CLAIMS

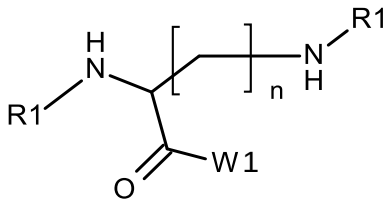
1. A compound comprising

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

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

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

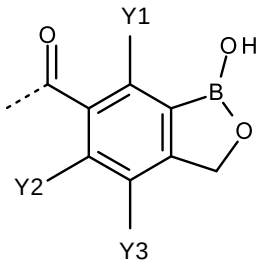
the *D*- or *L*-form of $NH\text{-}CH(COOH)\text{-}CH_2CH_2\text{-}C(=O)\text{-}*$,

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

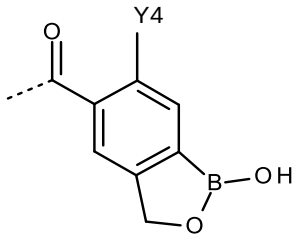
$NH\text{-}CH_2CH_2\text{-}C(=O)\text{-}NH\text{-}(CH_2)_2\text{-}O\text{-}(CH_2)_2\text{-}O\text{-}CH_2\text{-}CO\text{-}*$,

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

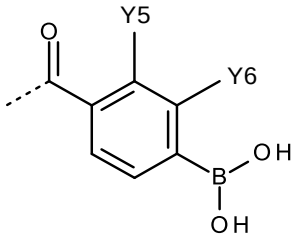
wherein R1 is selected from



Formula R1a , **Formula R1b**

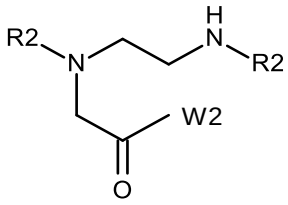


, and



Formula R1c ,

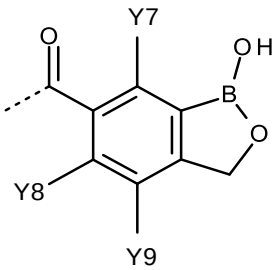
wherein Y1, Y2, Y3, Y4, Y5 and Y6 is independently selected from H, F, Cl, CHF_2, and CF_3;



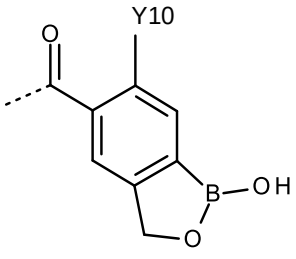
Formula M2

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

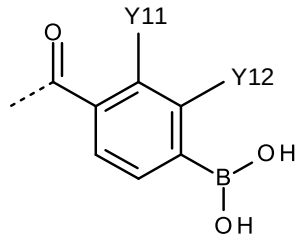
wherein R2 is selected from



Formula R2a , **Formula R2b**

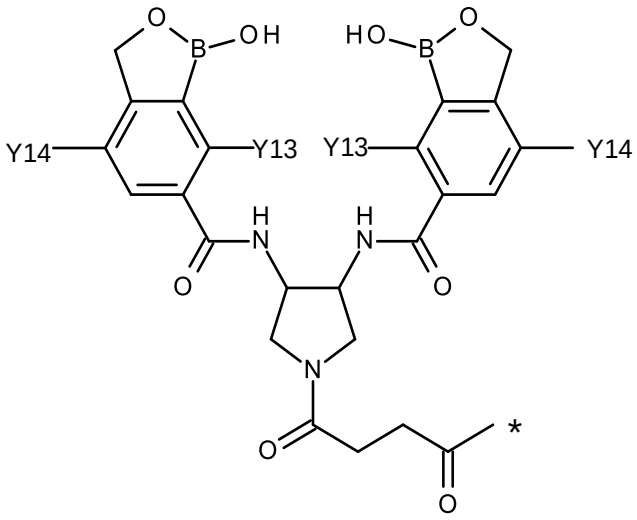


, and



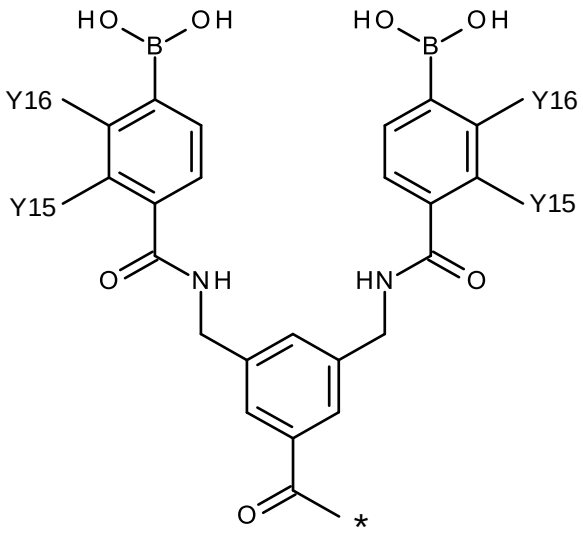
Formula R2c ,

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



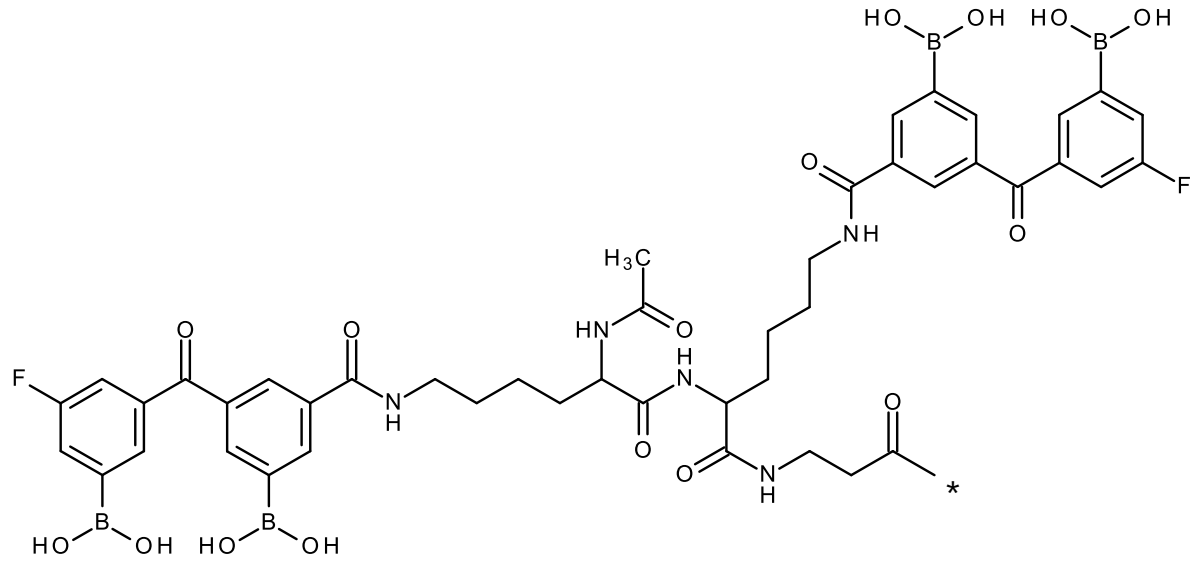
Formula M3 ,

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;



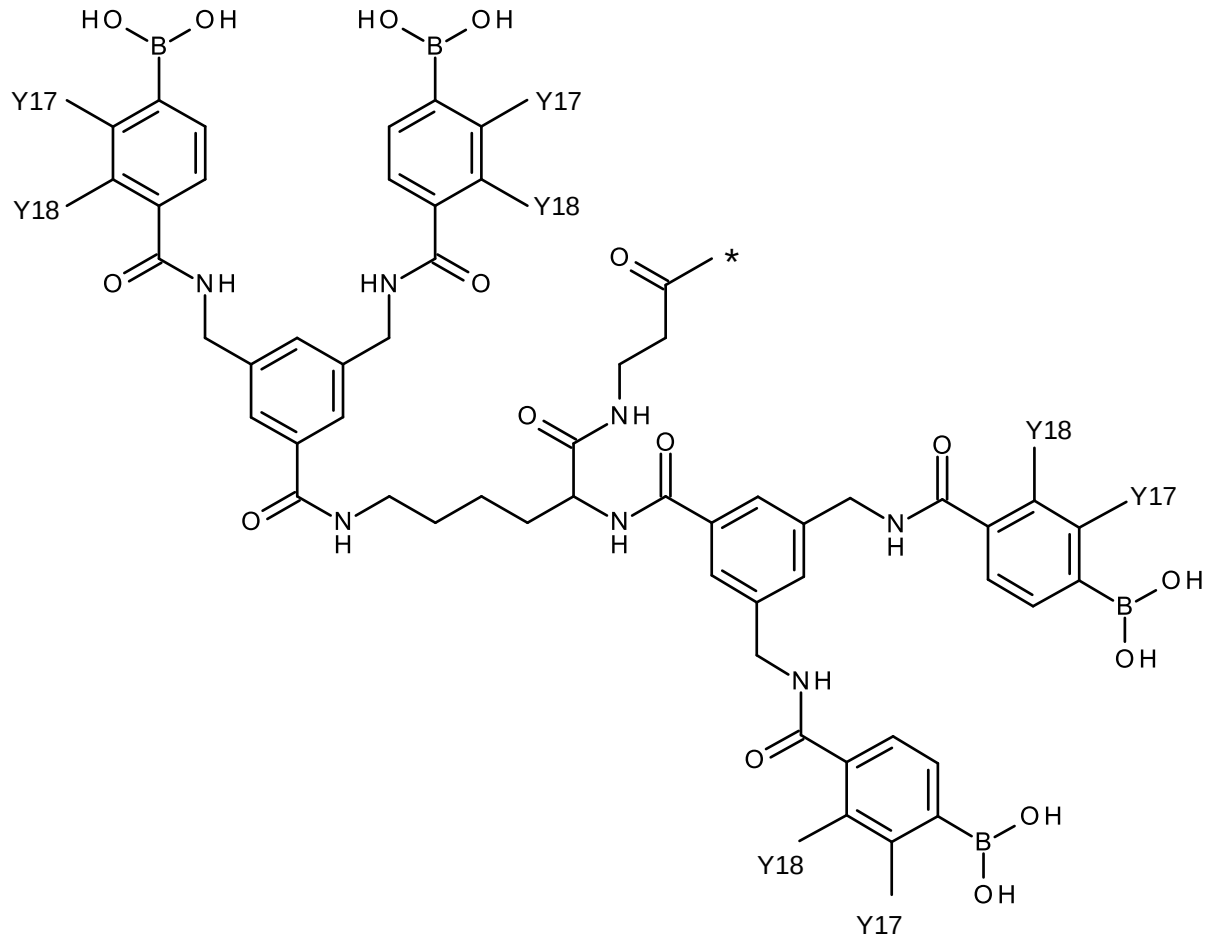
Formula M4 ,

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;



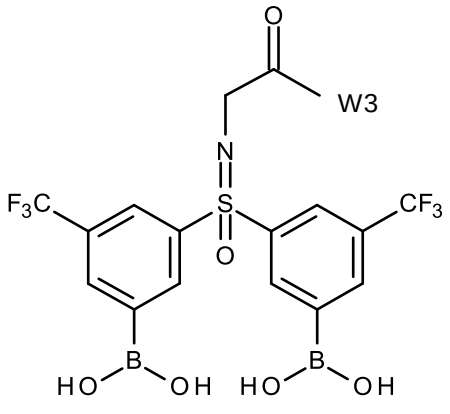
Formula M5

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

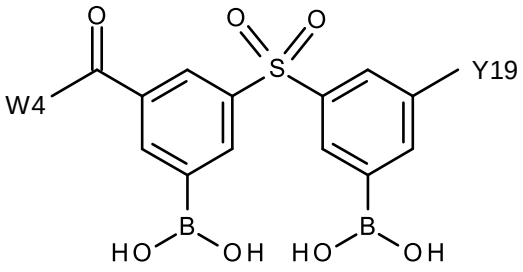
wherein the α-amino acid residue represents a *D*- or an *L*-amino acid form, and wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein Y17 and Y18 is independently selected from H, F, Cl, CHF_2, and CF_3;



Formula M7 ,

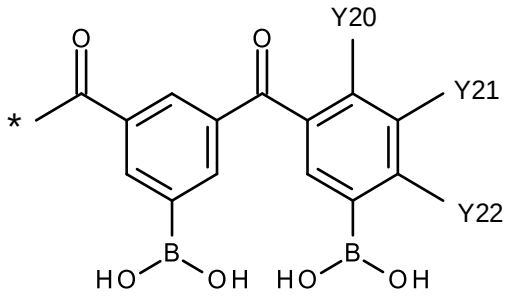
wherein W3 is absent and represents the point of attachment * to said human insulin or human insulin analogue, or W3 represents the *D*- or *L*-form of NH-CH(COOH)-CH_2CH_2-

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



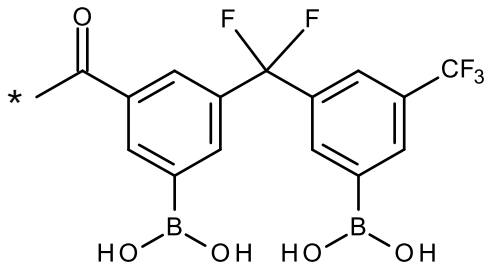
Formula M8 ,

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;



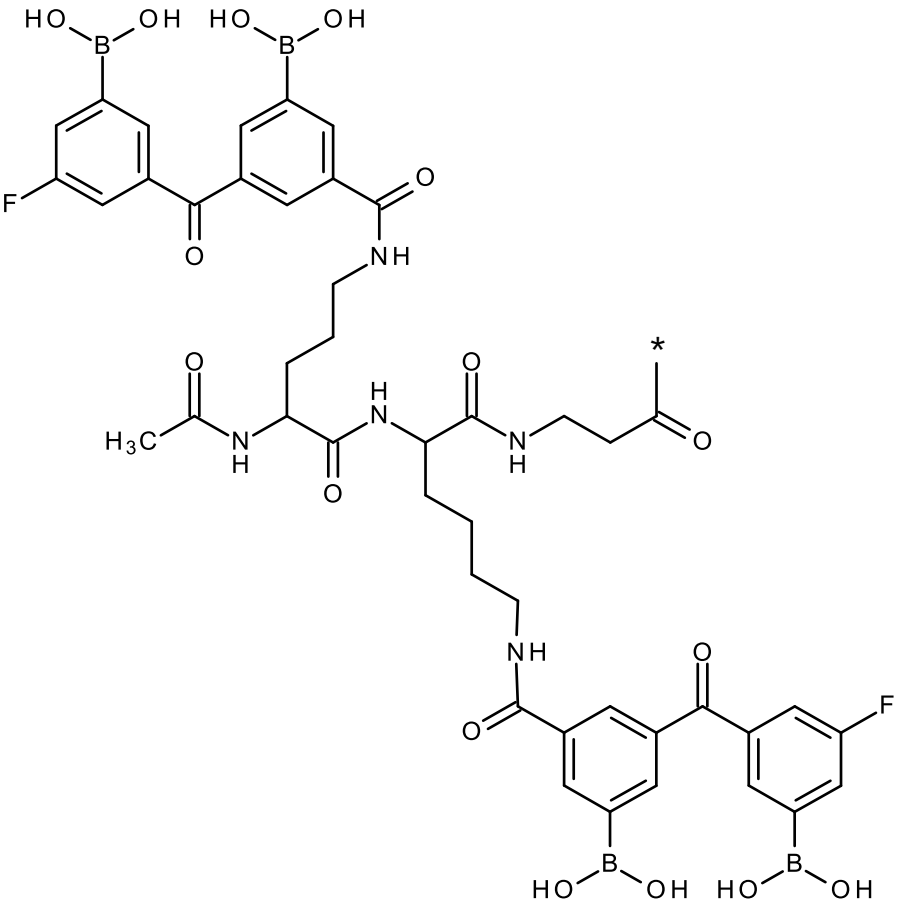
Formula M9 ,

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 ,

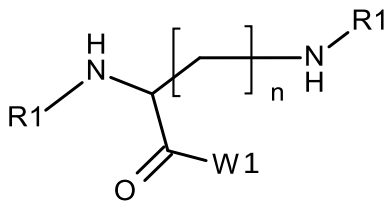
wherein * represents the point of attachment to said human insulin or human insulin analogue; and



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.

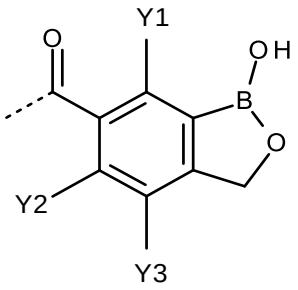
2. The compound according to claim 1, wherein each of the modifying groups **M** is independently selected from the group of



Formula M1 ,

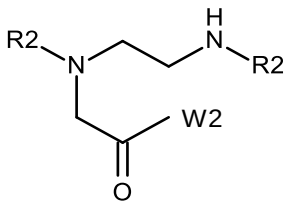
which represents a *D*- or an *L*-amino acid form, and wherein n is 1;

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



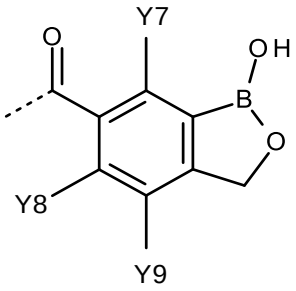
R1 is of **Formula R1a** ,

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



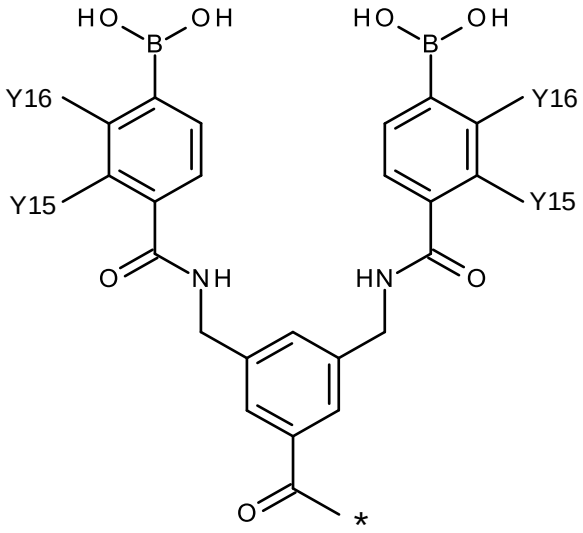
Formula M2 ,

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



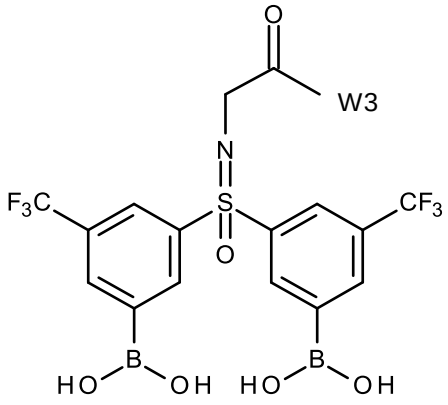
wherein R2 is of **Formula R2a** ,

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



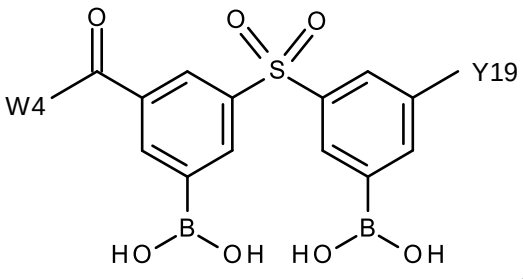
Formula M4 ,

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



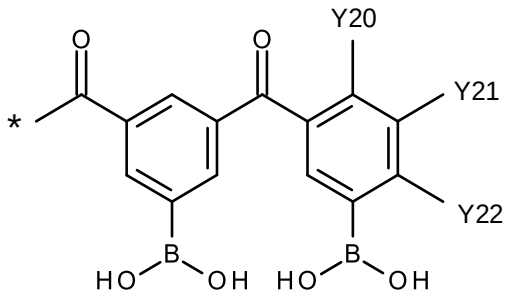
Formula M7 ,

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 ,

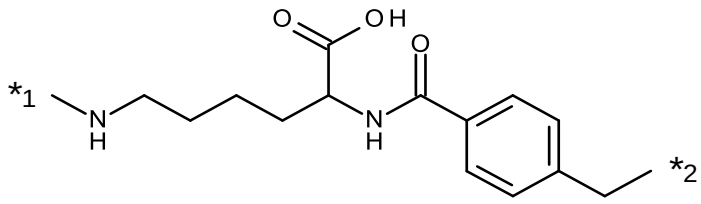
wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein each of Y20, Y21, and Y22 is independently selected from H and F; with the provisio that when Y21 is F, then Y20 and Y22 are H; and when Y21 is H, then Y20 and Y22 are F.

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

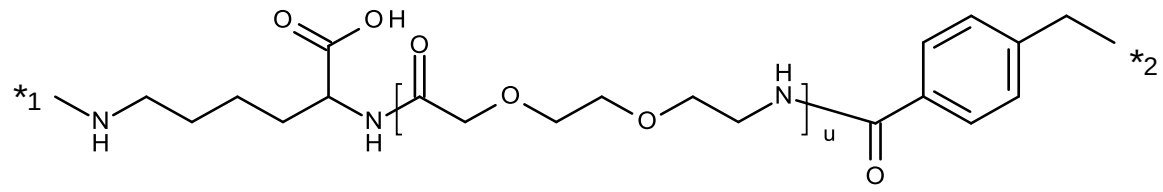
b) a peptide spacer or a linker L at the N-terminal of the B-chain of said human insulin or human insulin analogue;
wherein said peptide spacer comprises GKPG, $GKP(G_4S)_q$, $KP(G_4S)_r$, GKPRGFFYTP$(G_4S)_s$, or TYFFGRKPD$(G_4S)_t$, wherein each of q, r, s and t is independently selected from an integer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

wherein said linker L is selected from



Formula L1,

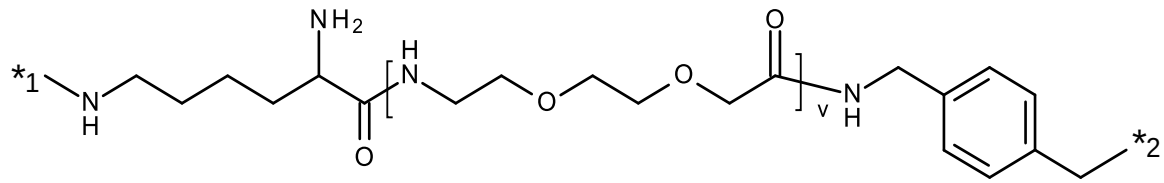
wherein *1 denotes the attachment point to the modifying group M and *2 denotes the attachment point to the amino group of the amino acid residue at the N-terminal of the B-chain of said human insulin or human insulin analogue;



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.

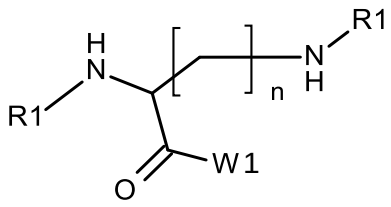
7. The compound according to any one of claims 1 to 6, wherein said human insulin or human insulin analogue is a human insulin analogue selected from the group of
desB30 human insulin;
A21Q desB30 human insulin;
A14E B25H desB30 human insulin;
A14E B1K B2P B25H desB27 desB30 human insulin;
A14E A22K 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. A compound according to any one of claims 1 to 7, 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;

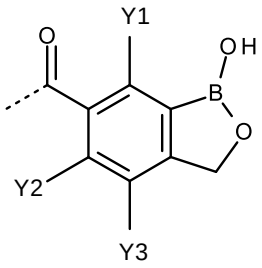
wherein said peptide spacer comprises GKPG, GKP$(G_4S)_q$, KP$(G_4S)_r$, GKPRGFFYTP$(G_4S)_s$, or TYFFGRKPD$(G_4S)_t$, wherein q is an integer from 1 to 3; r is 3; s is 2 and t is 3;

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



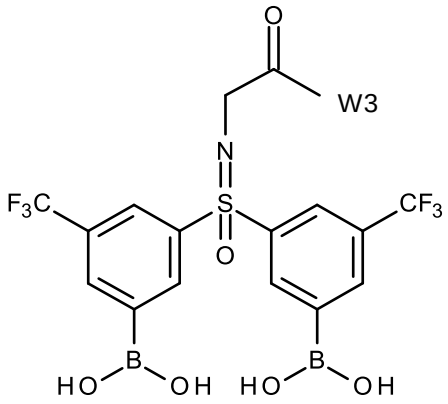
Formula M1 ,

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



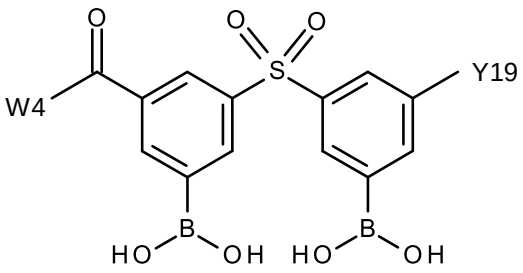
Formula R1a ,

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



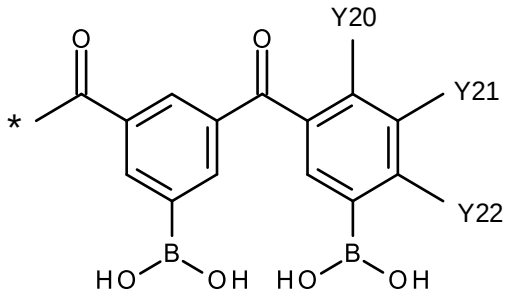
Formula M7 ,

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 ,

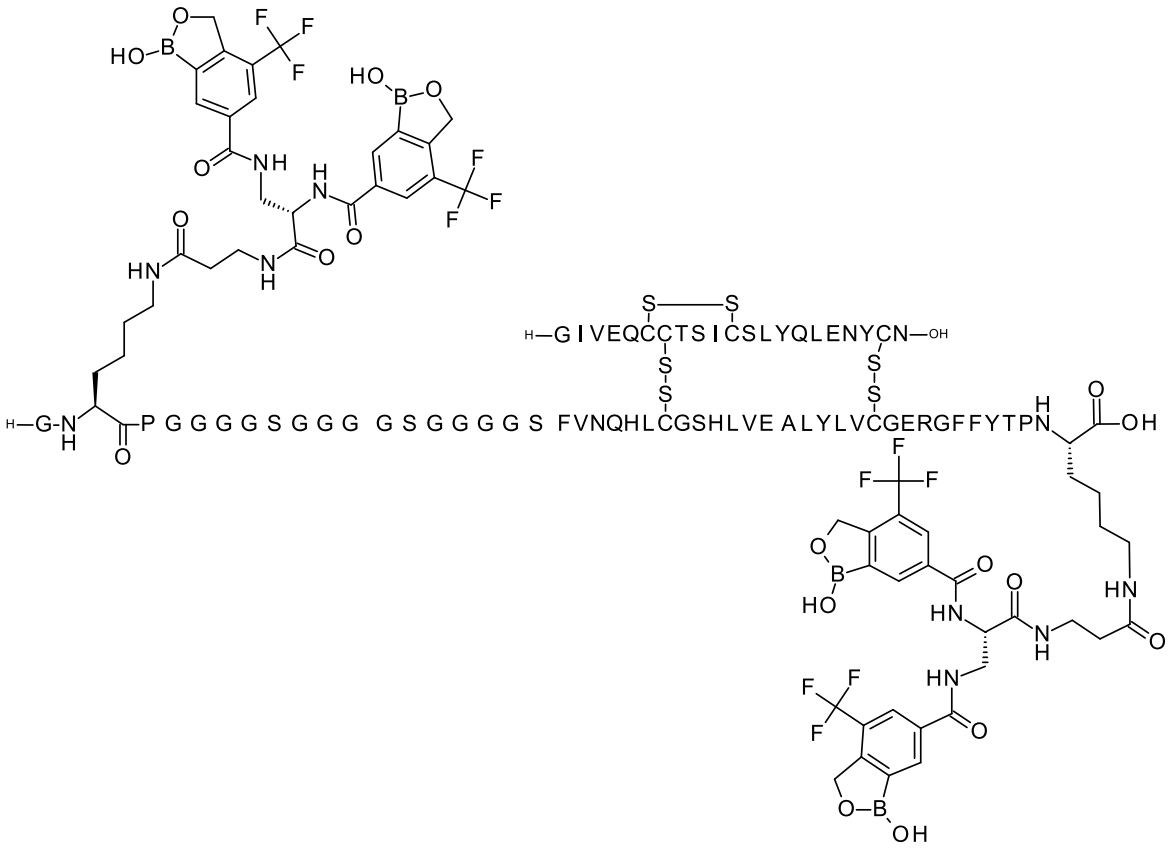
wherein * represents the point of attachment to said human insulin or human insulin analogue; and wherein each of Y20, Y21, and Y22 is independently selected from H, and F; with the provisio that when Y21 is F, then Y20 and Y22 are H; and when Y21 is H, then Y20 and Y22 are F; and

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

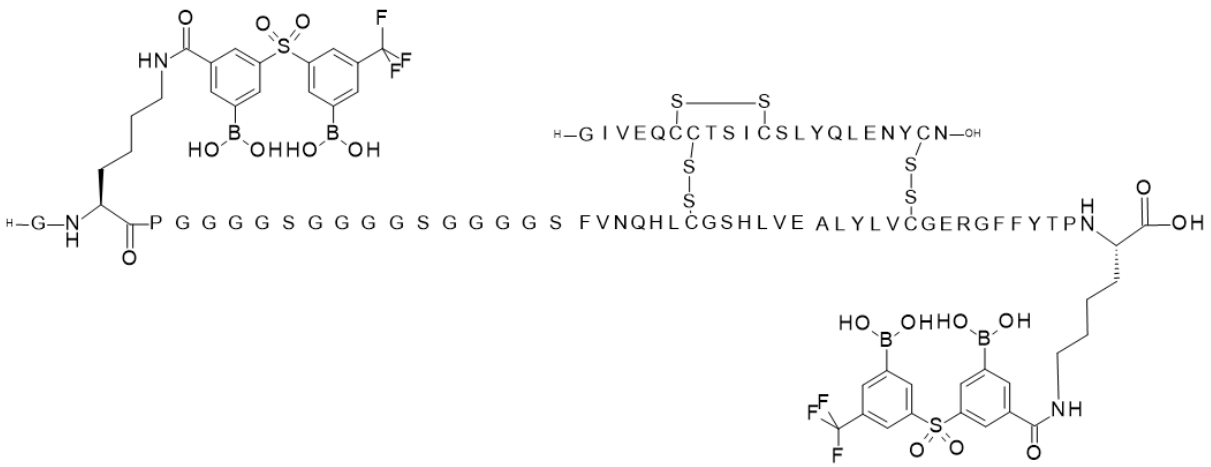
the epsilon amino group of a lysine residue in position 1 or position 4 of the B-chain of said human insulin analogue; or

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.

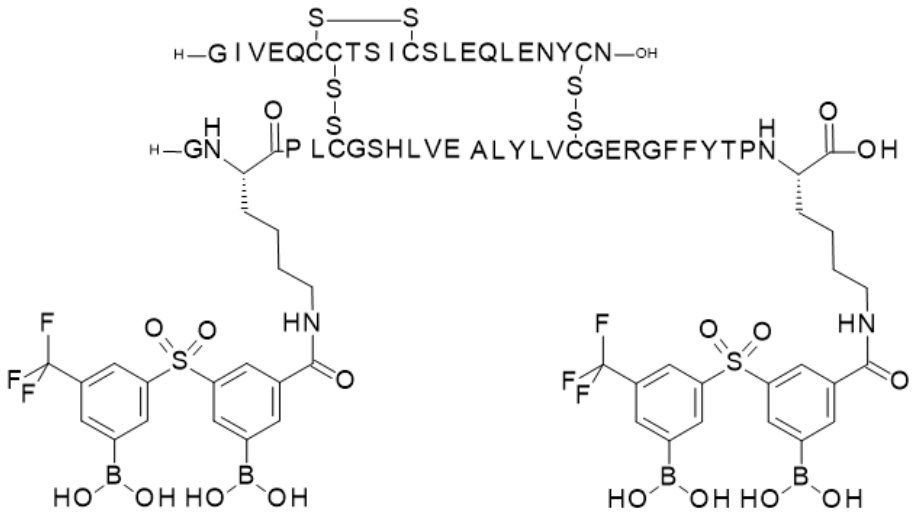
9. The compound according to any one of claims 1 to 8, wherein the compound is selected from the group of:



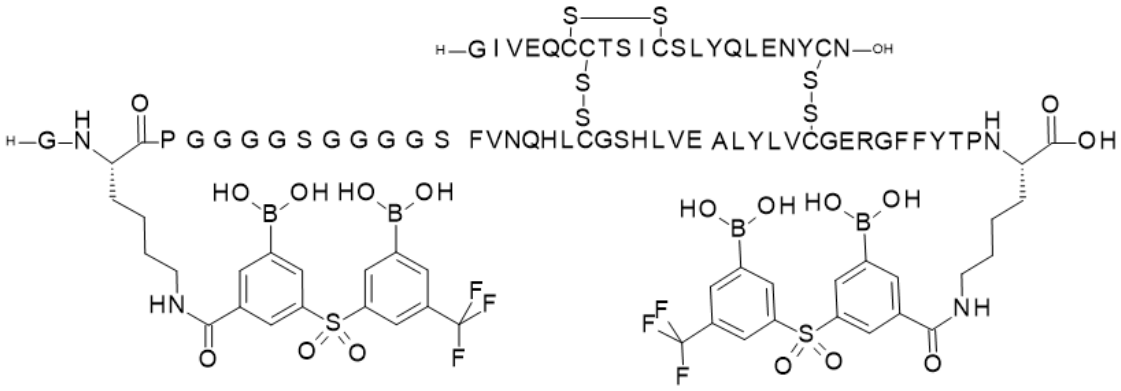
(the compound of Example 280);



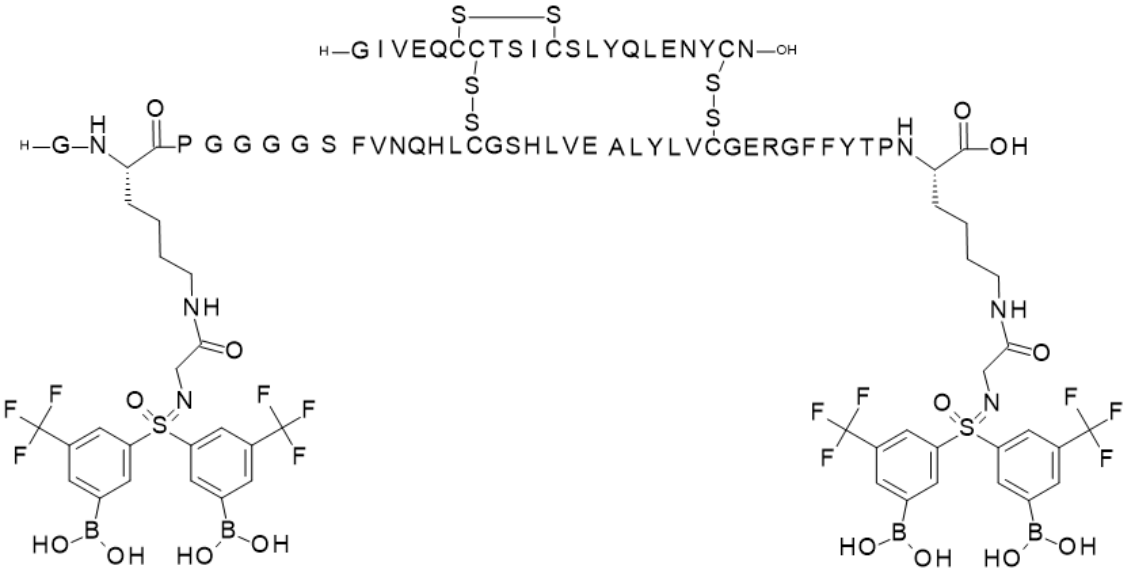
(the compound of Example 284);



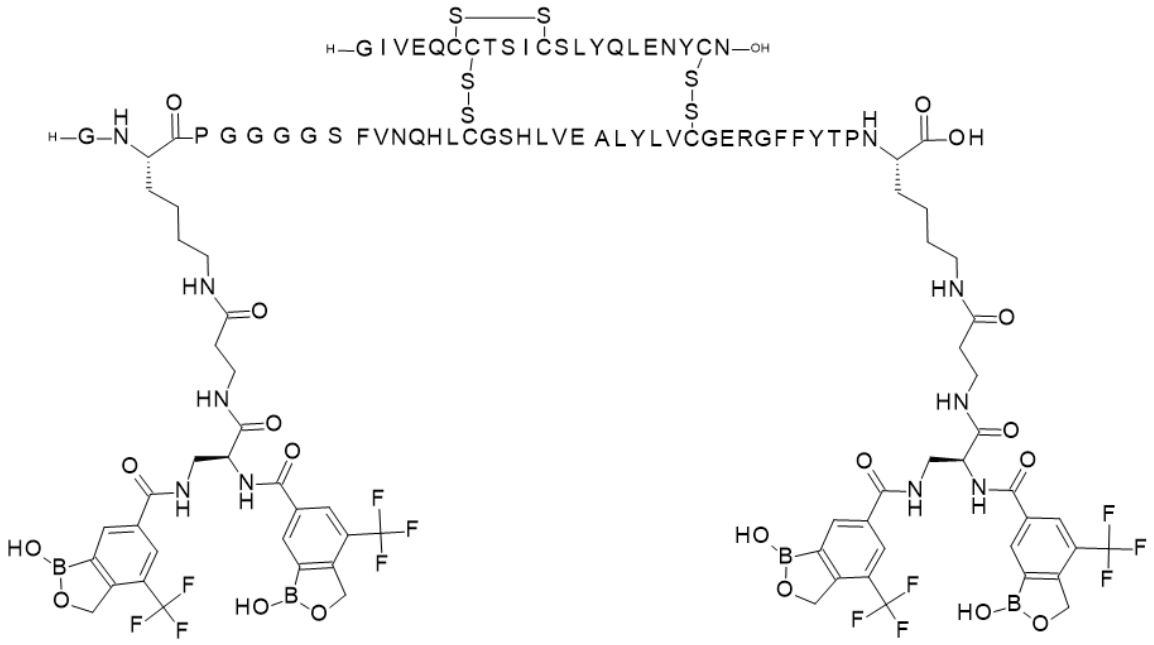
(the compound of Example 285);



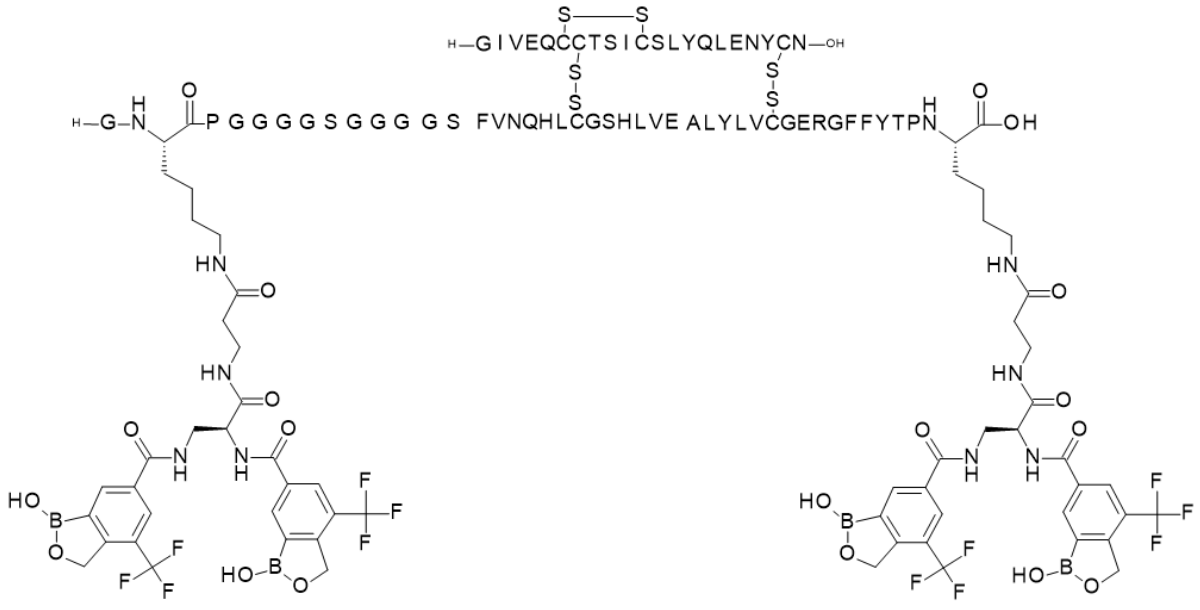
(the compound of Example 288);



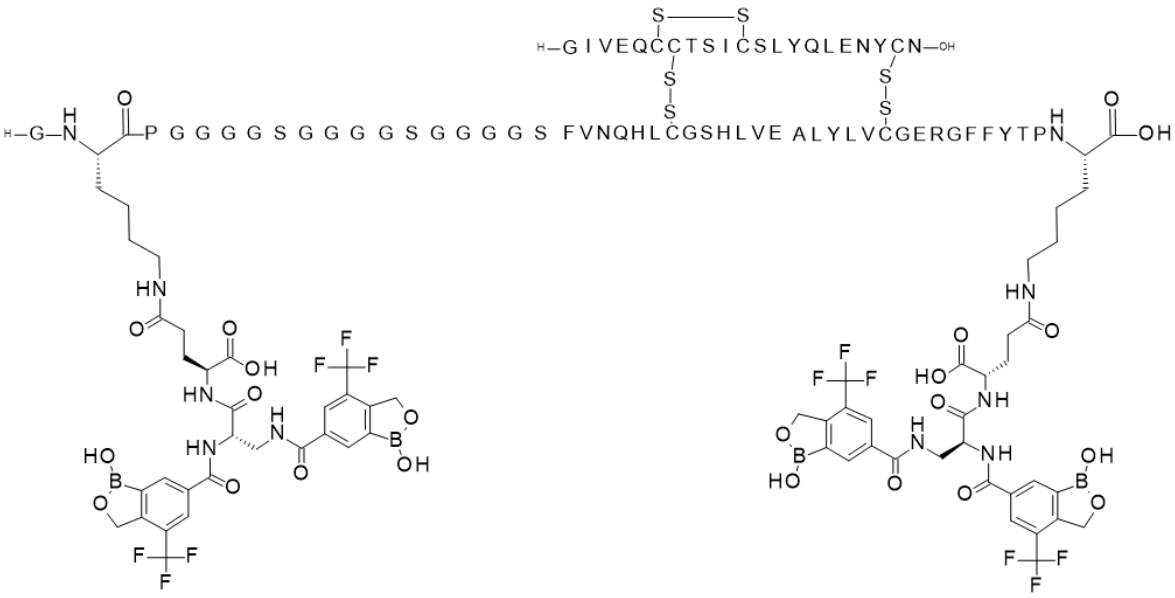
(the compound of Example 291);



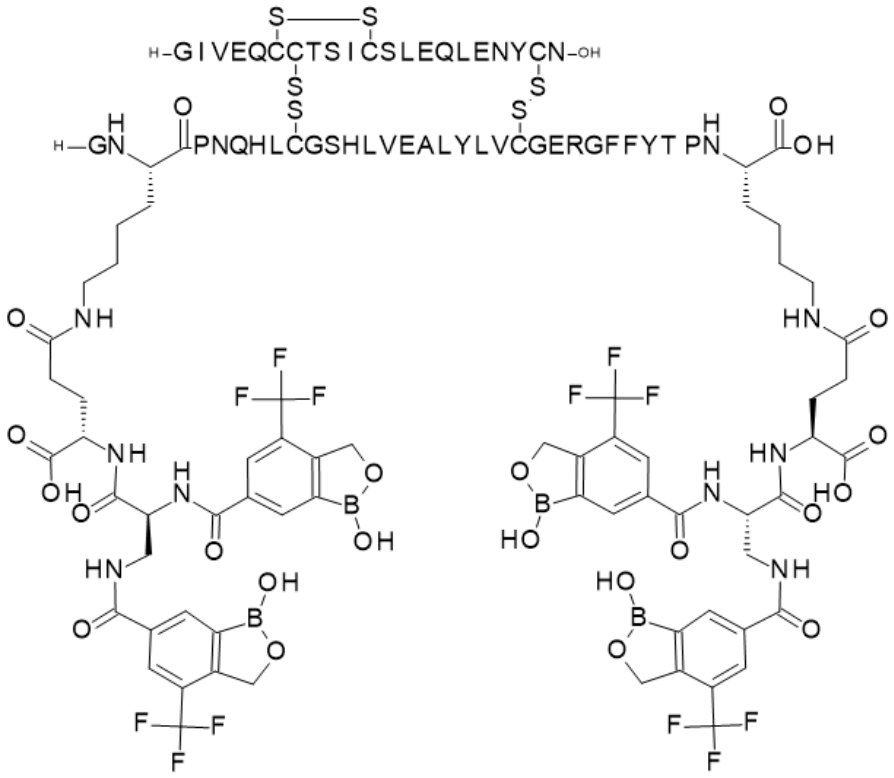
(the compound of Example 300);



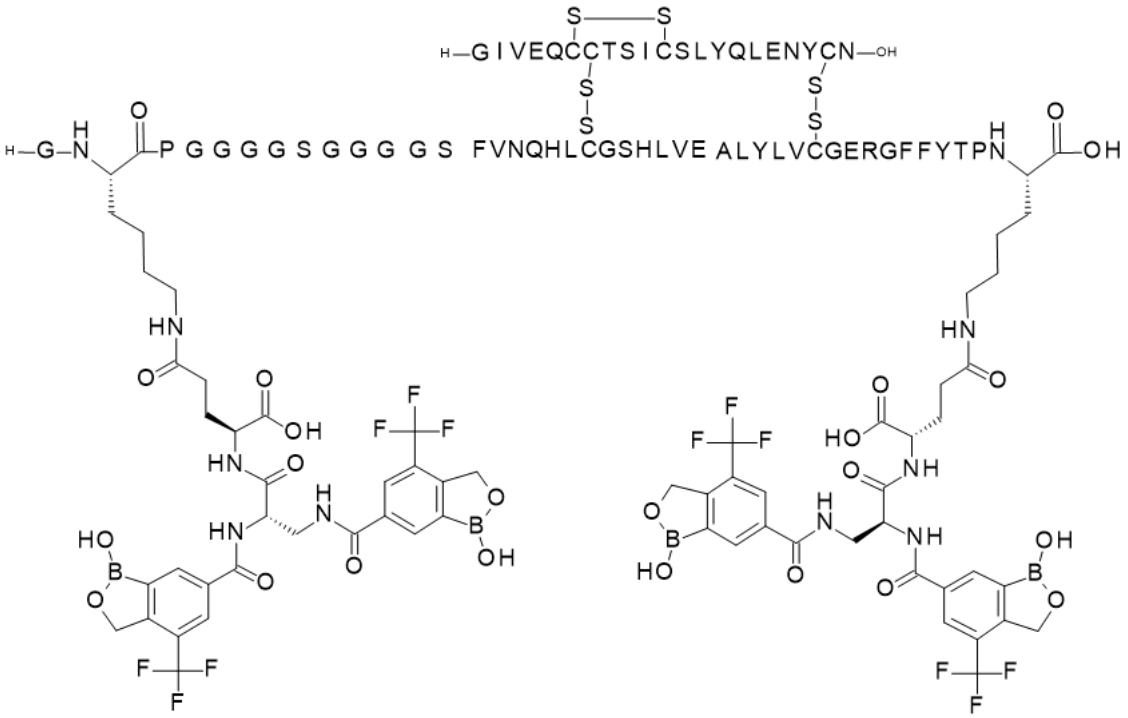
(the compound of Example 301);



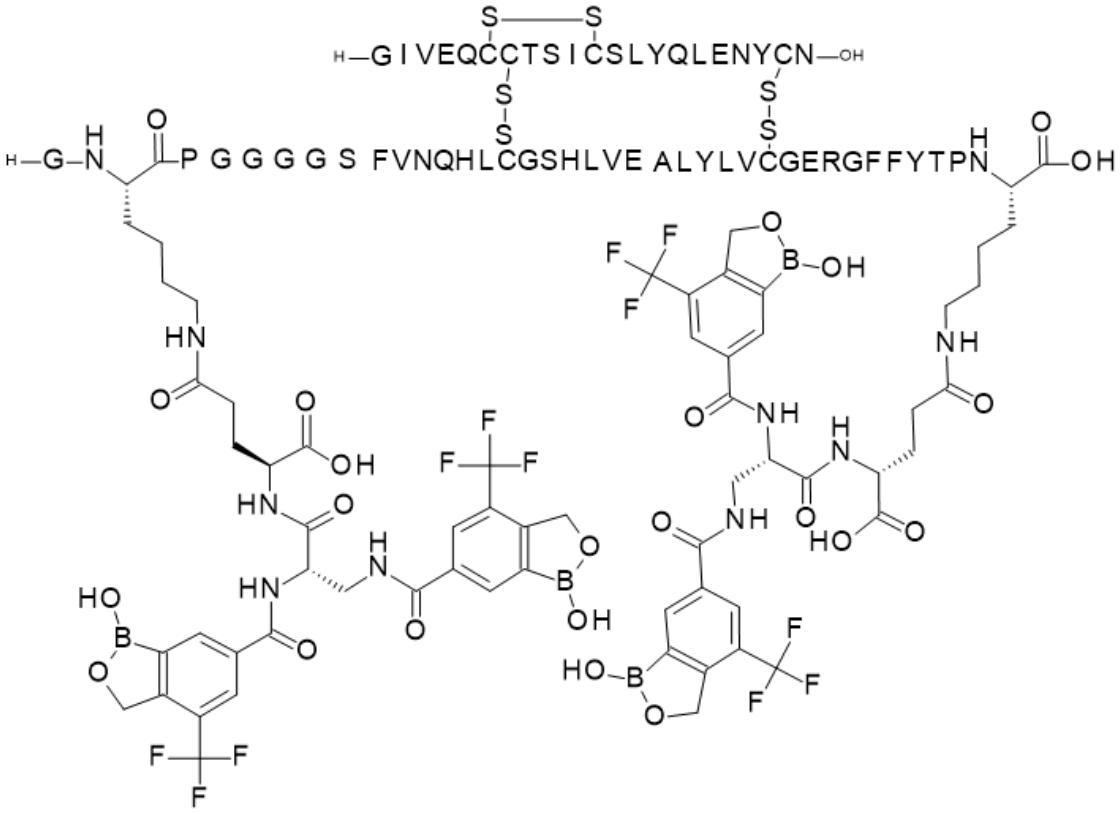
(the compound of Example 324);



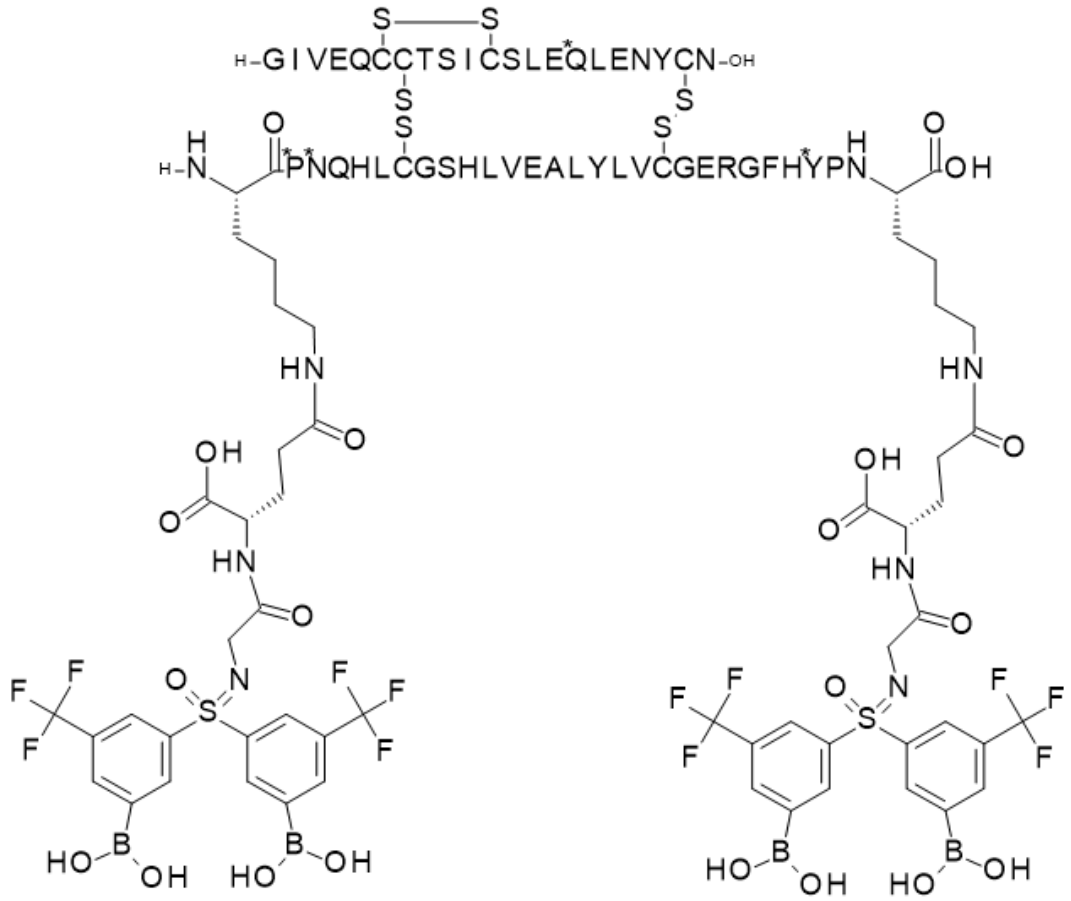
(the compound of Example 327);



(the compound of Example 331);



(the compound of Example 333); and



(the compound of Example 335).

10. 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. A composition comprising a compound according to any one of claims 1-9.

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

13. A compound according to any one of claims 1-9, 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. Use of a compound according to any one of claims 1-9 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).