

(43) International Publication Date
11 November 2010 (11.11.2010)(10) International Publication Number
WO 2010/128152 A1

(51) International Patent Classification:

C07H 7/06 (2006.01) A61K 31/7052 (2006.01)
 C07H 7/04 (2006.01) A61K 31/7056 (2006.01)
 A61K 31/70 (2006.01) A61K 31/706 (2006.01)
 A61K 31/7048 (2006.01) A61P 3/10 (2006.01)

(21) International Application Number:

PCT/EP2010/056286

(22) International Filing Date:

7 May 2010 (07.05.2010)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

939/DEL/2009 7 May 2009 (07.05.2009) IN
 61/176,399 7 May 2009 (07.05.2009) US
 61/327,287 23 April 2010 (23.04.2010) US

(71) Applicant (for all designated States except US): **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BEBERNITZ, Gregory Raymond** [US/US]; Novartis Institutes for BioMedical Research, Inc., 100 Technology Square, Cambridge, Massachusetts 02139 (US). **BHOSALE, Sandeep**

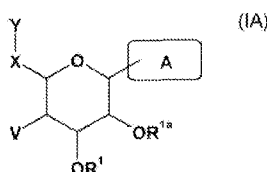
Bhauasaheb [IN/IN]; 1385, Sambhajinagar (HUDCO), A/ P & Tal. : Shirur, Pune, Maharashtra 412210 (IN). **BHUNIYA, Debnath** [IN/IN]; Post Khalisani, Howrah, West Bengal 711 037 (IN). **HAJARE, Atul Kashinath** [IN/IN]; Plot No. 28, Sadik Mala, Mali Lane, Bhingar, Ahmednagar, Maharashtra 414002 (IN). **MEN-GAWADE, Tanaji** [IN/IN]; A/P- Rajegaon, Tal- Dound, Pune, Maharashtra 413105 (IN). **MUKHOPADHYAY, Partha P.** [IN/IN]; Vill.- Barakuri, P.O.- Manbazar, Purulia, West Bengal 723131 (IN). **PALLE, P. Venkata** [US/IN]; 24 Gera Green Ville, Survey No. 64, Kharadi, Pune, Maharashtra 411 014 (IN). **REDDY, Dumbala Srinivas** [IN/IN]; Alpha 605, Jayabheri Silicon County, Hi-Tec City Road, Kondapur, Hyderabad, Andhra Pradesh 500 032 (IN).

(74) Agent: **CAMPBELL, Lachlan**; Novartis Pharma AG, Patent Department, CH-4002 Basel (CH).

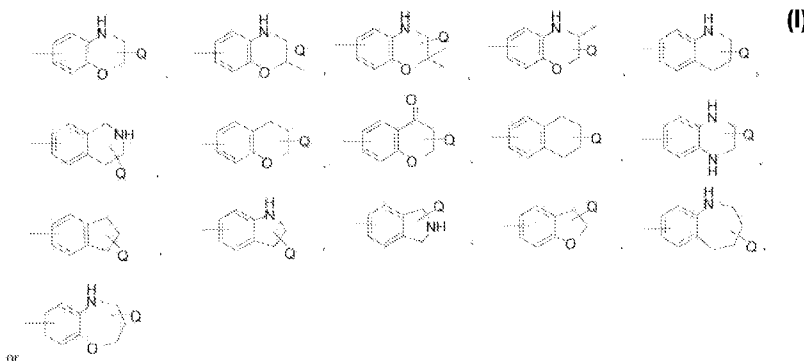
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI,

[Continued on next page]

(54) Title: FUSED HETEROCYCLIC C-GLYCOSIDES FOR THE TREATMENT OF DIABETES



(57) Abstract: The present invention provides compounds of Formula (IA) wherein A is selected from Formula (II) which have an inhibitory effect on the sodium dependent glucose transporter SGLT and their use in the treatment of diabetes.





NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK,

Published:

- with international search report (*Art. 21(3)*)
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (*Rule 48.2(h)*)

FUSED HETEROCYCLIC C-GLYCOSIDES FOR THE TREATMENT OF DIABETES

The invention relates to compounds which have an inhibitory effect on the sodium-dependent glucose cotransporter SGLT and their use in therapy.

This disclosure relates to a series of novel glycoside derivatives, their polymorphs, stereoisomers, prodrugs, solvates, pharmaceutically acceptable salts and formulations thereof. The disclosure also relates to the process for preparation of substituted glycoside derivatives along with their sodium-D-glucose cotransporter (SGLT) inhibition effects, which are beneficial for the prophylaxis, management, treatment, control of progression, or adjunct treatment of diseases and/or medical conditions where the inhibition of SGLT would be beneficial, such as diabetes (including Type-I and Type-II), obesity, dyslipidemia, insulin resistance, and other metabolic syndrome, and/or diabetes-related complications including retinopathy, nephropathy, neuropathy, ischemic heart disease, arteriosclerosis, β -cell dysfunction, and as therapeutic and/or prophylactic agents for obesity.

Diabetes mellitus is a metabolic disorder characterized by recurrent or persistent hyperglycemia (high blood glucose) and other signs, as distinct from a single disease or condition. Glucose level abnormalities can result in serious long-term complications, which include cardiovascular disease, chronic renal failure, retinal damage, nerve damage (of several kinds), microvascular damage and obesity.

Type 1 diabetes, also known as Insulin Dependent Diabetes Mellitus (IDDM), is characterized by loss of the insulin-producing β -cells of the islets of Langerhans of the pancreas leading to a deficiency of insulin. Type-2 diabetes previously known as adult-onset diabetes, maturity-onset diabetes, or Non-Insulin Dependent Diabetes Mellitus (NIDDM) – is due to a combination of increased hepatic glucose output, defective insulin secretion, and insulin resistance or reduced insulin sensitivity (defective responsiveness of tissues to insulin).

Chronic hyperglycemia can also lead to onset or progression of glucose toxicity characterized by decrease in insulin secretion from β -cell, insulin sensitivity; as a result diabetes mellitus is self-exacerbated [*Diabetes Care*, 1990, 13, 610].

Chronic elevation of blood glucose level also leads to damage of blood vessels. In diabetes, the resultant problems are grouped under "microvascular disease" (due to damage of small blood vessels) and "macrovascular disease" (due to damage of the arteries). Examples of microvascular disease include diabetic retinopathy, neuropathy and nephropathy, while examples of macrovascular disease include coronary artery disease, stroke, peripheral vascular disease, and diabetic myonecrosis.

Diabetic retinopathy, characterized by the growth of weakened blood vessels in the retina as well as macular edema (swelling of the macula), can lead to severe vision loss or blindness. Retinal damage (from microangiopathy) makes it the most common cause of blindness among non-elderly adults in the US. Diabetic neuropathy is characterized by compromised nerve function in the lower extremities. When combined with damaged blood vessels, diabetic neuropathy can lead to diabetic foot. Other forms of diabetic neuropathy may present as mononeuritis or autonomic neuropathy. Diabetic nephropathy is characterized by damage to the kidney, which can lead to chronic renal failure, eventually requiring dialysis. Diabetes mellitus is the most common cause of adult kidney failure worldwide. A high glycemic diet (i.e., a diet that consists of meals that give high postprandial blood sugar) is known to be one of the causative factors contributing to the development of obesity.

Type 2 diabetes is characterized by insulin resistance and/or inadequate insulin secretion in response to elevated glucose level. Therapies for type 2 diabetes are targeted towards increasing insulin sensitivity (such as TZDs), hepatic glucose utilization (such as biguanides), directly modifying insulin levels (such as insulin, insulin analogs, and insulin secretagogues), increasing incretin hormone action (such as exenatide and sitagliptin), or inhibiting glucose absorption from the diet (such as alpha glucosidase inhibitors) [*Nature* **2001**, 414, 821-827].

Glucose is unable to diffuse across the cell membrane and requires transport proteins. The transport of glucose into epithelial cells is mediated by a secondary active cotransport system, the sodium-D-glucose cotransporter (SGLT), driven by a sodium-gradient generated by the Na⁺/K⁺-ATPase. Glucose accumulated in the epithelial cell is further transported into the blood across the membrane by facilitated diffusion through GLUT transporters [*Kidney International* **2007**, 72, S27-S35].

SGLT belongs to the sodium/glucose cotransporter family SLCA5. Two different SGLT isoforms, SGLT1 and SGLT2, have been identified to mediate renal tubular glucose reabsorption in humans [*Curr. Opinon in Investigational Drugs* (2007): 8(4), 285-292 and references cited herein]. Both of them are characterized by their different substrate affinity. Although both of them show 59% homology in their amino acid sequence, they are functionally different. SGLT1 transports glucose as well as galactose, and is expressed both in the kidney and in the intestine, while SGLT2 is found exclusively in the S1 and S2 segments of the renal proximal tubule. As a consequence, glucose filtered in the glomerulus is reabsorbed into the renal proximal tubular epithelial cells by SGLT2, a low-affinity/high-capacity system, residing on the surface of epithelial cell lining in S1 and S2 tubular segments. Much smaller amounts of glucose are recovered by SGLT1, as a high-affinity/low-capacity system, on the more distal segment of the proximal tubule. In healthy human, more than 99% of plasma glucose that is filtered in the kidney glomerulus is reabsorbed, resulting in less than 1% of the total filtered glucose being excreted in urine. It is estimated that 90% of total renal glucose absorption is facilitated by SGLT2; remaining 10% is likely mediated by SGLT1 [*J. Parenter. Enterl Nutr.* **2004**, 28, 364-371].

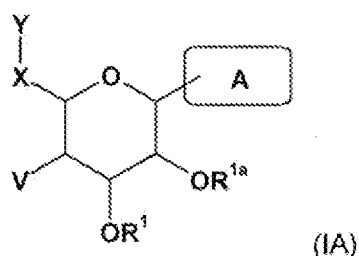
The SGLT2 was cloned as a candidate sodium glucose cotransporter, and its tissue distribution, substrate specificity, and affinities are reportedly very similar to those of the low-affinity sodium glucose co-transporter in the renal proximal tubule. A drug with a mode of action of SGLT2 inhibition will be a novel and complementary approach to existing classes of medication for diabetes and its associated diseases to meet the patient's needs for both blood glucose control, while preserving insulin secretion. In addition, SGLT2 inhibitors which lead to loss of excess glucose thereby excess calorie may have additional potential for the treatment of obesity.

Indeed small molecule SGLT2 inhibitors have been discovered and antidiabetic therapeutic potential of such molecules have been reported in literature [T-1095 (Diabetes, 1999, 48, 1794-1800, Dapagliflozin (Diabetes, 2008, 57, 1723-1729)]. Various O-aryl and O-heteroaryl glycosides have been reported as SGLT-2 inhibitors in patent publications such as: WO 01/74834, WO 03/020737, US 04/0018998, WO 01/68660, WO 01/16147, WO 04/099230, WO 05/011592, US 06/0293252, WO 05/021566. Various glucopyranosyl-substituted aromatic and heteroaromatic compounds

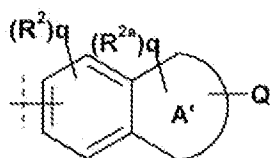
have also been reported as SGLT-2 inhibitors in patent publications such as: WO 01/27128, WO 04/080990, US 06/0025349, WO 05/085265, WO 05/085237, WO 06/054629, WO 06/011502. Glucopyranosyl-substituted aromatic or heteroaromatic compounds where, in general, the sugar moiety has been modified at C4, C5, or C6 positions of pyranose have been published (US 06/0009400, US 06/0019948, US 06/0035841, US 06/0074031, US 08/0027014, WO 08/016132).

For the purposes of this invention inhibition of SGLT means inhibitions exclusively of SGLT2, inhibitions exclusively of SGLT1 or inhibition of both SGLT1 and SGLT2.

Accordingly, in one aspect, the invention provides compounds of Formula (IA):



wherein



A is

A' is a heterocyclyl or carbocyclyl;

Q is L_a-X_a or R^{10} ;

L_a is $-Z'-Y'-Z''-$;

Z' and Z'' are each, independently, a bond, C_{1-4} alkylene or C_{2-4} alkenylene,

where Z' and Z'' together make no more than a 4-carbon chain and the hydrocarbon bonds may be optionally substituted by one or more hydroxy or halogens.

Y' is $-O-$, $-S(O)_p-$, $-N(R^3)-$, $-C(R')(R'')-$, $-C(O)-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-N(R^3)C(O)N(R^3)-$, $-N(R^3)SO_2-$, or $-SO_2N(R^3)-$;

V is halogen, $-OR^{1b}$ or hydrogen;

$m = 0-4$;

$n = 0-4$;

$p = 0-2$;

R' and R'' are independently, hydrogen, halogen, C₁₋₆ alkyl, perhaloalkyl, or taken together form a cyclic ring which may optionally have heteroatoms selected from O, N or S;

R¹, R^{1a} and R^{1b} are independently selected from hydrogen, C₁₋₆ alkyl, C₆₋₁₀aryl-C₁₋₄alkyl, -C(O)C₆₋₁₀aryl or -C(O)C₁₋₆alkyl;

R² and R^{2a} are independently halogen, hydroxy, C₁₋₄hydroxyalkyl, cyano, nitro, -NR⁴R⁵, -CH₂NR⁴R⁵, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₁₋₄ alkoxy, C₃₋₇ cycloalkoxy, -S(O)_pR³, -S(O)₂NR⁴R⁵, -OS(O)₂R³, -C(O)R³, -C(O)OR³, -CH₂C(O)OR³, -C(O)NR⁴R⁵, -CH₂C(O)NR⁴R⁵, -NR³C(O)NR⁴R⁵, -NR³C(O)OR³, C₁₋₆ haloalkyl, C₁₋₆ perhaloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, C₆₋₁₀aryl, C₆₋₁₀arylC₁₋₄alkyl, C₆₋₁₀aryloxy, C₂₋₁₀heterocyclyl, C₂₋₁₀heterocyclylC₁₋₄alkyl, C₁₋₁₀heteroarylC₁₋₄alkyl, C₁₋₁₀heteroaryl, C₁₋₁₀heteroaryloxy, or C₁₋₁₀heterocycloxy;

R³ is hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₆₋₁₀aryl, C₁₋₁₀heteroaryl, or C₂₋₁₀heterocyclyl;

q = 0-3;

X is [C(R⁶)(R⁷)]_i;

Y is H, C₁₋₄ alkyl, OR¹ or NR⁸R⁹

t = 1-3;

R⁶ and R⁷ are independently hydrogen or C₁₋₆ alkyl, or R⁶ and R⁷ form an oxo group and t=1, or when R⁶ and R⁷ are C₁₋₄alkyl on the same carbon they can be taken together to form a cyclic ring which may contain N, S or O atoms;

R⁴ and R⁵ are independently hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkylC₁₋₄alkyl, arylC₁₋₄alkyl, C₆₋₁₀aryl, C₁₋₁₀heteroaryl, C₁₋₁₀heteroarylC₁₋₄alkyl, C₂₋₁₀heterocyclyl, C₂₋₁₀heterocyclylC₁₋₄alkyl or

R⁴ and R⁵ taken together may form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N or S, the said ring system may further be optionally substituted; and

R⁸ and R⁹ are independently hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkylC₁₋₄alkyl, arylC₁₋₄alkyl, C₆₋₁₀aryl, C₁₋₁₀heteroaryl, C₁₋₁₀heteroarylC₁₋₄alkyl, C₂₋₁₀heterocyclyl, C₂₋₁₀heterocyclylC₁₋₄alkyl or

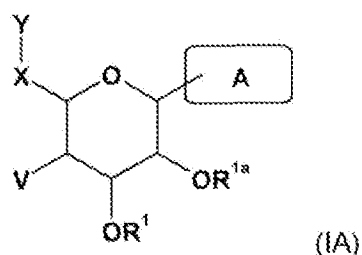
R⁸ and R⁹ along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may

optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted;

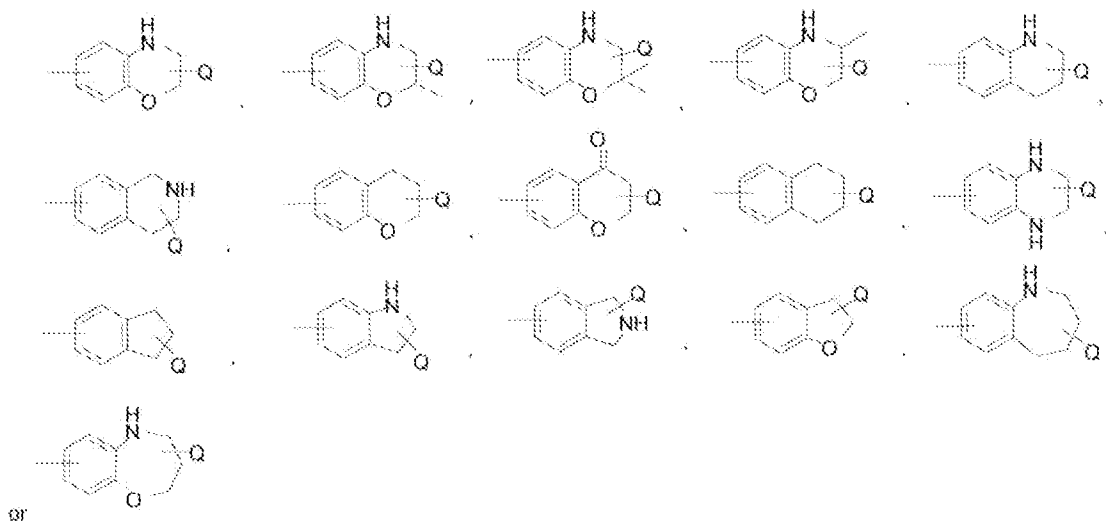
R^{10} is C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{3-7} cycloalkyl, C_{2-10} heterocyclyl, where C_{1-4} alkyl may be optionally substituted by one or more hydroxy or halogens; and X_a is halogen, hydroxy, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-4} alkyl, C_{1-4} hydroxyalkyl, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, trihalo C_{1-4} alkoxy, C_{3-7} cycloalkoxy, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-4} alkyl, C_{6-10} aryloxy, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{1-10} heteroaryloxy, or C_{1-10} heterocycloxy; or

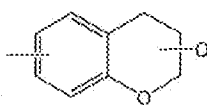
a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, or a prodrug thereof.

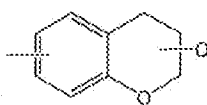
In another aspect, the invention provides compounds of Formula (IA):



wherein A is selected from:





provided that when A is , it is not substituted with hydroxy or methoxy;

Q is L_a-X_a or R^{10} ;

L_a is $-Z'-Y'-Z''-$;

Z' and Z'' are each, independently, a bond, C_{1-4} alkylene or C_{2-4} alkenylene, where Z' and Z'' together make no more than a 4-carbon chain and the hydrocarbon bonds may be optionally substituted by one or more hydroxy or halogens.

Y' is $-O-$, $-S(O)_p-$, $-N(R^3)-$, $-C(R')(R'')-$, $-C(O)-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-N(R^3)C(O)N(R^3)-$, $-N(R^3)SO_2-$, or $-SO_2N(R^3)-$;

V is halogen, $-OR^{1b}$ or hydrogen;

$m = 0-4$;

$n = 0-4$;

$p = 0-2$;

R' and R'' are independently, hydrogen, halogen, C_{1-6} alkyl, perhaloalkyl, or taken together form a cyclic ring which may optionally have heteroatoms selected from O, N or S;

R^1 , R^{1a} and R^{1b} are independently selected from hydrogen, C_{1-6} alkyl, C_{6-10} aryl- C_{1-4} alkyl, $-C(O)C_{6-10}$ aryl or $-C(O)C_{1-6}$ alkyl;

R^2 and R^{2a} are independently halogen, hydroxy, C_{1-4} hydroxyalkyl, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-4} alkoxy, C_{3-7} cycloalkoxy, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{3-7} cycloalkyl- C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl- C_{1-4} alkyl, C_{6-10} aryloxy, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl- C_{1-4} alkyl, C_{1-10} heteroaryl- C_{1-4} alkyl, C_{1-10} heteroaryl, C_{1-10} heteroaryloxy, or C_{1-10} heterocycloxy;

R^3 is hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{6-10} aryl, C_{1-10} heteroaryl, or C_{2-10} heterocyclyl;

$q = 0-3$;

X is $[C(R^6)(R^7)]_i$;

Y is H, C_{1-4} alkyl, OR^1 or NR^5R^9

$t = 1-3$;

R^6 and R^7 are independently hydrogen or C_{1-6} alkyl, or R^6 and R^7 form an oxo group and $t=1$, or when R^6 and R^7 are C_{1-4} alkyl on the same carbon they can be taken together to form a cyclic ring which may contain N, S or O atoms;

R^4 and R^5 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or

R^4 and R^5 taken together may form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N or S, the said ring system may further be optionally substituted; and

R^8 and R^9 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or

R^8 and R^9 along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted;

R^{10} is C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{3-7} cycloalkyl, C_{2-10} heterocyclyl, where C_{1-4} alkyl may be optionally substituted by one or more hydroxy or halogens and C_{6-10} aryl may be optionally substituted with one or more C_{1-4} alkyl, C_{1-4} alkoxy, or C_{1-4} haloalkyl; and

X_a is halogen, hydroxy, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{1-4} alkoxy, trihalo C_{1-4} alkoxy, an optionally substituted C_{3-7} cycloalkoxy, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, an optionally substituted C_{3-7} cycloalkyl, an optionally substituted C_{3-7} cycloalkyl C_{1-4} alkyl, an optionally substituted C_{6-10} aryl, an optionally substituted C_{6-10} aryl C_{1-4} alkyl, an optionally substituted C_{6-10} aryloxy, an optionally substituted C_{2-10} heterocyclyl, an optionally substituted C_{2-10} heterocyclyl C_{1-4} alkyl, an optionally substituted C_{1-10} heteroaryl, an optionally substituted C_{1-10} heteroaryl C_{1-4} alkyl, an optionally substituted C_{1-10} heteroaryloxy, or an optionally substituted C_{1-10} heterocycloxy; or a pharmaceutically acceptable salt thereof.

Definitions

For purposes of interpreting this specification, the following definitions will apply and whenever appropriate, terms used in the singular will also include the plural and vice versa.

As used herein, the term "alkyl" refers to a fully saturated branched or unbranched hydrocarbon moiety. Preferably the alkyl comprises 1 to 20 carbon atoms, more preferably 1 to 16 carbon atoms, 1 to 10 carbon atoms, 1 to 7 carbon atoms, or 1 to 4 carbon atoms. Representative examples of alkyl include methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *sec*-butyl, *iso*-butyl, *tert*-butyl, *n*-pentyl, isopentyl, neopentyl, *n*-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, *n*-heptyl, *n*-octyl, *n*-nonyl, or *n*-decyl.

"Alkylene" refers to a straight or branched divalent hydrocarbon chain consisting solely of carbon and hydrogen atoms, having from one to twelve carbon atoms, and linking the rest of the molecule to a radical group, e.g., methylene, ethylene, propylene, *n*-butylene, and the like. The alkylene is attached to the rest of the molecule through a single bond and to the radical group through a single bond. The points of attachment of the alkylene to the rest of the molecule and to the radical group can be through one carbon or any two carbons within the chain. Unless stated otherwise specifically in the specification, an alkylene group may be optionally substituted by one or more of the following groups: C₁₋₄ alkyl, trihaloC₁₋₄ alkyl, halogen (especially fluoro) or hydroxyl.

As used herein, the term "haloalkyl" refers to an alkyl as defined herein, that is substituted by one or more halo groups as defined herein. Preferably the haloalkyl can be monohaloalkyl, dihaloalkyl or polyhaloalkyl including perhaloalkyl. A monohaloalkyl can have one iodo, bromo, chloro or fluoro within the alkyl group. Dihalalkyl and polyhaloalkyl groups can have two or more of the same halo atoms or a combination of different halo groups within the alkyl. Preferably, the polyhaloalkyl contains up to 12, or 10, or 8, or 6, or 4, or 3, or 2 halo groups. Non-limiting examples of haloalkyl include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl. A perhaloalkyl refers to an alkyl having all hydrogen atoms replaced with halo atoms. C₁₋₆ haloalkyl refers to an alkyl group substituted by up to seven halogen groups, e.g. fluoro

groups. For example, where the substituent is fluoro, common haloalkyl groups are trifluoroalkyl, 2,2,2-trifluoroethyl or 2,2,2,1,1-pentafluoroethyl groups.

"Halogen" or "halo" may be fluorine, chlorine, bromine or iodine.

The term "alkenyl" refers to a monovalent group derived from a hydrocarbon having at least one carbon-carbon double bond. The term "C₂-C₆alkenyl" refers to a monovalent group derived from a hydrocarbon having two to six carbon atoms and comprising at least one carbon-carbon double bond.

The term "alkynyl" refers to a monovalent group derived from a hydrocarbon having at least one carbon-carbon triple bond. The term "C₂-C₆alkynyl" refers to a monovalent group derived from a hydrocarbon having two to six carbon atoms and comprising at least one carbon-carbon triple bond.

The term "aryl" refers to monocyclic or bicyclic aromatic hydrocarbon groups having 6-20 carbon atoms in the ring portion. Preferably, the aryl is a (C₆-C₁₀) aryl. Representative examples are phenyl, biphenyl, naphthyl, anthracyl, phenanthryl or tetrahydronaphthyl. An aryl group may optionally be substituted by 1-4 independently selected substituents. Preferred substituents for an aryl group are alkyl, trifluoromethyl, trifluoromethoxy, cycloalkyl, cycloalkoxy, halogen, hydroxy, alkoxy, acyl, alkyl-C(O)-O--, aryl-O--, heteroaryl-O--, amino, thiol, alkyl-S--, aryl-S--, nitro, cyano, carboxy, alkyl-O-C(O)--, carbamoyl, alkyl-S(O)--, alkylsulfonyl, alkylsulfonamido, and heterocyclyl.

The term "aryl" also refers to a bicyclic or polycyclic group in which a monocyclic aryl ring is fused to one or more heterocyclyl rings or carbocyclic rings, where the radical or point of attachment is on the aryl ring. Nonlimiting examples include benzoxazine, quinoline, isoquinoline, indole, isoindole, chroman, quinoxaline, benzoazepine, oxa-aza-benzocycloheptene, benzofuran, tetrahydronaphthalene and indan.

Furthermore, the term "aryl" as used herein, refers to an aromatic substituent which can be a single aromatic ring, or multiple aromatic rings that are fused together, linked covalently, or linked to a common group such as a methylene or ethylene moiety. The common linking group also can be a carbonyl as in benzophenone or oxygen as in diphenylether or nitrogen as in diphenylamine.

As used herein, the term "alkoxy" refers to alkyl-O-, wherein alkyl is defined herein above. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, *tert*-butoxy, pentyloxy, hexyloxy, cyclopropyloxy-, or cyclohexyloxy-. Preferably, alkoxy groups have about 1-7, more preferably about 1-4 carbons.

As used herein, the term "acyl" refers to a group R-C(O)- of from 1 to 10 carbon atoms of a straight, branched, or cyclic configuration or a combination thereof, attached to the parent structure through carbonyl functionality. Such group can be saturated or unsaturated, and aliphatic or aromatic. Preferably, R in the acyl residue is alkyl, or alkoxy, or aryl, or heteroaryl. Also preferably, one or more carbons in the acyl residue may be replaced by nitrogen, oxygen or sulfur as long as the point of attachment to the parent remains at the carbonyl. Examples of acyl include acetyl, benzoyl, propionyl, isobutyryl, *t*-butoxycarbonyl, benzyloxycarbonyl and the like. Lower acyl refers to acyl containing one to four carbons.

As used herein, the term "carbamoyl" refers to H₂NC(O)-, alkyl-NHC(O)-, (alkyl)₂NC(O)-, aryl-NHC(O)-, alkyl(aryl)-NC(O)-, heteroaryl-NHC(O)-, alkyl(heteroaryl)-NC(O)-, aryl-alkyl-NHC(O)-, or alkyl(aryl-alkyl)-NC(O)-.

As used herein, the term "sulfonyl" refers to R-SO₂-, wherein R is hydrogen, alkyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, alkoxy, aryloxy, cycloalkyl, or heterocyclyl.

As used herein, the term "sulfonamido" refers to alkyl-S(O)₂-NH-, aryl-S(O)₂-NH-, aryl-alkyl-S(O)₂-NH-, heteroaryl-S(O)₂-NH-, heteroaryl-alkyl-S(O)₂-NH-, alkyl-S(O)₂-N(alkyl)-, aryl-S(O)₂-N(alkyl)-, aryl-alkyl-S(O)₂-N(alkyl)-, heteroaryl-S(O)₂-N(alkyl)-, or heteroaryl-alkyl-S(O)₂-N(alkyl)-.

As used herein, the term "heterocyclyl" or "heterocyclo" refers to an optionally substituted, saturated or unsaturated non-aromatic ring or ring system, *e.g.*, which is a 4-, 5-, 6-, or 7-membered monocyclic, 7-, 8-, 9-, 10-, 11-, or 12-membered bicyclic or 10-, 11-, 12-, 13-, 14- or 15-membered tricyclic ring system and contains at least one heteroatom selected from O, S and N, where the N and S can also optionally be oxidized to various oxidation states. The heterocyclic group can be attached at a heteroatom or a carbon atom. The heterocyclyl can include fused or bridged rings as well as spirocyclic

rings. Examples of heterocycles include dihydrofuranyl, [1,3]dioxolane, 1, 4-dioxane, 1,4-dithiane, piperazinyl, 1,3-dioxolane, imidazolidinyl, imidazoliny, pyrrolidine, dihydropyran, oxathiolane, dithiolane, 1,3-dioxane, 1,3-dithianyl, oxathianyl, thiomorpholino, oxiranyl, aziridinyl, oxetanyl, azetidiny, tetrahydrofuranyl, pyrrolidinyl, tetrahydropyranyl, piperidinyl, morpholino, thiomorpholinyl, piperazinyl, azepiny, oxapiny, oxazepiny and diazepiny.

The term "heterocyclyl" further refers to heterocyclic groups as defined herein substituted with 1, 2 or 3 substituents selected from the groups consisting of the following:

- (a) alkyl;
- (b) hydroxy (or protected hydroxy);
- (c) halo;
- (d) oxo, i.e., =O;
- (e) amino (i.e. NH₂), alkylamino (i.e. NH-alkyl) or dialkylamino;
- (f) alkoxy;
- (g) cycloalkyl;
- (h) carboxyl;
- (i) heterocycloxy, wherein heterocycloxy denotes a heterocyclic group bonded through an oxygen bridge;
- (j) alkyl-O-C(O)---;
- (k) mercapto;
- (l) nitro;
- (m) cyano;
- (n) sulfamoyl or sulfonamido;
- (o) aryl;
- (p) alkyl-C(O)-O---;
- (q) aryl-C(O)-O---;
- (r) aryl-S---;
- (s) aryloxy;
- (t) alkyl-S---;
- (u) formyl, i.e., HC(O)---;
- (v) carbamoyl;
- (w) aryl-alkyl---; and

(x) aryl substituted with alkyl, cycloalkyl, alkoxy, hydroxy, amino, alkyl-C(O)-NH-, alkylamino, dialkylamino or halogen.

As used herein, the term "heterocyclalkyl" is a heterocycl as defined above bonded through an alkyl group, such as morpholine-CH₂-.

As used herein, the term "cycloalkyl" or "carbocycl" refers to saturated or unsaturated monocyclic, bicyclic or tricyclic hydrocarbon groups of 3-12 carbon atoms, preferably 3-9, or 3-7 carbon atoms, each of which can be optionally substituted by one, or two, or three, or more substituents, such as alkyl, halo, oxo, hydroxy, alkoxy, alkyl-C(O)-, acylamino, carbamoyl, alkyl-NH-, (alkyl)₂N-, thiol, alkyl-S-, nitro, cyano, carboxy, alkyl-O-C(O)-, sulfonyl, sulfonamido, sulfamoyl, or heterocycl. Exemplary monocyclic hydrocarbon groups include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentenyl, cyclohexyl or cyclohexenyl. Exemplary bicyclic hydrocarbon groups include bornyl, indyl, hexahydroindyl, tetrahydronaphthyl, decahydronaphthyl, bicyclo[2.1.1]hexyl, bicyclo[2.2.1]heptyl, bicyclo[2.2.1]heptenyl, 6,6-dimethylbicyclo[3.1.1]heptyl, 2,6,6-trimethylbicyclo[3.1.1]heptyl, or bicyclo[2.2.2]octyl. Exemplary tricyclic hydrocarbon groups include adamantyl.

As used herein, the term "sulfamoyl" refers to H₂NS(O)₂-, alkyl-NHS(O)₂-, (alkyl)₂NS(O)₂-, aryl-NHS(O)₂-, alkyl(aryl)-NS(O)₂-, (aryl)₂NS(O)₂-, heteroaryl-NHS(O)₂-, (aryl-alkyl)-NHS(O)₂-, or (heteroaryl-alkyl)-NHS(O)₂-.

As used herein, the term "aryloxy" refers to both an -O-aryl and an -O-heteroaryl group, wherein aryl and heteroaryl are defined herein.

As used herein, the term "heteroaryl" refers to a 5-14 membered monocyclic- or bicyclic- or polycyclic-aromatic ring system, having 1 to 8 heteroatoms selected from N, O or S. Preferably, the heteroaryl is a 5-10 or 5-7 membered ring system. A heteroaryl group may be optionally substituted with 1-4 independently selected substituents. Preferred substituents for an heteroaryl group include alkyl and halogen. Examples of monocyclic heteroaryl groups include pyridyl, thienyl, furanyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl and tetrazolyl. Examples of bicyclic heteroaryl groups include indolyl, benzofuranyl, quinolyl, isoquinolyl

indazolyl, indolyl, isoindolyl, indolizyl, benzamidazolyl, and quinolyl. More specific heteroaryl groups include 2- or 3-thienyl, 2- or 3-furyl, 2- or 3-pyrrolyl, 2-, 4-, or 5-imidazolyl, 3-, 4-, or 5-pyrazolyl, 2-, 4-, or 5-thiazolyl, 3-, 4-, or 5-isothiazolyl, 2-, 4-, or 5-oxazolyl, 3-, 4-, or 5-isoxazolyl, 3- or 5-1,2,4-triazolyl, 4- or 5-1,2,3-triazolyl, tetrazolyl, 2-, 3-, or 4-pyridyl, 3- or 4-pyridazinyl, 3-, 4-, or 5-pyrazinyl, 2-pyrazinyl, 2-, 4-, or 5-pyrimidinyl.

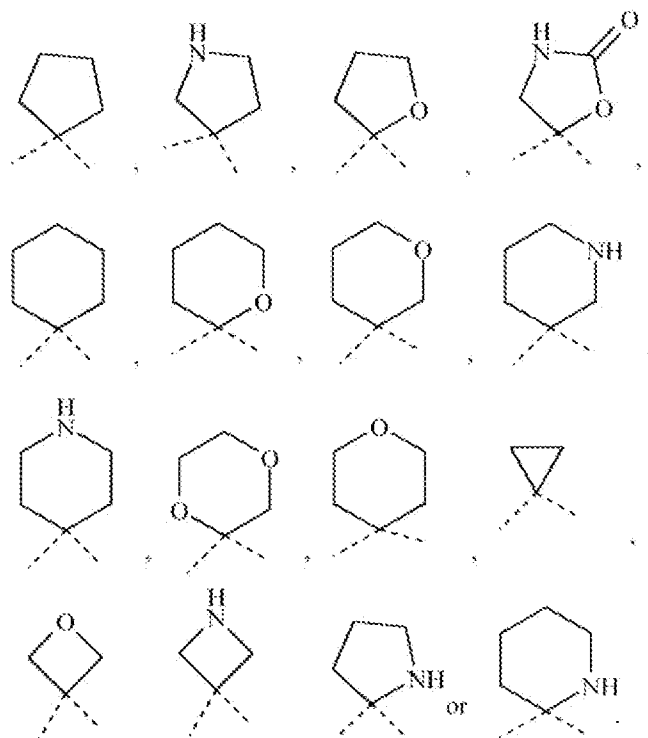
The term "heteroaryl" also refers to a group in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocyclyl rings, where the radical or point of attachment is on the heteroaromatic ring. Representative examples are 1-, 2-, 3-, 5-, 6-, 7-, or 8-indolizyl, 1-, 3-, 4-, 5-, 6-, or 7-isoindolyl, 2-, 3-, 4-, 5-, 6-, or 7-indolyl, 2-, 3-, 4-, 5-, 6-, or 7-indazolyl, 2-, 4-, 5-, 6-, 7-, or 8-purinyl, 1-, 2-, 3-, 4-, 6-, 7-, 8-, or 9-quinolizyl, 2-, 3-, 4-, 5-, 6-, 7-, or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7-, or 8-isoquinolyl, 1-, 4-, 5-, 6-, 7-, or 8-phthalazinyl, 2-, 3-, 4-, 5-, or 6-naphthyridinyl, 2-, 3-, 5-, 6-, 7-, or 8-quinazolinyl, 3-, 4-, 5-, 6-, 7-, or 8-cinnolyl, 2-, 4-, 6-, or 7-pteridinyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, or 8-4aH carbazolyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, or 8-carbazolyl, 1-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-carbolyl, 1-, 2-, 3-, 4-, 6-, 7-, 8-, 9-, or 10-phenanthridinyl, 1-, 2-, 3-, 4-, 5-, 6-, 7-, 8-, or 9-acridinyl, 1-, 2-, 4-, 5-, 6-, 7-, 8-, or 9-perimidinyl, 2-, 3-, 4-, 5-, 6-, 8-, 9-, or 10-phenanthrolinyl, 1-, 2-, 3-, 4-, 6-, 7-, 8-, or 9-phenazinyl, 1-, 2-, 3-, 4-, 6-, 7-, 8-, 9-, or 10-phenothiazinyl, 1-, 2-, 3-, 4-, 6-, 7-, 8-, 9-, or 10-phenoxazinyl, 2-, 3-, 4-, 5-, 6-, or 1-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, or 10-benzisoguinolyl, 2-, 3-, 4-, or thieno[2,3-b]furanyl, 2-, 3-, 5-, 6-, 7-, 8-, 9-, 10-, or 11-7H-pyrazino[2,3-c]carbazolyl, 2-, 3-, 5-, 6-, or 7-2H-furo[3,2-b]pyranyl, 2-, 3-, 4-, 5-, 7-, or 8-5H-pyrido[2,3-d]-o-oxazinyl, 1-, 3-, or 5-1H-pyrazolo[4,3-d]-oxazolyl, 2-, 4-, or 5-4H-imidazo[4,5-d]thiazolyl, 3-, 5-, or 8-pyrazino[2,3-d]pyridazinyl, 2-, 3-, 5-, or 6-imidazo[2,1-b]thiazolyl, 1-, 3-, 6-, 7-, 8-, or 9-furo[3,4-c]cinnolyl, 1-, 2-, 3-, 4-, 5-, 6-, 8-, 9-, 10-, or 11-4H-pyrido[2,3-c]carbazolyl, 2-, 3-, 6-, or 7-imidazo[1,2-b][1,2,4]triazinyl, 7-benzo[b]thienyl, 2-, 4-, 5-, 6-, or 7-benzoxazolyl, 2-, 4-, 5-, 6-, or 7-benzimidazolyl, 2-, 4-, 5-, 6-, or 7-benzothiazolyl, 1-, 2-, 4-, 5-, 6-, 7-, 8-, or 9-benzoxapinyl, 2-, 4-, 5-, 6-, 7-, or 8-benzoxazinyl, 1-, 2-, 3-, 5-, 6-, 7-, 8-, 9-, 10-, or 11-1H-pyrrolo[1,2-b][2]benzazapinyl. Typical fused heteroaryl groups include, but are not limited to 2-, 3-, 4-, 5-, 6-, 7-, or 8-quinolyl, 1-, 3-, 4-, 5-, 6-, 7-, or 8-isoquinolyl, 2-, 3-, 4-, 5-, 6-, or 7-indolyl, 2-, 3-, 4-, 5-, 6-, or 7-benzo[b]thienyl, 2-, 4-, 5-, 6-, or 7-benzoxazolyl, 2-, 4-, 5-, 6-, or 7-benzimidazolyl, 2-, 4-, 5-, 6-, or 7-benzothiazolyl.

A heteroaryl group may be mono-, bi-, tri-, or polycyclic, preferably mono-, bi-, or tricyclic, more preferably mono- or bicyclic.

Unless otherwise mentioned, alkyl, alkenyl, alkoxy, cycloalkyl, aryl, arylalkyl, heteroaryl, heterocyclyl, heterocyclylalkyl may be optionally substituted with one or more than one substituents selected from hydroxyl, cyano, nitro, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, C₁₋₆-alkoxy, C₂₋₆-alkenyloxy, C₂₋₆-alkynyloxy, halogen, haloalkyl, perhaloalkyl, C₁₋₆-alkylcarbonyl, (CH₂)_n-COOR³, amino, C₁₋₆-alkylamino, di-C₁₋₆-alkylamino, C₁₋₆-alkylaminocarbonyl, di-C₁₋₆-alkylaminocarbonyl, C₁₋₆-alkylcarbonylamino, C₁₋₆-alkylcarbonyl(C₁₋₆-alkyl)amino, C₁₋₆-alkylsulfonylamino, C₁₋₆-alkylsulfonyl(C₁₋₆-alkyl)amino, C₁₋₆-thioalkyl, C₁₋₆-alkylsulfanyl, C₁₋₆-alkylsulfinyl, C₁₋₆-alkylsulfonyl, aminosulfonyl, C₁₋₆-alkylaminosulfonyl and di-C₁₋₆-alkylaminosulfonyl, aminocarbonylC₁₋₆-alkyl, C₁₋₆-aminocarbonylC₁₋₆-alkyl, di-C₁₋₆-aminocarbonylC₁₋₆-alkyl, sulfanylC₁₋₆-alkyl, C₁₋₆-alkylsulfanylC₁₋₆-alkyl, sulfinylC₁₋₆-alkyl, C₁₋₆-alkylsulfinylC₁₋₆-alkyl, sulfonylC₁₋₆-alkyl, C₁₋₆-alkylsulfonylC₁₋₆-alkyl, cycloalkyl, aryl, heterocyclyl, heteroaryl, where each of the aforementioned hydrocarbon groups may be optionally substituted by one or more halogen, alkyl, hydroxyl, oxo, C₁₋₆-alkoxy, amino, C₁₋₆-alkylamino, di-C₁₋₆-alkylamino or cyano.

"Heteroaryl" and "heterocyclyl" is also intended to include oxidized S or N, such as sulfinyl, sulfonyl and N-oxide of tertiary ring nitrogen.

Two substituents on the same carbon may be taken together can form a cyclic ring, which may optionally have heteroatoms selected from O, N or S. Non limitative examples of such cyclic rings are as follows:



"Prodrugs" is meant to indicate a compound that may be converted under physiological conditions or by solvolysis to a biologically active compound of the invention. Thus, the term "prodrug" refers to a metabolic precursor of a compound of the invention that is pharmaceutically acceptable. A prodrug may be inactive when administered to a subject in need thereof, but is converted *in vivo* to an active compound of the invention.

Prodrugs are typically rapidly transformed *in vivo* to yield the parent compound of the invention, for example, by hydrolysis in blood or conversion in the gut or liver. The prodrug compound often offers advantages of solubility, tissue compatibility or delayed release in a mammalian organism (see, Bundgard, H., Design of Prodrugs (1985), pp. 7-9, 21-24 (Elsevier, Amsterdam)).

A discussion of prodrugs is provided in Higuchi, T., *et al.*, "Pro-drugs as Novel Delivery Systems," A.C.S. Symposium Series, Vol. 14, and in Bioreversible Carriers in Drug Design, ed. Edward B. Roche, Anglican Pharmaceutical Association and Pergamon Press, 1987.

"Optional" or "optionally" means that the subsequently described event or circumstances may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. For example, "optionally substituted aryl" means that the aryl radical may or may not be substituted and that the description includes both substituted aryl radicals and aryl radicals having no substitution.

"Pharmaceutically acceptable carrier, diluent or excipient" includes without limitation any adjuvant, carrier, excipient, glidant, sweetening agent, diluent, preservative, dye/colorant, flavor enhancer, surfactant, wetting agent, dispersing agent, suspending agent, stabilizer, isotonic agent, solvent, or emulsifier which has been approved by the United States Food and Drug Administration as being acceptable for use in humans or domestic animals.

"Pharmaceutically acceptable salt" includes both acid and base addition salts.

"Pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases, which are not biologically or otherwise undesirable, and which are formed with inorganic acids such as, but not limited to, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as, but not limited to, acetic acid, 2,2-dichloroacetic acid, adipic acid, alginic acid, ascorbic acid, aspartic acid, benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid, camphoric acid, camphor-10-sulfonic acid, capric acid, caproic acid, caprylic acid, carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, gluconic acid, glucuronic acid, glutamic acid, glutaric acid, 2-oxo-glutaric acid, glycerophosphoric acid, glycolic acid, hippuric acid, isobutyric acid, lactic acid, lactobionic acid, lauric acid, maleic acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, mucic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pantoic acid, propionic acid, pyroglutamic acid, pyruvic acid, salicylic acid, 4-aminosalicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid, thiocyanic acid, *p*-toluenesulfonic acid, trifluoroacetic acid, undecylenic acid, and the like.

"Pharmaceutically acceptable base addition salt" refers to those salts which retain the biological effectiveness and properties of the free acids, which are not biologically or otherwise undesirable. These salts are prepared from addition of an inorganic base or an organic base to the free acid. Salts derived from inorganic bases include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferred inorganic salts are the ammonium, sodium, potassium, calcium, and magnesium salts. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as ammonia, isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, diethanolamine, ethanolamine, deanol, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, benethamine, benzathine, ethylenediamine, glucosamine, methylglucamine, theobromine, triethanolamine, tromethamine, purines, piperazine, piperidine, *N*-ethylpiperidine, polyamine resins and the like. Particularly preferred organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline and caffeine.

Often crystallizations produce a solvate of the compound of the invention. As used herein, the term "solvate" refers to an aggregate that comprises one or more molecules of a compound of the invention with one or more molecules of solvent. The solvent may be water, in which case the solvate may be a hydrate. Alternatively, the solvent may be an organic solvent. Thus, the compounds of the present invention may exist as a hydrate, including a monohydrate, dihydrate, hemihydrate, sesquihydrate, trihydrate, tetrahydrate and the like, as well as the corresponding solvated forms. The compound of the invention may be true solvates, while in other cases, the compound of the invention may merely retain adventitious water or be a mixture of water plus some adventitious solvent.

A "pharmaceutical composition" refers to a formulation of a compound of the invention and a medium generally accepted in the art for the delivery of the biologically active

compound to mammals, e.g., humans. Such a medium includes all pharmaceutically acceptable carriers, diluents or excipients thereof.

As used herein, the terms "disease" and "condition" may be used interchangeably or may be different in that the particular malady or condition may not have a known causative agent (so that etiology has not yet been worked out) and it is therefore not yet recognized as a disease but only as an undesirable condition or syndrome, wherein a more or less specific set of symptoms have been identified by clinicians.

The compounds of the invention, or their pharmaceutically acceptable salts may contain one or more asymmetric centers and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (*R*)- or (*S*)- or as (*D*)- or (*L*)- for amino acids. The present invention is meant to include all such possible isomers, as well as their racemic and optically pure forms. Optically active (+) and (-), (*R*)- and (*S*)-, or (*D*)- and (*L*)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques, such as HPLC using a chiral column. When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both *E* and *Z* geometric isomers. Likewise, all tautomeric forms are also intended to be included.

A "stereoisomer" refers to a compound made up of the same atoms bonded by the same bonds but having different three-dimensional structures, which are not interchangeable. The present invention contemplates various stereoisomers and mixtures thereof and includes "enantiomers", which refers to two stereoisomers whose molecules are nonsuperimposable mirror images of one another.

The present invention includes all pharmaceutically acceptable isotopically-labeled compounds of Formula (I) wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number usually found in nature.

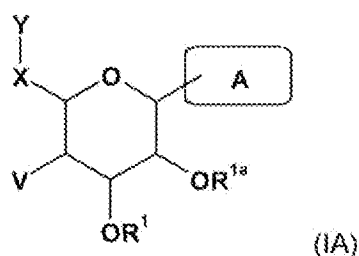
Examples of isotopes suitable for inclusion in the compounds of the invention comprises isotopes of hydrogen, such as ²H and ³H, carbon, such as ¹¹C, ¹³C and ¹⁴C, chlorine,

such as ^{36}Cl , fluorine, such as ^{18}F , iodine, such as ^{123}I and ^{125}I , nitrogen, such as ^{13}N and ^{15}N , oxygen, such as ^{15}O , ^{17}O and ^{18}O , phosphorus, such as ^{32}P , and sulphur, such as ^{35}S . Substitution with heavier isotopes such as deuterium, *i.e.* ^2H , may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be preferred in some circumstances. Isotopically-labeled compounds of Formula (I) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations Sections using an appropriate isotopically-labeled reagent in place of the non-labeled reagent previously employed.

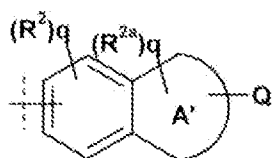
Embodiments of the Invention

Throughout this specification and in the claims that follow, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

In one embodiment of the present invention, the compounds are represented by Formula (IA):



wherein



A is

A' is a heterocyclyl or carbocyclyl;

Q is L_a-X_a or R¹⁰;

L_a is -Z'-Y-Z''-;

Z' and Z'' are each, independently, a bond, C₁₋₄ alkylene or C₂₋₄ alkenylene,

where Z' and Z'' together make no more than a 4-carbon chain and the hydrocarbon bonds may be optionally substituted by one or more hydroxy or halogens.

Y' is -O-, -S(O)_p-, -N(R³)-, -C(R')(R'')-, -C(O)-, -C(O)NR³-, -NR³C(O)-, -N(R³)C(O)N(R³)-, -N(R³)SO₂-, or -SO₂N(R³)-;

V is halogen, -OR^{1b} or hydrogen;

m = 0-4;

n = 0-4;

p = 0-2;

R' and R'' are independently, hydrogen, halogen, C₁₋₆ alkyl, perhaloalkyl, or taken together form a cyclic ring which may optionally have heteroatoms selected from O, N or S;

R¹, R^{1a} and R^{1b} are independently selected from hydrogen, C₁₋₆ alkyl, C₆₋₁₀aryl-C₁₋₄alkyl, -C(O)C₆₋₁₀aryl or -C(O)C₁₋₆alkyl;

R² and R^{2a} are independently halogen, hydroxy, C₁₋₄hydroxyalkyl, cyano, nitro, -NR⁴R⁵, -CH₂NR⁴R⁵, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₁₋₄ alkoxy, C₃₋₇ cycloalkoxy, -S(O)_pR³, -S(O)₂NR⁴R⁵, -OS(O)₂R³, -C(O)R³, -C(O)OR³, -CH₂C(O)OR³, -C(O)NR⁴R⁵, -CH₂C(O)NR⁴R⁵, -NR³C(O)NR⁴R⁵, -NR³C(O)OR³, C₁₋₆ haloalkyl, C₁₋₆ perhaloalkyl, C₃₋₇cycloalkylC₁₋₄alkyl, C₆₋₁₀aryl, C₆₋₁₀arylC₁₋₄alkyl, C₆₋₁₀aryloxy, C₂₋₁₀heterocyclyl, C₂₋₁₀heterocyclylC₁₋₄alkyl, C₁₋₁₀heteroarylC₁₋₄alkyl, C₁₋₁₀heteroaryl, C₁₋₁₀heteroaryloxy, or C₁₋₁₀heterocycloxy;

R³ is hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₆₋₁₀aryl, C₁₋₁₀heteroaryl, or C₂₋₁₀heterocyclyl;

q = 0-3;

X is [C(R⁶)(R⁷)]_i;

Y is H, C₁₋₄ alkyl, OR¹ or NR⁸R⁹

t = 1-3;

R⁶ and R⁷ are independently hydrogen or C₁₋₆ alkyl, or R⁶ and R⁷ form an oxo group and t=1, or when R⁶ and R⁷ are C₁₋₄alkyl on the same carbon they can be taken together to form a cyclic ring which may contain N, S or O atoms;

R⁴ and R⁵ are independently hydrogen, C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkylC₁₋₄alkyl, arylC₁₋₄alkyl, C₆₋₁₀aryl, C₁₋₁₀heteroaryl, C₁₋₁₀heteroarylC₁₋₄alkyl, C₂₋₁₀heterocyclyl, C₂₋₁₀heterocyclylC₁₋₄alkyl or

R⁴ and R⁵ taken together may form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N or S, the said ring system may further be optionally substituted; and

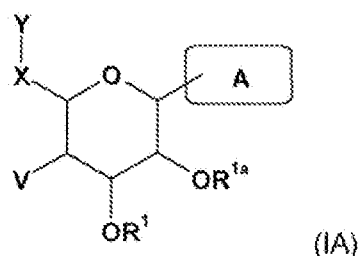
R^8 and R^9 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or

R^8 and R^9 along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted;

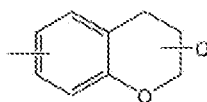
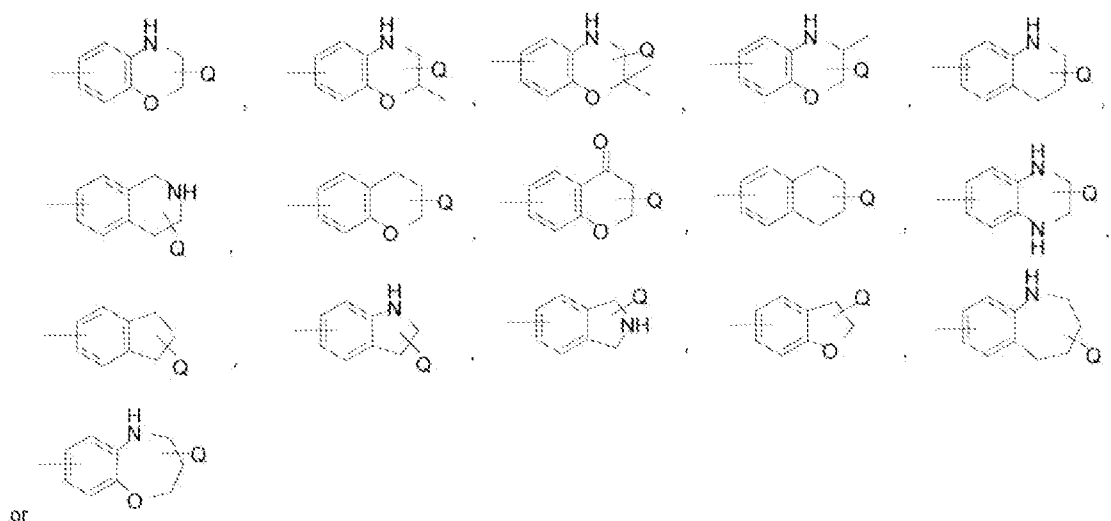
R^{10} is C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{3-7} cycloalkyl, C_{1-10} heterocycloalkyl, where C_{1-4} alkyl may be optionally substituted by one or more hydroxy or halogens; and

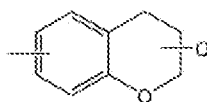
X_6 is halogen, hydroxy, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, trihalo C_{1-4} alkoxy, C_{3-7} cycloalkoxy, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-4} alkyl, C_{6-10} aryloxy, C_{1-10} heterocyclyl, C_{1-10} heterocyclyl C_{1-4} alkyl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{1-10} heteroaryloxy, or C_{1-10} heterocycloxy; or a stereoisomer, enantiomer or tautomer thereof, a pharmaceutically acceptable salt thereof, or a prodrug thereof.

In another embodiment, the invention provides compounds of Formula (IA):



wherein A is selected from:



provided that when A is , it is not substituted with hydroxy or methoxy;

Q is L_a-X_a or R^{10} ;

L_a is $-Z'-Y'-Z''-$;

Z' and Z'' are each, independently, a bond, C_{1-4} alkylene or C_{2-4} alkenylene, where Z' and Z'' together make no more than a 4-carbon chain and the hydrocarbon bonds may be optionally substituted by one or more hydroxy or halogens.

Y' is $-O-$, $-S(O)_p-$, $-N(R^3)-$, $-C(R^1)(R^2)-$, $-C(O)-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-N(R^3)C(O)N(R^3)-$, $-N(R^3)SO_2-$, or $-SO_2N(R^3)-$;

V is halogen, $-OR^{1b}$ or hydrogen;

$m = 0-4$;

$n = 0-4$;

$p = 0-2$;

R^1 and R^2 are independently, hydrogen, halogen, C_{1-6} alkyl, perhaloalkyl, or taken together form a cyclic ring which may optionally have heteroatoms selected from O, N or S;

R^1 , R^{1a} and R^{1b} are independently selected from hydrogen, C_{1-6} alkyl, C_{6-10} aryl- C_{1-4} alkyl, $-C(O)C_{6-10}$ aryl or $-C(O)C_{1-6}$ alkyl;

R^2 and R^{2a} are independently halogen, hydroxy, C_{1-4} hydroxyalkyl, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-4} alkoxy, C_{3-7} cycloalkoxy, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-$

$\text{CH}_2\text{C}(\text{O})\text{NR}^4\text{R}^5$, $-\text{NR}^3\text{C}(\text{O})\text{NR}^4\text{R}^5$, $-\text{NR}^3\text{C}(\text{O})\text{OR}^3$, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{3-7} cycloalkyl, C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-4} alkyl, C_{6-10} aryloxy, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{1-10} heteroaryl, C_{1-10} heteroaryloxy, or C_{1-10} heterocycloxy;

R^3 is hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{6-10} aryl, C_{1-10} heteroaryl, or C_{2-10} heterocyclyl;

$q = 0-3$;

X is $[\text{C}(\text{R}^6)(\text{R}^7)]_i$;

Y is H, C_{1-4} alkyl, OR^1 or NR^8R^9

$t = 1-3$;

R^6 and R^7 are independently hydrogen or C_{1-6} alkyl, or R^6 and R^7 form an oxo group and $t=1$, or when R^6 and R^7 are C_{1-4} alkyl on the same carbon they can be taken together to form a cyclic ring which may contain N, S or O atoms;

R^4 and R^5 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or

R^4 and R^5 taken together may form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N or S, the said ring system may further be optionally substituted; and

R^8 and R^9 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or

R^8 and R^9 along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted;

R^{10} is C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{3-7} cycloalkyl, C_{2-10} heterocyclyl, where C_{1-4} alkyl may be optionally substituted by one or more hydroxy or halogens and C_{6-10} aryl may be optionally substituted with one or more C_{1-4} alkyl, C_{1-4} alkoxy, or C_{1-4} haloalkyl; and

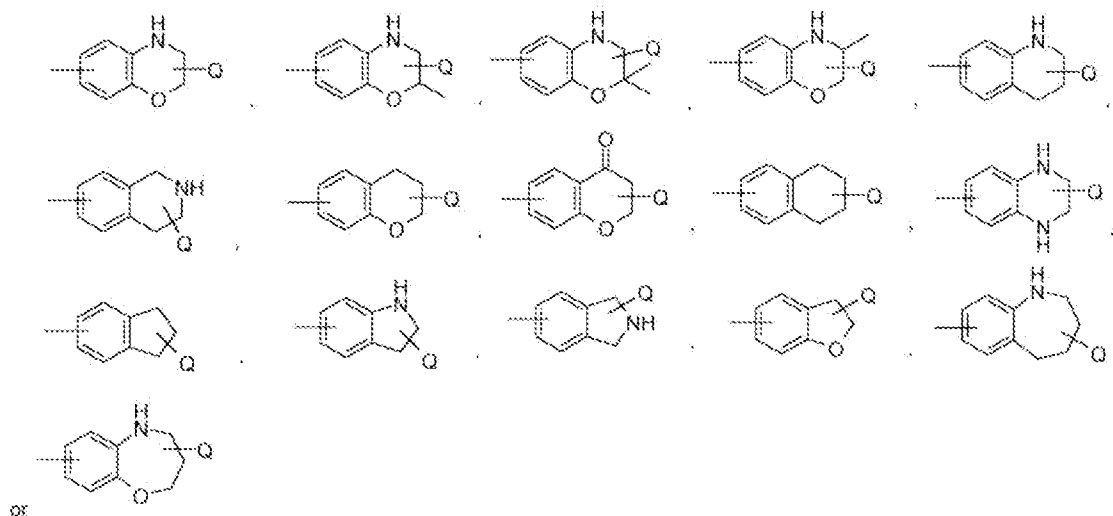
X_a is halogen, hydroxy, cyano, nitro, $-\text{NR}^4\text{R}^5$, $-\text{CH}_2\text{NR}^4\text{R}^5$, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{1-4} alkoxy, trihalo C_{1-4} alkoxy, an optionally substituted C_{3-7} cycloalkoxy, $-\text{C}(\text{O})\text{R}^3$, $-\text{C}(\text{O})\text{OR}^3$, $-\text{CH}_2\text{C}(\text{O})\text{OR}^3$, $-\text{C}(\text{O})\text{NR}^4\text{R}^5$, $-\text{CH}_2\text{C}(\text{O})\text{NR}^4\text{R}^5$, $-\text{NR}^3\text{C}(\text{O})\text{NR}^4\text{R}^5$, $-\text{NR}^3\text{C}(\text{O})\text{OR}^3$, $-\text{S}(\text{O})\text{R}^3$, $-\text{S}(\text{O})_2\text{NR}^4\text{R}^5$, $-\text{OS}(\text{O})_2\text{R}^3$, an

optionally substituted C₃₋₇cycloalkyl, an optionally substituted C₃₋₇cycloalkylC₁₋₄alkyl, an optionally substituted C₆₋₁₀ aryl, an optionally substituted C₆₋₁₀ arylC₁₋₄alkyl, an optionally substituted C₆₋₁₀ aryloxy, an optionally substituted C₂₋₁₀ heterocyclyl, an optionally substituted C₂₋₁₀ heterocyclylC₁₋₄alkyl, an optionally substituted C₁₋₁₀ heteroaryl, an optionally substituted C₁₋₁₀ heteroarylC₁₋₄alkyl, an optionally substituted C₁₋₁₀ heteroaryloxy, or an optionally substituted C₁₋₁₀ heterocycloxy; or a pharmaceutically acceptable salt thereof.

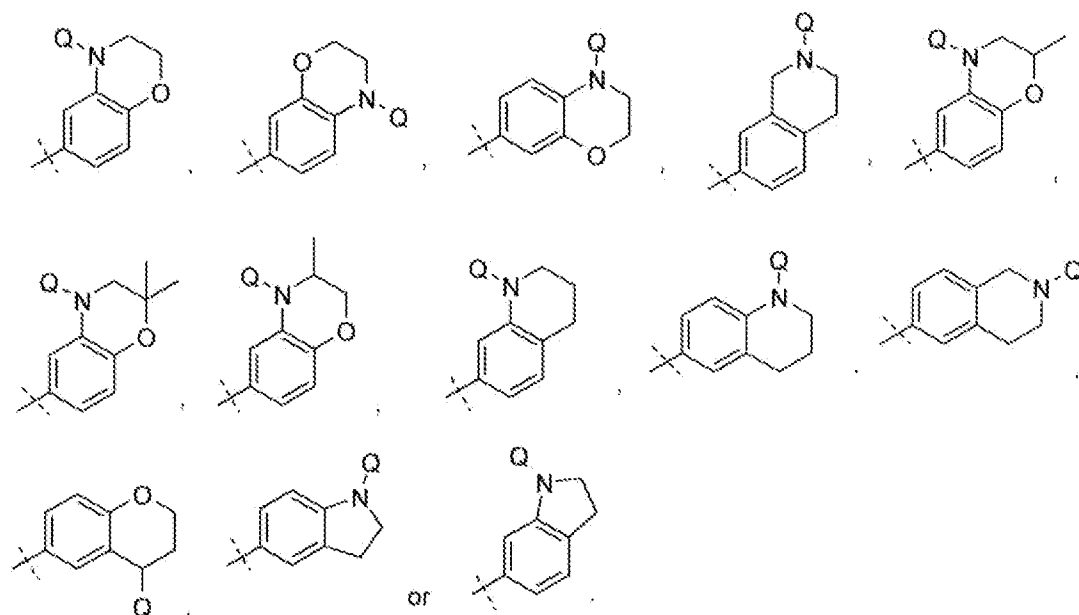
Various embodiments of the invention are described below. It will be appreciated that the features specified in each embodiment may be combined with other specified features, to provide further embodiments.

In one embodiment, the invention relates to compounds of Formula (IA), where A' is a C₂₋₁₀heterocyclyl.

In another embodiment, the invention relates to compounds of Formula (IA), wherein A is selected from:

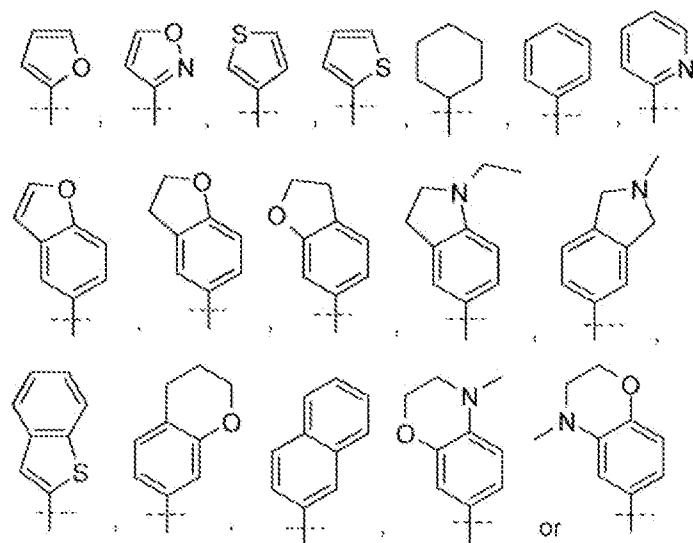


In another embodiment of the compounds of formula (IA), A is



In embodiment of the compound of Formula (IA), Q is L_a-X_a , wherein L_a is a C_{1-4} alkylene (e.g. methylene, ethylene or isopropylene).

In another embodiment of the compounds of formula (IA), X_n is



Each of which may be optionally substituted with one or more substituents which may be independently selected from halogen, hydroxyl, C₁₋₄ alkyl, C₃₋₇ cycloalkyl, C₃₋₇ cycloalkoxy, C₁₋₄ alkoxy, C₂₋₄ alkenyl, C₆₋₁₀ aryl, C₁₋₁₀ heteroaryl, cyano, -C(O)- C₁₋₄ alkyl, -C(O)-N- C₁₋₄ alkyl, -C(O)-N-di C₁₋₄ alkyl, -S- C₁₋₄ alkyl, SO₂- C₁₋₄ alkyl, trihalo C₁₋₄ alkoxy, -o- C₃₋₇ cycloalkyl and -O- C₃₋₇ cycloalkoxy.

In yet another embodiment X_a is an optionally substituted aryl, optionally substituted with one or more independently selected halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, -O- C_{3-7} cycloalkyl, -S- C_{1-4} alkyl, -SO₂- C_{1-4} alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , -CH₂ NR^4R^5 or -C(O)- C_{1-4} alkyl.

In another embodiment of the invention, the compound is of Formula (IA), wherein Q is R^{10} and R^{10} is methyl, ethyl, isopropyl, isobutyl, trifluoromethyl or cyclopentyl.

In another embodiment of the invention, the compound is of Formula (IA), wherein Q is R^{10} and R^{10} is a C_{6-10} aryl which may be optionally substituted with one or more substituents which may be independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, and C_{1-4} haloalkyl.

In another embodiment of Formula (IA) as described above

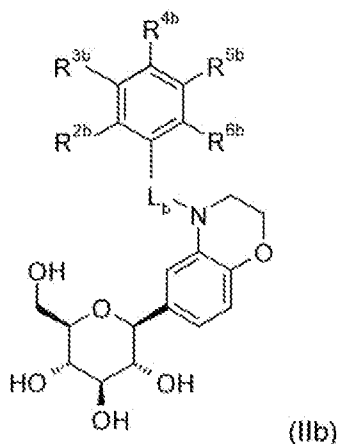
X is -CH₂-;

Y is OR¹;

V is OR¹

R^1 , R^{1a} and R^{1b} are hydrogen.

In another embodiment the invention provides a compound of formula (IIb):



wherein

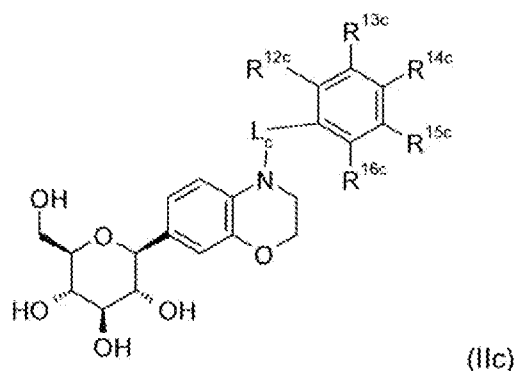
L_b is a bond or an optionally substituted C_{1-4} alkylene;

R^{12b} , R^{13b} , R^{14b} , R^{15b} and R^{16b} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, -O- C_{3-7} cycloalkyl, -S- C_{1-4} alkyl, -SO₂- C_{1-4} alkyl, trihalo C_{1-4} alkyl,

trihalo C₁₋₄ alkoxyl, C₆₋₁₀ aryl, C₁₋₁₀ heteroaryl, cyano, nitro, NR⁴R⁵, -CH₂NR⁴R⁵ or -C(O)-C₁₋₄ alkyl; or a pharmaceutically acceptable salt thereof.

In an exemplary embodiment of the compounds of formula (IIb) L_b is methylene; R^{11b}, R^{12b}, R^{13b}, R^{15b} and R^{16b} are each hydrogen; and R^{14b} is C₁₋₄ alkyl.

In one embodiment the invention provides a compound of formula (IIc):

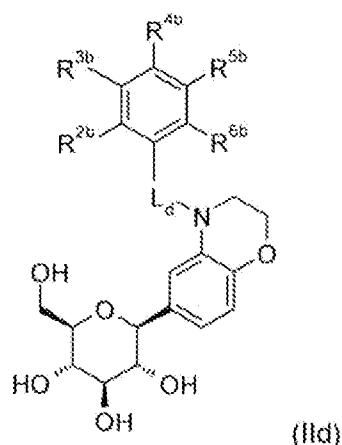


wherein

L_c is a bond or an optionally substituted C₁₋₄ alkylene;

R^{12c}, R^{13c}, R^{14c}, R^{15c} and R^{16c} are each, independently, hydrogen, halogen, C₁₋₄ alkyl, C₁₋₄ alkoxyl, C₃₋₇ cycloalkyl, -O-C₃₋₇ cycloalkyl, -S-C₁₋₄ alkyl, -SO₂-C₁₋₄ alkyl, trihalo C₁₋₄ alkyl, trihalo C₁₋₄ alkoxyl, C₆₋₁₀ aryl, C₁₋₁₀ heteroaryl, cyano, nitro, NR⁴R⁵, -CH₂NR⁴R⁵ or -C(O)-C₁₋₄ alkyl; or a pharmaceutically acceptable salt thereof.

In another embodiment the invention provides a compound of formula (IIId):



wherein

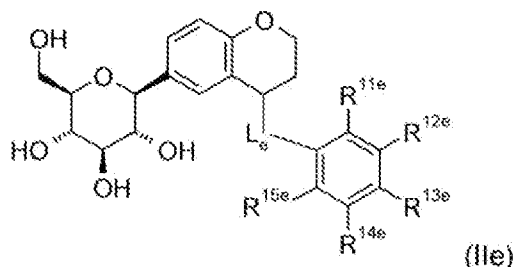
L_d is a bond or an optionally substituted C₁₋₄ alkylene;

R^{11d} , R^{12d} , R^{13d} , R^{14d} and R^{15d} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or a pharmaceutically acceptable salt thereof.

In an exemplary embodiment of the compounds of formula (IId) L_d is methylene; R^{11d} , R^{12d} , R^{14d} and R^{15d} are each hydrogen; and R^{13d} is C_{1-4} alkyl.

In yet another exemplary embodiment of the compounds of formula (IId) L_d is ethylene; R^{11d} , R^{12d} , R^{14d} and R^{15d} are each hydrogen; and R^{13d} is C_{1-4} alkoxy.

In one embodiment the invention provides a compound of formula (IIe):



wherein

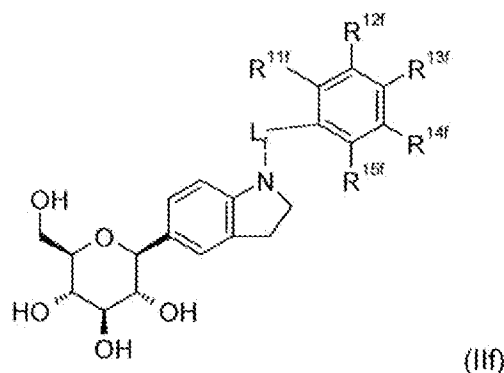
L_e is a bond or an optionally substituted C_{1-4} alkylene;

R^{11e} , R^{12e} , R^{13e} , R^{14e} and R^{15e} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or a pharmaceutically acceptable salt thereof.

In an exemplary embodiment of the compounds of formula (IIe) L_e is a bond; R^{11e} , R^{12e} , R^{14e} and R^{15e} are hydrogen; and R^{13e} is C_{1-4} alkyl or C_{1-4} alkoxy.

In yet another exemplary embodiment of the compounds of formula (IIe) L_e is methylene; R^{11e} , R^{12e} , R^{14e} and R^{15e} are hydrogen; and R^{13e} is C_{1-4} alkyl or C_{1-4} alkoxy.

In another embodiment the invention provides a compound of formula (IIf):



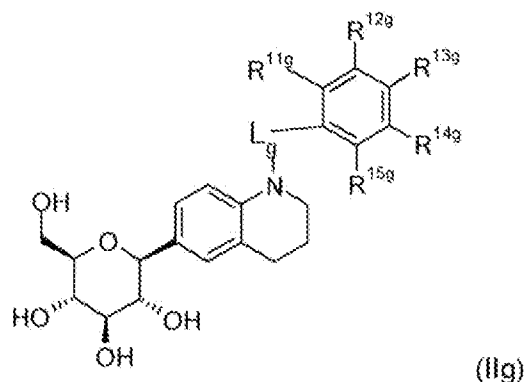
wherein

L_f is a bond or an optionally substituted C_{1-4} alkylene;

R^{11f} , R^{12f} , R^{13f} , R^{14f} and R^{15f} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or a pharmaceutically acceptable salt thereof.

In an exemplary embodiment of the compounds of formula (IIf) L_f is a bond; R^{11f} , R^{12f} , R^{14f} and R^{15f} are hydrogen; and R^{13f} is C_{1-4} alkyl.

In another embodiment the invention provides a compound of formula (IIg):

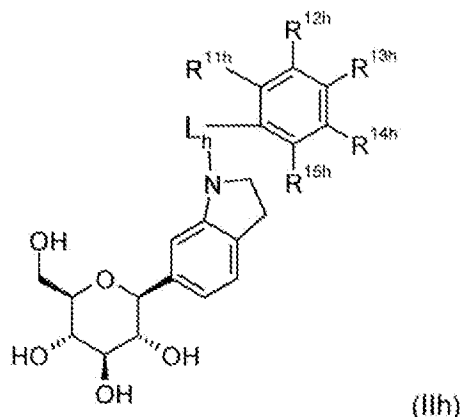


wherein

L_g is a bond or an optionally substituted C_{1-4} alkylene;

R^{11g} , R^{12g} , R^{13g} , R^{14g} and R^{15g} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or a pharmaceutically acceptable salt thereof.

In another embodiment the invention provides a compound of formula (IIh):



wherein

L_n is a bond or an optionally substituted C_{1-4} alkylene;

R^{11h} , R^{12h} , R^{13h} , R^{14h} and R^{15h} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or a pharmaceutically acceptable salt thereof.

In another embodiment individual compounds according to the invention are those listed in the Examples section below.

Isotopically-labeled compounds of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIg) and (IIh) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the accompanying Examples and Preparations using an appropriate isotopically-labeled reagents in place of the non-labeled reagent previously employed.

Pharmaceutically acceptable solvates in accordance with the invention include those wherein the solvent of crystallization may be isotopically substituted, e.g. D_2O , d_6 -acetone, d_6 -DMSO.

Compounds of the invention, i.e. compounds of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIg) and (IIh) that contain groups capable of acting as donors and/or acceptors for hydrogen bonds may be capable of forming co-crystals with suitable co-crystal formers. These co-crystals may be prepared from compounds of formula (I), (IA), (IIb), (IIc), (IId),

(IIe), (IIf), (IIg) and (IIh) by known co-crystal forming procedures. Such procedures include grinding, heating, co-subliming, co-melting, or contacting in solution compounds of formula (I), (IA), (IIb), (IIc), (IIe), (IIg) and (IIh) with the co-crystal former under crystallization conditions and isolating co-crystals thereby formed. Suitable co-crystal formers include those described in WO 2004/078163. Hence the invention further provides co-crystals comprising a compound of formula (I), (IA), (IIb), (IIc), (IIe), (IIg) and (IIh).

As used herein, the term "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, surfactants, antioxidants, preservatives (e.g., antibacterial agents, antifungal agents), isotonic agents, absorption delaying agents, salts, preservatives, drugs, drug stabilizers, binders, excipients, disintegration agents, lubricants, sweetening agents, flavoring agents, dyes, such like materials and combinations thereof, as would be known to one of ordinary skill in the art (see, for example, Remington's Pharmaceutical Sciences, 18th Ed. Mack Printing Company, 1990, pp. 1289- 1329). Except insofar as any conventional carrier is incompatible with the active ingredient, its use in the therapeutic or pharmaceutical compositions is contemplated.

The term "a therapeutically effective amount" of a compound of the present invention refers to an amount of the compound of the present invention that will elicit the biological or medical response of a subject, for example, reduction or inhibition of an enzyme or a protein activity, or ameliorate symptoms, alleviate conditions, slow or delay disease progression, or prevent a disease, etc. In one non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a subject, is effective to (1) at least partially alleviating, inhibiting, preventing and/or ameliorating a condition, or a disorder or a disease (i) mediated by SGLT-2 and SGLT-1, or (ii) associated with SGLT-2 and SGLT-1 activity, or (iii) characterized by abnormal activity of SGLT-2 and SGLT-1; or (2) reducing or inhibiting the activity of SGLT-2 and SGLT-1 or (3) reducing or inhibiting the expression of SGLT-2 and SGLT-1. In another non-limiting embodiment, the term "a therapeutically effective amount" refers to the amount of the compound of the present invention that, when administered to a cell, or a tissue, or a non-cellular biological material, or a medium, is effective to at least partially reducing or inhibiting the activity of

SGLT-2 and SGLT-1; or at least partially reducing or inhibiting the expression of SGLT-2 and SGLT-1.

As used herein, the term "patient" refers to an animal. Preferably, the animal is a mammal. A subject also refers to for example, primates (e.g., humans), cows, sheep, goats, horses, dogs, cats, rabbits, rats, mice, fish, birds and the like. In a preferred embodiment, the subject is a human.

As used herein, the term "inhibition" or "inhibiting" refers to the reduction or suppression of a given condition, symptom, or disorder, or disease, or a significant decrease in the baseline activity of a biological activity or process.

As used herein, the term "treating" or "treatment" of any disease or disorder refers in one embodiment, to ameliorating the disease or disorder (i.e., slowing or arresting or reducing the development of the disease or at least one of the clinical symptoms thereof). In another embodiment "treating" or "treatment" refers to alleviating or ameliorating at least one physical parameter including those which may not be discernible by the patient. In yet another embodiment, "treating" or "treatment" refers to modulating the disease or disorder, either physically, (e.g., stabilization of a discernible symptom), physiologically, (e.g., stabilization of a physical parameter), or both. In yet another embodiment, "treating" or "treatment" refers to preventing or delaying the onset or development or progression of the disease or disorder.

As used herein, the term "a," "an," "the" and similar terms used in the context of the present invention (especially in the context of the claims) are to be construed to cover both the singular and plural unless otherwise indicated herein or clearly contradicted by the context.

All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g. "such as") provided herein is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention otherwise claimed.

Any asymmetric atom (e.g., carbon or the like) of the compound(s) of the present invention can be present in racemic or enantiomerically enriched, for example the (*R*)-, (*S*)- or (*R,S*)- configuration. In certain embodiments, each asymmetric atom has at least 50 % enantiomeric excess, at least 60 % enantiomeric excess, at least 70 % enantiomeric excess, at least 80 % enantiomeric excess, at least 90 % enantiomeric excess, at least 95 % enantiomeric excess, or at least 99 % enantiomeric excess in the (*R*)- or (*S*)- configuration. Substituents at atoms with unsaturated bonds may, if possible, be present in *cis*- (*Z*)- or *trans*- (*E*)- form.

Accordingly, as used herein a compound of the present invention can be in the form of one of the possible isomers, rotamers, atropisomers, tautomers or mixtures thereof, for example, as substantially pure geometric (*cis* or *trans*) isomers, diastereomers, optical isomers (antipodes), racemates or mixtures thereof. Any resulting mixtures of isomers can be separated on the basis of the physicochemical differences of the constituents, into the pure or substantially pure geometric or optical isomers, diastereomers, racemates, for example, by chromatography and/or fractional crystallization. Any resulting racemates of final products or intermediates can be resolved into the optical antipodes by known methods, e.g., by separation of the diastereomeric salts thereof, obtained with an optically active acid or base, and liberating the optically active acidic or basic compound. In particular, a basic moiety may thus be employed to resolve the compounds of the present invention into their optical antipodes, e.g., by fractional crystallization of a salt formed with an optically active acid, e.g., tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, di-*O*, *O'*-*p*-toluoyl tartaric acid, mandelic acid, malic acid or camphor-10-sulfonic acid. Racemic products can also be resolved by chiral chromatography, e.g., high pressure liquid chromatography (HPLC) using a chiral adsorbent.

Compounds of the present invention are either obtained in the free form, as a salt thereof, or as prodrug derivatives thereof. When both a basic group and an acid group are present in the same molecule, the compounds of the present invention may also form internal salts, e.g., zwitterionic molecules.

Furthermore, the compounds of the present invention, including their salts, can also be obtained in the form of their hydrates, or include other solvents used for their crystallization.

The compounds of the present invention are useful as both prophylactic and therapeutic treatments for diseases or conditions related to the inhibition of SGLT-2 and SGLT-1.

Thus, as a further aspect, the invention relates to a method for treating a disease or condition related to the inhibition of SGLT-2, comprising administration of an effective therapeutic amount of a compound of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) or a pharmaceutically acceptable salt thereof.

Compounds of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) may be useful in the treatment of metabolic disorders, or conditions such as (such as e.g. retinopathy, nephropathy or neuropathies, diabetic foot, ulcers, macroangiopathies), metabolic acidosis or ketosis, reactive hypoglycaemia, hyperinsulinaemia, glucose metabolic disorder, insulin resistance, metabolic syndrome, dyslipidaemias of different origins, atherosclerosis and related diseases, obesity, high blood pressure, chronic heart failure, edema and hyperuricaemia.

Compounds of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) may be also suitable for preventing beta-cell degeneration such as apoptosis or necrosis of pancreatic beta cells, for improving or restoring the functionality of pancreatic cells, increasing the number and size of pancreatic beta cells, for use as diuretics in treating edema or for use as antihypertensives and for the prevention and treatment of acute renal failure.

As a further aspect, the invention relates to a method for treating a disorder selected from type 1 and type 2 diabetes mellitus, complications of diabetes, comprising administration of an effective amount of a compound of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) or a pharmaceutically acceptable salt thereof.

A compound of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) of the present invention may be usefully combined with another pharmacologically active compound, or

with two or more other pharmacologically active compounds, for use in therapy. For example, a compound of the formula (I), (IA), (IIb), (IIc), (IIId), (IIe), (IIIf), (IIg) and (IIh), or a pharmaceutically acceptable salt thereof, as defined above, may be administered simultaneously, sequentially or separately in combination with one or more agents for the treatment of disorders previously listed.

Therapeutic agents which are suitable for such a combination include, for example, antidiabetic agents such as metformin, sulphonylureas (e.g. glibenclamide, tolbutamide, glimepiride), nateglinide, repaglinide, thiazolidinediones (e.g. rosiglitazone, pioglitazone), PPAR-gamma-agonists (e.g. GI 262570) and antagonists, PPAR-gamma/alpha modulators (e.g. KRP 297), alpha- glucosidase inhibitors (e.g. acarbose, voglibose), DPPIV inhibitors (e.g. LAF237, MK-431), alpha2-antagonists, insulin and insulin analogues, GLP-1 and GLP-1 analogues (e.g. exendin-4) or amylin. The list also includes inhibitors of protein tyrosinephosphatase 1, substances that affect deregulated glucose production in the liver, such as e.g. inhibitors of glucose-6-phosphatase, or fructose-1,6-bisphosphatase, glycogen phosphorylase, glucagon receptor antagonists and inhibitors of phosphoenol pyruvate carboxykinase, glycogen synthase kinase or pyruvate dehydrokinase, lipid lowering agents such as for example HMG-CoA-reductase inhibitors (e.g. simvastatin, atorvastatin), fibrates (e.g. bezafibrate, fenofibrate), nicotinic acid and the derivatives thereof, PPAR-alpha agonists, PPAR-delta agonists, ACAT inhibitors (e.g. avasimibe) or cholesterol absorption inhibitors such as, for example, ezetimibe, bile acid-binding substances such as, for example, cholestyramine, inhibitors of ileac bile acid transport, HDL-raising compounds such as CETP inhibitors or ABC1 regulators or active substances for treating obesity, such as sibutramine or tetrahydrolipostatin, dexfenfluramine, axokine, antagonists of the cannabinoid receptor, MCH-1 receptor antagonists, MC4 receptor agonists, NPY5 or NPY2 antagonists or β 3-agonists such as SB-418790 or AD-9677 and agonists of the 5HT2c receptor. Moreover, combinations with drugs for influencing high blood pressure, chronic heart failure or atherosclerosis such as e.g. A-II antagonists or ACE inhibitors, ECE inhibitors, diuretics, β - blockers, Ca-antagonists, centrally acting antihypertensives, antagonists of the alpha-2- adrenergic receptor, inhibitors of neutral endopeptidase, thrombocyte aggregation inhibitors and others or combinations thereof are suitable. Examples of angiotensin II receptor antagonists are candesartan cilexetil, potassium losartan, eprosartan mesylate, valsartan, telmisartan, irbesartan, EXP-3174, L-158809, EXP-

3312, olmesartan, medoxomil, tasosartan, KT-3-671 , GA-01 13, RU-64276, EMD-90423, BR-9701 , etc. Angiotensin II receptor antagonists are preferably used for the treatment or prevention of high blood pressure and complications of diabetes, often combined with a diuretic such as hydrochlorothiazide.

A combination with uric acid synthesis inhibitors or uricosurics is suitable for the treatment or prevention of gout.

A combination with GABA-receptor antagonists, Na-channel blockers, topiramat, protein-kinase C inhibitors, advanced glycation end product inhibitors or aldose reductase inhibitors may be used for the treatment or prevention of complications of diabetes. Such combinations may offer significant advantages, including synergistic activity, in therapy.

The present invention is also in relation to a pharmaceutical composition comprising a compound of formula (I), (IA), (IIb), (IIc), (IIId), (IIe), (IIIf), (IIg) and (IIh) or its prodrug and pharmaceutically acceptable excipients.

In still another embodiment of the present invention, the prodrug is selected from a group comprising, esters and hydrates.

The term "prodrug" is also meant to include any covalently bonded carriers which release the active compound of the invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of the invention may be prepared by modifying functional groups present in the compound of the invention in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound of the invention. Prodrugs include compounds of the invention wherein a hydroxy, amino or mercapto or acid group is bonded to any group that, when the prodrug of the compound of the invention is administered to a mammalian subject, cleaves to form a free hydroxy, free amino or free mercapto or acid group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol or amides of amine functional groups in the compounds of the invention and the like.

In still another embodiment of the present invention, the excipients are selected from a group comprising, binders, anti-adherents, disintegrants, fillers, diluents, flavors, colors, glidants, lubricants, preservatives, sorbents and sweeteners or combination(s) thereof.

In still another embodiment of the present invention, the composition is formulated into various dosage forms selected from a group comprising tablet, troches, lozenges, aqueous or oily suspensions, ointment, patch, gel, lotion, dentifrice, capsule, emulsion, creams, spray, drops, dispersible powders or granules, emulsion in hard or soft gel capsules, syrups and elixirs.

Dosages of agents of the invention employed in practicing the present invention will of course vary depending, for example, on the particular condition to be treated, the effect desired and the mode of administration. In general, suitable daily dosages for oral administration are of the order of 0.1 to 10 mg/kg.

GENERAL SYNTHETIC ASPECTS

Within the scope of this text, only a readily removable group that is not a constituent of the particular desired end product of the compounds of the present invention is designated a "protecting group", unless the context indicates otherwise. The protection of functional groups by such protecting groups, the protecting groups themselves, and their cleavage reactions are described for example in standard reference works, such as J. F. W. McOmie, "Protective Groups in Organic Chemistry", Plenum Press, London and New York 1973.

Salts of compounds of the present invention having at least one salt-forming group may be prepared in a manner known per se. For example, salts of compounds of the present invention having acid groups may be formed, for example, by treating the compounds with metal compounds, such as alkali metal salts of suitable organic carboxylic acids, *e.g.* the sodium salt of 2-ethylhexanoic acid, with organic alkali metal or alkaline earth metal compounds, such as the corresponding hydroxides, carbonates or hydrogen carbonates, such as sodium or potassium hydroxide, carbonate or hydrogen carbonate, with corresponding calcium compounds or with ammonia or a suitable organic amine, stoichiometric amounts or only a small excess of the salt-forming agent preferably being used. Acid addition salts of compounds of the present invention are obtained in

customary manner, *e.g.* by treating the compounds with an acid or a suitable anion exchange reagent. Internal salts of compounds of the present invention containing acid and basic salt-forming groups, *e.g.* a free carboxy group and a free amino group, may be formed, *e.g.* by the neutralisation of salts, such as acid addition salts, to the isoelectric point, *e.g.* with weak bases, or by treatment with ion exchangers.

Salts can be converted in customary manner into the free compounds; metal and ammonium salts can be converted, for example, by treatment with suitable acids, and acid addition salts, for example, by treatment with a suitable basic agent.

Mixtures of isomers obtainable according to the invention can be separated in a manner known per se into the individual isomers; diastereoisomers can be separated, for example, by partitioning between polyphasic solvent mixtures, recrystallisation and/or chromatographic separation, for example over silica gel or by *e.g.* medium pressure liquid chromatography over a reversed phase column, and racemates can be separated, for example, by the formation of salts with optically pure salt-forming reagents and separation of the mixture of diastereoisomers so obtainable, for example by means of fractional crystallisation, or by chromatography over optically active column materials. Intermediates and final products can be worked up and/or purified according to standard methods, *e.g.* using chromatographic methods, distribution methods, (re-) crystallization, and the like.

The following applies in general to all processes mentioned herein before and hereinafter.

All the above-mentioned process steps can be carried out under reaction conditions that are known per se, including those mentioned specifically, in the absence or, customarily, in the presence of solvents or diluents, including, for example, solvents or diluents that are inert towards the reagents used and dissolve them, in the absence or presence of catalysts, condensation or neutralizing agents, for example ion exchangers, such as cation exchangers, *e.g.* in the H⁺ form, depending on the nature of the reaction and/or of the reactants at reduced, normal or elevated temperature, for example in a temperature range of from about -100 °C to about 190 °C, including, for example, from approximately -80 °C to approximately 150 °C, for example at from -80 to -60 °C, at room temperature,

at from -20 to 40 °C or at reflux temperature, under atmospheric pressure or in a closed vessel, where appropriate under pressure, and/or in an inert atmosphere, for example under an argon or nitrogen atmosphere.

At all stages of the reactions, mixtures of isomers that are formed can be separated into the individual isomers, for example diastereoisomers or enantiomers, or into any desired mixtures of isomers, for example racemates or mixtures of diastereoisomers, for example analogously to the methods described under "Additional process steps".

The solvents from which those solvents that are suitable for any particular reaction may be selected include those mentioned specifically or, for example, water, esters, such as lower alkyl-lower alkanates, for example ethyl acetate, ethers, such as aliphatic ethers, for example diethyl ether, or cyclic ethers, for example tetrahydrofuran or dioxane, liquid aromatic hydrocarbons, such as benzene or toluene, alcohols, such as methanol, ethanol or 1- or 2-propanol, nitriles, such as acetonitrile, halogenated hydrocarbons, such as methylene chloride or chloroform, acid amides, such as dimethylformamide or dimethyl acetamide, bases, such as heterocyclic nitrogen bases, for example pyridine or *N*-methylpyrrolidin-2-one, carboxylic acid anhydrides, such as lower alkanic acid anhydrides, for example acetic anhydride, cyclic, linear or branched hydrocarbons, such as cyclohexane, hexane or isopentane, methycyclohexane, or mixtures of those solvents, for example aqueous solutions, unless otherwise indicated in the description of the processes. Such solvent mixtures may also be used in working up, for example by chromatography or partitioning.

The compounds, including their salts, may also be obtained in the form of hydrates, or their crystals may, for example, include the solvent used for crystallization. Different crystalline forms may be present.

The invention relates also to those forms of the process in which a compound obtainable as an intermediate at any stage of the process is used as starting material and the remaining process steps are carried out, or in which a starting material is formed under the reaction conditions or is used in the form of a derivative, for example in a protected form or in the form of a salt, or a compound obtainable by the process according to the invention is produced under the process conditions and processed further *in situ*.

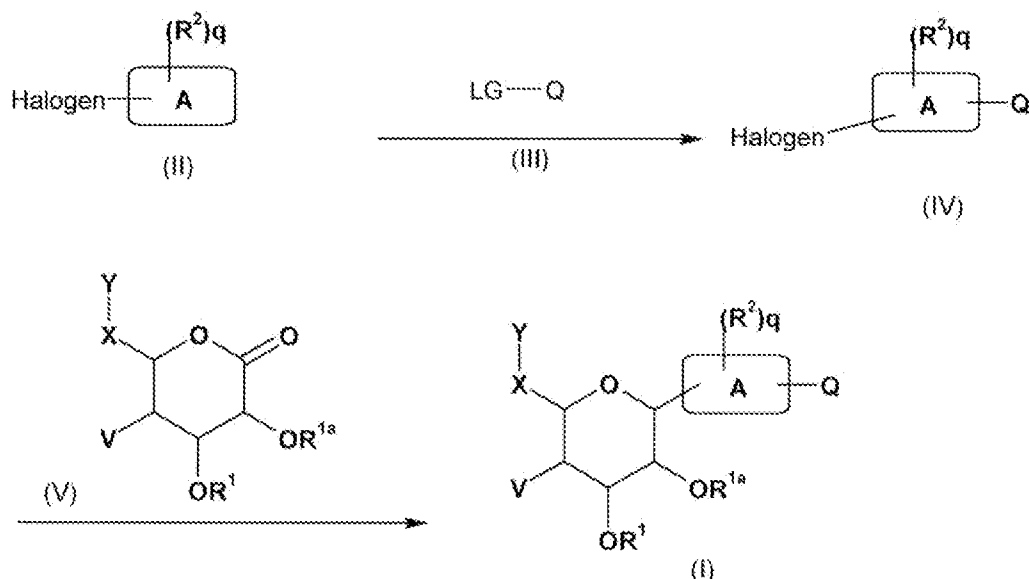
All starting materials, building blocks, reagents, acids, bases, dehydrating agents, solvents and catalysts utilized to synthesize the compounds of the present invention are either commercially available or can be produced by organic synthesis methods known to one of ordinary skill in the art (Houben-Weyl 4th Ed. 1952, Methods of Organic Synthesis, Thieme, Volume 21).

Typically, the compounds of formula (I), (IA), (IIb), (IIc), (IId), (IIe), (IIf), (IIg) and (IIh) can be prepared according to the Schemes provided *infra*.

Method of Preparation

The invention provides, in another aspect, a process for preparing a compound of formula (I). The schemes detailed below show general schemes for synthesizing compounds of formula (I). In the reactions described in the schemes herein below, any reactive group present, such as hydroxyl, amino, carbonyl or imino groups may be protected during the reaction by conventional protecting groups such as trimethylsilyl, tert-butyldimethylsilyl, benzyl, acetal, ketal etc., which are cleaved again after the reaction.

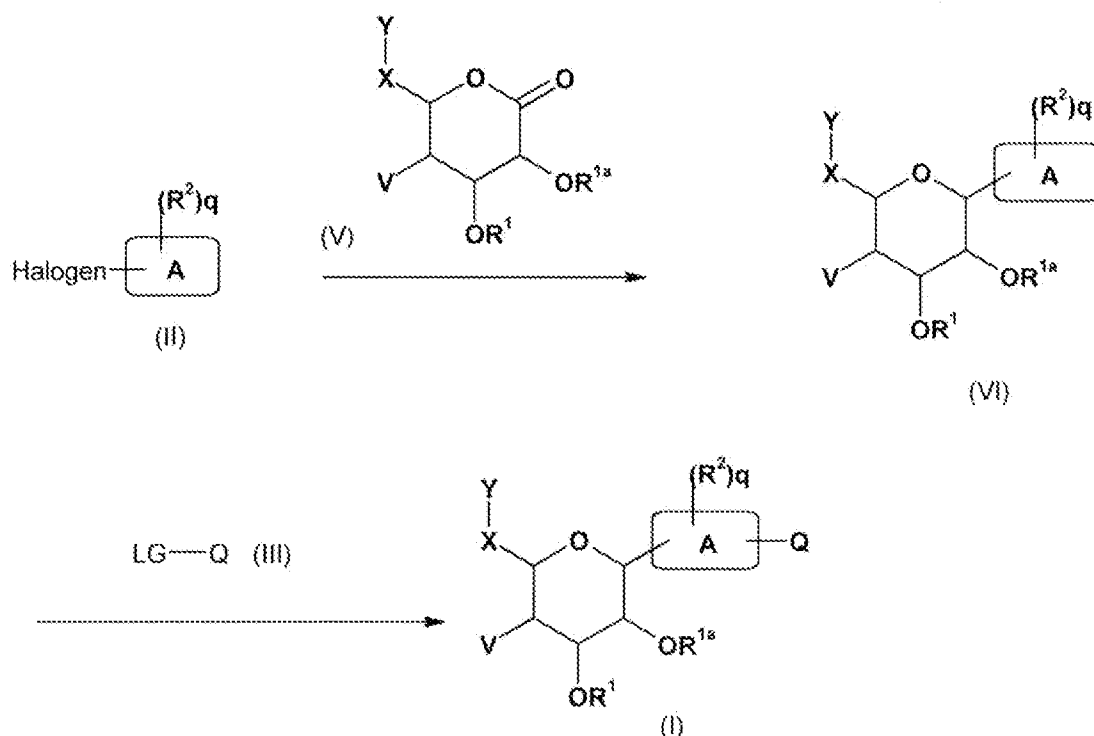
Scheme 1.



Compounds of formula (II) wherein all symbols are defined herein above may be reacted with compounds of formula (III) wherein LG is a leaving group such as halide, tosyl or

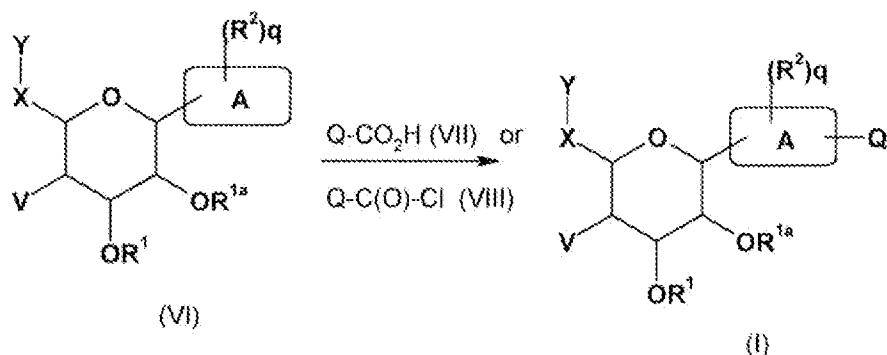
mesyl. The reaction may be carried out in the presence of a base and a solvent to provide compounds of formula (IV). Compounds of formula (IV) may be reacted with compounds of formula (V) wherein all symbols are defined wherein above. The reaction may be carried out in presence of a reagent such as alkyl-Li or Mg to provide compounds of formula (I) wherein Q is attached to a nitrogen in the heterocyclic ring all other symbols are defined herein above.

Scheme 2:



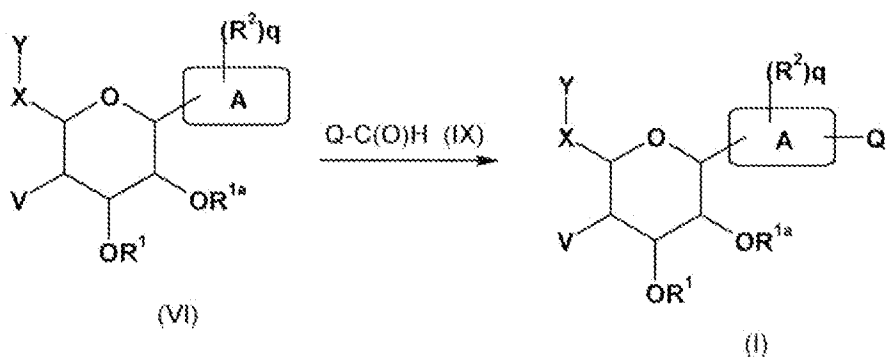
Compounds of formula (II) wherein all symbols are defined herein above may be reacted with compounds of formula (V) wherein all other symbols are defined herein above. The reaction may be carried out in presence of a reagent such as alkyl-Li or Mg to provide compounds of formula (VI). Compounds of formula (VI) may be reacted with compounds of formula (III) wherein LG is selected from halide, tosyl or mesyl. The reaction may be carried out in the presence of a base and a solvent or under Buchwald coupling conditions to provide compounds of formula (I) wherein Q is attached to the nitrogen of the bicyclic ring and all other symbols are defined herein above.

Scheme 3:



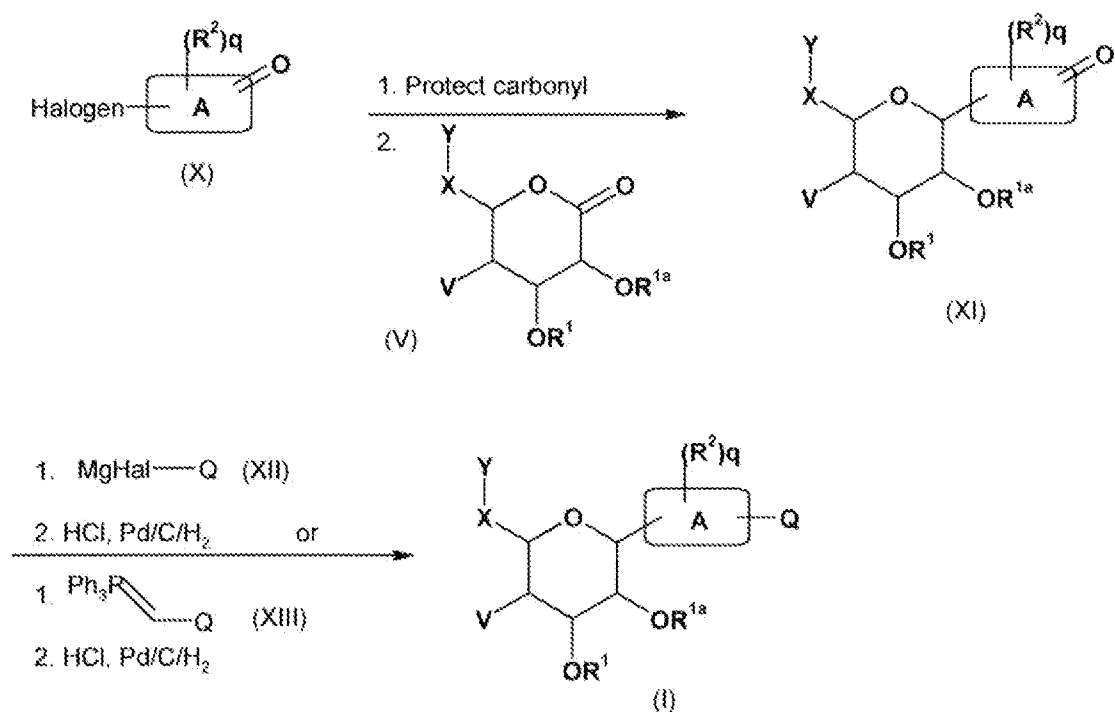
Alternatively, compounds of formula (VI) may be coupled with compounds of formula (VII) under peptide coupling conditions or compounds of formula (VIII) in the presence of a base, followed by reduction of resulting amides to provide compounds of formula (I) wherein Q attaches to a nitrogen via an amide bond and all other symbols are defined herein above.

Scheme 4:



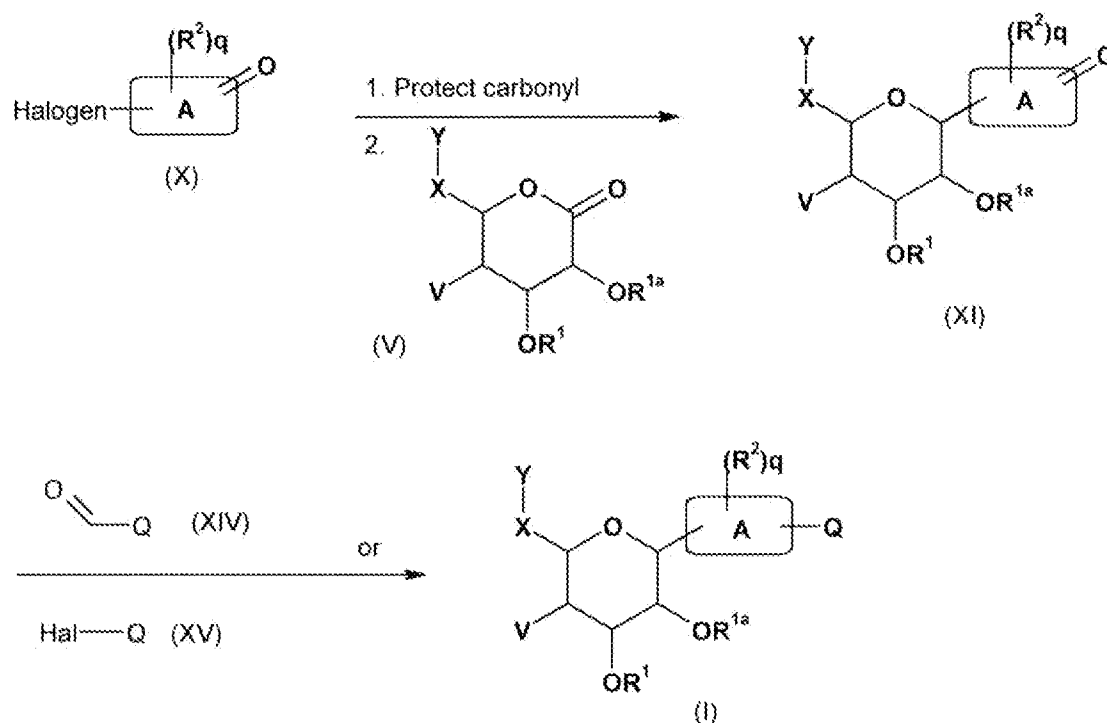
Alternatively, compounds of formula (VI) may be coupled with aldehydes of formula (IX) under reductive amination conditions to provide compounds of formula (I) wherein Q attaches to a nitrogen atom and all symbols are defined herein above.

Scheme 5:



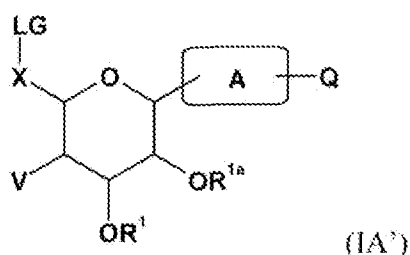
Carbonyl function of compounds of formula (X) wherein all symbols are defined herein above are protected to provide compounds of formula (XI) and may be reacted with compounds of formula (V) wherein all symbols are defined wherein above to provide compounds of formula (XII). The reaction may be carried out in presence of a reagent such as alkyl-Li or Mg. Compounds of formula (XII) may be reacted with a Grignard reagent of formula (XIII) or Wittig reagent of formula (XIV) followed by hydrogenation to provide compounds of formula (I) and all other symbols are defined herein above.

Scheme 6:



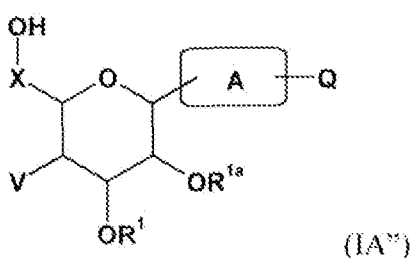
Carbonyl function of compounds of formula (X) wherein all symbols are defined herein above are protected to provide compounds of formula (XI) and may be reacted with compounds of formula (V) wherein A is a bond and all other symbols are defined wherein above to provide compounds of formula (XII). The reaction may be carried out in presence of a reagent such as alkyl-Li or Mg. Compounds of formula (XII) may be reacted with an aldehyde of formula (XV) in the presence of a base, followed by hydrogenation or compounds of formula (XII) may be reacted with alkyl halides of formula (XVI) in the presence of a base to provide compounds of formula (I) and all other symbols are defined herein above.

Compounds of formula (IA) where Y is NR^8R^9 and R^8 and R^9 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-4} alkyl, aryl C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl C_{1-4} alkyl or R^8 and R^9 along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted may be prepared by reaction of compounds of formula (IV)



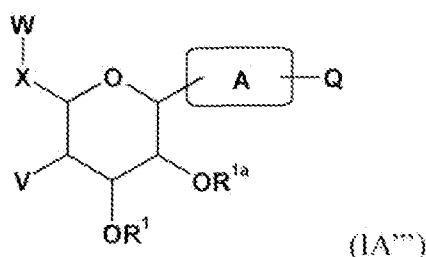
where V, R¹, R^{1a}, X and Q are as hereinbefore defined and LG is a suitable leaving group, with a compound of HNR⁸R⁹. Where X is an alkylene, suitable LG include mesylate or tosylate and the transformation may be carried out with a suitable base, e.g. triethylamine in a suitable solvent such as dimethylformamide, or similar conditions well known to those skilled in the art. Where X is carbonyl, suitable LG include halide and the transformation may be carried out with a suitable base in a suitable solvent under conditions well known to those skilled in the art.

Compounds of formula (IA') may be prepared from compounds of formula (IA'')



under suitable conditions for forming a leaving group, e.g. where LG is tosyl or mesyl, by reaction of the corresponding tosyl or mesyl halide, e.g. chloride, in a suitable solvent such as 2,6-lutidine, or under similar conditions well known to those skilled in the art.

Compounds of formula (IA) where Y is NR⁸R⁹ and R⁸ and R⁹ along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which is aromatic, may alternatively be prepared by reaction of compounds of formula (IA''')



where V, R¹, R^{1a}, X and Q are as hereinbefore defined and W is a suitable precursor to the formation of the desired ring. For example, where Y is a 1,2,3-triazolyl or tetrazolyl

group, W represents azide and the ring may be formed by reaction with a suitable reagent, e.g. for 1,2,3 triazole with a suitable alkynyl group or for a tetrazolyl with a suitable cyano-derivative under conditions well-known to those skilled in the art.

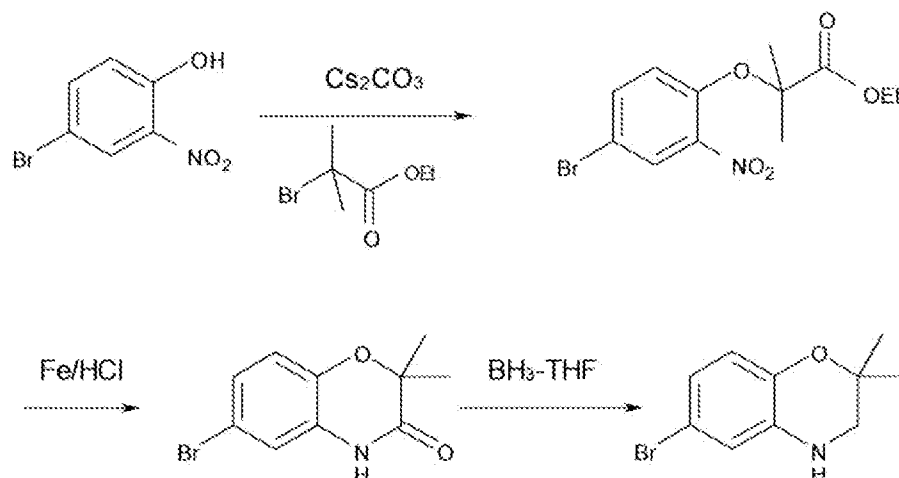
It will be understood that the processes detailed above and elsewhere herein are solely for the purpose of illustrating the invention and should not be construed as limiting. A process utilizing similar or analogous reagents and/or conditions known to one skilled in the art may also be used to obtain a compound of the invention.

Any mixtures of final products or intermediates obtained can be separated on the basis of the physico-chemical differences of the constituents, in a known manner, into the pure final products or intermediates, for example by chromatography, distillation, fractional crystallisation, or by the formation of a salt if appropriate or possible under the circumstances.

The following Examples are intended to illustrate the invention and are not to be construed as being limitations thereon. If not mentioned otherwise, all evaporations are performed under reduced pressure, between about 50 mmHg and 100 mmHg. The structure of final products, intermediates and starting materials is confirmed by standard analytical methods, e.g., microanalysis, melting point (m.p.) and spectroscopic characteristics, e.g. MS, IR and NMR. Abbreviations used are those conventional in the art.

EXAMPLES

Preparation 1. 6-Bromo-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazine



Step I: To a stirred solution of 4-bromo-2-nitro phenol (2.0 g, 9.17 mmol) in acetonitrile (18 ml) was added ethyl 2-bromo isobutyrate (2.15 g, 11.01 mmol), sodium iodide (138 mg, 0.91 mmol), cesium carbonate (3.59 g, 11.01 mmol) and heated at 60 °C for 18 h. Usual work up after quenching the reaction with water (50 ml) gave us the crude product which was purified by silica gel column chromatography to furnish 2-(4-bromo-2-nitro-phenoxy)-2-methyl propionic acid ethyl ester (2.73 g).

^1H NMR (400 MHz, CDCl_3): δ 1.29 (t, $J = 7.2$ Hz, 3H), 1.67 (s, 6H), 4.28 (q, $J = 7.2$ Hz, 2H), 6.91 (d, $J = 8.8$ Hz, 1H), 7.56 (dd, $J = 9.2, 2.4$ Hz, 1H), 7.91 (d, $J = 2.4$ Hz, 1H).

Step II: To a stirred solution of 2-(4-bromo-2-nitro-phenoxy)-2-methyl propionic acid ethyl ester (1.0 g, 3.01 mmol) in ethanol (15 ml) was added Iron powder (837 mg, 15.06 mmol), conc. hydrochloric acid 0.3 ml was added to the reaction mixture and heated to reflux for 4 h, filtered through celite, concentrated and diluted with water (50 ml). After usual work up, compound was purified by silica gel column chromatography to furnish 6-bromo-2,2-dimethyl-4H-benzo[1,4]oxazin-3-one (517 mg).

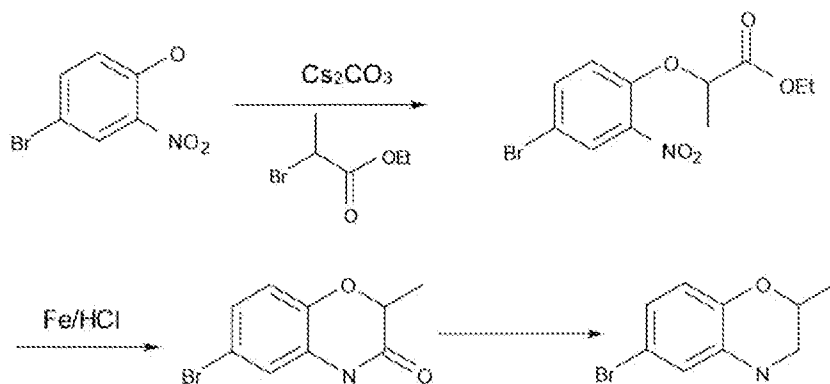
^1H NMR (400 MHz, CDCl_3): δ 1.56 (s, 6H), 6.86 (d, $J = 8.4$ Hz, 1H), 6.96 (d, $J = 2.4$ Hz, 1H), 7.12 (dd, $J = 8.4, 2.4$ Hz, 1H), 8.22 (bs, 1H)

Step III: To a stirred solution of 6-bromo-2,2-dimethyl-4H-benzo[1,4]oxazin-3-one (4.0g, 15.62 mmol) in THF (15 ml) was added 1.0 M Borane-tetrahydrofuran complex in THF (46.9 ml, 46.87 mmol) and refluxed for 6 h. The reaction mixture was cooled to 0 °C, quenched with methanol (30 ml) and concentrated under reduced pressure. The resulting residue was taken in ethyl acetate (100 ml), washed with aqueous saturated sodium bicarbonate solution (50 ml), water (50 ml), brine (50 ml), dried over sodium

sulphate, concentrated and purified by silica gel column chromatography to provide the titled compound (3.26 g).

^1H NMR (400 MHz, CDCl_3): δ 1.37 (s, 6H), 3.15 (s, 2H), 6.67 (d, $J = 8.4$ Hz, 1H), 6.82-6.85 (m, 2H).

Preparation 2. 6-Bromo-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazine

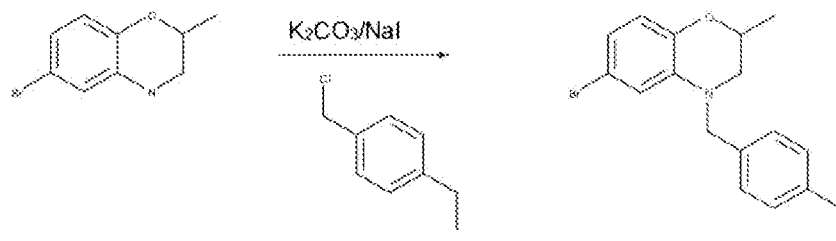


Step I: To a stirred solution of 4-bromo-2-nitro phenol (5.0 g, 22.93 mmol) in DMF (23 ml) was added ethyl 2-bromo propionate (6.22 g, 34.40 mmol), cesium carbonate (11.20 g, 34.40 mmol) and heated at 60°C for 18 h, quenched with water (50 ml). Usual work up provided crude 2-(4-bromo-2-nitro-phenoxy)-propionic acid ethyl ester (5.07 g), which was taken for next reaction.

Step II: To a stirred solution of 2-(4-bromo-2-nitro-phenoxy)-propionic acid ethyl ester (5.0 g, 15.72 mmol) in ethanol (78.0 ml) was added Iron powder (4.40 g, 78.61 mmol), conc. hydrochloric acid (1.5 ml) was added and heated to reflux for 4 h, filtered through celite, concentrated and quenched with water (50 ml). After usual work up, crude material obtained was purified by silica gel column chromatography to furnish the 6-bromo-2-methyl-4H-benzo[1,4]oxazin-3-one (3.21 g).

Step III: To a stirred solution of 6-bromo-2-methyl-4H-benzo[1,4]oxazin-3-one (3.0 g, 12.39 mmol) in THF (12.3 ml) was added 1.0 M borane-tetrahydrofuran complex in THF (37.2 ml, 37.19 mmol) and refluxed for 16 h. The reaction mixture was cooled to 0°C , quenched with methanol (30 ml) and concentrated under reduced pressure. The resulting residue was taken in ethyl acetate (50 ml), washed with aqueous saturated sodium bicarbonate solution (20 ml), water (20 ml), brine (20 ml), dried over sodium sulphate and concentrated to give the titled compound (2.32 g).

Preparation 3. 6-Bromo-4-(4-ethyl-benzyl)-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazine.

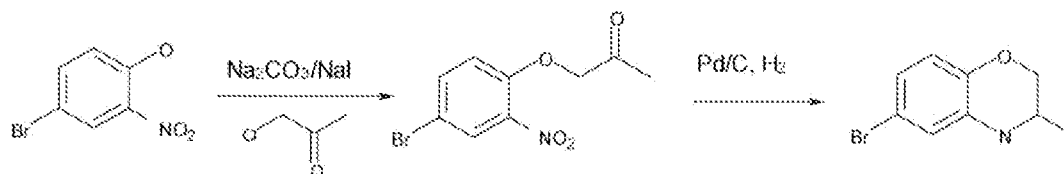


To a stirred solution of 6-bromo-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazine (obtained in preparation 2) (500 mg, 2.19 mmol) in DMF (2.1 ml) was added 4-ethylbenzyl chloride (410 mg, 2.63 mmol), sodium iodide (21.9 mg.), potassium carbonate (605 mg, 4.39 mmol) and heated at 60 °C for 16 h, quenched with water (40 ml). After usual work up, compound was purified by silica gel column chromatography (1% ethyl acetate in hexane) to furnish the titled compound (Yield = 605 mg).

¹H NMR (400 MHz, CDCl₃): δ 1.26 (t, J = 7.6 Hz, 3H), 1.46 (d, J = 8.6 Hz, 3H), 2.67 (q, J = 7.6 Hz, 2H), 3.08-3.13 (m, 1H), 3.23-3.26 (m, 1H), 4.23-4.27 (m, 1H), 4.42 (s, 2H), 6.70 (d, J = 8.4 Hz, 1H), 6.75 (d, J = 8.4, 1H), 6.84 (s, 1H), 7.20-7.23 (m, 4H);

MS (EI) *m/z* 346.0 (M+1)

Preparation 4. 6-Bromo-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazine



Step I: To a stirred solution of 4-bromo-2-nitro phenol (5.0 g, 22.93 mmol) in acetone (44 ml) was added 2-chloroacetone (3.21 g, 34.40 mmol), sodium carbonate (4.86 g, 45.87 mmol), sodium iodide (3.48 g, 22.93 mmol) and heated at 40 °C for 24 h. The reaction mixture was filtered through celite, concentrated, and quenched with water (50 ml). After usual work up, compound was precipitated with diisopropyl ether to furnish 1-(4-bromo-2-nitro-phenoxy)-propan-2-one (3.61 g).

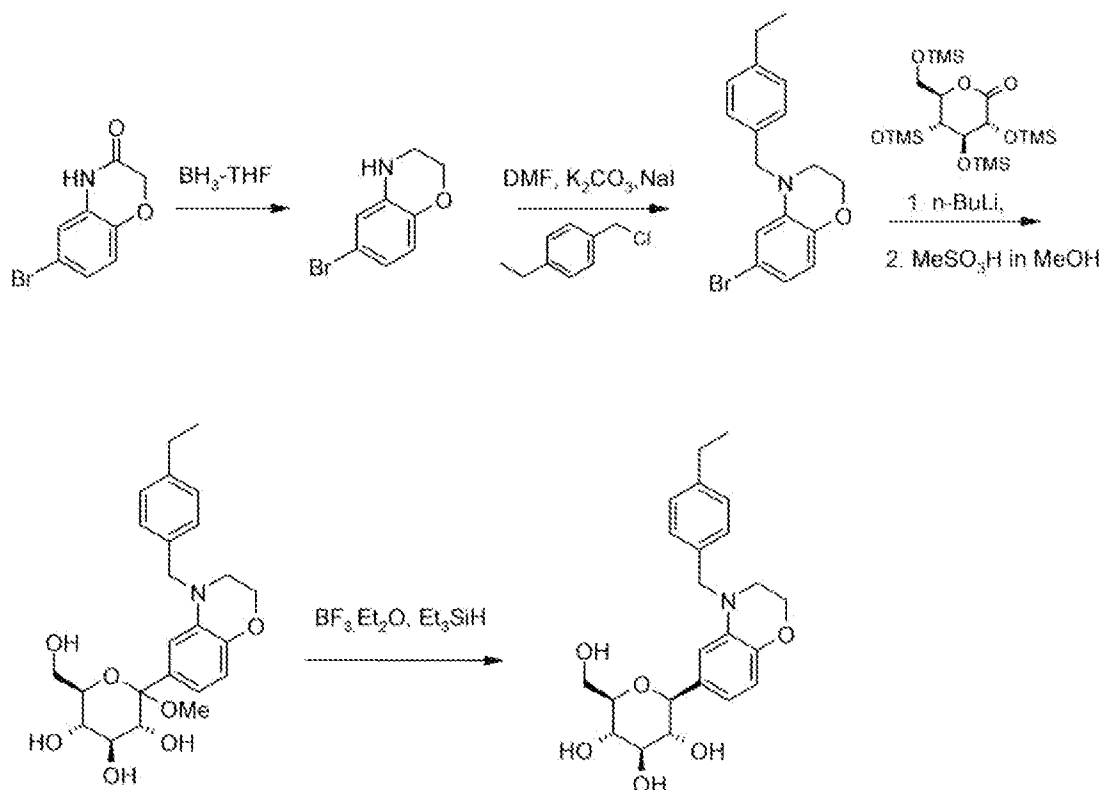
Step II: To a stirred solution of 1-(4-bromo-2-nitro-phenoxy)-propan-2-one (500 mg, 1.82 mmol) in methanol (18 ml) was added Raney-Nickel (100 mg, 20% w/w) and stirred under hydrogen pressure (balloon) for 16 h, filtered through celite, concentrated. After

usual work up, compound was purified by silica gel column chromatography to furnish the titled compound (213 mg).

^1H NMR (400 MHz, CDCl_3): δ 1.07 (d, $J = 6.4$ Hz, 3H), 3.36-3.39 (m, 1H), 3.57-3.62 (m, 1H), 4.10-4.13 (m, 1H), 6.09 (s, 1H), 6.53-6.59 (m, 2H), 6.68 (d, $J = 2.0$ Hz, 1H)

MS (EI) m/z 228 ($M+1$).

Example 1. (2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To an ice-cold stirred solution of D-glucono-1,5-lactone (5 g, 28.1 mmol) and N-methylmorpholine (22.7 ml, 230.2 mmol) in THF (50 ml) under argon was added trimethylsilyl chloride (21.4 ml, 168.4 mmol) via a dropping funnel and maintaining the temperature below 5°C . After 1 h, the reaction was heated to 35°C for 5 h. Then it was allowed to cool to 20°C as the reaction stirred overnight. Reaction mixture was cooled to 0°C and quenched by the addition of water (50 ml). The reaction mixture was diluted with toluene (50 ml) and the organic layer was separated and washed with sodium dihydrogen phosphate monobasic solution in water (50 ml), brine (50 ml), dried over

anhydrous sodium sulphate, filtered, and concentrated to provide 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (11.5 g).

Step II: To a stirred solution of 6-bromo-2H-1,4-benzoxazin-3(4H)-one (10 g, 43.85 mmol) in THF (25 ml) was added 1.0 M borane-tetrahydrofuran complex in THF (153.5 ml, 153.48 mmol) and refluxed for 14 h. The reaction mixture was cooled to room temperature, quenched with methanol (50 ml) and concentrated under reduced pressure. The resulting residue was taken in ethyl acetate (100 ml), washed with aqueous saturated sodium bicarbonate solution (100 ml), water (100 ml), brine (100 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (5% ethyl acetate in hexane) to provide 6-bromo-3,4-dihydro-2H-benzo[1,4]oxazine (8.5 g).

Step III: To a stirred solution of 6-bromo-3,4-dihydro-2H-benzo[1,4]oxazine (2.0 g, 9.34 mmol) in DMF (10 ml) was added 4-ethylbenzyl chloride (2.0 ml, 14.01 mmol), sodium iodide (250 mg, 0.93 mmol), potassium carbonate (2.58 g, 18.68 mmol) and heated at 60 °C for 20 h, quenched with water (40 ml). After usual work up, compound was purified by silica gel column chromatography (3% ethyl acetate in hexane) to furnish 6-bromo-4-(4-ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (2.2 g).

¹H NMR (400 MHz, CDCl₃): δ 1.25 (t, J = 8.0 Hz, 3H), 2.65 (q, J = 8.0 Hz, 2H), 3.35 (t, J = 4.4 Hz, 2H), 4.24 (t, J = 4.4 Hz, 2H), 4.41 (s, 2H), 6.89 (d, J = 8.4 Hz, 1H), 6.76 (dd, J = 8.4, 2.4 Hz, 1H), 6.85 (d, J = 2.0 Hz, 1H), 7.20-7.33 (m, 4H).

MS (ES) *m/z* 334.0 (M+2)

Step IV: To a stirred solution of 6-bromo-4-(4-ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (2.1 g, 6.32 mmol) in THF-toluene (30 ml of 1:2 mixture) was added 1.6 M solution of n-BuLi in hexanes (3.95 ml, 6.32 mmol) at -78 °C. The reaction mixture was stirred for 30 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (2.94 g, 6.32 mmol) in toluene (20 ml) at -78 °C. After stirring for 40 min., 0.6 N methanesulfonic acid in methanol (15 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate (10 ml). This reaction mixture was extracted with ethyl acetate (3 X 20 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography to furnish (3R,4S,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (1.0 g).

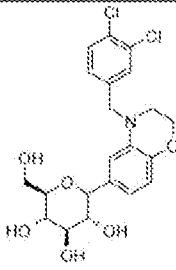
¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 7.6 Hz, 3H), 2.63 (q, J = 7.6 Hz, 2H), 2.98 (s, 3H), 3.10 (d, J = 9.2 Hz, 1H), 3.35-3.40 (m, 3H), 3.56 (m, 1H), 3.73 (t, J = 9.2 Hz, 1H),

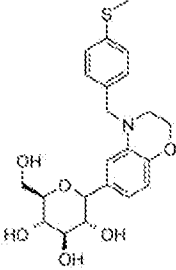
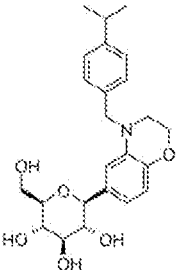
3.79 (dd, $J = 12.0, 5.6$ Hz, 1H), 3.92 (dd, $J = 11.6, 2.0$ Hz, 1H), 4.21-4.26 (m, 2H), 4.42 (d, $J = 15.6$ Hz, 1H), 4.54 (d, $J = 15.6$ Hz, 1H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.86 (dd, $J = 8.0, 1.2$ Hz, 1H), 7.02 (d, $J = 1.6$ Hz, 1H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H). MS (ES) m/z 446.3 ($M+1$).

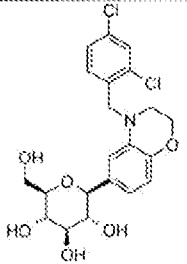
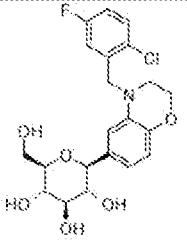
Step V: To a stirred solution of (3R,4S,5S,6R)-2-[4-(4-ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (1.0 g, 2.26 mmol) in acetonitrile-dichloromethane mixture (1:1 mixture, 10 ml) was added boron trifluoride diethyletharate complex (0.57 ml, 4.52 mmol), and triethylsilane (1.3 ml, 9.04 mmol) at -5°C . After stirring for 4 h at 0°C , reaction was quenched with aq. saturated sodium bicarbonate solution (8 ml). The volatiles were evaporated under reduced pressure; the resulting mixture was extracted with ethyl acetate (3 X 20 ml). The organic layer was washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish the titled compound (180 mg)

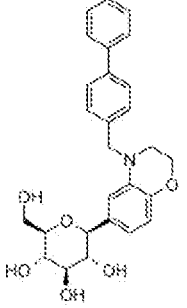
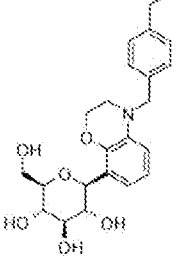
^1H NMR (400 MHz, CD_3OD): δ 1.24 (t, $J = 7.6$ Hz, 3H), 2.64 (q, $J = 7.6$ Hz, 2H), 3.29-3.44 (m, 6H), 3.67 (dd, $J = 12.0, 5.2$ Hz, 1H), 3.86 (d, $J = 11.6$ Hz, 1H), 3.97 (d, $J = 9.2$ Hz, 1H), 4.20 (t, $J = 4.0$ Hz, 2H), 4.42 (d, $J = 15.6$ Hz, 1H), 4.48 (d, $J = 15.6$ Hz, 1H), 6.67 (d, $J = 9.6$ Hz, 1H), 6.71 (d, $J = 8.0$ Hz, 1H), 6.88 (s, 1H), 7.17 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H). MS (ES) m/z 416.1 ($M+1$).

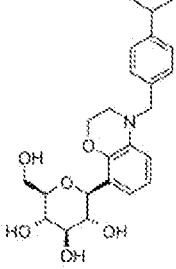
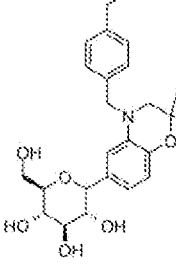
Examples 2-15 were prepared in an analogous procedure as described in example 1.

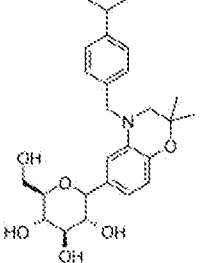
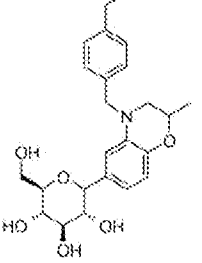
Example #	Structure	MS ($M+1$)	^1H NMR
Example 2	 (3R,4R,5S,6R)-2-[4-(3,4-Dichlorobenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol	<u>456.0</u>	^1H NMR (400 MHz, CDCl_3): (peaks correspond to major isomer) δ 2.20 (bs, 1H), 2.24 (bs, 1H), 3.20 (bs, 1H), 3.29-3.84 (m, 9H), 3.98 (d, $J = 9.6$ Hz, 1H), 4.24 (t, $J = 4.0$ Hz, 2H), 4.36 (s, 2H), 6.60 (s, 1H), 6.67 (d, $J = 8.4$ Hz, 1H), 6.80 (d, $J = 8.0$ Hz, 1H), 7.11 (d, $J = 7.6$ Hz, 1H), 7.38 (d, $J = 8.4$ Hz, 2H).

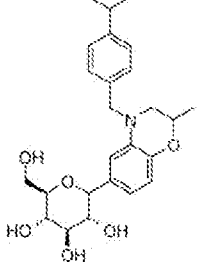
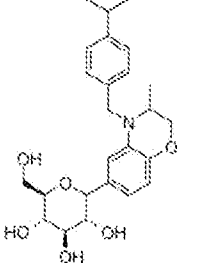
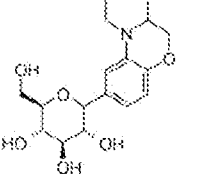
	hydroxymethyl- tetrahydro-pyran- 3,4,5-triol		
Example 3	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-methylsulfanylbenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	434.3	¹ H NMR (400 MHz, CD ₃ OD): (peaks correspond to major isomer) δ 2.45 (s, 3H), 3.29-3.44 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 4.42 (d, J = 15.6 Hz, 1H), 4.48 (d, J = 15.6 Hz, 1H), 6.67 (d, J = 9.6 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H).
Example 4	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-isopropylbenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	430.1	¹ H NMR (400 MHz, CD ₃ OD): δ 1.25 (d, J = 6.8 Hz, 6H), 2.88-2.92 (m, 1H), 3.29-3.44 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 4.42 (d, J = 15.6 Hz, 1H), 4.48 (d, J = 15.6 Hz, 1H), 6.67 (d, J = 9.6 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H).

Example 5	 (2S,3R,4R,5S,6R)- 2-[4-(2,4-Dichloro- benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin- 6-yl]-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol.	<u>455.9</u>	¹H NMR (400 MHz, CD₃OD): δ 3.27-3.43 (m, 6H), 3.65 (dd, J = 12.4, 4.8 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.94 (d, J = 9.2 Hz, 1H), 4.27 (t, J = 4.0 Hz, 2H), 4.52 (d, J = 17.2 Hz, 1H), 4.59 (d, J = 17.2 Hz, 1H), 6.62 (s, 1H), 6.69-6.75 (m, 2H), 7.33 (dd, J = 8.4, 1.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 2.0 Hz, 1H).
Example 6	 (2S,3R,4R,5S,6R)- 2-[4-(2-Chloro-5- fluoro-benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin- 6-yl]-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol.	<u>440.0</u>	¹H NMR (400 MHz, CD₃OD): δ 3.30-3.46 (m, 6H), 3.65 (dd, J = 12.4, 4.8 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.93 (d, J = 9.6 Hz, 1H), 4.29 (t, J = 4.0 Hz, 2H), 4.52 (d, J = 17.2 Hz, 1H), 4.59 (d, J = 17.2 Hz, 1H), 6.59 (s, 1H), 6.71-7.48 (series of m, 5H).

Example 7	 (2S,3R,4R,5S,6R)- 2-(4-Biphenyl-4- ylmethyl-3,4- dihydro-2H- benzo[1,4]oxazin- 6-yl)-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol	464.1	¹H NMR (400 MHz, CD₃OD): δ 3.33-3.46 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.25 (t, J = 4.0 Hz, 2H), 4.53 (d, J = 15.6 Hz, 1H), 4.58 (d, J = 15.6 Hz, 1H), 6.69 (d, J = 9.6 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.90 (s, 1H), 7.34 (t, J = 7.6 Hz, 1H), 7.42-7.46 (m, 4H), 7.60-7.64 (m, 4H).
Example 8	 (2S,3R,4R,5S,6R)- 2-[4-(4-Ethyl- benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin- 8-yl]-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol	416.4	¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 7.6 Hz, 3H), 2.62 (q, J = 6.8 Hz, 2H), 3.33-3.58 (m, 6H), 3.67 (d, J = 10.8 Hz, 1H), 3.87 (d, J = 12.4 Hz, 1H), 4.27 (s, 2H), 4.45 (s, 2H), 4.68 (d, J = 8.8 Hz, 1H), 6.66 (s, 1H), 6.75 (s, 2H), 7.16 (d, J = 6.8 Hz, 2H), 7.22 (d, J = 6.8 Hz, 2H).

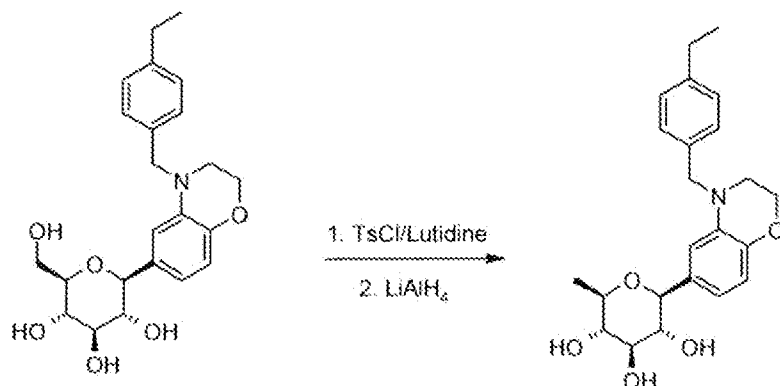
Example 9	 (2S,3R,4R,5S,6R)- 2-[4-(4-Ethyl- benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin- 8-yl]-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol	430.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.24 (d, J = 6.8 Hz, 6H), 2.86-2.91 (m, 1H), 3.33-3.56 (m, 6H), 3.67 (dd, J = 8.0, 3.2 Hz, 1H), 3.87 (d, J = 8.0 Hz, 1H), 4.24-4.30 (m, 2H), 4.45 (s, 2H), 4.69 (d, J = 9.2 Hz, 1H), 6.65-6.69 (m, 1H), 6.75-6.76 (m, 2H), 7.18 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H).
Example 10	 (3R,4R,5S,6R)-2- [4-(4-Ethyl-benzyl)- 2,2-dimethyl-3,4- dihydro-2H- benzo[1,4]oxazin- 6-yl]-6- hydroxymethyl- tetrahydro-pyran- 3,4,5-triol	444.1	¹ H NMR (400 MHz, DMSO-D ₆): (peaks correspond to major isomer) δ 1.18 (t, J = 7.5 Hz, 3H), 1.26 (s, 6H), 2.60 (q, J = 7.5 Hz, 2H), 3.07 (s, 2H), 3.36-3.42 (m, 1H), 3.57-3.61 (m, 1H), 3.72-3.75 (m, 1H), 3.80-3.86 (m, 3H), 3.97 (bt, 1H), 4.29 (d, J = 3.1 Hz, 1H), 4.40-4.44 (m, 2H), 4.61 (d, J = 5.5 Hz, 1H), 4.90 (d, J = 4.0 Hz, 1H), 5.29 (d, J = 4.4 Hz, 1H), 6.57-6.58 (m, 2H), 6.90 (s, 1H), 7.18 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H).

Example 11	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	458.1	¹H NMR (400 MHz, DMSO-D₆): (peaks correspond to major isomer) δ 1.12 (d, J = 6.8 Hz, 6H), 1.27 (s, 6H), 2.85-2.89 (m, 1H), 3.09 (s, 2H), 3.89-3.42 (m, 1H), 3.59-3.61 (m, 1H), 3.73-3.75 (m, 1H), 3.80-3.86 (m, 2H), 3.97 (bt, 1H), 4.29 (d, J = 3.6 Hz, 1H), 4.41-4.44 (m, 3H), 4.61 (d, J = 5.6 Hz, 1H), 4.90 (d, J = 4.0 Hz, 1H), 5.29 (d, J = 4.4 Hz, 1H), 6.57-6.58 (m, 2H), 6.91 (s, 1H), 7.21 (d, J = 7.9 Hz, 2H), 7.29 (d, J = 7.9 Hz, 2H).
Example 12	 (2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	430.2	¹H NMR (400 MHz, CD₃OD): (peaks correspond to major isomer) δ 1.24 (t, J = 7.5 Hz, 3H), 1.31 (d, J = 6.2 Hz, 3H), 2.64 (q, J = 7.5 Hz, 2H), 2.97-3.02 (m, 1H), 3.27-3.31 (m, 2H), 3.36-3.45 (m, 3H), 3.66-3.69 (m, 1H), 3.86 (d, J = 11.9 Hz, 1H), 3.96-3.99 (dd, J = 9.2 Hz, 2.0 Hz, 1H), 4.18-4.44 (m, 1H), 4.44-4.47 (m, 2H), 6.67 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 8.2 Hz, 1H), 6.88 (d, J = 2.6 Hz, 1H), 7.18 (d, J = 7.9 Hz, 2H), 7.24-7.27 (m, 2H).

Example 13	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropylbenzyl)-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	444.1	¹H NMR (400 MHz, DMSO-D₆): (peaks correspond to major isomer) δ 1.20 (d, J = 6.8 Hz, 6H), 1.27 (d, J = 6.2 Hz, 3H), 2.86-2.94 (m, 1H), 2.96-3.12 (m, 1H), 3.15-3.23 (m, 3H), 3.28-3.44 (m, 3H), 3.67-3.70 (m, 1H), 3.84 (d, J = 9.2 Hz, 1H), 4.19 (t, J = 6 Hz, 1H), 4.35-4.49 (m, 3H), 4.67 (d, J = 4.8 Hz, 1H), 4.92 (d, J = 4.4 Hz, 2H), 6.55 (d, J = 7.9 Hz, 1H), 6.64 (dd, J = 7.9 Hz, 1H), 6.81 (d, J = 5.2 Hz, 1H), 7.20-7.27 (m, 4H)
Example 14	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropylbenzyl)-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	444.1	¹H NMR (400 MHz, CD₃OD): (peaks correspond to major isomer) δ 1.16 (d, J = 6.4 Hz, 3H), 1.26 (d, J = 6.8 Hz, 6H), 2.87-2.94 (m, 2H), 3.41-3.51 (m, 3H), 3.62-3.65 (m, 1H), 3.83-3.86 (m, 1H), 3.92-3.97 (m, 1H), 4.01-4.07 (m, 2H), 4.09-4.36 (m, 1H), 4.37-4.65 (m, 2H), 6.66-6.68 (m, 1H), 6.72-6.77 (m, 2H), 7.21 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 7.7 Hz, 2H)
Example 15	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropylbenzyl)-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	340.1	¹H NMR (400 MHz, CD₃OD): (peaks correspond to major isomer) δ 1.17-1.22 (m, 6H), 3.37-3.52 (m, 7H), 3.68-3.72 (m, 1H), 3.88 (d, J = 12.0 Hz, 1H), 3.91-4.03

	(3R,4R,5S,6R)-2-(4-Ethyl-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol		(m, 3H), 6.62 (d, J = 8.2 Hz, 1H), 6.71 (d, J = 7.9 Hz, 1H), 6.77 (d, J = 1.3 Hz, 1H).
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Example 16. (2S,3R,4S,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-methyl-tetrahydro-pyran-3,4,5-triol



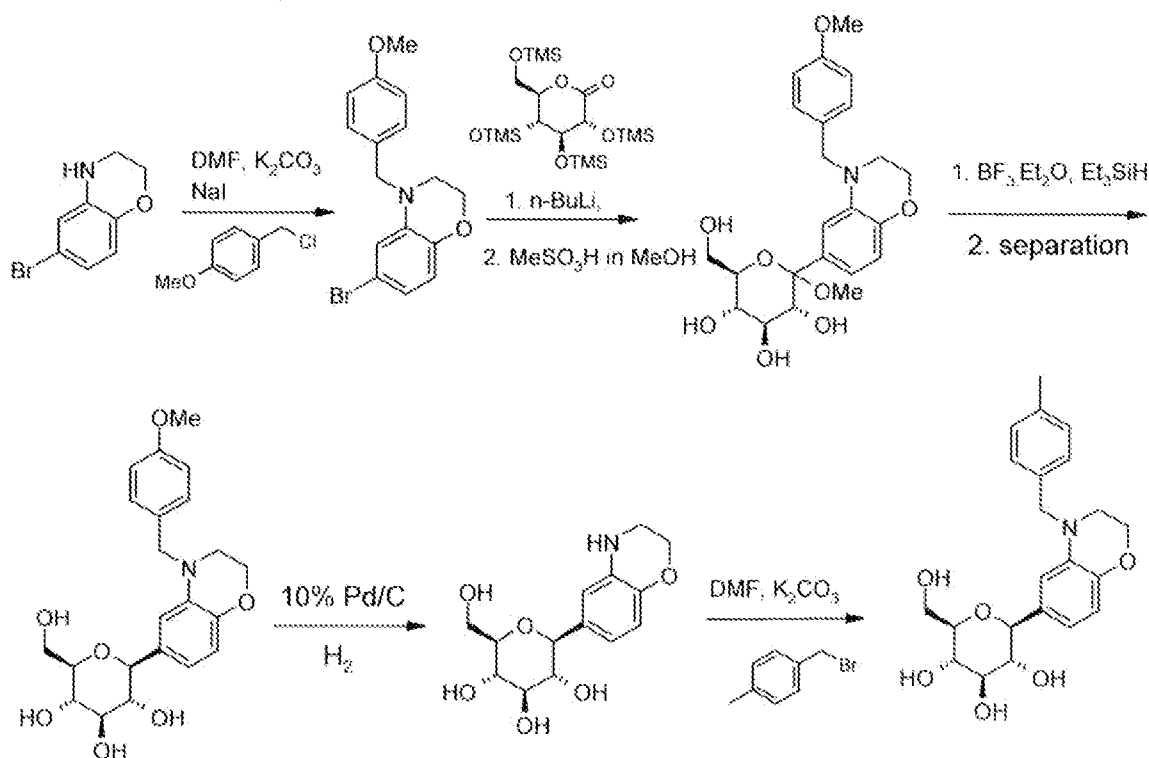
To a stirred solution of (2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (150 mg, 0.36 mmol) in lutidine (3 ml) was added tosyl chloride at 0 °C. After stirring for overnight at ambient temperature, reaction was quenched by the addition of water (5 ml). This mixture was extracted with ethyl acetate (2 X 10 ml). Organic layer was evaporated under reduced pressure and purified by column chromatography to give toluene-4-sulfonic acid (2R,3S,4R,5R,6S)-6-[4-(4-ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-3,4,5-trihydroxy-tetrahydro-pyran-2-ylmethyl ester (150 mg). MS (ES) *m/z* 570.1 (M+1).

To a stirred solution of lithium aluminium hydride (35 mg, 0.92 mmol) in dry THF (4 ml) was added a solution of Toluene-4-sulfonic acid (2R,3S,4R,5R,6S)-6-[4-(4-ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-3,4,5-trihydroxy-tetrahydro-pyran-2-ylmethyl ester (175 mg, 0.307 mmol) in THF (2 ml) at 0 °C. After stirring at ambient temperature for overnight, reaction mixture was cooled to 0 °C and quenched by the addition of aq.

saturated sodium sulfate solution. This was filtered through celite bed, washed with methanol, concentrated and purified to give the titled compound. (Yield = 5 mg).

^1H NMR (400 MHz, CD_3OD): δ 1.23-1.31 (m, 6H), 2.64 (q, $J = 7.6$ Hz, 2H), 3.09 (t, $J = 9.2$ Hz, 2H), 3.33-3.41 (m, 4H), 3.94 (d, $J = 8.8$ Hz, 1H), 4.21 (t, $J = 3.6$ Hz, 2H), 4.44 (s, 2H), 6.62 (d, $J = 8.0$ Hz, 1H), 6.71 (d, $J = 8.4$ Hz, 1H), 6.82 (s, 1H), 7.18 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H). MS (ES) m/z 400.3 ($M+1$).

Example 17. (2S,3R,4R,5S,6R)-2-[4-(4-Methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 6-bromo-3,4-dihydro-2H-benzo[1,4]oxazine (1.5 g, 7.0 mmol) in DMF (10 ml) was added 4-methoxybenzyl chloride (1.43 ml, 10.5 mmol), sodium iodide (105 mg, 0.7 mmol), and potassium carbonate (1.93 g, 14.0 mmol). The reaction mixture was heated at 60 °C for 20 h, quenched with water (40 ml). After usual work up, compound was purified by silica gel column chromatography to furnish 6-bromo-4-(4-methoxybenzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (2.2 g).

^1H NMR (400 MHz, CDCl_3): δ 3.28 (t, $J = 4.4$ Hz, 2H), 3.8 (s, 3H), 4.20 (t, $J = 4.4$ Hz, 2H), 4.34 (s, 2H), 6.64 (d, $J = 8.4$ Hz, 1H), 6.70 (dd, $J = 8.4, 2.0$ Hz, 1H), 6.80 (d, $J = 2.0$ Hz, 1H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H). MS (ES) m/z 336.1 ($M+2$).

Step II: To a stirred solution of 6-bromo-4-(4-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (20.0 g, 59.8 mmol) in THF-toluene (1:2 mixture, 150 ml) was added 1.6 M n-BuLi in hexanes (37.4 ml, 59.8 mmol) at -78 °C. The reaction mixture was stirred for 40 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (28.0 g, 59.8 mmol) in toluene (150 ml) at -78 °C. After stirring for 40 min., 0.6 N methanesulfonic acid in methanol (140 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate (30 ml). This was extracted with ethyl acetate (3 X 100 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography to furnish (3R,4S,5S,6R)-6-Hydroxymethyl-2-methoxy-2-[4-(4-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol (10.2 g). ¹H NMR (400 MHz, CD₃OD): δ 3.02 (s, 3H), 3.11 (d, J = 9.6 Hz, 1H), 3.31-3.33 (m, 2H), 3.39 (t, J = 9.2 Hz, 1H), 3.54-3.58 (m, 1H), 3.74 (t, J = 9.2 Hz, 1H), 3.78 (s, 3H), 3.81 (t, J = 5.6 Hz, 1H), 3.93 (dd, J = 11.6, 1.6 Hz, 1H), 3.99-4.24 (m, 2H), 4.39 (d, J = 15.2 Hz, 1H), 4.49 (d, J = 15.2 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.85-6.90 (m, 3H), 7.05 (s, 1H), 7.29 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 448.1 (M+1).

Step III: To a stirred solution of (3R,4S,5S,6R)-6-hydroxymethyl-2-methoxy-2-[4-(4-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol (10.0 g, 22.3 mmol) in acetonitrile-dichloromethane mixture (1:1, 100 ml) was added boron trifluoride diethyletherate complex (5.7 ml, 44.7 mmol) and triethylsilane (14.3 ml, 89.4 mmol) at -10 °C. After stirring for 4 h at 0 °C, reaction was quenched with aq. saturated sodium bicarbonate solution (30 ml). The volatiles were evaporated under reduced pressure, the resulting was extracted with ethyl acetate (3 X 70 ml). The ethyl acetate layers were mixed, washed with brine (1 X 15 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish (2S,3R,4R,5S,6R)-2-[4-(4-Methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

¹H NMR (400 MHz, CD₃OD): δ 3.28 (t, J = 4.4 Hz, 2H), 3.33-3.46 (m, 4H), 3.68 (dd, J = 11.6, 4.8 Hz, 1H), 3.79 (s, 3H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.19 (t, J = 4.0 Hz, 2H), 4.39 (d, J = 15.6 Hz, 1H), 4.44 (d, J = 15.6 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.89 (d, J = 8.4 Hz, 3H), 7.27 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 418.2 (M+1).

Step IV: To a stirred solution of (2S,3R,4R,5S,6R)-2-[4-(4-Methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (140 mg, 0.33

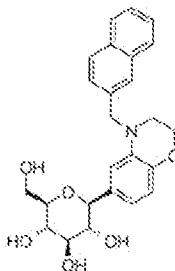
mmol) in methanol (5 ml) was added 10% palladium on charcoal (25 mg), 0.05 ml conc. HCl and stirred under hydrogen balloon pressure for 18 h. Reaction mixture was filtered through celite bed, washed with methanol and concentrated. The resulting residue was titrated in n-hexanes and dried under vacuum to furnish (2S,3R,4R,5S,6R)-2-(3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (90 mg). ¹H NMR (400 MHz, CD₃OD): δ 3.29-3.44 (m, 4H), 3.70-3.72 (m, 3H), 3.91 (d, J = 11.2 Hz, 1H), 4.15 (d, J = 9.6 Hz, 1H), 4.45 (t, J = 4.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 1H), 7.34 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H).

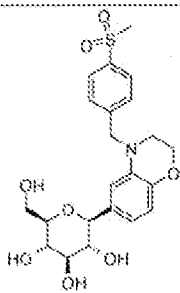
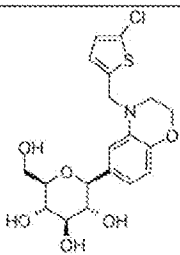
MS (ES) *m/z* 298.3 (M+1).

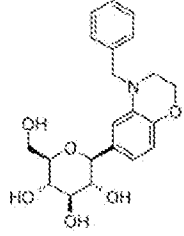
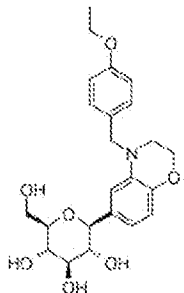
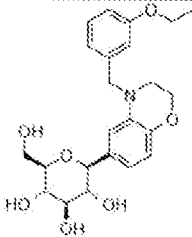
Step V: To a stirred solution of (2S,3R,4R,5S,6R)-2-(3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (70 mg, 0.23 mmol) in DMF (2 ml), was added potassium carbonate (65 mg, 0.47 mmol) and 4-methylbenzyl bromide (65 mg, 0.33 mmol). Reaction mixture was heated at 50 °C for 2h, quenched by the addition of water (3 ml). After usual work up product was purified by column chromatography to give the titled compound (20 mg).

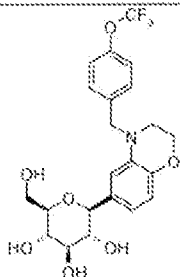
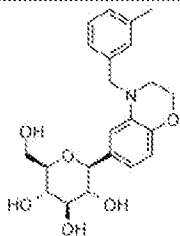
¹H NMR (400 MHz, CD₃OD): δ 2.33 (s, 3H), 3.29-3.46 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 12.0 Hz, 1H), 3.97 (d, J = 9.6 Hz, 1H), 4.20 (t, J = 4.4 Hz, 2H), 4.42 (d, J = 15.6 Hz, 1H), 4.48 (d, J = 15.6 Hz, 1H), 6.67 (d, J = 9.6 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 6.87 (s, 1H), 7.15 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H). MS (ES) *m/z* 402.3 (M+1).

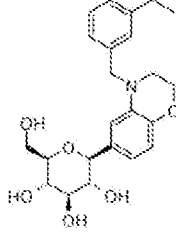
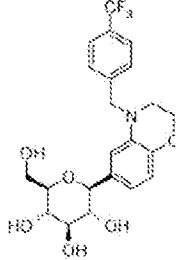
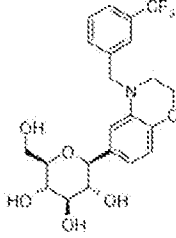
Examples 18-56 were prepared in an analogous procedure as described in example 17.

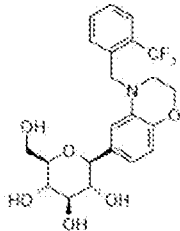
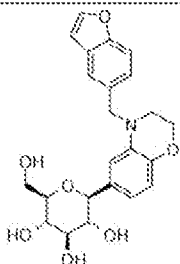
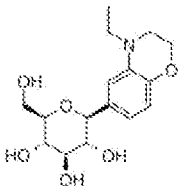
Example #	Structure	MS (M+1)	¹ H NMR
Example 18	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-(4-naphthalen-2-ylmethyl-	<u>438.0</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.31-3.44 (m, 6H), 3.63 (dd, J = 11.6, 4.8 Hz, 1H), 3.84 (d, J = 11.2 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.26 (t, J = 4.0 Hz, 2H), 4.64 (d, J = 15.6 Hz, 1H), 4.69 (d, J = 15.6 Hz, 1H), 6.70 (dd, J = 8.0, 1.2 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 1.2 Hz, 1H), 7.46-7.87 (m, 7H).

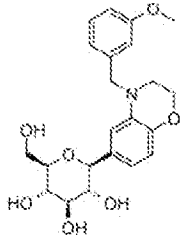
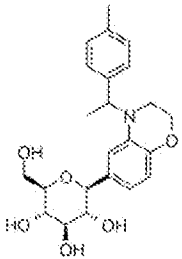
	3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-tetrahydro-pyran-3,4,5-triol		
Example 19	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methanesulfonyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	<u>466.0</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.13 (s, 3H), 3.26 (t, J = 9.2 Hz, 1H), 3.33-3.44 (m, 5H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.4 Hz, 1H), 3.94 (d, J = 9.6 Hz, 1H), 4.27 (t, J = 4.0 Hz, 2H), 4.61 (d, J = 16.8 Hz, 1H), 4.66 (d, J = 16.8 Hz, 1H), 6.68-6.73 (m, 3H), 7.63 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H).
Example 20	 (2S,3R,4R,5S,6R)-2-[4-(5-Chloro-thiophen-2-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>428.0</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.31-3.47 (m, 6H), 3.71 (dd, J = 12.0, 5.2 Hz, 1H), 3.89 (d, J = 12.0 Hz, 1H), 4.02 (d, J = 9.2 Hz, 1H), 4.21 (t, J = 4.4 Hz, 2H), 4.57 (d, J = 16.0 Hz, 1H), 4.65 (d, J = 16.0 Hz, 1H), 6.72 (s, 2H), 6.84 (d, J = 3.6 Hz, 1H), 6.88 (d, J = 4.0 Hz, 1H), 6.98 (s, 1H).

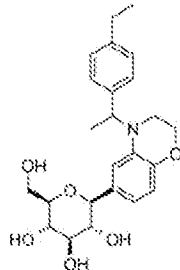
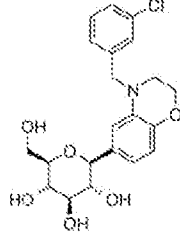
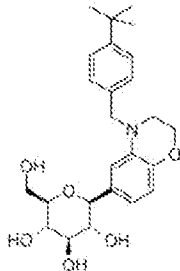
Example 21	 (2S,3R,4R,5S,6R)-2-(4-Benzyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	388.3	¹H NMR (400 MHz, CD₃OD): δ 3.31-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.95 (d, J = 9.6 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 4.45 (d, J = 16.0 Hz, 1H), 4.51 (d, J = 16.0 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 7.6 Hz, 1H), 6.85 (s, 1H), 7.23-7.33 (m, 5H).
Example 22	 (2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	432.4	¹H NMR (400 MHz, CD₃OD): δ 1.37 (t, J = 6.8 Hz, 3H), 3.26 (t, J = 4.0 Hz, 2H), 3.32-3.44 (m, 4H), 3.66 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.96 (d, J = 9.6 Hz, 1H), 4.01 (q, J = 6.8 Hz, 2H), 4.18 (t, J = 4.0 Hz, 2H), 4.37 (d, J = 16.0 Hz, 1H), 4.42 (d, J = 16.0 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 8.4 Hz, 2H), 6.89 (s, 1H), 7.22 (d, J = 8.0 Hz, 2H).
Example 23	 (2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	432.4	¹H NMR (400 MHz, CD₃OD): δ 1.37 (t, J = 6.8 Hz, 3H), 3.31-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.00 (q, J = 6.8 Hz, 2H), 4.20 (t, J = 4.0 Hz, 2H), 4.42 (d, J = 16.0 Hz, 1H), 4.43 (d, J = 16.0 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.79 (d, J = 8.4 Hz, 1H), 6.83 (s, 1H), 6.87 (s, 1H), 6.89 (d, J = 8.4 Hz, 1H), 7.22 (t, J = 8.0 Hz, 1H).

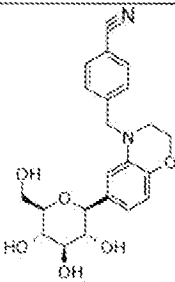
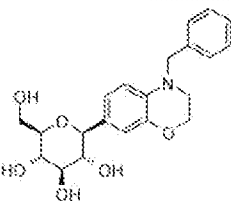
	benzo[1,4]oxazin-6-yl]- 6-hydroxymethyl- tetrahydro-pyran-3,4,5- triol		
Example 24	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethoxybenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	472.3	¹ H NMR (400 MHz, CD ₃ OD): δ 3.29-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 4.49 (d, J = 16.0 Hz, 1H), 4.54 (d, J = 16.0 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 6.82 (s, 1H), 7.24 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H).
Example 25	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methylbenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	402.3	¹ H NMR (400 MHz, CD ₃ OD): δ 2.33 (s, 3H), 3.32-3.44 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.21 (t, J = 4.0 Hz, 2H), 4.43 (d, J = 16.0 Hz, 1H), 4.44 (d, J = 16.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 6.8 Hz, 1H), 7.17 (s, 1H), 7.12 (d, J = 7.6 Hz, 1H).

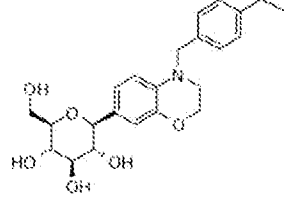
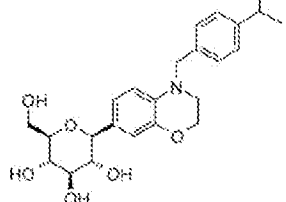
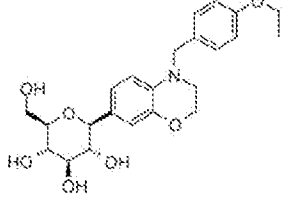
Example 26	 (2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	416.4	¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 4.8 Hz, 3H), 2.63 (q, J = 7.2 Hz, 2H), 3.32-3.44 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.21 (t, J = 4.0 Hz, 2H), 4.43 (d, J = 16.0 Hz, 1H), 4.44 (d, J = 16.0 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.86 (s, 1H), 7.09-7.23 (m, 4H).
Example 27	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	456.3	¹H NMR (400 MHz, CD₃OD): δ 3.27-3.42 (m, 6H), 3.64 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 11.6 Hz, 1H), 3.94 (d, J = 9.6 Hz, 1H), 4.23 (t, J = 4.0 Hz, 2H), 4.56 (d, J = 16.0 Hz, 1H), 4.61 (d, J = 16.0 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.77 (s, 1H), 7.53 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H).
Example 28	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	456.3	¹H NMR (400 MHz, CD₃OD): δ 3.27-3.42 (m, 6H), 3.64 (dd, J = 11.6, 4.8 Hz, 1H), 3.86 (d, J = 12.0 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.24 (t, J = 4.0 Hz, 2H), 4.54 (d, J = 15.6 Hz, 1H), 4.59 (d, J = 15.6 Hz, 1H), 6.69 (d, J = 7.6 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.79 (s, 1H), 7.52-7.655 (m, 4H).

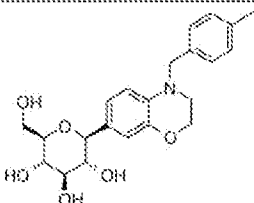
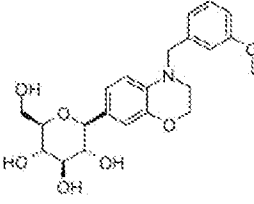
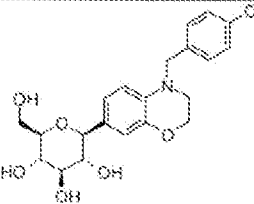
	3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol		
Example 29	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(2-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	<u>456.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.22-3.38 (m, 4H), 3.40 (t, J = 4.0 Hz, 2H), 3.59 (dd, J = 12.0, 5.2 Hz, 1H), 3.82 (d, J = 12.0 Hz, 1H), 3.89 (d, J = 9.6 Hz, 1H), 4.27 (t, J = 4.0 Hz, 2H), 4.64 (d, J = 17.2 Hz, 1H), 4.71 (d, J = 17.2 Hz, 1H), 6.58 (s, 1H), 6.68 (d, J = 7.6 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 5.2 Hz, 1H), 7.55-7.59 (m, 2H), 7.74 (d, J = 8.0 Hz, 1H).
Example 30	 (2S,3R,4R,5S,6R)-2-(4-Benzofuran-5-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>428.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.31-3.44 (m, 6H), 3.64 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 4.54 (d, J = 16.0 Hz, 1H), 4.59 (d, J = 16.0 Hz, 1H), 6.66 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H), 6.91 (s, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 8.8 Hz, 1H), 7.59 (s, 1H), 7.73 (s, 1H).
Example 31	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(2-ethyl-2H-benzo[1,4]oxazin-6-yl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	<u>326.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.15 (t, J = 2.5 Hz, 3H), 3.33-3.45 (m, 8H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 6.63-

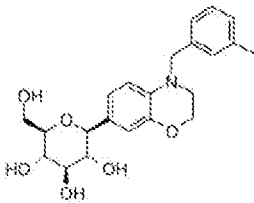
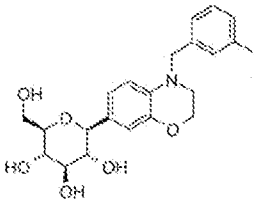
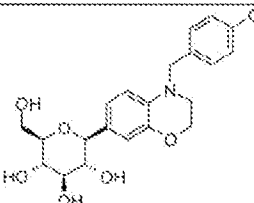
	(2S,3R,4R,5S,6R)-2-(4-Ethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-,4,5-triol		6.67 (m, 2H), 6.79 (s, 1H).
Example 32	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	418.4	¹ H NMR (400 MHz, CD ₃ OD): δ 3.33-3.45 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.78 (s, 3H), 3.85 (d, J = 11.6 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 4.44 (d, J = 16.8 Hz, 1H), 4.49 (d, J = 16.8 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.72 (d, J = 8.4 Hz, 1H), 6.80-6.85 (m, 2H), 6.92 (d, J = 8.4 Hz, 2H), 7.25 (t, J = 8.0 Hz, 1H).
Example 33	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(1-p-tolyl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	416.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.52-1.55 (m, 3H), 2.32 (s, 3H), 2.93-3.13 (m, 1H), 3.14-3.22 (m, 1H), 3.32-3.46 (m, 4H), 3.70 (dd, J = 12.0, 4.8 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97-4.02 (m, 2H), 4.08-4.13 (m, 1H), 5.16-5.22 (m, 1H), 6.63 (d, J = 8.4 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 7.15 (d, J = 7.2 Hz, 2H), 7.27 (t, J = 7.2 Hz, 2H).

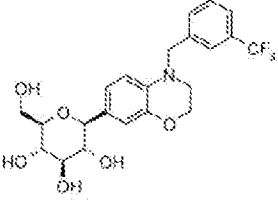
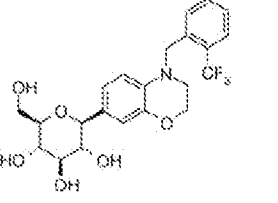
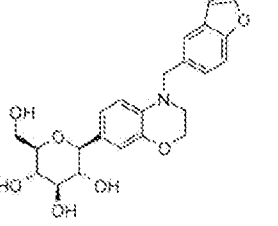
Example 34	 (2S,3R,4R,5S,6R)-2-[4-[1-(4-Ethyl-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>430.4</u>	¹H NMR (400 MHz, CD₃OD): δ 1.24 (t, J = 7.6 Hz, 3H), 1.53-1.56 (m, 3H), 2.64 (q, J = 7.6 Hz, 2H), 2.96-3.06 (m, 1H), 3.0(m, 1H), 3.33-3.45 (m, 5H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97-4.02 (m, 2H), 4.09-4.12 (m, 1H), 5.32-5.28 (m, 1H), 6.64 (d, J = 8.4 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 7.00 (d, J = 14.8 Hz, 1H), 7.18 (d, J = 6.8 Hz, 2H), 7.30 (t, J = 8.0 Hz, 2H).
Example 35	 (2S,3R,4R,5S,6R)-2-[4-(3-Chloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>422.3</u>	¹H NMR (400 MHz, CD₃OD): δ 3.28-3.42 (m, 5H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 4.46 (d, J = 16.0 Hz, 1H), 4.52 (d, J = 16.0 Hz, 1H), 4.6 (s, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.71 (d, J = 8.4 Hz, 1H), 6.78 (s, 1H), 7.25-7.36 (m, 4H).
Example 36	 (2S,3R,4R,5S,6R)-2-[4-(4-tert-Butyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>444.4</u>	¹H NMR (400 MHz, CD₃OD): δ 1.31 (s, 9H), 3.27-3.44 (m, 6H), 3.66 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.6 Hz, 1H), 4.19 (t, J = 4.0 Hz, 2H), 4.42 (d, J = 16.0 Hz, 1H), 4.47 (d, J = 16.0 Hz, 1H), 6.65 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.88 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H).

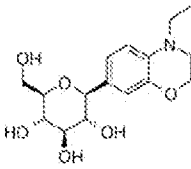
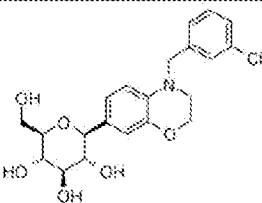
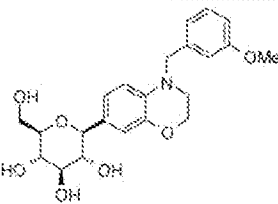
	3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol		
Example 37	 4-[6-((2S,3R,4R,5S,6R)-3,4,5-Trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yl)-2,3-dihydro-benzo[1,4]oxazin-4-ylmethyl]-benzonitrile	<u>413.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.26 (t, J = 8.8 Hz, 1H), 3.33-3.41 (m, 5H), 3.64 (dd, J = 12.0 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.92 (d, J = 9.2 Hz, 1H), 4.24 (t, J = 4.0 Hz, 2H), 4.55 (d, J = 17.2 Hz, 1H), 4.61 (d, J = 17.2 Hz, 1H), 6.66-6.72 (m, 3H), 7.53 (d, J = 8.0 Hz, 2H), 7.69 (d, J = 7.6 Hz, 2H).
Example 38	 (2S,4R,6R)-2-(4-Benzyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>388.3</u>	¹ H NMR (400 MHz, CD ₃ OD) δ 3.38-3.44 (m, 6H), 3.68 (dd, J = 12.0, 4.8 Hz, 1H), 3.86 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.23 (t, J = 4.4 Hz, 2H), 4.47 (s, 2H), 6.65 (d, J = 8.4 Hz, 1H), 6.78-6.82 (m, 2H), 7.23-7.30 (m, 5H).

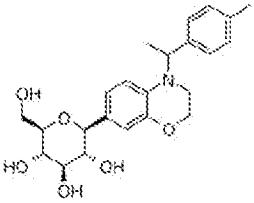
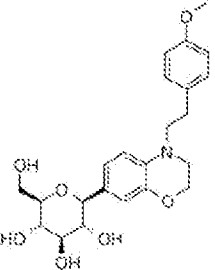
Example 39	 (2S,4R,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	416.4	¹H NMR (400 MHz, CD₃OD): δ 1.21 (t, J = 7.6 Hz, 3H), 2.62 (q, J = 7.6 Hz, 2H), 3.32-3.44 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 12 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.4 Hz, 2H), 4.43 (s, 2H), 6.67 (d, J = 8.8 Hz, 1H), 6.79-6.81 (m, 2H), 7.14 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H).
Example 40	 (2R,4R,6S)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	430.4	¹H NMR (400 MHz, CD₃OD) δ 1.23 (d, J = 6.8 Hz, 6H), 2.88 (m, 1H), 3.32-3.44 (m, 6H), 3.67 (dd, J = 12, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 8.8 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 4.43(s, 2H), 6.67 (d, J = 8.0 Hz, 1H), 6.80 (m, 2H), 7.17 (d, J = 8.4 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H).
Example 41	 (2S,4R,6R)-2-[4-(4-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	432.4	¹H NMR (400 MHz, CD₃OD) δ 1.37 (t, J = 7.2 Hz, 3H), 3.32-3.44 (m, 6H), 3.67 (dd, J = 11.6, 5.2 Hz, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.95-4.03 (m, 3H), 4.21 (t, J = 4.0 Hz, 2H), 4.39 (s, 2H), 6.70 (d, J = 8.8 Hz, 1H), 6.79-6.86 (m, 4H), 7.20 (d, J = 8.4 Hz, 2H).

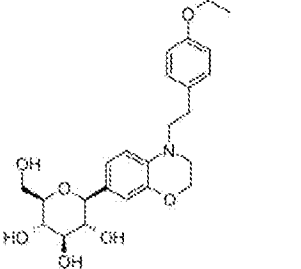
	tetrahydro-pyran-3,4,5-triol		
Example 42	 (2R,4R,6S)-2-Hydroxymethyl-6-[4-(4-methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>402.3</u>	¹ H NMR (400 MHz, CD ₃ OD) δ 2.33 (s, 3H), 3.34-3.46 (m, 6H), 3.68 (dd, J = 11.6, 4.4 Hz, 1H), 3.87 (d, J = 11.6 Hz, 1H), 3.98 (d, J = 8.8 Hz, 1H), 4.23 (t, J = 3.6 Hz, 2H), 4.44 (s, 2H), 6.68 (d, J = 8.0 Hz, 1H), 6.80-6.82 (m, 2H), 7.13 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H).
Example 43	 (2S,4R,6R)-2-[4-(3-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>432.4</u>	¹ H NMR (400 MHz, CD ₃ OD) δ 1.36 (t, J = 7.2 Hz, 3H), 3.32-3.44 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 12 Hz, 1H), 3.96-4.02 (m, 3H), 4.23 (t, J = 4.0 Hz, 2H), 4.44 (s, 2H), 6.64 (d, J = 8.4 Hz, 1H), 6.75-6.86 (m, 5H), 7.20 (t, J = 8.0 Hz, 1H).
Example 44	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>472.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.29-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.22 (t, J = 4.0 Hz, 2H), 4.51 (s, 2H), 6.61 (d, J = 8.4 Hz, 1H), 6.79-6.83 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H).

	benzo[1,4]oxazin-7-yl]- tetrahydro-pyran-3,4,5- triol		
Example 45	 (2R,3S,4R,5R,6S)-2- Hydroxymethyl-6-[4-(3- methyl-benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin-7-yl]- tetrahydro-pyran-3,4,5- triol	402.3	¹ H NMR (400 MHz, CD ₃ OD): δ 2.31 (s, 3H), 3.32-3.42 (m, 6H), 3.66 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 12.0 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.23 (t, J = 4.0 Hz, 2H), 4.43 (s, 2H), 6.79 (d, J = 8.0 Hz, 1H), 6.81 (s, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.06 (t, J = 7.6 Hz, 2H), 7.1 (s, 1H), 7.18 (t, J = 7.6 Hz, 1H).
Example 46	 (2S,3R,4R,5S,6R)-2-[4- (3-Ethyl-benzyl)-3,4- dihydro-2H- benzo[1,4]oxazin-7-yl]- 6-hydroxymethyl- tetrahydro-pyran-3,4,5- triol	416.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.21 (t, J = 7.6 Hz, 3H), 2.61 (q, J = 7.6 Hz, 2H), 3.32-3.44 (m, 6H), 3.67 (dd, J = 12.0, 4.8 Hz, 1H), 3.86 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 9.6 Hz, 1H), 4.23 (t, J = 4.4 Hz, 2H), 4.44 (s, 2H), 6.66 (d, J = 8.4 Hz, 1H), 6.79-6.82 (m, 2H), 7.09 (m, 2H), 7.14 (s, 1H), 7.21 (t, J = 7.6 Hz, 1H).
Example 47	 (2R,3S,4R,5R,6S)-2- Hydroxymethyl-6-[4-(4- trifluoromethyl-benzyl)- 3,4-dihydro-2H- benzo[1,4]oxazin-7-yl]- tetrahydro-pyran-3,4,5- triol	456.3	¹ H NMR (400 MHz, CD ₃ OD): δ 3.29-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.30 (t, J = 4.0 Hz, 2H), 4.66 (s, 2H), 6.57 (d, J = 8.0 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.83 (s, 1H), 7.50 (d, J = 8.4 Hz, 2H), 7.62 (d, J = 8.4 Hz, 2H).

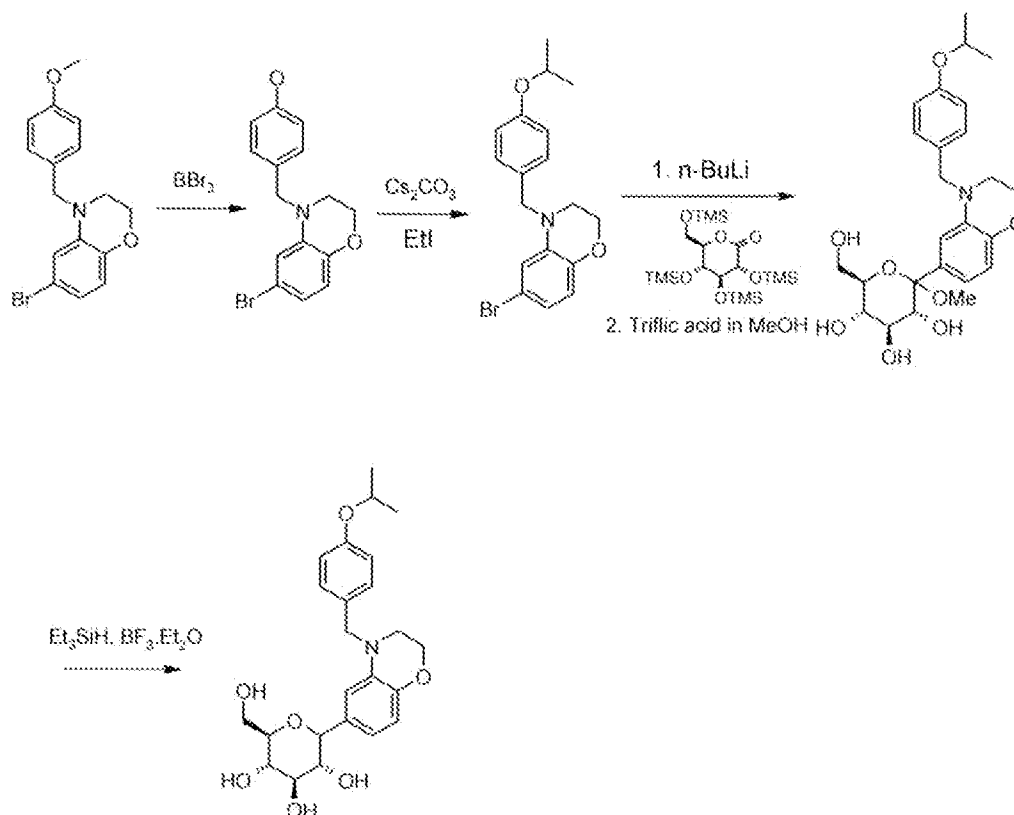
	3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol		
Example 48	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>456.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.29-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.30 (t, J = 4.0 Hz, 2H), 4.66 (s, 2H), 6.57 (d, J = 8.0 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 6.83 (s, 1H), 7.49-7.61 (m, 4H).
Example 49	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(2-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>456.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.29-3.43 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.30 (t, J = 4.0 Hz, 2H), 4.66 (s, 2H), 6.37 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.86 (s, 1H), 7.41-7.56 (m, 3H), 7.74 (d, J = 7.6 Hz, 1H).
Example 50	 (2S,3R,4R,5S,6R)-2-(4-benzofuran-2-ylmethyl)-6-[4-(3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-tetrahydro-pyran-3,4,5-triol	<u>428.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 3.31-3.44 (m, 6H), 3.64 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 4.30 (t, J = 4.0 Hz, 2H), 4.66 (s, 2H), 6.66 (d, J = 8.0 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H), 6.91 (s, 1H), 7.30 (d, J = 8.8 Hz, 1H).

	Benzofuran-5-ylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol		7.45 (d, J = 8.8 Hz, 1H), 7.59 (s, 1H), 7.73 (s, 1H).
Example 51	 (2S,3R,4R,5S,6R)-2-(4-Ethyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-4,5-triol	326.3	¹ H NMR (400 MHz, CD ₃ OD): δ 1.12 (t, J = 7.2 Hz, 3H), 3.28-3.45 (m, 8H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 6.70 (d, J = 8.0 Hz, 1H), 6.78 (s, 1H), 6.85 (dd, J = 9.6, 1.2 Hz, 1H).
Example 52	 (2S,3R,4R,5S,6R)-2-[4-(3-Chloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	422.3	¹ H NMR (400 MHz, CD ₃ OD) δ 3.33-3.45 (m, 6H), 3.67 (dd, J = 12.0, 4.8 Hz, 1H), 3.87 (d, J = 12 Hz, 1H), 3.98 (d, J = 9.2 Hz, 1H), 4.27 (t, J = 4.0 Hz, 2H), 4.49 (s, 2H), 6.60 (d, J = 8.0 Hz, 1H), 6.80-6.84 (m, 2H), 7.24-7.34 (m, 4H).
Example 53	 (2R,3S,4R,5R,6S)-2-(4-(3-Methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	418.4	¹ H NMR (400 MHz, CD ₃ OD): δ 3.32-3.45 (m, 6H), 3.67 (dd, J = 12.0, 4.8 Hz, 1H), 3.76 (s, 3H), 3.86 (d, J = 12 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.24 (t, J = 4.4 Hz, 2H), 4.45 (s, 2H), 6.64 (d, J = 8.4 Hz, 1H), 6.79-6.82 (m, 3H), 6.82-6.88 (m, 2H), 7.22 (t, J = 8.0 Hz, 1H).

	Hydroxymethyl-6-[4-(3-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol		
Example 54	 (2R,4R,6S)-2-Hydroxymethyl-6-[4-(1-p-tolyl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	416.4	¹ H NMR (400 MHz, CD ₃ OD): (peaks correspond to major isomer) δ 1.53 (d, J = 6.8 Hz, 3H), 2.31 (s, 3H), 3.05-3.10 (m, 1H), 3.21-3.21-3.26 (m, 1H), 3.32-3.47 (m, 4H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 8.8 Hz, 1H), 4.01-4.05 (m, 1H), 4.12-4.14 (m, 1H), 5.10 (q, J = 6.8 Hz, 1H), 6.82 (d, J = 10.4 Hz, 3H), 7.14 (d, J = 7.6 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H).
Example 55	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol	432.4	¹ H NMR (400 MHz, CD ₃ OD): δ 2.77 (t, J = 7.6 Hz, 2H), 3.19 (t, J = 4.0 Hz, 2H), 3.34-3.46 (m, 6H), 3.65 (dd, J = 12.0, 4.8 Hz, 1H), 3.73 (s, 3H), 3.84 (d, J = 11.2 Hz, 1H), 3.95 (d, J = 9.2 Hz, 1H), 4.05 (t, J = 4.0 Hz, 2H), 6.67 (d, J = 8.4 Hz, 1H), 6.55 (d, J = 8.0 Hz, 1H), 6.80-6.85 (m, 3H), 7.10 (d, J = 8.8 Hz, 2H).

Example 56	 (2S,4R,6R)-2-[4-[2-(4-Ethoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	446.4	¹H NMR (400 MHz, CD₃OD): δ 1.37 (t, J = 6.8 Hz, 3H), 2.80 (t, J = 7.2 Hz, 2H), 3.23 (t, J = 4.4 Hz, 2H), 3.22-3.50 (m, 6H), 3.68 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97-4.03 (m, 3H), 4.09 (t, J = 4 Hz, 2H), 6.71 (d, J = 8.4 Hz, 1H), 6.79-6.89 (m, 4H), 7.13 (d, J = 8.4 Hz, 2H).
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Example 57. (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 4-benzyl-6-bromo-4-(4-Methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (1.8 g, 5.4 mmol) in dichloromethane (10 ml) was added 1.0 M borontribromide solution in dichloromethane (27.0 ml, 27.0 mmol) at -78 °C. The reaction mixture was stirred for 3 h, quenched by the addition of aq. saturated sodium bicarbonate solution (15 ml). After usual work up, compound was purified by silica gel column chromatography (8% ethyl acetate in hexane) to furnish 4-(6-bromo-2,3-dihydro-benzo[1,4]oxazin-4-ylmethyl)-phenol (1.12 g).

¹H NMR (400 MHz, CDCl₃): δ 3.31 (t, J = 4.4 Hz, 2H), 4.22 (t, J = 4.4 Hz, 2H), 4.35 (s, 2H), 4.91 (s, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.75 (dd, J = 8.4, 2.0 Hz, 1H), 6.80-6.82 (m, 3H), 7.15 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 322.0 (M+2)

Step II: To a stirred solution of 4-(6-bromo-2,3-dihydro-benzo[1,4]oxazin-4-ylmethyl)-phenol (1.5 g, 4.68 mmol) in DMF (10 ml) was added cesium carbonate (3.0 g, 9.36 mmol), isopropyl bromide (0.9 ml, 9.36 mmol) and sodium iodide (70 mg, 0.47 mmol). The reaction mixture was heated to 60 °C for 20 h. Reaction mixture was cooled to room temperature and quenched by the addition of water (50 ml). After usual work up product was purified by silica gel column chromatography (3% ethyl acetate in hexane) to furnish 6-bromo-4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (1.4 g).

¹H NMR (400 MHz, CDCl₃): δ 1.33 (d, J = 6.0 Hz, 6H), 3.29 (t, J = 4.4 Hz, 2H), 4.21 (t, J = 4.4 Hz, 2H), 4.34 (s, 2H), 4.53 (q, J = 6.0 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 6.70 (dd, J = 8.4, 2.0 Hz, 1H), 6.81 (d, J = 1.6 Hz, 1H), 6.85 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H).

Step III: To a stirred solution of 6-bromo-4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazine (1.3 g, 3.59 mmol) in THF-toluene (1:2, mixture, 9 ml) was added 2.5 M n-BuLi in hexanes (1.6 ml, 3.92 mmol) at -78 °C. The reaction mixture was stirred for 40 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (1.67 g, 3.59 mmol) in toluene (9 ml) at -78 °C. After the reaction mixture was stirred for 40 min., quenched by the addition of water (9 ml). This was extracted with ethyl acetate (3 X 10 ml), washed with brine (1 X 5 ml), dried over sodium sulphate and concentrated. The resulting residue was taken in methanol (10 ml), and added triflic acid (150 µL), heated to 40 °C for 30 min. Reaction mixture was cooled to 30 °C, volatiles were removed under reduced pressure. The resulting residue was taken in aq. saturated sodium bicarbonate (6 ml) extracted with ethyl acetate (3 X 10 ml), washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (4% methanol in dichloromethane) to furnish (3R,4S,5S,6R)-6-

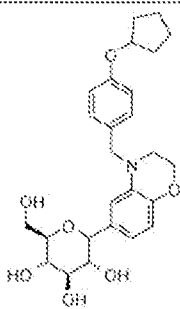
Hydroxymethyl-2-[4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-2-methoxy-tetrahydro-pyran-3,4,5-triol (950 mg).

^1H NMR (400 MHz, CD_3OD): δ 1.28 (dd, $J = 6.0, 1.6$ Hz, 6H), 2.99 (s, 3H), 3.09 (d, $J = 9.6$ Hz, 1H), 3.37-3.52 (m, 3H), 3.52-3.56 (m, 1H), 3.72 (t, $J = 9.2$ Hz, 1H), 3.78 (dd, $J = 12.0, 5.6$ Hz, 1H), 3.90 (dd, $J = 11.6, 2.0$ Hz, 1H), 4.10-4.38 (m, 2H), 4.36 (d, $J = 15.2$ Hz, 1H), 4.46 (d, $J = 15.6$ Hz, 1H), 4.52-4.61 (m, 1H), 6.68 (d, $J = 8.0$ Hz, 1H), 6.82-6.86 (m, 3H), 7.03 (d, $J = 1.6$ Hz, 1H), 7.24 (d, $J = 8.8$ Hz, 2H). MS (ES) m/z 476.3 ($M+1$).

Step IV: To a stirred solution of (3R,4S,5S,6R)-6-Hydroxymethyl-2-[4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-2-methoxy-tetrahydro-pyran-3,4,5-triol (560 mg, 1.15 mmol) in acetonitrile-dichloromethane (2:1 mixture, 7 ml) was added boron trifluoride diethyletharate complex (0.23 ml, 2.314 mmol) and triethylsilane (0.73 ml, 4.628 mmol) at -20°C . After stirring for 4 h at 0°C , reaction was quenched with aq. saturated sodium bicarbonate solution (4 ml). The volatiles were evaporated under reduced pressure, extracted with ethyl acetate (3 X 7 ml). The ethyl acetate layers were mixed, washed with brine (4 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish the titled compound (55 mg).

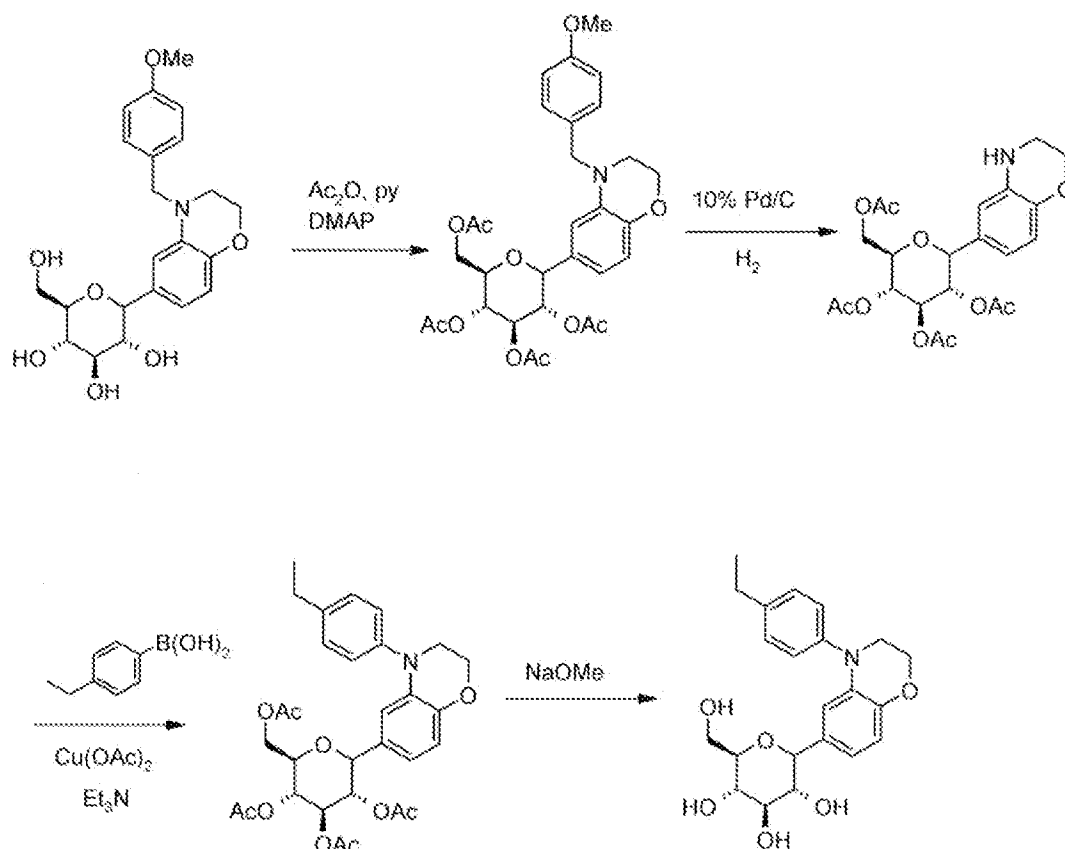
^1H NMR (400 MHz, CD_3OD): (peaks correspond to major isomer) δ 0.88 (dd, $J = 6.0, 1.6$ Hz, 6H), 2.85-3.04 (m, 6H), 3.25 (dd, $J = 11.6, 2.4$ Hz, 1H), 3.44 (d, $J = 11.6$, 1H), 3.56 (d, $J = 9.2$ Hz, 1H), 3.77 (bs, 2H), 3.94-4.19 (m, 3H), 6.24 (d, $J = 8.0$ Hz, 1H), 6.28 (d, $J = 8.0$ Hz, 1H), 6.44 (d, $J = 6.8$ Hz, 2H), 6.48 (s, 1H), 6.82 (d, $J = 7.2$ Hz, 2H). MS (EI) m/z 446.3 ($M+1$).

Example 58 was prepared in an analogous procedure as described in example 57.

Example #	Structure	MS ($M+1$)	^1H NMR
Example 58	 (3R,4R,5S,6R)-2-[4-(4-Cyclopentyloxy-	<u>472.4</u>	^1H NMR (400 MHz, CD_3OD): (peaks correspond to major isomer) δ 1.15-1.81 (m, 8H), 3.14 (s, 2H), 3.20-3.32 (m, 5H), 3.56 (dd, $J = 12.0, 5.2$ Hz, 1H), 3.73 (d, $J = 11.6$ Hz, 1H), 3.85 (d, $J = 9.2$ Hz, 1H), 4.06 (s, 2H), 4.25 (d, $J = 15.6$ Hz, 1H), 4.30 (d, $J = 15.6$ Hz, 1H), 6.54 (d, $J = 9.6$ Hz, 1H), 6.57 (d, $J = 9.6$ Hz, 1H), 6.72 (d, $J = 8.0$ Hz, 2H), 6.78 (s, 1H), 7.11 (d, $J = 8.0$ Hz, 2H).

	benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol		
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Example 59. (2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of (2R,3S,4R,5R,6S)-2-hydroxymethyl-6-[4-(4-methoxybenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol (590 mg, 1.41 mmol) in dichloromethane (10 ml) was added N,N'-dimethylaminopyridine (9 mg, 0.07 mmol), acetic anhydride (1.2 ml, 12.3 mmol) and pyridine (0.95 ml, 11.7 mmol) at 20 °C. After stirring for 20 h, reaction was quenched by the addition of water (5 ml). Organic layer was diluted with dichloromethane (30 ml), washed with 1N HCl (15 ml), water (10 ml), brine (10 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (20% ethyl acetate in hexane) to furnish [(2R,3R,4R,5S)-3,4,5-

triacetoxy-6-[4-[(4-methoxyphenyl)methyl]-2,3-dihydro-1,4-benzoxazin-6-yl]tetrahydropyran-2-yl]methyl acetate (617 mg).

¹H NMR (400 MHz, CDCl₃): (peaks correspond to major isomer) δ 1.80 (s, 3H), 1.99 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 3.28 (t, J = 4.0 Hz, 2H), 3.80 (s, 3H), 4.10-4.27 (m, 6H), 4.39 (s, 2H), 5.12 (t, J = 9.6 Hz, 1H), 5.19 (t, J = 9.6 Hz, 1H), 5.28 (t, J = 9.6 Hz, 1H), 6.66 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 6.79 (s, 1H), 6.87 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 586.4 (M+1).

Step II: To a stirred solution of [(2R,3R,4R,5S)-3,4,5-triacetoxy-6-[4-[(4-methoxyphenyl)methyl]-2,3-dihydro-1,4-benzoxazin-6-yl]tetrahydropyran-2-yl]methyl acetate (610 mg, 1.0 mmol) in methanol-dichloromethane (1:1 mixture, 8 ml) was added 10% palladium on charcoal (90 mg). The reaction mixture was stirred under hydrogen atmosphere in balloon pressure for 20 h at 20°C. Reaction mixture was filtered through celite bed, concentrated and purified by silica gel column chromatography to furnish [(2R,3R,4R,5S)-3,4,5-triacetoxy-6-(3,4-dihydro-2H-1,4-benzoxazin-6-yl)tetrahydropyran-2-yl]methyl acetate (430 mg).

MS (ES) *m/z* 466.3 (M+1).

Step III: To a stirred solution of acetic acid (2R,3R,4R,5S,6S)-3,4,5-triacetoxy-6-(3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-tetrahydro-pyran-2-ylmethyl ester (320 mg, 0.7 mmol), in dichloromethane (4 ml) was added copper (II) acetate (250 mg, 1.4 mmol), triethylamine (0.2 ml, 1.4 mmol), molecular sieves (300 mg), 4-ethylphenyl boronic acid (206 mg, 1.4 mmol). After 8 h, additional amount of 4-ethylphenyl boronic acid (206 mg) was added in portions. The reaction was stirred for 60 h, filtered through celite bed, filtrate was concentrated and purified by preparative HPLC to furnish [(2R,3R,4R,5S)-3,4,5-triacetoxy-6-[4-(4-ethylphenyl)-2,3-dihydro-1,4-benzoxazin-6-yl]tetrahydropyran-2-yl]methyl acetate (110 mg).

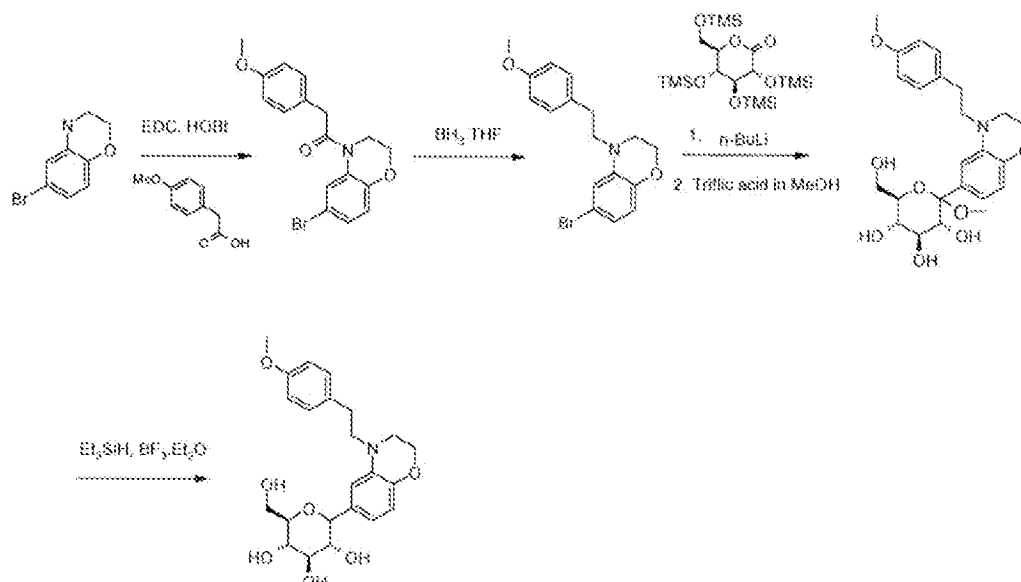
¹H NMR (400 MHz, CDCl₃): (peaks correspond to major isomer) δ 1.25 (t, J = 7.6 Hz, 3H), 1.78 (s, 3H), 1.94 (s, 3H), 1.97 (s, 3H), 2.00 (s, 3H), 2.65 (q, J = 7.6 Hz, 2H), 3.65 (t, J = 4.0 Hz, 2H), 3.85-3.89 (m, 1H), 4.09-4.305 (m, 5H), 4.95 (t, J = 9.6 Hz, 1H), 5.02 (t, J = 9.6 Hz, 1H), 5.27 (t, J = 9.6 Hz, 1H), 6.67 (dd, J = 8.0, 1.6 Hz, 1H), 6.75 (d, J = 8.4 Hz, 1H), 6.78 (d, J = 1.6 Hz, 1H), 7.14 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 570.4 (M+1).

Step IV: To a stirred solution of acetic acid (2R,3R,4R,5S,6S)-3,4,5-triacetoxy-6-[4-(4-ethyl-phenyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-2-ylmethyl ester (120 mg, 0.21 mmol) in methanol (3 ml) was added sodium methoxide (2 mg). The

reaction mixture was stirred for 20 h at 20 °C, concentrated and purified by preparative HPLC to furnish the titled compound. (Yield = 75 mg).

¹H NMR (400 MHz, CD₃OD): (peaks correspond to major isomer) δ 1.21 (t, J = 7.6 Hz, 3H), 2.60 (q, J = 7.6 Hz, 2H), 3.23-3.36 (m, 4H), 3.59 (dd, J = 11.2, 4.0 Hz, 1H), 3.63 (t, J = 4.4 Hz, 2H), 3.80 (d, J = 12.0 Hz, 1H), 3.86 (d, J = 9.2 Hz, 1H), 4.21 (t, J = 3.6 Hz, 2H), 6.76 (s, 2H), 6.84 (s, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H). MS (EI) *m/z* 402.3 (M+1).

Example 60. (2R,3S,4R,5R)-2-Hydroxymethyl-6-{4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-H-benzo[1,4]oxazin-6-yl}-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 6-bromo-3,4-dihydro-2H-benzo[1,4]oxazine (1.5 g, 7.0 mmol) in dichloromethane – dimethylformamide (1:1 mixture, 40 ml) was added 4-methoxyphenyl acetic acid (1.8 g, 10.5 mmol), HOBt (2.4 g, 17.5 mmol), diisopropylethylamine (4.8 ml, 28 mmol), EDCI.HCl (3.4 g, 17.5 mmol) at 0 °C. After 15 min, reaction mixture was heated to 70 °C for 15 h, quenched by the addition of water. After usual work up, the compound was purified by silica gel column chromatography (10% ethyl acetate in hexane) to furnish 1-(6-bromo-2,3-dihydro-benzo[1,4]oxazin-4-yl)-2-(4-methoxy-phenyl)-ethanone (1.8 g).

¹H NMR (400 MHz, CDCl₃): δ 3.79 (s, 3H), 3.86 (bs, 4H), 4.14 (bs, 2H), 6.76 (d, J = 8.4 Hz, 1H), 6.86 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.4 Hz, 4H). MS (ES) *m/z* 364.0 (M+2).

Step II: To a stirred solution of 1-(6-bromo-2,3-dihydro-benzo[1,4]oxazin-4-yl)-2-(4-methoxy-phenyl)-ethanone (1.0 g, 2.8 mmol) in THF (10 ml) was added 1.0M borane-

tetrahydrofuran complex solution in THF (8.3 ml, 8.3 mmol) at room temperature. The reaction mixture was refluxed for 15 h. Reaction was cooled to 25 °C, quenched by the addition of methanol; volatiles were removed under reduced pressure. The resulting residue was taken in ethyl acetate (30 ml) and washed with aqueous saturated sodium bicarbonate solution (20 ml), water (20 ml), brine (20 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (4% ethyl acetate in hexane) to furnish 6-bromo-4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazine (624 mg).

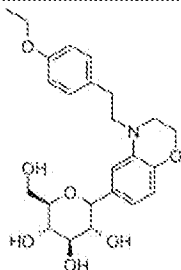
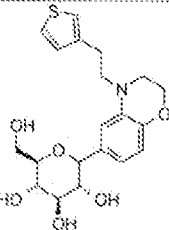
¹H NMR (400 MHz, CDCl₃): δ 2.81 (t, J = 7.2 Hz, 2H), 3.18 (d, J = 4.4 Hz, 2H), 3.43 (d, J = 7.2 Hz, 2H), 3.79 (s, 3H), 4.08 (t, J = 4.4 Hz, 2H), 6.62 (d, J = 8.4 Hz, 1H), 6.67 (dd, J = 8.4, 2.0 Hz, 1H), 6.74 (d, J = 4.0 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H). MS (ES) *m/z* 350.0 (M+2).

Step III: To a stirred solution of 6-bromo-4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazine (610 mg, 1.75 mmol) in THF-toluene (1:2 mixture, 9 ml) was added 2.5 M solution of *n*-BuLi in hexanes (0.77 ml, 1.92 mmol) at -78 °C. The reaction mixture was stirred for the 30 min. Then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (820 mg, 1.75 mmol) in toluene (9 ml) at -78 °C. After the reaction mixture was stirred for 30 min., quenched by the addition of water (10 ml), extracted with ethyl acetate (3 X 10 ml), washed with water (5 ml), brine (5 ml), dried over sodium sulphate and concentrated. The resulting residue was taken in methanol (8 ml), and added triflic acid (50 µL), heated to 40 °C for 40 min. Reaction mixture was cooled, quenched with aq. saturated sodium bicarbonate (3 ml), extracted with ethyl acetate (3 X 10 ml), washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (4% methanol in dichloromethane) to furnish the desired product (245 mg).

The above intermediate (220 mg, 0.48 mmol) was taken in acetonitrile-dichloromethane mixture (2.5:1 mixture, 3.5 ml) and cooled to -20 °C. To it was added boron trifluoride diethyletherate complex (0.09 ml, 0.72 mmol) and triethylsilane (0.11 ml, 0.95 mmol) and stirred for 45 min at 0 °C. Reaction was quenched with aq. saturated sodium bicarbonate solution (4 ml). The volatiles were evaporated under reduced pressure and the resulting was extracted with ethyl acetate (3 X 10 ml). The ethyl acetate layers were mixed and washed with brine (1 X 5 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC chromatography to furnish the titled compound (52 mg).

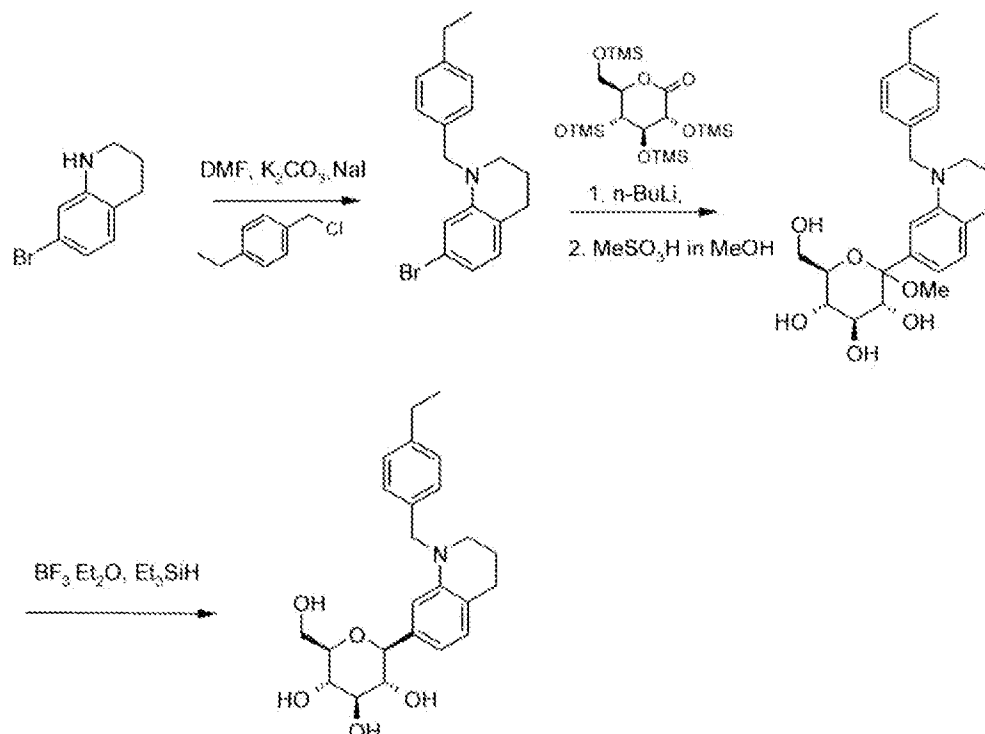
^1H NMR (400 MHz, CDCl_3): (peaks correspond to major isomer) δ 1.64 (br s, 1H), 2.38 (bs, 2H), 2.79 (t, $J = 7.2$ Hz, 2H), 3.22 (t, $J = 4.0$ Hz, 2H), 3.40-3.49 (m, 5H), 3.65 (t, $J = 6.0$ Hz, 2H), 3.77 (s, 3H), 3.78 (d, $J = 11.2$ Hz, 1H), 3.90 (d, $J = 11.2$ Hz, 1H), 4.04 (d, $J = 9.2$ Hz, 1H), 4.12 (t, $J = 4.0$ Hz, 2H), 6.59 (d, $J = 9.6$ Hz, 2H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.83 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.4$ Hz, 2H). MS (ES) m/z 432.1 ($M+1$).

Examples 61-62 were prepared in an analogous procedure as described in example 60.

Example #	Structure	MS ($M+1$)	^1H NMR
Example 61	 (3R,4R,5S,6R)-2-{4-[2-(4-Ethoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl}-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>446.3</u>	^1H NMR (400 MHz, CD_3OD): (peaks correspond to major isomer) δ 1.36 (t, $J = 7.2$ Hz, 3H), 3.25 (t, $J = 4$ Hz, 2H), 3.30-3.45 (m, 4H), 3.65 (dd, $J = 12.0, 4.8$ Hz, 1H), 3.84 (d, $J = 12$ Hz, 1H), 3.96-4.02 (m, 3H), 4.16 (t, $J = 4.0$ Hz, 2H), 4.35-4.42 (m, 2H), 6.64 (d, $J = 8.4$ Hz, 1H), 6.67 (d, $J = 8.4$ Hz, 1H), 6.85 (d, $J = 8.8$ Hz, 2H), 6.87 (s, 1H), 7.22 (d, $J = 8$ Hz, 2H).
Example 62	 (2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(2-thiophen-3-yl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	<u>408.1</u>	^1H NMR (400 MHz, CDCl_3): (peaks correspond to major isomer) δ 2.84-2.90 (m, 3H), 3.24 (s, 2H), 3.48-4.39 (m, 14H), 6.60 (d, $J = 8.4$ Hz, 2H), 6.72-6.99 (m, 4H).

	tetrahydro-pyran-3,4,5-triol		
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Example 63. (2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 7-bromo-1,2,3,4-tetrahydroquinoline hydrochloride (2.5 g, 10.05 mmol) in DMF (10 ml) was added potassium carbonate (2.76 g, 20.1 mmol), sodium iodide (150 mg, 1 mmol), 4-ethylbenzyl chloride (2.24 ml, 15.08 mmol) and heated to 60 °C for overnight. Reaction mixture was cooled to room temperature, quenched with addition of water (50 ml), extracted with ethyl acetate (3 X 30 ml). All organic layers were mixed and washed with water (50 ml), brine (50 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 7-bromo-1-(4-ethylbenzyl)-1,2,3,4-tetrahydroquinoline (3.0 g).

¹H NMR (400 MHz, CDCl₃): δ 1.25 (t, J = 7.6 Hz, 3H), 1.98 (m, 2H), 2.66 (q, J = 7.6 Hz, 2H), 2.75 (t, J = 6.4 Hz, 2H), 3.34 (t, J = 5.6 Hz, 2H), 4.44 (s, 2H), 6.68 (d, J = 7.2 Hz, 2H), 6.82 (d, J = 8.0 Hz, 1H), 7.17 (s, 4H). MS (ES) *m/z* 332.0 (M+2)

Step II: To a stirred solution of 7-Bromo-1-(4-ethylbenzyl)-1,2,3,4-tetrahydroquinoline (2.8 g, 8.78 mmol) in THF-toluene (1:2 mixture, 30 ml) was added 1.6 M n-BuLi in

hexanes (5.48 ml, 8.78 mmol) at -78 °C. The reaction mixture was stirred for 40 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (4.0 g, 8.78 mmol) in toluene (30 ml) at -78 °C. After stirring it for 40 min., 0.6 N methanesulfonic acid in methanol (30 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate (20 ml), extracted with ethyl acetate (3 X 50 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography to furnish (3R,4S,5S,6R)-2-[1-(4-ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (2.0 g).

¹H NMR (400 MHz, CD₃OD): δ 1.21 (t, J = 7.6 Hz, 3H), 1.97-2.02 (m, 2H), 2.62 (q, J = 7.6 Hz, 2H), 2.78-2.80 (m, 2H), 2.93 (s, 3H), 3.09 (d, J = 9.6 Hz, 1H), 3.37-3.42 (m, 3H), 3.52-3.56 (m, 1H), 3.71 (t, J = 8.8 Hz, 1H), 3.78 (dd, J = 12.0, 6.0 Hz, 1H), 3.90 (dd, J = 11.6, 1.6 Hz, 1H), 4.41 (d, J = 16.8 Hz, 1H), 4.61 (d, J = 16.4 Hz, 1H), 6.79 (d, J = 7.6 Hz, 1H), 6.81 (s, 1H), 6.92 (d, J = 7.6 Hz, 1H), 7.14 (d, J = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H).

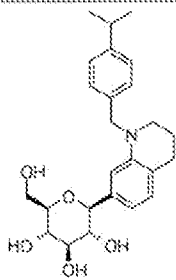
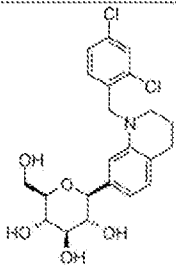
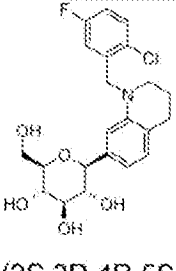
MS (ES) *m/z* 444.1 (M+1).

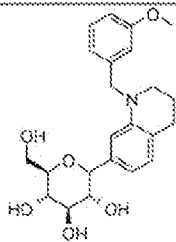
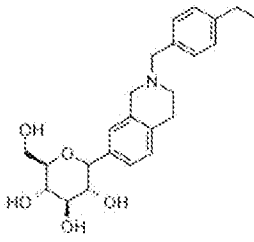
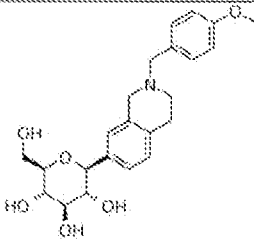
Step III: To a stirred solution of (3R,4S,5S,6R)-2-[1-(4-ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (2.0 g, 4.51 mmol) in acetonitrile-dichloromethane (1:1 mixture, 30 ml) was added boron trifluoride diethyletherate complex (1.14 ml, 9.02 mmol) and triethylsilane (2.68 ml, 18.04 mmol) at -10 °C. After stirring for 4 h at 0 °C, reaction was quenched with aq. saturated sodium bicarbonate solution (10 ml). The volatiles were evaporated under reduced pressure, extracted with ethyl acetate (3 X 20 ml). The ethyl acetate layers were mixed, washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish the titled compound (270 mg).

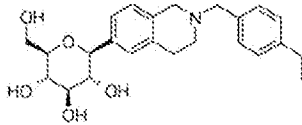
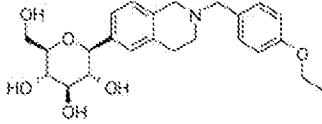
¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 7.6 Hz, 3H), 1.93-1.98 (m, 2H), 2.63 (q, J = 7.6 Hz, 2H), 2.76 (t, J = 6.4 Hz, 2H), 3.32-3.41 (m, 6H), 3.63 (dd, J = 11.6, 4.4 Hz, 1H), 3.83 (d, J = 11.6 Hz, 1H), 3.92 (d, J = 9.2 Hz, 1H), 4.43 (d, J = 16.8 Hz, 1H), 4.52 (d, J = 16.4 Hz, 1H), 6.60 (d, J = 7.6 Hz, 1H), 6.66 (s, 1H), 6.90 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H). MS (EI) *m/z* 414.1 (M+1).

Examples 64-71 were prepared in an analogous procedure as described in example 63.

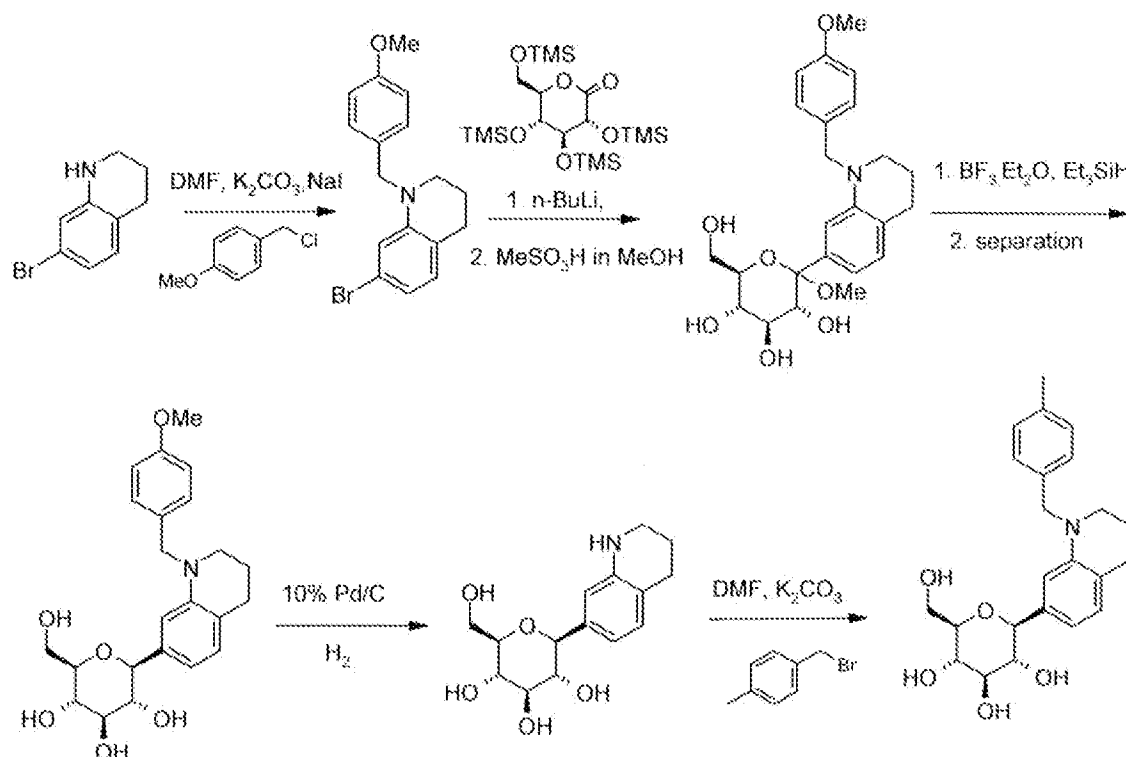
Example #	Structure	MS	¹ H NMR
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		(M+1)	
Example 64	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>428.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.25 (d, J = 6.8 Hz, 6H), 1.95-1.99 (m, 1H), 2.78 (t, J = 7.6 Hz, 2H), 3.33-3.43 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.6 Hz, 1H), 3.97 (d, J = 9.2 Hz, 1H), 4.20 (t, J = 4.0 Hz, 2H), 4.42 (d, J = 15.6 Hz, 1H), 4.48 (d, J = 15.6 Hz, 1H), 6.62 (d, J = 7.6 Hz, 1H), 6.69 (s, 1H), 6.92 (d, J = 7.6 Hz, 1H), 7.18 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H).
Example 65	 (3R,4R,5S,6R)-2-[1-(2,4-Dichloro-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>454.0</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 2.02-2.06 (m, 2H), 2.82 (t, J = 6 Hz, 2H), 3.26-3.41 (m, 6H), 3.63 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.90 (d, J = 8 Hz, 1H), 4.51 (d, J = 15.6 Hz, 1H), 4.61 (d, J = 18 Hz, 1H), 6.40 (s, 1H), 6.67 (d, J = 7.6 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 8.8 Hz, 1H), 7.27 (d, J = 8.8 Hz, 1H), 7.50 (s, 1H).
Example 66	 (2S,3R,4R,5S,6R)-2-[1-(2-Chloro-5-fluoro-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>438.1</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 2.02-2.08 (m, 2H), 2.84 (t, J = 6.0 Hz, 2H), 3.27-3.43 (m, 6H), 3.63 (dd, J = 12.0, 4.8 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.90 (d, J = 8.0 Hz, 1H), 4.51 (d, J = 15.6 Hz, 1H), 4.61 (d, J = 18 Hz, 1H), 6.40 (s, 1H), 6.67 (d, J = 7.6 Hz, 1H), 6.97-7.04 (m, 3H), 7.46 (dd, J = 5.2, 8.8 Hz, 1H).

	tetrahydro-quinolin-7-yl]- 6-hydroxymethyl- tetrahydro-pyran-3,4,5- triol		
Example 67	 (2R,3S,4R,5R)-2- Hydroxymethyl-6-[1-(3- methoxy-benzyl)-1,2,3,4- tetrahydro-quinolin-7-yl]- tetrahydro-pyran-3,4,5- triol	416.3	¹ H NMR (400 MHz, CD ₃ OD): (peaks correspond to major isomer) δ 1.94-1.98 (m, 2H), 2.76 (t, J = 5.6 Hz, 2H), 3.30-3.40 (m, 6H), 3.60-3.63 (m, 1H), 3.74 (s, 3H), 3.82 (d, J = 11.6 Hz, 1H), 3.90 (d, J = 9.6 Hz, 1H), 4.40-4.54 (m, 2H), 6.59-6.91 (m, 6H), 7.20 (t, J = 8.0 Hz, 1H).
Example 68	 (3R,4R,5S,6R)-2-[2-(4- Ethyl-benzyl)-1,2,3,4- tetrahydro-isoquinolin-7- yl]-6-hydroxymethyl- tetrahydro-pyran-3,4,5- triol	414.4	¹ H NMR (400 MHz, CD ₃ OD): (peaks correspond to major isomer) δ 1.23 (t, J = 7.6 Hz, 3H), 2.67 (q, J = 8.0 Hz, 2H), 3.06 (t, J = 6.0 Hz, 2H), 3.26-3.45 (m, 7H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.84 (d, J = 12.4, 2.0 Hz, 1H), 4.07 (d, J = 9.6 Hz, 3H), 4.16 (s, 2H), 7.16 (t, J = 4.0 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.39 (d, J = 7.6 Hz, 2H).
Example 69	 (2R,3S,4R,5R,6S)-2- Hydroxymethyl-6-[2-(4- methoxy-benzyl)-1,2,3,4- tetrahydro-quinolin-7-yl]- tetrahydro-pyran-3,4,5- triol	416.4	¹ H NMR (400 MHz, CD ₃ OD): δ 2.77 (t, J = 5.6 Hz, 2H), 2.89 (t, J = 5.6 Hz, 2H), 3.31-3.45 (m, 4H), 3.63-3.71 (m, 5H), 3.8 (s, 3H), 3.86 (d, J = 11.2 Hz, 1H), 4.06 (d, J = 9.6 Hz, 1H), 6.91 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 5.2 Hz, 2H), 7.19 (d, J = 8.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H).

	methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl]-tetrahydro-pyran-3,4,5-triol.		
Example 70	 (2S,3R,4R,5S,6R)-2-[2-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>414.4</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.28 (t, J = 8.8 Hz, 3H), 2.73 (q, J = 7.6 Hz, 2H), 3.12 (t, J = 6 Hz, 2H), 3.33-3.51 (m, 6H) 3.71 (dd, J = 11.2, 4.8 Hz, 1H), 3.88 (d, J = 11.2 Hz, 1H), 4.13 (d, J = 9.6 Hz, 1H), 4.16 (s, 2H), 4.22 (s, 2H), 7.10 (d, J = 8.4 Hz, 1H), 7.31-7.35 (m, 4H), 7.43 (d, J = 8. Hz, 2H).
Example 71	 (2S,3R,4R,5S,6R)-2-[2-(4-Ethoxy-benzyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>430.4</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.40 (t, J = 6.8 Hz, 3H), 3.12 (t, J = 5.6 Hz, 2H), 3.30-3.46 (m, 5H) 3.67 (dd, J = 11.2, 4.8 Hz, 1H), 3.88 (d, J = 11.2 Hz, 1H), 4.04-4.17 (m, 4H), 4.17 (s, 2H), 4.21 (s, 2H), 7.00 (d, J = 8.4 Hz, 2H), 7.08 (d, J = 8.4 Hz, 1H) 7.28-7.42 (m, 4H).

Example 72. (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 7-bromo-1,2,3,4-tetrahydroquinoline hydrochloride (5.0 g, 20.11 mmol) in DMF (20 ml) was added potassium carbonate (5.55 g, 40.2 mmol), sodium iodide (301mg, 2.01 mmol), 4-methoxybenzyl chloride (4.1 ml, 30.17 mmol) and heated to 60 °C for overnight. Reaction mixture was cooled to room temperature, quenched by the addition of water (100 ml), extracted with ethyl acetate (3 X 70 ml). All organic layers were mixed and washed with water (150 ml), brine (50 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 7-bromo-1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinoline (6.68 g).

¹H NMR (400MHz, CDCl₃): δ 2.00 (t, J= 6.0 Hz, 2H), 2.77 (t, J= 6.0 Hz, 2H), 3.35 (t, J= 6.0 Hz, 2H), 3.83 (s, 3H), 4.43 (s, 2H), 6.81-6.86(m, 2H), 6.90 (d, J = 8.4 Hz, 2H), 7.22 (d, J= 8.4 Hz, 2H), 7.29 (br s, 1H). MS (ES) m/z 334.0 (M+2).

Step II: To a stirred solution of 7-bromo-1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinoline (2.97 g, 8.9 mmol) in THF-toluene (1:2 mixture, 30 ml) was added 1.6 M n-BuLi in hexanes (5.58 ml, 8.9 mmol) at -78 °C. The reaction mixture was stirred for 40 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (4.16 g, 8.9 mmol) in toluene (20 ml) at -78 °C. After stirring it for 40 min., 0.6 N methanesulfonic acid in methanol (30 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium

bicarbonate (20 ml). This mixture was extracted with ethyl acetate (3 X 50 ml), dried over sodium sulphate, concentrated and purified by silica gel column chromatography (4% methanol in dichloromethane) to furnish (3R,4S,5S,6R)-6-hydroxymethyl-2-methoxy-2-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol (4.1 g).

¹H NMR (400MHz, CD₃OD): δ 2.00 (t, J= 6.0 Hz, 2H), 2.78 (t, J= 6.0 Hz, 2H), 2.98 (s, 3H), 3.09 (d, J= 9.2 Hz, 1H), 3.35-3.42 (m, 4H), 3.53-3.58 (m, 1H), 3.70-3.78 (m, 5H), 3.92(dd, J= 11.6, 2.0 Hz, 1H), 4.38 (d, J= 16.0 Hz, 1H), 4.56 (d, J= 16.0 Hz, 1H), 6.79 (d, J= 7.6 Hz, 1H), 6.85 (br s, 1H), 6.86 (d, J= 8.4 Hz, 2H), 6.91 (d, J= 7.6 Hz, 1H), 7.24 (d, J= 8.4 Hz, 1H). MS(ES) m/z 414 (M+1)

Step III: To a stirred solution of (3R,4S,5S,6R)-6-Hydroxymethyl-2-methoxy-2-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol (4.1 g, 9.2 mmol) in acetonitrile-dichloromethane mixture (1:1 mixture, 40 ml) was added boron trifluoride diethyletherate complex (2.33 ml, 18.4 mmol) and triethylsilane (5.86 ml, 36.8 mmol) at -10 °C and stirred for 4 h at 0 °C. Reaction was quenched with aq. saturated sodium bicarbonate solution (20 ml). The volatiles were evaporated under reduced pressure; the resulting mixture was extracted with ethyl acetate (3 X 30 ml). The ethyl acetate layers were mixed, washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol (1.04 g).

¹H NMR (400MHz, CD₃OD): δ 1.96 (t, J= 6.0 Hz, 2H), 2.77 (t, J= 6.0 Hz, 2H), 3.31-3.337 (m, 5H), 3.42 (br d, J= 8.8 Hz, 1H), 3.64 (d, J= 12.4 Hz, 1H), 3.67 (d, J= 5.0 Hz, 1H), 3.79 (s, 3H), 3.85 (d, J= 12.0 Hz, 1H), 3.94 (d, J= 9.2 Hz, 1H), 4.40 (d, J= 16.4 Hz, 1H), 4.50 (d, J= 16.4 Hz, 1H), 6.62 (d, J= 7.6 Hz, 1H), 6.70 (br s, 1H), 6.87 (d, J= 8.4 Hz, 1H), 6.91 (d, J= 7.6 Hz, 1H), 7.22 (d, J= 8.4 Hz, 2H). MS(ES) m/z 416.2 (M+1).

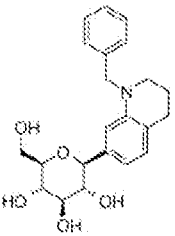
Step IV: To a stirred solution of (2R,3S,4R,5R,6S)-2-hydroxymethyl-6-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol (1.04 g, 2.5 mmol) in methanol (15ml) was added 10% palladium on charcoal (100 mg), 0.05 ml of conc. HCl and stirred under hydrogen balloon pressure for 18 h. Reaction mixture was filtered through celite bed, washed with methanol and concentrated. The resulting residue was titrated in n-hexanes and dried under vacuum to furnish (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-(1,2,3,4-tetrahydro-quinolin-7-yl)-tetrahydro-pyran-3,4,5-triol (710 mg).

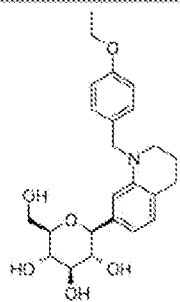
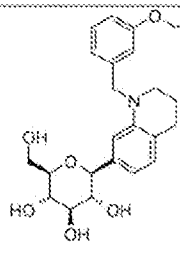
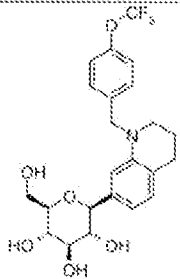
^1H NMR (400MHz, CD_3OD): δ 1.89 (t, J = 6.0 Hz, 2H), 2.73 (t, J = 6.0 Hz, 2H), 3.24 (t, J = 6.0 Hz, 2H), 3.35-3.45 (m, 4H), 3.62 (d, J = 12.0, 5.2 Hz, 1H), 3.86 (d, J = 11.2 Hz, 1H), 3.96 (d, J = 9.2 Hz, 1H), 6.59 (br s, 1H), 6.62 (d, J = 7.6 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H). MS(ES) m/z 296.3 ($M+1$).

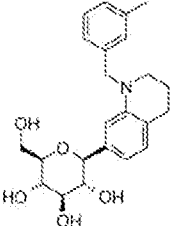
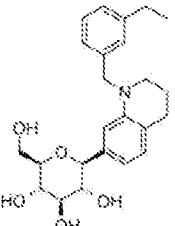
Step V: To a stirred solution of (2R,3S,4R,5R,6S)-2-hydroxymethyl-6-(1,2,3,4-tetrahydro-quinolin-7-yl)-tetrahydro-pyran-3,4,5-triol (50 mg, 0.16 mmol) in DMF (1 ml), was added potassium carbonate (47 mg, 0.33 mmol) and 4-methylbenzyl bromide (34 μl , 0.25 mmol). Reaction mixture was heated at 50 $^\circ\text{C}$ for 2 h, quenched by the addition of water (1 ml). After usual work up product was purified by column chromatography to furnish the titled compound (Yield = 27 mg).

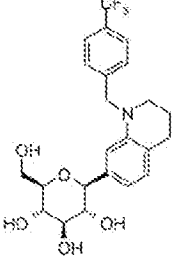
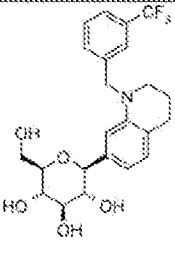
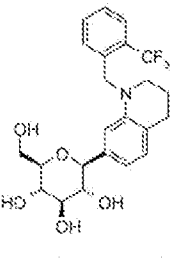
^1H NMR (400MHz, CD_3OD): δ 1.96 (t, J = 6.0 Hz, 2H), 2.31 (s, 3H), 2.76 (t, J = 6.0 Hz, 2H), 3.22-3.41 (m, 6H), 3.64 (dd, J = 12.4, 5.2 Hz, 1H), 3.84 (d, J = 12.0 Hz, 1H), 3.92 (d, J = 9.6 Hz, 1H), 4.42 (d, J = 16.4 Hz, 1H), 4.52 (d, J = 16.4 Hz, 1H), 6.60 (d, J = 7.2 Hz, 1H), 6.66 (br s, 1H), 6.90 (d, J = 8.0 Hz, 1H), 7.11 (d, J = 7.6 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H). MS(ES) m/z 400.4 ($M+1$)

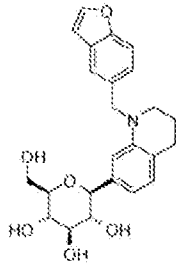
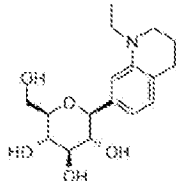
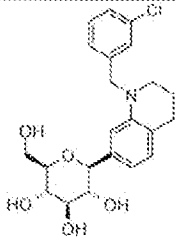
Examples 73-91 were prepared in an analogous procedure as described in example 72.

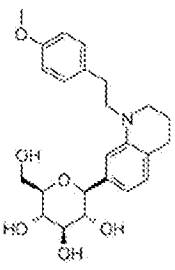
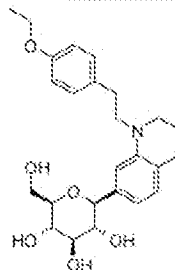
Example #	Structure	MS ($M+1$)	^1H NMR
Example 73	 (2S,3R,4R,5S,6R)-2-(1-Benzyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>386.3</u>	^1H NMR (400 MHz, CD_3OD): δ 1.94-2.00 (m, 2H), 2.77 (t, J = 6.0 Hz, 2H), 3.29-3.43 (m, 6H), 3.63 (dd, J = 11.6, 4.4 Hz, 1H), 3.83 (d, J = 11.6 Hz, 1H), 3.91 (d, J = 9.2 Hz, 1H), 4.57 (d, J = 16.8 Hz, 1H), 4.56 (d, J = 16.8 Hz, 1H), 6.461 (d, J = 7.6 Hz, 1H), 6.65 (s, 1H), 6.91 (d, J = 7.6 Hz, 1H), 7.20-7.30 (m, 5H).

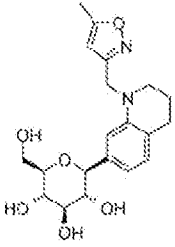
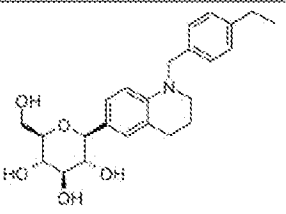
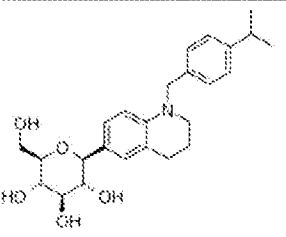
Example 74	 (2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	430.4	¹H NMR (400 MHz, CD₃OD): δ 1.35 (t, J = 7.2 Hz, 3H), 1.97-2.02 (m, 2H), 2.73 (t, J = 6.4 Hz, 2H), 3.32-3.42 (m, 6H), 3.63 (dd, J = 12.0, 5.2 Hz, 1H), 3.83 (d, J = 11.6 Hz, 1H), 3.91 (d, J = 9.6 Hz, 1H), 3.99 (q, J = 6.8 Hz, 2H), 4.38 (d, J = 16.4 Hz, 1H), 4.53 (d, J = 16.0 Hz, 1H), 6.58 (d, J = 7.6 Hz, 1H), 6.67 (s, 1H), 6.82 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 7.2 Hz, 1H), 7.17 (d, J = 8.8 Hz, 2H).
Example 75	 (2S,3R,4R,5S,6R)-2-[1-(3-Ethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	430.4	¹H NMR (400 MHz, CD₃OD): δ 1.36 (t, J = 6.8 Hz, 3H), 1.95-2.01 (m, 2H), 2.77 (t, J = 6.4 Hz, 2H), 3.32-3.42 (m, 6H), 3.63 (dd, J = 11.6, 3.6 Hz, 1H), 3.83 (d, J = 11.6 Hz, 1H), 3.91 (d, J = 9.6 Hz, 1H), 3.99 (q, J = 6.8 Hz, 2H), 4.43 (d, J = 16.4 Hz, 1H), 4.53 (d, J = 16.8 Hz, 1H), 6.61 (bd, J = 10.4 Hz, 2H), 6.76 (d, J = 8.0 Hz, 1H), 6.82 (s, 1H), 6.85 (d, J = 7.6 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H).
Example 76	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	470.3	¹H NMR (400 MHz, CD₃OD): δ 1.95-2.01 (m, 2H), 2.78 (t, J = 6.4 Hz, 2H), 3.28-3.43 (m, 6H), 3.64 (dd, J = 11.6, 4.4 Hz, 1H), 3.83 (d, J = 11.6 Hz, 1H), 3.92 (d, J = 9.2 Hz, 1H), 4.51 (d, J = 17.2 Hz, 1H), 4.58 (d, J = 16.8 Hz, 1H), 6.64 (d, J = 6.4 Hz, 2H), 6.92 (d, J = 8.0 Hz, 1H), 7.21 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H).

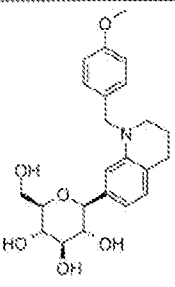
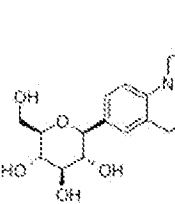
	trifluoromethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol		
Example 77	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-methyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	400.3	¹ H NMR (400 MHz, DMSO-d ₆): δ 1.86-2.01 (m, 2H), 2.31 (s, 3H), 2.70 (t, J = 6.0 Hz, 2H), 3.10-3.37 (m, 7H), 3.65 (dd, J = 11.6, 4.4 Hz, 1H), 3.79 (d, J = 9.2 Hz, 1H), 4.37 (t, J = 5.6 Hz, 1H), 4.34 (s, 2H), 4.61 (d, J = 5.6 Hz, 1H), 4.89 (t, J = 4.0 Hz, 2H), 6.50 (d, J = 7.2 Hz, 1H), 6.57 (s, 1H), 6.84 (d, J = 8.0 Hz, 1H), 7.06 (t, J = 5.6 Hz, 2H), 7.11 (s, 1H), 7.21 (t, J = 7.6 Hz, 1H).
Example 78	 (2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	414.3	¹ H NMR (400 MHz, CD ₃ OD): δ 1.20 (t, J = 7.6 Hz, 3H), 1.92-1.98 (m, 2H), 2.61 (q, J = 7.6 Hz, 2H), 2.76 (t, J = 6.0 Hz, 2H), 3.31-3.41 (m, 6H), 3.62 (dd, J = 11.2, 4.4 Hz, 1H), 3.82 (d, J = 11.6 Hz, 1H), 3.91 (d, J = 9.2 Hz, 1H), 4.43 (d, J = 16.8 Hz, 1H), 4.52 (d, J = 16.4 Hz, 1H), 6.60 (d, J = 7.6 Hz, 1H), 6.64 (s, 1H), 6.90 (d, J = 7.6 Hz, 1H), 7.06 (t, J = 8.4 Hz, 2H), 7.12 (s, 1H), 7.19 (t, J = 7.6 Hz, 1H).

Example 79	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	454.4	¹H NMR (400 MHz, CD₃OD): δ 1.97-2.01 (m, 2H), 2.79 (t, J = 6.0 Hz, 2H), 3.32-3.40 (m, 6H), 3.62 (dd, J = 11.6, 4.0 Hz, 1H), 3.82 (d, J = 11.6 Hz, 1H), 3.91 (d, J = 9.6 Hz, 1H), 4.52 (d, J = 17.2 Hz, 1H), 4.64 (d, J = 17.6 Hz, 1H), 6.59 (s, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.92 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H).
Example 80	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	454.3	¹H NMR (400 MHz, CD₃OD): δ 1.96-2.02 (m, 2H), 2.79 (t, J = 6.0 Hz, 2H), 3.26-3.45 (m, 6H), 3.62 (dd, J = 11.6, 4.4 Hz, 1H), 3.82 (d, J = 12.0 Hz, 1H), 3.91 (d, J = 9.2 Hz, 1H), 4.56 (d, J = 16.8 Hz, 1H), 4.64 (d, J = 17.2 Hz, 1H), 6.60 (s, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 7.50-7.59 (m, 4H).
Example 81	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(2-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	454.3	¹H NMR (400 MHz, CD₃OD): δ 1.90-2.11 (m, 2H), 2.84 (t, J = 6.4 Hz, 2H), 3.24 (t, J = 8.8 Hz, 2H), 3.32-3.40 (m, 4H), 3.57 (dd, J = 12.0, 5.2 Hz, 1H), 3.81 (d, J = 12.0 Hz, 1H), 3.86 (d, J = 9.2 Hz, 1H), 4.64 (d, J = 18.0 Hz, 1H), 4.68 (d, J = 18.4 Hz, 1H), 6.40 (s, 1H), 6.64 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 7.6 Hz, 1H), 7.41 (t, J = 7.2 Hz, 1H), 7.47 (d, J = 6.8

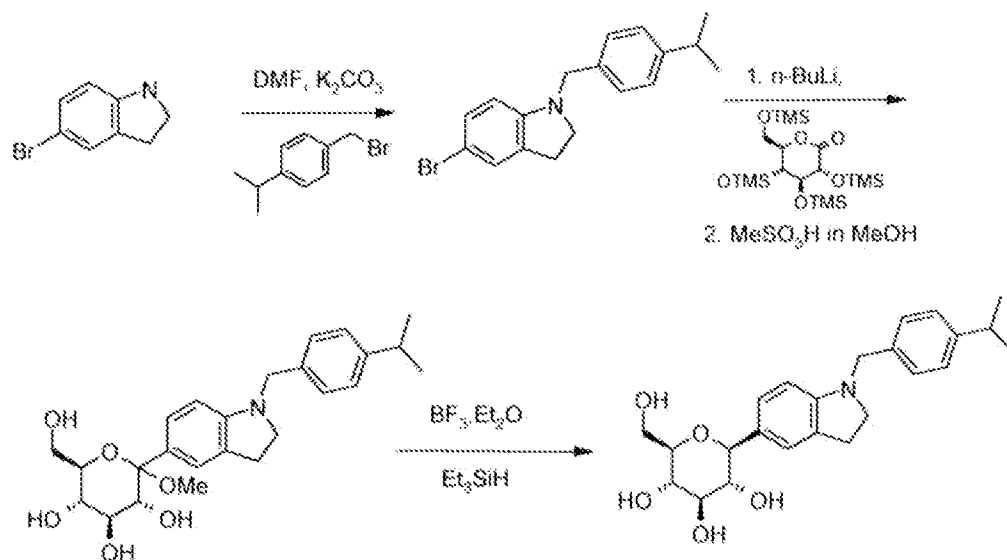
	1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol		Hz, 1H), 7.53 (t, J = 7.2 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H).
Example 82	 (2S,3R,4R,5S,6R)-2-(1-Benzofuran-5-ylmethyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>426.4</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.94-2.00 (m, 2H), 2.78 (t, J = 6.4 Hz, 2H), 3.29-3.40 (m, 6H), 3.62 (dd, J = 11.6, 4.0 Hz, 1H), 3.82 (d, J = 12.4 Hz, 1H), 3.91 (d, J = 9.6 Hz, 1H), 4.57 (d, J = 16.4 Hz, 1H), 4.65 (d, J = 16.4 Hz, 1H), 6.62 (d, J = 7.6 Hz, 1H), 6.71 (s, 1H), 6.78 (s, 1H), 6.92 (d, J = 7.2 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 8.4 Hz, 1H), 7.52 (s, 1H), 7.71 (d, J = 2.0 Hz, 1H).
Example 83	 (2S,3R,4R,5S,6R)-2-(1-Ethyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>324.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.14 (t, J = 7.2 Hz, 3H), 1.90-1.95 (m, 2H), 2.71 (t, J = 6.4 Hz, 2H), 3.26 (t, J = 6.4 Hz, 2H), 3.33-3.47 (m, 6H), 3.67 (dd, J = 12.0, 5.2 Hz, 1H), 3.87 (d, J = 12.0 Hz, 1H), 4.00 (d, J = 8.8 Hz, 1H), 6.59 (d, J = 7.2, 1H), 7.68 (s, 1H), 6.87 (d, J = 8.4 Hz, 1H).
Example 84	 (2S,3R,4R,5S,6R)-2-[1-(4-chlorophenyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>420.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.96-2.01 (m, 2H), 2.78 (t, J = 6.4 Hz, 2H), 3.27-3.42 (m, 6H), 3.47 (dd, J = 11.2, 4.4 Hz, 1H), 3.83 (d, J = 11.2 Hz, 1H), 3.92 (d, J = 9.2 Hz, 1H), 4.47 (d, J = 17.2 Hz, 1H), 4.55 (d, J = 17.2 Hz, 1H), 6.59 (s, 1H), 6.63 (d, J = 7.2 Hz,

	(3-Chloro-benzyl)- 1,2,3,4-tetrahydro- quinolin-7-yl]-6- hydroxymethyl- tetrahydro-pyran-3,4,5- triol		1H), 6.92 (d, J = 7.6 Hz, 1H), 7.21-7.31 (m, 4H).
Example 85	 (2R,3S,4R,5R,6S)-2- Hydroxymethyl-6-{1-[2- (4-methoxy-phenyl)- ethyl]-1,2,3,4- tetrahydro-quinolin-7- yl}-tetrahydro-pyran- 3,4,5-triol	430.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.83-1.89 (m, 2H), 2.69 (t, J = 6.0 Hz, 2H), 2.82 (t, J = 7.6 Hz, 2H), 3.20 (t, J = 5.6 Hz, 2H), 3.39-3.49 (m, 6H), 3.70 (dd, J = 11.2, 3.6 Hz, 1H), 3.78 (s, 3H), 3.90 (d, J = 11.6 Hz, 1H), 4.04 (d, J = 9.6 Hz, 1H), 6.60 (d, J = 7.2 Hz, 1H), 6.72 (s, 1H), 6.87 (t, J = 8.0 Hz, 3H), 7.18 (d, J = 7.6 Hz, 2H).
Example 86	 (2S,3R,4R,5S,6R)-2- {1-[2-(4-Ethoxy- phenyl)-ethyl]-1,2,3,4- tetrahydro-quinolin-7- yl}-6-hydroxymethyl- tetrahydro-pyran-3,4,5- triol	444.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.38 (t, J = 7.2 Hz, 3H), 1.83-1.88 (m, 2H), 2.69 (t, J = 6.0 Hz, 2H), 2.81 (t, J = 7.6 Hz, 2H), 3.19 (t, J = 5.2 Hz, 2H), 3.31-3.50 (m, 6H), 3.71 (dd, J = 12.0, 4.4 Hz, 1H), 3.90 (d, J = 12.0 Hz, 1H), 3.98-4.05 (m, 3H), 6.60 (d, J = 8.0 Hz, 1H), 6.72 (s, 1H), 6.84 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 7.6 Hz, 1H), 7.16 (d, J = 8.8 Hz, 2H).

Example 87	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(5-methyl-isoxazol-3-ylmethyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol	<u>391.3</u>	¹H NMR (400 MHz, CD₃OD): δ 1.92-1.98 (m, 2H), 2.37 (s, 3H), 2.73 (t, J = 6.0 Hz, 2H), 3.33-3.48 (m, 6H), 3.70 (dd, J = 12.0, 5.2 Hz, 1H), 3.87 (d, J = 10.4 Hz, 1H), 4.00 (d, J = 9.2 Hz, 1H), 4.49 (d, J = 16.4 Hz, 1H), 4.53 (d, J = 16.4 Hz, 1H), 6.08 (s, 1H), 6.66 (d, J = 7.6 Hz, 1H), 6.82 (s, 1H), 6.90 (d, J = 7.6 Hz, 1H).
Example 88	 (2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>414.4</u>	¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 8.0 Hz, 3H), 1.98-2.03 (m, 2H), 2.62 (q, J = 7.6 Hz, 2H), 2.81 (t, J = 12.4 Hz, 2H), 3.33-3.44 (m, 6H), 3.68 (dd, J = 11.2, 5.2 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 8.4 Hz, 1H), 4.47 (s, 2H), 6.50 (d, J = 8.8 Hz, 1H), 6.96-7.17 (m, 6H).
Example 89	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>428.4</u>	¹H NMR (400 MHz, CD₃OD): δ 1.24 (d, J = 6.8 Hz, 6H), 1.98-2.03 (m, 2H), 2.81 (t, J = 12.4 Hz, 2H), 2.85-2.90 (m, 1H), 3.33-3.44 (m, 5H), 3.67 (dd, J = 11.2, 5.2 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 8.4 Hz, 1H), 4.47 (s, 2H), 6.50 (d, J = 8.8 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.0 (s, 1H), 7.16 (s, 5H).

	quinolin-6-yl]- tetrahydro-pyran-3,4,5- triol		
Example 90	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-tetrahydro-pyran-3,4,5-triol	416.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.97-2.00 (m, 2H), 2.79 (t, J = 6.0 Hz, 2H), 3.33-3.44 (m, 6H) 3.67 (dd, J = 11.2, 4.8 Hz, 1H), 3.76 (s, 3H), 3.85 (d, J = 12 Hz, 1H), 3.95 (d, J = 8.8 Hz, 1H), 4.42 (s, 2H), 6.51 (d, J = 8.4 Hz, 1H), 6.84 (d, J = 8.4 Hz, 2H), 6.95-6.98 (m, 2H), 7.15 (d, J = 8.8 Hz, 2H).
Example 91	 (2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	414.4	¹ H NMR (400 MHz, CD ₃ OD): δ 1.22 (t, J = 8.0 Hz, 3H), 1.99-2.03 (m, 2H), 2.62 (q, J = 7.6 Hz, 2H), 2.81 (t, J = 12.4 Hz, 2H), 3.33-3.44 (m, 6H) 3.67 (dd, J = 11.2, 5.2 Hz, 1H), 3.87 (d, J = 11.2 Hz, 1H), 3.97 (d, J = 8.4 Hz, 1H), 4.47 (s, 2H), 6.50 (d, J = 8.8 Hz, 1H), 6.97-7.22 (m, 6H).

Example 92. (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 5-bromo-indoline (500 mg, 2.5 mmol) in DMF (4 ml) was added potassium carbonate (700 mg, 5.0 mmol), 4-isopropylbenzyl bromide (0.63 ml, 3.8 mmol) and heated to 60 °C for 3 h. Reaction mixture was cooled to room temperature, quenched by the addition of water (15 ml), extracted with ethyl acetate (3 X 10 ml). All organic layers were mixed and washed with water (20 ml), brine (20 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 5-bromo-1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indole (750 mg).

¹H NMR (400MHz, CDCl₃): δ 1.27 (d, J= 6.0 Hz, 6H), 2.91-2.99 (m, 3H), 3.47 (t, J= 8.0 Hz, 2H), 4.28 (s, 2H), 7.25-7.33 (m, 7H). MS(ES) m/z 330.2 (M+2).

Step II: To a stirred solution of 5-bromo-1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indole (740 mg, 2.24 mmol) in THF-toluene (1:2 mixture, 15 ml) was added 1.6 M n-BuLi in hexanes (1.4 ml, 2.24 mmol) at -78 °C. The reaction mixture was stirred for 40 min., then it was transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (1.05 g, 2.24 mmol) in toluene (10 ml) at -78 °C. After stirring it for 40 min., 0.6 N methanesulfonic acid in methanol (10 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate (5 ml). Usual work up and purification by silica gel column chromatography resulted in (3R,4S,5S,6R)-6-hydroxymethyl-2-[1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-2-methoxy-tetrahydro-pyran-3,4,5-triol (500 mg).

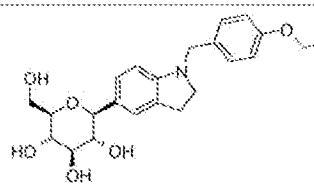
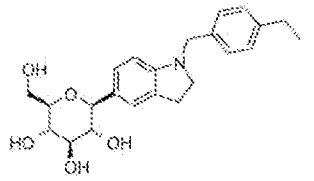
To a stirred solution of (3R,4S,5S,6R)-6-hydroxymethyl-2-[1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-2-methoxy-tetrahydro-pyran-3,4,5-triol (500 mg, 1.12 mmol) in

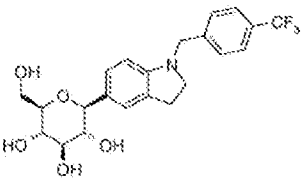
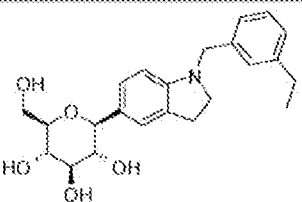
acetonitrile-dichloromethane (1:1 mixture, 10 ml) was added boron trifluoride diethyletharate complex (0.28 ml, 2.25 mmol) and triethylsilane (0.72 ml, 4.50 mmol) at -10 °C and stirred for 4 h at 0 °C. Reaction was quenched with aq. saturated sodium bicarbonate solution (5 ml), extracted with ethyl acetate (3 X 10 ml). The ethyl acetate layers were mixed, washed with brine (5 ml), dried over sodium sulphate, concentrated and purified by preparative HPLC to furnish the titled compound (45 mg).

¹H NMR (400 MHz, CD₃OD): δ 1.24 (t, J = 6.8 Hz, 6H), 2.87-2.94 (m, 3H), 3.26 (t, J = 8.4 Hz, 2H), 3.38-3.44 (m, 4H), 3.68 (dd, J = 11.2, 5.2, 1H), 3.87 (d, J = 11.2 Hz, 1H), 4.02 (d, J = 9.2 Hz, 1H), 4.22 (s, 2H), 6.54 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 7.14 (s, 1H), 7.19 (d, J = 7.6 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H).

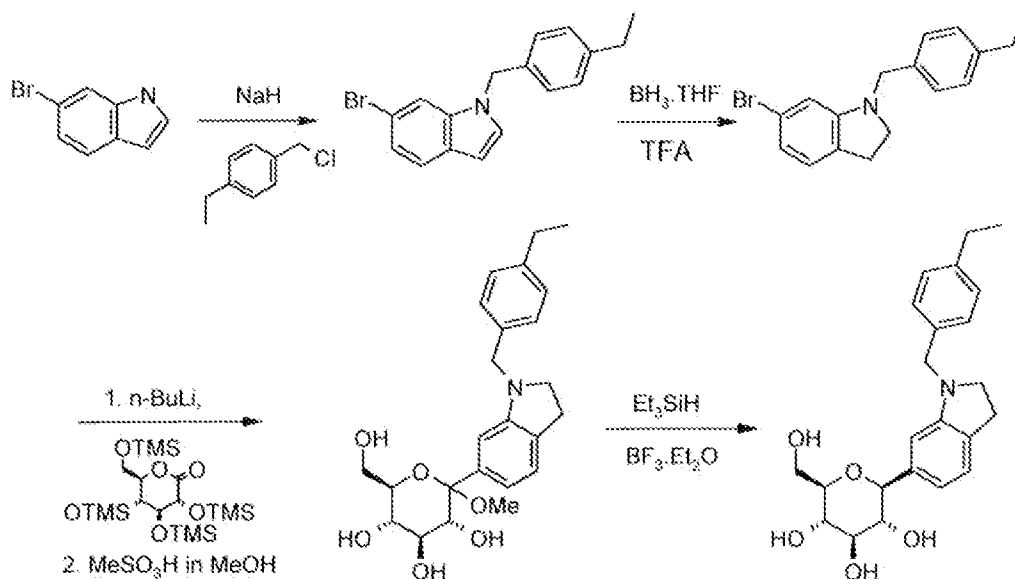
MS (EI) *m/z* 414.4 (M+1).

Examples 93-95 were prepared in an analogous procedure as described in example 92.

Example #	Structure	MS (M+1)	¹ H NMR
Example 93	 (2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>416.4</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.36 (t, J = 7.2 Hz, 3H), 2.91 (t, J = 8.4 Hz, 2H), 3.24 (t, J = 8.4 Hz, 2H), 3.33-3.47 (m, 4H), 3.68 (dd, J = 11.2, 5.2, 1H), 3.86 (d, J = 11.2 Hz, 1H), 3.98-4.03 (m, 3H), 4.16 (s, 2H), 6.56 (d, J = 8.0 Hz, 1H), 6.87 (d, J = 7.6 Hz, 2H), 7.08 (d, J = 8.0 Hz, 1H), 7.15 (s, 1H), 7.26 (d, J = 7.6 Hz, 2H)
Example 94	 (2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>400.4</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.21 (t, J = 7.6 Hz, 3H), 2.63 (q, J = 7.6 Hz, 2H), 2.90 (t, J = 8.4 Hz, 2H), 3.24 (t, J = 8.4 Hz, 2H), 3.30-3.44 (m, 4H), 3.68 (dd, J = 11.2, 5.2, 1H), 3.87 (d, J = 11.2 Hz, 1H), 4.02 (d, J = 9.2 Hz, 1H), 4.20 (s, 2H), 6.52 (d, J = 8.0 Hz, 1H), 7.05 (d, J = 8.0 Hz, 1H), 7.12-7.25 (m, 5H).

	triol		
Example 95	 (2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>440.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 2.97 (t, J = 8.4 Hz, 2H), 3.32-3.46 (m, 6H), 3.68 (dd, J = 12, 5.2, 1H), 3.86 (d, J = 11.2 Hz, 1H), 4.03 (d, J = 8.8 Hz, 1H), 4.35 (s, 2H), 6.49 (d, J = 8.0 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 7.16 (s, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H).
Example 96	 (2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	<u>400.3</u>	¹ H NMR (400 MHz, CD ₃ OD): δ 1.21 (t, J = 7.6 Hz, 3H), 2.62 (q, J = 7.6 Hz, 2H), 2.92 (t, J = 8.0 Hz, 2H), 3.25-3.45 (m, 6H), 3.67 (dd, J = 12.0, 4.4 Hz, 1H), 3.76 (d, J = 11.6 Hz, 1H), 4.01 (d, J = 9.2 Hz, 1H), 4.21 (s, 2H), 6.51 (d, J = 8.0 Hz, 1H), 7.05-7.23 (m, 6H).

Example 97: (2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To an ice-cold solution of 6-bromoindole (800 mg, 4.1 mmol) in DMF (8 ml) under argon was added sodium hydride (60% in mineral oil, 277 mg, 6.9 mmol) and stirred for 30 min followed by the addition of 4-ethylbenzyl chloride (2.2 ml, 14.7 mmol) and stirred further for 2h at room temperature. The reaction was quenched by the addition of water (20 ml). Crude product obtained after usual work up was purified by silica gel column chromatography to furnish 6-bromo-1-(4-ethyl-benzyl)-1H-indole (1.25 g).

¹H NMR (400 MHz, CDCl₃): δ 1.21 (t, J = 7.2 Hz, 3H), 2.62 (q, J = 7.2 Hz, 2H), 5.24 (s, 2H), 6.50-7.50 (m, 9H). MS (ES) *m/z* 315.9 (M+2)

Step II: To an ice cold solution of 6-bromo-1-(4-ethyl-benzyl)-1H-indole (1.24 g, 3.95 mmol) in trifluoroacetic acid (15 ml) was added 1.0 M borane-tetrahydrofuran complex in THF (7.9 ml, 7.9 mmol) and stirred for 3 h. The reaction was quenched by the addition of water and the mixture was concentrated under reduced pressure. The resulting residue was taken in 5N sodium hydroxide solution (15 ml) and extracted with ethyl acetate (2 X 10 ml). Combined organic layer was washed with water (15 ml), brine (15 ml), dried over anhydrous sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 6-bromo-1-(4-ethyl-benzyl)-2,3-dihydro-1H-indole (780 mg). MS (ES) *m/z* 318.0 (M+2)

Step III: To a stirred solution of 6-bromo-1-(4-ethyl-benzyl)-2,3-dihydro-1H-indole (700 mg, 2.21 mmol) in THF-toluene (9 ml of 1:2 mixture) was added 1.6 M solution of n-BuLi in hexanes (1.4 ml, 2.21 mmol) at -78 °C. The reaction mixture was stirred for 30 min. and was then transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-

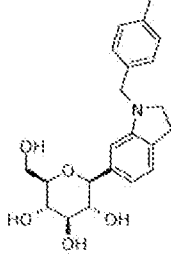
glucopyranone (1.03 g, 2.21 mmol) in toluene (9 ml) at -78 °C. After stirring for 40 min., 0.6 N methanesulfonic acid in methanol (10 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate solution (5 ml) and extracted with ethyl acetate (3 X 10 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish (3R,4S,5S,6R)-2-[1-(4-ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (765 mg).

¹H NMR (400 MHz, CD₃OD): δ 1.11(t, J = 7.2 Hz, 3H), 2.52 (q, J = 7.2 Hz, 2H), 2.78 (t, J = 8.0 Hz, 2H), 3.04 (s, 3H), 3.05-3.06 (m, 1H), 3.11 (t, J = 7.6 Hz, 2H), 3.31 (t, J = 9.2 Hz, 1H), 3.45-3.46 (m, 1H), 3.64 (t, J = 8.8 Hz, 1H), 3.70 (dd, J = 12.0, 5.6 Hz, 1H), 3.82 (d, J = 12.0 Hz, 1H), 4.14 (s, 2H), 6.79-6.82 (m, 2H), 6.93 (d, J = 7.6 Hz, 1H), 7.06 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H). MS (ES) *m/z* 430.0 (M+1).

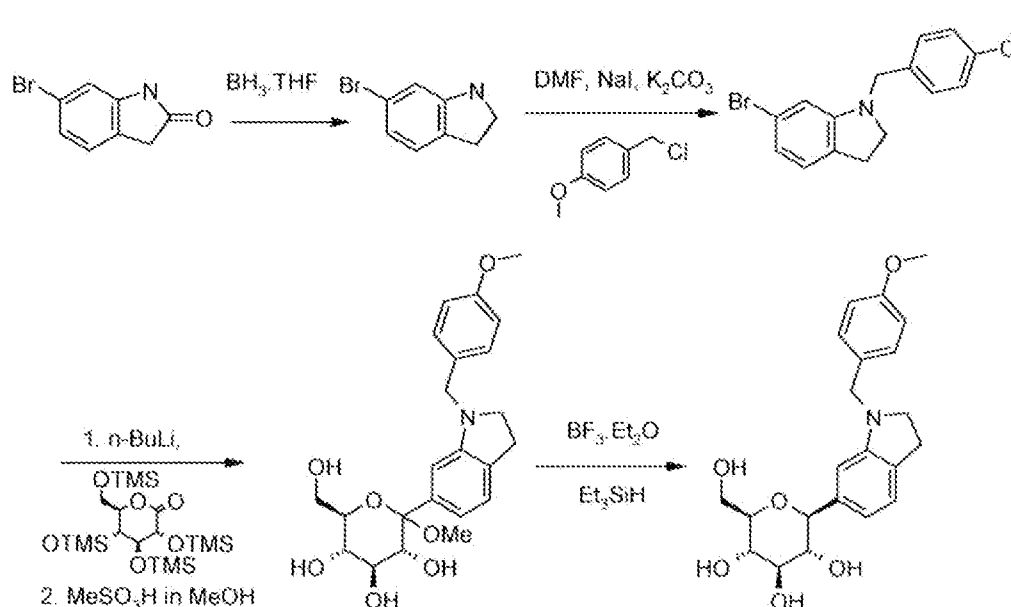
Step IV: To a stirred solution of (3R,4S,5S,6R)-2-[1-(4-ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-2-methoxy-tetrahydro-pyran-3,4,5-triol (490 g, 0.931 mmol) in acetonitrile-dichloromethane mixture (1:1 mixture, 8 ml) was added boron trifluoride diethyletherate complex (0.24 ml, 1.86 mmol), and triethylsilane (0.59 ml, 3.72 mol) at -5 °C. After stirring for 4 h at 0 °C, reaction was quenched with aq. saturated sodium bicarbonate solution (4 ml). The volatiles were evaporated under reduced pressure; the resulting mixture was extracted with ethyl acetate (3 X 8 ml). The organic layer was washed with brine (3 ml), dried over sodium sulfate, concentrated and purified by preparative HPLC to furnish (2S,3R,4R,5S,6R)-2-[1-(4-ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (60 mg).

¹H NMR (400 MHz, CD₃OD): δ 1.22 (t, J = 7.6 Hz, 3H), 2.63 (q, J = 7.6 Hz, 2H), 2.90 (t, J = 8.0 Hz, 2H), 3.23 (t, J = 8.0 Hz, 2H), 3.34-3.48 (m, 4H), 3.69 (dd, J = 12.0, 5.2 Hz, 1H), 3.86 (dd, J = 12.0, 2.0 Hz, 1H), 4.04 (d, J = 9.2 Hz, 1H), 4.22 (s, 2H), 6.70-6.72 (m, 2H), 7.02 (d, J = 8.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H). MS (ES) *m/z* 400.2 (M+1).

Following example was prepared using the procedures described above.

Example 98	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol	386.0	¹ H NMR (400 MHz, CD ₃ OD): δ 2.31 (s, 3H), 2.86 (t, J = 8.0 Hz, 2H), 3.19 (t, J = 8.0 Hz, 2H), 3.34-3.44 (m, 4H), 3.68 (dd, J = 11.6, 5.2 Hz, 1H), 3.86 (dd, J = 11.6, 1.2 Hz, 1H), 4.02 (d, J = 9.2 Hz, 1H), 4.20 (s, 2H), 6.69-6.71 (m, 2H), 7.00 (d, J = 7.6 Hz, 1H), 7.12 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H).
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Example 99: (2S,3R,4R,5S,6R)-2-[1-(4-Methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.



Step I: To a stirred solution of 6-bromoxindole (5.0 g, 23.6 mmol) in THF (25 ml) was added 1.0 M borane-tetrahydrofuran complex in THF (82.5 ml, 82.5 mmol) at room temperature. After complete addition, the reaction mixture was refluxed for 18 h. Reaction mixture was cooled to room temperature, quenched by the addition of methanol and solvents were evaporated under reduced pressure. The resulting residue

was taken in ethyl acetate (70 ml) and washed with aqueous sodium bicarbonate solution (50 ml) followed by water (50 ml) brine (50 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 6-bromo-indoline. (3.72 g). ^1H NMR (400 MHz, CDCl_3): δ 2.96 (t, $J = 8.4$ Hz, 2H), 3.57 (t, $J = 8.4$ Hz, 2H), 3.80 (bs, 1H), 6.74 (s, 1H), 6.78-6.95 (m, 2H). MS (EI) m/z 200.1 ($M+2$).

Step II: To a stirred solution of 6-bromo-indoline (3.7 g, 18.7 mmol) in DMF (30 ml) was added potassium carbonate (5.2 g, 37.4 mmol), 4-methoxybenzyl chloride (3.8 ml, 28.0 mmol), sodium iodide (1.4 g, 9.3 mmol) and heated to 50°C for 3 h. Reaction mixture was cooled to room temperature, quenched by the addition of water (50 ml), extracted with ethyl acetate (3 X 20 ml). The organic layer was washed with water (50 ml), brine (50 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish 6-bromo-1-(4-methoxy-benzyl)-2,3-dihydro-1H-indole (2.71 g). ^1H NMR (400 MHz, CDCl_3): δ 2.89 (t, $J = 8.4$ Hz, 2H), 3.31 (t, $J = 8.0$ Hz, 2H), 3.81 (s, 3H), 4.16 (s, 2H), 6.61 (s, 1H), 6.74 (d, $J = 7.6$ Hz, 1H), 6.86-7.25 (m, 5H). MS (EI) m/z 320.1 ($M+2$).

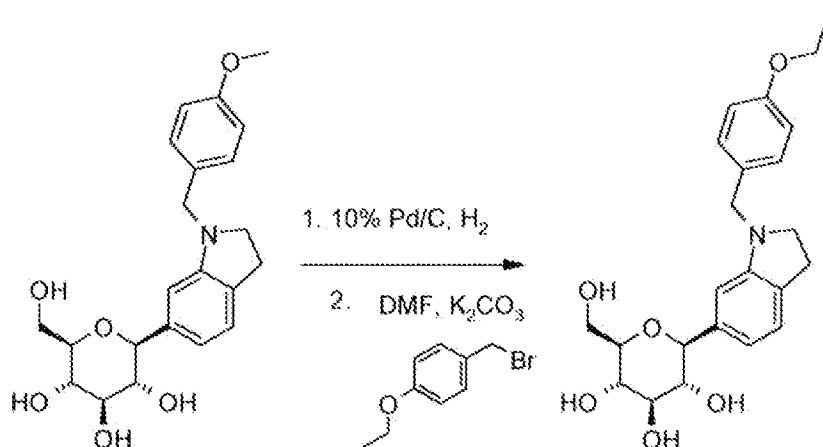
Step III: To a stirred solution of 6-bromo-1-(4-methoxy-benzyl)-2,3-dihydro-1H-indole (2.7 g, 8.5 mmol) in THF-toluene (1:2 mixture, 30 ml) was added 1.6 M *n*-BuLi in hexanes (5.3 ml, 8.5 mmol) at -78°C . The reaction mixture was stirred for 40 min., and then transferred to a stirred solution of 2,3,4,6-tetrakis-O-(trimethylsilyl)-D-glucopyranone (4.0 g, 8.5 mmol) in toluene (30 ml) at -78°C . After stirring the reaction for 40 min., 0.6 N methanesulfonic acid in methanol (30 ml) was added and stirred for 20 h at room temperature. Reaction was quenched by the addition of aq. saturated sodium bicarbonate solution (15 ml) and was extracted with ethyl acetate (3 X 20 ml), dried over sodium sulfate, concentrated and purified by silica gel column chromatography to furnish (3R,4S,5S,6R)-6-hydroxymethyl-2-methoxy-2-[1-(4-methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol (1.0 g). MS (EI) m/z 432.2 ($M+1$).

Step IV: To a stirred solution of (3R,4S,5S,6R)-6-hydroxymethyl-2-methoxy-2-[1-(4-methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol (550 mg, 1.27 mmol) in acetonitrile-dichloromethane (1:1 mixture, 10 ml) was added boron trifluoride diethyletherate complex (0.33 ml, 2.55 mmol) and triethylsilane (0.81 ml, 5.09 mmol) at -10°C and stirred for 4 h at 0°C . Reaction was quenched with aq. saturated sodium bicarbonate solution (5 ml), extracted with ethyl acetate (3 X 10 ml). The organic layer was washed with brine (5 ml), dried over sodium sulfate, concentrated and purified by

preparative HPLC to furnish (2R,3S,4R,5R,6S)-2-hydroxymethyl-6-[1-(4-methoxybenzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol (70 mg).

¹H NMR (400 MHz, CD₃OD): δ 2.84 (t, J = 8.0 Hz, 2H), 3.17 (t, J = 8 Hz, 2H), 3.28-3.42 (m, 4H), 3.54 (dd, J = 12.0, 5.2 Hz, 1H), 3.76 (s, 3H), 3.86 (d, J = 11.2 Hz, 1H), 4.02 (d, J = 9.2 Hz, 1H), 4.17 (s, 2H), 6.68-6.69 (m, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 7.6 Hz, 1H), 7.26 (d, J = 8.8 Hz, 2H). MS (EI) *m/z* 402.1 (M+1).

Example 100: (2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.



Step I: To a stirred solution of (2R,3S,4R,5R,6S)-2-hydroxymethyl-6-[1-(4-methoxybenzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol in methanol (4 ml) was added 10% palladium on charcoal (10 mg), 0.1 ml of conc. hydrochloric acid. Reaction mixture was stirred under hydrogen atmosphere (balloon pressure) for 18 h. Reaction mixture was filtered through celite bed, solvent was evaporated under reduced pressure to get (2S,3R,4R,5S,6R)-2-(2,3-dihydro-1H-indol-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (30 mg). MS (EI) *m/z* 282.0 (M+1).

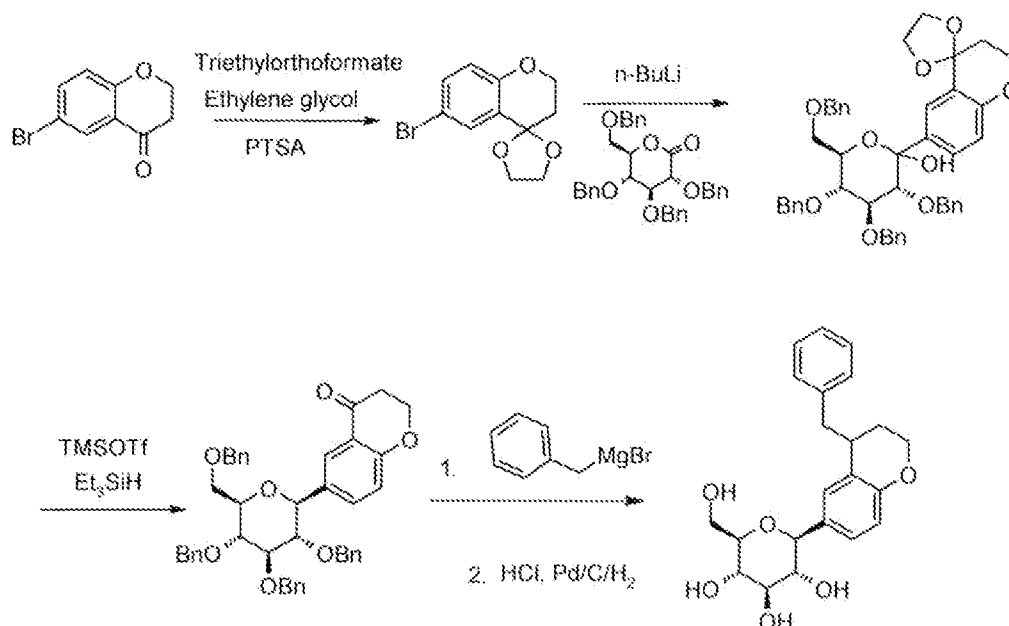
Step II: To a stirred solution of (2S,3R,4R,5S,6R)-2-(2,3-dihydro-1H-indol-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (30 mg, 0.107 mmol) in DMF (1 ml) was added potassium carbonate (0.03 mg, 0.213 mmol), 4-ethoxybenzyl bromide (0.034 g, 0.16 mmol) and heated to 60 °C for 3 h. Reaction mixture was cooled to room temperature, quenched by the addition of water (5 ml), extracted with ethyl acetate (2 X 8 ml). The organic layer was washed with brine (5 ml), dried over sodium sulfate, concentrated and purified by preparative HPLC to furnish (2S,3R,4R,5S,6R)-2-[1-(4-

ethoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol (10 mg).

^1H NMR (400 MHz, CD_3OD): δ 1.35 (t, $J = 6.8$ Hz, 3H), 2.84 (t, $J = 8.0$ Hz, 2H), 3.17 (t, $J = 8$ Hz, 2H), 3.28-3.42 (m, 4H), 3.67 (dd, $J = 12.0, 5.6$ Hz, 1H), 3.85 (dd, $J = 12.0, 2.0$ Hz, 1H), 3.97-4.02 (s, 3H), 4.17 (s, 2H), 6.67-6.69 (m, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 6.99 (d, $J = 7.6$ Hz, 1H), 7.24 (d, $J = 8.8$ Hz, 2H).

MS (EI) m/z 416.1 ($M+1$).

Example 101. (2S,3R,4R,5S,6R)-2-[4-benzyl-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol



Step I: To a stirred solution of 6-bromo-chroman-4-one (5.0 g, 22.03 mmol) in benzene (110 ml) was added ethylene glycol (2.73 g, 44.05 mmol), triethylorthoformate (6.52 g, 44.05 mmol), para-toluenesulfonic acid monohydrate (83 mg, 4.41 mmol) and azeotrope for 2h at 80 °C, quenched with saturated NaHCO_3 (50 ml). After usual work up, compound was purified by silica gel column chromatography to furnish 6'-bromospiro[1,3-dioxolane-2,4'-chromane] (4.83 g).

^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 2.07 (t, $J = 5.5$ Hz, 2H), 4.04-4.08 (m, 2H), 4.16-4.20 (m, 2H), 4.26 (t, $J = 5.5$ Hz, 2H), 6.79 (d, $J = 8.6$ Hz, 1H), 7.40 (dd, $J = 8.6$ Hz, 2.4 Hz, 1H), 7.48 (d, $J = 2.4$ Hz, 1H).

Step II: To a stirred solution of 8.2 (2.0 g, 7.38 mmol) in THF (8 ml) at -78 °C was added n-Butyl lithium (470 mg, 7.38 mmol) and stirred for 1h. Meanwhile tetra-O-Benzyl-

glucaranolactone (3.97 g, 7.38 mmol) in THF (6 ml) was cooled to -78°C and lithium salt prepared above was added to this at -78°C . This reaction mixture was stirred for 1h, quenched with saturated NH_4Cl (10 ml). After usual work up, compound was purified by silica gel column chromatography to furnish sugar derivaive (3.41 g).

To a stirred solution of above intermediate (1.0 g, 1.37 mmol) in DCM (15 ml) at -78°C was added triethylsilane (175 mg, 1.51 mmol) followed by trimethylsilyl trifluoromethanesulfonate (335 mg, 1.51 mmol) and stirred for 1h, quenched with saturated NaHCO_3 (20 ml). After usual work up, compound was purified by silica gel column chromatography to furnish the 6-((2S,3S,4R,5R,6R)-3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-chroman-4-one (Yield = 0.45 g).

^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 2.83 (t, $J = 6.2$ Hz, 2H), 3.46 (t, $J = 9.3$ Hz, 1H); 3.63-3.68 (m, 4H); 3.79 (t, $J = 8.2$ Hz, 1H), 3.89 (d, $J = 11.0$ Hz, 1H); 4.35 (d, $J = 9.5$ Hz, 1H); 4.43 (d, $J = 11.0$ Hz, 1H); 4.49-4.61 (m, 5 H); 4.78 (d, $J = 10.8$ Hz, 1H), 4.84 (s, 2H); 6.89-6.91 (m, 2H); 7.05 (d, $J = 8.6$ Hz, 1H); 7.19-7.23 (m, 5H); 7.29-7.36 (m, 13H); 7.60 (dd, $J = 8.6$ Hz, 1.5 Hz, 1H), 7.79 (d, $J = 1.5$ Hz, 1H). MS (ES) m/z 688.5 ($M+18$).

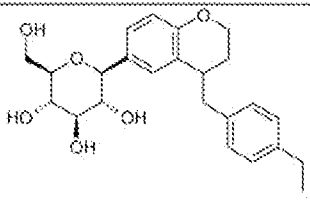
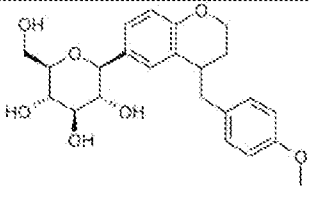
Step III: To a stirred suspension of magnesium (53 mg, 2.24 mmol) in THF (2.4 ml) was added one small crystal of iodine. Benzyl bromide (380 mg, 2.24 mmol) was added through syringe (initially 20 % of total amount was added for initiation) then slowly remaining amount was added and stirred for 1h. 6-((2S,3S,4R,5R,6R)-3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-chroman-4-one (300 mg, 0.45 mmol) was dissolved in THF (2 ml) and it was added to above prepared Grignard reagent stirred for 3h, quenched with saturated NH_4Cl (20 ml). Crude compound (4-Benzyl-6-((2S,3S,4R,5R,6R)-3,4,5-tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-chroman-4-ol, ~520 mg) obtained after usual work up was taken for next reaction.

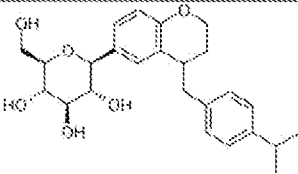
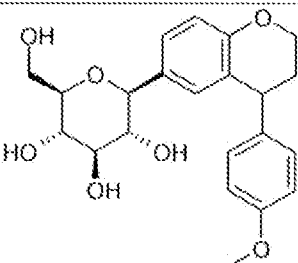
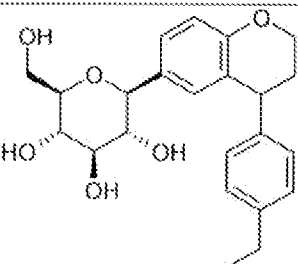
Step IV: To a stirred solution of crude 4-benzyl-6-((2S,3S,4R,5R,6R)-3,4,5-tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-chroman-4-ol (400 mg, 0.52 mmol) in 1,4-dioxane (5 ml) was added palladium on C 10 % w/w (80 mg, 20 % w/w) followed by methanol (5 ml) and one drop of conc.HCl was added. After stirring the reaction mixture for 18 h under hydrogen atmosphere (balloon pressure), filtered through celite and concentrated. The crude product was purified by preparative HPLC to furnish title compound (41 mg).

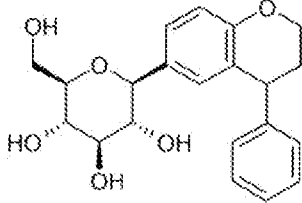
^1H NMR (400 MHz, $\text{DMSO}-d_6$): (peaks correspond to major isomer) δ 1.52-1.61 (m, 1H), 1.65-1.75 (m, 1H); 2.65 (t, $J = 12.8$ Hz, 1H), 2.88-3.11 (m, 1H); 3.21-3.48 (m, 6H); 3.69 (d, $J = 12.0$ Hz, 1H); 3.93 (t, $J = 9.0$ Hz, 1H); 4.10-4.18 (m, 2H), 4.22 (bs, 1H); 4.71 (bs,

1H); 4.93 (bs, 2H); 6.68 (d, J = 8.1 Hz, 1H); 7.05 (d, J = 7.8 Hz, 1H); 7.23 (s, 1H); 7.31 (bs, 5H) . MS (ES) *m/z* 404.4 (M+18)

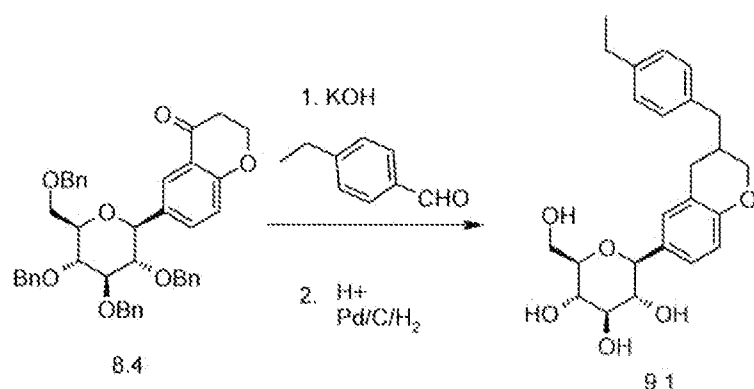
Examples 102-107 were prepared in an analogous procedure as described in example 101.

Example #	Structure	MS M+18	¹ H NMR
Example 102	 (2S,3R,4R,5S,6R)-2-[(4-ethylphenyl)methyl]chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol	432.4 (M+18)	¹ H NMR (400 MHz, DMSO-D ₆): δ 1.16 (t, J = 7.6 Hz, 3H); 1.51-1.62 (m, 1H), 1.63-1.76 (m, 1H); 2.57 (q, J = 7.6 Hz, 2H), 2.83-3.05 (m, 1H); 3.09-3.28 (m, 5H); 3.37-3.43 (m, 2H); 3.67 (dd, J = 5.6 Hz, 1H); 3.91 (dd, J = 8.8 Hz, 1H); 4.04-4.13 (m, 2H), 4.42 (t, J = 5.6 Hz, 1H); 4.69 (t, J = 4.0 Hz, 1H); 4.92 (t, J = 4.0 Hz, 2H); 6.67 (d, J = 8.3 Hz, 1H); 7.05-7.05 (m, 1H); 7.12-7.21 (m, 4H); 7.29 (bs, 1H).
Example 103	 (2R,3S,4R,5R,6S)-2-[(4-methoxyphenyl)methyl]chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol	434.4 (M+18)	¹ H NMR (400 MHz, CD ₃ OD) : δ 1.67-1.77 (m, 1H), 1.75-1.86 (m, 1H); 2.61-2.69 (m, 1H), 3.00-3.05 (m, 1H); 3.10-3.19 (m, 1H); 3.35-3.47 (m, 4H); 3.67-3.71 (m, 1H); 3.78 (s, 3H); 3.87 (d, J = 11.6 Hz, 1H); 4.01-4.19 (m, 3H), 6.72 (d, J = 8.6 Hz, 1H); 6.86 (d, J = 8.1 Hz, 2H); 7.12-7.16 (m, 3H); 7.27 (s, 1H) .

Example 104	 (2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-[4-[(4-isopropylphenyl)methyl]chroman-6-yl]tetrahydropyran-3,4,5-triol	446.5 (M+1 8)	¹H NMR (400 MHz, CD₃OD) : δ 1.45 (d, J = 6.6 Hz, 6H); 1.85-1.96 (m, 1H), 1.96-2.08 (m, 1H); 2.80-2.91 (m, 1H), 3.07-3.11 (m, 1H); 3.21-3.30 (m, 1H); 3.31-3.48 (m, 1H); 3.56-3.68 (m, 4H); 3.88-3.91 (m, 1H); 4.08 (d, J = 12.0 Hz, 1H); 4.22-4.38 (m, 3H), 6.93 (d, J = 8.1 Hz, 1H); 7.34-7.40 (m, 5H); 7.52 (s, 1H)
Example 105	 (2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-[4-(4-methoxyphenyl)chroman-6-yl]tetrahydropyran-3,4,5-triol	420.4 (M+1 8)	¹H NMR (400 MHz, DMSO-D₆) : δ 1.88-1.98 (m, 1H), 2.12-2.21 (m, 1H); 2.97-3.19 (m, 4H), 3.33-3.37 (m, 1H); 3.39-3.65 (m, 1H); 3.72 (s, 3H); 3.75-3.82 (m, 1H); 4.01-4.14 (m, 3H); 4.37-4.43 (m, 1H); 4.63 (d, J = 4.8 Hz, 1H), 4.87 (d, J = 2.4 Hz, 2H); 6.75 (d, J = 8.0 Hz, 2H); 6.88 (d, J = 8.4 Hz, 2H); 7.03-7.08 (m, 3H).
Example 106	 (2S,3R,4R,5S,6R)-2-[4-(4-ethylphenyl)chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol	418.4 (M+1 8)	¹H NMR (400 MHz, CD₃OD) : δ 1.21-1.26 (m, 3H), 2.01-2.08 (m, 1H); 2.21-2.31 (m, 1H), 2.60-2.66 (m, 2H); 3.21-3.30 (m, 1H); 3.37-3.41 (m, 3H); 3.61-3.68 (m, 1H); 3.82-3.85 (m, 1H); 3.93-3.96 (t, J = 11.2 Hz, 1H); 4.13-4.19 (m, 3H), 6.82 (d, J = 8.6 Hz, 1H); 6.91 (s, 1H); 7.06 (d, J = 7.6 Hz, 2H); 7.14 (d, J = 8.0 Hz, 2H); 7.20 (d, J = 8.4 Hz, 1H).

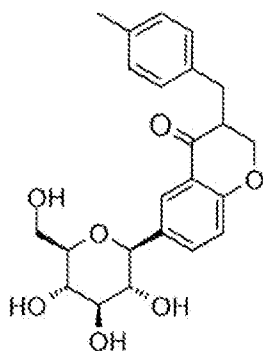
Example 107	 (2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-(4-phenylchroman-6-yl)tetrahydropyran-3,4,5-triol	390.4 (M+1) 8)	¹ H NMR (400 MHz, DMSO-D ₆) : δ 1.92-2.01 (m, 1H), 2.16-2.25 (m, 1H); 3.06-3.18 (m, 4H), 3.33-3.38 (m, 1H); 3.62-3.65 (m, 1H); 3.75-3.82 (dd, J = 9.8 Hz, 9.1 Hz, 1H); 4.03-4.20 (m, 3H); 4.35-4.45 (m, 1H); 4.64 (bs, 1H); 4.88 (bs, 2H); 6.77 (d, J = 8.3 Hz, 2H); 7.09 (d, J = 8.3 Hz, 1H); 7.12-7.34 (m, 5H).
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Example 108. (2S,3R,4R,5S,6R)-2-[3-[(4-ethylphenyl)methyl]chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol



Step I: To a stirred solution of 6-((2S,3S,4R,5R,6R)-3,4,5-Tris-benzyloxy-6-benzyloxymethyl-tetrahydro-pyran-2-yl)-chroman-4-one (300 mg, 0.45 mmol) in THF (2 ml) and methanol (5 ml) was added 4-ethylbenzaldehyde (66 mg, 0.49 mmol) followed by pyrrolidine (95 mg, 1.34 mmol) and stirred for 16h. Concentrated on rotavap then usual work up resulted in crude compound which was taken for hydrogenation step using the procedure described for above example to furnish the title compound (93 mg).

¹H NMR (400 MHz, CD₃OD) : (peaks correspond to major isomer) δ 1.20 (t, J = 7.28 Hz, 3H); 2.18-2.28 (m, 1H); 2.53-2.80 (m, 5H), 3.12-3.29 (m, 4H); 3.41-3.48 (m, 2H), 3.67-3.81 (m, 2H); 3.90 (d, J = 9.3 Hz, 1H); 4.12 (d, J = 10.4 Hz, 1H); 4.27-4.47 (m, 1H); 4.70 (d, J = 5.5 Hz, 1H); 4.92 (d, J = 4.4 Hz, 2H); 6.69 (d, J = 8.2 Hz, 1H); 7.00-7.04 (m, 2H); 7.17 (bs, 4H). MS (EI) *m/z* 432.4 (M+18)



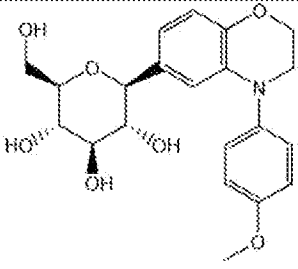
^1H NMR (400 MHz, CD_3OD) : (peaks correspond to major isomer) δ 2.33 (s, 3H); 2.70-2.75 (m, 1H); 2.81-2.97 (m, 1H); 3.15-3.18 (m, 1H); 3.43-3.50 (m, 4H); 3.72-3.75 (d, J = 11.9 Hz, 1H); 3.91 (d, J = 11.7 Hz, 1H); 4.16-4.21 (m, 2H); 4.36-4.40 (m, 1H); 7.00 (d, J = 8.6 Hz, 1H); 7.15 (bs, 4H); 7.63 (d, J = 8.4 Hz, 1H); 7.94 (s, 1H). MS (ES) m/z 432.4 (M+18)

Following examples were prepared using an analogous procedure as described in example 1.

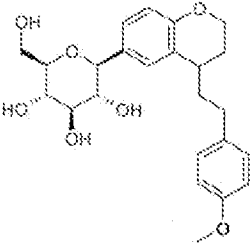
Example 109	(2S,3R,4R,5S,6R)-2-[4-(3-Ethylbenzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	415.9 (M+1)	^1H NMR (400 MHz, CD_3OD): δ 1.31 (t, J = 7.6 Hz, 3H), 2.72 (q, J = 7.2 Hz, 2H), 3.50-3.69 (m, 3H), 3.77 (dd, J = 12.0, 3.6 Hz, 1H), 3.87 (d, J = 10.4 Hz, 1H), 4.25-4.28 (m, 2H), 4.45 (s, 2H), 4.59 (s, 2H), 4.68 (d, J = 9.6 Hz, 2H), 6.62-6.64 (m, 1H), 6.74 (d, J = 4.8 Hz, 2H), 7.09 (t, J = 8.0 Hz, 2H), 7.14 (s, 1H), 7.21 (t, J = 7.6 Hz, 1H).
Example 110		431.9 (M+1)	^1H NMR (400 MHz, CD_3OD): δ 1.36 (t, J = 7.0 Hz, 3H), 3.25 (m, 2H), 3.65-3.70 (m, 1H), 3.86 (dd, J = 11.2, 2.8 Hz, 1H), 3.94-4.02 (m, 3H), 4.11 (dd, J = 8, 3.2 Hz, 1H), 4.21-4.23 (m,

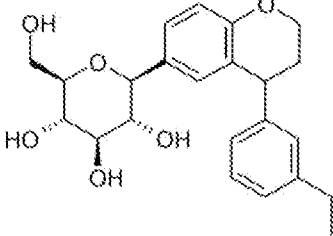
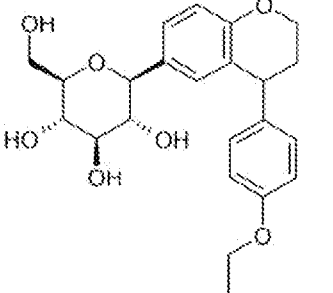
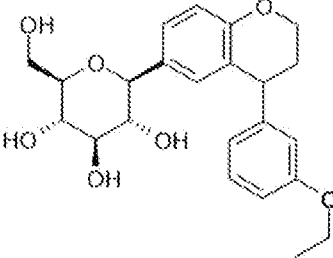
	(2S,3R,4R,5S,6R)-2-[4-(4-Ethoxyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	1H), 4.26-4.32 (m, 3H), 4.36 (s, 2H), 5.43(d, J = 3.2 Hz, 1H), 6.65-6.73 (m, 2H), 6.81-6.83 (m, J = 8.4 Hz, 3H), 7.21(d, J = 8 Hz, 2H).
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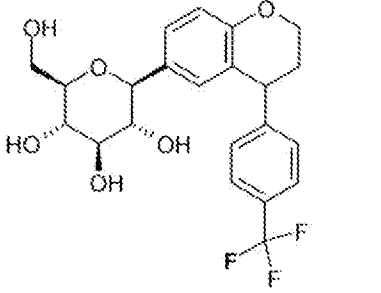
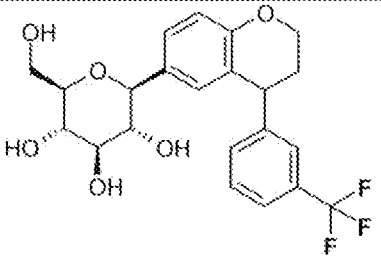
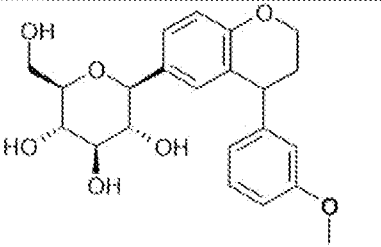
Following example was prepared using an analogous procedure as described in example 59.

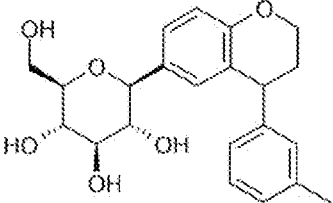
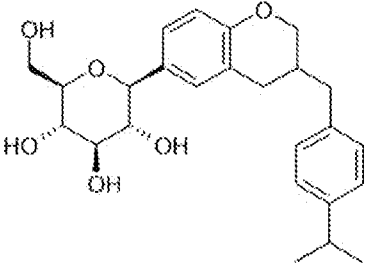
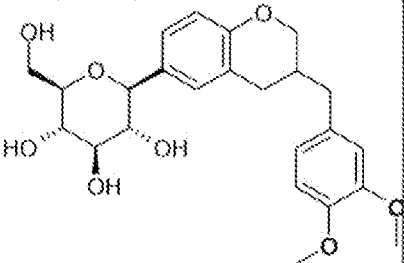
Example 111	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methoxy-phenyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol	404.2 (M+1) ¹ H NMR (400 MHz, CD ₃ OD): δ 3.24-3.35 (m, 5H), 3.59-3.62 (m, 3H), 3.79 (s, 3H), 3.84-4.25 (m, 3H), 6.68 (s, 1H), 6.73-6.77 (m, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 8.8 Hz, 2H).
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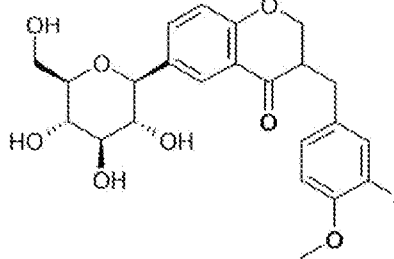
Following examples were prepared in an analogous procedure as described in example 101.

Example 112	 (2R,3S,4R,5R,6S)-2-	448.3(M+18) ¹ H NMR (400 MHz, CD ₃ OD): δ 1.78-1.88 (m, 2H); 1.91-2.06 (m, 2H); 2.60-2.65 (m, 1H); 2.69-2.72 (m, 2H); 3.30-3.44 (m, 4H); 3.64-3.67 (m, 1H); 3.74 (s, 3H); 3.85 (d, J = 12.0 Hz, 1H); 4.01
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	Hydroxymethyl-6-{4-[2-(4-methoxy-phenyl)-ethyl]-chroman-6-yl}-tetrahydro-pyran-3,4,5-triol		(d, J = 9.2 Hz, 1H); 4.09-4.20 (m, 2H); 6.68-6.70 (m, 1H); 6.81-6.84 (m, 2H); 7.08-7.15 (m, 4H).
Example 113	 (2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	418.2 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 1.17 (t, J = 7.6 Hz, 3H); 1.98-2.04 (m, 1H); 2.22-2.26 (m, 1H); 2.57 (q, J = 7.6 Hz, 2H); 3.20-3.36 (m, 4H); 3.57-3.59 (m, 1H); 3.78-3.81 (m, 1H); 3.93 (d, J = 9.2 Hz, 1H); 4.11-4.17 (m, 3H); 6.77-6.83 (m, 1H); 6.87-6.91 (m, 2H); 6.97-7.03 (m, 2H); 7.14-7.18 (m, 2H).
Example 114	 (2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	434.3 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 1.38 (t, J = 7.6 Hz, 3H); 2.01-2.05 (m, 1H); 2.23-2.26 (m, 1H); 3.23-3.41 (m, 4H); 3.61-3.65 (m, 1H); 3.83-3.86 (m, 1H); 3.95-4.05 (m, 3H); 4.13-4.15 (m, 3H); 6.79-6.90 (m, 4H); 7.04-7.06 (m, 2H); 7.17-7.21 (m, 1H).
Example 115	 (2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-	434.0 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 1.36 (t, J = 7.6 Hz, 3H); 2.03-2.08 (m, 1H); 2.25-2.30 (m, 1H); 3.23-3.43 (m, 4H); 3.62-3.68 (m, 1H); 3.82-3.87 (m, 1H); 3.94-4.02 (m, 3H); 4.15-4.19 (m, 3H); 6.67-6.93 (m, 5H); 7.17-7.20 (m, 2H).

	pyran-3,4,5-triol		
Example 116  (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethyl-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol		458.3 (M+18)	¹H NMR (400 MHz, CD₃OD): δ 2.06-2.09 (m, 1H), 2.33-2.36 (m, 1H); 3.23-3.41 (m, 4H), 3.62-3.65 (m, 1H), 3.83 (d, J = 12.0 Hz, 1H); 3.95-3.98 (m, 1H); 4.10-4.19 (m, 2H); 4.21-4.35 (m, 1H), 6.85-6.87 (m, 2H); 7.22-26 (m, 1H); 7.37 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H).
Example 117  (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol		458.3 (M+18)	¹H NMR (400 MHz, CD₃OD): δ 2.06-2.09 (m, 1H), 2.32-2.34 (m, 1H); 3.23-3.41 (m, 4H), 3.61-3.65 (m, 1H), 3.83-3.85 (m, 1H), 3.94-3.99 (m, 1H); 4.13-4.19 (m, 2H); 4.35-4.36 (m, 1H), 6.85-6.87 (m, 2H); 7.24 (d, J = 8.4 Hz, 1H); 7.39-7.41 (m, 1H), 7.51-7.55 (m, 3H).
Example 118  (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol		420.2 (M+18)	¹H NMR (400 MHz, CD₃OD): δ 2.04-2.10 (m, 1H), 2.25-2.34 (m, 1H); 3.23-3.44 (m, 4H), 3.62-3.68 (m, 1H), 3.75 (s, 3H), 3.82-3.86 (m, 1H); 3.94-3.99 (m, 1H), 4.15-4.21 (m, 3H); 6.70-6.92 (m, 4H); 7.16-7.24 (m, 3H).

Example 119	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-(4-m-tolyl-chroman-6-yl)-tetrahydro-pyran-3,4,5-triol	404.2 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 2.00-2.08 (m, 1H), 2.20-2.25 (m, 1H); 2.27 (s, 3H), 3.2-3.33 (m, 4H), 3.57-3.63 (m, 1H), 3.79-3.81 (m, 1H); 3.89-3.95 (m, 1H), 4.08-4.18 (m, 3H); 6.78-7.00 (m, 5H); 7.12-7.18 (m, 2H).
Example 120	 (2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[3-(4-isopropyl-benzyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol	446.4 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 1.25 (d, J = 6.6 Hz, 6H); 2.20-2.28 (m, 1H), 2.41-2.75 (m, 3H); 2.76-2.88 (m, 2H), 3.23-3.42 (m, 4H); 3.61-3.72 (m, 1H); 3.75-3.91 (m, 2H); 3.90-4.21 (m, 2H); 6.68 (d, J = 8.1 Hz, 1H); 7.08-7.24 (m, 6H)
Example 121	 (2S,3R,4R,5S,6R)-2-[3-(3,4-Dimethoxy-benzyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol	464.2 (M+18)	¹ H NMR (400 MHz, CD ₃ OD): δ 2.18-2.28 (m, 1H), 2.43-2.73 (m, 3H); 2.78-2.84 (m, 1H), 3.34-3.43 (m, 5H); 3.62-3.70 (m, 1H); 3.75-3.85 (m, 7H); 3.96-4.07 (m, 1H); 4.12-4.18 (m, 1H), 6.64-6.90 (m, 4H); 7.05-7.18 (m, 2H)

Example 122	 3-(3,4-Dimethoxy-benzyl)-6- ((2S,3R,4R,5S,6R)-3,4,5- trihydroxy-6-hydroxymethyl- tetrahydro-pyran-2-yl)- chroman-4-one	478.4 (M+18)	¹ H NMR (400 MHz, CD ₃ OD) : δ 2.62-2.73 (m, 1H), 2.85-2.93 (m, 1H); 3.11-3.18 (m, 1H), 3.21- 3.46 (m, 4H); 3.68-3.74 (m, 1H); 3.80-3.96 (m, 7H); 4.15-4.22 (m, 2H); 4.36-4.42 (m, 1H), 6.70- 6.98 (m, 4H); 7.58-7.62 (m, 1H), 7.92 (s, 1H)
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The below list of examples, but not limited to these, can also be synthesized following the general synthesis described herein above:

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(2,3-Dihydro-benzofuran-6-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(2,3-Dihydro-benzofuran-5-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(1-Ethyl-2,3-dihydro-1H-indol-5-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-Chroman-7-yl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Dimethylamino-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-[4-(tetrahydro-furan-3-yloxy)-benzyl]-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-7-hydroxymethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(5-Ethyl-pyridin-2-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-5-methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[2-(3-Ethyl-benzyl)-2,3-dihydro-1H-isoindol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[2-(3-Ethyl-phenyl)-6-hydroxymethyl-2,3-dihydro-1H-isoindol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3,4-Dimethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3,5-Diethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-5-methoxy-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-4-fluoro-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethoxy-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(2-methyl-2,3-dihydro-1H-isoindol-5-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(5-Ethyl-thiophen-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-tetrahydro-pyran-3,4,5-triol.

1-{6-[5-((2S,3R,4R,5S,6R)-3,4,5-Trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yl)-2,3-dihydro-indol-1-ylmethyl]-2,3-dihydro-benzo[1,4]oxazin-4-yl}-ethanone.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-phenyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Chloro-4-fluoro-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(5-methyl-pyridin-2-ylmethyl)-2,3-dihydro-1H-indol-5-yl]-tetrahydro-pyran-3,4,5-triol. (2S,3R,4R,5S,6R)-2-(1-Cyclohexylmethyl-2,3-dihydro-1H-indol-5-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1,4-Bis-(4-ethyl-benzyl)-1,2,3,4-tetrahydro-quinoxalin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-2,3,4,5-tetrahydro-1H-benzo[b]azepin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[9-(3-Ethyl-benzyl)-6,7,8,9-tetrahydro-5-oxa-9-aza-benzocyclohepten-3-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[9-(4-Ethyl-phenyl)-6,7,8,9-tetrahydro-5-oxa-9-aza-benzocyclohepten-3-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-(1-Benzo[b]thiophen-2-ylmethyl-2,3-dihydro-1H-indol-5-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-phenyl)-chroman-7-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-chroman-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenoxy)-chroman-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[3-(3-Ethyl-benzyl)-chroman-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[2-(3-Ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(5-Ethyl-furan-2-ylmethyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-[2-(3-methoxy-phenyl)-ethyl]-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-5-ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[8-(3-Ethyl-phenyl)-5,6,7,8-tetrahydro-naphthalen-2-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[3-(3-Ethyl-benzyl)-2,3-dihydro-benzofuran-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[3-(3-Ethyl-phenyl)-2,3-dihydro-benzofuran-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenyl)-3-methyl-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-benzyl)-indan-5-yl]-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-methyl-benzyl)-indan-5-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-4-fluoro-benzyl)-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-ylmethyl)-indan-5-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[2-(3-Ethyl-phenyl)-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(2-methyl-2,3-dihydro-1H-isoindol-5-ylmethyl)-indan-5-yl]-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-(5-Ethyl-thiophen-2-ylmethyl)-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[1-[1-(3-Ethyl-phenyl)-ethyl]-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[3-(3-Fluoro-4-methyl-benzyl)-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6R)-2-[3-(2,3-Dihydro-benzofuran-5-ylmethyl)-indan-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5S,6S)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-fluoromethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4R,5R,6R)-2-[1-(4-Ethyl-phenyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol.

(2S,3R,4S,5S,6R)-2-[1-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-methyl-tetrahydro-pyran-3,4,5-triol.

The inhibitory effect on the sodium-dependent glucose cotransporter SGLT, SGLT1 and SGLT2, of compounds of formula I may be demonstrated using the following test procedures

The ability of the substances to inhibit the SGLT-2 activity may be demonstrated in a test set-up in which a CHO-K1 cell line (ATCC No. CCL 6 1) or alternatively an HEK293 cell line (ATCC No. CRL-1573), which is stably transfected with an expression vector pZeoSV (Invitrogen, EMBL accession number L36849), which contains the cDNA for the coding sequence of the human sodium glucose cotransporter 2 (Genbank Acc. No. NM_003041) (CHO-hSGLT2 or HEK-hSGLT2). These cell lines transport 14 C-labelled alpha-methyl-glucopyranoside (14 C-AMG, Amersham) into the interior of the cell in sodium-dependent manner.

The SGLT-2 assay is carried out as follows: CHO-hSGLT2 cells are cultivated in Ham 's F12 Medium (BioWhittaker) with 10% foetal calf serum and 250 µg/mL zeocin (Invitrogen), and HEK293-hSGLT2 cells are cultivated in DMEM medium with 10% foetal calf serum and 250 µg/mL zeocin (Invitrogen). The cells are detached from the culture flasks by washing twice with PBS and subsequently treating with trypsin/EDTA. After the addition of cell culture medium the cells are centrifuged, resuspended in culture medium and counted in a Casy cell counter. Then 40,000 cells per well are seeded into a white, 96-well plate coated with poly-D-lysine and incubated overnight at 37°C, 5% CO₂. The cells are washed twice with 250 µl of assay buffer (Hanks Balanced Salt Solution, 137 mM NaCl, 5.4 mM KCl, 2.8 mM CaCl₂, 1.2 mM MgSO₄ and 10 mM HEPES (pH 7.4), 50 µg/mL of gentamycin). 250 µl of assay buffer and 5 µl of test compound are then added to each well and the plate is incubated for a further 15 minutes in the incubator. 5

μl of 10% DMSO are used as the negative control. The reaction is started by adding 5 μl of 14 C- AMG (0.05 μCi) to each well. After 2 hours' incubation at 37°C, 5% CO₂, the cells are washed again with 250 μl of PBS (200C) and then lysed by the addition of 25 μl of 0.1 N NaOH (5 min. at 37°C). 200 μl of MicroScint20 (Packard) are added to each well and incubation is continued for a further 20 min at 37°C. After this incubation the radioactivity of the 14 C-AMG absorbed is measured in a Topcount (Packard) using a 14 C scintillation program.

To determine the selectivity with respect to human SGLT1 an analogous test is set up in which the cDNA for hSGLT1 (Genbank Acc. No. NM000343) instead of hSGLT2 cDNA is expressed in CHO-K1 or HEK293 cells.

The compounds according to the invention may for example have EC₅₀ values below 1000 nM, particularly below 100 nM, most preferably below 10 nM. The title compounds of the above Examples were evaluated in the above described assay and the results of which are collated in Table 1.

TABLE 1

Example Number	SGLT2 IC ₅₀ nM (n = 1-4)
1	66
4	110
17	56
63	90
64	309
99	13
102	76
103	117
105	21
106	33

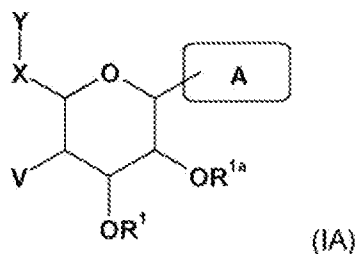
It can be seen that the compounds of the invention are useful as inhibitors of SGLT and therefore useful in the treatment of diseases and conditions mediated by SGLT such as the metabolic disorders disclosed herein.

It will be understood that the invention has been described by way of example only and modifications may be made whilst remaining within the scope and spirit of the invention.

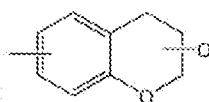
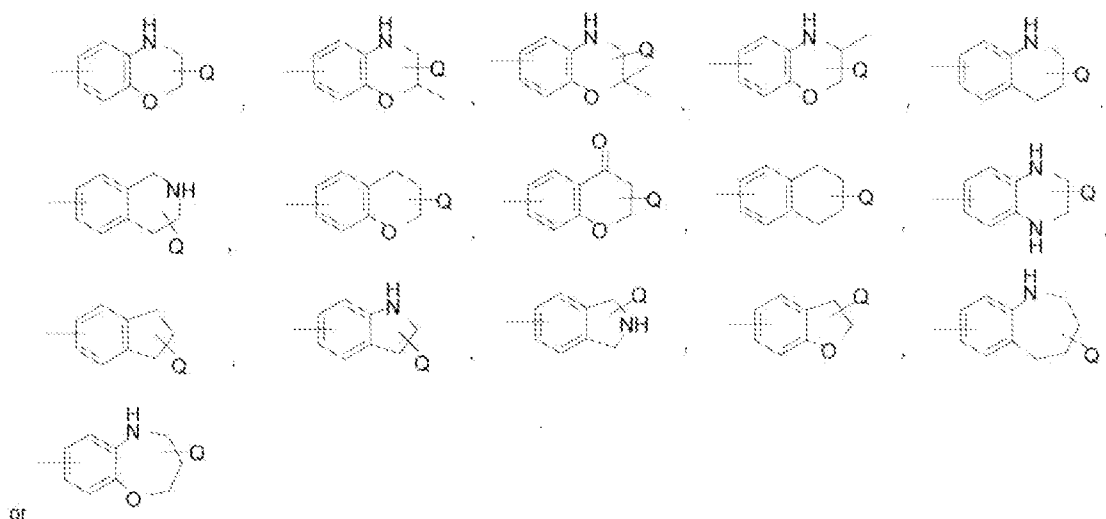
CLAIMS

We Claim:

1. A compound represented by Formula (IA):



wherein A is selected from:



provided that when A is , it is not substituted with hydroxy or methoxy;

Q is L_a-X_a or R^{10} ;

L_a is $-Z'-Y'-Z''-$;

Z' and Z'' are each, independently, a bond, C_{1-4} alkylene or C_{2-4} alkenylene,

where Z' and Z'' together make no more than a 4-carbon chain and the hydrocarbon bonds may be optionally substituted by one or more hydroxy or halogens.

Y' is $-O-$, $-S(O)_p-$, $-N(R^3)-$, $-C(R^1)(R^2)-$, $-C(O)-$, $-C(O)NR^3-$, $-NR^3C(O)-$, $-N(R^3)C(O)N(R^3)-$, $-N(R^3)SO_2-$, or $-SO_2N(R^3)-$;

V is halogen, $-OR^{1b}$ or hydrogen;

$m = 0-4$;

$n = 0-4$;

$p = 0-2$;

R' and R'' are independently, hydrogen, halogen, C_{1-6} alkyl, perhaloalkyl, or taken together form a cyclic ring which may optionally have heteroatoms selected from O, N or S;

R^1 , R^{1a} and R^{1b} are independently selected from hydrogen, C_{1-6} alkyl, C_{6-10} aryl- C_{1-4} alkyl, $-C(O)C_{6-10}$ aryl or $-C(O)C_{1-6}$ alkyl;

R^2 and R^{2a} are independently halogen, hydroxy, C_{1-4} hydroxyalkyl, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{1-4} alkoxy, C_{3-7} cycloalkoxy, $-S(O)_pR^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{3-7} cycloalkyl, C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl- C_{1-4} alkyl, C_{6-10} aryloxy, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl- C_{1-4} alkyl, C_{1-10} heteroaryl- C_{1-4} alkyl, C_{1-10} heteroaryl, C_{1-10} heteroaryloxy, or C_{1-10} heterocycloxy;

R^3 is hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{6-10} aryl, C_{1-10} heteroaryl, or C_{2-10} heterocyclyl;

$q = 0-3$;

X is $[C(R^6)(R^7)]_i$;

Y is H, C_{1-4} alkyl, OR^1 or NR^5R^9

$t = 1-3$;

R^6 and R^7 are independently hydrogen or C_{1-6} alkyl, or R^6 and R^7 form an oxo group and $t=1$, or when R^6 and R^7 are C_{1-4} alkyl on the same carbon they can be taken together to form a cyclic ring which may contain N, S or O atoms;

R^4 and R^5 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-4} alkyl, aryl- C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl- C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl- C_{1-4} alkyl or

R^4 and R^5 taken together may form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N or S, the said ring system may further be optionally substituted; and

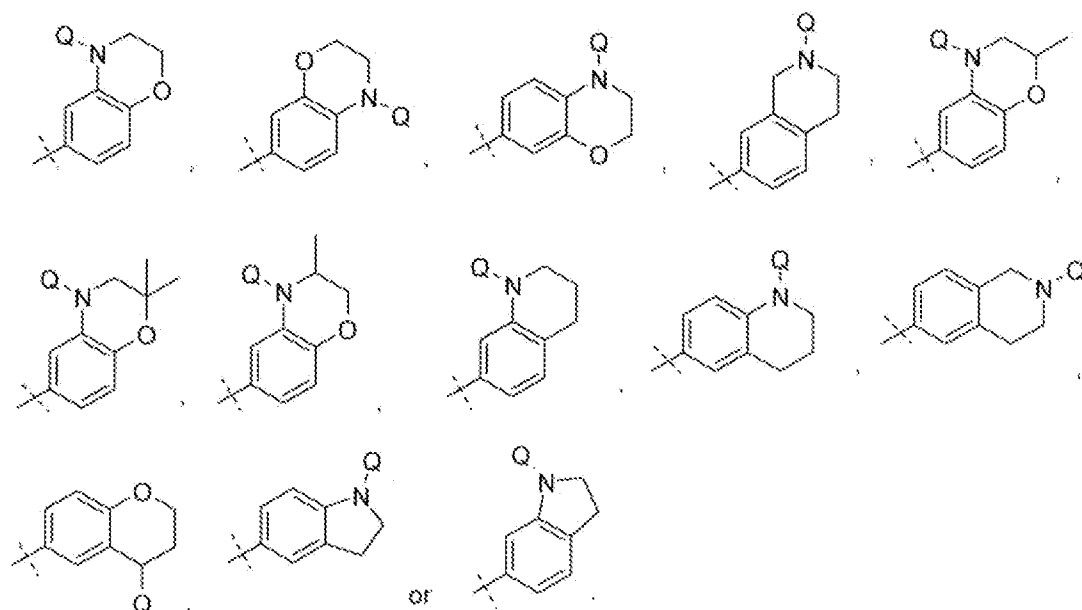
R^8 and R^9 are independently hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl- C_{1-4} alkyl, aryl- C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{1-10} heteroaryl- C_{1-4} alkyl, C_{2-10} heterocyclyl, C_{2-10} heterocyclyl- C_{1-4} alkyl or

R^5 and R^9 along with the nitrogen to which they are bound form a monocyclic or a bicyclic ring system which may be saturated, partially saturated or aromatic and may optionally have additional heteroatoms selected from O, N and S, the said ring system may further be optionally substituted;

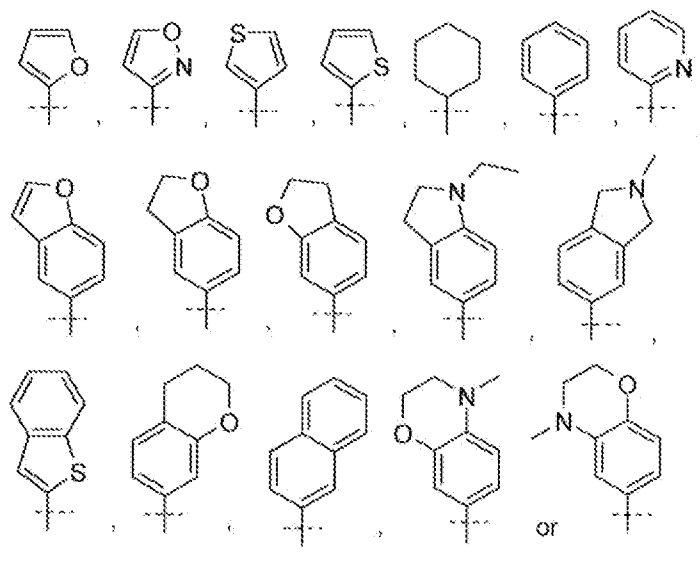
R^{10} is C_{1-4} alkyl, C_{6-10} aryl, C_{1-10} heteroaryl, C_{3-7} cycloalkyl, C_{2-10} heterocyclyl, where C_{1-4} alkyl may be optionally substituted by one or more hydroxy or halogens and C_{6-10} aryl may be optionally substituted with one or more C_{1-4} alkyl, C_{1-4} alkoxy, or C_{1-4} haloalkyl; and

X_9 is halogen, hydroxy, cyano, nitro, $-NR^4R^5$, $-CH_2NR^4R^5$, C_{1-4} alkyl, C_{1-4} hydroxylalkyl, C_{1-6} haloalkyl, C_{1-6} perhaloalkyl, C_{1-4} alkoxy, trihalo C_{1-4} alkoxy, an optionally substituted C_{3-7} cycloalkoxy, $-C(O)R^3$, $-C(O)OR^3$, $-CH_2C(O)OR^3$, $-C(O)NR^4R^5$, $-CH_2C(O)NR^4R^5$, $-NR^3C(O)NR^4R^5$, $-NR^3C(O)OR^3$, $-S(O)_2R^3$, $-S(O)_2NR^4R^5$, $-OS(O)_2R^3$, an optionally substituted C_{3-7} cycloalkyl, an optionally substituted C_{3-7} cycloalkyl C_{1-4} alkyl, an optionally substituted C_{6-10} aryl, an optionally substituted C_{6-10} aryl C_{1-4} alkyl, an optionally substituted C_{6-10} aryloxy, an optionally substituted C_{2-10} heterocyclyl, an optionally substituted C_{2-10} heterocyclyl C_{1-4} alkyl, an optionally substituted C_{1-10} heteroaryl, an optionally substituted C_{1-10} heteroaryl C_{1-4} alkyl, an optionally substituted C_{1-10} heteroaryloxy, or an optionally substituted C_{1-10} heterocycloxy; or a pharmaceutically acceptable salt thereof.

2. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein A is



3. The compound according to Claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein Q is L_8-X_8 , wherein L_8 is a C_{1-4} alkylene.
4. The compound according to any one Claims 1-3, or a pharmaceutically acceptable salt thereof, wherein X_8 is



each of which may be optionally substituted with one or more substituent which are independently selected from halogen, hydroxyl, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkoxyl, C_{1-4} alkoxy, C_{2-4} alkenyl, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, $-C(O)-C_{1-4}$ alkyl, $-C(O)-N-C_{1-4}$ alkyl, $-C(O)-N-di-C_{1-4}$ alkyl, $-S-C_{1-4}$ alkyl, SO_2-C_{1-4} alkyl, trihalo C_{1-4} alkoxy, $-O-C_{3-7}$ cycloalkyl and $-O-C_{3-7}$ cycloalkoxyl.

5. The compound according to any one Claims 1-3, or a pharmaceutically acceptable salt thereof, wherein X_8 is an C_{6-10} aryl which is optionally substituted with one or more substituent which are independently selected from halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ and $-C(O)-C_{1-4}$ alkyl.
6. The compound according to Claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein Q is R^{10} .

7. The compound according to Claim 6, or a pharmaceutically acceptable salt thereof, wherein R^{10} is methyl, ethyl, isopropyl, isobutyl, trifluoromethyl or cyclopentyl.

8. The compound according to any one of Claims 1-7, or a pharmaceutically acceptable salt thereof, wherein

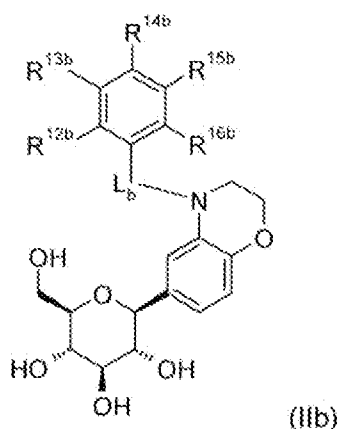
X is $-\text{CH}_2-$;

Y is OR^1 ;

V is OR^1 ; and

R^1 , R^{1a} and R^{1b} are hydrogen.

9. The compound according to Claim 1, wherein the compound is of formula (IIb):



wherein

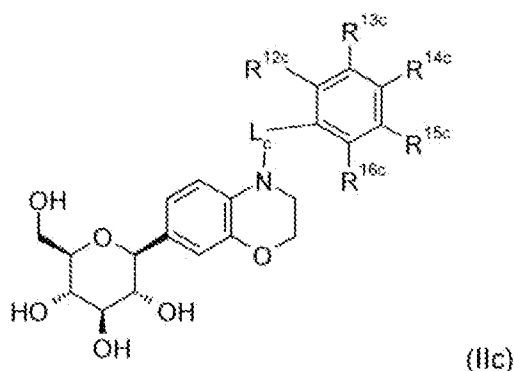
L_b is a bond or an optionally substituted C_{1-4} alkylene;

R^{12b} , R^{13b} , R^{14b} , R^{15b} and R^{16b} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-\text{O}-\text{C}_{3-7}$ cycloalkyl, $-\text{S}-\text{C}_{1-4}$ alkyl, $-\text{SO}_2-\text{C}_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-\text{CH}_2\text{NR}^4\text{R}^5$ or $-\text{C}(\text{O})-\text{C}_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

10. The compound according to Claim 9, or a pharmaceutically acceptable salt thereof, wherein L_b is methylene; R^{11b} , R^{12b} , R^{13b} , R^{15b} and R^{16b} are each hydrogen; and R^{14b} is C_{1-4} alkyl.

11. The compound according to Claim 1, wherein the compound is of formula (IIc):



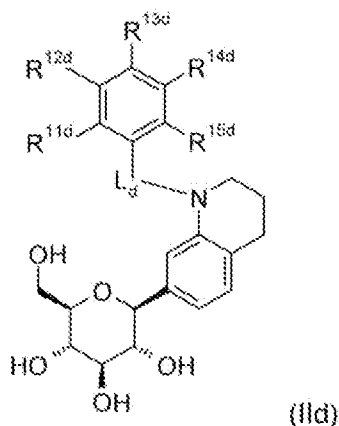
wherein

L_c is a bond or an optionally substituted C_{1-4} alkylene;

R^{12c} , R^{13c} , R^{14c} , R^{15c} and R^{16c} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

12. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of formula (IId):



wherein

L_d is a bond or an optionally substituted C_{1-4} alkylene;

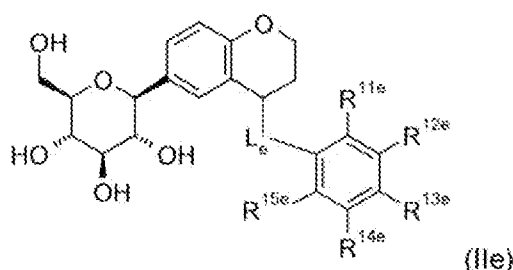
R^{11d} , R^{12d} , R^{13d} , R^{14d} and R^{15d} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

13. The compound according to Claim 12, or a pharmaceutically acceptable salt thereof, wherein L_d is methylene; R^{11d} , R^{12d} , R^{14d} and R^{15d} are each hydrogen; and R^{13d} is C_{1-4} alkyl.

14. The compound according to Claim 12, or a pharmaceutically acceptable salt thereof, wherein L_d is ethylene; R^{11d} , R^{12d} , R^{14d} and R^{15d} are each hydrogen; and R^{13d} is C_{1-4} alkoxy.

15. The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is of formula (IIe):



wherein

L_e is a bond or an optionally substituted C_{1-4} alkylene;

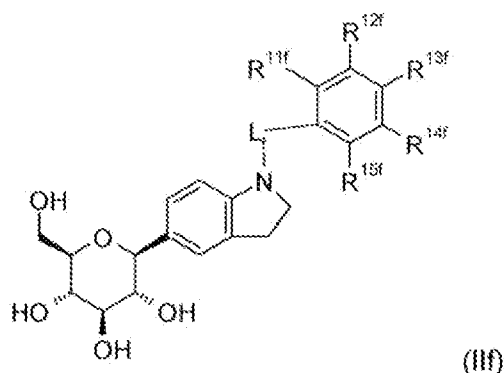
R^{11e} , R^{12e} , R^{13e} , R^{14e} and R^{15e} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro, NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

16. The compound according to Claim 15, or a pharmaceutically acceptable salt thereof, wherein L_e is a bond; R^{11e} , R^{12e} , R^{14e} and R^{15e} are hydrogen; and R^{13e} is C_{1-4} alkyl or C_{1-4} alkoxy.

17. The compound according to claim 15, wherein L_e is methylene; R^{11e} , R^{12e} , R^{14e} and R^{15e} are hydrogen; and R^{13e} is C_{1-4} alkyl or C_{1-4} alkoxy.

18. The compound according to Claim 1, wherein the compound is of formula (IIIf):



wherein

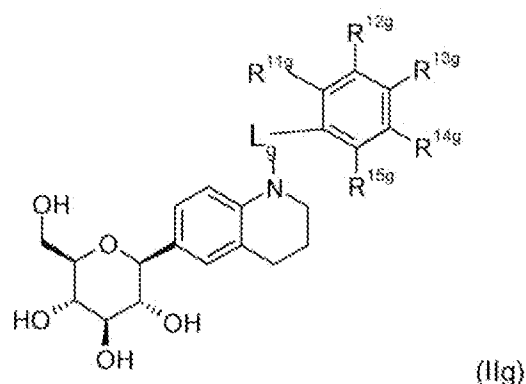
L_f is a bond or an optionally substituted C_{1-4} alkylene;

R^{11f} , R^{12f} , R^{13f} , R^{14f} and R^{15f} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

19. The compound according to claim 18, or a pharmaceutically acceptable salt thereof, wherein L_f is a bond; R^{11f} , R^{12f} , R^{14f} and R^{15f} are hydrogen; and R^{13f} is C_{1-4} alkyl.

20. The compound according to Claim 1, wherein the compound is of formula (IIg):



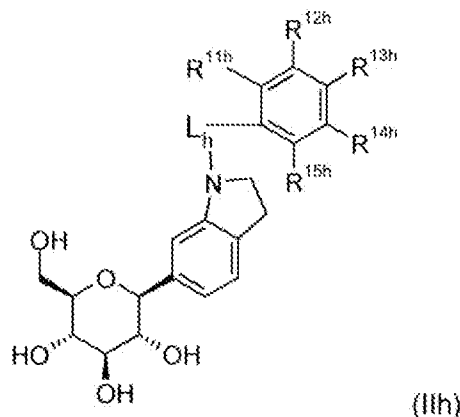
wherein

L_g is a bond or an optionally substituted C_{1-4} alkylene;

R^{11g} , R^{12g} , R^{13g} , R^{14g} and R^{15g} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

21. The compound according to Claim 1, wherein the compound is of formula (IIh):



wherein

L_h is a bond or an optionally substituted C_{1-4} alkylene;

R^{11h} , R^{12h} , R^{13h} , R^{14h} and R^{15h} are each, independently, hydrogen, halogen, C_{1-4} alkyl, C_{1-4} alkoxy, C_{3-7} cycloalkyl, $-O-C_{3-7}$ cycloalkyl, $-S-C_{1-4}$ alkyl, $-SO_2-C_{1-4}$ alkyl, trihalo C_{1-4} alkyl, trihalo C_{1-4} alkoxy, C_{6-10} aryl, C_{1-10} heteroaryl, cyano, nitro NR^4R^5 , $-CH_2NR^4R^5$ or $-C(O)-C_{1-4}$ alkyl; or

a pharmaceutically acceptable salt thereof.

22. The compound according to Claim 1, wherein the compound is selected from the group consisting of:

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[4-(3,4-Dichloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-methylsulfanyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(2,4-Dichloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(2-Chloro-5-fluoro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Biphenyl-4-ylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-2,2-dimethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-benzyl)-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropylbenzyl)-2-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-(4-Ethyl-3-methyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4S,5S,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-methyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-(4-naphthalen-2-ylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methanesulfonyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(5-Chloro-thiophen-2-ylmethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Benzyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(2-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Benzofuran-5-ylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Ethyl-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(1-p-tolyl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-[1-(4-Ethyl-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Chloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-tert-Butyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

4-[6-((2S,3R,4R,5S,6R)-3,4,5-Trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yl)-2,3-dihydro-benzo[1,4]oxazin-4-ylmethyl]-benzonitrile;

(2S,4R,6R)-2-(4-Benzyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,4R,6R)-2-[4-(4-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,4R,6S)-2-Hydroxymethyl-6-[4-(4-isopropyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,4R,6R)-2-[4-(4-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,4R,6S)-2-Hydroxymethyl-6-[4-(4-methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,4R,6R)-2-[4-(3-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(2-trifluoromethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Benzofuran-5-ylmethyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(4-Ethyl-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Chloro-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,4R,6S)-2-Hydroxymethyl-6-[4-(1-p-tolyl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,4R,6R)-2-[4-[2-(4-Ethoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(4-isopropoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[4-(4-Cyclopentyloxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-[2-(4-methoxy-phenyl)-ethyl]-3,4-dihydro-H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[4-[2-(4-Ethoxy-phenyl)-ethyl]-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[4-(2-thiophen-3-yl-ethyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[1-(2,4-Dichloro-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(2-Chloro-5-fluoro-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R)-2-Hydroxymethyl-6-[1-(3-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(3R,4R,5S,6R)-2-[2-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[2-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-isoquinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[2-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[2-(4-Ethoxy-benzyl)-1,2,3,4-tetrahydro-isoquinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(1-Benzyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(3-Ethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-trifluoromethoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-methyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(3-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(2-trifluoromethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(1-Benzofuran-5-ylmethyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-(1-Ethyl-1,2,3,4-tetrahydro-quinolin-7-yl)-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(3-Chloro-benzyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-[2-(4-methoxy-phenyl)-ethyl]-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-[2-(4-Ethoxy-phenyl)-ethyl]-1,2,3,4-tetrahydro-quinolin-7-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(5-methyl-isoxazol-3-ylmethyl)-1,2,3,4-tetrahydro-quinolin-7-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methoxy-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-1,2,3,4-tetrahydro-quinolin-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-isopropyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(3-Ethyl-benzyl)-2,3-dihydro-1H-indol-5-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[1-(4-methyl-benzyl)-2,3-dihydro-1H-indol-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Methoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[1-(4-Ethoxy-benzyl)-2,3-dihydro-1H-indol-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-benzyl-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-[(4-ethylphenyl)methyl]chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-[4-[(4-methoxyphenyl)methyl]chroman-6-yl]tetrahydropyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-[4-[(4-isopropylphenyl)methyl]chroman-6-yl]tetrahydropyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-[4-(4-methoxyphenyl)chroman-6-yl]tetrahydropyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-ethylphenyl)chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-(hydroxymethyl)-6-(4-phenylchroman-6-yl)tetrahydropyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[3-[(4-ethylphenyl)methyl]chroman-6-yl]-6-(hydroxymethyl)tetrahydropyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-benzyl)-3,4-dihydro-2H-benzo[1,4]oxazin-8-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-methoxy-phenyl)-3,4-dihydro-2H-benzo[1,4]oxazin-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-[2-(4-methoxy-phenyl)-ethyl]-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethyl-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(4-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[4-(3-Ethoxy-phenyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(4-trifluoromethyl-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-trifluoromethyl-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[4-(3-methoxy-phenyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-(4-m-tolyl-chroman-6-yl)-tetrahydro-pyran-3,4,5-triol;

(2R,3S,4R,5R,6S)-2-Hydroxymethyl-6-[3-(4-isopropyl-benzyl)-chroman-6-yl]-tetrahydro-pyran-3,4,5-triol;

(2S,3R,4R,5S,6R)-2-[3-(3,4-Dimethoxy-benzyl)-chroman-6-yl]-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol;

3-(3,4-Dimethoxy-benzyl)-6-((2S,3R,4R,5S,6R)-3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yl)-chroman-4-one; or

a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition, comprising:

a compound according to any one of Claim 1-22, or a pharmaceutically acceptable salt thereof, and pharmaceutically acceptable carriers and excipients.

24. A method of treating a disease or condition related to the inhibition of SGLT, comprising:

administering an effective amount of the compound according to any one of Claim 1-22, or a pharmaceutically acceptable salt thereof.

25. The method of claim 24, wherein the disease or condition related to the inhibition of SGLT is metabolic disorders or conditions, metabolic acidosis or ketosis, reactive hypoglycaemia, hyperinsulinaemia, glucose metabolic disorder, insulin resistance, metabolic syndrome, dyslipidaemias of different origins, atherosclerosis, obesity, high blood pressure, chronic heart failure, edema or hyperuricaemia.

26. The method of Claim 24, wherein the disease or condition related to the inhibition of SGLT is pancreatic beta cell degeneration, hypertension, edema, or acute renal failure.

27. The method of Claim 24, wherein the disease or condition related to the inhibition of SGLT is type 1, type 2 diabetes mellitus or complications of diabetes.

28. A combination, comprising:

the compound according to any one of Claims 1-22, or a pharmaceutically acceptable salt thereof; and

one or more additional pharmacologically active compounds selected from antidiabetic agents; uric acid synthesis inhibitors; drugs for influencing high blood pressure, chronic heart failure or atherosclerosis; GABA-receptor antagonists; Na-channel blockers; topiramate; protein-kinase C inhibitors; advanced glycation end product inhibitors; and aldose reductase inhibitors.

29. A compound according to any one of Claims 1-22, or a pharmaceutically acceptable salt thereof, for use as a medicament.

30. A compound according to any one of Claims 1-22, or a pharmaceutically acceptable salt thereof, for use in the treatment of a disease or condition mediated by the inhibition of SGLT.

31. The compound of claim 30, wherein the disease or condition related to the inhibition of SGLT is metabolic disorders, metabolic acidosis or ketosis, reactive hypoglycaemia, hyperinsulinaemia, glucose metabolic disorder, insulin resistance, metabolic syndrome, dyslipidaemias of different origins, atherosclerosis, obesity, high blood pressure, chronic heart failure, edema or hyperuricaemia.
32. The compound of Claim 30, wherein the disease or condition related to the inhibition of SGLT is pancreatic beta cell degeneration, hypertension, edema, or acute renal failure.
33. The compound of Claim 30, wherein the disorder or diseases related to the inhibition of SGLT is type 1, type 2 diabetes mellitus or complications of diabetes.
34. A pharmaceutical composition according to Claim 23 for use as a medicament.

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/056286

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07H7/06 C07H7/04 A61K31/70 A61K31/7048 A61K31/7052
A61K31/7056 A61K31/706 A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BEILSTEIN Data, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 803 721 A1 (CHUGAI PHARMACEUTICAL CO LTD [JP]) 4 July 2007 (2007-07-04) cited in the application claim 2	1-17, 20, 22-34
Y	WO 2005/012318 A2 (JANSSEN PHARMACEUTICA NV [BE]; TANABE SEIYAKU CO [JP]; RYBCZYNSKI PHIL) 10 February 2005 (2005-02-10) claim 1	1-17, 20, 22-34
Y	EP 1 609 798 A1 (KISSEI PHARMACEUTICAL [JP]) 28 December 2005 (2005-12-28) page 66 - page 74	1-17, 20, 22-34
X, P	WO 2009/124638 A1 (MERCK PATENT GMBH, GERMANY) 15 October 2009 (2009-10-15) claims 1-7	1-8, 22-34 9-17, 20



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

11 June 2010

Date of mailing of the international search report

31/08/2010

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Mezzato, Stefano

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2010/056286

Box No. II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

9-17, 20(completely); 1-8, 22-34(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 9-17, 20(completely); 1-8, 22-34(partially)

compounds of formula (IA) of claim 1, wherein A is a benzo-fused 6-membered ring, corresponding to the first 10 A-rings of claim 1

2. claims: 18, 19, 21(completely); 1-8, 22-34(partially)

compounds of formula (IA) of claim 1, wherein A is a benzo-fused 5-membered ring, corresponding to A-rings 11-14 of claim 1

3. claims: 1, 3-8, 23-34(all partially)

compounds of formula (IA) of claim 1, wherein A is a benzo-fused 7-membered ring, corresponding to the last two A-rings of claim 1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2010/056286

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