



(86) Date de dépôt PCT/PCT Filing Date: 1994/04/04

(87) Date publication PCT/PCT Publication Date: 1994/10/13

(45) Date de délivrance/Issue Date: 2004/05/11

(85) Entrée phase nationale/National Entry: 1994/11/29

(86) N° demande PCT/PCT Application No.: JP 1994/000549

(87) N° publication PCT/PCT Publication No.: 1994/022826

(30) Priorité/Priority: 1993/04/07 (5-80712) JP

(51) Cl.Int.⁵/Int.Cl.⁵ C07D 211/58, A61K 31/535,
A61K 31/435, C07D 401/00, C07D 417/06,
C07D 405/06, C07D 413/00, C07D 409/00

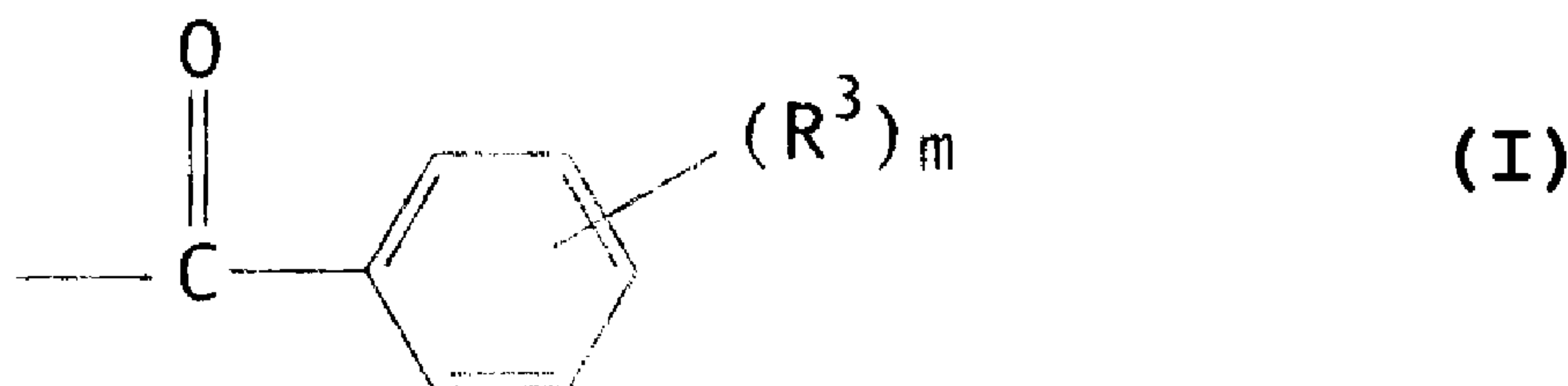
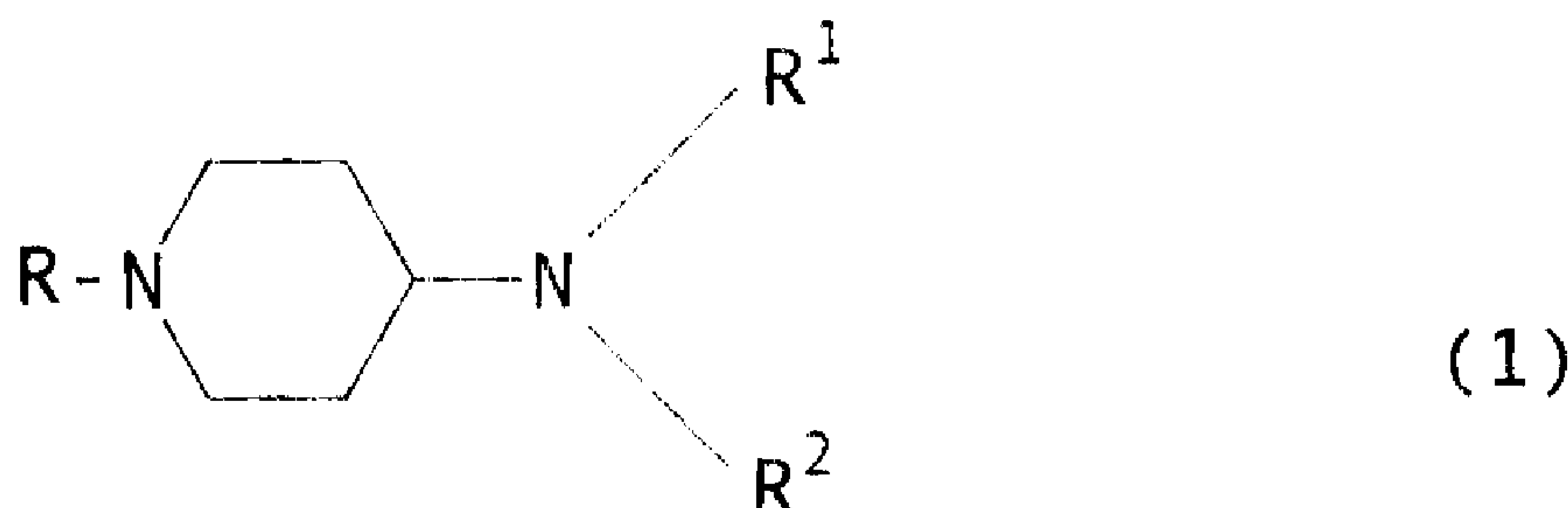
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(54) Titre : AGENT DE VASODILATION PERIPHERIQUE CONTENANT UN DERIVE DE LA PIPERIDINE COMME
INGREDIENT ACTIF

(54) Title: PERIPHERAL VASODILATING AGENT CONTAINING PIPERIDINE DERIVATIVE AS ACTIVE INGREDIENT



(57) Abrégé/Abstract:

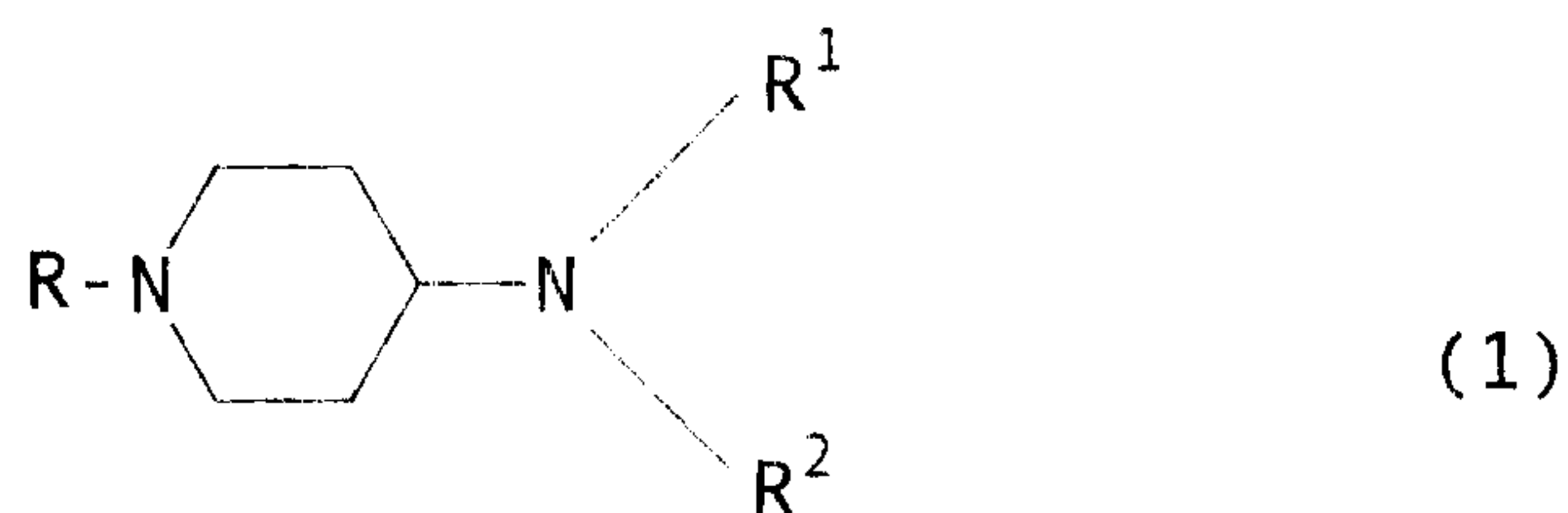
Disclosed is a novel peripheral vasodilating agent containing a piperidine derivative represented by the general formula (1): (see formula I) (wherein R¹ is hydrogen or lower alkyl which may have a hydroxyl group; R² is a phenylalkyl group, a phenoxyalkyl group, or the like; R is a group the formula (see formula II) lower alkanoyl having substituent, pyridyl carbonyl, or the like; m is 1-3; and R³ is H or a substituent such as nitro, alkyl, halogen) or pharmaceutically acceptable salt thereof having excellent peripheral vasodilating activity.



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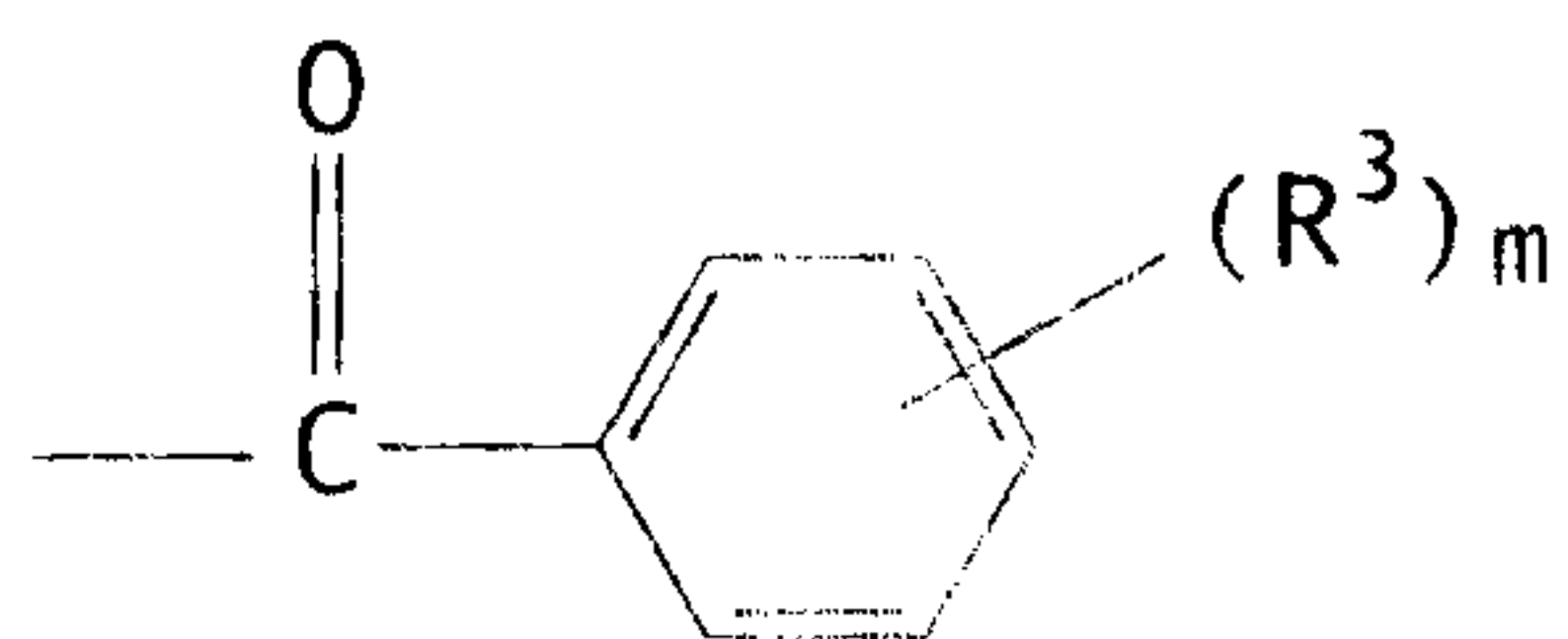
ABSTRACT

Disclosed is a novel peripheral vasodilating agent containing a piperidine derivative represented by the general formula (1):



(wherein R^1 is hydrogen or lower alkyl which may have a hydroxyl group; R^2 is a phenylalkyl group, a phenoxyalkyl group, or the like; R is a group the formula

10



lower alkanoyl having substituent, pyridyl carbonyl, or the like; m is 1-3; and R^3 is H or a substituent such as nitro, alkyl, halogen) or pharmaceutically acceptable salt thereof

15

having excellent peripheral vasodilating activity.

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

THIS IS VOLUME __1__ OF __2__

NOTE: For additional volumes please contact the Canadian Patent Office.

DESCRIPTION

PERIPHERAL VASODILATING AGENT CONTAINING N-ACYLATED 4-AMINO
PIPERIDINE DERIVATIVES AS ACTIVE INGREDIENTS

[Industrial Field of Utilization]

5 The present invention relates to novel
peripheral vasodilating agents each containing, as an
active ingredient, a piperidine derivative having an
excellent peripheral vasodilating activity.

10 [Prior Art and Problems to Be Solved by the Invention]

 Various compounds having a peripheral vasodil-
ating activity have been used for the treatment of
various disturbances in peripheral circulations. As
such compounds, there are known, for example, nicotinic
15 acid derivatives such as Inositol Nicotinate, Ecofrol,
Nicametate, NicotinyI Alcohol Tartarate and the like;
norephedrin derivatives such as Nylidrin hydrochloride,
Isoxsuprine hydrochloride and the like; Bamethan sulfate
and compounds similar thereto; imidazoline derivatives
20 such as Tolazoline hydrochloride and the like; and
Trimethylcyclohexyl mandelate.

 Some of these known peripheral vasodilating
compounds, however, have effects to the heart such as
effect to heart rate, hypotensive effect, myocardinal
25 contraction effect and the like, and other adverse
effects. Therefore, development of new peripheral

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vasodilating compound is still desired.

In addition to the above, various compounds, each of which having chemical structural formula similar to that of the piperidine derivative represented by the below-mentioned general formula (1), have been known in some prior art references for exampl:

(A) Prior art references (Patents) filed by the present applicant's company (Otsuka Pharmaceutical Co., Ltd.):

10 o U. S. Patent Nos. 4,487,772; 4,454,130;
4,468,402;

 o U. S. Patent Nos. 4,886,809; 5,071,856
(EP-A-0255134);

 o Japanese Patent Kokai (Laid-open) No. Sho
15 57-171974 (1982) [Japanese Patent Publication No. Sho
64-9313 (1989)];

 o Japanese Patent Kokai (Laid-open) No. Sho
57-154129 (1982) [Japanese Patent Publication No. Sho
64-53248 (1989)];

20 o Japanese Patent Kokai (Laid-open) Nos. Sho
54-16478 (1979);

 o Japanese Patent Kokai (Laid-open) No. Sho
55-85520 (1980);

 o Japanese Patent Kokai (Laid-open) No. Sho
25 51-65770 (1976);

 o Japanese Patent Koaki (Laid-open) No. Sho
51-68574 (1976);

 o Japanese Patent Kokai (Laid-open) No. Sho

51-118771 (1976);

o Japanese Patent Kokai (Laid-open) Nos. Sho
52-282 (1977); and Sho 52-283 (1977);

o Japanese Patent Kokai (Laid-open) No. Sho
5 52-118474 (1977);

o U. S. Patent Nos. 4,455,422; 4,567,187;
4,460,593; and 4,619,932;

o U. S. Patent No. 5,008,274; (EP-A-0240015);

o Japanese Patent Kokai (Laid-open) No. Sho
10 52-83380;

o Japanese Patent Kokai (Laid-open) No. Hei
1-61468.

(B) Prior art references filed by and/or written by
persons who belong to other than the present
15 applicant's company:

o J. Org. Chem. 1990, (55), pp. 2552-2554;

o Japanese Patent Kokai (Laid-open) No. Sho
64-79151 [Japanese Patent Koaki (Laid-open) No. Hei
2-169569; EP-A-0296560A2; U. S. Patent Nos. 5,100,901; &
20 4,895,841)];

o Swiss Patent No. 535,767 [Chem. Abstr., 79, (7):
42395k];

o J. Pharm. Sci., 1987, 76, (1), pp. 32-34 [Chem.,
Abstr., 106, (25): 207384f];

o Japanese Patent Kokai (Laid-open) No. Sho
25 59-5610 (EP-A-0097000A2);

o Japanese Patent Kokai (Laid-open) No. Hei
1-316356 (EP-A-318029A);

- o Japanese Patent Kokai (Laid-open) Nos. Sho 63-150237, Sho 63-170311 [Chem, Abstr., 109, (15): 128570x, DE-A-3740383];
- o J. Org. Chem., 1984, 49, (15), pp. 2795-2799;
- 5 o Japanese Patent Kokai (Laid-open) No. Sho 41-19506 [Chem. Abstr., 66, (11): 46341c];
- o Japanese Patent Kokai (Laid-open) No. Hei 4-282366 [EP-A-481299, Chem. Abstr., 117, (9): 90151m; EP-A-457686, (Chem. Abstr., 116, (11): 106097r];
- 10 o Japanese Patent Kokai (Laid-open) No, Sho 60-226862 [EP-A-156433, Chem. Abstr., 104, (15): 129918a];
- o Japanese Patent Kokai (Laid-open) No. Sho 57-192383; Japanese Patent Kokai (Laid-open) Nos. Sho 15 56-92884; 56-125385; 56-161386; 56-164183; 56-164184, 56-166188, 57-40482; Chem. Pharm. Bull., 1985, 33, (3), pp. 1116-1128; J. Heterocyclic Chem., 20, pp. 565-573 (1983);
- o Japanese Patent Kokai (Laid-open) No. Sho 20 60-149583 [EP-A-144101, Chem. Abstr., 104, (9): 68856e]; Japanese Patent Kokai (Laid-open) No. Sho 59-21680 [EP-A-99139, Chem. Abstr., 101, (3): 23473z];
- o DE-A-2311570 [Japanese Patent Kokai (Laid-open) No. Sho 49-273].
- 25 (C) Prior art reference in which compounds having chemical structural formulae similar to those of piperidine compounds of the present invention, but the former do not overlapped with the latter:

- o Chem., Abstr., 98, (7): 53690e [U. S. Patent No. 4,350,634, Japanese Patent Kokai (Laid-open) No., Sho 54-36259]; Chem. Abstr., 91, (7): 56817t [Japanese Patent Kokai (Laid-open) No. Sho 54-8589];
- 5 o Chem. Abstr., 107, (13): 115499q [Japanese Patent Kokai (Laid-open) No. Sho 62-89679]:
 - o Chem. Abstr., 114, (11); 101745z [DE-A-3907974];
 - o Chem. Abstr., 91, (7): 56817t [Swiss Patent No. 77/8589];
- 10 o Chem. Abstr., 100, (9): 68324x [EP-A-90733];
 - o Synth. Commun., 1985, 15, (2), pp. 157-163 [Chem. Abstr., 103, (7): 53339u]
 - o EP-A-297661A
 - o Chem. Abstr., 106, (3): 18371p [Japanese Patent
 - 15 Kokai (Laid-open) No. Sho 61-161262];
 - o Chem. Abstr., 113, (21): 190946k [Japanese Patent Kokai (Laid-open) No. Hei 2-138161];
 - o Chem. Abstr., 113, (3): 23909u [EP-A-344577];
 - Chem. Abstr., 114, (21): 206799y [Japanese Patent Kokai
 - 20 (Laid-open) No. Hei 2-306951];
 - o Chem. Abstr., 113, (1): 6232a [J. Med. Chem., 1990, 33, (6), pp 1688-1697];
 - o British Patent No. 2,216,516
 - o Japanese Patent Koaki (Laid-open) No. Sho
 - 25 54-92974 [EP-A-1175];
 - o Japanese Patent Kokai (Laid-open) No. Sho 61-183283 [EP-A-191603];
 - o South African Patent No. 6701679 [Japanese Patent

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Kokai (Laid-open) Nos. Sho 44-17387 & 43-29585]

o U. S. Patent No. 3,963,996

o Can. J. Pharm. Sci., 16, (1), pp 52-56, 1981

[Chem. Abstr. 96, (19): 162500x];

5 o Japanese Patent Kokai (Laid-open) No. Sho

62-48665 [DE-A-3529994]

o DT-2034640

These compounds being disclosed in the above-mentioned prior art references indeed possess certain
10 pharma-cological activities, for example myocardial contraction increasing activity (positive inotropic activity), coronary blood flow increasing activity, hypotensive activity and antiinflammatory activity, etc. However, such known compounds do not possess any
15 peripheral vasodilating activities at all.

[Means for Solving the Problems]

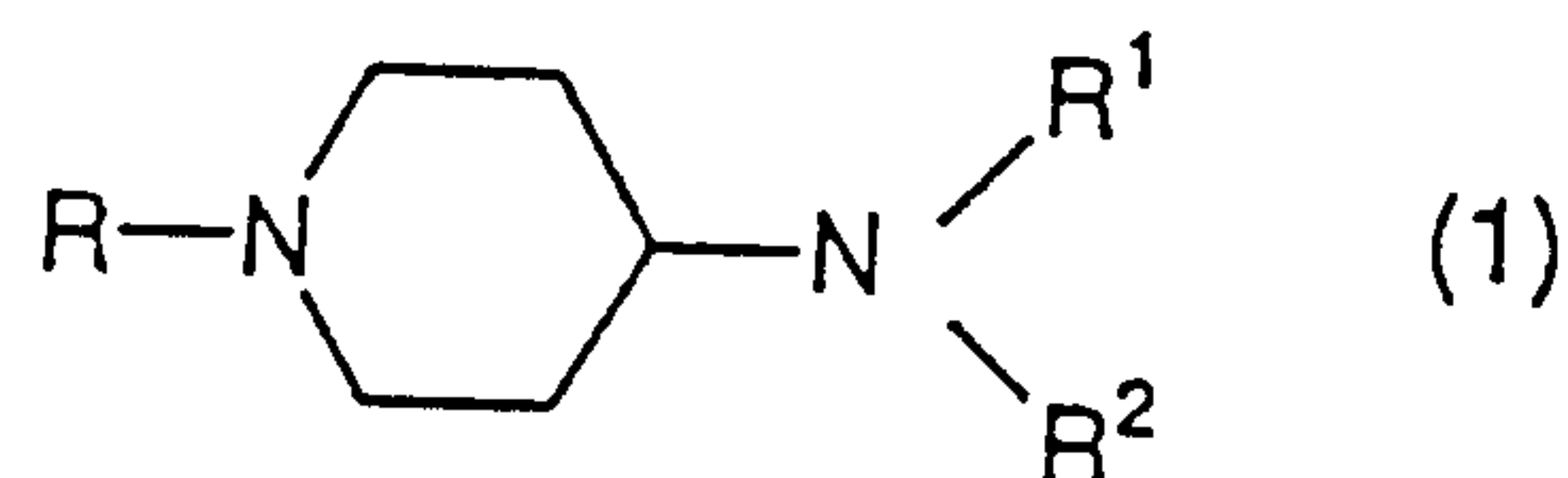
The present inventors made an extensive study in order to develop a peripheral vasodilating agent of new type and, as a result, found that the piperidine
20 derivatives of the general formula (1) shown below or salts thereof have an excellent peripheral vasodilating activity.

Each of the piperidine derivatives of the present invention, when contained in and used as a
25 peripheral vasodilating agent, is useful as an agent for improving peripheral circulatory disturbances caused by arterial diseases (e.g. Berger disease, obstructive

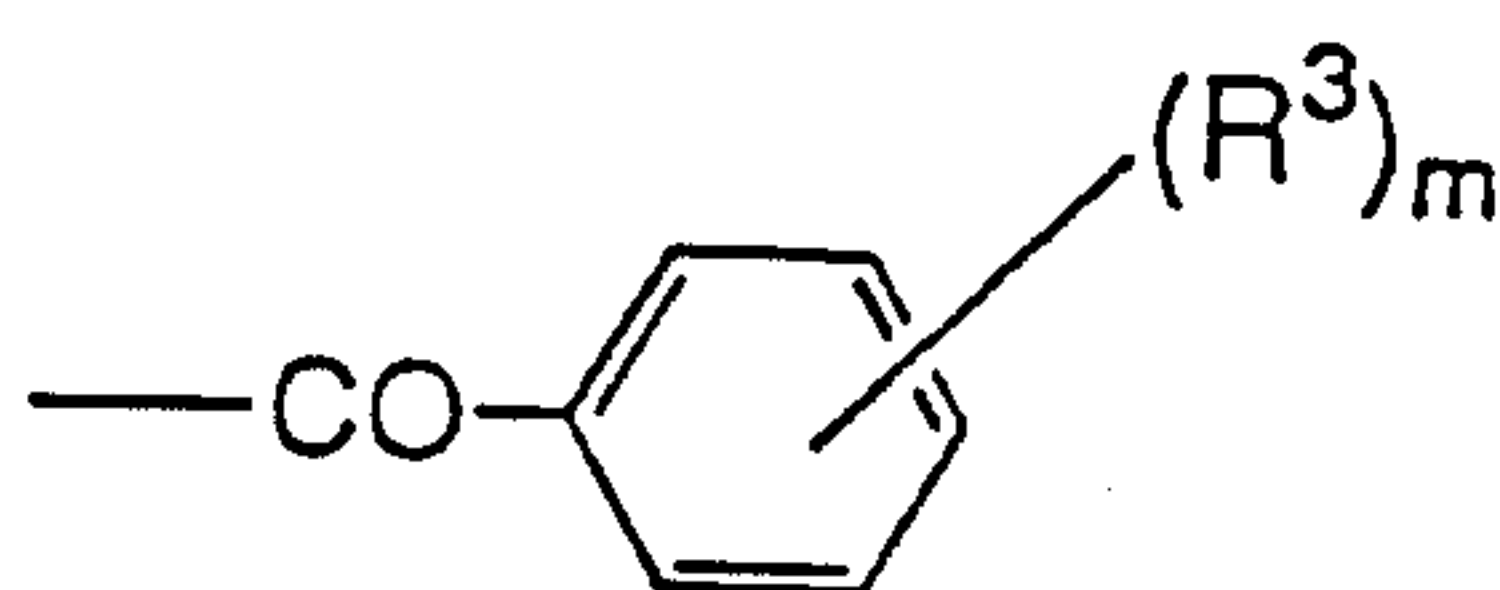
arteriosclerosis, Raynaud disease and Raynaud syndrome),
venous diseases (e.g. venous thrombosis and thrombophle-
bites) and other diseases (e.g. congelation, frostbite,
feeling of cold and decubitus), and is effective for the
5 preventions and treatments of feeling of coldness accom-
panied by oversensitivity to the cold and hypnagogic
disturbance, etc.

The piperidine derivatives of general formula
(1) and their salts according to the present invention
10 are characterized particularly in that while they have
an excellent peripheral vasodilating activity, they show
low pharmacological side-effects to the heart, i.e. a
low effect to heart rate, a low hypotensive effect and a
low myocardial contraction effect.

15 The piperidine derivatives contained in the
peripheral vasodilating agents of the present invention
as an active ingredient are represented by the following
general formula (1).



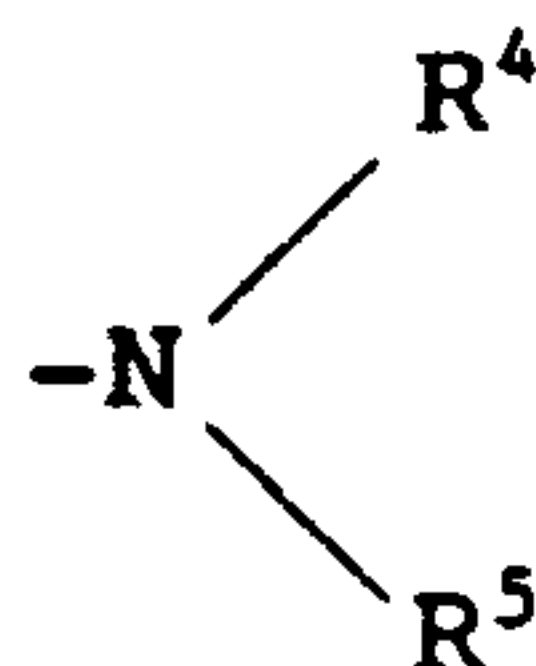
[wherein, R is a group of the formula:



(wherein, $\underline{m}$ is an integer of 1 to 3;

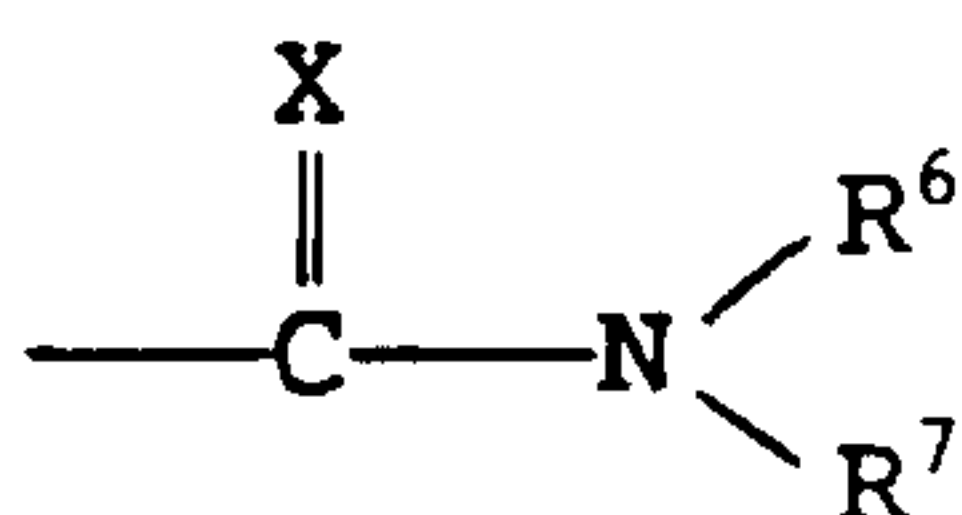
R^3 is a hydrogen atom; a nitro group; a lower alkyl group; a halogen atom; a cyano group; a lower alkanoyl group; an aminocarbonyl group which may have 1
5 to 2 substituents selected from the group consisting of a lower alkyl group and a phenyl group; a lower alkoxy-carbonyl group; a carboxy group; a lower alkoxy group; a hydroxyl group; a hydroxyamino group; a lower alkylthio-lower alkyl group; a lower alkylsulfonyl-lower alkyl
10 group; a hydroxyl group-substituted lower alkyl group; a lower alkenyl group; a lower alkoxycarbonyl group-substituted lower alkenyl group; a phenyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a hydroxyl group, a phenyl-lower
15 alkoxy group, a lower alkanoyloxy group, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a lower alkyl group and a lower alkoxy group; an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s); a morpholinyl group-
20 substituted lower alkoxy group; a 1,2,4-triazolyl group which may have oxo group(s) as substituent(s) on the 1,2,4-triazole ring; a 1,2,3,4-tetrazolyl group; an imidazolyl group which may have 1 to 2 substituents selected from the group consisting of a phenyl group and
25 a lower alkyl group on the imidazole ring; a pyrazolyl group which may have lower alkyl group(s) as substituent(s) on the pyrazole ring; a pyridyl group; a pyrrolyl group; a pyrrolydiny group which may have oxo group(s)

as substituent(s) on the pyrrolidine ring; a piperidinyl group which may have oxo group(s) as substituent(s) on the piperidine ring; a benzimidazolyl group; an imidazolidinyl group which may have oxo group(s) as substituent(s) on the imidazolidine ring; a 2-oxazolinyl group; a 1,2,4-triazolyl-lower alkyl group; a phenoxy group; a phenyl-lower alkoxy group; a lower alkanoyloxy group; a phenyl-lower alkoxycarbonyl group; an amino-lower alkyl group which may have substituent(s) selected from the group consisting of a lower alkyl group and a lower alkanoyl group; or a group of the formula:



(wherein, R^4 and R^5 are the same or different and are each a hydrogen atom, a lower alkyl group, a lower alkanoyl group, a lower alkanoyl group having 1 to 3 halogen atoms, a benzoyl group, a pyridylcarbonyl group, a lower alkenylcarbonyl group, an anilinothiocarbonyl group, an aminothiocarbonyl group which may have lower alkyl group(s) as substituent(s) or an aminocarbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group, a phenyl group and a lower alkenyl group));

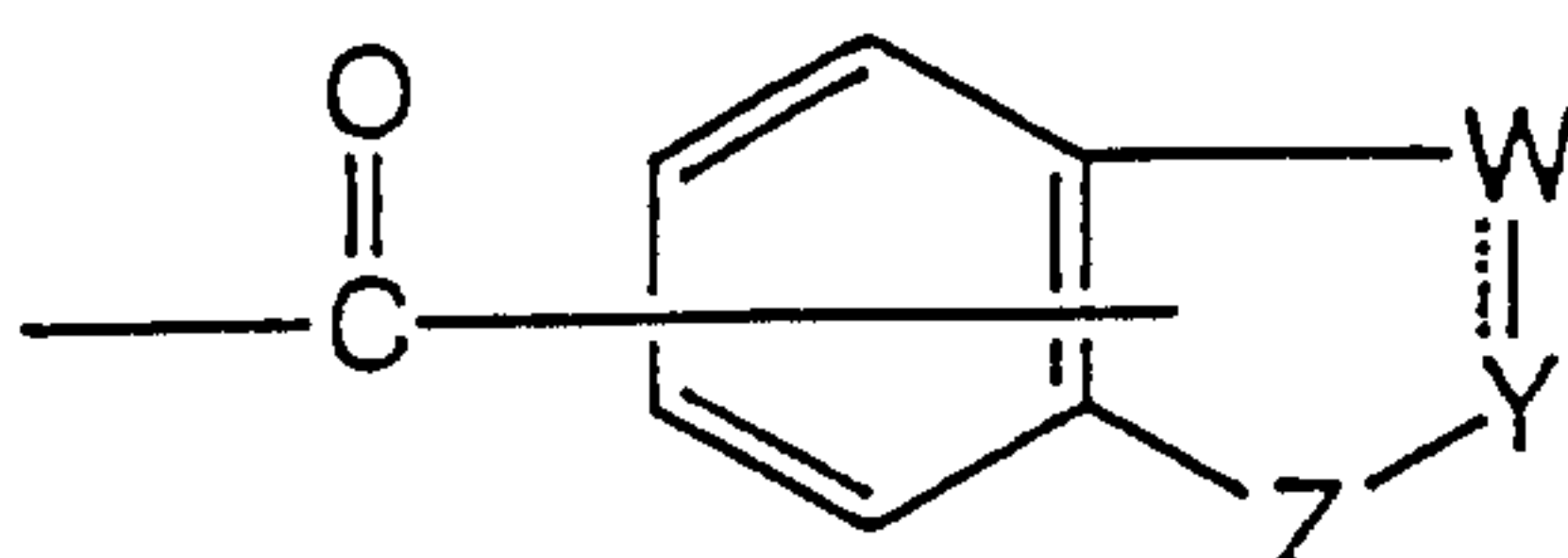
a group of the formula:



(wherein, X is an oxygen atom or a sulfur atom;

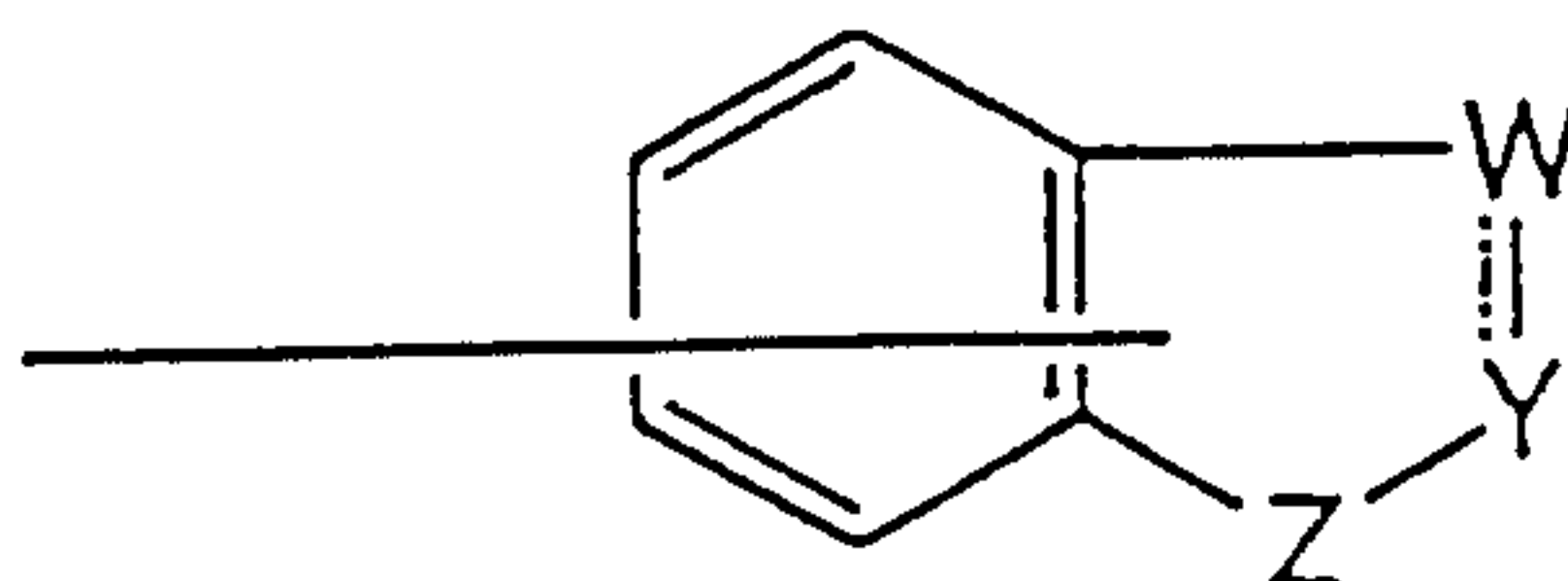
R⁶ and R⁷ are the same or different and are each a hydrogen atom, a lower alkyl group or a phenyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom and a nitro group); a lower alkanoyl group which may have hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s) as substituent(s); a lower alkanoyl group having 1 to 3 halogen atoms; a lower alkoxy carbonyl group; a pyridyl carbonyl group which may have, on the pyridine ring, substituent(s) selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxy carbonyl group, a hydroxyl group-substituted lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkanoyl group; a furoyl group which has, on the furan ring, substituent(s) selected from the group consisting of a nitro group, a hydroxyl group-substituted lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a thienyl carbonyl group which may have, on the thiophene ring, substituent(s) selected from the group consisting of a nitro group, a

lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); a fluorenylcarbonyl group which may have, on the fluorene ring, substituent(s) selected from the group
 5 consisting of an oxo group and a nitro group; or a group of the formula:



(wherein, Z is a group of the formula: $-\text{CH}_2-$ or $-\text{NH}-$ or a sulfur atom; Y and W are each a group of the formula: $=\text{CH}-$ or a nitrogen atom; the dotted line in the bonding
 10 of the formula: $\begin{array}{c} -\text{W} \\ \vdots \\ \text{Y} \end{array}$ is a single bond or a double bond;

and the group of the formula:



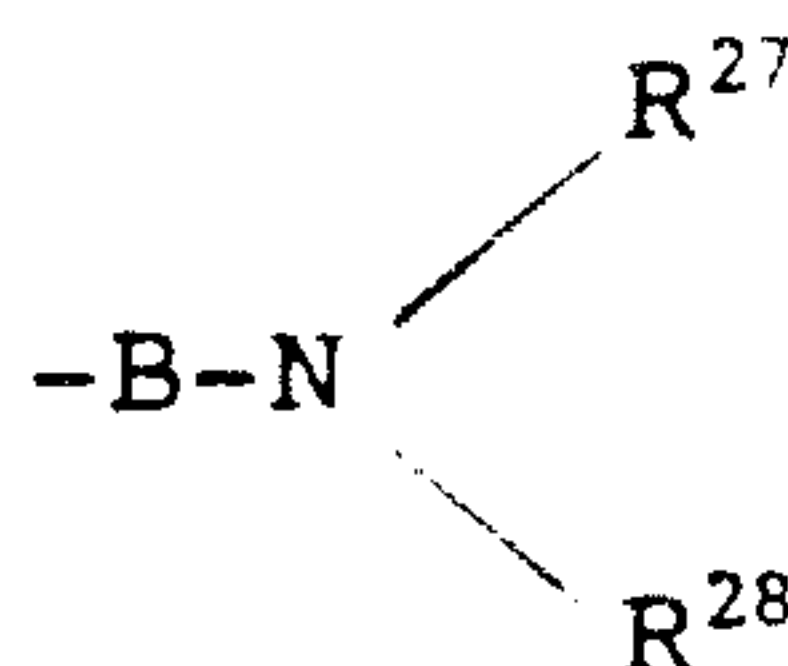
may have 1-4 substituents selected from the group consisting of an oxo group, a lower alkyl group, a lower alkoxy group, a hydroxyl group, a lower alkylthio group, a halogen atom, a nitro group and an amino group));

R^1 is a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituent(s);

R^2 is a phenyl-lower alkyl group which may
 20 have, on the phenyl ring, substituent(s) selected from

the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy group-substituted lower alkoxy group and an amino group which may have substituent(s) selected from the group consisting of a lower alkanoyl group, a lower alkoxy-carbonyl group and aminocarbonyl group(s) which may each have lower alkyl group(s) as substituent(s), which phenyl-lower alkyl group may have lower alkoxycarbonyl group(s) or hydroxyl group-substituted lower alkyl group(s) as substituent(s) in the lower alkyl moiety; a phenoxy-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), and a hydroxyl group; a pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring; a thienyl-lower alkyl group; a furyl-lower alkyl group; a group of the formula:

25



(wherein, B is a lower alkylene group; and R^{27} and R^{28} are the same or different and are each a hydrogen atom, a lower alkyl group, a phenyl group, a lower alkanoyl group or a benzoyl group); a phthalimido-substituted
5 lower alkyl group, a cycloalkyl-lower alkyl group; a phenyl-lower alkenyl group; a cycloalkyl group which may have phenyl group(s) as substituent(s); or a 2,3-dihydro-1H-indenyl group which may have, on the 2,3-dihydro-1H-indene ring, substituent(s) selected from the
10 group consisting of a lower alkoxy group, a hydroxyl group, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s);

R^1 , R^2 and the nitrogen atom bonded thereto may form a pyrrolidine ring, a piperidine ring, a morpholine
15 ring or a 1,2,3,4-tetrahydroisoquinoline ring, which heterocyclic group may have substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy group and a phenyl group;

provided that, when m is 1 and R^3 is an amino
20 group, R^3 must not be substituted at the 4-position of the benzoyl group].

Of the compounds of general formula (1), those having substituents having the following definitions are novel compounds not yet disclosed in any literature.
25 The present invention includes these novel compounds.

That is, said novel compounds are those compounds of general formula (1) wherein R is any of the above-mentioned groups, other than an unsubstituted

lower alkanoyl group and a lower alkoxycarbonyl group and
R¹ and R² form, together with the nitrogen atom bonded
thereto, a pyrrolidine ring, a piperidine ring or a
1,2,3,4-tetrahydroisoquinoline ring, each having thereon
5 substituent(s) selected from the group consisting of a
hydroxyl group, a lower alkoxy group and a phenyl group,
or wherein R³ in R is a group of the formula: -CX-NR⁶R⁷
and R² is a phenyl-lower alkyl group which may have the
above-mentioned substituent(s), a phenoxy-lower alkyl
10 group which may have the above-mentioned substituent(s),
or a pyridyl-lower alkyl group which may have the above-
mentioned substituent(s), each lower alkyl moiety of
said groups being a C₁₋₂ alkyl group.

Specific examples of the individual groups mentioned with respect to general formula (1) and throughout the present specification are as follows.

"Lower alkyl group" includes C₁₋₆ straight- or
5 branched-chain alkyl groups such as methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl and hexyl groups and the like.

"Halogen atom" includes, for example, a fluorine atom, a chlorine atom, a bromine atom and an
10 iodine atom.

"Lower alkanoyl group" includes C₁₋₆ straight- or branched-chain alkanoyl groups such as formyl, acetyl, propionyl, butyryl, isobutyryl, pentanoyl, tert-butylcarbonyl and hexanoyl groups and the like.

15 "Aminocarbonyl group which may have lower alkyl group(s)" can be exemplified by aminocarbonyl groups which may each have C₁₋₆ straight- or branched-chain alkyl group(s), such as carbamoyl, methylaminocarbonyl, ethylaminocarbonyl, propylaminocarbonyl,
20 isopropylaminocarbonyl, butylaminocarbonyl, tert-butylaminocarbonyl, pentylaminocarbonyl, hexylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, dipropylaminocarbonyl, dibutylaminocarbonyl, dipentylaminocarbonyl, dihexylaminocarbonyl, N-methyl-N-
25 ethylaminocarbonyl, N-ethyl-N-propylaminocarbonyl, N-methyl-N-butylaminocarbonyl and N-methyl-N-hexylaminocarbonyl groups and the like.

"Lower alkylsulfonyl-lower alkyl group"

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includes C₁₋₆ straight- or branched-chain alkylsulfonyl group-substituted C₁₋₆ straight- or branched-chain alkyl groups such as methylsulfonylmethyl, 3-ethylsulfonylpropyl, 4-methylsulfonylbutyl, 2-methylsulfonylethyl, 6-propylsulfonylhexyl, 5-isopropylsulfonylpentyl, 1,1-dimethyl-2-butylsulfonylethyl and 2-methyl-3-methylsulfonylpropyl groups and the like.

"Lower alkylthio-lower alkyl group" includes C₁₋₆ straight- or branched-chain alkylthio group-substituted C₁₋₆ straight- or branched-chain alkyl groups such as methylthiomethyl, 3-ethylthiopropyl, 4-methylthiobutyl, 2-methylthioethyl, 6-propylthiohexyl, 5-isopropylthiopentyl, 1,1-dimethyl-2-butylthioethyl and 2-methyl-3-methylthiopropyl groups and the like.

"Hydroxyl-substituted lower alkyl group" can be exemplified by C₁₋₆ straight- or branched-chain alkyl groups each having 1-3 hydroxyl groups, such as hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxypropyl, 4-hydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5,5,4-trihydroxypentyl, 5-hydroxypentyl, 6-hydroxyhexyl, 1-hydroxyisopropyl and 2-methyl-3-hydroxypropyl groups and the like.

"Lower alkenyl group" includes C₂₋₆ straight- or branched-chain alkenyl groups such as vinyl, allyl, 2-butenyl, 3-butenyl, 1-methylallyl, 2-pentenyl and 2-hexenyl groups and the like.

"Lower alkoxycarbonyl-substituted lower alkenyl group" can be exemplified by C₁₋₆ straight- or

branched-chain alkoxycarbonyl-substituted C₂₋₆ straight-
or branched-chain alkenyl groups such as 3-methoxy-
carbonylallyl, 2-ethoxycarbonylvinyl, 3-isopropoxy-
carbonyl-1-methylallyl, 5-butoxycarbonyl-2-pentenyl, 6-
5 pentyloxycarbonyl-2-hexenyl and 4-hexyloxycarbonyl-2-
butenyl groups and the like.

"Phenyl group which may have, on the phenyl
ring, substituent(s) selected from the group consisting
of a hydroxyl group, a phenyl-lower alkoxy group, a
10 lower alkanoyloxy group, a nitro group, an amino group
which may have lower alkanoyl group(s) as substi-
tuent(s), a lower alkyl group and a lower alkoxy group"
can be exemplified by phenyl groups which may each have,
on the phenyl ring, 1-3 substituents selected from the
15 group consisting of a hydroxyl group, a phenylalkoxy
group whose alkoxy moiety is a C₁₋₆ straight- or
branched-chain alkoxy group, a C₁₋₆ straight- or
branched-chain alkanoyloxy group, a nitro group, an
amino group which may have C₁₋₆ straight- or branched-
20 chain alkanoyl group(s) as substituent(s), a C₁₋₆
straight- or branched-chain alkyl group and a C₁₋₆
straight- or branched-chain alkoxy group, such as
phenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-
hydroxyphenyl, 2,3-dihydroxyphenyl, 2,4-dihydroxyphenyl,
25 3,4-dihydroxyphenyl, 2,6-dihydroxyphenyl, 3,4,5-trihyd-
roxyphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-
methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-
ethoxyphenyl, 4-isopropoxyphenyl, 4-pentyloxyphenyl,

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2,4-dimethoxyphenyl, 4-hexyloxyphenyl, 3,4-dimethoxyphenyl, 3-ethoxy-4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-diethoxyphenyl, 2,4-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3,4-dipentyloxyphenyl, 5 3,4,5-trimethoxyphenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-propylphenyl, 3-propylphenyl, 4-propylphenyl, 2-isopropylphenyl, 3-pentylphenyl, 4-hexylphenyl, 3,4-dimethylphenyl, 3,5-dimethylphenyl, 10 2,6-dimethylphenyl, 2,3-dimethylphenyl, 2,4-dimethylphenyl, 3,4-diethylphenyl, 3,5-diethylphenyl, 3,4,5-trimethylphenyl, 2-methoxy-3-methylphenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2,4-dinitrophenyl, 2,6-dinitrophenyl, 2,4,6-trinitrophenyl, 4-aminophenyl, 15 4-propionylaminophenyl, 2-acetylaminophenyl, 3-formylaminophenyl, 2-butyrylamino-phenyl, 3-isobutyrylamino-phenyl, 4-pentanoylamino-phenyl, 4-tert-butylcarbonylaminophenyl, 3-hexanoylamino-phenyl, 3,4-diamino-phenyl, 3,4,5-triamino-phenyl, 3,4-diacetylaminophenyl, 4-acetyloxyphenyl, 3,4-dibenzyloxyphenyl, 2,4-diacetyl- 20 oxyphenyl, 4-benzyloxyphenyl, 3-propionyloxyphenyl, 2-butyryloxyphenyl, 4-pentanoyloxyphenyl, 4-helanoxyloxyphenyl, 4-(2-phenylethoxy)phenyl, 3-(3-phenylpropoxy)phenyl, 4-(4-phenylbutoxy)phenyl, 2-(5-phenyl- 25 pentyloxy)phenyl and 4-(6-phenylhexyloxy)phenyl groups and the like.

"Amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s)" can be exemplified by

amino-substituted C₁₋₆ straight- or branched-chain alkoxy groups which may each have one to two C₁₋₆ straight- or branched-chain alkyl groups as substituent(s), such as aminomethoxy, 1-aminoethoxy, 2-aminoethoxy, 3-aminopropoxy, 4-aminobutoxy, 5-aminopentyloxy, 6-aminohexyloxy, 1,1-dimethyl-2-aminoethoxy, 2-methyl-3-aminopropoxy, methylaminomethoxy, ethylaminomethoxy, propylaminomethoxy, isopropylaminomethoxy, butylaminomethoxy, tert-butylaminomethoxy, pentylaminomethoxy, hexylaminomethoxy, dimethylaminomethoxy, diethylaminomethoxy, dipropylaminomethoxy, dibutylaminomethoxy, dipentylaminomethoxy, dihexylaminomethoxy, N-methyl-N-ethylaminomethoxy, N-methyl-N-propylaminomethoxy, N-methyl-N-butylaminomethoxy, N-methyl-N-hexylaminomethoxy, 1-methylaminoethoxy, 2-ethylaminoethoxy, 3-propylaminopropoxy, 4-butylaminobutoxy, 1,1-dimethyl-2-pentylaminoethoxy, 5-hexylaminopentyloxy, 6-dimethylaminoethoxy, 2-diethylaminoethoxy, 1-(N-methyl-N-hexylamino)ethoxy, 3-dihexylaminopropoxy, 4-dibutylaminobutoxy and 2-(N-methyl-N-pentylamino)ethoxy groups and the like.

"Morpholinyl-substituted lower alkoxy group" includes morpholinyl-substituted alkoxy groups whose alkoxy moieties are each a C₁₋₆ straight- or branched-chain alkoxy group, such as morpholinomethoxy, 2-morpholinoethoxy, 1-(2-morpholinyl)ethoxy, 3-(3-morpholinyl)propoxy, 4-morpholinobutoxy, 5-(2-morpholinyl)pentyloxy and 6-(3-morpholinyl)hexyloxy groups and the like.

"1,2,4-Triazolyl group which may have oxo group(s) as substituent(s) on the 1,2,4-triazole ring" includes 1,2,4-triazolyl, 3-oxo-1,2,4-triazolyl, 5-oxo-1,2,4-triazolyl, etc.

5 "Imidazolyl group which may have, on the imidazole ring, 1-2 substituents selected from the group consisting of a phenyl group and a lower alkyl group" includes imidazolyl groups which may each have, on the imidazole ring, 1-2 substituents selected from the group
10 consisting of a phenyl group and a C₁₋₆ straight- or branched-chain alkyl group, such as imidazolyl, 4-phenylimidazolyl, 2-ethylimidazolyl, 2-ethyl-4-methylimidazolyl, 2-methyl-4-phenylimidazolyl, 2-propylimidazolyl, 4-butylimidazolyl, 4-pentylimidazolyl,
15 2-hexylimidazolyl and 2-phenylimidazolyl groups and the like.

"Pyrazolyl group which may have lower alkyl group(s) on the pyrazole ring" can be exemplified by pyrazolyl groups which may each have, on the pyrazole
20 ring, C₁₋₆ straight- or branched-chain alkyl group(s), such as pyrazolyl, 3-methylpyrazolyl, 4-ethylpyrazolyl, 1-methylpyrazolyl, 3-propylpyrazolyl, 4-butylpyrazolyl, 3-pentylpyrazolyl and 4-hexylpyrazolyl groups and the like.

25 "Pyrrolidinyl group which may have oxo group(s) as substituent(s) on the pyrrolidine ring" includes pyrrolidinyl, 2-oxopyrrolidinyl, 3-oxopyrrolidinyl, etc.

"Piperidinyl group which may have oxo group(s) as substituent(s) on the piperidine ring" includes piperidinyl, 2-oxopiperidinyl, 3-oxopiperidinyl, 4-oxopiperidinyl, etc.

5 "Imidazolidinyl group which may have oxo group(s) as substituent(s) on the imidazolidine ring" includes imidazolidinyl, 2-oxoimidazolidinyl, 4-oxoimidazolidinyl, 5-oxoimidazolidinyl, etc.

"1,2,4-Triazolyl-lower alkyl group" can be
10 exemplified by 1,2,4-triazolylalkyl groups whose alkyl moieties are each a C₁₋₆ straight- or straight-chained alkyl group", such as (1,2,4-triazol-1-yl)methyl, 2-(1,2,4-triazol-3-yl)ethyl, 1-(1,2,4-triazol-5-yl)ethyl, 3-(1,2,4-triazol-1-yl)propyl, 4-((1,2,4-triazol-3-yl)butyl, 5-(1,2,4-triazol-5-yl)pentyl, 6-(1,2,4-triazol-1-yl)hexyl, 1,1-dimethyl-2-(1,2,4-triazol-1-yl)ethyl and 2-methyl-3-(1,2,4-triazol-1-yl)propyl
15 groups and the like.

"Lower alkenylcarbonyl group" includes C₂₋₆
20 straight- or branched-chain alkenylcarbonyl groups such as vinylcarbonyl, allylcarbonyl, 2-butenylcarbonyl, 3-butenylcarbonyl, 1-methylallylcarbonyl, 2-pentenylcarbonyl and 2-hexenylcarbonyl groups and the like.

"Aminothiocarbonyl group which may have lower
25 alkyl group(s) as substituent(s)" can be exemplified by aminothiocarbonyl groups which may each have C₁₋₆ straight- or branched-chain alkyl group(s) as substituent(s), such as aminothiocarbonyl, methylaminothio-

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carbonyl, ethylaminothiocarbonyl, propylaminothio-
carbonyl, isopropylaminothiocarbonyl, butylaminothio-
carbonyl, tert-butylaminothiocarbonyl, pentylaminothio-
carbonyl, hexylaminothiocarbonyl, dimethylaminothio-
5 carbonyl, diethylaminothiocarbonyl, dipropylaminothio-
carbonyl, dibutylaminothiocarbonyl, dipentylamino-
thiocarbonyl, dihexylaminothiocarbonyl, N-methyl-N-
ethylaminothiocarbonyl, N-ethyl-N-propylaminothio-
carbonyl, N-methyl-N-butylaminothiocarbonyl and N-
10 methyl-N-hexylaminothiocarbonyl groups and the like.

"Aminocarbonyl group which may have 1-2
substituents selected from the group consisting of a
lower alkyl group, a phenyl group and a lower alkenyl
group" can be exemplified by aminocarbonyl groups which
15 may each have 1-2 substituents selected from the group
consisting of a C₁₋₆ straight- or branched-chain alkyl
group, a phenyl group and a C₂₋₆ straight- or branched-
chain alkenyl group, such as aminocarbonyl, phenylamino-
carbonyl, diphenylaminocarbonyl, methylaminocarbonyl,
20 ethylaminocarbonyl, propylaminocarbonyl, isopropyl-
aminocarbonyl, butylaminocarbonyl, tertbutylamino-
carbonyl, pentylaminocarbonyl, hexylaminocarbonyl,
dimethylaminocarbonyl, diethylaminocarbonyl, dipropyl-
aminocarbonyl, dibutylaminocarbonyl, dipentylamino-
25 carbonyl, dihexylaminocarbonyl, N-methyl-N-ethylamino-
carbonyl, N-ethyl-N-propylaminocarbonyl, N-methyl-N-
butylaminocarbonyl, N-methyl-N-hexylaminocarbonyl, N-
methyl-N-phenylaminocarbonyl, N-ethyl-N-phenylamino-

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carbonyl, vinylaminocarbonyl, allylaminocarbonyl, (2-butenyl)aminocarbonyl, (3-butenyl)aminocarbonyl, (1-methylallyl)aminocarbonyl, (2-pentenyl)aminocarbonyl, (2-hexenyl)aminocarbonyl, N-methyl-N-allylaminocarbonyl
5 and diallylaminocarbonyl groups and the like.

"Phenyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom and a nitro groups" can be exemplified by phenyl groups which may
10 each have, on the phenyl ring, 1-3 substituents selected from the group consisting of a C₁₋₆ straight- or branched-chain alkoxy group, a halogen atom and a nitro group, such as phenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 4-isopropoxyphenyl, 4-pentyloxyphenyl,
15 2,4-dimethoxyphenyl, 4-hexyloxyphenyl, 3,4-dimethoxyphenyl, 3-ethoxy-4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-diethoxyphenyl, 2,5-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3,4-dipentyloxyphenyl, 3,4,5-trimethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,6-dichlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 3,4-difluorophenyl, 3,5-dibromophenyl, 3,4,5-trichlorophenyl, 2-methoxy-3-chlorophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2,4-dinitrophenyl, 2,6-dinitrophenyl and

2,4,6-trinitrophenyl groups and the like.

"Amino group which may have lower alkyl group(s)" can be exemplified by amino groups which may each have one to two C₁₋₆ straight- or branched-chain alkyl groups as substituent(s), such as amino, methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, dipentylamino, dihexylamino, N-methyl-N-ethylamino, N-ethyl-N-propylamino, N-methyl-N-butylamino and N-methyl-N-hexylamino groups and the like.

"Lower alkanoyl group which may have, as substituent(s), hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s)" can be exemplified by the above-mentioned alkanoyl groups and also by C₂₋₆ straight- or branched-chain alkanoyl groups which may each have, as substituent(s), hydroxyl group(s) or amino group(s) which may each have one to two C₁₋₆ straight- or branched-chain alkyl groups, such as 2-hydroxyacetyl, 3-hydroxypropionyl, 2-hydroxypropionyl, 4-hydroxybutyryl, 2,2-dimethyl-3-hydroxypropionyl, 5-hydroxypentanoyl, 6-hydroxyhexanoyl, 3-methyl-4-hydroxybutyryl, 2-aminoacetyl, 4-aminobutyryl, 4-methylaminobutyryl, 2-dimethylaminoacetyl, 2-methylaminoacetyl, 4-dimethylaminoacetyl, 3-ethylaminopropionyl, 2-isopropylaminopropionyl, 2,2-dimethyl-3-butylaminopropionyl, 5-pentylaminopentanoyl, 6-hexylaminohexanoyl, 3-methyl-4-(N-methyl-N-ethylamino)butyryl

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groups and the like. Incidentally, "lower alkanoyl group having, as substituent, hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s)" includes the above-mentioned groups other than unsubstituted lower alkanoyl groups.

"Lower alkanoyl group having 1-3 halogen atoms" includes C₁₋₆ straight- or branched-chain alkanoyl groups each having 1-3 halogen atoms, such as 2,2,2-trifluoroacetyl, 2,2,2-trichloroacetyl, 2-chloroacetyl, 2-bromoacetyl, 2-fluoroacetyl, 2-iodoacetyl, 2,2-difluoroacetyl, 2,2-dibromoacetyl, 3,3,3-trifluoropropionyl, 3,3,3-trichloropropionyl, 3-chloropropionyl, 2,3-dichloropropionyl, 4,4,4-trichlorobutyryl, 4-fluorobutyryl, 5-chloropentanoyl, 3-chloro-2-methylpropionyl, 6-bromohexanoyl and 5,6-dibromohexanoyl groups and the like.

"Lower alkoxy carbonyl group" can be exemplified by C₁₋₆ straight- or branched-chain alkoxy carbonyl groups such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, pentyloxycarbonyl and hexyloxycarbonyl groups and the like.

"Amino group which may have lower alkanoyl group(s)" can be exemplified by amino groups which may each have C₁₋₆ straight- or branched-chain alkanoyl group(s), such as amino, formylamino, acetylamino, propionylamino, butyrylamino, isobutyrylamino, pentanoylamino, tert-butylcarbonylamino and hexanoyl-

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amino groups and the like.

"Pyridylcarbonyl group which may have, on the pyridine ring, substituent(s) selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), lower alkoxy-carbonyl group(s), hydroxyl-substituted lower alkyl group(s), phenyl group(s) and 1,2,4-triazolyl group(s)" can be exemplified by pyridylcarbonyl groups which may each have, on the pyridine ring, 1-3 substituents selected from the group consisting of a nitro group, an amino group which may have C₁₋₆ straight- or branched-chain alkanoyl group(s) as substituent(s), halogen atom(s), C₁₋₆ straight- or branched-chain alkyl group(s), pyrrolyl group(s), C₁₋₆ straight- or branched-chain alkylthio group(s), C₁₋₆ straight- or branched-chain alkanoyl group(s), hydroxyl group(s), aminocarbonyl group(s) which may each have C₁₋₆ straight- or branched-chain alkyl group(s) as substituent(s), C₁₋₆ straight- or branched-chain alkoxy-carbonyl group(s), C₁₋₆ straight- or branched-chain alkyl group(s) each having 1-3 hydroxyl groups, phenyl group(s) and 1,2,4-triazolyl group(s), such as pyridylcarbonyl, 2-nitropyridylcarbonyl, 3-nitropyridylcarbonyl, 4-nitropyridylcarbonyl, 2-aminopyridylcarbonyl, 3-aminopyridylcarbonyl, 4-amino-

pyridylcarbonyl, 2-propionylaminopyridylcarbonyl, 3-acetylaminopyridylcarbonyl, 4-butyrylamino-
pyridylcarbonyl, 2-pentanoylamino-
pyridylcarbonyl, 3-hexanoylamino-
pyridylcarbonyl, 2-chloropyridylcarbonyl,
5 3-bromopyridylcarbonyl, 4-fluoropyridylcarbonyl, 2-iodopyridylcarbonyl, 2,4-dichloropyridylcarbonyl, 2-methylpyridylcarbonyl, 3-ethylpyridylcarbonyl, 4-propylpyridylcarbonyl, 2-butylpyridylcarbonyl, 3-pentylpyridylcarbonyl, 4-hexylpyridylcarbonyl, 2,4-
10 dimethylpyridylcarbonyl, 2,4,6-trimethylpyridylcarbonyl, 2-(1-pyrrolyl)pyridylcarbonyl, 2-amino-3-methylpyridylcarbonyl, 2-propionylaminopyridylcarbonyl, 2-(1-1,2,4-triazol-1-yl)pyridylcarbonyl, 2-methylthiopyridylcarbonyl, 3-ethylthiopyridylcarbonyl, 4-propylthio-
15 pyridylcarbonyl, 2-butylthiopyridylcarbonyl, 3-pentylthiopyridylcarbonyl, 4-hexylthiopyridylcarbonyl, 2-acetylpyridylcarbonyl, 2-acetyl-4-methylpyridylcarbonyl, 3-propionylpyridylcarbonyl, 4-butylpyridylcarbonyl, 2-formylpyridylcarbonyl, 3-pentanoyl-
20 pyridylcarbonyl, 4-hexanoylpyridylcarbonyl, 2-hydroxypyridylcarbonyl, 3-hydroxypyridylcarbonyl, 4-hydroxypyridylcarbonyl, 2,4-dihydroxypyridylcarbonyl, 2,4,6-trihydroxypyridylcarbonyl, 2-hydroxy-3-chloropyridylcarbonyl, 2-ethylaminocarbonylpyridylcarbonyl, 3-methylaminocarbonylpyridylcarbonyl, 4-propylamino-
25 carbonylpyridylcarbonyl, 2-butylaminocarbonylpyridylcarbonyl, 3-pentylaminocarbonylpyridylcarbonyl, 4-hexylaminocarbonylpyridylcarbonyl, 2-carbamoylpyridyl-

carbonyl, 2-dimethylaminocarbonylpyridylcarbonyl, 2-methoxycarbonylpyridylcarbonyl, 3-ethoxycarbonylpyridylcarbonyl, 4-propoxycarbonylpyridylcarbonyl, 2-butoxycarbonylpyridylcarbonyl, 3-pentyloxycarbonylpyridylcarbonyl, 4-hexyloxycarbonylpyridylcarbonyl, 2-hydroxymethylpyridylcarbonyl, 2,4-dimethyl-3-propionylaminopyridylcarbonyl, 3-propionylamino-4-methylpyridylcarbonyl, 3-(2-hydroxyethyl)pyridylcarbonyl, 4-(3-hydroxypropyl)pyridylcarbonyl, 2-(4-hydroxybutyl)pyridylcarbonyl, 3-(5-hydroxypentyl)pyridylcarbonyl, 4-(6-hydroxyhexyl)pyridylcarbonyl, 2-(2,3-dihydroxypropyl)pyridylcarbonyl, 4-(5,5,4-trihydroxybutyl)pyridylcarbonyl, 2-phenylpyridylcarbonyl and 3-phenylpyridylcarbonyl groups and the like.

"1,2,4-Triazolyl-lower alkanoyl group" can be exemplified by 1,2,4-triazolylalkanoyl groups whose alkanoyl moieties are each a C₂₋₆ straight- or branched-chain alkanoyl group, such as 2-(1,2,4-triazol-1-yl)acetyl, 3-(1,2,4-triazol-3-yl)propionyl, 2-(1,2,4-triazol-5-yl)propionyl, 4-(1,2,4-triazol-1-yl)butyryl, 2,2-dimethyl-3-(1,2,4-triazol-1-yl)propionyl, 5-(1,2,4-triazol-3-yl)pentanoyl, 6-(1,2,4-triazol-5-yl)hexanoyl and 3-methyl-4-(1,2,4-triazol-1-yl)butyryl groups and the like.

"Lower alkyl group which may have hydroxyl group(s) as substituent(s)" can be exemplified by (a) the above-mentioned lower alkyl groups and (b) C₁₋₆ straight- or branched-chain alkyl groups each having 1-3

hydroxyl groups, obtained by introducing said hydroxyl group(s) into the lower alkyl group (a).

"Lower alkylthio group" can be exemplified by C₁₋₆ straight- or branched-chain alkylthio groups such as methylthio, ethylthio, propylthio, isopropylthio, butylthio, tert-butylthio, pentylthio and hexylthio groups and the like.

"Lower alkylsulfinyl group" can be exemplified by C₁₋₆ straight- or branched-chain alkylsulfinyl groups such as methylsulfinyl, ethylsulfinyl, isopropylsulfinyl, butylsulfinyl, tert-butylsulfinyl, pentylsulfinyl, hexylsulfinyl groups and the like.

"Carboxy-substituted lower alkoxy group" includes carboxyalkoxy groups whose alkoxy moities are each a C₁₋₆ straight- or branched-chain alkoxy group, such as carboxymethoxy, 2-carboxyethoxy, 1-carboxyethoxy, 3-carboxypropoxy, 4-carboxybutoxy, 5-carboxypentyloxy, 6-carboxyhexyloxy, 1,1-dimethyl-2-carboxyethoxy and 2-methyl-3-carboxypropoxy groups and the like.

"Amino group which may have, as substituent(s), lower alkanoyl group(s), lower alkoxycarbonyl group(s), or aminocarbonyl group(s) which may each have lower alkyl group(s)" can be exemplified by amino groups which may have, as substituent(s), C₁₋₆ straight- or branched-chain alkanoyl group(s), C₁₋₆ straight- or branched-chain alkoxycarbonyl group(s), or aminocarbonyl group(s) which may each have C₁₋₆ straight- or branched-

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chain alkyl group(s), such as amino, carbamoylamino, methylaminocarbonylamino, ethylaminocarbonylamino, propylaminocarbonylamino, isopropylaminocarbonylamino, butylaminocarbonylamino, tert-butylaminocarbonylamino, 5 pentylaminocarbonylamino, hexylaminocarbonylamino, dimethylaminocarbonylamino, diethylaminocarbonylamino, dipropylaminocarbonylamino, dibutylaminocarbonylamino, dipentylaminocarbonylamino, dihexylaminocarbonylamino, N-acetyl-N-ethylaminocarbonylamino, N-propionyl-N- 10 propylaminocarbonylamino, N-methoxycarbonyl-N-butylaminocarbonylamino, N-ethoxycarbonyl-N-hexylaminocarbonylamino, formylamino, acetylamino, propionylamino, butyrylamino, isobutyrylamino, pentanoylamino, tert-butylcarbonylamino, hexanoylamino, methoxycarbonylamino, 15 ethoxycarbonylamino, propoxycarbonylamino, isopropoxycarbonylamino, butoxycarbonylamino, tert-butoxycarbonylamino, pentyloxycarbonylamino and hexyloxycarbonylamino groups and the like.

"Phenoxy-lower alkyl group which may have, on 20 the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a nitro group, a hydroxyl group and a amino group which may have lower alkanoyl group(s)" can be exemplified by phenoxyalkyl groups which may each 25 have, on the phenyl ring, 1-3 substituents selected from the group consisting of a C₁₋₆ straight- or branched-chain alkoxy group, a C₁₋₆ straight- or branched-chain alkyl group, a halogen atom, a nitro group, a hydroxyl

group and an amino group which may have C₁₋₆ straight- or branched-chain alkanoyl group(s), and whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as phenoxymethyl, 2-phenoxyethyl, 1-phenoxyethyl, 3-phenoxypropyl, 4-phenoxybutyl, 5-phenoxypentyl, 6-phenoxyhexyl, 1,1-dimethyl-2-phenoxyethyl, 2-methyl-3-phenoxypropyl, (2-hydroxyphenoxy)methyl, 2-(4-hydroxyphenoxy)ethyl, 1-(3-hydroxyphenoxy)ethyl, 3-(2-hydroxyphenoxy)propyl, 4-(3-hydroxyphenoxy)butyl, 5-(4-hydroxyphenoxy)pentyl, 6-(2-hydroxyphenoxy)hexyl, (2-methoxyphenoxy)methyl, 2-(4-methoxyphenoxy)ethyl, 1-(3-ethoxyphenoxy)ethyl, 3-(2-propoxyphenoxy)propyl, 4-(3-butoxyphenoxy)butyl, 5-(4-pentyloxyphenoxy)pentyl, 6-(2-hexyloxyphenoxy)hexyl, 1,1-dimethyl-2-(2,4-dimethoxyphenoxy)ethyl, 2-methyl-3-(3,4,5-trimethoxyphenoxy)propyl, (2,3-dihydroxyphenoxy)methyl, (3,4,5-trihydroxyphenoxy)methyl, 2-(3,4-dimethoxyphenoxy)ethyl, 2-(3-methoxy-4-hydroxyphenoxy)-ethyl, (2-methylphenoxy)methyl, 2-(4-methylphenoxy)-ethyl, 2-(3-methylphenoxy)ethyl, 1-(4-methylphenoxy)-ethyl, 3-(2-ethylphenoxy)propyl, 4-(3-ethylphenoxy)-butyl, 1,1-dimethyl-2-(4-ethylphenoxy)ethyl, 5-(4-isopropylphenoxy)pentyl, 6-(4-hexylphenoxy)hexyl, (3,4-dimethylphenoxy)methyl, (3,4,5-trimethylphenoxy)methyl, (2,5-dimethylphenoxy)methyl, (2-chlorophenoxy)methyl, (4-chlorophenoxy)methyl, (3-chlorophenoxy)methyl, 2-(3-chlorophenoxy)ethyl, (2-fluorophenoxy)methyl, 1-(4-chlorophenoxy)ethyl, 3-(2-fluorophenoxy)propyl, 4-(3-

fluorophenoxy)butyl, 5-(4-fluorophenoxy)pentyl, 1,1-dimethyl-2-(2-bromophenoxy)ethyl, 6-(3-bromophenoxy)-hexyl, (4-bromophenoxy)methyl, 2-(2-iodophenoxy)ethyl, 1-(3-iodophenoxy)ethyl, 3-(4-iodophenoxy)propyl, (3,4-dichlorophenoxy)methyl, (3,5-dichlorophenoxy)methyl, (2,6-dichlorophenoxy)methyl, (2,3-dichlorophenoxy)-methyl, (2,4-dichlorophenoxy)methyl, (3,4-difluorophenoxy)methyl, (3,5-dibromophenoxy)methyl, (3,4,5-trichlorophenoxy)methyl, (2-methoxy-3-chlorophenoxy)methyl, (2-nitrophenoxy)methyl, 2-(3-nitrophenoxy)ethyl, 2-(4-nitrophenoxy)ethyl, 1-(2-nitrophenoxy)ethyl, 3-(3-nitrophenoxy)propyl, 4-(4-nitrophenoxy)butyl, 5-(2-nitrophenoxy)pentyl, 2-(3-methyl-4-nitrophenoxy)ethyl, 2-(3-methyl-4-aminophenoxy)ethyl, 6-(3-nitrophenoxy)-hexyl, 2-(3,4-dinitrophenoxy)ethyl, 2-(3,4,5-trinitrophenoxy)ethyl, (2-aminophenoxy)methyl, 2-(3-aminophenoxy)ethyl, 2-(4-aminophenoxy)ethyl, 1-(2-aminophenoxy)ethyl, 3-(3-aminophenoxy)propyl, 4-(4-aminophenoxy)butyl, 5-(2-aminophenoxy)pentyl, 6-(3-aminophenoxy)hexyl, 2-(3,4-diaminophenoxy)ethyl, 2-(3,4,5-triaminophenoxy)ethyl, (2-propionylaminophenoxy)-ethyl, 3-(3-butyrylaminophenoxy)propyl, 4-(4-pentanoylaminophenoxy)butyl, 5-(5-hexanoylaminophenoxy)pentyl, 2-(4-acetylaminophenoxy)ethyl and 6-(2-acetylaminophenoxy)hexyl groups and the like.

"Pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring" can be exemplified by pyridylalkyl groups which

may each have, on the pyridine ring, one to three C₁₋₆ straight- or branched-chain alkyl groups and whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as (2-pyridyl)methyl, 2-(2-pyridyl)ethyl, 2-(3-pyridyl)ethyl, 1-(4-pyridyl)ethyl, 3-(2-pyridyl)propyl, 4-(3-pyridyl)butyl, 5-(4-pyridyl)pentyl, 6-(2-pyridyl)hexyl, 1,1-dimethyl-2-(3-pyridyl)ethyl, 2-methyl-3-(4-pyridyl)propyl, (4-methyl-2-pyridyl)methyl, 2-(2-methyl-6-pyridyl)ethyl, 1-(3-propyl-4-pyridyl)ethyl, 3-(4-butyl-2-pyridyl)propyl, 4-(2-pentyl-3-pyridyl)butyl, 5-(3-hexyl-4-pyridyl)pentyl, 6-(3,4-dimethyl-2-pyridyl)hexyl, 1,1-dimethyl-2-(2,4,6-trimethyl-3-pyridyl)ethyl and 2-methyl-3-(2,3-dimethyl-4-pyridyl)propyl groups and the like.

"Phenyl-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy-lower alkoxy group and an amino group which may have lower alkanoyl group(s), lower alkoxycarbonyl group(s) or aminocarbonyl group(s) which may each have lower alkyl group(s), and whose lower alkyl moiety may have, as substituent(s), lower alkoxycarbonyl group(s) or hydroxyl-substituted lower alkyl group(s)" can be exemplified by phenylalkyl

groups whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, which may each have, on the phenyl ring, 1-3 substituents selected from the group consisting of a C₁₋₆ straight- or branched-chain alkoxy group, a hydroxyl group, a nitro group, a C₁₋₆ straight- or branched-chain alkyl group, a halogen atom, a C₁₋₆ straight- or branched-chain alkylthio group, a C₁₋₆ straight- or branched-chain alkylsulfinyl group, a C₁₋₆ straight- or branched-chain alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-substituted C₁₋₆ straight- or branched-chain alkoxy group which may have one to two C₁₋₆ straight- or branched-chain alkyl groups as substituent(s), a carboxyalkoxy group whose alkoxy moiety is a C₁₋₆ straight- or branched-chain alkoxy group, and an amino group which may have, as substituent(s), C₁₋₆ straight- or branched-chain alkanoyl group(s), C₁₋₆ straight- or branched-chain alkoxycarbonyl group(s) or aminocarbonyl group(s) which may each have C₁₋₆ straight- or branched-chain alkyl group(s) as substituent(s), and whose alkyl moieties may each have, as substituent(s), C₁₋₆ straight- or branched-chain alkoxycarbonyl group(s) or C₁₋₆ straight- or branched-chain alkyl group(s) each having 1-3 hydroxyl groups, such as benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 2-phenylpropyl, 4-phenylbutyl, 1,1-dimethyl-2-phenylethyl, 5-phenylpentyl, 6-phenylhexyl, 2-methyl-3-phenylpropyl, 1-methoxycarbonyl-2-phenylethyl, 1-hydroxymethyl-2-phenylethyl, 1-ethoxycarbonyl-3-phenylpropyl, 1-(2-

hydroxyethyl)-4-phenylpropyl, 1-hydroxymethyl-2-(4-methoxyphenyl)ethyl, 2-(4-methoxyphenyl)ethyl, 2-(3-methoxyphenyl)ethyl, 1-(4-methoxyphenyl)ethyl, 2-methoxybenzyl, 3-(2-ethoxyphenyl)propyl, 4-(3-ethoxyphenyl)butyl, 1,1-dimethyl-2-(4-ethoxyphenyl)ethyl, 5-(4-isopropoxyphenyl)pentyl, 6-(4-hexyloxyphenyl)hexyl, 3,4-dimethoxybenzyl, 3,4,5-trimethoxybenzyl, 2,5-dimethylbenzyl, 3-methoxybenzyl, 4-methoxybenzyl, 2,4-diethoxybenzyl, 2,3-dimethoxybenzyl, 2,4-dimethoxybenzyl, 2,6-dimethoxybenzyl, 4-ethylthiobenzyl, 2-(4-methylthiophenyl)ethyl, 1-(2-propylthiophenyl)ethyl, 3-(2-butylthiophenyl)propyl, 4-(3-pentylthiophenyl)butyl, 1,1-dimethyl-2-(4-hexylthiophenyl)ethyl, 5-(2-methylthiophenyl)pentyl, 6-(methylthiophenyl)hexyl, 2-hydroxybenzyl, 4-hydroxybenzyl, 2-(3-hydroxyphenyl)ethyl, 1-(4-hydroxyphenyl)ethyl, 2-(4-hydroxyphenyl)ethyl, 2-(2-hydroxyphenyl)ethyl, 3-(2-hydroxyphenyl)propyl, 4-(3-hydroxyphenyl)butyl, 5-(2-hydroxyphenyl)pentyl, 6-(3-hydroxyphenyl)hexyl, 3,4-dihydroxybenzyl, 3,4,5-trihydroxybenzyl, 2-methylbenzyl, 2-(4-methylphenyl)ethyl, 2-(3-methylphenyl)ethyl, 1-(4-methylphenyl)ethyl, 3-(2-ethylphenyl)propyl, 4-(3-ethylphenyl)butyl, 1,1-dimethyl-2-(4-ethylphenyl)ethyl, 5-(4-isopropylphenyl)pentyl, 6-(4-hexylphenyl)hexyl, 3,4-dimethylbenzyl, 3,4,5-trimethyl benzyl, 2,5-dimethylbenzyl, 2-chlorobenzyl, 4-chloro benzyl, 3-chlorobenzyl, 2-(3-chlorophenyl)ethyl, 2-fluorobenzyl, 1-(4-chlorophenyl)ethyl, 3-(2-fluoro phenyl)propyl, 4-(3-fluorophenyl)butyl, 5-

(4-fluorophenyl)pentyl, 1,1-dimethyl-2-(2-bromophenyl)-
ethyl, 6-(3-bromophenyl)hexyl, 4-bromobenzyl, 2-(2-
iodophenyl) ethyl, 1-(3-iodophenyl)ethyl, 3-(4-iodo-
phenyl)propyl, 3,4-dichlorobenzyl, 3,5-dichlorobenzyl,
5 2,6-dichlorobenzyl, 2,3-dichlorobenzyl, 2,4-dichloro-
benzyl, 3,4-difluorobenzyl, 3,5-dibromobenzyl, 3,4,5-
trichlorobenzyl, 2-methoxy-3-chlorobenzyl, 2-nitro-
benzyl, 2-(3-nitrophenyl)ethyl, 2-(4-nitrophenyl)ethyl,
1-(2-nitrophenyl)ethyl, 3-(3-nitrophenyl)propyl, 4-(4-
10 nitrophenyl)butyl, 5-(2-nitrophenyl)pentyl, 6-(3-
nitrophenyl)hexyl, 2-(3,4-dinitrophenyl)ethyl, 2-(3,4,5-
trinitrophenyl)ethyl, 2-aminobenzyl, 2-(3-aminophenyl)
ethyl, 2-(4-aminophenyl)ethyl, 1-(2-aminophenyl)ethyl,
3-(3-aminophenyl)propyl, 4-(4-aminophenyl)butyl, 5-(2-
15 aminophenyl)pentyl, 6-(3-aminophenyl)hexyl, 2-(3,4-
diaminophenyl)ethyl, 2-(3,4,5-triaminophenyl)ethyl, 4-
ethylsulfinylbenzyl, 2-(4-methylsulfinyl)ethyl, 1-(2-
propylsulfinylphenyl)ethyl, 3-(2-butylsulfinylphenyl)-
propyl, 4-(3-pentylsulfinylphenyl)butyl, 1,1-dimethyl-2-
20 (4-hexylsulfinylphenyl)pentyl, 6-(3-methylsulfinyl-
phenyl)hexyl, 3-methoxycarbonylbenzyl, 2-(4-methoxy-
carbonylphenyl)ethyl, 1-(2-ethoxycarbonylphenyl)ethyl,
3-(3-propoxycarbonylphenyl)propyl, 4-(4-butoxycarbonyl-
phenyl)butyl, 5-(2-pentyloxycarbonylphenyl)pentyl, 6-(3-
25 hexyloxycarbonylphenyl)hexyl, 3-carbamoylbenzyl, 2-(4-
carbamoylphenyl)ethyl, 1-(2-carbamoylphenyl)ethyl, 3-(3-
carbamoylphenyl)propyl, 4-(4-carbamoylphenyl)butyl, 5-
(2-carbamoylphenyl)pentyl, 6-(3-carbamoylphenyl)hexyl,

3-carboxybenzyl, 2-(4-carboxyphenyl)ethyl, 1-(2-carboxyphenyl)ethyl, 3-(3-carboxyphenyl)propyl, 4-(4-carboxyphenyl)butyl, 5-(2-carboxyphenyl)pentyl, 6-(3-carboxyphenyl)hexyl, 2-aminomethoxybenzyl, 2-[2-(2-dimethylaminoethoxy)phenyl]ethyl, 1-[3-(3-propylamino propoxy)phenyl]ethyl, 3-[4-(5-hexylaminopentyloxy)phenyl]propyl, 4-{2-[2-(N-methyl-N-pentylamino)ethoxy]-phenyl}butyl, 5-[3-(6-aminohexyloxy)phenyl]pentyl, 3-(2-carboxyethoxy)benzyl, 2-(2-carboxymethoxyphenyl)ethyl, 1-[3-(1-carboxyethoxy)phenyl]ethyl, 3-[4-(3-carboxypropoxy)phenyl]propyl, 4-[2-(4-carboxybutoxy)phenyl]butyl, 5-[3-(5-carboxypentyloxy)phenyl]pentyl, 6-[4-(6-carboxyhexyloxy)phenyl]hexyl, 2-(2-acetylaminophenyl)ethyl, 2-(4-acetylaminophenyl)ethyl, 2-(2-methylaminocarbonylaminophenyl)ethyl, 2-(3-acetylaminophenyl)ethyl, 2-(3-methylaminocarbonylaminophenyl)ethyl, 2-(4-methylaminocarbonylaminophenyl)ethyl, 2-(3-ethoxycarbonylaminophenyl)ethyl, 1-(2-propionylaminophenyl)ethyl, 3-(3-butyrylaminophenyl)propyl, 4-(4-pentanoylaminophenyl)butyl, 5-(5-hexanoylaminophenyl)pentyl, 6-(2-acetylaminophenyl)hexyl, 2-methoxycarbonylamino)benzyl, 1-(4-propoxycarbonylaminophenyl)ethyl, 3-(3-butoxycarbonylaminophenyl)propyl, 4-(2-pentyloxy-carbonylaminophenyl)butyl, 5-(3-hexyloxycarbon-ylaminophenyl)benzyl, 6-(2-methoxycarbonylaminophenyl)hexyl, 2-aminocarbonylaminobenzyl, 1-(3-propylaminocarbonylaminophenyl)ethyl, 3-(4-hexylaminocarbonylaminophenyl)propyl, 4-[2-(N-methyl-N-pentylamino-

carbonylamino)phenyl]butyl, 5-(3-dimethylamino-carbonylamino)phenyl]pentyl, 6-(2-ethylamino-carbonylamino)phenyl]hexyl, 3,4-diacetylaminobenzyl, 3,4-dimethoxycarbonylamino)benzyl, 3-carboxy-4-hydroxybenzyl
5 and 3-methyl-4-methoxybenzyl groups and the like.

"Aminocarbonyl group which may have 1-2 substituents selected from the group consisting of lower alkyl groups and phenyl groups" can be exemplified by aminocarbonyl groups which may each have 1-2 substituents selected from the group consisting of C₁₋₆ straight- or branched-chain alkyl groups and phenyl groups, such as aminocarbonyl, phenylaminocarbonyl, diphenylaminocarbonyl, methylaminocarbonyl, ethylaminocarbonyl, propylaminocarbonyl, isopropylaminocarbonyl, butylaminocarbonyl, tert-butylaminocarbonyl, pentylaminocarbonyl, hexylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, dipropylaminocarbonyl, dibutylaminocarbonyl, dipentylaminocarbonyl, dihexylaminocarbonyl, N-methyl-N-ethylaminocarbonyl, N-ethyl-N-propylaminocarbonyl, N-methyl-N-butylaminocarbonyl, N-methyl-N-hexylaminocarbonyl, N-methyl-N-phenylaminocarbonyl and N-ethyl-N-phenylaminocarbonyl groups and the like.

"Furoyl group which may have, on the furan ring, substituent(s) selected from the group consisting of a nitro group, a hydroxyl-substituted lower alkyl group, a lower alkanoyl group and an amino groups which may have lower alkanoyl group(s)" can be exemplified by

furoyl groups which may each have, on the furan ring, 1-3 substituents selected from the group consisting of a nitro group, a C₁₋₆ straight- or branched-chain alkyl group having 1-3 hydroxyl groups as substituent(s), C₁₋₆ straight- or branched-chain alkanoyl group and an amino group which may have C₁₋₆ straight- or branched-chain alkanoyl group(s), such as furoyl, 2-nitrofuroyl, 3-nitrofuroyl, 2,4-dinitrofuroyl, 2-formylfuroyl, 2-acetylfuroyl, 3-propionylfuroyl, 2-butyrylfuroyl, 3-pentanoylfuroyl, 2-hexanoylfuroyl, 2-aminofuroyl, 2,3-diaminofuroyl, 2-propionylaminofuroyl, 3-acetylaminofuroyl, 2-(1-hydroxyethyl)furoyl, 3-hydroxymethylfuroyl, 2-(3-hydroxypropyl)furoyl, 2-butyrylaminofuroyl, 3-pentanoylaminofuroyl, 2-(4-hydroxybutyl)furoyl, 3-(5-hydroxypentyl)furoyl, 2-hexanoylaminofuroyl, 3-nitro-2-acetylaminofuroyl, 3-(5,5,4-trihydroxypentyl)furoyl, 2-(6-hydroxyhexyl)furoyl, 2-(2,3-dihydroxypropyl)furoyl and 2-propionylamino-3,4-dinitrofuroyl groups and the like.

"Thienylcarbonyl group which may have, on the thiophene ring, substituent(s) selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s)" can be exemplified by thienylcarbonyl groups which may each have, on the thienyl ring, 1-3 substituents selected from the group consisting of a nitro group, a C₁₋₆ straight- or branched-chain alkyl group, a halogen atom and an amino group which may have

C₁₋₆ straight- or branched-chain alkanoyl group(s), such as thienylcarbonyl, 2-nitrothienylcarbonyl, 3-nitrothienylcarbonyl, 2,4-dinitrothienylcarbonyl, 2-methylthienylcarbonyl, 3-ethylthienylcarbonyl, 2-propylthienylcarbonyl, 3-butylthienylcarbonyl, 2-pentylthienylcarbonyl, 3-hexylthienylcarbonyl, 2,3,4-trimethylthienylcarbonyl, 2,3-dimethylthienylcarbonyl, 2-chlorothienylcarbonyl, 3-bromothienylcarbonyl, 2-fluorothienylcarbonyl, 3-iodothienylcarbonyl, 2,3-dichlorothienylcarbonyl, 2,3,4-trichlorothienylcarbonyl, 2-aminothienylcarbonyl, 2,3-diaminothienylcarbonyl, 2-propionylaminothienylcarbonyl, 3-acetylaminothienylcarbonyl, 2-butyrylaminothienylcarbonyl, 3-pentanoylaminothienylcarbonyl, 2-hexanoylaminothienylcarbonyl, 2-propionylamino-3-methylthienylcarbonyl and 4-chloro-2-acetylaminothienylcarbonyl groups and the like.

"Fluorenylcarbonyl group which may have, on the fluorene ring, substituent(s) selected from the group consisting of an oxo group and a nitro group" can be exemplified by fluorenylcarbonyl groups which may each have, on the fluorene ring, 1-3 substituents selected from the group consisting of an oxo group and an nitro group, such as fluorenylcarbonyl, 9-oxofluorenylcarbonyl, 2-nitrofluorenylcarbonyl, 3-nitrofluorenylcarbonyl, 4-nitrofluorenylcarbonyl, 2-nitro-9-oxofluorenylcarbonyl, 3-nitro-9-oxofluorenylcarbonyl, 4-nitro-9-oxofluorenylcarbonyl and 2,8-dinitro-9-oxofluorenylcarbonyl groups and the like.

"Thienyl-lower alkyl group" can be exemplified by thienylalkyl groups whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as (2-thienyl)methyl, 2-(2-thienyl)ethyl, 1-(3-thienyl)ethyl, 3-(2-thienyl)propyl, 4-(3-thienyl)butyl, 5-(2-thienyl)pentyl, 6-(2-thienyl)hexyl, 1,1-dimethyl-2-(2-thienyl)ethyl and 2-methyl-3-(3-thienyl)propyl groups and the like.

"Furyl-lower alkyl group" can be exemplified by furylalkyl groups whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as (2-furyl)methyl, 2-(2-furyl)ethyl, 1-(3-furyl)ethyl, 3-(2-furyl)propyl, 4-(3-furyl)butyl, 5-(2-furyl)pentyl, 6-(2-furyl)hexyl, 1,1-dimethyl-2-(2-furyl)ethyl and 2-methyl-3-(3-furyl)propyl groups and the like.

"Lower alkylene group" can be exemplified by C₁₋₆ straight- or branched-chain alkylene groups such as methylene, ethylene, trimethylene, tetramethylene, pentamethylene, hexamethylene, 2-ethyltrimethylene, 2,2-dimethyltrimethylene, 1-methyltrimethylene, methylmethylene and ethylmethylene groups and the like.

"Phthalimido-substituted lower alkyl group" can be exemplified by phthalimidoalkyl groups whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as phthalimidomethyl, 2-phthalimidoethyl, 1-phthalimidoethyl, 3-phthalimidopropyl, 4-phthalimidobutyl, 5-phthalimidopentyl, 6-phthalimidoethyl, 1,1-dimethyl-2-phthalimidoethyl and 2-

methyl-3-phthalimidopropyl groups and the like.

"Cycloalkyl-lower alkyl group" can be exemplified by C₃-C₈ cycloalkyl-alkyl groups whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as cyclohexylmethyl, 2-cyclopropylethyl, 2-cyclohexylethyl, 1-cyclobutylethyl, 3-cyclopentylpropyl, 4-cyclohexylbutyl, 2,2-dimethyl-3-cycloheptylpropyl, 5-cyclooctylpentyl and 6-cyclohexylhexyl groups and the like.

"Phenyl-lower alkenyl group" can be exemplified by phenylalkenyl groups whose alkenyl moieties are each a C₂₋₆ straight- or branched-chain alkenyl group, such as styryl, 3-phenyl-1-propenyl, 3-phenyl-2-propenyl, 4-phenyl-3-butenyl, 4-phenyl-2-butenyl, 5-phenyl-4-pentenyl, 5-phenyl-3-pentenyl, 5-phenyl-2-pentenyl, 6-phenyl-5-hexenyl, 6-phenyl-4-hexenyl, 6-phenyl-3-hexenyl, 6-phenyl-2-hexenyl, 2-methyl-4-phenyl-3-butenyl, 2-methyl-styryl and 1-methyl-styryl groups and the like.

"2,3-Dihydro-1H-indenyl group which may have, on the 2,3-dihydro-1H-indene ring, substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s)" can be exemplified by 2,3-dihydro-1H-indenyl groups which may each have, on the 2,3-dihydro-1H-indene ring, 1-3 substituents selected from the group consisting of a C₁₋₆ straight- or branched-chain alkoxy group, a hydroxyl

group, a nitro group and an amino group which may have C₁₋₆ straight- or branched-chain alkanoyl group(s), such as 2,3-dihydro-1H-indenyl, 1-methoxy-2,3-dihydro-1H-indenyl, 5-methoxy-2,3-dihydro-1H-indenyl, 2-ethoxy-2,3-dihydro-1H-indenyl, 3-methoxy-2,3-dihydro-1H-indenyl, 6-ethoxy-2,3-dihydro-1H-indenyl, 4-propoxy-2,3-dihydro-1H-indenyl, 7-butoxy-2,3-dihydro-1H-indenyl, 5-pentyloxy-2,3-dihydro-1H-indenyl, 6-hexyloxy-2,3-dihydro-1H-indenyl, 3,5,7-trimethoxy-2,3-dihydro-1H-indenyl, 5,7-dimethoxy-2,3-dihydro-1H-indenyl, 5-hydroxy-2,3-dihydro-1H-indenyl, 6-hydroxy-2,3-dihydro-1H-indenyl, 4-hydroxy-2,3-dihydro-1H-indenyl, 7-hydroxy-2,3-dihydro-1H-indenyl, 1-hydroxy-2,3-dihydro-1H-indenyl, 2-hydroxy-2,3-dihydro-1H-indenyl, 3-hydroxy-2,3-dihydro-1H-indenyl, 1,3,5-trihydroxy-2,3-dihydro-1H-indenyl, 3,5-dihydroxy-2,3-dihydro-1H-indenyl, 1-nitro-2,3-dihydro-1H-indenyl, 2-nitro-2,3-dihydro-1H-indenyl, 3-nitro-2,3-dihydro-1H-indenyl, 4-nitro-2,3-dihydro-1H-indenyl, 5-nitro-2,3-dihydro-1H-indenyl, 6-nitro-2,3-dihydro-1H-indenyl, 7-nitro-2,3-dihydro-1H-indenyl, 5,7-dinitro-2,3-dihydro-1H-indenyl, 1-amino-2,3-dihydro-1H-indenyl, 2-amino-2,3-dihydro-1H-indenyl, 3-amino-2,3-dihydro-1H-indenyl, 4-amino-2,3-dihydro-1H-indenyl, 5-amino-2,3-dihydro-1H-indenyl, 6-amino-2,3-dihydro-1H-indenyl, 7-amino-2,3-dihydro-1H-indenyl, 1,5-diamino-2,3-dihydro-1H-indenyl, 1,2,5-triamino-2,3-dihydro-1H-indenyl, 5-acetylamino-2,3-dihydro-1H-indenyl, 2-propionylamino-2,3-dihydro-1H-indenyl, 1-butyrylamino-2,3-dihydro-1H-

indenyl, 3-pentanoylamino-2,3-dihydro-1H-indenyl, 4-hexanoylamino-2,3-dihydro-1H-indenyl, 6-acetylamino-2,3-dihydro-1H-indenyl, 7-formylamino-2,3-dihydro-1H-indenyl, 2,5-diacetylamino-2,3-dihydro-1H-indenyl, 1-hydroxy-5-amino-2,3-dihydro-1H-indenyl, 1-methoxy-5-nitro-2,3-dihydro-1H-indenyl and 1-hydroxy-5-acetylamino-2,3-dihydro-1H-indenyl groups and the like.

"Phenyl-lower alkoxy group" can be exemplified by phenylalkoxy groups whose alkoxy moieties are each a C₁₋₆ straight- or branched-chain alkoxy group, such as benzyloxy, 2-phenylethoxy, 1-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 1,1-dimethyl-2-phenylethoxy, 5-phenylpentyloxy, 6-phenylhexyloxy and 2-methyl-3-phenylpropoxy groups and the like.

"Lower alkanoyloxy group" can be exemplified by C₁₋₆ straight- or branched-chain alkanoyloxy groups such as formyloxy, acetyloxy, propionyloxy, butyryloxy, isobutyryloxy, pentanoyloxy, tert-butylcarbonyloxy and hexanoyloxy groups and the like.

"Phenyl-lower alkoxycarbonyl group" can be exemplified by phenylalkoxycarbonyl groups whose alkoxycarbonyl moieties are each a C₁₋₆ straight- or branched-chain alkoxycarbonyl group, such as benzyloxycarbonyl, 2-phenylethoxycarbonyl, 1-phenylethoxycarbonyl, 3-phenylpropoxycarbonyl, 4-phenylbutoxycarbonyl, 1,1-dimethyl-2-phenylethoxycarbonyl, 5-phenylpentyloxycarbonyl, 6-phenylhexyloxycarbonyl and 2-methyl-3-phenylpropoxycarbonyl groups and the like.

"Amino-lower alkyl group which may have substituent(s) selected from the group consisting of a lower alkyl group and a lower alkanoyl group" can be exemplified by C₁₋₆ straight- or branched-chain alkyl groups each having an amino group which may have 1-2 substituents selected from the group consisting of a C₁₋₆ straight- or branched-chain alkyl group and a C₁₋₆ straight- or branched-chain alkanoyl group, such as aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminopropyl, 5-aminopentyl, 5-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, methylaminomethyl, ethylaminomethyl, 1-ethylaminoethyl, 2-propylaminoethyl, 3-isopropylaminopropyl, 4-butylaminobutyl, 5-pentylaminopentyl, 6-hexylaminoethyl, dimethylaminomethyl, 2-diethylaminoethyl, 2-dimethylaminoethyl, (N-ethyl-N-propylamino)methyl, 2-(N-methyl-N-hexylamino)ethyl, formylaminomethyl, acetylaminomethyl, 1-acetylaminomethyl, 2-propionylaminomethyl, 3-butyrylaminopropyl, 4-pentanoylaminobutyl, 5-hexanoylaminopentyl, 6-acetylaminohexyl and (N-ethyl-N-acetylamino)methyl groups and the like.

"Cycloalkyl group which may have phenyl group(s)" can be exemplified by C₃₋₈ cycloalkyl groups which may each have phenyl group(s), such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, 1-phenylcyclopropyl, 1-phenylcyclobutyl, 1-phenylcyclopentyl, 1-phenylcyclohexyl, 1-phenylcycloheptyl and 1-phenylcyclooctyl groups and the

like.

"Furoyl group having, on the furan ring, substituent(s) selected from the group consisting of a nitro group, a hydroxyl-substituted lower alkyl group, a lower alkanoyl group and a amino group which may have lower alkanoyl group(s)" can be exemplified by the above-mentioned furoyl groups other than unsubstituted furoyl group.

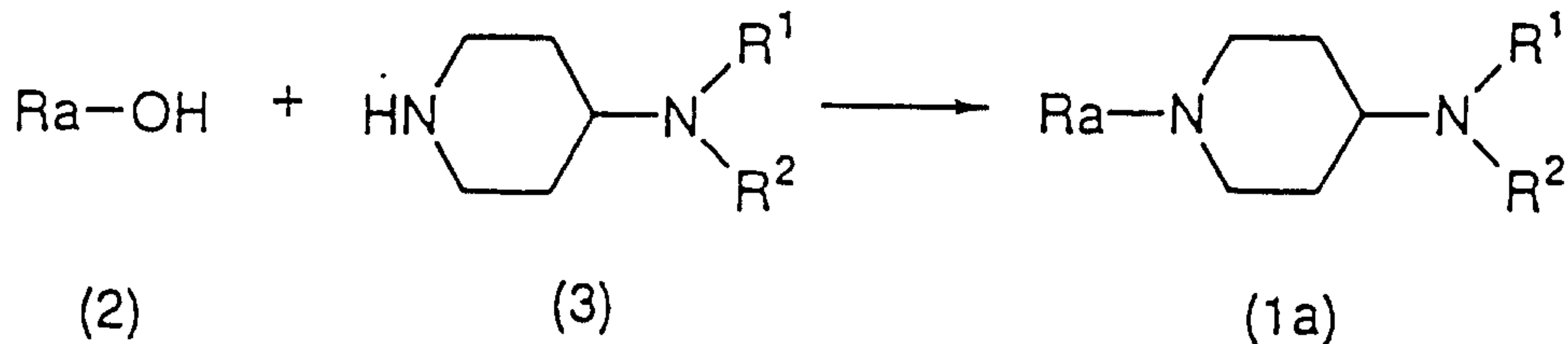
"Phenyl-C₁₋₂ alkyl group" can be exemplified by benzyl, 1-phenylethyl and 2-phenylethyl groups and the like.

"Phenyl-lower alkyl group having lower alkylthio group(s) on the phenyl ring" can be exemplified by phenylalkyl groups which each have, on the phenyl ring, one to three C₁₋₆ straight- or branched-chain alkylthio groups and whose alkyl moieties are each a C₁₋₆ straight- or branched-chain alkyl group, such as 4-ethylthiobenzyl, 2-(4-methylthiophenyl)ethyl, 1-(2-propylthiophenyl)ethyl, 3-(2-butylthiophenyl)propyl, 4-(3-pentylthiophenyl)butyl, 1,1-dimethyl-2-(4-hexylthiophenyl)ethyl, 5-(2-methylthiophenyl)pentyl, 6-(3-methylthiophenyl)hexyl, 3,4-dimethylthiobenzyl and 2,4,6-trimethylthiobenzyl groups and the like.

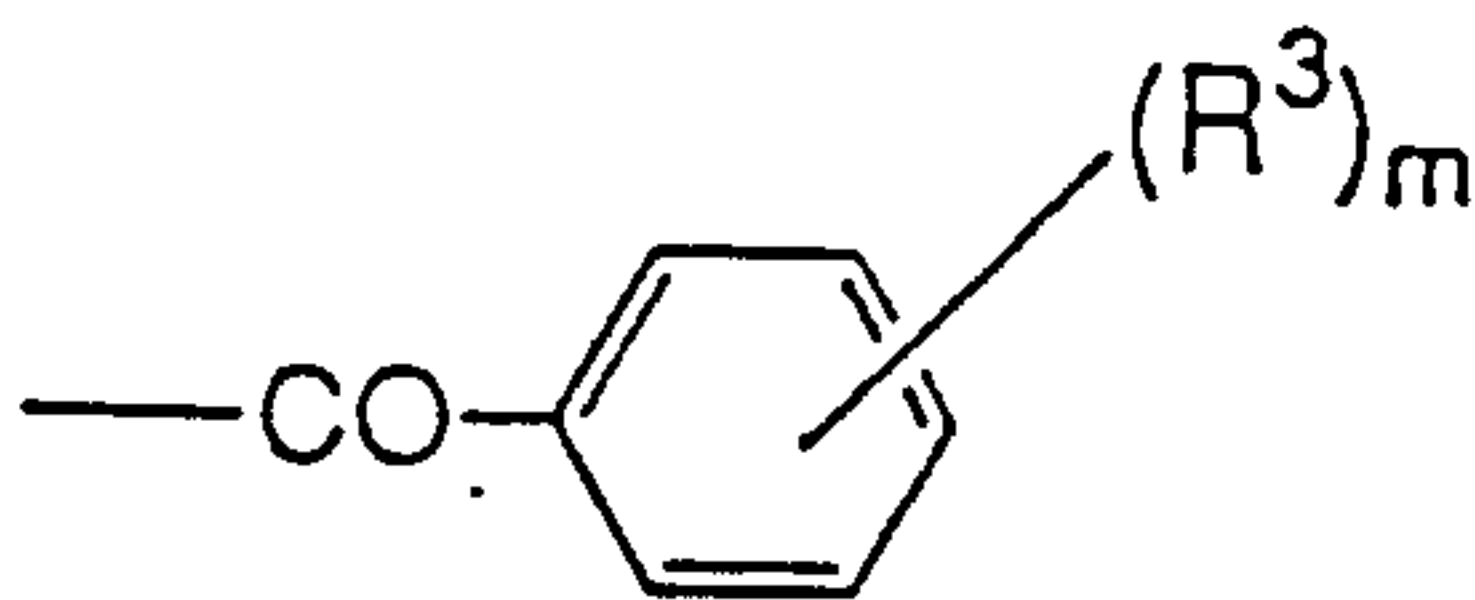
"Cycloalkyl group having phenyl group(s)" can be exemplified by the above-mentioned cycloalkyl groups which may each have phenyl ring(s), other than unsubstituted cycloalkyl groups.

The compounds of the present invention represented by general formula (1) can be produced by various processes. Preferable processes for production of said compounds include, for example, the followings.

5 [Reaction formula-1]

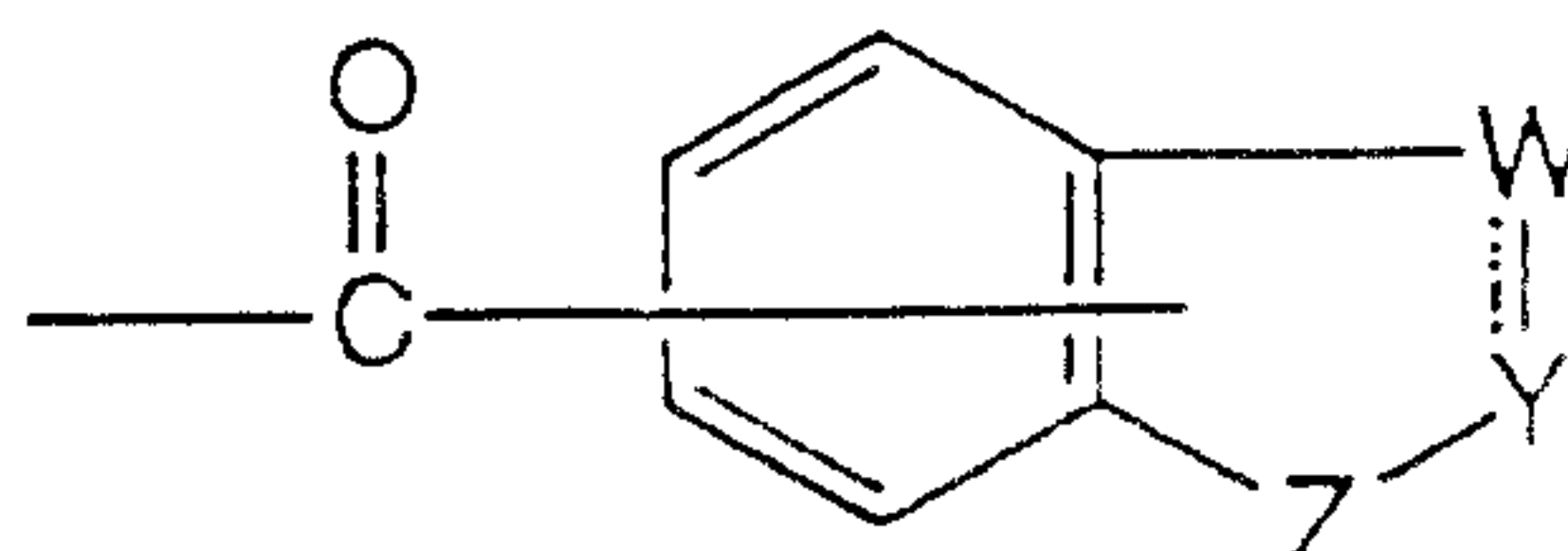


[wherein, Ra represents a group of the formula:



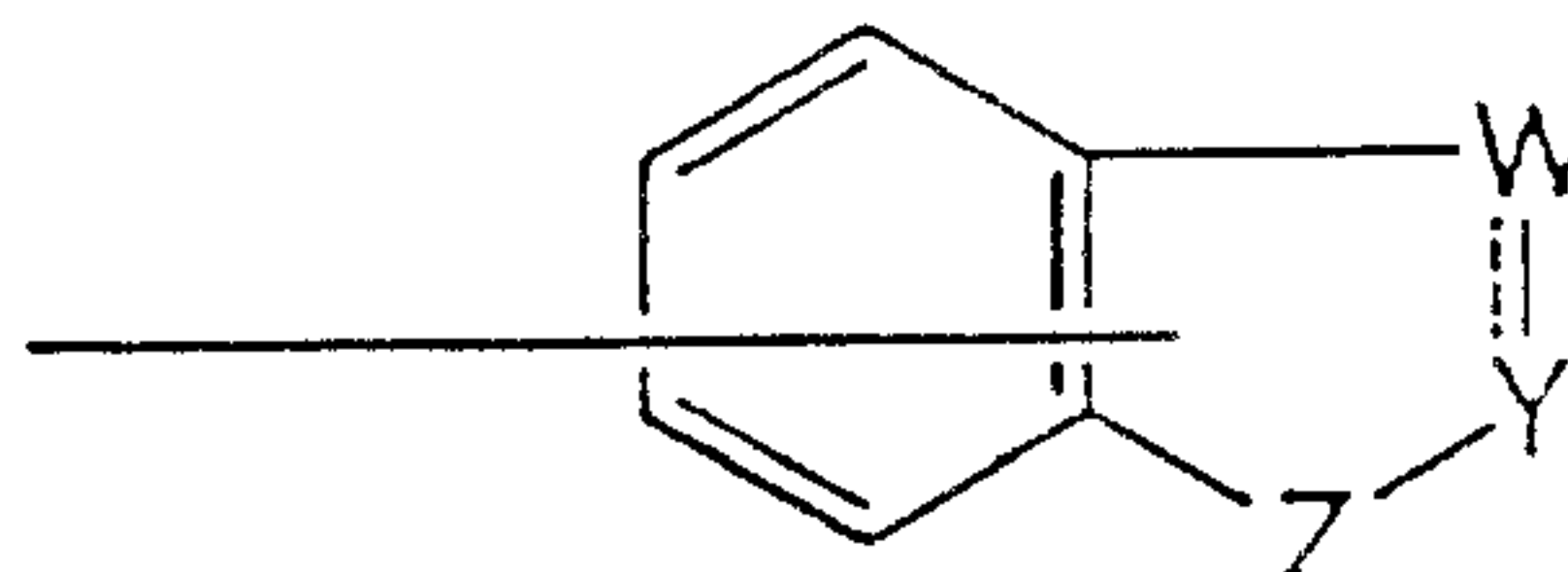
(wherein, R^3 and m are the same as defined above); a lower alkanoyl group which may have hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s) as substituent(s); a lower alkanoyl group having 1-3 halogen atoms; a lower alkoxycarbonyl group; a pyridyl-carbonyl group which may have, on the pyridine ring, substituent(s) selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, a aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxycarbonyl group, a

hydroxyl-substituted lower alkyl group, a phenyl group
 and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower
 alkanoyl group; a furoyl group which may have, on the
 furan ring, substituent(s) selected from the group
 5 consisting of a nitro group, a hydroxyl-substituted
 lower alkyl group, a lower alkanoyl group and an amino
 group which may have lower alkanoyl group(s) as
 substituent(s); a thienylcarbonyl group which may have,
 on the thiophene ring, substituent(s) selected from the
 10 group consisting of a nitro group, a lower alkyl group,
 a halogen atom and an amino group which may have lower
 alkanoyl group(s) as substituent(s); a fluorenylcarbonyl
 group which may have, on the fluorene ring, substi-
 tuent(s) selected from the group consisting of an oxo
 15 group and a nitro group; or a group of the formula



(wherein, Y, W, Z, the dotted line in the bond -W , and
 Y

the substituent(s) on the group of the formula:



are the same as mentioned above); and

20 R^1 and R^2 are the same as defined above].

The process shown by the above reaction

formula 1 is carried out by reacting a carboxylic acid derivative represented by general formula (2) or a compound obtained by activating the carboxyl group of said derivative, with an amine represented by general formula (3) or a compound obtained by activating the amino group of said amine, according to an ordinary amido-bond formation reaction. In the reaction, the known conditions used in amido-bond formation reaction can be employed easily. The process includes, for example, (a) a mixed acid anhydride process which comprises reacting a carbostyryl derivative (2) with an alkylhalocarboxylic acid to form a mixed acid anhydride and reacting the anhydride with an amine (3); (b) an active ester process which comprises converting a carbostyryl derivative (2) into an active ester such as p-nitrophenyl ester, N-hydroxysuccinimide ester, 1-hydroxybenzotriazole ester or the like and reacting the active ester with an amine (3); (c) a carbodiimide process which comprises subjecting a carbostyryl derivative (2) and an amine (3) to a condensation reaction in the presence of an activating agent such as dicyclohexylcarbodiimide, carbonyldiimidazole or the like; and (d) other processes. The other processes (d) include, for example, a process which comprises converting a carbostyryl derivative (2) into a carboxylic acid anhydride using a dehydrating agent such as acetic anhydride or the like and reacting the carboxylic acid anhydride with an amine (3); a process which comprises

reacting an ester of a carboxylic acid derivative (2)
and a lower alcohol with an amine (3) at a high pressure
at a high temperature; and a process which comprises
reacting an acid halide of a carboxylic acid derivative
5 (2), i.e. a carboxylic acid halide with an amine (3).
There may be also employed, for example, a process which
comprises activating a carboxylic acid derivative (2)
with a phosphorus compound such as triphenylphosphine,
diethyl cyanophosphonate, diethyl chlorophosphate, N,N-
10 bis(2-oxo-3-oxazolidinyl)phosphorodiamidic chloride,
diphenylphosphoramidate or the like and reacting the
resulting compound with an amine (3).

The mixed acid anhydride used in the mixed
acid anhydride process (a) can be obtained by an
15 ordinary Schotten-Baumann reaction. The anhydride is
reacted with an amine (3) generally without being
isolated, whereby a compound of general formula (1) can
be produced. The Schotten-Baumann reaction is conducted
in the presence or absence of a basic compound. The
20 basic compound is a compound conventionally used in the
Schotten-Baumann reaction and includes, for example,
organic bases such as triethylamine, trimethylamine,
pyridine, dimethylaniline, N-methylmorpholine, 4-
dimethylaminopyridine, 1,5-diazabicyclo[4.3.0]nonene-5
25 (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-
diazabicyclo[2.2.2]octane (DABCO) and the like, and
inorganic bases such as potassium carbonate, sodium
carbonate, potassium hydrogencarbonate, sodium

hydrogencarbonate and the like. The reaction is conducted generally at -20°C to 100°C , preferably at $0-50^{\circ}\text{C}$, and the reaction time is 5 minutes to 10 hours, preferably 5 minutes to 2 hours. The reaction of the

5 resulting mixed acid anhydride with an amine (3) is conducted generally at -20°C to 150°C , preferably at $10-50^{\circ}\text{C}$, and the reaction time is 5 minutes to 10 hours, preferably 5 minutes to 5 hours. The mixed acid

10 anhydride process (a) is conducted in an appropriate solvent or in the absence of any solvent. The solvent may be any solvent conventionally used in the mixed acid anhydride process, and can be exemplified by halogenated hydrocarbons such as methylene chloride, chloroform, dichloroethane and the like; aromatic hydrocarbons such

15 as benzene, toluene, xylene and the like; ethers such as diethyl ether, tetrahydrofuran, dimethoxyethane and the like; esters such as methyl acetate, ethyl acetate and the like; and aprotic polar solvents such as N,N-

20 dimethylformamide, dimethyl sulfoxide, hexamethylphosphoric triamide and the like. The alkylhalocarboxylic acid used in the mixed acid anhydride process (a) includes, for example, methyl chloroformate, methyl bromoformate, ethyl chloroformate, ethyl bromoformate and isobutyl chloroformate. The alkylhalocarboxylic

25 acid is used in an amount of generally at least 1 mole, preferably about 1-2 moles per mole of the carbostyryl derivative (2). The amine (3) is used in an amount of generally at least 1 mole, preferably about 1-2 moles

per mole of the carboxylic acid derivative (2).

The active ester process (b), when, for example, N-hydroxysuccinimide ester is used, is conducted in an appropriate solvent which does not adversely affect the reaction. Specific examples of the solvent are
5 halogenated hydrocarbons such as methylene chloride, chloroform, dichloroethane and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as diethyl ether, tetrahydrofuran,
10 dimethoxyethane and the like; esters such as methyl acetate, ethyl acetate and the like; and aprotic polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, hexamethylphosphoric triamide and the like. The reaction is conducted at 0-150°C, preferably at 10-
15 100°C and is complete in 5-30 hours. With respect to the desirable proportions of the amine (3) and the N-hydroxysuccinimide ester, the former is used in an amount of generally at least 1 mole, preferably 1-2 moles per mole of the latter.

20 The process which comprises reacting a carboxylic acid halide with an amine (3) [this is a process included in the other processes (d)], can be conducted in the presence of a dehydrohalogenating agent in an appropriate solvent. As the dehydrohalogenating
25 agent, an ordinary basic compound is used. The basic compound can be selected from various known basic compounds and can be exemplified by not only the basic compounds usable in the above Schotten-Baumann reaction

but also sodium hydroxide, potassium hydroxide, sodium hydride, potassium hydride, silver carbonate and alcoholates (e.g. sodium methylate and sodium ethylate). The solvent can be exemplified by the solvents usable in the mixed acid anhydride process (a), alcohols (e.g. methanol, ethanol, propanol, butanol, 3-methoxy-1-butanol, ethyl cellosolve and methyl cellosolve), water, pyridine, acetone, acetonitrile and mixtures thereof. The proportions of the amine (3) and the carboxylic acid halide used are not particularly restricted and can be appropriately selected from a wide range, but the carboxylic acid halide is used in an amount of generally at least about 1 mole, preferably about 1-2 moles per mole of the amine (3). The reaction is conducted generally at about -30°C to 180°C, preferably at about 0-150°C and is complete generally in about 5 minutes to 30 hours.

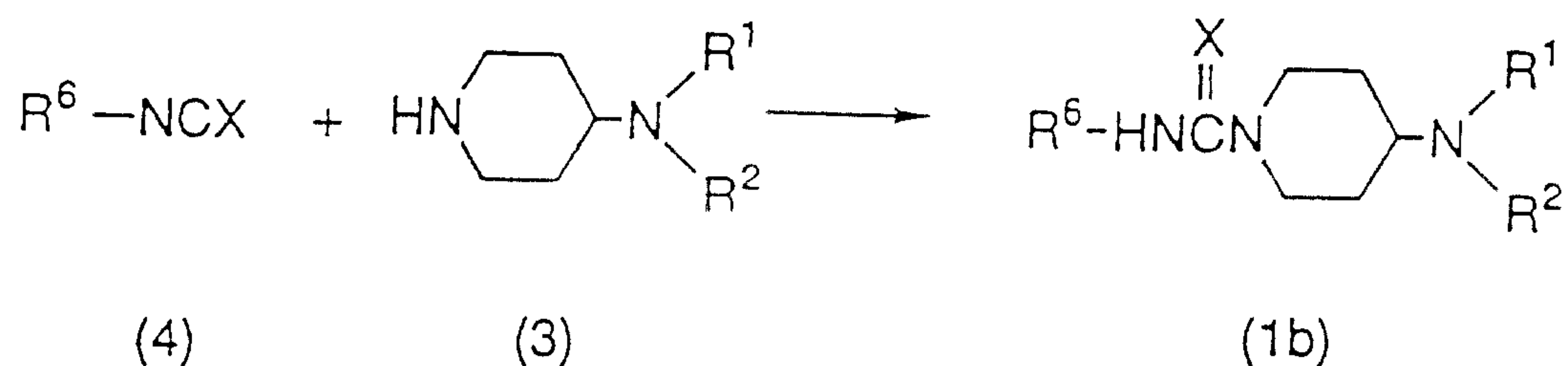
In the above process, the carboxylic acid halide can be produced, for example, by reacting a carboxylic acid derivative (2) with a halogenating agent in the presence or absence of a solvent. The solvent may be any solvent which does not adversely affect the reaction, and includes, for example, aromatic hydrocarbons (e.g. benzene, toluene and xylene), halogenated hydrocarbons (e.g. chloroform, methylene chloride and carbon tetrachloride), ethers (e.g. dioxane, tetrahydrofuran and diethyl ether), aprotic polar solvents (e.g. N,N-dimethylformamide and dimethyl sulfoxide) and

mixtures thereof. The halogenating agent may be an ordinary halogenating agent used for converting the hydroxyl group of carboxyl group into a halogen atom, and can be exemplified by thionyl chloride, phosphorus oxychloride, phosphorus oxybromide, phosphorus pentachloride and phosphorus pentabromide. The proportions of the carboxylic acid derivative (2) and the halogenating agent used are not particularly restricted and can be appropriately selected. The latter is used generally in large excess of the former when the reaction is conducted in the absence of any solvent, and in an amount of generally at least about 1 mole, preferably 2-4 moles per mole of the former when the reaction is conducted in a solvent. The reaction temperature and reaction time are not particularly restricted, either. However, the reaction temperature is generally about room temperature to 150°C, preferably room temperature to 100°C and the reaction time is about 10 minutes to 6 hours.

The process which comprises activating a carboxylic acid derivative (2) with a phosphorus compound such as triphenylphosphine, diethyl cyanophosphate, diethyl chlorophosphonate, N,N-bis(2-oxo-3-oxazolidinyl)phosphinic acid chloride, diphenyl phosphoryl azide or the like and reacting the resulting compound with an amine (3), can be conducted in an appropriate solvent. The solvent can be any solvent which does not adversely affect the reaction. Specific

examples thereof are halogenated hydrocarbons such as methylene chloride, chloroform, dichloroethane and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as diethyl ether, 5 tetrahydrofuran, dimethoxyethane and the like; esters such as methyl acetate, ethyl acetate and the like; and aprotic polar solvents such as N,N-dimethylformamide, dimethyl sulfoxide, hexamethylphosphoric triamide and the like. In the reaction, since the amine (3) acts 10 also as a basic compound, the use of the amine (3) in excess of the stoichiometric amount allows the reaction to proceed favorably. However, it is possible to use, as necessary, other basic compound, for example, an organic base (e.g. triethylamine, trimethylamine, 15 pyridine, dimethylaniline, N-methylmorpholine, DBN, DBU or DABCO) or an inorganic base (e.g. potassium carbonate, sodium carbonate, potassium hydrogencarbonate or sodium hydrogencarbonate). The reaction is conducted at about 0-150°C, preferably at about 0-100°C and is com- 20 plete in about 10 minutes to 30 hours. The phosphorus compound and the amine (3) are used each in an amount of generally at least about 1 mole, preferably 1-3 moles per mole of the carboxylic acid derivative (2).

[Reaction formula-2]

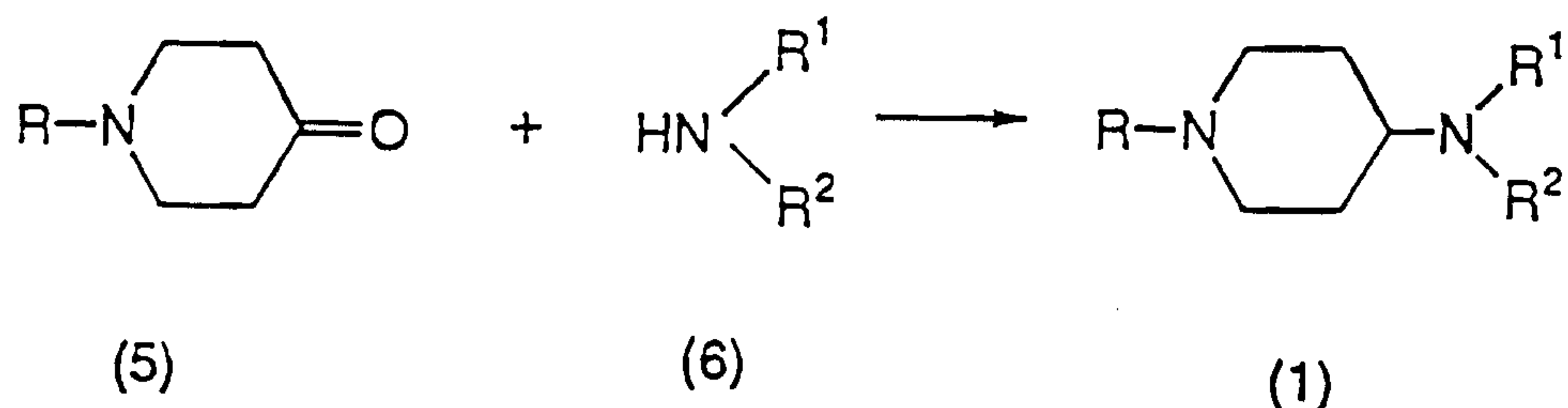


(wherein, R¹, R², R⁶ and X are the same as defined above).

The reaction of the compound (3) with the compound (4) is conducted in the presence or absence of a basic compound, preferably in the absence of any basic compound, in an appropriate solvent or in the absence of any solvent. The solvent and basic compound can each be any of those mentioned with respect to the Reaction formula-1 process for reacting a carboxylic acid halide with an amine (3).

The desirable amount of the compound (4) is generally about 1-15 moles, preferably about 1-10 moles per mole of the compound (3). The reaction is conducted generally at about 0-200°C, preferably at about room temperature to 150°C generally in about 5 minutes to 30 hours. In the reaction, a boron compound such as boron trifluoride-diethyl ether or the like may be added.

[Reaction formula-3]



(wherein, R, R¹ and R² are the same as defined above).

(a) The reaction of the compound of general formula (5) with the compound of general formula (6) is conducted in the absence of any solvent or in the presence of an appropriate solvent, in the presence or absence of a dehydrating agent. The solvent includes, for example, alcohols such as methanol, ethanol, isopropanol and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; halogenated hydrocarbons such as dichloromethane, dichloroethane, chloroform, carbon tetrachloride and the like; aprotic polar solvents such as N,N-dimethylformamide, N,N-dimethylacetamide, N-methylpyrrolidone and the like; and mixed solvents thereof. The dehydrating agent includes, for example, drying agents conventionally used for drying of solvents, such as molecular sieve and the like; mineral acids such as hydrochloric acid, sulfuric acid and the like; Lewis acids such as boron trifluoride and the like; and organic acids such as p-toluenesulfonic acid and the like. The reaction is conducted generally at room temperature to 250°C, preferably at about 50-200°C and is complete generally in about 1-48 hours.

The amount of the compound of general formula (6) used is not particularly restricted but desirably is generally at least equimolar, preferably equimolar to a large excess over the compound of general formula (5).

5 The desirable amount of the dehydrating agent used is generally a large excess when a drying agent is used, and is a catalytic amount when an acid is used.

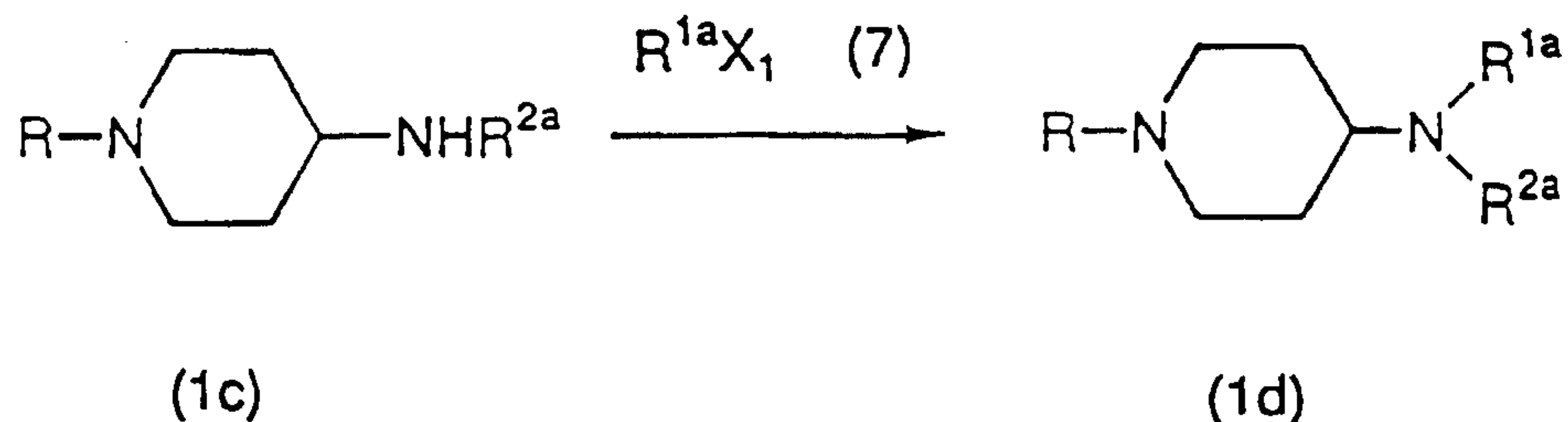
The above reaction produces a Schiff base as an intermediate. The intermediate is reduced to convert
10 to a desired compound (1). Various methods can be employed for this reduction and, for example, a method using a hydride as a reducing agent is preferably used. The hydride includes, for example, lithium aluminum hydride, sodium boron hydride and diborane. The amount
15 of the hydride used is generally at least 1 mole, preferably 1-15 moles per mole of the compound (5). The reduction is conducted generally using an appropriate solvent such as water, lower alcohol (e.g. methanol, ethanol or isopropanol), ether (e.g. tetrahydrofuran,
20 diethyl ether or diglyme) or the like generally at about -60°C to 50°C, preferably at -30°C to room temperature for about 10 minutes to 15 hours. When lithium aluminum hydride or diborane is used as a reducing agent, it is preferable to use an anhydrous solvent such as diethyl
25 ether, tetrahydrofuran, diglyme or the like.

(b) When the above reaction of the compound (5) with the compound (6) is conducted in the absence of any solvent or in the presence of an appropriate solvent

in the presence of a reducing agent, a compound (1) can be obtained in one step. The solvent can be exemplified by water; alcohols such as methanol, ethanol, isopropanol and the like; acetic acid; ethers such as dioxane, tetrahydrofuran, diethyl ether, diglyme and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; and mixed solvents thereof. The reaction can be conducted by, for example, a process using formic acid or a hydride reducing agent such as sodium borohydride, sodium cyanoborohydride, lithium aluminum hydride or the like, and a catalytic reduction process using a catalytic reduction catalyst such as palladium black, palladium carbon, platinum oxide, platinum black, platinum carbon, Raney nickel or the like. When formic acid is used as the reducing agent, the reaction is conducted generally at about room temperature to 200°C, preferably at about 50-150°C and is complete in about 1-10 hours. The desirable amount of formic acid used is a large excess over the compound of general formula (5). When a hydride reducing agent is used, the reaction is conducted generally at about -30°C to 100°C, preferably at about 0-70°C and is complete in about 30 minutes to 12 hours. The desirable amount of the reducing agent used is generally 1-20 moles, preferably 1-5 moles per mole of the compound of general formula (5). When lithium aluminum hydride is used as the reducing agent, it is preferable to use, as the solvent, for example, an ether (e.g. dioxane,

tetrahydrofuran, diethyl ether or diglyme) or an aromatic hydrocarbon (e.g. benzene, toluene or xylene). When a catalytic reduction catalyst is used, the reaction is conducted in a hydrogen atmosphere of generally normal pressure to 20 atm., preferably normal pressure to 10 atm. generally at -30°C to 100°C, preferably at 0-60°C. The desirable amount of the catalyst used is generally 0.1-40% by weight, preferably 0.1-20% by weight based on the compound of general formula (5). The amount of the compound (5) used is not particularly restricted and can be appropriately selected from a wide range, but desirably is generally at least equimolar to the compound of general formula (6), preferably equimolar to a large excess over the compound (6).

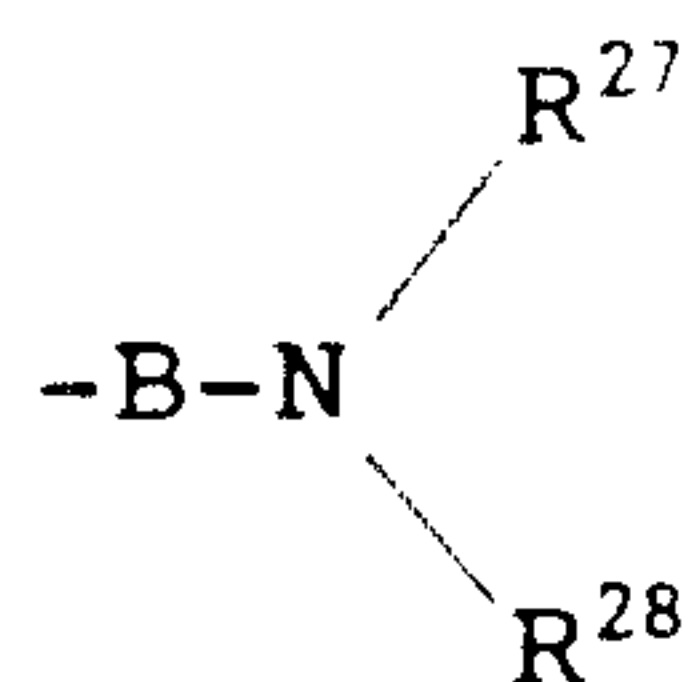
[Reaction formula-4]



[wherein, R is the same as defined above;

R^{2a} represents a hydrogen atom; a lower alkyl group which may have hydroxyl group(s) as substituent(s); a
 5 phenyl-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower
 10 alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy-substituted lower alkoxy group and an amino group which may have, as substituent(s), lower alkanoyl group(s), lower alkoxy-
 15 carbonyl group(s), or aminocarbonyl group(s) which may each have lower alkyl group(s) as substituent(s), which phenyl-lower alkyl group may have lower alkoxycarbonyl group(s) or hydroxyl-substituted lower alkyl group(s) as substituent(s) in the lower alkyl moiety; a phenoxy-
 20 lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom,

a nitro group, a hydroxyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring; a
 5 thienyl-lower alkyl group; a furyl-lower alkyl group; a group of the formula:



10 (wherein, B, R²⁷ and R²⁸ are the same as defined above); a phthalimido-substituted lower alkyl group; a cycloalkyl-lower alkyl group; a phenyl-lower alkenyl group; a cycloalkyl group which may have a phenyl group as a substituent; or a 2,3-dihydro-1H-indenyl group
 15 which may have, on the 2,3-dihydro-1H-indene ring, substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s);

R^{1a} represents the above-mentioned R^{2a} other
 20 than hydrogen atom; and

X¹ represents a halogen atom, a lower-alkanesulfonyloxy group, an arylsulfonyloxy group or an aralkylsulfonyloxy group, provided that, when R^{2a} is the same as defined above, except a hydrogen atom and a
 25 lower alkyl group which may have hydroxyl group(s) as substituent(s), then R^{1a} should be a lower alkyl group which may have hydroxyl group(s) as substituent(s); further, when R^{2a} is a hydrogen atom or a lower alkyl

group which may have hydroxyl group(s) as substituent(s), then R^{1a} should be the same as defined above, except a lower alkyl group which may have hydroxyl group(s) as substituent(s)].

5 In the compound represented by the above
general formula (7), specific examples of the halogen
atom represented by X¹ are chlorine, fluorine, bromine
and iodine atoms; specific examples of the lower alkane-
sulfonyloxy group are methanesulfonyloxy, ethane-
10 sulfonyloxy, propanesulfonyloxy, isopropanesulfonyloxy,
butanesulfonyloxy, tert-butanesulfonyloxy, pentane-
sulfonyloxy and hexanesulfonyloxy; specific examples of
the arylsulfonyloxy group are substituted or unsubsti-
tuted arylsulfonyloxy groups such as phenylsulfonyloxy,
15 4-methylphenylsulfonyloxy, 2-methylphenylsulfonyloxy, 4-
nitrophenylsulfonyloxy, 4-methoxyphenylsulfonyloxy, 3-
chlorophenylsulfonyloxy, α -naphthylsulfonyloxy and the
like; and specific examples of the aralkylsulfonyloxy
group are substituted or unsubstituted aralkyl-
20 sulfonyloxy groups such as benzylsulfonyloxy, 2-
phenylethylsulfonyloxy, 4-phenylbutylsulfonyloxy, 4-
methylbenzylsulfonyloxy, 2-methylbenzylsulfonyloxy, 4-
nitrobenzylsulfonyloxy, 4-methoxybenzylsulfonyloxy, 3-
chlorobenzylsulfonyloxy, α -naphthylmethylsulfonyloxy and
25 the like.

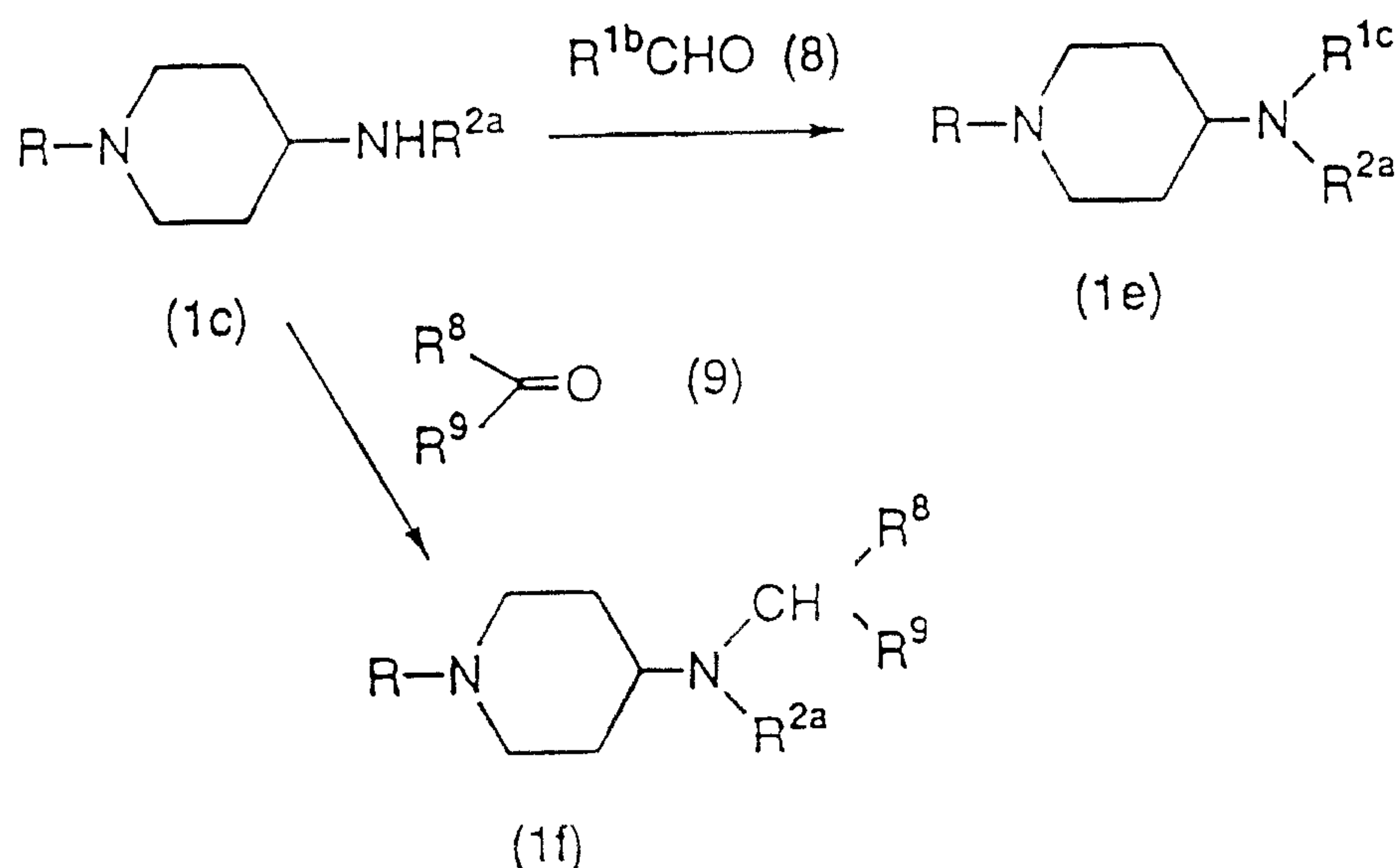
The reaction of the compound of general
formula (1c) with the compound of general formula (7) is
conducted generally in an appropriate inert solvent, in

the presence or absence of a basic compound. The inert solvent can be exemplified by aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as tetrahydrofuran, dioxane, diethylene glycol dimethyl ether and the like; lower alcohols such as methanol, ethanol, isopropanol, butanol and the like; acetic acid; ethyl acetate; acetone; acetonitrile; dimethyl sulf-oxide; N,N-dimethylformamide; hexamethylphosphoric triamide; and the like. The basic compound can be exemplified by alkali metal carbonates such as sodium carbonate, potassium carbonate, sodium hydrogen-carbonate, potassium hydrogencarbonate and the like; alkali metal hydroxides such as sodium hydroxide, potassium hydroxide and the like; sodium hydride; potassium; sodium; sodium amide; metal alcholates such as sodium methyllate, sodium ethyllate and the like; and organic bases such as pyridine, diisopropylethylamine, dimethylaminopyridine, triethylamine, 1,5-diazabicyclo-[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO) and the like. The proportions of the compound of general formula (1c) and the compound of general formula (7) used are not particularly restricted and can be appropriately selected from a wide range, but it is desirable to use the latter compound in an amount of at least about 1 mole, preferably about 1-5 moles per mole of the former. The reaction is conducted generally at about 0-200°C, preferably at about 0-170°C and is complete

generally in about 30 minutes to 30 hours.

An alkali metal halide such as sodium iodide, potassium iodide or the like may be added to the reaction system.

[Reaction formula-5]



[wherein, R and R^{2a} are the same as defined above;

R^{1b} represents a phenyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxy carbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy-substituted lower alkoxy group and an amino group which may have, as substituent(s), lower alkanoyl group(s), lower alkoxy carbonyl group(s) or aminocarbonyl group(s) which may each have lower alkyl group(s) as substituent(s); a pyridyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring; a thienyl group; a furyl group; a phthalimido group; a

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cycloalkyl group; or the above-mentioned R^{2a} group other than hydrogen atom, 2,3-dihydro-1H-indenyl group which may have, on the 2,3-dihydro-1H-indene ring, substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s) as substituent(s), a phenyl-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy group-substituted lower alkoxy group and an amino group which may have substituent(s) selected from the group consisting of a lower alkanoyl group, a lower alkoxy-carbonyl group and aminocarbonyl group(s) which may each have lower alkyl group(s) as substituent(s), which phenyl-lower alkyl group has lower alkoxycarbonyl group(s) or hydroxyl group-substituted lower alkyl group(s) as substituent(s) in the lower alkyl moiety, and cycloalkyl group which may have phenyl group(s) as substituent(s);

25 R^{1c} represents -CH₂-R^{1b};

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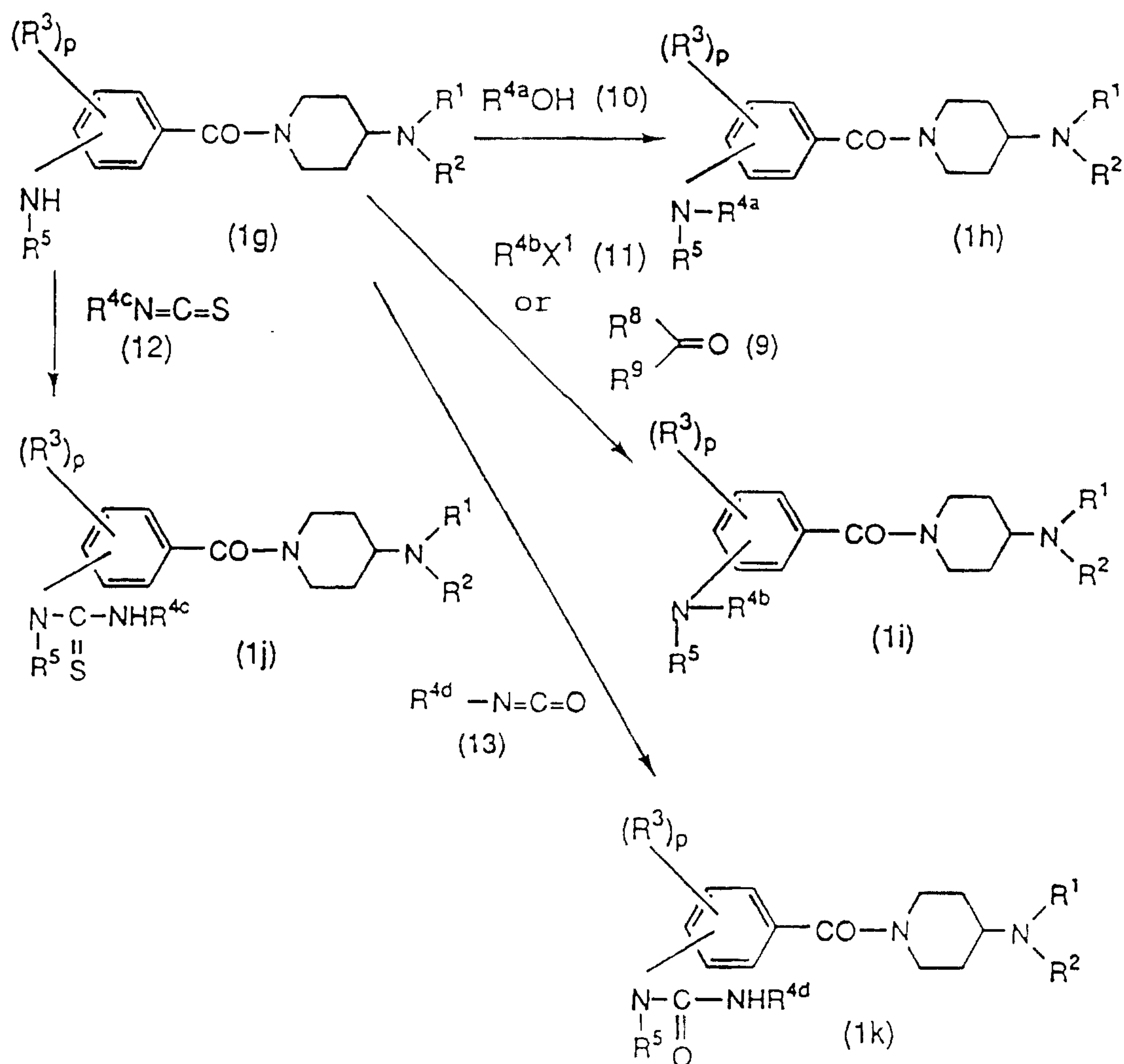
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R^8 and R^9 independently represent a hydrogen atom or a lower alkyl group provided that, in compound (1e), R^{2a} is a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituent(s), further, 5 in compound (1f), R^{2a} is the same as defined above, except both a hydrogen atom and a lower alkyl group which may have hydroxyl group(s) as substituent(s)].

The reaction of the compound (1c) with the

compound (8) can be conducted under the same conditions as used in the reaction of the compound (5) with the compound (6) by the process (a) in the reaction formula-3. The reaction of the compound (1c) with the compound
5 (9) can be conducted under the same conditions as used in the reaction of the compound (5) with the compound (6) by the process (b) in the Reaction formula-3.

[Reaction formula-6]



[wherein, R^1 , R^2 , R^3 , R^5 , R^8 , R^9 and X^1 are the same as defined above; p is an integer of 1-2; R^{4a} represents a lower alkanoyl group, a lower alkanoyl group having 1-3 halogen atoms as substituent(s), a benzoyl group, a pyridylcarbonyl group or a lower alkenylcarbonyl group; R^{4b} represents a lower alkyl group; R^{4c} represents a phenyl group or a lower alkyl group; and R^{4d} represents a lower alkyl group, a phenyl group or a lower alkenyl group].

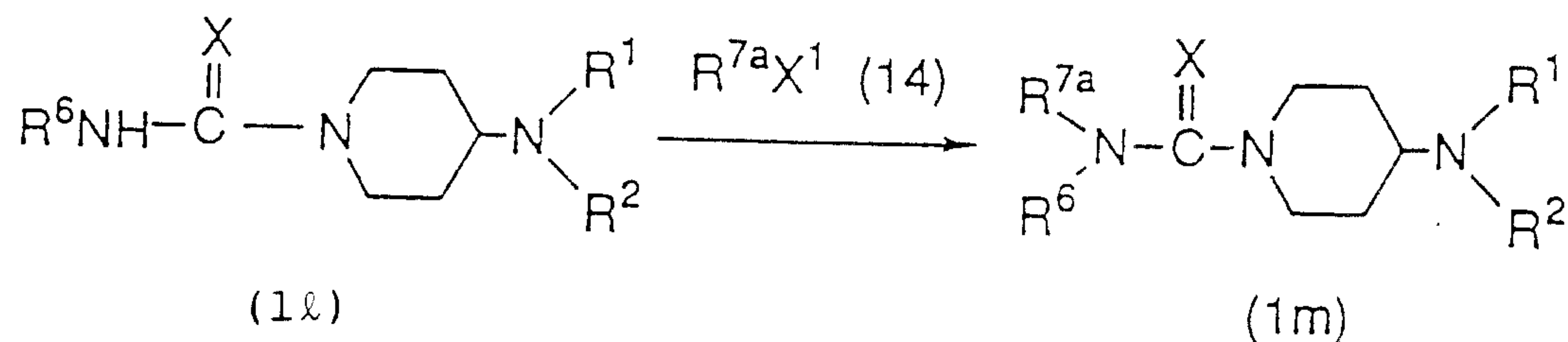
The reaction of the compound (1g) with the compound (10) can be conducted under the same conditions as used in the reaction of the compound (2) with the compound (3) in the Reaction formula-1.

5 The reaction of the compound (1g) with the compound (11) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the Reaction formula-4.

10 The reaction of the compound (1g) with the compound (9) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (9) in the Reaction formula-5.

15 The reaction of the compound (1g) with the compound (12) or the compound (13) can be conducted under the same conditions as used in the reaction of the compound (4) with the compound (3) in the Reaction formula-2.

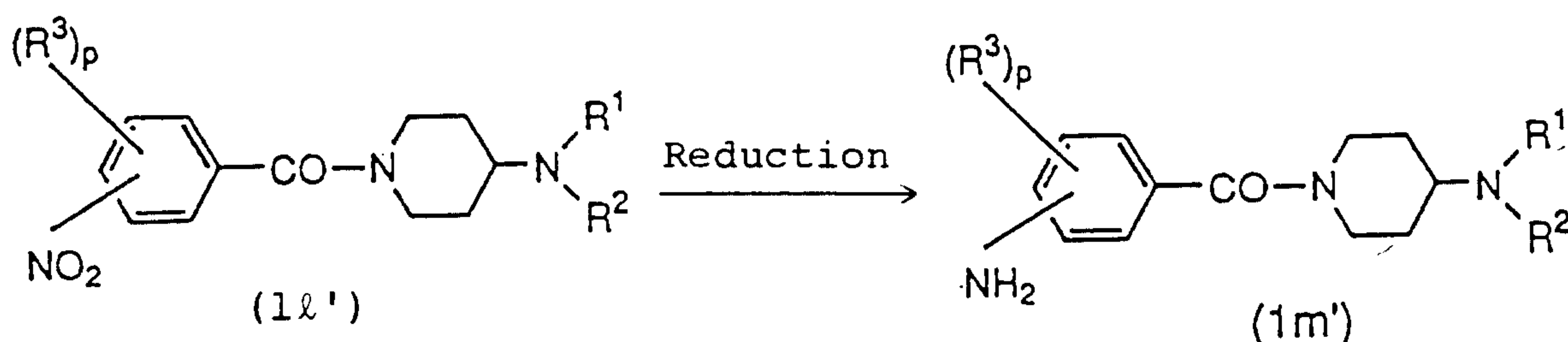
[Reaction formula-7]



(wherein R^1 , R^2 , R^6 , X and X^1 are the same as defined above; and R^{7a} represents a lower alkyl group).

The reaction of the compound (1l) with the
 5 compound (14) can be conducted under the same conditions
 as used in the reaction of the compound (1c) with the
 compound (7) in the Reaction formula-4.

[Reaction formula-8]



(wherein, R^1 , R^2 , R^3 and p are the same as defined above).

The reduction of the compound (1l') is conducted, for example, (1) using a catalytic reduction catalyst in an appropriate solvent, or (2) using, as a reducing agent, a mixture between a metal or a metal salt and an acid, or between a metal or a metal salt and an alkali metal hydroxide, a sulfide, an ammonium salt or the like in an appropriate inert solvent.

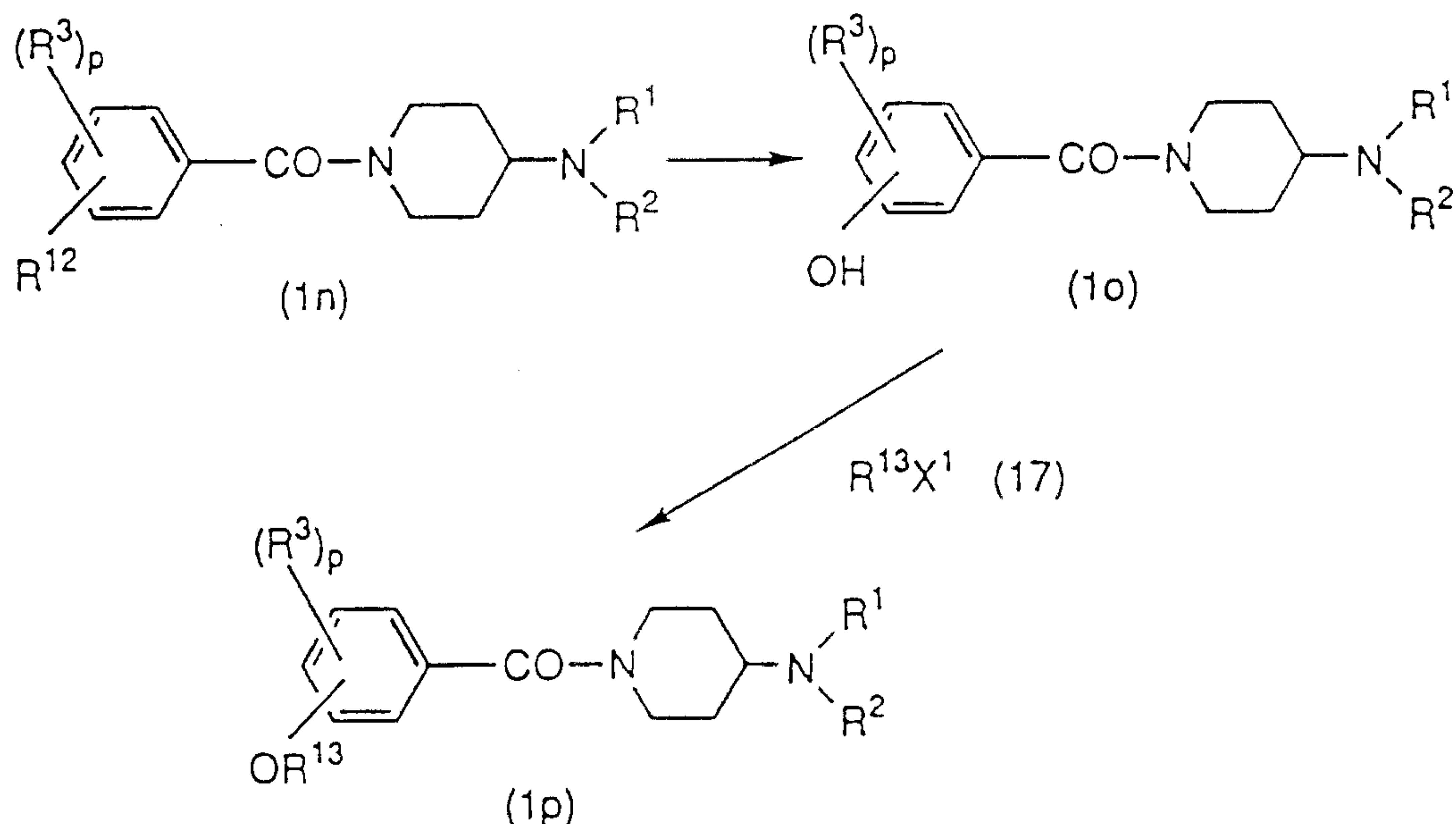
(1) When the reduction is conducted by the above method using a catalytic reduction catalyst in an appropriate solvent, the solvent includes, water; acetic acid; alcohols such as methanol, ethanol, isopropanol and the like; hydrocarbons such as hexane, cyclohexane and the like; halogenated hydrocarbons such as methylene chloride, chloroform, carbon tetrachloride and the like; ethers such as dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether and the like; esters such as ethyl acetate, methyl acetate and the like; aprotic polar solvents such as N,N-dimethylformamide and the like; and mixed solvents thereof. The catalytic

reduction catalyst includes, for example, palladium, palladium hydroxide carbon, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite and Raney nickel. The desirable amount of the catalyst used
5 is generally about 0.02-1 time the amount of the starting material. The reaction temperature is generally about -20°C to 150°C, preferably about 0-100°C, and the hydrogen pressure is generally 1-10 atm. The reaction is complete generally in about 0.5-24 hours. An acid
10 such as hydrochloric acid or the like may be added in the reaction.

(2) When the reduction is conducted by the above method using a reducing agent in an appropriate inert solvent, the reducing agent includes, for example,
15 a mixture between iron, zinc, tin or stannous chloride and an acid (e.g. hydrochloric acid or sulfuric acid), and a mixture between iron, ferrous sulfate, zinc or tin and an alkali metal hydroxide (e.g. sodium hydroxide), a sulfide (e.g. ammonium sulfide), ammonia water or an
20 ammonium salt (e.g. ammonium chloride). The solvent can be exemplified by water, acetic acid, methanol, ethanol and dioxane. The conditions for reduction can be appropriately selected depending upon the type of the reducing agent used. For example, when a mixture of
25 stannous chloride and hydrochloric acid is used as a reducing agent, the reaction can be conducted favorably by employing a reaction temperature of about 0°C to 100°C and a reaction time of about 0.5-10 hours. The reducing

agent is used in an amount of at least 1 mole, generally 1-5 moles per mole of the starting material compound.

[Reaction formula-9]



(wherein, R^1 , R^2 , R^3 , X^1 and p are the same as defined above; R^{12} represents a lower alkoxy group, a phenyl-lower alkoxy group or a lower alkanoyl group; and R^{13} represents a lower alkyl group, a phenyl-lower alkyl group, a lower alkanoyl group, an amino-lower alkyl group which may have lower alkyl group(s) as substituent(s), or a morpholinyl-substituted lower alkyl group).

The reaction for converting a compound (1n) wherein R^{12} is a lower alkoxy group, into a compound (1o), can be conducted by heat-treating the compound (1n) at 30-150°C, preferably at 50-120°C in a mixture of an acid (e.g. hydrobromic acid or hydrochloric acid) and a solvent (e.g. water, methanol, ethanol, isopropyl alcohol or acetic acid). Alternatively, the reaction

can be conducted by hydrolyzing the compound (1n). The hydrolysis is conducted in the presence of an appropriate solvent in the presence of an acid. The solvent includes, for example, water; lower alcohols such as methanol, ethanol, isopropyl alcohol and the like; ethers such as dioxane, tetrahydrofuran and the like; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride and the like; polar solvents such as acetonitrile and the like; and mixed solvents thereof. The acid includes, for example, mineral acids such as hydrochloric acid, sulfuric acid, hydrobromic acid and the like; Lewis acids such as boron trifluoride, aluminum chloride, boron trifluoride and the like; iodides such as sodium iodide, potassium iodide and the like; and mixtures between said Lewis acid and said iodide. The reaction proceeds favorably generally at room temperature to 150°C, preferably at room temperature to 100°C and is complete generally in about 0.5-15 hours.

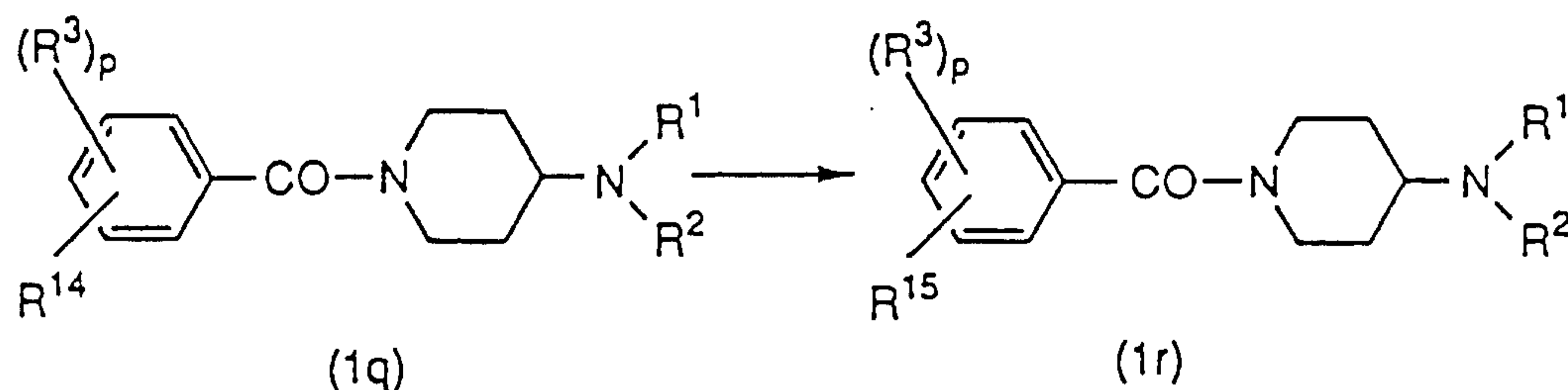
The reaction for converting a compound (1n) wherein R^{12} is a phenyl-lower alkoxy group, into a compound (1o), can be conducted under the same conditions as used in the reaction of the compound (5) with the compound (6) by the process (b) (the catalytic reduction process using a catalytic reduction catalyst) in the reaction formula-3.

The reaction for converting a compound (1n) wherein R^{12} is a lower alkanoyloxy group, into a compound

(10), can be conducted under the same conditions as used in the below-mentioned hydrolysis of a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one lower-alkoxycarbonyl group as
5 a substituent on the phenyl ring.

The reaction of the compound (10) with the compound (17) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the Reaction formula-4.

[Reaction formula-10]



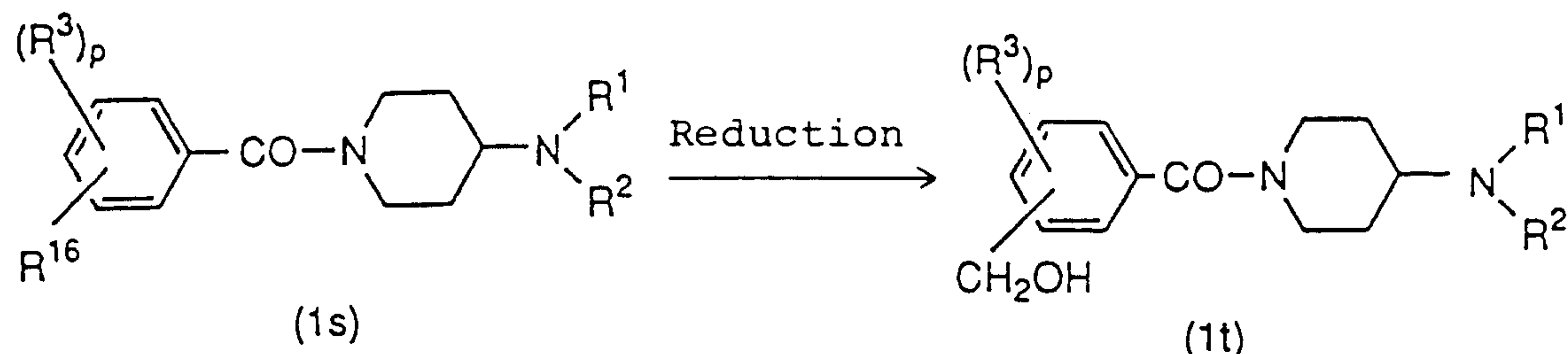
(wherein, R^1 , R^2 , R^3 and p are the same as defined above; R^{14} represents a lower alkylthio-lower alkyl group; and R^{15} represents a lower alkylsulfonyl-lower alkyl group).

5 The reaction for converting a compound (1q) into a compound (1r) is conducted in an appropriate solvent in the presence of an oxidizing agent. The solvent can be exemplified by water, organic acids such as formic acid, acetic acid, trifluoroacetic acid and
10 the like; alcohols such as methanol, ethanol, isopropyl alcohol and the like; halogenated hydrocarbons such as chloroform, dichloromethane and the like; and mixed solvents thereof. The oxidizing agent includes, for example, peracids such as performic acid, peracetic
15 acid, trifluoroperacetic acid, perbenzoic acid, m-chloroperbenzoic acid, o-carboxyperbenzoic acid and the like; hydrogen peroxide; sodium metaperiodate; bichromic acid; bichromates such as sodium bichromate, potassium bichromate and the like; permanganic acid; permanganates
20 such as potassium permanganate, sodium permanganate and the like; and lead salts such as lead tetracetate and

- 80 -

the like. The oxidizing agent is used in an amount of generally at least 2 moles, preferably 2-4 moles per mole of the starting material. The reaction is conducted generally at about 0-40°C, preferably at about 0°C
5 to room temperature and is complete in about 1-15 hours.

[Reaction formula-11]

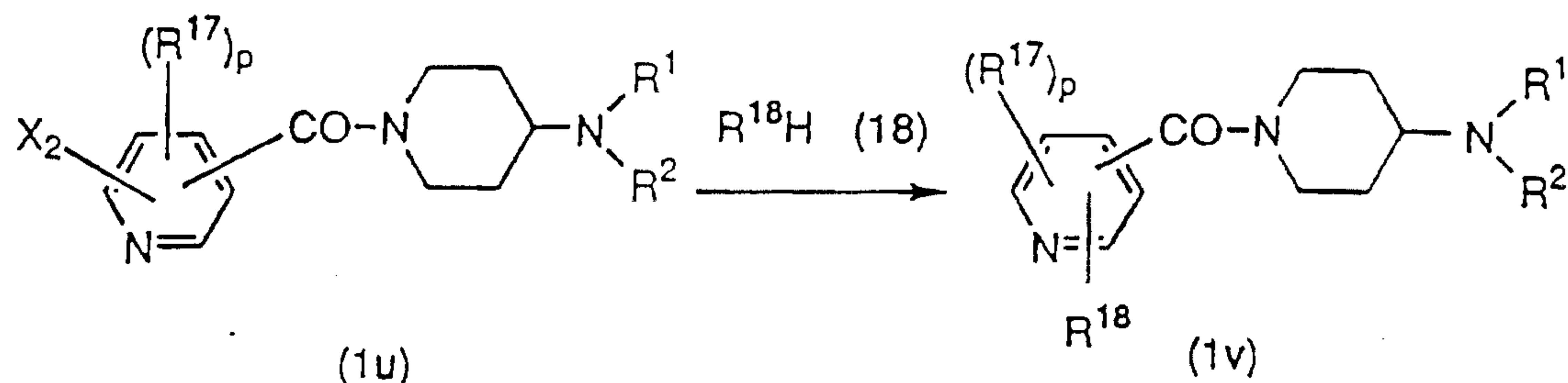


(wherein, R^1 , R^2 , R^3 and p are the same as defined above; and R^{16} represents a lower alkoxy carbonyl group).

The reduction of the compound (1s) is

- 5 preferably conducted using a hydride reducing agent. The hydride reducing agent includes, for example, lithium aluminum hydride, sodium borohydride and diborane. The amount of the hydride reducing agent used is at least 1 mole, preferably 1-15 moles per mole of
- 10 the starting material. The reduction is conducted generally in an appropriate solvent, for example, water, a lower alcohol (e.g. methanol, ethanol, isopropanol or tert-butanol), an ether (e.g. tetrahydrofuran, diethyl ether, diisopropyl ether or diglyme), or a mixed solvent
- 15 thereof, generally at about -60°C to 150°C , preferably at about -30°C to 100°C for about 10 minutes to 5 hours.
- When the reducing agent is lithium aluminum hydride or diborane, it is preferable to use an anhydrous solvent such as tetrahydrofuran, diethyl ether, diisopropyl
- 20 ether, diglyme or the like.

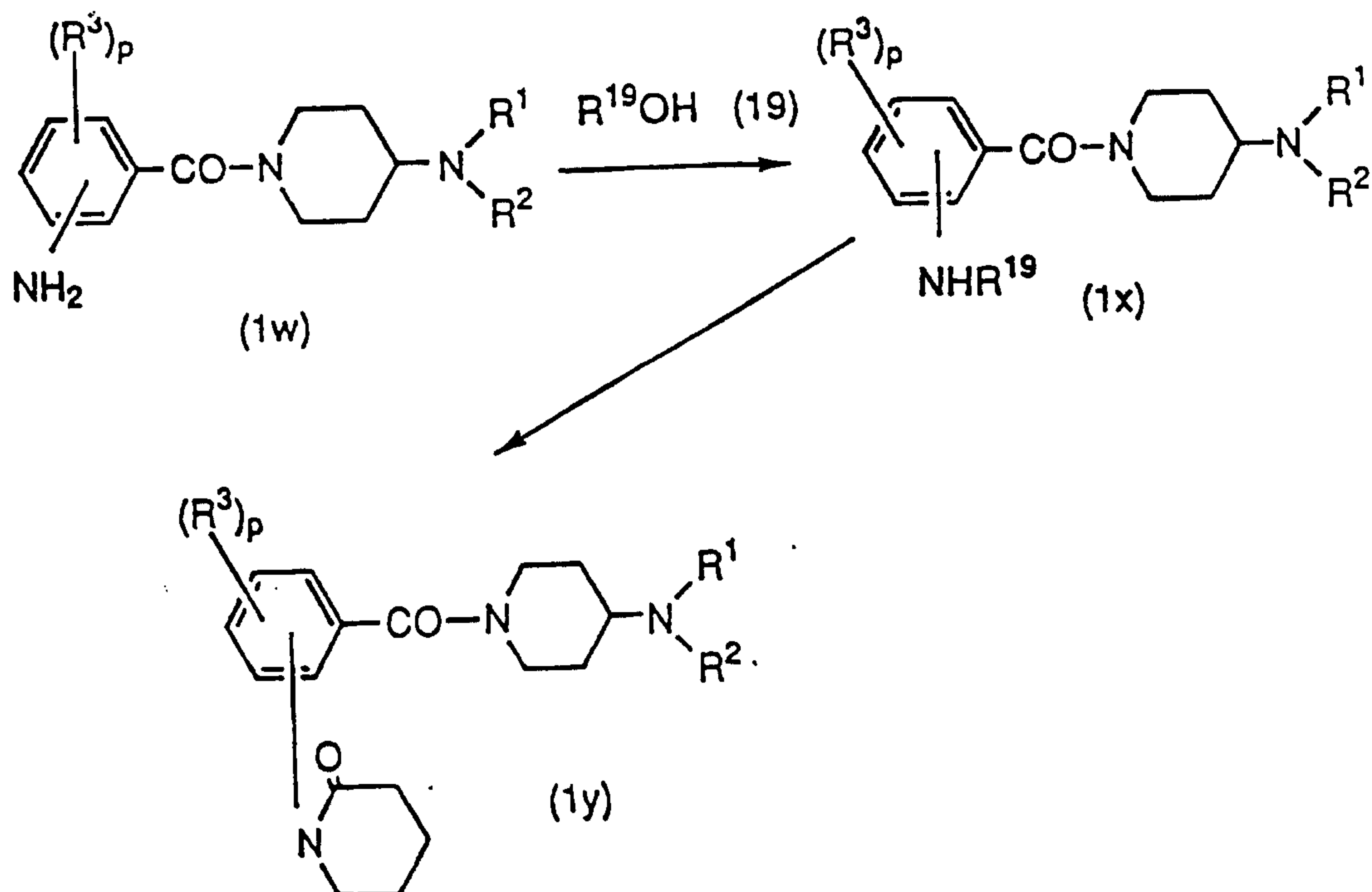
[Reaction formula-12]



[wherein, R^1 , R^2 and p are the same as defined above; R^{17} represents a hydrogen atom, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxy carbonyl group, a hydroxyl-substituted lower alkyl group, a phenyl group or a 1,2,4-triazolyl group; R^{18} represents an amino group which may have lower alkanoyl group(s) as substituent(s), a pyrrolyl group or a 1,2,4-triazolyl group; and X_2 represents a halogen atom].

The reaction of the compound (1u) with the compound (18) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the Reaction formula-4.

[Reaction formula-13]



(wherein, R^1 , R^2 , R^3 and p are the same as defined above; and R^{19} represents a lower alkanoyl group having 1-3 halogen atoms).

5 The reaction of the compound (1w) with the compound (19) can be conducted under the same conditions as used in the reaction of the compound (2) with the compound (3) in the Reaction formula-1.

10 The reaction for converting a compound (1x) into a compound (1y) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the Reaction formula-4.

A compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one amino group on the phenyl ring, can be converted, by reacting with a compound of general formula (15):



(wherein, R^{10} represents a lower alkanoyl group or a lower alkoxycarbonyl group) or with a compound of general formula (16):



10 (wherein, R^{11} represents a lower alkyl group), into a compound of general formula (1) wherein R^1 or R^2 is a phenyl-lower alkyl group having, on the phenyl ring, at least one amino group having lower alkanoyl group(s), lower alkoxycarbonyl group(s) or aminocarbonyl group(s)
15 each having lower alkyl group(s).

The reaction of the starting material with the compound (15) can be conducted under the same conditions as used in the reaction of the compound (2) with the compound (3) in the Reaction formula-1. The reaction of
20 the starting material with the compound (16) can be conducted under the same conditions as used in the reaction of the compound (4) with the compound (3) in the reaction formula-2.

A compound of general formula (1) wherein R^2
25 is a phenyl-lower alkyl group having at least one lower alkoxy group on the phenyl ring, or R^2 form a heterocyclic ring having at least one lower alkoxy group on

the heterocyclic ring, or R^2 is a phenoxy-lower alkyl group having at least one lower alkoxy group on the phenyl ring, can be converted, by dealkylation, into a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one hydroxyl group on the phenyl ring, or R^2 form a heterocyclic ring having at least one hydroxyl group on the heterocyclic ring, or R^1 or R^2 is a phenoxy-lower alkyl group having at least one hydroxyl group on the phenyl ring. Said dealkylating reaction can be carried out under the same condition being employed in Reaction formula-9 for obtaining a compound (1o) from a compound (1m).

A compound of general formula (1) wherein R^1 or R^2 is a phenyl-lower alkyl group having at least one hydroxyl group on the phenyl ring, or R^1 and R^2 form a heterocyclic ring having at least one hydroxyl group on the heterocyclic ring, or R^2 is a phenoxy-lower alkyl group having at least one hydroxyl group on the phenyl ring, can be converted, by reacting with a compound of general formula (20):



(wherein, R^{20} represents a lower alkyl group and X^2 is the same as defined above), into a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one lower alkoxy group on the phenyl ring, or R^1 and R^2 form a heterocyclic ring having at least one lower alkoxy group on the heterocyclic ring,

or R^2 is a phenoxy-lower alkyl group having at least one lower alkoxy group on the phenyl ring.

The reaction can be conducted under the same conditions as used in the reaction of the compound (10) with the compound (17) in the Reaction formula-9.

A compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one nitro group on the phenyl ring, or R is a pyridylcarbonyl group having at least one nitro group on the pyridine ring, can be converted, by reduction, into a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one amino group on the phenyl ring, or R is a pyridylcarbonyl group having at least one amino group on the pyridine ring.

The reduction can be conducted under the same conditions as used in the reduction of the compound (10') in the Reaction formula-8.

A compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one lower alkoxy carbonyl group on the phenyl ring, can be converted, by hydrolysis, into a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one carboxy group on the phenyl ring.

The hydrolysis can be carried out in an appropriate solvent or in the absence of any solvent, in the presence of an acid or a basic compound. The solvent includes, for example, water; lower alcohols

such as methanol, ethanol, isopropanol and the like; ketones such as acetone, methyl ethyl ketone and the like; ethers such as dioxane, tetrahydrofuran, ethylene glycol dimethyl ether and the like; fatty acids such as formic acid, acetic acid and the like; and mixed solvents thereof. The acid includes, for example, mineral acids such as hydrochloric acid, sulfuric acid, hydrobromic acid and the like; and organic acids such as formic acid, acetic acid, aromatic sulfonic acid and the like. The basic compound includes, for example, metal carbonates such as sodium carbonate, potassium carbonate and the like; and metal hydroxides such as sodium hydroxide, potassium hydroxide, calcium hydroxide and the like. The reaction proceeds favorably generally at about room temperature to 200°C, preferably at about room temperature to 150°C and is complete generally in about 0.5-25 hours.

In a compound (1), wherein R^1 or R^2 is a phenyl-lower alkyl group having at least one lower alkoxy-carbonyl group as substituent on the phenyl ring, such compound can be prepared by esterifying a starting compound (1), wherein R^1 or R^2 is a phenyl-lower alkyl group having at least one carboxyl group on the phenyl-ring.

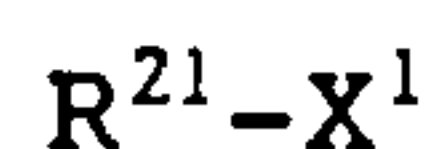
Said esterification can be conducted by reacting the starting compound (1), in the presence of a mineral acid for example hydrochloric acid, sulfuric acid or the like; or a halogenating agent for example

thionyl chloride, phosphorus oxychloride, phosphorus trichloride, phosphorus pentachloride or the like, with an alcohol for example methanol, ethanol, isopropanol or the like; at temperature of generally from 0 to 150°, preferably at 50 to 100°C, for about 1 to 10 hours. Further the objective esterified compound (1) can be obtained by esterifying the starting compound (1) with a halogenated lower alkyl for example methyl iodide, under the same reaction condition being employed in Reaction formula-4 for reacting a compound (1c) with a compound (7).

A compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one carbamoyl group on the phenyl ring, or R is a benzoyl group having at least one aminocarbonyl group which may have lower alkyl group(s), can be obtained by reacting a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one lower alkoxy-carbonyl group or at least one carboxy group on the phenyl ring, or R is a benzoyl group having at least one lower alkoxy-carbonyl group, with NH_3 or an amine which has lower alkyl group(s), under the same conditions as used in the reaction of the compound (2) with the compound (3) in the Reaction formula-1.

A compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having, on the phenyl

ring, at least one amino-lower alkoxy group which may have lower alkyl group(s), or at least one carboxy-substituted lower alkoxy group, can be obtained by reacting a compound of general formula (1) wherein R² is
5 a phenyl-lower alkyl group having at least one hydroxyl group on the phenyl ring, with a compound of general formula:

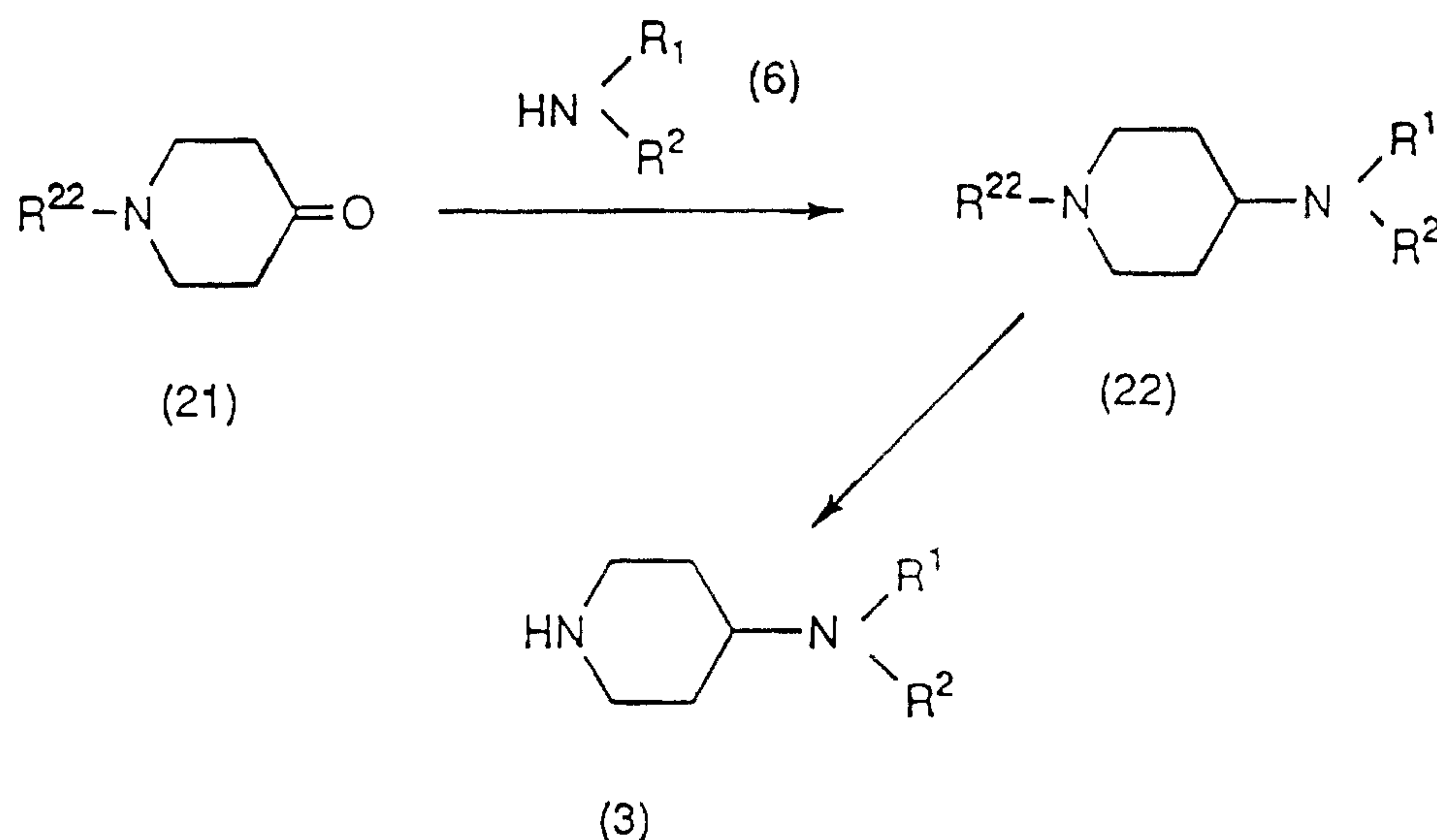


(wherein, R²¹ represents an amino-lower alkyl group which
10 may have lower alkyl group(s), or a carboxy-substituted lower alkyl group, and X¹ is the same as defined above) under the same conditions as used in the reaction of the compound (1o) with the compound (17) in the Reaction formula-9.

15 A compound of general formula (1) wherein R² is a phenyl-lower alkyl group having at least one lower alkylthio group on the phenyl ring, can be converted, by oxidation under the same conditions as used in the reaction for converting a compound (1q) into a compound
20 (1r) in the reaction formula-10 (the desirable amount of the oxidizing agent used is at least 1 mole, preferably 1-2 moles per mole of the starting material), into a compound of general formula (1) wherein R² is a phenyl-lower alkyl group having at least one lower alkyl-
25 sulfinyl group on the phenyl ring.

The compound (3) as starting material can be produced, for example, by the process of the following Reaction formula-14.

[Reaction formula-14]



- 5 (wherein, R^{22} represents a phenyl-lower alkyl group, a benzoyl group, or a phenyl-lower alkoxy carbonyl group, and R^1 and R^2 are the same as defined above).

10 The reaction of the compound (21) with the compound (6) can be conducted under the same conditions as used in the reaction of the compound (5) with the compound (6) in the reaction formula-3. The reaction for converting a compound (22) wherein R^{22} is a phenyl-lower alkyl group or a phenyl-lower alkoxy carbonyl group, into a compound (3), can be conducted by

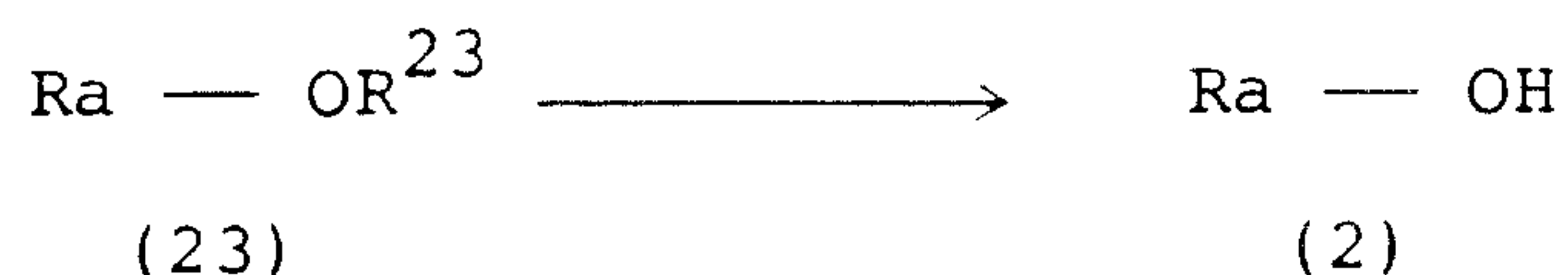
15 reduction. The reaction for converting a compound of general formula (1) wherein R^{22} is a benzoyl group, into a compound (3), can be conducted by hydrolysis.

The reduction can be conducted under the same conditions as used in the reduction of the compound (11') by the catalytic reduction method (1) in the reaction formula-8 or in the reaction for converting a compound (1n) into a compound (1o) in the reaction formula-9. The hydrolysis can be conducted under the same conditions as used in the hydrolysis of a compound of general formula (1) wherein R¹ is a phenyl-lower alkyl group having at least one lower alkoxycarbonyl group on the phenyl ring.

A compound of general formula(3) wherein either of R¹ and R² is a hydrogen atom, can be converted, by a reaction under the same conditions as used in the reaction formula-4 or 5, into a compound of general formula (3) wherein either of R¹ and R² is a group other than hydrogen atom.

The compound (2) as a starting material can be produced, for example, by the process of the following reaction formula.

[Reaction formula-15]



5 (wherein, Ra is the same as defined above and R²³ represents a lower alkyl group or a phenyl-lower alkyl group).

A compound (23) wherein R²³ is a lower alkyl group, can be converted into a compound (2) by
 10 hydrolysis. The hydrolysis can be conducted under the same conditions as used in the hydrolysis of a compound of general formula (1) wherein R² is a phenyl-lower alkyl group having at least one lower alkoxy carbonyl group on the phenyl ring. A compound (23) wherein R²³ is
 15 a phenyl-lower alkyl group, can be converted into a compound (2) by reduction. The reduction can be conducted under the same conditions as used in the reduction of the compound (11') by the catalytic reduction method (1) in the Reaction formula-8.

A compound of general formula (1) wherein R is a pyridylcarbonyl group having at least one lower alkoxy carbonyl group on the pyridine ring, or a furoyl group having at least one lower alkanoyl group on the furan ring, can be converted, by reduction under the same conditions as used in the reduction of the compound (1s) in the reaction formula-11, into a compound of general formula (1) wherein R is a pyridylcarbonyl group having at least one hydroxymethyl group on the pyridine ring, or a furoyl group having at least one hydroxyl-substituted lower alkyl group on the furan ring.

A compound of general formula (1) wherein R³ is an amino group, can be converted into a compound of general formula (1) wherein R³ is a cyano group, by reacting the former compound with a metal nitrite (e.g. sodium nitrite or potassium nitrite) in an appropriate solvent and, without isolating the reaction product, reacting said product with a metal cyanide (e.g. copper cyanide).

The solvent can be exemplified by water; alcanoic acids such as acetic acid and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; alcohols such as methanol, ethanol, isopropanol and the like; halogenated hydrocarbons such as chloroform, dichloromethane, dichloroethane and the like; ethers such as dioxane, tetrahydrofuran and the like; polar solvents such as DMF, DMSO, HMPA and the

like; and mixed solvents thereof. The desirable amounts of the metal nitrite and metal cyanide used are each generally at least 1 mole, preferably 1-1.5 moles per mole of the starting material. The reaction proceeds
5 generally at about 0-150°C, preferably at about 0-100°C and is complete generally in about 10 minutes to 5 hours.

A compound of general formula (1) wherein R is a furoyl group having at least one nitro group on the
10 furan ring or a thienylcarbonyl group having at least one nitro group on the thiophene ring, can be converted, by reduction under the same conditions as used in the reduction of the compound (11') in the Reaction formula-8, into a compound of general formula (1) wherein R is a
15 furoyl group having at least one amino group on the furan ring or a thienylcarbonyl group having at least one amino group on the thiophene ring.

A compound of general formula (1) wherein R is a furoyl group having at least one amino group on the
20 furan ring or a thienylcarbonyl group having at least one amino group on the thiophene ring, can be converted, by reaction with an agent for introducing a lower alkanoyl group, into a compound of general formula (1) wherein R is a furoyl group having, on the furan ring,
25 at least one amino group having a lower alkanoyl group, or a thienylcarbonyl group having, on the thiophene

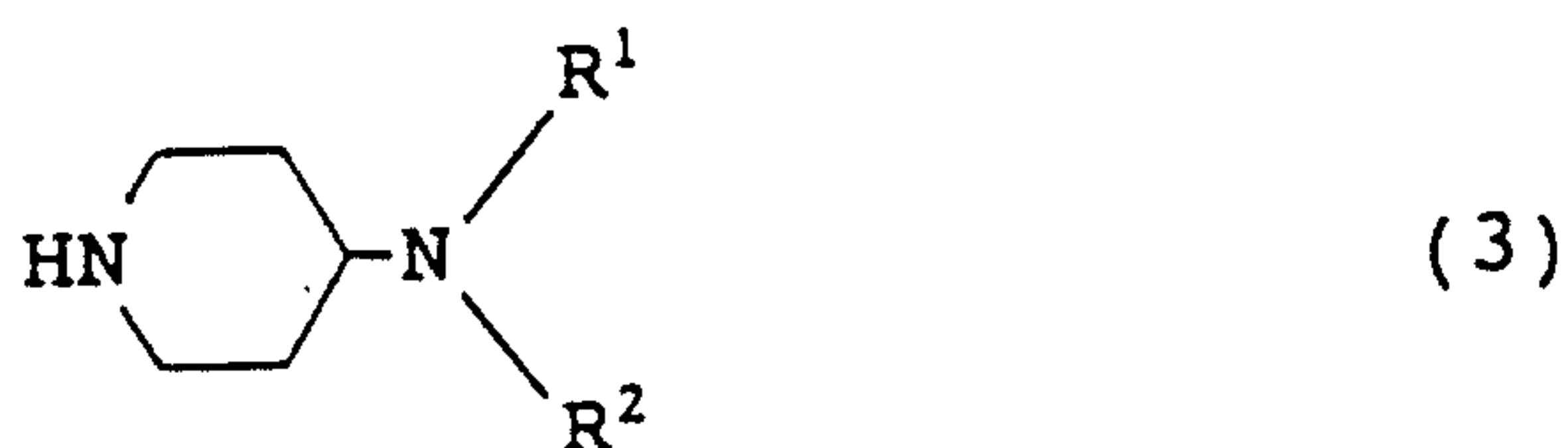
ring, at least one amino group having a lower alkanoyl group.

The agent for introducing a lower alkanoyl group includes, for example, lower alkanolic acids such as formic acid, acetic acid, propionic acid and the like; lower alkanolic acid anhydrides such as acetic anhydride, propionic anhydride and the like; and lower alkanolic acid halides such as acetyl chloride, propionyl bromide and the like. When the agent for introducing a lower alkanoyl group is an acid anhydride or an acid halide, it is possible to allow a basic compound to be present in the reaction system. The basic compound includes, for example, alkali metals such as metallic sodium, metallic potassium and the like; their hydroxides, carbonates and bicarbonates; and organic bases such as pyridine, piperidine and the like. The reaction proceeds in the presence or absence of a solvent, but is conducted generally in an appropriate solvent. The solvent includes, for example, ketones such as acetone, methyl ethyl ketone and the like; ethers such as diethyl ether, dioxane and the like, aromatic hydrocarbons such as benzene, toluene, xylene and the like; esters such as methyl acetate, ethyl acetate and the like; acetic acid; acetic anhydride; water; and pyridine. The desirable amount of the agent for introducing a lower alkanoyl group is at least about equimolar, generally equimolar to a large excess over the starting material. The reaction favorably proceeds

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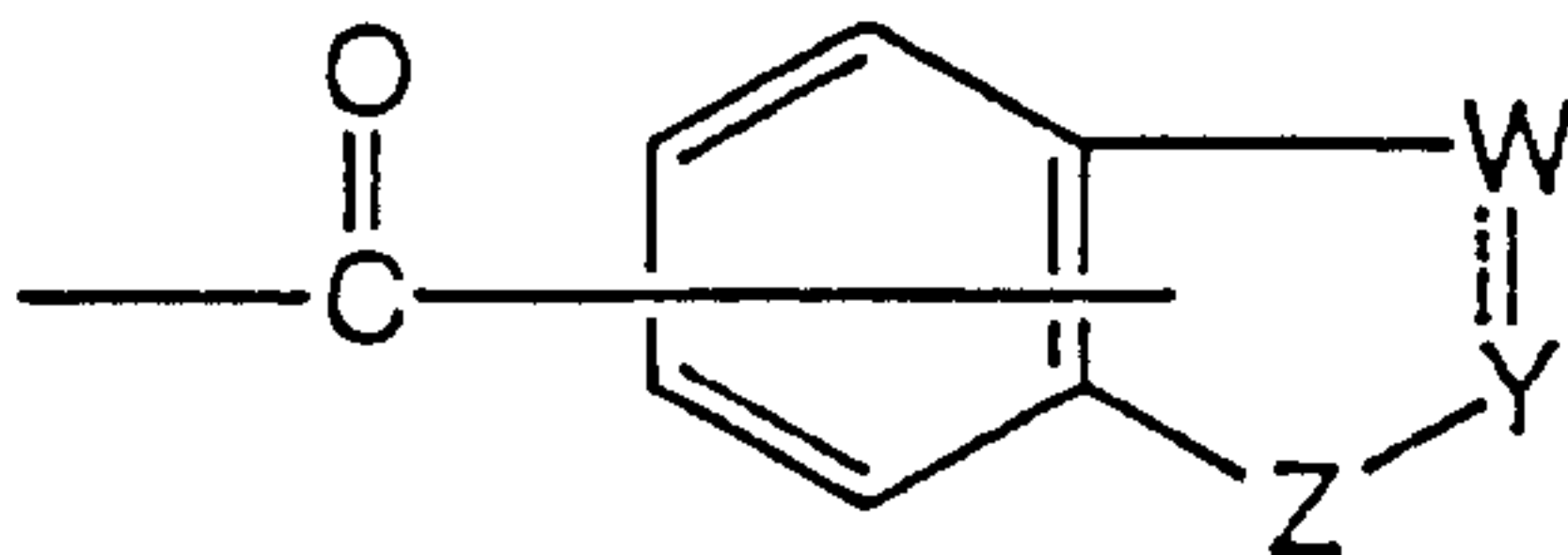
generally at about 0-150°C, preferably at about 0-100°C and is complete generally in about 5 minutes to 24 hours. When the agent for introducing a lower alkanoyl group is a lower alkanonic acid, it is desirable to add to the
 5 reaction system a dehydrating agent such as mineral acid (e.g. sulfuric acid or hydrochloric acid), sulfonic acid (e.g. p-toluenesulfonic acid, benzenesulfonic acid or ethanesulfonic acid) or the like. The reaction temperature is particularly preferably about 50-120°C.

10 A compound of general formula (1) wherein R is a formyl group, can be obtained by reacting a compound of general formula (3):



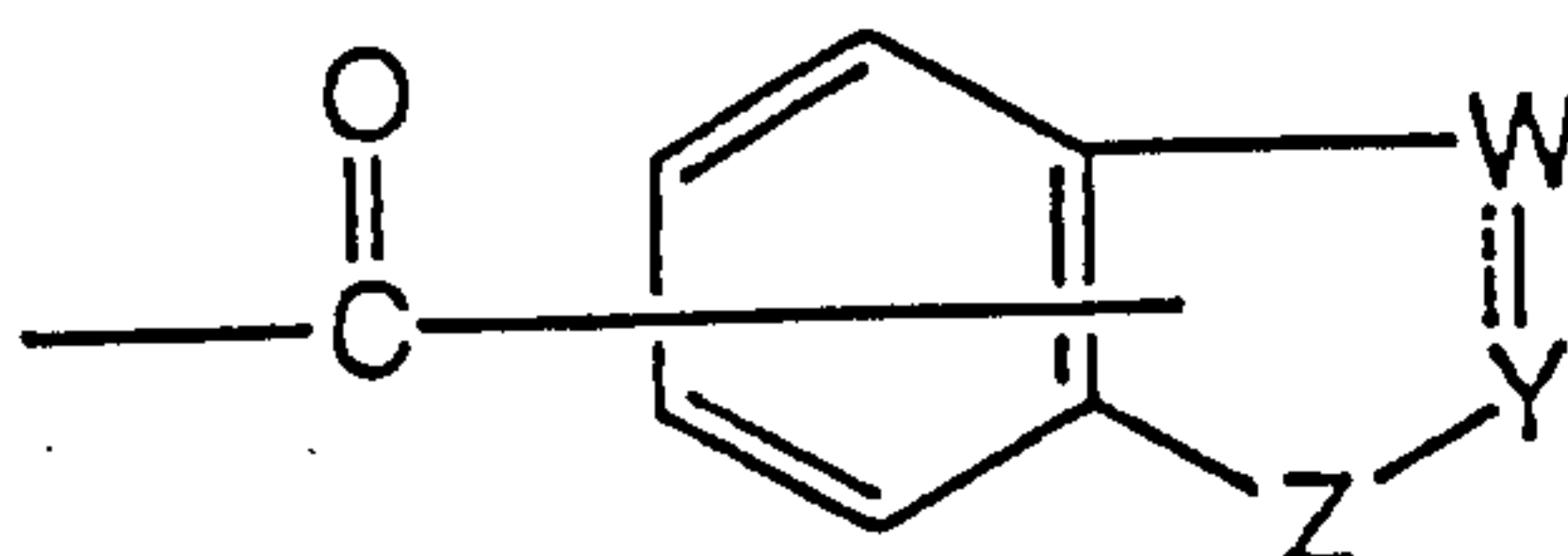
with a di-lower alkylformamide such as dimethyl-
 formamide or the like. The desirable amount of the di-
 15 lower alkylformamide used is generally a large excess over the compound (3). The reaction is conducted generally at about room temperature to 200°C, preferably at about room temperature to 150°C and is complete in about 1-30 hours.

20 A compound of general formula (1) wherein R is a group of the formula:



(wherein, W, Y, Z and the dotted line in $\begin{array}{c} -W \\ \vdots \\ Y \end{array}$ are the same

as defined above) and said group has at least one lower alkylthio group thereon, can be converted, by desulfurization, into a compound of general formula (1) wherein
 5 R is a group of the formula:



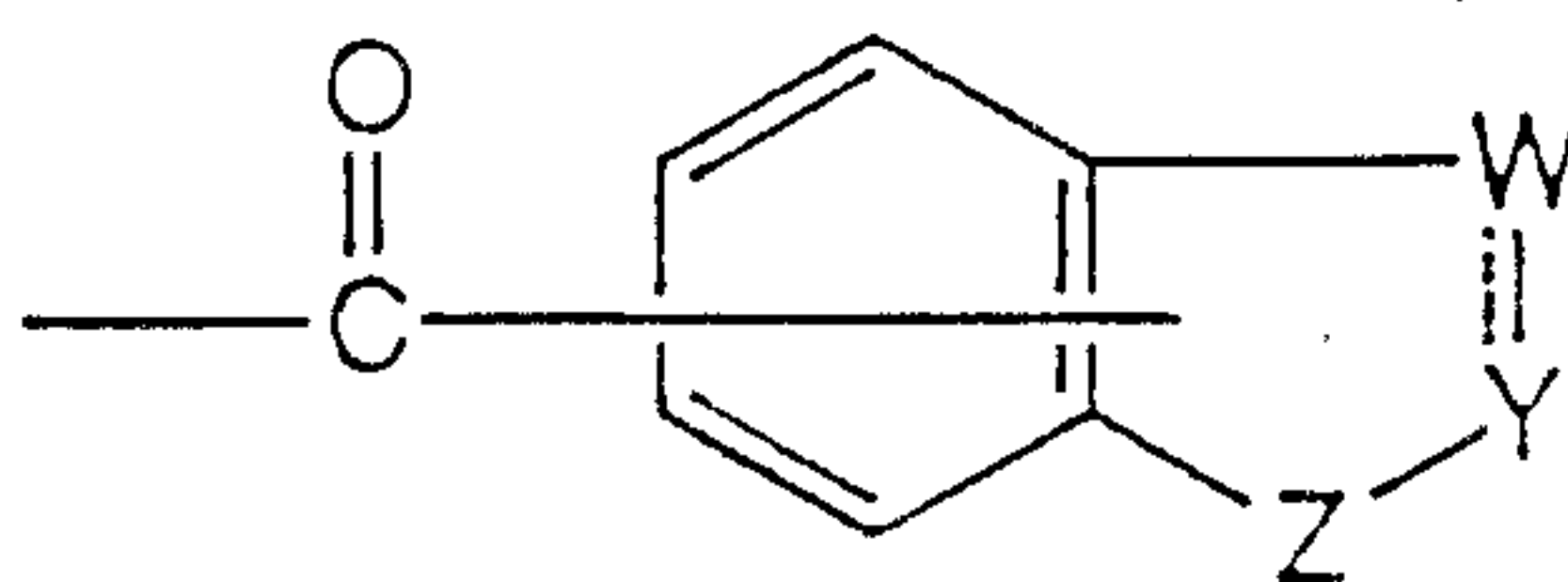
(wherein, W, Y, Z and the dotted line in $\begin{array}{c} -W \\ \vdots \\ Y \end{array}$ are the same

as defined above) and said may have thereon at least one
 10 lower alkylthio group, the number of said at least one alkylthio group being smaller by at least one than the number of the at least one alkylthio group of the compound before desulfurization.

The desulfurization is conducted generally in
 15 the presence of an appropriate catalyst in a solvent. The catalyst can be exemplified by aluminum amalgam, lithium-lower alkylamine, Raney nickel, Raney cobalt, triethyl phosphite and triphenylphosphine. Raney nickel is preferable. The solvent can be exemplified by
 20 alcohols such as methanol, ethanol, isopropanol and the

like, and ethers such as dioxane, tetrahydrofuran, diethyl ether and the like. The reaction is conducted at about 0-200°C, preferably at about room temperature to 100°C and is complete in about 10 minutes to 5 hours.

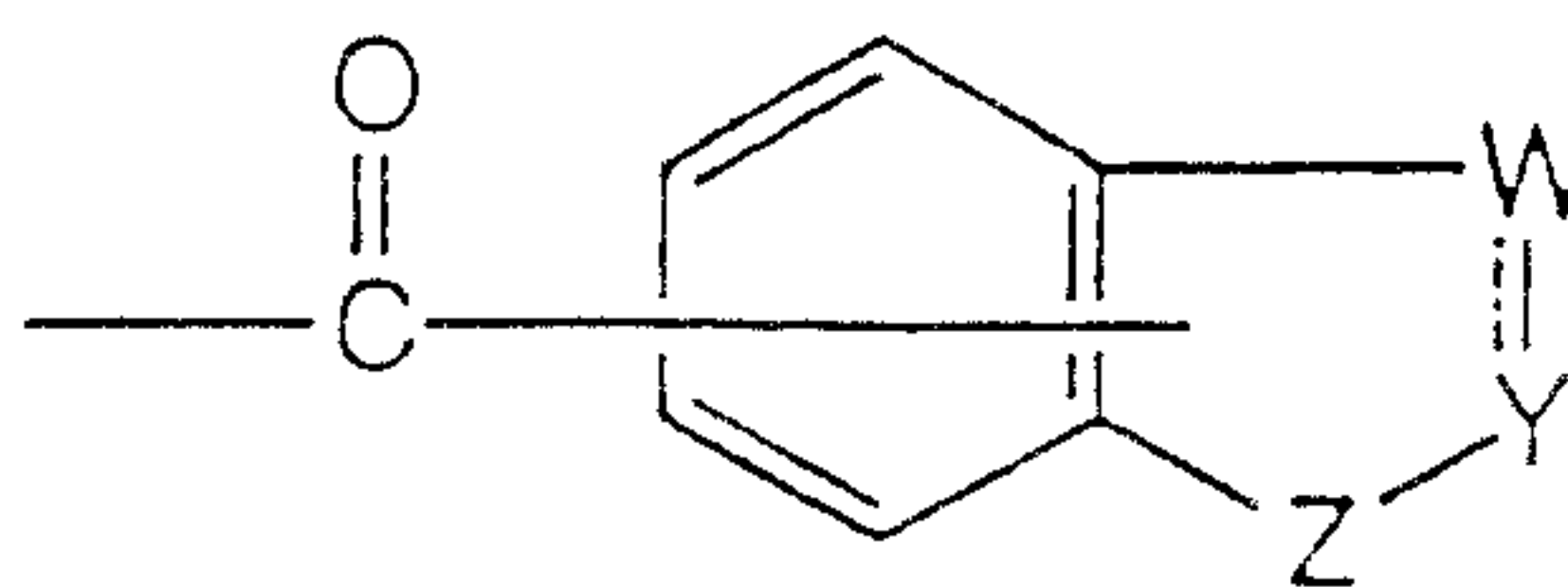
- 5 A compound of general formula (1) wherein R is a group of the formula:



(wherein, W, Y, Z and the dotted line in $\begin{array}{c} \text{---} \text{W} \\ \vdots \\ \text{Y} \end{array}$ are the same

as defined above) and said group has at least one

- 10 halogen atom thereon, can be converted, by dehalogenation, into a compound of general formula (1) wherein R is a group of the formula:



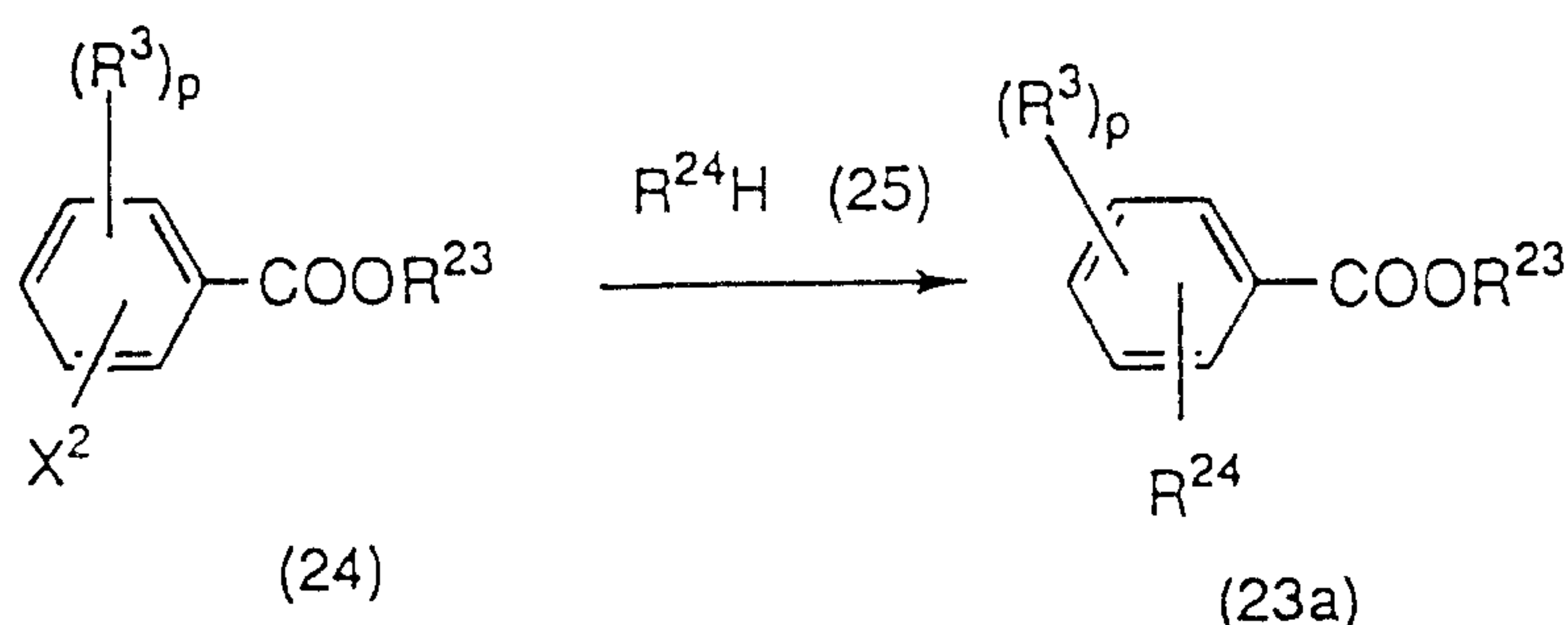
(wherein, W, Y, Z and the dotted line in $\begin{array}{c} \text{---} \text{W} \\ \vdots \\ \text{Y} \end{array}$ are the same

- 15 as defined above) and said group may have thereon at least one halogen atom, the number of said at least one halogen atom being smaller by at least one than the number of the at least one halogen atom of the compound before dehalogenation.

The dehalogenation can be conducted under the same conditions as used in the reduction of the compound (11') by the method using a catalytic reduction catalyst in the Reaction formula-8. The dehalogenation favorably
5 proceeds when a basic compound such as triethylamine or the like is added.

The compound (23) as starting material can be produced, for example, by the processes of the following reaction formulas.

[Reaction formula-16]

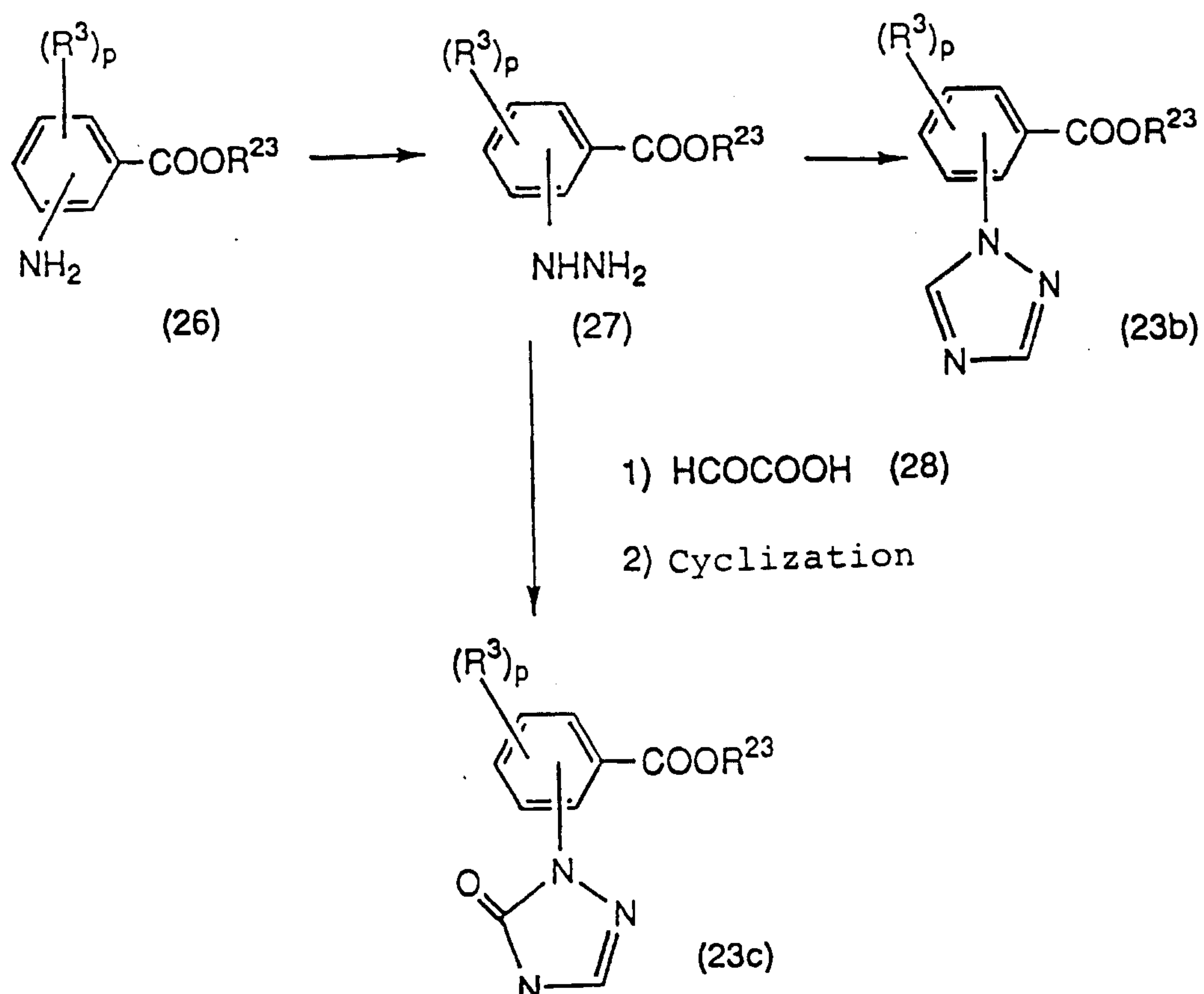


- 5 (wherein, R^3 , R^{23} , p and X^2 are the same as defined above; and R^{24} represents a 1,2,4-triazolyl group which may have oxo group(s) on the 1,2,4-triazole ring, a 1,2,3,4-tetrazolyl group, an imidazolidinyl group which may have 1-2 substituents selected from the group
- 10 consisting of a phenyl group and a lower alkyl group, on the imidazole ring, a pyrazolyl group which may have lower alkyl group(s) on the pyrazole ring, a pyrrolyl group, a pyrrolidinyl group which may have oxo group(s) on the pyrrolidine ring, a piperidinyl group which may
- 15 have oxo group(s) on the piperidine ring, an benzoimidazolyl group, an imidazolidinyl group which may have oxo group(s) on the imidazolidine ring, or a 2-oxazolidinyl group).

The reaction of the compound (24) with the

20 compound (25) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the reaction formula-4.

[Reaction formula-17]



(wherein, R^3 , R^{23} and p are the same as defined above).

The reaction for converting a compound (26) into a compound (27) can be conducted by reacting the compound (26) with an acid (e.g. sulfuric acid, hydrochloric acid, hydrobromic acid or fluoroboric acid) and sodium nitrite in a solvent such as lower alkanolic acid (e.g. acetic acid), water or the like to form a diazonium salt and then reacting the diazonium salt with sulfurous acid or a metal salt (e.g. sodium hydrogen-sulfite or stannous chloride) in a solvent such as water or the like.

The desirable amount of sodium nitrite used is generally 1-2 moles, preferably 1-1.5 moles per mole of

the compound (26). The desirable reaction temperature is generally about -20°C to room temperature, preferably about -5°C to room temperature, and the reaction time is generally about 5 minutes to 5 hours.

5 In the subsequent reaction of the diazonium salt with sulfurous acid, the desirable reaction temperature is generally about $0-150^{\circ}\text{C}$, preferably about $0-100^{\circ}\text{C}$, and the reaction time is generally about 1-50 hours.

10 The reaction for converting the compound (27) into a compound (23b) can be conducted by reacting the compound (27) with 1,3,5-triazine in an appropriate solvent. The solvent can be any solvent mentioned with respect to the reaction of the compound (5) with the
15 compound (6) in the reaction formula-3. The reaction is desirably conducted generally at about room temperature to 150°C , preferably at about room temperature to 100°C and is complete generally in about 1-10 hours.

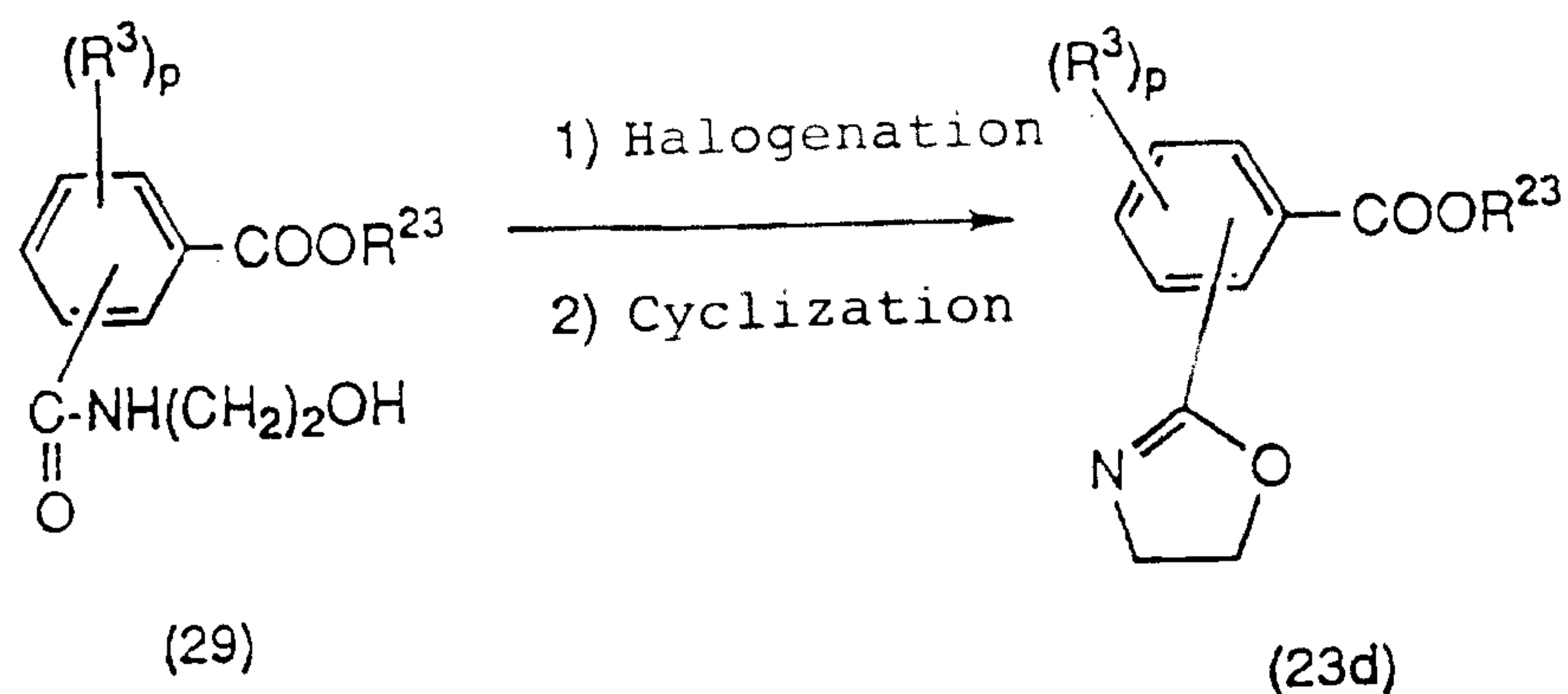
 The amount of 1,3,5-triazine used is generally
20 0.1-5 moles, preferably 0.1-2 moles per mole of the compound (27).

 The reaction of the compound (27) with a compound (28) can be conducted in an appropriate solvent in the presence of an acid or a basic compound. The
25 solvent includes, for example, water; alcohols such as methanol, ethanol, isopropanol and the like; aromatic hydrocarbons such as benzene, toluene, xylene and the like; and aprotic polar solvents such as dimethyl-

formamide, dimethylacetamide, N-methylpyrrolidone and the like. The acid includes, for example, mineral acids such as hydrochloric acid, sulfuric acid, boron trifluoride and the like; and organic acids such as p-toluenesulfonic acid and the like. The basic compound can be exemplified by inorganic bases such as potassium carbonate, sodium carbonate, potassium hydrogen-carbonate, sodium hydrogencarbonate and the like, and organic bases such as sodium acetate and the like. The desirable amount of the compound (28) used is at least 1 mole, preferably 1-2 moles per mole of the compound (27). The desirable amount of the acid or basic compound used is at least 1 mole, preferably 1-5 moles per mole of the compound (27). The reaction is conducted generally at about room temperature to 150°C, preferably at about room temperature to 100°C and is complete in about 5 minutes to 5 hours.

The subsequent cyclization can be conducted by reaction with diphenyl phosphoryl azide in the above-mentioned solvent in the presence of an appropriate basic compound. The basic compound can be any basic compound used in the reaction of the compound (1c) with the compound (7) in the reaction formula-4. The desirable amount of diphenyl phosphoryl azide used is at least 1 mole, preferably 1-2 moles per mole of the compound (27). The reaction is conducted generally at about room temperature to 200°C, preferably at about 50-150°C and is complete in about 1-10 hours.

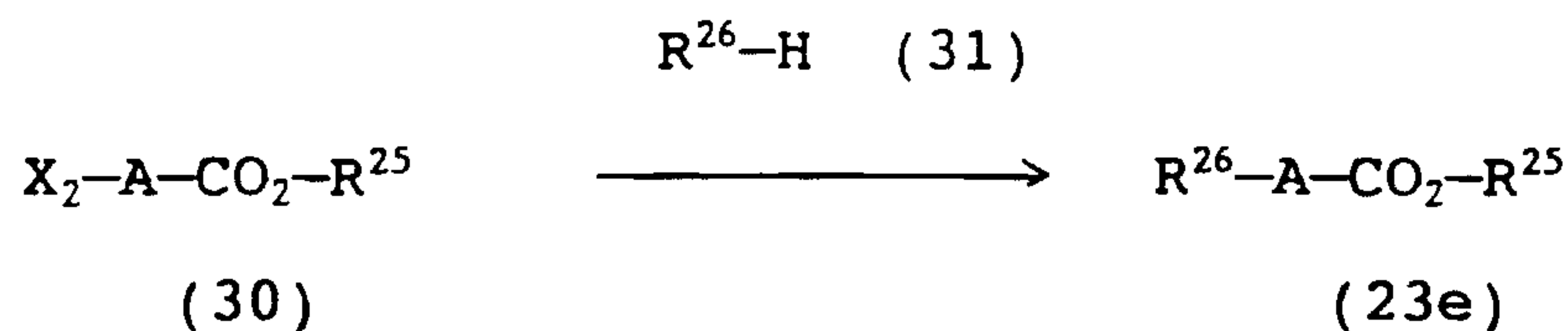
[Reaction formula-18]



(wherein, R^3 , R^{23} and p are the same as defined above).

The halogenation of the compound (29) can be conducted under the same conditions as used in the reaction for production of a carboxylic acid halide in the reaction formula-1. The subsequent cyclization can be conducted in an appropriate solvent in the presence of a basic compound. The solvent and basic compound can be each any of those mentioned with respect to the reaction of the compound (1c) with the compound (7) in the reaction formula-4. The cyclization is conducted generally at about 0-70°C, preferably at about 0°C to room temperature and is complete in about 5 minutes to 5 hours.

[Reaction formula-19]

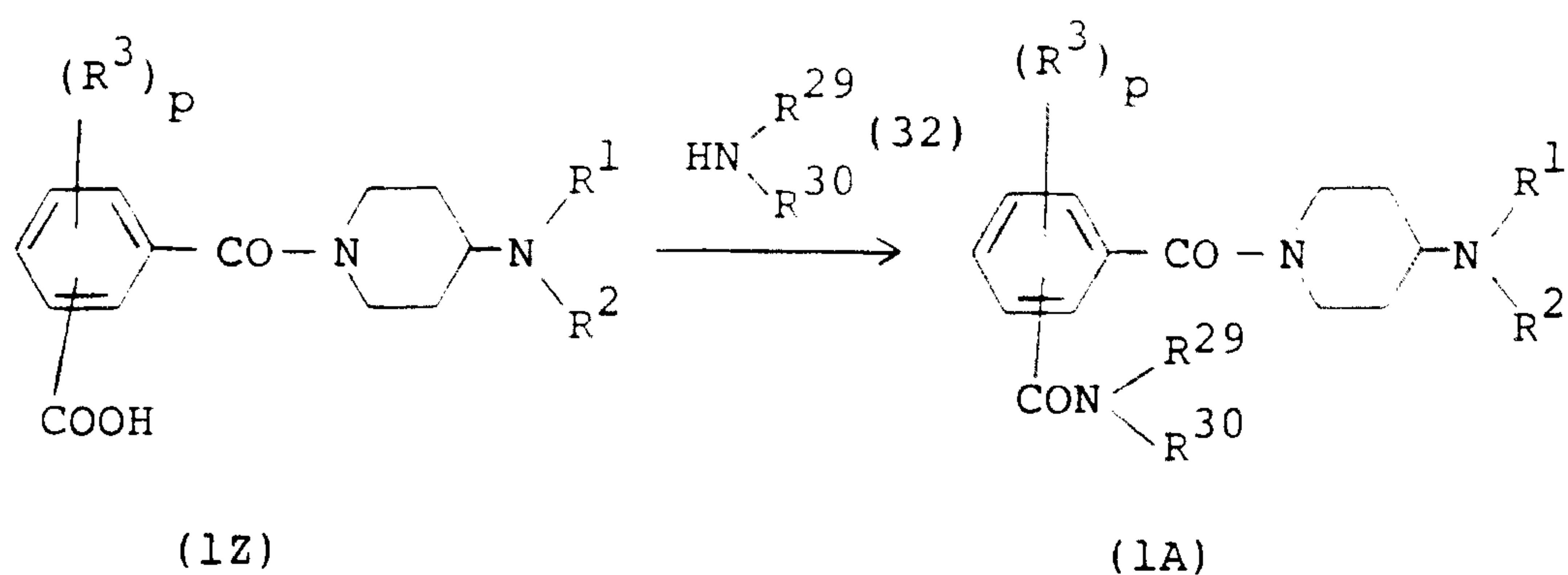


5 [wherein, X₂ is the same as defined above; A represents a lower alkylene group; R²⁵ represents a phenyl-lower alkyl group; and R²⁶ represents a 1,2,4-triazolyl group or an amino group which may have lower alkyl group(s)].

The lower alkylene group can be exemplified by
 10 C¹⁻⁶ straight- or branched-chain alkylene group such as methylene, ethylene, trimethylene, 2-methyltrimethylene, 2,2-dimethyltrimethylene, 1-methyltrimethylene, methylnmethylene, ethylnmethylene, tetramethylene, pentamethylene, hexamethylene and the like.

15 The reaction of the compound (30) with the compound (31) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the Reaction formula-4.

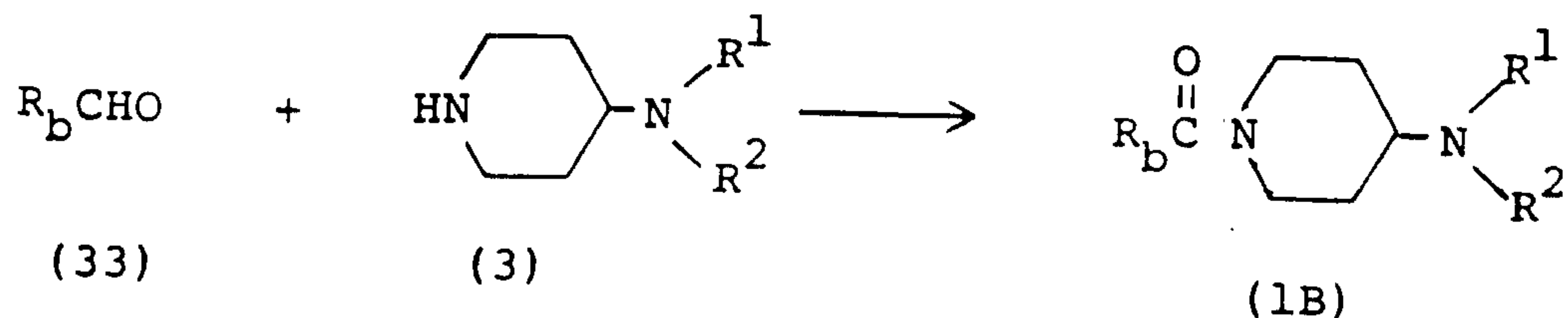
[Reaction formula-20]



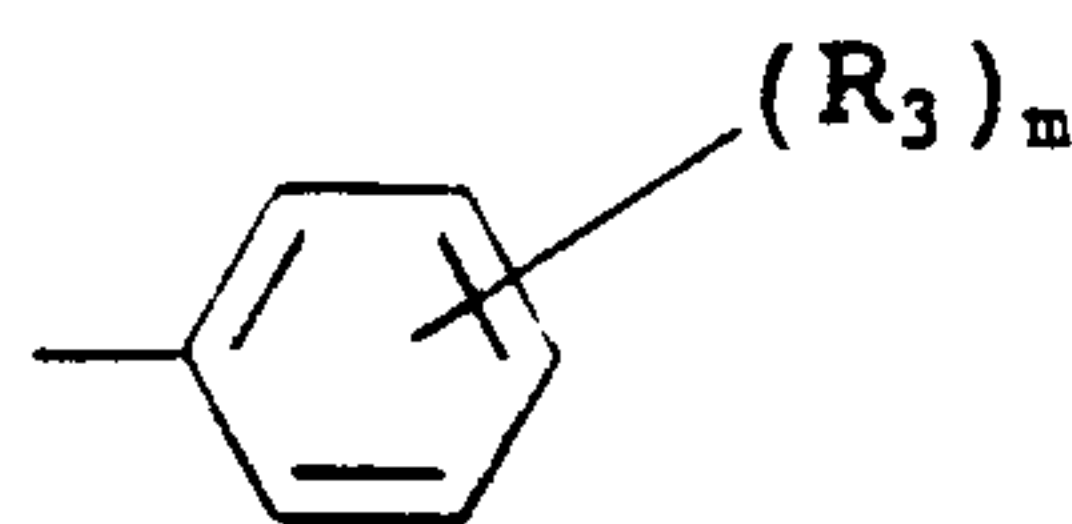
(wherein, R^1 , R^2 , R^3 and p are the same as defined above;
 and R^{29} and R^{30} , which may be the same or different, each
 represent a hydrogen atom, a lower alkyl group or a
 5 phenyl group).

The reaction of the compound (1Z) with the
 compound (32) can be conducted under the same conditions
 as used in the reaction of the compound (2) with the
 compound (3) in the Reaction formula-1.

[Reaction formula-21]



[wherein, R^1 and R^2 are the same as defined above; and R_b represents a group of the formula:

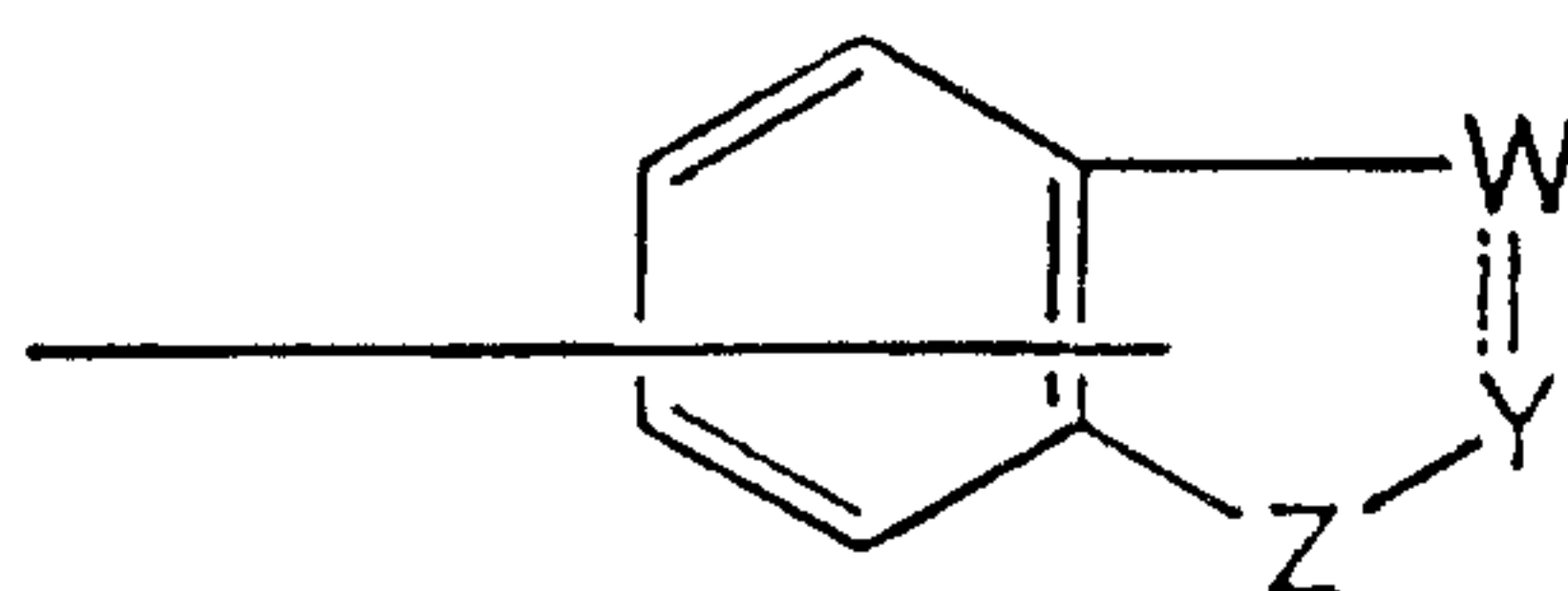


5 (R^3 and m are the same as defined above); a lower alkyl group which may have hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s); a lower alkyl group having 1-3 halogen atoms; a pyridyl group which may have, on the pyridine ring, substituent(s) selected

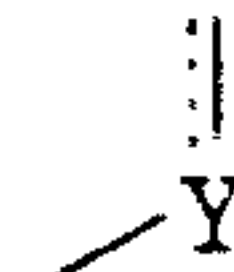
10 from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which

15 may have lower alkyl group(s) as substituent(s), a lower alkoxy carbonyl group, a hydroxyl-substituted lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkyl group; a furyl group which may have, on the furan ring, substituent(s) selected

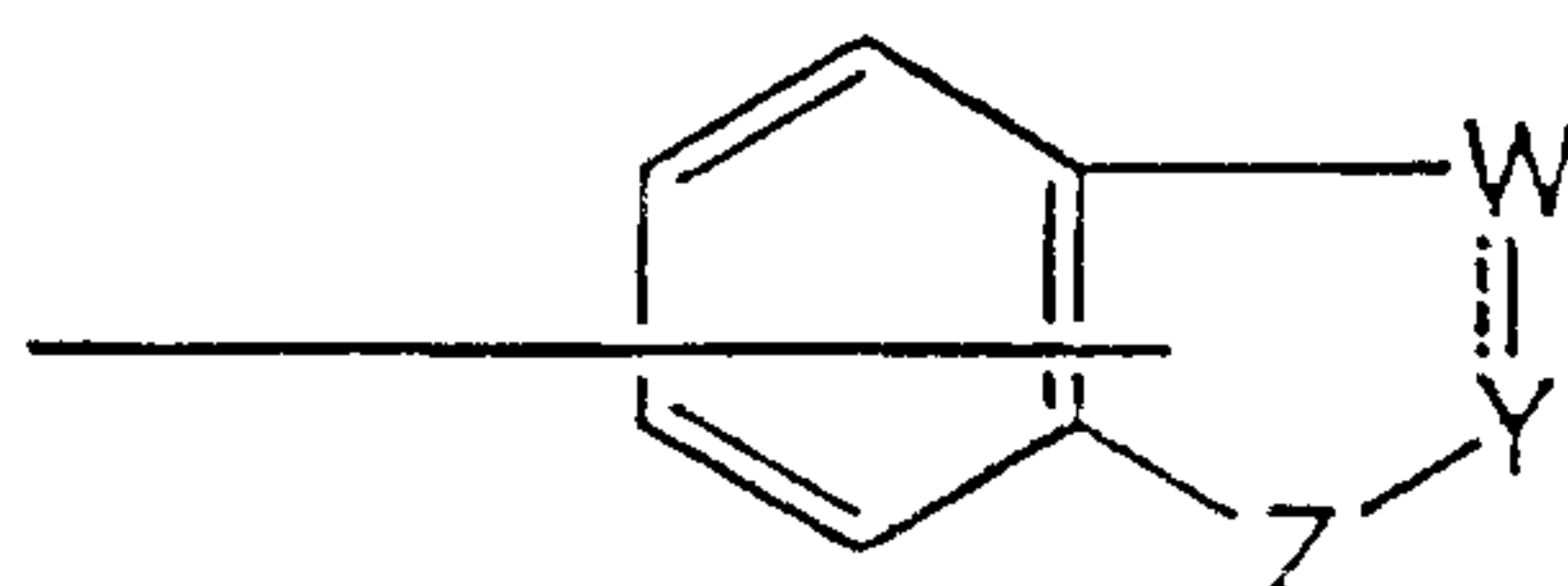
from the group consisting of a nitro group, a hydroxyl-substituted lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s); a thienyl group which may have, on the thiophene ring, substituent(s) selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s); a fluorenyl group which may have, on the fluorene ring, substituent(s) selected from the group consisting of an oxo group and a nitro group; or a group of the formula:



(wherein, Y, W, Z, the dotted line in the bond -W and



the substituent on the group



are the same as mentioned above)].

The reaction of the compound (33) with the compound (3) can be conducted by reaction with a metal cyanide (e.g. sodium cyanide) and subsequent reaction with an oxidizing agent both in an appropriate solvent. The solvent can be any solvent used in the reaction for converting a compound (1q) into a compound (1r) in the

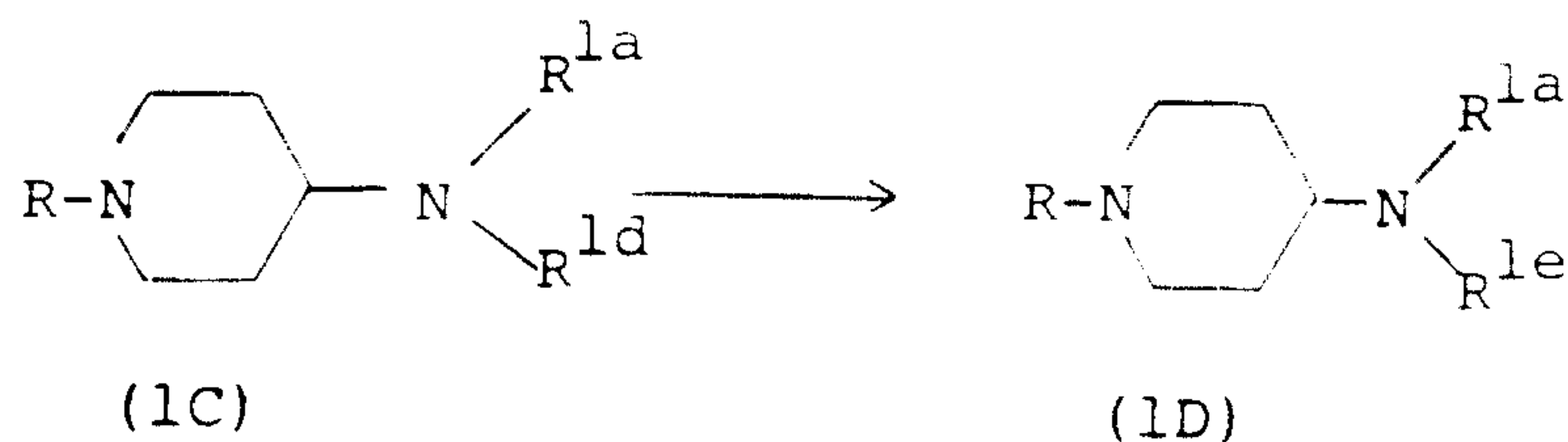
reaction formula-10. The oxidizing agent can be manganese dioxide or any oxidizing agent used in the reaction for converting the compound (1q) into the compound (1r) in the Reaction formula-10.

5 The desirable amount of the metal cyanide used is at least 1 mole, preferably 1-10 moles per mole of the compound (33). The desirable amount of the oxidizing agent used is generally a large excess over the compound (33). The desirable amount of the compound (3)

10 is at least 1 mole, preferably 1-2 moles per mole of the compound (33). The reaction with the metal cyanide and the reaction with the oxidizing agent are conducted generally at about 0-40°C, preferably at about 0°C to room temperature and is complete in about few minutes to

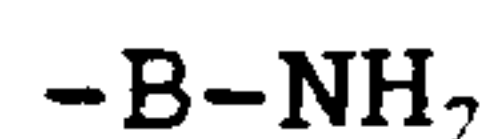
15 5 hours.

[Reaction formula-22]



[wherein, R and R^{1a} are the same as defined above; R^{1d} represents a phthalimido-substituted lower alkyl group; and R^{1e} represents a group of the formula:

5



(wherein, B is the same as defined above)].

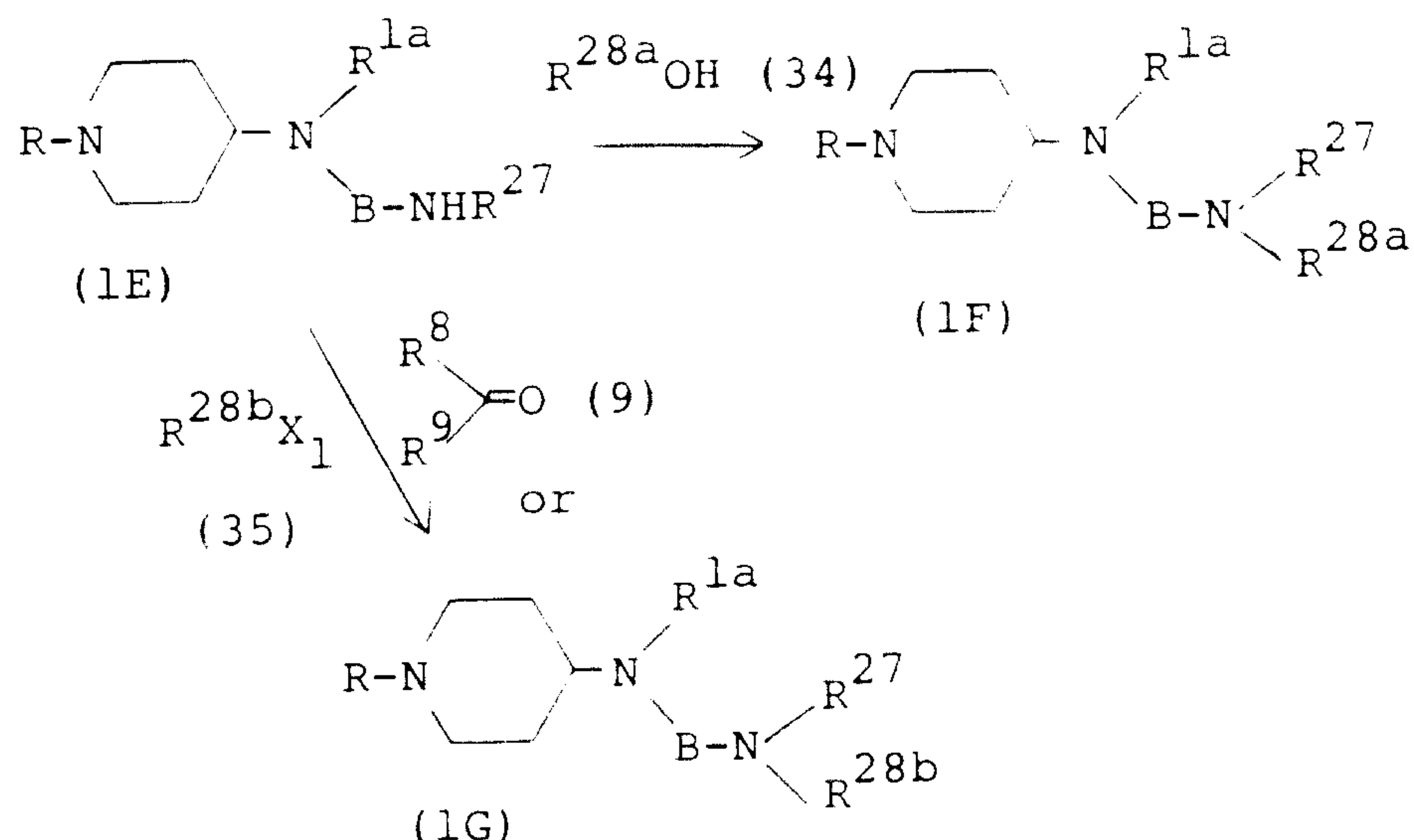
The reaction for converting a compound (1C) into a compound (1D) can be carried out by reacting the compound (1C) with hydrazine in an appropriate solvent or by hydrolysis of the compound (1C). As to the solvent to be used in the reaction of the compound (1C) with hydrazine, there can be exemplified by water; aromatic hydrocarbons such as benzene, toluene, xylene and the like; ethers such as tetrahydrofuran, dioxane, diethyl ether, diethylene glycol dimethyl ether and the like; alcohols such as methanol, isopropanol, butanol and the like; acetic acid; and inert solvents such as ethyl acetate, acetone, acetonitrile, dimethylformamide, dimethyl sulfoxide, hexamethylphosphoric triamide and the like. The reaction is conducted generally at about room temperature to 120°C, preferably at about 0-100°C and is complete generally in about 5 minutes to 5 hours. The desirable amount of hydrazine used is at least about

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1 mole, preferably about 1-5 moles per mole of the compound (1C).

The hydrolysis can be conducted under the same conditions as used in the above-mentioned hydrolysis of
5 a compound of general formula (1) wherein R^2 is a phenyl-lower alkyl group having at least one lower alkoxycarbonyl group on the phenyl ring.

[Reaction formula-23]



(wherein, R, R^{1a}, R⁸, R⁹, R²⁷, B and X₁ are the same as defined above; R^{28a} represents a lower alkanoyl group or a benzoyl group; and R^{28b} represents a lower alkyl group).

The reaction of the compound (1E) with the compound (34) can be conducted under the same conditions as used in the reaction of the compound (2) with the compound (3) in the reaction formula-1.

The reaction of the compound (1E) with the compound (35) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (7) in the reaction formula-4.

The reaction of the compound (1E) with the compound (9) can be conducted under the same conditions as used in the reaction of the compound (1c) with the compound (9) in the reaction formula-5.

The piperidine derivatives represented by general formula (1) according to the present invention can each form an acid addition salt easily by being reacted with a pharmacologically acceptable acid. The acid can be exemplified by inorganic acids such as hydrochloric acid, sulfuric acid, phosphoric acid, hydrobromic acid and the like, and organic acids such as oxalic acid, maleic acid, fumaric acid, malic acid, tartaric acid, citric acid, benzoic acid and the like.

Of the present piperidine derivatives represented by general formula (1), those having an acidic group can each form a salt easily by being reacted with a pharmacologically acceptable basic compound. The basic compound can be exemplified by sodium hydroxide, potassium hydroxide, calcium hydroxide, sodium carbonate and potassium hydrogencarbonate.

Each of the intended compounds obtained by the above reaction formulas can be easily separated from the reaction system and purified by ordinary means. The means for separation can be exemplified by solvent extraction, dilution, recrystallization, column chromatography and preparative thin-layer chromatography.

Needless to say, the present piperidine derivatives of general formula (1) include optical isomers.

Each of the compounds of general formula (1) is used generally in the form of ordinary pharmaceutical preparation. The pharmaceutical preparation is prepared

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by using diluents or excipients ordinarily used, such as filler, bulking agent, binder, humectant, disintegrator, surfactant, lubricant and the like. The pharmaceutical preparation can be prepared in various forms depending upon the purpose of remedy, and the typical forms include tablets, pills, a powder, a solution, a suspension, an emulsion, granules, an ointment, suppositories, an injection (e.g. solution or suspension), etc. In preparing tablets, there can be used various carriers exemplified by excipients such as lactose, white sugar, sodium chloride, glucose, urea, starch, calcium carbonate, kaolin, crystalline cellulose, silicic acid and the like; binders such as water, ethanol, propanol, simple syrup, lactose solution, starch solution, gelatin solution, carboxymethyl cellulose, shellac, methyl cellulose, potassium phosphate, polyvinylpyrrolidone and the like; disintegrators such as dry starch, sodium alginate, powdered agar, powdered laminarin, sodium hydrogencarbonate, calcium carbonate, polyoxyethylene sorbitan-fatty acid esters, sodium lauryl sulfate, stearic acid monoglyceride, starch, lactose and the like; disintegration inhibitors such as white sugar, stearin, cacao butter, hydrogenated oil and the like; absorption promoters such as quaternary ammonium salts, sodium lauryl sulfate and the like; humectants such as glycerine, starch and the like; adsorbents such as starch, lactose, kaolin, bentonite, colloidal silicic acid and the like; and lubricants such

as refined talc, stearic acid salts, boric acid powder, polyethylene glycol and the like. The tablets can be prepared, as necessary, in the form of ordinary coated tablets, such as sugar-coated tablets, gelatin-coated tablets, enteric coated tablets or film-coated tablets, or in the form of double-layered tablets or multi-layered tablets. In preparing pills, there can be used various carriers exemplified by excipients such as glucose, lactose, starch, cacao butter, hardened vegetable oils, kaolin, talc and the like; binders such as powdered acacia, powdered tragacanth, gelatin, ethanol and the like; and disintegrators such as laminarin, agar and the like. In preparing suppositories, there can be used carriers exemplified by a polyethylene glycol, cacao butter, a higher alcohol, a higher alcohol ester, gelatin and a semi-synthetic glyceride. Capsules can be prepared generally by mixing the present compound with various carriers mentioned above and filling the mixture into a hard gelatin capsule or a soft capsule according to an ordinary method. In preparing an injection (solution, emulsion or suspension), it is sterilized and is preferably made isotonic to the blood. In preparing the solution, emulsion or suspension, there can be used diluents such as water, ethyl alcohol, polyethylene glycol, propylene glycol, ethoxylated isostearyl alcohol, polyoxy-isostearyl alcohol and polyoxyethylene sorbitan-fatty acid esters. In this case, the injection may contain sodium chloride, glucose or glycerine in an

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amount sufficient to make the injection isotonic, and may further contain a solubilizing agent, a buffer solution, a soothing agent, etc. all ordinarily used. The pharmaceutical preparation may furthermore contain,
5 as necessary, a coloring agent, a preservative, a perfume, a flavoring agent, a sweetening agent and other drugs. In preparing the present pharmaceutical preparation in the form of a paste, a cream or a gel, there can be used diluents such as white petrolatum, paraffin,
10 glycerin, cellulose derivatives, polyethylene glycol, silicon, bentonite and the like.

The amount of the present compound to be contained in the pharmaceutical preparation of the present invention is not particularly restricted and can
15 be appropriately selected from a wide range, but the desirable amount is generally 1-70% by weight, preferably 1-30% by weight in the pharmaceutical preparation.

The method for administering the pharmaceutical preparation is not particularly restricted. It
20 is decided depending upon the form of preparation, the age, distinction of sex and other conditions of patient, the disease condition of patient, etc. For example, tablets, pills, a solution, a suspension, an emulsion, granules or capsules are administered orally. An
25 injection is intravenously administered singly or in admixture with an ordinary auxiliary solution of glucose, amino acids or the like, or, as necessary, is singly administered intramuscularly, intradermally,

subcutaneously or intraperitoneally. Suppositories are administered intrarectally.

The dose of the pharmaceutical preparation is appropriately selected depending upon the administration method, the age, distinction of sex and other conditions of patient, the disease condition of patient, etc., but the desirable dose is generally about 0.01-10 mg per kg of body weight per day in terms of the amount of the active ingredient, i.e. the present compound of general formula (1). The desirable content of the active ingredient in each unit of administration form is 0.1-200 mg.

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[Examples]

The present invention is described more specifically below with reference to Preparation Examples, Reference Examples, Examples and

5 Pharmacological Test.

Preparation Example 1

	4-[N-methyl-N-(2-phenylethyl)amino]-1-[3-(2-dimethylaminoethoxy)-4-(1,2,4-triazol-1-yl)-benzoyl]piperidine	5 mg
10	Starch	132 mg
	Magnesium stearate	18 mg
	Lactose	<u>45 mg</u>
	Total	200 mg

Tablets each containing the above components

15 in the above amounts were prepared according to an ordinary method.

Preparation Example 2

20	4-[N-methyl-N-(2-phenylethyl)amino]-1-[3-(2-dimethylaminoethoxy)-4-(1,2,4-triazol-1-yl)-benzoyl]piperidine	500 mg
	Polyethylene glycol (molecular weight: 4000)	0.3 g
	Sodium chloride	0.9 g
25	Polyoxyethylene sorbitan mono-oleate	0.4 g
	Sodium metabisulfite	0.1 g
	Methylparaben	0.18 g

Propylparaben 0.02 g

Distilled water for injection 100 ml

The above parabens, sodium metabisulfite and sodium chloride were dissolved in the above distilled water at 80°C with stirring. The resulting solution was cooled to 40°C. Therein were dissolved the above compound (present compound), polyethylene glycol and polyoxyethylene sorbitan mono-oleate in this order. To the resulting solution was added the above distilled water to obtain a final volume, followed by filtration through an appropriate filter paper for sterilization. The sterile filtrate was poured into vials each in an amount of 1 ml to prepare an injection.

Reference Example 1

2 g of p-toluenesulfonic acid was added to a solution of 230 g of 4-oxo-1-benzylpiperidine and 221 g of 2-phenethylamine in 1 liter of toluene. The mixture
5 was refluxed for 1 hour while removing the generated water using a Dean-Stark trap. The reaction mixture was concentrated under reduced pressure. To the residue was added 1 liter of ethanol. To the mixture being ice-cooled was slowly added 22 g of sodium boron hydride.
10 The resulting mixture was stirred at room temperature for 4 hours. The reaction mixture was ice-cooled, and then was made acidic by slow addition of concentrated hydrochloric acid. The resulting crystals were collected by filtration. The crystals were dissolved in
15 water. The solution was made alkaline with a 25% aqueous sodium hydroxide solution and then extracted with methylene chloride. The extract was water-washed, dried with anhydrous sodium sulfate, and concentrated under reduced pressure to obtain 222.2 g of 4-(2-
20 phenylethylamino)-1-benzylpiperidine as a light yellow oily substance.

¹H-NMR (200 MHz, CDCl₃) δ ppm: 1.20-1.75 (3H, m),
1.75-1.90 (2H, m), 1.90-2.10 (2H, m), 2.37-2.58
(1H, m), 2.70-3.00 (6H, m), 3.48 (2H, m), 7.12-7.45
25 (10H, m)

Reference Example 2

136 ml of formic acid was added to 210 g of 4-

(2-phenylethylamino)-1-benzylpiperidine. Since the temperature of the mixture increased to about 90°C, the mixture was ice-cooled. To the reaction mixture was added 64 ml of 37% formalin at 50-60°C; the ice bath was removed; and the mixture was stirred for 1 hour. To the
5 resulting reaction mixture were added 1 liter of ethanol and 120 ml of concentrated hydrochloric acid, followed by concentration under reduced pressure. To the residue was added 1 liter of ethanol. The resulting insolubles were collected by filtration and then washed with
10 ethanol to obtain 251.7 g of 4-[N-methyl-N-(2-phenylethyl)amino]-1-benzylpiperidine dihydrochloride as a white powder.

¹H-NMR (200 MHz, D₂O) δ ppm: 1.88-2.20 (2H, m),
2.20-2.43 (2H, m), 2.90 (3H, s), 3.00-3.25 (4H, m),
15 3.37-3.56 (2H, m), 3.56-3.81 (3H, m), 4.33 (2H, s),
7.25-7.54 (5H, m), 7.54-7.60 (5H, m)

Reference Example 3

60 ml of concentrated hydrochloric acid and 13.3 g of 10% palladium-carbon were added to a solution
20 of 266 g of 4-[N-methyl-N-(2-phenylethyl)amino]-1-benzylpiperidine in 1 liter of ethanol and 500 ml of water. The mixture was stirred at a hydrogen pressure of 1 atm. at 60°C for 5 hours. 10% palladium-carbon was removed by filtration and then washed with ethanol. The
25 filtrate and the washings were combined and concentrated under reduced pressure. The residue was added to ice

water. The mixture was made alkaline with a 25% aqueous sodium hydroxide solution and then extracted with methylene chloride. The extract was water-washed and then concentrated under reduced pressure. The residue
5 was subjected to vacuum distillation to obtain 131.9 g of 4-[N-methyl-N-(2-phenylethyl)amino]piperidine as a colorless oil.

Boiling point: 137-139°C/0.2 mmHg

Reference Example 4

10 60 ml of 5 N hydrochloric acid was added to a solution of 5.8 g of 4-{N-methyl-N-[2-(4-methylthio-phenyl)ethyl]amino}-1-benzoylpiperidine in 20 ml of ethanol. The mixture was refluxed by heating, for 12 hours. To the reaction mixture was added 100 ml of
15 ethanol, followed by concentration under reduced pressure. To the residue was added ice water. The mixture was made basic with a 25% aqueous sodium hydroxide solution and then extracted with chloroform. The extract was water-washed, dried with anhydrous
20 sodium sulfate, and concentrated under reduced pressure to obtain 3.7 g of 4-{N-methyl-N-[2-(4-methylthio-phenyl)ethyl]amino}piperidine as a light yellow oily substance.

Reference Example 5

25 A suspension of 16.4 g of ethyl 4-fluorobenzoate, 20 g of triazole and 20 g of potassium

carbonate in 50 ml of dimethyl sulfoxide was stirred in a nitrogen atmosphere at 130°C for 1.5 hours. The reaction mixture was poured into ice water. The mixture was extracted with ethyl acetate. The extract was
5 water-washed, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluant: methylene chloride/methanol = 100/1 to 50/1). The former eluate portion was subjected to crystallization
10 with diisopropyl ether. The resulting crystals were recrystallized from ethanol-water to obtain 3.1 g of ethyl 4-(1,2,4-triazol-1-yl)benzoate as colorless needle-like crystals.

Melting point: 97-99°C

15 The latter eluate portion was subjected to precipitation with diethyl ether. The precipitate was collected by filtration to obtain 1.3 g of ethyl 4-(1,2,4-triazol-4-yl)benzoate as a white powder.

Melting point: 209-211°C.

20 Reference Example 6

5.5 ml of a 5 N aqueous sodium hydroxide solution was added to a solution of 1.2 g of ethyl 4-(1,2,4-triazol-4-yl)benzoate in 15 ml of ethanol. The mixture was stirred at 50-60°C for 1 hour. The reaction
25 mixture was concentrated under reduced pressure. To the residue was added ice water. The mixture was made acidic with acetic acid. The resulting crystals were

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collected by filtration, water-washed, and dried to obtain 0.95 g of 4-(1,2,4-triazol-4-yl)benzoic acid as a white powder. Melting point: 300°C or above

¹H-NMR (250 MHz, DMSO-d₆) δ ppm: 7.87 (2H, d, J=8.5 Hz), 8.09 (2H, d, J=8.5 Hz), 9.24 (2H, s), 13.21 (1H, brs)

Reference Example 7

A solution of 5.75 g of sodium nitrite in 30 ml of water was dropwise added to a solution of 11.7 g of methyl 3-aminobenzoate and 20 ml of concentrated hydrochloric acid in 200 ml of water, at about 0°C with cooling with ice-methanol. The mixture was stirred at the same temperature for 5 minutes. The mixture was then added to 650 ml of a 6% aqueous sulfurous acid solution being ice-cooled. The resulting mixture was stirred at 50-60°C for 2 days. The reaction mixture was allowed to cool and then extracted with ethyl acetate. The aqueous layer was made basic with an aqueous sodium hydroxide solution and extracted with ethyl acetate. The extract was washed with water and an aqueous sodium chloride solution in this order, then dried with anhydrous sodium sulfate, and concentrated under reduced pressure. To the residue was added ethanol. The mixture was made acidic with concentrated hydrochloric acid and then concentrated under reduced pressure. To the residue was added a slight amount of ethanol. The resulting insolubles were collected by filtration,

washed with ethanol, and dried to obtain 3.1 g of methyl 3-hydrazinobenzoate hydrochloride as a white powder.

Melting point: 184.5-185.5°C

Reference Example 8

5 1.04 g of 1,3,5-triazine was added to a solution of 3.7 g of methyl 3-hydrazinobenzoate hydrochloride in 20 ml of ethanol. The mixture was refluxed by heating, for 3 hours. The reaction mixture was allowed to cool and mixed with chloroform. The
10 resulting insolubles were removed by filtration. The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (eluant: methylene chloride/methanol = 100/0 to 100/1) and then subjected to crystallization from diisopropyl
15 ether. The crystals were collected by filtration to obtain 2.0 g of methyl 3-(1,2,4-triazol-1-yl)benzoate as colorless needle-like crystals.

Melting point: 115-120°C

20 Reference Example 9

 5.6 ml of concentrated hydrochloric acid was added to a suspension of 7.5 g of methyl 4-hydrazinobenzoate in 150 ml of water. Thereto was dropwise added a solution of 4.6 g of glyoxylic acid in 20 ml of water.
25 The mixture was stirred for 10 minutes. The resulting crude crystals were collected by filtration, water-washed, and suspended in 150 ml of toluene. The

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suspension was concentrated under reduced pressure. This procedure was repeated again and the resulting concentrate was dried. The concentrate was suspended in 150 ml of toluene. To the suspension were added 6.3 ml
5 of triethylamine and 9.7 ml of diphenyl phosphoryl azide in this order. The mixture was refluxed for 1 hour and then allowed to cool. The resulting insolubles were collected by filtration, washed with ethyl acetate, and recrystallized from methanol to obtain 4.3 g of methyl
10 4-(5-oxo-1,2,4-triazol-1-yl)benzoate as orange needle-like crystals.

¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 3.85 (3H, s), 8.05 (2H, d, J=9.2 Hz), 8.07 (2H, d, J=9.2 Hz), 8.20 (1H, s), 12.12 (1H, brs)

15 Reference Example 10

2.2 ml of thionyl chloride was added to 2.23 g of methyl 4-(2-hydroxyethyl)aminocarbonylbenzoate. The mixture was stirred for 15 minutes. Thereto was added 10 ml of diethyl ether. The reaction mixture was added
20 to 20 ml of a 5 N aqueous sodium hydroxide solution being cooled with an ice-methanol cryogen. The mixture was stirred for a while. The resulting precipitate was collected by filtration and water-washed to obtain a white powder. The powder was dissolved in 20 ml of
25 methanol. Thereto was added 4 ml of 5 N sodium hydroxide. The mixture was stirred at 40°C for 15 minutes and then concentrated under reduced pressure.

To the residue was added ice water. The mixture was made acidic with acetic acid. The resulting crystals were collected by filtration, washed with water and methanol in this order, and dried to obtain 1.6 g of 4-(2-oxazolin-2-yl)benzoic acid as a white powder.

Melting point: 300°C or above

¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 3.99 (2H, t, J=9.4 Hz), 4.43 (2H, t, J=9.4 Hz), 7.97 (2H, d, J=8.6 Hz), 8.02 (2H, d, J=8.6 Hz), 13.22 (1H, s)

10 Reference Example 11

4.7 g of 1,2,4-triazole and 9.5 g of potassium carbonate were added to a solution of 15 g of benzyl 4-bromobutyrate in 150 ml of acetonitrile. The mixture was refluxed by heating, for 1 hour. The reaction mixture was concentrated under reduced pressure. To the residue was added 30 ml of methylene chloride. The insolubles were collected by filtration and washed. The filtrate and the washings were combined and purified by silica gel column chromatography (eluant: methylene chloride/methanol = 50/1) to obtain 11.6 g of benzyl 4-(1,2,4-triazol-1-yl)butyrate as a colorless oily substance.

¹H-NMR (200 MHz, CDCl₃) δ ppm: 2.14-2.32 (2H, m), 2.32-2.44 (2H, m), 4.24 (2H, t, J=6.7 Hz), 5.13 (2H, s), 7.30-7.45 (5H, m), 7.94 (1H, s), 8.00 (1H, s)

Reference Example 12

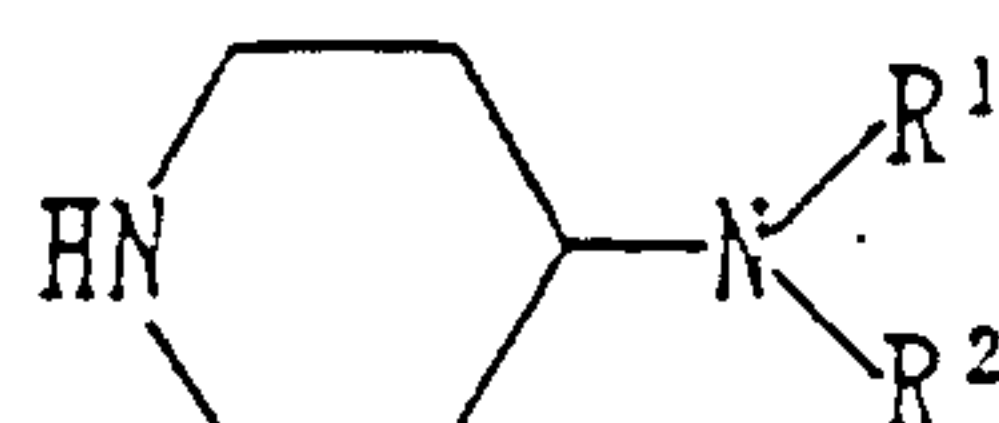
0.5 g of 5% palladium carbon was added to a solution of 11 g of benzyl 4-(1,2,4-triazol-1-yl)butyrate in 150 ml of ethanol. The mixture was stirred at a hydrogen pressure of 1 atm. at room temperature for 1 hour. Thereto was added 100 ml of ethanol. The mixture was heated and made uniform. Palladium carbon was collected by filtration and washed with ethanol. The filtrate and the washings were combined and concentrated under reduced pressure. To the residue was added a small amount of ethanol. The resulting insolubles were collected by filtration to obtain 6.2 g of 4-(1,2,4-triazol-1-yl)butyric acid as a white powder.

¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 1.98 (2H, quint, J=6.8 Hz), 2.21 (2H, t, J=6.8 Hz), 4.20 (2H, t, J=6.8 Hz), 7.96 (1H, s), 8.50 (1H, s), 12.19 (1H, s)

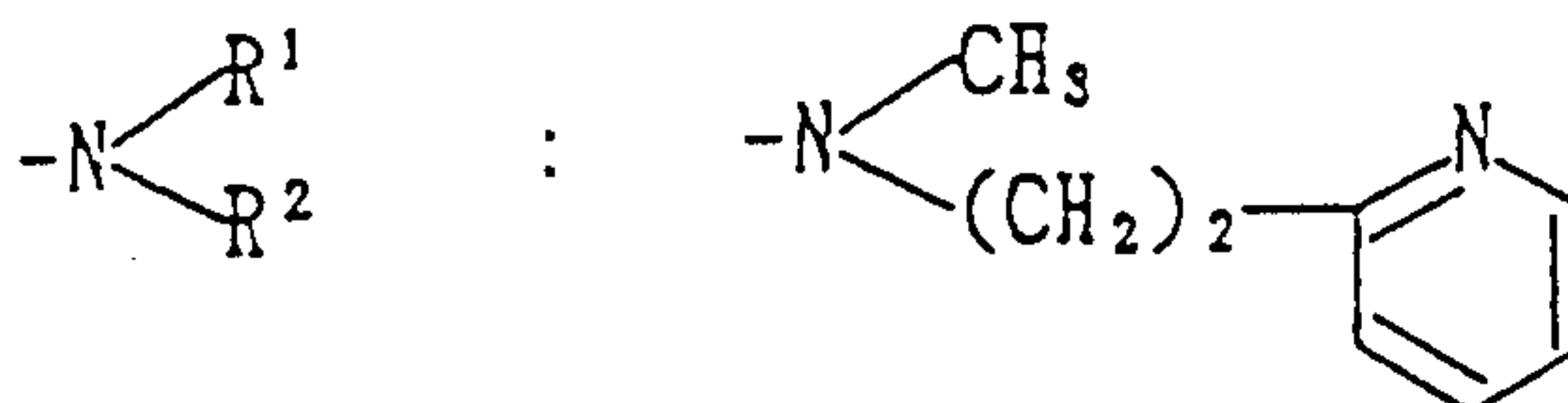
Reference Examples 13-28

Using suitable starting materials, the compounds shown in Table 1 were obtained in the same manner as in Reference Example 3 or 4.

[Table 1]

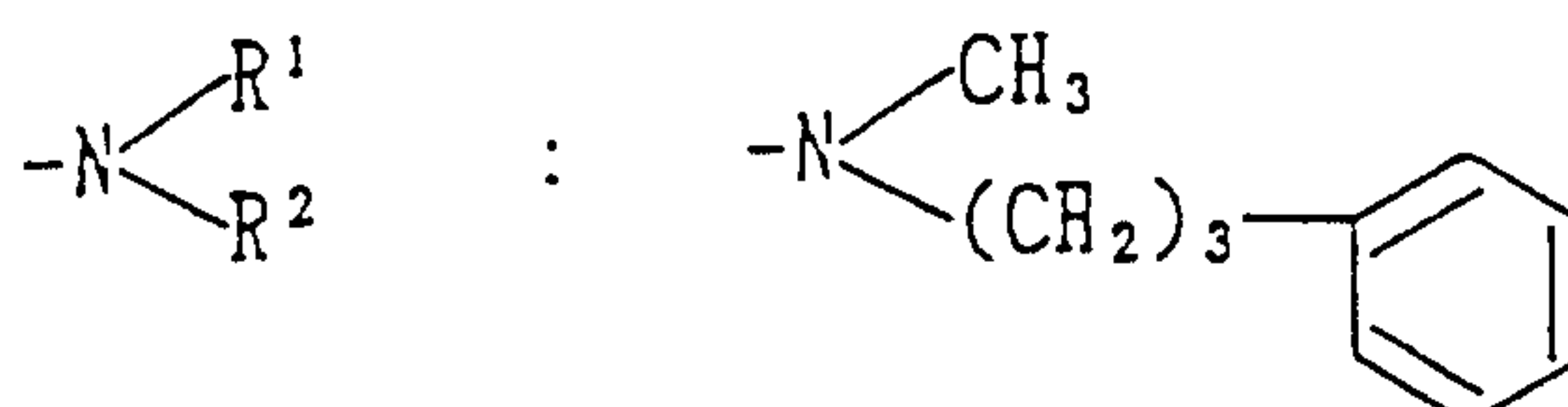


Reference Example 13
Structural formula:



Crystal form: colorless oil
Salt form: free
NMR value: 1)

Reference Example 14
Structural formula:

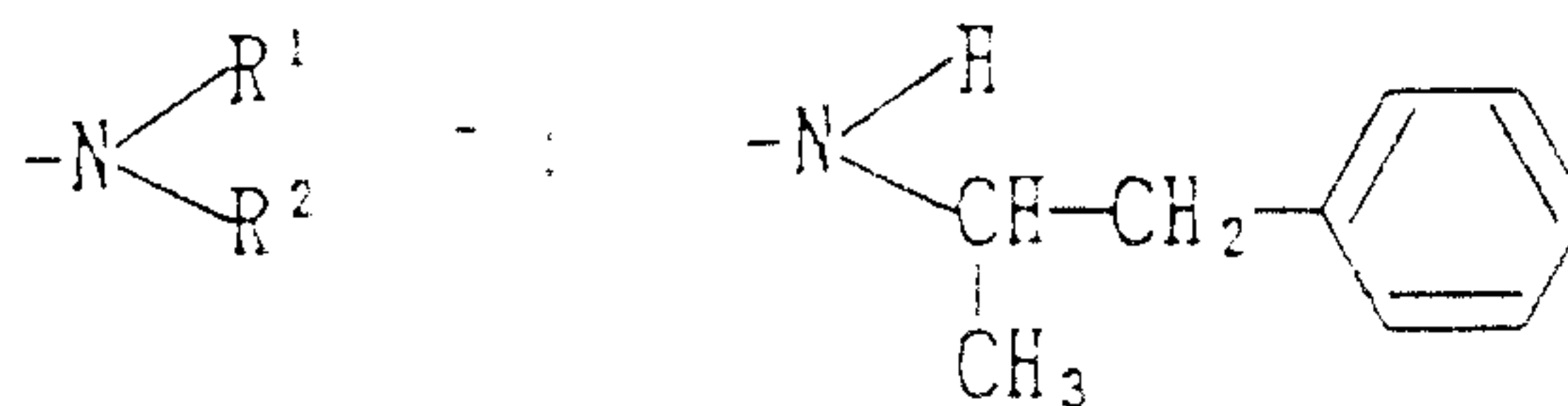


Crystal form: colorless oil
Salt form: free
NMR value: 2)

[Table 1 (Continued)]

Reference Example 15

Structural formula:



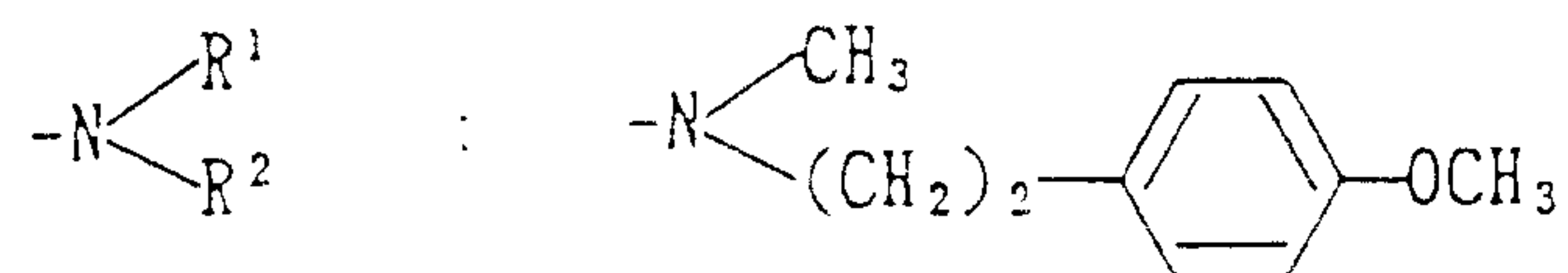
Crystal form: colorless oil

Salt form: free

NMR value: 3)

Reference Example 16

Structural formula:



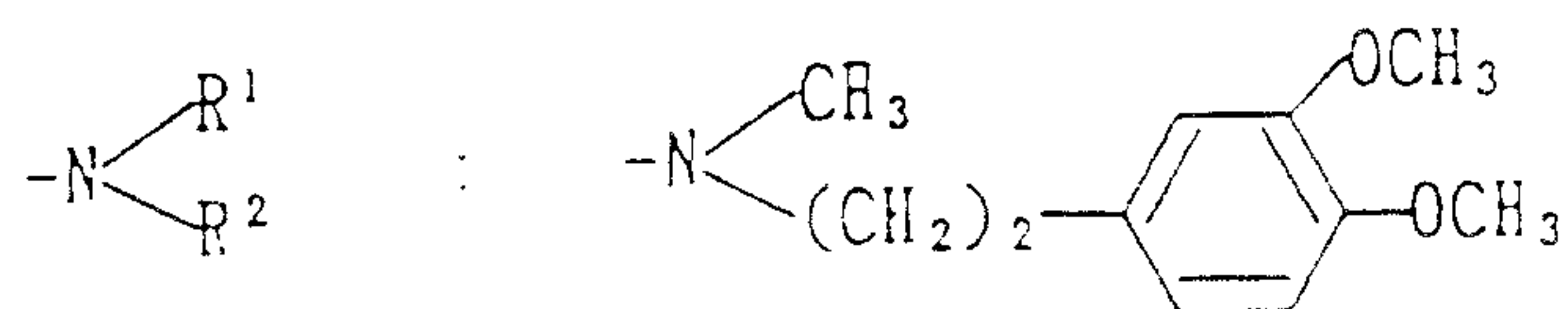
Crystal form: yellow oil

Salt form: free

NMR value: 4)

Reference Example 17

Structural formula:



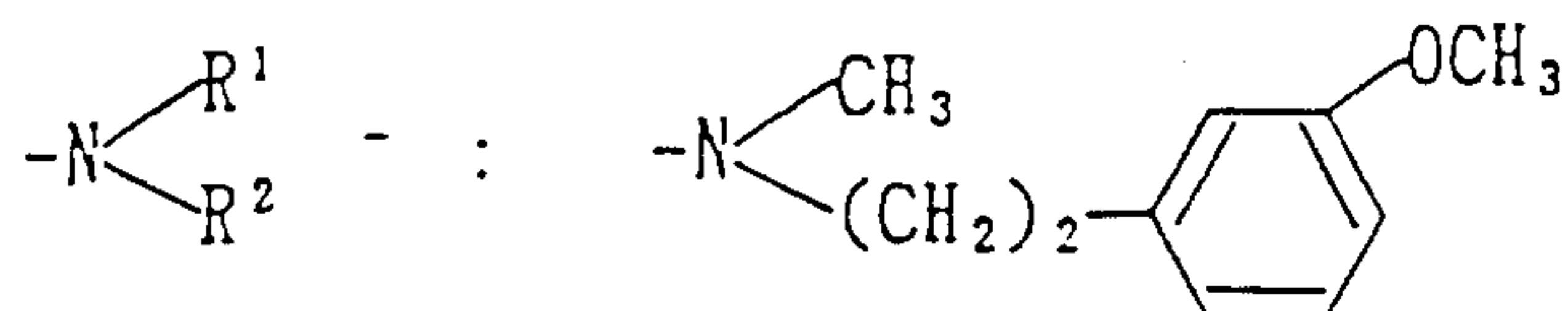
Crystal form: colorless oil

Salt form: free

NMR value: 5)

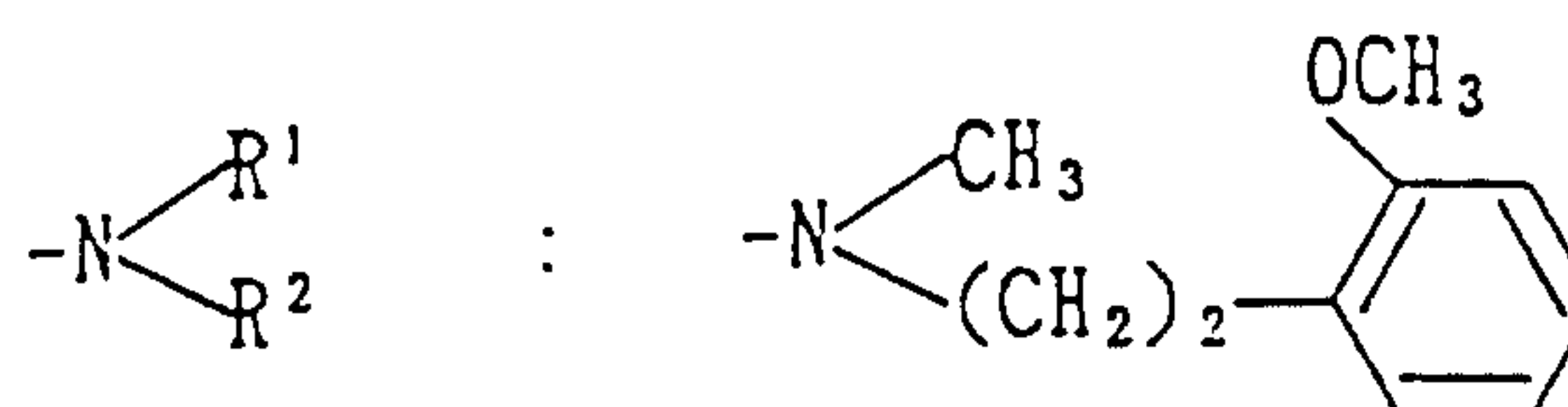
{Table 1 (Continued)}

Reference Example 18
Structural formula:



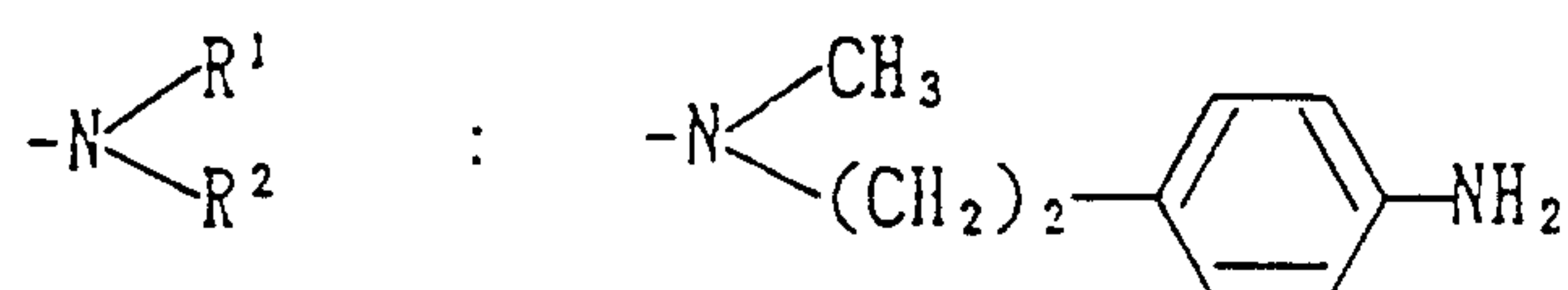
Crystal form: light yellow oil
Salt form: free
NMR value: 6)

Reference Example 19
Structural formula:



Crystal form: yellow oil
Salt form: free
NMR value: 7)

Reference Example 20
Structural formula:

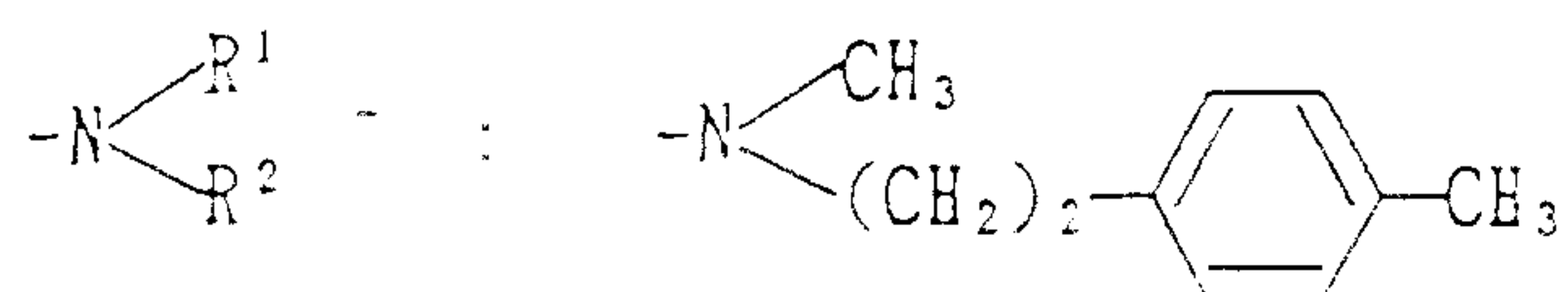


Crystal form: yellow oil
Salt form: free
NMR value: 8)

(Table 1 (Continued))

Reference Example 21

Structural formula:



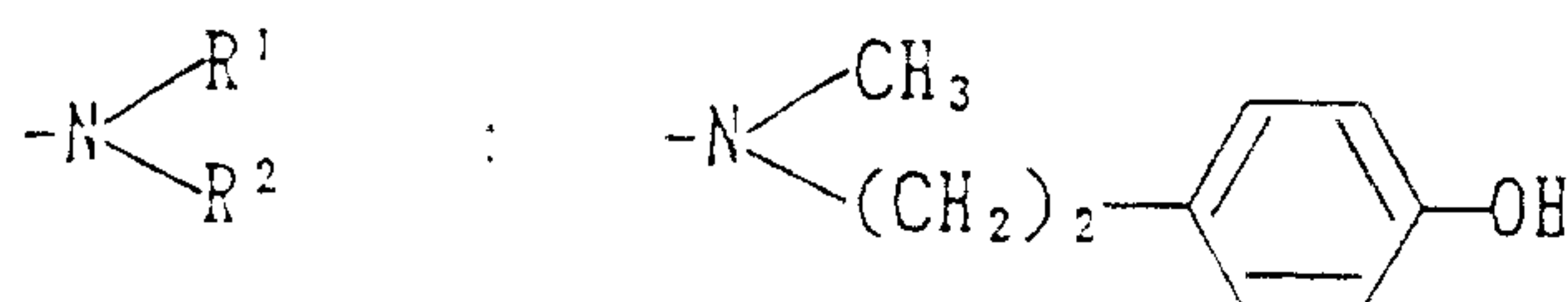
Crystal form: yellow oil

Salt form: free

NMR value: 9)

Reference Example 22

Structural formula:



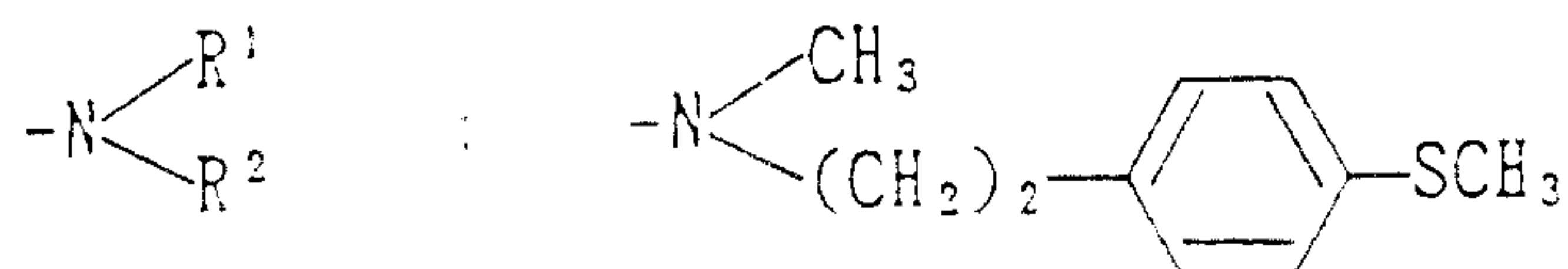
Crystal form: white powder

Salt form: dihydrobromide

NMR value: 10)

Reference Example 23

Structural formula:



Crystal form: light yellow oil

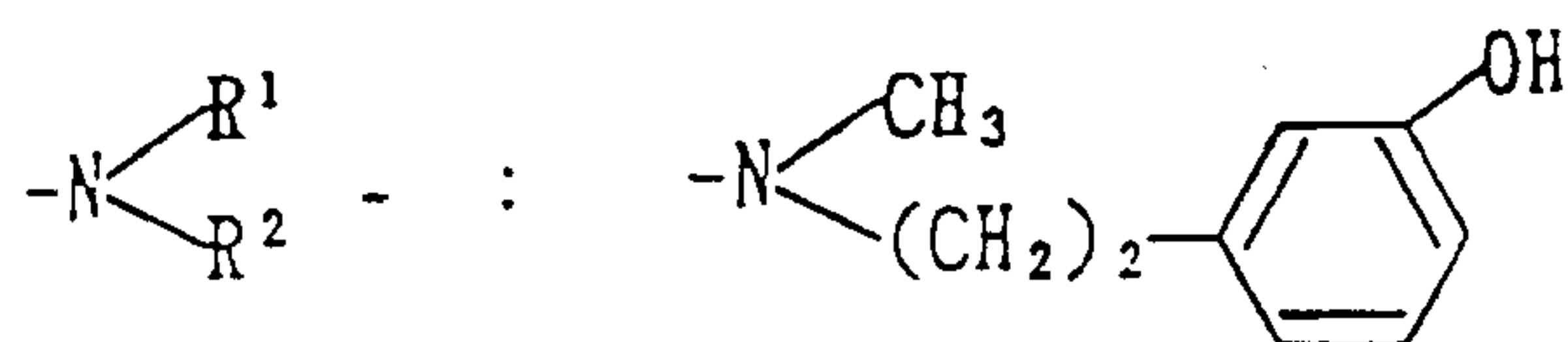
Salt form: free

NMR value: 11)

(Table 1 (Continued))

Reference Example 24

Structural formula:



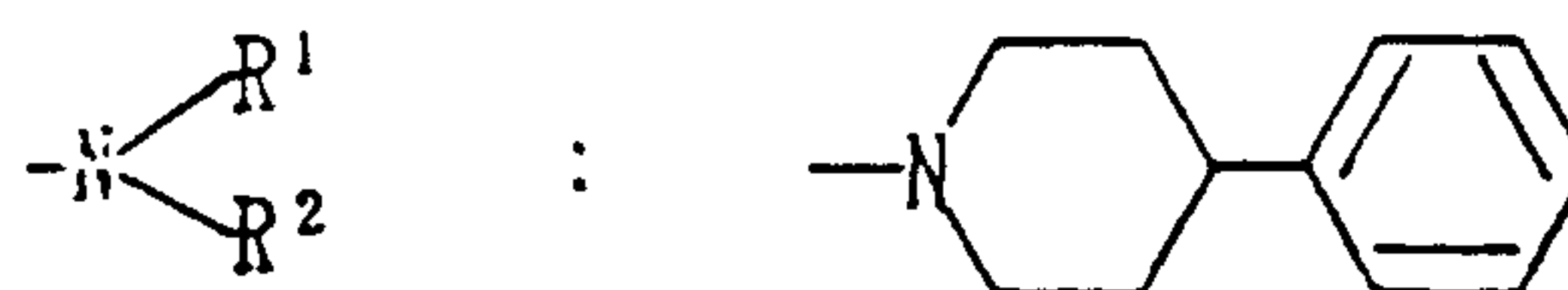
Crystal form: yellow oil

Salt form: free

NMR value: 12)

Reference Example 25

Structural formula:



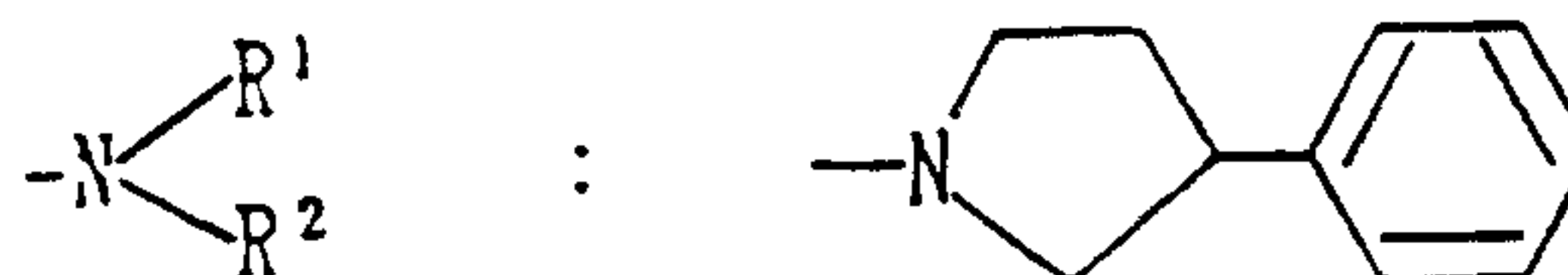
Crystal form: white powder

Melting point (°C): 82-83

Salt form: free

Reference Example 26

Structural formula:



Crystal form: colorless oil

Boiling point (°C): 170-180/0.4 mmHg

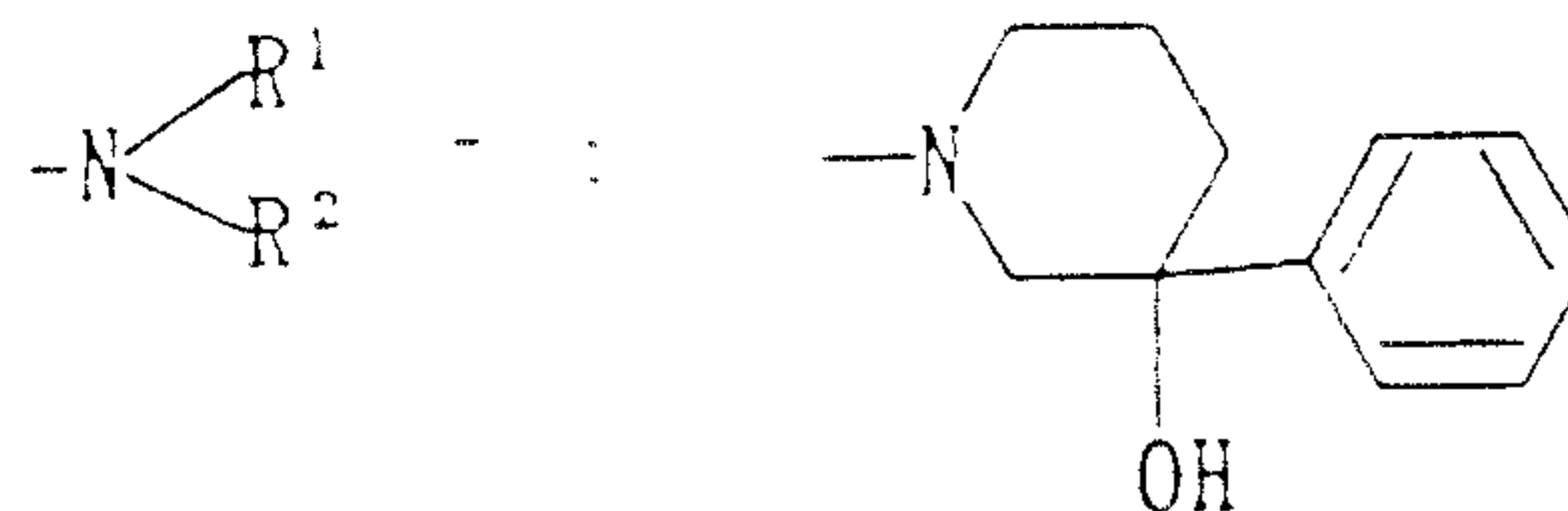
Salt form: free

NMR value: 13)

(Table 1 (continued))

Reference Example 27

Structural formula:



Crystal form: white powder

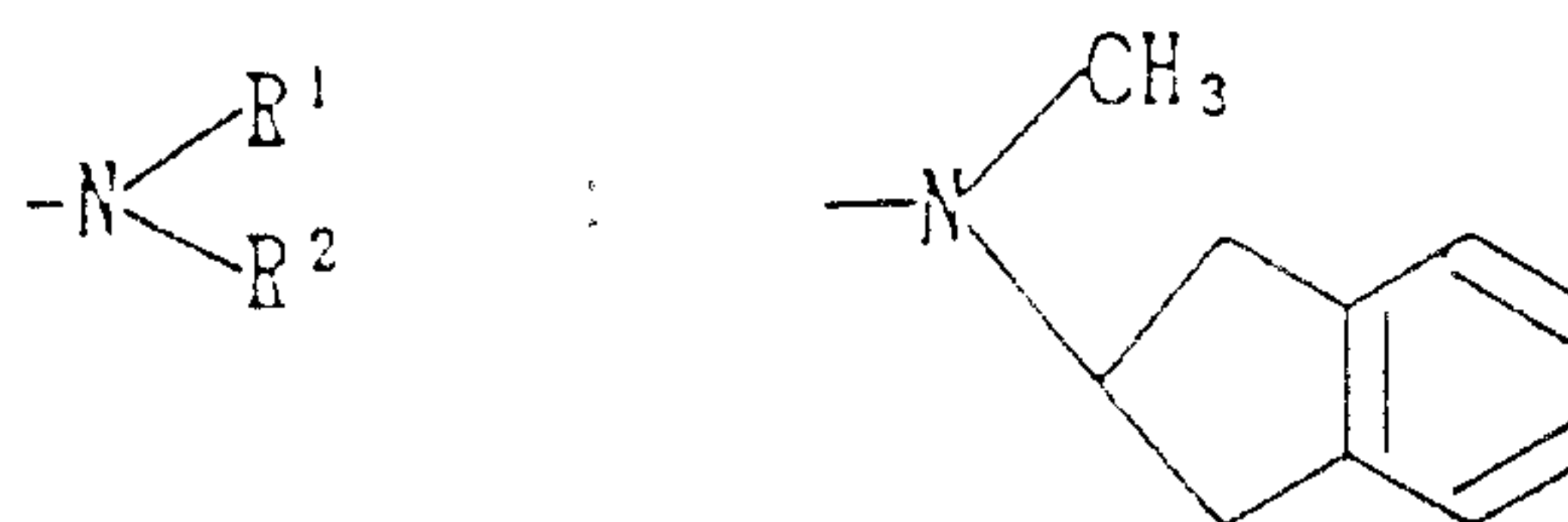
Melting point ($^{\circ}$): 250 or above (decompd.)

Salt form: dihydrochloride

NMR value: 14)

Reference Example 28

Structural formula:



Crystal form: light orange oil

Salt form: free

NMR value: 15)

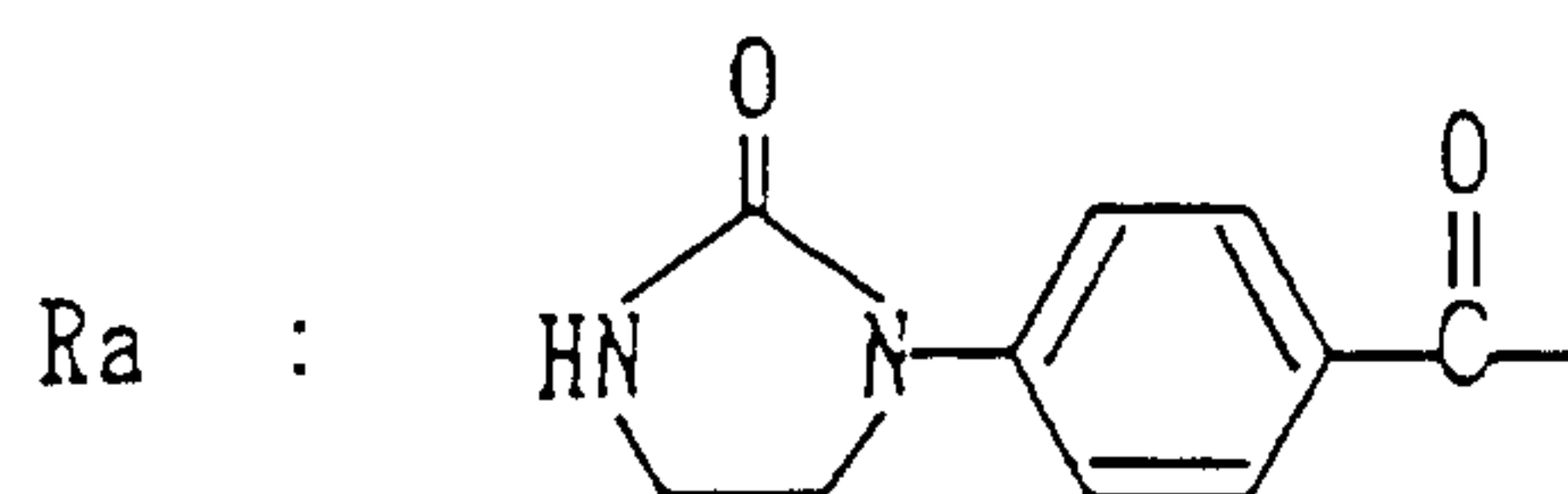
Reference Examples 29 - 40

By the method similar to that of employed in Reference Example 5, and by using suitable starting materials, there were prepared compounds of Reference Examples 29 - 40 as shown in the following Table 2.

[Table 2]

Ra-OR²³

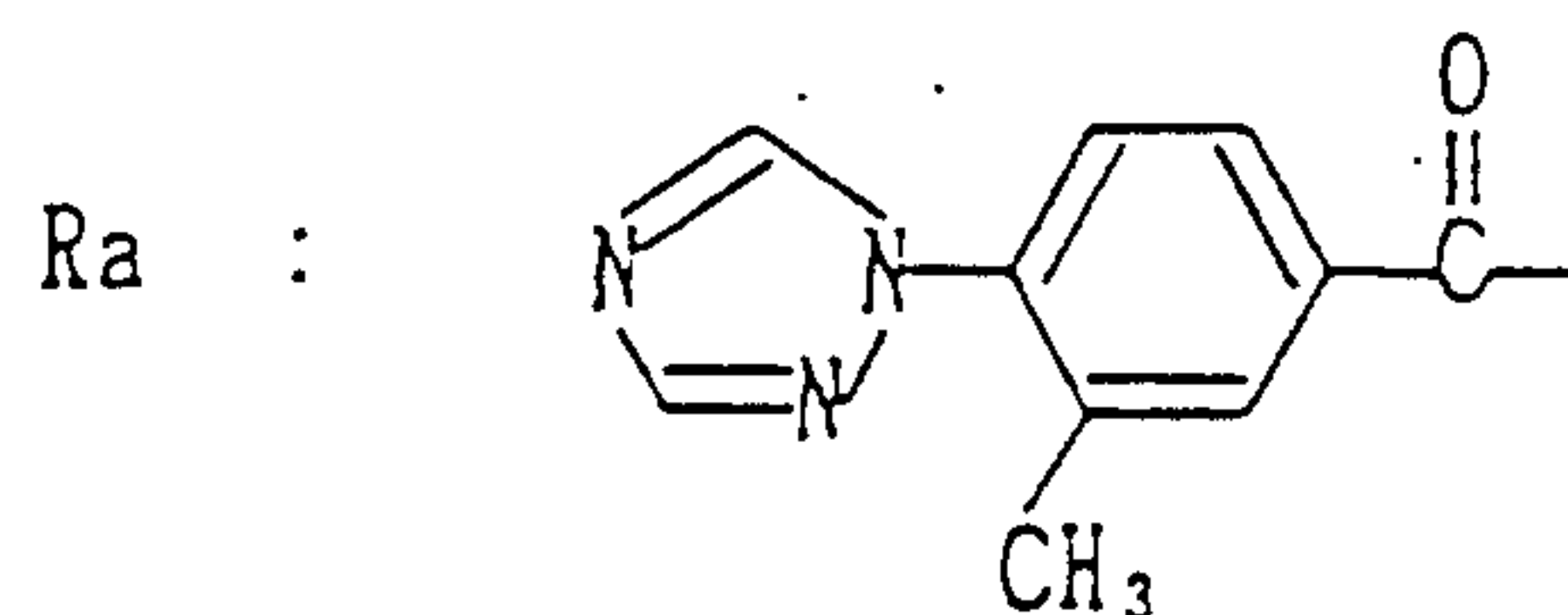
Reference Example 29
Structural formula:



R²³ : C₂H₅

Crystal form: white powder
Salt form: free
NMR value: 16)

Reference Example 30
Structural formula:

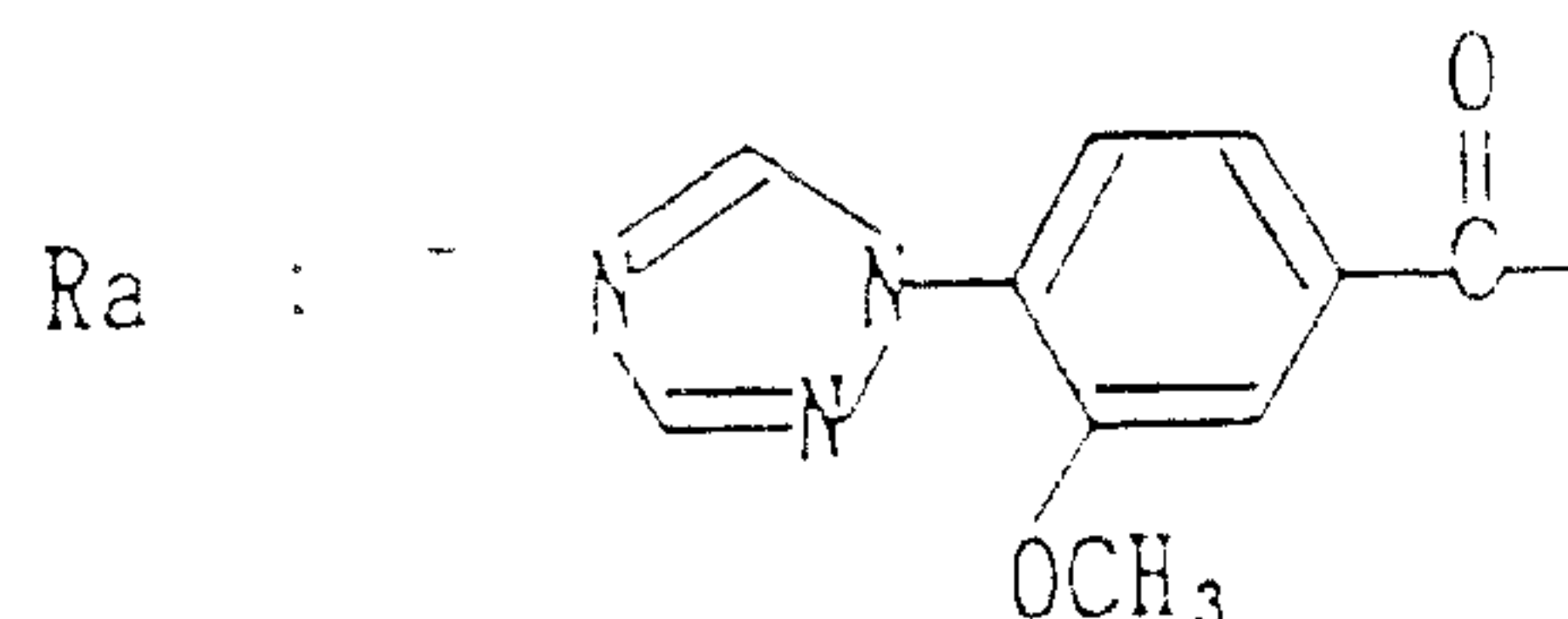


R²³ : CH₃

Crystal form: light yellow needles
Recrystallization solvent: ethyl acetate-n-hexane
Melting point (°C): 126-129
Salt form: free

(Table 2 (continued))

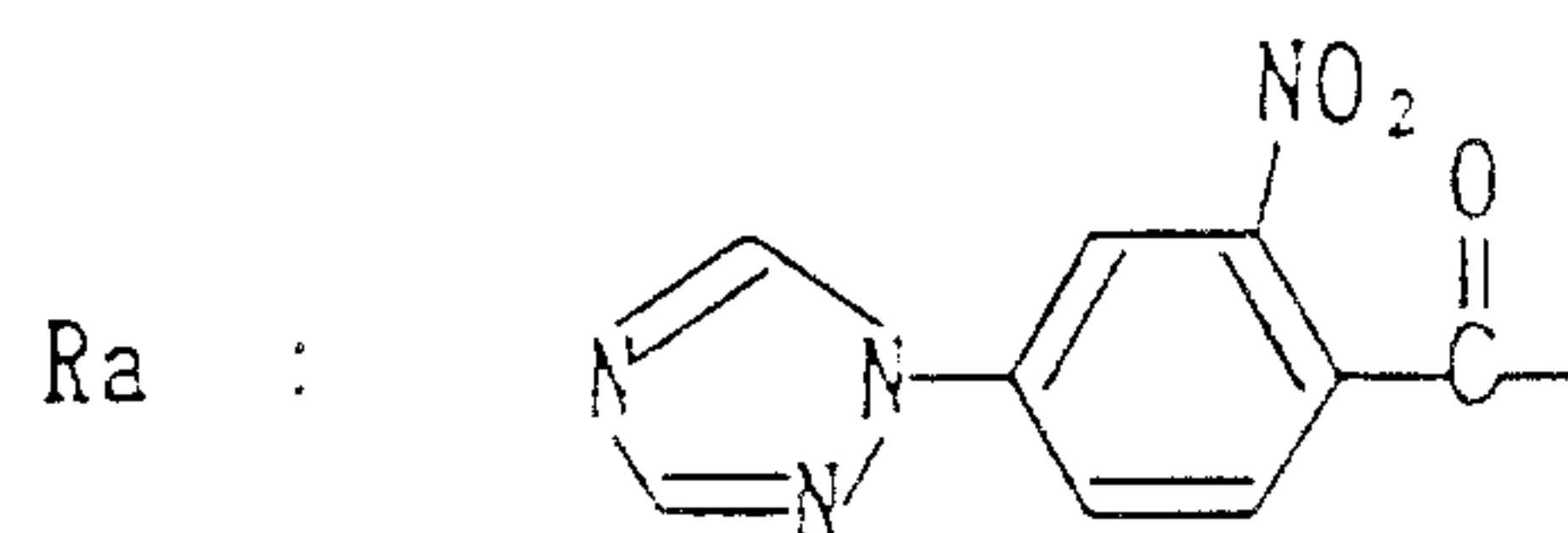
Reference Example 31
Structural formula:



R²³ : CH₃

Crystal form: light red prisms
Melting point (°C): 105-107
Salt form: free

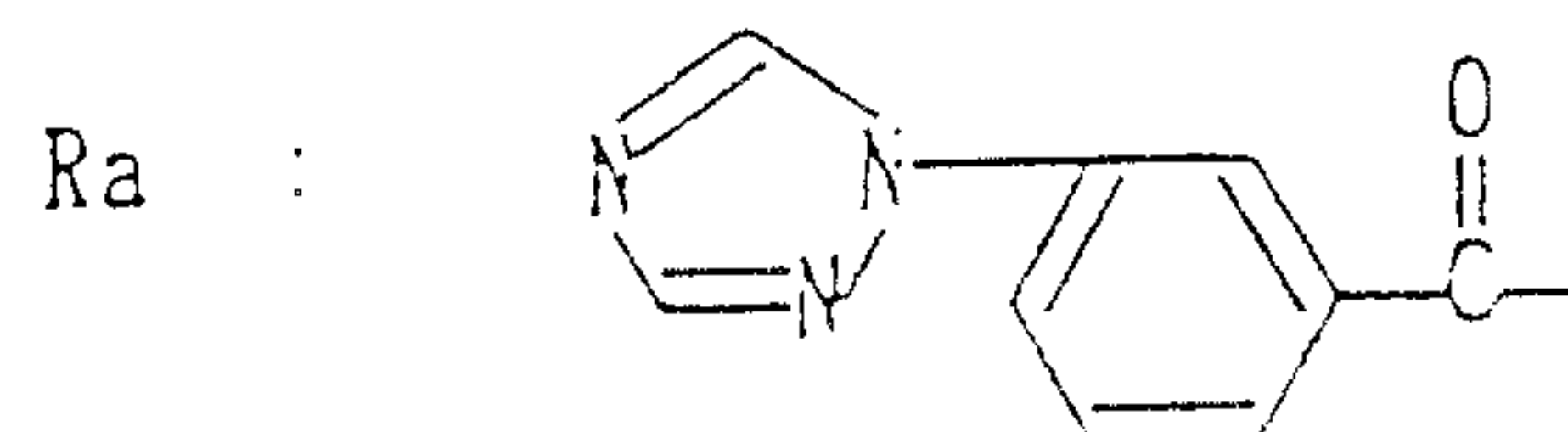
Reference Example 32
Structural formula:



R²³ : CH₃

Crystal form: white powder
Salt form: free
NMR value: 17)

Reference Example 33
Structural formula:



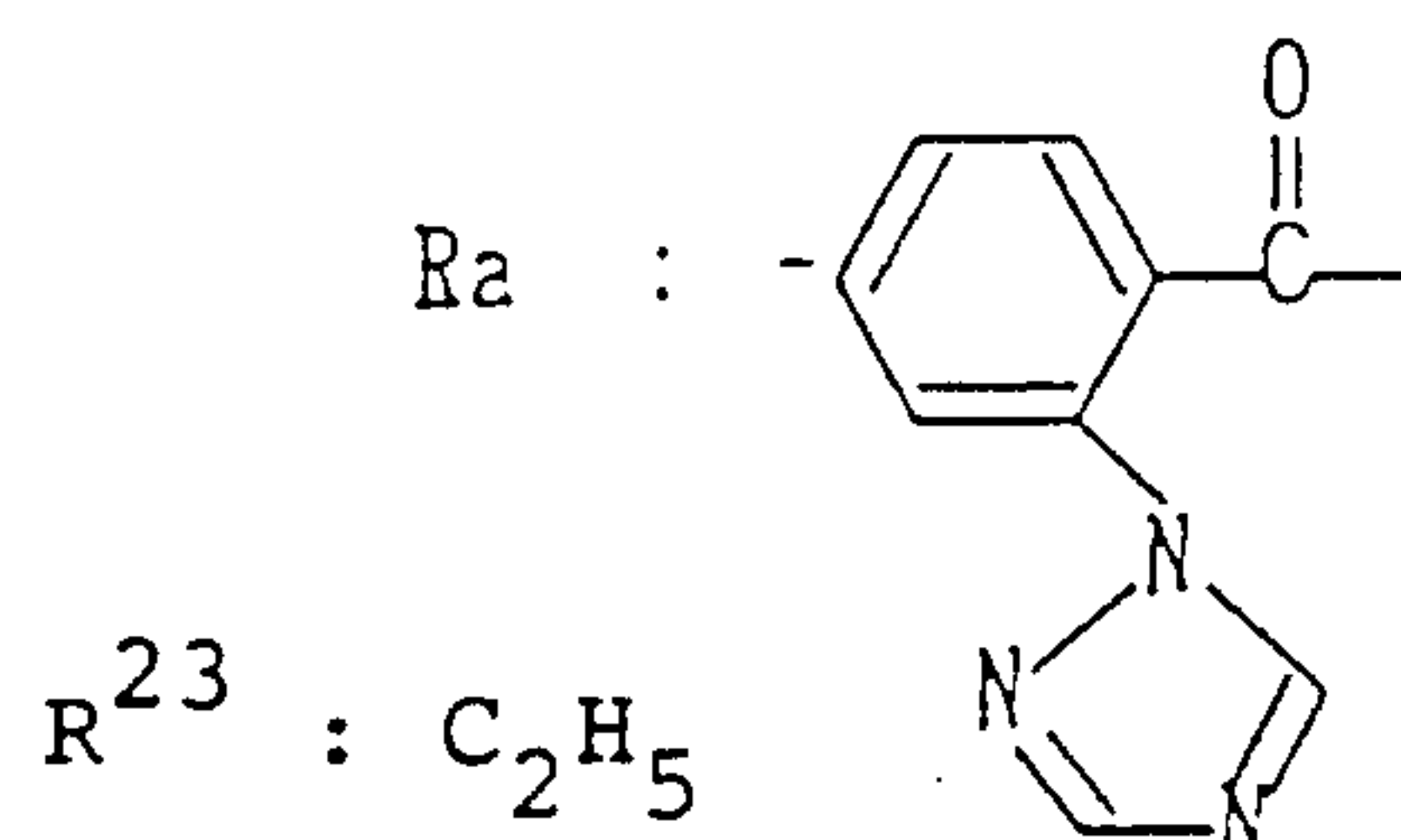
R²³ : CH₃

Crystal form: colorless needles
Salt form: free
NMR value: 18)

{Table 2 (continued)}

Reference Example 34

Structural formula:



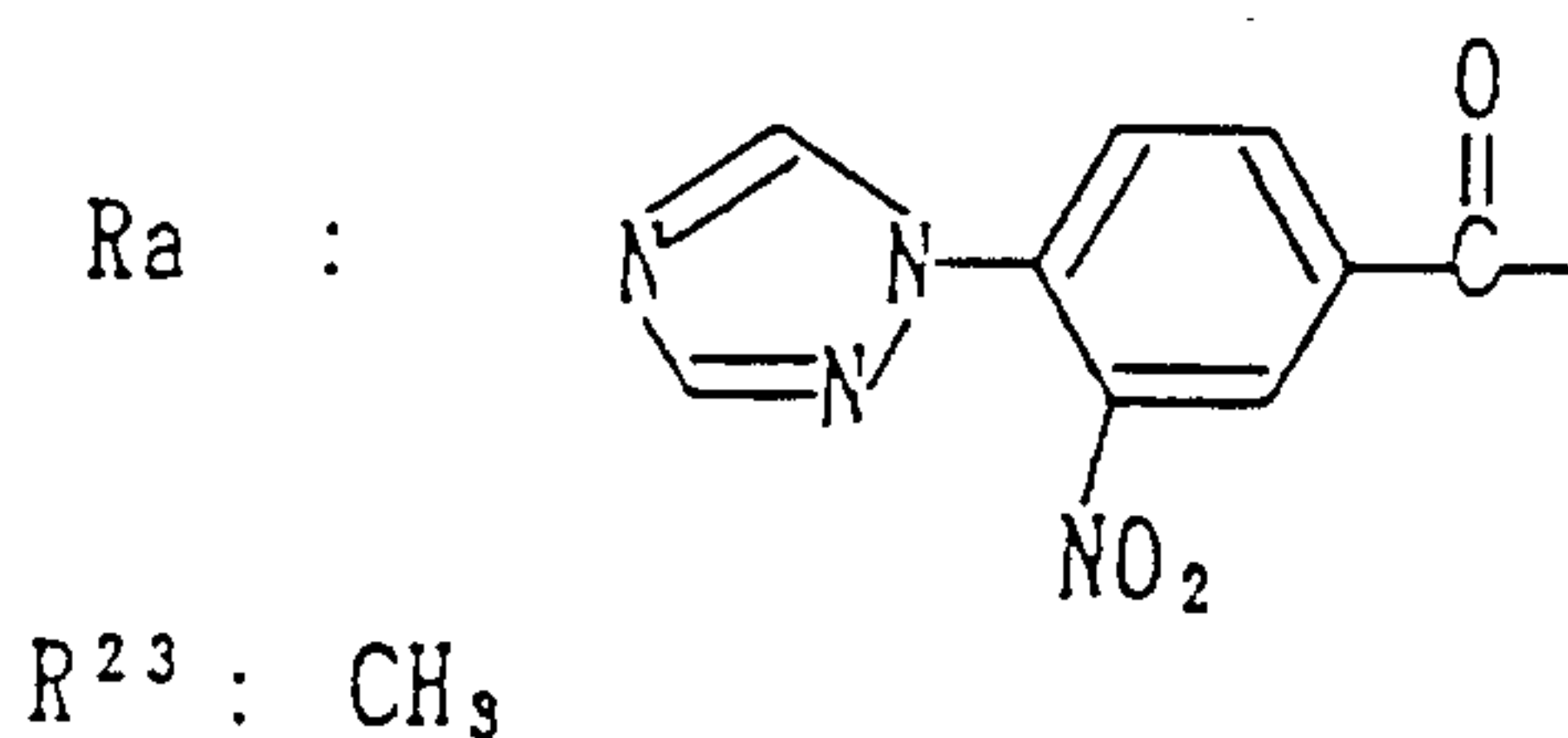
Crystal form: colorless oil

Salt form: free

NMR value: 19)

Reference Example 35

Structural formula:



Crystal form: colorless needles

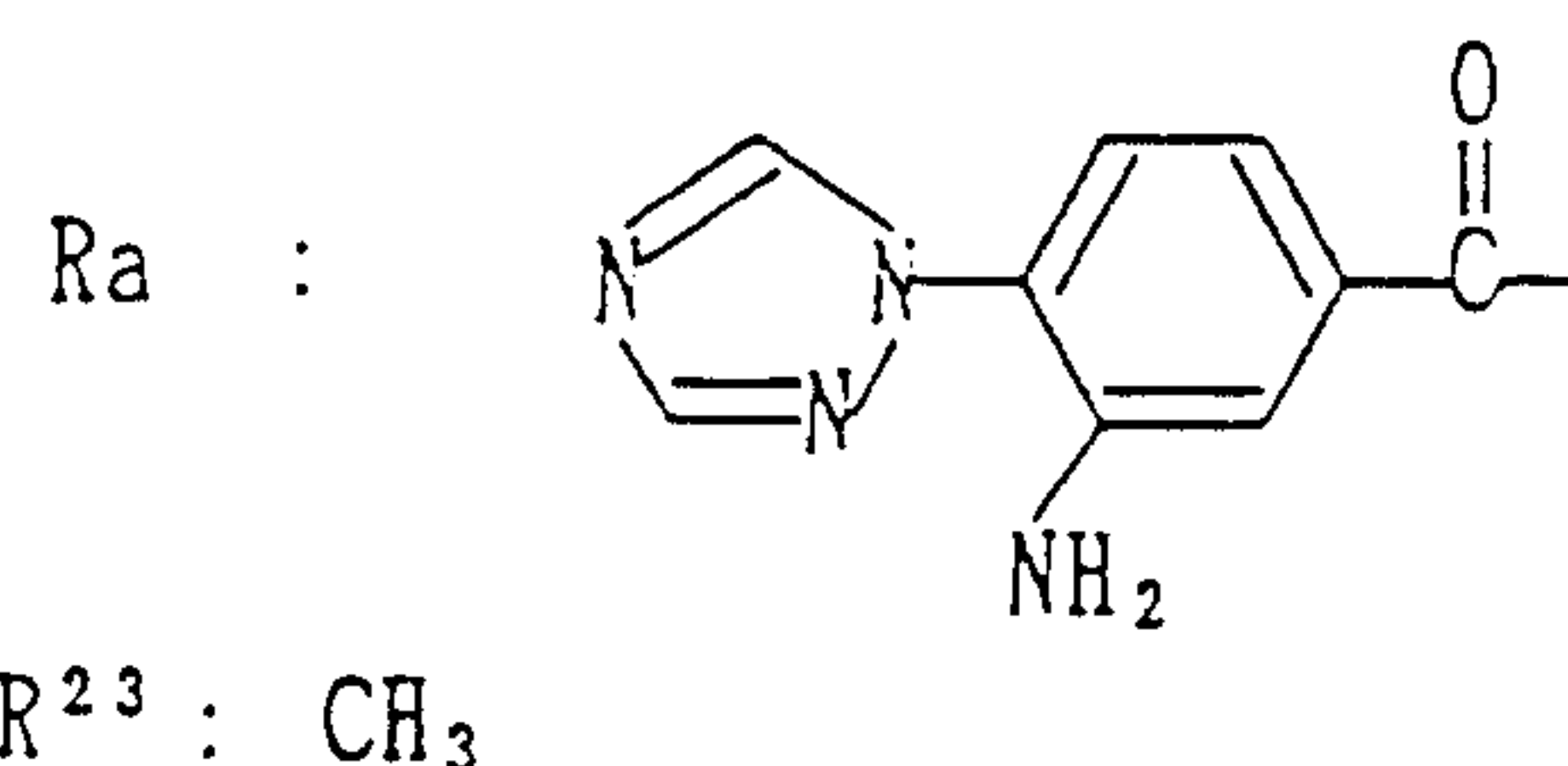
Recrystallization solvent: methanol-water

Melting point (°C): 99.5-100.5

Salt form: free

Reference Example 36

Structural formula:



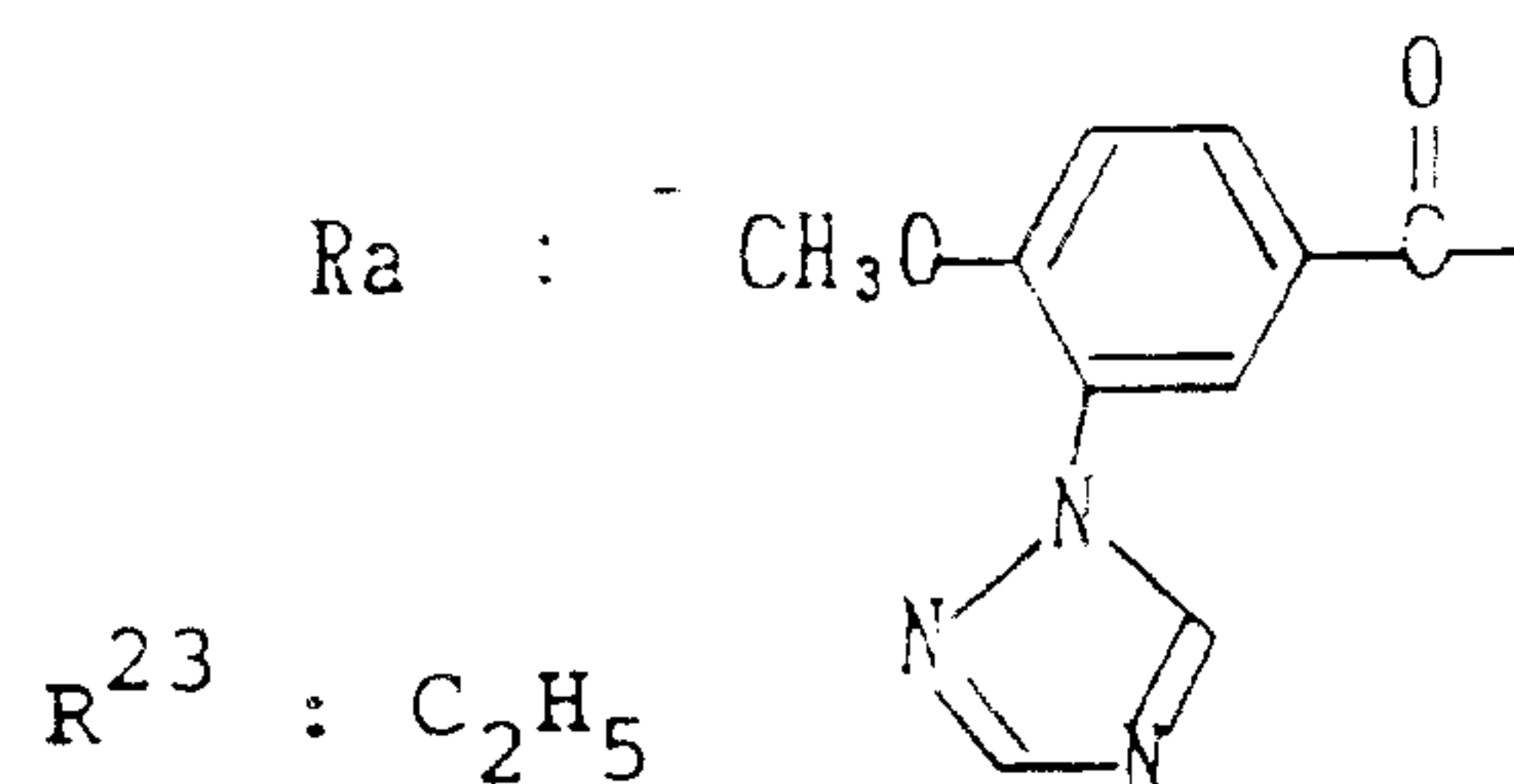
Crystal form: colorless needles

Melting point (°C): 135.5-137.5

Salt form: free

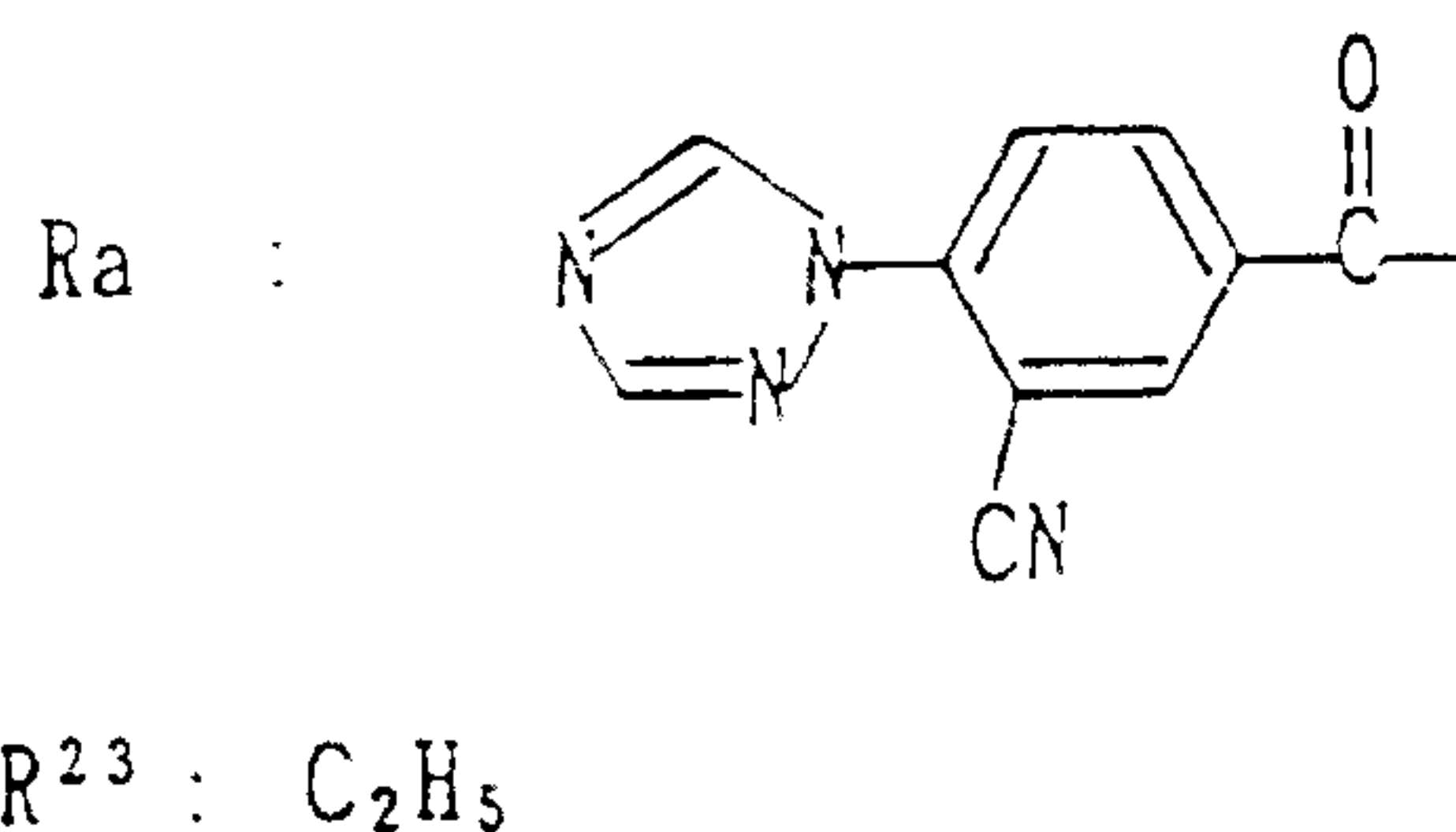
[Table 2 (continued)]

Reference Example 37
Structural formula:



Crystal form: colorless needles
Recrystallization solvent: ethanol
Melting point (°C): 134-136
Salt form: free

Reference Example 38
Structural formula:

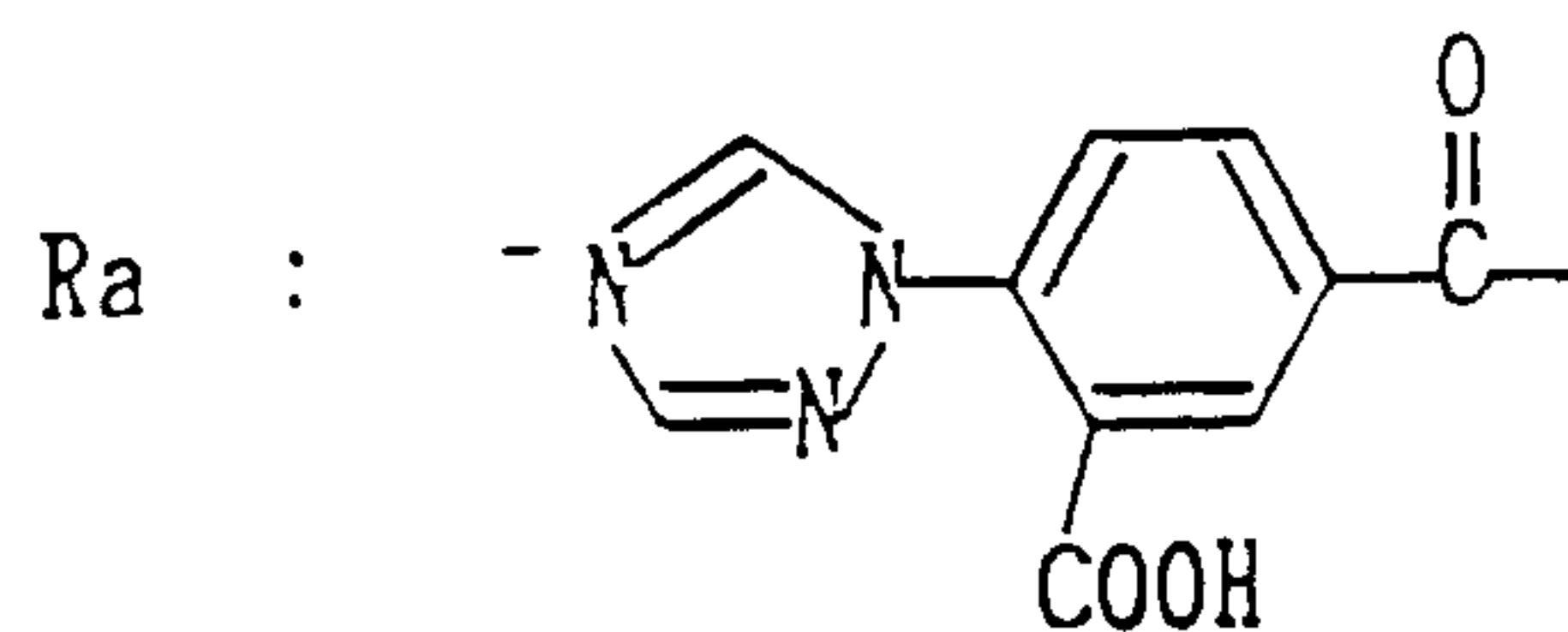


Crystal form: colorless scales
Recrystallization solvent: ethanol
Melting point (°C): 108-110
Salt form: free

[Table 2 (continued)]

Reference Example 39

Structural formula:



Crystal form: colorless needles

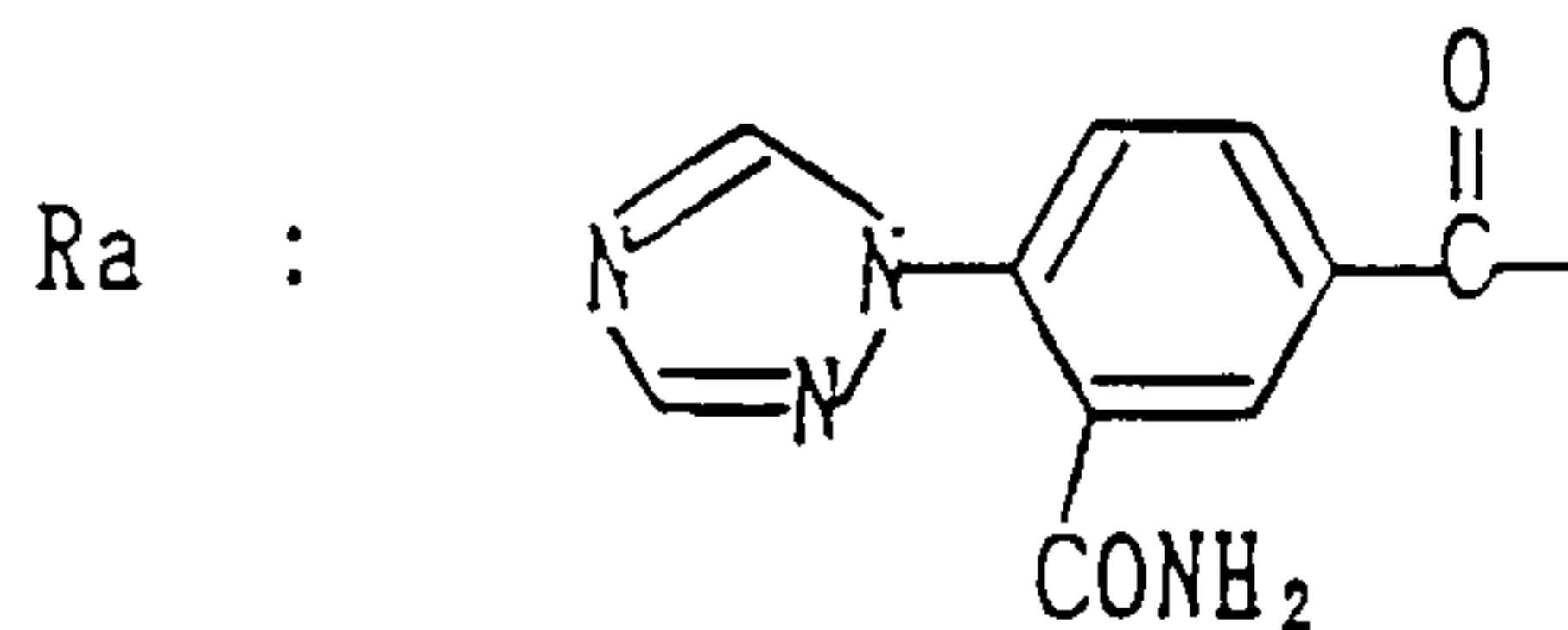
Recrystallization solvent: ethanol

Melting point (°C): 201-202.5

Salt form: free

Reference Example 40

Structural formula:



Crystal form: colorless prisms

Melting point (°C): 163-164.5

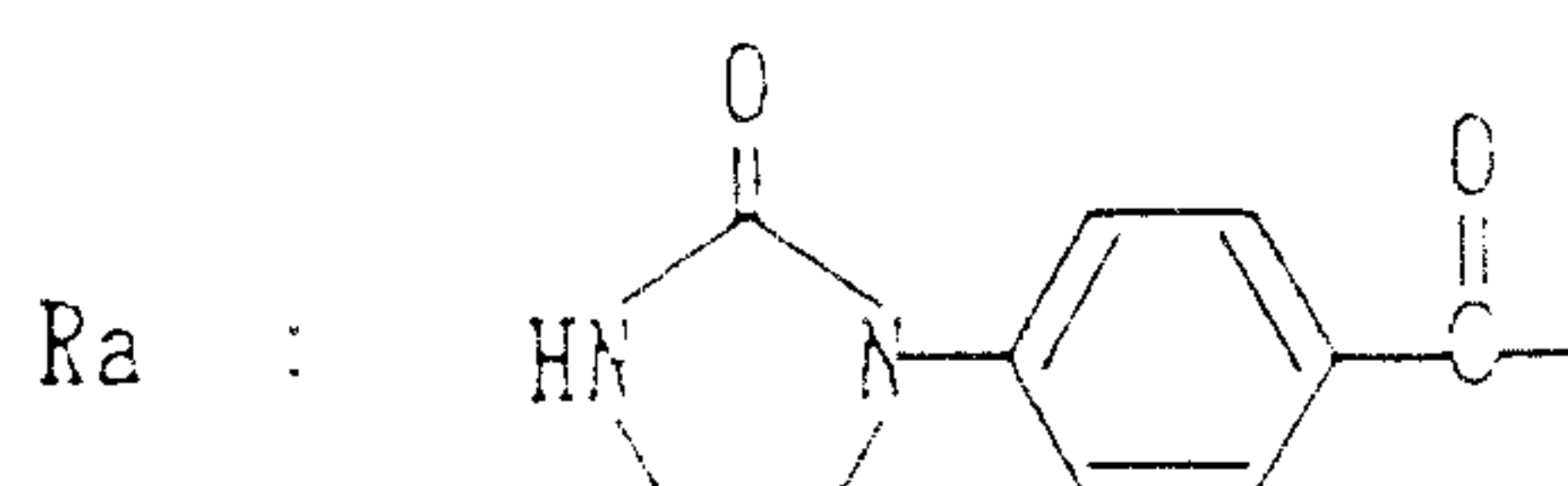
Salt form: free

Reference Examples 41 - 73

By the method similar to that of employed in Reference Example 6 or 12, and by using suitable starting materials, there were prepared compounds of Reference Examples 41 - 73 as shown in the following Table 3.

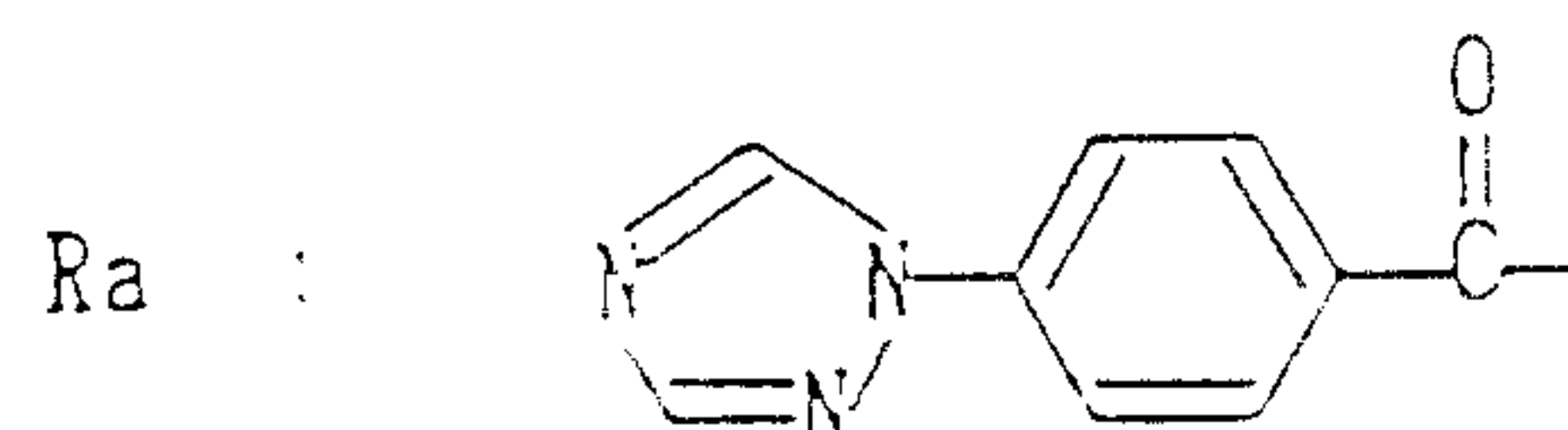
[Table 3] Ra-OH

Reference Example 41
Structural formula:



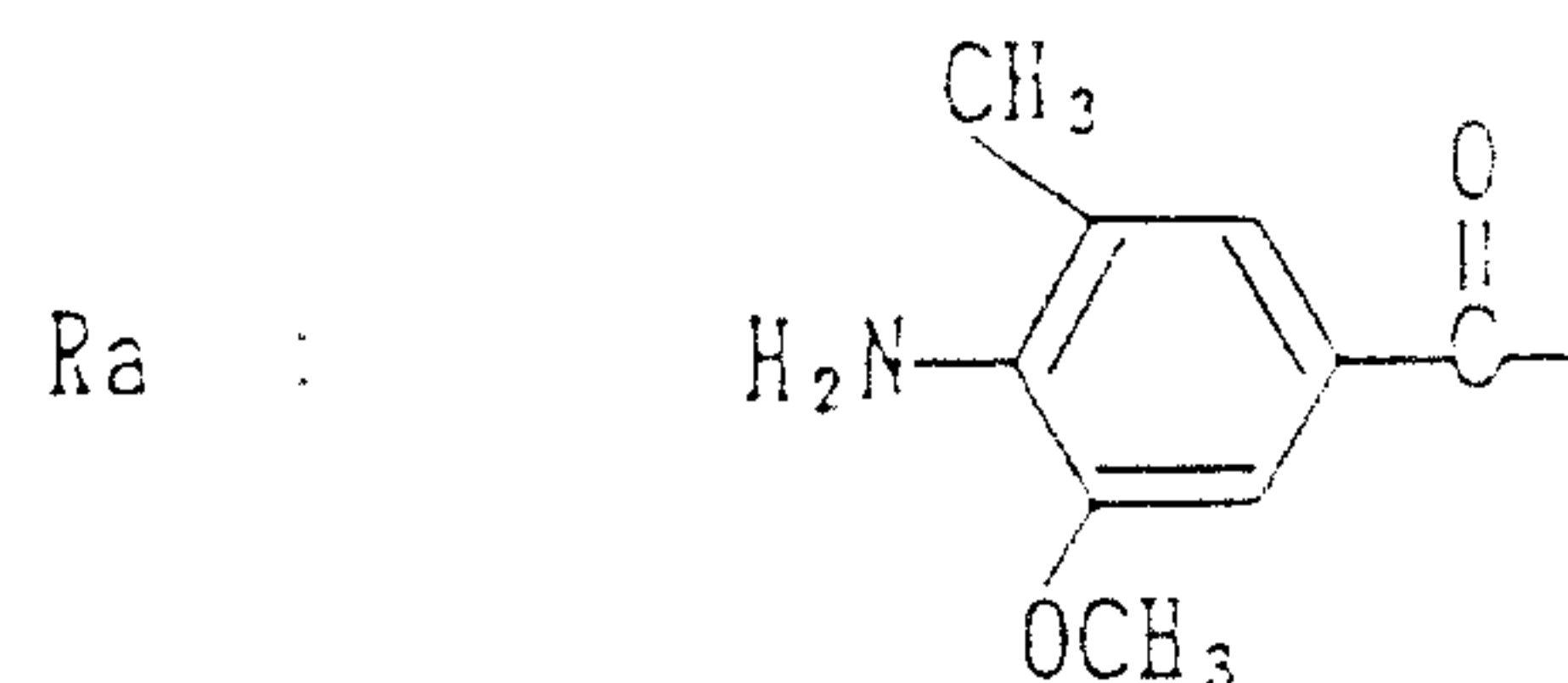
Crystal form: white powder
Salt form: free
NMR value: 20)

Reference Example 42
Structural formula:



Crystal form: white powder
Melting point (°C): 300 or above
Salt form: free
NMR value: 21)

Reference Example 43
Structural formula:

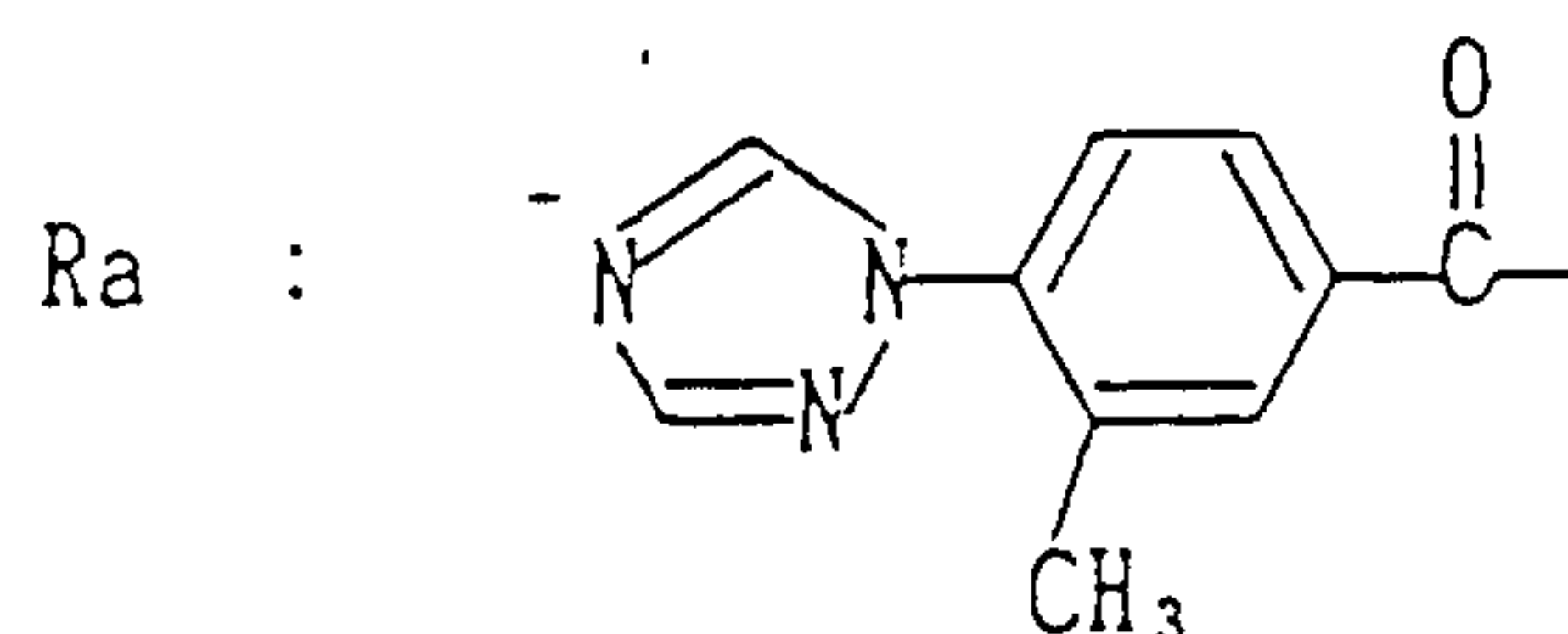


Crystal form: white powder
Salt form: free
NMR value: 22)

{Table 3 (continued)}

Reference Example 44

Structural formula:



Crystal form: white powder

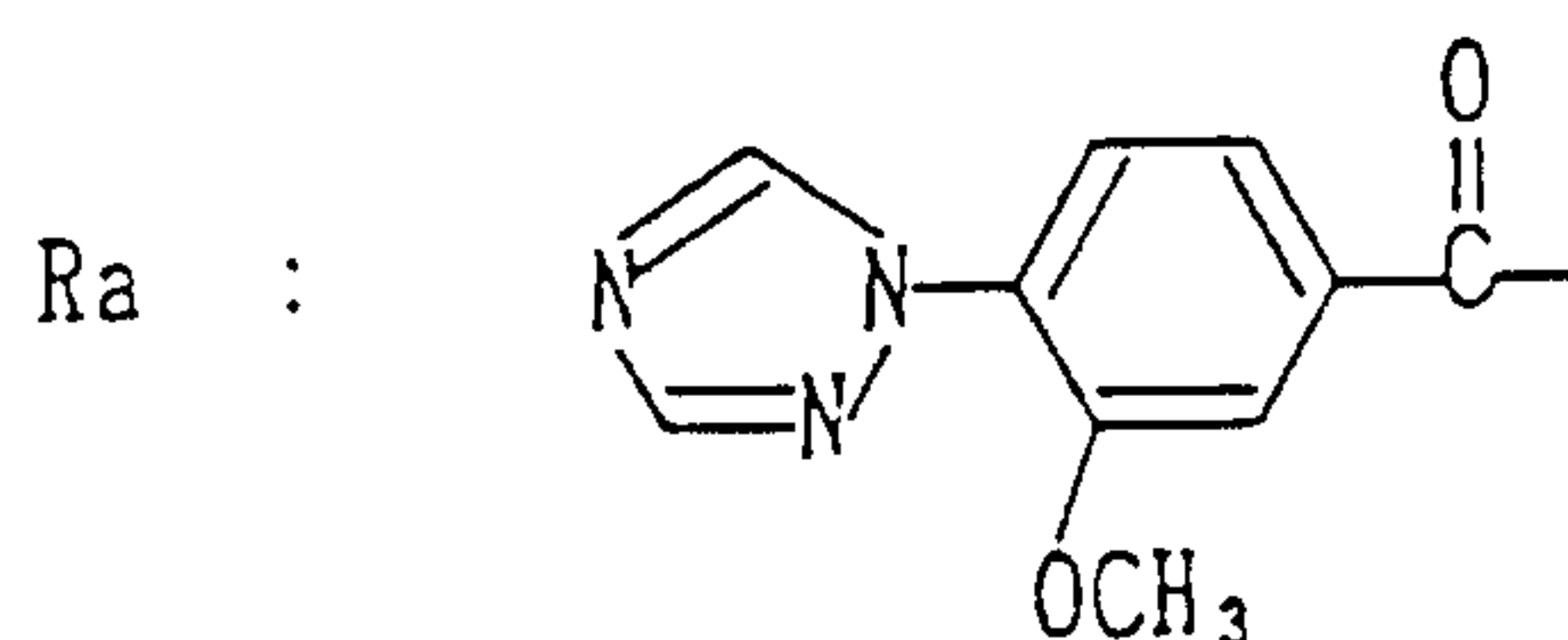
Melting point (°C): 224-231

Salt form: free

NMR value: 23)

Reference Example 45

Structural formula:



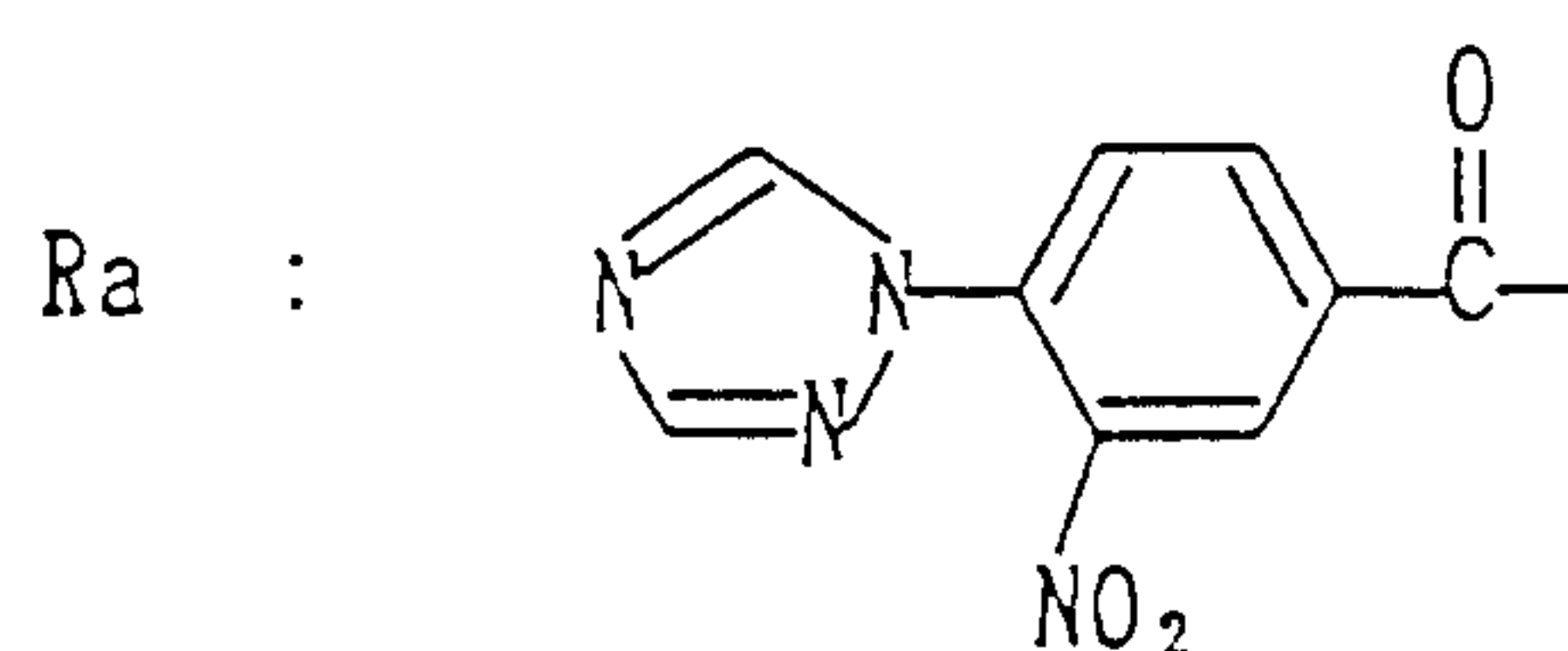
Crystal form: light red powder

Melting point (°C): 268-271

Salt form: free

Reference Example 46

Structural formula:



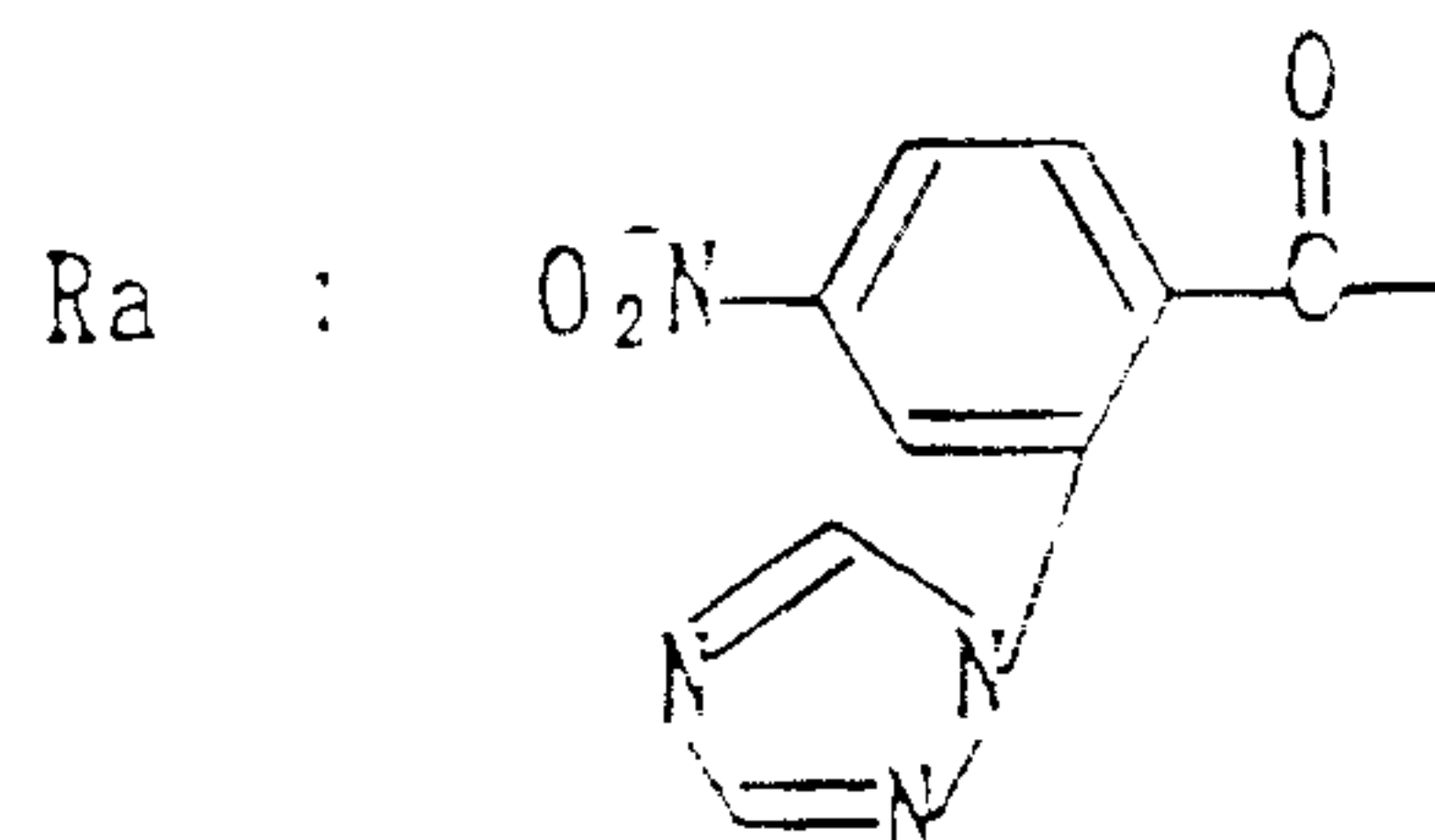
Crystal form: light yellow powder

Melting point (°C): 278-279

Salt form: free

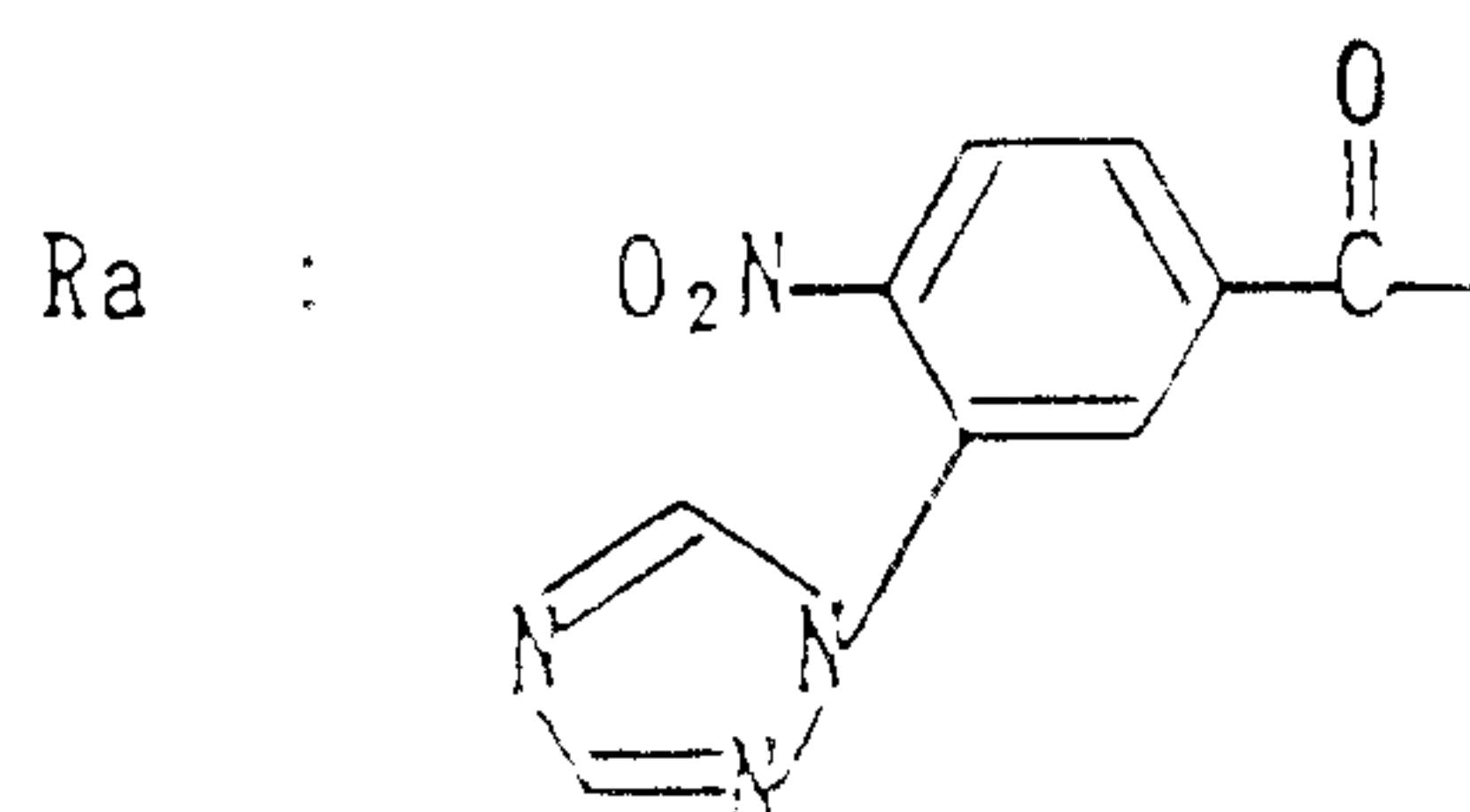
{Table 3 (continued)}

Reference Example 47
Structural formula:



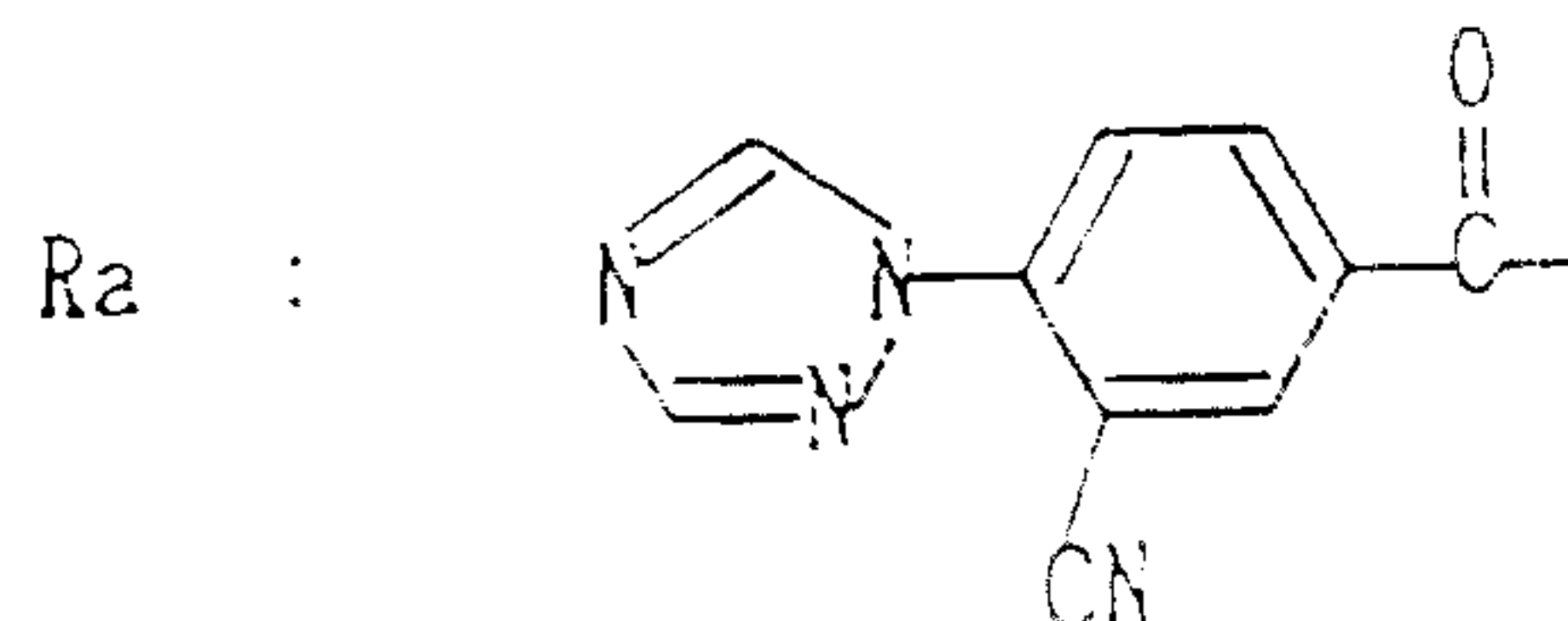
Crystal form: white powder
Salt form: free
NMR value: 24)

Reference Example 48
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 25)

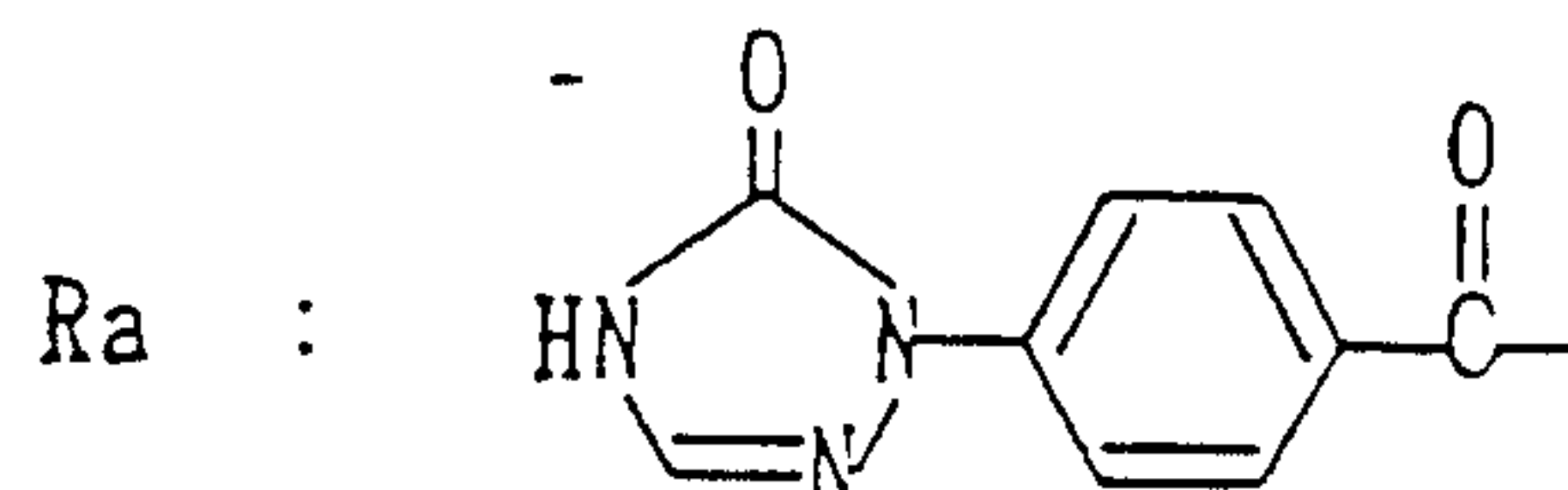
Reference Example 49
Structural formula:



Crystal form: light red needles
Salt form: free
NMR value: 26)

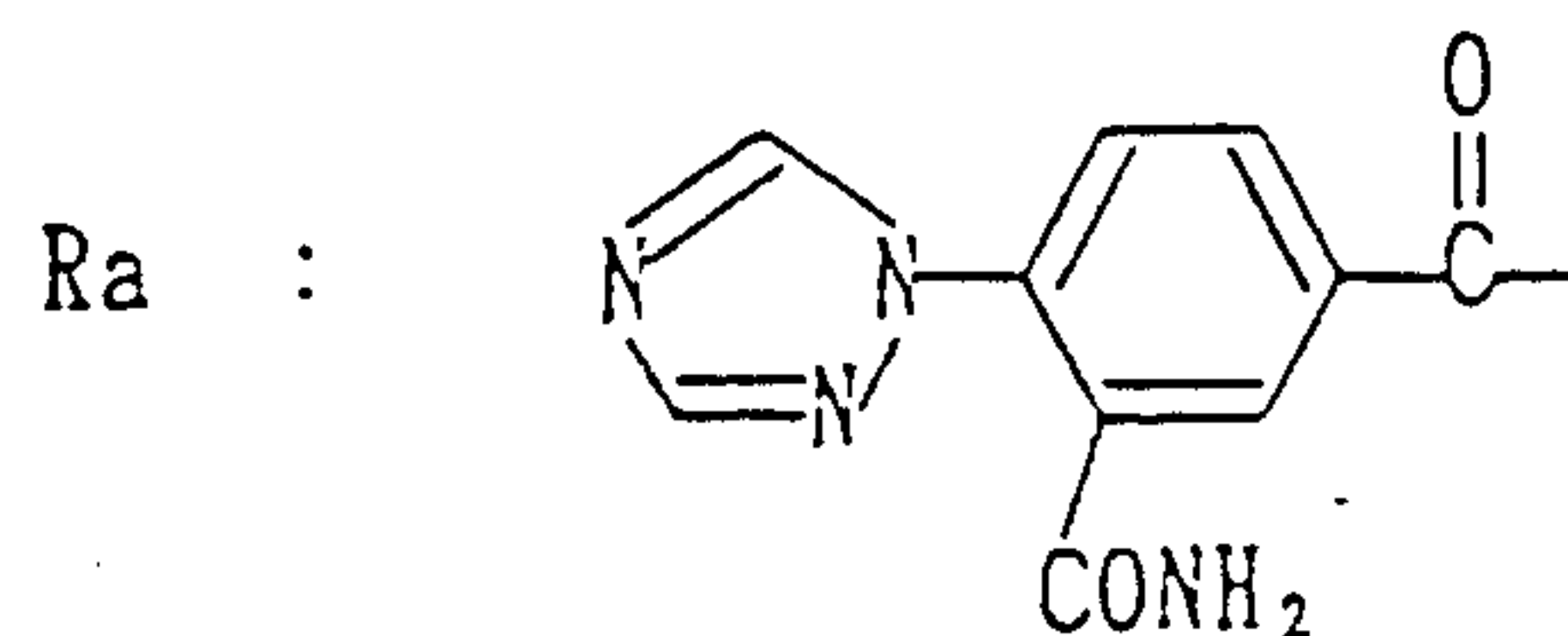
[Table 3 (continued)]

Reference Example 50
Structural formula:



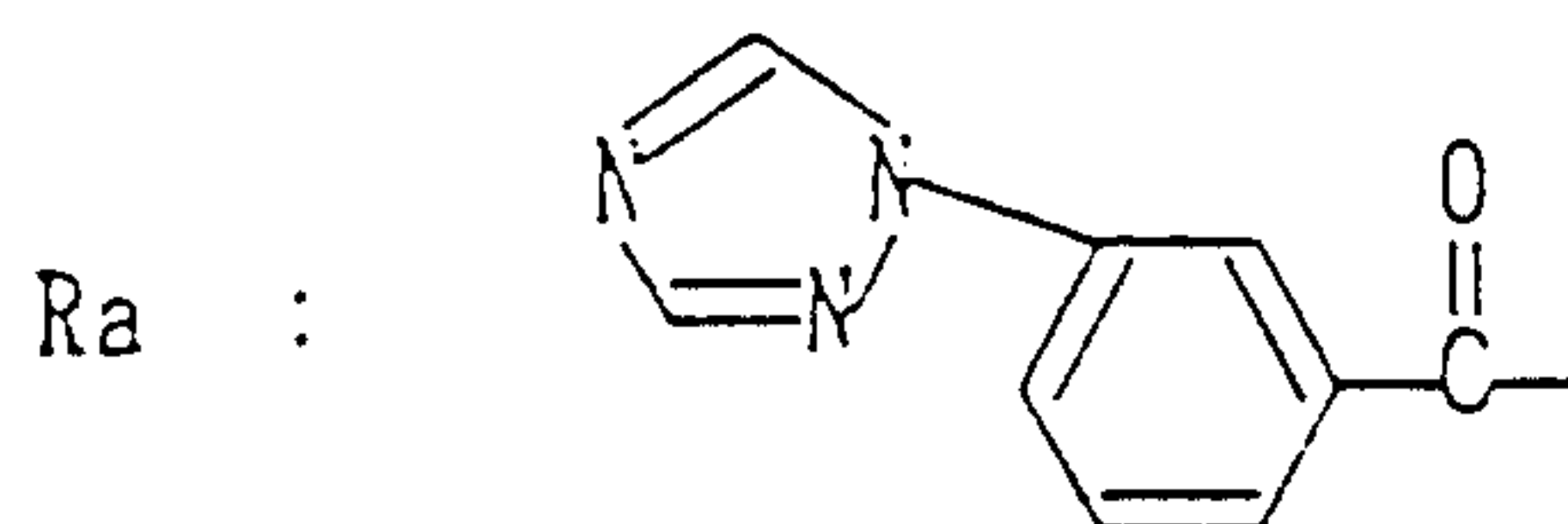
Crystal form: light brown powder
Salt form: free
NMR value: 27)

Reference Example 51
Structural formula:



Crystal form: colorless needles
Melting point (°C): 277-279 (decompd.)
Salt form: free

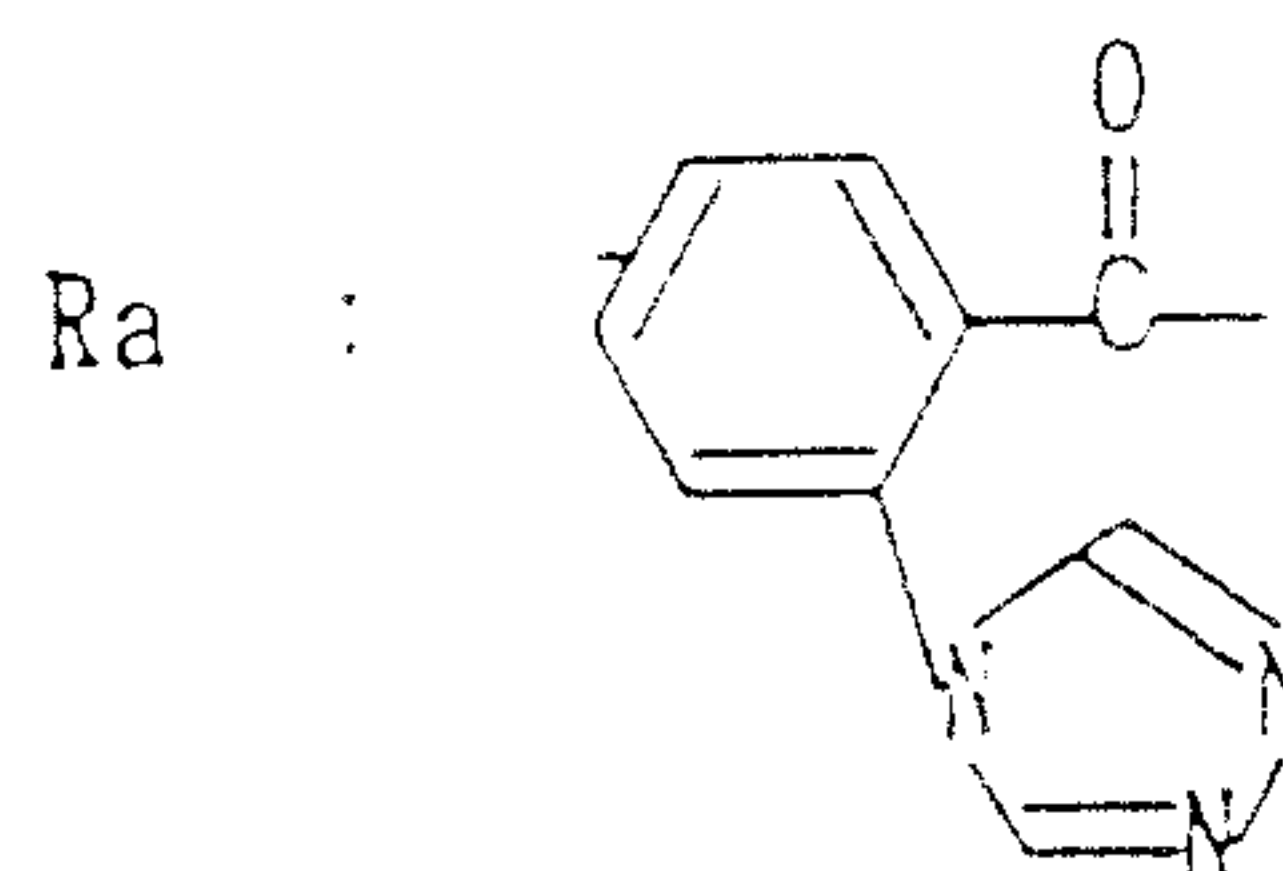
Reference Example 52
Structural formula:



Crystal form: white powder
Melting point (°C): 260-267
Salt form: free
NMR value: 28)

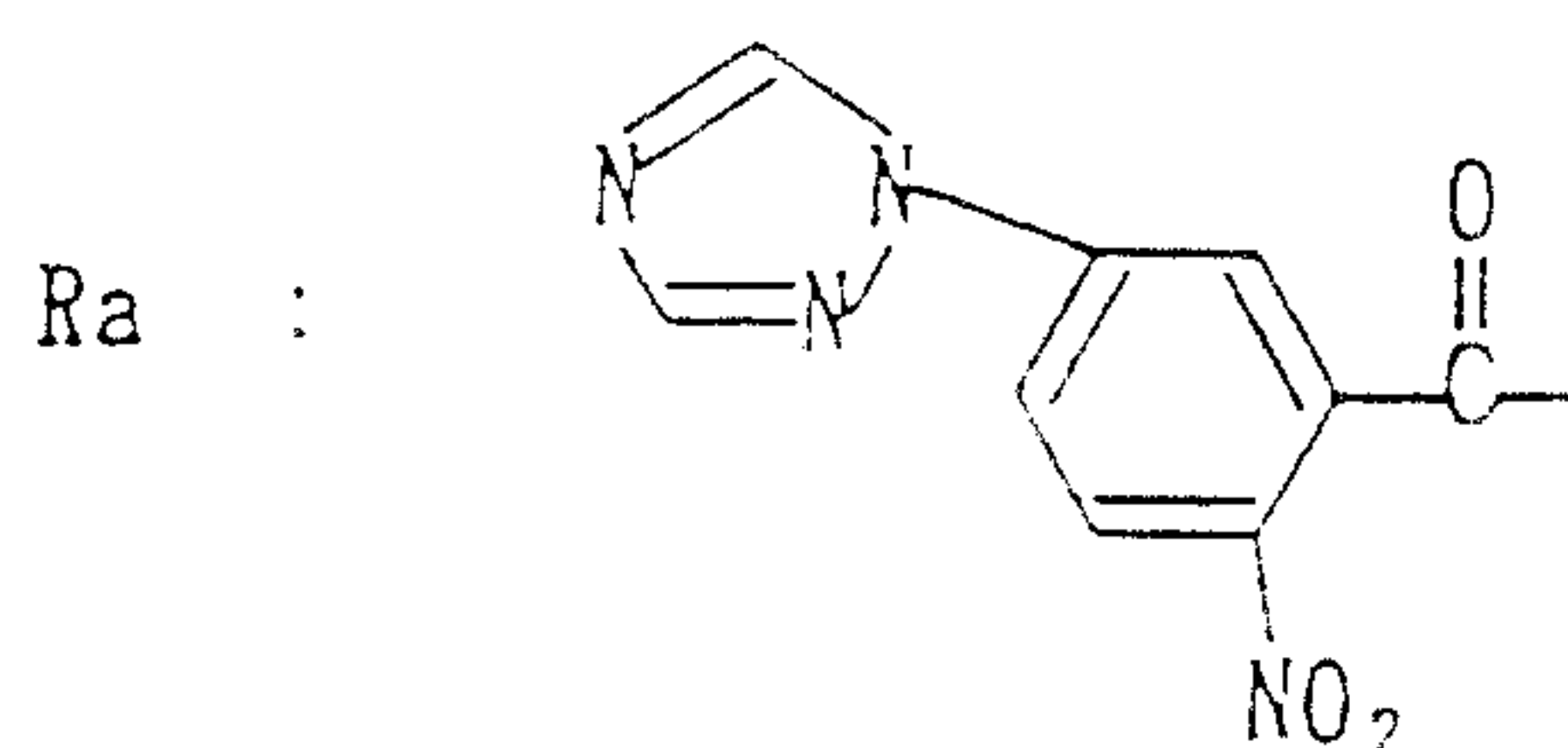
{Table 3 (continued)}

Reference Example 53
Structural formula:



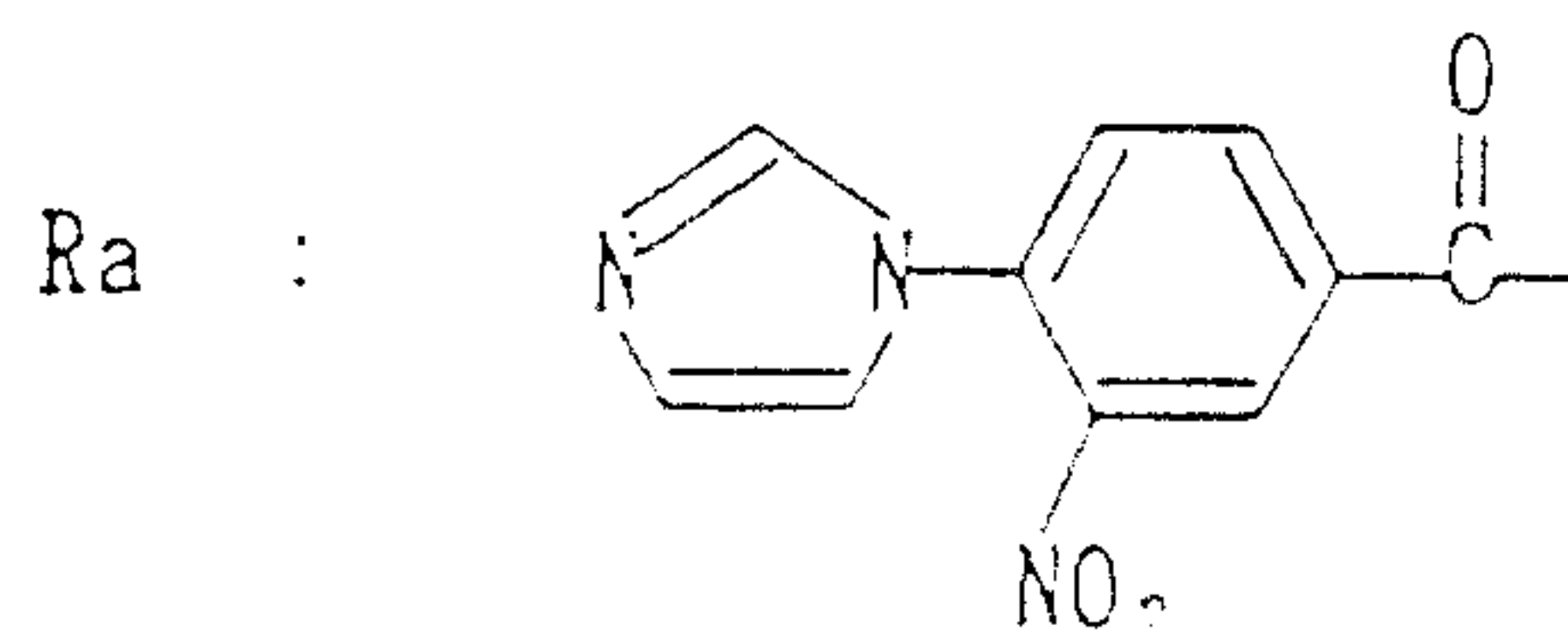
Crystal form: colorless needles
Salt form: free
NMR value: 29)

Reference Example 54
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 30)

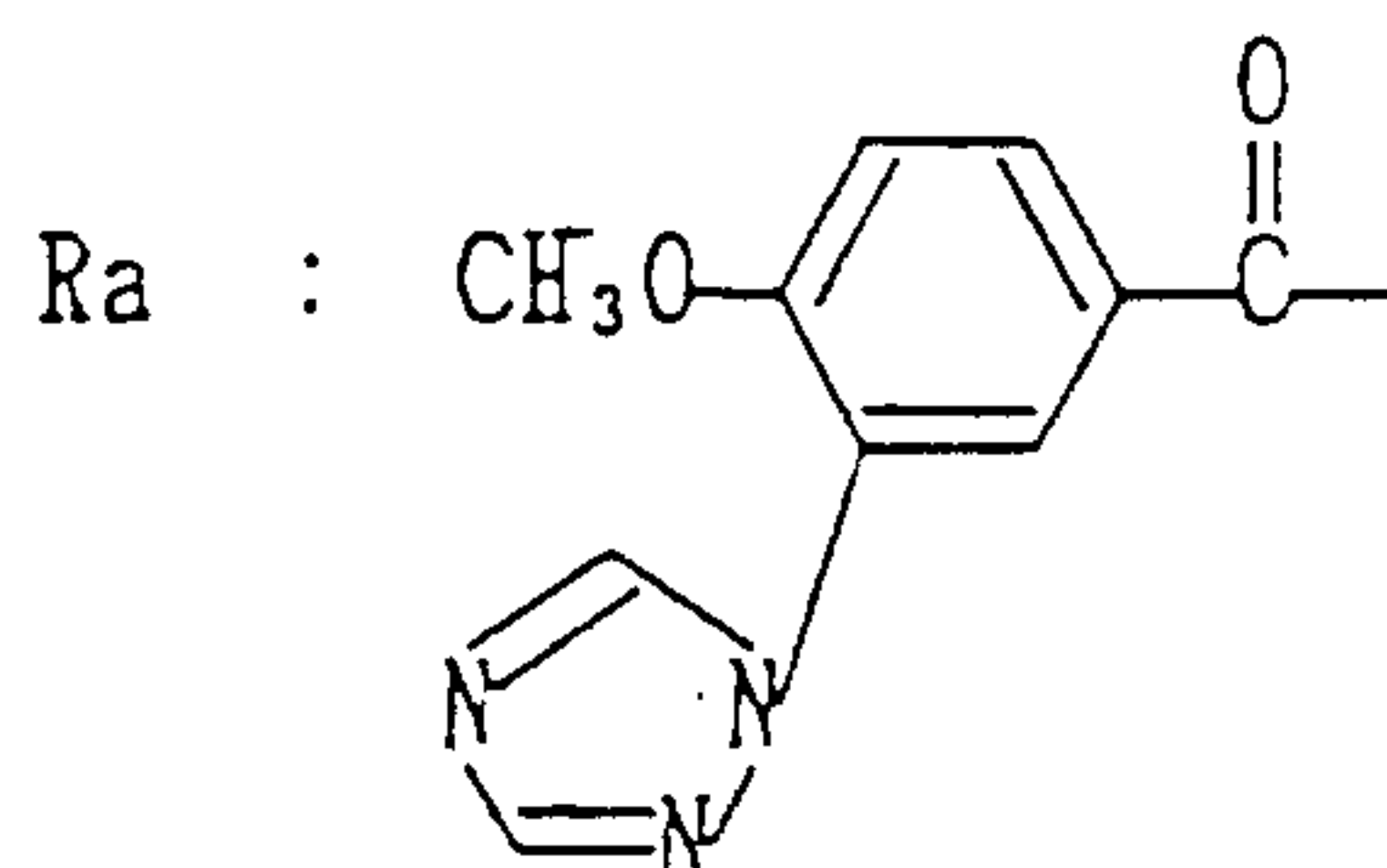
Reference Example 55
Structural formula:



Crystal form: light yellow powder
Melting point (°C): 261-263 (decompd.)
Salt form: free

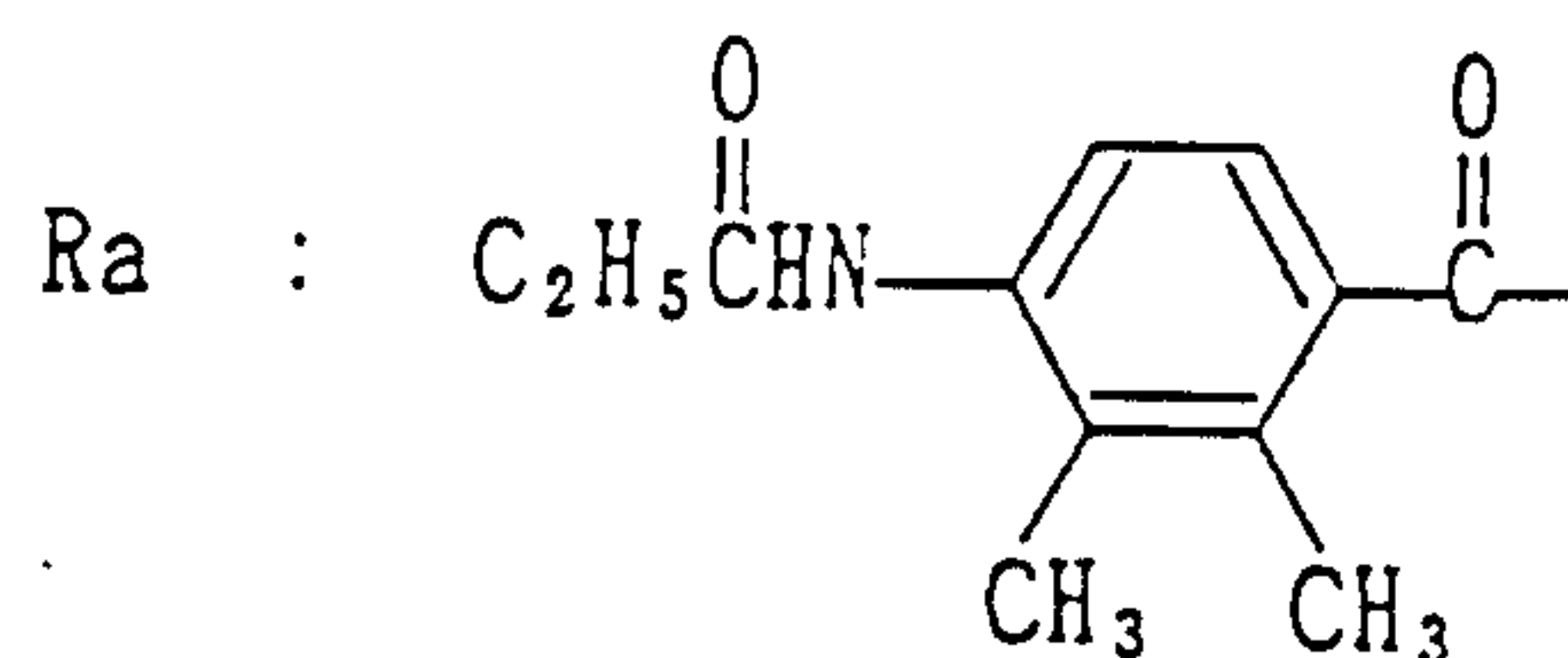
{Table 3 (continued)}

Reference Example 56
Structural formula:



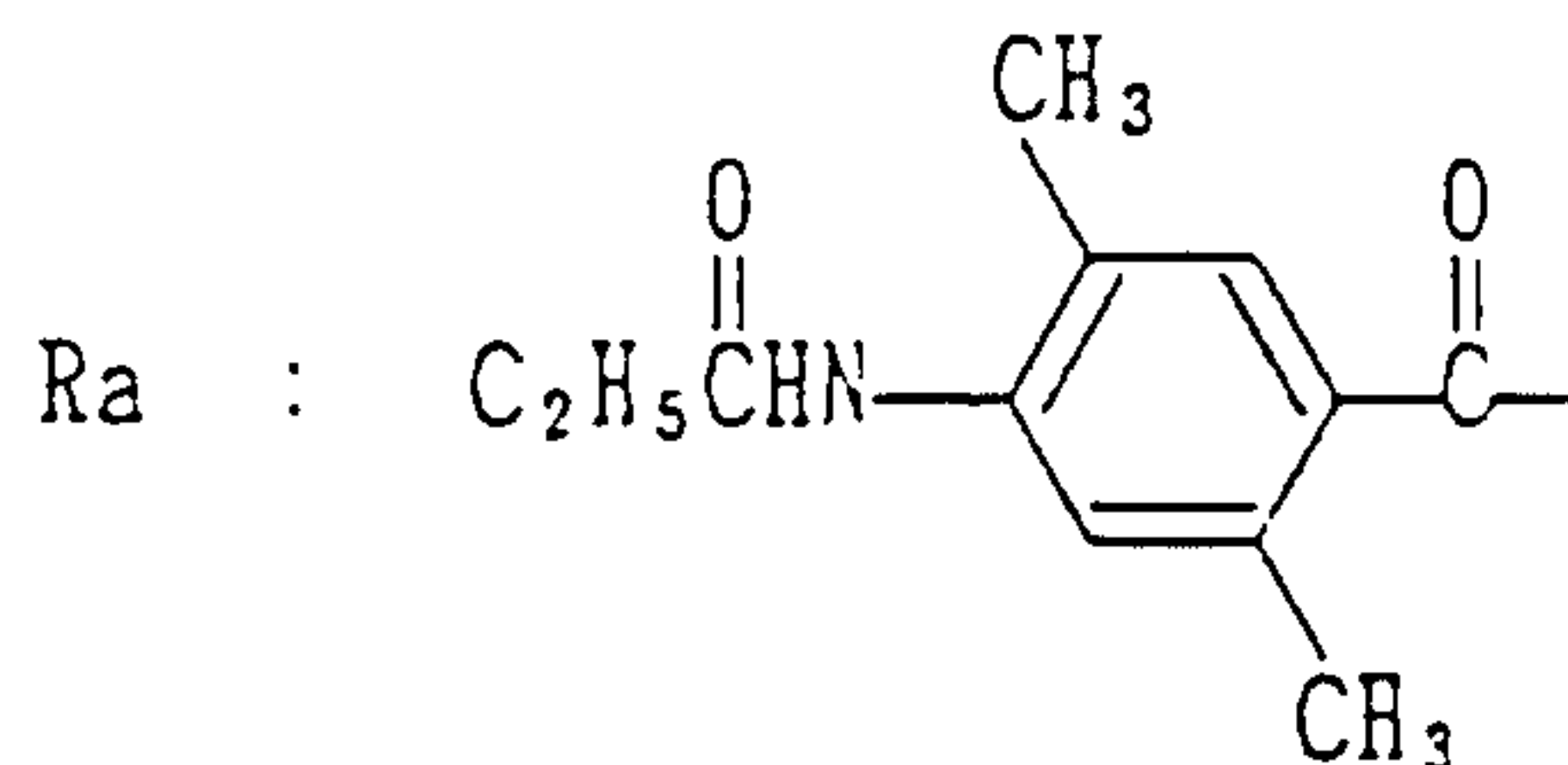
Crystal form: white powder
Salt form: free
NMR value: 31)

Reference Example 57
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 32)

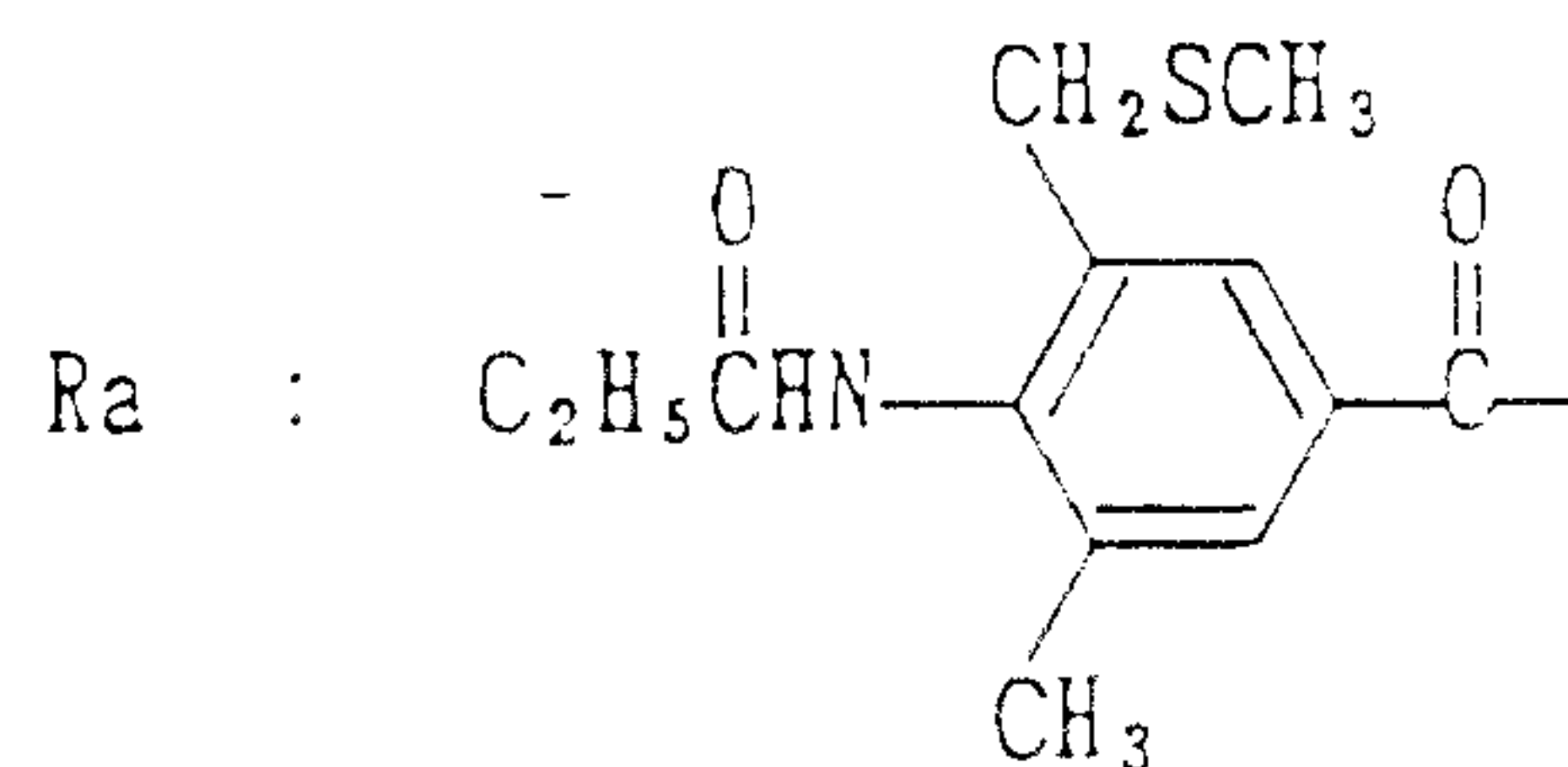
Reference Example 58
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 33)

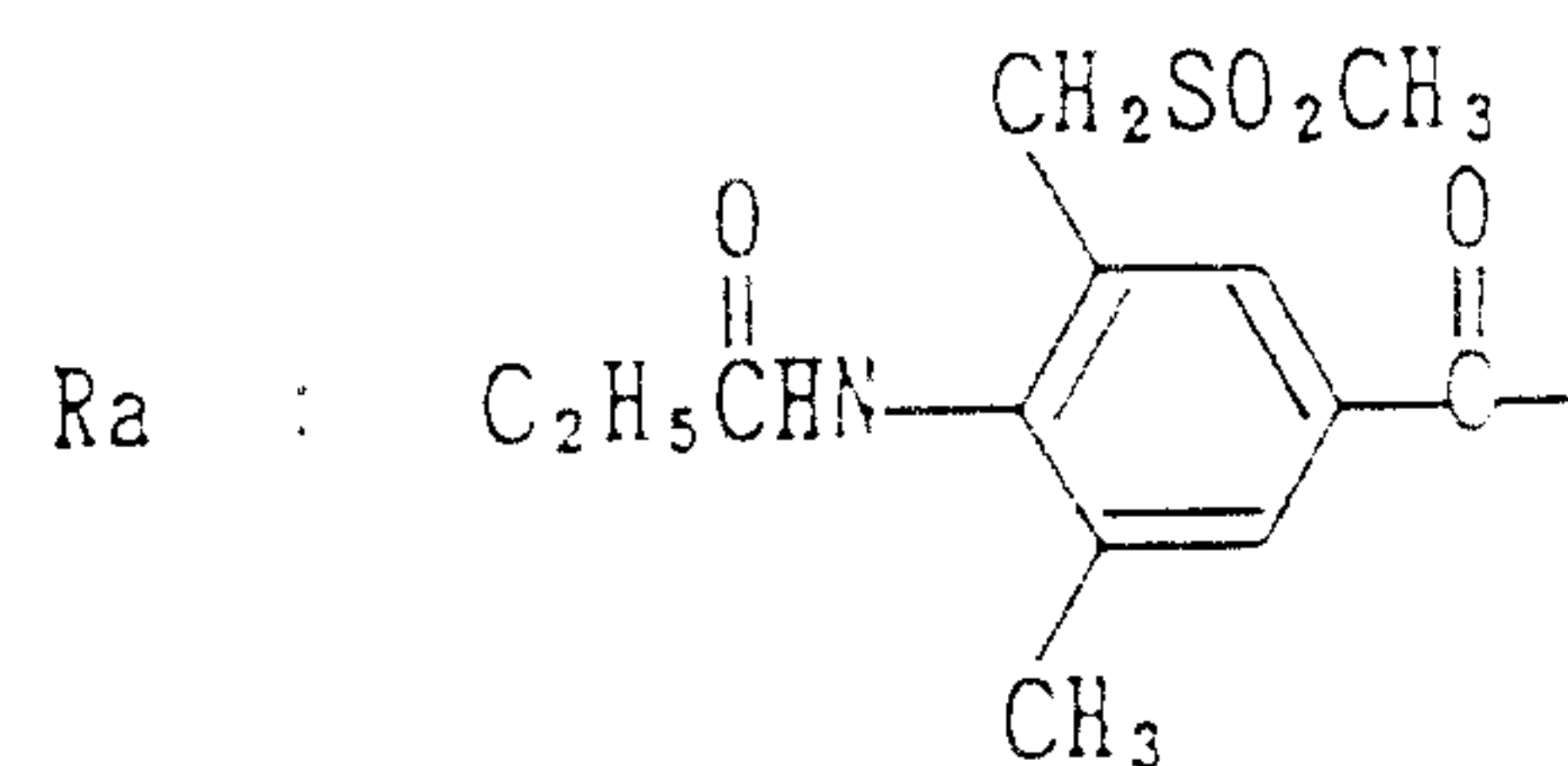
{Table 3 (continued)}

Reference Example 59
Structural formula:



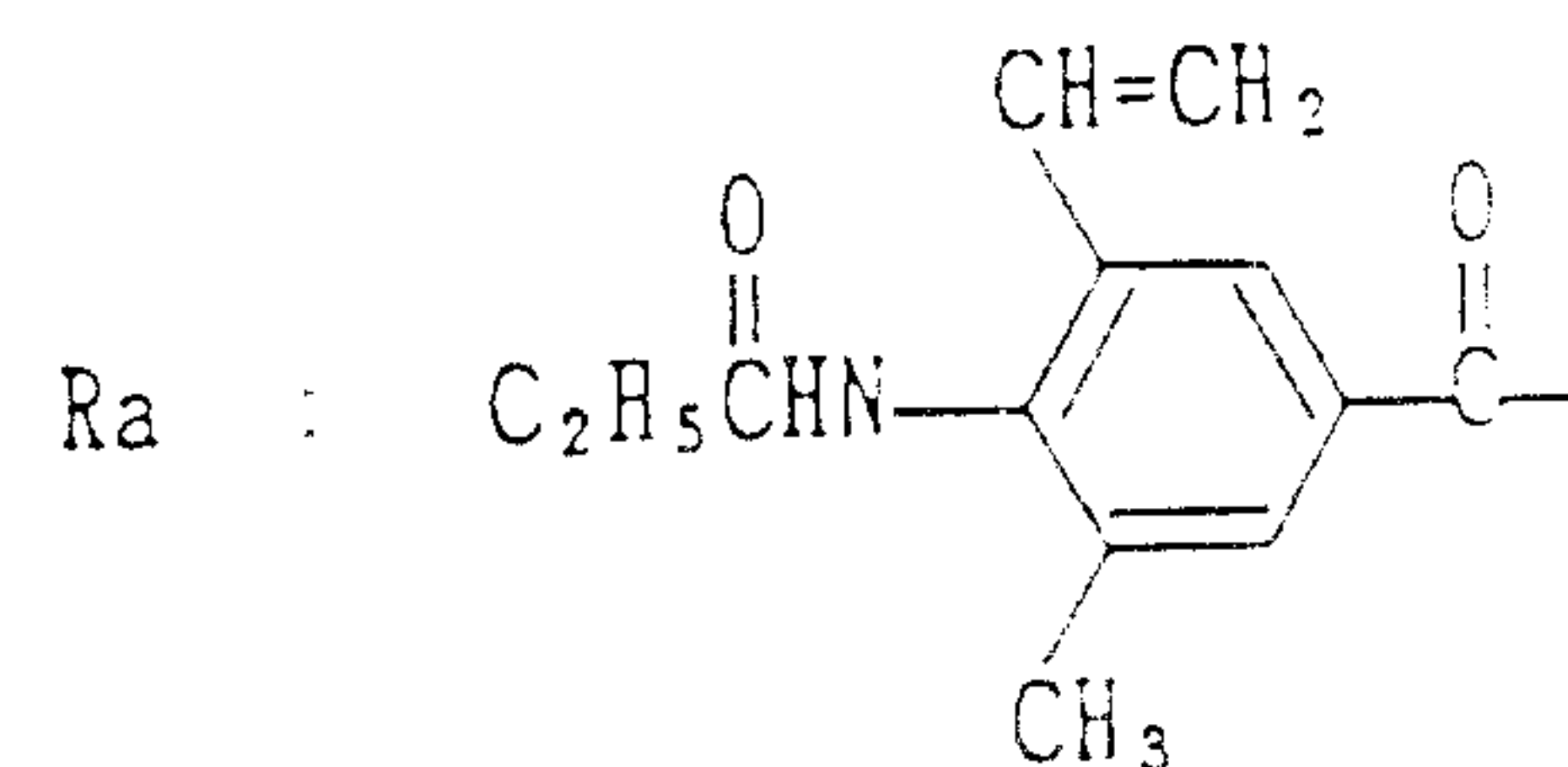
Crystal form: white powder
Salt form: free
NMR value: 34)

Reference Example 60
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 35)

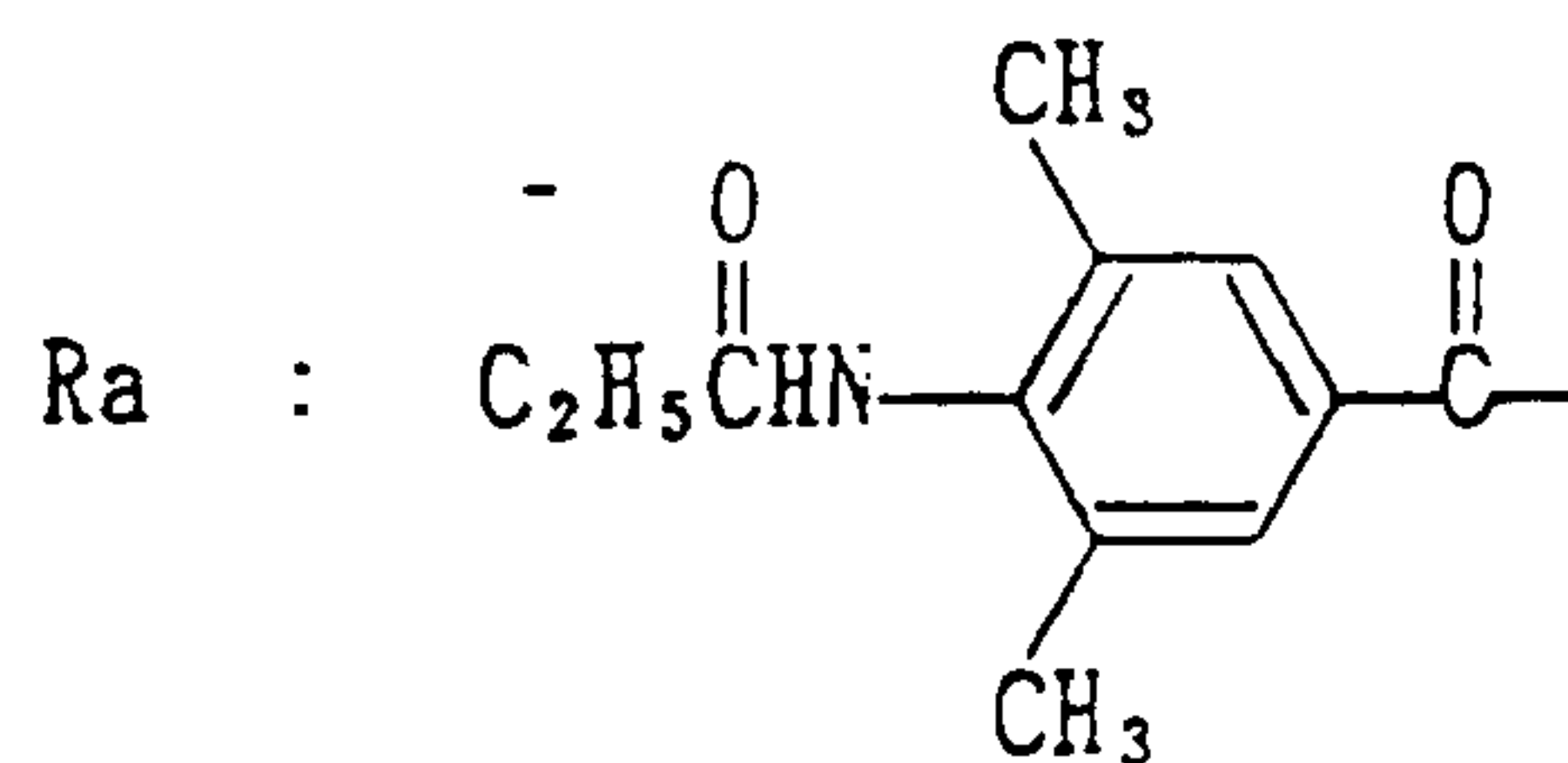
Reference Example 61
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 36)

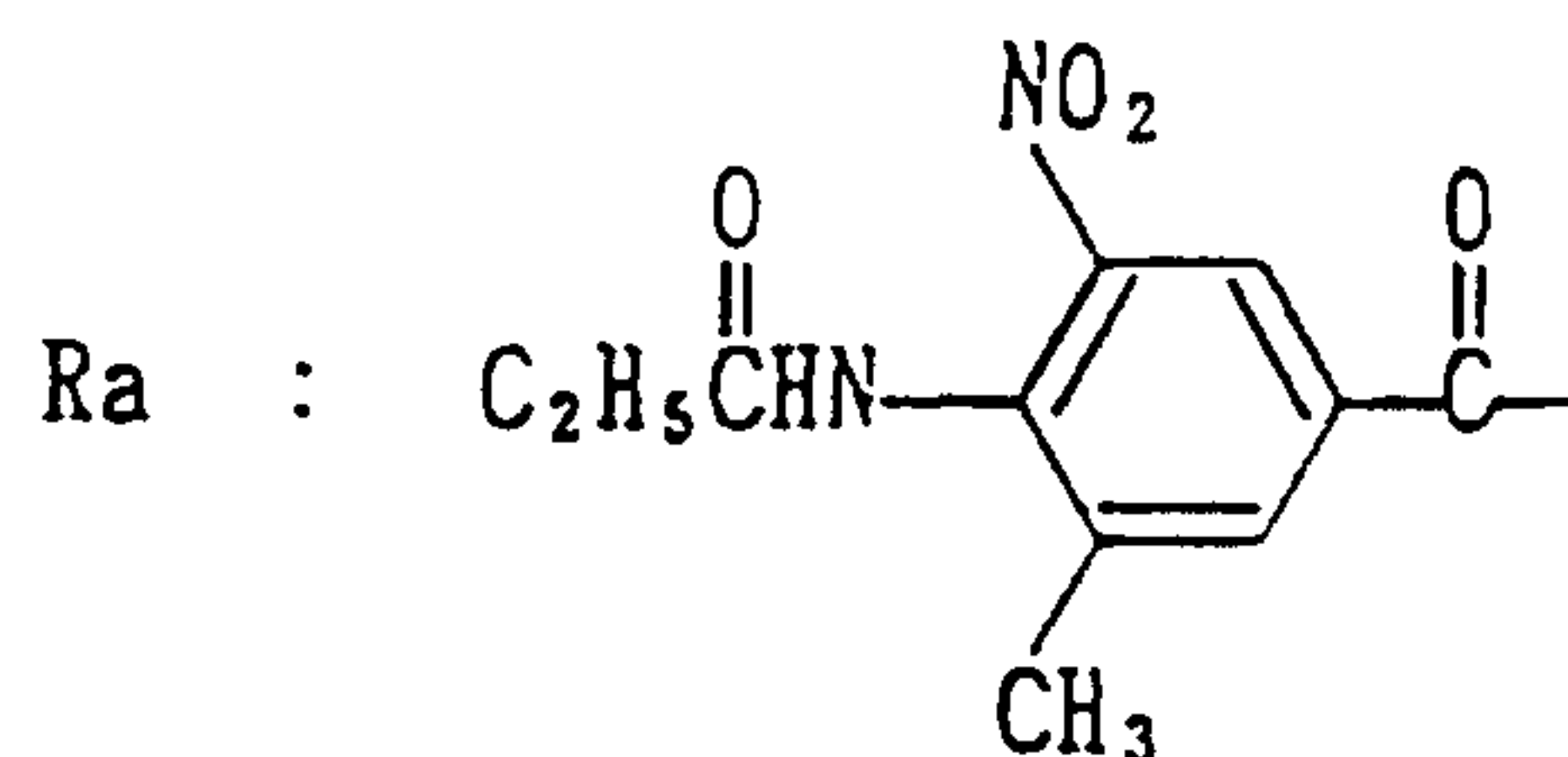
{Table 3 (continued)}

Reference Example 62
Structural formula:



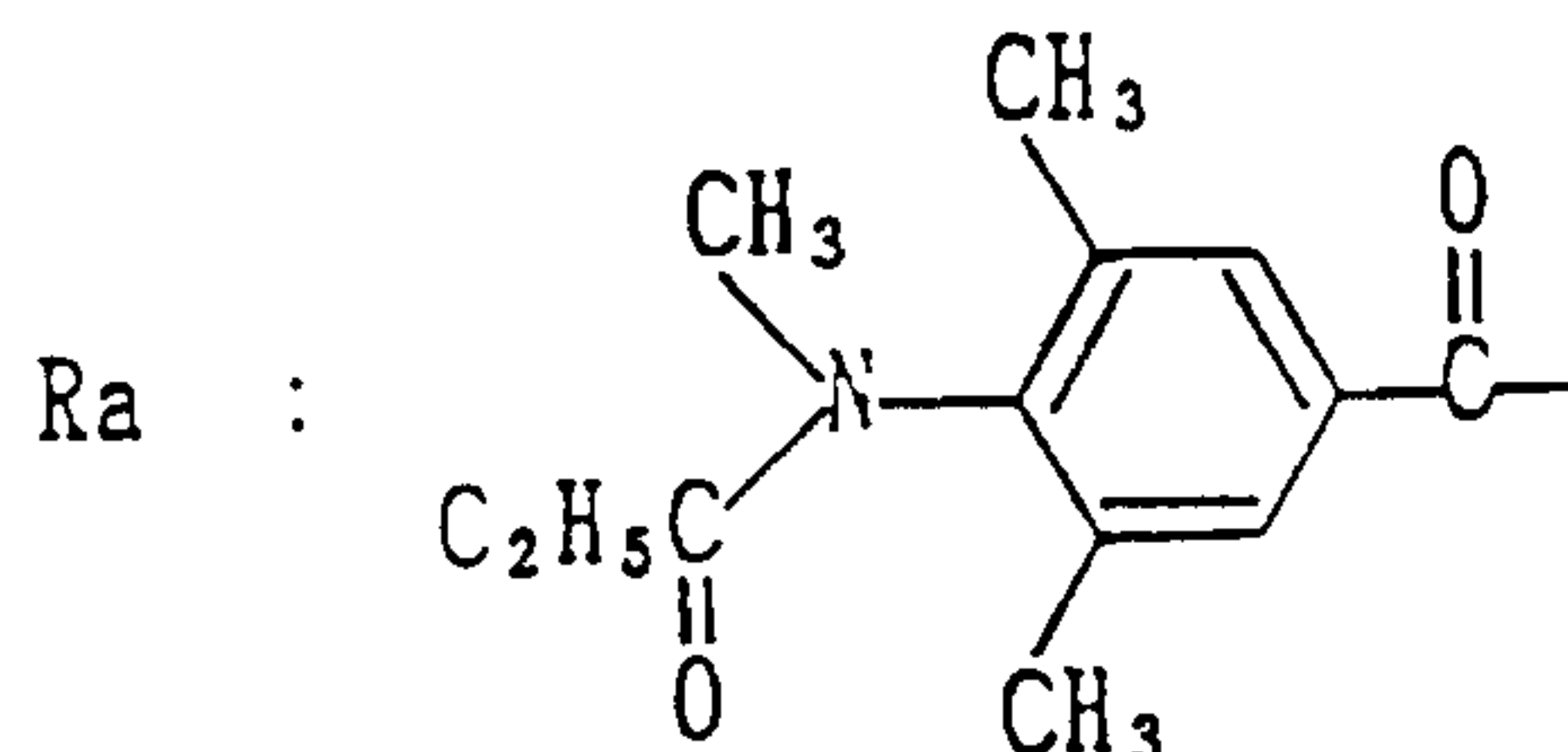
Crystal form: colorless needles
Melting point (°C): 250-252
Salt form: free

Reference Example 63
Structural formula:



Crystal form: light yellow powder
Salt form: free
NMR value: 37)

Reference Example 64
Structural formula:

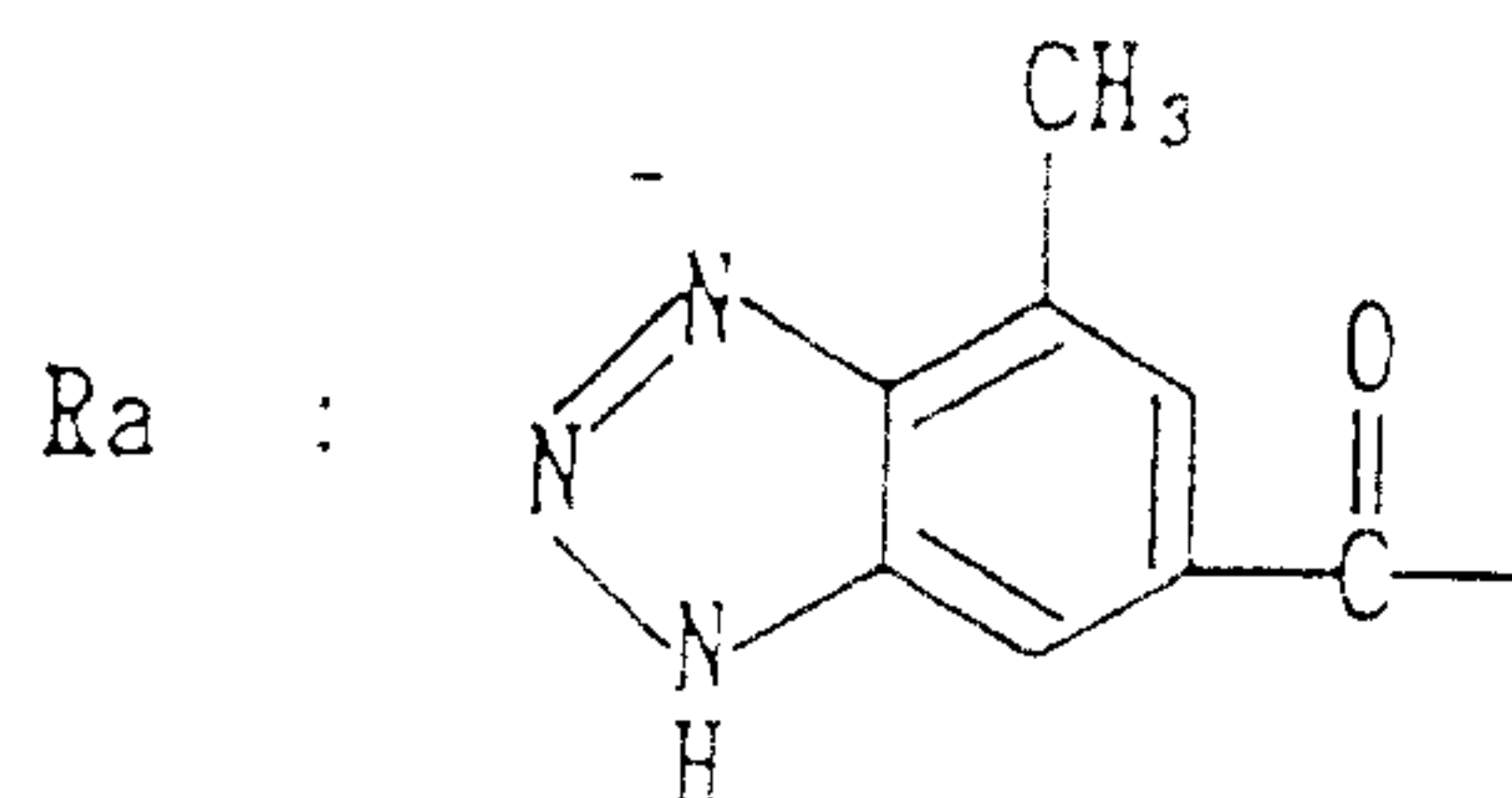


Crystal form: light yellow powder
Salt form: free
NMR value: 38)

{Table 3 (continued)}

Reference Example 65

Structural formula:



Crystal form: white powder

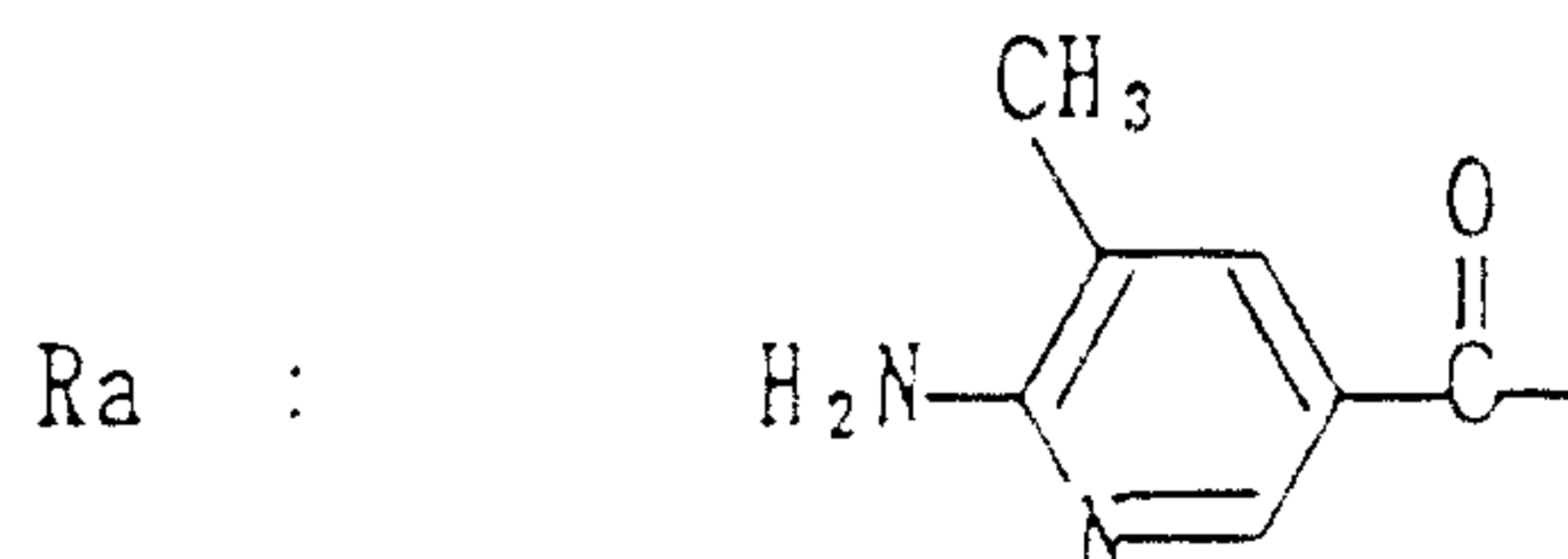
Melting point (°C): 300 or above

Salt form: free

NMR value: 39)

Reference Example 66

Structural formula:



Crystal form: white powder

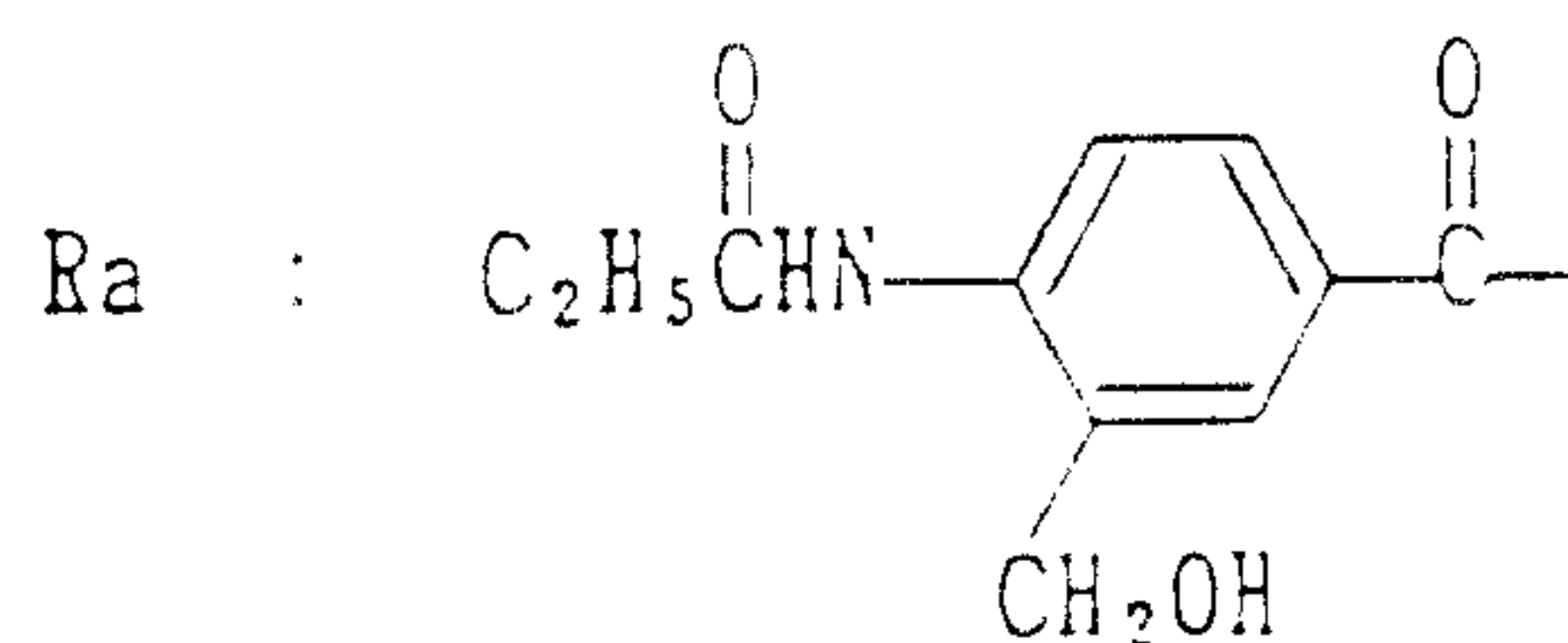
Melting point (°C): 300 or above

Salt form: free

NMR value: 40)

Reference Example 67

Structural formula:



Crystal form: white powder

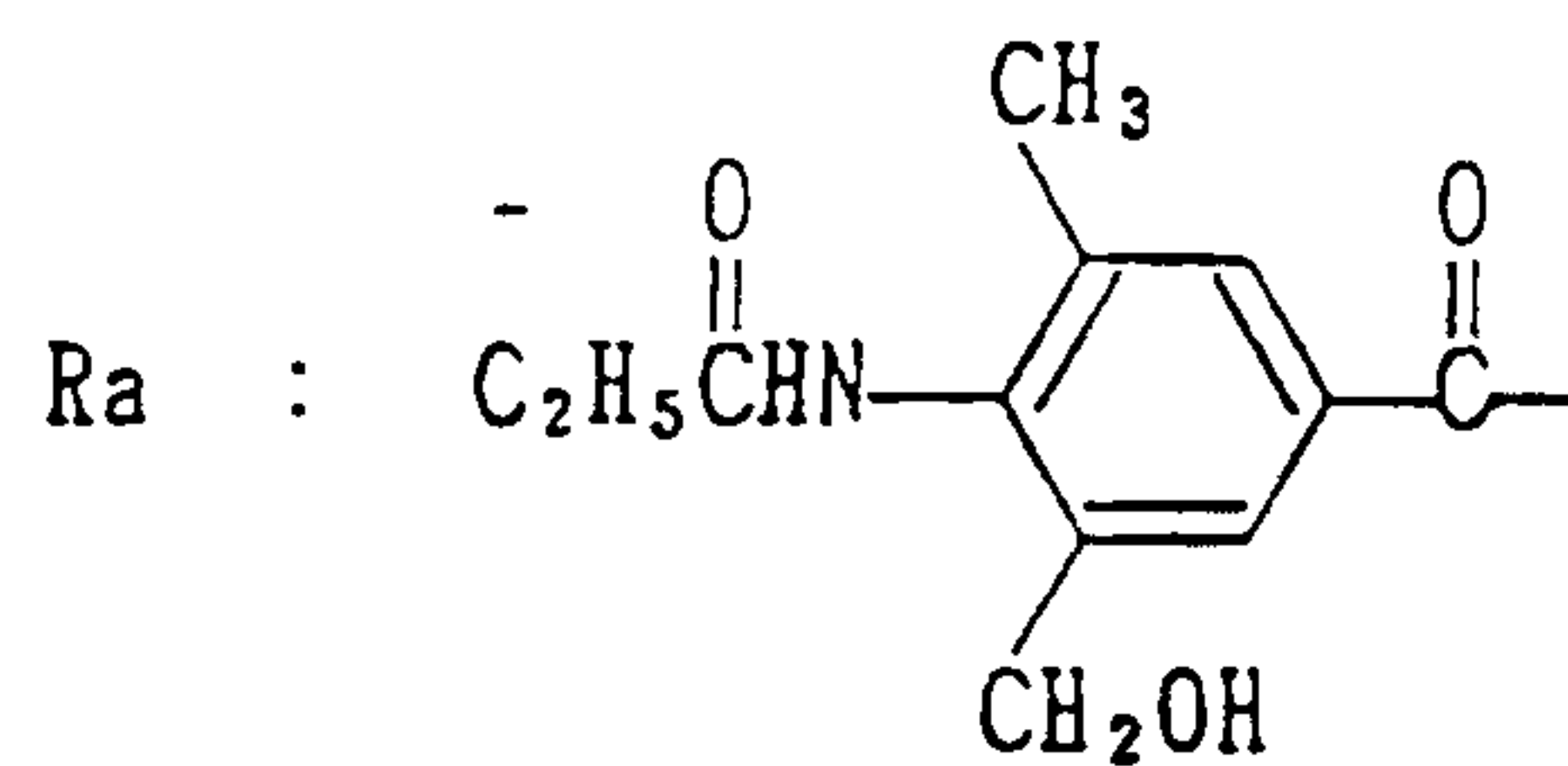
Salt form: free

NMR value: 41)

(Table 3 (continued))

Reference Example 68

Structural formula:



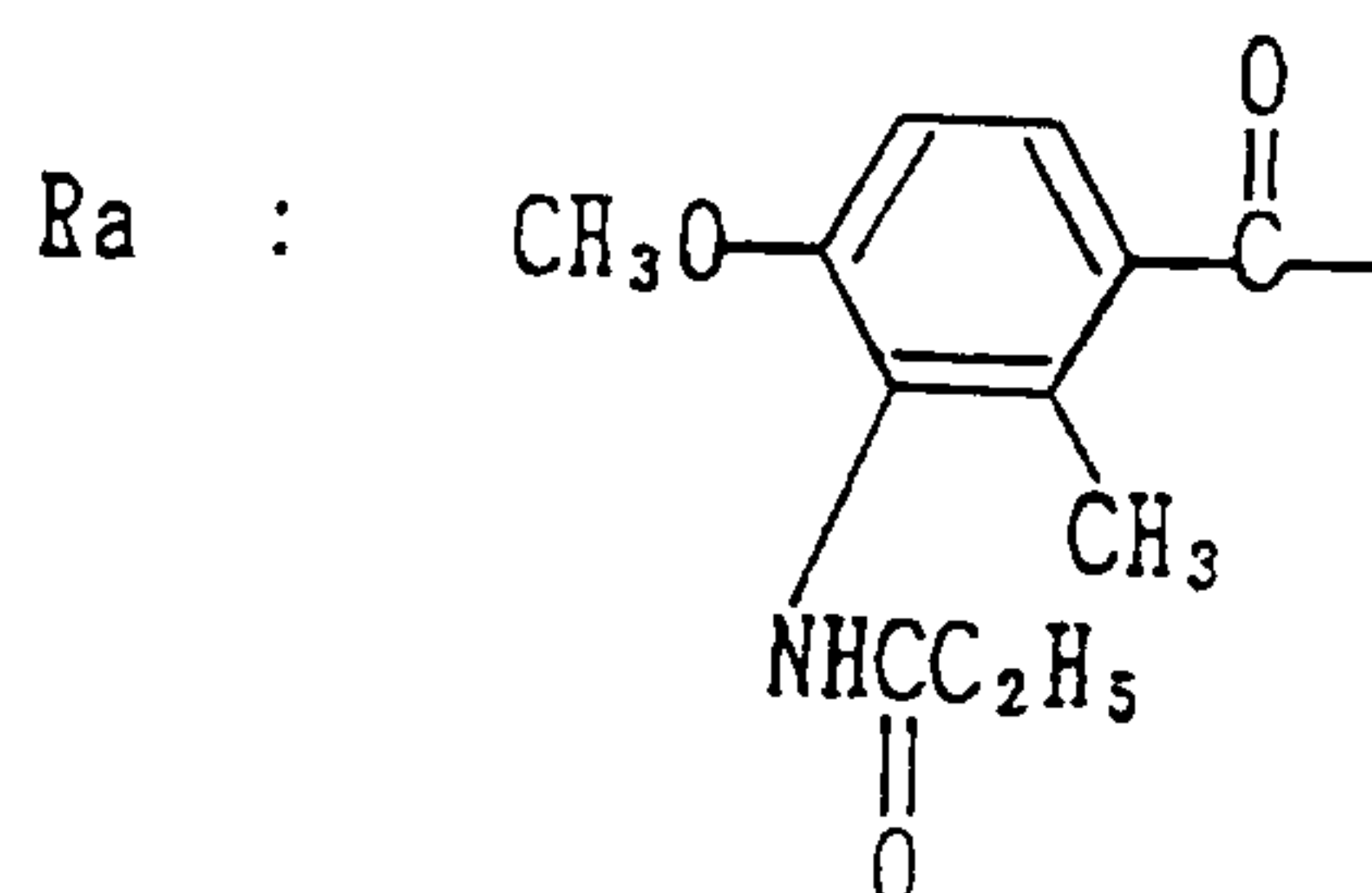
Crystal form: white powder

Salt form: free

NMR value: 42)

Reference Example 69

Structural formula:



Crystal form: white powder

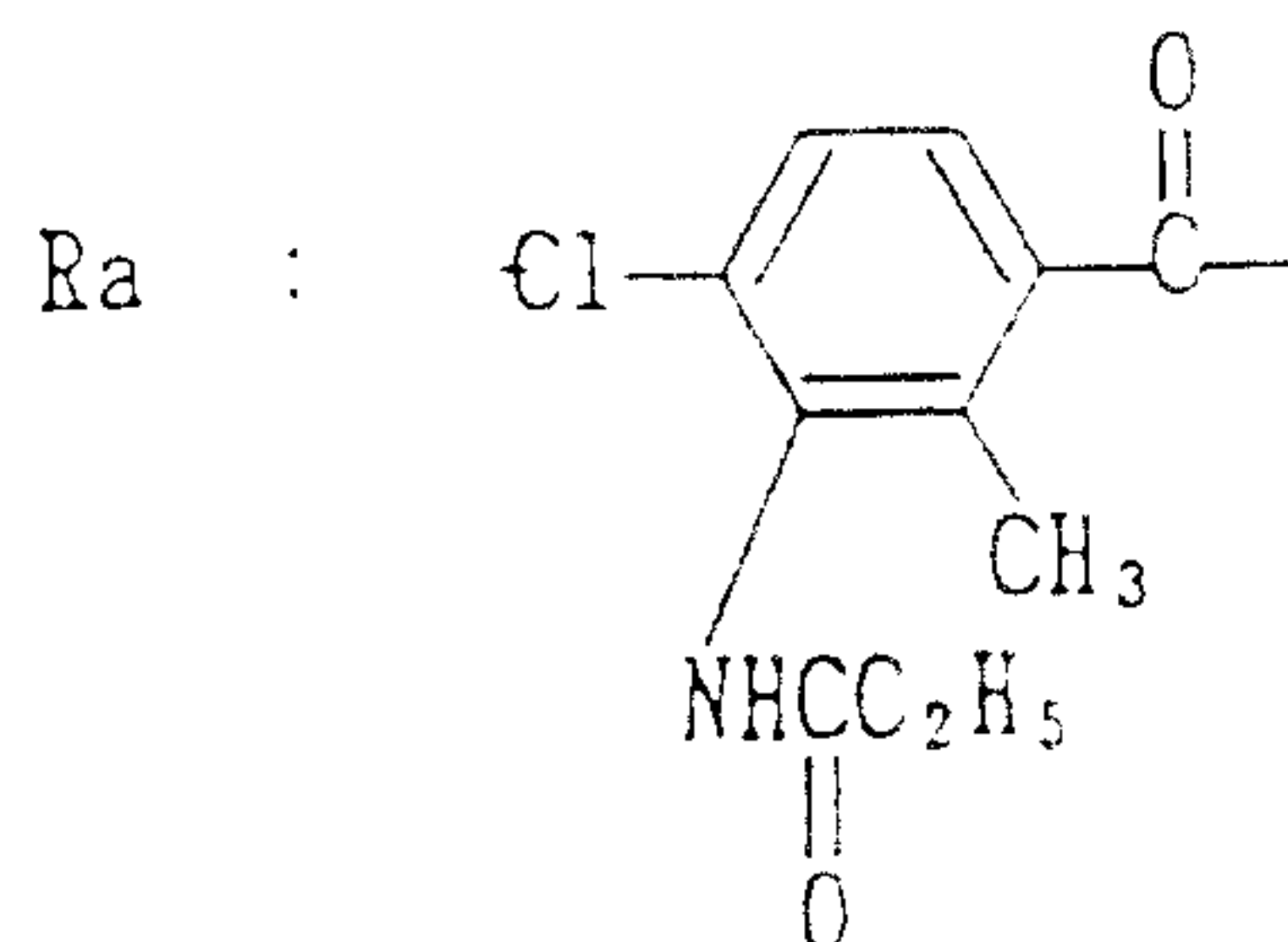
Salt form: free

NMR value: 43)

[Table 3 (continued)]

Reference Example 70

Structural formula:



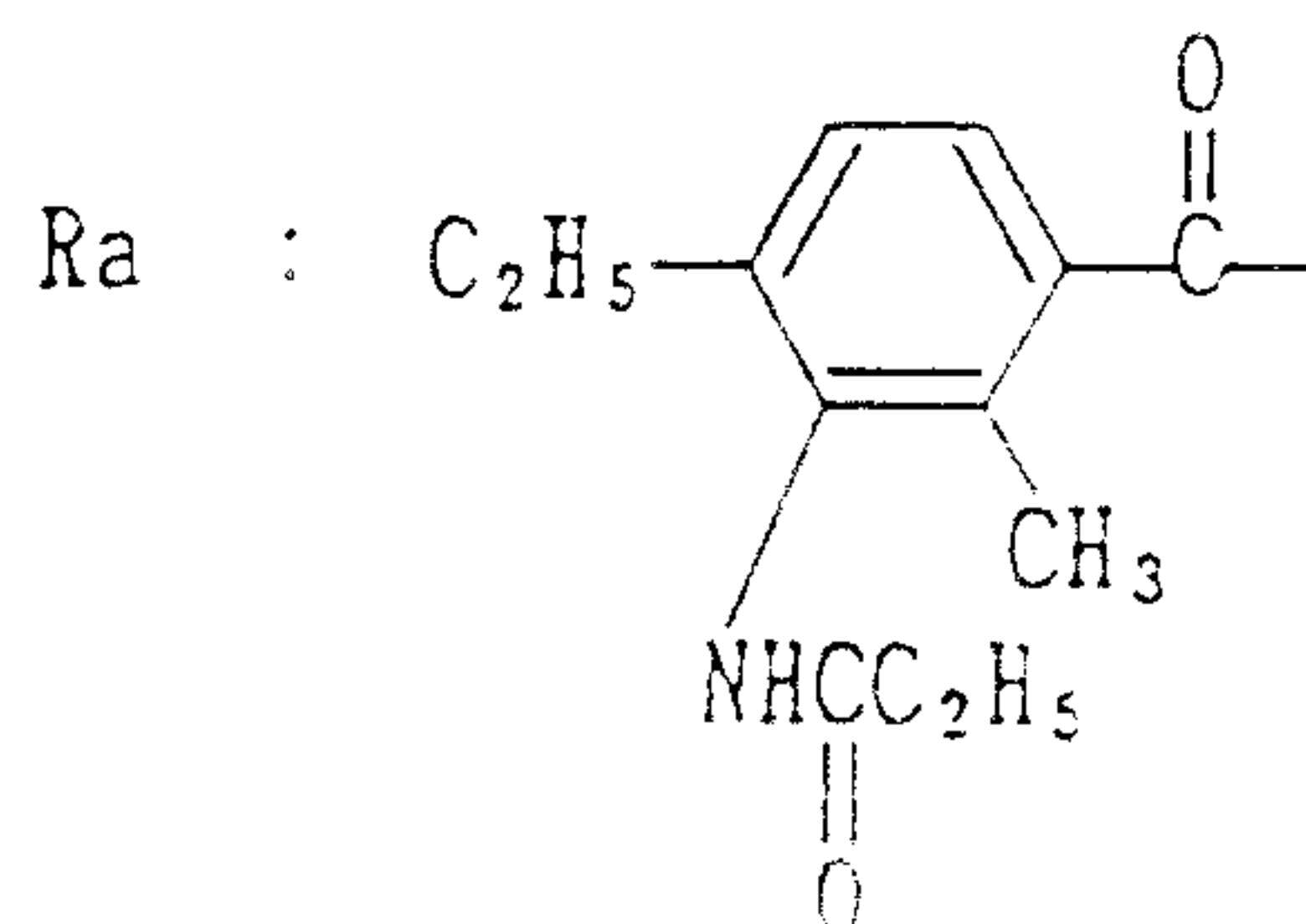
Crystal form: white powder

Salt form: free

NMR value: 44)

Reference Example 71

Structural formula:



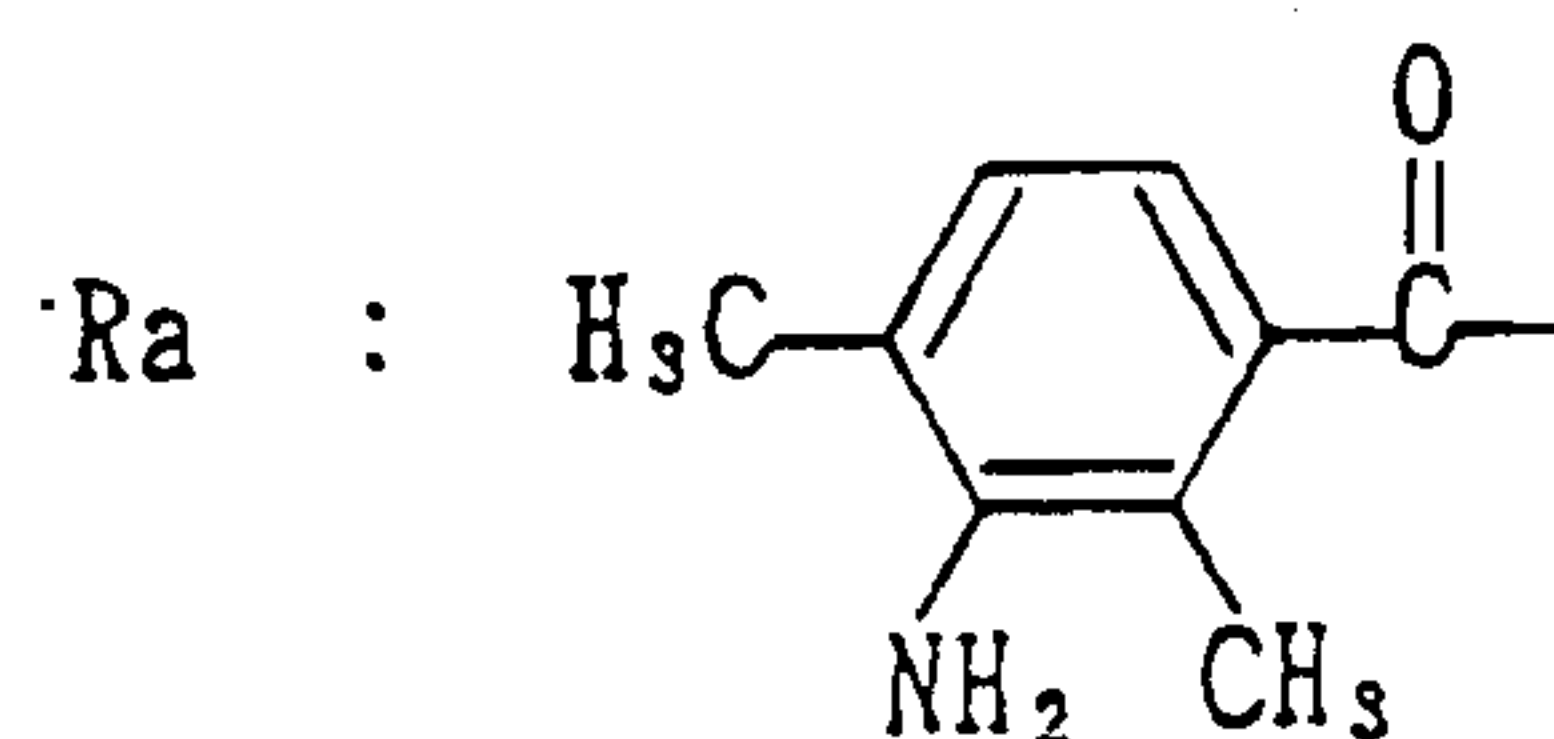
Crystal form: white powder

Salt form: free

NMR value: 45)

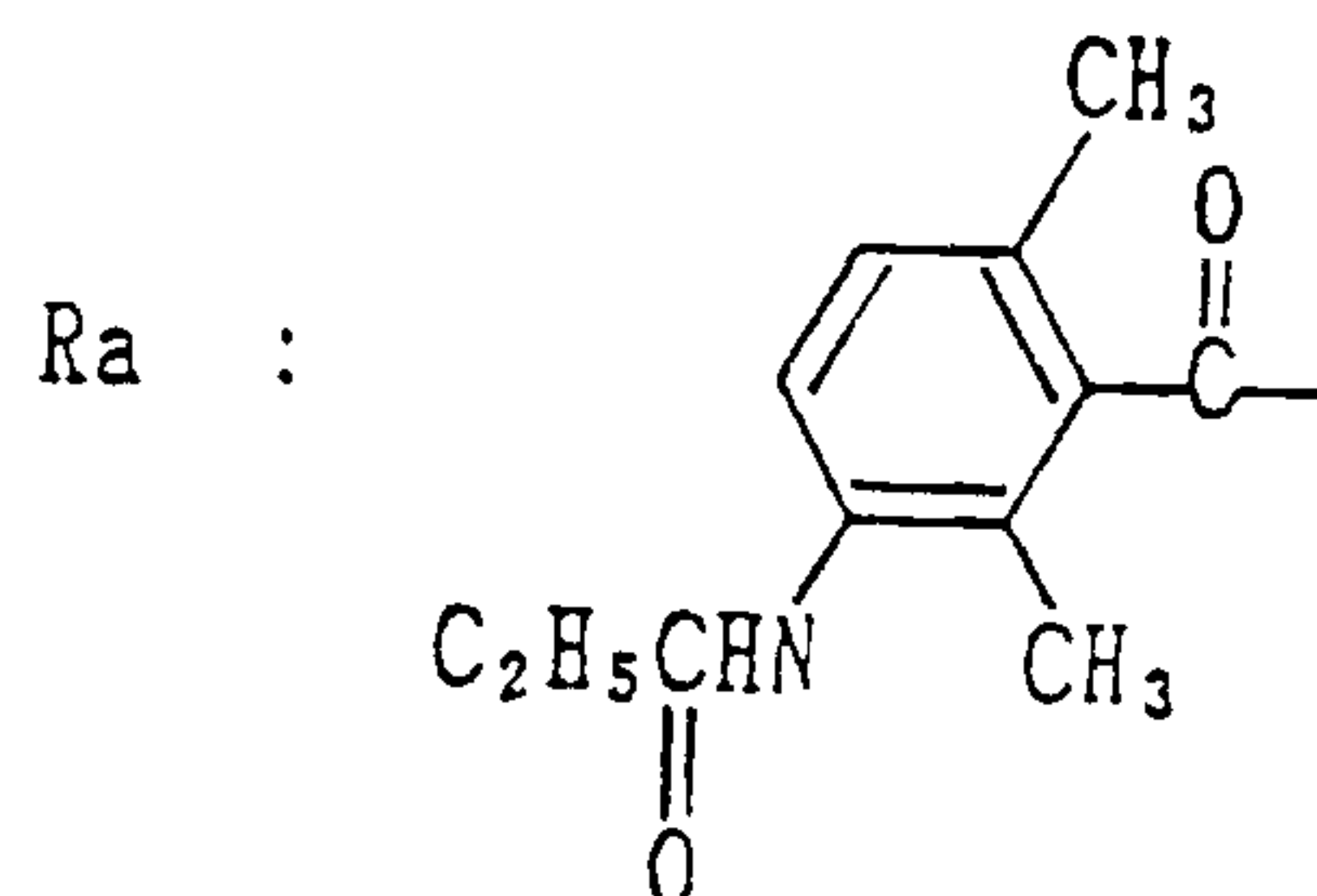
[Table 3 (continued)]

Reference Example 72
Structural formula:



Crystal form: white powder
Recrystallization solvent: ethanol
Melting point (°C): 142-144
Salt form: free

Reference Example 73
Structural formula:



Crystal form: white powder
Salt form: free
NMR value: 46)

The NMR data 1) to 46) for the compounds prepared in Reference Examples 13 through 73 are as follows:

- 1) ^1H -NMR (250 MHz, CdCl_3) δ ppm: 1.30-1.49 (2H, m),
5 1.66-1.91 (2H, m), 2.36 (3H, s), 2.40-2.68 (3H, m),
2.80-3.04 (4H, m), 3.04-3.21 (2H, m), 7.06-7.15 (1H, m),
7.15-7.23 (1H, m), 7.54-7.66 (1H, m), 8.50-8.59 (1H, m).
- 2) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.25-1.55 (2H, m),
1.55-1.94 (6H, m), 2.26 (3H, s), 2.35-2.75 (5H, m),
10 3.04-3.25 (2H, m), 7.06-7.39 (5H, m).
- 3) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 0.86-1.70 (4H, m),
1.04 (3H, d, $J=6.2$ Hz), 1.70-2.05 (2H, m), 2.41-2.85
(4H, m), 2.89-3.25 (2H, m), 7.07-7.45 (5H, m).
- 4) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.43 (2H, dq, $J=4.0$
15 Hz, 12.2 Hz), 1.70-1.90 (2H, m), 2.34 (3H, s), 2.45-2.80
(7H, m), 3.08-3.25 (2H, m), 3.79 (3H, s), 6.83 (2H, d,
 $J=8.7$ Hz), 7.11 (2H, d, $J=8.7$ Hz)
- 5) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.32-1.60 (2H, m),
1.60-1.89 (3H, m), 2.35 (3H, s), 2.43-2.88 (7H, m),
20 3.02-3.28 (2H, m), 3.86 (3H, s), 3.89 (3H, s), 6.69-6.89
(3H, m).
- 6) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.43 (2H, dq, $J=4.0$
Hz, 12.2 Hz), 1.70-1.88 (2H, m), 2.35 (3H, s), 2.45-2.90
(7H, m), 3.07-3.25 (2H, m), 3.80 (3H, s), 6.68-6.85 (3H,
25 m), 7.13-7.38 (1H, m).
- 7) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.41 (2H, dq, $J=12$
Hz, 4Hz), 1.65-2.03 (3H, m), 2.30-2.95 (7H, m), 2.37

(3H, s), 3.05-3.28 (2H, m), 3.82 (3H, s), 6.75-7.00 (2H, m), 7.09-7.32 (2H, m).

8) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.25-1.57 (2H, m), 1.57-2.00 (3H, m), 2.34 (3H, s), 2.40-2.67 (7H, m), 3.02-3.24 (2H, m), 3.53 (1H, brs), 6.62 (2H, d, $J=8.4$ Hz), 6.98 (2H, d, $J=8.4$ Hz).

9) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.32-1.64 (2H, m), 1.66-1.95 (2H, m), 2.31 (3H, s), 2.34 (3H, s), 2.38-2.88 (7H, m), 3.07-3.38 (3H, m), 7.08 (4H, s).

10) 10) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 1.70-2.44 (4H, m), 2.45-3.98 (9H, m), 2.81 (3H, d, $J=4.6\text{Hz}$), 6.75 (2H, d, $J=8.4\text{Hz}$), 7.14 (2H, d, $J=8.4\text{Hz}$), 8.39-9.78 (3H, m), 9.79-10.28 (1H, m).

11) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.20-1.53 (3H, m), 1.66-1.85 (2H, m), 2.34 (3H, s), 2.40-2.76 (7H, m), 2.46 (3H, s), 3.05-3.22 (2H, m), 7.12 (2H, d, $J=8.5$ Hz), 7.20 (2H, d, $J=8.5$ Hz).

12) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 1.55-1.95 (4H, m), 2.28 (3H, s), 2.59-2.98 (7H, m), 3.15-3.48 (2H, m), 3.44 (1H, brs), 6.53-6.72 (3H, m), 7.06 (1H, t, $J=7.7$ Hz), 9.33 (1H, brs)

13) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.28-1.55 (2H, m), 1.55-2.05 (4H, m), 2.10-2.80 (6H, m), 2.87-3.48 (5H, m), 7.12-7.40 (5H, m).

14) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 1.63-2.40 (8H, m), 2.70-3.02 (2H, m), 3.02-3.65 (7H, m), 6.09 (1H, brs), 7.25-7.48 (3H, m), 7.53-7.65 (2H, m), 9.33 (3H, brs).

- 15) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.42-1.65 (2H, m), 1.68-1.85 (2H, m), 1.92 (1H, brs), 2.28 (3H, s), 2.53-2.85 (3H, m), 2.89 (2H, dd, $J=9.5$ Hz, 14.9 Hz), 3.04 (2H, dd, $J=7.4$ Hz, 14.9 Hz), 3.00-3.25 (2H, m), 3.49-3.68 (1H, m), 7.06-7.24 (4H, m).
- 16) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.39 (3H, t, $J=7.1$ Hz), 3.52-3.70 (2H, m), 3.86-4.06 (2H, m), 4.36 (2H, q, $J=7.1$ Hz), 5.62 (1H, brs), 7.61 (2H, d, $J=8.9$ Hz), 8.02 (2H, d, $J=8.9$ Hz).
- 10 17) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 3.95 (3H, s), 7.96 (1H, d, $J=8.4$ Hz), 8.05 (1H, dd, $J=2.0$ Hz, 8.4 Hz), 8.17 (1H, s), 8.28 (1H, d, $J=2.0$ Hz), 8.77 (1H, s)
- 18) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 3.98 (3H, s), 7.61 (1H, dd, $J=7.9$ Hz, 8.1 Hz), 7.94 (1H, ddd, $J=1.1$ Hz, 2.3 Hz, 8.1 Hz), 8.08 (1H, ddd, $J=1.1$ Hz, 1.8 Hz, 7.9 Hz), 8.14 (1H, s), 8.34 (1H, dd, $J=1.8$ Hz, 2.3 Hz), 8.66 (1H, s)
- 15 19) ^1H -NMR (200 MHz, CDCl_3) δ ppm: 1.16 (3H, t, $J=7.1$ Hz), 4.19 (2H, d, $J=7.1$ Hz), 7.45-7.73 (3H, m), 8.01 (1H, dd, $J=1.8$ Hz, 7.6 Hz), 8.11 (1H, s), 8.34 (1H, s)
- 20 20) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 3.40-3.60 (2H, m), 3.76-4.04 (2H, m), 7.20 (1H, brs), 7.66 (2H, d, $J=9.0$ Hz), 7.88 (2H, d, $J=9.0$ Hz), 12.60 (1H, brs).
- 21) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 8.02 (2H, d, $J=6.8$ Hz), 8.11 (2H, d, $J=6.8$ Hz), 8.30 (1H, s), 9.43 (1H, s), 13.18 (1H, brs).
- 25 22) ^1H -NMR (200 MHz, $\text{DMSO}-d_6$) δ ppm: 2.13 (3H, s), 3.38 (2H, brs), 3.82 (3H, s), 5.23 (1H, brs), 7.23 (1H, d,

- J=1.4 Hz), 7.32 (1H, d, J=1.4 Hz).
- 23) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 2.29 (3H, s), 7.57 (1H, d, J=8.2 Hz), 7.92 (1H, dd, J=1.6 Hz, 8.2 Hz), 8.01 (1H, d, J=1.6 Hz), 8.27 (1H, s), 9.07 (1H, s), 13.19 (1H, brs).
- 24) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 8.00-8.60 (3H, m), 9.03 (1H, s), 9.52 (1H, s), 12.37-14.20 (1H, m).
- 25) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 8.20-8.27 (2H, m), 8.29 (1H, s), 8.31-8.38 (1H, m), 9.25 (1H, s).
- 10 26) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 6.9 (1H, brs), 7.78 (1H, d, J=8.5 Hz), 8.33 (1H, dd, J=1.7 Hz, 8.5 Hz), 8.39 (1H, s), 8.41 (1H, d, J=1.7 Hz), 9.25 (1H, s).
- 27) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 9.99 (2H, d, J=9.4 Hz), 10.00 (2H, d, J=9.4 Hz), 10.15 (1H, s), 14.07 (1H, brs), 14.86 (1H, brs).
- 15 28) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 7.70 (1H, dd, J=7.8 Hz, 8.0 Hz), 7.97 (1H, ddd, J=1.2 Hz, 1.8 Hz, 7.8 Hz), 8.14 (1H, ddd, J=1.2 Hz, 2.4 Hz, 8.0 Hz), 8.28 (1H, s), 8.39 (1H, dd, J=1.8 Hz, 2.4 Hz), 9.43 (1H, s), 13.38 (1H, brs).
- 20 29) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 7.55-7.70 (3H, m), 7.90 (1H, dd, J=2.0 Hz, 7.6 Hz), 8.17 (1H, s), 8.90 (1H, s), 13.12 (1H, brs).
- 30) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 3.38 (1H, s), 7.89 (1H, dd, J=2.2 Hz, 8.5 Hz), 8.80 (1H, dd, J=0.6 Hz, 2.2 Hz), 8.32 (1H, s), 9.49 (1H, s).
- 25 31) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 3.98 (3H, s), 7.41 (1H, d, J=8.6 Hz), 8.02 (1H, dd, J=2.2 Hz, 8.6 Hz), 8.18

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(1H, d, J=2.2 Hz), 8.23 (1H, s), 9.02 (1H, s), 13.04 (1H, brs).

32) ¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 1.11 (3H, t, J=7.6 Hz), 2.13 (3H, s), 3.37 (2H, q, J=7.6 Hz), 2.44 (3H, s),
5 7.29 (1H, d, J=8.4 Hz), 7.54 (1H, d, J=8.4 Hz), 9.41 (1H, brs), 12.70 (1H, brs).

33) ¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 1.11 (3H, t, J=7.6 Hz), 2.21 (3H, s), 2.39 (2H, q, J=7.6 Hz), 2.45 (3H, s),
7.50 (1H, s), 7.70 (1H, s), 9.24 (1H, brs), 12.59 (1H, brs).
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34) ¹H-NMR (200 MHz, CDCl₃) δ ppm: 1.32 (3H, t, J=7.6 Hz), 1.97 (3H, s), 2.26 (3H, s), 2.51 (2H, q, J=7.6 Hz),
3.63 (2H, s), 7.69 (1H, s), 7.82 (1H, s), 7.93 (1H, s), 11.00 (1H, brs)

15 35) ¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 1.14 (3H, t, J=7.6 Hz), 2.23 (3H, s), 2.41 (2H, q, J=7.6 Hz), 2.92 (3H, s),
4.53 (2H, s), 7.80-7.92 (1H, m), 7.92-8.05 (1H, m), 9.45 (1H, brs), 13.00 (1H, brs).

36) ¹H-NMR (200 MHz, DMSO-d₆) δ ppm: 1.12 (3H, t, J=7.6 Hz), 2.18 (3H, s), 2.37 (2H, q, J=7.6 Hz), 5.35 (1H, d, J=11.0 Hz),
20 5.81 (1H, d, J=17.6 Hz), 6.80 (1H, dd, J=11.0 Hz, 17.6 Hz), 7.75 (1H, d, J=1.6 Hz), 8.00 (1H, d, J=1.6 Hz), 9.47 (1H, brs), 12.96 (1H, brs).

37) ¹H-NMR (200 MHz, CDCl₃) δ ppm: 1.24 (3H, t, J=7.6 Hz), 2.36 (3H, s), 2.50 (2H, q, J=7.6 Hz), 8.14 (1H, d, J=1.7 Hz),
25 8.40 (1H, d, J=1.7 Hz), 9.15 (1H, brs).

- 38) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 0.92 (3H, t, $J=7.5$ Hz), 1.79 (2H, q, $J=7.5$ Hz), 2.20 (6H, s), 3.03 (3H, s), 7.77 (2H, s), 12.98 (1H, brs).
- 39) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 2.66 (3H, s), 7.80
5 (1H, s), 8.33 (1H, s).
- 40) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 2.04 (3H, s), 6.50 (2H, brs), 7.65 (1H, d, $J=1.9$ Hz), 8.36 (1H, d, $J=1.9$ Hz).
- 41) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.10 (3H, t, $J=7.6$
10 Hz), 2.39 (2H, q, $J=7.6$ Hz), 4.55 (2H, s), 4.50-6.00 (1H, m), 7.70-7.90 (2H, m), 7.92-8.10 (1H, m), 9.41 (1H, brs), 12.74 (1H, brs).
- 42) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.12 (3H, t, $J=7.6$
15 Hz), 2.18 (3H, s), 2.34 (2H, q, $J=7.6$ Hz), 4.42 (2H, s), 7.62-7.76 (1H, m), 7.87-8.01 (1H, m), 9.31 (1H, brs), 12.79 (1H, brs).
- 43) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.12 (3H, t, $J=7.6$
20 Hz), 2.32 (3H, s), 2.34 (2H, q, $J=7.6$ Hz), 3.82 (3H, s), 6.97 (1H, d, $J=8.7$ Hz), 7.81 (1H, d, $J=8.7$ Hz), 9.10 (1H, s), 12.57 (1H, s).
- 44) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.15 (3H, t, $J=7.6$ Hz), 2.36 (3H, s), 2.38 (2H, q, $J=7.6$ Hz), 7.47 (1H, d, $J=8.4$ Hz), 7.70 (1H, d, $J=8.4$ Hz), 9.60 (1H, s), 13.13 (1H, brs).
- 25 45) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.11 (3H, t, $J=7.6$ Hz), 1.15 (3H, t, $J=7.6$ Hz), 2.32 (3H, s), 2.37 (2H, q, $J=7.6$ Hz), 2.48-2.70 (2H, m), 7.18 (1H, d, $J=8.2$ Hz), 7.65 (1H, d, $J=8.2$ Hz), 9.34 (1H, s), 12.79 (1H, s).

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46) ^1H -NMR (200 MHz, DMSO- d_6) δ ppm: 1.09 (3H, t, $J=7.5$ Hz), 2.10 (3H, s), 2.23 (3H, s), 2.32 (2H, q, $J=7.5$ Hz), 7.04 (1H, d, $J=8.0$ Hz), 7.23 (1H, d, $J=8.0$ Hz), 9.28 (1H, brs).

Reference Examples 74-80

By the method similar to that employed in Reference Example 3 or 4, and by using suitable starting materials, there were prepared compounds of Reference Examples 74-80 as shown in the following Table 4.

Reference Examples 81-147

By the method similar to that employed in Reference Example 6 or 12, and by using suitable starting materials, there were prepared compounds of Reference Examples 81-147 as shown in the following Table 5.

Reference Example 148

By the method similar to that employed in Reference Example 5, and by using suitable starting materials, there was prepared compound of Reference Example 148 as shown in the following Table 6.

Reference Examples 149-156

By the method similar to that employed in Reference Example 3 or 4, and by using suitable starting materials, there were prepared compounds of Reference Examples 149-156 as shown in the following Table 7.

Reference Examples 157-159

By the method similar to that employed in Reference Example 6 or 12, and by using suitable

starting materials, there were prepared compounds of Reference Examples 157-159 as shown in the following Table 8.

Reference Examples 160-161

- 5 By the method similar to that employed in Reference Example 5, and by using suitable starting materials, there were prepared compounds of Reference Examples 160-161 as shown in the following Table 9.

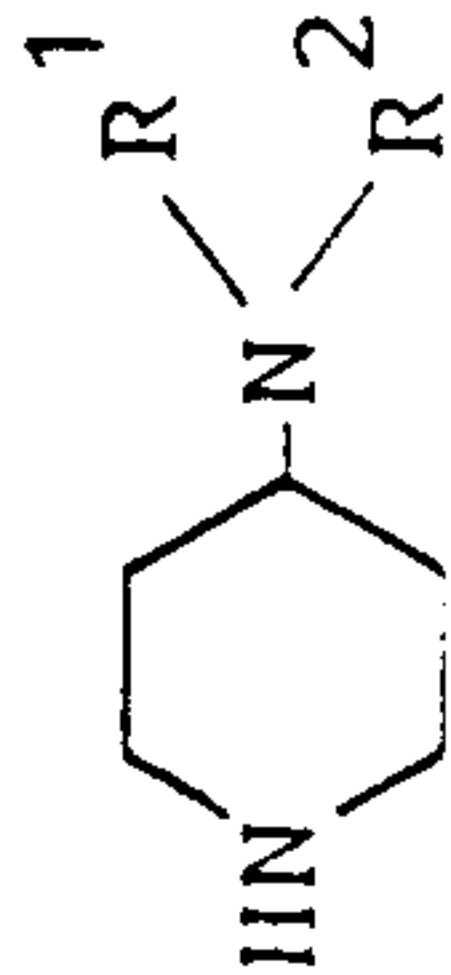
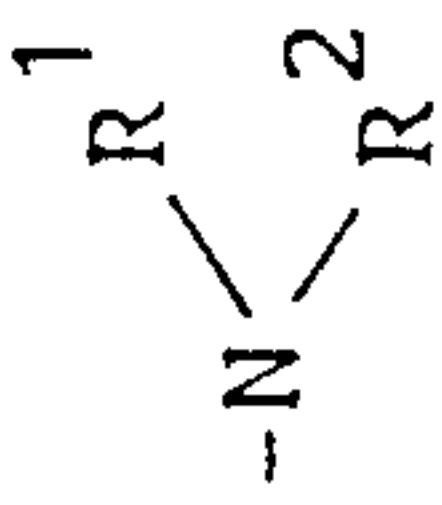
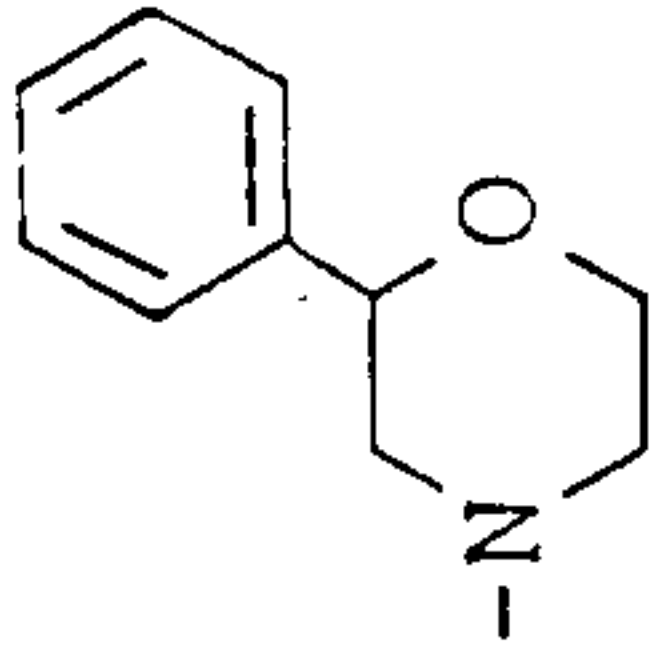
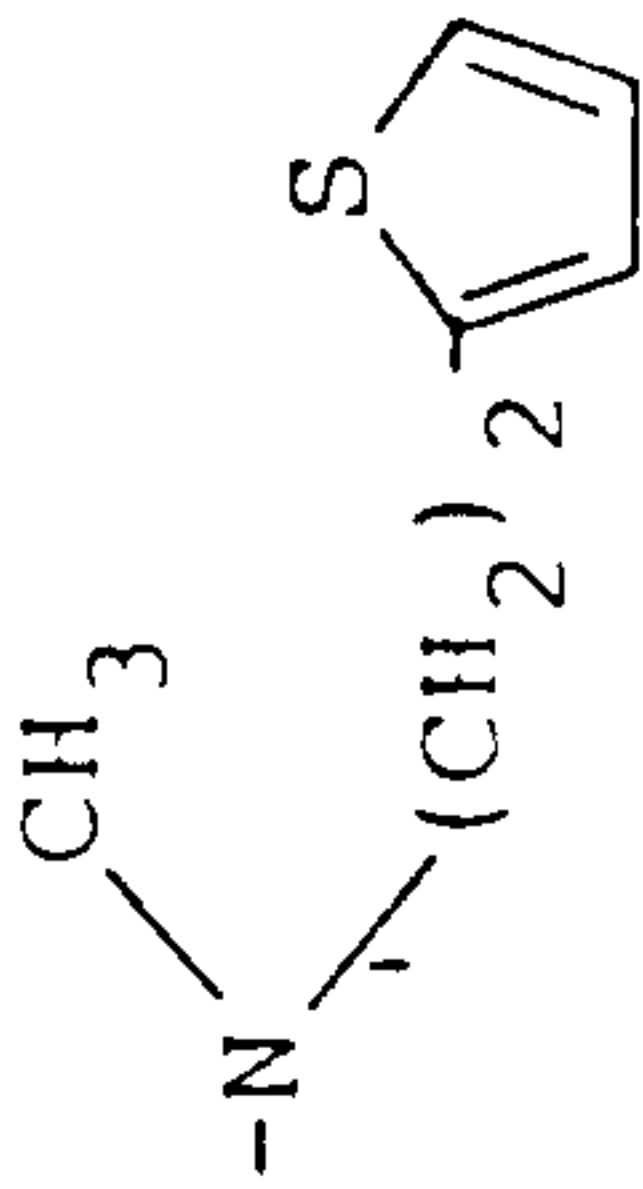
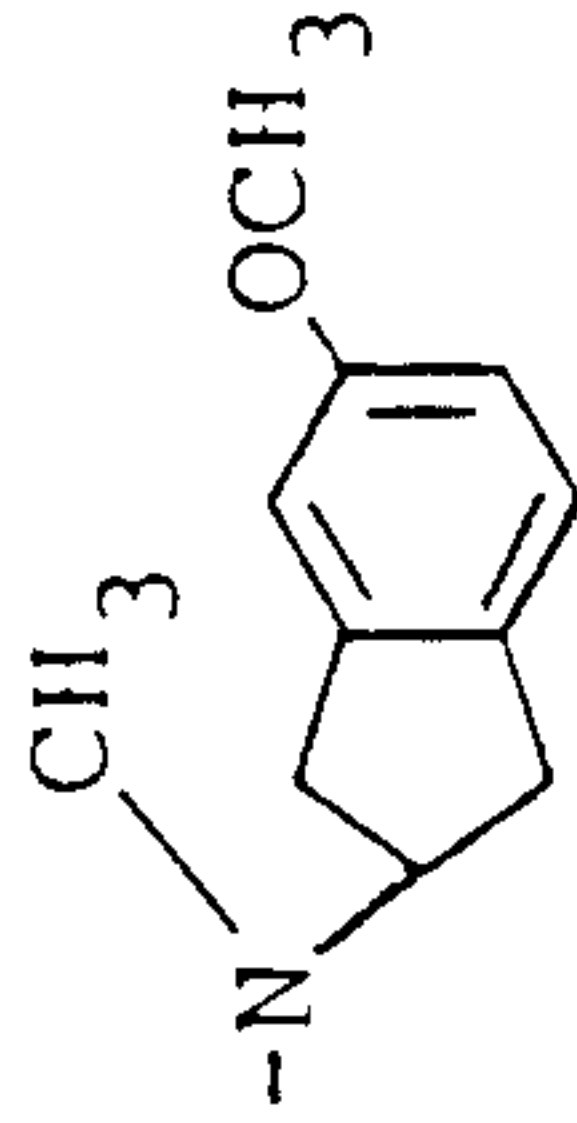
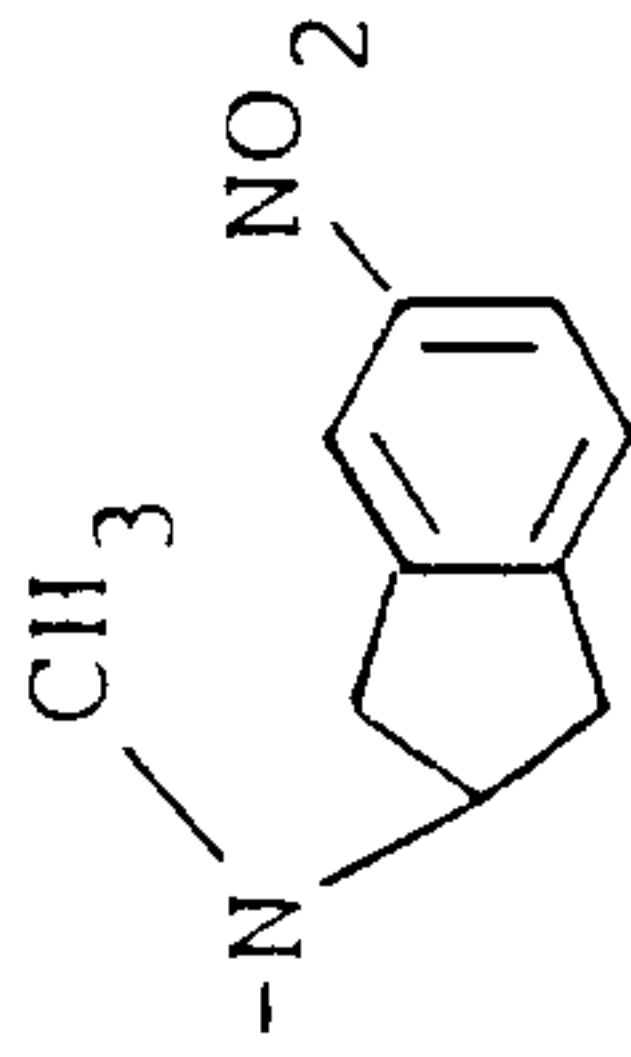


Table 4

Reference Example No.		Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
74		Colorless oil	(-)	See Attached Sheet (Λ).
75		White powder	251-254 (Decompd.) (2HCl)	
76		Orange red oil	(-)	See Attached Sheet (Λ).
77		Brown oil	(-)	See Attached Sheet (Λ).

(To be continued)

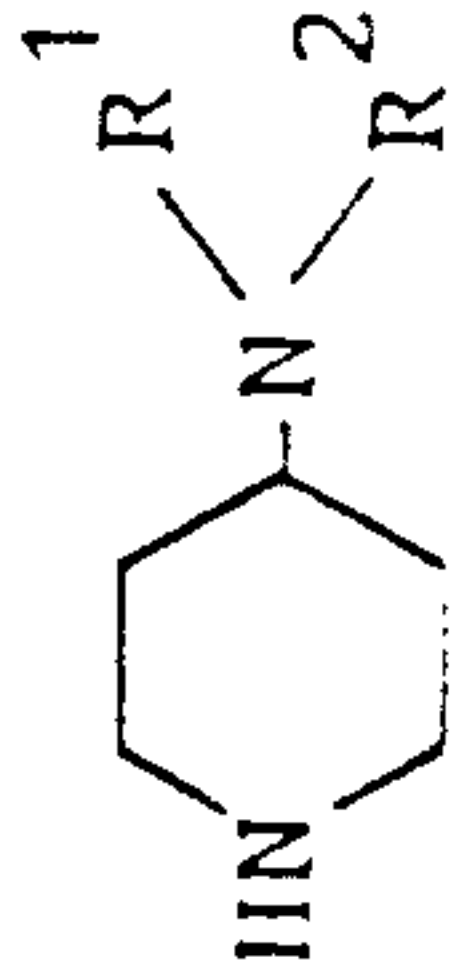
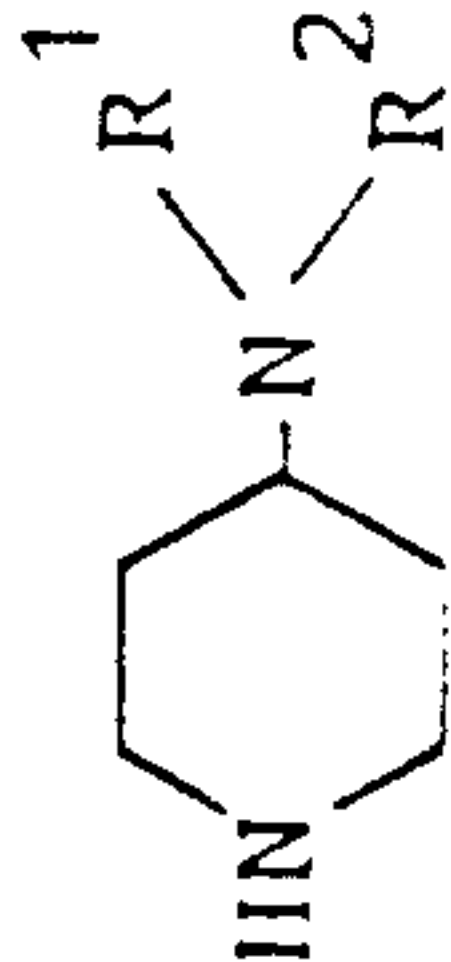
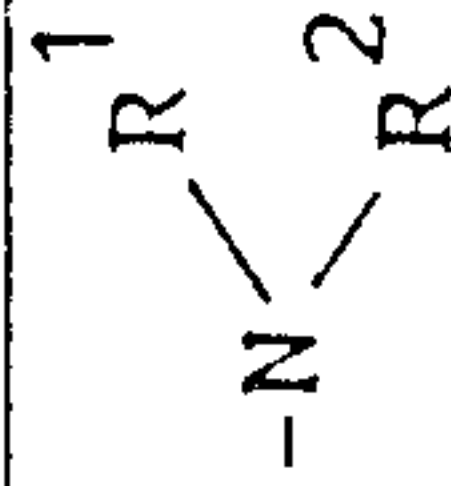
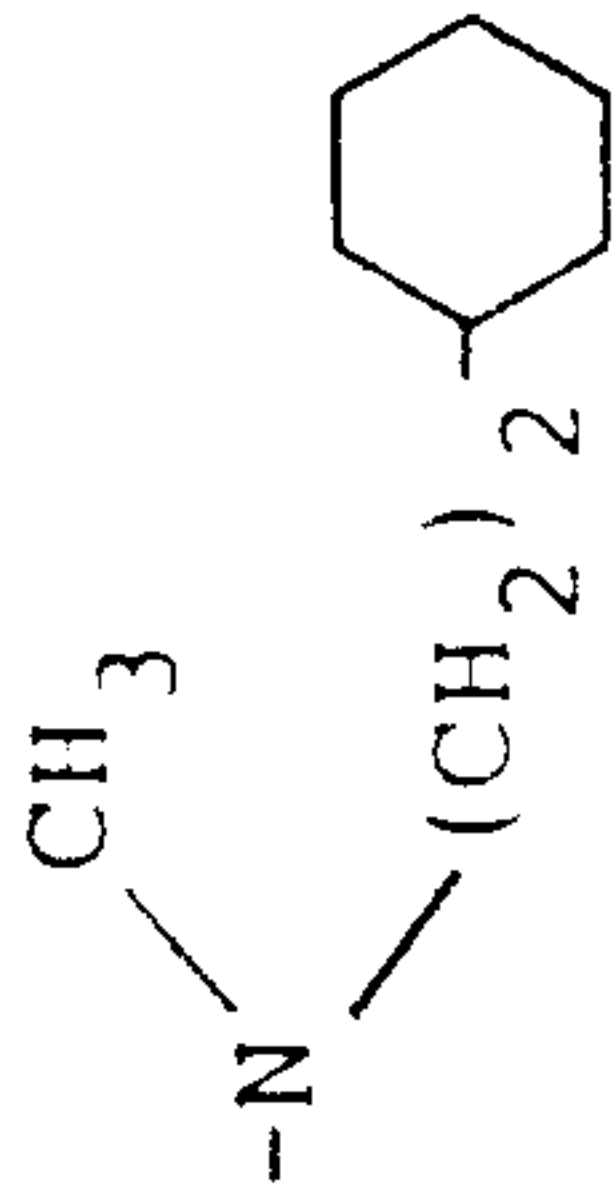
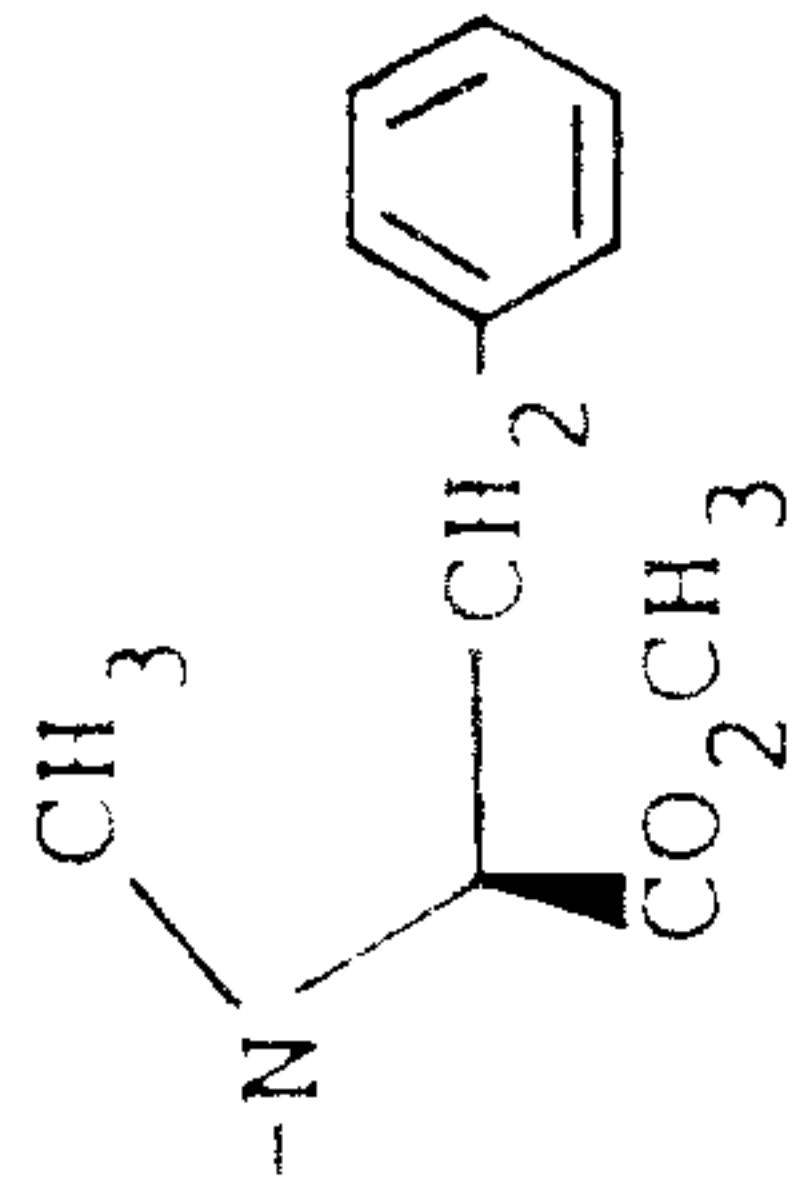
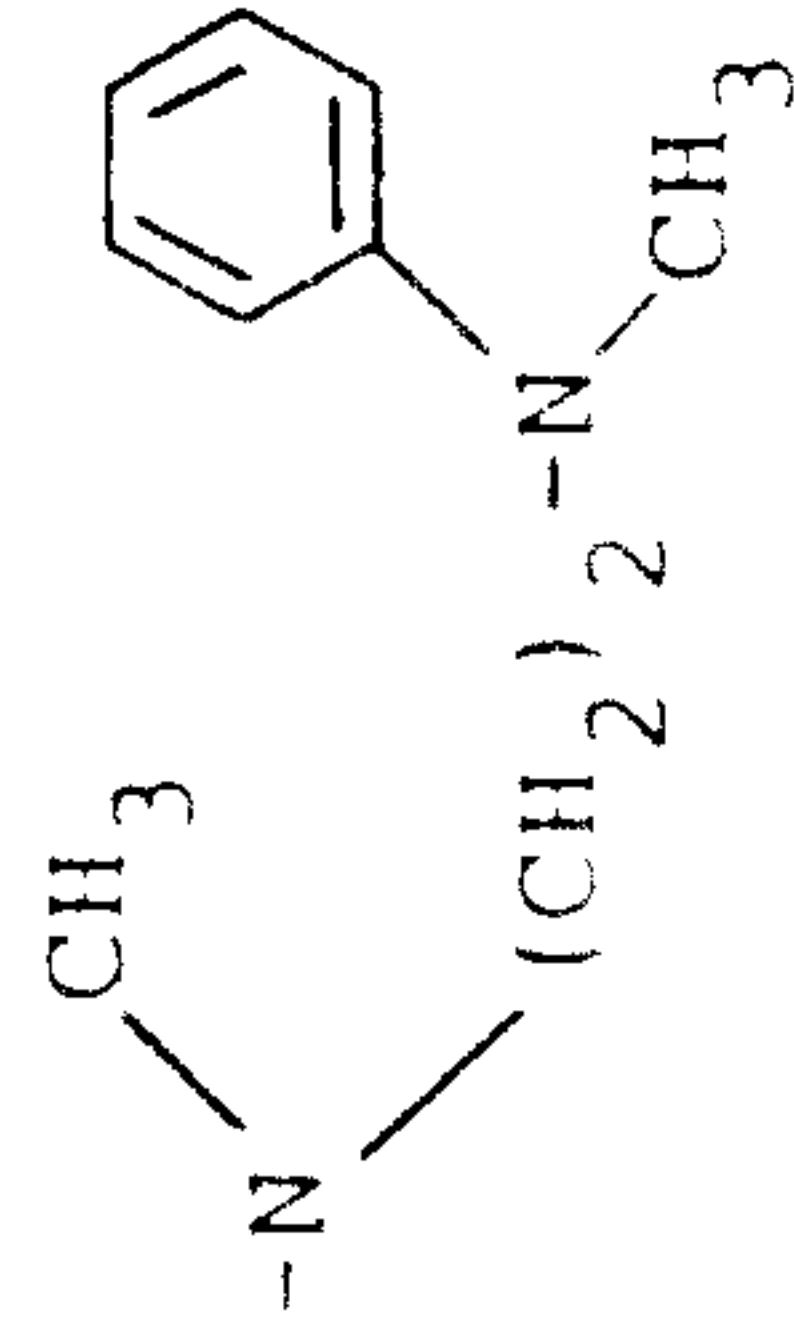


Table 4

(Continued)			Reference Example No.		Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
	78				Colorless oil	(-)	See Attached Sheet (A).
	79				Colorless oil	(-)	See Attached Sheet (A).
	80				Light yellow oil	(-)	See Attached Sheet (A).

Attached Sheet (A) for Table 4

Reference Example No.	¹ H-NMR (200 MHz) δ ppm
74	(CDCl ₃): 1.22-1.70 (3H, m), 1.75-2.00 (2H, m), 2.13-2.72 (5H, m), 2.72-3.04 (2H, m), 3.04-3.23 (2H, m), 3.82 (1H, dt, J= 2.5 Hz, 11.3 Hz), 4.00-4.16 (1H, m), 4.55 (1H, dd, J=10.3 Hz, 2.4 Hz), 7.20-7.46 (5H, m)
76	(CDCl ₃): 1.41-1.67 (3H, m), 1.67-1.86 (2H, m), 2.27 (3H, s), 2.52-3.11 (7H, m), 3.11-3.28 (2H, m), 3.46-3.71 (1H, m), 3.77 (3H, s), 6.69 (1H, d, J=8.1 Hz), 6.74 (1H, s), 7.07 (1H, d, J=8.1 Hz)
77	(CDCl ₃): 1.41-1.69 (3H, m), 1.69-1.94 (2H, m), 2.27 (3H, s), 2.52-2.86 (3H, m), 2.86- 3.30 (6H, m), 3.69 (1H, quint, J=7.4 Hz), 7.23-7.36 (1H, m), 7.96-8.10 (2H, m)
78	(CDCl ₃): 0.79-1.09 (2H, m), 1.09-1.55 (8H, m), 1.55-1.88 (7H, m), 1.88-2.05 (1H, m), 2.24 (3H, m), 2.35-2.72 (5H, m), 3.05- 3.22 (2H, m)
79	(CDCl ₃): 1.22-1.60 (2H, m), 1.60-1.88 (2H, m), 1.92-2.10 (1H, m), 2.42 (3H, s), 2.49- 2.74 (3H, m), 2.82-3.00 (1H, m), 3.00- 3.24 (3H, m), 3.60 (3H, s), 3.60-3.77 (1H, m), 7.10-7.39 (5H, m)
80	(CDCl ₃): 1.29-1.55 (2H, m), 1.68-1.91 (2H, m), 2.33 (3H, s), 2.39-2.72 (5H, m), 2.95 (3H, s), 3.07-3.23 (2H, m), 3.35-3.52 (2H, m), 6.61-6.79 (3H, m), 7.18-7.32 (2H, m)

Table 5 Ra-OH

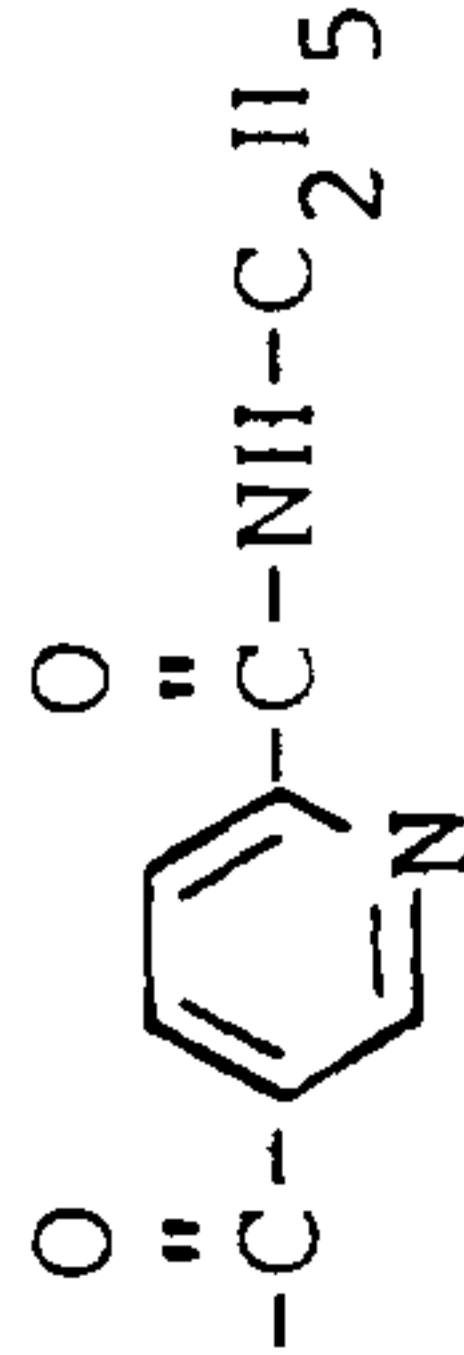
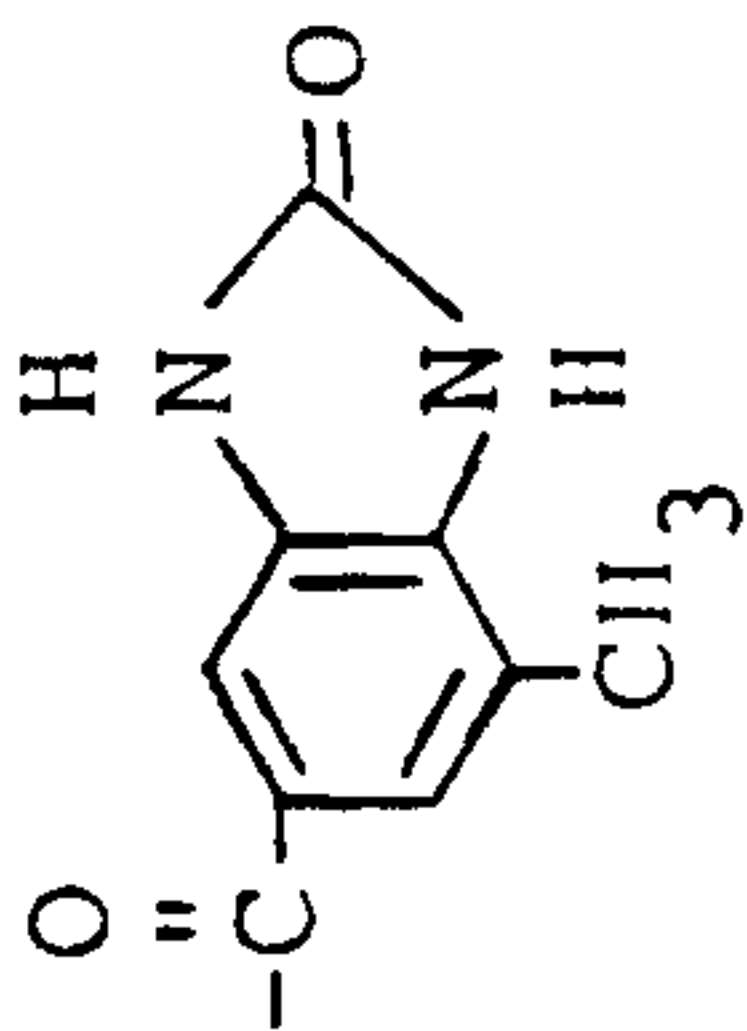
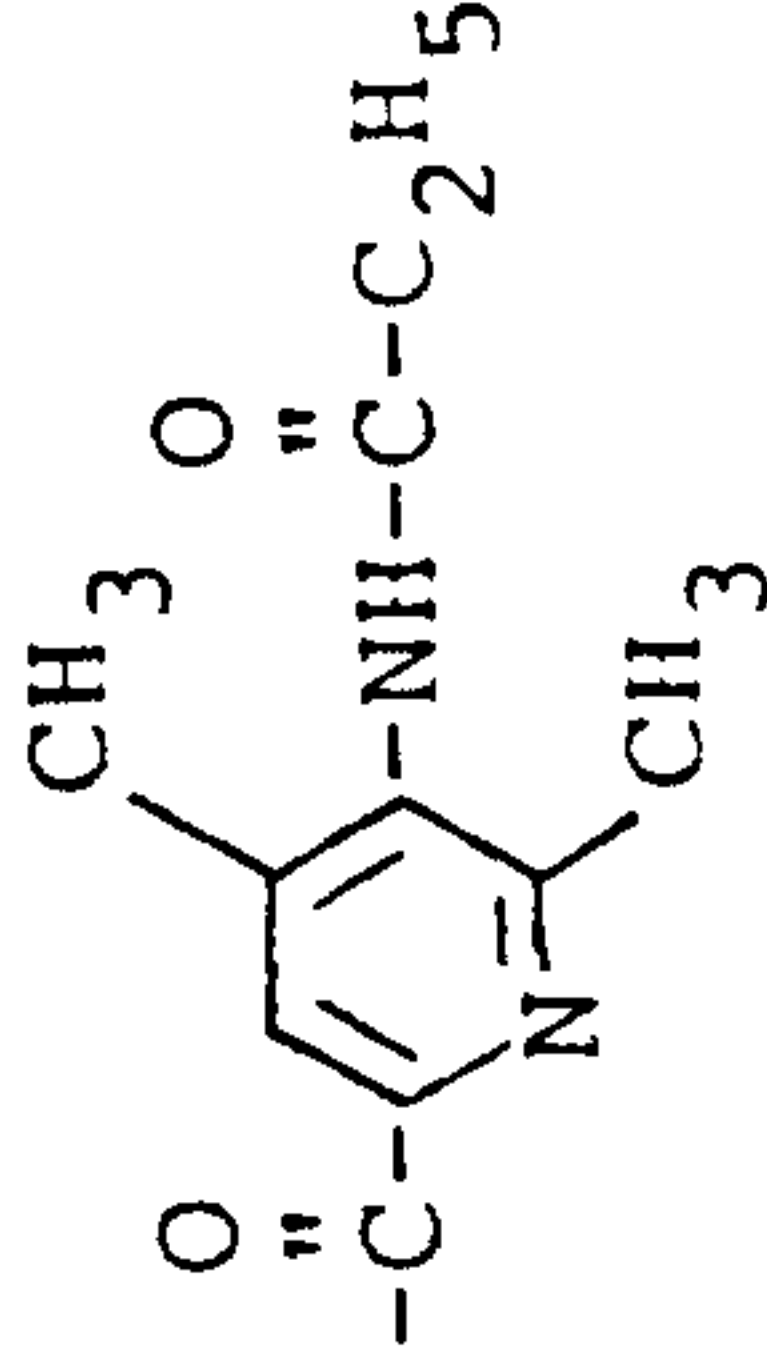
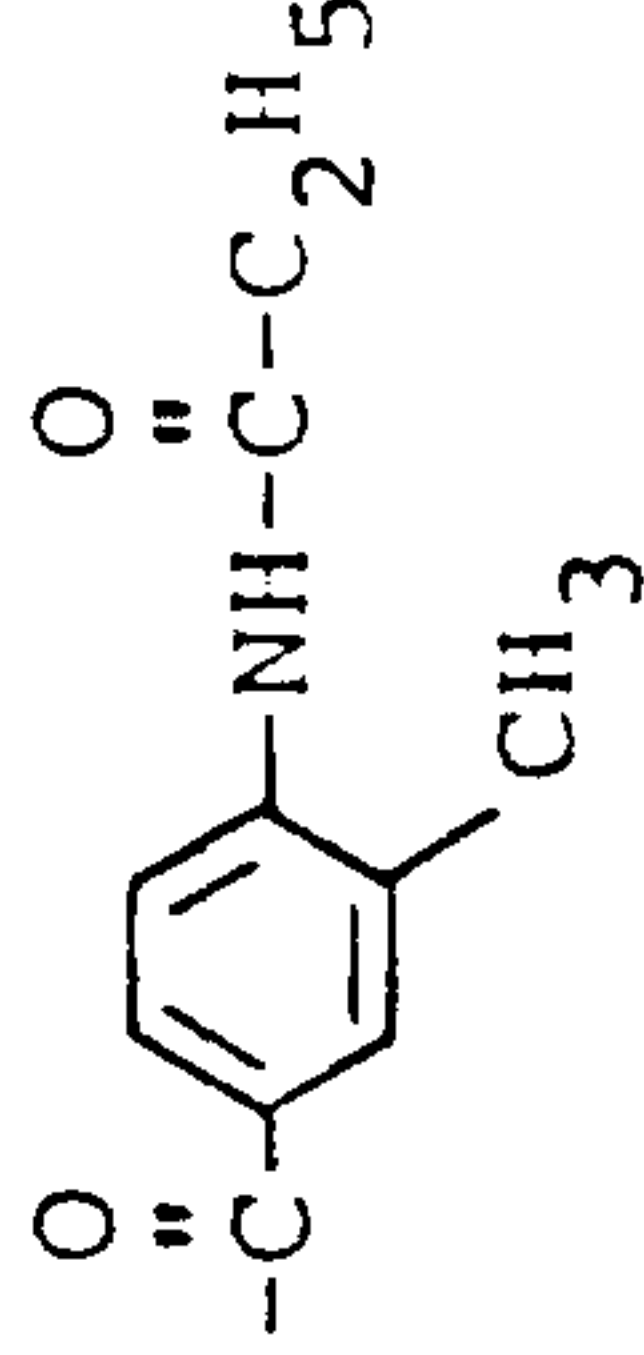
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
81		White powder	216 - 218 (-)	
82		White powder	(-)	See Attached Sheet (B).
83		White powder	240 (Decompd.) (-)	See Attached Sheet (B).
84		White powder	167 (-)	

(To be continued)

Ra-OH

Table 5

(Continued)

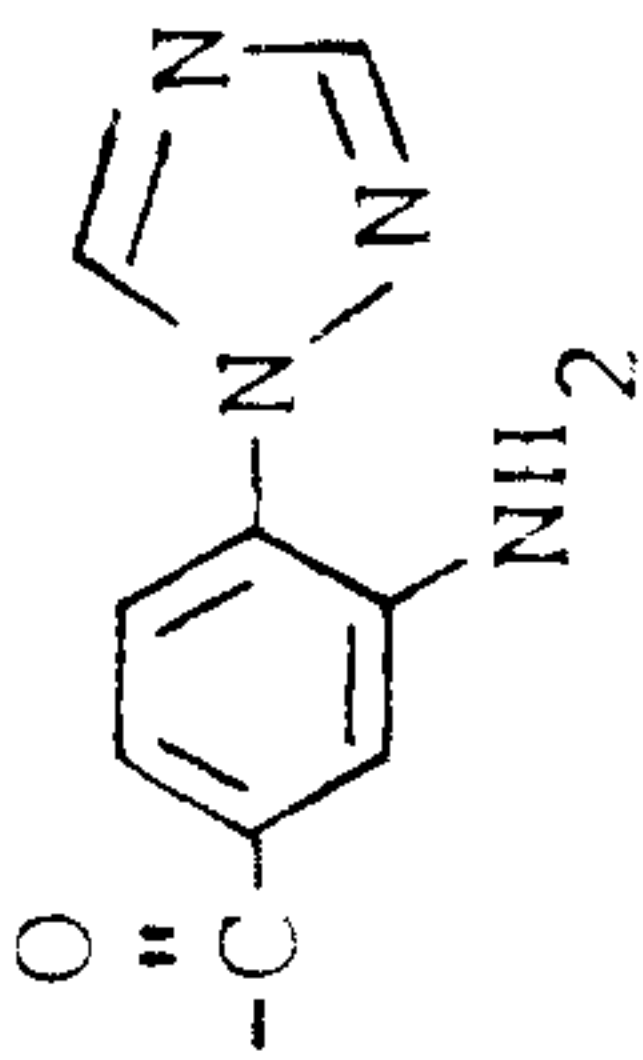
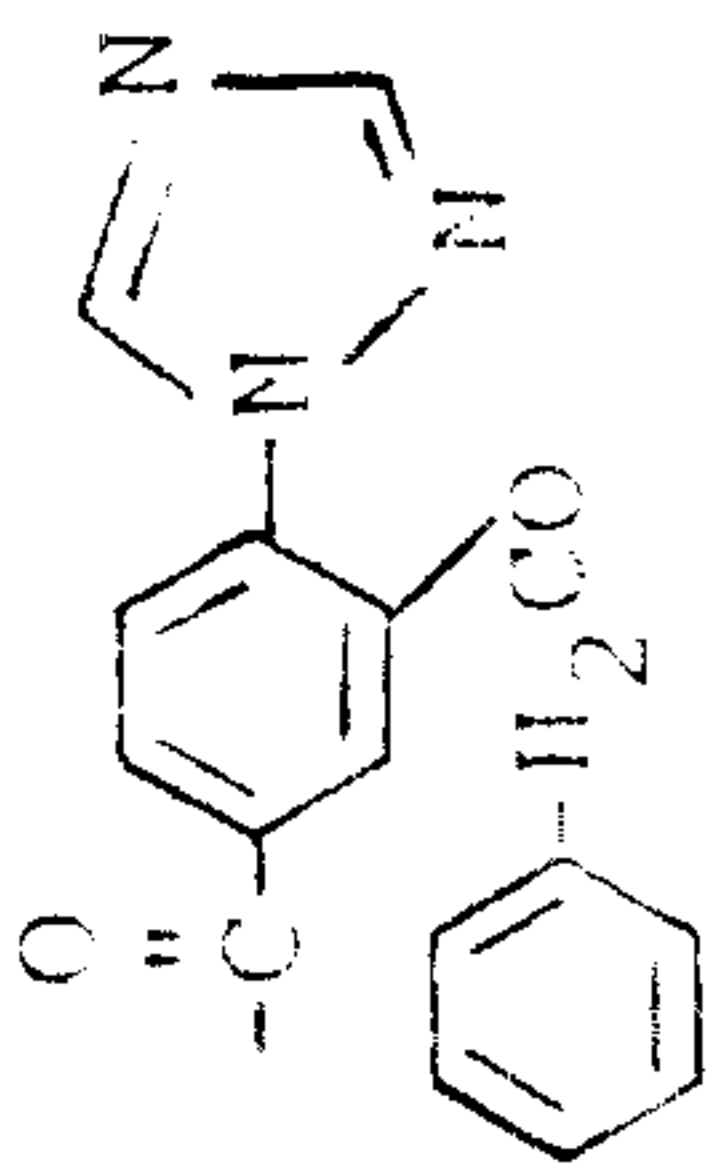
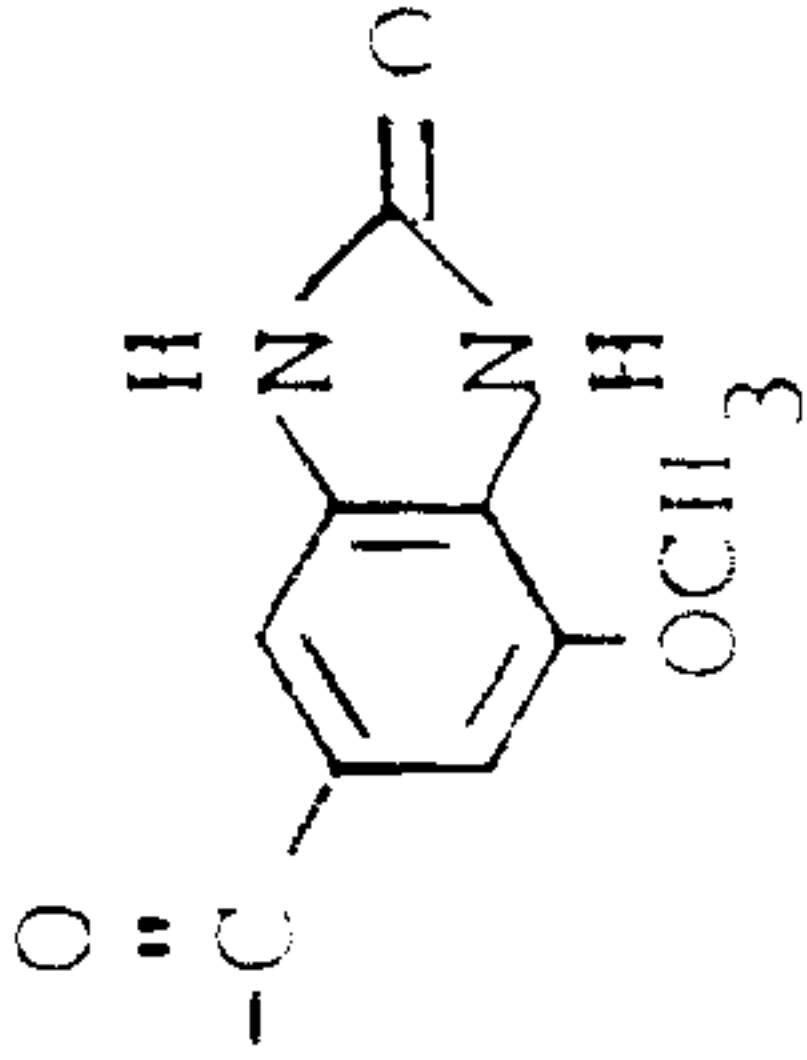
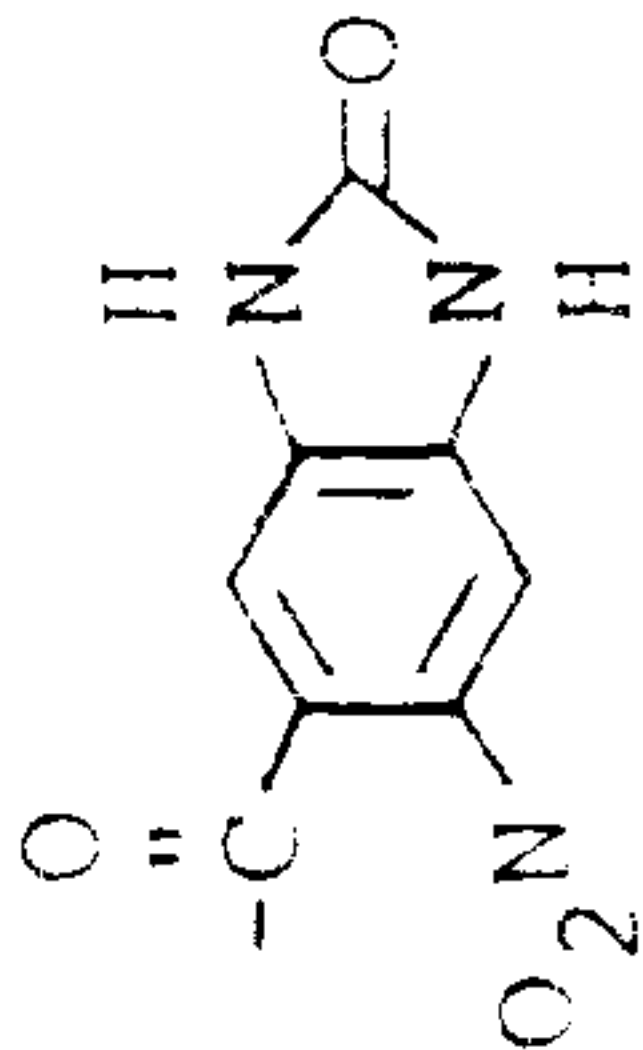
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
85		White powder	234 - 235 (-)	
86		Light brown powder	300 or above (-)	See Attached Sheet (B).
87		White amorphous	(-)	See Attached Sheet (B).
88		Colorless needles	118 (-)	

(To be continued)

Ra-OII

Table 5

(Continued)

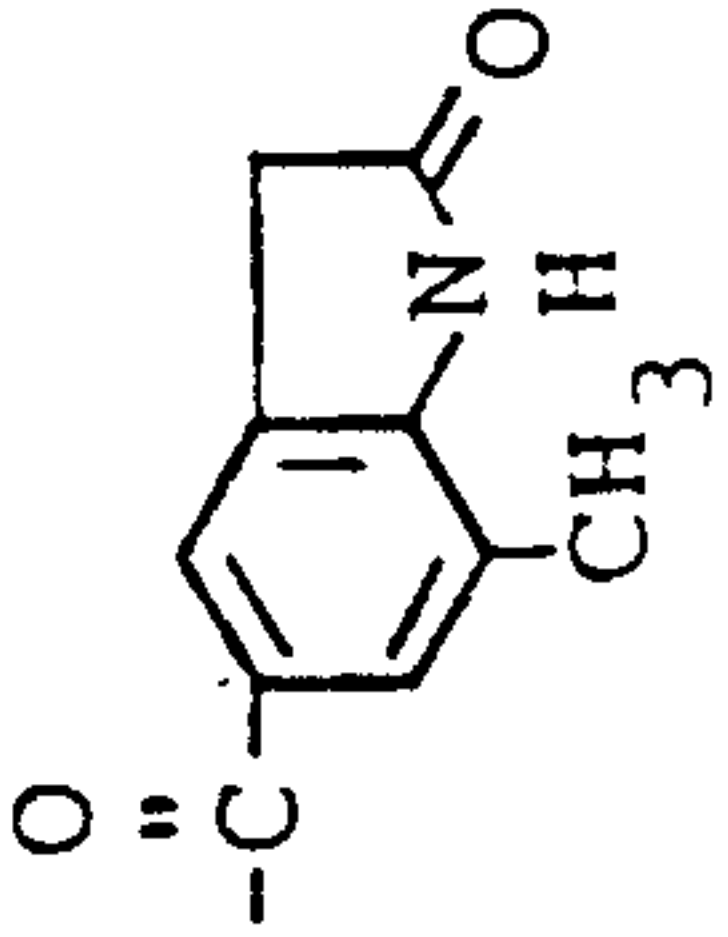
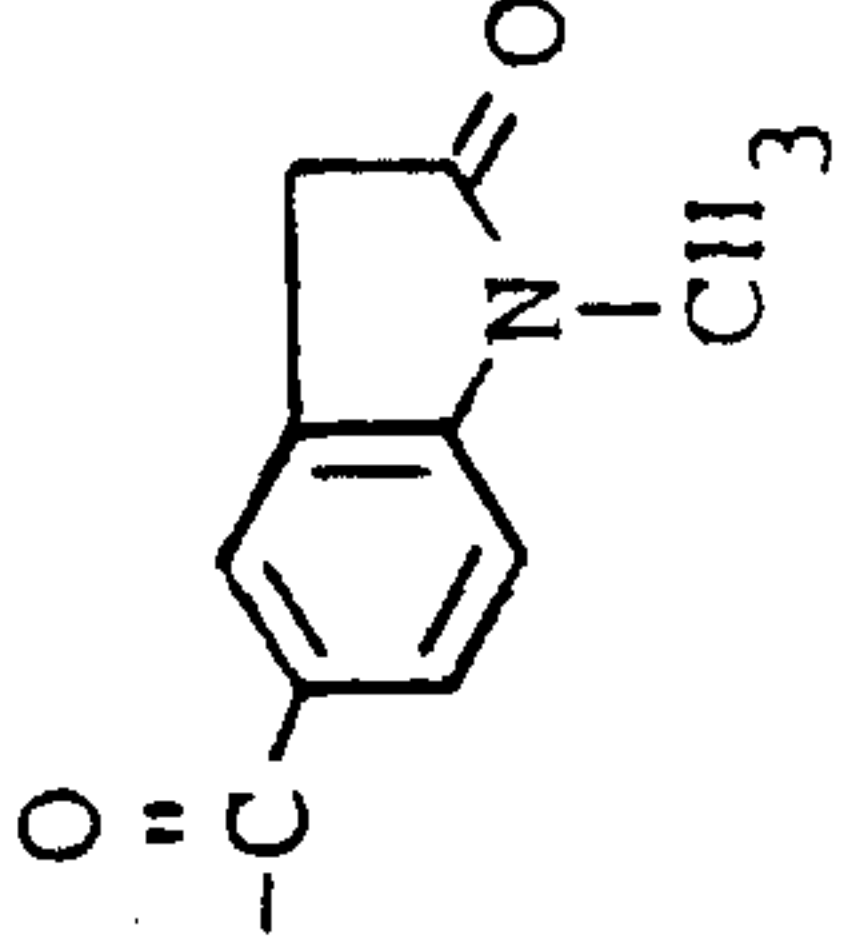
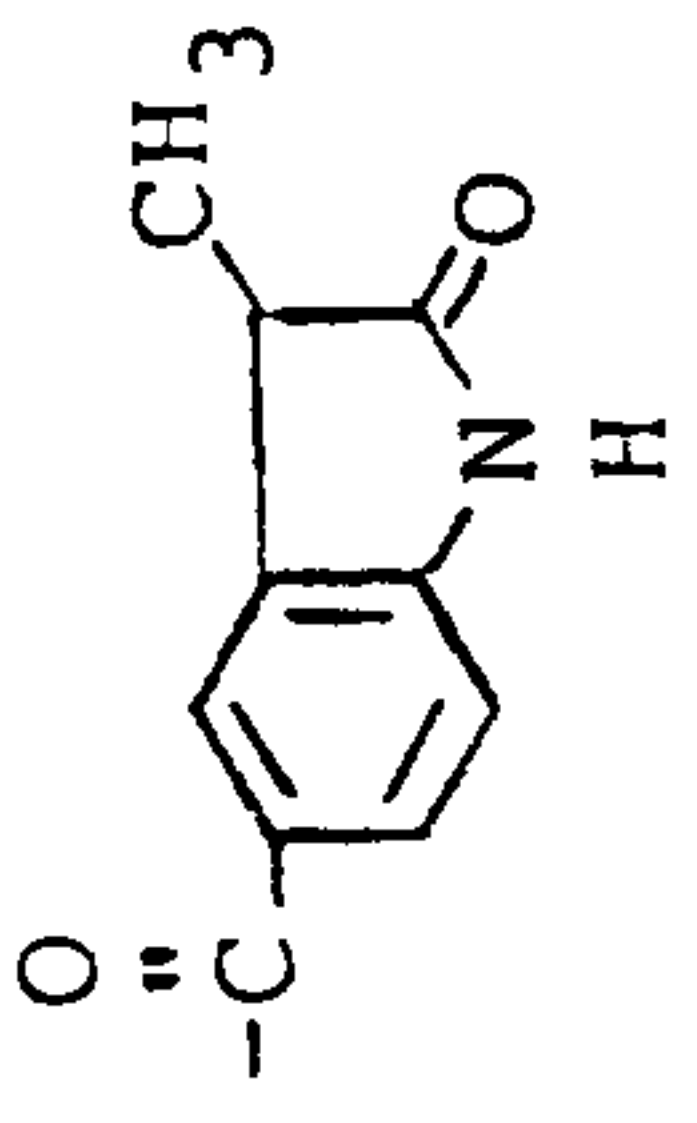
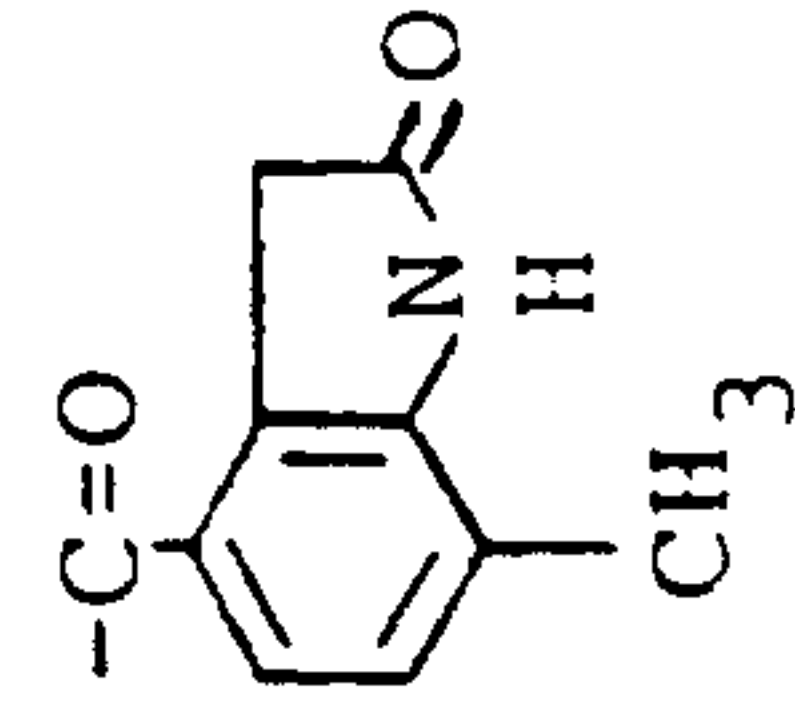
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
89		White powder	259 - 261 (Decompd.)	
90		White powder	(-)	See Attached Sheet (B).
91		Light brown powder	300 or above (-)	See Attached Sheet (B).
92		Light yellow powder	300 or above (-)	See Attached Sheet (B).

(To be continued)

Ra-OH

Table 5

(Continued)

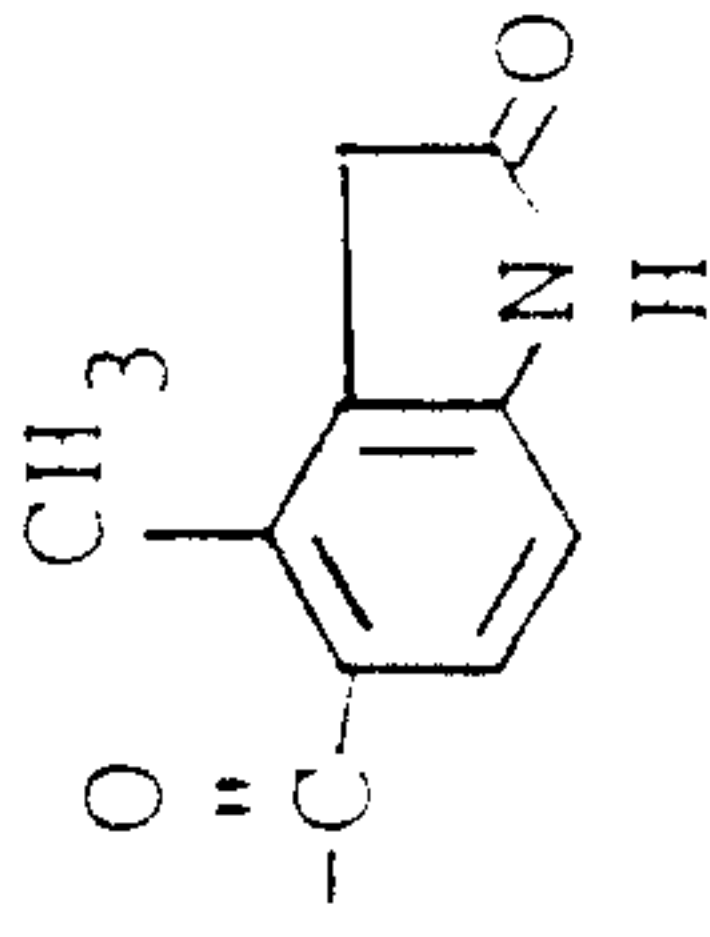
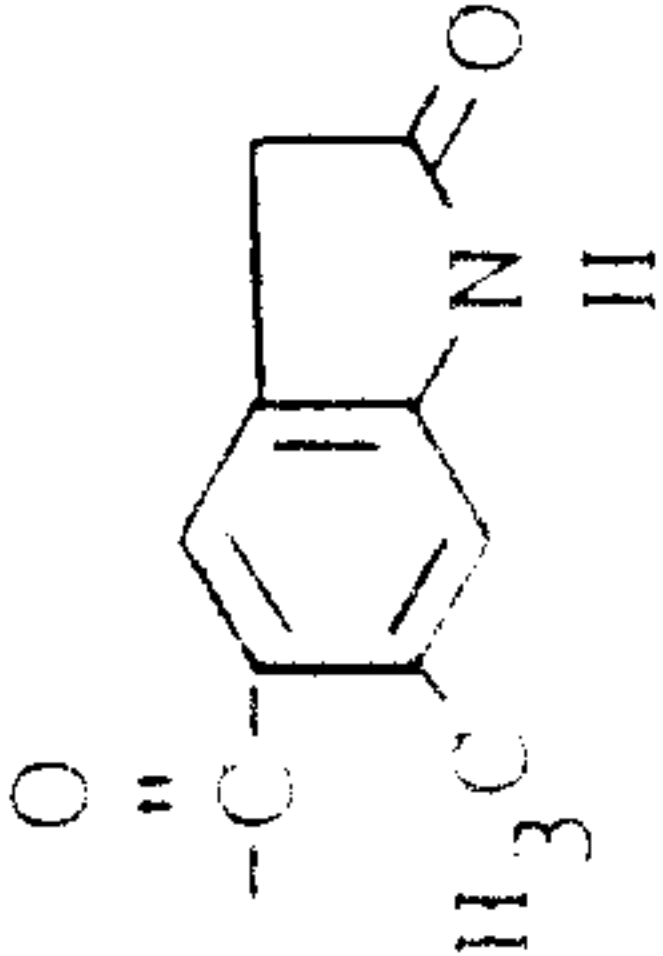
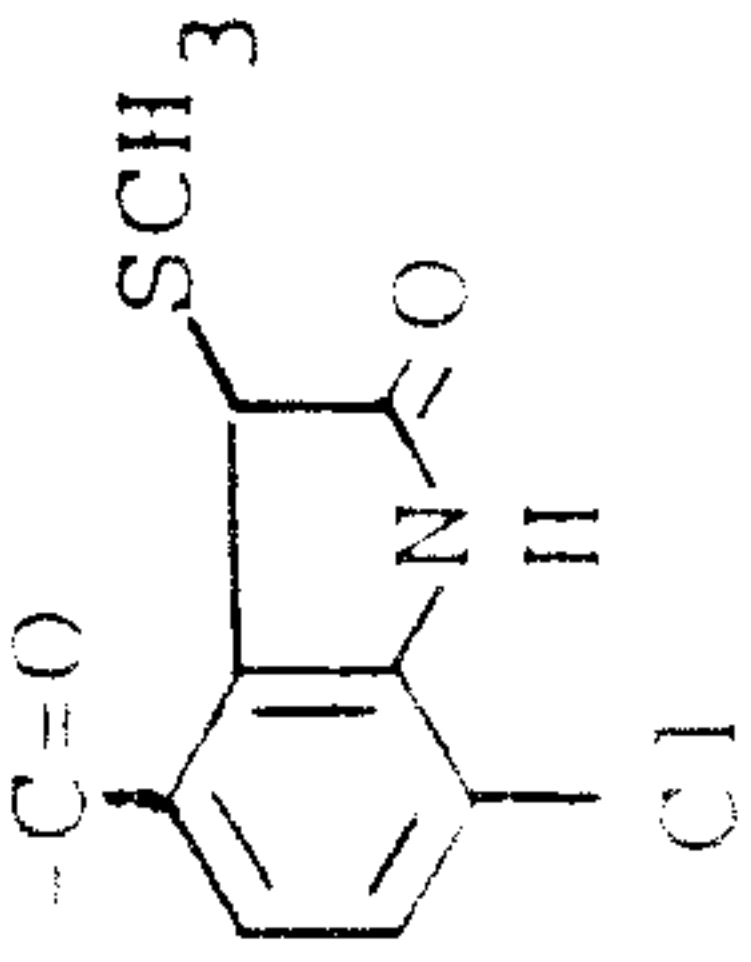
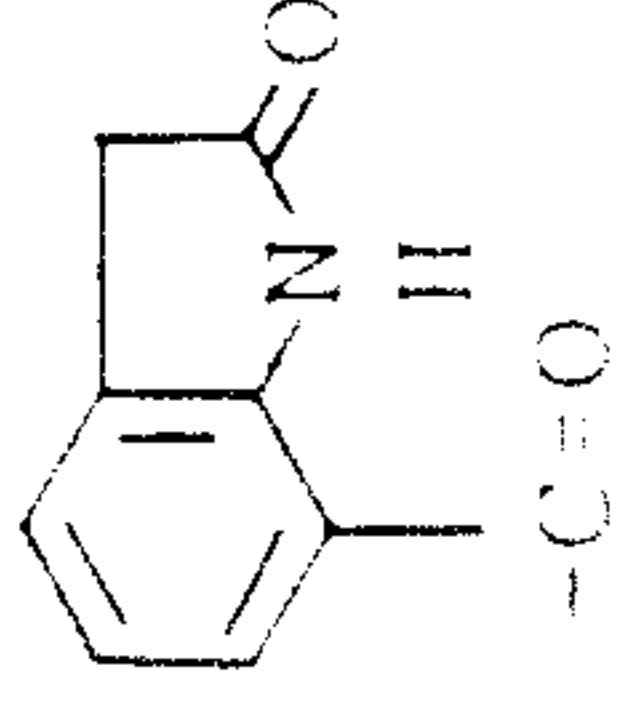
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
93		White powder	(-)	See Attached Sheet (B).
94		White powder	(-)	See Attached Sheet (B).
95		White powder	(-)	See Attached Sheet (B).
96		White powder	(-)	See Attached Sheet (B).

(To be continued)

Ra-OH

Table 5

(Continued)

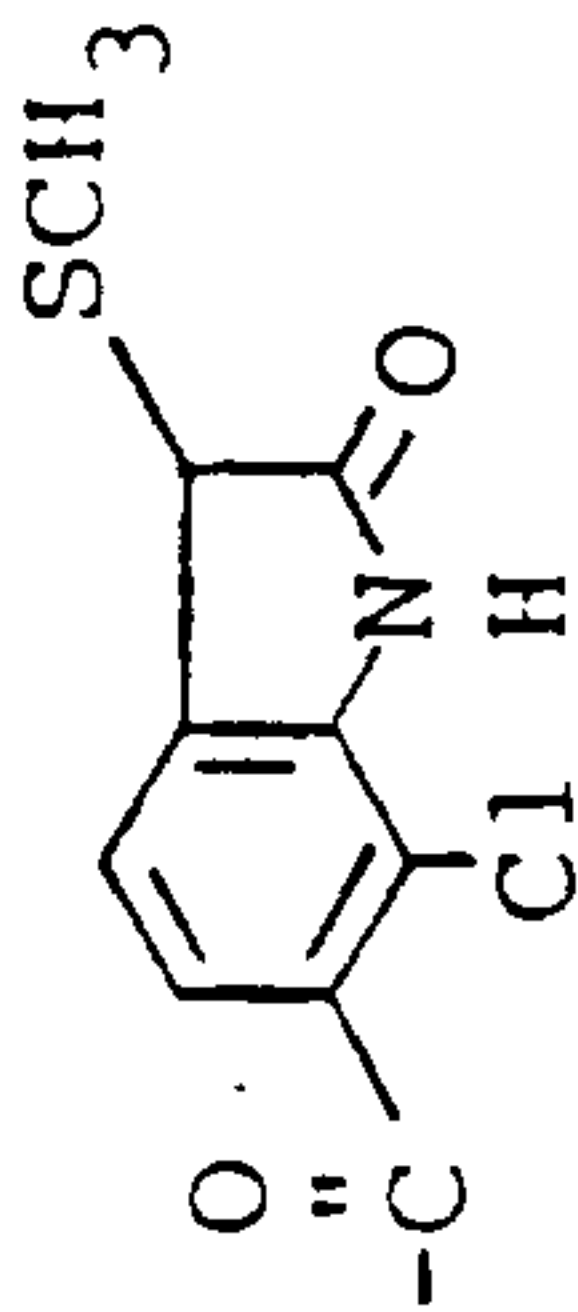
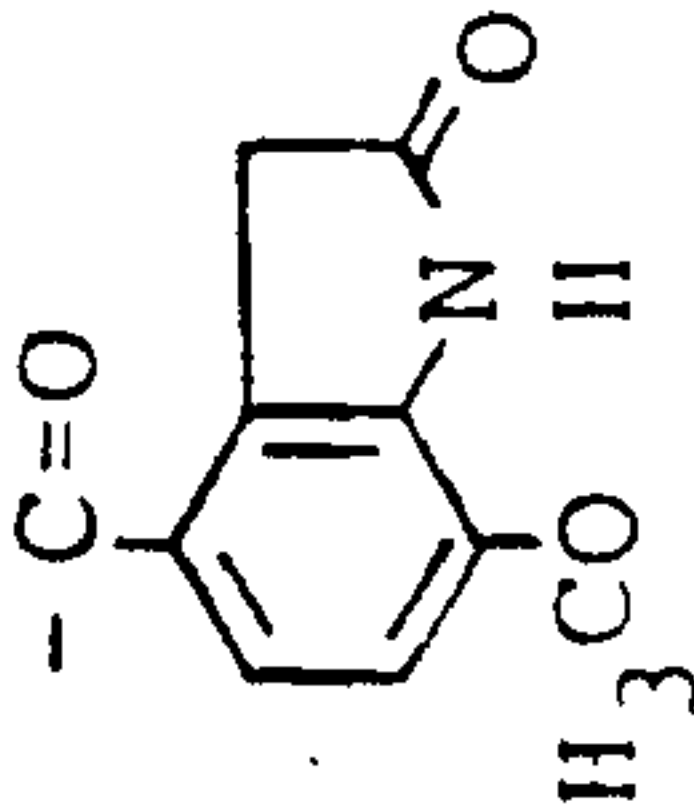
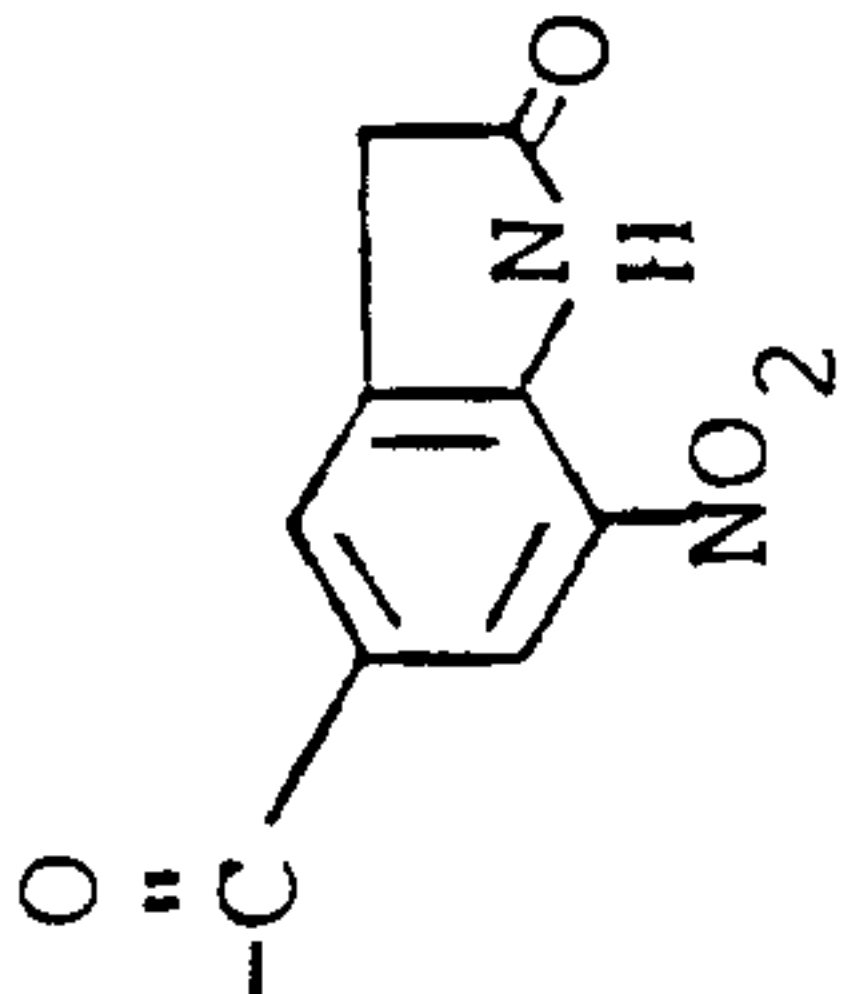
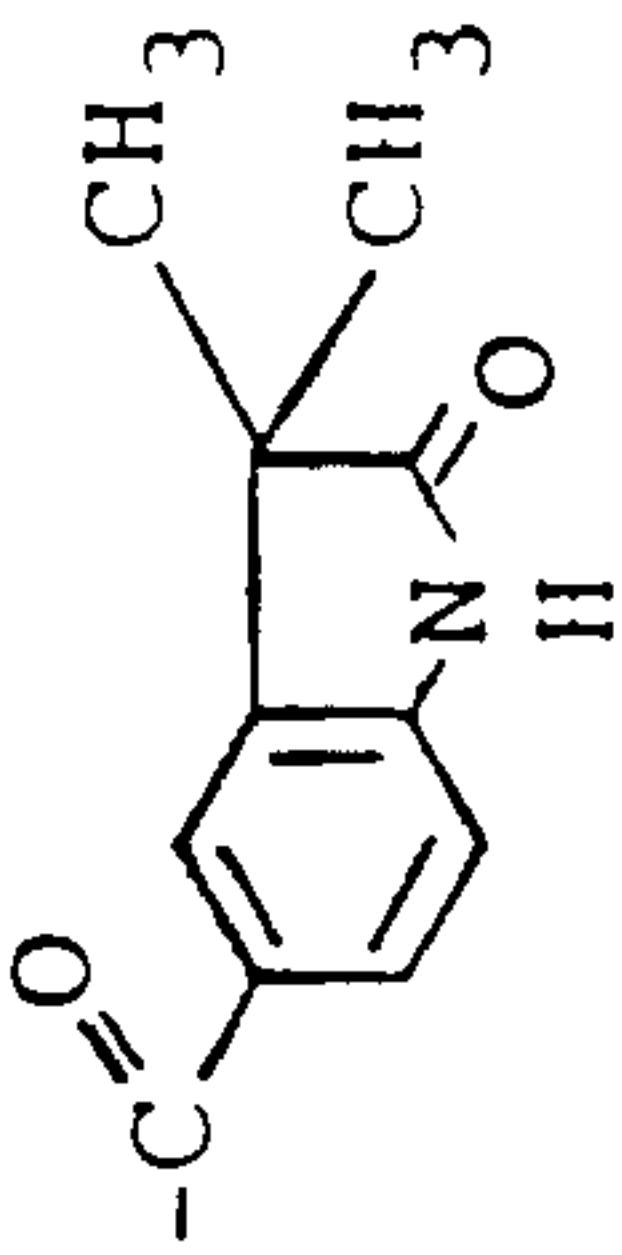
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
97		White powder	(-)	See Attached Sheet (B).
98		White powder	(-)	See Attached Sheet (B).
99		White powder	(-)	See Attached Sheet (B).
100		White powder	(-)	See Attached Sheet (B).

(To be continued)

Table 5 Ra-OH

Table 5

(Continued)

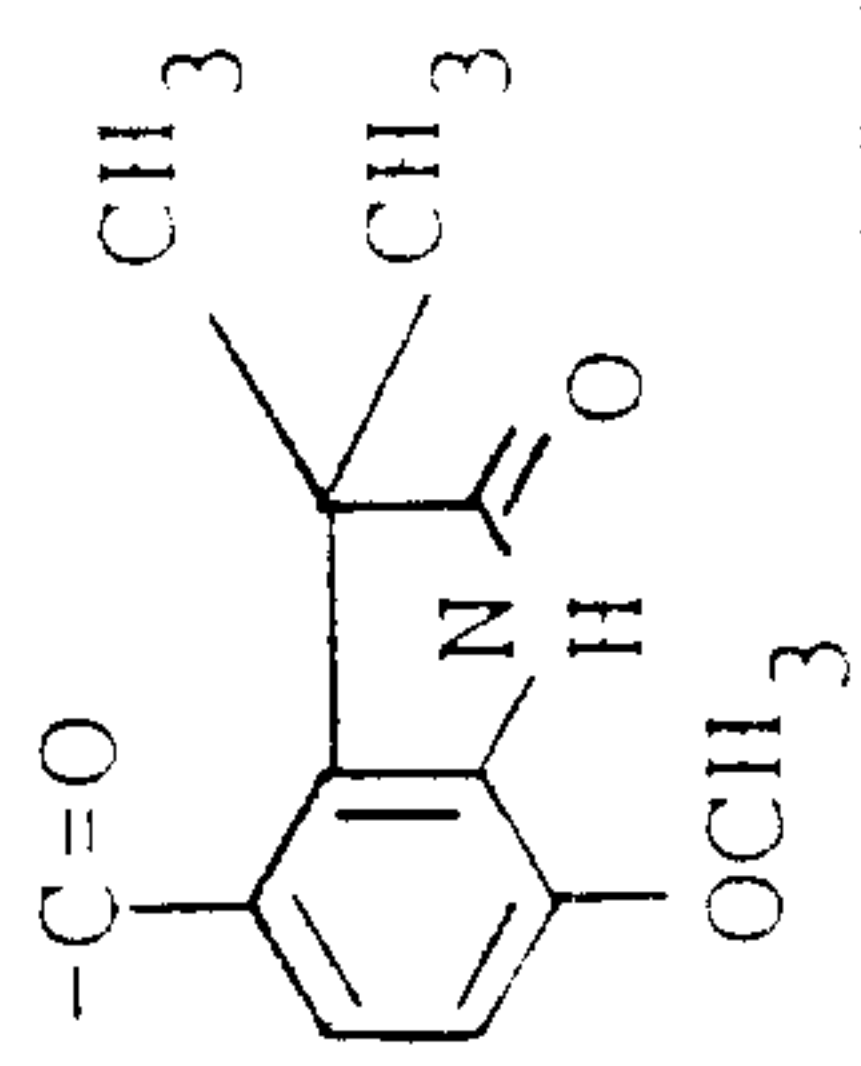
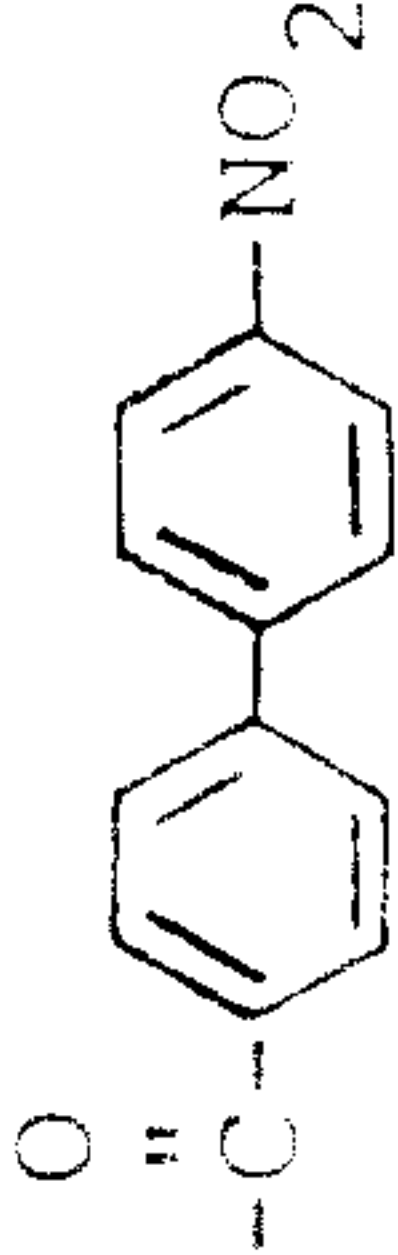
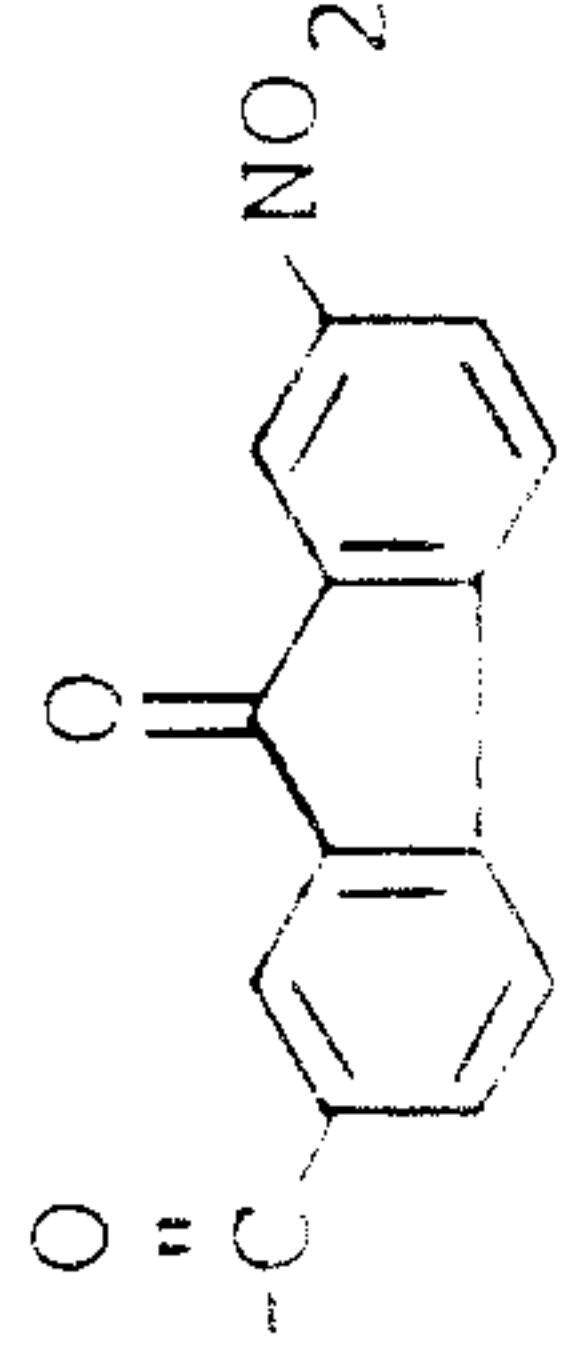
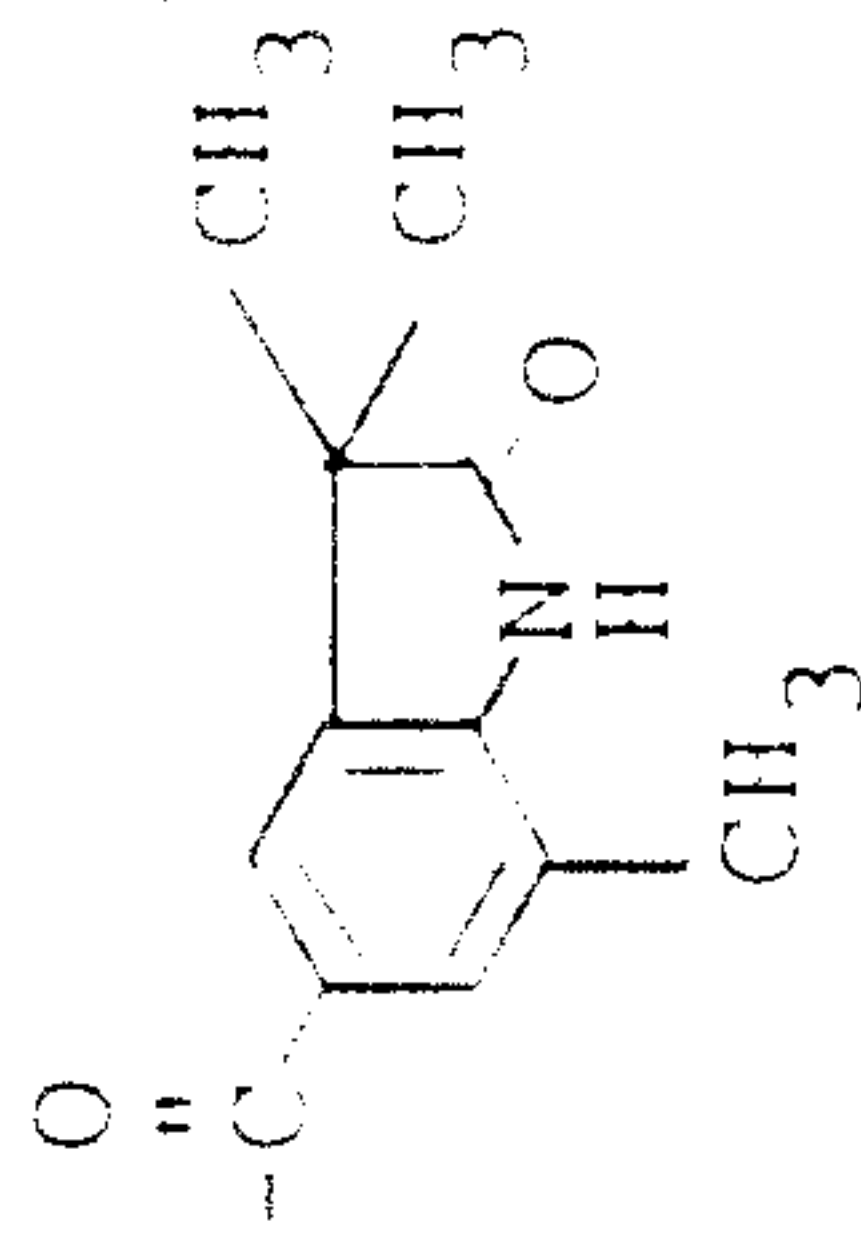
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
101		White powder	(-)	See Attached Sheet (B).
102		White powder	(-)	See Attached Sheet (B).
103		White powder	(-)	See Attached Sheet (B).
104		White powder	(-)	See Attached Sheet (B).

(To be continued)

Ra-OH

Table 5

(Continued)

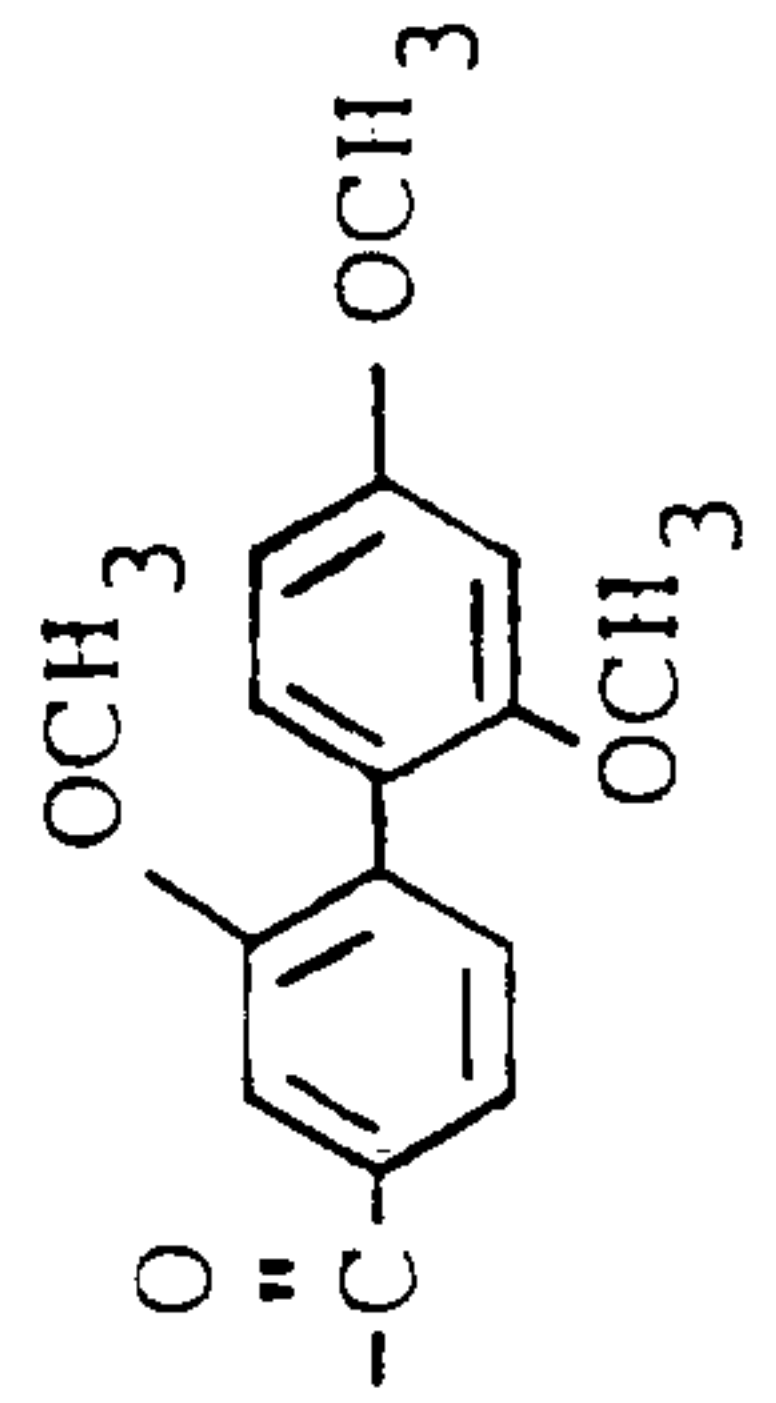
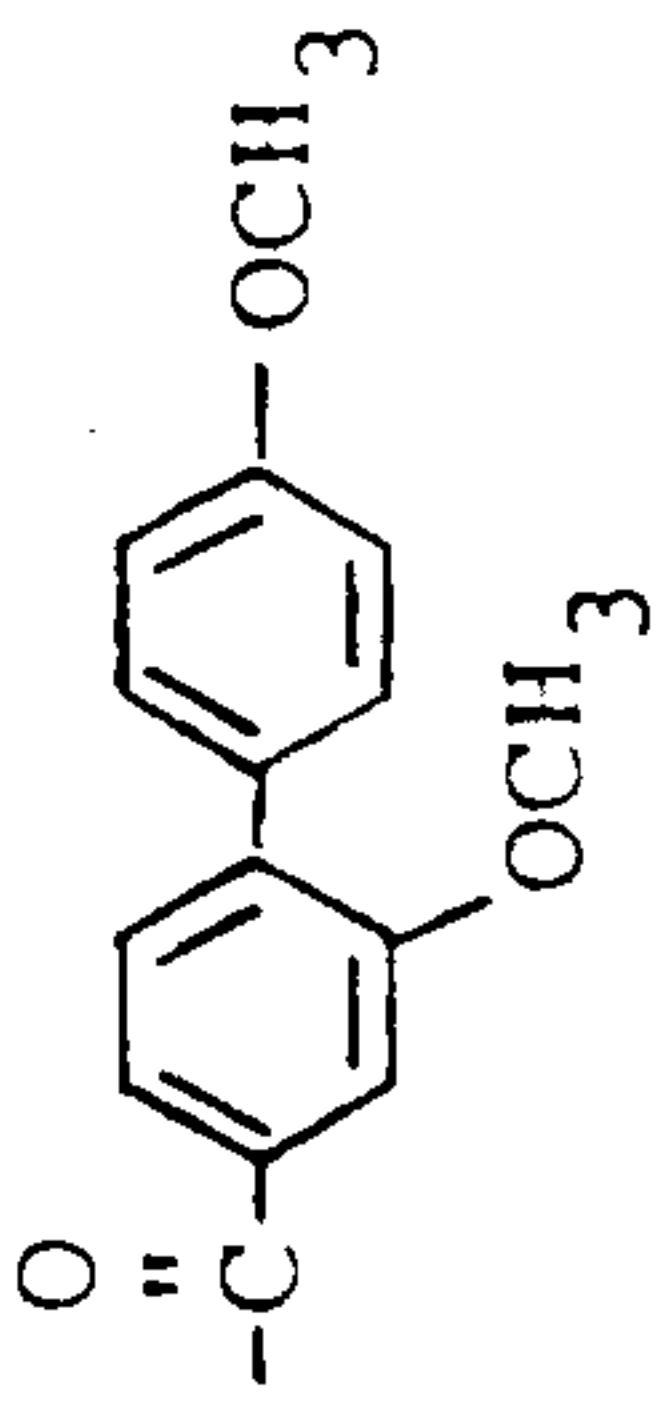
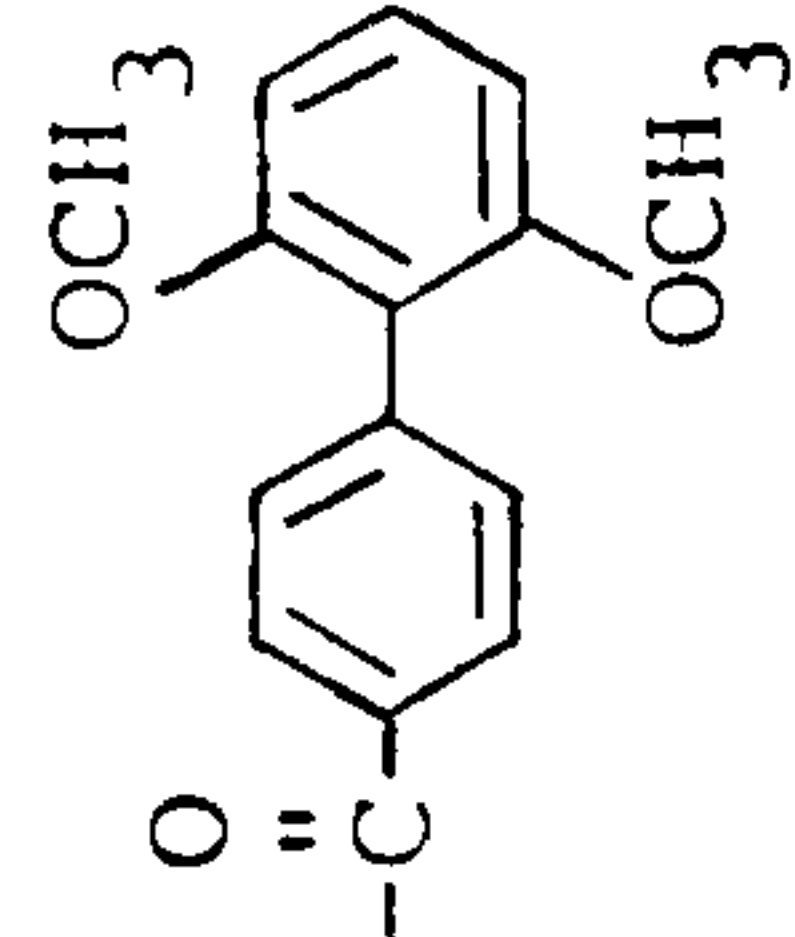
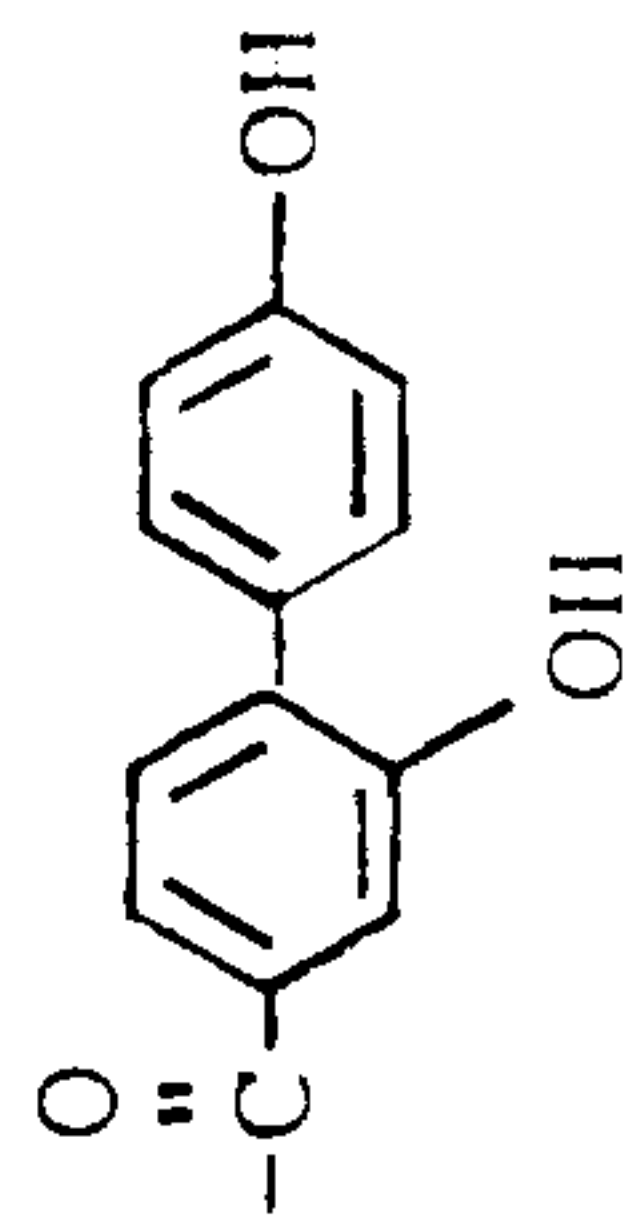
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
105		White powder	(-)	See Attached Sheet (B).
106		Light yellow prisms (Dimethylformamide)	322 - 326 (-)	
107		Yellow powder (Dimethylformamide)	308 - 314 (-)	See Attached Sheet (B).
108		White powder	(-)	See Attached Sheet (B).

(To be continued)

Ra-OH

Table 5

(Continued)

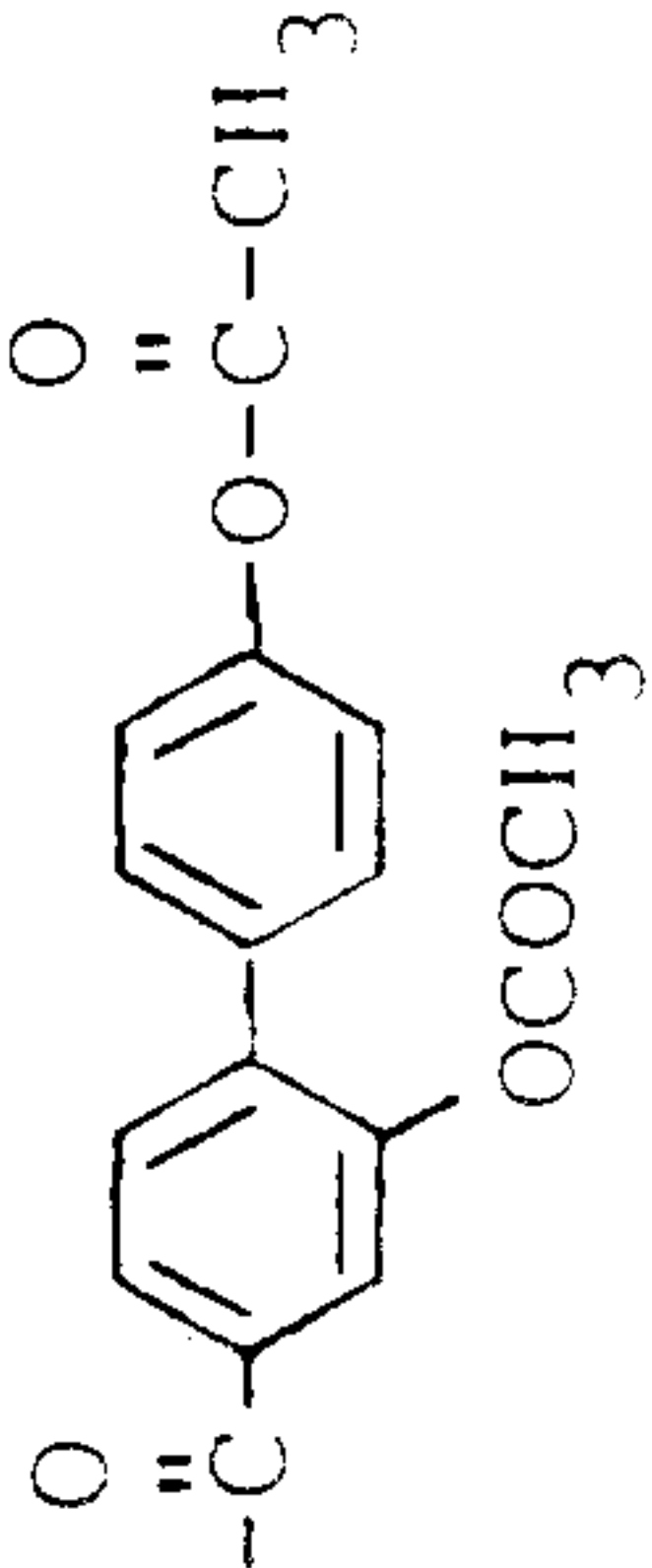
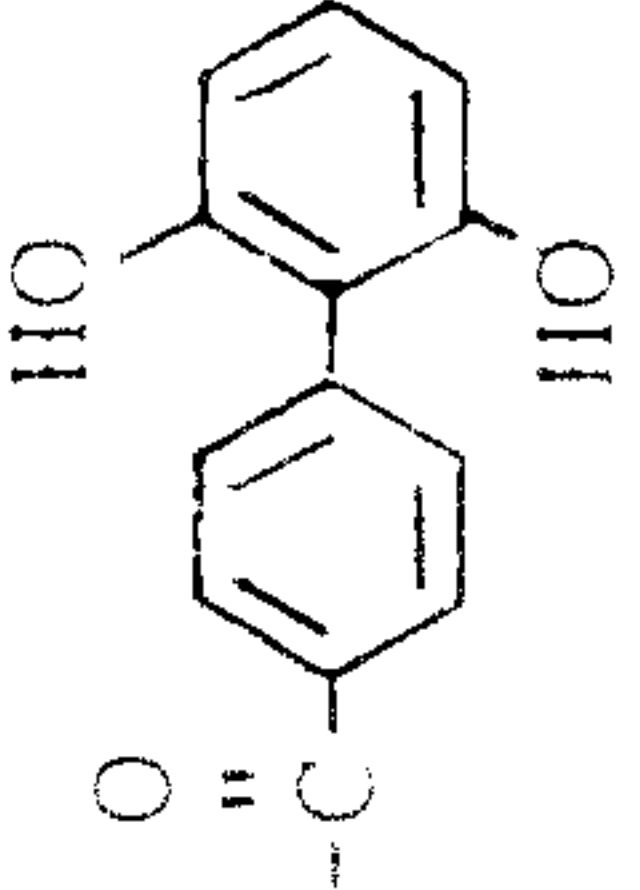
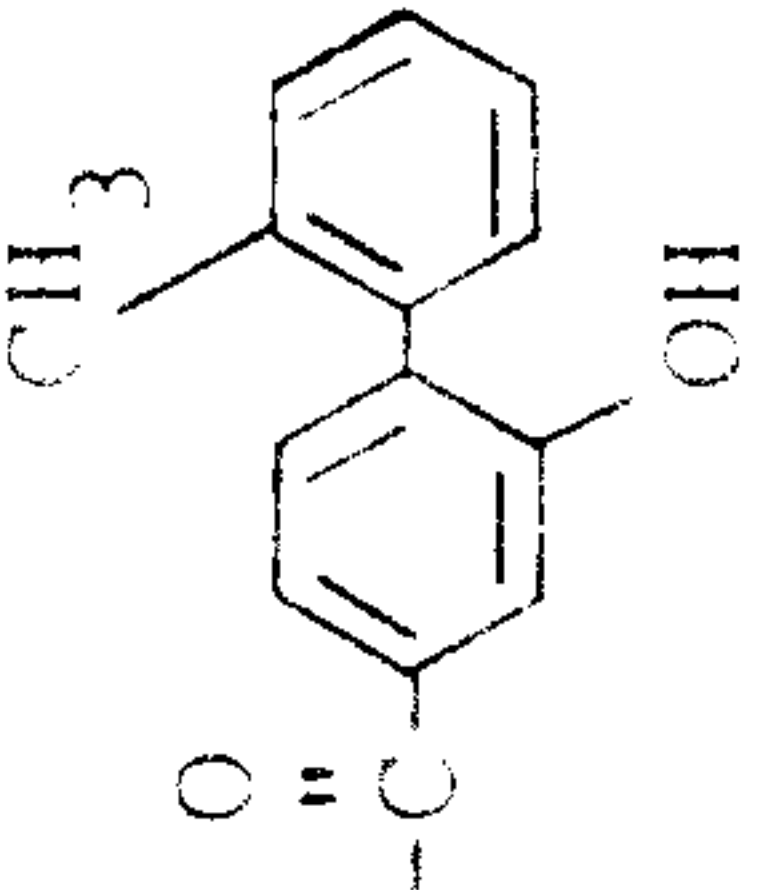
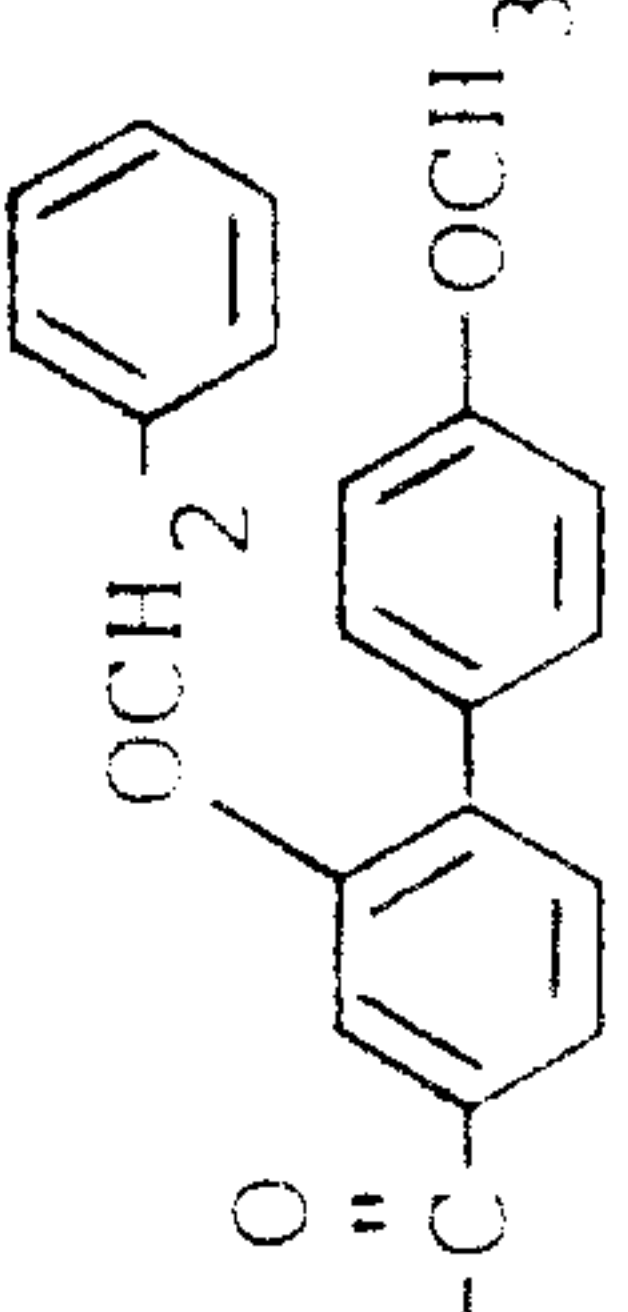
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
109		White powder	(-)	See Attached Sheet (B).
110		White powder	198 (-)	
111		Light grey powder	225 - 226 (-)	
112		White powder	244 - 246 (-)	

(To be continued)

Ra-OH

Table 5

(Continued)

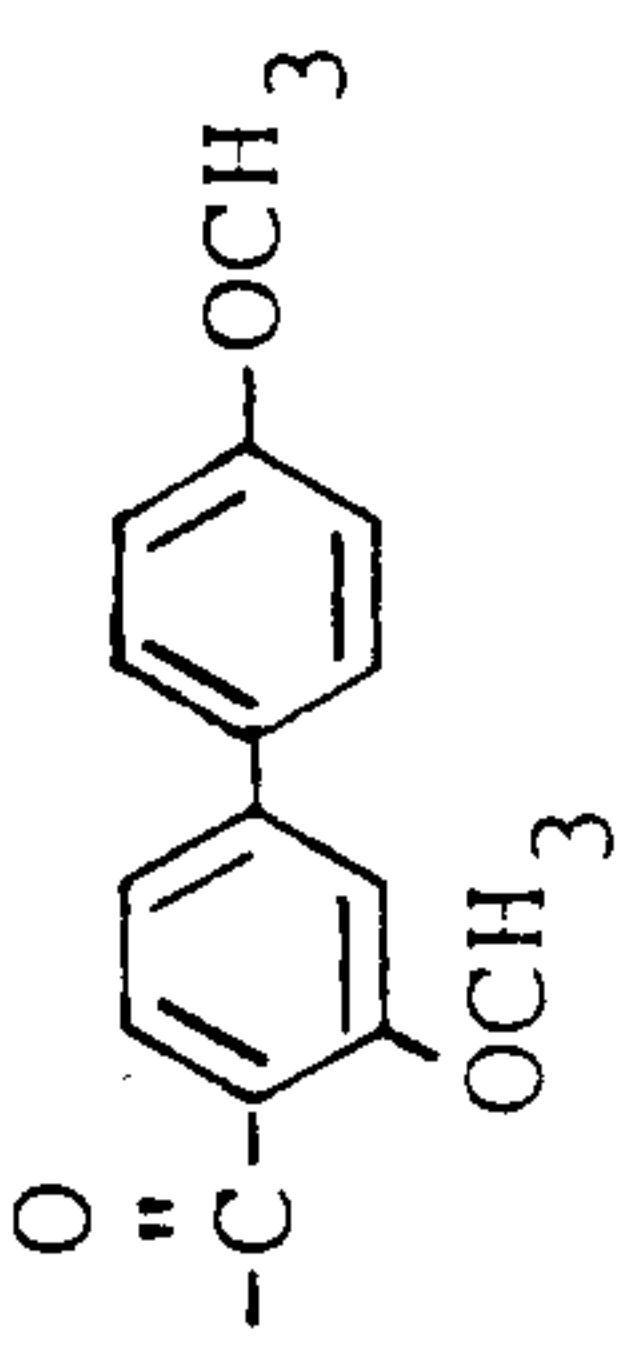
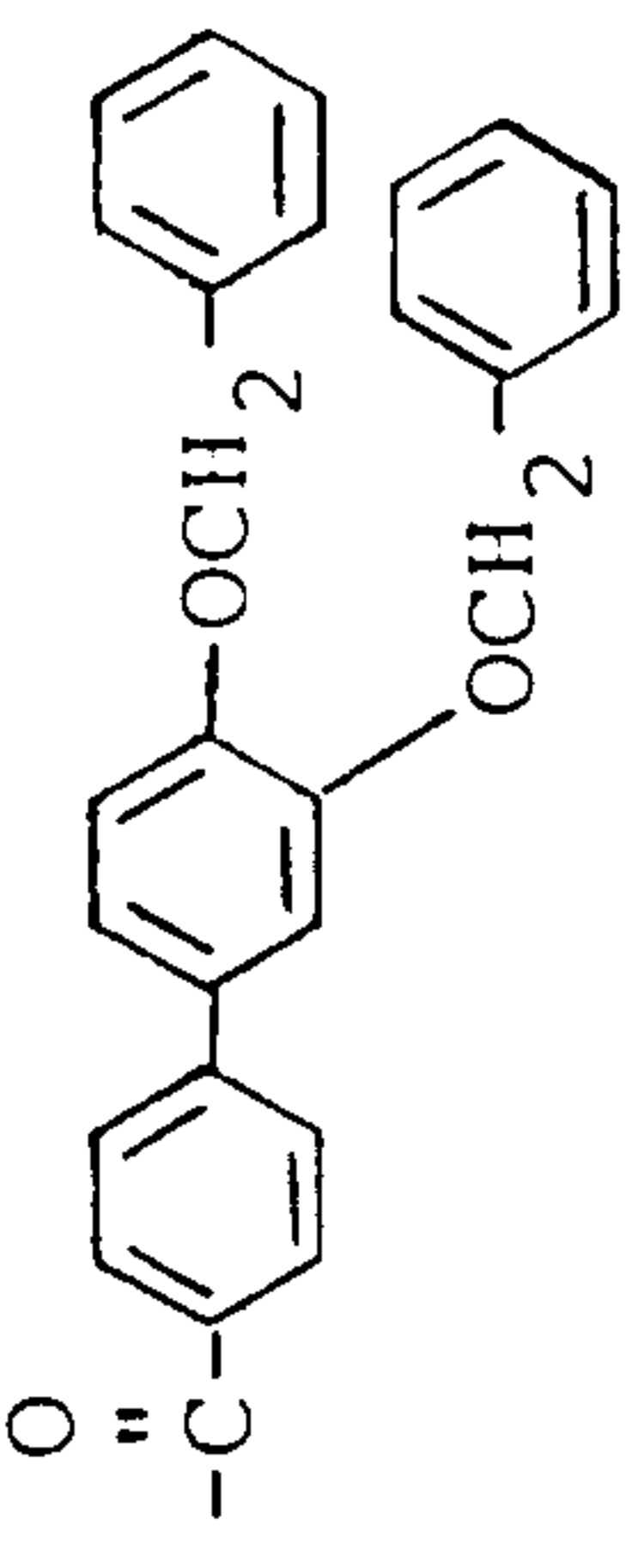
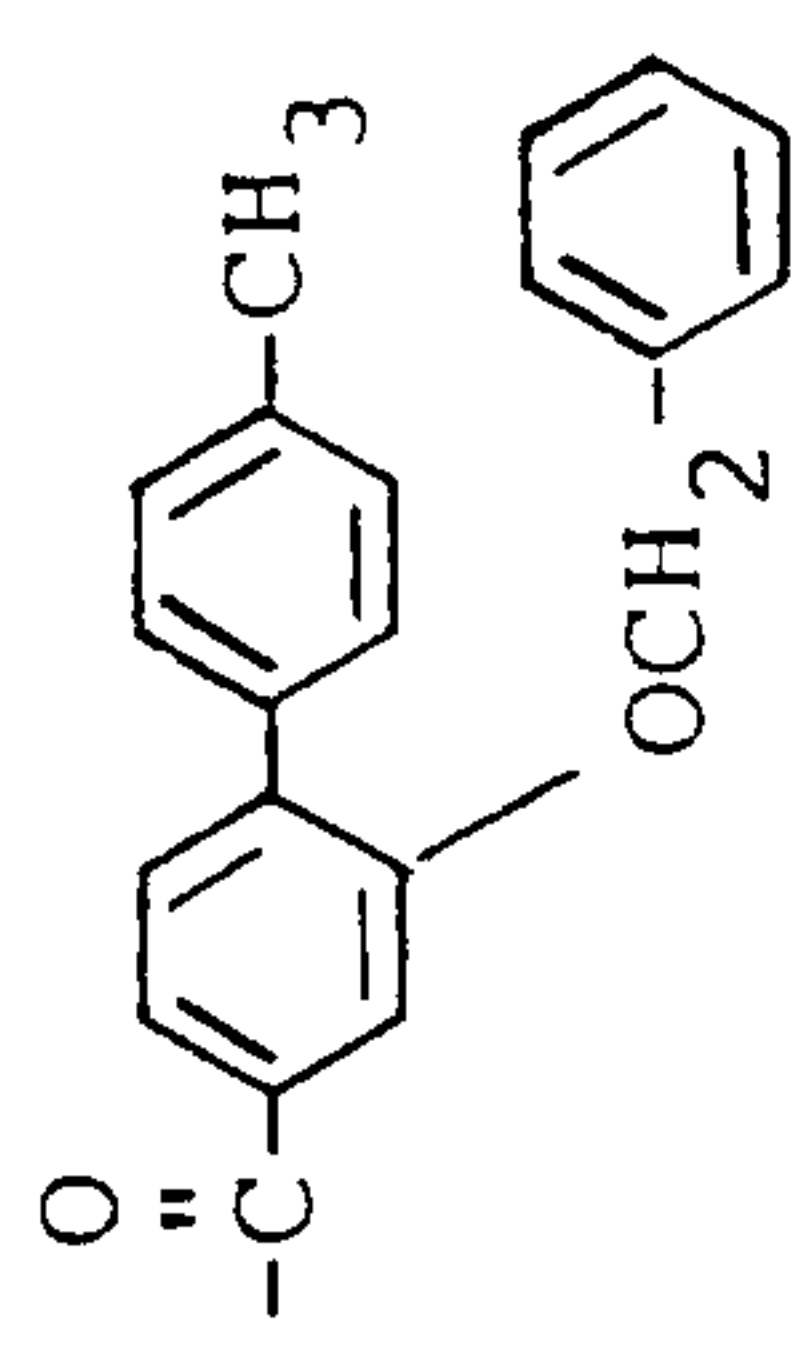
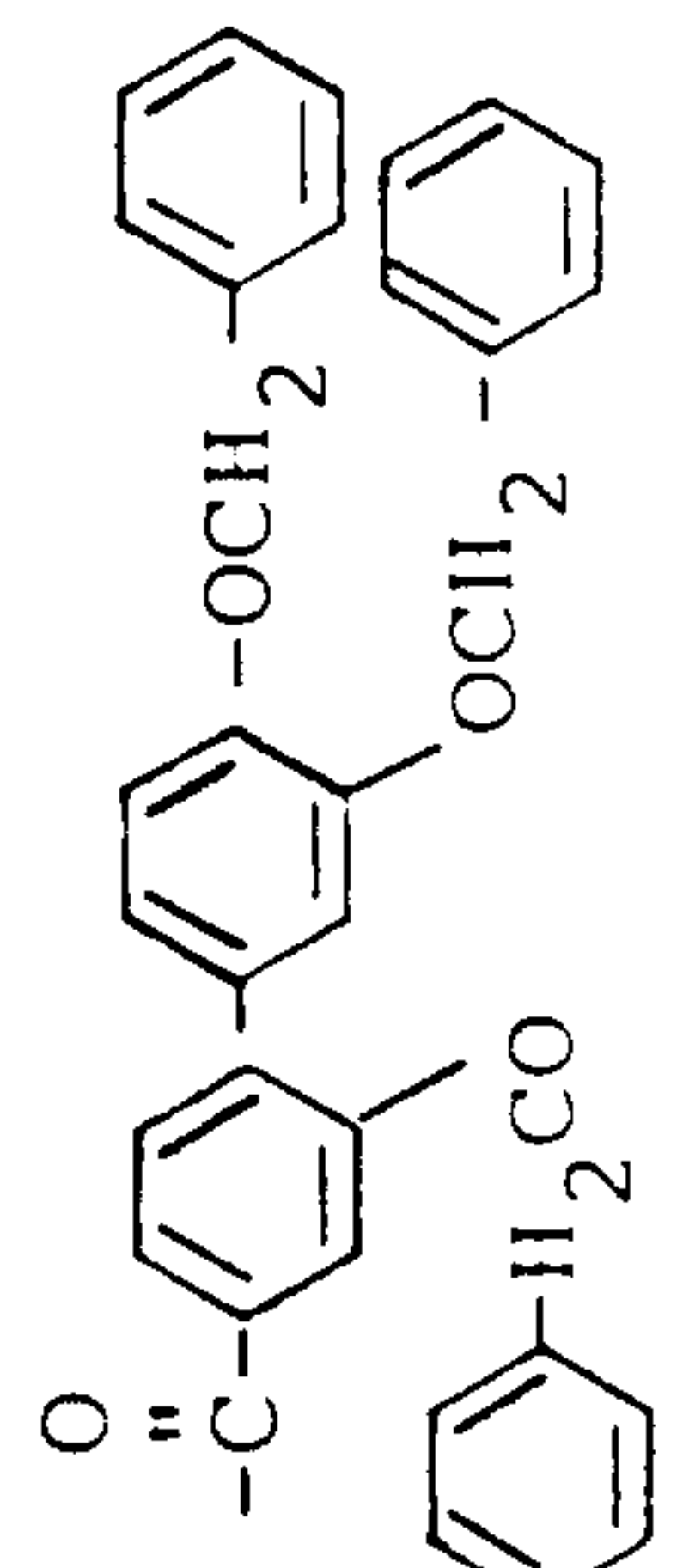
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
113		Colorless needles	192 - 196 (-)	
114		Light green powder	195 - 203 (-)	See Attached Sheet (B).
115		White powder	145 - 146 (-)	
116		White powder	180 - 183 (-)	

(To be continued)

Ra-OH

Table 5

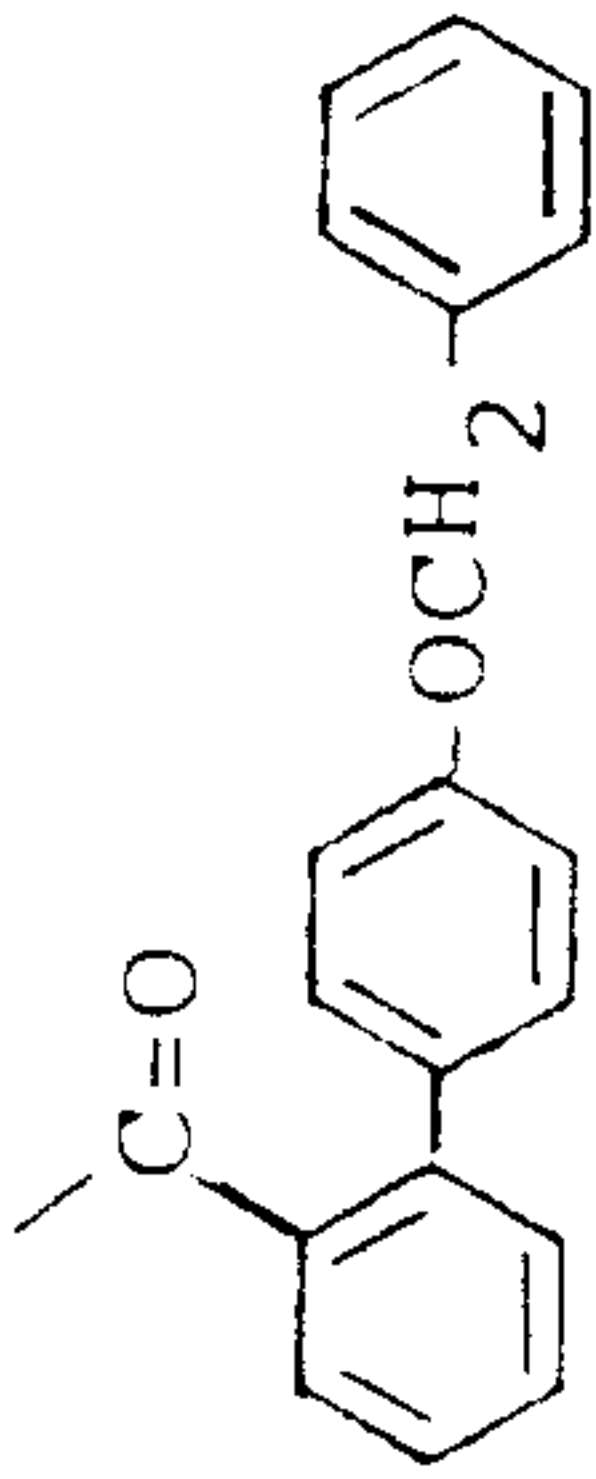
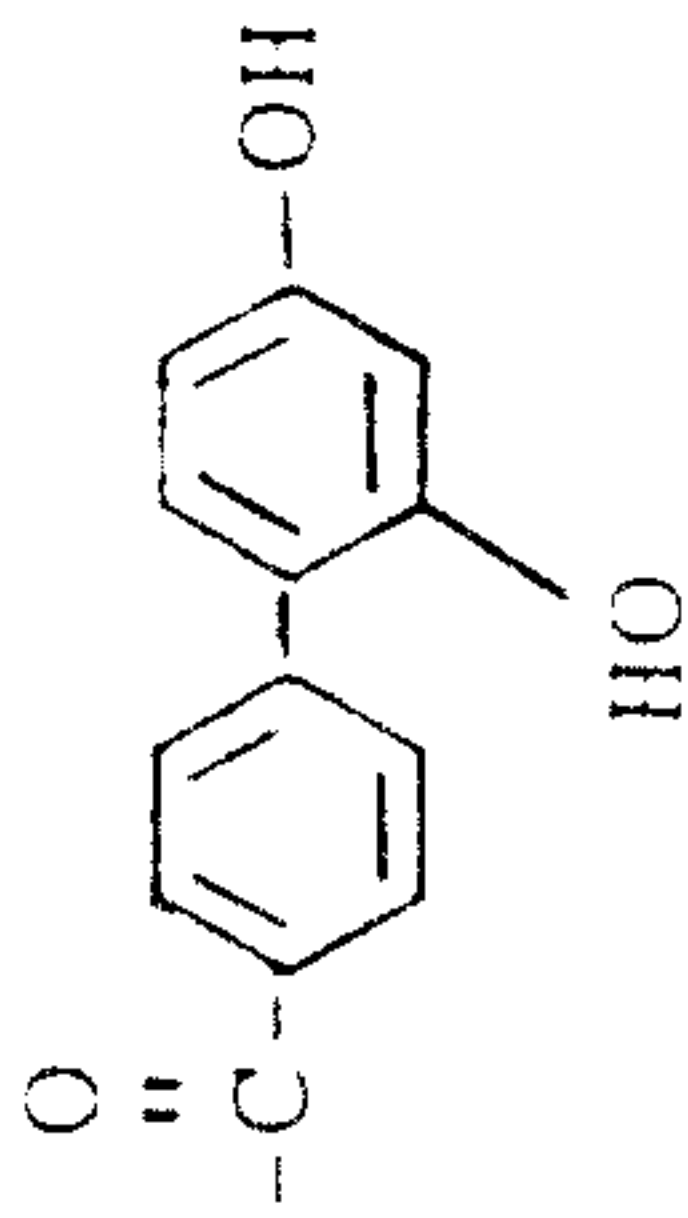
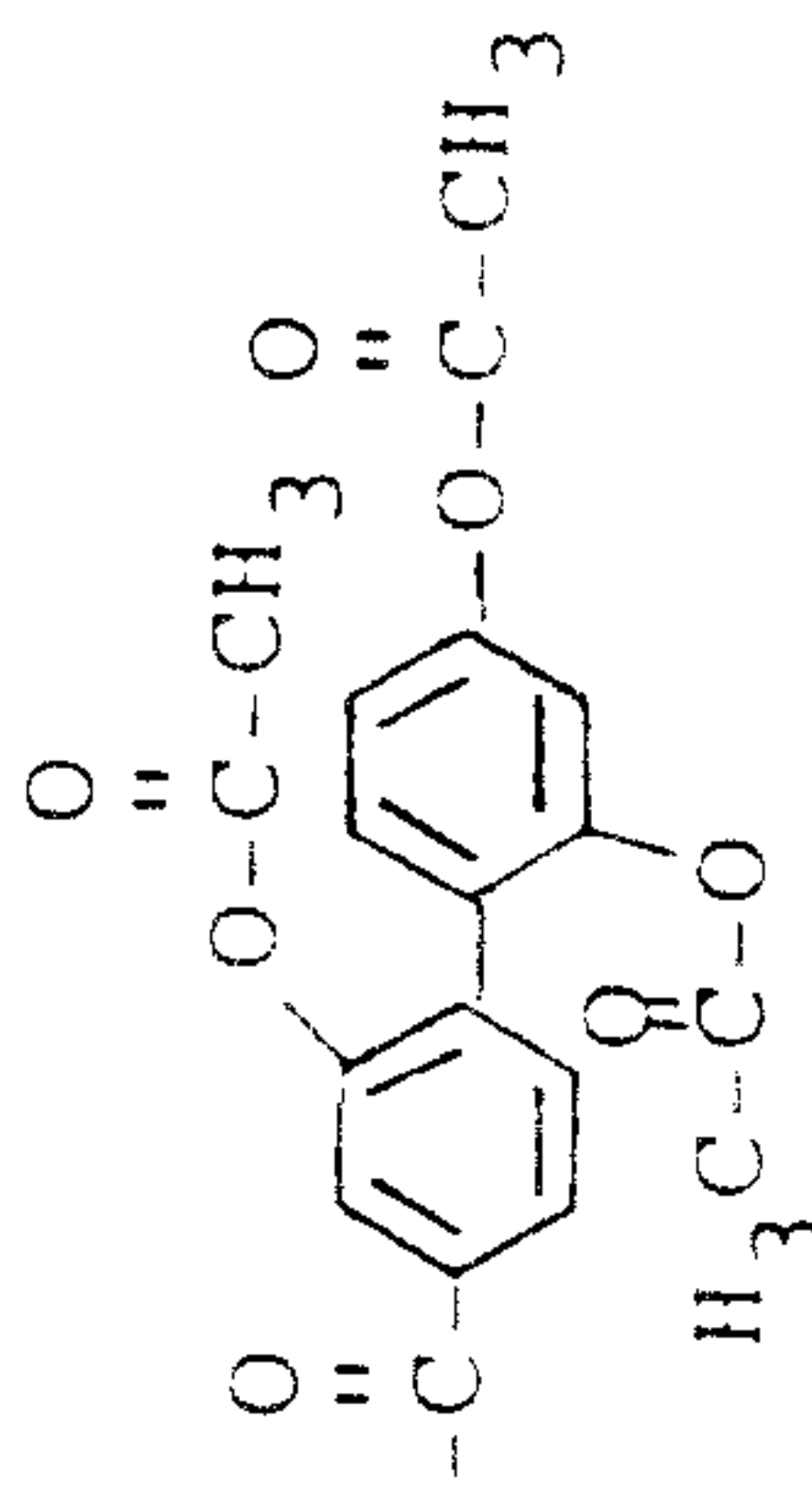
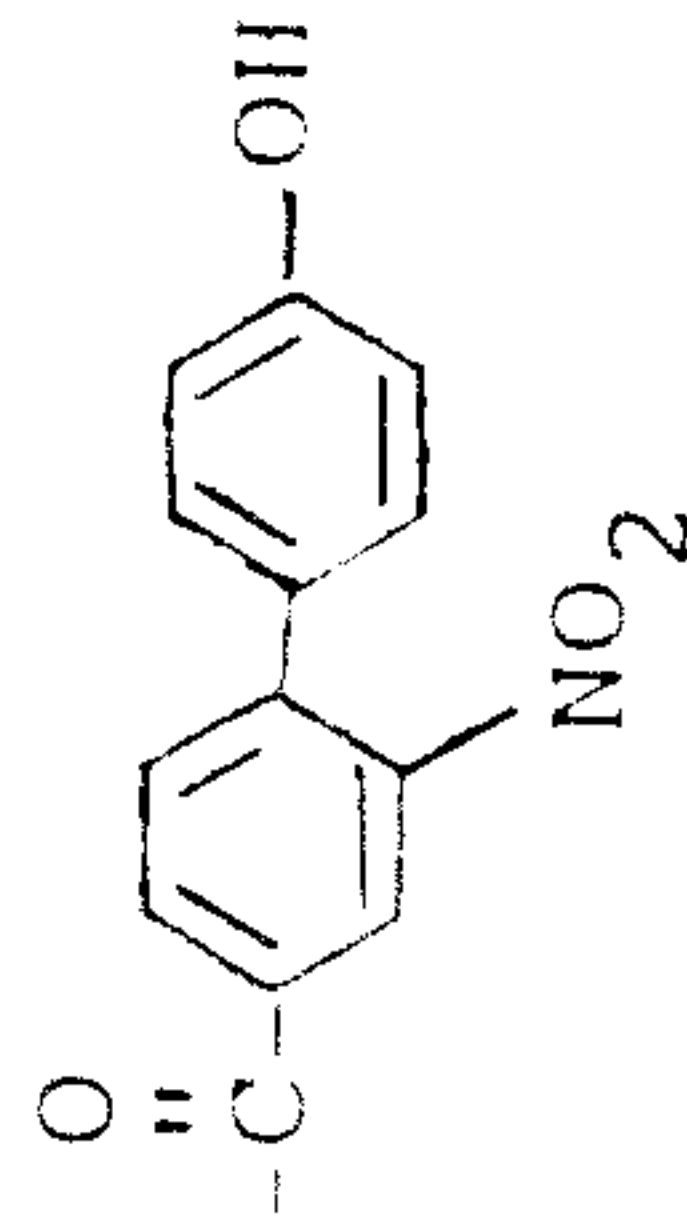
(Continued)

Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
117		White powder	146 - 147 (-)	
118		White powder	260 - 262 (-)	
119		White powder	197 - 199 (-)	
120		White powder	(-)	See Attached Sheet (B).

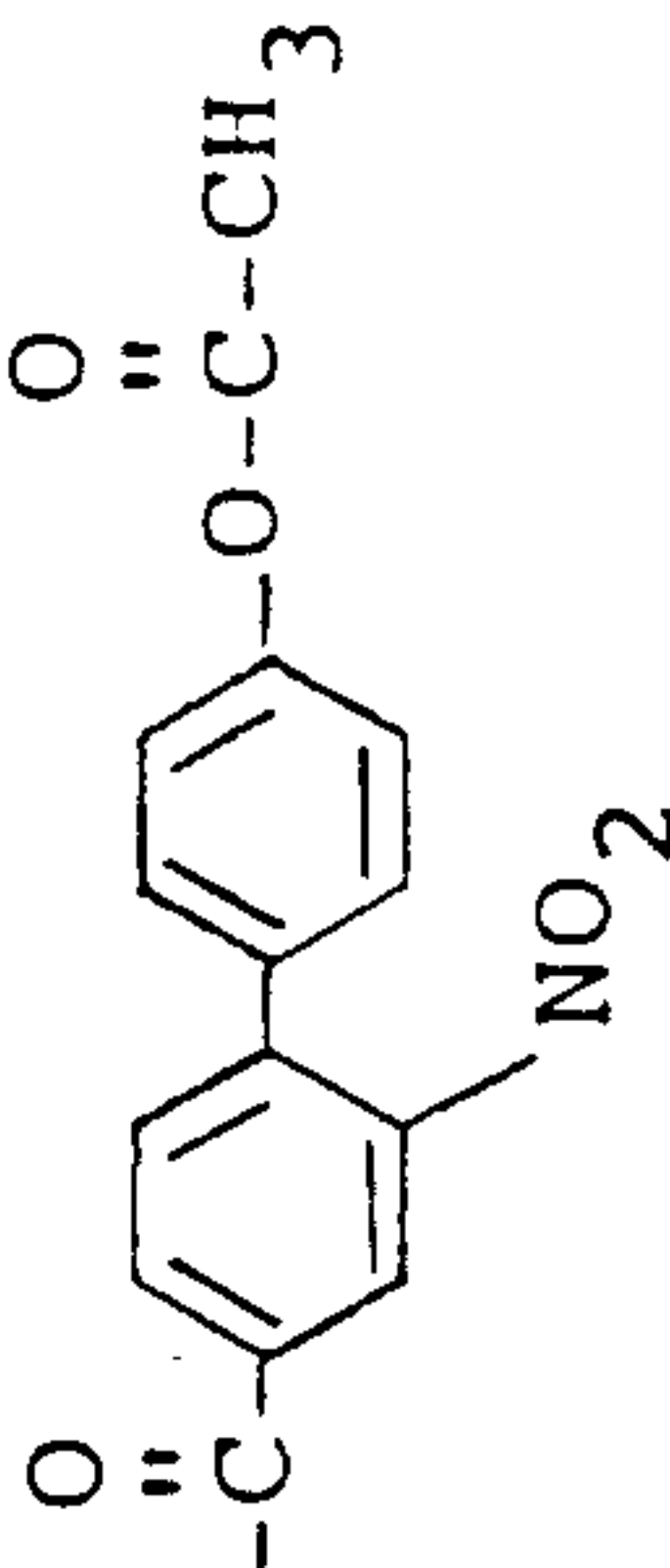
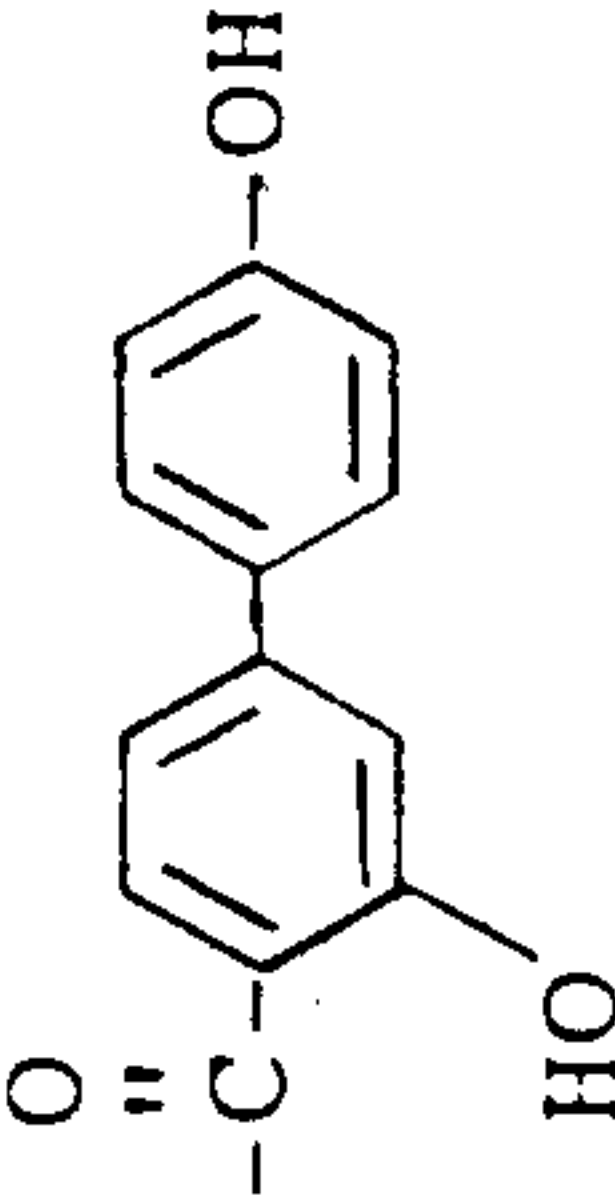
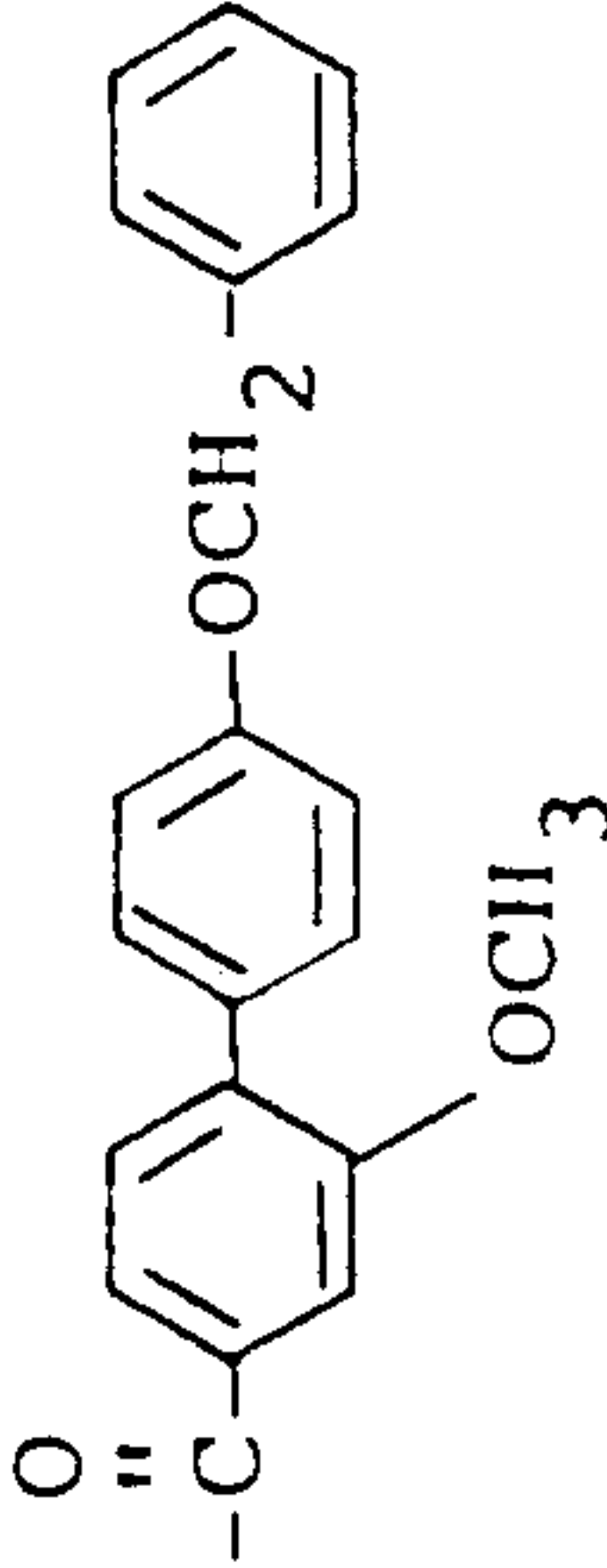
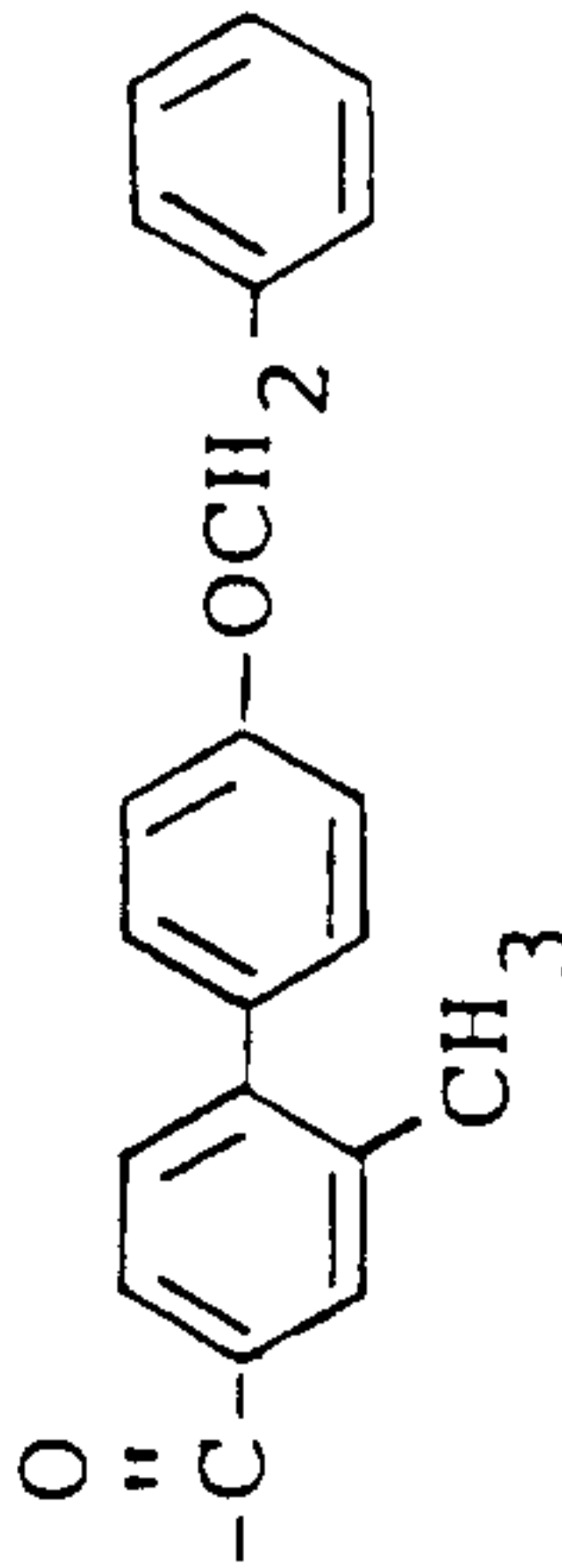
(To be continued)

Table 5

(Continued)

Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
121		White powder	157 - 159 (-)	
122		White powder	(-)	See Attached Sheet (B).
123		White amorphous	(-)	See Attached Sheet (B).
124		Light yellow powder	229 - 231 (-)	

(To be continued)

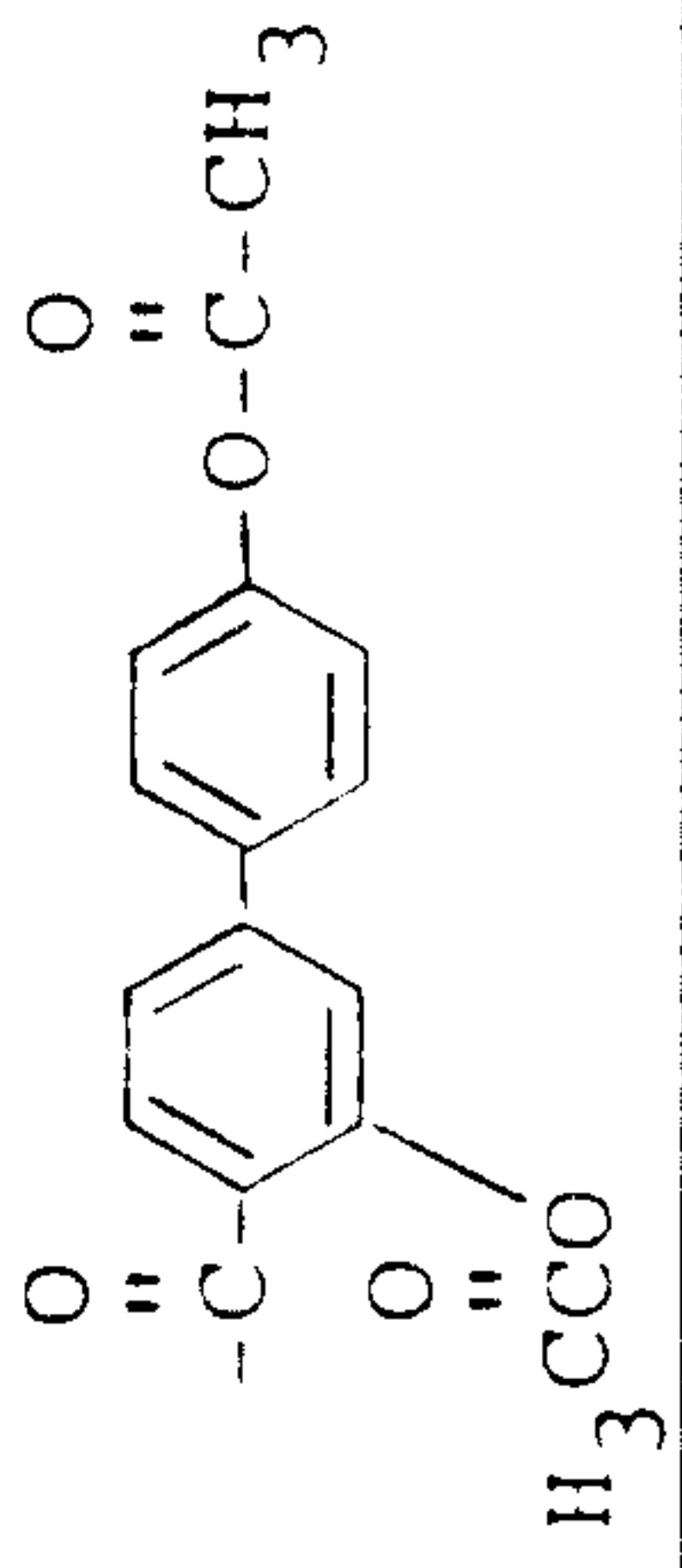
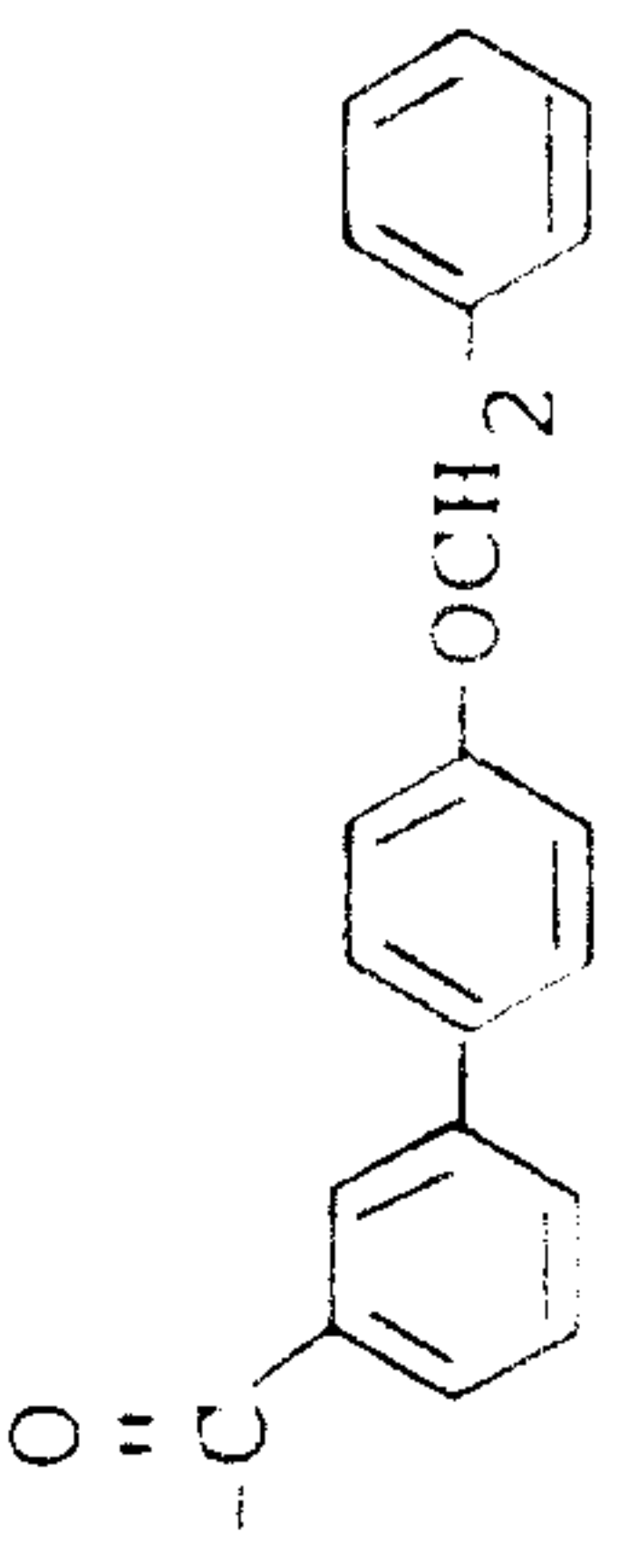
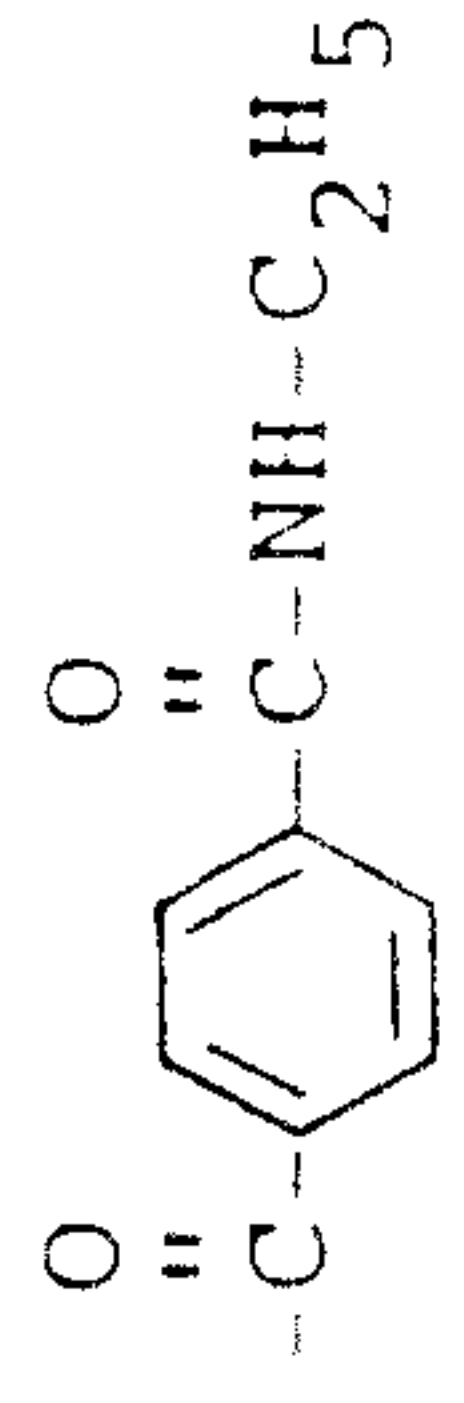
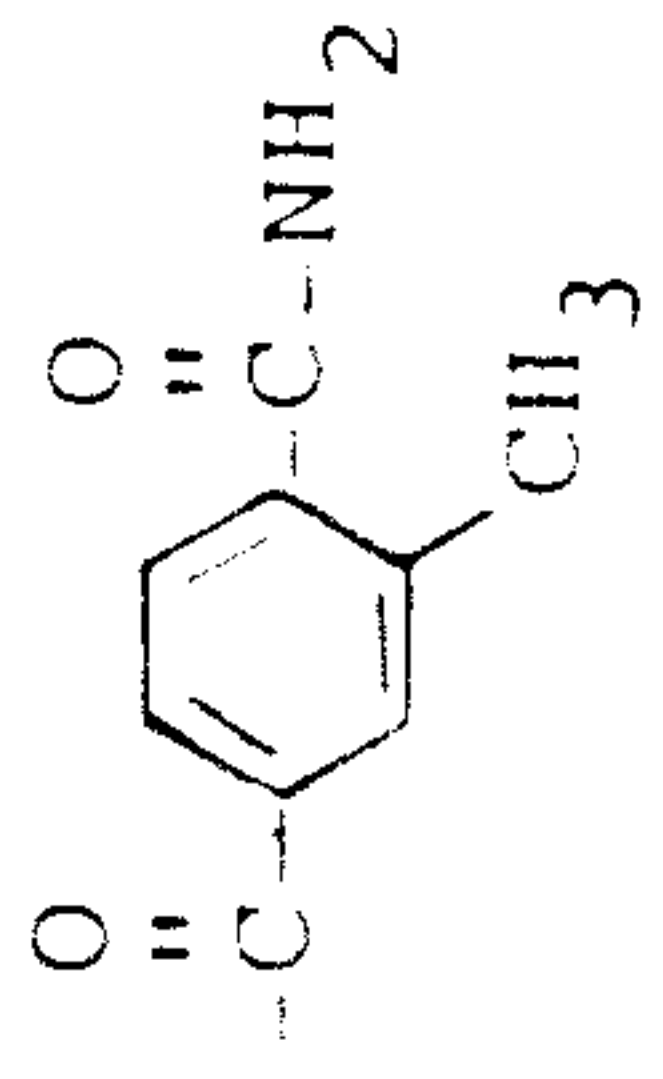
(Continued)		Table 5			Ra-OH	
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm		
125		Light yellow powder	192 - 195 (-)			
126		Light gray powder	249 - 251 (-)			
127		White powder	201 - 205 (-)			
128		White powder	194 - 198 (-)			

(To be continued)

Ra-OH

Table 5

(Continued)

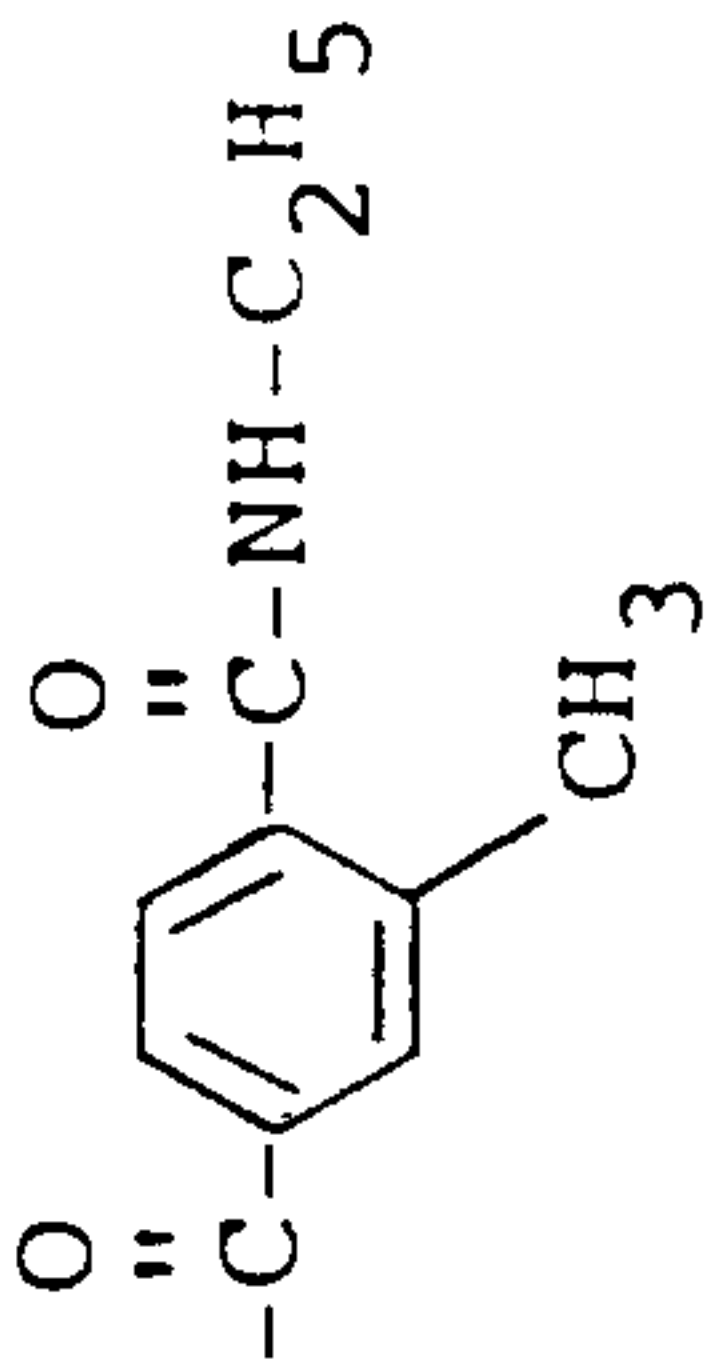
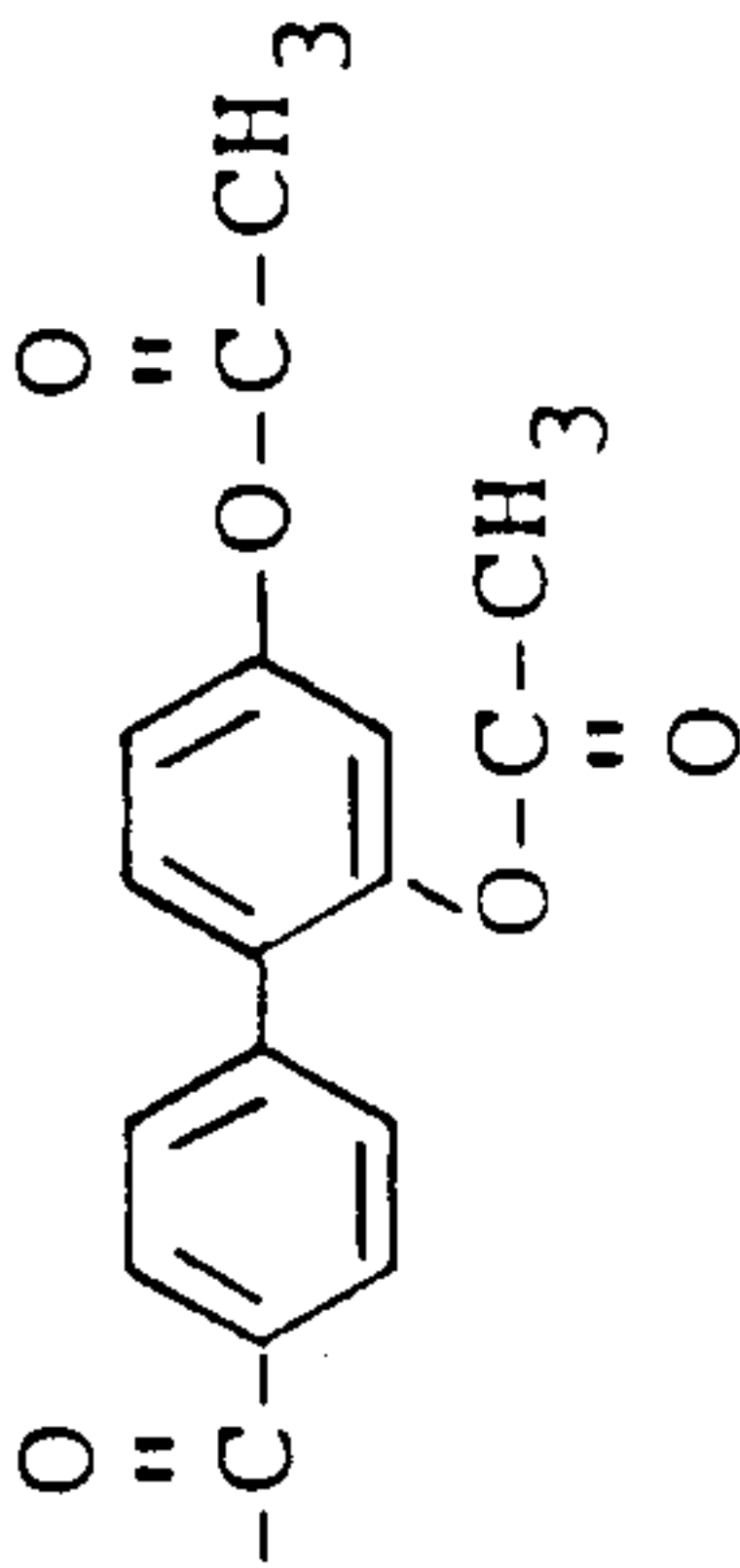
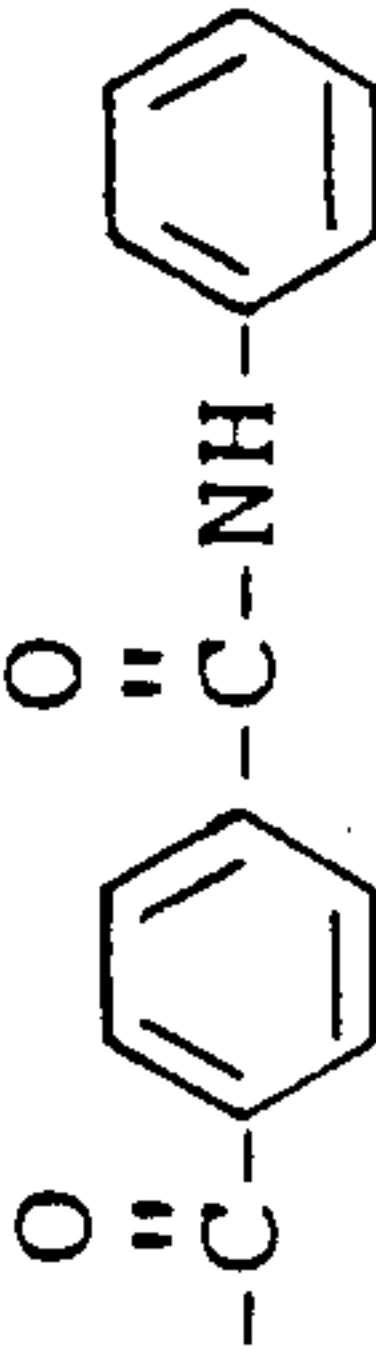
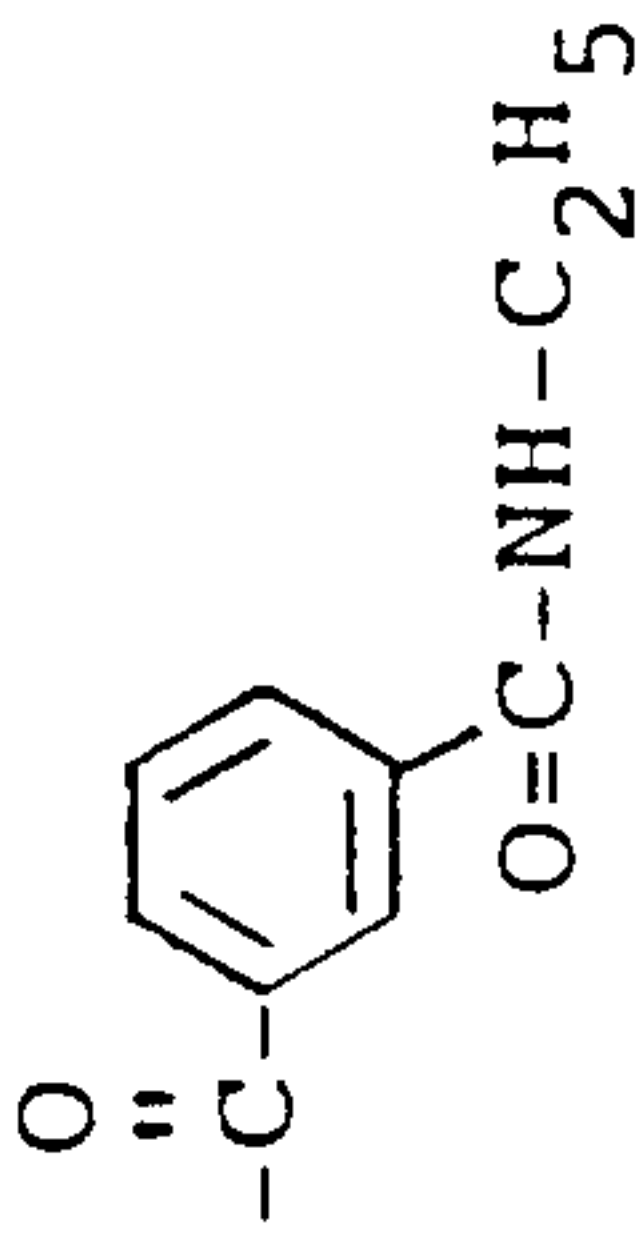
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
129		Light brown prisms (Dimethylformamide-water)	189 - 191 (-)	
130		White powder	216 - 219 (-)	
131		White powder	(-)	See Attached Sheet (B).
132		Light orange powder	244 - 247 (-)	

(To be continued)

Ra-OH

Table 5

(Continued)

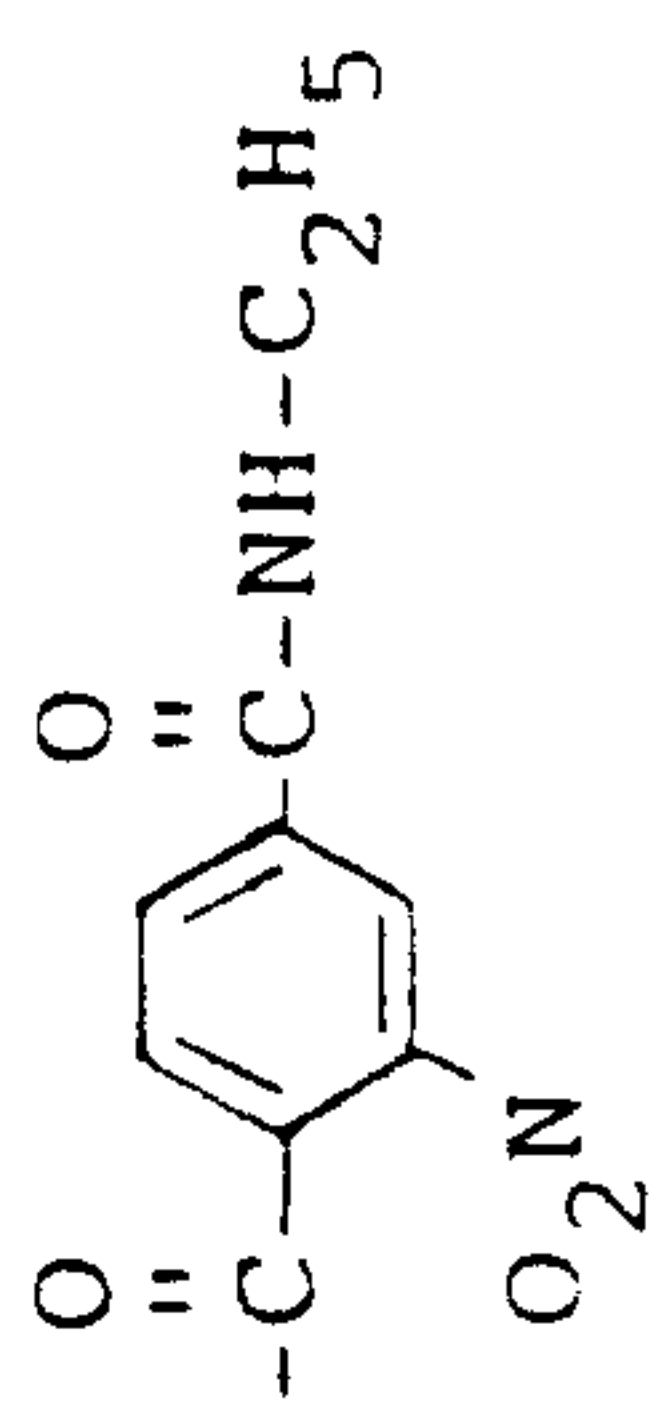
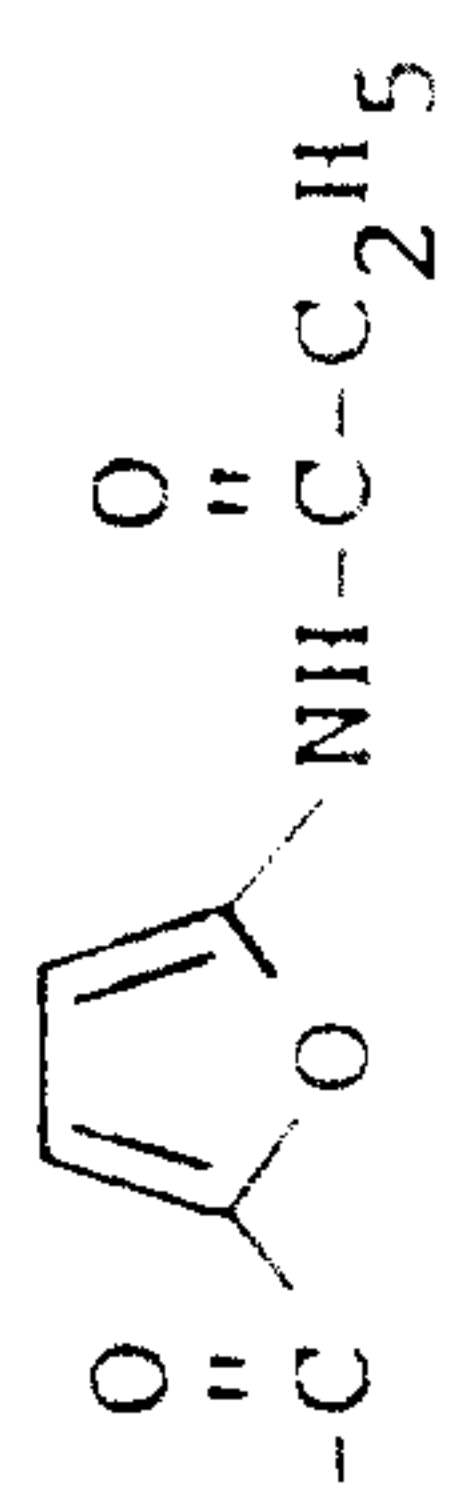
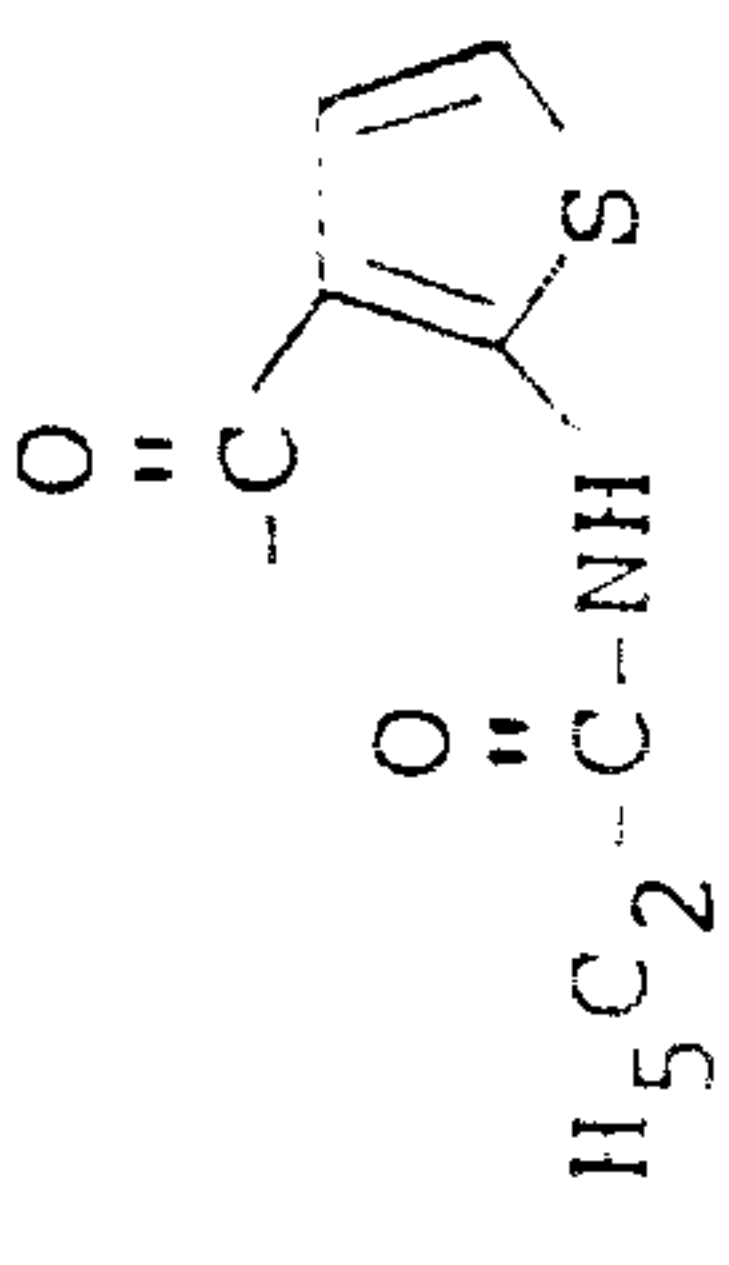
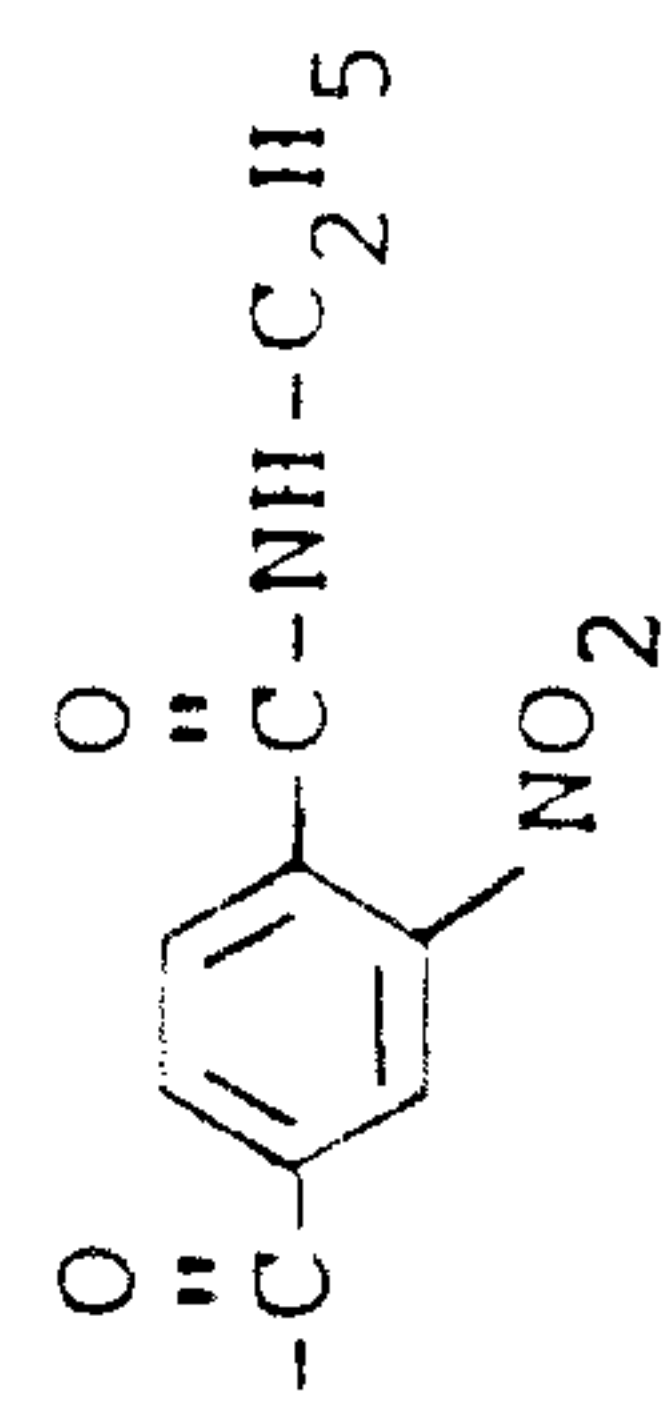
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
133		White powder	169 - 170 (-)	
134		Light brown powder (Dimethylformamide-water)	204 - 208	,
135		White powder	(-)	See Attached Sheet (B).
136		White powder	(-)	See Attached Sheet (B).

(To be continued)

Ra-OH

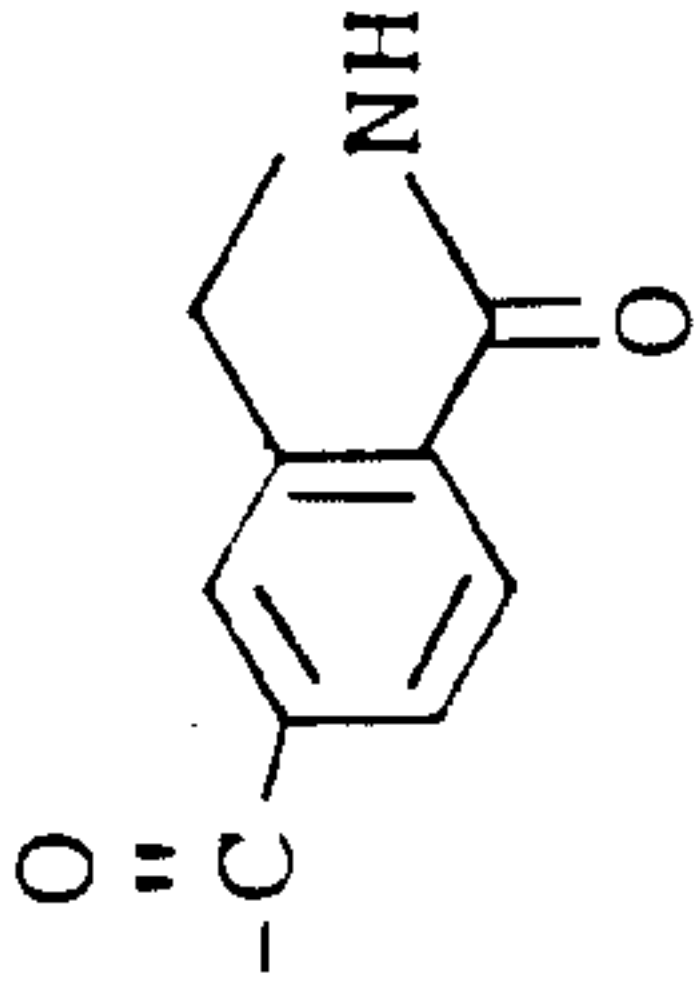
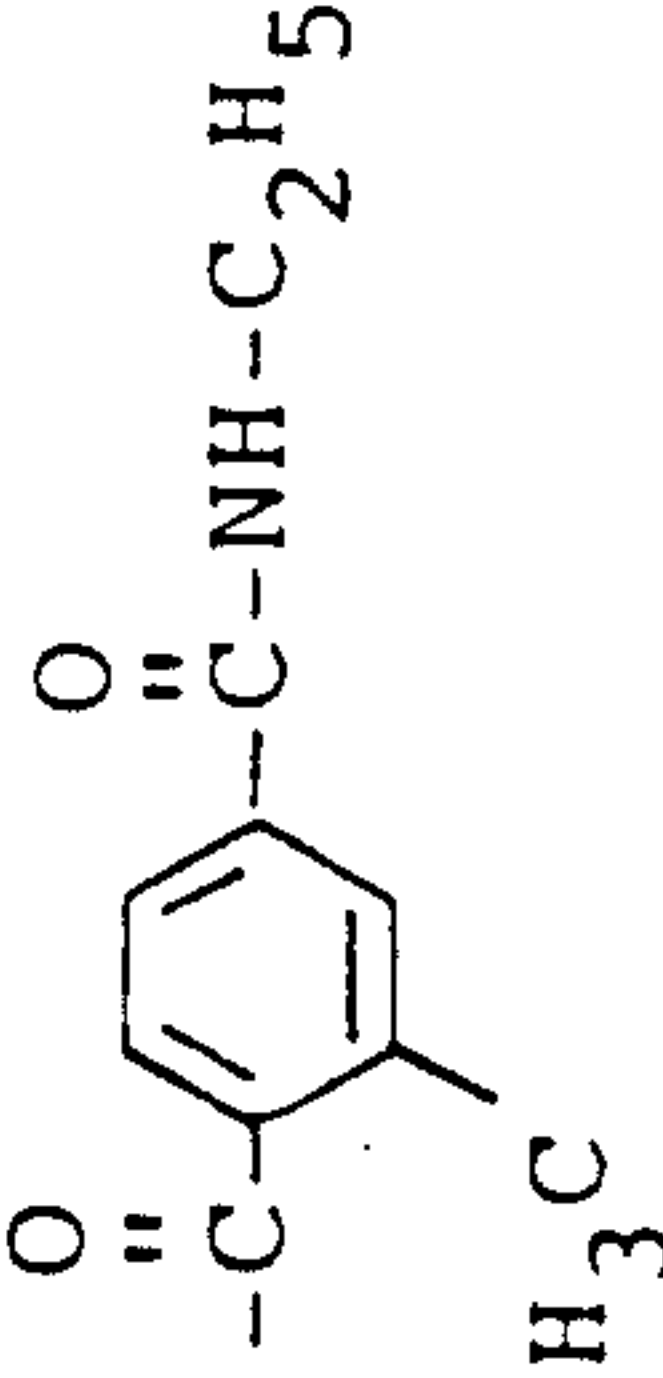
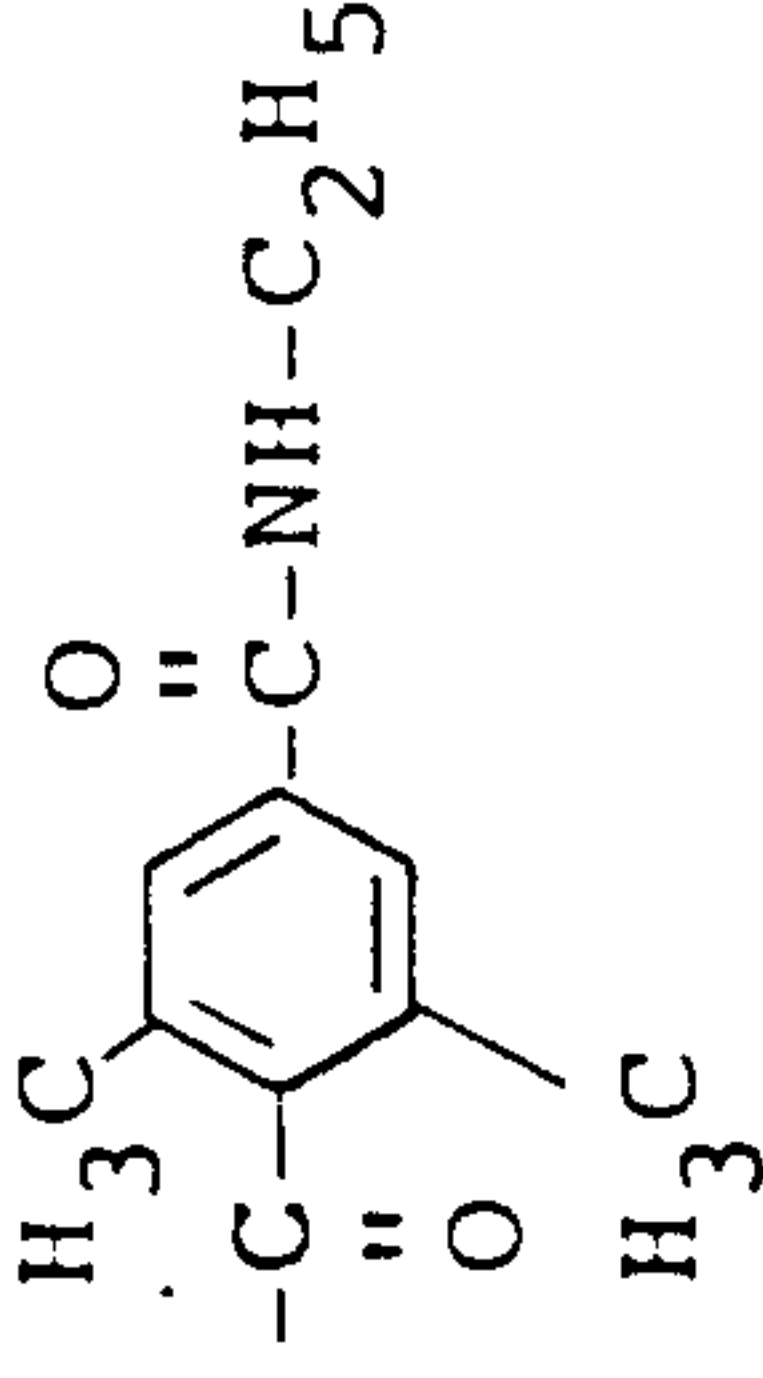
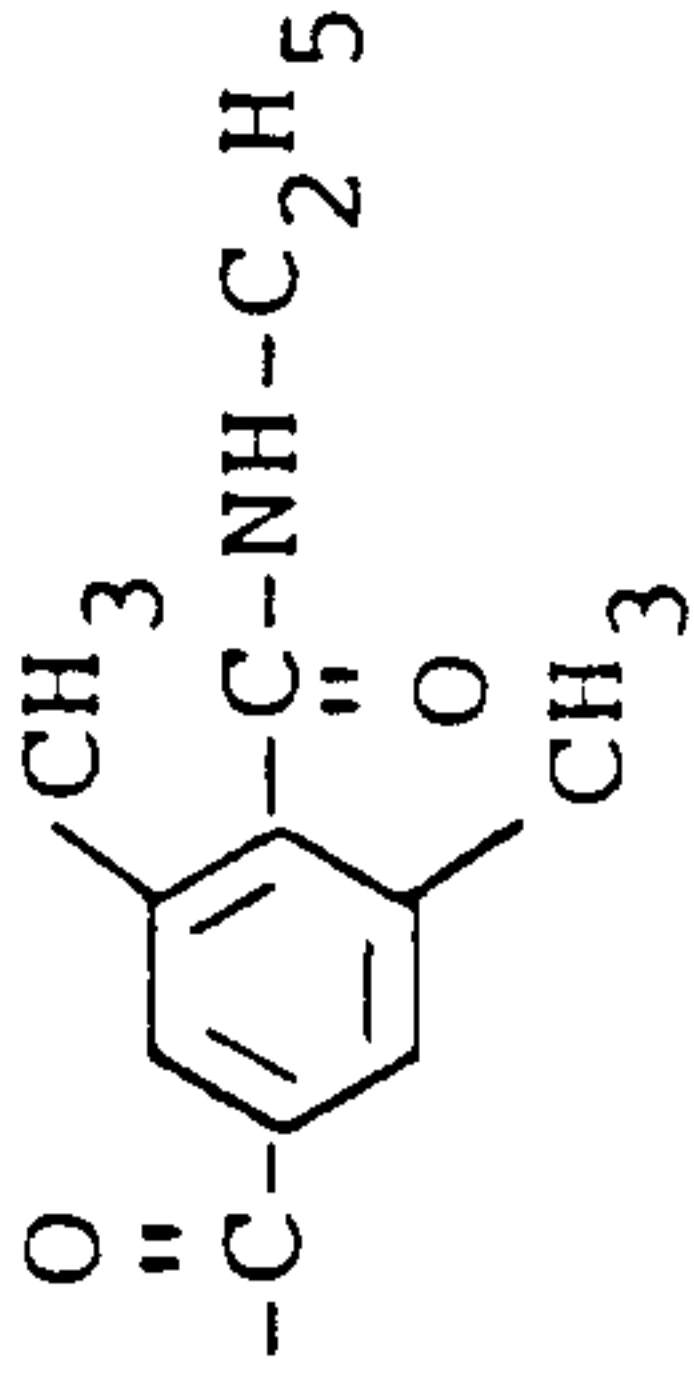
Table 5

(Continued)

Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
137		White powder	(-)	See Attached Sheet (B).
138		Light brown powder	(-)	See Attached Sheet (B).
139		White powder (Ethanol)	180 - 181.5 (Decompd.)	
140		White powder	(-)	See Attached Sheet (B).

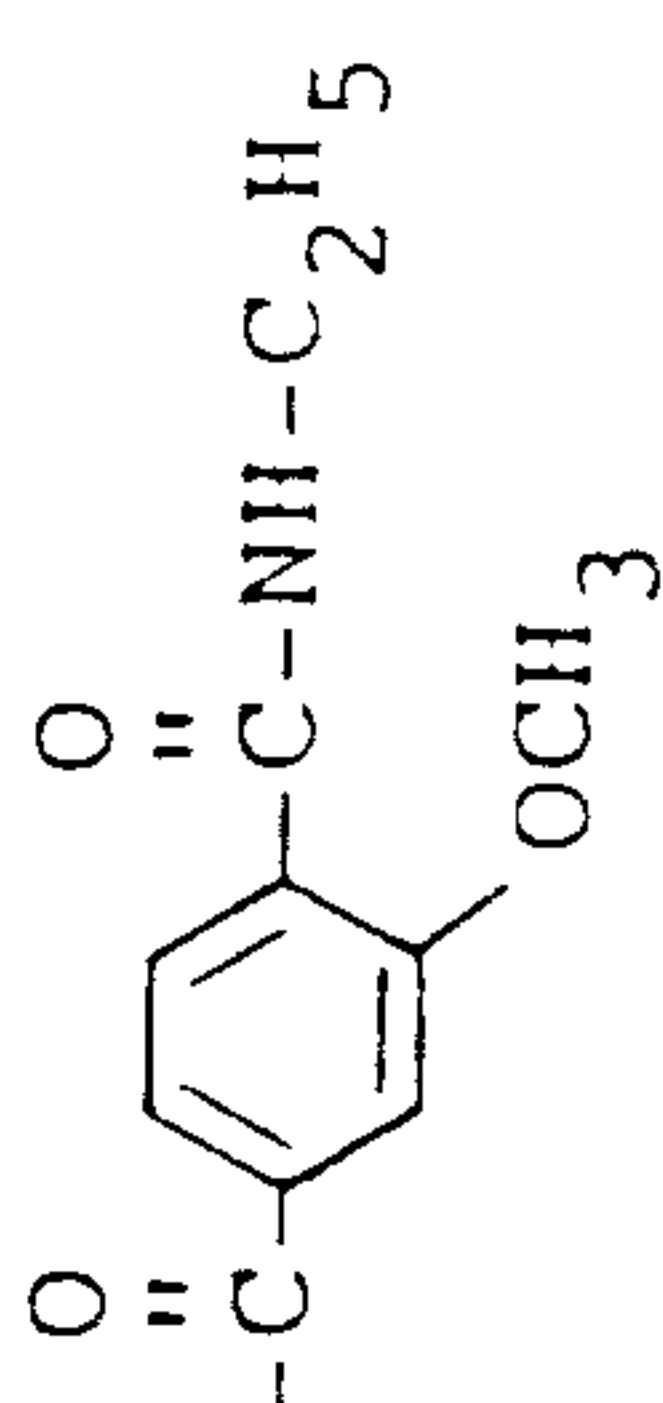
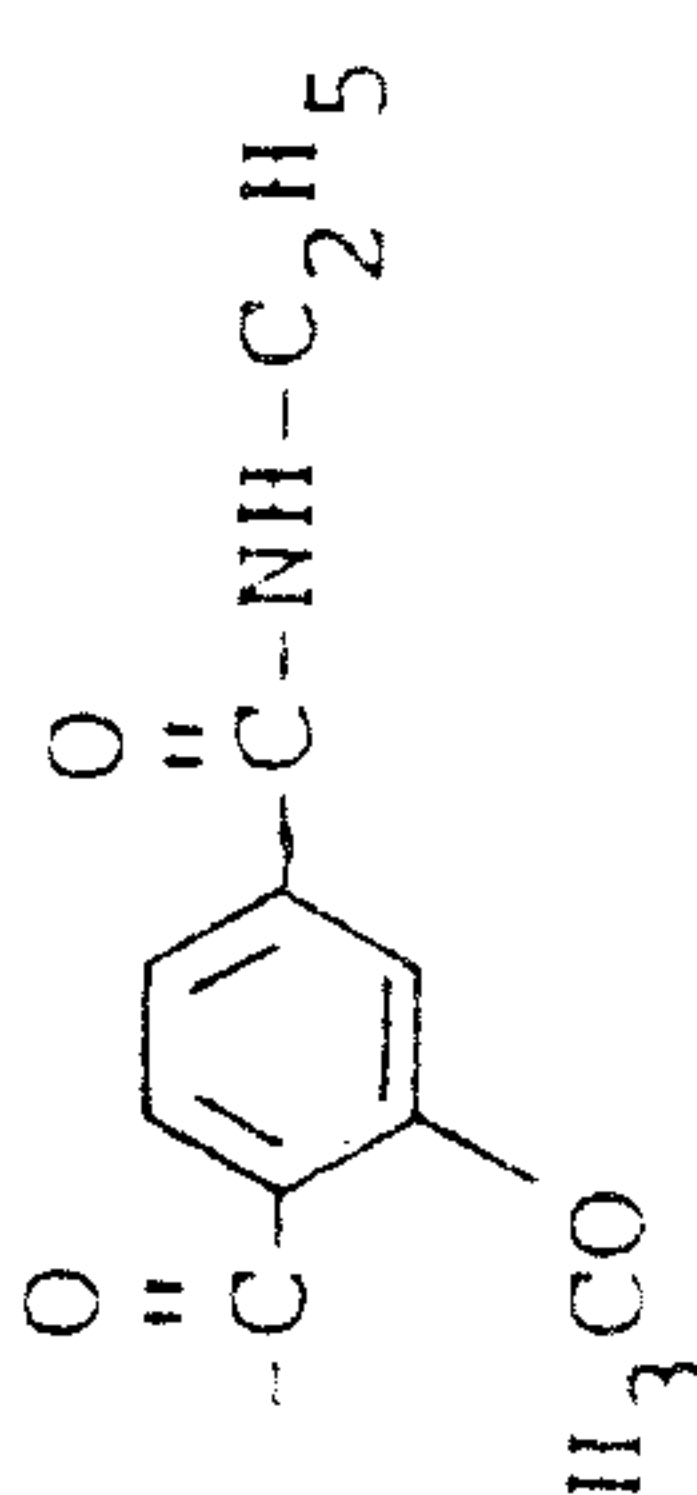
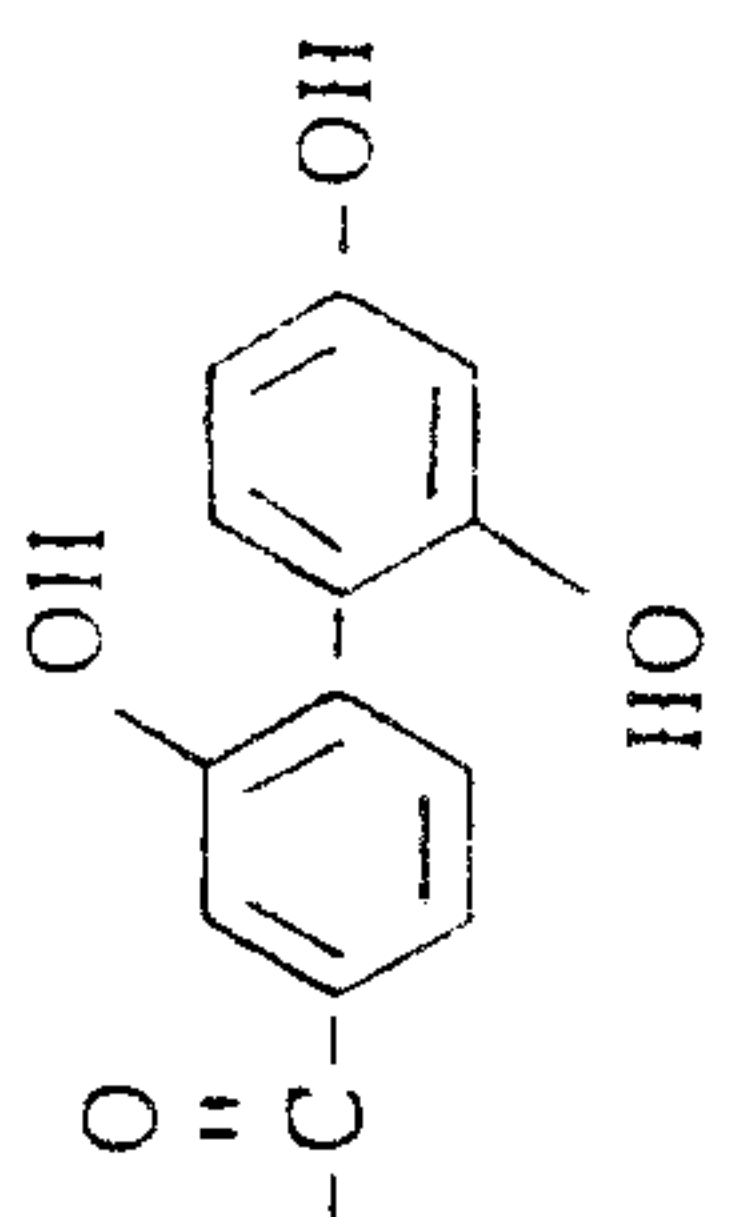
(To be continued)

Table 5 Ra-OH

(Continued)	Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
	141		White powder	Higher than 300 (-)	See Attached Sheet (B).
	142		Colorless needles	189 - 190 (-)	,
	143		White powder	225 - 228 (-)	
	144		White powder	201 - 204 (-)	

(To be continued)

Table 5 Ra-OH

(Continued)				
Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
145		Colorless needles	197 - 200 (-)	
146		White powder	93 - 95 (-)	
147		White powder	(-)	See Attached Sheet (R).

Attached Sheet (B) for Table 5

Reference Example No.	$^1\text{H-NMR}$ (200 MHz) δ ppm
82	(DMSO- d_6): 2.13 (3H, s), 6.34 (2H, brs), 7.73 (1H, d, $J=1.5$ Hz), 7.79 (1H, d, $J=1.5$ Hz)
83	(250 MHz; DMSO- d_6): 1.12 (3H, t, $J=12.6$ Hz), 2.32 (3H, s), 2.46 (2H, q, $J=12.6$ Hz), 7.93 (1H, s), 8.75 (1H, s), 9.64 (1H, s), 2.60-4.33 (1H, brs)
86	(DMSO- d_6): 2.30 (3H, s), 7.32 (1H, s), 7.43 (1H, s), 10.82 (1H, s), 11.07 (1H, s), 12.27 (1H, brs)
87	(DMSO- d_6): 1.11 (3H, t, $J=7.6$ Hz), 2.21 (3H, s), 2.39 (2H, q, $J=7.6$ Hz), 2.39 (3H, s), 3.00-6.50 (1H, brs), 7.80 (1H, s), 9.91 (1H, s)
90	(DMSO- d_6): 5.35 (2H, s), 7.26-7.58 (5H, m), 7.72 (1H, dd, $J=1.5$ Hz, 8.3 Hz), 7.78-7.95 (2H, m), 8.25 (1H, s), 9.04 (1H, s), 13.28 (1H, brs)
91	(DMSO- d_6): 3.88 (3H, s), 7.20 (1H, s), 7.23 (1H, s), 10.82 (1H, s), 11.12 (1H, s), 12.66 (1H, brs)
92	(DMSO- d_6): 7.22 (1H, s), 7.49 (1H, s), 11.39 (1H, s), 11.42 (1H, s)
93	(DMSO- d_6): 2.23 (3H, s), 3.54 (2H, s), 7.55-7.62 (1H, m), 7.62-7.68 (1H, m), 10.73 (1H, s), 11.45-13.40 (1H, m)
94	(DMSO- d_6): 3.14 (3H, s), 3.61 (2H, s), 7.04 (1H, d, $J=8.5$ Hz), 7.79 (1H, d, $J=1.5$ Hz), 7.90 (1H, dd, $J=8.5$ Hz, 1.5 Hz), 12.30-12.92 (1H, m)
95	(DMSO- d_6): 1.35 (3H, d, $J=7.5$ Hz), 3.48 (1H, q, $J=7.5$ Hz), 6.90 (1H, d, $J=8.5$ Hz), 7.75-7.90 (2H, m), 10.69 (1H, s), 12.38-12.83 (1H, m)

Attached Sheet (B) for Table 5

Reference Example No.	$^1\text{H-NMR}$ (200 MHz) δ ppm
96	(DMSO- d_6): 2.24 (3H, s), 3.68 (2H, s), 7.11 (1H, d, $J=8.0$ Hz), 7.41 (1H, d, $J=8.0$ Hz), 10.58 (1H, s), 12.70-13.00 (1H, m)
97	(DMSO- d_6): 2.41 (3H, s), 3.47 (2H, s), 6.71 (1H, d, $J=8.0$ Hz), 7.78 (1H, d, $J=8.0$ Hz), 10.60 (1H, s), 12.15-12.60 (1H, m)
98	(DMSO- d_6): 2.50 (3H, s), 3.46 (2H, s), 6.66 (1H, s), 7.68 (1H, s), 10.59 (1H, s), 12.10-12.60 (1H, m)
99	(DMSO- d_6): 1.92 (3H, s), 4.69 (1H, s), 7.42 (2H, s), 11.11 (1H, s), 13.15-13.40 (1H, m)
100	(DMSO- d_6): 3.51 (2H, s), 6.89-7.08 (1H, m), 7.30-7.47 (1H, m), 7.57-7.70 (1H, m), 9.72 (1H, s), 11.35-14.25 (1H, m)
101	(DMSO- d_6): 1.94 (3H, s), 4.75 (2H, s), 7.31 (1H, d, $J=7.5$ Hz), 7.47 (1H, d, $J=7.5$ Hz), 11.10 (1H, s), 13.10-13.54 (1H, m)
102	(DMSO- d_6): 3.67 (2H, s), 3.87 (3H, s), 7.02 (1H, d, $J=9.0$ Hz), 7.53 (1H, d, $J=9.0$ Hz), 10.53 (1H, s), 10.68 (1H, s)
103	(DMSO- d_6): 3.75 (2H, s), 7.68 (1H, s), 7.84 (1H, d, $J=2.0$ Hz), 8.51 (1H, d, $J=2.0$ Hz), 12.30-12.98 (1H, m)
104	(DMSO- d_6): 1.26 (6H, s), 6.92 (1H, d, $J=8.5$ Hz), 7.79 (1H, d, $J=1.5$ Hz), 7.81 (1H, dd, $J=8.5$ Hz, 1.5 Hz), 10.68 (1H, s), 12.62 (1H, s)
105	(DMSO- d_6): 1.39 (6H, s), 3.87 (3H, s), 7.00 (1H, d, $J=8.5$ Hz), 7.58 (1H, d, $J=8.5$ Hz), 10.51 (1H, s), 12.50-12.90 (1H, m)
107	(250 MHz; DMSO- d_6): 8.00 (1H, s), 8.05 (1H, d, $J=8$ Hz), 8.10 (1H, d, $J=8$ Hz), 8.18-8.30 (2H, m), 8.48 (1H, dd, $J=8.2$ Hz, 2.0 Hz), 13.39 (1H, brs)

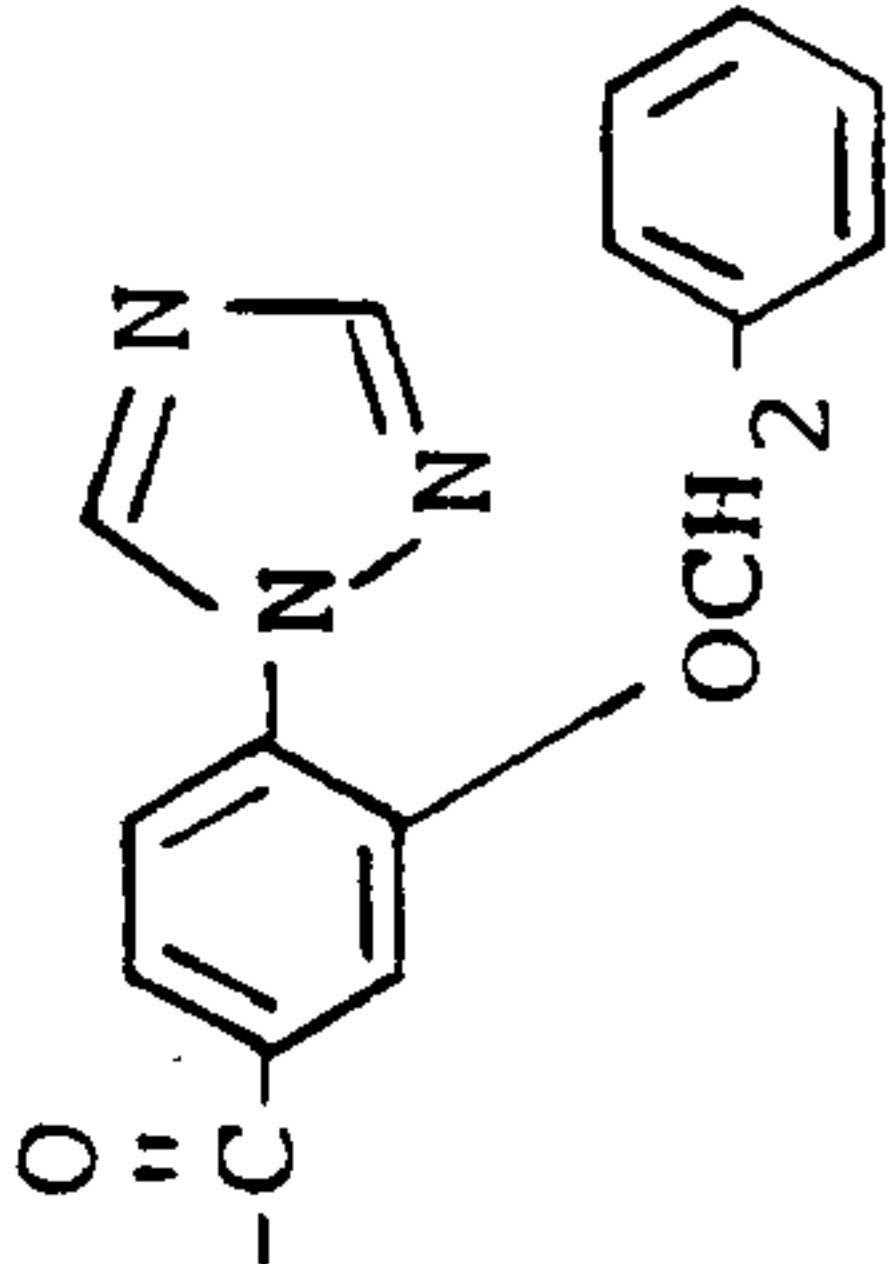
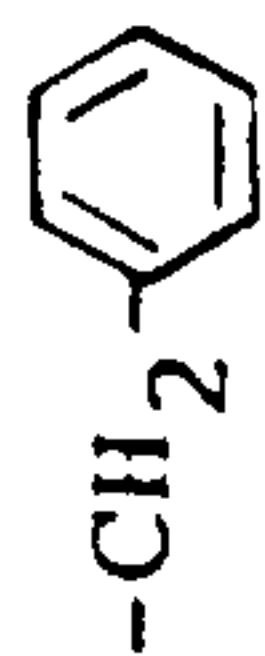
Attached Sheet (B) for Table 5

Reference Example No.	$^1\text{H-NMR}$ (200 MHz) δ ppm
108	(DMSO- d_6): 1.26 (6H, s), 2.24 (3H, s), 7.63 (1H, d, $J=0.5$ Hz), 7.66 (1H, d, $J=0.5$ Hz), 10.72 (1H, s), 12.35-12.70 (1H, m)
109	(DMSO- d_6): 3.68 (3H, s), 3.73 (3H, s), 3.79 (3H, s), 6.50-6.60 (1H, m), 6.62 (1H, d, $J=2.0$ Hz), 7.05 (1H, d, $J=8.0$ Hz), 7.15-7.28 (1H, m), 7.46-7.62 (2H, m), 12.84-13.01 (1H, m)
114	(DMSO- d_6): 6.39 (2H, d, $J=8.1$ Hz), 6.93 (1H, t, $J=8.1$ Hz), 7.42 (2H, d, $J=8.5$ Hz), 7.89 (2H, d, $J=8.5$ Hz), 9.22 (2H, brs), 10.29-14.49 (1H, brs)
120	(DMSO- d_6): 5.00 (2H, s), 5.16 (4H, s), 7.11 (2H, s), 7.20-7.56 (17H, m), 7.60 (1H, d, $J=7.9$ Hz), 7.69 (1H, s)
122	(DMSO- d_6): 6.32 (1H, dd, $J=8.5$ Hz, 2.5 Hz), 6.43 (1H, d, $J=2.5$ Hz), 7.12 (1H, d, $J=8.5$ Hz), 7.61 (2H, d, $J=8.5$ Hz), 7.90 (2H, d, $J=8.5$ Hz), 8.71-10.34 (2H, m), 11.47-13.68 (1H, m)
123	(CDCl $_3$): 2.06 (3H, s), 2.08 (3H, s), 2.32 (3H, s), 7.05 (1H, d, $J=2.0$ Hz), 7.10 (1H, dd, $J=8.5$ Hz, 2.0 Hz), 7.32 (1H, d, $J=8.5$ Hz), 7.43 (1H, d, $J=8.0$ Hz), 7.91 (1H, d, $J=1.5$ Hz), 8.05 (1H, dd, $J=8.0$ Hz, 1.5 Hz), 9.20-10.20 (1H, m)
131	(DMSO- d_6): 1.12 (3H, t, $J=7.0$ Hz), 3.17-3.40 (2H, m), 7.84-8.10 (4H, m), 8.50-8.79 (1H, m), 13.05-13.31 (1H, m)
135	(DMSO- d_6): 7.05-7.20 (1H, m), 7.28-7.46 (2H, m), 7.70-7.88 (2H, m), 7.98-8.15 (4H, m), 10.39 (1H, s), 13.11-13.35 (1H, m)
136	(DMSO- d_6): 1.12 (3H, t, $J=7.0$ Hz), 3.14-3.43 (2H, m), 7.58 (1H, t, $J=8.0$ Hz), 7.96-8.17 (2H, m), 8.41 (1H, t, $J=1.5$ Hz), 8.56-8.78 (1H, m), 13.05-13.24 (1H, m)

Attached Sheet (B) for Table 5

Reference Example No.	$^1\text{H-NMR}$ (200 MHz) δ ppm
137	(DMSO- d_6): 1.13 (3H, t, $J=7.0$ Hz), 3.15-3.45 (2H, m), 7.93 (1H, d, $J=8.0$ Hz), 8.10-8.30 (1H, m), 8.30-8.50 (1H, m), 8.70-8.98 (1H, m), 13.50-13.90 (1H, m)
138	(DMSO- d_6): 1.05 (3H, t, $J=7.6$ Hz), 2.33 (2H, q, $J=7.6$ Hz), 6.32 (1H, d, $J=3.6$ Hz), 7.19 (1H, d, $J=3.6$ Hz), 11.37 (1H, s), 12.74 (1H, brs)
140	(DMSO- d_6): 1.11 (3H, t, $J=7.0$ Hz), 3.12-3.38 (2H, m), 7.70 (1H, d, $J=8.0$ Hz), 8.26 (1H, dd, $J=8.0$ Hz, 1.5 Hz), 8.42 (1H, d, $J=1.5$ Hz), 8.73 (1H, t, $J=5.5$ Hz), 13.22-14.22 (1H, m)
141	(DMSO- d_6): 4.42 (2H, s), 7.75 (1H, d, $J=8.0$ Hz), 8.03 (1H, d, $J=8.0$ Hz), 8.12 (1H, s), 8.78 (1H, s), 13.24 (1H, brs)
147	(DMSO- d_6): 6.26 (1H, dd, $J=8.0$ Hz, 2.0 Hz), 6.37 (1H, d, $J=2.0$ Hz), 6.96 (1H, d, $J=8.0$ Hz), 7.21 (1H, d, $J=8.0$ Hz), 7.36 (1H, dd, $J=8.0$ Hz, 1.5 Hz), 7.45 (1H, d, $J=1.5$ Hz), 9.19 (1H, s), 9.29 (1H, s), 9.40 (1H, s), 12.33-12.95 (1H, m)

Table 6 Ra-OR²³

Reference Example No.	Ra	R ²³	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm:
148			Colorless needles (Ethanol)	(-)	(CDCl ₃): 5.25 (2H, s), 5.39 (2H, s), 7.30-7.45 (10H, m), 7.84 (1H, dd, J=1.7Hz, 8.4Hz), 7.90 (1H, d, J=1.7Hz), 8.01 (1H, d, J=8.4Hz), 8.08 (1H, s), 8.92 (1H, s)

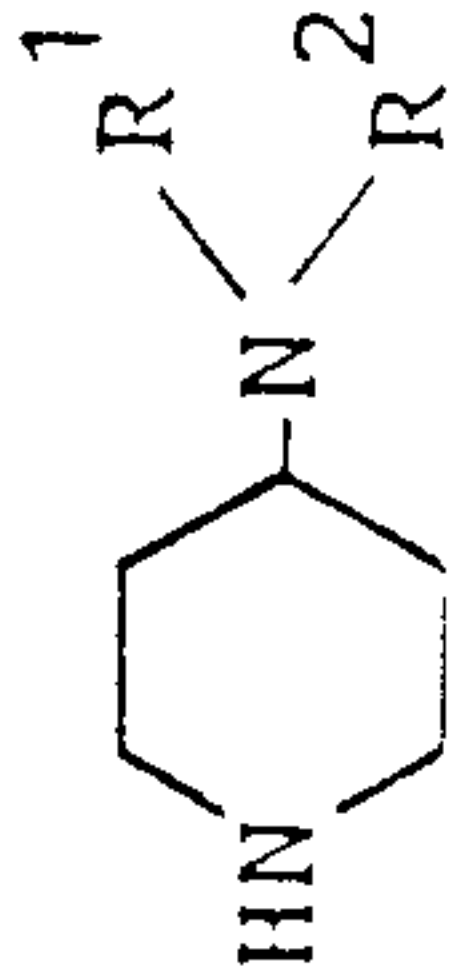


Table 7

Reference Example No.		Crystal form (Recrystallization solvent)	Melting point (°C)	¹ H-NMR (200 MHz) ppm
149		White powder (Ethanol)	235 - 238 (2HCl)	
150		White powder (Ethanol)	182 - 185 (2HCl)	
151		Colorless oil	(-)	See Attached Sheet (C).
152		Colorless oil	(-)	See Attached Sheet (C).

(To be continued)

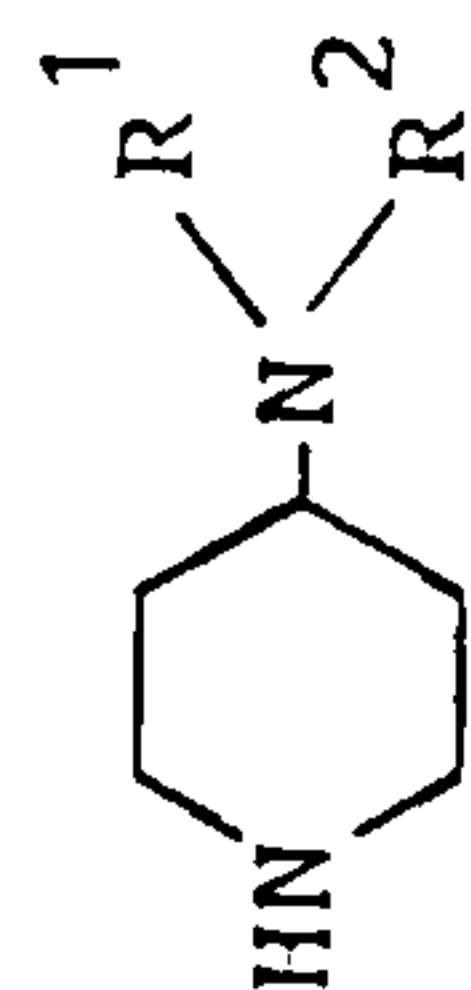


Table 7

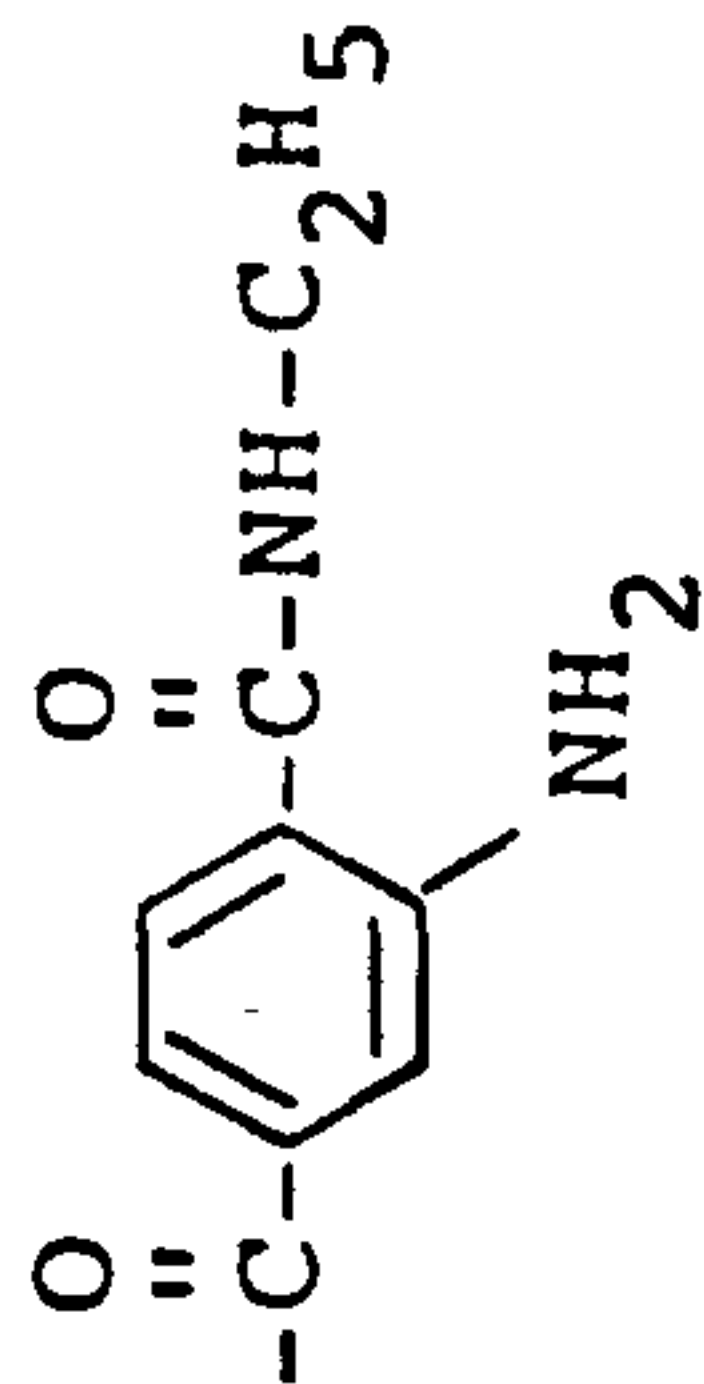
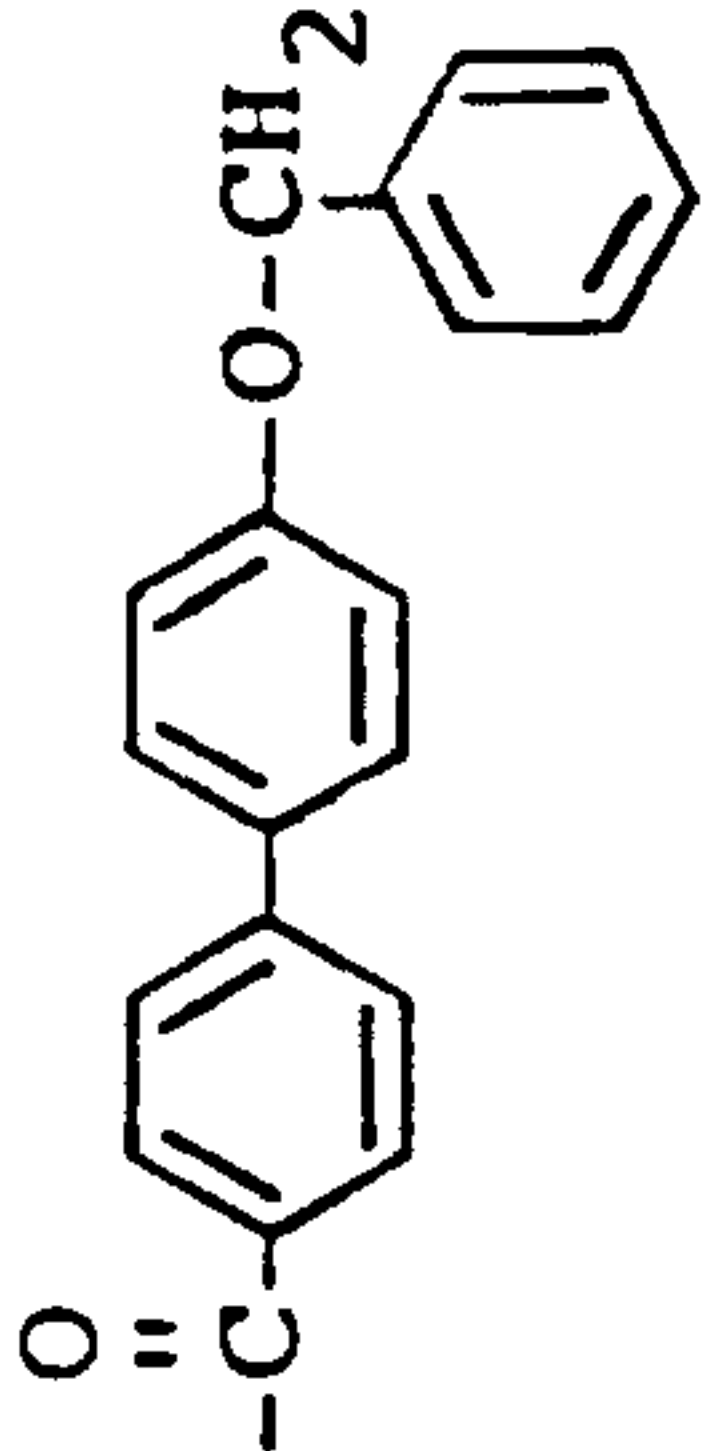
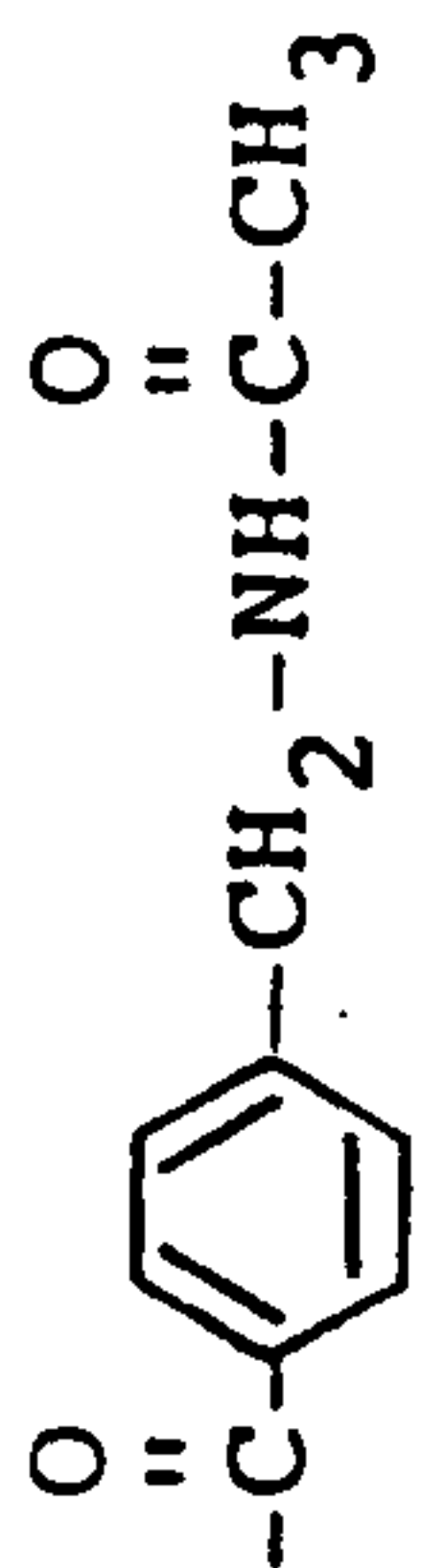
(Continued)

Reference Example No.		Crystal form (Recrystallization solvent)	Melting point (°C)	¹ H-NMR (200 MHz) ppm
153		Colorless oil	(-)	See Attached Sheet (C).
154		Light brown oil	(-)	See Attached Sheet (C).
155		Colorless oil	(-)	See Attached Sheet (C).
156		Light yellow oil	(-)	See Attached Sheet (C).

Attached Sheet (C) for Table 7

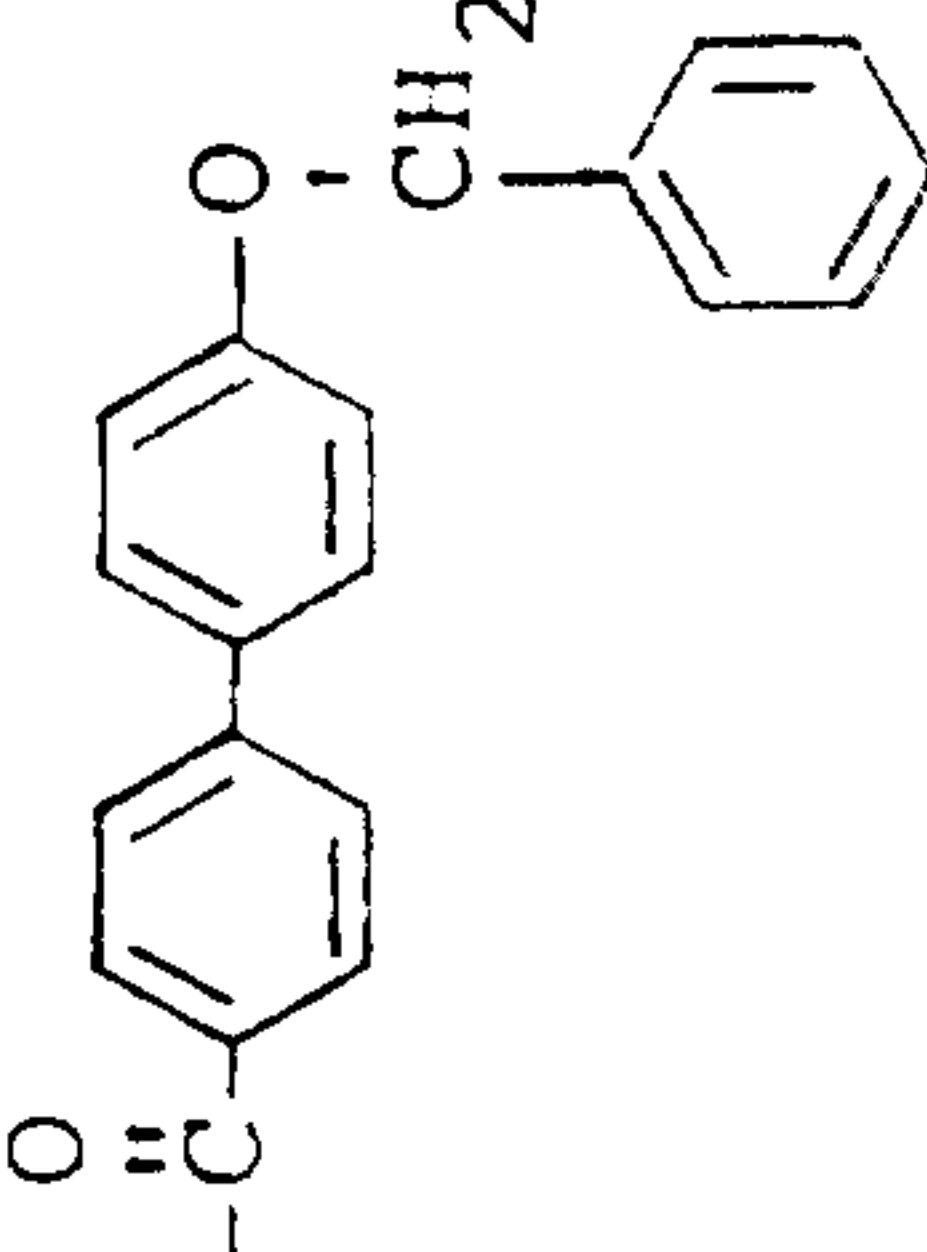
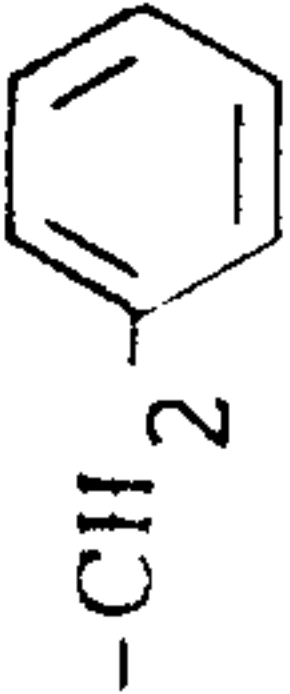
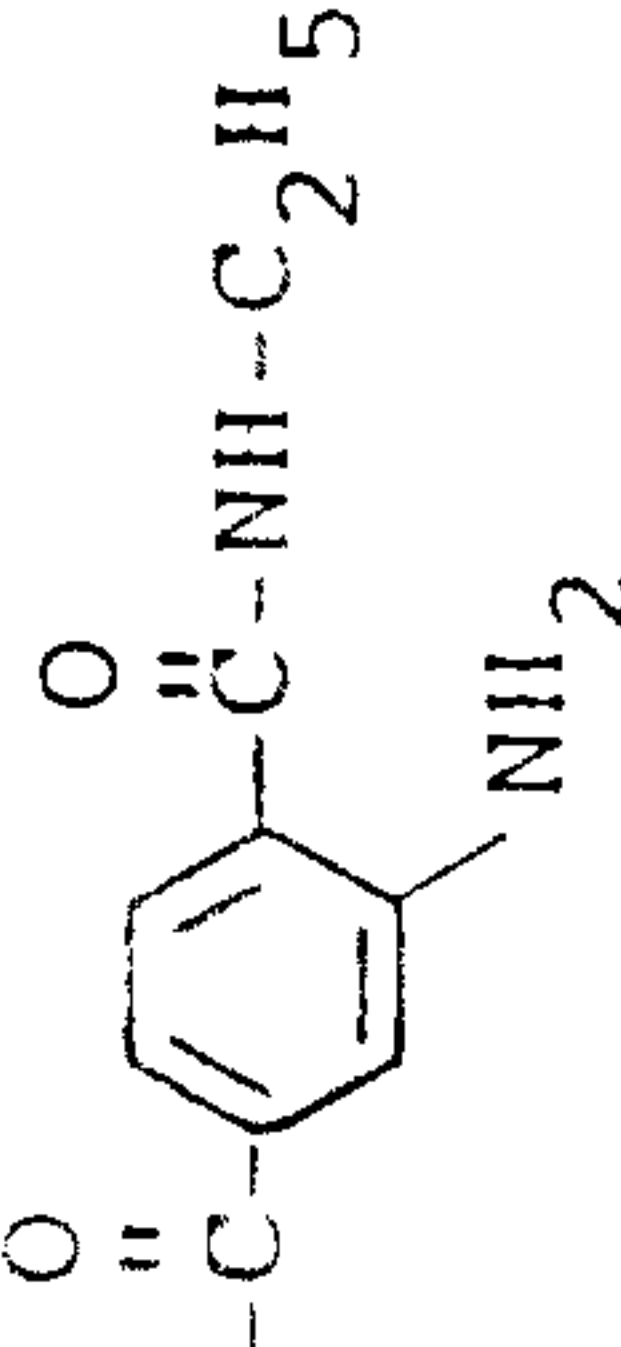
Reference Example No.	$^1\text{H-NMR}$ (200 MHz) δ ppm
151	(250 MHz; CDCl_3): 1.31-1.56 (2H, m), 1.72-1.90 (2H, m), 2.16 (3H, s), 2.21 (3H, s), 2.37 (3H, s), 2.45-2.70 (3H, m), 2.85 (2H, t, $J=6.0$ Hz), 3.04-3.26 (2H, m), 4.01 (2H, t, $J=6.0$ Hz), 6.66-6.80 (2H, m), 6.90-7.20 (1H, m), 7.41 (1H, d, $J=8.5$ Hz)
152	(CDCl_3): 1.30-1.56 (2H, m), 1.72-1.90 (2H, m), 2.11 (3H, s), 2.37 (3H, s), 2.44-2.72 (3H, m), 2.85 (2H, t, $J=6.0$ Hz), 3.03-3.29 (2H, m), 4.01 (2H, t, $J=6.0$ Hz), 6.75-6.92 (2H, m), 7.32-7.47 (2H, m), 7.96 (1H, s)
153	(CDCl_3): 1.32-1.61 (2H, m), 1.70-1.92 (3H, m), 2.38 (3H, s), 2.46-2.75 (3H, m), 2.87 (2H, t, $J=6.1$ Hz), 3.09-3.28 (2H, m), 4.02 (2H, t, $J=6.1$ Hz), 6.73-6.85 (1H, m), 6.85-6.99 (2H, m), 7.18 (1H, t, $J=8.4\text{Hz}$)
154	(CDCl_3): 1.31-1.59 (2H, m), 1.70-1.93 (3H, m), 2.32 (3H, s), 2.50-2.70 (3H, m), 2.70-2.89 (4H, m), 3.05-3.26 (2H, m), 6.02 (1H, d, $J=3.1$ Hz), 6.28 (1H, dd, $J=1.9$ Hz, 3.1 Hz), 7.30 (1H, d, $J=1.9$ Hz)
155	(CDCl_3): 1.32-1.61 (2H, m), 1.71-1.95 (3H, m), 2.28 (3H, s), 2.38 (3H, s), 2.47-2.75 (3H, m), 2.87 (2H, t, $J=6.2$ Hz), 3.09-3.28 (2H, m), 4.02 (2H, t, $J=6.2$ Hz), 6.80 (2H, d, $J=8.6$ Hz), 7.07 (2H, d, $J=8.6$ Hz)
156	(250 MHz; CDCl_3): 0.95-1.07 (1H, m), 1.07-1.18 (1H, m), 1.41-1.63 (2H, m), 1.79-2.03 (4H, m), 2.39 (3H, s), 2.30-2.70 (4H, m), 3.08-3.22 (2H, m), 7.04 (2H, d, $J=8.5$ Hz), 7.10-7.31 (3H, m)

Table 8 Ra-OH

Reference Example No.	Ra	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
157		Colorless needles	(-)	(DMSO-d ₆): 1.09 (3H, t, J=7.0Hz), 3.11-3.37 (2H, m), 6.51 (2H, brs), 7.02 (1H, dd, J=8.0Hz, 1.5Hz), 7.30 (1H, d, J=1.5Hz), 7.51 (1H, d, J=8.0Hz), 8.34 (1H, t, J=5.5Hz), 12.60-13.05 (1H, m)
158		White powder	(-)	(DMSO-d ₆): 5.16 (2H, s), 7.02-7.19 (2H, m), 7.30-7.58 (7H, m), 7.58-7.70 (2H, m), 7.82-8.02 (2H, m)
159		Colorless prisms (Methanol)	195-198 (-)	

Ra-OR²³

Table 9

Reference Example No.	Ra	R ²³	Crystal form (Recrystallization solvent)	Melting point (°C) (Salt form)	¹ H-NMR (200 MHz) ppm
160			White powder	(-)	(CDCl ₃): 5.12 (2H, s) 5.38 (2H, s), 7.00-7.16 (2H, m), 7.30-7.53 (10H, m), 7.53-7.70 (4H, m), 8.06-8.20 (2H, m)
161			White powder	(-)	(CDCl ₃): 1.25 (3H, t, J=7.0Hz), 3.36-3.58 (2H, s), 3.90 (3H, m), 5.57 (2H, brs), 5.88-6.33 (1H, m), 7.23-7.33 (1H, m), 7.33-7.43 (2H, m)

Example 1

42 ml of diethyl cyanophosphonate and 34 ml of triethylamine were dropwise added, in this order, to a solution of 49.2 g of 3,5-dimethyl-4-propionylamino-
5 benzoic acid and 46.8 g of 4-[N-methyl-N-(2-phenylethyl)amino]piperidine in 300 ml of DMF, at 5-10°C (the container inside temperature) with cooling in an ice-methanol bath. The bath was removed and the mixture was stirred for 30 minutes. The mixture was then poured
10 into 2 liters of ice water. The resulting mixture was extracted with ethyl acetate (500 ml x 2). The extract was washed with water (600 ml x 2) and a saturated aqueous sodium chloride solution in this order, and then concentrated under reduced pressure. To the residue was
15 added 1 liter of ethanol for dissolution. To the solution was added 20 ml of concentrated hydrochloric acid. The mixture was concentrated under reduced pressure. The concentration was stopped when the liquid volume became half of the original volume. The concentrate was
20 ice-cooled. The resulting crystals were collected by filtration and recrystallized from water to obtain 81 g of 4-[N-methyl-N-(2-phenylethyl)amino]-1-(3,5-dimethyl-4-propionylaminobenzoyl)piperidine hydrochloride as a white powder.

25 Melting point: 260-263°C (decompd.)

Using suitable starting materials, the compounds of Examples 2-257 described later were

obtained in the same manner as in Example 1.

Example 2

1.0 ml of phenyl isocyanate was added to a solution of 1.0 g of 4-[N-methyl-N-(2-phenylethyl)-
5 amino]piperidine in 15 ml of chloroform. The mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated under reduced pressure. To the residue was added diethyl ether for crystallization. The resulting crystals were collected
10 by filtration and recrystallized from ethyl acetate to obtain 0.7 g of 4-[N-methyl-N-(2-phenylethyl)amino]-1-anilinocarbonylpiperidine as colorless prism-like crystals.

Melting point: 105-107°C

15

Using suitable starting materials, the compounds of Examples 46 and 258-262 described later were obtained in the same manner as in Example 2.

Example 3

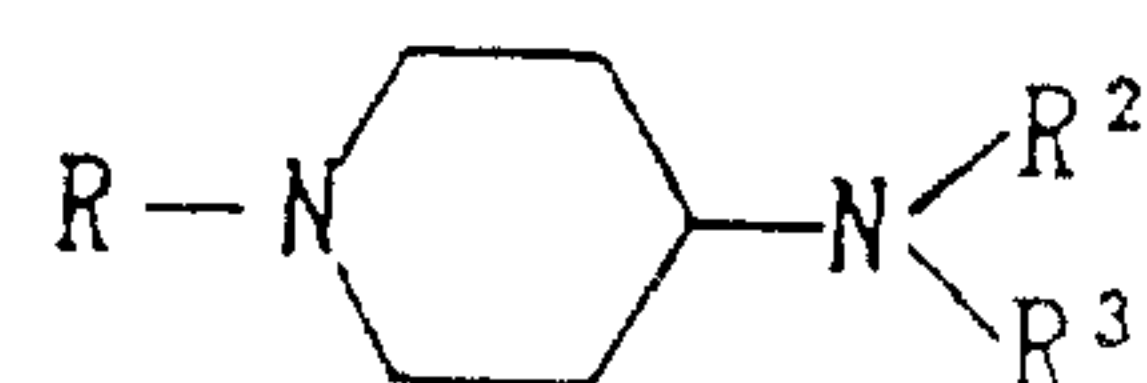
20 A catalytic amount of p-toluenesulfonic acid was added to a solution of 0.45 g of 4-oxo-1-[4-(1,2,4-triazol-1-yl)benzoyl]piperidine and 0.39 g of 2-(4-chlorophenyl)ethylamine in 10 ml of toluene. The mixture was refluxed by heating, for 5 hours while
25 removing the generated water using a Dean-Stark trap. The reaction mixture was concentrated under reduced

pressure. To the residue was added 10 ml of ethanol. Thereto was added 70 mg of sodium borohydride at room temperature. The mixture was stirred at room temperature overnight. The reaction mixture was made acidic with concentrated hydrochloric acid and then concentrated under reduced pressure. To the residue was added ice water. The mixture was made basic with an aqueous sodium hydroxide solution and extracted with two 30-ml portions of ethyl acetate. The extract was washed with water and a saturated aqueous sodium chloride solution in this order, dried with sodium sulfate, and concentrated under reduced pressure to remove the solvent. The residue was purified by silica gel column chromatography (eluant: methylene chloride/methanol = 25/1) and then recrystallized from ethyl acetate to obtain 4-[2-(4-chlorophenyl)ethylamino]-1-[4-(1,2,4-triazol-1-yl)benzoyl]piperidine as a white powder.

Melting point: 131-132.5°C

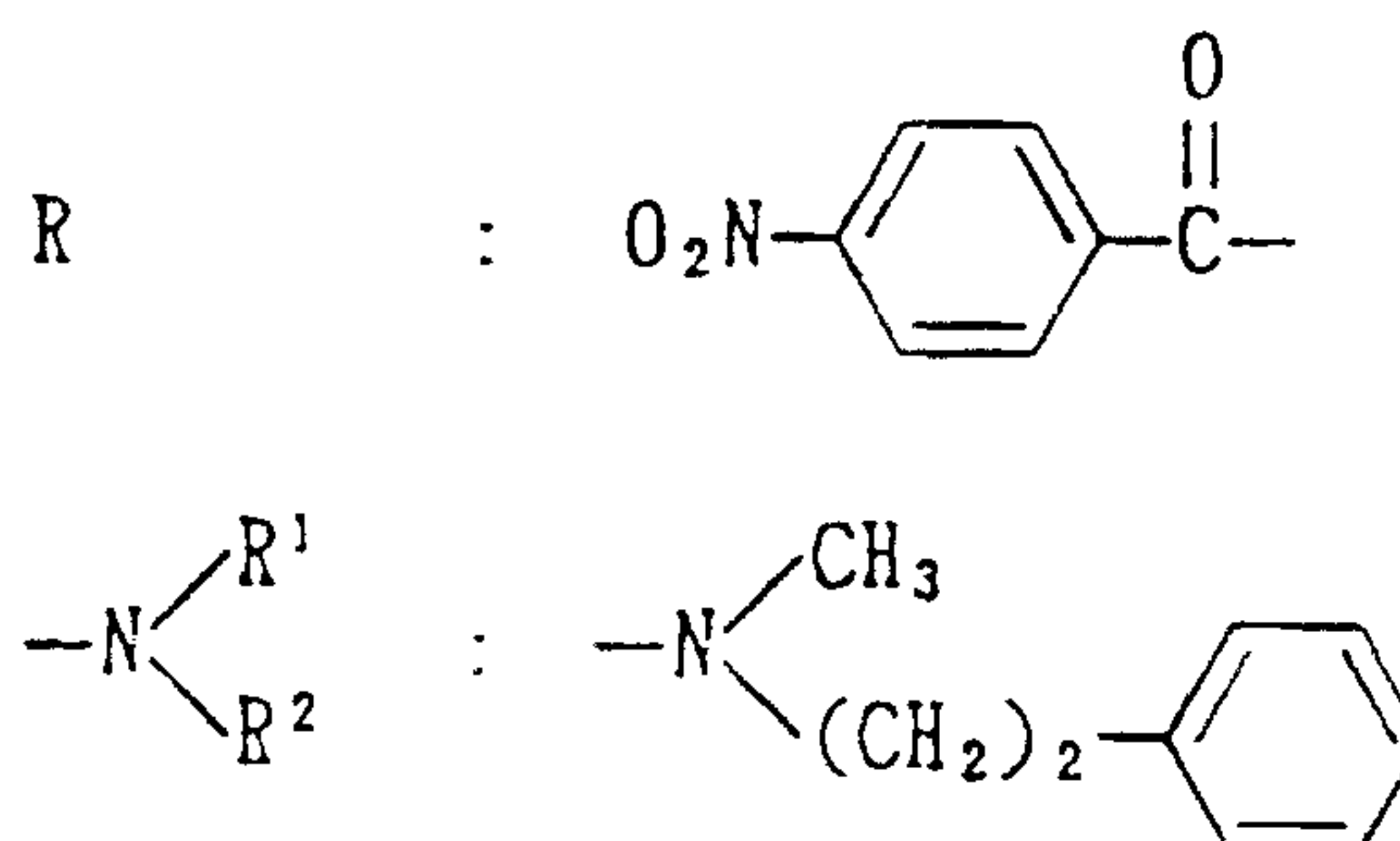
By the method similar to that of employed in Example 3, and by using suitable materials, there were prepared compounds of Examples 1 and 2 as mentioned above, as well as compounds of Examples 4 - 90 and 92 - 262 as shown in following Table 10.

[Table 10]



Example 4

Structural formula:



Crystal form: colorless scales

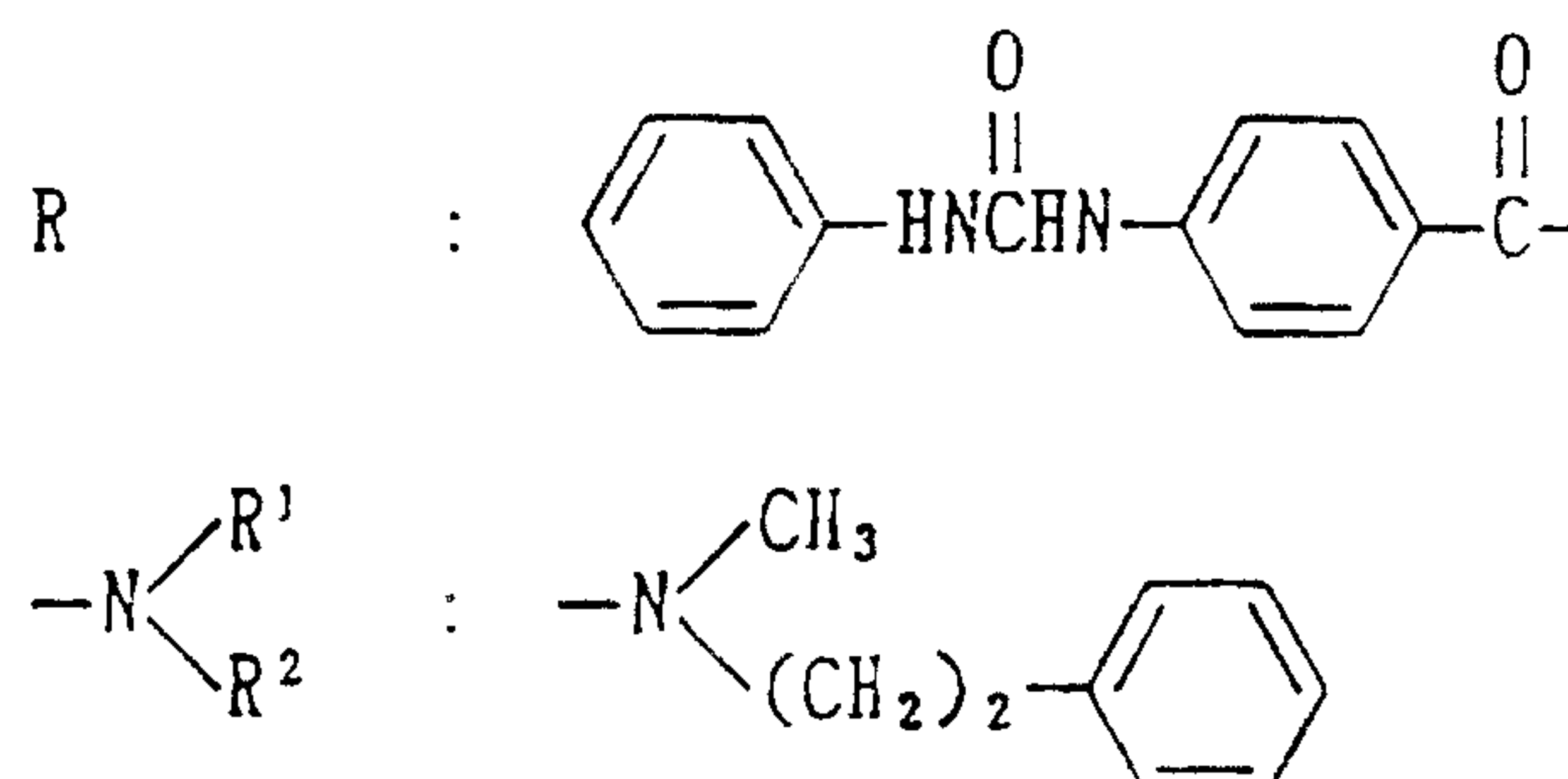
Recrystallization solvent: ethanol-water

Melting point (°C): 188-190

Salt form: fumarate

Example 5

Structural formula:



Crystal form: colorless scales

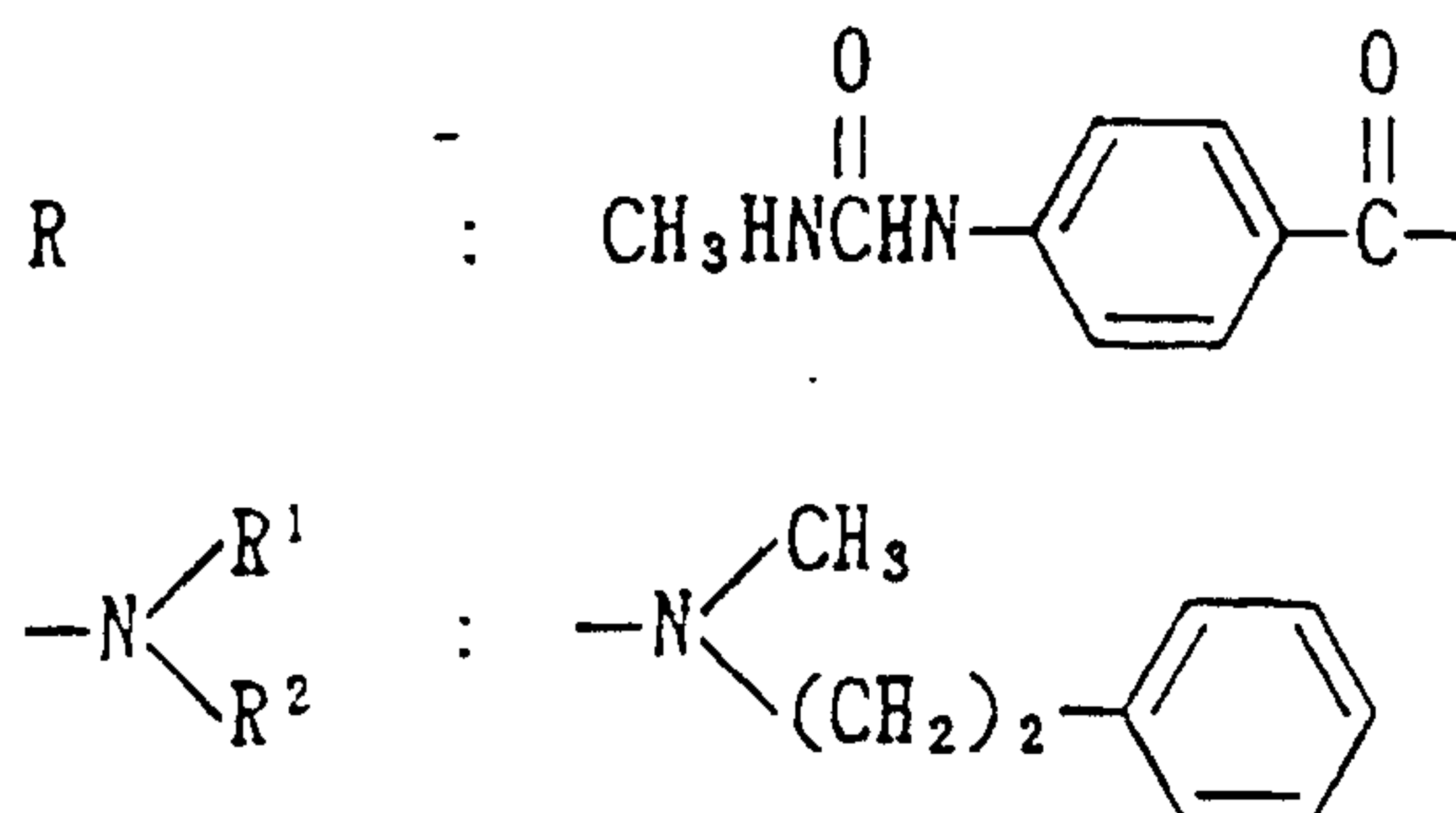
Recrystallization solvent: ethanol

Melting point (°C): 150-152

Salt form: free

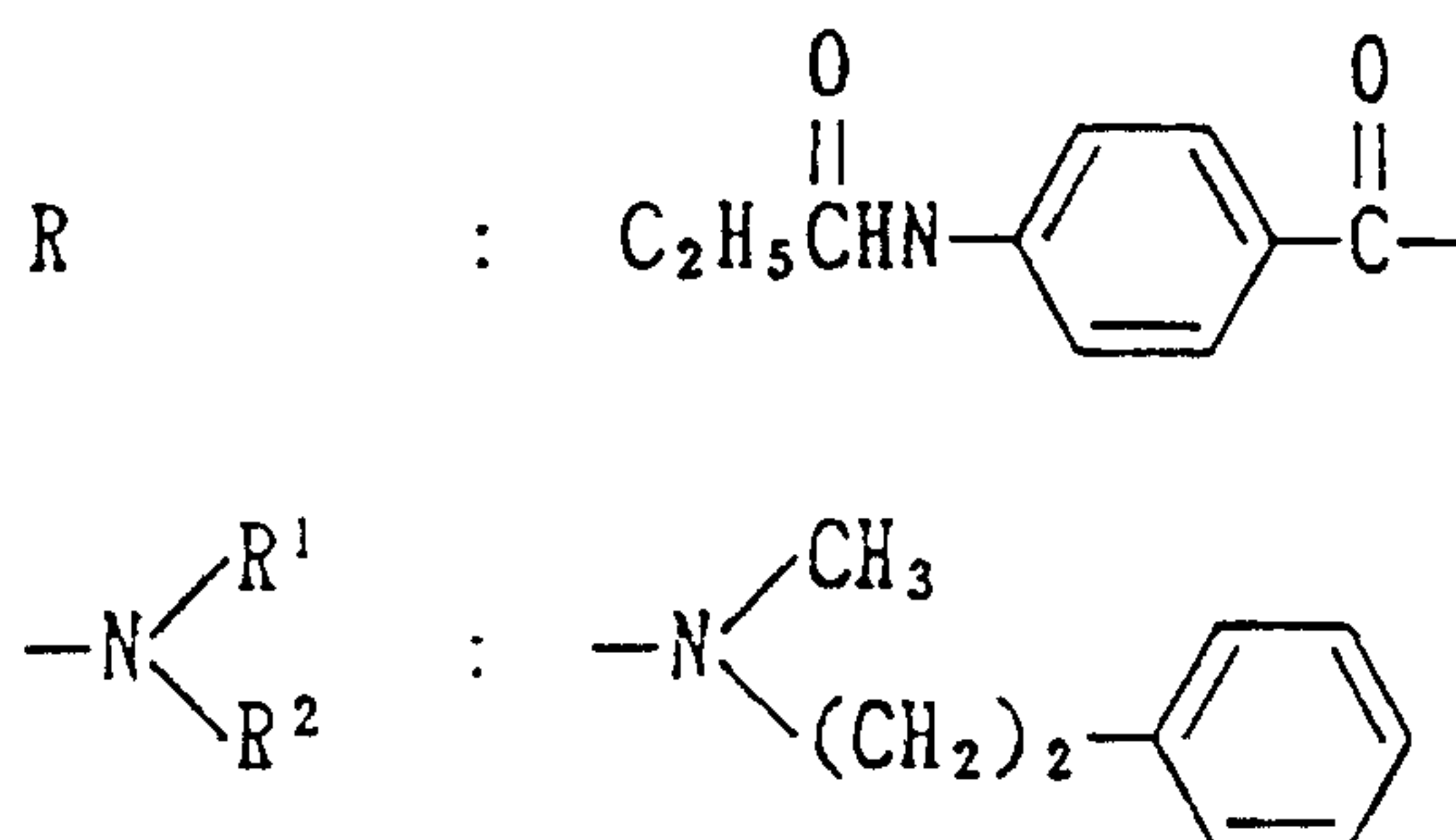
[Table 10 (continued)]

Example 6
Structural formula:



Crystal form: colorless scales
Recrystallization solvent: ethanol
Melting point (°C): 235-237
Salt form: hydrochloride

Example 7
Structural formula:

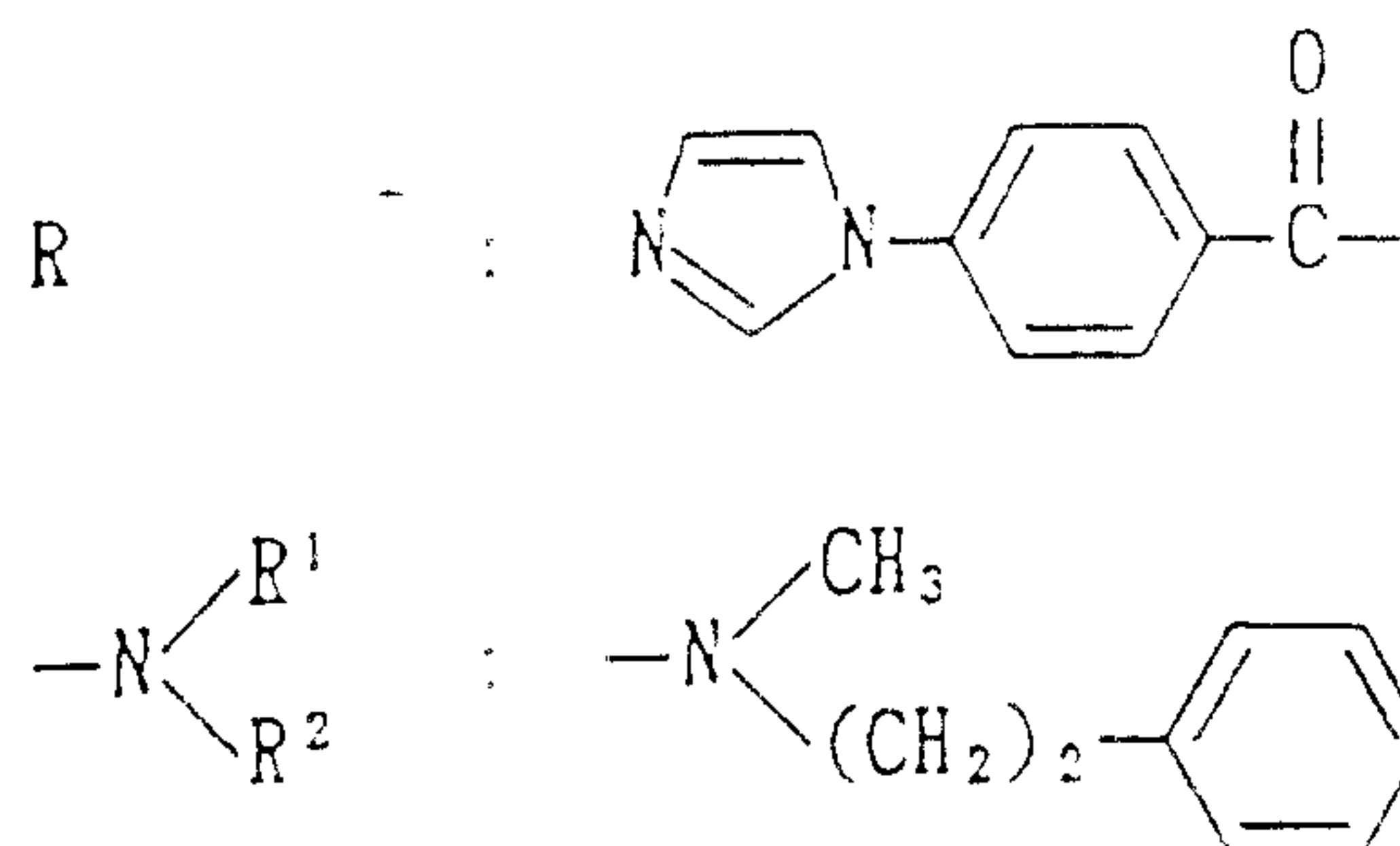


Crystal form: white powder
Recrystallization solvent: ethanol
Melting point (°C): 158-160
Salt form: 1/2 fumarate

{Table 10 (continued)}

Example 8

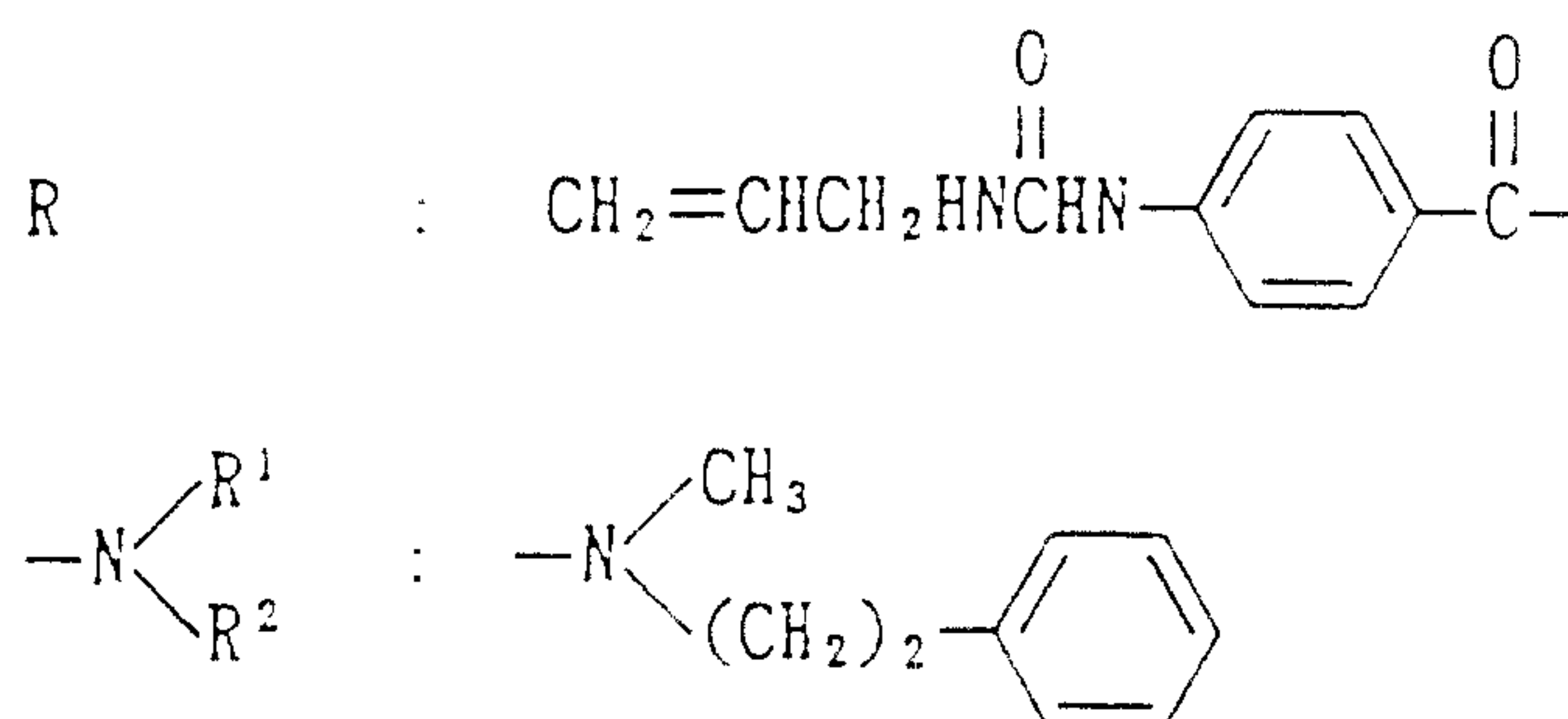
Structural formula:



Crystal form: light yellow amorphous
Salt form: hydrochloride
NMR value: 47)

Example 9

Structural formula:

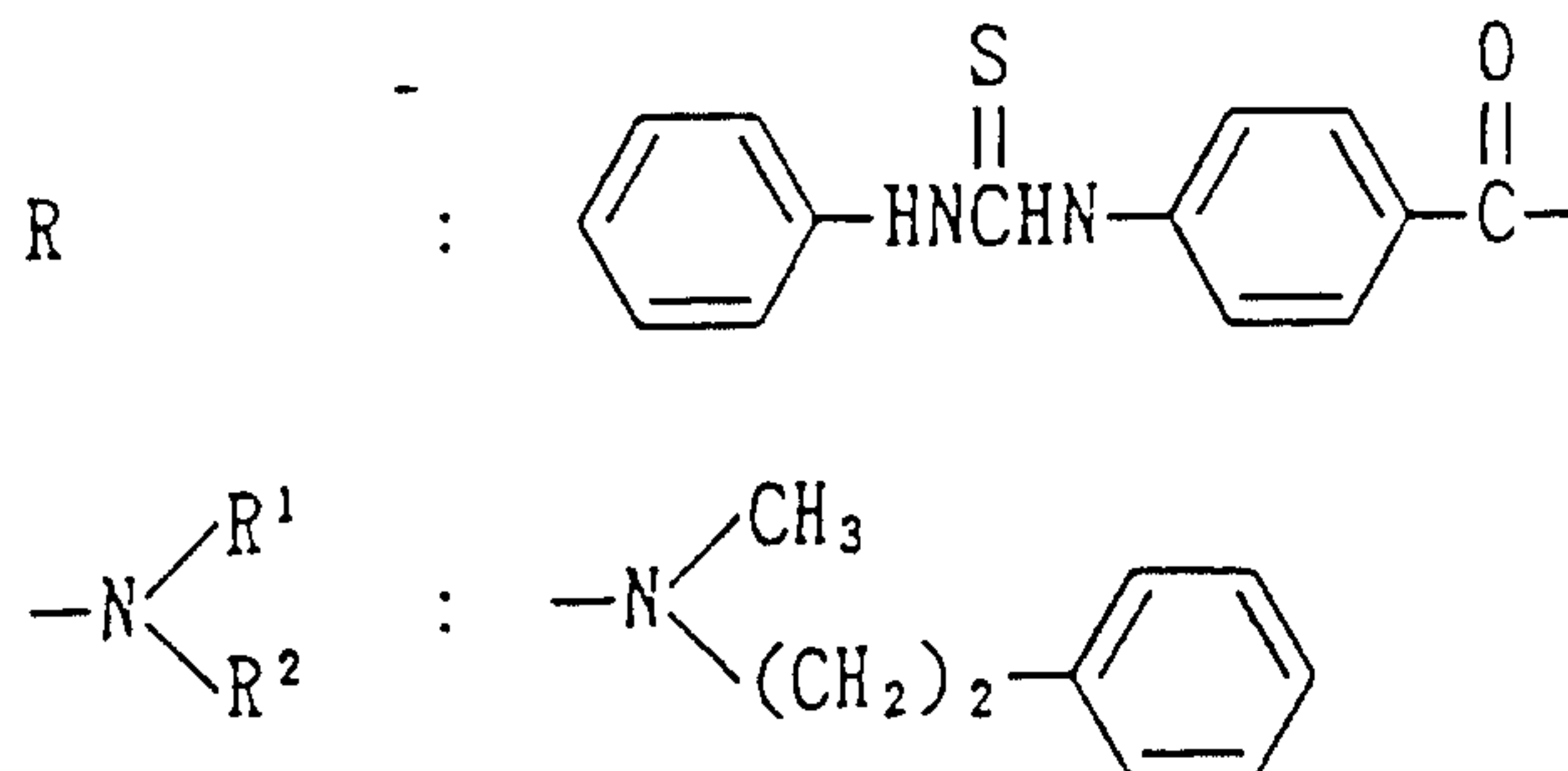


Crystal form: white powder
Recrystallization solvent: ethanol
Melting point (°C): 218-220 (decompd.)
Salt form: hydrochloride

[Table 10 (continued)]

Example 10

Structural formula:



Crystal form: white powder

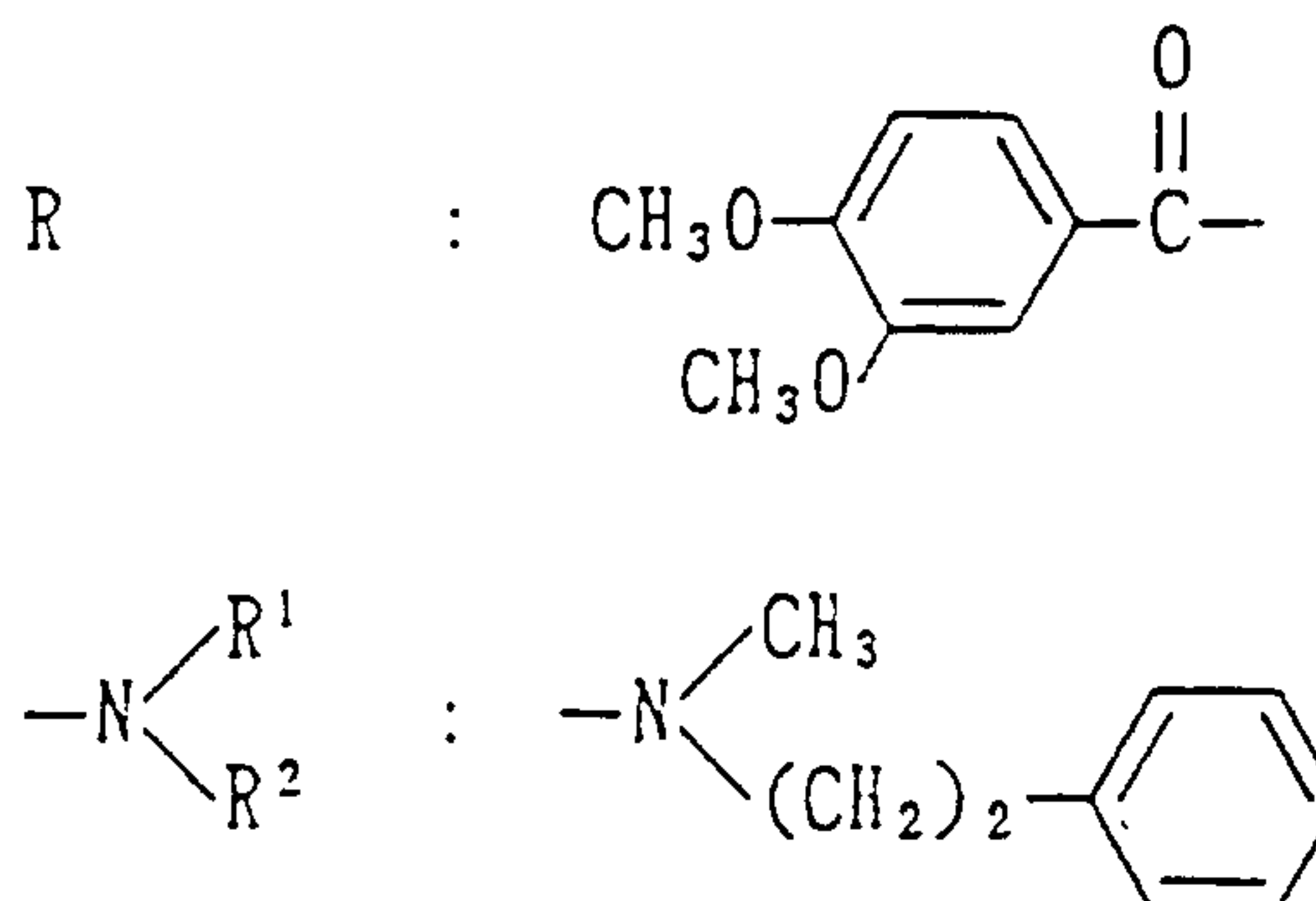
Recrystallization solvent: ethyl acetate

Melting point (°C): 139-141

Salt form: free

Example 11

Structural formula:



Crystal form: colorless prisms

Recrystallization solvent: ethanol-water

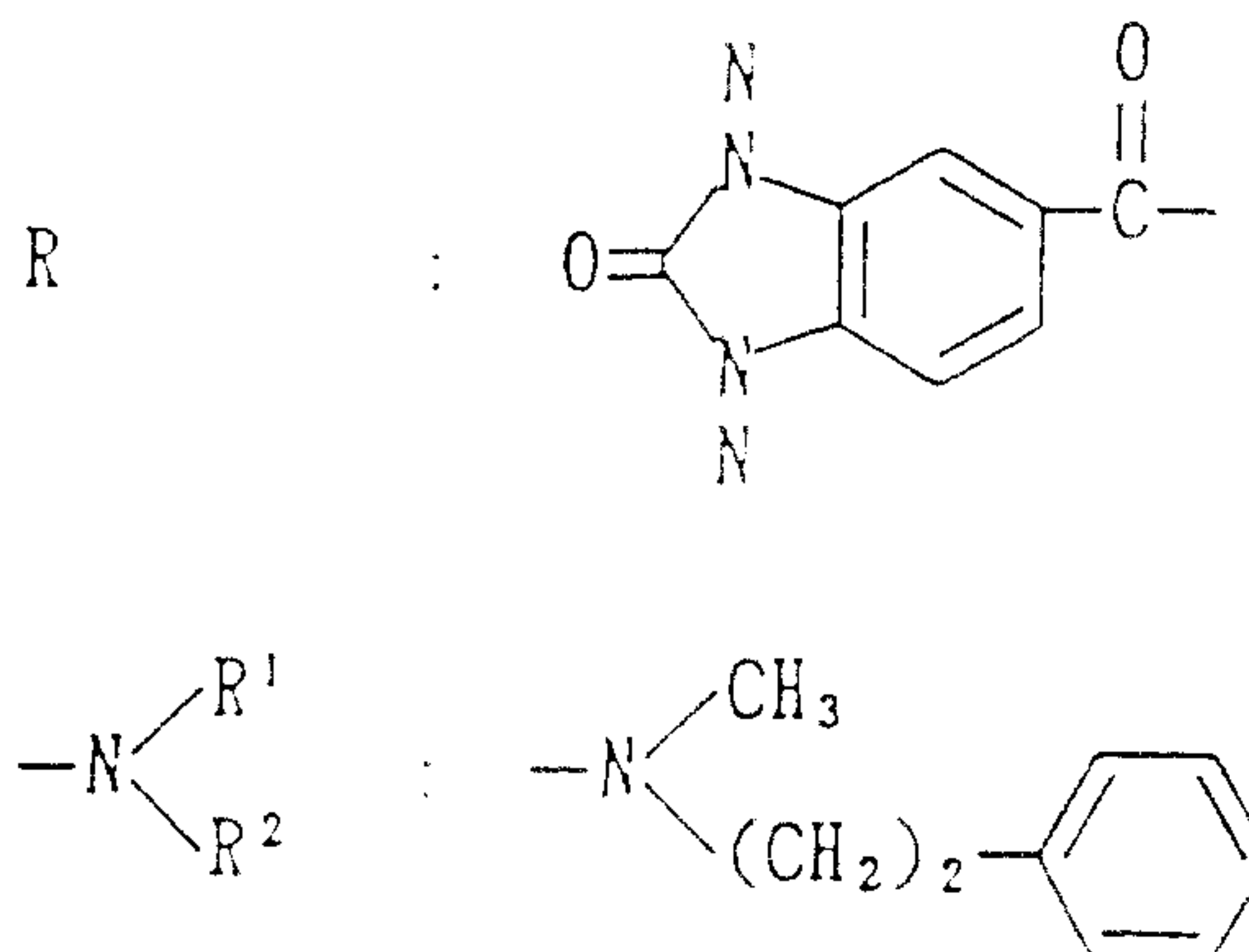
Melting point (°C): 126-128

Salt form: oxalate

[Table 10 (continued)]

Example 12

Structural formula:



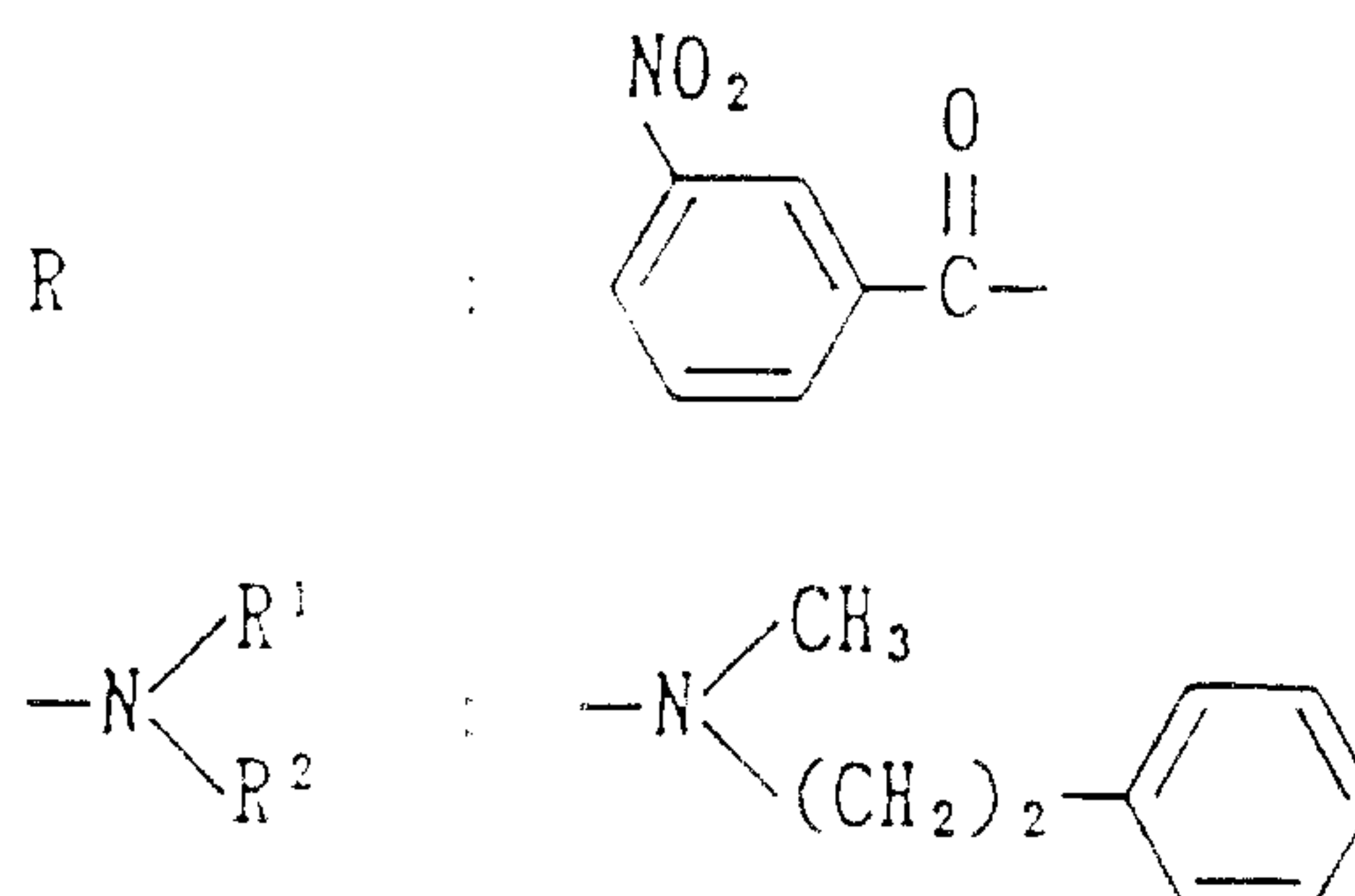
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 48)

Example 13

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-water

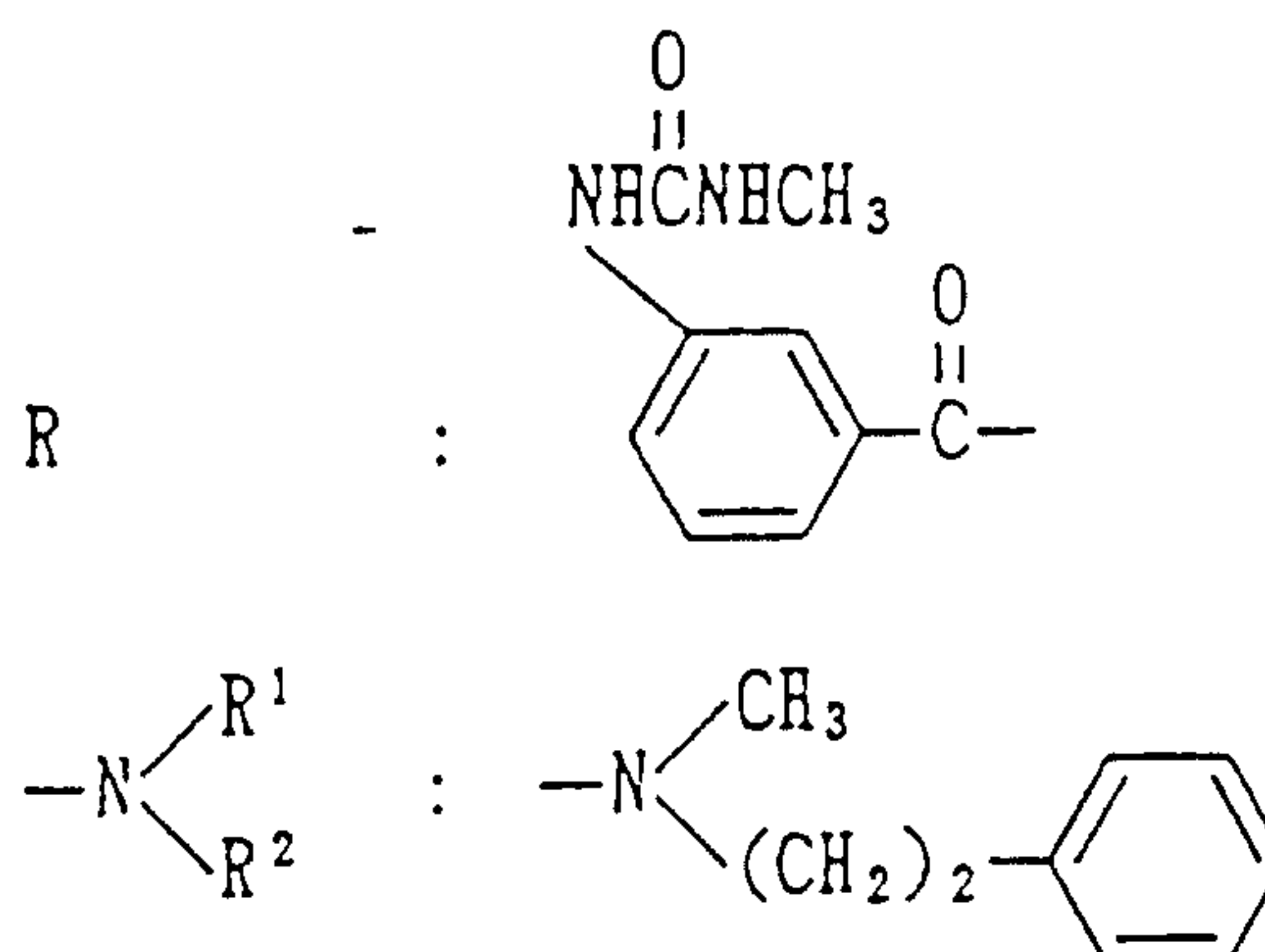
Melting point (°C): 189-191

Salt form: fumarate

{Table 10 (continued)}

Example 14

Structural formula:



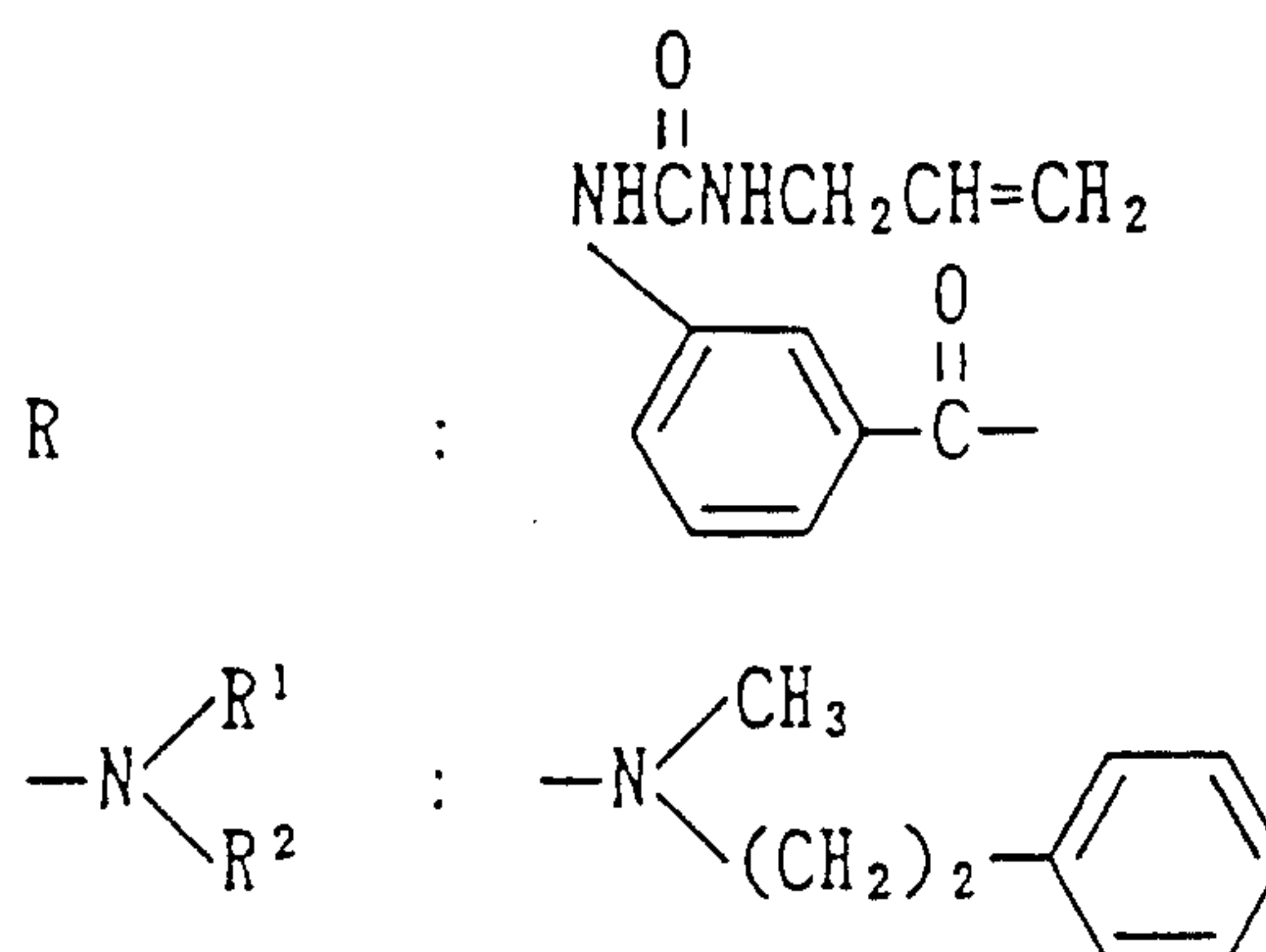
Crystal form: light orange amorphous

Salt form: hydrochloride

NMR value: 49)

Example 15

Structural formula:



Crystal form: light orange amorphous

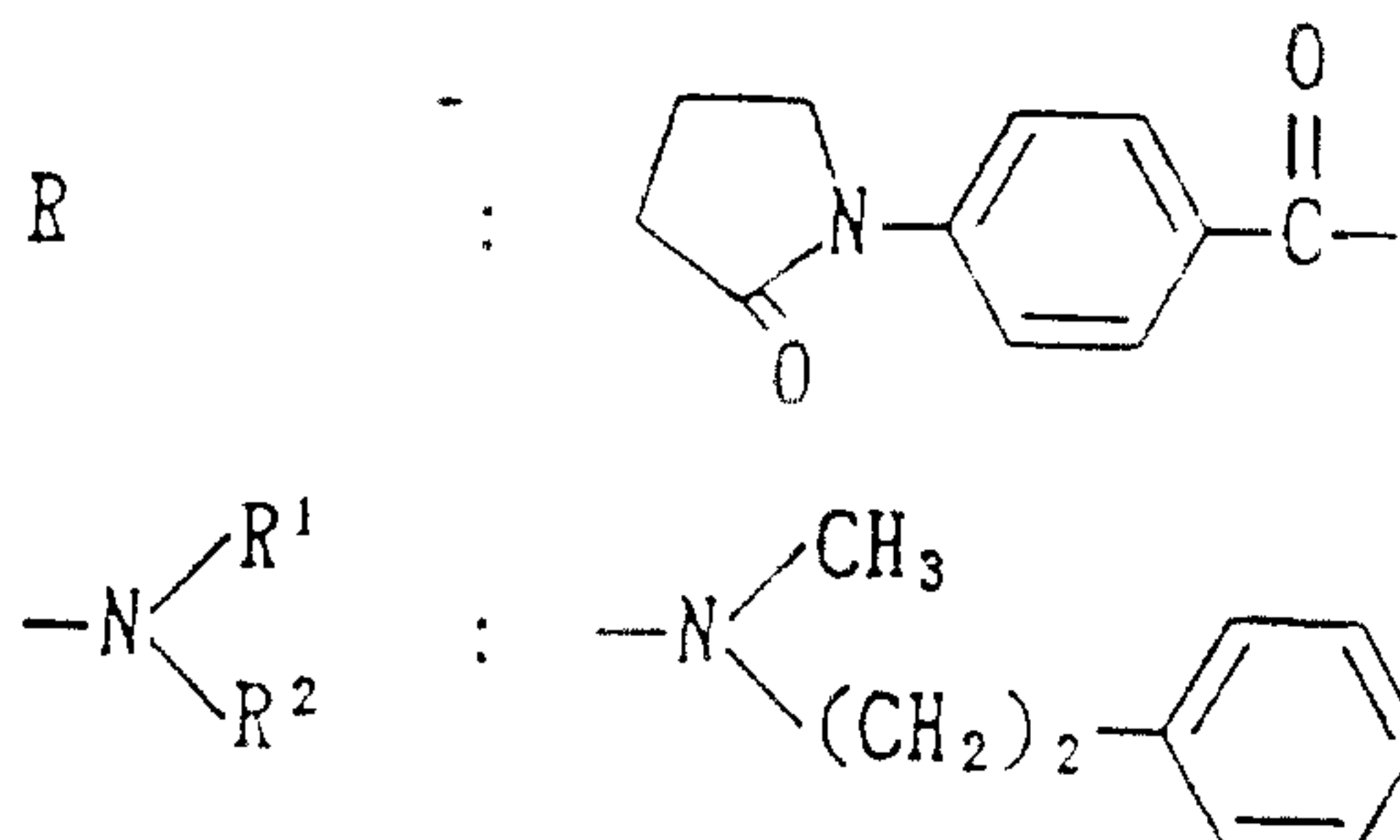
Salt form: hydrochloride

NMR value: 50)

{Table 10 (continued)}

Example 16

Structural formula:



Crystal form: white powder

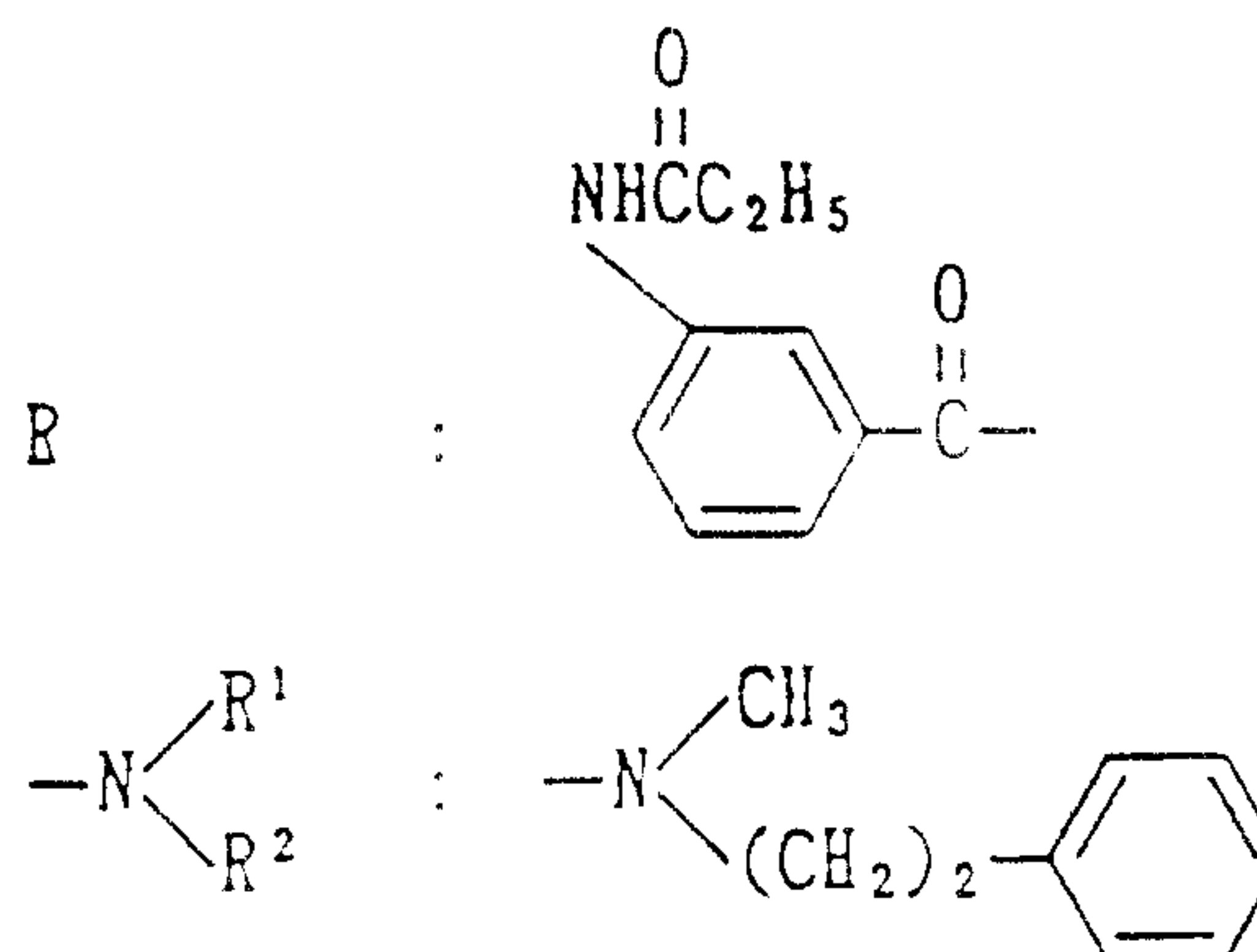
Recrystallization solvent: ethanol

Melting point (°C): 138-140

Salt form: oxalate

Example 17

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

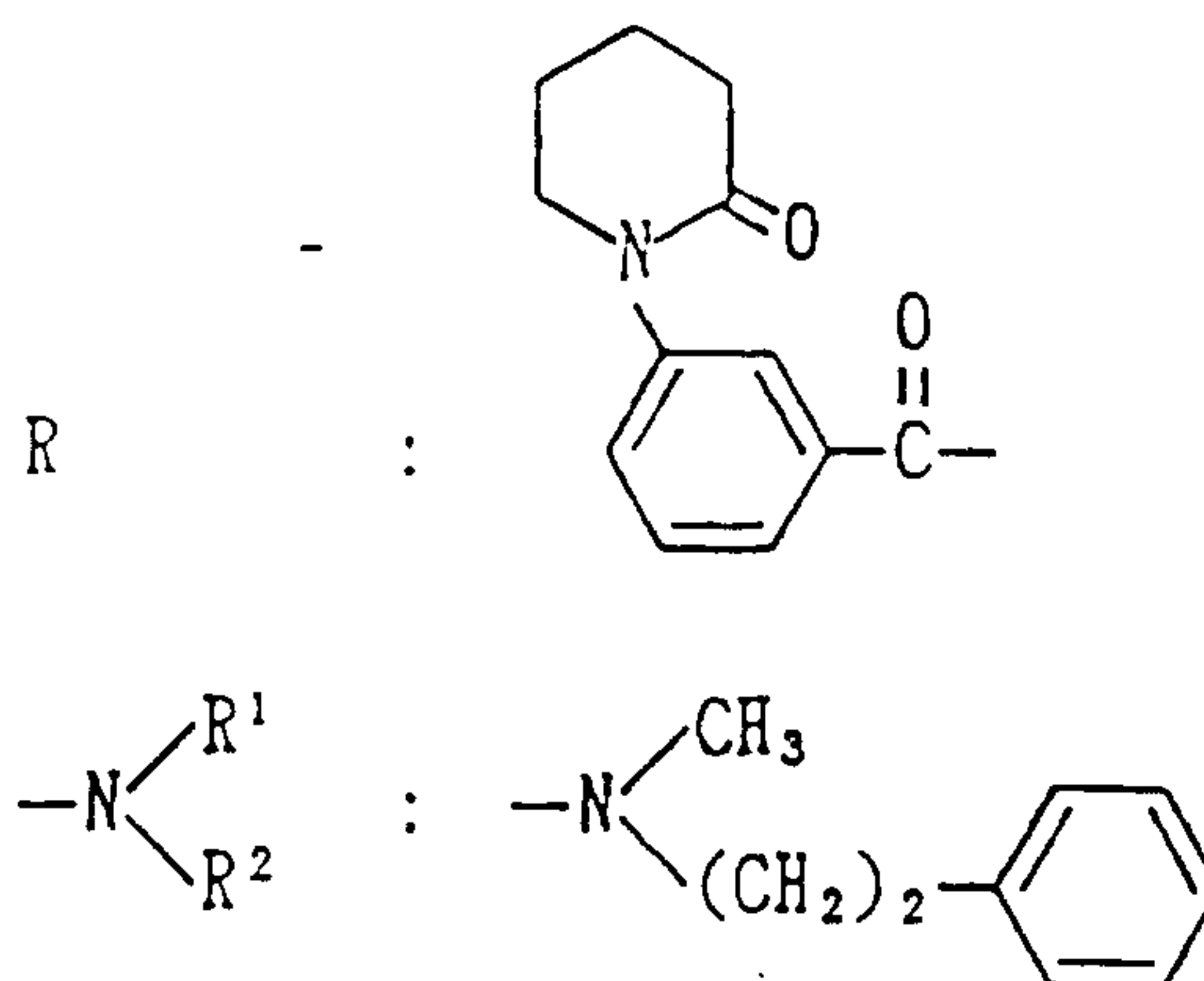
Melting point (°C): 244-246

Salt form: hydrochloride

[Table 10 (continued)]

Example 18

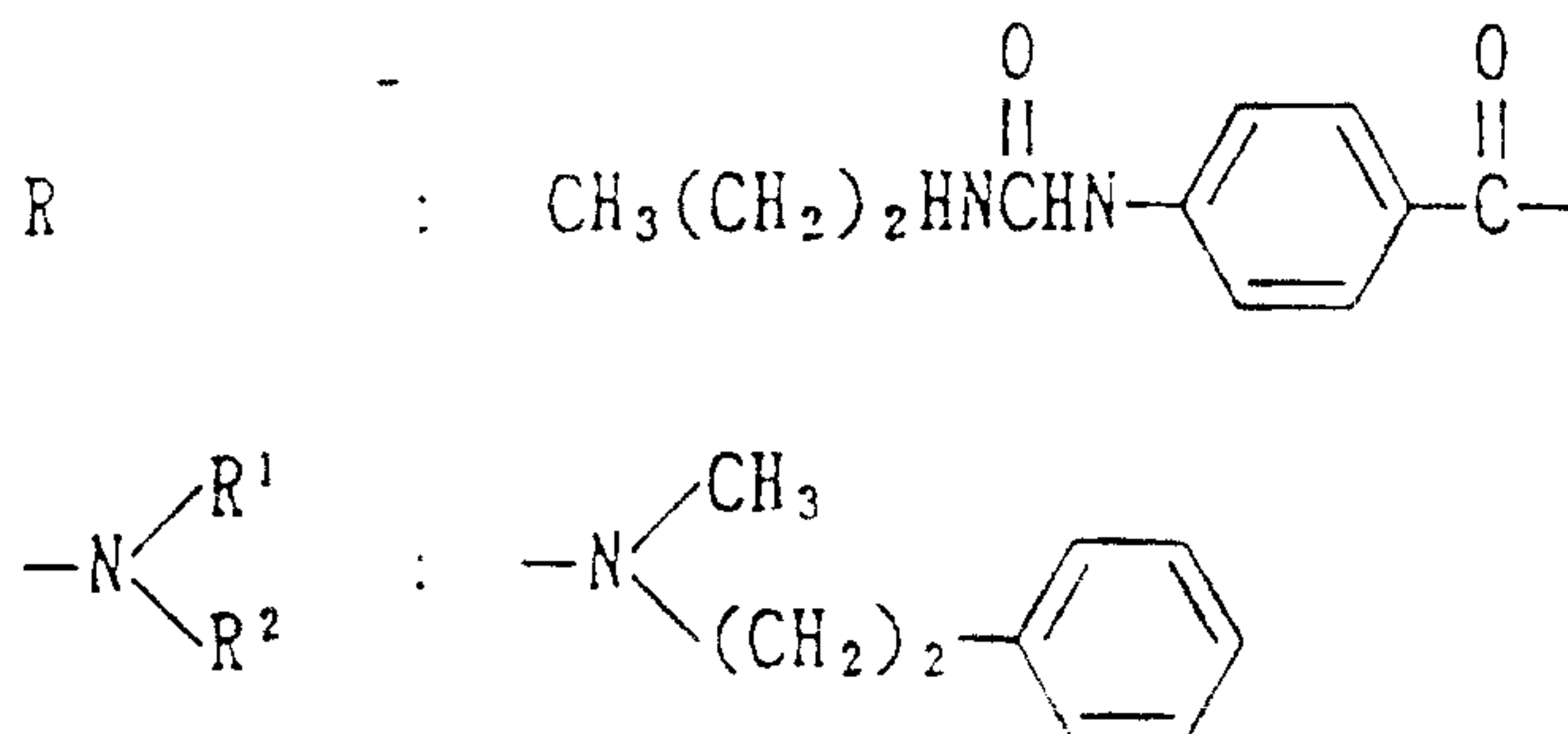
Structural formula:



{Table 10 (continued)}

Example 20

Structural formula:



Crystal form: white powder

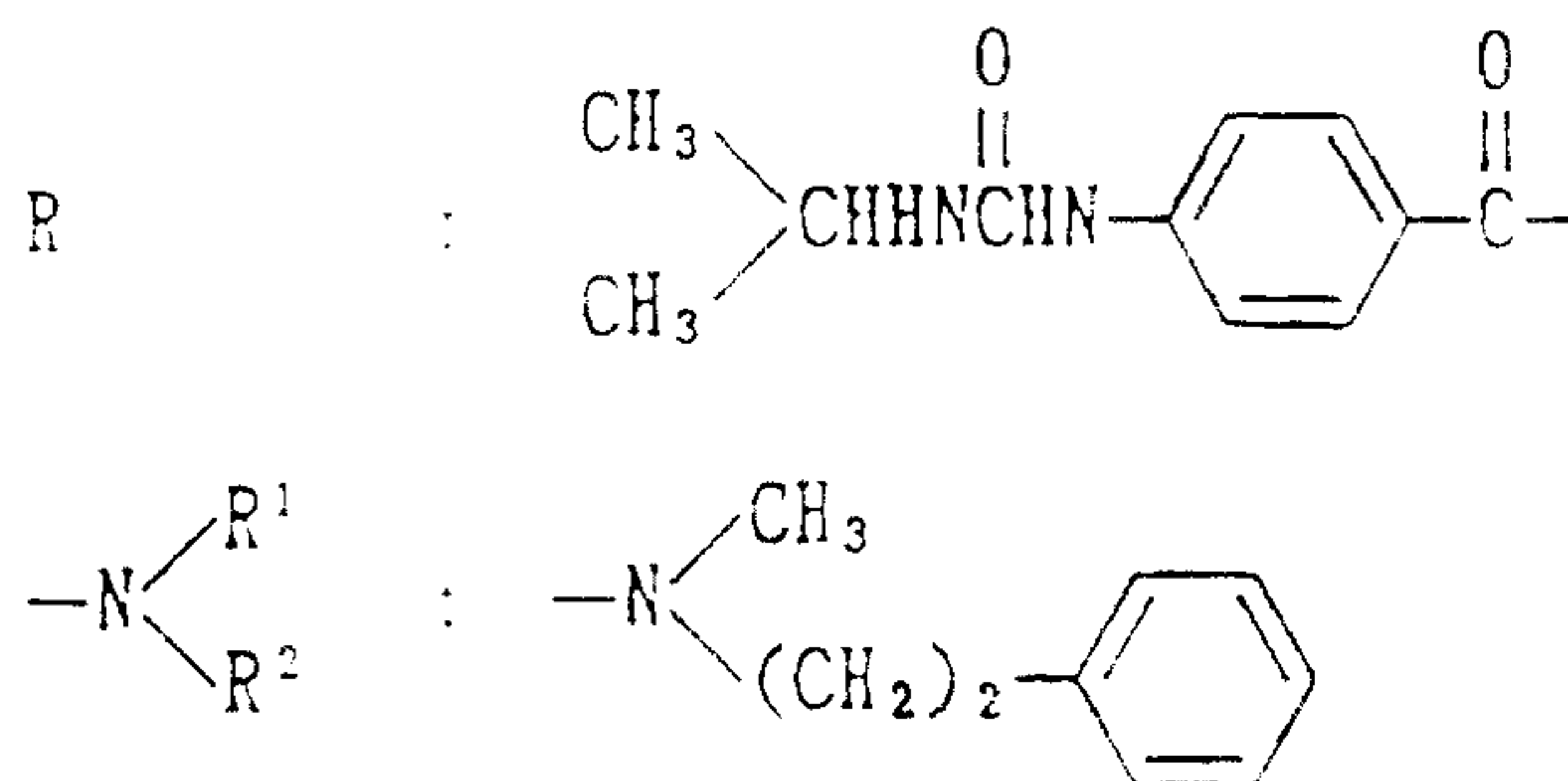
Recrystallization solvent: ethanol

Melting point (°C): 234-237 (decompd.)

Salt form: hydrochloride

Example 21

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

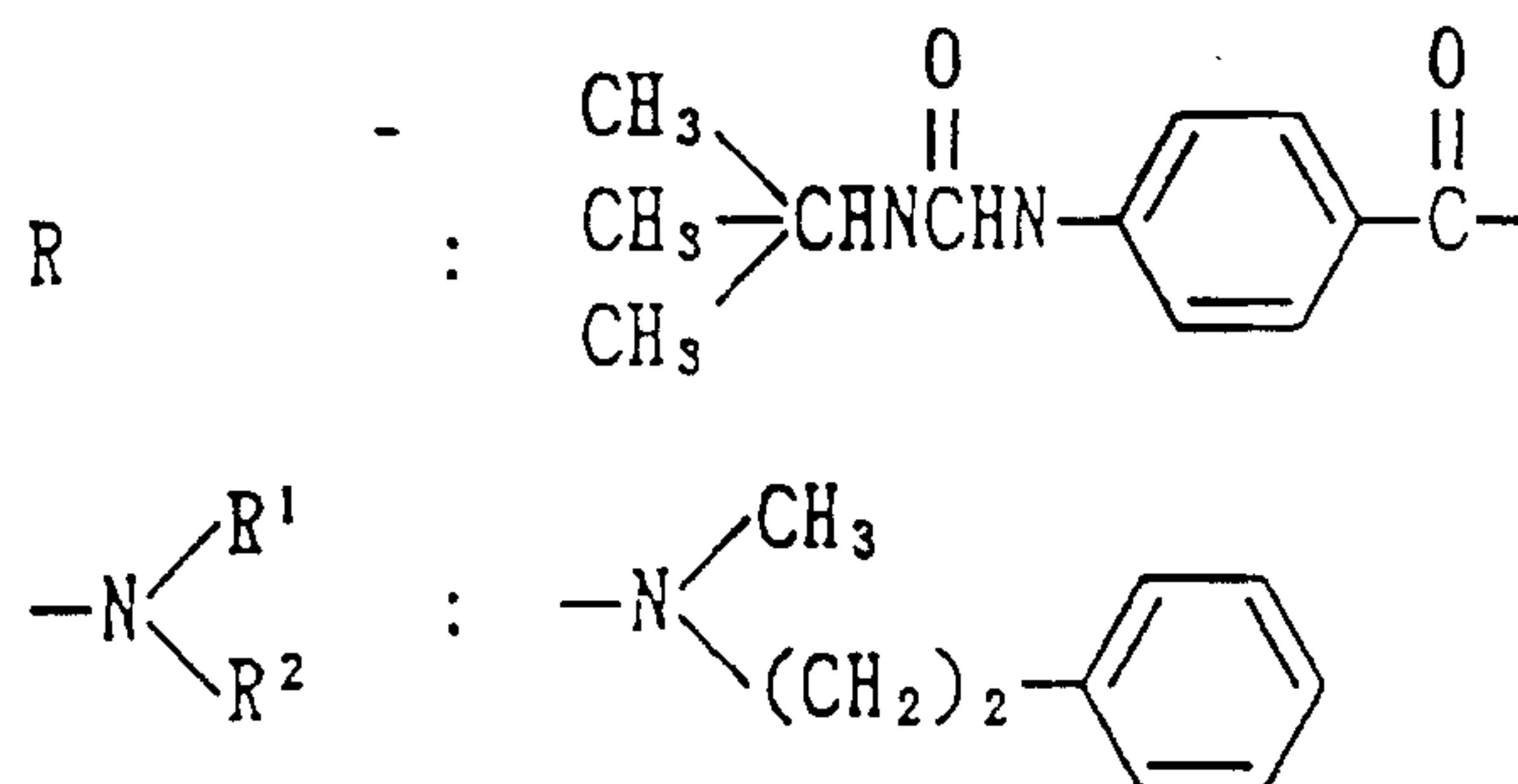
Melting point (°C): 238-240 (decompd.)

Salt form: hydrochloride

{Table 10 (continued)}

Example 22

Structural formula:



Crystal form: white powder

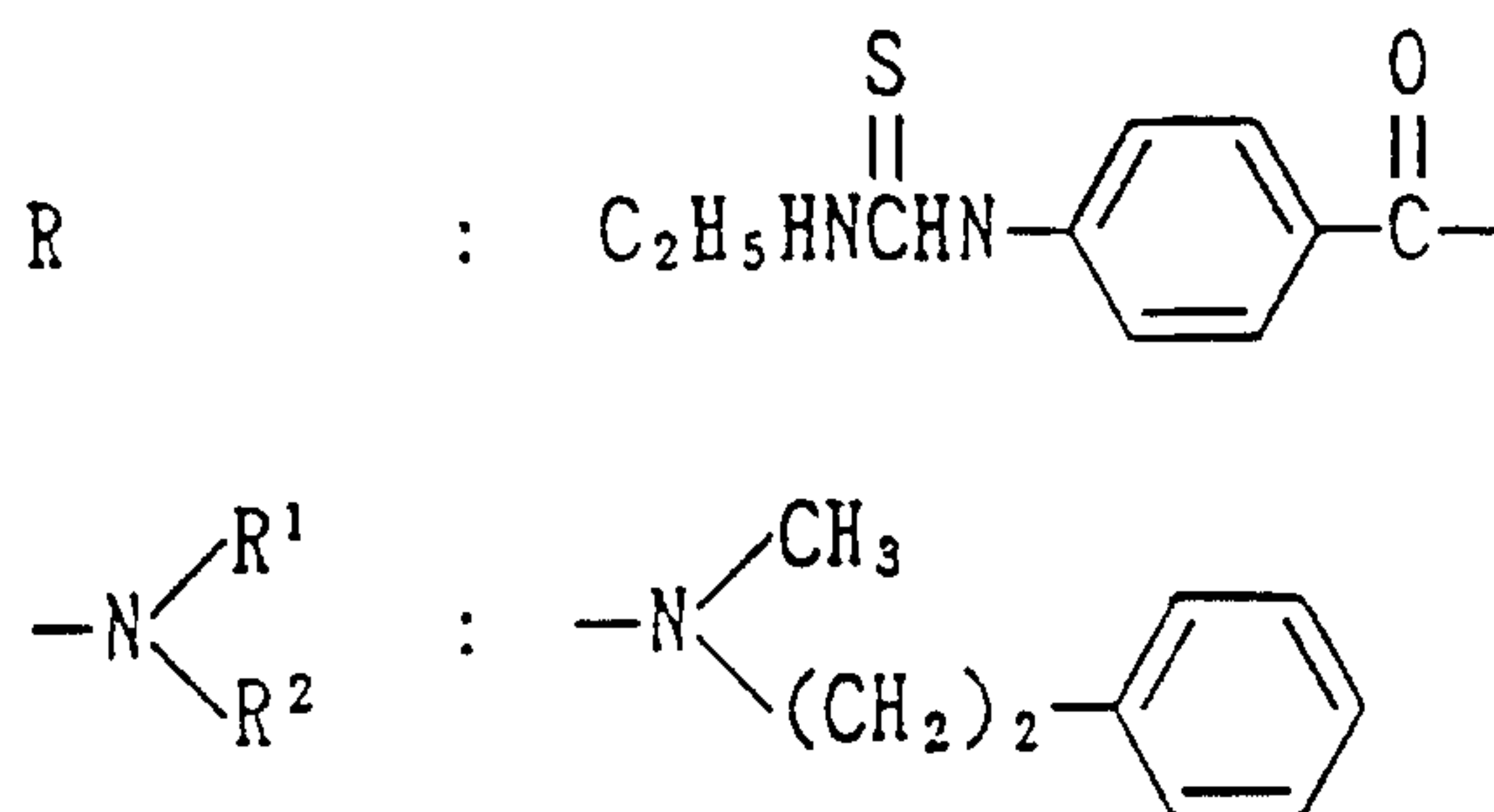
Recrystallization solvent: ethanol

Melting point (°C): 228-230 (decompd.)

Salt form: hydrochloride

Example 23

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-water

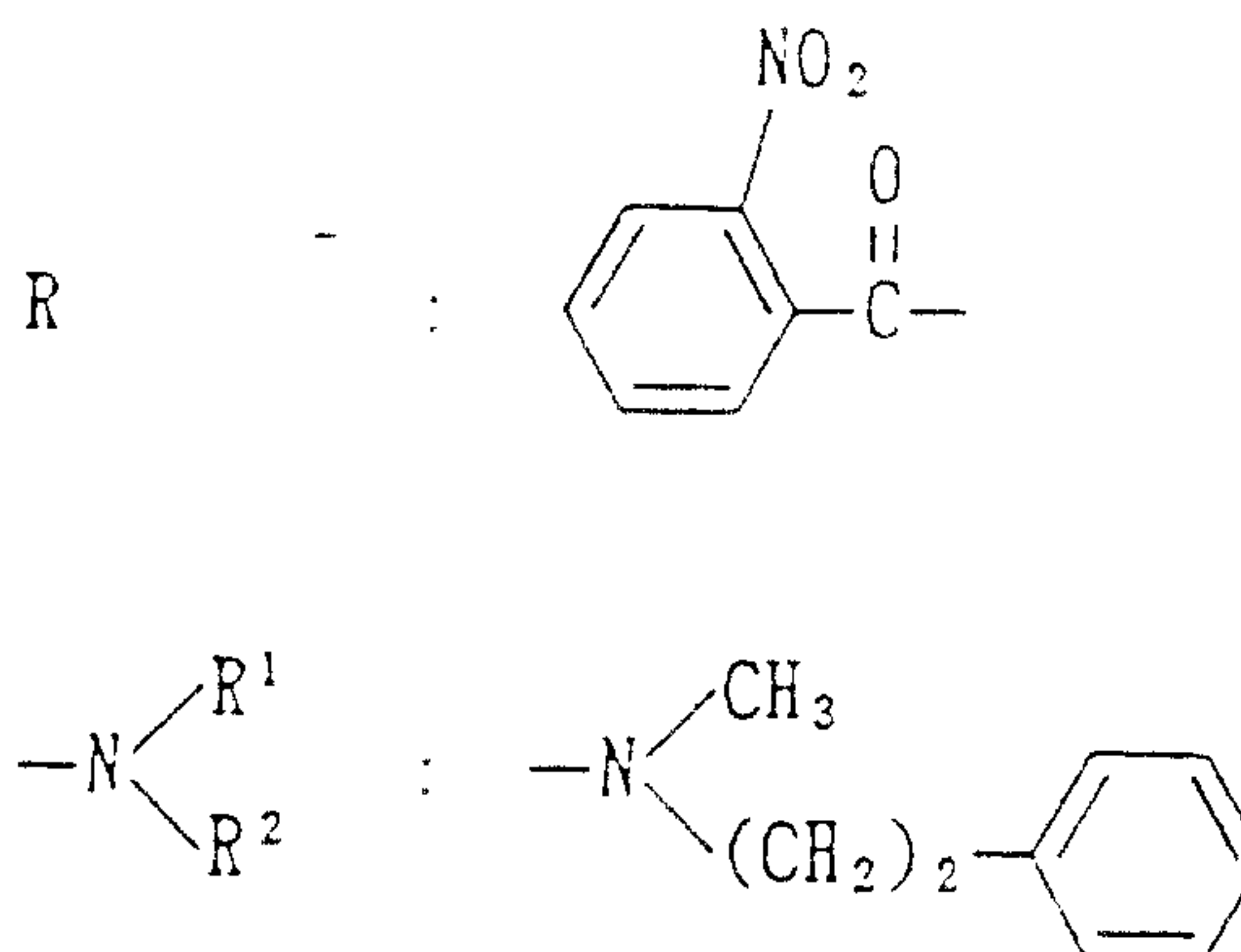
Melting point (°C): 234-236

Salt form: hydrochloride

{Table 10 (continued)}

Example 24

Structural formula:



Crystal form: white powder

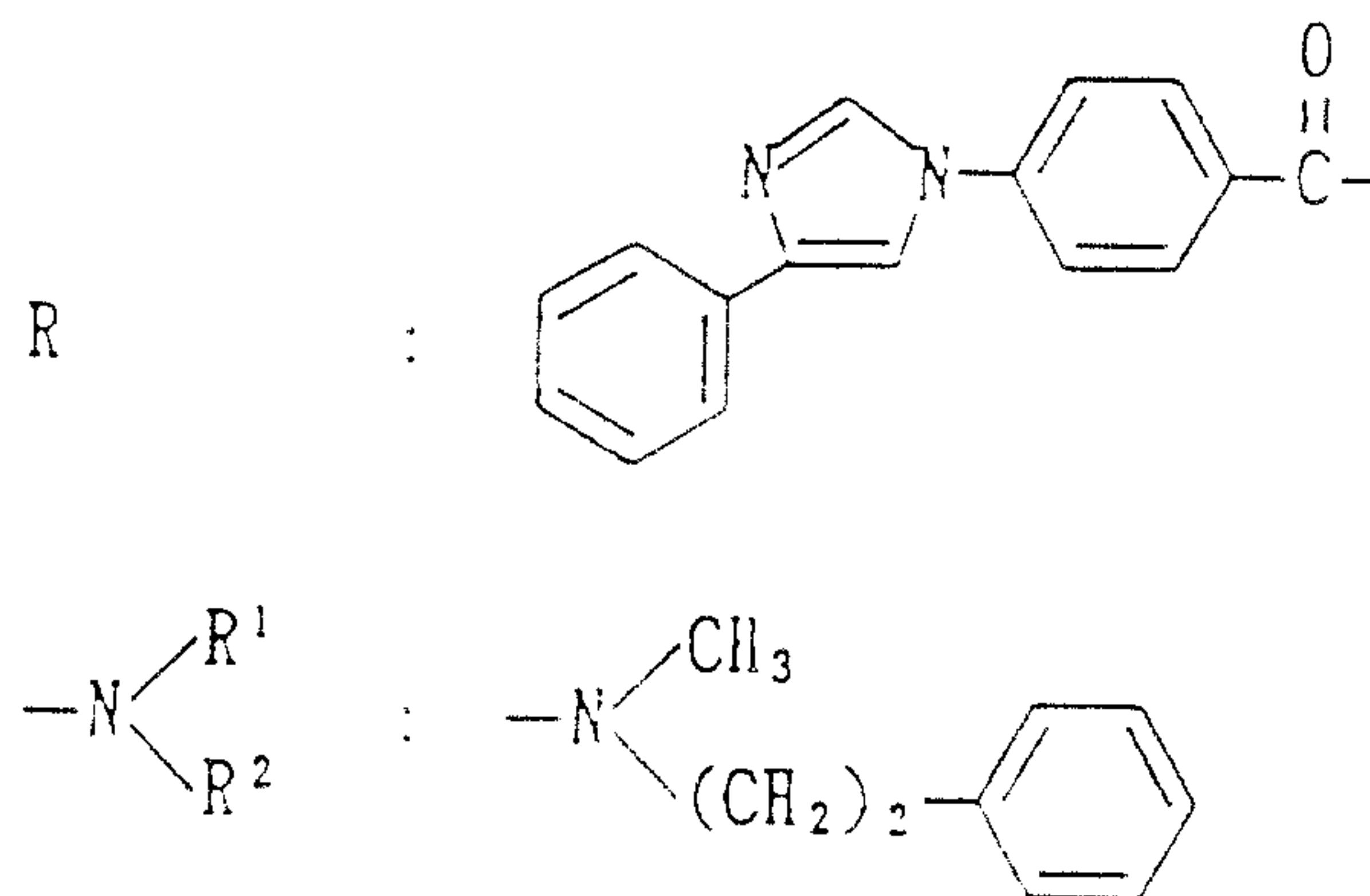
Recrystallization solvent: ethanol-water

Melting point (°C): 220-222 (decompd.)

Salt form: oxalate

Example 25

Structural formula:



Crystal form: colorless scales

Recrystallization solvent: ethyl acetate

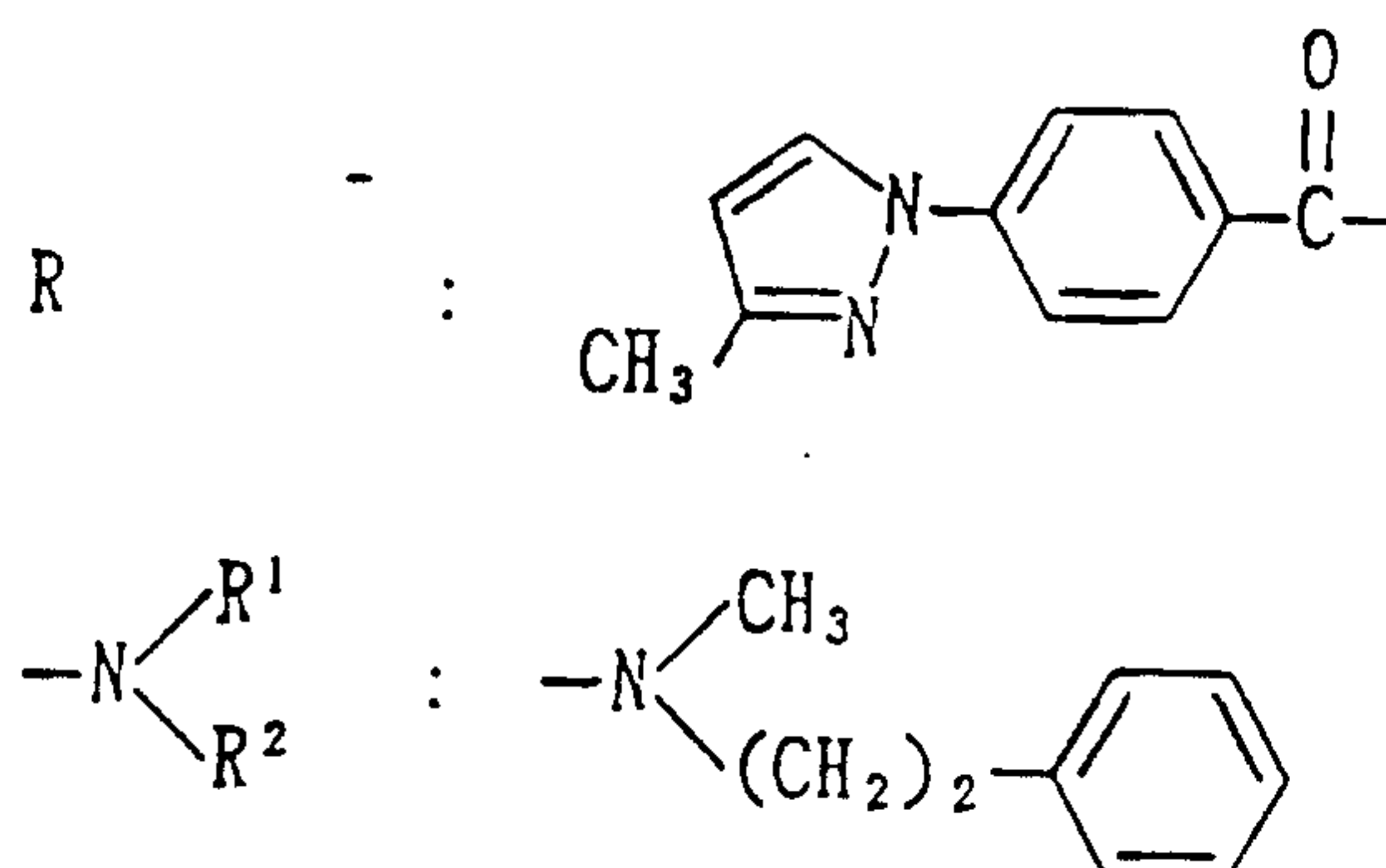
Melting point (°C): 132-134

Salt form: free

{Table 10 (continued)}

Example 26

Structural formula:



Crystal form: colorless prisms

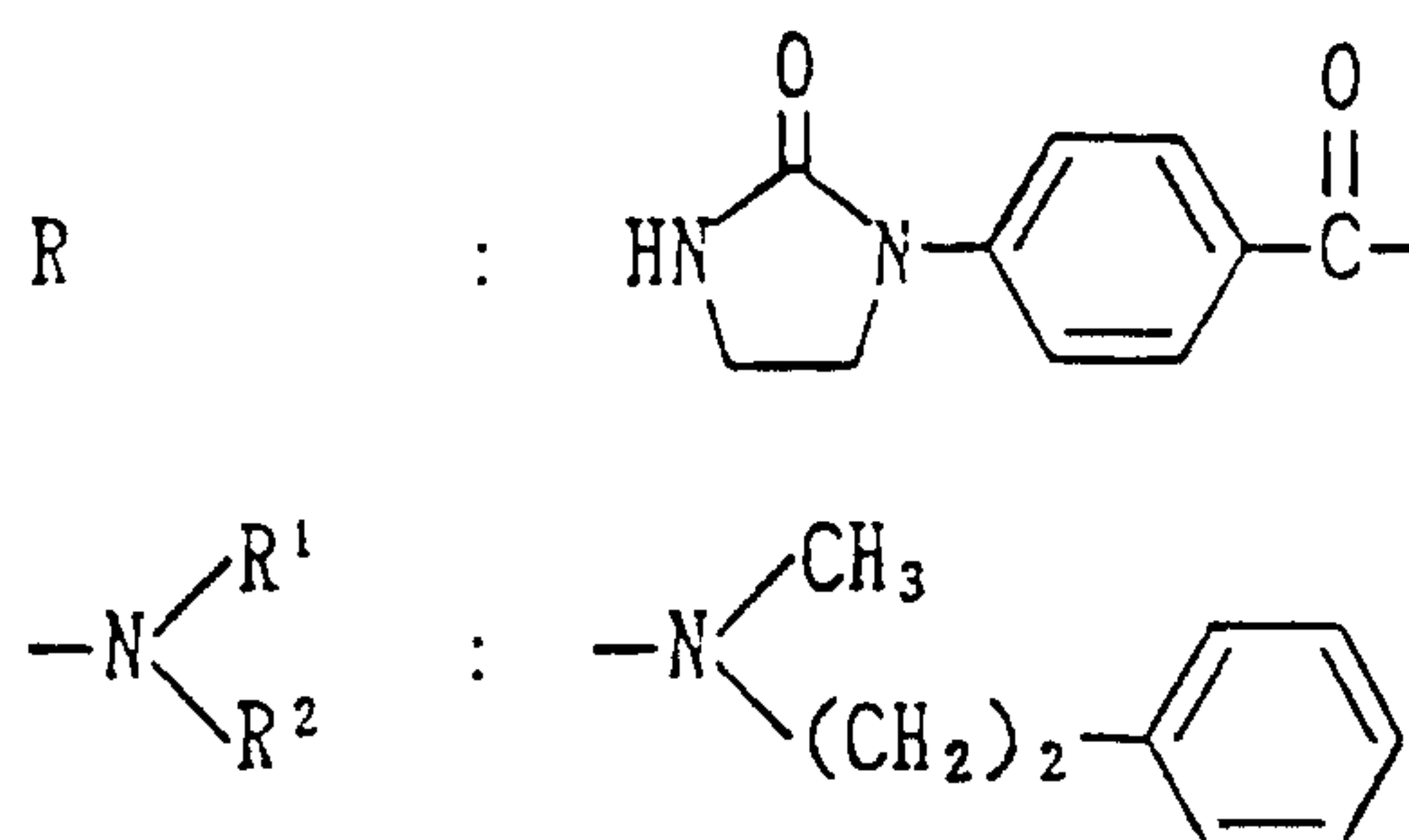
Recrystallization solvent: ethanol

Melting point (°C): 236-238

Salt form: hydrochloride

Example 27

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate

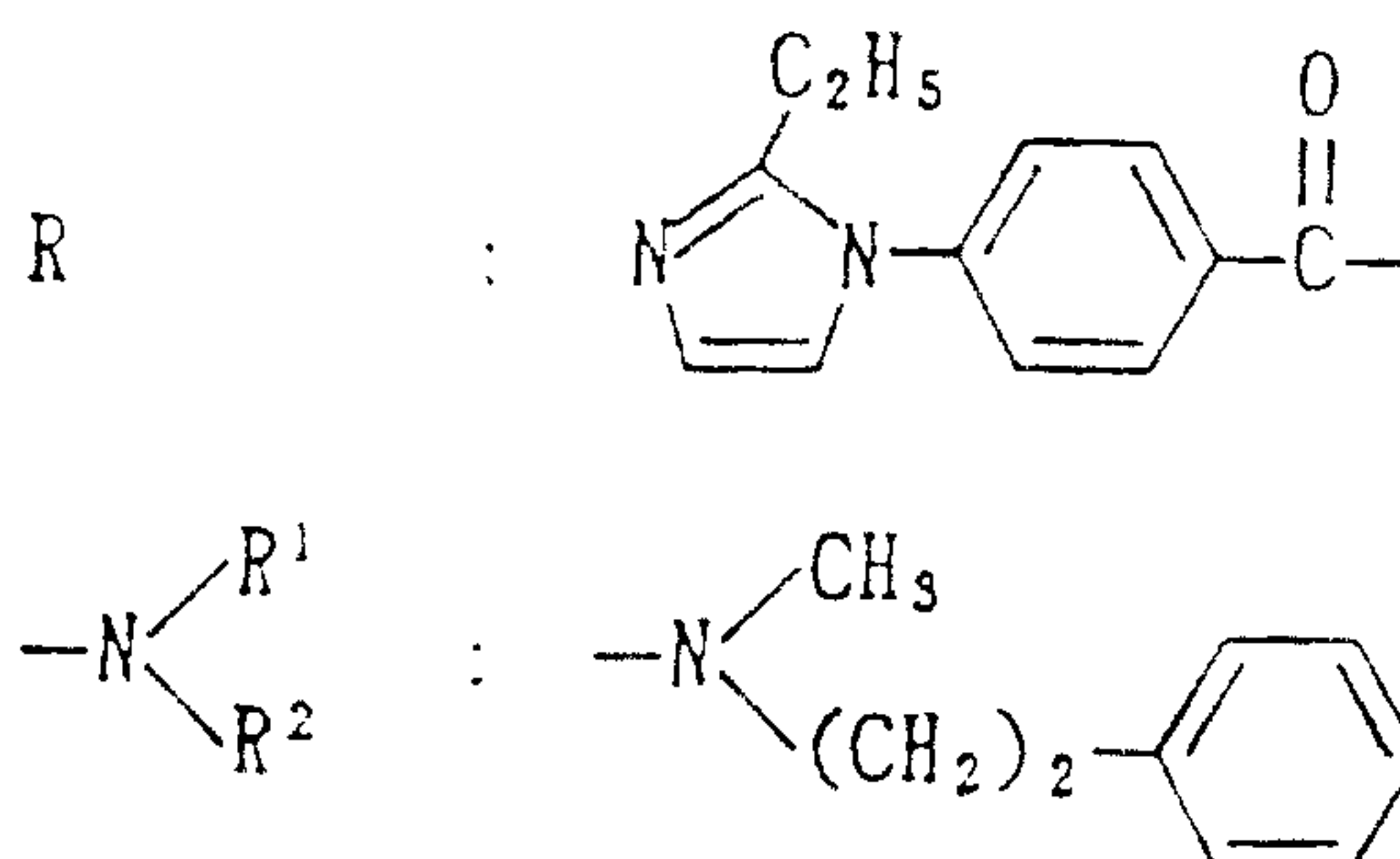
Melting point (°C): 118-120

Salt form: free

[Table 10 (continued)]

Example 28

Structural formula:



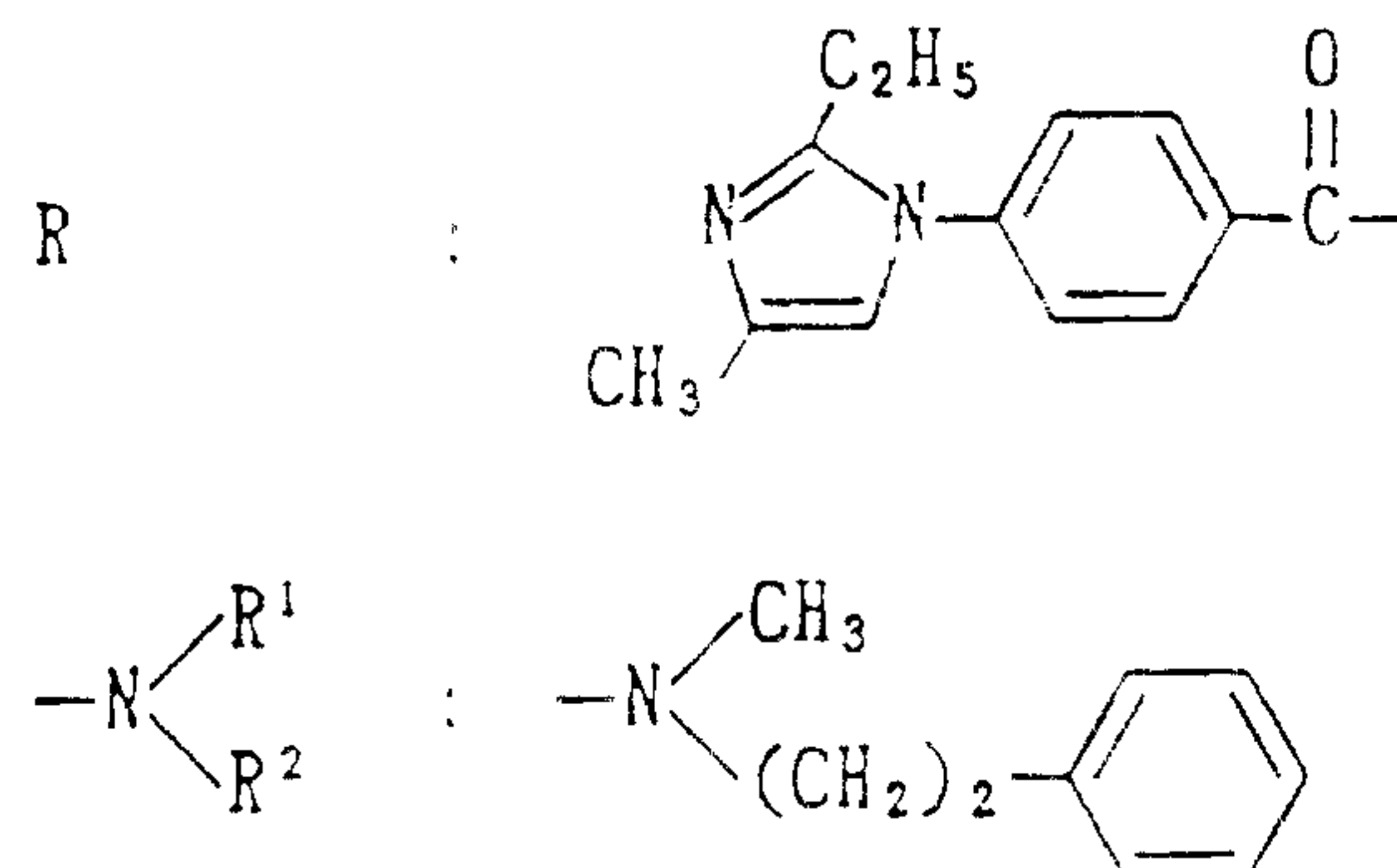
Crystal form: white amorphous

Salt form: trihydrochloride

NMR value: 52)

Example 29

Structural formula:



Crystal form: white amorphous

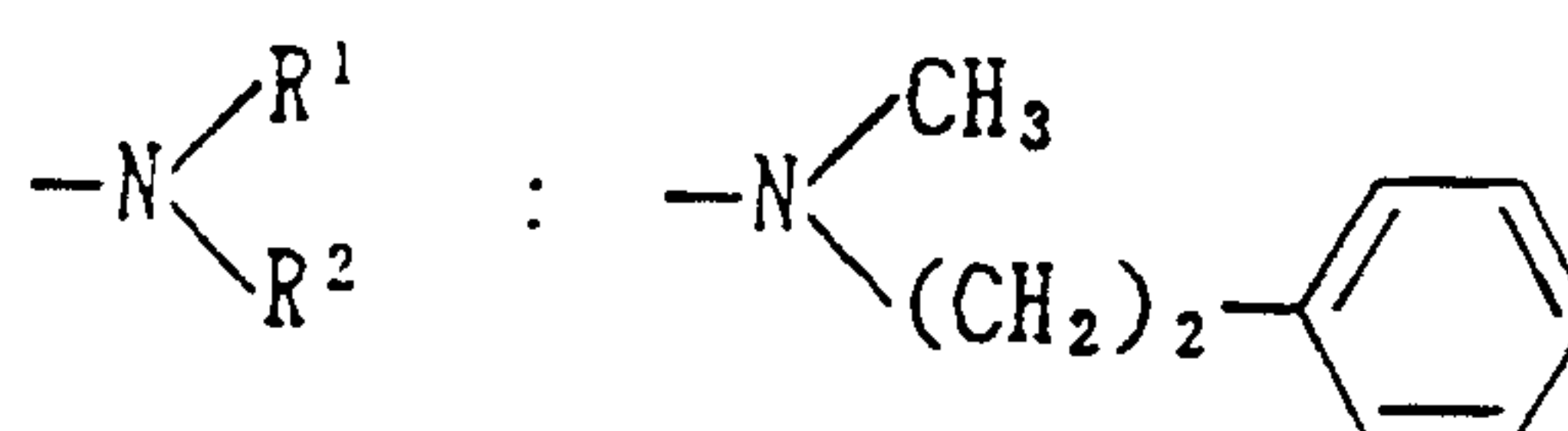
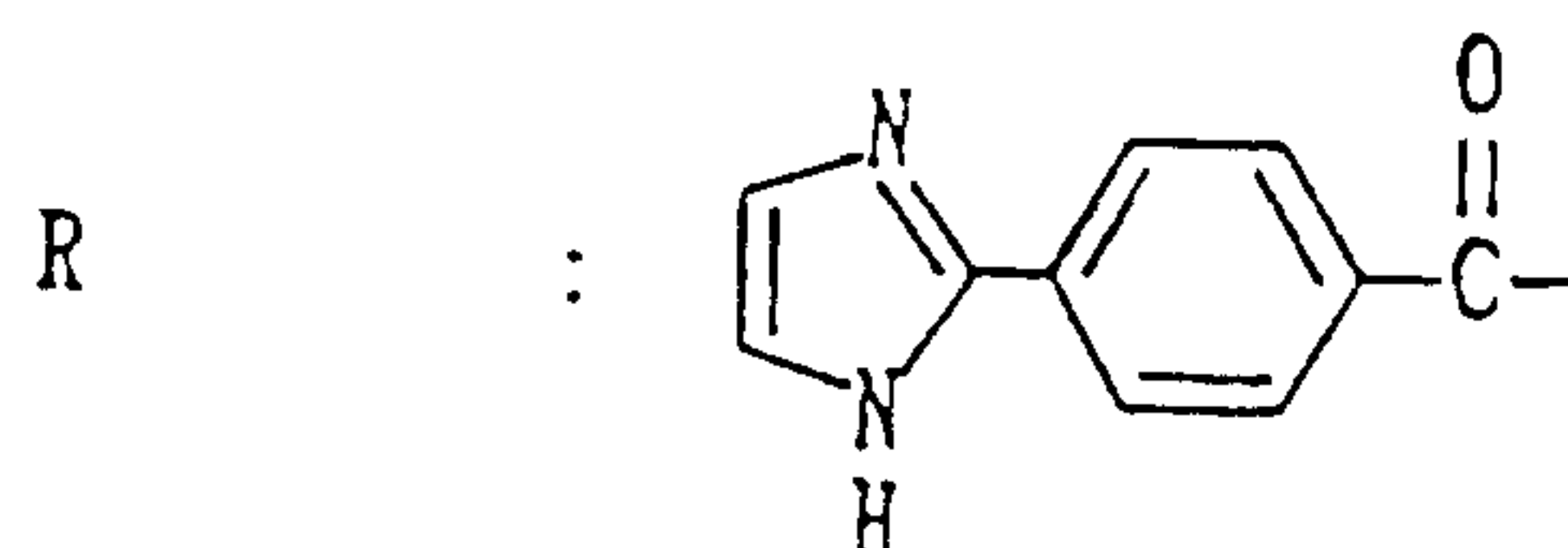
Salt form: trihydrochloride

NMR value: 53)

[Table 10 (continued)]

Example 30

Structural formula:



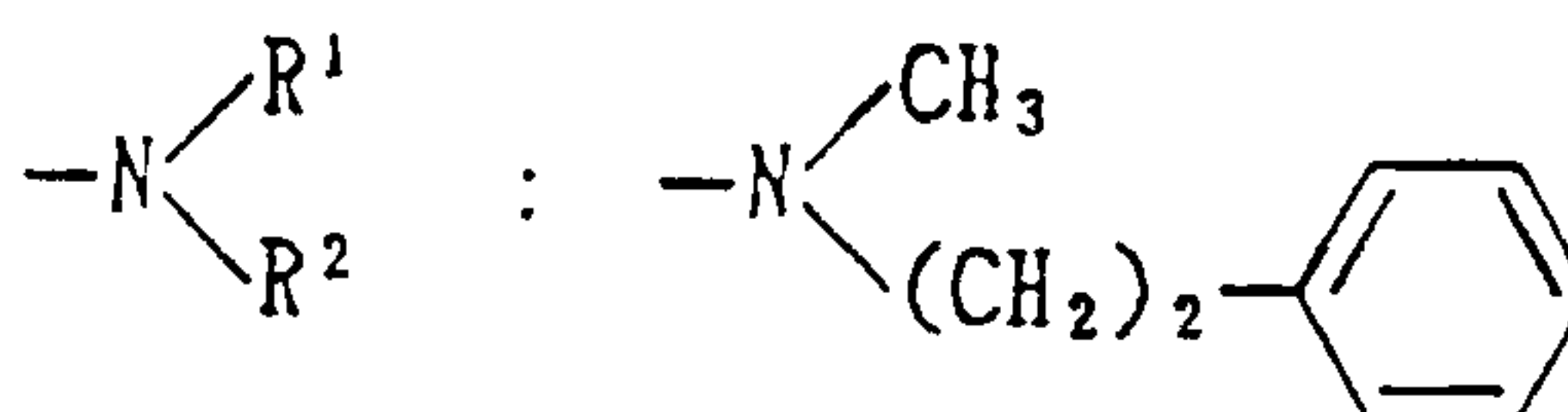
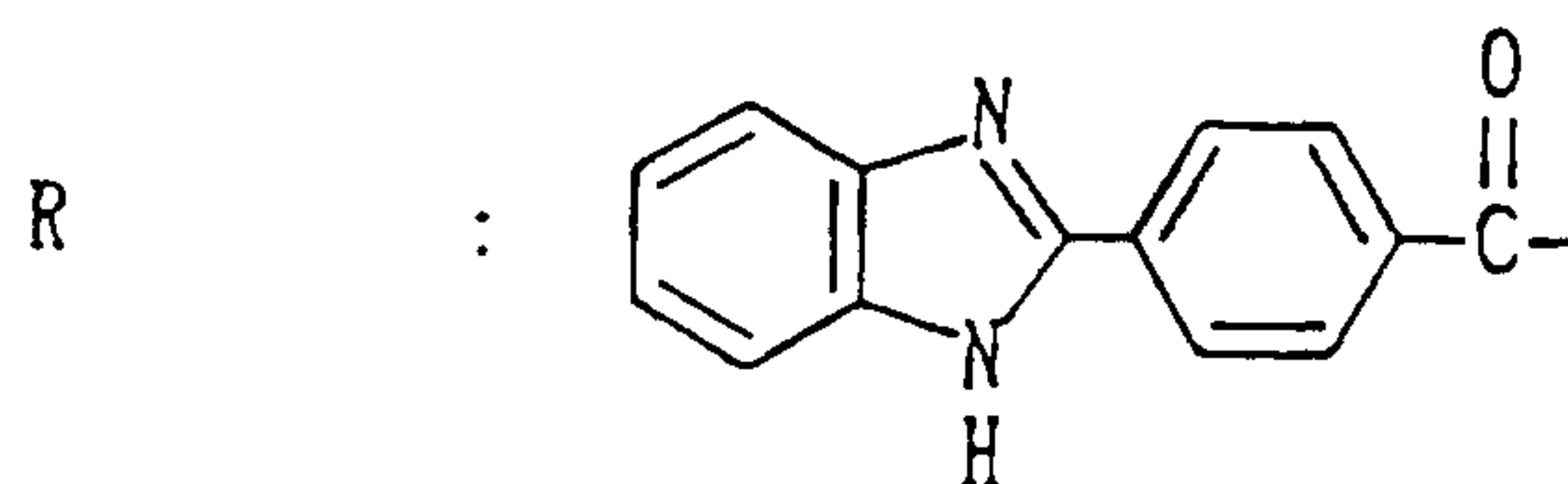
Crystal form: white amorphous

Salt form: trihydrochloride

NMR value: 54)

Example 31

Structural formula:



Crystal form: colorless scales

Recrystallization solvent: ethanol

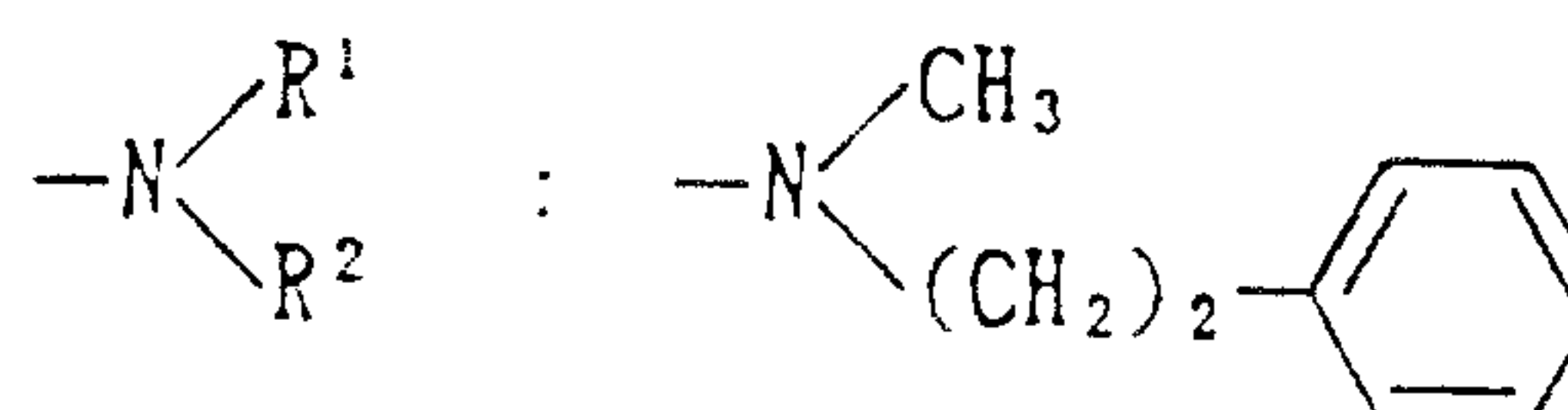
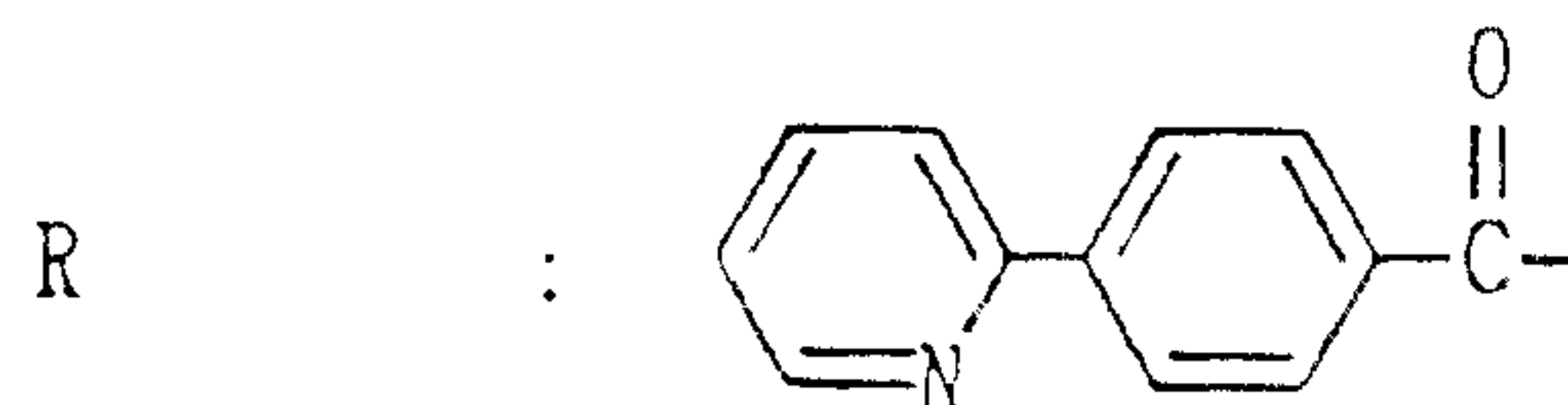
Melting point (°C): 120-123

Salt form: free

{Table 10 (continued)}

Example 32

Structural formula:



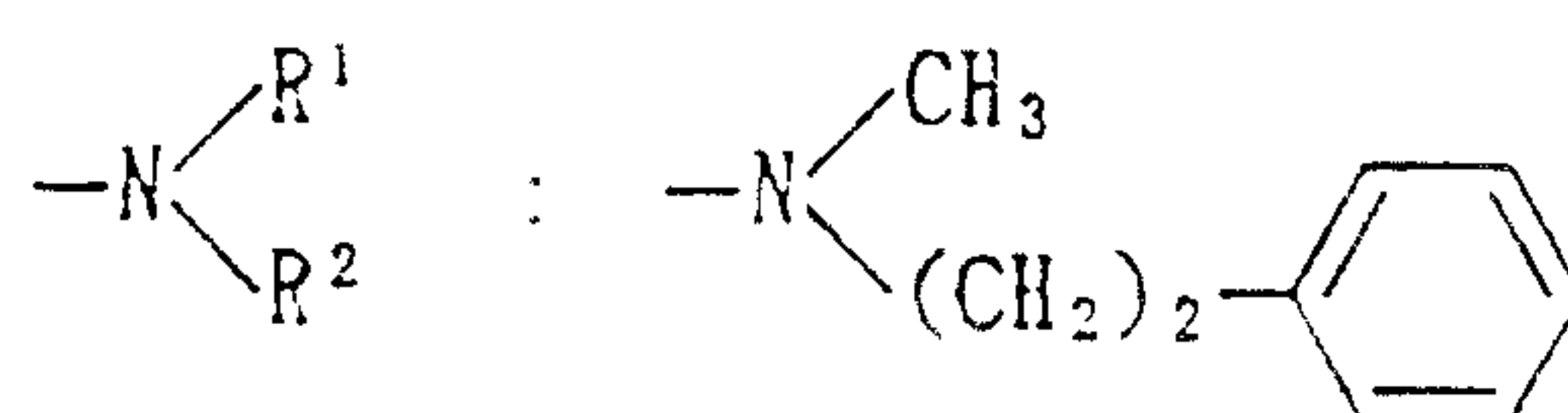
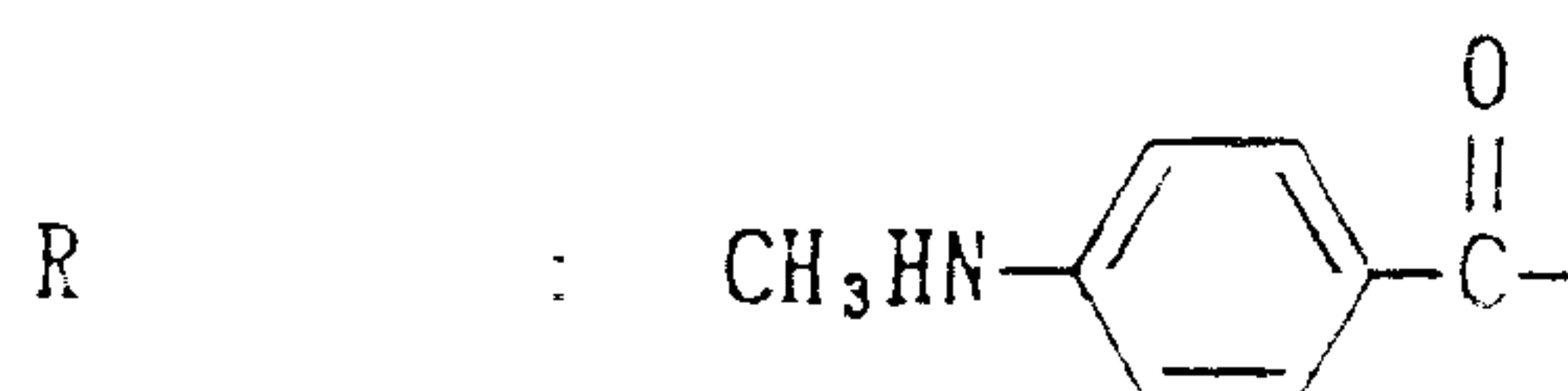
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 55)

Example 33

Structural formula:



Crystal form: white amorphous

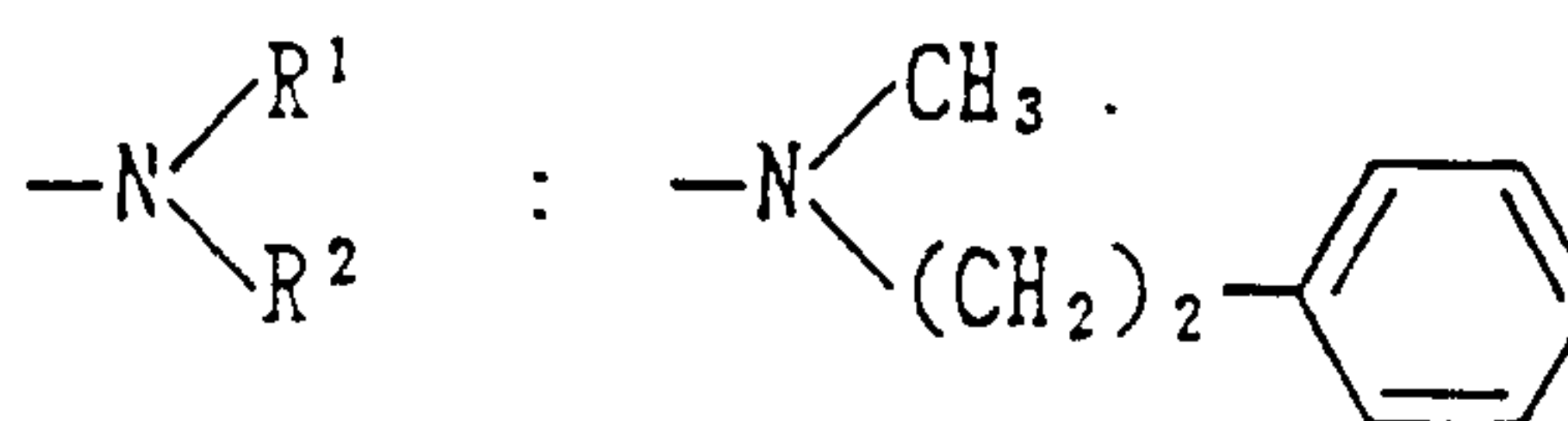
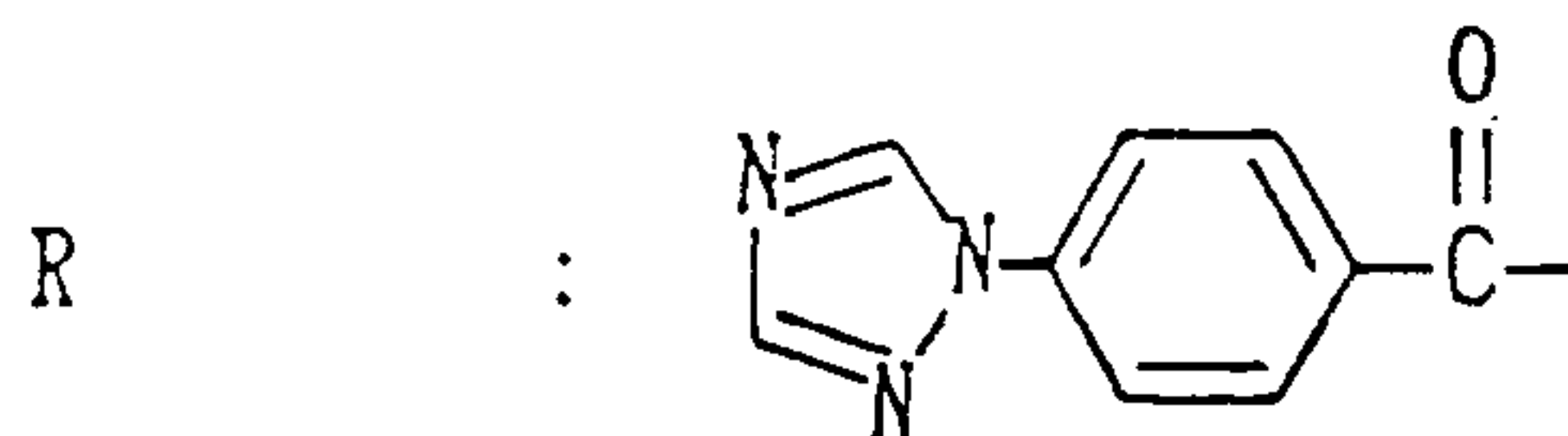
Salt form: dihydrochloride

NMR value: 56)

{Table 10 (continued)}

Example 34

Structural formula:



Crystal form: colorless prisms

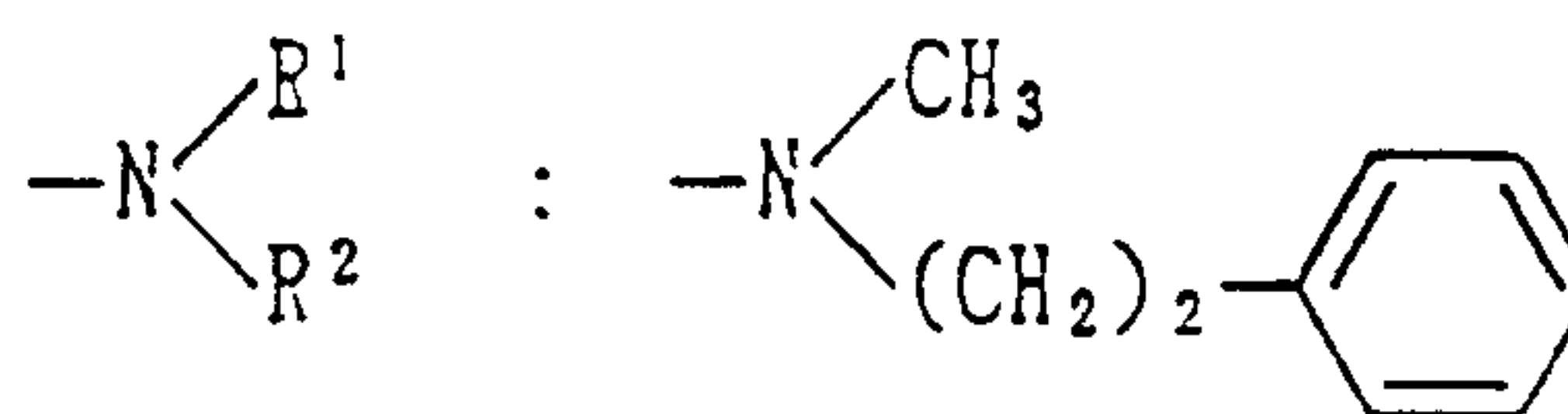
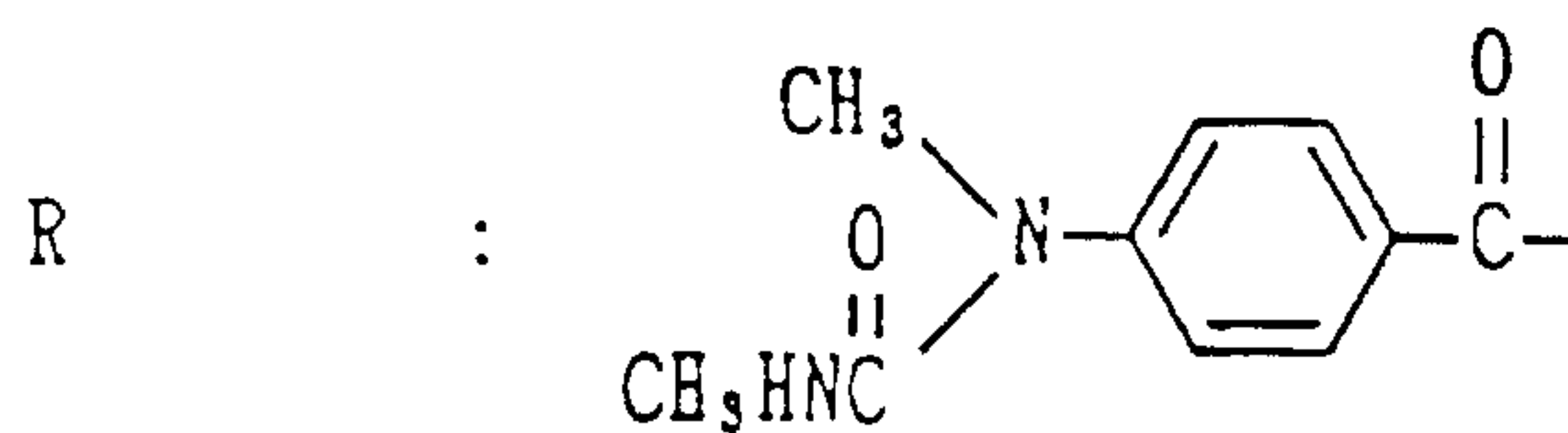
Recrystallization solvent: ethyl acetate

Melting point (°C): 134-136

Salt form: free

Example 35

Structural formula:



Crystal form: white powder

Recrystallization solvent: isopropanol

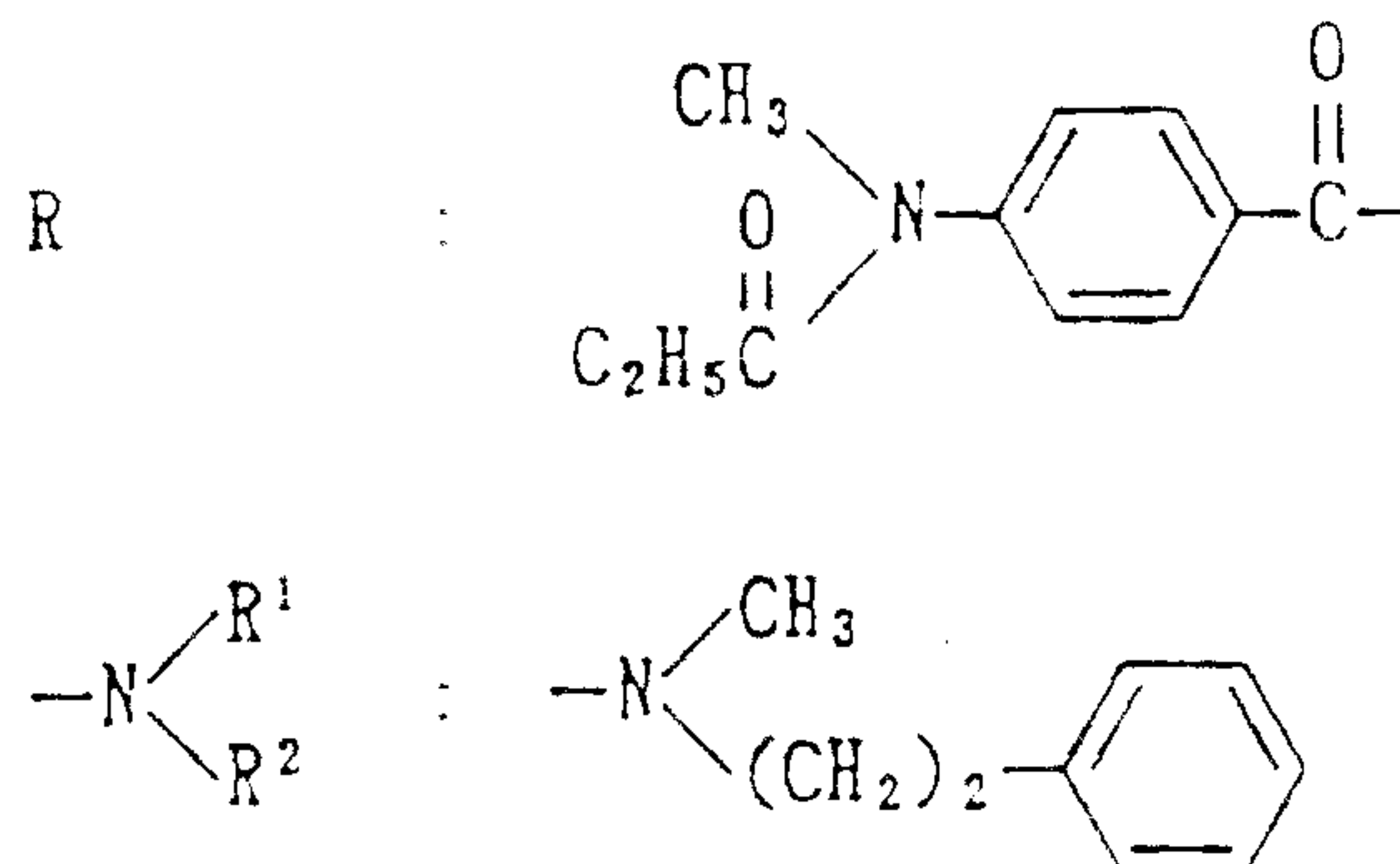
Melting point (°C): 145-148

Salt form: hydrochloride

{Table 10 (continued)}

Example 36

Structural formula:



Crystal form: white powder

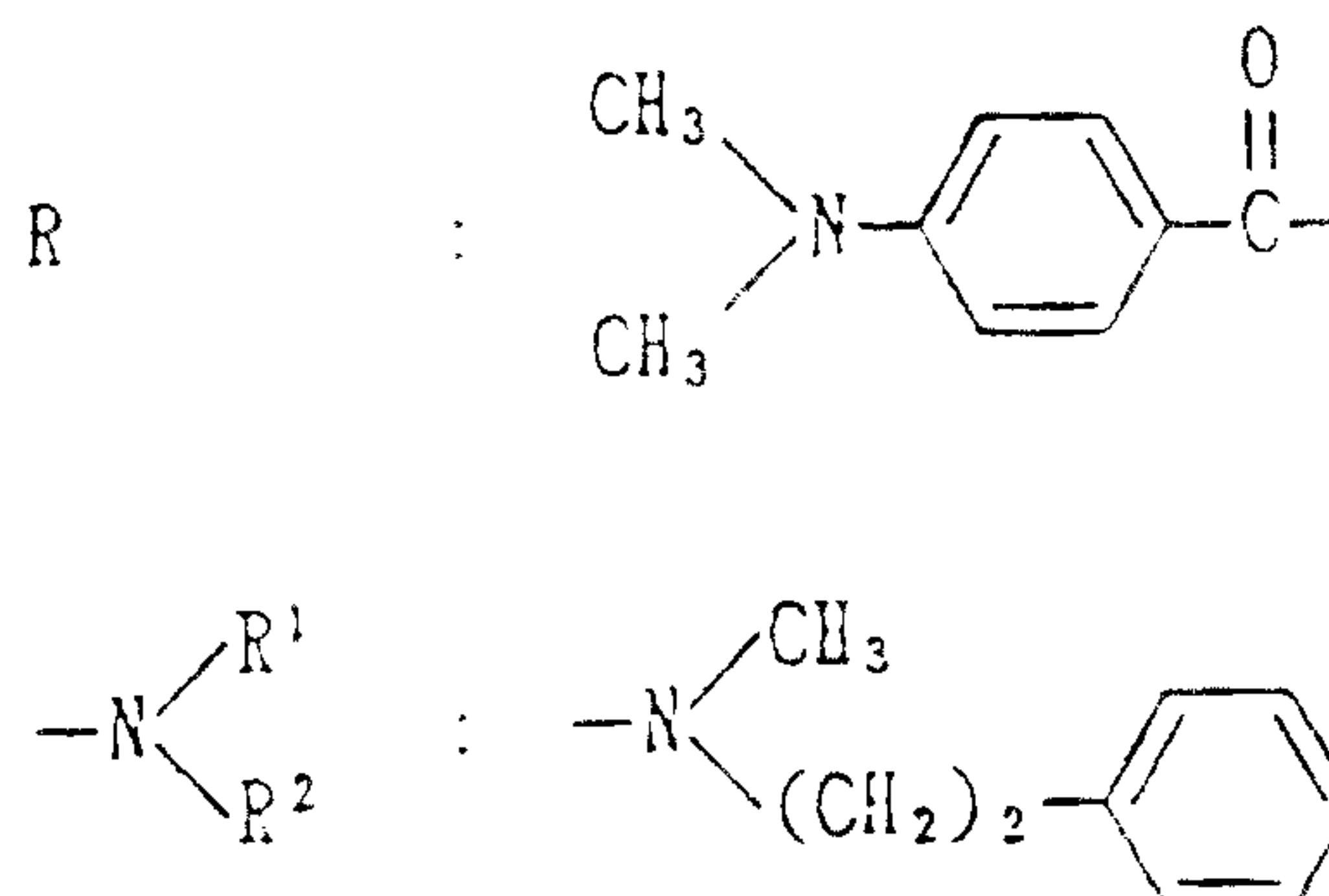
Recrystallization solvent: ethanol

Melting point (°C): 225-227

Salt form: hydrochloride

Example 37

Structural formula:



Crystal form: white powder

Recrystallization solvent: isopropanol

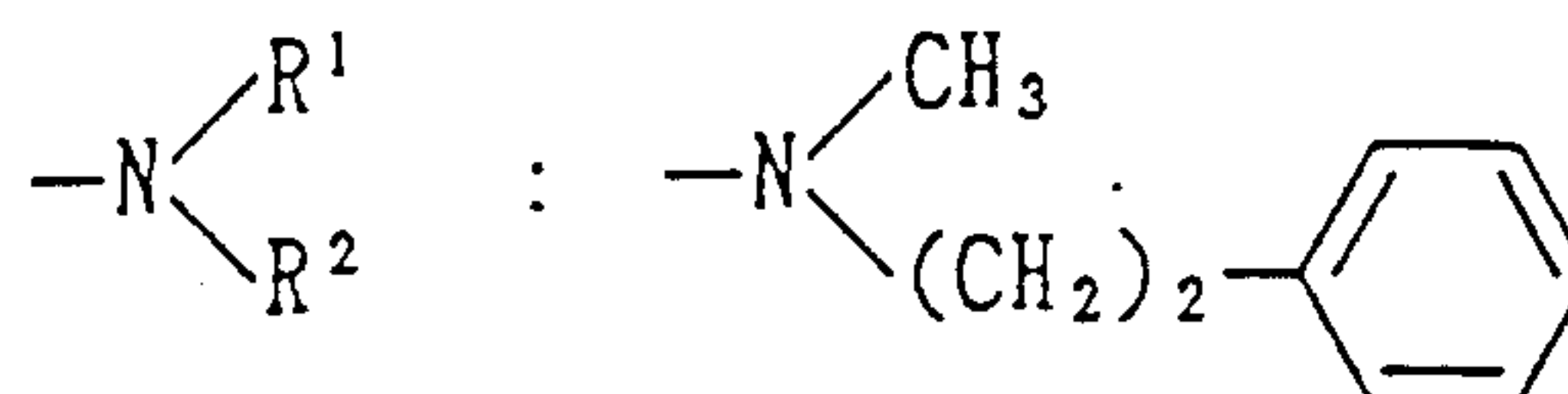
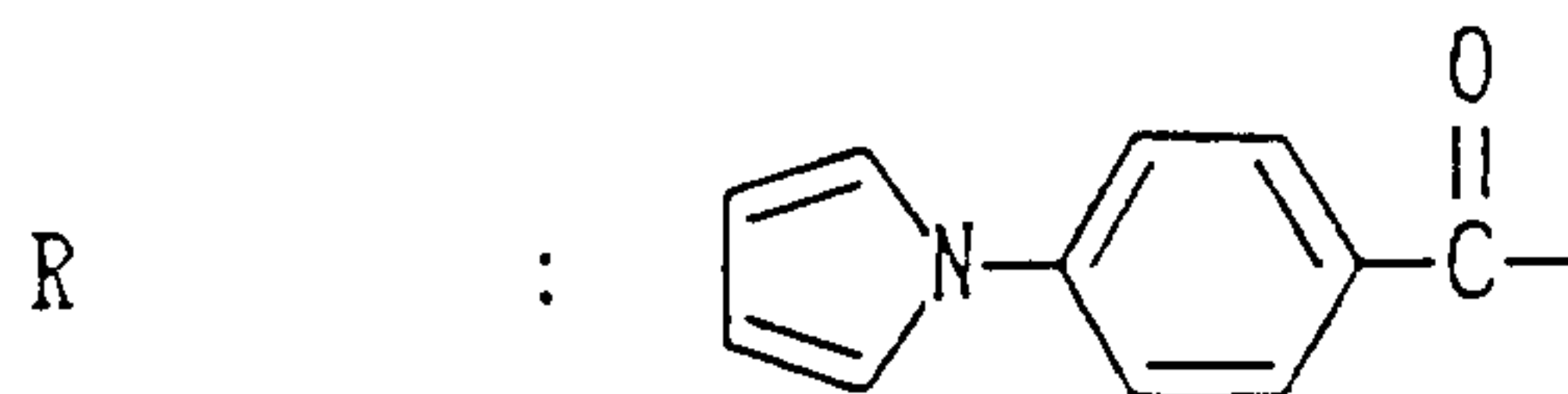
Melting point (°C): 220-222

Salt form: hydrochloride

[Table 10 (continued)]

Example 38

Structural formula:



Crystal form: colorless scales

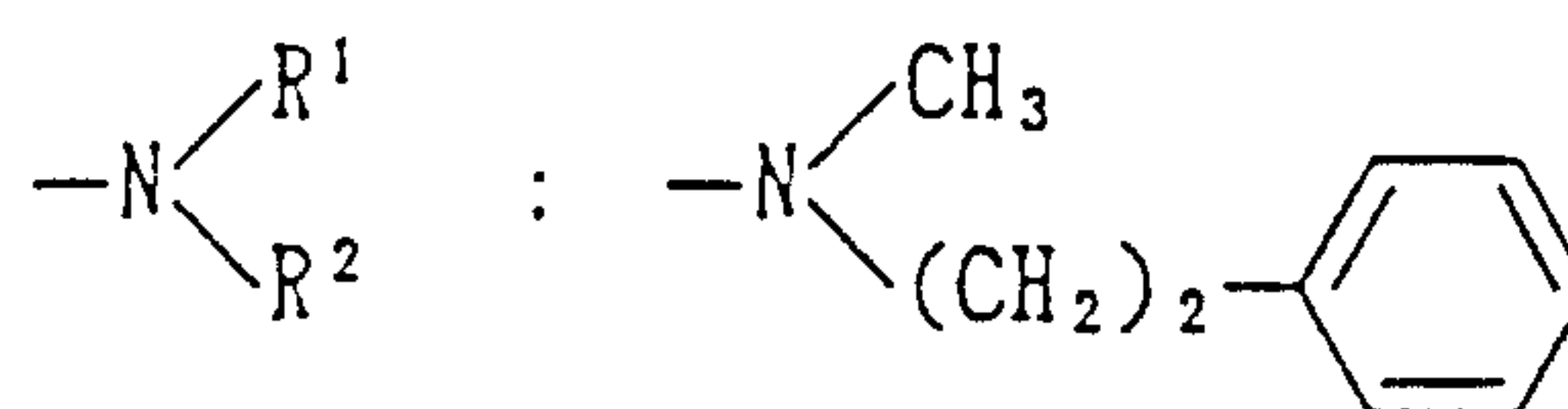
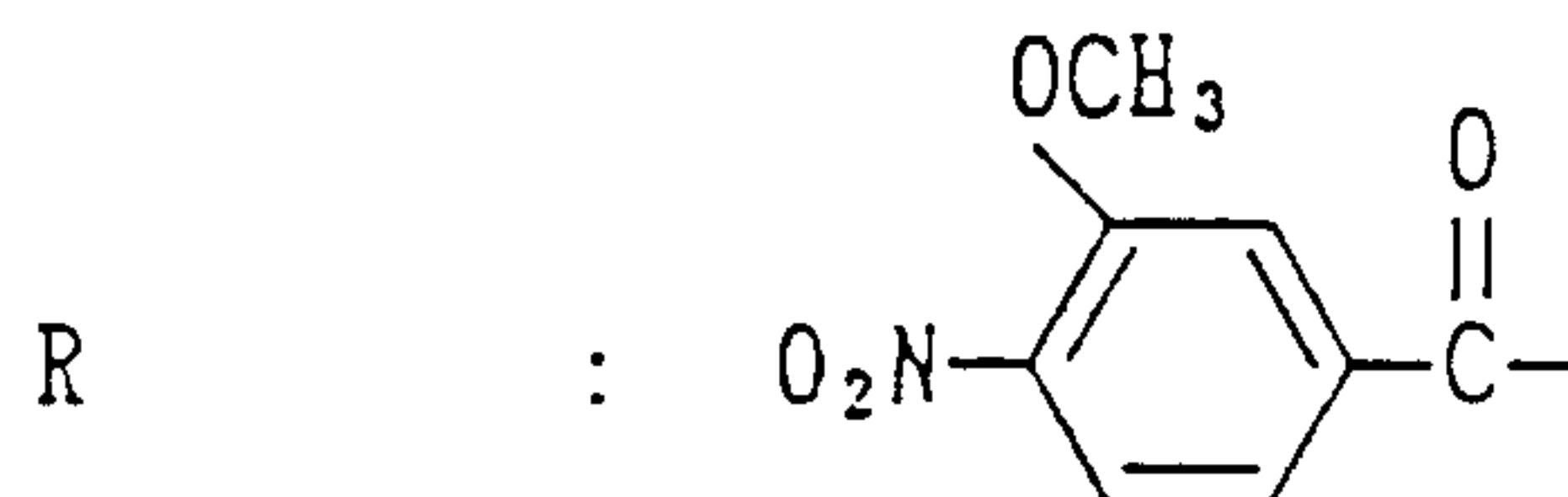
Recrystallization solvent: ethanol-water

Melting point (°C): 246-248 (decompd.)

Salt form: hydrochloride

Example 39

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

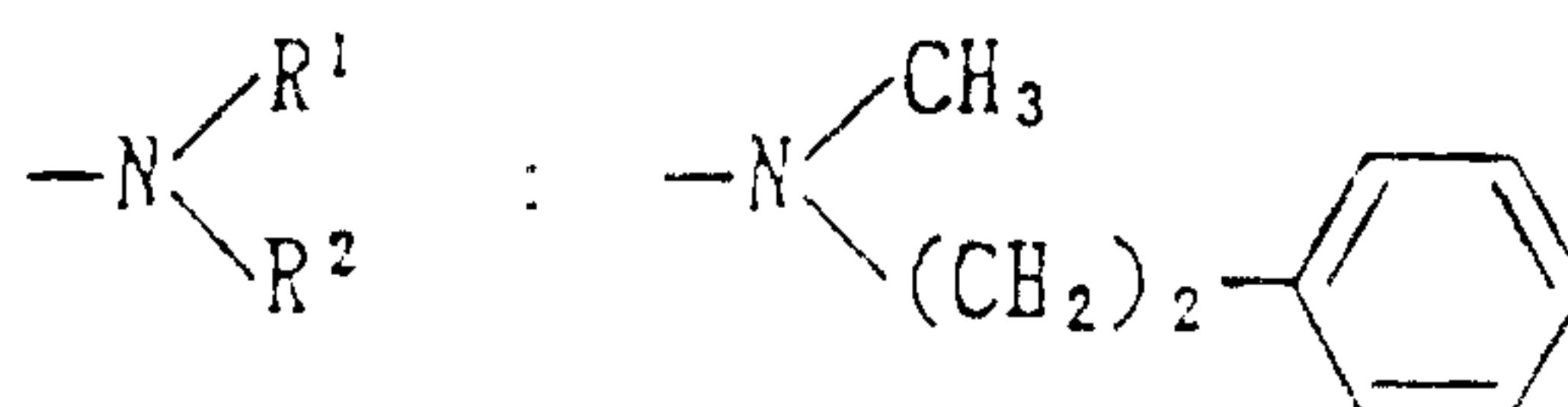
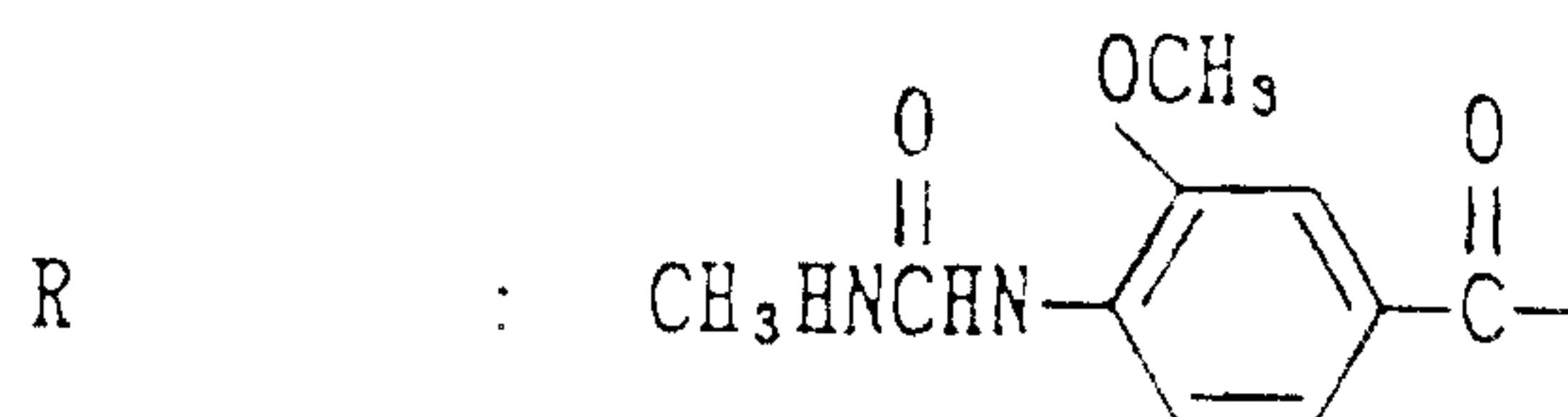
Melting point (°C): 130-132 (decompd.)

Salt form: oxalate

{Table 10 (continued)}

Example 40

Structural formula:



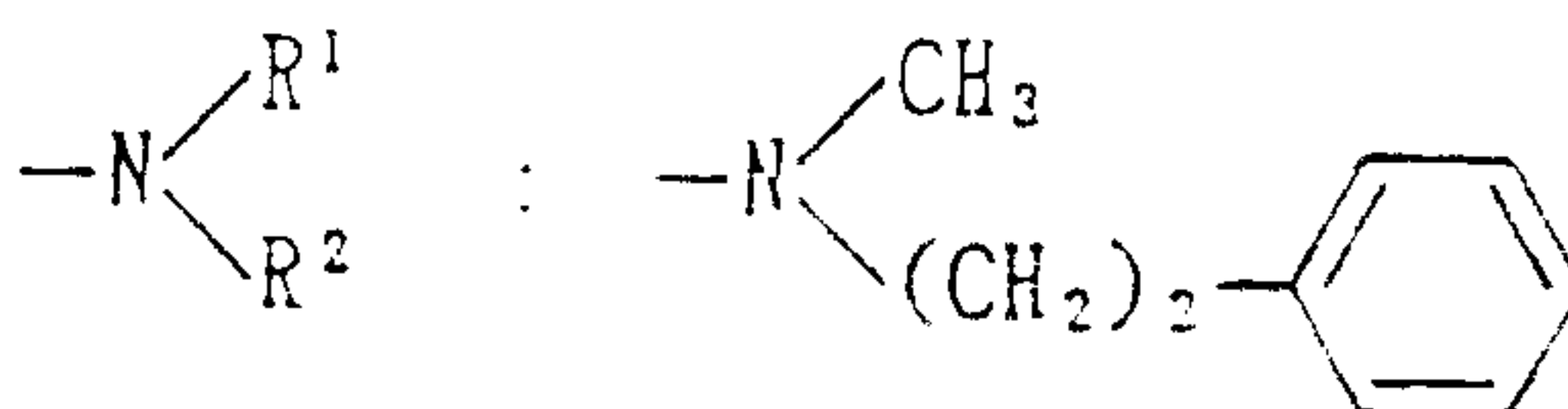
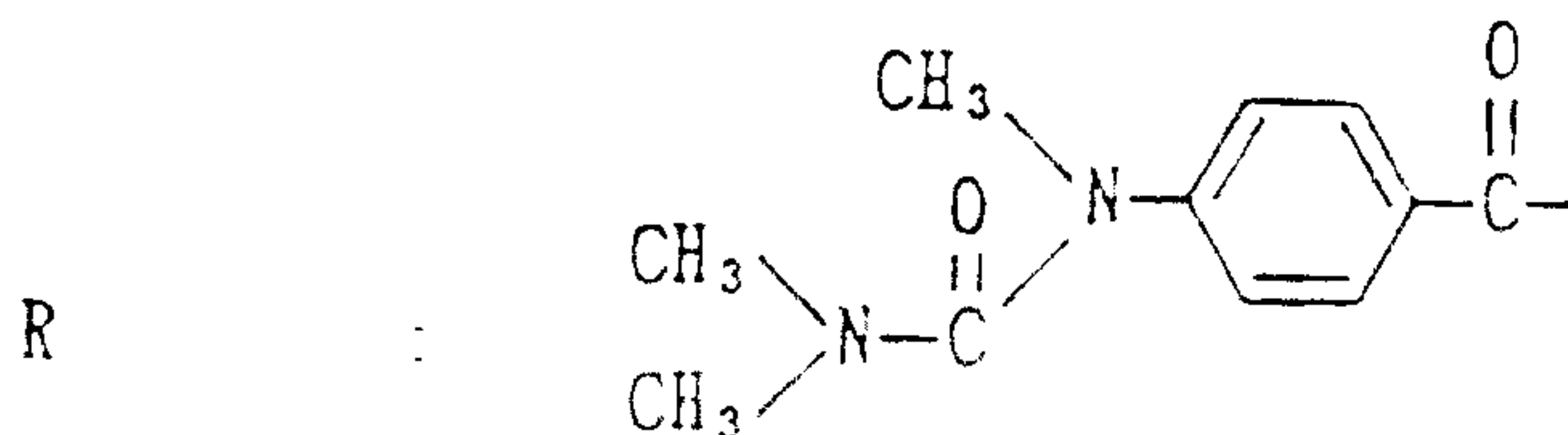
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 57)

Example 41

Structural formula:



Crystal form: colorless prisms

Recrystallization solvent: isopropanol

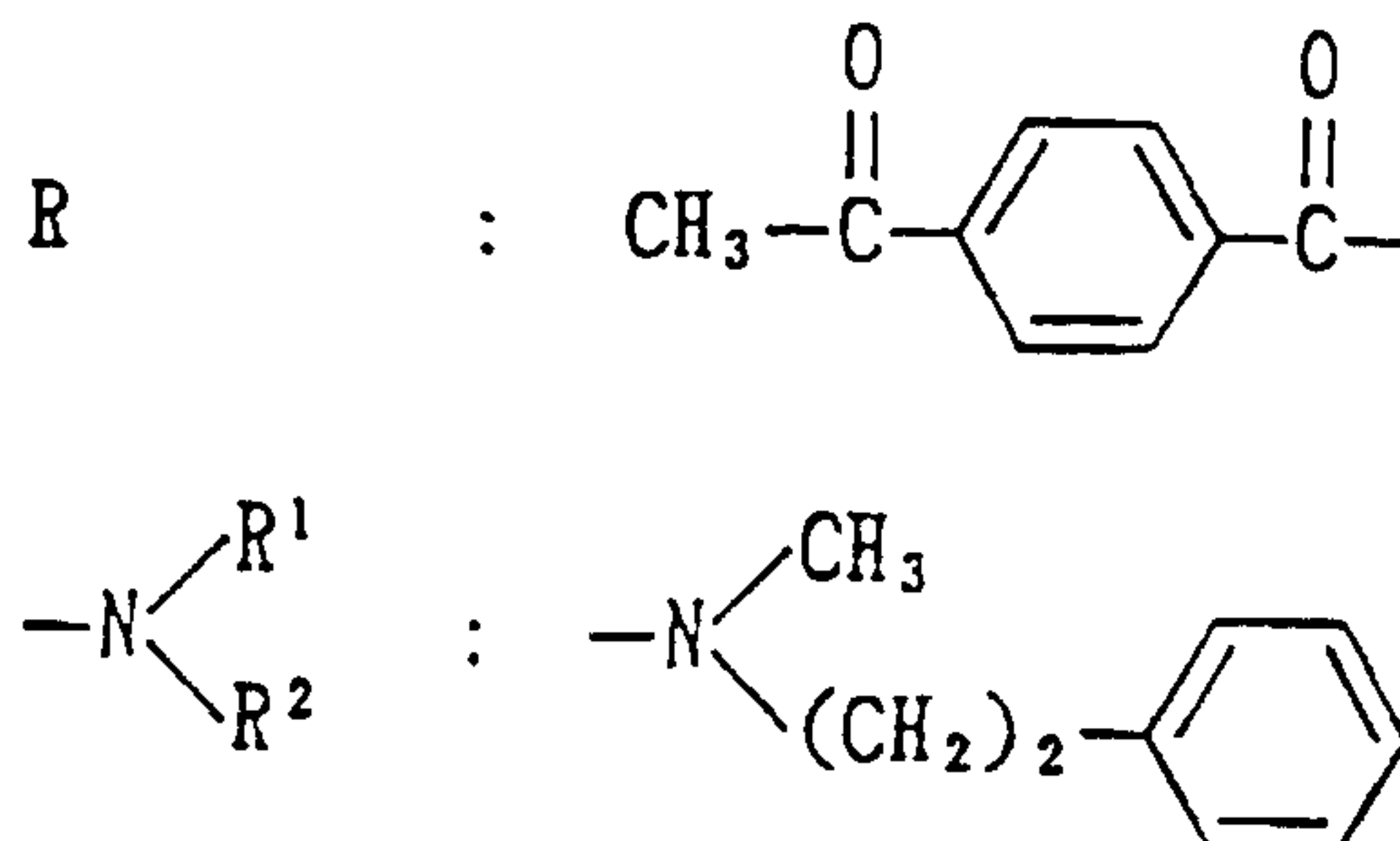
Melting point (°C): 218-220

Salt form: hydrochloride

[Table 10 (continued)]

Example 42

Structural formula:



Crystal form: white powder

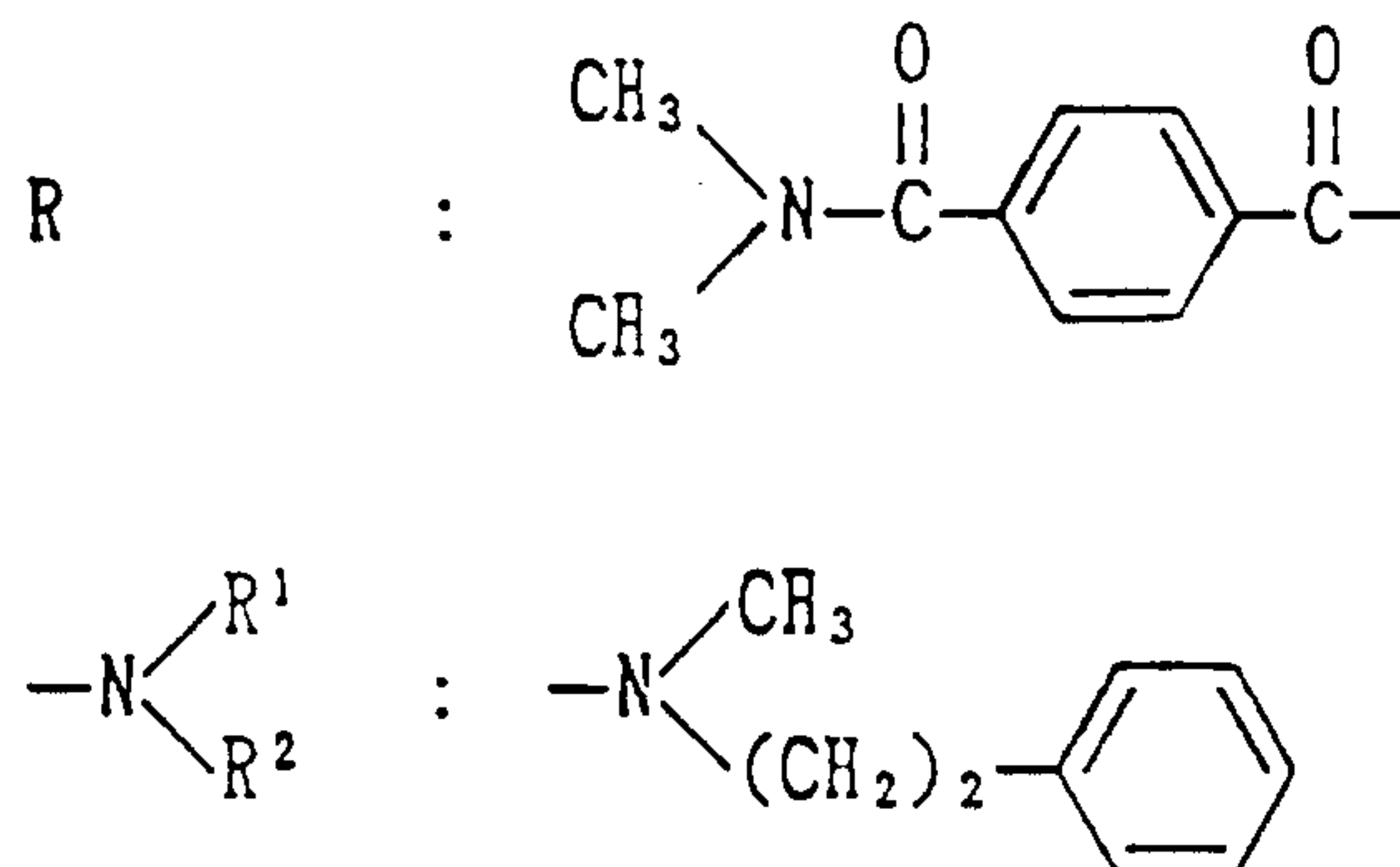
Recrystallization solvent: ethanol

Melting point (°C): 203-205

Salt form: hydrochloride

Example 43

Structural formula:



Crystal form: light yellow powder

Recrystallization solvent: ethyl acetate-n-hexane

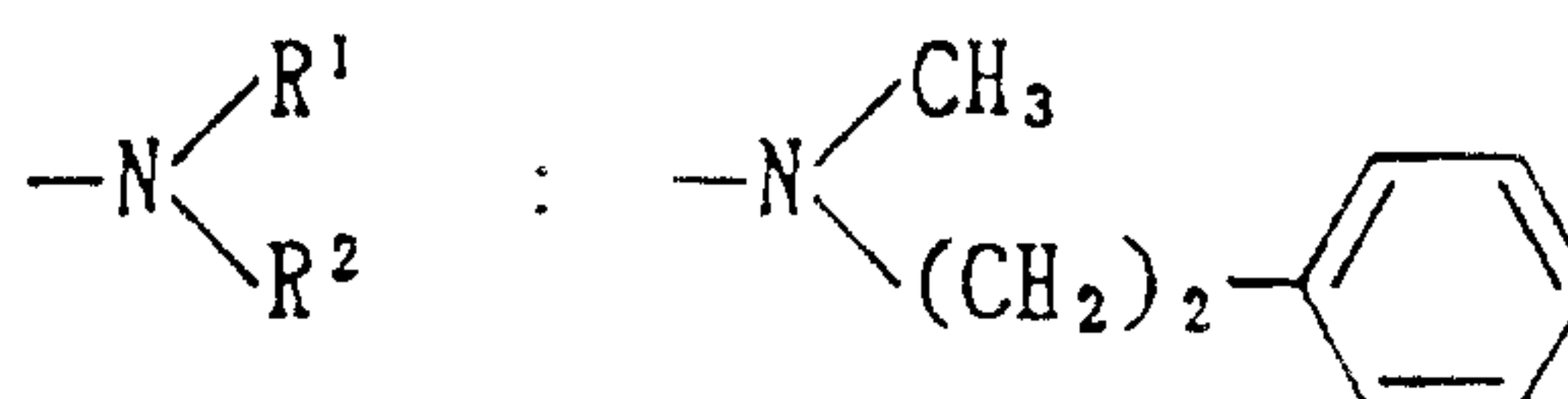
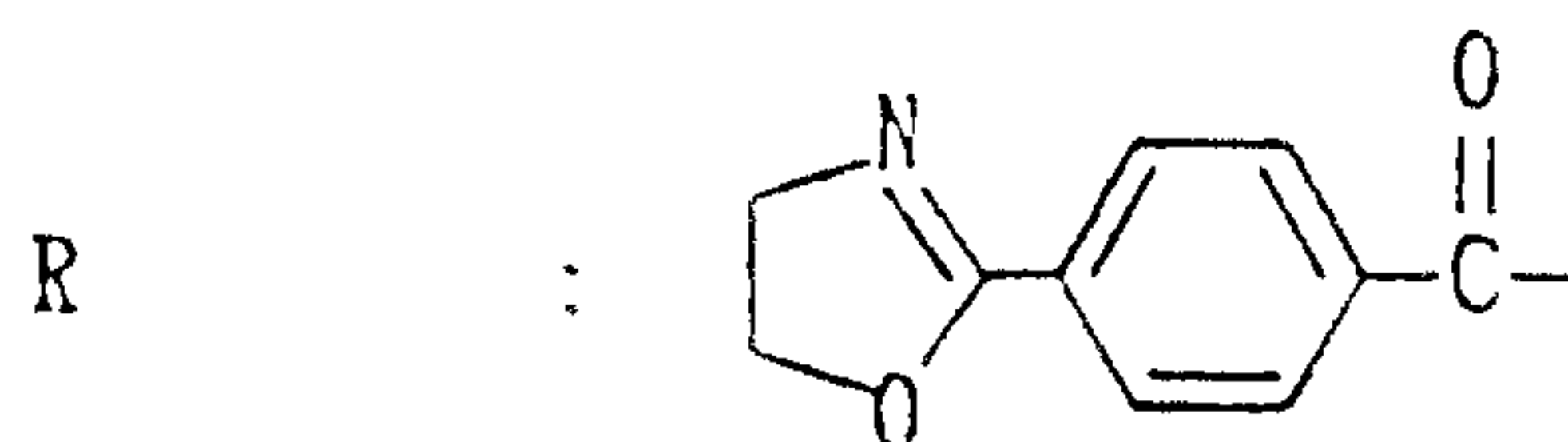
Melting point (°C): 84-87

Salt form: free

[Table 10 (continued)]

Example 44

Structural formula:



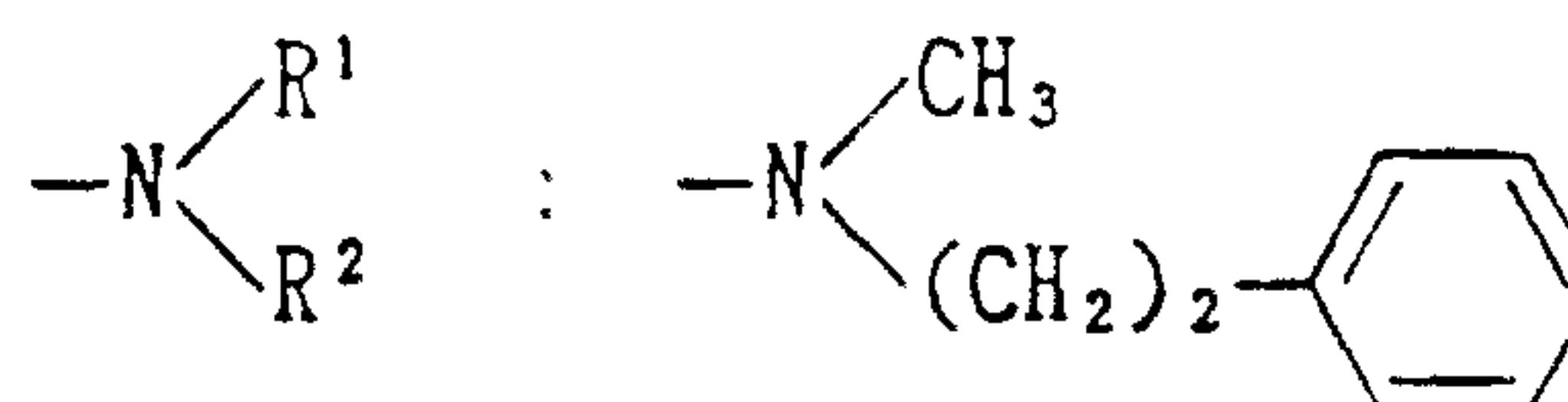
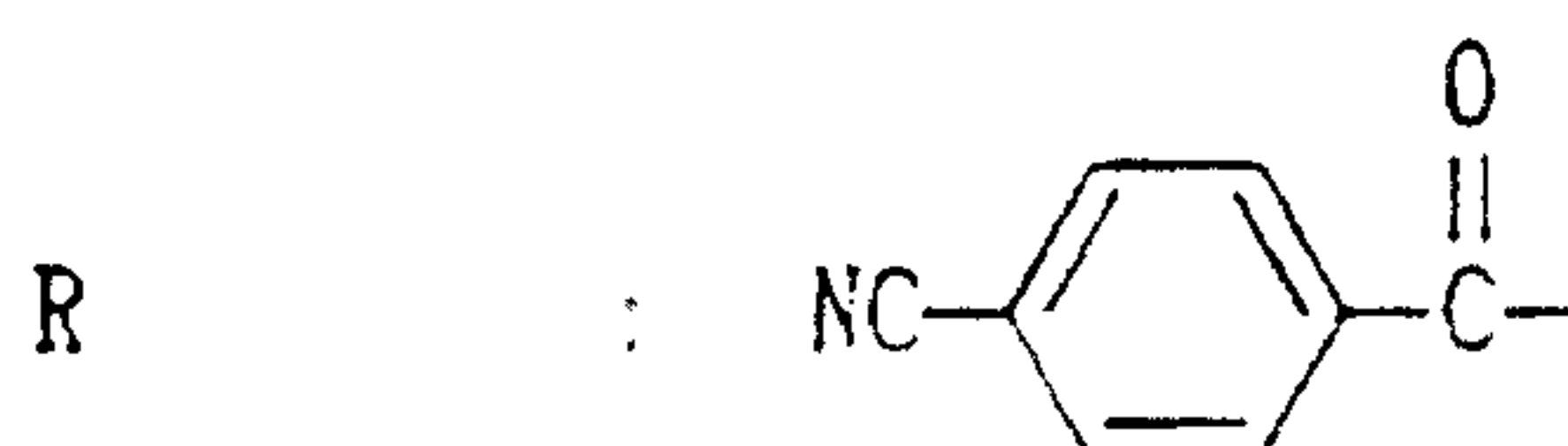
Crystal form: colorless thick syrup

Salt form: free

NMR value: 159)

Example 45

Structural formula:



Crystal form: light yellow needles

Recrystallization solvent: ethanol

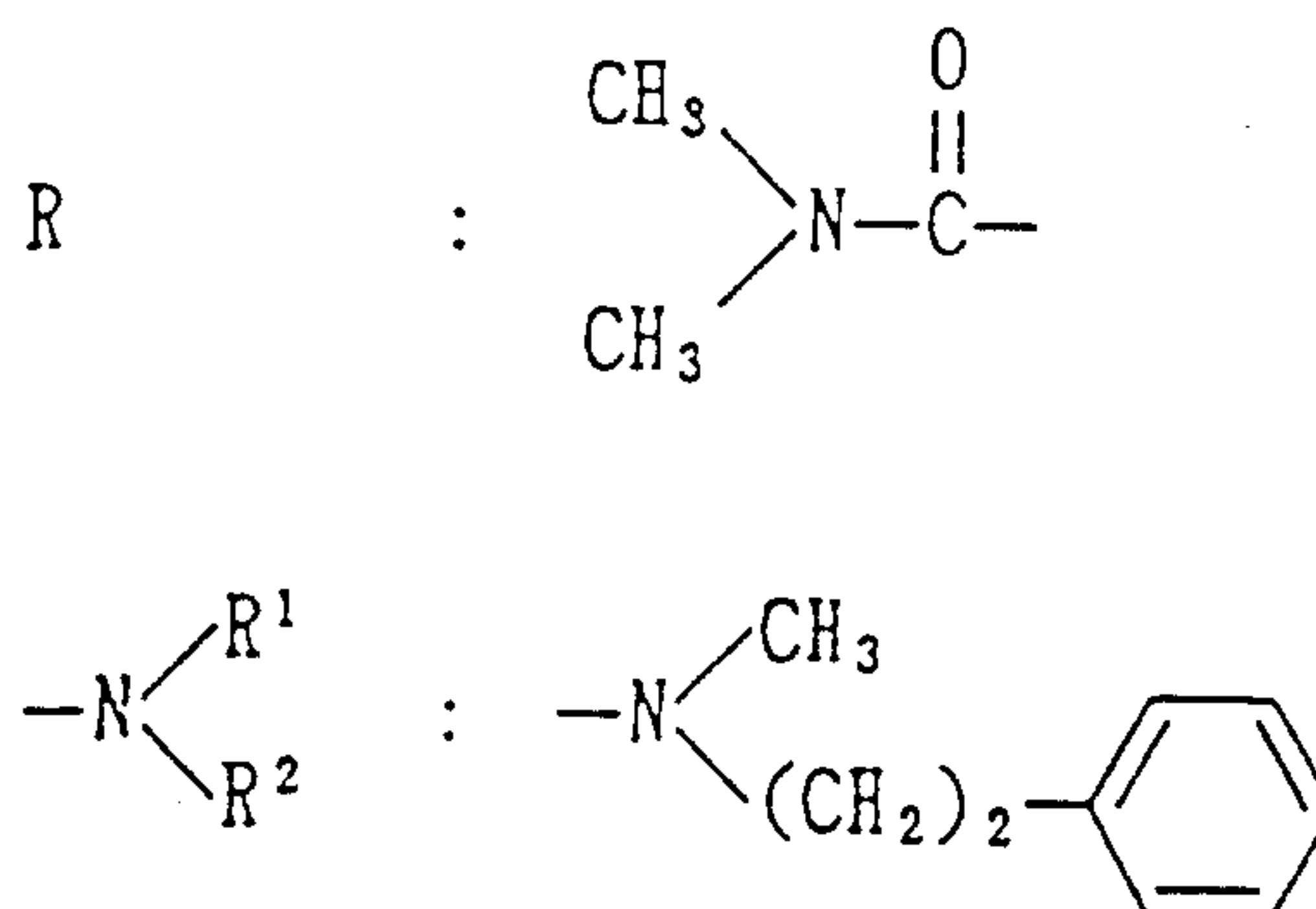
Melting point (°C): 200-202

Salt form: hydrochloride

[Table 10 (continued)]

Example 46

Structural formula:



Crystal form: colorless prisms

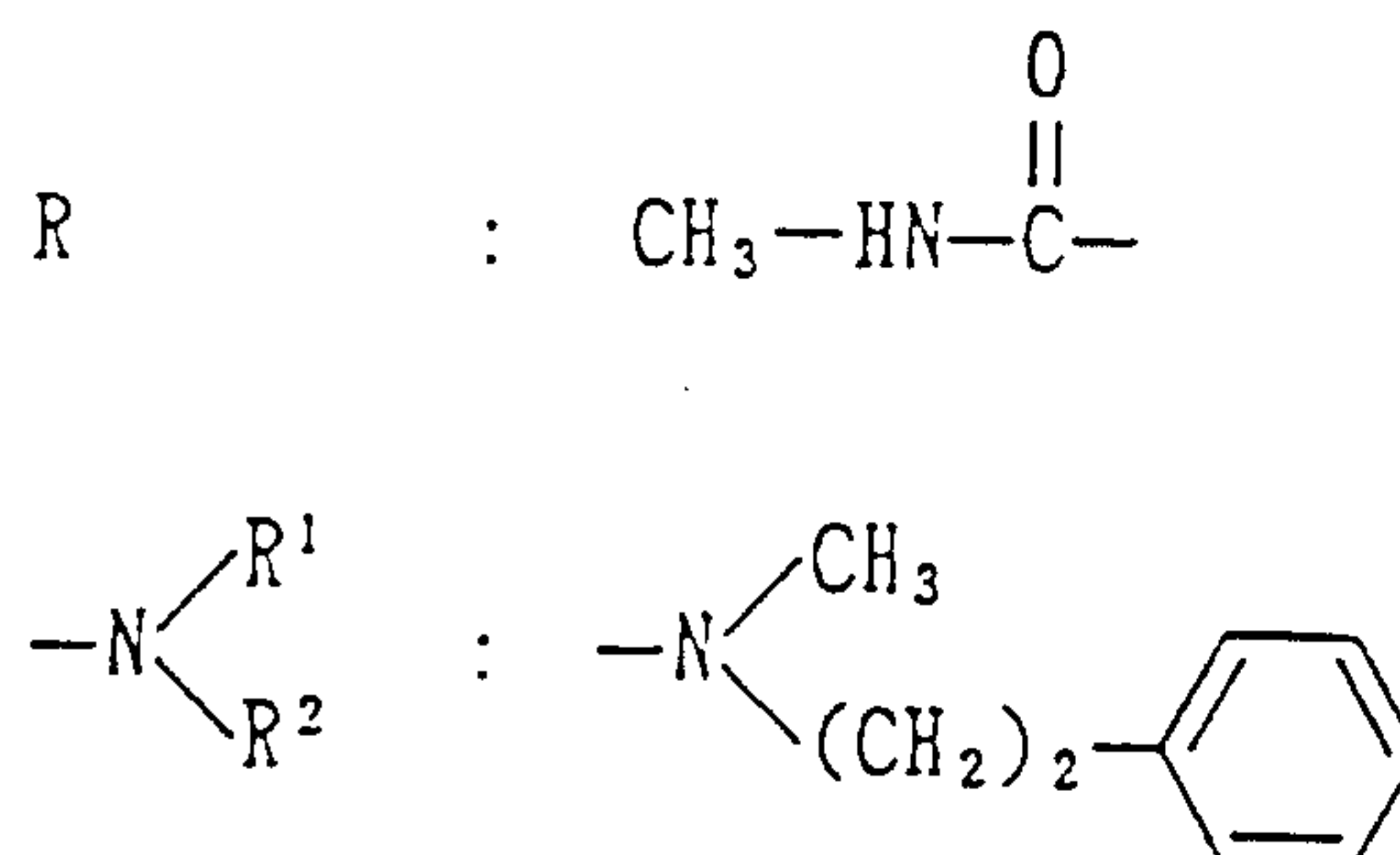
Recrystallization solvent: ethanol

Melting point (°C): 210-212

Salt form: hydrochloride

Example 47

Structural formula:



Crystal form: colorless prisms

Recrystallization solvent: ethyl acetate-ethanol

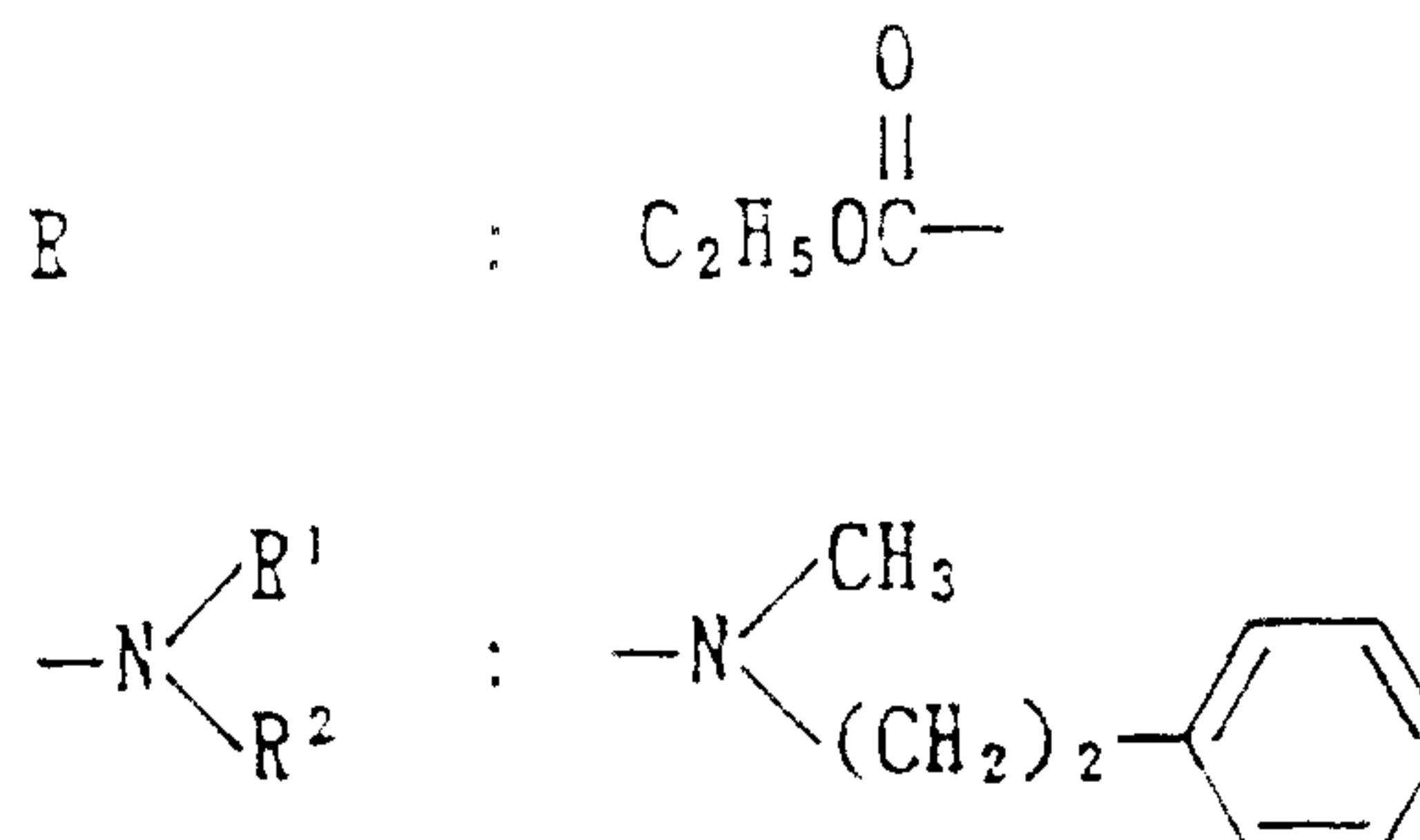
Melting point (°C): 140-142

Salt form: hydrochloride

(Table 10 (continued))

Example 48

Structural formula:



Crystal form: colorless needles

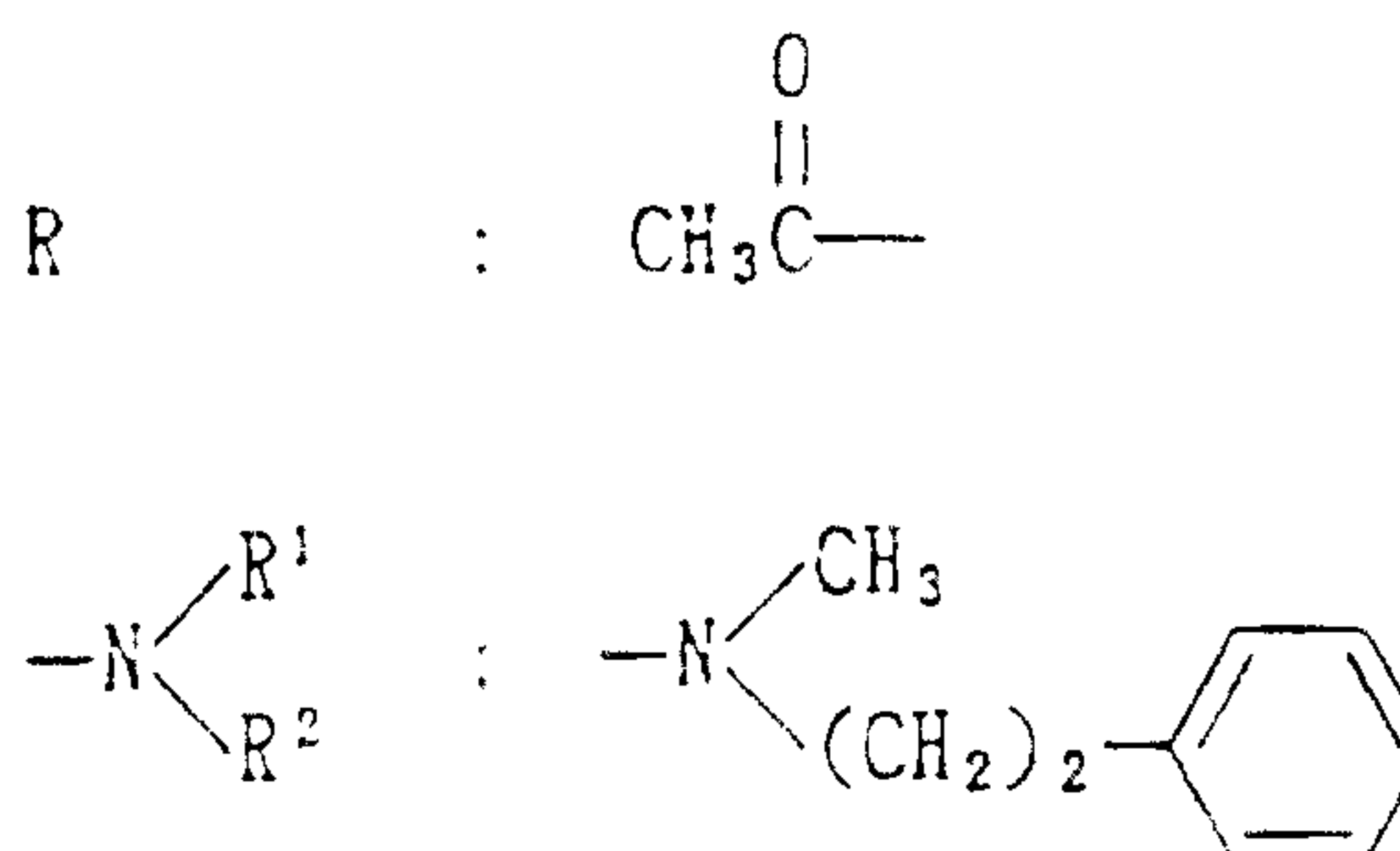
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 156-157

Salt form: hydrochloride

Example 49

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-ethanol

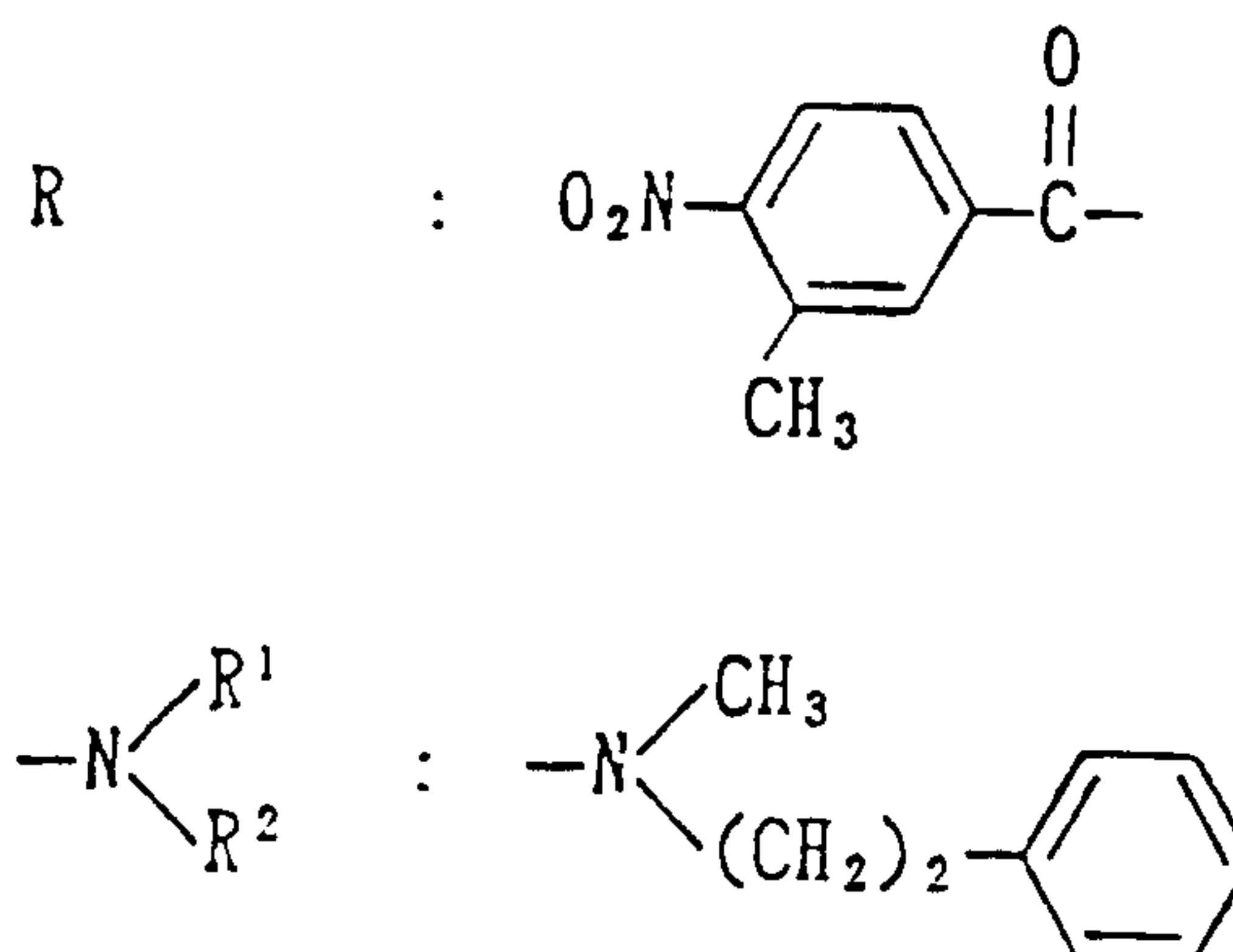
Melting point (°C): 186-188

Salt form: hydrochloride

[Table 10 (continued)]

Example 50

Structural formula:



Crystal form: white powder

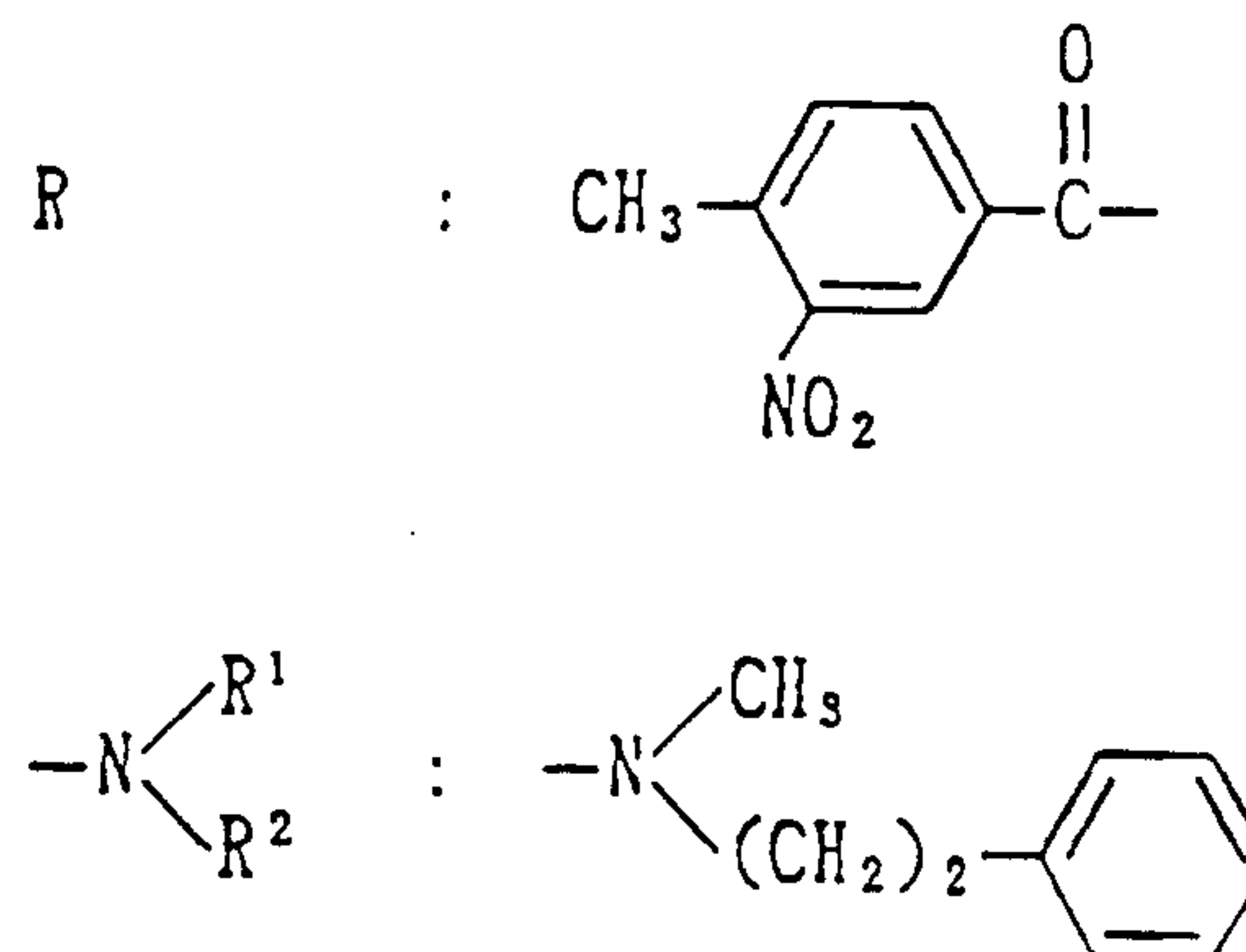
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 187-189

Salt form: hydrochloride

Example 51

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-ethanol

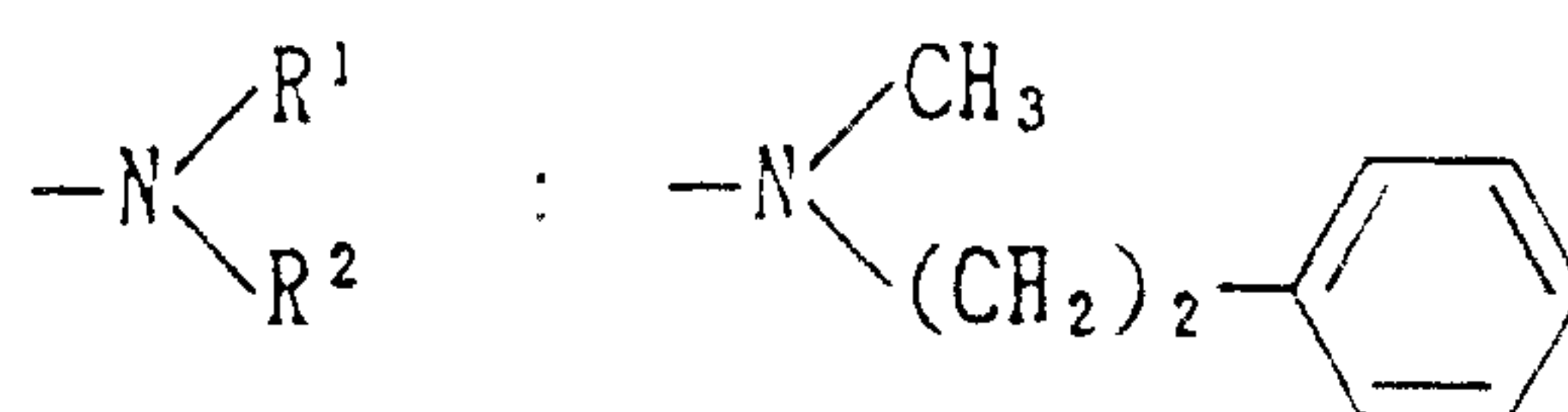
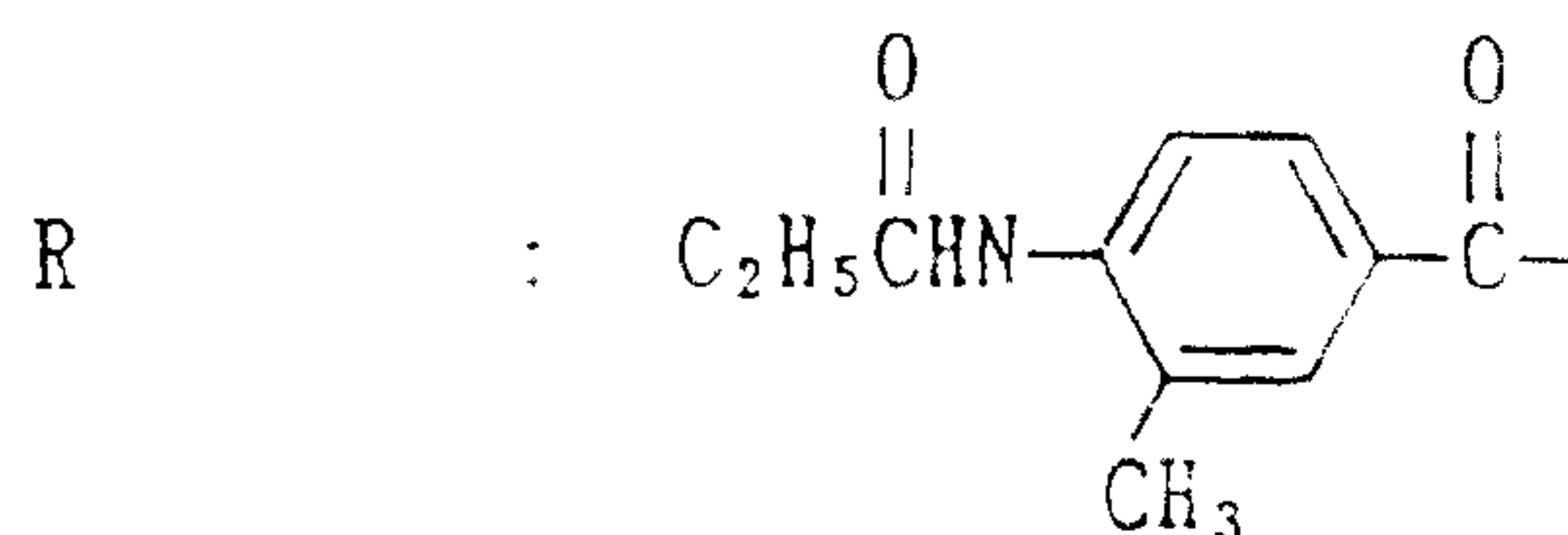
Melting point (°C): 203-205

Salt form: hydrochloride

{Table 10 (continued)}

Example 52

Structural formula:



Crystal form: white powder

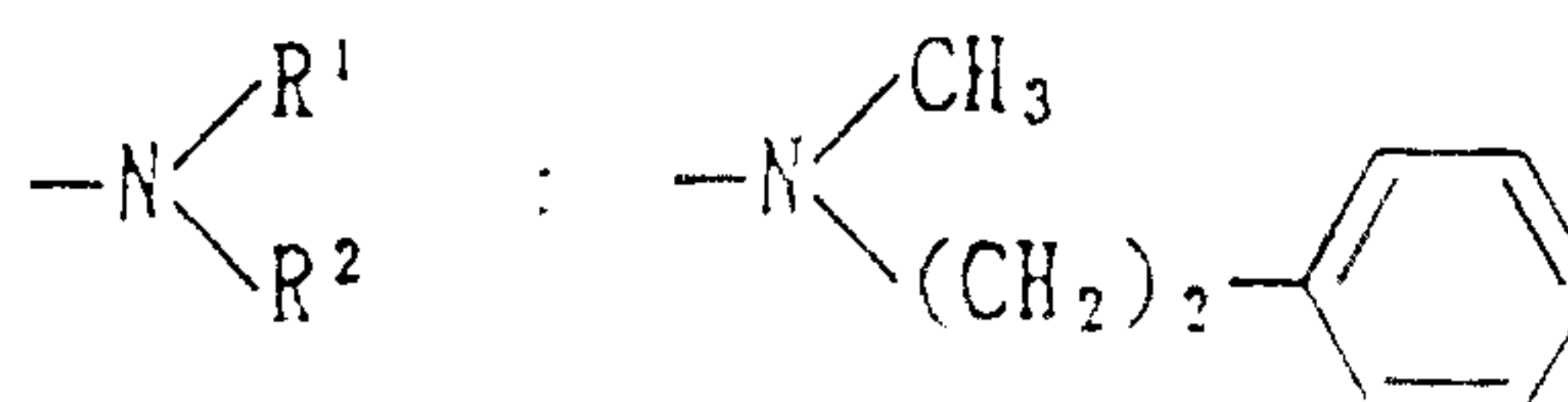
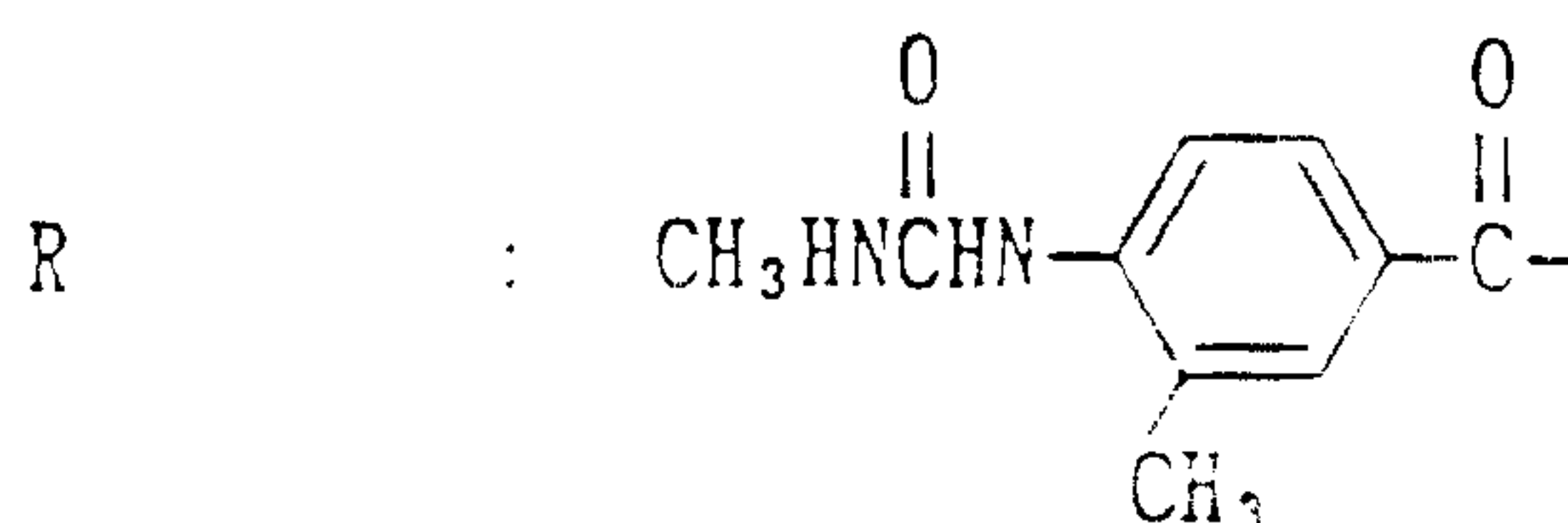
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 139-141

Salt form: hydrochloride

Example 53

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

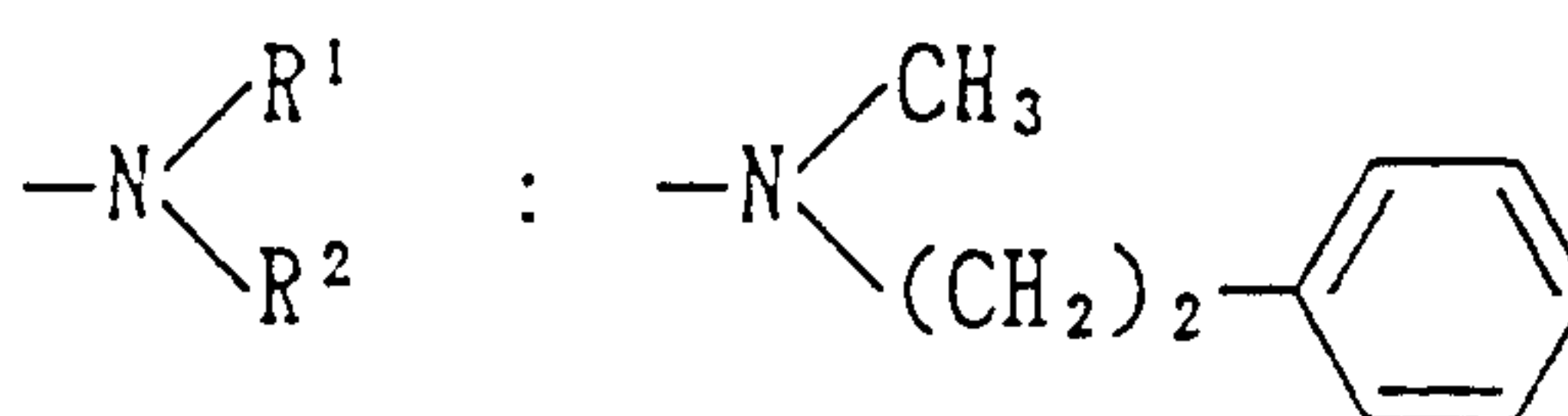
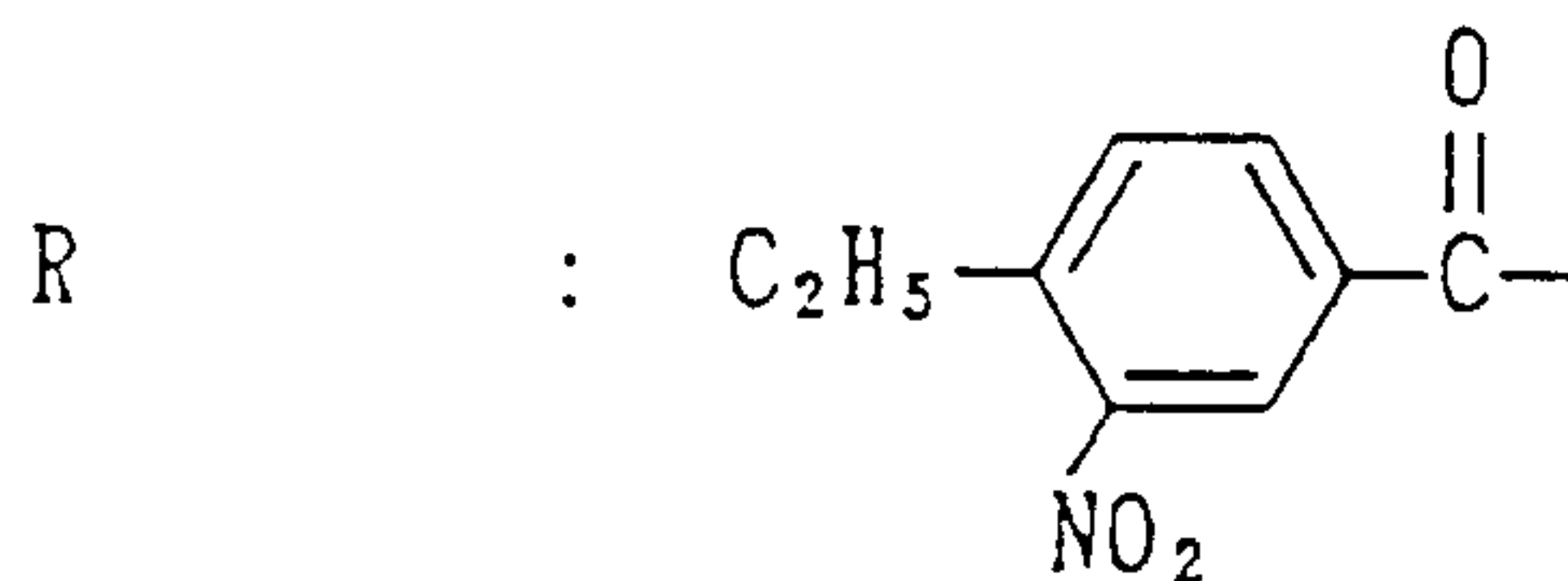
Melting point (°C): 224-227 (decompd.)

Salt form: hydrochloride

{Table 10 (continued)}

Example 54

Structural formula:



Crystal form: white powder

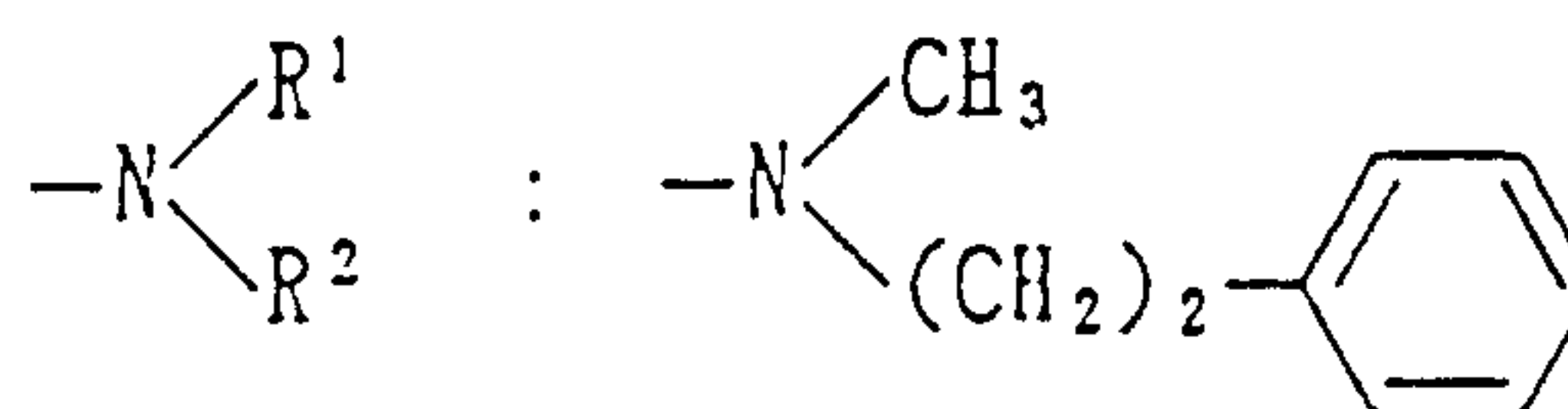
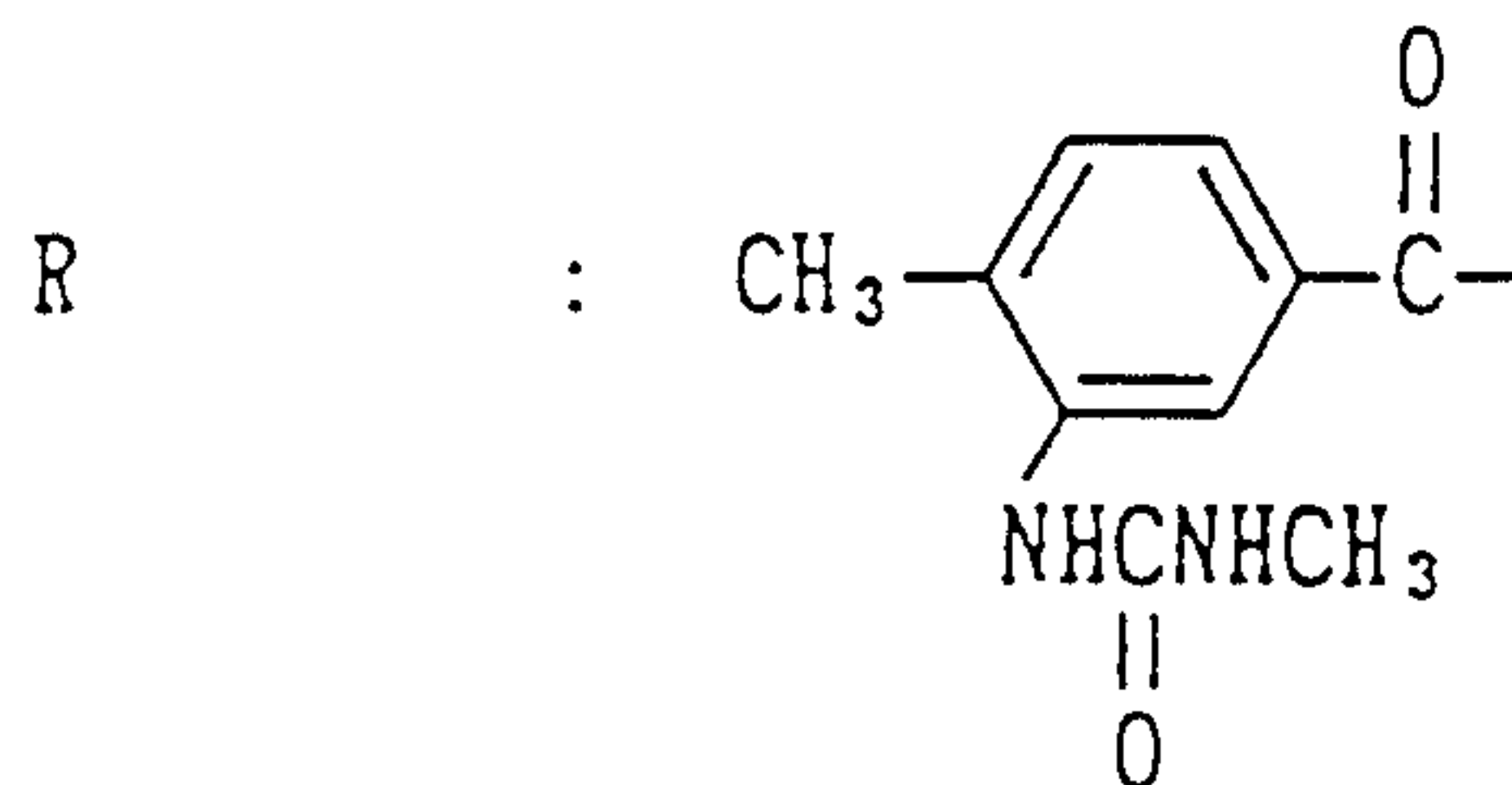
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 193-197

Salt form: hydrochloride

Example 55

Structural formula:



Crystal form: white amorphous

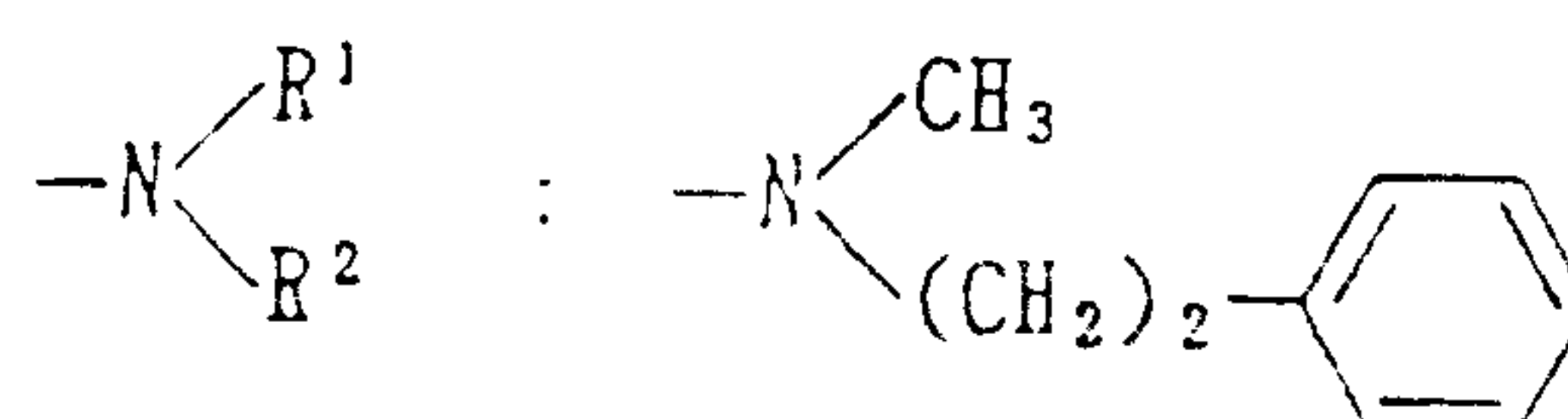
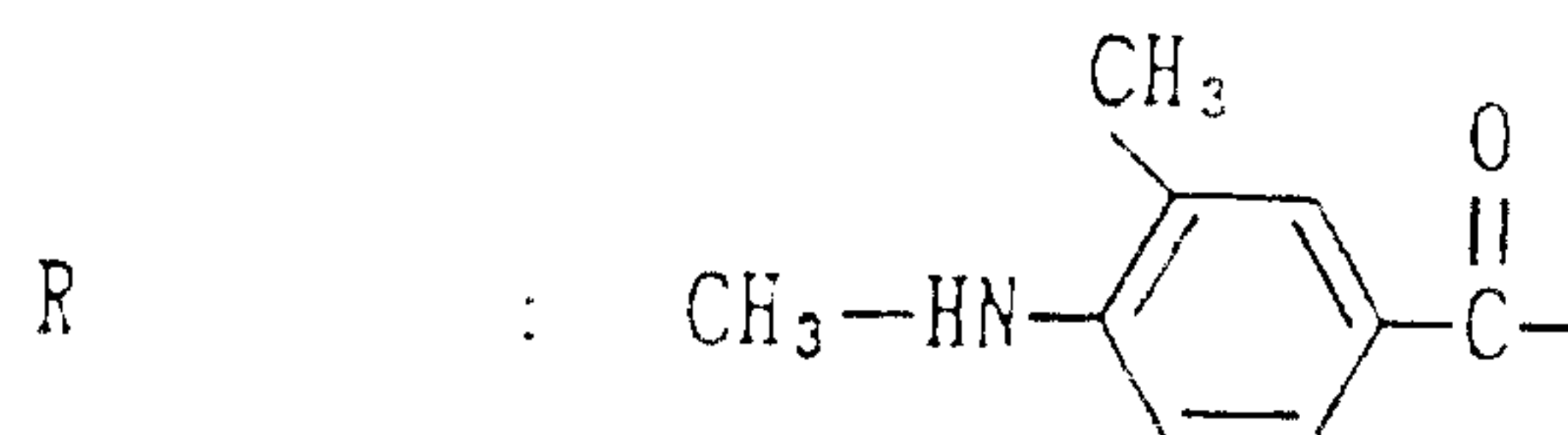
Salt form: hydrochloride

NMR value: 58)

{Table 10 (continued)}

Example 56

Structural formula:



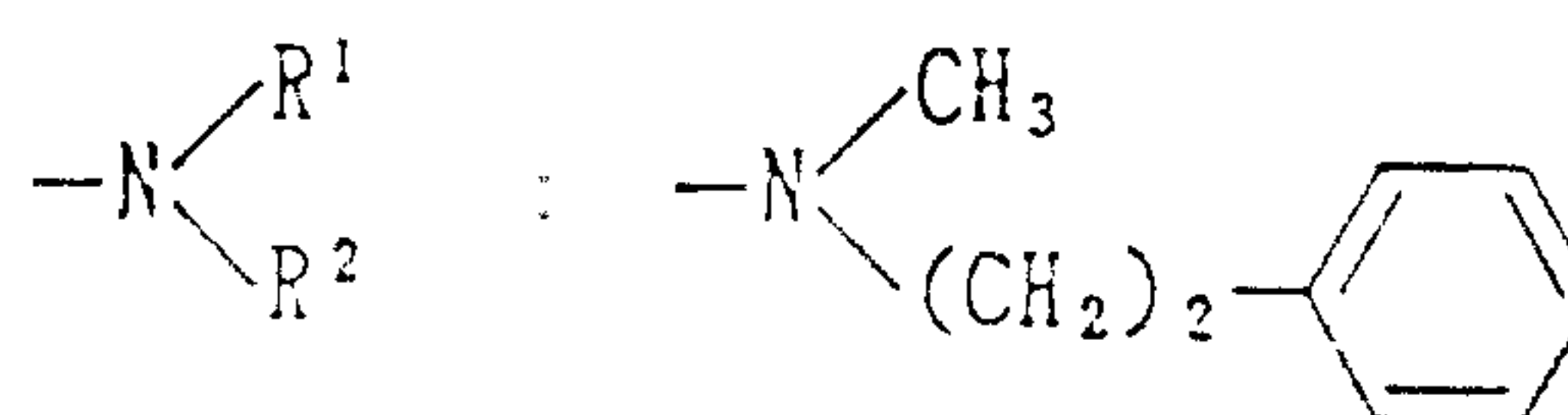
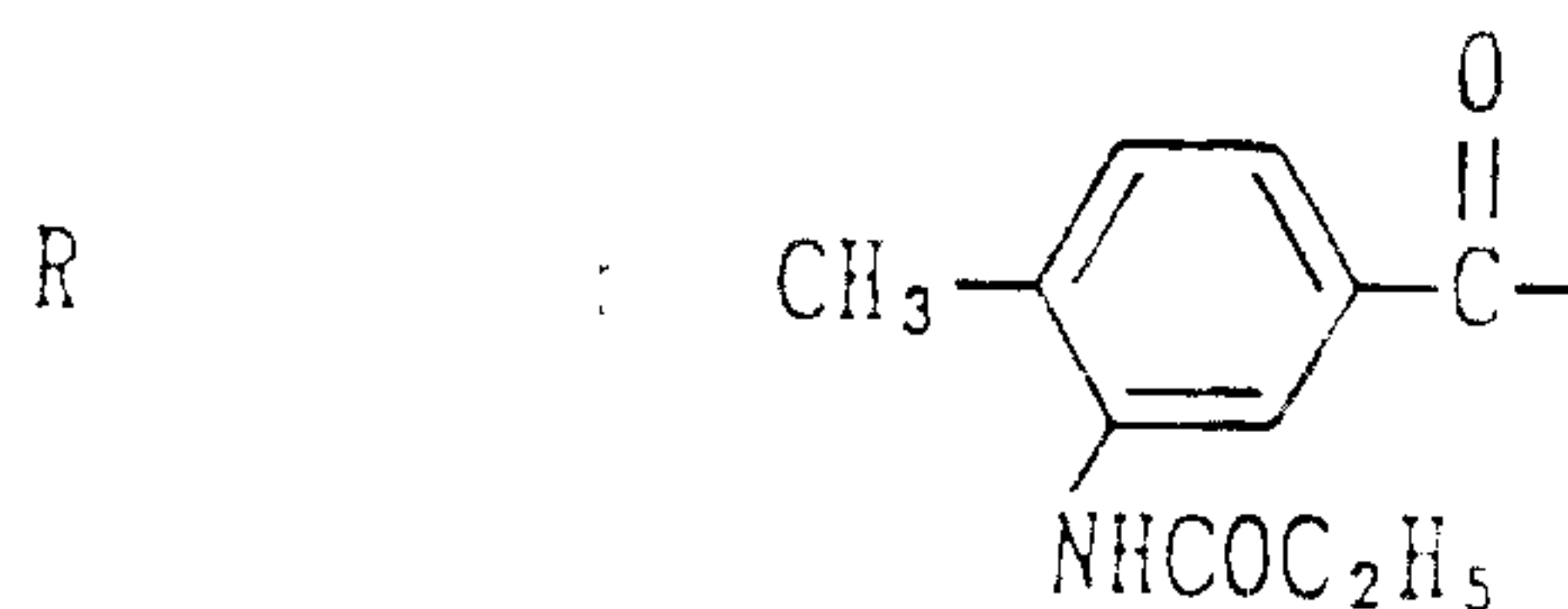
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 160)

Example 57

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

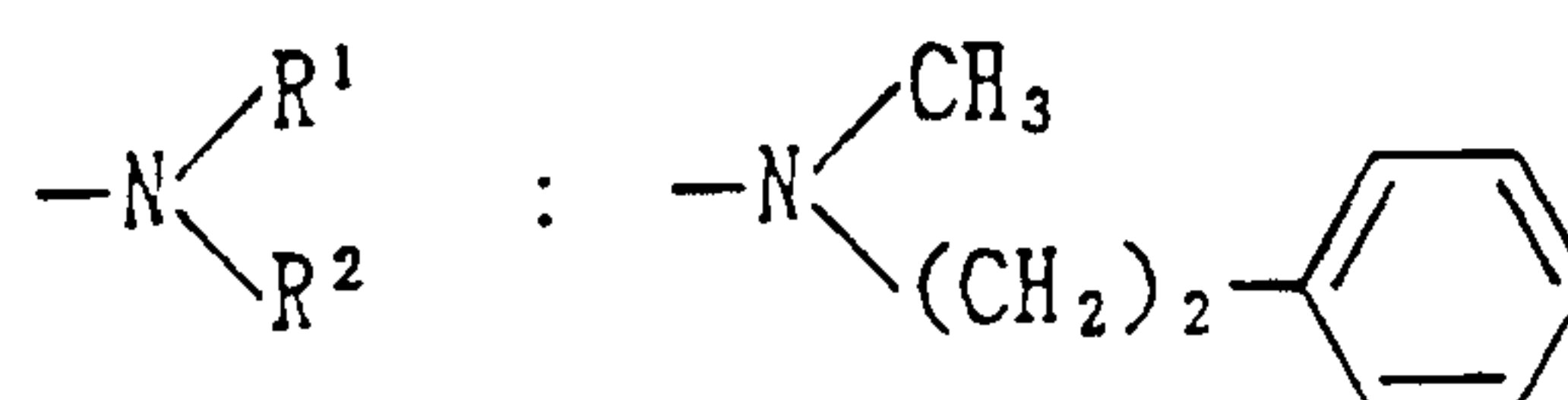
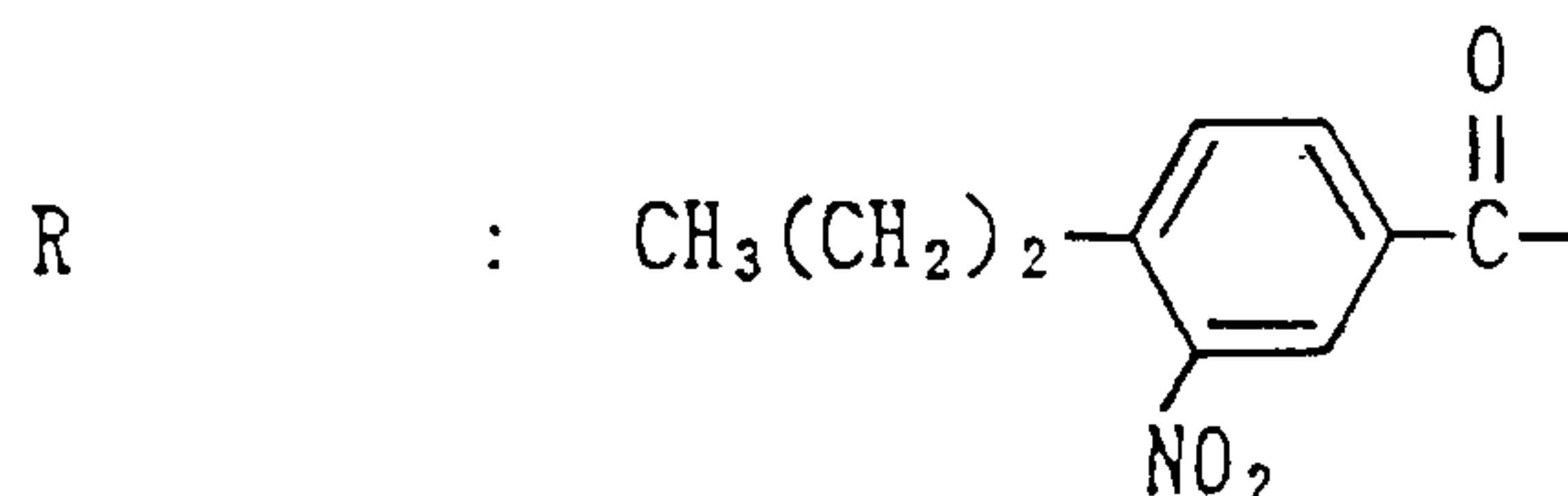
Melting point (°C): 216-218.5

Salt form: hydrochloride

[Table 10 (continued)]

Example 58

Structural formula:



Crystal form: colorless prisms

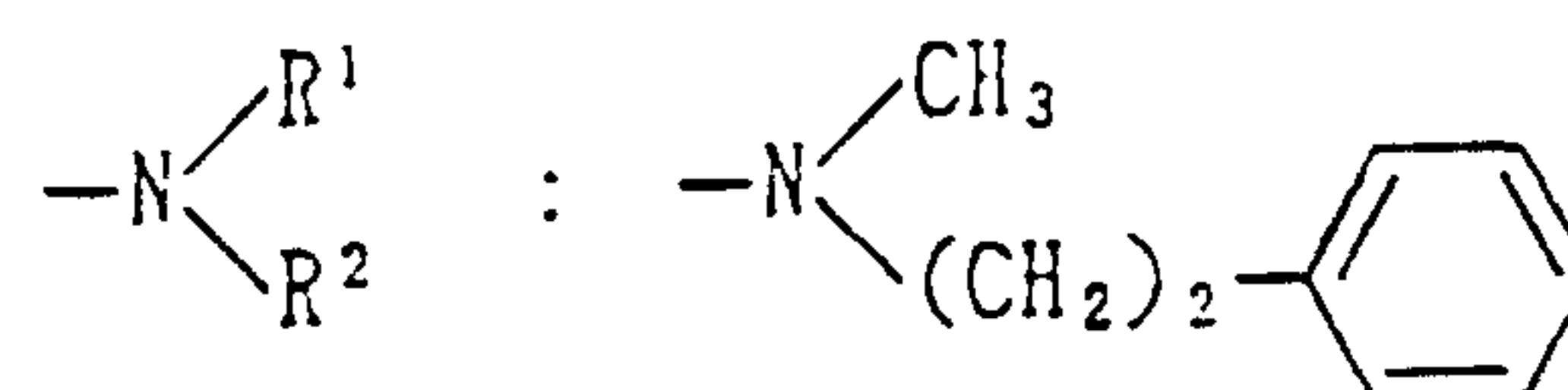
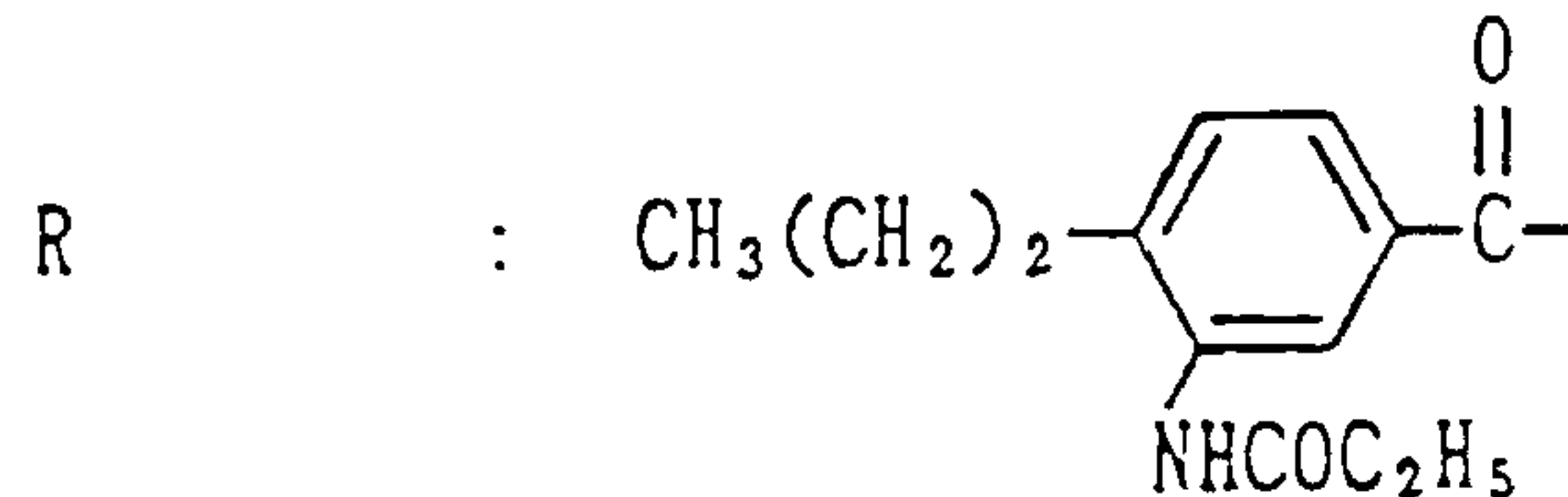
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 174-178

Salt form: hydrochloride

Example 59

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate

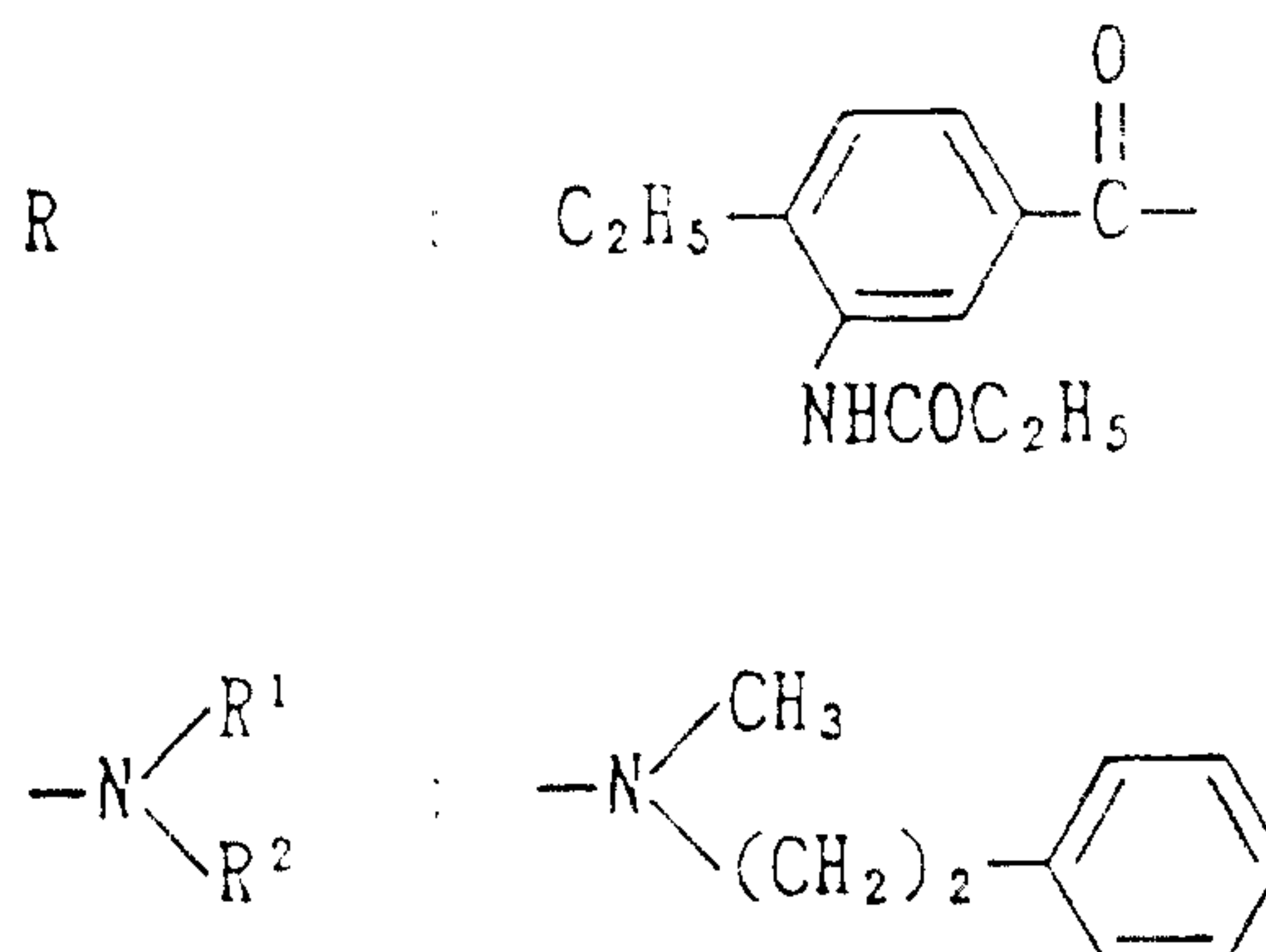
Melting point (°C): 175-176

Salt form: hydrochloride

{Table 10 (continued)}

Example 60

Structural formula:



Crystal form: colorless scales

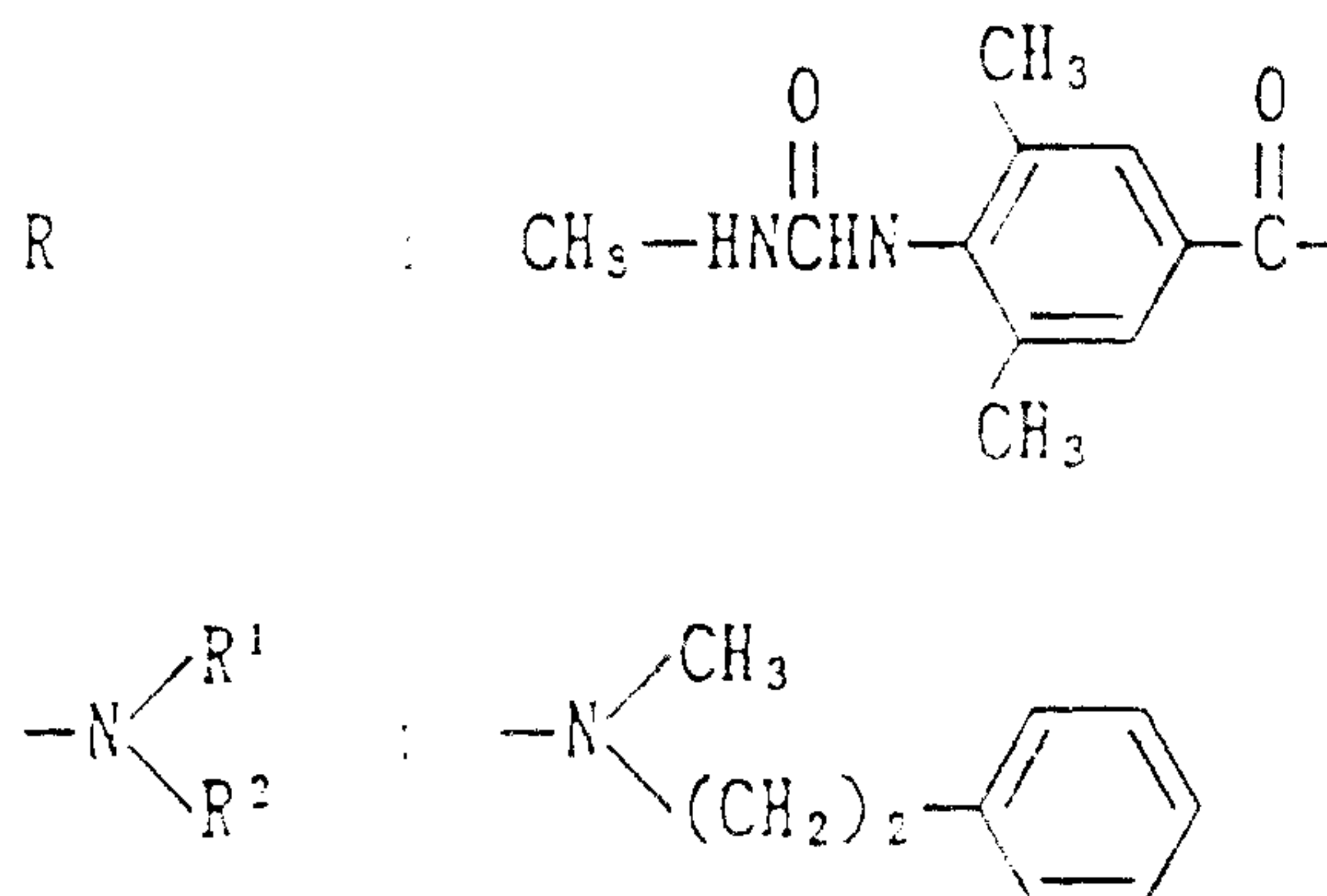
Recrystallization solvent: ethyl acetate

Melting point (°C): 144-147

Salt form: hydrochloride

Example 61

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

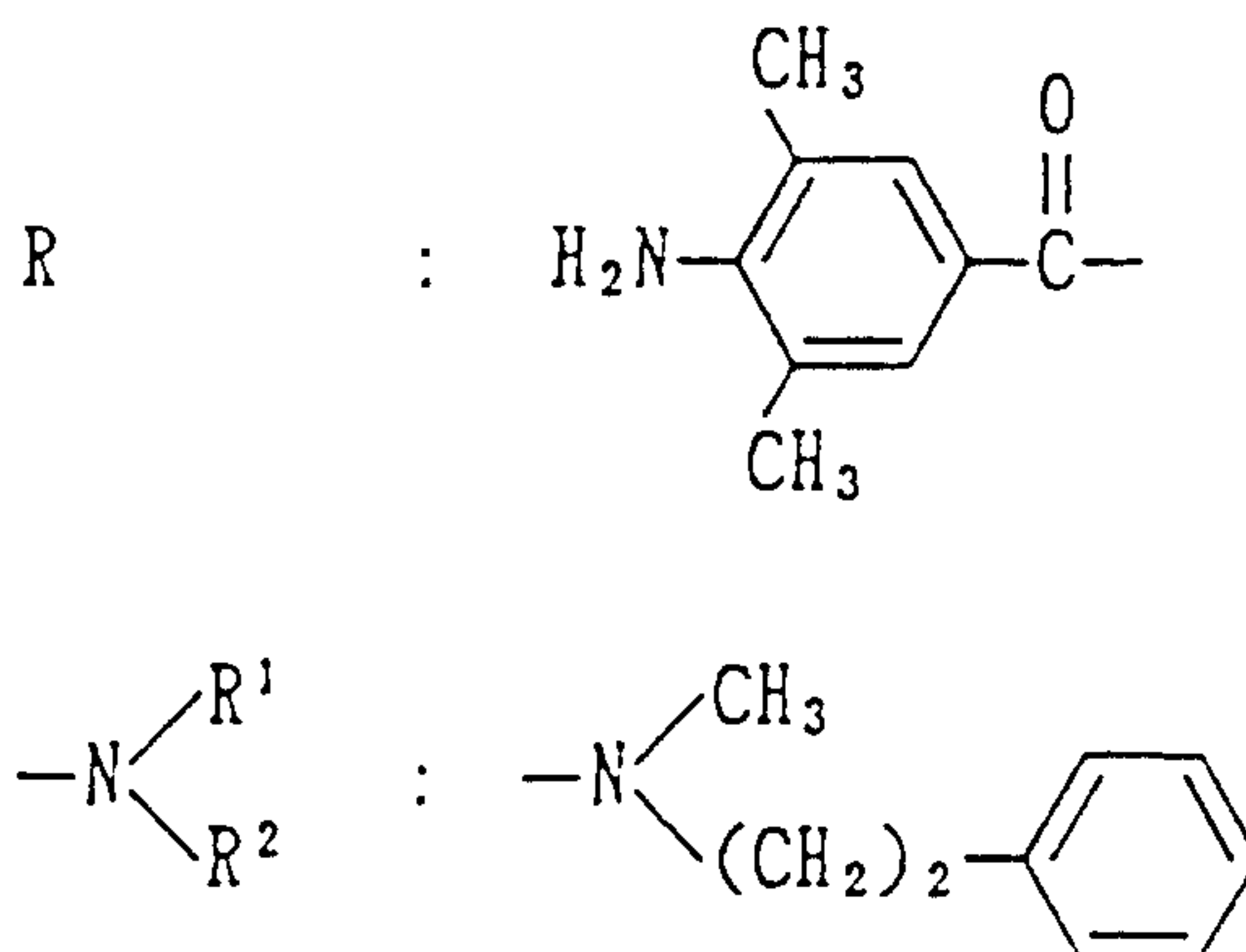
Melting point (°C): 230-235

Salt form: hydrochloride

[Table 10 (continued)]

Example 62

Structural formula:



Crystal form: white powder

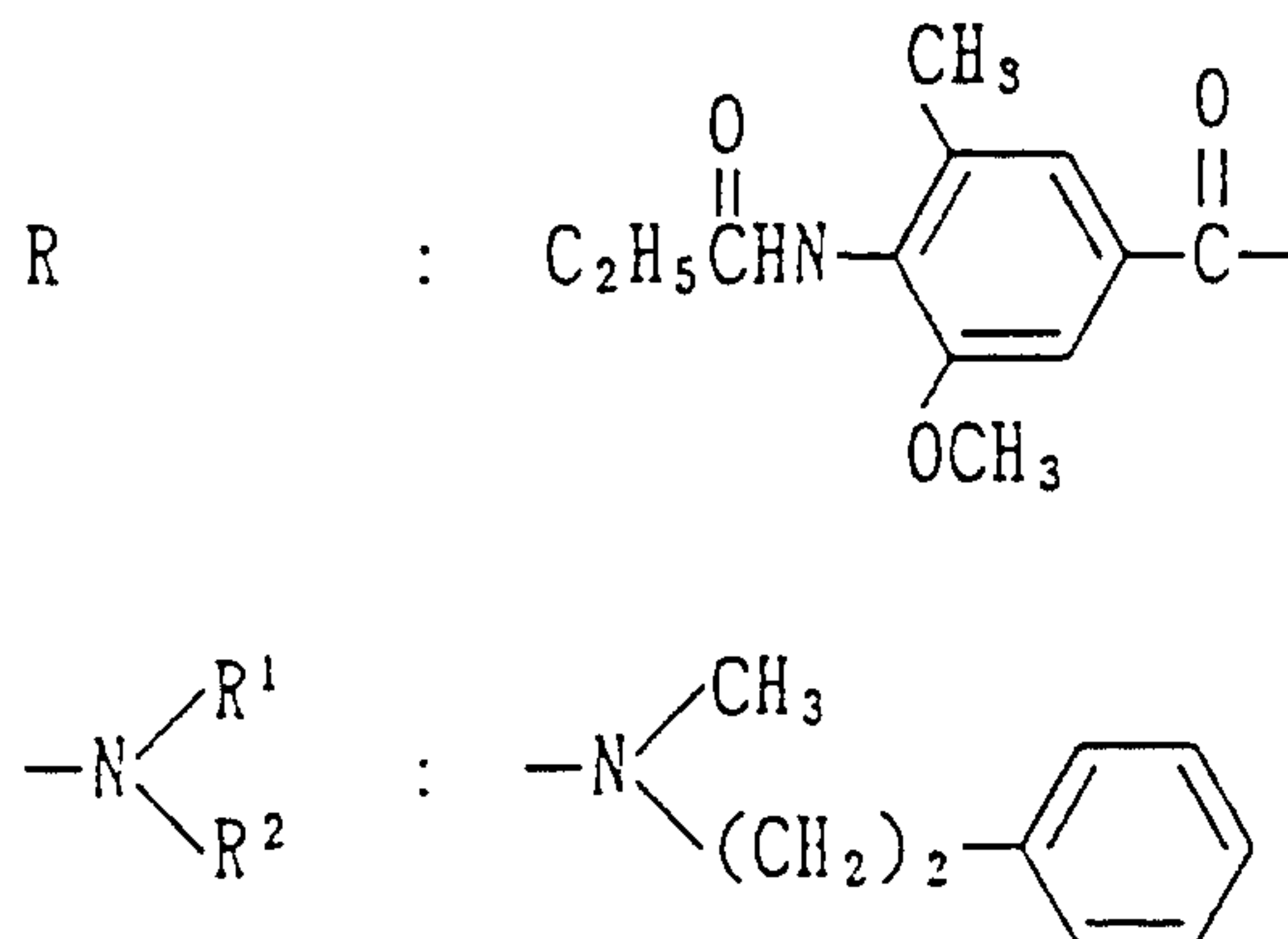
Recrystallization solvent: ethanol

Melting point (°C): 196-197

Salt form: oxalate

Example 63

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

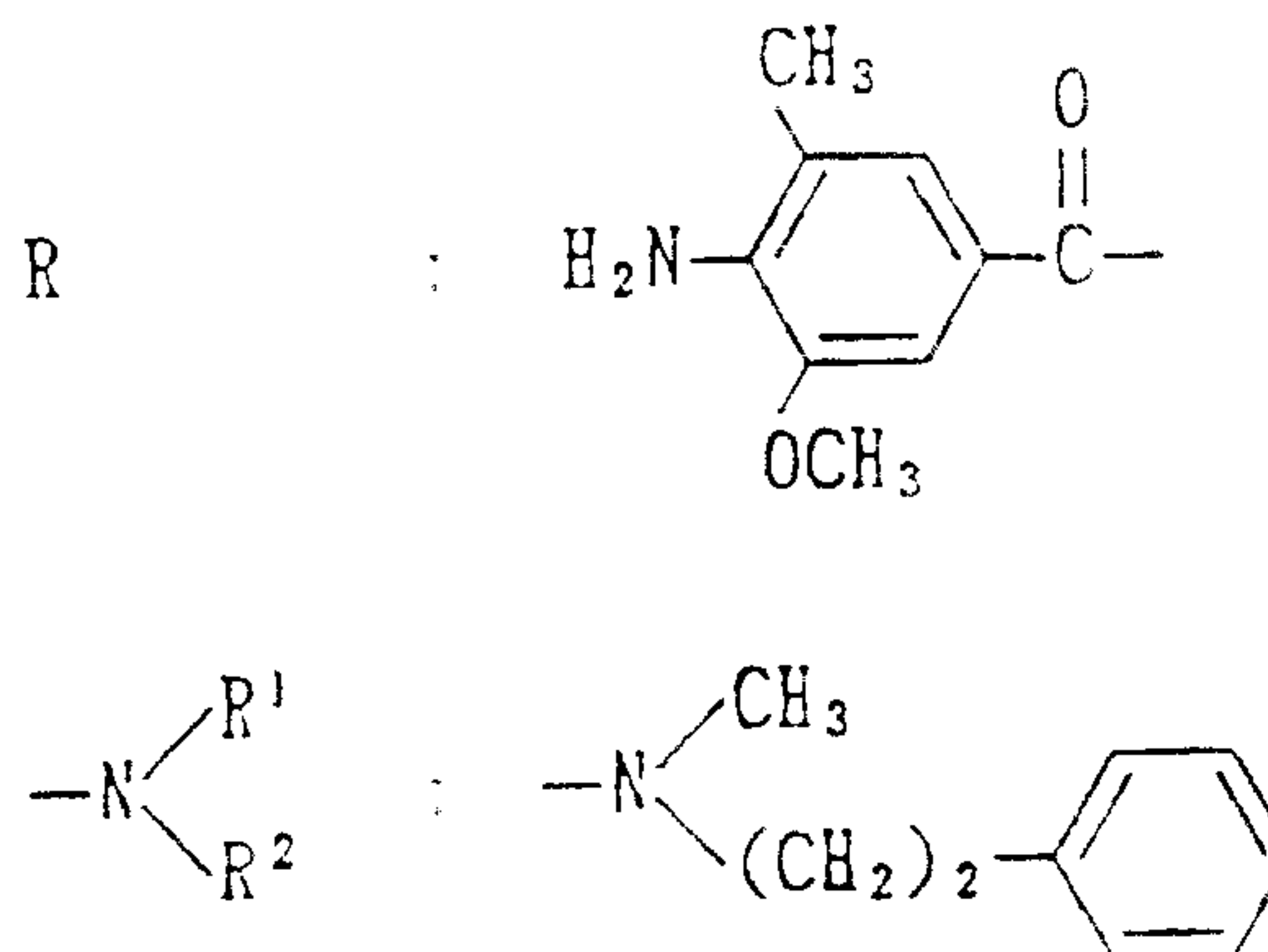
Melting point (°C): 214-218

Salt form: hydrochloride

{Table 10 (continued)}

Example 64

Structural formula:



Crystal form: white powder

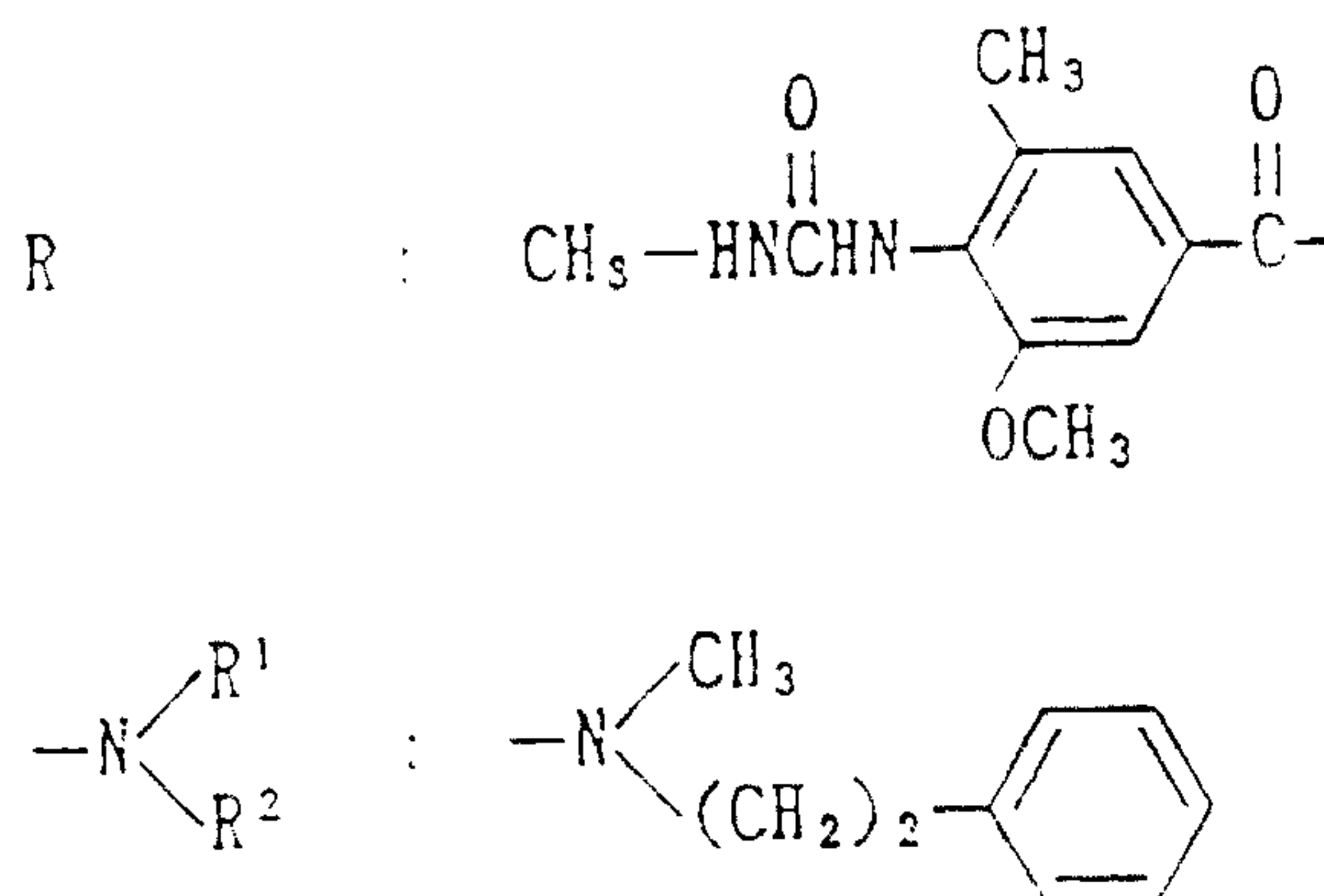
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 198.5-200

Salt form: oxalate

Example 65

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

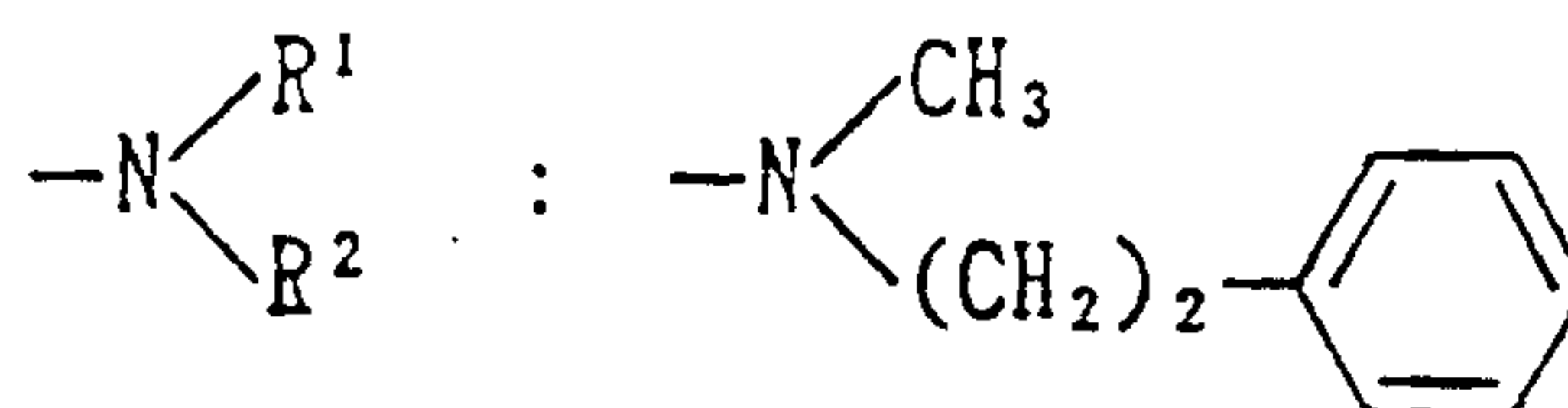
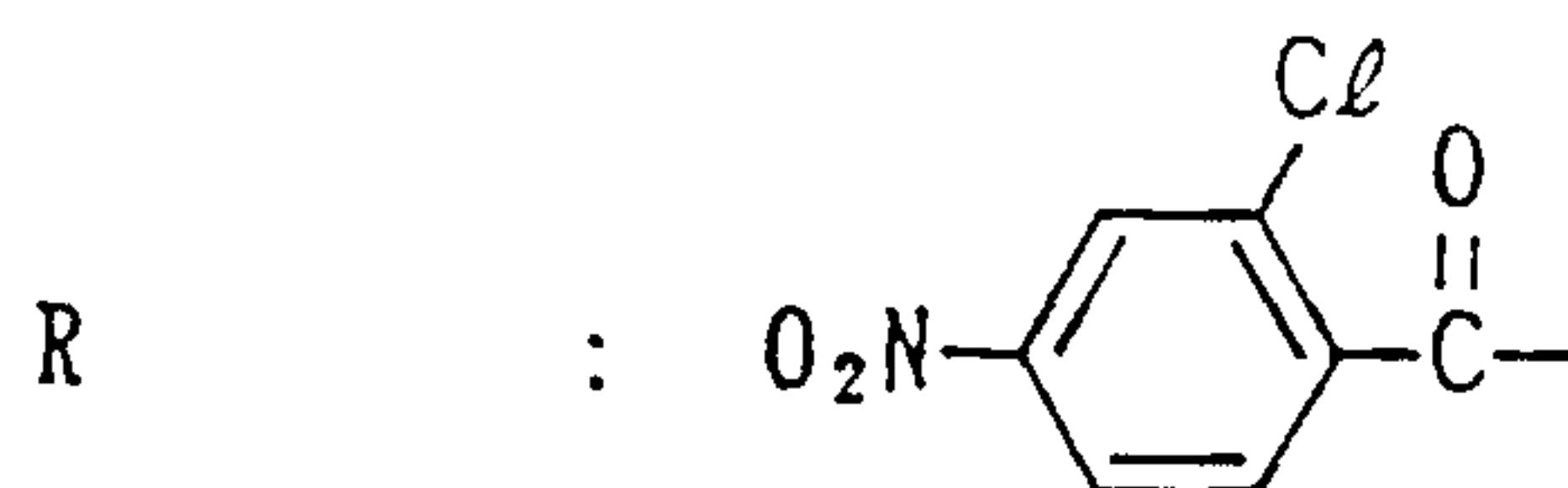
Melting point (°C): 132-133

Salt form: oxalate

{Table 10 (continued)}

Example 66

Structural formula:



Crystal form: white powder

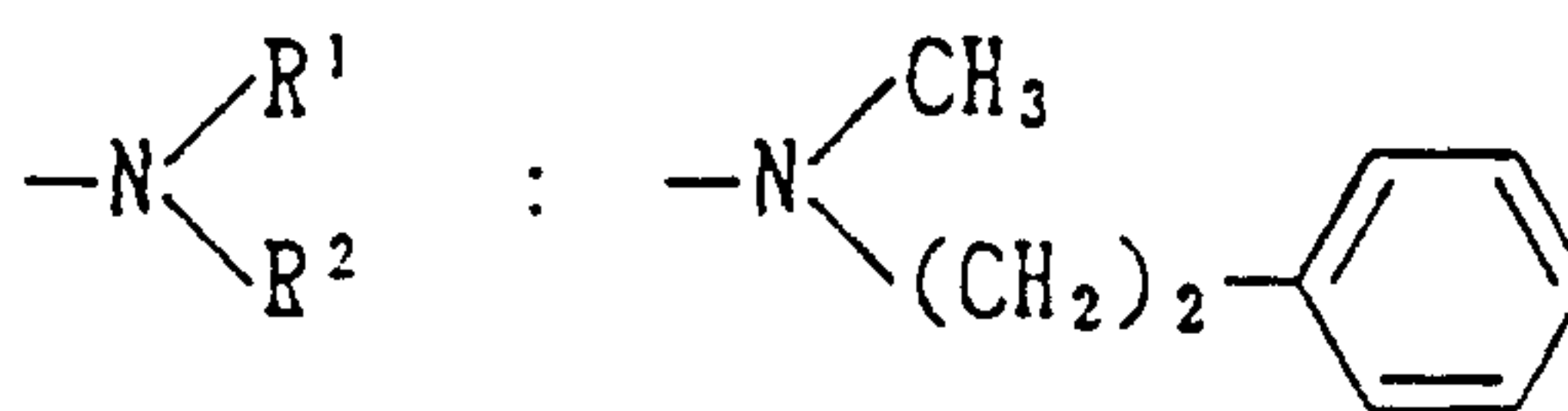
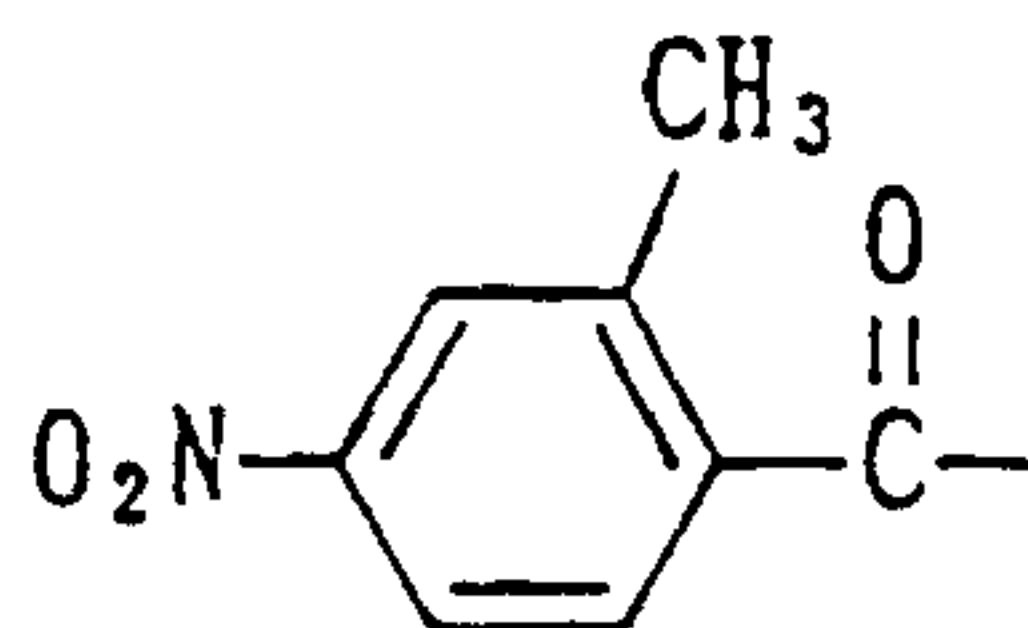
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 229-230.5

Salt form: hydrochloride

Example 67

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

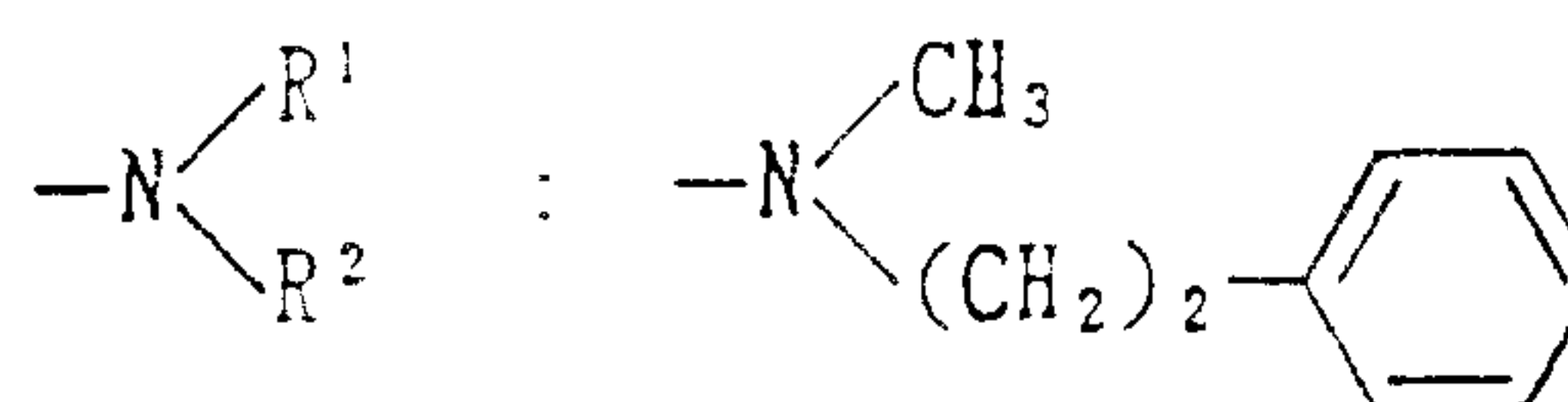
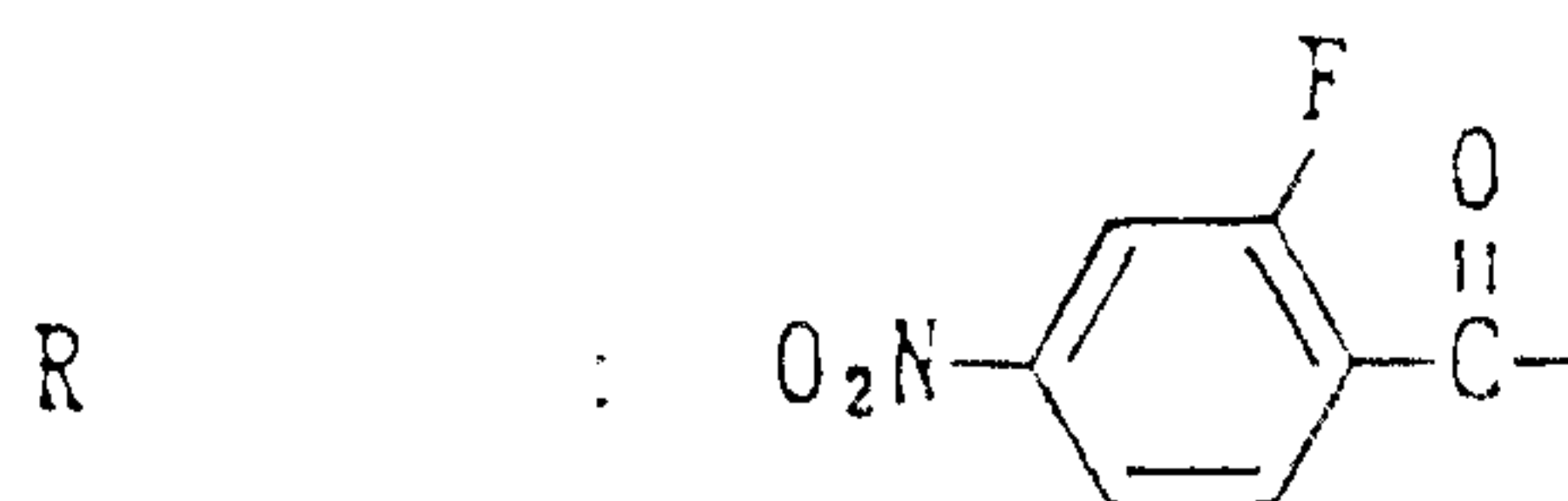
Melting point (°C): 232-232.5

Salt form: hydrochloride

[Table 10 (continued)]

Example 68

Structural formula:



Crystal form: white powder

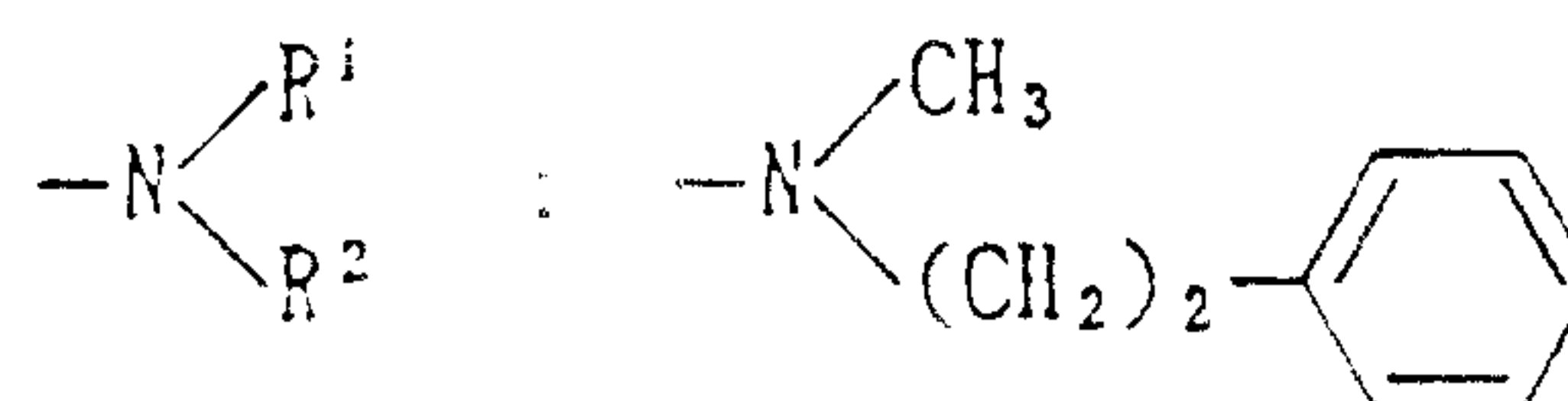
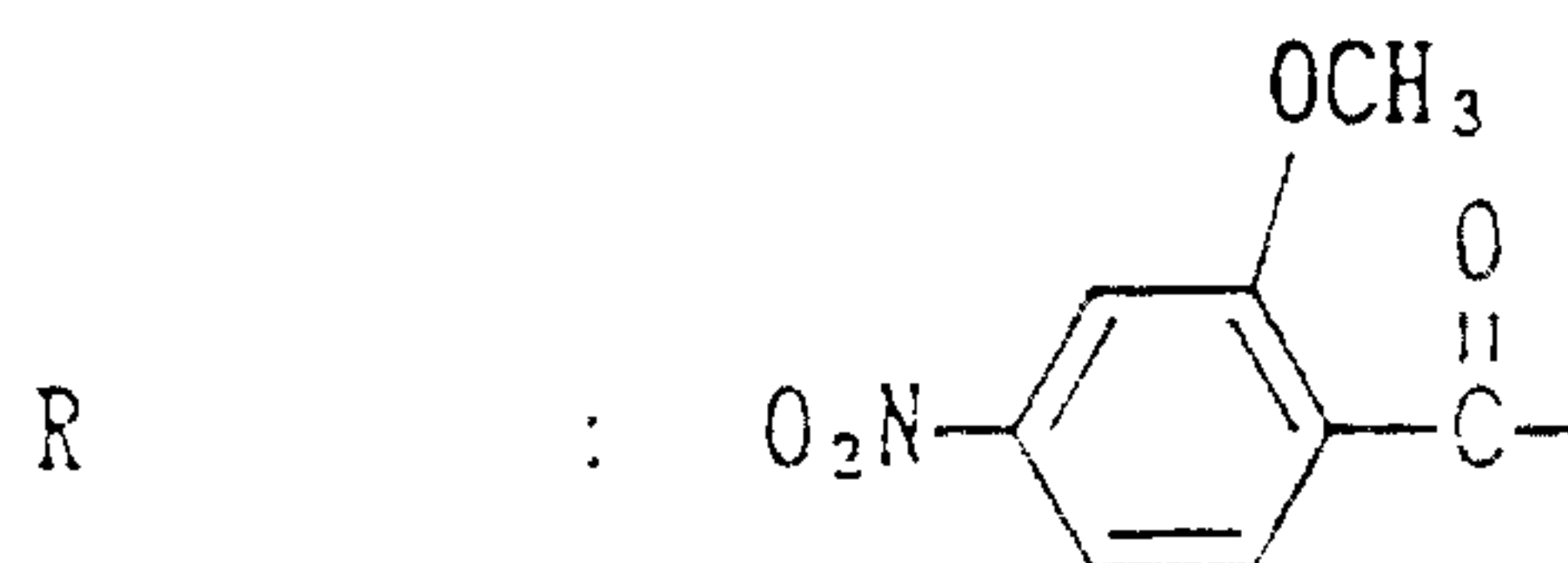
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 222-223

Salt form: hydrochloride

Example 69

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

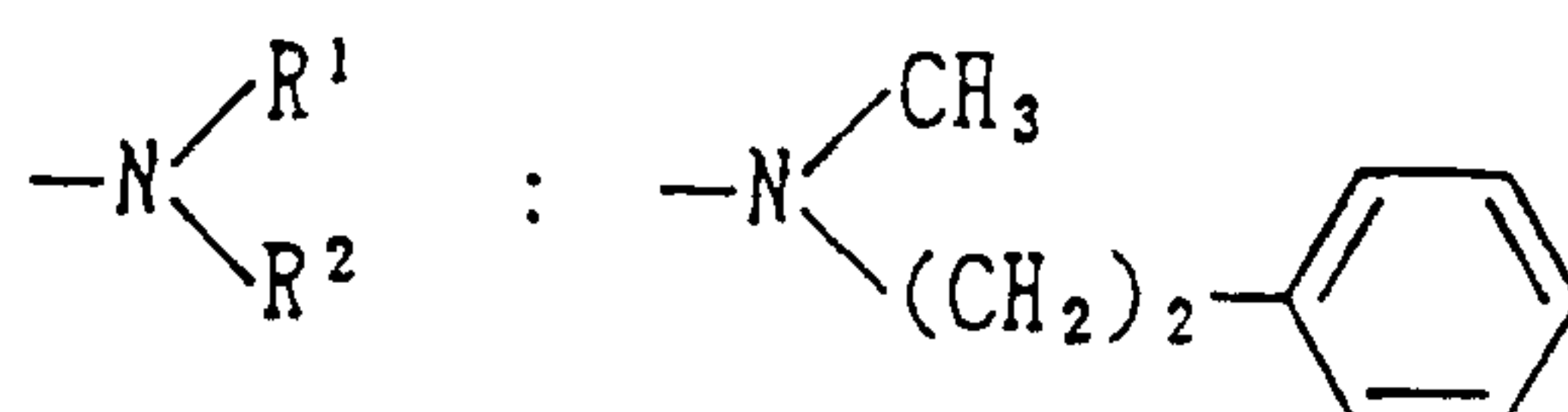
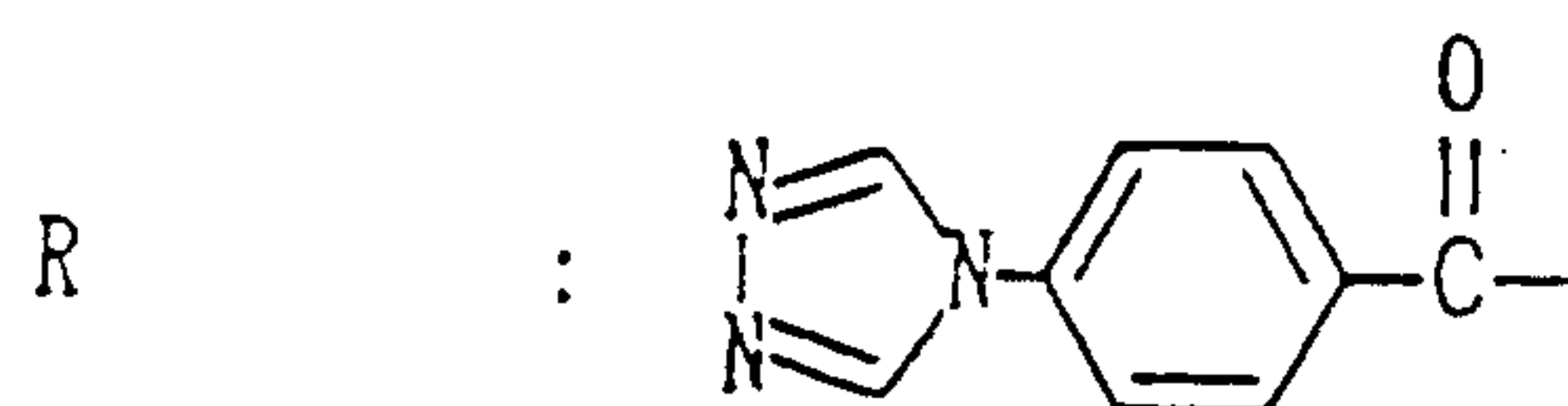
Melting point (°C): 203-204.5

Salt form: hydrochloride

{Table 10 (continued)}

Example 70

Structural formula:



Crystal form: white powder

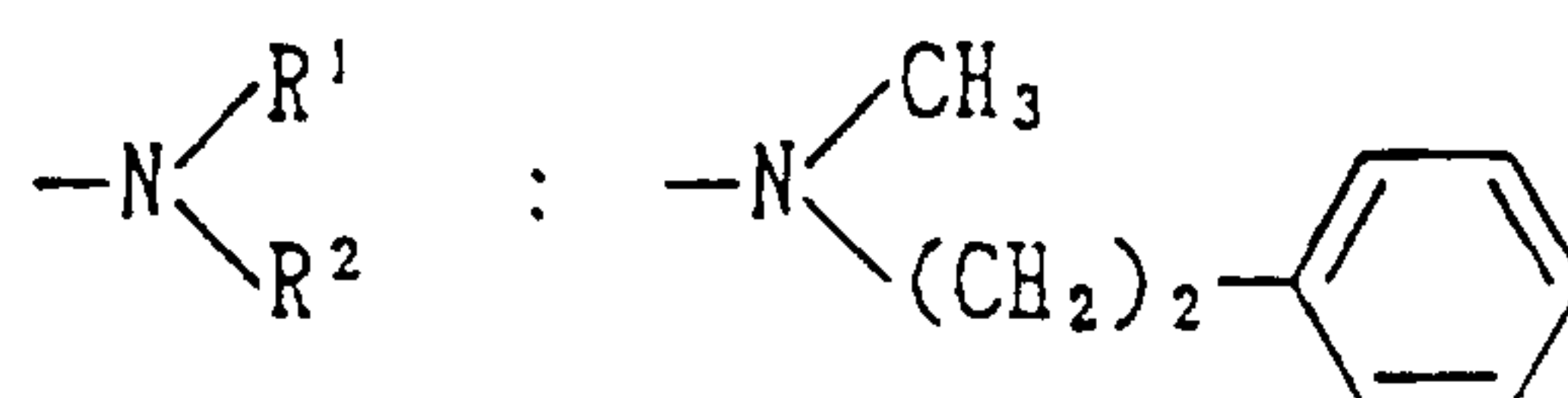
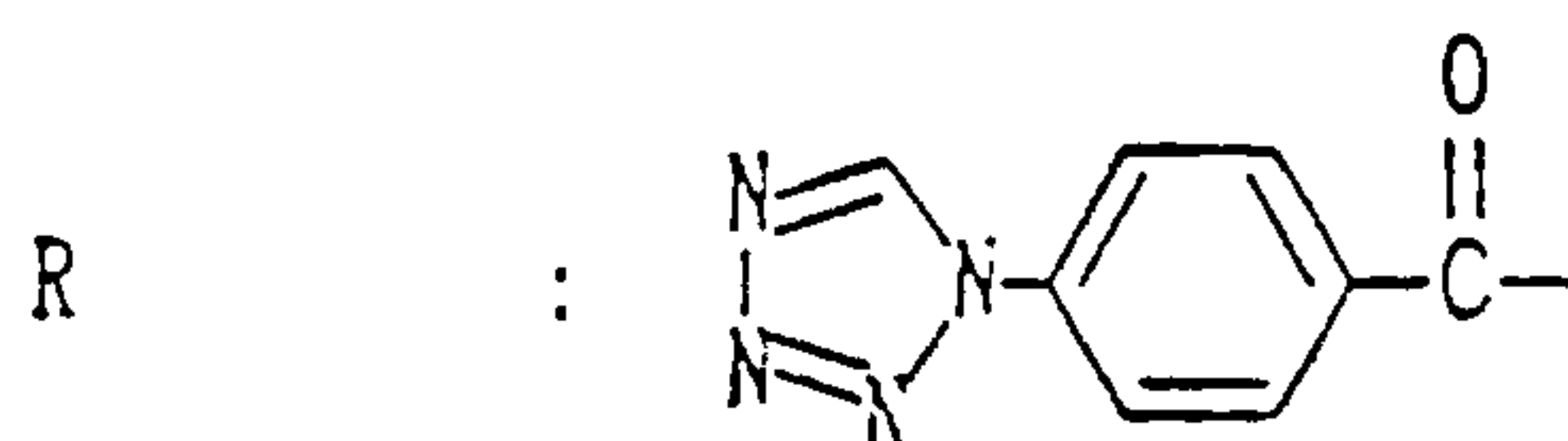
Melting point (°C): 226-237

Salt form: dihydrochloride

NMR value: 59)

Example 71

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-n-hexane

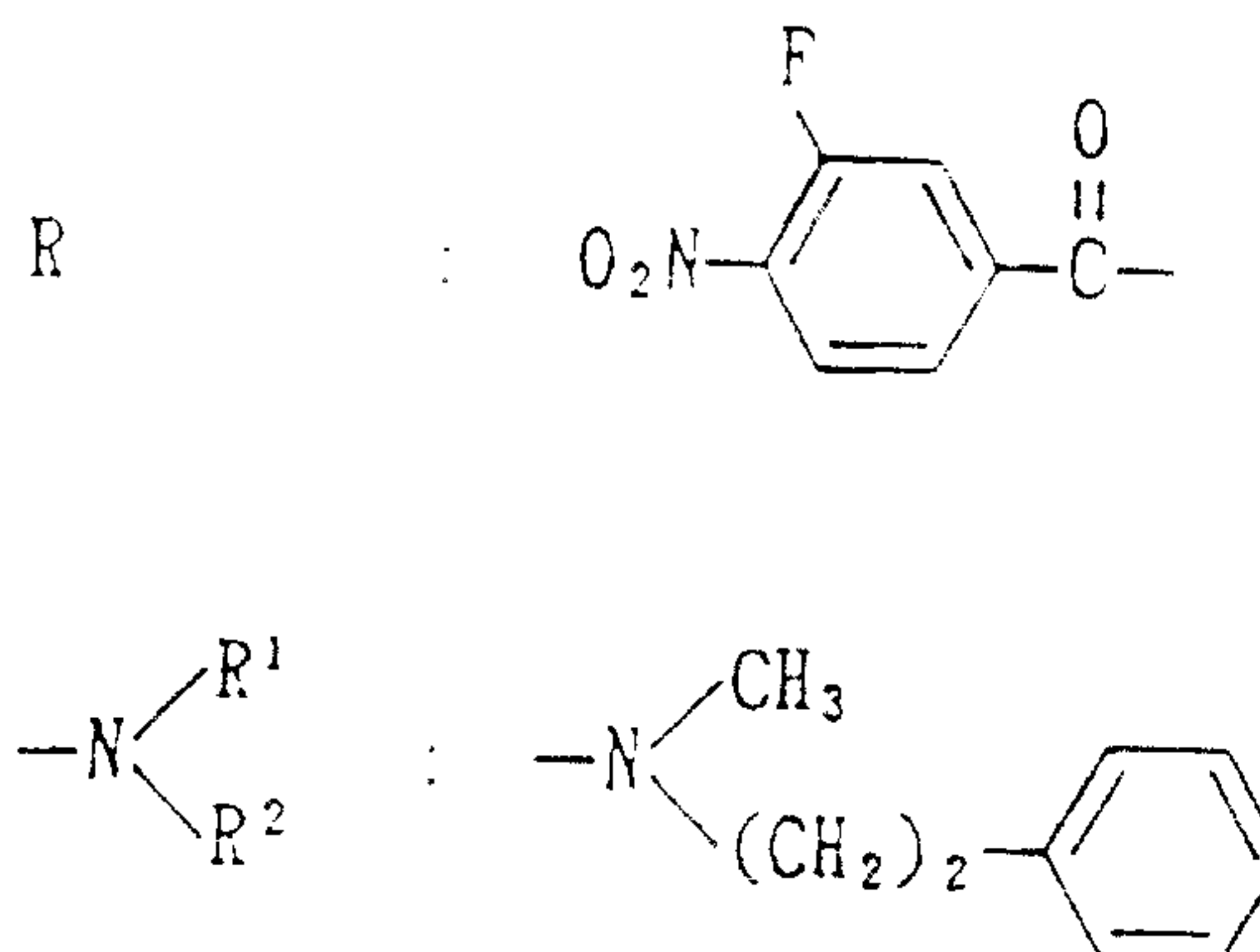
Melting point (°C): 70-72

Salt form: free

[Table 10 (continued)]

Example 72

Structural formula:



Crystal form: yellow powder

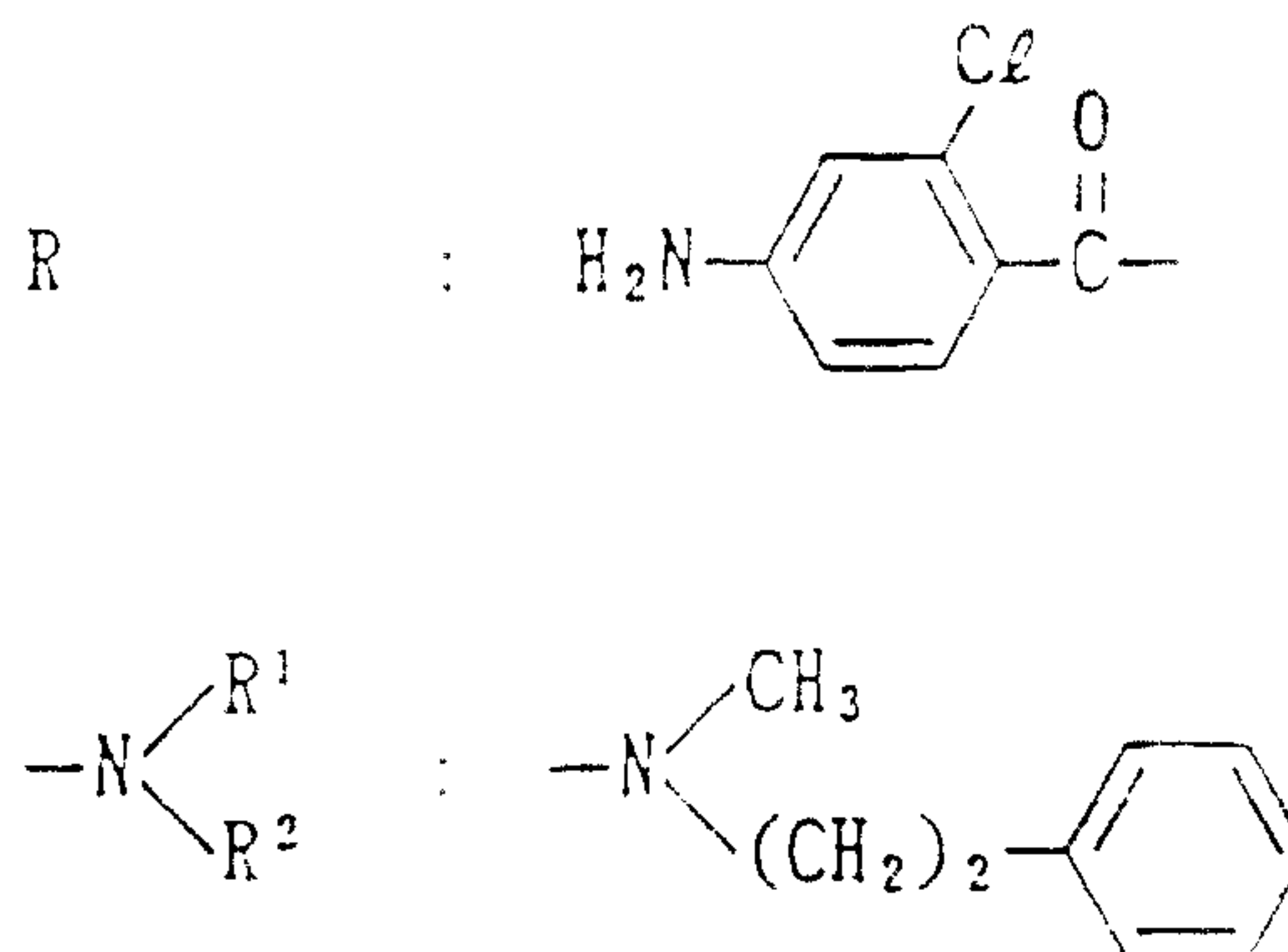
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 210-210.5

Salt form: hydrochloride

Example 73

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

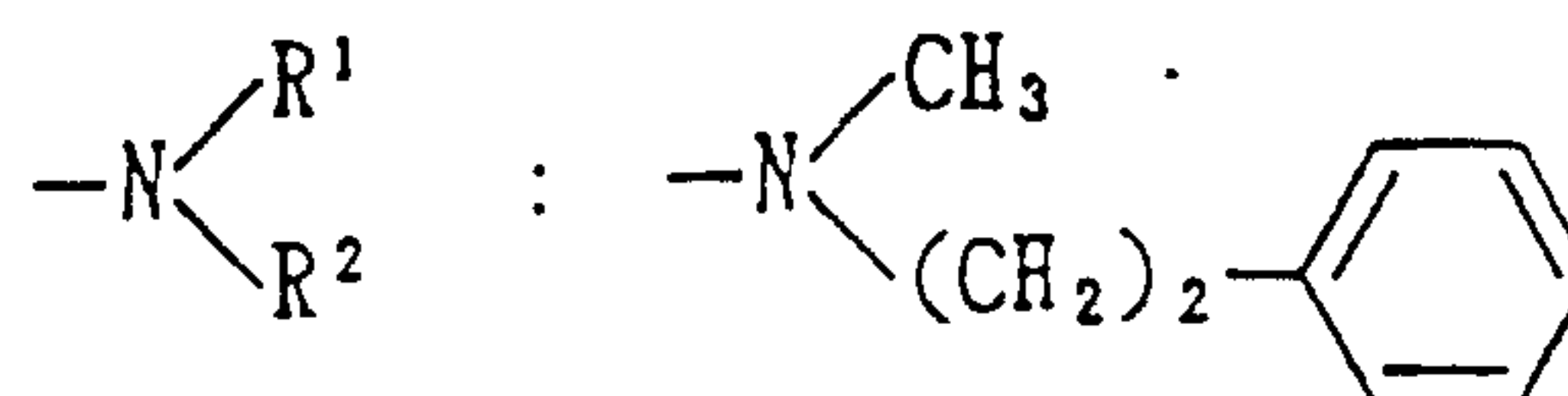
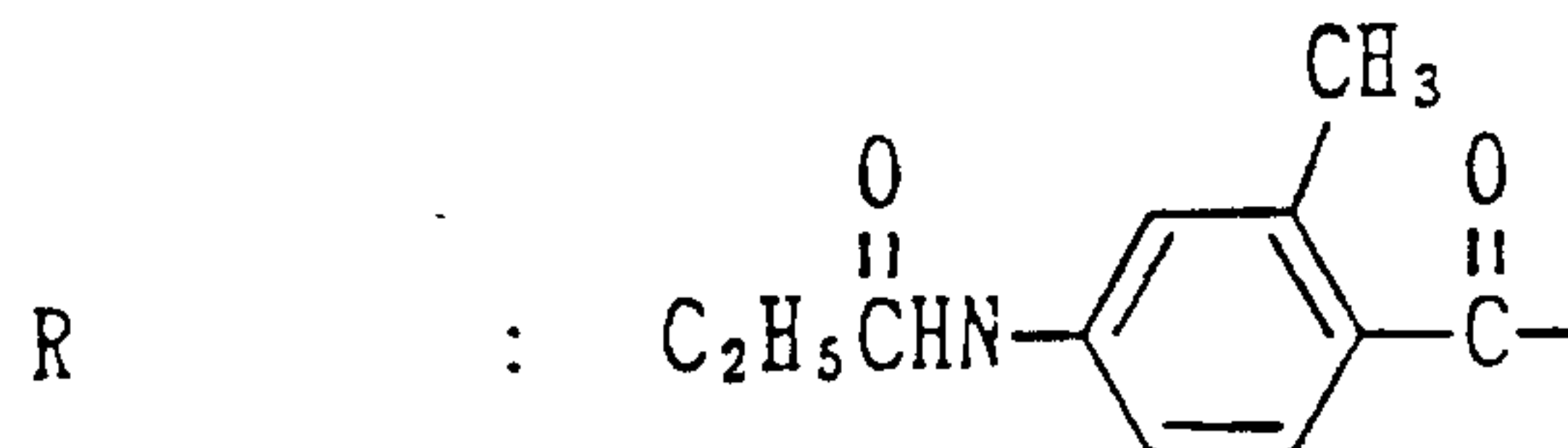
Melting point (°C): 128.5-130

Salt form: oxalate

{Table 10 (continued)}

Example 74

Structural formula:



Crystal form: white powder

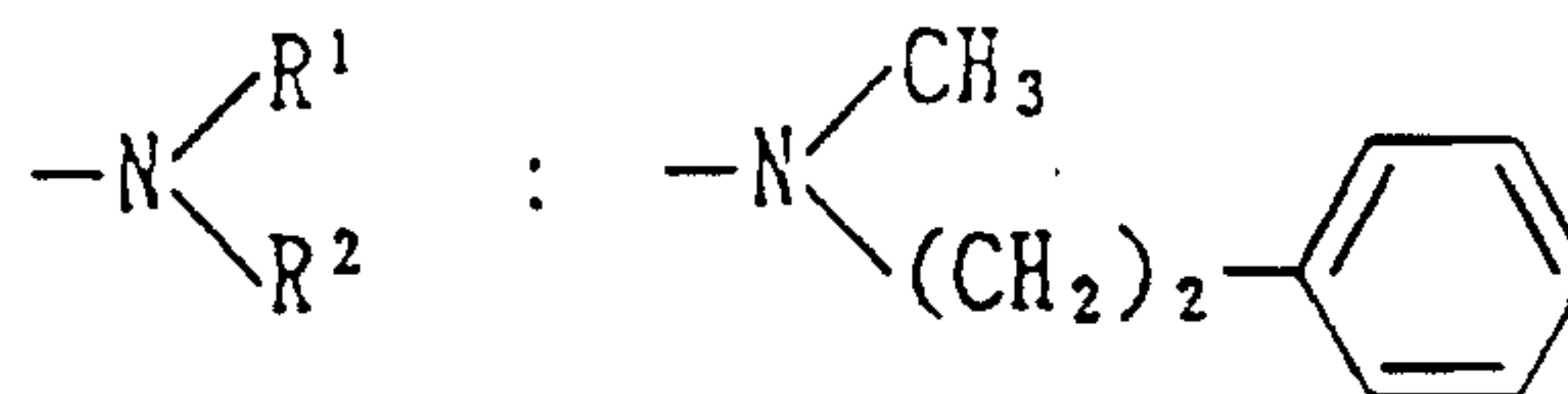
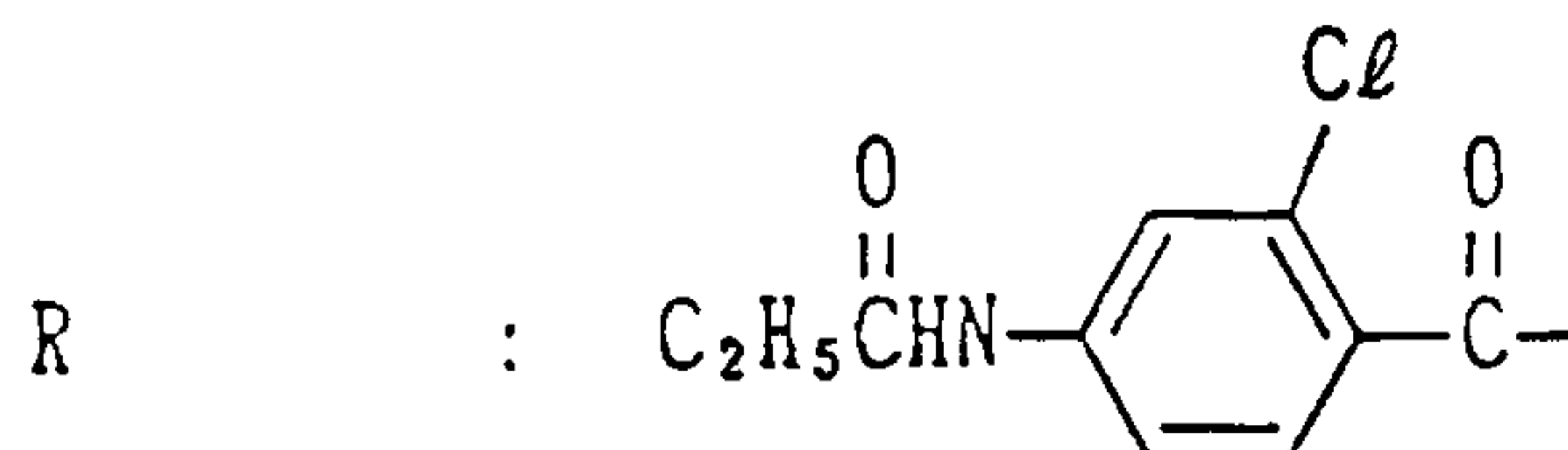
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 231.5-232.5

Salt form: hydrochloride

Example 75

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

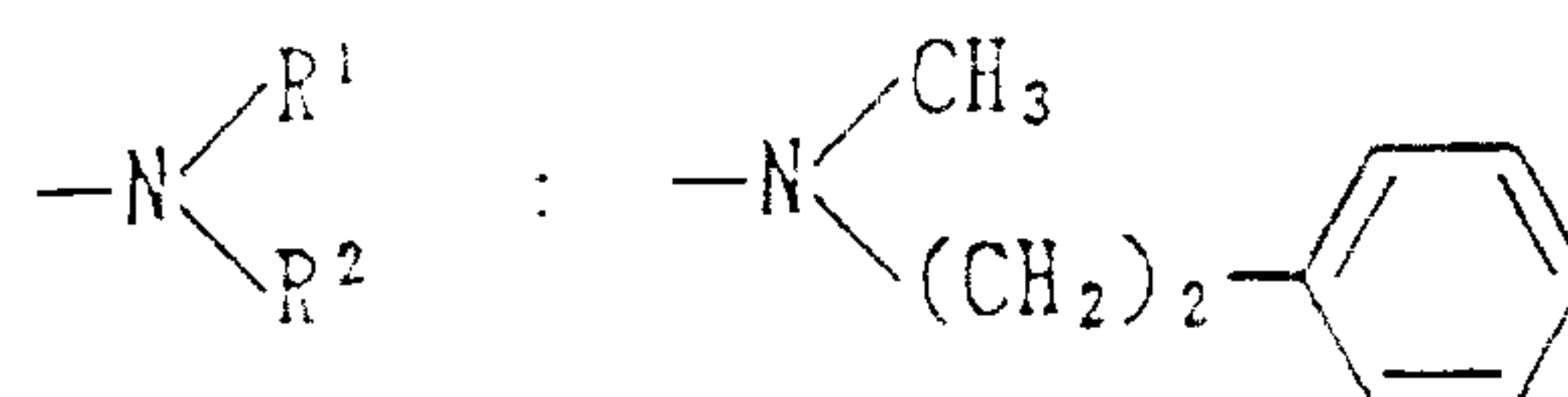
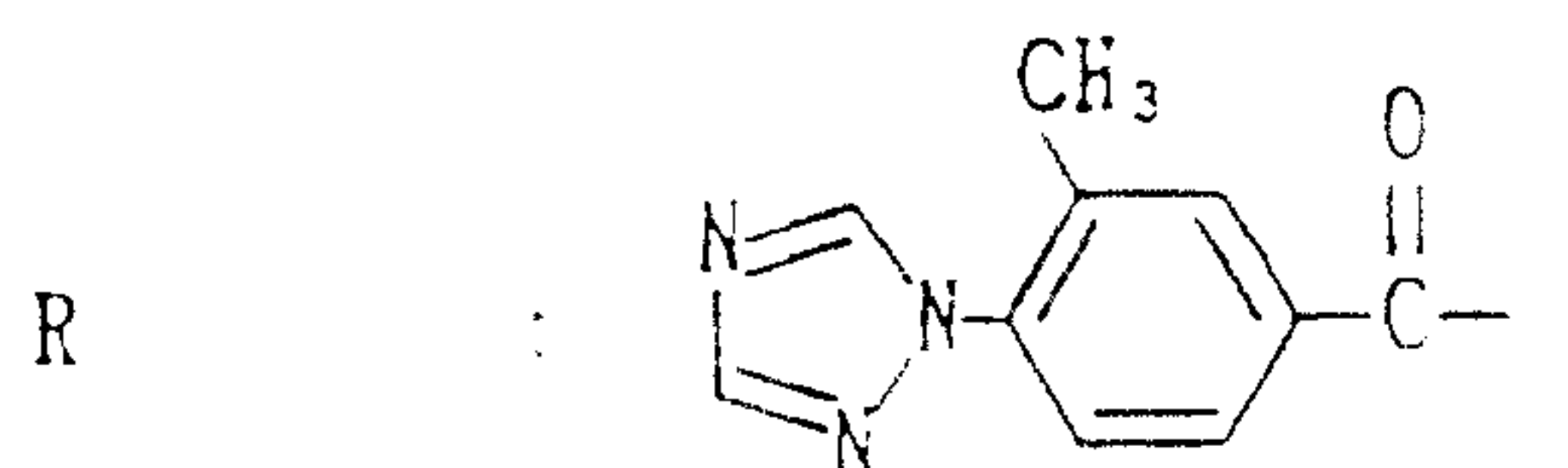
Melting point (°C): 195-196

Salt form: hydrochloride

{Table 10 (continued)}

Example 76

Structural formula:



Crystal form: white powder

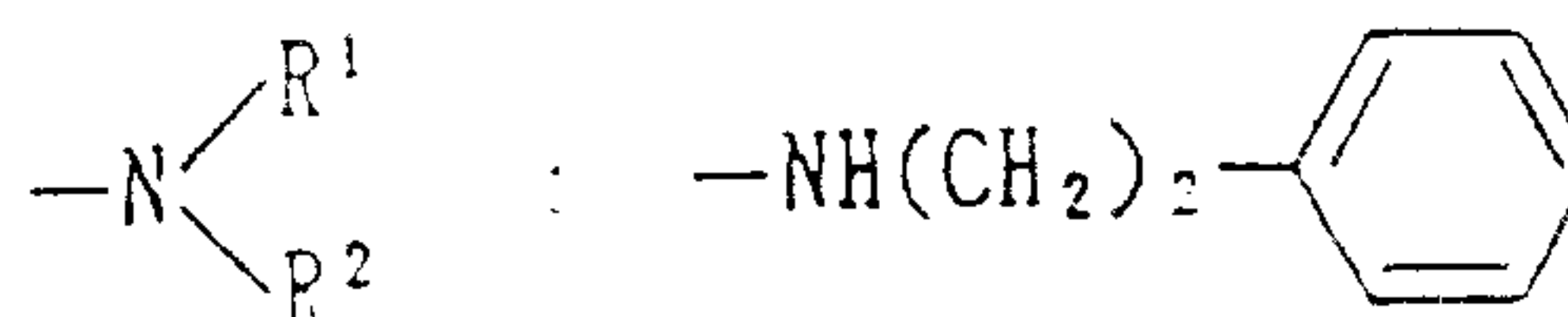
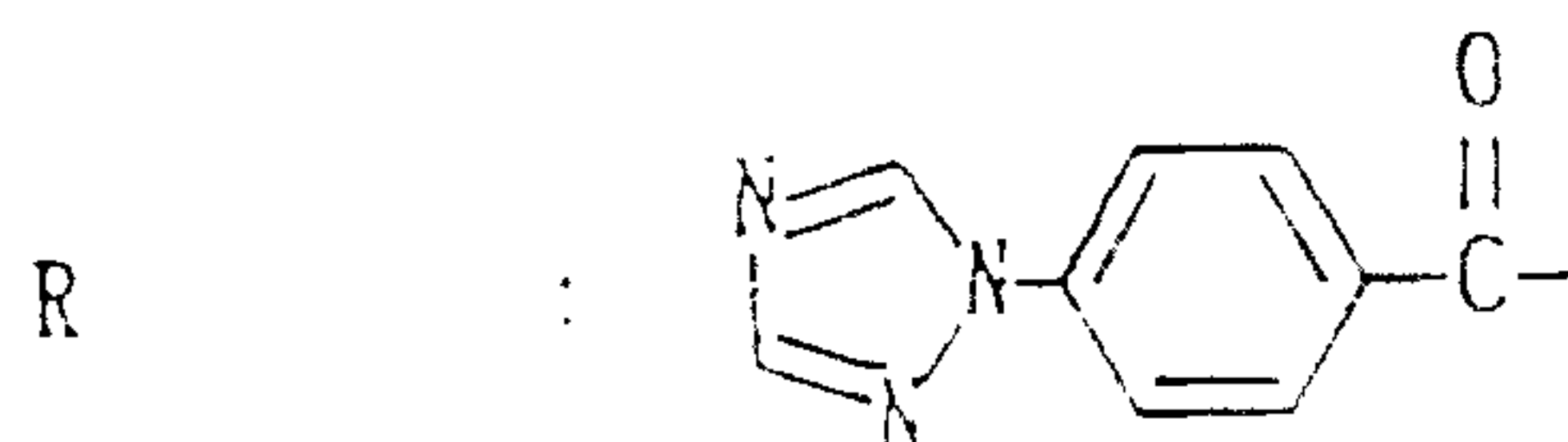
Recrystallization solvent: ethyl acetate-n-hexane

Melting point (°C): 92-94

Salt form: free

Example 77

Structural formula:



Crystal form: colorless thick syrup

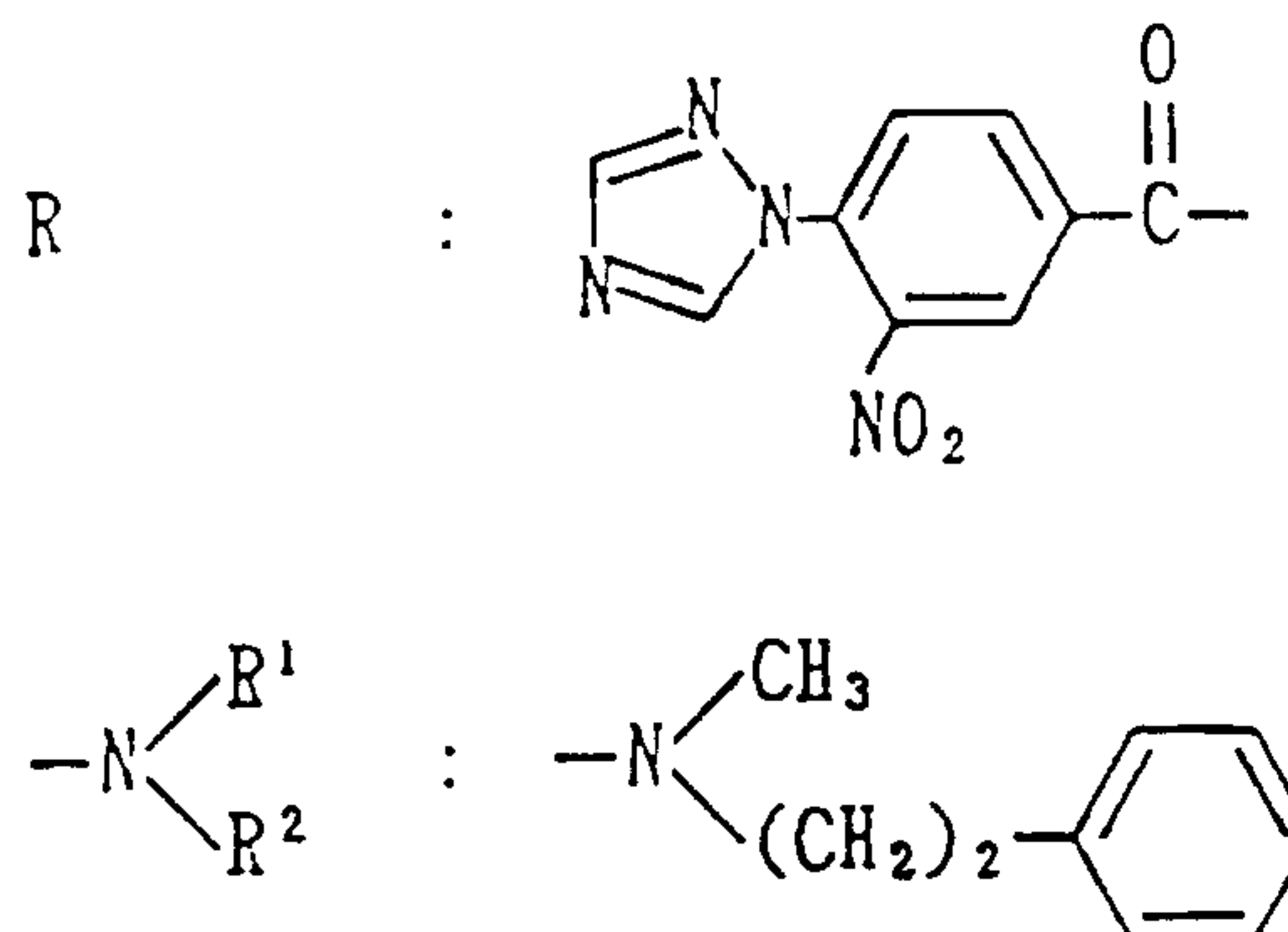
Salt form: free

NMR value: 63)

[Table 10 (continued)]

Example 78

Structural formula:



Crystal form: white powder

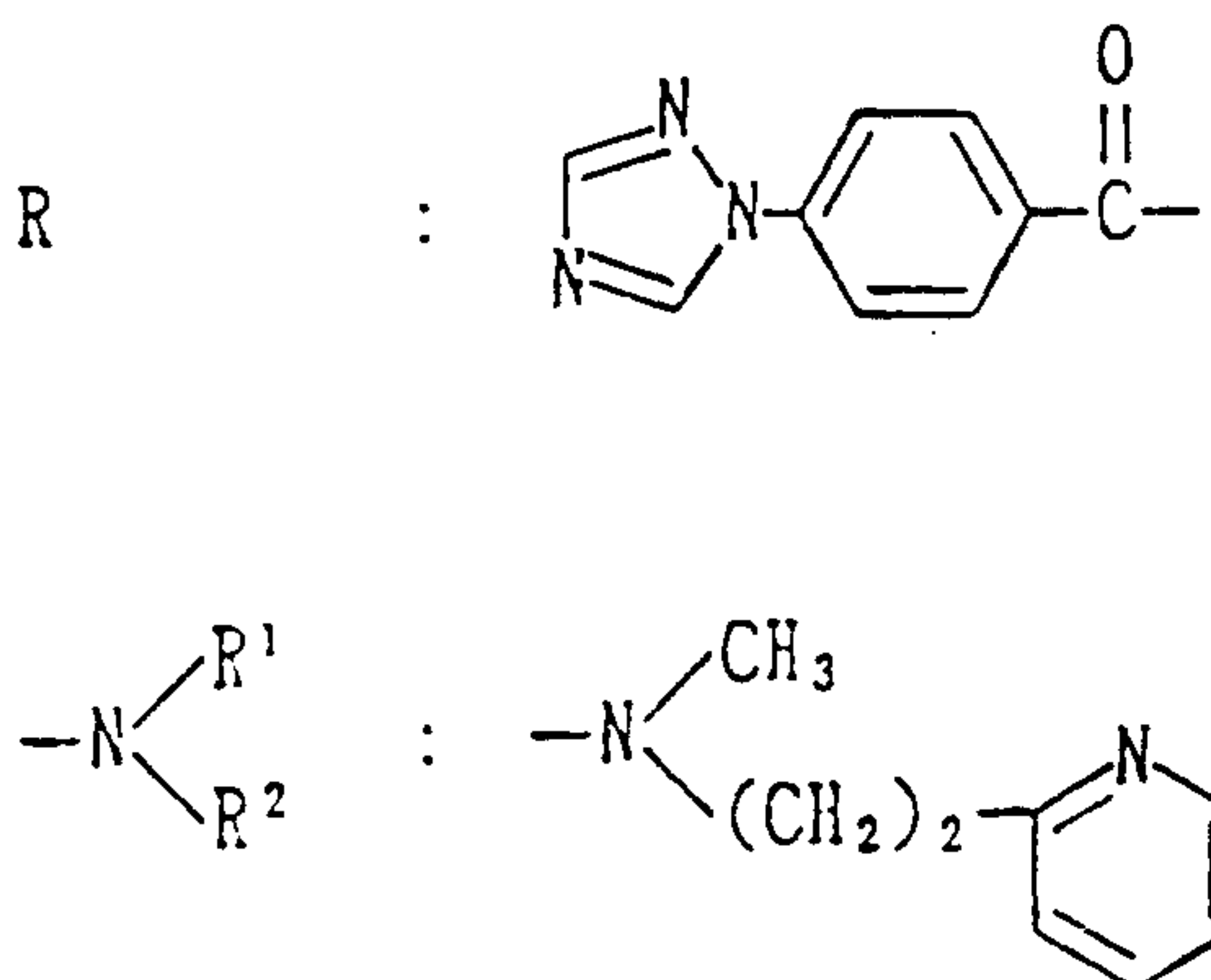
Recrystallization solvent: ethyl acetate-diethyl ether

Melting point (°C): 118.5-120.5

Salt form: free

Example 79

Structural formula:



Crystal form: white amorphous

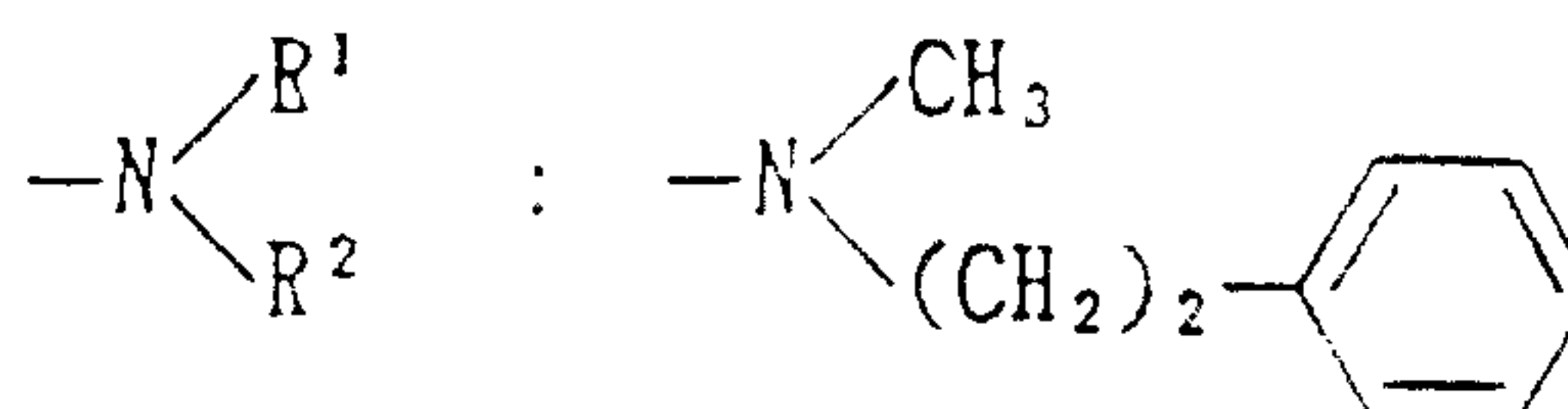
Salt form: dihydrochloride

NMR value: 60)

{Table 10 (continued)}

Example 80

Structural formula:



Crystal form: yellow prisms

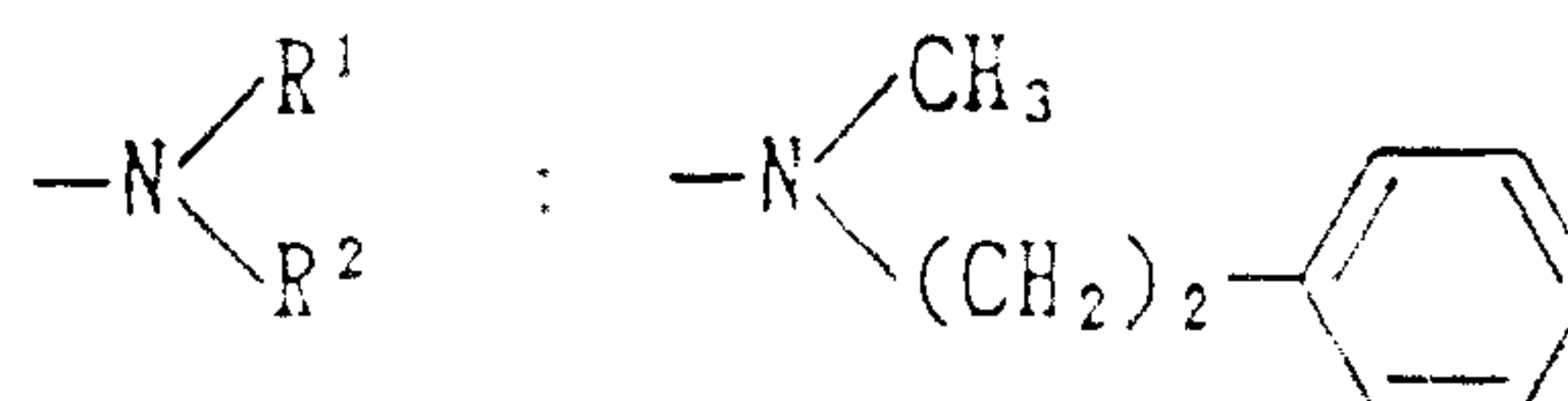
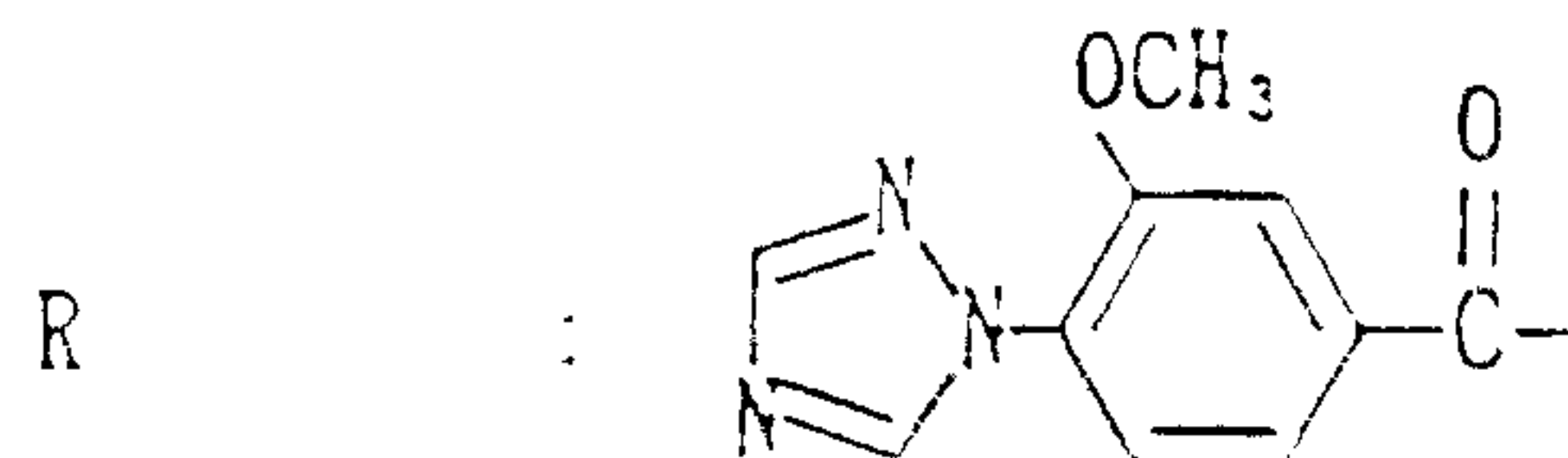
Recrystallization solvent: ethanol

Melting point (°C): 171-171.5

Salt form: free

Example 81

Structural formula:



Crystal form: white amorphous

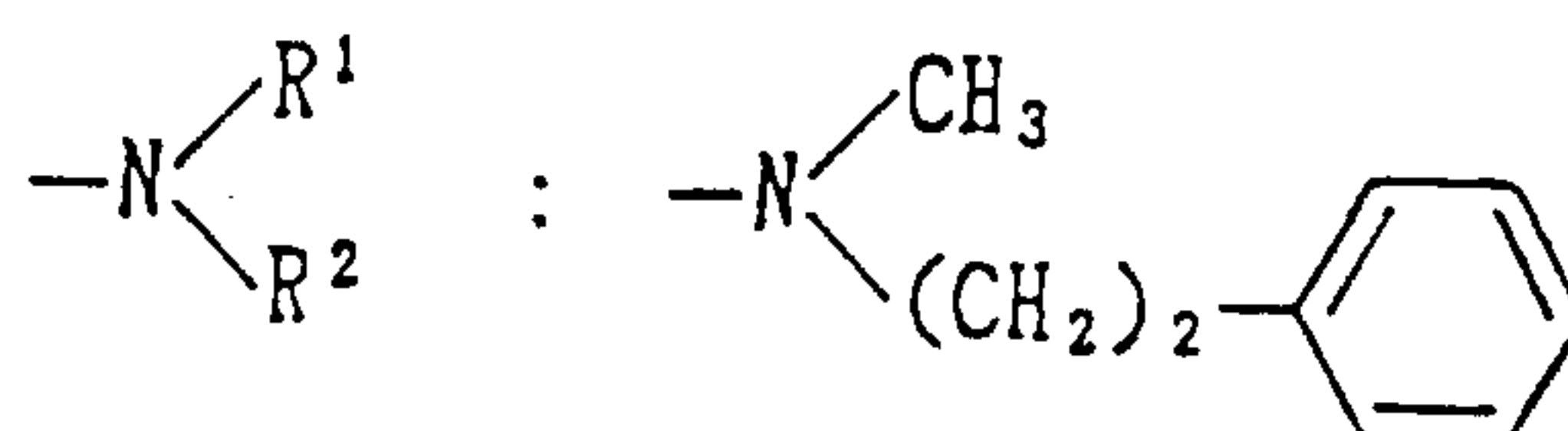
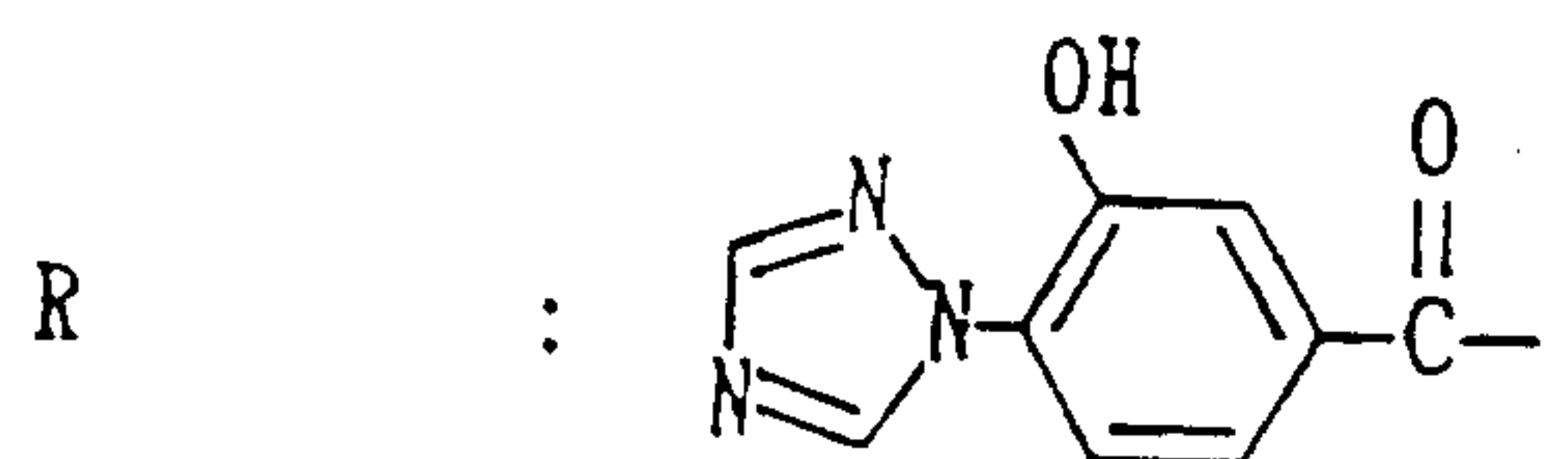
Salt form: hydrochloride

NMR value: 61)

[Table 10 (continued)]

Example 82

Structural formula:



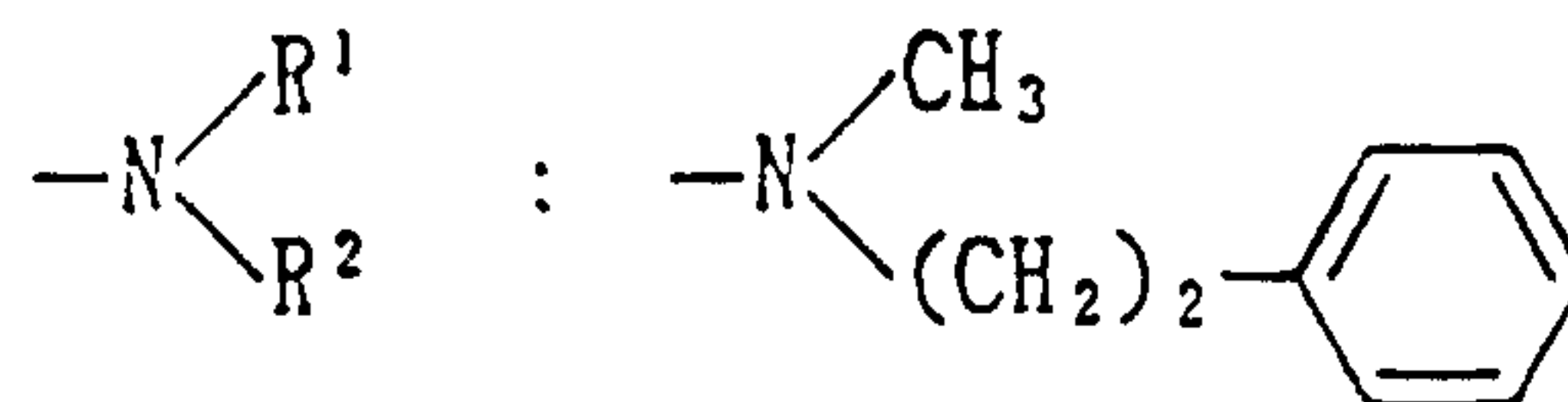
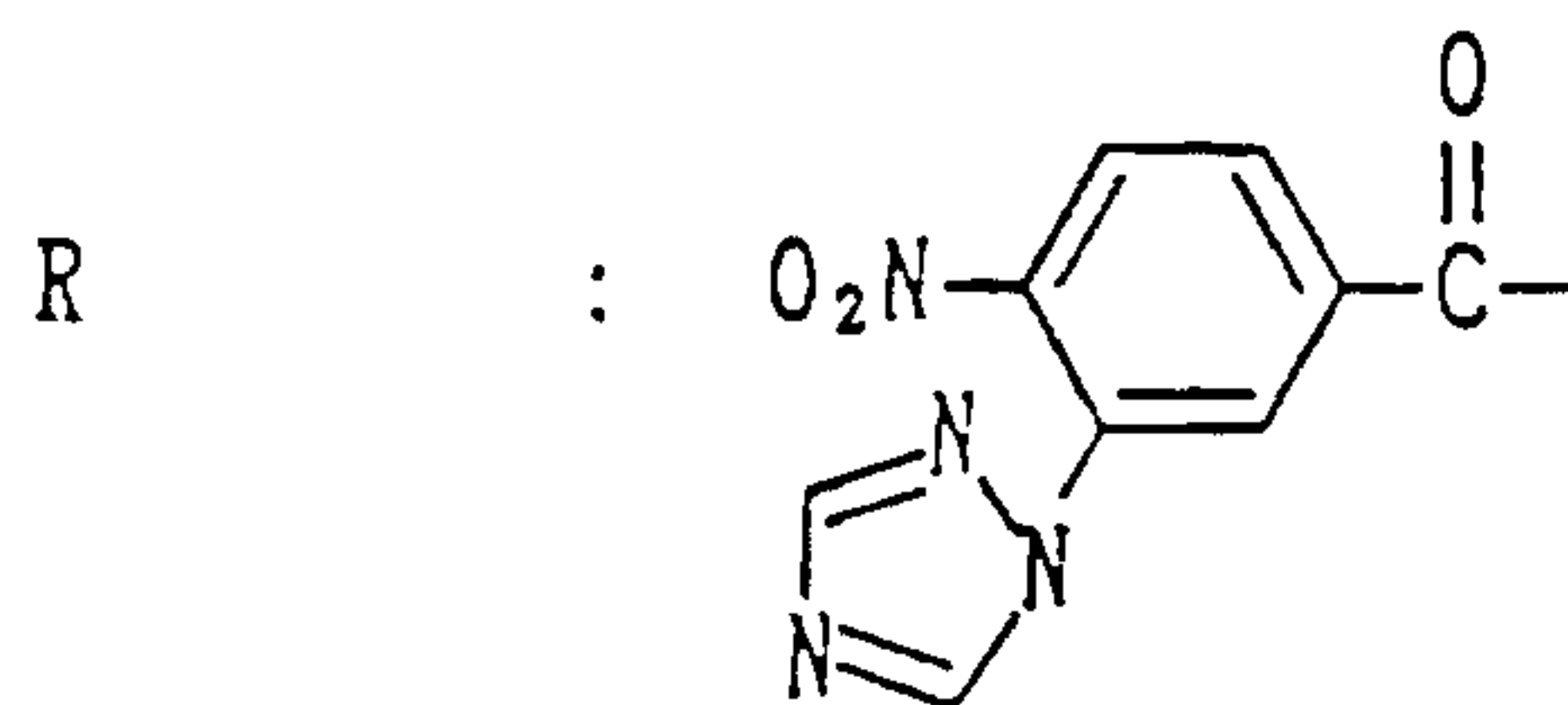
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 62)

Example 83

Structural formula:



Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 64)

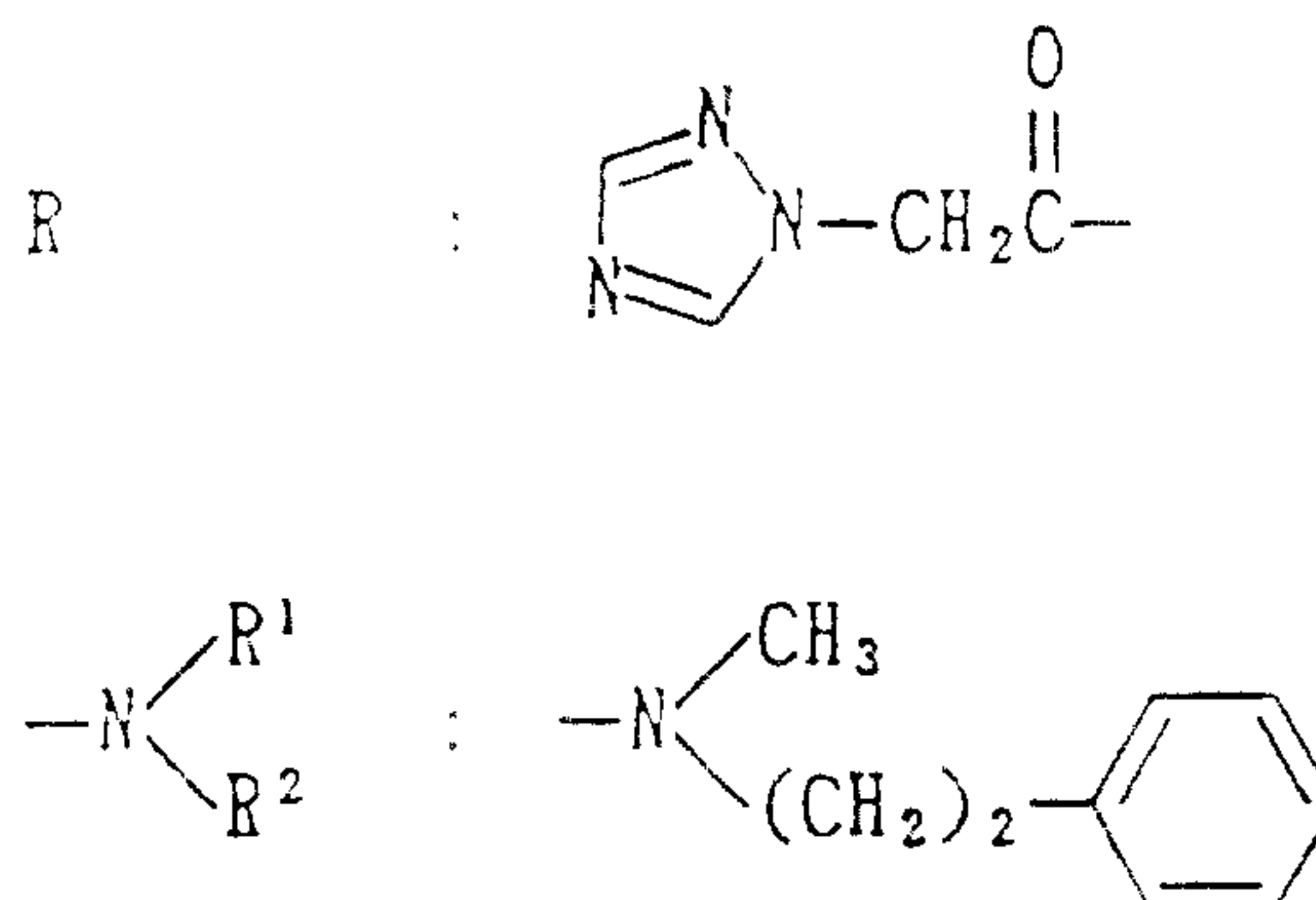
2136999

- 234 -

{Table 10 (continued)}

Example 84

Structural formula:



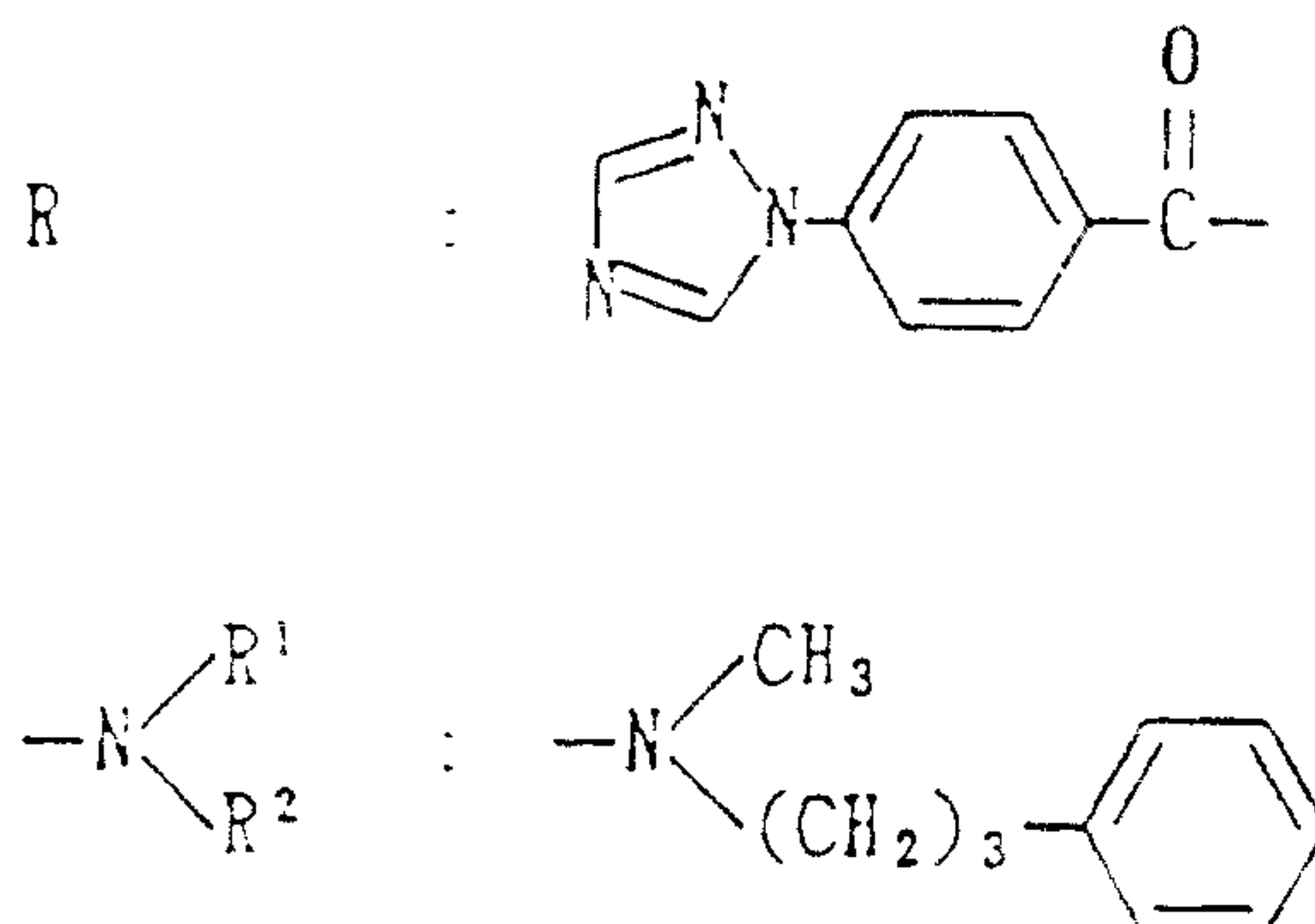
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 65)

Example 85

Structural formula:



Crystal form: white amorphous

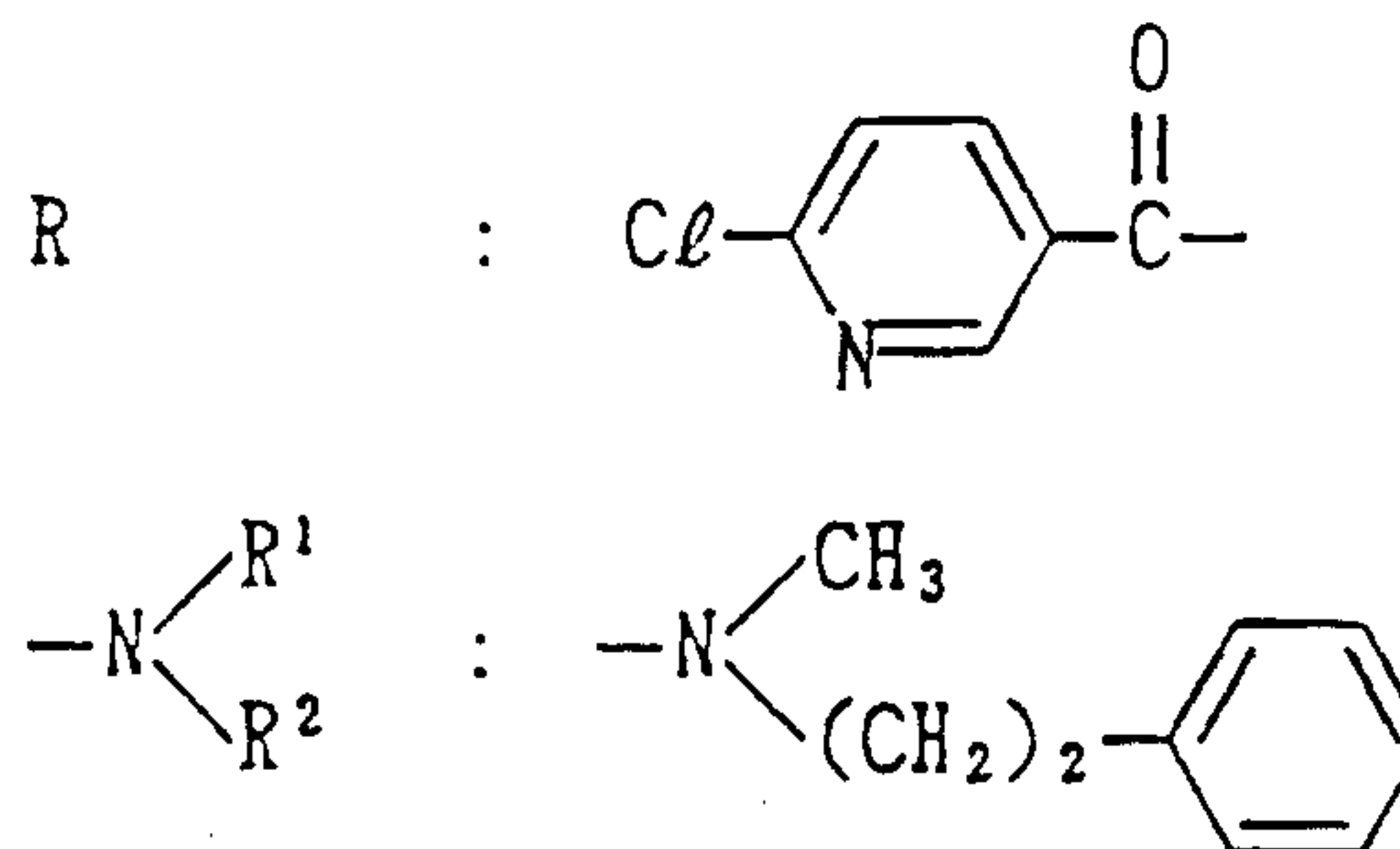
Salt form: hydrochloride

NMR value: 66)

{Table 10 (continued)}

Example 86

Structural formula:



Crystal form: white powder

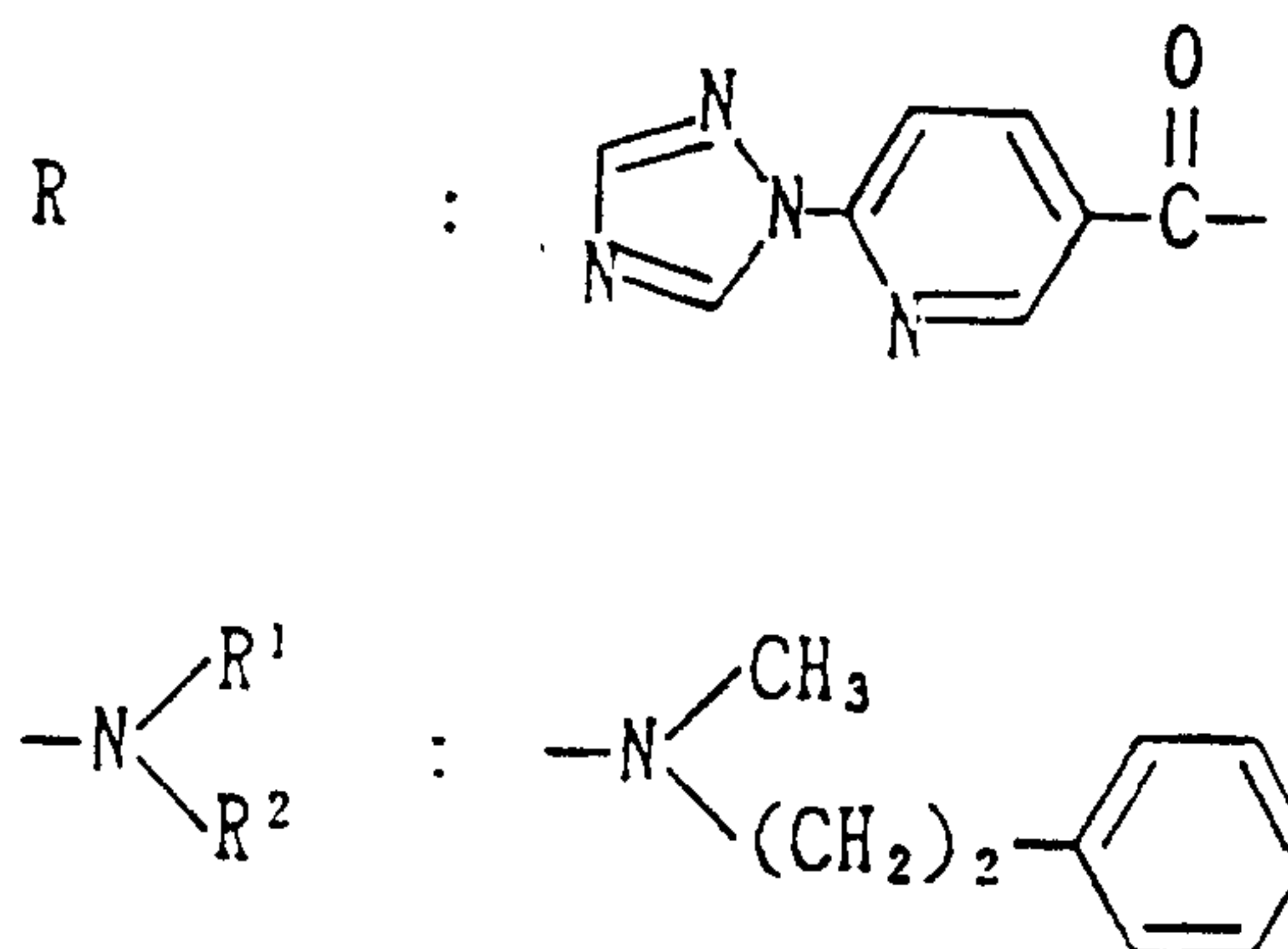
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 210-212

Salt form: hydrochloride

Example 87

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-diethyl ether

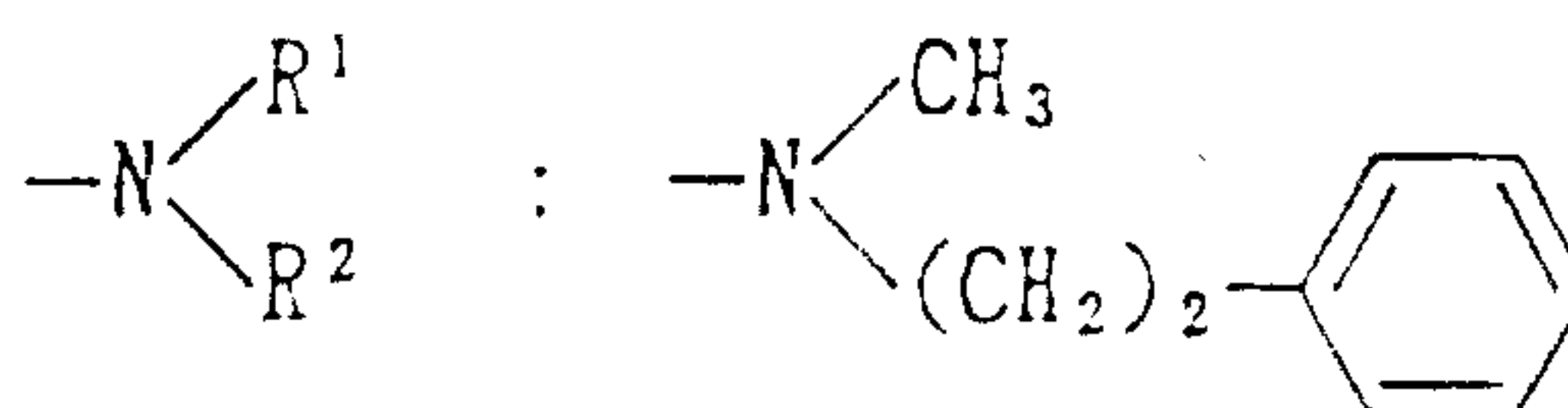
Melting point (°C): 85-86

Salt form: free

{Table 10 (continued)}

Example 88

Structural formula:



Crystal form: white powder

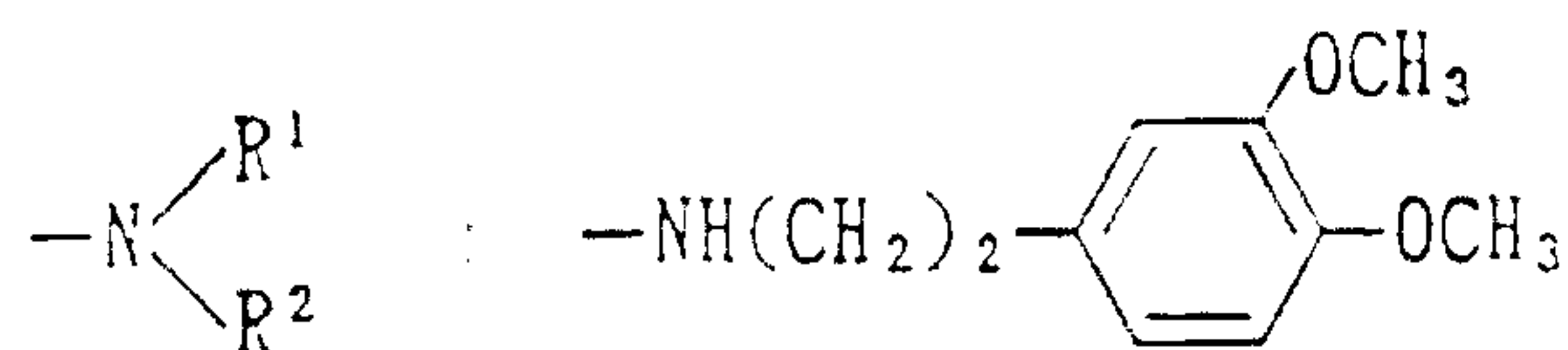
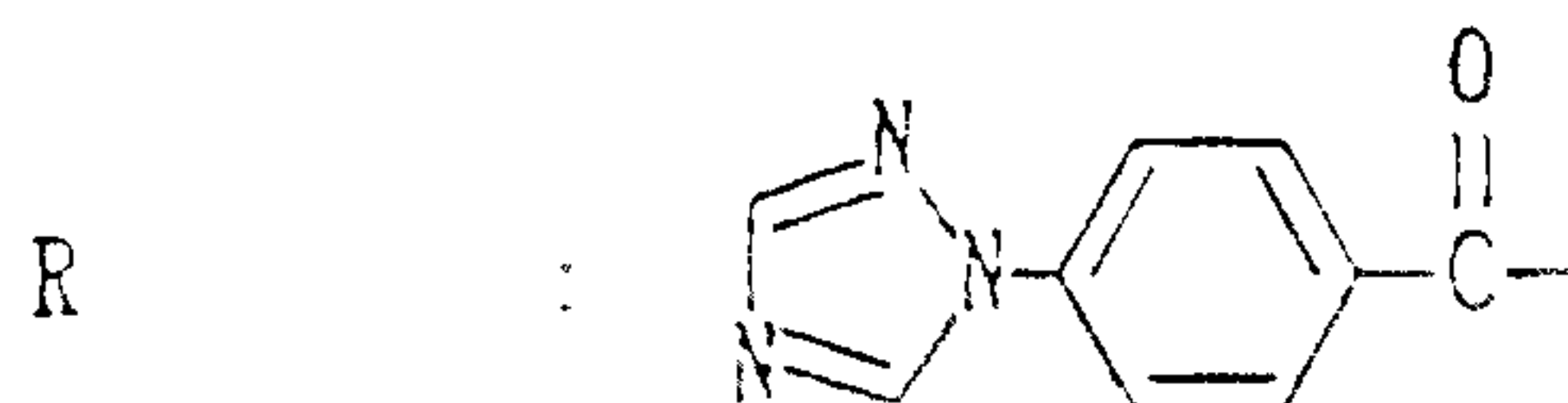
Recrystallization solvent: ethanol

Melting point (°C): 164-168

Salt form: oxalate

Example 89

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-n-hexane

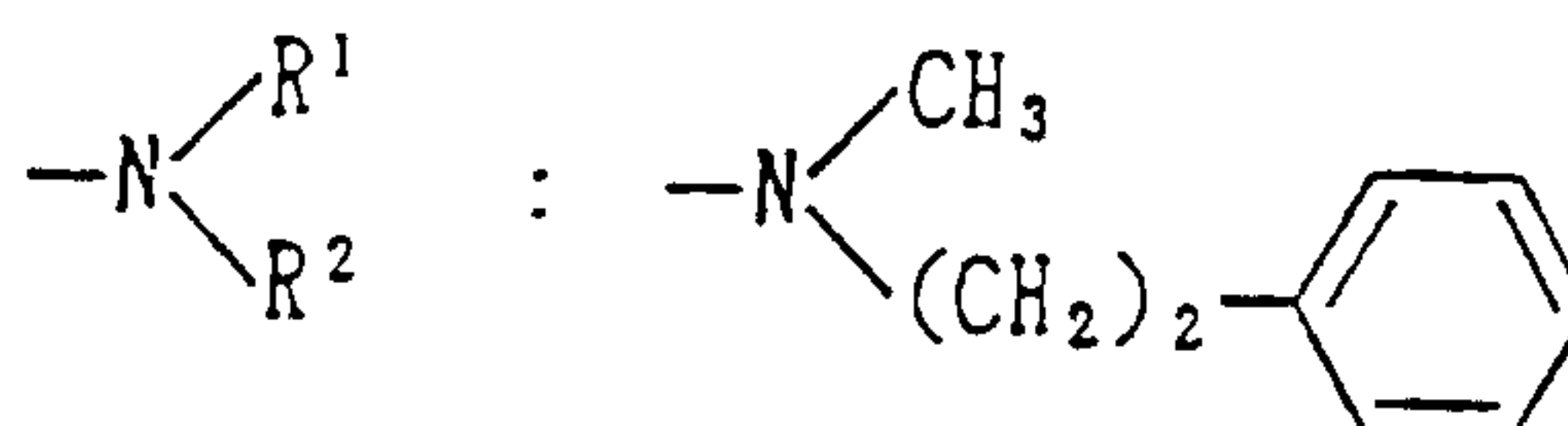
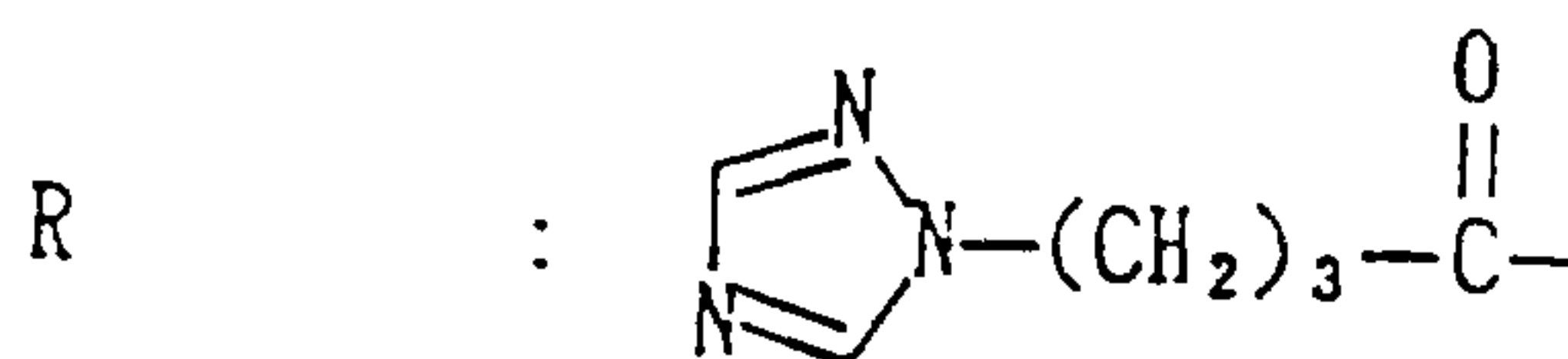
Melting point (°C): 114.5-116

Salt form: free

{Table 10 (continued)}

Example 90

Structural formula:



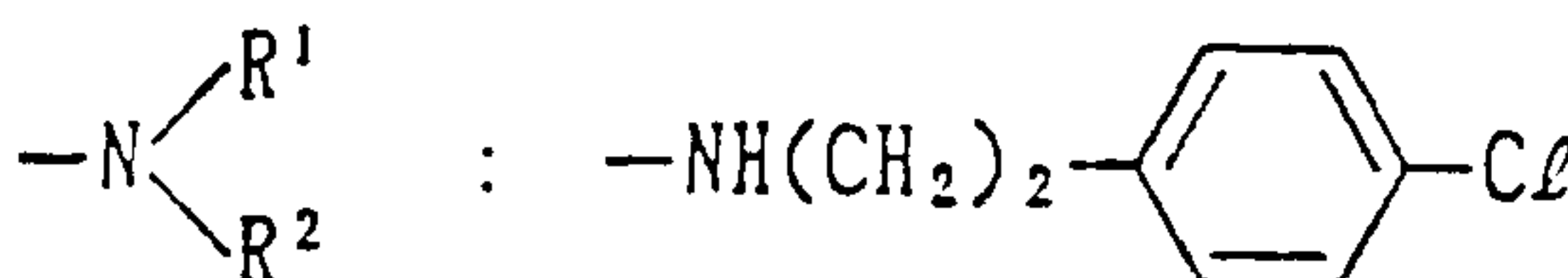
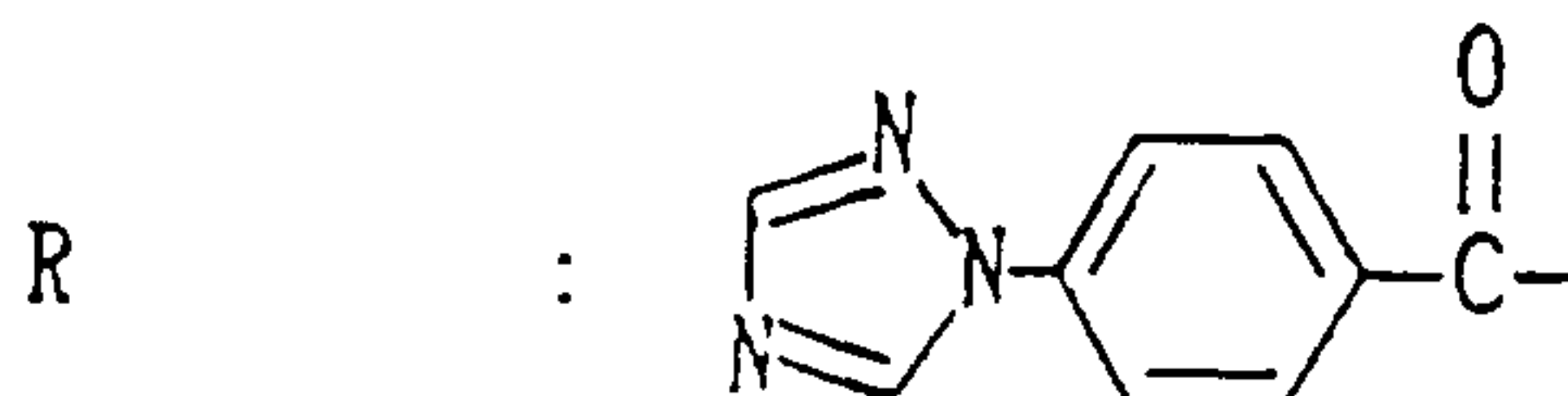
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 67)

Example 91

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate

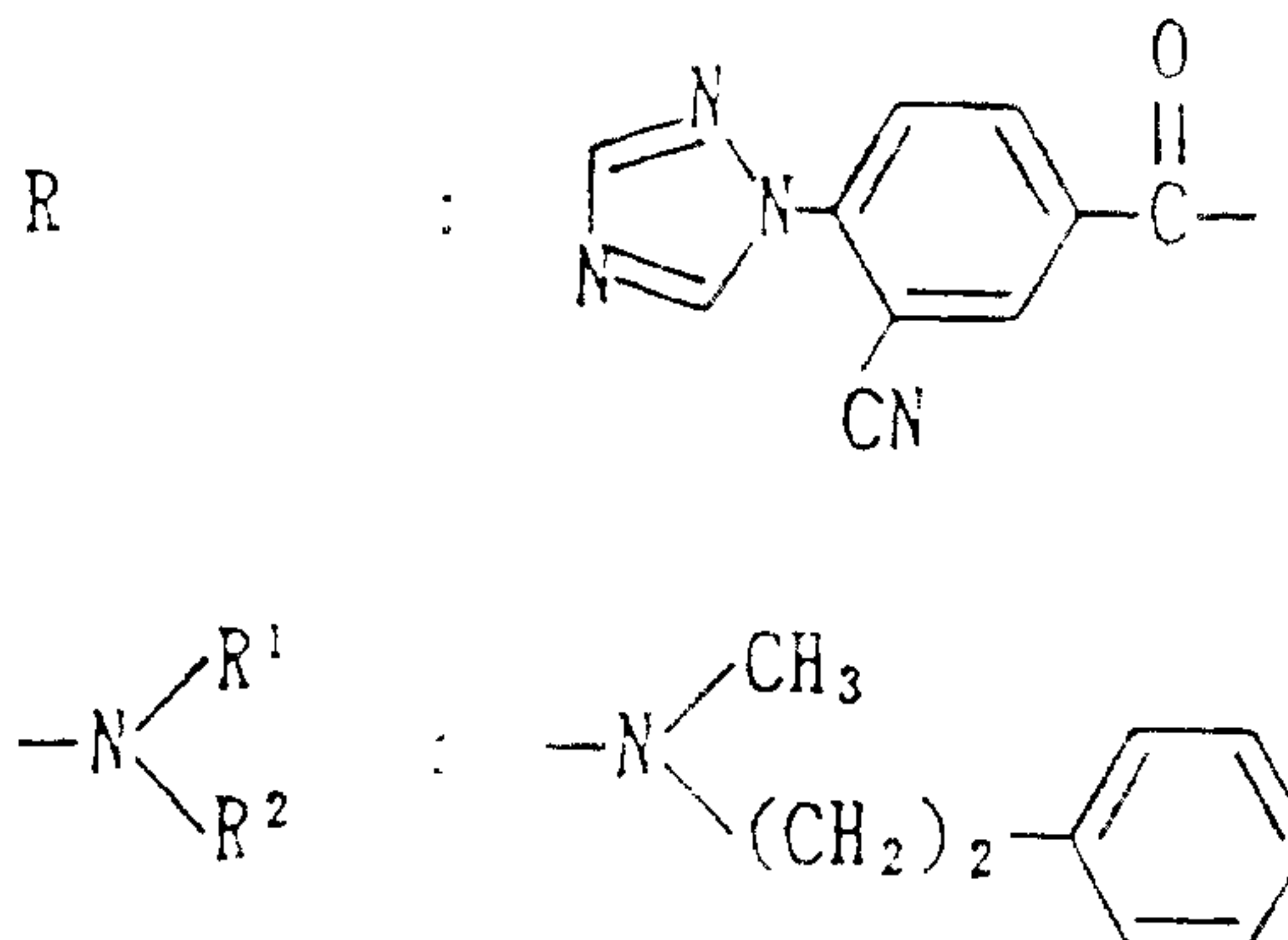
Melting point (°C): 131-132.5

Salt form: free

{Table 10 (continued)}

Example 92

Structural formula:



Crystal form: white powder

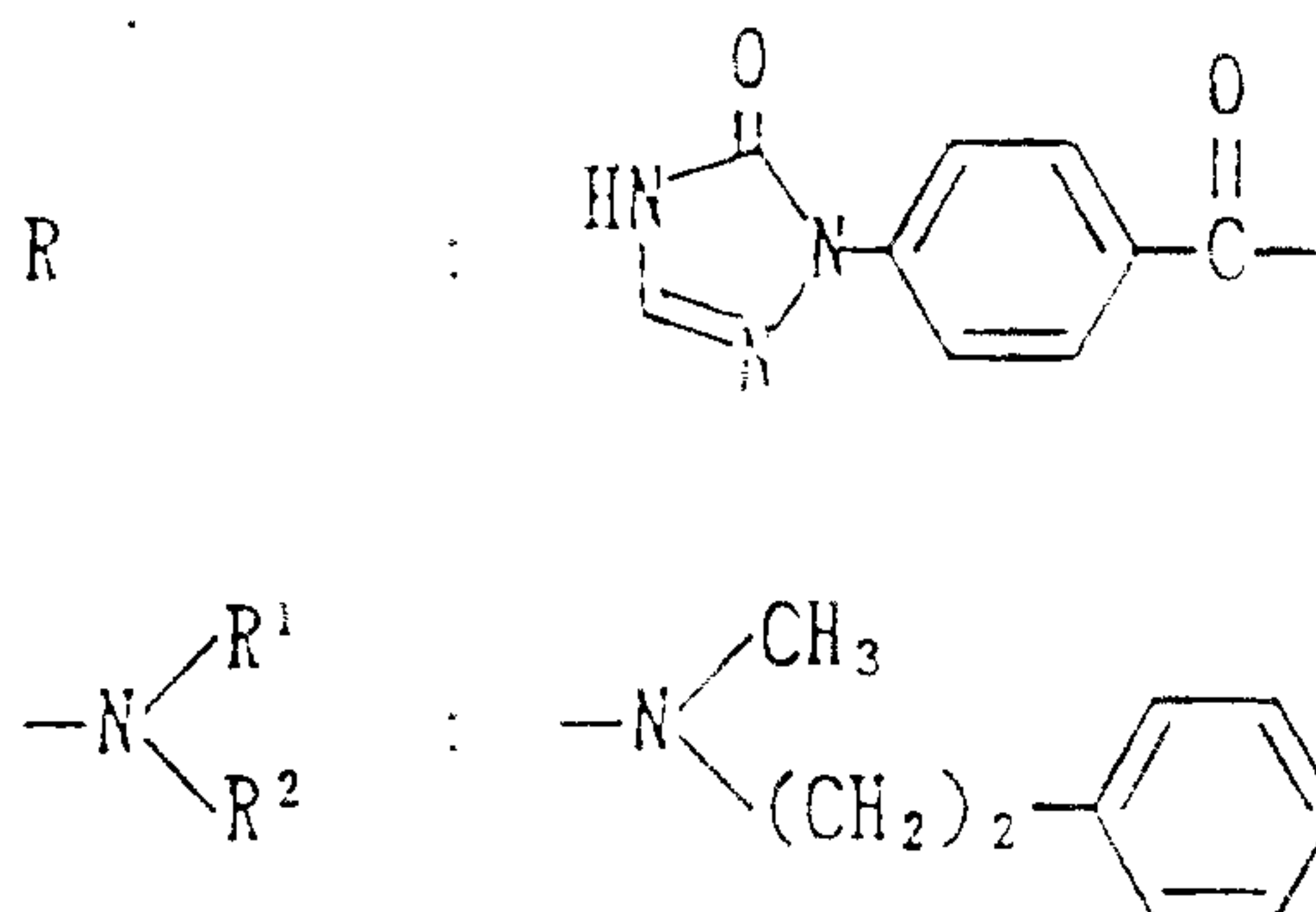
Recrystallization solvent: ethanol

Melting point (°C): 223-225.5

Salt form: hydrochloride

Example 93

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-water

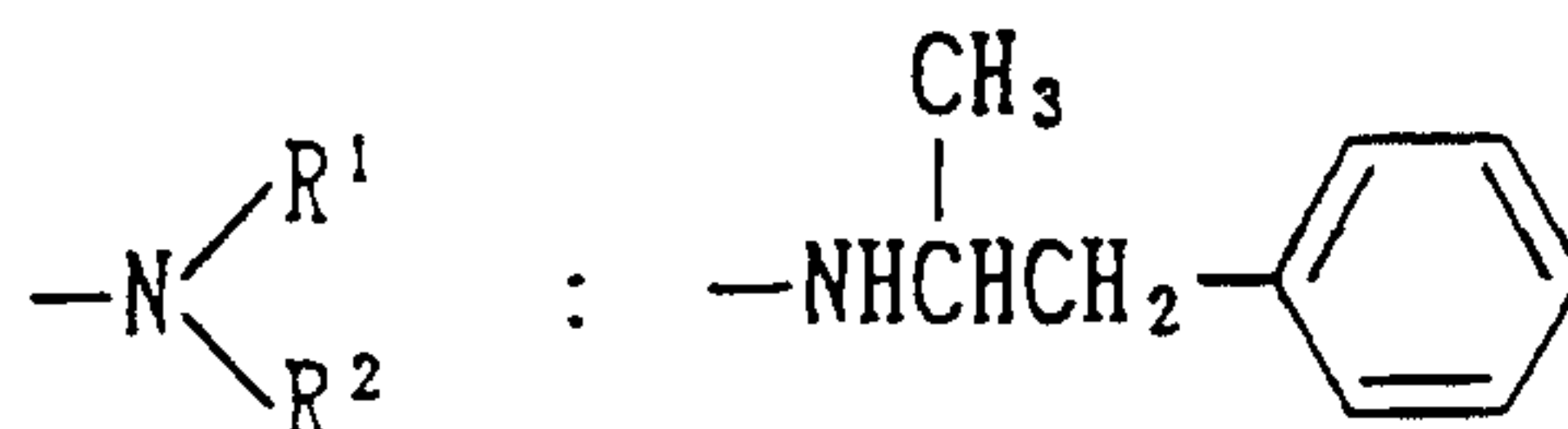
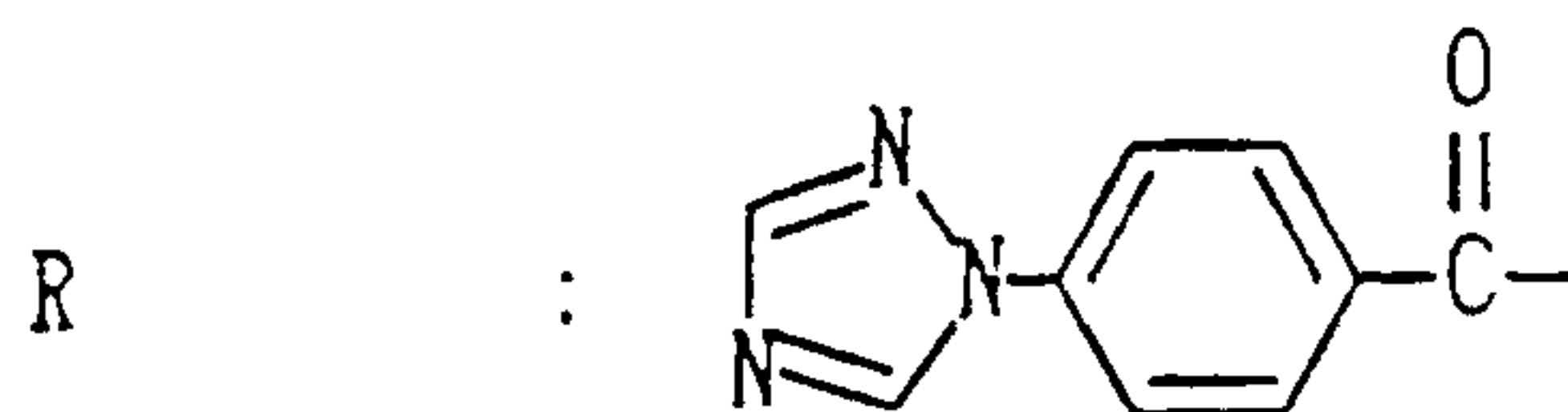
Melting point (°C): 279-281 (decompd.)

Salt form: hydrochloride

[Table 10 (continued)]

Example 94

Structural formula:



Crystal form: white powder

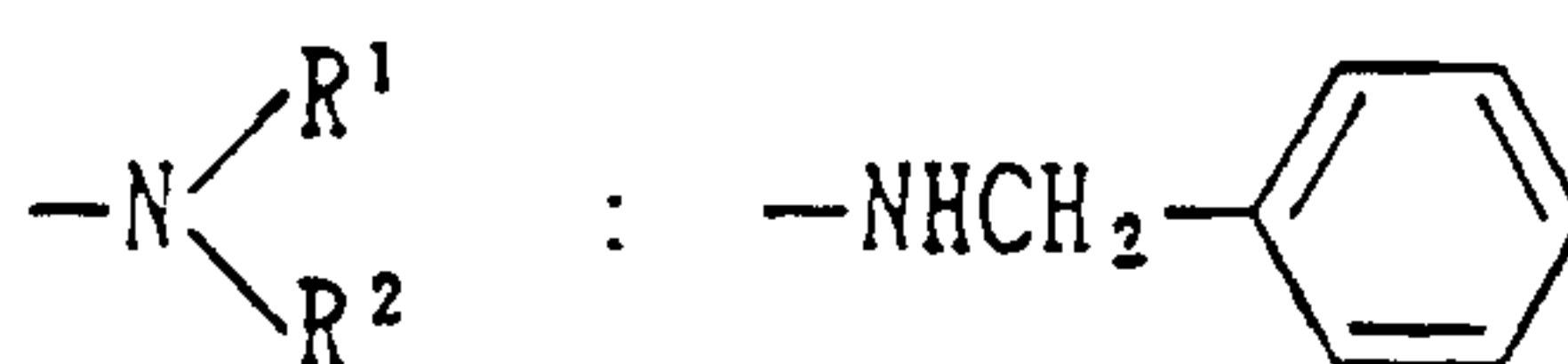
Recrystallization solvent: ethanol

Melting point (°C): 224-227

Salt form: oxalate

Example 95

Structural formula:



Crystal form: white powder

Recrystallization solvent: dichloromethane-ethyl acetate

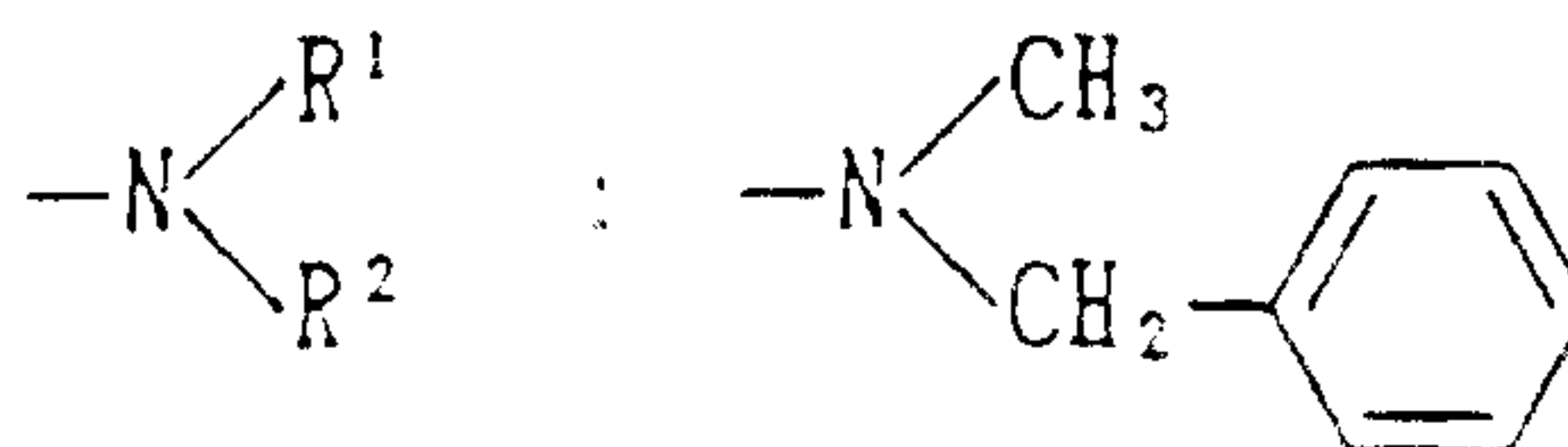
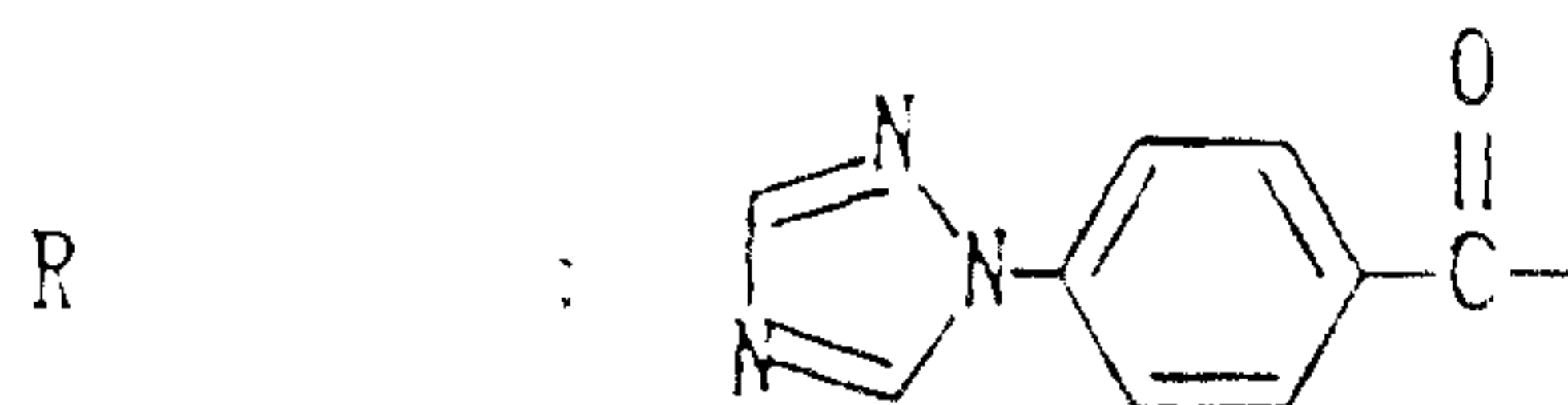
Melting point (°C): 137-138

Salt form: free

{Table 10 (continued)}

Example 96

Structural formula:



Crystal form: white powder

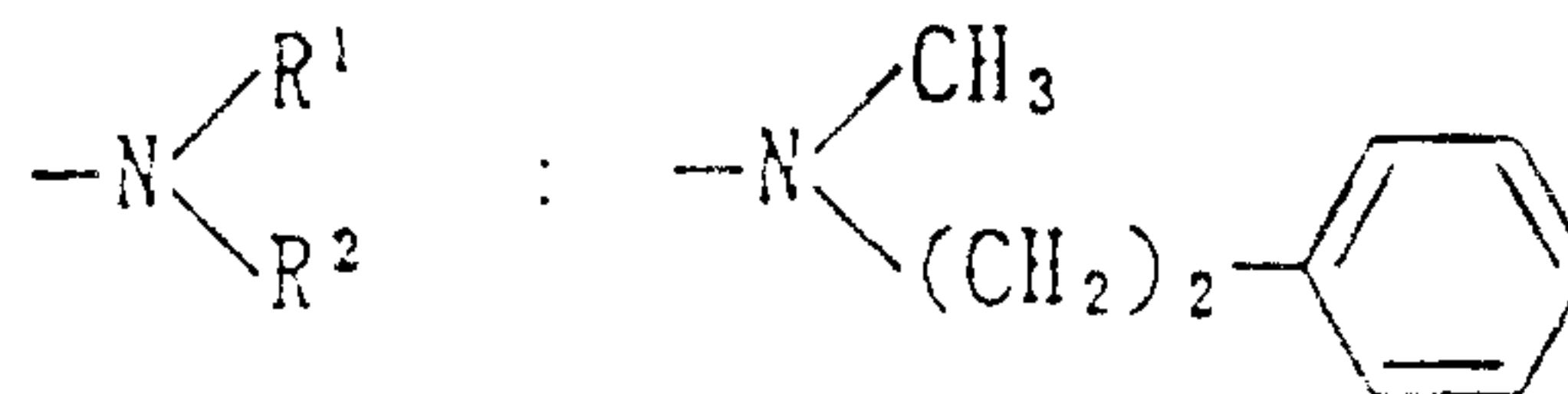
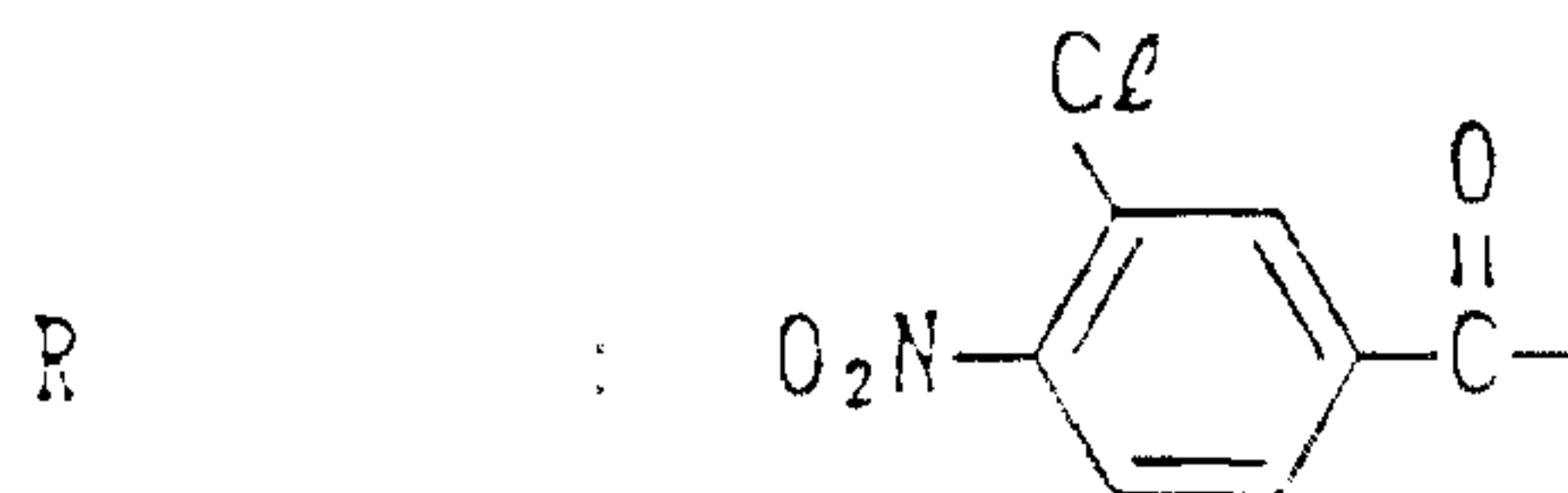
Recrystallization solvent: dichloromethane-diethyl ether

Melting point (°C): 168-169

Salt form: free

Example 97

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

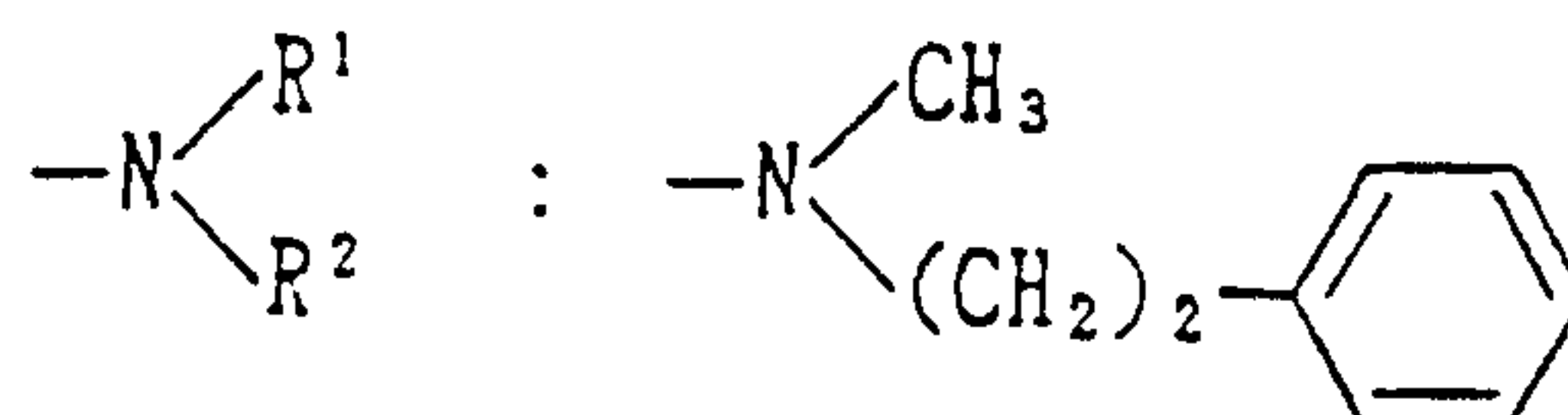
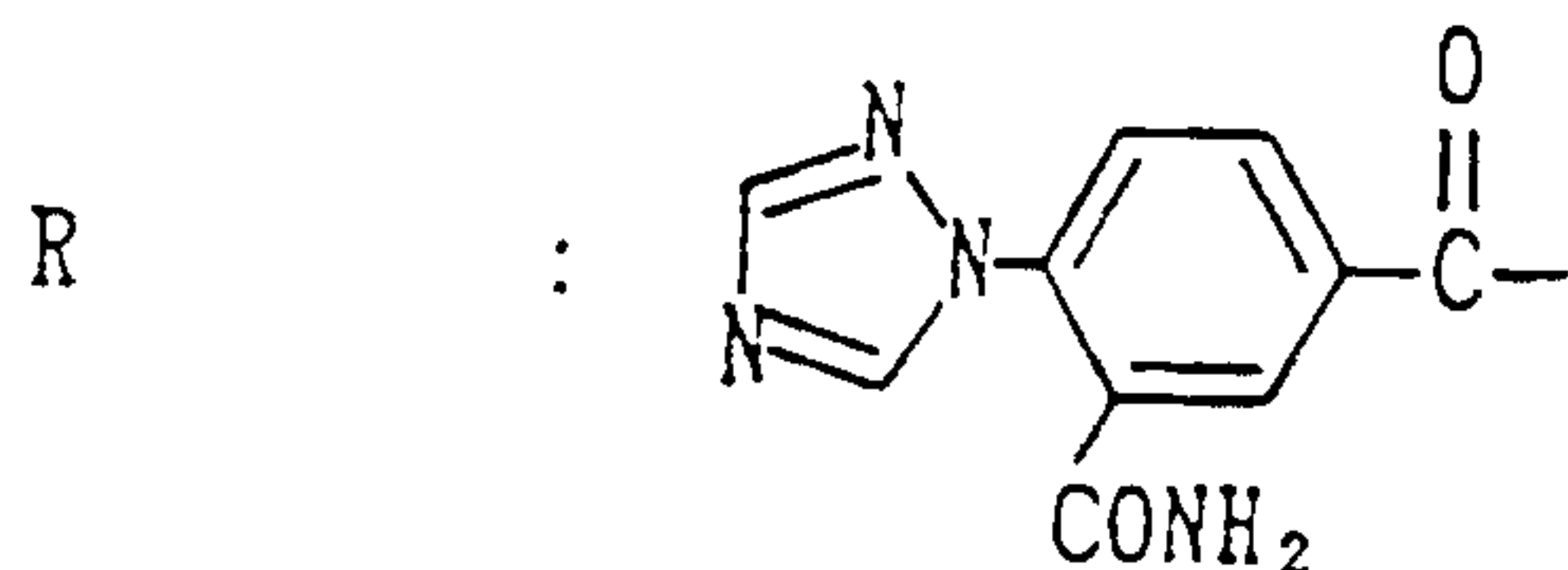
Melting point (°C): 203-205

Salt form: hydrochloride

{Table 10 (continued)}

Example 98

Structural formula:



Crystal form: colorless prisms

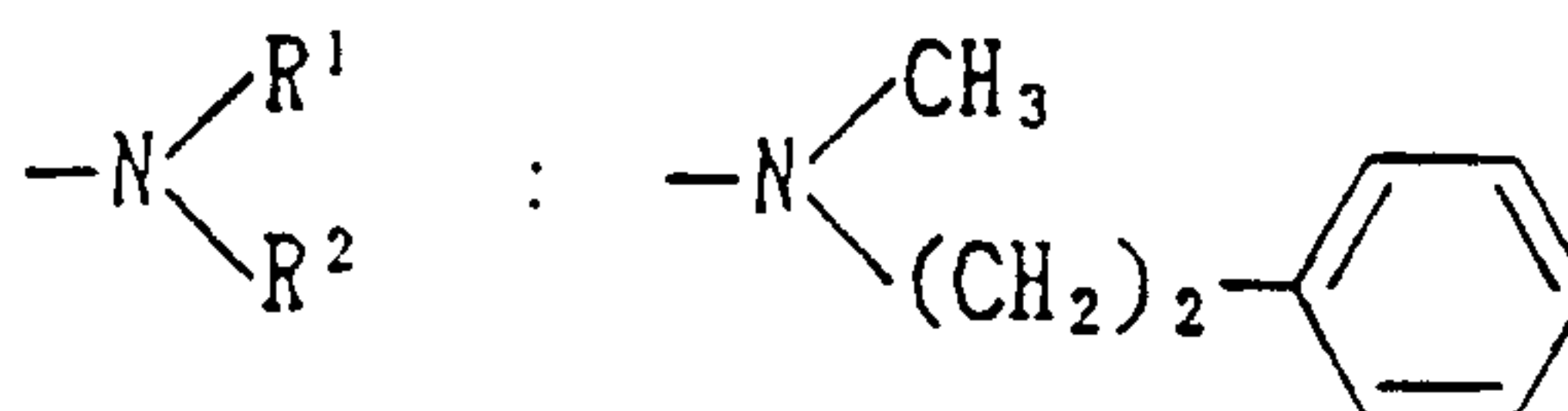
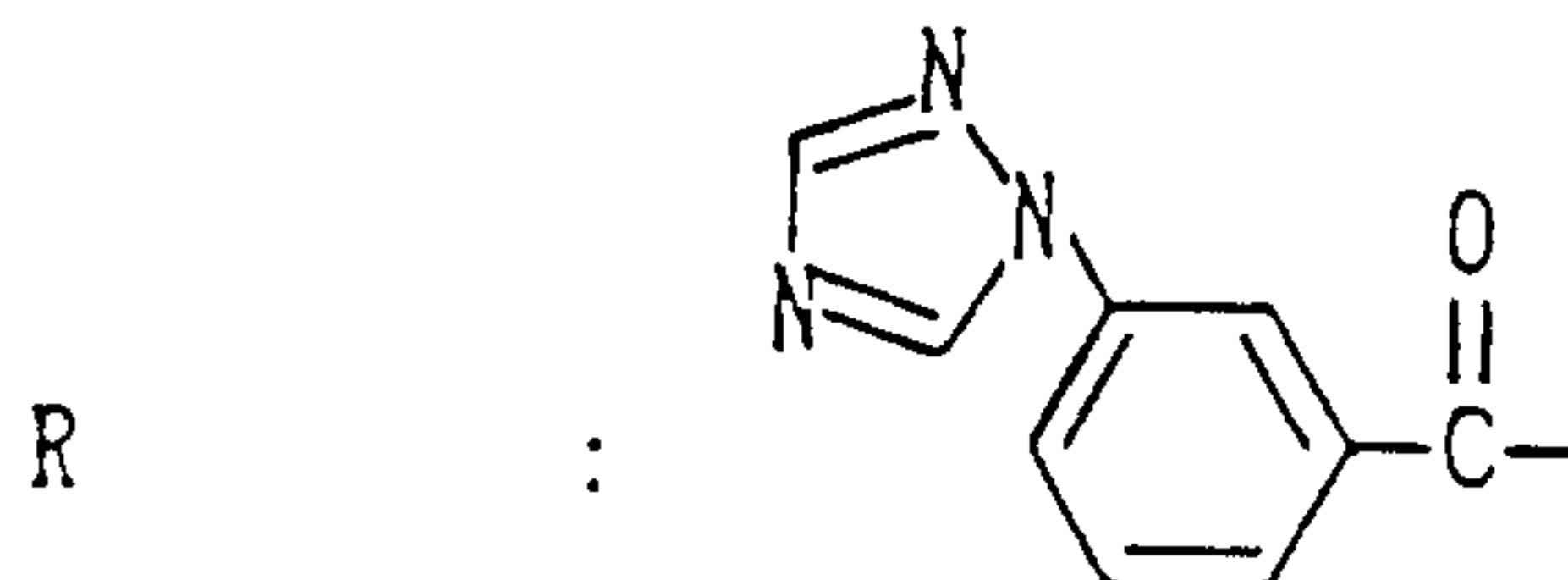
Recrystallization solvent: ethyl acetate

Melting point (°C): 103-105.5

Salt form: free

Example 99

Structural formula:



Crystal form: white amorphous

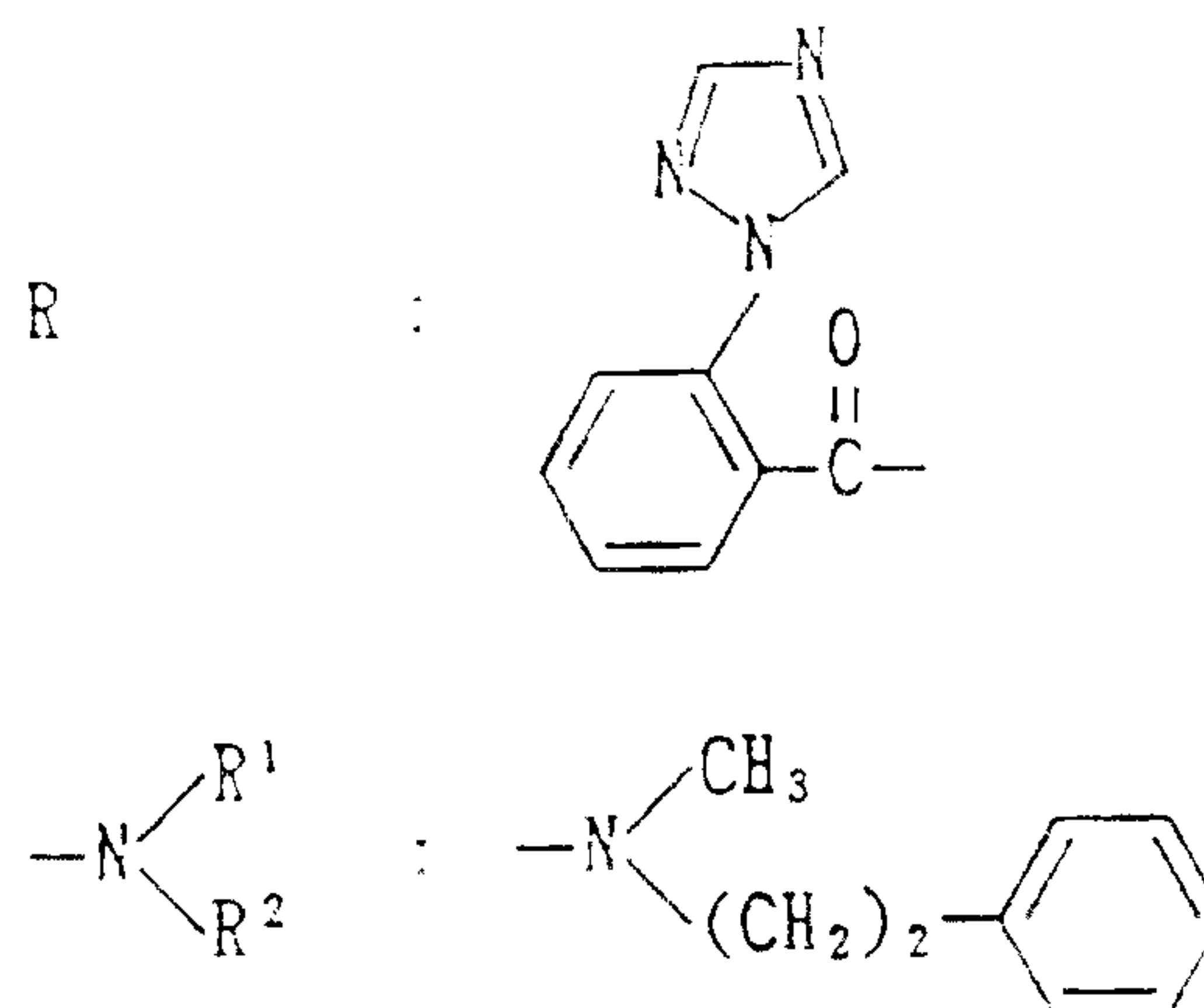
Salt form: hydrochloride

NMR value: 68)

[Table 10 (continued)]

Example 100

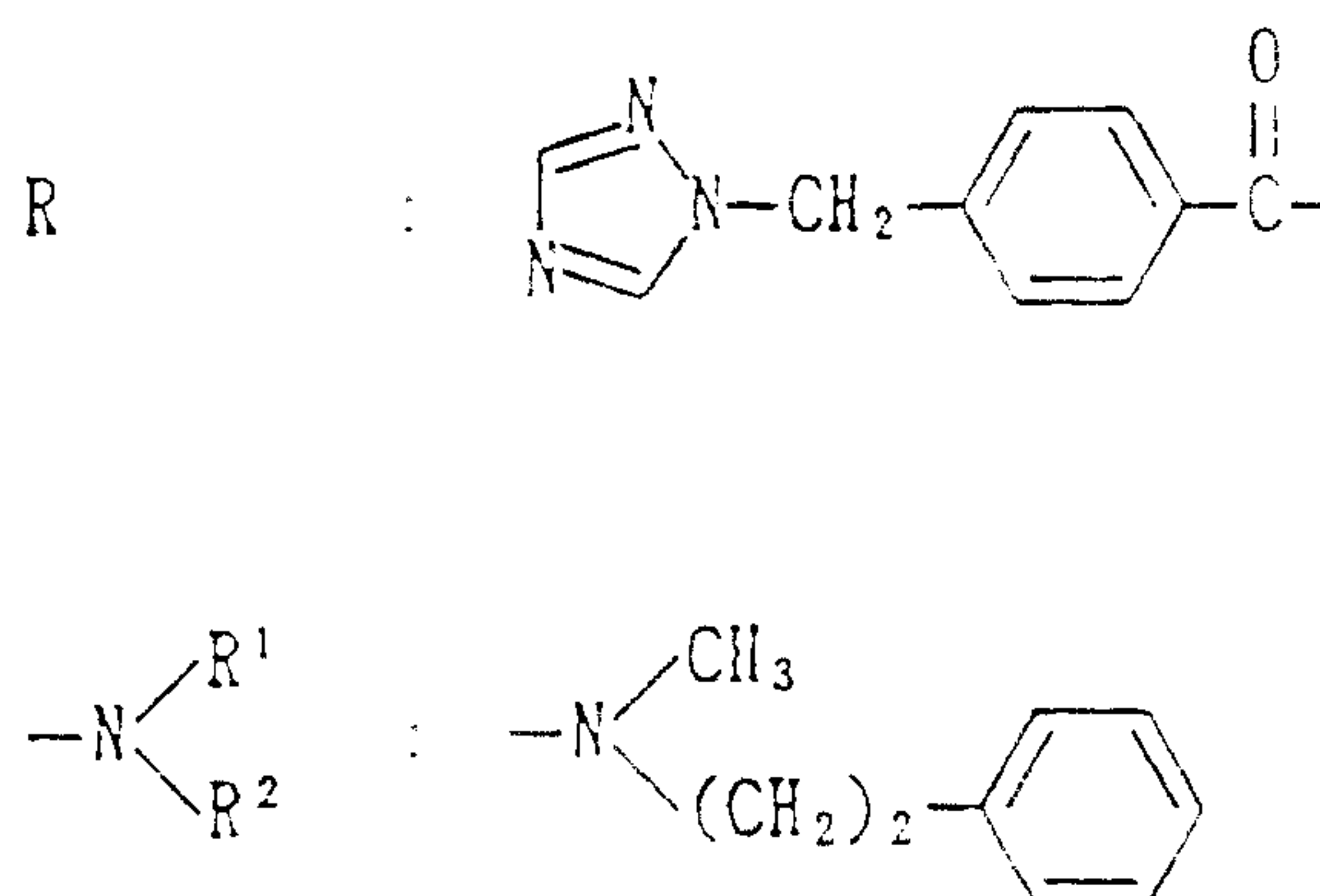
Structural formula:



Crystal form: white amorphous
Salt form: hydrochloride
NMR value: 69)

Example 101

Structural formula:

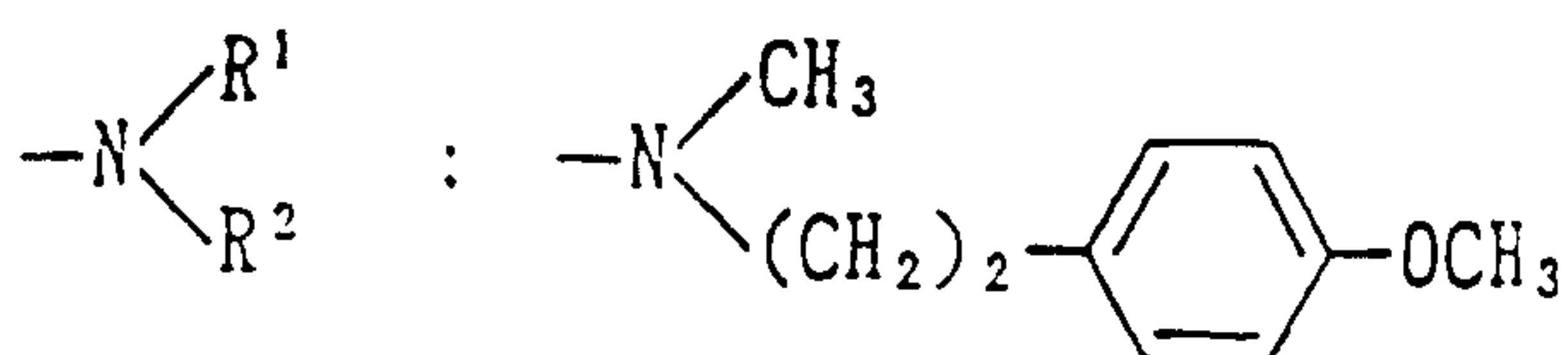


Crystal form: white amorphous
Salt form: hydrochloride
NMR value: 70)

[Table 10 (continued)]

Example 102

Structural formula:



Crystal form: white powder

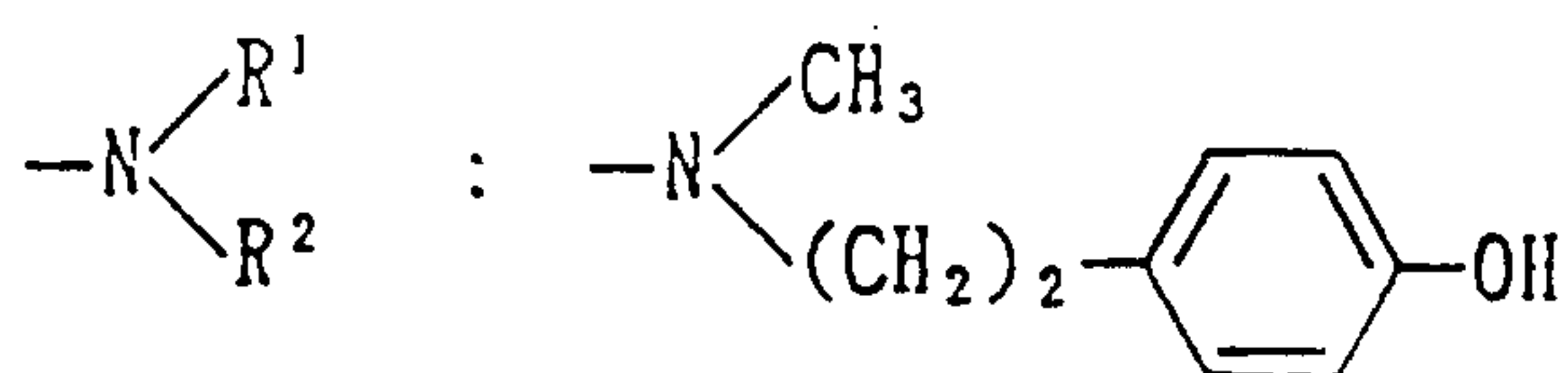
Recrystallization solvent: ethyl acetate-diethyl ether

Melting point (°C): 96-98

Salt form: free

Example 103

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-ethanol

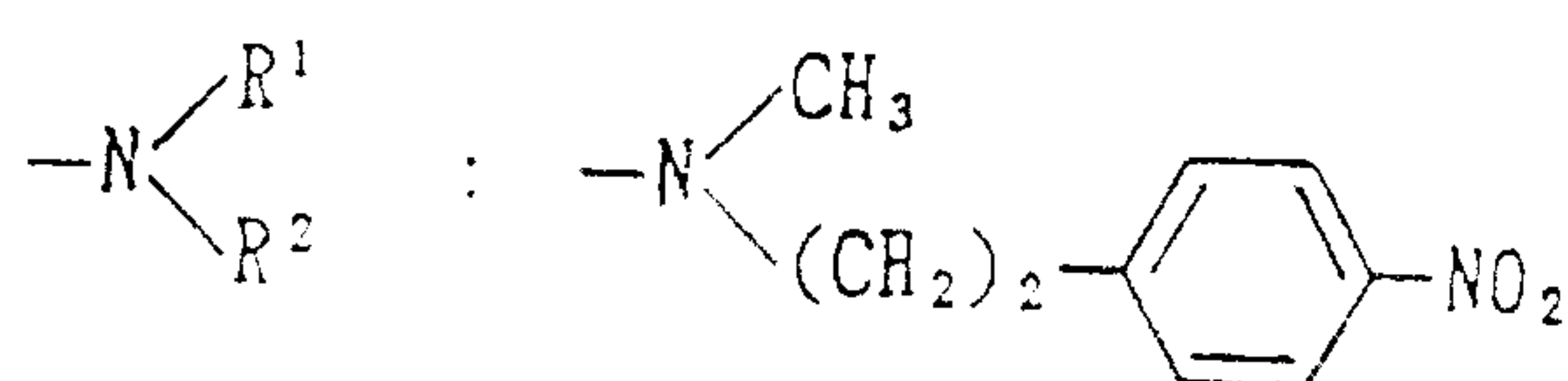
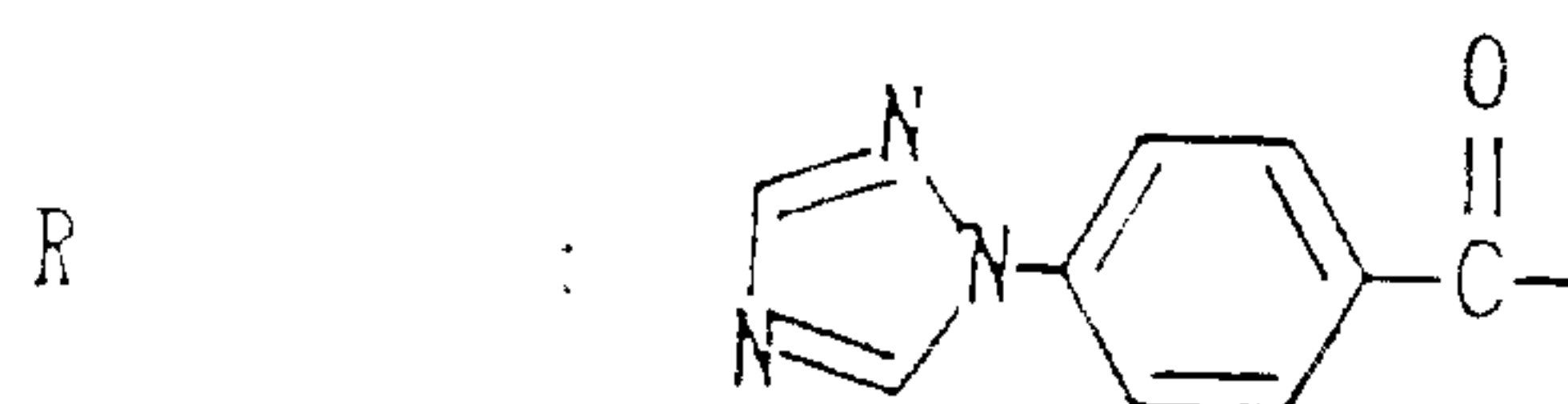
Melting point (°C): 181-182

Salt form: free

[Table 10 (continued)]

Example 104

Structural formula:



Crystal form: yellow powder

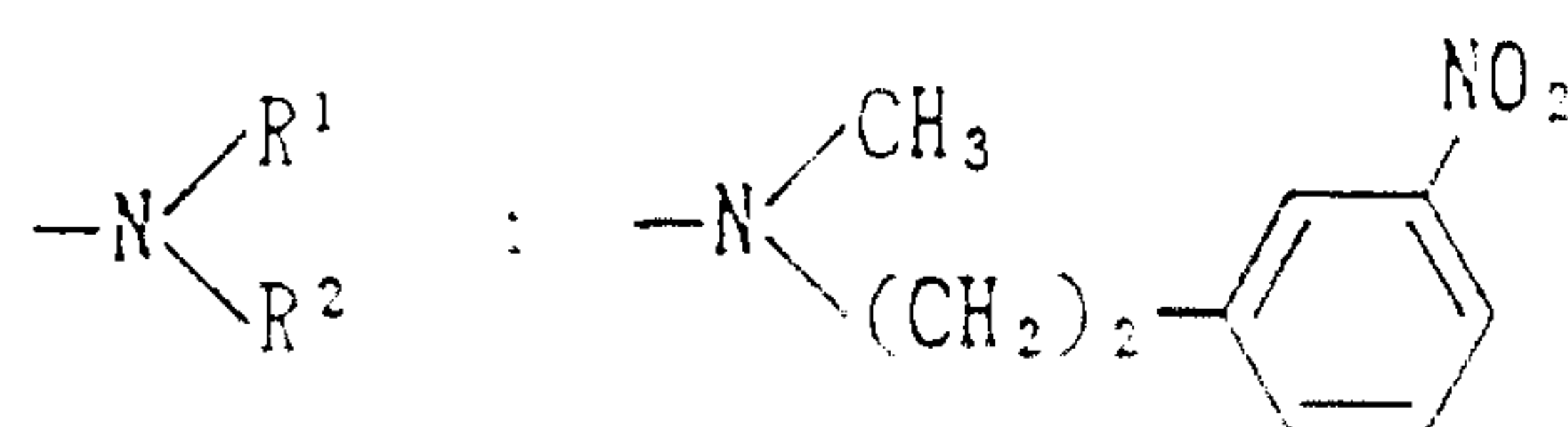
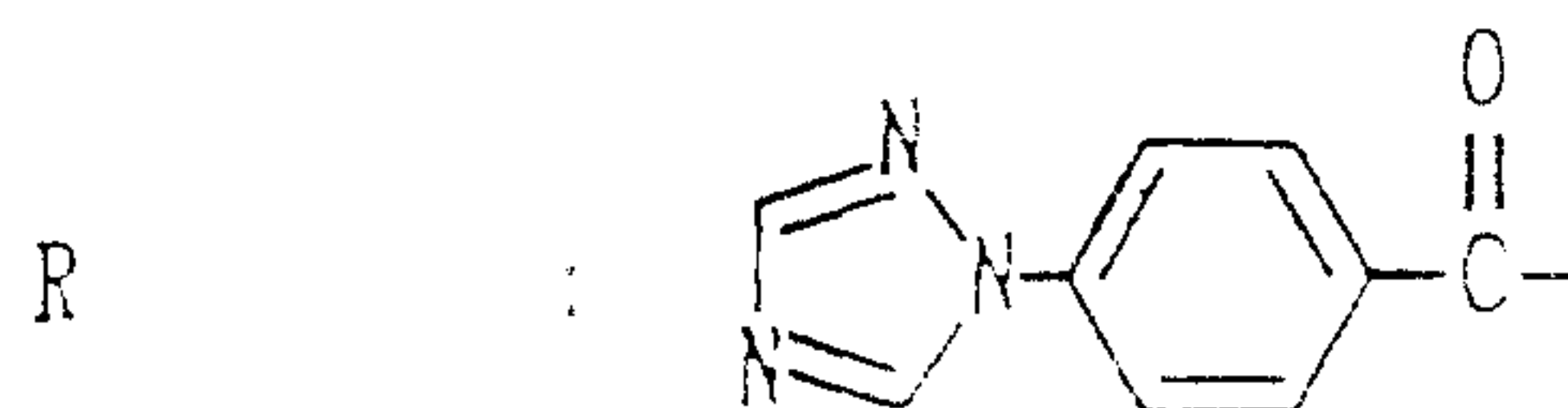
Recrystallization solvent: ethyl acetate

Melting point (°C): 160.4-162.0

Salt form: free

Example 105

Structural formula:



Crystal form: light yellow powder

Recrystallization solvent: ethyl acetate-diethyl ether

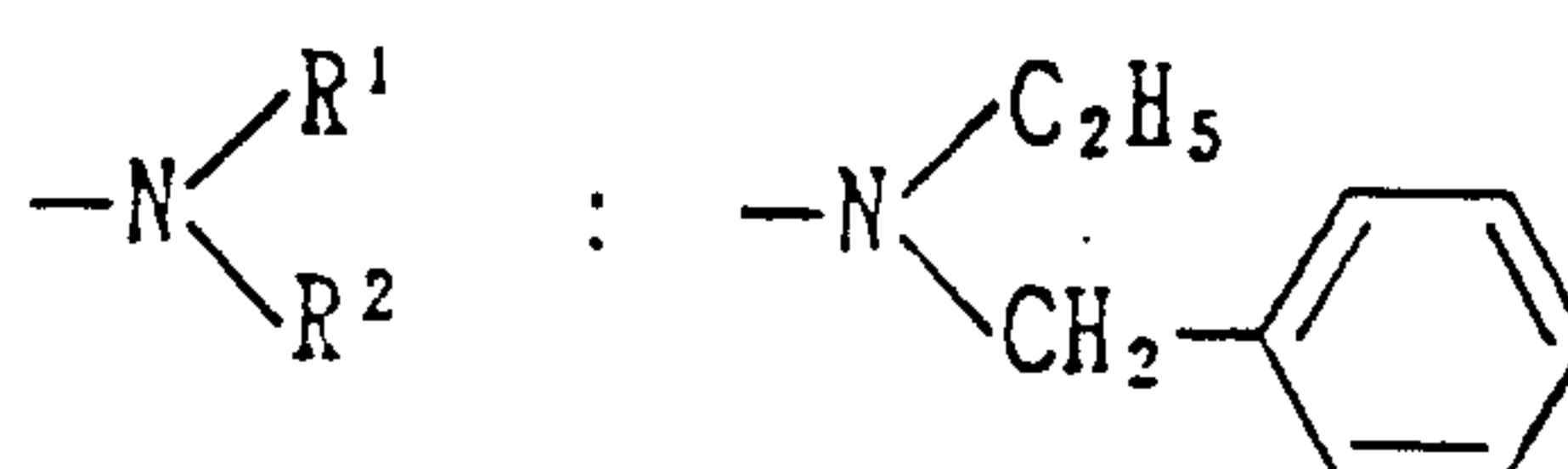
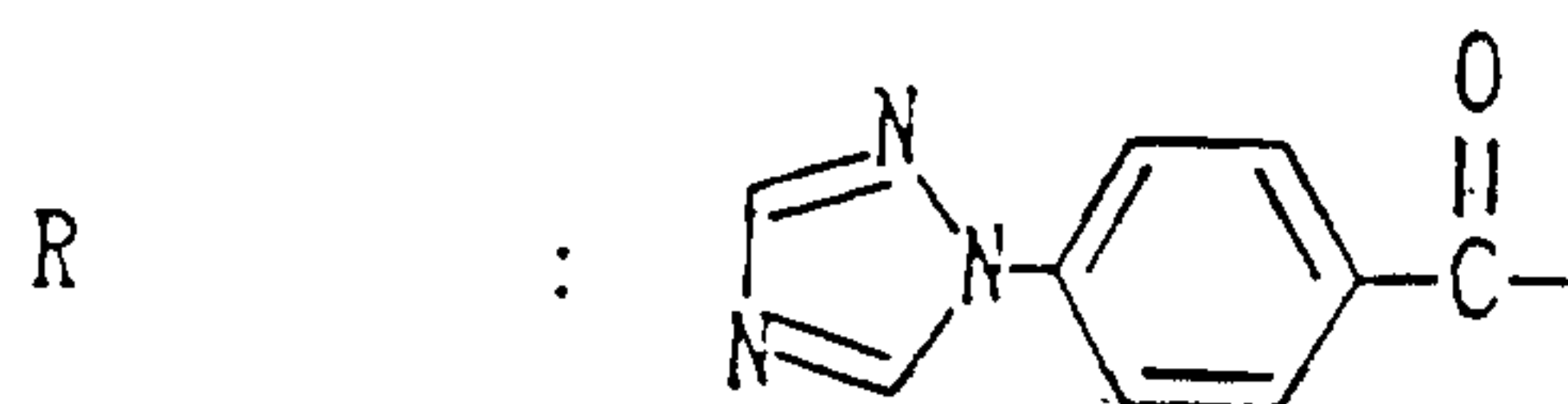
Melting point (°C): 88.5-89.0

Salt form: free

[Table 10 (continued)]

Example 106

Structural formula:



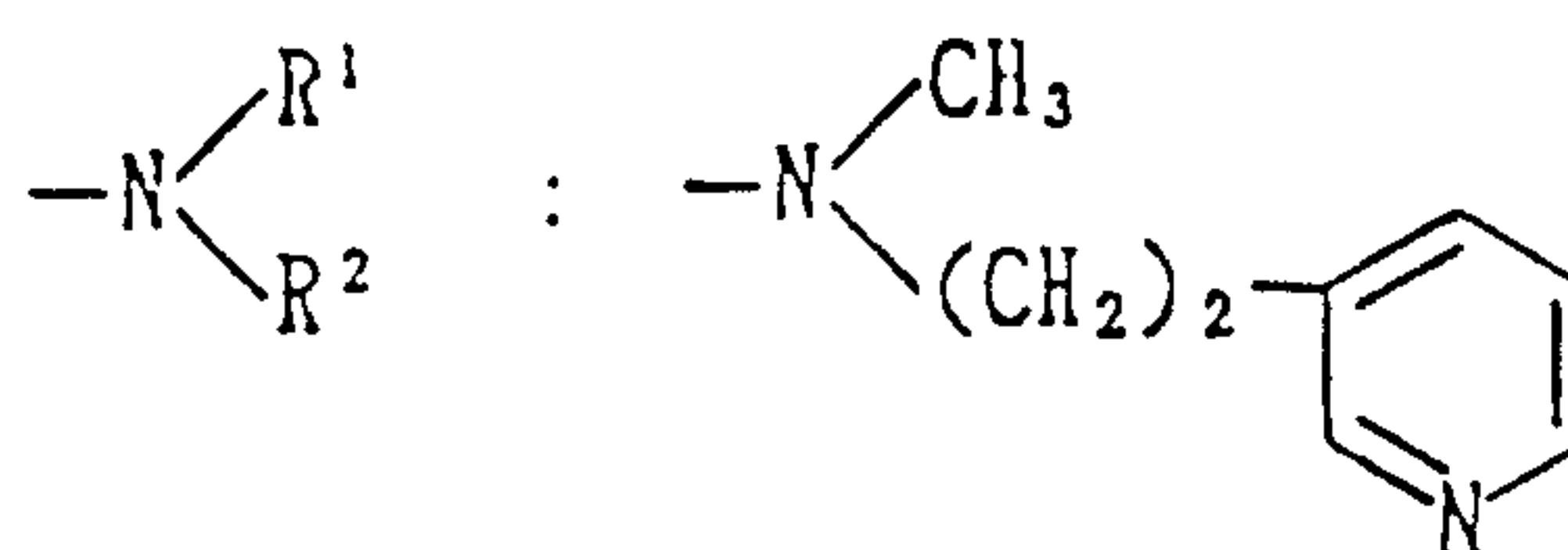
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 71)

Example 107

Structural formula:



Crystal form: white amorphous

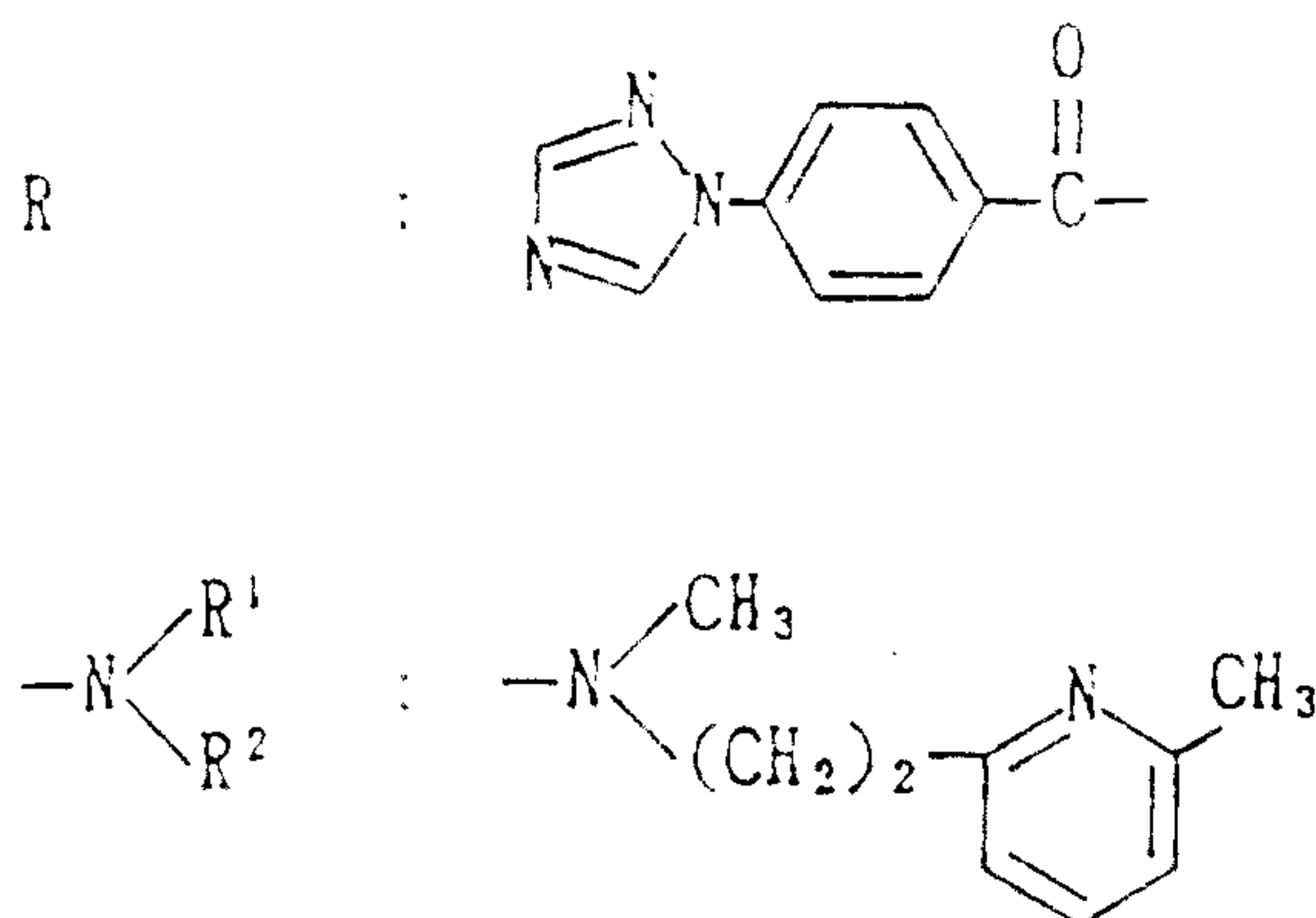
Salt form: trihydrochloride

NMR value: 72)

[Table 10 (continued)]

Example 108

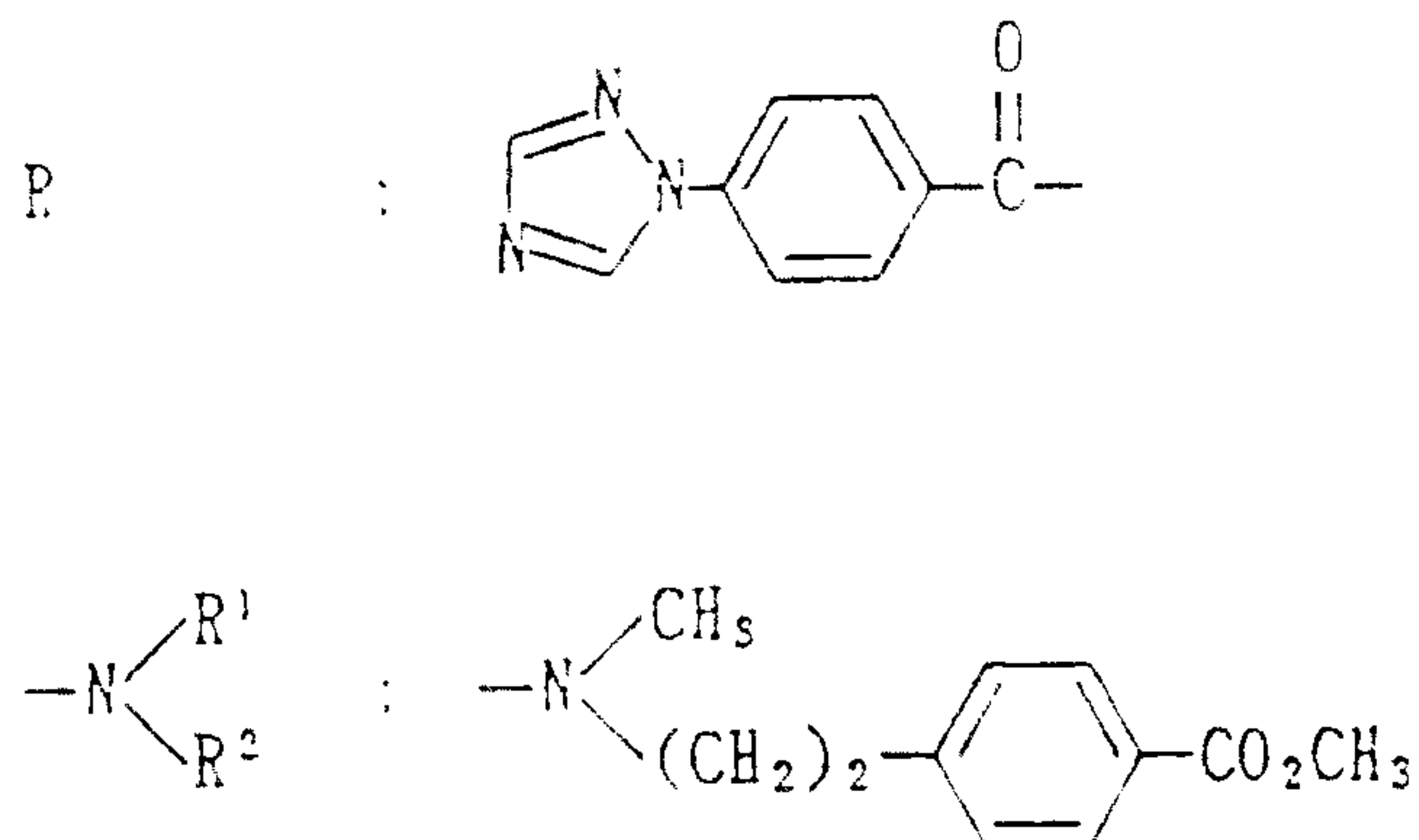
Structural formula:



Crystal form: white amorphous
Salt form: trihydrochloride
NMR value: 73)

Example 109

Structural formula:

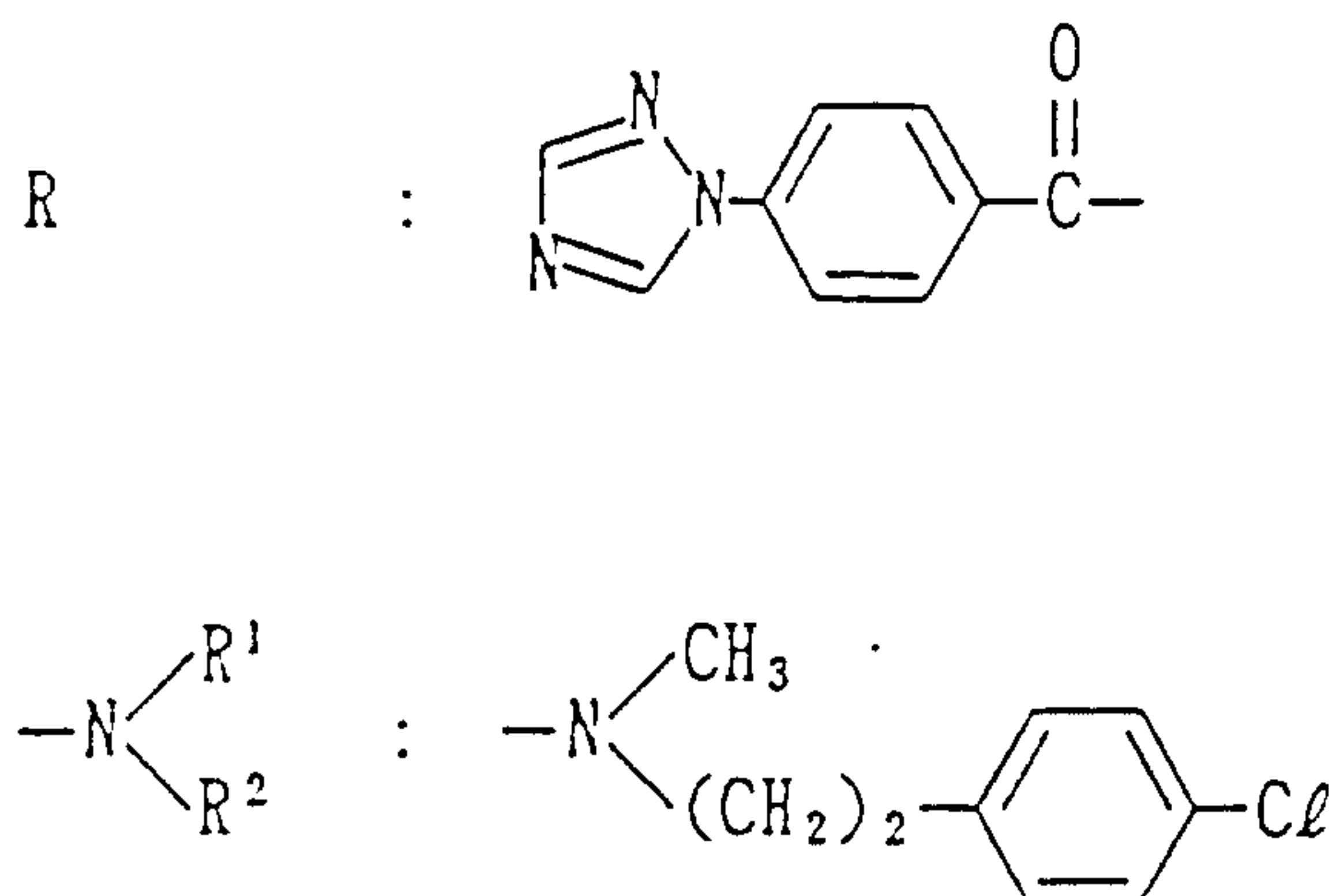


Crystal form: white powder
Recrystallization solvent: ethyl acetate
Melting point (°C): 112-113
Salt form: free

[Table 10 (continued)]

Example 110

Structural formula:



Crystal form: white powder

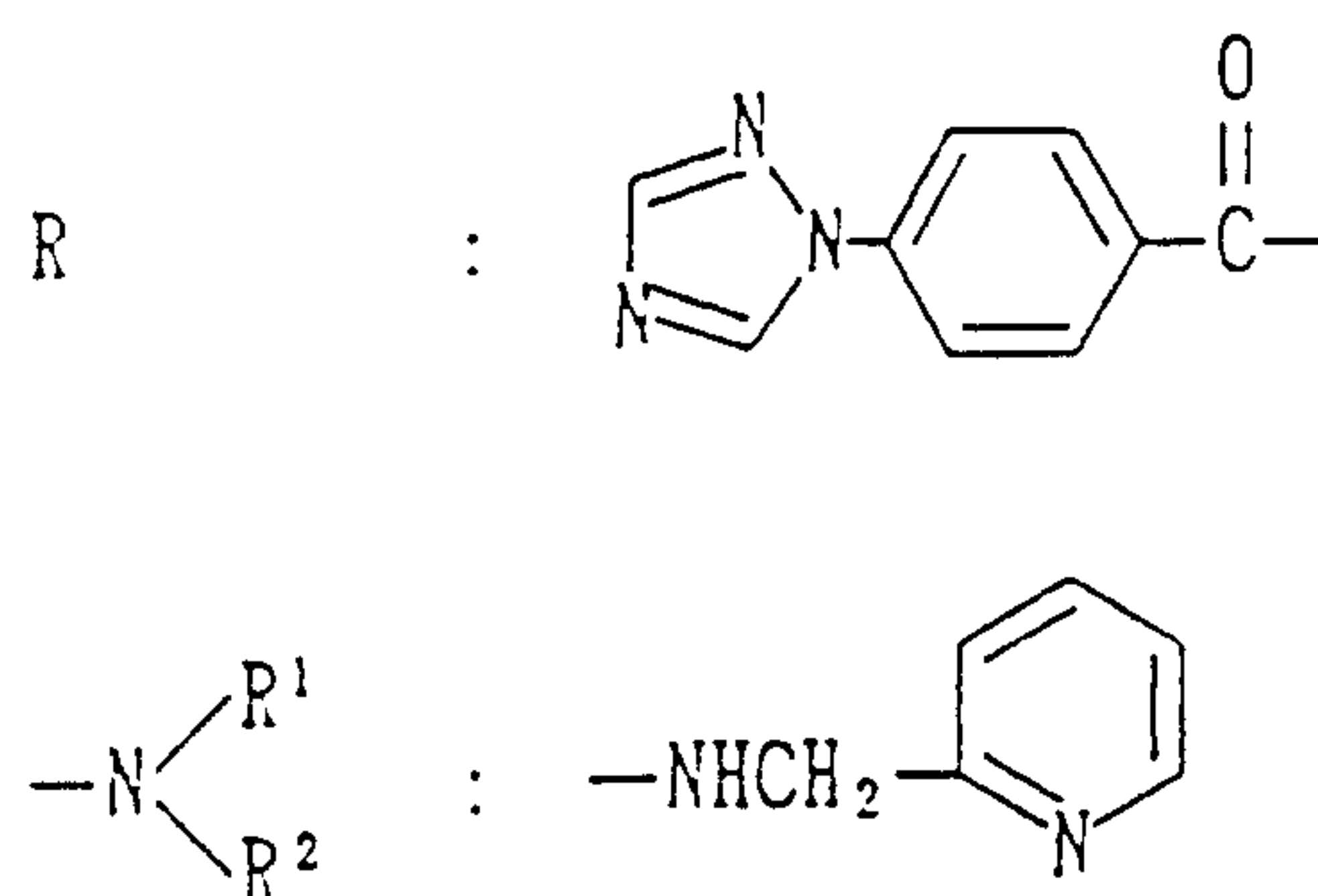
Recrystallization solvent: ethyl acetate

Melting point (°C): 147-148

Salt form: free

Example 111

Structural formula:



Crystal form: white powder

Recrystallization solvent: dichloromethane-diethyl ether

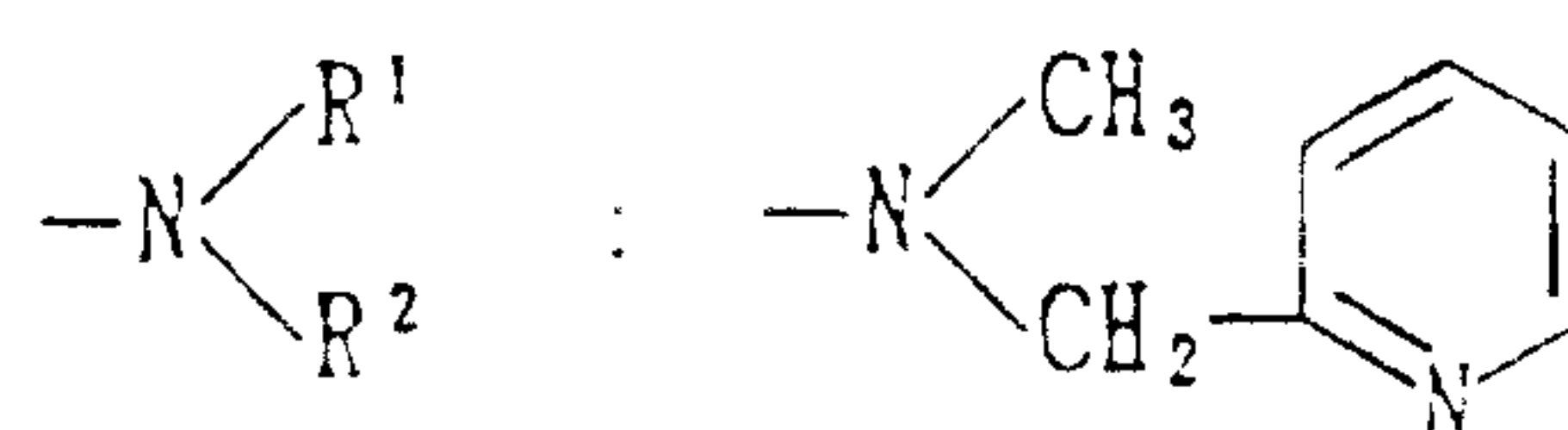
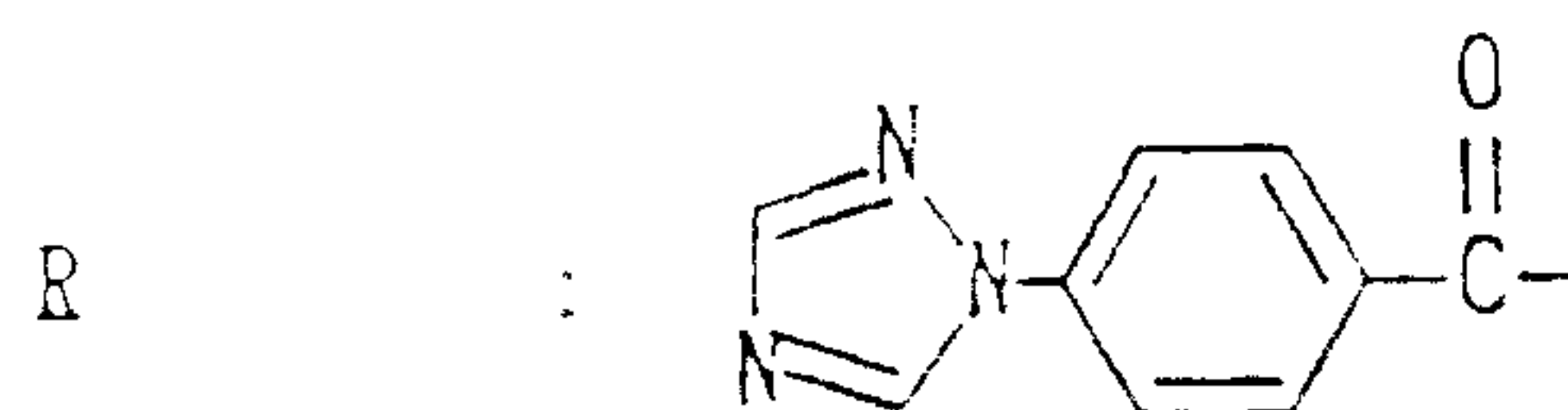
Melting point (°C): 133-134

Salt form: free

[Table 10 (continued)]

Example 112

Structural formula:



Crystal form: white powder

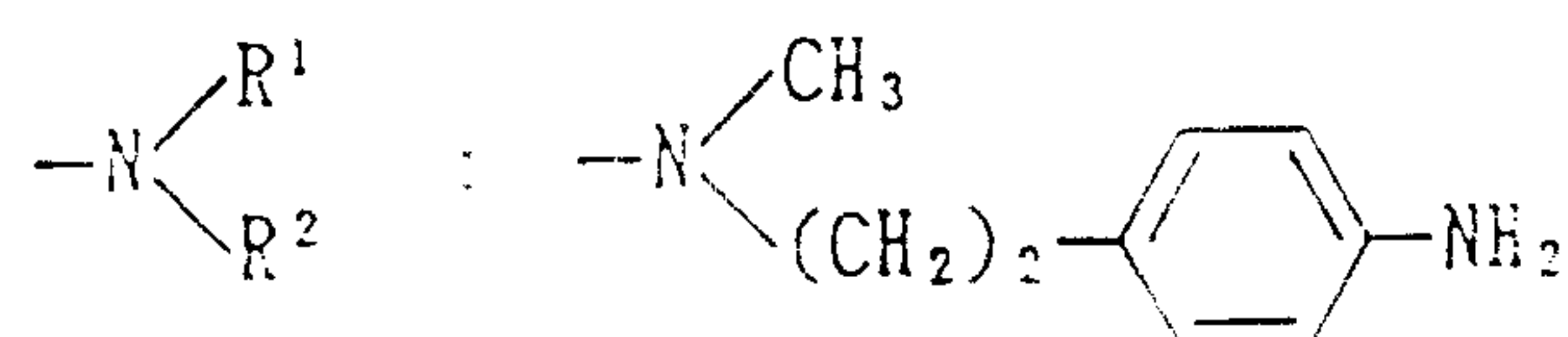
Recrystallization solvent: dichloromethane-diethyl ether

Melting point (°C): 131-131.5

Salt form: free

Example 113

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-diethyl ether

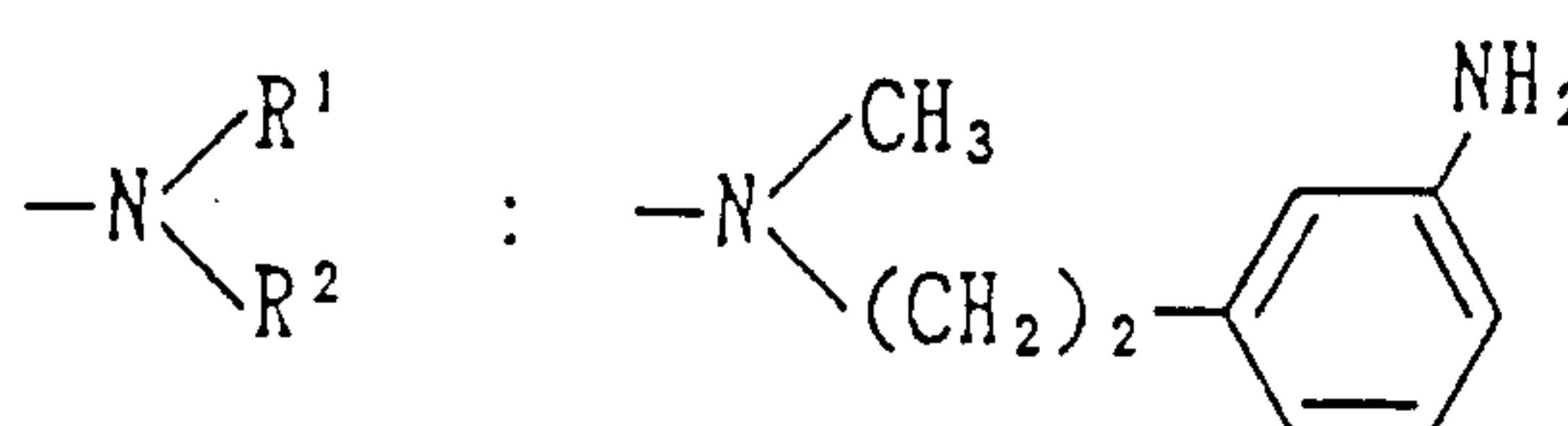
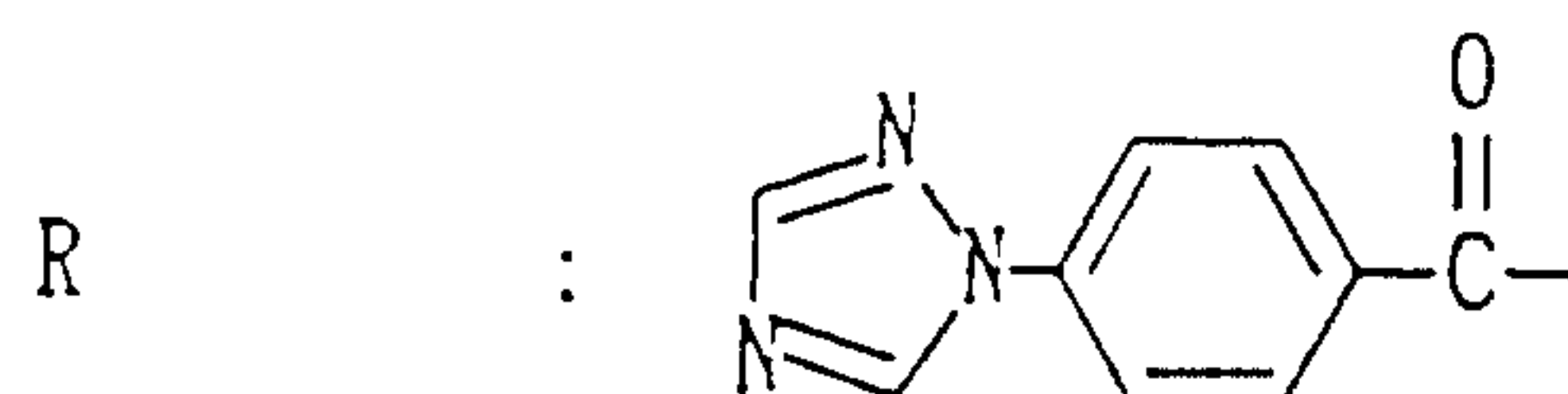
Melting point (°C): 112-113

Salt form: free

{Table 10 (continued)}

Example 114

Structural formula:



Crystal form: light yellow powder

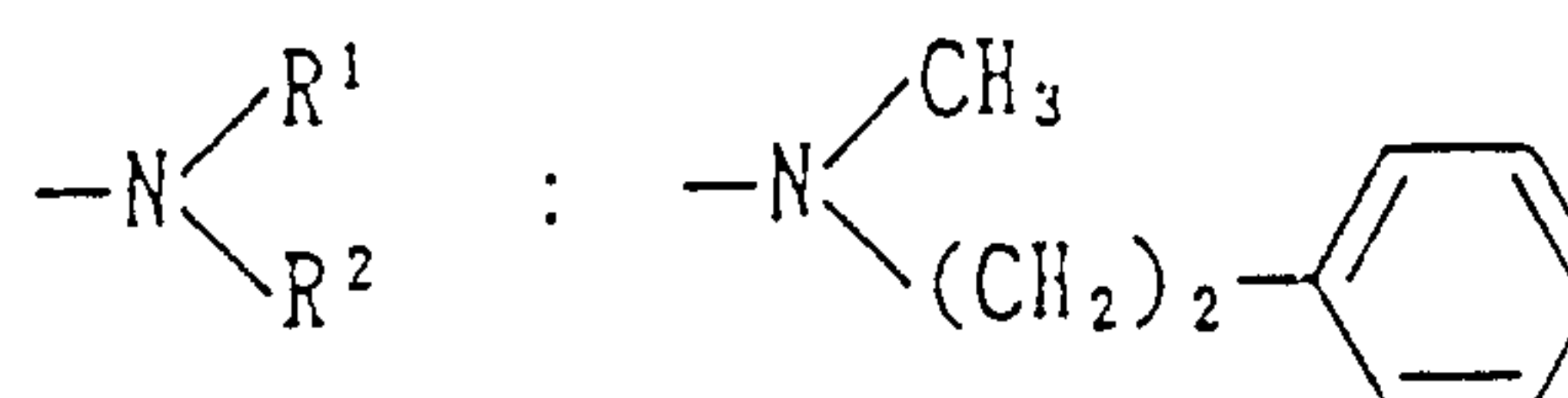
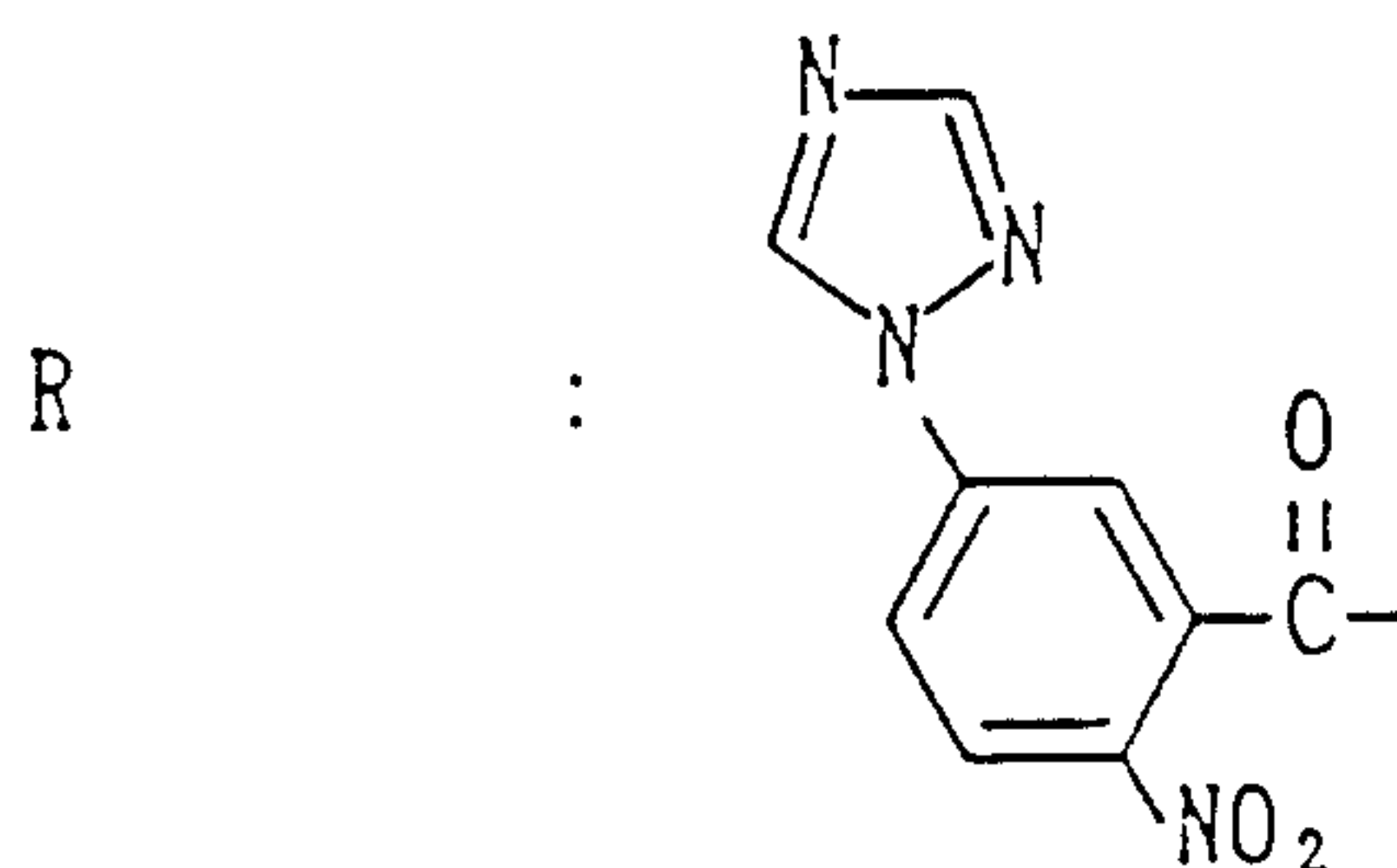
Recrystallization solvent: ethyl acetate

Melting point (°C): 150-151

Salt form: free

Example 115

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

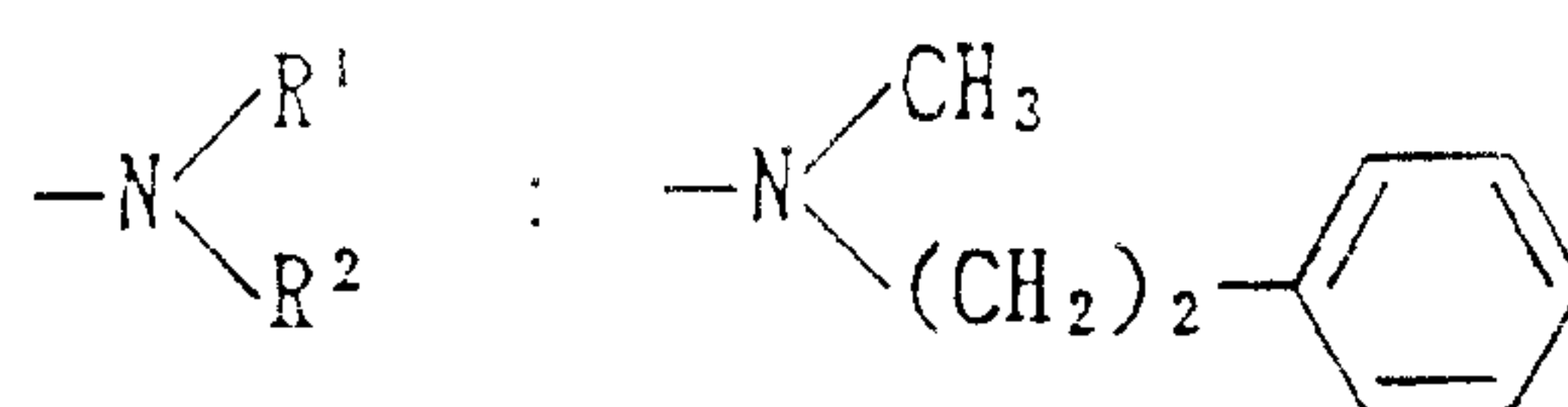
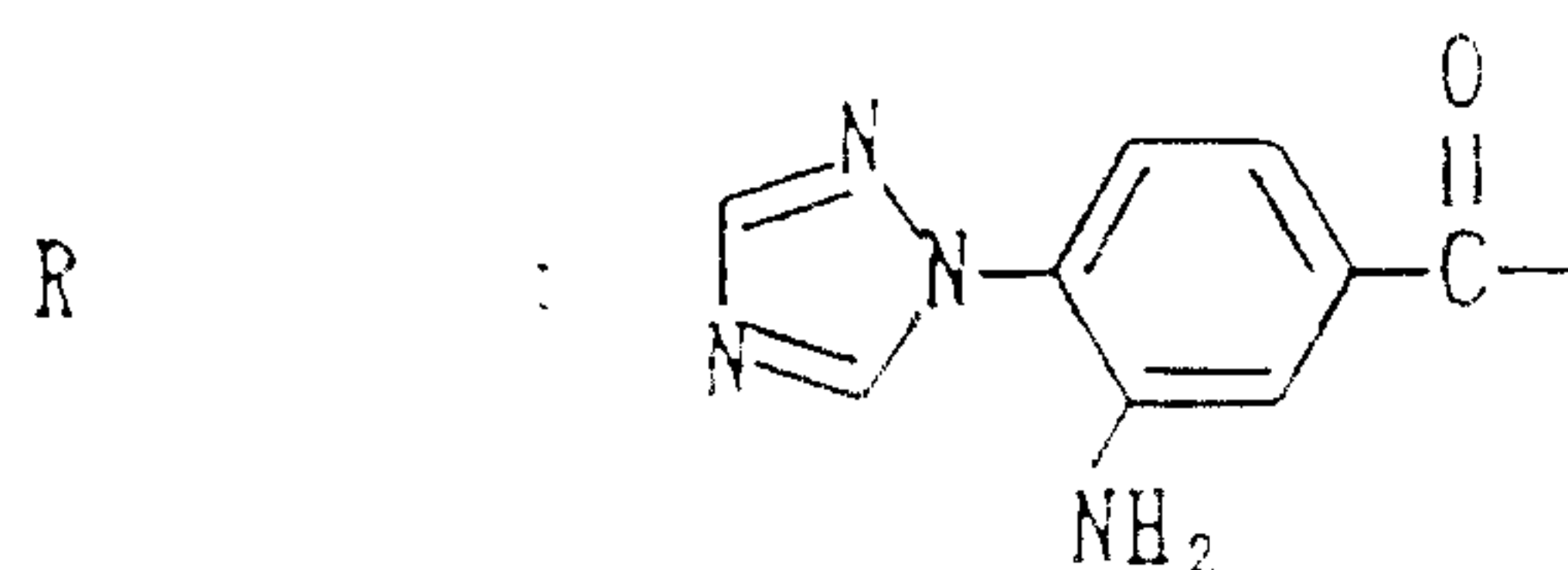
Melting point (°C): 155-160

Salt form: free

{Table 10 (continued)}

Example 116

Structural formula:



Crystal form: white powder

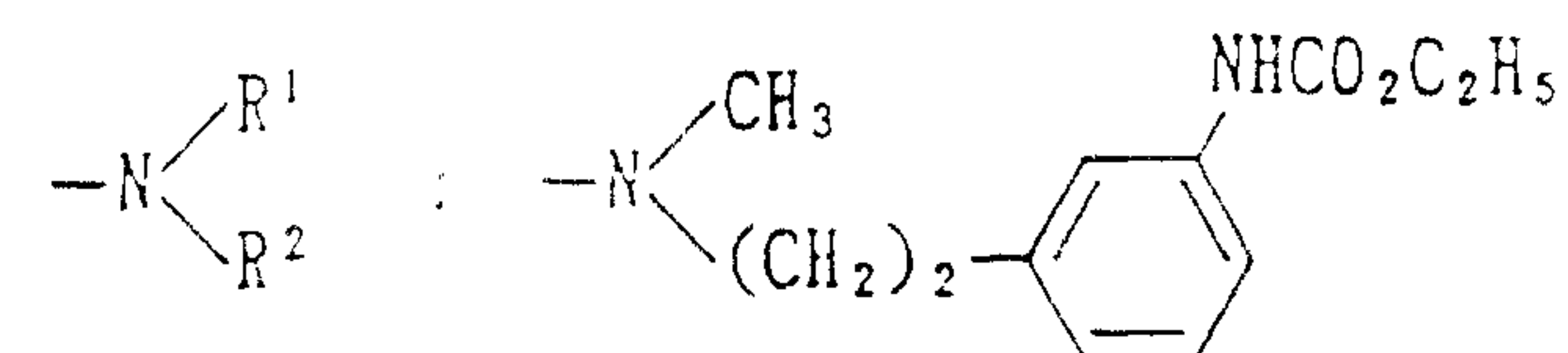
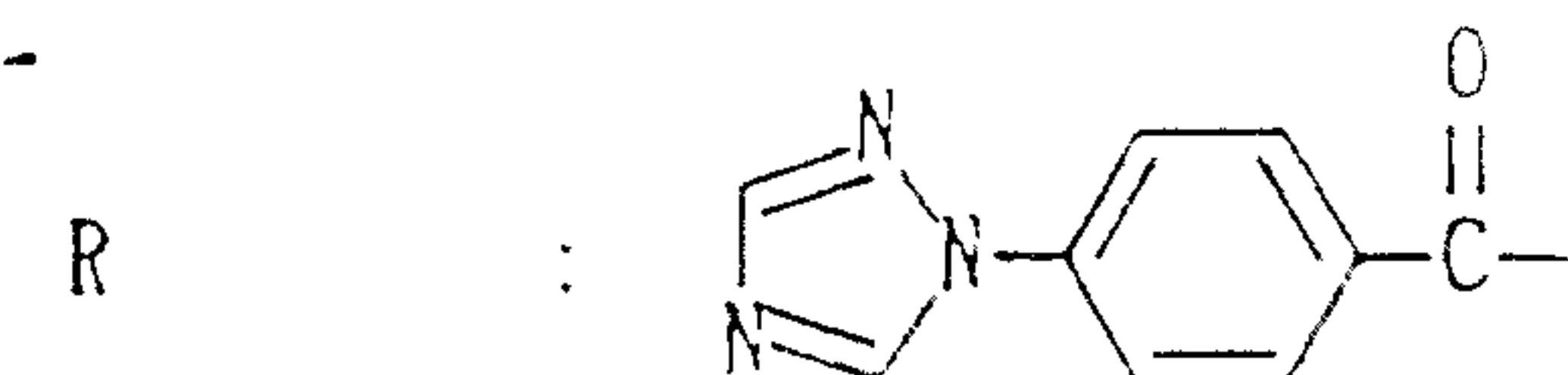
Recrystallization solvent: ethyl acetate-n-hexane

Melting point (°C): 117-118

Salt form: free

Example 117

Structural formula:



Crystal form: white amorphous

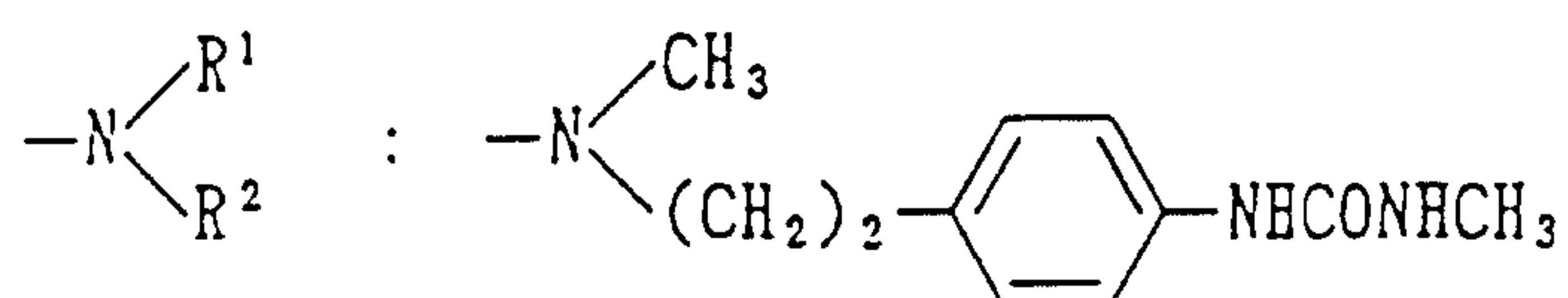
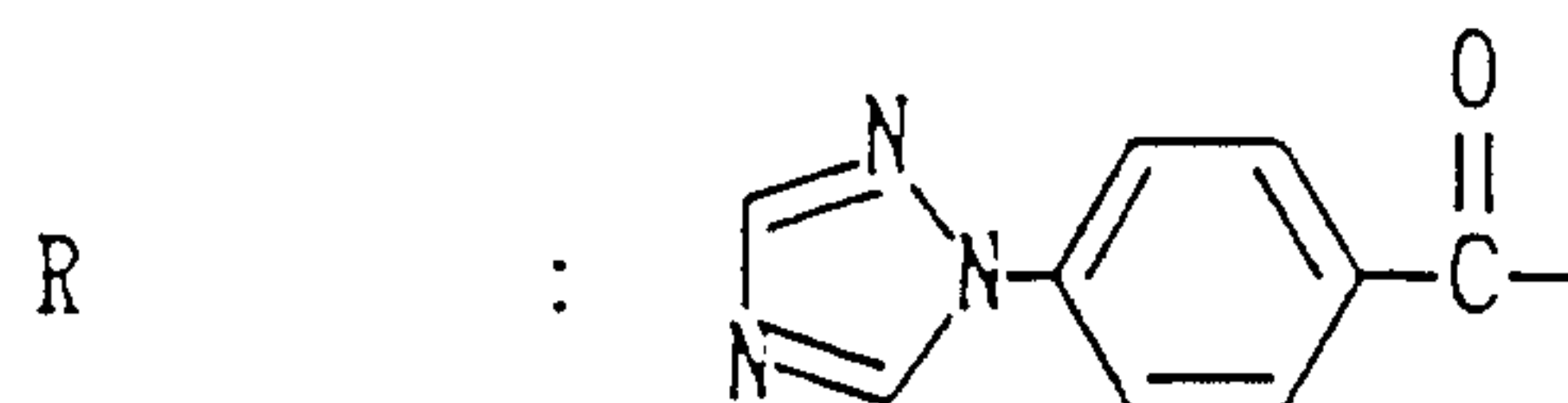
Salt form: free

NMR value: 74)

[Table 10 (continued)]

Example 118

Structural formula:



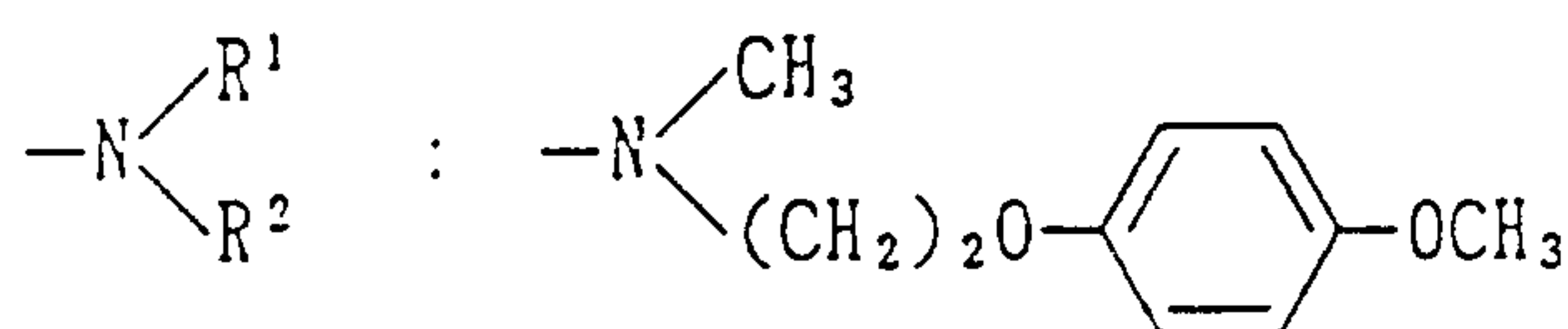
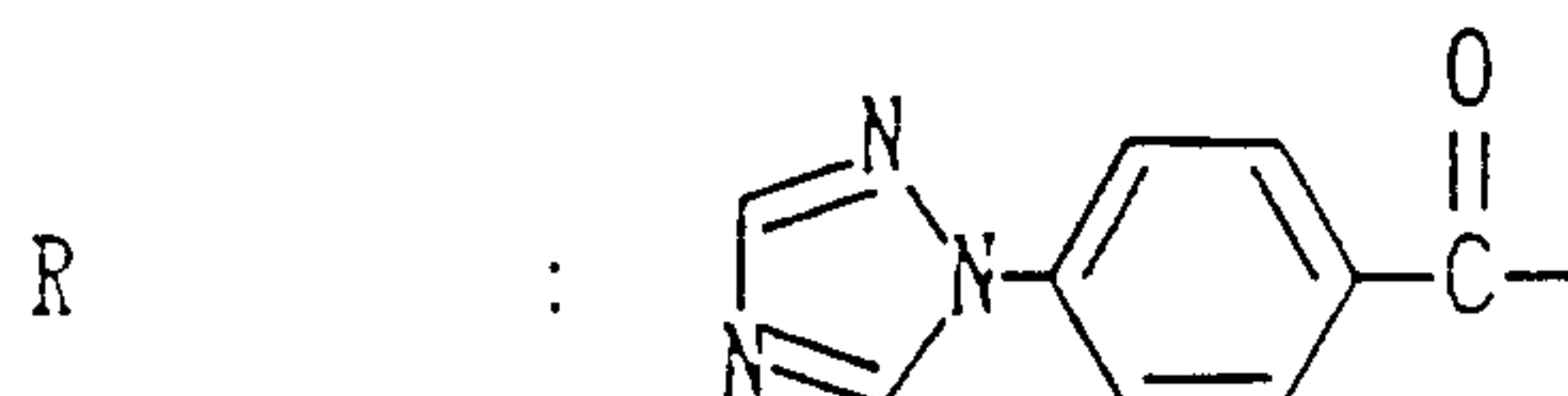
Crystal form: white amorphous

Salt form: free

NMR value: 75)

Example 119

Structural formula:



Crystal form: white amorphous

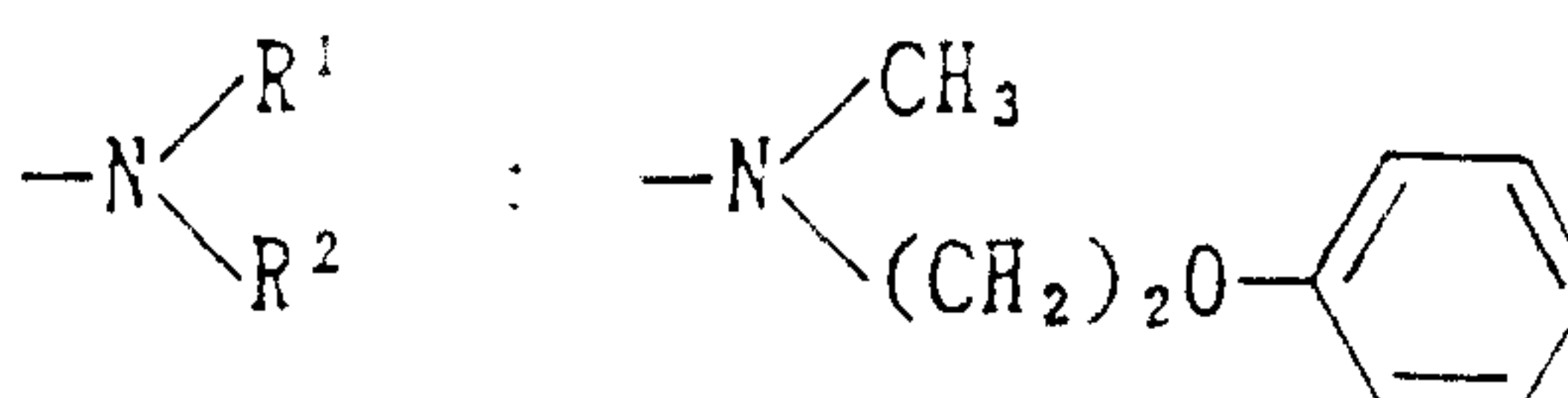
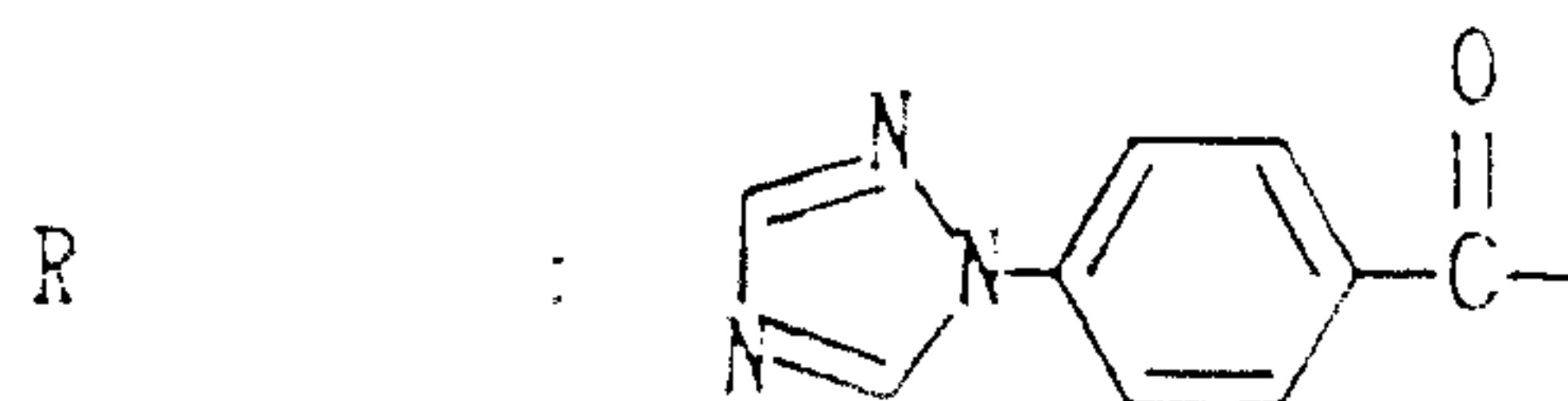
Salt form: hydrochloride

NMR value: 76)

[Table 10 (continued)]

Example 120

Structural formula:



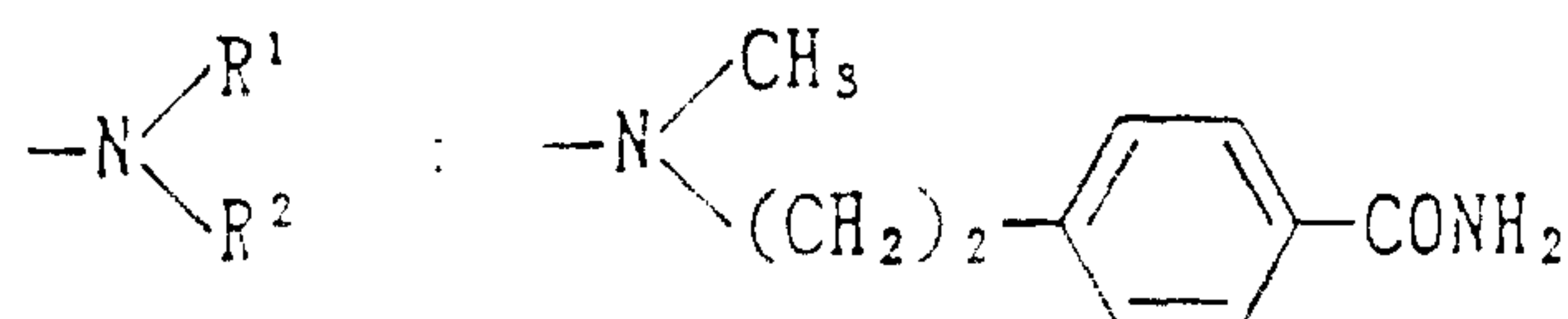
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 77)

Example 121

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

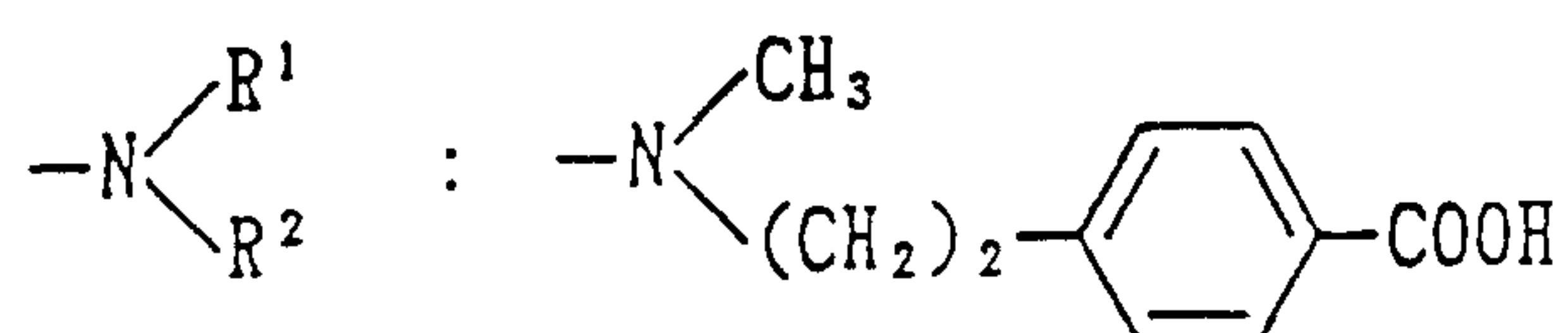
Melting point (°C): 194.5-195.5

Salt form: free

{Table 10 (continued)}

Example 122

Structural formula:



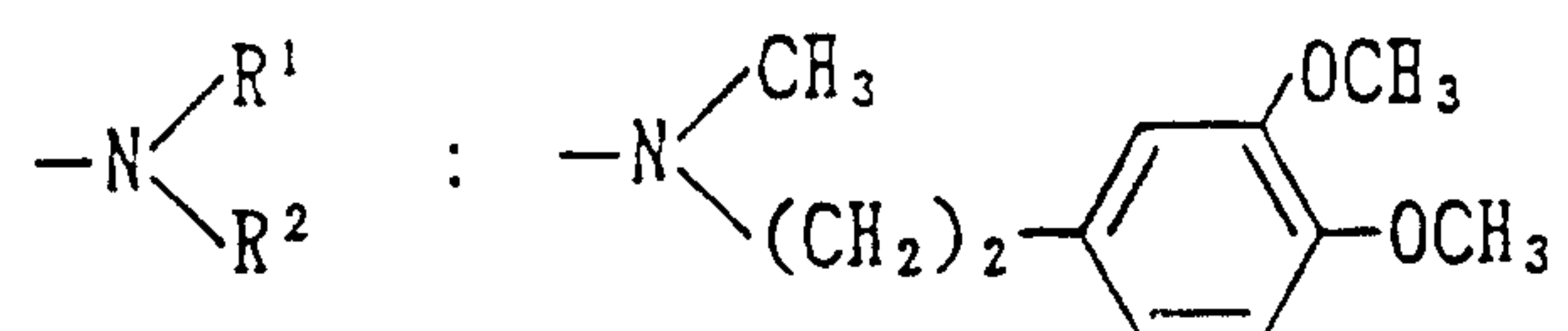
Crystal form: white amorphous

Salt form: free

NMR value: 78)

Example 123

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

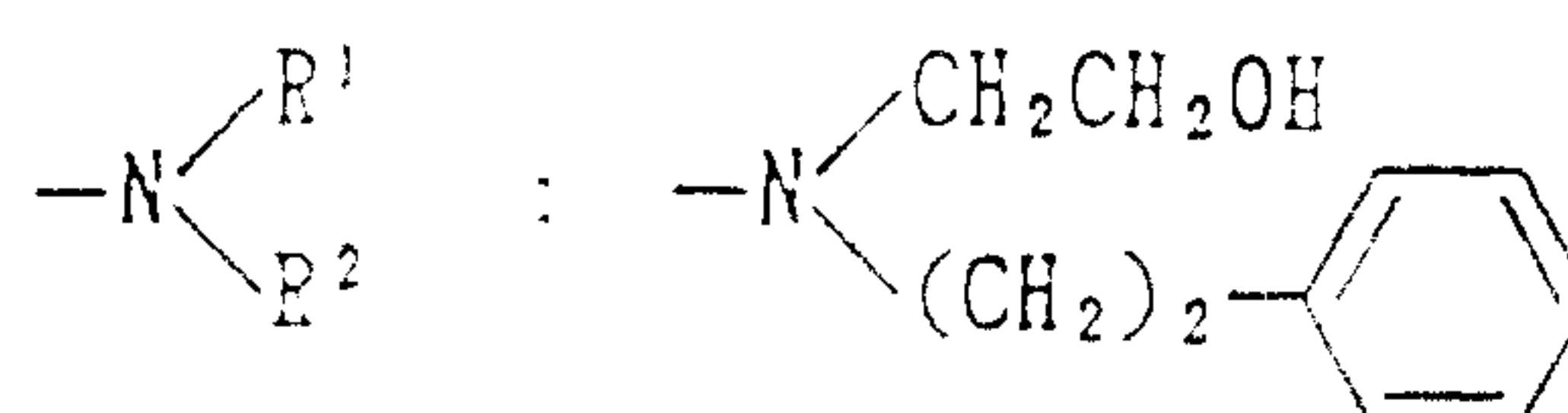
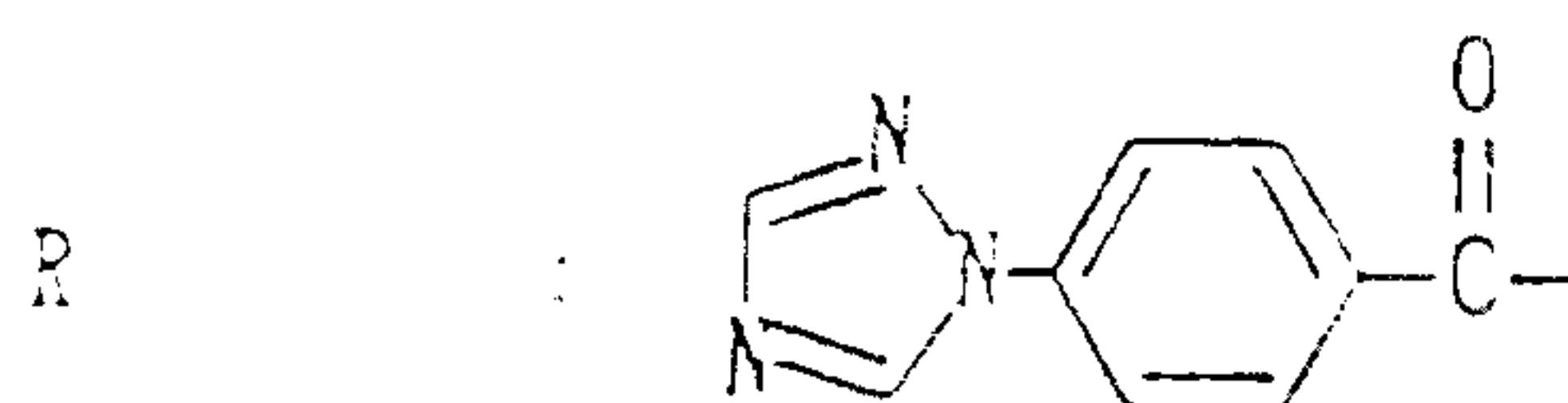
Melting point (°C): 214-216

Salt form: hydrochloride

{Table 10 (continued)}

Example 124

Structural formula:



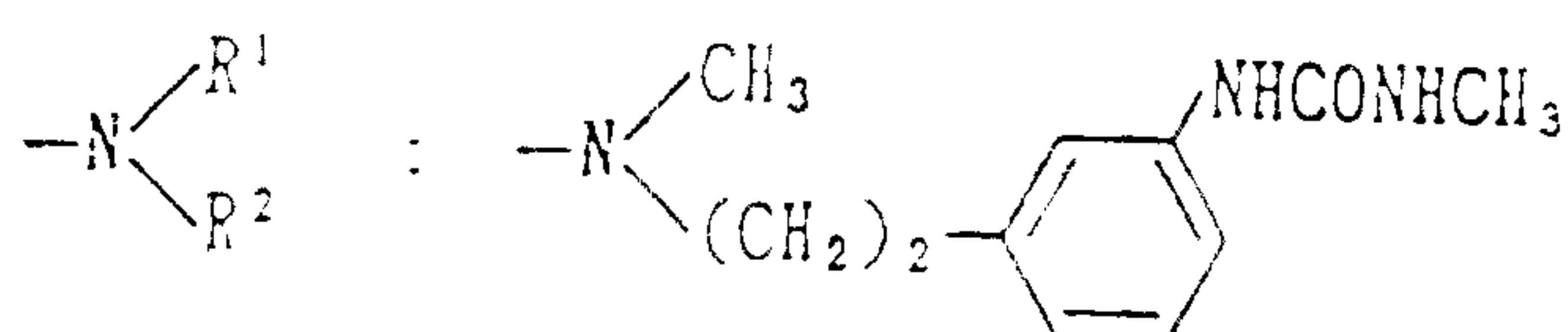
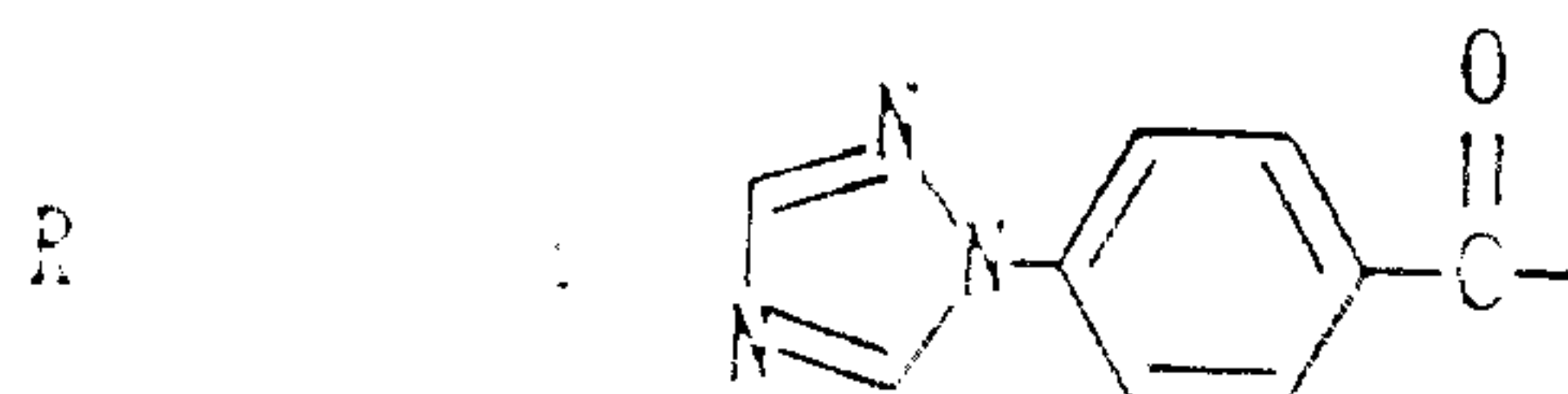
Crystal form: white amorphous

Salt form: free

NMR value: 79)

Example 125

Structural formula:



Crystal form: white amorphous

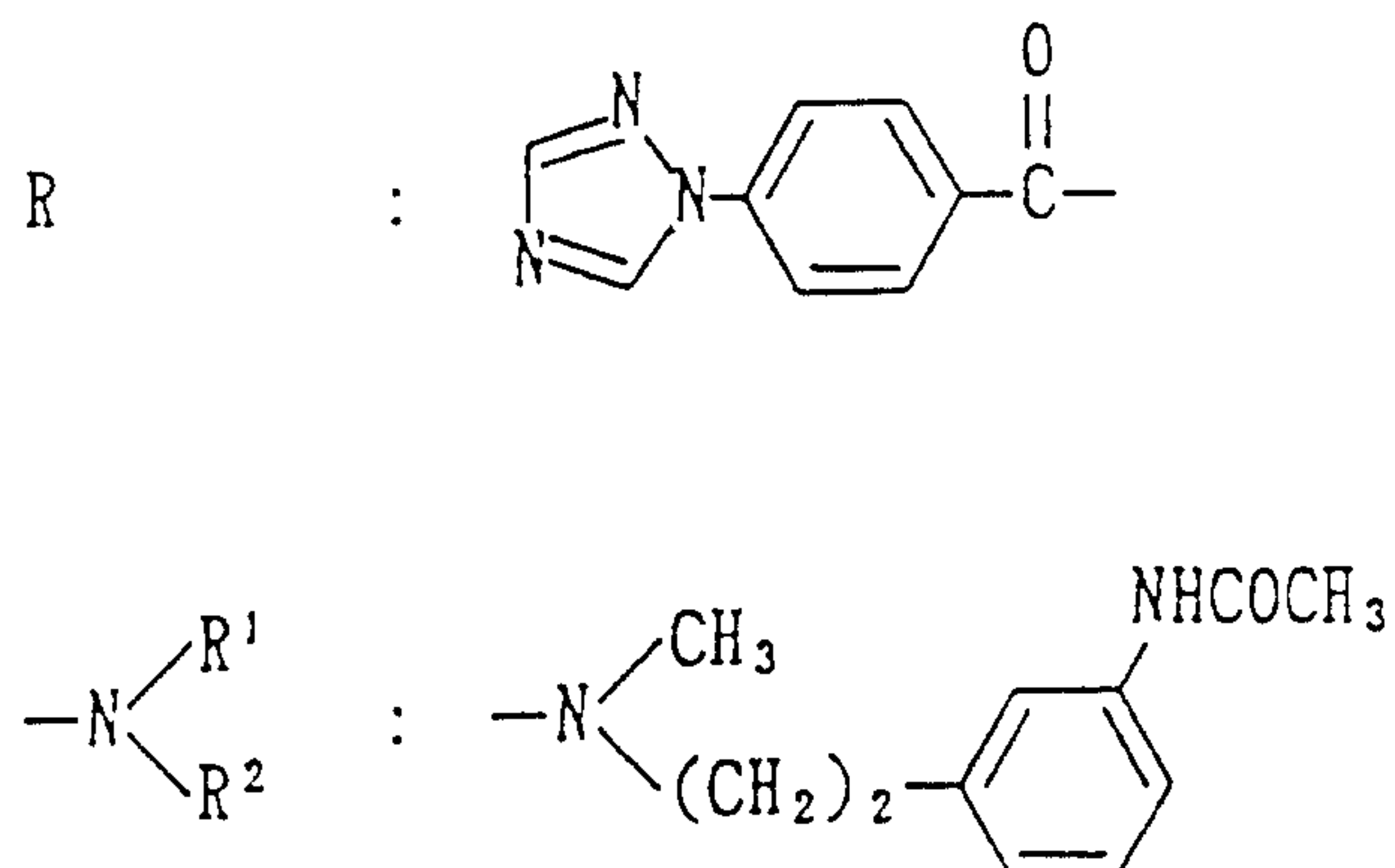
Salt form: free

NMR value: 80)

{Table 10 (continued)}

Example 126

Structural formula:



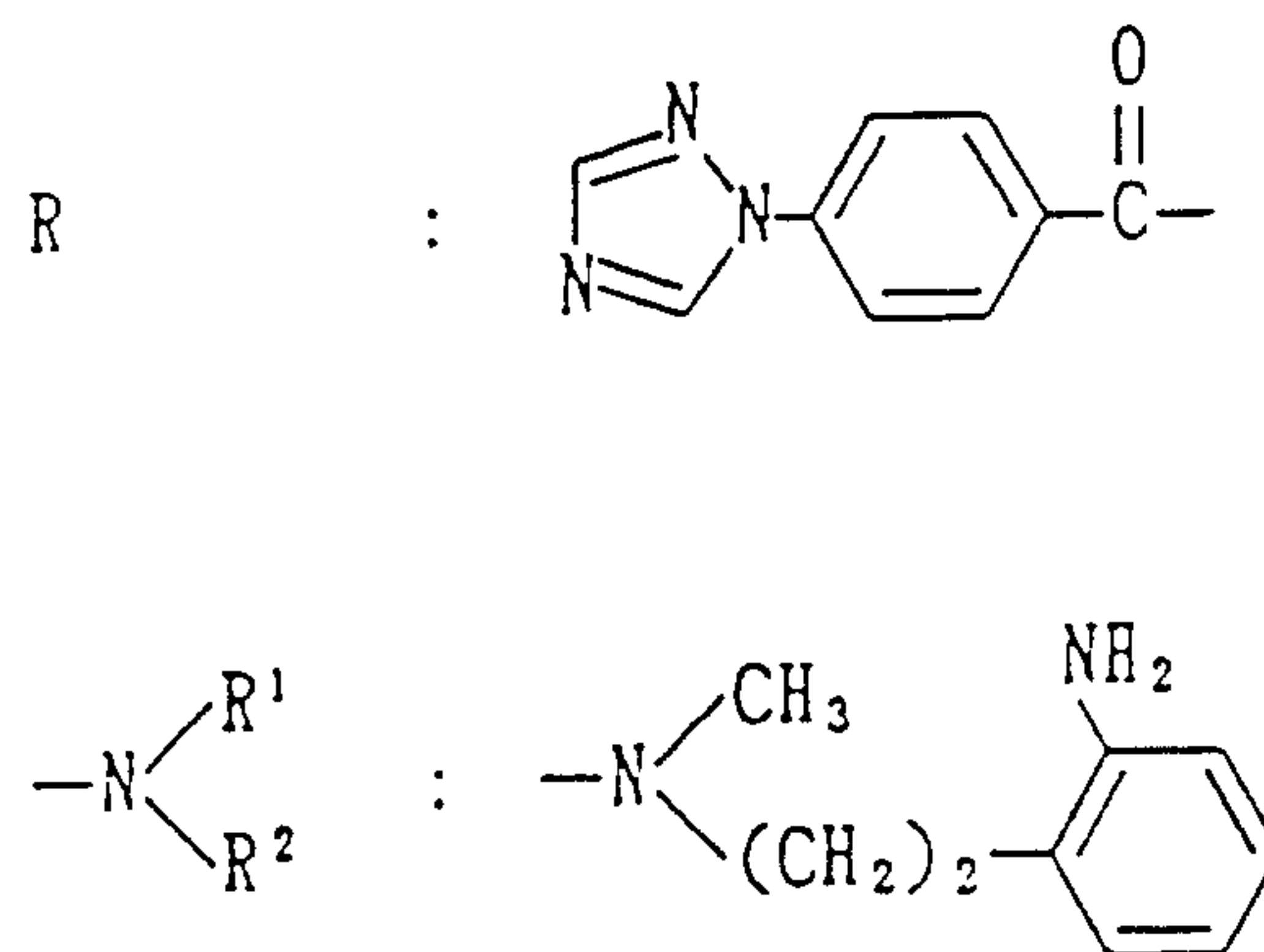
Crystal form: white amorphous

Salt form: free

NMR value: 81)

Example 127

Structural formula:



Crystal form: white amorphous

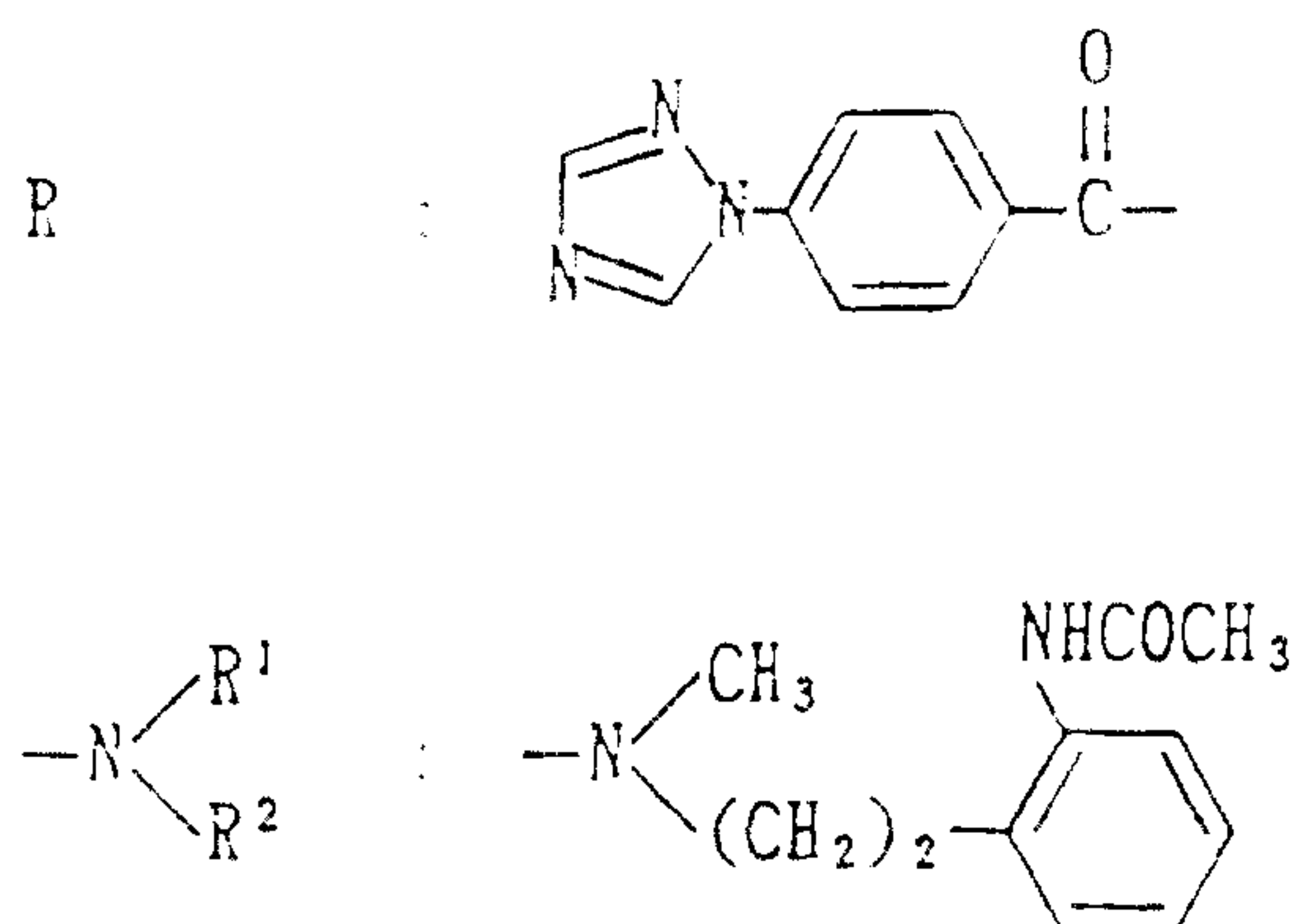
Salt form: hydrochloride

NMR value: 82)

[Table 10 (continued)]

Example 128

Structural formula:



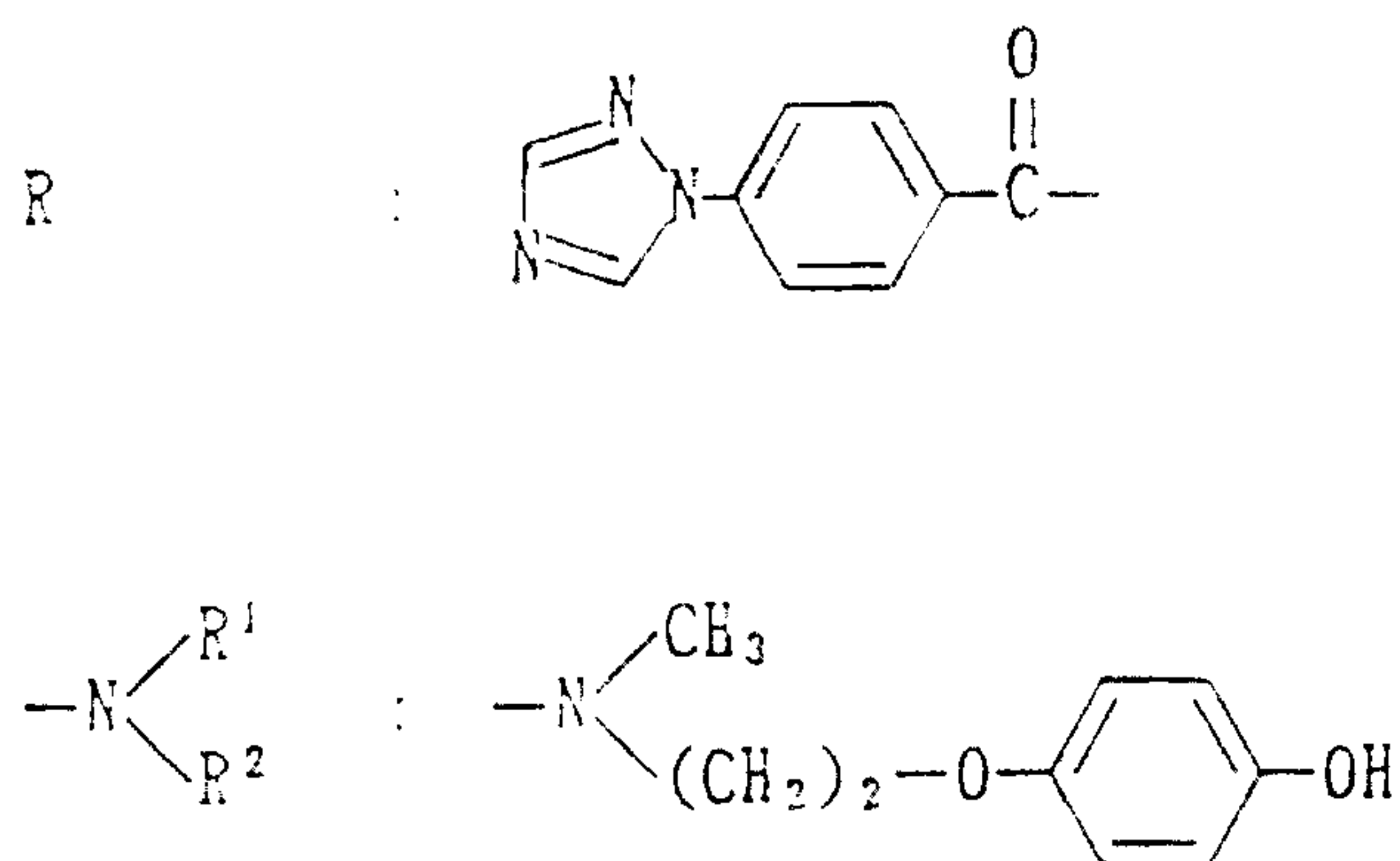
Crystal form: white amorphous

Salt form: free

NMR value: 83)

Example 129

Structural formula:



Crystal form: white powder

Recrystallization solvent: dichloromethane-diethyl ether

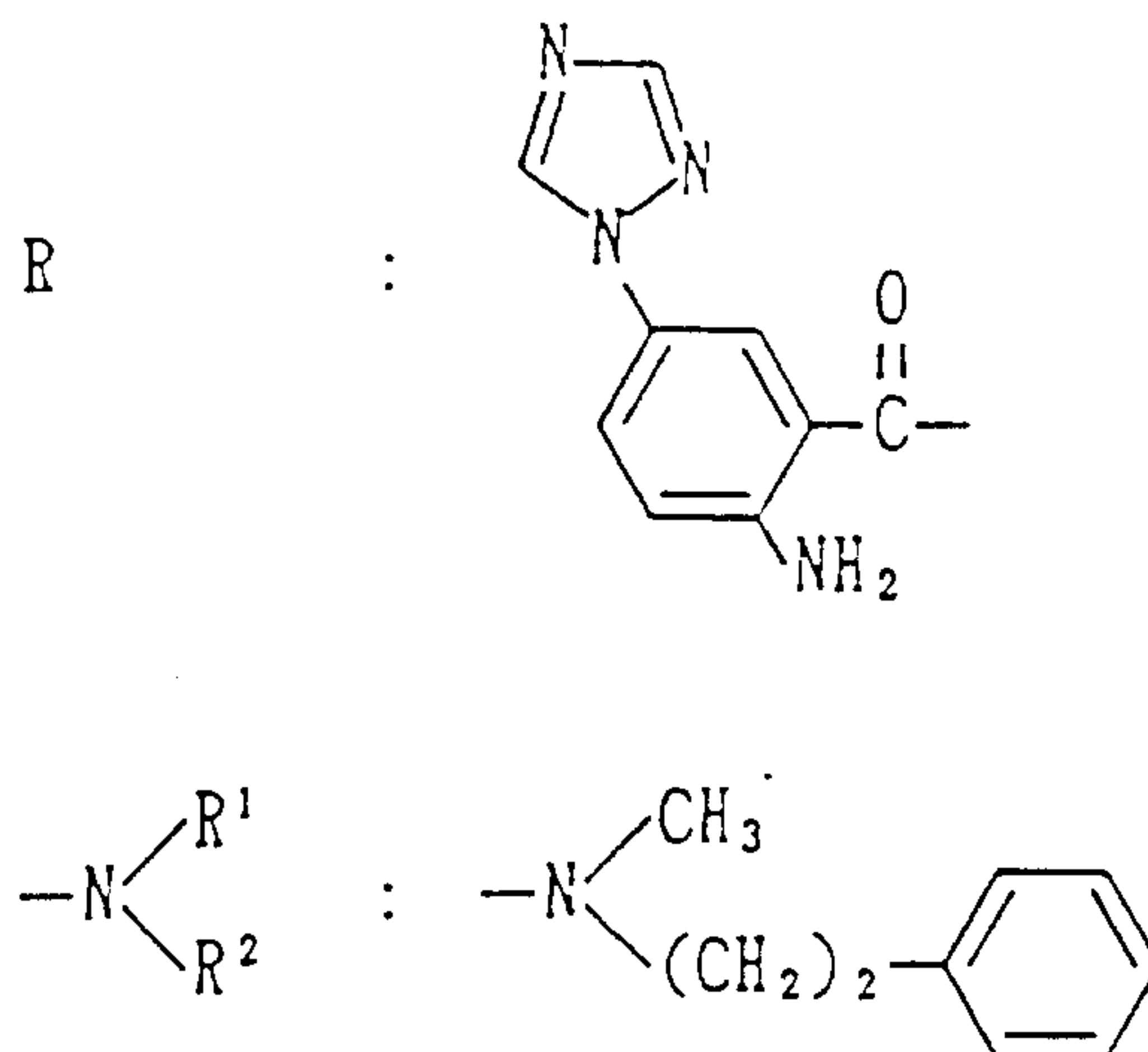
Melting point (°C): 191-193

Salt form: free

{Table 10 (continued)}

Example 130

Structural formula:



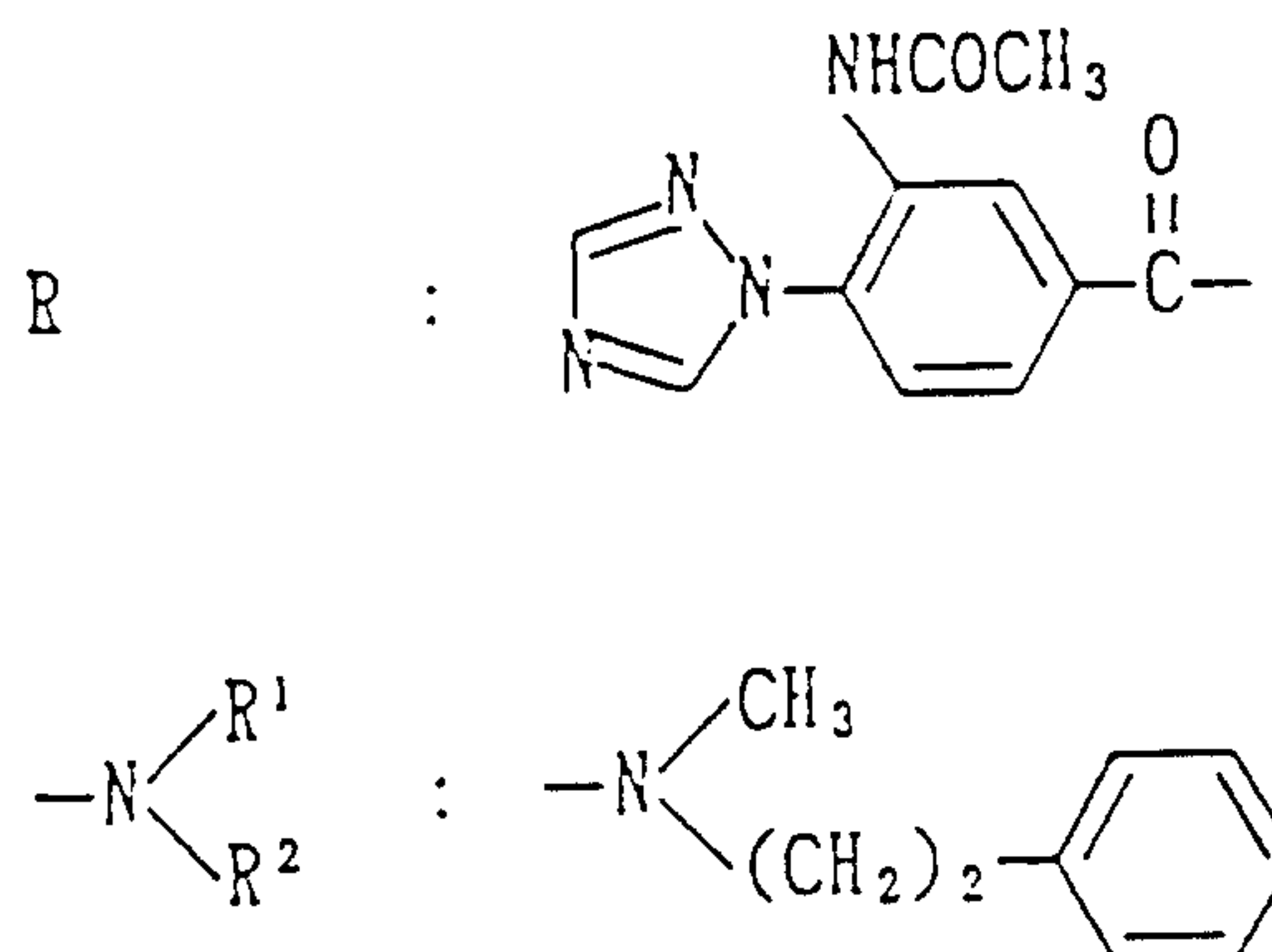
Crystal form: light yellow amorphous

Salt form: hydrochloride

NMR value: 84)

Example 131

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol

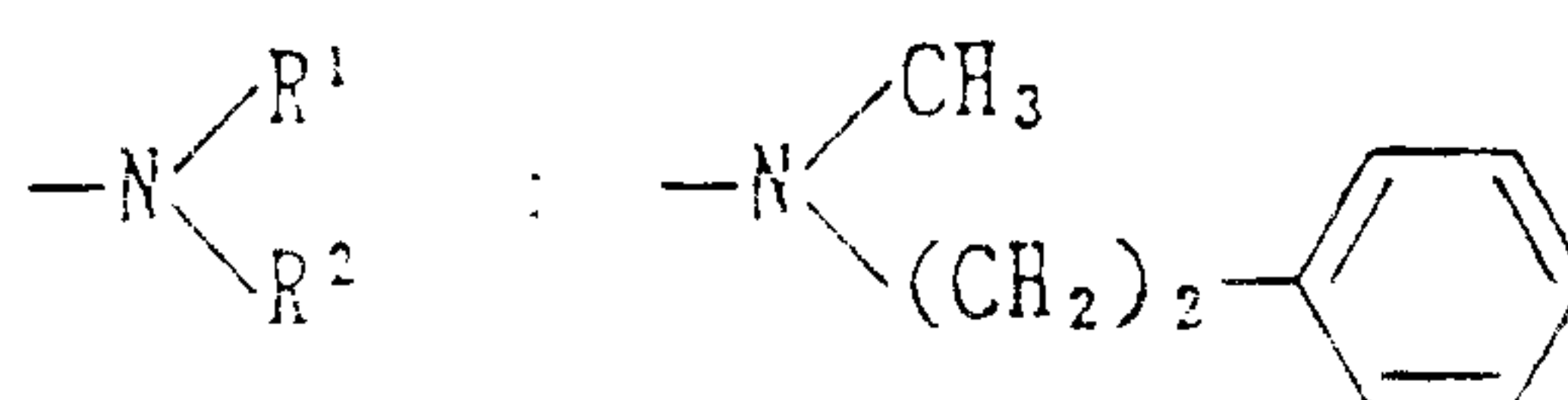
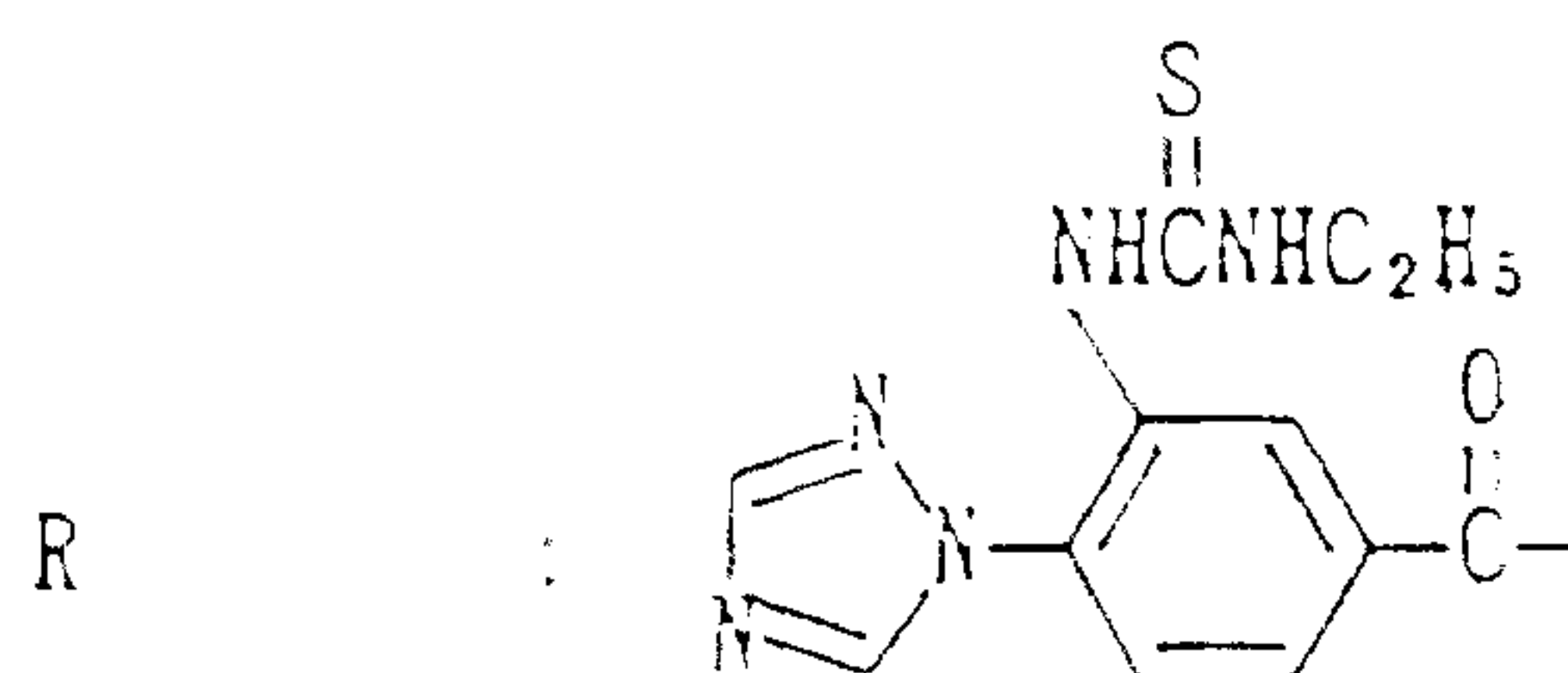
Melting point (°C): 256-257

Salt form: hydrochloride

[Table 10 (continued)]

Example 132

Structural formula:



Crystal form: white powder

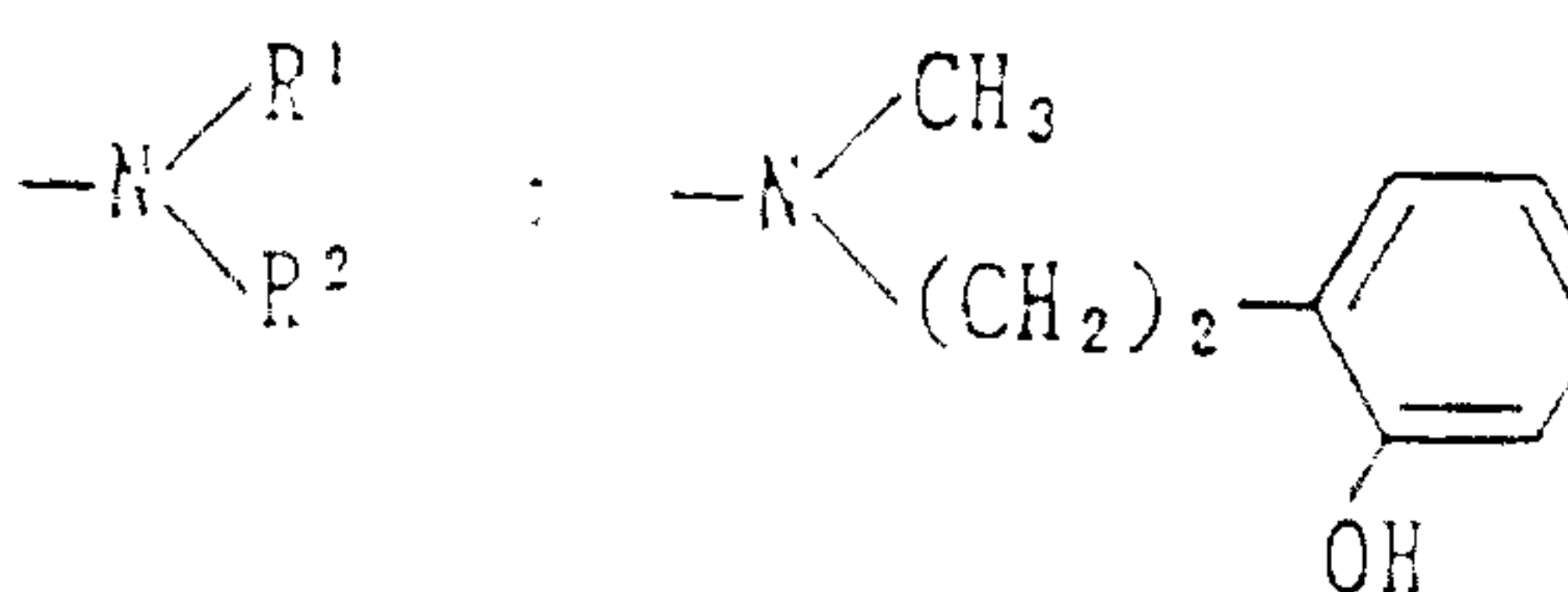
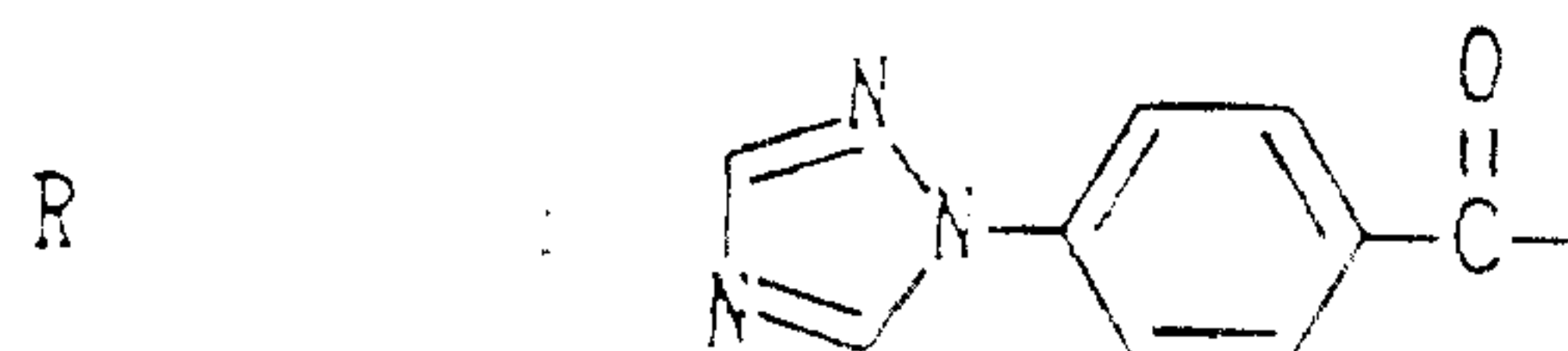
Recrystallization solvent: ethyl acetate-n-hexane

Melting point (°C): 141-142

Salt form: free

Example 133

Structural formula:



Crystal form: white amorphous

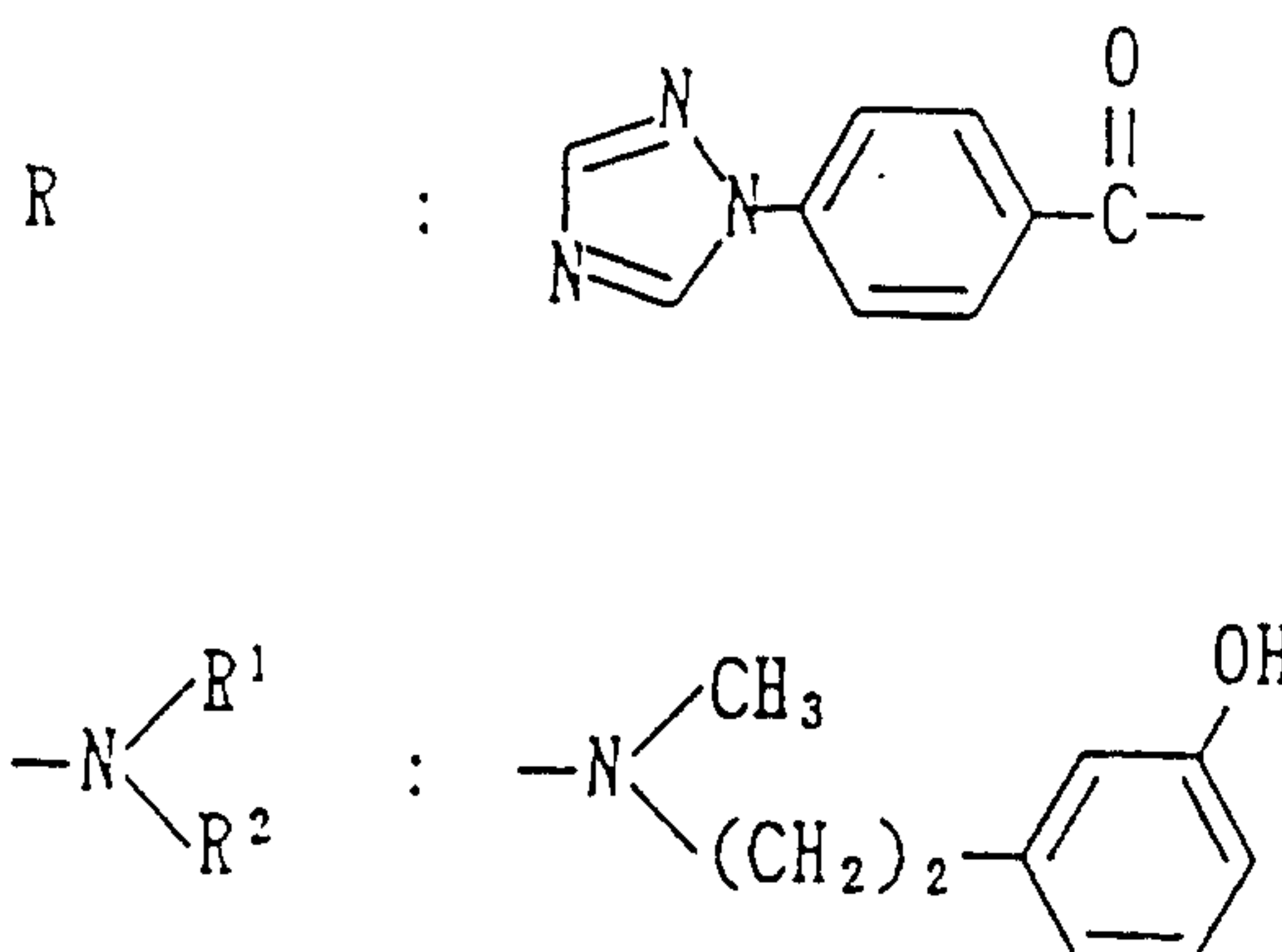
Salt form: hydrochloride

NMR value: 85)

[Table 10 (continued)]

Example 134

Structural formula:



Crystal form: light yellow powder

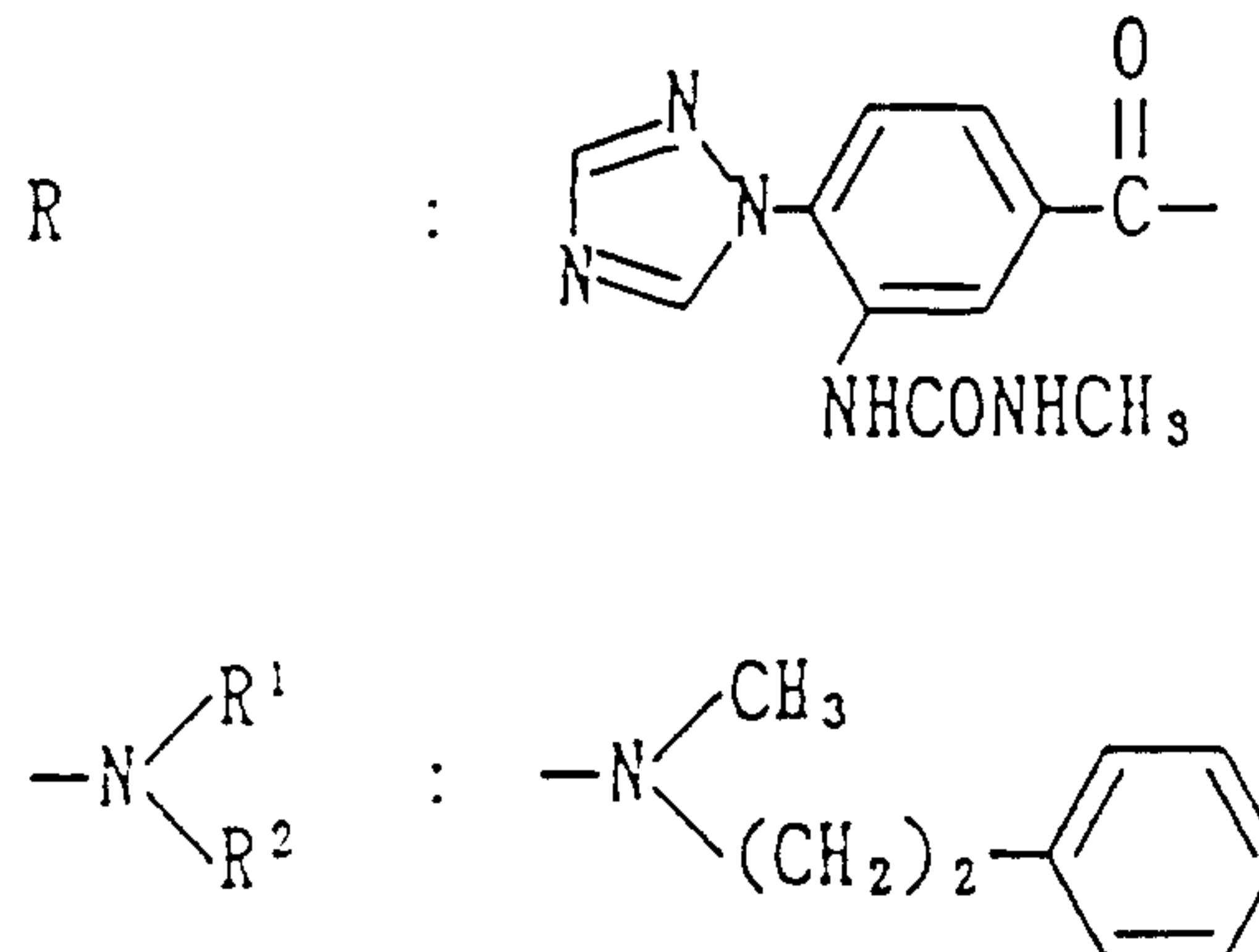
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 180-181

Salt form: free

Example 135

Structural formula:



Crystal form: white amorphous

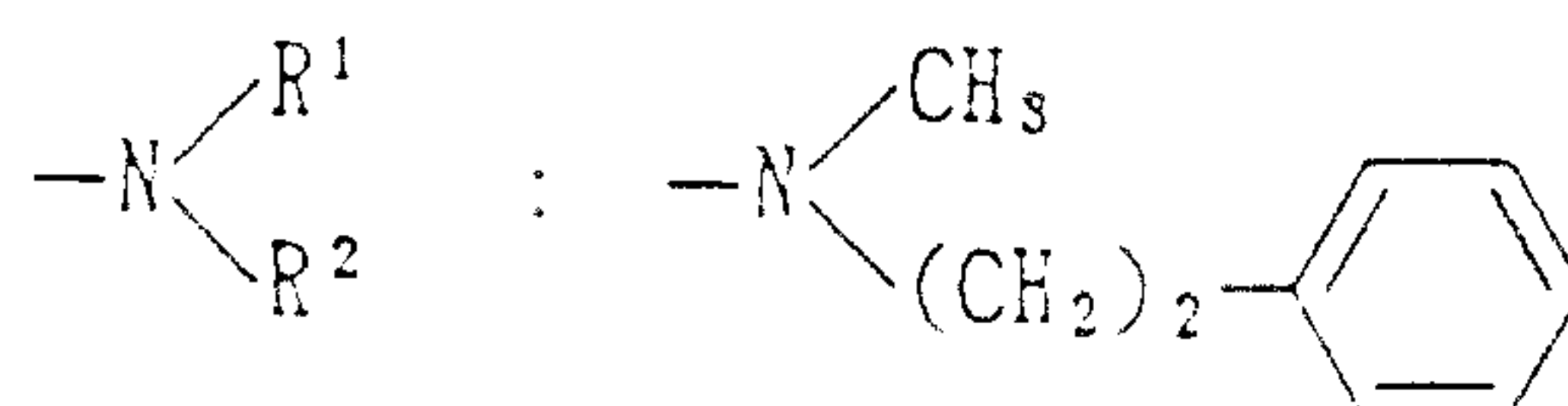
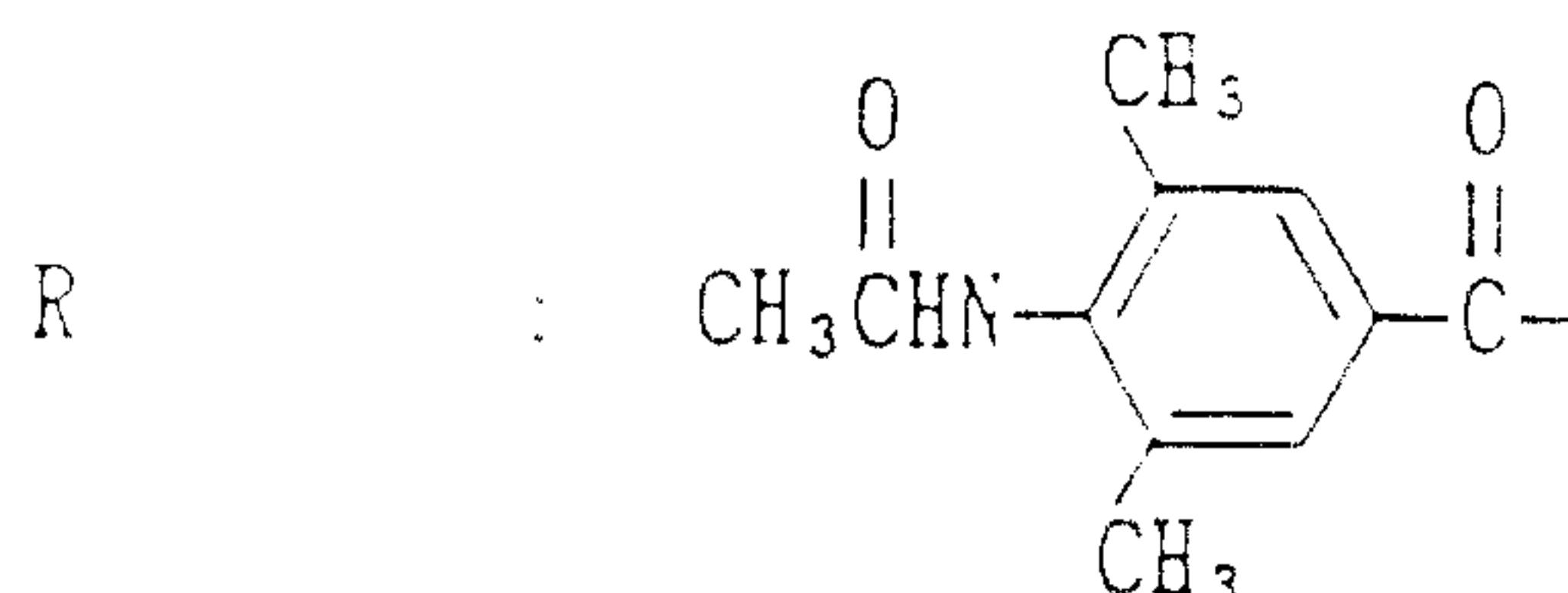
Salt form: hydrochloride

NMR value: 86)

{Table 10 (continued)}

Example 136

Structural formula:



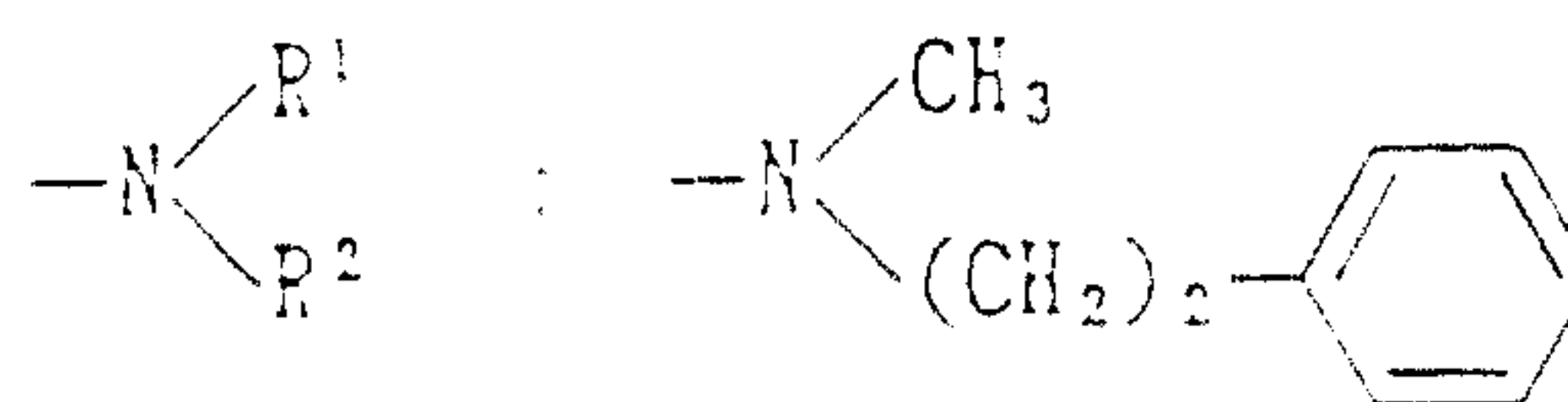
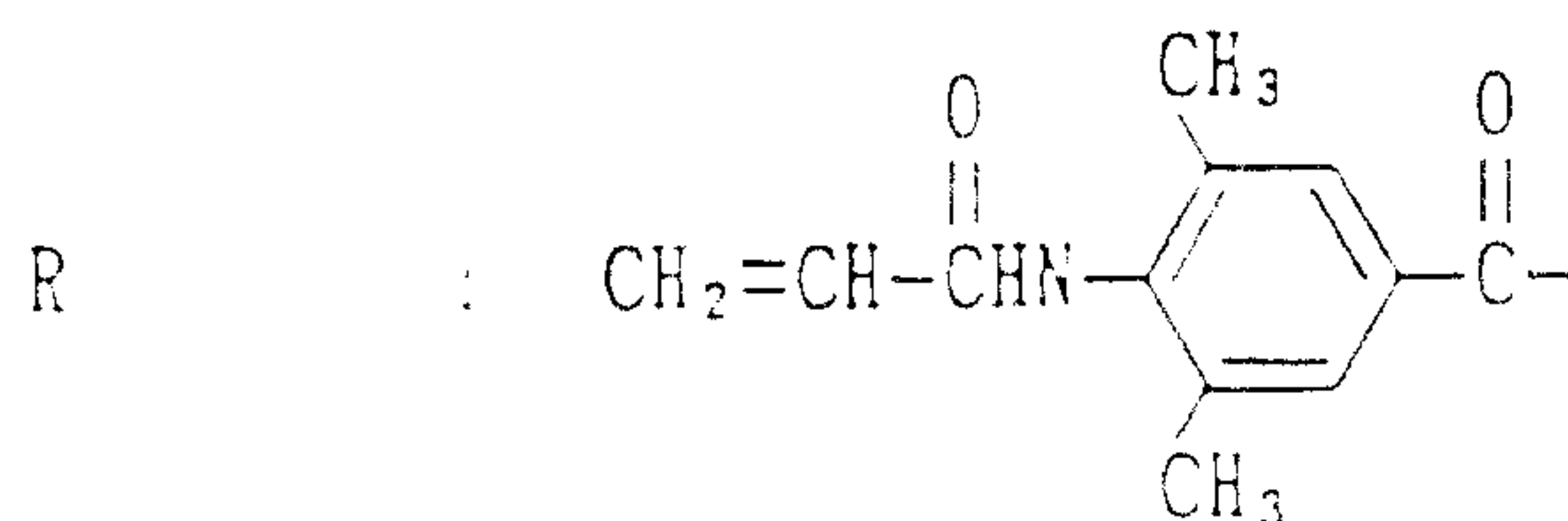
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 87)

Example 137

Structural formula:



Crystal form: yellow amorphous

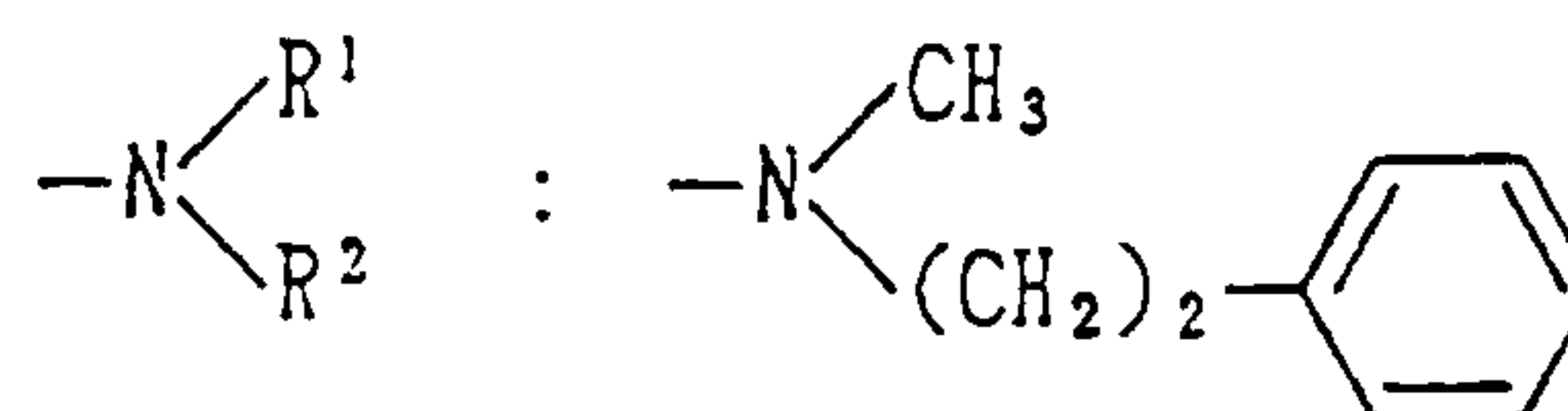
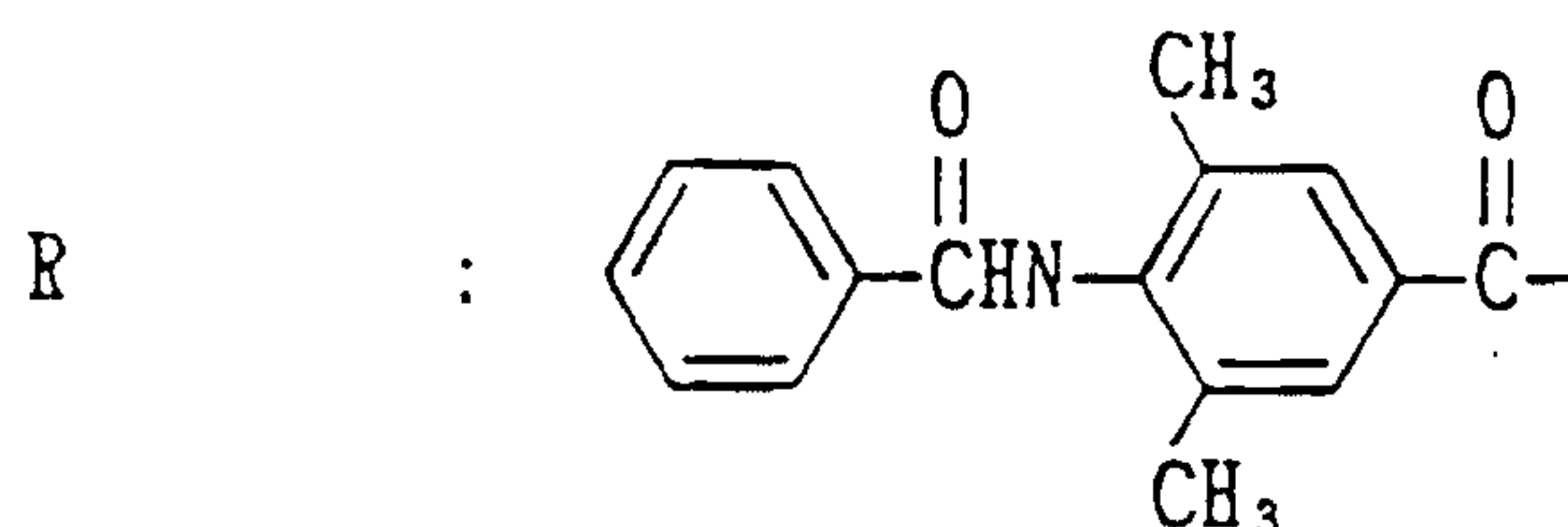
Salt form: hydrochloride

NMR value: 88)

{Table 10 (continued)}

Example 138

Structural formula:



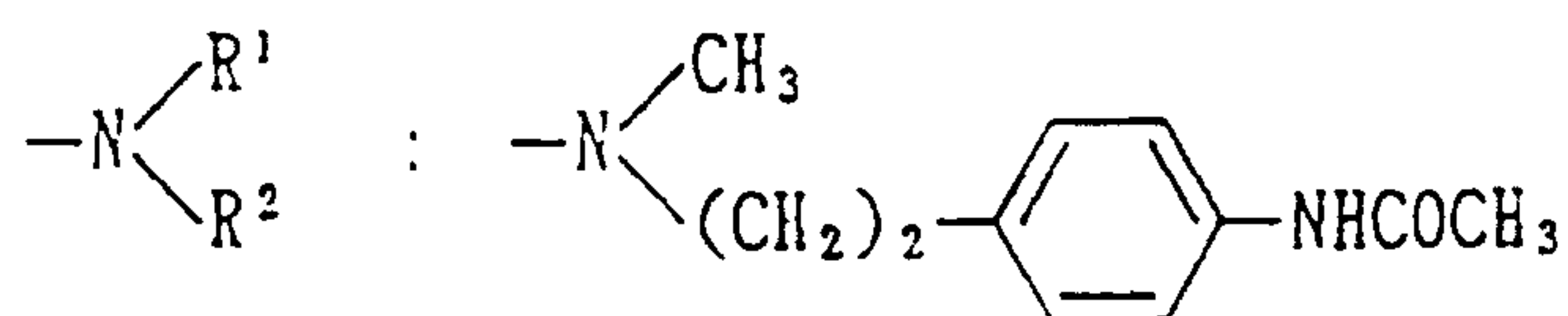
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 89)

Example 139

Structural formula:



Crystal form: white amorphous

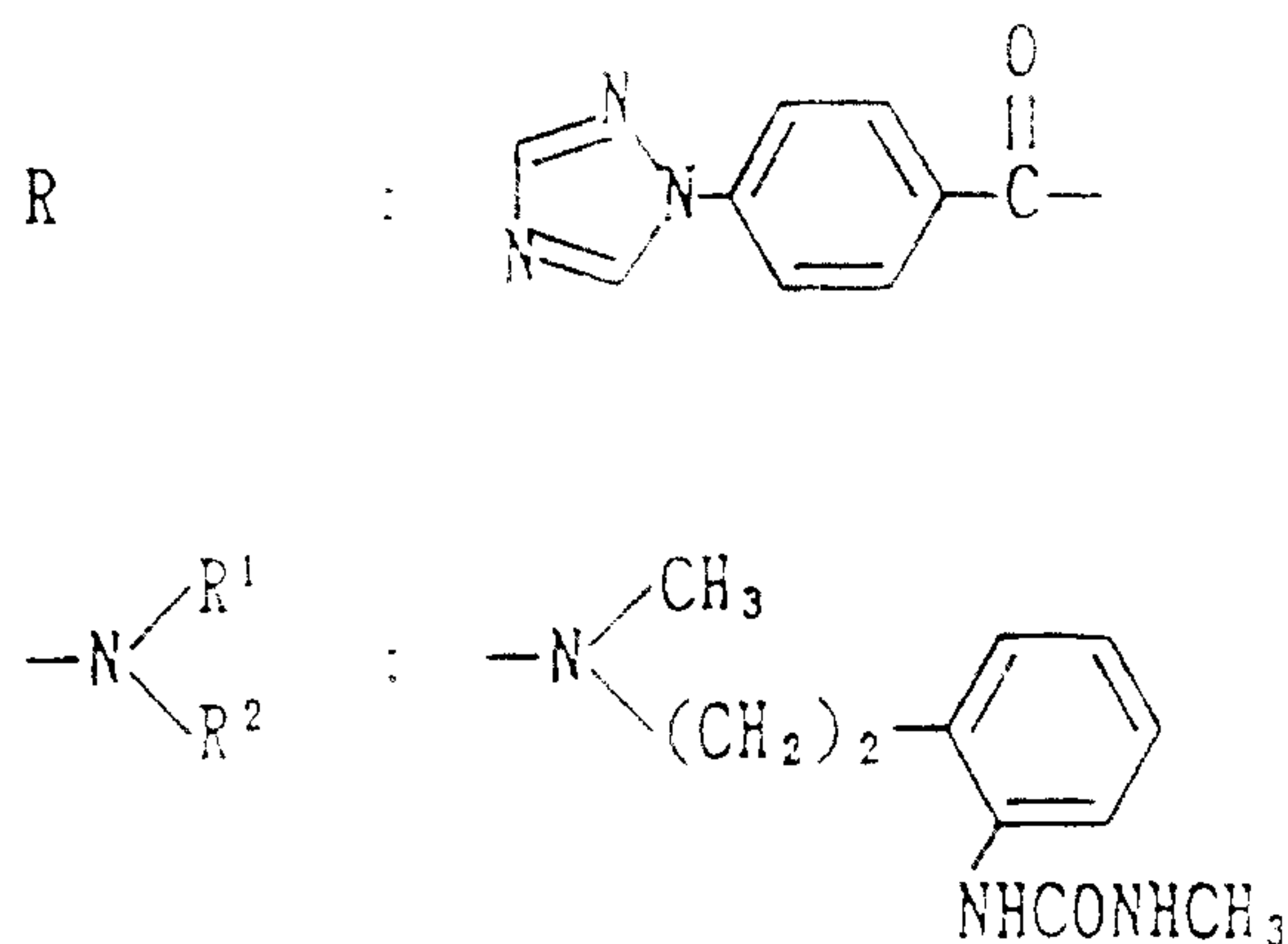
Salt form: free

NMR value: 90)

{Table 10 (continued)}

Example 140

Structural formula:



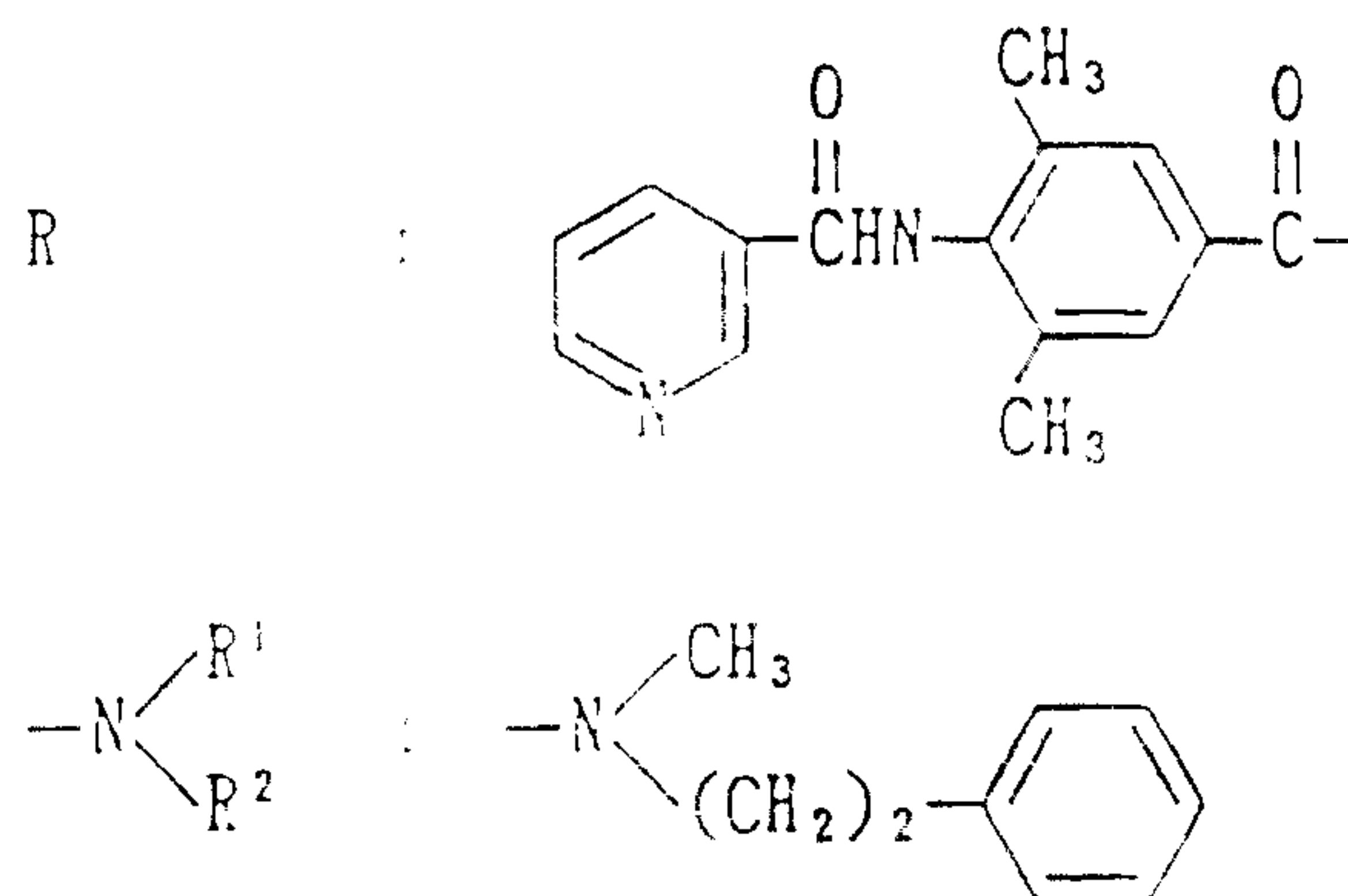
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 91)

Example 141

Structural formula:



Crystal form: orange amorphous

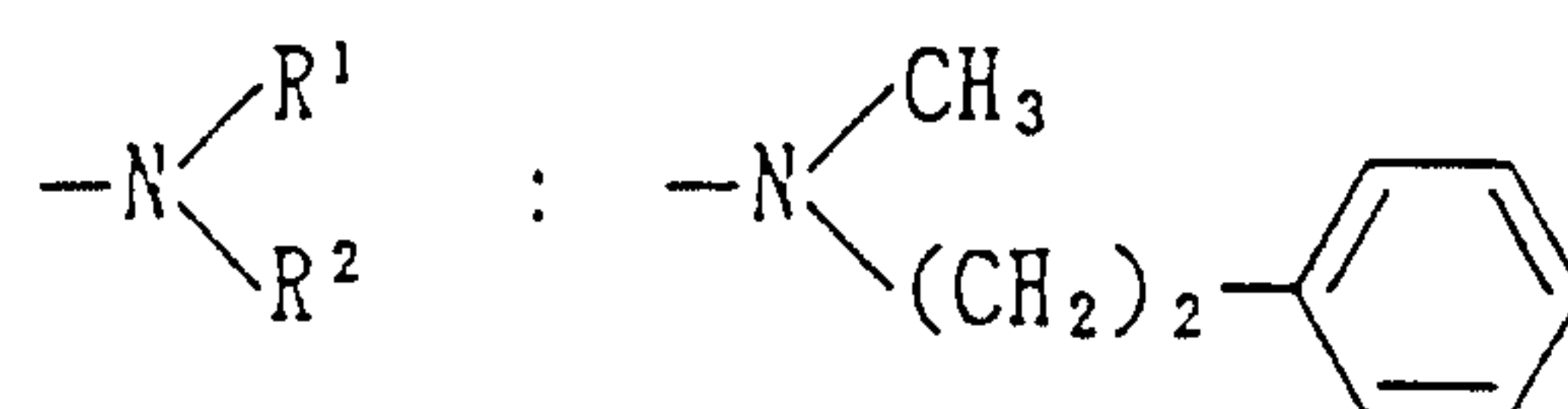
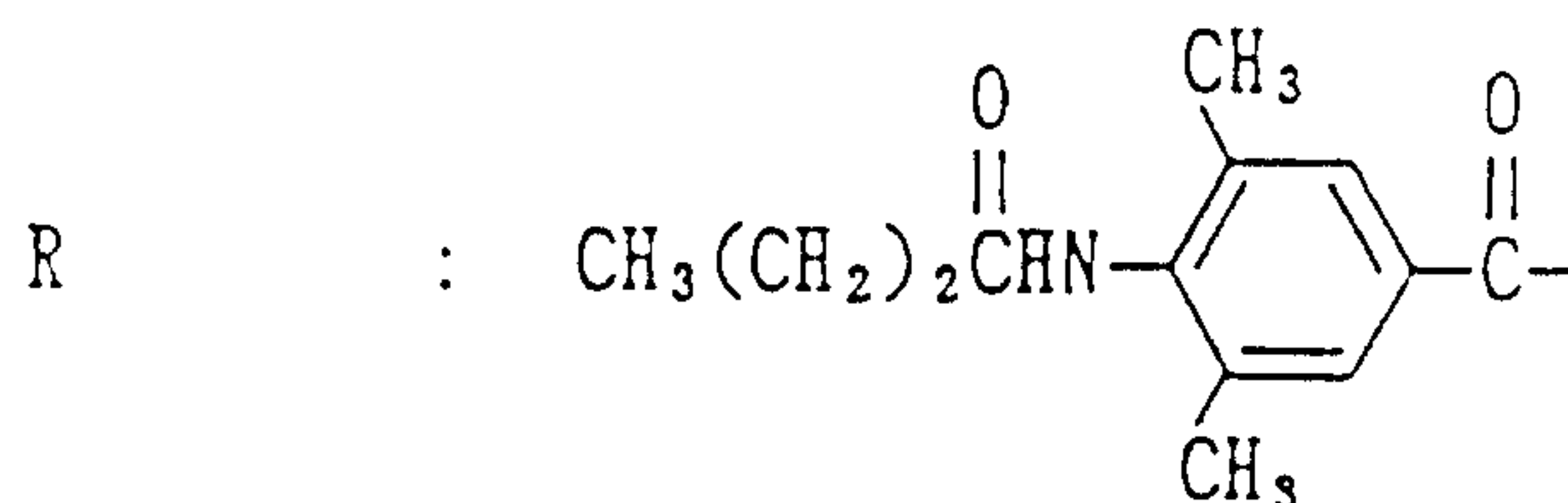
Salt form: dihydrochloride

NMR value: 92)

[Table 10 (continued)]

Example 142

Structural formula:



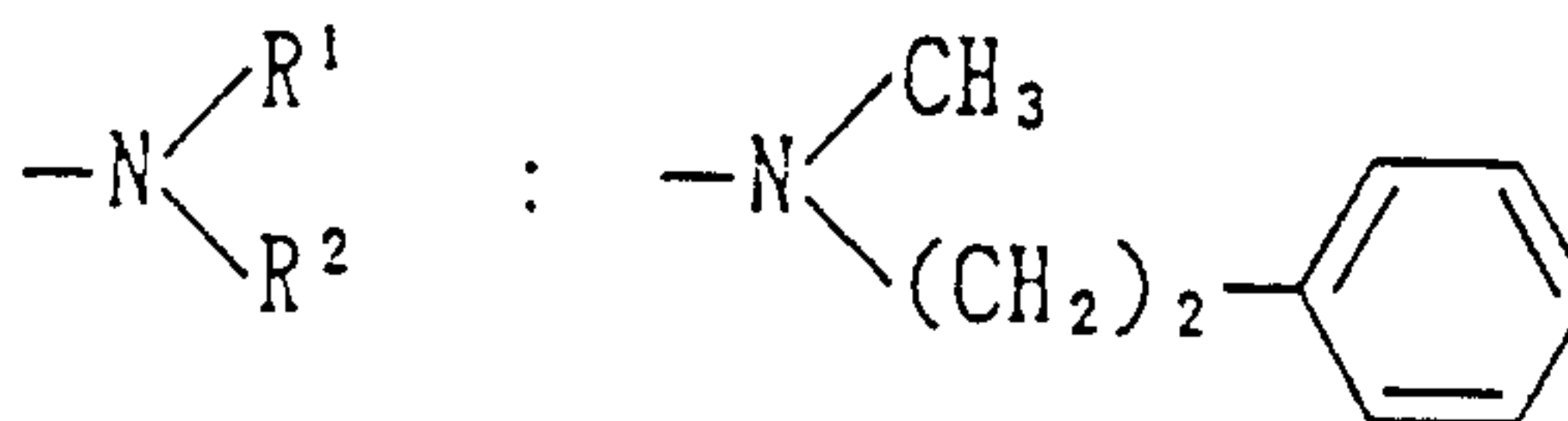
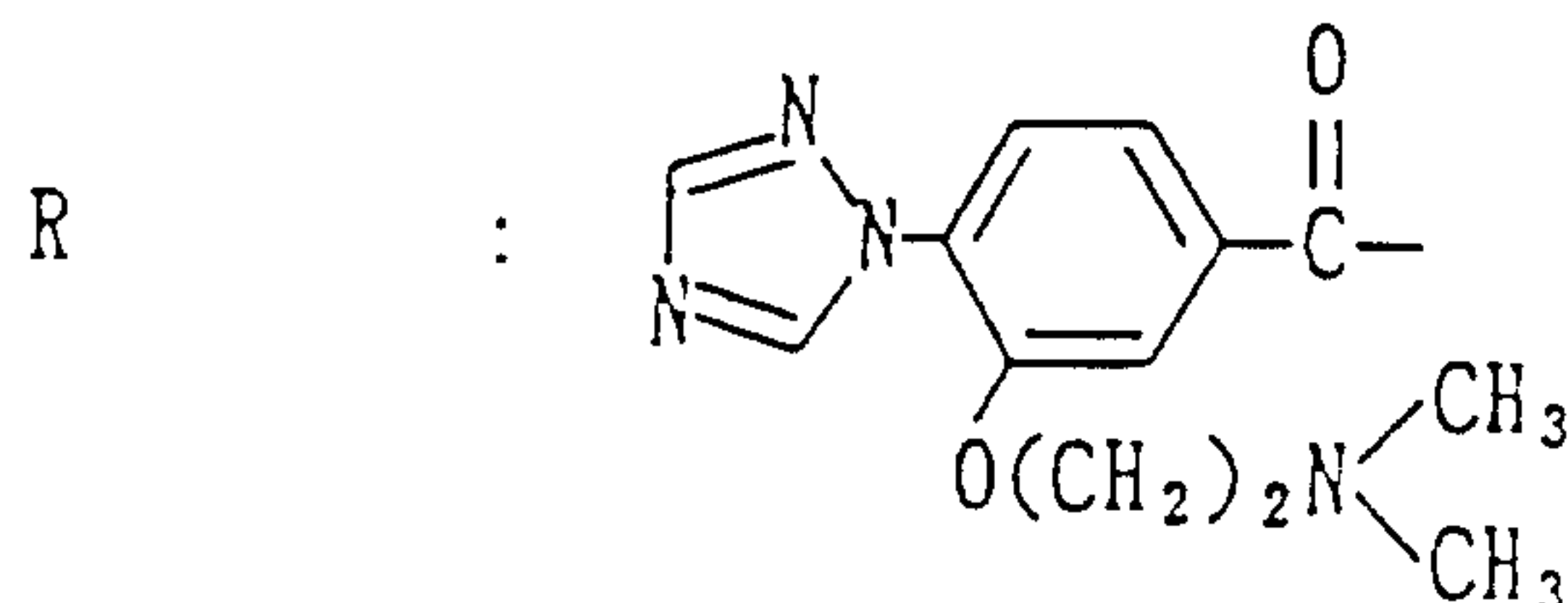
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 93)

Example 143

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-n-hexane

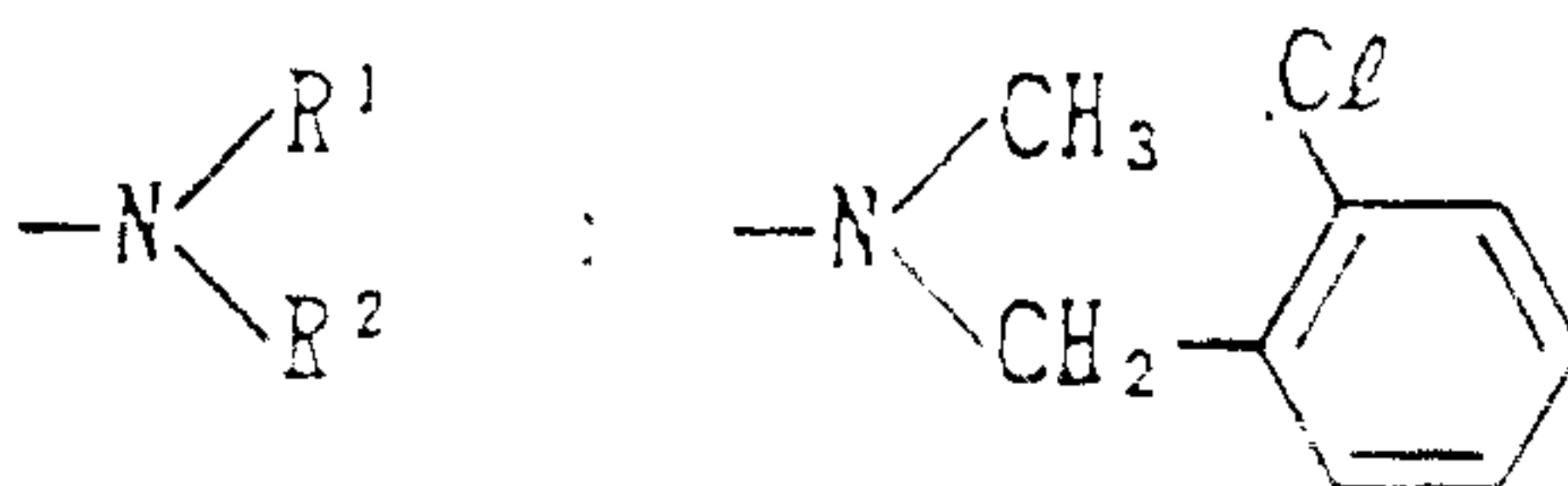
Melting point (°C): 83-85

Salt form: free

[Table 10 (continued)]

Example 144

Structural formula:



Crystal form: white powder

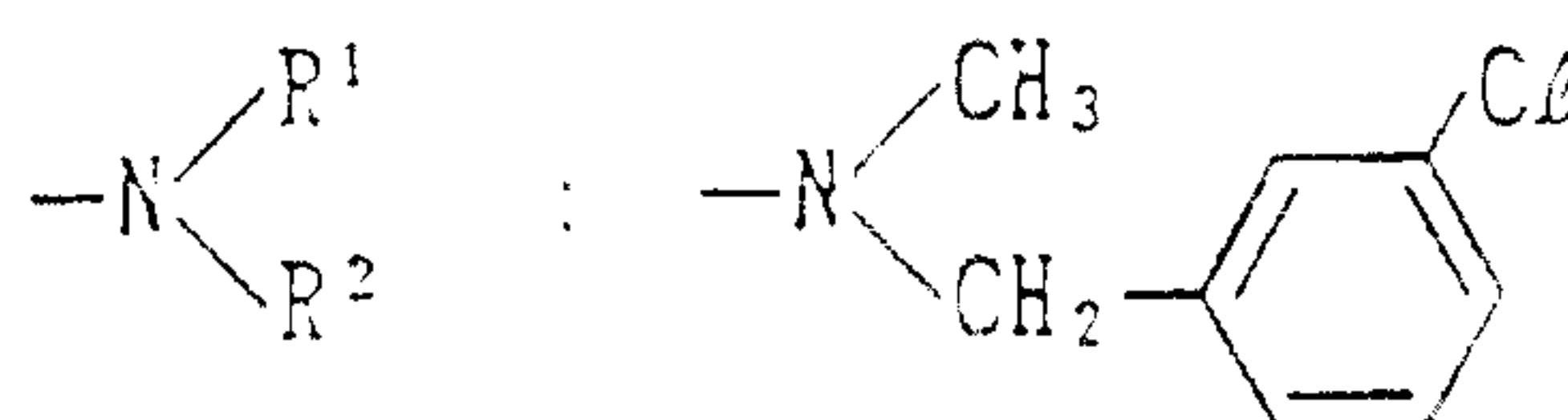
Recrystallization solvent: dichloromethane-diethyl ether

Melting point (°C): 140-142.5

Salt form: free

Example 145

Structural formula:



Crystal form: white powder

Recrystallization solvent: dichloromethane-diethyl ether

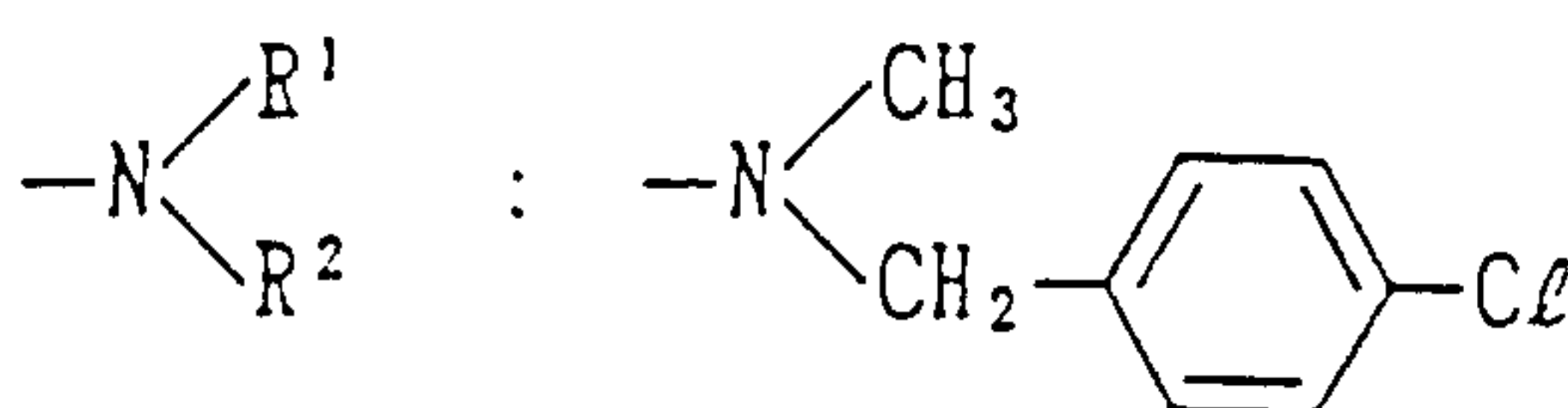
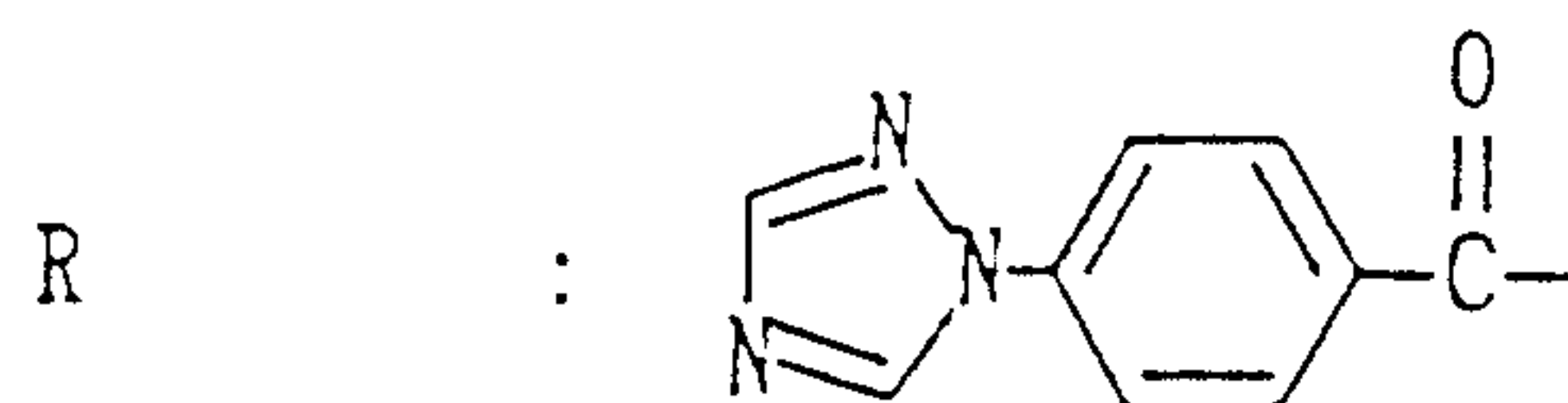
Melting point (°C): 133-134

Salt form: free

[Table 10 (continued)]

Example 146

Structural formula:



Crystal form: colorless needles

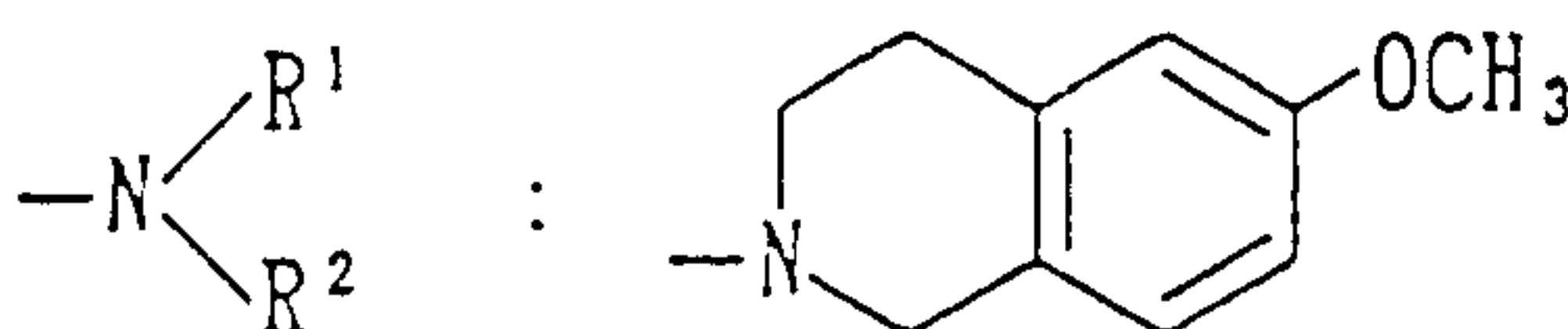
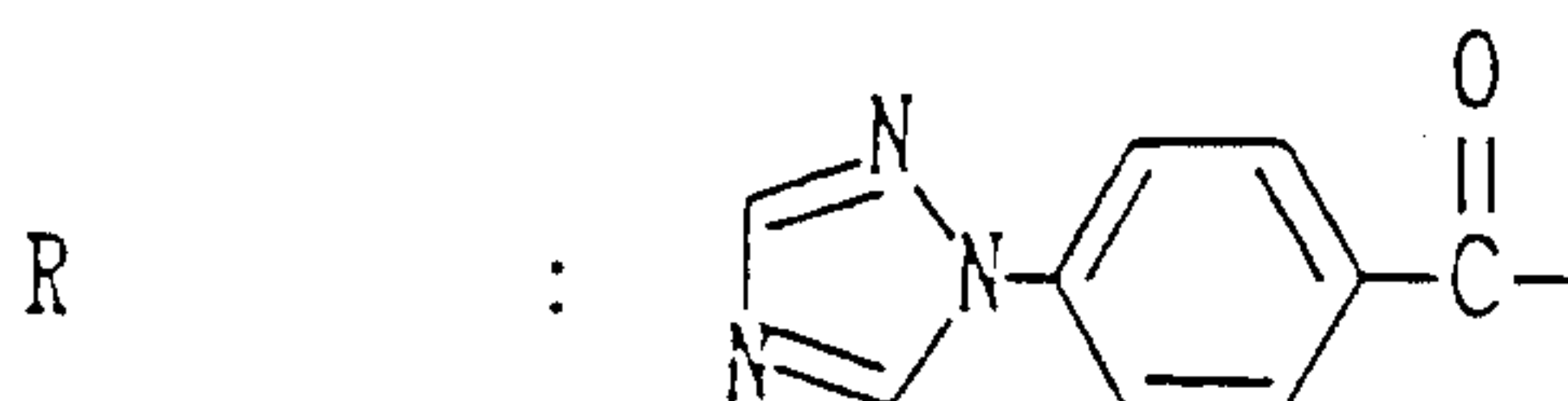
Recrystallization solvent: dichloromethane-diethyl ether

Melting point (°C): 168-170

Salt form: free

Example 147

Structural formula:



Crystal form: light yellow amorphous

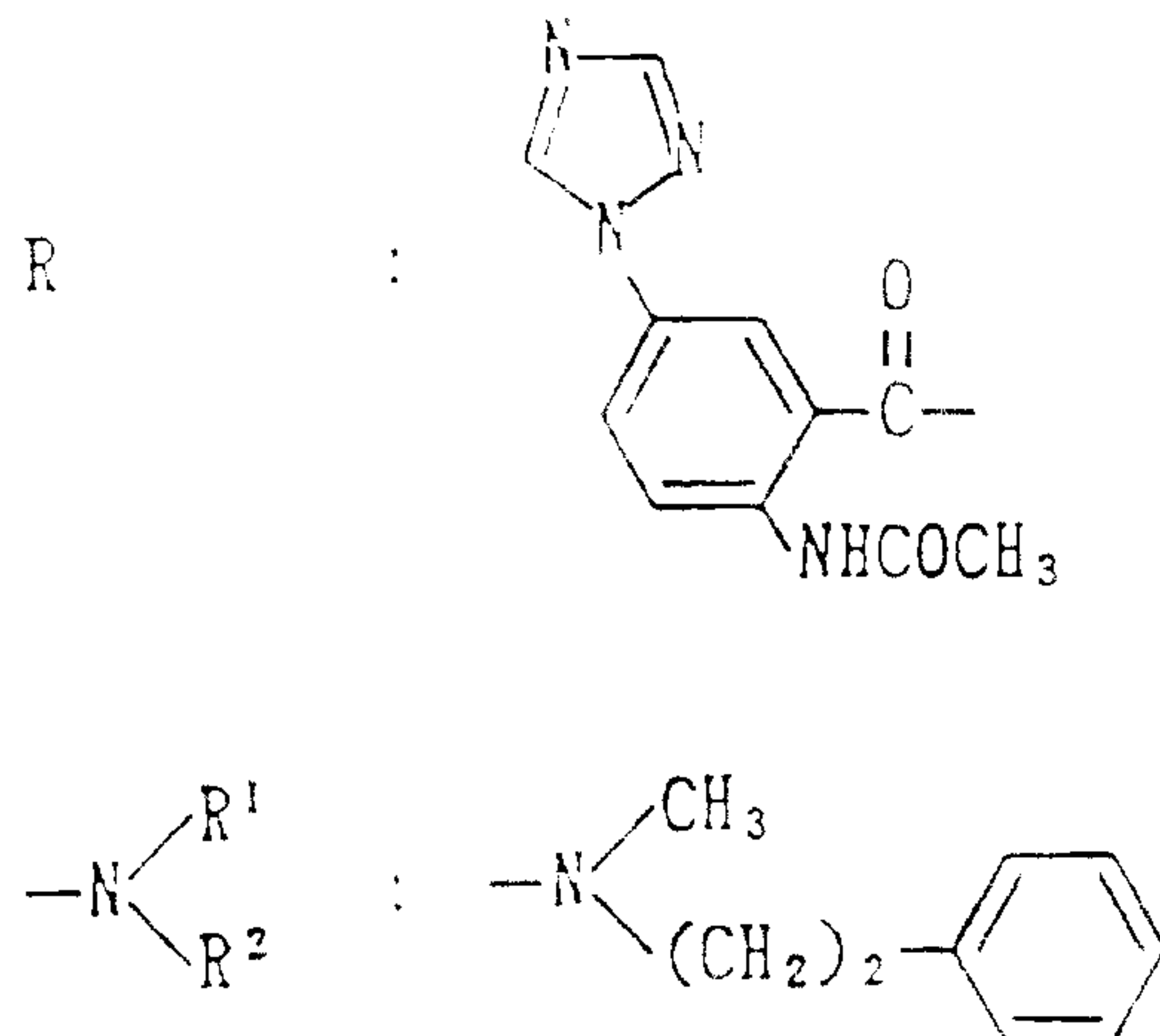
Salt form: free

NMR value: 94)

{Table 10 (continued)}

Example 148

Structural formula:



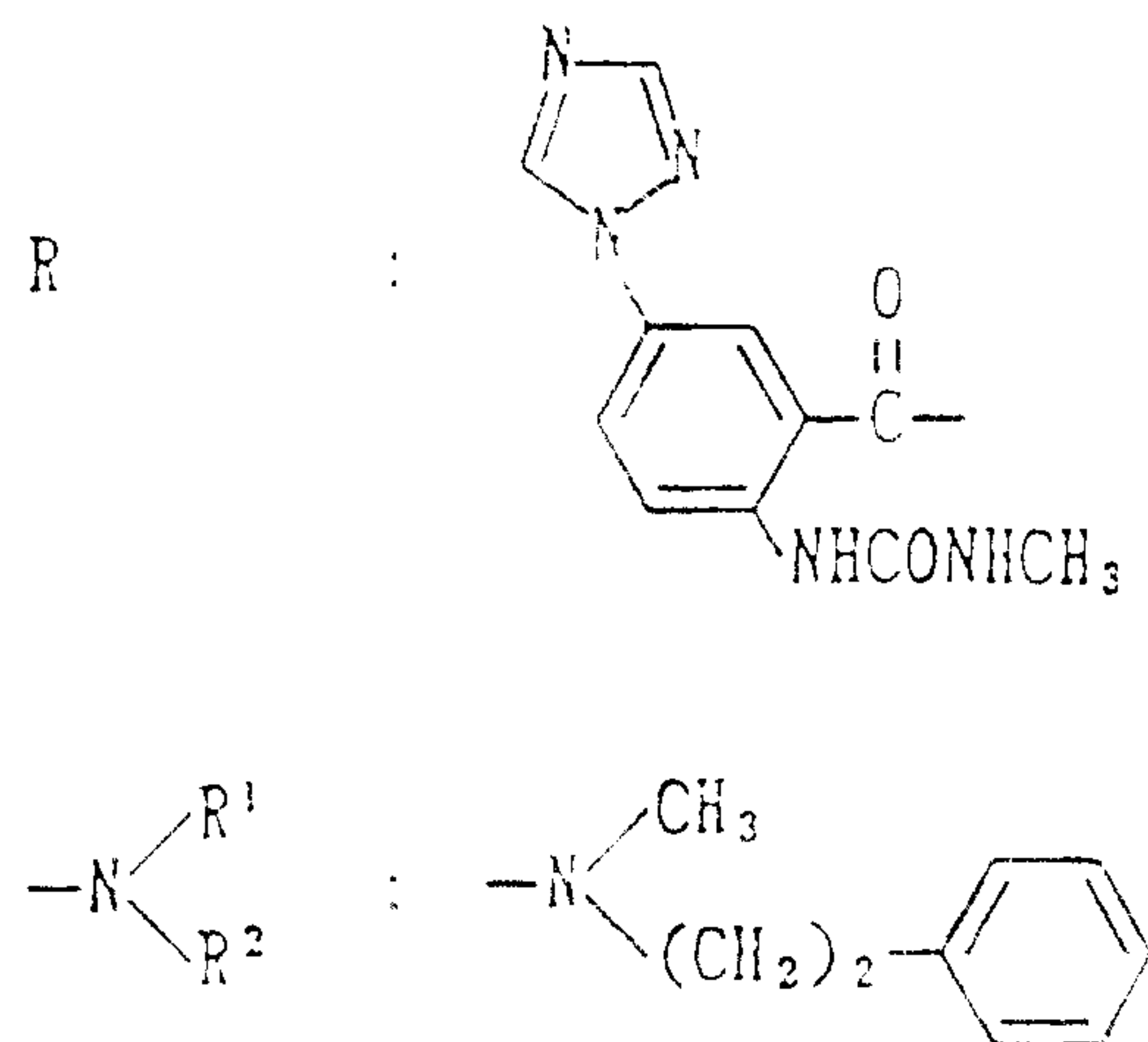
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 95)

Example 149

Structural formula:



Crystal form: white amorphous

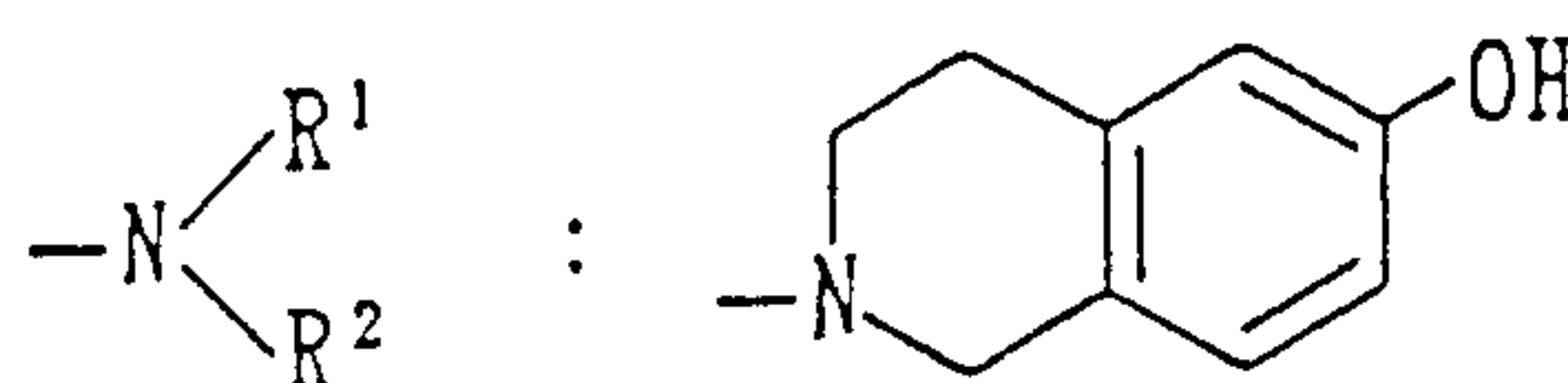
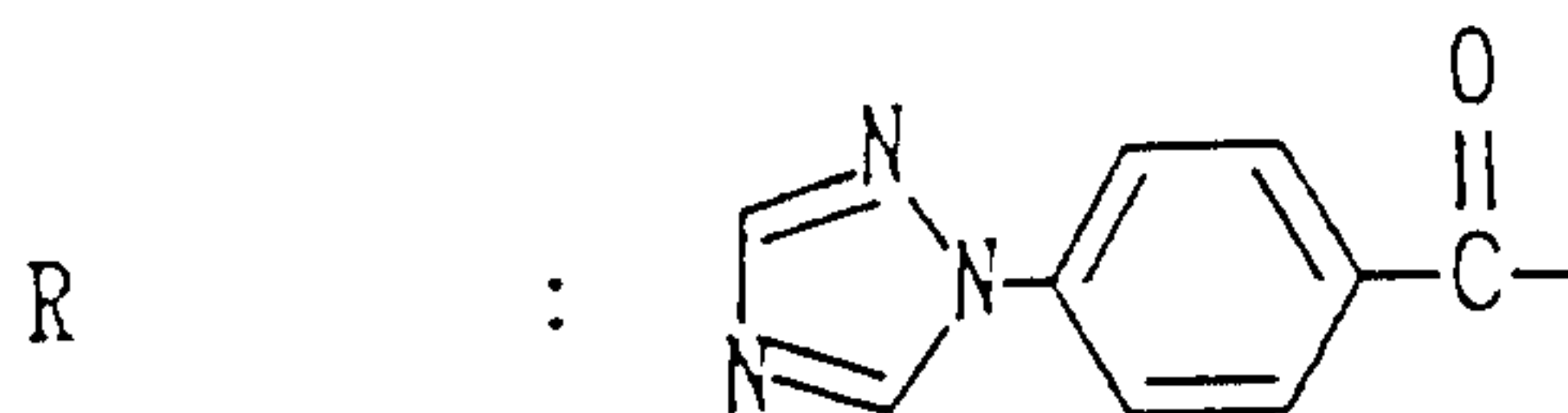
Salt form: free

NMR value: 96)

{Table 10 (continued)}

Example 150

Structural formula:



Crystal form: light yellow powder

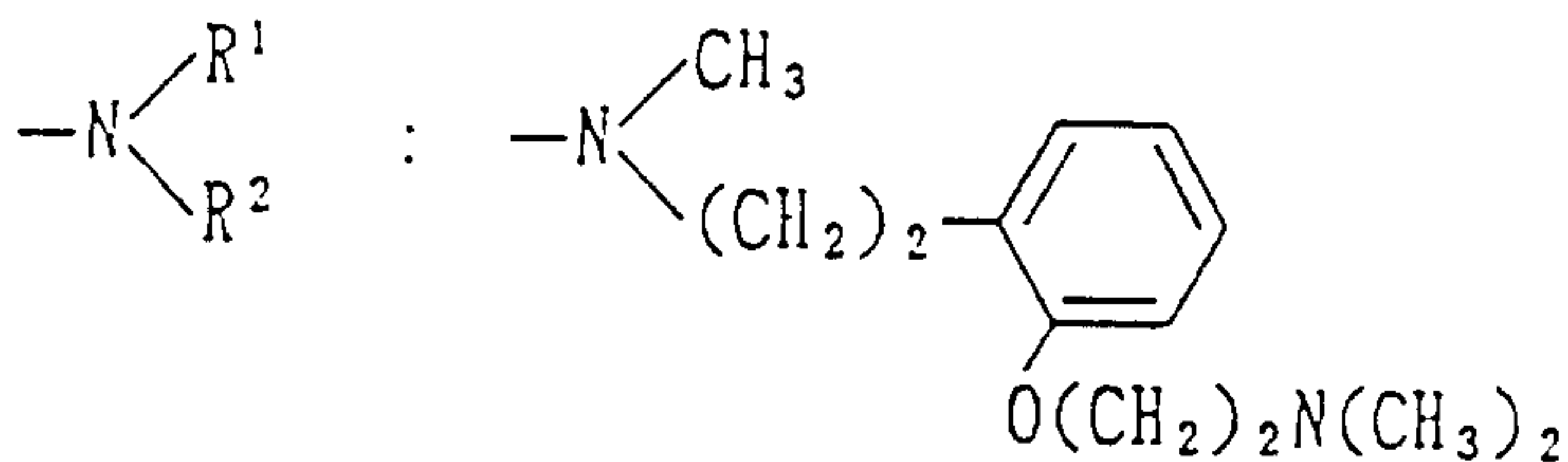
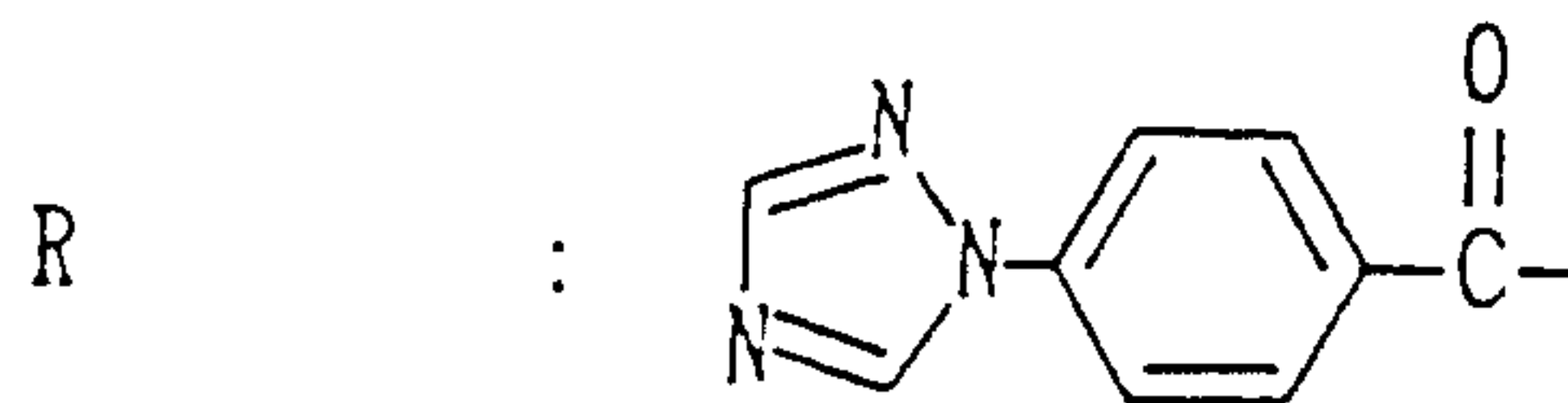
Recrystallization solvent: dimethylformamide-ethanol

Melting point (°C): 249-251

Salt form: free

Example 151

Structural formula:



Crystal form: white amorphous

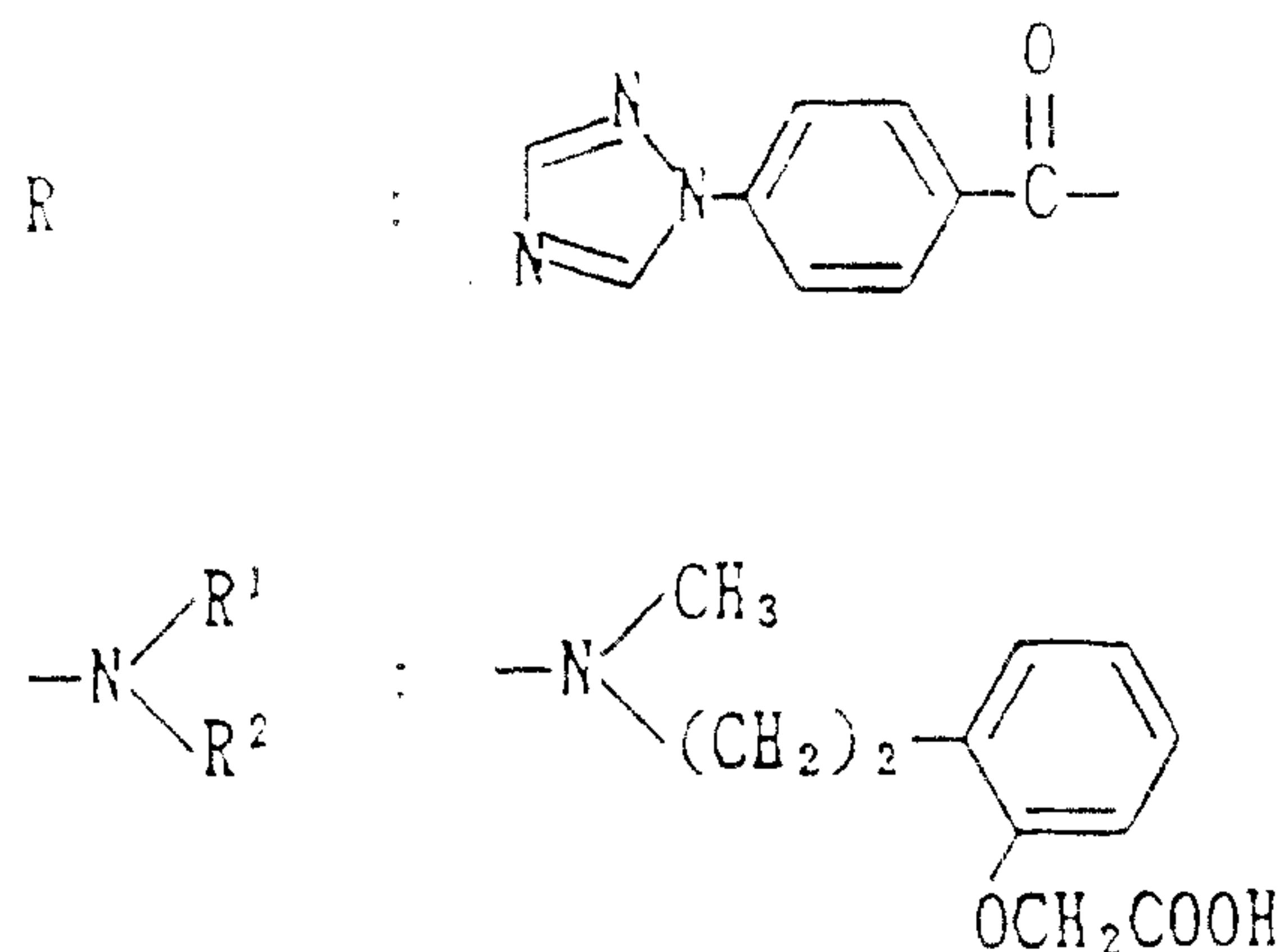
Salt form: dihydrochloride

NMR value: 97).

(Table 10 (continued))

Example 152

Structural formula:



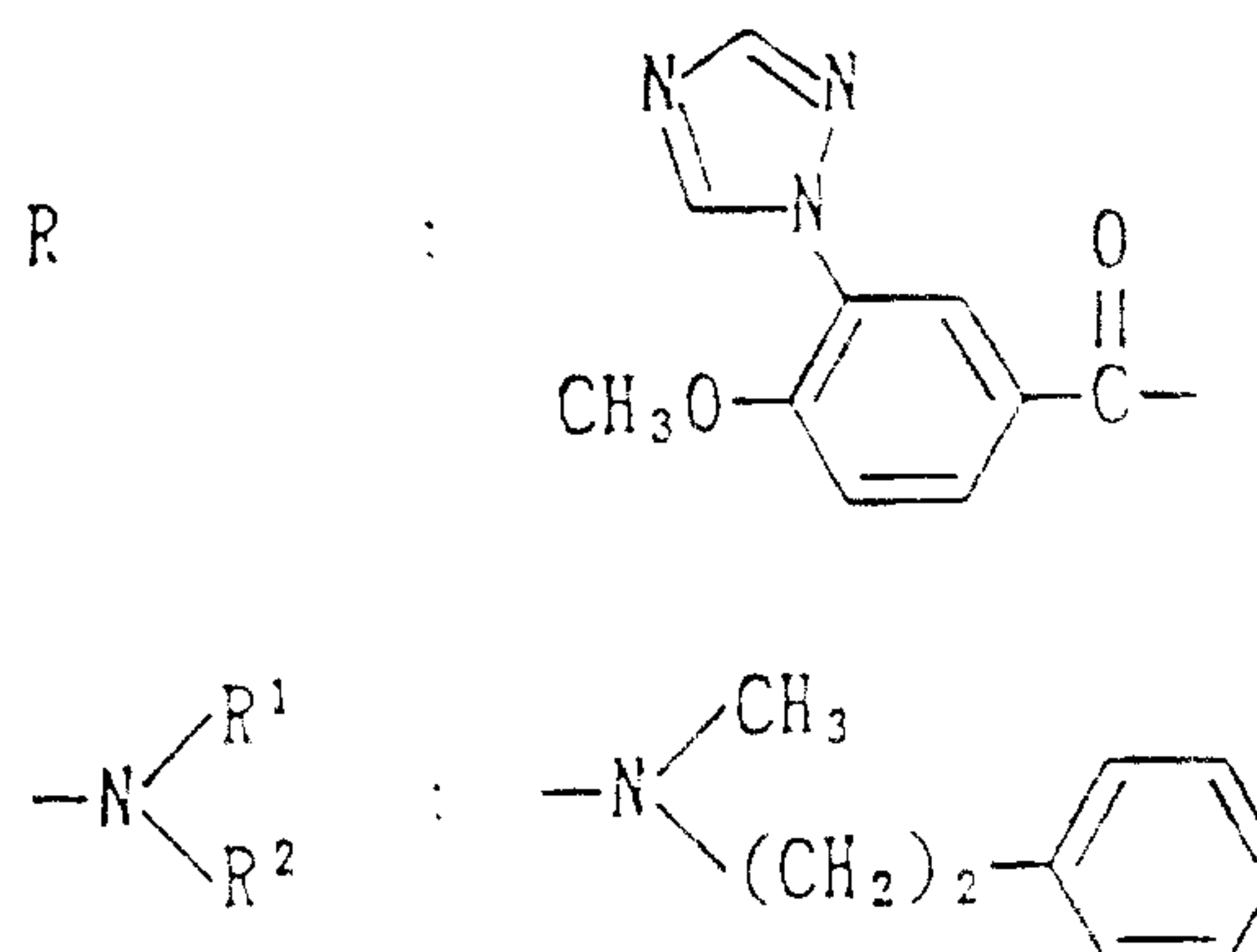
Crystal form: white amorphous

Salt form: free

NMR value: 98)

Example 153

Structural formula:



Crystal form: white amorphous

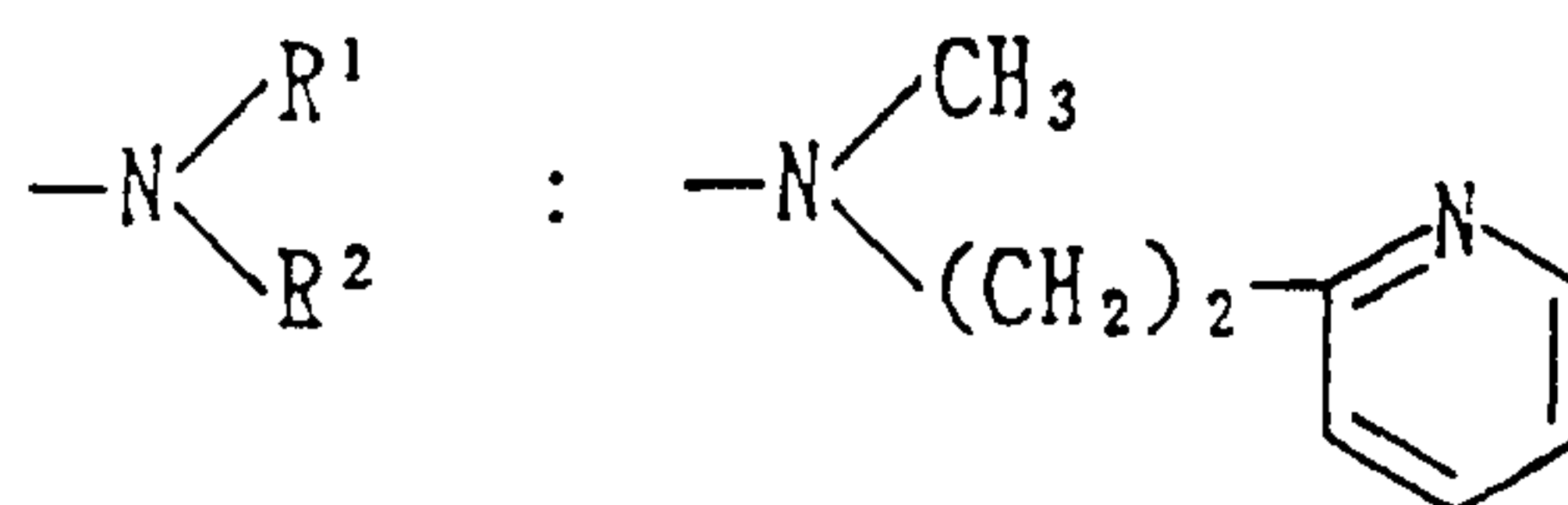
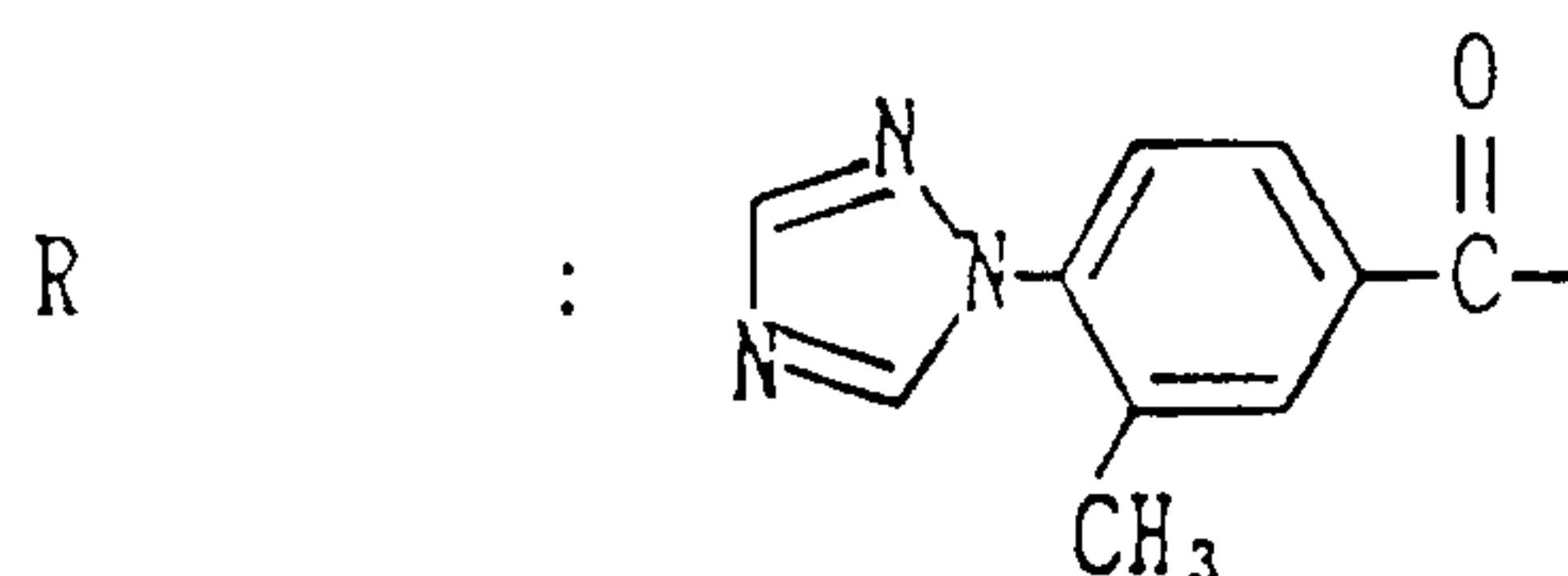
Salt form: hydrochloride

NMR value: 99)

[Table 10 (continued)]

Example 154

Structural formula:



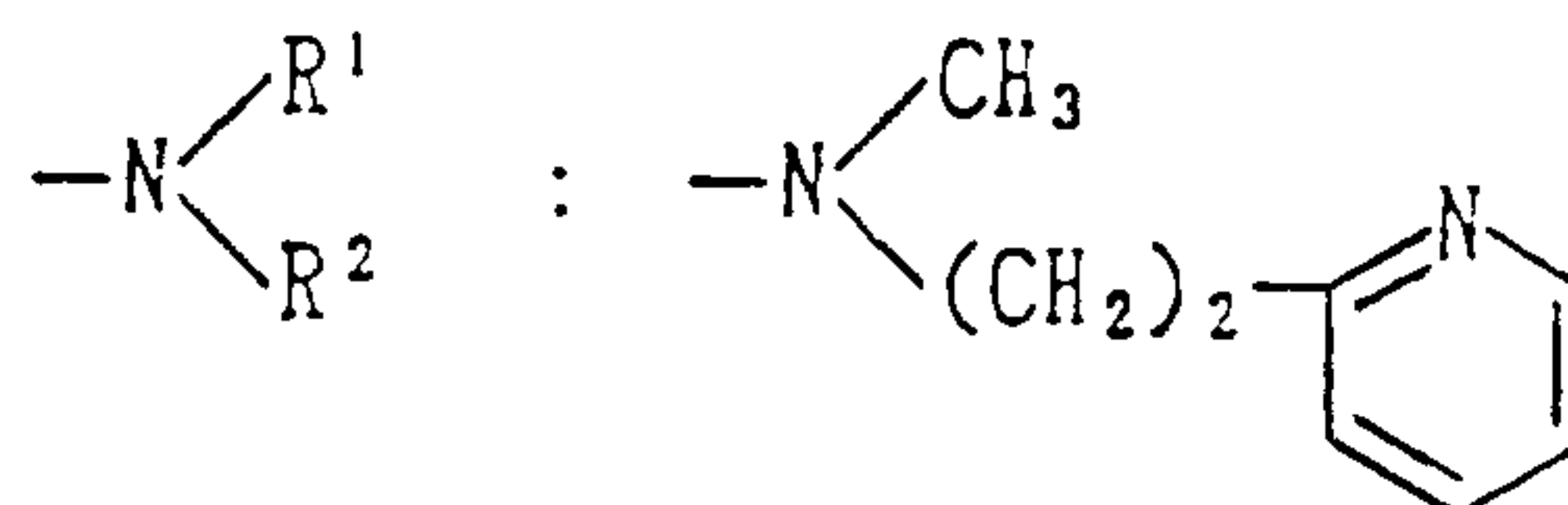
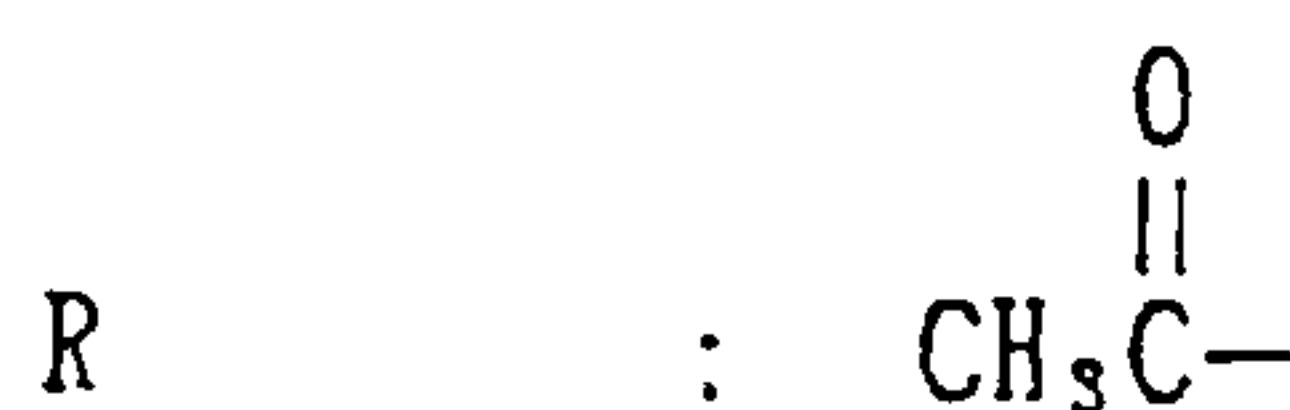
Crystal form: yellow amorphous

Salt form: dihydrochloride

NMR value: 100)

Example 155

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-diethyl ether

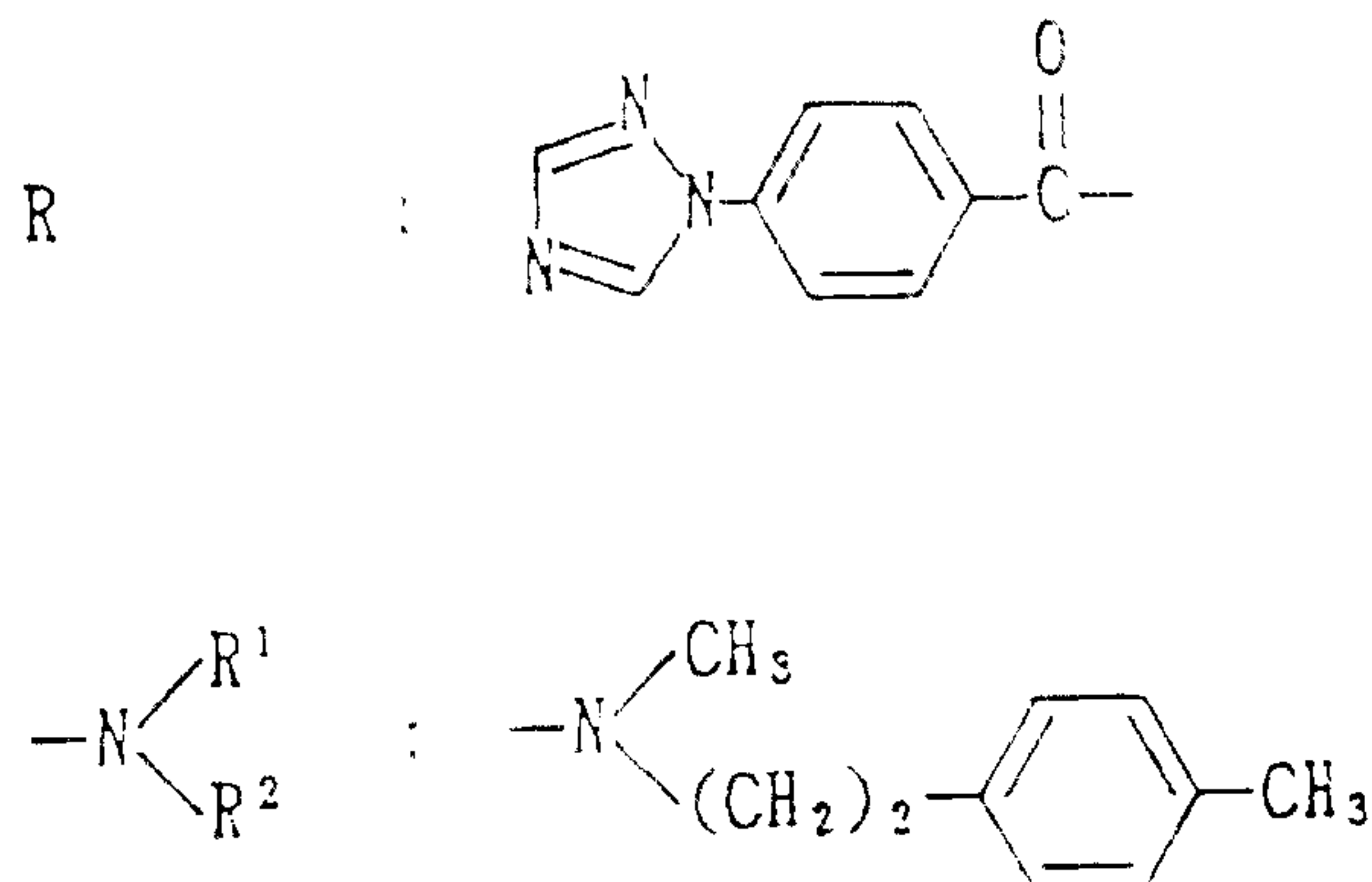
Melting point (°C): 192-193.5

Salt form: dihydrochloride

[Table 10 (continued)]

Example 156

Structural formula:



Crystal form: white powder

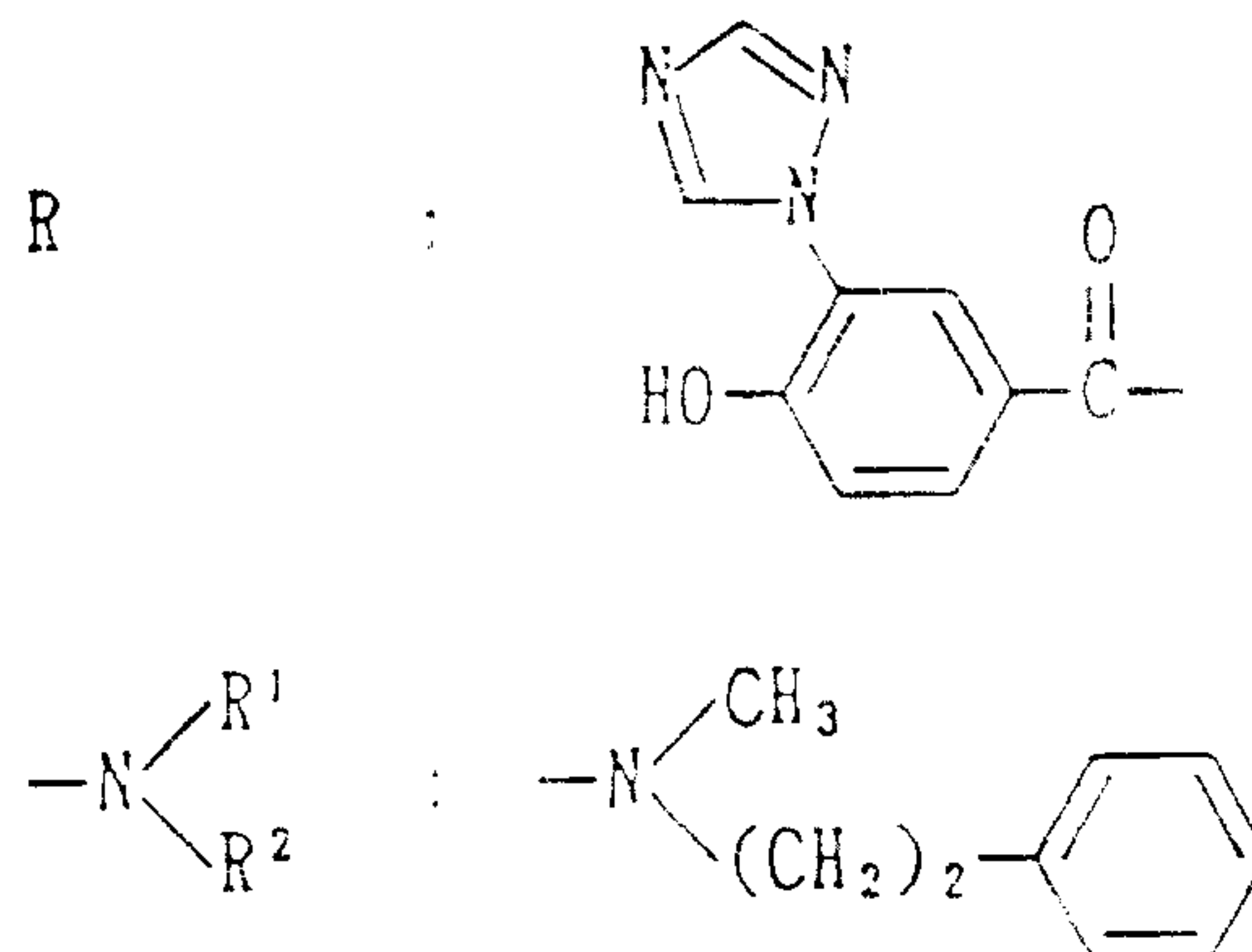
Recrystallization solvent: ethanol-diethyl ether

Melting point (°C): 219-220.5

Salt form: free

Example 157

Structural formula:



Crystal form: white amorphous

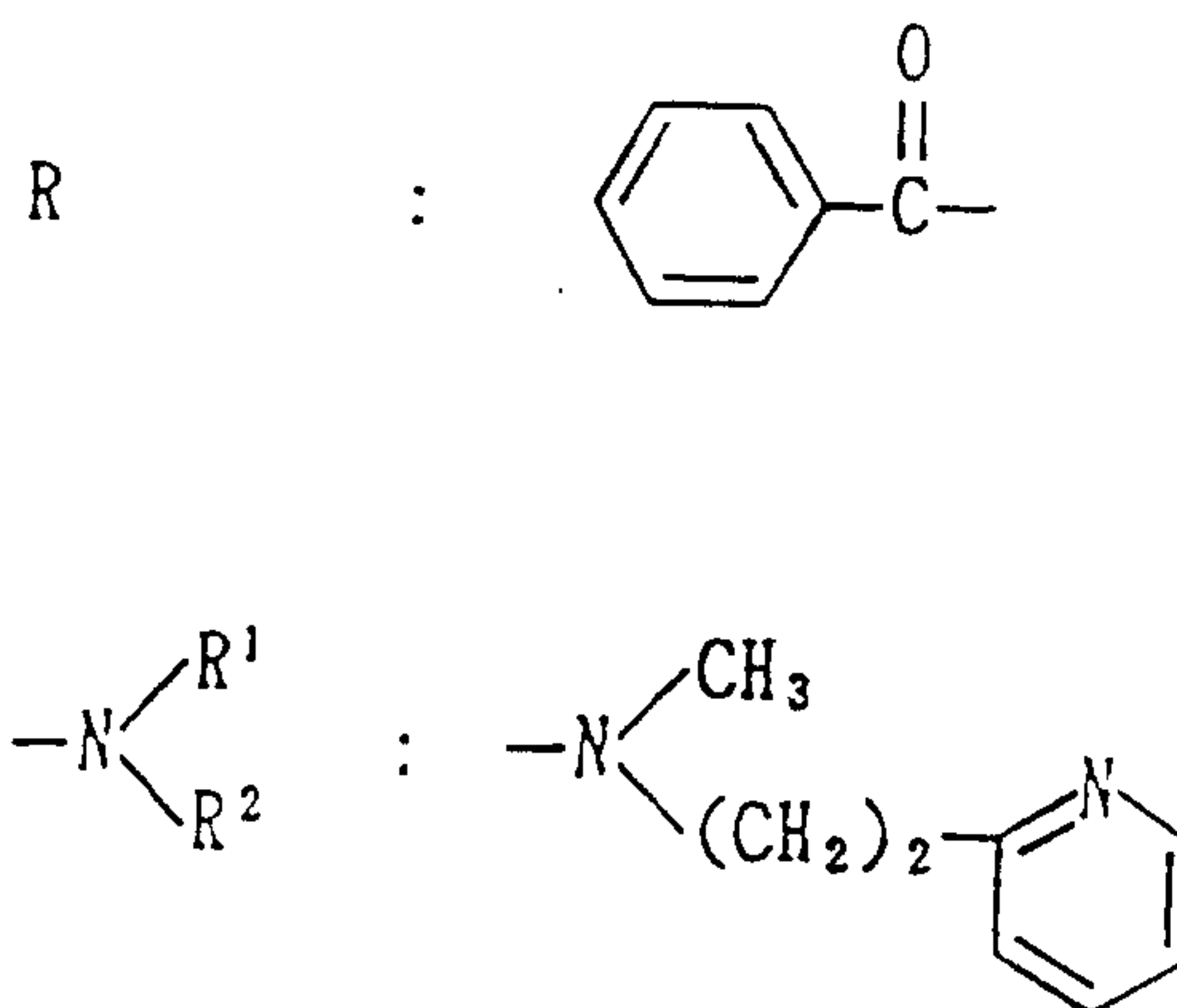
Salt form: hydrochloride

NMR value: 101)

{Table 10 (continued)}

Example 158

Structural formula:



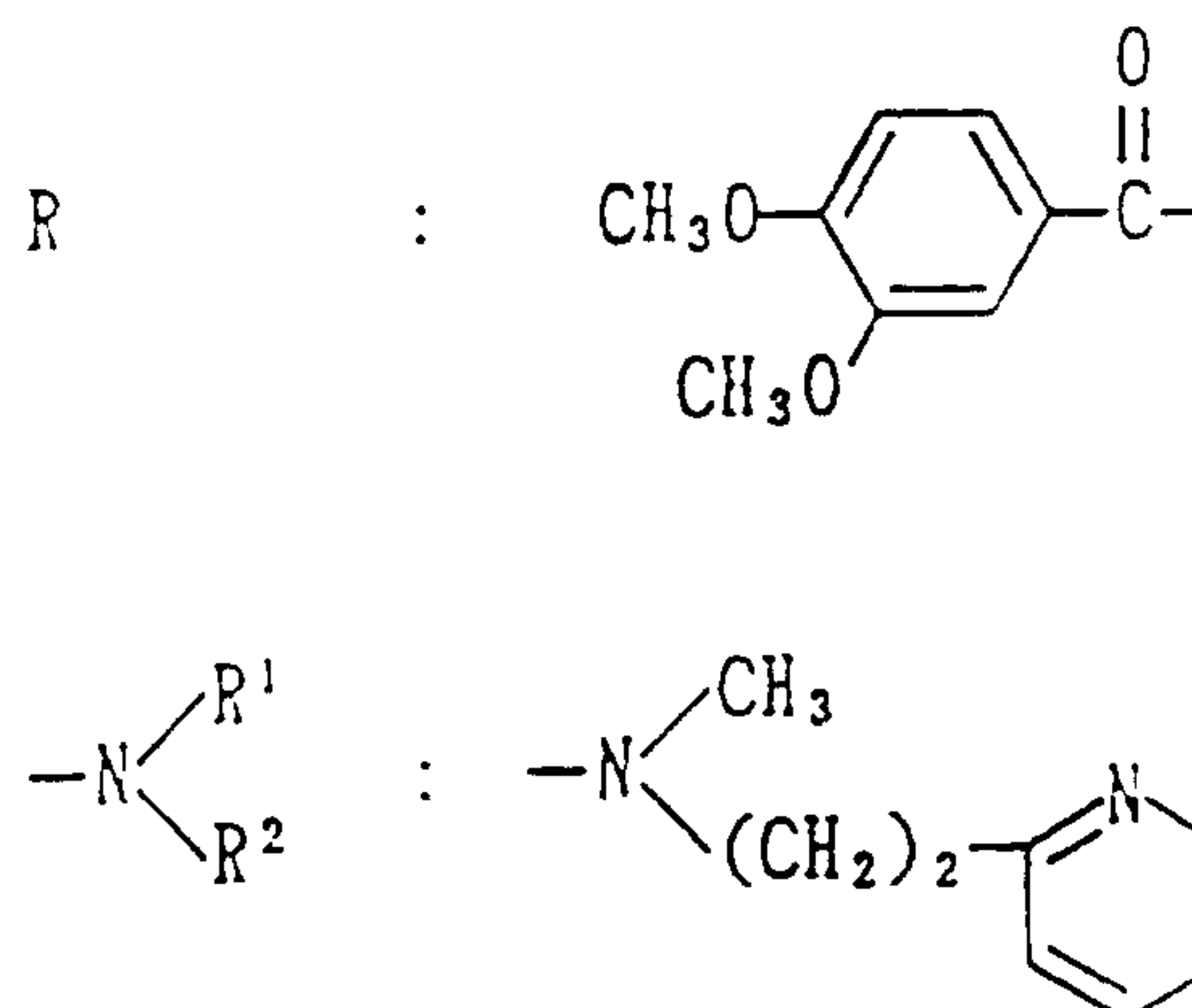
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 102)

Example 159

Structural formula:



Crystal form: white amorphous

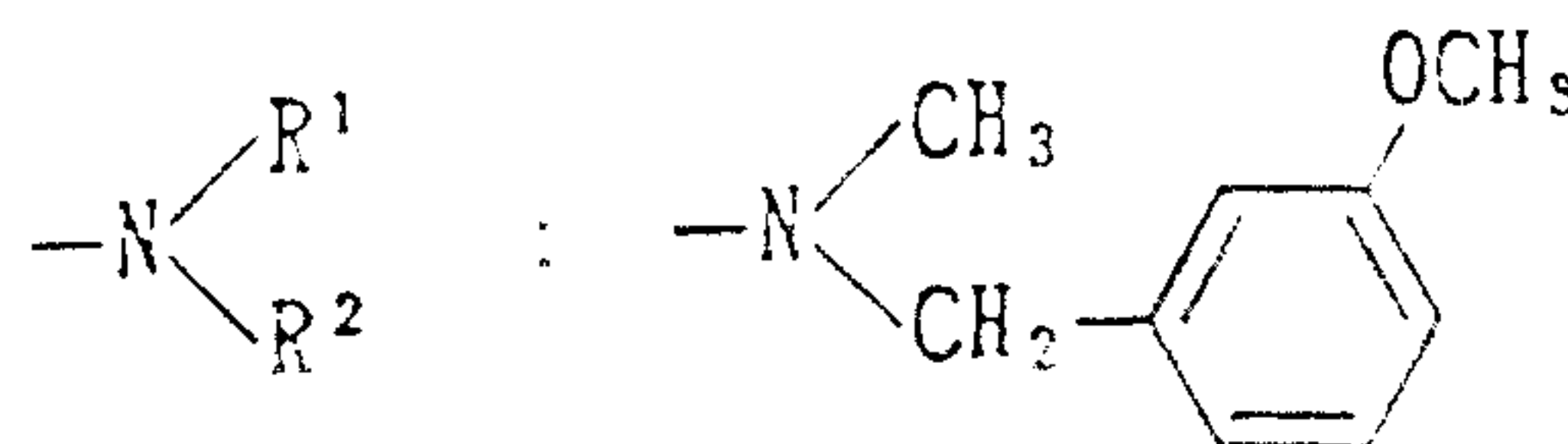
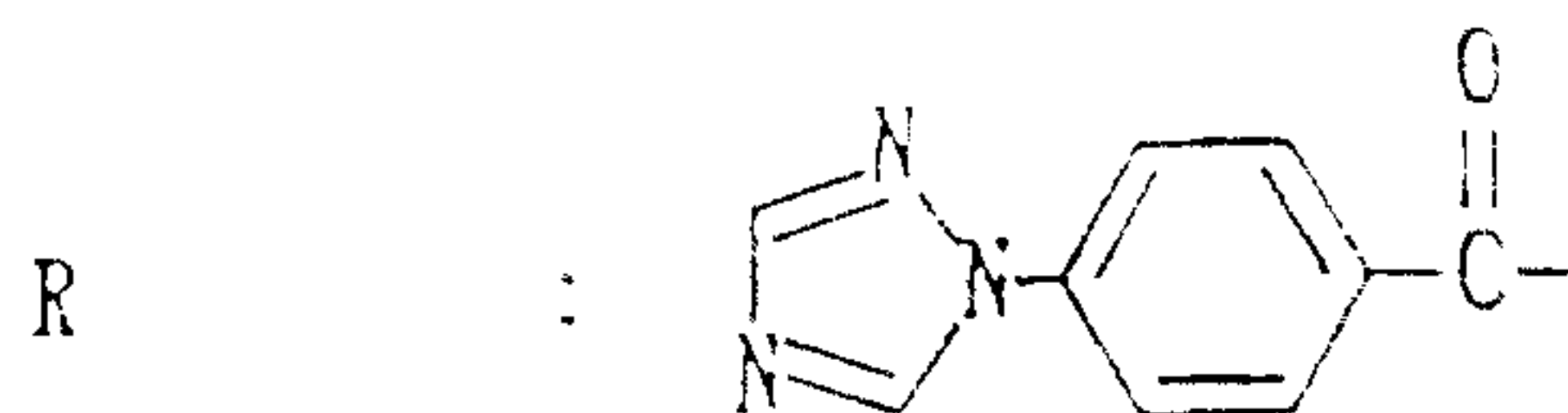
Salt form: dihydrochloride

NMR value: 103)

[Table 10 (continued)]

Example 160

Structural formula:



Crystal form: white powder

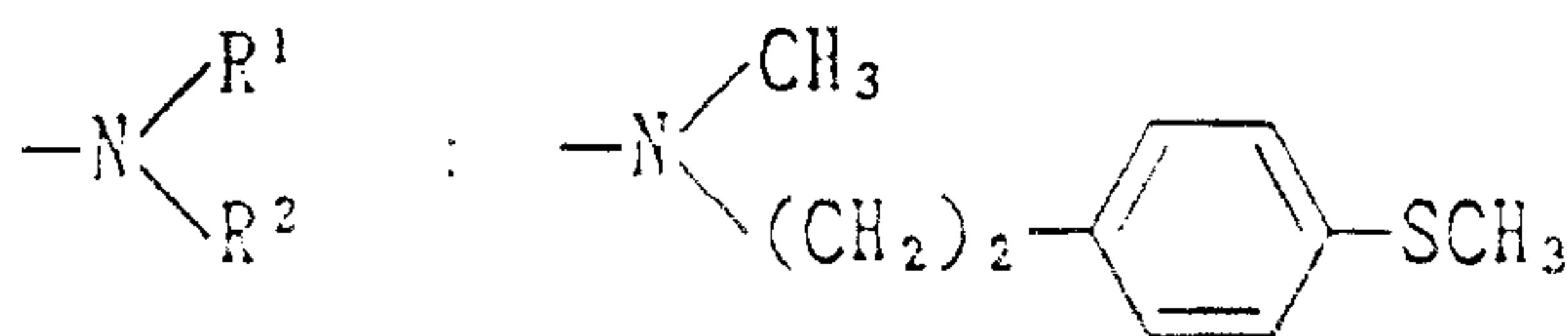
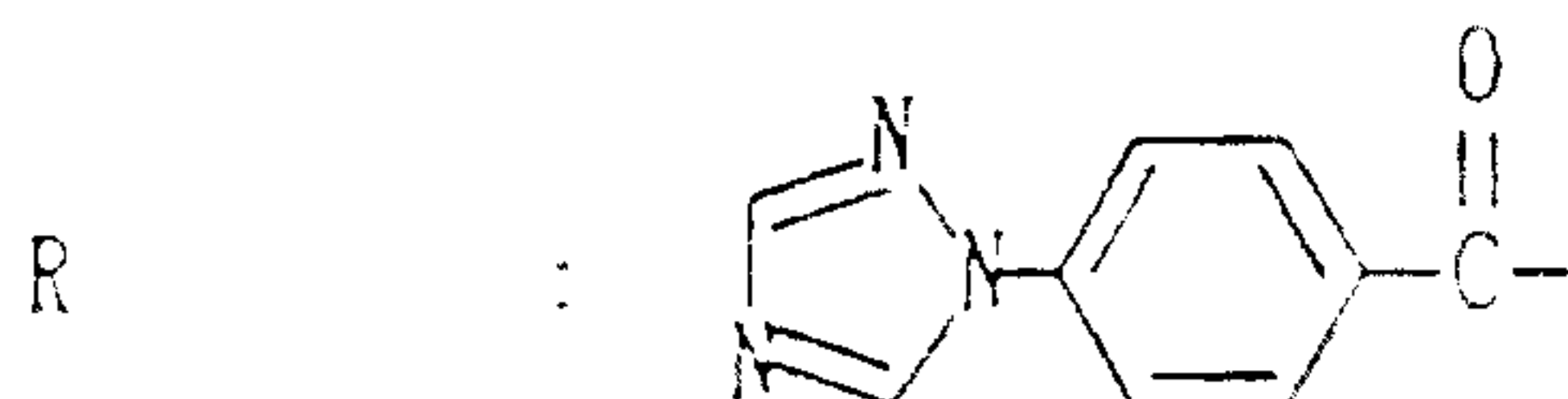
Recrystallization solvent: dichloromethane-diethyl ether

Melting point (°C): 105-107

Salt form: free

Example 161

Structural formula:



Crystal form: colorless prisms

Recrystallization solvent: ethyl acetate

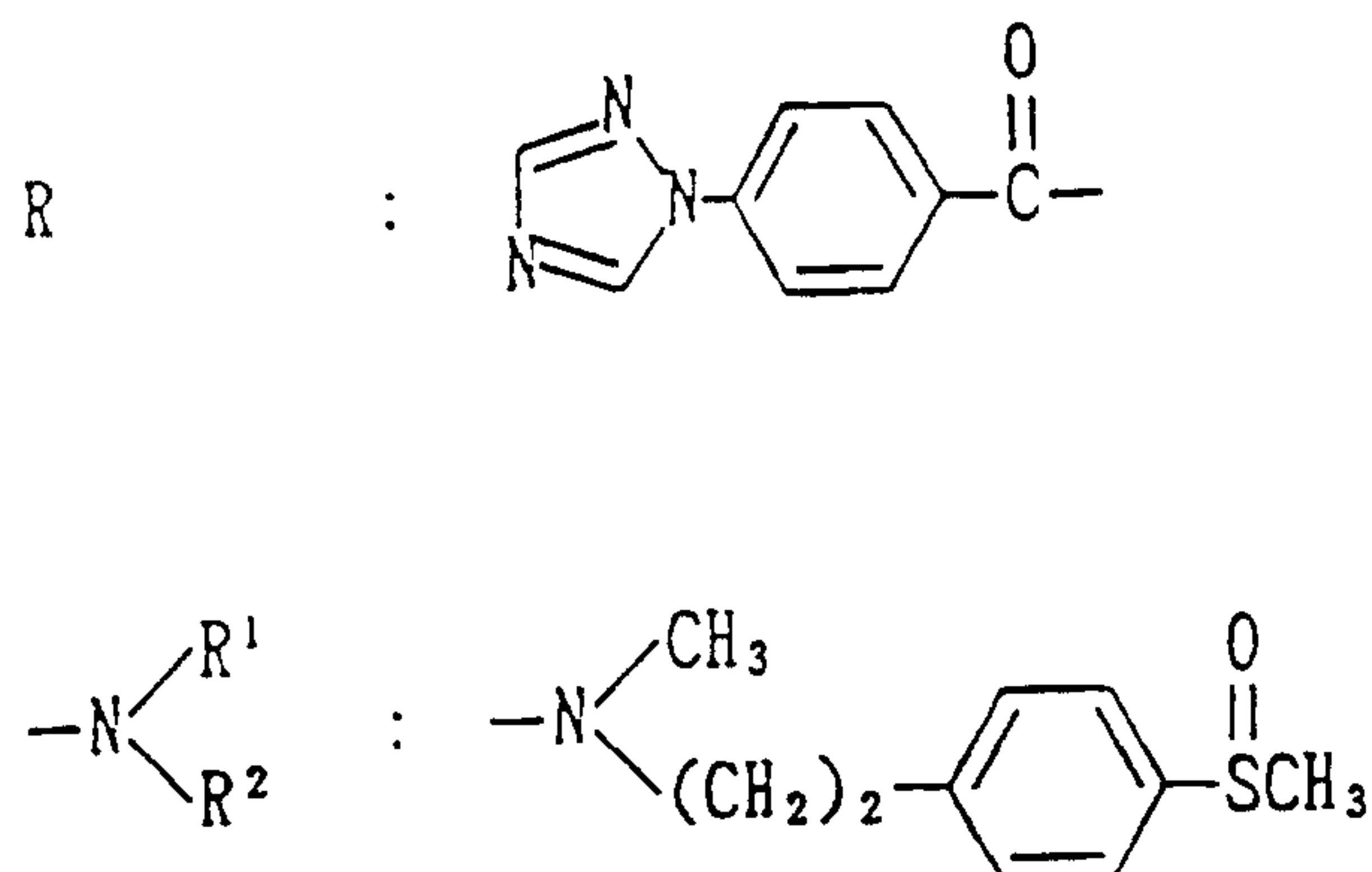
Melting point (°C): 98-101

Salt form: free

[Table 10 (continued)]

Example 162

Structural formula:



Crystal form: white powder

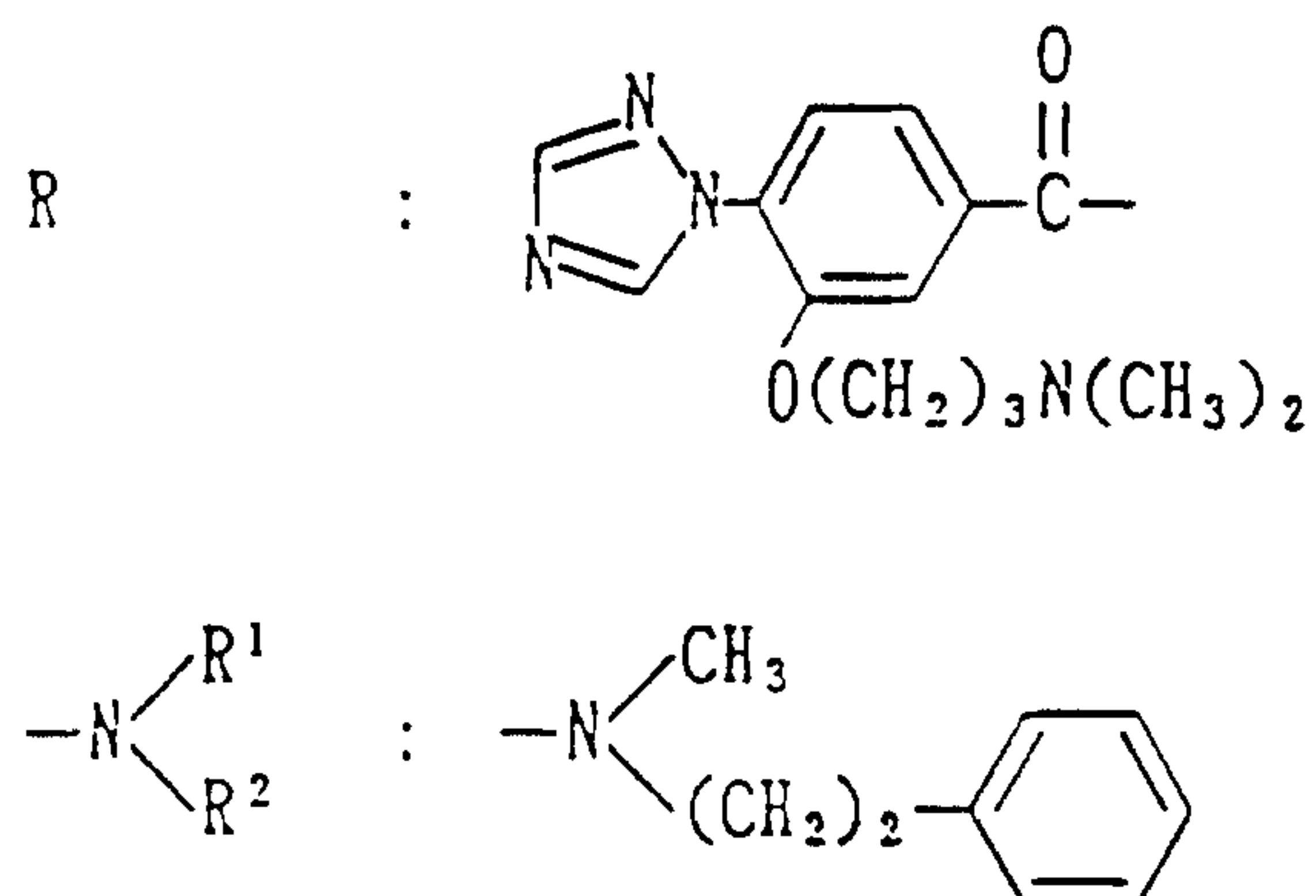
Recrystallization solvent: ethanol-water

Melting point (°C): 235-236

Salt form: hydrochloride

Example 163

Structural formula:



Crystal form: white amorphous

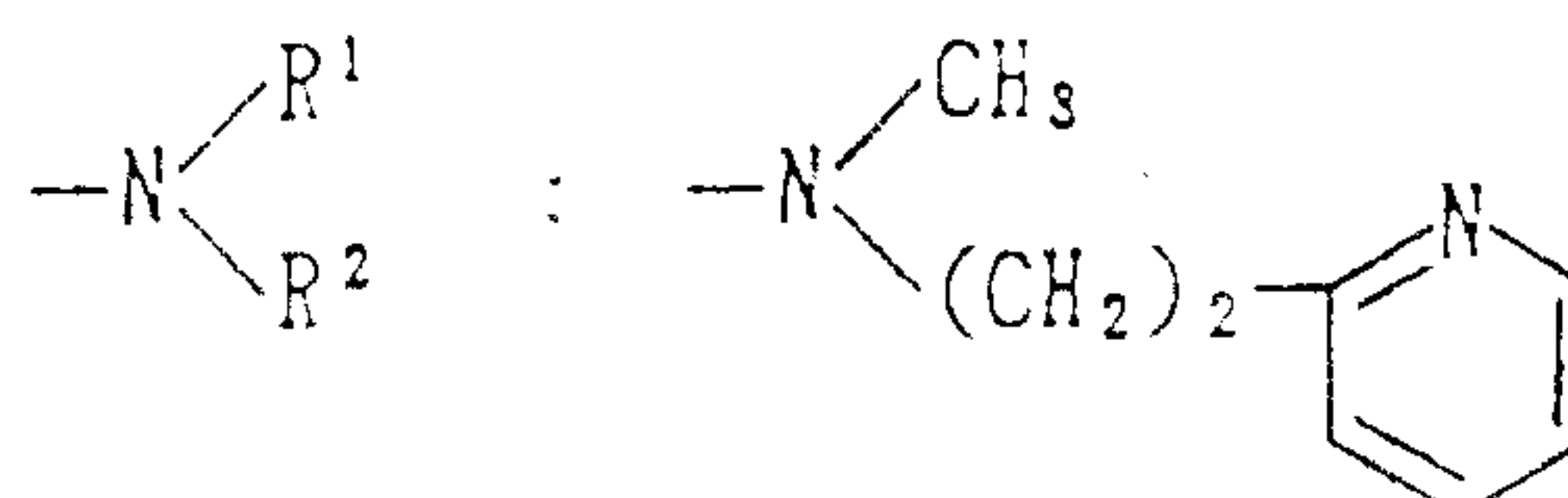
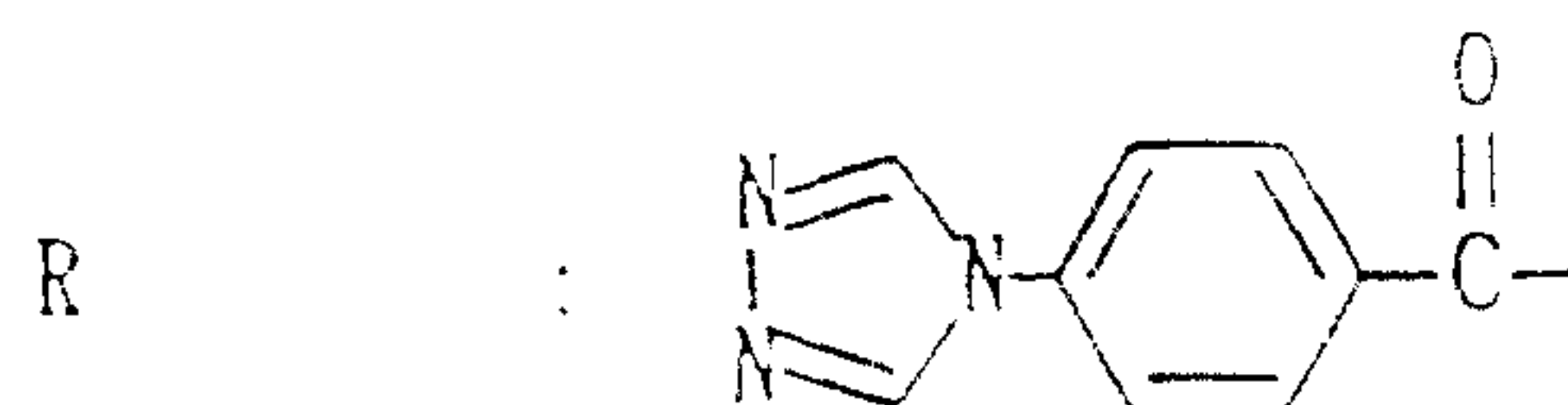
Salt form: dihydrochloride

NMR value: 104)

[Table 10 (continued)]

Example 164

Structural formula:



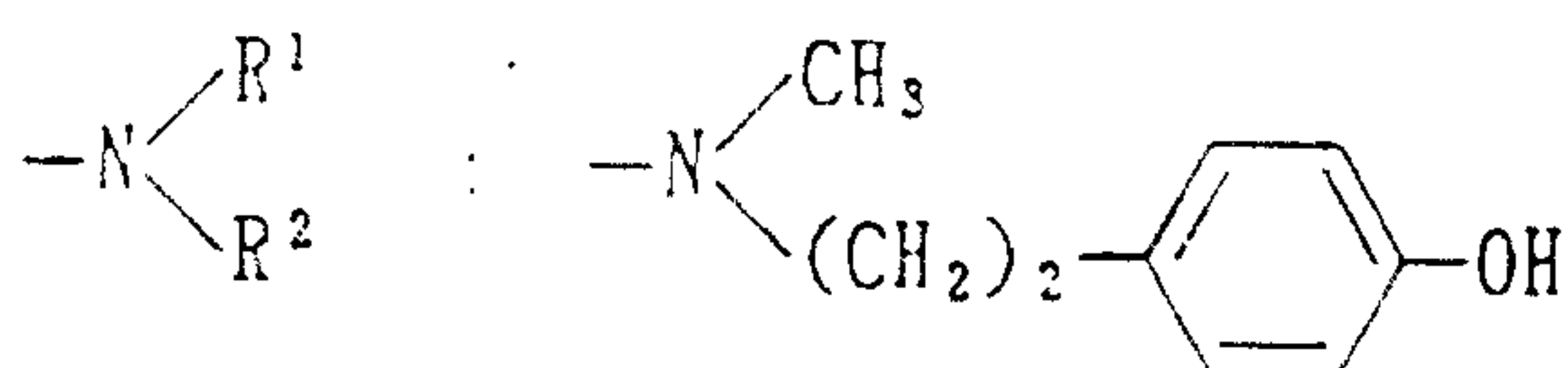
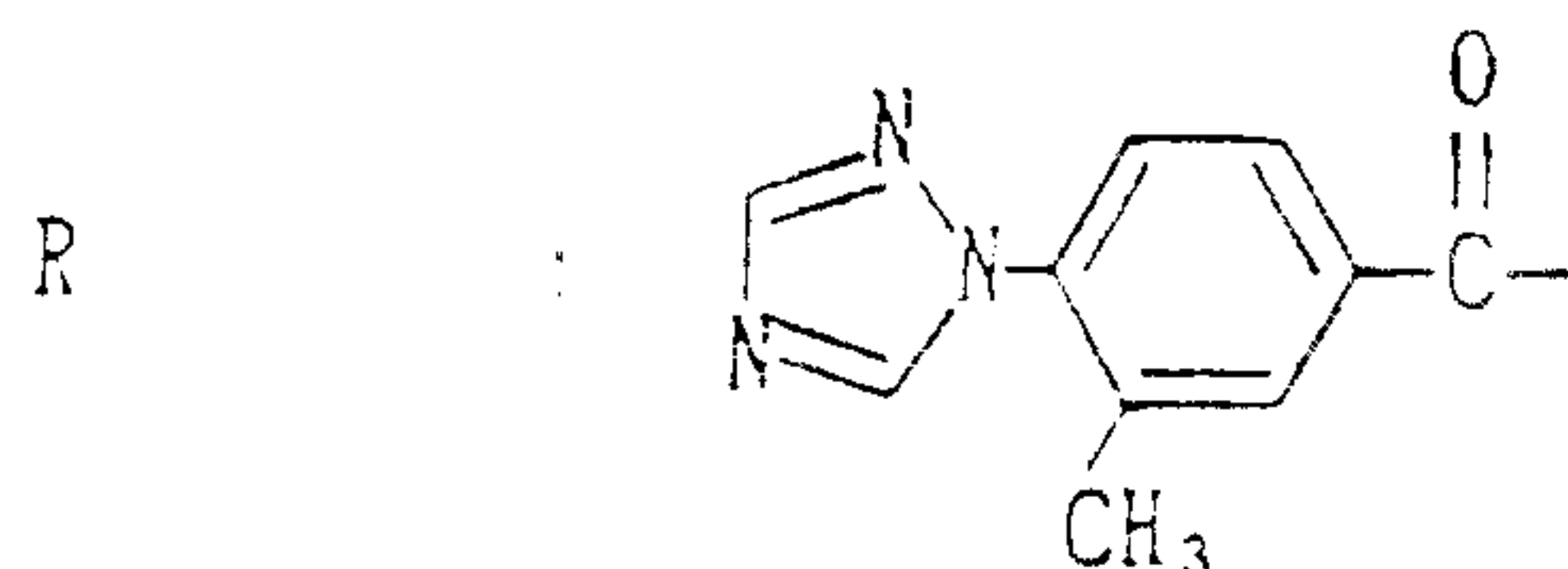
Crystal form: pink amorphous

Salt form: dihydrochloride

NMR value: 105)

Example 165

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-diethyl ether

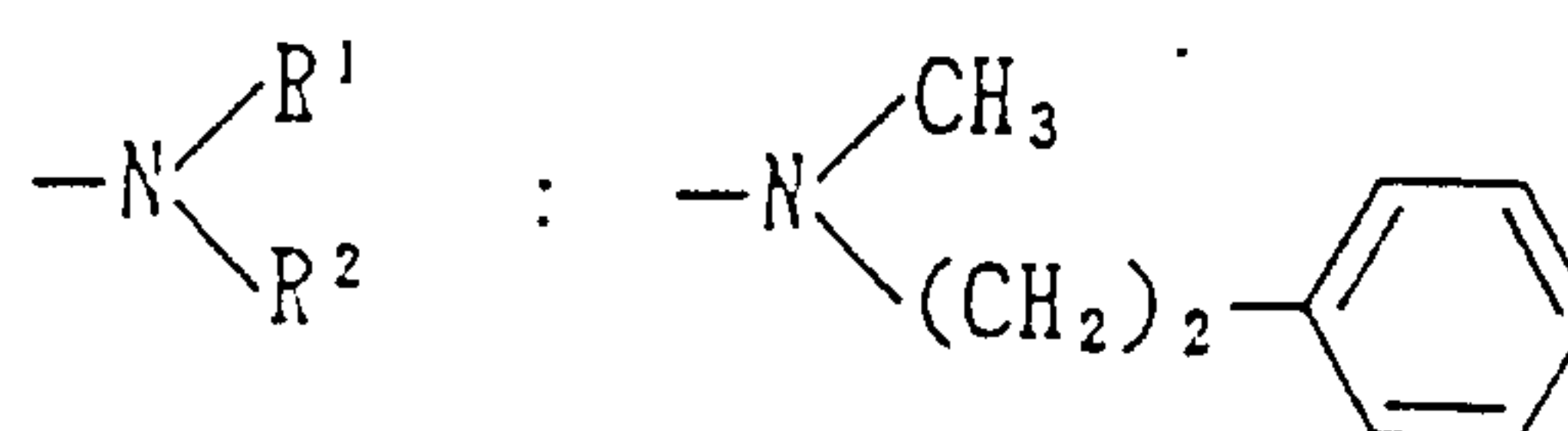
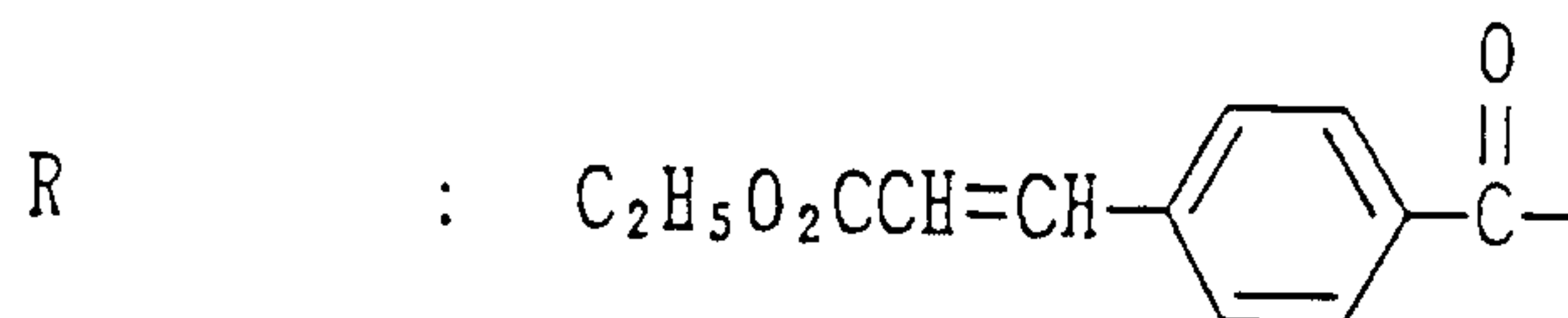
Melting point (°C): 188-189

Salt form: free

[Table 10 (continued)]

Example 166

Structural formula:



Crystal form: white powder

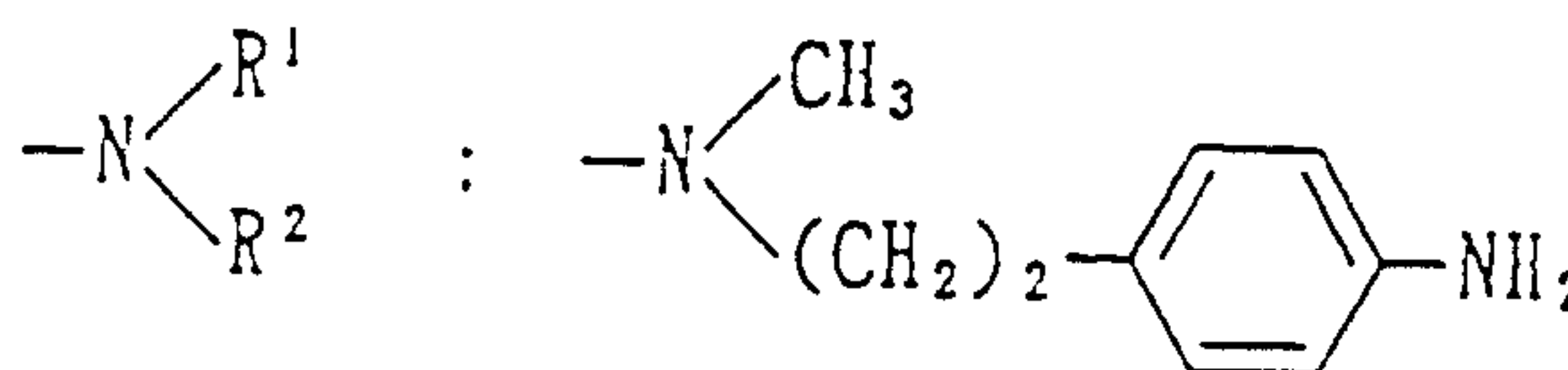
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 225.5-226.5

Salt form: hydrochloride

Example 167

Structural formula:



Crystal form: light yellow amorphous

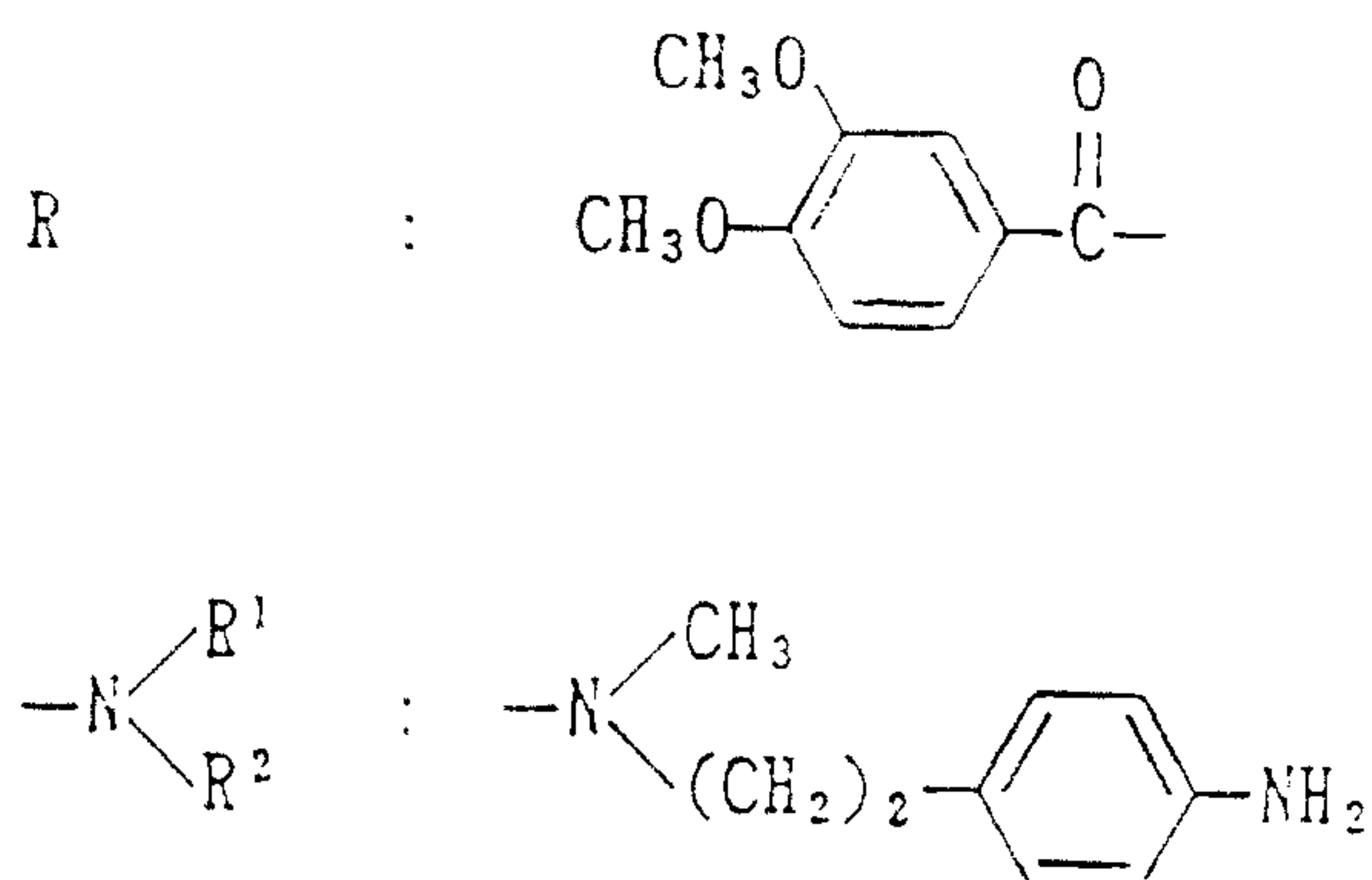
Salt form: dihydrochloride

NMR value: 106.)

[Table 10 (continued)]

Example 168

Structural formula:



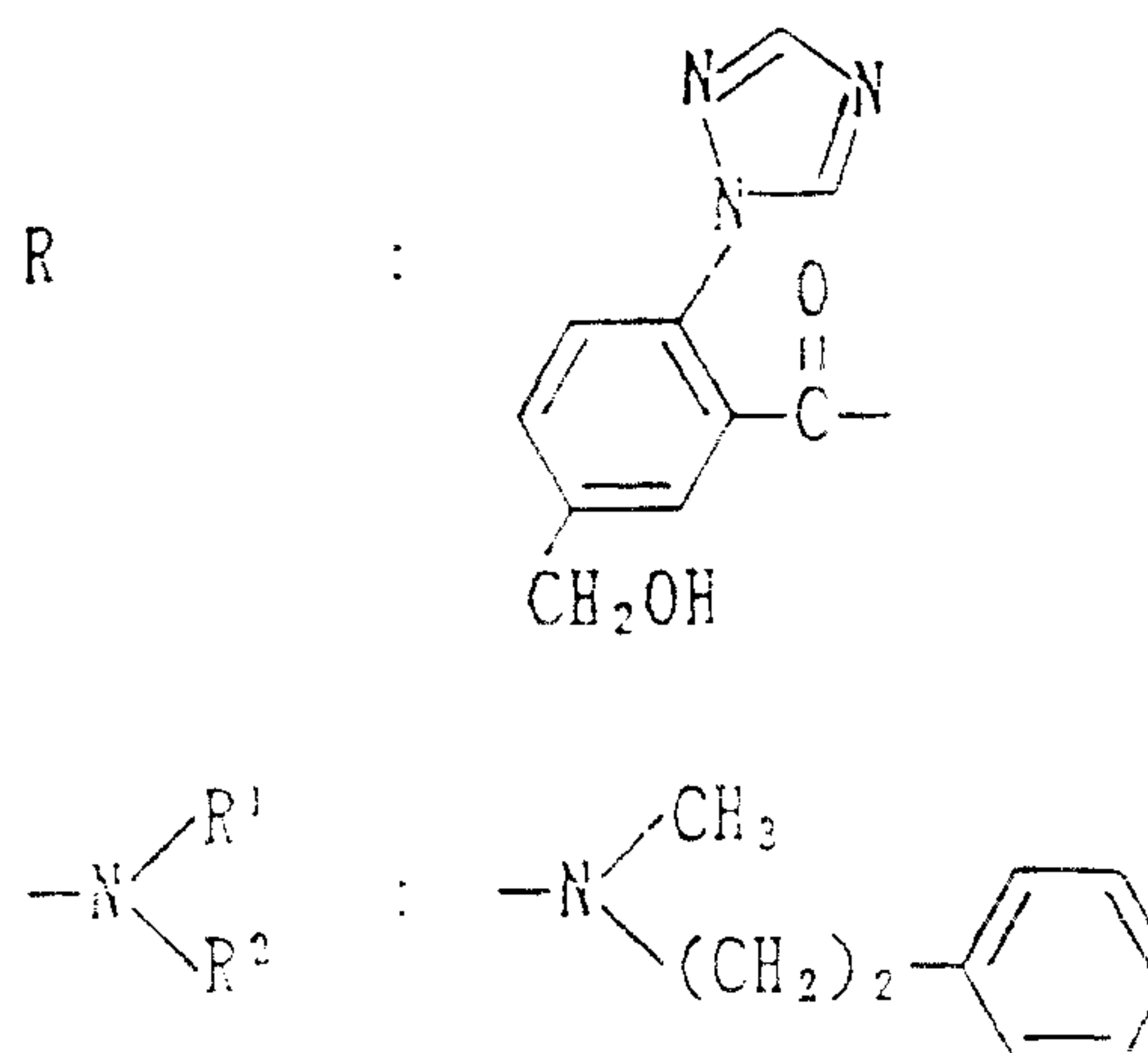
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 107)

Example 169

Structural formula:



Crystal form: white amorphous

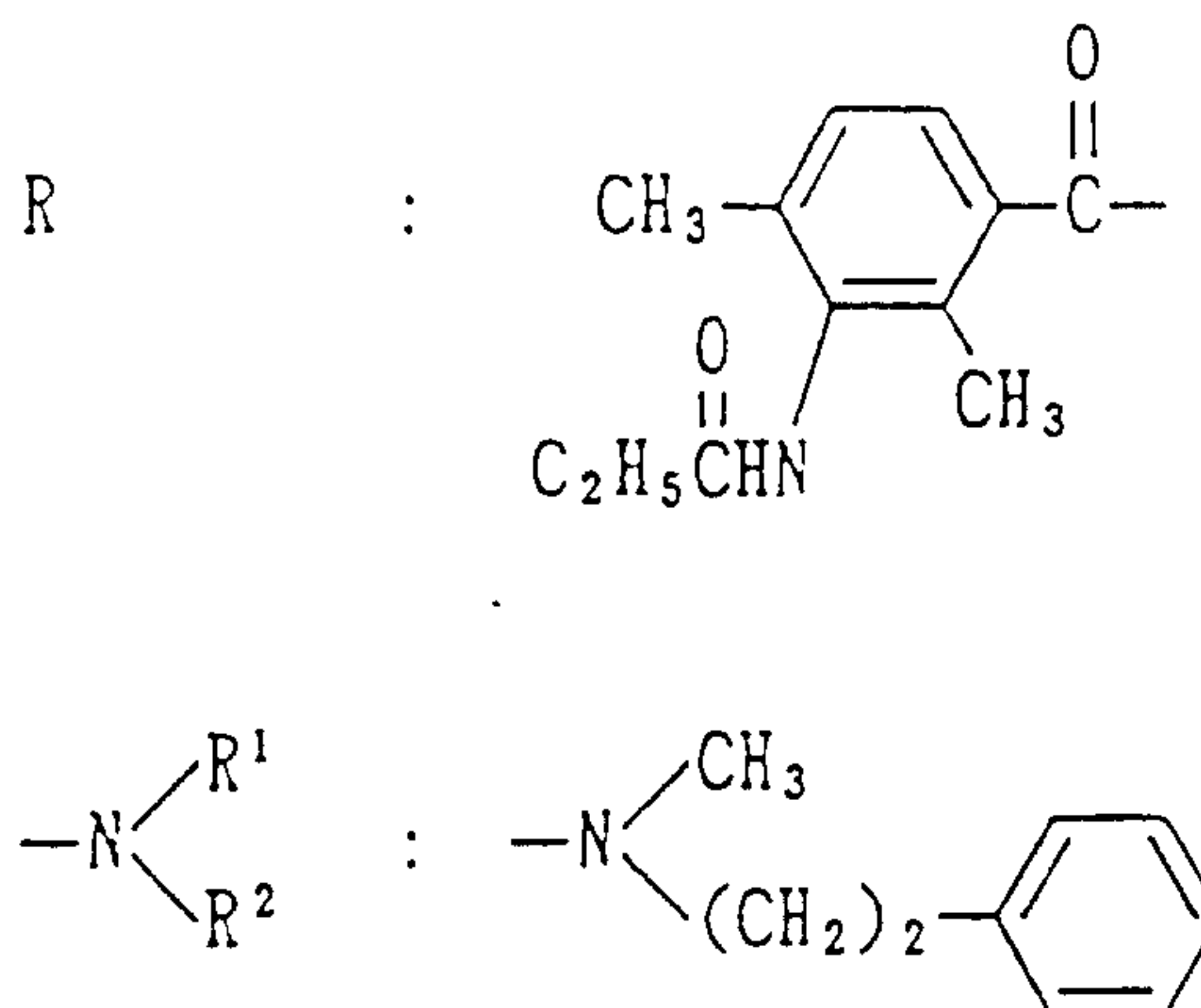
Salt form: hydrochloride

NMR value: 108)

{Table 10 (continued)}

Example 170

Structural formula:



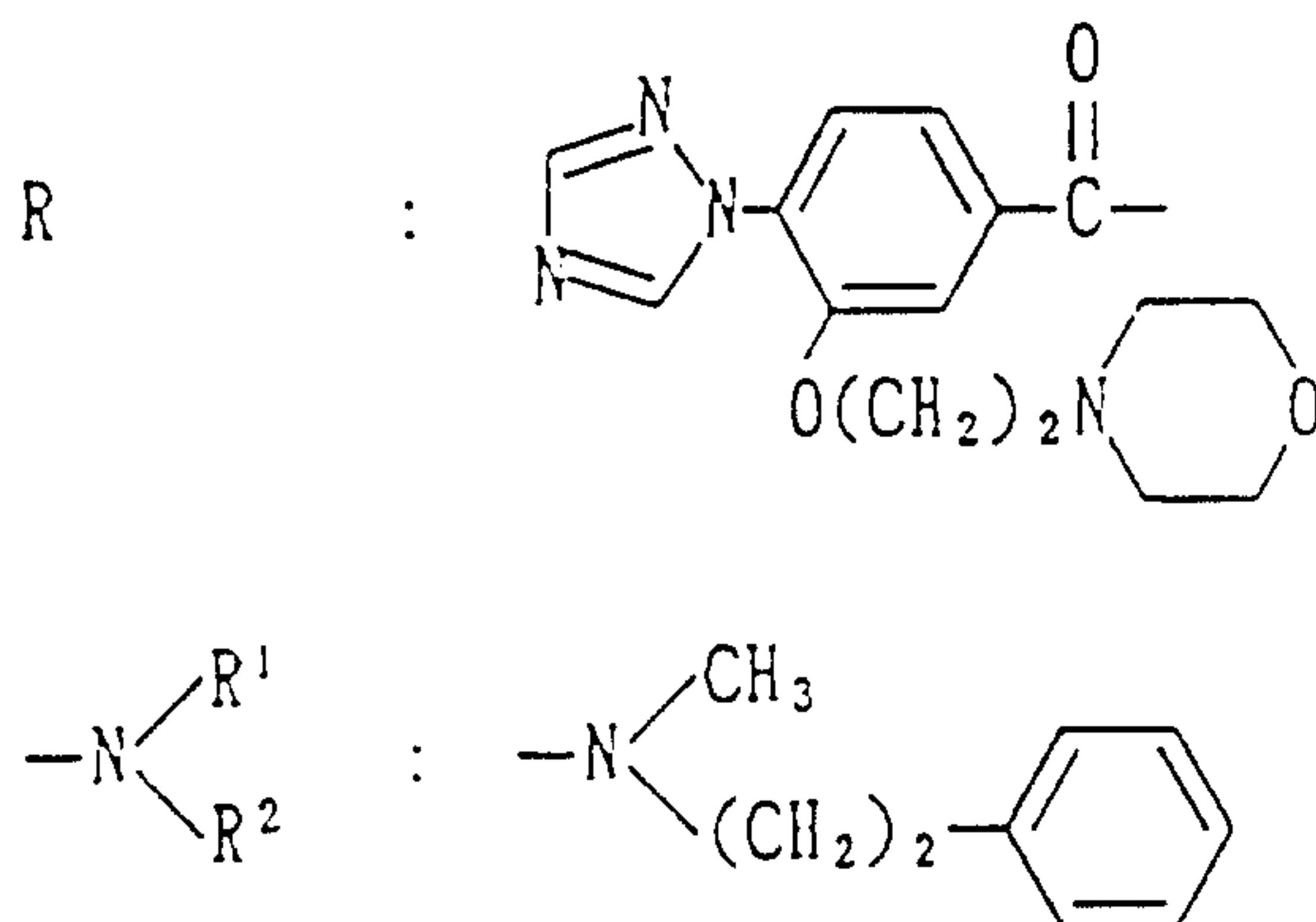
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 109)

Example 171

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-n-hexane

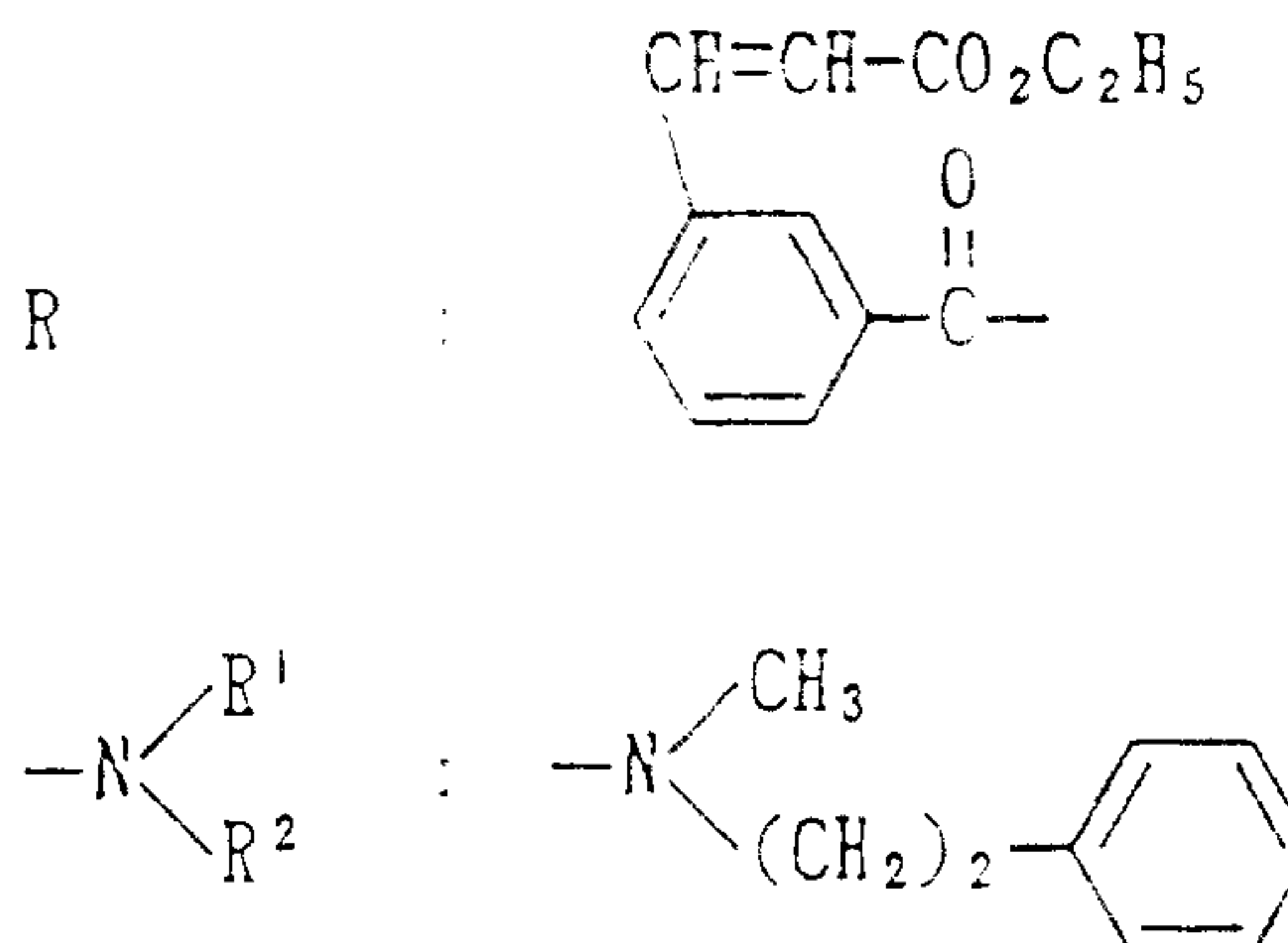
Melting point (°C): 84.5-87

Salt form: free

{Table 10 (continued)}

Example 172

Structural formula:



Crystal form: white powder

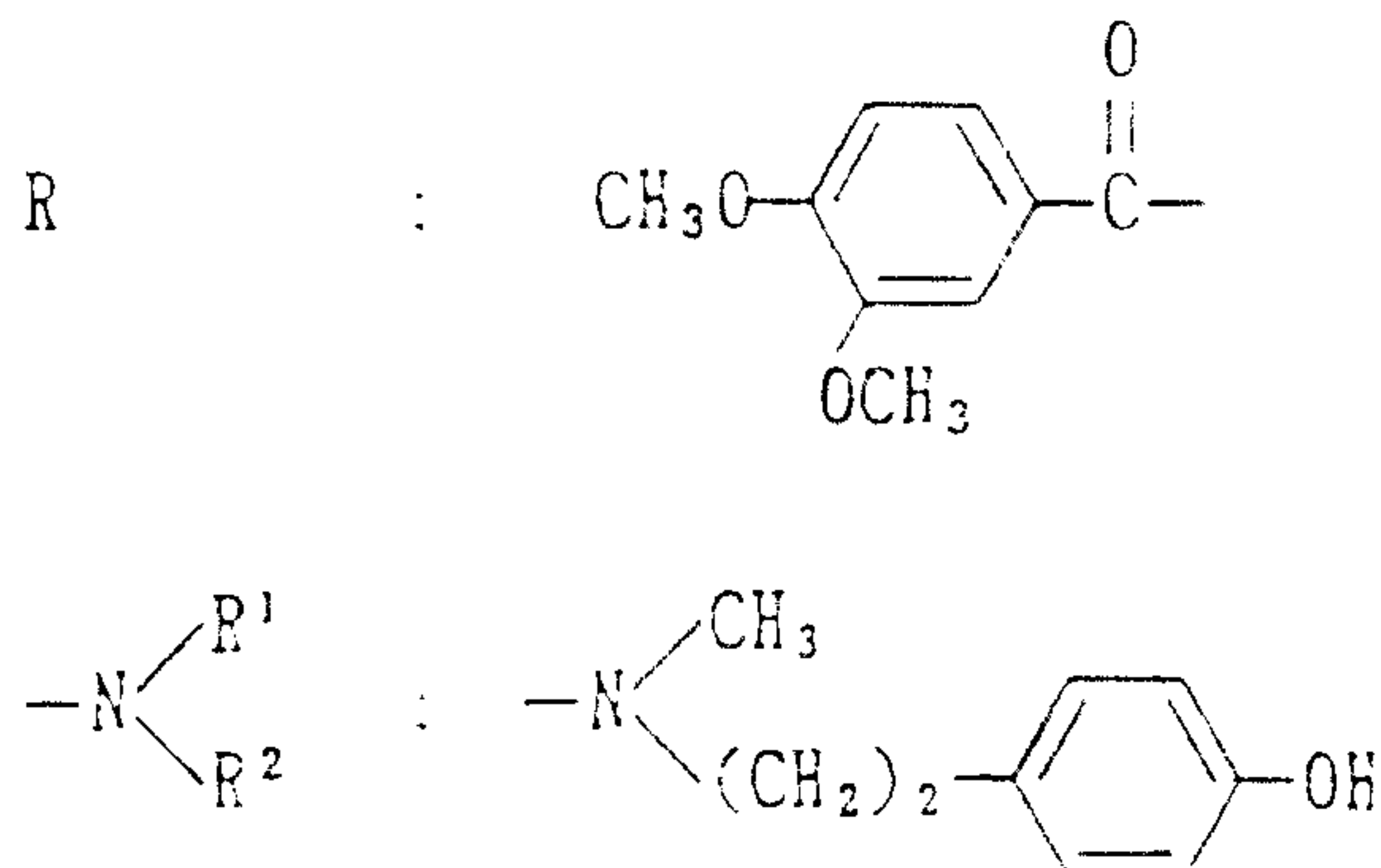
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 162.5-163.5

Salt form: hydrochloride

Example 173

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-diethyl ether

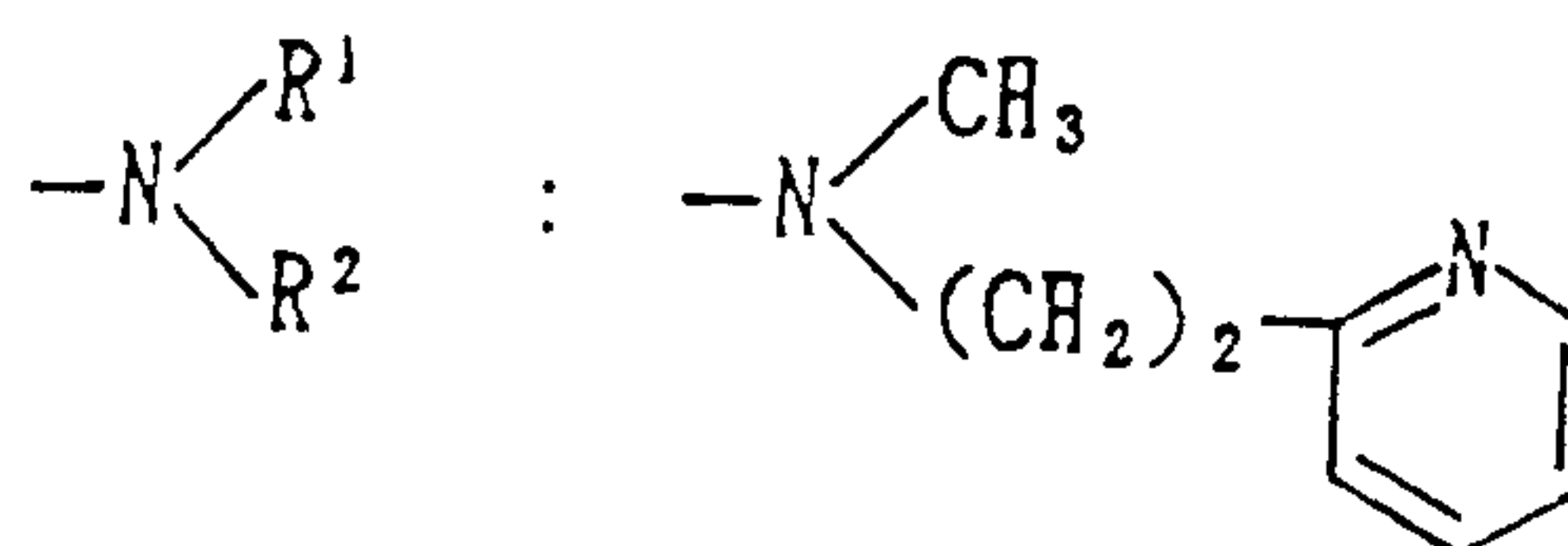
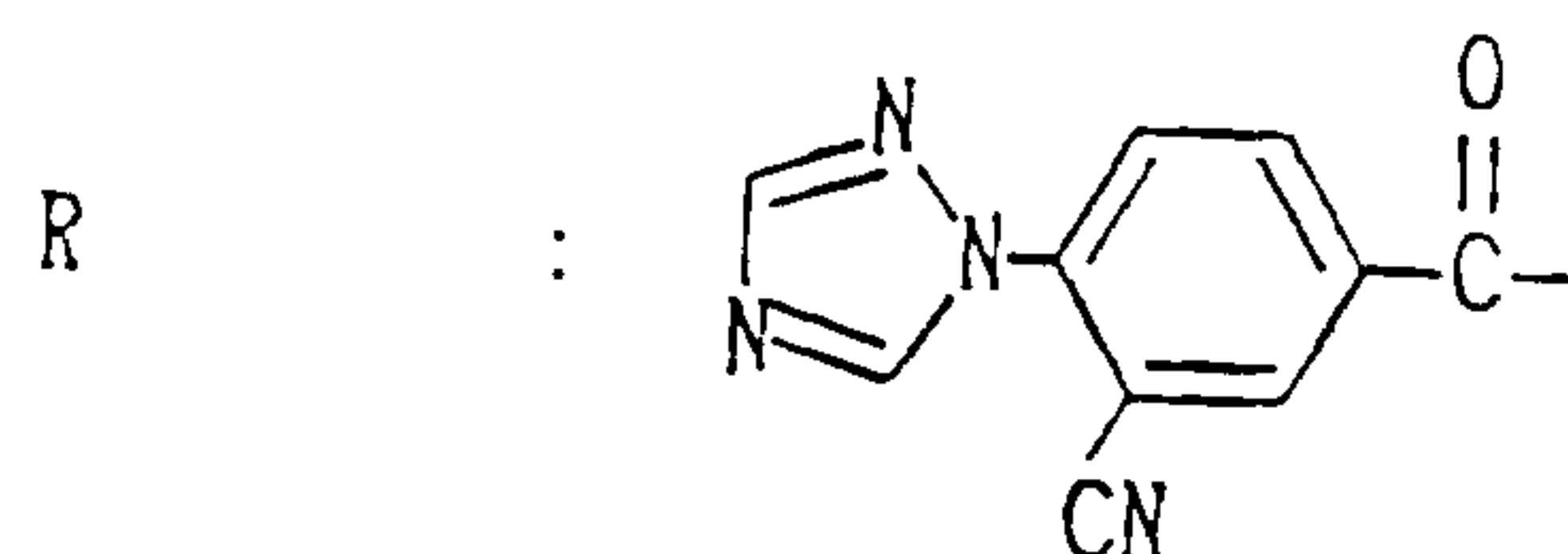
Melting point (°C): 211-214

Salt form: hydrochloride

[Table 10 (continued)]

Example 174

Structural formula:



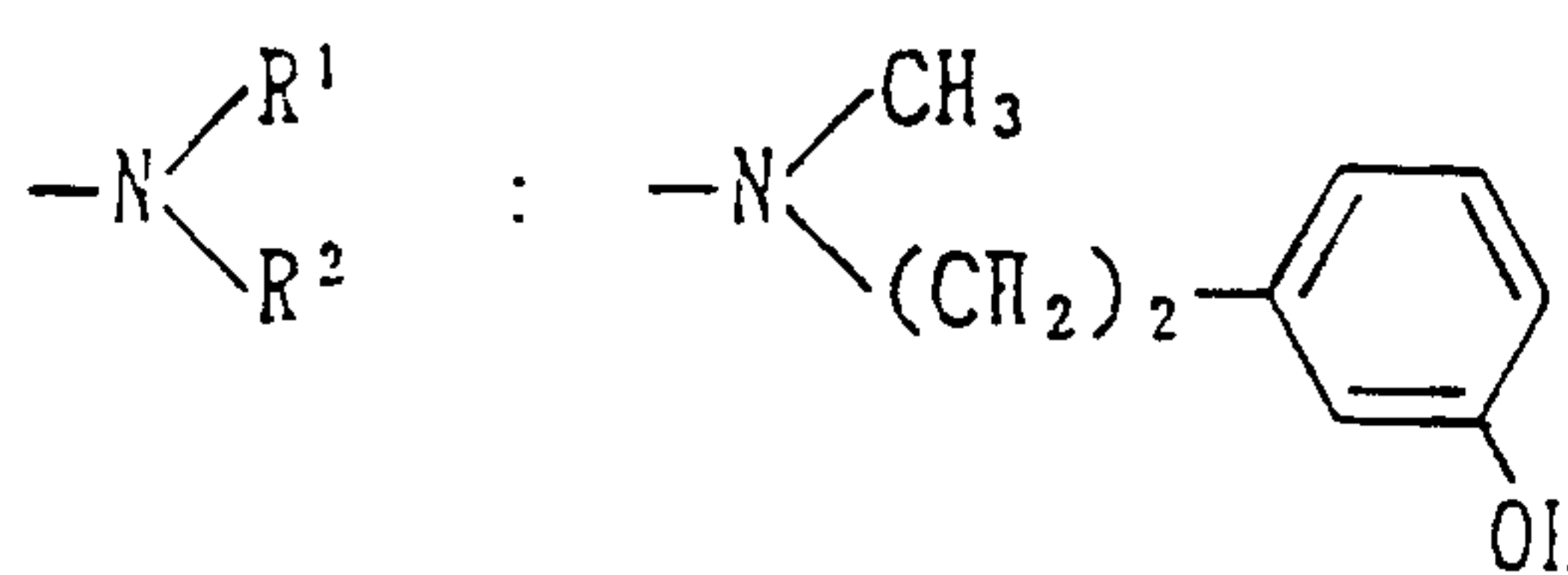
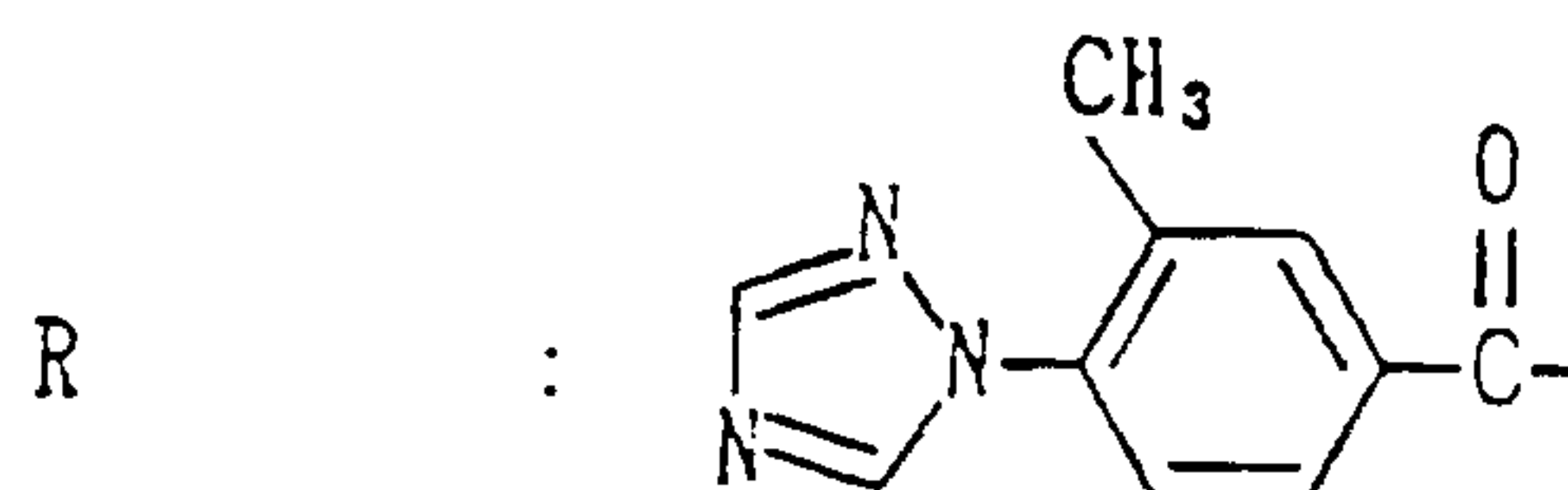
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 110)

Example 175

Structural formula:



Crystal form: white amorphous

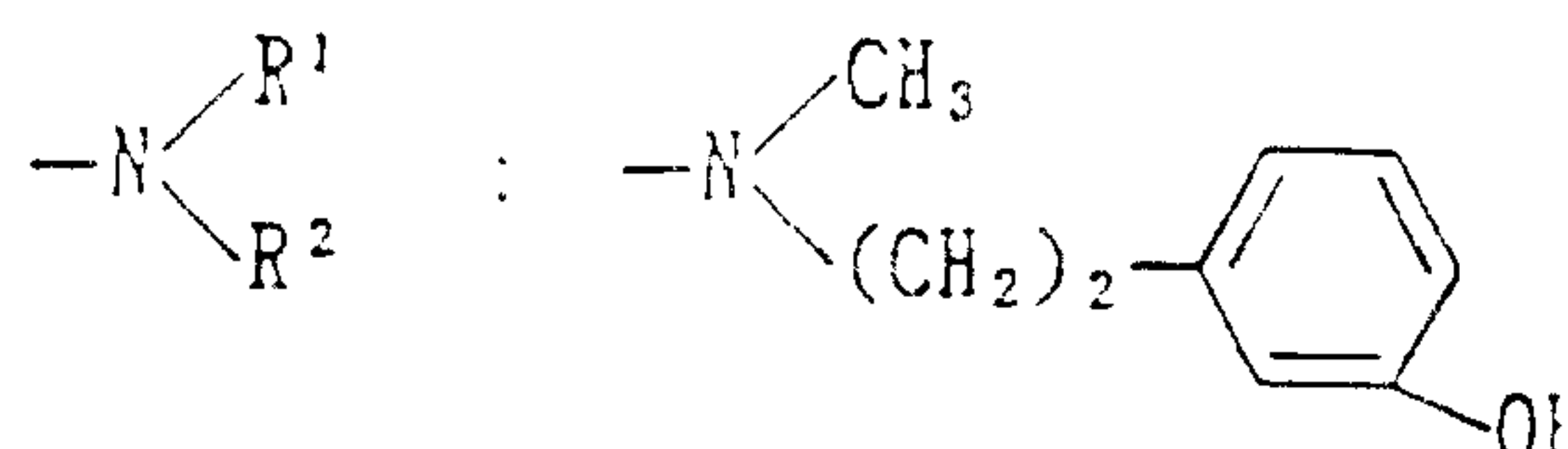
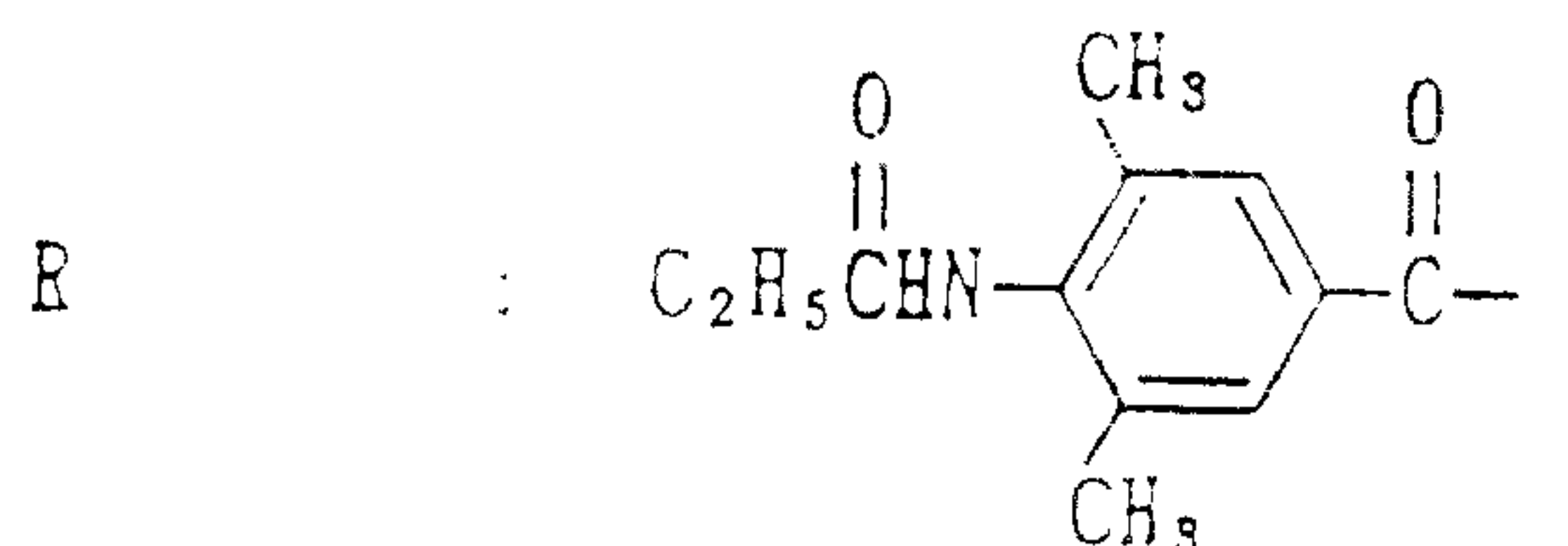
Salt form: hydrochloride

NMR value: 111)

[Table 10 (continued)]

Example 176

Structural formula:



Crystal form: white powder

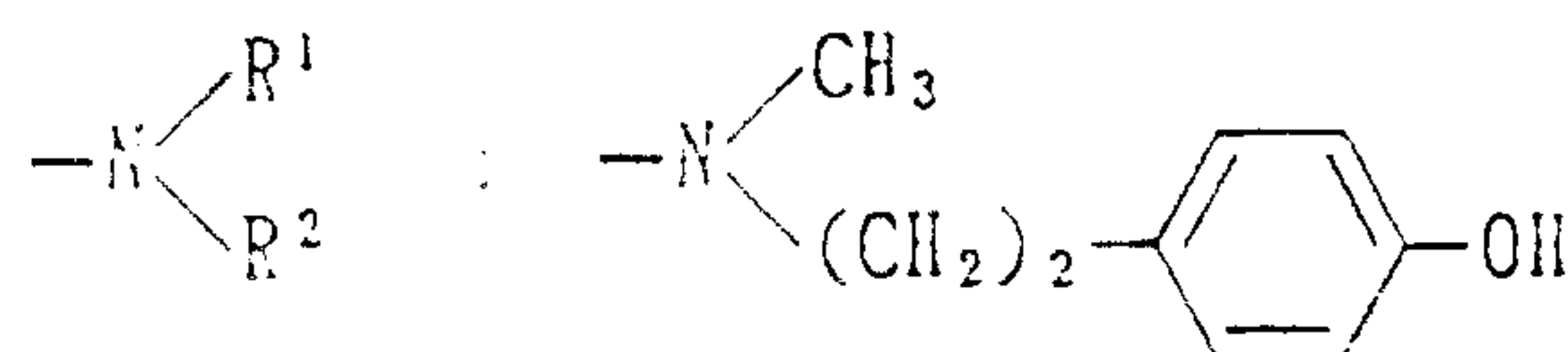
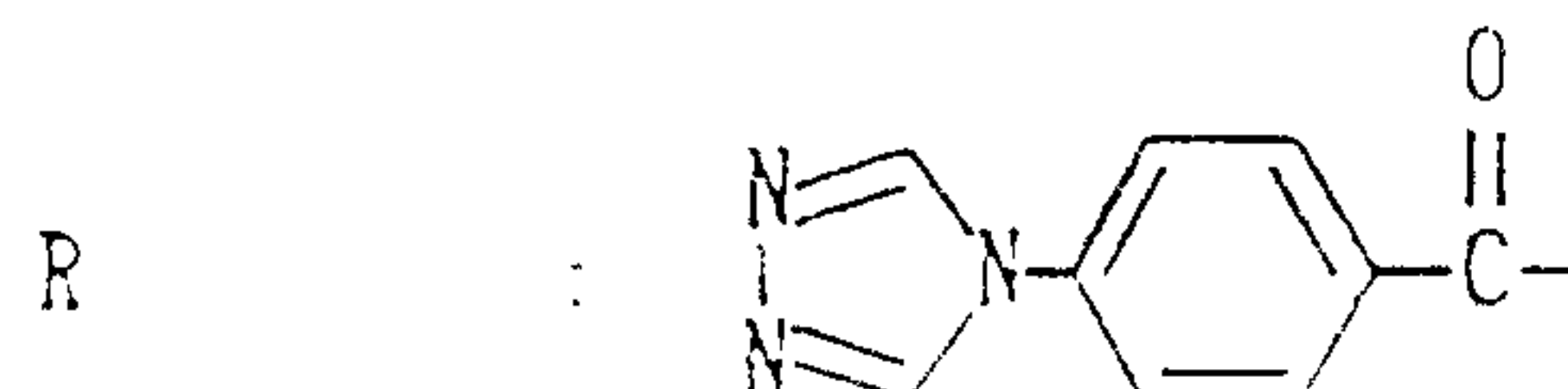
Recrystallization solvent: ethanol-water

Melting point (°C): 198-200

Salt form: free

Example 177

Structural formula:



Crystal form: white powder

Recrystallization solvent: methanol

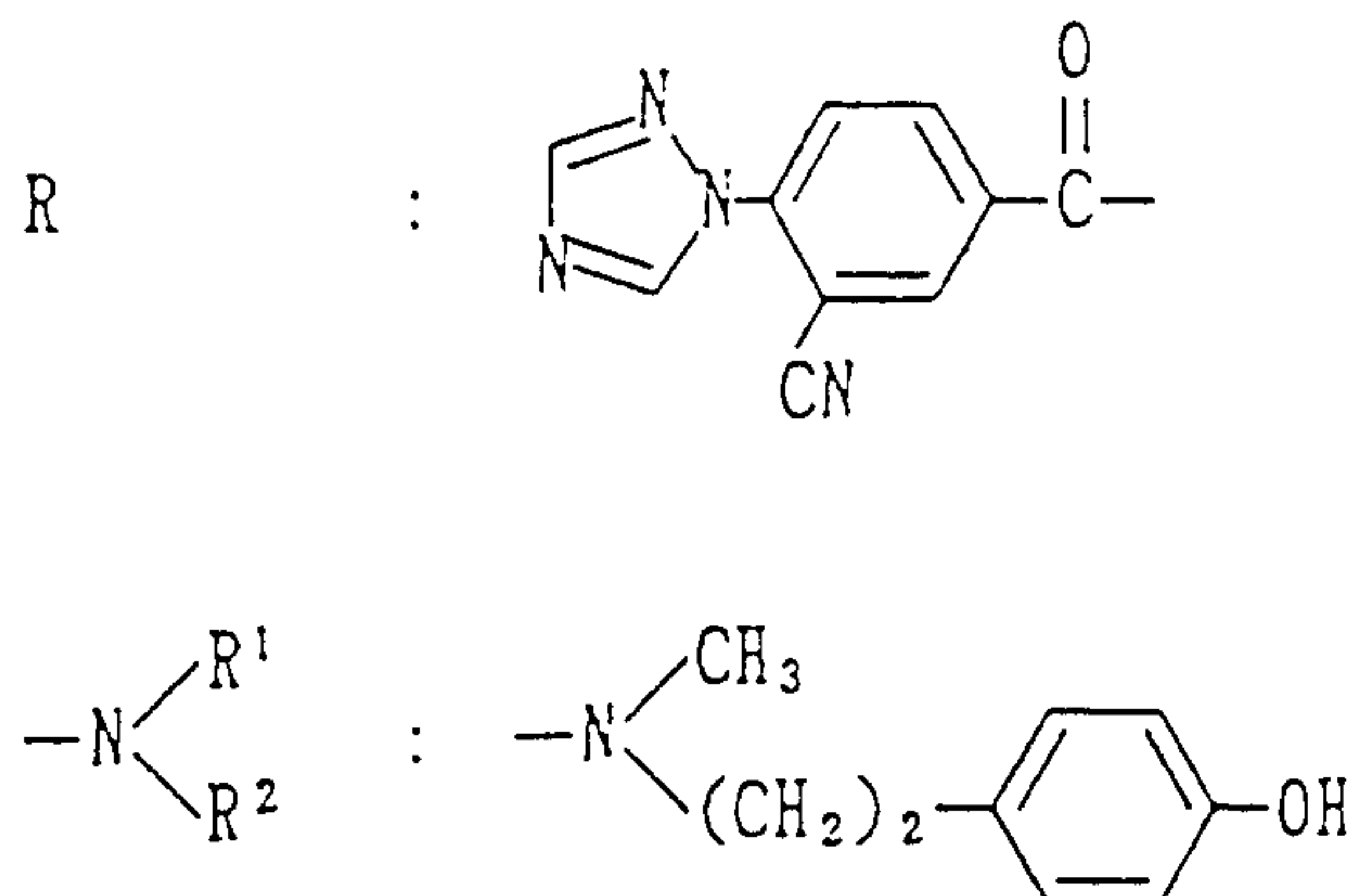
Melting point (°C): 209-210

Salt form: free

[Table 10 (continued)]

Example 178

Structural formula:



Crystal form: white powder

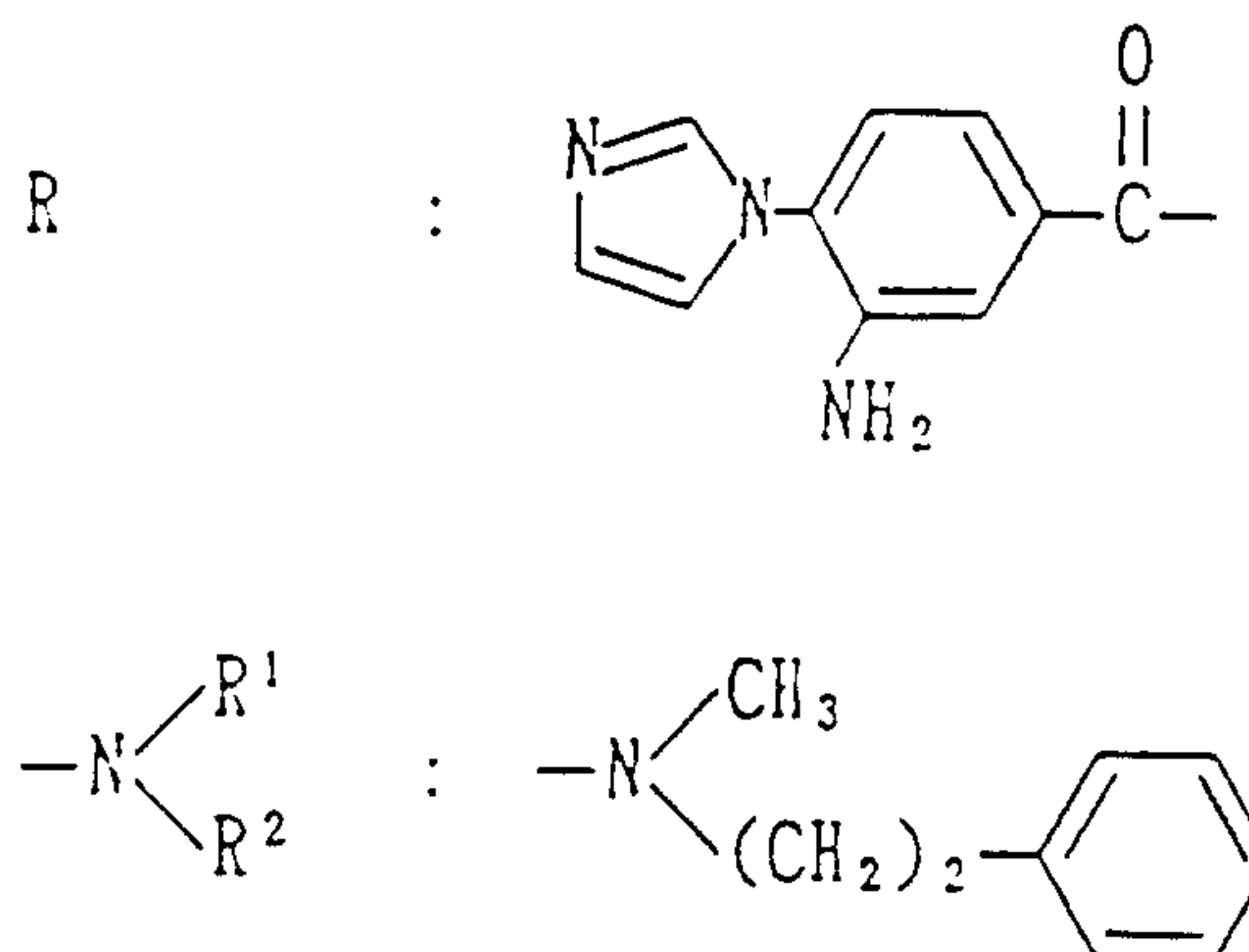
Recrystallization solvent: water-ethanol

Melting point (°C): 255-258 (decompd.)

Salt form: hydrobromide

Example 179

Structural formula:



Crystal form: white amorphous

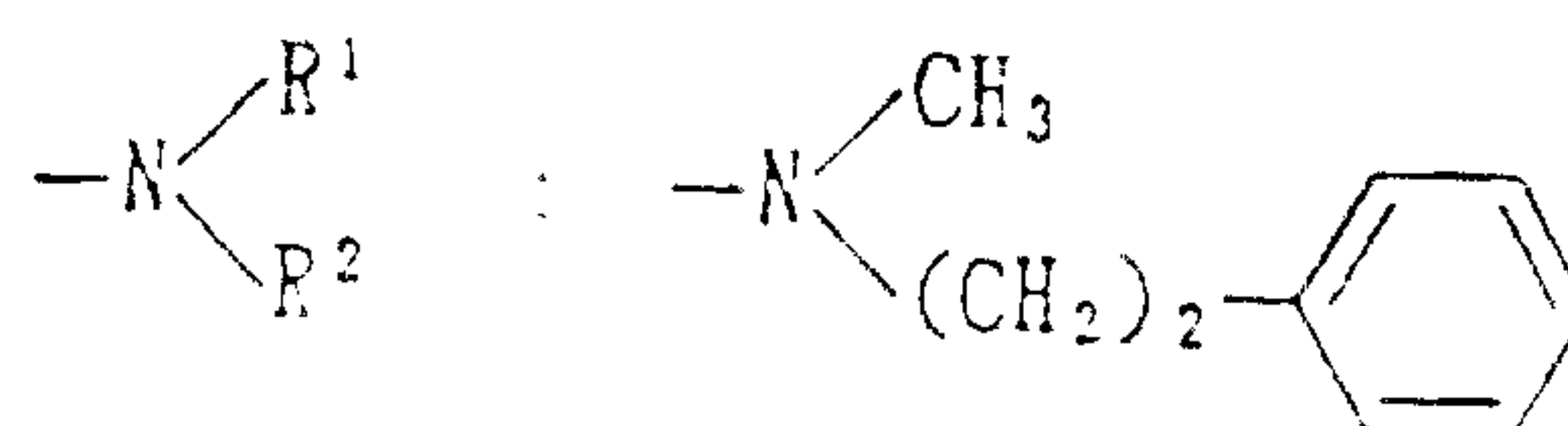
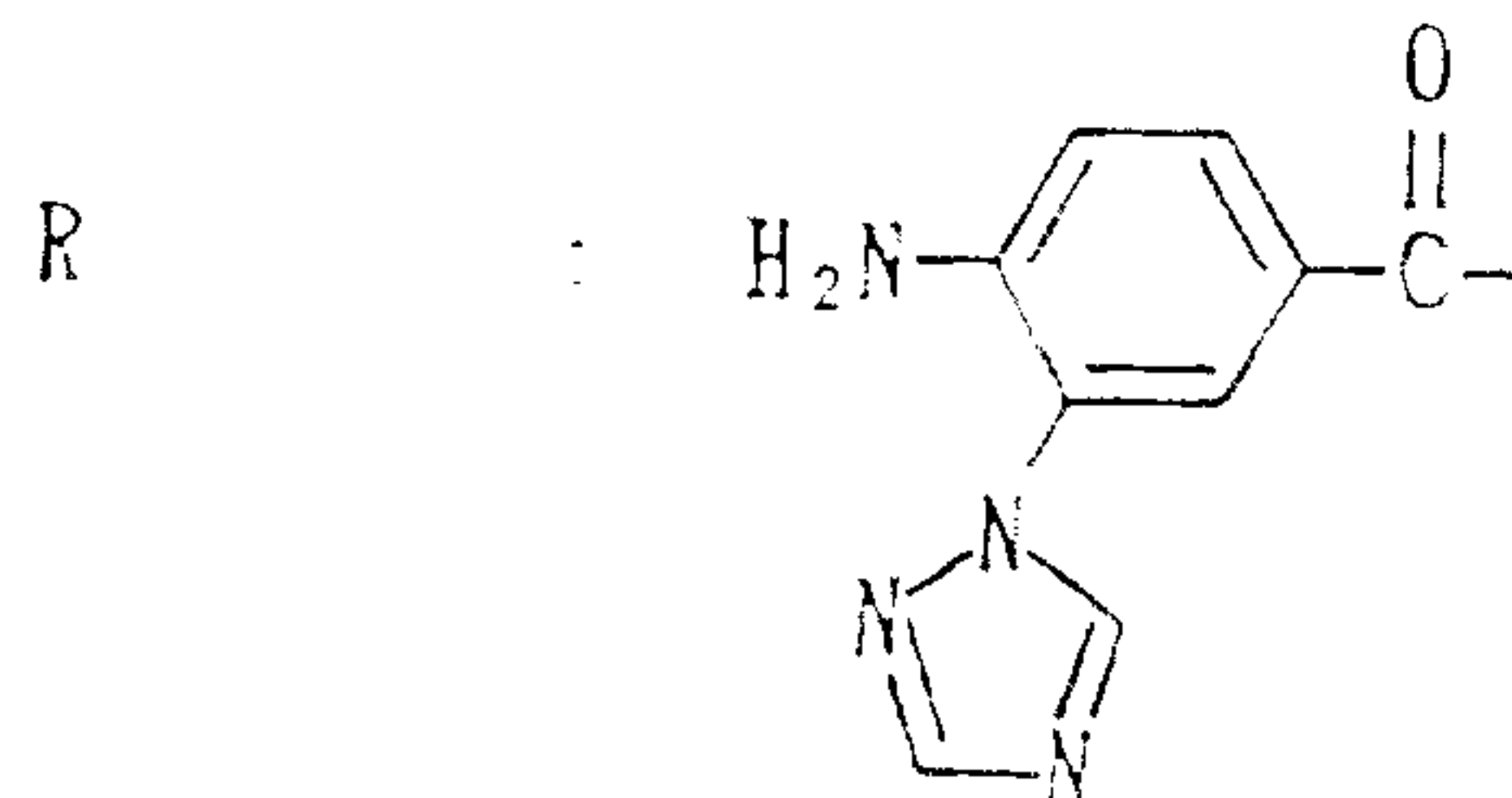
Salt form: hydrochloride

NMR value: 112)

[Table 10 (continued)]

Example 180

Structural formula:



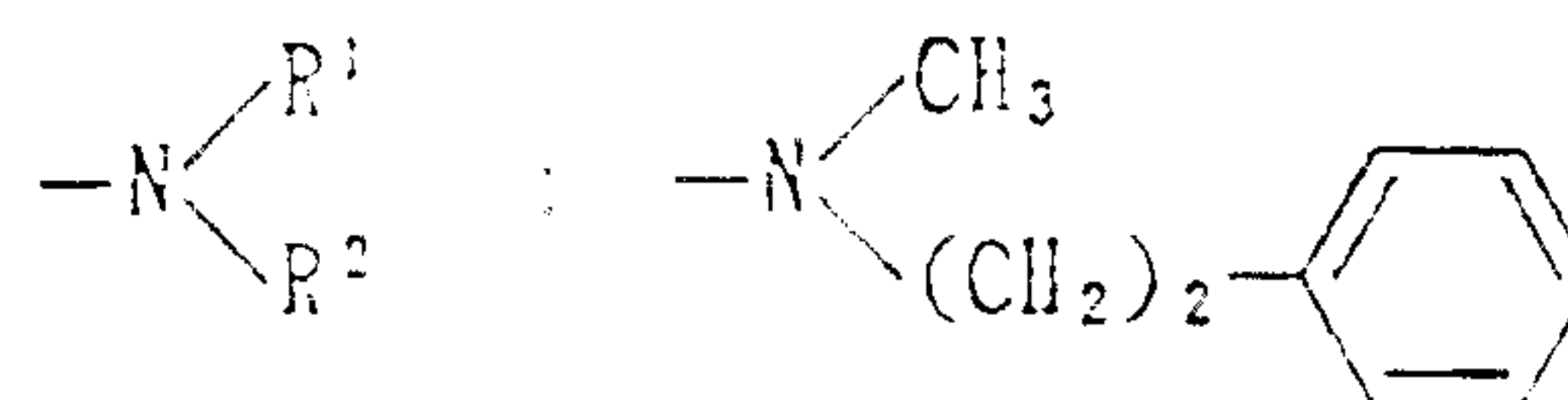
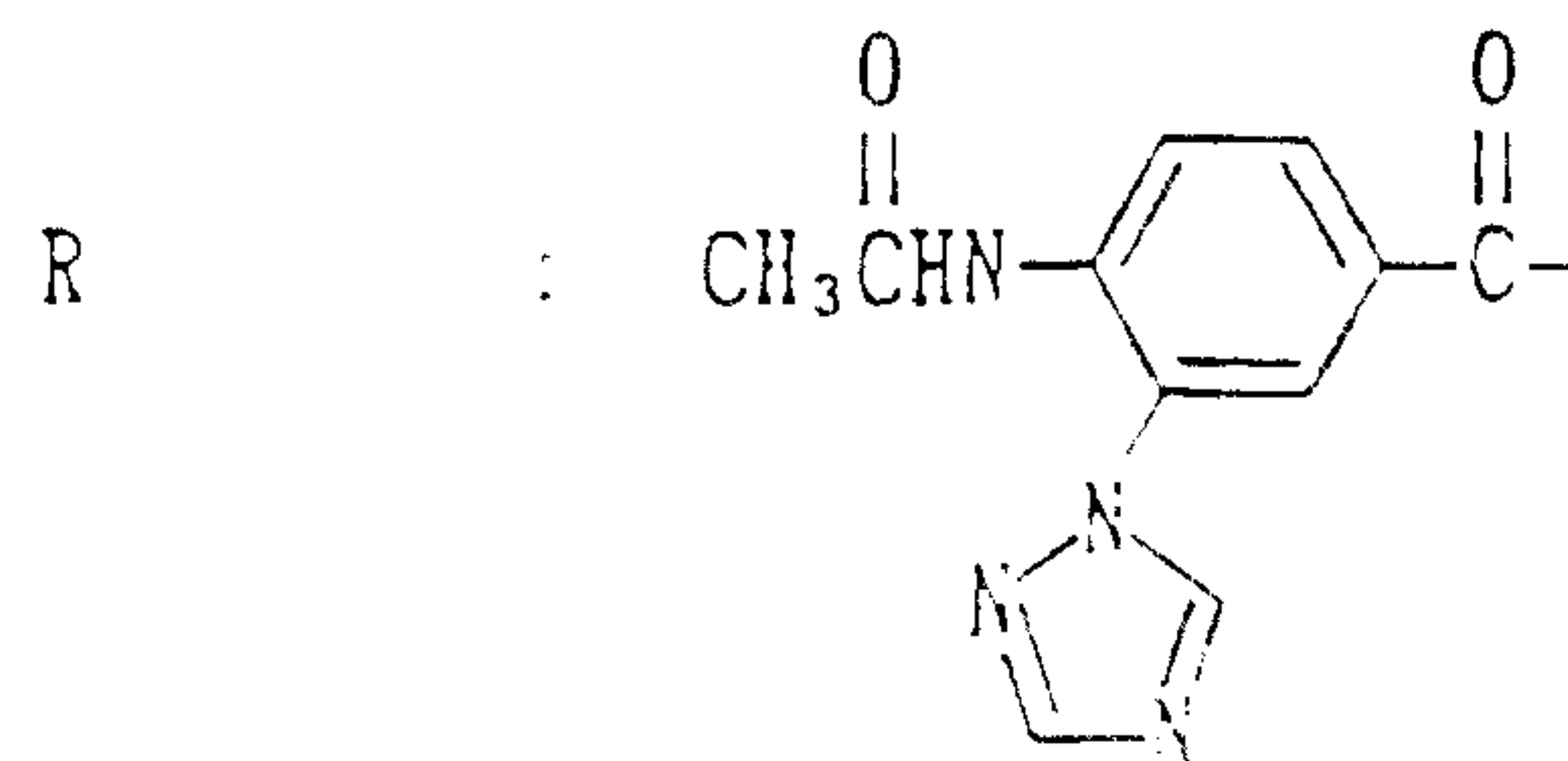
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 113)

Example 181

Structural formula:



Crystal form: white amorphous

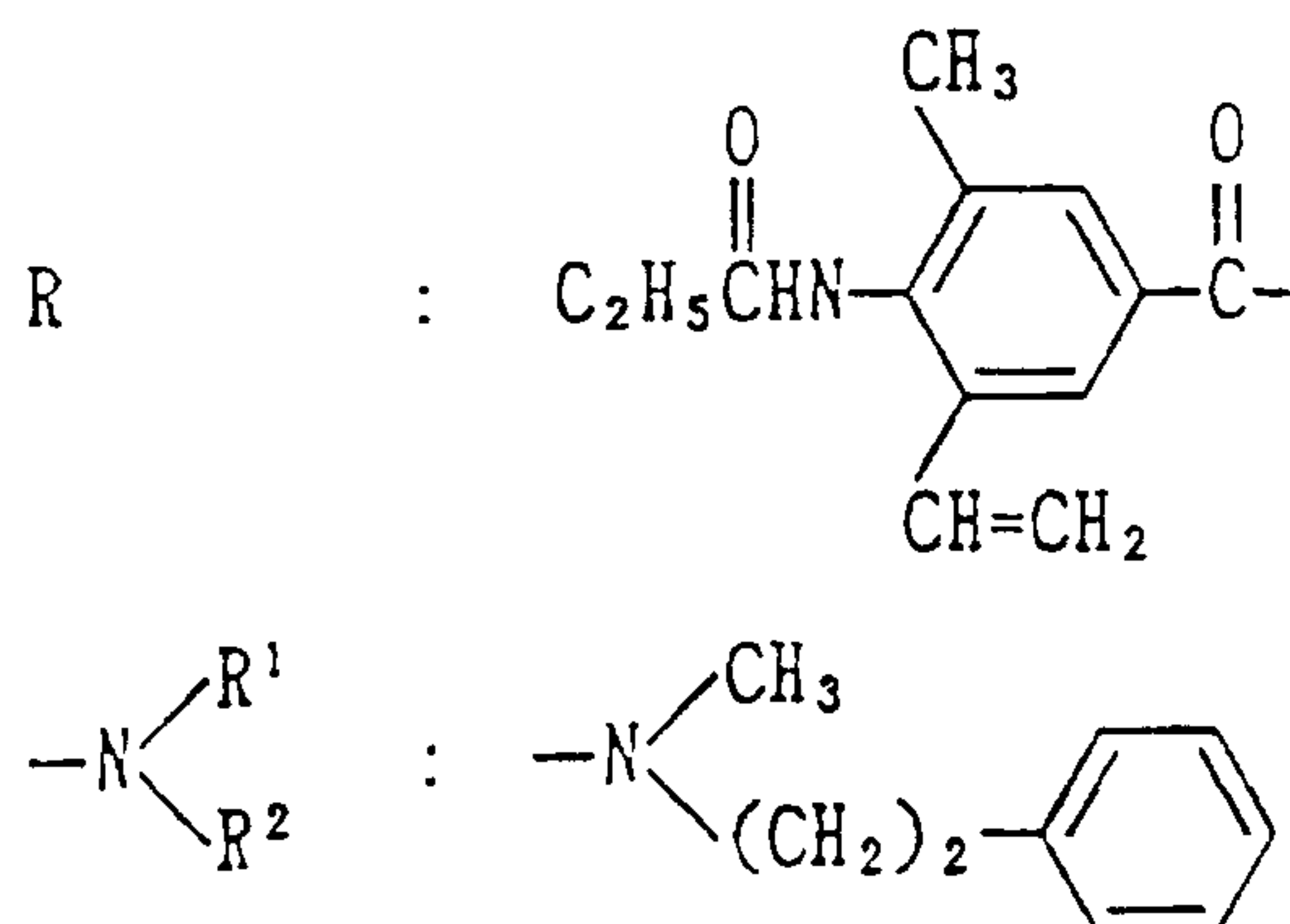
Salt form: hydrochloride

NMR value: 114)

[Table 10 (continued)]

Example 182

Structural formula:



Crystal form: white powder

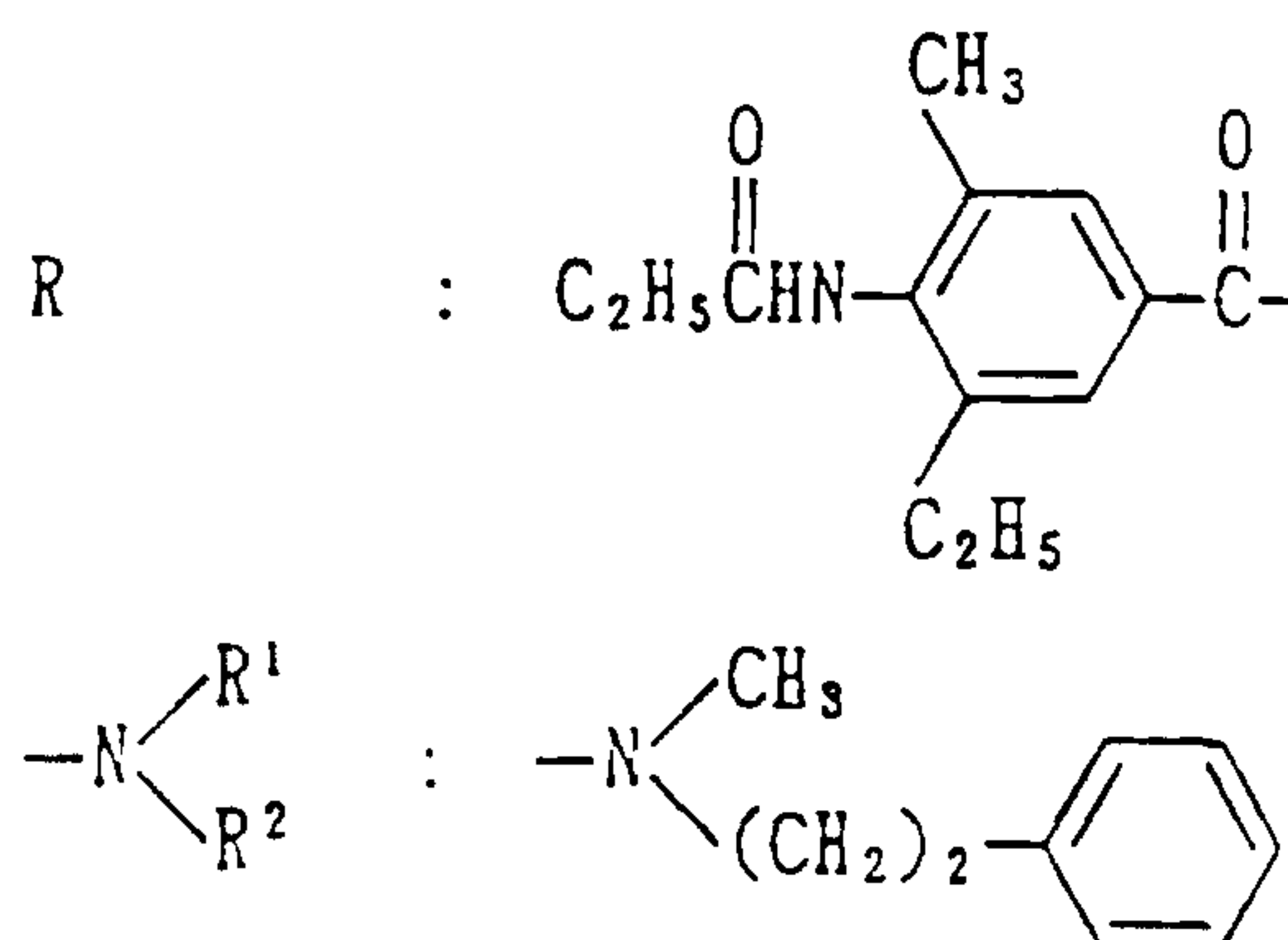
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 234-235.5

Salt form: hydrochloride

Example 183

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

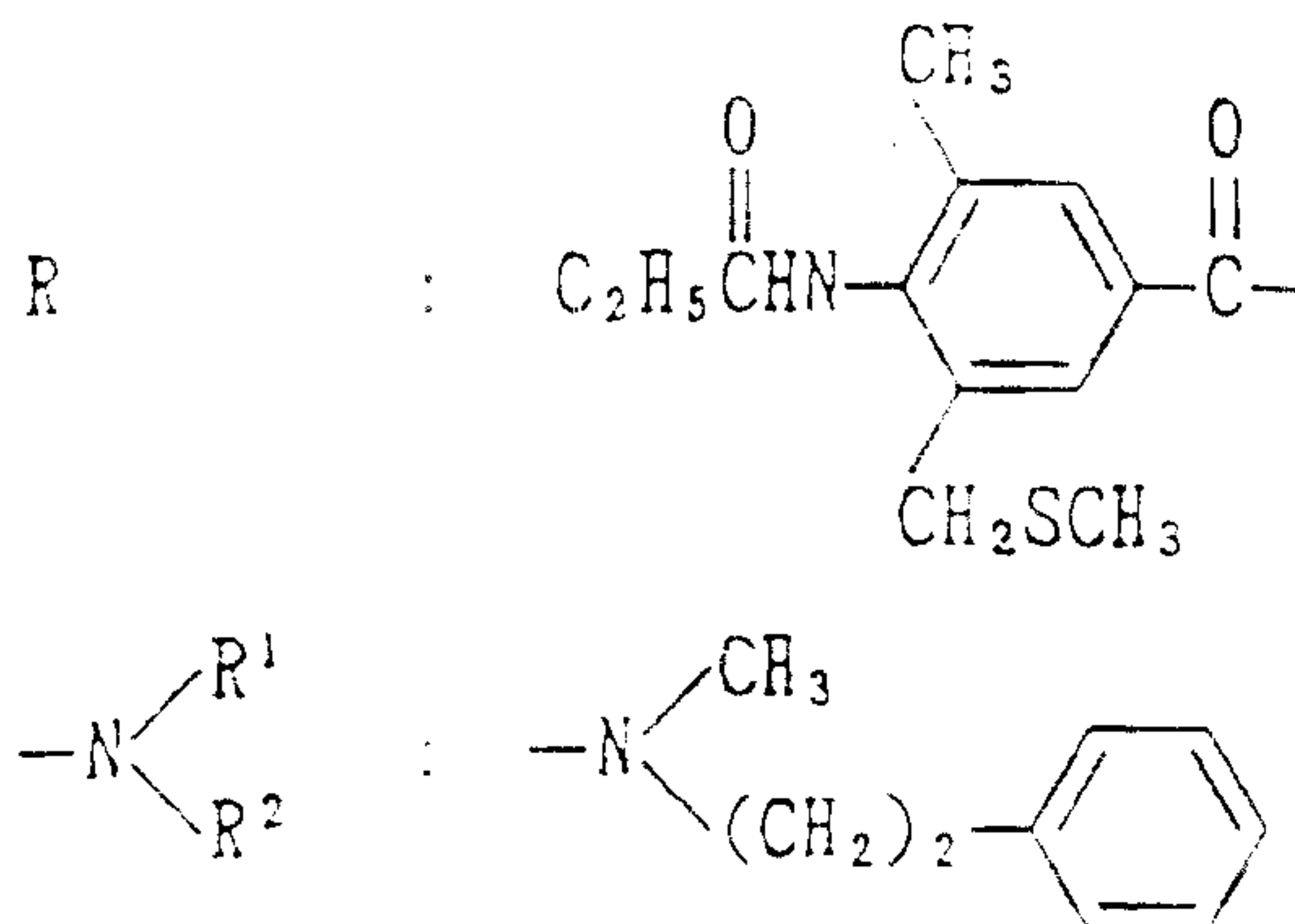
Melting point (°C): 247.5-248.5

Salt form: hydrochloride

[Table 10 (continued)]

Example 184

Structural formula:



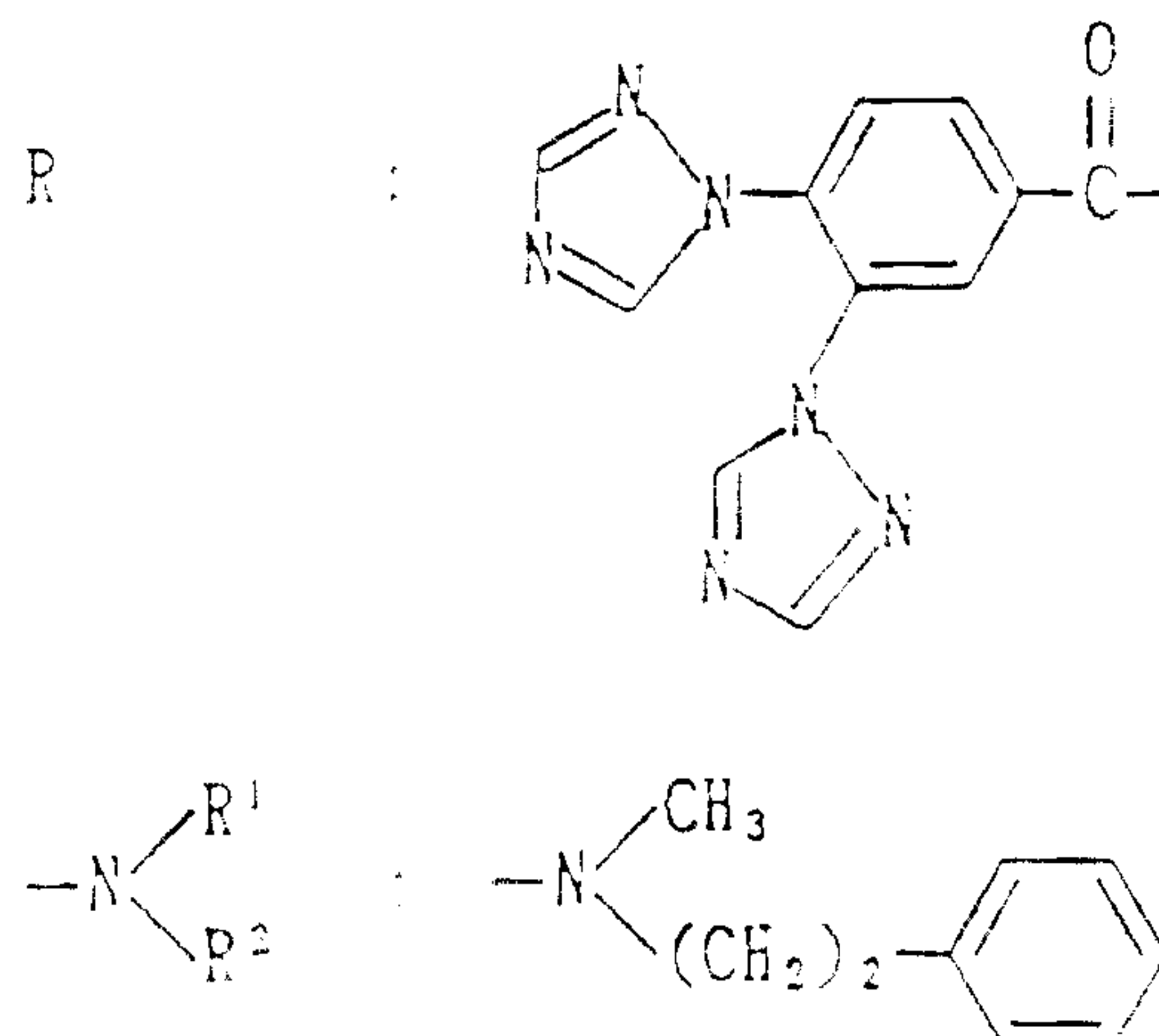
Crystal form: white powder

Salt form: hydrochloride

NMR value: 115)

Example 185

Structural formula:



Crystal form: white powder

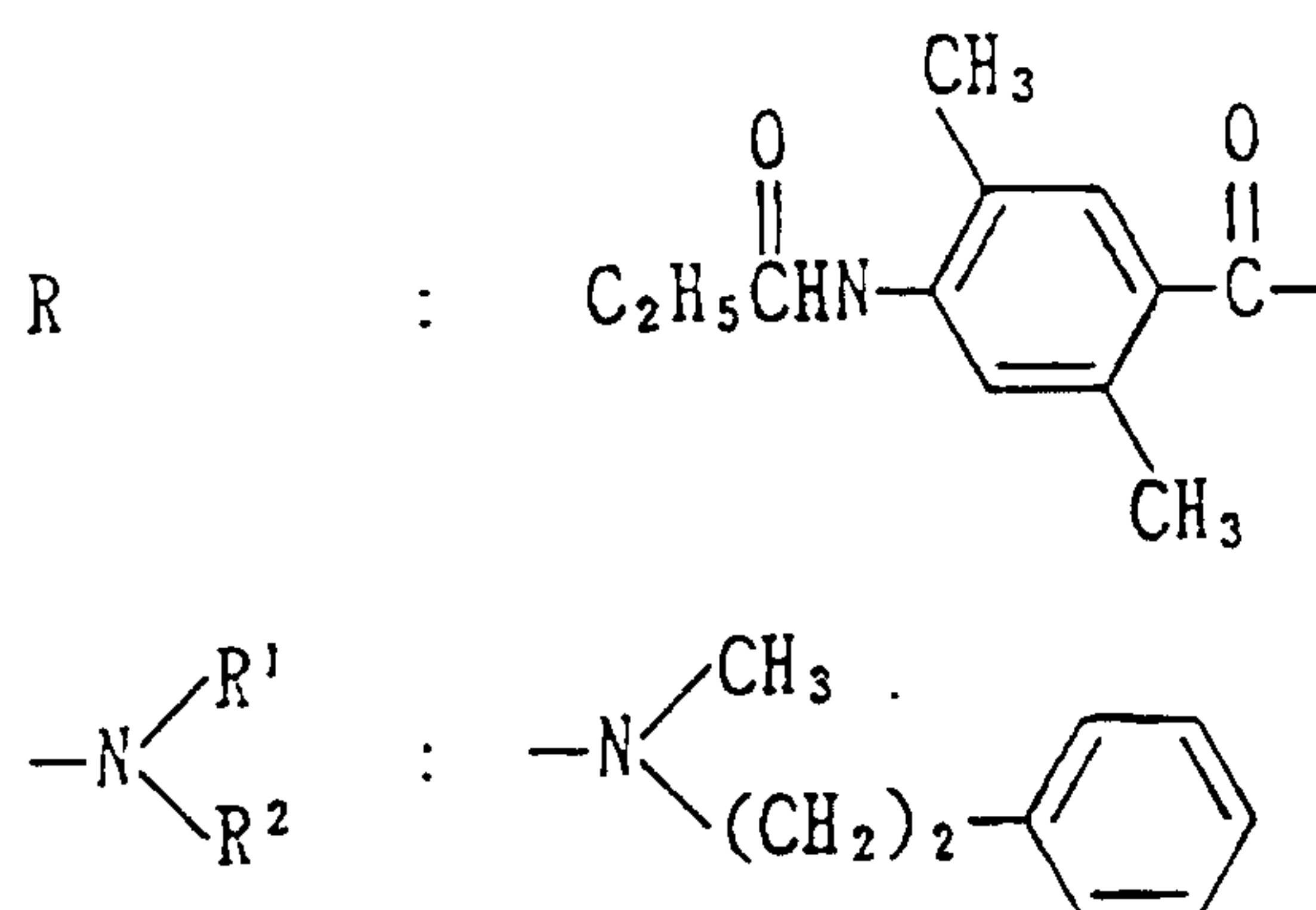
Salt form: hydrochloride

NMR value: 116)

[Table 10 (continued)]

Example 186

Structural formula:



Crystal form: white powder

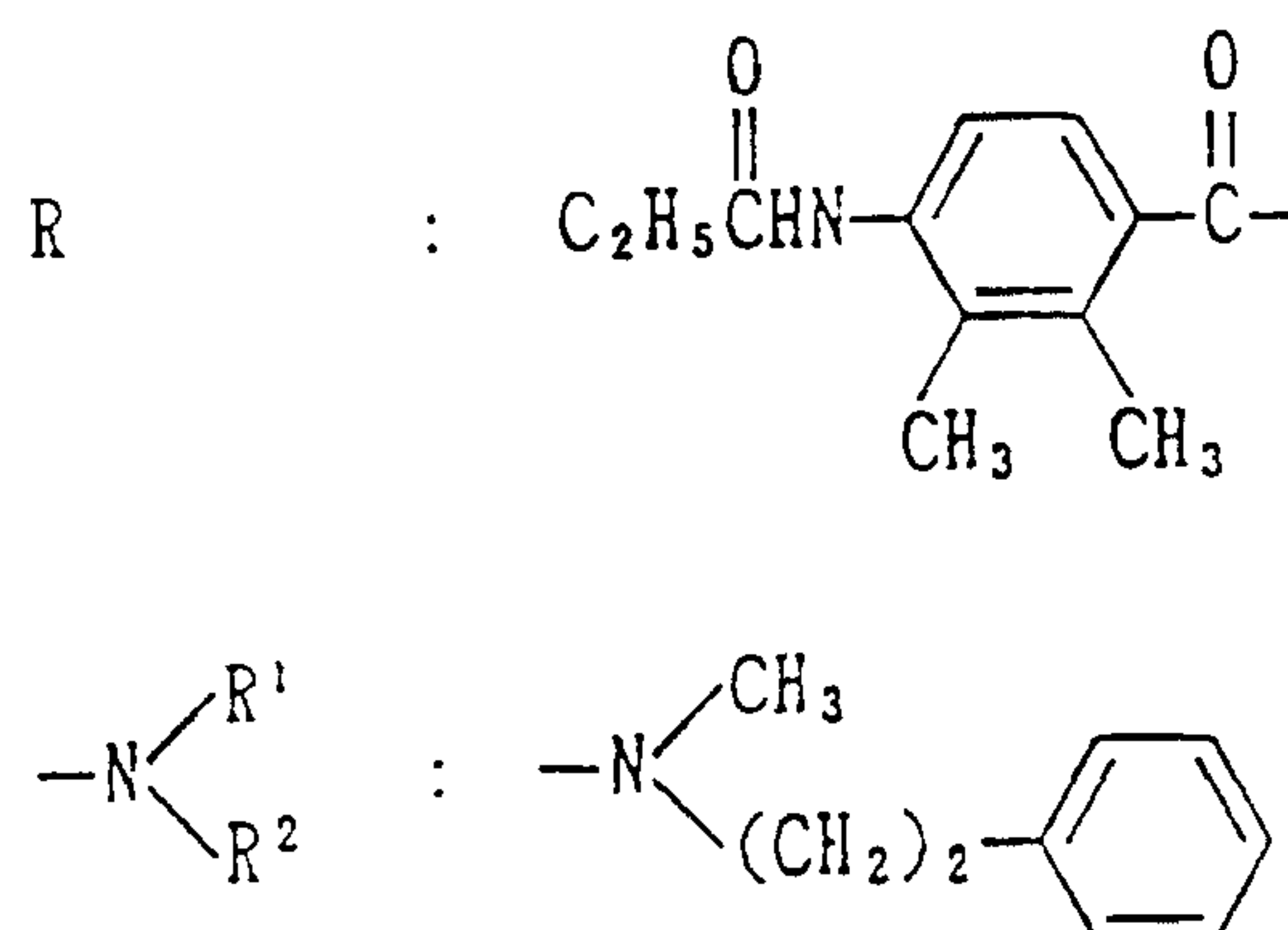
Recrystallization solvent: ethanol-ethyl acetate

Melting point (°C): 209-211

Salt form: hydrochloride

Example 187

Structural formula:



Crystal form: white amorphous

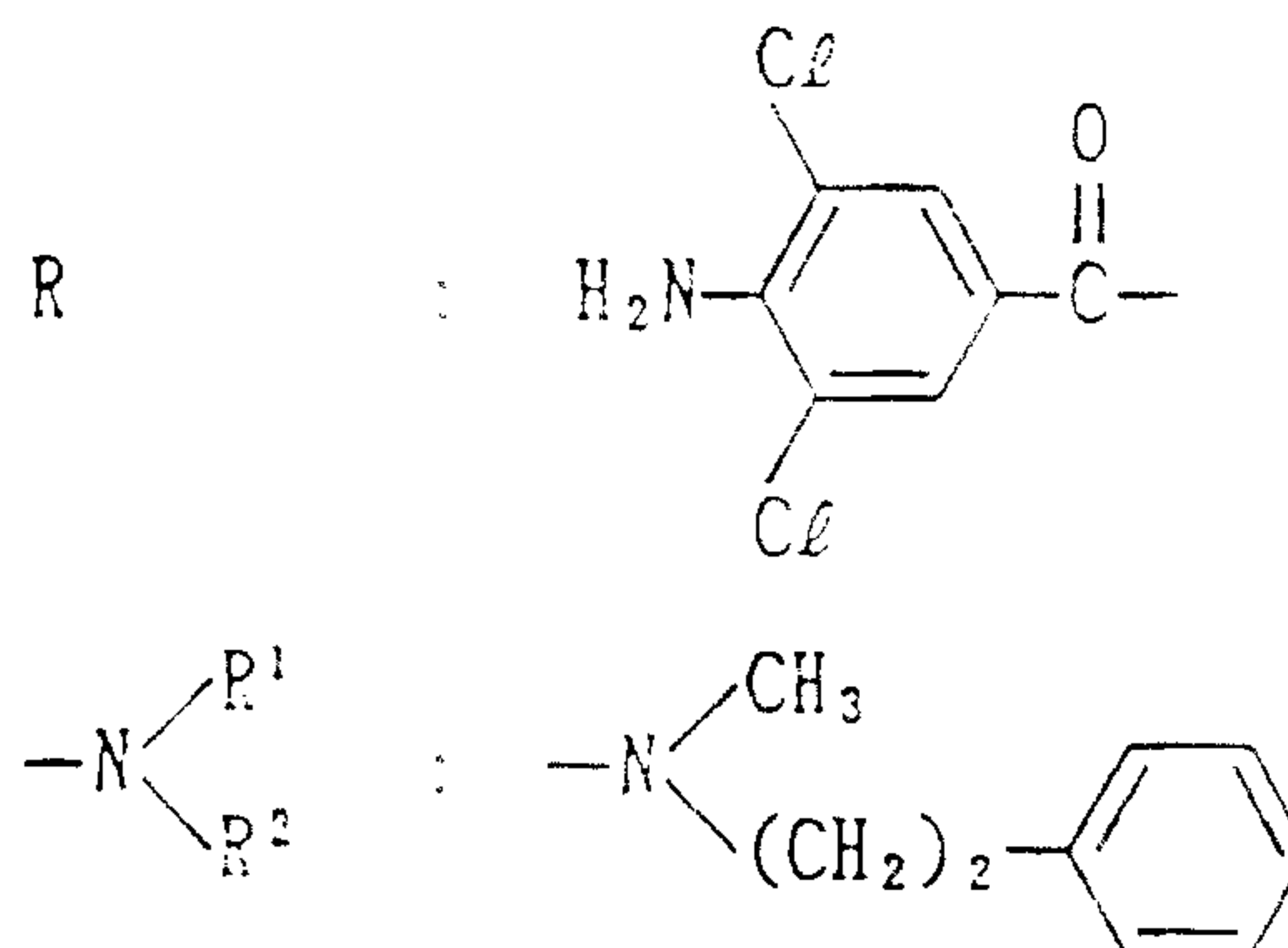
Salt form: hydrochloride

NMR value: 117)

{Table 10 (continued)}

Example 188

Structural formula:



Crystal form: white needles

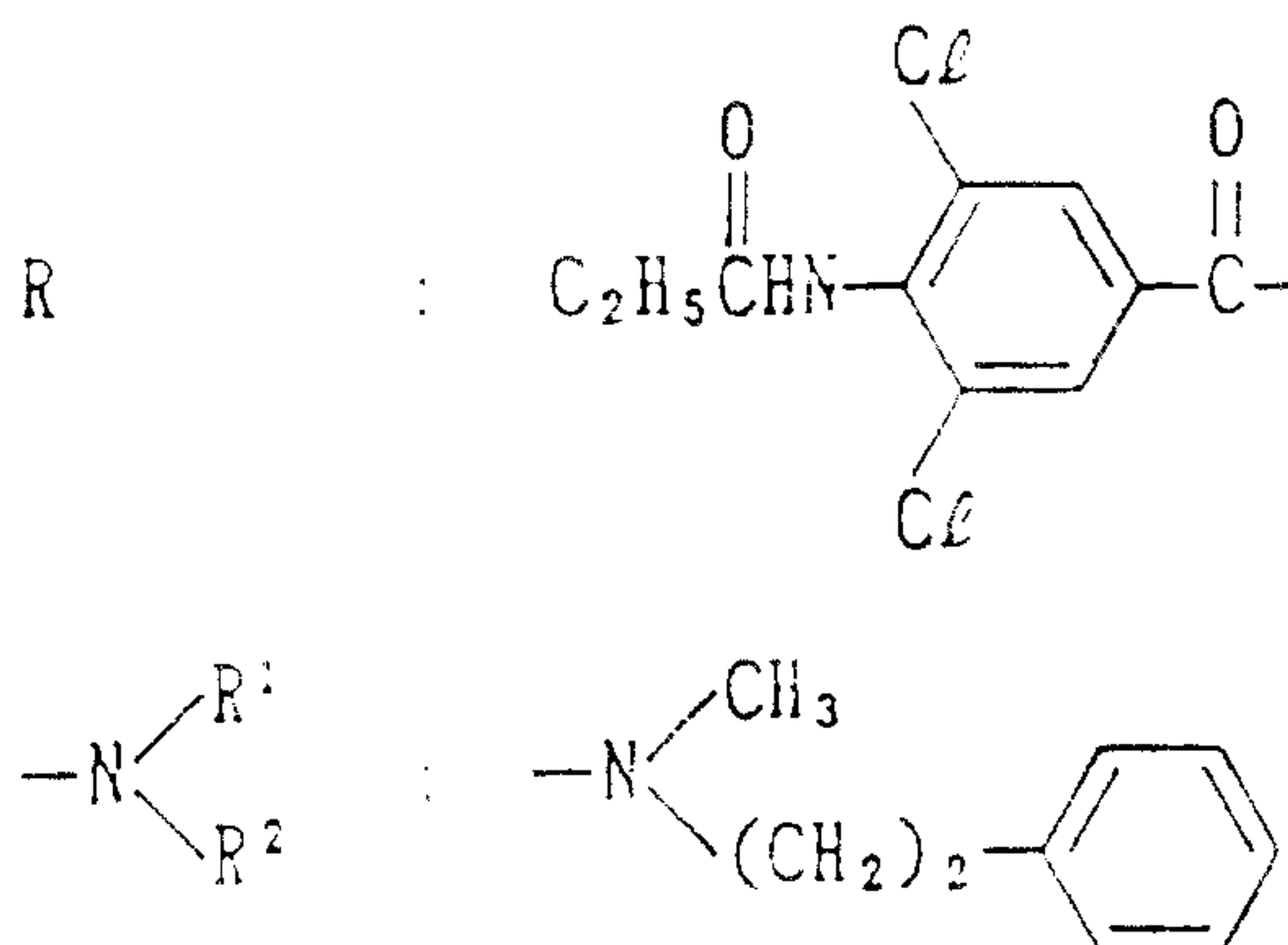
Recrystallization solvent: dichloromethane-n-hexane

Melting point (°C): 109-111

Salt form: free

Example 189

Structural formula:



Crystal form: white powder

Recrystallization solvent: methanol-water

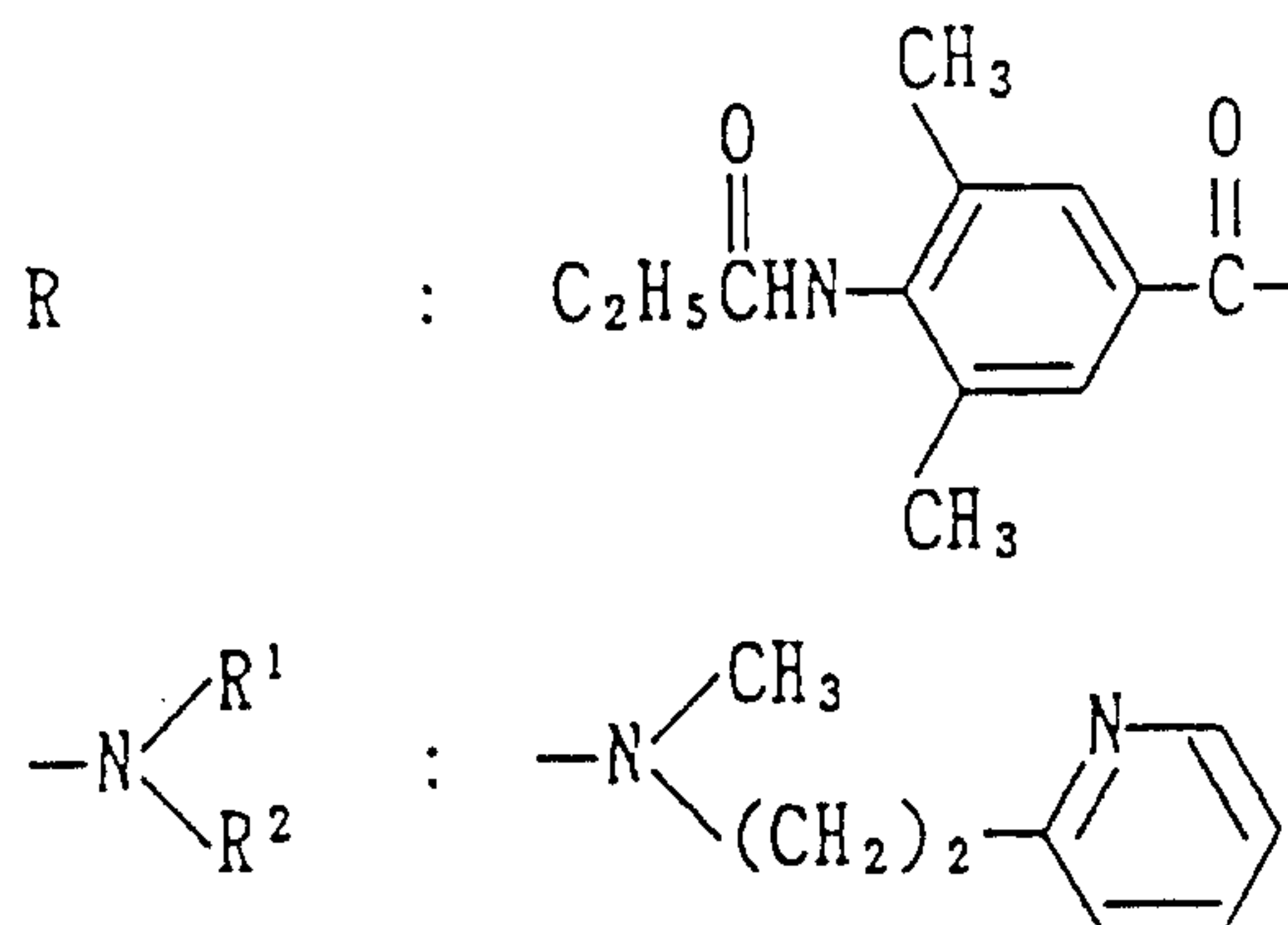
Melting point (°C): 258-260

Salt form: hydrochloride

{Table 10 (continued)}

Example 190

Structural formula:



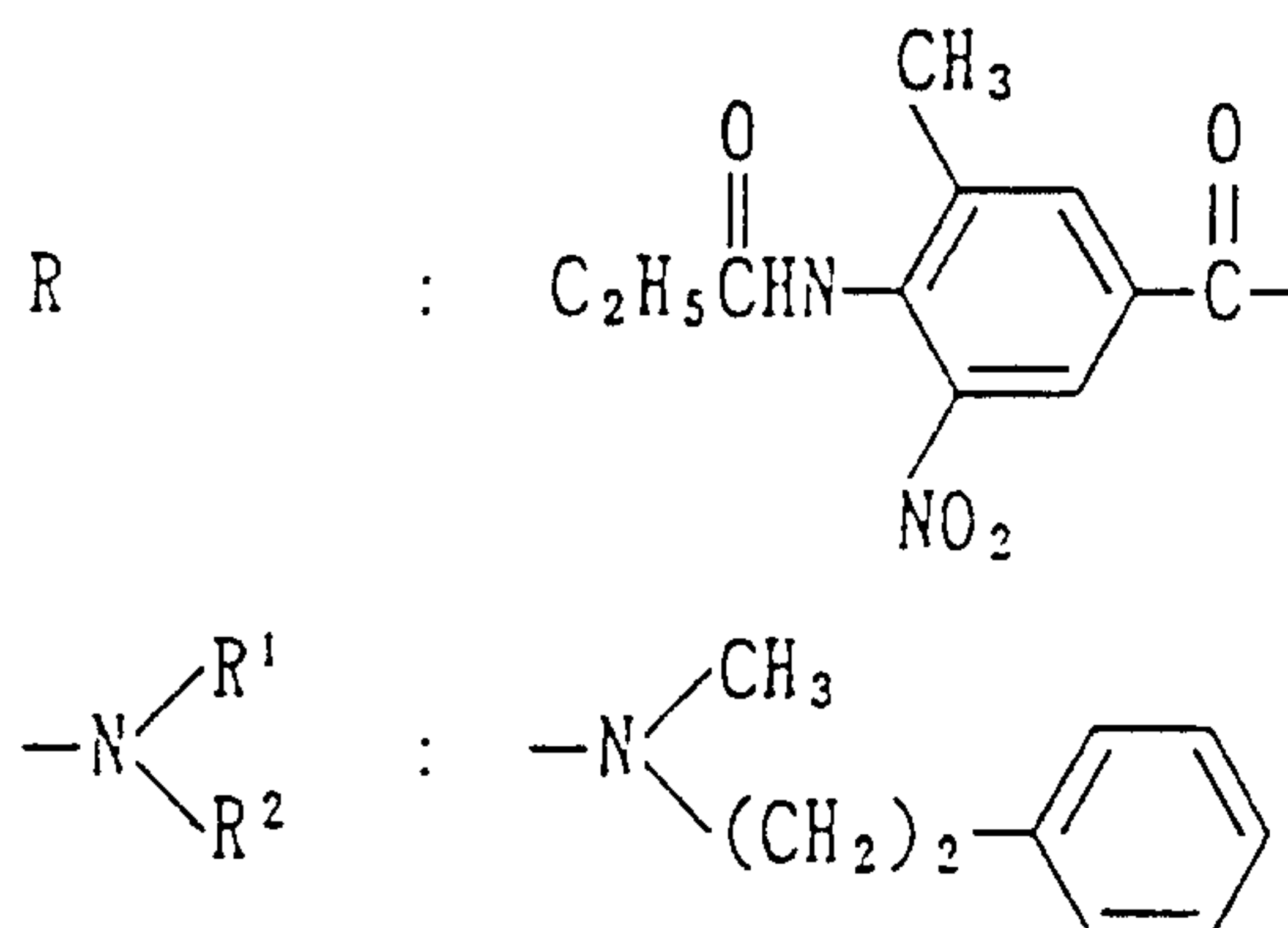
Crystal form: light yellow amorphous

Salt form: dihydrochloride

NMR value: 118)

Example 191

Structural formula:



Crystal form: light yellow powder

Recrystallization solvent: ethyl acetate-n-hexane

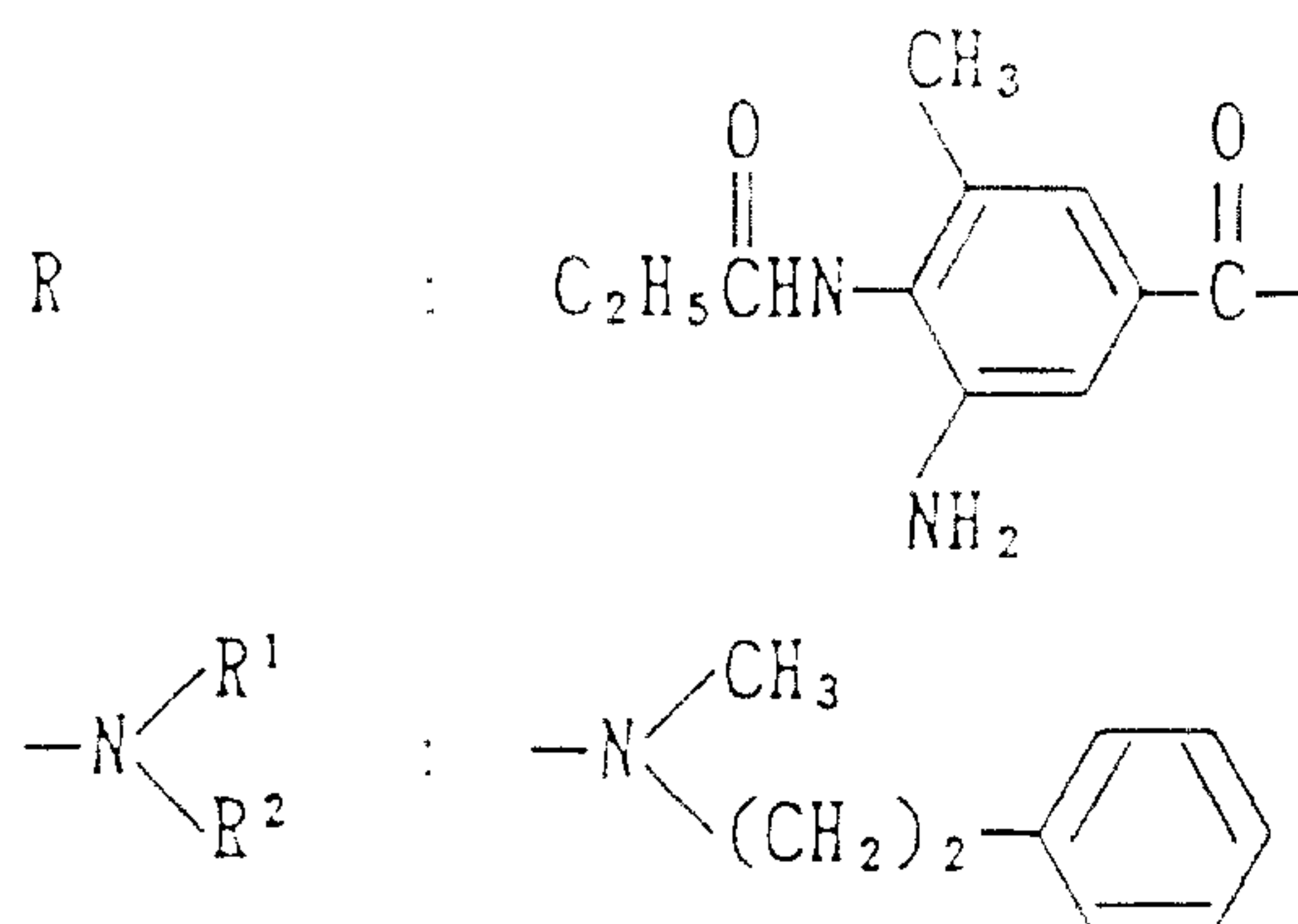
Melting point (°C): 126-128

Salt form: free

{Table 10 (continued)}

Example 192

Structural formula:



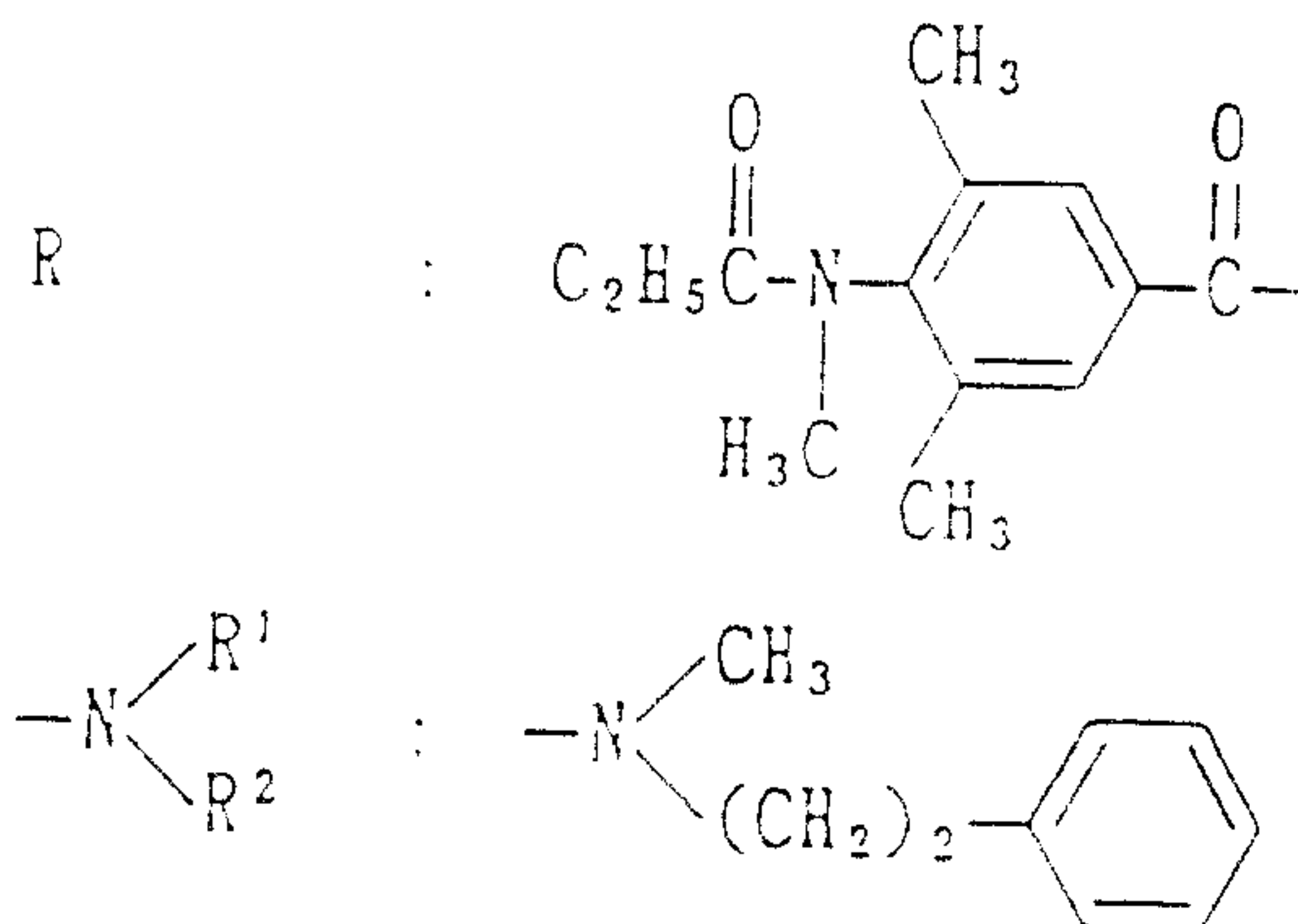
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 119)

Example 193

Structural formula:



Crystal form: white amorphous

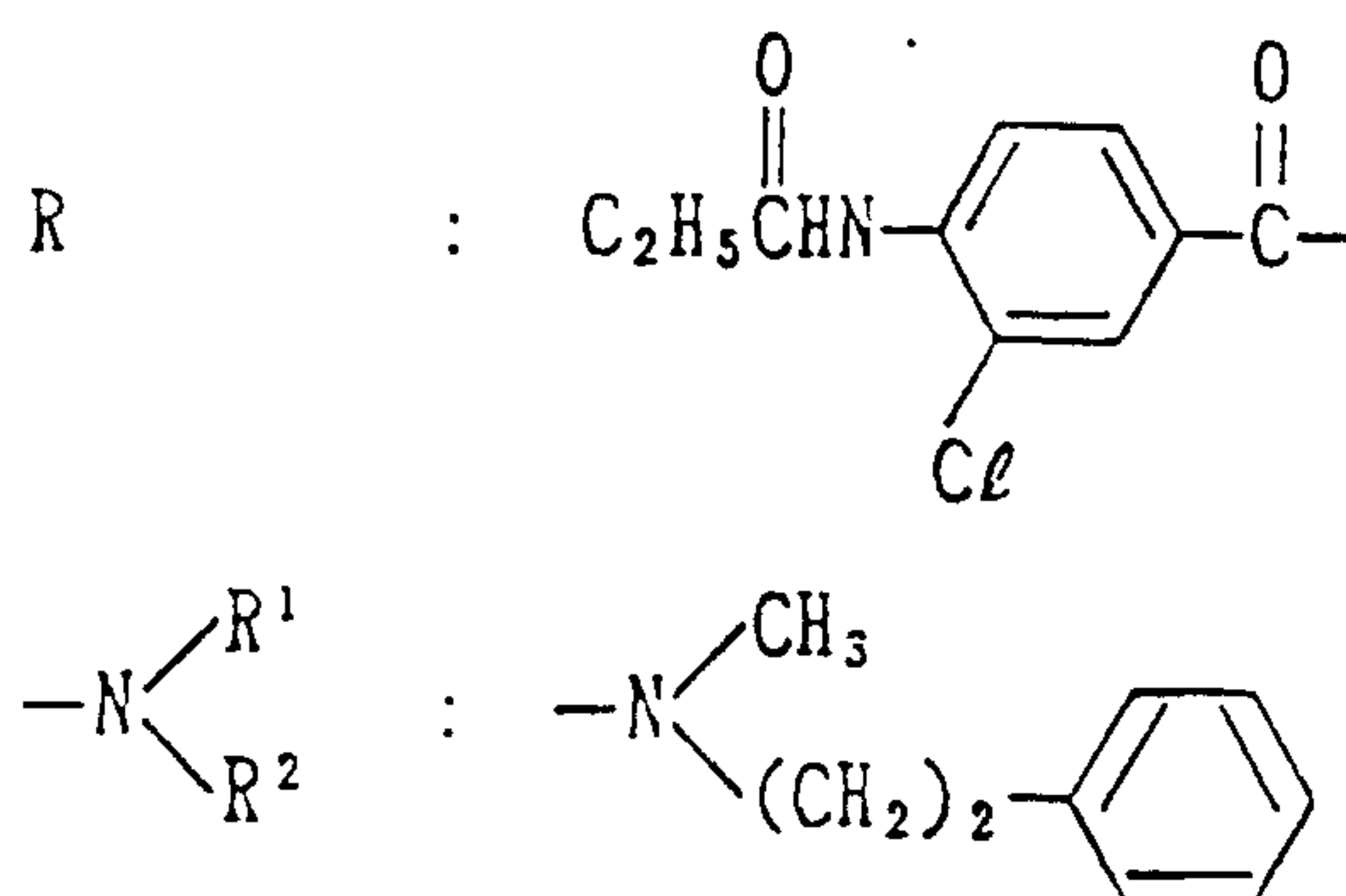
Salt form: hydrochloride

NMR value: 120)

[Table 10 (continued)]

Example 194

Structural formula:



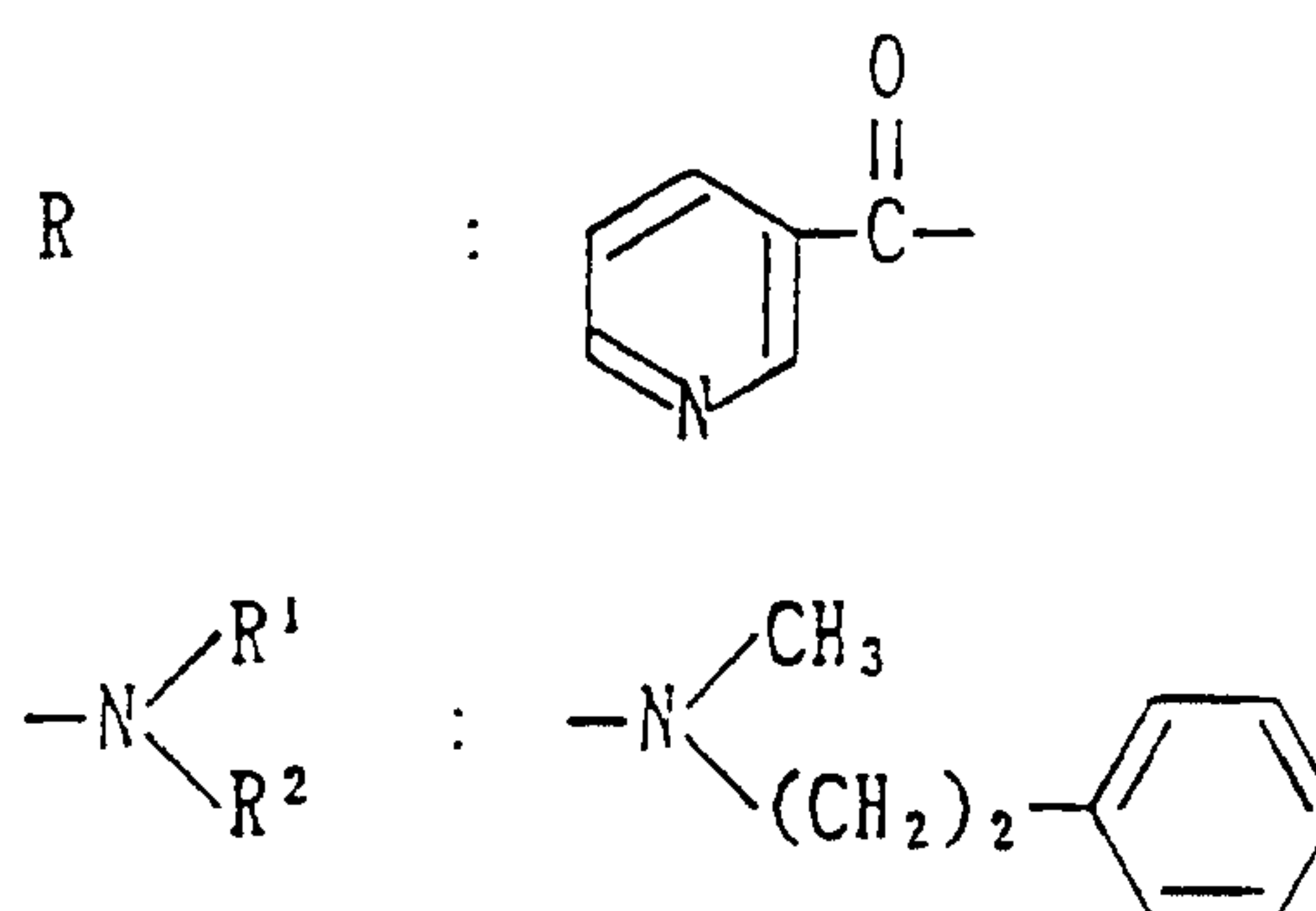
Crystal form: light yellow amorphous

Salt form: hydrochloride

NMR value: 121)

Example 195

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-water

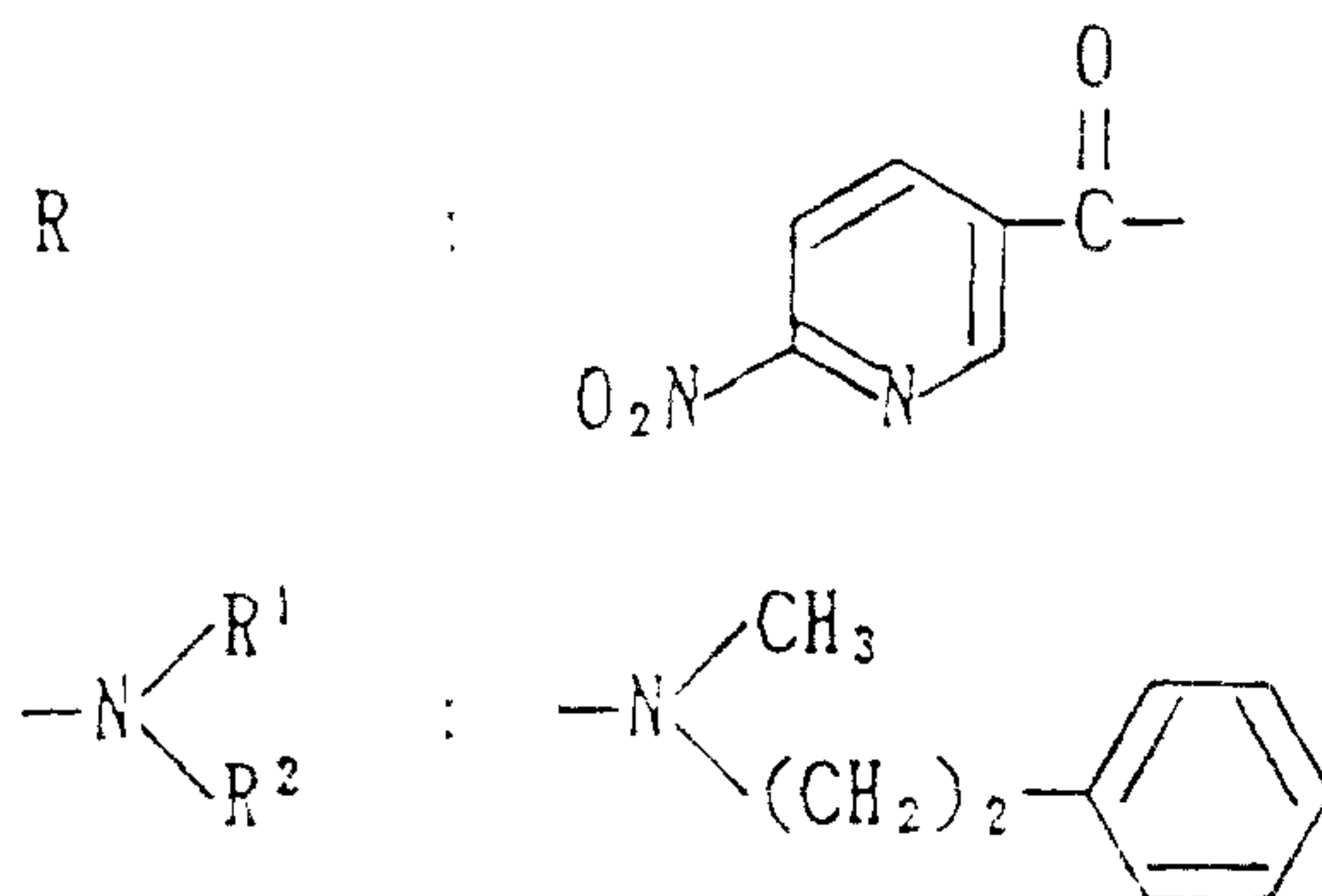
Melting point (°C): 236-237 (decompd.)

Salt form: dihydrochloride

[Table 10 (continued)]

Example 196

Structural formula:



Crystal form: white powder

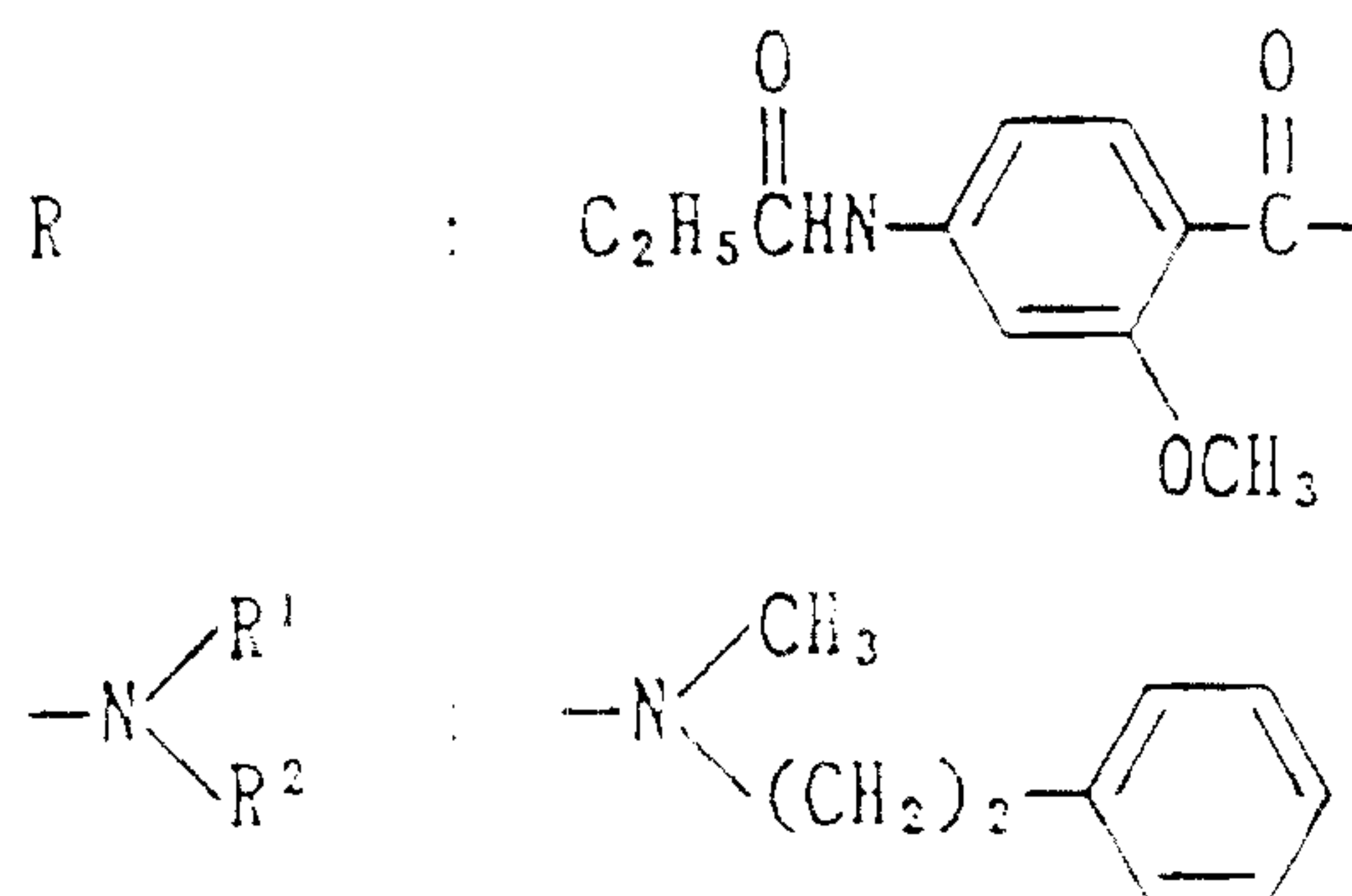
Recrystallization solvent: ethanol-water

Melting point (°C): 219-220 (decompd.)

Salt form: hydrochloride

Example 197

Structural formula:



Crystal form: white amorphous

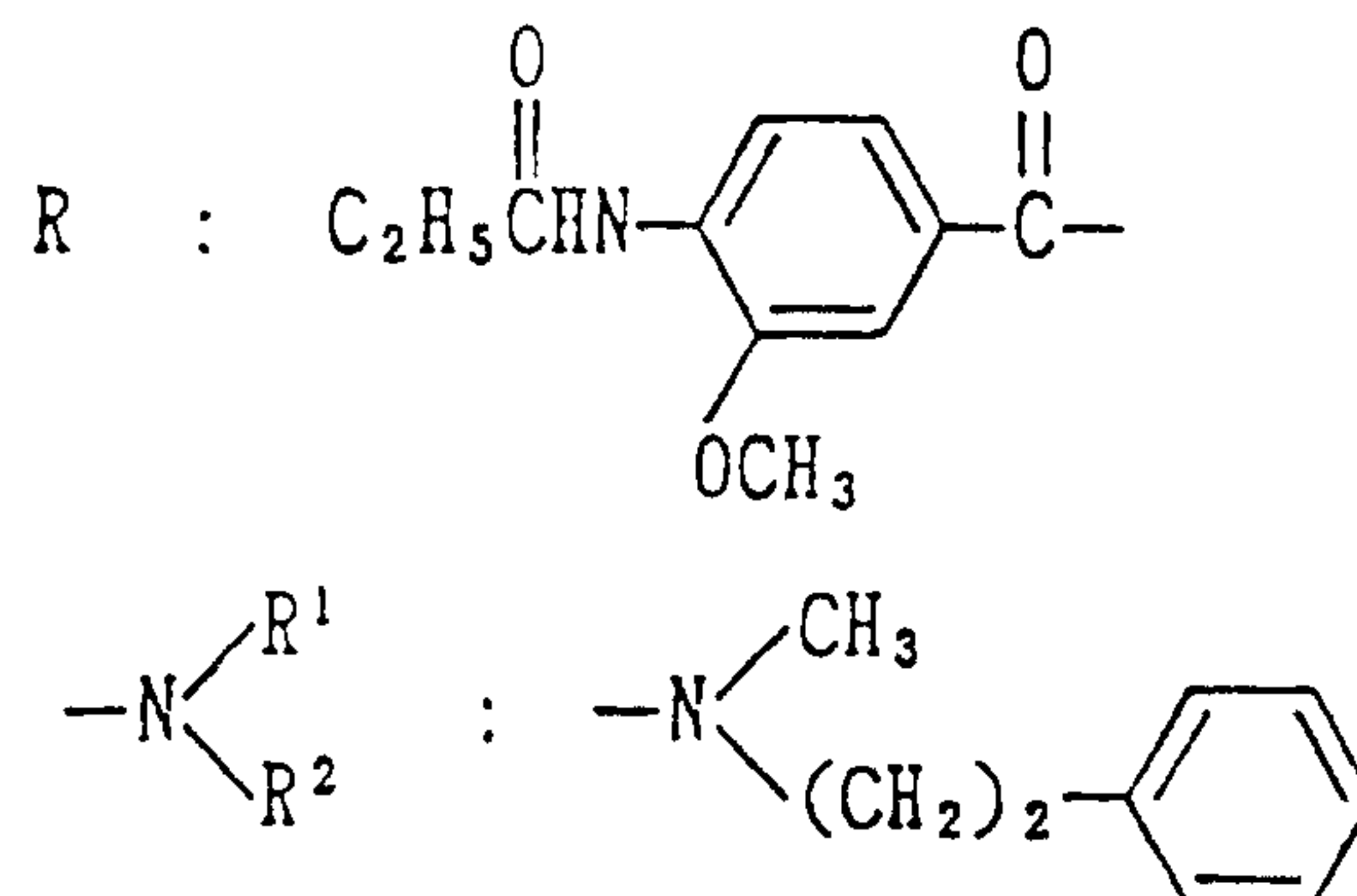
Salt form: hydrochloride

NMR value: 122)

[Table 10 (continued)]

Example 198

Structural formula:



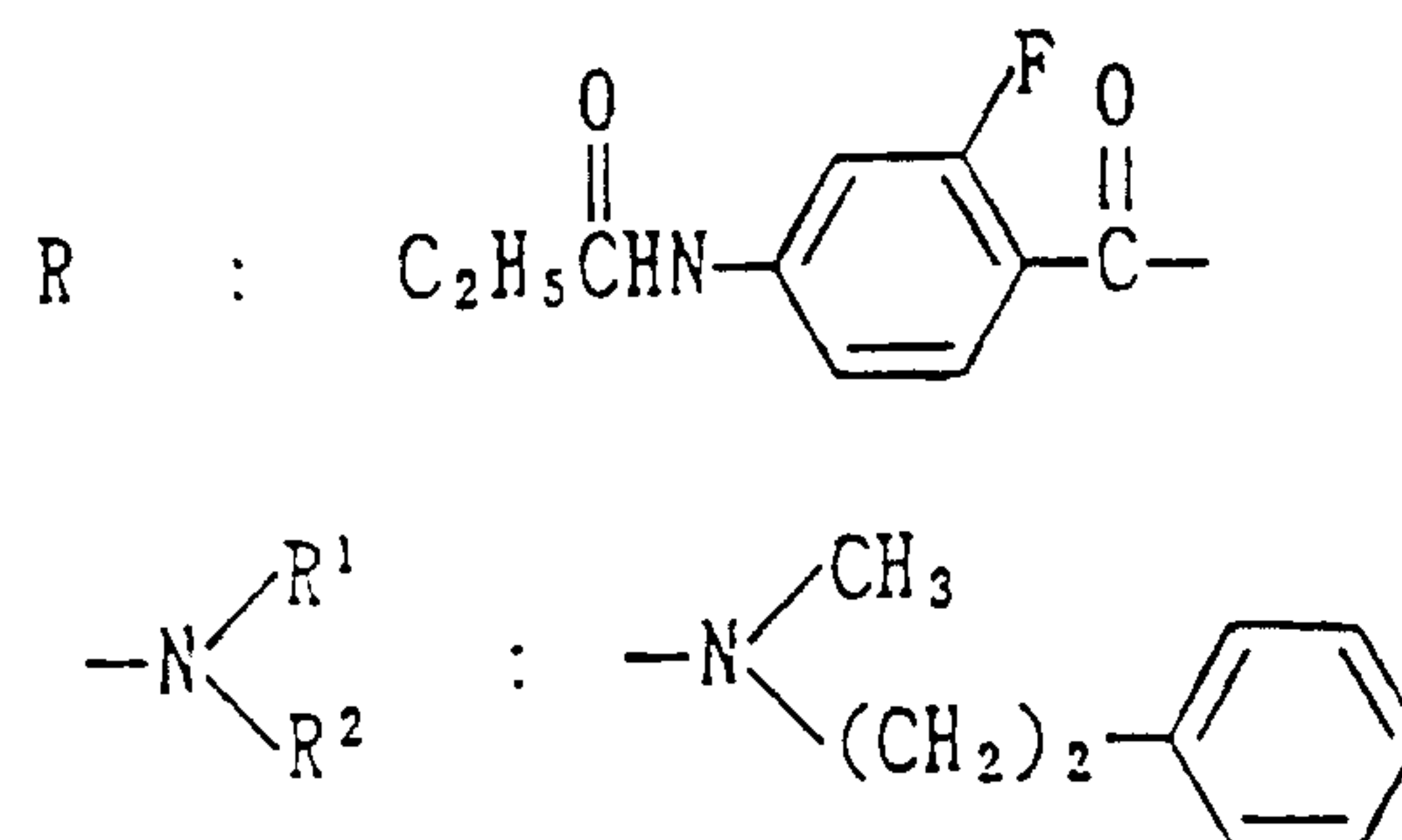
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 123)

Example 199

Structural formula:



Crystal form: white amorphous

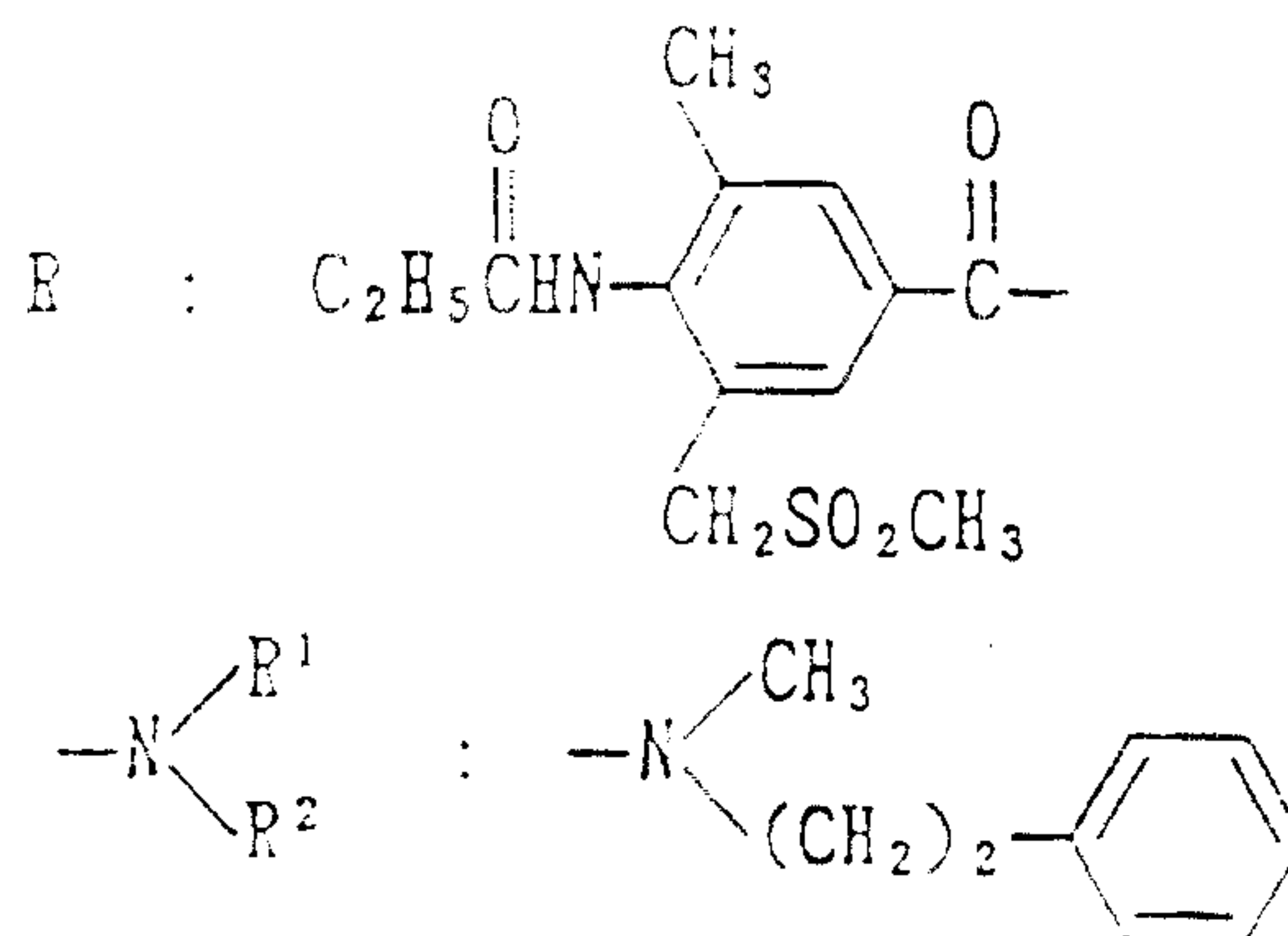
Salt form: hydrochloride

NMR value: 124)

{Table 10 (continued)}

Example 200

Structural formula:



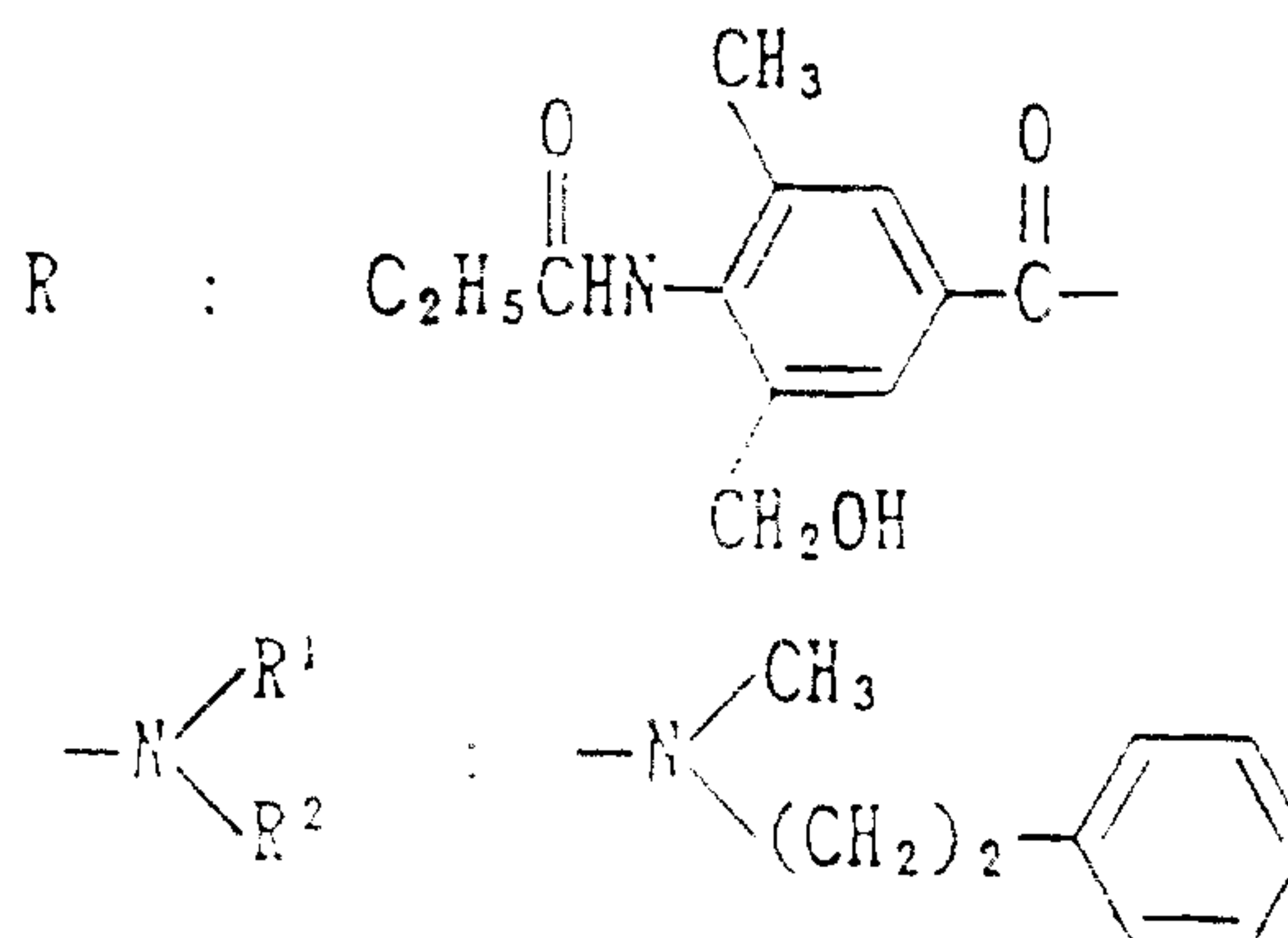
Crystal form: white amorphous

Salt form: hydrochloride

NMR value: 125)

Example 201

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-ethyl acetate

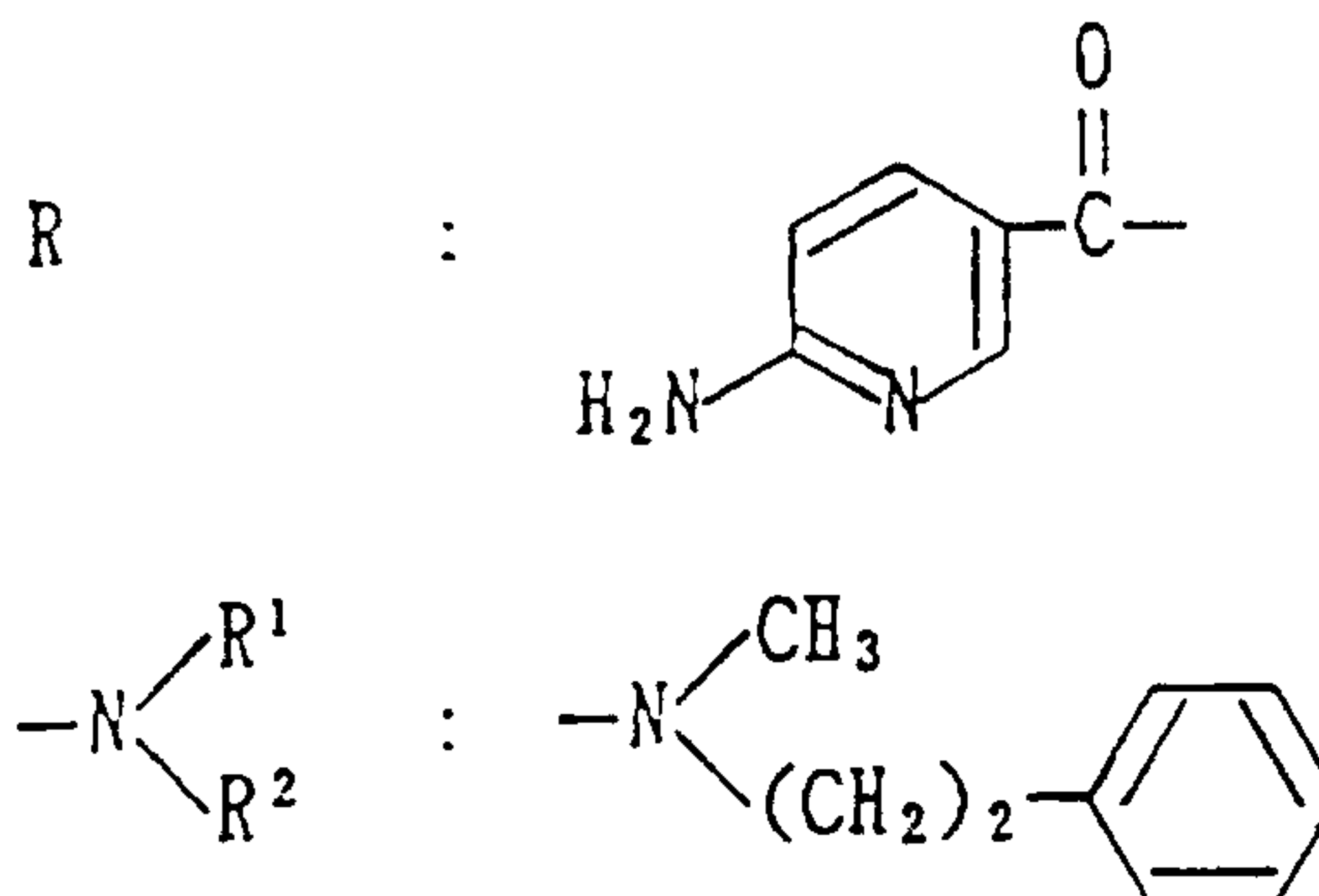
Melting point (°C): 158-159

Salt form: oxalate

{Table 10 (continued)}

Example 202

Structural formula:



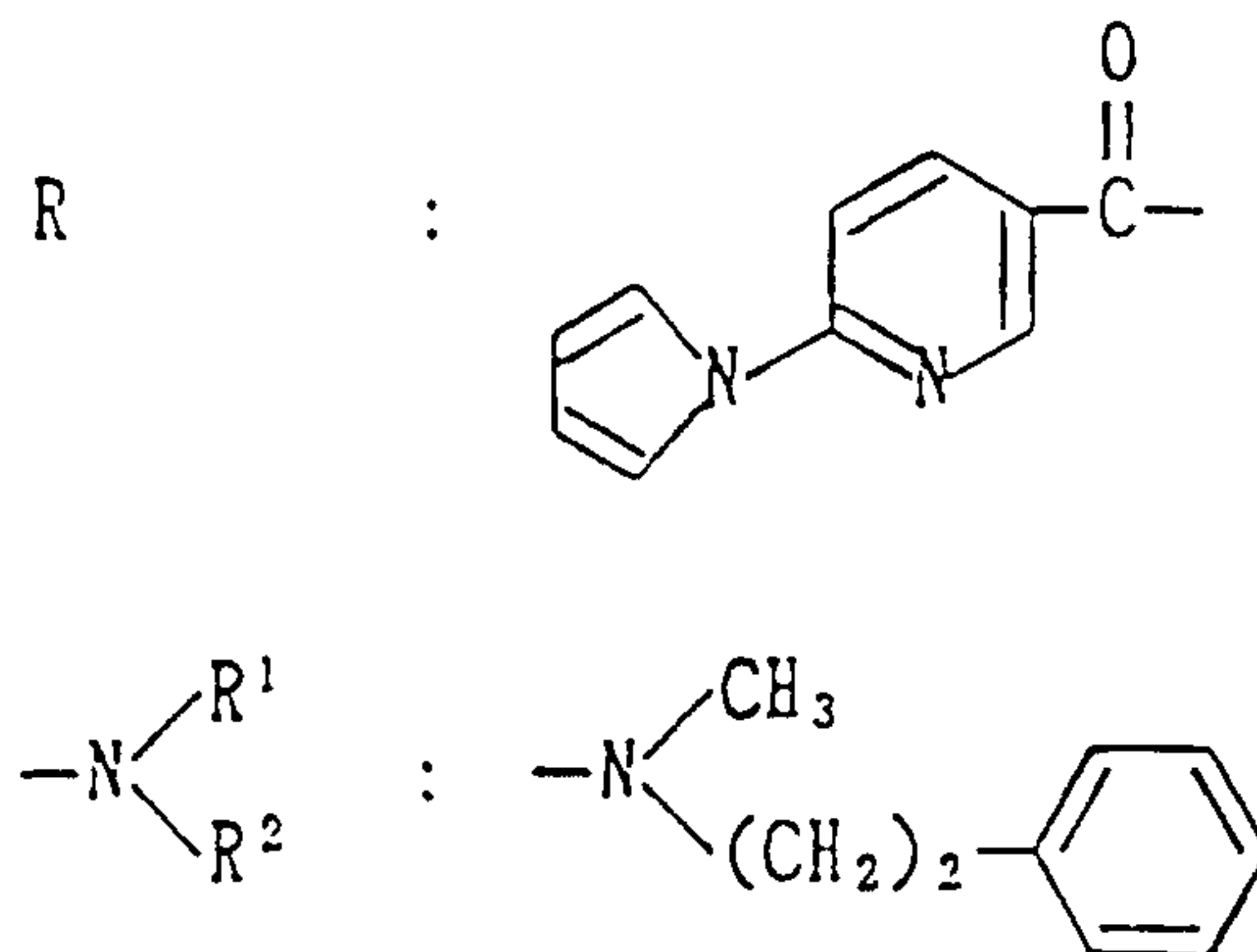
Crystal form: white amorphous

Salt form: dihydrochloride

NMR value: 126)

Example 203

Structural formula:



Crystal form: colorless scales

Recrystallization solvent: ethanol

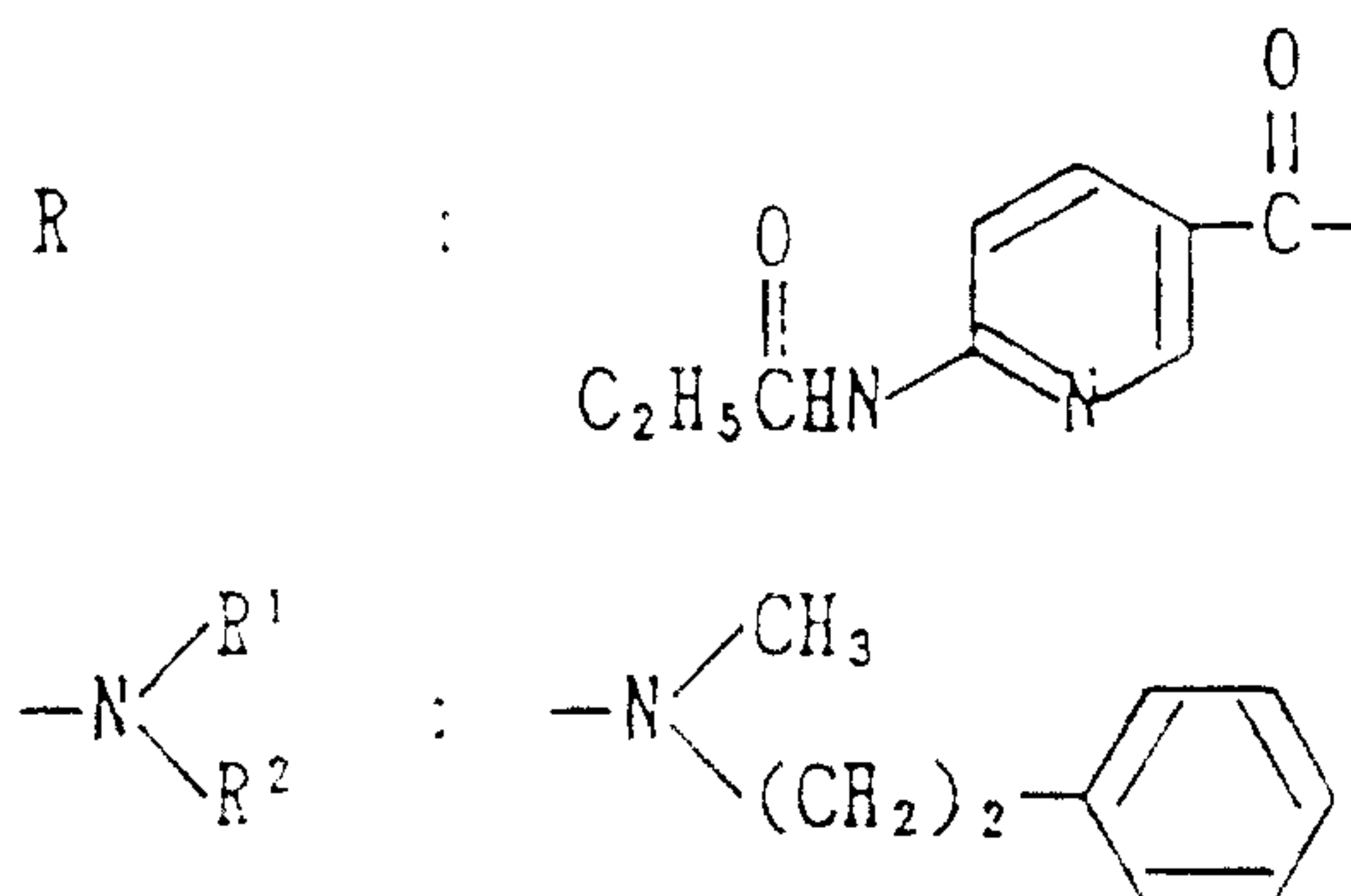
Melting point (°C): 115-116

Salt form: free

[Table 10 (continued)]

Example 204

Structural formula:



Crystal form: white powder

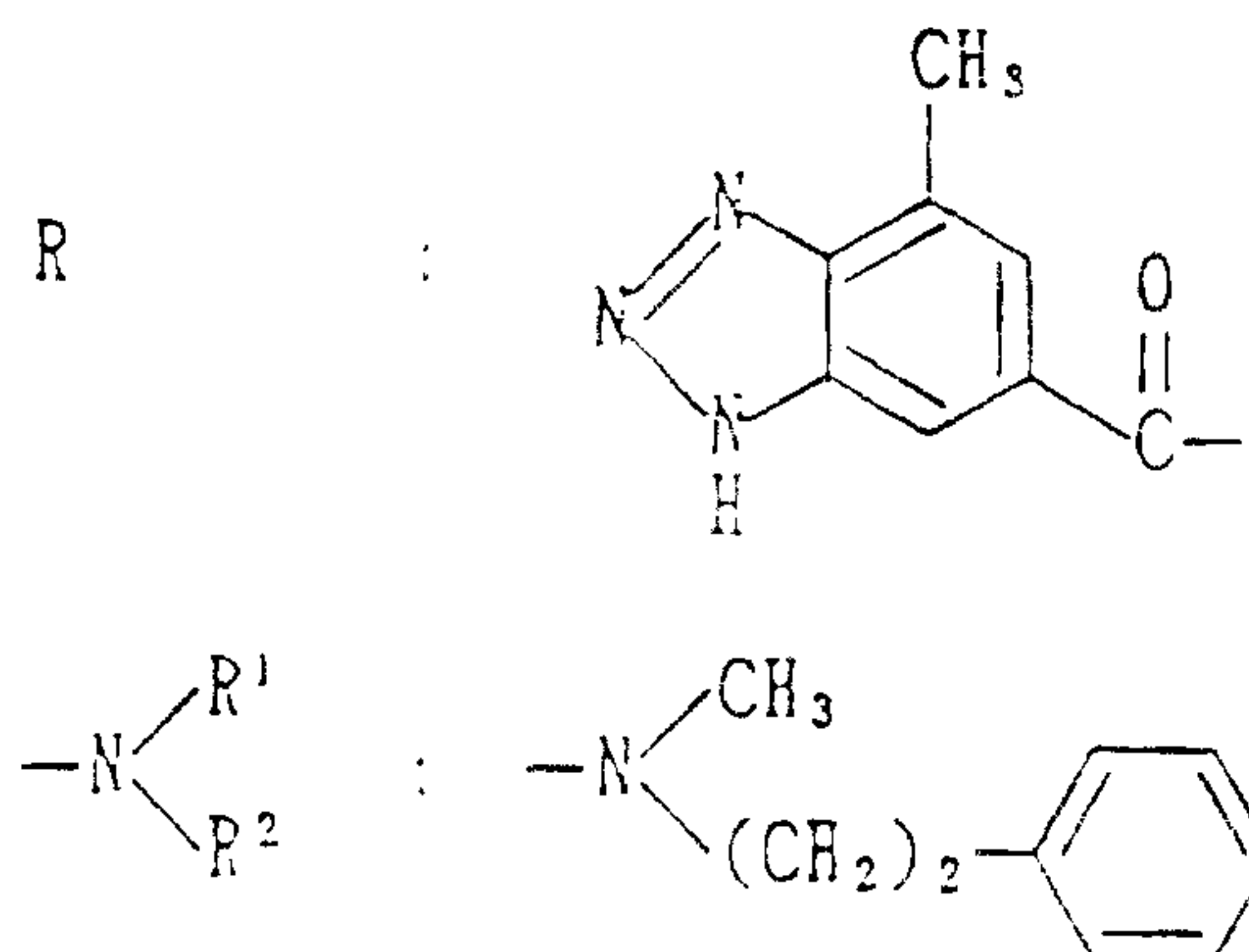
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 173-175

Salt form: hydrochloride

Example 205

Structural formula:



Crystal form: white amorphous

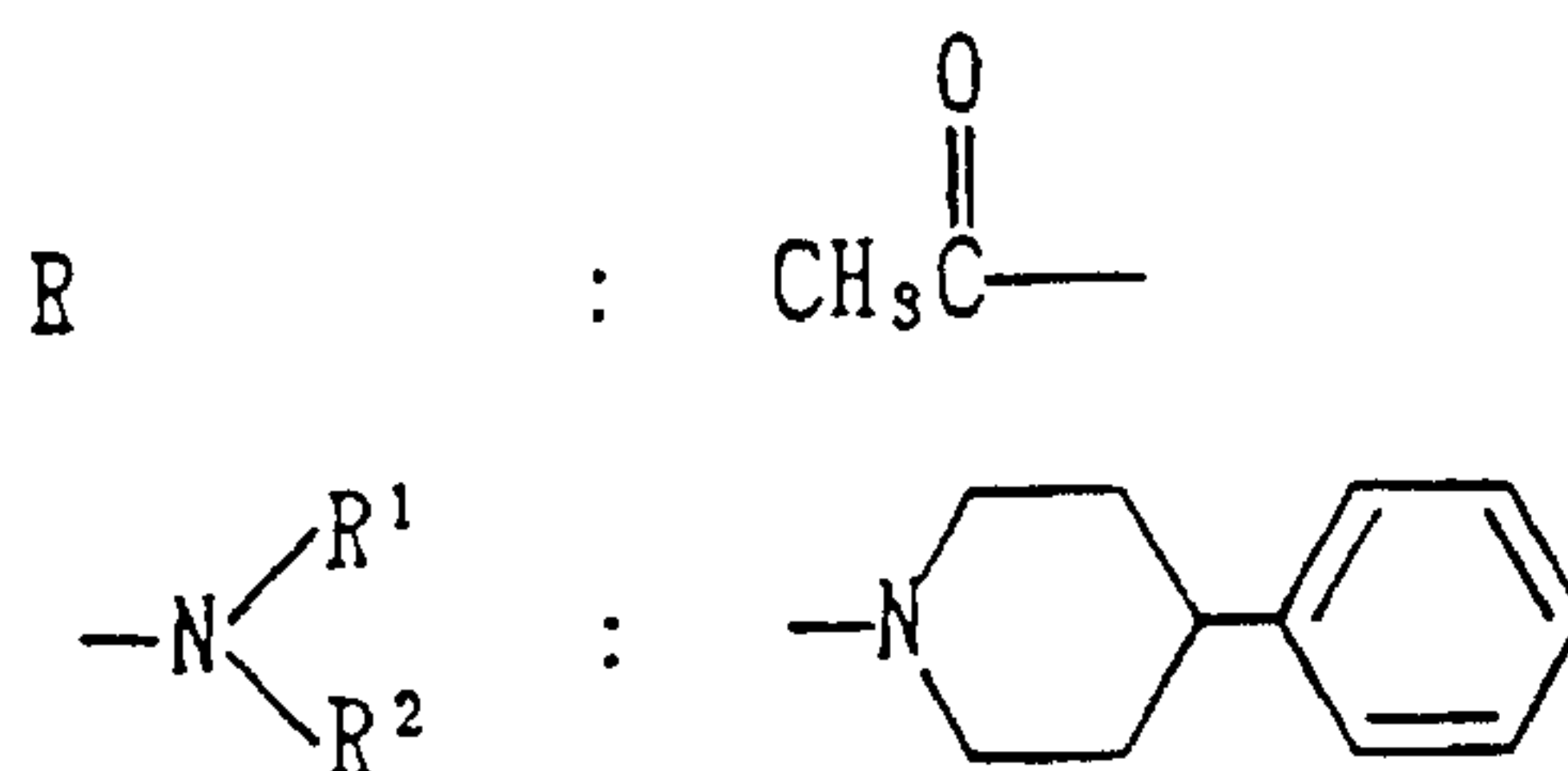
Salt form: hydrochloride

NMR value: 127)

[Table 10 (continued)]

Example 206

Structural formula:



Crystal form: white powder

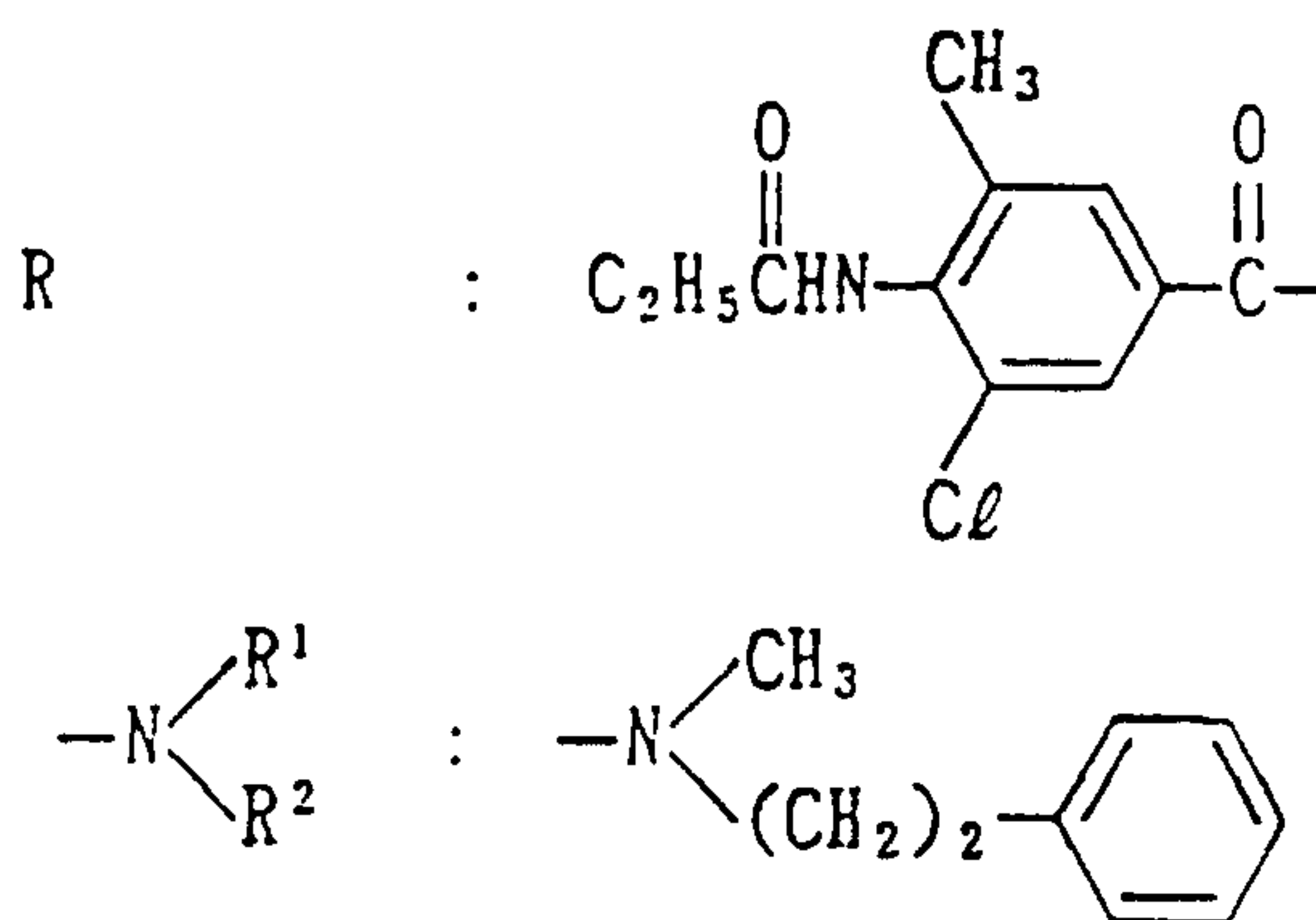
Recrystallization solvent: ethyl acetate-n-hexane

Melting point (°C): 104-105

Salt form: free

Example 207

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethanol-water

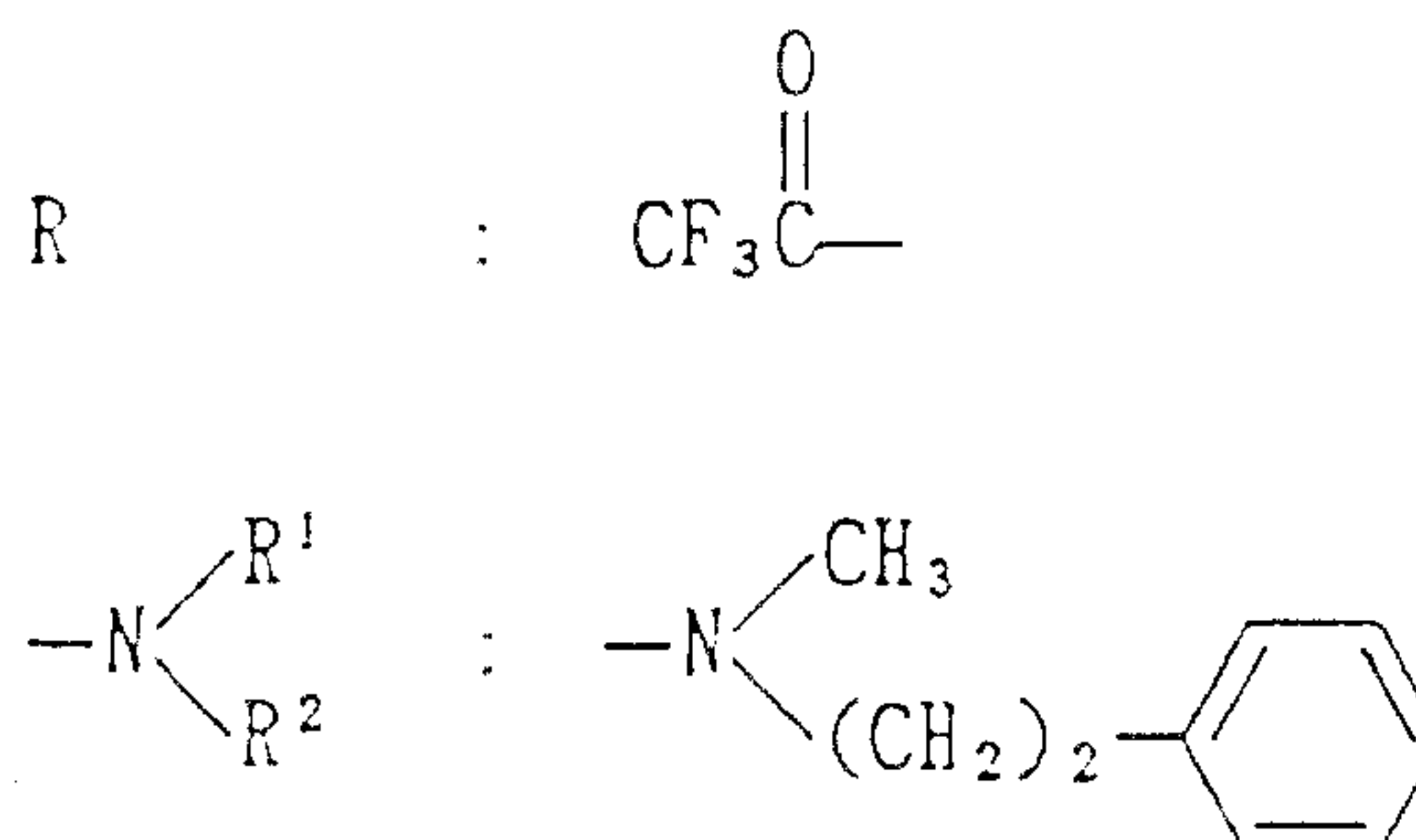
Melting point (°C): 243-246 (decompd.)

Salt form: hydrochloride

{Table 10 (continued)}

Example 208

Structural formula:



Crystal form: colorless prisms

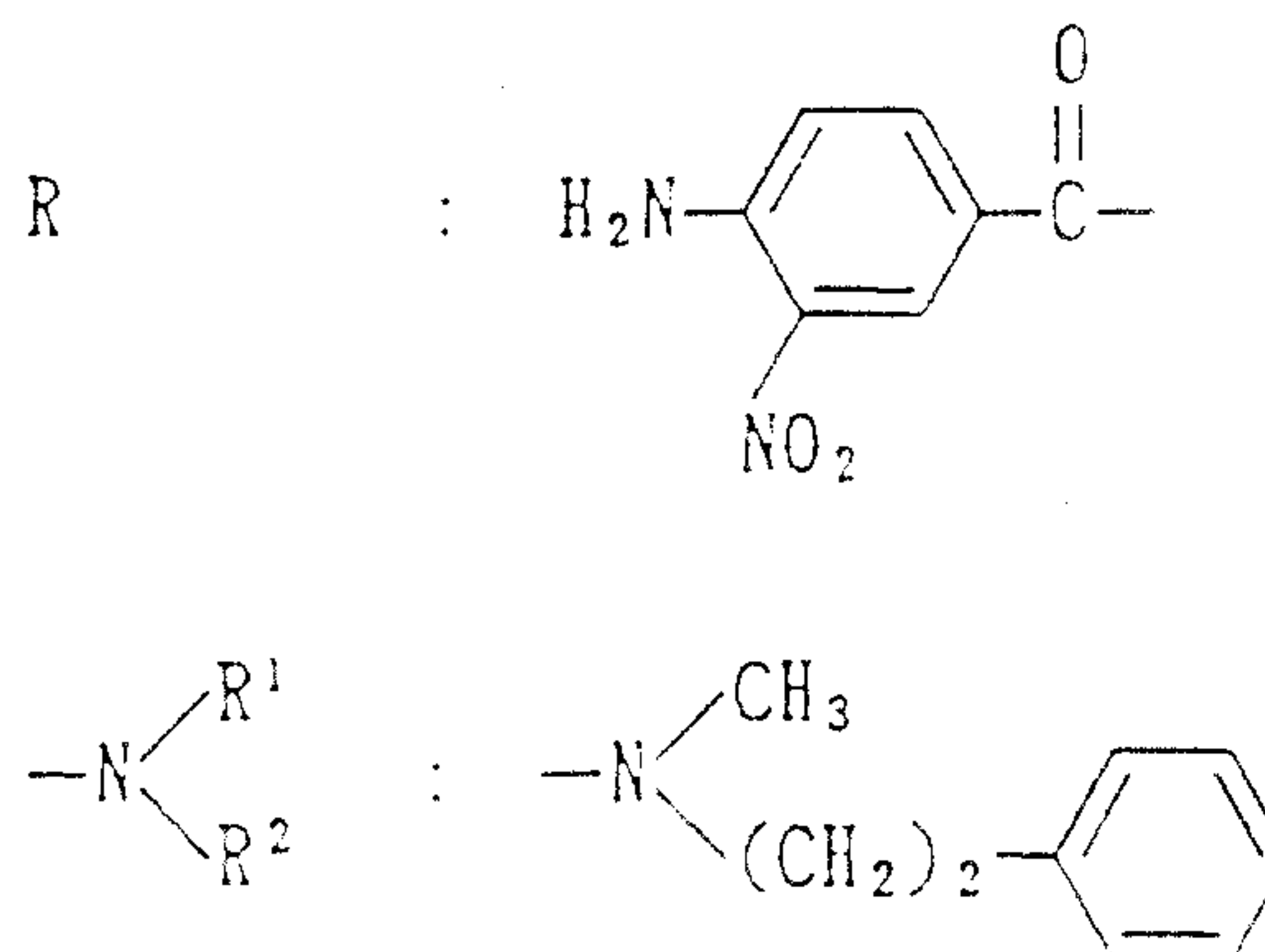
Recrystallization solvent: ethanol

Melting point (°C): 177-178

Salt form: hydrochloride

Example 209

Structural formula:



Crystal form: yellow amorphous

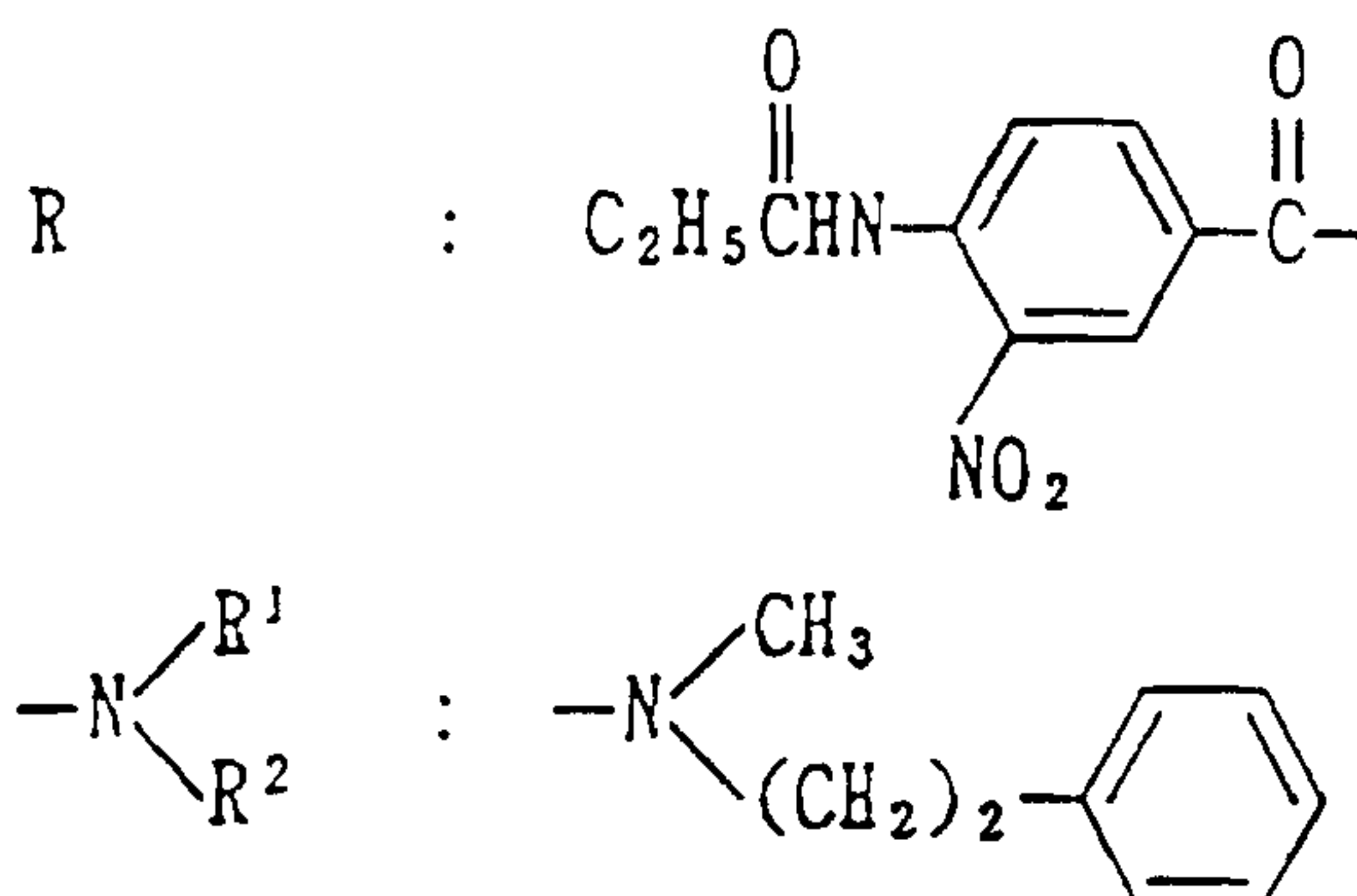
Salt form: hydrochloride

NMR value: 128)

{Table 10 (continued)}

Example 210

Structural formula:



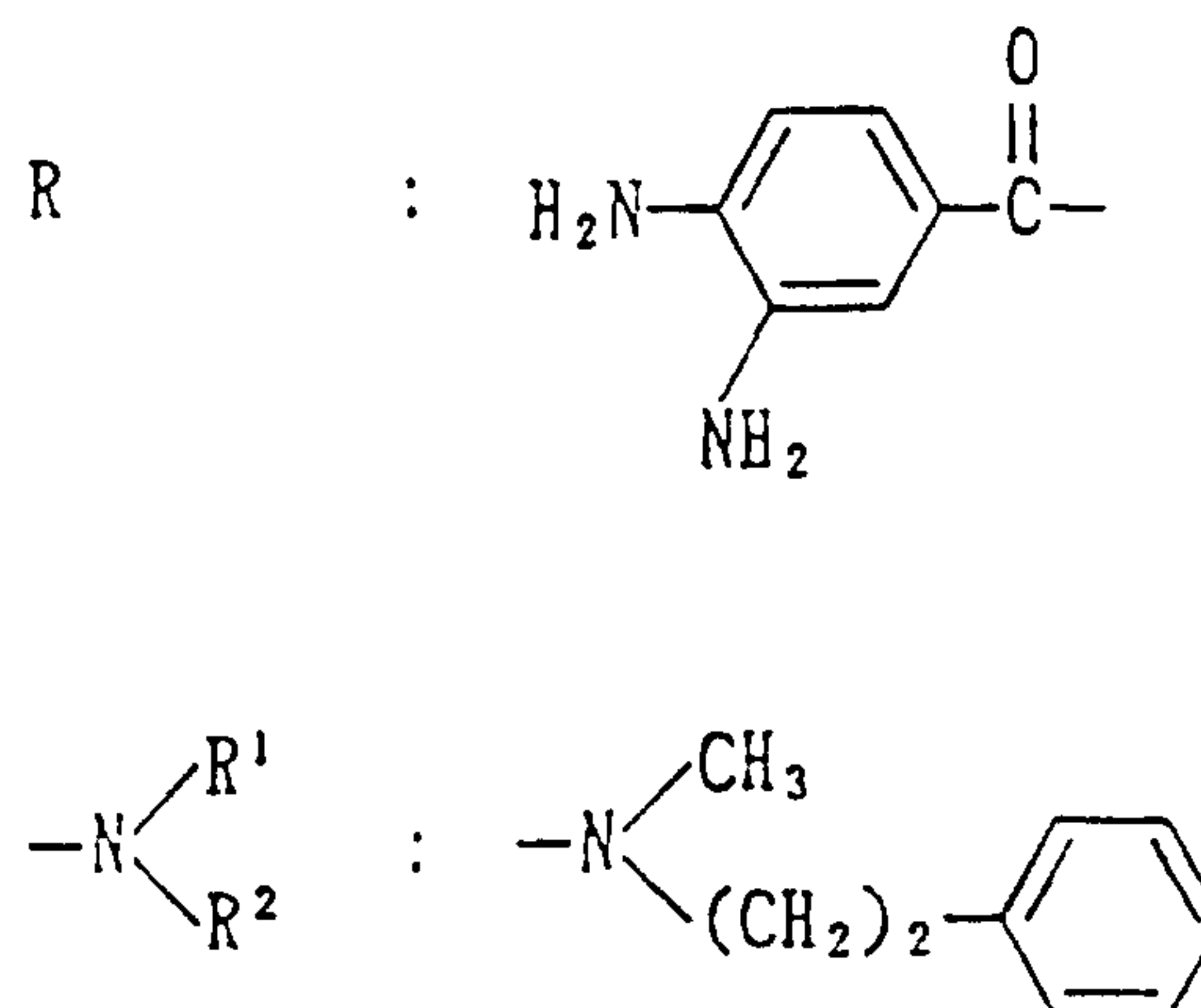
Crystal form: yellow amorphous

Salt form: hydrochloride

NMR value: 129)

Example 211

Structural formula:



Crystal form: white amorphous

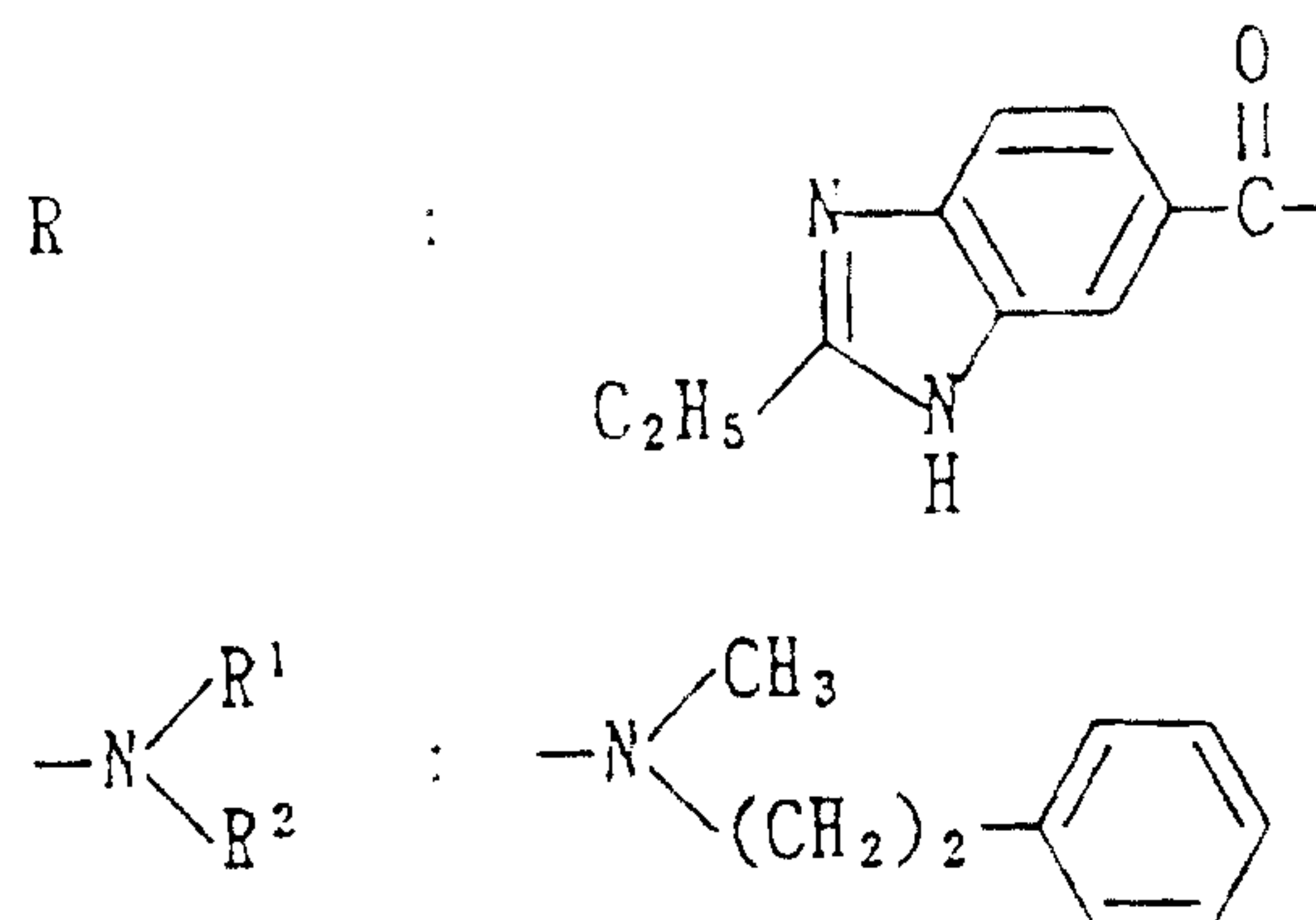
Salt form: dihydrochloride

NMR value: 130)

{Table 10 (continued)}

Example 212

Structural formula:



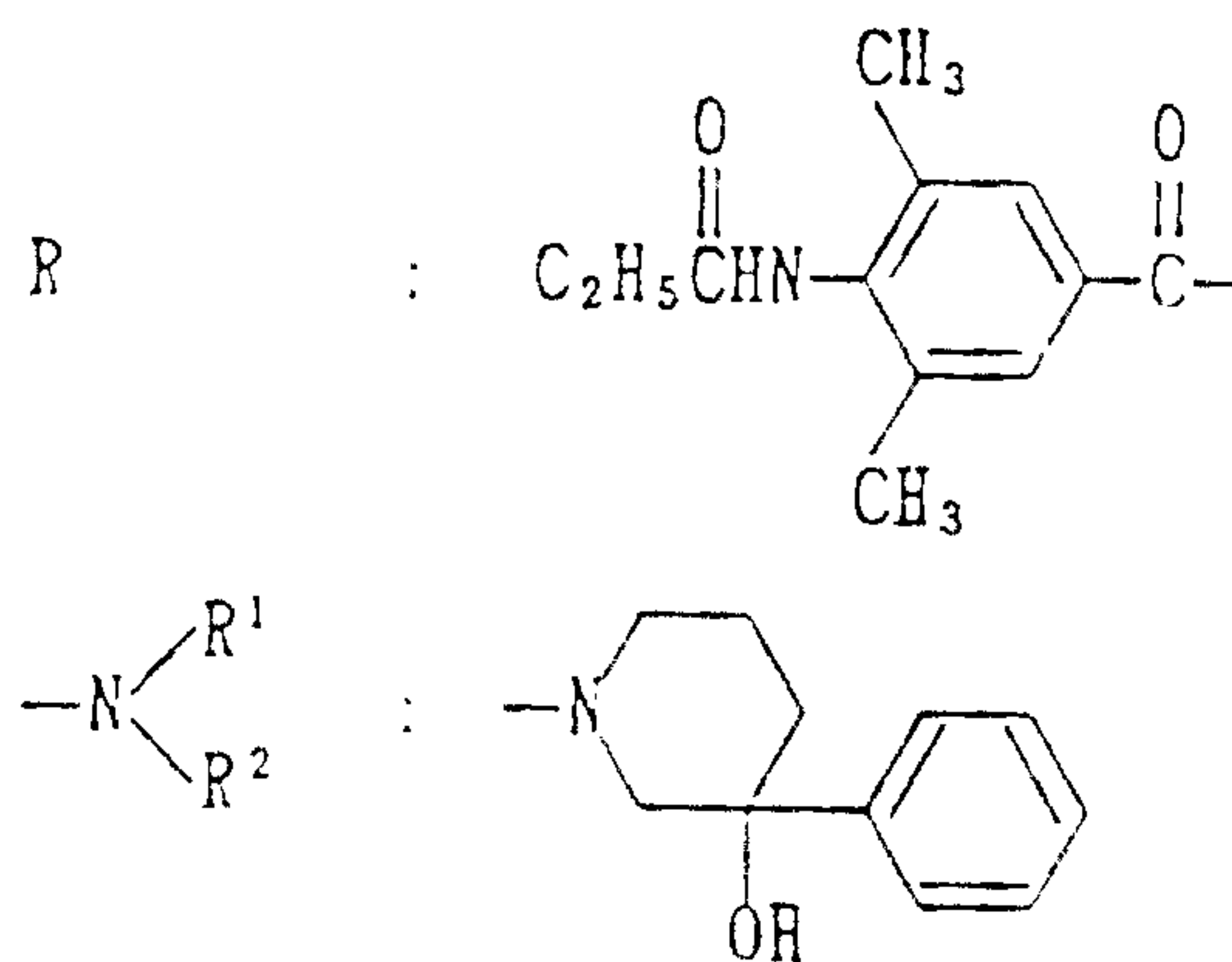
Crystal form: light yellow amorphous

Salt form: hydrochloride

NMR value: 131)

Example 213

Structural formula:



Crystal form: white powder

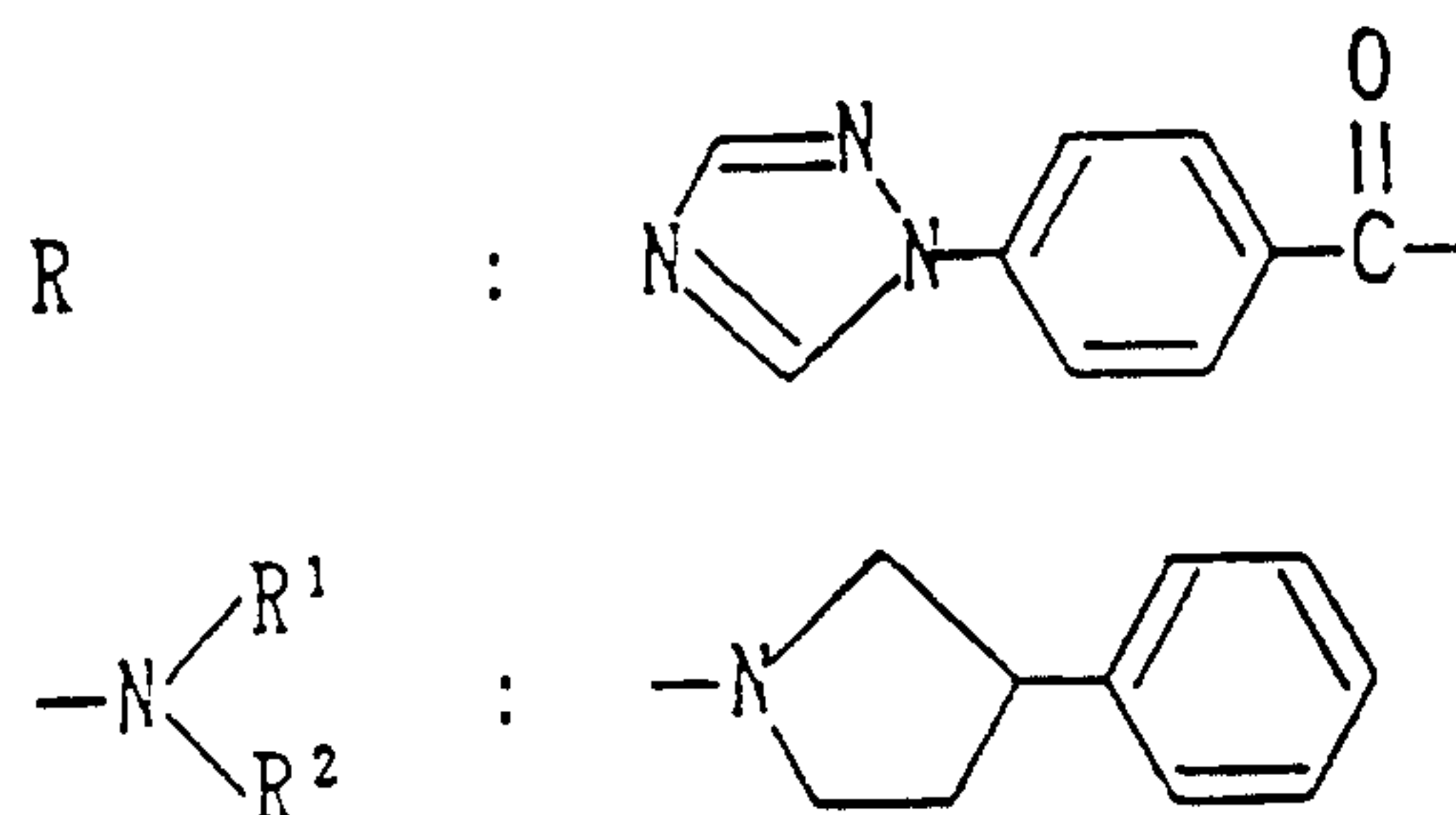
Melting point (°C): 243-245.5 (decompd.)

Salt form: hydrochloride

{Table 10 (continued)}

Example 214

Structural formula:



Crystal form: white powder

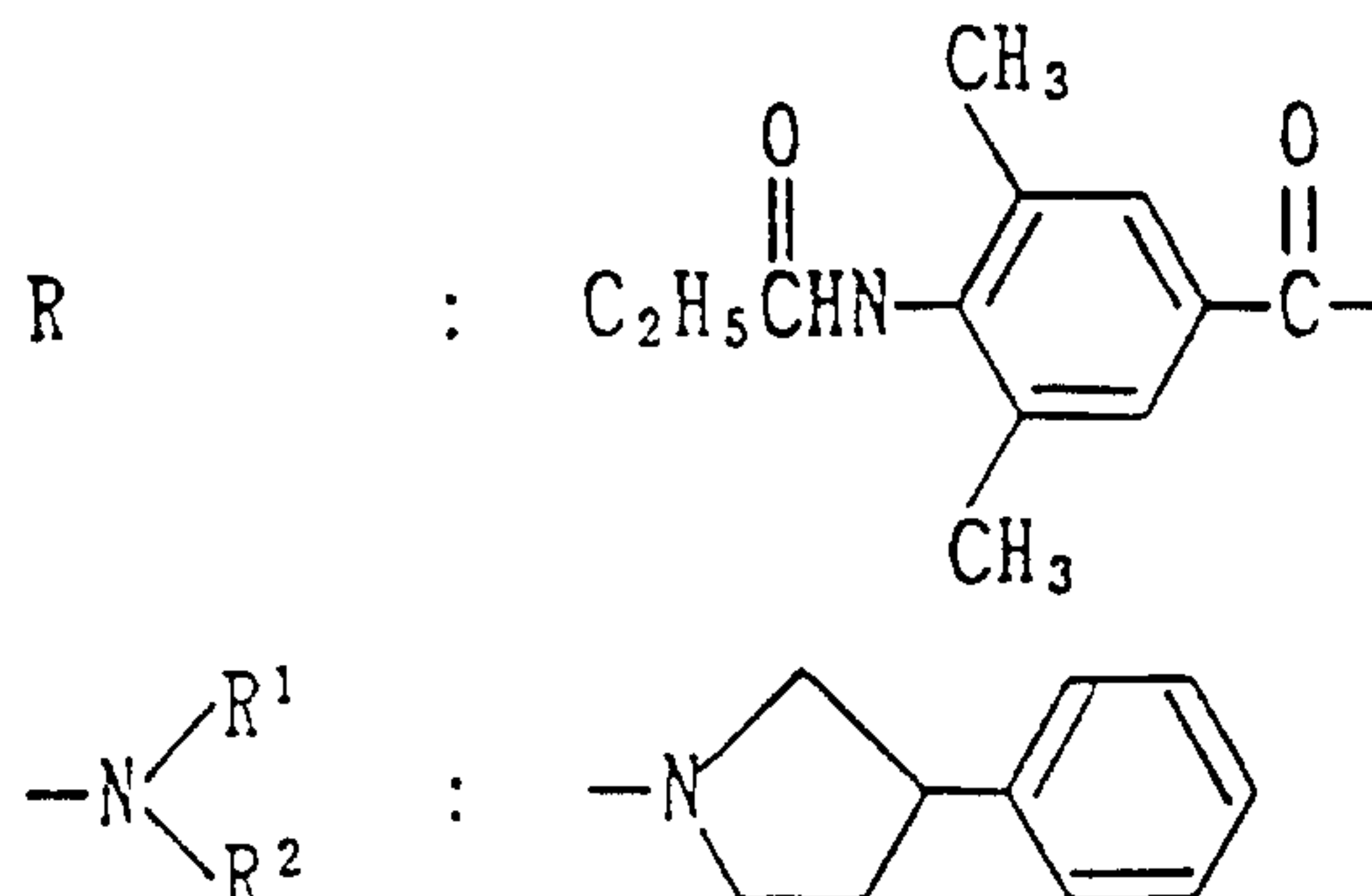
Recrystallization solvent: ethanol

Melting point (°C): 220-222

Salt form: hydrochloride

Example 215

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-ethanol

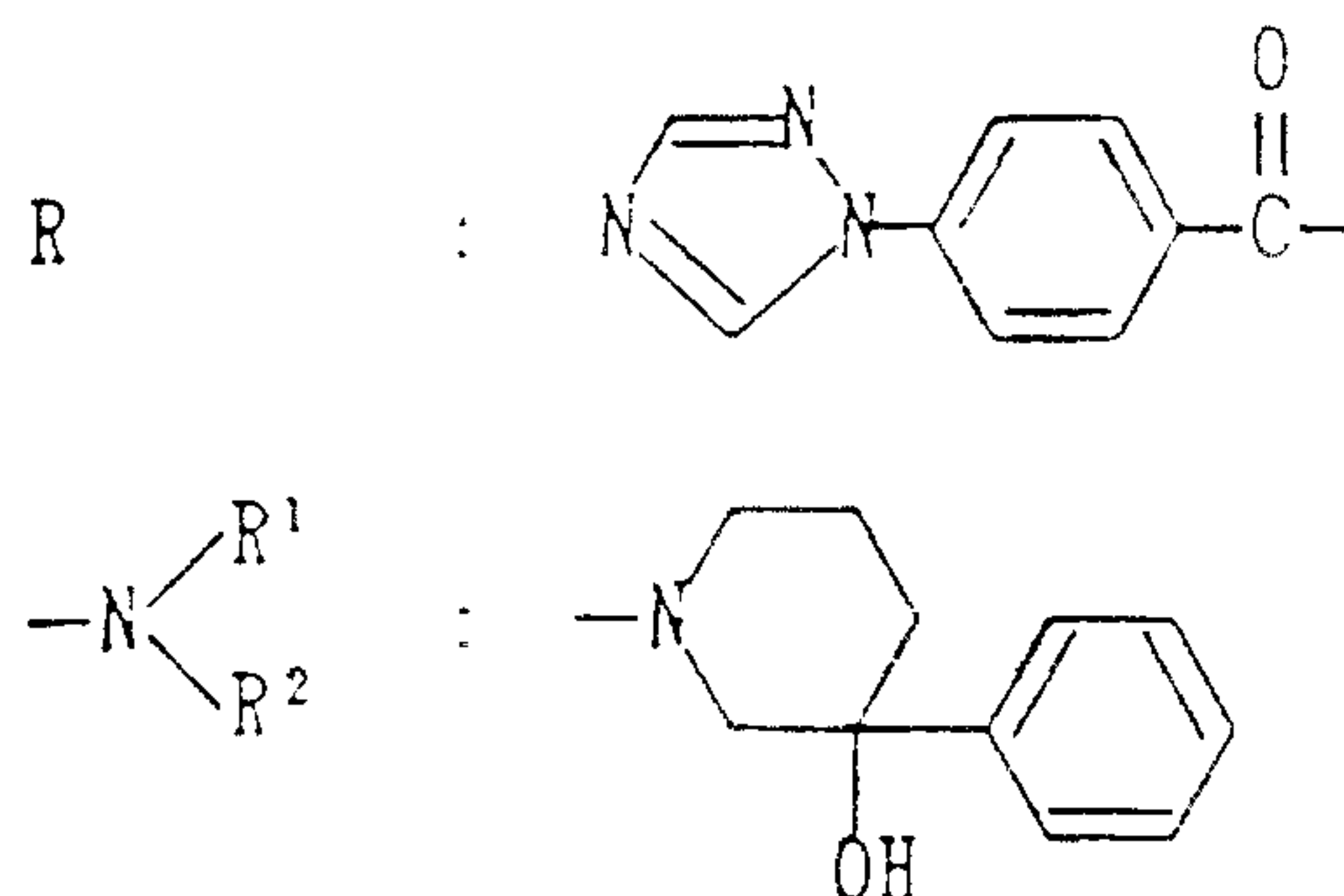
Melting point (°C): 244-246

Salt form: hydrochloride

{Table 10 (continued)}

Example 216

Structural formula:



Crystal form: white powder

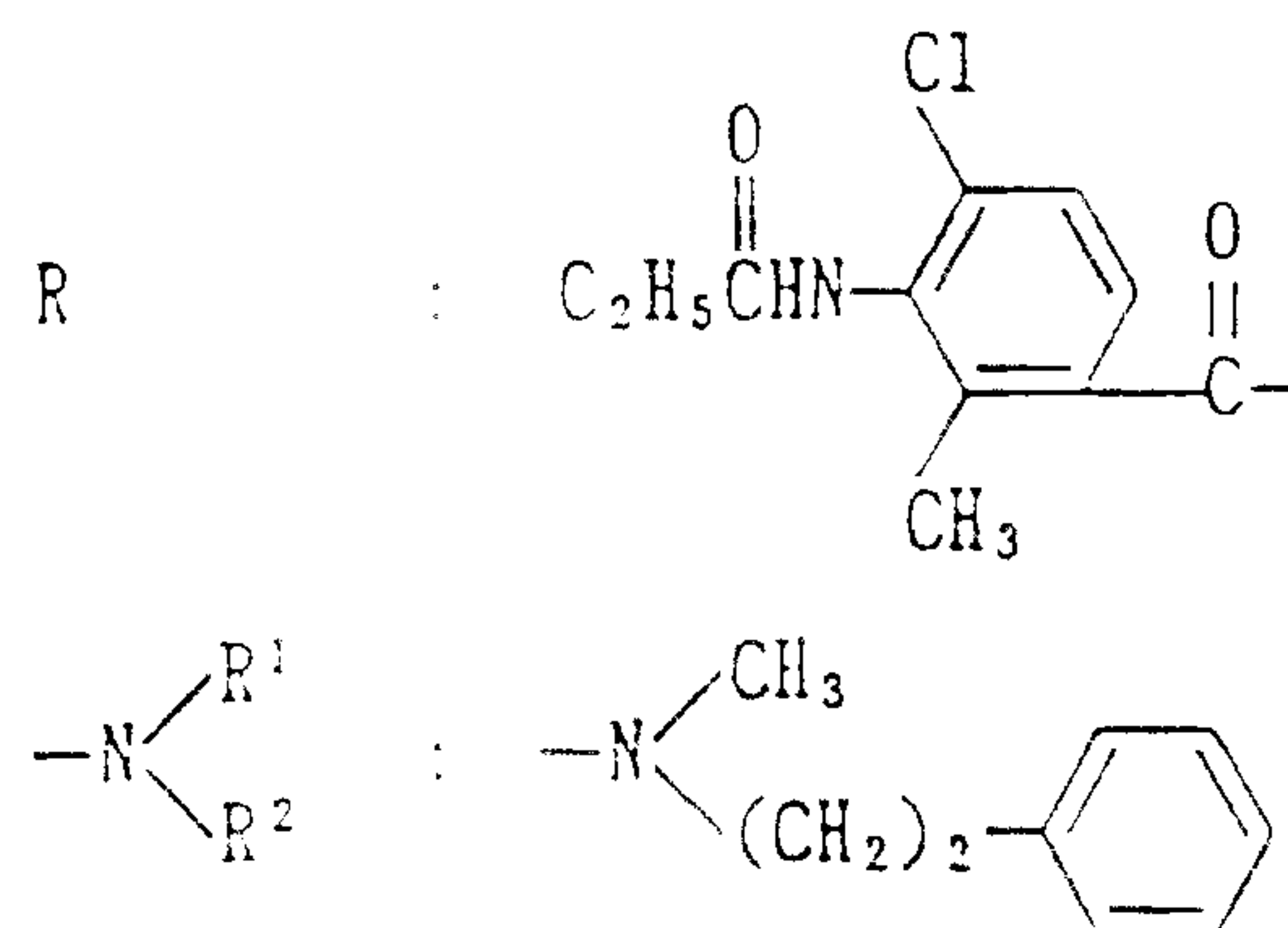
Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 237-239 (decompd.)

Salt form: hydrochloride

Example 217

Structural formula:



Crystal form: white powder

Recrystallization solvent: ethyl acetate-ethanol

Melting point (°C): 184.5-185

Salt form: hydrochloride

DEMANDES OU BREVETS VOLUMINEUX

**LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS
COMPREND PLUS D'UN TOME.**

CECI EST LE TOME __1__ DE __2__

NOTE: Pour les tomes additionels, veuillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

**THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE
THAN ONE VOLUME.**

THIS IS VOLUME __1__ OF __2__

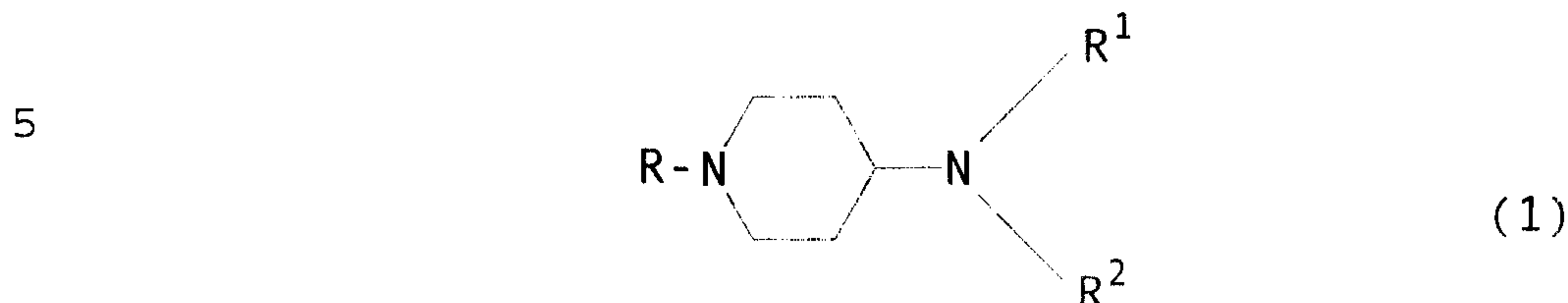
NOTE: For additional volumes please contact the Canadian Patent Office.

25711-737

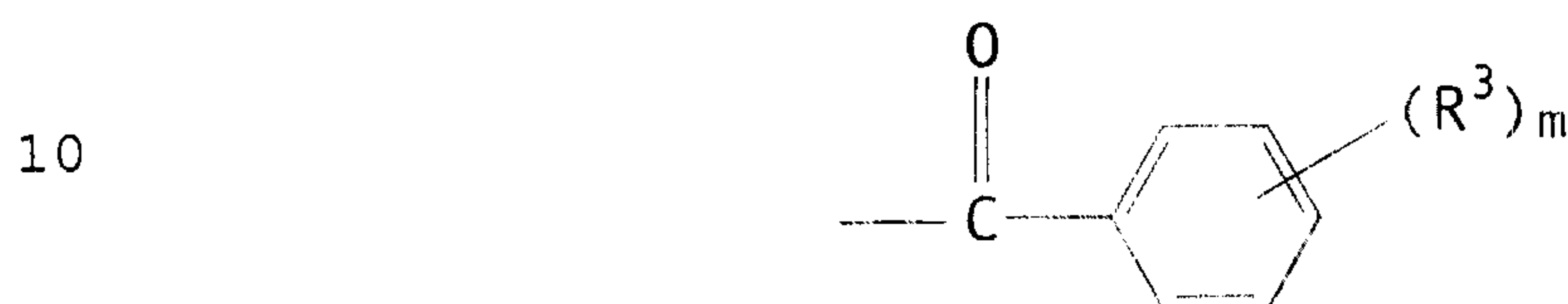
- 466 -

CLAIMS:

1. A piperidine derivative or salt thereof represented by the general formula (1):



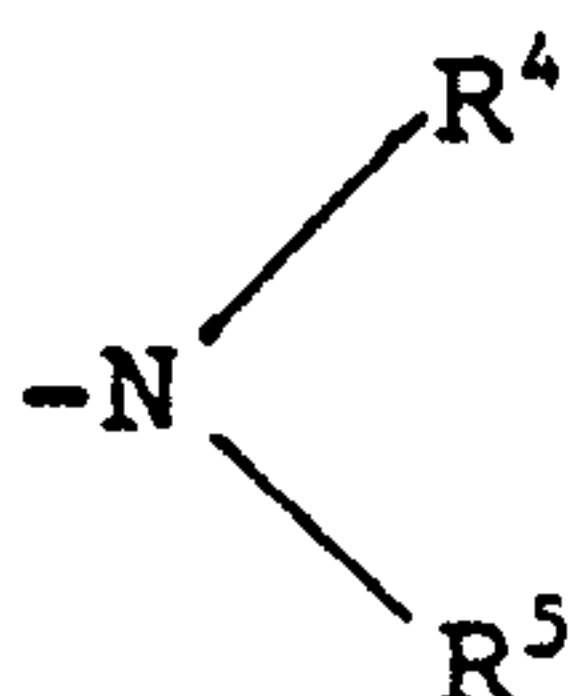
wherein, R is a group of the formula:



(wherein, m is an integer of 1 to 3;

R^3 is a nitro group; a lower alkyl group; a halogen atom; a cyano group; a lower alkanoyl group; an
 15 aminocarbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group and a phenyl group; a lower alkoxycarbonyl group; a carboxy group, a lower alkoxy group; a hydroxyl group; a hydroxyamino group; a lower alkylthio-lower alkyl group; a
 20 lower alkylsulfonyl-lower alkyl group; a hydroxyl group substituted-lower alkyl group; a lower alkenyl group; a lower alkoxy-carbonyl group substituted-lower alkenyl group; a phenyl group which may have substituent(s), on the phenyl ring, selected from the group consisting of a hydroxyl
 25 group, a phenyl-lower alkoxy group, a lower alkanoyloxy group, a nitro

group, an amino group which may have lower alkanoyl group(s) as substituent(s), a lower alkyl group and a lower alkoxy group; an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s); a morpholinyl group substituted-lower alkoxy group; 1,2,4-triazolyl group which may have oxo group(s) as substituent(s) on the 1,2,4-triazole ring; a 1,2,3,4-tetrazolyl group; an imidazolyl group which may have 1 to 2 substituent(s) selected from the group consisting of a phenyl group and a lower alkyl group on the imidazole ring; a pyrazolyl group which may have lower alkyl group(s) as substituent(s) on the pyrazole ring; a pyridyl group; a pyrrolyl group; a pyrrolidinyl group which may have oxo group(s) as substituent(s) on the pyrrolidine ring; a piperidinyl group which may have oxo group(s) as substituent(s) on the piperidine ring; a benzimidazolyl group; an imidazolidinyl group which may have oxo group(s) as substituent(s) on the imidazolidine ring; a 2-oxazolinyl group; a 1,2,4-triazolyl-lower alkyl group; a phenoxy group; a phenyl-lower alkoxy group; a lower alkanoyloxy group; a phenyl-lower alkoxycarbonyl group; an amino-lower alkyl group which may have, substituent(s) selected from the group consisting of a lower alkyl group and a lower alkanoyl group; a group of the formula:



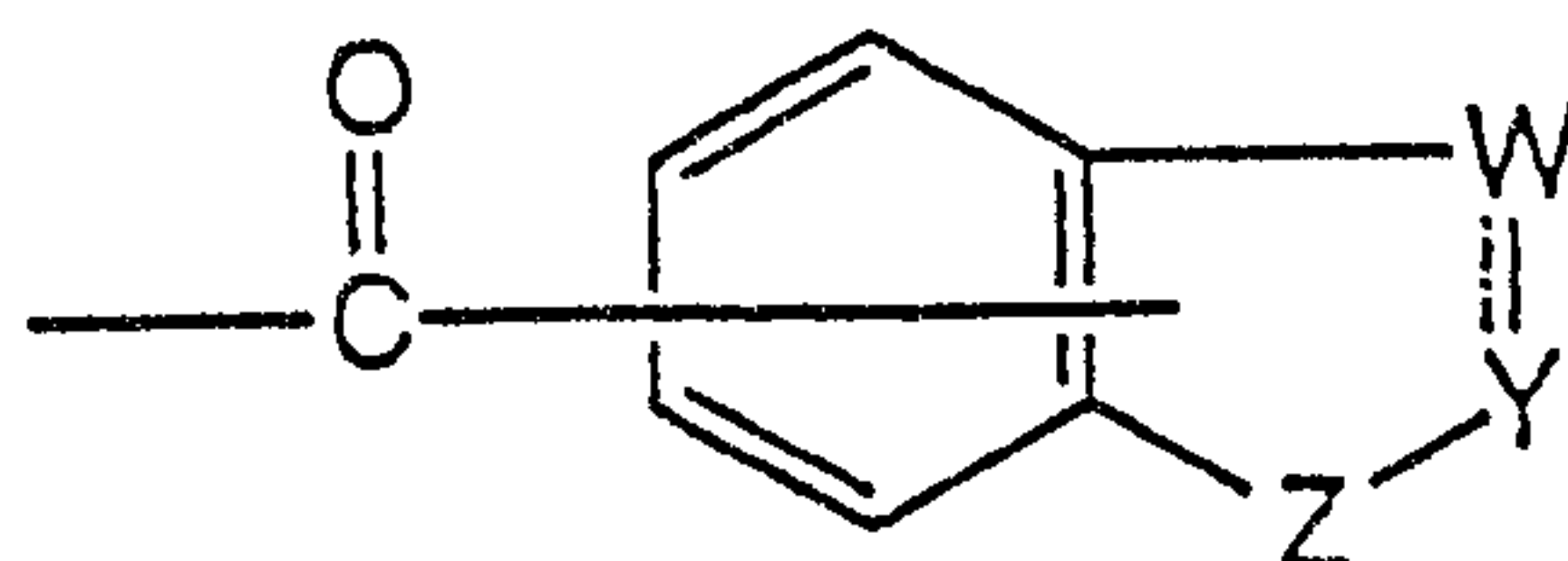
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(wherein, R^4 and R^5 are each the same or different, and are each a hydrogen atom, a lower alkyl group, a lower alkanoyl group, a lower alkanoyl group having 1 to 3 halogen atoms, a benzoyl group, a pyridylcarbonyl group, a lower alkenyl-carbonyl group, an anilinothiocarbonyl group, an aminothio-carbonyl group which may have lower alkyl group(s) as substituent(s) or an aminocarbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group, a phenyl group and a lower alkenyl group)); or

R is a lower alkanoyl group having as substituent(s), hydroxyl group(s) or amino group(s) which may have lower alkyl group(s) as substituent(s); a pyridylcarbonyl group which may have as substituent(s), on the pyridine ring, selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxycarbonyl group, a hydroxyl group substituted-lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkanoyl group; a furoyl group which has substituents, on the furan ring, selected from the group consisting of a nitro group, a hydroxyl group substituted-lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl

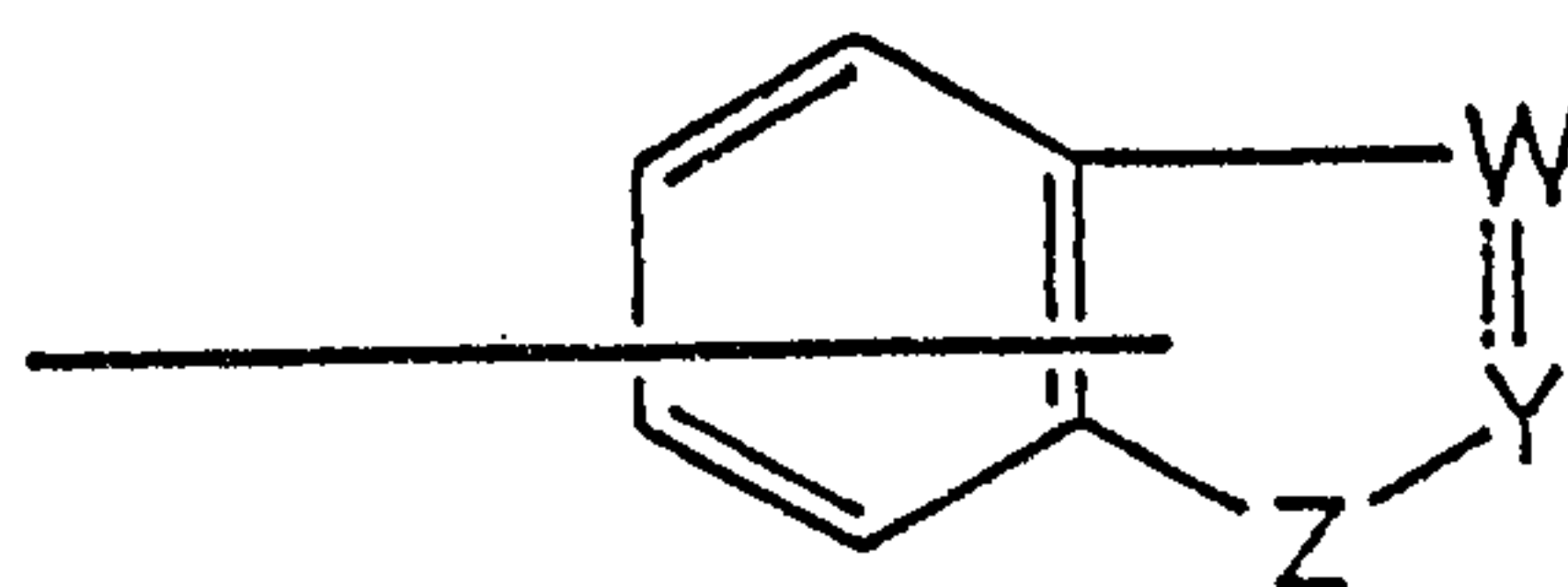
group(s) as substituent(s); a thienylcarbonyl group which may have substituent(s), on the thiophene ring, selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); a fluorenylcarbonyl group which may have substituent(s), on the fluorene ring, selected from the group consisting of an oxo group and a nitro group; or a group of the formula:



(wherein, Z is a group of the formula: $-\text{CH}_2-$ or $-\text{NH}-$ or a sulfur atom; Y and W are each a group of the formula: $=\text{CH}-$ or a nitrogen atom; and the dotted line in the bonding of the formula: ---W is a single bond or double



bond; and the group of the formula:



may have 1 to 4 substituents selected from the group consisting of an oxo group, a lower alkyl group, a lower alkoxy group, a hydroxyl group, a lower alkylthio group, a halogen atom, a nitro group and an amino group);

R^1 is a hydrogen atom or a lower alkyl group

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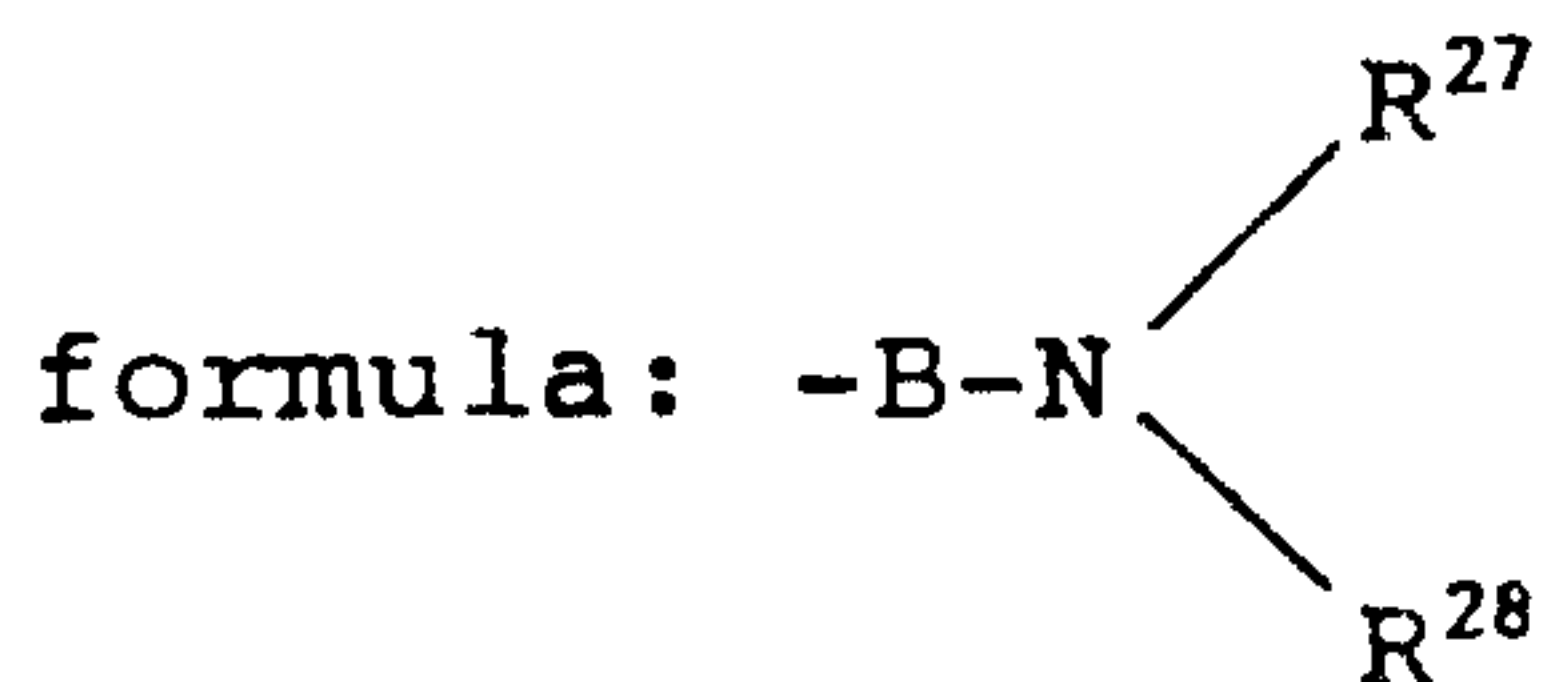
which may have hydroxyl group as substituents; and

R^2 is a phenyl-lower alkyl group which may have as substituents, on the phenyl ring, selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxy-carbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy group substituted-lower alkoxy group and an amino group which may have as substituent(s) selected from the group consisting of a lower alkanoyl group, a lower alkoxy-carbonyl group, and aminocarbonyl group which may have lower alkyl group(s) as substituent(s), where the

afore-mentioned phenyl-lower alkyl group may further have a lower alkoxy-carbonyl group or a hydroxyl group substituted-lower alkyl group as a substituent in the lower alkyl moiety; a phenoxy-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), and a hydroxyl group; a pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring; a thienyl-lower alkyl group; a furyl-lower alkyl group; a group of the

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(wherein B is a lower alkylene group and R^{27} and R^{28} are the same or different and are each a hydrogen atom, a lower alkyl group, a phenyl group, a lower alkanoyl group or a benzoyl group);

a phthalimide substituted-lower alkyl group; a cycloalkyl-lower alkyl group; a phenyl-lower alkenyl group; a cycloalkyl group having phenyl group(s) as substituent(s); or a 2,3-dihydro-1H-indenyl group which may have substituent(s)

selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s) as substituent(s); or

R^1 and R^2 and the adjacent nitrogen atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or a 1,2,3,4-tetrahydroisoquinoline ring, each having substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy group and a phenyl group;

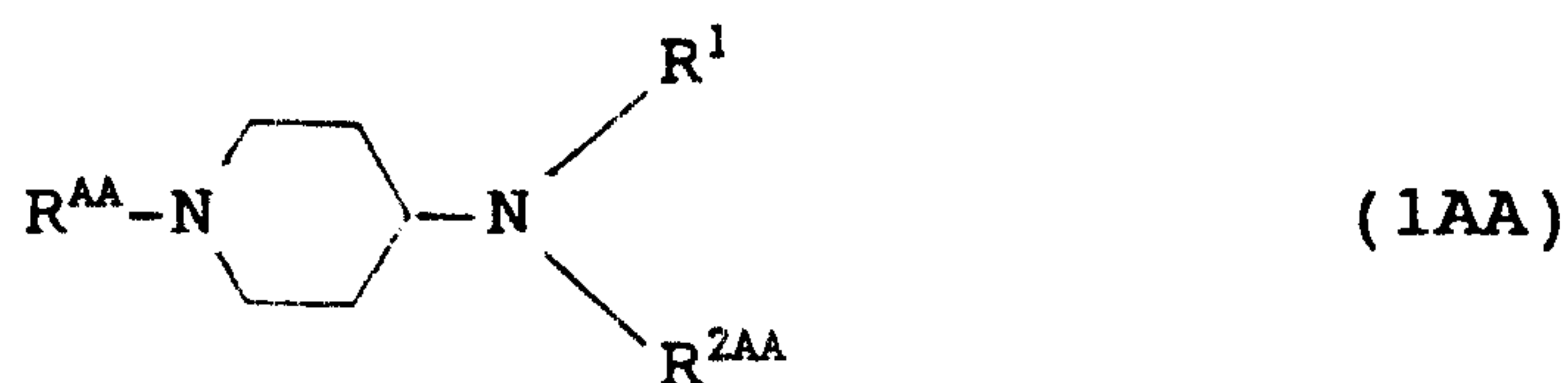
provided that (a) when $\underline{m}$ is 1, then R^3 is not an amino group; and (b) when $\underline{m}$ is 2 and one of R^3 is an amino group, then the other one of R^3 is not a halogen atom, a lower alkyl group, a lower alkoxy group, a hydroxyl group, a nitro group, an amino group,

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mono- or di-lower alkyl substituted-amino group.

2. A piperidine derivative or salt thereof represented by the general formula (1AA):



wherein, R^{AA} is a benzoyl group or a lower alkanoyl group;

R^1 is the same as defined in Claim 1; and

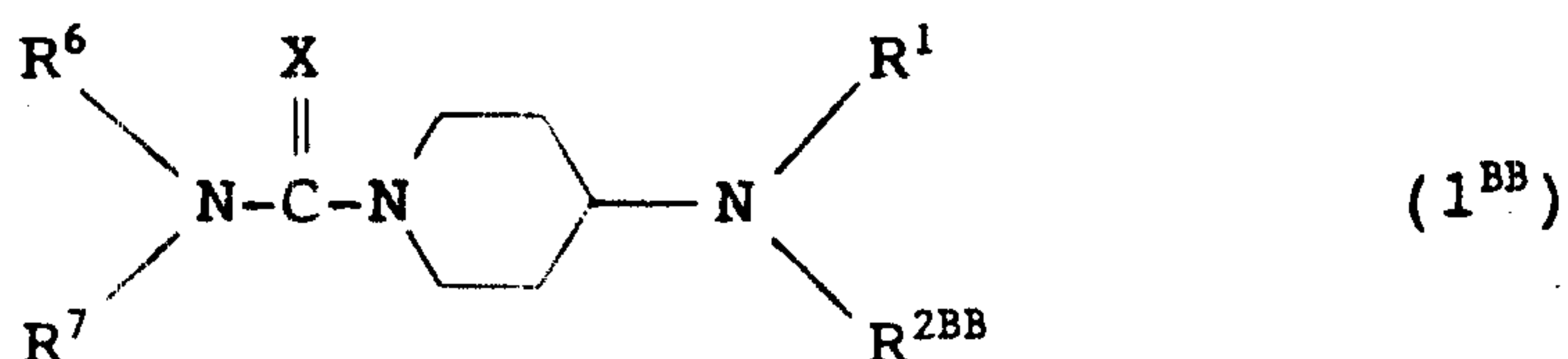
R^{2AA} is a thienyl-lower alkyl group, a phenyl-lower alkyl group having a lower alkylthio group as substituents in the phenyl ring, or a 2,3-dihydro-1H-indenyl group which may have a substituent selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s) as substituent(s); or

R^1 and R^{2AA} and the adjacent nitrogen atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or 1,2,3,4-tetrahydroisoquinoline ring, each having substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy group and a phenyl group.

3. A piperidine derivative or salt thereof represented by the general formula (1^{BB}):

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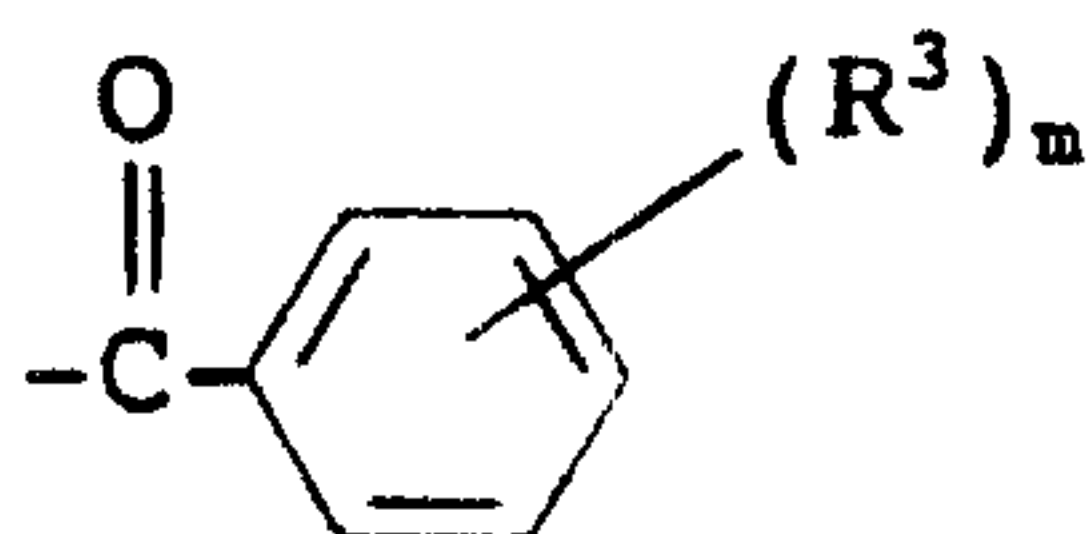
wherein, X is an oxygen atom or a sulfur atom;

R⁶ and R⁷ are each the same or different, and are each a hydrogen atom, a lower alkyl group or a phenyl group which may have as substituents, in the phenyl ring, selected from the group consisting of a lower alkoxy group, a halogen atom and a nitro group;

R¹ is as defined in claim 1; and

R^{2BB} is a phenyl-C₁-C₂ alkyl group.

4. The piperidine derivative or salt thereof according to claim 1, wherein R is a group of the formula:



wherein R³ and m are as defined in claim 1.

5. The piperidine derivative or salt thereof according to claim 1, wherein R is a lower alkanoyl group having, as substituent(s), hydroxyl group(s) or amino group(s) which may have lower alkyl group(s) as substituent(s); or 1,2,4-triazolyl-lower alkanoyl group.

6. The piperidine derivative or salt thereof according to claim 1, wherein R is a pyridylcarbonyl

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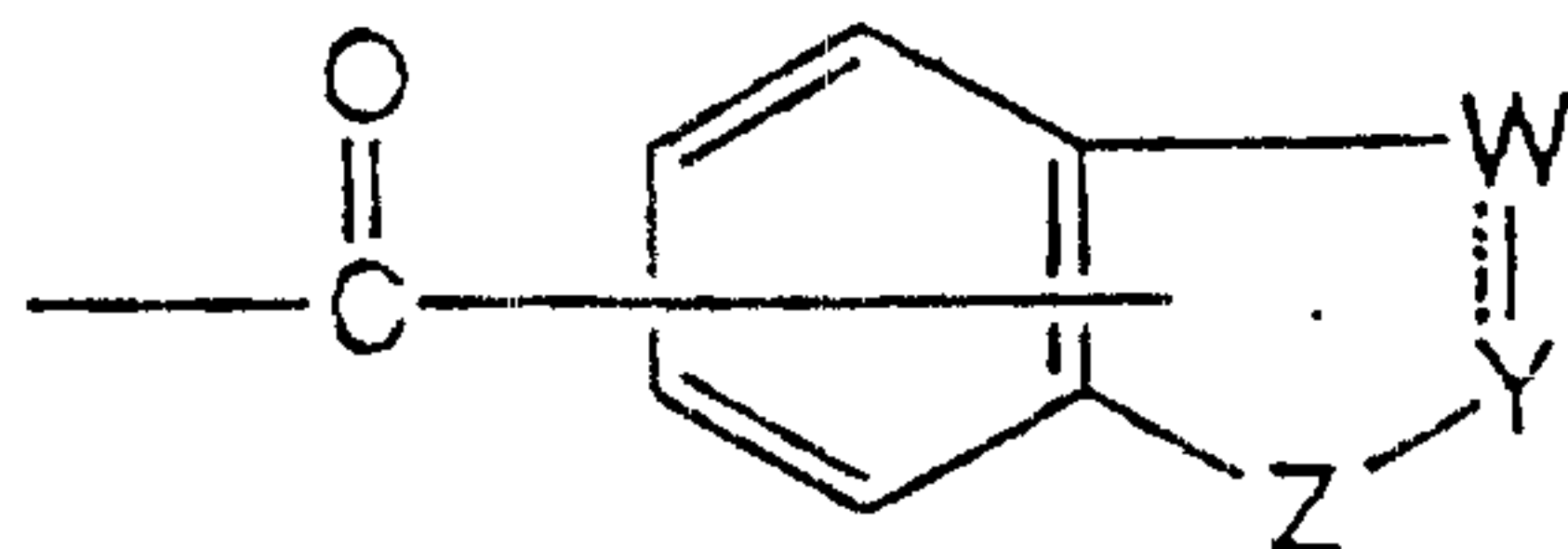
group in which the pyridine ring may have at least one substituent selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxycarbonyl group, a hydroxyl group(s)-substituted lower alkyl group, a phenyl group and a 1,2,4-triazolyl group.

7. The piperidine derivative or salt thereof according to claim 1, wherein R is a furoyl group having substituent(s), on the furan ring, selected from the group consisting of a nitro group, a hydroxyl group(s)-substituted lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a thienylcarbonyl group which may have substituent(s), on the thiophene ring, selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); or a fluorenyl-carbonyl group which may have substituent(s), on the fluorene ring, selected from the group consisting of an oxo group and a nitro group.

8. The piperidine derivative or salt thereof according to claim 1, wherein R is a group of the formula:

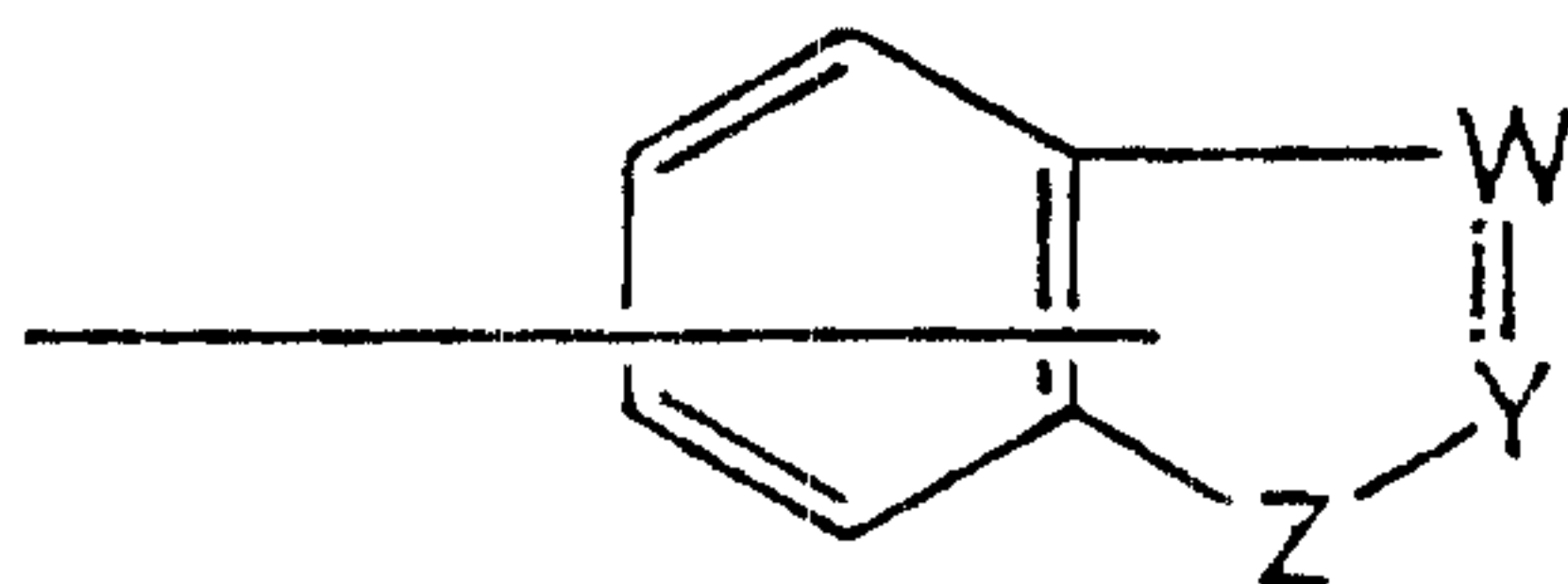
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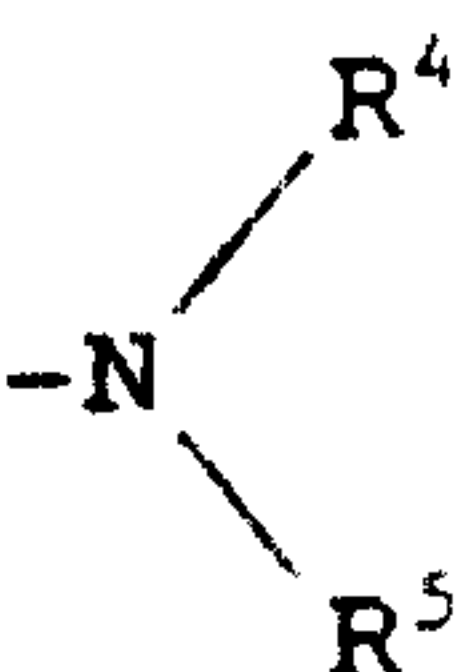
wherein W, Y, Z and the dotted line in the bonding of the formula:  and the substituent(s) on the group

of the formula:



are the same as defined in claim 1.

9. The piperidine derivative or salt thereof according to Claim 4, wherein R^3 is a lower alkyl group, an amino-carbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group and a phenyl group, a phenyl group which may have substituent(s), on the phenyl ring, selected from the group consisting of a hydroxyl group, a phenyl-lower alkoxy group, a lower alkanoyloxy group, a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a lower alkyl group and a lower alkoxy group, 1,2,4-triazolyl group which may have oxo group(s) as substituent(s) on the 1,2,4-triazole ring;

or a group of the formula: 

(wherein R^4 and R^5 are the same as defined in claim 1).

10. The piperidine derivative or salt thereof according to Claim 4, wherein R^1 is a hydrogen atom.
11. The piperidine derivative or salt thereof according to Claim 4, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).
12. The piperidine derivative or salt thereof according to Claim 5, wherein R^1 is a hydrogen atom.
13. The piperidine derivative or salt thereof according to Claim 5, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).
14. The piperidine derivative or salt thereof according to Claim 6, wherein R^1 is a hydrogen atom.
15. The piperidine derivative or salt thereof according to Claim 6, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).
16. The piperidine derivative or salt thereof according to Claim 7, wherein R^1 is a hydrogen atom.
17. The piperidine derivative or salt thereof according to Claim 7, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).
18. The piperidine derivative or salt thereof according to Claim 8, wherein R^1 is a hydrogen atom.
19. The piperidine derivative or salt thereof according to Claim 8, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).
20. The piperidine derivative or salt thereof according to Claim 9, wherein R^1 is a hydrogen atom.

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21. The piperidine derivative or salt thereof according to Claim 9, wherein R^1 is a lower alkyl group which may have hydroxyl group(s) as substituent(s).

22. The piperidine derivative or salt thereof according to any one of claims 10 to 21, wherein R^2 is a phenyl-lower alkyl group in which (1) the phenyl ring may have substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxy-carbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy group-substituted lower alkoxy group and an amino group which may have substituent(s) selected from the group consisting of a lower alkanoyl group, a lower alkoxycarbonyl group and an aminocarbonyl group which may each have lower alkyl group(s) as substituent(s) and (2) the lower alkyl moiety may have lower alkoxycarbonyl group(s) or hydroxyl group-substituted lower alkyl group(s) as substituent(s).

23. The piperidine derivative or salt thereof according to any one of claims 10 to 21, wherein R^2 is a phenoxy-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a nitro group, an amino group which may have lower

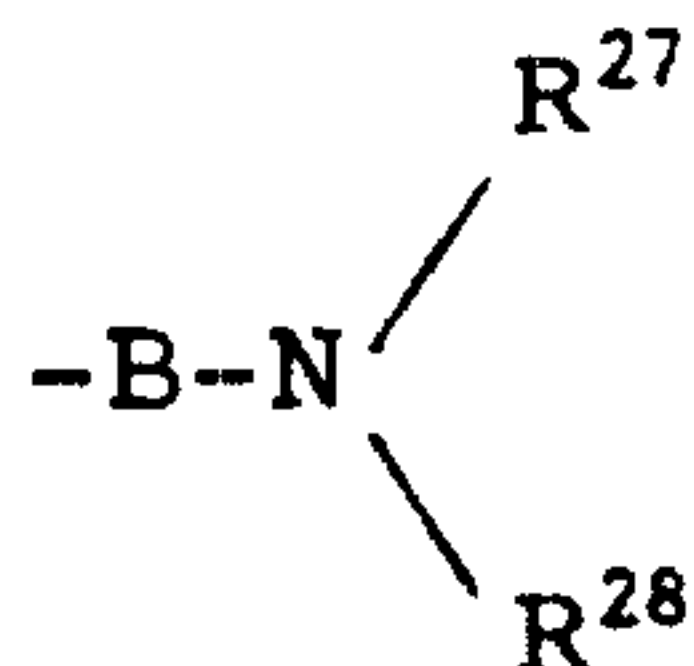
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alkanoyl group(s) as substituent(s), and a hydroxyl group.

24. The piperidine derivative or salt thereof according to any one of claims 10 to 21, wherein R^2 is a pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring, or a thienyl-lower alkyl group.

25. The piperidine derivative or salt thereof according to any one of claims 10 to 21, wherein R^2 is a 2,3-dihydro-1H-indenyl group which may have, substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s) as substituent(s); a furyl-lower alkyl group; a group of the formula:



(wherein B, R^{27} and R^{28} are the same as defined in claim 1); a phthalimido-substituted lower alkyl group; a cycloalkyl-lower alkyl group; a phenyl-lower alkenyl group; or a cycloalkyl group having phenyl group(s) as substituent(s).

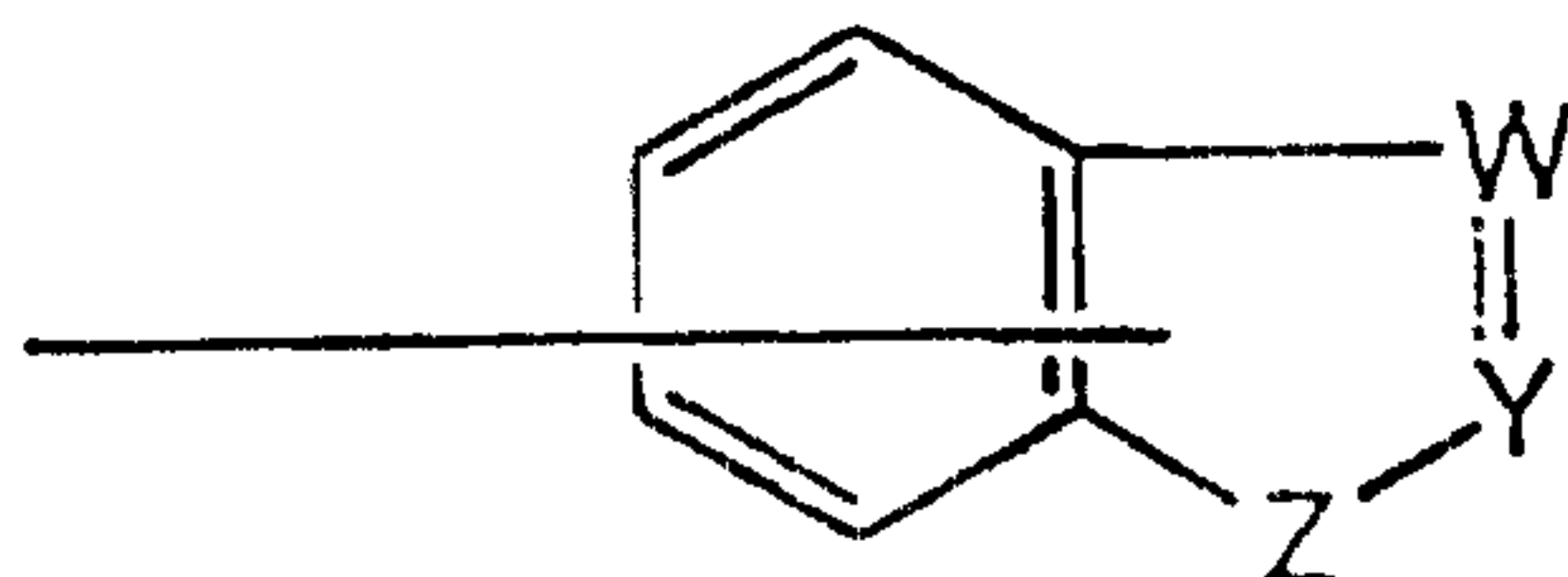
26. The piperidine derivative or salt thereof according to any one of claims 4 to 8, wherein R^1 and R^2 together with the adjacent nitrogen atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or a 1,2,3,4-tetrahydro-isoquinoline

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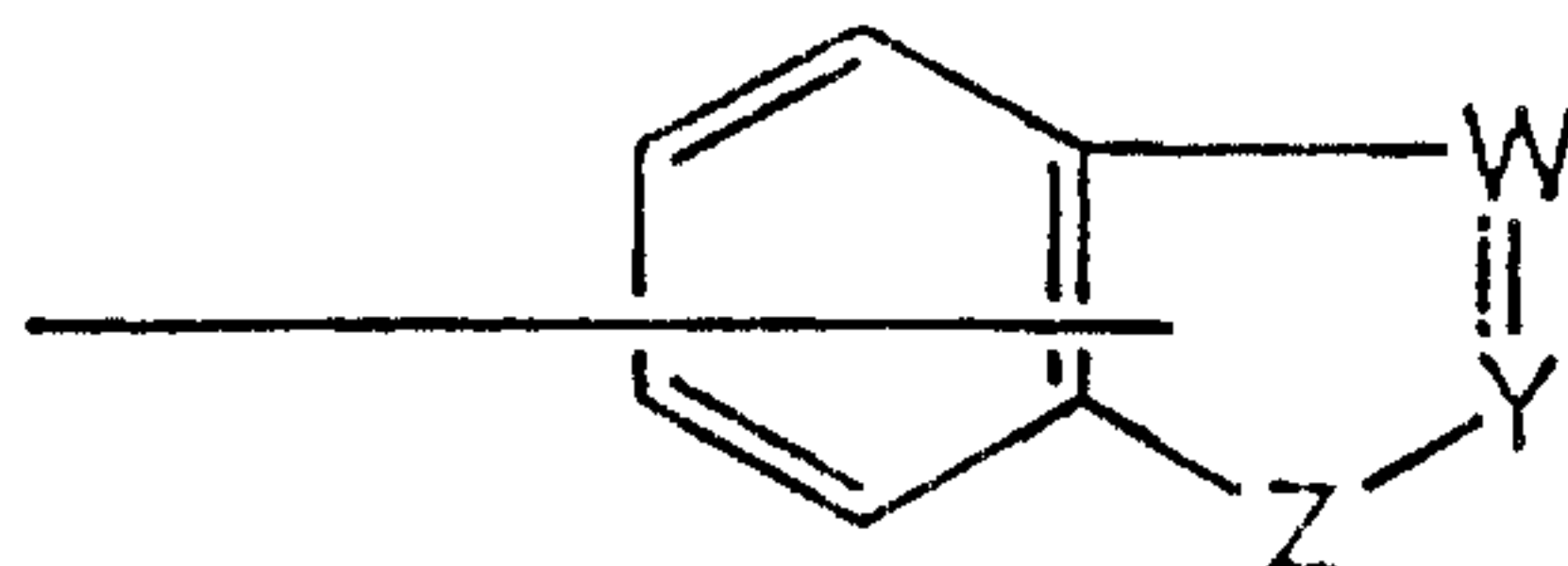
ring, each having substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy group and a phenyl group.

27. The piperidine derivative or salt thereof according to claim 8, wherein the group of the formula:



is an indolinyl group or a benzo-1,2,3-triazolyl group.

28. The piperidine derivative or salt thereof according to claim 8, wherein the group of the formula:



is an indolyl group, a benzimidazolyl group, a benzo-thiazolyl group, a 2,3-dihydrobenzimidazolyl group or an isoindolinyl group.

29. The piperidine derivative or salt thereof according to claim 2, wherein R^{AA} is a benzoyl group; R^1 and R^{2AA} together with the nitrogen atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or a 1,2,3,4-tetrahydroisoquinoline ring, each having substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy

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group and a phenyl group.

30. The piperidine derivative or salt thereof according to Claim 2, wherein R^{AA} is a benzoyl group; and R^{2AA} is a thienyl-lower alkyl group; a phenyl-lower alkyl group having lower alkylthio group(s) as substituent(s); or a 2,3-dihydro-1H-indenyl group which may have substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s) as substituent(s), on the 2,3-dihydro-1H-indene ring.

31. The piperidine derivative or salt thereof according to Claim 2, wherein R^{AA} is a lower alkanoyl group; and R^{2AA} is a thienyl-lower alkyl group or a phenyl-lower alkyl group having lower alkylthio group(s) as substituent(s) on the phenyl ring.

32. The piperidine derivative or salt thereof according to Claim 2, wherein R^{AA} is a lower alkanoyl group; and R^{2AA} is a 2,3-dihydro-1H-indenyl group which may have substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl groups(s) as substituent(s); or R^1 and R^{2AA} together with the adjacent nitrogen atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or a 1,2,3,4-tetrahydroisoquinoline ring, each having substituent(s) selected from the group consisting of a hydroxyl group, a lower alkoxy

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group and a phenyl group.

33. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-(3-methyl-4-propionylaminobenzoyl)piperidine.

34. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-(3,5-dimethyl-4-propionylaminobenzoyl)piperidine.

35. 4-{N-Methyl-N-[2-(2-thienyl)ethyl]amino}-1-(3-methyloxindol-5-yl)carbonylpiperidine.

36. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-(5-propionylaminopyridin-2-yl)carbonylpiperidine.

37. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-[4-(4-hydroxyphenyl)benzoyl]piperidine.

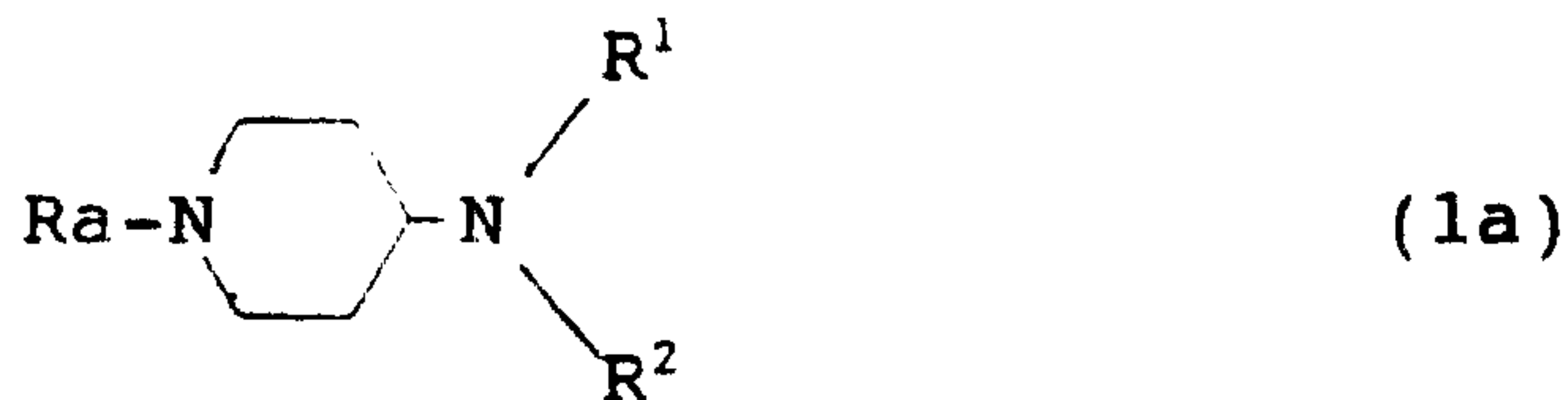
38. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-[3-amino-4-(4-hydroxyphenyl)benzoyl]piperidine.

39. 4-[N-Methyl-N-(2-phenoxyethyl)amino]-1-[4-(4-hydroxyphenyl)benzoyl]piperidine.

40. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-(4-methyl-benzo-1,2,3-triazol-6-yl)carbonylpiperidine.

41. 4-[N-Methyl-N-(2-phenylethyl)amino]-1-(4-ethylaminocarbonylbenzoyl)piperidine.

42. A process for preparing a piperidine derivative of the general formula (1a):

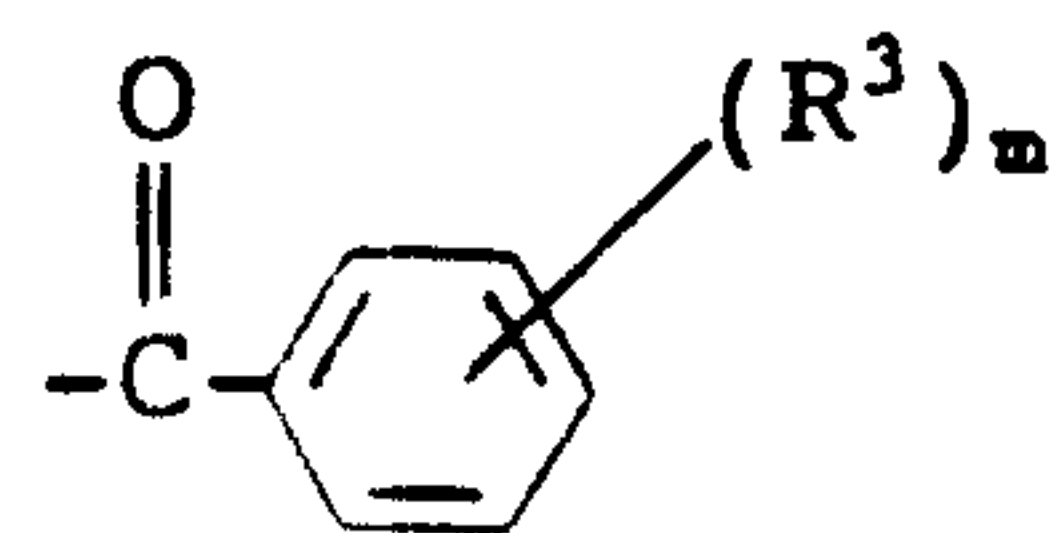


or a salt thereof, wherein, R^1 and R^2 are as defined in claim 1; and

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Ra is a group of the formula:



(wherein, R³ and m are as defined in claim 1);

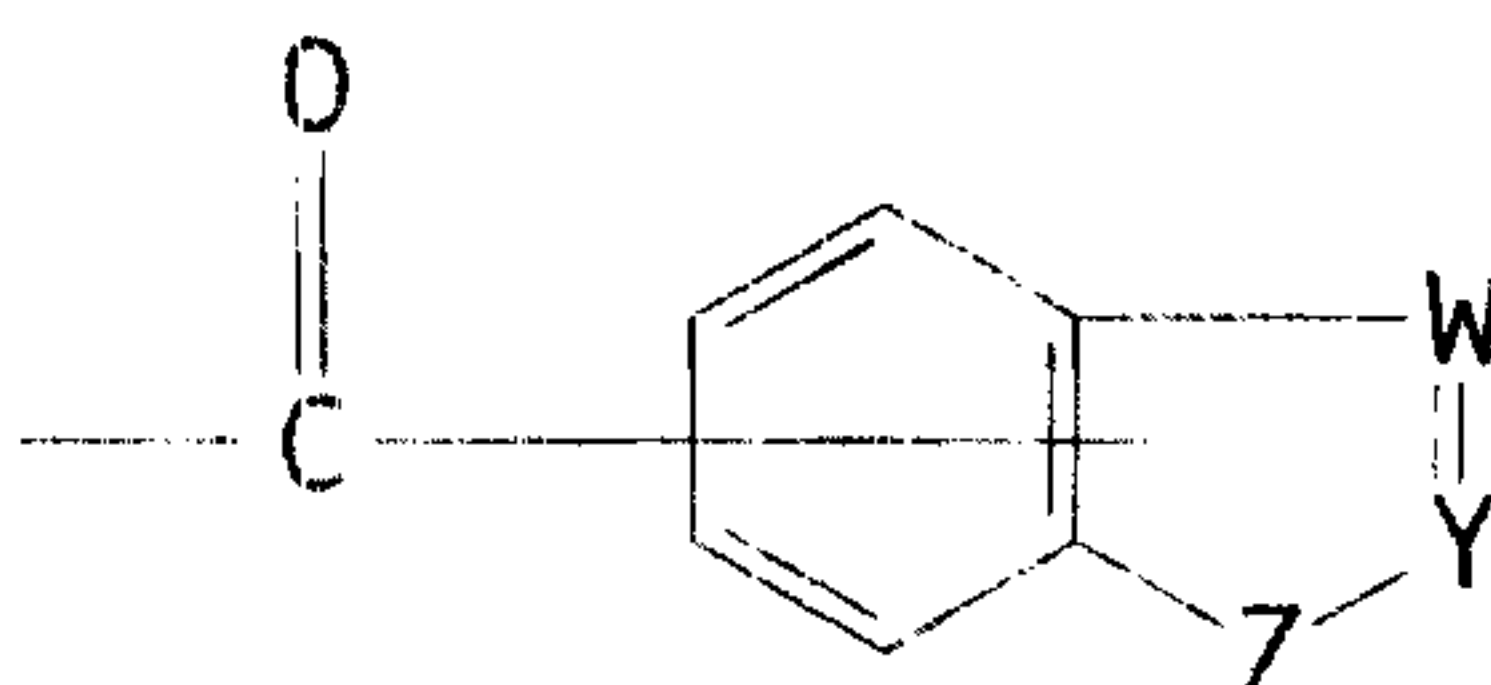
a lower alkanoyl group which may have hydroxyl group or amino group which may have lower alkyl group(s) as substituent(s); a lower alkanoyl group having 1 to 3 halogen atoms; a lower alkoxycarbonyl group; a pyridyl-carbonyl group which may have substituent(s), on the pyridine ring, selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxycarbonyl group, a hydroxyl group substituted-lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkanoyl group; a furoyl group which may have substituent(s), on the furyl ring, selected from the group consisting of a nitro group, a hydroxyl group substituted-lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a thienylcarbonyl group which may have substituent(s), on the thienyl ring, selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); a fluorenylcarbonyl group which may have

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substituent(s), on the fluorene ring, selected from the group consisting of an oxo group and a nitro group; or a group of the formula:

5



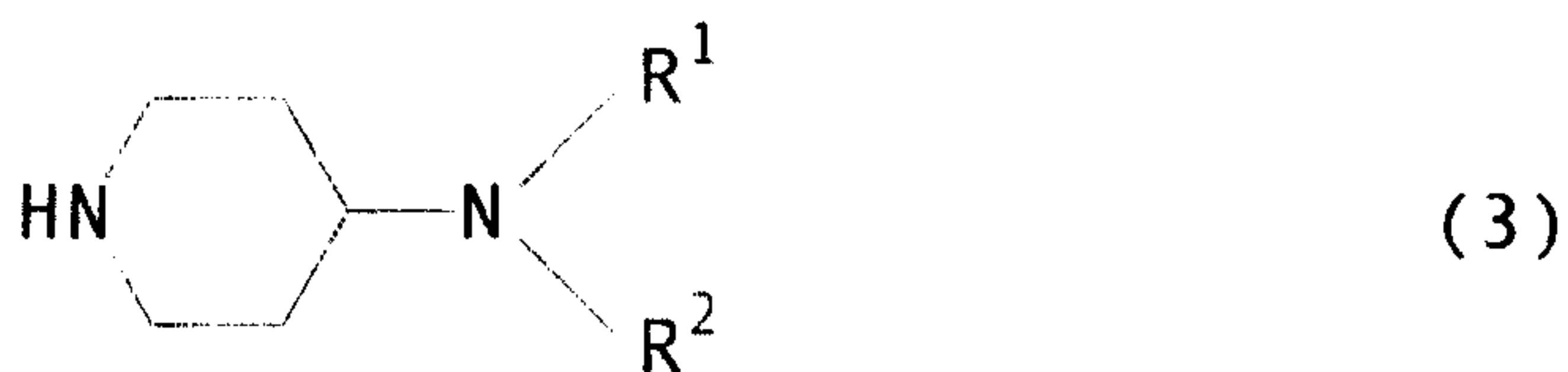
(wherein, Z, Y and W are as defined in claim 1 and which may have 1 to 4 substituents as defined in claim 1), which process comprises:

10 reacting a carboxylic acid derivative represented by the general formula (2):



(wherein Ra is as defined above), or a carboxylic acid derivative obtained by activating the carboxyl group of the
15 derivative,

with an amine compound represented by the general formula (3):



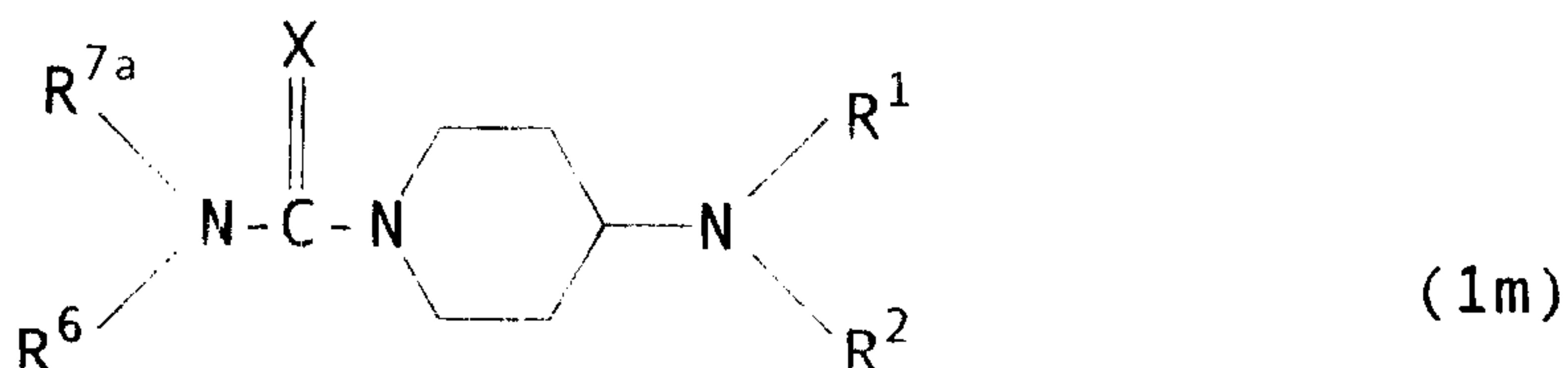
20

(wherein R¹ and R² have the meanings given above), or an amine compound obtained by activating the amino group of thereof.

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43. A process for preparing a piperidine derivative represented by the general formula (1m):



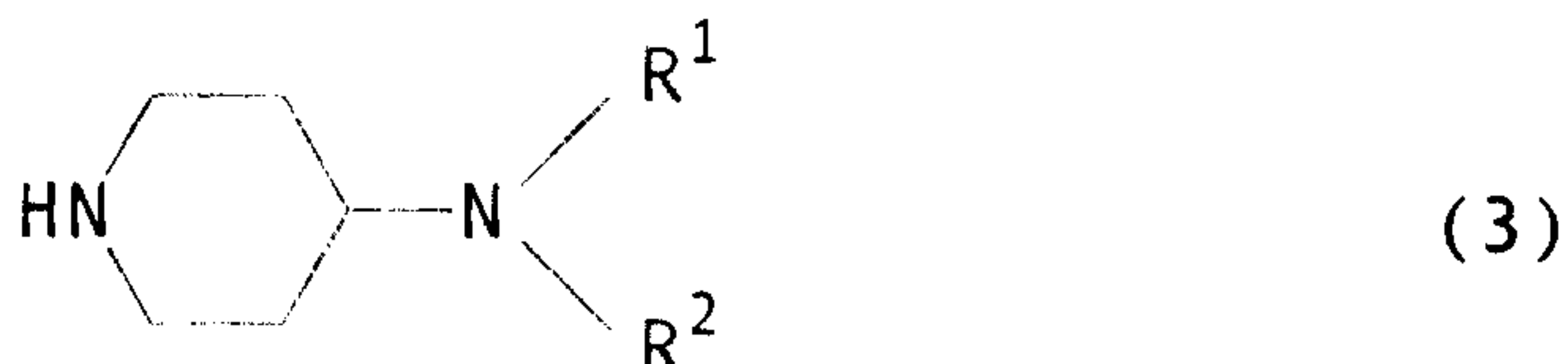
5

(wherein R¹ is as defined in claim 1; R² is a phenyl-C₁-C₂ alkyl group;

R⁶ is a hydrogen atom, a lower alkyl group in which the phenyl ring has substituents, selected from the group consisting of a lower alkoxy group, a halogen atom and a nitro group;

X is an oxygen atom or a sulfur atom and R^{7a} is a lower alkyl group),

which comprises reacting a piperidine derivative represented by the general formula (3):



(wherein R¹ and R² have the meanings given above),

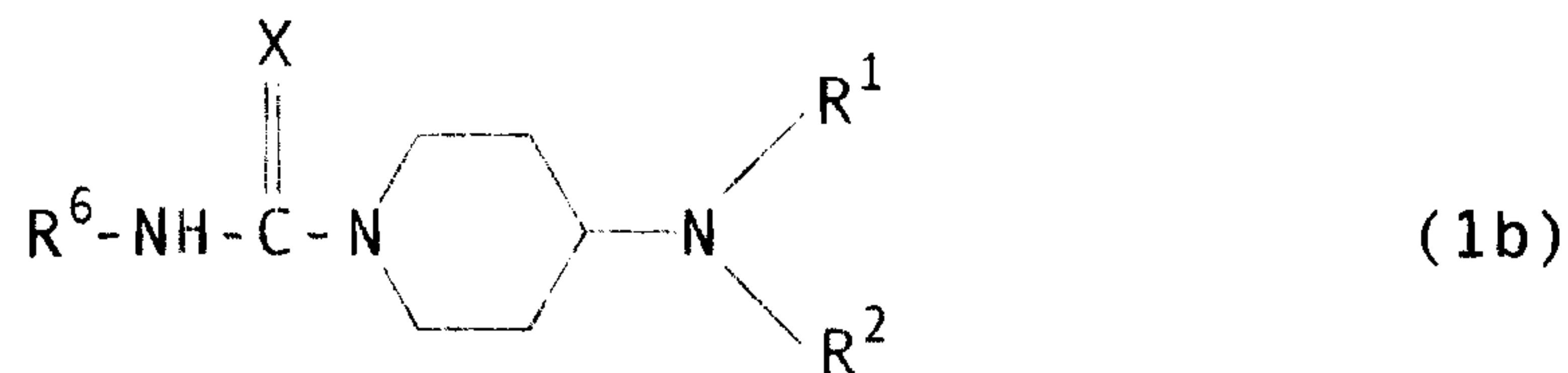
20 with a compound represented by the general formula (4):



(wherein R⁶ and X have the meanings given above), to obtain a piperidine derivative represented by the general formula (1b):

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5 (wherein R^1 , R^2 , R^6 and X have the meanings given above), and

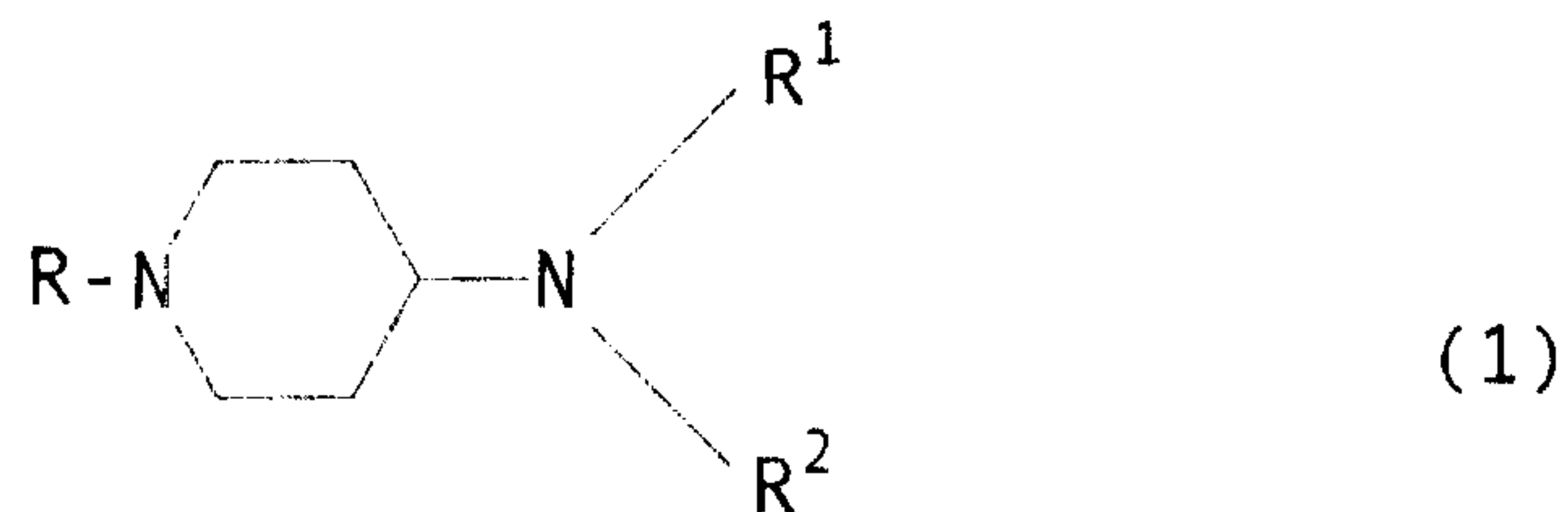
then reacting the thus obtained piperidine derivative of the general formula (1b) with a compound of the general formula (14):



10 (wherein R^{7a} has the meaning given above; and

X^1 is a halogen atom, a lower alkane sulfonyloxy group, an arylsulfonyloxy group or an aralkylsulfonyloxy group) to obtain the desired piperidine derivative of the general formula (1m).

15 44. A process for preparing a piperidine derivative represented by the general formula (1):



20 or salt thereof (wherein R, R^1 and R^2 are as defined in claim 1), which comprises reacting a compound represented by the general formula (5):



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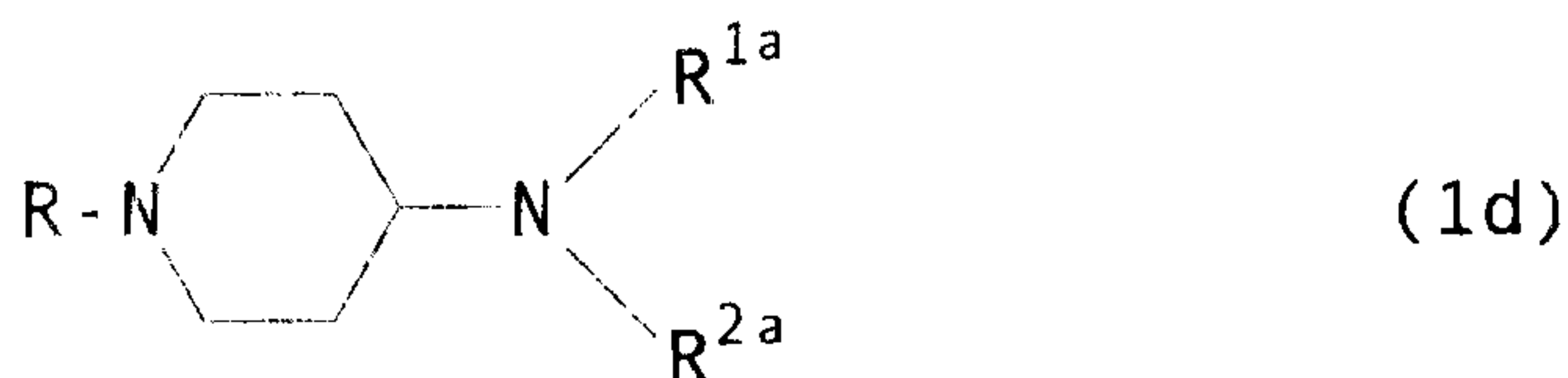
(wherein R has the meaning given above),

with an amine compound represented by the general formula (6):



(wherein R^1 and R^2 have the meanings given above) and a reducing agent.

45. A process for preparing a piperidine derivative represented by the general formula (1d):



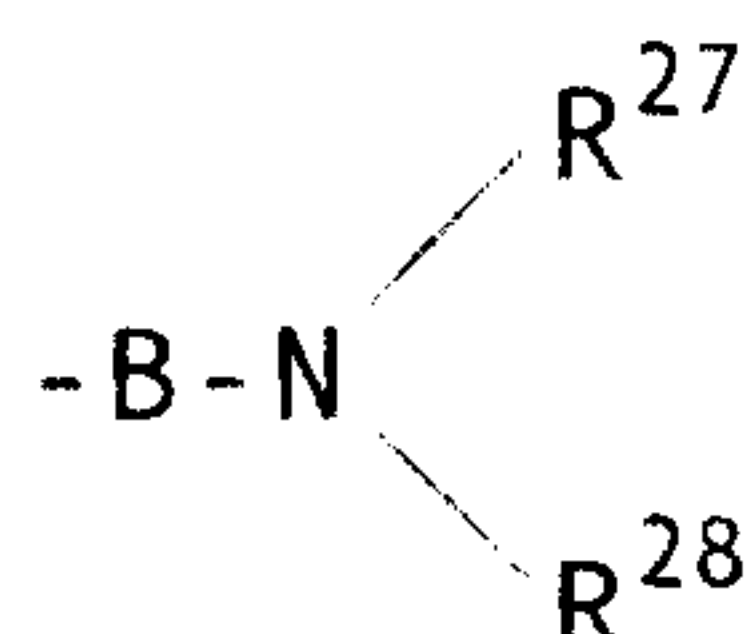
wherein R is as defined in claim 1;

15 R^{2a} is a hydrogen atom; a lower alkyl group which may have hydroxyl group(s) as substituent(s); a phenyl-lower alkyl group which may have substituent(s), (1) on the phenyl ring, selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a
20 lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxyl group, an amino-lower alkoxy

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group which may have lower alkyl group(s) as substituent(s),
 a carboxy-substituted lower alkoxy group and an amino group
 which may have, as substituent(s), lower alkanoyl group(s),
 lower alkoxy-carbonyl group(s), or aminocarbonyl group(s)
 5 which may each have lower alkyl group(s) as substituent(s)
 and (2) in the lower alkyl moiety, lower alkoxycarbonyl
 group(s) or hydroxyl-substituted lower alkyl group(s); a
 phenoxy-lower alkyl group which may have, on the phenyl
 ring, substituent(s) selected from the group consisting of a
 10 lower alkoxy group, a lower alkyl group, a halogen atom, a
 nitro group, a hydroxyl group and an amino group which may
 have lower alkanoyl group(s) as substituent(s); a pyridyl-
 lower alkyl group which may have lower alkyl group(s) as
 substituent(s) on the pyridine ring; a thienyl-lower alkyl
 15 group; a furyl-lower alkyl group; a group of the formula:



(wherein, B, R²⁷ and R²⁸ are as defined in claim 1); a
 20 phthalimido-substituted lower alkyl group; a cycloalkyl-
 lower alkyl group; a phenyl-lower alkenyl group; a
 cycloalkyl group which may have a phenyl group as a
 substituent; or a 2,3-dihydro-1H-indenyl group which may
 have substituent(s) selected from the group consisting of a
 25 lower alkoxy group, a hydroxyl group, a nitro group and an
 amino group which may have lower alkanoyl group(s); and

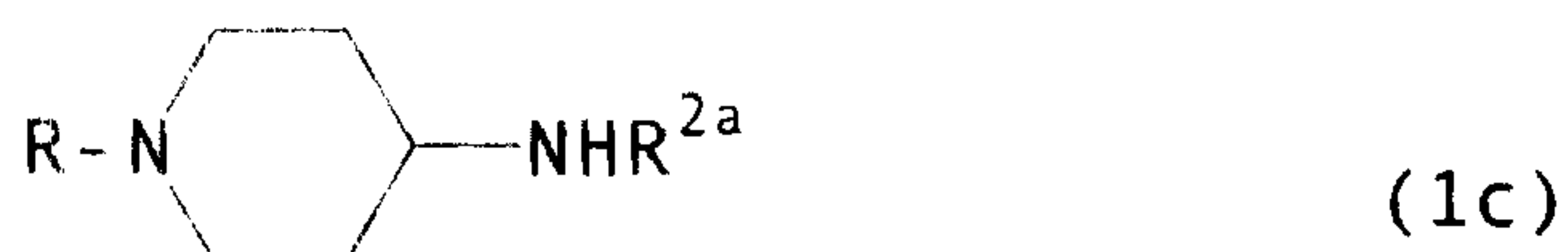
R^{1a} is the same as R^{2a}, excluding a hydrogen atom,

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provided that, when R^{2a} is as defined above except a hydrogen atom and a lower alkyl group which may have hydroxyl group(s) as substituent(s), then R^{1a} is a lower alkyl group which may have hydroxyl group(s) as substituent(s); further, when R^{2a} is a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituent(s), then R^{1a} is as defined above except a lower alkyl group which may have hydroxyl group(s) as substituent(s), which process comprises:

10 reacting a compound of the general formula (1c):



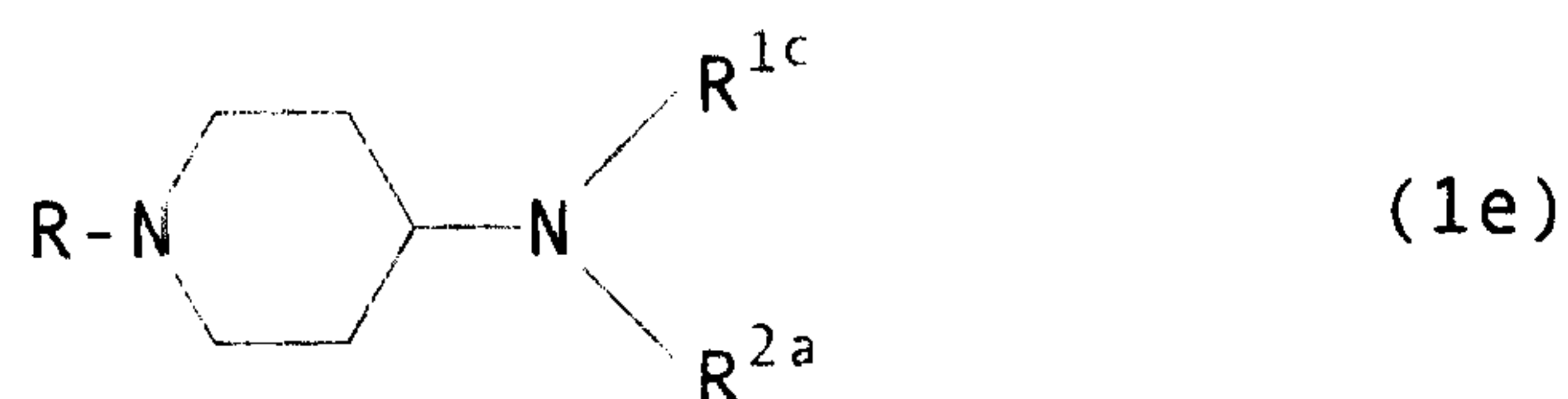
(wherein R and R^{2a} are as defined above),

15 with a compound of the general formula (7):



(wherein R^{1a} is as defined above and X^1 is a halogen atom, a lower alkane-sulfonyloxy group, an arylsulfonyloxy group or an aralkylsulfonyloxy group).

20 46. A process for preparing a piperidine derivative represented by the general formula (1e):



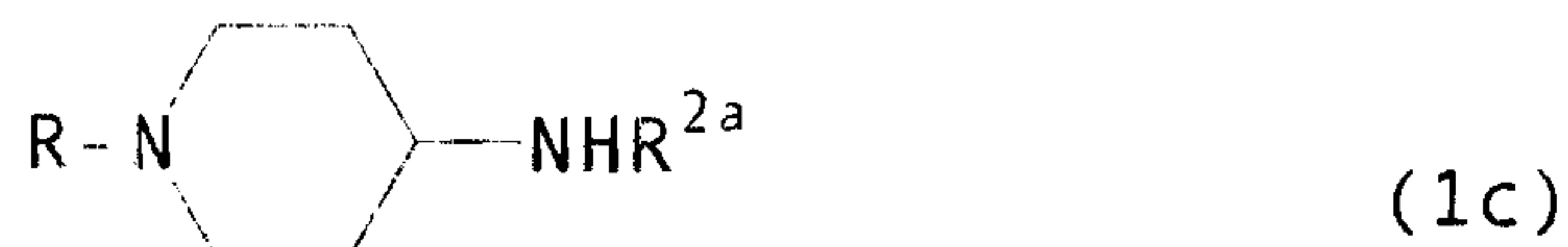
25 (wherein R is as defined in claim 1;

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and R^{2a} is a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituent(s); and R^{1c} is $R^{1b}-CH_2-$ in which R^{1b} is defined hereinunder), which process comprises:

5 reacting a compound of the general formula (1c):



(wherein R and R^{2a} have the meanings given above),

10 with a compound represented by the general formula (8):

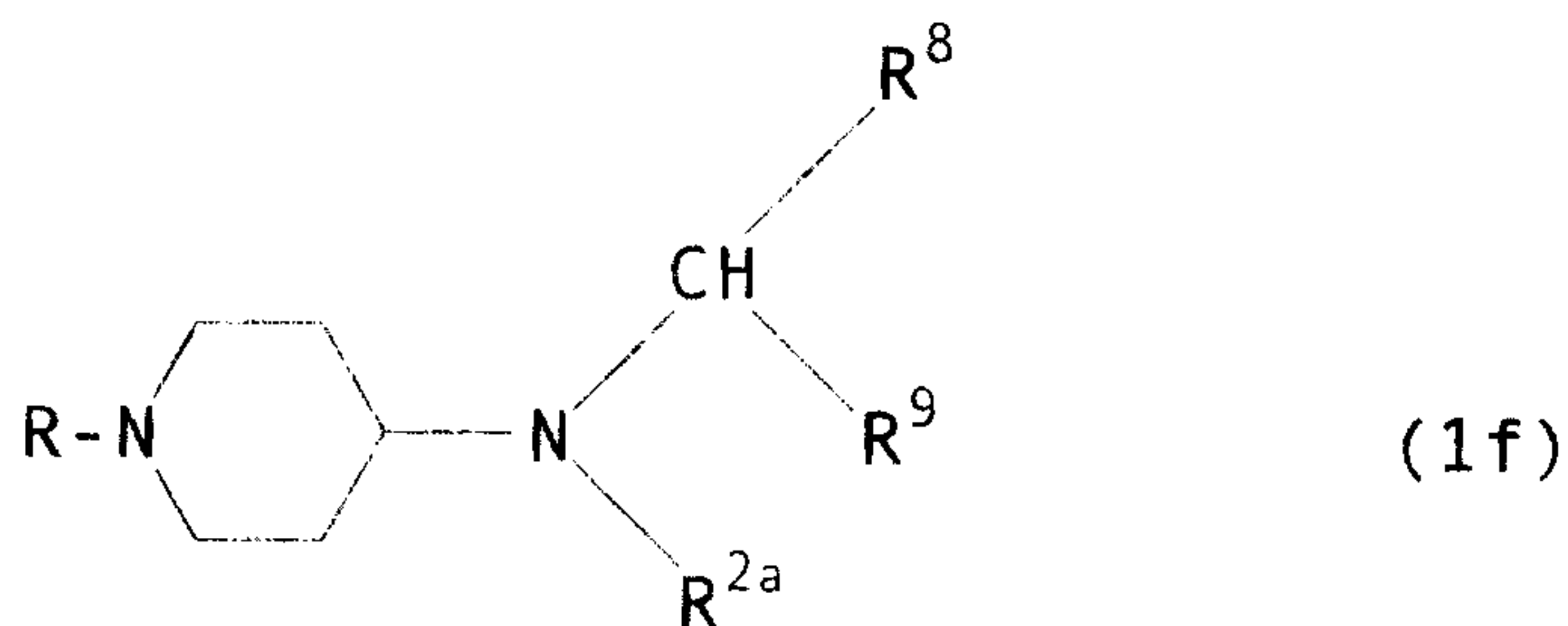


(wherein R^{1b} is a phenyl group which may have substituent(s) selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower
 15 alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxyl group, an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s), a carboxy-substituted lower alkoxy group and an amino group which may
 20 have, as substituent(s), lower alkanoyl group(s), lower alkoxycarbonyl group(s) or aminocarbonyl group(s) which may have lower alkyl group(s) as substituent(s); a pyridyl group which may have lower alkyl group(s) as substituent(s); a thienyl group; a furyl group; a phthalimido group; a
 25 cycloalkyl group) and a reducing agent.

47. A process for preparing a piperidine derivative represented by the general formula (1f):

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5

(wherein R is as defined in claim 1;

R^{2a} is a hydrogen atom; a lower alkyl group which may have hydroxyl group(s) as substituent(s); a phenyl-lower alkyl group which may have substituent(s), (1) on the phenyl
 10 ring, selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxyl group, an amino-lower alkoxy
 15 group which may have lower alkyl group(s) as substituent(s), a carboxy-substituted lower alkoxy group and an amino group which may have, as substituent(s), lower alkanoyl group(s), lower alkoxy-carbonyl group(s), or aminocarbonyl group(s) which may each have lower alkyl group(s) as substituent(s)
 20 and (2) in the lower alkyl moiety, lower alkoxycarbonyl group(s) or hydroxyl-substituted lower alkyl group(s); a phenoxy-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a
 25 nitro group, a hydroxyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a pyridyl-

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lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring; a thienyl-lower alkyl group; a furyl-lower alkyl group; a group of the formula:

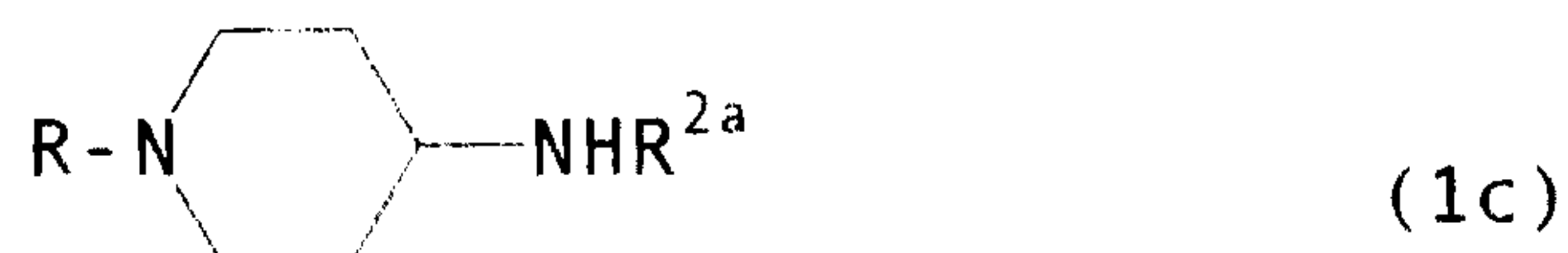


(wherein, B, R²⁷ and R²⁸ are as defined in claim 1); a phthalimido-substituted lower alkyl group; a cycloalkyl-lower alkyl group; a phenyl-lower alkenyl group; a cycloalkyl group which may have a phenyl group as a substituent; or a 2,3-dihydro-1H-indenyl group which may have substituent(s) selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group(s); and

15 R⁸ and R⁹ independently represent a hydrogen atom or a lower alkyl group,

provided that R^{2a} is other than a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituents(s)), which process comprises:

20 reacting a piperidine derivative represented by the general formula (1c):



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(wherein R and R^{2a} have the meanings given above),

with a compound of the general formula (9):

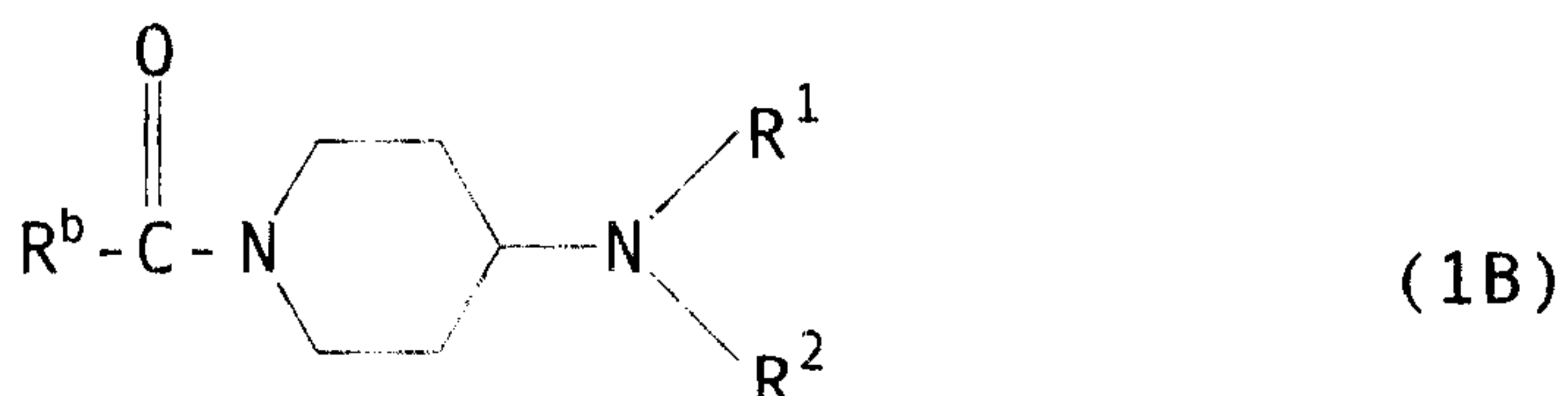


5

(wherein R⁸ and R⁹ have the meanings given above) and a reducing agent.

48. A process for preparing a piperidine derivative represented by the general formula (1B):

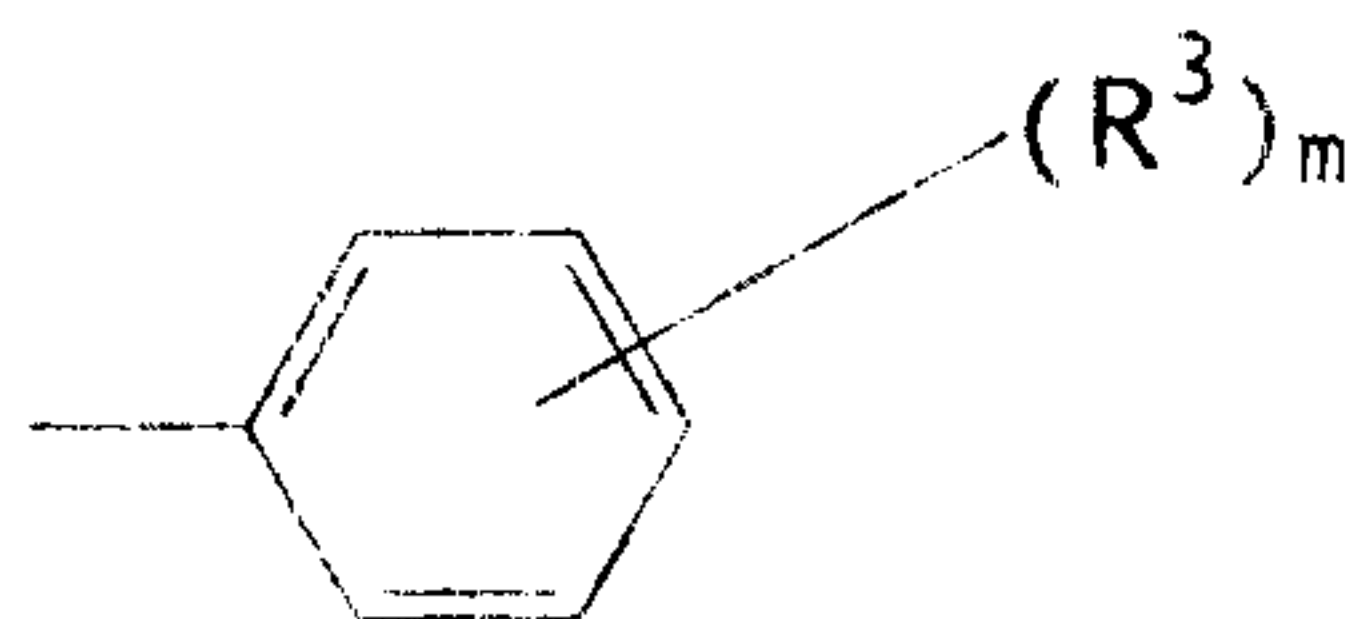
10



wherein R¹ and R² are as defined in claim 1; and

R^b is a group of the formula:

15



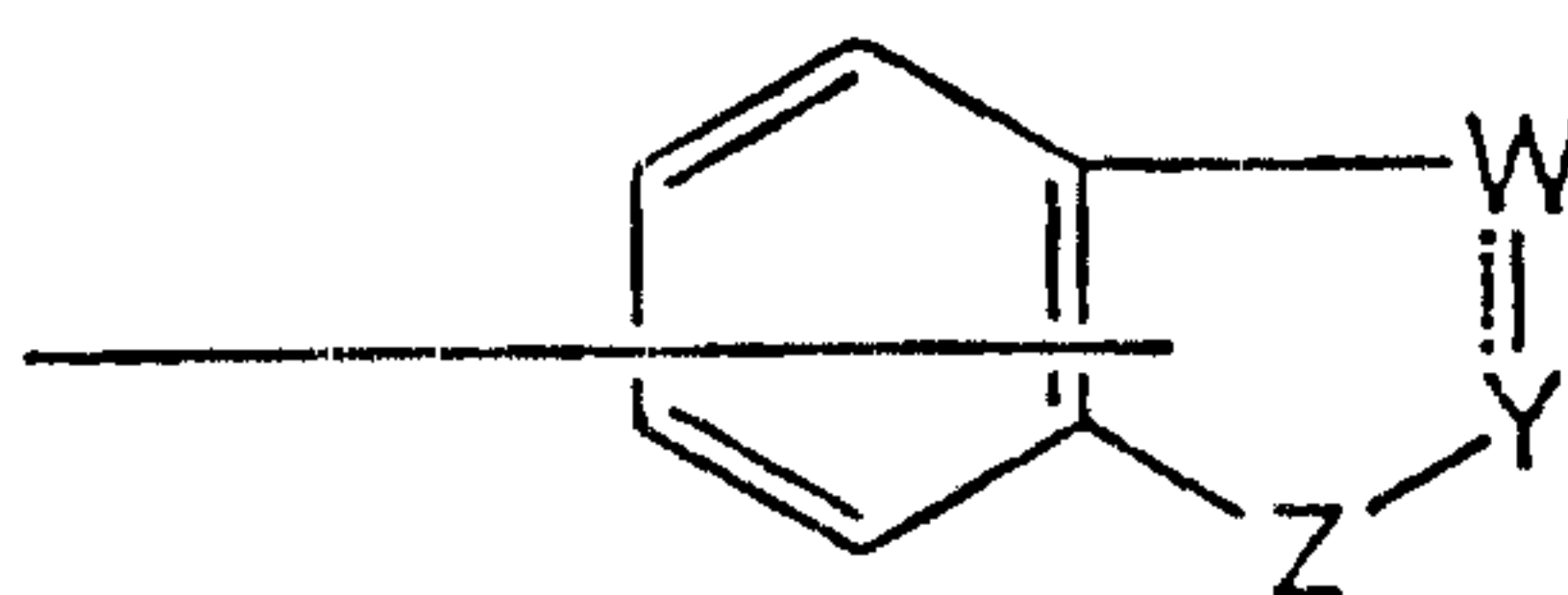
(wherein R³ and m are as defined in claim 1);

a lower alkyl group which may have hydroxyl group(s) or amino group(s) which may each have lower alkyl group(s);

20

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a lower alkyl group having 1 to 3 halogen atoms; a pyridyl group which may have, on the pyridine ring, substituent(s) selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxycarbonyl group, a hydroxyl group-substituted lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkyl group; a furyl group which may have, on the furan ring, substituent(s) selected from the group consisting of a nitro group, a hydroxyl group-substituted lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a thienyl group which may have, on the thiophene ring, substituent(s) selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); a fluorenyl group which may have, on the fluorene ring, substituent(s) selected from the group consisting of an oxo group and a nitro group; or a group of the formula:



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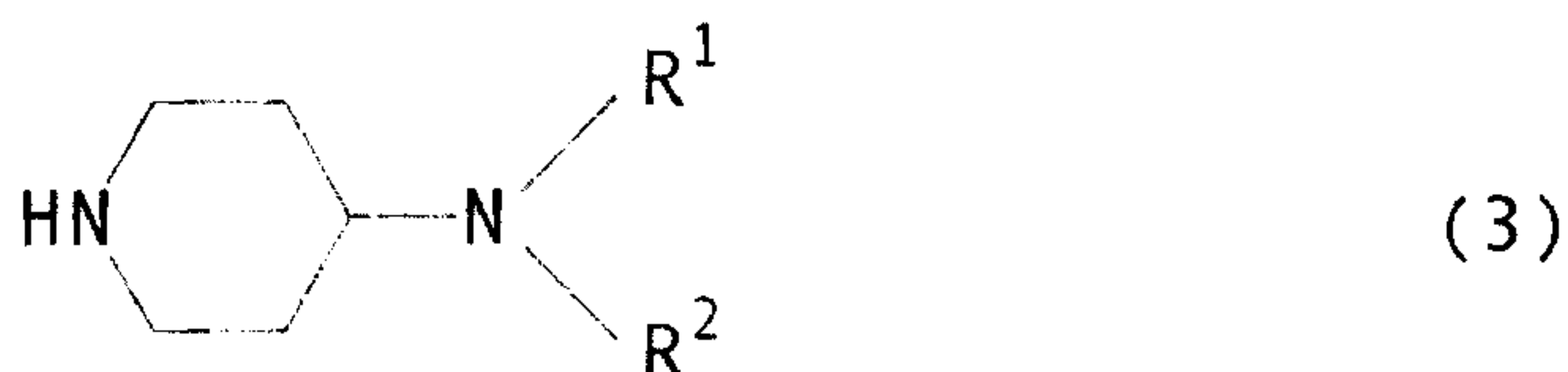
(wherein Y, W, Z, the dotted line are as defined in claim 1) which may have 1 to 4 substituents defined in claim 1, which process comprises:

reacting a compound of the formula (33):



(wherein R^b is defined above),

with a piperidine compound of the formula (3):



(wherein R^1 and R^2 are the same as defined above) and a metal cyanide, and subsequently with an oxidizing agent.

49. A peripheral vasodilating agent that is a pharmaceutical preparation containing:

15 an effective amount of the piperidine derivative claimed in any one of claims 1 to 41 or a physiologically acceptable acid addition salt thereof, and

a pharmaceutically acceptable diluent or excipient.

20 50. The peripheral vasodilating agent according to claim 49, which is used for improving peripheral circulatory disturbance caused by arterial disease.

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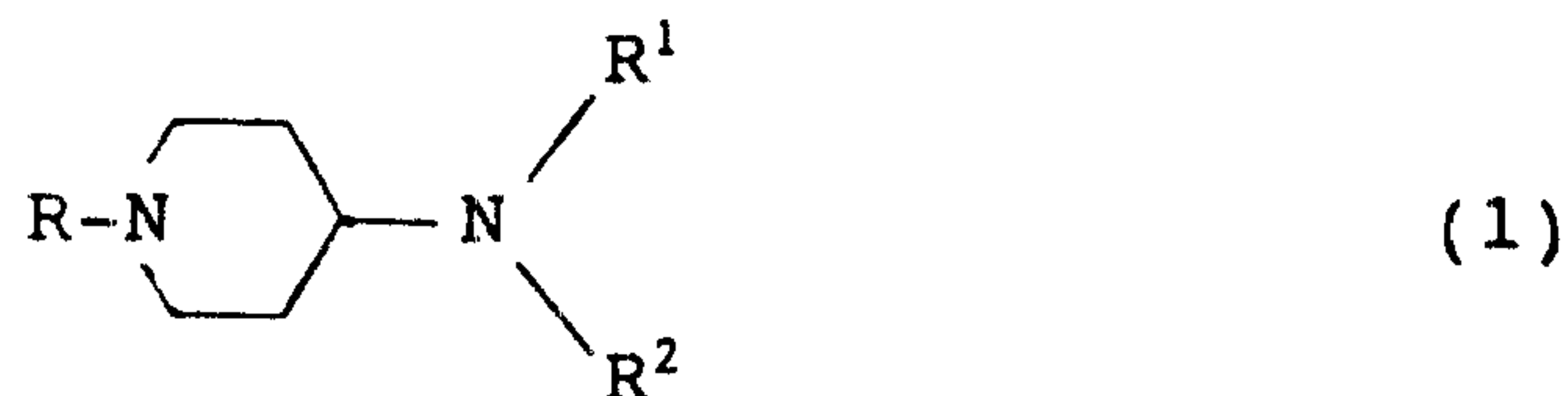
51. The peripheral vasodilating agent according to claim 49, which is used for improving peripheral circulatory disturbance caused by venous disease.

52. A peripheral vasodilating agent that is a
5 pharmaceutical preparation containing:

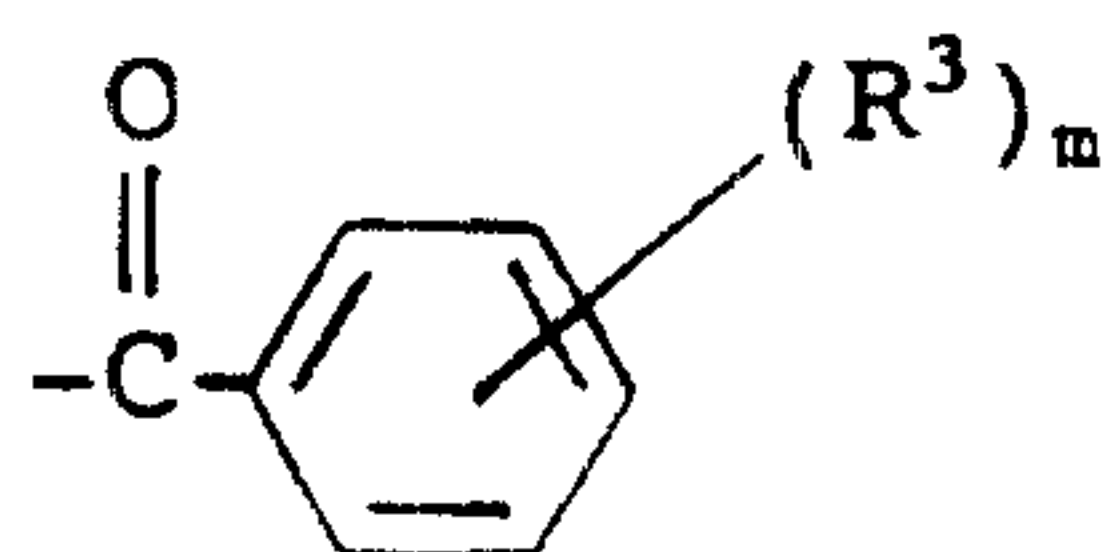
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(a) an effective amount of a piperidine derivative represented by the general formula (1):



wherein, R is a benzoyl group of the formula:



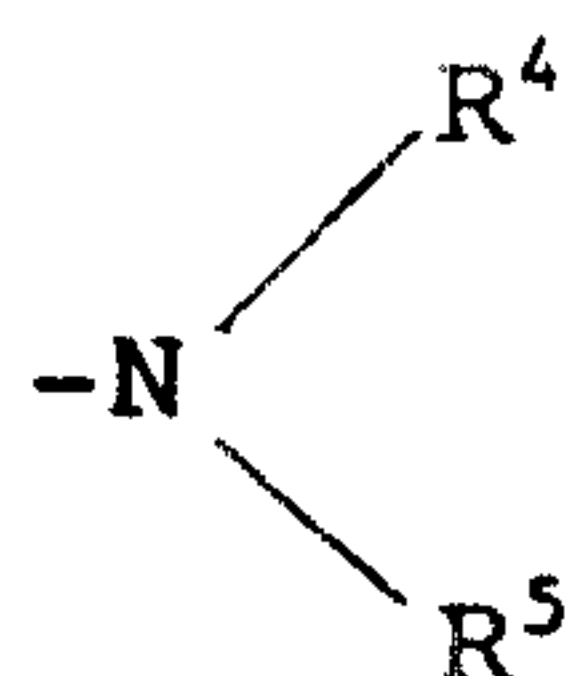
(wherein, m is an integer of 1 to 3;

R^3 is a hydrogen atom, a nitro group; a lower alkyl group; a halogen atom; a cyano group; a lower alkanoyl group; an aminocarbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group and a phenyl group; a lower alkoxycarbonyl group; a carboxy group, a lower alkoxy group; a hydroxyl group; a hydroxyamino group; a lower alkylthio-lower alkyl group; a lower alkylsulfonyl-lower alkyl group; a hydroxyl group substituted-lower alkyl group; a lower alkenyl group; a lower alkoxycarbonyl group substituted-lower alkenyl group; a phenyl group which may have substituent(s), on the phenyl ring, selected from the group consisting of a hydroxyl group a phenyl-lower alkoxy group, a lower alkanoyloxy group,

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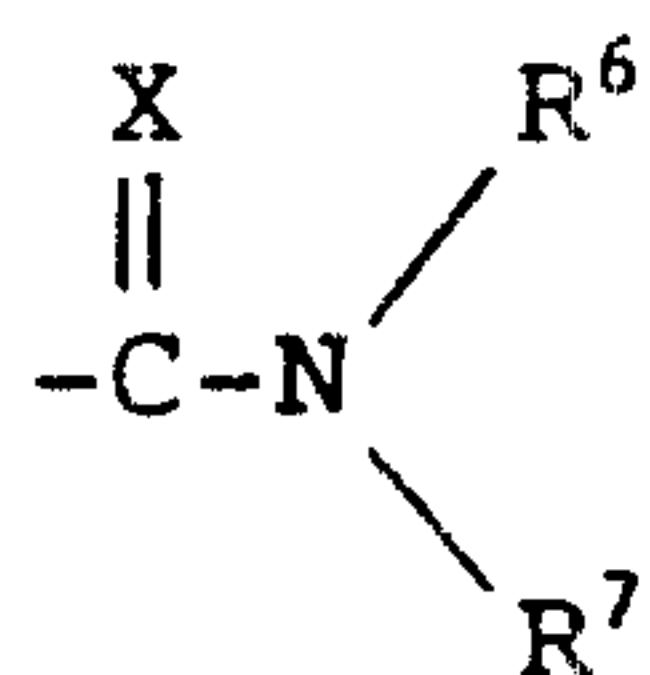
a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a lower alkyl group and a lower alkoxy group; an amino-lower alkoxy group which may have lower alkyl group(s) as substituent(s); a morpholinyl group substituted-lower alkoxy group; 1,2,4-triazolyl group which may have oxo group(s) as substituent(s) on the 1,2,4-triazole ring; a 1,2,3,4-tetrazolyl group; an imidazolyl group which may have 1 to 2 substituents, on the imidazole ring, selected from the group consisting of a phenyl group and a lower alkyl group; a pyrazolyl group which may have lower alkyl group(s) as substituent(s) on the pyrazole ring; a pyridyl group; a pyrrolyl group; a pyrrolidinyl group which may have oxo group(s) as substituent(s) on the pyrrolidine ring; a piperidinyl group which may have oxo group(s) as substituent(s) on the piperidine ring; a benzimidazolyl group; an imidazolidinyl group which may have oxo group(s) as substituent(s) on the imidazolidine ring; a 2-oxazolinyl group; a 1,2,4-triazolyl-lower alkyl group; a phenoxy group; a phenyl-lower alkoxy group; a lower alkanoyloxy group; a phenyl-lower alkoxy-carbonyl group; an amino-lower alkyl group in which the amino moiety may have, substituent(s) selected from the group consisting of a lower alkyl group and a lower alkanoyl group; a group of the formula:



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(wherein, R^4 and R^5 are each the same or different, and are each a hydrogen atom, a lower alkyl group, a lower alkanoyl group, a lower alkanoyl group having 1 to 3 halogen atoms, a benzoyl group, a pyridylcarbonyl group, a lower alkenyl-carbonyl group, an anilinothiocarbonyl group, an aminothio-carbonyl group which may have lower alkyl group as substituent(s) or an aminocarbonyl group which may have 1 to 2 substituents selected from the group consisting of a lower alkyl group, a phenyl group and a lower alkenyl group)); a group of the formula:

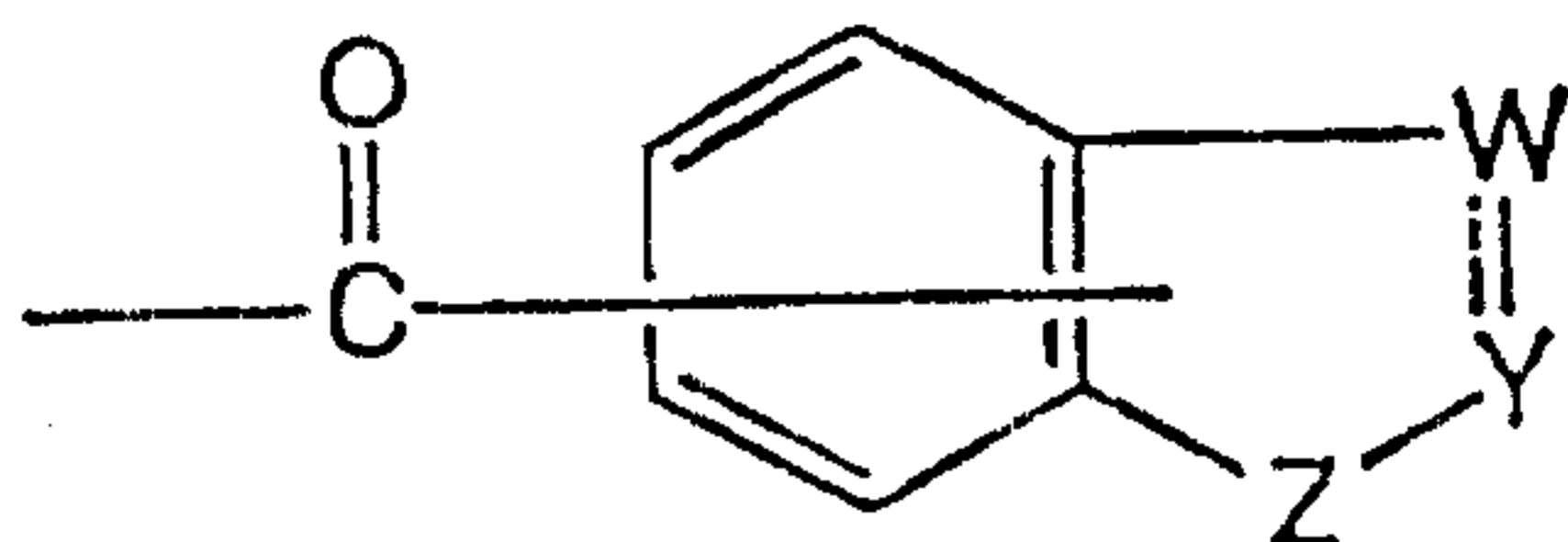


(wherein, X is an oxygen atom or a sulfur atom;

R^6 and R^7 are the same or different, and are each a hydrogen atom, a lower alkyl group, or a phenyl group which may have substituent(s), on the phenyl ring, selected from the group consisting of a lower alkoxy group, a halogen atom and a nitro group),
 a lower alkanoyl group which may have hydroxyl group or amino group which may have lower alkyl group(s) as substituent(s); a lower alkanoyl group having 1 to 3 halogen atoms, a lower alkoxy carbonyl group, a pyridyl-carbonyl group which may have substituent(s), on the pyridine ring, selected from the group consisting of a nitro group, an amino group which may have lower alkanoyl group(s) as substituent(s), a halogen atom, a lower alkyl group, a pyrrolyl group, a lower alkylthio

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group, a lower alkanoyl group, a hydroxyl group, an aminocarbonyl group which may have lower alkyl group(s) as substituent(s), a lower alkoxy carbonyl group, a hydroxyl group substituted-lower alkyl group, a phenyl group and a 1,2,4-triazolyl group; a 1,2,4-triazolyl-lower alkanoyl group; a furoyl group which may have substituent(s), on the furan ring, selected from the group consisting of a nitro group, a hydroxyl group substituted-lower alkyl group, a lower alkanoyl group and an amino group which may have lower alkanoyl group(s) as substituent(s); a thienylcarbonyl group which may have substituent(s), on the thiophene ring, selected from the group consisting of a nitro group, a lower alkyl group, a halogen atom and an amino group which may have lower alkanoyl group(s) as substituent(s); a fluorenylcarbonyl group which may have substituent(s), on the fluorene ring, selected from the group consisting of an oxo group and a nitro group; or a group of the formula:

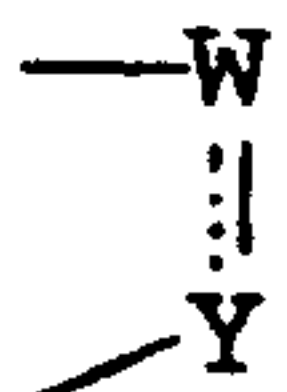


(wherein, Z is a group of the formula: $-\text{CH}_2-$ or $-\text{NH}-$ or a sulfur atom;

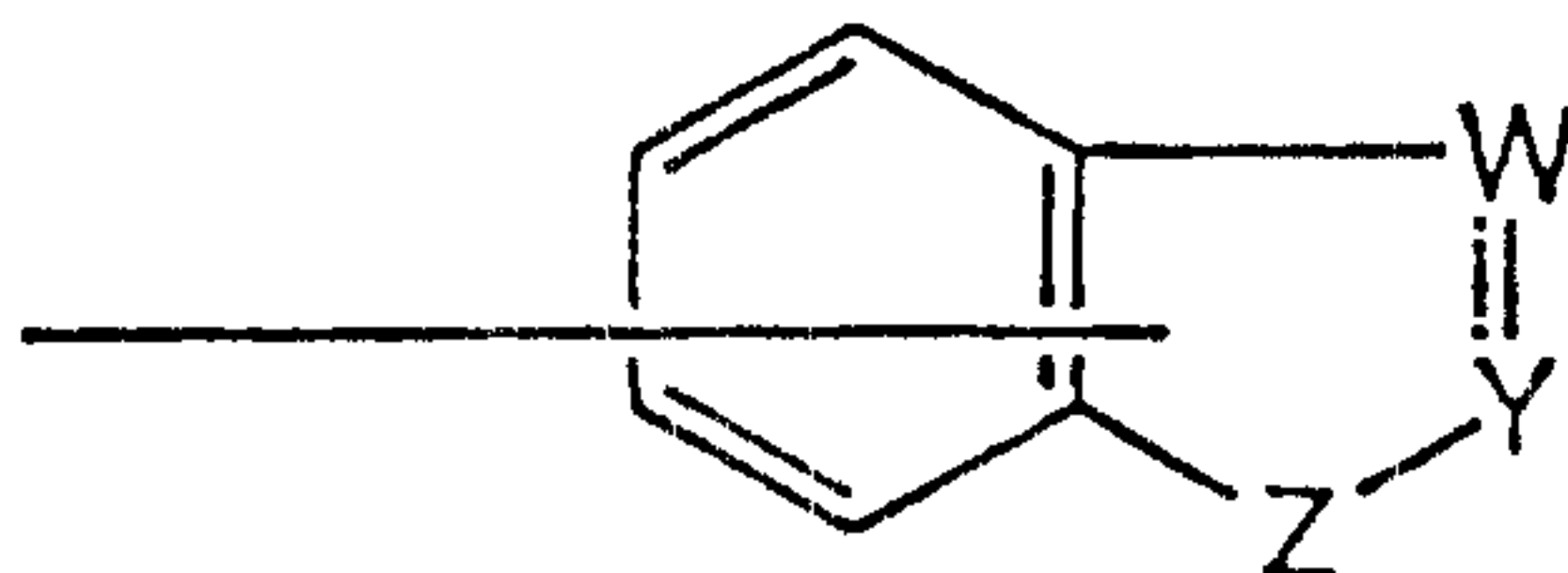
Y and W are each a group of the formula: $=\text{CH}-$ or a nitrogen atom;

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and the dotted line in the bonding of the formula: 

is a single bond or a double bond); and a group of the formula:



may have 1 to 4 substituent(s) selected from the group consisting of an oxo group, a lower alkyl group, a lower alkoxy group, a hydroxyl group, a lower alkylthio group, a halogen atom, a nitro group and an amino group;

R^1 is a hydrogen atom or a lower alkyl group which may have hydroxyl group(s) as substituent(s);

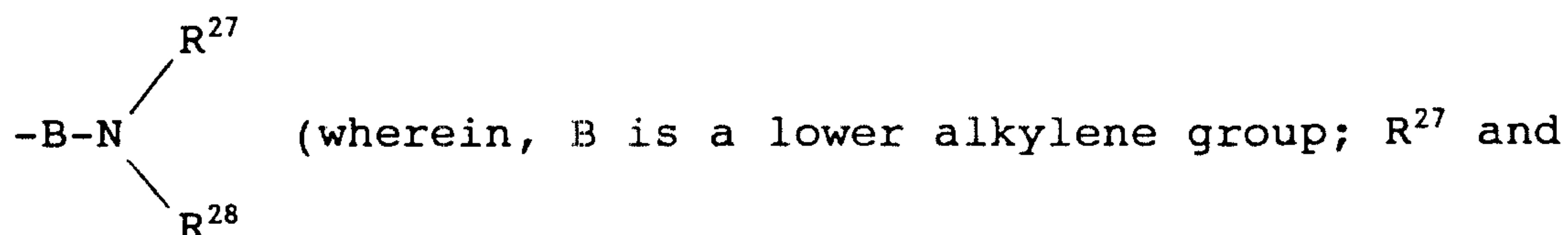
R^2 is a phenyl-lower alkyl group which may have as substituent(s), on the phenyl ring, selected from the group consisting of a lower alkoxy group, a halogen atom, a hydroxyl group, a nitro group, a lower alkyl group, a lower alkylthio group, a lower alkylsulfinyl group, a lower alkoxycarbonyl group, a carbamoyl group, a carboxy group, an amino-lower alkoxy group in which the amino moiety may have lower alkyl group(s) as substituent(s), a carboxy group substituted-lower alkoxy group and an amino group which may have as substituent(s) selected from the group consisting of a lower alkanoyl group, a lower alkoxycarbonyl group, and aminocarbonyl group which may have lower alkyl group as substituent(s);

further, a phenyl-lower alkyl group which may

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have a lower alkoxy-carbonyl group or a hydroxyl group substituted-lower alkyl group as substituent(s) in the lower alkyl moiety; a phenoxy-lower alkyl group which may have, on the phenyl ring, substituent(s) selected from the group consisting of a lower alkoxy group, a lower alkyl group, a halogen atom, a nitro group, an amino group which may have a lower alkanoyl group as substituent(s), and a hydroxyl group, a pyridyl-lower alkyl group which may have lower alkyl group(s) as substituent(s) on the pyridine ring, a thienyl-lower alkyl group; a furyl-lower alkyl group, a group of the formula:



R²⁸ are each the same or different, and are each a hydrogen atom, a lower alkyl group, a phenyl group, a lower alkanoyl group or a benzoyl group), a phthalimide substituted-lower alkyl group, a cycloalkyl-lower alkyl group, a phenyl-lower alkenyl group, a cycloalkyl group which may have phenyl group(s) as substituent(s), or a 2,3-dihydro-1H-indenyl group which may have as substituent(s), on the 2,3-dihydro-1H-indene ring, selected from the group consisting of a lower alkoxy group, a hydroxyl group, a nitro group and an amino group which may have lower alkanoyl group as substituents; or

R¹ and R² and the adjacent nitrogen

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atom being bonded thereto form a pyrrolidine ring, a piperidine ring, a morpholine ring or a 1,2,3,4-tetrahydroisoquinoline ring, each of which may have substituent(s) selected from the group consisting of a
5 hydroxyl group, a lower alkoxy group and a phenyl group;

provided that, when $\underline{m}$ is 1 and R^3 is an amino group, then R^3 should not be substituted at the 4-position in the benzoyl group), or a physiologically acceptable acid addition salt thereof, and

10 (b) a pharmaceutically acceptable diluent or excipient.

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