used in combination, and even then may not provide adequate glycemic control or may produce undesired side effects. Such side effects include lactic acidosis (biguanides), hypoglycemia (sulfonylureas), and edema and weight gain (thiazolidinediones).

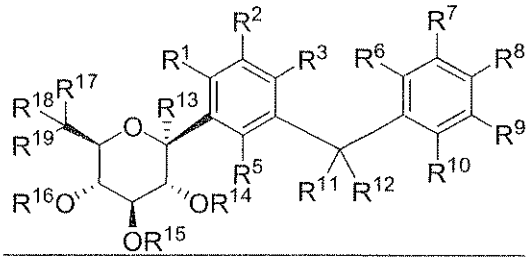
One promising target for therapeutic intervention in diabetes and related disorders is the glucose transport system of the kidneys. Cellular glucose transport is conducted by either facilitative ("passive") glucose transporters (GLUTs) or sodium-dependent ("active") glucose cotransporters (SGLTs). SGLT1 is found predominantly in the intestinal brush border, while SGLT2 is localized in the renal proximal tubule and is reportedly responsible for the majority of glucose reuptake by the kidneys. Recent studies suggest that inhibition of renal SGLT may be a useful approach to treating hyperglycemia by increasing the amount of glucose excreted in the urine (Arakawa et al., *Br J Pharmacol* 132:578-86, 2001; Oku et al., *Diabetes* 48:1794-1800, 1999). The potential of this therapeutic approach is further supported by recent findings that mutations in the SGLT2 gene occur in cases of familial renal glucosuria, an apparently benign syndrome characterized by urinary glucose excretion in the presence of normal serum glucose levels and the absence of general renal dysfunction or other disease (Santer et al., *J Am Soc Nephrol* 14:2873-82, 2003).

Therefore, compounds that inhibit SGLT, particularly SGLT2, are promising candidates for use as antidiabetic drugs and new antidiabetic agents providing improved glycemic control and lacking these adverse effects are highly desired.

SUMMARY OF THE INVENTION

The present ~~invention~~disclosure provides compositions that include compounds having an inhibitory effect on sodium-dependent glucose cotransporter SGLT. The ~~invention~~disclosure also provides pharmaceutical compositions and methods of using the compounds, independently or in combination with other therapeutic agents, for treating diseases and conditions which are affected by SGLT inhibition such as: type 1 diabetes mellitus, type 2 diabetes mellitus, hyperglycemia, diabetic complications, insulin resistance, metabolic syndrome (Syndrome X), hyperinsulinemia, hypertension, hyperuricemia, obesity, edema, dyslipidemia, chronic heart failure, and atherosclerosis.

In one aspect, the invention features a composition comprising a compound having the structure:



or any stereoisomer or tautomer thereof, or any pharmaceutically acceptable salt or solvate thereof, wherein

each R^{11}, R^{12}, R^{13}, R^{17}, and R^{18} is, independently, -H, -D, or halogen;

one of R^1, R^2, R^3 and R^5 represents hydrogen, deuterium, halo, cyano, nitro, amino, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl, C_1-C_6 alkoxy, C_3-C_{10} cycloalkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, C_5-C_7 cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, (C_2-C_4 alkenyl)C_1-C_3 alkoxy, (C_2-C_4 alkynyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkoxy, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkyl, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkoxy, (C_1-C_4 alkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkenyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkynyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkoxy, (C_1-C_4 alkylamino)C_1-C_3 alkyl, di-(C_1-C_3 alkylamino)C_1-C_3 alkyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkenyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkynyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkoxy, (C_3-C_7 cycloalkyl)C_2-C_5 alkenyl, (C_3-C_7 cycloalkyl)C_3-C_5 alkenyloxy, (C_3-C_7 cycloalkyl)C_3-C_5 alkynyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkenyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkynyloxy, C_3-C_6 cycloalkylidenmethyl, (C_1-C_4 alkyl)carbonyl, arylcarbonyl, heteroarylcarbonyl, aminocarbonyl, (C_1-C_4 alkyl)aminocarbonyl, di-(C_1-C_3 alkyl)aminocarbonyl, hydroxycarbonyl, (C_1-C_4 alkoxy)carbonyl, C_1-C_4 alkylamino, di-(C_1-C_3 alkyl)amino, (C_1-C_4 alkyl)carbonylamino, arylcarbonylamino, heteroarylcarbonylamino, C_1-C_4 alkylsulfonylamino, arylsulfonylamino, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_3-C_{10} cycloalkylthio, C_3-C_{10} cycloalkylsulfinyl, C_3-C_{10} cycloalkylsulfonyl, C_5-C_{10} cycloalkenylthio, C_5-C_{10} cycloalkenylsulfinyl, C_5-C_{10} cycloalkenylsulfonyl, arylthio, arylsulfinyl or arylsulfonyl;

two of the remaining groups R^1, R^2, R^3 and R^5 each independently represent hydrogen, deuterium, halo, cyano, nitro, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_1-C_3 alkoxy or C_3-C_{10} cycloalkoxy; and

one of the remaining groups R^1, R^2, R^3 and R^5 represents hydrogen or deuterium; one of the groups R^6, R^7, R^8, R^9 and R^{10} represents hydrogen, deuterium, halo, cyano, nitro, amino, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl, C_1-C_6 alkoxy, C_3-C_{10} cycloalkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, (C_1-C_3 alkoxy)C_3-C_7 cycloalkoxy, C_5-C_7 cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, (C_2-C_4 alkenyl)C_1-C_3 alkoxy, (C_2-C_4 alkynyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkoxy, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkyl, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkoxy, (C_1-C_4 alkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkenyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkynyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkoxy, (C_1-C_4 alkylamino)C_1-C_3 alkyl, di-(C_1-C_3 alkylamino)C_1-C_3 alkyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkenyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkynyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkoxy, (C_3-C_7 cycloalkyl)C_2-C_5 alkenyl, (C_3-C_7 cycloalkyl)C_3-C_5 alkenyloxy, (C_3-C_7 cycloalkyl)C_3-C_5 alkynyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkenyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkynyloxy, C_3-C_6 cycloalkylidenmethyl, (C_1-C_4 alkyl)carbonyl, arylcarbonyl, heteroarylcarbonyl, aminocarbonyl, (C_1-C_4 alkyl)aminocarbonyl, di-(C_1-C_3 alkyl)aminocarbonyl, hydroxycarbonyl, (C_1-C_4 alkoxy)carbonyl, C_1-C_4 alkylamino, di-(C_1-C_3 alkyl)amino, (C_1-C_4 alkyl)carbonylamino, arylcarbonylamino, heteroarylcarbonylamino, C_1-C_4 alkylsulfonylamino, arylsulfonylamino, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_3-C_{10} cycloalkylthio, C_3-C_{10} cycloalkylsulfinyl, C_3-C_{10} cycloalkylsulfonyl, C_5-C_{10} cycloalkenylthio, C_5-C_{10} cycloalkenylsulfinyl, C_5-C_{10} cycloalkenylsulfonyl, arylthio, arylsulfinyl or arylsulfonyl; two of the remaining groups R^6, R^7, R^8, R^9 and R^{10} each independently represent hydrogen, deuterium, halo, cyano, nitro, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_1-C_3 alkoxy or C_3-C_{10} cycloalkoxy; and two of the remaining groups R^6, R^7, R^8, R^9 and R^{10} each independently represent hydrogen or deuterium;

R^{14}, R^{15} and R^{16} each independently represent hydrogen, (C_1-C_{18} alkyl)carbonyl, (C_1-C_{18} alkyl)oxycarbonyl, arylcarbonyl, aryl-(C_1-C_3 alkyl)carbonyl, (C_3-C_{10} cycloalkyl)carbonyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, (C_5-C_7 cycloalkenyl)C_1-C_3 alkyl, (aryl)C_1-C_3 alkyl, (heteroaryl)C_1-C_3 alkyl, C_3-C_7 cycloalkyl, C_5-C_7 cycloalkenyl, aryl, heteroaryl, (C_3-C_7 cycloalkyl)C_1-C_3 alkyl, (C_5-C_7 cycloalkenyl)C_1-C_3 alkyl, (aryl)C_1-C_3 alkyl, (heteroaryl)C_1-C_3 alkyl, C_1-C_4

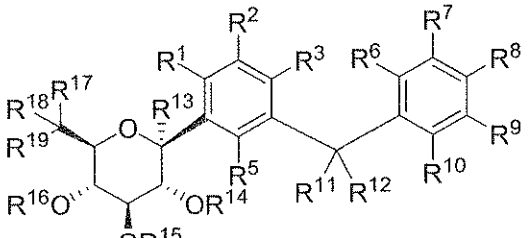
alkylsulfonyl, arylsulfonyl, (aryl)C_1-C_3 alkylsulfonyl, trimethylsilyl or *t*-butyldimethylsilyl;

R^{19} represents hydroxy, (C_1-C_{18} alkyl)carbonyloxy, (C_1-C_{18} alkyl)oxycarbonyloxy, arylcarbonyloxy, aryl-(C_1-C_3 alkyl)carbonyloxy, (C_3-C_{10} cycloalkyl)carbonyloxy, hydrogen, deuterium, halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_5-C_7 cycloalkenyl)C_1-C_3 alkyl, (aryl)C_1-C_3 alkyl, (heteroaryl)C_1-C_3 alkyl, C_1-C_6 alkoxy, C_2-C_6 alkenyloxy, C_2-C_6 alkynyloxy, C_3-C_7 cycloalkoxy, C_5-C_7 cycloalkenyloxy, aryloxy, heteroaryloxy, (C_3-C_7 cycloalkyl)C_1-C_3 alkoxy, (C_5-C_7 cycloalkenyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, aminocarbonyl, hydroxycarbonyl, (C_1-C_4 alkyl)aminocarbonyl, di-(C_1-C_3 alkyl)aminocarbonyl, (C_1-C_4 alkoxy)carbonyl, (aminocarbonyl)C_1-C_3 alkyl, (C_1-C_4 alkyl)aminocarbonyl-(C_1-C_3)alkyl, di-(C_1-C_3 alkyl)aminocarbonyl-(C_1-C_3)alkyl, (hydroxycarbonyl)C_1-C_3 alkyl, (C_1-C_4 alkoxy)carbonyl-(C_1-C_3)alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_5-C_7 cycloalkenyloxy)C_1-C_3 alkyl, (aryloxy)C_1-C_3 alkyl, (heteroaryloxy)C_1-C_3 alkyl, C_1-C_4 alkylsulfonyloxy, arylsulfonyloxy, (aryl)C_1-C_3 alkylsulfonyloxy, trimethylsilyloxy, *t*-butyldimethylsilyloxy, or cyano,

wherein alkyl, alkenyl, alkynyl, cycloalkyl and cycloalkenyl groups or portions optionally may be partly or completely substituted with fluorine or deuterium and may be mono- or disubstituted by identical or different substituents selected from chlorine, hydroxy, C_1-C_3 alkoxy and C_1-C_3 alkyl, and in cycloalkyl and cycloalkenyl groups or portions one or two methylene groups are optionally replaced independently of one another by NR^a, O, S, CO, SO or SO_2; R^a independently represents hydrogen, C_1-C_4 alkyl or (C_1-C_4 alkyl)carbonyl, wherein alkyl groups or portions optionally may be partly or completely substituted with fluorine or deuterium; and wherein

at least one of R^1-R^{19} is –D or comprises –D, wherein said composition has an isotopic enrichment factor for deuterium of at least 5 for said compound.

In another aspect, the invention features a composition having a structure according to the following formula,



, wherein

each R^1, R^2, R^3 and R^5 is, independently, -H, -D, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted alkcycloalkyl;

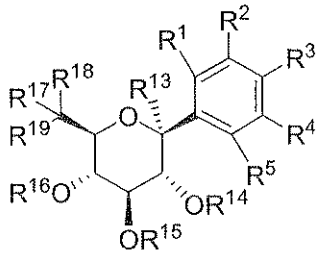
each R^6, R^7, R^8, R^9, R^{10}, and R^{19} is, independently, -H, -D, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted carbamoyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, and optionally substituted alkcycloalkyl;

each R^{11}, R^{12}, R^{13}, R^{17}, and R^{18} is, independently, -H, -D, or halogen; and

each R^{14}, R^{15}, and R^{16} is, independently, -H, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkcycloalkyl, $-C(O)R^A$, $-C(O)OR^A$, or $-C(O)NR^AR^B$, wherein each R^A and R^B is, independently, hydrogen, deuterium, or an optionally deuterated substituent selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, and optionally substituted aryl;

wherein at least one of R^1, $-R^{19}$ is -D or comprises -D, wherein said composition has an isotopic enrichment factor for deuterium of at least 5 for said compound.

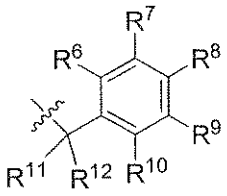
Also disclosed are compounds having the structure:



(I),

or any stereoisomer or tautomer thereof, or any pharmaceutically acceptable prodrug, salt, or solvate thereof, wherein

- each R^1, R^2, R^3, R^4 and R^5 is, independently, -H, -D, a substituent that is optionally deuterated, or group Q:



(Q) ;

- each R^6, R^7, R^8, R^9, R^{10}, R^{14}, R^{15}, R^{16}, and R^{19} is, independently, -H, -D, or a substituent that is optionally deuterated; and
- each R^{11}, R^{12}, R^{13}, R^{17} and R^{18} is, independently, -H, -D, or halogen;

wherein

- one of R^1, R^2, R^3, R^4 and R^5 is group Q;

at least one of R^1-R^{19} is –D or comprises –D.

In certain ~~embodiments~~examples of compounds of formula I:

one of R^1, R^2, R^3, R^4 and R^5 is group Q;

one of the remaining groups R^1, R^2, R^3, R^4 and R^5 represents hydrogen, deuterium, halo, cyano, nitro, amino, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl, C_1-C_6 alkoxy, C_3-C_{10} cycloalkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, C_5-C_7 cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, (C_2-C_4 alkenyl)C_1-C_3 alkoxy, (C_2-C_4 alkynyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkoxy, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkyl, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkoxy, (C_1-C_4 alkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkenyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkynyl, (C_3-C_7

(aminocarbonyl)C_1-C_3 alkyl, (C_1-C_4 alkyl)aminocarbonyl-(C_1-C_3)alkyl, di-(C_1-C_3 alkyl)aminocarbonyl-(C_1-C_3)alkyl, (hydroxycarbonyl)C_1-C_3 alkyl, (C_1-C_4 alkoxy)carbonyl-(C_1-C_3)alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_5-C_7 cycloalkenyloxy)C_1-C_3 alkyl, (aryloxy)C_1-C_3 alkyl, (heteroaryloxy)C_1-C_3 alkyl, C_1-C_4 alkylsulfonyloxy, arylsulfonyloxy, (aryl)C_1-C_3 alkylsulfonyloxy, trimethylsilyloxy, *t*-butyldimethylsilyloxy, or cyano,

wherein alkyl, alkenyl, alkynyl, cycloalkyl and cycloalkenyl groups or portions optionally may be partly or completely substituted with fluorine or deuterium and may be mono- or disubstituted by identical or different substituents selected from chlorine, hydroxy, C_1-C_3 alkoxy and C_1-C_3 alkyl, and in cycloalkyl and cycloalkenyl groups or portions one or two methylene groups are optionally replaced independently of one another by NR^a, O, S, CO, SO or SO_2; R^a independently represents hydrogen, C_1-C_4 alkyl or (C_1-C_4 alkyl)carbonyl, wherein alkyl groups or portions optionally may be partly or completely substituted with fluorine or deuterium.

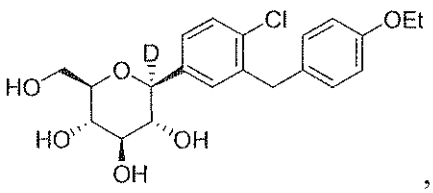
In other ~~embodiments~~examples, R^{11} and R^{12} may be both –D. R^{13} is, for example, –D. One of R^1, R^2, R^3, or R^5 may be halogen, e.g., R^3 is –Cl. R^4 may be Q.

In various ~~embodiments~~examples, each R^1, R^2, R^3, R^4 and R^5 is, independently, -H, -D, group Q, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, or optionally substituted alkcycloalkyl; each R^6, R^7, R^8, R^9, R^{10}, and R^{19} is, independently, -H, -D, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted carbamoyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, or optionally substituted alkcycloalkyl; and each R^{14}, R^{15}, and R^{16} is, independently, -H, -D, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkcycloalkyl, -C(O)R^A, -C(O)OR^A, or -C(O)NR^AR^B, wherein each R^A and R^B is, independently, hydrogen, deuterium, or an optionally deuterated substituent selected from optionally substituted alkyl, optionally

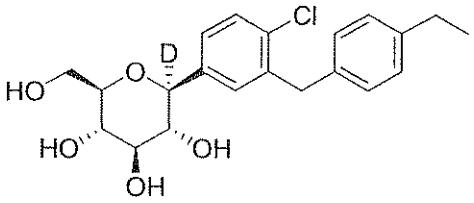
substituted alkenyl, optionally substituted cycloalkyl, and optionally substituted aryl. For example, R^4 is Q and R^8 is -D, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, or optionally substituted alkcycloalkyl. In further embodiments, R^2 is H; R^3 is halogen, e.g., Cl; R^5, R^6, R^7, R^9, and R^{10} are H; R^8 is a deuterated substituent; R^{11} and R^{12} are both –D; R^{13} is –D; and/or R^{14}, R^{15}, and R^{16} are, independently, selected from H, D, -$C(O)R^A$, -$C(O)OR^A$, or -$C(O)NR^AR^B$.

In some ~~embodiments~~examples, R^8 is a deuterated substituent.

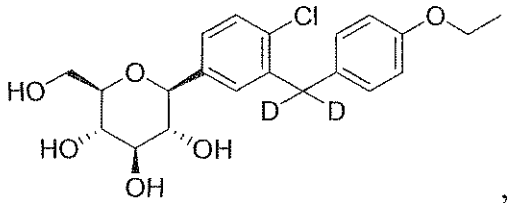
In some ~~embodiments~~examples, the composition includes a compound selected from the group consisting of:



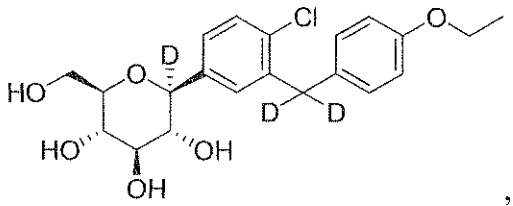
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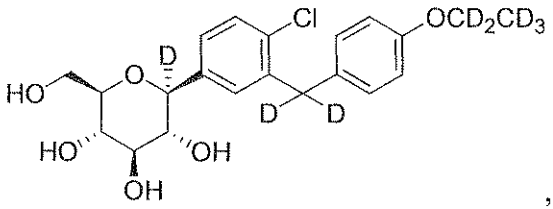
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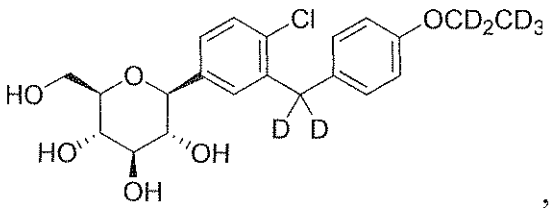
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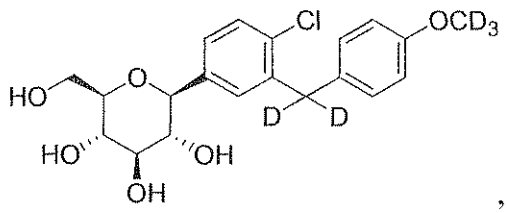
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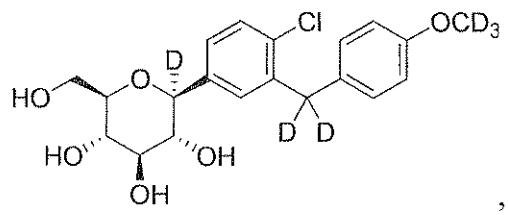
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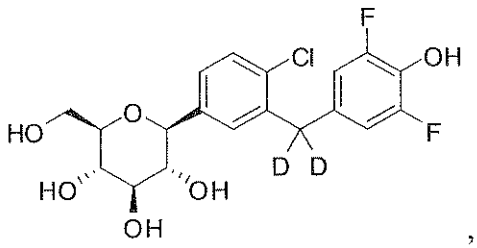
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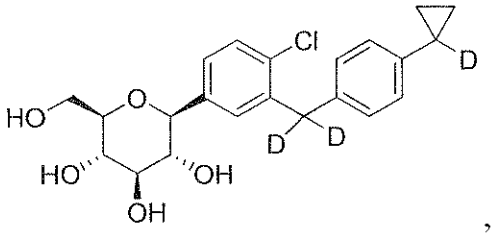
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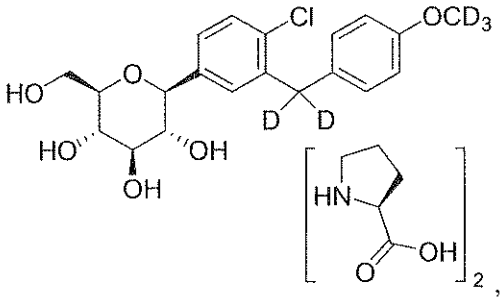
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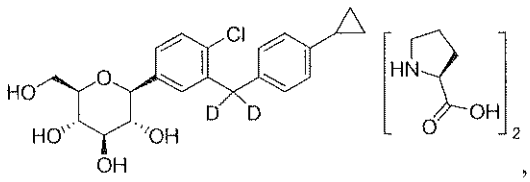
,

or any stereoisomer or tautomer thereof, or any pharmaceutically acceptable prodrug, salt, or solvate thereof.

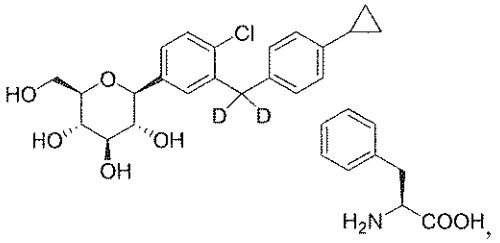
In any of the compositions described herein, the composition further includes an amino acid (e.g., as a co-crystal with any of the compounds of Formula (I) or (II) described herein). In some ~~embodiments~~examples, the amino acid is L-phenylalanine or L-proline. In some ~~embodiments~~examples, the co-crystal of a compound of Formula (I) with 1 or 2 amino acids is selected from the following:



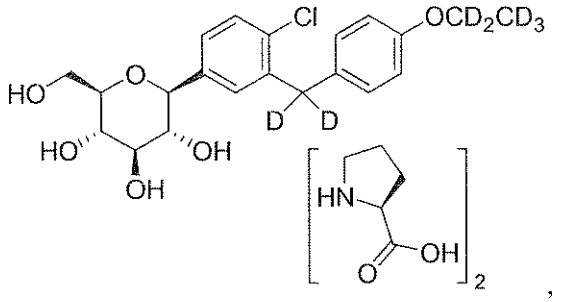
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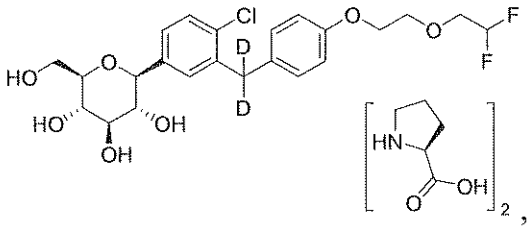
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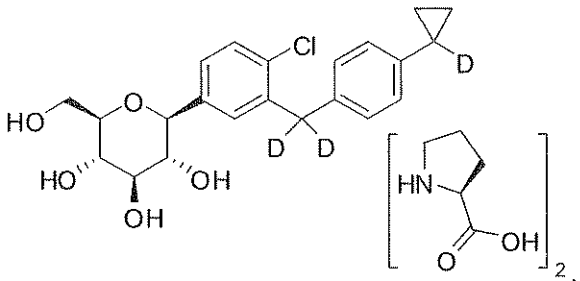
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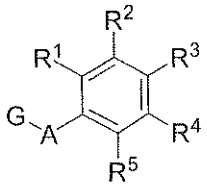
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and

In some ~~embodiments~~examples, R^1-R^{19} include 1, 2, 3, 4, or 5 deuterium atoms.

In further ~~embodiments~~examples, the composition further includes a pharmaceutically acceptable carrier, and the compound of Formula (I) is present in an effective amount.

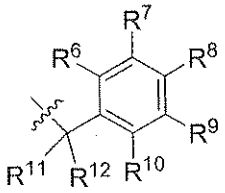
The ~~invention~~disclosure also features compounds having the formula:



(II),

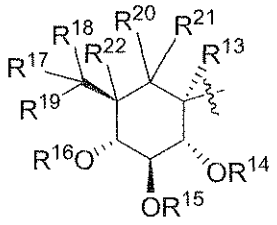
or any diastereomer, tautomer, or isomer thereof, or any pharmaceutically acceptable prodrug, salt, or solvate thereof, wherein

- each R^1, R^2, R^3, R^4 and R^5 is, independently, -H, -D, a substituent that is optionally deuterated, or group Q:

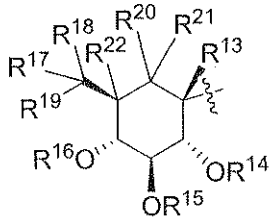


(Q) ;

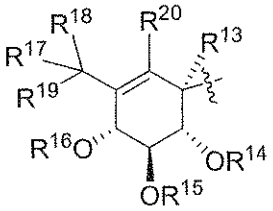
- A is selected from the group consisting of oxygen and a single bond;
- G is selected from the group consisting of:



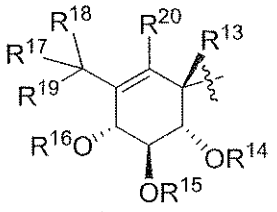
G^1



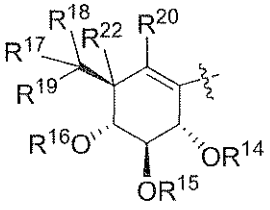
G^2



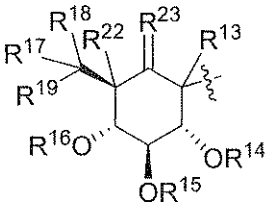
G^3



G^4



G^5



G^6

- each R^6, R^7, R^8, R^9, R^{10}, R^{14}, R^{15}, R^{16}, R^{19}, and R^{21},is, independently, -H, -D, or a substituent that is optionally deuterated; and
- each R^{11}, R^{12}, R^{13}, R^{17}, R^{18}, R^{20}, and R^{22} is, independently, -H, -D, or halogen;

wherein

- one of R^1, R^2, R^3, R^4, and R^5 is group Q;
- R^{23} is CH_2, NH, O, or S; and

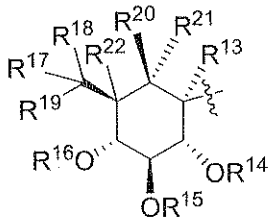
at least one of R^1-R^{23} is –D or includes –D. In certain embodiments, G is G^6. In further embodiments, R^{21} is hydroxy.

In other ~~embodiments~~examples of compounds of formula II:

one of R^1, R^2, R^3, R^4 and R^5 is group Q;

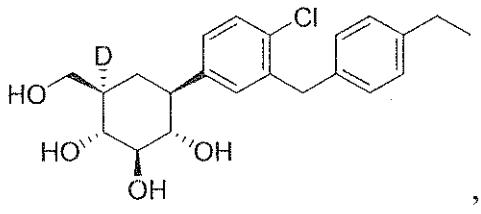
one of the remaining groups R^1, R^2, R^3, R^4 and R^5 represents hydrogen, deuterium, halo, cyano, nitro, amino, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl, C_1-C_6 alkoxy, C_3-C_{10} cycloalkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, C_5-C_7 cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, (C_2-C_4 alkenyl)C_1-C_3 alkoxy, (C_2-C_4 alkynyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkoxy, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkyl, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkoxy, (C_1-C_4 alkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkenyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkynyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkoxy, (C_1-C_4 alkylamino)C_1-C_3 alkyl, di-(C_1-C_3 alkylamino)C_1-C_3 alkyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkenyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkynyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkoxy, (C_3-C_7 cycloalkyl)C_2-C_5 alkenyl, (C_3-C_7 cycloalkyl)C_3-C_5 alkenyloxy, (C_3-C_7 cycloalkyl)C_3-C_5 alkynyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkenyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkynyloxy, C_3-C_6 cycloalkylidenmethyl, (C_1-C_4 alkyl)carbonyl, arylcarbonyl, heteroarylcarbonyl, aminocarbonyl, (C_1-C_4 alkyl)aminocarbonyl, di-(C_1-C_3 alkyl)aminocarbonyl, hydroxycarbonyl, (C_1-C_4 alkoxy)carbonyl, C_1-C_4 alkylamino, di-(C_1-C_3 alkyl)amino, (C_1-C_4 alkyl)carbonylamino, arylcarbonylamino, heteroarylcarbonylamino, C_1-C_4 alkylsulfonylamino, arylsulfonylamino, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_3-C_{10} cycloalkylthio, C_3-C_{10} cycloalkylsulfinyl, C_3-C_{10} cycloalkylsulfonyl, C_5-C_{10} cycloalkenylthio, C_5-C_{10} cycloalkenylsulfinyl, C_5-C_{10} cycloalkenylsulfonyl, arylthio, arylsulfinyl or arylsulfonyl;

In various ~~embodiments~~examples, G is G^1, R^{22} is –D, and/or R^{11} and R^{12} are both –D. In some embodiments, G^1 has the following structure:

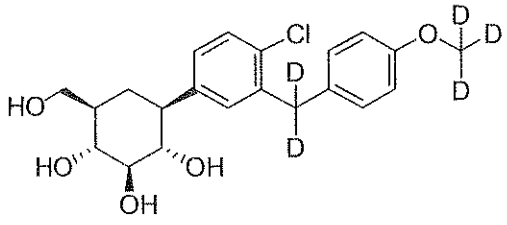


In other ~~embodiments~~examples, each R^1, R^2, R^3, R^4 and R^5 is, independently, -H, -D, group Q, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, or optionally substituted alkcycloalkyl; each R^6, R^7, R^8, R^9, R^{10}, and R^{19} is, independently, -H, -D, halogen, or an optionally deuterated substituent selected from hydroxyl, optionally substituted carbamoyl, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, or optionally substituted alkcycloalkyl; and each R^{14}, R^{15}, and R^{16} is, independently, hydrogen, deuterium, optionally substituted alkyl, haloalkyl, optionally substituted alkoxyalkyl, optionally substituted alkoxy, haloalkoxy, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted alkcycloalkyl, $-C(O)R^A$, $-C(O)OR^A$, or $-C(O)NR^AR^B$, wherein each R^A and R^B is, independently, hydrogen, deuterium, or an optionally deuterated substituent selected from optionally substituted alkyl, optionally substituted alkenyl, optionally substituted cycloalkyl, and optionally substituted aryl. For example, R^4 is Q and R^8 is an optionally deuterated substituent selected from optionally substituted alkyl and optionally substituted alkoxy.

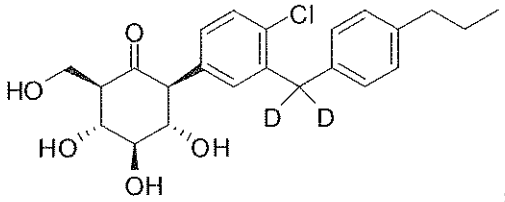
In some ~~embodiments~~examples, the compound of Formula (II) is selected from the following group:

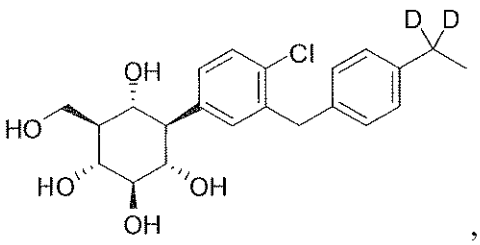


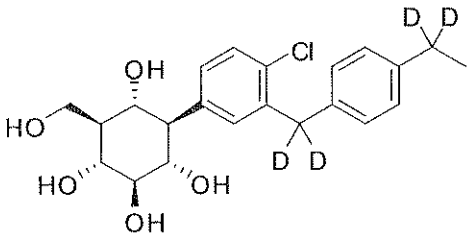
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or any stereoisomer or tautomer thereof, or any pharmaceutically acceptable prodrug, salt, or solvate thereof.

In certain ~~embodiments~~examples, the composition further includes a pharmaceutically acceptable carrier, and the compound of Formula (II) is present in an effective amount.

Where a group is described as having optional substituents (e.g., any of R^1-R^{19} in Formula (I) or any of R^1-R^{21} in Formula (II)), such substituents may be selected from the group consisting of halo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, C_2-C_6 alkynyl, C_3-C_8 cycloalkenyl, (C_3-C_8 cycloalkyl)C_1-C_6 alkyl, (C_3-C_8 cycloalkyl)C_2-C_6 alkenyl, (C_3-C_8 cycloalkyl)C_1-C_6 alkoxy, (C_3-C_8 cycloalkoxy)C_1-C_6 alkoxy,C_3-C_7 heterocyclyl, (C_3-C_7 heterocyclyl)C_1-C_6 alkyl, (C_3-C_7 heterocyclyl)C_2-C_6 alkenyl, (C_3-C_7 heterocyclyl)C_1-C_6 alkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, (C_1-C_6 haloalkoxy)C_1-C_6 alkoxy, hydroxy, carboxy, oxo, thio, C_1-C_6 alkylthio, aryl, heteroaryl, aryloxy, heteroaryloxy, aralkyl, aralkoxy, heteroaralkoxy, nitro, cyano, amino, C_1-C_6 alkylamino, di-(C_1-C_6 alkyl)amino, carbamoyl, (C_1-C_6 alkyl)carbonyl, (C_1-C_6 alkoxy)carbonyl, (C_1-C_6 alkyl)aminocarbonyl, di-(C_1-C_6 alkyl)aminocarbonyl, arylcarbonyl, aryloxycarbonyl, (C_1-C_6 alkyl)sulfonyl, and arylsulfonyl, or any substituent group as described herein. Such substituents may be undeuterated or deuterated. In a deuterated substituent, at least one hydrogen has been replaced with deuterium; e.g., 2, 3, 4, 5, or 6 hydrogens are replaced with deuterium. In some deuterated substituents, all hydrogens have been replaced with deuterium. In some ~~embodiments~~examples, a substituent is not further substituted. Additional

optional substituents for various groups are described herein. Compounds of the ~~invention~~disclosure may include, for example, 1-5 deuterium atoms.

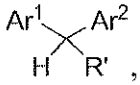
The ~~invention~~disclosure further features compositions including any of the above compounds of formula I or II and having an isotopic enrichment factor for deuterium of at least 5, e.g., at least 500, 1000, or 3000. The ~~invention~~disclosure also features pharmaceutical compositions including any of the above compounds of formula I or II and a pharmaceutically acceptable carrier and having an isotopic enrichment factor for deuterium of at least 5, e.g., at least 500, 1000, or 3000. A pharmaceutical composition is formulated, for example, for nonimmediate release, e.g., as an oral, parenteral, systemic, or buccal administration, or as a depot preparation.

In another aspect, the invention features the use of the composition as defined herein in the manufacture of a medicament for treating or preventing a disease affected by inhibition of the sodium-dependent glucose transporter (SGLT).

Any of the compounds and compositions of the ~~invention~~disclosure described herein may also be employed in methods for treating or preventing a disease affected by inhibition of the sodium-dependent glucose transporter (SGLT) such as type 1 diabetes mellitus, type 2 diabetes mellitus, hyperglycemia, diabetic complications, insulin resistance, metabolic syndrome (Syndrome X), hyperinsulinemia, hypertension, hyperuricemia, obesity, edema, dyslipidemia, chronic heart failure, or atherosclerosis. These methods may further include administering a second therapeutic agent, e.g., an antidiabetic agent, a lipid-lowering/lipid-modulating agent, an agent for treating diabetic complications, an anti-obesity agent, an antihypertensive agent, an antihyperuricemic agent, an agent for treating chronic heart failure, or an agent for treating atherosclerosis.

Also disclosed is~~In another aspect, the invention features~~ a method of enriching the deuterium content of a diarylmethylene compound, wherein said method includes

(a) combining:

(i) a diarylmethylene compound having a structure according to , wherein R' is H or D, and each Ar^1 and Ar^2 is, independently, an optionally substituted aryl group; and

(ii) a mixture that includes deuterium oxide and sodium hydride, e.g., dispersed in mineral oil; and

(iii) a phase-transfer catalyst;

wherein the combination of reagents (i), (ii), and (iii) results in the incorporation of deuterium at the methylene bridge of said diarylmethylene compound; and

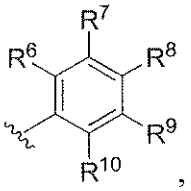
(b) optionally combining the product obtained in step (a) one or more times with the reagents (ii) and (iii).

In some ~~embodiments~~examples, the mixture of (ii) further includes mineral oil. In other embodiments, the mixture of step (a) stirs at 20-30 °C for at least 30 minutes (e.g., for 1-24 hours).

In some ~~embodiments~~examples, the sodium hydride is dispersed in mineral oil as a 50%-75% (w/w) dispersion, e.g., a 60% dispersion.

In other ~~embodiments~~examples, the phase-transfer catalyst is a tetraalkylammonium salt, e.g., tetrabutylammonium bisulfate.

In still other ~~embodiments~~examples, R' and R" are each optionally substituted phenyl. In further embodiments, each R' and R" has the following structure:



, wherein each R^6, R^7, R^8, R^9, and R^{10} is, independently, hydrogen, deuterium, halo, cyano, nitro, amino, hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_{10} cycloalkyl, C_5-C_{10} cycloalkenyl, C_1-C_6 alkoxy, C_3-C_{10} cycloalkoxy, (C_1-C_6 alkoxy)C_1-C_6 alkoxy, C_5-C_7 cycloalkenyloxy, aryl, heteroaryl, aryloxy, heteroaryloxy, (C_2-C_4 alkenyl)C_1-C_3 alkoxy, (C_2-C_4 alkynyl)C_1-C_3 alkoxy, (aryl)C_1-C_3 alkoxy, (heteroaryl)C_1-C_3 alkoxy, (C_3-C_{10} cycloalkyl)C_1-C_3 alkyl, (C_3-C_{10} cycloalkyl)C_1-C_3 alkoxy, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkyl, (C_5-C_{10} cycloalkenyl)C_1-C_3 alkoxy, (C_1-C_4 alkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkenyl, (C_3-C_7 cycloalkoxy)C_2-C_4 alkynyl, (C_3-C_7 cycloalkoxy)C_1-C_3 alkoxy, (C_1-C_4 alkylamino)C_1-C_3 alkyl, di-(C_1-C_3 alkylamino)C_1-C_3 alkyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkenyl, tri-(C_1-C_4 alkyl)silyl-C_2-C_6 alkynyl, tri-(C_1-C_4 alkyl)silyl-C_1-C_6 alkoxy, (C_3-C_7 cycloalkyl)C_2-C_5 alkenyl, (C_3-C_7 cycloalkyl)C_3-C_5 alkenyloxy, (C_3-C_7 cycloalkyl)C_3-C_5 alkynyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkenyloxy, (C_5-C_8 cycloalkenyl)C_3-C_5 alkynyloxy, C_3-C_6 cycloalkylidenmethyl, (C_1-C_4 alkyl)carbonyl, arylcarbonyl, heteroarylcarbonyl, aminocarbonyl, (C_1-C_4 alkyl)aminocarbonyl, di-(C_1-C_3