(19) IPOS INTELLECTUAL PROPERTY OFFICE OF SINGAPORE

(11) Publication number: **SG 188402 A1**

(43) Publication date: **30.04.2013**

(51) Int. Cl: **C07D 403/04, C07D 409/04, C07D 241/38, C07D 243/10, C07D 401/04, C07D 403/10, C07D 405/04, C07D 405/10, C07D 409/10, C07D 413/10, C07D 417/04, C07D 417/10, C07D 471/04, C07D 491/04, C07D 495/04;**

(12) Patent Application

(21) Application number: **2013016258**

(22) Date of filing: **12.09.2011**

(30) Priority: **JP 2010-204747 13.09.2010**

(71) Applicant: **OTSUKA PHARMACEUTICAL CO., LTD. 9, KANDA-TSUKASAMACHI 2-CHOME, CHIYODA-KU, TOKYO 1018535 JP**

(72) Inventor: **ITO, NOBUAKI C/O OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, DOSHOMACHI, CHUO-KU, OSAKA-SHI, OSAKA 5410045 (JP) JP
SASAKI, HIROFUMI C/O OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, DOSHOMACHI, CHUO-KU, OSAKA-SHI, OSAKA 5410045 (JP) JP
TAI, KUNINORI C/O OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, DOSHOMACHI, CHUO-KU, OSAKA-SHI, OSAKA 5410045 (JP) JP
SHINOHARA, TOMOICHI C/O OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, DOSHOMACHI, CHUO-KU, OSAKA-SHI, OSAKA 5410045 (JP) JP**

(54) **Title:**
HETEROCYCLIC COMPOUNDS FOR TREATING OR PREVENTING DISORDERS CAUSED BY REDUCED NEUROTRANSMISSION OF SEROTONIN, NOREPHNEPHRINE OR DOPAMINE.

(57) **Abstract:**
A heterocyclic compound represented by the general formula (1) or a salt thereof: wherein m, l, and n respectively represent an integer of 1 or 2; X represents -O- or -CH2-; R1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a protecting group, or a tri-lower alkylsilyloxy-lower alkyl group; R2 and R3, which are the same or different, each independently represent hydrogen or a lower alkyl group; or R2 and R3 are bonded to form a cyclo-C3-C8 alkyl group; and R4 represents an aromatic group or a heterocyclic group, wherein the aromatic or heterocyclic group may have one or more arbitrary substituent(s).

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 March 2012 (22.03.2012)

PCT

(10) International Publication Number
WO 2012/036253 A1

(51) International Patent Classification:
C07D 403/04 (2006.01) ***C07D 409/10*** (2006.01)
C07D 409/04 (2006.01) ***C07D 413/10*** (2006.01)
C07D 241/38 (2006.01) ***C07D 417/04*** (2006.01)
C07D 243/10 (2006.01) ***C07D 417/10*** (2006.01)
C07D 401/04 (2006.01) ***C07D 471/04*** (2006.01)
C07D 403/10 (2006.01) ***C07D 491/04*** (2006.01)
C07D 405/04 (2006.01) ***C07D 495/04*** (2006.01)
C07D 405/10 (2006.01)

(21) International Application Number: PCT/JP2011/071174

(22) International Filing Date: 12 September 2011 (12.09.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
2010-204747 13 September 2010 (13.09.2010) JP

(71) Applicant *(for all designated States except US)*: **OTSUKA PHARMACEUTICAL CO., LTD.** [JP/JP]; 9, Kanda-Tsukasamachi 2-chome, Chiyoda-ku, Tokyo, 1018535 (JP).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ITO, Nobuaki** [JP/JP]; c/o OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, Doshomachi, Chuo-ku, Osaka-shi, Osaka, 5410045 (JP). **SASAKI, Hirofumi** [JP/JP]; c/o OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, Doshomachi, Chuo-ku, Osaka-shi, Osaka, 5410045 (JP). **TAI, Kuninori** [JP/JP]; c/o OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, Doshomachi, Chuo-ku, Osaka-shi, Osaka, 5410045 (JP). **SHINOHARA, Tomoichi** [JP/JP]; c/o OTSUKA PHARMACEUTICAL CO., LTD., 1-7-1, Doshomachi, Chuo-ku, Osaka-shi, Osaka, 5410045 (JP).

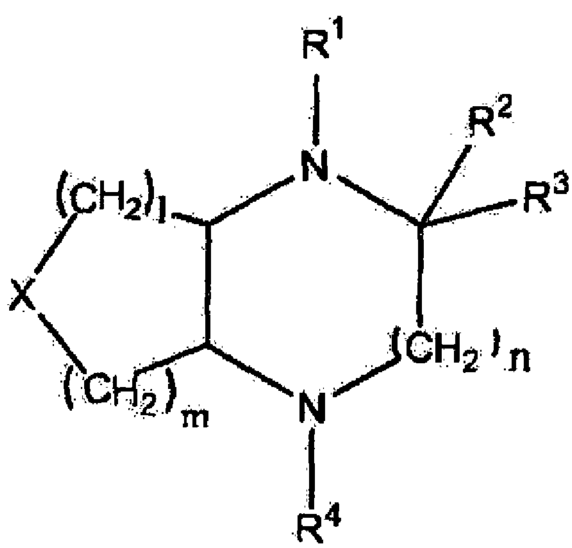
(74) Agents: **ASAMURA, Kiyoshi** et al.; Tennoz Central Tower, 2-2-24 Higashi-Shinagawa, Shinagawa-ku, Tokyo, 1408776 (JP).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH,

[Continued on next page]

(54) **Title**: HETEROCYCLIC COMPOUNDS FOR TREATING OR PREVENTING DISORDERS CAUSED BY REDUCED NEUROTRANSMISSION OF SEROTONIN, NOREPHNEPHRINE OR DOPAMINE.



(57) **Abstract**: A heterocyclic compound represented by the general formula (1) or a salt thereof: wherein m, l, and n respectively represent an integer of 1 or 2; X represents -O- or $-CH_2-$; R^1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a protecting group, or a tri-lower alkylsilyloxy-lower alkyl group; R^2 and R^3, which are the same or different, each independently represent hydrogen or a lower alkyl group; or R_2 and R_3 are bonded to form a cyclo-C3-C8 alkyl group; and R^4 represents an aromatic group or a heterocyclic group, wherein the aromatic or heterocyclic group may have one or more arbitrary substituent(s).

WO 2012/036253 A1

GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

DESCRIPTION

HETEROCYCLIC COMPOUND

TECHNICAL FIELD

[0001]

The present invention relates to a novel heterocyclic compound.

BACKGROUND ART

[0002]

Three monoamines known as serotonin, norepinephrine, and dopamine function as neurotransmitters *in vivo*. Therefore, drugs having inhibitory effects on the reuptake of these monoamines have been used widely as therapeutic drugs for diseases associated with the central or peripheral nervous system.

[0003]

Most of drugs previously used in the treatment of depression selectively inhibit the reuptake of norepinephrine or serotonin. Examples of such drugs include imipramine (first-generation antidepressant), maprotiline (second-generation antidepressant), selective serotonin reuptake inhibitors (SSRIs, third-generation antidepressants) typified by fluoxetine, and serotonin and/or norepinephrine reuptake inhibitors (SNRIs, fourth-generation antidepressants) typified by venlafaxine (S. Miura, Japanese Journal of Clinical Psychopharmacology, 2000, 3: 311-318).

[0004]

However, all of these drugs require a period as long as 3 weeks or longer for exerting their therapeutic effects and, in addition, fail to exert sufficient therapeutic effects on approximately 30% of patients with depression (Phil Skolnick, European Journal of Pharmacology, 1999, 375: 31-40).

DISCLOSURE OF INVENTION

[0005]

An object of the present invention is to provide a drug that has a wide therapeutic spectrum and can exert sufficient therapeutic effects in a short period, compared with antidepressants known in the art.

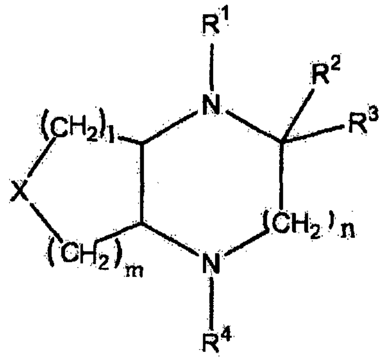
[0006]

The present inventors have conducted diligent studies to attain the object and have consequently found that a heterocyclic compound represented by the general formula (1) shown below can be used in the production of the desired drug. The present invention has been completed based on these findings.

[0007]

The present invention provides a heterocyclic compound or a salt thereof according to any one of Items 1 to 15 shown below, a pharmaceutical composition comprising the compound or an use of the compounds, a method for treating or preventing diseases or a methods for producing the compounds.

Item 1. A heterocyclic compound represented by the general formula (1) or a salt thereof:



wherein m, l, and n respectively represent an integer of 1 or 2; X represents -O- or $-CH_2-$;

R^1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a protecting group, or a tri-lower alkylsilyloxy-lower alkyl group;

R^2 and R^3, which are the same or different, each independently represent hydrogen or a lower alkyl group; or R_2 and R_3 are bonded to form a cyclo-C3-C8 alkyl group; and

R^4 represents an aromatic group or a heterocyclic group, wherein the aromatic or heterocyclic group may have one or more arbitrary substituent(s).

Item 2. The heterocyclic compound represented by the general formula (1) or a salt thereof according to item 1, wherein

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(3) a benzothienyl group,

(4) a naphthyl group,

(5) a benzofuryl group,

(6) a quinolyl group,

(7) an isoquinolyl group,

(8) a pyridyl group,

(9) a thienyl group,
(10) a dihydrobenzoxazinyl group,
(11) a dihydrobenzodioxinyl group,
(12) a dihydroquinolyl group,
(13) a chromanyl group,
(14) a quinoxalinyl group,
(15) a dihydroindenyl group,
(16) a dihydrobenzofuryl group,
(17) a benzodioxolyl group,
(18) an indazolyl group,
(19) a benzothiazolyl group,
(20) an indolinyl group,
(21) a thienopyridyl group,
(22) a tetrahydrobenzazepinyl group,
(23) a tetrahydrobenzodiazepinyl group,
(24) a dihydrobenzodioxepinyl group,
(25) a fluorenyl group,
(26) a pyridazinyl group,
(27) a tetrahydroquinolyl group,
(28) a carbazolyl group,
(29) a phenanthryl group,
(30) a dihydroacenaphthylenyl group,
(31) a pyrrolopyridyl group,
(32) an anthryl group,
(33) a benzodioxinyl group,
(34) a pyrrolidinyl group,
(35) a pyrazolyl group,
(36) an oxadiazolyl group,
(37) a pyrimidinyl group,
(38) a tetrahydronaphthyl group,
(39) a dihydroquinazolinyl group,
(40) a benzoxazolyl group,
(41) a thiazolyl group,
(42) a quinazolinyl group,

(43) a phthalazinyl group,

(44) a pyrazinyl group, and

(45) a chromenyl group, wherein

these aromatic or heterocyclic groups may have one or more substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-3) a lower alkanoyl group,

(1-4) a halogen-substituted lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group,

(1-7) a lower alkoxy group,

(1-8) a lower alkylthio group,

(1-9) an imidazolyl group,

(1-10) a tri-lower alkylsilyl group,

(1-11) an oxadiazolyl group which may have a lower alkyl group(s),

(1-12) a pyrrolidinyl group which may have an oxo group(s),

(1-13) a phenyl group which may have a lower alkoxy group(s),

(1-14) a lower alkylamino-lower alkyl group,

(1-15) an oxo group,

(1-16) a pyrazolyl group which may have a lower alkyl group(s),

(1-17) a thienyl group,

(1-18) a furyl group,

(1-19) a thiazolyl group which may have a lower alkyl group(s),

(1-20) a lower alkylamino group,

(1-21) a pyrimidyl group which may have a lower alkyl group(s),

(1-22) a phenyl-lower alkenyl group,

(1-23) a phenoxy group which may have a halogen atom(s),

(1-24) a phenoxy-lower alkyl group,

(1-25) a pyrrolidinyl-lower alkoxy group,

(1-26) a lower alkylsulfamoyl group,

(1-27) a pyridazinyloxy group which may have a lower alkyl group(s),

(1-28) a phenyl-lower alkyl group,

(1-29) a lower alkylamino-lower alkoxy group,

(1-30) an imidazolyl-lower alkyl group,

(1-31) a phenyl-lower alkoxy group,

(1-32) a hydroxy group,

(1-33) a lower alkoxycarbonyl group,

(1-34) a hydroxy-lower alkyl group,

(1-35) an oxazolyl group,

(1-36) a piperidyl group,

(1-37) a pyrrolyl group,

(1-38) a morpholinyl-lower alkyl group,

(1-39) a piperazinyl-lower alkyl group which may have a lower alkyl group(s),

(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have a lower alkyl group(s).

Item 3. The heterocyclic compound represented by the general formula (1) or a salt thereof according to item 2, wherein

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(3) a benzothienyl group,

(4) a naphthyl group,

(5) a benzofuryl group,

(6) a quinolyl group,

(7) an isoquinolyl group,

(8) a pyridyl group,

(9) a thienyl group,

(10) a dihydrobenzoxazinyl group,

(11) a dihydrobenzodioxinyl group,

(12) a dihydroquinolyl group,

(13) a chromanyl group,

(14) a quinoxalinyl group,

(15) a dihydroindenyl group,

(16) a dihydrobenzofuryl group,

(17) a benzodioxolyl group,

(18) an indazolyl group,

(19) a benzothiazolyl group,
(20) an indolinyl group,
(21) a thienopyridyl group,
(22) a tetrahydrobenzazepinyl group,
(23) a tetrahydrobenzodiazepinyl group,
(24) a dihydrobenzodioxepinyl group,
(25) a fluorenyl group,
(26) a pyridazinyl group,
(27) a tetrahydroquinolyl group,
(28) a carbazolyl group,
(29) a phenanthryl group,
(30) a dihydroacenaphthylenyl group,
(31) a pyrrolopyridyl group,
(32) an anthryl group,
(33) a benzodioxinyl group,
(34) a pyrrolidinyl group,
(35) a pyrazolyl group,
(36) an oxadiazolyl group,
(37) a pyrimidinyl group,
(38) a tetrahydronaphthyl group,
(39) a dihydroquinazolinyl group,
(40) a benzoxazolyl group,
(41) a thiazolyl group,
(42) a quinazolinyl group,
(43) a phthalazinyl group,
(44) a pyrazinyl group, and
(45) a chromenyl group, wherein
these aromatic or heterocyclic groups may have 1 to 4 substituent(s) selected from
(1-1) a halogen atom,
(1-2) a lower alkyl group,
(1-3) a lower alkanoyl group,
(1-4) a halogen-substituted lower alkyl group,
(1-5) a halogen-substituted lower alkoxy group,
(1-6) a cyano group,

(1-7) a lower alkoxy group,
(1-8) a lower alkylthio group,
(1-9) an imidazolyl group,
(1-10) a tri-lower alkylsilyl group,
(1-11) an oxadiazolyl group which may have 1 lower alkyl group,
(1-12) a pyrrolidinyl group which may have 1 oxo group,
(1-13) a phenyl group which may have 1 lower alkoxy group,
(1-14) a lower alkylamino-lower alkyl group,
(1-15) an oxo group,
(1-16) a pyrazolyl group which may have 1 lower alkyl group,
(1-17) a thienyl group,
(1-18) a furyl group,
(1-19) a thiazolyl group which may have 1 lower alkyl group,
(1-20) a lower alkylamino group,
(1-21) a pyrimidyl group which may have 1 lower alkyl group,
(1-22) a phenyl-lower alkenyl group,
(1-23) a phenoxy group which may have 1 halogen atom,
(1-24) a phenoxy-lower alkyl group,
(1-25) a pyrrolidinyl-lower alkoxy group,
(1-26) a lower alkylsulfamoyl group,
(1-27) a pyridazinyloxy group which may have 1 lower alkyl group,
(1-28) a phenyl-lower alkyl group,
(1-29) a lower alkylamino-lower alkoxy group,
(1-30) an imidazolyl-lower alkyl group,
(1-31) a phenyl-lower alkoxy group,
(1-32) a hydroxy group,
(1-33) a lower alkoxycarbonyl group,
(1-34) a hydroxy-lower alkyl group,
(1-35) an oxazolyl group,
(1-36) a piperidyl group,
(1-37) a pyrrolyl group,
(1-38) a morpholinyl-lower alkyl group,
(1-39) a piperazinyl-lower alkyl group which may have 1 lower alkyl group,
(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have 1 lower alkyl group.

Item 4. The heterocyclic compound represented by the general formula (1) or a salt thereof according to item 3, wherein

m represents 2; l and n respectively represent an integer of 1; X represents $-CH_2-$;

R^1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a benzyl group, or a tri-lower alkylsilyloxy-lower alkyl group; and

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(4) a naphthyl group,

(5) a benzofuryl group, and

(31) a pyrrolopyridyl group, wherein

these aromatic or heterocyclic groups may have 1 to 4 substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-3) a lower alkanoyl group,

(1-4) a halogen-substituted lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group,

(1-7) a lower alkoxy group,

(1-8) a lower alkylthio group,

(1-9) an imidazolyl group,

(1-10) a tri-lower alkylsilyl group,

(1-11) an oxadiazolyl group which may have 1 lower alkyl group,

(1-12) a pyrrolidinyl group which may have 1 oxo group,

(1-13) a phenyl group which may have 1 lower alkoxy group,

(1-14) a lower alkylamino-lower alkyl group,

(1-15) an oxo group,

(1-16) a pyrazolyl group which may have 1 lower alkyl group,

(1-17) a thienyl group,

(1-18) a furyl group,

(1-19) a thiazolyl group which may have 1 lower alkyl group, (1-20) a lower alkylamino group,

(1-21) a pyrimidyl group which may have 1 lower alkyl group,

(1-22) a phenyl-lower alkenyl group,

(1-23) a phenoxy group which may have 1 halogen atom,

(1-24) a phenoxy-lower alkyl group,

(1-25) a pyrrolidinyl-lower alkoxy group,

(1-26) a lower alkylsulfamoyl group,

(1-27) a pyridazinyloxy group which may have 1 lower alkyl group,

(1-28) a phenyl-lower alkyl group,

(1-29) a lower alkylamino-lower alkoxy group,

(1-30) an imidazolyl-lower alkyl group,

(1-31) a phenyl-lower alkoxy group,

(1-32) a hydroxy group,

(1-34) a hydroxy-lower alkyl group,

(1-35) an oxazolyl group,

(1-36) a piperidyl group,

(1-37) a pyrrolyl group,

(1-38) a morpholinyl-lower alkyl group,

(1-39) a piperazinyl-lower alkyl group which may have a lower alkyl group(s),

(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have 1 lower alkyl group.

Item 5. The heterocyclic compound represented by the general formula (1) or a salt thereof according to item 4, wherein

R^1 represents hydrogen;

R^2 and R^3, which are the same or different, each independently represent a lower alkyl group; or R^2 and R^3 are bonded to form a cyclo-C3-C8 alkyl group; and

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(4) a naphthyl group,

(5) a benzofuryl group, and

(31) a pyrrolopyridyl group, wherein

these aromatic or heterocyclic groups may have 1 to 2 substituent(s) selected from
(1-1) a halogen atom,
(1-2) a lower alkyl group,
(1-5) a halogen-substituted lower alkoxy group,
(1-6) a cyano group, and
(1-7) a lower alkoxy group.

Item 6. The heterocyclic compound represented by the general formula (1) or a salt thereof according to item 5, which is selected from
(4a*S*,8a*R*)-1-(4-chlorophenyl)-3,3-dimethyldecahydroquinoxaline,
2-chloro-4-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)benzonitrile,
(4a*S*,8a*R*)-1-(3-chloro-4-fluorophenyl)-3,3-dimethyldecahydroquinoxaline,
(4a*S*,8a*R*)-1-(7-fluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline,
5-((4a*R*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-1-methyl-1*H*-indole-2-carbonitrile,
(4a'*R*,8a'*S*)-4'-(7-methoxybenzofuran-4-yl)octahydro-1'*H*-spiro[cyclobutane-1,2'-quinoxaline],
(4a*S*,8a*R*)-1-(6,7-difluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline,
5-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-1*H*-indole-2-carbonitrile,
(4a*S*,8a*R*)-1-(7-chloro-2,3-dihydro-1*H*-inden-4-yl)-3,3-dimethyldecahydroquinoxaline,
6-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-2-naphthonitrile,
(4a*S*,8a*S*)-3,3-dimethyl-1-(1*H*-pyrrolo[2,3-*b*]pyridin-4-yl)decahydroquinoxaline, and
(4a*S*,8a*S*)-1-(4-(difluoromethoxy)-3-fluorophenyl)-3,3-dimethyldecahydroquinoxaline.

Item 7. A pharmaceutical composition comprising a heterocyclic compound represented by the general formula (1) or a salt thereof according to item 1 as an active ingredient and a pharmaceutically acceptable carrier.

Item 8. A prophylactic and/or therapeutic agent for disorders caused by reduced neurotransmission of serotonin, norepinephrine or dopamine, comprising as an active ingredient a heterocyclic compound of general formula (1) or a salt thereof according to item 1.

Item 9. a prophylactic and/or therapeutic agent according to item 8, wherein the disorder is selected from the group consisting of depression, depression status caused by adjustment disorder, anxiety caused by adjustment disorder, anxiety caused by various diseases, generalized anxiety disorder, phobia, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, acute stress disorder, hypochondria, dissociative amnesia, avoidant personality disorder, body dysmorphic disorder, eating disorder, obesity, chemical dependence, pain, fibromyalgia, Alzheimer's disease, memory deficit, Parkinson's disease, restless leg syndrome, endocrine disorder, vasospasm, cerebellar ataxia, gastrointestinal disorder, negative syndrome of schizophrenia, premenstrual syndrome, stress urinary incontinence, Tourette's disorder, attention deficit hyperactivity disorder (ADHD), autism, Asperger syndrome, impulse control disorder, trichotillomania, kleptomania, gambling disorder, cluster headache, migraine, chronic paroxysmal hemicrania, chronic fatigue syndrome, precocious ejaculation, male impotence, narcolepsy, primary hypersomnia, cataplexy, sleep apnea syndrome and headache.

Item 10. a prophylactic and/or therapeutic agent according to item 9, wherein the depression is selected from the group consisting of major depressive disorder; bipolar I disorder; bipolar II disorder; mixed state; dysthymic disorder; rapid cycler; atypical depression; seasonal affective disorder; postpartum depression; hypomelancholia; recurrent brief depressive disorder; refractory depression; chronic depression; double depression; alcohol-induced mood disorder; mixed anxiety-depressive disorder; depression caused by various physical diseases such as Cushing('s) syndrome, hypothyroidism, hyperparathyroidism, Addison's disease, amenorrhea-galactorrhea syndrome, Parkinson's disease, Alzheimer's disease, cerebrovascular dementia, brain infarct、brain hemorrhage、subarachnoid hemorrhage, diabetes millitus, virus infection, multiple sclerosis, chronic fatigue syndrome, coronary artery disease, pain, cancer, etc.; presenile depression; senile depression; depression in children and adolescents; depression induced by drugs such as interferon, etc.

Item 11. A prophylactic and/or therapeutic agent according to item 9, wherein the anxiety caused by various diseases is selected from the group consisting of anxiety caused by head injury, brain infection, inner ear impairment, cardiac failure, cardiac dysrhythmia, hyperadrenalism, hyperthyroidism, asthma and chronic obstructive pulmonary disease.

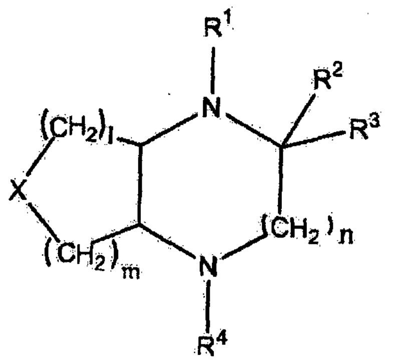
Item 12. A prophylactic and/or therapeutic agent according to item 9, wherein the pain is selected from the group consisting of chronic pain, psychogenic pain, neuropathic pain, phantom limb pain, postherpetic neuralgia, traumatic cervical syndrome, spinal cord injury pain, trigeminal neuralgia, diabetic neuropathy.

Item 13. Use of a heterocyclic compound of the general formula (1) or a salt thereof according to any one of items 1 to 6 as a drug.

Item 14. Use of a heterocyclic compound of the general formula (1) or a salt thereof according to any one of items 1 to 6 as a serotonine reuptake inhibitor and/or a norepinephrine reuptake inhibitor and/or a dopamine reuptake inhibitor.

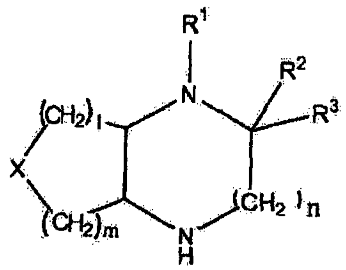
Item 15. A method for treating and/or preventing disorders caused by reduced neurotransmission of serotonin, norephnephrine or dopamine, comprising administering a heterocyclic compound of general formula (1) or a salt thereof according to items 1 to 6 to a human or an animal.

Item 16. A process for producing a heterocyclic compound of general formula (1):



or salts thereof, wherein m, l and n respectively represent an integer of 1 or 2; X, R^1, R^2, and R^3 are defined in the above in item 1,

the process comprising reacting the compound represented by the general formula;



wherein m, l and n respectively represent an integer of 1 or 2; X, R^1, R^2, and R^3 are defined in the above in item 1 and the compound represented by the general formula;

R^4 —— X_1

wherein R^4 and X^1 are defined in the below.

[0008]

Each group shown in the general formula is specifically as shown below.

The term "lower" means a group having 1 to 6 (preferably 1 to 4, more preferably 1 to 3) carbon atoms, unless otherwise specified.

[0009]

A heterocyclic ring group includes saturated or unsaturated monocyclic or polycyclic heterocyclic rings comprising at least one hetero atoms selected from an oxygen atom(s), a sulfur atom(s) and nitrogen atom(s). More preferably, it includes the following heterocyclic ring:

[0010]

3 to 8 unsaturated-membered, preferably 5 or 6-membered heteromonocyclic ring containing 1 to 4 nitrogen atoms, for example, pyrrolyl , pyrroliny, imidazolyl, pyrazolyl, pyridyl groups and N-oxide thereof, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1, 2, 4-triazolyl, 1H-1, 2, 3-triazolyl, 2H-1, 2, 3-triazolyl gourps etc.), tetrazolyl group (e.g., 1H-tetrazolyl, 2H-tetrazolyl groups, etc.), dihydrotriazinyl (e.g., 4, 5-dihydro-1, 2, 4-triazinyl, 2, 5-dihydro-1, 2, 4-triazinyl groups) groups, etc. can be mentioned. Preferably, imidazolyl, pyridazinyl, pyridyl, pyrazinyl, pyrimidinyl, pyrazolyl groups, etc. can be mentioned.

[0011]

3 to 8-membered, preferably 5 or 6-membered unsaturated heteromonocyclic ring containing 1 to 4 nitrogen atoms, for example, azetidinyl, pyrrolidinyl, imidazolidinyl, piperidinyl, pyrazolidinyl, pyperazinyl groups, etc. can be mentioned. Preferably, pyrrolidinyl group can be mentioned.

[0012]

7 to 12-membered partially saturated or unsaturated condensed hetero ring group containing 1 to 5 nitrogen atoms, for example, indolyl, dihydroindolyl, (e.g., 2, 3-dihydro-1H-dihydroindolyl group, etc.), isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, dihydroisoquinolyl (e.g., 3, 4-dihydro-1H-isoquinolyl group, etc.), tetrahydroquinolyl, tetrahydroisoquinolyl (e.g., 1, 2, 3, 4-tetrahydro-1H-isoquinolyl, 5, 6, 7, 8-tetrahydroisoquinolyl groups, etc.), carbostyril, dihydrocarbostyril (e.g., 3, 4-dihydrocarbostyril group, etc.), indazolyl, benzotriazolyl, tetrazolopyridyl, tetrazolopyridazinyl (e.g., tetrazolo[1, 5-b]pyridazinyl group, etc.), dihydrotriazolopyridazinyl, imidazopyridyl (e.g., imidazo[1, 2-a]pyridyl group, etc.), naphthyridyl, cinnolinyl, quinoxalinyl, pyrazolopyridyl (e.g., pyrazolo[2, 3-a]pyridyl group, etc.), pyrrolopyridyl, carbazolyl, Indolinyl, tetrahydrobenzodiazepinyl, tetrahydrobenzoazepinyl, quinazolinyl, phthalazinyl groups, etc. can be mentioned. Preferably, quinolyl, isoquinolyl, quinoxalinyl, indolyl, indazolyl, pyrrolopyridyl, tetrahydroquinolyl, carbazolyl, indolinyl, quinazolyl, phthalazinyl, tetrahydrobenzodiazepinyl, or tetrahydrobenzoazepinyl groups, etc. can be mentioned.

[0013]

3 to 8 membered, preferably 5 or 6 membered unsaturated heteromono ring containing 1 to 2 oxygen atoms, for example, furyl group, etc. can be mentioned.

[0014]

7 to 12-membered partially saturated or unsaturated condensed hetero ring group containing 1 to 3 oxygen atoms, for example, benzofuryl, dihydrobenzofuyl (e.g., 2, 3-dihydrobenzo [b] furyl group, etc.), chromanyl, benzodioxanyl (e.g., 1,4-benzodioxanyl group, etc.), dihydrobenzoxadinyl (e.g, 2, 3-dihydrobenzo-1,4-oxadinyl), benzodioxolyl (e.g., benzo[1,,3] dioxolyl group, etc.), benzodioxynyl, dihydrobenzodioxynyl, dihydrobenzodioxepinyl groups, etc. can be mentioned. Preferably, benzofuryl, benzodioxynyl, benzodioxolyl, dihydrobenzofuryl, dihydrobenzodioxepinyl, dihydrobenzodioxsepinylyl, chromenyl, or chromanyl groups can be mentioned.

[0015]

3 to 8-membered, preferably 5 or 6-membered unsaturated heteromonocyclic ring containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1, 2, 4-oxadiazolyl, 1, 3, 4-oxadiazoyl, 1, 2, 5-oxadiazoyl groups, etc.) groups, etc. can be mentioned. Preferably, oxazolyl, oxadiazolyl groups can be mentioned.

[0016]

3 to 8-membered, preferably 5 or 6-membered saturated heteromonocyclic ring containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, morpholinyl group, etc. can be mentioned.

[0017]

7 to 12-membered partially saturated or unsaturated condensed hetero ring containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, benzoxazoly, benzoxazdiazolyl, benzisoxazolyl, furopyridyl (e.g., furo[2, 3-b] pyridyl, furo[3, 2-c]pyridyl groups, etc.), dihydrobenzoxadinyl groups, etc. can be mentioned. Preferably, benzoxazolyl, dihydrobenzoxadinyl groups can be mentioned.

[0018]

3 to 8-membered, preferably 5 or 6-membered unsaturated heteromonocyclic ring containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, 1, 2-thiazolyl, thiazolynyl, thiadiazolyl (e.g., 1,2,4-tiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1, 2, 3-thiadiazolyl groups, etc.) groups, etc. can be mentioned. Preferably, thiazolyl group can be mentioned.

[0019]

3 to 8-membered, preferably, 5 or 6-membered saturated heteromonocyclic ring containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolydinyl group, etc. can be mentioned.

[0020]

3 to 8-membered, preferably, 5 or 6-membered unsaturated heteromonocyclic ring containing 1 sulfur atom, for example, thienyl group, etc. can be mentioned.

[0021]

7 to 12-membered unsaturated condensed hetero ring containing 1 to 3 sulfur atoms, for example, benzothienyl group (e.g., benzo [b] thienyl group, etc.), etc. can be mentioned.

[0022]

7 to 12-membered partially saturated or unsaturated condensed hetero ring group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, benzothiazolyl, benzothadiazolyl, thienopyridyl (e.g., thieno[2, 3-b] pyridyl, thieno[2, 3-c] pyridyl, thieno[3, 2-c]pyridyl groups, etc.), imidazothiazolyl (e.g., imidazo[2, 1-b] thiazolyl group, etc.), dihydroimidazothiazolyl (e.g., 2, 3-dihydroimidazo[2, 1-b] thiazolyl group, etc.), thienopyradinyl (e.g., thieno[2, 3-b] pyradinyl group, etc.), groups, etc. can be mentioned. Preferably, thienopyridyl or benzothiazolyl groups can be mentioned.

[0023]

The above heterocyclic ring can be substituted by one or more optional substituents.

[0024]

As an aromatic ring, it includes, for example, C_{6-14} aryl groups can be mentioned. The preferable examples of the aryl groups are a phenyl, naphthyl, anthryl, phenanthryl, acenaphthylenyl, biphenyl, indenyl groups. Among them, phenyl, naphtyl, anthryl, phenanthryl groups are preferable. The aryl groups can be partially saturated. As the partially unsaturated aryl groups are, for example, dihydroindenyl, fluorenyl, dihydroacenaphthylenyl, tetrahydronaphthyl groups. Here, the above heterocyclic rings can be substituted by one or more optional substituents.

[0025]

As a saturated hydrocarbon group, it includes, for example, lower alkyl, cyclo C3-C8 alkyl groups, etc.

[0026]

As an unsaturated hydrocarbon group, it includes, for example, lower alkenyl, lower alkynyl, phenyl groups, etc.

[0027]

A characteristic group is a generic term used to refer to groups bind directly to a mother structure other than a carbon-carbon binding (atoms or atomic groups other than hydrogen), and –C≡N and >C=X (X=O, S, Se, Te, NH, NR). As the characteristic group, it includes, for example, carboxy, carbamoyl, cyano, hydroxy, amino groups, etc.

[0028]

The optional substituents are the above heterocyclic rings, aromatic ring groups, saturated hydrocarbon groups, unsaturated hydrocarbon groups, characteristic groups, etc. Preferably, the substituents (1-1) to (1-43) described in item 2 above can be mentioned.

[0029]

Examples of the lower alkyl group can include linear or branched alkyl groups having 1 to 6 carbon atoms (preferably 1 to 4 carbon atoms), unless otherwise specified. More specifically, it includes methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, sec-butyl, n-pentyl, 1-ethylpropyl, isopentyl, neopentyl, n-hexyl, 1,2,2-trimethylpropyl, 3,3-dimethylbutyl, 2-ethylbutyl, isohexyl, and 3-methylpentyl groups, etc.

[0030]

Examples of a lower alkoxy group can include linear or branched alkoxy groups having 1 to 6 carbon atoms (preferably 1 to 4 carbon atoms), unless otherwise specified. More specifically, it includes methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, tert-butoxy, sec-butoxy, n-pentyloxy, 1-ethylpropoxy, isopentyloxy, neopentyloxy, n-hexyloxy, 1,2,2-trimethylpropoxy, 3,3-dimethylbutoxy, 2-ethylbutoxy, isohexyloxy, and 3-methylpentyloxy groups, etc.

[0031]

Examples of a halogen atom include fluorine, chlorine, bromine, and iodine atoms, unless otherwise specified.

[0032]

Examples of a halogen-substituted lower alkyl group can include the lower alkyl groups exemplified above which are substituted by 1 to 7 (more preferably 1 to 3) halogen atoms, unless otherwise specified. More specifically, it includes fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, bromomethyl, dibromomethyl, dichlorofluoromethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, pentafluoroethyl, 2-fluoroethyl, 2-chloroethyl, 3,3,3-trifluoropropyl, heptafluoropropyl, 2,2,3,3,3-pentafluoropropyl, heptafluoroisopropyl, 3-chloropropyl, 2-chloropropyl, 3-bromopropyl, 4,4,4-trifluorobutyl, 4,4,4,3,3-pentafluorobutyl, 4-chlorobutyl, 4-bromobutyl, 2-chlorobutyl, 5,5,5-trifluoropentyl, 5-chloropentyl, 6,6,6-trifluorohexyl, 6-chlorohexyl, and perfluorohexyl groups, etc.

[0033]

Examples of a halogen-substituted lower alkoxy group can include the lower alkoxy groups exemplified above which are substituted by 1 to 7 (preferably 1 to 3) halogen atoms, unless otherwise specified. More specifically, it includes fluoromethoxy, difluoromethoxy, trifluoromethoxy, chloromethoxy, dichloromethoxy, trichloromethoxy, bromomethoxy, dibromomethoxy, dichlorofluoromethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy, pentafluoroethoxy, 2-fluoroethoxy, 2-chloroethoxy, 3,3,3-trifluoropropoxy, heptafluoropropoxy, heptafluoroisopropoxy, 3-chloropropoxy, 2-chloropropoxy, 3-bromopropoxy, 4,4,4-trifluorobutoxy, 4,4,4,3,3-pentafluorobutoxy, 4-chlorobutoxy, 4-bromobutoxy, 2-chlorobutoxy, 5,5,5-trifluoropentyloxy, 5-chloropentyloxy, 6,6,6-trifluorohexyloxy, 6-chlorohexyloxy, and perfluorohexyloxy groups, etc.

[0034]

Examples of a cyclo-C3-C8 alkyl group include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl groups, etc., unless otherwise specified.

[0035]

Examples of a lower alkanoyl group can include linear or branched alkanoyl groups having 1 to 6 carbon atoms (preferably 1 to 4 carbon atoms), unless otherwise specified. More specifically, it includes formyl, acetyl, propionyl, butyryl, isobutyryl, pentanoyl, tert-butylcarbonyl, and hexanoyl groups, etc.

[0036]

Examples of a lower alkylthio group can include thio groups which are substituted by linear or branched alkyl groups having 1 to 6 carbon atoms (preferably 1 to 4 carbon atoms), unless otherwise specified. More specifically, it includes methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, isobutylthio, tert-butylthio, sec-butylthio, n-pentylthio, 1-ethylpropylthio, isopentylthio, neopentylthio, n-hexylthio, 1,2,2-trimethylpropylthio, 3,3-dimethylbutylthio, 2-ethylbutylthio, isohexylthio, and 3-methylpentylthio groups, etc.

[0037]

Examples of a lower alkenyl group can include linear or branched alkenyl groups having 1 to 3 double bonds and 2 to 6 carbon atoms (preferably 2 to 4 carbon atoms), unless otherwise specified, and the lower alkenyl group encompasses both trans and cis forms. More specifically, it includes vinyl, 1-propenyl, 2-propenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 2-methyl-2-propenyl, 2-butenyl, 1-butenyl, 3-butenyl, 2-pentenyl, 1-pentenyl, 3-pentenyl, 4-pentenyl, 1,3-butadienyl, 1,3-pentadienyl, 2-penten-4-yl, 2-hexenyl, 1-hexenyl, 5-hexenyl, 3-hexenyl, 4-hexenyl, 3,3-dimethyl-1-propenyl, 2-ethyl-1-propenyl, 1,3,5-hexatrienyl, 1,3-hexadienyl, and 1,4-hexadienyl groups, etc.

[0038]

Examples of a hydroxy-lower alkyl group can include the lower alkyl groups exemplified above (preferably, linear or branched alkyl groups having 1 to 6 carbon atoms (more preferably 1 to 4 carbon atoms)) which have 1 to 5, preferably 1 to 3 hydroxy groups, unless otherwise specified. More specifically, it includes hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxypropyl, 4-hydroxybutyl, 3,4-dihydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5-hydroxypentyl, 6-hydroxyhexyl, 3,3-dimethyl-3-hydroxypropyl, 2-methyl-3-hydroxypropyl, 2,3,4-trihydroxybutyl, and perhydroxyhexyl groups, etc.

[0039]

Examples of a lower alkylamino group can include amino groups having 1 to 2 of the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 (more preferably 1 to 4, even more preferably 1 to 3) carbon atoms) exemplified above, unless otherwise specified. More specifically, it includes methylamino, dimethylamino, diethylamino, and diisopropylamino groups, etc.

[0040]

Examples of a lower alkylsulfamoyl group can include sulfamoyl groups having 1 to 2 of the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 (more preferably 1 to 4, even more preferably 1 to 3) carbon atoms) exemplified above, unless otherwise specified. More specifically, it includes methylsulfamoyl, ethylsulfamoyl, dimethylsulfamoyl, diethylsulfamoyl, and ethylmethylsulfamoyl groups, etc.

[0041]

A tri-lower alkylsilyl group can be exemplified by silyl groups which are substituted by 3 linear or branched alkyl groups having 1 to 6 carbon atoms, such as triisopropylsilyl, tert-butyldimethylsilyl, trimethylsilyl, n-butylethylmethylsilyl, tert-butyldipropylsilyl, n-pentyldiethylsilyl, and n-hexyl-n-propylmethylsilyl groups, etc.

[0042]

Examples of a tri(lower alkyl)silyloxy-lower alkyl group can include tri(lower alkyl)silyloxy-lower alkyl groups whose lower alkyl moiety is any of the lower alkyl groups exemplified above (preferably, linear or branched alkyl groups having 1 to 6 carbon atoms (more preferably 1 to 4 carbon atoms)), unless otherwise specified. More specifically, it includes trimethylsilyloxymethyl, 1- (or 2-)trimethylsilyloxyethyl, 1- (or 2- or 3-)trimethylsilyloxypropyl, triethylsilyloxymethyl, 1- (or 2-)triethylsilyloxyethyl, 1- (or 2- or 3-)triethylsilyloxypropyl, triisopropylsilyloxymethyl, 1- (or 2-)triisopropylsilyloxyethyl, and 1- (or 2- or 3-)triisopropylsilyloxypropyl groups, etc.

[0043]

Examples of a phenoxy-lower alkyl group can include the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 (more preferably 1 to 4, even more preferably 1 to 3) carbon atoms) exemplified above which have 1 to 3, preferably 1 phenoxy group, unless otherwise specified. More specifically, it includes phenoxymethyl, 1-phenoxyethyl, 2-phenoxyethyl, 3-phenoxypropyl, 2-phenoxypropyl, 4-phenoxybutyl, 5-phenoxypentyl, 4-phenoxypentyl, 6-phenoxyhexyl, 2-methyl-3-phenoxypropyl, and 1,1-dimethyl-2-phenoxyethyl groups, etc.

[0044]

Examples of a phenyl-lower alkoxy group can include the lower alkoxy groups (preferably linear or branched alkoxy groups having 1 to 6 (more preferably 1 to 4, even more preferably 1 to 3) carbon atoms) exemplified above which have 1 to 3, preferably 1 phenyl group, unless otherwise specified. More specifically, it includes benzyloxy, 2-phenylethoxy, 1-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 5-phenylpentyloxy, 6-phenylhexyloxy, 1,1-dimethyl-2-phenylethoxy, and 2-methyl-3-phenylpropoxy groups, etc.

[0045]

Examples of a phenyl-lower alkenyl group can include the lower alkenyl groups (preferably linear or branched alkenyl groups having 2 to 6 (more preferably 2 to 4) carbon atoms) exemplified above which have 1 to 3, preferably 1 phenyl group, unless otherwise specified. More specifically, it includes styryl, 3-phenyl-2-propenyl (commonly called cinnamyl), 4-phenyl-2-butenyl, 4-phenyl-3-butenyl, 5-phenyl-4-pentenyl, 5-phenyl-3-pentenyl, 6-phenyl-5-hexenyl, 6-phenyl-4-hexenyl, 6-phenyl-3-hexenyl, 4-phenyl-1,3-butadienyl, and 6-phenyl-1,3,5-hexatrienyl groups, etc.

[0046]

Examples of a lower alkylamino-lower alkyl group can include lower alkyl groups which have 1 to 2 of the lower alkylamino groups exemplified above, unless otherwise specified. More specifically, it includes methylaminomethyl, ethylaminomethyl, dimethylaminomethyl, 1- (or 2-)dimethylaminoethyl, 1- (or 2- or 3-)dimethylaminopropyl, diisopropylaminomethyl, 1- (or 2-)diethylaminoethyl, and bis(dimethylamino)methyl groups, etc.

[0047]

Examples of a lower alkylamino-lower alkoxy group can include lower alkoxy groups which have 1 to 2 of the lower alkylamino groups exemplified above, unless otherwise specified. More specifically, it includes methylaminomethoxy, ethylaminomethoxy, dimethylaminomethoxy, 1- (or 2-)dimethylaminoethoxy, 1- (or 2- or 3-)dimethylaminopropoxy, diisopropylaminomethoxy, 1- (or 2-)diethylaminoethoxy, and bis(dimethylamino)methoxy groups, etc.

[0048]

Examples of a dihydrobenzodioxinyl group include 2,3-dihydrobenzo[b][1,4]dioxinyl, 3,4-dihydrobenzo[c][1,2]dioxinyl, and 2,4-dihydrobenzo[d][1,3] dioxinyl groups, etc.

[0049]

Examples of an imidazolyl-lower alkyl group can include the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 (more preferably 1 to 4) carbon atoms) exemplified above which have 1 to 3, preferably 1 imidazolyl group. More specifically, it includes 1- (or 2- or 4- or 5-)imidazolylmethyl, 1- (or 2-){1- (or 2- or 4- or 5-)imidazolyl}ethyl, and 1- (or 2- or 3-){1- (or 2- or 4- or 5-)imidazolyl}propyl groups, etc.

[0050]

A dihydroindenyl group includes (1-, 2-, 4-, or 5-)-1,2-dihydroindenyl groups, etc.

[0051]

A dihydroquinolyl group includes 1,2-dihydroquinolyl, 3,4-dihydroquinolyl, 1,4-dihydroquinolyl, 4a,8a-dihydroquinolyl, 5,6-dihydroquinolyl, 7,8-dihydroquinolyl, and 5,8-dihydroquinolyl groups, etc.

[0052]

A fluorenyl group includes 1H-fluorenyl, 2H-fluorenyl, 3H-fluorenyl, 4aH-fluorenyl, 5H-fluorenyl, 6H-fluorenyl, 7H-fluorenyl, 8H-fluorenyl, 8aH-fluorenyl, and 9H-fluorenyl groups, etc.

[0053]

A dihydrobenzofuryl group includes 2,3-dihydro-(2-, 3-, 4-, 5-, 6-, or 7-)benzofuryl groups, etc.

[0054]

A dihydrobenzoxazinyl group includes (2-, 3-, 4-, 5-, 6-, 7-, or 8-)3,4-dihydro-2H-benzo[b][1.4]oxazinyl and (1-, 2-, 4-, 5-, 6-, 7-, or 8-)2,4-dihydro-1H-benzo[d][1.3]oxazinyl groups, etc.

[0055]

A tetrahydrobenzodiazepinyl group includes (1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-) 2,3,4,5-tetrahydro-1H-benzo[b][1.4]diazepinyl and (1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-)2,3,4,5-tetrahydro-1H-benzo[e][1.4]diazepinyl groups, etc.

[0056]

Examples of a tetrahydrobenzodiazepinyl group can include (1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-)2,3,4,5-tetrahydro-1H-benzo[b][1.4]diazepinyl and (1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-)2,3,4,5-tetrahydro-1H-benzo[e][1.4]diazepinyl groups, etc.

[0057]

A dihydrobenzodioxepinyl group includes 3,4-dihydro-2H-1,5-benzodioxepinyl, 4,5-dihydro-3H-1,2-benzodioxepinyl, and 3,5-dihydro-2H-1,4-benzodioxepinyl groups, etc.

[0058]

Examples of a pyrrolidinyl group which may have an oxo group(s) include pyrrolidinyl group which may have 1 to 2 (preferably 1) oxo groups, unless otherwise specified. More specifically, it includes (1-, 2-, or 3-)pyrrolidinyl, (2- or 3-)oxo-1-pyrrolidinyl, (3-, 4-, or 5-)oxo-2-pyrrolidinyl, and (2-, 4-, or 5-)oxo-3-pyrrolidinyl groups, etc.

[0059]

Examples of an oxadiazolyl group which may have a lower alkyl group(s) can include oxadiazolyl group which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 5-methyl-1,3,4-oxadiazolyl, 5-ethyl-1,3,4-oxadiazolyl, 5-propyl-1,3,4-oxadiazolyl, 5-butyl-1,3,4-oxadiazolyl, 5-pentyl-1,3,4-oxadiazolyl, and 5-hexyl-1,3,4-oxadiazolyl groups, etc.

[0060]

Examples of a pyrazolyl group which may have a lower alkyl group(s) can include pyrazolyl group which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 1-methyl-1H-pyrazolyl, 1-ethyl-1H-pyrazolyl, 1-propyl-1H-pyrazolyl, 1-isopropyl-1H-pyrazolyl, 1-butyl-1H-pyrazolyl, 1-tert-butyl-1H-pyrazolyl, and 1,3-dimethyl-1H-pyrazolyl groups, etc.

[0061]

Examples of a thiazolyl group which may have a lower alkyl group(s) can include thiazolyl group which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 2-methylthiazolyl, 2-ethylthiazolyl, 2-propylthiazolyl, 2-isopropylthiazolyl, 2-butylthiazolyl, 2-tert-butylthiazolyl, and 2,5-dimethylthiazolyl groups, etc.

[0062]

Examples of a pyrimidyl group which may have a lower alkyl group(s) can include pyrimidyl group which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 2-

methylpyrimidyl, 2-ethylpyrimidyl, 2-propylpyrimidyl, 2-isopropylpyrimidyl, 2-butylpyrimidyl, 2-tert-butylpyrimidyl, and 2,4-dimethylpyrimidyl groups, etc.

[0063]

Examples of a pyridazinyl group which may have a lower alkyl group(s) can include pyridazinyl group which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 3-methylpyridazinyl, 3-ethylpyridazinyl, 3-propylpyridazinyl, 3-isopropylpyridazinyl, 3-butylpyridazinyl, 3-tert-butylpyridazinyl, and 3,4-dimethylpyridazinyl groups, etc.

[0064]

Examples of a pyridazinyloxy group which may have a lower alkyl group(s) can include oxy group which is substituted by pyridazinyl which may have 1 to 2 (preferably 1) of the lower alkyl groups exemplified above, unless otherwise specified. More specifically, it includes 6-methylpyridazinyl-3-yloxy and 4-methylpyridazinyl-3-yloxy groups, etc.

[0065]

Examples of a pyrrolidinyl-lower alkoxy group can include lower alkoxy groups (preferably linear or branched alkoxy groups having 1 to 6 (more preferably 1 to 4, even more preferably 1 to 3) carbon atoms) exemplified above which have 1 to 3, preferably 1 pyrrolidinyl group, unless otherwise specified. Specific examples thereof include (1-, 2-, or 3-) pyrrolidinylmethoxy, 2-[(1-, 2-, or 3-)pyrrolidinyl]ethoxy, 1-[(1-, 2-, or 3-)pyrrolidinyl]ethoxy, 3-[(1-, 2-, or 3-)pyrrolidinyl]propoxy, 4-[(1-, 2-, or 3-)pyrrolidinyl]butoxy, 5-[(1-, 2-, or 3-) pyrrolidinyl]pentyloxy, 6-[(1-, 2-, or 3-)pyrrolidinyl]hexyloxy, 1,1-dimethyl-2-[(1-, 2-, or 3-) pyrrolidinyl]ethoxy, and 2-methyl-3-[(1-, 2-, or 3-)pyrrolidinyl]propoxy groups, etc.

[0066]

Examples of a protecting group include protecting groups routinely used, such as substituted or unsubstituted lower alkanoyl [e.g., formyl, acetyl, propionyl, and trifluoroacetyl], phthaloyl, lower alkoxycarbonyl [e.g., tertiary butoxycarbonyl and tertiary amyloxycarbonyl], substituted or unsubstituted aralkyloxycarbonyl [e.g., benzyloxycarbonyl and p-nitrobenzyloxycarbonyl], 9-fluorenylmethoxycarbonyl, substituted or unsubstituted arenesulfonyl [e.g., benzenesulfonyl and tosyl], nitrophenylsulfenyl, aralkyl [e.g., trityl and benzyl], and lower alkylsilyl groups [e.g., triisopropylsilyl].

[0067]

Examples of a phenyl-lower alkyl group can include the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 (more preferably 1 to 4 carbon atoms) exemplified above which have 1 to 3, preferably 1 phenyl group, unless otherwise specified.

More specifically, it includes benzyl, phenethyl, 3-phenylpropyl, benzhydryl, trityl, 4-phenylbutyl, 5-phenylpentyl, and 6-phenylhexyl groups, etc.

[0068]

Examples of a morpholinyl-lower alkyl group can include the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 carbon atoms) exemplified above which have 1 to 2 (preferably 1) morpholinyl groups, unless otherwise specified. More specifically, it includes 2-morpholinyl methyl, 3-morpholinyl methyl, 4-morpholinyl methyl, 2-(2-morpholinyl)ethyl, 2-(3-morpholinyl)ethyl, 2-(4-morpholinyl)ethyl), 1-(2-morpholinyl)ethyl, 1-(3-morpholinyl)ethyl, 1-(4-morpholinyl)ethyl, 3-(2-morpholinyl)propyl, 3-(3-morpholinyl)propyl, 3-(4-morpholinyl)propyl, 4-(2-morpholinyl)butyl, 4-(3-morpholinyl)butyl, 4-(4-morpholinyl)butyl, 5-(2-morpholinyl)pentyl, 5-(3-morpholinyl)pentyl, 5-(4-morpholinyl)pentyl, 6-(2- morpholinyl)hexyl, 6-(3- morpholinyl)hexyl, 6-(4- morpholinyl)hexyl, 3-methyl-3-(2-morpholinyl)propyl, 3-methyl-3-(3- morpholinyl)propyl, 1, 1-dimethyl-2-(2-morpholinyl)ethyl, 1,1-dimethyl-2-(3- morpholinyl)ethyl, and 1,1-dimethyl-2-(4-morpholinyl)ethyl groups, etc.

[0069]

Examples of a pyrrolidinyl -lower alkyl group can include the lower alkyl groups exemplified above which have 1 to 3 (preferably 1) pyrrolidinyl groups, unless otherwise specified. More specifically, it includes (1-, 2-, or 3-) pyrrolidinylmethyl, 2-[(1-, 2- or 3-) pyrrolidinyl]ethyl, 1-[(1-, 2- or 3-)] pyrrolidinyl]ethyl, 3-[(1-, 2- or 3-)] pyrrolidinyl]propyl, 4-[(1-, 2- or 3-)] pyrrolidinyl]butyl, 5-[(1-, 2- or 3-)] pyrrolidinyl]pentyl, 6-[(1-, 2- or 3-)] pyrrolidinyl]hexyl, 1, 1-dimethyl-2-[(1-, 2- or 3-)] pyrrolidinyl]ethyl, and 2-methyl-3-[(1-, 2- or 3-)] pyrrolidinyl]propyl groups, etc.

[0070]

Examples of a piperidyl-lower alkyl group can include the lower alkyl groups (preferably linear or branched alkyl groups having 1 to 6 carbon atoms) exemplified above which have 1 to 2 (preferably 1) piperidyl groups, unless otherwise specified. More specifically, it includes (1-, 2-, 3- or 4-) piperidylmethyl, 2-[(1-, 2-, 3- or 4-)piperidyl]ethyl, 1-[(1-, 2-, 3- or 4-)piperidyl]ethyl, 3-[(1-, 2-, 3- or 4-)piperidyl]propyl, 4-[(1-, 2-, 3- or 4-)piperidyl]butyl, 1,1-dimethyl-2-[(1-, 2-, 3- or 4-)piperidyl]ethyl, 5-[(1-, 2-, 3- or 4-)piperidyl]pentyl, 6-[(1-, 2-, 3- or 4-)piperidyl]hexyl, 1-[(1-, 2-, 3- or 4-)piperidyl]isopropyl, and 2-methyl-3-[(1-, 2-, 3- or 4-)piperidyl]propyl groups, etc.

[0071]

Examples of a lower alkoxycarbonyl group can include linear or branched alkoxy groups having preferably 1 to 6 carbon atoms and having a lower alkoxycarbonyl moiety as exemplified above. More specifically, it includes methoxycarbonyl, ethoxycarbonyl, n-propxycarbonyl, isopropoxycarbonyl, n-butoxycarbonyl, isobutoxycarbonyl, tert-butoxycarbonyl, sec-butoxycarbonyl, n-pentyloxycarbonyl, neopentyloxycarbonyl, n-hexyloxycarbonyl, isohexyloxycarbonyl, 3-methylpentyloxycarbonyl groups, etc.

[0072]

Examples of a piperazinyl group which may have a lower alkyl group(s) include piperazinyl groups which may have 1 to 2 (preferably 1) lower alkyl groups, unless otherwise specified. More specifically, it includes 2-methylpiperazinyl, 4-methylpiperazinyl, 2-ethylpiperazinyl, 2-propylpiperazinyl, 2-isopropylpiperazinyl, 2-butylpiperazinyl, 2-tert butylpiperazinyl, and 2, 4-dimethylpiperazinyl groups, etc.

[0073]

Examples of a piperazinyl-lower alkyl group which may have a lower alkyl group(s) include piperazinyl groups exemplified above which may have 1 to 2 (preferably 1) lower alkyl groups, unless otherwise specified. More specifically, it includes 1-(4-methylpiperazinyl)methyl, 1-(2-methyl piperazinyl)methyl, 2-(1-methyl piperazinyl)ethyl, 3-(1-methyl piperazinyl)propyl, 4-(1-methyl piperazinyl)butyl groups, etc.

[0074]

Examples of a phenyl group which may have a lower alkoxy group(s) include phenyl groups exemplified above which may have 1 to 2 (preferably 1) lower alkoxy groups, unless otherwise specified. More specifically, it includes 4-methoxyphenyl, 4-ethoxyphenyl, 4-propoxyphenyl, 4-isopropylphenyl, 4-butoxyphenyl, 4-tert butoxyphenyl groups, etc. can be mentioned As a phenoxy group exemplified above which may have a halogen atom(s) include phenoxy groups which may have 1 to 4 (preferably 1) halogen atoms, unless otherwise specified. More specifically, it includes 4-fluorophenoxy, 3, 4-difluorophenoxy, 3, 4, 5-trifluorophenoxy, and 3-chloro-4,5-difluorophenoxy groups, etc.

[0075]

A tetrahydroquinolyl group includes, for example, 1, 2, 3, 4- tetrahydroquinolyl, 5, 6, 7, 8-tetrahydroquinolyl, 4a, 5, 8, 8a-tetrahydroquinolyl, 3, 4, 4a, 8a-tetrahydroquinolyl, 4a, 5, 8, 8a-tetrahydroquinolyl, and 4a, 5, 6, 7- tetrahydroquinolyl groups, etc.

[0076]

A dihydroacenaphthylenyl group includes, for example, 1, 2-dihydroacenaphthylenyl, $2a^1$, 3-dihydroacenaphthylenyl, 5, 6- dihydroacenaphthylenyl, 3, 7-dihydroacenaphthylenyl, $2a^1$, 6-dihydroacenaphthylenyl, 1, $2a^1$-dihydroacenaphthylenyl, and 6, 8a-dihydroacenaphthylenyl groups, etc. More preferably , it is 1, 2-dihydroacenaphthylenyl group can be mentioned.

[0077]

A tetrahydronaphthyl group includes, for example, 1, 2, 3, 4-tetrahydronaphthyl, 1, 2, 3, 5-tetrahydronaphthyl, and 5, 6, 7, 8-tetrahydronaphthyl, 2, 3, 7, 8-tetrahydronaphthyl groups, etc. can be mentioned.

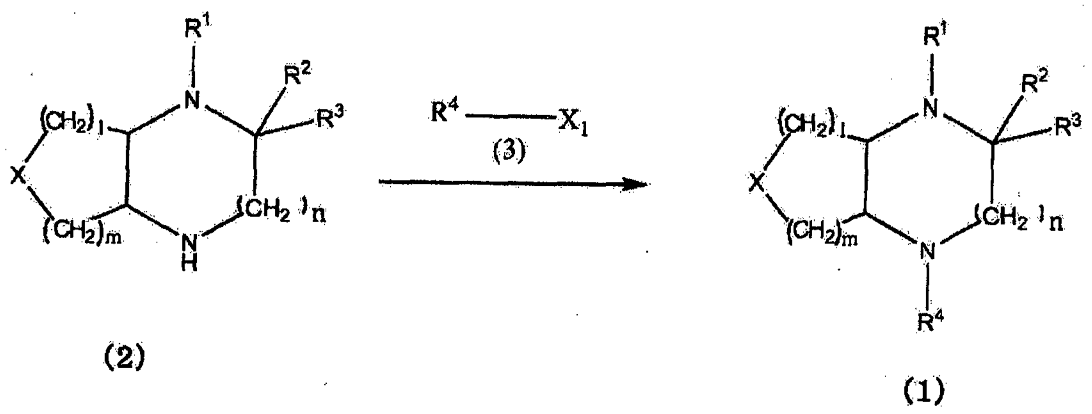
[0078]

A dihydroquinazolinyl group includes, for example, 1, 2-dihydroquinazolinyl, 3, 4-dihydroquinazolinyl, 4a, 5-dihydroquinazolinyl, 5, 6-dihydroquinazolinyl, 6, 7-dihydroquinazolinyl, 7,8-dihydroquinazolinyl, 8,8a-dihydroquinazolinyl, and 4a, 8a-dihydroquinazolinyl groups, etc. can be mentioned.

[0079]

The heterocyclic compound represented by the general formula (1) can be produced by various methods. As an example, the heterocyclic compound represented by the general formula (1) is produced by methods represented by the reaction formulas shown below.

Reaction Formula-1



wherein R^1, R^2, R^3, R^4, X, l, m, and n are defined as above; and X_1 represents a leaving group.

[0080]

In the general formula (3), the leaving group represented by X_1 can be exemplified by halogen atoms, lower alkanesulfonyloxy groups, arylsulfonyloxy groups, aralkylsulfonyloxy groups, trihalomethanesulfonyloxy groups, sulfonio groups, and toluenesulfoxy groups. Preferable examples of the leaving groups for the present reaction include halogen atoms.

[0081]

Examples of the halogen atoms represented by X_1 can include fluorine, chlorine, bromine, and iodine atoms.

[0082]

The lower alkanesulfonyloxy groups represented by X_1 can be exemplified specifically by linear or branched alkanesulfonyloxy groups having 1 to 6 carbon atoms, such as methanesulfonyloxy, ethanesulfonyloxy, n-propanesulfonyloxy, isopropanesulfonyloxy, n-butanesulfonyloxy, tert-butanesulfonyloxy, n-pentanesulfonyloxy, and n-hexanesulfonyloxy groups.

[0083]

Examples of the arylsulfonyloxy groups represented by X_1 can include: phenylsulfonyloxy groups which may have 1 to 3 groups selected from the group consisting of linear or branched alkyl groups having 1 to 6 carbon atoms, linear or branched alkoxy groups having 1 to 6 carbon atoms, nitro groups, and halogen atoms as substituents on the phenyl ring; and naphthylsulfonyloxy groups. The phenylsulfonyloxy groups which may have the substituents can be exemplified specifically by phenylsulfonyloxy, 4-methylphenylsulfonyloxy, 2-methylphenylsulfonyloxy, 4-nitrophenylsulfonyloxy, 4-methoxyphenylsulfonyloxy, 2-nitrophenylsulfonyloxy, and 3-chlorophenylsulfonyloxy groups. The naphthylsulfonyloxy groups can be exemplified specifically by α-naphthylsulfonyloxy and β-naphthylsulfonyloxy groups.

[0084]

Examples of the aralkylsulfonyloxy groups represented by X_1 can include: linear or branched alkanesulfonyloxy groups having 1 to 6 carbon atoms, which are substituted by a phenyl group which may have 1 to 3 groups selected from the group consisting of linear or branched alkyl groups having 1 to 6 carbon atoms, linear or branched alkoxy groups having 1 to 6 carbon atoms, nitro groups, and halogen atoms as substituents on the phenyl ring; and linear or branched alkanesulfonyloxy groups having 1 to 6 carbon atoms, which are substituted by a naphthyl group. The alkanesulfonyloxy groups which are substituted by the phenyl group can be exemplified specifically by benzylsulfonyloxy, 2-phenylethylsulfonyloxy, 4-phenylbutylsulfonyloxy, 4-methylbenzylsulfonyloxy, 2-methylbenzylsulfonyloxy, 4-nitrobenzylsulfonyloxy, 4-methoxybenzylsulfonyloxy, and 3-chlorobenzylsulfonyloxy. The alkanesulfonyloxy groups which are substituted by the naphthyl group can be exemplified specifically by α-naphthylmethylsulfonyloxy and β-naphthylmethylsulfonyloxy groups.

[0085]

The perhaloalkanesulfonyloxy groups represented by X_1 can be exemplified specifically by trifluoromethanesulfonyloxy groups.

[0086]

Examples of the sulfonio groups represented by X_1 can specifically include dimethylsulfonio, diethylsulfonio, dipropylsulfonio, di-(2-cyanoethyl)sulfonio, di-(2-nitroethyl)sulfonio, di-(aminoethyl)sulfonio, di-(2-methylaminoethyl)sulfonio, di-(2-dimethylaminoethyl)sulfonio, di-(2-hydroxyethyl)sulfonio, di-(3-hydroxypropyl)sulfonio, di-(2-methoxyethyl)sulfonio, di-(2-carbamoylethyl)sulfonio, di-(2-carbamoylethyl)sulfonio, di-(2-carboxyethyl)sulfonio, and di-(2-methoxycarbonylethyl)sulfonio, and diphenylsulfonio groups.

[0087]

A compound represented by the general formula (2) and the compound represented by the general formula (3) can be reacted in the presence of a palladium catalyst in the presence or absence of a basic compound without or in an inert solvent to thereby produce the compound (1).

[0088]

Examples of the inert solvent can include, for example: water; ether solvents such as dioxane, tetrahydrofuran, diethyl ether, 1,2-dimethoxyethane, diethylene glycol dimethyl ether, and ethylene glycol dimethyl ether; aromatic hydrocarbon solvents such as benzene, toluene, and xylene; lower alcohol solvents such as methanol, ethanol, and isopropanol; ketone solvents such as acetone and methyl ethyl ketone; and polar solvents such as N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), hexamethylphosphoric triamide, and acetonitrile. These inert solvents are used alone or as a mixture of two or more of them.

[0089]

The palladium compound used in the present reaction is not particularly limited. Examples thereof include: tetravalent palladium catalysts such as sodium hexachloropalladium (IV) acid tetrahydrate and potassium hexachloropalladium (IV) acid; divalent palladium catalysts such as palladium (II) chloride, palladium (II) bromide, palladium (II) acetate, palladium (II) acetylacetonate, dichlorobis(benzonitrile)palladium (II), dichlorobis(acetonitrile)palladium (II), dichlorobis(triphenylphosphine)palladium (II), dichlorotetraammine palladium (II), dichloro(cycloocta-1,5-diene)palladium (II), and palladium (II) trifluoroacetate 1,1'-bis(diphenylphosphino)ferrocenedichloropalladium (II)-dichloromethane complex; and zerovalent palladium catalysts such as tris(dibenzylideneacetone)dipalladium (0), tris(dibenzylideneacetone)dipalladium (0)-chloroform complex, and tetrakis(triphenylphosphine)palladium (0). These palladium compounds are used alone or as a mixture of two or more of them.

[0090]

In the present reaction, the amount of the palladium catalyst used is not particularly limited and usually ranges from 0.000001 to 20 mol in terms of palladium with respect to 1 mol of the compound of the general formula (2). More preferably, the amount of the palladium compound used ranges from 0.0001 to 5 mol in terms of palladium with respect to 1 mol of the compound of the general formula (2).

[0091]

The present reaction proceeds advantageously in the presence of an appropriate ligand. For example, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP), tri-o-tolylphosphine, bis(diphenylphosphino)ferrocene, triphenylphosphine, tri-t-butylphosphine, tricyclohexylphosphine, and 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (XANTPHOS) can be used as the ligand for the palladium catalyst. These ligands are used alone or as a mixture of two or more of them.

[0092]

Furthermore, in the present invention, the tertiary phosphine may be prepared in a complex form in advance and added thereto. Examples of the complex can include tri-t-butylphosphonium tetrafluoroborate and tri-t-butylphosphonium tetraphenylborate.

[0093]

The ratio between the palladium catalyst and the ligand used is not particularly limited. The amount of the ligand used is approximately 0.1 to 100 mol, preferably approximately 0.5 to 15 mol, with respect to 1 mol of the palladium catalyst.

[0094]

Inorganic and organic bases known in the art can be used widely as the basic compound.

[0095]

Examples of the inorganic bases can include: alkali metal hydroxides such as sodium hydroxide, potassium hydroxide, cesium hydroxide, and lithium hydroxide; alkali metal carbonates such as sodium carbonate, potassium carbonate, cesium carbonate, and lithium carbonate; alkali metal bicarbonates such as lithium bicarbonate, sodium bicarbonate, and potassium bicarbonate; alkali metals such as sodium and potassium; phosphates such as sodium phosphate and potassium phosphate; amides such as sodium amide; and alkali metal hydrides such as sodium hydride and potassium hydride.

[0096]

Examples of the organic bases can include: alkali metal lower alkoxides such as sodium methoxide, sodium ethoxide, sodium t-butoxide, potassium methoxide, potassium ethoxide, and potassium t-butoxide; and amines such as triethylamine, tripropylamine, pyridine, quinoline, piperidine, imidazole, N-ethyldiisopropylamine, dimethylaminopyridine, trimethylamine, dimethylaniline, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 1,4-diazabicyclo[2.2.2]octane (DABCO).

[0097]

These basic compounds are used alone or as a mixture of two or more of them. More preferable examples of the basic compound used in the present reaction include alkali metal carbonates such as sodium carbonate, potassium carbonate, cesium carbonate, and lithium carbonate, and sodium t-butoxide.

[0098]

The amount of the basic compound used is usually 0.5 to 10 mol, preferably 0.5 to 6 mol, with respect to 1 mol of the compound of the general formula (2).

[0099]

The ratio between the compound of the general formula (2) and the compound of the general formula (3) used in the Reaction Formula-1 may be at least 1 mol, preferably approximately 1 to 5 mol of the latter compound with respect to 1 mol of the former compound.

[0100]

The reaction can be performed in an atmosphere of inert gas such as nitrogen or argon under the atmospheric pressure or can be performed under increased pressure.

[0101]

The present reaction is usually performed under temperature conditions involving room temperature to 200°C, preferably room temperature to 150°C, and generally completed in approximately 1 to 30 hours. It is also achieved by heating at 100 to 200°C for 5 minutes to 1 hour using a microwave reactor.

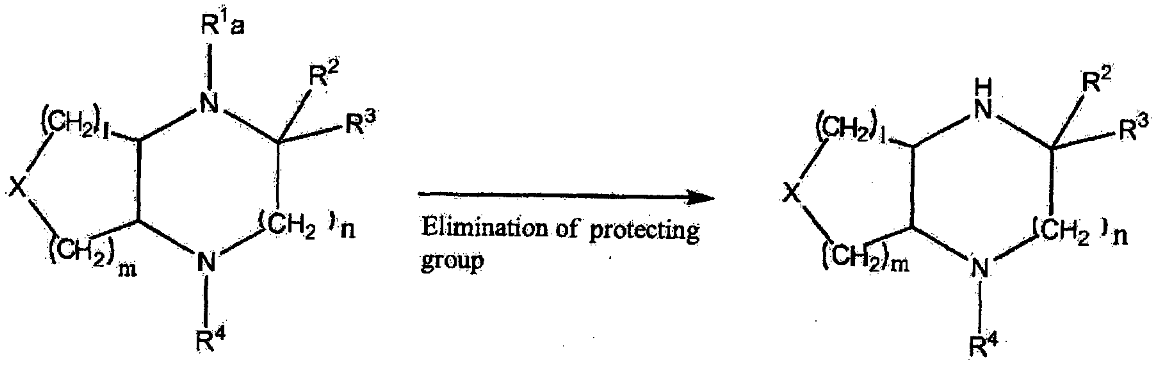
[0102]

After the completion of the reaction, the reaction product can be treated by a standard method to obtain the compound of interest.

[0103]

The compound represented by the general formula (2) used as a starting material in the Reaction Formula-1 is produced from compounds known in the art, for example, by methods represented by Reaction Formulas-3 and 4 shown below. The compound represented by the general formula (3) is an easily obtainable compound known in the art or a compound easily produced by a method known in the art.

Reaction Formula-2



(1a) (1b)

wherein R^2, R^3, R^4, X, l, m, and n are defined as above; and R^{1a} represents a protecting group.

[0104]

Examples of the protecting group include the protecting groups exemplified above.

[0105]

The compound represented by the general formula (1b) can be produced by subjecting a compound represented by the general formula (1a) to the elimination reaction of the protecting group.

[0106]

A method routinely used such as hydrolysis or hydrogenolysis can be applied to the elimination reaction of the protecting group.

[0107]

The present reaction is usually performed in a solvent routinely used that does not adversely affect the reaction. Examples of the solvent include: water; alcohol solvents such as methanol, ethanol, isopropanol, n-butanol, trifluoroethanol, and ethylene glycol; ketone solvents such as acetone and methyl ethyl ketone; ether solvents such as tetrahydrofuran, dioxane, diethyl ether, dimethoxyethane, and diglyme; ester solvents such as methyl acetate and ethyl acetate; aprotic polar solvents such as acetonitrile, N,N-dimethylformamide, dimethyl sulfoxide, and N-methylpyrrolidone; halogenated hydrocarbon solvents such as methylene chloride and ethylene chloride; and other organic solvents.

[0108]

(i) Hydrolysis:

[0109]

The hydrolysis is preferably performed in the presence of a base or an acid (including Lewis acids).

[0110]

Inorganic and organic bases known in the art can be used widely as the base. Preferable examples of the inorganic bases include alkali metals (e.g., sodium and potassium), alkaline earth metals (e.g., magnesium and calcium), and hydrides, carbonates, or bicarbonates thereof. Preferable examples of the organic bases include trialkylamines (e.g., trimethylamine and triethylamine), picoline, and 1,5-diazabicyclo[4.3.0]non-5-ene.

[0111]

Organic and inorganic acids known in the art can be used widely as the acid. Preferable examples of the organic acids include: fatty acids such as formic acid, acetic acid, and propionic acid; and trihaloacetic acids such as trichloroacetic acid and trifluoroacetic acid. Preferable examples of the inorganic acids include hydrochloric acid, hydrobromic acid, sulfuric acid, hydrogen chloride, and hydrogen bromide. Examples of the Lewis acids include boron trifluoride-ether complexes, boron tribromide, aluminum chloride, and ferric chloride.

[0112]

When trihaloacetic acid or Lewis acid is used as the acid, the reaction is preferably performed in the presence of a cation scavenger (e.g., anisole and phenol).

[0113]

The amount of the base or the acid used is not particularly limited as long as it is an amount necessary for hydrolysis.

[0114]

The reaction temperature is usually 0 to 120°C, preferably room temperature to 100°C, more preferably room temperature to 80°C. The reaction time is usually 30 minutes to 24 hours, preferably 30 minutes to 12 hours, more preferably 1 to 8 hours.

[0115]

(ii) Hydrogenolysis:

Hydrogenolysis methods known in the art can be applied widely to the hydrogenolysis. Examples of such hydrogenolysis methods include chemical reduction and catalytic reduction.

[0116]

Preferable reducing agents used in chemical reduction are the combinations of hydrides (e.g., hydrogen iodide, hydrogen sulfide, lithium aluminum hydride, sodium borohydride, and sodium cyanoborohydride), metals (e.g., tin, zinc, and iron), or metal compounds (e.g., chromium chloride and chromium acetate) with organic or inorganic acids (e.g., formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, and hydrobromic acid).

[0117]

Preferable catalysts used in catalytic reduction are platinum catalysts (e.g., platinum plates, platinum sponge, platinum black, colloidal platinum, platinum oxide, and platinum wires), palladium catalysts (e.g., palladium sponge, palladium black, palladium oxide, palladium-carbon, palladium/barium sulfate, and palladium/barium carbonate), nickel catalysts (e.g., reduced nickel, nickel oxide, and Raney nickel), cobalt catalysts (e.g., reduced cobalt and Raney cobalt), iron catalysts (e.g., reduced iron), etc.

[0118]

When these acids used in chemical reduction are in a liquid state, they can also be used as solvents.

[0119]

The amount of the reducing agent used in chemical reduction or the catalyst used in catalytic reduction is not particularly limited and may be an amount usually used.

[0120]

The reaction of the present invention can be performed in an atmosphere of inert gas such as nitrogen or argon under the atmospheric pressure or can be performed under increased pressure.

[0121]

The reaction temperature is usually 0 to 120°C, preferably room temperature to 100°C, more preferably room temperature to 80°C. The reaction time is usually 30 minutes to 24 hours, preferably 30 minutes to 10 hours, more preferably 30 minutes to 4 hours.

[0122]

After the completion of the reaction, the reaction product can be treated by a standard method to obtain the compound of the general formula (1b) of interest.

[0123]

The deprotection reaction of the protecting group is not limited to the reaction conditions described above. For example, reaction described in T.W. Green, P.G.M. Wuts, "Protective Groups in Organic Synthesis", 4th ed., or John Wiley & Sons; New York, 1991, P. 309 can also be applied to the present reaction step.

[0124]

The compound represented by the general formula (2) is a novel compound, which is useful as an intermediate for the compound represented by the general formula (1), as described above.

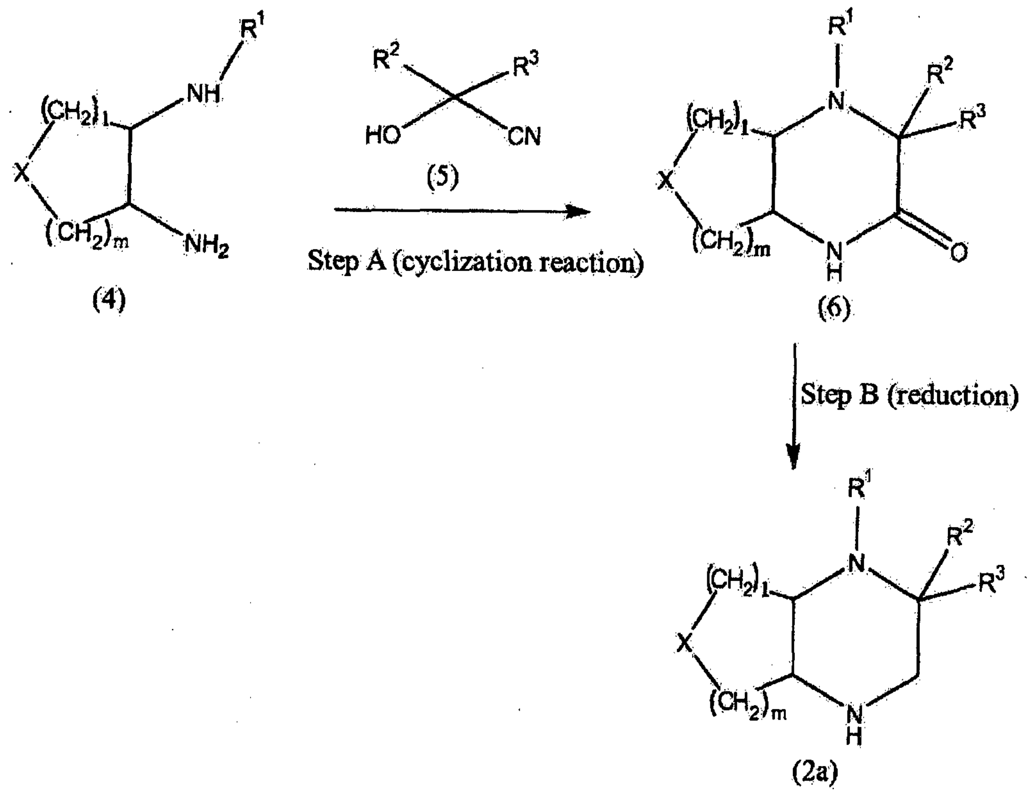
[0125]

The compound of the general formula (2) is produced according to, for example, Reaction Formulas-3, 4, or 5 shown below.

[0126]

Hereinafter, each reaction formula will be described.

Reaction Formula-3



wherein R^1, R^2, R^3, X, l, m, and n are defined as above.

[0127]

The compound represented by the general formula (2a) is produced by subjecting a compound represented by the general formula (4) and a compound represented by the general formula (5) to cyclization reaction to form a compound represented by the general formula (6) (Step A), which is then reduced (Step B).

[0128]

Step A

The reaction between the compound represented by the general formula (4) and the compound represented by the general formula (5) can be performed in the presence or absence of a base without or in an inert solvent.

[0129]

Examples of the inert solvent can include, for example: water; ethers such as dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether, and ethylene glycol dimethyl ether; aromatic hydrocarbons such as benzene, toluene, and xylene; lower alcohols such as methanol, ethanol, and isopropanol; ketones such as acetone and methyl ethyl ketone; and polar solvents such as N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), hexamethylphosphoric triamide, and acetonitrile.

[0130]

Basic compounds known in the art can be used widely. Examples thereof can include: alkali metal hydroxides such as sodium hydroxide, potassium hydroxide, cesium hydroxide, and lithium hydroxide; alkali metal carbonates such as sodium carbonate, potassium carbonate, cesium carbonate, and lithium carbonate; alkali metals such as sodium and potassium; other inorganic bases such as sodium amide, sodium hydride, and potassium hydride; alkali metal alcoholates such as sodium methoxide, sodium ethoxide, potassium methoxide, and potassium ethoxide; and other organic bases such as triethylamine, tripropylamine, pyridine, quinoline, piperidine, imidazole, N-ethyldiisopropylamine, dimethylaminopyridine, trimethylamine, dimethylaniline, N-methylmorpholine, 1,5-diazacyclo[4.3.0]non-5-ene (DBN), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and 1,4-diazabicyclo[2.2.2]octane (DABCO).

[0131]

These basic compounds are used alone or as a mixture of two or more of them.

[0132]

The amount of the basic compound used is usually 0.5 to 10 mol, preferably 0.5 to 6 mol, with respect to the compound of the general formula (4).

[0133]

The reaction can be performed by adding, if necessary, alkali metal iodide (e.g., potassium iodide and sodium iodide) as a reaction promoter.

[0134]

The ratio between the compound of the general formula (4) and the compound of the general formula (5) used in the reaction formula may be usually at least 0.5 mol, preferably approximately 0.5 to 5 mol of the latter compound with respect to 1 mol of the former compound.

[0135]

The reaction of the present invention can be performed in an atmosphere of inert gas such as nitrogen or argon under the atmospheric pressure or can be performed under increased pressure.

[0136]

The reaction is usually performed under temperature conditions involving 0°C to 200°C, preferably room temperature to 150°C, and generally completed in approximately 1 to 30 hours.

[0137]

The compound of the general formula (4) and the compound of the general formula (5) used as starting materials in the Step A are easily obtainable compounds known in the art or compounds easily produced by a method known in the art.

[0138]

Step B

The compound represented by the general formula (2a) can be produced by subjecting the compound represented by the general formula (6) to reduction reaction without or in an inert solvent.

[0139]

Examples of such reduction methods include chemical reduction and catalytic reduction.

[0140]

Examples of the inert solvent can include: water; ethers such as dioxane, tetrahydrofuran, diethyl ether, diethylene glycol methyl ether, and ethylene glycol dimethyl ether; aromatic hydrocarbons such as benzene, toluene, and xylene; lower alcohols such as methanol, ethanol, and isopropanol; ketones such as acetone and methyl ethyl ketone; and polar solvents such as N,N-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), hexamethylphosphoric triamide, and acetonitrile.

[0141]

Preferable reducing agents used in chemical reduction are the combinations of hydrides (e.g., hydrogen iodide, hydrogen sulfide, lithium aluminum hydride, boron hydride, sodium borohydride, and sodium cyanoborohydride), metals (e.g., tin, zinc, and iron), or metal compounds (e.g., chromium chloride and chromium acetate) with organic or inorganic acids (e.g., formic acid, acetic acid, propionic acid, trifluoroacetic acid, p-toluenesulfonic acid, hydrochloric acid, and hydrobromic acid).

[0142]

Preferable catalysts used in catalytic reduction are platinum catalysts (e.g., platinum plates, platinum sponge, platinum black, colloidal platinum, platinum oxide, and platinum wires), palladium catalysts (e.g., palladium sponge, palladium black, palladium oxide, palladium-carbon, palladium/barium sulfate, and palladium/barium carbonate), nickel catalysts (e.g., reduced nickel, nickel oxide, and Raney nickel), cobalt catalysts (e.g., reduced cobalt and Raney cobalt), iron catalysts (e.g., reduced iron), etc.

[0143]

When these acids used in chemical reduction are in a liquid state, they can also be used as solvents.

[0144]

The amount of the reducing agent used in chemical reduction or the catalyst used in catalytic reduction is not particularly limited and may be an amount usually used.

[0145]

The reaction of the present invention can be performed in an atmosphere of inert gas such as nitrogen or argon under the atmospheric pressure or can be performed under increased pressure.

[0146]

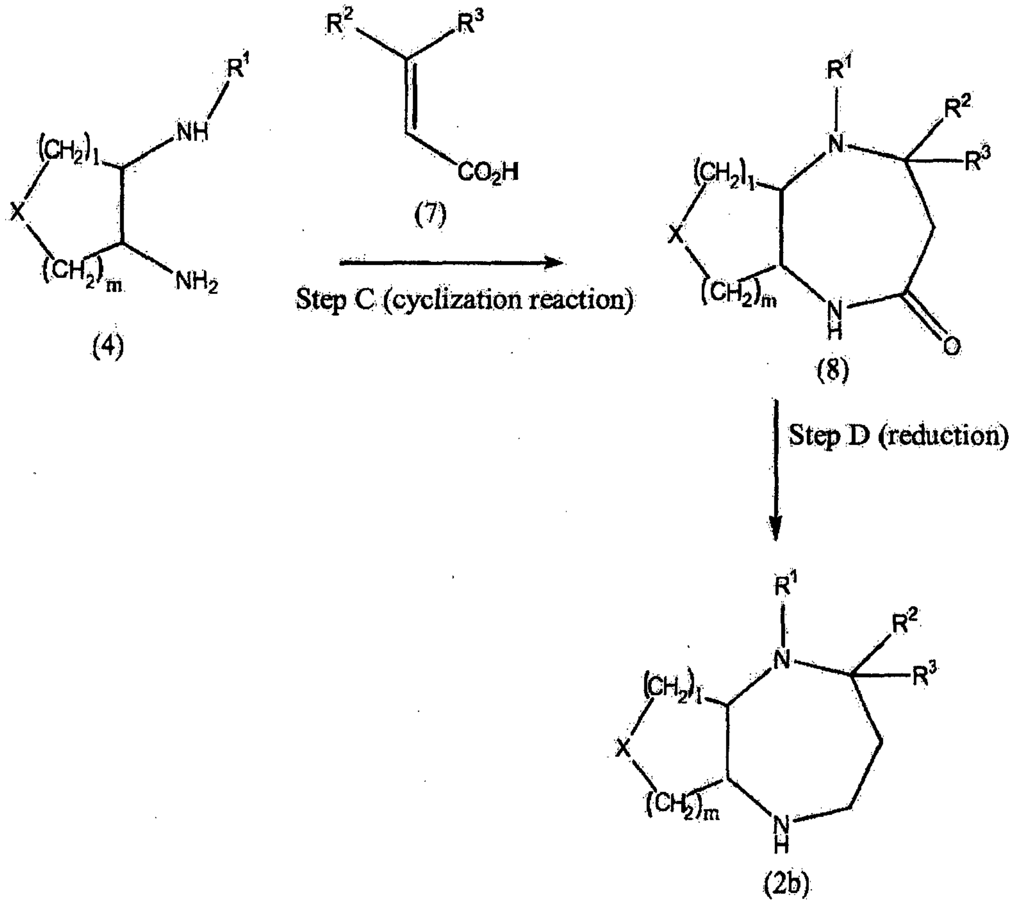
The reaction temperature is usually 0 to 120°C, preferably room temperature to 100°C, more preferably room temperature to 80°C. The reaction time is usually 30 minutes to 24 hours, preferably 30 minutes to 10 hours, more preferably 30 minutes to 4 hours.

[0147]

After the completion of the reaction, the reaction product can be treated by a standard method to obtain the compound of the general formula (2a) of interest.

[0148]

Reaction Formula-4



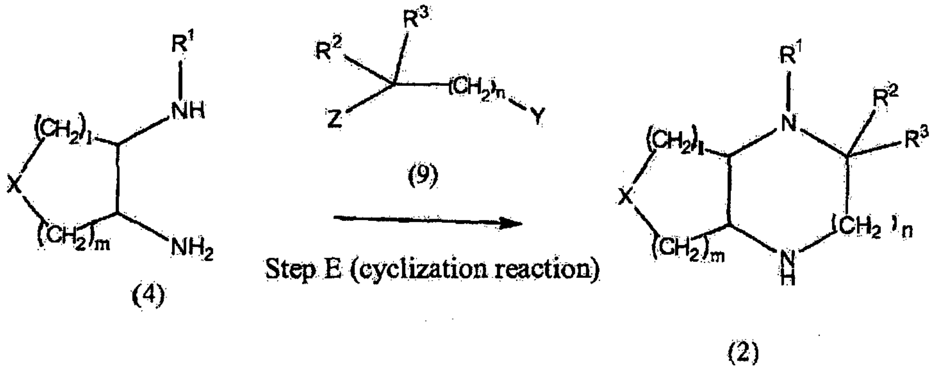
wherein R^1, R^2, R^3, X, l, m, and n are defined as above.

[0149]

The compound represented by the general formula (2b) is produced by subjecting the compound represented by the general formula (4) and a compound represented by the general formula (7) to cyclization reaction to form a compound represented by the general formula (8) (Step C), which is then reduced (Step D). The reaction conditions are the same reaction conditions as in the Reaction Formula-3.

[0150]

Reaction Formula-5



wherein R^1, R^2, R^3, R^4, l, m, n, and X are defined as above; and Y and Z, which are the same or different, each independently represent a leaving group.

[0151]

Examples of the leaving groups represented by Y and Z in the general formula (9) include the leaving groups exemplified above.

[0152]

Step E

The compound represented by the general formula (2) can be produced by subjecting the compound represented by the general formula (4) and a compound represented by the general formula (9) to cyclization reaction. The cyclization reaction is usually performed in the presence or absence of a basic compound.

[0153]

The present reaction is usually performed in a solvent routinely used that does not adversely affect the reaction. Examples of the solvent include: water; alcohol solvents such as methanol, ethanol, isopropanol, n-butanol, trifluoroethanol, and ethylene glycol; ketone solvents such as acetone and methyl ethyl ketone; ether solvents such as tetrahydrofuran, dioxane, diethyl ether, dimethoxyethane, and diglyme; ester solvents such as methyl acetate and ethyl acetate; aprotic polar solvents such as acetonitrile, N,N-dimethylformamide, dimethyl sulfoxide, and N-methylpyrrolidone; halogenated hydrocarbon solvents such as methylene chloride and ethylene chloride; and other organic solvents.

[0154]

A transition metal catalyst and a ligand may be used in this reaction. Examples of the transition metal include ruthenium chloride, dichlorotris(triphenylphosphine)ruthenium, dibromotris(triphenylphosphine)ruthenium, dihydridotetrakis(triphenylphosphine)ruthenium, (η^4-cyclooctadiene)(η^6-cyclooctatriene)ruthenium, dichlorotricarbonylruthenium dimers, dodecacarbonyltriruthenium, (η^5-pentamethylcyclopentadienyl)chloro(η^4-

cyclooctatriene)ruthenium, palladium acetate, palladium chloride, dichlorobis(triphenylphosphine)palladium, tetrakis(triphenylphosphine)palladium, bis(dibenzylideneacetone)palladium, rhodium chloride, chlorotris(triphenylphosphine)rhodium, hydridocarbonyltris(triphenylphosphine)rhodium, hydridotris(triphenylphosphine)rhodium, di-μ-chlorotetracarbonyldirhodium, chlorocarbonylbis(triphenylphosphine)iridium, (η^5-pentamethylcyclopentadienyl)dichloroiridium dimers, nickel tetrakis(triphenylphosphine), dicobaltoctacarbonyl, and (η^5-cyclopentadienyl)dicarbonylcobalt.

[0155]

Examples of the ligand include: unidentate phosphine ligands typified by trimethylphosphine, triethylphosphine, tri-n-propylphosphine, tri-i-propylphosphine, tri-n-butylphosphine, tri-t-butylphosphine, tricyclohexylphosphine, triphenylphosphine, and tri(o-tolyl)phosphine; bidentate phosphine ligands typified by 1,2-bis(diphenylphosphino)ethane, 1,3-bis(diphenylphosphino)propane, 1,4-bis(diphenylphosphino)butane, and 1,2-(diethylphosphino)ethane; and phosphite ligands typified by triethyl phosphite, tributyl phosphite, triphenyl phosphite, and tri(o-tolyl) phosphite.

[0156]

This reaction may be performed in the presence of a base. Inorganic and organic bases known in the art can be used widely as the base. Examples of the inorganic bases include alkali metals (e.g., sodium and potassium), alkali metal bicarbonates (e.g., lithium bicarbonate, sodium bicarbonate, and potassium bicarbonate), alkali metal hydroxides (e.g., lithium hydroxide, sodium hydroxide, potassium hydroxide, and cesium hydroxide), alkali metal carbonates (e.g., lithium carbonate, sodium carbonate, potassium carbonate, and cesium carbonate), alkali metal lower alkoxides (e.g., sodium methoxide and sodium ethoxide), and alkali metal hydrides (e.g., sodium hydride and potassium hydride). Examples of the organic bases include trialkylamines (e.g., trimethylamine, triethylamine, and N-ethyldiisopropylamine), pyridine, quinoline, piperidine, imidazole, picoline, dimethylaminopyridine, dimethylaniline, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,4-diazabicyclo[2.2.2]octane (DABCO), and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). When these bases are in a liquid state, they can also be used as solvents. These bases are used alone or as a mixture of two or more of them. The amount of the base used is usually 0.1 to 10 mol, preferably 0.1 to 3 mol, with respect to 1 mol of the compound of the general formula (7).

[0157]

The reaction can also be performed in the presence of a mixture of an oxidizing agent and a reducing agent.

[0158]

Examples of the oxidizing agent include manganese dioxide, chromic acid, lead tetraacetate, silver oxide, copper oxide, halogen acid, dimethyl sulfoxide (Swern oxidation), organic peroxides, and oxygen. A method such as electrode oxidation may be used.

[0159]

Examples of the reducing agent include borohydride reagents such as sodium borohydride and aluminum hydride reagents such as lithium aluminum hydride.

[0160]

The ratio between the compound of the general formula (9) and the compound of the general formula (4) used in the reaction formula is usually at least 1 mol, preferably approximately 1 to 5 mol of the former compound with respect to 1 mol of the latter compound.

[0161]

The reaction of the present invention can be performed in an atmosphere of inert gas such as nitrogen or argon under the atmospheric pressure or can be performed under increased pressure.

[0162]

The reaction temperature is not particularly limited. The reaction is usually performed under cooling, at room temperature, or under heating. The reaction is preferably performed under temperature conditions involving room temperature to 100°C, for 30 minutes to 30 hours, preferably 30 minutes to 5 hours.

[0163]

After the completion of the reaction, the reaction product can be treated by a standard method to obtain the compound of the general formula (2) of interest.

[0164]

Examples of preferable salts of the compound of the general formula (1) include pharmacologically acceptable salts, for example: metal salts such as alkali metal salts (e.g., sodium salt and potassium salt) and alkaline earth metal salts (e.g., calcium salt and magnesium salt); ammonium salt; salts of inorganic bases such as alkali metal carbonates (e.g., lithium carbonate, potassium carbonate, sodium carbonate, and cesium carbonate), alkali metal bicarbonates (e.g., lithium bicarbonate, sodium bicarbonate, and potassium bicarbonate), and alkali metal hydroxides (e.g., lithium hydroxide, sodium hydroxide, potassium hydroxide, and cesium hydroxide); salts of organic bases such as tri-(lower) alkylamine (e.g., trimethylamine, triethylamine, and N-ethyldiisopropylamine), pyridine, quinoline, piperidine, imidazole, picoline, dimethylaminopyridine, dimethylaniline, N-(lower) alkyl-morpholine (e.g., N-methylmorpholine), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU), and 1,4-diazabicyclo [2.2.2] octane (DABCO); inorganic acid salts such as hydrochloride, hydrobromide, hydroiodide, sulfate, nitrate, and phosphate; and organic acid salts such as formate, acetate, propionate, oxalate, malonate, succinate, fumarate, maleate, lactate, malate, citrate, tartrate, carbonate, picrate, methanesulfonate, ethanesulfonate, p-toluenesulfonate, and glutamate.

[0165]

Moreover, compounds in a form of a solvate (e.g., a hydrate or an ethanolate) added to the raw material or the compound of interest shown in each reaction formula are also included in each general formula. Preferable examples of the solvate include hydrates.

[0166]

Each compound of interest obtained according to each of the reaction formulas can be isolated and purified from the reaction mixture, for example, by separating, after cooling, the reaction mixture into a crude reaction product by isolation procedures such as filtration, concentration, and extraction and subjecting the crude reaction product to usual purification procedures such as column chromatography and recrystallization.

[0167]

The compound represented by the general formula (1) of the present invention also encompasses isomers such as geometric isomers, stereoisomers, and optical isomers, of course.

[0168]

Various isomers can be isolated by a standard method using difference in physicochemical properties among the isomers. For example, racemic compounds can be converted to sterically pure isomers by a general optical resolution method [e.g., method involving conversion to diastereomeric salts with a general optically active acid (tartaric acid, etc.) and subsequent optical resolution]. Diastereomeric mixtures can be separated by, for example, fractional crystallization or chromatography. Optically active compounds can also be produced using appropriate optically active starting materials.

[0169]

The present invention also encompasses isotope-labeled compounds which are the same as the compound represented by the general formula (1) except that one or more atom(s) is substituted by one or more atoms(s) having a particular atomic mass or mass number. Examples of the isotope that can be incorporated in the compound of the present invention include hydrogen, carbon, nitrogen, oxygen, sulfur, fluorine, and chlorine isotopes such as ^{2}H,

^{3}H, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{18}F, and ^{36}Cl. These particular isotope-labeled compounds of the present invention containing any of the isotopes and/or other isotopes of other atoms, for example, radioisotope (e.g., ^{3}H and ^{14}C)-incorporated compounds, are useful in assay for the distribution of drugs and/or substrates in tissues. Tritiated (i.e., ^{3}H) and carbon-14 (i.e., ^{14}C) isotopes are particularly preferable because of their easy preparation and detectability. Furthermore, substitution by heavier isotopes such as heavy hydrogen (i.e., ^{2}H) can be expected to bring about particular therapeutic advantages attributed to improved metabolic stability, for example, increased *in-vivo* half-life, or reduced necessary doses. The isotope-labeled compounds of the present invention can be prepared generally by substituting an unlabeled reagent by an easily obtainable isotope-labeled reagent by a method disclosed in the reaction formulas and/or Examples below.

[0170]

A pharmaceutical preparation comprising the compound of the present invention as an active ingredient will be described.

[0171]

The pharmaceutical preparation is obtained by making the compound of the present invention into usual dosage forms of pharmaceutical preparations and prepared using a diluent and/or an excipient usually used, such as fillers, extenders, binders, humectants, disintegrants, surfactants, and lubricants.

[0172]

Such a pharmaceutical preparation can be selected from among various forms according to a therapeutic purpose. Typical examples thereof include tablets, pills, powders, solutions, suspensions, emulsions, granules, capsules, suppositories, and injections (solutions, suspensions, etc.).

[0173]

Carries known in the art for use for forming a tablet form can be used widely. Examples thereof include: excipients such as lactose, sucrose, sodium chloride, glucose, urea, starch, calcium carbonate, kaolin, and crystalline cellulose; binders such as water, ethanol, propanol, simple syrup, glucose solutions, starch solutions, gelatin solutions, carboxymethylcellulose, shellac, methylcellulose, potassium phosphate, and polyvinyl pyrrolidone; disintegrants such as dry starch, sodium alginate, agar powder, laminaran powder, sodium bicarbonate, calcium carbonate, polyoxyethylene sorbitan fatty acid esters, sodium lauryl sulfate, stearic acid monoglyceride, starch, and lactose; disintegration inhibitors such as sucrose, stearin, cacao butter, and hydrogenated oil; absorption promoters such as quaternary ammonium bases and sodium lauryl sulfate; humectants such as glycerin and starch; adsorbents such as starch, lactose, kaolin, bentonite, and colloidal silicic acid; and lubricants such as purified talc, stearate, boric acid powder, and polyethylene glycol.

[0174]

Furthermore, the tablets can be coated, if necessary, with a usual coating material to prepare, for example, sugar-coated tablets, gelatin-coated tablets, enteric coated tablets, film-coated tablets, and bilayer or multilayer tablets.

[0175]

Carries known in the art for use for forming a pill form can be used widely. Examples thereof include: excipients such as glucose, lactose, starch, cacao butter, hydrogenated plant oil, kaolin, and talc; binders such as gum arabic powder, powdered tragacanth, gelatin, and ethanol; and disintegrants such as laminaran and agar.

[0176]

Carries known in the art for use for forming a suppository form can be used widely. Examples thereof include polyethylene glycol, cacao butter, higher alcohol, esters of higher alcohol, gelatin, and semisynthetic glyceride.

[0177]

When the compound represented by the general formula (1) is prepared as injections, solutions, emulsions, and suspensions are preferably sterile and isotonic with blood. Diluents known in the art for use for forming forms of these solutions, emulsions, and suspensions can be used widely. Examples thereof include water, ethanol, propylene glycol, ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, and polyoxyethylene sorbitan fatty acid esters. In this case, the pharmaceutical preparation may contain common salt, glucose, or glycerin in an amount sufficient for preparing an isotonic solution and may contain usual solubilizers, buffers, soothing agents, and the like, and if necessary, coloring agents, preservatives, perfumes, flavoring agents, sweetening agents, and the like, and/or other drugs.

[0178]

The amount of the compound of the present invention contained in the pharmaceutical preparation is not particularly limited and can be selected appropriately from within a wide range. The compound of the present invention is usually contained in an amount of preferably approximately 1 to 70% by weight in the pharmaceutical preparation.

[0179]

A method for administering the pharmaceutical preparation according to the present invention is not particularly limited. The pharmaceutical preparation is administered by a method according to various dosage forms, the age, sex, and disease state of a patient, and other conditions. For example, tablets, pills, solutions, suspensions, emulsions, granules, and capsules are orally administered. Moreover, injections can be administered through an intravenous route alone or as a mixture with a usual replacement fluid such as glucose or amino acid or can be administered alone through intramuscular, intradermal, hypodermic, or intraperitoneal route, if necessary. Suppositories are rectally administered.

[0180]

The dose of the pharmaceutical preparation may be selected appropriately according to use, the age, sex, and disease state of a patient, and other conditions. The pharmaceutical preparation is usually administered once or several times a day at a daily dose of approximately 0.001 to 100 mg, preferably approximately 0.001 to 50 mg, per kg of body weight.

[0181]

The dose varies depending on various conditions. Thus, in some cases, a dose smaller than this range suffices. In other cases, a dose exceeding this range is required.

[0182]

A heterocyclic compound of the present invention has reuptake inhibitory effects on 1, 2, or 3 monoamines (serotonin, norepinephrine, and dopamine).

[0183]

The heterocyclic compound of the present invention has remarkably strong uptake inhibitory activity in *in-vitro* or *ex-vivo* tests on any one, any two, or all of the 3 monoamines, compared with existing compounds having monoamine uptake inhibitory activity. Moreover, the heterocyclic compound of the present invention exhibits remarkably strong activity in brain microdialysis study against increase in any one, any two, or all of the 3 monoamines, compared with existing compounds having monoamine uptake inhibitory activity.

[0184]

The heterocyclic compound of the present invention has a wide therapeutic spectrum, compared with antidepressants known in the art.

[0185]

The heterocyclic compound of the present invention exerts sufficient therapeutic effects even in short-term administration.

[0186]

The heterocyclic compound of the present invention has excellent bioavailability, weak inhibitory activity on metabolic enzymes in the liver, few side effects, and excellent safety.

[0187]

The heterocyclic compound of the present invention is excellent in transfer into the brain.

[0188]

The heterocyclic compound of the present invention also exerts strong activity in a mouse forced swimming test used in depression screening. Moreover, the heterocyclic compound of the present invention also exerts strong activity in a rat forced swimming test used in depression screening. Moreover, the heterocyclic compound of the present invention also exerts strong activity in a reserpine-induced hypothermia test used in depression screening.

[0189]

The heterocyclic compound of the present invention exerts strong activity in a marble burying behavior test of anxiety or stress disease model mice and in fear-conditioned stress models.

[0190]

The heterocyclic compound of the present invention has reuptake inhibitory effects on 1, 2, or 3 monoamines (serotonin, norepinephrine, and dopamine) and is therefore effective for treating various disorders associated with the reduced neurotransmission of serotonin, norepinephrine, or dopamine.

[0191]

Such disorders include depression (e.g.: major depressive disorder; bipolar I disorder; bipolar II disorder; mixed state; dysthymic disorder; rapid cycler; atypical depression; seasonal affective disorder; postpartum depression; hypomelancholia; recurrent brief depressive disorder; refractory depression/chronic depression; double depression; alcohol-induced mood disorder; mixed anxiety-depressive disorder; depression caused by various physical diseases such as Cushing syndrome, hypothyroidism, hyperparathyroidism, Addison's disease, amenorrhea-galactorrhea syndrome, Parkinson's disease, Alzheimer's disease, cerebrovascular dementia, brain infarct, brain hemorrhage, subarachnoid hemorrhage, diabetes mellitus, virus infection, multiple sclerosis, chronic fatigue syndrome, coronary artery disease, pain, and cancer, etc.; presenile depression; senile depression; depression in children and adolescents; depression induced by drugs such as interferon, etc.); depression status caused by adjustment disorder, anxiety caused by adjustment disorder, anxiety caused by various diseases [e.g.: nerve disorders (head injury, brain infection, and inner ear impairment); cardiovascular disorders (cardiac failure and arrhythmia); endocrine disorders (hyperadrenalism and hyperthyroidism); and respiratory disorders (asthma and chronic obstructive pulmonary disease)], generalized anxiety disorder, phobia (e.g., agoraphobia, social fear, simple phobia, social phobia, social anxiety disorder, ereuthrophobia, anthrophobia, acrophobia, odontophobia, trypanophobia, specific phobia, simple phobia, animal phobia, claustrophobia, nyctophobia and phobic anxiety), obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, acute stress syndrome, hypochondriasis disorder, dissociative amnesia, avoidant personality disorder, body dysmorphic disorder, eating disorders (e.g., anorexia nervosa and bulimia nervosa), obesity, chemical dependence (e.g., addition to alcohol, cocaine, heroin, phenobarbital, nicotine, and benzodiazepines), pain (e.g., chronic pain, psychogenic pain, neuropathic pain, phantom limb pain, postherpetic neuralgia, traumatic cervical syndrome, spinal cord injury (SCI) pain, trigeminal neuralgia, diabetic neuropathy), fibromyalgia (FMS), Alzheimer's disease, memory deficit (e.g., dementia, amnestic disorder, and age-related cognitive decline (ARCD)), Parkinson's disease (e.g., non-motor/ psychotic symptoms, dementia in Parkinson disease, neuroleptic-induced Parkinson's syndrome, and tardive dyskinesia), restless leg diseases, endocrine disorders (e.g., hyperprolactinemia), vasospasm (particularly, in the cerebral vasculature), cerebellar ataxia, gastrointestinal disorders (which encompass changes in secretion and motility), negative syndromes of schizophrenia, premenstrual syndrome, stress urinary incontinence, Tourette's Disorder, attention deficit hyperactivity disorder (ADHD), autism, Asperger syndrome, impulse control disorder, trichotillomania, kleptomania, gambling disorder, cluster headache, migraine, chronic paroxysmal hemicrania, chronic fatigue syndrome, precocious ejaculation, male impotence, narcolepsy, primary hypersomnia, cataplexy, sleep apnea syndrome and headache (associated with angiopathy).

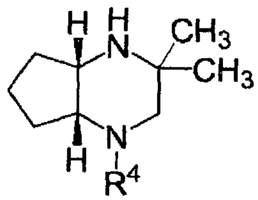
Examples

[0192]

Hereinafter, the present invention will be described more specifically with reference to Reference Examples, Examples, and Pharmacological Tests. The chemical structures of racemic bodies and optically active forms are indicated, for example, as shown below.

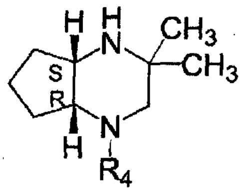
Racemic body

Relative configuration



Optically active form

Absolute configuration

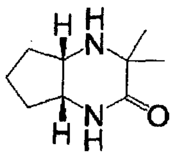


[0193]

Reference Example 1

Production of cis-3,3-dimethyloctahydrocyclopentapyrazin-2-one

Relative configuration



90% acetone cyanohydrin (9.79 g, 104 mmol) was added to an aqueous (100 mL) solution of cis-cyclopentane-1,2-diamine (9.88 g, 98.6 mmol) at room temperature, and the mixture was stirred under reflux for 16 hours. The solvent was removed from the reaction mixture under reduced pressure, followed by azeotropy with ethanol. The obtained residue was purified by silica gel column chromatography (methylene chloride/methanol=1/10) to obtain cis-3,3-dimethyloctahydrocyclopentapyrazin-2-one (5.00 g, 30%) in a white powder form.

^{1}H-NMR($CDCl_3$)δppm : 1.20(1 H,brs),1.34(3 H,s),1.39(3 H,s),1.40-2.20(6 H,m),3.50-3.70(2 H,m),5.89(1 H,brs).

[0194]

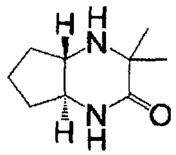
Compounds of Reference Examples 2 to 12 shown below were produced in the same way as in Reference Example 1 using appropriate starting materials.

[0195]

Reference Example 2

Trans-3,3-dimethyloctahydrocyclopentapyrazin-2-one

Relative configuration



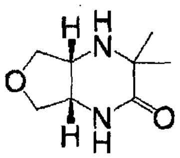
^{1}H-NMR(CDCl$_3$)δppm : 1.26-1.55(9 H,m),1.75-2.00(4 H,m),2.85-3.02(1 H,m),3.05-3.20(1 H,m),6.02(1 H,brs).

[0196]

Reference Example 3

Cis-3,3-dimethylhexahydrofuro[3,4-b]pyrazin-2-one

Relative configuration



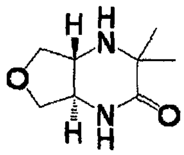
^{1}H-NMR(CDCl$_3$)δppm : 1.37(3H,s),1.40(3H,s),1.50-1.85(1H,br),3.73-4.10(6H,m),6.02-6.22(1H,br).

[0197]

Reference Example 4

Trans-3,3-dimethylhexahydrofuro[3,4-b]pyrazin-2-one

Relative configuration



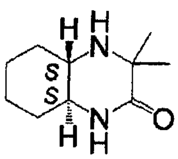
^{1}H-NMR(CDCl$_3$)δppm : 1.38-1.43 (1H, br), 1.44 (3H, s), 1.47 (3H, s), 3.38-3.52 (1H, m), 3.52-3.65 (3H, m), 4.00-4.14 (2H, m), 6.28-6.45 (1H, br).

[0198]

Reference Example 5

(4aS,8aS)-3,3-dimethyloctahydroquinoxalin-2-one

Absolute configuration



^{1}H-NMR(CDCl$_3$)δppm : 1.14-1.37 (6H, m), 1.38 (3H, s), 1.42 (3H, s), 1.69 (1H, brs), 1.74-1.84

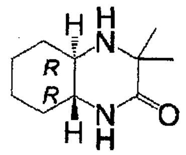
(2H, m), 2.57-2.65 (1H, m), 2.96-3.04 (1H, m), 5.61(1H,s)

[0199]

Reference Example 6

(4aR,8aR)-3,3-dimethyloctahydroquinoxalin-2-one

Absolute configuration



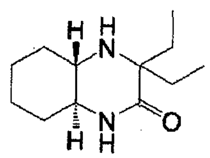
^{1}H-NMR($CDCl_3$)δppm : 1.14-1.37 (6H, m), 1.38 (3H, s), 1.42 (3H, s), 1.63 (1H, brs), 1.73-1.83 (2H, m), 2.57-2.66 (1H, m), 2.95-3.04 (1H, m), 5.55 (1H,s)

[0200]

Reference Example 7

Trans-3,3-diethyloctahydroquinoxalin-2-one

Relative configuration



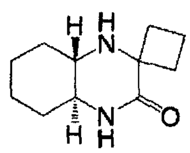
^{1}H-NMR($CDCl_3$)δppm : 0.92 (3H, t, J = 7.5 Hz), 0.93 (3H ,t, J = 7.3 Hz), 1.13-1.49 (7H, m), 1.60-1.99 (6H, m), 2.55-2.60 (1H, m), 2.91-3.00 (1H, m), 5.69(1H, brs)

[0201]

Reference Example 8

Trans-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxalin]-3'-one

Relative configuration



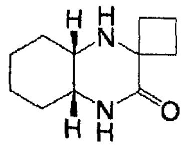
^{1}H-NMR($CDCl_3$)δppm : 1.14-1.46 (4H, m), 1.70-2.17 (9H, m), 2.43-2.52 (1H, m), 2.55-2.66 (1H, m), 2.78-2.88 (1H, m), 2.97-3.06 (1H, m), 5.65 (1H, brs)

[0202]

Reference Example 9

Cis-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxalin]-3'-one

Relative configuration



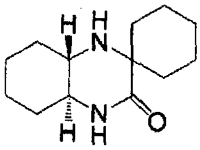
^{1}H-NMR($CDCl_3$)δppm : 1.1-1.3 (1H, m), 1.35-2.15 (12H, m), 2.5-2.6 (1H, m), 2.75-2.85 (1H, m), 3.15-3.3 (2H, m), 5.65(1H, br).

[0203]

Reference Example 10

Trans-octahydro-1'H-spiro[cyclohexane-1,2'-quinoxalin]-3'-one

Relative configuration



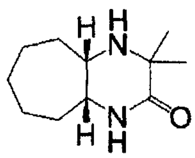
^{1}H-NMR($CDCl_3$)δppm : 1.18-1.88 (18H, m), 2.03-2.13 (1H, m), 2.47-2.58 (1H, m), 2.92-3.00 (1H, m), 5.59 (1H, s)

[0204]

Reference Example 11

Cis-3,3-dimethyldecahydrocycloheptapyrazin-2-one

Relative configuration



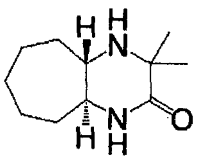
^{1}H-NMR($CDCl_3$)δppm : 1.12-2.00 (16 H, m), 2.03-2.20 (1H, m), 3.35-3.55 (2H, m), 5.88 (1H, brs).

[0205]

Reference Example 12

Trans-3,3-dimethyldecahydrocycloheptapyrazin-2-one

Relative configuration



^{1}H-NMR($CDCl_3$)δppm : 1.35 (3H, s), 1.39 (3H, s), 1.42-1.90 (11H, m), 2.73-2.85 (1H, m), 3.13-

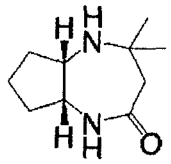
3.26 (1H, m), 5.51 (1H, brs).

[0206]

Reference Example 13

Production of cis-4,4-dimethyloctahydrocyclopenta[b][1,4]diazepin-2-one

Relative configuration



A toluene (200 mL) suspension of cis-cyclopentane-1,2-diamine (19.7 g, 197 mmol) and 3-methyl-2-butenoic acid (19.7 g, 197 mmol) was stirred under reflux for 24 hours under azeotropic conditions using a Dean-Stark apparatus. The reaction mixture was cooled to room temperature and then concentrated under reduced pressure, and the deposited crystal was collected by filtration. The obtained crystal was washed with ether and then dried to obtain cis-4,4-dimethyloctahydrocyclopenta[b][1,4]diazepin-2-one (8.60 g, 24%) in a light brown powder form.

^{1}H-NMR($CDCl_3$)δppm : 1.10-1.56 (10 H, m), 1.65-1.80 (1 H, m), 2.02-2.30 (3 H, m), 2.60(1 H, d, J = 12.8 Hz), 3.18-3.37 (1 H, m), 3.68-3.85 (1 H, m), 5.73(1H,brs).

[0207]

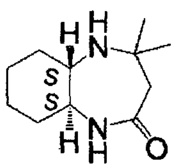
Compounds of Reference Examples 14 and 15 below were produced in the same way as in Reference Example 13 using appropriate starting materials.

[0208]

Reference Example 14

(5aS,9aS)-4,4-dimethyldecahydro[b][1,4]diazepin-2-one

Absolute configuration



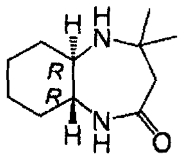
^{1}H-NMR($CDCl_3$)δppm : 1.00-1.45 (11H, m), 1.63-1.83 (3H, m), 1.83-2.00 (1H, m), 2.31-2.43 (1H, m), 2.65-2.81 (2H, m), 3.00-3.16 (1H, m), 5.54-5.90 (1H, br).

[0209]

Reference Example 15

(5aR,9aR)-4,4-dimethyldecahydro[b][1,4]diazepin-2-one

Absolute configuration



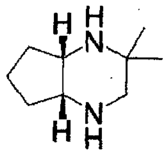
^{1}H-NMR($CDCl_3$)δppm : 1.02-1.36 (11H, m), 1.64-1.83 (3H, m), 1.83-1.97 (1H, m), 2.37 (1H, dd, J = 2.4, 13.9 Hz), 2.66-2.81 (2H, m), 3.01-3.15 (1H, m), 5.75-5.92 (1H, brs).

[0210]

Reference Example 16

Production of cis-2,2-dimethyloctahydro-1H-cyclopenta[b]pyrazine

Relative configuration



Lithium aluminum hydride (541 mg, 14.3 mmol) was added to an anhydrous dioxane (40 mL) solution of cis-3,3-dimethyloctahydrocyclopentapyrazin-2-one (2.00 g, 11.9 mmol) with stirring at room temperature, and the mixture was gradually heated and stirred for 10 minutes under reflux. The reaction mixture was cooled to ice temperature. Then, sodium sulfate decahydrate was added thereto in small portions until no hydrogen gas was generated. Then, the mixture was stirred at room temperature for 1 hour. Insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by basic silica gel column chromatography (ethyl acetate/hexane=1/10) to obtain cis-2,2-dimethyloctahydro-1H-cyclopenta[b]pyrazine (1.67 g, 91%) in a pale yellow oil form.

^{1}H-NMR($CDCl_3$)δppm :1.04 (3 H, s), 1.16 (3 H, s), 1.28-2.02 (8 H, m), 2.37 (1 H, d, J = 12.9 Hz), 2.70 (1 H, d, J = 12.9 Hz), 3.00-3.15 (1 H, m), 3.15-3.32 (1 H, m).

[0211]

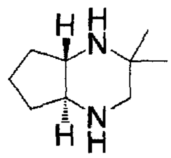
Compounds of Reference Examples 17 to 34 below were produced in the same way as in Reference Example 16 using appropriate starting materials.

[0212]

Reference Example 17

Trans-2,2-dimethyloctahydro-1H-cyclopenta[b]pyrazine

Relative configuration



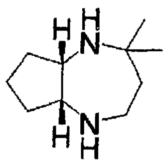
^{1}H-NMR($CDCl_3$)δppm : 1.08 (3H, s), 1.19-1.92 (11H, m), 2.15-2.30 (1H, m), 2.55-2.74 (2H, m), 2.77 (1H, d, J = 12.2 Hz).

[0213]

Reference Example 18

Cis-2,2-dimethyldecahydrocyclopenta[b][1,4]diazepine

Relative configuration



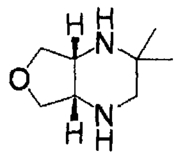
^{1}H-NMR($CDCl_3$)δppm : 1.11 (3H, s), 1.14 (3H, s), 1.15-1.45 (6H, m), 1.55-1.67 (1H, m), 1.67-1.77 (1H, m), 1.97-2.12 (2H, m), 2.68-2.80 (1H, m), 2.98-3.11 (2H, m), 3.16-3.28 (1H, m).

[0214]

Reference Example 19

Cis-2,2-dimethyloctahydrofuro[3,4-b]pyrazine

Relative configuration



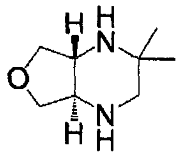
^{1}H-NMR($CDCl_3$)δppm : 1.08 (3H, s), 1.18 (3H, s), 1.40-1.80 (2H, br), 2.41(1H, d, J = 13.2 Hz), 2.69 (1H, d, J = 13.2 Hz), 3.33-3.43 (1H, m), 3.43-3.55 (1H, m), 3.63-3.72 (1H, m), 3.75-3.96 (3H, m).

[0215]

Reference Example 20

Trans-2,2-dimethyloctahydrofuro[3,4-b]pyrazine

Relative configuration



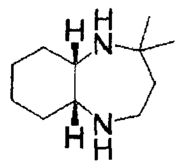
^{1}H-NMR($CDCl_3$)δppm : 1.13 (3H, s), 1.30 (3H, s), 1.44-1.65 (2H, m), 2.64-2.78 (2H, m), 2.83 (1H, d, J = 12.2 Hz), 3.11-3.22 (1H, m), 3.46 (1H, dd, J = 7.3, 10.5 Hz), 3.55 (1H, dd, J = 7.4, 10.5 Hz), 3.94 (1H, t, J = 7.1 Hz), 4.00 (1H, t, J = 7.2 Hz).

[0216]

Reference Example 21

Cis-2,2-dimethyldecahydro-1H-benzo[b][1,4]diazepine

Relative configuration



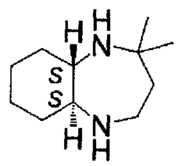
^{1}H-NMR($CDCl_3$)δppm : 1.08 (3H, s), 1.13 (3H, s), 1.18-1.84 (12H, m), 2.65-2.93 (3H, m), 3.14-3.22 (1H, m).

[0217]

Reference Example 22

(5aS,9aS)-2,2-dimethyldecahydro-1H-benzo[b][1,4]diazepine

Absolute configuration



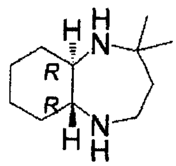
^{1}H-NMR($CDCl_3$)δppm : 1.00-1.35 (11H, m), 1.50-1.85 (7H, m), 2.20-2.31 (1H, m), 2.31-2.43 (1H,m), 2.79-2.90 (1H, m), 2.90-3.04 (1H, m).

[0218]

Reference Example 23

(5aR,9aR)-2,2-dimethyldecahydro-1H-benzo[b][1,4]diazepine

Absolute configuration



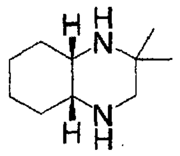
^{1}H-NMR($CDCl_3$)δppm : 1.00-1.35 (11H, m), 1.50-1.85 (7H, m), 2.20-2.31 (1H, m), 2.31-2.43 (1H, m), 2.79-2.90 (1H, m), 2.90-3.04 (1H, m).

[0219]

Reference Example 24

Cis-2,2-dimethyldecahydroquinoxaline

Relative configuration



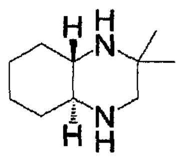
^{1}H-NMR($CDCl_3$)δppm : 1.06 (3H, s), 1.19 (3H, s), 1.20-1.40 (5H, m), 1.53-1.60 (3H, m), 1.70-1.77 (1H, m), 1.92-2.15 (1H, m), 2.36 (1H, d, J = 12.7 Hz), 2.66-2.72 (1H, m), 2.72 (1H, d, J = 12.7 Hz), 3.16-3.28 (1H, m).

[0220]

Reference Example 25

Trans-2,2-dimethyldecahydroquinoxaline

Relative configuration



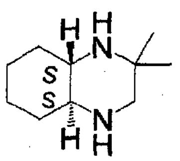
^{1}H-NMR($CDCl_3$)δppm : 1.05 (3H, s), 1.08-1.74 (10H, m), 1.23 (3H, s), 2.02-2.12 (1H, m), 2.40-2.50 (1H, m), 2.60 (1H, d, J = 12.1 Hz), 2.73 (1H, d, J = 12.1 Hz).

[0221]

Reference Example 26

(4aS,8aS)-2,2-dimethyldecahydroquinoxaline

Absolute configuration



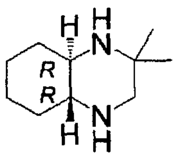
^{1}H-NMR($CDCl_3$)δppm : 1.01-1.43 (6H, m), 1.05 (3H, s), 1.23 (3H, s), 1.58-1.63 (1H, m), 1.68-1.74 (3H, m), 2.03-2.19 (1H, m), 2.40-2.49 (1H, m), 2.60 (1H, d, J = 12.1 Hz), 2.73 (1H, d, J = 12.1 Hz).

[0222]

Reference Example 27

(4aR,8aR)-2,2-dimethyldecahydroquinoxaline

Absolute configuration



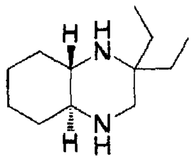
^{1}H-NMR(CDCl$_3$)δppm : 1.05 (3H, s), 1.09-1.56 (6H, m), 1.23 (3H, s), 1.58-1.63 (1H, m), 1.66-1.75 (3H, m), 2.03-2.12 (1H, m), 2.41-2.50 (1H, m), 2.61 (1H, d, J = 12.1 Hz), 2.75 (1H, d, J = 12.1 Hz).

[0223]

Reference Example 28

Trans-2,2-diethyldecahydroquinoxaline

Relative configuration



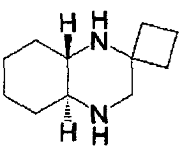
^{1}H-NMR(CDCl$_3$)δppm : 0.79 (3H, t, J = 7.5 Hz), 0.81 (3H, t, J = 7.5 Hz), 0.86-1.02 (1H, m), 1.08-1.40 (8H, m), 1.47-1.60 (2H, m), 1.67-1.87 (3H, m), 2.06-2.15 (1H, m), 2.33-2.42 (1H, m), 2.57 (1H, d, J = 12.1 Hz), 2.81 (1H, d, J = 12.1 Hz).

[0224]

Reference Example 29

Trans-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Relative configuration



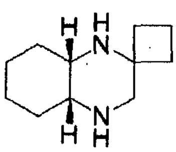
MS(M+1) 181

[0225]

Reference Example 30

Cis-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Relative configuration



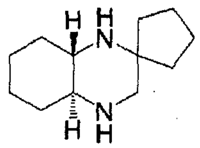
MS(M+1) 181

[0226]

Reference Example 31

Trans-octahydro-1'H-spiro[cyclopentane-1,2'-quinoxaline]

Relative configuration



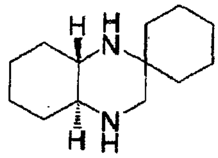
^{1}H-NMR($CDCl_3$)δppm : 1.10-1.97 (18H, m), 2.10-2.21 (1H, m), 2.29-2.38 (1H, m), 2.71 (1H, d, J = 12.2 Hz), 2.76 (1H, d, J = 12.2 Hz).

[0227]

Reference Example 32

Trans-octahydro-1'H-spiro[cyclohexane-1,2'-quinoxaline]

Relative configuration



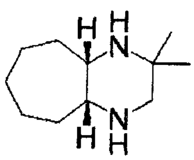
^{1}H-NMR($CDCl_3$)δppm : 1.12-1.76 (20H, m), 2.12-2.20 (1H, m), 2.44-2.53 (1H, m), 2.55 (1H, d, J = 12.2 Hz), 2.98 (1H, d, J = 12.2 Hz).

[0228]

Reference Example 33

Cis-2,2-dimethyldecahydro-1H-cyclohepta[b]pyrazine

Relative configuration



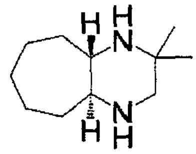
^{1}H-NMR($CDCl_3$)δppm : 1.00-2.02 (18H, m), 2.42 (1H, d, J = 12.4 Hz), 2.58 (1H, d, J = 12.4 Hz), 2.75-2.86 (1H, m), 3.13-3.25 (1H, m).

[0229]

Reference Example 34

Trans-2,2-dimethyldecahydro-1H-cyclohepta[b]pyrazine

Relative configuration



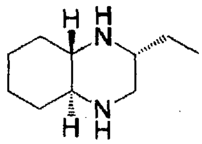
^{1}H-NMR($CDCl_3$)δppm : 1.05 (3H, s), 1.21 (3H, s), 1.23-1.80 (12H, m), 2.09-2.20 (1H, m), 2.46-2.60 (2H, m), 2.68 (1H, d, J = 11.8 Hz).

[0230]

Reference Example 35

Production of (2RS,4aSR,8aSR)-2-ethyldecahydroquinoxaline

Relative configuration



Dichloro(pentamethylcyclopentadienyl)iridium (III) dimer (70 mg, 0.090 mmol) and sodium bicarbonate (73 mg, 0.87 mmol) were added to an aqueous (20 mL) solution of trans-cyclohexane-1,2-diamine (2.00 g, 17.5 mmol) and (±)-1,2-butanediol (1.69 mL, 18.4 mmol) with stirring at room temperature. Degassing and argon substitution were repeated 3 times, and the mixture was then stirred for 24 hours under reflux. The reaction mixture was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (methylene chloride/methanol) to obtain (2R*,4aS*,8aS*)-2-ethyldecahydroquinoxaline (2.03 g, yield: 69%) in a yellow solid form.

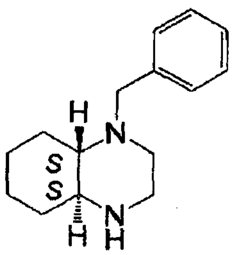
^{1}H-NMR($CDCl_3$)δppm : 0.92 (3H, t, J = 7.5 Hz), 1.10-1.60 (7H, m), 1.64-1.83 (5H, m), 2.16-2.31 (2H, m), 2.44 (1H, dd, J = 11.5, 10.4 Hz), 2.58-2.67 (1H, m), 3.02 (1H, dd, J = 11.5, 2.7 Hz).

[0231]

Reference Example 36

Production of (4aS,8aS)-1-benzyldecahydroquinoxaline

Absolute configuration



Benzaldehyde (3.05 mL, 30.0 mmol) was added to a methanol (300 mL) solution of (1S,2S)-cyclohexane-1,2-diamine (3.43 g, 30.0 mmol) with stirring at room temperature, and the mixture was stirred overnight at the same temperature. The reaction mixture was cooled to 0°C. Sodium borohydride (2.27 g, 60.0 mmol) was added thereto, and the mixture was stirred at 0°C for 2 hours. To the reaction mixture, water (30 mL) was added, and the product was extracted twice with methylene chloride (50 mL). The organic layers were combined and dried over magnesium sulfate, and the solvent was then distilled off under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (ethyl acetate/hexane) to obtain (1S,2S)-N-benzylcyclohexane-1,2-diamine (cas no. 207450-11-1) (2.95 g, yield: 48%) in a pale yellow oil form.

[0232]

The obtained (1S,2S)-N-benzylcyclohexane-1,2-diamine (2.90 g, 14.2 mmol) was dissolved in methylene chloride (284 nL). To the solution, 60% sodium hydride (1.99 g, 49.7 mmol) was added with ice-cooling and stirring in a nitrogen atmosphere. After 5 minutes, (2-bromoethyl)diphenylsulfonium trifluoromethanesulfonate (6.92 g, 15.6 mmol) was added to the reaction mixture with ice-cooling and stirring, and the mixture was stirred overnight at room temperature. To the reaction mixture, a saturated aqueous solution of ammonium chloride was added dropwise in small portions, and the product was then extracted twice with methylene chloride (100 mL). The organic layers were combined and dried over magnesium sulfate, and the solvent was then distilled off under reduced pressure. The obtained residue was purified by NH-silica gel column chromatography (ethyl acetate/hexane) to obtain (4aS,8aS)-1-benzyldecahydroquinoxaline (2.28 g, 70%) in a light brown solid form.

^{1}H-NMR($CDCl_3$)δppm : 1.05-1.4 (4H, m), 1.50 (1H, br), 1.6-1.9 (4H, m), 2.05-2.2 (1H, m), 2.2-2.3 (1H, m), 2.4-2.5 (1H, m), 2.65-2.75 (1H, m), 2.8-2.95 (2H, m), 3.14 (1H, d, J = 13.4Hz), 4.11 (1H, d, J = 13.4Hz), 7.15-7.4 (5H, m).

[0233]

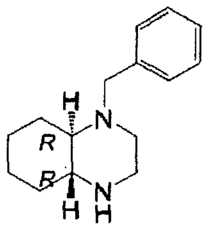
Compounds of Reference Examples 37 to 39 below were produced in the same way as in Reference Example 36 using appropriate starting materials.

[0234]

Reference Example 37

(4aS,8aS)-1-benzyldecahydroquinoxaline

Absolute configuration



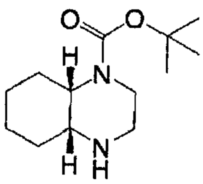
^{1}H-NMR($CDCl_3$)δppm : 1.05-1.4 (4H, m), 1.50 (1H, br), 1.6-1.9 (4H, m), 2.05-2.2 (1H, m), 2.2-2.3 (1H, m), 2.4-2.5 (1H, m), 2.65-2.75 (1H, m), 2.8-2.95 (2H, m), 3.13 (1H, d, J = 13.4Hz), 4.11 (1H, d, J = 13.4Hz), 7.15-7.4 (5H, m).

[0235]

Reference Example 38

Cis-decahydroquinoxaline-1-carboxylic acid tert-butyl ester

Relative configuration



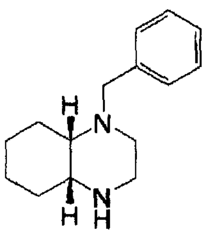
^{1}H-NMR($CDCl_3$)δppm : 1.05-1.15 (1H, m), 1.2-1.75 (19H, m), 1.75-1.85 (1H, m), 1.85-2.2 (1H, m), 3.70 (1H, br), 4.83(1H, br).

[0236]

Reference Example 39

Cis-1-benzyldecahydroquinoxaline

Relative configuration



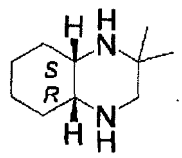
^{1}H-NMR(CDCl$_3$)δppm : 1.0-2.0 (10H, m), 2.2-2.4 (1H, m), 2.45-2.7 (2H, m), 2.75-3.1 (2H, m), 3.63 (2H, br), 7.05-7.45 (5H, m).

[0237]

Reference Example 40

Production of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline

Absolute configuration

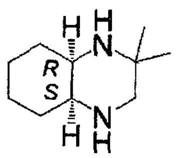


[0238]

Reference Example 41

(4aS,8aR)-2,2-dimethyldecahydroquinoxaline

Absolute configuration



(-)-dibenzoyl-L-tartaric acid monohydrate (13.8 g, 36.7 mmol) in ethanol (140 mL) was added to an ethanol (140 mL) solution of cis-2,2-dimethyldecahydroquinoxaline (13.7 g, 81.4 mmol) with stirring at room temperature. The reaction mixture was stirred for 30 minutes under reflux and cooled to room temperature, and the deposited white crystal was then collected by filtration. The obtained crystal was washed with ethanol (20 mL) and then dried to obtain a white solid <1> (13.1 g). The filtrate and washes obtained in obtaining the solid <1> were concentrated under reduced pressure. The obtained residue was dissolved in ethanol (100 mL). To the solution, an ethanol (130 mL) solution of (+)-dibenzoyl-D-tartaric acid (13.1 g, 36.6 mmol) was added with stirring at room temperature, and the deposited crystal was collected by filtration. The obtained crystal was washed with ethanol (20 mL) and then dried to obtain a light brown solid <2> (16.6 g).

[0239]

A methanol (130 mL)/water (10 mL) suspension of the solid <1> was stirred for 30 minutes under reflux. Then, the reaction mixture was cooled to room temperature, and the deposited crystal was collected by filtration. The deposited crystal was washed with methanol (10 mL) and then dried to obtain (4aR,8aS)-2,2-dimethyldecahydroquinoxaline dibenzoyl-L-tartrate (11.4 g, 21.6 mmol) in a white solid form (the absolute configuration of cis-2.2-dimethyldecahydroquinoxaline was determined by the X-ray crystallographic analysis of the white solid). This solid was dissolved in a 1 N aqueous sodium hydroxide solution (44 mL), and the product was extracted with ether (100 mL) three times and with methylene chloride (100 mL) three times. The extracted organic layers were combined, dried over magnesium sulfate, and then concentrated under reduced pressure to obtain (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (3.44 g, yield: 25%) in a white solid form.

^{1}H-NMR ($CDCl_3$) δppm : 1.06 (3H, s), 1.20 (3H, s), 1.2-1.4 (4H, m), 1.45-1.95 (5H, m), 1.95-2.15 (1H, m), 2.36 (1H, d, J = 12.7Hz), 2.65-2.75 (2H, m), 3.15-3.25 (1H, m).

[0240]

A methanol (130 mL)/water (10 mL) suspension of the solid <2> was stirred for 1 hour under reflux. Then, the reaction mixture was cooled to room temperature, and the deposited crystal was collected by filtration. The deposited crystal was washed with methanol (10 mL) and then dried to obtain (4aS,8aR)-2,2-dimethyldecahydroquinoxaline dibenzoyl-D-tartrate (16.0 g, 30.4 mmol) in a white solid form. This solid was dissolved in a 1 N aqueous sodium hydroxide solution (65 mL), and the product was extracted with methylene chloride (100 mL) three times. The extracted organic layers were combined, dried over magnesium sulfate, and then concentrated under reduced pressure to obtain (4aS,8aR)-2,2-dimethyldecahydroquinoxaline (4.63 g, yield: 34%) in a light brown solid form.

^{1}H-NMR($CDCl_3$)δppm : 1.06 (3H, s), 1.19 (3H, s), 1.2-1.45 (5H, m), 1.45-1.65 (3H, m), 1.65-1.8 (1H, m), 1.95-2.15 (1H, m), 2.36 (1H, d, J = 12.7Hz), 2.6-2.8 (2H, m), 3.15-3.25 (1H, m).

[0241]

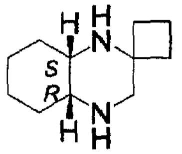
Compounds of Reference Examples 42 to 45 below were produced in the same way as in Reference Examples 40 and 41 using appropriate starting materials.

[0242]

Reference Example 42

(4a'R,8a'S)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Absolute configuration



MS(M+1) 181

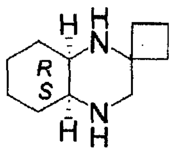
^{1}H-NMR ($CDCl_3$) δppm : 1.20-2.20 (16H, m), 2.69 (1H, d, J = 12.4 Hz), 2.72-2.82 (1H, m), 2.87-3.02 (2H, m).

[0243]

Reference Example 43

(4a'S,8a'R)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Absolute configuration



MS(M+1) 181

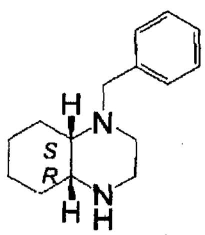
^{1}H-NMR ($CDCl_3$) δppm : 1.20-2.20 (16H, m), 2.68 (1H, d, J = 12.5 Hz), 2.72-2.82 (1H, m), 2.87-3.02 (2H, m).

[0244]

Reference Example 44

(4aR,8aS)-1-benzyldecahydroquinoxaline

Absolute configuration



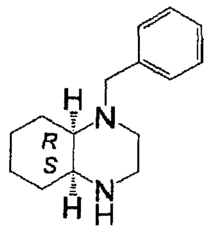
^{1}H-NMR($CDCl_3$)δppm : 1.0-1.25 (1H, m), 1.25-1.65 (5H, m), 1.65-2.05 (3H, m), 2.2-2.4 (1H, m), 2.45-2.7 (2H, m), 2.75-3.1 (3H, m), 3.63 (2H, br), 7.15-7.4 (5H, m).

[0245]

Reference Example 45

(4aS,8aR)-1-benzyldecahydroquinoxaline

Absolute configuration



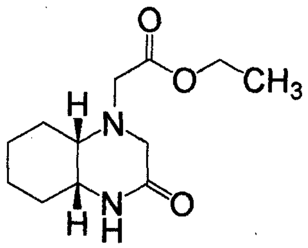
^{1}H-NMR($CDCl_3$)δppm : 1.05-1.25 (1H, m), 1.25-1.65 (5H, m), 1.65-2.05 (3H, m), 2.2-2.4 (1H, m), 2.5-2.7 (2H, m), 2.75-3.1 (3H, m), 3.63 (2H, br), 7.15-7.4 (5H, m).

[0246]

Reference Example 46

Production of (trans-3-oxodecahydroquinoxalin-1-yl)acetic acid ethyl ester

Relative configuration



Trans-cyclohexane-1,2-diamine (3.00 g, 26.3 mmol) was diluted with ethanol (15 ml). To the solution, bromoethyl acetate (6.12 mL, 55.2 mmol) was added dropwise with ice-cooling, and the mixture was then stirred overnight at room temperature.

[0247]

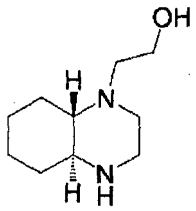
To the reaction solution, water was added, and the mixture was stirred. The product was extracted with methylene chloride. The organic layer was washed with saturated saline and dried over magnesium sulfate, followed by filtration. The filtrate was concentrated under reduced pressure. The obtained residue was separated and purified by silica gel column chromatography (methylene chloride/methanol) to obtain (trans-3-oxodecahydroquinoxalin-1-yl)acetic acid ethyl ester (2.35 g, yield: 74.4%) in an orange particulate solid form.

^{1}H-NMR($CDCl_3$)δppm : 1.13-1.41 (4H, m), 1.28 (3H, t, J = 7.1 Hz), 1.72-1.97 (4H, m), 2.59-2.67 (1H, m), 3.06-3.13 (1H, m), 3.35 (1H, d, J = 17.4 Hz), 3.48 (1H, d, J = 16.8 Hz), 3.52 (1H, d, J = 17.4 Hz), 3.60 (1H, d, J = 16.8 Hz), 4.17 (2H, q, J = 7.1 Hz), 6.79 (1H, brs).

[0248]

[Reference Example 47] Production of 2-(trans-decahydroquinoxalin-1-yl)ethanol

Relative configuration



Lithium aluminum hydride (1.00 g, 26.4 mmol) was suspended in anhydrous dioxane (40 ml). To the suspension, an anhydrous dioxane (10 ml) solution of (trans-3-oxodecahydroquinoxalin-1-yl)acetic acid ethyl ester (2.35 g, 9.78 mmol) was added dropwise with stirring at room temperature, and the mixture was then stirred under reflux for 10 minutes. The reaction mixture was cooled on ice, and sodium sulfate decahydrate was added thereto in small portions until no gas was generated. This mixture was filtered through celite and washed with methylene chloride, and the filtrate was then concentrated under reduced pressure to obtain 2-(trans-decahydroquinoxalin-1-yl)ethanol (1.74 g, yield: 97%) in a brown oil form.

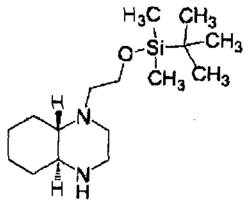
^{1}H-NMR($CDCl_3$)δppm : 0.95-1.11 (1H, m), 1.15-1.44 (3H, m), 1.68-1.80 (5H, m), 1.85-1.94 (1H, m), 2.05-2.44 (4H, m), 2.87-2.97 (3H, m), 3.04-3.16 (1H, m), 3.46-3.54 (1H, m), 3.60-3.69 (1H, m).

[0249]

Reference Example 48

Production of trans-1-[2-(tert-butyldimethylsilyloxy)ethyl]decahydroquinoxaline

Relative configuration



Triethylamine (4.61 mL, 33.0 mmol) and subsequently tert-butyldimethylsilyl chloride (4.27 g, 28.3 mmol) were added to a methylene chloride (40 mL) solution of 2-(trans-decahydroquinoxalin-1-yl)ethanol (1.74 g, 9.44 mmol) with ice-cooling and stirring, and the mixture was stirred overnight at room temperature. To the reaction mixture, water (100 mL) was added to terminate the reaction. The product was extracted with methylene chloride (100 mL). The organic layer was washed with water twice and with saturated saline once, then dried over magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (methylene chloride/methanol) to obtain trans-1-[2-(tert-butyldimethylsilyloxy)ethyl]decahydroquinoxaline (2.00 g, yield: 71%) in a light brown oil form.

^{1}H-NMR($CDCl_3$)δppm : 0.06 (6H, s), 0.89 (9H, s), 0.98-1.36 (4H, m), 1.65-1.79 (4H, m), 1.85-1.95 (1H, m), 2.08-2.14 (1H, m), 2.24-2.39 (1H, m), 2.45-2.61 (2H, m) ,2.79-3.03 (4H, m), 3.62-3.80 (2H, m).

[0250]

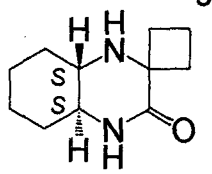
Compounds of Reference Examples 50 and 51 below were produced in the same way as in Reference Example 1 using appropriate starting materials.

[0251]

Reference Example 50

(4a'S,8a'S)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxalin]-3'-one

Absolute configuration



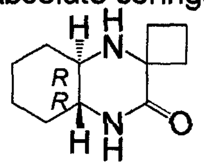
^{1}H-NMR ($CDCl_3$) δppm : 0.99-1.38 (4H, m), 1.55-1.78 (5H, m), 1.78-1.94 (3H, m), 2.21-2.33 (2H, m), 2.48-2.59 (1H, m), 2.63 (1H, brs), 2.76-2.87 (1H, m), 7.36 (1H, s).

[0252]

Reference Example 51

(4a'R,8a'R)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxalin]-3'-one

Absolute configuration



^{1}H-NMR ($CDCl_3$) δppm : 0.97-1.36 (4H, m), 1.55-1.77 (5H, m), 1.77-1.92 (3H, m), 2.20-2.32 (2H, m), 2.47-2.57 (1H, m), 2.63 (1H, brs), 2.76-2.86 (1H, m), 7.36 (1H, s).

[0253]

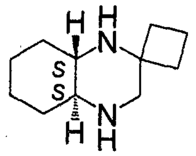
Compounds of Reference Examples 52 and 53 below were produced in the same way as in Reference Example 16 using appropriate starting materials.

[0254]

Reference Example 52

(4a'S,8a'S)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Absolute configuration



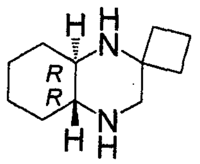
^{1}H-NMR ($CDCl_3$) δppm : 1.05-1.90 (15H, m), 2.15-2.30 (3H, m), 2.69 (1H, dd, J = 1.5, 12.2 Hz), 3.01 (1H, d, J = 12.2 Hz).

[0255]

Reference Example 53

(4a'R,8a'R)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Absolute configuration



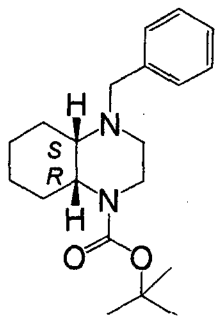
^{1}H-NMR ($CDCl_3$) δppm : 1.05-1.91 (15H, m), 2.15-2.30 (3H, m), 2.69 (1H, d, J = 12.2 Hz), 3.01 (1H, d, J = 12.2 Hz).

[0256]

Reference Example 54

Production of (4aS,8aR)-tert-butyl 4-benzyldecahydroquinoxaline-1-carboxylate

Absolute configuration



Di-tert-butyl dicarbonate (1.70 g, 7.79 mmol) was added to a MeOH (16 ml) solution of (4aR,8aS)-1-benzyldecahydroquinoxaline (1.63 g, 7.08 mmol), and the mixture was stirred at room temperature for 2 hours. The solvent was distilled off, and the residue was then purified by basic silica gel column chromatography (Hex-AcOEt) to obtain (4aS,8aR)-tert-butyl 4-benzyldecahydroquinoxaline-1-carboxylate (2.38 g, yield: quantitative) in a colorless oil form.

^{1}H-NMR ($CDCl_3$) δppm : 1.26-1.66 (14H, m), 1.79-1.96 (2H, m), 2.14-2.33 (2H, m), 2.40-2.45 (1H, m), 2.66 (1H, brs), 2.86 (1H, d, J = 13.2 Hz), 3.03 (1H, brs), 3.50-4.10 (2H, br), 4.16 (1H, d, J = 13.2 Hz), 7.21-7.36 (5H, m).

[0257]

A compound of Reference Example 55 below was produced in the same way as in

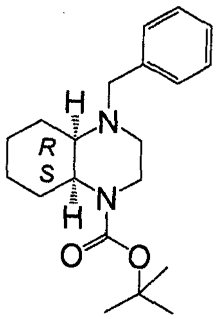
Reference Example 54 using appropriate starting materials.

[0258]

Reference Example 55

(4aR,8aS)-tert-butyl 4-benzyldecahydroquinoxaline-1-carboxylate

Absolute configuration



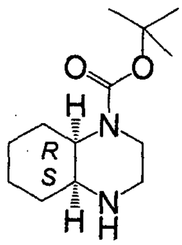
^{1}H-NMR ($CDCl_3$) δppm : 1.26-1.66 (14H, m), 1.79-1.96 (2H, m), 2.14-2.33 (2H, m), 2.40-2.45 (1H, m), 2.65 (1H, brs), 2.86 (1H, d, J = 13.2 Hz), 3.03 (1H, brs), 3.51-4.10 (2H, br), 4.16 (1H, d, J = 13.2 Hz), 7.21-7.36 (5H, m).

[0259]

Reference Example 56

Production process of (4aS,8aR)-tert-butyl decahydroquinoxaline-1-carboxylate

Absolute configuration



Pearlman's catalyst (0.24 g) was added to an EtOH (25 ml) solution of (4aS,8aR)-tert-butyl 4-benzyldecahydroquinoxaline-1-carboxylate (2.4 g, 7.26 mmol). This suspension was stirred at room temperature for 1 hour in a hydrogen atmosphere. The catalyst was filtered through celite, and the residue was washed with EtOH. Then, the filtrate was concentrated under reduced pressure to obtain (4aS,8aR)-tert-butyl decahydroquinoxaline-1-carboxylate (1.67 g, yield: 96%) in a colorless oil form.

^{1}H-NMR ($CDCl_3$) δppm : 1.16-1.53 (14H, m), 1.53-1.82 (3H, m), 1.83-2.00 (1H, m), 2.68-2.83 (1H, m), 2.85-3.10 (3H, m), 3.65-4.06 (2H, m).

[0260]

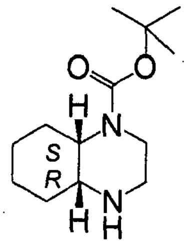
A compound of Reference Example 57 below was produced in the same way as in Reference Example 56 using appropriate starting materials.

[0261]

Reference Example 57

(4aR,8aS)-tert-butyl decahydroquinoxaline-1-carboxylate

Absolute configuration



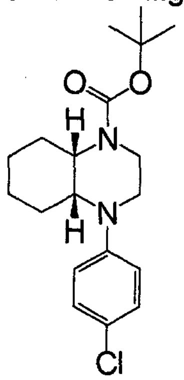
^{1}H-NMR ($CDCl_3$) δppm : 1.18-1.55 (14H, m), 1.55-1.82 (3H, m), 1.85-2.00 (1H, m), 2.68-2.82 (1H, m), 2.85-3.10 (3H, m), 3.65-4.04 (2H, m).

[0262]

Reference Example 58

Production process of cis tert-butyl 4-(4-chlorophenyl)decahydroquinoxaline-1-carboxylate

Relative configuration



A toluene (4 ml) suspension of *cis* tert-butyl decahydroquinoxaline-1-carboxylate (240 mg, 0.999 mmol), 1-bromo-4-chlorobenzene (211 mg, 1.10 mmol), $Pd(OAc)_2$ (11.2 mg, 0.0499 mmol), $t\text{-}Bu_3P.HBF_4$ (14.5 mg, 0.0500 mmol), and NaOt-Bu (135 mg, 1.40 mmol) was stirred for 5 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Insoluble matter was filtered through celite, and the celite layer was washed with AcOEt (5 ml×2). Then, the filtrate was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a white solid (87 mg, yield: 25%).

^{1}H-NMR ($CDCl_3$) δppm : 1.10-1.40 (4H, m), 1.40-1.52 (10H, m), 1.63-1.71 (1H, m), 1.73-1.82 (1H, m), 2.15-2.28 (1H, m), 2.74 (1H, dt, J = 3.6, 11.8 Hz), 2.90-2.97 (1H, m), 3.05-3.11 (1H, m), 3.27 (1H, dt, J = 3.4, 12.6 Hz), 3.77-3.86 (1H, m), 4.01-4.10 (1H, m), 7.08-7.13 (2H, m), 7.25-7.30 (2H, m).

[0263]

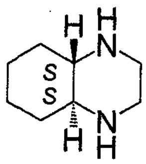
Compounds of Reference Examples 59 to 63 below were produced in the same way as in Reference Example 35 using appropriate starting materials.

[0264]

Reference Example 59

(4aS,8aS)-decahydroquinoxaline

Absolute configuration



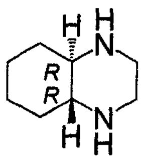
^{1}H-NMR ($CDCl_3$) δppm :1.12-1.58 (6H, m), 1.62-1.78 (4H, m), 2.20-2.29 (2H, m), 2.82-3.02 (4H, m).

[0265]

Reference Example 60

(4aR,8aR)-decahydroquinoxaline

Absolute configuration



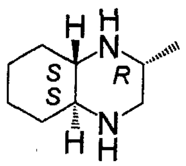
^{1}H-NMR ($CDCl_3$) δppm :1.14-1.27 (2H,m), 1.27-1.57(4H, m), 1.62-1.79 (4H, m), 2.19-2.30(2H, m), 2.83-3.03(4H, m).

[0266]

Reference Example 61

(2R,4aS,8aS)-2-methyldecahydroquinoxaline

Absolute configuration



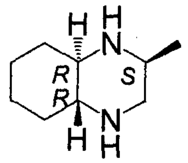
^{1}H-NMR ($CDCl_3$) δppm :1.02 (3H, d, J = 6.3 Hz), 1.11-1.51 (6H, m), 1.62-1.79 (4H, m), 2.14-2.22 (1H, m), 2.24-2.33 (1H, m), 2.44 (1H, dd, J = 10.2, 11.7 Hz), 2.81-2.91 (1H, m), 2.94 (1H, dd, J = 2.9, 11.7 Hz).

[0267]

Reference Example 62

(2S,4aR,8aR)-2-methyldecahydroquinoxaline

Absolute configuration



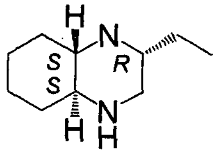
^{1}H-NMR ($CDCl_3$) δppm : 1.02 (3H, d, J = 6.3 Hz), 1.10-1.49 (6H, m), 1.62-1.80 (4H, m), 2.14-2.22 (1H, m), 2.24-2.33 (1H, m), 2.44 (1H, dd, J = 10.3, 11.7 Hz), 2.80-2.91 (1H, m), 2.94 (1H, dd, J = 2.9, 11.7 Hz).

[0268]

Reference Example 63

(2R,4aS,8aS)-2-ethyldecahydroquinoxaline

Absolute configuration



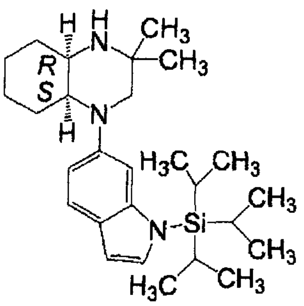
^{1}H-NMR ($CDCl_3$) δppm : 0.92 (3H, t, J = 7.5 Hz), 1.1-1.55 (8H, m), 1.6-1.8 (4H, m), 2.14-2.32 (2H, m), 2.39-2.5 (1H, m), 2.57-2.68 (1H, m), 3.01 (1H, dd, J = 2.6, 11.6 Hz).

[0269]

Example 1

Production of (4aR,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-indol-6-yl)decahydroquinoxaline

Absolute configuration



A toluene (8 mL) suspension of (4aS,8aR)-2,2-dimethyldecahydroquinoxaline (337 mg, 2.00 mmol), 6-bromo-1-(triisopropylsilyl)-1H-indole (846 mg, 2.40 mmol), sodium tert-butoxide (269 mg, 2.80 mmol), palladium (II) acetate (22.5 mg, 0.0902 mmol), and tri-tert-butylphosphine tetrafluoroborate (29.1 mg, 0.101 mmol) was stirred for 5 hours under reflux in a nitrogen atmosphere. The reaction mixture was cooled to room temperature. Then, water (0.5 mL) and ethyl acetate (10 mL) were added thereto, and the mixture was stirred, followed by addition of magnesium sulfate. Insoluble matter was filtered through celite, and the filtrate was then concentrated under reduced pressure. The obtained residue was purified by NH-silica gel column chromatography (n-hexane:ethyl acetate) to obtain colorless, amorphous (4aR,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-indol-6-yl)decahydroquinoxaline (0.75 g, yield: 85%).

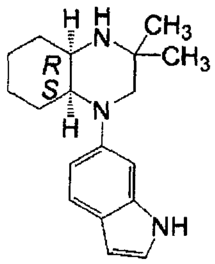
^{1}H-NMR($CDCl_3$)δppm : 1.1-1.2 (18H, m), 1.21 (3H, s), 1.29 (3H ,s), 1.3-1.55(5H, m), 1.55-1.8 (7H, m), 2.79 (1H, d, J = 11.6Hz), 2.91 (1H, d, J = 11.6Hz), 3.45-3.6 (2H, m), 6.49 (1H, dd, J = 0.7, 3.2Hz), 6.82 (1H, dd, J = 2.0, 8.6Hz), 6.93 (1H, s), 7.08 (1H, d, J = 3.2Hz), 7.45 (1H, d, J = 8.6Hz).

[0270]

Example 2

Production of (4aR,8aS)-1-(1H-indol-6-yl)-3,3-dimethyldecahydroquinoxaline

Absolute configuration



Tetra-n-butyl ammonium fluoride (1 M in THF) (3.41 mL, 3.41 mol) was added to a tetrahydrofuran (15 mL) solution of (4aR,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-indol-6-yl)decahydroquinoxaline (0.750 g, 1.71 mmol) with stirring at room temperature, and the mixture was stirred at room temperature for 1 hour. The solvent was distilled off from the reaction mixture under reduced pressure. The obtained residue was purified by NH-silica gel column chromatography (ethyl acetate/hexane) to obtain a white solid. The obtained solid was recrystallized from diisopropyl ether/hexane to obtain (4aR,8aS)-1-(1H-indol-6-yl)-3,3-dimethyldecahydroquinoxaline (305 mg, yield: 63%).

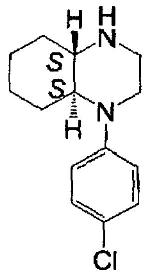
^{1}H-NMR($CDCl_3$)δppm : 1.0-1.55 (11H, m), 1.55-1.85 (4H, m), 2.79 (1H, d, J = 11.6Hz), 2.94 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.6-3.75 (1H, m), 6.35-6.5 (1H, m), 6.79(1H, s), 6.86 (1H, dd, J = 2.1, 8.7Hz), 7.03 (1H, dd, J = 2.7, 2.7Hz), 7.47 (1H, d, J = 8.6Hz), 7.92 (1H, br).

[0271]

Example 3

Production of (4aS,8aS)-1-(4-chlorophenyl)decahydroquinoxaline

Absolute configuration



1-chloroethyl chloroformate (229 μL, 2.10 mmol) was added to a methylene chloride (6.5 mL) solution of (4aS,8aS)-1-benzyl-4-(4-chlorophenyl)decahydroquinoxaline (0.650 g, 1.91 mmol) with ice-cooling and stirring. The mixture was stirred at room temperature for 15 hours, and the reaction mixture was then concentrated under reduced pressure. The obtained residue was dissolved in methanol (6.5 mL), and this solution was stirred for 1 hour under reflux. The solvent was distilled off from the reaction mixture. To the obtained residue, acetone (5 mL) was added, and the mixture was stirred. The deposited crystal was collected by filtration. The obtained crystal was washed with acetone (1 mL) and then dried to obtain (4aS,8aS)-1-(4-chlorophenyl)decahydroquinoxaline (253 mg, yield: 53%) in a white powder form.

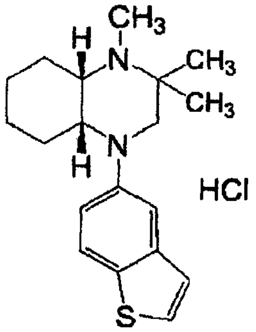
^{1}H-NMR(DMSO-d_6)δppm : 0.85-1.05 (1H, m), 1.1-1.4 (2H, m), 1.4-1.65 (3H, m), 1.65-1.8 (1H, m), 1.9-2.05 (1H, m), 2.8-3.0 (2H, m), 3.05-3.2 (3H, m), 3.2-3.5 (1H, m), 7.1-7.2 (2H, m), 7.35-7.45 (2H, m), 9.2-9.65 (2H, m).

[0272]

Example 4

Production of cis-4-(benzo[b]thiophen-5-yl)-1,2,2-trimethyldecahydroquinoxaline hydrochloride

Relative configuration



A 37% aqueous formaldehyde solution (0.81 mL, 9.9 mmol) was added to a methanol (10 mL) solution of cis-1-(benzo[b]thiophen-5-yl)-3,3-dimethyldecahydroquinoxaline (298 mg, 0.992 mmol) with stirring at room temperature. After 30 minutes, sodium cyanoborohydride (311 mg, 4.96 mmol) and acetic acid (0.30 mL) were added to the reaction solution at room temperature, and the mixture was stirred overnight. The solvent was distilled off from the reaction mixture under reduced pressure. Then, a saturated aqueous solution of sodium bicarbonate (50 mL) was added thereto, followed by extraction with ethyl acetate (50 mL) twice. The organic layer was washed with water twice and with saturated saline once, then dried over magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (methylene chloride:methanol=10:1) to obtain a brown oil. 4 N hydrochloric acid/ethyl acetate (0.6 mL) was added to an ethanol solution of the obtained oil with stirring at room temperature, and the deposited crystal was collected by filtration. The obtained crystal was washed with ethyl acetate and then dried under reduced pressure to obtain cis-4-(benzo[b]thiophen-5-yl)-1,2,2-trimethyldecahydroquinoxaline hydrochloride (258 mg, yield: 74%) in a white powder form.

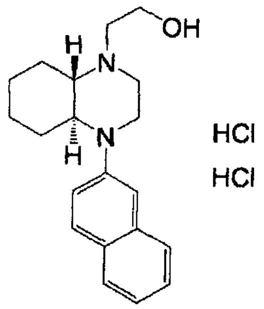
^{1}H-NMR($CDCl_3$)δppm : 1.17-1.34 (1H, m), 1.37-1.74 (2H, m), 1.47 (3H, s), 1.87-2.04 (1H, m), 1.90 (3H, s), 2.20-2.30 (1H, m), 2.39-2.54 (1H, m), 2.64-2.88 (2H, m), 2.75 (3H, d, J = 4.9 Hz), 3.12 (1H, d, J = 13.2 Hz), 3.69-3.74 (1H, m), 3.85-3.93 (1H, m), 3.87 (1H, d, J = 13.2 Hz), 7.01 (1H, dd, J = 8.8, 2.3 Hz), 7.21-7.32 (2H, m), 7.44 (1H, d, J = 5.4 Hz), 7.75 (1H, d, J = 8.8 Hz), 11.20 (1H, brs).

[0273]

Example 5

Production of 2-(trans-4-(naphthalen-2-yl)decahydroquinoxalin-1-yl)ethanol dihydrochloride

Relative configuration



Tetra-n-butyl ammonium fluoride (1 M in THF) (2.1 mL, 2.1 mmol) was added to a THF (10 mL) solution of trans-1-(2-(tert-butyldimethylsilyloxy)ethyl)-4-(naphthalen-2-yl)decahydroquinoxaline (820 mg, 1.93 mmol) with stirring at room temperature, and the mixture was stirred overnight. To the reaction mixture, ethyl acetate was added, and the resultant mixture was washed with water twice and with saturated saline once, then dried over magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (methylene chloride:methanol=10:1) to obtain a colorless, amorphous solid (534 mg). A 319 mg aliquot of the obtained solid was dissolved in ethanol. To the solution, 4 N hydrochloric acid/ethyl acetate (1.0 mL) was added with stirring at room temperature, and the deposited crystal was collected by filtration. The obtained crystal was washed with ethyl acetate and then dried under reduced pressure to obtain 2-(trans-4-(naphthalen-2-yl)decahydroquinoxalin-1-yl)ethanol dihydrochloride (365 mg, yield: 49%) in a white powder form.

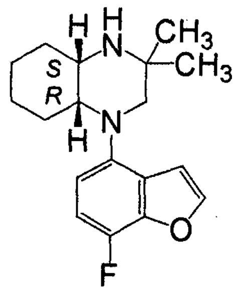
^{1}H-NMR($CDCl_3$)δppm : 1.23-1.76 (4H, m), 1.86-2.08 (3H, m) ,2.43-2.48 (1H, m), 3.18-3.25 (1H, m), 3.72-3.77 (2H, m), 3.93-3.98 (1H, m), 3.93-4.78 (1H, br), 4.08-4.20 (2H, m), 4.39-4.55 (1H, m), 4.57-4.78 (2H, m), 4.97-5.06 (1H, m), 7.61-7.68 (3H, m), 7.81-8.07 (3H, m), 8.17-8.69 (1H, br), 12.73 (1H, brs), 14.91 (1H, brs).

[0274]

Example 77

Production of (4aS,8aR)-1-(7-fluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline

Absolute configuration



A toluene (4 ml) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (168 mg, 0.998 mmol), 4-bromo-7-fluorobenzofuran (258 mg, 1.20 mmol), $Pd(OAc)_2$ (11.2 mg, 0.0499 mmol), t-$Bu_3P.HBF_4$ (14.5 mg, 0.0500 mmol), and NaOt-Bu (135 mg, 1.40 mmol) was stirred for 4 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Insoluble matter was filtered, and the residue was washed with AcOEt (5 ml×2). Then, the filtrate was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a colorless oil (167 mg). This oil was crystallized from hexane (1 mL) to obtain (4aS,8aR)-1-(7-fluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline (107 mg, yield: 35%) in a white powder form.

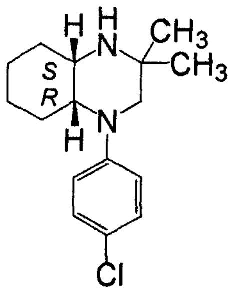
^{1}H-NMR ($CDCl_3$) δppm : 1.0-1.45 (11H, m), 1.6-1.8 (3H, m), 1.8-1.95 (1H, m), 2.70 (1H, d, J = 11.3Hz), 3.04 (1H, d, J = 11.3Hz), 3.50 (1H, ddd, J = 3.8, 3.8, 12.1Hz), 3.55-3.65 (1H, m), 6.47 (1H, dd, J = 3.4, 8.6Hz), 6.84 (1H, dd, J = 2.5, 2.5Hz), 6.89 (1H, dd, J = 8.6, 10.4Hz), 7.60 (1H, d, J = 2.2Hz).

[0275]

Example 106

Production of (4aS,8aR)-1-(4-chlorophenyl)-3,3-dimethyldecahydroquinoxaline hydrochloride

Absolute configuration



A toluene (10 ml) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (252 mg, 1.50 mmol), 1-bromo-4-chlorobenzene (345 mg, 1.80 mmol), $Pd(OAc)_2$ (16.8 mg, 0.0748 mmol), t-$Bu_3P.HBF_4$ (21.8 mg, 0.0751 mmol), and NaOt-Bu (202 mg, 2.10 mmol) was stirred for 5 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Then, insoluble matter was filtered through celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt). The obtained oil was dissolved in 1 N HCl-EtOH (3 mL), and the solvent was distilled off under reduced pressure. The deposited crystal was recrystallized from ethanol/acetone to obtain (4aS,8aR)-1-(4-chlorophenyl)-3,3-dimethyldecahydroquinoxaline hydrochloride (262 mg, yield: 55%) in a white powder form.

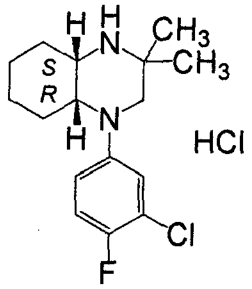
^{1}H-NMR (DMSO-d_6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.1 (5H, m), 2.93 (1H, d, J = 13.6Hz), 3.40 (1H, d, J = 13.8Hz), 3.65-3.85 (1H, m), 3.9-4.1 (1H, m), 6.8-7.05 (2H, m), 7.1-7.35 (2H, m), 8.14 (1H, br), 9.77 (1H, br).

[0276]

Example 112

Production of (4aS,8aR)-1-(3-chloro-4-fluorophenyl)-3,3-dimethyldecahydroquinoxaline hydrochloride

Absolute configuration



A toluene (10 ml) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (168 mg, 0.998 mmol), 4-bromo-2-chloro-1-fluorobenzene (251 mg, 1.20 mmol), $Pd(OAc)_2$ (11.2 mg, 0.0500 mmol), $t\text{-}Bu_3P.HBF_4$ (14.5 mg, 0.0500 mmol), and NaOt-Bu (135 mg, 1.40 mmol) was stirred for 5 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Then, insoluble matter was filtered. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt). The obtained oil was dissolved in 1 N HCl-EtOH (3 mL), and ethanol was distilled off under reduced pressure. The deposited crystal was recrystallized from ethanol/acetone to obtain (4aS,8aR)-1-(3-chloro-4-fluorophenyl)-3,3-dimethyldecahydroquinoxaline hydrochloride (153 mg, yield: 46%) in a white powder form.

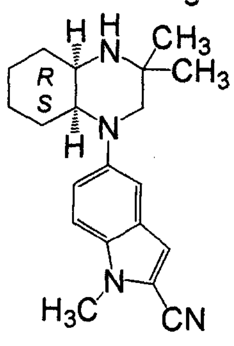
^{1}H-NMR (DMSO-d_6) δppm : 1.15-1.45 (6H, m), 1.51 (3H, s), 1.6-1.9 (4H, m), 1.9-2.05 (1H, m), 2.94 (1H, d, J = 13.5Hz), 3.3-3.45 (1H, m), 3.65-3.8 (1H, m), 3.95-4.1 (1H, m), 6.85-7.0 (1H, m), 7.12 (1H, dd, J = 3.0, 6.2Hz), 7.25 (1H, dd, J = 9.1, 9.1Hz), 8.13 (1H, br), 9.86 (1H, br).

[0277]

Example 150

Production of 5-((4aR,8aS)-3,3-dimethyldecahydroquinoxalin-1-yl)-1-methyl-1H-indole-2-carbonitrile

Absolute configuration



A toluene (4 ml) suspension of (4aS,8aR)-2,2-dimethyldecahydroquinoxaline

(168 mg, 0.998 mmol), 5-bromo-1-methyl-1H-indole-2-carbonitrile (259 mg, 1.10 mmol), $Pd(OAc)_2$ (11.2 mg, 0.0499 mmol), t-$Bu_3P.HBF_4$ (14.5 mg, 0.0500 mmol), and NaOt-Bu (135 mg, 1.40 mmol) was stirred for 4 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Insoluble matter was filtered through celite, and the residue was washed with CH_2Cl_2:MeOH (3:1) (5 mL×2). Then, the filtrate was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a colorless oil. This oil was crystallized from hexane (1 mL) to obtain (4aS,8aR)-1-(7-fluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline (148 mg, yield: 46%) in a pale yellow powder form.

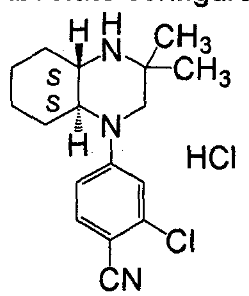
^{1}H-NMR ($CDCl_3$) δppm : 0.7-2.3 (15H, m), 2.7-3.2 (2H, m), 3.5-3.8 (2H, m), 3.85 (3H, s), 6.95-7.05 (2H, m), 7.15-7.3 (2H, m).

[0278]

Example 237

Production of (4aS,8aS)-1-(3-chloro-4-cyanophenyl)-3,3-dimethyldecahydroquinoxaline hydrochloride

Absolute configuration



A toluene (10 ml) suspension of (4aS,8aS)-2,2-dimethyldecahydroquinoxaline (400 mg, 2.38 mmol), 4-bromo-2-chlorobenzonitrile (669 mg, 3.09 mmol), $Pd(OAc)_2$ (53 mg, 0.24 mmol), t-$Bu_3P.HBF_4$ (70 mg, 0.24 mmol), and t-BuONa (320 mg, 3.33 mmol) was stirred for 5 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled. Then, insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH) to obtain an orange amorphous solid. This amorphous solid was dissolved in ethyl acetate (5 mL). A crystal deposited by the addition of 4 N HCl/AcOEt (0.6 mL) was collected by filtration and dried under reduced pressure to obtain (4aS,8aS)-1-(3-chloro-4-cyanophenyl)-3,3-dimethyldecahydroquinoxaline (304 mgm, 48%) in a pale orange powder form.

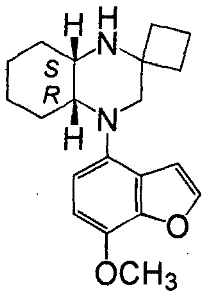
^{1}H-NMR ($CDCl_3$) δppm : 1.05-1.20 (1H, m), 1.23-1.44 (2H, m), 1.54-2.10 (4H, m), 1.63 (3H, s), 1.68 (3H, s), 2.35-2.40 (1H, m), 2.89 (1H, d, J = 12.7 Hz), 3.19 (2H, br), 3.34 (1H, d, J = 12.7 Hz), 7.06 (1H, dd, J = 8.4, 2.0 Hz), 7.20 (1H, d, J = 2.0 Hz), 7.61 (1H, d, J = 8.4 Hz), 9.62 (1H, brs), 9.90 (1H, br)

[0279]

Example 579

Production of (4a'R,8a'S)-4'-(7-methoxybenzofuran-4-yl)octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline]

Absolute configuration



A toluene (4 ml) suspension of (4a'R,8a'S)-octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline] (180 mg, 0.998 mmol), 4-bromo-7-methoxybenzofuran (250 mg, 1.10 mmol), $Pd(OAc)_2$ (11.2 mg, 0.0499 mmol), t-$Bu_3P.HBF_4$ (14.5 mg, 0.0500 mmol), and NaOt-Bu (135 mg, 1.40 mmol) was stirred for 4 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Insoluble matter was filtered, and the residue was washed with AcOEt (5 mL×2). Then, the filtrate was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a colorless amorphous solid. This solid was crystallized from hexane (1 mL) to obtain (4a'R,8a'S)-4'-(7-methoxybenzofuran-4-yl)octahydro-1'H-spiro[cyclobutane-1,2'-quinoxaline] (107 mg, yield: 35%) in a white powder form.

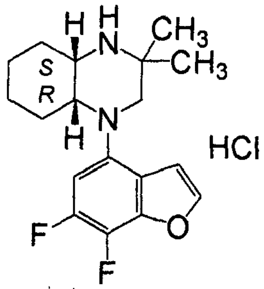
^{1}H-NMR ($CDCl_3$) δppm : 0.95-1.1 (2H, m), 1.3-1.4 (1H, m), 1,4-2.1 (11H, m), 2.25-2.4 (1H, m), 3.01 (1H, d, J = 11.0Hz), 3.17 (1H, d, J = 11.1Hz), 3.40 (1H, br), 3.45-3.5 (1H, m), 3.97 (3H, s), 6.58 (1H, d, J = 8.4Hz), 6.70 (1H, d, J = 8.4Hz), 6.80 (1H, d, J = 2.1Hz), 7.58 (1H, d, J = 2.1Hz).

[0280]

Example 580

Production of (4aS,8aR)-1-(6,7-difluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline hydrochloride

Absolute configuration



A toluene (6 ml) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (252 mg, 1.50 mmol), 4-bromo-6,7-difluorobenzofuran (384 mg, 1.65 mmol), $Pd(OAc)_2$ (16.8 mg, 0.0748 mmol), t-$Bu_3P.HBF_4$ (21.8 mg, 0.0751 mmol), and NaOt-Bu (202 mg, 2.10 mmol) was stirred for 3 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Then, insoluble matter was filtered through celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a pale yellow oil (193 mg). This oil was dissolved in ethanol (2 mL). To the solution, 1 N HCl-EtOH (1.2 mL) was added, and the mixture was stirred. The deposited crystal was collected by filtration, washed with ethyl acetate, and then dried under reduced pressure to obtain (4aS,8aR)-1-(6,7-difluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline hydrochloride (167 mg, yield: 31%) in a white powder form.

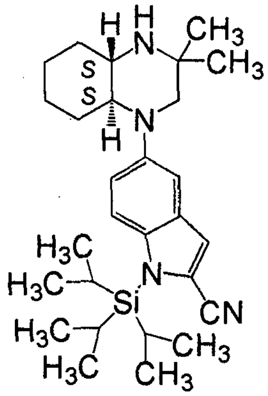
^{1}H-NMR (DMSO-d_6) δppm : 1.01-1.17 (2H, m), 1.34-1.44 (1H, m), 1.48 (3H, s), 1.52 (3H, s), 1.59-2.07 (5H, m), 3.00 (1H, d, J = 13.0Hz), 3.28 (1H, d, J = 13.2Hz), 3.75-3.9 (1H, m), 4.0-4.15 (1H, m), 6.83 (1H, dd, J = 5.9, 13.5Hz), 7.36 (1H ,dd, J = 2.6, 2.6Hz), 8.0-8.2 (2H, m), 9.7-9.9 (1H, m).

[0281]

Example 581

Production of (4aS,8aS)-1-(2-cyano-1-(triisopropylsilyl)-1H-indol-5-yl) 3,3-dimethyldecahydroquinoxaline

Absolute configuration



A toluene (5 ml) suspension of (4aS,8aS)-2,2-dimethyldecahydroquinoxaline (200 mg, 1.19 mmol), 5-bromo-1-(triisopropylsilyl)-1H-indole-2-carbonitrile (493 mg, 1.31 mmol), $Pd(OAc)_2$ (13.3 mg, 0.0594 mmol), $tBu_3P.HBF_4$ (17.2 mg, 0.0594 mmol), and t-BuONa (137 mg, 1.43 mmol) was stirred at 100°C for 4 hours in a nitrogen atmosphere. Insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane) to obtain (4aS,8aS)-1-(2-cyano-1-(triisopropylsilyl)-1H-indol-5-yl) 3,3-dimethyldecahydroquinoxaline (430 mg, 78%) in a white amorphous solid form.

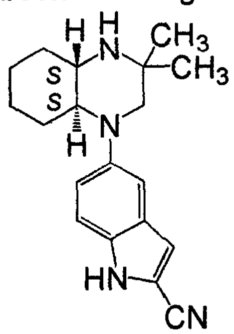
^{1}H-NMR ($CDCl_3$) δppm : 0.75-1.38 (26H, m), 1.41 (3H, s), 1.54-1.77 (4H, m), 2.01 (3H, quintet, J = 7.5 Hz), 2.25-2.32 (1H, m), 2.65 (1H, d, J = 11.2 Hz), 2.75-2.85 (2H, m), 7.11 (1H, dd, J = 2.0, 9.1 Hz), 7.32 (1H, d, J = 2.0 Hz), 7.33 (1H, d, J = 0.5 Hz), 7.50 (1H, d, J = 9.1 Hz).

[0282]

Example 582

Production of (4aS,8aS)-1-(2-cyano-1H-indol-5-yl) 3,3-dimethyldecahydroquinoxaline

absolute configuration



Tetrabutylammonium fluoride (1 M THF solution, 0.73 mL, 0.73 mmol) was added to an anhydrous tetrahydrofuran (5 mL) solution of (4aS,8aS)-1-(2-cyano-1-(triisopropylsilyl)-1H-indol-5-yl) 3,3-dimethyldecahydroquinoxaline (170 mg, 0.366 mmol) at room temperature, and the reaction solution was stirred at room temperature for 1 hour. The reaction solution was concentrated under reduced pressure, and the obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane=1/10→1/1). The solvent was removed under reduced pressure. The obtained residue was recrystallized from ethyl acetate/n-hexane to obtain (4aS,8aS)-1-(2-cyano-1H-indol-5-yl) 3,3-dimethyldecahydroquinoxaline (30 mg, yield: 27%) in a white powder form.

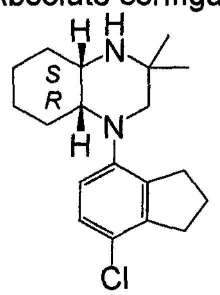
^{1}H-NMR (DMSO-d_6) δppm : 0.82-1.00 (4H, m), 1.08-1.34 (6H, m), 1.42-1.67 (5H, m), 2.19-2.27 (1H, m), 2.55 (1H, d, J = 10.9 Hz), 2.59-2.69 (2H, m), 7.11 (1H, dd, J = 1.8, 8.8 Hz), 7.26 (1H, d, J = 0.8 Hz), 7.32 (1H, d, J = 1.8 Hz), 7.36 (1H, d, J = 8.8 Hz) 12.25 (1H, brs).

[0283]

Example 583

Production of (4aS,8aR)-1-(7-chloro-2,3-dihydro-1H-inden-4-yl)-3,3-dimethyldecahydroquinoxaline

Absolute configuration



A toluene (1 mL) solution of bis(tri-tert-butylphosphine)palladium (25.6 mg, 0.0501 mmol) was added to a toluene (4 ml) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (168 mg, 0.998 mmol), 4-bromo-7-chloro-2,3-dihydro-1H-indene (255 mg, 1.10 mmol), and NaOt-Bu (135 mg, 1.40 mmol), and the mixture was stirred for 4 hours under reflux in a nitrogen atmosphere. The reaction solution was cooled to room temperature. Then, water (0.5 mL) and AcOEt (10 mL) were added thereto, and the mixture was stirred. $MgSO_4$ was further added thereto, and the mixture was stirred. Insoluble matter was filtered through celite, and the residue was washed with AcOEt (5 mL×2). Then, the filtrate was concentrated under reduced pressure. The obtained residue was purified by basic silica gel column chromatography (Hex-AcOEt) to obtain a white solid (167 mg). This solid was recrystallized from ethanol/water to obtain (4aS,8aR)-1-(7-chloro-2,3-dihydro-1H-inden-4-yl)-3,3-dimethyldecahydroquinoxaline (136 mg, yield: 43%) in a white powder form.

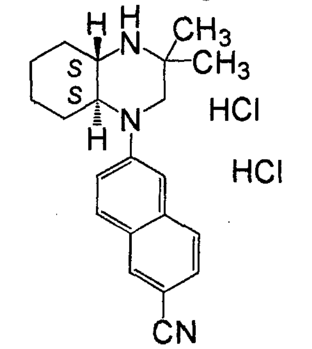
1H-NMR (CDCl3) δppm : 0.97-1.12 (3H, m), 1.16 (3H, s), 1.27 (3H, s), 1.31-1.44 (2H, m), 1.45-1.76 (3H, m), 1.78-1.92 (1H, m), 1.94-2.06 (1H, m), 2.12-2.23 (1H, m), 2.51 (1H, d, J = 11.2Hz), 2.85-3.05 (5H, m), 3.1-3.2 (1H, m), 3.45-3.55 (1H, m), 6.58 (1H, d, J = 8.4Hz), 7.03 (1H, d, J = 8.4Hz).

[0284]

Example 584

Production of (4aS,8aS)-1-(6-cyanonaphthalen-2-yl)-3,3-dimethyldecahydroquinoxaline dihydrochloride

absolute configuration



A toluene (5 mL) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (200 mg, 1.19 mmol), 6-bromo-2-naphthonitrile (303 mg, 1.31 mmol), $Pd(OAc)_2$ (13.3 mg, 0.0594 mmol), $tBu_3P.HBF_4$ (17.2 mg, 0.0594 mmol), and t-BuONa (137 mg, 1.43 mmol) was stirred at 100°C for 4 hours. Insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane). The solvent was removed under reduced pressure. The obtained residue was dissolved in ethyl acetate. To this solution, 1 N hydrochloric acid-ethanol was added, and the deposited crystal was collected by filtration. The obtained crystal was dried under reduced pressure to obtain (4aS,8aS)-1-(6-cyanonaphthalen-2-yl)-3,3-dimethyldecahydroquinoxaline dihydrochloride (303 mg, yield: 65%) in a white powder form.

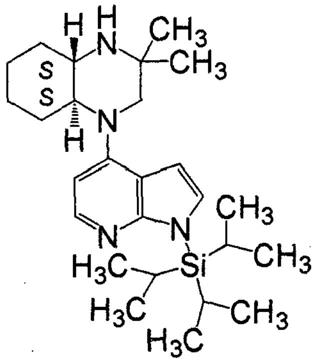
^{1}H-NMR (DMSO-d_6) δppm : 1.10-1.50 (6H, m), 1.56-1.90 (7H, m), 2.00-2.14 (1H, m), 3.08-3.45 (4H, m), 4.68-5.32 (1H, br), 7.45 (1H, dd, J = 2.0, 8.9 Hz), 7.64 (1H, d, J = 1.8 Hz), 7.73 (1H, dd, J = 1.6, 8.6 Hz), 8.00 (1H, d, J = 8.6 Hz), 8.04 (1H, d, J = 8.6 Hz), 8.49 (1H, s), 9.10-9.28 (1H, br), 10.04-10.28 (1H, br).

[0285]

Example 585

Production of (4aS,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridin-4-yl)decahydroquinoxaline

Absolute configuration



A toluene (5 mL) suspension of (4aS,8aS)-2,2-dimethyldecahydroquinoxaline (200 mg, 1.19 mmol), 4-bromo-1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridine (462 mg, 1.31 mmol), $Pd(OAc)_2$ (13.3 mg, 0.0594 mmol), $tBu_3P.HBF_4$ (17.2 mg, 0.0594 mmol), and t-BuONa (137 mg, 1.43 mmol) was stirred at 100°C for 4 hours in a nitrogen atmosphere. Insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane) to obtain (4aS,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridin-4-yl)decahydroquinoxaline (439 mg, 84%) in a white amorphous solid form.

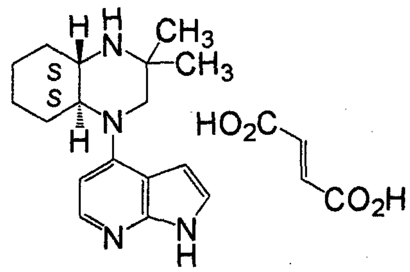
^{1}H-NMR ($CDCl_3$) δppm : 0.95-1.20 (22H, m), 1.36-1.45 (3H, m), 1.52 (3H, s), 1.65-1.92 (7H, m), 2.11-2.20 (1H, m), 2.57-2.67 (2H, m), 2.83-2.95 (1H, m), 3.26- (1H, d, J = 11.7 Hz), 6.55 (1H, d, J = 3.5 Hz), 6.63 (1H, d, J = 5.3 Hz), 7.18 (1H, d, J = 3.5 Hz), 8.12 (1H, d, J = 5.3 Hz).

[0286]

Example 586

Production of (4aS,8aS)-3,3-dimethyl-1-(1H-pyrrolo[2,3-b]pyridin-4-yl)decahydroquinoxaline fumarate

Absolute configuration



Tetrabutylammonium fluoride (1 M THF solution, 1.95 mL, 1.95 mmol) was added to an anhydrous tetrahydrofuran (5 mL) solution of (4aS,8aS)-3,3-dimethyl-1-(1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridin-4-yl)decahydroquinoxaline (430 mg, 0.976 nmol), and the mixture was stirred at room temperature for 1 hour. The reaction solution was concentrated under reduced pressure, and the obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane=1/10→1/1) to obtain a product (370 mg, 1.30 mmol) in an oil form. This oil was dissolved in ethanol (5 mL). To this solution, an ethanol (5 mL) solution of fumaric acid (151 mg) was added, and ethanol was removed under reduced pressure. The obtained solid was recrystallized from ethanol/ethyl acetate to obtain 5-((4aS,8aS)-3,3-dimethyldecahydroquinoxalin-1-yl)-1H-indole-2-carbonitrile (246 mg, yield: 63%) in a white powder form.

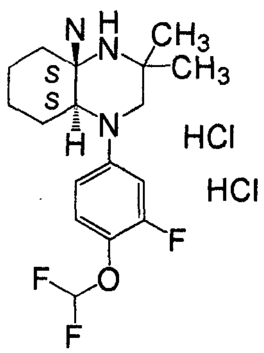
^{1}H-NMR (DMSO-d_6) δppm : 0.94-1.09 (1H, m), 1.20 (3H, s), 1.26-1.55 (7H, m), 1.68-1.78 (1H, m), 1.85-2.04 (2H, m), 2.81-2.93 (1H, m), 2.95-3.23 (3H, m), 6.36-6.42 (1H, m), 6.49 (2H, s), 6.71 (1H, d, J = 5.2 Hz), 7.32-7.38 (1H, m), 8.09 (1H, d, J = 5.2 Hz), 8.50-11.20 (1H, br), 11.59 (1H, s).

[0287]

Example 587

Production of (4aS,8aS)-1-(4-(difluoromethoxy)-3-fluorophenyl)-3,3-dimethyldecahydroquinoxaline dihydrochloride

Absolute configuration



A toluene (5 mL) suspension of (4aR,8aS)-2,2-dimethyldecahydroquinoxaline (200 mg, 1.19 mmol), 4-bromo-1-difluoromethoxy-2-fluorobenzene (315 mg, 1.31 mmol), $Pd(OAc)_2$ (13.3 mg, 0.0594 mmol), $tBu_3P.HBF_4$ (17.2 mg, 0.0594 mmol), and t-BuONa (137 mg, 1.43 mmol) was stirred at 100°C for 4 hours. Insoluble matter was filtered through celite, and the filtrate was concentrated. The obtained residue was purified by basic silica gel column chromatography (AcOEt/hexane). The solvent was removed under reduced pressure. The obtained residue was dissolved in ethyl acetate. To this solution, 1 N hydrochloric acid-ethanol was added, and the deposited crystal was collected by filtration. The obtained crystal was dried under reduced pressure to obtain (4aS,8aS)-1-(4-difluoromethoxy-3-fluorophenyl)-3,3-dimethyldecahydroquinoxaline dihydrochloride (193 mg, yield: 40%) in a white powder form.

^{1}H-NMR (DMSO-d_6) δppm :1.01-1.39 (6H, m), 1.49-1.67 (6H, m), 1.67-1.77 (1H, m), 1.96-2.05 (1H, m), 2.81-2.95 (2H, m), 3.02 (1H, d, J = 12.5 Hz), 3.10-3.23 (1H, m), 4.30-4.80 (1H, br), 6.96-7.01 (1H, m), 7.02 (0.25H, s), 7.17 (1H, dd, J = 2.5, 12.1 Hz), 7.20 (0.5H, s), 7.33 (1H, t, J = 8.9 Hz), 7.39 (0.25H, s), 9.04-9.21 (1H, m), 9.70-9.85 (1H, m).

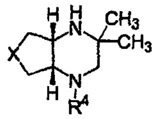
[0288]

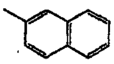
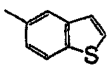
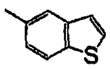
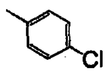
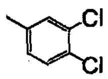
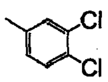
Compounds of Examples 6 to 76, 78 to 105, 107 to 111, 113 to 149, 151 to 236, 238 to 578, 588 to 1656 shown in tables below were produced in the same way as in the Examples using corresponding appropriate starting materials. In these tables, for example, the produced compounds have physical properties such as a crystalline form, m.p. (melting point), salt, ^{1}H-NMR, and MS (mass spectrum).

[0289]

Table 1

Relative configuration

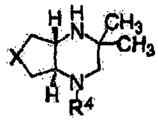


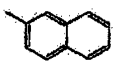
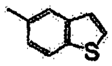
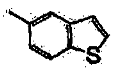
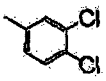
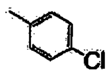
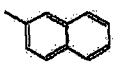
Example	X	R^4	1H-NMR	Salt
6	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.39 (3H, s), 1.49 (3H, s), 1.56-2.20 (6 H, m), 3.04 (1H, d, J = 13.3 Hz), 3.61 (1H, d, J = 13.3 Hz), 3.75-3.90 (1H, m), 4.40-4.55 (1 H, m), 7.17-7.30 (2 H, m), 7.33-7.48 (2 H, m), 7.65-7.83 (3 H, m), 8.35-8.60 (1 H, brm), 9.70-9.95 (1 H, brm).	Hydrochloride
7	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.39 (3H, s), 1.48 (3H, s), 1.55-2.19 (6H, m), 3.01 (1H, d, J = 13.2 Hz), 3.45 (1H, d, J = 13.2 Hz), 3.70-3.87 (1H, m), 4.28-4.45 (1H, m), 7.17 (1H, dd, J = 2.2, 9.0 Hz), 7.29 (1H, d, J = 5.4 Hz), 7.37 (1H, d, J = 2.2 Hz), 7.67 (1H, d, J = 5.4 Hz), 7.81 (1H, J = 8.9 Hz), 8.42-8.65 (1H, br), 9.80-10.05 (1H, br).	Hydrochloride
8	-O-		1H-NMR (DMSO-d6) δppm : 1.42 (3H, s), 1.49 (3H, s), 3.07 (1H, d, J = 13.4 Hz), 3.53 (1H, d, J = 13.4 Hz), 3.72 (1H, t, J = 8.8 Hz), 3.90-4.17 (4H, m), 4.79-4.94 (1H, m), 7.19 (1H, dd, J = 2.4, 8.9 Hz), 7.30 (1H, dd, J = 0.5, 5.4 Hz), 7.41 (1H, d, J = 2.4 Hz), 7.69 (1H, d, J = 5.4 Hz), 7.83 (1H, d, J = 8.9 Hz), 8.60-8.85 (1H, br), 10.41-10.65 (1H, br).	Hydrochloride
9	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.33 (3H, s), 1.44 (3H, s), 1.55-2.19 (6H, m), 2.92 (1H, d, J = 13.5 Hz), 3.48 (1H, d, J = 13.5 Hz), 3.66-3.82 (1H, m), 4.20-4.35 (1H, m), 6.98 (2H, d, J = 9.0 Hz), 7.23 (2H, d, J = 9.0 Hz), 8.40-8.66 (1H, br), 9.75-10.05 (1H, br).	Hydrochloride
10	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.32 (3H, s), 1.43 (3H, s), 1.55-2.15 (6H, m), 2.93 (1H, d, J = 13.6 Hz), 3.58 (1H, d, J = 13.6 Hz), 3.65-3.82 (1H, m), 4.20-4.40 (1H, m), 6.97 (1H, dd, J = 2.9, 9.0 Hz), 7.19 (1H, d, J = 2.9 Hz), 7.40 (1H, d, J = 9.0 Hz), 8.40-8.52 (1H, br), 9.70-9.95 (1H, br).	Hydrochloride
11	-O-		1H-NMR (DMSO-d6) δppm : 1.34 (3H, s), 1.44 (3H, s), 2.99 (1H, d, J = 13.8 Hz), 3.60-3.73 (2H, m), 3.85-4.11 (4H, m), 4.71-4.90 (1H, m), 6.95-7.08 (1H, m), 7.20-7.30 (1H, m), 7.42 (1H, d, J 9.0 Hz), 8.60-8.89 (1H, br), 10.20-10.61 (1H, br).	Hydrochloride

[0290]

Table 2

Relative configuration

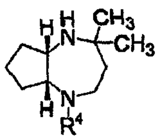


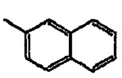
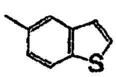
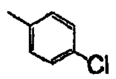
Example	X	R^4	NMR	Salt
12	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.30-1.50 (4H, m), 1.60 (3H, s), 1.65-2.05 (4H, m), 2.05-2.23 (1H, m), 2.82-2.96 (1H, m), 3.06-3.25 (1H, m), 3.25-3.45 (2H, m), 4.00-5.25 (1H, br), 7.29 (1H, dd, J = 2.1, 8.8 Hz), 7.35-7.60 (3H, m), 7.78-7.94 (3H, m), 9.33-9.67 (1H, br), 9.73-10.08 (1H, br).	Dihydrochloride
13	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.30-1.53 (4H, m), 1.60 (3H, s), 1.65-2.07 (5H, m), 2.94 (1H, d, J = 12.4 Hz), 3.06-3.45 (3H, m), 4.40-5.68 (1H, br), 7.18 (1H, dd, J = 1.7, 8.7 Hz), 7.42 (1H, d, J = 5.4 Hz), 7.65 (1H, d, J = 1.7 Hz), 7.76 (1H, d, J = 5.4 Hz), 7.93 (1H, d, J = 8.7 Hz), 9.40-9.70 (1H, br), 9.80-10.12 (1H, br).	Dihydrochloride
14	-O-		1H-NMR (DMSO-d6) δppm : 1.44 (3H, s), 1.62 (3H, s), 2.80 (1H, d, J = 12.7 Hz), 3.34 (1H, d, J = 12.7 Hz), 3.46-3.61 (2H, m), 3.75-3.95 (2H, m), 4.00-4.10 (1H, m), 4.11-4.28 (1H, m), 4.75-5.61 (1H, br), 7.12 (1H, dd, J = 2.1, 8.7 Hz), 7.40 (1H, d, J = 5.4 Hz), 7.62 (1H, d, J = 2.1 Hz), 7.75 (1H, d, J = 5.4 Hz), 7.91 (1H, d, J = 8.7 Hz), 9.68-10.08 (1H, br), 10.08-10.30 (1H, br).	Dihydrochloride
15	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.25-1.45 (4H, m), 1.52 (3H, s), 1.65-1.88 (3H, m), 1.88-2.10 (2H, m), 2.84 (1H, d, J = 12.8 Hz), 2.94-3.10 (1H, m), 3.18-3.39 (2H, m), 4.03-4.70 (1H, br), 7.09 (1H, dd, J = 2.6, 8.7 Hz), 7.33 (1H, d, J = 2.6 Hz), 7.52 (1H, d, J = 8.7 Hz), 9.26-9.59 (1H, br),9.72-10.04 (1H, br).	Dihydrochloride
16	$-CH_2-$		1H-NMR (DMSO-d6) δppm : 1.24-1.45 (4H, m), 1.53 (3H, s), 1.63-2.04 (5H, m), 2.82 (1H, d, J = 12.6 Hz), 2.90-3.08 (1H, m), 3.13 (1H, d, J = 12.6 Hz), 3.26-3.36 (1H, m), 4.35-5.05 (1H, br), 7.05-7.18 (2H, m), 7.30-7.40 (2H, m), 9.30-9.65 (1H, br), 9.75-10.02 (1H, br).	Dihydrochloride
17	-O-		1H-NMR (DMSO-d6) δppm : 1.46 (3H, s), 1.64 (3H, s), 2.89 (1H, d, J = 12.9 Hz), 3.47-3.66 (3H, m), 3.81-3.97 (2H, m), 4.01-4.15 (1H, m), 4.34-4.45 (1H, m), 7.26 (1H, dd, J = 2.3, 8.8 Hz), 7.38-7.44 (1H, m), 7.44-7.50 (1H, m), 7.50-7.54 (1H, m), 7.80-7.87 (2H, m), 7.89 (1H, d, J = 8.1 Hz), 9.84-10.04 (1H, br), 10.04-10.20 (1H, br).	Hydrochloride

[0291]

Table 3

Relative configuration

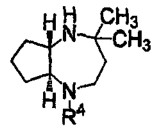


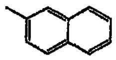
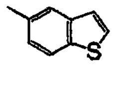
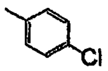
Example	R^4	NMR	Salt
18		1H-NMR (DMSO-d6) δ ppm (80°C) : 1.40 (3 H, s), 1.43-1.70 (5 H, m), 1.72-1.92 (2 H, m), 1.95-2.23 (4 H, m), 3.39-3.52 (2 H, m), 3.85-4.02 (1 H, br), 4.02-4.14 (1 H, m), 5.64-6.00 (1 H, br), 7.31-7.38 (1 H, m), 7.38-7.47 (2 H, m), 7.50-7.57 (1 H, m), 7.72-7.85 (3 H, m),8.44-8.80 (1 H, br), 9.04-9.40 (1 H, br).	Dihydrochloride
19		1H-NMR (DMSO-d6) δ ppm (80°C) : 1.31-1.51 (5H, m), 1.54 (3H, s), 1.63-1.76 (2H, m), 1.87-2.12 (3H, m), 2.12-2.23 (1H, m), 3.22-3.44 (2H, m), 3.85-4.02 (2H, m), 5.00-5.90 (1H, br), 7.33 (1H, d, J = 8.6 Hz), 7.36 (1H, d, J = 5.4 Hz), 7.70 (1H, d, J = 5.4 Hz), 7.77 (1H, s), 7.89 (1H, d, J = 8.6 Hz), 8.25-8.74 (1H, br), 9.00-9.54 (1H, br).	Dihydrochloride
20		1H-NMR (DMSO-d6) δppm : 1.34 (3H, s), 1.39-1.55 (5H, m), 1.67-1.90 (3H, m), 1.90-2.16 (3H, m), 3.17-3.38 (2H, m), 3.76-4.02 (2H, m), 7.10-7.20 (2H, m), 7.25-7.37 (2H, m), 7.37-7.90 (1H, br), 8.45-8.69 (1H, br), 8.69-9.19 (1H, br).	Dihydrochloride

[0292]

Table 4

Relative configuration

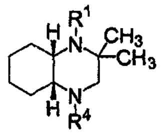


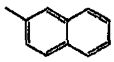
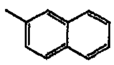
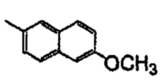
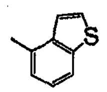
Example	R^4	NMR	Salt
21		1H-NMR (DMSO-d6) δ ppm (80℃) : 1.43 (3H, s), 1.47 (3H, s), 1.51-1.65 (1H, m), 1.72-1.90 (3H, m), 1.93-2.09 (2H, m), 2.12-2.29 (2H, m), 3.69-3.80 (1H, m), 3.81-3.92 (1H, m), 3.96-4.11 (1H, m), 4.11-4.70 (2H, br), 7.22-7.45 (4H, m), 7.70-7.85 (3H, m), 9.15-9.49 (1H, br), 9.49-9.58 (1H, br).	Dihydrochloride
22		1H-NMR (DMSO-d6) δ ppm (80℃) : 1.46 (3H, s), 1.49 (3H, s), 1.65-1.94 (5H, m), 2.10-2.44 (3H, m), 3.69-3.80 (1H, m), 3.86-4.00 (1H, m), 4.00-4.20 (1H, m), 4.60-4.85 (1H, m), 4.85-6.06 (1H, br), 7.36-7.55 (2H, m), 7.76 (1H, d, J = 5.4 Hz), 7.78 (1H, brs), 7.99 (1H, d, J = 8.6 Hz), 9.40-9.68 (1H, br), 9.68-10.11 (1H, br).	Dihydrochloride
23		1H-NMR (DMSO-d6) δ ppm (80℃) : 1.44 (6H, s), 1.47-1.64 (1H, m), 1.67-1.84 (3H, m), 1.86-2.13 (3H, m), 2.14-2.30 (1H, m), 3.60-3.80 (2H, m), 3.92-4.07 (1H, m), 5.80-6.70 (1H, br), 7.04 (1H, d, J = 8.9 Hz), 7.28 (1H, d, J = 8.9 Hz), 9.40-9.75 (2H, br).	Dihydrochloride

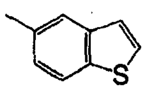
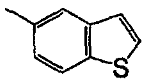
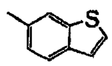
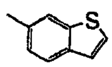
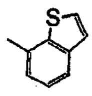
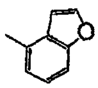
[0293]

Table 5

Relative configuration



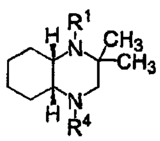
Example	R^1	R^4	NMR	Salt
24	-H		1H-NMR (DMSO) δppm : 1.29-1.57 (3H, m), 1.46 (3H, s), 1.57 (3H, s), 1.69-1.91 (4H, m), 1.98-2.09 (1H, m), 3.07 (1H, d, J = 13.5 Hz), 3.51 (1H, d, J = 13.5 Hz), 3.73-3.92 (1H, m), 4.11-4.30 (1H, m), 7.18 (1H, d, J = 2.2 Hz), 7.22-7.28 (1H, m), 7.36-7.43 (2H, m), 7.68-7.80 (3H, m), 8.02-8.31 (1H, m), 9.62-9.91 (1H, br)	Hydrochloride
25	$-CH_3$		1H-NMR (CDCl3) δppm : 1.21-1.36 (1H, m), 1.40-1.53 (1H, m), 1.48 (3H, s), 1.58-1.77 (2H, m), 1.93 (3H, s), 1.98-2.05 (1H, m), 2.18-2.34 (1H, m), 2.37-2.58 (1H, m), 2.67-2.88 (1H, m), 2.82 (3H, d, J = 4.9 Hz), 3.26 (1H, d, J = 13.4 Hz), 3.64-3.77 (1H, m), 3.91 (1H, d, J = 13.4 Hz), 3.97-4.04 (1H, m), 7.07-7.09 (1H, m), 7.17-7.22 (1H, m), 7.30-7.35 (1H, m), 7.40-7.48 (1H, m), 7.66-7.83 (3H, m), 11.27 (1H, brs)	Hydrochloride
26	-H		1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.57 (3H, s), 1.6-1.95 (4H, m), 1.95-2.15 (1H, m), 3.05 (1H, d, J = 13.3Hz), 3.40 (1H, d, J = 13.4Hz), 3.75-3.9 (4H, m), 4.05-4.2 (1H, m), 4.93 (1H, br), 7.07 (1H, dd, J = 2.5, 8.9Hz), 7.1-7.2 (2H, m), 7.36 (1H, dd, J = 2.3, 9.1Hz), 7.63 (1H, d, J = 9.0Hz), 7.70 (1H, d, J = 9.1Hz), 8.05-8.3 (1H, m), 9.75-10.05 (1H, m).	Dihydrochloride
27	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.1 (2H, m), 1.25-1.45 (1H, m), 1.45-1.7 (7H, m), 1.7-2.1 (4H, m), 2.85 (1H, d, J = 12.7Hz), 3.43 (1H, d, J = 12.8Hz), 3.55-3.7 (1H, m), 4.1-4.3 (1H, m), 6.92 (1H, d, J = 7.7Hz), 7.28 (1H, dd, J = 7.8, 7.8Hz), 7.6-7.7 (2H, m), 7.74 (1H, d, J = 5.5Hz), 7.9-8.2 (1H, m), 9.55-9.85 (1H, m).	Hydrochloride

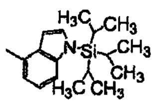
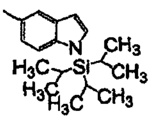
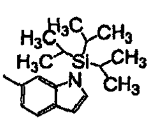
28	-H		1H-NMR (CDCl3) δppm : 1.18-1.28 (1H, m), 1.38-1.50 (2H, m), 1.66 (3H, s), 1.72-2.00 (2H, m), 1.90 (3H, s), 2.07-2.22 (1H, m), 2.39-2.52 (2H, m), 3.05 (1H, d, J = 12.8 Hz), 3.43 (1H, d, J = 12.8 Hz), 3.77-3.90 (1H, m), 3.91-4.01 (1H, m), 7.04 (1H, dd, J = 8.8, 2.2 Hz), 7.21-7.25 (2H ,m), 7.43 (1H, d, J = 5.4 Hz), 7.75 (1H, d, J =8.8 Hz), 8.55-8.97 (1H, br), 9.99-10.37 (1H, br)	Hydrochloride
29	$-CH_3$		1H-NMR (CDCl3) δppm : 1.17-1.34 (1H, m), 1.37-1.74 (2H, m), 1.47 (3H, s), 1.87-2.04 (1H, m), 1.90 (3H, s), 2.20-2.30 (1H, m), 2.39-2.54 (1H, m), 2.64-2.88 (2H, m), 2.75 (3H, d, J = 4.9 Hz), 3.12 (1H, d, J = 13.2 Hz), 3.69-3.74 (1H, m), 3.85-3.93 (1H, m), 3.87 (1H, d, J = 13.2 Hz), 7.01 (1H, dd, J = 8.8, 2.3 Hz), 7.21-7.32 (2H, m), 7.44 (1H, d, J = 5.4 Hz), 7.75 (1H, d, J = 8.8 Hz), 11.20 (1H, brs)	Hydrochloride
30	-H		1H-NMR (CDCl3) δppm : 1.11-1.33 (1H, m), 1.36-1.54 (2H, m), 1.65 (3H, s), 1.72-2.00 (2H, m), 1.90 (3H, s), 2.07-2.29 (1H, m), 2.34-2.60 (2H, m), 3.08 (1H, d, J = 13.2 Hz), 3.42 (1H, d, J = 13.2 Hz), 3.76-4.02 (2H, m), 7.02 (1H, dd, J = 8.7, 2.2 Hz), 7.17-7.31 (3H ,m), 7.70 (1H, d, J = 8.7 Hz), 8.64-9.00 (1H, br), 10.08-10.37 (1H, br)	Hydrochloride
31	$-CH_3$		1H-NMR (CDCl3) δppm : 1.20-1.33 (1H, m), 1.38-1.74 (3H, m), 1.46 (3H, s), 1.90 (3H, s), 1.97-2.11 (1H, m), 2.20-2.30 (1H, m), 2.41-2.56 (1H, m), 2.66-2.89 (1H, m), 2.81 (3H, d, J = 4.8 Hz), 3.16 (1H, d, J = 13.3 Hz), 3.61-3.74 (1H, m), 3.68 (1H, d, J = 13.3 Hz), 3.89-3.99 (1H, m), 6.99 (1H, dd, J = 8.7, 2.1 Hz), 7.20-7.31 (3H, m), 7.70 (1H, d, J = 8.7 Hz), 11.04-11.44 (1H, br)	Hydrochloride
32	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.2 (2H, m), 1.25-1.45 (1H, m), 1.53 (6H, s), 1.6-1.7 (1H, m), 1.7-1.9 (2H, m), 1.9-2.15 (2H, m), 2.92 (1H, d, J = 2.8Hz), 3.48 (1H, d, J = 12.7Hz), 3.75-4.0 (2H, m), 7.02 (1H, d, J = 7.6Hz), 7.34 (1H, dd, J = 7.7, 7.7Hz), 7.48 (1H, d, J = 5.4Hz), 7.61 (1H, d, J = 7.8Hz), 7.76 (1H, d, J = 5.4Hz), 8.17 (1H, br), 9.78 (1H, br).	Hydrochloride
33	-H		1H-NMR (DMSO-d6) δppm : 0.85-1.15 (2H, m), 1.3-1.45 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.6-2.1 (5H, m), 3.04 (1H, d, J = 12.9Hz), 3.2-3.45 (1H, m), 3.75-3.95 (1H, m), 3.95-4.15 (1H, m), 6.6-6.8 (1H, m), 7.1-7.3 (3H, m), 7.94 (1H, d, J = 2.1Hz), 8.07 (1H, br), 9.77 (1H, br).	Hydrochloride

[0294]

Table 6

Relative configuration

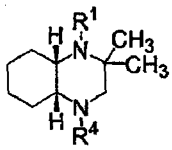


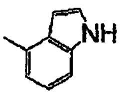
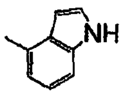
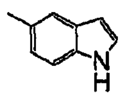
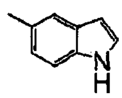
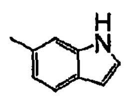
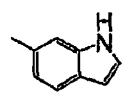
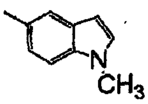
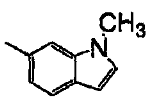
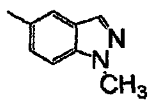
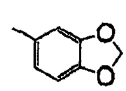
Example	R^1	R^4	NMR	Salt
34	-H		1H-NMR (CDCl3) δppm : 1.15 (18H, d, J = 7.5Hz), 1.20 (3H, s), 1.25-1.45 (6H, m), 1.45-1.8 (8H, m), 1.8-2.0 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.5Hz), 3.6-3.65 (1H, m), 3.65-3.8 (1H, m), 6.50 (1H, d, J = 7.2Hz), 6.64 (1H, d, J = 2.7Hz), 7.00 (1H, dd, J = 7.9, 7.9Hz), 7.11 (1H, d, J = 8.3Hz), 7.16 (1H, d, J = 3.2Hz).	–
35	-H		1H-NMR (CDCl3) δppm : 1.13 (18H, d, J = 7.5Hz), 1.21 (3H, s), 1.25-1.3 (5H, m), 1.35-1.45 (2H, m), 1.53 (1H, br), 1.6-1.8 (7H, m), 2.80 (1H, d, J = 11.7Hz), 2.93 (1H, d, J = 11.5Hz), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 6.48 (1H, d, J = 2.6Hz), 6.85 (1H, dd, J = 2.4, 9.0Hz), 7.02 (1H, d, J = 2.4Hz), 7.16 (1H, d, J = 3.2Hz), 7.36 (1H, d, J = 9.1Hz).	–
36	-H		1H-NMR (CDCl3) δppm : 1.1-1.2 (18H, m), 1.21 (3H, s), 1.25-1.3 (4H, m), 1.3-1.85 (11H, m), 2.79 (1H, d, J = 11.6Hz), 2.91 (1H, d, J = 11.6Hz), 3.45-3.65 (2H, m), 6.45-6.5 (1H, m), 6.82 (1H, dd, J = 2.0, 8.6Hz), 6.93 (1H, s), 7.08 (1H, d, J = 3.2Hz), 7.45 (1H, d, J = 8.6Hz).	–

[0295]

Table 7

Relative configuration

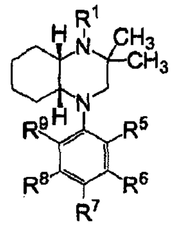


Example	R^1	R^4	NMR	Salt
37	-H		1H-NMR (CDCl3) δppm : 0.95-1.15 (3H, m), 1.21 (3H, s), 1.25-1.45 (6H, m), 1.45-1.8 (2H, m), 1.8-1.95 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.5Hz), 3.6-3.7 (1H, m), 3.75-3.85 (1H, m), 6.50 (1H, dd, J = 0.9, 7.4Hz), 6.55-6.6 (1H, m), 7.00 (1H, d, J = 8.1Hz), 7.07 (1H, dd, J = 7.7, 7.7Hz), 7.14 (1H, dd, J = 2.8, 2.8Hz), 8.18 (1H, br).	—
38	$-CH_3$		1H-NMR (CDCl3) δppm : 1.0-1.15 (5H, m), 1.19 (3H, s), 1.2-1.5 (3H, m), 1.6-1.7 (1H, m), 2.0-2.3 (5H, m), 2.76 (1H, d, J = 11.5Hz), 3.05-3.15 (1H, m), 3.38 (1H, d, J = 11.4Hz), 3.6-3.9 (1H, m), 6.49 (1H, d, J = 7.4Hz), 6.55-6.6 (1H, m), 6.99 (1H, d, J = 7.4Hz), 7.07 (1H, dd, J =7.8, 7.8Hz), 7.13 (1H, dd, J = 2.8, 2.8Hz), 8.11 (1H, br).	—
39	-H		1H-NMR (CDCl3) δppm : 1.0-1.85 (15H, m), 2.82 (1H, d, J = 11.5Hz), 2.88 (1H, d, J = 11.5Hz), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 6.4-6.45 (1H, m), 6.95 (1H, dd, J = 2.3, 8.8Hz), 7.04 (1H, d, J = 2.2Hz), 7.13 (1H, dd, J = 2.8, 2.8Hz), 7.25-7.3 (1H, m), 7.98 (1H, br).	—
40	$-CH_3$		1H-NMR (CDCl3) δppm : 1.06 (3H, s), 1.1-1.55 (8H, m), 1.6-1.75 (1H, m), 1.95-2.15 (2H, m), 2.18 (3H, s), 2.80 (1H, d, J = 11.4Hz), 2.95-3.0 (1H, m), 3.10 (1H, d, J = 11.4Hz), 3.55-3.7 (1H, m), 6.35-6.45 (1H, m), 6.94 (1H, dd, J = 2.3, 8.8Hz), 7.03 (1H, d, J = 2.0Hz), 7.12 (1H, dd, J = 2.8, 2.8Hz), 7.2-7.3 (1H, m), 7.94 (1H, br).	—
41	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.4 (9H, m), 1.4-1.9 (5H, m), 2.82 (1H, d, J = 11.9Hz), 2.95 (1H, d, J = 12.0Hz), 3.0-4.5 (4H, m), 6.25 (1H, dd, J = 2.4, 2.4Hz), 6.47 (1H, s), 6.7-6.8 (2H, m), 7.10 (1H, dd, J = 2.7, 2.7Hz), 7.34 (1H, d, J = 9.3Hz), 10.65 (1H, s).	Hemifumarate
42	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.95-1.5 (11H, m), 1.55-1.7 (1H, m), 1.85-2.1 (2H, m), 2.18 (3H, s), 2.65-4.2 (8H, m), 6.2-6.25 (1H, m), 6.60 (2H, s), 6.7-6.8 (2H, s), 7.09 (1H, dd, J = 2.4, 3.0Hz), 7.33 (1H, d, J = 8.5Hz), 10.60 (1H, s).	Fumarate
43	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.4 (9H, m), 1.45-1.9 (5H, m), 2.88 (2H, dd, J = 12.3, 15.1Hz), 3.5-3.6 (1H, m), 3.6-3.75 (4H, m), 6.24 (1H, dd, J = 0.6, 3.0Hz), 6.47 (1H, s), 6.85-7.0 (2H, m), 7.18 (1H, d, J = 3.0Hz), 7.27 (1H, d, J = 9.5Hz).	Hemifumarate
44	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.4-1.9 (6H, m), 2.85 (1H, d, J = 12.1Hz), 3.03 (1H, d, J = 12.1Hz), 3.5-3.6 (1H, m), 3.69 (3H, s), 3.75-3.85 (1H, m), 6.24 (1H, d, J = 3.1Hz), 6.49 (2H, s), 6.7-6.85 (2H, m), 7.07 (1H, d, J = 3.1Hz), 7.34 (1H, d, J = 8.6Hz).	Fumarate
45	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.3 (2H, m), 1.3-1.45 (7H, m), 1.5-1.95 (5H, m), 2.9-3.1 (2H, m), 3.71 (1H, br), 3.8-3.95 (1H, m), 3.98 (3H, s), 6.54 (3H, s), 7.04 (1H, s), 7.27 (1H, dd, J = 1.9, 9.2Hz), 7.51 (1H, d, J = 9.1Hz), 7.83 (1H, s), 10.6 (4H, br).	3/2 Fumarate
46	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.45 (4H, m), 1.50 (3H, s), 1.6-1.9 (4H, m), 1.9-2.1 (1H, m), 2.92 (1H, d, J = 13.2Hz), 3.11 (1H, d, J = 13.2Hz), 3.5-4.05 (3H, m), 5.91 (2H, d, J = 1.0Hz), 6.32 (1H, dd, J = 2.4, 8.5Hz), 6.71 (1H, d, J = 2.3Hz), 6.76 (1H, d, J = 8.4Hz), 8.06 (1H, br), 9.83 (1H, br).	Dihydrochloride

[0296]

Table 8

Relative configuration



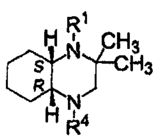
Example	R^1	R^5	R^6	R^7	R^8	R^9	NMR	Salt
47	-H	-H	-H	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.5 (4H, m), 1.53 (3H, s), 1.6-1.95 (4H, m), 1.95-2.15 (1H, m), 2.94 (1H, d, J = 13.3Hz), 3.24 (1H, d, J = 13.2Hz), 3.65-3.85 (1H, m), 3.85-4.0 (1H, m), 5.30 (1H, br), 6.9-7.0 (2H, m), 7.0-7.1 (2H, m), 8.0-8.35 (1H, m), 10.03 (1H, d, J = 10.5Hz).	Dihydrochloride
48	-H	-H	-H	-F	-F	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.35 (6H, m), 1.52 (3H, s), 1.6-1.95 (4H, m), 1.95-2.15 (1H, m), 2.93 (1H, d, J = 13.5Hz), 3.36 (1H, d, J = 13.5Hz), 3.65-3.8 (1H, m), 3.9-4.1 (1H, m), 6.6-6.8 (1H, m), 6.9-7.1 (1H, m), 7.25 (1H, dd, J = 9.5, 19.7Hz), 8.0-8.4 (1H, m), 10.02 (1H, d, J = 11.3Hz).	Hydrochloride
49	-H	-H	-F	-H	-F	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.6 (9H, m), 1.6-2.05 (5H, m), 2.95 (1H, d, J = 14.0Hz), 3.56 (1H, d, J = 13.9Hz), 3.6-3.75 (1H, m), 4.0-4.15 (1H, m), 6.35-6.55 (1H, m), 6.5-6.75 (2H, m), 8.05-8.4 (1H, m), 9.65-10.2 (1H, m).	Hydrochloride
50	-H	-H	-F	-OCH$_3$	-F	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.50 (3H, s), 1.6-1.9 (4H, m), 1.9-2.05 (1H, m), 2.90 (1H, d, J = 13.7Hz), 3.42 (1H, d, J = 13.7Hz), 3.6-3.75 (1H, m), 3.78 (3H, s), 3.9-4.05 (1H, m), 6.65-6.8 (2H, m), 8.17 (1H, br), 9.86 (1H, br).	Hydrochloride
51	-CH$_3$	-H	-F	-OCH$_3$	-F	-H	1H-NMR (DMSO-d6) δppm : 0.96 (3H, s), 1.05-1.2 (4H, m), 1.2-1.5 (4H, m), 1.55-1.75 (1H, m), 1.85-2.1 (2H, m), 2.16 (3H, s), 2.75-2.9 (2H, m), 3.12 (1H, d, J = 12.4Hz), 3.65-3.85 (4H, m), 6.55-6.85 (5H, m).	3/2 Fumarate
52	-H	-H	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.05 (5H, m), 2.94 (1H, d, J = 13.7Hz), 3.48 (1H, d, J = 14.0Hz), 3.65-3.8 (1H, m), 4.0-4.15 (1H, m), 6.77 (1H, dd, J = 1.5, 7.8Hz), 6.90 (1H, dd, J = 2.3, 8.4Hz), 6.95-7.0 (1H, m), 7.21 (1H, dd, J = 8.1, 8.1Hz), 8.14 (1H, br), 9.55-10.0 (1H, m).	Hydrochloride
53	-CH$_3$	-H	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.97 (3H, s), 1.05-1.2 (4H, m), 1.2-1.5 (4H, m), 1.6-1.75 (1H, m), 1.9-2.1 (2H, m), 2.15 (3H, s), 2.65-5.05 (6H, m), 6.61 (2H, s), 6.66 (1H, dd, J = 1.2, 7.8Hz), 6.75-6.9 (2H, m), 7.15 (1H, dd, J = 8.1, 8.1Hz).	Fumarate
54	-H	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.52 (3H, s), 1.6-2.1 (5H, m), 2.93 (1H, d, J = 13.6Hz), 3.39 (1H, d, J = 13.9Hz), 3.65-3.8 (1H, m), 3.9-4.1 (1H, m), 6.9-7.0 (2H, m), 7.15-7.3 (2H, m), 7.95-8.4 (1H, m), 9.65-10.1 (1H, m).	Hydrochloride
55	-CH$_3$	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.99 (3H, s), 1.05-1.5 (8H, m), 1.55-1.75 (1H, m), 1.85-2.1 (2H, m), 2.17 (3H, s), 2.8-2.95 (2H, m), 3.12 (1H, d, J = 12.3Hz), 3.7-3.85 (1H, m), 6.61 (2H, s), 6.8-6.9 (2H, m), 7.1-7.2 (2H, m).	Fumarate
56	-H	-H	-Cl	-Cl	-H	-H	1H-NMR (DMSO) δppm : 1.21-1.62 (2H, m), 1.38 (3H, s), 1.53 (3H, s), 1.67-2.09 (8H, m), 2.95 (1H, d, J = 13.6 Hz), 3.48 (1H, d, J = 13.6 Hz), 3.70-3.74 (1H, m), 4.04-4.10 (1H, m), 6.95 (1H, dd, J = 8.7, 2.6 Hz), 7.17 (1H, d, J = 2.6 Hz), 7.40 (1H, d, J = 8.7 Hz), 8.03-8.52 (1H, br), 9.77-10.21 (1H, br)	Hydrochloride

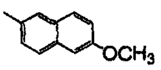
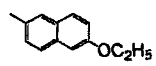
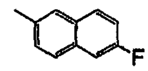
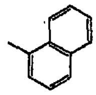
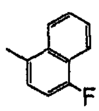
57	$-CH_3$	-H	-Cl	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.23-1.72 (4H, m), 1.42 (3H, s), 1.69 (3H, s), 2.01-2.11 (1H, m), 2.20-2.29 (1H, m), 2.37-2.55 (1H, m), 2.68-2.83 (1H, m), 2.79 (3H, d, J = 4.8 Hz), 3.09 (1H, d, J = 13.5 Hz), 3.54-3.65 (1H, m), 3.76-3.83 (1H, m), 3.78 (1H, d, J = 13.5 Hz), 6.88 (1H, dd, J = 9.0, 2.9 Hz), 6.92 (1H, d, J = 2.9 Hz), 7.30 (1H, d, J = 9.0 Hz), 11.48 (1H, brs)	Hydrochloride
58	-H	-H	-Cl	-F	-H	-H	1H-NMR (DMSO) δppm : 1.24-1.57 (3H, m), 1.37 (3H, s), 1.52 (3H, s), 1.64-1.81 (4H, m), 1.87-2.01 (1H, m), 2.92 (1H, d, J = 13.1 Hz), 3.45 (1H, d, J = 13.1 Hz), 3.65-3.79 (1H, m), 3.90-4.06 (1H, m), 6.89-6.94 (1H, m), 7.08-7.11 (1H, m), 7.20-7.27 (1H, m), 7.90-8.21 (1H, br), 9.55-9.81 (1H, br)	Hydrochloride

[0297]

Table 9

Absolute configuration

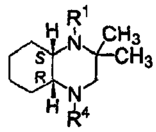


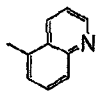
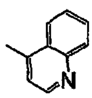
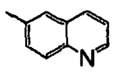
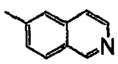
Example	R^1	R^4	NMR	Salt
59	-H		1H-NMR (CDCl3) δppm : 1.15-1.35 (8H, m), 1.35-1.85 (7H, m), 2.82 (1H, d, J = 11.7Hz), 3.05 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.88 (3H, s), 6.97 (1H, d, J = 2.4Hz), 7.0-7.1 (2H, m), 7.22-7.29 (1H, m), 7.55 (1H, d, J = 8.8Hz), 7.61 (1H, d, J = 9.0Hz).	–
60	-H		1H-NMR (CDCl3) δppm : 1.15-1.3 (8H, m), 1.3-1.5 (6H, m), 1.65-1.85 (4H, m), 2.82 (1H, d, J = 11.7Hz), 3.04 (1H, d, J = 11.7Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 4.11 (2H, q, J = 7.0Hz), 6.96 (1H, d, J = 2.4Hz), 7.03 (1H, d, J = 2.4Hz), 7.06 (1H, dd, J = 2.5, 8.8Hz), 7.2-7.3 (1H, m), 7.55 (1H, d, J = 8.9Hz), 7.59 (1H, d, J = 9.0Hz).	–
61	-H		1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.56 (3H, s), 1.65-2.1 (5H, m), 3.06 (1H, d, J = 13.4Hz), 3.48 (1H, d, J = 13.4Hz), 3.8-3.9 (1H, m), 4.1-4.2 (1H, m), 4.42 (1H, br), 7.24 (1H, d, J = 2.2Hz), 7.31 (1H, ddd, J = 4.5, 12.8, 12.8Hz), 7.47 (1H, dd, J = 2.3, 9.2Hz), 7.54 (1H, dd, J = 2.6, 10.2Hz), 7.75-7.8 (2H, m), 8.1-8.25 (1H, m), 9.75-9.95 (1H, m).	Dihydrochloride
62	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.1 (2H, m), 1.3-1.4 (1H, m), 1.5-1.65 (7H, m), 1.65-1.85 (2H, m), 1.9-2.1 (2H, m), 2.81 (1H, d, J = 1.26Hz), 3.4-3.6 (2H, m), 4.2-4.35 (1H, m), 7.13 (1H, d, J = 7.0Hz), 7.43 (1H, dd, J = 7.8, 7.8Hz), 7.5-7.6 (2H, m), 7.65 (1H, d, J = 8.2Hz), 7.85-7.95 (1H, m), 7.95-8.15 (1H, m), 8.2-8.3 (1H, m), 9.65-9.85 (1H, m).	Hydrochloride
63	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.15 (2H, m), 1.3-1.4 (1H, m), 1.5-1.7 (7H, m), 1.7-1.85 (2H, m), 1.9-2.1 (2H, m), 2.77 (1H, d, J = 12.6Hz), 3.3-3.45 (1H, m), 3.52 (1H, d, J = 12.6Hz), 4.2-4.3 (1H, m), 7.05-7.15 (1H, m), 7.25 (1H, dd, J = 8.2, 10.5Hz), 7.6-7.7 (2H, m), 8.0-8.15 (2H, m), 8.3-8.4 (1H, m), 9.7-9.95 (1H, m).	Hydrochloride

[0298]

Table 10

Absolute configuration

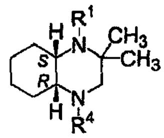


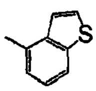
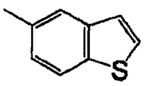
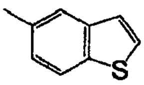
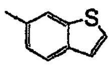
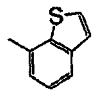
Example	R^1	R^4	NMR	Salt
64	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.1 (2H, m), 1.3-1.4 (1H, m), 1.5-1.7 (7H, m), 1.7-1.9 (2H, m), 1.95-2.15 (2H, m), 2.89 (1H, d, J = 12.7Hz), 3.0-4.2 (4H, m), 4.3-4.4 (1H, m), 7.35-7.5 (1H, m), 7.8-8.05 (3H, m), 8.05-8.3 (1H, m), 9.1-9.4 (2H, m), 10.0-10.25 (1H, m).	Trihydrochloride
65	-H		1H-NMR (CDCl3) δppm : 0.9-1.05 (3H, m), 1.24 (3H, s), 1.35-1.45 (5H, m), 1.55-1.8 (3H, m), 1.9-2.05 (1H, m), 2.71 (1H, d, J = 11.3Hz), 3.25 (1H, d, J = 11.3Hz), 3.65-3.75 (1H, m), 3.75-3.85 (1H, m), 6.76 (1H, d, J = 5.0Hz), 7.45-7.5 (1H, m), 7.6-7.7 (1H, m), 8.0-8.1 (2H, m), 8.68 (1H, d, J = 5.0Hz).	–
66	-H		1H-NMR (DMSO-d6) δppm : 1.35-1.5 (6H, m), 1.62 (3H, s), 1.7-2.0 (3H, m), 2.0-2.15 (2H, m), 2.7-4.3 (4H, m), 4.25-4.4 (1H, m), 7.57 (1H, d, J = 2.6Hz), 7.90 (1H, d, J = 5.2, 8.5Hz), 8.04 (1H, dd, J = 2.7, 9.6Hz), 8.24 (1H, d, J = 9.5Hz), 8.5-8.6 (1H, m), 8.79 (1H, d, J = 8.4Hz), 8.93 (1H, dd, J = 1.3, 5.2Hz), 10.22 (1H, d, J = 10.1Hz).	Dihydrochloride
67	-H		1H-NMR (DMSO-d6) δppm : 1.41 (3H, s), 1.45-1.6 (3H, m), 1.62 (3H, s), 1.7-1.85 (2H, m), 1.85-2.0 (1H, m), 2.05-2.25 (2H, m), 3.27 (1H, d, J = 14.5Hz), 3.37 (1H, br), 3.75-3.85 (1H, m), 4.09 (1H, d, J = 14.4Hz), 4.4-4.5 (1H, m), 7.50 (1H, d, J = 2.1Hz), 7.85 (1H, dd, J = 2.4, 9.5Hz), 7.93 (1H, d, J = 6.8Hz), 8.25-8.35 (2H, m), 8.6-8.75 (1H, m), 9.36 (1H, s), 10.2-10.4 (1H, m).	Dihydrochloride

[0299]

Table 11

Absolute configuration

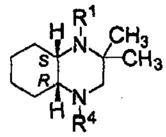


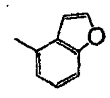
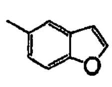
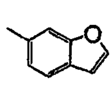
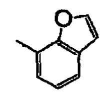
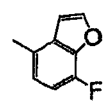
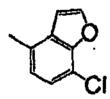
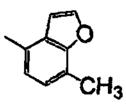
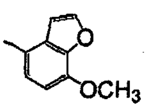
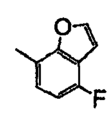
Example	R^1	R^4	NMR	Salt
68	-H		1H-NMR (CDCl3) δppm : 0.9-1.1 (2H, m), 1.22 (3H, s), 1.3-1.45 (6H, m), 1.45-1.8 (3H, m), 1.8-2.0 (1H, m), 2.65 (1H, d, J = 11.3Hz), 3.19 (1H, d, J = 11.3Hz), 3.45-3.55 (1H, m), 3.65-3.75 (1H, m), 6.79 (1H, d, J = 7.6Hz), 7.15-7.3 (1H, m), 7.38 (1H, d, J = 5.5Hz), 7.44 (1H, d, J = 5.5Hz), 7.51 (1H, d, J = 8.0Hz).	—
69	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.5 (4H, m), 1.55 (3H, s), 1.6-2.15 (5H, m), 3.03 (1H, d, J = 13.2Hz), 3.35 (1H, d, J = 13.2Hz), 3.71 (1H, br), 3.75-3.9 (1H, m), 3.95-4.15 (1H, m), 7.16 (1H, dd, J = 2.1, 9.0Hz), 7.29 (1H, d, J = 5.4Hz), 7.35 (1H, d, J = 2.0Hz), 7.68 (1H, d, J = 5.4Hz), 7.82 (1H, d, J = 8.9Hz), 8.05-8.25 (1H, m), 9.75-10.0 (1H, m).	Dihydrochloride
70	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.95-1.5 (11H, m), 1.55-1.75 (1H, m), 1.85-2.1 (2H, m), 2.19 (3H, s), 2.65-5.05 (6H, m), 6.61 (2H, s), 7.10 (1H, dd, J = 2.4, 9.0Hz), 7.24 (1H, d, J = 2.3Hz), 7.27 (1H, dd, J = 0.5, 5.4Hz), 7.62 (1H, d, J = 5.4Hz), 7.75 (1H, d, J = 8.9Hz).	Fumarate
71	-H		1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.54 (3H, s), 1.6-2.1 (5H, m), 3.03 (1H, d, J = 13.4Hz), 3.43 (1H, d, J = 13.6Hz), 3.7-3.9 (1H, m), 4.0-4.2 (1H, m), 7.14 (1H, dd, J = 2.2, 8.9Hz), 7.27 (1H, d, J = 5.4Hz), 7.4-7.55 (2H, m), 7.71 (1H, d, J = 8.8Hz), 8.14 (1H, br), 9.84 (1H, br).	Hydrochloride
72	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.2 (2H, m), 1.3-1.45 (1H, m), 1.45-1.7 (7H, m), 1.7-1.9 (2H, m), 1.9-2.2 (2H, m), 2.91 (1H, d, J = 12.8Hz), 3.48 (1H, d, J = 12.9Hz), 3.75-4.0 (2H, m), 7.01 (1H, d, J = 7.5Hz), 7.34 (1H, dd, J = 7.7, 7.7Hz), 7.48 (1H, d, J = 5.4Hz), 7.61 (1H, d, J = 7.7Hz), 7.76 (1H, d, J = 5.4Hz), 8.24 (1H, br), 9.94 (1H, br).	Hydrochloride

[0300]

Table 12

Absolute configuration

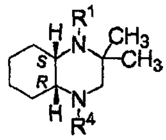


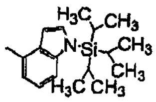
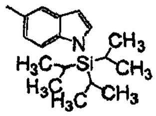
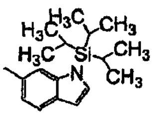
Example	R^1	R^4	NMR	Salt
73	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.3-1.45 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.55-2.05 (5H, m), 3.04 (1H, d, J = 12.9Hz), 3.2-3.4 (1H, m), 3.75-3.9 (1H, m), 4.0-4.15 (1H, m), 6.71 (1H, dd, J = 3.0, 5.5Hz), 7.15-7.25 (3H, m), 7.94 (1H, d, J = 2.2Hz), 8.08 (1H, br), 9.80 (1H, br).	Hydrochloride
74	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.5 (4H, m), 1.54 (3H, s), 1.6-1.95 (4H, m), 1.95-2.1 (1H, m), 3.03 (1H, d, J = 13.1Hz), 3.21 (1H, d, J = 13.1Hz), 3.75-3.9 (1H, m), 3.9-4.0 (1H, m), 4.83 (1H, br), 6.8-6.85 (1H, m), 7.03 (1H, dd, J = 2.5, 9.0Hz), 7.13 (1H, d, J = 2.4Hz), 7.46 (1H, d, J =9.0Hz), 7.90 (1H, d, J = 2.2Hz), 8.11 (1H, br), 9.91 (1H, br).	Dihydrochloride
75	-H		1H-NMR (DMSO-d6) δppm : 1.15-1.5 (6H, m), 1.55 (3H, s), 1.6-1.95 (4H, m), 1.95-2.15 (1H, m), 3.01 (1H, d, J = 13.4Hz), 3.36 (1H, d, J = 13.1Hz), 3.7-3.85 (1H, m), 3.95-4.05 (1H, m), 4.50 (1H, br), 6.80 (1H, d, J = 2.1Hz), 6.98 (1H, dd, J = 1.9, 8.7Hz), 7.13 (1H, s), 7.47 (1H, d, J = 8.6Hz), 7.79 (1H, d, J = 0.7H), 8.20 (1H, br), 9.85-10.2 (1H, m).	Dihydrochloride
76	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.45 (1H, m), 1.50 (3H, s), 1.54 (3H, s), 1.6-1.9 (3H, m), 1.9-2.1 (2H, m), 3.2-3.4 (2H, m), 3.9-4.0 (1H, m), 4.15-4.25 (1H, m), 6.80 (1H, d, J = 7.2Hz), 6.93 (1H, d, J = 2.2Hz), 7.12 (1H, dd, J = 7.7, 7.7Hz), 7.21 (1H, dd, J = 0.8, 7.7Hz), 7.97 (1H, d, J = 2.2Hz), 8.1-8.35 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride
77	-H		1H-NMR (CDCl3) δppm : 1.0-1.45 (11H, m), 1.6-1.8 (3H, m), 1.8-1.95 (1H, m), 2.70 (1H, d, J = 11.3Hz), 3.04 (1H, d, J = 11.3Hz), 3.50 (1H, ddd, J = 3.8, 3.8, 12.1Hz), 3.55-3.65 (1H, m), 6.47 (1H, dd, J = 3.4, 8.6Hz), 6.84 (1H, dd, J = 2.5, 2.5Hz), 6.89 (1H, dd, J = 8.6, 10.4Hz), 7.60 (1H, d, J = 2.2Hz).	–
78	-H		1H-NMR (CDCl3) δppm : 1.0-1.15 (2H, m), 1.20 (3H, s), 1.25-1.45 (6H, m), 1.6-1.8 (3H, m), 1.8-1.95 (1H, m), 2.79 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.4Hz), 3.55-3.65 (2H, m), 6.53 (1H, d, J = 8.4Hz), 6.84 (1H, d, J = 2.2Hz), 7.14 (1H, d, J = 8.4Hz), 7.61 (1H, d, J = 2.2Hz).	–
79	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.1 (2H, m), 1.3-1.4 (1H, m), 1.51 (3H, s), 1.52 (3H, s), 1.6-1.7 (1H, m), 1.7-1.95 (3H, m), 1.95-2.05 (1H, m), 2.39 (3H, s), 2.95 (1H, d, J = 12.8Hz), 3.28 (1H, d, J = 12.9Hz), 3.7-3.8 (1H, m), 4.0-4.15 (1H, m), 6.61 (1H, d, J = 7.9Hz), 6.99 (1H, d, J = 8.0Hz), 7.20 (1H, d, J = 2.2Hz), 7.95 (1H, d, J = 2.2Hz), 7.95-8.15 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride
80	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.1 (2H, m), 1.3-1.4 (1H, m), 1.52 (6H, s), 1.55-1.65 (1H, m), 1.65-1.95 (3H, m), 1.95-2.1 (1H, m), 2.85 (1H, d, J = 12.7Hz), 3.27 (1H, d, J = 12.8Hz), 3.6-3.7 (1H, m), 3.87 (3H, s), 4.0-4.15 (1H, m), 6.61 (1H, d, J = 8.4Hz), 6.79 (1H, d, J = 8.4Hz), 7.21 (1H, d, J = 2.2Hz), 7.95 (1H, d, J = 2.2Hz), 7.95-8.15 (1H, m), 9.75-10.0 (1H, m).	Hydrochloride
81	-H		1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.50 (3H, s), 1.53 (3H, s), 1.6-1.9 (3H, m), 1.9-2.1 (2H, m), 3.17 (1H, d, J = 13.0Hz), 3.29 (1H, d, J = 13.2Hz), 3.9-4.0 (1H, m), 4.0-4.1 (1H, m), 6.80 (1H, dd, J = 4.4, 8.7Hz), 6.98 (1H, dd, J = 8.9, 8.9Hz), 7.06 (1H, d, J = 2.2Hz), 8.06 (1H, d, J = 2.2Hz), 8.1-8.3 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride

[0301]

Table 13

Absolute configuration

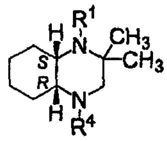


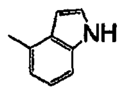
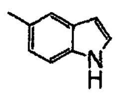
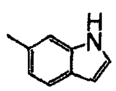
Example	R^1	R^4	NMR	Salt
82	-H		1H-NMR (CDCl3) δppm : 1.1-1.2 (20H, m), 1.20 (3H, s), 1.3-1.45 (6H, m), 1.55-1.8 (6H, m), 1.8-2.0 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.5Hz), 3.6-3.7 (1H, m), 3.7-3.8 (1H, m), 6.50 (1H, d, J = 7.4Hz), 6.64 (1H, d, J = 3.1Hz), 7.00 (1H, dd, J = 7.9, 7.9Hz), 7.11 (1H, d, J = 8.3Hz), 7.16 (1H, d, J = 3.2Hz).	–
83	-H		1H-NMR (CDCl3) δppm : 1.13 (18H, d, J = 7.5Hz), 1.21 (3H, s), 1.28 (3H, s), 1.3-1.6 (5H, m), 1.55-1.8 (7H, m), 2.80 (1H, d, J = 11.6Hz), 2.93 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 6.48 (1H, d, J = 3.1Hz), 6.85 (1H, dd, J = 2.4, 9.0Hz), 7.02 (1H, d, J = 2.4Hz), 7.16 (1H, d, J = 3.1Hz), 7.35 (1H, d, J = 9.0Hz).	–
84	-H		1H-NMR (CDCl3) δppm : 1.1-1.2 (18H, m), 1.21 (3H, s), 1.29 (3H, s), 1.3-1.5 (5H, m), 1.55-1.8 (7H, m), 2.79 (1H, d, J = 11.6Hz), 2.91 (1H, d, J = 11.6Hz), 3.45-3.6 (2H, m), 6.48 (1H, d, J = 3.2Hz), 6.62 (1H, dd, J = 2.0, 8.6Hz), 6.93 (1H, s), 7.08 (1H, d, J = 3.2Hz), 7.45 (1H, d, J = 8.6Hz).	–

[0302]

Table 14

Absolute configuration

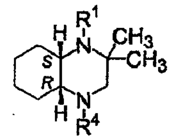


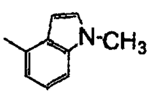
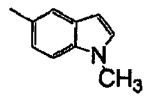
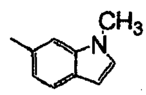
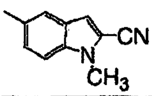
Example	R^1	R^4	NMR	Salt
85	-H		1H-NMR (CDCl3) δppm : 0.9-1.15 (2H, m), 1.21 (3H, s), 1.25-1.45 (5H, m), 1.5-1.8 (4H, m), 1.8-2.0 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.5Hz), 3.6-3.75 (1H, m), 3.75-3.85 (1H, m), 6.50 (1H, dd, J = 0.9, 7.4Hz), 6.55-6.6 (1H, m), 6.95-7.05 (1H, m), 7.07 (1H, dd, J = 7.7, 7.7Hz), 7.14 (1H, dd, J = 2.8, 2.8Hz), 8.15 (1H, br).	–
86	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.35 (7H, bs), 1.45-1.9 (5H, m), 2.93 (2H, s), 3.6-3.8 (2H, m), 6.2-6.3 (1H, m), 6.50 (2H, s), 6.86 (1H, dd, J = 2.1, 8.8Hz), 6.95 (1H, d, J = 1.8Hz), 7.15-7.3 (2H, m), 10.80 (1H, s).	Fumarate
87	-H		1H-NMR (CDCl3) δppm : 1.05-1.85 (15H, m), 2.79 (1H, d, J = 11.6Hz), 2.94 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.6-3.75 (1H, m), 6.35-6.45 (1H, m), 6.79 (1H, s), 6.86 (1H, dd, J = 2.1, 8.7Hz), 7.03 (1H, dd, J = 2.4, 3.2Hz), 7.47 (1H, d, J = 8.7Hz), 7.89 (1H, br).	–

[0303]

Table 15

Absolute configuration

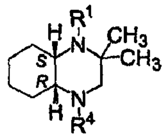


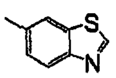
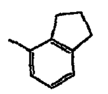
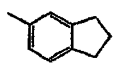
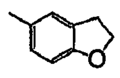
Example	R¹	R⁴	NMR	Salt
88	-H		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (2H, m), 1.25-1.4 (4H, m), 1.40 (3H, s), 1.5-2.0 (5H, m), 2.82 (1H, d, J = 8.2Hz), 3.21 (1H, d, J = 12.2Hz), 3.74 (3H, s), 3.8-3.9 (2H, m), 6.44 (1H, dd, J = 2.5, 5.8Hz), 6.5-6.55 (3H, m), 6.95-7.05 (2H, m), 7.22 (1H, d, J = 3.1Hz).	Fumarate
89	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.32 (7H, bs), 1.45-1.85 (6H, m), 2.85-2.95 (2H, m), 3.63 (1H, br), 3.65-3.8 (4H, m), 6.24 (1H, dd, J = 0.6, 3.0Hz), 6.50 (2H, s), 6.9-7.0 (2H, m), 7.19 (1H, d, J = 3.0Hz), 7.28 (1H, d, J = 8.6Hz).	Fumarate
90	-H		1H-NMR (DMSO-d6) δppm : 1.05-1.3 (2H, m), 1.3-1.45 (7H, m), 1.5-1.9 (5H, m), 2.90 (1H, d, J = 12.4Hz), 3.08 (1H, d, J = 12.3Hz), 3.62 (1H, br), 3.70 (3H, s), 3.8-3.9 (1H, m), 6.25 (1H, d, J = 3.0Hz), 6.52 (2H, s), 6.75-6.85 (2H, m), 7.09 (1H, d, J = 3.1Hz), 7.35 (1H, d, J = 8.6Hz).	Fumarate
91	-H		1H-NMR (CDCl3) δppm : 0.6-2.4 (15H, m), 2.7-3.3 (2H, m), 3.4-3.8 (2H, m), 3.85 (3H, s), 6.95-7.05 (2H, m), 7.15-7.3 (2H, m).	-

[0304]

Table 16

Absolute configuration

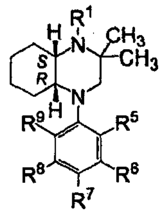


Example	R¹	R⁴	NMR	Salt
92	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.45-1.75 (4H, m), 1.8-1.95 (1H, m), 2.80 (1H, d, J = 12.3Hz), 3.20 (1H, d, J = 12.3Hz), 3.4-3.5 (1H, m), 3.8-3.9 (1H, m), 6.51 (1H, s), 7.20 (1H, dd, J = 2.5, 9.1Hz), 7.51 (1H, d, J = 2.4Hz), 7.85 (1H, d, J = 9.1Hz), 9.01 (1H, s).	Hemifumarate
93	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.45 (1H, m), 1.48 (3H, s), 1.50 (3H, s), 1.55-1.7 (1H, m), 1.7-2.15 (6H, m), 2.7-2.95 (5H, m), 3.28 (1H, d, J = 12.8Hz), 3.35-3.45 (1H, m), 3.75-3.95 (1H, m), 6.68 (1H, d, J = 7.8Hz), 6.90 (1H, d, J = 7.2Hz), 7.05 (1H, dd, J = 7.6, 7.6Hz), 7.95-8.2 (1H, m), 9.75-10.0 (1H, m).	Hydrochloride
94	-H		1H-NMR (DMSO-d6) δppm : 1.15-1.3 (2H, m), 1.3-1.5 (4H, m), 1.53 (3H, s), 1.6-1.9 (4H, m), 1.9-2.1 (3H, m), 2.74 (2H, t, J = 7.3Hz), 2.79 (2H, t, J = 7.4Hz), 2.93 (1H, d, J = 13.2Hz), 3.22 (1H, d, J = 13.3Hz), 3.65-3.8 (1H, m), 3.85-4.0 (1H, m), 6.70 (1H, dd, J = 2.2, 8.2Hz), 6.8-6.85 (1H, m), 7.05 (1H, d, J = 8.2Hz), 7.8-8.4 (2H, m), 9.85-10.2 (1H, m).	Dihydrochloride
95	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.5 (4H, m), 1.51 (3H, s), 1.6-1.9 (4H, m), 2.0-2.1 (1H, m), 2.95 (1H, d, J = 13.0Hz), 3.02 (1H, d, J = 13.0Hz), 3.11 (2H, t, J = 8.6Hz), 3.7-3.85 (2H, m), 4.44 (2H, t, J = 8.6Hz), 4.7-5.6 (1H, m), 6.6-6.7 (2H, m), 6.85-6.95 (1H, m), 8.09 (1H, br), 9.94 (1H, br).	Dihydrochloride

[0305]

Table 17

Absolute configuration



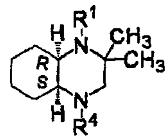
Example	R^1	R^5	R^6	R^7	R^8	R^9	NMR	Salt
96	-H	-F	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.25 (2H, m), 1.35-1.45 (1H, m), 1.46 (3H, s), 1.49 (3H, s), 1.6-1.85 (3H, m), 1.85-2.05 (2H, m), 2.93 (1H, d, J = 13.1Hz), 3.27 (1H, d, J = 13.2Hz), 3.55-3.65 (1H, m), 3.8-3.9 (1H, m), 6.95-7.05 (1H, m), 7.05-7.2 (3H, m), 8.0-8.2 (1H, m), 9.55-9.75 (1H, m).	Hydrochloride
97	-H	-H	-H	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.45 (4H, m), 1.53 (3H, s), 1.6-1.95 (4H, m), 1.95-2.15 (1H, m), 2.94 (1H, d, J = 13.3Hz), 3.24 (1H, d, J = 13.3Hz), 3.65-3.85 (1H, m), 3.85-4.0 (1H, m), 4.2-5.8 (1H, m), 6.85-7.0 (2H, m), 7.0-7.1 (2H, m), 8.19 (1H, br), 10.05 (1H, br).	Dihydrochloride
98	-H	-H	-F	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.35-1.45 (4H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 2.0-2.1 (1H, m), 2.90 (1H, d, J = 13.3Hz), 3.22 (1H, d, J = 13.2Hz), 3.65-3.8 (4H, m), 3.85-3.95 (1H, m), 6.6-6.7 (1H, m), 6.89 (1H, dd, J = 2.9, 14.7Hz), 7.02 (1H, dd, J = 9.5, 9.5Hz), 8.05-8.25 (1H, m), 9.94 (1H, br).	Dihydrochloride
99	-H	-H	$-OCH_3$	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.55 (3H, s), 1.6-1.95 (4H, m), 2.0-2.15 (1H, m), 2.95 (1H, d, J = 13.2Hz), 3.24 (1H, d, J = 13.2Hz), 3.7-3.8 (1H, m), 3.82 (3H, s), 3.9-4.0 (1H, m), 6.4-6.5 (1H, m), 6.70 (1H, dd, J = 2.8, 7.6Hz), 7.03 (1H, dd, J = 8.9, 11.3Hz), 8.0 (1H, br), 8.15-8.35 (1H, m), 10.0-10.15 (1H, m).	Dihydrochloride
100	-H	-F	-F	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.3 (2H, m), 1.35-1.45 (1H, m), 1.46 (3H, s), 1.50 (3H, s), 1.6-1.85 (3H, m), 1.9-2.05 (2H, m), 3.00 (1H, d, J = 13.2Hz), 3.28 (1H, d, J = 13.2Hz), 3.6-3.7 (1H, m), 3.8-3.9 (1H, m), 6.85-6.95 (1H, m), 6.95-7.05 (1H, m), 7.05-7.15 (1H, m), 8.05-8.35 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride
101	-H	-H	-H	-F	-F	-H	1H-NMR (DMSO-d6) δppm : 1.05-1.4 (9H, m), 1.4-1.9 (5H, m), 2.72 (1H, d, J = 12.5Hz), 2.8-4.6 (6H, m), 6.54 (2H, s), 6.6-6.7 (1H, m), 6.85-7.0 (1H, m), 7.20 (1H, dd, J = 9.5, 19.9Hz).	Fumarate
102	-H	-H	-F	-F	-F	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.51 (3H, s), 1.65-2.1 (5H, m), 2.92 (1H, d, J = 13.8Hz), 3.46 (1H, d, J = 13.8Hz), 3.65-3.75 (1H, m), 4.0-4.1 (1H, m), 6.8-6.95 (2H, m), 8.15-8.35 (1H, m), 9.85-10.1 (1H, m).	Hydrochloride
103	-H	-H	-F	$-OCH_3$	-F	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.55 (9H, m), 1.6-1.85 (4H, m), 1.85-2.05 (1H, m), 2.90 (1H, d, J = 13.8Hz), 3.43 (1H, d, J = 12.8Hz), 3.65-3.75 (1H, m), 3.78 (3H, s), 3.95-4.05 (1H, m), 6.6-6.8 (2H, m), 8.06 (1H, br), 9.57 (1H, br).	Hydrochloride
104	-H	-Cl	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.4 (1H, m), 1.48 (3H, s), 1.50 (3H, s), 1.6-1.85 (3H, m), 1.85-2.1 (2H, m), 2.74 (1H, d, J = 12.8Hz), 3.41 (1H, d, J = 13.1Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 7.05-7.15 (1H, m), 7.17 (1H, dd, J = 1.4, 8.0Hz), 7.25-7.35 (1H, m), 7.44 (1H, d, J = 1.5, 7.9Hz), 8.02 (1H, br), 9.63 (1H, br).	Hydrochloride

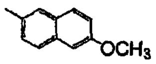
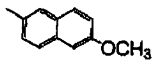
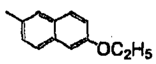
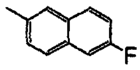
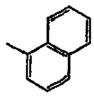
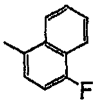
105	-H	-H	-Cl	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.51 (3H, s), 1.6-1.9 (4H, m), 1.95-2.1 (1H, m), 2.92 (1H, d, J = 13.3Hz), 3.20 (1H, d, J = 13.1Hz), 3.7-3.8 (4H, m), 3.9-4.0 (1H, m), 5.9 (1H, br), 6.88 (1H, dd, J = 2.9, 9.1Hz), 7.0-7.05 (1H, m), 8.11 (1H, br), 9.90 (1H, br).	Dihydrochloride
106	-H	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.1 (5H, m), 2.93 (1H, d, J = 13.6Hz), 3.40 (1H, d, J = 13.6Hz), 3.65-3.85 (1H, m), 3.9-4.1 (1H, m), 6.8-7.05 (2H, m), 7.1-7.35 (2H, m), 8.14 (1H, br), 9.77 (1H, br).	Hydrochloride
107	$-CH_3$	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98 (3H, s), 1.05-1.2 (4H, m), 1.2-1.45 (4H, m), 1.55-1.75 (1H, m), 1.85-2.1 (2H, m), 2.16 (3H, s), 2.65-4.2 (4H, m), 6.61 (2H, s), 6.8-6.9 (2H, m), 7.1-7.2 (2H, m), 12.8 (2H, br).	Fumarate
108	-H	-H	$-OCH_3$	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.5-1.6 (3H, m), 1.6-1.95 (4H, m), 2.0-2.1 (1H, m), 2.95 (1H, d, J = 13.5Hz), 3.3-3.5 (1H, m), 3.7-3.8 (1H, m), 3.84 (3H, s), 4.0-4.1 (1H, m), 6.52 (1H, dd, J = 2.6, 8.9Hz), 6.63 (1H, d, J = 2.6Hz), 7.19 (1H, d, J = 8.8Hz), 8.19 (1H, br), 9.75-10.1 (1H, m).	Hydrochloride
109	-H	-Cl	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.47 (3H, s), 1.49 (3H, s), 1.6-1.85 (3H, m), 1.85-2.05 (2H, m), 2.76 (1H, d, J = 12.8Hz), 3.42 (1H, d, J = 13.0Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 7.18 (1H, dd, J = 1.6, 7.9Hz), 7.31 (1H, dd, J = 8.0, 8.0Hz), 7.37 (1H, dd, J = 1.5, 8.0Hz), 8.01 (1H, br), 9.5-9.7 (1H, m).	Hydrochloride
110	-H	-H	-Cl	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.52 (3H, s), 1.6-2.15 (5H, m), 2.95 (1H, d, J = 13.7Hz), 3.49 (1H, d, J = 13.4Hz), 3.6-3.8 (1H, m), 3.95-4.15 (1H, m), 6.95 (1H, dd, J = 2.6, 9.1Hz), 7.05-7.25 (1H, m), 7.40 (1H, d, J = 9.0Hz), 7.95-8.4 (1H, m), 9.6-10.15 (1H, m).	Hydrochloride
111	$-CH_3$	-H	-Cl	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.96 (3H, s), 1.05-1.2 (4H, m), 1.2-1.5 (4H, m), 1.6-1.75 (1H, m), 1.85-2.05 (2H, m), 2.14 (3H, s), 2.75-2.95 (2H, m), 3.17 (1H, d, J = 12.4Hz), 3.7-3.9 (1H, m), 6.62 (3H, s), 6.87 (1H, dd, J = 2.9, 9.1Hz), 7.04 (1H, d, J = 2.9Hz), 7.33 (1H, d, J = 9.0Hz), 11.0 (3H, br).	3/2 Fumarate
112	-H	-H	-Cl	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.51 (3H, s), 1.6-1.9 (4H, m), 1.9-2.05 (1H, s), 2.01 (1H, d, J = 8.2Hz), 3.3-3.45 (1H, m), 3.65-3.8 (1H, m), 3.95-4.1 (1H, m), 6.85-7.0 (1H, m), 7.12 (1H, dd, J = 3.0, 6.2Hz), 7.25 (1H, dd, J = 9.1, 9.1Hz), 8.13 (1H, br), 9.86 (1H, br).	Hydrochloride
113	-H	-H	-F	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.1 (5H, m), 2.94 (1H, d, J = 13.7Hz), 3.50 (1H, d, J = 13.6Hz), 3.65-3.8 (1H, m), 3.95-4.15 (1H, m), 6.80 (1H, dd, J = 2.6, 9.1Hz), 7.01 (1H, dd, J = 2.7, 13.4Hz), 7.34 (1H, dd, J = 9.0, 9.0Hz), 8.22 (1H, br), 9.90 (1H, br).	Hydrochloride

[0306]

Table 18

Absolute configuration

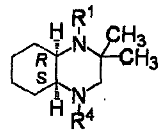


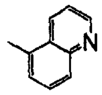
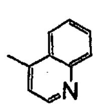
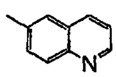
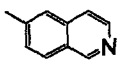
Example	R^1	R^4	NMR	Salt
114	-H		1H-NMR (CDCl3) δppm : 1.15-1.35 (8H, m), 1.35-1.85 (7H, m), 2.82 (1H, d, J = 11.7Hz), 3.05 (1H, d, J = 11.7Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.88 (3H, s), 6.97 (1H, d, J = 2.3Hz), 7.03 (1H, d, J = 2.4Hz), 7.06 (1H, dd, J = 2.6, 8.8Hz), 7.26 (1H, dd, J = 2.5, 9.0Hz), 7.55 (1H, d, J = 8.8Hz), 7.61 (1H, d, J = 9.0Hz).	–
115	$-CH_3$		1H-NMR (CDCl3) δppm : 1.05 (3H, s), 1.15-1.5 (8H, m), 1.65-1.8 (1H, m), 2.0-2.15 (2H, m), 2.18 (3H, s), 2.9-3.0 (2H, m), 3.09 (1H, d, J = 11.7Hz), 3.7-3.8 (1H, m), 3.88 (3H, s), 6.95 (1H, d, J = 2.4Hz), 7.0-7.1 (2H, m), 7.15-7.3 (1H, m), 7.55 (1H, d, J = 8.7Hz), 7.59 (1H, d, J = 9.1Hz).	–
116	-H		1H-NMR (CDCl3) δppm : 1.15-1.3 (8H, m), 1.3-1.85 (10H, m), 2.82 (1H, d, J = 11.7Hz), 3.04 (1H, d, J = 11.7Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 4.11 (2H, q, J = 7.0Hz), 6.96 (1H, d, J = 2.4Hz), 7.03 (1H, d, J = 2.4Hz), 7.06 (1H, dd, J = 2.5, 8.8Hz), 7.2-7.3 (1H, m), 7.55 (1H, d, J = 8.9Hz), 7.59 (1H, d, J = 9.0Hz).	–
117	-H		1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.57 (3H, s), 1.65-2.15 (5H, m), 3.06 (1H, d, J = 13.4Hz), 3.47 (1H, d, J = 13.5Hz), 3.8-3.9 (1H, m), 4.15-4.25 (1H, m), 5.02 (1H, br), 7.24 (1H, d, J = 2.2Hz), 7.31 (1H, ddd, J = 4.5, 12.8, 12.8Hz), 7.47 (1H, dd, J = 2.2, 9.2Hz), 7.54 (1H, dd, J = 2.6, 10.2Hz), 7.75-7.8 (2H, m), 8.15-8.3 (1H, m), 9.9-10.0 (1H, m).	Dihydrochloride
118	-H		1H-NMR (DMSO-d6) δppm : 0.85-1.1 (2H, m), 1.3-1.45 (1H, m), 1.45-1.7 (7H, m), 1.7-1.9 (2H, m), 1.9-2.1 (2H, m), 2.81 (1H, d, J = 12.6Hz), 3.45-3.6 (2H, m), 4.15-4.3 (1H, m), 7.12 (1H, d, J = 7.1Hz), 7.43 (1H, dd, J = 7.8, 7.8Hz), 7.5-7.6 (2H, m), 7.65 (1H, d, J = 8.2Hz), 7.85-7.95 (1H, m), 8.0-8.2 (1H, m), 8.2-8.3 (1H, m), 9.7-9.95 (1H, m).	Hydrochloride
119	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.15 (2H, m), 1.3-1.4 (1H, m), 1.5-1.7 (7H, m), 1.7-1.9 (2H, m), 1.9-2.1 (2H, m), 2.77 (1H, d, J = 12.6Hz), 3.3-3.45 (1H, m), 3.52 (1H, d, J = 12.6Hz), 4.2-4.3 (1H, m), 7.05-7.15 (1H, m), 7.25 (1H, dd, J = 8.2, 10.5Hz), 7.6-7.7 (2H, m), 8.0-8.2 (2H, m), 8.3-8.4 (1H, m), 9.8-10.0 (1H, m).	Hydrochloride

[0307]

Table 19

Absolute configuration

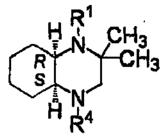


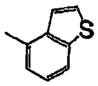
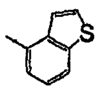
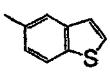
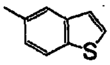
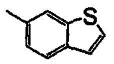
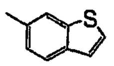
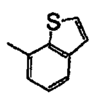
Example	R^1	R^4	NMR	Salt
120	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.1 (2H, m), 1.3-1.4 (1H, m), 1.5-1.7 (7H, m), 1.7-1.85 (2H, m), 1.95-2.1 (2H, m), 2.89 (1H, d, J = 12.8Hz), 3.0-3.9 (4H, m), 4.3-4.4 (1H, m), 7.41 (1H, d, J = 7.0Hz), 7.8-7.9 (1H, m), 7.9-8.0 (2H, m), 8.1-8.2 (1H, m), 9.1-9.25 (2H, m), 9.98 (1H, br).	Trihydrochloride
121	-H		1H-NMR (CDCl3) δppm : 0.9-1.05 (3H, m), 1.24 (3H, s), 1.35-1.45 (6H, m), 1.55-1.8 (3H, m), 1.9-2.05 (1H, m), 2.71 (1H, d, J = 11.3Hz), 3.25 (1H, d, J = 11.4Hz), 3.65-3.75 (1H, m), 3.75-3.85 (1H, m), 6.76 (1H, d, J = 5.0Hz), 7.45-7.5 (1H, m), 7.6-7.7 (1H, m), 8.0-8.1 (2H, m), 8.68 (1H, d, J = 5.0Hz).	—
122	-H		1H-NMR (DMSO-d6) δppm : 1.35-1.5 (6H, m), 1.61 (3H, s), 1.7-2.0 (3H, m), 2.0-2.15 (2H, m), 2.8-4.2 (4H, m), 4.25-4.4 (1H, m), 7.56 (1H, d, J = 2.6Hz), 7.89 (1H, d, J = 5.2, 8.5Hz), 8.04 (1H, dd, J = 2.7, 9.6Hz), 8.23 (1H, d, J = 9.5Hz), 8.45-8.6 (1H, m), 8.78 (1H, d, J = 8.3Hz), 8.92 (1H, dd, J = 1.3, 5.2Hz), 10.21 (1H, d, J = 10.6Hz).	Dihydrochloride
123	-H		1H-NMR (DMSO-d6) δppm : 1.41 (3H, s), 1.45-1.6 (3H, m), 1.63 (3H, s), 1.7-1.85 (2H, m), 1.85-2.05 (1H, m), 2.05-2.25 (2H, m), 3.28 (1H, d, J = 14.5Hz), 3.39 (1H, br), 3.75-3.85 (1H, m), 4.10 (1H, d, J = 14.4Hz), 4.4-4.5 (1H, m), 7.51 (1H, d, J = 2.0Hz), 7.86 (1H, dd, J = 2.4, 9.5Hz), 7.94 (1H, d, J = 6.8Hz), 8.25-8.35 (2H, m), 8.65-8.85 (1H, m), 9.37 (1H, s), 10.3-10.45 (1H, m).	Dihydrochloride

[0308]

Table 20

Absolute configuration

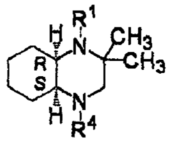


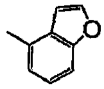
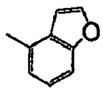
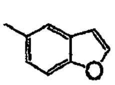
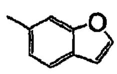
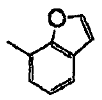
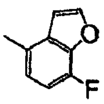
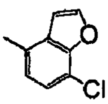
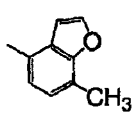
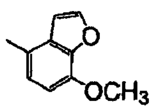
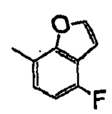
Example	R^1	R^4	NMR	Salt
124	-H		1H-NMR (CDCl3) δppm : 0.9-1.15 (2H, m), 1.21 (3H, s), 1.3-1.45 (5H, m), 1.45-1.8 (4H, m), 1.8-2.0 (1H, m), 2.64 (1H, d, J = 11.2Hz), 3.18 (1H, d, J = 11.2Hz), 3.45-3.55 (1H, m), 3.65-3.75 (1H, m), 6.78 (1H, d, J = 7.7Hz), 7.15-7.3 (1H, m), 7.37 (1H, d, J = 5.5Hz), 7.45 (1H, d, J = 5.6Hz), 7.51 (1H, d, J = 8.0Hz).	—
125	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.8-1.05 (2H, m), 1.13 (3H, s), 1.15-1.45 (6H, m), 1.5-1.65 (1H, m), 2.0-2.2 (2H, m), 2.23 (3H, s), 2.61 (1H, d, J = 11.6Hz), 2.8-3.9 (3H, m), 6.61 (4H, s), 6.81 (1H, d, J = 7.6Hz), 7.24 (1H, dd, J = 7.8, 7.8Hz), 7.46 (1H, d, J = 5.6Hz), 7.58 (1H, d, J = 8.0Hz), 7.69 (1H, d, J = 5.5Hz), 13.0 (4H, br).	Difumarate
126	-H		1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.35-1.5 (4H, m), 1.54 (3H, s), 1.6-2.1 (5H, m), 3.03 (1H, d, J = 13.2Hz), 3.25-3.4 (1H, m), 3.75-3.9 (1H, m), 3.95-4.15 (1H, m), 7.16 (1H, dd, J = 2.2, 8.9Hz), 7.29 (1H, d, J = 5.4Hz), 7.35 (1H, d, J = 2.1Hz), 7.68 (1H, d, J = 5.4Hz), 7.82 (1H, d, J = 8.9Hz), 7.95-8.3 (1H, m), 9.65-9.95 (1H, m).	Hydrochloride
127	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.95-1.5 (11H, m), 1.55-1.75 (1H, m), 1.85-2.1 (2H, m), 2.18 (3H, s), 2.6-4.75 (6H, m), 6.61 (2H, s), 7.10 (1H, dd, J = 2.4, 9.0Hz), 7.24 (1H, d, J = 2.3Hz), 7.27 (1H, d, J = 5.4Hz), 7.62 (1H, d, J = 5.3Hz), 7.75 (1H, d, J = 8.9Hz).	Fumarate
128	-H		1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.53 (3H, s), 1.6-2.05 (5H, m), 3.03 (1H, d, J = 13.5Hz), 3.44 (1H, d, J = 13.5Hz), 3.75-3.9 (1H, m), 4.0-4.15 (1H, m), 7.14 (1H, dd, J = 2.2, 8.9Hz), 7.27 (1H, d, J = 5.4Hz), 7.44 (1H, d, J = 5.4Hz), 7.48 (1H, d, J = 1.8Hz), 7.71 (1H, d, J = 8.8Hz), 7.95-8.2 (1H, m), 9.55-9.8 (1H, m).	Hydrochloride
129	$-CH_3$		1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.61 (3H, s), 1.65-1.9 (3H, m), 2.05-2.3 (2H, m), 2.74 (3H, d, J = 4.7Hz), 3.27 (1H, d, J = 13.9Hz), 3.58 (1H, d, J = 13.8Hz), 3.7-3.85 (1H, m), 4.1-4.25 (1H, m), 7.15 (1H, dd, J = 2.3, 8.9Hz), 7.28 (1H, d, J = 5.4Hz), 7.44 (1H, d, J = 5.4Hz), 7.49 (1H, d, J = 1.9Hz), 7.72 (1H, d, J = 8.8Hz), 9.42 (1H, br).	Hydrochloride
130	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.2 (2H, m), 1.3-1.45 (1H, m), 1.53 (6H, s), 1.55-1.7 (1H, m), 1.7-1.9 (2H, m), 1.9-2.15 (2H, m), 2.92 (1H, d, J = 12.9Hz), 3.48 (1H, d, J = 12.8Hz), 3.75-4.0 (2H, m), 7.02 (1H, d, J = 7.6Hz), 7.35 (1H, dd, J = 7.7, 7.7Hz), 7.48 (1H, d, J = 5.4Hz), 7.61 (1H, d, J = 7.9Hz), 7.76 (1H, d, J = 5.4Hz), 8.18 (1H, br), 9.81 (1H, br).	Hydrochloride

[0309]

Table 21

Absolute configuration

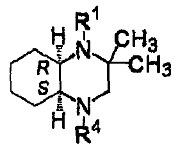


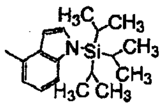
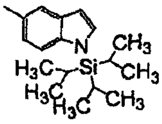
Example	R^1	R^4	NMR	Salt
131	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.3-1.45 (1H, m), 1.52 (3H, s), 1.54 (3H, s), 1.6-2.1 (5H, m), 3.03 (1H, d, J = 13.0Hz), 3.30 (1H, d, J = 13.4Hz), 3.75-3.9 (1H, m), 4.0-4.15 (1H, m), 6.65-6.75 (1H, m), 7.1-7.25 (3H, m), 7.94 (1H d, J = 2.2Hz), 8.0-8.25 (1H, m), 9.7-10.05 (1H, m).	Hydrochloride
132	$-CH_3$		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.3-1.4 (1H, m), 1.43 (3H, s), 1.55-1.9 (6H, m), 2.1-2.35 (2H, m), 2.75 (3H, d, J = 4.7Hz), 3.21 (1H, d, J = 13.3Hz), 3.55 (1H, d, J = 13.3Hz), 3.85-4.1 (2H, m), 6.65-6.75 (1H, m), 7.15-7.25 (3H, m), 7.95 (1H, d, J = 2.2Hz), 9.48 (1H, br).	Hydrochloride
133	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (2H, m), 1.35-1.5 (4H, m), 1.55 (3H, s), 1.6-1.95 (4H, m), 1.95-2.1 (1H, m), 3.03 (1H, d, J = 13.1Hz), 3.20 (1H, d, J = 12.9Hz), 3.75-3.9 (1H, m), 3.9-4.0 (1H, m), 5.29 (1H, br), 6.8-6.85 (1H, m), 7.03 (1H, dd, J = 2.4, 9.0Hz), 7.13 (1H, d, J = 2.3Hz), 7.45 (1H, d, J =9.0Hz), 7.89 (1H, d, J = 2.2Hz), 8.15 (1H, br), 9.99 (1H, br).	Dihydrochloride
134	-H		1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.56 (3H, s), 1.6-2.0 (4H, m), 2.0-2.15 (1H, m), 3.01 (1H, d, J = 13.4Hz), 3.35 (1H, d, J = 13.3Hz), 3.65-3.85 (1H, m), 3.95-4.15 (1H, m), 6.75-6.85 (1H, m), 6.98 (1H, dd, J = 2.1, 8.7Hz), 7.13 (1H, s), 7.47 (1H, d, J = 8.8Hz), 7.5-8.0 (2H, m), 8.15-8.35 (1H, m), 10.0-10.2 (1H, m).	Dihydrochloride
135	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.45 (1H, m), 1.50 (3H, s), 1.55 (3H, s), 1.6-1.9 (3H, m), 1.9-2.1 (2H, m), 3.2-3.4 (2H, m), 3.85-4.0 (1H, m), 4.15-4.25 (1H, m), 6.80 (1H, d, J = 7.0Hz), 6.94 (1H, d, J = 2.2Hz), 7.12 (1H, dd, J = 7.7, 7.7Hz), 7.21 (1H, dd, J = 0.8, 7.7Hz), 7.97 (1H, d, J = 2.2Hz), 8.1-8.35 (1H, m), 9.75-9.95 (1H, m).	Hydrochloride
136	-H		1H-NMR (CDCl3) δppm : 1.0-1.45 (11H, m), 1.6-1.8 (3H, m), 1.8-1.95 (1H, m), 2.70 (1H, d, J = 11.3Hz), 3.04 (1H, d, J = 11.4Hz), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 6.47 (1H, dd, J = 3.4, 8.6Hz), 6.84 (1H, dd, J = 2.5, 2.5Hz), 6.89 (1H, dd, J = 8.6, 10.4Hz), 7.60 (1H, d, J = 2.1Hz).	–
137	-H		1H-NMR (CDCl3) δppm : 1.0-1.15 (2H, m), 1.20 (3H, s), 1.25-1.45 (6H, m), 1.6-1.8 (3H, m), 1.8-1.95 (1H, m), 2.79 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.4Hz), 3.55-3.65 (2H, m), 6.53 (1H, d, J = 8.4Hz), 6.84 (1H, d, J = 2.2Hz), 7.14 (1H, d, J = 8.4Hz), 7.61 (1H, d, J = 2.2Hz).	–
138	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.1 (2H, m), 1.3-1.4 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.6-1.7 (1H, m), 1.7-2.0 (3H, m), 2.0-2.05 (1H, m), 2.39 (3H, s), 2.95 (1H, d, J = 12.8Hz), 3.28 (1H, d, J = 12.9Hz), 3.7-3.8 (1H, m), 4.0-4.15 (1H, m), 6.61 (1H, d, J = 7.9Hz), 6.99 (1H, d, J = 8.1Hz), 7.20 (1H, d, J = 2.2Hz), 7.95 (1H, d, J = 2.2Hz), 8.0-8.15 (1H, m), 9.57-9.95 (1H, m).	Hydrochloride
139	-H		1H-NMR (DMSO-d6) δppm : 0.9-1.1 (2H, m), 1.3-1.4 (1H, m), 1.52 (6H, s), 1.55-1.65 (1H, m), 1.65-1.95 (3H, m), 1.95-2.1 (1H, m), 2.86 (1H, d, J = 12.8Hz), 3.27 (1H, d, J = 12.6Hz), 3.6-3.7 (1H, m), 3.87 (3H, s), 4.0-4.15 (1H, m), 6.61 (1H, d, J = 8.4Hz), 6.79 (1H, d, J = 8.4Hz), 7.21 (1H, d, J = 2.2Hz), 7.95 (1H, d, J = 2.1Hz), 7.95-8.15 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride
140	-H		1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.50 (3H, s), 1.54 (3H, s), 1.6-1.9 (3H, m), 1.9-2.1 (2H, m), 3.17 (1H, d, J = 13.1Hz), 3.29 (1H, d, J = 13.2Hz), 3.9-4.0 (1H, m), 4.0-4.1 (1H, m), 6.80 (1H, dd, J = 4.4, 8.7Hz), 6.98 (1H, dd, J = 8.9, 8.9Hz), 7.06 (1H, d, J = 2.2Hz), 8.06 (1H, d, J = 2.2Hz), 8.1-8.3 (1H, m), 9.75-9.95 (1H, m).	Hydrochloride

[0310]

Table 22

Absolute configuration

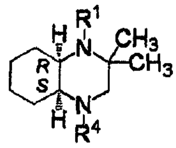


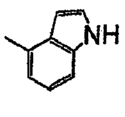
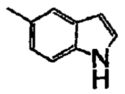
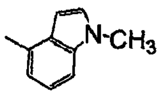
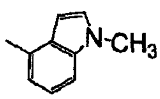
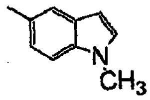
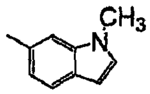
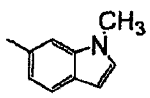
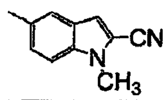
Example	R^1	R^4	NMR	Salt
141	-H		1H-NMR (CDCl3) δppm : 1.1-1.2 (20H, m), 1.20 (3H, s), 1.3-1.45 (6H, m), 1.55-1.8 (6H, m), 1.8-2.0 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.6Hz), 3.6-3.7 (1H, m), 3.7-3.8 (1H, m), 6.50 (1H, d, J = 7.5Hz), 6.64 (1H, d, J = 3.2Hz), 7.00 (1H, dd, J = 7.9, 7.9Hz), 7.11 (1H, d, J = 8.3Hz), 7.16 (1H, d, J = 3.2Hz).	–
142	-H		1H-NMR (CDCl3) δppm : 1.13 (18H, d, J = 7.5Hz), 1.21 (3H, s), 1.28 (3H, s), 1.3-1.6 (5H, m), 1.6-1.8 (7H, m), 2.80 (1H, d, J = 11.7Hz), 2.93 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 6.48 (1H, dd, J = 0.7, 3.1Hz), 6.85 (1H, dd, J = 2.4, 9.0Hz), 7.02 (1H, d, J = 2.3Hz), 7.16 (1H, d, J = 3.1Hz), 7.36 (1H, d, J = 9.0Hz).	–

[0311]

Table 23

Absolute configuration

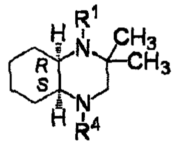


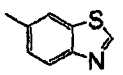
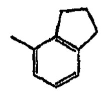
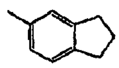
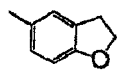
Example	R¹	R⁴	NMR	Salt
143	-H		1H-NMR (CDCl3) δppm : 0.9-1.15 (2H, m), 1.21 (3H, s), 1.25-1.45 (5H, m), 1.45-1.8 (4H, m), 1.8-2.0 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.11 (1H, d, J = 11.5Hz), 3.6-3.75 (1H, m), 3.75-3.9 (1H, m), 6.50 (1H, d, J = 7.3Hz), 6.55-6.65 (1H, m), 7.00 (1H, d, J = 8.0Hz), 7.07 (1H, dd, J = 7.7, 7.7Hz), 7.14 (1H, dd, J = 2.8, 2.8Hz), 8.16 (1H, br).	–
144	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.33 (7H, bs), 1.45-1.9 (5H, m), 2.8-3.0 (2H, m), 3.0-4.05 (5H, m), 6.2-6.3 (1H, m), 6.50 (2H, s), 6.86 (1H, dd, J = 2.2, 8.8Hz), 6.95 (1H, d, J = 1.9Hz), 7.15-7.3 (2H, m), 10.79 (1H, s).	Fumarate
145	-H		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (2H, m), 1.25-1.4 (4H, m), 1.42 (3H, s), 1.5-2.0 (5H, m), 2.84 (1H, d, J = 12.3Hz), 3.24 (1H, d, J = 12.3Hz), 3.74 (3H, s), 3.8-3.95 (2H, m), 6.45 (1H, dd, J = 2.2, 6.2Hz), 6.5-6.55 (3H, m), 6.95-7.05 (2H, m), 7.23 (1H, d, J = 3.1Hz).	Fumarate
146	$-CH_3$		1H-NMR (CDCl3) δppm : 1.0-1.5 (11H, m), 1.6-1.7 (1H, m), 2.05-2.3 (5H, m), 2.75 (1H, d, J = 11.4Hz), 3.05-3.15 (1H, m), 3.38 (1H, d, J = 11.5Hz), 3.75 (3H, s), 3.8-3.9 (1H, m), 6.45-6.55 (2H, m), 6.92 (1H, d, J = 8.2Hz), 6.96 (1H, d, J = 3.1Hz), 7.10 (1H, dd, J = 0.7, 3.1Hz).	–
147	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.33 (7H, bs), 1.45-1.85 (6H, m), 2.85-2.95 (2H, m), 3.64 (1H, br), 3.7-3.8 (4H, m), 6.24 (1H, dd, J = 0.7, 3.0Hz), 6.51 (2H, s), 6.9-7.0 (2H, m), 7.19 (1H, d, J = 3.0Hz), 7.28 (1H, d, J = 8.6Hz).	Fumarate
148	-H		1H-NMR (DMSO-d6) δppm : 1.05-1.3 (2H, m), 1.3-1.45 (7H, m), 1.5-1.9 (5H, m), 2.93 (1H, d, J = 12.3Hz), 3.09 (1H, d, J = 12.4Hz), 3.65 (1H, br), 3.70 (3H, s), 3.8-3.95 (1H, m), 6.25 (1H, d, J = 3.0Hz), 6.51 (2H, s), 6.75-6.85 (2H, m), 7.09 (1H, d, J = 3.1Hz), 7.36 (1H, d, J = 9.2Hz).	Fumarate
149	$-CH_3$		1H-NMR (CDCl3) δppm : 1.06 (3H, s), 1.1-1.5 (8H, m), 1.65-1.75 (1H, m), 2.0-2.15 (2H, m), 2.18 (3H, s), 2.87 (1H, d, J = 11.4Hz), 2.95-3.0 (1H, m), 3.10 (1H, d, J = 11.4Hz), 3.65-3.75 (4H, m), 6.34 (1H, dd, J = 0.7, 3.1Hz), 6.62 (1H, d, J = 1.8Hz), 6.8-6.9 (2H, m), 7.44 (1H, d, J = 8.7Hz).	–
150	-H		1H-NMR (CDCl3) δppm : 0.7-2.3 (15H, m), 2.7-3.2 (2H, m), 3.5-3.8 (2H, m), 3.85 (3H, s), 6.95-7.05 (2H, m), 7.15-7.3 (2H, m).	–

[0312]

Table 24

Absolute configuration

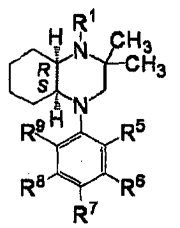


Example	R^1	R^4	NMR	Salt
151	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.45-1.8 (4H, m), 1.8-1.95 (1H, m), 2.81 (1H, d, J = 12.3Hz), 3.22 (1H, d, J = 12.4Hz), 3.45-3.5 (1H, m), 3.85-3.95 (1H, m), 6.52 (1H, s), 7.20 (1H, dd, J = 2.5, 9.1Hz), 7.51 (1H, d, J = 2.4Hz), 7.85 (1H, d, J = 9.1Hz), 9.02 (1H, s).	Hemifumarate
152	-H		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.45 (1H, m), 1.48 (3H, s), 1.50 (3H, s), 1.55-1.7 (1H, m), 1.7-2.15 (6H, m), 2.7-2.95 (5H, m), 3.28 (1H, d, J = 12.8Hz), 3.35-3.45 (1H, m), 3.8-3.9 (1H, m), 6.68 (1H, d, J = 7.8Hz), 6.90 (1H, d, J = 7.3Hz), 7.05 (1H, dd, J = 7.6, 7.6Hz), 7.95-8.2 (1H, m), 9.7-9.95 (1H, m).	Hydrochloride
153	-H		1H-NMR (DMSO-d6) δppm : 1.15-1.3 (2H, m), 1.35-1.5 (4H, m), 1.53 (3H, s), 1.6-1.9 (4H, m), 1.9-2.1 (3H, m), 2.74 (2H, t, J = 7.3Hz), 2.79 (2H, t, J = 7.4Hz), 2.93 (1H, d, J = 13.3Hz), 3.22 (1H, d, J = 13.3Hz), 3.65-3.8 (1H, m), 3.85-4.0 (1H, m), 6.70 (1H, dd, J = 2.2, 8.2Hz), 6.8-6.85 (1H, m), 7.05 (1H, d, J = 8.2Hz), 7.33 (1H, br), 8.0-8.3 (1H, m), 9.9-10.1 (1H, m).	Dihydrochloride
154	-H		1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.5 (4H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 2.0-2.1 (1H, m), 2.95 (1H, d, J = 13.0Hz), 3.02 (1H, d, J = 13.0Hz), 3.11 (2H, t, J = 8.6Hz), 3.7-3.85 (2H, m), 4.44 (2H, t, J = 8.6Hz), 5.98 (1H, br), 6.6-6.7 (2H, m), 6.85-6.95 (1H, m), 8.0-8.25 (1H, m), 9.9-10.2 (1H, m).	Dihydrochloride

[0313]

Table 25

Absolute configuration



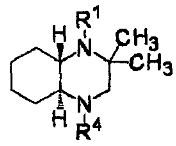
Example	R^1	R^5	R^6	R^7	R^8	R^9	NMR	Salt
155	-H	-F	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.25 (2H, m), 1.3-1.45 (1H, m), 1.46 (3H, s), 1.49 (3H, s), 1.65-1.85 (3H, m), 1.85-2.05 (2H, m), 2.93 (1H, d, J = 13.0Hz), 3.27 (1H, d, J = 13.1Hz), 3.55-3.65 (1H, m), 3.8-3.9 (1H, m), 6.95-7.05 (1H, m), 7.05-7.2 (3H, m), 8.09 (1H, br), 9.68 (1H, br).	Hydrochloride
156	-H	-H	-H	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.52 (3H, s), 1.6-2.15 (5H, m), 2.94 (1H, d, J = 13.3Hz), 3.25 (1H, d, J = 13.1Hz), 3.35-3.4 (3H, m), 6.85-7.0 (2H, m), 7.0-7.1 (2H, m), 8.16 (1H, br), 9.94 (1H, br).	Dihydrochloride
157	$-CH_3$	-H	-H	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98 (3H, s), 1.0-1.1 (1H, m), 1.16 (3H, s), 1.2-1.45 (4H, m), 1.55-1.7 (1H, m), 1.85-2.05 (2H, s), 2.15 (3H, s), 2.35-4.55 (4H, m), 6.59 (2H, s), 6.8-6.9 (2H, m), 6.9-7.05 (2H, m), 12.9 (2H, br).	Fumarate
158	-H	-H	-F	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.35-1.45 (4H, m), 1.51 (3H, s), 1.6-1.9 (4H, m), 1.95-2.1 (1H, m), 2.90 (1H, d, J = 13.4Hz), 3.22 (1H, d, J = 13.3Hz), 3.65-3.8 (4H, m), 3.85-3.95 (1H, m), 6.6-6.7 (1H, m), 6.89 (1H, dd, J = 2.9, 14.7Hz), 7.02 (1H, dd, J = 9.5, 9.5Hz), 8.12 (1H, m), 9.90 (1H, br).	Hydrochloride
159	-H	-H	$-OCH_3$	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.54 (3H, s), 1.6-1.95 (4H, m), 2.0-2.15 (1H, m), 2.95 (1H, d, J = 13.3Hz), 3.24 (1H, d, J = 13.2Hz), 3.7-3.8 (1H, m), 3.82 (3H, s), 3.9-4.05 (1H, m), 6.4-6.5 (1H, m), 6.70 (1H, dd, J = 2.8, 7.6Hz), 7.03 (1H, dd, J = 8.9, 11.3Hz), 7.75 (1H, br), 8.15-8.35 (1H, m), 10.0-10.15 (1H, m).	Hydrochloride
160	-H	-F	-F	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.3 (2H, m), 1.35-1.45 (1H, m), 1.46 (3H, s), 1.50 (3H, s), 1.6-1.85 (4H, m), 1.9-2.05 (3H, m), 3.00 (1H, d, J = 13.2Hz), 3.28 (1H, d, J = 13.4Hz), 3.6-3.7 (1H, m), 3.8-3.9 (1H, m), 6.85-6.95 (1H, m), 6.95-7.05 (1H, m), 7.05-7.15 (1H, m), 8.1-8.3 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride
161	-H	-H	-F	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.52 (3H, s), 1.6-2.15 (5H, m), 2.93 (1H, d, J = 13.5Hz), 3.2-3.45 (1H, m), 3.65-3.8 (1H, m), 3.9-4.1 (1H, m), 6.65-6.8 (1H, m), 6.95-7.1 (1H, m), 7.25 (1H, dd, J = 9.4, 19.8Hz), 8.0-8.35 (1H, m), 9.75-10.1 (1H, m).	Hydrochloride
162	$-CH_3$	-H	-F	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 0.97 (3H, s), 1.05-1.2 (4H, m), 1.2-1.45 (4H, m), 1.6-1.75 (1H, m), 1.85-2.05 (2H, s), 2.14 (3H, s), 2.65-4.05 (4H, m), 6.55-6.7 (3H, m), 6.8-6.95 (1H, m), 7.18 (1H, dd, J = 9.5, 20.0Hz), 13.0 (2H, br).	Fumarate

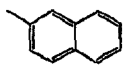
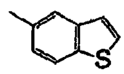
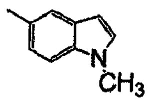
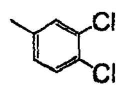
163	-H	-H	-F	-F	-F	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.50 (3H, s), 1.65-1.9 (4H, m), 1.95-2.05 (1H, m), 2.92 (1H, d, J = 13.8Hz), 3.47 (1H, d, J = 13.8Hz), 3.65-3.8 (1H, m), 4.0-4.1 (1H, m), 6.8-6.95 (2H, m), 8.1-8.3 (1H, m), 9.75-9.95 (1H, m).	Hydrochloride
164	-H	-H	-F	$-OCH_3$	-F	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.50 (3H, s), 1.6-1.9 (4H, m), 1.9-2.1 (1H, m), 2.90 (1H, d, J = 13.6Hz), 3.42 (1H, d, J = 13.8Hz), 3.6-3.75 (1H, m), 3.78 (3H, s), 3.95-4.05 (1H, m), 6.6-6.85 (2H, m), 8.16 (1H, br), 9.85 (1H, br).	Hydrochloride
165	-H	-Cl	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.45 (1H, m), 1.49 (3H, s), 1.51 (3H, s), 1.6-1.85 (3H, m), 1.9-2.1 (2H, m), 2.73 (1H, d, J = 12.8Hz), 3.41 (1H, d, J = 12.8Hz), 3.45-3.55 (1H, m), 3.75-3.9 (1H, m), 7.05-7.15 (1H, m), 7.17 (1H, dd, J = 1.4, 8.0Hz), 7.25-7.35 (1H, m), 7.44 (1H, d, J = 1.5, 8.0Hz), 8.09 (1H, br), 9.7-9.9 (1H, m).	Hydrochloride
166	-H	-H	-Cl	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 2.0-2.1 (1H, m), 2.92 (1H, d, J = 13.2Hz), 3.19 (1H, d, J = 13.1Hz), 3.7-3.8 (4H, m), 3.85-3.95 (1H, m), 5.9 (1H, br), 6.88 (1H, dd, J = 2.9, 9.0Hz), 7.0-7.05 (1H, m), 8.15 (1H, br), 10.00 (1H, br).	Dihydrochloride
167	-H	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.1 (5H, m), 2.93 (1H, d, J = 13.7Hz), 3.2-3.5 (1H, m), 3.65-3.85 (1H, m), 3.9-4.1 (1H, m), 6.96 (2H, d, J = 9.0Hz), 7.24 (2H, d, J = 8.9Hz), 8.14 (1H, br), 9.45-10.0 (1H, m).	Hydrochloride
168	$-CH_3$	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.97 (3H, s), 1.05-1.2 (4H, m), 1.2-1.45 (4H, m), 1.6-1.75 (1H, m), 1.85-2.05 (2H, m), 2.14 (3H, s), 2.65-4.35 (4H, m), 6.61 (2H, s), 6.8-6.9 (2H, m), 7.1-7.2 (2H, m), 12.9 (2H, br).	Fumarate
169	-H	-Cl	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.47 (3H, s), 1.49 (3H, s), 1.6-1.85 (3H, m), 1.9-2.05 (2H, m), 2.76 (1H, d, J = 12.8Hz), 3.42 (1H, d, J = 13.0Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 7.18 (1H, dd, J = 1.5, 7.9Hz), 7.31 (1H, dd, J = 8.0, 8.0Hz), 7.37 (1H, dd, J = 1.5, 8.0Hz), 8.02 (1H, br), 9.61 (1H, br).	Hydrochloride
170	-H	-H	-Cl	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.51 (3H, s), 1.6-2.1 (5H, m), 2.95 (1H, d, J = 13.7Hz), 3.49 (1H, d, J = 13.7Hz), 3.65-3.8 (1H, m), 4.0-4.15 (1H, m), 6.95 (1H, dd, J = 3.0, 9.1Hz), 7.18 (1H, d, J = 2.9Hz), 7.40 (1H, d, J = 9.0Hz), 7.95-8.35 (1H, m), 9.6-10.05 (1H, m).	Hydrochloride
171	$-CH_3$	-H	-Cl	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.95 (3H, s), 1.05-1.2 (4H, m), 1.2-1.5 (4H, m), 1.55-1.75 (1H, m), 1.85-2.05 (2H, m), 2.13 (3H, s), 2.75-2.9 (2H, m), 3.17 (1H, d, J = 12.4Hz), 3.75-3.85 (1H, m), 6.62 (3H, s), 6.87 (1H, dd, J = 2.9, 9.1Hz), 7.04 (1H, d, J = 2.9Hz), 7.33 (1H, d, J = 9.0Hz), 11.0 (3H, br).	3/2 Fumarate
172	-H	-H	-Cl	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.45 (6H, m), 1.50 (3H, s), 1.6-1.9 (4H, m), 1.9-2.1 (1H, s), 2.00 (1H, d, J = 8.2Hz), 3.25-3.45 (1H, m), 3.65-3.85 (1H, m), 3.9-4.1 (1H, m), 6.85-7.0 (1H, m), 7.12 (1H, dd, J = 3.0, 6.3Hz), 7.25 (1H, dd, J = 9.1, 9.1Hz), 8.12 (1H, br), 9.82 (1H, br).	Hydrochloride
173	-H	-H	-F	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.45 (6H, m), 1.50 (3H, s), 1.6-2.1 (5H, m), 2.94 (1H, d, J = 13.8Hz), 3.51 (1H, d, J = 13.9Hz), 3.65-3.85 (1H, m), 3.95-4.15 (1H, m), 6.80 (1H, dd, J = 2.5, 8.9Hz), 7.01 (1H, dd, J = 2.8, 13.4Hz), 7.34 (1H, dd, J = 9.0, 9.0Hz), 8.16 (1H, br), 9.77 (1H, br).	Hydrochloride
174	-H	-H	$-OCH_3$	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.2-1.5 (6H, m), 1.53 (3H, s), 1.65-1.95 (4H, m), 1.95-2.1 (1H, m), 2.95 (1H, d, J = 13.5Hz), 3.3-3.45 (1H, m), 3.7-3.8 (1H, m), 3.84 (3H, s), 4.0-4.1 (1H, m), 6.52 (1H, dd, J = 2.7, 8.9Hz), 6.63 (1H, d, J = 2.6Hz), 7.19 (1H, d, J = 8.8Hz), 8.18 (1H, br), 9.88 (1H, br).	Hydrochloride

[0314]

Table 26

Relative configuration

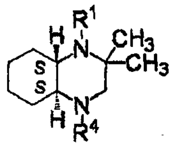


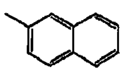
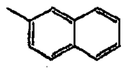
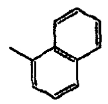
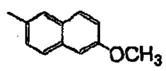
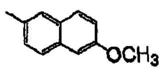
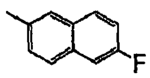
Example	R^1	R^4	NMR	Salt
175	-H		1H-NMR (CDCl3) δppm : 1.04-1.21 (1H, m), 1.25-1.46 (2H, m), 1.64-1.88 (3H, m), 1.67 (3H, s), 1.77 (3H, s), 2.00-2.12 (1H, m), 2.34-2.40 (1H, m), 2.88 (1H, d, J = 12.5 Hz), 3.13-3.29 (2H, m), 3.42 (1H, d, J = 12.5 Hz), 7.29-7.34 (1H, m), 7.41-7.51 (2H, m), 7.60 (1H, s), 7.77-7.82 (3H, m), 9.51 (1H, brs), 9.79 (1H, brs)	Hydrochloride
176	-H		1H-NMR (CDCl3) δppm : 1.00-1.11 (1H, m), 1.25-1.39 (2H, m), 1.58-1.81 (3H, m), 1.65 (3H, s), 1.75 (3H, s), 1.96-2.10 (1H, m), 2.32-2.37 (1H, m), 2.82 (1H, d, J = 12.5 Hz), 3.06-3.15 (1H, m), 3.18-3.36 (2H, m), 3.39 (1H, d, J = 12.5 Hz), 7.19 (1H, d, J = 8.5 Hz), 7.291H, d, J = 5.4 Hz), 7.47 (1H, d, J = 5.4 Hz), 7.64 (1H, s), 7.81 (1H, d, J = 8.5 Hz), 9.46 (1H, brs), 9.75 (1H, brs)	Hydrochloride
177	-H		1H-NMR (DMSO) δppm : 0.92-1.37 (3H, m), 1.27 (3H, s), 1.40-1.60 (3H, m), 1.52 (3H, s), 1.60-1.75 (1H, m), 1.80-1.90 (1H, m), 2.60-2.73 (1H, m), 2.78 (1H, d, J = 12.1 Hz), 2.97 (1H, d, J = 12.1 Hz), 3.00-3.12 (1H, m), 3.13-3.69 (3H, br), 3.76 (3H, s), 6.36 (1H, d, J = 3.0 Hz), 6.50 (2H, s), 6.94 (1H, dd, J = 8.6, 1.6 Hz), 7.28 (1H, d, J = 1.6 Hz), 7.30 (1H, d, J = 3.0 Hz), 7.36 (1H, d, J = 8.6 Hz)	Fumarate
178	-H		1H-NMR (CDCl3) δppm : 0.97-1.09 (1H, m), 1.23-1.38 (2H, m), 1.62-1.68 (3H, m), 1.63 (3H, s), 1.68 (3H, s), 1.92-2.05 (1H, m), 2.29-2.36 (1H, m), 2.73 (1H, d, J = 12.4 Hz), 2.94-3.03 (1H, m), 3.11-3.22 (1H, m), 3.28 (1H, d, J = 12.4 Hz), 7.02 (1H, dd, J = 8.5, 2.4 Hz), 7.25 (1H, d, J = 2.4 Hz), 7.39 (1H, d, J = 8.5 Hz), 9.50 (1H, brs), 9.78 (1H, brs)	Hydrochloride

[0315]

Table 27

Absolute configuration

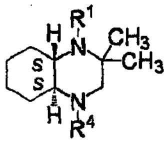


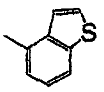
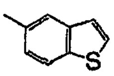
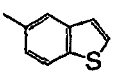
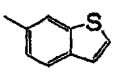
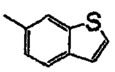
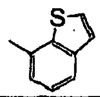
Example	R^1	R^4	NMR	Salt
179	-H		1H-NMR (CDCl3) δppm : 1.26-2.30 (8H, m), 1.79 (3H, s), 2.17 (3H, s), 2.51-2.57 (1H, m), 3.36 (1H, d, J = 13.2 Hz), 3.90-4.30 (2H, m), 4.08 (1H, d, J = 13.2 Hz), 7.56-7.69 (2H, m), 7.83-8.01 (4H, m), 8.50 (1H, brs), 10.07 (1H, brs), 10.26 (1H, brs)	Dihydrochloride
180	$-CH_3$		1H-NMR (CDCl3) δppm : 1.20-1.36 (1H, m), 1.42-1.76 (4H, m), 1.76 (3H, s), 1.91-1.93 (1H, m), 2.03-2.18 (1H, m), 2.16 (3H, s), 2.30-2.53 (2H, m), 2.85 (3H, d, J = 4.9 Hz), 3.49 (1H, d, J = 13.6 Hz), 4.06-4.21 (1H, m), 4.68 (1H, d, J = 13.6 Hz), 4.95-5.05 (1H, m), 7.55-7.67 (2H, m), 7.89-8.05 (4H, m), 8.95 (1H, br), 13.17 (1H, brs)	Dihydrochloride
181	-H		1H-NMR (DMSO-d6) δppm: 0.94-1.25 (2H, m), 1.25-1.45 (5H, m), 1.45-1.55 (1H, m), 1.55-1.80 (5H, m), 1.95-2.10 (1H, m), 2.82 (1H, d, J = 12.4 Hz), 2.97-3.11 (2H, m), 3.36-3.51 (1H, m), 7.40 (1H, d, J = 7.3 Hz), 7.50-7.59 (3H, m), 7.79 (1H, d, J = 8.2 Hz), 7.89-7.96 (1H, m), 8.42-8.48 (1H, m), 8.97-9.24 (1H, br), 9.50-9.80 (1H, br).	Hydrochloride
182	-H		1H-NMR (CDCl3) δppm : 1.21-2.12 (8H, m), 1.77 (3H, s), 2.11 (3H, s), 2.49-2.55 (1H, m), 3.27 (1H, d, J = 13.1 Hz), 3.64-4.22 (3H, m), 3.94 (3H,s), 7.15-7.24 (2H, m), 7.68-7.85 (3H, m), 8.25 (1H, brs), 10.04 (2H, brs)	Dihydrochloride
183	$-CH_3$		1H-NMR (CDCl3) δppm : 1.20-1.50 (2H, m), 1.63-2.28 (7H, m), 1.70 (3H, s), 1.95 (3H, s), 2.81 (3H, d, J = 4.9 Hz), 3.27 (1H, d, J = 13.2 Hz), 3.49-3.85 (1H, m), 3.94 (3H, s), 4.22-4.70 (2H, br), 7.14-7.25 (2H, m), 7.68-7.82 (3H, m), 7.97-8.60 (1H, br), 12.21 (1H, brs)	Dihydrochloride
184	-H		1H-NMR (DMSO-d6) δppm : 1.01-1.48 (6H, m), 1.48-1.85 (7H, m), 1.95-2.12 (1H, m), 2.88-3.33 (4H, m), 4.45-5.45 (1H, br), 7.30-7.48 (2H, m), 7.62-7.75 (2H, m), 7.89 (1H, d, J = 8.8 Hz), 7.99 (1H, dd, J = 5.8, 9.1 Hz), 9.07-9.38 (1H, br), 9.60-9.88 (1H, br).	Dihydrochloride

[0316]

Table 28

Absolute configuration

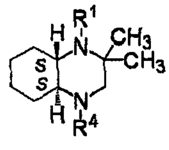


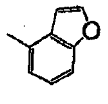
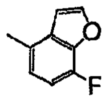
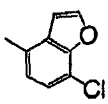
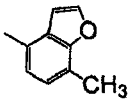
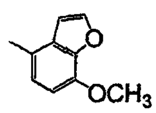
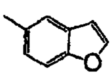
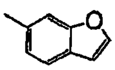
Example	R^1	R^4	NMR	Salt
185	-H		1H-NMR (CDCl3) δppm : 0.96-1.07 (1H, m), 1.25-1.33 (2H, m), 1.48-1.86 (3H, m), 1.65 (3H, s), 1.85 (3H, s), 1.95-2.12 (1H, m), 2.37-2.42 (1H, m), 2.86 (1H, d, J = 12.7 Hz), 3.20-3.35 (2H, m), 3.32 (1H, d, J = 12.7 Hz), 7.26 (1H, d, J = 7.7 Hz), 7.35 (1H, dd, J = 7.7, 7.7 Hz), 7.41 (1H, d, J = 5.5 Hz), 7.53 (1H, d, J = 5.5 Hz), 7.72 (1H, d, J = 7.7 Hz), 9.57 (1H, brs), 9.67 (1H, brs)	Hydrochloride
186	-H		1H-NMR (CDCl3) δppm : 1.18-2.18 (8H, m), 1.76 (3H, s), 2.17 (3H, s), 2.47-2.54 (1H, m), 3.26 (1H, d, J = 12.9 Hz), 3.72-4.05 (2H, m), 3.92 (1H, d, J = 12.9 Hz), 7.41 (1H, d, J = 5.5 Hz), 7.59 (1H, d, J = 5.5 Hz), 7.65-7.80 (1H, m), 7.96 (1H, d, J = 8.7 Hz), 8.34 (1H, brs), 10.15 (2H, brs)	Dihydrochloride
187	$-CH_3$		1H-NMR (CDCl3) δppm : 1.23-1.76 (5H, m), 1.75 (3H, s), 1.84-2.21 (2H, m), 2.14 (3H, s), 2.24-2.44 (2H, m), 2.86 (3H, d, J = 4.9 Hz), 3.49 (1H, d, J = 13.6 Hz), 4.06-4.20 (1H, m), 4.65 (1H, d, J = 13.6 Hz), 4.90-5.01 (1H, m), 7.46 (1H, d, J = 5.5 Hz), 7.65 (1H, d, J = 5.5 Hz), 7.74-8.30 (2H, br), 7.97-8.10 (1H, m), 13.12 (1H, brs)	Dihydrochloride
188	-H		1H-NMR (CDCl3) δppm : 1.26-2.06 (8H, m), 1.75 (3H, s), 2.05 (3H, s), 2.46-2.52 (1H, m), 3.23 (1H, d, J = 13.4 Hz), 3.70-4.05 (2H, br), 3.86 (1H, d, J = 13.4 Hz), 7.36 (1H, d, J = 5.5 Hz), 7.56 (1H, d, J = 5.5 Hz), 7.67 (1H, brs), 7.89 (1H, d, J = 8.6 Hz), 8.38 (1H, brs), 10.03 (2H, brs)	Dihydrochloride
189	$-CH_3$		1H-NMR (CDCl3) δppm : 1.18-1.35 (1H, m), 1.39-1.53 (1H, m), 1.55-1.75 (2H, m), 1.74 (3H, s), 1.84-1.96 (1H, m), 2.02-2.39 (4H, m), 2.08 (3H, s), 2.84 (3H, d, J = 4.9 Hz), 3.42 (1H, d, J = 13.5 Hz), 3.98-4.07 (1H, m), 4.56 (1H, d, J = 13.5 Hz), 4.76-4.84 (1H, m), 7.39 (1H, d, J = 5.5 Hz), 7.63 (1H, d, J = 5.5 Hz), 7.90-7.99 (2H, m), 8.780 (1H, br), 13.05 (1H, brs)	Dihydrochloride
190	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.48 (6H, m), 1.48-1.80 (7H, m), 1.90-2.07 (1H, m), 2.87-3.16 (3H, m), 3.16-3.32 (1H, m), 7.23 (1H, d, J = 7.5 Hz), 7.40-7.52 (2H, m), 7.67-7.79 (2H, m), 8.92-9.22 (1H, br), 9.40-9.70 (1H, br).	Hydrochloride

[0317]

Table 29

Absolute configuration

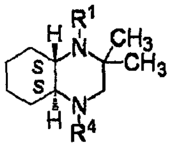


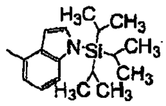
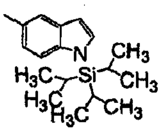
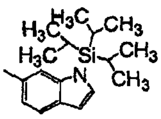
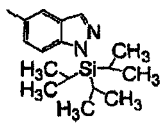
Example	R^1	R^4	NMR	Salt
191	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.46 (6H, m), 1.46-1.85 (7H, m), 1.95-2.12 (1H, m), 2.80-3.40 (4H, m), 5.50-6.60 (1H, br), 6.75-7.20 (2H, m), 7.20-7.37 (1H, m), 7.37-1.53 (1H, m), 7.99 (1H, s), 9.00-9.50 (1H, br), 9.60-10.05 (1H, br).	Dihydrochloride
192	-H		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 0.98-1.26 (2H, m), 1.26-1.51 (5H, m), 1.51-1.61 (1H, m), 1.61-1.78 (5H, m), 1.99-2.08 (1H, m), 2.80 (1H, d, J = 12.3 Hz), 3.05-3.32 (3H, m), 3.58-4.12 (1H, br), 7.01 (1H, dd, J = 3.8, 8.5 Hz), 7.08-7.18 (2H, m), 8.01 (1H, d, J = 2.1 Hz), 9.10-9.35 (1H, br), 9.38-9.75 (1H, br).	Dihydrochloride
193	-H		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 0.98-1.27 (2H, m), 1.27-1.46 (4H, m), 1.46-1.60 (2H, m), 1.60-1.80 (5H, m), 1.98-2.10 (1H, m), 2.84 (1H, d, J = 12.4 Hz), 3.05-3.35 (3H, m), 3.45-3.90 (1H, br), 7.05 (1H, d, J = 8.2 Hz), 7.08-7.13 (1H, br), 7.36 (1H, d, J = 8.2 Hz), 8.03 (1H, d, J = 2.2 Hz), 8.98-9.35 (1H, br), 9.35-9.72 (1H, br).	Dihydrochloride
194	-H		1H-NMR (CDCl3) δppm: 0.82-1.05 (2H, m), 1.07 (3H, s), 1.19-1.43 (3H, m), 1.49 (3H, s), 1.56-1.68 (1H, m), 1.68-1.90 (3H, m), 2.35-2.51 (4H, m), 2.51-2.70 (1H, m), 2.78-2.92 (2H, m), 6.83-6.89 (2H, m), 7.01 (1H, d, J = 7.8 Hz), 7.56 (1H, d, J = 2.1 Hz).	–
195	-H		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 0.96-1.25 (2H, m), 1.25-1.60 (6H, m), 1.60-1.79 (5H, m), 1.98-2.10 (1H, m), 2.76 (1H, d, J = 12.3 Hz), 2.99-3.37 (3H, m), 3.93 (3H, s), 4.52-4.86 (1H, br), 6.86 (1H, d, J = 8.4 Hz), 6.95 (1H, d = 8.4 Hz), 6.98-7.09 (1H, br), 7.87 (1H, d, J = 2.1 Hz), 9.02-9.40 (1H, br), 9.40-9.75 (1H, br).	Dihydrochloride
196	-H		1H-NMR (CDCl3) δppm : 1.18-1.36 (1H, m), 1.41-1.63 (2H, m), 1.73-2.10 (5H, m), 1.78 (3H, s), 2.17 (3H, s), 2.36-2.69 (1H, m), 3.36 (1H, d, J = 12.8 Hz), 3.82-4.40 (2H, br), 4.09 (1H, d, J = 12.8 Hz), 6.88 (1H, d, J = 2.0 Hz), 7.62 (1H, d, J = 8.7 Hz), 7.74 (1H, d, J = 2.0 Hz), 7.70-8.76 (2H, br), 9.50-10.65 (2H, br)	Dihydrochloride
197	-H		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.03-1.44 (6H, m), 1.51-1.79 (7H, m), 2.00-2.10 (1H, m), 2.87 (1H, d, J = 12.4 Hz), 2.94-3.05 (1H, m), 3.10-3.23 (2H, m), 4.64-5.12 (1H, br), 6.88 (1H, d, J = 1.4 Hz), 7.05-7.09 (1H, m), 7.33-7.36 (1H, br), 7.59 (1H, d, J = 8.2 Hz), 7.89 (1H, J = 2.2 Hz), 8.97-9.26 (1H, br), 9.45-9.82 (1H, br).	Dihydrochloride

[0318]

Table 30

Absolute configuration

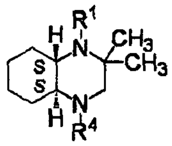


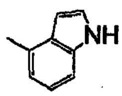
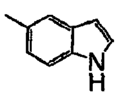
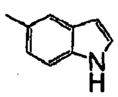
Example	R¹	R⁴	NMR	Salt
198	-H		1H-NMR (CDCl3) δppm : 0.93-1.80 (35H, m), 1.80-2.05 (1H, br), 2.40-2.70 (2H, m), 2.81-2.95 (1H, m), 3.00-3.15 (1H, m), 6.72 (1H, d, J = 2.7 Hz), 6.80 (1H, d, J = 7.4 Hz), 7.00-7.13 (1H, m), 7.17 (1H, d, J = 3.2 Hz), 7.23-7.34 (1H, m).	–
199	-H		1H-NMR (CDCl3) δppm : 0.99-1.50 (5H, m), 1.07 (3H, s), 1.13 (9H, s), 1.15 (9H, s), 1.42 (3H, s), 1.58-1.73 (7H, m), 2.23-2.31 (1H, m), 2.68 (1H, d, J = 11.2 Hz), 2.73-2.79 (1H, m), 2.83 (1H, d, J = 11.2 Hz), 6.55 (1H, dd, J = 3.2, 0.7 Hz), 6.92 (1H, dd, J = 8.8, 2.1 Hz), 7.21 (1H, d, J = 3.2 Hz), 7.34 (1H, d, J = 2.1 Hz), 7.37 (1H, d, J = 8.8 Hz)	–
200	-H		1H-NMR (CDCl3) δppm : 0.85-1.85 (36H, m), 2.25-2.39 (1H, m), 2.60 (1H, d, J = 11.2 Hz), 2.76-2.90 (2H, m), 6.54-6.60 (1H, m), 6.90 (1H, dd, J = 1.7, 8.3 Hz), 7.17-7.32 (2H, m), 7.50 (1H, d, J = 8.3 Hz).	–
201	-H		1H-NMR (CDCl3) δppm : 1.01-1.44 (5H, m), 1.08 (3H, s), 1.13 (9H, s), 1.15 (9H, s), 1.42 (3H, s), 1.56-1.83 (7H, m), 2.25-2.33 (1H, m), 2.67 (1H, d, J = 11.3 Hz), 2.77-2.83 (1H, m), 2.82 (1H, d, J = 11.3 Hz), 7.13 (1H, dd, J = 8.9, 2.0 Hz), 7.43 (1H, d, J = 2.0 Hz), 7.45 (1H, d, J = 8.9 Hz), 8.15 (1H, d, J = 0.8 Hz)	–

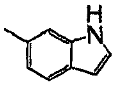
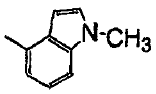
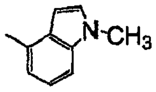
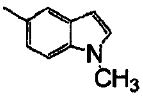
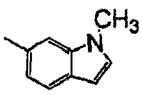
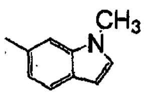
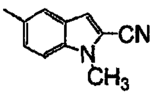
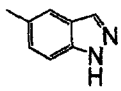
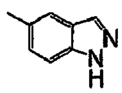
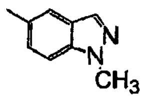
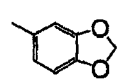
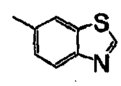
[0319]

Table 31

Absolute configuration



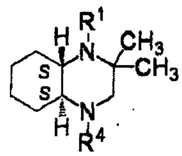
Example	R¹	R⁴	NMR	Melting point (°C)	Salt
202	-H		1H-NMR (CDCl3) δppm : 0.80-1.18 (5H, m), 1.18-1.46 (3H, m), 1.46-1.66 (4H, m), 1.66-2.05 (3H, m), 2.40-2.70 (2H, m), 2.80-2.98 (1H, m), 3.03 (1H, d, J = 11.3 Hz), 6.64-6.72 (1H, m), 6.83 (1H, dd, J = 1.6, 6.6 Hz), 7.07-7.20 (3H, m), 8.16-8.35 (1H, br).		–
203	-H		1H-NMR (CDCl3) δppm : 0.95-1.08 (1H, m), 1.07 (3H, s), 1.13-1.37 (4H, m), 1.43 (3H, s), 1.55-1.73 (4H, m), 2.25-2.33 (1H, m), 2.68 (1H, d, J = 11.1 Hz), 2.75-2.83 (1H, m), 2.81 (1H, d, J = 11.1 Hz), 6.48-6.50 (1H, m), 7.01 (1H, dd, J = 8.6, 1.9 Hz), 7.17-7.20 (1H, m), 7.30 (1H, d, J = 8.6 Hz), 7.38 (1H, d, J = 1.9 Hz), 8.11 (1H, brs)		–
204	$-CH_3$		1H-NMR (CDCl3) δppm : 1.01-1.30 (3H, m), 1.09 (3H, s), 1.22 (3H, s), 1.50-1.76 (4H, m), 1.99-2.15 (1H, m), 2.25 (3H, s), 2.27-2.36 (1H, m), 2.54-2.64 (1H, m), 2.70 (1H, d, J = 11.2 Hz), 2.91 (1H, d, J = 11.2 Hz), 6.48-6.50 (1H, m), 7.02 (1H, dd, J = 8.6, 1.5 Hz), 7.17-7.20 (1H, m), 7.31 (1H, d, J = 8.6 Hz), 7.39(1H, s), 8.10 (1H, brs)		–

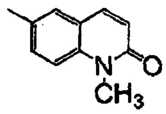
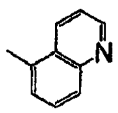
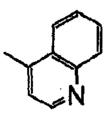
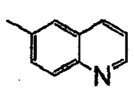
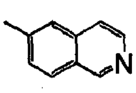
205	-H		1H-NMR (CDCl3) δppm : 0.80-1.40 (8H, m), 1.43 (3H, s), 1.55-1.86 (4H, m), 2.27-2.40 (1H, m), 2.68 (1H, d, J = 11.3 Hz), 2.75-2.91 (2H, m), 6.48-6.56 (1H, m), 6.94 (1H, dd, J = 1.8, 8.4 Hz), 7.13-7.22 (2H, m), 7.53 (1H, d, J = 8.4 Hz), 8.15-8.48 (1H, br).		–
206	-H		1H-NMR (MeOH-d4) δppm : 0.87-1.95 (14H, m), 2.66-3.02 (3H, m), 3.09-3.30 (3H, m), 3.69 (3H, s), 6.43 (1H, s), 6.58 (1H, s), 6.77 (1H, d, J = 7.6 Hz), 6.93-7.20 (3H, m).		Hemifumarate
207	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.85-1.55 (11H, m), 1.63-1.85 (2H, m), 2.05-2.20 (1H, m), 2.41 (3H, brs), 2.60-3.00 (4H, m), 3.00-4.80 (5H, m), 6.35-6.52 (1H, br), 6.56 (2H, s), 6.79 (1H, d, J = 7.5 Hz), 7.03-7.15 (1H, m), 7.15-7.30 (2H, m).		Fumarate
208	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.89-1.40 (10H, m), 10.40-10.58 (2H, m), 10.63-10.80 (1H, m), 2.01-2.27 (1H, m), 2.39 (3H, s), 2.55-2.78 (3H, m), 2.92-3.06 (1H,m), 4.65 (5H, m), 6.35 (1H, d, J = 2.6 Hz), 6.65 (2H, s), 6.90-7.00 (1H, m), 7.24-7.32 (2H, m), 7.34 (1H, d, J = 8.6 Hz).		Fumarate
209	-H		1H-NMR (DMSO-d6) δppm : 0.90-1.63 (12H, m), 1.63-1.77 (1H, m), 1.82-1.99 (1H, m), 2.60-2.88 (2H, m), 2.91-3.14 (2H, m), 3.75 (3H, s), 3.80-5.30 (2H, br), 6.36 (1H, d, J = 3.0 Hz), 6.48 (2H, s), 6.85 (1H, d, J = 8.4 Hz), 7.14 (1H, s), 7.27 (1H, d, J = 3.0 Hz), 7.46 (1H, d, J = 8.4 Hz), 8.76-10.00 (1H, br).		Fumarate
210	$-CH_3$		1H-NMR (DMSO-d6) δppm : 0.90-1.35 (10H, m), 1.40-1.55 (2H, m), 1.55-1.80 (1H, m), 2.02-2.16 (1H, m), 2.39 (3H, s), 2.55-2.80 (3H,m), 2.90-3.08 (1H, m), 3.15-4.70 (5H,m), 6.32-6.40 (1H, m), 6.56 (2H, s), 6.85 (1H, dd, J = 1.5, 8.4 Hz), 7.14 (1H, s), 7.26 (1H, d, J = 3.1 Hz), 7.45 (1H, d, J = 8.4 Hz).		Fumarate
211	-H			209.8 - 214.2	Fumarate
212	-H		1H-NMR (CDCl3) δppm : 0.96-1.16 (1H, m), 1.09 (3H, s), 1.19-1.39 (4H, m), 1.44 (3H, s), 1.52-1.62 (2H, m), 1.69-1.82 (2H, m), 2.27-2.35 (1H, m), 2.68 (1H, d, J = 11.1 Hz), 2.75-2.85 (1H, m), 2.81 (1H, d, J = 11.1 Hz), 7.22 (1H, dd, J = 8.8, 1.9 Hz), 7.37-7.46 (2H, m), 8.01 (1H, s), 9.54-10.80 (1H, br)		–
213	$-CH_3$		1H-NMR (CDCl3) δppm : 0.99-1.30 (4H, m), 1.10 (3H, s), 1.22 (3H, s), 1.41-1.67 (2H, br), 1.70-1.80 (1H, m), 1.98-2.16 (1H, m), 2.26 (3H, s), 2.20-2.37 (1H, m), 2.57-2.64 (1H, m), 2.69 (1H, d, J = 11.1 Hz), 2.89 (1H, d, J = 11.1 Hz), 5.85 (1H, s), 7.21-7.28 (1H, m), 7.40-7.53 (2H, m), 8.01 (1H, s)		–
214	-H		1H-NMR (DMSO-d6) δppm : 1.00-1.51 (7H, m), 1.51-1.85 (6H, m), 1.92-2.20 (1H, brs), 2.60-3.70 (4H, m), 4.04 (3H, s), 6.85-7.90 (3H, m), 7.90-8.18 (1H, brs), 8.75-10.40 (3H, brm).		Dihydrochloride
215	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.40 (6H, m), 1.40-1.65 (6H, m), 1.65-1.80 (1H, m), 1.85-2.00 (1H, m), 2.65-2.80 (2H, m), 2.85-3.00 (1H, m), 3.00-3.21(1H, m), 3.98-4.55 (1H, br), 6.00 (2H, s), 6.55-6.65(1H, m), 6.73 (1H, d, J = 1.6 Hz), 6.86 (1H, d, J = 8.2 Hz), 8.65-8.95 (1H, br), 9.22-9.52 (1H, br).		Dihydrochloride
216	-H		1H-NMR (DMSO) δppm : 1.04-1.46 (4H, m), 1.35 (3H, s), 1.50-1.75 (4H, m), 1.59 (3H, s), 1.94-1.99 (1H, m), 2.82-2.92 (1H, m), 2.97 (1H, d, J = 12.3 Hz), 3.07 (1H, d, J = 12.3 Hz), 3.13-3.28 (1H, m), 7.28 (1H, dd, J = 8.5, 1.8 Hz), 7.81 (1H, d, J = 1.8 Hz), 8.12 (1H, d, J = 8.5 Hz), 8.85-9.05 (1H, br), 9.41 (1H, s), 9.48-9.56 (1H, br)		Dihydrochloride

[0320]

Table 32

Absolute configuration

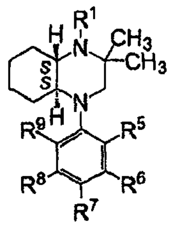


Example	R^1	R^4	NMR	Melting point (°C)	Salt
217	-H		1H-NMR (DMSO-d6) δppm: 1.00-1.44 (6H, m), 1.50-1.79 (7H, m), 1.96-2.08 (1H, m), 2.82-3.00 (2H, m), 3.00-3.25 (2H, m), 3.61 (3H, s), 6.62 (1H, d, J = 9.5 Hz), 7.38-7.46 (1H, m), 7.48-7.58 (2H, m), 7.91 (1H, d, J = 9.5 Hz), 7.98-8.62 (1H, br), 9.14-9.37 (1H, br), 9.65-9.88 (1H, br).		Dihydrochloride
218	-H		1H-NMR (CDCl3) δppm: 0.87-1.03 (1H, m), 1.09 (3H, m), 1.15-1.46 (4H, m), 1.46-1.65 (5H, m), 1.65-1.88 (2H, m), 2.47-2.60 (1H, m), 2.65 (1H, d, J = 11.3 Hz), 2.76 (1H, d, J = 11.3 Hz), 2.90-3.04 (1H, m), 7.25 (1H, d, J = 7.3 Hz), 7.40 (1H, dd, J = 4.2, 8.5 Hz), 7.65-7.72 (1H, m), 7.91 (1H, d, J = 8.5 Hz), 8.85 (1H, d, J= 8.5 Hz), 8.90 (1H, dd, J = 1.7, 4.2 Hz).		–
219	-H		1H-NMR (CDCl3) δppm: 0.93-1.12 (5H, m), 1.22-1.48 (3H, m), 1.55-1.70 (4H, m), 1.73-1.90 (3H, m), 2.50 (1H, d, J = 11.5 Hz), 2.55-2.65 (1H, m), 2.92-3.05 (2H, m), 7.09 (1H, d, J = 4.8 Hz), 7.49-7.56 (1H, m), 7.65-7.72 (1H, m), 8.05-8.10 (1H, m), 8.36 (1H, dd, J = 1.0, 8.4 Hz), 8.84 (1H, d, J = 4.8 Hz).		–
220	-H		1H-NMR (CDCl3) δppm: 0.80-1.17 (5H, m), 1.21-1.50 (6H, m), 1.61-1.88 (4H, m), 2.42-2.50 (1H, m), 2.74 (1H, d, J = 11.4 Hz), 2.80-2.90 (1H, m), 2.96 (1H, d, J = 11.4 Hz), 7.31-7.39 (2H, m), 7.50 (1H, dd, J = 2.4, 9.0 Hz), 8.01 (1H, d, J = 9.0 Hz), 8.06 (1H, dd, J = 1.1, 8.3 Hz), 8.81 (1H, dd, J = 1.7, 4.2 Hz).		–
221	-H		1H-NMR (CDCl3) δppm: 1.04-1.20 (4H, m), 1.20-1.48 (7H, m), 1.67-1.86 (3H, m), 1.96 (1H, dd, J = 3.0, 13.0), 2.61-2.70 (1H, m), 2.82-2.95 (2H, m), 3.07 (1H, d, J = 12.0 Hz), 7.20 (1H, d, J = 1.8 Hz), 7.32 (1H, dd, J = 2.1, 8.8 Hz), 7.50 (1H, d, J = 5.8 Hz), 7.84 (1H, d, J = 8.8 Hz), 8.41 (1H, d, J = 5.8 Hz), 9.09 (1H, s).		–

[0321]

Table 33

Absolute configuration



Example	R^1	R^5	R^6	R^7	R^8	R^9	NMR	Salt
222	-H	-H	-H	-F	-H	-H	1H-NMR (CDCl3) δppm : 1.21-1.36 (1H, m), 1.44-1.61 (2H, m), 1.68-2.00 (3H, m), 1.78 (3H, s), 2.09-2.33 (1H, m), 2.22 (3H, s), 2.51-2.55 (1H, m), 3.42 (1H, d, J = 13.2 Hz), 3.92-4.12 (1H, m), 4.15 (1H, d, J = 13.2 Hz), 4.37-4.44 (1H, m), 7.22-7.27 (4H, m), 7.90-8.46 (1H, br), 9.90-10.18 (1H, m), 10.32-10.60 (1H, brs)	Dihydrochloride
223	$-CH_3$	-H	-H	-F	-H	-H	1H-NMR (CDCl3) δppm : 0.90-1.10 (1H, m), 1.14-1.38 (2H, m), 1.40-1.75 (2H, m), 1.53 (3H, s), 1.69 (3H, s), 1.85-1.95 (1H, m), 2.01-2.23 (2H, m), 2.72 (3H, d, J = 5.0 Hz), 2.75 (1H, d, J = 12.9 Hz), 2.87-3.06 (1H, m), 3.40-3.50 (1H, m), 3.80 (1H, d, J = 12.9 Hz), 6.98-7.04 (2H, m), 7.18-7.23 (2H, m), 12.10 (1H, brs)	Dihydrochloride
224	-H	-H	-F	-F	-H	-H	1H-NMR (CDCl3) δppm : 1.17-1.46 (3H, m), 1.53-1.74 (2H, m), 1.66 (3H, s), 1.79 (3H, s), 1.79 (1H, brs), 1.88-2.05 (1H, m), 2.24-2.46 (1H, m), 2.88 (1H, d, J = 12.5 Hz), 3.10-3.40 (2H, m), 3.43 (1H, d, J = 12.5 Hz), 7.13-7.18 (2H, m), 7.20-7.28 (1H, m), 9.40-9.75 (1H, br), 9.76-10.08 (1H, br)	Hydrochloride
225	$-CH_3$	-H	-F	-F	-H	-H	1H-NMR (CDCl3) δppm : 1.19-1.41 (3H, m), 1.61 (8H, brs), 1.80-2.02 (1H, m), 2.04-2.24 (2H, m), 2.74 (3H, d, J = 5.0 Hz), 2.87 (1H, d, J = 12.8 Hz), 3.08-3.20 (1H, m), 3.62-3.78 (1H, m), 3.92 (1H, d, J = 12.8 Hz), 7.11-7.19 (2H, m), 7.27-7.32 (1H, m), 12.08 (1H, brs)	Hydrochloride
226	-H	-H	-Cl	-F	-H	-H	1H-NMR (CDCl3) δppm : 1.13-1.42 (3H, m), 1.47-1.81 (3H, m), 1.65 (3H, s), 1.74 (3H, s), 1.88-2.05 (1H, m), 2.32-2.38 (1H, m), 2.80 (1H, d, J = 12.5 Hz), 3.07-3.16 (1H, m), 3.19-3.29 (1H, m), 3.36 (1H, d, J = 12.5 Hz), 7.07-7.21 (2H, m), 7.34 (1H, dd, J = 6.5, 2.3 Hz), 9.56 (1H, brs), 9.82-9.86 (1H, br)	Hydrochloride
227	-H	-H	$-CH_3$	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.45 (6H, m), 1.45-1.81 (7H, m), 1.81-2.10 (1H, m), 2.22 (3H, d, J = 1.5 Hz), 2.78-3.00 (2H, m), 3.00-3.27 (2H, m), 4.10-4.98 (1H, br), 6.96-7.23 (3H, m), 9.00-9.40 (1H, br), 9.58-9.92 (1H, br).	Dihydrochloride
228	-H	-H	$-OCH_3$	-F	-H	-H	1H-NMR (DMSO-d6) δ ppm at 80 °C: 1.00-1.43 (6H, m), 1.49-1.77 (7H, m), 1.97-2.08 (1H, m), 2.81 (1H, d, J = 12.3 Hz), 2.84-2.93 (1H, m), 3.04-3.18 (2H, m), 3.83 (3H, s), 4.30-4.57 (1H, br), 6.68-6.74 (1H, m), 6.86 (1H, dd, J = 2.5, 7.9 Hz), 7.11 (1H, dd, J = 8.6, 11.4 Hz), 8.94-9.25 (1H, br), 9.49-9.80 (1H, br).	Dihydrochloride
229	-H	-H	-F	$-CH_3$	-H	-H	1H-NMR (CDCl3) δppm : 1.21-1.51 (2H, m), 1.62-1.97 (5H, m), 1.72 (3H, s), 2.03 (3H, s), 2.29 (3H, s), 2.44-2.49 (1H, m), 3.21 (1H, d, J = 12.9 Hz), 3.66-3.87 (2H, m), 3.21 (1H, d, J = 12.9 Hz), 7.25-7.31 (1H, m), 7.47-7.62 (2H, m), 10.00 (2H, brs)	Hydrochloride

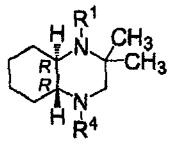
230	-CH₃	-H	-F	-CH₃	-H	-H	1H-NMR (CDCl3) δppm : 1.20-1.40 (3H, m), 1.48-1.75 (2H, m), 1.61 (3H, s), 1.64 (3H, s), 1.84-1.93 (1H, m), 2.11-2.16 (2H, m), 2.26 (3H, d, J = 1.9 Hz), 2.73 (3H, d, J = 5.0 Hz), 2.90 (1H, d, J = 12.9 Hz), 3.12-3.24 (1H, m), 3.65-3.80 (1H, m), 3.92 (1H, d, J = 12.9 Hz), 7.09-7.21 (3H, m), 12.33 (1H, brs)	Hydrochloride
231	-H	-H	-F	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.01-1.12 (1H, m), 1.20-1.39 (2H, m), 1.56-2.04 (4H, m), 1.63 (3H, s), 1.69 (3H, s), 2.31-2.36 (1H, m), 2.76 (1H, d, J = 12.4 Hz), 2.97-3.04 (1H, m), 3.13-3.24 (1H, m), 3.29 (1H, d, J = 12.4 Hz), 6.91-7.01 (2H, m), 7.34 (1H, dd, J = 8.4, 8.3 Hz), 9.50 (1H, brs), 9.80 (1H, brs)	Hydrochloride
232	-CH₃	-H	-F	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.00-1.13 (1H, m), 1.17-1.40 (2H, m), 1.53 (3H, s), 1.60 (3H, s), 1.60-1.81 (3H, m), 1.90-1.94 (1H, m), 2.04-2.25 (1H, m), 2.72 (3H, d, J = 4.9 Hz), 2.78 (1H, d, J = 12.8 Hz), 2.92-3.04 (1H, m), 3.46-3.55 (1H, m), 3.81 (1H, d, J = 12.8 Hz), 7.00-7.06 (2H, m), 7.32-7.39 (1H, m), 12.26 (1H, brs)	Hydrochloride
233	-H	-H	-F	-OCH₃	-F	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.34 (3H, m), 1.33 (3H, s), 1.51 (3H, s), 1.54-1.73 (4H, m), 1.96-2.01 (1H, m), 2.76-2.83 (1H, m), 2.89 (1H, d, J = 12.5 Hz), 2.98 (1H, d, J = 12.5 Hz), 3.08-3.18 (1H, m), 3.87 (3H, s), 4.76 (1H, s), 6.86-6.96 (2H, m), 9.01-9.09 (1H, m), 9.70-9.75 (1H, m)	Dihydrochloride
234	-H	-H	-F	-OCH₃	-H	-H	1H-NMR (DMSO-d6) δppm : 1.05-1.45 (6H, m), 1.45-1.60 (7H, m), 1.95-2.08 (1H, m), 2.70-2.90 (2H, m), 2.95-3.23 (2H, m), 3.81 (3H, s), 4.65-5.40 (1H, br), 6.88-7.08 (2H, m), 7.08-7.22 (1H, m), 8.90-9.25 (1H, br), 9.55-9.85 (1H, br).	Dihydrochloride
235	-H	-H	-Cl	-H	-H	-H	1H-NMR (CDCl3) δppm : 1.05-1.13 (1H, m), 1.23-1.35 (2H, m), 1.50-1.78 (3H, m), 1.63 (3H, s), 1.71 (3H, s), 1.92-2.08 (1H, m), 2.31-2.36 (1H, m), 2.78 (1H, d, J = 12.7 Hz), 3.00-3.09 (1H, m), 3.15-3.26 (1H, m), 3.31 (1H, d, J = 12.7 Hz), 7.07-7.10 (1H, m), 7.15-7.19 (2H, m), 7.23-7.29 (1H, m), 9.50 (1H, brs), 9.79 (1H, brs)	Hydrochloride
236	-CH₃	-H	-Cl	-H	-H	-H	1H-NMR (CDCl3) δppm : 1.18-1.50 (2H, m), 1.60-1.81 (2H, m), 1.71 (3H, s), 1.91-2.30 (5H, m), 2.00 (3H, s), 2.80 (3H, d, J = 4.9 Hz), 3.32 (1H, d, J = 13.4 Hz), 3.81-3.94 (1H, m), 4.42 (1H, d, J = 13.4 Hz), 4.61-4.70 (1H, m), 7.42-7.50 (2H, m), 7.97 (1H, brs), 8.13 (1H, brs), 13.7 (1H, brs)	Dihydrochloride
237	-H	-H	-Cl	-CN	-H	-H	1H-NMR (CDCl3) δppm : 1.05-1.20 (1H, m), 1.23-1.44 (2H, m), 1.54-2.10 (4H, m), 1.63 (3H, s), 1.68 (3H, s), 2.35-2.40 (1H, m), 2.89 (1H, d, J = 12.7 Hz), 3.19 (2H, br), 3.34 (1H, d, J = 12.7 Hz), 7.06 (1H, dd, J = 8.4, 2.0 Hz), 7.20 (1H, d, J = 2.0 Hz), 7.61 (1H, d, J = 8.4 Hz), 9.62 (1H, brs), 9.90 (1H, br)	Hydrochloride
238	-CH₃	-H	-Cl	-CN	-H	-H	1H-NMR (CDCl3) δppm : 1.01-1.15 (1H, m), 1.23-1.46 (2H, m), 1.50 (3H, s), 1.61 (3H, s), 1.61-1.98 (3H, m), 2.09-2.27 (2H, m), 2.72 (3H, d, J = 4.9 Hz), 2.87 (1H, d, J = 13.0 Hz), 2.91-3.03 (1H, m), 3.63-3.72 (1H, m), 3.84 (1H, d, J = 13.0 Hz), 7.14 (1H, dd, J = 8.4, 2.1 Hz), 7.26 (1H, d, J = 2.1 Hz), 7.62 (1H, d, J = 8.4 Hz), 12.38 (1H, brs)	Hydrochloride
239	-H	-H	-Cl	-CH₃	-H	-H	1H-NMR (CDCl3) δppm : 1.25-2.04 (7H, m), 1.75 (3H, s), 2.13 (3H, s), 2.40 (3H, s), 2.48-2.53 (1H, m), 3.33 (1H, d, J = 13.1 Hz), 3.88-3.92 (1H, m), 3.97 (1H, d, J = 13.1 Hz), 4.10-4.17 (1H, m), 7.36 (1H, d, J = 8.4 Hz), 7.78 (1H, d, J = 8.4 Hz), 8.00 (1H, s), 10.03-10.07 (1H, m), 10.20-10.30 (1H, m)	Hydrochloride

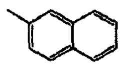
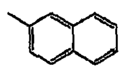
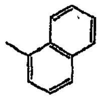
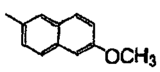
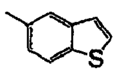
240	$-CH_3$	-H	-Cl	$-CH_3$	-H	-H	1H-NMR (CDCl3) δppm : 1.14-1.41 (3H, m), 1.47-1.74 (2H, m), 1.58 (3H, s), 1.60 (3H, s), 1.89-1.93 (1H, m), 2.10-2.22 (2H, m), 2.35 (3H, s), 2.72 (3H, d, J = 4.9 Hz), 2.83 (1H, d, J = 12.9 Hz), 3.00-3.15 (1H, m), 3.45-3.67 (1H, m), 3.85 (1H, d, J = 12.9 Hz), 7.11-7.22 (2H, m), 7.32 (1H, s), 12.24 (1H, brs)	Hydrochloride
241	-H	-H	-Cl	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 0.95-1.41 (6H, m), 1.41-1.80 (7H,m), 1.88-2.05 (1H, m), 2.69-2.90 (2H, m), 2.93-3.05 (1H, m), 3.05-3.24 (1H,m), 3.83 (3H, s), 4.15-5.35 (1H, br), 7.02-7.25 (3H, m), 8.87-9.18 (1H, br), 9.40-9.72 (1H, br).	Dihydrochloride
242	-H	-H	-H	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.13-1.24 (1H, m), 1.25-1.36 (2H, m), 1.60-1.83 (3H, m), 1.64 (3H, s), 1.74 (3H, s), 1.89-2.02 (1H, m), 2.32-2.37 (1H, m), 2.80 (1H, d, J = 12.5 Hz), 3.12-3.16 (1H, m), 3.22-3.29 (1H, m), 3.36 (1H, d, J = 12.5 Hz), 7.19-7.22 (2H, m), 7.29-7.33 (2H, m), 9.52 (1H, brs), 9.81 (1H, brs)	Hydrochloride
243	$-CH_3$	-H	-H	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.02-1.40 (3H, m), 1.48-1.75 (2H, m), 1.61 (3H, s), 1.63 (3H, s), 1.80-2.02 (1H, m), 2.11-2.16 (2H, m), 2.74 (3H, d, J = 5.0 Hz), 2.88 (1H, d, J = 12.9 Hz), 3.10-3.22 (1H, m), 3.66-3.78 (1H, m), 3.93 (1H, d, J = 12.9 Hz), 7.30-7.38 (4H, m), 12.28 (1H, brs)	Hydrochloride
244	-H	-H	$-CH_3$	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.90-1.79 (13H, m), 1.79-1.95 (1H, m), 2.29 (3H, s), 2.58-3.08 (4H, m), 3.10-4.90 (3H, br), 6.48 (2H, s), 6.89-7.00 (1H, m), 7.07 (1H, d, J = 2.3 Hz), 7.33 (1H, d, J = 8.5 Hz).	Fumarate
245	-H	-H	$-OCH_3$	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.45 (6H ,m), 1.45-1.82 (7H, m), 1.95-2.10 (1H, m), 2.78-3.10 (3H, m), 3.10-3.27 (1H, m), 3.85 (3H, s), 4.00-4.55 (1H, br), 6.73 (1H, dd, J = 2.1, 8,4 Hz), 6.80 (1H, d, J = 2.1 Hz), 7.37 (1H, d, J = 8.4 Hz), 8.90-9.19 (1H, br), 9.51-9.85 (1H, br).	Dihydrochloride
246	-H	-H	-Cl	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.15-1.45 (3H, m), 1.58-1.81 (3H, m), 1.65 (3H, s), 1.75 (3H, s), 1.88-2.04 (1H, m), 2.32-2.38 (1H, m), 2.82 (1H, d, J = 12.6 Hz), 3.12-3.31 (2H, m), 3.38 (1H, d, J = 12.6 Hz), 7.15 (1H, dd, J = 8.5, 2.3 Hz), 7.40 (1H, d, J = 2.3 Hz), 7.42 (1H, d, J = 8.5 Hz), 9.57 (1H, br), 9.82 (1H, br)	Hydrochloride
247	$-CH_3$	-H	-Cl	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.23-1.49 (2H, m), 1.60-1.75 (2H, m), 1.69 (3H, s), 1.91 (3H, s), 1.91-2.15 (3H, m), 2.22-2.28 (1H, m), 2.79 (3H, d, J = 4.9 Hz), 3.23 (1H, d, J = 13.2 Hz), 3.64-3.76 (1H, m), 4.33 (1H, d, J = 13.2 Hz), 4.43-4.52 (1H, m), 7.56(1H, d, J = 8.7 Hz), 7.82 (1H, dd, J = 8.7, 2.3 Hz), 8.14 (1H, d, J = 2.3 Hz), 12.88 (1H, brs)	Hydrochloride
248	-H	-H	-H	$-OCH_3$	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.50 (7H, m), 1.50-1.82 (6H, m), 1.96-2.18 (1H, m), 2.60-3.60 (4H, m), 3.76 (3H, s), 6.85-7.10 (2H, m), 7.10-7.68(2H, m), 8.60-10.90 (3H, m).	Dihydrochloride
249	-H	-H	$-OCH_3$	-F	-H	-H	1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.00-1.43 (6H, m), 1.49-1.77 (7H, m), 1.97-2.08 (1H, m), 2.81 (1H, d, J = 12.3 Hz), 2.84-2.93 (1H, m), 3.04-3.18 (2H, m), 3.83 (3H, s), 4.30-4.57 (1H, br), 6.68-6.74 (1H, m), 6.86 (1H, dd, J = 2.5, 7.9 Hz), 7.11 (1H, dd, J = 8.6, 11.4 Hz), 8.94-9.25 (1H, br), 9.49-9.80 (1H, br).	Dihydrochloride

[0322]

Table 34

Absolute configuration

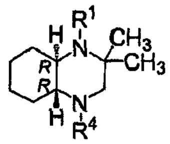


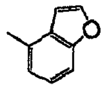
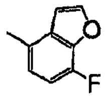
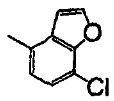
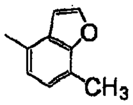
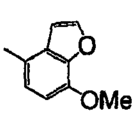
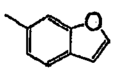
Example	R^1	R^4	NMR	Salt
250	-H		1H-NMR (CDCl3) δppm : 1.10-1.47 (3H, m), 1.48-2.16 (4H, m), 1.69 (3H, s), 1.78 (3H, s), 2.30-2.54 (1H, m), 2.95 (1H, d, J = 12.5 Hz), 3.20-3.50 (2H, br), 3.52 (1H, d, J = 12.5 Hz), 7.37-7.52 (2H, m), 7.60-8.00 (4H, m), 9.18-10.05 (2H, br)	Hydrochloride
251	$-CH_3$		1H-NMR (CDCl3) δppm : 1.20-1.35 (1H, m), 1.41-1.55 (1H, m), 1.59-1.82 (2H, m), 1.75 (3H, s), 1.91-2.01 (1H, m), 2.02-2.15 (2H, m), 2.14 (3H, s), 2.30-2.44 (2H, m), 2.85 (3H, d, J = 4.8 Hz), 3.49 (1H, d, J = 13.5 Hz), 4.07-4.19 (1H, m), 4.66 (1H, d, J = 13.5 Hz), 4.92-5.01 (1H, m), 7.59-7.66 (2H, m), 7.89-8.04 (4H, m), 8.87 (1H, br), 13.11 (1H, brs)	Dihydrochloride
252	-H		1H-NMR (DMSO-d6) δppm: 0.94-1.25 (2H, m), 1.25-1.45 (5H, m), 1.45-1.55 (1H, m), 1.55-1.80 (5H, m), 1.95-2.10 (1H, m), 2.82 (1H, d, J = 12.4 Hz), 2.97-3.11 (2H, m), 3.36-3.51 (1H, m), 7.40 (1H, d, J = 7.3 Hz), 7.50-7.59 (3H, m), 7.79 (1H, d, J = 8.2 Hz), 7.89-7.96 (1H, m), 8.42-8.48 (1H, m), 8.97-9.24 (1H, br), 9.50-9.80 (1H, br).	Hydrochloride
253	-H		1H-NMR (CDCl3) δppm : 1.23-2.17 (8H, m), 1.76 (3H, s), 2.09 (3H, s), 2.48-2.53 (1H, m), 3.27 (1H, d, J = 1.23 Hz), 3.66-4.18 (3H, m), 3.94 (3H,s), 7.15 (1H, d, J = 2.4 Hz), 7.23 (1H, dd, J = 9.0, 2.4 Hz), 7.74 (1H, brs), 7.79-7.85 (2H, m), 8.24 (1H, brs), 9.87-10.19 (2H, br)	Dihydrochloride
254	-H		1H-NMR (CDCl3) δppm : 1.20-2.05 (8H, m), 1.73 (3H, s), 2.00 (3H, s), 2.44-2.48 (1H, m), 3.15 (1H, d, J = 10.7 Hz), 3.55-3.88 (3H, br), 7.38 (1H, d, J = 5.5 Hz), 7.49-7.69 (1H, m), 7.55 (1H, d, J = 5.5 Hz), 7.92 (1H, d, J = 8.6 Hz), 8.14 (1H, brs), 9.94 (2H, brs)	Dihydrochloride

[0323]

Table 35

Absolute configuration

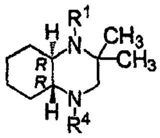


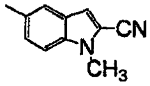
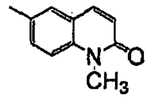
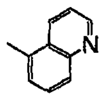
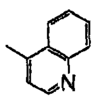
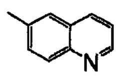
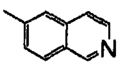
Example	R[1]	R[4]	NMR	Salt
255	-H		1H-NMR (DMSO-d6) δppm : 0.95-1.82 (13H, m), 1.97-2.12 (1H, m), 2.80-3.35 (4H, m), 6.07-6.72 (1H, br), 6.72-7.20 (2H, m), 7.23-7.35 (1H, m), 7.35-7.53 (1H, m), 7.99 (1H, brs), 9.00-9.50 (1H, br), 9.55-10.10 (1H, br).	Dihydrochloride
256	-H		1H-NMR (DMSO-d6) δ ppm at 80 °C: 0.96-1.26 (2H, m), 1.26-1.51 (5H, m), 1.51-1.61 (1H, m), 1.61-1.78 (5H, m), 1.99-2.08 (1H, m), 2.80 (1H, d, J = 12.3 Hz), 3.05-3.32 (3H, m), 3.58-4.12 (1H, br), 7.01 (1H, dd, J = 3.8, 8.5 Hz), 7.08-7.18 (2H, m), 8.01 (1H, d, J = 2.1 Hz), 9.10-9.35 (1H, br), 9.38-9.75 (1H, br).	Dihydrochloride
257	-H		1H-NMR (DMSO-d6) δ ppm at 80 °C: 0.98-1.27 (2H, m), 1.27-1.46 (4H, m), 1.46-1.60 (2H, m), 1.60-1.80 (5H, m), 1.98-2.10 (1H, m), 2.84 (1H, d, J = 12.4 Hz), 3.05-3.35 (3H, m), 3.45-3.90 (1H, br), 7.05 (1H, d, J = 8.2 Hz), 7.08-7.13 (1H, br), 7.36 (1H, d, J = 8.2 Hz), 8.03 (1H, d, J = 2.2 Hz), 8.98-9.35 (1H, br), 9.35-9.72 (1H, br).	Dihydrochloride
258	-H		1H-NMR (CDCl3) δppm: 0.82-1.05 (2H, m), 1.07 (3H, s), 1.19-1.43 (3H, m), 1.49 (3H, s), 1.56-1.68 (1H, m), 1.68-1.90 (3H, m), 2.35-2.51 (4H, m), 2.51-2.70 (1H, m), 2.78-2.92 (2H, m), 6.83-6.89 (2H, m), 7.01 (1H, d, J = 7.8 Hz), 7.56 (1H, d, J = 2.1 Hz).	–
259	-H		1H-NMR (DMSO-d6) δ ppm at 80 °C: 0.96-1.25 (2H, m), 1.25-1.60 (6H, m), 1.60-1.79 (5H, m), 1.98-2.10 (1H, m), 2.76 (1H, d, J = 12.3 Hz), 2.99-3.37 (3H, m), 3.93 (3H, s), 4.52-4.86 (1H, br), 6.86 (1H, d, J = 8.4 Hz), 6.95 (1H, d, = 8.4 Hz), 6.98-7.09 (1H, br), 7.87 (1H, d, J = 2.1 Hz), 9.02-9.40 (1H, br), 9.40-9.75 (1H, br).	Dihydrochloride
260	-H		1H-NMR (DMSO-d6) δ ppm at 80 °C: 1.03-1.44 (6H, m), 1.51-1.79 (7H, m), 2.00-2.10 (1H, m), 2.87 (1H, d, J = 12.4 Hz), 2.94-3.05 (1H, m), 3.10-3.23 (2H, m), 4.64-5.12 (1H, br), 6.88 (1H, d, J = 1.4 Hz), 7.05-7.09 (1H, m), 7.33-7.36 (1H, br), 7.59 (1H, d, J = 8.2 Hz), 7.89 (1H, J = 2.2 Hz), 8.97-9.26 (1H, br), 9.45-9.82 (1H, br).	Dihydrochloride

[0324]

Table 36

Absolute configuration

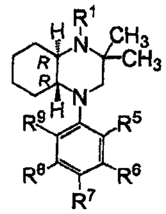


Example	R^1	R^4	NMR	Melting point (°C)	Salt
261	-H			209.8 - 214.2	Fumarate
262	-H		1H-NMR (DMSO-d6) δppm: 1.00-1.44 (6H, m), 1.50-1.79 (7H, m), 1.98-2.08 (1H, m), 2.82-3.00 (2H, m), 3.00-3.25 (2H, m), 3.61 (3H, s), 6.62 (1H, d, J = 9.5 Hz), 7.38-7.46 (1H, m), 7.48-7.58 (2H, m), 7.91 (1H, d, J = 9.5 Hz), 7.98-8.62 (1H, br), 9.14-9.37 (1H, br), 9.65-9.88 (1H, br).		Dihydrochloride
263	-H		1H-NMR (CDCl3) δppm: 0.87-1.03 (1H, m), 1.09 (3H, m), 1.15-1.46 (4H, m), 1.46-1.65 (5H, m), 1.65-1.88 (2H, m), 2.47-2.60 (1H, m), 2.65 (1H, d, J = 11.3 Hz), 2.76 (1H, d, J = 11.3 Hz), 2.90-3.04 (1H, m), 7.25 (1H, d, J = 7.3 Hz), 7.40 (1H, dd, J = 4.2, 8.5 Hz), 7.65-7.72 (1H, m), 7.91 (1H, d, J = 8.5 Hz), 8.85 (1H, d, J= 8.5 Hz), 8.90 (1H, dd, J = 1.7, 4.2 Hz).		–
264	-H		1H-NMR (CDCl3) δppm: 0.93-1.12 (5H, m), 1.22-1.48 (3H, m), 1.55-1.70 (4H, m), 1.73-1.90 (3H, m), 2.50 (1H, d, J = 11.5 Hz), 2.55-2.65 (1H, m), 2.92-3.05 (2H, m), 7.09 (1H, d, J = 4.8 Hz), 7.49-7.56 (1H, m), 7.65-7.72 (1H, m), 8.05-8.10 (1H, m), 8.36 (1H, dd, J = 1.0, 8.4 Hz), 8.84 (1H, d, J = 4.8 Hz).		–
265	-H		1H-NMR (CDCl3) δppm: 0.80-1.17 (5H, m), 1.21-1.50 (6H, m), 1.61-1.88 (4H, m), 2.42-2.50 (1H, m), 2.74 (1H, d, J = 11.4 Hz), 2.80-2.90 (1H, m), 2.96 (1H, d, J = 11.4 Hz), 7.31-7.39 (2H, m), 7.50 (1H, dd, J = 2.4, 9.0 Hz), 8.01 (1H, d, J = 9.0 Hz), 8.06 (1H, dd, J = 1.1, 8.3 Hz), 8.81 (1H, dd, J = 1.7, 4.2 Hz).		–
266	-H		1H-NMR (CDCl3) δppm: 1.04-1.20 (4H, m), 1.20-1.48 (7H, m), 1.67-1.86 (3H, m), 1.96 (1H, dd, J = 3.0, 13.0), 2.61-2.70 (1H, m), 2.82-2.95 (2H, m), 3.07 (1H, d, J = 12.0 Hz), 7.20 (1H, d, J = 1.8 Hz), 7.32 (1H, dd, J = 2.1, 8.8 Hz), 7.50 (1H, d, J = 5.8 Hz), 7.84 (1H, d, J = 8.8 Hz), 8.41 (1H, d, J = 5.8 Hz), 9.09 (1H, s).		–

[0325]

Table 37

Absolute configuration

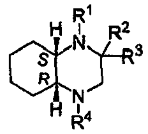


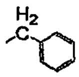
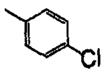
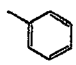
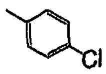
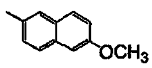
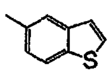
Example	R1	R5	R6	R7	R8	R9	NMR	Salt
267	-H	-H	-H	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 0.99-1.44 (6H, m), 1.44-1.80 (7H, m), 1.93-2.10 (1H, m), 2.75-2.99 (2H, m), 2.99-3.28 (2H,m), 5.08-6.60 (1H, br), 7.10-7.33 (4H, m), 8.96-9.42 (1H, br), 9.58-9.94 (1H, br).	Dihydrochloride
268	-H	-H	-OCH$_3$	-F	-H	-H	1H-NMR (DMSO-d6) δ ppm at 80 °C: 1.00-1.43 (6H, m), 1.49-1.77 (7H, m), 1.97-2.08 (1H, m), 2.81 (1H, d, J = 12.3 Hz), 2.84-2.93 (1H, m), 3.04-3.18 (2H, m), 3.83 (3H, s), 4.30-4.57 (1H, br), 6.68-6.74 (1H, m), 6.86 (1H, dd, J = 2.5, 7.9 Hz), 7.11 (1H, dd, J = 8.6, 11.4 Hz), 8.94-9.25 (1H, br), 9.49-9.80 (1H, br).	Dihydrochloride
269	-H	-H	-Cl	-CN	-H	-H	1H-NMR (CDCl3) δppm : 1.02-1.17 (1H, m), 1.25-1.44 (2H, m), 1.62-2.05 (4H, m), 1.63 (3H, s), 1.66 (3H, s), 2.35-2.41 (1H, m), 2.89 (1H, d, J = 12.8 Hz), 3.20 (2H, br), 3.35 (1H, d, J = 12.8 Hz), 7.07 (1H, dd, J = 8.4, 2.0 Hz), 7.20 (1H, d, J = 2.0 Hz), 7.61 (1H, d, J = 8.4 Hz), 9.61 (1H, brs), 9.89 (1H, br)	Hydrochloride
270	-H	-H	-H	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 0.95-1.45 (6H, m), 1.45-1.80 (7H, m), 1.88-2.06 (1H, m), 2.70-3.05 (3H, m), 3.08-3.28 (1H, m), 3.50-3.94 (1H, br), 7.13 (2H, d, J = 8.7 Hz), 7.39 (2H, d, J = 8.7 Hz), 8.66-9.20 (1H, br), 9.20-9.80 (1H, br).	Dihydrochloride
271	-H	-H	-OCH$_3$	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.45 (6H, m), 1.45-1.83 (7H, m), 1.90-2.08 (1H, m), 2.70-2.87 (1H, m), 2.87-3.08 (2H, m), 3.08-3.28 (1H, m), 3.85 (3H, s), 6.72 (1H, dd, J = 2.2, 8.4 Hz), 6.79 (1H, d, J = 2.2 Hz), 7.36 (1H, d, J = 8.4 Hz), 8.73-9.10 (1H, br), 9.34-9.70 (1H, br).	Hydrochloride
272	-H	-H	-Cl	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 0.98-1.14 (1H, m), 1.26-1.39 (2H, m), 1.55-1.78 (3H, m), 1.62 (3H, s), 1.68 (3H, s), 1.92-2.05 (1H, m), 2.30-2.35 (1H, m), 2.73 (1H, d, J = 12.5 Hz), 2.95-3.03 (1H, m), 3.11-3.23 (1H, m), 3.28 (1H, d, J = 12.5 Hz), 7.20 (1H, dd, J = 8.5, 2.4 Hz), 7.25 (1H, d, J = 2.4 Hz), 7.39 (1H, d, J = 8.5 Hz), 9.49 (1H, br), 9.79 (1H, br)	Hydrochloride
273	-CH$_3$	-H	-Cl	-Cl	-H	-H	1H-NMR (CDCl3) δppm : 1.23-1.49 (2H, m), 1.60-1.74 (2H, m), 1.69 (3H, s), 1.87-2.15 (3H, m), 1.91 (3H, s), 2.21-2.28 (1H, m), 2.78 (3H, d, J = 4.9 Hz), 3.22 (1H, d, J = 13.2 Hz), 3.63-3.75 (1H, m), 4.32 (1H, d, J = 13.2 Hz), 4.42-4.51 (1H, m), 7.56(1H, d, J = 8.7 Hz), 7.81 (1H, dd, J = 8.7, 2.0 Hz), 8.14 (1H, d, J = 2.0 Hz), 12.71 (1H, brs)	Hydrochloride

[0326]

Table 38

Absolute configuration

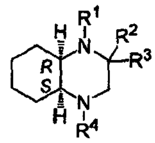


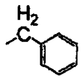
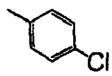
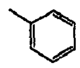
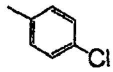
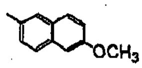
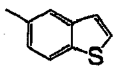
Example	R^1	R^2,R^3	R^4	NMR	Salt
274		-H, -H		1H-NMR (CDCl3) δppm : 1.25-1.7 (5H, m), 1.75-1.9 (1H, m), 2.05-2.2 (2H, m), 2.3-2.4 (1H, m), 2.6-2.7 (1H, m), 2.8-2.9 (1H, m), 2.92 (1H, d, J = 13.1Hz), 3.0-3.15 (2H, m), 3.65-3.75 (1H, m), 4.20 (1H, d, J = 13.1Hz), 6.7-6.8 (2H, m), 7.1-7.2 (2H, m), 7.2-7.3 (1H, m), 7.3-7.4 (4H, m).	–
275	-H	-H, -H		1H-NMR (DMSO-d6) δppm : 1.2-1.4 (2H, m), 1.4-1.5 (1H, m), 1.5-1.95 (4H, m), 1.95-2.05 (1H, m), 2.95-3.2 (2H, m), 3.25-3.4 (1H, m), 3.4-3.6 (2H, m), 3.95-4.1 (1H, m), 6.48 (1H, br), 6.80 (1H, dd, J = 7.2, 7.2Hz), 6.9-7.0 (2H, m), 7.2-7.3 (2H, m), 9.22 (1H, br), 9.87 (1H, br).	Dihydrochloride
276	-H	$-(CH_2)_3-$		1H-NMR (DMSO-d6) δppm : 1.25-1.4 (2H, m), 1.4-2.35 (10H, m), 2.3-2.6 (2H, m), 3.04 (1H, d, J = 13.3Hz), 3.35-3.5 (1H, m), 3.67 (1H, d, J = 13.4Hz), 3.7-4.3 (2H, m), 6.95-7.05 (2H, m), 7.2-7.3 (2H, m), 8.95-9.2 (1H, m), 10.1-10.3 (1H, m).	Dihydrochloride
277	-H	$-(CH_2)_3-$		1H-NMR (CDCl3) δppm : 1.05-1.35 (3H, m), 1.35-1.45 (1H, m), 1.45-1.65 (3H, m), 1.65-1.9 (5H, m), 1.9-2.0 (1H, m), 2.0-2.1 (1H, m), 2.2-2.3 (1H, m), 2.93 (1H, d, J = 11.4Hz), 3.25-3.35 (1H, m), 3.39 (1H, d, J = 11.4Hz), 3.7-3.8 (1H, m), 3.89 (3H, s), 7.01 (1H, d, J = 2.4Hz), 7.04 (1H, d, J = 2.5Hz), 7.07 (1H, dd, J = 2.6, 8.8Hz), 7.25-7.3 (1H, m), 7.58 (1H, d, J = 8.9Hz), 7.61 (1H, d, J = 9.1Hz).	–
278	-H	$-(CH_2)_3-$		1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.4-2.15 (10H, m), 2.35-2.6 (2H, m), 3.14 (1H, d, J = 12.5Hz), 3.4-3.55 (1H, m), 3.64 (1H, d, J = 13.1Hz), 3.95-4.05 (1H, m), 4.05-4.4 (1H, m), 7.19 (1H, dd, J = 2.4, 8.9Hz), 7.31 (1H, d, J = 5.3Hz), 7.41 (1H, d, J = 2.0Hz), 7.69 (1H, d, J = 5.4Hz), 7.83 (1H, d, J = 8.9Hz), 8.9-9.1 (1H, m), 11-12.5 (1H, m).	Dihydrochloride

[0327]

Table 39

Absolute configuration

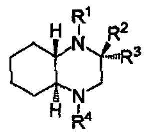


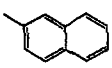
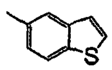
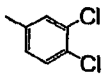
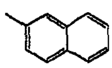
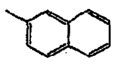
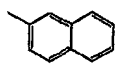
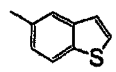
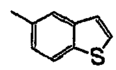
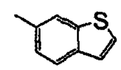
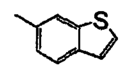
Example	R^1	R^2, R^3	R^4	NMR	Melting point (°C)	Salt
279		-H, -H		1H-NMR (CDCl3) δppm : 1.25-1.5 (4H, m), 1.55-1.7 (1H, m), 1.75-1.85 (1H, m), 2.05-2.2 (2H, m), 2.3-2.4 (1H, m), 2.6-2.7 (1H, m), 2.8-2.9 (1H, m), 2.92 (1H, d, J = 13.2Hz), 3.0-3.15 (2H, m), 3.65-3.8 (1H, m), 4.20 (1H, d, J = 13.1Hz), 6.7-6.8 (2H, m), 7.1-7.2 (2H, m), 7.2-7.3 (1H, m), 7.3-7.4 (4H, m).		–
280	-H	-H, -H		1H-NMR (DMSO-d6) δppm : 1.2-1.4 (2H, m), 1.4-1.5 (1H, m), 1.5-1.95 (4H, m), 1.95-2.05 (1H, m), 3.0-3.2 (2H, m), 3.25-3.4 (1H, m), 3.4-3.6 (2H, m), 3.95-4.1 (1H, m), 5.65 (1H, br), 6.79 (1H, dd, J = 7.2, 7.2Hz), 6.9-7.0 (2H, m), 7.2-7.3 (2H, m), 9.16 (1H, br), 9.81 (1H, br).		Dihydrochloride
281	-H	$-(CH_2)_3-$		1H-NMR (DMSO-d6) δppm : 1.25-1.4 (2H, m), 1.4-2.15 (10H, m), 2.3-2.6 (2H, m), 3.03 (1H, d, J = 12.5Hz), 3.35-3.5 (1H, m), 3.65-3.85 (2H, m), 3.9-4.0 (1H, m), 6.95-7.05 (2H, m), 7.2-7.3 (2H, m), 8.9-9.15 (1H, m), 10.05-12.5 (1H, m).		Dihydrochloride
282	-H	$-(CH_2)_3-$		1H-NMR (CDCl3) δppm : 1.05-1.35 (3H, m), 1.35-1.45 (1H, m), 1.45-1.65 (3H, m), 1.65-1.9 (5H, m), 1.9-2.0 (1H, m), 2.0-2.1 (1H, m), 2.2-2.3 (1H, m), 2.93 (1H, d, J = 11.4Hz), 3.25-3.35 (1H, m), 3.39 (1H, d, J = 11.4Hz), 3.7-3.8 (1H, m), 3.89 (3H, s), 7.01 (1H, d, J = 2.4Hz), 7.04 (1H, d, J = 2.5Hz), 7.07 (1H, dd, J = 2.6, 8.8Hz), 7.25-7.3 (1H, m), 7.58 (1H, d, J = 8.8Hz), 7.61 (1H, d, J = 9.0Hz).		–
283	-H	$-(CH_2)_3-$		1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.4-2.15 (10H, m), 2.4-2.6 (2H, m), 3.15 (1H, d, J = 12.1Hz), 3.4-3.55 (1H, m), 3.64 (1H, d, J = 13.0Hz), 3.95-4.1 (1H, m), 4.2-4.6 (1H, m), 7.19 (1H, dd, J = 2.4, 8.9Hz), 7.31 (1H, d, J = 5.2Hz), 7.41 (1H, d, J = 2.0Hz), 7.69 (1H, d, J = 5.4Hz), 7.83 (1H, d, J = 8.9Hz), 8.9-9.1 (1H, m), 10.1-10.3 (1H, m).		Dihydrochloride

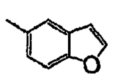
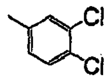
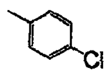
[0328]

Table 40

Relative configuration



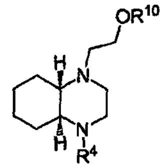
Example	R^1	R^2	R^3	R^4	NMR	Salt
284	-H	-H	$-CH_3$		1H-NMR (CDCl3) δppm : 1.18-1.48 (2H, m), 1.62-2.08 (8H, m), 2.56-2.61 (1H, m), 3.63-3.66 (1H, m), 4.23 (1H, brs), 4.67 (3H, brs), 7.61-8.26 (7H, m), 9.60-9.81 (1H, m), 11.36 (1H, br), 14.02 (1H, brs)	Dihydrochloride
285	-H	-H	$-CH_3$		1H-NMR (DMSO) δppm : 1.02-1.43 (3H, m), 1.30 (3H, d, J = 6.4 Hz), 1.44-1.68 (4H, m), 1.95-2.20 (1H, m), 2.97-3.53 (6H, m), 7.26-7.46 (1H, br), 7.50 (1H, d, J = 5.4 Hz), 7.69-8.00 (1H, br), 7.86 (1H, d, J = 5.4 Hz), 8.09 (1H, d, J = 8.2 Hz), 9.28-10.12 (2H, br)	Dihydrochloride
286	-H	-H	$-CH_3$		1H-NMR (DMSO) δppm : 0.87-1.06 (1H, m), 1.17-1.35 (2H, m), 1.24 (3H, d, J = 6.3 Hz), 1.41-1.84 (4H, m), 1.92-2.07 (1H, m), 2.88-3.08 (3H, m), 3.24 (1H, d, J = 12.4 Hz), 3.31-3.52 (1H, br), 7.16 (1H, dd, J = 8.6, 2.1 Hz), 7.40 (1H, d, J = 2.1 Hz), 7.60 (1H, d, J = 8.6 Hz), 9.02-9.33 (1H, br), 9.50-9.85 (1H, br)	Hydrochloride
287	-H	-H	$-C_2H_5$		1H-NMR (CDCl3) δppm : 1.05 (3H, t, J = 7.3 Hz), 1.24-1.48 (2H, m), 1.51-2.14 (6H, br), 2.18-2.41 (1H, br), 2.43-2.76 (1H, m), 2.83-5.31 (5H, br), 7.33-8.24 (6H, br), 9.15-10.20 (1.3H, br), 11.04-11.78 (0.3H, br), 13.30-13.79 (0.4H, br)	Hydrochloride
288	$-CH_3$	-H	$-C_2H_5$		1H-NMR (CDCl3) δppm : 1.06 (3H, t, J = 7.5 Hz), 1.22-2.25 (10H, m), 2.26-2.45 (2H, m), 2.94 (3H, s), 3.31-4.97 (4H, br), 7.36-8.02 (7H, m), 12.47-13.27 (1H, br)	Dihydrochloride
289	-H	$-C_2H_5$	$-C_2H_5$		1H-NMR (CDCl3) δppm : 0.80-2.47 (11H, m), 0.99 (3H, t, J = 7.4 Hz), 1.17 (3H, t, J = 7.3 Hz), 2.66-2.76 (1H, m), 2.86-3.18 (1H, br), 3.38-3.43 (1H, m), 3.65-4.01 (2H, m), 4.02-4.36 (1H, m), 7.54-7.61 (2H, m), 7.80-7.96 (5H, m), 9.37 (1H, brs), 9.80-10.49 (1H, br)	Dihydrochloride
290	-H	-H	$-C_2H_5$		1H-NMR (CDCl3) δppm : 1.07 (3H, t, J = 7.5 Hz), 1.25-1.42 (2H, m), 1.48-1.85 (7H, m), 1.93-2.10 (2H, m), 2.16-2.40 (1H, m), 2.50-2.69 (1H, m), 2.91-5.05 (4H, br), 7.33-8.76 (4H, br & m), 9.19-9.85 (1H, br), 11.09-11.67 (0.4H, br), 13.40-13.82 (0.6H, br)	Dihydrochloride
291	-H	$-C_2H_5$	$-C_2H_5$		1H-NMR (CDCl3) δppm : 0.80-2.44 (11H, m), 0.97 (3H, t, J = 7.4 Hz), 1.15 (3H, t, J = 7.4 Hz), 2.60-2.66 (1H, m), 2.78-3.09 (1H, m), 3.20-3.37 (1H, m), 3.45-4.16 (3H, m), 7.37 (1H, d, J = 5.4 Hz), 7.49-7.71 (1H, m), 7.55 (1H, d, J = 5.4 Hz), 7.86-7.96 (1H, m), 8.01-8.47 (1H, br), 9.02-9.48 (1H, br), 9.69-10.18 (1H, br)	Dihydrochloride
292	-H	-H	$-C_2H_5$		1H-NMR (CDCl3) δppm : 1.07 (3H, t, J = 7.5 Hz), 1.23-1.50 (3H, m), 1.51-2.13 (8H, m), 2.16-2.39 (1H, m), 2.50-2.71 (1H, m), 2.90-5.09 (4H, br), 7.30-7.46 (1H, m), 7.46-8.33 (3H, br), 9.10-9.91 (1H, br), 10.95-11.65 (0.4H, br), 13.37-13.92 (0.6H, br)	Dihydrochloride
293	-H	$-C_2H_5$	$-C_2H_5$		1H-NMR (CDCl3) δppm : 0.80-2.45 (10H, m), 0.97 (3H, t, J = 7.3 Hz), 1.45 (3H, t, J = 7.3 Hz), 2.60-2.66 (1H, m), 2.74-3.05 (1H, m), 3.11-3.42 (1H, m), 3.51-3.97 (3H, m), 7.37 (1H, d, J = 5.4 Hz), 7.50-7.68 (2H, m), 7.53 (1H, d, J = 5.5 Hz), 7.83-7.88 (1H, m), 8.02-8.53 (1H, br), 9.12-9.46 (1H, br), 9.66-10.18 (1H, br)	Dihydrochloride

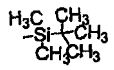
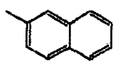
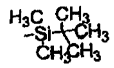
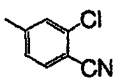
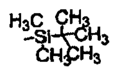
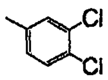
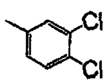
294	-H	$-C_2H_5$	$-C_2H_5$		1H-NMR (CDCl3) δppm : 0.87-2.38 (11H, m), 0.98 (3H, t, J = 7.4 Hz), 1.14 (3H, t, J = 7.2 Hz), 2.49-2.73 (1H, m), 2.73-3.11 (1H, m), 3.31-3.42 (1H, m), 3.52-4.26 (3H, m), 6.82 (1H, d, J = 1.9 Hz), 7.54-7.68 (2H, m), 7.71 (1H, d, J = 1.9 Hz), 7.79-8.30 (1H, br), 8.94-9.51 (1H, br), 9.75-10.34 (1H, br)	Dihydrochloride
295	-H	-H	$-C_2H_5$		1H-NMR (CDCl3) δppm : 1.08 (3H, t, J = 7.5 Hz), 1.25-1.43 (2H, m), 1.54-2.05 (6H, m), 2.15-2.34 (1H, m), 2.50-2.64 (1H, m), 3.56 (1H, d, J = 11.1 Hz), 3.84-4.04 (1H, m), 4.10-4.46 (3H, m), 7.62 (1H, d, J = 8.6 Hz), 7.72 (1H, d, J = 8.6 Hz), 7.97 (1H, s), 9.25-9.53 (1H, br), 10.75-11.16 (1H, br)	Hydrochloride
296	-H	-H	$-C_3H_7$		1H-NMR (DMSO-d6) δppm : 0.93 (3H, t, J = 7.3Hz), 1.2-1.4 (2H, m), 1.4-1.6 (3H, m), 1.6-1.9 (6H, m), 2.05-2.15 (1H, m), 2.8-2.9 (1H, m), 3.25 (1H, br), 3.5-3.6 (2H, m), 4.0-4.1 (1H, m), 6.95-7.05 (2H, m), 7.2-7.3 (2H m), 8.35-8.6 (1H, m), 9.3-9.5 (1H, m).	Hydrochloride

[0329]

Table 41

Relative configuration

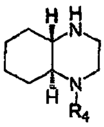


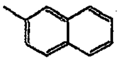
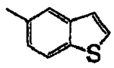
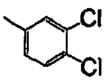
Example	R^{10}	R^4	NMR	Salt
297			1H-NMR (CDCl3) δppm : 0.08 (6H, s), 0.91 (9H, s), 1.04-1.35 (4H, m), 1.53-1.80 (3H, m), 2.18-2.33 (2H, m), 2.60-2.76 (2H, m), 2.80-3.01 (3H, m), 3.09-3.13 (2H, m), 3.69-3.85 (2H, m), 7.29-7.48 (3H, m), 7.52-7.53 (1H, m), 7.73-7.80 (3H, m)	–
298			1H-NMR (CDCl3) δppm : 0.06 (6H, s), 0.90 (9H, s), 1.04-1.37 (5H, m), 1.61-1.75 (2H, m), 1.79-1.84 (2H, m), 2.15-2.20 (1H, m), 2.32-2.40 (1H, m), 2.58-2.68 (1H, m), 2.71-2.90 (3H, m), 2.97-3.14 (2H, m), 3.19-3.26 (1H, m), 3.64-3.79 (2H, m), 6.93 (1H, dd, J = 8.5, 2.1 Hz), 7.07 (1H, d, J = 2.1 Hz), 7.52 (1H, d, J = 8.5 Hz)	–
299			1H-NMR (CDCl3) δppm : 0.07 (6H, s), 0.81-1.90 (3H, m), 0.90 (9H, s), 1.55-1.78 (4H, m), 2.14-2.24 (2H, m), 2.46-2.54 (1H, m), 2.57-2.67 (1H, m), 2.72-2.82 (1H, m), 2.85-2.97 (4H, m), 3.66-3.81 (2H, m), 6.97 (1H, dd, J = 8.6, 2.4 Hz), 7.22 (1H, d, J = 2.4 Hz), 7.34 (1H, d, J = 8.6 Hz)	–
300	-H		1H-NMR (CDCl3) δppm : 1.25-1.53 (2H, m), 1.61-1.70 (1H, m), 1.74-1.80 (2H, m), 1.89-2.04 (2H, m), 2.38-2.43 (1H, m), 3.08-3.16 (1H, m), 3.53-3.59 (1H, m), 3.66-3.73 (1H, m), 3.88-3.94 (1H, m), 4.06-4.14 (3H, m), 4.35-4.43 (2H, m), 4.61-4.78 (1H, m), 7.61 (1H, d, J = 8.7 Hz), 7.71 (1H, d, J = 8.7 Hz), 8.00 (1H, brs), 12.52 (1H, brs)	Hydrochloride

[0330]

Table 42

Relative configuration

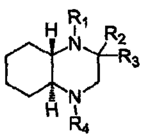


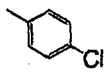
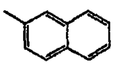
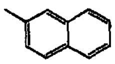
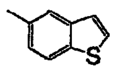
Example	R⁴	NMR	Salt
301		1H-NMR (CDCl3) δppm : 1.25-1.50 (2H, m), 1.60-2.05 (5H, m), 2.35-2.70 (1H, m), 2.81-5.38 (6H, br), 7.32-8.69 (7H, br), 9.47-10.31 (1H, br), 10.55-11.77 (0.45H, br), 13.51-14.36 (0.55H, br)	Hydrochloride
302		1H-NMR (CDCl3) δppm : 1.25-1.51 (2H, m), 1.63-2.09 (5H, m), 2.50-2.56 (1H, m), 3.56-3.91 (2H, m), 3.91-5.16 (4H, br), 7.46 (1H, d, J = 5.5 Hz), 7.55-8.76 (3H, br), 7.66 (1H, d, J = 5.5 Hz), 9.46-10.11 (1H, br), 10.94-11.83 (1H, br), 13.61-14.25 (1H, br)	Dihydrochloride
303		1H-NMR (CDCl3) δppm : 1.24-1.49 (2H, br), 1.51-2.00 (5H, m), 2.33-2.54 (1H, m), 3.30-3.79 (5H, m), 3.81-4.15 (1H, br),7.34 (1H, d, J = 8.6 Hz), 7.50 (1H, d, J = 8.6 Hz), 7.59 (1H, s), 10.01 (1H, brs), 10.14-10.56 (1H, br)	Hydrochloride

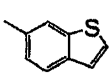
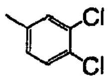
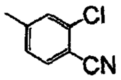
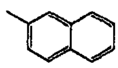
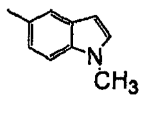
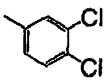
[0331]

Table 43

Relative configuration



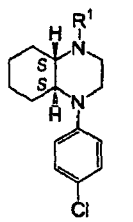
Example	R¹	R², R³	R⁴	NMR	Salt
304	-H	-(CH₂)₅-		1H-NMR (DMSO-d6) δppm : 1.2-1.35 (2H, m), 1.4-2.1 (10H, m), 2.3-2.5 (2H, m), 3.03 (1H, d, J = 13.2Hz), 3.35-3.45 (1H, m), 3.68 (1H, d, J = 13.4Hz), 3.9-4.0 (1H, m), 4.35 (1H, br), 6.95-7.05 (2H, m), 7.2-7.3 (2H, m), 8.9-9.1 (1H, m), 10.0-10.15 (1H, m).	Dihydrochloride
305	-H	-(CH₂)₄-		1H-NMR (CDCl3) δppm : 1.20-1.58 (2H, m), 1.60-2.17 (10H, m), 2.29-2.37 (1H, m), 2.46-2.67 (2H, m), 2.96-3.29 (1H, br), 3.33 (1H, d, J = 13.2 Hz), 3.60-3.98 (1H, br), 3.98-4.41 (2H, br), 7.56-7.60 (2H, m), 7.80-7.98 (4H, m), 8.11-8.71 (1H, br), 9.63-10.08 (1H, br), 10.13-10.87 (1H, br)	Hydrochloride
306	-CH₃	-(CH₂)₄-		1H-NMR (CDCl3) δppm : 1.20-1.33 (1H, m), 1.40-2.08 (12H, m), 2.24-2.44 (2H, m), 2.58-2.69 (1H, m), 2.83 (3H, d, J = 4.8 Hz), 3.45 (1H, d, J = 13.4 Hz), 3.58-3.83 (1H, m), 3.87-4.14 (1H, m), 4.08 (1H, d, J = 13.4 Hz), 4.74-4.98 (1H, m), 7.55-7.65 (2H, m), 7.88-8.03 (4H, m), 8.42-9.20 (1H, br), 13.33 (1H, brs)	Dihydrochloride
307	H	-(CH₂)₄-		1H-NMR (CDCl3) δppm : 1.18-1.35 (1H, m), 1.41-2.17 (12H, m), 2.30-2.38 (1H, m), 2.51-2.67 (2H, m), 3.00-3.32 (1H, br), 3.36 (1H, d, J = 12.4 Hz), 3.65-4.47 (3H, br), 7.43 (1H, d, J = 5.5 Hz), 7.61 (1H, d, J = 5.5 Hz), 7.66-7.96 (1H, br), 7.99 (1H, d, J = 8.6 Hz), 8.12-8.19 (1H, br), 9.65-10.02 (1H, br), 10.29-10.83 (1H, br)	Dihydrochloride

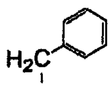
308	H	-(CH2)4-		1H-NMR (CDCl3) δppm : 1.20-1.36 (1H, m), 1.41-2.21 (12H, m), 2.29-2.37 (1H, m), 2.49-2.56 (1H, m), 2.61-2.67 (1H, m), 3.07-3.30 (1H, br), 3.36 (1H, d, J = 13.1 Hz), 3.66-3.97 (1H, br), 3.98-4.32 (2H, br), 7.38 (1H, d, J = 5.5 Hz), 7.59 (1H, d, J = 5.5 Hz), 7.67-7.90 (1H, br), 7.93 (1H, d, J = 8.6 Hz), 8.11-8.93 (1H, br), 9.56-10.03 (1H, br), 10.20-10.61 (1H, br)	Dihydrochloride
309	H	-(CH2)4-		1H-NMR (CDCl3) δppm : 0.91-1.13 (1H, m), 1.23-1.38 (2H, m), 1.46-2.12 (10H, m), 2.33-2.48 (3H, m), 2.76 (1H, d, J = 12.5 Hz), 2.94-3.12 (2H, m), 3.32 (1H, d, J = 12.5 Hz), 7.03 (1H, dd, J = 8.5,2.4 Hz), 7.26 (1H, d, J = 2.4 Hz), 7.39 (1H, d, J = 8.5 Hz), 9.75 (2H, brs)	Hydrochloride
310	H	-(CH2)4-		1H-NMR (DMSO) δppm : 0.96-2.27 (16H, m), 2.97-3.59 (4H, m), 7.10 (1H, d, J = 8.7 Hz), 7.31 (1H, s), 7.78 (1H, d, J = 8.7 Hz), 8.93-9.28 (1H, br), 9.32-9.67 (1H, br)	Hydrochloride
311	H	-(CH2)5-		1H-NMR (CDCl3) δppm : 1.18-2.19 (16H, m), 2.30-2.35 (1H, m), 2.47-2.52 (1H, m), 3.04 (1H, br), 3.44-3.67 (3H, m), 7.47-7.61 (3H, m), 7.83-7.89 (4H, m), 9.64 (2H, br)	Hydrochloride
312	H	-(CH2)5-		1H-NMR (CDCl3) δppm : 0.89-1.01 (1H, m), 1.08-1.70 (15H, m), 1.86-1.90 (1H, m), 2.42-2.47 (1H, m), 2.64-2.73 (1H, m), 2.79 (1H, d, J = 12.2 Hz), 3.00-3.08 (1H, m), 3.15 (1H, d, J = 12.2 Hz), 3.76 (3H, s), 3.47-4.70 (3H, br), 6.36 (1H, d, J = 3.0 Hz), 6.49 (2H, s), 6.93 (1H, dd, J = 8.6, 1.4 Hz), 7.27 (1H, d, J = 1.4 Hz), 7.29 (1H, d, J = 3.0 Hz), 7.36 (1H, d, J = 8.6 Hz)	Fumarate
313	H	-(CH2)5-		1H-NMR (CDCl3) δppm : 0.96-1.08 (1H, m), 1.23-1.45 (6H, m), 1.06-2.13 (8H, m), 2.20-2.25 (1H, m), 2.35-2.40 (1H, m), 2.62-2.67 (1H, m), 3.03-3.31 (4H, m), 7.03 (1H, dd, J = 8.5, 2.4 Hz), 7.26 (1H, d, J = 2.4 Hz), 7.40 (1H, d, J = 8.5 Hz), 9.49 (2H, brs)	Hydrochloride

[0332]

Table 44

Absolute configuration

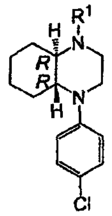


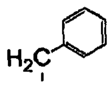
Example	R^1	NMR	Salt
314		1H-NMR (CDCl3) δppm : 0.9-1.1 (1H, m), 1.15-1.4 (3H, m), 1.55-1.7 (2H, m), 1.75-1.85 (1H, m), 2.1-2.2 (1H, m), 2.25-2.45 (2H, m), 2.55-2.7 (1H, m), 2.7-2.8 (1H, m), 2.85-2.95 (2H, m), 3.21 (1H, d, J = 13.4Hz), 4.18 (1H, d, J = 13.4Hz), 7.05-7.1 (2H, m), 7.2-7.35 (7H, m).	–
315	-H	1H-NMR (CDCl3) δppm : 0.9-1.4 (4H, m), 1.5-1.65 (2H, m), 1.7-1.9 (2H, m), 2.05-2.2 (1H, m), 2.32 (3H, s), 2.45-2.6 (2H, m), 2.8-2.9 (1H, m), 2.9-3.1 (2H, m), 7.0-7.1 (2H, m), 7.2-7.3 (2H, m).	–

[0333]

Table 45

Absolute configuration

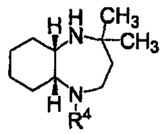


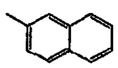
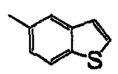
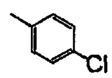
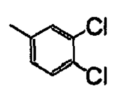
Example	R^1	NMR	Salt
316		1H-NMR (CDCl3) δppm : 0.95-1.1 (1H, m), 1.15-1.45 (3H, m), 1.5-1.7 (2H, m), 1.75-1.85 (1H, m), 2.1-2.25 (1H, m), 2.25-2.45 (2H, m), 2.55-2.7 (1H, m), 2.7-2.8 (1H, m), 2.85-3.0 (2H, m), 3.21 (1H, d, J = 13.3Hz), 4.18 (1H, d, J = 13.4Hz), 7.0-7.1 (2H, m), 7.2-7.35 (7H, m).	–
317	–H	1H-NMR (DMSO-d6) δppm : 0.85-1.05 (1H, m), 1.1-1.4 (2H, m), 1.4-1.65 (3H, m), 1.65-1.8 (1H, m), 1.9-2.05 (1H, m), 2.8-3.0 (2H, m), 3.0-3.2 (3H, m), 3.2-3.5 (1H, m), 7.1-7.2 (2H, m), 7.35-7.45 (2H, m), 9.2-9.7 (2H, m).	Hydrochloride
318	$-CH_3$	1H-NMR (CDCl3) δppm : 0.9-1.4 (4H, m), 1.5-1.65 (2H, m), 1.7-1.9 (2H, m), 2.05-2.2 (1H, m), 2.32 (3H, s), 2.45-2.6 (2H, m), 2.8-2.9 (1H, m), 2.9-3.1 (2H, m), 7.0-7.15 (2H, m), 7.2-7.3 (2H, m).	–

[0334]

Table 46

Relative configuration

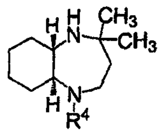


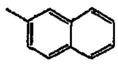
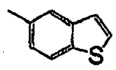
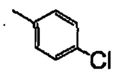
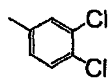
Example	R^4	NMR	Salt
319		1H-NMR (DMSO-d6) δppm : 1.35 (3H, s), 1.45-1.67 (6H, m), 1.67-2.00 (4H, m), 2.16-2.30 (2H, m), 2.30-2.43 (1H, m), 3.39-3.48 (1H, m), 3.62-3.72 (1H, m), 3.88-3.96 (1H, m), 3.09-4.08 (1H, m), 6.05-6.75 (1H, br), 7.10 (1H, s), 7.20-7.25 (1H, m), 7.25-7.34 (1H, m), 7.33-7.40 (1H, m), 7.66-7.80 (3H, m), 8.22-8.35 (1H, br), 9.30-9.45 (1H, br).	Dihydrochloride
320		1H-NMR (DMSO-d6) δppm at 80 °C: 1.37-1.55 (5H, m), 1.55-1.70 (4H, m), 1.71-2.00 (4H, m), 2.19-2.40 (3H, m), 3.35-3.50 (1H, m), 3.52-3.66 (1H, m), 3.84-3.97 (2H, m), 5.53-5.86 (1H, br), 7.06 (1H, dd, J = 2.4, 8.9 Hz), 7.28 (1H, d, J = 5.4 Hz), 7.36 (1H, d, J = 2.4 Hz), 7.60 (1H, d, J = 5.4 Hz), 7.76 (1H, d, J = 8.9 Hz), 8.07-8.40 (1H, br), 9.20-9.57 (1H, br).	Dihydrochloride
321		1H-NMR (DMSO-d6) δppm : 1.32 (3H, s), 1.43-1.61 (6H, m), 1.65-1.89 (4H, m), 2.07-2.17 (1H, m), 2.17-2.27 (1H, m), 2.27-2.40 (1H, m), 3.27-3.36 (1H, m), 3.40-3.55 (1H, m), 3.79-3.90 (2H, m), 5.00-6.60 (1H, br), 6.84 (2H, d, J = 8.9 Hz), 7.19 (2H, d, J = 8.9 Hz), 8.19-8.35 (1H, br), 9.25-9.44 (1H, br).	Dihydrochloride
322		1H-NMR (DMSO-d6) δppm : 1.32 (3H, s), 1.40-1.63 (6H, m), 1.63-1.90 (4H, m), 2.07-2.25 (2H, m), 2.30-2.33 (1H, m), 3.27-3.38 (1H, m), 3.48-3.59 (1H, m), 3.78-3.86 (1H, m), 3.86-3.95 (1H, m), 5.30-6.75 (1H, br), 6.83 (1H, d, J = 3.0, 9.1 Hz), 7.02 (1H, d, J = 3.0 Hz), 7.35 (1H, d, J = 9.1 Hz), 8.23-8.40 (1H, br), 9.22-9.45 (1H, br).	Dihydrochloride

[0335]

Table 47

Relative configuration

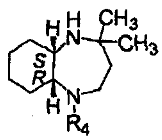


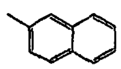
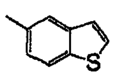
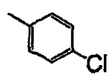
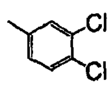
Example	R4	NMR	Salt
323		1H-NMR (DMSO-d6) δppm : 1.39 (3H, s), 1.43-1.65 (7H, m), 1.71-1.90 (4H, m), 1.93-2.06 (1H, m), 2.35-2.45 (1H, m), 3.60-3.79 (4H, m), 5.40-6.15 (1H, br), 6.90 (1H, s), 7.09-7.20 (2H, m), 7.30-7.40 (1H, m), 7.65-7.72 (2H, m), 7.75 (1H, d, J = 9.0 Hz), 8.60-8.80 (1H, br), 8.80-9.00 (1H, br).	Dihydrochloride
324		1H-NMR (DMSO-d6) δppm at 80 °C: 1.38-1.54 (10H, m), 1.69-2.02 (5H, m), 2.41-2.50 (1H, m), 3.55-3.85 (4H, m), 4.97-5.80 (1H, br), 6.94-7.10 (1H, br), 7.18-7.40 (2H, m), 7.59 (1H, d, J = 5.4 Hz), 7.78 (1H, d, J = 8.9 Hz), 8.75-8.92 (1H, br), 8.92-9.30 (1H, br).	Dihydrochloride
325		1H-NMR (DMSO-d6) δppm : 1.33-1.52 (10H, m), 1.64-1.82 (4H, m), 1.82-1.93 (1H, m), 2.30-2.40 (1H, m), 3.40-3.54 (2H, m), 3.54-3.70 (2H, m), 4.45-5.20 (1H, br), 6.66 (2H, d, J = 9.0 Hz), 7.19 (2H, d, J = 9.0 Hz), 8.55-8.70 (1H, br), 8.75-8.92 (1H, br).	Dihydrochloride
326		1H-NMR (DMSO-d6) δppm : 1.33-1.59 (10H, m), 1.61-1.90 (5H, m), 2.33-2.45 (1H, m), 3.45-3.56 (2H, m), 3.56-3.71 (2H, m), 5.05-6.00 (1H, br), 6.65 (1H, dd, J = 2.8, 9.1 Hz), 6.78 (1H, d, J = 2.8 Hz), 7.34 (1H, d, J = 9.1 Hz), 8.70-8.89 (1H, br), 9.00-9.15 (1H, br).	Dihydrochloride

[0336]

Table 48

Absolute configuration

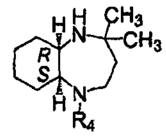


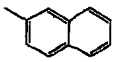
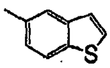
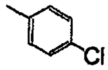
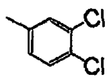
Example	R4	NMR	Salt
327		1H-NMR (DMSO-d6) δppm : 1.35 (3H, s), 1.45-1.67 (6H, m), 1.67-2.00 (4H, m), 2.16-2.30 (2H, m), 2.30-2.43 (1H, m), 3.39-3.48 (1H, m), 3.62-3.72 (1H, m), 3.88-3.96 (1H, m), 3.09-4.08 (1H, m), 6.05-6.75 (1H, br), 7.10 (1H, s), 7.20-7.25 (1H, m), 7.25-7.34 (1H, m), 7.33-7.40 (1H, m), 7.66-7.80 (3H, m), 8.22-8.35 (1H, br), 9.30-9.45 (1H, br).	Dihydrochloride
328		1H-NMR (DMSO-d6) δppm at 80 °C: 1.37-1.55 (5H, m), 1.55-1.70 (4H, m), 1.71-2.00 (4H, m), 2.19-2.40 (3H, m), 3.35-3.50 (1H, m), 3.52-3.66 (1H, m), 3.84-3.97 (2H, m), 5.53-5.86 (1H, br), 7.06 (1H, dd, J = 2.4, 8.9 Hz), 7.28 (1H, d, J = 5.4 Hz), 7.36 (1H, d, J = 2.4 Hz), 7.60 (1H, d, J = 5.4 Hz), 7.76 (1H, d, J = 8.9 Hz), 8.07-8.40 (1H, br), 9.20-9.57 (1H, br).	Dihydrochloride
329		1H-NMR (DMSO-d6) δppm : 1.33-1.52 (10H, m), 1.64-1.82 (4H, m), 1.82-1.93 (1H, m), 2.30-2.40 (1H, m), 3.40-3.54 (2H, m), 3.54-3.70 (2H, m), 4.45-5.20 (1H, br), 6.66 (2H, d, J = 9.0 Hz), 7.19 (2H, d, J = 9.0 Hz), 8.55-8.70 (1H, br), 8.75-8.92 (1H, br).	Dihydrochloride
330		1H-NMR (DMSO-d6) δppm : 1.32 (3H, s), 1.40-1.63 (6H, m), 1.63-1.80 (4H, m), 2.07-2.25 (2H, m), 2.30-2.33 (1H, m), 3.27-3.38 (1H, m), 3.48-3.59 (1H, m), 3.78-3.86 (1H, m), 3.86-3.95 (1H, m), 5.30-6.75 (1H, br), 6.83 (1H, d, J = 3.0, 9.1 Hz), 7.02 (1H, d, J = 3.0 Hz), 7.35 (1H, d, J = 9.1 Hz), 8.23-8.40 (1H, br), 9.22-9.45 (1H, br).	Dihydrochloride

[0337]

Table 49

Absolute configuration

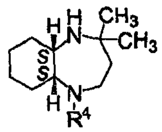


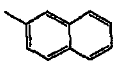
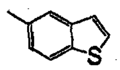
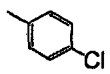
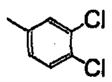
Example	R⁴	NMR	Salt
331		1H-NMR (DMSO-d6) δppm : 1.35 (3H, s), 1.45-1.67 (6H, m), 1.67-2.00 (4H, m), 2.16-2.30 (2H, m), 2.30-2.43 (1H, m), 3.39-3.48 (1H, m), 3.62-3.72 (1H, m), 3.88-3.96 (1H, m), 3.09-4.08 (1H, m), 6.05-6.75 (1H, br), 7.10 (1H, s), 7.20-7.25 (1H, m), 7.25-7.34 (1H, m), 7.33-7.40 (1H, m), 7.66-7.80 (3H, m), 8.22-8.35 (1H, br), 9.30-9.45 (1H, br).	Dihydrochloride
332		1H-NMR (DMSO-d6) δppm at 80 °C: 1.37-1.55 (5H, m), 1.55-1.70 (4H, m), 1.71-2.00 (4H, m), 2.19-2.40 (3H, m), 3.35-3.50 (1H, m), 3.52-3.66 (1H, m), 3.84-3.97 (2H, m), 5.53-5.86 (1H, br), 7.06 (1H, dd, J = 2.4, 8.9 Hz), 7.28 (1H, d, J = 5.4 Hz), 7.36 (1H, d, J = 2.4 Hz), 7.60 (1H, d, J = 5.4 Hz), 7.78 (1H, d, J = 8.9 Hz), 8.07-8.40 (1H, br), 9.20-9.57 (1H, br).	Dihydrochloride
333		1H-NMR (DMSO-d6) δppm : 1.33-1.52 (10H, m), 1.64-1.82 (4H, m), 1.82-1.93 (1H, m), 2.30-2.40 (1H, m), 3.40-3.54 (2H, m), 3.54-3.70 (2H, m), 4.45-5.20 (1H, br), 6.66 (2H, d, J = 9.0 Hz), 7.19 (2H, d, J = 9.0 Hz), 8.55-8.70 (1H, br), 8.75-8.92 (1H, br).	Dihydrochloride
334		1H-NMR (DMSO-d6) δppm : 1.32 (3H, s), 1.40-1.63 (6H, m), 1.63-1.90 (4H, m), 2.07-2.25 (2H, m), 2.30-2.33 (1H, m), 3.27-3.38 (1H, m), 3.48-3.59 (1H, m), 3.78-3.86 (1H, m), 3.86-3.95 (1H, m), 5.30-6.75 (1H, br), 6.83 (1H, d, J = 3.0, 9.1 Hz), 7.02 (1H, d, J = 3.0 Hz), 7.35 (1H, d, J = 9.1 Hz), 8.23-8.40 (1H, br), 9.22-9.45 (1H, br).	Dihydrochloride

[0338]

Table 50

Absolute configuration

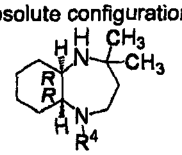


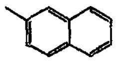
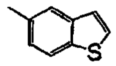
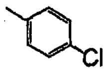
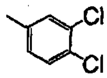
Example	R⁴	NMR	Salt
335		1H-NMR (DMSO-d6) δppm : 1.39 (3H, s), 1.43-1.65 (7H, m), 1.71-1.90 (4H, m), 1.93-2.06 (1H, m), 2.35-2.45 (1H, m), 3.60-3.79 (4H, m), 5.40-6.15 (1H, br), 6.90 (1H, s), 7.09-7.20 (2H, m), 7.30-7.40 (1H, m), 7.65-7.72 (2H, m), 7.75 (1H, d, J = 9.0 Hz), 8.60-8.80 (1H, br), 8.80-9.00 (1H, br).	Dihydrochloride
336		1H-NMR (DMSO-d6) δppm at 80 °C: 1.38-1.54 (10H, m), 1.69-2.02 (5H, m), 2.41-2.50 (1H, m), 3.55-3.85 (4H, m), 4.97-5.80 (1H, br), 6.94-7.10 (1H, br), 7.18-7.40 (2H, m), 7.59 (1H, d, J = 5.4 Hz), 7.78 (1H, d, J = 8.9 Hz), 8.75-8.92 (1H, br), 8.92-9.30 (1H, br).	Dihydrochloride
337		1H-NMR (DMSO-d6) δppm : 1.33-1.52 (10H, m), 1.64-1.82 (4H, m), 1.82-1.93 (1H, m), 2.30-2.40 (1H, m), 3.40-3.54 (2H, m), 3.54-3.70 (2H, m), 4.45-5.20 (1H, br), 6.66 (2H, d, J = 9.0 Hz), 7.19 (2H, d, J = 9.0 Hz), 8.55-8.70 (1H, br), 8.75-8.92 (1H, br).	Dihydrochloride
338		1H-NMR (DMSO-d6) δppm : 1.33-1.59 (10H, m), 1.61-1.90 (5H, m), 2.33-2.45 (1H, m), 3.45-3.56 (2H, m), 3.56-3.71 (2H, m), 5.05-6.00 (1H, br), 6.65 (1H, dd, J = 2.8, 9.1 Hz), 6.78 (1H, d, J = 2.8 Hz), 7.34 (1H, d, J = 9.1 Hz), 8.70-8.89 (1H, br), 9.00-9.15 (1H, br).	Dihydrochloride

[0339]

Table 51

Absolute configuration

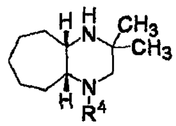


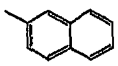
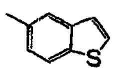
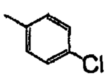
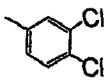
Example	R^4	NMR	Salt
339		1H-NMR (DMSO-d6) δppm : 1.39 (3H, s), 1.43-1.65 (7H, m), 1.71-1.90 (4H, m), 1.93-2.06 (1H, m), 2.35-2.45 (1H, m), 3.60-3.79 (4H, m), 5.40-6.15 (1H, br), 6.90 (1H, s), 7.09-7.20 (2H, m), 7.30-7.40 (1H, m), 7.65-7.72 (2H, m), 7.75 (1H, d, J = 9.0 Hz), 8.60-8.80 (1H, br), 8.80-9.00 (1H, br).	Dihydrochloride
340		1H-NMR (DMSO-d6) δ ppm at 80 °C: 1.38-1.54 (10H, m), 1.69-2.02 (5H, m), 2.41-2.50 (1H, m), 3.55-3.85 (4H, m), 4.97-5.80 (1H, br), 6.94-7.10 (1H, br), 7.18-7.40 (2H, m), 7.59 (1H, d, J = 5.4 Hz), 7.78 (1H, d, J = 8.9 Hz), 8.75-8.92 (1H, br), 8.92-9.30 (1H, br).	Dihydrochloride
341		1H-NMR (DMSO-d6) δppm : 1.33-1.52 (10H, m), 1.64-1.82 (4H, m), 1.82-1.93 (1H, m), 2.30-2.40 (1H, m), 3.40-3.54 (2H, m), 3.54-3.70 (2H, m), 4.45-5.20 (1H, br), 6.86 (2H, d, J = 9.0 Hz), 7.19 (2H, d, J = 9.0 Hz), 8.55-8.70 (1H, br), 8.75-8.92 (1H, br).	Dihydrochloride
342		1H-NMR (DMSO-d6) δppm : 1.33-1.59 (10H, m), 1.61-1.90 (5H, m), 2.33-2.45 (1H, m), 3.45-3.56 (2H, m), 3.56-3.71 (2H, m), 5.05-6.00 (1H, br), 6.85 (1H, dd, J = 2.8, 9.1 Hz), 6.78 (1H, d, J = 2.8 Hz), 7.34 (1H, d, J = 9.1 Hz), 8.70-8.89 (1H, br), 9.00-9.15 (1H, br).	Dihydrochloride

[0340]

Table 52

Relative configuration

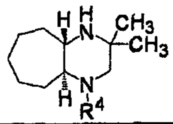


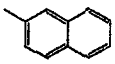
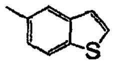
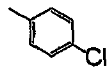
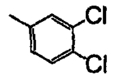
Example	R^4	NMR	Salt
343		1H-NMR (DMSO-d6) δppm : 1.10-1.92 (14H, m), 2.23-2.44 (2H, m), 2.94 (1H, d, J = 13.3), 3.51 (1H, d, J = 13.3 Hz), 3.76-3.94 (1H, m), 4.10-4.22 (1H, m), 5.80-6.30 (1H, br), 7.11 (1H, d, J = 1.6 Hz), 7.22-7.31 (1H, m), 7.36-7.50 (2H, m), 7.66-7.85 (3H, m), 8.66-8.92 (1H, br), 9.80-9.08 (1H, br).	Dihydrochloride
344		1H-NMR (DMSO-d6) δppm : 1.10-1.38 (3H, m), 1.38-1.65 (8H, m), 1.65-1.92 (3H, m), 2.15-2.40 (2H, m), 2.89 (1H, d, J = 13.3 Hz), 3.37 (1H, d, J = 13.3 Hz), 3.77-3.95 (1H, m), 4.00-4.14 (1H, m), 7.17 (1H, dd, J = 2.3, 8.9 Hz), 7.28-7.38 (2H, m), 7.68 (1H, d, J = 5.4 Hz), 7.83 (1H, d, J = 8.9 Hz), 8.44-8.74 (1H, br), 9.65-9.90 (1H, br).	Hydrochloride
345		1H-NMR (DMSO-d6) δppm : 1.10-1.95 (14H, m), 2.16-2.45 (2H, m), 2.82 (1H, d, J = 13.5), 3.40 (1H, d, J = 13.5 Hz), 3.70-3.89 (1H, m), 3.89-4.07 (1H, m), 6.93 (2H, d, J = 9.0 Hz), 7.26 (2H, d, J = 9.0 Hz), 8.54-8.88 (1H, br), 9.66-9.99 (1H, br).	Hydrochloride
346		1H-NMR (DMSO-d6) δppm : 1.10-1.90 (14H, m), 2.19-2.45 (2H, m), 2.83 (1H, d, J = 13.6 Hz), 3.50 (1H, d, J = 13.6 Hz), 3.68-3.86 (1H, br), 3.94-4.07 (1H, br), 6.92 (1H, dd, J = 2.9, 9.0 Hz), 7.14 (1H, d, J = 2.9 Hz), 7.42 (1H, d, J = 9.0 Hz), 8.55-8.88 (1H, br), 9.62-9.98 (1H, br).	Hydrochloride

[0341]

Table 53

Relative configuration

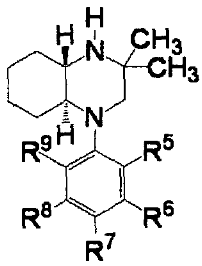


Example	R^4	NMR	Salt
347		1H-NMR (DMSO-d6) δppm : 1.37 (3H, s), 1.42-1.88 (12H, m), 2.10-2.25 (1H, m), 3.13 (1H, d, J = 13.4 Hz), 3.28-3.63 (3H, m), 3.92-4.48 (1H, br), 7.26-7.51 (4H, m), 7.76-7.92 (3H, m), 8.85-9.15 (1H, br), 9.50-9.70 (1H, br).	Dihydrochloride
348		1H-NMR (DMSO-d6) δppm : 1.00 (3H, s), 1.20-1.70 (13H, m), 1.70-1.85 (1H, m), 2.70-2.95 (4H, m), 7.05 (1H, dd, J = 2.1, 8.7 Hz), 7.34 (1H, d, J = 5.4 Hz), 7.39 (1H, d, J = 2.1 Hz), 7.67 (1H, d, J = 5.4 Hz), 7.82 (1H, d, J = 8.7 Hz).	—
349		1H-NMR (DMSO-d6) δppm : 1.33 (3H, s), 1.37-1.81 (12H, m), 2.07-2.22 (1H, m), 3.00 (1H, d, J = 13.6 Hz), 3.21-3.50 (3H, m), 3.88-4.20 (1H, br), 6.97 (2H, d, J = 8.8 Hz), 7.31 (2H, d, J = 8.8 Hz), 8.66-9.00 (1H, br), 9.33-9.65 (1H, m).	Dihydrochloride
350		1H-NMR (DMSO-d6) δppm : 1.33 (3H, s), 1.36 (3H, s), 1.50-1.90 (9H, m), 2.07-2.28 (1H, m), 3.07 (1H, d, J = 14.2 Hz), 3.32-3.66 (3H, m), 6.88 (1H, dd, J = 2.8, 8.9 Hz), 7.09 (1H, d, J = 2.8 Hz), 7.43 (1H, d, J = 8.9 Hz), 8.70-8.92 (1H, br), 9.35-9.58 (1H, br).	Hydrochloride

[0342]

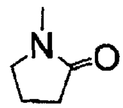
Table 54

Relative configuration



Example	R^5	R^6	R^7	R^8	R^9	MS(M+1)
351	-H	-H	-H	-H	-H	245
352	-H	-H	$-CH_3$	-H	-H	259
353	-H	$-CH_3$	-H	-H	-H	259
354	-H	-F	-H	-H	-H	263
355	-H	-H	-CN	-H	-H	270
356	-H	$-CH_3$	$-CH_3$	-H	-H	273
357	-H	$-C_2H_5$	-H	-H	-H	273
358	-H	$-CH_3$	-H	$-CH_3$	-H	273
359	-H	-H	$-C_2H_5$	-H	-H	273
360	-H	$-OCH_3$	-H	-H	-H	275
361	-H	-F	-H	-F	-H	281
362	-H	$-CH_3$	-CN	-H	-H	284
363	-H	-H	$-(CH_2)_2CH_3$	-H	-H	287
364	-H	$-CH(CH_3)_2$	-H	-H	-H	287
365	-H	-H	$-CH(CH_3)_2$	-H	-H	287
366	-H	-F	-CN	-H	-H	288

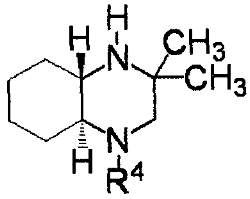
367	-H	-CN	-H	-F	-H	288
368	-H	$-N(CH_3)_2$	-H	-H	-H	288
369	-H	-H	$-N(CH_3)_2$	-H	-H	288
370	-H	$-OC_2H_5$	-H	-H	-H	289
371	-H	$-CH_3$	$-OCH_3$	-H	-H	289
372	-H	-H	$-OCH_2CH_3$	-H	-H	289
373	-H	$-CH_3$	-F	$-CH_3$	-H	291
374	-H	-H	$-SCH_3$	-H	-H	291
375	-H	$-SCH_3$	-H	-H	-H	291
376	$-OCH_3$	-H	-H	-F	-H	293
377	-H	-F	-H	-Cl	-H	297
378	-H	-F	-F	-F	-H	299
379	-H	-H	$-C(CH_3)_3$	-H	-H	301
380	-H	$-CH_3$	$-OCH_3$	$-CH_3$	-H	303
381	-H	$-OCH(CH_3)_2$	-H	-H	-H	303
382	-H	$-OCH_3$	$-OCH_3$	-H	-H	305
383	-H	-H	$-SCH_2CH_3$	-H	-H	305
384	$-OCH_3$	-H	-H	-Cl	-H	309
385	-H	$-OCH_3$	-F	-F	-H	311
386	-H	-H		-H	-H	311

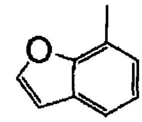
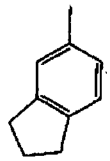
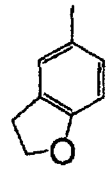
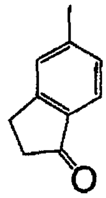
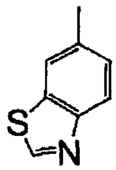
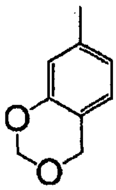
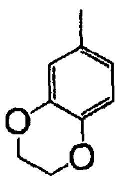
387	-H	$-CF_3$	-H	-H	-H	313
388	-H	-H	$-CF_3$	-H	-H	313
389	-Cl	-H	-Cl	-H	-H	313
390	-H	-Cl	-H	-Cl	-H	313
391	-H	$-CF_3$	$-CH_3$	-H	-H	327
392	-H	-H		-H	-H	328
393	-H	-H	$-OCF_3$	-H	-H	329
394	-H	$-CF_3$	-H	-F	-H	331
395	-F	-H	$-CF_3$	-H	-H	331
396	-H	-F	$-CF_3$	-H	-H	331
397	-F	$-CF_3$	-H	-H	-H	331
398	-H	$-CF_3$	-F	-H	-H	331
399	-H	$-CF_3$	$-OCH_3$	-H	-H	343
400	-H	$-CF_3$	-Cl	-H	-H	347

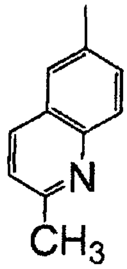
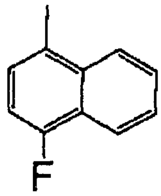
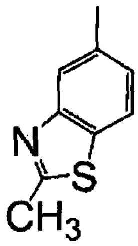
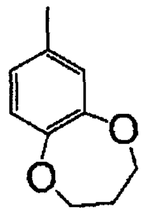
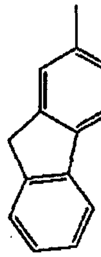
[0343]

Table 55

Relative configuration



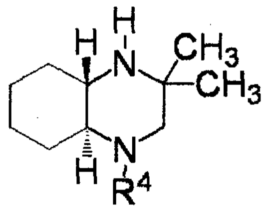
Example	R^4	MS(M+1)
401		285
402		285
403		287
404		299
405		302
406		303
407		303

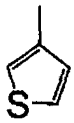
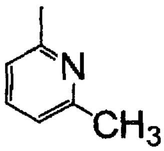
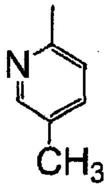
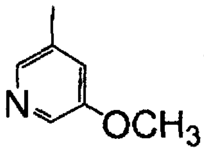
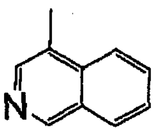
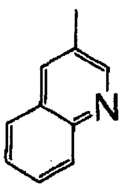
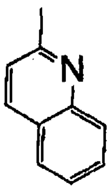
408		310
409		313
410		316
411		317
412		333

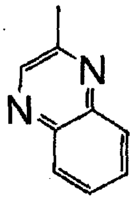
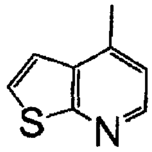
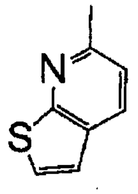
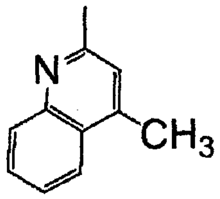
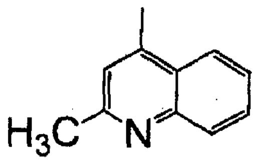
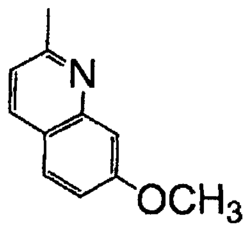
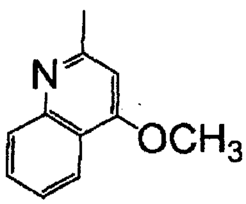
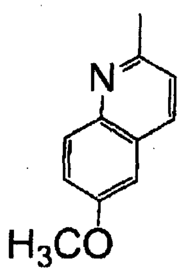
[0344]

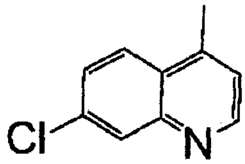
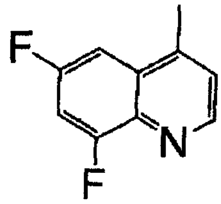
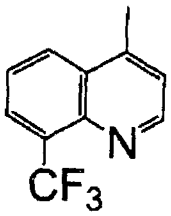
Table 56

Relative configuration



Example	R^4	MS(M+1)
413		251
414		260
415		260
416		276
417		296
418		296
419		296

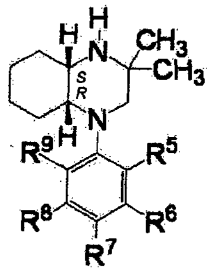
420		297
421		302
422		302
423		310
424		310
425		326
426		326
427		326

428		330
429		332
430		364

[0345]

Table 57

Absolute configuration

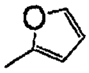
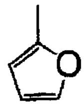
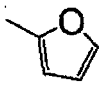
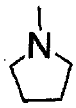
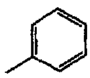
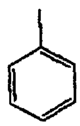
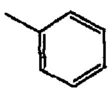


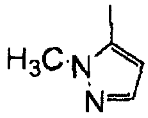
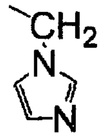
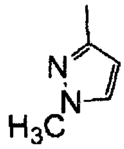
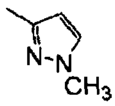
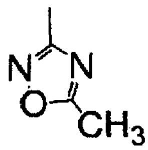
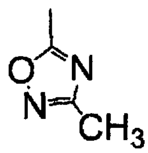
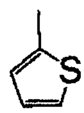
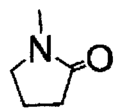
Example	R^5	R^6	R^7	R^8	R^9	MS(M+1)
431	-H	-H	-H	-H	-H	245
432	-H	-H	$-CH_3$	-H	-H	259
433	-H	$-CH_3$	-H	-H	-H	259
434	$-CH_3$	-H	-H	-H	-H	259
435	-H	-CN	-H	-H	-H	270
436	-CN	-H	-H	-H	-H	270
437	-H	-H	-CN	-H	-H	270
438	-H	$-CH_3$	$-CH_3$	-H	-H	273
439	-H	$-CH_3$	-H	$-CH_3$	-H	273
440	$-CH_3$	$-CH_3$	-H	-H	-H	273
441	-H	-H	$-C_2H_5$	-H	-H	273

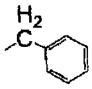
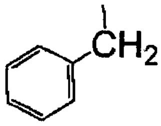
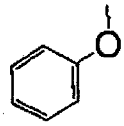
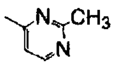
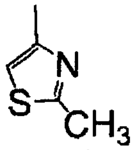
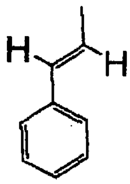
442	-H	$-OCH_3$	-H	-H	-H	275
443	$-OCH_3$	-H	-H	-H	-H	275
444	$-CH_3$	-F	-H	-H	-H	277
445	-H	$-CH_3$	-F	-H	-H	277
446	-F	-H	-H	$-CH_3$	-H	277
447	-H	-F	$-CH_3$	-H	-H	277
448	$-CH_3$	-H	-F	-H	-H	277
449	-F	-H	-H	-F	-H	281
450	-F	-H	-F	-H	-H	281
451	-H	$-CH_3$	-CN	-H	-H	284
452	-H	$-C(O)CH_3$	-H	-H	-H	287
453	-H	-H	$-C(O)CH_3$	-H	-H	287
454	$-CH_3$	-H	$-CH_3$	$-CH_3$	-H	287
455	-H	-H	$-CH(CH_3)_2$	-H	-H	287
456	-F	-H	-CN	-H	-H	288
457	-H	-F	-CN	-H	-H	288

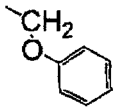
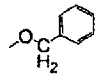
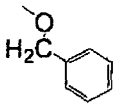
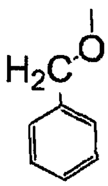
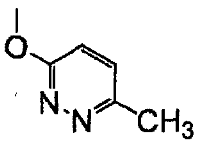
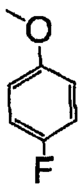
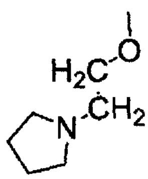
458	-H	-CN	-F	-H	-H	288
459	-H	-N(CH_3)$_2$	-H	-H	-H	288
460	-H	-H	-N(CH_3)$_2$	-H	-H	288
461	-CH_3	-H	-OCH_3	-H	-H	289
462	-H	-CH_3	-OCH_3	-H	-H	289
463	-H	-CH_3	-F	-CH_3	-H	291
464	-CH_3	-F	-CH_3	-H	-H	291
465	-H	-H	-SCH_3	-H	-H	291
466	-H	-SCH_3	-H	-H	-H	291
467	-OCH_3	-H	-H	-F	-H	293
468	-CH_3	-Cl	-H	-H	-H	293
469	-H	-CH_3	-Cl	-H	-H	293
470	-H	-Cl	-CH_3	-H	-H	293
471	-CH_3	-H	-Cl	-H	-H	293
472	-F	-H	-H	-Cl	-H	297
473	-H	-F	-H	-Cl	-H	297

474	-F	-H	-Cl	-H	-H	297
475	-F	-F	-H	-F	-H	299
476	-H	-H	$-(CH_2)_3CH_3$	-H	-H	301
477	-H	-H	$-C(CH_3)_3$	-H	-H	301
478	-H	-H	$-CH_2N(CH_3)_2$	-H	-H	302
479	-H	$-CH_2N(CH_3)_2$	-H	-H	-H	302
480	$-OCH(CH_3)_2$	-H	-H	-H	-H	303
481	-H	$-CH_3$	$-OCH_3$	$-CH_3$	-H	303
482	-H	-Cl	-CN	-H	-H	304
483	-H	$-OCH_3$	-H	$-OCH_3$	-H	305
484	-H	$-OCH_3$	$-OCH_3$	-H	-H	305
485	$-OCH_3$	-H	-H	$-OCH_3$	-H	305
486	$-OCH_3$	-F	-H	-F	-H	311
487	-H	$-OCH_3$	-F	-F	-H	311
488	$-OCH_3$	-H	-F	-F	-H	311
489	-H	-H	$-OCHF_2$	-H	-H	311

490		-H	-H	-H	-H	311
491	-H	-H		-H	-H	311
492	-H		-H	-H	-H	311
493	-H		-H	-H	-H	311
494	$-CF_3$	-H	-H	-H	-H	313
495	-H	$-CF_3$	-H	-H	-H	313
496	-H	-H	$-CF_3$	-H	-H	313
497	-Cl	-H	-Cl	-H	-H	313
498	-H	-Cl	-H	-Cl	-H	313
499	-H	-H		-H	-H	314
500	-H	$-CH_3$	$-N(CH_3)_2$	$-CH_3$	-H	316
501		-H	-H	-H	-H	321
502	-H	-H		-H	-H	321
503	-H		-H	-H	-H	321
504	-H	-Cl	$-OC_2H_5$	-H	-H	323

505	-H	-H		-H	-H	325
506	-H		-H	-H	-H	325
507	-H	-H		-H	-H	325
508	-H		-H	-H	-H	325
509	-H	$-CF_3$	$-CH_3$	-H	-H	327
510	-H	-H		-H	-H	327
511	-H	-H		-H	-H	327
512	-H	-H		-H	-H	327
513	-H	-H		-H	-H	328
514	-H	$-OCF_3$	-H	-H	-H	329
515	$-OCF_3$	-H	-H	-H	-H	329
516	-H	-H	$-OCF_3$	-H	-H	329

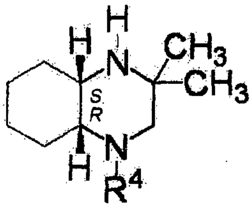
517	-H	-F	$-CF_3$	-H	-H	331
518	-H	$-CF_3$	-F	-H	-H	331
519	-H	-H	$-O(CH_2)_2N(CH_3)_2$	-H	-H	332
520	-H	$-OCH_3$	$-OCH_3$	$-OCH_3$	-H	335
521		-H	-H	-H	-H	335
522	-H	-H		-H	-H	335
523	-H	-H		-H	-H	337
524	-H		-H	-H	-H	337
525	-H	-H		-H	-H	342
526	-H	$-CF_3$	$-OCH_3$	-H	-H	343
527	-H	-H	$-O(CH_2)_5CH_3$	-H	-H	345
528	-H	-H	$-O(CH_2)_3N(CH_3)_2$	-H	-H	346
529	-H	-H		-H	-H	347
530	-H	-Cl	$-CF_3$	-H	-H	347

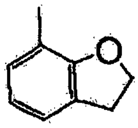
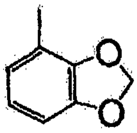
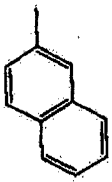
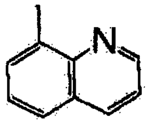
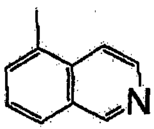
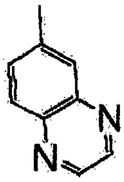
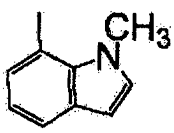
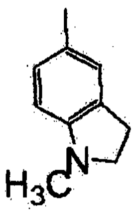
531	-H	$-CF_3$	-Cl	-H	-H	347
532	-Cl	-Cl	-H	-Cl	-H	347
533	-H		-H	-H	-H	351
534		-H	-H	-H	-H	351
535	-H		-H	-H	-H	351
536	-H	-H		-H	-H	351
537	-H	-H	$-SO_2N(CH_3)_2$	-H	-H	352
538	-H	-H		-H	-H	353
539	-H		-H	-H	-H	355
540	-H	-H		-H	-H	358
541	-H	-H	$-CH_2N(i\text{-}Pr)_2$	-H	-H	358
542	-H	$-CF_3$	-H	$-CF_3$	-H	381

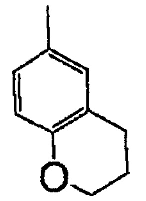
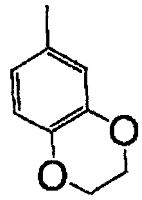
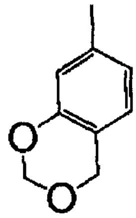
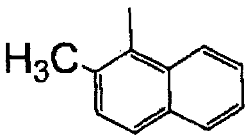
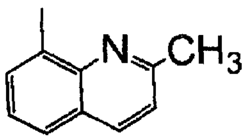
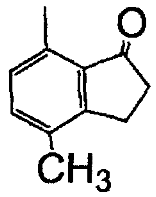
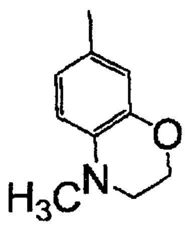
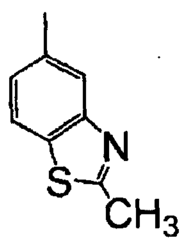
[0346]

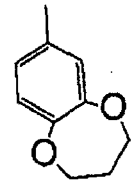
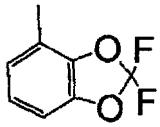
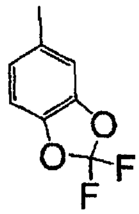
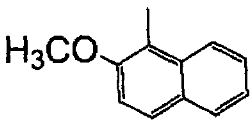
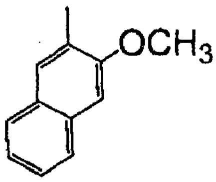
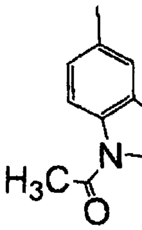
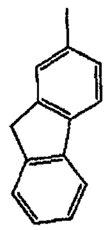
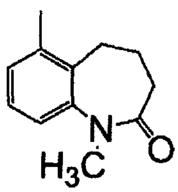
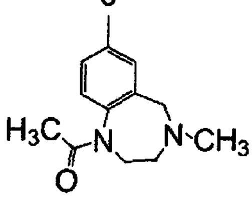
Table 58

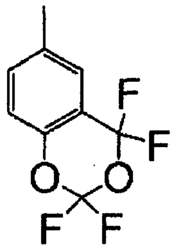
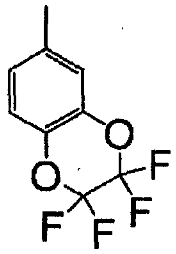
Absolute configuration



Example	R^4	MS(M+1)
543		287
544		289
545		295
546		296
547		296
548		297
549		298
550		300

551		301
552		303
553		303
554		309
555		310
556		313
557		316
558		316

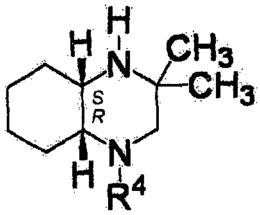
559		317
560		325
561		325
562		325
563		325
564		328
565		333
566		342
567		371

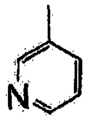
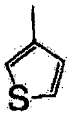
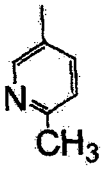
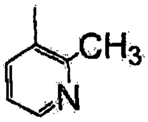
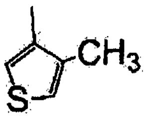
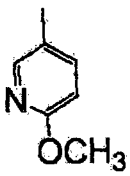
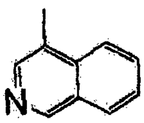
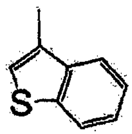
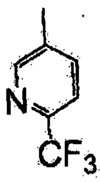
568		375
569		375

[0347]

Table 59

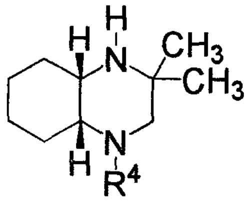
Absolute configuration

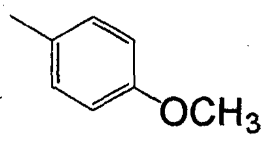


Example	R^4	MS(M+1)
570		246
571		251
572		260
573		260
574		265
575		276
576		296
577		301
578		314

[0348]
Table 63

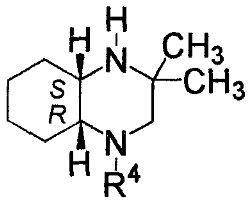
relative configuration

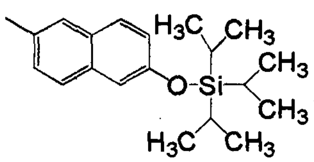
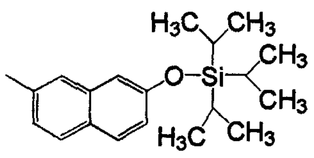


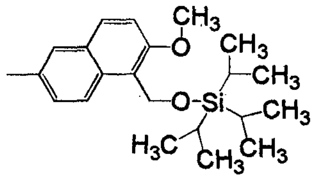
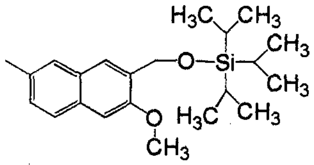
Example	R^4	NMR	Salt
588		1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.3-1.45 (4H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 1.95-2.1 (1H, m), 2.93 (1H, d, J = 13.1Hz), 3.11 (1H, d, J = 13.3Hz), 3.68 (3H, d, J = 0.6Hz), 3.7-4.4 (3H, m), 6.82 (2H, d, J = 9.0Hz), 6.89 (2H, d, J = 9.1Hz), 8.09 (1H, br), 9.83 (1H, br)	2 Hydrochloride

[0349]
Table 64

absolute configuration

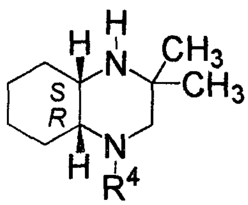


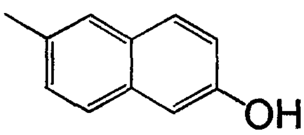
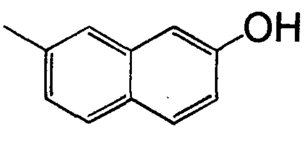
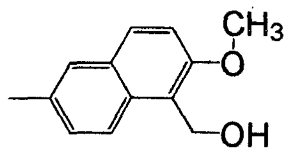
Example	R^4	NMR	Salt
589		1H-NMR (CDCl3) δppm : 1.07-1.15 (18H, m), 1.17-1.34 (12H, m), 1.35-1.50 (2H, m), 1.64-1.86 (4H, m), 2.82 (1H, d, J = 11.6Hz), 3.04 (1H, d, J = 11.7Hz), 3.47-3.53 (1H, m), 3.69-3.78 (1H, m), 6.95 (1H, d, J = 2.3Hz), 7.03 (1H, dd, J = 2.4, 8.8Hz), 7.10 (1H, d, J = 2.4Hz), 7.23 (1H, d, J = 2.4, 9.1Hz), 7.51 (1H, d, J = 8.9Hz), 7.55 (1H, d, J = 9.1Hz).	-
590		1H-NMR (CDCl3) δppm : 1.13 (18H, d, J = 7.3Hz), 1.20-1.36 (12H, m), 1.36-1.64 (2H, m), 1.68-1.86 (4H, m), 2.83 (1H, d, J = 12.0Hz), 3.12 (1H, d, J = 11.9Hz), 3.45-3.55 (1H, m), 3.75-3.85 (1H, m), 6.82 (1H, d, J = 2.3Hz), 6.86 (1H, dd, J = 2.4, 8.7Hz), 7.02 (1H, d, J = 2.3Hz), 7.10 (1H, dd, J = 2.4, 9.0Hz), 7.53 (1H, d, J = 8.7Hz), 7.59 (1H, d, J = 9.0Hz).	-

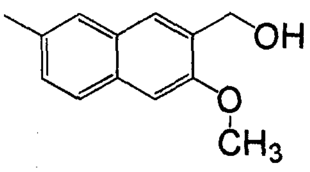
591		1H-NMR (CDCl3) δppm : 1.03-1.12 (18H, m), 1.12-1.32 (12H, m), 1.32-1.65 (2H, m), 1.66-1.84 (4H, m), 2.82 (1H, d, J = 11.7Hz), 3.08 (1H, d, J = 11.8Hz), 3.47-3.53 (1H, m), 3.73-3.81 (1H, m), 3.88 (3H, s), 5.17 (1H, d, J = 11.0Hz), 5.24 (1H, d, J = 11.0Hz), 6.94 (1H, d, J = 2.5Hz), 7.16 (1H, d, J = 9.0Hz), 7.31 (1H, dd, J = 2.5, 9.4Hz), 7.58 (1H, d, J = 9.0Hz), 8.12 (1H, d, J = 9.4Hz).	-
592		1H-NMR (CDCl3) δppm : 1.14 (18H, d, J = 6.6Hz), 1.19-1.35 (13H, m), 1.35-1.65 (1H, m), 1.65-1.84 (4H, m), 2.83 (1H, d, J = 11.6Hz), 3.04 (1H, d, J = 11.6Hz), 3.5-3.6 (1H, m), 3.7-3.8 (1H, m), 3.87 (3H, s), 4.93 (2H, d, J = 1.0Hz), 6.96 (1H, s), 6.99 (1H, d, J = 2.2Hz), 7.21 (1H, dd, J =2.4, 9.0Hz), 7.59 (1H, d, J = 9.0Hz), 7.77 (1H, s).	-

[0350]
Table 65

absolute configuration

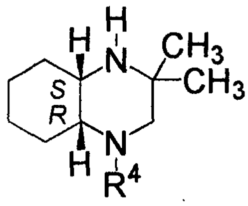


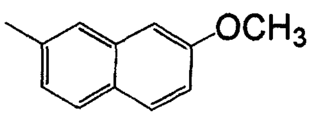
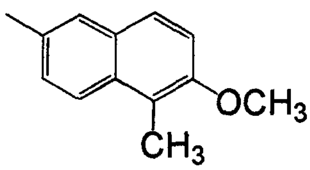
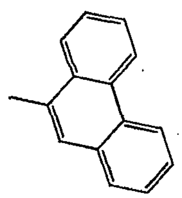
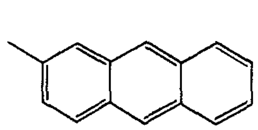
Example.	R^4	NMR	Salt
593		1H-NMR (CDCl3) δppm : 1.15-1.33 (9H, m), 1.33-1.50 (2H, m), 1.64-1.84 (4H, m), 2.82 (1H, d, J = 11.8Hz), 3.04 (1H, d, J = 11.8Hz), 3.49-3.56 (1H, m), 3.69-3.78 (1H, m), 6.96 (1H, d, J = 2.4Hz), 6.99-7.06 (2H, m), 7.22-7.28 (1H, m), 7.52-7.58 (2H, m).	-
594		1H-NMR (CDCl3) δppm : 1.17-1.36 (9H, m), 1.36-1.52 (2H, m), 1.65-1.86 (4H, m), 2.83 (1H, d, J = 11.9Hz), 3.13 (1H, d, J = 12.0Hz), 3.45-3.55 (1H, m), 3.75-3.85 (1H, m), 6.8-6.85 (2H, m), 6.94 (1H, d, J =2.4Hz), 7.10 (1H, d, J = 2.4, 9.1Hz), 7.57 (1H, d, J = 8.7Hz), 7.60 (1H, d, J = 9.1Hz).	-
595		1H-NMR (DMSO-d6) δppm : 1.1-1.2 (1H, m), 1.2-1.4 (8H, m), 1.5-1.9 (5H, m), 2.89 (1H, d, J = 12.4Hz), 3.22 (1H, d, J = 12.5Hz), 3.62 (1H, br), 3.85 (3H, s), 3.95-4.05 (1H, m), 4.85 (2H, s), 6.53 (2H, s), 7.07 (1H, d, J = 2.4Hz), 7.28 (1H, d, J = 9.1Hz), 7.39 (1H, dd, J = 2.5, 9.5Hz), 7.67 (1H, d, J = 9.0H), 7.98 (1H, d, J = 9.4Hz).	Fumarate

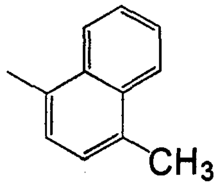
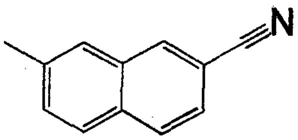
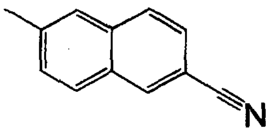
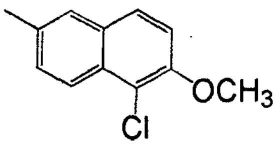
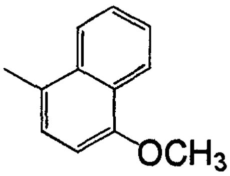
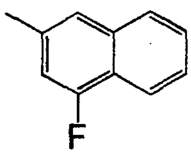
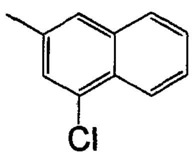
596		1H-NMR (CDCl3) δppm : 0.99 (1H, br), 1.15-1.35 (8H, m), 1.35-1.5 (2H, m), 1.5-1.85 (4H, m), 2.44 (1H, br), 2.81 (1H, d, J = 11.7Hz), 3.05 (1H, d, J = 11.8H), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.93 (3H, s), 4.79 (2H, s), 6.98 (1H, d, J = 2.4Hz), 7.02 (1H, s), 7.21-7.28 (1H, m), 7.54 (1H, s), 7.60 (1H, d, J = 9.0Hz).	-

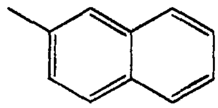
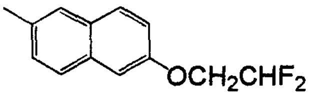
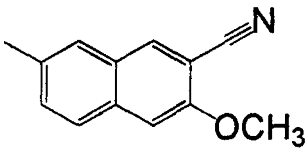
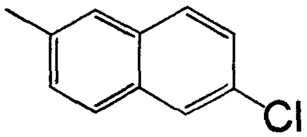
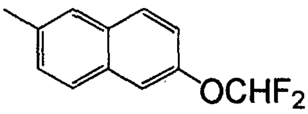
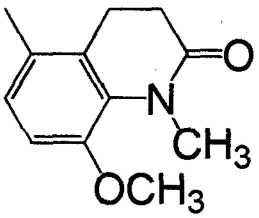
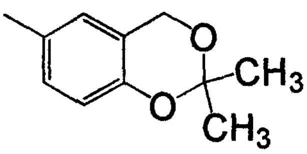
[0351]
Table 66

absolute configuration



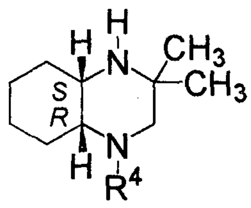
Example.	R^4	NMR	Salt
597		1H-NMR (CDCl3) δppm : 1.15-1.65 (11H, m), 1.65-1.9 (4H, m), 2.84 (1H, d, J = 12.0Hz), 3.13 (1H, d, J = 11.9Hz), 3.50 (1H, bs), 3.75-3.85 (1H, m), 3.89 (3H, s), 6.89 (1H, dd, J = 2.5, 8.8Hz), 6.92 (1H, d, J = 2.3Hz), 6.97 (1H, d, J = 2.4Hz), 7.11 (1H, dd, J = 2.4, 9.0Hz), 7.57 (1H, d, J = 8.8Hz), 7.60 (1H, d, J = 9.0Hz).	-
598		1H-NMR (CDCl3) δppm : 1.08 (1H, br), 1.15-1.35 (8H, m), 1.35-1.5 (2H, m), 1.65-1.85 (4H, m), 2.50 (3H ,s), 2.82 (1H, d, J = 11.8Hz), 3.07 (1H, d, J = 11.7Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.90 (3H, s), 6.96 (1H, d, J = 2.6Hz), 7.18 (1H, d, J = 9.0Hz), 7.30 (1H, dd, J = 2.6, 9.4Hz), 7.51 (1H, d, J = 8.9Hz), 7.81 (1H, d, J = 9.4Hz).	-
599		1H-NMR (CDCl3) δppm : 0.81-1.00 (1H, m), 1.03-1.13 (1H, m), 1.27 (3H, s), 1.33-1.43 (2H, m), 1.46 (3H, s), 1.54-1.72 (2H, m), 1.72-1.82 (1H, m), 1.85-2.0 (1H, m), 2.69 (1H, d, J = 11.1Hz), 3.3-3.4 (2H, m), 3.75-3.85 (1H, m), 7.15 (1H, s), 7.5-7.55 (2H, m), 7.6-7.7 (2H, m), 7.7-7.8 (1H, m), 8.3-8.4 (1H, m), 8.55-8.65 (1H, m), 8.65-8.75 (1H, m).	-
600		1H-NMR (CDCl3) δppm : 1.00 (1H, br), 1.19-1.37 (8H, m), 1.39-1.51 (2H, m), 1.68-1.79 (3H, m), 1.79-1.93 (1H, m), 2.90 (1H, d, J = 11.8Hz), 3.18 (1H, d, J = 11.9Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 7.05 (1H, d, J = 2.1Hz), 7.3-7.45 (3H, m), 7.8-7.95 (3H, m), 8.15 (1H, s), 8.25 (1H, s).	-

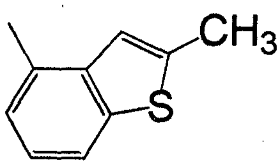
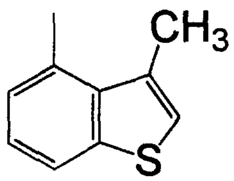
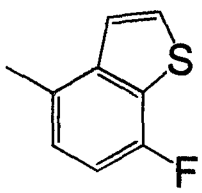
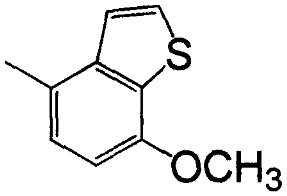
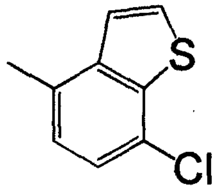
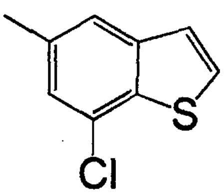
601		1H-NMR (DMSO-d6) δppm : 0.85-1.0 (1H, m), 1.0-1.1 (1H, m), 1.3-1.4 (1H, m), 1.5-1.65 (7H, m), 1.65-1.85 (2H, m), 1.85-2.1 (2H, m), 2.59 (3H, s), 2.76 (1H, d, J = 12.6Hz), 3.3-3.5 (1H, m), 3.51 (1H, d, J = 13.1Hz), 4.15-4.3 (1H, m), 7.02 (1H, d, J = 7.5Hz), 7.28 (1H, d, J = 8.0Hz), 7.5-7.65 (2H, m), 7.95-8.15 (2H, m), 8.25-8.35 (1H, m), 9.6-9.8 (1H, m).	Hydrochloride
602		1H-NMR (DMSO-d6) δppm : 1.29-1.51 (6H, m), 1.56 (3H, s), 1.65-2.1 (5H, m), 3.09 (1H, d, J = 13.6Hz), 3.62 (1H, d, J = 13.5Hz), 3.8-3.9 (1H, m), 4.2-4.3 (1H, m), 7.32 (1H, d, J = 2.2Hz), 7.50 (1H, dd, J = 1.6, 8.4Hz), 7.63 (1H, dd, J = 2.5, 9.2Hz), 7.87-7.98 (2H, m), 8.11-8.29 (2H, m), 9.74 (1H, br).	Hydrochloride
603		1H-NMR (DMSO-d6) δppm : 1.32-1.54 (6H, m), 1.58 (3H, s), 1.67-1.90 (3H, m), 1.90-2.14 (2H, m), 3.11 (1H, d, J = 13.8Hz), 3.71 (1H, d, J = 13.8Hz), 3.75-3.9 (1H, m), 4.25-4.35 (1H, m), 7.29 (1H, d, J = 2.2Hz), 7.5-7.65 (2H, m), 7.81 (1H, d, J = 8.6Hz), 7.91 (1H, d, J = 9.2Hz), 8.25-8.45 (2H, m), 9.9-10.1 (1H, m).	Hydrochloride
604		1H-NMR (CDCl3) δppm : 0.96 (1H, br), 1.15-1.35 (8H, m), 1.35-1.5 (2H, m), 1.65-1.9 (4H, m), 2.83 (1H, d, J = 11.8Hz), 3.09 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.75-3.85 (1H, m), 3.99 (3H, s), 6.95 (1H, d, J = 2.4Hz), 7.20 (1H, d, J = 9.0Hz), 7.37 (1H, dd, J = 2.5, 9.4Hz), 7.56 (1H, d, J = 9.0Hz), 8.06 (1H, d, J = 9.3Hz).	-
605		1H-NMR (DMSO-d6) δppm : 0.9-1.0 (1H, m), 1.1-1.2 (1H, m), 1.3-1.4 (1H, m), 1.52 (3H, s), 1.55-1.7 (4H, m), 1.7-1.85 (2H, m), 1.85-2.05 (2H, m), 2.73 (1H, d, J = 12.5Hz), 3.3-3.6 (2H, m), 3.94 (3H, s), 4.15-4.3 (1H, m), 6.88 (1H, d, J = 8.2Hz), 7.06 (1H, d, J = 8.1Hz), 7.5-7.55 (1H, m), 7.55-7.6 (1H, m), 7.95 (1H, br), 8.16 (1H, dd, J = 1.0, 8.3Hz), 8.24 (1H, d, J = 8.1Hz), 9.45-9.6 (1H, m).	Hydrochloride
606		1H-NMR (DMSO-d6) δppm : 1.26-1.51 (6H, m), 1.57 (3H, s), 1.66-2.12 (5H, m), 3.06 (1H, d, J = 13.6Hz), 3.57 (1H, d, J = 13.6Hz), 3.74-3.86 (1H, m), 4.15-4.26 (1H, m), 7.05 (1H, d, J = 1.8Hz), 7.28-7.37 (2H, m), 7.43-7.52 (1H, m), 7.75 (1H, d, J = 8.4Hz), 7.84 (1H, d, J = 8.2Hz), 8.23 (1H, br), 9.90 (1H, br).	Hydrochloride
607		1H-NMR (DMSO-d6) δppm : 1.28-1.52 (6H, m), 1.57 (3H, s), 1.64-1.97 (4H, m), 2.02-2.16 (1H, m), 3.08 (1H, d, J = 13.5Hz), 3.56 (1H, d, J = 13.6Hz), 3.8-3.9 (1H, m), 3.95-4.1 (1H, m), 7.23 (1H, d, J = 2.0Hz), 7.36-7.45 (1H, m), 7.45-7.54 (1H, m), 7.65 (1H, d, J = 2.3Hz), 7.78 (1H, d, J = 8.1Hz), 7.97 (1H, d, J = 8.3Hz), 8.1-8.35 (1H, m), 9.90 (1H, br).	Hydrochloride

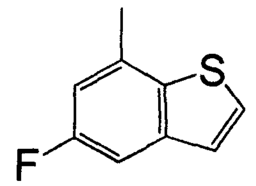
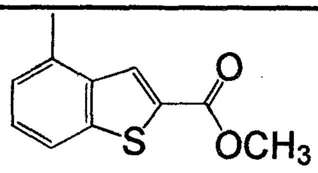
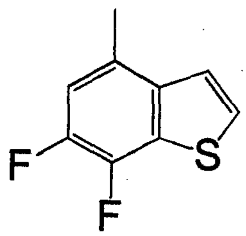
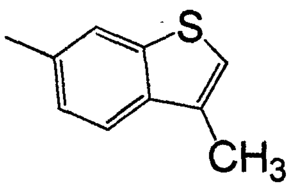
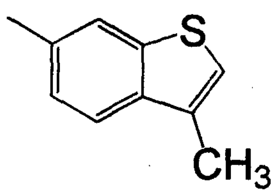
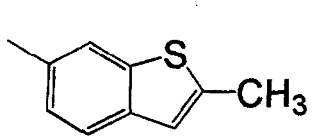
608		1H-NMR (DMSO-d6) δppm : 1.26-1.52 (6H, m), 1.57 (3H, s), 1.66-2.02 (4H, m), 2.02-2.12 (1H, m), 3.07 (1H, d, J = 13.4Hz), 3.51 (1H, d, J = 13.4Hz), 3.65-3.9 (2H, m), 4.15-4.25 (1H, m), 7.18 (1H, d, J = 2.2Hz), 7.22-7.3 (1H, m), 7.35-7.47 (2H, m), 7.65-7.85 (3H, m), 8.1-8.3 (1H, m), 9.8-10.0 (1H, m).	2 Hydrochloride
609		1H-NMR (DMSO-d6) δppm : 1.06-1.16 (1H, m), 1.16-1.39 (8H, m), 1.46-1.78 (4H, m), 1.78-1.93 (1H, m), 2.81 (1H, d, J = 12.2Hz), 2.9-4.0 (5H, m), 4.30-4.42 (2H, m), 6.27-6.58 (2H, m), 7.06 (1H, d, J = 2.1Hz), 7.10 (1H, dd, J = 2.6, 8.9Hz), 7.26 (1H, d, J = 2.5Hz), 7.35 (1H, dd, J = 2.6, 9.4Hz), 7.61-7.68 (2H, m).	1/2 Fumarate
610		1H-NMR (DMSO-d6) δppm : 1.23-1.52 (6H, m), 1.59 (3H, s), 1.64-2.03 (4H, m), 2.03-2.16 (1H, m), 3.07 (1H, d, J = 13.3Hz), 3.45 (1H, d, J = 14.0Hz), 3.75-3.85 (1H, m), 3.95 (3H, s), 4.1-4.2 (1H, m), 4.77 (1H, br), 7.25 (1H, d, J = 2.2Hz), 7.46 (1H, s), 7.58 (1H, dd, J =2.4, 9.2Hz), 7.81 (1H, d, J = 9.2Hz), 8.23 (1H, s), 8.25-8.4 (1H, m), 10.13 (1H, br).	2 Hydrochloride
611		1H-NMR (DMSO-d6) δppm : 1.12-1.20 (1H, m), 1.21-1.39 (8H, m), 1.47-1.79 (4H, m), 1.79-1.95 (1H, m), 2.84 (1H, d, J = 12.3Hz), 2.85-3.75 (5H, m), 3.9-4.0 (1H, m), 6.54 (2H, s), 7.12 (1H, d, J = 2.2Hz), 7.34 (1H, dd, J = 2.2, 8.7Hz), 7.43 (1H, dd, J = 2.4, 9.2Hz), 7.65-7.75 (2H, m), 7.80 (1H, d, J = 2.1Hz).	Fumarate
612		1H-NMR (DMSO-d6) δppm : 1.05-1.19 (1H, m), 1.19-1.40 (8H, m), 1.46-1.80 (4H, m), 1.80-1.96 (1H, m), 2.83 (1H, d, J = 12.3Hz), 2.9-4.3 (5H, m), 6.51 (1H, s), 7.05-7.45 (4H, m), 7.49 (1H, d, J = 2.3Hz), 7.7-7.8 (2H, m).	1/2 Fumarate
613		1H-NMR (DMSO-d6) δppm : 1.0-1.15 (2H, m), 1.3-1.4 (1H, m), 1.48 (3H, s), 1.50 (3H, s), 1.55-1.65 (1H, m), 1.7-1.8 (2H, m), 1.8-2.0 (2H, m), 2.25-2.35 (1H, m), 2.4-2.5 (1H, m), 2.6-2.75 (2H, m), 2.95-3.1 (2H, m), 3.21 (3H, s), 3.3-3.5 (1H, m), 3.78 (3H, s), 3.85-3.95 (1H, m), 6.78 (1H, d, J = 8.9Hz), 6.93 (1H, d, J = 8.9Hz), 7.99 (1H, br), 9.64 (1H, br).	Hydrochloride
614		1H-NMR (DMSO-d6) δppm : 1.08-1.37 (9H, m), 1.42 (6H, s), 1.47-1.85 (5H, m), 2.76 (1H, d, J = 12.4Hz), 2.95 (1H, d, J = 12.3Hz), 3.53 (1H, br), 3.63-3.73 (1H, m), 4.74 (2H, s), 6.52 (2H, s), 6.58 (1H, d, J = 2.7Hz), 6.65 (1H, d, J = 8.9Hz), 6.76 (1H, dd, J = 2.8, 9.0Hz).	Fumarate

[0352]
Table 67

absolute configuration

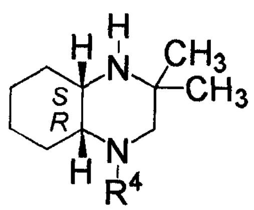


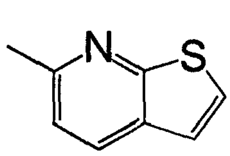
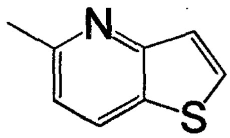
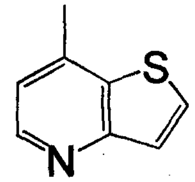
Example	R^4	NMR	Salt
615		1H-NMR (CDCl3) δppm : 0.91-1.09 (3H, m), 1.20 (3H, s), 1.31-1.43 (5H, m), 1.54-1.78 (3H, m), 1.81-1.95 (1H, m), 2.55-2.65 (4H, m), 3.15 (1H, d, J = 11.2Hz), 3.4-3.5 (1H, m), 3.65-3.7 (1H, m), 6.72-6.77 (1H, m), 7.05 (1H, s), 7.13 (1H, dd, J = 7.8, 7.8Hz), 7.37 (1H, d, J = 8.0Hz).	-
616		1H-NMR (CDCl3) δppm : 0.85-1.08 (3H, m), 1.21 (3H, s), 1.29-1.42 (5H, m), 1.52-1.68 (2H, m), 1.68-1.88 (2H, m), 2.58 (1H, d, J = 11.0Hz), 2.77 (3H, d, J = 0.9Hz), 3.02-3.12 (1H, m), 3.20 (1H, d, J = 11.0Hz), 3.66 (1H, br), 6.91 (1H, d, J = 7.5Hz), 6.98 (1H, d, J = 0.8Hz), 7.19 (1H, dd, J = 7.8, 7.8Hz), 7.52 (1H, dd, J = 0.7, 8.0Hz).	-
617		1H-NMR (CDCl3) δppm : 0.90-1.08 (3H, m), 1.20 (3H, s), 1.32-1.43 (5H, m), 1.45-1.78 (3H, m), 1.81-1.95 (1H, m), 2.57 (1H, d, J = 11.1Hz), 3.14 (1H, d, J = 11.1Hz), 3.33-3.42 (1H, m), 3.62-3.71 (1H, m), 6.71 (1H, dd, J = 4.1, 8.4Hz), 6.92 (1H, dd, J = 8.9, 8.9Hz), 7.41 (1H, d, J = 5.4hz), 7.46 (1H, dd, J = 3.7, 5.4Hz).	-
618		1H-NMR (CDCl3) δppm : 0.9-1.1 (2H, m), 1.20 (3H, s), 1.3-1.45 (5H, m), 1.45-1.8 (4H, m), 1.8-1.95 (1H, m), 2.56 (1H, d, J = 11.1Hz), 3.14 (1H, d, J = 11.1Hz), 3.3-3.4 (1H, m), 3.6-3.7 (1H, m), 3.96 (3H, s), 6.66 (1H, d, J = 8.2Hz), 6.74 (1H, d, J = 8.2Hz), 7.39 (1H, d, J = 5.4Hz), 7.45 (1H, d, J = 5.4Hz).	-
619		1H-NMR (CDCl3) δppm : 0.92-1.08 (3H, m), 1.20 (3H, s), 1.30-1.43 (5H, m), 1.47-1.78 (3H, m), 1.82-1.96 (1H, m), 2.61 (1H, d, J = 11.2Hz), 3.13 (1H, d, J = 11.2Hz), 3.42-3.52 (1H, m), 3.63-3.71 (1H, m), 6.74 (1H, d, J = 8.2Hz), 7.21 (1H, d, J = 8.2Hz), 7.43 (1H, d, J = 5.5Hz), 7.47 (1H, d, J = 5.5Hz).	-
620		1H-NMR (CDCl3) δppm : 0.94 (1H, br), 1.14-1.33 (8H, m), 1.33-1.49 (2H, m), 1.65-1.85 (4H, m), 2.80 (1H, d, J = 11.7Hz), 2.97 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.6-3.7 (1H, m), 7.04 (1H, d, J = 2.1Hz), 7.10 (1H, d, J = 2.2Hz), 7.20 (1H, d, J = 5.4Hz), 7.41 (1H, d, J = 5.5Hz).	-

621		1H-NMR (DMSO-d6) δppm : 1.02-1.19 (2H, m), 1.32-1.44 (1H, m), 1.51 (3H, s), 1.52 (3H, s), 1.58-1.88 (3H, m), 1.92-2.09 (2H, m), 3.00 (1H, d, J = 13.0Hz), 3.46 (1H, d, J = 13.1Hz), 3.9-4.0 (1H, m), 3.95-4.08 (1H, m), 6.96 (1H, dd, J = 2.0, 11.0Hz), 7.41 (1H, dd, J = 2.2, 9.1Hz), 7.46 (1H, d, J = 5.4Hz), 7.86 (1H, d, J = 5.4Hz), 8.14 (1H, br), 9.76 (1H, br).	Hydrochloride
622		1H-NMR (CDCl3) δppm : 0.92-1.12 (2H, m), 1.13-2.02 (13H, m), 2.66 (1H, d, J = 11.6Hz), 3.22 (1H, br), 3.45-3.6 (1H, m), 3.77 (1H, br), 3.96 (3H, s), 6.81 (1H, d, J = 7.6Hz), 7.33 (1H, dd, J = 7.8, 7.8Hz), 7.46 (1H, d, J = 7.8Hz), 8.13 (1H, s).	-
623		1H-NMR (DMSO-d6) δppm : 0.94-1.12 (2H, m), 1.28-1.43 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.58-2.07 (5H, m), 2.84 (1H, d, J = 12.6Hz), 3.41(1H, d, J = 13.0Hz), 3.6-3.7 (1H, m), 4.15-4.25 (1H, m), 7.11 (1H, dd, J = 6.5, 12.6Hz), 7.77 (1H, dd, J = 3.8, 5.4Hz), 7.84 (1H, d, J = 5.4Hz), 8.05 (1H, br), 9.85 (1H, br).	Hydrochloride
624		1H-NMR (DMSO-d6) δppm : 1.17-1.52 (6H, m), 1.52-1.63 (3H, m), 1.63-1.74 (1H, m), 1.74-1.98 (3H, m), 1.98-2.16 (1H, m), 2.33 (3H, d, J = 1.0Hz), 3.03 (1H, d, J = 13.4Hz), 3.33-3.5 (1H, m), 3.53-3.97 (2H, m), 4.03-4.18 (1H, m), 7.03-7.12 (1H, m), 7.15 (1H, dd, J = 2.1, 8.9Hz), 7.4-7.5 (1H, m), 7.59 (1H, d, J = 8.8Hz), 8.1-8.35 (1H, m), 9.8-10.1 (1H, m).	2 Hydrochloride
625		1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.49-1.93 (6H, m), 2.31 (3H, d, J = 1.2Hz), 2.83 (1H, d, J = 12.4Hz), 3.19 (1H, d, J = 12.4Hz), 3.25-3.85 (3H, m), 3.85-3.95 (1H, m), 6.52 (2H, s), 7.01 (1H, d, J = 1.2Hz), 7.10 (1H, dd, J = 2.3, 9.0Hz), 7.34 (1H, d, J = 2.2Hz), 7.55 (1H, d, J = 8.8Hz).	Fumarate
626		1H-NMR (DMSO-d6) δppm : 1.09-1.17 (1H, m), 1.17-1.41 (8H, m), 1.45-1.76 (4H, m), 1.76-1.89 (1H, m), 2.47 (3H, d, J = 1.1Hz), 2.78 (1H, d, J = 12.2Hz), 3.11 (1H, d, J = 12.2Hz), 3.47 (3H, m), 3.75-3.85 (1H, m), 6.50 (1H, s), 6.90 (1H, s), 6.99 (1H, dd, J = 2.3, 8.9Hz), 7.25 (1H, d, J = 2.2Hz), 7.48 (1H, d, J = 8.8Hz).	1/2 Fumarate

[0353]
Table 68

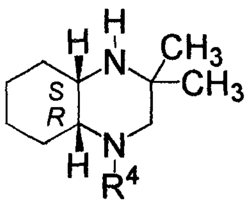
absolute configuration

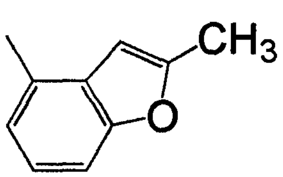
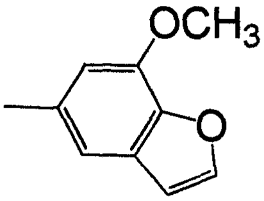


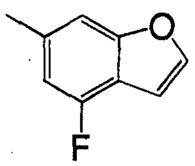
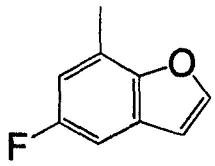
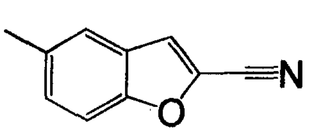
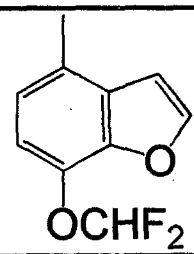
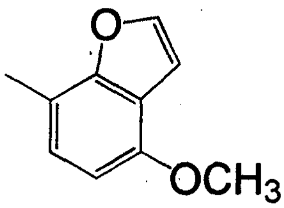
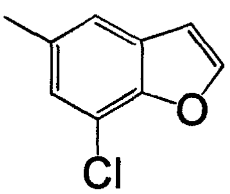
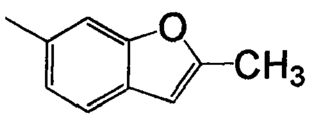
Example	R^4	NMR	Salt
627		1H-NMR (CDCl3) δppm : 0.99 (1H, br), 1.20 (3H, s), 1.22 (3H, s), 1.29-1.51 (4H, m), 1.68-1.82 (3H, m), 1.82-1.95 (1H, m), 2.79 (1H, d, J =12.8Hz), 3.35-3.45 (1H, m), 3.91 (1H, d, J = 12.8Hz), 4.2-4.3 (1H, m), 6.66 (1H, d, J = 9.0Hz), 7.03 (2H, s), 7.77 (1H, d, J = 8.9Hz).	-
628		1H-NMR (DMSO-d6) δppm : 1.35-1.63 (9H, m), 1.69-1.97 (3H, m), 1.97-2.16 (2H, m), 3.05-3.35 (1H, m), 3.35-4.3 (2H, m), 4.3-4.8 (2H, m), 7.1-7.35 (1H, m), 7.4-7.75 (1H, m), 8.0-8.2 (1H, m), 8.25-8.7 (2H, m), 9.85-10.35 (1H, m).	2 Hydrochloride
629		1H-NMR (DMSO-d6) δppm : 1.43-1.54 (5H, m), 1.64 (3H, s), 1.71-1.83 (2H, m), 1.83-2.06 (2H, m), 2.06-2.17 (1H, m), 2.4-2.6 (1H, m), 3.56 (1H, d, J = 15.1Hz), 3.85-4.0 (1H, m), 4.25 (1H, d, J = 15.0Hz), 4.65-4.75 (1H, m), 7.28 (1H, d, J = 7.2Hz), 7.69 (1H, d, J = 5.7Hz), 8.5-8.6 (2H, m), 8.9-9.1 (1H, m), 10.35-10.65 (1H, m), 15.15 (1H, br).	2 Hydrochloride

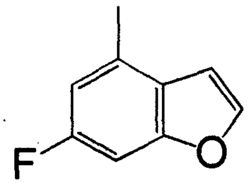
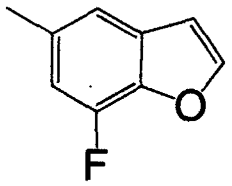
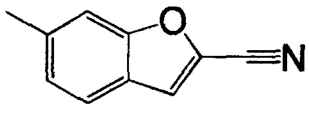
[0354]
Table 69

absolute configuration



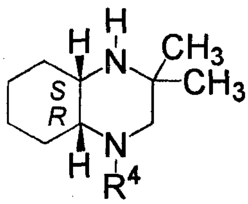
Example	R^4	NMR	Salt
630		1H-NMR (CDCl3) δppm : 0.85-1.17 (3H, m), 1.20 (3H, s), 1.31 (3H, s), 1.33-1.45 (2H, m), 1.5-1.78 (3H, m), 1.81-1.95 (1H, m), 2.45 (3H, d, J = 1.0Hz), 2.80 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.5Hz), 3.55-3.64 (2H, m), 6.39 (1H, s), 6.56 (1H, dd, J =0.5, 7.7Hz), 6.99 (1H, d, J = 8.2Hz), 7.06 (1H, dd, J = 7.9, 7.9Hz).	-
631		1H-NMR (CDCl3) δppm : 1.10-1.27 (5H, m), 1.29 (3H, s), 1.35-1.48 (2H, m), 1.48-1.83 (5H, m), 2.77-2.89 (2H, m), 3.49-3.55 (1H, m), 3.55-3.63 (1H, m), 4.01 (3H, s), 6.50 (1H, d, J = 2.0Hz), 6.58 (1H, d, J = 2.1Hz), 6.63 (1H, d, J = 2.1Hz), 7.53 (1H, d, J =2.0Hz).	-

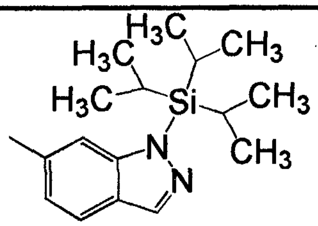
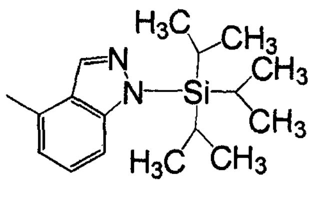
632		1H-NMR (DMSO-d6) δppm : 1.05-1.22 (2H, m), 1.34-1.45 (1H, m), 1.48 (3H, s), 1.53 (3H, s), 1.60-2.07 (5H, m), 3.13 (1H ,d, J = 13.2Hz), 3.28 (1H, d, J = 13.4Hz), 3.88-3.89 (1H, m), 3.89-4.02 (1H, m), 6.62 (1H, dd, J = 2.1, 12.3Hz), 7.09 (1H, dd, J = 1.3, 8.7Hz), 7.22 (1H, dd, J = 0.7, 2.2Hz), 7.96 (1H, d, J = 2.3Hz), 8.05-8.2 (1H, m), 9.7-9.95 (1H, m).	Hydrochloride
633		1H-NMR (DMSO-d6) δppm : 1.16-1.35 (2H, m), 1.35-1.45 (1H, m), 1.47 (3H, s), 1.54 (3H, s), 1.66-1.92 (3H, m), 1.92-2.14 (2H, m), 3.25 (1H, d, J = 13.5Hz), 3.45 (1H, d, J = 13.4Hz), 3.85-4.0 (1H, m), 4.2-4.35 (1H, m), 6.68 (1H, dd, J = 2.4, 12.1Hz), 6.89-7.04 (2H, m), 8.02 (1H, d, J = 2.2Hz), 8.26 (1H, br), 9.89 (1H, br).	Hydrochloride
634		1H-NMR (DMSO-d6) δppm : 1.18-1.36 (2H, m), 1.36-1.49 (4H, m), 1.49-1.57 (3H, m), 1.62-1.94 (4H, m), 1.94-2.12 (1H, m), 3.03 (1H, d, J = 13.3Hz), 3.25-3.4 (1H, m), 3.75-3.9 (1H, m), 3.95-4.15 (1H, m), 7.22 (1H, s), 7.37 (1H, dd, J = 2.5, 9.3Hz), 7.62 (1H, d, J = 9.2Hz), 7.95 (1H, s), 8.18 (1H, br), 9.6-10.1 (1H, m).	Hydrochloride
635		1H-NMR (DMSO-d6) δppm : 0.85-1.1 (2H, m), 1.2-1.35 (7H, m), 1.45-1.85 (4H, m), 1.85-2.05 (1H, m), 2.81 (1H, d, J = 12.0Hz), 2.9-4.4 (5.5H, m), 6.52 (1.5H, s), 6.60 (1H, d, J = 8.6Hz), 7.0-7.4 (3H, m), 8.00 (1H, d, J = 2.2Hz).	3/4 Fumarate
636		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.35-1.44 (1H, m), 1.50 (3H, s), 1.53 (3H, s), 1.59-2.07 (5H, m), 3.05 (1H, d, J = 12.8Hz), 3.27 (1H, d, J = 13.0Hz), 3.84 (3H, s), 3.89-4.02 (2H, m), 6.66 (1H, d, J = 8.5Hz), 6.75 (1H, d, J = 8.4Hz), 6.93 (1H, J = 2.2Hz), 7.92 (1H, d, J = 2.2Hz), 8.0-8.2 (1H, m), 9.55-9.8 (1H, m).	Hydrochloride
637		1H-NMR (DMSO-d6) δppm : 1.21-1.37 (2H, m), 1.37-1.49 (4H, m), 1.52 (3H ,s), 1.63-1.92 (4H, m), 1.92-2.10 (1H, m), 3.02 (1H, d, J = 13.2Hz), 3.29 (1H, d, J = 13.5Hz), 3.75-3.9 (1H, m), 3.95-4.1 (1H, m), 6.92 (1H, d, J = 2.2Hz), 7.12 (1H, d, J = 2.1Hz), 7.16 (1H, d, J = 2.1Hz), 8.01 (1H, d, J = 2.1Hz), 8.06 (1H, br), 9.72 (1H, br)	Hydrochloride
638		1H-NMR (DMSO-d6) δppm : 1.18-1.37 (2H, m), 1.37-1.48 (4H, m), 1.55 (3H, s), 1.61-1.98 (4H, m), 1.99-2.15 (1H, m), 2.38 (3H, s), 3.00 (1H, d, J = 13.3Hz), 3.28 (1H, d, J = 13.2Hz), 3.7-3.85 (1H, m), 3.95-4.05 (1H, m), 4.34 (1H, br), 6.40 (1H, s), 6.89 (1H, dd, J = 2.1, 8.6Hz), 7.05 (1H, d, J = 1.4Hz), 7.33 (1H, d, J = 8.5Hz), 8.22 (1H, br), 10.07 (1H, br).	2 Hydrochloride

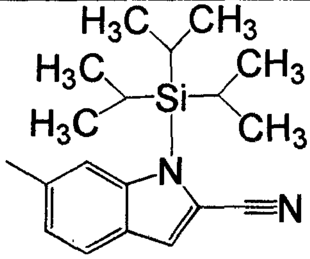
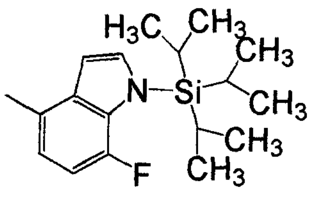
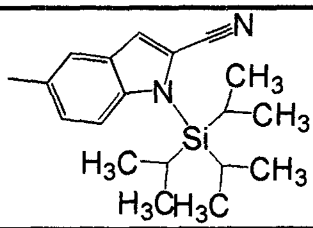
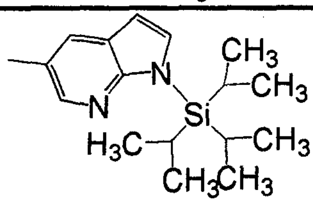
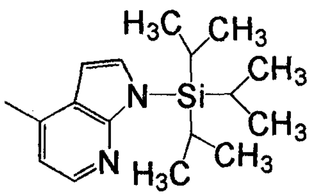
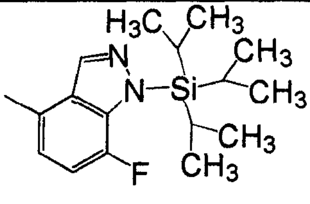
639		1H-NMR (DMSO-d6) δppm : 1.28-1.48 (6H, m), 1.52 (3H, s), 1.64-1.93 (4H, m), 1.95-2.06 (1H, m), 2.99 (1H, d, J = 13.6Hz), 3.46 (1H, d, J = 13.4Hz), 3.5-3.95 (2H, m), 4.05-4.15 (1H, m), 6.83-6.92 (2H, m), 7.01 (1H, s), 7.83 (1H, d, J = 2.1Hz), 8.14 (1H, br), 9.82 (1H, br).	2 Hydrochloride
640		1H-NMR (DMSO-d6) δppm : 1.18-1.49 (6H, m), 1.53 (3H, s), 1.62-1.93 (4H, m), 1.95-2.12 (1H, m), 3.00 (1H, d, J = 13.2Hz), 3.30 (1H, d, J = 13.2Hz), 3.7-3.85 (1H, m), 3.95-4.1 (1H, m), 4.95 (1H, br), 6.91 (1H, dd, J = 2.1, 3.0Hz), 6.94 (1H, d, J 2.1Hz), 7.01 (1H, dd, J = 2.1, 14.3Hz), 7.99 (1H, d, J = 2.1Hz), 8.14 (1H, br), 9.89 (1H, br).	2 Hydrochloride
641		1H-NMR (DMSO-d6) δppm : 1.12-1.29 (8H, m), 1.29-1.40 (2H, m), 1.45-1.76 (4H, m), 1.82-1.96 (1H, m), 2.80 (1H, d, J = 12.6Hz), 2.85-3.85 (4H, m), 3.85-3.95 (1H, m), 6.55 (2H, s), 7.08 (1H, s), 7.12 (1H, dd, J = 2.1, 9.0Hz), 7.56 (1H, d, J = 8.9Hz), 7.88 (1H, d, J = 0.6Hz).	Fumarate

[0355]
Table 70

absolute configuration

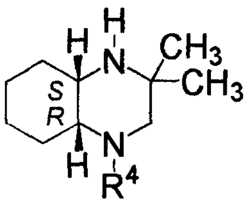


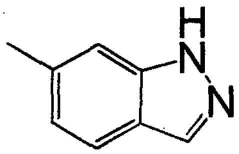
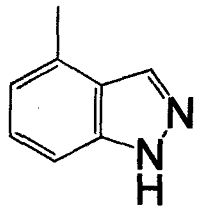
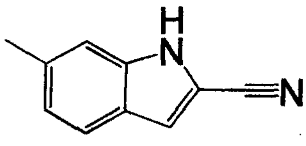
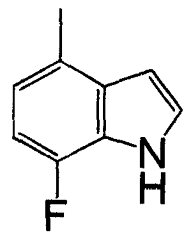
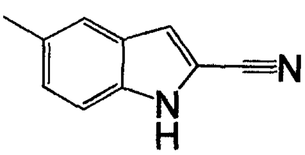
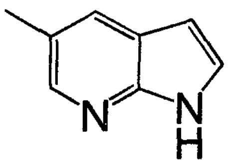
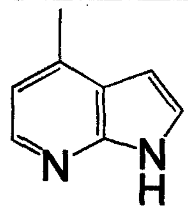
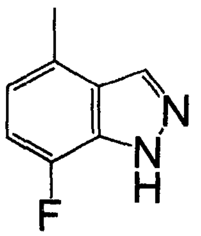
Example.	R^4	NMR	Salt
642		1H-NMR (CDCl3) δppm : 1.10-1.20 (20H, m), 1.22 (3H, s), 1.25-1.36 (4H, m), 1.37-1.50 (2H, m), 1.64-1.88 (7H, m), 2.82 (1H, d, J = 11.8Hz), 3.02 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.6-3.7 (1H, m), 6.82 (1H, s), 6.86 (1H, dd, J = 2.0, 8.9Hz), 7.54 (1H, d, J = 8.8Hz), 8.04 (1H, d, J = 0.9Hz).	-
643		1H-NMR (CDCl3) δppm : 1.11-1.19 (19H, m), 1.21 (3H, s), 1.23-1.32 (2H, m), 1.35 (3H, s), 1.37-1.47 (2H, m), 1.63-1.86 (6H, m), 1.90-2.04 (1H, m), 3.04 (1H, d, J = 11.9Hz), 3.09 (1H, d, J = 12.0Hz), 3.55-3.65 (1H, m), 3.8-3.9 (1H, m), 6.41 (1H, d, J = 7.5Hz), 7.05 (1H, d, J = 8.5Hz), 7.16 (1H, dd, J = 7.6, 8.3Hz), 8.26 (1H, d, J = 0.8Hz).	-

644		1H-NMR (CDCl3) δppm : 1.14-1.23 (21H, m), 1.23-1.33 (6H, m), 1.38-1.50 (2H, m), 1.63-1.88 (4H, m), 1.93-2.06 (3H, m), 2.82 (1H, d, J = 11.8Hz), 3.00 (1H, d, J = 11.8Hz), 3.44-3.50 (1H, m), 3.56-3.65 (1H, m), 6.88-6.94 (2H, m), 7.28 (1H, d, J = 0.4Hz), 7.42-7.47 (1H, m).	-
645		1H-NMR (CDCl3) δppm : 1.02-1.17 (21H, m), 1.19 (3H, s), 1.31-1.42 (5H, m), 1.59-1.77 (6H, m), 1.79-1.92 (1H, m), 2.67 (1H, d, J = 11.3Hz), 3.09 (1H, d, J = 11.3Hz), 3.45-3.6 (1H, m), 3.6-3.7 (1H, m), 6.39 (1H, dd, J = 3.4, 8.3Hz), 6.65 (1H, dd, J = 3.2, 3.2Hz), 6.72 (1H, d, J = 8.2, 12.7Hz), 7.25 (1H, d, J = 3.2Hz).	-
646		1H-NMR (CDCl3) δppm : 0.95 (1H, br), 1.15-1.30 (26H, m), 1.32-1.49 (2H, m), 1.63-1.82 (4H, m), 1.93-2.08 (3H, m), 2.78 (1H, d, J = 11.6Hz), 2.93 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.6-3.7 (1H, m), 6.92 (1H, d, J = 2.4Hz), 7.07 (1H, dd, J = 2.6, 9.4Hz), 7.23-7.28 (1H, m), 7.46 (1H, d, J = 9.4Hz).	-
647		1H-NMR (CDCl3) δppm : 1.07-1.16 (19H, m), 1.17-1.32 (8H, m), 1.32-1.48 (2H, m), 1.61-1.89 (7H, m), 2.8-2.9 (2H, m), 3.5-3.55 (1H, m), 3.55-3.65 (1H, m), 6.40 (1H, d, J = 3.4Hz), 7.21 (1H, d, J = 3.4Hz), 7.31 (1H, d, J = 2.7Hz), 8.06 (1H, d, J = 2.7Hz).	-
648		1H-NMR (CDCl3) δppm : 1.03-1.17 (19H, m), 1.19-1.36 (8H, m), 1.36-1.49 (2H, m), 1.63-1.90 (6H, m), 1.95-2.11 (1H, m), 3.05 (1H, d, J = 12.5Hz), 3.38 (1H, d, J = 12.5Hz), 3.45-3.55 (1H, m), 3.95-4.05 (1H, m), 6.33 (1H, d, J = 5.6Hz), 6.54 (1H, d, J = 3.6Hz), 7.10 (1H, d, J = 3.6Hz), 7.98 (1H, d, J = 5.6Hz).	-
649		1H-NMR (CDCl3) δppm : 1.1-1.18 (19H, m), 1.18-1.22 (4H, m), 1.34 (3H, s), 1.36-1.44 (2H, m), 1.61-1.83 (7H, m), 1.85-1.98 (1H, m), 2.81 (1H, d, J = 11.5Hz), 3.07 (1H, d, J = 11.4Hz), 3.6-3.65 (1H, m), 3.65-3.75 (1H, m), 6.30 (1H, dd, J = 3.0, 8.2Hz), 6.86 (1H, dd, J = 8.2, 12.0Hz), 8.24 (1H, d, J = 3.1Hz).	-

[0356]
Table 71

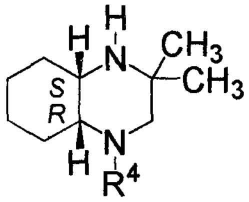
absolute configuration

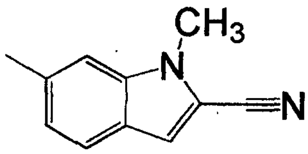
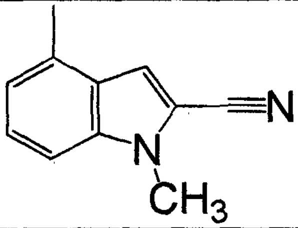
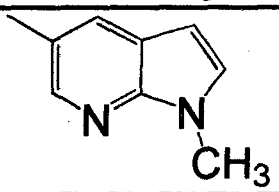
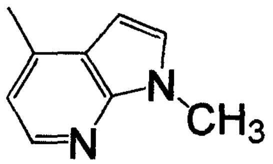
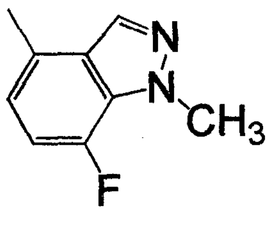
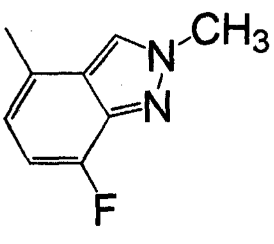


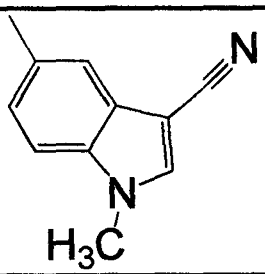
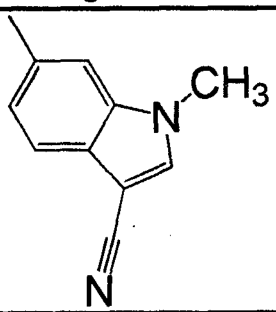
Example.	R^4	NMR	Salt
650		1H-NMR (CDCl3) δppm : 1.03 (1H, br), 1.15-1.34 (8H, m), 1.34-1.52 (2H, m), 1.62-1.90 (4H, m), 2.81 (1H, d, J = 11.8Hz), 3.05 (1H, d, J = 11.8Hz), 3.43-3.55 (1H, m), 3.69-3.81 (1H, m), 6.71 (1H, s), 6.92 (1H, d, J = 2.0, 9.0Hz), 7.56 (1H, d, J = 8.8Hz), 7.89 (1H, d, J = 0.9Hz), 9.76 (1H, br).	-
651		1H-NMR (CDCl3) δppm : 0.95-1.25 (6H, m), 1.33 (3H, s), 1.37-1.47 (2H, m), 1.64-1.80 (3H, m), 1.88-2.00 (1H, m), 3.02 (1H, d, J = 11.8Hz), 3.09 (1H, d, J = 11.8Hz), 3.62-3.68 (1H, m), 3.83-3.92 (1H, m), 6.4-6.45 (1H, m), 6.97 (1H, d, J = 8.3Hz), 7.23 (1H, dd, J = 7.7, 8.1Hz), 8.11 (1H, d, J = 1.0Hz), 10.05 (1H, br).	-
652		1H-NMR (CDCl3) δppm : 0.95 (1H, br), 1.15-1.33 (8H, m), 1.33-1.50 (2H, m), 1.64-1.88 (4H, m), 2.80 (1H, d, J = 11.8Hz), 3.03 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.65-3.75 (1H, m), 6.66 (1H, s), 6.95 (1H, dd, J = 2.1, 9.0Hz), 7.06 (1H, dd, J = 0.8, 2.0Hz), 7.46 (1H, d, J = 9.0Hz), 8.22 (1H, bs).	-
653		1H-NMR (CDCl3) δppm : 0.93-1.13 (3H, m), 1.20 (3H, s), 1.27-1.45 (5H, m), 1.58-1.79 (3H, m), 1.79-1.94 (1H, m), 2.70 (1H, d, J = 11.3Hz), 3.08 (1H, d, J = 11.3Hz), 3.6-3.7 (2H, m), 6.35 (1H, dd, J = 3.8, 8.3Hz), 6.61 (1H, dd, J = 3.3, 5.5Hz), 6.76 (1H, dd, J = 8.3, 10.7Hz), 7.18 (1H, dd, J = 2.8, 2.8Hz), 8.33 (1H, br).	-
654		1H-NMR (CDCl3) δppm : 0.80-1.25 (6H, m), 1.28 (3H, s), 1.31-1.48 (2H, m), 1.63-1.82 (4H, m), 2.81 (1H, d, J = 11.6Hz), 2.89 (1H, d, J = 11.6Hz), 3.5-3.6 (1H, m), 3.6-3.7 (1H, m), 6.95 (1H, d, J = 2.1Hz), 7.03 (1H, dd, J = 0.7, 2.0Hz), 7.17 (1H, dd, J = 2.3, 9.1Hz), 7.28 (1H, d, J = 9.0Hz), 8.64 (1H, br).	-
655		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.25-1.35 (7H, m), 1.45-1.9 (5H, m), 2.55-4.35 (6H, m), 6.27 (1H, dd, J = 1.9, 3.3Hz), 6.49 (1H, s), 7.33 (1H, dd, J = 2.9, 2.9Hz), 7.40 (1H, d, J = 2.5Hz), 8.04 (1H, d, J = 2.6Hz), 11.30 (1H, s).	1/2 Fumarate
656		1H-NMR (CDCl3) δppm : 1.00 (1H, br), 1.18-1.36 (7H, m), 1.36-1.52 (3H, m), 1.64-1.83 (3H, m), 1.98-2.13 (1H, m), 3.09 (1H, d, J = 12.6Hz), 3.43 (1H, d, J = 12.5Hz), 3.52 (1H, br), 4.0-4.1 (1H, m), 6.36 (1H, d, J = 5.7Hz), 6.51 (1H, d, J = 3.6Hz), 7.13 (1H, d, J = 3.6Hz), 8.03 (1H, d = 5.7Hz), 9.99 (1H, br).	-
657		1H-NMR (CDCl3) δppm : 1.03-1.17 (2H, m), 1.22 (3H, s), 1.33 (3H, s), 1.36-1.45 (2H, m), 1.62-1.79 (3H, m), 1.83-1.96 (1H, m), 2.83 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.5Hz), 3.65-3.7 (1H, m), 3.7-3.8 (1H, m), 6.28 (1H, dd, J = 3.3, 8.3Hz), 6.91 (1H, dd, J = 8.3, 10.3Hz), 8.12 (1H, d, J = 3.3Hz), 10.26 (1H, br).	-

[0357]
Table 72

absolute configuration

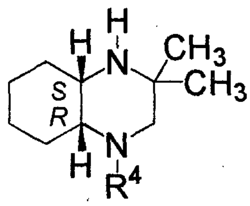


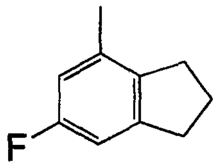
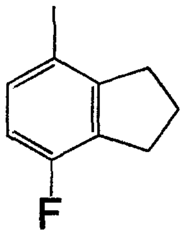
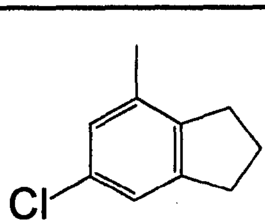
Example.	R^4	NMR	Salt
658		1H-NMR (CDCl3) δppm : 0.75-1.65 (11H, m), 1.65-1.9 (4H, m), 2.82 (1H, d, J = 11.7Hz), 3.03 (1H, d, J = 11.7Hz), 3.46-3.54 (1H, m), 3.71-3.79 (1H, m), 3.80 (3H, s), 6.51 (1H, d, J = 1.6Hz), 6.96 (1H, dd, J = 2.1, 9.0Hz), 7.02 (1H, s), 7.46 (1H, d, J = 9.0Hz).	-
659		1H-NMR (CDCl3) δppm : 0.85-1.15 (3H, m), 1.20 (3H, s), 1.32 (3H, s), 1.35-1.45 (1H, m), 1.6-1.8 (4H, m), 1.85-2.0 (1H, m), 2.80 (1H, d, J = 11.5Hz), 3.10 (1H, d, J = 11.6Hz), 3.6-3.7 (1H, m), 3.7-3.8 (1H, m), 3.85 (3H, s), 6.52 (1H, d, J = 7.6Hz), 6.89 (1H, d, J = 8.4Hz)7.20 (1H, s), 7.25-7.3 (1H, m).	-
660		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.25-1.4 (7H, m), 1.45-1.9 (5H, m), 2.93 (2H, s), 3.38 (3H, br), 3.63 (1H, br), 3.70-3.83 (4H, m), 6.28 (1H, d, J = 3.4Hz), 6.53 (2H, s), 7.39 (1H, d, J = 3.3Hz), 7.43 (1H, d, J = 2.6Hz), 8.10 (1H, d, J = 2.6Hz).	Fumarate
661		1H-NMR (DMSO-d6) δppm : 1.15-1.4 (9H, m), 1.5-1.8 (4H, m), 1.95-2.15 (1H, m), 3.09 (1H, d, J = 12.9Hz), 3.43 (1H, d, J = 12.8Hz), 3.55-3.65 (1H, m), 3.73 (3H, s), 4.05-4.15 (1H, m), 6.41 (1H, d, J = 5.6Hz), 6.49 (1H, d, J = 3.6Hz), 6.55 (2H, s), 7.26 (1H, d, J = 3.6Hz), 7.93 (1H, d, J = 5.6Hz).	Fumarate
662		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.30-1.42 (1H, m), 1.51 (3H, s), 1.54 (3H, s), 1.57-1.66 (1H, m), 1.69-1.98 (3H, m), 1.98-2.09 (1H, m), 2.99 (1H, d, J = 12.9Hz), 3.26 (1H, d, J = 12.8Hz), 3.9-4.0 (1H, m), 4.05-4.2 (4H, s), 6.39 (1H, dd, J = 3.0, 8.3Hz), 7.05 (1H, dd, J = 8.2, 11.8Hz), 8.14 (1H, br), 8.38 (1H ,d, J = 2.3Hz), 9.95 (1H, br).	Hydrochloride
663		1H-NMR (DMSO-d6) δppm : 1.00-1.16 (2H, m), 1.34-1.44 (1H, m), 1.50 (3H, s), 1.52 (3H, s), 1.58-1.95 (4H, m), 1.98-2.09 (1H, m), 2.98 (1H, d, J = 13.0Hz), 3.24 (1H, d, J = 13.0Hz), 3.85-3.95 (1H, m), 3.95-4.1 (1H, m), 4.17 (3H, s), 6.24 (1H, dd, J = 3.2, 8.0Hz), 6.85 (1H, dd, J = 8.0, 11.5Hz), 7.95-8.2 (1H, m), 8.74 (1H, d, J = 2.7Hz), 9.75-9.95 (1H, m).	Hydrochloride

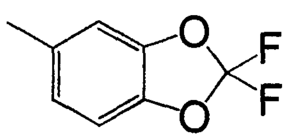
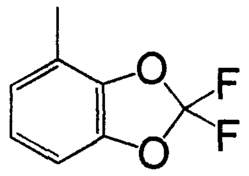
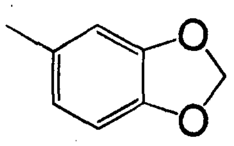
664		1H-NMR (DMSO-d6) δppm : 1.05-1.3 (2H, m), 1.3-1.45 (7H, m), 1.5-1.7 (2H, m), 1.7-1.9 (3H, m), 2.97 (1H ,d, J = 12.4Hz), 3.17 (1H ,d, J = 12.7Hz), 3.72 (1H, br), 3.81 (3H, s), 3.9-4.0 (1H, m), 6.58 (6H, s), 6.98 (1H, d, J = 2.0Hz), 7.14 (1H, dd, J = 2.2, 9.1Hz), 7.49 (1H, d, J = 9.0Hz), 8.10 (1H, s).	3 Fumarate
665		1H-NMR (DMSO-d6) δppm : 1.05-1.15 (1H, m), 1.15-1.35 (9H, m), 1.45-1.75 (3H, m), 1.75-1.9 (1H, m), 2.80 (1H, d, J = 11.9Hz), 3.0-3.6 (4H, m), 3.77 (3H, s), 3.8-3.9 (1H, m), 6.51 (1H, s), 6.90 (1H, d, J = 1.8Hz), 7.03 (1H, dd, J = 2.0, 8.9Hz), 7.43 (1H, d, J = 8.8Hz), 7.99 (1H, s).	1/2 Fumarate

[0358]
Table 73

absolute configuration

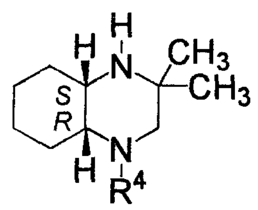


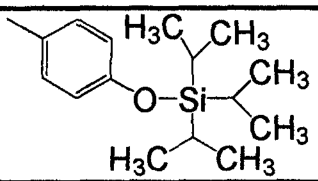
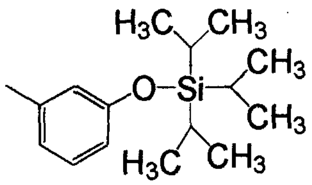
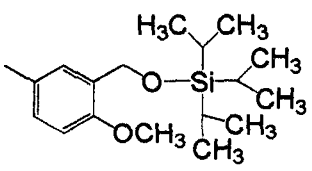
Example.	R^4	NMR	Salt
666		1H-NMR (DMSO-d6) δppm : 1.00-1.25 (2H, m), 1.31-1.42 (1H, m), 1.46 (3H, s), 1.49 (3H, s), 1.58-1.69 (1H, m), 1.69-1.84 (2H, m), 1.84-2.05 (3H, m), 2.05-2.2 (1H, m), 2.70-2.92 (5H, m), 3.24 (1H, d, J = 13.0Hz), 3.45-3.57 (1H, m), 3.80-3.93 (1H, m), 6.53 (1H, dd, J = 2.0, 11.6Hz), 6.66-6.76 (1H, m), 7.9-8.2 (1H, m), 9.7-10.0 (1H, m).	Hydrochloride
667		1H-NMR (DMSO-d6) δppm : 1.00-1.21 (2H, m), 1.29-1.41 (1H, m), 1.48 (6H, s), 1.55-1.67 (1H, m), 1.67-2.06 (5H, m), 2.07-2.21 (1H, m), 2.70 (1H, d, J = 12.7Hz), 2.78-3.00 (4H, m), 3.21-3.39 (2H, m), 3.78-3.89 (1H, m), 6.74 (1H, dd, J = 4.4, 8.6Hz), 6.88 (1H, dd, J = 8.6, 8.6Hz), 8.01 (1H, br), 9.74 (1H, br).	Hydrochloride
668		1H-NMR (DMSO-d6) δppm : 1.10-1.24 (1H, m), 1.34-1.42 (1H, m), 1.45 (3H, s), 1.48 (3H, s), 1.58-2.03 (6H, m), 2.03-2.19 (1H, m), 2.72-2.95 (5H, m), 3.27 (1H, d, J = 12.9Hz), 3.38-3.55 (1H, m), 3.79-3.95 (1H, m), 4.28-4.11 (1H, m), 6.72 (1H, d, J = 1.5Hz), 6.94 (1H, s), 7.9-8.1 (1H, m), 9.6-9.8 (1H, m).	Hydrochloride

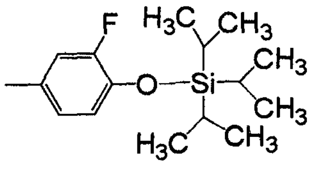
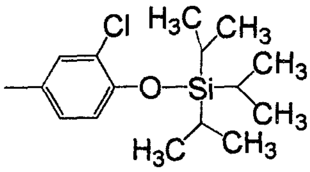
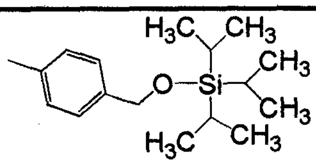
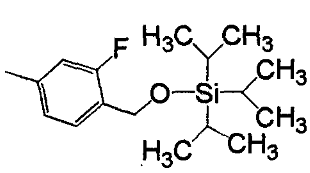
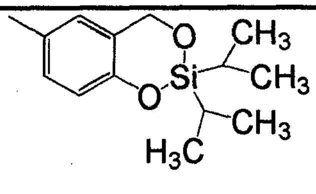
669		1H-NMR (DMSO-d6) δppm : 1.20-1.48 (6H, m), 1.51 (3H, s), 1.63-1.93 (4H, m), 1.93-2.10 (1H, m), 2.96 (1H, d, J = 13.4Hz), 3.29 (1H, d, J = 14.0Hz), 3.7-3.85 (1H, m), 3.9-4.05 (1H, m), 6.70 (1H, dd, J = 2.5, 8.9Hz), 7.12 (1H, d, J = 2.4Hz), 7.23 (1H, d, J = 8.9Hz), 8.15 (1H, br), 9.86 (1H, br).	Hydrochloride
670		1H-NMR (DMSO-d6) δppm : 1.1-1.25 (9H, m), 1.25-1.4 (1H, m), 1.45-1.75 (4H, m), 1.9-2.05 (1H, m), 2.92 (1H, d, J = 12.2Hz), 3.06 (1H, d, J = 12.3Hz), 3.1-3.63 (3H, m), 3.63-3.70 (1H, m), 6.57 (2H, s), 6.71 (1H, d, J = 8.6Hz), 6.75-6.81 (1H, m), 7.04 (1H, dd, J = 8.3, 8.3Hz).	Fumarate
671		1H-NMR (DMSO-d6) δppm : 1.15-1.31 (2H, m), 1.35-1.46 (4H, m), 1.50 (3H, s), 1.61-1.87 (4H, m), 1.93-2.07 (1H, m), 2.92 (1H, d, J = 13.2Hz), 3.11 (1H, d, J = 13.2Hz), 3.7-3.8 (1H, m), 3.8-3.9 (1H, m), 5.88-5.95 (2H, m), 6.32 (1H, d, J = 2.4, 8.5Hz), 6.71 (1H, d, J = 2.4Hz), 6.76 (1H, d, J = 8.5Hz), 7.9-8.15 (1H, m), 9.7-9.9 (1H, m).	Hydrochloride

[0359]
Table 74

absolute configuration

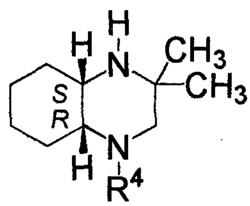


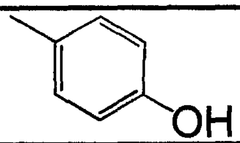
Example.	R^4	NMR	Salt
672		1H-NMR (CDCl3) δppm : 1.02-1.15 (19H, m), 1.15-1.28 (11H, m), 1.29-1.46 (2H, m), 1.60-1.76 (4H, m), 2.67 (1H, d, J = 11.6Hz), 2.83 (1H, d, J = 11.6Hz), 3.4-3.55 (2H, m), 6.69-6.74 (2H, m), 6.74-6.79 (2H, m).	-
673		1H-NMR (CDCl3) δppm : 1.11 (18H, d, J = 7.0Hz), 1.16-1.33 (11H, m), 1.33-1.59 (3H, m), 1.65-1.78 (4H, m), 2.68 (1H, d, J = 11.8Hz), 2.97 (1H, d, J = 11.9Hz), 3.4-3.45 (1H, m), 3.55-3.6 (1H, m), 6.28 (1H, dd, J = 1.9, 7.6Hz), 6.37 (1H, dd, J = 2.3, 2.3Hz), 6.43 (1H, dd, J = 2.4, 7.8Hz), 7.03 (1H, dd, J = 8.1, 8.1Hz).	-
674		1H-NMR (CDCl3) δppm : 1.04-1.15 (19H, m), 1.15-1.30 (11H, m), 1.32-1.47 (2H, m), 1.47-1.77 (4H, m), 2.70 (1H, d, J = 11.7Hz), 2.92 (1H, d, J = 11.7Hz), 3.41-3.48 (1H, m), 3.54-3.63 (1H, m), 3.75 (3H, s), 4.78-4.88 (2H, m), 6.65 (1H, dd, J = 3.0, 8.7Hz), 6.71 (1H, d, J = 8.8Hz), 7.22 (1H, d, J = 2.9Hz).	-

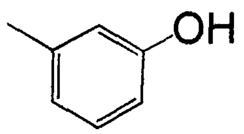
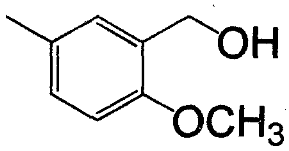
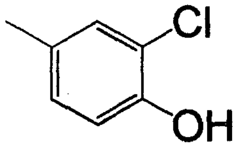
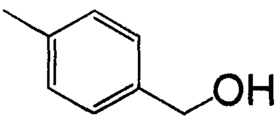
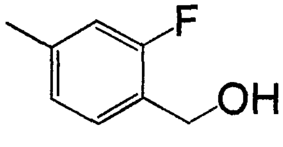
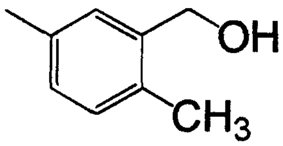
675		1H-NMR (CDCl3) δppm : 1.06-1.14 (18H, m), 1.15-1.29 (12H, m), 1.29-1.48 (2H, m), 1.58-1.76 (4H, m), 2.65 (1H, d, J = 11.8Hz), 2.83 (1H, d, J = 11.6Hz), 3.35-3.45 (1H, m), 3.45-3.55 (1H, m), 6.40-6.48 (1H, m), 6.55 (1H, dd, J = 2.9, 14.1Hz), 6.79 (1H, dd, J = 9.4, 9.4Hz).	-
676		1H-NMR (CDCl3) δppm : 1.11 (18H, d, J = 7.3Hz), 1.16-1.21 (4H, m), 1.21-1.33 (7H, m), 1.34-1.47 (2H, m), 1.47-1.78 (5H, m), 2.66 (1H, d, J = 11.6Hz), 2.81 (1H, d, J = 11.6Hz), 3.4-3.55 (2H, m), 6.61 (1H, d, J = 3.0, 8.9Hz), 6.78 (1H, d, J = 8.9Hz), 6.81 (1H, d, J = 3.0Hz).	-
677		1H-NMR (CDCl3) δppm : 1.06-1.11 (18H, m), 1.11-1.22 (7H, m), 1.23 (3H, s), 1.25-1.80 (8H, m), 2.71 (1H, d, J = 11.8Hz), 3.01 (1H, d, J = 11.9Hz), 3.4-3.5 (1H, m), 3.6-3.7 (1H, m), 4.73 (2H, s), 6.79-6.85 (2H, m), 7.18-7.23 (2H, m),	-
678		1H-NMR (CDCl3) δppm : 1.05-1.12 (18H, m), 1.12-1.48 (13H, m), 1.48-1.82 (5H, m), 2.70 (1H, d, J = 11.9Hz), 2.99 (1H, d, J = 12.0Hz), 3.35-3.45 (1H, m), 3.55-3.65 (1H, m), 4.77 (2H, s), 6.47 (1H, dd, J = 2.4, 13.9Hz), 6.61 (1H, dd, J = 2.4, 8.6Hz), 7.32 (1H, dd, J = 8.8, 8.8Hz).	-
679		1H-NMR (CDCl3) δppm : 1.03 (18H, d, J = 2.4Hz), 1.13-1.27 (9H, m), 1.27-1.77 (6H, m), 2.67 (1H, d, J = 11.5Hz), 2.80 (1H, d, J = 11.5Hz), 3.4-3.55 (2H, m), 4.96 (2H, s), 6.42 (1H, d, J = 2.8Hz), 6.70 (1H, dd, J = 2.9, 8.8Hz), 6.80 (1H, d, J = 8.8Hz).	-

[0360]
Table 75

absolute configuration

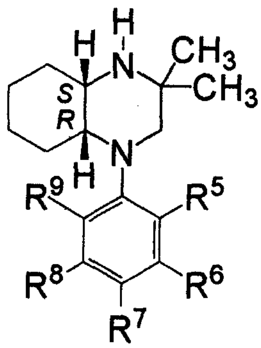


Example.	R^4	NMR	Salt
680		1H-NMR (CDCl3) δppm : 1.02-1.30 (9H, m), 1.30-1.49 (2H, m), 1.50-1.83 (4H, m), 2.70 (1H, d, J = 10.4Hz), 2.81 (1H, d, J = 11.4Hz), 3.4-3.6 (2H, m), 6.75 (4H, bs).	-

681		1H-NMR (CDCl3) δppm : 1.16-1.30 (8H, m), 1.30-1.49 (3H, m), 1.60-1.83 (4H, m), 2.71 (1H, d, J = 12.0Hz), 3.03 (1H, d, J = 12.0Hz), 3.38-3.45 (1H, m), 3.56-3.68 (1H, m), 6.17-6.23 (1H, m), 6.33 (1H, dd, J = 2.3, 2.3Hz), 6.43 (1H, dd, J = 2.2, 8.3Hz), 7.06 (1H, dd, J = 8.1, 8.1Hz).	-
682		1H-NMR (DMSO-d6) δppm : 1.1-1.25 (2H, m), 1.3-1.4 (7H, m), 1.5-1.9 (5H, m), 2.87 (1H, d, J = 12.4Hz), 2.97 (1H, d, J = 12.6Hz), 3.63-3.78 (5H, m), 4.44 (2H, s), 6.54 (3H, s), 6.73 (1H, dd, J = 2.9, 8.8Hz), 6.80 (1H, d, J = 8.8Hz), 6.99 (1H, d, J = 2.8Hz).	3/2 Fumarate
683		1H-NMR (CDCl3) δppm : 1.09-2.34 (16H, m), 2.81 (1H, d, J = 12.1Hz), 2.85-3.1 (1H, m), 3.5-3.6 (1H, m), 3.6-3.75 (1H, m), 6.73 (1H, dd, J = 2.8, 8.9Hz), 6.81 (1H, d, J = 2.8Hz), 6.92 (1H, d, J = 8.8Hz).	-
684		1H-NMR (CDCl3) δppm : 1.15-1.60 (12H, m), 1.61-1.83 (4H, m), 2.72 (1H, d, J = 12.0Hz), 3.03 (1H, d, J = 11.9Hz), 3.4-3.45 (1H, m), 3.6-3.7 (1H, m), 4.56 (2H, s), 6.80-6.86 (2H, m), 7.20-7.25 (2H, m).	-
685		1H-NMR (CDCl3) δppm : 0.92 (1H, br), 1.16-1.36 (8H, m), 1.37-1.48 (2H, m), 1.57 (1H, br), 1.62-1.84 (4H, m), 2.71 (1H, d, J = 12.0Hz), 3.02 (1H, d, J = 12.0H), 3.35-3.45 (1H, m), 3.55-3.65 (1H, m), 4.62 (2H, s), 6.51 (1H, dd, J = 2.5, 14.0Hz), 6.59 (1H, dd, J = 2.5, 8.5Hz), 7.19 (1H, dd, J = 8.8, 8.8Hz).	-
686		1H-NMR (CDCl3) δppm : 0.92-1.02 (1H, m), 1.02-1.18 (7H, m), 1.19-1.32 (1H, m), 1.35-1.66 (5H, m), 1.69-1.83 (1H, m), 2.60 (1H, d, J =11.3Hz), 2.69 (1H, d, J = 11.3Hz), 3.32 (1H, br), 3.41-3.50 (1H, m), 4.43 (2H, d, J = 4.6Hz), 4.88 (1H, t, J = 5.4Hz), 6.55 (1H, dd, J = 2.9, 8.7Hz), 6.60 (1H, d, J = 8.6Hz), 6.83 (1H, d, J = 2.7Hz), 8.55 (1H, s).	-

[0361]
Table 76

absolute configuration



Example	R^5	R^6	R^7	R^8	R^9	NMR	Salt

687	-H	-H	-OCH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.45 (4H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 1.95-2.1 (1H, m), 2.93 (1H, d, J = 13.1Hz), 3.10 (1H, d, J = 13.0Hz), 3.68 (3H, s), 3.7-3.9 (2H, m), 4.35-5.75 (1H, m), 6.75-6.85 (2H, m), 6.85-6.95 (2H, m), 8.11 (1H, br), 9.92 (1H, br).	2 Hydrochloride
688	-CH3	-Cl	-H	-H	-H	1H-NMR (CDCl3) δppm : 0.93-1.1 (2H, m), 1.17 (3H, s), 1.31 (3H, s), 1.35-1.43 (2H, m), 1.55-1.75 (3H, m), 1.78-1.93 (1H, m), 2.37 (3H, s), 2.42 (1H, d, J = 11.0Hz), 2.83-2.91 (1H, m), 3.10 (1H, d, J = 11.0Hz), 3.5-3.6 (1H, m), 6.79 (1H, dd, J = 2.1, 7.1Hz), 6.99-7.09 (2H, m).	-
689	-CH3	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.17 (2H, m), 1.3-1.43 (1H, m), 1.49 (3H, s), 1.52 (3H, s), 1.56-1.68 (1H, m), 1.68-1.87 (2H, m), 1.87-2.1 (2H, m), 2.30 (3H, s), 2.62 (1H, d, J = 12.6Hz), 3.11-3.23 (1H, m), 3.25-3.45 (1H, m), 3.78-3.92 (1H, m), 6.92-7.04 (2H, m), 7.08-7.22 (2H, m), 8.03 (1H, br), 9.65-9.95 (1H, m). "	Hydrochloride

690	-H	-H	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.18-1.35 (2H, m), 1.35-1.48 (4H, m), 1.52 (3H, s), 1.62-1.9 (4H, m), 1.98-2.04 (1H, m), 2.19 (3H, s), 2.91 (1H, d, J = 13.3Hz), 3.25 (1H, d, J = 13.3Hz), 3.7-3.8 (1H, m), 3.9-4.0 (1H, m), 4.1-4.45 (1H, m), 6.8-6.87 (2H, m), 6.98-7.07 (2H, m), 8.05-8.25 (1H, m), 9.8-10.05 (1H, m). "	2 Hydrochloride
691	-CH3	-CH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.15 (2H, m), 1.3-1.42 (1H, m), 1.49 (3H, s), 1.52 (3H, s), 1.55-1.67 (1H, m), 1.67-1.83 (2H, m), 1.83-2.008 (2H, m), 2.20 (3H, s), 2.22 (3H, s), 2.59 (1H, d, J = 12.6Hz), 3.05-3.15 (1H, m), 3.25-3.4 (1H, m), 3.82-3.96 (1H, m), 6.82 (1H, d, J = 7.8Hz), 6.91 (1H, d, J = 7.4Hz), 7.03 (1H, dd, J = 7.7, 7.7Hz), 7.98 (1H, br), 9.65-9.8 (1H, m).	Hydrochloride
692	-H	-CH3	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.22-1.47 (6H, m), 1.53 (3H, s), 1.63-1.93 (4H, m), 1.97-2.08 (1H, m), 2.27 (3H, s), 2.93 (1H, d, J = 13.6Hz), 3.36 (1H, d, J = 13.5Hz), 3.7-3.8 (1H, m), 3.8-4.1 (2H, m), 6.79 (1H, dd, J = 3.0, 8.9Hz), 6.93 (1H, d, J = 2.9Hz), 7.20 (1H, d, J = 8.8Hz), 8.1-8.3 (1H, m), 9.85-10.05 (1H, m).	2 Hydrochloride

693	-H	-CH3	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.16-1.33 (2H, m), 1.36-1.45 (4H, m), 1.52 (3H, s), 1.62-1.9 (4H, m), 2.0-2.08 (1H, m), 2.18 (3H, d, J = 1.7Hz), 2.93 (1H, d, J = 13.3Hz), 3.21 (1H, d, J = 13.2Hz), 3.7-3.8 (1H, m), 3.9-4.0 (1H, m), 4.15-4.55 (1H, m), 6.72-6.8 (1H, m), 6.81-6.89 (1H, m), 6.97 (1H, dd, J = 9.1, 9.1Hz), 8.05-8.25 (1H, m), 9.85-10.1 (1H, m).	2 Hydrochloride
694	-CH3	-F	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.45 (1H, m), 1.49 (3H, s), 1.51 (3H, s), 1.56-1.84 (3H, m), 1.84-2.06 (2H, m), 2.20 (3H, d, J = 2.2Hz), 2.67 (1H, d, J = 12.7Hz), 3.15-3.25 (1H, m), 3.29-3.42 (1H, m), 3.85-4.0 (1H, m), 6.83 (1H, d, J = 8.0Hz), 6.89 (1H, dd, J = 8.8, 8.8Hz), 7.16 (1H, dd, J = 7.9, 15.3Hz), 8.02 (1H, br), 9.72 (1H, br).	Hydrochloride
695	-H	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.46 (6H, m), 1.52 (3H, s), 1.63-1.95 (4H, m), 1.95-2.1 (1H, m), 2.95 (1H, d, J = 13.7Hz), 3.47 (1H, d, J = 13.6Hz), 3.7-3.8 (1H, m), 4.0-4.1 (1H, m), 6.77 (1H, dd, J = 1.4, 7.8Hz), 6.90 (1H, d, J = 2.2, 8.4Hz), 6.96-7.01 (1H, m), 7.21 (1H, dd, J = 8.1, 8.1Hz), 8.17 (1H, br), 9.85 (1H, br).	Hydrochloride

696	-CH3	-OCH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.3-1.4 (1H, m), 1.48 (3H, s), 1.51 (3H, s), 1.55-1.65 (1H, m), 1.65-1.85 (2H, m), 1.85-2.05 (2H, m), 2.13 (3H, s), 2.62 (1H, d, J = 12.6Hz), 3.1-3.2 (1H, m), 3.3-3.4 (1H, m), 3.76 (3H, s), 3.8-3.9 (1H, m), 6.61 (1H, d, J = 7.9Hz), 6.72 (1H, d, J = 8.1Hz), 7.10 (1H, dd, J = 8.1, 8.1Hz), 8.01 (1H, br), 9.71 (1H, br).	Hydrochloride
697	-H	-Cl	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.24-1.47 (6H, m), 1.51 (3H, s), 1.63-1.91 (4H, m), 1.91-2.08 (1H, m), 2.20 (3H, s), 2.91 (1H, d, J = 13.5Hz), 3.23-3.42 (1H, m), 3.66-3.80 (1H, m), 3.94-4.08 (1H, m), 6.84 (1H, dd, J = 2.6, 8.5Hz), 6.97 (1H, d, J = 2.6Hz), 7.16 (1H, d, J = 8.6Hz), 8.12 (1H, br), 9.82 (1H, br).	Hydrochloride
698	-H	-F	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.45 (6H, m), 1.51 (3H, s), 1.65-1.9 (4H, m), 2.0-2.05 (1H, m), 2.10 (3H, s), 2.91 (1H, d, J = 13.6Hz), 3.3-3.45 (1H, m), 3.7-3.8 (1H, m), 3.95-4.05 (1H, m), 6.67 (1H, dd, J = 2.5, 8.5Hz), 6.74 (1H, dd, J = 2.4, 13.5Hz), 7.08 (1H, dd, J = 8.9, 8.9Hz), 8.0-8.3 (1H, m), 9.75-10.0 (1H, m).	Hydrochloride

699	-H	-H	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.21-1.35 (2H, m), 1.35-1.48 (4H, m), 1.53 (3H, s), 1.63-1.95 (4H, m), 1.98-2.12 (1H, m), 2.94 (1H, d, J = 13.4Hz), 3.32 (1H, d, J = 13.3Hz), 3.7-3.8 (1H, m), 3.9-4.05 (1H, m), 6.85-7.26 (5H, m), 8.20 (1H, br), 9.99 (1H, br).	Hydrochloride
700	-H	-H	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.49 (6H, m), 1.49-1.57 (3H, m), 1.65-1.95 (4H, m), 1.95-2.09 (1H, m), 2.96 (1H, d, J = 13.6Hz), 3.39-3.48 (1H, m), 3.71-3.83 (1H, m), 3.98-4.09 (1H, m), 6.98-7.05 (2H, m), 7.16-7.24 (2H, m), 8.16 (1H, br), 9.65-10.1 (1H, m).	Hydrochloride
701	-H	-Cl	-CN	-H	-H	1H-NMR (DMSO-d6) δppm : 1.10 (3H, s), 1.15-1.25 (4H, m), 1.25-1.45 (2H, m), 1.45-1.7 (4H, m), 1.85-2.0 (1H, m), 2.76 (1H, d, J = 12.8Hz), 2.85-3.85 (4H, m), 3.85-3.95 (1H, m), 6.56 (1H, s), 6.94 (1H, dd, J = 2.5, 9.1Hz), 7.09 (1H, d, J = 2.4Hz), 7.59 (1H, d, J = 9.0Hz).	1/2 Fumarate
702	-H	-F	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.25-1.5 (6H, m), 1.52 (3H ,s), 1.65-2.1 (5H, m), 2.97 (1H, d, J = 13.8Hz), 3.54 (1H, d, J = 13.6Hz), 3.65-3.8 (1H, m), 4.0-4.15 (1H, m), 6.81 (1H, dd, J = 2.2, 9.3Hz), 7.05 (1H, dd, J = 2.9, 14.4Hz), 7.34 (1H, dd, J = 9.0, 9.0Hz), 8.24 (1H, br), 9.92 (1H, br).	Hydrochloride

703	-H	-F	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.10-1.37 (9H, m), 1.44-1.75 (4H, m), 1.75-1.90 (1H, m), 2.68 (1H, d, J = 12.4Hz), 3.15 (1H, d, J = 12.4Hz), 3.25-3.45 (1H, m), 3.7-3.8 (1H, m), 6.51 (1H, m), 6.67 (1H, d, J = 2.1, 9.1Hz), 6.81-7.24 (3H, m)	1/2 Fumarate
704	-H	-Cl	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.07-1.36 (9H, m), 1.43-1.58 (1H, m), 1.58-1.72 (3H, m), 1.73-1.89 (1H, m), 2.67 (1H, d, J = 12.2Hz), 3.0-3.7 (4H, m), 3.7-3.8 (1H, m), 6.52 (1H, s), 6.82-7.24 (4H, m).	1/2 Fumarate
705	-H	-CHF2	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.41 (9H, m), 1.48-1.92 (5H, m), 2.75 (1H, d, J = 12.7Hz), 2.8-4.4 (6H, m), 6.46 (1H, d, J = 7.8Hz), 6.54 (2H, s), 6.62 (1H, s), 6.76 (1H, dd, J = 2.1, 8.5Hz), 7.0-7.4 (2H, m).	Fumarate
706	-H	-OCHF2	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 0.97-1.36 (9H, m), 1.43-1.73 (4H, m), 1.73-1.87 (1H, m), 2.67 (1H, d, J = 12.1Hz), 2.95-3.8 (5H, m), 6.52 (1H, s), 6.7-6.8 (2H, m), 7.0-7.4 (2H, m).	1/2 Fumarate
707	-H	-OCHF2	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.11-1.37 (9H, m), 1.45-1.74 (4H, m), 1.77-1.91 (1H, m), 2.69 (1H, d, J = 12.3Hz), 2.75-4.2 (5H, m), 6.52 (1H, s), 6.73-6.83 (2H, m), 7.03-7.43 (2H, m).	1/2 Fumarate

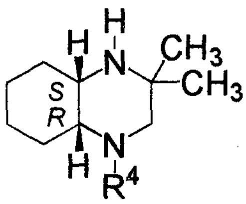
708	-H	-CN	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.06-1.21 (7H, m), 1.21-1.36 (2H, m), 1.41-1.70 (4H, m), 1.74-1.89 (1H, m), 2.68 (1H, d, J = 12.3Hz), 2.9-3.75 (4H, m), 3.75-3.85 (1H, m), 6.54 (1H, s), 6.99-7.14 (4H, m).	1/2 Fumarate
709	-H	-OCHF2	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.45-1.75 (4H, m), 1.75-1.9 (1H, m), 2.69 (1H, d, J = 12.2Hz), 2.8-4.3 (5H, m), 6.52 (1H, s), 6.71-7.38 (5H, m).	1/2 Fumarate
710	-H	-F	-OCHF2	-F	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.22 (7H, m), 1.25-1.40 (2H, m), 1.42-1.72 (4H, m), 1.76-1.92 (1H, m), 2.66 (1H, d, J = 12.5Hz), 2.8-4.35 (5H, m), 6.53 (1H, s), 6.66-6.76 (2H, m), 7.05 (1H, t, J = 72.9Hz).	1/2 Fumarate
711	-H	-H	-OCH2CHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.31 (2H, m), 1.32-1.49 (4H, m), 1.52 (3H, s), 1.62-1.89 (4H m), 1.98-2.08 (1H, m), 2.93 (1H, d, J = 13.1Hz), 3.16 (1H, d, J = 13.2Hz), 3.7-3.8 (1H, m), 3.80-4.27 (4H, m), 6.18-6.50 (1H, m), 6.90 (4H, s), 8.0-8.25 (1H, m), 9.8-10.1 (1H, m).	2 Hydrochloride

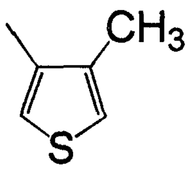
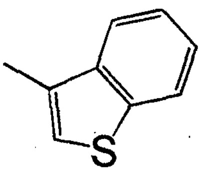
712	-H	-F	-OCH2CF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.20-1.46 (6H, m), 1.51 (3H, s), 1.63-1.89 (4H m), 1.92-2.08 (1H, m), 2.91 (1H, d, J = 13.4Hz), 3.29 (1H, d, J = 12.8Hz), 3.67-3.79 (1H, m), 3.88-4.01 (1H, m), 4.20-4.33 (2H, m), 6.18-6.52 (1H, m), 6.68 (1H, dd, J = 1.8, 9.1Hz), 6.91 (1H, dd, J = 2.9, 14.7Hz), 7.10 (1H, dd, J = 9.5, 9.5Hz), 8.0-8.2 (1H, m), 9.75-9.95 (1H, m).	Hydrochloride
713	-H	-CH3	-OCHCF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.06-1.16 (1H, m), 1.16-1.37 (8H, m), 1.45-1.88 (5H, m), 2.17 (3H, s), 2.69 (1H, d, J = 12.0Hz), 3.04 (1H, d, J = 12.0Hz), 3.1-3.9 (4H, m), 6.50 (1H, s), 6.71 (1H, dd, J = 3.0, 8.9Hz), 6.75-7.16 (3H, m).	1/2 Fumarate
714	-H	-OCH3	-OCHCF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.18 (1H, m), 1.18-1.27 (7H, m), 1.27-1.38 (1H, m), 1.44-1.60 (1H, m), 1.60-1.74 (3H, m), 1.74-1.88 (1H, m), 2.71 (1H, d, J = 12.1Hz), 3.08 (1H, d, J = 12.2Hz), 3.15-3.85 (7H, m), 6.40 (1H, dd, J = 2.7, 8.9Hz), 6.50 (1H, s), 6.57 (1H, d, J = 2.6Hz), 6.62-7.02 (2H, m).	1/2 Fumarate

715	-OCHCF2	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.94-1.14 (1H, m), 1.14-1.15 (1H, m), 1.18 (3H, s), 1.26 (3H, s), 1.28-1.43 (2H, m), 1.48 (1H, br), 1.61-1.73 (3H, m), 1.76-1.90 (1H, m), 2.49 (1H, d, J = 11.2Hz), 3.05 (1H, d, J = 11.2Hz), 3.45-3.6 (2H, m), 6.55 (1H, dd, J = 70.2, 81.4Hz), 6.91 (1H, dd, J = 1.4, 8.0Hz), 6.93-6.99 (1H, m), 7.07-7.18 (2H, m)	-

[0362]
Table 77

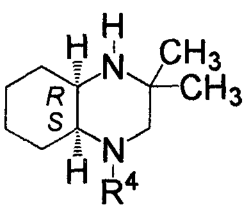
absolute configuration

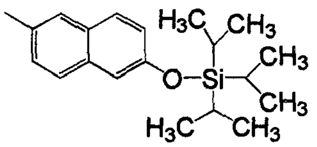
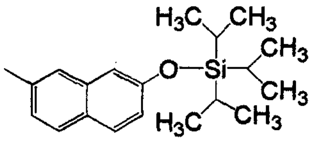
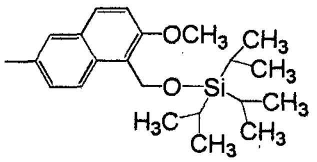
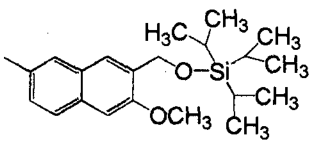


Example	R^4	NMR	Salt
716		1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.47 (3H, s), 1.50 (3H, s), 1.6-2.05 (5H, m), 2.15 (3H, d, J = 0.7Hz), 2.70 (1H, d, J = 12.8Hz), 3.20 (1H, d, J = 12.9Hz), 3.25-3.4 (1H, m), 3.8-3.9 (1H, m), 6.77 (1H, d, J = 3.2Hz), 7.09 (1H, dd, J = 1.0, 3.3Hz), 7.9-8.1 (1H, m), 9.6-9.75 (1H, m).	-
717		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.3-1.45 (1H, m), 1.52 (3H, s), 1.56 (3H, s), 1.6-1.7 (1H, m), 1.7-2.1 (4H, m), 2.87 (1H, d, J = 12.8Hz), 3.36 (1H, d, J = 13.1Hz), 3.65-3.75 (1H, m), 4.1-4.2 (1H, m), 7.06 (1H, s), 7.35-7.45 (2H, m), 7.9-8.0 (2H, m), 8.0-8.15 (1H, m), 9.6-9.8 (1H, m).	Hydrochloride

[0363]
Table 78

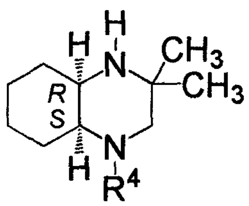
absolute configuration

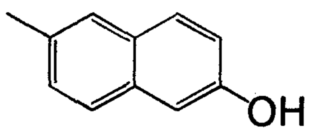


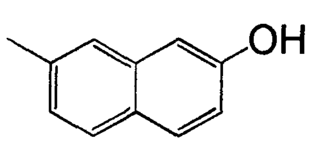
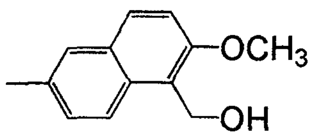
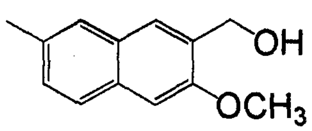
Example	R4	NMR	Salt
718		1H-NMR (CDCl3) δppm : 1.08-1.15 (18H, m), 1.19-1.34 (12H, m), 1.35-1.48 (2H, m), 1.64-1.85 (4H, m), 2.82 (1H, d, J = 11.6Hz), 3.04 (1H, d, J = 11.7Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 6.95 (1H, d, J = 2.2Hz), 7.03 (1H, dd, J = 2.5, 8.8Hz), 7.10 (1H, d, J = 2.4Hz), 7.23 (1H, d, J = 2.5, 9.1Hz), 7.51 (1H, d, J = 8.8Hz), 7.55 (1H, d, J = 9.1Hz).	-
719		1H-NMR (CDCl3) δppm : 1.13 (18H, d, J = 7.3Hz), 1.18-1.36 (12H, m), 1.36-1.65 (2H, m), 1.65-1.87 (4H, m), 2.83 (1H, d, J = 11.9Hz), 3.12 (1H, d, J = 11.9Hz), 3.45-3.55 (1H, m), 3.75-3.85 (1H, m), 6.82 (1H, d, J = 2.3Hz), 6.86 (1H, dd, J = 2.4, 8.7Hz), 7.02 (1H, d, J = 2.3Hz), 7.10 (1H, dd, J = 2.4, 9.0Hz), 7.53 (1H, d, J = 8.7Hz), 7.59 (1H, d, J = 9.0Hz).	-
720		1H-NMR (CDCl3) δppm : 1.04-1.12 (18H, m), 1.12-1.32 (12H, m), 1.32-1.64 (2H, m), 1.65-1.86 (4H, m), 2.82 (1H, d, J = 11.8Hz), 3.08 (1H, d, J = 11.8Hz), 3.47-3.53 (1H, m), 3.73-3.81 (1H, m), 3.88 (3H, s), 5.17 (1H, d, J = 11.0Hz), 5.24 (1H, d, J = 11.0Hz), 6.94 (1H, d, J = 2.5Hz), 7.16 (1H, d, J = 9.0Hz), 7.31 (1H, dd, J = 2.5, 9.4Hz), 7.58 (1H, d, J = 9.0Hz), 8.12 (1H, d, J = 9.4Hz).	-
721		1H-NMR (CDCl3) δppm : 1.14 (18H, d, J = 6.7Hz), 1.19-1.33 (13H, m), 1.33-1.65 (1H, m), 1.65-1.84 (4H, m), 2.83 (1H, d, J = 11.6Hz), 3.04 (1H, d, J = 11.6Hz), 3.5-3.6 (1H, m), 3.7-3.8 (1H, m), 3.87 (3H, s), 4.93 (2H, d, J = 0.9Hz), 6.96 (1H, s), 6.99 (1H, d, J = 2.2Hz), 7.21 (1H, dd, J =2.4, 9.0Hz), 7.59 (1H, d, J = 9.0Hz), 7.77 (1H, s).	-

[0364]
Table 79

absolute configuration

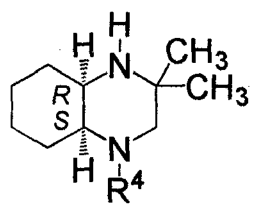


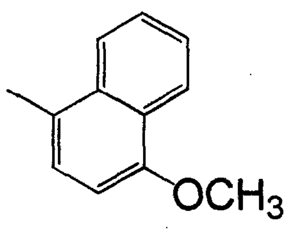
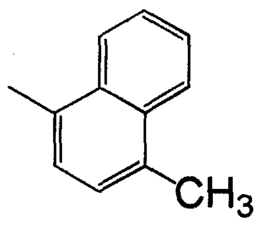
Example	R4	NMR	Salt
722		1H-NMR (CDCl3) δppm : 1.14-1.51 (11H, m), 1.65-1.85 (4H, m), 2.83 (1H, d, J = 11.7Hz), 3.05 (1H, d, J = 11.8Hz), 3.52-3.57 (1H, m), 3.69-3.79 (1H, m), 6.97 (1H, d, J = 2.3Hz), 6.99-7.06 (2H, m), 7.22-7.28 (1H, m), 7.52-7.58 (2H, m).	-

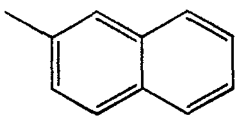
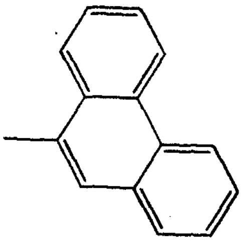
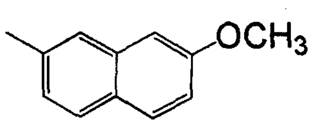
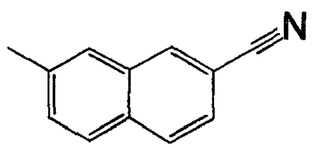
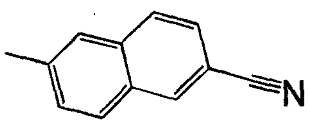
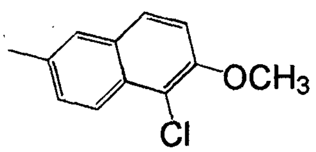
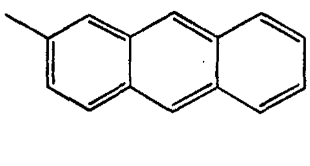
723		1H-NMR (CDCl3) δppm : 1.18-1.36 (9H, m), 1.35-1.51 (2H, m), 1.66-1.86 (4H, m), 2.84 (1H, d, J = 11.9Hz), 3.13 (1H, d, J = 12.0Hz), 3.45-3.55 (1H, m), 3.75-3.85 (1H, m), 6.8-6.85 (2H, m), 6.94 (1H, d, J =2.4Hz), 7.10 (1H, d, J = 2.4, 9.1Hz), 7.57 (1H, d, J = 8.7Hz), 7.60 (1H, d, J = 9.0Hz).	-
724		1H-NMR (DMSO-d6) δppm : 1.1-1.2 (1H, m), 1.2-1.4 (8H, m), 1.5-1.9 (5H, m), 2.86 (1H, d, J = 12.2Hz), 3.20 (1H, d, J = 12.5Hz), 3.58 (1H, br), 3.85 (3H, s), 3.9-4.0 (1H, m), 4.85 (2H, s), 6.54 (2H, s), 7.05 (1H, d, J = 2.4Hz), 7.28 (1H, d, J = 9.1Hz), 7.39 (1H, dd, J = 2.5, 9.5Hz), 7.66 (1H, d, J = 9.0H), 7.97 (1H, d, J = 9.4Hz).	Fumarate
725		1H-NMR (CDCl3) δppm : 0.97 (1H, br), 1.15-1.35 (8H, m), 1.35-1.5 (2H, m), 1.65-1.85 (4H, m), 2.42 (1H, t, J = 6.5Hz), 2.82 (1H, d, J = 11.8Hz), 3.05 (1H, d, J = 11.7H), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.94 (3H, s), 4.79 (2H, d, J = 5.9Hz), 6.98 (1H, d, J = 2.4Hz), 7.02 (1H, s), 7.21-7.28 (1H, m), 7.54 (1H, s), 7.60 (1H, d, J = 9.0Hz).	-

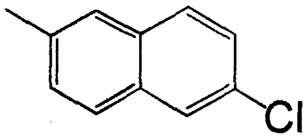
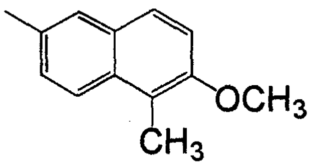
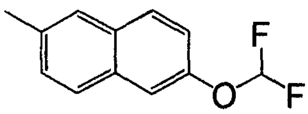
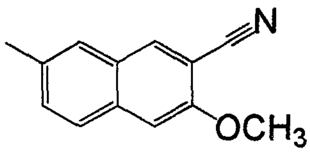
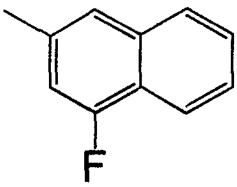
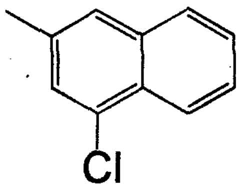
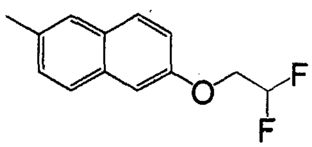
[0365]
Table 80

absolute configuration



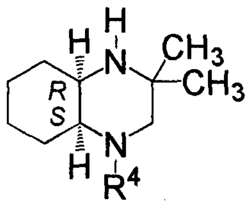
Example	R^4	NMR	Salt
726		1H-NMR (DMSO-d6) δppm : 0.9-1.05 (1H, m), 1.05-1.2 (1H, m), 1.3-1.45 (1H, m), 1.52 (3H, s), 1.55-1.65 (4H, m), 1.65-1.85 (2H, m), 1.85-2.05 (2H, m), 2.73 (1H, d, J = 12.5Hz), 3.25-3.6 (2H, m), 3.94 (3H, s), 4.15-4.3 (1H, m), 6.88 (1H, d, J = 8.2Hz), 7.06 (1H, d, J = 8.0Hz), 7.5-7.55 (1H, m), 7.55-7.6 (1H, m), 7.96 (1H, br), 8.16 (1H, dd, J = 1.0, 8.3Hz), 8.24 (1H, d, J = 8.1Hz), 9.4-9.6 (1H, m).	Hydrochloride
727		1H-NMR (DMSO-d6) δppm : 0.85-1.0 (1H, m), 1.0-1.15 (1H, m), 1.3-1.4 (1H, m), 1.5-1.65 (7H, m), 1.65-1.85 (2H, m), 1.85-2.1 (2H, m), 2.59 (3H, s), 2.76 (1H, d, J = 12.5Hz), 3.3-3.45 (1H, m), 3.51 (1H, d, J = 12.5Hz), 4.15-4.3 (1H, m), 7.02 (1H, d, J = 7.5Hz), 7.28 (1H, d, J = 7.4Hz), 7.5-7.65 (2H, m), 7.95-8.15 (2H, m), 8.25-8.35 (1H, m), 9.6-9.8 (1H, m).	Hydrochloride

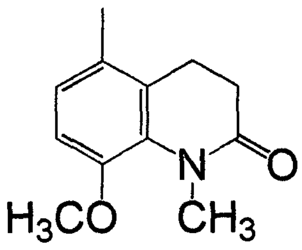
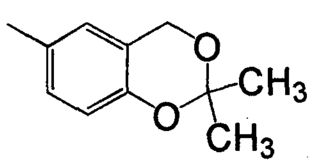
728		1H-NMR (DMSO-d6) δppm : 1.23-1.54 (6H, m), 1.58 (3H, s), 1.64-2.02 (4H, m), 2.02-2.15 (1H, m), 3.07 (1H, d, J = 13.4Hz), 3.50 (1H, d, J = 13.4Hz), 3.75-3.9 (1H, m), 3.9-4.53 (2H, m), 7.18 (1H, d, J = 2.2Hz), 7.22-7.32 (1H, m), 7.32-7.46 (2H, m), 7.65-7.82 (3H, m), 8.26 (1H, br), 10.02 (1H, br).	2 Hydrochloride
729		1H-NMR (CDCl3) δppm : 0.83-0.99 (1H, m), 1.021.13 (1H, m), 1.27 (3H, s), 1.32-1.42 (2H, m), 1.46 (3H, s), 1.54-1.71 (2H, m), 1.71-1.81 (1H, m), 1.85-1.99 (1H, m), 2.69 (1H, d, J = 11.1Hz), 3.3-3.45 (2H, m), 3.75-3.85 (1H, m), 7.15 (1H, s), 7.5-7.55 (2H, m), 7.6-7.7 (2H, m), 7.7-7.8 (1H, m), 8.3-8.4 (1H, m), 8.55-8.65 (1H, m), 8.65-8.75 (1H, m).	-
730		1H-NMR (CDCl3) δppm : 0.9-1.65 (11H, m), 1.65-1.9 (4H, m), 2.84 (1H, d, J = 12.0Hz), 3.13 (1H, d, J = 11.9Hz), 3.50 (1H, bs), 3.75-3.85 (1H, m), 3.89 (3H, s), 6.89 (1H, dd, J = 2.5, 8.8Hz), 6.92 (1H, d, J = 2.4Hz), 6.97 (1H, d, J = 2.4Hz), 7.11 (1H, dd, J = 2.5, 9.0Hz), 7.57 (1H, d, J = 8.8Hz), 7.60 (1H, d, J = 9.0Hz).	-
731		1H-NMR (DMSO-d6) δppm : 1.3-1.5 (6H, m), 1.55 (3H, s), 1.65-2.05 (5H, m), 3.08 (1H, d, J = 13.6Hz), 3.62 (1H, d, J = 13.6Hz), 3.8-3.9 (1H, m), 4.2-4.3 (1H, m), 7.32 (1H, d, J = 2.1Hz), 7.50 (1H, dd, J = 1.6, 8.4Hz), 7.63 (1H, dd, J = 2.5, 9.2Hz), 7.85-8.0 (2H, m), 8.11-8.2 (1H, m), 8.26 (1H, s), 9.6-9.75 (1H, m).	Hydrochloride
732		1H-NMR (DMSO-d6) δppm : 1.32-1.54 (6H, m), 1.57 (3H, s), 1.66-2.13 (5H, m), 3.10 (1H, d, J = 13.9Hz), 3.72 (1H, d, J = 13.7Hz), 3.75-3.9 (1H, m), 4.25-4.35 (1H, m), 7.29 (1H, d, J = 2.2Hz), 7.5-7.65 (2H, m), 7.81 (1H, d, J = 8.6Hz), 7.91 (1H, d, J = 9.2Hz), 8.15-8.45 (2H, m), 9.92 (1H, br).	Hydrochloride
733		1H-NMR (DMSO) δppm : 1.0-1.35 (9H, m), 1.4-1.6 (2H, m), 1.6-1.7 (3H, m), 1.8-1.95 (1H, m), 2.72 (1H, d, J = 12.3Hz), 3.12 (1H, d, J = 11.1Hz), 3.3-3.4 (1H, m), 3.8-3.9 (1H, m), 3.92 (3H, s), 7.09 (1H, d, J = 1.8Hz), 7.39 (1H, d, J = 9.2Hz), 7.49 (1H, dd, J = 2.4, 9.5Hz), 7.71 (1H, d, J = 9.0Hz), 7.89 (1H, d, J = 9.4Hz).	-
734		1H-NMR (CDCl3) δppm : 1.00 (1H, br), 1.19-1.37 (8H, m), 1.38-1.51 (2H, m), 1.67-1.79 (3H, m), 1.79-1.93 (1H, m), 2.90 (1H, d, J = 11.8Hz), 3.18 (1H, d, J = 11.9Hz), 3.53 (1H, br), 3.8-3.9 (1H, m), 7.05 (1H, d, J = 2.1Hz), 7.3-7.45 (3H, m), 7.8-7.95 (3H, m), 8.15 (1H, s), 8.25 (1H, s).	-

735		1H-NMR (DMSO-d6) δppm : 1.15-1.25 (1H, m), 1.25-1.4 (8H, m), 1.5-1.95 (5H, m), 2.88 (1H, d, J = 12.6Hz), 3.31 (1H, d, J = 12.4Hz), 3.54 (1H, br), 3.95-4.05 (1H, m), 6.54 (2H, s), 7.13 (1H, d, J = 2.1Hz), 7.34 (1H, dd, J = 2.2, 8.7Hz), 7.44 (1H, dd, J = 2.4, 9.2Hz), 7.67-7.76 (2H, m), 7.81 (1H, d, J = 2.1Hz).	Fumarate
736		1H-NMR (CDCl3) δppm : 1.09 (1H, br), 1.15-1.35 (8H, m), 1.35-1.5 (2H, m), 1.65-1.85 (4H, m), 2.50 (3H ,s), 2.82 (1H, d, J = 11.6Hz), 3.07 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.90 (3H, s), 6.96 (1H, d, J = 2.5Hz), 7.18 (1H, d, J = 9.0Hz), 7.30 (1H, dd, J = 2.6, 9.4Hz), 7.51 (1H, d, J = 9.0Hz), 7.81 (1H, d, J = 9.3Hz).	-
737		1H-NMR (DMSO-d6) δppm : 1.06-1.19 (1H, m), 1.19-1.39 (8H, m), 1.47-1.80 (4H, m), 1.80-1.96 (1H, m), 2.83 (1H, d, J = 12.2Hz), 2.9-4.4 (5H, m), 6.51 (1H, s), 7.05-7.45 (4H, m), 7.49 (1H, d, J = 2.4Hz), 7.7-7.8 (2H, m).	1/2 Fumarate
738		1H-NMR (DMSO-d6) δppm : 1.23-1.54 (6H, m), 1.60 (3H, s), 1.66-2.06 (4H, m), 2.06-2.20 (1H, m), 3.07 (1H, d, J = 13.4Hz), 3.45 (1H, d, J = 13.9Hz), 3.75-3.9 (1H, m), 3.95 (3H, s), 4.1-4.2 (1H, m), 4.77 (1H, br), 7.25 (1H, d, J = 2.2Hz), 7.46 (1H, s), 7.58 (1H, dd, J =2.4, 9.2Hz), 7.81 (1H, d, J = 9.2Hz), 8.23 (1H, s), 8.25-8.4 (1H, m), 10.18 (1H, br).	2 Hydrochloride
739		1H-NMR (DMSO-d6) δppm : 1.27-1.50 (6H, m), 1.58 (3H, s), 1.65-2.13 (5H, m), 3.06 (1H, d, J = 13.6Hz), 3.56 (1H, d, J = 13.6Hz), 3.73-3.87 (1H, m), 4.14-4.26 (1H, m), 7.05 (1H, d, J = 1.8Hz), 7.28-7.38 (2H, m), 7.43-7.52 (1H, m), 7.75 (1H, d, J = 8.5Hz), 7.84 (1H, d, J = 8.2Hz), 8.15-8.4 (1H, m), 9.9-10.1 (1H, m).	Hydrochloride
740		1H-NMR (DMSO-d6) δppm : 1.28-1.50 (6H, m), 1.57 (3H, s), 1.66-2.00 (4H, m), 2.00-2.18 (1H, m), 3.08 (1H, d, J = 13.5Hz), 3.56 (1H, d, J = 13.5Hz), 3.75-3.9 (1H, m), 3.95-4.1 (1H, m), 7.23 (1H, d, J = 2.0Hz), 7.36-7.45 (1H, m), 7.45-7.54 (1H, m), 7.65 (1H, d, J = 2.4Hz), 7.78 (1H, d, J = 8.1Hz), 7.97 (1H, d, J = 8.4Hz), 8.1-8.35 (1H, m), 9.8-10.1 (1H, m).	Hydrochloride
741		1H-NMR (DMSO-d6) δppm : 1.06-1.17 (1H, m), 1.17-1.39 (8H, m), 1.46-1.79 (4H, m), 1.79-1.92 (1H, m), 2.82 (1H, d, J = 12.1Hz), 2.9-4.2 (5H, m), 4.30-4.41 (2H, m), 6.27-6.59 (2H, m), 7.06 (1H, d, J = 2.1Hz), 7.10 (1H, dd, J = 2.6, 8.9Hz), 7.26 (1H, d, J = 2.5Hz), 7.36 (1H, dd, J = 2.4, 9.2Hz), 7.60-7.68 (2H, m).	1/2 Fumarate

[0366]
Table 81

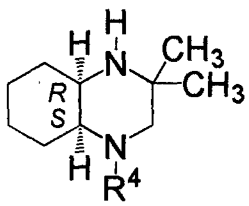
absolute configuration

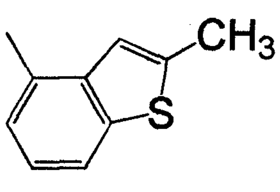
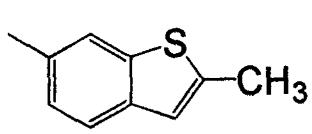


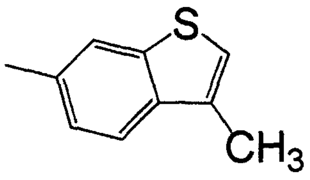
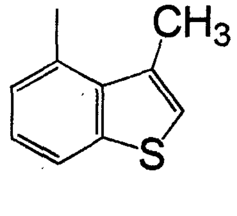
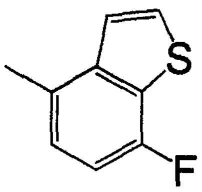
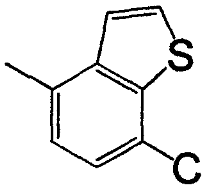
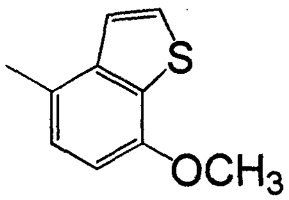
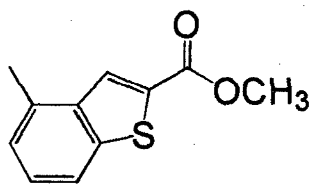
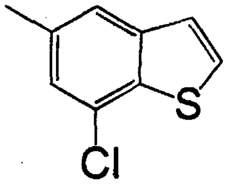
Example	R^4	NMR	Salt
742		1H-NMR (DMSO-d6) δppm : 1.0-1.15 (2H, m), 1.3-1.45 (1H, m), 1.48 (3H, s), 1.50 (3H, s), 1.55-1.65 (1H, m), 1.65-1.8 (2H, m), 1.8-2.0 (2H, m), 2.25-2.35 (1H, m), 2.4-2.5 (1H, m), 2.6-2.75 (2H, m), 2.95-3.1 (2H, m), 3.21 (3H, s), 3.3-3.5 (1H, m), 3.78 (3H, s), 3.85-3.95 (1H, m), 6.78 (1H, d, J = 8.9Hz), 6.93 (1H, d, J = 8.9Hz), 7.97 (1H, br), 9.59 (1H, br).	Hydrochloride
743		1H-NMR (DMSO-d6) δppm : 1.08-1.37 (9H, m), 1.42 (6H, s), 1.48-1.83 (5H, m), 2.74 (1H, d, J = 12.2Hz), 2.94 (1H, d, J = 12.3Hz), 3.51 (1H, br), 3.6-3.75 (1H, m), 4.73 (2H, s), 6.53 (2H, s), 6.57 (1H, d, J = 2.6Hz), 6.65 (1H, d, J = 8.9Hz), 6.75 (1H, dd, J = 2.8, 9.0Hz).	Fumarate

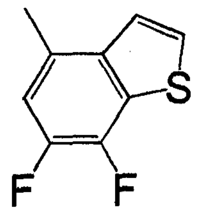
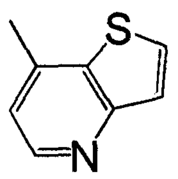
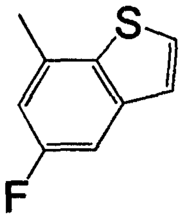
[0367]
Table 82

absolute configuration



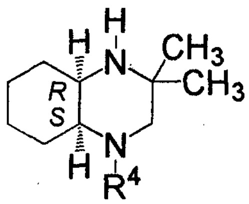
Example	R^4	NMR	Salt
744		1H-NMR (CDCl3) δppm : 0.94-1.09 (3H, m), 1.20 (3H, s), 1.34 (3H, s), 1.36-1.44 (2H, m), 1.45-1.79 (3H, m), 1.81-1.94 (1H, m), 2.55-2.65 (4H, m), 3.15 (1H, d, J = 11.2Hz), 3.4-3.5 (1H, m), 3.65-3.7 (1H, m), 6.74 (1H, dd, J = 0.6, 7.6Hz), 7.05 (1H, s), 7.13 (1H, dd, J = 7.8, 7.8Hz), 7.38 (1H, d, J = 8.0Hz).	-
745		1H-NMR (DMSO-d6) δppm : 1.1-1.2 (1H, m), 1.2-1.4 (8H, m), 1.45-1.75 (4H, m), 1.75-1.9 (1H, m), 2.47 (3H, d, J = 1.2Hz), 2.6-2.7 (6H, m), 6.49 (1H, s), 6.90 (1H, s), 6.99 (1H, dd, J = 2.3, 8.8Hz), 7.25 (1H, d, J = 2.1Hz), 7.48 (1H, d, J = 8.8Hz).	1/2 Fumarate

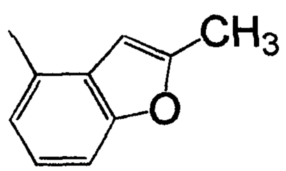
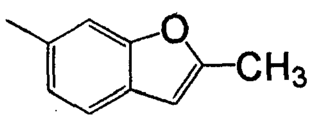
746		1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.5-1.95 (5H, m), 2.31 (3H, d, J = 1.2Hz), 2.6-5.0 (7H, m), 6.52 (2H, s), 7.01 (1H, d, J = 1.2Hz), 7.11 (1H, dd, J = 2.3, 8.9Hz), 7.34 (1H, d, J = 2.2Hz), 7.55 (1H, d, J = 8.8Hz).	1/2 Fumarate
747		1H-NMR (DMSO-d6) δppm : 0.93-1.10 (2H, m), 1.28-1.42 (1H, m), 1.51-1.66 (7H, m), 1.70-2.00 (3H, m), 2.00-2.18 (1H, m), 2.69 (3H, s), 2.80 (1H, d, J = 12.5Hz), 3.2-3.3 (1H, m), 3.48 (1H, d, J = 12.6Hz), 3.85-3.95 (1H, m), 7.02 (1H, d, J = 7.5Hz), 7.26 (1H, d, J = 7.8, 7.8Hz), 7.36 (1H, d, J = 0.6Hz), 7.69 (1H, d, J = 7.6Hz), 7.95-8.15 (1H, m), 9.95-10.1 (1H, m).	Hydrochloride
748		1H-NMR (CDCl3) δppm : 0.92-1.08 (3H, m), 1.20 (3H, s), 1.32-1.43 (5H, m), 1.45-1.78 (3H, m), 1.81-1.94 (1H, m), 2.57 (1H, d, J = 11.1Hz), 3.14 (1H, d, J = 11.1Hz), 3.33-3.41 (1H, m), 3.63-3.70 (1H, m), 6.71 (1H, dd, J = 4.1, 8.4Hz), 6.92 (1H, dd, J = 8.9, 8.9Hz), 7.41 (1H, d, J = 5.4Hz), 7.46 (1H, dd, J = 3.7, 5.4Hz).	-
749		1H-NMR (CDCl3) δppm : 0.92-1.08 (3H, m), 1.20 (3H, s), 1.29-1.42 (5H, m), 1.45-1.78 (3H, m), 1.82-1.96 (1H, m), 2.61 (1H, d, J = 11.2Hz), 3.15 (1H, d, J = 11.1Hz), 3.42-3.50 (1H, m), 3.64-3.71 (1H, m), 6.74 (1H, d, J = 8.2Hz), 7.21 (1H, d, J = 8.2Hz), 7.43 (1H, d, J = 5.5Hz), 7.47 (1H, d, J = 5.5Hz).	-
750		1H-NMR (CDCl3) δppm : 0.9-1.1 (2H, m), 1.20 (3H, s), 1.3-1.45 (5H, m), 1.45-1.8 (4H, m), 1.8-1.95 (1H, m), 2.56 (1H, d, J = 11.1Hz), 3.14 (1H, d, J = 11.1Hz), 3.3-3.4 (1H, m), 3.6-3.7 (1H, m), 3.96 (3H, s), 6.66 (1H, d, J = 8.2Hz), 6.74 (1H, d, J = 8.2Hz), 7.39 (1H, d, J = 5.4Hz), 7.45 (1H, d, J = 5.4Hz).	-
751		1H-NMR (CDCl3) δppm : 0.95-1.1 (2H, m), 1.22 (3H, s), 1.3-1.45 (5H, m), 1.45-1.85 (4H, m), 1.85-2.0 (1H, m), 2.65 (1H, d, J = 11.2Hz), 3.17 (1H, d, J = 11.2Hz), 3.45-3.55 (1H, m), 3.7-3.8 (1H, m), 3.96 (3H, s), 6.77-6.82 (1H, m), 7.33 (1H, dd, J = 7.9, 7.9Hz), 7.45 (1H, d, J = 8.1Hz), 8.14 (1H, d, J = 0.5Hz).	-
752		1H-NMR (CDCl3) δppm : 0.93 (1H, br), 1.16-1.33 (8H, m), 1.33-1.49 (2H, m), 1.64-1.85 (4H, m), 2.80 (1H, d, J = 11.6Hz), 2.97 (1H, d, J = 11.7Hz), 3.48 (1H, br), 3.6-3.7 (1H, m), 7.04 (1H, d, J = 2.1Hz), 7.10 (1H, d, J = 2.2Hz), 7.20 (1H, d, J = 5.4Hz), 7.41 (1H, d, J = 5.5Hz).	-

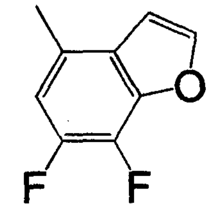
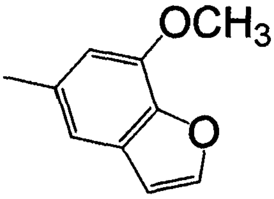
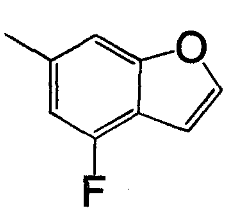
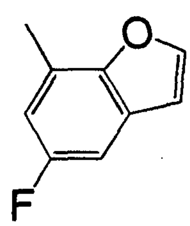
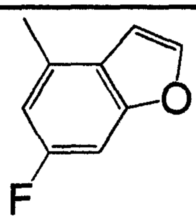
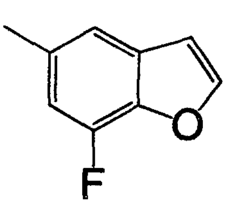
753		1H-NMR (DMSO-d6) δppm : 0.94-1.14 (2H, m), 1.29-1.44 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.58-2.07 (5H, m), 2.84 (1H, d, J = 12.9Hz), 3.41(1H, d, J = 13.0Hz), 3.6-3.7 (1H, m), 4.15-4.25 (1H, m), 7.11 (1H, dd, J = 6.5, 12.6Hz), 7.77 (1H, dd, J = 3.8, 5.4Hz), 7.84 (1H, d, J = 5.4Hz), 8.04 (1H, br), 9.81 (1H, br).	Hydrochloride
754		1H-NMR (DMSO-d6) δppm : 1.38-1.57 (5H, m), 1.64 (3H, s), 1.70-2.02 (4H, m), 2.03-2.14 (1H, m), 2.37-2.54 (1H, m), 3.55 (1H, d, J = 15.0Hz), 3.9-4.0 (1H, m), 4.23 (1H, d, J = 15.3Hz), 4.6-4.75 (1H, m), 7.27 (1H, d, J = 7.2Hz), 7.67 (1H, d, J = 5.7Hz), 8.45-8.6 (2H, m), 8.88 (1H, br), 10.33 (1H, m), 14.95 (1H, br).	2 Hydrochloride
755		1H-NMR (DMSO-d6) δppm : 1.0-1.19 (2H, m), 1.31-1.46 (1H, m), 1.51 (3H, s), 1.52 (3H, s), 1.60-1.89 (3H, m), 1.93-2.08 (2H, m), 3.00 (1H, d, J = 12.9Hz), 3.46 (1H, d, J = 13.0Hz), 3.90-4.01 (1H, m), 3.95-4.08 (1H, m), 6.96 (1H, dd, J = 2.1, 11.0Hz), 7.41 (1H, dd, J = 2.2, 9.1Hz), 7.46 (1H, d, J = 5.4Hz), 7.86 (1H, d, J = 5.4Hz), 8.16 (1H, br), 9.78 (1H, br).	Hydrochloride

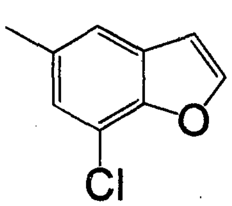
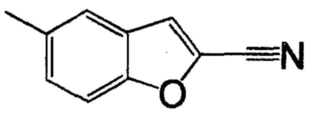
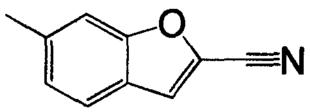
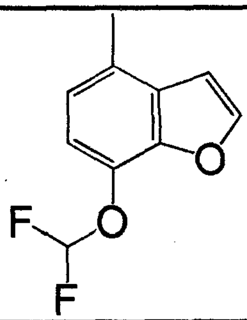
[0368]
Table 83

absolute configuration



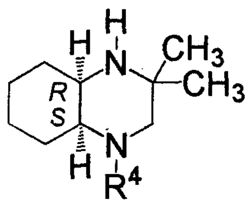
Example	R^4	NMR	Salt
756		1H-NMR (CDCl3) δppm : 1.02-1.17 (3H, m), 1.20 (3H, s), 1.31 (3H, s), 1.34-1.46 (2H, m), 1.47-1.79 (3H, m), 1.81-1.95 (1H, m), 2.45 (3H, d, J = 1.0Hz), 2.80 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.5Hz), 3.55-3.65 (2H, m), 6.39 (1H, dd, J = 1.0, 1.0Hz), 6.56 (1H, dd, J = 0.8, 7.7Hz), 6.95-7.05 (1H, m), 7.06 (1H, dd, J = 7.9, 7.9Hz).	-
757		1H-NMR (DMSO-d6) δppm : 1.17-1.37 (2H, m), 1.37-1.52 (4H, m), 1.56 (3H, s), 1.61-1.73 (1H, m), 1.73-1.99 (3H, m), 2.00-2.15 (1H, m), 2.37 (3H, d, J = 0.9Hz), 3.00 (1H, d, J = 13.3Hz), 3.28 (1H, d, J = 13.2Hz), 3.7-3.85 (1H, m), 3.95-4.1 (1H, m), 4.92 (1H, br), 6.40 (1H, d, J = 0.8Hz), 6.89 (1H, dd, J = 2.1, 8.6Hz), 7.05 (1H, d, J = 1.5Hz), 7.33 (1H, d, J = 8.5Hz), 8.15-8.35 (1H, m), 10.0-10.2 (1H, m).	2 Hydrochloride

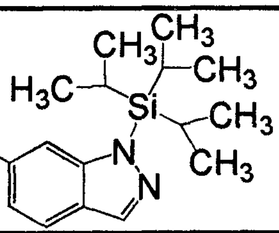
758		1H-NMR (DMSO-d6) δppm : 1.01-1.19 (2H, m), 1.33-1.44 (1H, m), 1.48 (3H, s), 1.51 (3H, s), 1.59-2.07 (5H, m), 3.01 (1H, d, J = 13.0Hz), 3.28 (1H, d, J = 13.1Hz), 3.75-3.9 (1H, m), 4.0-4.15 (1H, m), 6.83 (1H, dd, J = 5.9, 13.5Hz), 7.36 (1H ,dd, J = 2.6, 2.6Hz), 8.0-8.2 (2H, m), 9.7-9.9 (1H, m).	Hydrochloride
759		1H-NMR (DMSO-d6) δppm : 1.0-1.2 (2H, m), 1.34-1.44 (1H, m), 1.50 (3H, s), 1.53 (3H, s), 1.60-2.06 (5H, m), 3.05 (1H, d, J = 12.8Hz), 3.27 (1H, d, J = 13.0Hz), 3.84 (3H, s), 3.88-4.00 (2H, m), 6.66 (1H, d, J = 8.5Hz), 6.75 (1H, d, J = 8.5Hz), 6.93 (1H, J = 2.2Hz), 7.92 (1H, d, J = 2.2Hz), 8.0-8.25 (1H, m), 9.55-9.8 (1H, m).	Hydrochloride
760		1H-NMR (CDCl3) δppm : 0.99-1.27 (5H, m), 1.28 (3H, s), 1.33-1.47 (2H, m), 1.48-1.84 (5H, m), 2.77-2.90 (2H, m), 3.45-3.55 (1H, m), 3.55-3.65 (1H, m), 4.01 (3H, s), 6.51 (1H, d, J = 2.0Hz), 6.58 (1H, d, J = 2.1Hz), 6.63 (1H, d, J = 2.1Hz), 7.53 (1H, d, J =2.0Hz).	-
761		1H-NMR (DMSO-d6) δppm : 1.05-1.25 (2H, m), 1.35-1.45 (1H, m), 1.48 (3H, s), 1.52 (3H, s), 1.6-2.05 (5H, m), 3.13 (1H ,d, J = 13.2Hz), 3.28 (1H, d, J = 13.5Hz), 3.9-4.0 (1H, m), 4.0-4.1 (1H, m), 6.63 (1H, dd, J = 2.1, 12.3Hz), 7.09 (1H, dd, J = 1.3, 8.7Hz), 7.22 (1H, dd, J = 0.7, 2.2Hz), 7.96 (1H, d, J = 2.3Hz), 8.0-8.2 (1H, m), 9.6-9.9 (1H, m).	Hydrochloride
762		1H-NMR (DMSO-d6) δppm : 1.16-1.34 (2H, m), 1.35-1.45 (1H, m), 1.47 (3H, s), 1.54 (3H, s), 1.66-1.89 (3H, m), 1.92-2.11 (2H, m), 3.25 (1H, d, J = 13.6Hz), 3.45 (1H, d, J = 13.4Hz), 3.83-4.02 (1H, m), 4.20-4.38 (1H, m), 6.68 (1H, dd, J = 2.0, 12.2Hz), 6.87-7.05 (2H, m), 8.02 (1H, d, J = 2.1Hz), 8.24 (1H, br), 9.7-10.0 (1H, m).	Hydrochloride
763		1H-NMR (DMSO-d6) δppm : 1.27-1.47 (6H, m), 1.53 (3H, s), 1.61-1.96 (4H, m), 1.97-2.09 (1H, m), 3.00 (1H, d, J = 13.6Hz), 3.45 (1H, d, J = 13.5Hz), 3.71-3.81 (1H, m), 4.05-4.15 (1H, m), 6.81-6.93 (2H, m), 6.98-7.04 (1H, m), 7.83 (1H, d, J = 2.2Hz), 8.1-8.3 (1H, m), 9.8-10.0 (1H, m).	Hydrochloride
764		1H-NMR (DMSO-d6) δppm : 1.18-1.48 (6H, m), 1.53 (3H, s), 1.62-1.93 (4H, m), 1.95-2.13 (1H, m), 3.00 (1H, d, J = 13.3Hz), 3.30 (1H, d, J = 13.2Hz), 3.7-3.85 (1H, m), 3.95-4.1 (1H, m), 4.83 (1H, br), 6.91 (1H, dd, J = 2.2, 3.0Hz), 6.94 (1H, d, J 2.1Hz), 7.01 (1H, dd, J = 2.1, 14.2Hz), 7.99 (1H, d, J = 2.1Hz), 8.12 (1H, br), 9.86 (1H, br).	2 Hydrochloride

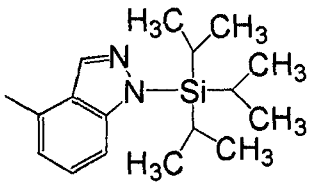
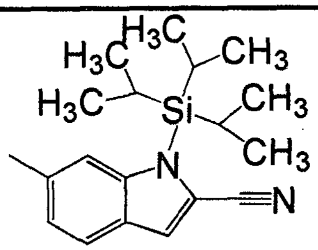
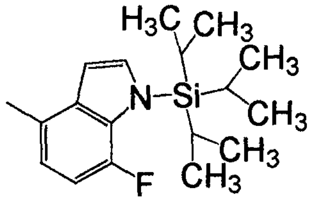
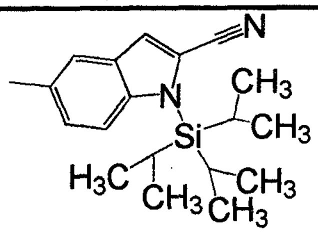
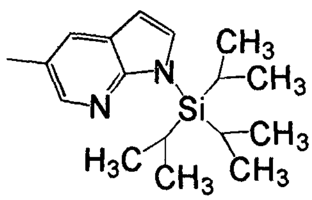
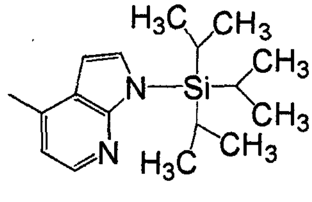
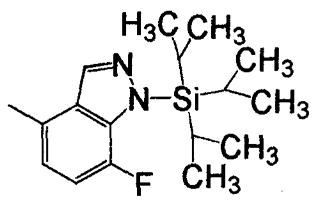
765		1H-NMR (DMSO-d6) δppm : 1.21-1.37 (2H, m), 1.37-1.47 (4H, m), 1.52 (3H ,s), 1.62-1.90 (4H, m), 1.95-2.08 (1H, m), 3.02 (1H, d, J = 13.2Hz), 3.29 (1H, d, J = 13.2Hz), 3.75-3.9 (1H, m), 3.95-4.1 (1H, m), 6.92 (1H, d, J = 2.2Hz), 7.12 (1H, d, J = 2.2Hz), 7.16 (1H, d, J = 2.2Hz), 8.01 (1H, d, J = 2.1Hz), 8.06 (1H, br), 9.74 (1H, br)	Hydrochloride
766		1H-NMR (DMSO-d6) δppm : 1.19-1.36 (2H, m), 1.38-1.48 (4H, m), 1.52 (3H, s), 1.62-1.89 (4H, m), 1.93-2.06 (1H, m), 3.03 (1H, d, J = 13.3Hz), 3.25-3.4 (1H, m), 3.75-3.9 (1H, m), 4.0-4.1 (1H, m), 7.22 (1H, d, J = 2.4Hz), 7.37 (1H, dd, J = 2.5, 9.3Hz), 7.62 (1H, d, J = 9.2Hz), 7.95 (1H, d, J =0.7Hz), 8.06 (1H, br), 9.64 (1H, br).	Hydrochloride
767		1H-NMR (DMSO-d6) δppm : 1.15-1.29 (8H, m), 1.29-1.40 (2H, m), 1.48-1.80 (4H, m), 1.80-1.96 (1H, m), 2.83 (1H, d, J = 12.8Hz), 2.9-3.85 (4H, m), 3.9-4.0 (1H, m), 6.55 (2H, s), 7.09 (1H, s), 7.13 (1H, dd, J = 2.1, 8.9Hz), 7.56 (1H, d, J = 8.9Hz), 7.89 (1H, d, J = 0.6Hz).	Fumarate
768		1H-NMR (DMSO-d6) δppm : 0.85-1.1 (2H, m), 1.2-1.35 (7H, m), 1.4-1.8 (4H, m), 1.85-2.05 (1H, m), 2.78 (1H, d, J = 11.8Hz), 2.85-4.5 (5H, m), 6.5 (1H, s), 6.58 (1H, d, J = 8.6Hz), 7.0-7.4 (3H, m), 7.99 (1H, d, J = 2.2Hz).	1/2 Fumarate

[0369]
Table 84

absolute configuration

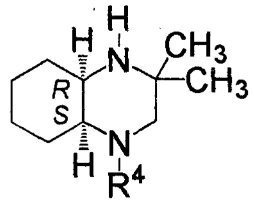


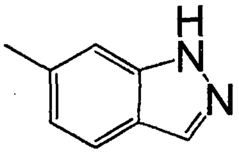
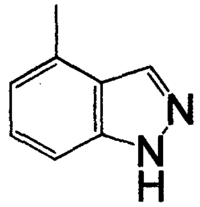
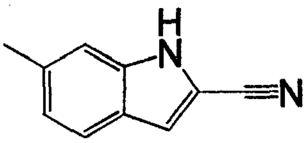
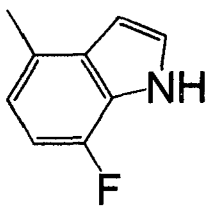
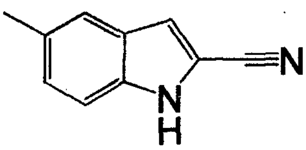
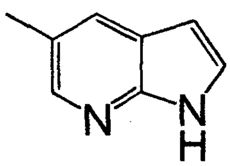
Example.	R^4	NMR	Salt
769		1H-NMR (CDCl3) δppm : 1.11-1.18 (20H, m), 1.22 (3H, s), 1.26-1.36 (4H, m), 1.37-1.49 (2H, m), 1.64-1.87 (7H, m), 2.82 (1H, d, J = 11.8Hz), 3.02 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.6-3.7 (1H, m), 6.82 (1H, s), 6.86 (1H, dd, J = 2.0, 8.9Hz), 7.54 (1H, d, J = 8.8Hz), 8.04 (1H, d, J = 0.8Hz).	-

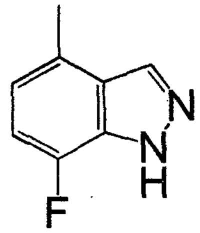
770		1H-NMR (CDCl3) δppm : 1.11-1.19 (19H, m), 1.21 (3H, s), 1.23-1.31 (2H, m), 1.35 (3H, s), 1.37-1.46 (2H, m), 1.62-1.85 (6H, m), 1.95-2.04 (1H, m), 3.03 (1H, d, J = 11.9Hz), 3.09 (1H, d, J = 12.0Hz), 3.55-3.65 (1H, m), 3.8-3.9 (1H, m), 6.41 (1H, d, J = 7.5Hz), 7.05 (1H, d, J = 8.4Hz), 7.16 (1H, dd, J = 7.6, 8.3Hz), 8.26 (1H, d, J = 0.8Hz).	-
771		1H-NMR (CDCl3) δppm : 1.17-1.23 (21H, m), 1.25-1.33 (5H, m), 1.33-1.50 (3H, m), 1.62-1.90 (4H, m), 1.93-2.05 (3H, m), 2.82 (1H, d, J = 11.8Hz), 3.00 (1H, d, J = 11.8Hz), 3.45-3.50 (1H, m), 3.55-3.65 (1H, m), 6.88-6.95 (2H, m), 7.28 (1H, s), 7.41-7.48 (1H, m).	-
772		1H-NMR (CDCl3) δppm : 0.93-1.17 (21H, m), 1.19 (3H, s), 1.23-1.44 (5H, m), 1.58-1.78 (6H, m), 1.78-1.93 (1H, m), 2.67 (1H, d, J = 11.2Hz), 3.09 (1H, d, J = 11.2Hz), 3.5-3.6 (1H, m), 3.6-3.7 (1H, m), 6.39 (1H, dd, J = 3.4, 8.3Hz), 6.65 (1H, dd, J = 3.2, 3.2Hz), 6.72 (1H, d, J = 8.2, 12.7Hz), 7.25 (1H, d, J = 3.2Hz).	-
773		1H-NMR (CDCl3) δppm : 1.12-1.29 (27H, m), 1.30-1.48 (2H, m), 1.62-1.82 (4H, m), 1.93-2.07 (3H, m), 2.78 (1H, d, J = 11.6Hz), 2.93 (1H, d, J = 11.6Hz), 3.45-3.55 (1H, m), 3.6-3.7 (1H, m), 6.92 (1H, d, J = 2.4Hz), 7.07 (1H, dd, J = 2.5, 9.4Hz), 7.24 (1H, s), 7.46 (1H ,d, J = 9.4Hz).	-
774		1H-NMR (CDCl3) δppm : 1.09-1.16 (19H, m), 1.20 (3H, s), 1.23-1.32 (5H, m), 1.33-1.48 (2H, m), 1.61-1.90 (7H, m), 2.81-2.91 (2H, m), 3.49-3.55 (1H, m), 3.55-3.63 (1H, m), 6.40 (1H, d, J = 3.4Hz), 7.21 (1H, d, J = 3.4Hz), 7.31 (1H, d, J = 2.8Hz), 8.06 (1H, d, J = 2.7Hz).	-
775		1H-NMR (CDCl3) δppm : 1.07-1.17 (19H, m), 1.21 (3H, s), 1.23-1.35 (5H, m), 1.37-1.49 (2H, m), 1.63-1.90 (6H, m), 1.96-2.09 (1H, m), 3.05 (1H, d, J = 12.6Hz), 3.38 (1H, d, J = 12.5Hz), 3.48-3.54 (1H, m), 3.94-4.02 (1H, m), 6.33 (1H, d, J = 5.6Hz), 6.54 (1H, d, J = 3.6Hz), 7.10 (1H, d, J = 3.6Hz), 7.98 (1H, d, J = 5.5Hz).	-
776		1H-NMR (CDCl3) δppm : 1.1-1.18 (19H, m), 1.18-1.22 (4H, m), 1.34 (3H, s), 1.36-1.44 (2H, m), 1.61-1.84 (7H, m), 1.86-1.98 (1H, m), 2.81 (1H, d, J = 11.4Hz), 3.07 (1H, d, J = 11.4Hz), 3.6-3.65 (1H, m), 3.65-3.75 (1H, m), 6.30 (1H, dd, J = 3.0, 8.2Hz), 6.86 (1H, dd, J = 8.2, 12.0Hz), 8.24 (1H, d, J = 3.1Hz).	-

[0370]
Table 85

absolute configuration

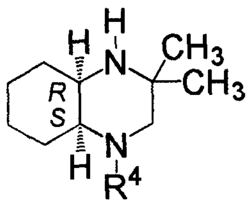


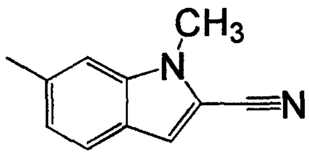
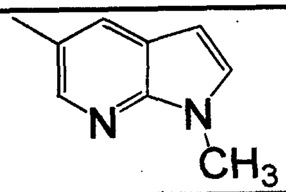
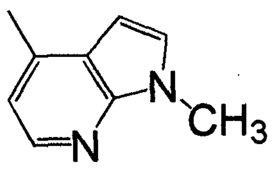
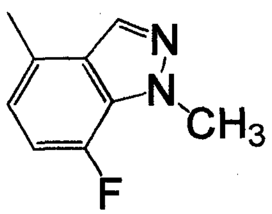
Example.	R^4	NMR	Salt
777		1H-NMR (CDCl3) δppm : 1.07 (1H, br), 1.16-1.33 (8H, m), 1.35-1.50 (2H, m), 1.64-1.88 (4H, m), 2.81 (1H, d, J = 11.8Hz), 3.05 (1H, d, J = 11.8Hz), 3.46-3.53 (1H, m), 3.68-3.79 (1H, m), 6.71 (1H, s), 6.92 (1H, d, J = 2.0, 9.0Hz), 7.5-7.6 (1H, m), 7.89 (1H, d, J = 0.9Hz), 9.7 (1H, br).	-
778		1H-NMR (CDCl3) δppm : 0.94-1.24 (6H, m), 1.33 (3H, s), 1.37-1.47 (2H, m), 1.63-1.80 (3H, m), 1.88-2.02 (1H, m), 3.02 (1H, d, J = 11.8Hz), 3.09 (1H, d, J = 11.9Hz), 3.62-3.68 (1H, m), 3.83-3.92 (1H, m), 6.43 (1H, d, J = 7.6Hz), 6.97 (1H, d, J = 8.3Hz), 7.23 (1H, dd, J = 7.7, 8.1Hz), 8.10 (1H, d, J = 0.9Hz), 9.96 (1H, br).	-
779		1H-NMR (CDCl3) δppm : 0.95 (1H, br), 1.15-1.35 (8H, m), 1.35-1.52 (2H, m), 1.52-1.90 (4H, m), 2.81 (1H, d, J = 11.9Hz), 3.03 (1H, d, J = 11.8Hz), 3.45-3.55 (1H, m), 3.65-3.8 (1H, m), 6.66 (1H, s), 6.95 (1H, dd, J = 2.1, 9.0Hz), 7.06 (1H, dd, J = 0.8, 2.0Hz), 7.46 (1H, d, J = 9.0Hz), 8.23 (1H, bs).	-
780		1H-NMR (CDCl3) δppm : 0.95-1.11 (3H, m), 1.20 (3H, s), 1.28-1.44 (5H, m), 1.59-1.79 (3H, m), 1.79-1.93 (1H, m), 2.70 (1H, d, J = 11.3Hz), 3.08 (1H, d, J = 11.3Hz), 3.6-3.7 (2H, m), 6.35 (1H, dd, J = 3.8, 8.3Hz), 6.61 (1H, dd, J = 3.2, 5.6Hz), 6.76 (1H, dd, J = 8.3, 10.7Hz), 7.17 (1H, dd, J = 2.8, 2.8Hz), 8.39 (1H, br).	-
781		1H-NMR (CDCl3) δppm : 1.01 (1H, br), 1.10-1.26 (5H, m), 1.28 (3H, s), 1.31-1.48 (2H, m), 1.61-1.83 (4H, m), 2.81 (1H, d, J = 11.5Hz), 2.89 (1H, d, J = 11.5Hz), 3.5-3.6 (1H, m), 3.6-3.7 (1H, m), 6.95 (1H, d, J = 2.1Hz), 7.04 (1H, dd, J = 0.8, 2.0Hz), 7.17 (1H, dd, J = 2.3, 9.1Hz), 7.28 (1H, d, J = 9.1Hz), 8.68 (1H, br).	-
782		1H-NMR (DMSO-d6) δppm : 1.00-1.37 (9H, m), 1.47-1.9 (5H, m), 2.90 (2H, s), 2.95-4.35 (4H, m), 6.27 (1H, dd, J = 1.9, 3.3Hz), 6.49 (1H, s), 7.34 (1H, dd, J = 2.9, 2.9Hz), 7.40 (1H, d, J = 2.5Hz), 8.04 (1H, d, J = 2.6Hz), 11.30 (1H, s).	1/2 Fumarate

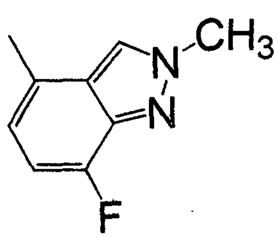
783		1H-NMR (CDCl3) δppm : 0.81-1.37 (8H, m), 1.37-1.51 (3H, m), 1.65-1.83 (3H, m), 1.98-2.13 (1H, m), 3.09 (1H, d, J = 12.6Hz), 3.4-3.5 (1H, m), 3.5-3.55 (1H, m), 4.0-4.1 (1H, m), 6.36 (1H, d, J = 5.7Hz), 6.50 (1H, d, J = 3.6Hz), 7.1-7.2 (1H, m), 8.0-8.1 (1H, m), 9.7-10.6 (1H, m).	-
784		1H-NMR (CDCl3) δppm : 1.02-1.17 (2H, m), 1.22 (3H, s), 1.34 (3H, s), 1.36-1.45 (2H, m), 1.62-1.80 (3H, m), 1.83-1.96 (1H, m), 2.84 (1H, d, J = 11.5Hz), 3.05 (1H, d, J = 11.5Hz), 3.65-3.7 (1H, m), 3.7-3.8 (1H, m), 6.28 (1H, dd, J = 3.3, 8.3Hz), 6.91 (1H, dd, J = 8.2, 10.4Hz), 8.12 (1H, d, J = 3.4Hz), 10.38 (1H, br).	-

[0371]
Table 86

absolute configuration

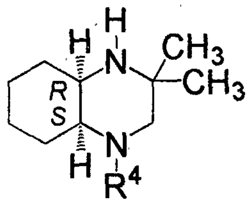


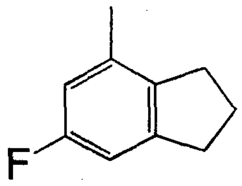
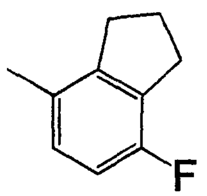
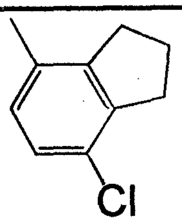
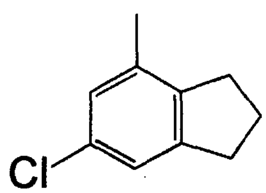
Ex. No.	R^4	NMR	Salt
785		1H-NMR (CDCl3) δppm : 1.15-1.32 (9H, m), 1.33-1.50 (2H, m), 1.64-1.88 (4H, m), 2.82 (1H, d, J = 11.7Hz), 3.03 (1H, d, J = 11.7Hz), 3.46-3.54 (1H, m), 3.71-3.79 (1H, m), 3.80 (3H, s), 6.51 (1H, d, J = 1.7Hz), 6.96 (1H, dd, J = 2.1, 9.0Hz), 7.02 (1H, s), 7.46 (1H, d, J = 9.0Hz).	-
786		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.25-1.4 (7H, m), 1.45-1.9 (5H, m), 2.94 (2H, s), 3.36 (3H, br), 3.66 (1H, br), 3.7-3.8 (4H, m), 6.29 (1H, d, J = 3.3Hz), 6.54 (2H, s), 7.39 (1H, d, J = 3.3Hz), 7.43 (1H, d, J = 2.2Hz), 8.10 (1H, d, J = 2.5Hz).	Fumarate
787		1H-NMR (DMSO-d6) δppm : 1.15-1.4 (9H, m), 1.5-1.8 (4H, m), 2.0-2.15 (1H, m), 3.09 (1H, d, J = 12.9Hz), 3.43 (1H, d, J = 12.4Hz), 3.55-3.65 (1H, m), 3.73 (3H, s), 4.05-4.15 (1H, m), 6.41 (1H, d, J = 5.6Hz), 6.49 (1H, d, J = 3.6Hz), 6.55 (2H, s), 7.26 (1H, d, J = 3.6Hz), 7.93 (1H, d, J = 5.6Hz).	Fumarate
788		1H-NMR (DMSO-d6) δppm : 0.97-1.13 (2H, m), 1.33-1.44 (1H, m), 1.51 (3H, s), 1.53 (3H, s), 1.58-1.67 (1H, m), 1.67-1.96 (3H, m), 1.96-2.07 (1H, m), 3.00 (1H, d, J = 12.9Hz), 3.26 (1H, d, J = 13.0Hz), 3.85-4.0 (1H, m), 4.05-4.2 (4H, m), 6.40 (1H, dd, J = 3.0, 8.3Hz), 7.05 (1H, dd, J = 8.2, 11.8Hz), 8.0-8.2 (1H, m), 8.38 (1H ,d, J = 2.3Hz), 9.65-9.9 (1H, m).	Hydrochloride

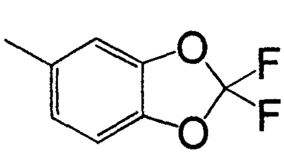
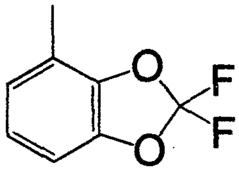
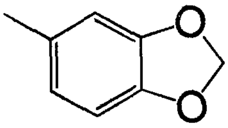
789		1H-NMR (DMSO-d6) δppm : 1.00-1.16 (2H, m), 1.34-1.44 (1H, m), 1.50 (3H, s), 1.53 (3H, s), 1.58-1.96 (4H, m), 1.98-2.09 (1H, m), 2.98 (1H, d, J = 12.9Hz), 3.24 (1H, d, J = 13.0Hz), 3.85-3.95 (1H, m), 3.95-4.08 (1H, m), 4.17 (3H, s), 6.24 (1H, dd, J = 3.2, 8.0Hz), 6.85 (1H, dd, J = 8.0, 11.5Hz), 7.95-8.2 (1H, m), 8.74 (1H, d, J = 2.8Hz), 9.7-10.0 (1H, m).	Hydrochloride

[0372]
Table 87

absolute configuration

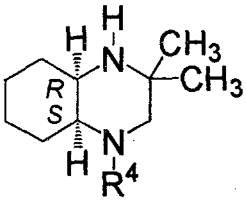


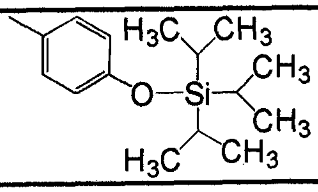
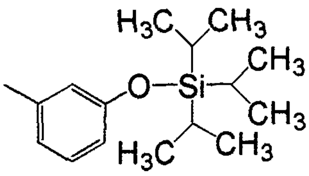
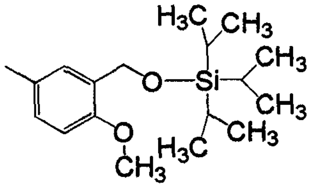
Exam ple	R^4	NMR	Salt
790		1H-NMR (DMSO-d6) δppm : 1.01-1.25 (2H, m), 1.32-1.42 (1H, m), 1.46 (3H, s), 1.48 (3H, s), 1.58-2.03 (6H, m), 2.05-2.18 (1H, m), 2.70-2.93 (5H, m), 3.24 (1H, d, J = 12.9Hz), 3.45-3.57 (1H, m), 3.81-3.93 (1H, m), 6.53 (1H, d, J = 11.4Hz), 6.70 (1H, d, J = 8.4Hz), 8.02 (1H, br), 9.72 (1H, br).	Hydrochloride
791		1H-NMR (DMSO-d6) δppm : 0.90-1.21 (2H, m), 1.28-1.41 (1H, m), 1.48 (6H, s), 1.57-1.67 (1H, m), 1.67-2.06 (5H, m), 2.08-2.21 (1H, m), 2.70 (1H, d, J = 12.4Hz), 2.78-3.00 (4H, m), 3.22-3.42 (2H, m), 3.77-3.92 (1H, m), 6.74 (1H, dd, J = 4.3, 8.6Hz), 6.88 (1H, dd, J = 8.6, 8.6Hz), 8.01 (1H, br), 9.73 (1H, br).	Hydrochloride
792		1H-NMR (CDCl3) δppm : 0.75-1.15 (3H, m), 1.17 (3H, s), 1.27 (3H, s), 1.3-1.45 (2H, m), 1.45-1.75 (3H, m), 1.75-1.95 (1H, m), 1.95-2.1 (1H, m), 2.1-2.25 (1H, m), 2.52 (1H, d, J = 11.2Hz), 2.85-3.05 (5H, m), 3.1-3.2 (1H, m), 3.45-3.55 (1H, m), 6.58 (1H, d, J = 8.4Hz), 7.03 (1H, d, J = 8.4Hz).	-
793		1H-NMR (DMSO-d6) δppm : 1.11-1.24 (1H, m), 1.34-1.42 (1H, m), 1.45 (3H, s), 1.47 (3H, s), 1.59-2.03 (6H, m), 2.05-2.17 (1H, m), 2.7-2.95 (5H, m), 3.27 (1H, d, J = 12.9Hz), 3.38-3.55 (1H, m), 3.79-3.95 (1H, m), 4.28-4.11 (1H, m), 6.72 (1H, d, J = 1.5Hz), 6.94 (1H, s), 7.9-8.1 (1H, m), 9.6-9.8 (1H, m).	Hydrochloride

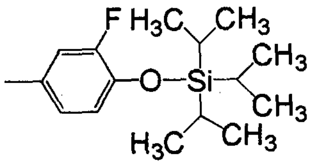
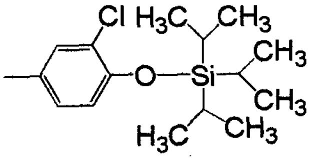
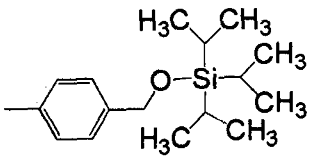
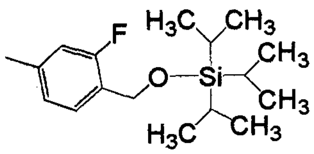
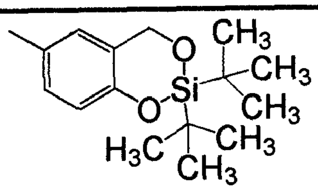
794		1H-NMR (DMSO-d6) δppm : 1.20-1.48 (6H, m), 1.52 (3H, s), 1.62-1.93 (4H, m), 1.96-2.12 (1H, m), 2.97 (1H, d, J = 13.4Hz), 3.29 (1H, d, J = 13.4Hz), 3.7-3.85 (1H, m), 3.9-4.05 (1H, m), 6.70 (1H, dd, J = 2.4, 8.9Hz), 7.12 (1H, d, J = 2.4Hz), 7.23 (1H, d, J = 8.9Hz), 8.18 (1H, br), 9.94 (1H, br).	Hydrochloride
795		1H-NMR (DMSO-d6) δppm : 1.1-1.25 (9H, m), 1.25-1.35 (1H, m), 1.45-1.75 (4H, m), 1.9-2.05 (1H, m), 2.94 (1H, d, J = 12.2Hz), 3.07 (1H, d, J = 12.3Hz), 3.11-3.62 (3H, m), 3.63-3.71 (1H, m), 6.57 (2H, s), 6.72 (1H, d, J = 8.0Hz), 6.75-6.81 (1H, m), 7.04 (1H, dd, J = 8.3, 8.3Hz).	Fumarate
796		1H-NMR (CDCl3) δppm : 0.65-1.3 (9H, m), 1.3-1.95 (6H, m), 2.69 (1H, d, J = 11.5Hz), 2.79 (1H, d, J = 11.6Hz), 3.4-3.55 (2H, m), 5.84-5.90 (2H, m), 6.25 (1H, dd, J = 11.6Hz), 6.51 (1H, d, J = 2.4Hz), 6.69 (1H, d, J = 8.5Hz).	-

[0373]
Table 88

absolute configuration



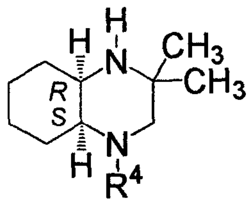
Example.	R^4	NMR	Salt
797		1H-NMR (CDCl3) δppm : 1.01-1.13 (19H, m), 1.14-1.28 (11H, m), 1.31-1.46 (2H, m), 1.60-1.76 (4H, m), 2.67 (1H, d, J = 11.6Hz), 2.83 (1H, d, J = 11.5Hz), 3.4-3.55 (2H, m), 6.69-6.74 (2H, m), 6.74-6.80 (2H, m).	-
798		1H-NMR (CDCl3) δppm : 1.07-1.16 (19H, m), 1.16-1.33 (11H, m), 1.33-1.47 (2H, m), 1.62-1.80 (4H, m), 2.68 (1H, d, J = 12.0Hz), 2.97 (1H, d, J = 11.9Hz), 3.4-3.45 (1H, m), 3.55-3.6 (1H, m), 6.25-6.35 (1H, m), 6.37 (1H ,dd, J = 2.4, 7.8Hz), 6.43 (1H, dd, J = 1.9, 8.3Hz), 7.03 (1H, dd, J = 8.1, 8.1Hz).	-
799		1H-NMR (CDCl3) δppm : 1.07-1.14 (19H, m), 1.14-1.29 (11H, m), 1.29-1.47 (2H, m), 1.59-1.77 (4H, m), 2.70 (1H, d, J = 11.7Hz), 2.92 (1H, d, J = 11.7Hz), 3.4-3.5 (1H, m), 3.55-3.65 (1H, m), 3.75 (3H, s), 4.78-4.89 (2H, m), 6.65 (1H, dd, J = 3.1, 8.8Hz), 6.71 (1H, d, J = 8.8Hz), 7.22 (1H, d, J = 3.0Hz).	-

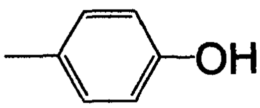
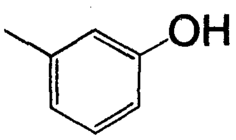
800		1H-NMR (CDCl3) δppm : 1.06-1.13 (18H, m), 1.14-1.29 (12H, m), 1.32-1.48 (2H, m), 1.48-1.76 (4H, m), 2.65 (1H, d, J = 11.8Hz), 2.83 (1H, d, J = 11.6Hz), 3.35-3.45 (1H, m), 3.45-3.55 (1H, m), 6.39-6.48 (1H, m), 6.55 (1H, dd, J = 2.9, 14.1Hz), 6.79 (1H, dd, J = 9.4, 9.4Hz).	-
801		1H-NMR (CDCl3) δppm : 1.11 (18H, d, J = 7.2Hz), 1.15-1.21 (4H, m), 1.21-1.33 (7H, m), 1.34-1.47 (2H, m), 1.47-1.77 (5H, m), 2.66 (1H, d, J = 11.5Hz), 2.81 (1H, d, J = 11.6Hz), 3.4-3.55 (2H, m), 6.61 (1H, d, J = 3.0, 8.9Hz), 6.78 (1H, d, J = 8.9Hz), 6.81 (1H, d, J = 3.0Hz).	-
802		1H-NMR (CDCl3) δppm : 1.04-1.11 (18H, m), 1.11-1.22 (7H, m), 1.23 (3H, s), 1.26-1.49 (4H, m), 1.64-1.79 (4H, m), 2.71 (1H, d, J = 11.9Hz), 3.01 (1H, d, J = 11.9Hz), 3.4-3.5 (1H, m), 3.6-3.7 (1H, m), 4.73 (2H, s), 6.79-6.86 (2H, m), 7.18-7.23 (2H, m).	-
803		1H-NMR (CDCl3) δppm : 1.03-1.12 (18H, m), 1.12-1.48 (13H, m), 1.50-1.82 (5H, m), 2.70 (1H, d, J = 12.0Hz), 2.99 (1H, d, J = 12.0Hz), 3.35-3.45 (1H, m), 3.55-3.65 (1H, m), 4.77 (2H, s), 6.47 (1H, dd, J = 2.4, 14.0Hz), 6.61 (1H, dd, J = 2.4, 8.6Hz), 7.32 (1H, dd, J = 8.8, 8.8Hz).	-
804		1H-NMR (CDCl3) δppm : 1.03 (18H, d, J = 2.4Hz), 1.13-1.27 (9H, m), 1.27-1.77 (6H, m), 2.67 (1H, d, J = 11.6Hz), 2.80 (1H, d, J = 11.5Hz), 3.4-3.55 (2H, m), 4.96 (2H, s), 6.42 (1H, d, J = 2.9Hz), 6.70 (1H, dd, J = 2.9, 8.8Hz), 6.80 (1H, d, J = 8.8Hz).	-

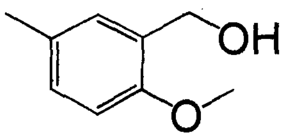
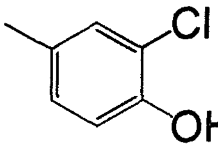
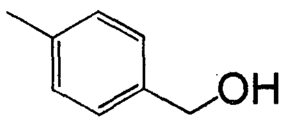
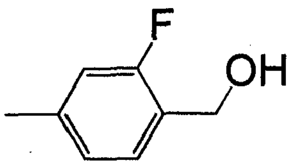
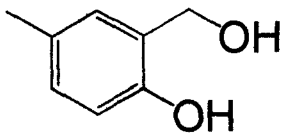
[0374]

Table 89

absolute configuration



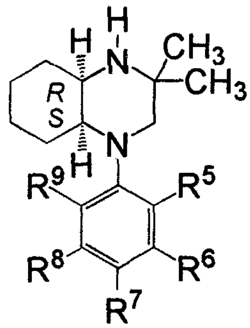
Example.	R^4	NMR	Salt
805		1H-NMR (CDCl3) δppm : 1.00-1.48 (11H, m), 1.54-1.87 (4H, m), 2.70 (1H, d, J = 10.4Hz), 2.81 (1H, d, J = 11.5Hz), 3.3-3.65 (2H, m), 6.75 (4H, bs).	-
806		1H-NMR (CDCl3) δppm : 1.14-1.49 (11H, m), 1.60-1.83 (4H, m), 2.71 (1H, d, J = 12.1Hz), 3.03 (1H, d, J = 12.0Hz), 3.37-3.44 (1H, m), 3.56-3.67 (1H, m), 6.16-6.23 (1H, m), 6.33 (1H, dd, J = 2.3, 2.3Hz), 6.43 (1H, dd, J = 2.1, 8.4Hz), 7.06 (1H, dd, J = 8.1, 8.1Hz).	-

807		1H-NMR (DMSO-d6) δppm : 1.0-1.25 (2H, m), 1.25-1.4 (7H, m), 1.4-1.85 (5H, m), 2.78 (1H, d, J = 12.3Hz), 2.90 (1H, d, J = 12.1Hz), 2.95-4.1 (9H, m), 4.44 (2H, s), 6.50 (2H, s), 6.71 (1H, dd, J = 2.8, 8.8Hz), 6.79 (1H, d, J = 8.9Hz), 6.97 (1H, d, J = 2.7Hz).	Fumarate
808		1H-NMR (CDCl3) δppm : 1.10-1.27 (9H, m), 1.31-1.48 (1H, m), 1.49-2.01 (6H, m), 2.68 (1H, d, J = 11.5Hz), 2.78 (1H, d, J = 11.5Hz), 3.4-3.55 (2H, m), 6.73 (1H, dd, J = 2.8, 8.9Hz), 6.78 (1H, d, J = 2.8Hz), 6.89 (1H, d, J = 8.9Hz).	-
809		1H-NMR (CDCl3) δppm : 1.17-1.61 (12H, m), 1.62-1.83 (4H, m), 2.72 (1H, d, J = 11.9Hz), 3.03 (1H, d, J = 11.9Hz), 3.4-3.45 (1H, m), 3.6-3.7 (1H, m), 4.56 (2H, s), 6.80-6.86 (2H, m), 7.20-7.25 (2H, m).	-
810		1H-NMR (CDCl3) δppm : 0.91 (1H, br), 1.17-1.48 (10H, m), 1.56 (1H, br), 1.62-1.84 (4H, m), 2.71 (1H, d, J = 12.1Hz), 3.02 (1H, d, J = 12.0H), 3.35-3.45 (1H, m), 3.55-3.65 (1H, m), 4.62 (2H, d, J = 3.2Hz), 6.51 (1H, dd, J = 2.5, 14.0Hz), 6.59 (1H, dd, J = 2.5, 8.5Hz), 7.19 (1H, dd, J = 8.8, 8.8Hz).	-
811		1H-NMR (CDCl3) δppm : 0.92-1.02 (1H, m), 1.02-1.13 (4H, m), 1.15 (3H, s), 1.21-1.30 (1H, m), 1.35-1.65 (5H, m), 1.69-1.83 (1H, m), 2.60 (1H, d, J =11.3Hz), 2.69 (1H, d, J = 11.3Hz), 3.32 (1H, br), 3.41-3.49 (1H, m), 4.43 (2H, d, J = 4.6Hz), 4.88 (1H, t, J = 5.4Hz), 6.55 (1H, dd, J = 2.8, 8.7Hz), 6.60 (1H, d, J = 8.6Hz), 6.83 (1H, d, J = 2.7Hz), 8.55 (1H, s).	-

[0375]

Table 90

absolute configuration



Example	R^5	R^6	R^7	R^8	R^9	NMR	Salt

812	-H	-H	-OCH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.3 (2H, m), 1.35-1.45 (4H, m), 1.52 (3H, s), 1.6-1.9 (4H, m), 1.95-2.1 (1H, m), 2.93 (1H, d, J = 13.1Hz), 3.11 (1H, d, J = 13.0Hz), 3.68 (3H, s), 3.7-3.9 (2H, m), 4.35-5.35 (1H, m), 6.75-6.85 (2H, m), 6.85-6.95 (2H, m), 8.09 (1H, br), 9.90 (1H, br).	2 Hydrochloride
813	-CH3	-Cl	-H	-H	-H	1H-NMR (CDCl3) δppm : 0.93-1.09 (3H, m), 1.16 (3H, s), 1.23-1.34 (4H, m), 1.34-1.44 (2H, m), 1.44-1.75 (2H, m), 1.79-1.92 (1H, m), 2.37 (3H, s), 2.41 (1H, d, J = 11.0Hz), 2.83-2.91 (1H, m), 3.10 (1H, d, J = 11.1Hz), 3.51-3.57 (1H, m), 6.79 (1H, dd, J = 2.1, 7.1Hz), 6.99-7.08 (2H, m).	-
814	-CH3	-H	-H	-H	-H	1H-NMR (CDCl3) δppm : 0.78-1.13 (3H, m), 1.16 (3H, s), 1.28-1.42 (5H, m), 1.54-1.76 (4H, m), 1.81-1.95 (1H, m), 2.34 (3H, s), 2.43 (1H, d, J = 11.1Hz), 2.87-2.96 (1H, m), 3.13 (1H, d, J = 11.1Hz), 3.47-3.58 (1H, m), 6.88 (1H, dd, J = 1.0, 7.9Hz), 6.91-6.97 (1H, m), 7.07-7.15 (1H, m), 7.17 (1H, dd, J = 0.7, 7.5Hz).	Hydrochloride
815	-H	-H	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.16-1.33 (2H, m), 1.34-1.48 (4H, m), 1.49-1.56 (3H, m), 1.61-1.93 (4H, m), 1.97-2.11 (1H, m), 2.19 (3H, s), 2.91 (1H, d, J = 13.2Hz), 3.19-3.32 (1H, m), 3.68-3.80 (1H, m), 3.87-3.99 (1H, m), 4.35-6.4 (1H, m), 6.83 (2H, d, J = 8.4Hz), 7.02 (2H, d, J = 8.1Hz), 8.0-8.35 (1H, m), 9.8-10.2 (1H, m).	2 Hydrochloride

816	-CH3	-CH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.96-1.18 (2H, m), 1.28-1.45 (1H, m), 1.49 (3H, s), 1.52 (3H, s), 1.56-1.67 (1H, m), 1.67-1.83 (2H, m), 1.83-2.10 (2H, m), 2.20 (3H, s), 2.22 (3H, s), 2.59 (1H, d, J = 12.6Hz), 3.0-3.15 (1H, m), 3.25-3.4 (1H, m), 3.8-3.95 (1H, m), 6.82 (1H, d, J = 7.8Hz), 6.90 (1H, d, J = 7.4Hz), 7.03 (1H, dd, J = 7.7, 7.7Hz), 8.02 (1H, br), 9.65-9.9 (1H, m).	Hydrochloride
817	-H	-CH3	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.21-1.49 (6H, m), 1.53 (3H, s), 1.63-1.96 (4H, m), 1.96-2.16 (1H, m), 2.26 (3H, s), 2.93 (1H, d, J = 13.5Hz), 3.36 (1H, d, J = 13.4Hz), 3.65-3.8 (1H, m), 3.95-4.05 (1H, m), 4.43 (1H, br), 6.79 (1H, dd, J = 2.9, 8.8Hz), 6.93 (1H, d, J = 2.8Hz), 7.20 (1H, d, J = 8.8Hz), 8.1-8.4 (1H, m), 9.8-10.2 (1H, m).	Hydrochloride
818	-H	-CH3	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.16-1.35 (2H, m), 1.35-1.48 (4H, m), 1.52 (3H, s), 1.62-1.95 (4H, m), 1.95-2.14 (1H, m), 2.18 (3H, d, J = 1.6Hz), 2.93 (1H, d, J = 13.2Hz), 3.21 (1H, d, J = 13.1Hz), 3.7-3.8 (1H, m), 3.85-4.0 (1H, m), 4.05-5.8 (1H, m), 6.71-6.81 (1H, m), 6.85 (1H, dd, J = 2.9, 6.6Hz), 6.97 (1H, dd, J = 9.1, 9.1Hz), 8.05-8.3 (1H, m), 9.85-10.2 (1H, m).	Hydrochloride

819	-CH3	-F	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.20 (2H, m), 1.3-1.43 (1H, m), 1.50 (3H, s), 1.51 (3H, s), 1.56-1.69 (1H, m), 1.69-1.87 (2H, m), 1.87-2.08 (2H, m), 2.20 (3H, d, J = 2.3Hz), 2.67 (1H, d, J = 12.6Hz), 3.15-3.25 (1H, m), 3.36 (1H, d, J = 12.8Hz), 3.8-4.0 (1H, m), 6.83 (1H, d, J = 8.0Hz), 6.89 (1H, dd, J = 8.8, 8.8Hz), 7.16 (1H, dd, J = 7.9, 15.2Hz), 8.08 (1H, br), 9.7-10.0 (1H, m).	Hydrochloride
820	-H	-F	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.14-1.41 (9H, m), 1.50-1.90 (5H, m), 2.09 (3H, d, J =0.8Hz), 2.78 (1H, d, J = 12.8Hz), 3.19 (1H, d, J = 12.8Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 6.52 (2H, s), 6.60-6.71 (2H, m), 7.05 (1H, dd, J = 8.9, 8.9Hz).	Fumarate
821	-H	-Cl	-CH3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.15-1.40 (9H, m), 1.5-1.9 (5H, m), 2.19 (3H, d, J =0.8Hz), 2.78 (1H, d, J = 12.7Hz), 3.18 (1H, d, J = 12.7Hz), 3.5-3.6 (1H, m), 3.8-3.9 (1H, m), 6.54 (2H, s), 6.80 (1H, dd, J = 2.6, 8.5Hz), 6.90 (1H, d, J = 2.6Hz), 7.13 (1H, d, J = 8.5Hz).	Fumarate
822	-H	-Cl	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.12-1.21 (4H, m), 1.22 (3H, s), 1.24-1.37 (2H, m), 1.45-1.77 (4H, m), 1.77-1.92 (1H, m), 2.72 (1H, d, J = 12.5Hz), 3.18 (1H, d, J = 12.4Hz), 3.40 (1H, brs), 3.75-3.85 (1H, m), 6.50 (1H, s), 6.67 (1H, dd, J = 1.6, 7.7Hz), 6.8-6.9 (2H, m), 7.16 (1H, dd, J = 8.1, 8.1Hz).	1/2 Fumarate

823	-CH3	-OCH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.0-1.17 (2H, m), 1.29-1.43 (1H, m), 1.48 (3H, s), 1.51 (3H, s), 1.56-2.05 (5H, m), 2.12 (3H, s), 2.62 (1H, d, J = 12.6Hz), 3.05-3.2 (1H, m), 3.3-3.4 (1H, m), 3.76 (3H, s), 3.85-3.95 (1H, m), 6.61 (1H, d, J = 7.9Hz), 6.72 (1H, d, J = 8.2Hz), 7.10 (1H, dd, J = 8.1, 8.1Hz), 7.99 (1H, br), 9.5-9.8 (1H, m).	Hydrochloride
824	-H	-H	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.21-1.36 (2H, m), 1.36-1.46 (4H, m), 1.52 (3H, s), 1.63-1.92 (4H, m), 1.93-2.09 (1H, m), 2.94 (1H, d, J = 13.4Hz), 3.33 (1H, d, J = 13.3Hz), 3.5-4.4 (2H, m), 6.84-7.26 (5H, m), 8.13 (1H, br), 9.84 (1H, br).	2 Hydrochloride
825	-H	-H	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.26-1.48 (6H, m), 1.50 (3H, s), 1.63-1.92 (4H, m), 1.92-2.06 (1H, m), 2.96 (1H, d, J = 13.6Hz), 3.44 (1H, d, J = 13.5Hz), 3.72-3.83 (1H, m), 3.98-4.09 (1H, m), 6.96-7.07 (2H, m), 7.15-7.27 (2H, m), 8.08 (1H, br), 9.67 (1H, br).	Hydrochloride
826	-H	-Cl	-CN	-H	-H	1H-NMR (DMSO-d6) δppm : 1.10 (3H, s), 1.15-1.25 (4H, m), 1.25-1.45 (2H, m), 1.45-1.75 (4H, m), 1.85-2.0 (1H, m), 2.75 (1H, d, J = 13.0Hz), 2.9-3.85 (4H, m), 3.85-3.95 (1H, m), 6.56 (1H, s), 6.94 (1H, dd, J = 2.5, 9.1Hz), 7.09 (1H, d, J = 2.4Hz), 7.59 (1H, d, J = 9.0Hz).	1/2 Fumarate
827	-H	-F	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.28-1.46 (6H, m), 1.51 (3H ,s), 1.63-2.10 (5H, m), 2.97 (1H, d, J = 13.8Hz), 3.54 (1H, d, J = 13.8Hz), 3.65-3.8 (1H, m), 4.0-4.15 (1H, m), 6.81 (1H, dd, J = 2.2, 9.2Hz), 7.05 (1H, dd, J = 2.9, 14.4Hz), 7.34 (1H, dd, J = 9.2, 9.2Hz), 8.22 (1H, br), 9.89 (1H, br).	Hydrochloride

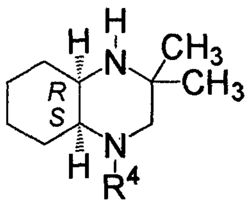
828	-H	-F	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.09-1.37 (9H, m), 1.44-1.73 (4H, m), 1.75-1.90 (1H, m), 2.66 (1H, d, J = 12.1Hz), 3.0-3.7 (4H, m), 3.7-3.8 (1H, m), 6.52 (1H, m), 6.67 (1H, d, J = 2.1, 9.3Hz), 6.80-7.22 (3H, m)	1/2 Fumarate
829	-H	-Cl	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.37 (9H, m), 1.43-1.59 (1H, m), 1.59-1.74 (3H, m), 1.75-1.90 (1H, m), 2.69 (1H, d, J = 12.3Hz), 2.8-4.2 (5H, m), 6.52 (1H, s), 6.82-7.25 (4H, m).	1/2 Fumarate
830	-H	-OCHF2	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.13-1.41 (9H, m), 1.46-1.93 (5H, m), 2.75 (1H, d, J = 12.5Hz), 2.8-4.4 (6H, m), 6.46 (1H, d, J = 8.1Hz), 6.54 (2H, s), 6.62 (1H, s), 6.76 (1H, dd, J = 8.4Hz), 7.0-7.4 (2H, m).	1/2 Fumarate
831	-H	-OCHF2	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.36 (9H, m), 1.44-1.59 (1H, m), 1.59-1.74 (3H, m), 1.74-1.87 (1H, m), 2.65-4.5 (6H, m), 6.52 (1H, s), 6.7-6.8 (2H, m), 7.0-7.4 (2H, m).	1/2 Fumarate
832	-H	-OCHF2	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.10-1.38 (9H, m), 1.44-1.74 (4H, m), 1.76-1.91 (1H, m), 2.69 (1H, d, J = 12.3Hz), 2.75-4.2 (5H, m), 6.53 (1H, s), 6.75-6.85 (2H, m), 7.05-7.45 (2H, m).	1/2 Fumarate
833	-H	-CN	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.06-1.23 (7H, m), 1.23-1.37 (2H, m), 1.43-1.74 (4H, m), 1.75-1.89 (1H, m), 2.69 (1H, d, J = 12.4Hz), 2.9-3.75 (4H, m), 3.75-3.85 (1H, m), 6.53 (1H, s), 7.00-7.41 (4H, m).	1/2 Fumarate
834	-H	-OCHF2	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.1-1.4 (9H, m), 1.44-1.76 (4H, m), 1.76-1.90 (1H, m), 2.69 (1H, d, J = 12.2Hz), 2.8-4.25 (5H, m), 6.52 (1H, s), 6.71-7.36 (5H, m).	1/2 Fumarate

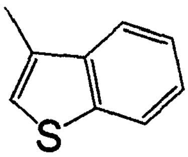
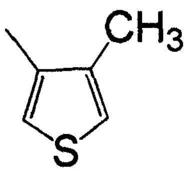
835	-H	-F	-OCHF2	-F	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.23 (7H, m), 1.24-1.40 (2H, m), 1.43-1.73 (4H, m), 1.76-1.91 (1H, m), 2.67 (1H, d, J = 12.5Hz), 2.8-4.2 (5H, m), 6.53 (1H, s), 6.67-6.77 (2H, m), 7.05 (1H, t, J = 72.9Hz).	1/2 Fumarate
836	-H	-H	-OCH2CHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.13-1.31 (2H, m), 1.32-1.47 (4H, m), 1.53 (3H, s), 1.61-1.90 (4H m), 1.97-2.12 (1H, m), 2.93 (1H, d, J = 13.1Hz), 3.15 (1H, d, J = 13.1Hz), 3.69-3.81 (1H, m), 3.83-3.93 (1H, m), 4.10-4.46 (3H, m), 6.12-6.53 (1H, m), 6.90 (4H, s), 8.0-8.25 (1H, m), 9.9-10.1 (1H, m).	2 Hydrochloride
837	-H	-F	-OCH2CHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.20-1.46 (6H, m), 1.51 (3H, s), 1.63-1.91 (4H m), 1.93-2.10 (1H, m), 2.91 (1H, d, J = 13.4Hz), 3.29 (1H, d, J = 13.2Hz), 3.67-3.80 (1H, m), 3.89-4.01 (1H, m), 4.20-4.35 (2H, m), 6.18-6.51 (1H, m), 6.68 (1H, dd, J = 1.8, 9.1Hz), 6.91 (1H, dd, J = 2.9, 14.7Hz), 7.10 (1H, dd, J = 9.5, 9.5Hz), 8.05-8.2 (1H, m), 9.75-9.95 (1H, m).	Hydrochloride
838	-H	-CH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.06-1.15 (1H, m), 1.15-1.38 (8H, m), 1.42-1.88 (5H, m), 2.17 (3H, s), 2.68 (1H, d, J = 11.9Hz), 3.04 (1H, d, J = 12.1Hz), 3.1-3.9 (4H, m), 6.50 (1H, s), 6.71 (1H, dd, J = 2.9, 8.9Hz), 6.75-7.16 (3H, m).	1/2 Fumarate
839	-H	-OCH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.10-1.39 (9H, m), 1.45-1.90 (5H, m), 2.72 (1H, d, J = 12.2Hz), 2.95-4.1 (8H, m), 6.40 (1H, dd, J = 2.8, 8.9Hz), 6.50 (1H, s), 6.57 (1H, d, J = 2.7Hz), 6.63-7.03 (2H, m).	1/2 Fumarate

840	-OCHF2	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.94-1.14 (1H, m), 1.14-1.17 (1H, m), 1.18 (3H, s), 1.26 (3H, s), 1.29-1.55 (3H, m), 1.59-1.73 (3H, m), 1.76-1.90 (1H, m), 2.49 (1H, d, J = 11.2Hz), 3.04 (1H, d, J = 11.2Hz), 3.5-3.6 (2H, m), 6.55 (1H, dd, J = 70.2, 81.4Hz), 6.91 (1H, dd, J = 1.4, 8.0Hz), 6.93-6.99 (1H, m), 7.07-7.18 (2H, m)	-

[0376]
Table 91

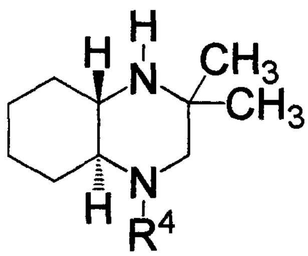
absolute configuration



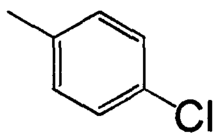
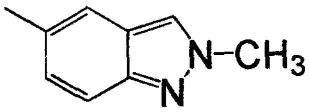
Example	R^4	NMR	Salt
841		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.35-1.45 (1H, m), 1.51 (3H, s), 1.56 (3H, s), 1.6-2.05 (5H, m), 2.87 (1H, d, J = 12.8Hz), 3.3-3.4 (1H, m), 3.65-3.75 (1H, m), 4.1-4.2 (1H, m), 7.05 (1H, s), 7.35-7.45 (2H, m), 7.9-8.1 (3H, m), 9.5-9.7 (1H, m).	Hydrochloride
842		1H-NMR (CDCl3) δppm : 0.89-1.18 (5H, m), 1.25-1.74 (9H, m), 1.74-1.86 (1H, m), 2.19 (3H, d, J = 0.9Hz), 2.52 (1H, d, J = 11.2Hz), 2.93 (1H, d, J = 11.2Hz), 3.03-3.10 (1H, m), 3.47-3.52 (1H, m), 6.35 (1H, d, J = 3.3Hz), 6.84-6.88 (1H, m).	-

[0377]
Table 92

relative configuration

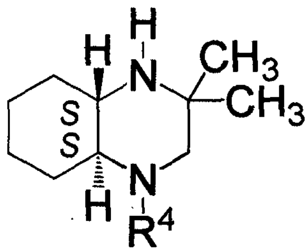


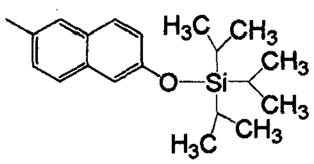
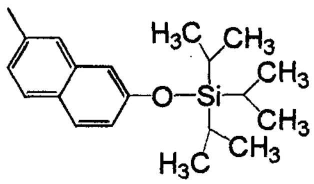
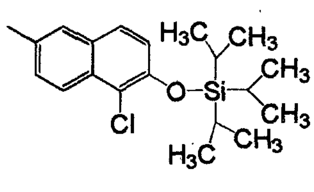
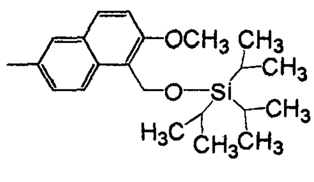
Example	R^4	NMR	Salt

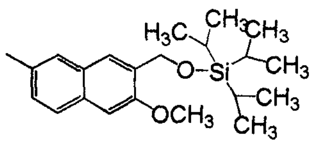
843		1H-NMR (CDCl3)δppm 1.13-1.24 (1H, m), 1.25-1.36 (2H, m), 1.60-1.83 (3H, m), 1.64 (3H, s), 1.74 (3H, s), 1.89-2.02 (1H, m), 2.32-2.37 (1H, m), 2.80 (1H, d, J = 12.5 Hz), 3.12-3.16 (1H, m), 3.22-3.29 (1H, m), 3.36 (1H, d, J = 12.5 Hz), 7.19-7.22 (2H, m), 7.29-7.33 (2H, m), 9.52 (1H, brs), 9.81 (1H, brs)	Hydrochloride
844		1H-NMR (DMSO-d6) δppm : 1.00-1.98 (13H, m), 1.98-2.28 (1H, br), 2.65-3.90 (4H, br), 4.18 (3H, s), 6.70-7.95 (3H, m), 8.22-8.60 (1H, br), 8.80-11.33 (3H, brm).	2 Hydrochloride

[0378]
Table 93

absolute configuration

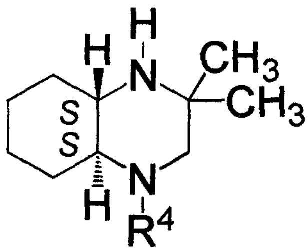


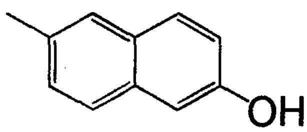
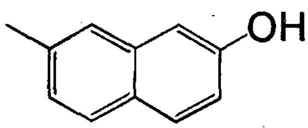
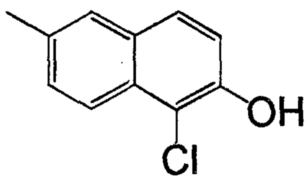
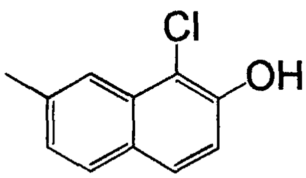
Example	R^4	NMR	Salt
845		1H-NMR (CDCl3) δppm : 1.03-1.17 (23H, m), 1.17-1.41 (6H, m), 1.43 (3H, s), 1.59-1.68 (1H, m), 1.68-1.80 (3H, m), 2.32-2.40 (1H, m), 2.68 (1H, d, J = 11.3 Hz), 2.78-2.85 (1H, m), 2.88 (1H, d, J = 11.3 Hz), 7.08 (1H, dd, J = 2.4, 8.8 Hz), 7.16 (1H, d, J = 2.4 Hz), 7.22 (1H, dd, J = 2.1, 8.7 Hz), 7.37 (1H, d, J = 1.8 Hz), 7.57-7.64 (2H, m).	-
846		1H-NMR (CDCl3) δppm : 0.82-1.17 (23H, m), 1.20-1.46 (9H, m), 1.60-1.70 (1H, m), 1.70-1.85 (3H, m), 2.35-2.45 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.77-2.86 (1H, m), 2.91 (1H, d, J = 11.3 Hz), 7.02 (1H, dd, J = 2.4, 8.8 Hz), 7.09-7.15 (2H, m), 7.27 (1H, d, J = 1.9 Hz), 7.60-7.68 (2H, m).	-
847		1H-NMR (CDCl3) δppm : 0.97-1.41 (29H, m), 1.43 (3H, s), 1.60-1.70 (1H, m), 1.70-1.80 (3H, m), 2.35-2.43 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.78-2.87 (1H, m), 2.89 (1H, d, J = 11.3 Hz), 7.11 (1H, d, J = 8.9 Hz), 7.34 (1H, dd, J = 2.1, 9.0 Hz), 7.37 (1H, d, J = 1.9 Hz), 7.53 (1H, d, J = 8.9 Hz), 8.10 (1H, d, J = 8.9 Hz).	-
848		1H-NMR (CDCl3) δppm :0.74-1.42 (29H, m), 1.44 (3H, s), 1.58-1.83 (4H, m), 2.35-2.43 (1H, m), 2.68 (1H, d, J = 11.3 Hz), 2.78-2.87 (1H, m), 2.91 (1H, d, J = 11.3 Hz), 3.91 (3H, s), 5.19-5.27 (2H, m), 7.21 (1H, d, J = 9.1 Hz), 7.29 (1H, d, J = 2.2, 9.1 Hz), 7.37 (1H, d, J = 2.1 Hz), 7.69 (1H, d, J = 9.0 Hz), 8.16 (1H, d, J = 9.1 Hz).	-

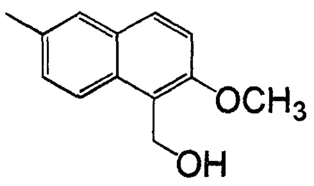
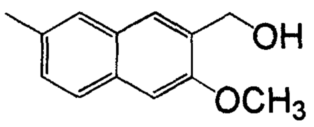
849		1H-NMR (CDCl3) δppm : 0.96-1.19 (23H, m), 1.19-1.42 (6H, m), 1.44 (3H, s), 1.57-1.78 (4H, m), 2.32-2.41 (1H, m), 2.71 (1H, d, J = 11.3 Hz), 2.77-2.86 (1H, m), 2.87 (1H, d, J = 11.3 Hz), 3.89 (3H, s), 4.94 (2H, d, J = 1.1 Hz), 7.02 (1H, s), 7.22 (1H, dd, J = 2.0, 8.6 Hz), 7.44 (1H, d, J = 1.8 Hz), 7.64 (1H, d, J = 8.6 Hz), 7.88 (1H, s).	-

[0379]
Table 94

absolute configuration

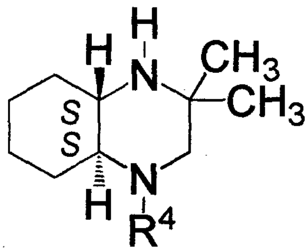


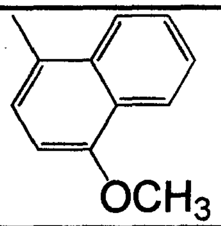
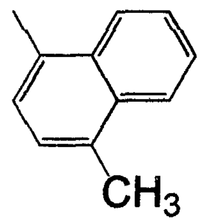
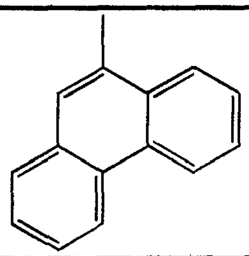
Example	R^4	NMR	Salt
850		1H-NMR (DMSO-d6) δppm : 0.88-1.03 (4H, m), 1.11-1.37 (6H, m), 1.45-1.68 (5H, m), 2.26-2.35 (1H, m), 2.58 (1H, d, J = 10.9 Hz), 2.62-2.70 (1H, m), 2.73 (1H, d, J = 10.9 Hz), 7.02 (1H, dd, J = 2.4, 8.7 Hz), 7.05 (1H, d, J = 2.4 Hz), 7.16 (1H, dd, J = 2.1, 8.7 Hz), 7.37 (1H, d, J = 1.8 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.67 (1H, d, J = 8.9 Hz), 9.57 (1H, brs).	-
851		1H-NMR (DMSO-d6) δppm : 0.88-1.02 (4H, m), 1.10-1.37 (6H, m), 1.44-1.74 (5H, m), 2.32-2.41 (1H, m), 2.60 (1H, d, J = 11.1 Hz), 2.63-2.72 (1H, m), 2.80 (1H, d, J = 11.1 Hz), 6.94 (1H, dd, J = 2.4, 8.8 Hz), 7.00 (1H, dd, J = 2.0, 8.8 Hz), 7.02 (1H, d, J = 2.4 Hz), 7.21 (1H, d, J = 1.8 Hz), 7.64 (2H, d, J = 8.7 Hz), 9.63 (1H, s).	-
852		1H-NMR (DMSO-d6) δppm : 0.90-1.08 (4H, m), 1.15-1.40 (6H, m), 1.51-1.73 (4H, m), 2.35-2.47 (1H, m), 2.65 (1H, d, J = 11.2 H), 2.70-2.85 (2H, m), 2.90-3.75 (1H, br), 7.23 (1H, d, J = 8.9 Hz), 7.34 (1H, dd, J = 2.1, 9.0 Hz), 7.46 (1H, d, J = 2.0 Hz), 7.70 (1H, d, J = 8.9 Hz), 7.92 (1H, d, J = 9.0 Hz), 9.05-11.25 (1H, br).	-
853		1H-NMR (DMSO-d6) δppm : 0.95-1.10 (4H, m), 1.17-1.40 (6H, m), 1.56-1.80 (4H, m), 2.49-2.60 (1H, m), 2.73-2.87 (2H, m), 2.92 (1H, d, J = 11.5 Hz), 3.18-3.46 (1H, br), 7.10-7.18 (2H, m), 7.50 (1H, d, J = 2.0 Hz), 7.67 (1H, d, J = 8.8 Hz), 7.75 (1H, d, J = 8.7 Hz), 9.95-10.75 (1H, br).	-

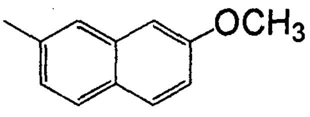
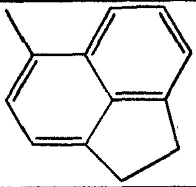
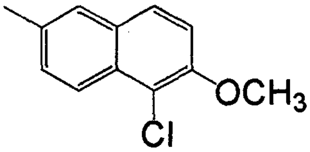
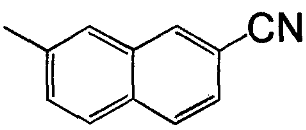
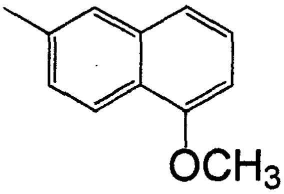
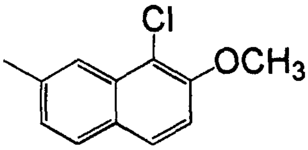
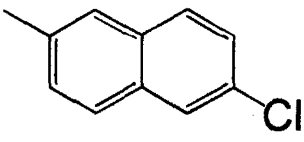
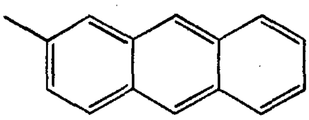
854		1H-NMR (DMSO-d6) δppm : 0.90-1.07 (4H, m), 1.13-1.37 (6H, m), 1.47-1.70 (5H, m), 2.30-2.40 (1H, m), 2.61 (1H, d, J = 11.0 Hz), 2.65-2.74 (1H, m), 2.77 (1H, d, J = 11.0 Hz), 3.88 (3H, s), 4.82 (1H, t, J = 5.1 Hz), 4.89 (2H, d, J = 5.1 Hz), 7.27 (1H, dd, J = 2.1, 9.1 Hz), 7.35 (1H, d, J = 9.1 Hz), 7.42 (1H, d, J = 2.1 Hz), 7.80 (1H, d, J = 9.1 Hz), 8.03 (1H, d, J = 9.1 Hz).	-
855		1H-NMR (DMSO-d6) δppm : 0.95-1.10 (1H, m), 1.10-1.50 (9H, m), 1.53-1.73 (3H, m), 1.77-1.87 (1H, m), 2.58-2.70 (1H, m), 2.85 (2H, s), 2.89-3.00 (1H, m), 3.87 (3H, s), 4,61 (2H, s), 6.46 (1H, s), 7.20 (1H, dd, J = 2.0, 8.7 Hz), 7.22 (1H, s), 7.46 (1H, d, J = 1.6 Hz), 7.73 (1H, d, J = 8.7 Hz), 7.79 (1H, s). (3H not found)	1/2 Fumarate

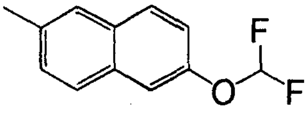
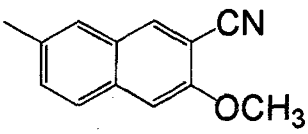
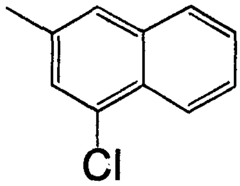
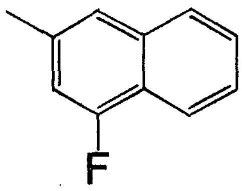
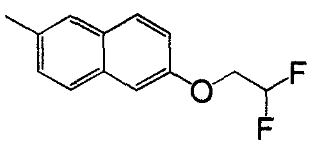
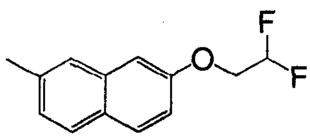
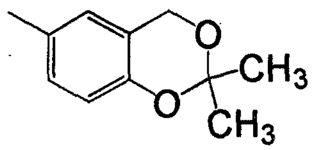
[0380]
Table 95

absolute configuration



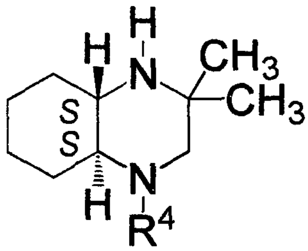
Example	R^4	NMR	Salt
856		1H-NMR (CDCl3) δppm : 0.91-1.05 (1H, m), 1.08 (3H, s), 1.12-1.62 (9H, m), 1.68-1.78 (2H, m), 2.42-2.50 (1H, m), 2.62 (1H, d, J = 11.3 Hz), 2.75 (1H, d, J = 11.3 Hz), 2.91-3.00 (1H,m), 3.98 (3H, s), 6.78 (1H, d, J = 8.1 Hz), 7.20 (1H, d, J = 8.1 Hz), 7.43-7.54 (2H, m), 8.21-8.26 (1H, m), 8.50-8.54 (1H, m).	-
857		1H-NMR (DMSO-d6) δppm : 0.93-1.22 (2H, m), 1.26-1.44 (5H, m), 1.44-1.54 (1H,m), 1.56-1.77 (5H, m), 1.99-2.08 (1H, m), 2.62 (3H, s), 2.76 (1H, d, J = 12.4 Hz), 2.98-3.08 (2H, m), 3.33-3.50 (1H, m), 7.28 (1H, d, J = 7.5 Hz), 7.38 (1H, d, J = 7.5 Hz), 7.54-7.61 (2H, m), 7.97-8.03 (1H, m), 8.43-8.52 (1H, m), 9.10-9.25 (1H, br), 9.62-9.77 (1H, br).	Hydrochloride
858		1H-NMR (DMSO-d6) δppm : 1.00-1.30 (2H, m), 1.30-1.45 (4H, m), 1.45-1.62 (2H, m), 1.62-1.81 (5H, m), 2.00-2.13 (1H, m), 2.91 (1H, d, J = 12.6 Hz), 3.05-3.20 (2H, m), 3.41-3.57 (1H, m), 3.75-4.30 (1H, br), 7.61-7.77 (5H, m), 7.98-8.05 (1H, m), 8.54-8.61 (1H, m), 8.77-8.88 (2H, m), 9.19-9.35 (1H, m), 9.669.81 (1H, m).	2 Hydrochloride

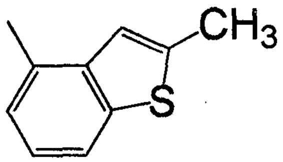
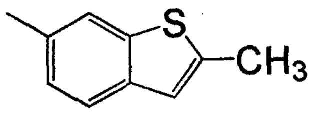
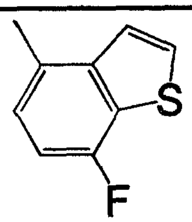
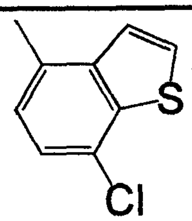
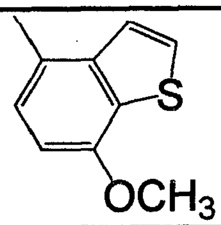
859		1H-NMR (DMSO-d6) δppm : 0.90-1.45 (6H, m), 1.53-1.80 (7H, m), 1.97-2.12 (1H, m), 2.83-3.40 (4H, m), 3.86 (3H, s), 7.05-7.25 (2H, m), 7.32 (1H, d, J = 2.4 Hz), 7.42-7.68 (1H, br), 7.75-7.87 (2H, m), 8.25-9.55 (2H, br), 9.55-10.02 (1H, br).	2 Hydrochloride
860		1H-NMR (DMSO-d6) δppm : 0.85-1.00 (1H, m), 1.10-1.70 (12H, m), 1.75-1.86 (1H, m), 2.65-2.80 (3H, m), 2.99-3.10 (1H, m), 3.25-3.43 (4H, m), 6.46 (1H, s), 7.20-7.34 (3H, m), 7.45 (1H, dd, J = 7.0, 8.2 Hz), 7.88 (1H, d, J = 8.2 Hz), 8.07-9.40 (1H, br).	1/2 Fumarate
861		1H-NMR (DMSO-d6) δppm : 1.04-1.43 (6H, m), 1.54-1.80 (7H, m), 1.97-2.10 (1H, m), 2.86-3.07 (2H, m), 3.07-3.30 (2H, m), 3.98 (3H, s), 7.43 (1H, d, J = 9.1 Hz), 7.55 (1H, d, J = 9.2 Hz), 7.66 (1H, brs), 7.95 (1H, d, J = 9.1 Hz), 8.04 (1H, d, J = 9.1 Hz), 8.11-8.95 (1H, br), 9.08-9.35 (1H, m), 9.60-9.86 (1H, m).	2 Hydrochloride
862		1H-NMR (CDCl3) δppm : 0.84-0.97 (1H, br), 1.03-1.17 (4H, m), 1.22-1.46 (6H, m), 1.61-1.74 (1H, m), 1.74-1.88 (3H, m), 2.45-2.55 (1H, m), 2.76 (1H, d, J = 11.5 Hz), 2.82-2.90 (1H, m), 2.98 (1H, d, J = 11.5 Hz), 7.38-7.43 (2H, m), 7.50 (1H, dd, J = 1.6, 8.4 Hz), 7.77-7.86 (2H, m), 8.12 (1H, s).	-
863		1H-NMR (DMSO-d6) δppm : 1.05-1.43 (6H, m), 1.54-1.80 (7H, m), 1.98-2.10 (1H, m), 2.90-3.32 (4H, m), 3.95 (3H, s), 6.91 (1H, d, J = 7.2 Hz), 7.24-7.36 (1H, br), 7.38-7.49 (2H, m), 7.50-7.68 (1H, br), 8.11 (1H, d, J = 8.9 Hz), 9.00-9.45 (1H, br), 9.55-9.98 (1H, br), 10.50-12.10 (1H, br).	2 Hydrochloride
864		1H-NMR (DMSO-d6) δppm : 1.10-1.47 (6H, m), 1.54-1.80 (7H, m), 2.01-2.14 (1H, m), 2.95-3.37 (4H,m), 4.00 (3H, s), 7.30 (1H, d, J = 8.3 Hz), 7.51 (1H, d, J = 9.1 Hz), 7.73 (1H, brs), 7.95 (2H, d, J = 9.1 Hz), 9.39 (1H, brs), 9.90 (1H, brs), 11.80 (1H, brs).	2 Hydrochloride
865		1H-NMR (DMSO-d6) δppm : 1.03-1.44 (6H, m), 1.53-1.79 (7H, m), 1.97-2.09 (1H, m), 2,92-3.06 (2H, m), 3.06-3.16 (1H, m), 3.16-3.30 (1H, m), 6.24-7.14 (1H, m), 7.36 (1H, dd, J = 2.1, 8.8 Hz), 7.49 (1H, dd, J = 2.1, 8.8 Hz), 7.64 (1H, brs), 7.88 (1H, d, J = 8.8 Hz), 7.94 (1H, d, J = 8.8 Hz), 8.00 (1H, d, J = 2.1 Hz), 9.10-9.39 (1H, brs), 9.63-9.87 (1H, brs).	2 Hydrochloride
866		1H-NMR (CDCl3) δppm : 0.75-1.19 (5H, m), 1.24-1.43 (3H, m), 1.45 (3H, s), 1.64-1.73 (1H, m), 1.73-1.82 (2H, m), 1.90-2.00 (1H, m), 2.45-2.54 (1H, m), 2.72 (1H, d, J = 11.5 Hz), 2.83-2.92 (1H, m), 3.02 (1H, d, J = 11.5 Hz), 7.26 (1H, dd, J = 2.1, 9.0 Hz), 7.37-7.47 (2H, m), 7.50 (1H, brs), 7.91 (1H, d, J = 9.0 Hz), 7.94-7.99 (2H, m), 8.30 (1H, s), 8.34 (1H, s).	-

867		1H-NMR (DMSO-d6) δppm : 1.15-1.45 (6H, m), 1.53-1.80 (7H, m), 1.97-2.10 (1H, m), 2.94-3.09 (2H, m), 3.09-3.18 (1H, m), 3.18-3.31 (1H, m), 4.00-4.62 (1H, br), 7.16 (0.25H, s), 7.32-7.40 (2.5H, m), 7.53 (0.25H, s), 7.61-7.72 (2H, m), 7.90 (1H, d, J = 8.8 Hz), 7.98 (1H, d, J = 9.0 Hz).9.10-9.45 (1H, br), 9.61-9.90 (1H, br).	2 Hydrochloride
868		1H-NMR (DMSO-d6) δppm : 1.05-1.47 (6H, m), 1.55-1.80 (7H, m), 1.99-2.10 (1H, m), 2.41-3.05 (2H, m), 3.05-3.16 (1H, m), 3.16-3.30 (1H, m), 3.75-4.60 (4H, m), 7.45 (1H, dd, J = 2.0, 8.8 Hz), 7.57 (1H, s), 7.67 (1H, s), 7.90 (1H, d, J = 8.9 Hz), 8.48 (1H, s), 9.10-9.40 (1H, br), 9.61-9.90 (1H, br).	3 Hydrochloride
869		1H-NMR (DMSO-d6) δppm : 1.05-1.45 (6H, m), 1.54-1.80 (7H, m), 1.96-2.07 (1H, m), 2.93-3.04 (1H, m), 3.04-3.16 (2H, m), 3.18-3.32 1H, m), 4.23-4.51 (1H, br), 7.46-7.50 (1H, m), 7.58-7.67 (3H, m), 7.97-8.04 (1H, m), 8.08-8.14 (1H, m), 9.03-9.25 (1H, br), 9.51-9.75 (1H, br).	2 Hydrochloride
870		1H-NMR (DMSO-d6) δppm : 1.08-1.45 (6H, m), 1.52-1.80 (7H, m), 1.99-2.10 (1H, m), 2.96-3.17 (3H, m), 3.17-3.30 (1H, m), 4.45-4.55 (1H, br), 7.16 (1H, dd, J = 1.7, 12.3 Hz), 7.48 (1H, s), 7.51-7.64 (2H, m), 7.98 (2H, d, J = 8.2 Hz), 9.15-9.36 (1H, br), 9.70-9.90 (1H, br).	2 Hydrochloride
871		1H-NMR (CDCl3) δppm : 1.00-1.15 (4H, m), 1.15-1.52 (7H, m), 1.57-1.68 (1H, m), 1.68-1.79 (3H, m), 2.34-2.42 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.77-2.86 (1H, m), 2.88 (1H, d, J = 11.3 Hz), 4.28 (2H, dt, J = 4.1, 13.1 Hz), 6.15 (1H, tt, J = 4.1, 55.2 Hz), 7.10 (1H, d, J = 2.5 Hz), 7.14 (1H, dd, J = 2.6, 8.9 Hz), 7.27 (1H, dd, J = 2.1, 8.7 Hz), 7.41 (1H, d, J = 2.0 Hz), 7.63-7.72 (2H, m).	-
872		1H-NMR (CDCl3) δppm : 1.00-1.15 (4H, m), 1.20-1.70 (8H, m), 1.70-1.88 (3H, m), 2.39-2.48 (1H, m), 2.70 (1H, d, J = 11.4 Hz), 2.80-2.89 (1H, m), 2.93 (1H, d, J = 11.4 Hz), 4.29 (2H, dt, J = 4.2, 13.1 Hz), 6.15 (1H, tt, J = 4.1, 55.2 Hz), 7.03-7.11 (2H, m), 7.16 (1H, dd, J = 2.1, 8.7 Hz), 7.33 (1H, d, J = 2.0 Hz), 7.65-7.74 (2H, m).	-
873		1H-NMR (DMSO-d6) δppm : 0.90-1.06 (1H, m), 1.06-1.64 (17H, m), 1.64-1.74 (1H, m), 1.80-1.83 (1H, m), 2.50-2.62 (1H, m), 2.71 (1H, d, J = 11.9 Hz), 2.86 (1H, d, J = 11.9 Hz), 2.92-3.02 (1H, m), 4.78 (2H, s), 6.48 (2H, s), 6.73 (1H, d, J = 8.6 Hz), 6.83 (1H, d, J = 2.2 Hz), 6.91 (1H, dd, J = 2.3, 8.6 Hz). 9.37-11.61 (1H, br).	Fumarate

[0381]
Table 96

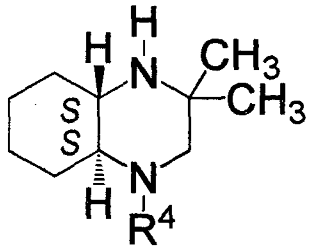
absolute configuration

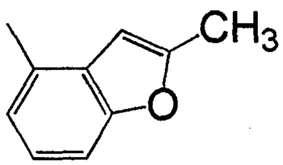
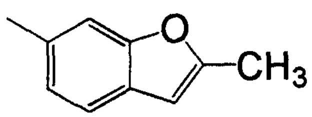
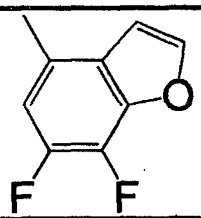
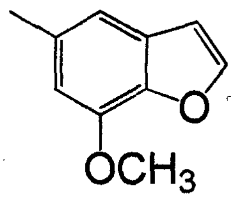
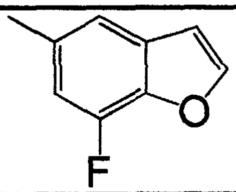
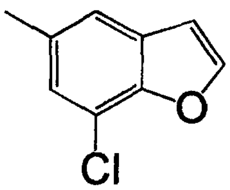
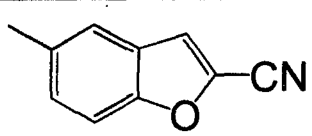


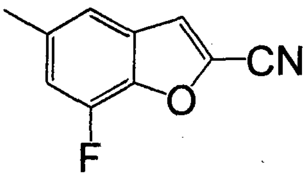
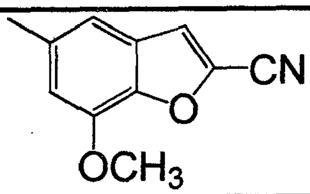
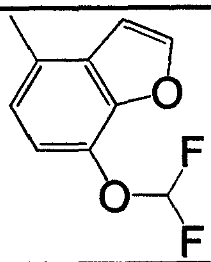
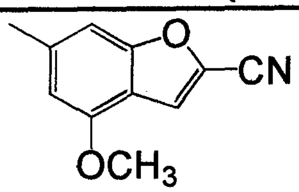
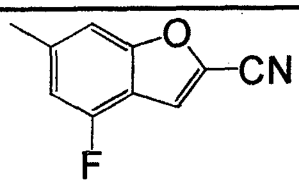
Example	R^4	NMR	Salt
874		1H-NMR (DMSO-d6) δppm : 0.96-1.10 (1H, m), 1.10-1.25 (1H, m), 1.26-1.41 (4H, m), 1.47-1.78 (7H, m), 1.94-2.05 (1H, m), 2.56 (3H, s), 2.84 (1H, d, J = 12.4 Hz), 2.90-3.02 (2H, m), 3.23-3.35 (1H, m), 7.15 (1H, d, J = 7.6 Hz), 7.22-7.33 (2H, m), 7.68 (1H, d, J = 7.9 Hz), 8.91-9.09 (1H, brm), 9.54-9.70 (1H, brm).	Hydrochloride
875		1H-NMR (DMSO-d6) δ ppm (80℃): 1.03-1.46 (6H, m), 1.51-1.78 (7H, m), 2.01-2.11 (1H, m), 2.53 (3H, s), 2.88 (1H, d, J = 12.4 Hz), 2.97-3.08 (1H, m), 3.10-3.25 (2H, m), 7.05 (1H, s), 7.13 (1H, d, J = 8.4 Hz), 7.60-7.68 (2H, m), 9.20 (1H, brs), 9.70 (1H, brs).	Hydrochloride
876		1H-NMR (DMSO-d6) δppm : 0.95-1.40 (6H, m), 1.40-1.78 (7H, m), 1.95-2.05 (1H, m), 2.85 (1H, d, J = 12.5 Hz), 2.90-3.00 (1H, m), 3.03 (1H, d, J = 12.5 Hz), 3.28-3.44 (1H, m), 7.26 (2H, d, J = 7.0 Hz), 7.64 (1H, dd, J = 4.0, 5.2 Hz), 7.86 (1H, d, J = 5.4 Hz), 9.07 (1H, brs), 9.64 (1H, brs).	Hydrochloride
877		1H-NMR (DMSO-d6) δppm : 0.97-1.45 (6H, m), 1.45-1.80 (7H, m), 1.94-2.09 (1H, m), 2.88 (1H, d, J = 12.5 Hz), 2.93-3.05 (2H, m), 3.26-3.45 (1H, m), 7.28 (1H, d, J = 8.2 Hz), 7.50 (1H, d, J = 8.2 Hz), 7.64 (1H, d, J = 5.4 Hz), 7.88 (1H, d, J = 5.4 Hz), 9.06 (1H, brs), 9.59 (1H, brs).	Hydrochloride
878		1H-NMR (DMSO-d6) δppm : 0.90-1.79 (13H, m), 1.35-2.06 (1H, m), 2.75-3.05 (4H, m), 3.94 (3H, s), 6.94 (1H, d, J = 7.9 Hz), 7.18 (1H, d, J = 7.9 Hz), 7.55 (1H, d, J = 5.4 Hz), 7.71 (1H, d, J = 5.4 Hz), 8.80 (1H, brs), 9.31 (1H, brs).	Hydrochloride

[0382]
Table 97

absolute configuration

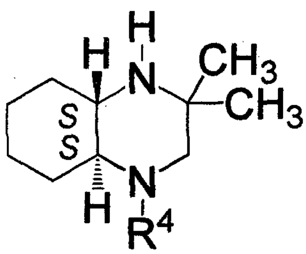


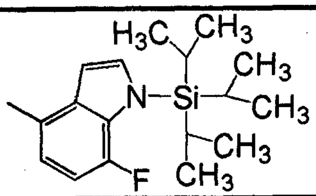
Example	R^4	NMR	Salt
879		1H-NMR (DMSO-d6) δppm : 0.97-1.10 (1H, m), 1.10-1.41 (5H, m), 1.50-1.78 (7H, m), 1.94-2.05 (1H, m), 2.44 (3H, s), 2.75-3.09 (3H, m), 3.09-3.30 (1H, m), 6.58 (1H, brs), 6.98 (1H, d, J = 7.2 Hz), 7.19 (1H, t, J = 7.8 Hz), 7.31 (1H, d, J = 7.8 Hz), 9.00 (1H, brs), 9.59 (1H, brs).	Hydrochloride
880		1H-NMR (DMSO-d6) δppm : 1.00-1.43 (6H, m), 1.44-1.78 (7H, m), 1.90-2.07 (1H, m), 2.42 (3H, d, J = 0.9 Hz), 2.75-3.30 (4H, m), 3.48-4.50 (1H, br), 6.54 (1H, s), 7.04 (1H, brs), 7.30 (1H, brs), 7.48 (1H, d, J = 8.6 Hz), 9.11 (1H, brs), 9.70 (1H, brs).	2 Hydrochloride
881		1H-NMR (DMSO-d6) δppm : 0.99-1.15 (1H, m), 1.15-1.42 (5H, m), 1.47-1.77 (7H, m), 1.93-2.05 (1H, m), 2.75-3.18 (3H, m), 3.27 (1H, brs), 7.08 (1H, brs), 7.22 (1H, brs), 8.14 (1H, s), 9.00 (1H, brs), 9.67 (1H, brs).	Hydrochloride
882		1H-NMR (CDCl3) δppm : 0.75-1.14 (5H, m), 1.14-1.40 (3H, m), 1.42 (3H, s), 1.56-1.68 (2H, m), 1.68-1.79 (2H, m), 2.20-2.30 (1H, m), 2.65 (1H, d, J = 11.1 Hz), 2.74-2.85 (2H, m), 3.99 (3H, s), 6.61 (1H, d, J = 1.7 Hz), 6.70 (1H, d, J = 2.1 Hz), 6.95 (1H, d, J = 1.7 Hz), 7.59 (1H, d, J = 2.1 Hz).	-
883		1H-NMR (DMSO-d6) δppm : 1.01-1.42 (6H, m), 1.49-1.68 (6H, m), 1.68-1.78 (1H, m), 1.95-2.05 (1H, m), 2.80-2.95 (2H, m), 3.01-3.10 (1H, m), 3.10-3.24 (1H, m), 6.50-7.80 (4H, m), 8.10 (1H, d, J = 2.1 Hz), 9.13 (1H, brs), 9.71 (1H, brs).	2 Hydrochloride
884		1H-NMR (DMSO-d6) δppm : 1.00-1.41 (6H, m), 1.45-1.67 (6H, m), 1.67-1.77 (1H,m), 1.92-2.03 (1H, m), 2.80-2.94 (2H, m), 3.01-3.10 (1H, m), 3.10-3.25 (1H, m), 3.65-4.00 (1H, br), 7.05 (1H, d, J = 2.1 Hz), 7.18 (1H, d, J = 1.7 Hz), 7.43 (1H, d, J = 1.7 Hz), 8.12 (1H, d, J = 2.1 Hz), 9.10 (1H, brs), 9.60 (1H, brs).	2 Hydrochloride
885		1H-NMR (DMSO-d6) δppm : 0.92-1.07 (1H, m), 1.07-1.88 (13H, m), 2.60-3.01 (4H, m), 3.10-4.92 (2H, br), 6.45 (3H, s), 7.35 (1H, dd, J = 2.1, 8.9 Hz), 7.54 (1H, d, J = 2.0 Hz), 7.68 (1H, d, J = 8.9 Hz), 8.04 (1H, d, J = 0.8 Hz).	Fumarate

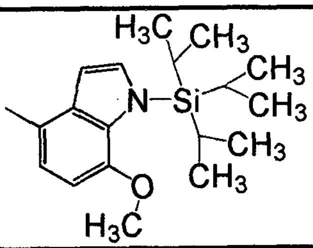
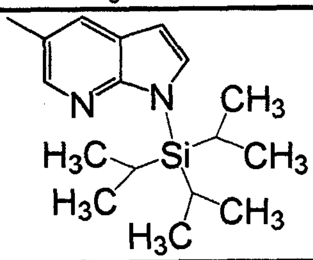
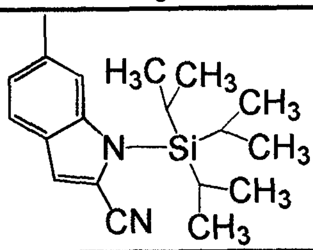
886		1H-NMR (CDCl3) δppm : 0.96-1.12 (4H, m), 1.16-1.44 (6H, m), 1.55-1.80 (5H, m), 2.20-2.30 (1H, m), 2.62 (1H, d, J = 11.2 Hz), 2.75-2.85 (2H, m), 7.04 (1H, dd, J = 1.8, 11.8 Hz), 7.15 (1H, d, J = 1.8 Hz), 7.42 (1H, d, J = 2.5 Hz).	-
887		1H-NMR (CDCl3) δppm : 0.96-1.15 (4H, m), 1.15-1.39 (3H, m), 1.42 (3H, s), 1.55-1.69 (3H, m), 1.69-1.80 (2H, m), 2.23-2.34 (1H, m), 2.65 (1H, d, J = 11.1 Hz), 2.75-2.85 (2H, m), 4.01 (3H, s), 6.76 (1H, d, J = 1.7 Hz), 6.97 (1H, d, J = 1.7 Hz), 7.38 (1H, s).	-
888		1H-NMR (DMSO-d6) δppm : 0.99-1.42 (6H, m), 1.50-1.78 (7H, m), 1.72-2.05 (1H, m), 2.75-3.11 (3H, m), 3.16-3.40 (1H, br), 4.95-6.80 (1H, br), 6.95-7.11 (2H, m), 7.12-7.21 (1.25H, m), 7.33 (0.5H, s), 7.51 (0.25H, s), 8.08 (1H, brs), 9.05 (1H, brs), 9.64 (1H, brs).	2 Hydrochloride
889		1H-NMR (CDCl3) δppm : 0.99-1.12 (4H, m), 1.20-1.43 (7H, m), 1.62-1.83 (4H, m), 2.34-2.42 (1H, m), 2.70 (1H, d, J = 11.5 Hz), 2.76-2.85 (1H, m), 2.91 (1H, d, J = 11.5 Hz), 3.92 (3H, s), 6.45 (1H, d, J = 1.4 Hz), 6.80-6.83 (1H, m), 7.45 (1H, d, J = 0.9 Hz).	-
890		1H-NMR (CDCl3) δppm : 1.01-1.15 (4H, m), 1.20-1.45 (7H, m), 1.67-1.90 (4H, m), 2.44-2.53 (1H, m), 2.77-2.87 (2H, m), 2.98 (1H, d, J = 11.9 Hz), 6.74 (1H, dd, J = 1.6, 11.5 Hz), 6.90-6.94 (1H, m), 7.43 (1H, d, J = 0.9 Hz).	-

[0383]
Table 98

absolute configuration

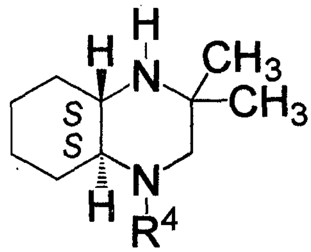


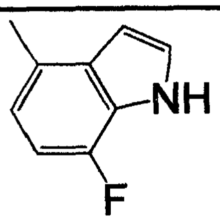
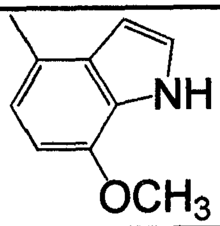
Example	R^4	NMR	Salt
891		1H-NMR (CDCl3) δppm : 0.83-1.43 (26H, m), 1.52 (3H, s), 1.55-1.91 (7H, m), 2.34-2.61 (2H, m), 2.80-3.00 (2H, m), 6.69-6.84 (3H, m), 7.24 (1H, d, J = 3.2 Hz).	-

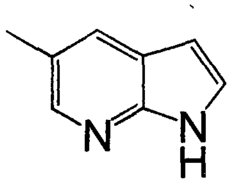
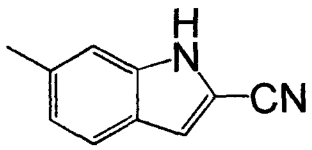
892		1H-NMR (CDCl3) δppm : 0.76-1.40 (26H, m), 1.52 (3H, s), 1.56-1.95 (7H, m), 2.36-2.64 (2H, m), 2.80-3.01 (2H, m), 3.88 (3H, s), 6.54 (1H, d, J = 8.1 Hz), 6.69 (1H, d, J = 3.1 Hz), 6.73 (1H, d, J = 8.1 Hz), 7.24 (1H, d, J = 3.1 Hz).	-
893		1H-NMR (CDCl3) δppm : 0.98-1.17 (23H, m), 1.17-1.40 (3H, m), 1.42 (3H, s), 1.55-1.66 (2H, m), 1.66-1.76 (2H, m), 1.84 (3H, quint, J = 7.5 Hz), 2.27-2.38 (1H, m), 2.72(1H, d, J = 11.2 Hz), 2.77-2.85 (2H, m), 6.47 (1H, d, J = 3.4 Hz), 7.27 (1H, d, J = 3.4 Hz), 7.61 (1H, d, J = 2.4 Hz), 8.06 (1H, d, J = 2.4 Hz).	-
894		1H-NMR (CDCl3) δppm : 0.90-1.40 (26H, m), 1.43 (3H, s), 1.59-1.80 (4H, m), 1.95-2.06 (3H, m), 2.30-2.39 (1H, m), 2.58 (1H, d, J = 11.3 Hz), 2.79-2.89 (2H, m), 6.98 (1H, d, J = 1.5, 8.5 Hz), 7.31 (1H, s), 7.34 (1H, d, J = 0.6 Hz), 7.52 (1H, d, J = 8.5 Hz).	-

[0384]
Table 99

absolute configuration

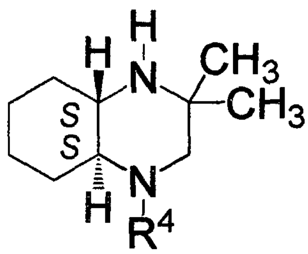


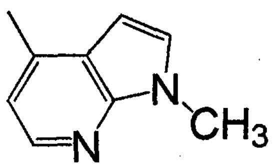
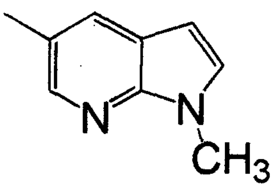
Example	R^4	NMR	Salt
895		1H-NMR (DMSO-d6) δppm : 0.77-0.92 (1H, m), 0.95 (3H, s), 1.08-1.35 (3H, m), 1.40 (3H, s), 1.47-1.58 (2H, m), 1.58-1.82 (3H, m), 2.27-2.48 (2H, m), 2.60-2.85 (2H, m), 6.47 (1H, brs), 6.58-6.65 (1H, m), 6.81 (1H, dd, J = 8.3, 10.9 Hz), 7.30 (1H, t, J = 2.6 Hz), 11.47 (1H, s).	-
896		1H-NMR (CDCl3) δppm : 0.77-0.99 (4H, m), 1.08-1.90 (11H, m), 2.21-2.46 (2H, m), 2.58-2.85 (2H, m), 3.86 (3H, s), 6.38 (1H, brs), 6.47-6.63 (2H, m), 7.13 (1H, t, J = 2.6 Hz), 11.07 (1H, s).	-

897		1H-NMR (DMSO-d6) δppm : 0.91-1.08 (1H,m), 1.08-1.60 (11H, m), 1.61-1.72(1H, m), 1.78-1.90 (1H, m), 2.60-2.71 (1H, m), 2.75 (1H, d, J = 11.7 Hz), 2.90-3.05 (2H, m), 6.39 (1H, dd, J = 1.8, 3.4 Hz), 6.47 (1H, s), 7.42-7.49 (1H,m), 7.73 (1H, d, J = 2.0 Hz), 7.98 (1H, d, J = 2.2 Hz), 8.18-10.97 (2H, br), 11.59 (1H, s).	1/2 Fumarate
898		1H-NMR (DMSO-d6) δppm : 0.81-1.02 (4H, m), 1.10-1.36 (6H, n), 1.36-2.05 (5H, m), 2.25-2.35 (1H, m), 2.57 (1H, d, J = 11.0 Hz), 2.62-2.70 (1H, m), 2.75 (1H, d, J = 11.0 Hz), 6.91 (1H, dd, J = 1.7, 8.6 Hz), 7.03 (1H, s), 7.27 (1H, d, J = 0.6 Hz), 7.55 (1H, d, J = 8.6 Hz) 11.93-12.33 (1H, br).	-

[0385]
Table 100

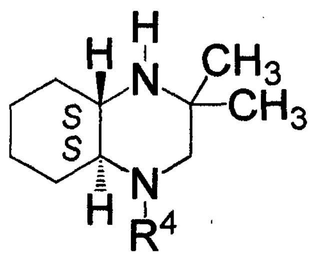
absolute configuration

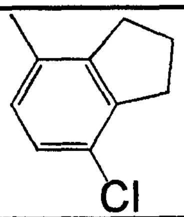
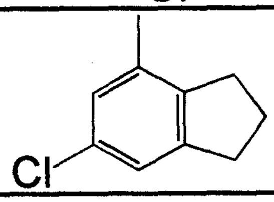
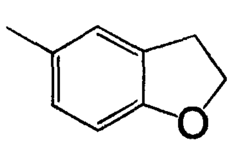
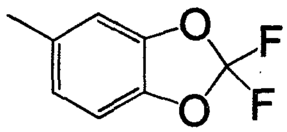


Example	R^4	NMR	Salt
899		1H-NMR (CDCl3) δppm : 0.75-1.13 (5H, m), 1.25-1.45 (3H, m), 1.48 (3H, s), 1.62-1.85 (3H, m), 2.08-2.19 (1H, m), 2.66-2.78 (2H, m), 2.85-2.94 (1H, m), 3.27 (1H, d, J = 11.9 Hz), 3.85 (3H, s), 6.46 (1H, d, J = 3.5 Hz), 6.63 (1H, d, J = 5.4 Hz), 7.06 (1H, d, J = 3.5 Hz), 8.20 (1H, d, J = 5.4 Hz).	-
900		1H-NMR (DMSO-d6) δppm : 0.91-1.62 (11H, m), 1.62-1.84 (2H, m), 1.82-1.95 (1H, m), 2.65-2.83 (2H, m), 2.99-3.10 (2H,m), 3.79 (3H, s), 6.41 (1H, d, J = 3.4 Hz), 6.48 (2H, s), 7.50 (1H, d, J = 3.4 Hz), 7.76 (1H, d, J = 2.2 Hz), 8.04 (1H, d, J = 2.2 Hz), 8.35-11.00 (2H, br)	Fumarate

[0386]
Table 101

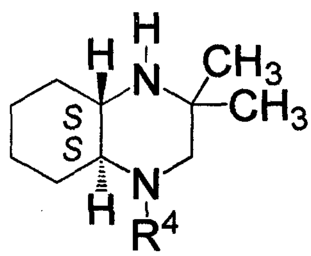
absolute configuration

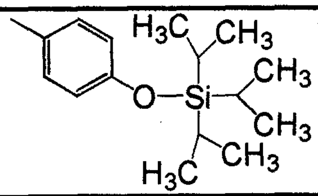
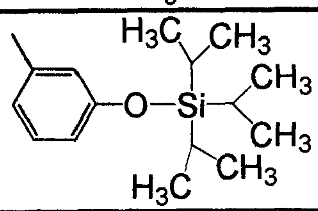


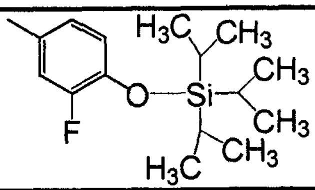
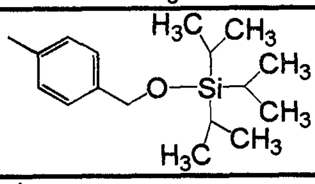
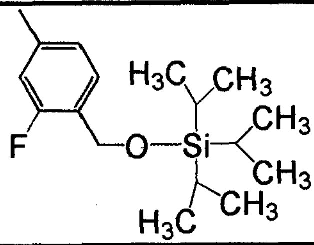
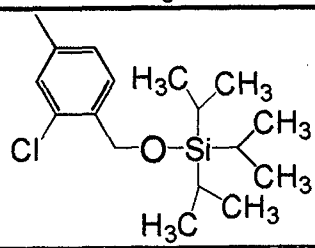
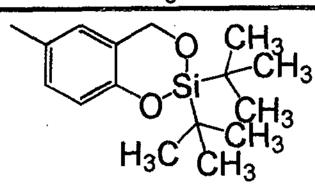
Example	R^4	NMR	Salt
901		1H-NMR (DMSO-d6) δppm : 0.86-1.01 (1H, m), 1.12-1.40 (5H, m), 1.51-1.76 (7H,m), 1.72-2.10 (3H, m), 2.67-2.81 (2H, m), 2.81-3.00 (5H, m), 3.05-3.20 (1H, m), 6.65-7.10 (2H, m), 7.21 (1H, d, J = 8.4 Hz), 9.03-9.20 (1H, m), 9.59-9.77 (1H, m).	2 Hydrochloride
902		1H-NMR (DMSO-d6) δppm : 0.88-1.04 (1H, m), 1.15-1.41 (5H, m), 1.48-1.80 (7H,m), 1.90-2.10 (3H, m), 2.65-3.05 (7H, m), 3.05-3.22 (1H, m), 4.90-6.25 (1H, br), 6.94 (1H, s), 7.11 (1H, s), 9.21 (1H, brs), 9.70 (1H, brs).	2 Hydrochloride
903		1H-NMR (DMSO-d6) δppm : 0.93-1.22 (2H, m), 1.22-1.43 (4H, m), 1.43-1.79 (7H, m), 1.90-2.10 (1H, m), 2.58-3.40 (6H, m), 4.52 (2H, t, J = 8.6 Hz), 5.30-6.20 (1H, br), 6.50-7.45 (3H, m), 8.65-9.38 (1H, br), 9.38-9.92 (1H, br).	2 Hydrochloride
904		1H-NMR (DMSO-d6) δppm : 0.96-1.13 (1H, m), 1.13-1.42 (5H, m), 1.49-1.66 (6H, m), 1.66-1.77 (1H, m), 1.93-2.05 (1H, m), 2.74-2.90 (2H, m), 2.98 (1H, d, J = 12.5 Hz), 3.08-3.20 (1H, m), 4.35-4.68 (1H, br), 6.95 (1H, dd, J = 2.0, 8.6 Hz), 7.26 (1H, d, J = 2.0 Hz), 7.36 (1H, d, J = 8.6 Hz), 8.98-9.20 (1H, br), 9.60-9.85 (1H, br).	2 Hydrochloride

[0387]
Table 102

absolute configuration

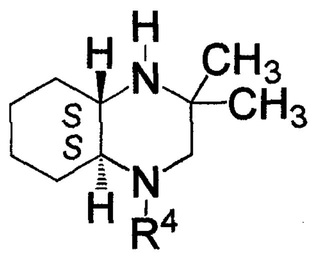


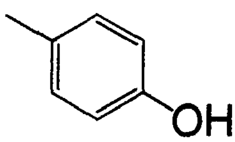
Example	R^4	NMR	Salt
905		1H-NMR (CDCl3) δppm : 0.75-1.04 (2H, m), 1.04-1.13 (21H, m), 1.15-1.37 (6H, m), 1.38 (3H, s), 1.52-1.75 (4H, m), 2.12-2.20 (1H, m), 2.58 (1H, d, J = 11.1 Hz), 2.69-2.78 (2H, m), 6.76-6.81 (2H, m), 6.92-6.97 (2H, m).	
906		1H-NMR (CDCl3) δppm : 0.88-1.14 (23H, m), 1.16-1.37 (6H, m), 1.38 (3H, s), 1.60-1.77 (4H, m), 2.20-2.29 (1H, m), 2.57 (1H, d, J = 11.3 Hz), 2.72-2.82 (2H, m), 6.60-6.65 (2H, m), 6.65-6.70 (1H, m), 7.07-7.14 (1H, m).	

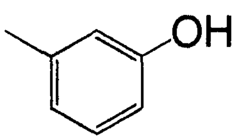
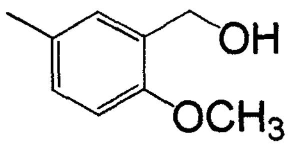
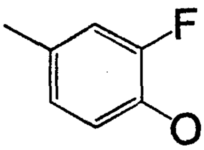
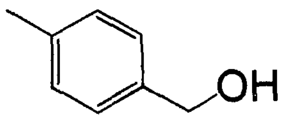
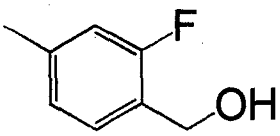
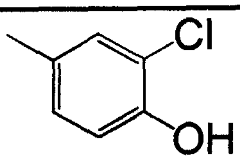
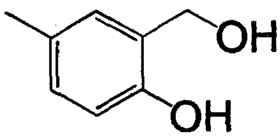
907		1H-NMR (CDCl3) δppm : 0.75-1.15 (23H, m), 1.17-1.40 (9H, m), 1.52-1.75 (4H, m), 2.10-2.17 (1H, m), 2.55 (1H, d, J = 11.1 Hz), 2.70-2.77 (2H, m), 6.69-6.74 (1H, m), 6.78-6.87 (2H, m).	
908		1H-NMR (CDCl3) δppm :0.81-1.38 (29H, m), 1.39 (3H, s), 1.58-1.76 (4H, m), 2.23-2.32 (1H, m), 2.61 (1H, d, J = 11.2 Hz), 2.72-2.82 (2H, m), 4.79 (2H, s), 7.02-7.08 (2H, m), 7.24-7.30 (2H, m).	
909		1H-NMR (CDCl3) δppm :0.75-1.35 (29H, m), 1.37 (3H, s), 1.62-1.78 (4H, m), 2.22-2.30 (1H, m), 2.60 (1H, d, J = 11.4 Hz), 2.71-2.85 (2H, m), 5.30 (2H, s), 6.72 (1H, dd, J = 2.0, 12.0 Hz), 6.86 (1H, J = 2.0, 8.2 Hz), 7.44 (1H, t, J = 8.4 Hz).	
910		1H-NMR (CDCl3) δppm :0.75-1.39 (32H, m), 1.53-1.75 (4H, m), 2.10-2.17 (1H, m), 2.56 (1H, d, J = 11.1 Hz), 2.68-2.77 (2H, m), 6.80 (1H, d, J = 8.6 Hz), 6.84 (1H, dd, J = 2.4, 8.6 Hz), 7.08 (1H, d, J = 2.4 Hz).	
911		1H-NMR (CDCl3) δppm : 0.85-1.09 (23H, m), 1.09-1.36 (3H, m), 1.37 (3H, s), 1.50-1.75 (4H, m), 2.11-2.19 (1H, m), 2.57 (1H, d, J = 11.1 Hz), 2.67-2.77 (2H, m), 4.95 (2H, s), 6.67 (1H, d, J = 2.5 Hz), 6.82 (1H, d, J = 8.5 Hz), 6.91 (1H, dd, J = 2.5, 8.5 Hz).	

[0388]
Table 103

absolute configuration

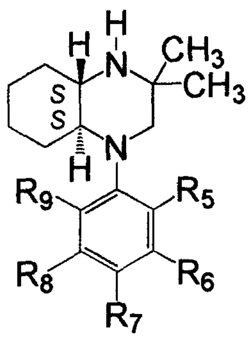


Example	R^4	NMR	Salt
912		1H-NMR (CDCl3) δppm : 0.92-1.06 (1H, m), 1.09 (3H, s), 1.12-1.37 (3H, m), 1.40 (3H, s), 1.55-1.66 (2H, m), 1.66-1.78 (2H, m), 2.15-2.25 (1H, m), 2.57-2.65 (1H, m), 2.69-2.83 (2H, m), 3.15-4.30 (2H, br), 6.72-6.79 (2H, m), 6.95-7.01 (2H, m).	-

913		1H-NMR (DMSO-d6) δppm : 0.82-1.00 (4H, m), 1.09-1.35 (6H, m), 1.40-1.52 (1H, m), 1.52-1.70 (4H, m), 2.12-2.25 (1H, m), 2.45-2.55 (1H, m), 2.55-2.65 (1H, m), 2.66 (1H, d, J = 11.0 Hz), 6.40-6.51 (3H, m), 7.00-7.10 (1H, m), 9.21 (1H, s).	-
914		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (1H, m), 1.05-1.38 (5H, m), 1.38-1.62 (6H, m), 1.64-1.74 (1H,m), 1.82-1.94 (1H, m), 2.53-2.62 (1H, m), 2.70 (1H, d, J = 12.0 Hz), 2.86 (1H, d, J = 12.0 Hz), 2.95-3.06 (1H, m), 3.74 (3H, s), 4.45 (2H, s), 4.65-5.60 (1H, br), 6.46 (1H, s), 6.87 (1H, d, J = 8.6 Hz), 6.94 (1H, dd, J = 2.5, 8.6 Hz), 7.15 (1H, d, J = 2.2 Hz), 8.59-10.40 (1H, br).	1/2 Fumarate
915		1H-NMR (DMSO-d6) δppm : 0.82-0.99 (4H, m), 1.05-1.32 (6H, m), 1.41-1.50 (1H, m), 1.50-1.65 (3H, m), 2.05-2.14 (1H, m), 2.47 (1H, d, J = 10.8 Hz), 2.53-2.62 (2H, m), 2.95-3.65 (1H, br), 6.67-6.72 (1H, m), 6.79-6.87 (2H, m), 8.65-10.50 (1H, m).	-
916		1H-NMR (CDCl3) δppm : 0.85-1.10 (5H, m), 1.15-1.42 (6H, m), 1.56-2.05 (5H, m), 2.25-2.15 (1H, m), 2.56-2.65 (1H, m), 2.72-2.84 (2H, m), 4.64 (2H, s), 7.04-7.10 (2H, m), 7.25-7.32 (2H, m).	-
917		1H-NMR (CDCl3) δppm : 0.95-1.44 (11H, m), 1.44-2.20 (5H, m), 2.25-2.35 (1H, m), 2.61 (1H, d, J = 11.4 Hz), 2.72-2.86 (2H, m), 4.69 (2H, s), 6.75 (1H, dd, J = 2.0, 12.1 Hz), 6.83 (1H, dd, J = 2.0, 8.1 Hz), 7.29 (1H, t, J = 8.4 Hz).	-
918		1H-NMR (CDCl3) δppm : 0.90-1.11 (4H, m), 1.14-1.42 (6H, m), 1.53-1.77 (4H, m), 2.12-2.21 (1H, m), 2.57 (1H, d, J = 11.2 Hz), 2.67-2.80 (2H, m), 2.81-3.38 (2H, br), 6.89-6.97 (2H, m), 7.07 (1H, dd, J = 0.5. 1.9 Hz).	-
919		1H-NMR (DMSO-d6) δppm : 0.78-0.93 (1H, m), 0.95 (3H, s), 1.04-1.32 (6H, m), 1.37-1.66 (5H, m), 2.05-2.14 (1H, m), 2.45-2.62 (3H, m), 4.43 (2H, s), 4.65-5.20 (1H, br), 6.65 (1H, d, J = 8.4 Hz), 6.74 (1H, dd, J = 2.5, 8.4 Hz), 7.03 (1H, d, J = 2.5 Hz), 8.81-9.28 (1H, br).	-

[0389]
Table 104

absolute configuration



Example	R^5	R^6	R^7	R^8	R^9	NMR	Salt
920	-CH3	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.88-1.03 (1H, m), 1.10-1.25 (1H, m), 1.25-1.40 (4H, m), 1.45-1.66 (6H, m), 1.67-1.89 (1H, m), 1.92-2.03 (1H, m), 2.26 (3H, m), 2.65 (1H, d, J = 12.5 Hz), 2.80 (1H, d, J = 12.5 Hz), 2.88-3.00 (1H, m), 3.15-3.28 (1H, m), 7.06-7.17 (2H, m), 7.19-7.26 (2H, m), 9.04 (1H, brs), 9.58 (1H, brs).	Hydrochloride
921	-CH3	-CH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.87-1.02 (1H, m), 1.10-1.24 (1H, m), 1.24-1.40 (4H, m), 1.40-1.64 (6H, m), 1.67-1.77 (1H, m), 1.95-2.04 (1H, m), 2.21 (3H, s), 2.22 (3H, s), 2.59 (1H, d, J = 12.5 Hz), 2.82 (1H, d, J = 12.5 Hz), 2.86-2.95 (1H, m), 3.15-3.37 (1H, m), 6.97-7.03 (2H, m), 7.07-1.15 (1H, m), 9.11 (1H, brs), 9.65 (1H, brs).	Hydrochloride
922	-H	-F	-CN	-H	-H	1H-NMR (DMSO-d6) δppm : 1.22-1.65 (10H, m), 1.65-1.84 (2H, m), 1.90-2.00 (1H, m), 2.10-2.20 (1H, m), 3.38-3.61 (4H, m), 3.78 (1H, d, J = 14.5 Hz), 6.83 (1H, dd, J = 2.3, 8.9 Hz), 6.97 (1H, dd, J = 2.0, 13.7 Hz), 7.65 (1H, t, J = 8.5 Hz), 8.93-9.15 (1H, m), 9.51-9.71 (1H, m).	2 Hydrochloride
923	-H	-H	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.15 (1H, m), 1.15-1.41 (5H, m), 1.50-1.67 (6H,m), 1.67-1.77 (1H, m), 1.95-2.05 (1H, m), 2.81-2.95 (2H, m), 3.01 (1H, d, J = 12.5 Hz), 3.11-3.25 (1H, m), 5.42-6.30 (1H, br), 7.20-7.27 (2H, m), 7.31-7.37 (2H, m), 9.02-9.20 (1H, brm), 9.60-9.80 (1H, brm).	2 Hydrochloride

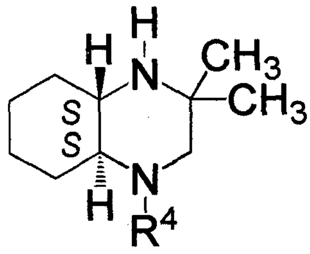
924	-H	-F	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.04-1.20 (1H, m), 1.20-1.41 (5H, m), 1.49-1.78 (7H, m), 1.96-2.06 (1H, m), 2.85-3.11 (3H, m), 3.15-3.28 (1H, m), 5.10-6.60 (1H, br), 7.00-7.15 (1H, m), 7.22-7.29 (1H, m), 7.47-7.54 (1H, m), 9.09 (1H, brs), 9.71 (1H, brs).	2 Hydrochloride
925	-H	-H	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.11 (1H, m), 1.11-1.25 (1H, m), 1.25-1.40 (4H, m), 1.48-1.65 (6H, m), 1.65-1.76 (1H, m), 1.92-2.03 (1H, m), 2.75-2.90 (2H, m), 2.99 (1H, d, J = 12.8 Hz), 3.10-3.23 (1H, m), 4.85-5.90 (1H, br), 7.01 (0.25H, s), 7.13-7.22 (4.5H, m), 7.38 (0.25H, s), 9.06 (1H, brs), 9.63 (1H, brs).	2 Hydrochloride
926	-H	-Cl	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.42 (6H, m), 1.50-1.66 (6H, m), 1.66-1.77 (1H, m), 1.95-2.05 (1H, m), 2.81-2.94 (2H, m), 3.02 (1H, d, J = 12.5 Hz), 3.10-3.23 (1H, m), 3.88-4.25 (1H, br), 7.15 (1H, dd, J = 2.6, 8.8 Hz), 7.24 (1H, t, J = 73.3 Hz), 7.32 (1H, d, J = 2.6 Hz), 7.34 (1H, d, J = 8.8 Hz), 9.05-9.22 (1H, m), 9.62-9.80 (1H, m).	2 Hydrochloride
927	-H	-OCHF2	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.16 (1H, m), 1.16-1.41 (5H, m), 1.50-1.67 (6H, m), 1.67-1.78 (1H, m), 1.96-2.06 (1H, m), 2.84-2.97 (2H, m), 3.04 (1H, d, J = 12.5 Hz), 3.11-3.25 (1H, m), 6.89 (1H, s), 6.96 (1H, dd, J = 2.1, 8.1 Hz), 7.00 (1H, d, J = 8.1 Hz), 7.27 (1H, t, J = 74.1 Hz), 7.39 (1H, t, J = 8.1 Hz), 8.30-9.30 (2H, br), 9.69-9.89 (1H, br).	2 Hydrochloride

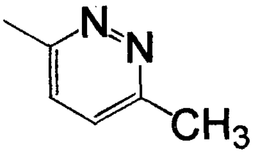
928	-H	-OCHF2	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.04-1.40 (6H, m), 1.50-1.69 (6H, m), 1.69-1.79 (1H, m), 1.92-2.04 (1H,m), 2.78-2.89 (1H, m), 2.89-3.06 (2H, m), 3.15-3.27 (1H, m), 7.01-7.08 (2H, m), 7.32 (1H, t, J = 73,3 Hz), 7.54 (1H, d, J = 8.4 Hz), 8.81-9.11 (1H, m), 9.40-9.69 (1H, m).	Hydrochloride
929	-H	-OCHF2	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.40 (6H, m), 1.47-1.65 (6H, m), 1.67-1.77 (1H, m), 1.90-2.00 (1H, m), 2.70-2.80 (1H, m), 2.87 (1H, d, J = 12.5 Hz), 2.96 (1H, d, J = 12.5 Hz), 3.10-3.24 (1H, m), 7.02-7.11 (2.25H, m), 7.27 (0.5H, s), 7.37 (1H, dd, J = 8.8, 10.5 Hz), 7.46 (0.25H, s), 8.80-9.00 (1H, br), 9.39-9.58 (1H, br).	Hydrochloride
930	-H	-CN	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.03-1.15 (1H, m), 1.17-1.41 (5H, m), 1.48-1.82 (7H, m), 1.93-2.05 (1H, m), 2.82-2.91 (1H, m), 2.94 (1H, d, J = 12.7 Hz), 3.01 (1H, d, J = 12.7 Hz), 3.08-3.25 (1H, m), 4.00-4.60 (1H, br), 7.39 (1H, t, J= 72.6 Hz), 7.42 (1H, d, J = 8.9 Hz), 7.51 (1H, dd, J = 2.7, 9.0 Hz), 7.69 (1H, d, J = 2.7 Hz), 8.90-9.10 (1H, br), 9.40-9.65 (1H, br).	2 Hydrochloride
931	-H	-F	-OCHF2	-F	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.42 (6H, m), 1.42-1.80 (7H, m), 1.96-2.07 (1H, m), 2.90-3.00 (1H, m), 3.05 (1H, d, J = 13.0 Hz), 3.10 (1H, d, J = 13.0 Hz), 3.17-3.29 (1H, m), 3.55-3.85 (1H, br), 6.97-7.06 (2.25H, m), 7.19 (0.5H, s), 7.37 (0.25H, s), 8.90-9.07 (1H, br), 9.51-9.70 (1H, br).	2 Hydrochloride

932	-H	-H	-OCH2CHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.80 (13H, m), 1.91-2.14 (1H, m), 2.61-3.50 (4H, m), 4.20-4.40 (2H, m), 4.61-6.20 (1H, br), 6.39 (1H, tt, J = 3.4, 54.5 Hz), 6.85-7.65 (4H, brm), 8.84-10.20 (2H, br).	2 Hydrochloride
933	-H	-F	-OCH2CHF2	-H	-H	1H-NMR (CDCl3) δppm : 0.95-1.09 (4H, m), 1.15-1.44 (7H, m), 1.57-1.78 (4H, m), 2.13-2.22 (1H, m), 2.56 (1H, d, J =11.1 Hz), 2.70-2.79 (2H, m), 4.21 (2H, dt, J = 4.2, 13.1 Hz), 6.08 (1H, tt, J = 4.2, 55.1 Hz), 6.77-6.83 (1H, m), 6.84-6.95 (2H, m).	-
934	-H	-Cl	-OCH2CHF2	-H	-H	1H-NMR (CDCl3) δppm : 0.93-1.10 (4H, m), 1.15-1.41 (7H, m), 1.53-1.77 (4H, m), 2.14-2.23 (1H, m), 2.57 (1H, d, J = 11.0 Hz), 2.68-2.79 (2H, m), 4.20 (2H, dt, J = 4.2, 13.0 Hz), 6.12 (1H, tt, J = 4.2, 55.1 Hz), 6.87 (1H, d, J = 8.7 Hz), 6.96 (1H, dd, J = 2.5, 8.7 Hz), 7.13 (1H, d, J = 2.5 Hz).	-
935	-H	-CH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.96-1.10 (1H, m), 1.12-1.40 (5H, m), 1.47-1.63 (6H, m), 1.67-1.76 (1H, m), 1.90-2.01 (1H, m), 2.21 (3H, m), 2.70-2.87 (2H, m), 2.96 (1H, d, J = 12.1 Hz), 3.07-3.22 (1H, m), 4.40-6.50 (1H, br), 6.94 (0.25H, s), 6.97-7.03 (1H, m), 7.03-7.08 (1H, m), 7.09-7.15 (1.5H, m), 7.31 (0.25H, s), 9.01 (1H, brs), 9.56 (1H, brs).	2 Hydrochloride
936	-H	-OCH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.40 (6H, m), 1.50-1.79 (7H, m), 1.96-2.06 (1H, m), 2.78-2.95 (2H, m), 2.98-3.22 (2H,m), 3.82 (3H, s), 6.75 (1H, d, J = 7.8 Hz), 6.80-6.93 (1.25H, m), 7.01 (0.5H, s), 7.11-7.21 (1.25H, m), 7.21-7.75 (1H, br), 9.14 (1H, brs), 9.77 (1H, brs).	2 Hydrochloride

[0390]
Table 105

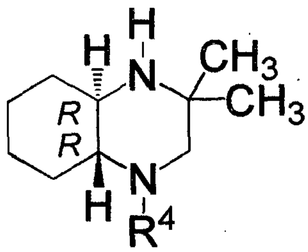
absolute configuration

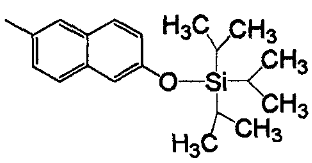
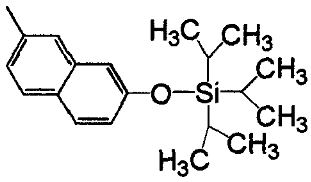
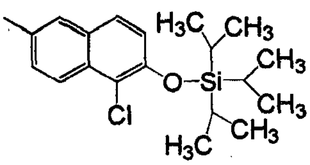


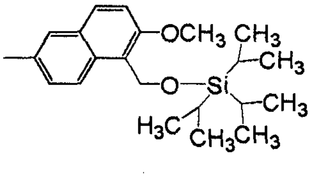
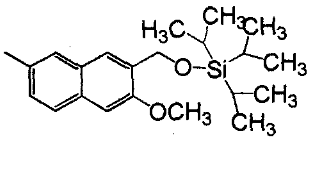
Example	R^4	NMR	Salt
937		1H-NMR (DMSO-d6) δppm : 1.15-1.60 (10H, m), 1.60-1.86 (2H, m), 1.95-2.15 (2H, m), 2.47 (3H, s), 3.37 (1H, d, J = 14.2 Hz), 3.41-3.66 (2H, m), 3.88 (1H, d, J = 14.2 Hz), 5.32-7.05 (1.5H, br), 7.18 (1H, d, J = 9.2 Hz), 7.36 (1H, d, J = 9.2 Hz), 7.45-9.40 (1.5 H, br).	Oxalate

[0391]
Table 106

absolute configuration

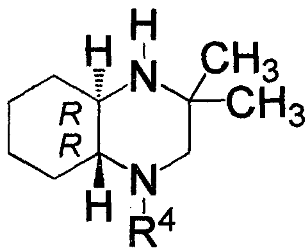


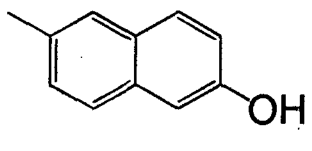
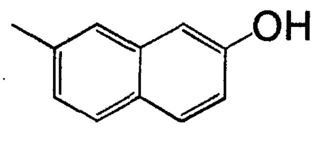
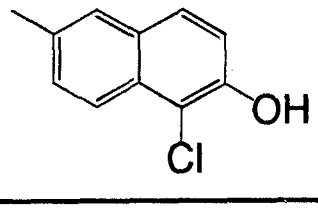
Example	R^4	NMR	Salt
938		1H-NMR (CDCl3) δppm : 0.98-1.17 (23H, m), 1.17-1.40 (6H, m), 1.43 (3H, s), 1.59-1.68 (1H, m), 1.68-1.80 (3H, m), 2.32-2.41 (1H, m), 2.68 (1H, d, J = 11.3 Hz), 2.77-2.85 (1H, m), 2.88 (1H, d, J = 11.3 Hz), 7.08 (1H, dd, J = 2.4, 8.8 Hz), 7.16 (1H, d, J = 2.4 Hz), 7.22 (1H, dd, J = 2.1, 8.7 Hz), 7.37 (1H, d, J = 1.8 Hz), 7.57-7.64 (2H, m).	-
939		1H-NMR (CDCl3) δppm : 0.82-1.18 (23H, m), 1.20-1.40 (6H, m), 1.43 (3H, s), 1.59-1.70 (1H, m), 1.70-1.85 (3H, m), 2.35-2.45 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.77-2.86 (1H, m), 2.91 (1H, d, J = 11.3 Hz), 7.02 (1H, dd, J = 2.4, 8.8 Hz), 7.09-7.15 (2H, m), 7.27 (1H, d, J = 1.9 Hz), 7.61-7.68 (2H, m).	-
940		1H-NMR (CDCl3) δppm : 0.97-1.41 (29H, m), 1.43 (3H, s), 1.59-1.70 (1H, m), 1.70-1.80 (3H, m), 2.34-2.44 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.78-2.87 (1H, m), 2.89 (1H, d, J = 11.3 Hz), 7.11 (1H, d, J = 8.9 Hz), 7.34 (1H, dd, J = 2.1, 9.0 Hz), 7.37 (1H, d, J = 1.9 Hz), 7.53 (1H, d, J = 8.9 Hz), 8.10 (1H, d, J = 8.9 Hz).	-

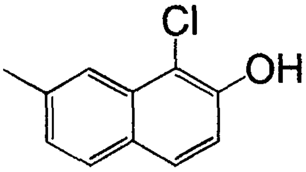
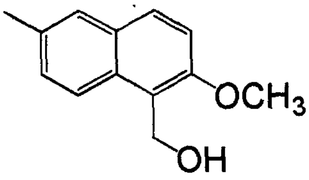
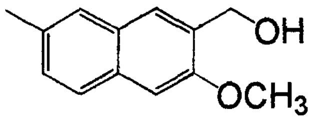
941		1H-NMR (CDCl3) δppm :0.75-1.42 (29H, m), 1.44 (3H, s), 1.58-1.83 (4H, m), 2.34-2.42 (1H, m), 2.68 (1H, d, J = 11.3 Hz), 2.78-2.87 (1H, m), 2.91 (1H, d, J = 11.3 Hz), 3.91 (3H, s), 5.19-5.27 (2H, m), 7.21 (1H, d, J = 9.1 Hz), 7.29 (1H, d, J = 2.2, 9.1 Hz), 7.37 (1H, d, J = 2.1 Hz), 7.69 (1H, d, J = 9.0 Hz), 8.16 (1H, d, J = 9.1 Hz).	-
942		1H-NMR (CDCl3) δppm : 0.95-1.18 (23H, m), 1.18-1.40 (6H, m), 1.44 (3H, s), 1.57-1.77 (4H, m), 2.33-2.41 (1H, m), 2.71 (1H, d, J = 11.2 Hz), 2.77-2.85 (1H, m), 2.87 (1H, d, J = 11.2 Hz), 3.89 (3H, s), 4.94 (2H, d, J = 1.0 Hz), 7.02 (1H, s), 7.22 (1H, dd, J = 2.0, 8.6 Hz), 7.43 (1H, d, J = 1.8 Hz), 7.64 (1H, d, J = 8.6 Hz), 7.88 (1H, s).	-

[0392]
Table 107

absolute configuration

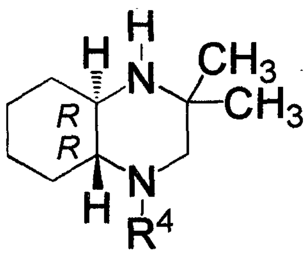


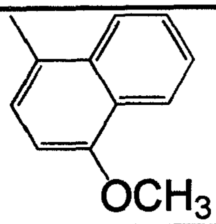
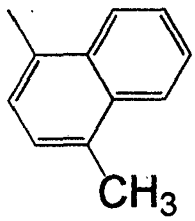
Example	R^4	NMR	Salt
943		1H-NMR (DMSO-d6) δppm : 0.88-1.03 (4H, m), 1.10-1.37 (6H, m), 1.45-1.68 (5H, m), 2.25-2.36 (1H, m), 2.58 (1H, d, J = 10.9 Hz), 2.62-2.71 (1H, m), 2.73 (1H, d, J = 10.9 Hz), 7.02 (1H, dd, J = 2.4, 8.7 Hz), 7.05 (1H, d, J = 2.4 Hz), 7.16 (1H, dd, J = 2.1, 8.7 Hz), 7.37 (1H, d, J = 1.8 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.67 (1H, d, J = 8.8 Hz), 9.57 (1H, brs).	-
944		1H-NMR (DMSO-d6) δppm : 0.88-1.04 (4H, m), 1.12-1.37 (6H, m), 1.45-1.74 (5H, m), 2.32-2.41 (1H, m), 2.60 (1H, d, J = 11.1 Hz), 2.63-2.72 (1H, m), 2.80 (1H, d, J = 11.1 Hz), 6.94 (1H, dd, J = 2.4, 8.8 Hz), 6.97-7.04 (2H, m), 7.21 (1H, d, J = 1.8 Hz), 7.64 (2H, d, J = 8.8 Hz), 9.62 (1H, s).	-
945		1H-NMR (DMSO-d6) δppm : 0.90-1.10 (4H, m), 1.15-1.40 (6H, m), 1.51-1.75 (4H, m), 2.35-2.48 (1H, m), 2.60-2.88 (3H, m), 2.96-3.88 (1H, br), 7.23 (1H, d, J = 8.9 Hz), 7.34 (1H, dd, J = 2.1, 9.0 Hz), 7.47 (1H, d, J = 2.0 Hz), 7.70 (1H, d, J = 8.9 Hz), 7.92 (1H, d, J = 9.0 Hz), 8.92-11.38 (1H, br).	-

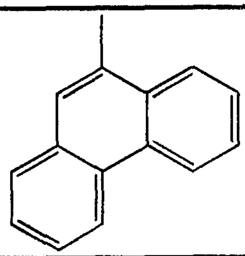
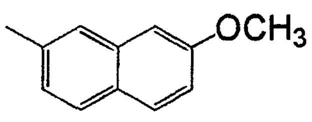
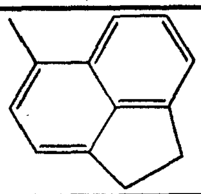
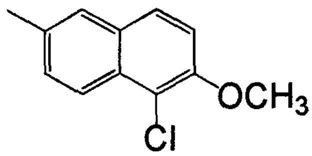
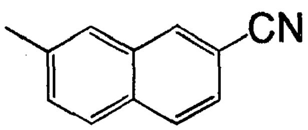
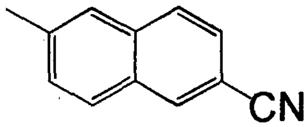
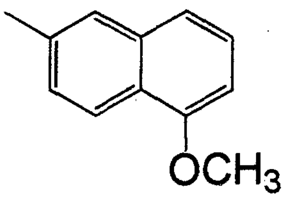
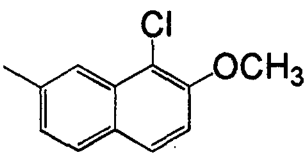
946		1H-NMR (DMSO-d6) δppm : 0.93-1.12 (4H, m), 1.15-1.41 (6H, m), 1.54-1.80 (4H, m), 2.48-2.60 (1H, m), 2.70-2.87 (2H, m), 2.92 (1H, d, J = 11.5 Hz), 3.03-4.36 (1H, br), 7.08-7.18 (2H, m), 7.50 (1H, d, J = 2.0 Hz), 7.67 (1H, d, J = 8.8 Hz), 7.75 (1H, d, J = 8.7 Hz), 8.89-11.11 (1H, br).	-
947		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (4H, m), 1.13-1.37 (6H, m), 1.47-1.70 (5H, m), 2.30-2.39 (1H, m), 2.61 (1H, d, J = 11.0 Hz), 2.64-2.73 (1H, m), 2.78 (1H, d, J = 11.0 Hz), 3.88 (3H, s), 4.81 (1H, t, J = 5.2 Hz), 4.88 (2H, d, J = 5.2 Hz), 7.27 (1H, dd, J = 2.2, 9.1 Hz), 7.35 (1H, d, J = 9.1 Hz), 7.42 (1H, d, J = 2.1 Hz), 7.80 (1H, d, J = 9.1 Hz), 8.03 (1H, d, J = 9.1 Hz).	-
948		1H-NMR (DMSO-d6) δppm : 0.95-1.10 (1H, m), 1.10-1.50 (9H, m), 1.53-1.73 (3H, m), 1.77-1.87 (1H, m), 2.58-2.70 (1H, m), 2.85 (2H, s), 2.89-3.00 (1H, m), 3.87 (3H, s), 4,61 (2H, s), 6.46 (1H, s), 7.20 (1H, dd, J = 2.0, 8.7 Hz), 7.22 (1H, s), 7.46 (1H, d, J = 1.6 Hz), 7.73 (1H, d, J = 8.7 Hz), 7.79 (1H, s).	1/2 Fumarate

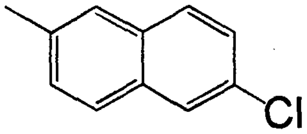
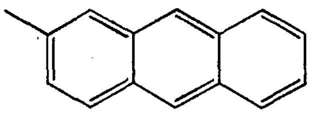
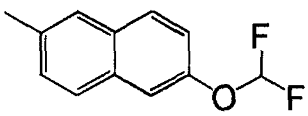
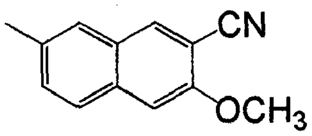
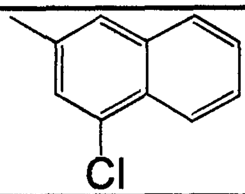
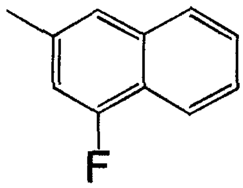
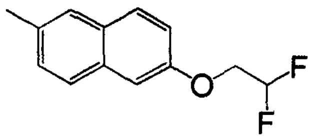
[0393]
Table 108

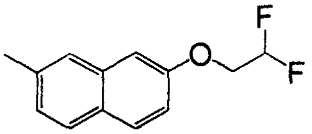
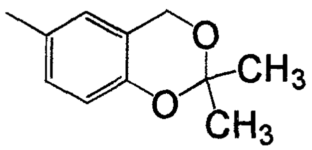
absolute configuration



Example	R^4	NMR	Salt
949		1H-NMR (CDCl3) δppm : 0.91-1.05 (1H, m), 1.08 (3H, s), 1.12-1.62 (9H, m), 1.68-1.78 (2H, m), 2.42-2.50 (1H, m), 2.62 (1H, d, J = 11.3 Hz), 2.75 (1H, d, J = 11.3 Hz), 2.91-3.00 (1H,m), 3.98 (3H, s), 6.78 (1H, d, J = 8.1 Hz), 7.20 (1H, d, J = 8.1 Hz), 7.43-7.54 (2H, m), 8.21-8.26 (1H, m), 8.50-8.54 (1H, m).	-
950		1H-NMR (DMSO-d6) δppm : 0.93-1.22 (2H, m), 1.26-1.44 (5H, m), 1.44-1.54 (1H,m), 1.56-1.77 (5H, m), 1.99-2.08 (1H, m), 2.62 (3H, s), 2.76 (1H, d, J = 12.4 Hz), 2.98-3.08 (2H, m), 3.33-3.50 (1H, m), 7.28 (1H, d, J = 7.5 Hz), 7.38 (1H, d, J = 7.5 Hz), 7.54-7.61 (2H, m), 7.97-8.03 (1H, m), 8.43-8.52 (1H, m), 9.10-9.25 (1H, br), 9.62-9.77 (1H, br).	Hydrochloride

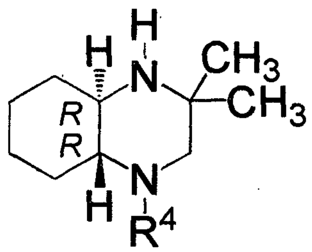
951		1H-NMR (DMSO-d6) δppm : 1.00-1.30 (2H, m), 1.30-1.45 (4H, m), 1.45-1.65 (2H, m), 1.65-1.85 (5H, m), 2.00-2.13 (1H, m), 2.91 (1H, d, J = 12.6 Hz), 3.05-3.20 (2H, m), 3.41-3.57 (1H, m), 3.93-4.29 (1H, br), 7.61-7.77 (5H, m), 7.98-8.05 (1H, m), 8.55-8.61 (1H, m), 8.77-8.88 (2H, m), 9.19-9.35 (1H, m), 9.669.81 (1H, m).	2 Hydrochloride
952		1H-NMR (DMSO-d6) δppm : 0.96-1.45 (6H, m), 1.55-1.80 (7H, m), 2.00-2.12 (1H, m), 2.85-3.40 (4H, m), 3.87 (3H, s), 7.05-7.26 (2H, m), 7.32 (1H, d, J = 2.5 Hz), 7.42-7.73 (1H, br), 7.73-7.90 (2H, m), 8.75-9.60 (2H, br), 9.60-10.15 (1H, br).	2 Hydrochloride
953		1H-NMR (DMSO-d6) δppm : 0.85-1.00 (1H, m), 1.10-1.70 (12H, m), 1.75-1.87 (1H, m), 2.62-2.81 (3H, m), 2.98-3.12 (1H, m), 3.20-3.45 (4H, m), 6.46 (1H, s), 7.15-7.35 (3H, m), 7.35-7.52 (1H, m), 7.88 (1H, d, J = 8.1 Hz), 8.05-9.35 (1H, br).	1/2 Fumarate
954		1H-NMR (DMSO-d6) δppm : 1.05-1.45 (6H, m), 1.55-1.80 (7H, m), 1.99-2.10 (1H, m), 2.91-3.08 (2H, m), 3.08-3.30 (2H, m), 3.98 (3H, s), 7.44 (1H, d, J = 9.0 Hz), 7.56 (1H, d, J = 9.2 Hz), 7.67 (1H, brs), 7.96 (1H, d, J = 9.1 Hz), 8.05 (1H, d, J = 9.1 Hz), 8.15-9.10 (1H, br), 9.17-9.40 (1H, m), 9.69-9.89 (1H, m).	2 Hydrochloride
955		1H-NMR (CDCl3) δppm : 0.80-0.98 (1H, br), 1.03-1.17 (4H, m), 1.22-1.47 (6H, m), 1.63-1.74 (1H, m), 1.74-1.89 (3H, m), 2.45-2.55 (1H, m), 2.76 (1H, d, J = 11.5 Hz), 2.81-2.90 (1H, m), 2.98 (1H, d, J = 11.5 Hz), 7.38-7.44 (2H, m), 7.49 (1H, dd, J = 1.6, 8.4 Hz), 7.76-7.81 (1H, m), 7.83 (1H, d, J = 8.4 Hz), 8.12 (1H, s).	-
956		1H-NMR (DMSO-d6) δppm : 1.12-1.45 (6H, m), 1.55-1.90 (7H, m), 2.00-2.14 (1H, m), 3.08-3.40 (4H, m), 4.52-5.08 (1H, br), 7.45 (1H, dd, J = 2.0, 8.9 Hz), 7.64 (1H, d, J = 1.7 Hz), 7.73 (1H, dd, J = 1.6, 8.5 Hz), 8.00 (1H, d, J = 8.9 Hz), 8.04 (1H, d, J = 8.6 Hz), 8.49 (1H, s), 9.10-9.25 (1H, br), 9.60-9.75 (1H, br).	2 Hydrochloride
957		1H-NMR (DMSO-d6) δppm : 1.03-1.45 (6H, m), 1.50-1.80 (7H, m), 1.98-2.10 (1H, m), 2.90-3.30 (4H, m), 3.95 (3H, s), 6.91 (1H, d, J = 7.1 Hz), 7.23-7.34 (1H, br), 7.38-7.49 (2H, m), 7.48-7.65 (1H, br), 8.10 (1H, d, J = 8.9 Hz), 9.10-9.36 (1H, br), 9.60-9.88 (1H, br), 10.00-11.50 (1H, br).	2 Hydrochloride
958		1H-NMR (DMSO-d6) δppm : 1.10-1.48 (6H, m), 1.55-1.80 (7H, m), 1.981-2.10 (1H, m), 2.95-3.10 (2H,m),3.10-3.21 (1H, m), 3.21-3.85 (1H, m), 3.99 (3H, s), 7.26 (1H, dd, J = 1.5, 8.7 Hz), 7.50 (1H, d, J = 9.1 Hz), 7.66 (1H, brs), 7.93 (2H, d, J = 9.1 Hz), 9.20 (1H, brs), 9.72 (1H, brs), 9.89-10.70 (1H, brs).	2 Hydrochloride

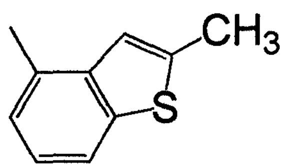
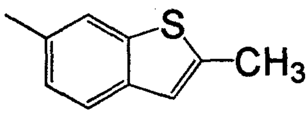
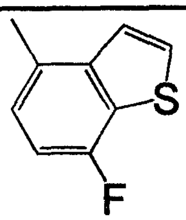
959		1H-NMR (DMSO-d6) δppm : 1.10-1.43 (6H, m), 1.56-1.80 (7H, m), 1.99-2.09 (1H, m), 2.95-3.06 (2H, m), 3.11 (1H, d, J = 12.5 Hz), 3.17-3.30 (1H, m), 6.05-7.25 (1H, br), 7.36 (1H, dd, J = 1.9, 8.8 Hz), 7.49 (1H, dd, J = 2.1, 8.8 Hz), 7.64 (1H, brs), 7.88 (1H, d, J = 8.9 Hz), 7.94 (1H, d, J = 8.9 Hz), 8.00 (1H, d, J = 1.8 Hz), 9.15-9.34 (1H, br), 9.69-9.85 (1H, br).	2 Hydrochloride
960		1H-NMR (CDCl3) δppm : 0.75-1.19 (5H, m), 1.24-1.44 (3H, m), 1.41 (3H, s), 1.59-1.73 (1H, m), 1.73-1.82 (2H, m), 1.90-2.00 (1H, m), 2.45-2.54 (1H, m), 2.73 (1H, d, J = 11.5 Hz), 2.81-2.92 (1H, m), 3.02 (1H, d, J = 11.5 Hz), 7.26 (1H, dd, J = 2.1, 9.0 Hz), 7.38-7.47 (2H, m), 7.51 (1H, d, J = 1.3 Hz), 7.91 (1H, d, J = 9.1 Hz), 7.94-7.99 (2H, m), 8.30 (1H, s), 8.34 (1H, s).	-
961		1H-NMR (DMSO-d6) δppm : 1.15-1.48 (6H, m), 1.55-1.80 (7H, m), 1.95-2.09 (1H, m), 2.91-3.05 (2H, m), 3.05-3.16 (1H, m), 3.16-3.30 (1H, m), 3.70-4.4.10 (1H, br), 7.16 (0.25H, s), 7.32-7.40 (2.5H, m), 7.53 (0.25H, s), 7.62-7.70 (2H, m), 7.90 (1H, d, J = 8.8 Hz), 7.98 (1H, d, J = 9.0 Hz).9.05-9.25 (1H, br), 9.54-9.78 (1H, br).	2 Hydrochloride
962		1H-NMR (DMSO-d6) δppm : 1.05-1.50 (6H, m), 1.55-1.80 (7H, m), 1.97-2.10 (1H, m), 2.40-3.05 (2H, m), 3.05-3.16 (1H, m), 3.16-3.31 (1H, m), 3.65-4.25 (4H, m), 7.44 (1H, dd, J = 2.0, 8.8 Hz), 7.56 (1H, s), 7.65 (1H, s), 7.89 (1H, d, J = 8.8 Hz), 8.47 (1H, s), 9.05-9.35 (1H, br), 9.53-9.84 (1H, br).	2 Hydrochloride
963		1H-NMR (DMSO-d6) δppm : 1.08-1.46 (6H, m), 1.54-1.80 (7H, m), 1.97-2.08 (1H, m), 2.95-3.17 (3H, m), 3.17-3.31 1H, m), 4.65-4.45 (1H, br), 7.46-7.50 (1H, m), 7.57-7.67 (3H, m), 7.97-8.04 (1H, m), 8.07-8.15 (1H, m), 9.13-9.35 (1H, br), 9.62-9.80 (1H, br).	2 Hydrochloride
964		1H-NMR (DMSO-d6) δppm : 1.08-1.47 (6H, m), 1.53-1.82 (7H, m), 1.98-2.09 (1H, m), 2.93-3.17 (3H, m), 3.17-3.30 (1H, m), 4.30-4.85 (1H, br), 7.15 (1H, dd, J = 1.6, 12.4 Hz), 7.47 (1H, d, J = 1.3 Hz), 7.51-7.64 (2H, m), 7.97 (2H, d, J = 8.2 Hz), 9.10-9.30 (1H, br), 9.67-9.85 (1H, br).	2 Hydrochloride
965		1H-NMR (CDCl3) δppm : 1.00-1.15 (4H, m), 1.17-1.52 (7H, m), 1.58-1.68 (1H, m), 1.68-1.79 (3H, m), 2.34-2.42 (1H, m), 2.69 (1H, d, J = 11.3 Hz), 2.77-2.86 (1H, m), 2.88 (1H, d, J = 11.3 Hz), 4.28 (2H, dt, J = 4.1, 13.1 Hz), 6.15 (1H, tt, J = 4.1, 55.2 Hz), 7.10 (1H, d, J = 2.5 Hz), 7.14 (1H, dd, J = 2.6, 8.9 Hz), 7.27 (1H, dd, J = 2.1, 8.7 Hz), 7.41 (1H, d, J = 2.0 Hz), 7.63-7.72 (2H, m).	-

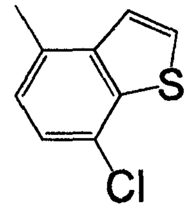
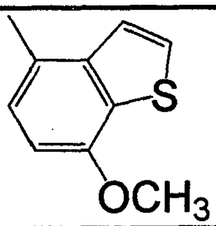
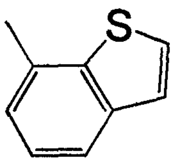
966		1H-NMR (CDCl3) δppm : 1.00-1.15 (4H, m), 1.20-1.70 (8H, m), 1.70-1.88 (3H, m), 2.39-2.48 (1H, m), 2.70 (1H, d, J = 11.4 Hz), 2.79-2.88 (1H, m), 2.93 (1H, d, J = 11.4 Hz), 4.29 (2H, dt, J = 4.2, 13.1 Hz), 6.15 (1H, tt, J = 4.1, 55.2 Hz), 7.03-7.11 (2H, m), 7.16 (1H, dd, J = 2.1, 8.6 Hz), 7.33 (1H, d, J = 2.0 Hz), 7.65-7.74 (2H, m).	-
967		1H-NMR (DMSO-d6) δppm : 0.91-1.05 (1H, m), 1.07-1.36 (5H, m), 1.36-1.63 (12H, m), 1.63-1.74 (1H, m), 1.80-1.83 (1H, m), 2.50-2.62 (1H, m), 2.71 (1H, d, J = 12.0 Hz), 2.86 (1H, d, J = 12.0 Hz), 2.92-3.02 (1H, m), 4.78 (2H, s), 6.48 (2H, s), 6.73 (1H, d, J = 8.6 Hz), 6.83 (1H, d, J = 2.3 Hz), 6.91 (1H, dd, J = 2.3, 8.6 Hz). 9.52-11.33 (1H, br).	Fumarate

[0394]
Table 109

absolute configuration

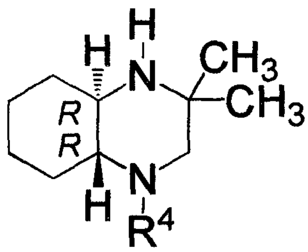


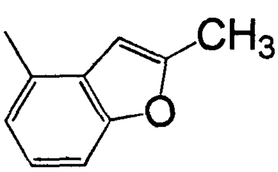
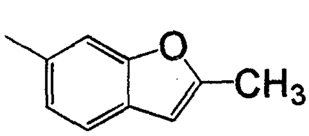
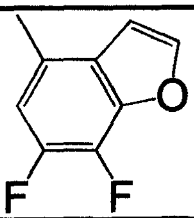
Example.	R^4	NMR	Salt
968		1H-NMR (DMSO-d6) δppm : 0.96-1.10 (1H, m), 1.10-1.25 (1H, m), 1.26-1.41 (4H, m), 1.47-1.78 (7H, m), 1.94-2.05 (1H, m), 2.56 (3H, s), 2.84 (1H, d, J = 12.4 Hz), 2.90-3.02 (2H, m), 3.23-3.35 (1H, m), 7.15 (1H, d, J = 7.6 Hz), 7.22-7.33 (2H, m), 7.68 (1H, d, J = 7.9 Hz), 8.91-9.09 (1H, brm), 9.54-9.70 (1H, brm).	Hydrochloride
969		1H-NMR (DMSO-d6) δ ppm (80 °C): 1.03-1.46 (6H, m), 1.50-1.79 (7H, m), 2.02-2.12 (1H, m), 2.53 (3H, s), 2.88 (1H, d, J = 12.4 Hz), 3.02-3.12 (1H, m), 3.12-3.27 (2H, m), 7.05 (1H, s), 7.13 (1H, d, J = 8.6 Hz), 7.62-7.68 (2H, m), 9.25 (1H, brs), 9.75 (1H, brs).	Hydrochloride
970		1H-NMR (DMSO-d6) δppm : 0.95-1.41 (6H, m), 1.40-1.76 (7H, m), 1.96-2.05 (1H, m), 2.84 (1H, d, J = 12.4 Hz), 2.93-3.01 (1H, m), 3.04 (1H, d, J = 12.4 Hz), 3.28-3.44 (1H, m), 7.25 (2H, d, J = 7.0 Hz), 7.64 (1H, dd, J = 4.0, 5.3 Hz), 7.86 (1H, d, J = 5.3 Hz), 9.04-9.19 (1H, brm), 9.63-9.75 (1H, brm).	Hydrochloride

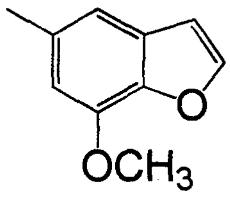
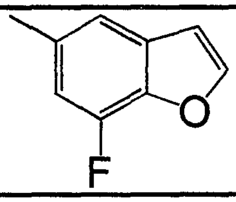
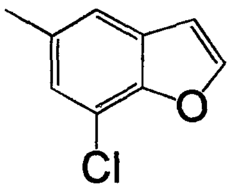
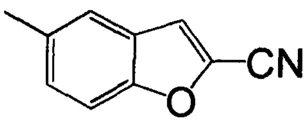
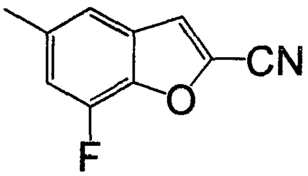
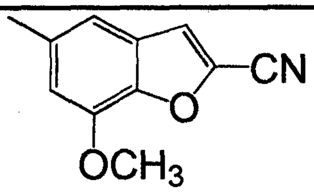
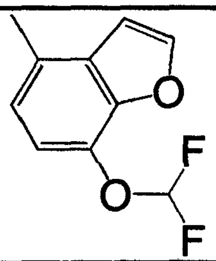
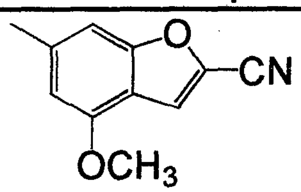
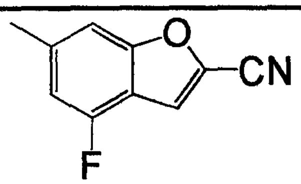
971		1H-NMR (DMSO-d6) δppm : 0.97-1.43 (6H, m), 1.45-1.78 (7H, m), 1.96-2.06 (1H, m), 2.87 (1H, d, J = 12.4 Hz), 2.94-3.06 (2H, m), 3.26-3.43 (1H, m), 7.28 (1H, d, J = 8.1 Hz), 7.50 (1H, d, J = 8.1 Hz), 7.64 (1H, d, J = 5.4 Hz), 7.88 (1H, d, J = 5.4 Hz), 9.12 (1H, brs), 9.66 (1H, brs).	Hydrochloride
972		1H-NMR (DMSO-d6) δppm : 0.92-1.80 (13H, m), 1.36-2.05 (1H, m), 2.75-3.05 (4H, m), 3.94 (3H, s), 6.94 (1H, d, J = 7.9 Hz), 7.18 (1H, d, J = 7.9 Hz), 7.55 (1H, d, J = 5.4 Hz), 7.71 (1H, d, J = 5.4 Hz), 8.81 (1H, brs), 9.31 (1H, brs).	Hydrochloride
973		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (1H, m), 1.15-1.3 (1H, m), 1.3-1.45 (5H, m), 1.5-1.7 (6H, m), 1.7, 1.8 (1H, m), 1.9-2.0 (1H, m), 2.85-3.1 (3H, m), 3.2-3.4 (1H, m), 7.24 (1H, d, J =7.2Hz), 7.42 (1H, dd, J = 7.7, 7.7Hz), 7.70-7.77 (2H, m), 8.84 (1H, br), 9.28 (1H, br).	Hydrochloride

[0395]
Table 110

absolute configuration



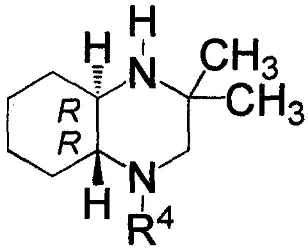
Example.	R^4	NMR	Salt
974		1H-NMR (DMSO-d6) δppm : 0.97-1.10 (1H, m), 1.10-1.41 (5H, m), 1.50-1.78 (7H, m), 1.94-2.05 (1H, m), 2.44 (3H, s), 2.75-3.09 (3H, m), 3.09-3.30 (1H, m), 6.58 (1H, brs), 6.98 (1H, d, J = 7.2 Hz), 7.19 (1H, t, J = 7.8 Hz), 7.31 (1H, d, J = 7.8 Hz), 9.00 (1H, brs), 9.59 (1H, brs).	Hydrochloride
975		1H-NMR (DMSO-d6) δppm : 1.00-1.44 (6H, m), 1.44-1.79 (7H, m), 1.95-2.08 (1H, m), 2.42 (3H, d, J = 0.9 Hz), 2.78-3.30 (4H, m), 3.78-4.64 (1H, br), 6.55 (1H, s), 7.04 (1H, brs), 7.32 (1H, brs), 7.48 (1H, d, J = 8.6 Hz), 8.91-9.35 (1H, br), 9.54-9.90 (1H, br).	2 Hydrochloride
976		1H-NMR (DMSO-d6) δppm : 1.00-1.14 (1H, m), 1.14-1.42 (5H, m), 1.43-1.77 (7H, m), 1.93-2.03 (1H, m), 2.72-3.12 (3H, m), 3.27 (1H, brs), 7.08 (1H, brs), 7.24 (1H, brs), 8.14 (1H, s), 8.95 (1H, brs), 9.57 (1H, brs).	Hydrochloride

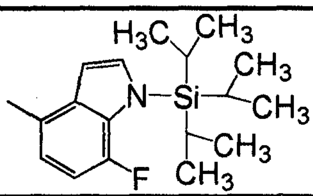
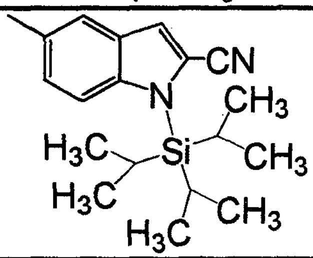
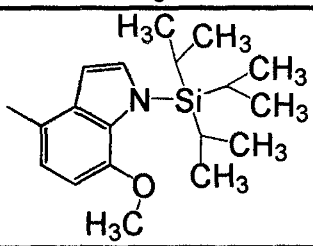
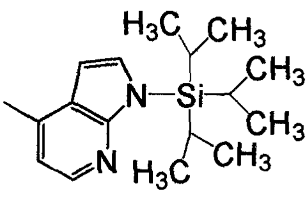
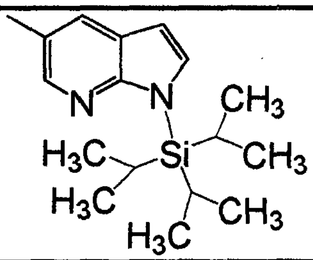
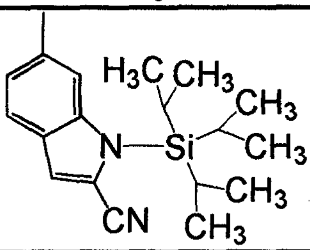
977		1H-NMR (CDCl3) δppm : 0.86-1.13 (5H, m), 1.13-1.40 (3H, m), 1.42 (3H, s), 1.57-1.68 (2H, m), 1.68-1.79 (2H, m), 2.20-2.30 (1H, m), 2.65 (1H, d, J = 11.1 Hz), 2.74-2.85 (2H, m), 3.99 (3H, s), 6.61 (1H, d, J = 1.8 Hz), 6.70 (1H, d, J = 2.1 Hz), 6.95 (1H, d, J = 1.8 Hz), 7.59 (1H, d, J = 2.1 Hz).	-
978		1H-NMR (DMSO-d6) δppm : 1.02-1.42 (6H, m), 1.49-1.78 (7H, m), 1.96-2.06 (1H, m), 2.82-2.97 (2H, m), 3.04-3.25 (2H, m), 6.55-7.25 (3H, m), 7.30 (1H, s), 8.11 (1H, d, J = 2.1 Hz), 9.11-9.30 (1H, m), 9.70-9.88 (1H, m).	2 Hydrochloride
979		1H-NMR (DMSO-d6) δppm : 1.00-1.40 (6H, m), 1.45-1.78 (7H, m), 1.95-2.05 (1H, m), 2.82-2.95 (2H, m), 3.02-3.24 (2H, m), 3.78-4.47 (1H, br), 7.05 (1H, d, J = 2.2 Hz), 7.19 (1H, d, J = 1.7 Hz), 7.44 (1H, d, J = 1.7 Hz), 8.12 (1H, d, J = 2.2 Hz), 9.15 (1H, brs), 9.66 (1H, brs).	2 Hydrochloride
980		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (1H, m), 1.12-1.84 (13H, m), 2.55-2.95 (4H, m), 3.10-4.75 (2H, br), 6.43 (3H, s), 7.34 (1H, dd, J = 2.1, 8.9 Hz), 7.53 (1H, d, J = 2.0 Hz), 7.68 (1H, d, J = 8.9 Hz), 8.03 (1H, d, J = 0.8 Hz).	Fumarate
981		1H-NMR (CDCl3) δppm : 0.96-1.15 (4H, m), 1.15-1.45 (6H, m), 1.48-1.80 (5H, m), 2.21-2.30 (1H, m), 2.62 (1H, d, J = 11.1 Hz), 2.75-2.85 (2H, m), 7.04 (1H, dd, J = 1.8, 11.8 Hz), 7.15 (1H, d, J = 1.8 Hz), 7.42 (1H, d, J = 2.5 Hz).	-
982		1H-NMR (CDCl3) δppm : 0.96-1.15 (4H, m), 1.15-1.40 (3H, m), 1.42 (3H, s), 1.55-1.70 (3H, m), 1.70-1.80 (2H, m), 2.23-2.35 (1H, m), 2.66 (1H, d, J = 11.1 Hz), 2.75-2.86 (2H, m), 4.01 (3H, s), 6.76 (1H, d, J = 1.7 Hz), 6.97 (1H, d, J = 1.7 Hz), 7.38 (1H, s).	-
983		1H-NMR (DMSO-d6) δppm : 0.99-1.42 (6H, m), 1.50-1.78 (7H, m), 1.72-2.05 (1H, m), 2.75-3.11 (3H, m), 3.16-3.40 (1H, br), 4.95-6.80 (1H, br), 6.95-7.11 (2H, m), 7.12-7.21 (1.25H, m), 7.33 (0.5H, s), 7.51 (0.25H, s), 8.08 (1H, brs), 9.05 (1H, brs), 9.64 (1H, brs).	2 Hydrochloride
984		1H-NMR (CDCl3) δppm : 0.99-1.12 (4H, m), 1.20-1.43 (7H, m), 1.62-1.83 (4H, m), 2.34-2.42 (1H, m), 2.70 (1H, d, J = 11.5 Hz), 2.76-2.85 (1H, m), 2.91 (1H, d, J = 11.5 Hz), 3.92 (3H, s), 6.45 (1H, d, J = 1.4 Hz), 6.80-6.83 (1H, m), 7.45 (1H, d, J = 0.9 Hz).	-
985		1H-NMR (CDCl3) δppm : 1.01-1.15 (4H, m), 1.20-1.45 (7H, m), 1.67-1.90 (4H, m), 2.44-2.53 (1H, m), 2.77-2.87 (2H, m), 2.98 (1H, d, J = 11.9 Hz), 6.74 (1H, dd, J = 1.6, 11.5 Hz), 6.90-6.94 (1H, m), 7.43 (1H, d, J = 0.9 Hz).	-

[0396]

Table 111

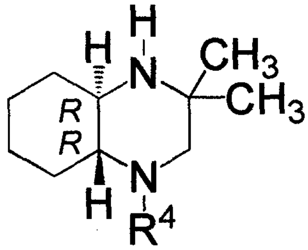
absolute configuration

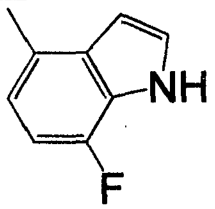
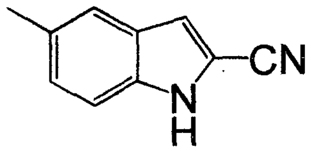
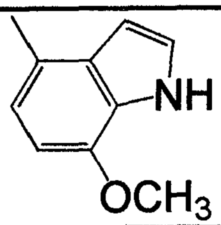
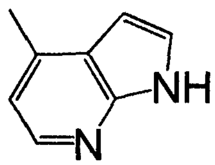
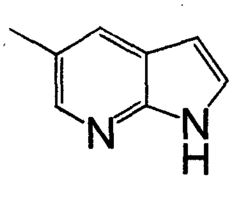
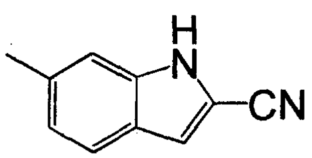


Example	R^4	NMR	Salt
986		1H-NMR (CDCl3) δppm : 0.83-1.44 (26H, m), 1.52 (3H, s), 1.55-1.90 (7H, m), 2.36-2.62 (2H, m), 2.80-3.00 (2H, m), 6.69-6.84 (3H, m), 7.24 (1H, d, J = 3.2 Hz).	-
987		1H-NMR (CDCl3) δppm : 0.80-1.38 (26H, m), 1.42 (3H, s), 1.58-1.77 (4H, m), 2.01 (3H, sextet, J = 7.5 Hz), 2.25-2.34 (1H, m), 2.65 (1H, d, J = 11.2 Hz), 2.75-2.85 (2H, m), 7.11 (1H, dd, J = 2.1, 9.1 Hz), 7.32 (1H, d, J = 2.1 Hz), 7.33 (1H, d, J = 0.5 Hz), 7.50 (1H, d, J = 9.1 Hz).	-
988		1H-NMR (CDCl3) δppm : 0.76-1.40 (26H, m), 1.52 (3H, s), 1.56-1.94 (7H, m), 2.35-2.64 (2H, m), 2.79-3.01 (2H, m), 3.88 (3H, s), 6.54 (1H, d, J = 8.1 Hz), 6.69 (1H, d, J = 3.1 Hz), 6.74 (1H, d, J = 8.1 Hz), 7.24 (1H, d, J = 3.2 Hz).	-
989		1H-NMR (CDCl3) δppm : 0.95-1.20 (22H, m), 1.20-1.45 (3H, m), 1.52 (3H, s), 1.62-1.90 (7H, m), 2.10-2.20 (1H, m), 2.57-2.68 (2H, m), 2.83-2.95 (1H, m), 3.26 (1H, d, J = 11.7 Hz), 6.55 (1H, d, J = 3.5 Hz), 6.63 (1H, d, J = 5.2 Hz), 7.18 (1H, d, J = 3.5 Hz), 8.12 (1H, d, J = 5.2 Hz).	-
990		1H-NMR (CDCl3) δppm : 0.96-1.17 (23H, m), 1.17-1.40 (3H, m), 1.42 (3H, s), 1.55-1.66 (2H, m), 1.66-1.76 (2H, m), 1.84 (3H, quint, J = 7.5 Hz), 2.28-2.37 (1H, m), 2.72(1H, d, J = 11.2 Hz), 2.76-2.85 (2H, m), 6.47 (1H, d, J = 3.4 Hz), 7.27 (1H, d, J = 3.4 Hz), 7.61 (1H, d, J = 2.4 Hz), 8.06 (1H, d, J = 2.4 Hz).	-
991		1H-NMR (CDCl3) δppm : 0.89-1.40 (26H, m), 1.43 (3H, s), 1.60-1.80 (4H, m), 1.95-2.07 (3H, m), 2.30-2.40 (1H, m), 2.58 (1H, d, J = 11.3 Hz), 2.80-2.90 (2H, m), 6.98 (1H, d, J = 1.6, 8.5 Hz), 7.31 (1H, s), 7.34 (1H, d, J = 0.6 Hz), 7.52 (1H, d, J = 8.5 Hz).	-

[0397]
Table 112

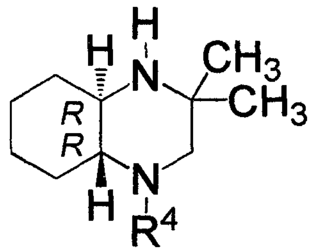
absolute configuration

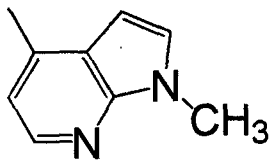
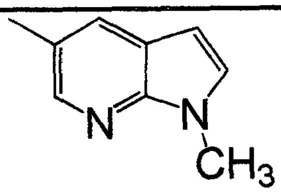


Example	R4	NMR	Salt
992		1H-NMR (DMSO-d6) δppm : 0.77-0.92 (1H, m), 0.95 (3H, s), 1.09-1.35 (3H, m), 1.40 (3H, s), 1.46-1.57 (2H, m), 1.58-1.83 (3H, m), 2.29-2.47 (2H, m), 2.60-2.85 (2H, m), 6.47 (1H, brs), 6.58-6.65 (1H, m), 6.81 (1H, dd, J = 8.3, 11.0 Hz), 7.30 (1H, t, J = 2.7 Hz), 11.47 (1H, s).	-
993		1H-NMR (DMSO-d6) δppm : 0.83-1.00 (4H, m), 1.08-1.34 (6H, m), 1.41-1.67 (5H, m), 2.19-2.27 (1H, m), 2.55 (1H, d, J = 10.8 Hz), 2.59-2.69 (2H, m), 7.11 (1H, dd, J = 1.8, 8.8 Hz), 7.26 (1H, d, J = 0.8 Hz), 7.32 (1H, d, J = 1.8 Hz), 7.37 (1H, d, J = 8.8 Hz), 12.25 (1H, brs).	-
994		1H-NMR (CDCl3) δppm : 0.75-0.99 (4H, m), 1.08-1.90 (11H, m), 2.20-2.45 (2H, m), 2.58-2.86 (2H, m), 3.86 (3H, s), 6.38 (1H, brs), 6.47-6.66 (2H, m), 7.13 (1H, t, J = 2.5 Hz), 11.07 (1H, s).	-
995		1H-NMR (DMSO-d6) δppm : 0.95-1.09 (1H, m), 1.21 (3H, s), 1.25-1.65 (7H, m), 1.69-1.79 (1H, m), 1.86-2.03 (2H, m), 2.88 (1H, d, J = 12.4 Hz), 2.96-3.21 (3H, m), 6.39 (1H, d, J = 2.6 Hz), 6.49 (2H, s), 6.72 (1H, d, J = 5.3 Hz), 7.33-7.38 (1H, m), 8.09 (1H, d, J = 5.3 Hz), 8.35-11.15 (1H, br), 11.58 (1H, s).	Fumarate
996		1H-NMR (DMSO-d6) δppm : 0.95-1.10 (1H,m), 1.10-1.23 (1H, m), 1.23-1.38 (4H, m), 1.38-1.60 (6H, m), 1.63-1.75 (1H,m), 1.84-1.95 (1H, m), 2.72-2.85 (2H,m), 3.00-3.13 (2H, m), 6.38-6.43 (1H, m), 6.50 (1H, s), 7.43-7.48 (1H, m), 7.75 (1H, d, J = 1.9 Hz), 7.99 (1H, d, J = 2.2 Hz), 8.35-11.30 (2H, br), 11.61 (1H, s).	1/2 Fumarate
997		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (4H, m), 1.10-1.36 (6H, m), 1.35-2.10 (5H, m), 2.25-2.35 (1H, m), 2.56 (1H, d, J = 11.0 Hz), 2.62-2.70 (1H, m), 2.75 (1H, d, J = 11.0 Hz), 6.91 (1H, dd, J = 1.2, 8.6 Hz), 7.02 (1H, s), 7.27 (1H, s), 7.55 (1H, d, J = 8.6 Hz) 11.93-12.33 (1H, br).	-

[0398]
Table 113

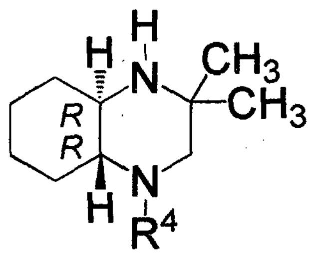
absolute configuration

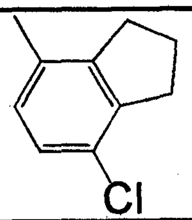
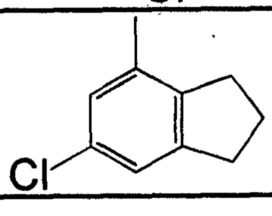


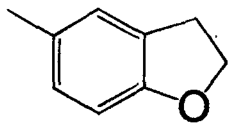
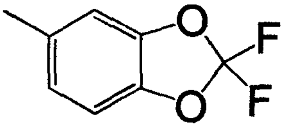
Example	R⁴	NMR	Salt
998		1H-NMR (CDCl3) δppm : 0.72-1.19 (5H, m), 1.25-1.45 (3H, m), 1.48 (3H, s), 1.65-1.82 (3H, m), 2.08-2.20 (1H, m), 2.65-2.80 (2H, m), 2.80-2.95 (1H, m), 3.27 (1H, d, J = 11.9 Hz), 3.85 (3H, s), 6.45 (1H, d, J = 3.5 Hz), 6.63 (1H, d, J = 5.3 Hz), 7.06 (1H, d, J = 3.5 Hz), 8.20 (1H, d, J = 5.3 Hz).	-
999		1H-NMR (DMSO-d6) δppm : 0.95-1.60 (11H, m), 1.60-1.83 (2H, m), 1.83-1.95 (1H, m), 2.65-2.83 (2H, m), 3.00-3.10 (2H, m), 3.79 (3H, s), 6.41 (1H, d, J = 3.4 Hz), 6.48 (2H, s), 7.50 (1H, d, J = 3.4 Hz), 7.77 (1H, d, J = 2.2 Hz), 8.04 (1H, d, J = 2.2 Hz), 8.35-10.85 (2H, br).	Fumarate

[0399]
Table 114

absolute configuration

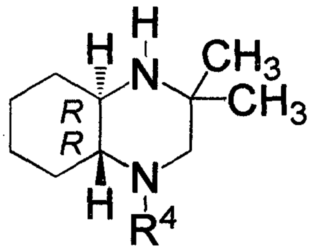


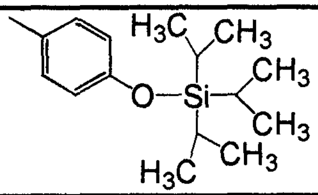
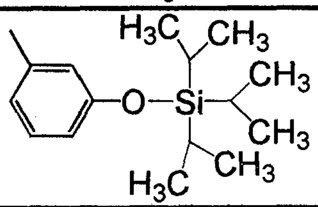
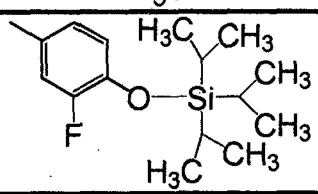
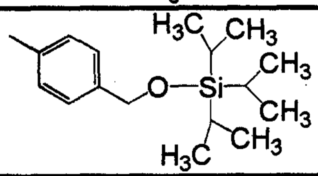
Example	R⁴	NMR	Salt
1000		1H-NMR (DMSO-d6) δppm : 0.87-1.00 (1H, m), 1.15-1.40 (5H, m), 1.50-1.78 (7H,m), 1.90-2.11 (3H, m), 2.65-2.80 (2H, m), 2.80-3.05 (5H, m), 3.09-3.25 (1H, m), 3.48 (1H, brs), 6.99 (1H, d, J = 8.3 Hz), 7.21 (1H, d, J = 8.3 Hz), 8.90-9.10 (1H, m), 9.40-9.64 (1H, m).	2 Hydrochloride
1001		1H-NMR (DMSO-d6) δppm : 0.89-1.04 (1H, m), 1.20-1.40 (5H, m), 1.46-1.78 (7H,m), 1.88-2.09 (3H, m), 2.64-3.00 (7H, m), 3.05-3.25 (1H, m), 3.25-3.50 (1H, br), 6.96 (1H, s), 7.12 (1H, s), 8.70-9.10 (1H, brs), 9.15-9.55 (1H, brs).	2 Hydrochloride

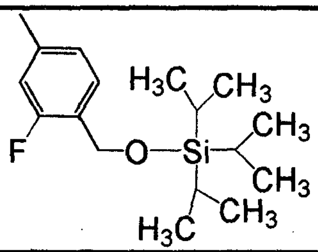
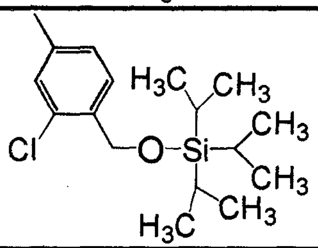
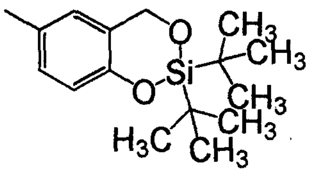
1002		1H-NMR (DMSO-d6) δppm : 0.90-1.21 (2H, m), 1.22-1.43 (4H, m), 1.43-1.80 (7H, m), 1.90-2.10 (1H, m), 2.58-3.40 (6H, m), 4.52 (2H, t, J = 8.6 Hz), 5.35-6.40 (1H, br), 6.55-7.60 (3H, m), 8.60-10.20 (2H, br).	2 Hydrochloride
1003		1H-NMR (DMSO-d6) δppm : 0.98-1.13 (1H, m), 1.13-1.40 (5H, m), 1.47-1.65 (6H, m), 1.65-1.77 (1H, m), 1.91-2.06 (1H, m), 2.74-2.90 (2H, m), 2.99 (1H, d, J = 12.5 Hz), 3.08-3.21 (1H, m), 4.05-5.00 (1H, br), 6.95 (1H, dd, J = 2.0, 8.6 Hz), 7.26 (1H, d, J = 2.0 Hz), 7.36 (1H, d, J = 8.6 Hz), 8.94-9.20 (1H, br), 9.55-9.85 (1H, br).	2 Hydrochloride

[0400]
Table 115

absolute configuration

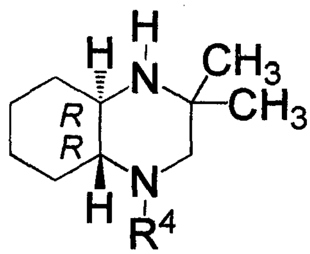


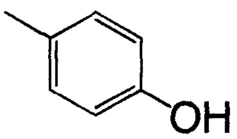
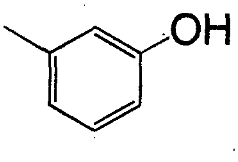
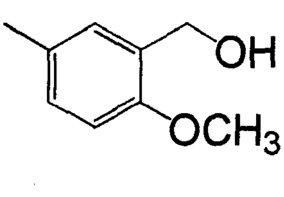
Example	R^4	NMR	Salt
1004		1H-NMR (CDCl3) δppm : 0.78-1.04 (2H, m), 1.04-1.14 (21H, m), 1.15-1.35 (6H, m), 1.38 (3H, s), 1.51-1.75 (4H, m), 2.12-2.20 (1H, m), 2.58 (1H, d, J = 11.1 Hz), 2.69-2.78 (2H, m), 6.76-6.81 (2H, m), 6.92-6.97 (2H, m).	-
1005		1H-NMR (CDCl3) δppm : 0.85-1.15 (23H, m), 1.15-1.37 (6H, m), 1.38 (3H, s), 1.60-1.77 (4H, m), 2.20-2.29 (1H, m), 2.58 (1H, d, J = 11.3 Hz), 2.72-2.82 (2H, m), 6.60-6.65 (2H, m), 6.65-6.70 (1H, m), 7.07-7.13 (1H, m).	-
1006		1H-NMR (CDCl3) δppm : 0.75-1.13 (23H, m), 1.13-1.39 (9H, m), 1.50-1.75 (4H, m), 2.08-2.18 (1H, m), 2.55 (1H, d, J = 11.2 Hz), 2.69-2.78 (2H, m), 6.68-6.74 (1H, m), 6.77-6.86 (2H, m).	-
1007		1H-NMR (CDCl3) δppm :0.92-1.38 (29H, m), 1.39 (3H, s), 1.58-1.76 (4H, m), 2.23-2.31 (1H, m), 2.61 (1H, d, J = 11.3 Hz), 2.71-2.82 (2H, m), 4.79 (2H, s), 7.02-7.08 (2H, m), 7.22-7.31 (2H, m).	-

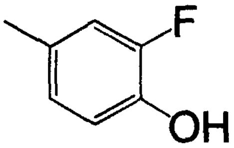
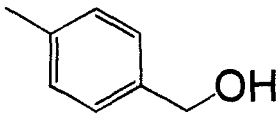
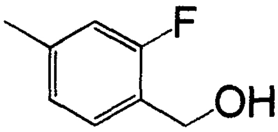
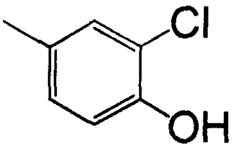
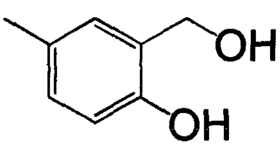
1008		1H-NMR (CDCl3) δppm :0.72-1.35 (29H, m), 1.36 (3H, s), 1.60-1.78 (4H, m), 2.21-2.30 (1H, m), 2.60 (1H, d, J = 12.1 Hz), 2.71-2.84 (2H, m), 5.30 (2H, s), 6.72 (1H, dd, J = 2.0, 12.0 Hz), 6.86 (1H, J = 2.0, 8.2 Hz), 7.44 (1H, t, J = 8.4 Hz).	-
1009		1H-NMR (CDCl3) δppm :0.72-1.39 (32H, m), 1.52-1.75 (4H, m), 2.08-2.18 (1H, m), 2.56 (1H, d, J = 11.1 Hz), 2.67-2.77 (2H, m), 6.80 (1H, d, J = 8.6 Hz), 6.84 (1H, dd, J = 2.4, 8.6 Hz), 7.08 (1H, d, J = 2.4 Hz).	-
1010		1H-NMR (CDCl3) δppm : 0.86-1.09 (23H, m), 1.09-1.36 (3H, m), 1.37 (3H, s), 1.50-1.75 (4H, m), 2.11-2.19 (1H, m), 2.57 (1H, d, J = 11.1 Hz), 2.67-2.77 (2H, m), 4.95 (2H, s), 6.67 (1H, d, J = 2.5 Hz), 6.82 (1H, d, J = 8.5 Hz), 6.91 (1H, dd, J = 2.5, 8.5 Hz).	-

[0401]
Table 116

absolute configuration

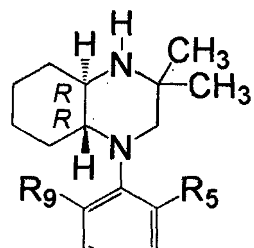


Example	R^4	NMR	Salt
1011		1H-NMR (CDCl3) δppm : 0.92-1.06 (1H, m), 1.09 (3H, s), 1.12-1.39 (3H, m), 1.41 (3H, s), 1.55-1.66 (2H, m), 1.66-1.79 (2H, m), 2.17-2.25 (1H, m), 2.61 (1H, d, J = 11.3 Hz), 2.70-2.83 (2H, m), 3.53-4.70 (2H, br), 6.73-6.79 (2H, m), 6.94-7.01 (2H, m).	-
1012		1H-NMR (DMSO-d6) δppm : 0.82-1.00 (4H, m), 1.09-1.35 (6H, m), 1.40-1.52 (1H, m), 1.52-1.70 (4H, m), 2.15-2.25 (1H, m), 2.44-2.55 (1H, m), 2.55-2.64 (1H, m), 2.66 (1H, d, J = 12.2 Hz), 6.39-6.51 (3H, m), 6.99-7.09 (1H, m), 9.21 (1H, s).	-
1013		1H-NMR (DMSO-d6) δppm : 0.90-1.03 (1H, m), 1.05-1.53 (10H, m), 1.53-1.62 (1H, m), 1.62-1.74 (1H, m), 1.80-1.90 (1H,m), 2.48-2.59 (1H, m), 2.68 (1H, J = 11.8 Hz), 2.84 (1H, d, J = 11.8 Hz), 2.90-3.01 (1H, m), 3.74 (3H, s), 4.45 (2H, s), 6.45 (1H, s), 6.86 (1H, d, J = 8.6 Hz), 6.94 (1H, dd, J = 2.5, 8.6 Hz), 7.15 (1H, d, J = 2.5 Hz), 8.10-10.15 (1H, br).	1/2 Fumarate

1014		1H-NMR (DMSO-d6) δppm : 0.83-1.00 (4H, m), 1.05-1.31 (6H, m), 1.40-1.51 (1H, m), 1.51-1.65 (3H, m), 2.05-2.14 (1H, m), 2.47 (1H, d, J = 10.8 Hz), 2.53-2.62 (2H, m), 3.10-3.60 (1H, br), 6.67-6.73 (1H, m), 6.79-6.87 (2H, m), 9.00-10.10 (1H, m).	-
1015		1H-NMR (CDCl3) δppm : 0.84-1.12 (5H, m), 1.16-1.45 (6H, m), 1.59-2.14 (5H, m), 2.25-2.35 (1H, m), 2.56-2.65 (1H, m), 2.72-2.85 (2H, m), 4.64 (2H, m), 7.07 (2H, dd, J = 1.3, 8.1 Hz), 7.29 (2H, d, J = 8.1 Hz).	-
1016		1H-NMR (CDCl3) δppm : 0.95-1.44 (11H, m), 1.44-2.22 (5H, m), 2.26-2.35 (1H, m), 2.62 (1H, d, J = 11.4 Hz), 2.72-2.87 (2H, m), 4.69 (2H, s), 6.75 (1H, dd, J = 2.0, 12.0 Hz), 6.81 (1H, dd, J = 2.0, 8.1 Hz), 7.29 (1H, t, J = 8.4 Hz).	-
1017		1H-NMR (CDCl3) δppm : 0.89-1.12 (4H, m), 1.14-1.43 (6H, m), 1.53-1.77 (4H, m), 2.12-2.21 (1H, m), 2.57 (1H, d, J = 11.2 Hz), 2.67-2.80 (2H, m), 2.80-3.30 (2H, br), 6.89-6.96 (2H, m), 7.05-7.09 (1H, m).	-
1018		1H-NMR (DMSO-d6) δppm : 0.78-0.94 (1H, m), 0.95 (3H, s), 1.04-1.32 (6H, m), 1.39-1.66 (5H, m), 2.05-2.15 (1H, m), 2.45-2.62 (3H, m), 4.43 (2H, s), 4.70-5.15 (1H, br), 6.65 (1H, d, J = 8.4 Hz), 6.74 (1H, dd, J = 2.5, 8.4 Hz), 7.03 (1H, d, J = 2.5 Hz), 8.80-9.30 (1H, br).	-

[0402]
Table 117

absolute configuration



Example	R^5	R^6	R^7	R^8	R^9	NMR	Salt

1019	-CH3	-H	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.88-1.03 (1H, m), 1.10-1.25 (1H, m), 1.25-1.40 (4H, m), 1.45-1.66 (6H, m), 1.67-1.89 (1H, m), 1.92-2.03 (1H, m), 2.26 (3H, m), 2.65 (1H, d, J = 12.5 Hz), 2.80 (1H, d, J = 12.5 Hz), 2.88-3.00 (1H, m), 3.15-3.28 (1H, m), 7.06-7.17 (2H, m), 7.19-7.26 (2H, m), 9.04 (1H, brs), 9.58 (1H, brs).	Hydrochloride
1020	-CH3	-CH3	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 0.89-1.02 (1H, m), 1.09-1.23 (1H, m), 1.24-1.40 (4H, m), 1.40-1.66 (6H, m), 1.67-1.76 (1H, m), 1.93-2.02 (1H, m), 2.21 (3H, s), 2.22 (3H, s), 2.60 (1H, d, J = 12.5 Hz), 2.76-2.95 (2H, m), 3.15-3.35 (1H, m),6.97-7.03 (2H, m), 7.07-1.15 (1H, m), 9.07 (1H, brs), 9.61 (1H, brs).	Hydrochloride
1021	-H	-F	-CN	-H	-H	1H-NMR (DMSO-d6) δppm : 1.21-1.65 (10H, m), 1.65-1.84 (2H, m), 1.90-2.00 (1H, m), 2.10-2.20 (1H, m), 3.38-3.61 (3H, m), 3.78 (1H, d, J = 14.5 Hz), 6.83 (1H, dd, J = 2.3, 8.9 Hz), 6.97 (1H, dd, J = 2.0, 13.7 Hz), 7.65 (1H, t, J = 8.5 Hz), 8.93-9.15 (1H, m), 9.51-9.71 (1H, m).	Fumarate

1022	-H	-H	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.15 (1H, m), 1.15-1.40 (5H, m), 1.50-1.67 (6H,m), 1.67-1.77 (1H, m), 1.95-2.05 (1H, m), 2.80-2.95 (2H, m), 3.01 (1H, d, J = 12.4 Hz), 3.11-3.25 (1H, m), 5.15-5.32 (1H, br), 7.20-7.27 (2H, m), 7.31-7.37 (2H, m), 9.10 (1H, brs), 9.68 (1H, brm).	2 Hydrochloride
1023	-H	-F	-OCF3	-H	-H	1H-NMR (DMSO-d6) δppm : 1.04-1.20 (1H, m), 1.20-1.41 (5H, m), 1.479-1.78 (7H, m), 1.97-2.07 (1H, m), 2.86-3.11 (3H, m), 3.15-3.27 (1H, m), 4.45-6.85 (1H, br), 7.00-7.16 (1H, m), 7.22-7.29 (1H, m), 7.46-7.55 (1H, m), 9.12 (1H, brs), 9.77 (1H, brs).	2 Hydrochloride
1024	-H	-H	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.40 (6H, m), 1.49-1.77 (7H, m), 1.95-2.06 (1H, m), 2.76-2.95 (2H, m), 3.03 (1H, d, J = 12.3 Hz), 3.10-3.23 (1H, m), 6.20-6.90 (1H, br), 7.01 (0.25H, s), 7.13-7.23 (4.5H, m), 7.38 (0.25H, s), 9.17 (1H, brs), 9.74 (1H, brm).	2 Hydrochloride

1025	-H	-F	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm :1.03-1.40 (6H, m), 1.50-1.67 (6H, m), 1.67-1.77 (1H, m), 1.96-2.05 (1H, m), 2.81-2.95 (2H, m), 3.02 (1H, d, J = 12.5 Hz), 3.10-3.23 (1H, m), 3.88-4.20 (1H, br), 6.96-7.01 (1H, m), 7.02 (0.25H, s), 7.17 (1H, dd, J = 2.5, 12.1 Hz), 7.20 (0.5H, s), 7.33 (1H, t, J = 8.9 Hz), 7.39 (0.25H, s), 9.08-9.22 (1H, m), 9.70-9.88 (1H, m).	2 Hydrochloride
1026	-H	-Cl	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.15 (1H, m), 1.15-1.41 (5H, m), 1.50-1.67 (6H, m), 1.67-1.78 (1H, m), 1.93-2.04 (1H, m), 2.78-2.95 (2H, m), 2.95-3.06 (1H, m), 3.10-3.25 (1H, m), 3.50-4.05 (1H, br), 7.15 (1H, dd, J = 2.5, 8.8 Hz), 7.24 (1H, t, J = 73.3 Hz), 7.32 (1H, d, J = 2.5 Hz), 7.34 (1H, d, J = 8.8 Hz), 8.90-9.20 (1H, br), 9.44-9.75 (1H, br).	2 Hydrochloride
1027	-H	-OCHF2	-H	-H	-H	1H-NMR (DMSO-d6) δppm : 1.01-1.15 (1H, m), 1.15-1.42 (5H, m), 1.50-1.68 (6H, m), 1.68-1.78 (1H, m), 1.96-2.06 (1H, m), 2.83-2.96 (2H, m), 3.03 (1H, d, J = 12.7 Hz), 3.10-3.25 (1H, m), 6.89 (1H, s), 6.96 (1H, dd, J = 2.1, 8.1 Hz), 7.00 (1H, d, J = 8.1 Hz), 7.27 (1H, t, J = 74.1 Hz), 7.39 (1H, t, J = 8.1 Hz), 7.85-8.90 (1H, br), 9.00-9.25 (1H, br), 9.65-9.85 (1H, br).	2 Hydrochloride

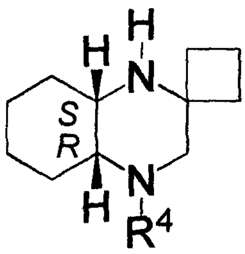
1028	-H	-OCHF2	-Cl	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.41 (6H, m), 1.49-1.80 (7H, m), 1.91-2.07 (1H,m), 2.78-2.90 (1H, m), 2.90-3.05 (2H, m), 3.10-3.27 (1H, m), 3.90-4.65 (1H, br), 7.01-7.08 (2H, m), 7.32 (1H, t, J = 73,3 Hz), 7.54 (1H, d, J = 8.4 Hz), 8.85-9.10 (1H, m), 9.39-9.70 (1H, m).	2 Hydrochloride
1029	-H	-OCHF2	-F	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.40 (6H, m), 1.47-1.65 (6H, m), 1.67-1.77 (1H, m), 1.90-2.00 (1H, m), 2.70-2.80 (1H, m), 2.87 (1H, d, J = 12.5 Hz), 2.96 (1H, d, J = 12.5 Hz), 3.10-3.24 (1H, m), 7.02-7.11 (2.25H, m), 7.27 (0.5H, s), 7.37 (1H, dd, J = 8.8, 10.5 Hz), 7.46 (0.25H, s), 8.80-9.00 (1H, br), 9.39-9.58 (1H, br).	Hydrochloride
1030	-H	-CN	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.02-1.15 (1H, m), 1.17-1.40 (5H, m), 1.48-1.81 (7H, m), 1.93-2.07 (1H, m), 2.82-2.91 (1H, m), 2.94 (1H, d, J = 12.6 Hz), 3.01 (1H, d, J = 12.6 Hz), 3.08-3.25 (1H, m), 3.70-4.20 (1H, br), 7.39 (1H, t, J= 72.6 Hz), 7.42 (1H, d, J = 8.9 Hz), 7.51 (1H, dd, J = 2.7, 9.0 Hz), 7.69 (1H, d, J = 2.7 Hz), 8.90-9.10 (1H, br), 9.35-9.70 (1H, br).	2 Hydrochloride

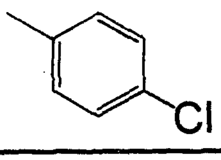
1031	-H	-F	-OCHF2	-F	-H	1H-NMR (DMSO-d6) δppm : 1.08-1.40 (6H, m), 1.43-1.80 (7H, m), 1.95-2.07 (1H, m), 2.88-2.99 (1H, m), 3.05 (1H, d, J = 13.1 Hz), 3.09 (1H, d, J = 13.1 Hz), 3.17-3.30 (1H, m), 3.48-3.70 (1H, br), 6.97-7.06 (2.25H, m), 7.19 (0.5H, s), 7.37 (0.25H, s), 8.81-9.04 (1H, br), 9.45-9.65 (1H, br).	2 Hydrochloride
1032	-H	-H	-OCH2CHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.98-1.85 (13H, m), 1.90-2.20 (1H, m), 2.60-3.80 (4H, m), 4.20-4.40 (2H, m), 4.40-5.40 (1H, br), 6.38 (1H, tt, J = 3.4, 54.5 Hz), 6.85-7.70 (4H, brm), 8.84-10.40 (2H, br).	2 Hydrochloride
1033	-H	-F	OCH2CHF2	-H	-H	1H-NMR (CDCl3) δppm : 0.94-1.11 (4H, m), 1.14-1.41 (7H, m), 1.57-1.78 (4H, m), 2.13-2.22 (1H, m), 2.56 (1H, d, J = 11.1 Hz), 2.70-2.79 (2H, m), 4.21 (2H, dt, J = 4.2, 13.1 Hz), 6.08 (1H, tt, J = 4.2, 55.1 Hz), 6.77-6.83 (1H, m), 6.83-6.95 (2H, m).	-
1034	-H	Cl	OCH2CHF2	-H	-H	1H-NMR (CDCl3) δppm : 0.93-1.11 (4H, m), 1.15-1.41 (7H, m), 1.55-1.77 (4H, m), 2.14-2.23 (1H, m), 2.57 (1H, d, J = 11.0 Hz), 2.68-2.78 (2H, m), 4.20 (2H, dt, J = 4.2, 13.0 Hz), 6.12 (1H, tt, J = 4.2, 55.1 Hz), 6.87 (1H, d, J = 8.7 Hz), 6.96 (1H, dd, J = 2.5, 8.7 Hz), 7.13 (1H, d, J = 2.5 Hz).	

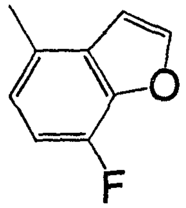
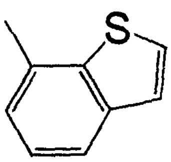
1035	-H	-CH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 0.97-1.10 (1H, m), 1.12-1.40 (5H, m), 1.47-1.63 (6H, m), 1.67-1.76 (1H, m), 1.90-2.01 (1H, m), 2.20 (3H, m), 2.70-2.80 (1H, m), 2.83 (1H, d, J = 12.3 Hz), 2.95 (1H, d, J = 12.3 Hz), 3.08-3.22 (1H, m), 4.60-5.40 (1H, br), 6.94 (0.25H, s), 6.99 (1H, dd, J = 2.5, 8.5 Hz), 7.05 (1H, d, J = 2.5 Hz), 7.09-7.15 (1.5H, m), 7.31 (0.25H, s), 8.85-9.01 (1H, m), 9.40-9.55 (1H, m).	2 Hydrochloride
1036	-H	-OCH3	-OCHF2	-H	-H	1H-NMR (DMSO-d6) δppm : 1.00-1.40 (6H, m), 1.50-1.80 (7H, m), 1.95-2.06 (1H, m), 2.75-2.94 (2H, m), 2.96-3.07 (1H, m), 3.09-3.22 (1H,m), 3.82 (3H, s), 6.08-6.65 (1H, br), 6.73 (1H, d, J = 8.2 Hz), 6.80-6.89 (1.25H, m), 7.01 (0.5H, s), 7.14 (1H, d, J = 8.4 Hz), 7.19 (0.25H, s), 9.09 (1H, brs), 9.72 (1H, brs).	2 Hydrochloride

[0403]
Table 118

absolute configuration

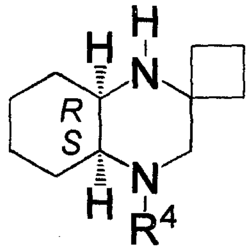


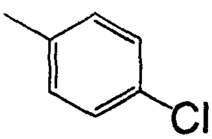
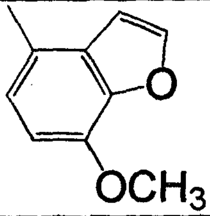
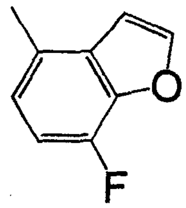
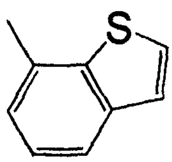
Example	R^4	NMR	Salt
1037		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (3H, m), 1.4-1.55 (1H, m), 1.55-1.95 (8H, m), 1.95-2.05 (2H, m), 2.68 (1H, d, J = 11.9Hz), 2.8-4.0 (5H, m), 6.55 (1H, s), 6.85-6.95 (2H, m), 7.14-7.22 (2H, m).	1/2 Fumarate

1038		1H-NMR (CDCl3) δppm : 0.95-1.15 (2H, m), 1.3-1.4 (1H, m), 1.4-2.1 (11H, m), 2.25-2.4 (1H, m), 3.04 (1H, d, J = 11.1Hz), 3.17 (1H, d, J = 10.9Hz), 3.41 (1H, br), 3.45-3.58 (1H, m), 6.54 (1H, dd, J = 3.3, 8.4Hz), 6.82 (1H, dd, J = 2.5, 2.5Hz), 6.91 (1H, dd, J = 8.6, 10.4Hz), 7.59 (1H, d, J = 2.1Hz).	-
1039		1H-NMR (DMSO-d6) δppm : 0.95-1.5 (3H, m), 1.5-1.7 (2H, m), 1.7-2.3 (6H, m), 2.3-2.7 (3H, m), 3.0-3.4 (1H, m), 3.59 (2H, br), 3.73 (1H, br), 7.07 (1H, br), 7.3-7.45 (1H, m), 7.48 (1H, d, J = 5.4Hz), 7.64 (1H, br), 7.75 (1H, d, J = 5.4Hz), 8.75-10.3 (2H, m).	Hydrochloride

[0404]
Table 119

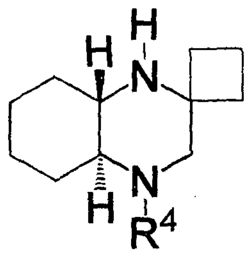
absolute configuration

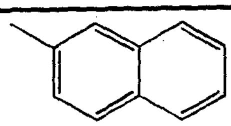


Example	R^4	NMR	Salt
1040		1H-NMR (DMSO-d6) δppm : 1.1-1.35 (3H, m), 1.4-1.55 (1H, m), 1.55-1.95 (8H, m), 1.95-2.05 (2H, m), 2.68 (1H, d, J = 11.9Hz), 2.8-4.0 (5H, m), 6.55 (1H, s), 6.85-6.95 (2H, m), 7.14-7.22 (2H, m).	1/2 Fumarate
1041		1H-NMR (CDCl3) δppm : 0.95-1.1 (2H, m), 1.3-1.4 (1H, m), 1,4-2.1 (11H, m), 2.25-2.4 (1H, m), 3.01 (1H, d, J = 11.0Hz), 3.17 (1H, d, J = 11.1Hz), 3.40 (1H, br), 3.45-3.5 (1H, m), 3.97 (3H, s), 6.58 (1H, d, J = 8.4Hz), 6.70 (1H, d, J = 8.4Hz), 6.80 (1H, d, J = 2.1Hz), 7.58 (1H, d, J = 2.1Hz).	-
1042		1H-NMR (CDCl3) δppm : 0.95-1.15 (2H, m), 1.3-1.4 (1H, m), 1.4-2.1 (11H, m), 2.25-2.4 (1H, m), 3.04 (1H, d, J = 11.1Hz), 3.17 (1H, d, J = 10.9Hz), 3.41 (1H, br), 3.45-3.58 (1H, m), 6.54 (1H, dd, J = 3.3, 8.4Hz), 6.82 (1H, dd, J = 2.5, 2.5Hz), 6.91 (1H, dd, J = 8.6, 10.4Hz), 7.59 (1H, d, J = 2.1Hz).	-
1043		1H-NMR (DMSO-d6) δppm : 0.95-1.5 (3H, m), 1.5-1.7 (2H, m), 1.7-2.3 (6H, m), 2.3-2.7 (3H, m), 3.0-3.4 (1H, m), 3.59 (2H, br), 3.73 (1H, br), 7.07 (1H, br), 7.3-7.45 (1H, m), 7.48 (1H, d, J = 5.4Hz), 7.64 (1H, br), 7.75 (1H, d, J = 5.4Hz), 8.75-10.3 (2H, m).	Hydrochloride

[0405]
Table 120

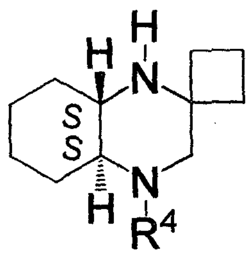
relative configuration

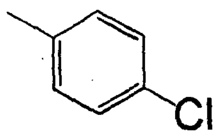
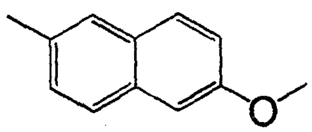
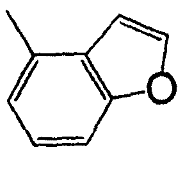


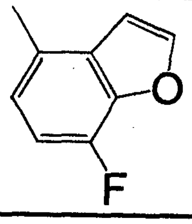
Example	R4	NMR	Salt
1044		1H-NMR (CDCl3) δppm : 0.90-2.30 (10H, m), 2.36-3.40 (7H, m), 3.50-3.70 (1H, m), 7.30-7.55 (3H, m), 7.55-7.75 (1H, m), 7.75-7.90 (3H, m), 9.75-10.40 (2H, br).	2 Hydrochloride

[0406]
Table 121

absolute configuration

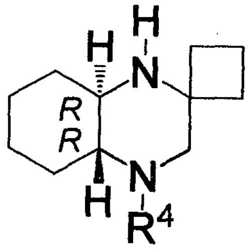


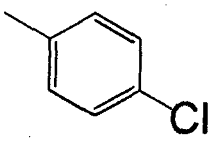
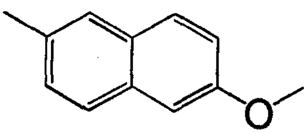
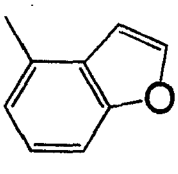
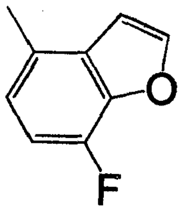
Example	R4	NMR	Salt
1045		1H-NMR (DMSO-d6) δppm : 0.85-1.0 (1H, m), 1.12-1.40 (2H, m), 1.42-1.63 (3H, m), 1.65-1.78 (1H, m), 1.84-1.97 (3H, m), 1.97-2.06 (1H, m).2.24-2.38 (2H, m), 2.39-2.49 (1H, m), 2.73-2.93 (2H, m), 3.03 (1H, d, J = 12.5Hz), 3.23 (1H, d, J = 12.5Hz), 3.6 (1H, br), 7.15-7.25 (2H, m), 7.37-7.46 (2H, m), 9.37 (1H, br), 9.87 (1H, br).	2 Hydrochloride
1046		1H-NMR (CDCl3) δppm : 0.95-1.1 (1H, m), 1.15-1.45 (3H, m), 1.45-1.95 (10H, m), 2.45-2.7 (3H, m), 2.80 (1H, dd, J = 1.7, 11.2Hz), 3.19 (1H, d, J = 11.1Hz), 3.91 (3H, s), 7.08-7.15 (2H, m), 7.29 (1H, dd, J = 2.1, 8.7Hz), 7.45 (1H, d, J = 2.0Hz), 7.63-7.71 (2H, m).	-
1047		1H-NMR (DMSO-d6) δppm : 0.85-1.1 (1H, m), 1.1-1.45 (2H, m), 1.45-1.65 (3H, m), 1.65-1.8 (1H, m), 1.8-2.0 (3H, m), 2.0-2.15 (1H, m), 2.25-2.65 (3H, m), 2.85-3.35 (2H, m), 3.6-4.35 (3H, m), 6.9-7.2 (2H, m), 7.31 (1H, dd, J = 8.0, 8.0Hz), 7.46 (1H, d, J = 8.2Hz), 8.00 (1H, d, J = 1.6Hz), 9.3-10.3 (2H, m).	2 Hydrochloride

1048		1H-NMR (DMSO-d6) δppm : 0.8-1.0 (1H, m), 1.1-1.6 (5H, m), 1.6-2.0 (5H, m), 2.1-2.5 (3H, m), 2.75-2.95 (2H, m), 2.95-3.13 (1H, m), 3.17 (1H, d, J = 12.6Hz), 6.56 (4H, s), 6.99-7.14 (2H, m), 7.20 (1H, dd, J = 8.6, 10.7Hz), 8.09 (1H, d, J = 2.0Hz), 11.4 (5H, br).	2 Fumarate

[0407]
Table 122

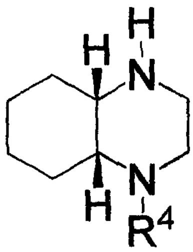
absolute configuration

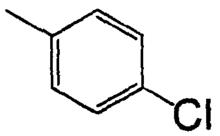
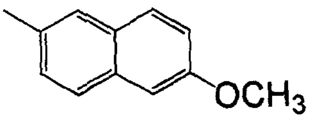
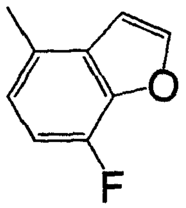
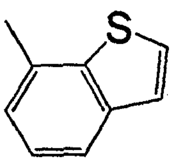
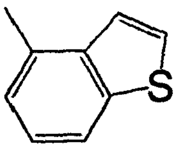
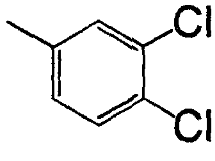


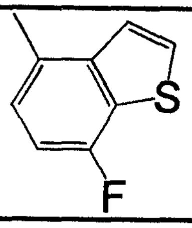
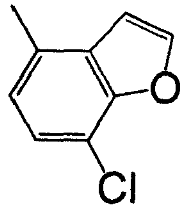
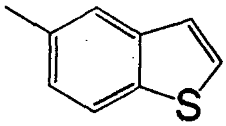
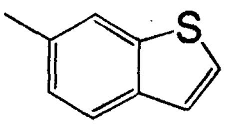
Example	R^4	NMR	Salt
1049		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (1H, m), 1.1-1.4 (2H, m), 1.4-1.65 (3H, m), 1.65-1.8 (1H, m), 1.8-2.0 (3H, m), 2.0-2.1 (1H, m), 2.25-2.4 (2H, m), 2.4-2.6 (1H, m), 2.75-2.95 (2H, m), 3.0-3.1 (1H, m), 3.23 (1H, d, J = 12.6Hz), 3.5-4.0 (1H, m), 7.15-7.25 (2H, m), 7.35-7.45 (2H, m), 9.3-9.6 (1H, m), 9.85-10.1 (1H, m).	2 Hydrochloride
1050		1H-NMR (CDCl3) δppm : 0.95-1.1 (1H, m), 1.1-1.45 (3H, m), 1.45-1.95 (10H, m), 2.45-2.7 (3H, m), 2.80 (1H, dd, J = 1.7, 11.2Hz), 3.19 (1H, d, J = 11.2Hz), 3.91 (3H, s), 7.07-7.15 (2H, m), 7.29 (1H, dd, J = 2.1, 8.7Hz), 7.45 (1H, d, J = 2.0Hz), 7.63-7.71 (2H, m).	-
1051		1H-NMR (DMSO-d6) δppm : 0.85-1.1 (1H, m), 1.1-1.4 (2H, m), 1.4-1.65 (3H, m), 1.65-1.8 (1H, m), 1.8-2.0 (3H, m), 2.0-2.15 (1H, m), 2.25-2.65 (3H, m), 2.8-3.45 (2H, m), 3.5-4.25 (3H, m), 6.9-7.2 (2H, m), 7.31 (1H, dd, J = 8.0, 8.0Hz), 7.46 (1H, d, J = 8.2Hz), 8.00 (1H, d, J = 1.8Hz), 9.3-10.3 (2H, m).	2 Hydrochloride
1052		1H-NMR (DMSO-d6) δppm : 0.8-0.95 (1H, m), 1.1-1.4 (3H, m), 1.45-1.6 (2H, m), 1.6-1.7 (1H, m), 1.7-1.9 (4H, m), 2.0-2.15 (1H, m), 2.15-2.3 (1H, m), 2.35-2.5 (1H, m), 2.65-2.85 (2H, m), 2.85-3.0 (1H, m), 3.13 (1H, d, J = 11.7Hz), 6.53 (3H, s), 7.0-7.1 (2H, m), 7.18 (1H, dd, J = 8.6, 10.8Hz), 8.07 (1H, d, J = 2.1Hz), 10.3 (4H, br).	1.5 Fumarate

[0408]
Table 123

relative configuration

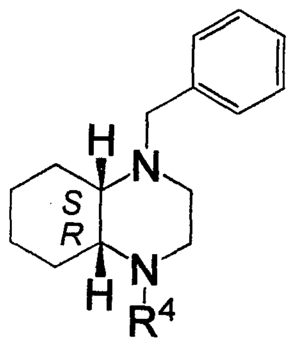


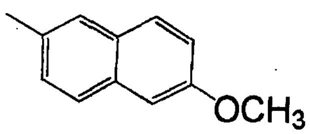
Example.	R^4	NMR	Salt
1053		1H-NMR (CDCl3) δppm : 1.14-1.29 (1H, m), 1.29-1.38 (1H, m), 1.38-1.58 (3H, m), 1.62-1.86 (4H, m), 2.95-3.05 (2H, m), 3.1-3.25 (3H, m), 3.6-3.7 (1H, m), 6.74-6.82 (2H, m), 7.14-7.21 (2H, m).	-
1054		1H-NMR (CDCl3) δppm : 1.14-1.36 (2H, m), 1.37-1.65 (3H, m), 1.65-1.77 (2H, m), 1.77-1.91 (2H, m), 3.01-3.17 (2H, m), 3.19-3.28 (3H, m), 3.75-3.83 (1H, m), 3.88 (3H, s), 6.97-7.11 (3H, m), 7.23-7.30 (1H, m), 7.57 (1H, d, J = 8.8Hz), 7.62 (1H, d, J = 9.0Hz).	-
1055		1H-NMR (DMSO-d6) δppm : 0.97-1.14 (2H, m), 1.32-1.43 (1H, m), 1.43-1.67 (2H, m), 1.68-2.03 (3H, m), 3.01-3.14 (2H, m), 3.25-3.43 (2H, m), 3.55-3.64 (1H, m), 3.66-3.77 (1H, m), 6.55 (4H, s), 6.68 (1H, br), 7.10 (1H, dd, J = 8.7, 10.7Hz), 7.22 (1H, br), 8.05 (1H, d, J = 2.2Hz), 11.27 (5H, br).	2 Fumarate
1056		1H-NMR (DMSO-d6) δppm : 0.95-1.15 (2H, m), 1.28-1.40 (1H, m), 1.43-1.72 (3H, m), 1.94 (2H, br), 2.90-3.12 (2H, m), 3.19-3.30 (1H, m), 3.34-3.57 (2H, m), 3.70-3.87 (1H, br), 6.53 (2H, s), 7.00 (1H, br), 7.34 (1H, dd, J = 7.7, 7.7Hz), 7.45 (1H, d, J = 5.4Hz), 7.5-7.65 (1H, m), 7.72 (1H, d, J = 5.4Hz), 10.5 (3H, br).	Fumarate
1057		1H-NMR (CDCl3) δppm : 0.96-1.18 (2H, m), 1.33-1.72 (5H, m), 1.72-1.91 (1H, m), 1.92-2.07 (1H, m), 2.82-2.92 (1H, m), 3.03-3.17 (1H, m), 3.17-3.27 (1H, m), 3.38 (1H, br), 3.42-3.52 (1H, m), 3.52-3.61 (1H, m), 6.85 (1H, d, J = 7.6Hz), 7.21-7.28 (1H, m), 7.37 (1H, d, J = 5.5Hz), 7.40-7.47 (1H, m), 7.52 (1H, d, J = 8.0Hz).	-
1058		1H-NMR (DMSO-d6) δppm : 1.26-1.42 (2H, m), 1.42-1.63 (2H, m), 1.63-1.91 (3H, m), 1.91-2.04 (1H, m), 3.01-3.18 (2H, m), 3.24-3.42 (1H, m), 3.47-3.55 (1H, m), 3.55-3.65 (1H, m), 4.06-4.19 (1H, m), 6.95 (1H, dd, J = 2.9, 9.0Hz), 7.18 (1H, d, J = 2.9Hz), 7.43 (1H, d, J = 9.0Hz). 9.00 (1H, br), 9.62 (1H, br).	Hydrochloride

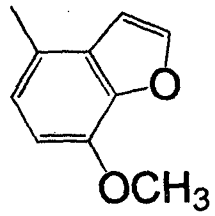
1059		1H-NMR (DMSO-d6) δppm : 0.9-1.15 (2H, m), 1.25-1.4 (1H, m), 1.4-1.7 (3H, m), 1.91 (2H, br), 2.82-2.92 (1H, m), 2.97-3.10 (1H, m), 3.15-3.60 (7H, m), 6.52 (2H, s), 6.94 (1H, br), 7.15 (1H, dd, J = 8.9, 8.9Hz), 7.59 (1H, br), 7.83 (1H, d, J = 5.3Hz).	Fumarate
1060		1H-NMR (DMSO-d6) δppm : 1.0-1.15 (2H, m), 1.28-1.40 (1H, m), 1.4-1.65 (2H, m), 1.65-1.77 (1H, m), 1.78-1.98 (2H, m), 2.95-3.15 (2H, m), 3.15-3.25 (1H, m), 3.25-3.4 (1H, m), 3.43 (1H, br), 3.7-3.8 (1H, m), 6.53 (2H, s), 6.68 (1H, d, J = 8.5Hz), 7.19 (1H, bs), 7.26 (1H, d, J = 8.4Hz), 8.04 (1H, d, J = 2.2Hz).	Fumarate
1061		1H-NMR (DMSO-d6) δppm : 1.17-1.32 (2H, m), 1.34-1.56 (2H, m), 1.59-1.85 (3H, m), 1.86-1.96 (1H, m), 2.95-3.14 (2H, m), 3.23-3.40 (3H, m), 3.90-3.99 (1H, m), 6.51 (2H, s), 7.13 (1H, dd, J = 2.3, 8.9Hz), 7.27-7.34 (2H, m), 7.66 (1H, d, J = 5.4Hz), 7.80 (1H, d, J = 8.9Hz).	Fumarate
1062		1H-NMR (DMSO-d6) δppm : 1.16-1.40 (3H, m), 1.40-1.55 (1H, m), 1.57-1.73 (2H, m), 1.73-1.87 (2H, m), 2.85-3.03 (3H, m), 3.04-3.83 (4H, m), 3.85-3.93 (1H, m), 6.49 (1H, s), 7.09 (1H, dd, J = 2.2, 8.9Hz), 7.25 (1H, d, J = 5.3Hz), 7.35-7.41 (2H, m), 7.67 (1H, d, J = 8.8Hz).	1/2 Fumarate

[0409]
Table 124

absolute configuration

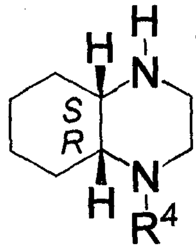


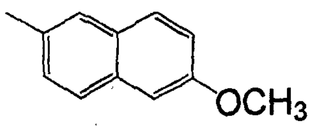
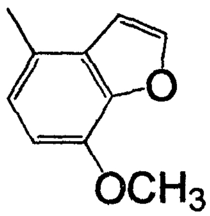
Example.	R^4	NMR	Salt
1063		1H-NMR (CDCl3) δppm : 1.23-1.43 (3H m), 1.44-1.57 (1H, m), 1.58-1.72 (1H, m), 1.74-1.84 (1H, m), 2.08-2.27 (2H, m), 2.33-2.42 (1H, m), 2.72-2.79 (1H, m), 2.86-2.93 (1H, m), 2.97 (1H, d, J = 13.2Hz); 3.14-3.25 (2H, m), 3.81-3.90 (4H, m), 4.22 (1H, d, J = 13.1Hz), 6.97 (1H, bs), 7.02-7.09 (2H, m), 7.22-7.30 (2H, m), 7.31-7.38 (2H, m), 7.38-7.43 (2H, m), 7.55 (1H, d, J = 8.7Hz), 7.61 (1H, d, J = 9.0Hz).	-

1064		1H-NMR (CDCl3) δppm : 1.0-1.2 (2H, m), 1.2-1.4 (1H, m), 1.4-1.9 (3H, m), 2.0-2.5 (3H, m), 2.75-3.2 (4H, m), 3.38 (1H, br), 3.60 (1H, br), 3.96 (3H, s), 4.19 (1H, br), 6.54 (1H, br), 6.68 (1H, d, J = 8.2Hz), 6.82 (1H, br), 7.22-7.29 (1H, m), 7.29-7.38 (2H, m), 7.38-7.44 (2H, m), 7.58 (1H, d, J = 2.2Hz).	-

[0410]
Table 125

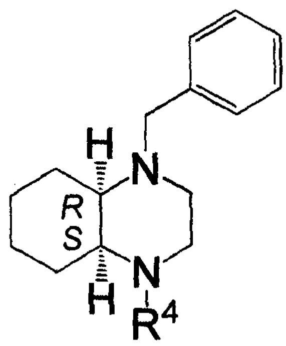
absolute configuration

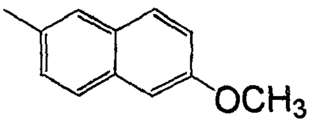
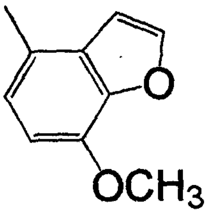


Example.	R^4	NMR	Salt
1065		1H-NMR (CDCl3) δppm : 1.15-1.56 (5H, m), 1.65-1.76 (2H, m), 1.76-1.90 (2H, m), 3.01-3.18 (2H, m), 3.20-3.28 (3H, m), 3.76-3.83 (1H, m), 3.88 (3H, s), 7.01 (1H, d, J = 2.4Hz), 7.04 (1H, d, J = 2.5Hz), 7.07 (1H, dd, J = 2.6, 8.8Hz), 7.25 (1H, dd, J = 2.5, 9.0Hz), 7.57 (1H, d, J = 8.8Hz), 7.62 (1H, d, J =9.0Hz).	-
1066		1H-NMR (DMSO-d6) δppm : 0.93-1.22 (2H, m), 1.33-1.47 (1H, m), 1.47-1.70 (1H, m), 1.70-1.94 (2H, m), 1.94-2.19 (1H, m), 2.88-3.22 (2H, m), 3.27-3.48 (2H, m), 3.59-3.78 (2H, m), 3.88 (3H, s), 6.69 (1H, br), 6.82 (1H, d, J = 8.3Hz), 7.13 (1H, d, J = 1.9Hz), 7.95 (1H, d, J = 2.1Hz), 8.5 (1H, br), 9.00 (1H, br), 9.68 (1H, br).	2 Hydrochloride

[0411]
Table 126

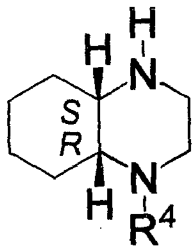
absolute configuration

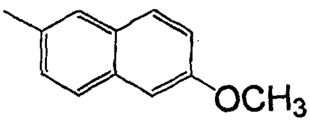
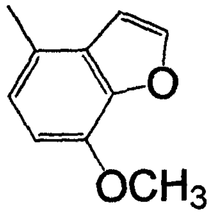


Example.	R⁴	NMR	Salt
1067		1H-NMR (CDCl3) δppm : 1.22-1.43 (3H m), 1.45-1.56 (1H, m), 1.58-1.72 (1H, m), 1.74-1.84 (1H, m), 2.08-2.27 (2H, m), 2.32-2.42 (1H, m), 2.73-2.79 (1H, m), 2.86-2.93 (1H, m), 2.97 (1H, d, J = 13.1Hz), 3.14-3.25 (2H, m), 3.8-3.9 (4H, m), 4.22 (1H, d, J = 13.2Hz), 6.97 (1H, bs), 7.02-7.09 (2H, m), 7.22-7.30 (2H, m), 7.31-7.37 (2H, m), 7.37-7.43 (2H, m), 7.55 (1H, d, J = 8.7Hz), 7.61 (1H, d, J = 9.0Hz).	-
1068		1H-NMR (CDCl3) δppm : 1.0-1.2 (2H, m), 1.2-1.4 (1H, m), 1.4-1.85 (3H, m), 2.05-2.5 (3H, m), 2.65-3.15 (4H, m), 3.2-3.5 (1H, m), 3.60 (1H, br), 3.96 (3H, s), 4.05-4.4 (1H, m), 6.54 (1H, br), 6.68 (1H, d, J = 8.2Hz), 6.82 (1H, br), 7.22-7.29 (1H, m), 7.29-7.38 (2H, m), 7.38-7.44 (2H, m), 7.58 (1H, d, J = 2.2Hz).	-

[0412]
Table 127

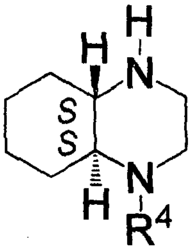
absolute configuration

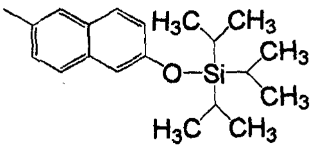
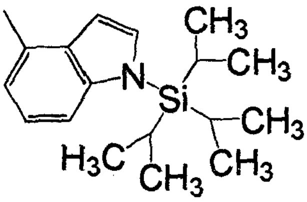
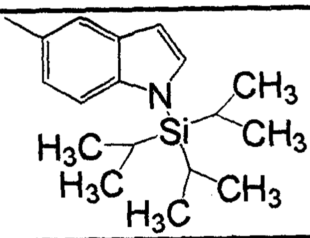
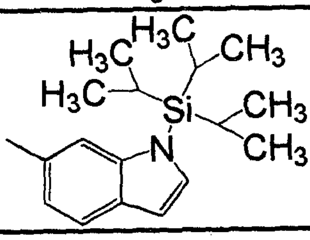


Example.	R⁴	NMR	Salt
1069		1H-NMR (CDCl3) δppm : 1.15-1.56 (5H, m), 1.65-1.76 (2H, m), 1.76-1.89 (2H, m), 3.00-3.20 (2H, m), 3.20-3.28 (3H, m), 3.76-3.83 (1H, m), 3.88 (3H, s), 7.01 (1H, d, J = 2.4Hz), 7.04 (1H, d, J = 2.4Hz), 7.07 (1H, dd, J = 2.6, 8.8Hz), 7.26 (1H, dd, J = 2.5, 9.0Hz), 7.57 (1H, d, J = 8.8Hz), 7.62 (1H, d, J =9.0Hz).	-
1070		1H-NMR (DMSO-d6) δppm : 0.94-1.19 (2H, m), 1.35-1.47 (1H, m), 1.47-1.70 (1H, m), 1.70-1.91 (2H, m), 1.91-2.18 (1H, m), 3.0-3.25 (2H, m), 3.25-3.55 (2H, m), 3.6-3.8 (2H, m), 3.88 (3H, s), 6.69 (1H, br), 6.82 (1H, d, J = 8.4Hz), 7.13 (1H, d, J = 2.2Hz), 7.95 (1H, d, J = 2.1Hz), 8.90 (1H, br), 9.56 (1H, br).	Hydrochloride

[0413]
Table 128

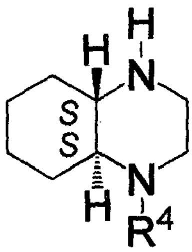
absolute configuration



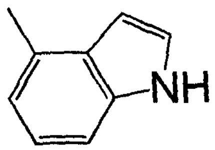
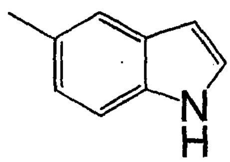
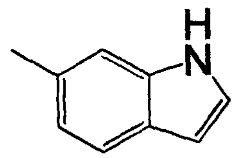
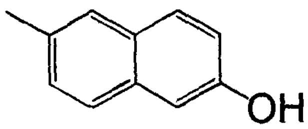
Example	R^4	NMR	Salt
1071		1H-NMR (CDCl3) δppm : 0.96-1.19 (19H, m), 1.19-1.41 (6H, m), 1.50-1.67 (2H, m), 1.67-1.82 (3H, m), 2.48-2.65 (2H, m), 2.94-3.09 (2H, m), 3.09-3.25 (2H, m), 7.09 (1H, dd, J = 2.4, 8.9 Hz), 7.17 (1H, d, J = 2.4 Hz), 7.28 (1H, dd, J = 2.1, 11.0 Hz), 7.45 (1H, d, J = 2.0 Hz), 7.59-7.66 (2H, m).	-
1072		1H-NMR (CDCl3) δppm : 0.95-1.09 (1H, m), 1.14 (18H, d, J = 7.5 Hz), 1.20-1.45 (3H, m), 1.48-1.85 (8H, m), 2.58-2.74 (2H, m), 2.90-3.00 (1H, m), 3.00-3.08 (1H, m), 3.17-3.30 (2H, m), 6.74 (1H, dd, J = 0.7, 3.2 Hz), 6.85 (1H, d, J = 7.3 Hz), 7.03-7.10 (1H, m), 7.17 (1H, d, J = 3.2 Hz), 7.26 (1H, d, J = 8.3 Hz).	-
1073		1H-NMR (CDCl3) δppm : 0.95-1.09 (1H, m), 1.09-1.42 (21H, m), 1.53-1.80 (8H, m), 2.41-2.50 (1H, m), 2.54-2.64 (1H, m), 2.95-3.10 (3H, m), 3.13-3.23 (1H, m), 6.56 (1H, d, J = 0.4, 3.1 Hz), 6.97 (1H, dd, J = 2.1, 8.8 Hz), 7.23 (1H, d, J = 3.1 Hz), 7.37-7.44 (2H, m).	-
1074		1H-NMR (CDCl3) δppm : 0.94-1.06 (1H, m), 1.05-1.25 (19H, m), 1.25-1.45 (2H, m), 1.53-1.80 (8H, m), 2.42-2.50 (1H, m), 2.55-2.65 (1H, m), 2.90-3.00 (1H, m), 3.00-3.13 (2H, m), 3.16-3.25 (1H, m), 6.56 (1H, dd, J = 0.7, 3.2 Hz), 6.97 (1H, dd, J = 1.7, 8.3 Hz), 7.20 (1H, d, J = 3.2 Hz), 7.32 (1H, s), 7.52 (1H, d, J = 8.3 Hz).	-

[0414]
Table 129

absolute configuration

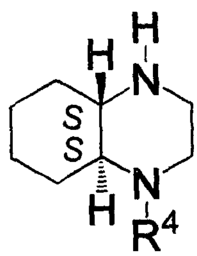


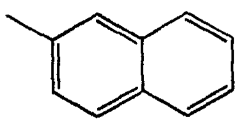
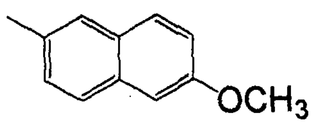
Example	R^4	NMR	Salt

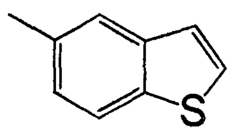
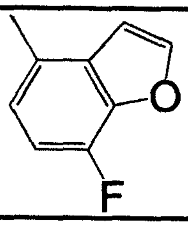
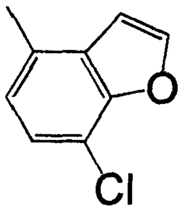
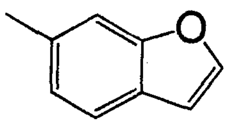
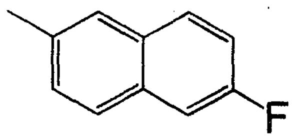
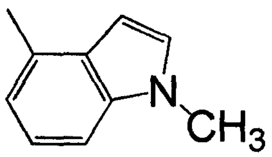
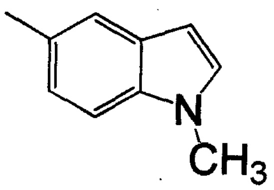
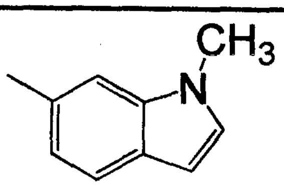
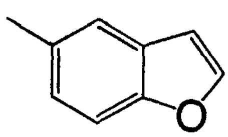
1075		1H-NMR (CDCl3) δppm : 0.95-1.09 (1H, m), 1.20-1.55 (4H, m), 1.55-1.63 (1H, m), 1.66-1.86 (3H, m), 2.59-2.77 (2H, m), 2.81-3.01 (1H, m), 3.01-3.09 (1H, m), 3.18-3.30 (2H, m), 6.66-6.71 (1H, m), 6.87 (1H, dd, J = 1.1, 7.2 Hz), 7.10-7.21 (3H, m), 8.25 (1H, brs).	-
1076		1H-NMR (CDCl3) δppm : 0.96-1.10 (1H, m), 1.10-1.43 (3H, m), 1.43-1.65 (3H, m), 1.65-1.84 (2H, m), 2.42-2.53 (1H, m), 2.53-2.66 (1H, m), 2.97-3.12 (3H, m), 3.15-3.26 (1H, m), 6.51 (1H, dd, J = 1.0, 2.1 Hz), 7.06 (1H, dd, J = 2.0, 8.6 Hz), 7.17-7.23 (1H, m), 7.32 (1H, d, J = 8.6 Hz), 7.44 (1H, d, J = 2.0 Hz), 8.36 (1H, brs).	-
1077		1H-NMR (DMSO-d6) δppm : 0.81-0.96 (1H, m), 1.06-1.35 (3H, m), 1.43-1.57 (2H, m), 1.58-1.74 (2H, m), 2.01 (1H, brs), 2.30-2.41 (2H, m), 2.75-2.97 (4H, m), 6.31-6.37 (1H, m), 6.80 (1H, dd, J = 1.8, 8.4 Hz), 7.10 (1H, s), 7.25 (1H, t, J = 2.7 Hz), 7.41 (1H, d, J = 8.4 Hz), 10.89 (1H, s).	-
1078		1H-NMR (DMSO-d6) δppm : 0.85-0.98 (1H, m), 1.12-1.35 (3H, m), 1.48-1.73 (4H, m), 2.17 (1H, brs), 2.32-2.50 (2H, m), 2.76-3.01 (4H, m), 6.99-7.08 (2H, m), 7.20 (1H, dd, J = 2.1, 8.7 Hz), 7.41 (1H, d, J = 1.8 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.67 (1H, d, J = 8.8 Hz), 9.56 (1H, brs).	-

[0415]
Table 130

absolute configuration



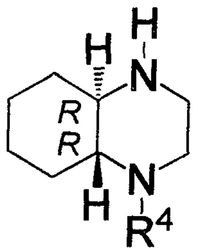
Example	R^4	NMR	Salt
1079		1H-NMR (CDCl3) δppm : 1.00-1.14 (1H, m), 1.20-1.45 (3H, m), 1.45-1.60 (1H, m), 1.60-1.68 (1H, m), 1.68-1.85 (3H, m), 2.53-2.66 (2H, m), 2.95-3.10 (2H, m), 3.15-3.26 (2H, m), 7.33 (1H, dd, J = 2.1, 8.8 Hz), 7.37-7.47 (2H, m), 7.51 (1H, d, J = 2.1 Hz), 7.74-7.82 (3H, m).	-
1080		1H-NMR (CDCl3) δppm : 0.98-1.12 (1H, m), 1.17-1.82 (8H, m), 2.48-2.64 (2H, m), 2.95-3.25 (4H, m), 3.90 (3H, s), 7.08-7.14 (2H, m), 7.31 (1H, dd, J = 2.1, 8.7 Hz), 7.47 (1H, d, J = 2.0 Hz), 7.63-7.70 (2H, m).	-

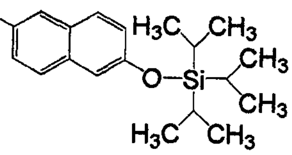
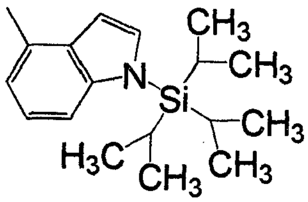
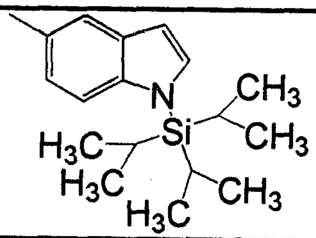
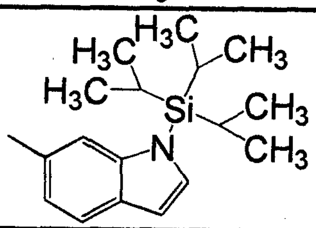
1081		1H-NMR (CDCl3) δppm : 0.97-1.10 (1H, m), 1.15-1.69 (6H, m), 1.69-1.84 (2H, m), 2.45-2.54 (1H, m), 2.54-2.63 (1H, m), 2.93-3.13 (3H, m), 3.13-3.25 (1H, m), 7.19 (1H, dd, J = 2.0, 8.6 Hz), 5.27 (1H, d, J = 5.4 Hz), 7.42 (1H, d, J = 5.4 Hz), 7.59 (1H, d, J = 2.0 Hz), 7.79 (1H, d, J = 8.6 Hz).	-
1082		1H-NMR (DMSO-d6) δppm : 0.95-1.22 (2H, m), 1.22-1.37 (1H, m), 1.39-1.51 (1H, m), 1.51-1.68 (2H, m), 1,68-1,78 (1H, m), 1.99-2.11 (1H, m), 2.92-3.75 (6H, brm), 4.30-5.75 (1H, br), 7.00-7.30 (2H, m), 7.30-7.52 (1H, m), 8.15 (1H, s), 9.45-10.15 (2H, brm).	2 Hydrochloride
1083		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (1H, m), 1.10-1.38 (2H, m), 1.49-1.66 (3H, m), 1.67-1.78 (1H, m), 1.96-2.08 (1H, m), 2.94-3.10 (1H, m), 3.10-3.42 (5H, m), 3.53-4.15 (1H, br), 7.08 (1H, d, J = 8.3 Hz), 7.21 (1H, brs), 7.40 (1H, d, J = 8.3 Hz), 8.12 (1H, d, J = 2.1 Hz), 9.51 (2H, brs).	2 Hydrochloride
1084		1H-NMR (DMSO-d6) δppm : 1.10-1.52 (4H, m), 1.52-1.69 (2H, m), 1.69-1.81 (1H, m), 2.03-2.22 (1H, m), 3.20-4.30 6H, m), 7.05 (1H, s), 7.25-7.70 (1H, m), 7.70-8.05 (2H, m), 8.14 (1H, s), 9.60-10.47 (2H, m). (1H not found)	2 Hydrochloride
1085		1H-NMR (CDCl3) δppm : 1.00-1.13 (1H, m), 1.19-1.45 (3H, m), 1.58-1.90 (5H, m), 2.52-2.65 (2H, m), 2.95-3.25 (4H, m), 7.22 (1H, dt, J = 2.5, 8.8 Hz), 7.36 (1H, dd, J = 2.0, 8.8 Hz), 7.40 (1H, dd, J = 2.5, 9.9 Hz), 7.51 (1H, d, J = 2.0 Hz), 7.69-7.78 (2H, m).	-
1086		1H-NMR (DMSO-d6) δppm : 0.79-0.97 (1H, m), 1.05-1.56 (4H, m), 1.56-1.72 (2H, m), 1.77-1.90 (1H, m), 2.62-2.75 (1H, m), 2.79-3.19 (5H, m), 3.19-3.70 (1H, br), 3.75 (3H, s), 6.37-6.56 (2H, m), 6.78 (1H, d, J = 7.2 Hz), 7.30-7.14 (1H, m), 7.14-7.33 (2H, m).	Fumarate
1087		1H-NMR (DMSO-d6) δppm : 0.86-1.00 (1H, m), 1.04-1.47 (4H, m), 1.47-1.57 (1H, m), 1.61-1.71 (1H, m), 1.77-1.86 (1H, m), 2.55-2.72 (2H, m), 2.92-3.16 (4H, m), 3.75 (3H, s), 5.25-6.25 (1H, br), 6.35 (1H, dd, J = 0.4, 3.0 Hz), 6.96 (1H, dd, J = 1.9, 8.6 Hz), 7.25-7.33 (2H, m), 7.35 (1H, d, J = 8.6 Hz). (2H not found)	Oxalate
1088		1H-NMR (CDCl3) δppm : 0.95-1.11 (1H, m), 1.11-1.42 (3H, m), 1.53-1.82 (5H, m), 2.45-2.55 (1H, m), 2.55-2.64 (1H, m), 2.98-3.12 (3H, m), 3.15-3.25 (1H, m), 3.75 (3H, s), 6.43 (1H, dd, J = 0.8, 3.1 Hz), 6.98-7.03 (2H, m), 7.12-7.15 (1H, m), 7.53 (1H, d, J = 8.4 Hz).	-
1089		1H-NMR (DMSO-d6) δppm : 0.87-1.02 (1H, m), 1.08-1.50 (4H, m), 1.50-1.60 (1H, m), 1.62-1.72 (1H, m), 1.75-1.86 (1H, m), 2.57-2.76 (2H, m), 2.92-3.16 (4H, m), 3.20-4.38 (1H, br), 6.91 (1H, s), 7.09 (1H, dd, J = 1.9, 8.5 Hz), 7.41 (1H, d, J = 1.9 Hz), 7.52 (1H, d, J = 8.5 Hz), 7.97 (1H, d, J = 1.8 Hz). (2H not found)	Oxalate

[0416]

Table 131

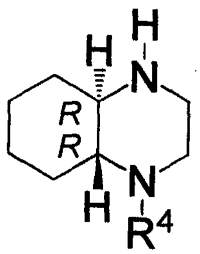
absolute configuration



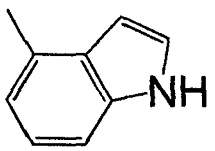
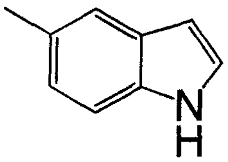
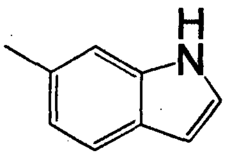
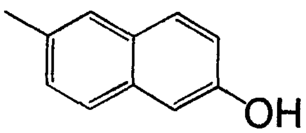
Example	R^4	NMR	Salt
1090		1H-NMR (CDCl3) δppm : 0.99-1.18 (19H, m), 1.20-1.41 (6H, m), 1.49-1.68 (2H, m), 1.68-1.82 (3H, m), 2.49-2.64 (2H, m), 2.94-3.10 (2H, m), 3.10-3.25 (2H, m), 7.09 (1H, dd, J = 2.4, 8.8 Hz), 7.17 (1H, d, J = 2.4 Hz), 7.28 (1H, dd, J = 2.1, 11.0 Hz), 7.45 (1H, d, J = 2.0 Hz), 7.59-7.66 (2H, m).	-
1091		1H-NMR (CDCl3) δppm : 0.93-1.10 (1H, m), 1.14 (18H, d, J = 7.5 Hz), 1.20-1.45 (3H, m), 1.49-1.85 (8H, m), 2.58-2.74 (2H, m), 2.90-3.00 (1H, m), 3.00-3.08 (1H, m), 3.17-3.30 (2H, m), 6.74 (1H, dd, J = 0.7, 3.2 Hz), 6.85 (1H, d, J = 7.3 Hz), 7.03-7.10 (1H, m), 7.17 (1H, d, J = 3.2 Hz), 7.26 (1H, d, J = 8.3 Hz).	-
1092		1H-NMR (CDCl3) δppm : 0.95-1.10 (1H, m), 1.10-1.41 (21H, m), 1.53-1.80 (8H, m), 2.41-2.50 (1H, m), 2.53-2.62 (1H, m), 2.95-3.10 (3H, m), 3.13-3.23 (1H, m), 6.56 (1H, d, J = 0.4, 3.1 Hz), 6.97 (1H, dd, J = 2.1, 8.8 Hz), 7.23 (1H, d, J = 3.1 Hz), 7.37-7.44 (2H, m).	-
1093		1H-NMR (CDCl3) δppm : 0.94-1.06 (1H, m), 1.05-1.25 (19H, m), 1.25-1.45 (2H, m), 1.53-1.80 (8H, m), 2.42-2.50 (1H, m), 2.55-2.65 (1H, m), 2.90-3.00 (1H, m), 3.00-3.13 (2H, m), 3.16-3.25 (1H, m), 6.56 (1H, dd, J = 0.7, 3.2 Hz), 6.97 (1H, dd, J = 1.7, 8.3 Hz), 7.20 (1H, d, J = 3.2 Hz), 7.32 (1H, s), 7.52 (1H, d, J = 8.3 Hz).	-

[0417]
Table 132

absolute configuration

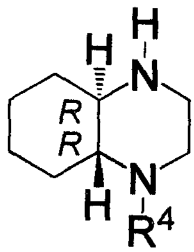


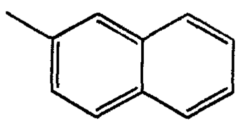
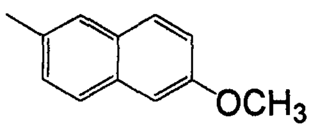
Example.	R^4	NMR	Salt

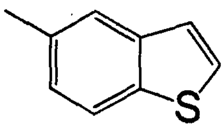
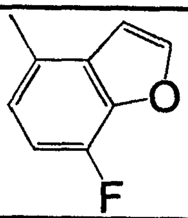
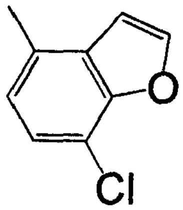
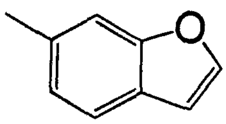
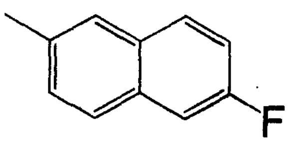
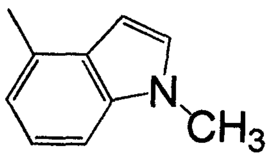
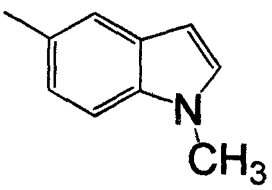
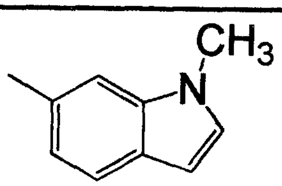
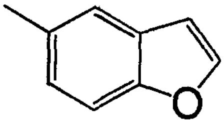
1094		1H-NMR (CDCl3) δppm : 0.95-1.09 (1H, m), 1.18-1.55 (4H, m), 1.55-1.63 (1H, m), 1.66-1.85 (3H, m), 2.59-2.77 (2H, m), 2.81-3.01 (1H, m), 3.01-3.09 (1H, m), 3.18-3.30 (2H, m), 6.67-6.71 (1H, m), 6.87 (1H, dd, J = 1.1, 7.2 Hz), 7.10-7.20 (3H, m), 8.15-8.47 (1H, br).	-
1095		1H-NMR (CDCl3) δppm : 0.96-1.10 (1H, m), 1.11-1.43 (3H, m), 1.52-1.84 (5H, m), 2.42-2.52 (1H, m), 2.54-2.64 (1H, m), 2.97-3.10 (3H, m), 3.14-3.25 (1H, m), 6.51 (1H, dd, J = 1.0, 2.1 Hz), 7.06 (1H, dd, J = 2.0, 8.6 Hz), 7.17-7.23 (1H, m), 7.32 (1H, d, J = 8.6 Hz), 7.44 (1H, d, J = 2.0 Hz), 8.20 (1H, brs).	-
1096		1H-NMR (DMSO-d6) δppm : 0.81-0.95 (1H, m), 1.05-1.35 (3H, m), 1.41-1.57 (2H, m), 1.58-1.74 (2H, m), 2.05 (1H, brs), 2.30-2.41 (2H, m), 2.75-2.97 (4H, m), 6.30-6.38 (1H, m), 6.80 (1H, dd, J = 1.8, 8.4 Hz), 7.10 (1H, s), 7.25 (1H, t, J = 2.7 Hz), 7.41 (1H, d, J = 8.4 Hz), 10.89 (1H, s).	-
1097		1H-NMR (DMSO-d6) δppm : 0.85-0.99 (1H, m), 1.12-1.36 (3H, m), 1.48-1.76 (4H, m), 2.17 (1H, brs), 2.31-2.50 (2H, m), 2.76-3.01 (4H, m), 6.99-7.08 (2H, m), 7.20 (1H, dd, J = 2.0, 8.7 Hz), 7.41 (1H, d, J = 1.6 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.67 (1H, d, J = 8.8 Hz), 9.57 (1H, brs).	-

[0418]
Table 133

absolute configuration

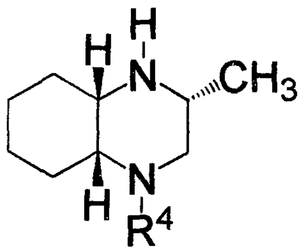


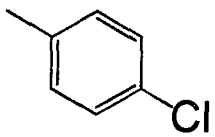
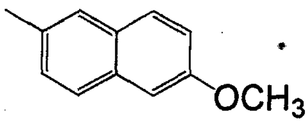
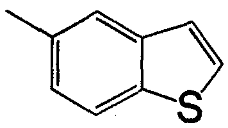
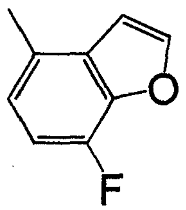
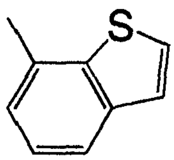
Example.	R^4	NMR	Salt
1098		1H-NMR (CDCl3) δppm : 1.00-1.14 (1H, m), 1.20-1.45 (3H, m), 1.45-1.68 (2H, m), 1.68-1.85 (3H, m), 2.53-2.66 (2H, m), 2.95-3.10 (2H, m), 3.15-3.26 (2H, m), 7.33 (1H, dd, J = 2.1, 8.8 Hz), 7.37-7.47 (2H, m), 7.51 (1H, d, J = 2.1 Hz), 7.74-7.82 (3H, m).	-
1099		1H-NMR (CDCl3) δppm : 0.98-1.12 (1H, m), 1.17-1.45 (3H, m), 1.45-1.85 (5H, m), 2.49-2.64 (2H, m), 2.95-3.25 (4H, m), 3.90 (3H, s), 7.08-7.14 (2H, m), 7.31 (1H, dd, J = 2.1, 8.7 Hz), 7.47 (1H, d, J = 2.0 Hz), 7.63-7.70 (2H, m).	-

1100		1H-NMR (CDCl3) δppm : 0.97-1.10 (1H, m), 1.15-1.69 (6H, m), 1.69-1.84 (2H, m), 2.45-2.54 (1H, m), 2.54-2.63 (1H, m), 2.93-3.13 (3H, m), 3.13-3.25 (1H, m), 7.19 (1H, dd, J = 2.0, 8.6 Hz), 5.27 (1H, d, J = 5.4 Hz), 7.42 (1H, d, J = 5.4 Hz), 7.59 (1H, d, J = 2.0 Hz), 7.79 (1H, d, J = 8.6 Hz).	-
1101		1H-NMR (DMSO-d6) δppm : 0.91-1.10 (1H, m), 1.10-1.37 (2H, m), 1.41-1.66 (3H, m), 1.66-1.79 (1H, m), 1.06-2.09 (1H, m), 2.95-3.55 (6H, m), 3.70-4.95 (1H, br), 7.00-7.17 (1H, m), 7.17-7.40 (2H, m), 8.08-8.19 (1H, m), 9.33-9.90 (2H, m).	2 Hydrochloride
1102		1H-NMR (DMSO-d6) δppm : 0.92-1.09 (1H, m), 1.10-1.39 (2H, m), 1.47-1.68 (3H, m), 1.68-1.78 (1H, m), 1.99-2.09 (1H, m), 2.94-3.14 (1H, br), 3.14-3.50 (5H, brm), 4.05-5.03 (1H, br), 7.08-7.19 (1H, m), 7.25-7.36 (1H, m), 7.41 (1H, d, J = 8.2 Hz), 8.14 (1H, d, J = 1.6 Hz), 9.70 (2H, brs).	2 Hydrochloride
1103		1H-NMR (DMSO-d6) δppm : 1.12-1.51 (4H, m), 1.53-1.68 (2H, m), 1.69-1.79 (1H, m), 2.07-2.19 (1H, m), 3.20-4.27 6H, m), 7.04 (1H, s), 7.30-7.65 (1H, m), 7.65-8.05 (2H, m), 8.13 (1H, s), 9.65-10.40 (2H, m). (1H not found)	2 Hydrochloride
1104		1H-NMR (CDCl3) δppm : 1.00-1.13 (1H, m), 1.18-1.45 (3H, m), 1.58-1.90 (5H, m), 2.52-2.65 (2H, m), 2.95-3.11 (2H, m), 3.11-3.25 (2H, m), 7.22 (1H, dt, J = 2.5, 8.8 Hz), 7.36 (1H, dd, J = 2.0, 8.8 Hz), 7.40 (1H, dd, J = 2.5, 9.9 Hz), 7.51 (1H, d, J = 2.0 Hz), 7.69-7.78 (2H, m).	-
1105		1H-NMR (DMSO-d6) δppm : 0.80-0.96 (1H, m), 1.05-1.56 (4H, m), 1.56-1.72 (2H, m), 1.77-1.90 (1H, m), 2.62-2.75 (1H, m), 2.77-2.90 (1H, m), 2.90-3.19 (4H, m), 3.19-3.70 (1H, br), 3.75 (3H, s), 6.37-6.54 (2H, m), 6.78 (1H, d, J = 7.3 Hz), 7.30-7.14 (1H, m), 7.14-7.31 (2H, m).	Fumarate
1106		1H-NMR (DMSO-d6) δppm : 0.86-1.00 (1H, m), 1.04-1.47 (4H, m), 1.47-1.57 (1H, m), 1.61-1.70 (1H, m), 1.77-1.87 (1H, m), 2.55-2.72 (2H, m), 2.90-3.16 (4H, m), 3.75 (3H, s), 5.25-6.25 (1H, br), 6.35 (1H, d, J = 2.9 Hz), 6.96 (1H, dd, J = 1.7, 8.6 Hz), 7.25-7.33 (2H, m), 7.35 (1H, d, J = 8.6 Hz). (2H not found)	Oxalate
1107		1H-NMR (CDCl3) δppm : 0.96-1.10 (1H, m), 1.10-1.44 (3H, m), 1.48-1.82 (5H, m), 2.45-2.55 (1H, m), 2.55-2.64 (1H, m), 2.98-3.12 (3H, m), 3.15-3.25 (1H, m), 3.75 (3H, s), 6.43 (1H, dd, J = 0.8, 3.1 Hz), 6.98-7.03 (2H, m), 7.12-7.15 (1H, m), 7.53 (1H, d, J = 8.5 Hz).	-
1108		1H-NMR (DMSO-d6) δppm : 0.87-1.02 (1H, m), 1.08-1.50 (4H, m), 1.50-1.60 (1H, m), 1.62-1.72 (1H, m), 1.75-1.86 (1H, m), 2.54-2.76 (2H, m), 2.92-3.17 (4H, m), 3.20-5.40 (1H, br), 6.91 (1H, d, J = 1.2 Hz), 7.10 (1H, dd, J = 1.9, 8.6 Hz), 7.41 (1H, d, J = 1.9 Hz), 7.52 (1H, d, J = 8.6 Hz), 7.97 (1H, d, J = 2.0 Hz). (2H not found)	Oxalate

[0419]
Table 134

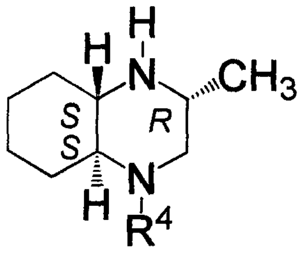
relative configuration

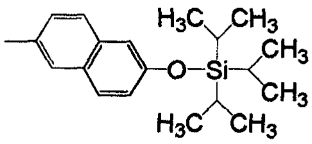
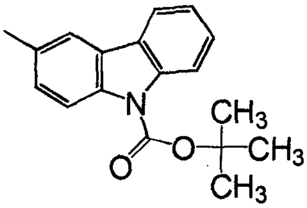


Example.	R^4	NMR	Salt
1109		1H-NMR (DMSO-d6) δppm : 1.22-1.52 (6H, m), 1.56-1.97 (4H, m), 2.00-2.18 (1H, m), 2.75-2.95 (1H, m), 3.20-3.40 (1H, m), 3.40-3.60 (2H,m), 3.96-4.10 (1H, m), 4.20-4.57 (1H, br), 6.91-7.01 (2H, m), 7.19-7.31 (2H, m), 8.69 (1H, brs), 10.11 (1H, brs).	2 Hydrochloride
1110		1H-NMR (CDCl3) δppm : 1.15-1.33 (6H, m), 1.48-1.58 (2H, m), 1.66-1.85 (4H, m), 2.68 (1H, t, J = 11.8 Hz), 3.02-3.12 (1H, m), 3.23 (1H, dd, J = 3.3, 11.4 Hz), 3.29-3.24 (1H, m), 3.76 (1H, td, J = 3.3, 11.4 Hz), 3.88 (3H, s), 7.00 (1H, d, J = 2.3 Hz), 7.02-7.30 (2H, m), 7.22-7.29 (1H, m), 7.57 (1H, d, J = 8.8 Hz), 7.61 (1H, d, J = 9.0 Hz).	-
1111		1H-NMR (DMSO-d6) δppm : 1.17-1.36 (2H, m), 1.36-1.51 (4H, m), 1.62-2.00 (4H, m), 2.06-2.17 (1H, m), 2.94-3.05 (1H, m), 3.30-3.50 (1H, m), 3.50-3.64 (2H, m), 4.04-4.13 (1H, m), 4.59-5.50 (1H, br), 7.17 (1H, d, J = 8.9 Hz), 7.31 (1H, d, J = 5.4 Hz), 7.38 (1H, brs), 7.62 (1H, d, J = 5.4 Hz), 7.83 (1H, d, J = 8.9 Hz), 8.68 (1H, brs), 10.12 (1H, brs).	2 Hydrochloride
1112		1H-NMR (DMSO-d6) δppm : 0.99-1.17 (2H, m), 1.30-1.49 (4H, m), 1.55-1.75 (2H, m), 1.75-1.98 (2H, m), 1.98-2.13 (1H, m), 3.12-3.28 (2H, m), 3.28-3.50 (1H, m), 3.67-3.85 (2H, m), 6.67 (1H, dd, J = 3.4, 8.6Hz), 7.10 (1H, dd, J = 8.6, 10.7Hz), 7.28 (1H, dd, J = 2.6, 2.6Hz), 8.07 (1H, d, J = 2.2Hz). 8.43 (1H, br), 9.94 (1H, br).	Hydrochloride
1113		1H-NMR (DMSO-d6) δppm : 1.03-1.21 (2H, m), 1.37-1.48 (4H, m), 1.58-1.85 (3H, m), 1.95-2.14 (2H, m), 3.23 (1H, d, J = 10.6Hz), 3.36-3.55 (2H, m), 3.64-3.76 (1H, m), 3.85-3.96 (1H, m), 7.01 (1H, d, J = 7.6Hz), 7.34 (1H, dd, J = 7.7, 7.7Hz), 7.46 (1H, d, J = 5.4Hz), 7.57-7.62 (1H, m), 7.75 (1H, d, J = 5.4Hz), 8.35-8.6 (1H, m), 9.82 (1H, br).	Hydrochloride

[0420]
Table 134

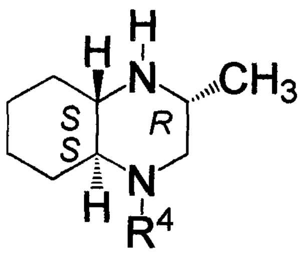
absolute configuration

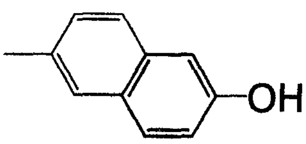


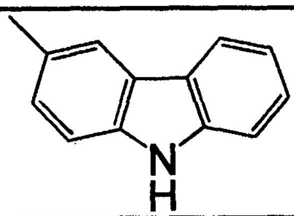
Example.	R^4	NMR	Salt
1114		1H-NMR (CDCl3) δppm : 0.95-1.10 (4H, m), 1.13 (18H, d, J = 7.3 Hz), 1.19-1.47 (7H, m), 1.59-1.67 (1H, m), 1.70-1.84 (3H, m), 2.45-2.53 (1H, m), 2.57 (1H, dd, J = 10.3, 11.0 Hz), 2.62-2.70 (1H, m), 3.12 (1H, dd, J = 2.7, 11.2 Hz), 3.16-3.24 (1H, m), 7.09 (1H, dd, J = 2.4, 8.9 Hz), 7.17 (1H, d, J = 2.4 Hz), 7.27 (1H, dd, J = 2.1, 8.7 Hz), 7.44 (1H, d, J = 2.0 Hz), 7.59-7.65 (2H, m).	-
1115		1H-NMR (CDCl3) δppm : 0.94-1.12 (4H, m), 1.15-1.46 (4H, m), 1.57-1.68 (2H, m), 1.68-1.85 (11H, m), 2.42-2.51 (1H, m), 2.59-2.70 (2H, m), 3.10 (1H, dd, J = 2.7, 11.2 Hz), 3.15-3.25 (1H, m), 7.29 (1H, dd, J = 2.2, 8.6 Hz), 7.30-7.37 (1H, m), 7.42-7.49 (1H, m), 7.76 (1H, d, J = 2.1 Hz), 7.93 (1H, d, J = 7.2 Hz), 8.21 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 8.3 Hz).	-

[0421]
Table 135

absolute configuration

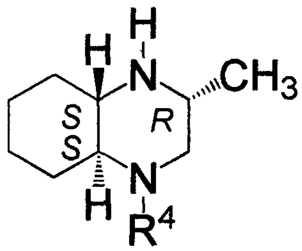


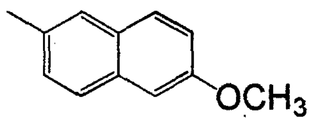
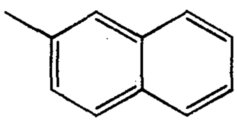
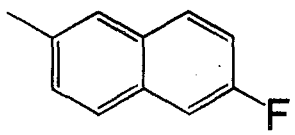
Example.	R^4	NMR	Salt
1116		1H-NMR (DMSO-d6) δppm : 0.85-0.99 (4H, m), 1.13-1.35 (3H, m), 1.49-1.75 (4H, m), 1.99 (1H, brs), 2.32-2.50 (3H, m), 2.92-3.02 (2H, m), 7.00-7.09 (2H, m), 7.19 (1H, dd, J = 2.1, 8.7 Hz), 7.41 (1H, d, J = 1.8 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.66 (1H, d, J = 8.8 Hz), 9.56 (1H, brs).	-

1117		1H-NMR (DMSO-d6) δppm : 1.10-1.57 (7H, m), 1.57-1.71 (2H, m), 1.71-1.82 (1H, m), 2.11-2.22 (1H,m), 3.00-3.40 (6H, m), 7.22 (1H, t, J = 7.4 Hz), 7.35-7.85 (4H, m), 8.09 (1H, d, J = 7.8 Hz), 8.37 (1H, brs), 9.96 (2H, brs), 11.61 (1H, brs).	2 Hydrochloride

[0422]
Table 136

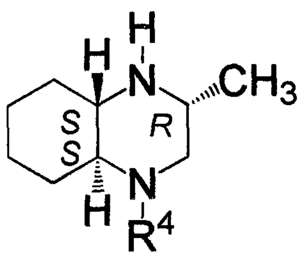
absolute configuration

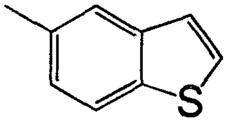
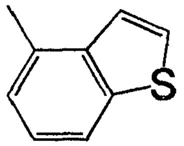
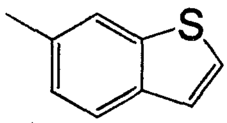


Example.	R^4	NMR	Salt
1118		1H-NMR (CDCl3) δppm : 0.98-1.11 (4H, m), 1.17-1.58 (4H, m), 1.58-1.85 (4H, m), 2.44-2.53 (1H, m), 2.56-2.70 (2H, m), 3.12 (1H, dd, J = 2.8, 11.2 Hz), 3.15-3.25 (1H, m), 3.90 (3H, s), 7.08-7.16 (2H, m), 7.30 (1H, dd, J = 2.0, 8.7 Hz), 7.46 (1H, d, J = 2.0 Hz), 7.65 (1H, d, J = 4.8 Hz), 7.67 (1H, d, J = 4.9 Hz).	-
1119		1H-NMR (DMSO-d6) δppm : 0.95-1.05 (1H, m), 1.11 (3H, d, J = 6.3Hz), 1.15-1.5 (3H, m), 1.5-1.6 (1H, m), 1.65-1.75 (2H, m), 1.85-1.95 (1H, m), 2.65-2.85 (3H, m), 2.85-4.35 (4H, m), 6.50 (1H, s), 7.33 (1H, dd, J = 2.1, 8.7Hz), 7.4-7.5 (2H, m), 7.57 (1H, d, J = 1.8Hz), 7.8-7.9 (3H, m).	1/2 Fumarate
1120		1H-NMR (CDCl3) δppm : 0.98-1.12 (4H, m), 1.18-1.48 (4H, m), 1.58-1.69 (1H, m), 1.69-1.85 (3H, m), 2.46-2.54 (1H, m), 2.57 (1H, dd, J = 10.2, 11.0 Hz), 2.62-2.70 (1H, m), 3.10-3.25 (2H, m), 7.22 (1H, dt, J = 2.6, 8.8 Hz), 7.35 (1H, dd, J = 1.8, 8.7 Hz), 7.40 (1H, dd, J = 2.5, 9.9 Hz), 7.50 (1H, d, J = 1.9 Hz), 7.68-7.77 (2H, m).	-

[0423]
Table 137

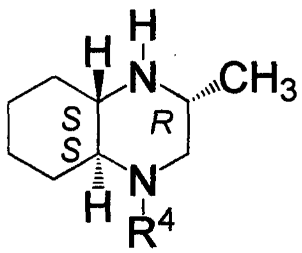
absolute configuration

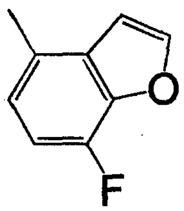
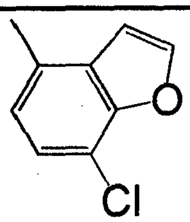


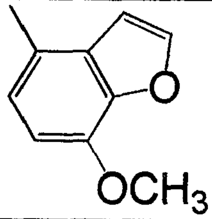
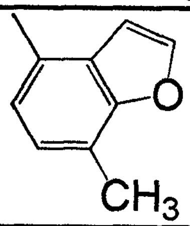
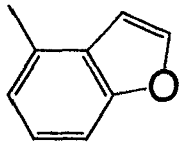
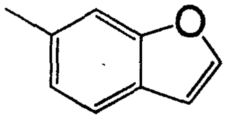
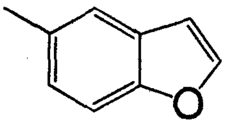
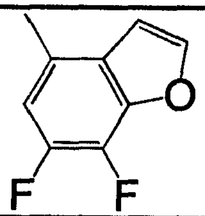
Example.	R^4	NMR	Salt
1121		1H-NMR (CDCl3) δppm : 0.97-1.17 (4H, m), 1.17-1.49 (4H, m), 1.53-1.89 (4H, m), 2.42-2.55 (1H, m), 2.55-2.71 (2H, m), 3.08 (1H, dd, J = 2.8, 11.3 Hz), 3.13-3.26 (1H, m), 7.19 (1H, dd, J = 2.0, 8.6 Hz), 7.27 (1H, d, J = 5.4 Hz), 7.42 (1H, d, J = 5.4 Hz), 7.58 (1H, d, J = 2.0 Hz), 7.78 (1H, d ,J = 8.6 Hz).	-
1122		1H-NMR (CDCl3) δppm : 0.85-1.02 (1H, m), 1.05 (3H, d, J = 6.4 Hz), 1.17-1.54 (4H, m), 1,54-1.63 (1H, m), 1.63-1.83 (3H, m), 2.40-2.55 (1H, m), 2.55-2.65 (1H, m), 2.65-2.74 (1H, m), 3.10 (1H, dd, J = 2.8, 11.4 Hz), 3.15-3.26 (1H, m), 7.12 (1H, dd, J = 0.7, 7.6 Hz), 7.30 (1H, t, J = 7.8 Hz), 7.35 (1H, d, J = 5.5 Hz), 7.57 (1H, d, J = 5.5 Hz), 7.64 (1H, d, J = 8.0 Hz).	-
1123		1H-NMR (DMSO-d6) δppm : 0.90-1.04 (1H, m), 1.12 (3H, d, J = 6.4 Hz), 1.17-1.35 (2H, m), 1.35-1.49 (1H, m), 1.50-1.62 (2H, m), 1.64-1.74 (1H, m), 1.84-1.94 (1H, m), 2.65-2.84 (3H, m), 3.10 (1H, dd, J = 2.9, 11.7 Hz), 3.21-3.34 (1H, m), 4.30-6.30 (1H, br), 6.49 (2H, s), 7.18 (1H, dd, J = 1.7, 8.4 Hz), 7.39 (1H, d, J = 5.4 Hz), 7.67 (1H, d, J = 5.4 Hz), 7.75 (1H, d, J = 1.7 Hz), 7.81 (1H, d, J = 8.4 Hz).	Fumarate

[0424]
Table 138

absolute configuration

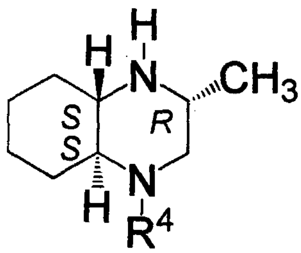


Example.	R^4	NMR	Salt
1124		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 0.96-1.38 (6H, m), 1.40-1.50 (1H, m), 1.50-1.80 (3H, m), 2.06-2.17 (1H, m), 3.01-3.20 (2H, m), 3.27-3.40 (2H, m), 3.50-3.65 (1H, m), 5.90-6.39 (1H, br), 7.05-7.22 (2H, m), 7.32 (1H, brs), 8.03 (1H, d, J = 2.0 Hz), 9.64 (1H, brs), 9.81 (1H, brs).	2 Hydrochloride
1125		1H-NMR (DMSO-d6) δppm: 0.85-1.00 (1H, m), 1.05-1.38 (5H, m), 1.38-1.75 (4H, m), 1.87-2.00 (1H, m), 2.65-3.00 (3H, m), 3.12 (1H, dd, J = 2.8, 11.9 Hz), 3.30-3.47 (1H, m), 6.53 (2H, s), 7.04 (1H, d, J = 8.3 Hz), 7.14 (1H, brs), 7.37 (1H, d, J = 8.3 Hz), 8.08 (1H, d, J = 2.2 Hz). (3H, not found)	Fumarate

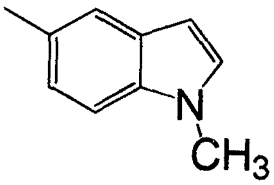
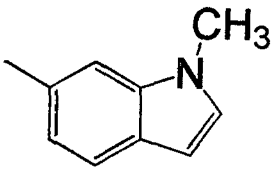
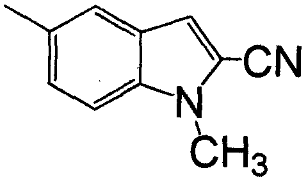
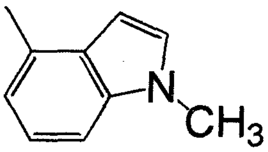
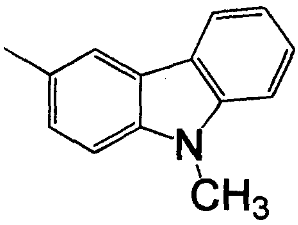
1126		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.02-1.38 (6H, m), 1.38-1.50 (1H, m), 1.50-1.79 (3H, m), 2.05-2.16 (2H, m), 3.10-3.29 (2H, m), 3.29-3.57 (2H, br), 3.57-3.73 (1H, br), 3.94 (3H, s), 4.30-4.25 (1H, br), 6.91 (1H, d, J = 8.4 Hz), 7.16 (1H, brs), 7.31 (1H, brs), 7.93 (1H, s), 9.72 (1H, brs).	2 Hydrochloride
1127		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.03-1.38 (6H, m), 1.40-1.79 (4H, m), 2.06-2.18 (1H, m), 2.45 (3H, s), 3.12-3.31 (2H, m), 3.31-3.56 (2H, m), 3.56-3.77 (1H, m), 5.39-6.13 (1H, br), 7.08-7.21 (2H, m), 7.21-7.40 (1H, m), 7.95 (1H, d, J = 2.0 Hz), 9.79 (2H, brs).	2 Hydrochloride
1128		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.02-1.39 (6H, m), 1.45-1.80 (4H, m), 2.08-2.18 (1H, m), 3.10-3.30 (2H, m), 3.32-3.55 (2H, m), 3.55-3.74 (1H, m), 5.50-6.15 (1H, br), 7.16-7.25 (1H, m), 7.25-7.36 (2H, m), 7.47 (1H, d, J = 8.2 Hz), 7.94 (1H, d, J = 2.0 Hz), 9.55-10.05 (2H, brm).	2 Hydrochloride
1129		1H-NMR (DMSO-d6) δppm : 0.89-1.03 (1H, m), 1.08-1.35 (5H, m), 1.35-1.60 (3H, m), 1.63-1.73 (1H, m), 1.84-1.96 (1H, m), 2.62-2.85 (3H, m), 3.08 (1H, dd, J = 2.8, 11.8 Hz), 3.22-3.35 (1H, m), 6.50 (2H, s), 6.91 (1H, dd, J = 0.9, 2.1 Hz), 7.07 (1H, dd, J = 1.7, 8.3 Hz), 7.36 (1H, s), 7.58 (1H, d, J = 8.2 Hz), 7.95 (1H, d, J = 2.2 Hz). (3H not found)	Fumarate
1130		1H-NMR (DMSO-d6) δppm : 1.09-1.55 (7H, m), 1.55-1.80 (3H, m), 2.10-2.22 (1H,m), 3.35-4.13 (5H, m), 4.13-5.22 (1H, br), 7.12 (1H, s), 7.60 (1H, brs), 7.81 (1H, s), 7.98 (1H, brs), 8.15 (1H, s), 10.09 (2H, brs).	2 Hydrochloride
1131		1H-NMR (DMSO-d6) δppm : 0.90-1.06 (1H, m), 1.15-1.38 (5H, m), 1.47-1.67 (3H, m), 1.67-1.80 (1H, m), 1.99-2.11 (1H, m), 2.80-3.30 (4H, m), 3.40-3.60 (1H, m), 4.40-5.10 (1H, br), 7.13-7.38 (2H, m), 8.15 (1H, d, J = 2.0 Hz), 9.05-9.58 (1H, br), 9.70-9.95 (1H, br).	2 Hydrochloride

[0425]
Table 139

absolute configuration

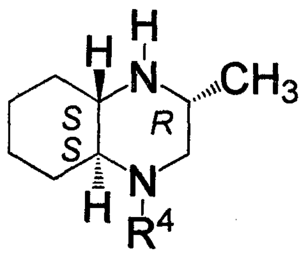


Example.	R^4	NMR	Salt

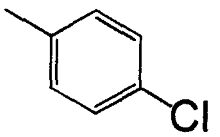
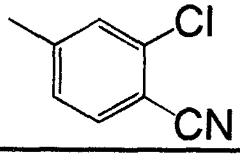
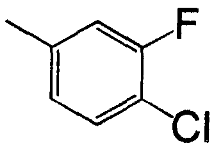
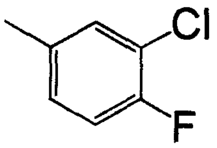
1132		1H-NMR (CDCl3) δppm : 0.94-1.10 (4H, m), 1.13-1.65 (6H, m), 1.65-1.83 (2H, m), 2.37-2.47 (1H, m), 2.55-2.69 (2H, m), 3.05 (1H, dd, J = 2.8, 11.2 Hz), 3.12-3.23 (1H, m), 3.77 (3H, s), 6.42 (1H, d, J = 0.7, 3.1 Hz), 7.03 (1H, d, J = 3.1 Hz), 7.08 (1H, d, J = 2.0, 8.6 Hz), 7.22-7.30 (1H, m), 7.41 (1H, d, J = 1.8 Hz).	-
1133		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (1H, m), 1.09-1.35 (5H, m), 1.39-1.60 (3H, m), 1.64-1.76 (1H, m), 1.88-2.00 (1H, m), 2.68-2.79 (1H, m), 2.79-2.94 (2H, m), 3.01-3.11 (1H, m), 3.28-3.40 (1H, m), 3.75 (3H, s), 6.36 (1H, d, J = 0.6, 3.1 Hz), 6.51 (2H, s), 6.87 (1H, d, J = 1.7, 8.4 Hz), 7.18 (1H, s), 7.27 (1H, d, J = 3.1 Hz), 7.47 (1H, d, J = 8.3 Hz). (3H not found)	Fumarate
1134		1H-NMR (CDCl3) δppm : 0.82-0.92 (1H, m), 0.94 (3H, d, J = 6.3 Hz), 1.06-1.34 (4H, m), 1.38-1.58 (2H, m), 1.59-1.75 (2H, m), 2.28-2.37 (1H, m), 2.37-2.49 (2H, m), 2.89 (1H, dd, J = 2.6, 10.8 Hz), 2.94-3.04 (1H, m), 3.86 (3H, s), 7.21 (1H, dd, J = 1.9, 8.9 Hz), 7.31 (1H, s), 7.36 (1H, d, J = 1.7 Hz), 7.51 (1H, d, J = 8.9 Hz).	-
1135		1H-NMR (DMSO-d6) δppm : 0.82-0.96 (1H, m), 1.01-1.35 (5H, m), 1.35-1.85 (4H, m), 1.85-1.96 (1H, m), 2.53-3.05 (3H, m), 3.05-3.23 (1H, m), 3.23-3.40 (1H, m), 3.76 (3H, s), 6.39-6.57 (3H, m), 6.79 (1H, d, J = 8.0 Hz), 7.09 (1H, t, J = 7.8 Hz), 7.17-7.28 (2H, m). (3H not found)	Fumarate
1136		1H-NMR (DMSO-d6) δppm : 0.93-1.10 (1H, m), 1.10-1.35 (5H, m), 1.41-1.59 (3H, m), 1.64-1.78 (1H, m), 1.91-2.04 (1H, m), 2.75-3.04 (3H, m), 3.11 (1H, dd, J = 2.0, 12.0 Hz), 3.32-3.46 (1H, m), 3.85 (3H, s), 6.53 (2H, s), 7.15-7.23 (1H, m), 7.29 (1H, dd, J = 1.9, 8.6 Hz), 7.42-7.49 (1H, m), 7.53 (1H, d, J = 8.6 Hz), 7.56 (1H, d, J = 8.3 Hz), 7.94 (1H, d, J = 1.8 Hz), 8.15 (1H, d, J = 7.7 Hz). (3H, not found)	Fumarate

[0426]
Table 140

absolute configuration

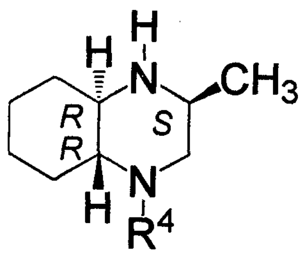


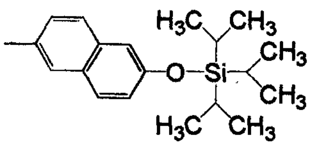
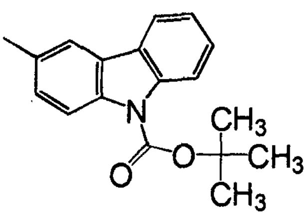
Example	R^4	NMR	Salt

1137		1H-NMR (CDCl3) δppm : 0.88-1.08 (4H, m), 1.15-1,57 (4H,m), 1.60-1.68 (2H, m), 1.68-1.80 (2H, m), 2.31-2.39 (1H, m), 2.46 (1H, dd, J = 10.4, 11.0 Hz), 2.55-2.63 (1H, m), 3.00 (1H, dd, J = 2.8, 11.2 Hz), 3.07-3.18 (1H, m), 7.03-7.09 (2H, m), 7.23-7.29 (2H, m).	-
1138		1H-NMR (CDCl3) δppm : 0.98-1.10 (4H, m), 1.20-1.46 (4H, m), 1.65-1.90 (4H, m), 2.46-2.67 (3H, m), 3.10-3.25 (2H, m), 6.98 (1H, dd, J = 2.1, 8.5 Hz), 7.12 (1H, d, J = 2.1 Hz), 7.54 (1H, d, J = 8.5 Hz)	-
1139		1H-NMR (DMSO-d6) δppm : 0.89-1.03 (1H, m), 1.11 (3H ,d, J = 6.4 Hz), 1.17-1.34 (2H, m), 1.34-1.47 (1H, m), 1.51-1.74 (3H, m), 1.82-1.94 (1H, m), 2.64-2.74 (2H, m), 2.74-2.84 (1H, m), 3.14 (1H, dd, J = 3.0, 11.9 Hz), 3.20-3.33 (1H, m), 6.51 (2H, s), 6.97-7.04 (1H, m), 7.19 (1H, dd, J = 2.4, 11.3 Hz), 7.50 (1H, t, J = 8.7 Hz), 8.90-11.40 (2H, br). (1H not found)	Fumarate
1140		1H-NMR (DMSO-d6) δppm : 0.89-1.03 (1H, m), 1.10 (3H, d, J = 6.4 Hz), 1.14-1.45 (3H, m), 1.48-1.62 (2H, m), 1.65-1.73 (1H, m), 1.82-1.92 (1H, m), 2.58-2.81 (3H, m), 3.05 (1H, dd, J = 3.0, 11.7 Hz), 3.19-3.30 (1H, m), 6.51 (2H, s), 7.11-7.18 (1H, m), 7.31-7.41 (2H, m), 9.00-11.60 (2H, br). (1H not found)	Fumarate

[0427]
Table 141

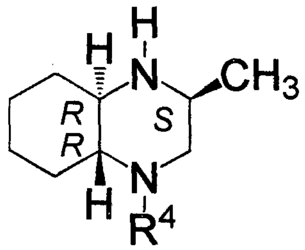
absolute configuration

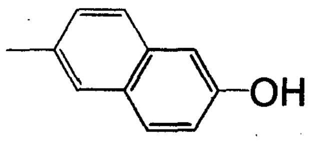
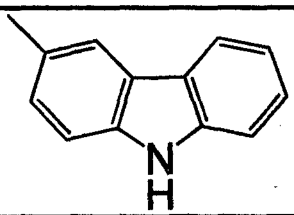


Example	R^4	NMR	Salt
1141		1H-NMR (CDCl3) δppm : 0.96-1.10 (4H, m), 1.13 (18H, d, J = 7.3 Hz), 1.19-1.50 (7H, m), 1.58-1.67 (1H, m), 1.68-1.84 (3H, m), 2.45-2.53 (1H, m), 2.57 (1H, dd, J = 10.3, 11.0 Hz), 2.62-2.70 (1H, m), 3.12 (1H, dd, J = 2.7, 11.2 Hz), 3.15-3.24 (1H, m), 7.09 (1H, dd, J = 2.4, 8.9 Hz), 7.17 (1H, d, J = 2.4 Hz), 7.27 (1H, dd, J = 2.1, 8.7 Hz), 7.44 (1H, d, J = 2.0 Hz), 7.59-7.65 (2H, m).	-
1142		1H-NMR (CDCl3) δppm : 0.94-1.12 (4H, m), 1.15-1.46 (4H, m), 1.57-1.68 (2H, m), 1.68-1.85 (11H, m), 2.42-2.51 (1H, m), 2.59-2.70 (2H, m), 3.10 (1H, dd, J = 2.7, 11.2 Hz), 3.15-3.25 (1H, m), 7.29 (1H, dd, J = 2.2, 8.6 Hz), 7.30-7.37 (1H, m), 7.42-7.49 (1H, m), 7.76 (1H, d, J = 2.1 Hz), 7.93 (1H, d, J = 7.2 Hz), 8.21 (1H, d, J = 8.8 Hz), 8.29 (1H, d, J = 8.3 Hz).	-

[0428]
Table 142

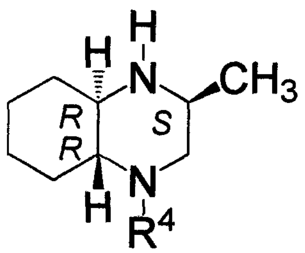
absolute configuration

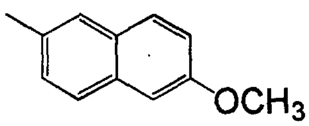


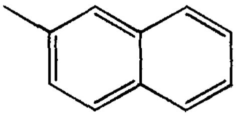
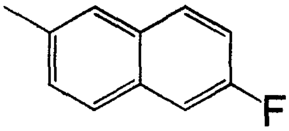
Example	R^4	NMR	Salt
1143		1H-NMR (DMSO-d6) δppm : 0.83-1.00 (4H, m), 1.12-1.35 (3H, m), 1.48-1.75 (4H, m), 1.99 (1H, brs), 2.31-2.50 (3H, m), 2.92-3.03 (2H, m), 6.99-7.09 (2H, m), 7.19 (1H, dd, J = 2.0, 8.7 Hz), 7.41 (1H, d, J = 1.7 Hz), 7.58 (1H, d, J = 8.8 Hz), 7.66 (1H, d, J = 8.8 Hz), 9.57 (1H, brs).	-
1144		1H-NMR (DMSO-d6) δppm : 1.10-1.57 (7H, m), 1.57-1.71 (2H, m), 1.71-1.82 (1H, m), 2.11-2.22 (1H,m), 3.00-3.40 (6H, m), 7.22 (1H, t, J = 7.4 Hz), 7.35-7.85 (4H, m), 8.09 (1H, d, J = 7.8 Hz), 8.37 (1H, brs), 9.96 (2H, brs), 11.61 (1H, brs).	2 Hydrochloride

[0429]
Table 143

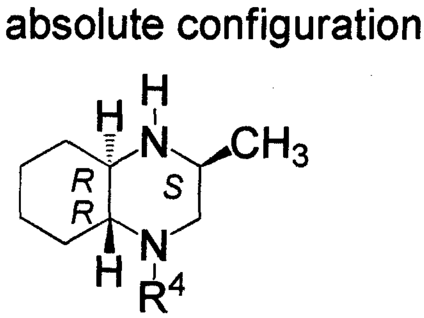
absolute configuration

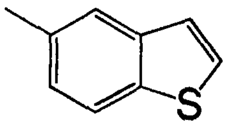
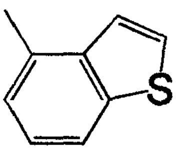
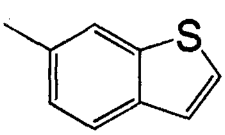


Example	R^4	NMR	Salt
1145		1H-NMR (CDCl3) δppm : 0.98-1.12 (4H, m), 1.18-1.58 (4H, m), 1.58-1.85 (4H, m), 2.45-2.53 (1H, m), 2.56-2.70 (2H, m), 3.12 (1H, dd, J = 2.8, 11.2 Hz), 3.16-3.25 (1H, m), 3.90 (3H, s), 7.08-7.16 (2H, m), 7.30 (1H, dd, J = 2.01, 8.7 Hz), 7.46 (1H, d, J = 2.0 Hz), 7.65 (1H, d, J = 4.9 Hz), 7.67 (1H, d, J = 4.9 Hz).	-

1146		1H-NMR (DMSO-d6) δppm : 0.92-1.06 (1H, m), 1.11 (3H, d, J = 6.4Hz), 1.16-1.51 (3H, m), 1.52-1.64 (1H, m), 1.64-1.78 (2H, m), 1.82-1.94 (1H, m), 2.65-2.85 (3H, m), 2.85-4.2 (4H, m), 6.50 (1H, s), 7.33 (1H, dd, J = 2.1, 8.7Hz), 7.39-7.51 (2H, m), 7.56 (1H, d, J = 1.9Hz), 7.80-7.89 (3H, m).	1/2 Fumarate
1147		1H-NMR (CDCl3) δppm : 0.98-1.12 (4H, m), 1.18-1.48 (4H, m), 1.60-1.69 (1H, m), 1.69-1.85 (3H, m), 2.46-2.54 (1H, m), 2.57 (1H, dd, J = 10.2, 11.0 Hz), 2.62-2.71 (1H, m), 3.10-3.25 (2H, m), 7.22 (1H, dt, J = 2.6, 8.8 Hz), 7.35 (1H, dd, J = 1.8, 8.7 Hz), 7.40 (1H, dd, J = 2.5, 9.9 Hz), 7.50 (1H, d, J = 1.9 Hz), 7.68-7.77 (2H, m).	-

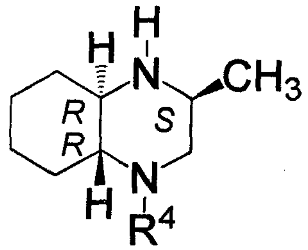
[0430]
Table 144

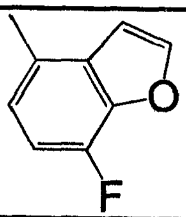
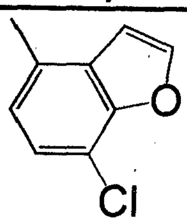
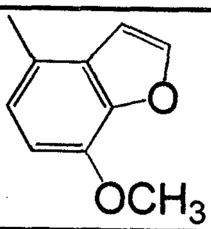
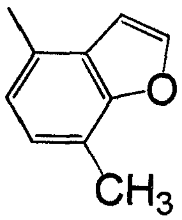
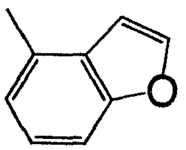
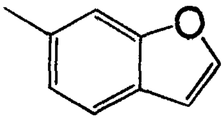


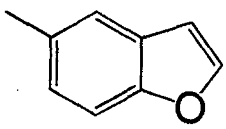
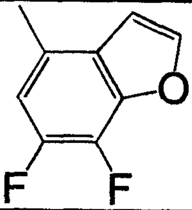
Example	R^4	NMR	Salt
1148		1H-NMR (CDCl3) δppm : 0.97-1.17 (4H, m), 1.17-1.89 (8H, m), 2.41-2.50 (1H, m), 2.53-2.69 (2H, m), 3.08 (1H, dd, J = 2.8, 11.2 Hz), 3.13-3.22 (1H, m), 7.18 (1H, dd, J = 2.0, 8.5 Hz), 7.27 (1H, d, J = 5.4 Hz), 7.42 (1H, d, J = 5.4 Hz), 7.58 (1H, d, J = 2.0 Hz), 7.78 (1H, d ,J = 8.5 Hz).	-
1149		1H-NMR (CDCl3) δppm : 0.86-1.02 (1H, m), 1.05 (3H, d, J = 6.4 Hz), 1.17-1.54 (4H, m), 1,54-1.63 (1H, m), 1.63-1.83 (3H, m), 2.39-2.55 (1H, m), 2.55-2.65 (1H, m), 2.65-2.74 (1H, m), 3.10 (1H, dd, J = 2.8, 11.4 Hz), 3.15-3.26 (1H, m), 7.12 (1H, dd, J = 0.7, 7.6 Hz), 7.30 (1H, t, J = 7.8 Hz), 7.35 (1H, d, J = 5.5 Hz), 7.57 (1H, d, J = 5.5 Hz), 7.64 (1H, d, J = 8.0 Hz).	-
1150		1H-NMR (DMSO-d6) δppm : 0.90-1.04 (1H, m), 1.10-1.35 (5H, m), 1.35-1.62 (3H, m), 1.64-1.74 (1H, m), 1.84-1.95 (1H, m), 2.65-2.84 (3H, m), 3.11 (1H, dd, J = 2.8, 11.8 Hz), 3.21-3.35 (1H, m), 6.49 (2H, s), 7.19 (1H, dd, J = 1.8, 8.5 Hz), 7.39 (1H, d, J = 5.4 Hz), 7.68 (1H, d, J = 5.4 Hz), 7.75 (1H, d, J = 1.8 Hz), 7.81 (1H, d, J = 8.5 Hz), 7.50-9.40 (1H, br).	Fumarate

[0431]
Table 145

absolute configuration

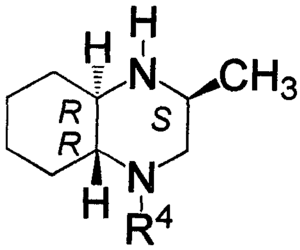


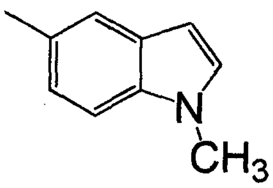
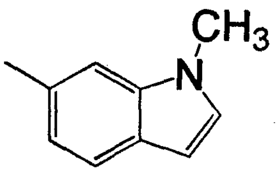
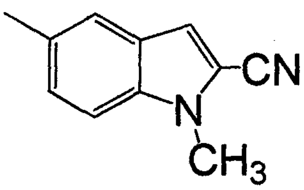
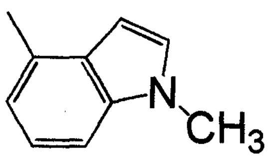
Example	R^4	NMR	Salt
1151		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 0.96-1.39 (6H, m), 1.40-1.50 (1H, m), 1.50-1.80 (3H, m), 2.05-2.15 (1H, m), 2.98-3.20 (2H, m), 3.20-3.40 (2H, m), 3.42-3.64 (1H, m), 5.23-6.05 (1H, br), 7.05-7.21 (2H, m), 7.30 (1H, brs), 8.03 (1H, s), 9.56 (1H, brs), 9.77 (1H, brs).	2 Hydrochloride
1152		1H-NMR (DMSO-d6) δppm: 0.85-1.00 (1H, m), 1.05-1.38 (5H, m), 1.38-1.75 (4H, m), 1.87-2.00 (1H, m), 2.65-3.00 (3H, m), 3.12 (1H, dd, J = 2.8, 11.9 Hz), 3.30-3.47 (1H, m), 6.53 (2H, s), 7.04 (1H, d, J = 8.3 Hz), 7.14 (1H, brs), 7.37 (1H, d, J = 8.3 Hz), 8.08 (1H, d, J = 2.2 Hz). (3H, not found)	Fumarate
1153		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.00-1.38 (6H, m), 1.38-1.50 (1H, m), 1.50-1.79 (3H, m), 2.05-2.14 (2H, m), 3.09-3.25 (2H, m), 3.25-3.50 (2H, br), 3.54-3.70 (1H, br), 3.94 (3H, s), 4.35-5.05 (1H, br), 6.90 (1H, d, J = 8.4 Hz), 7.07-7.20 (1H, m), 7.27 (1H, brs), 7.92 (1H, d, J = 1.8 Hz), 9.68 (1H, brs).	2 Hydrochloride
1154		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.05-1.38 (6H, m), 1.38-1.52 (1H, m), 1.52-1.62 (1H, m), 1.62-1.79 (2H, m), 2.09-2.18 (1H, m), 2.46 (3H, s), 3.17-3.37 (2H, m), 3.37-3.66 (2H, m), 3.66-3.75 (1H, m), 6.25-7.10 (1H, br), 7.14 (1H, d, J = 7.8 Hz), 7.19-7.30 (1H, m), 7.40 (1H, brs), 7.97 (1H, d, J = 2.1 Hz), 9.88 (2H, brs).	2 Hydrochloride
1155		1H-NMR (DMSO-d6) δ ppm at 80 ℃: 1.00-1.38 (6H, m), 1.45-1.80 (4H, m), 2.08-2.18 (1H, m), 3.06-3.27 (2H, m), 3.27-3.49 (2H, m), 3.53-3.70 (1H, m), 4.94-5.68 (1H, br), 7.13-7.22 (1H, m), 7.25-7.35 (2H, m), 7.45 (1H, d, J = 8.2 Hz), 7.93 (1H, d, J = 1.5 Hz), 9.45-10.00 (2H, brm).	2 Hydrochloride
1156		1H-NMR (DMSO-d6) δppm : 0.89-1.03 (1H, m), 1.05-1.35 (5H, m), 1.35-1.61 (3H, m), 1.61-1.75 (1H, m), 1.82-1.96 (1H, m), 2.62-2.86 (3H, m), 3.08 (1H, d, J = 11.6 Hz), 3.21-3.36 (1H, m), 6.50 (2H, s), 6.91 (1H, d, J = 2.0 Hz), 7.07 (1H, dd, J = 1.3, 8.3 Hz), 7.36 (1H, s), 7.58 (1H, d, J = 8.2 Hz), 7.95 (1H, d, J = 2.2 Hz). (3H not found)	Fumarate

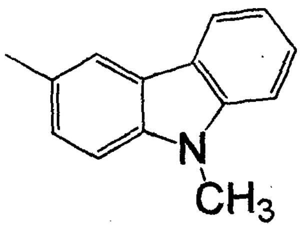
1157		1H-NMR (DMSO-d6) δppm : 1.09-1.55 (7H, m), 1.55-1.80 (3H, m), 2.10-2.22 (1H,m), 3.30-4.10 (5H, m), 4.10-5.20 (1H, br), 7.11 (1H, s), 7.58 (1H, brs), 7.80 (1H, s), 7.97 (1H, brs), 8.15 (1H, s), 10.06 (2H, brs).	2 Hydrochloride
1158		1H-NMR (DMSO-d6) δppm : 0.90-1.10 (1H, m), 1.15-1.38 (5H, m), 1.47-1.69 (3H, m), 1.69-1.80 (1H, m), 2.00-2.11 (1H, m), 2.80-3.40 (4H, m), 3.40-3.60 (1H, m), 5.35-6.36 (1H, br), 7.13-7.44 (2H, m), 8.15 (1H, d, J = 2.0 Hz), 9.08-9.66 (1H, br), 9.66-10.08 (1H, br).	2 Hydrochloride

[0432]
Table 146

absolute configuration

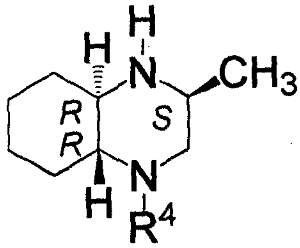


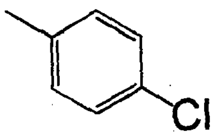
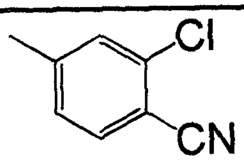
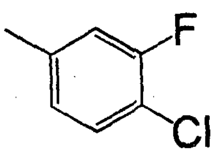
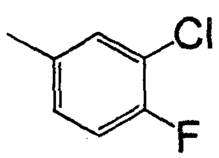
Example	R^4	NMR	Salt
1159		1H-NMR (CDCl3) δppm : 0.95-1.10 (4H, m), 1.10-1.54 (4H, m), 1.54-1.65 (2H, m), 1.65-1.83 (2H, m), 2.37-2.47 (1H, m), 2.55-2.69 (2H, m), 3.05 (1H, dd, J = 2.8, 11.2 Hz), 3.12-3.23 (1H, m), 3.77 (3H, s), 6.42 (1H, d, J = 0.7, 3.1 Hz), 7.03 (1H, d, J = 3.1 Hz), 7.08 (1H, d, J = 2.0, 8.6 Hz), 7.22-7.30 (1H, m), 7.41 (1H, d, J = 1.8 Hz).	-
1160		1H-NMR (DMSO-d6) δppm : 0.90-1.05 (1H, m), 1.09-1.35 (5H, m), 1.39-1.60 (3H, m), 1.64-1.75 (1H, m), 1.88-2.00 (1H, m), 2.67-2.95 (3H, m), 3.07 (1H, dd, J = 2.8, 12.0 Hz), 3.28-3.40 (1H, m), 3.75 (3H, s), 6.36 (1H, d, J = 0.6, 3.0 Hz), 6.51 (2H, s), 6.87 (1H, d, J = 1.6, 8.4 Hz), 7.18 (1H, s), 7.27 (1H, d, J = 3.0 Hz), 7.47 (1H, d, J = 8.3 Hz). (3H not found)	Fumarate
1161		1H-NMR (CDCl3) δppm : 0.82-0.92 (1H, m), 0.94 (3H, d, J = 6.3 Hz), 1.06-1.34 (4H, m), 1.38-1.58 (2H, m), 1.59-1.75 (2H, m), 2.28-2.37 (1H, m), 2.37-2.49 (2H, m), 2.89 (1H, dd, J = 2.6, 10.8 Hz), 2.94-3.04 (1H, m), 3.86 (3H, s), 7.21 (1H, dd, J = 1.9, 8.9 Hz), 7.31 (1H, s), 7.36 (1H, d, J = 1.7 Hz), 7.51 (1H, d, J = 8.9 Hz).	-
1162		1H-NMR (DMSO-d6) δppm : 0.80-0.99 (1H, m), 1.00-1.35 (5H, m), 1.35-1.98 (5H, m), 2.53-3.25 (4H, m), 3.23-3.40 (1H, m), 3.76 (3H, s), 6.40-6.58 (3H, m), 6.79 (1H, d, J = 8.0 Hz), 7.09 (1H, t, J = 7.8 Hz), 7.17-7.28 (2H, m). (3H not found)	Fumarate

1163		1H-NMR (DMSO-d6) δppm : 0.93-1.08 (1H, m), 1.10-1.35 (5H, m), 1.401-1.60 (3H, m), 1.64-1.75 (1H, m), 1.90-2.03 (1H, m), 2.72-3.00 (3H, m), 3.11 (1H, dd, J = 2.0, 12.0 Hz), 3.32-3.43 (1H, m), 3.85 (3H, s), 6.52 (2H, s), 7.15-7.23 (1H, m), 7.29 (1H, dd, J = 1.9, 8.6 Hz), 7.43-7.49 (1H, m), 7.53 (1H, d, J = 8.6 Hz), 7.56 (1H, d, J = 8.2 Hz), 7.94 (1H, d, J = 1.8 Hz), 8.14 (1H, d, J = 7.7 Hz). (3H, not found)	Fumarate

[0433]
Table 147

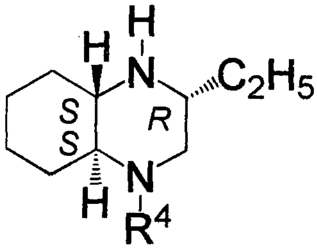
absolute configuration

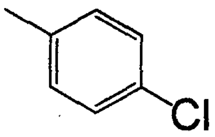
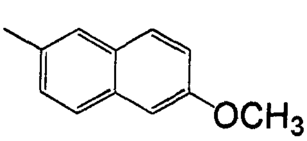
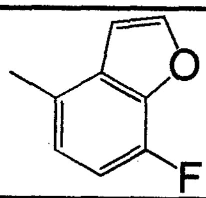
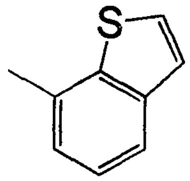
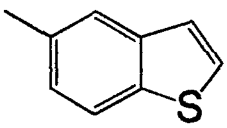
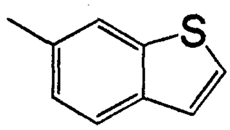


Example	R^4	NMR	Salt
1164		1H-NMR (CDCl3) δppm : 0.88-1.08 (4H, m), 1.15-1,42 (3H, m), 1.42-1.60 (1H, br), 1.60-1.69 (2H, m), 1.69-1.82 (2H, m), 2.31-2.39 (1H, m), 2.46 (1H, dd, J = 10.4, 11.0 Hz), 2.55-2.63 (1H, m), 3.00 (1H, dd, J = 2.8, 11.2 Hz), 3.07-3.18 (1H, m), 7.02-7.09 (2H, m), 7.23-7.29 (2H, m).	-
1165		1H-NMR (CDCl3) δppm : 0.98-1.10 (4H, m), 1.22-1.46 (4H, m), 1.65-1.90 (4H, m), 2.46-2.67 (3H, m), 3.10-3.25 (2H, m), 6.98 (1H, dd, J = 2.1, 8.6 Hz), 7.12 (1H, d, J = 2.1 Hz), 7.54 (1H, d, J = 8.6 Hz)	-
1166		1H-NMR (DMSO-d6) δppm : 0.90-1.03 (1H, m), 1.12 (3H ,d, J = 6.4 Hz), 1.17-1.34 (2H, m), 1.34-1.48 (1H, m), 1.52-1.74 (3H, m), 1.84-1.94 (1H, m), 2.65-2.75 (2H, m), 2.74-2.84 (1H, m), 3.14 (1H, dd, J = 3.0, 11.9 Hz), 3.22-3.34 (1H, m), 6.51 (2H, s), 6.97-7.04 (1H, m), 7.19 (1H, dd, J = 2.4, 11.3 Hz), 7.51 (1H, t, J = 8.6 Hz), 8.60-11.75 (2H, br). (1H not found)	Fumarate
1167		1H-NMR (DMSO-d6) δppm : 0.88-1.02 (1H, m), 1.11 (3H, d, J = 6.4 Hz), 1.14-1.45 (3H, m), 1.48-1.62 (2H, m), 1.65-1.73 (1H, m), 1.82-1.92 (1H, m), 2.60-2.81 (3H, m), 3.05 (1H, dd, J = 3.0, 11.8 Hz), 3.19-3.30 (1H, m), 6.51 (2H, s), 7.11-7.18 (1H, m), 7.30-7.41 (2H, m), 8.85-11.65 (2H, br). (1H not found)	Fumarate

[0434]
Table 148

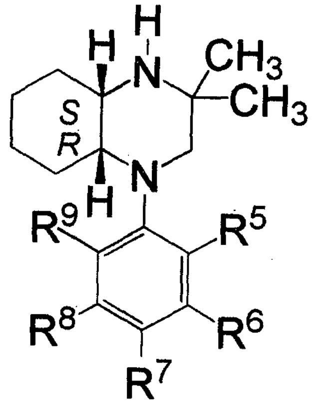
absolute configuration

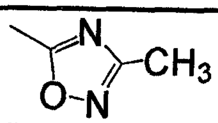
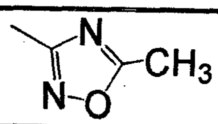
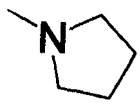
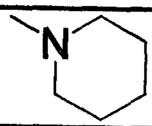
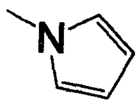
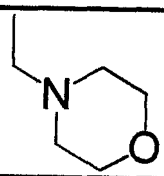
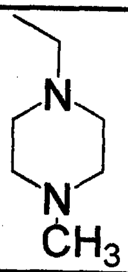


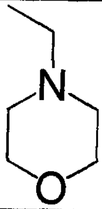
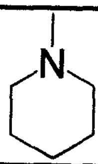
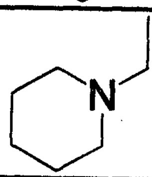
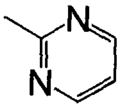
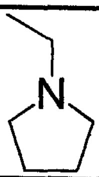
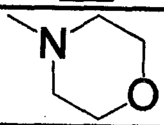
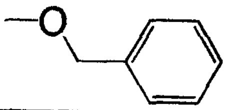
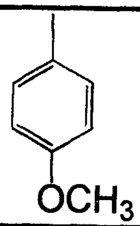
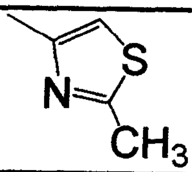
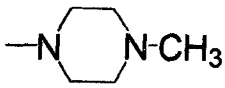
Example	R^4	NMR	Salt
1168		1H-NMR (DMSO-d6) δppm : 0.8-1.0 (4H, m), 1.1-1.6 (7H, m), 1.6-1.7 (1H, m), 1.8-1.9 (1H, m), 2.5-2.75 (3H, m), 2.85-3.9 (5H, m), 6.5-6.55 (2H, m), 7.1-7.2 (2H, m), 7.3-7.4 (2H, m).	Fumarate
1169		1H-NMR (CDCl3) δppm : 0.94 (3H, t, J = 7.5Hz), 0.95-1.1 (1H, m), 1.15-1.5 (5H, m), 1.5-1.85 (5H, m), 2.46-2.69 (3H, m), 2.91-3.01 (1H, m), 3.18 (1H, dd, J = 2.7, 11.2Hz), 3.91 (3H, s), 7.08-7.14 (2H, m), 7.31 (1H ,dd, J = 2.1, 8.7Hz), 7.47 (1H, d, J = 2.0Hz), 7.64-7.71 (2H, m).	-
1170		1H-NMR (DMSO-d6) δppm : 0.82-1.03 (4H, m), 1.09-1.36 (2H, m), 1.41-1.59 (4H, m), 1.59-1.75 (2H, m), 1.92-2.06 (1H, m), 2.71-3.07 (3H, m), 3.10-3.20 (1H, m), 3.20-3.32 (1H, m), 6.56 (4H, s), 6.97-7.26 (3H, m), 11.5 (5H, m).	2 Fumarate
1171		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (4H, m), 1.1-1.4 (2H, m), 1.45-1.65 (4H, m), 1.65-1.85 (2H, m), 2.05-2.15 (1H, m), 2.85-3.22 (3H, m), 3.22-3.38 (2H, m), 4.09 (1H, br), 7.24 (1H, d, J = 7.5Hz), 7.35-7.5 (2H, m), 7.7-7.8 (2H, m), 9.15-9.35 (1H, m), 9.35-9.55 (1H, m).	2 Hydrochloride
1172		1H-NMR (CDCl3) δppm : 0.93 (3H, t, J = 7.5Hz), 0.98-1.09 (1H, m), 1.14-1.50 (5H, m), 1.55-1.85 (5H, m), 2.44-2.53 (1H, m), 2.55-2.68 (2H, m), 2.91-3.00 (1H, m), 3.15 (1H, dd, J = 2.7, 11.1Hz), 7.20 (1H, dd, J = 2.0, 8.6Hz), 7.27 (1H, dd, J = 0.5, 5.4Hz), 7.43 (1H, d, J = 5.4Hz), 7.59 (1H, d, J = 2.0Hz), 7.79 (1H, d, J = 8.6Hz).	-
1173		1H-NMR (DMSO-d6) δppm : 0.85-1.05 (4H, m), 1.15-1.35 (2H, m), 1.35-1.5 (2H, m), 1.5-1.6 (3H, m), 1.65-1.75 (1H, m), 1.85-1.95 (1H, m), 2.65-2.85 (3H, m), 3.05-3.2 (2H, m), 3.6 (3H, br), 6.51 (2H, s), 7.19 (1H, dd, J = 1.9, 8.5Hz), 7.39 (1H, dd, J = 0.5, 5.4Hz), 7.68 (1H, d, J = 5.4Hz), 7.76 (1H, d, J = 1.8Hz), 7.81 (1H, d, J = 8.5Hz).	Fumarate

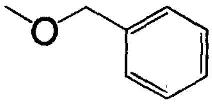
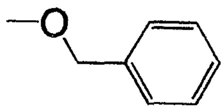
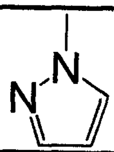
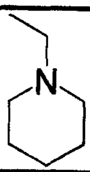
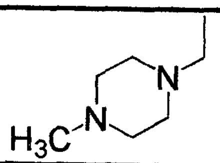
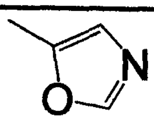
[0435]
Table 149

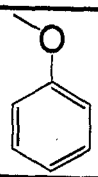
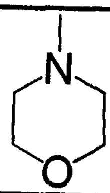
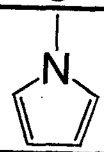
absolute configuration



Example	R5	R6	R7	R8	R9	MS(M+1)
1174	-H		-H	-H	-H	327
1175	-H	-H		-H	-H	317
1176	-H		-H	-H	-H	327
1177	-H		-H	-H	-H	314
1178	-H		-H	-H	-H	328
1179	-H		-H	-H	-H	310
1180	-H	-H		-H	-H	344
1181	-H		-H	-H	-H	357

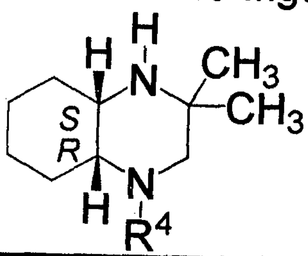
1182	-H		-H	-H	-H	344
1183	-H	-H		-H	-H	328
1184	-H	-H		-H	-H	342
1185	-H		-H	-H	-H	323
1186	-H		-H	-H	-H	328
1187	-H		-H	-H	-H	330
1188	-H	-Cl		-H	-H	385
1189	-H	-H		-H	-H	351
1190	-H		-H	-H	-H	342
1191	-OCH3	-OCH3	-H	-H	-H	305
1192	-H	-H	-O(CH2)2CH3	-H	-H	303
1193	-H	-H		-H	-H	343

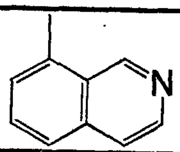
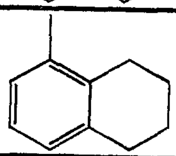
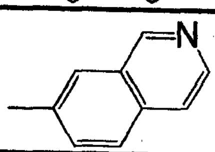
1194	-F	-H	-OCH3	-H	-H	293
1195	-Cl	-H	-H	-CF3	-H	347
1196	-Cl	-H	-H	-H	-H	297
1197	-H		-OCH3	-H	-H	381
1198	-OCH3	-H	-Cl	-H	-H	309
1199	-F	-Cl	-H	-H	-H	297
1200	-CH3	-H	-OCH3	-Cl	-H	323
1201	-H	-OCH3		-H	-H	381
1202	-H	-H		-H	-H	311
1203	-H		-H	-H	-H	342
1204	-H	-H		-H	-H	357
1205	-H	-H	-OCH(CH3)2	-H	-H	303
1206	-H		-H	-H	-H	312
1207	-OCH2CH3	-H	-H	-H	-H	289

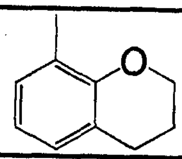
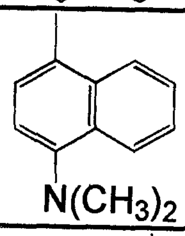
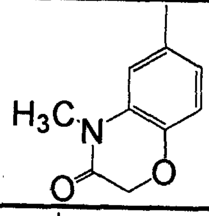
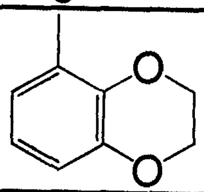
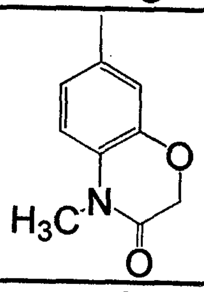
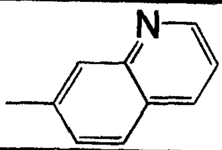
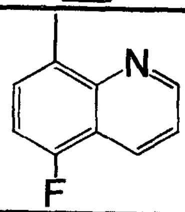
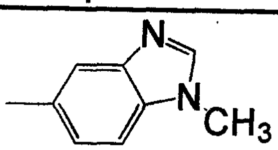
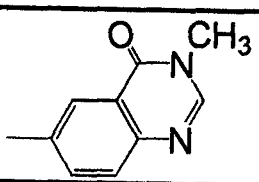
1208	-H		-H	-H	-H	337
1209	-Cl	-CF3	-H	-H	-H	347
1210	-H	-H	-CH2CH(CH3)2	-H	-H	301
1211	-CN	-H	-Cl	-H	-H	304
1212	-H	-H		-H	-H	330
1213	-H	-H		-H	-H	310

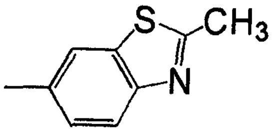
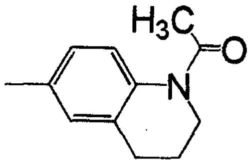
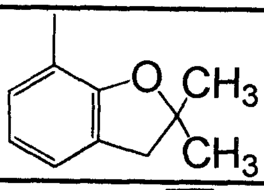
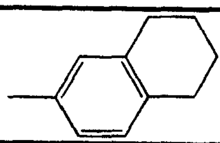
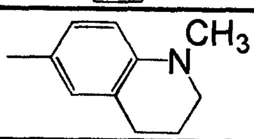
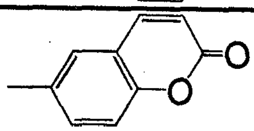
[0436]
Table 150

absolute configuration



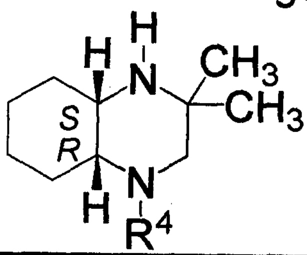
Example	R⁴	MS(M+1)
1214		296
1215		299
1216		296

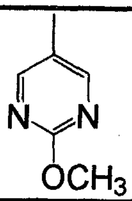
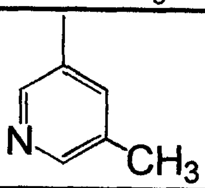
1217		301
1218		338
1219		330
1220		303
1221		330
1222		296
1223		314
1224		299
1225		327

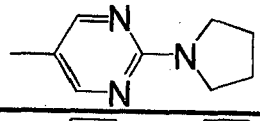
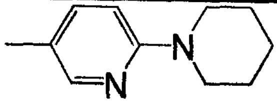
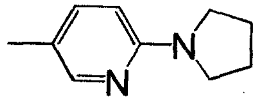
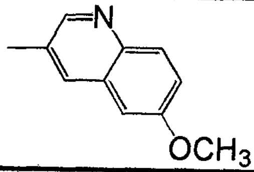
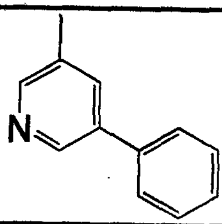
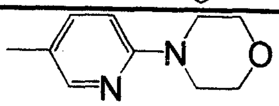
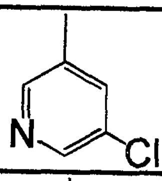
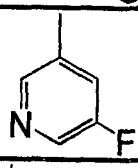
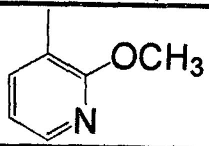
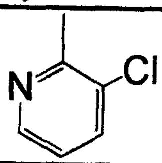
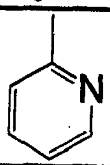
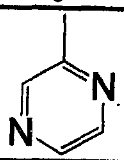
1226		316
1227		342
1228		315
1229		299
1230		314
1231		313

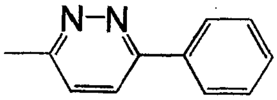
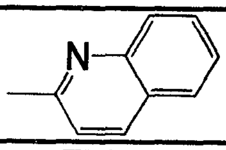
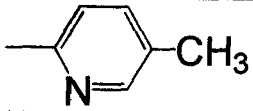
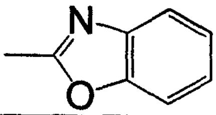
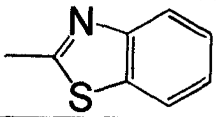
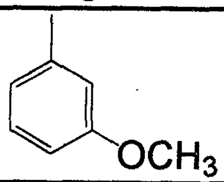
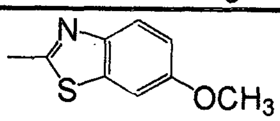
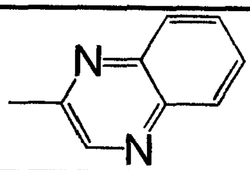
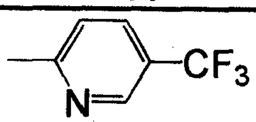
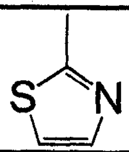
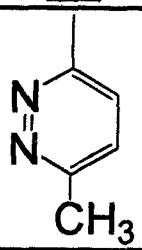
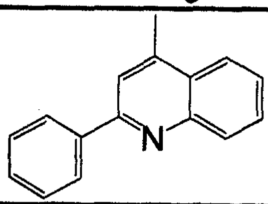
[0437]
Table 151

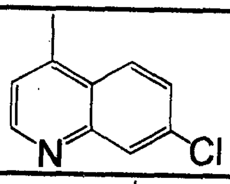
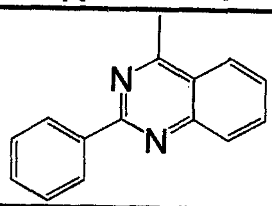
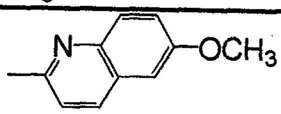
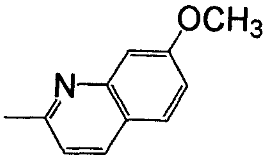
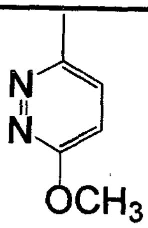
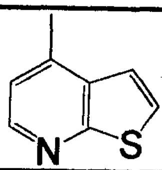
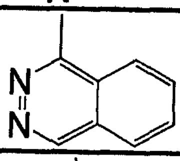
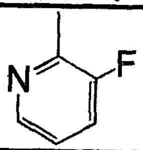
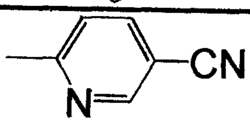
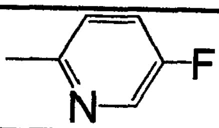
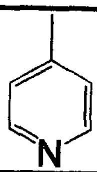
absolute configuration

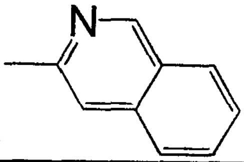
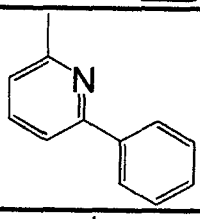
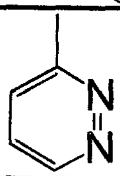
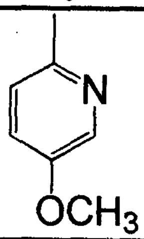
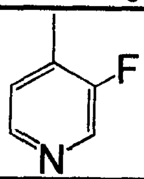
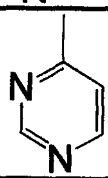
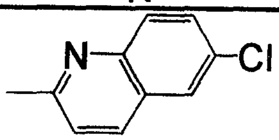
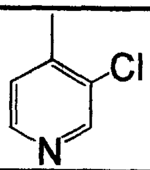
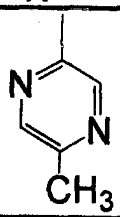
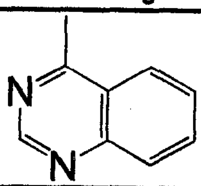


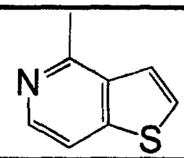
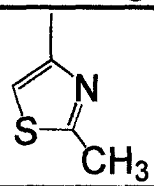
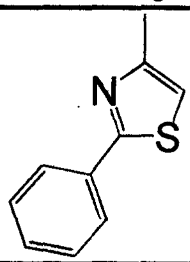
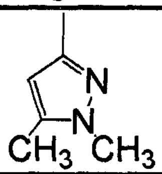
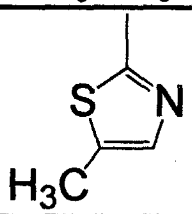
Example.	R^4	MS(M+1)
1232		277
1233		260

1234		316
1235		329
1236		315
1237		326
1238		322
1239		331
1240		280
1241		264
1242		276
1243		280
1244		246
1245		247

1246		323
1247		296
1248		260
1249		286
1250		302
1251		276
1252		332
1253		297
1254		314
1255		252
1256		261
1257		372

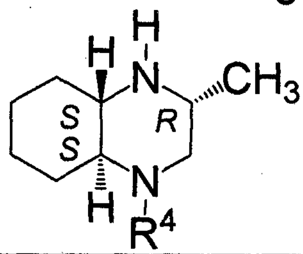
1258		330
1259		373
1260		326
1261		326
1262		277
1263		302
1264		297
1265		264
1266		271
1267		264
1268		246

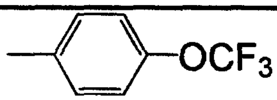
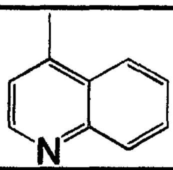
1269		296
1270		322
1271		247
1272		276
1273		264
1274		247
1275		330
1276		280
1277		261
1278		297

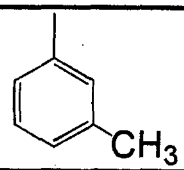
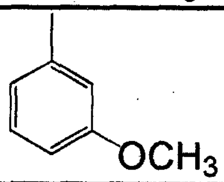
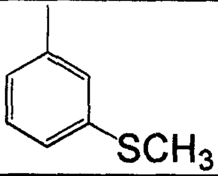
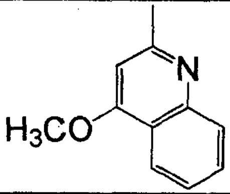
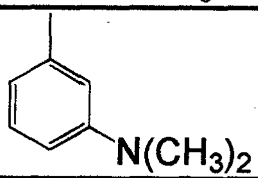
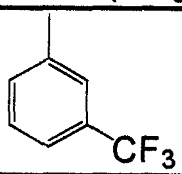
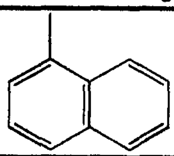
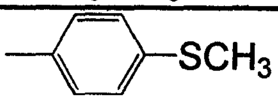
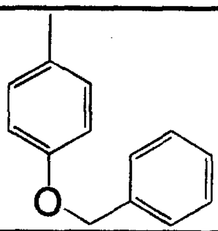
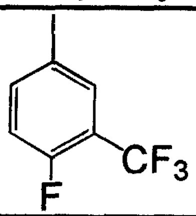
1279		302
1280		266
1281		328
1282		263
1283		266

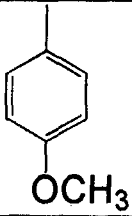
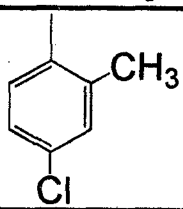
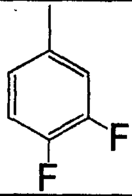
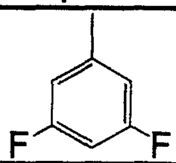
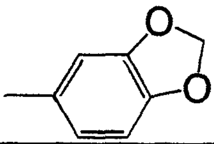
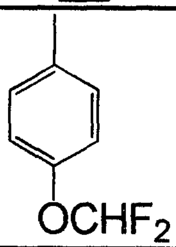
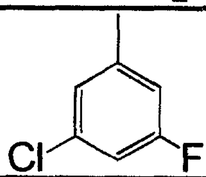
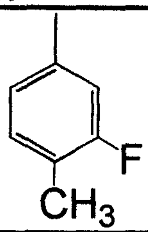
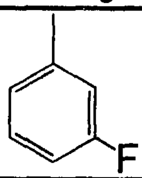
[0438]
Table 152

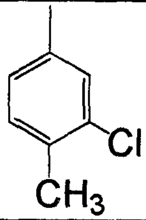
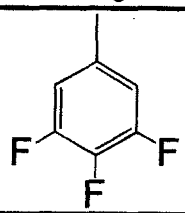
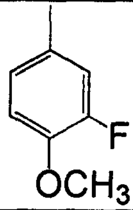
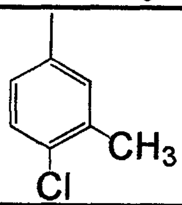
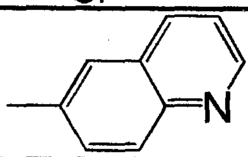
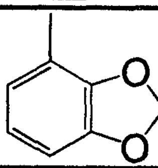
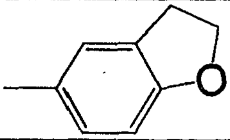
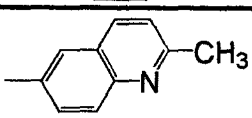
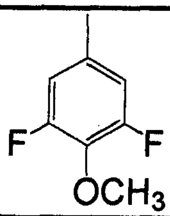
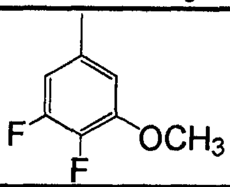
absolute configuration

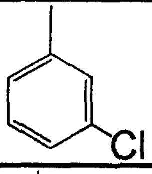
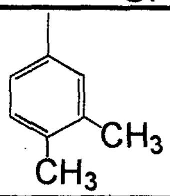
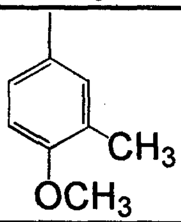
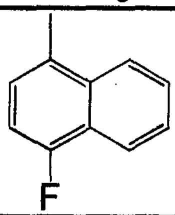
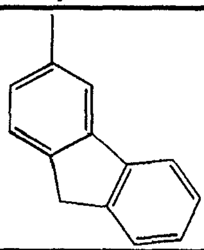
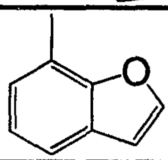
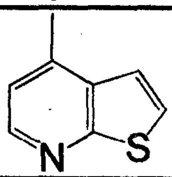
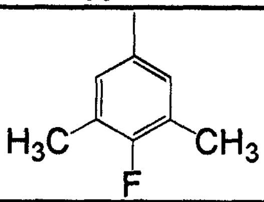
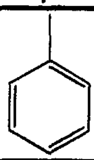


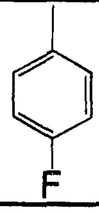
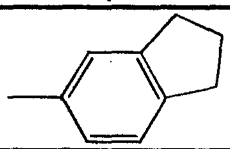
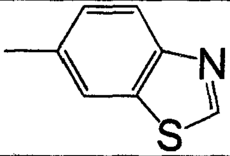
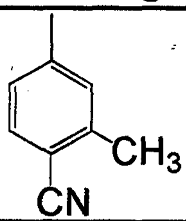
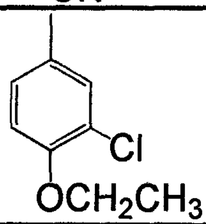
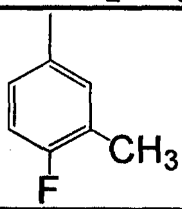
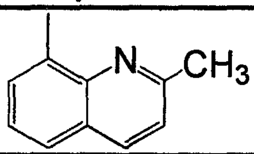
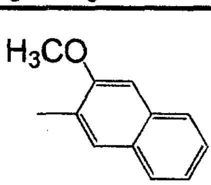
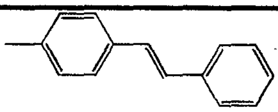
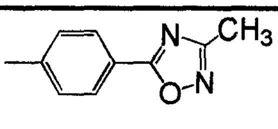
Exam ple.	R^4	MS(M+1)
1284		315
1285		282

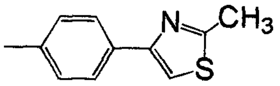
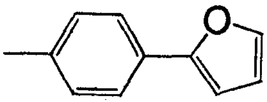
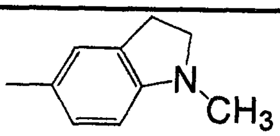
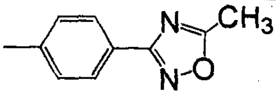
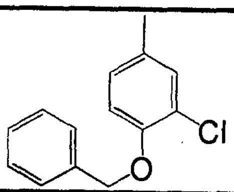
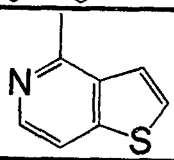
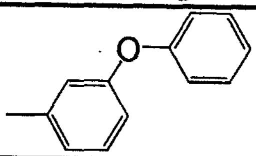
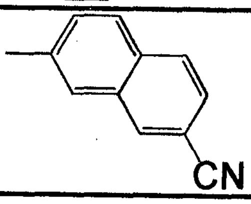
1286		245
1287		261
1288		277
1289		312
1290		274
1291		299
1292		281
1293		277
1294		337
1295		317

1296		261
1297		279
1298		267
1299		267
1300		275
1301		297
1302		283
1303		263
1304		249

1305		279
1306		285
1307		279
1308		279
1309		282
1310		275
1311		273
1312		296
1313		297
1314		297

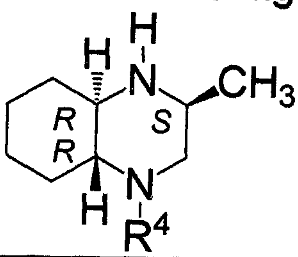
1315		265
1316		259
1317		275
1318		299
1319		319
1320		271
1321		288
1322		277
1323		231

1324		249
1325		271
1326		288
1327		270
1328		309
1329		263
1330		296
1331		311
1332		333
1333		313

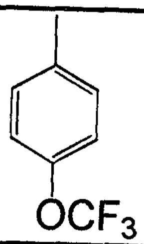
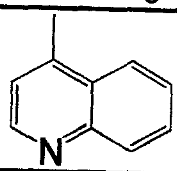
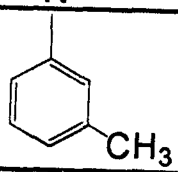
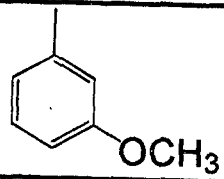
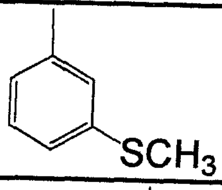
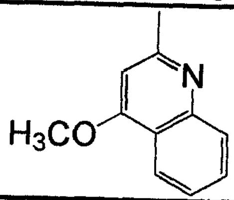
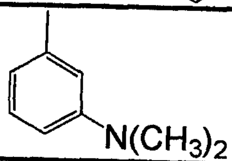
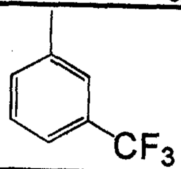
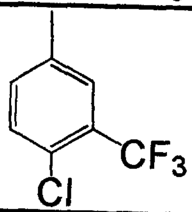
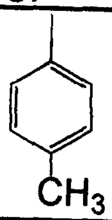
1334		328
1335		297
1336		286
1337		313
1338		371
1339		288
1340		323
1341		306

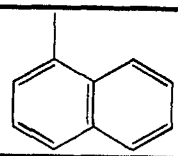
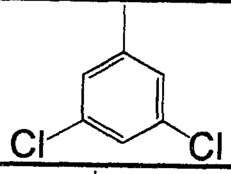
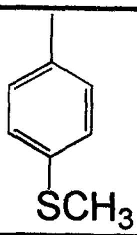
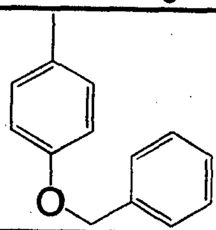
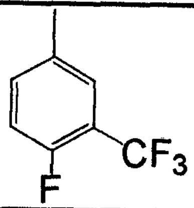
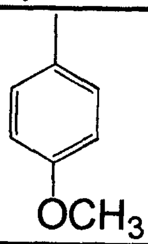
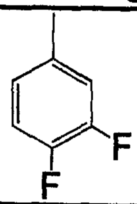
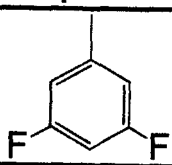
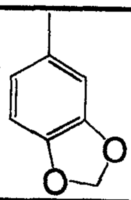
[0439]
Table 153

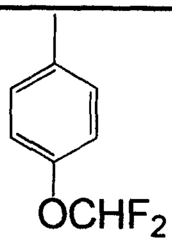
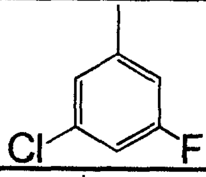
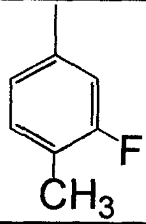
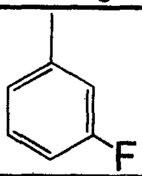
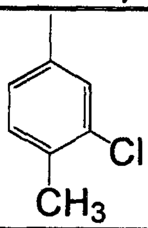
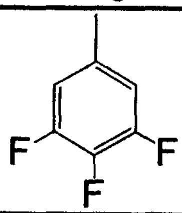
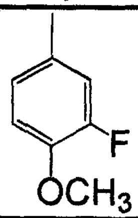
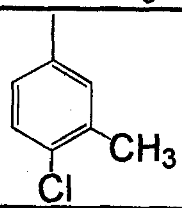
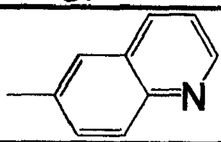
absolute configuration

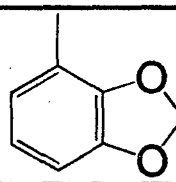
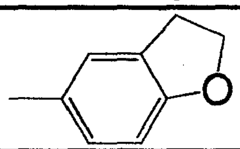
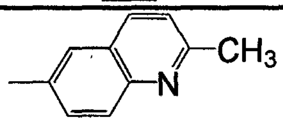
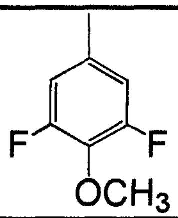
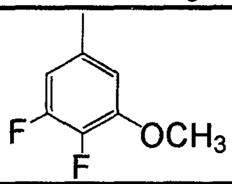
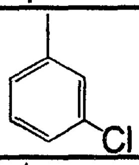
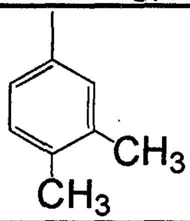
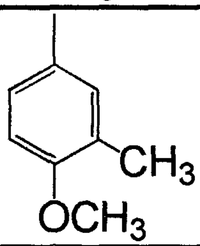
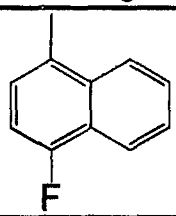


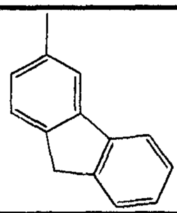
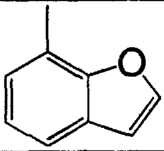
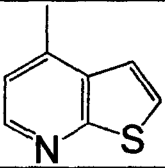
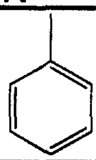
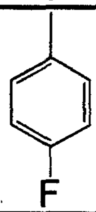
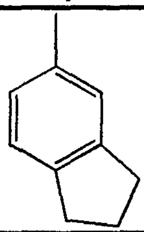
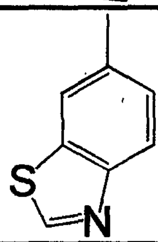
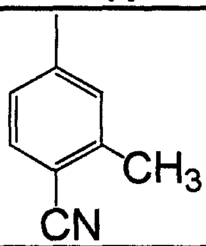
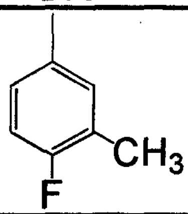
Example.	R^4	MS(M+1)

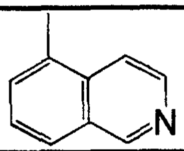
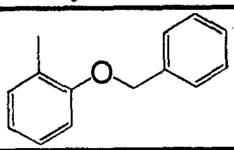
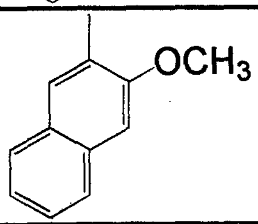
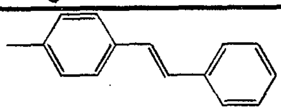
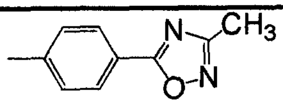
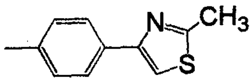
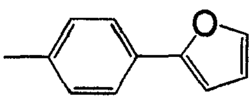
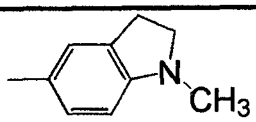
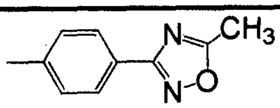
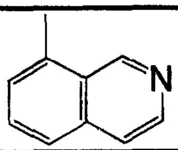
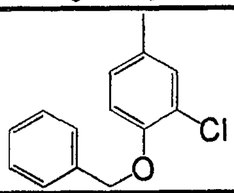
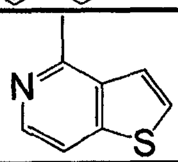
1342		315
1343		282
1344		245
1345		261
1346		277
1347		312
1348		274
1349		299
1350		333
1351		245

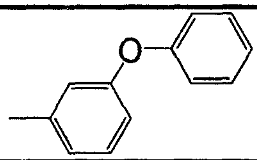
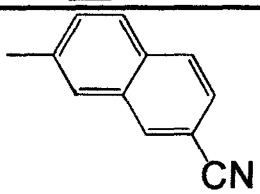
1352		281
1353		299
1354		277
1355		337
1356		317
1357		261
1358		267
1359		267
1360		275

1361		297
1362		283
1363		263
1364		249
1365		279
1366		285
1367		279
1368		279
1369		282

1370		275
1371		273
1372		296
1373		297
1374		297
1375		265
1376		259
1377		275
1378		299

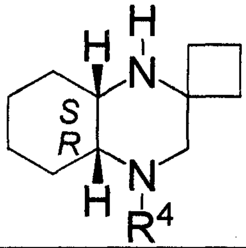
1379		319
1380		271
1381		288
1382		231
1383		249
1384		271
1385		288
1386		270
1387		263

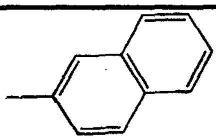
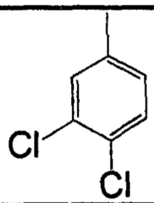
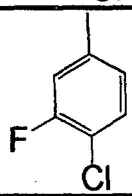
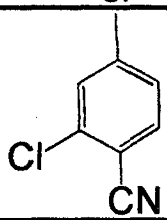
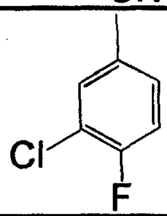
1388		282
1389		337
1390		311
1391		333
1392		313
1393		328
1394		297
1395		286
1396		313
1397		282
1398		371
1399		288

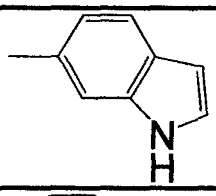
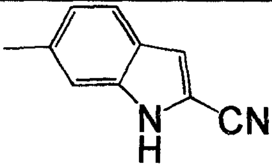
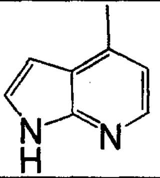
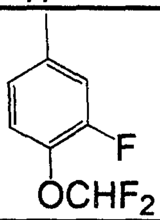
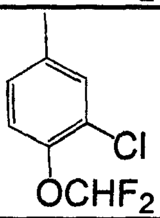
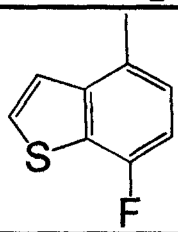
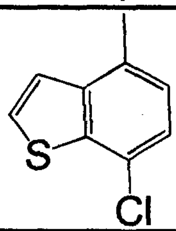
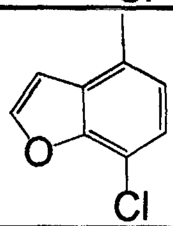
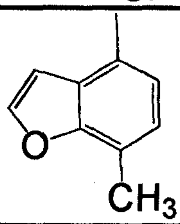
1400		323
1401		306

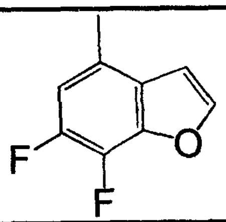
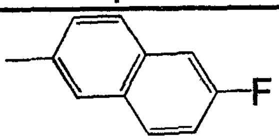
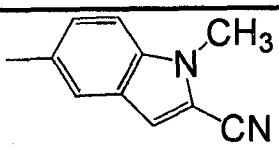
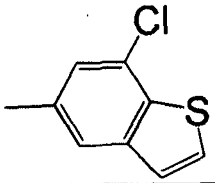
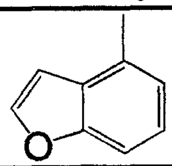
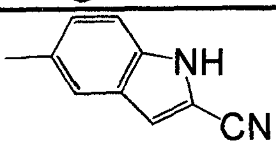
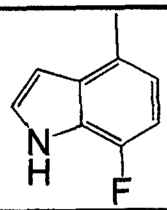
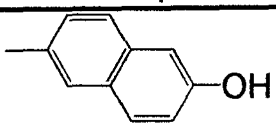
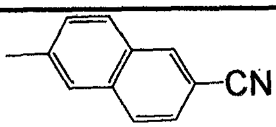
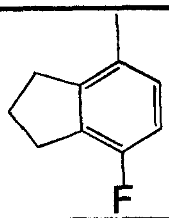
[0440]
Table 154

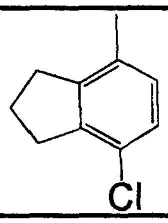
absolute configuration



Example.	R^4	MS(M+1)
1402		307
1403		325
1404		309
1405		316
1406		309

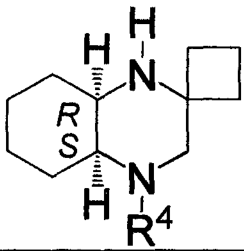
1407		296
1408		321
1409		297
1410		341
1411		357
1412		331
1413		347
1414		331
1415		311

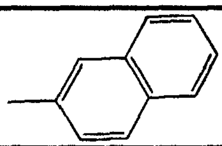
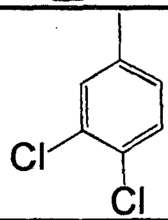
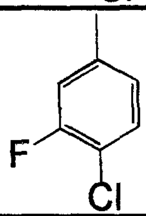
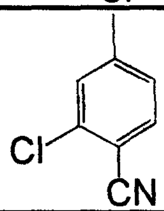
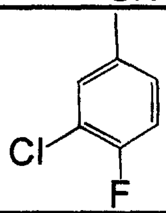
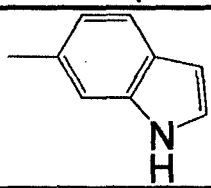
1416		333
1417		325
1418		335
1419		347
1420		297
1421		321
1422		314
1423		323
1424		332
1425		315

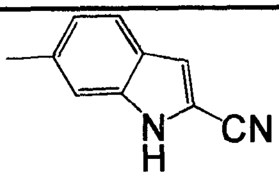
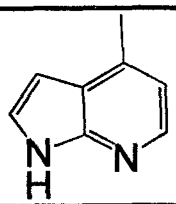
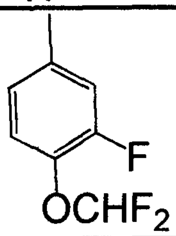
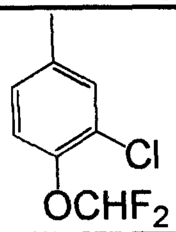
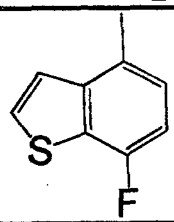
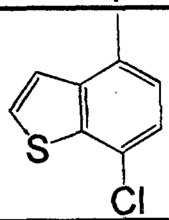
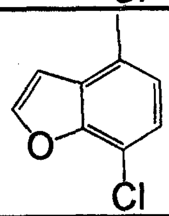
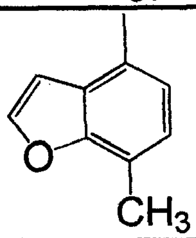
1426		331

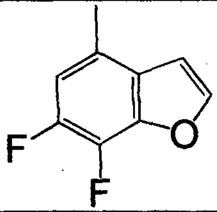
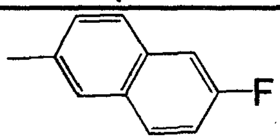
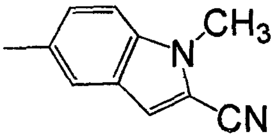
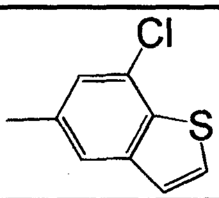
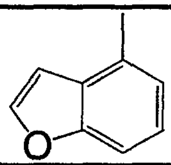
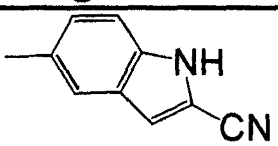
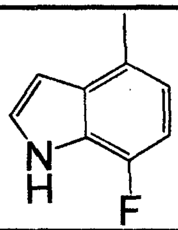
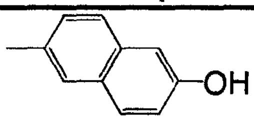
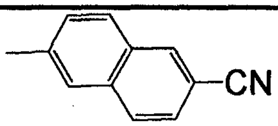
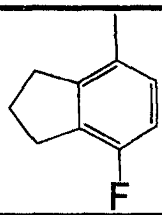
[0441]
Table 155

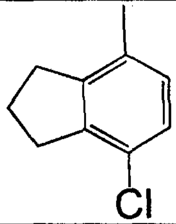
absolute configuration



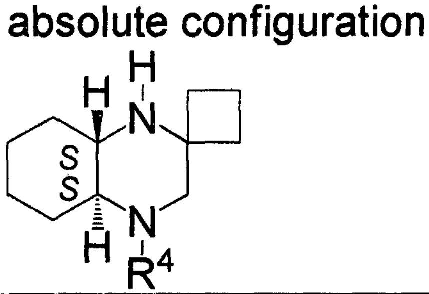
Example.	R^4	MS(M+1)
1427		307
1428		325
1429		309
1430		316
1431		309
1432		296

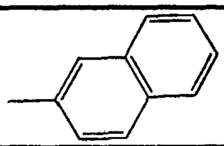
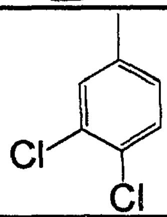
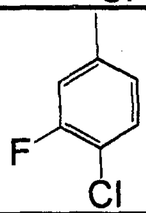
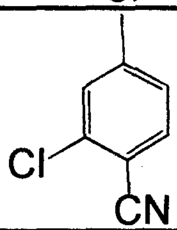
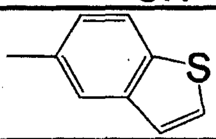
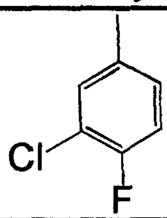
1433		321
1434		297
1435		341
1436		357
1437		331
1438		347
1439		331
1440		311

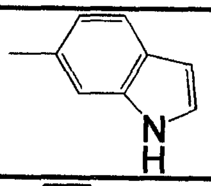
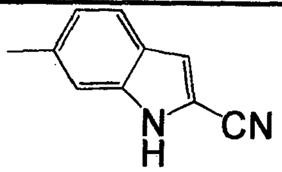
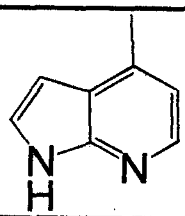
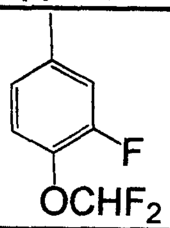
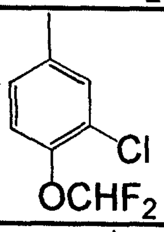
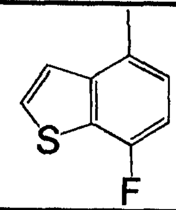
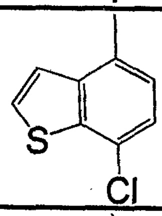
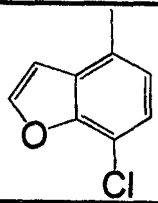
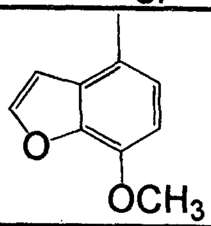
1441		333
1442		325
1443		335
1444		347
1445		297
1446		321
1447		314
1448		323
1449		332
1450		315

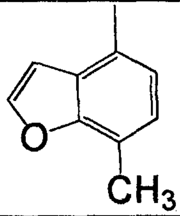
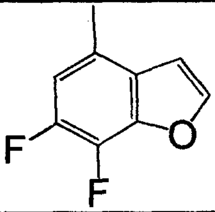
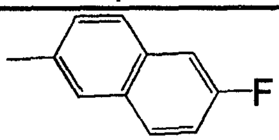
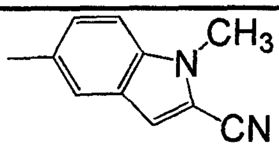
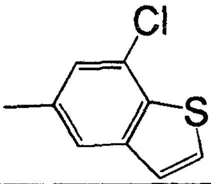
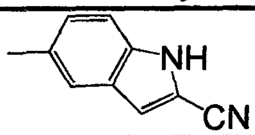
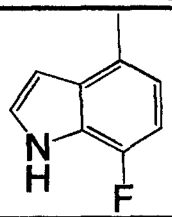
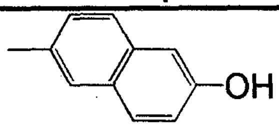
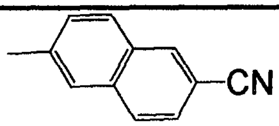
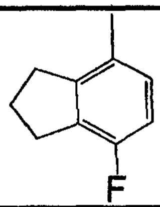
1451		331

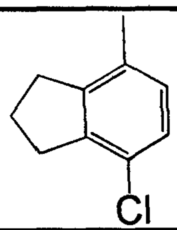
[0442]
Table 156



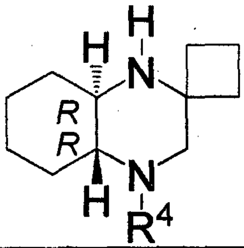
Example.	R^4	MS(M+1)
1452		307
1453		325
1454		309
1455		316
1456		313
1457		309

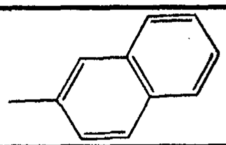
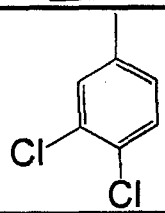
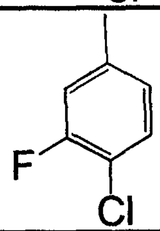
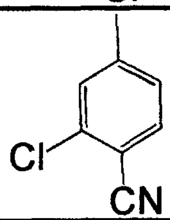
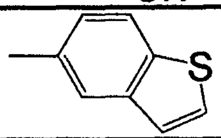
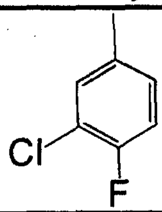
1458		296
1459		321
1460		297
1461		341
1462		357
1463		331
1464		347
1465		331
1466		327

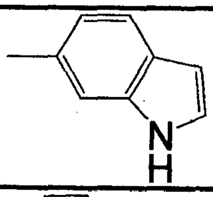
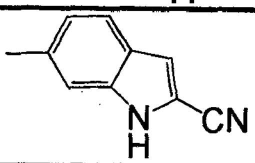
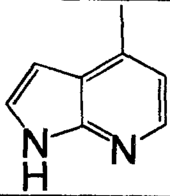
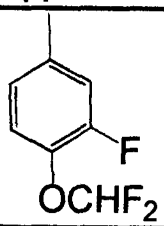
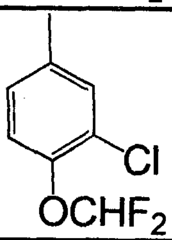
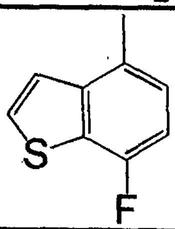
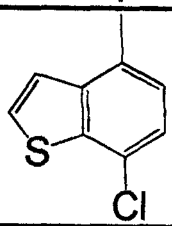
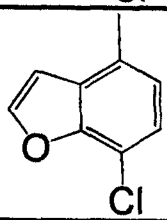
1467		311
1468		333
1469		325
1470		335
1471		347
1472		321
1473		314
1474		323
1475		332
1476		315

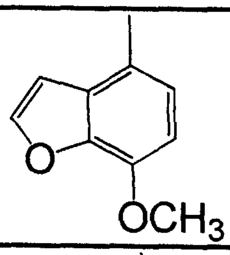
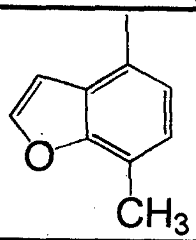
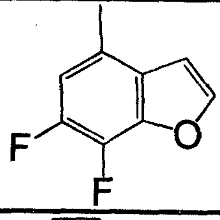
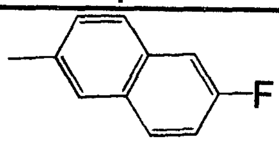
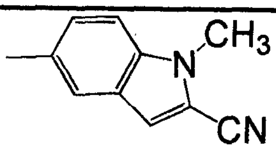
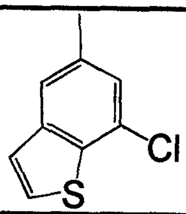
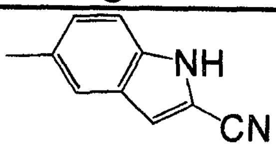
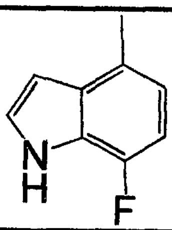
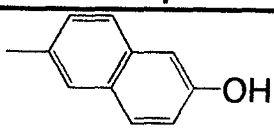
1477		331

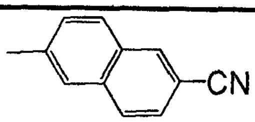
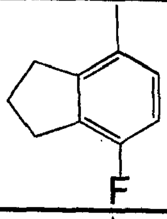
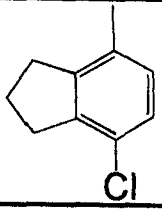
[0443]
Table 157



Example.	R^4	MS(M+1)
1478		307
1479		325
1480		309
1481		316
1482		313
1483		309

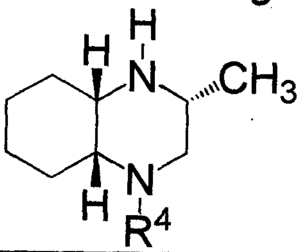
1484		296
1485		321
1486		297
1487		341
1488		357
1489		331
1490		347
1491		331

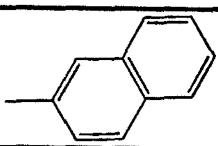
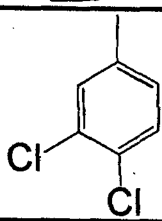
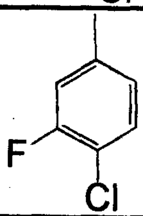
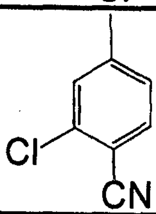
1492		327
1493		311
1494		333
1495		325
1496		335
1497		347
1498		321
1499		314
1500		323

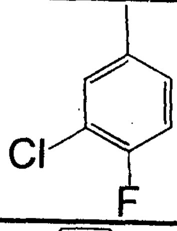
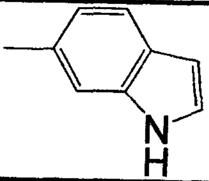
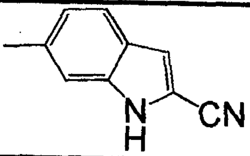
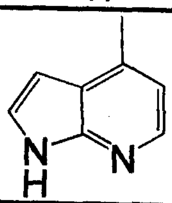
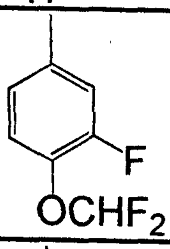
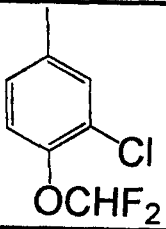
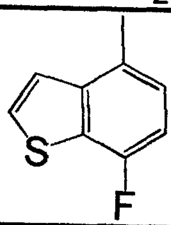
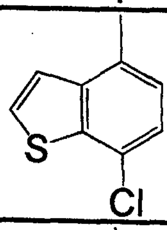
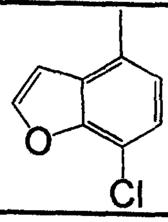
1501		332
1502		315
1503		331

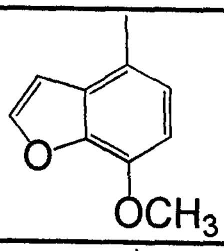
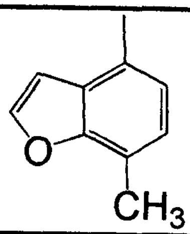
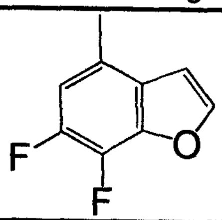
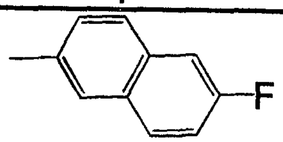
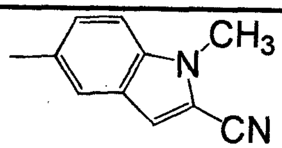
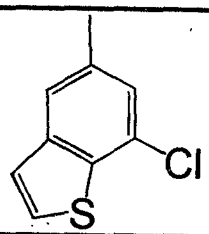
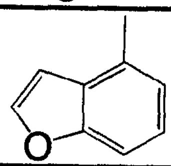
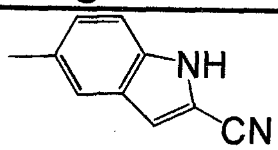
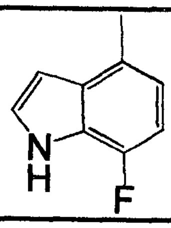
[0444]
Table 158

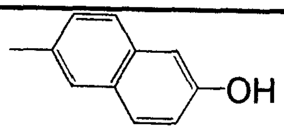
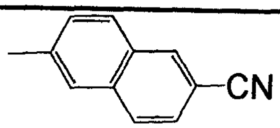
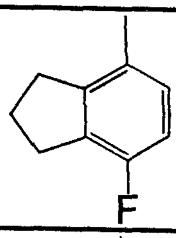
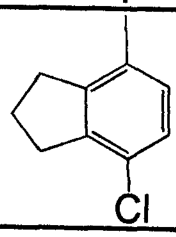
relative configuration



Exam ple.	R^4	MS(M+1)
1504		281
1505		299
1506		283
1507		290

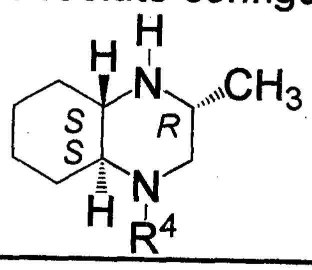
1508		283
1509		270
1510		295
1511		271
1512		315
1513		331
1514		305
1515		321
1516		305

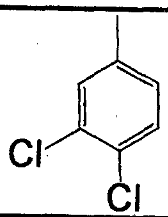
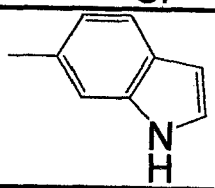
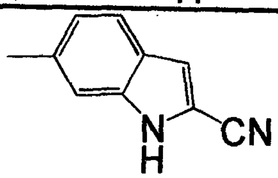
1517		301
1518		285
1519		307
1520		299
1521		309
1522		321
1523		271
1524		295
1525		288

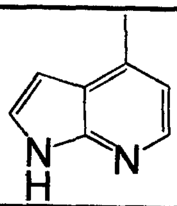
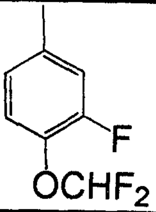
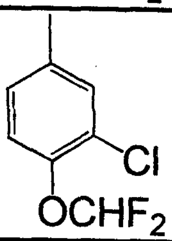
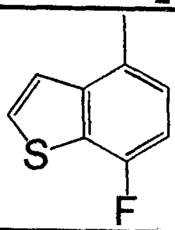
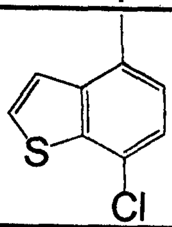
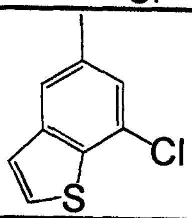
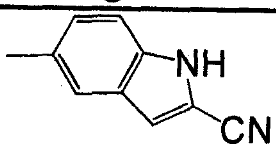
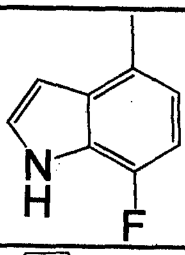
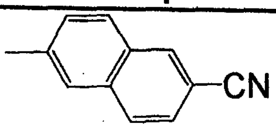
1526		297
1527		306
1528		289
1529		305

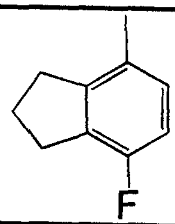
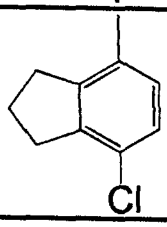
[0445]
Table 159

absolute configuration



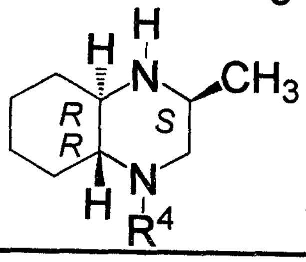
Example.	R^4	MS(M+1)
1530		299
1531		270
1532		295

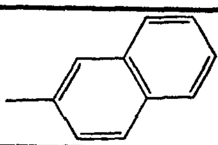
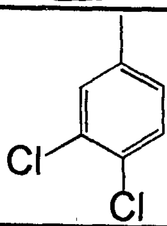
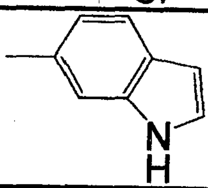
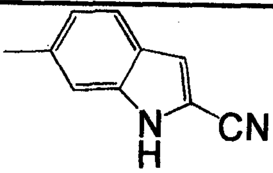
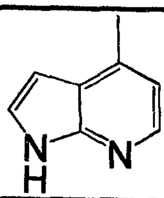
1533		271
1534		315
1535		331
1536		305
1537		321
1538		321
1539		295
1540		288
1541		306

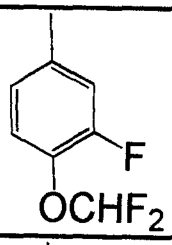
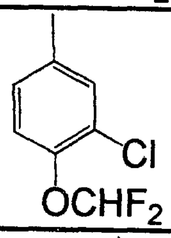
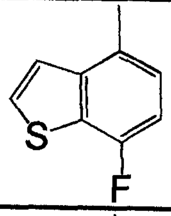
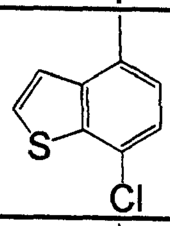
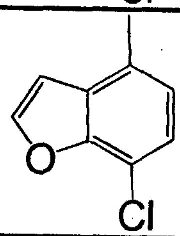
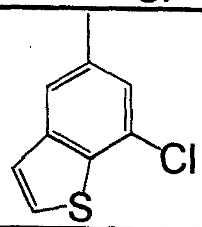
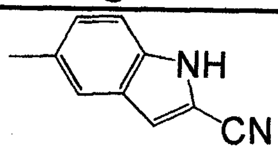
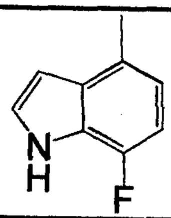
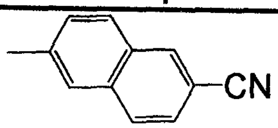
1542		289
1543		305

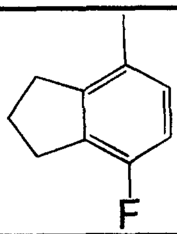
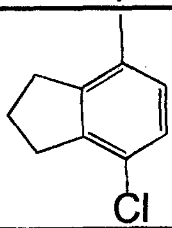
[0446]
Table 160

absolute configuration



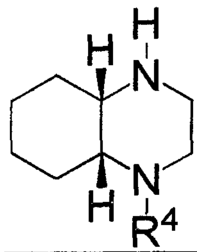
Example.	R^4	MS(M+1)
1544		281
1545		299
1546		270
1547		295
1548		271

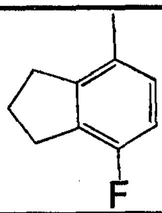
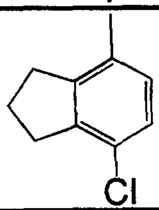
1549		315
1550		331
1551		305
1552		321
1553		305
1554		321
1555		295
1556		288
1557		306

1558		289
1559		305

[0447]
Table 161

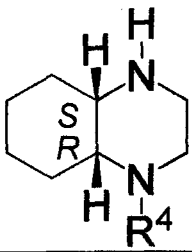
relative configuration



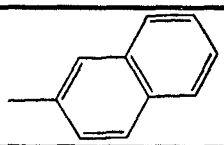
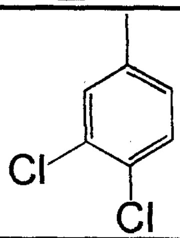
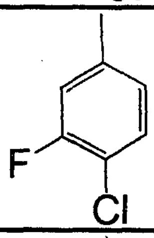
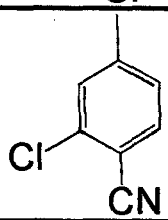
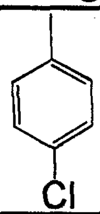
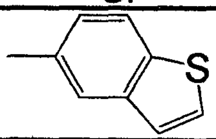
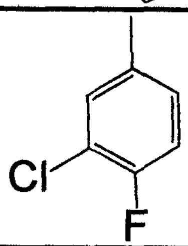
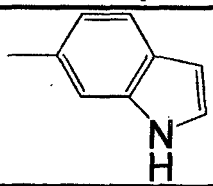
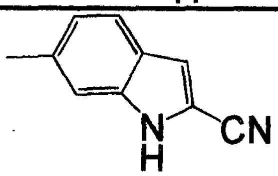
Example.	R4	MS(M+1)
1560		275
1561		291

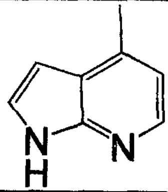
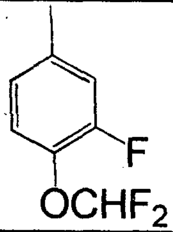
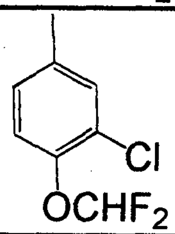
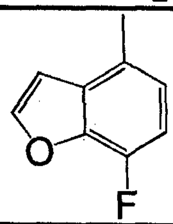
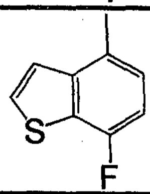
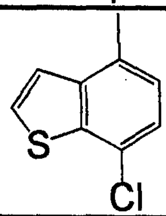
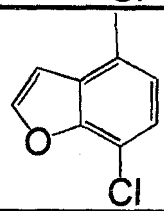
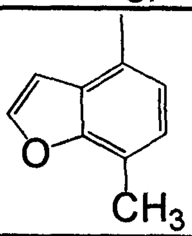
[0448]
Table 162

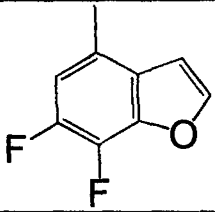
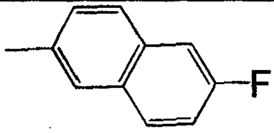
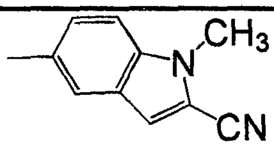
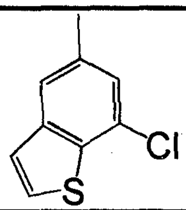
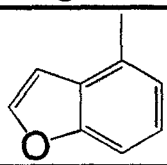
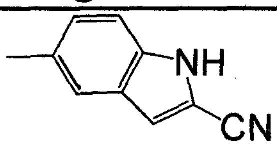
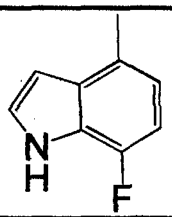
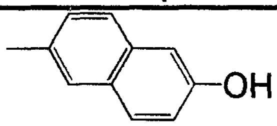
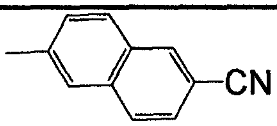
absolute configuration



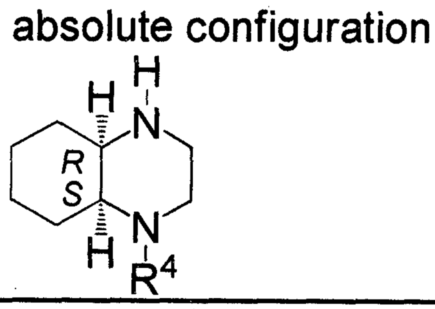
Example.	R4	MS(M+1)

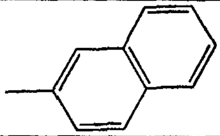
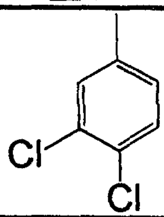
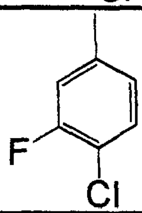
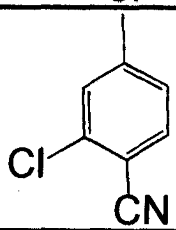
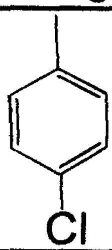
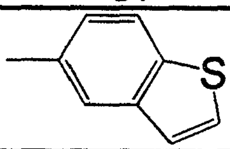
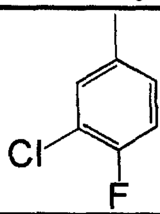
1562		267
1563		285
1564		269
1565		276
1566		251
1567		273
1568		269
1569		256
1570		281

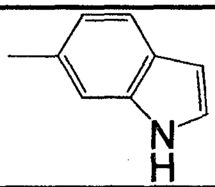
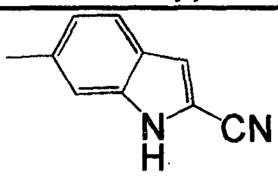
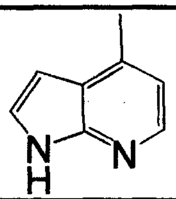
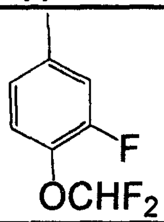
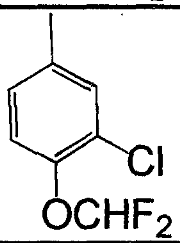
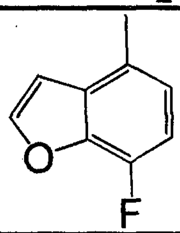
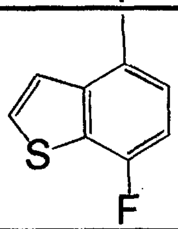
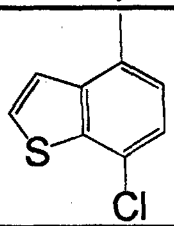
1571		257
1572		301
1573		317
1574		275
1575		291
1576		307
1577		291
1578		271

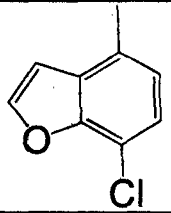
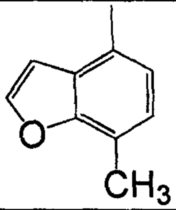
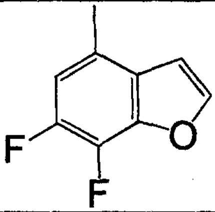
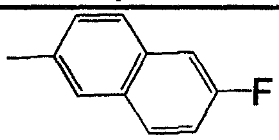
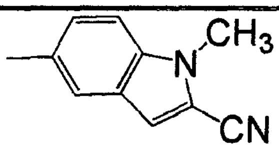
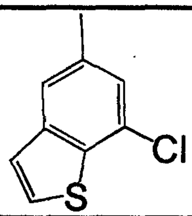
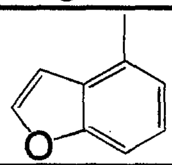
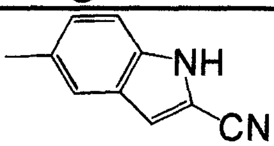
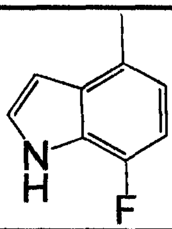
1579		293
1580		285
1581		295
1582		307
1583		257
1584		281
1585		274
1586		283
1587		292

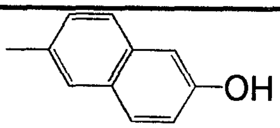
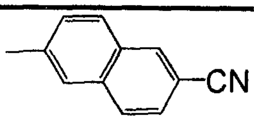
[0449]
Table 163



Example.	R^4	MS(M+1)
1588		267
1589		285
1590		269
1591		276
1592		251
1593		273
1594		269

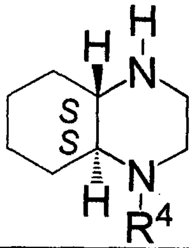
1595		256
1596		281
1597		257
1598		301
1599		317
1600		275
1601		291
1602		307

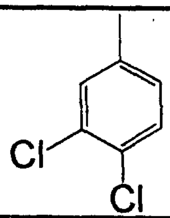
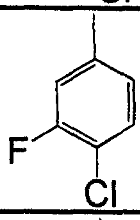
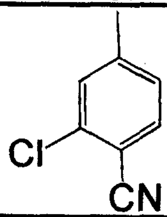
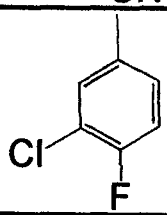
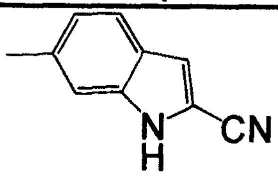
1603		291
1604		271
1605		293
1606		285
1607		295
1608		307
1609		257
1610		281
1611		274

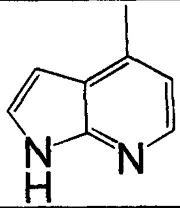
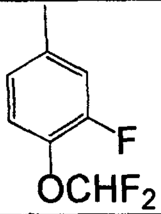
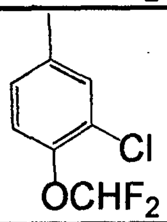
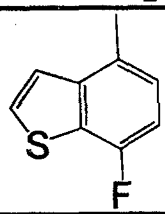
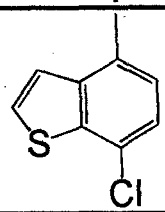
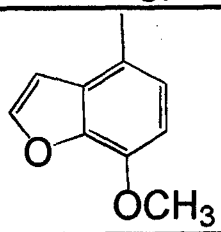
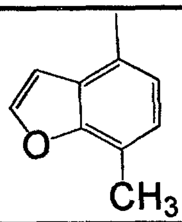
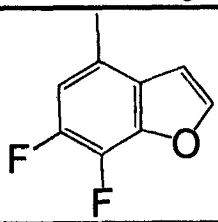
1612		283
1613		292

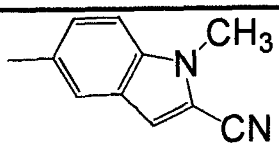
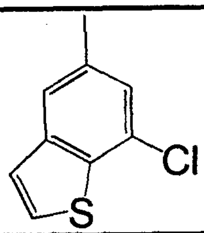
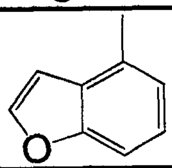
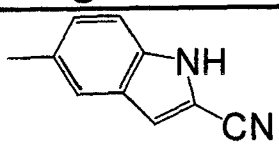
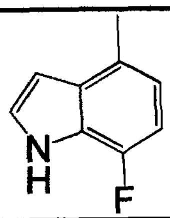
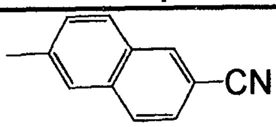
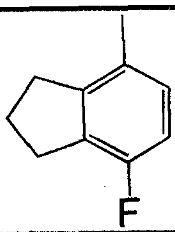
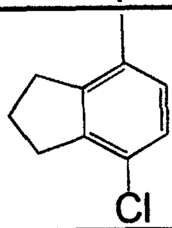
[0450]
Table 164

absolute configuration



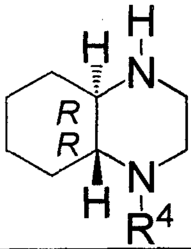
Example.	R^4	MS(M+1)
1614		285
1615		269
1616		276
1617		269
1618		281

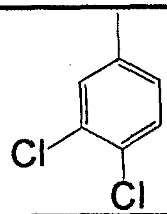
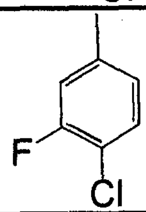
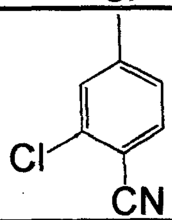
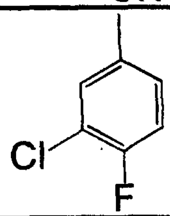
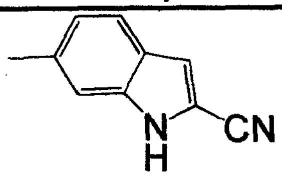
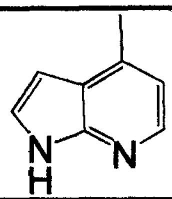
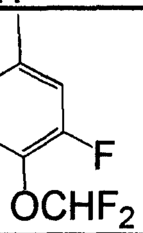
1619		257
1620		301
1621		317
1622		291
1623		307
1624		287
1625		271
1626		293

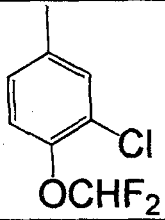
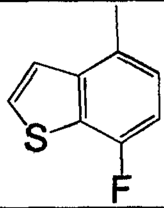
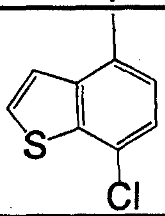
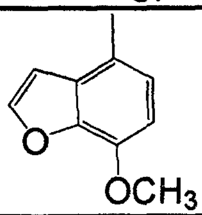
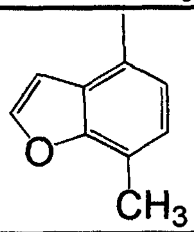
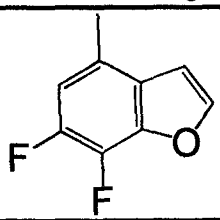
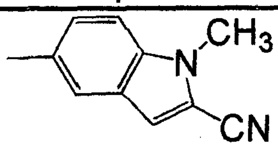
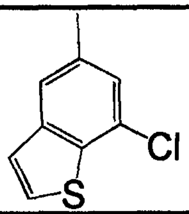
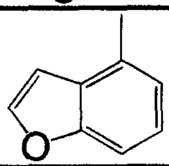
1627		295
1628		307
1629		257
1630		281
1631		274
1632		292
1633		275
1634		291

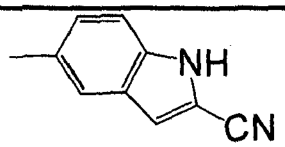
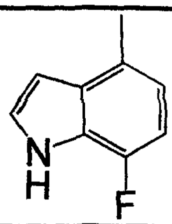
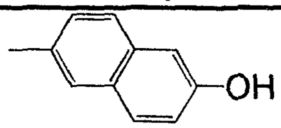
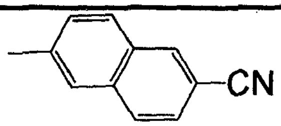
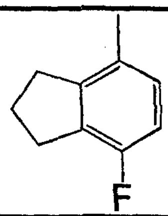
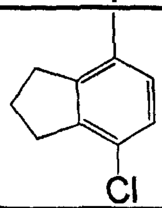
[0451]
Table 165

absolute configuration



Example.	R^4	MS(M+1)
1635		285
1636		269
1637		276
1638		269
1639		281
1640		257
1641		301

1642		317
1643		291
1644		307
1645		287
1646		271
1647		293
1648		295
1649		307
1650		257

1651		281
1652		274
1653		283
1654		292
1655		275
1656		291

[0452]

Pharmacological Study 1

Measurement of serotonin (5-HT) uptake inhibitory activity of test compound using rat brain synaptosome

Male Wistar rats were decapitated, and their brains were removed and dissected to remove the frontal cortex. The separated frontal cortex was placed in a 20-fold weight of a 0.32 molarity (M) sucrose solution and homogenized with a potter homogenizer. The homogenate was centrifuged at 1000 g at 4°C for 10 minutes, and the supernatant was further centrifuged at 20000 g at 4°C for 20 minutes. The pellet was suspended in an incubation buffer (20 mM HEPES buffer (pH 7.4) containing 10 mM glucose, 145 mM sodium chloride, 4.5 mM potassium chloride, 1.2 mM magnesium chloride, and 1.5 mM calcium chloride). The suspension was used as a crude synaptosome fraction.

[0453]

Uptake reaction was performed using each well of a 96-well round-bottom plate and a 200 μl volume in total of a solution containing pargyline (final concentration: 10 μM) and ascorbic acid (final concentration: 0.2 mg/ml).

[0454]

Specifically, a solvent, unlabeled 5-HT, and serially diluted test compounds were separately added to the wells, and the synaptosome fraction was added in an amount 1/10 of the final volume to each well and preincubated at 37°C for 10 minutes. Then, a tritium-labeled 5-HT solution (final concentration: 8 nM) was added thereto to initiate uptake reaction at 37°C. 10 minutes later, the uptake reaction was terminated by suction filtration through a 96-well glass fiber filter plate. Furthermore, the filter was washed with a cold saline and then sufficiently dried. MicroScint-O (PerkinElmer Co., Ltd.) was added thereto, and the residual radioactivity on the filter was measured.

[0455]

An uptake value obtained by the addition of only the solvent was defined as 100%, and an uptake value (nonspecific uptake value) obtained by the addition of the unlabeled 5-HT (final concentration: 10 μM) was defined as 0%. A 50% inhibitory concentration was calculated from the test compound concentrations and inhibitory activities thereat. The results are shown in Table 60.

[0456]

[Table 60]

Test compound	50% Inhibitory concentration (nM)
Compound of Example 2	7.1
Compound of Example 7	1.0
Compound of Example 8	2.4
Compound of Example 10	6.2
Compound of Example 13	5.1
Compound of Example 15	12.5
Compound of Example 27	5.8
Compound of Example 33	2.6
Compound of Example 72	2.6
Compound of Example 77	0.8
Compound of Example 85	7.2
Compound of Example 106	9.7
Compound of Example 112	7.1
Compound of Example 118	13.7
Compound of Example 120	9.2
Compound of Example 124	8.5
Compound of Example 125	4.7
Compound of Example 130	5.3
Compound of Example 131	6.1
Compound of Example 132	8.8
Compound of Example 136	1.3
Compound of Example 150	5.4
Compound of Example 165	12.0
Compound of Example 186	5.2
Compound of Example 187	5.8
Compound of Example 188	6.0
Compound of Example 191	3.2
Compound of Example 192	2.9
Compound of Example 193	3.4
Compound of Example 196	4.4
Compound of Example 233	7.4
Compound of Example 246	6.8
Compound of Example 247	42.8
Compound of Example 273	44.0
Compound of Example 276	7.2
Compound of Example 281	5.8
Compound of Example 285	19.7
Compound of Example 288	56.1
Compound of Example 300	89.1
Compound of Example 307	19.3
Compound of Example 322	9.6
Compound of Example 344	6.8
Compound of Example 346	10.0
Compound of Example 348	6.4
Compound of Example 405	6.4
Compound of Example 409	35.6
Compound of Example 468	3.8
Compound of Example 577	5.2
Compound of Example 579	4.5
Compound of Example 580	2.5
Compound of Example 582	4.1
Compound of Example 586	5.2
Compound of Example 587	0.9
Compound of Example 593	4.9

Compound of Example 610	4.6
Compound of Example 621	7.0
Compound of Example 641	2.2
Compound of Example 654	1.5
Compound of Example 717	4.2
Compound of Example 778	87.5
Compound of Example 780	6.5
Compound of Example 781	6.2
Compound of Example 791	1.4
Compound of Example 805	42.6
Compound of Example 841	28.1
Compound of Example 850	7.3
Compound of Example 867	4.7
Compound of Example 884	7.3
Compound of Example 895	5.4
Compound of Example 918	10.0
Compound of Example 962	18.7
Compound of Example 983	6.5
Compound of Example 993	4.8
Compound of Example 1026	2.4
Compound of Example 1047	0.7
Compound of Example 1083	5.1
Compound of Example 1113	5.4
Compound of Example 1121	8.5
Compound of Example 1124	7.1
Compound of Example 1318	40.7
Compound of Example 1326	37.8
Compound of Example 1333	84.2
Compound of Example 1341	6.8
Compound of Example 1534	38.1

[0457]

Pharmacological Study 2

Measurement of norepinephrine (NE) uptake inhibitory activity of test compound using rat brain synaptosome

Male Wistar rats were decapitated, and their brains were removed and dissected to remove the hippocampus. The separated hippocampus was placed in a 20-fold weight of a 0.32 molarity (M) sucrose solution and homogenized with a potter homogenizer. The homogenate was centrifuged at 1000 g at 4°C for 10 minutes, and the supernatant was further centrifuged at 20000 g at 4°C for 20 minutes. The pellet was suspended in an incubation buffer (20 mM HEPES buffer (pH 7.4) containing 10 mM glucose, 145 mM sodium chloride, 4.5 mM potassium chloride, 1.2 mM magnesium chloride, and 1.5 mM calcium chloride). The suspension was used as a crude synaptosome fraction.

[0458]

Uptake reaction was performed using each well of a 96-well round-bottom plate and a 200 μl volume in total of a solution containing pargyline (final concentration: 10 μM) and ascorbic acid (final concentration: 0.2 mg/ml).

[0459]

Specifically, a solvent, unlabeled NE, and serially diluted test compounds were separately added to the wells, and the synaptosome fraction was added in an amount 1/10 of the final volume to each well and preincubated at 37°C for 10 minutes. Then, a tritium-labeled NE solution (final concentration: 12 nM) was added thereto to initiate uptake reaction at 37°C. Ten minutes later, the uptake reaction was terminated by suction filtration through a 96-well glass fiber filter plate. Furthermore, the filter was washed with a cold saline and then sufficiently dried. MicroScint-O (PerkinElmer Co., Ltd.) was added thereto, and the residual radioactivity on the filter was measured.

[0460]

An uptake value obtained by the addition of only the solvent was defined as 100%, and an uptake value (nonspecific uptake value) obtained by the addition of the unlabeled NE (final concentration: 10 μM) was defined as 0%. A 50% inhibitory concentration was calculated from the test compound concentrations and inhibitory activities thereat. The results are shown in Table 61.

[0461]

[Table 61]

Test compound	50% Inhibitory concentration (nM)
Compound of Example 2	4.6
Compound of Example 7	9.5
Compound of Example 8	60.9
Compound of Example 10	8.8
Compound of Example 13	14.3
Compound of Example 15	11.0
Compound of Example 27	0.9
Compound of Example 33	0.7
Compound of Example 72	1.0
Compound of Example 77	3.9
Compound of Example 85	4.9
Compound of Example 106	37.2
Compound of Example 112	87.3
Compound of Example 118	3.7
Compound of Example 120	9.2
Compound of Example 124	0.8
Compound of Example 125	1.9
Compound of Example 130	0.5
Compound of Example 131	0.7
Compound of Example 132	3.1
Compound of Example 136	0.5
Compound of Example 150	23.6
Compound of Example 165	2.4
Compound of Example 186	3.8
Compound of Example 187	6.0
Compound of Example 188	0.8

Compound of Example 191	2.1
Compound of Example 192	3.6
Compound of Example 193	4.4
Compound of Example 196	1.7
Compound of Example 233	3.2
Compound of Example 246	3.8
Compound of Example 247	6.6
Compound of Example 273	6.8
Compound of Example 276	4.5
Compound of Example 281	2.0
Compound of Example 285	1.4
Compound of Example 288	22.0
Compound of Example 300	9.9
Compound of Example 307	40.4
Compound of Example 322	40.1
Compound of Example 344	7.5
Compound of Example 346	8.8
Compound of Example 348	4.6
Compound of Example 405	4.4
Compound of Example 409	9.1
Compound of Example 468	7.5
Compound of Example 577	5.9
Compound of Example 579	5.1
Compound of Example 580	5.4
Compound of Example 582	6.0
Compound of Example 586	4.0
Compound of Example 587	1.9
Compound of Example 593	3.3
Compound of Example 610	5.9
Compound of Example 621	0.7
Compound of Example 641	76.0
Compound of Example 654	1.0
Compound of Example 717	4.8
Compound of Example 778	4.2
Compound of Example 780	0.6
Compound of Example 781	3.0
Compound of Example 791	0.7
Compound of Example 805	30.4
Compound of Example 841	0.9
Compound of Example 850	1.0
Compound of Example 867	11.7
Compound of Example 884	4.8
Compound of Example 895	3.0
Compound of Example 918	0.8
Compound of Example 962	31.9
Compound of Example 983	47.6
Compound of Example 993	8.7
Compound of Example 1026	4.2
Compound of Example 1047	0.7
Compound of Example 1083	2.5
Compound of Example 1113	1.7
Compound of Example 1121	0.7
Compound of Example 1124	0.8
Compound of Example 1318	6.6
Compound of Example 1326	1.8
Compound of Example 1333	39.6
Compound of Example 1341	42.7
Compound of Example 1534	4.0

[0462]

Pharmacological Study 3

Measurement of dopamine (DA) uptake inhibitory activity of test compound using rat brain synaptosome

Male Wistar rats were decapitated, and their brains were removed and dissected to remove the corpus striatum. The separated corpus striatum was placed in a 20-fold weight of a 0.32 molarity (M) sucrose solution and homogenized with a potter homogenizer. The homogenate was centrifuged at 1000 g at 4°C for 10 minutes, and the supernatant was further centrifuged at 20000 g at 4°C for 20 minutes. The pellet was suspended in an incubation buffer (20 mM HEPES buffer (pH 7.4) containing 10 mM glucose, 145 mM sodium chloride, 4.5 mM potassium chloride, 1.2 mM magnesium chloride, and 1.5 mM calcium chloride). The suspension was used as a crude synaptosome fraction.

[0463]

Uptake reaction was performed using each well of a 96-well round-bottom plate and a 200 μl volume in total of a solution containing pargyline (final concentration: 10 μM) and ascorbic acid (final concentration: 0.2 mg/ml).

[0464]

Specifically, a solvent, unlabeled DA, and serially diluted test compounds were separately added to the wells, and the synaptosome fraction was added in an amount 1/10 of the final volume to each well and preincubated at 37°C for 10 minutes. Then, a tritium-labeled DA solution (final concentration: 2 nM) was added thereto to initiate uptake reaction at 37°C. Ten minutes later, the uptake reaction was terminated by suction filtration through a 96-well glass fiber filter plate. Furthermore, the filter was washed with a cold saline and then sufficiently dried. MicroScint-O (PerkinElmer Co., Ltd.) was added thereto, and the residual radioactivity on the filter was measured.

[0465]

An uptake value obtained by the addition of only the solvent was defined as 100%, and an uptake value (nonspecific uptake value) obtained by the addition of the unlabeled DA (final concentration: 10 μM) was defined as 0%. A 50% inhibitory concentration was calculated from the test compound concentrations and inhibitory activities thereat. The results are shown in Table 62.

[0466]

[Table 62]

Test compound	50% Inhibitory concentration (nM)
Compound of Example 2	85.9
Compound of Example 7	78.9
Compound of Example 8	377.8
Compound of Example 10	64.8
Compound of Example 13	85.4
Compound of Example 15	68.4
Compound of Example 27	31.9
Compound of Example 33	15.1
Compound of Example 72	47.9
Compound of Example 77	41.2
Compound of Example 85	95.7
Compound of Example 106	336.8
Compound of Example 112	263.7
Compound of Example 118	8.3
Compound of Example 120	187.2
Compound of Example 124	9.1
Compound of Example 125	5.2
Compound of Example 130	3.9
Compound of Example 131	8.3
Compound of Example 132	3.9
Compound of Example 136	7.7
Compound of Example 150	200.5
Compound of Example 165	6.8
Compound of Example 186	29.8
Compound of Example 187	12.1
Compound of Example 188	7.9
Compound of Example 191	13.5
Compound of Example 192	8.6
Compound of Example 193	5.7
Compound of Example 196	18.3
Compound of Example 233	38.8
Compound of Example 246	8.8
Compound of Example 247	8.7
Compound of Example 273	8.7
Compound of Example 276	10.9
Compound of Example 281	6.6
Compound of Example 285	43.9
Compound of Example 288	74.7
Compound of Example 300	81.3
Compound of Example 307	68.2
Compound of Example 322	67.7
Compound of Example 344	9.8
Compound of Example 346	7.8
Compound of Example 348	27.3
Compound of Example 405	74.8
Compound of Example 409	165.3
Compound of Example 468	54.0
Compound of Example 577	47.9
Compound of Example 579	46.5
Compound of Example 580	202.0
Compound of Example 582	68.8
Compound of Example 586	93.0
Compound of Example 587	76.1
Compound of Example 593	9.7

Compound of Example 610	13.2
Compound of Example 621	128.5
Compound of Example 641	9.7
Compound of Example 654	9.0
Compound of Example 717	60.1
Compound of Example 778	4.9
Compound of Example 780	4.3
Compound of Example 781	5.2
Compound of Example 791	160.9
Compound of Example 805	83.8
Compound of Example 841	5.1
Compound of Example 850	7.0
Compound of Example 867	85.7
Compound of Example 884	52.8
Compound of Example 895	19.9
Compound of Example 918	42.0
Compound of Example 962	69.5
Compound of Example 983	172.6
Compound of Example 993	38.6
Compound of Example 1026	12.3
Compound of Example 1047	1.1
Compound of Example 1083	53.7
Compound of Example 1113	26.0
Compound of Example 1121	29.9
Compound of Example 1124	49.3
Compound of Example 1318	83.5
Compound of Example 1326	91.8
Compound of Example 1333	73.0
Compound of Example 1341	113.3
Compound of Example 1534	214.8

[0467]

Pharmacological Study 4

Forced swimming test

This test was conducted according to the method of Porsolt et al. (Porsolt, R.D., et al., Behavioural despair in mice: A primary screening test for antidepressants. Arch. int. Pharmacodyn. Ther., 229, pp 327-336 (1977)).

[0468]

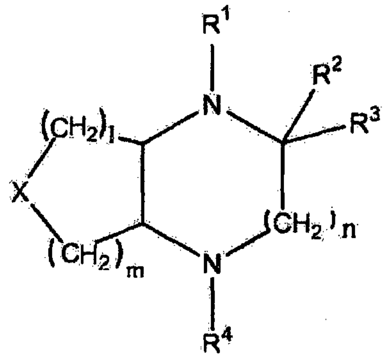
A test compound was suspended in a 5% gum arabic/saline (w/v), and this suspension was orally administered to male ICR mice (CLEA Japan, Inc. (JCL), 5 to 6 week old). One hour later, the mice were placed in a water tank having a water depth of 9.5 cm and a water temperature of 21 to 25°C and immediately thereafter allowed to try to swim for 6 minutes. Then, a time during which the mouse was immobile (immobility time) was measured for the last 4 minutes. A SCANET MV-20 AQ system manufactured by Melquest Ltd. was used in the measurement and analysis of the immobility time.

[0469]

In this experiment, the animals treated with the test compounds exhibited a reduction in immobility time. This demonstrates that the test compounds are useful as antidepressants.

CLAIMS

1. A heterocyclic compound represented by the general formula (1) or a salt thereof:



wherein m, l, and n respectively represent an integer of 1 or 2; X represents -O- or $-CH_2-$;
R^1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a protecting group, or a tri-lower alkylsilyloxy-lower alkyl group;
R^2 and R^3, which are the same or different, each independently represent hydrogen or a lower alkyl group; or R_2 and R_3 are bonded to form a cyclo-C3-C8 alkyl group; and
R^4 represents an aromatic group or a heterocyclic group, wherein the aromatic or heterocyclic group may have one or more arbitrary substituent(s).

2. The heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 1, wherein
R^4 represents any of
(1) a phenyl group,
(2) an indolyl group,
(3) a benzothienyl group,
(4) a naphthyl group,
(5) a benzofuryl group,
(6) a quinolyl group,
(7) an isoquinolyl group,
(8) a pyridyl group,
(9) a thienyl group,
(10) a dihydrobenzoxazinyl group,
(11) a dihydrobenzodioxinyl group,
(12) a dihydroquinolyl group,
(13) a chromanyl group,
(14) a quinoxalinyl group,

(15) a dihydroindenyl group,

(16) a dihydrobenzofuryl group,

(17) a benzodioxolyl group,

(18) an indazolyl group,

(19) a benzothiazolyl group,

(20) an indolinyl group,

(21) a thienopyridyl group,

(22) a tetrahydrobenzazepinyl group,

(23) a tetrahydrobenzodiazepinyl group,

(24) a dihydrobenzodioxepinyl group,

(25) a fluorenyl group,

(26) a pyridazinyl group,

(27) a tetrahydroquinolyl group,

(28) a carbazolyl group,

(29) a phenanthryl group,

(30) a dihydroacenaphthylenyl group,

(31) a pyrrolopyridyl group,

(32) an anthryl group,

(33) a benzodioxinyl group,

(34) a pyrrolidinyl group,

(35) a pyrazolyl group,

(36) an oxadiazolyl group,

(37) a pyrimidinyl group,

(38) a tetrahydronaphthyl group,

(39) a dihydroquinazolinyl group,

(40) a benzoxazolyl group,

(41) a thiazolyl group,

(42) a quinazolinyl group,

(43) a phthalazinyl group,

(44) a pyrazinyl group, and

(45) a chromenyl group, wherein

these aromatic or heterocyclic groups may have one or more substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-3) a lower alkanoyl group,

(1-4) a halogen-substituted lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group,

(1-7) a lower alkoxy group,

(1-8) a lower alkylthio group,

(1-9) an imidazolyl group,

(1-10) a tri-lower alkylsilyl group,

(1-11) an oxadiazolyl group which may have a lower alkyl group(s),

(1-12) a pyrrolidinyl group which may have an oxo group(s),

(1-13) a phenyl group which may have a lower alkoxy group(s),

(1-14) a lower alkylamino-lower alkyl group,

(1-15) an oxo group,

(1-16) a pyrazolyl group which may have a lower alkyl group(s),

(1-17) a thienyl group,

(1-18) a furyl group,

(1-19) a thiazolyl group which may have a lower alkyl group(s),

(1-20) a lower alkylamino group,

(1-21) a pyrimidyl group which may have a lower alkyl group(s),

(1-22) a phenyl-lower alkenyl group,

(1-23) a phenoxy group which may have a halogen atom(s),

(1-24) a phenoxy-lower alkyl group,

(1-25) a pyrrolidinyl-lower alkoxy group,

(1-26) a lower alkylsulfamoyl group,

(1-27) a pyridazinyloxy group which may have a lower alkyl group(s),

(1-28) a phenyl-lower alkyl group,

(1-29) a lower alkylamino-lower alkoxy group,

(1-30) an imidazolyl-lower alkyl group,

(1-31) a phenyl-lower alkoxy group,

(1-32) a hydroxy group,

(1-33) a lower alkoxycarbonyl group,

(1-34) a hydroxy-lower alkyl group,

(1-35) an oxazolyl group,

(1-36) a piperidyl group,

(1-37) a pyrrolyl group,

(1-38) a morpholinyl-lower alkyl group,

(1-39) a piperazinyl-lower alkyl group which may have a lower alkyl group(s),

(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have a lower alkyl group(s).

3. The heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 2, wherein

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(3) a benzothienyl group,

(4) a naphthyl group,

(5) a benzofuryl group,

(6) a quinolyl group,

(7) an isoquinolyl group,

(8) a pyridyl group,

(9) a thienyl group,

(10) a dihydrobenzoxazinyl group,

(11) a dihydrobenzodioxinyl group,

(12) a dihydroquinolyl group,

(13) a chromanyl group,

(14) a quinoxalinyl group,

(15) a dihydroindenyl group,

(16) a dihydrobenzofuryl group,

(17) a benzodioxolyl group,

(18) an indazolyl group,

(19) a benzothiazolyl group,

(20) an indolinyl group,

(21) a thienopyridyl group,

(22) a tetrahydrobenzazepinyl group,

(23) a tetrahydrobenzodiazepinyl group,

(24) a dihydrobenzodioxepinyl group,

(25) a fluorenyl group,

(26) a pyridazinyl group,

(27) a tetrahydroquinolyl group,

(28) a carbazolyl group,

(29) a phenanthryl group,

(30) a dihydroacenaphthylenyl group,

(31) a pyrrolopyridyl group,

(32) an anthryl group,

(33) a benzodioxinyl group,

(34) a pyrrolidinyl group,

(35) a pyrazolyl group,

(36) an oxadiazolyl group,

(37) a pyrimidinyl group,

(38) a tetrahydronaphthyl group,

(39) a dihydroquinazolinyl group,

(40) a benzoxazolyl group,

(41) a thiazolyl group,

(42) a quinazolinyl group,

(43) a phthalazinyl group,

(44) a pyrazinyl group, and

(45) a chromenyl group, wherein

these aromatic or heterocyclic groups may have 1 to 4 substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-3) a lower alkanoyl group,

(1-4) a halogen-substituted lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group,

(1-7) a lower alkoxy group,

(1-8) a lower alkylthio group,

(1-9) an imidazolyl group,

(1-10) a tri-lower alkylsilyl group,

(1-11) an oxadiazolyl group which may have 1 lower alkyl group,

(1-12) a pyrrolidinyl group which may have 1 oxo group, (1-13) a phenyl group which may have 1 lower alkoxy group,

(1-14) a lower alkylamino-lower alkyl group,

(1-15) an oxo group,

(1-16) a pyrazolyl group which may have 1 lower alkyl group,

(1-17) a thienyl group,

(1-18) a furyl group,

(1-19) a thiazolyl group which may have 1 lower alkyl group,

(1-20) a lower alkylamino group,

(1-21) a pyrimidyl group which may have 1 lower alkyl group,

(1-22) a phenyl-lower alkenyl group,

(1-23) a phenoxy group which may have 1 halogen atom,

(1-24) a phenoxy-lower alkyl group,

(1-25) a pyrrolidinyl-lower alkoxy group,

(1-26) a lower alkylsulfamoyl group,

(1-27) a pyridazinyloxy group which may have 1 lower alkyl group,

(1-28) a phenyl-lower alkyl group,

(1-29) a lower alkylamino-lower alkoxy group,

(1-30) an imidazolyl-lower alkyl group,

(1-31) a phenyl-lower alkoxy group,

(1-32) a hydroxy group,

(1-33) a lower alkoxycarbonyl group,

(1-34) a hydroxy-lower alkyl group,

(1-35) an oxazolyl group,

(1-36) a piperidyl group,

(1-37) a pyrrolyl group,

(1-38) a morpholinyl-lower alkyl group,

(1-39) a piperazinyl-lower alkyl group which may have 1 lower alkyl group,

(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have 1 lower alkyl group.

4. The heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 3, wherein

m represents 2; l and n respectively represent an integer of 1; X represents $-CH_2-$;

R^1 represents hydrogen, a lower alkyl group, a hydroxy-lower alkyl group, a benzyl group, or a tri-lower alkylsilyloxy-lower alkyl group; and

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(4) a naphthyl group,

(5) a benzofuryl group, and

(31) a pyrrolopyridyl group, wherein

these aromatic or heterocyclic groups may have 1 to 4 substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-3) a lower alkanoyl group,

(1-4) a halogen-substituted lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group,

(1-7) a lower alkoxy group,

(1-8) a lower alkylthio group,

(1-9) an imidazolyl group,

(1-10) a tri-lower alkylsilyl group,

(1-11) an oxadiazolyl group which may have 1 lower alkyl group,

(1-12) a pyrrolidinyl group which may have 1 oxo group,

(1-13) a phenyl group which may have 1 lower alkoxy group,

(1-14) a lower alkylamino-lower alkyl group,

(1-15) an oxo group,

(1-16) a pyrazolyl group which may have 1 lower alkyl group,

(1-17) a thienyl group,

(1-18) a furyl group,

(1-19) a thiazolyl group which may have 1 lower alkyl group,

(1-20) a lower alkylamino group,

(1-21) a pyrimidyl group which may have 1 lower alkyl group,

(1-22) a phenyl-lower alkenyl group,

(1-23) a phenoxy group which may have 1 halogen atom,

(1-24) a phenoxy-lower alkyl group,

(1-25) a pyrrolidinyl-lower alkoxy group, (1-26) a lower alkylsulfamoyl group,

(1-27) a pyridazinyloxy group which may have 1 lower alkyl group,

(1-28) a phenyl-lower alkyl group,

(1-29) a lower alkylamino-lower alkoxy group,

(1-30) an imidazolyl-lower alkyl group,

(1-31) a phenyl-lower alkoxy group,

(1-32) a hydroxy group,

(1-34) a hydroxy-lower alkyl group,

(1-35) an oxazolyl group,

(1-36) a piperidyl group,

(1-37) a pyrrolyl group,

(1-38) a morpholinyl-lower alkyl group,

(1-39) a piperazinyl-lower alkyl group which may have a lower alkyl group(s),

(1-40) a piperidyl-lower alkyl group,

(1-41) a pyrrolidinyl-lower alkyl group,

(1-42) a morpholinyl group, and

(1-43) a piperazinyl group which may have 1 lower alkyl group.

5. The heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 4, wherein

R^1 represents hydrogen;

R^2 and R^3, which are the same or different, each independently represent a lower alkyl group; or R^2 and R^3 are bonded to form a cyclo-C3-C8 alkyl group; and

R^4 represents any of

(1) a phenyl group,

(2) an indolyl group,

(4) a naphthyl group,

(5) a benzofuryl group, and

(31) a pyrrolopyridyl group, wherein

these aromatic or heterocyclic groups may have 1 to 2 substituent(s) selected from

(1-1) a halogen atom,

(1-2) a lower alkyl group,

(1-5) a halogen-substituted lower alkoxy group,

(1-6) a cyano group, and

(1-7) a lower alkoxy group.

6. The heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 5, which is selected from

(4a*S*,8a*R*)-1-(4-chlorophenyl)-3,3-dimethyldecahydroquinoxaline,

2-chloro-4-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)benzonitrile,

(4a*S*,8a*R*)-1-(3-chloro-4-fluorophenyl)-3,3-dimethyldecahydroquinoxaline,

(4a*S*,8a*R*)-1-(7-fluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline,

5-((4a*R*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-1-methyl-1*H*-indole-2-carbonitrile,

(4a'*R*,8a'*S*)-4'-(7-methoxybenzofuran-4-yl)octahydro-1'*H*-spiro[cyclobutane-1,2'-quinoxaline],

(4a*S*,8a*R*)-1-(6,7-difluorobenzofuran-4-yl)-3,3-dimethyldecahydroquinoxaline,

5-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-1*H*-indole-2-carbonitrile,

(4a*S*,8a*R*)-1-(7-chloro-2,3-dihydro-1*H*-inden-4-yl)-3,3-dimethyldecahydroquinoxaline,

6-((4a*S*,8a*S*)-3,3-dimethyloctahydroquinoxalin-1(2*H*)-yl)-2-naphthonitrile,

(4a*S*,8a*S*)-3,3-dimethyl-1-(1*H*-pyrrolo[2,3-*b*]pyridin-4-yl)decahydroquinoxaline, and

(4a*S*,8a*S*)-1-(4-(difluoromethoxy)-3-fluorophenyl)-3,3-dimethyldecahydroquinoxaline.

7. A pharmaceutical composition comprising a heterocyclic compound represented by the general formula (1) or a salt thereof according to claim 1 as an active ingredient and a pharmaceutically acceptable carrier.

8. A prophylactic and/or therapeutic agent for disorders caused by reduced neurotransmission of serotonin, norepinephrine or dopamine, comprising as an active ingredient a heterocyclic compound of general formula (1) or a salt thereof according to claim 1.

9. A prophylactic and/or therapeutic agent according to claim 8, wherein the disorder is selected from the group consisting of depression, depression status caused by adjustment disorder, anxiety caused by adjustment disorder, anxiety caused by various diseases, generalized anxiety disorder, phobia, obsessive-compulsive disorder, panic disorder, posttraumatic stress disorder, acute stress disorder, hypochondria, dissociative amnesia, avoidant personality disorder, body dysmorphic disorder, eating disorder, obesity, chemical dependence, pain, fibromyalgia, Alzheimer's disease, memory deficit, Parkinson's disease, restless leg syndrome, endocrine disorder, vasospasm, cerebellar ataxia, gastrointestinal disorder, negative syndrome of schizophrenia, premenstrual syndrome, stress urinary incontinence, Tourette's disorder, attention deficit hyperactivity disorder (ADHD), autism, Asperger syndrome, impulse control disorder, trichotillomania, kleptomania, gambling disorder, cluster headache, migraine,

chronic paroxysmal hemicrania, chronic fatigue syndrome, precocious ejaculation, male impotence, narcolepsy, primary hypersomnia, cataplexy, sleep apnea syndrome and headache.

10. A prophylactic and/or therapeutic agent according to claim 9, wherein the depression is selected from the group consisting of major depressive disorder; bipolar I disorder; bipolar II disorder; mixed state; dysthymic disorder; rapid cycler; atypical depression; seasonal affective disorder; postpartum depression; hypomelancholia; recurrent brief depressive disorder; refractory depression; chronic depression; double depression; alcohol-induced mood disorder; mixed anxiety-depressive disorder; depression caused by various physical diseases such as Cushing('s) syndrome, hypothyroidism, hyperparathyroidism, Addison's disease, amenorrhea-galactorrhea syndrome, Parkinson's disease, Alzheimer's disease, cerebrovascular dementia, brain infarct、brain hemorrhage、subarachnoid hemorrhage, diabetes millitus, virus infection, multiple sclerosis, chronic fatigue syndrome, coronary artery disease, pain, cancer, etc.; presenile depression; senile depression; depression in children and adolescents; depression induced by drugs such as interferon, etc.

11. A prophylactic and/or therapeutic agent according to claim 9, wherein the anxiety caused by various diseases is selected from the group consisting of anxiety caused by head injury, brain infection, inner ear impairment, cardiac failure, arrhythmia, hyperadrenalism, hyperthyroidism, asthma and chronic obstructive pulmonary disease.

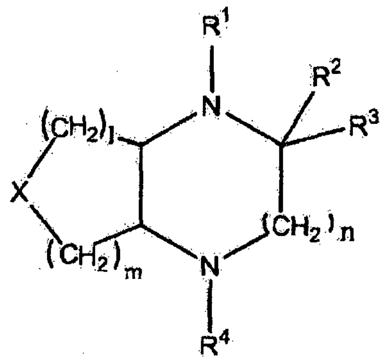
12. A prophylactic and/or therapeutic agent according to claim 9, wherein the pain is selected from the group consisting of chronic pain, psychogenic pain, neuropathic pain, phantom limb pain, postherpetic neuralgia, traumatic cervical syndrome, spinal cord injury pain, trigeminal neuralgia, diabetic neuropathy.

13. Use of a heterocyclic compound of the general formula (1) or a salt thereof according to any one of claims 1 to 6 as a drug.

14. Use of a heterocyclic compound of the general formula (1) or a salt thereof according to any one of claims 1 to 6 as a serotonine reuptake inhibitor and/or a norepinephrine reuptake inhibitor and/or a dopamine reuptake inhibitor.

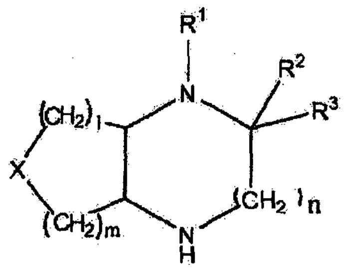
15. A method for treating and/or preventing disorders caused by reduced neurotransmission of serotonin, norephnephrine or dopamine, comprising administering a heterocyclic compound of general formula (1) or a salt thereof according to claims 1 to 6 to a human or an animal.

16. A process for producing a heterocyclic compound of general formula (1):



or salts thereof, wherein m, l and n respectively represent an integer of 1 or 2; X, R^1, R^2, and R^3 are defined in the above in claim 1,

the process comprising reacting the compound represented by the general formula;



wherein m, l and n respectively represent an integer of 1 or 2; X, R^1, R^2, and R^3 are defined in the above in claim 1 and the compound represented by the general formula;

R^4 ——— X_1

wherein R^4 and X^1 are defined in the above in claim 1.