CLAIMS

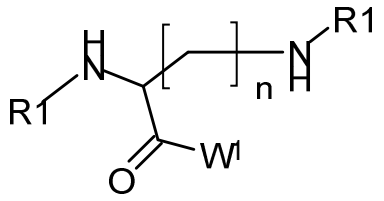
1. A compound comprising

i) human insulin or a human insulin analogue; and

ii) two or more modifying groups M, wherein each of the modifying groups M comprises two aryl moieties, wherein a boron atom is attached to each of the two aryl moieties; and

wherein each of the two or more modifying groups M is attached, optionally via a spacer, to the amino group of the N-terminal amino acid residue of the A-chain or B-chain of said human insulin or human insulin analogue or to the epsilon amino group of a lysine in said human insulin or human insulin analogue; and

wherein each of the modifying groups M is independently selected from the group of



Formula M1 ,

which represents a *D*- or an *L*-amino acid form, and

wherein n represents an integer in the range of 1 to 4;

wherein W1 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W1 represents

$NH\text{-}CH_2\text{-}C(=O)\text{-}*$,

$NH\text{-}CH_2CH_2\text{-}C(=O)\text{-}*$,

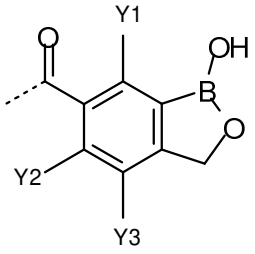
the *D*- or *L*-form of $NH\text{-}CH(COOH)\text{-}CH_2CH_2\text{-}C(=O)\text{-}*$,

the *D*- or *L*-form of $NH\text{-}CH(COOH)\text{-}CH_2CH_2\text{-}C(=O)\text{-}NH\text{-}CH_2CH_2\text{-}C(=O)\text{-}*$, or

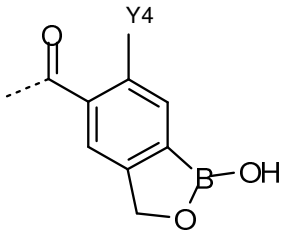
$NH\text{-}CH_2CH_2\text{-}C(=O)\text{-}NH\text{-}(CH_2)_2\text{-}O\text{-}(CH_2)_2\text{-}O\text{-}CH_2\text{-}CO\text{-}*$,

wherein * represents the point of attachment to said human insulin or human insulin analogue; and

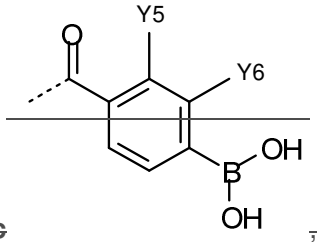
wherein R1 is selected from



Formula R1a , and **Formula R1b**

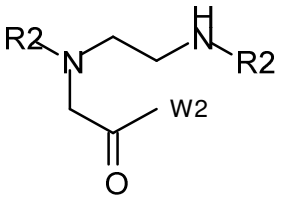


~~, and~~



~~**Formula R1c**~~ ~~,~~

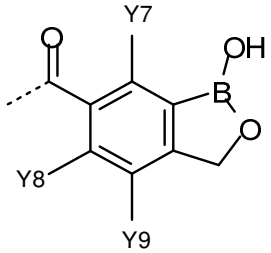
wherein Y1, Y2, Y3, and Y4~~, Y5 and Y6~~ is independently selected from H, F, Cl, CHF_2, and CF_3;



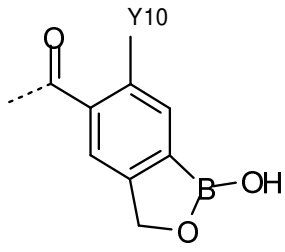
Formula M2

wherein W2 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W2 represents the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, or NH-$CH_2CH_2CH_2$-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and

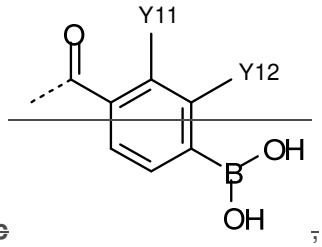
wherein R2 is selected from



Formula R2a , and **Formula R2b**

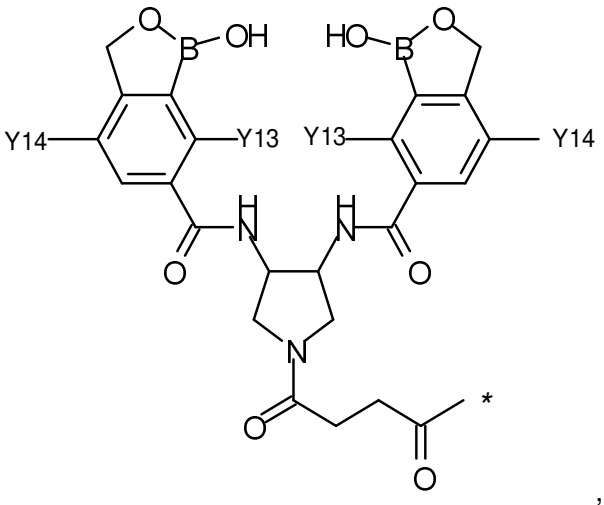


~~, and~~



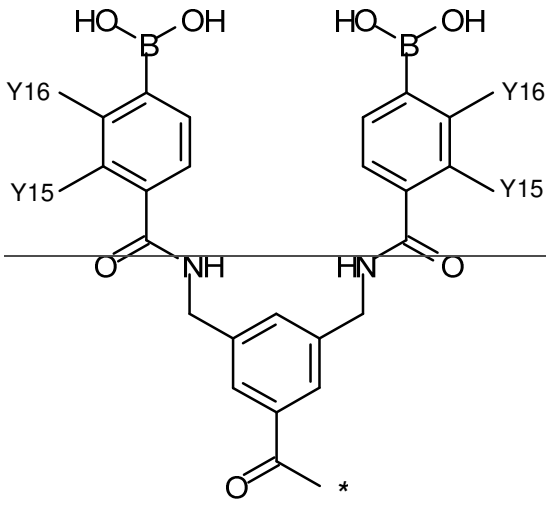
~~**Formula R2c**~~ ~~,~~

wherein Y7, Y8, Y9, and Y10~~, Y11 and Y12~~ is independently selected from H, F, Cl, CHF_2, and CF_3; and



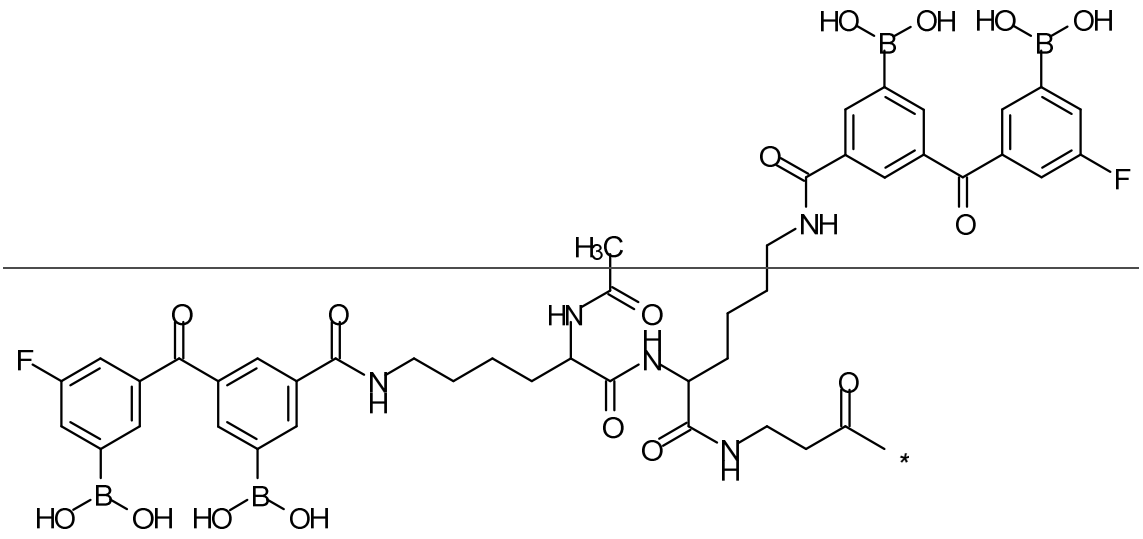
Formula M3 ,

which represents a *R,R or S,S, or R,S* stereoisomer of the 3,4-diamino-pyrrolidine; and wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y13 and Y14 is independently selected from H, F, Cl, CHF_2, and CF_3;



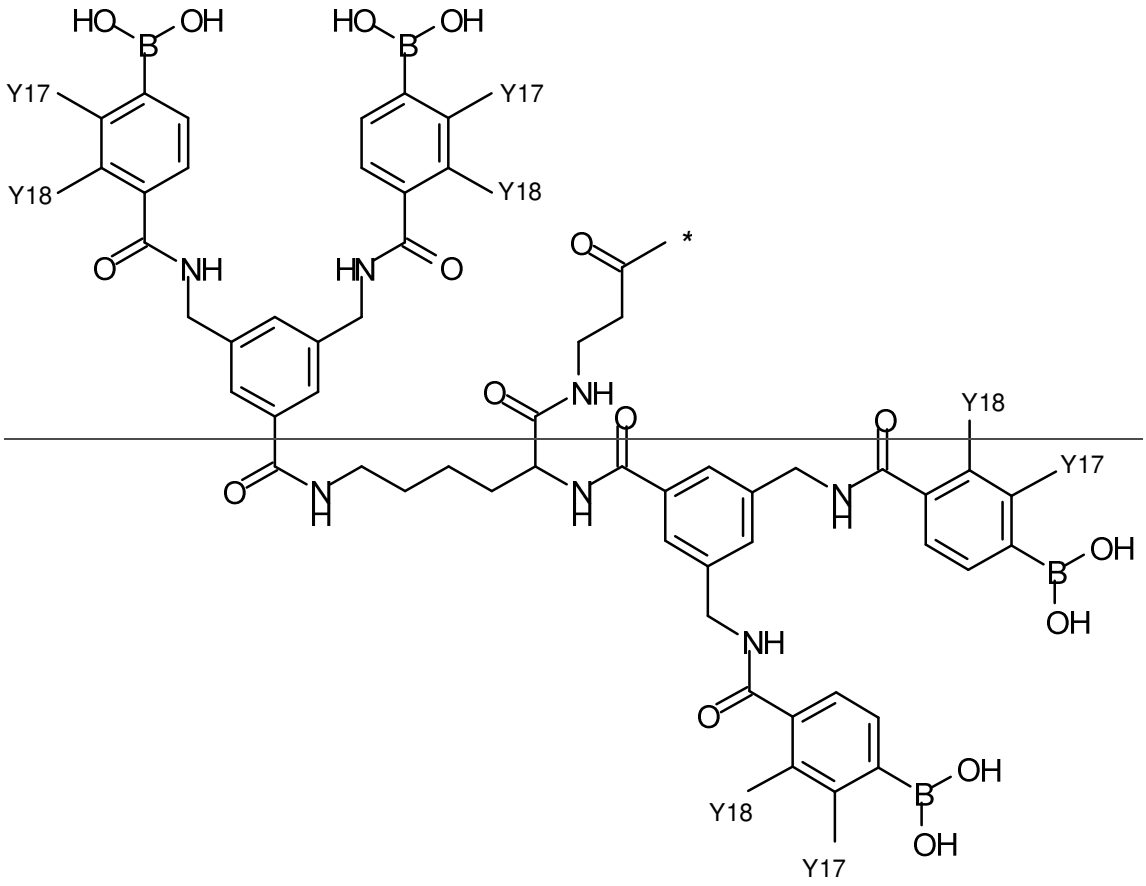
Formula M4

wherein * represents the point of attachment to said human insulin or human insulin analogue, and wherein Y15 and Y16 is independently selected from H, F, Cl, CHF_2, and CF_3;



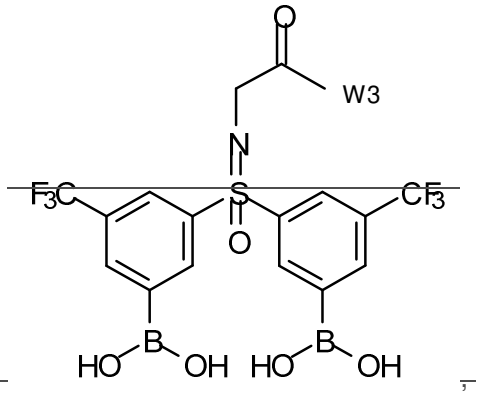
Formula M5

wherein each of the amino acid residues represents a *D*- or an *L*-amino acid form, and wherein * represents the point of attachment to said human insulin or human insulin analogue;



Formula M6

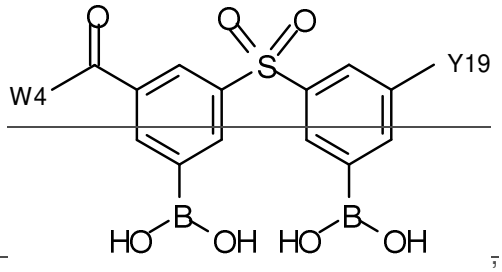
wherein the α-amino acid residue represents a *D*- or an *L*-amino acid form, and wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y17 and Y18 is independently selected from H, F, Cl, CHF_2, and CF_3;



Formula M7

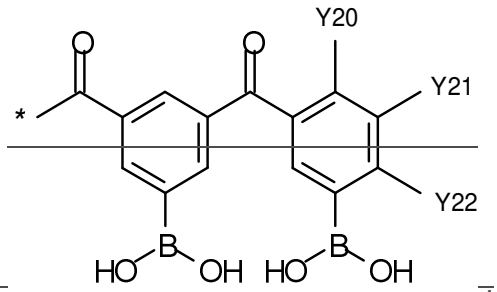
wherein W3 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W3 represents the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-

~~C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue;~~



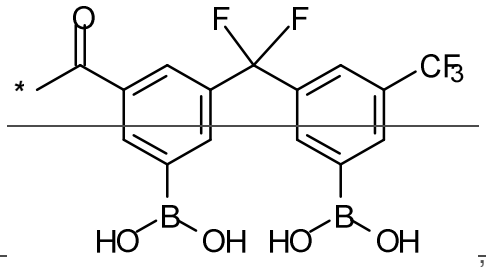
~~**Formula M8**~~ ,

~~wherein W4 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W4 represents NH-CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y19 is H, F, Cl, CHF_2, and CF_3 or SF_5;~~



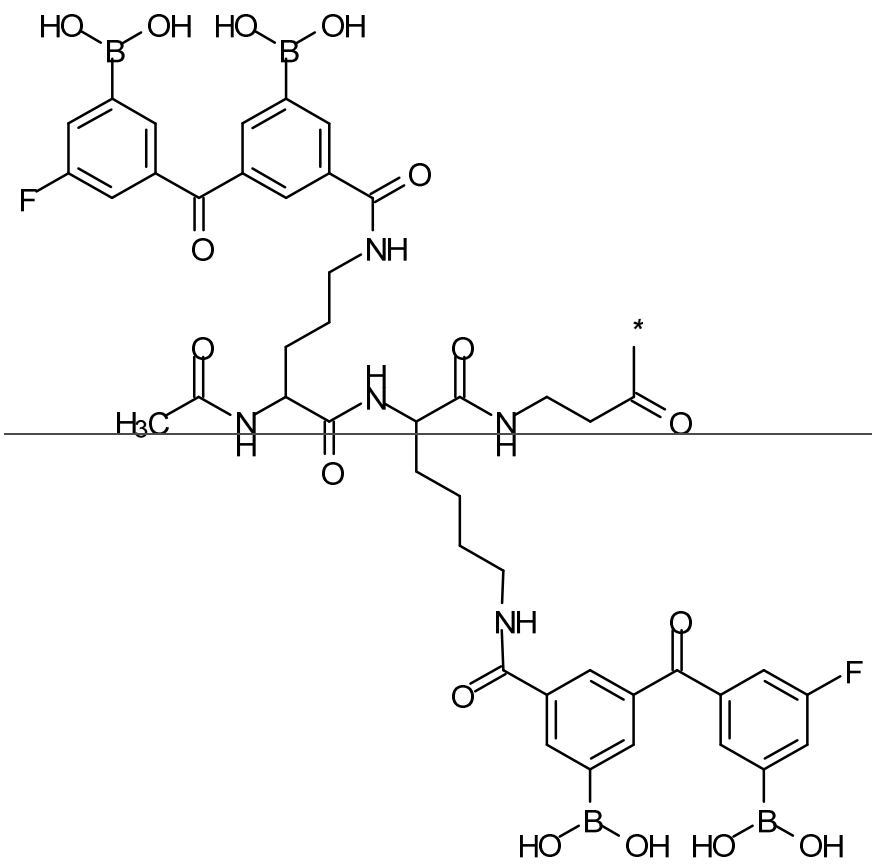
~~**Formula M9**~~ ,

~~wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein each of Y20, Y21, and Y22 is independently selected from H, F, Cl, CHF_2, and CF_3;~~



~~**Formula M10**~~ ,

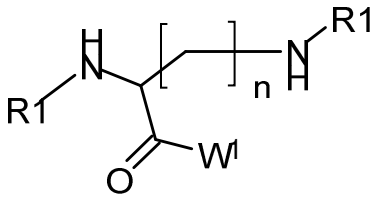
~~wherein * represents the point of attachment to said human insulin or human insulin analogue; and~~



~~Formula M11~~

wherein each of the amino acid residues represents a *D*- or an *L*-amino acid form, and wherein * represents the point of attachment to said human insulin or human insulin analogue.

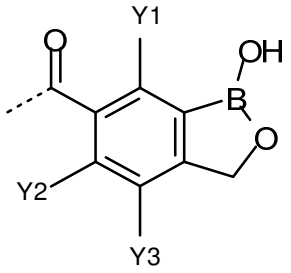
2. The compound according to claim 1, wherein each of the modifying groups **M** is independently selected from the group of



Formula M1 ,

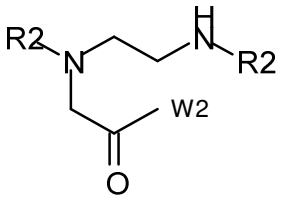
which represents a *D*- or an *L*-amino acid form, and wherein n is 1;

W1 represents NH-CH_2CH_2-C(=O)-* or the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and



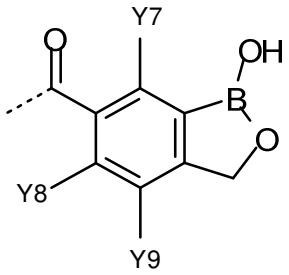
R1 is of **Formula R1a** ,

wherein Y1 and Y2 are H; and Y3 is F or CF_3; and



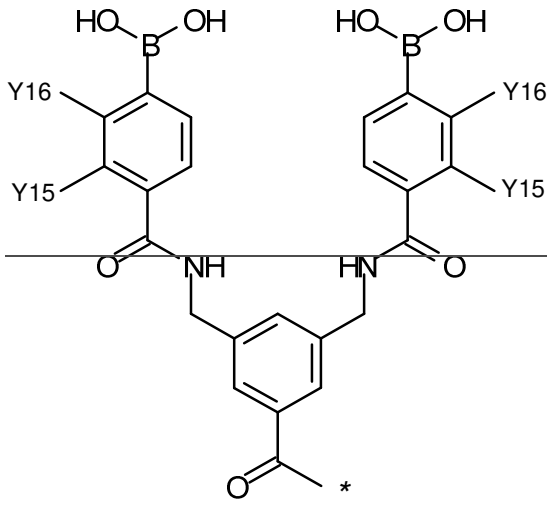
Formula M2 ,

wherein W2 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W2 represents the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and



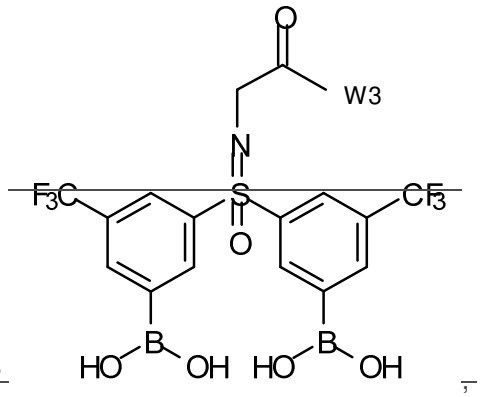
wherein R2 is of **Formula R2a** ,

wherein Y7 and Y8 are H; and Y9 is Cl, CHF_2, or CF3;



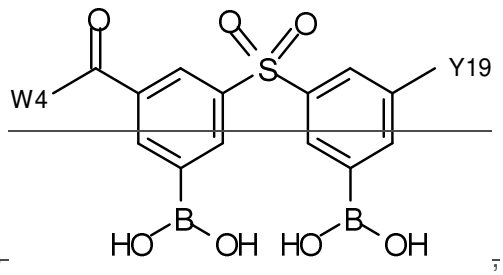
Formula M4

wherein * represents the point of attachment to said human insulin or human insulin analogue, and wherein Y15 is H, and Y16 is F;



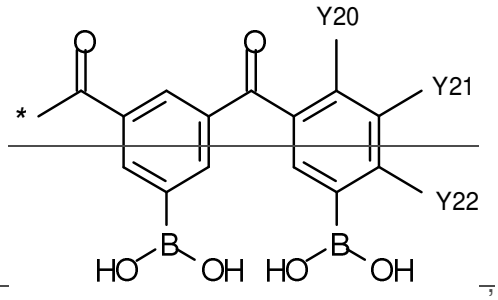
Formula M7

wherein W3 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W3 represents the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue;



Formula M8

~~wherein W4 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W4 represents NH CH_2 C(=O) *, wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y19 is CF3; and~~



~~**Formula M9**~~ ~~,~~

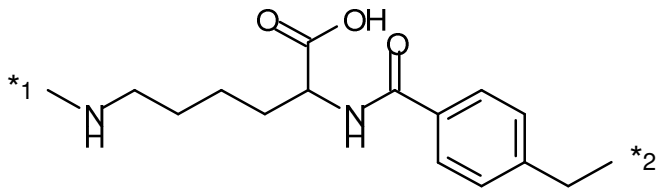
~~wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein each of Y20, Y21, and Y22 is independently selected from H and F; with the provisio that when Y21 is F, then Y20 and Y22 are H; and when Y21 is H, then Y20 and Y22 are F.~~

3. The compound according to any one of claims 1-2, wherein said human insulin or human insulin analogue optionally comprises a spacer selected from the group of

a) a peptide spacer at the C-terminal of the A-chain of said human insulin or human insulin analogue,
wherein said peptide spacer comprises $(GES)_pK$, wherein p is an integer from 3 to 12; or

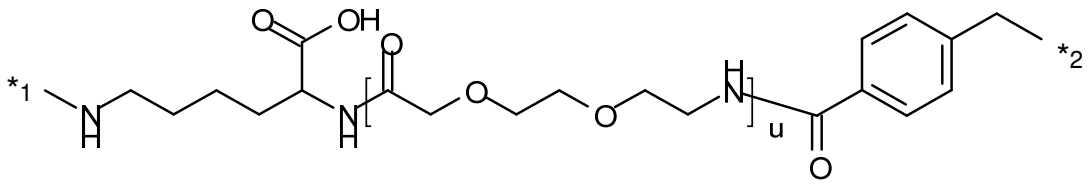
b) a peptide spacer or a linker L at the N-terminal of the B-chain of said human insulin or human insulin analogue;
wherein said peptide spacer comprises GKPG, $GKP(G_4S)_q$, $KP(G_4S)_r$, $GKPRGFFYTP(G_4S)_s$, or $TYFFGRKPD(G_4S)_t$, wherein each of q, r, s and t is independently selected from an integer from 1 to 5; and

wherein said linker L is selected from



Formula L1,

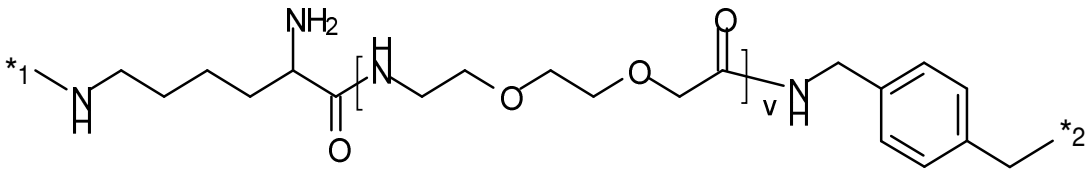
wherein *1 denotes the attachment point to the modifying group M and *2 denotes the attachment point to the amino group of the amino acid residue at the N-terminal of the B-chain of said human insulin or human insulin analogue;



Formula L2,

wherein *1 denotes the attachment point to the modifying group M and *2 denotes the attachment point to the amino group of the amino acid residue at N-terminal of the B-chain of said human insulin or human insulin analogue, and

wherein u is 1, 2 or 3; and



Formula L3,

wherein *1 denotes the attachment point to the modifying group M and *2 denotes the attachment point to the amino group of the amino acid residue at N-terminal of the B-chain of said human insulin or human insulin analogue, and

wherein v is 2 or 3.

4. The compound according to claim 3, wherein q is an integer selected from 1 to 3; r is 3; s is 2; and t is 3.

5. The compound according to any one of claims 1 to 4, wherein each modifying group M is attached to an attachment point selected from one of the following groups:

a) the amino group of the N-terminal amino acid residue of the A-chain of said human insulin or human insulin analogue;
b) the epsilon amino group of a lysine in position 22 of the A-chain of said human insulin analogue; or

the epsilon amino group of the lysine in said optional peptide spacer at the C-terminal of the A-chain of said human insulin or human insulin analogue;

c) the amino group of the N-terminal amino acid residue of the B-chain of said human insulin or human insulin analogue;

the epsilon amino group of a lysine residue in position 1 or position 4 of the B-chain of said human insulin analogue;

the epsilon amino group of a lysine in said optional peptide spacer at the N-terminal of the B-chain of said human insulin or human insulin analogue; or

the distal amino group marked with *1 in said optional linker L at the N-terminal of the B-chain of said human insulin or human insulin analogue; and

d) the epsilon amino group of a lysine in position 22 or position 29 of the B-chain of said human insulin or human insulin analogue.

~~6. The compound according to any one of claims 1 to 5, having exactly two, three or four modifying groups M.~~

~~7.~~6. The compound according to any one of claims 1 to ~~6~~ 5, wherein said human insulin or human insulin analogue is a human insulin analogue selected from the group of

desB30 human insulin;

A21Q desB30 human insulin;

A14E B25H desB30 human insulin;

A14E B1K B2P B25H desB27 desB30 human insulin;

A14E A22K B25H desB27 desB30 human insulin;

A14E A22K B25H B27P B28G desB30 human insulin;

A14E desB1-B2 B4K B5P desB30 human insulin;

A14E desB1-B2 B3G B4K B5P desB30 human insulin;

A14E B-1G B1K B2P desB30 human insulin;

A22K desB30 human insulin;

A22K B29R desB30 human insulin;

A22K B22K B29R desB30 human insulin; and

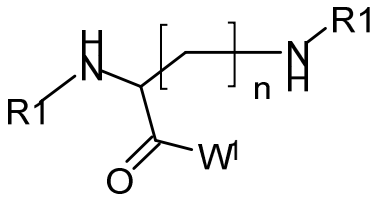
A-2K A-1P desB30 human insulin.

~~8.~~7. A compound according to any one of claims 1 to ~~7~~ 6, comprising

i) human insulin or a human insulin analogue, wherein said human insulin or human insulin analogue optionally comprises a peptide spacer at the N-terminal of the B-chain of said human insulin or human insulin analogue;

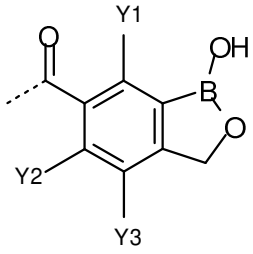
wherein said peptide spacer comprises GKPG, GKP$(G_4S)_q$, KP$(G_4S)_r$, GKPRGFFYTP$(G_4S)_s$, or TYFFGRKPD$(G_4S)_t$, wherein q is an integer from 1 to 3; r is 3; s is 2 and t is 3;

ii) two **modifying groups M,** wherein each of the modifying groups **M** is independently selected from the group of



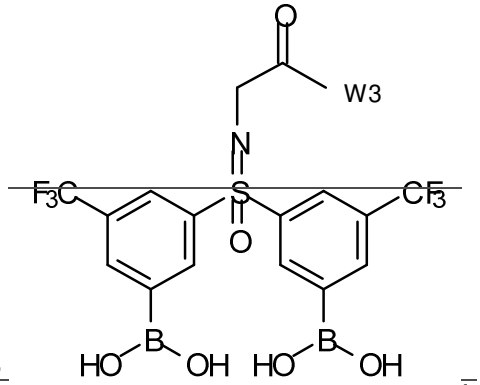
Formula M1 ,

which represents a *D*- or an *L*-amino acid form, and wherein n is 1; W1 represents NH-CH_2CH_2-C(=O)-*, or the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein R1 is of



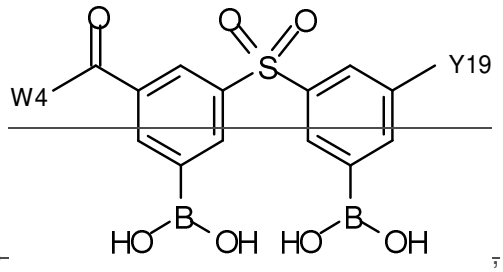
Formula R1a ,

wherein Y1 and Y2 is H, and Y3 is CF_3; and



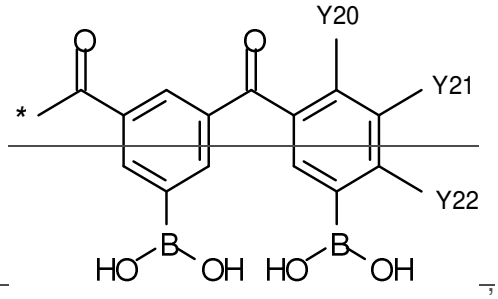
Formula M7

wherein W3 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W3 represents the *D*- or *L*- form of NH-CH(COOH)-CH_2CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue;



Formula M8

wherein W4 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W4 represents NH-CH_2-C(=O)-*, wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y19 is CF_3;



Formula M9

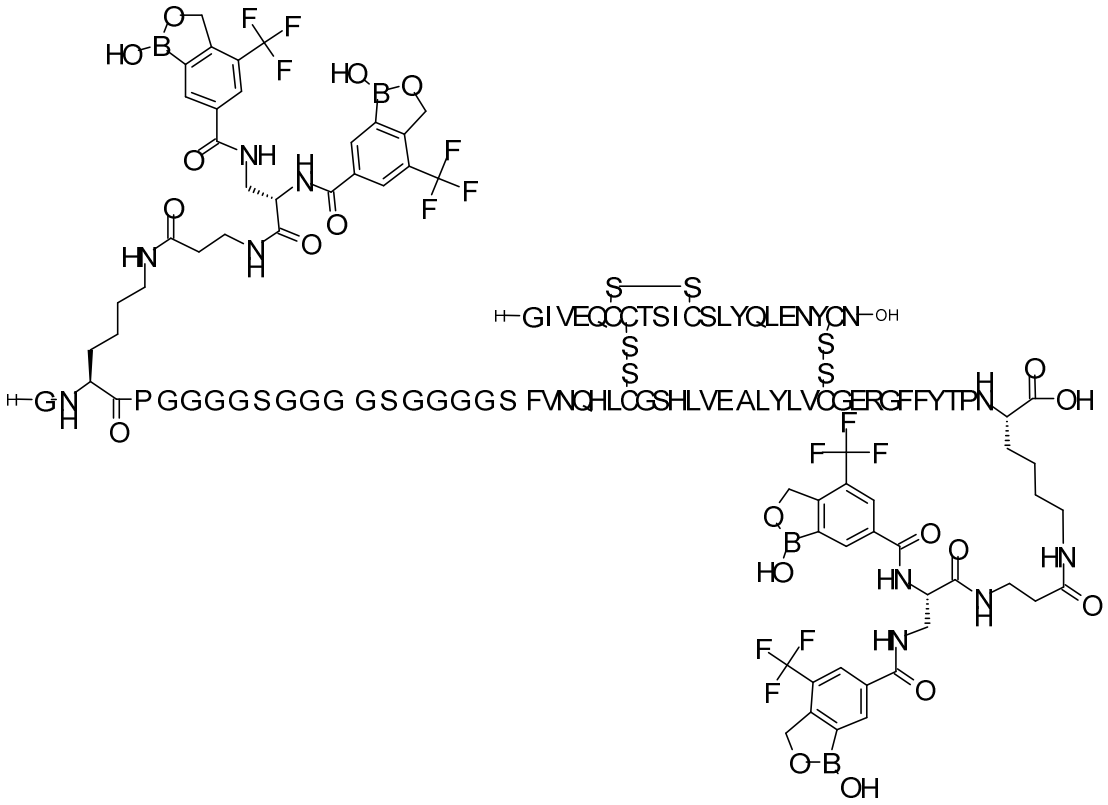
wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein each of Y20, Y21, and Y22 is independently selected from H, and F; with the provisio that when Y21 is F, then Y20 and Y22 are H; and when Y21 is H, then Y20 and Y22 are F; and

wherein one modifying group M is attached to the epsilon amino group of a lysine in position 29 of the B-chain of said human insulin or human insulin analogue; and one modifying group M is attached to

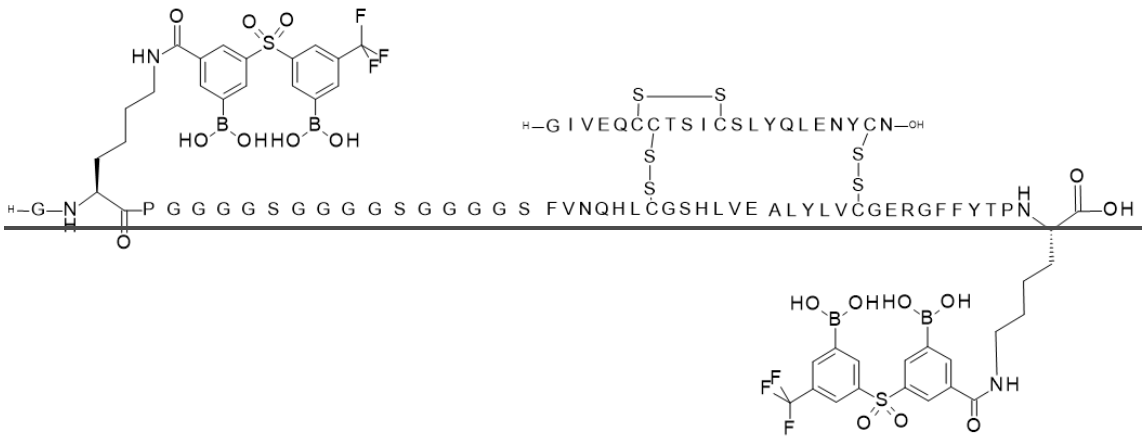
the epsilon amino group of a lysine residue in position 1 or position 4 of the B-chain of said human insulin analogue; or

the epsilon amino group of a lysine in said optional peptide spacer at the N-terminal of the B-chain of said human insulin or human insulin analogue.

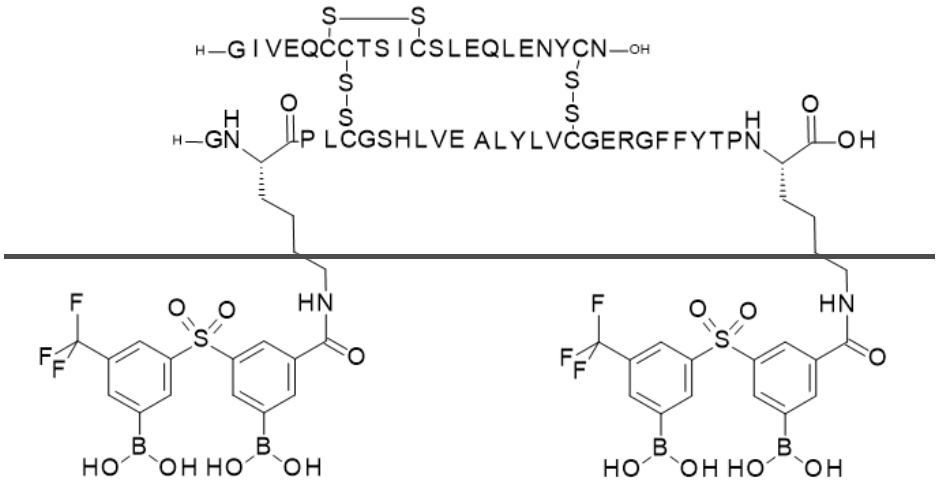
~~9.~~8. The compound according to any one of claims 1 to ~~8~~ 7, wherein the compound is selected from the group of:



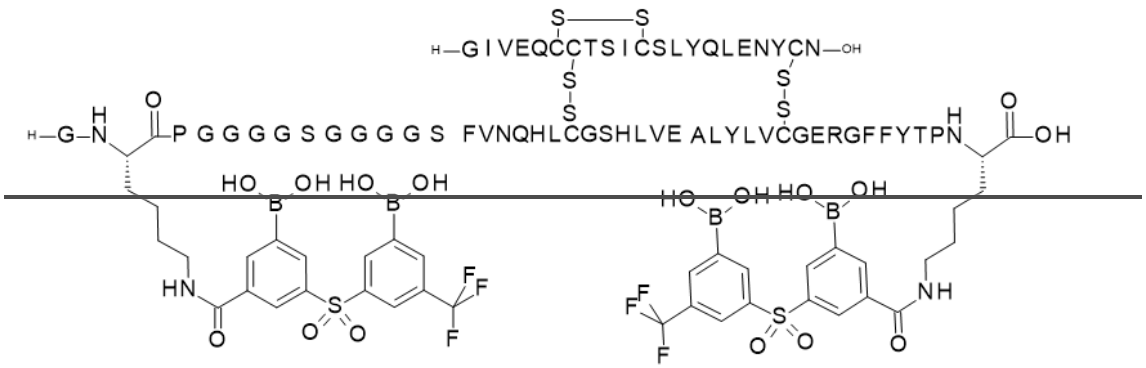
(the compound of Example 280);



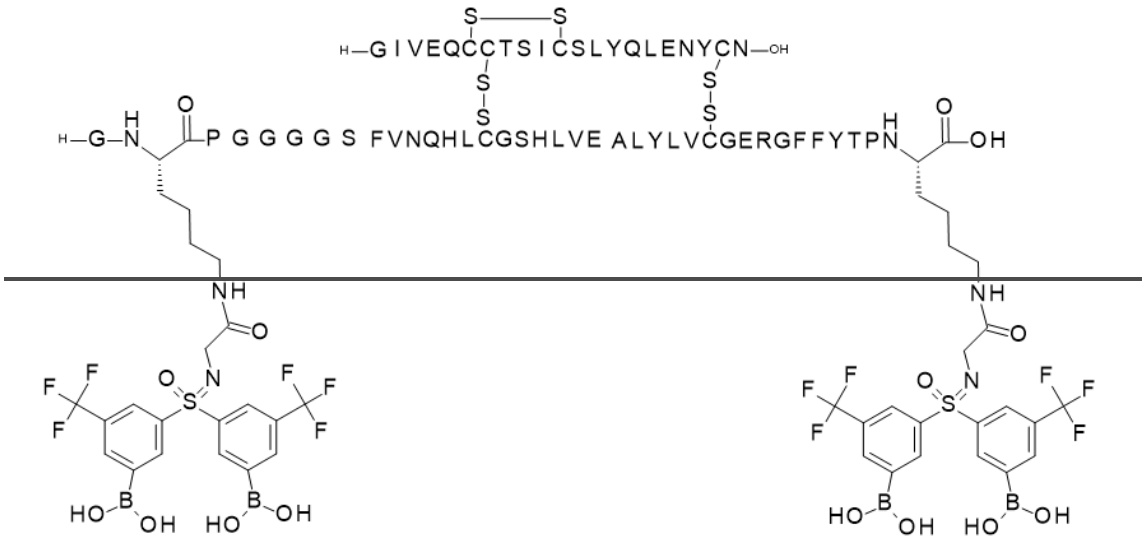
(the compound of Example 284);



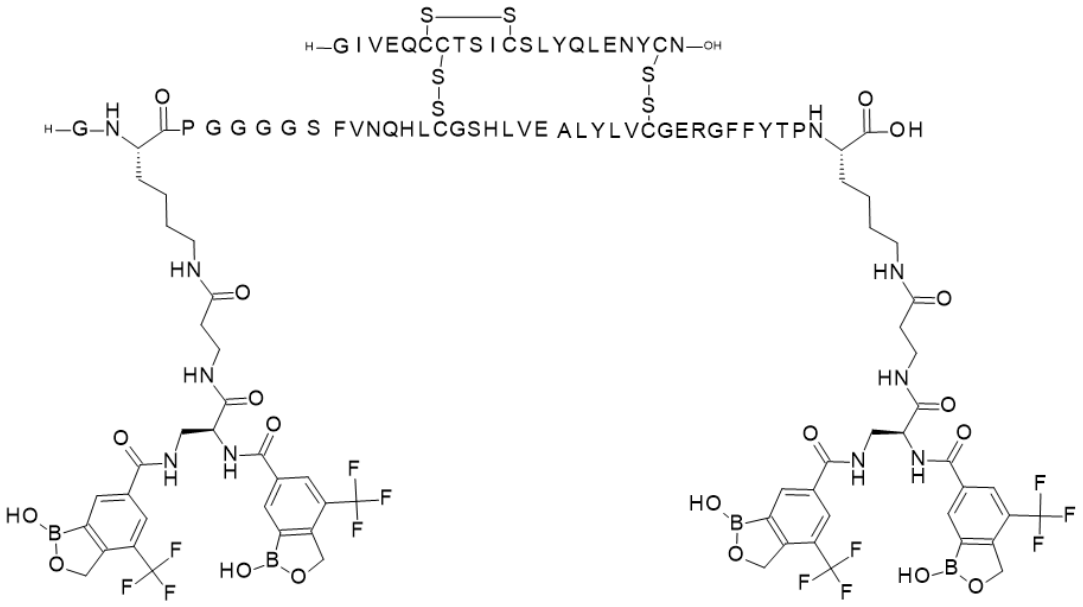
(the compound of Example 285);



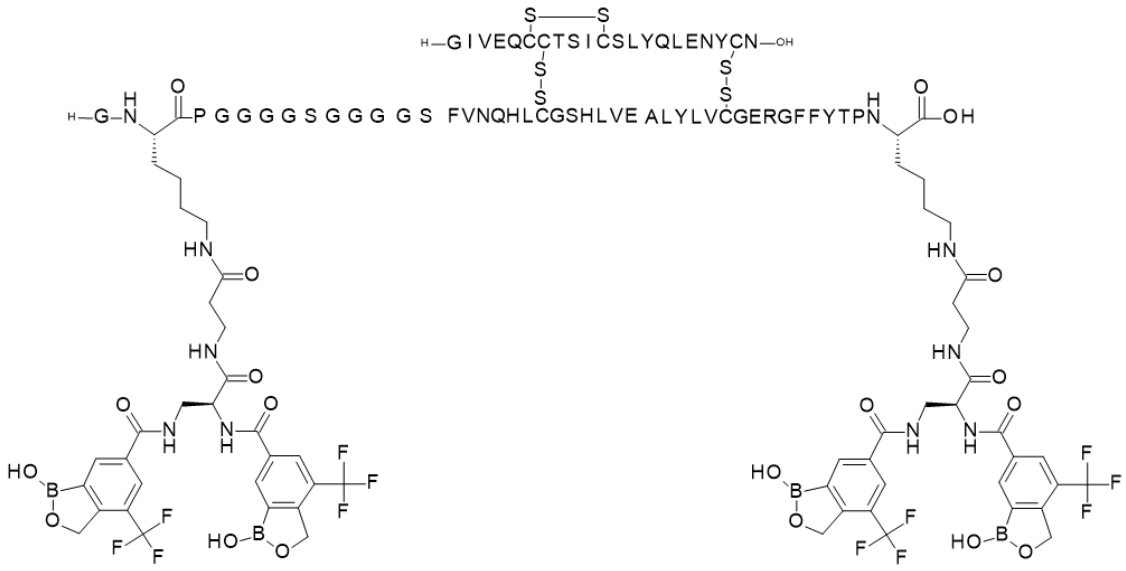
~~(the compound of Example 288);~~



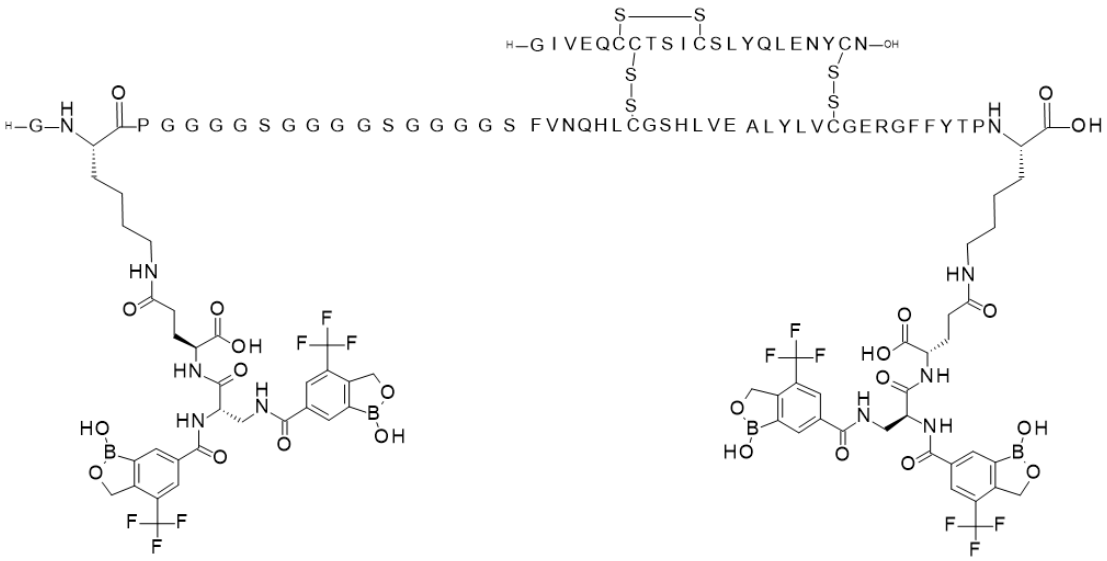
~~(the compound of Example 291);~~



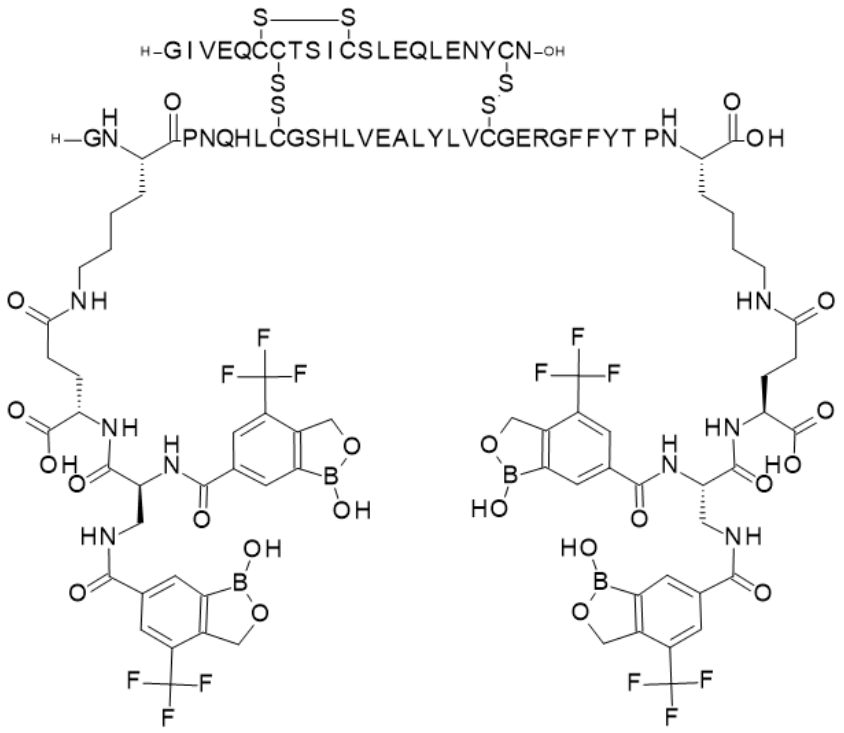
(the compound of Example 300);



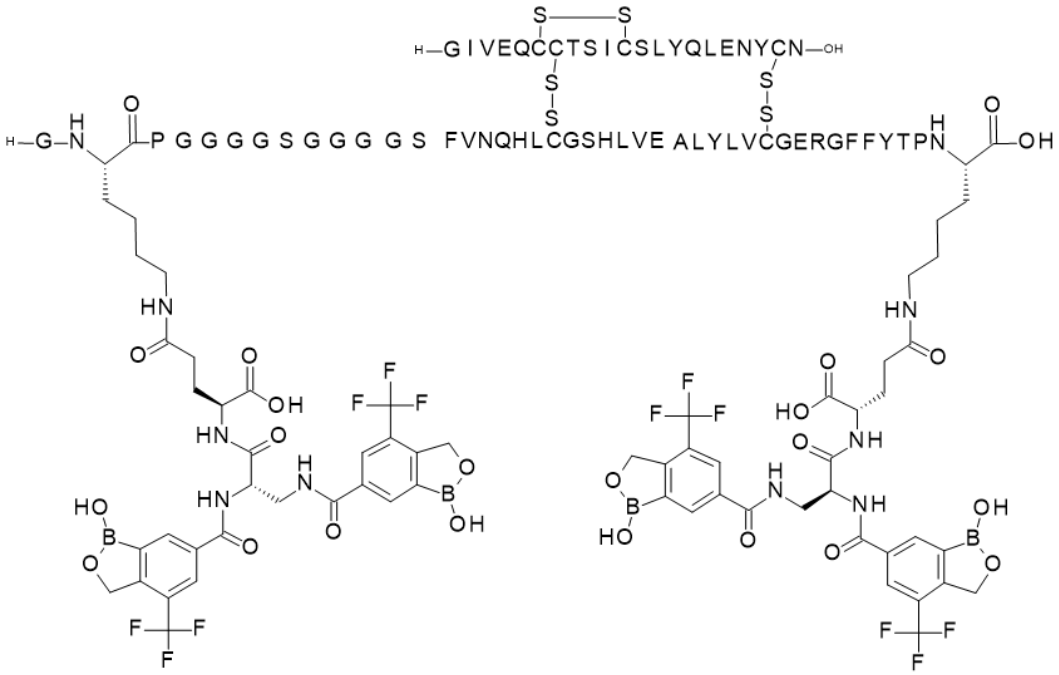
(the compound of Example 301);



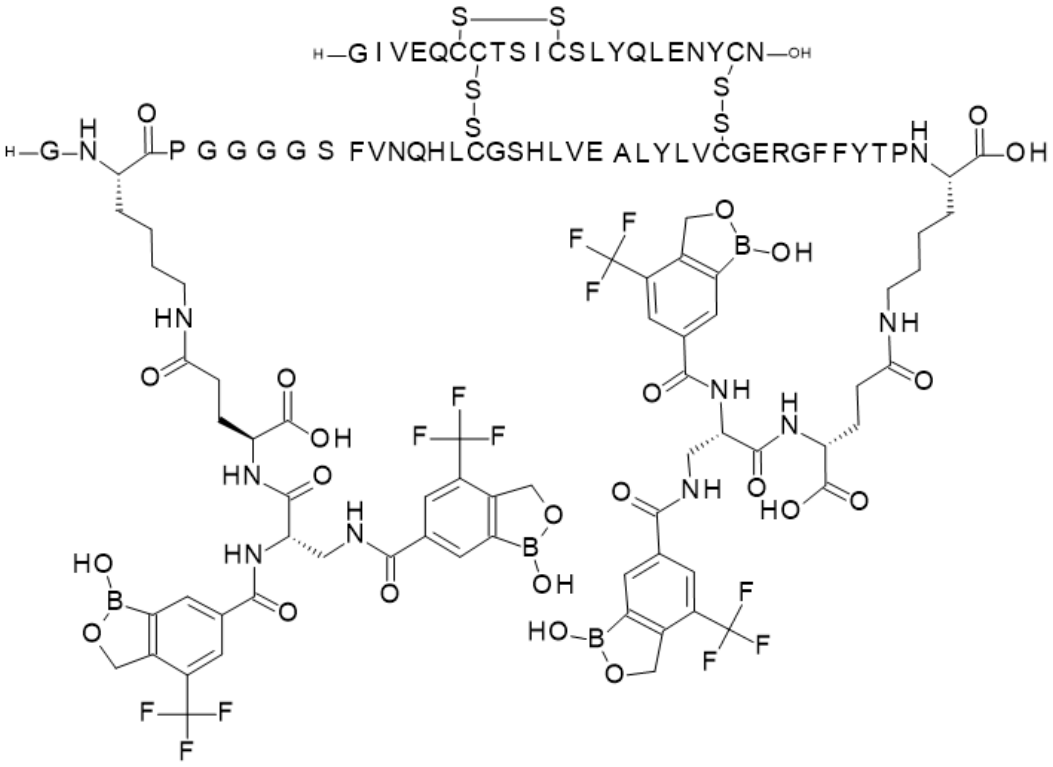
(the compound of Example 324);



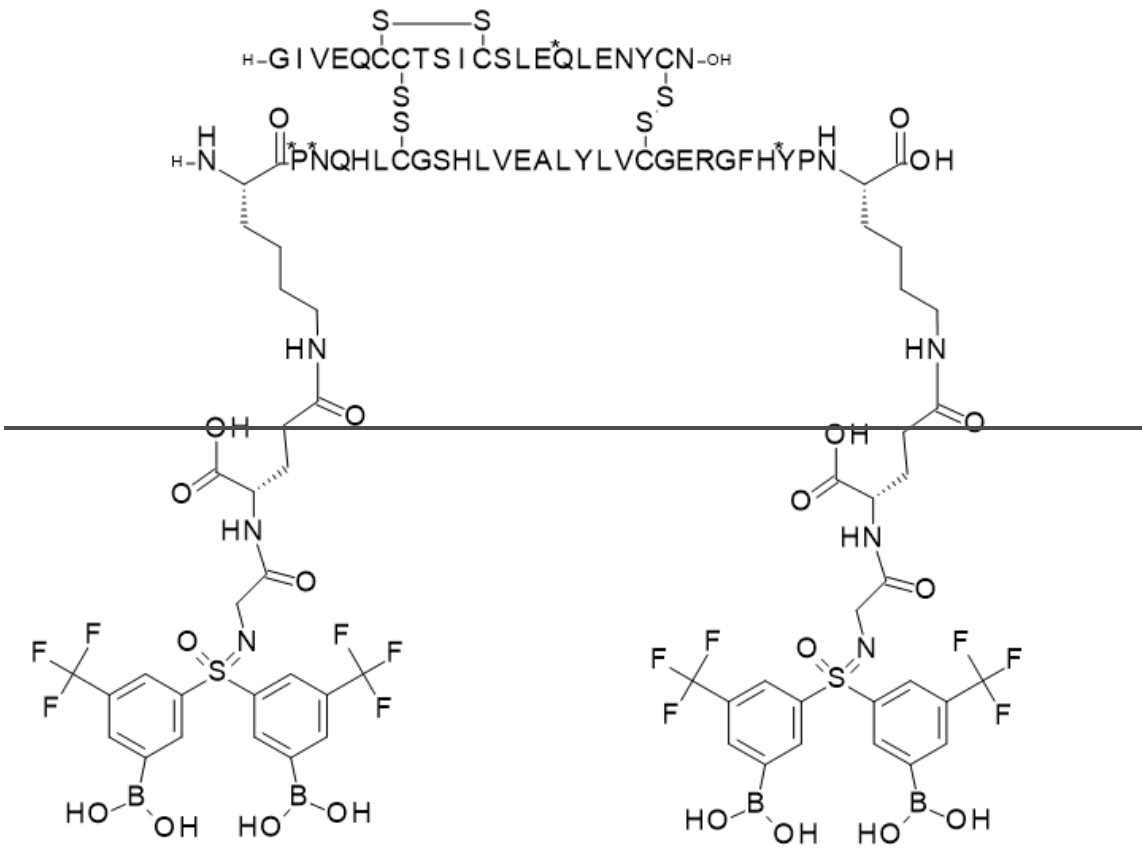
(the compound of Example 327);



(the compound of Example 331); and

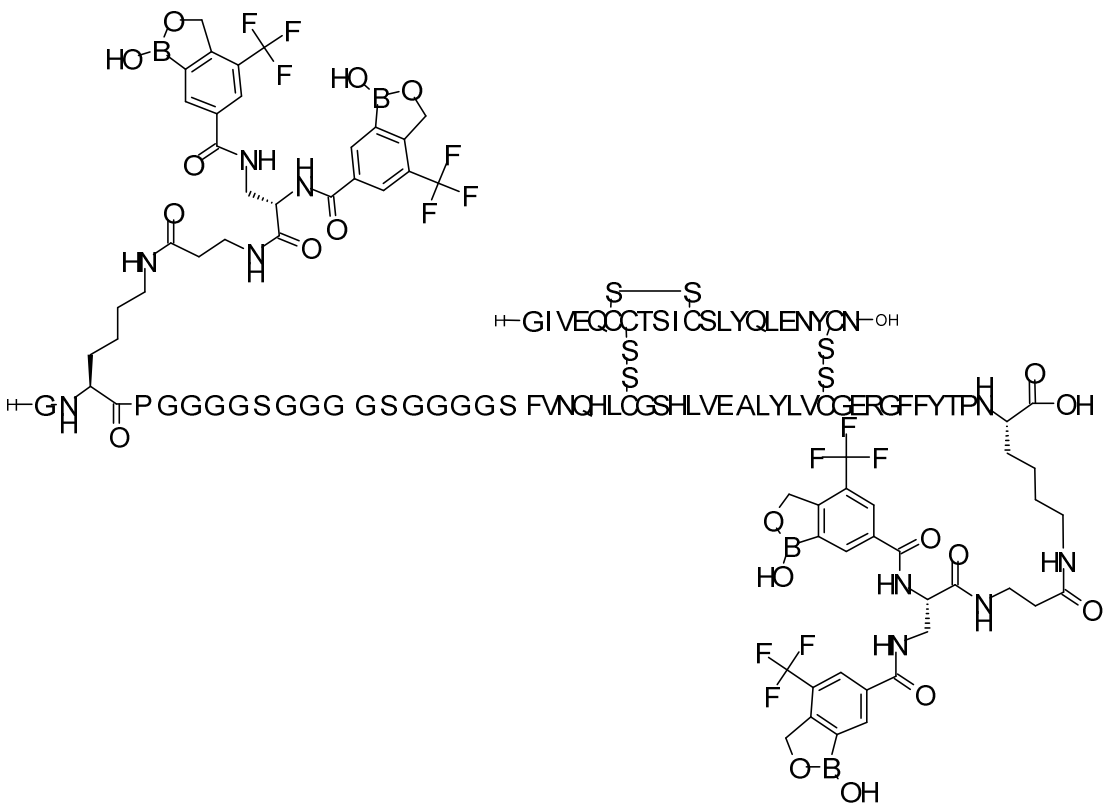


(the compound of Example 333).; and



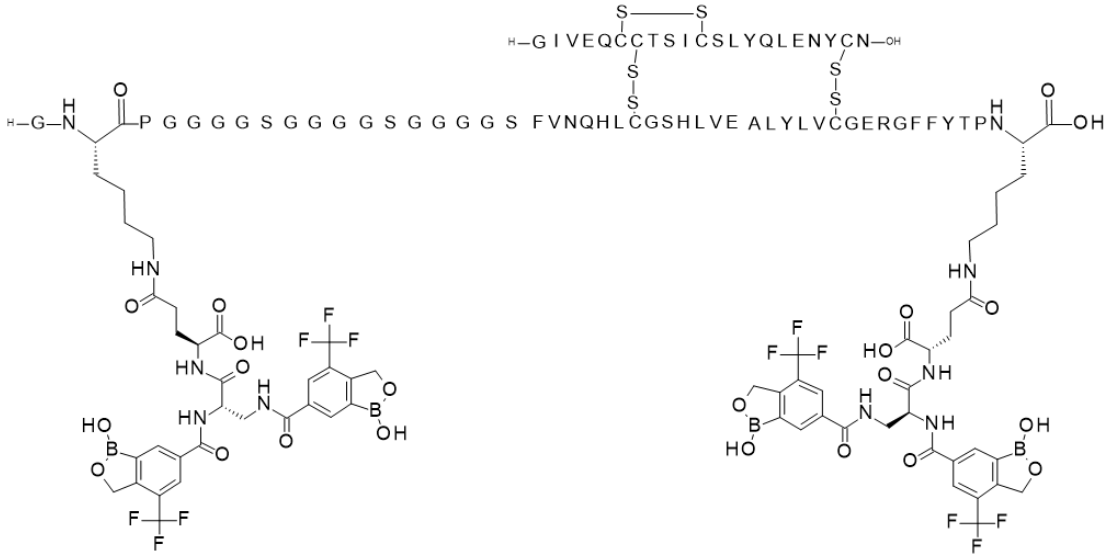
~~(the compound of Example 335).~~

9. The compound according to any one of claims 1 to 8, wherein the compound is



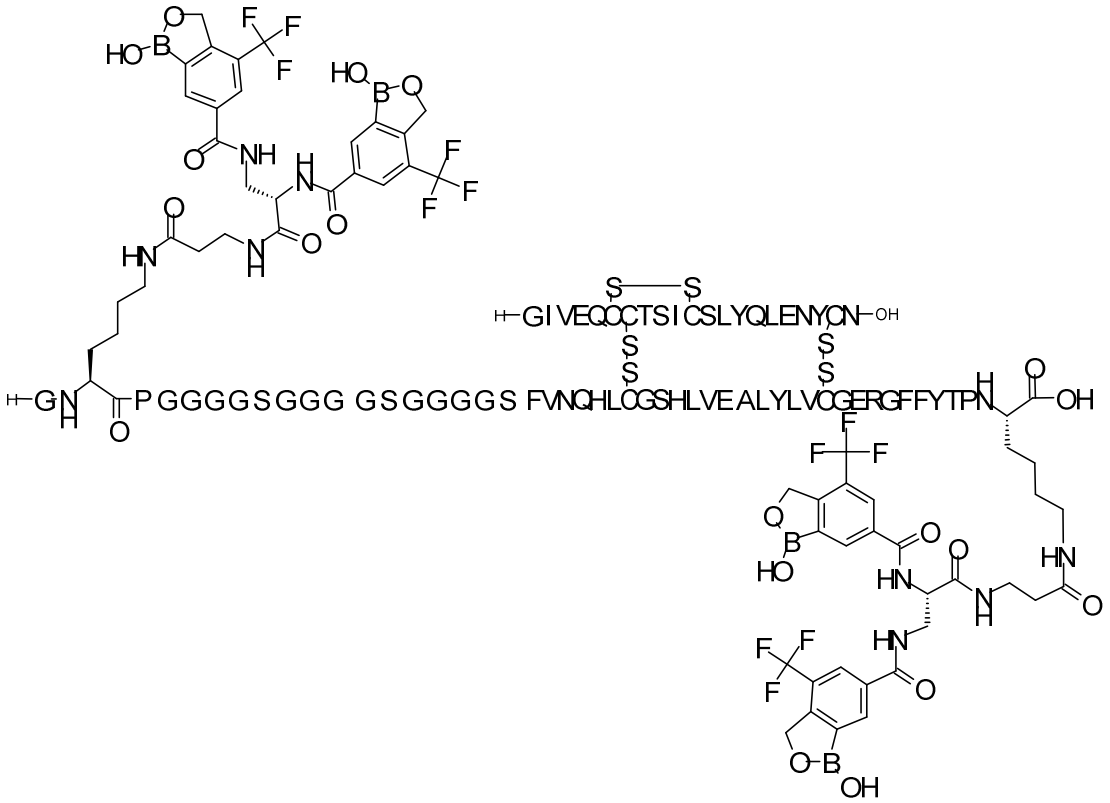
(the compound of Example 280).

10. The compound according to any one of claims 1 to 8, wherein the compound is



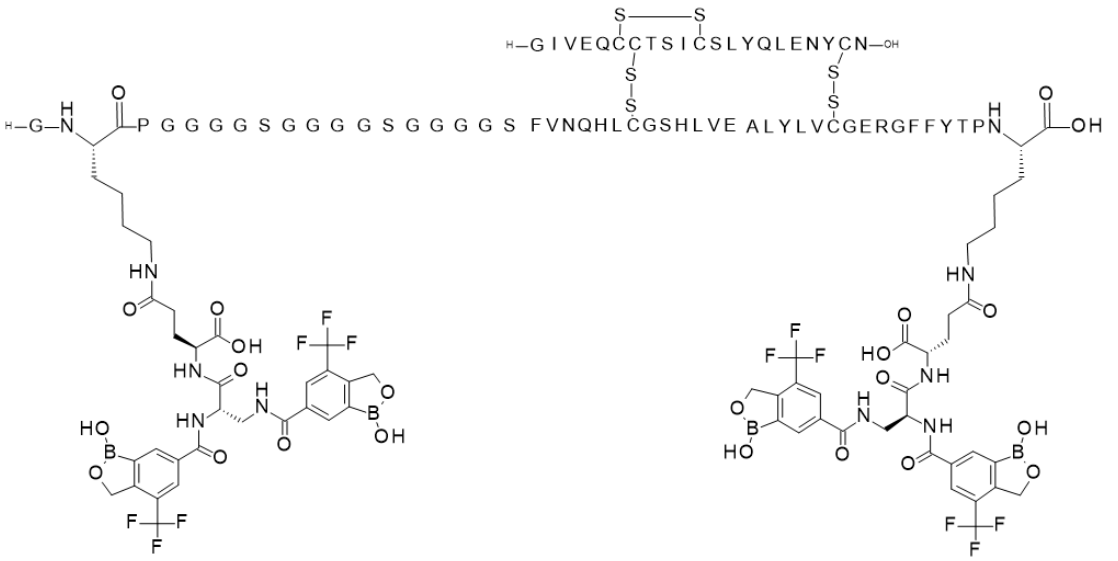
(the compound of Example 324).

11. A compound, wherein the compound is



(the compound of Example 280).

12. A compound, wherein the compound is



(the compound of Example 324).

~~10.~~13. An intermediate product selected from the group consisting of

A14E desB1-B2 B4K B5P desB30 human insulin (SEQ ID NO:4 and SEQ ID NO:16);

A14E desB1-B2 B3G B4K B5P desB30 human insulin (SEQ ID NO:4 and SEQ ID NO:17);

A14E B-1G B1K B2P desB30 human insulin (SEQ ID NO:4 and SEQ ID NO:18);

A22K B22K B29R desB30 human insulin (SEQ ID NO:6 and SEQ ID NO:20);

A21Q (GES)3K desB30 human insulin (SEQ ID NO:8 and SEQ ID NO:11);

A21Q (GES)6K desB30 human insulin (SEQ ID NO:9 and SEQ ID NO:11);

A21Q (GES)12K desB30 human insulin (SEQ ID NO:10 and SEQ ID NO:11);

B1-KPGGGGSGGGGSGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:21);

B1-KPGGGGSGGGGSGGGGS A14E B25H desB30 human insulin (SEQ ID NO:4 and SEQ ID NO:22);

B1-GKPGGGGSGGGGSGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:23);

B1-GKPGGGGSGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:24);

B1-GKPGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:25);

B1-GKPG desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:26);

B1-GKPRGFFYTPGGGGSGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:27); and

B1-TYFFGRKPDGGGGSGGGGSGGGGS desB30 human insulin (SEQ ID NO:1 and SEQ ID NO:28).

~~11.~~14. A composition comprising a compound according to any one of claims ~~1-9~~ 1 to 12.

~~12.~~15. A compound according to any one of claims ~~1-9~~ 1 to 12, for use as a medicament.

~~13.~~16. A compound according to any one of claims ~~1-9~~ 1 to 12, for use in the prevention or treatment of diabetes, diabetes of Type 1, diabetes of Type 2, impaired glucose tolerance, hyperglycemia, and metabolic syndrome (metabolic syndrome X, insulin resistance syndrome).

~~14.~~17. Use of a compound according to any one of claims ~~1-9~~ 1 to 12 in the manufacture of a medicament for the treatment or prevention of diabetes, diabetes of Type 1, diabetes of Type 2, impaired glucose tolerance, hyperglycemia, and metabolic syndrome (metabolic syndrome X, insulin resistance syndrome).