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C07D 207/452 (2006.01)

C07D 207/456 (2006.01)

C07D 405/12 (2006.01)

C07D 491/22 (2006.01)

Norwegian Industrial Property Office

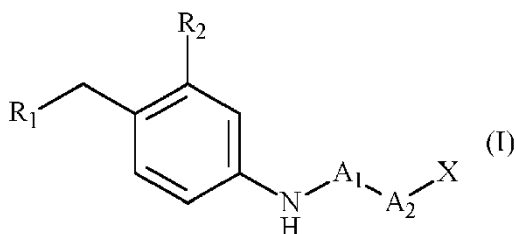
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	Designated validation states	MA; TN
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(54)	Title	PARA-AMINO-BENZYL LINKERS, PROCESS FOR THEIR PREPARATION AND THEIR USE IN CONJUGATES
(56)	References Cited:	WO-A1-2011/130598 WO-A1-2019/108974 WO-A1-2017/214282

Enclosed is a translation of the patent claims in Norwegian. Please note that as per the Norwegian Patents Acts, section 66i the patent will receive protection in Norway only as far as there is agreement between the translation and the language of the application/patent granted at the EPO. In matters concerning the validity of the patent, language of the application/patent granted at the EPO will be used as the basis for the decision. The patent documents published by the EPO are available through Espacenet (<http://worldwide.espacenet.com>) or via the search engine on our website here: <https://search.patentstyret.no/>

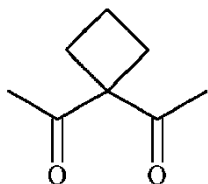
Patentkrav

1. Para-amino-benzylbindeleddforbindelse av formel (I):

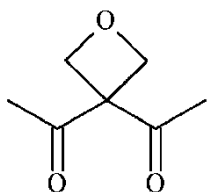


hvor:

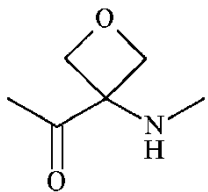
- R_1 representerer en hydroksygruppe eller et halogenatom;
- R_2 representerer en $-S(O)_2(OH)$ -gruppe, en $-S(O)_2(O^-M^+)$ -gruppe, en lineær eller forgrenet $-(C_1-C_4)alkyl-S(O)_2(OH)$ -gruppe, en lineær eller forgrenet $-(C_1-C_4)alkyl-S(O)_2(O^-M^+)$ -gruppe, en lineær eller forgrenet -halogen $(C_1-C_4)alkyl-S(O)_2(OH)$ -gruppe, eller en lineær eller forgrenet -halogen $(C_1-C_4)alkyl-S(O)_2(O^-M^+)$ -gruppe;
- A_1 representerer en $-C(O)-CH(R_3)-NH$ -gruppe;
- A_2 representerer en $-C(O)-CH(R_4)-NH$ -gruppe, en



-gruppe, en



-gruppe, eller en



-gruppe;

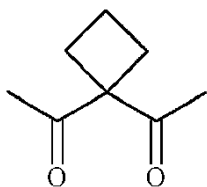
- R_3 og R_4 , uafhængig af hverandre, repræsenterer sidekæden til en aminosyre;
- X repræsenterer et hydrogenatom, en hydroksygruppe eller en beskyttende gruppe;
- M^+ repræsenterer et farmasøytisk akseptabelt enverdig kation.

2. Para-amino-benzylbindeleddforbindelse ifølge krav 1, hvori R_1 repræsenterer en hydroksygruppe, et bromatom, et kloratom eller et jodatom.

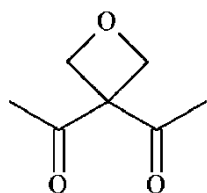
3. Para-amino-benzylbindeleddforbindelse ifølge krav 1, hvori R_2 repræsenterer en $-S(O)_2(OH)$ -gruppe, en $-S(O)_2(O^{\cdot}M^+)$ -gruppe, en $-CH_2-S(O)_2(OH)$ -gruppe, en $-CH_2-S(O)_2(O^{\cdot}M^+)$ -gruppe, en $-CH_2-CH_2-S(O)_2(OH)$ -gruppe, en $-CH_2-CH_2-S(O)_2(O^{\cdot}M^+)$ -gruppe, en $-CH_2-CH_2-CH_2-S(O)_2(OH)$ -gruppe eller en $-CH_2-CH_2-CH_2-S(O)_2(O^{\cdot}M^+)$ -gruppe.

4. Para-amino-benzylbindeleddforbindelse ifølge krav 1, hvori A_1 repræsenterer en $-C(O)-CH(R_3)-NH$ -gruppe hvor R_3 repræsenterer en $-(CH_2)_3-NH-CO-NH_2$ -gruppe eller en metylgruppe.

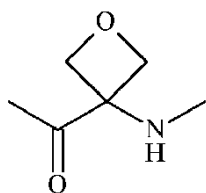
5. Para-amino-benzylbindeleddforbindelse ifølge krav 1, hvori A_2 repræsenterer en $-C(O)-CH(R_4)-NH$ -gruppe hvor R_4 repræsenterer en isopropylgruppe; en



-gruppe; en



-gruppe; eller en



-gruppe.

6. Para-amino-benzylbindeleddforbindelse ifølge krav 1, hvori A₁ representerer en -C(O)-CH(R₃)-NH-gruppe og A₂ representerer en -C(O)-CH(R₄)-NH-gruppe, hvor R₃ og R₄, uavhengig av hverandre, representerer sidekjedven til en aminosyre.

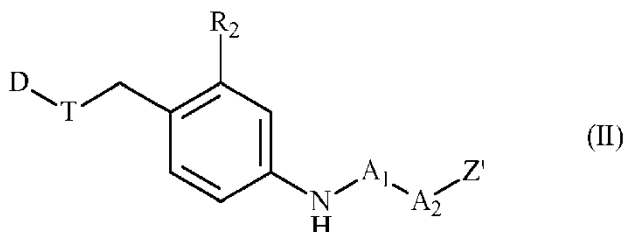
7. Para-amino-benzylbindeleddforbindelse ifølge krav 1, som er:

- natrium-5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-(hydroksymetyl)benzensulfonat;
- natrium-5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]propanoyl]amino]-2-(hydroksymetyl)benzensulfonat;
- 5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]propanoyl]amino]-2-(hydroksymetyl)benzensulfonsyre;
- natrium-[5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-(hydroksymetyl)fenyl]metansulfonat;
- 2-(klormetyl)-5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]benzensulfonsyre;
- 2-(klormetyl)-5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metyl-butanoyl]amino]propanoyl]amino]benzensulfonsyre;

- 5-[[[(2S)-2-[[[(2S)-2-(9H-fluoren-9-ylmetoksykarbonylamino)-3-metylbutanoyl]amino]-5-ureido-pentanoyl]amino]-2-(jodmetyl)benzensulfonsyre;
- natrium-*N*-{[(9H-fluoren-9-yl)metoksy]karbonyl}-*L*-valyl-*N*⁵-karbamoyl-*N*-[4-(hydroksymetyl)-3-(2-sulfonatoetyl)fenyl]-*L*-ornitinamid;
- *N*-{[(9H-fluoren-9-yl)metoksy]karbonyl}-*L*-valyl-*N*⁵-karbamoyl-*N*-[4-(hydroksymetyl)-3-(3-sulfopropyl)fenyl]-*L*-ornitinamid.

8. Para-amino-benzylbindeleddforbindelse av formel (I) ifølge et hvilket som helst av kravene 1 til 7 for anvendelse i fremstillingen av et antistoff-legemiddelkonjugat.

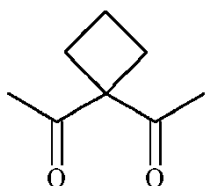
9. Bindeledd-legemiddelforbindelse av formel (II):



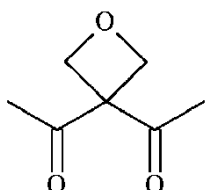
hvor:

- D representerer en legemiddeldel;
- T er en binding, -O-C(O)-N(CH₃)-CH₂-CH₂-N(CH₃)-C(O)-*, -O-*, -NR₅*, -NRs-C(O)-* eller -O-C(O)-*, hvori * indikerer festepunktet til D;
- R₂ representerer en -S(O)₂(OH)-gruppe, en -S(O)₂(O⁻M⁺)-gruppe, en lineær eller forgrenet -(C₁-C₄)alkyl-S(O)₂(OH)-gruppe, en lineær eller forgrenet -(C₁-C₄)alkyl-S(O)₂(O⁻M⁺)-gruppe, en lineær eller forgrenet -halogen(C₁-C₄)alkyl-S(O)₂(OH)-gruppe, eller en lineær eller forgrenet -halogen(C₁-C₄)alkyl-S(O)₂(O⁻M⁺)-gruppe;
- A₁ representerer en -C(O)-CH(R₃)-NH-gruppe;

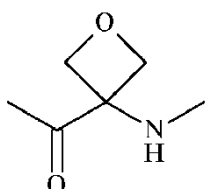
- A₂ representerer en -C(O)-CH(R₄)-NH-gruppe, en



-gruppe, en



-gruppe, eller en



-gruppe;

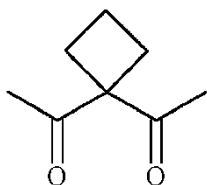
- R₃ og R₄, uafhængig af hverandre, representerer sidekæden til en aminosyre;
- R₅ representerer et hydrogenatom eller en (C₁-C₄)-alkylgruppe;
- Z' representerer en afstandsenhedsforløber;
- M⁺ representerer et farmasøytisk akseptabelt enverdig kation.

10. Bindeledd-legemiddelforbindelse ifølge krav 9, hvori R₂ representerer en -S(O)₂(OH)-gruppe, en -S(O)₂(O⁻M⁺)-gruppe, en -CH₂-S(O)₂(OH)-gruppe, en -CH₂-S(O)₂(O⁻M⁺)-gruppe, en -CH₂-CH₂-S(O)₂(OH)-gruppe, en -CH₂-CH₂-S(O)₂(O⁻M⁺)-gruppe, en -CH₂-CH₂-CH₂-S(O)₂(OH)-gruppe eller en -CH₂-CH₂-CH₂-S(O)₂(O⁻M⁺)-gruppe.

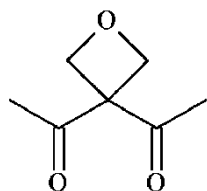
11. Bindeledd-legemiddelforbindelse ifølge krav 9, hvori A₁ representerer en -C(O)-CH(R₃)-NH-gruppe hvor R₃ representerer en -(CH₂)₃-NH-CO-NH₂-gruppe

eller en metylgruppe.

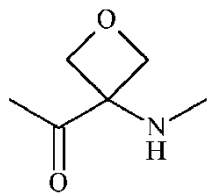
12. Bindeledd-legemiddelforbindelse ifølge krav 9, hvori A_2 representerer en -C(O)-CH(R₄)-NH-gruppe hvor R₄ representerer en isopropylgruppe; en



-gruppe; en



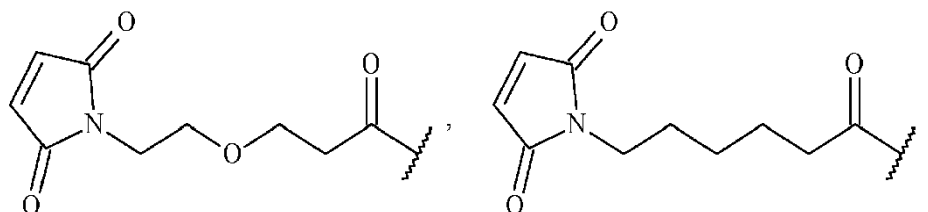
-gruppe; eller en

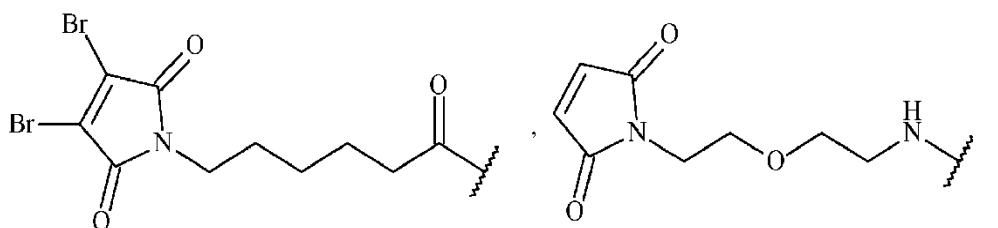


-gruppe.

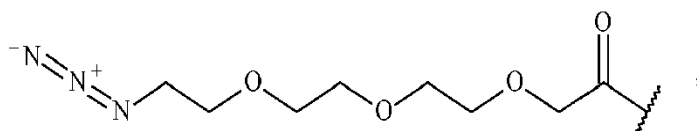
13. Bindeledd-legemiddelforbindelse ifølge krav 9, hvori T representerer en binding eller -O-C(O)-*, hvori * indikerer festepunktet til D.

14. Bindeledd-legemiddelforbindelse ifølge krav 9, hvori Z' representerer en gruppe valgt fra:



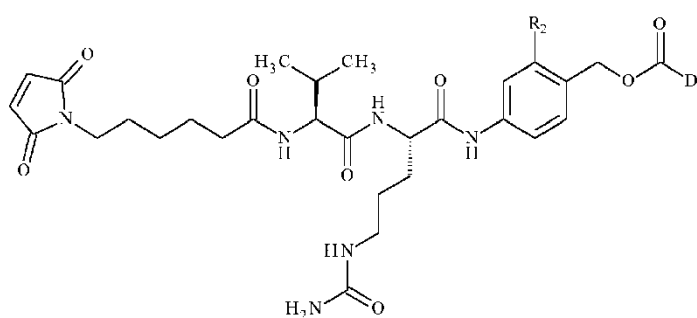
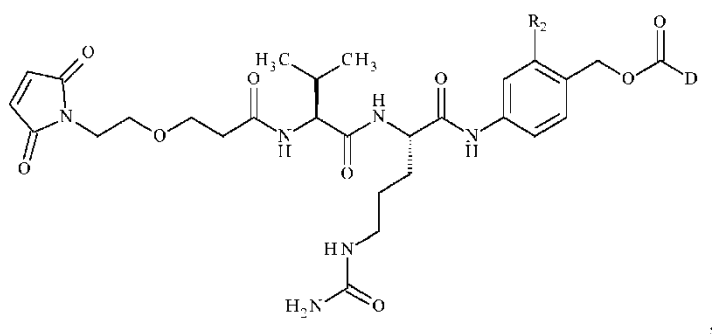


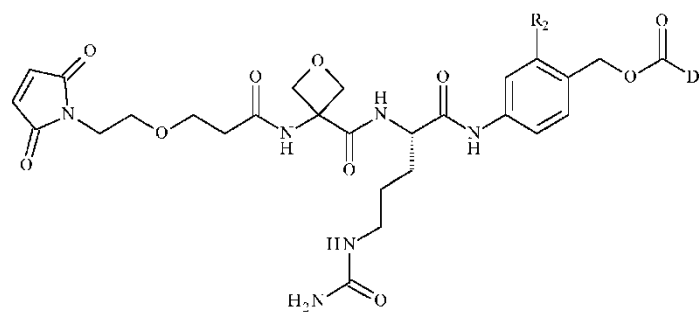
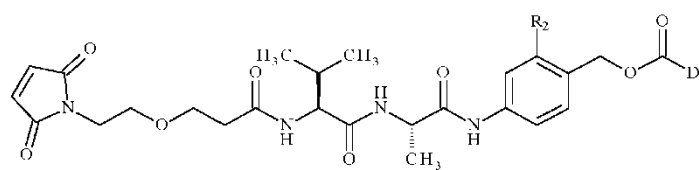
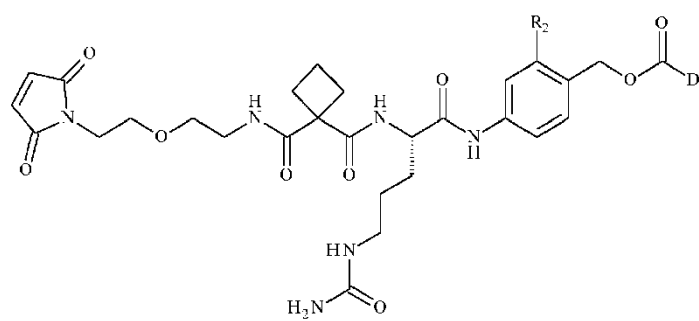
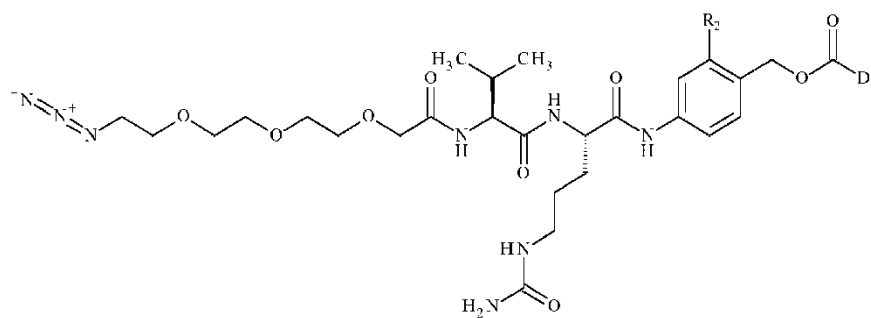
eller

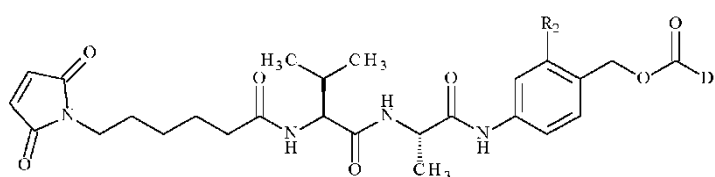
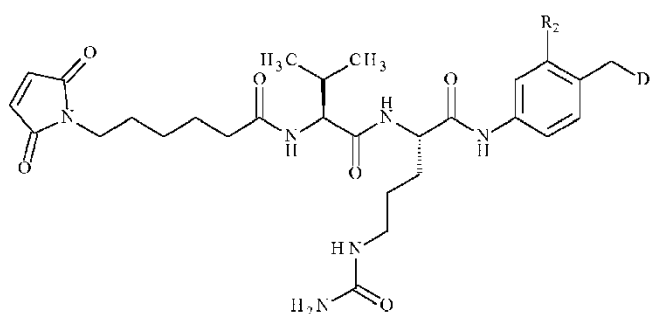
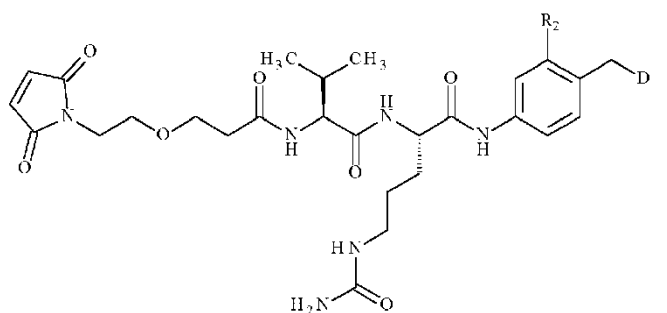


hvor den bølgete linjen indikerer det kovalente festestedet til N-enden eller karbonylgruppen til A₂-gruppen.

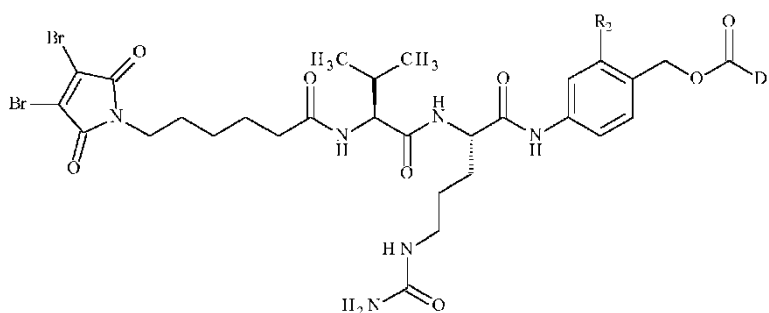
15. Bindeledd-legemiddelforbindelse ifølge krav 9, som er:







og



hvor R_2 og D er som definert i krav 9.

16. Bindeledd-legemiddelforbindelse ifølge krav 9, som er:

- natrium-5-[[[(2S)-2-[[[(2S)-2-[3-[2-(2,5-dioksopyrrol-1-yl)etoksy]propanoylamino]-3-metyl-butanoyl]amino]-5-ureido-

pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-propyl]karbamoyl]-2-metyl-propyl]-metyl-karbamoyl]oksymetyl]benzensulfonat;

- natrium-5-[[[(2S)-2-[[[(2S)-2-[6-(2,5-dioksopyrrol-1-yl)heksanoylamino]-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-propyl]karbamoyl]-2-metyl-propyl]-metyl-karbamoyl]oksymetyl]benzensulfonat;

- natrium-5-[[[(2S)-2-[[[(2S)-2-[[2-[2-(2-(2-azidoetoksy)etoksy]etoksy]acetyl]amino]-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-propyl]karbamoyl]-2-metyl-propyl]-metyl-karbamoyl]oksymetyl]benzensulfonat;

- 5-[[[(2S)-2-[[1-[2-[2-(2,5-dioksopyrrol-1-yl)etoksy]etylkarbamoyl]syklobutankarbonyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-propyl]karbamoyl]-2-metyl-propyl]-metyl-karbamoyl]oksymetyl]benzensulfonsyre;

- natrium-5-[[[(2S)-2-[[[(2S)-2-[3-[2-(2,5-dioksopyrrol-1-yl)etoksy]propanoylamino]-3-metyl-butanoyl]amino]propanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[[[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-

metyl-propyl]karbamoyl]-2-metyl-propyl]-
 metylkarbamoyl]oksymetyl]benzensulfonat;
 - 5-[[[(2S)-2-[[[(2S)-2-[3-[2-(2,5-dioksopyrrol-1-yl)etoksy]propanoylamino]-
 3-metyl-butanoyl]amino]propanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-[(S,2R)-4-
 [(2S)-2-[(1R,2R)-3-[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-etyl]amino]-1-
 metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1S)-1-
 metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-propyl]karbamoyl]-
 2-metyl-propyl]-metylkarbamoyl]oksymetyl]benzensulfonsyre;
 - 5-[[[(2S)-2-[[3-[2-[2-(2,5-dioksopyrrol-1-yl)etoksy]etylkarbamoyl]oksetan-
 3-karbonyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-
 [[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[(1R,2S)-2-hydroksy-1-metyl-2-fenyl-
 etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-
 1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metyl-
 propyl]karbamoyl]-2-metyl-propyl]-metyl-
 karbamoyl]oksymetyl]benzensulfonsyre;
 - [5-[[[(2S)-2-[[[(2S)-2-[3-[2-(2,5-dioksopyrrol-1-yl)etoksy]propanoylamino]-
 3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1S)-1-[[[(1S)-1-
 [[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[(1R,2S)-2-hydroksy-1-metyl-2-
 fenyletyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-
 metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-
 metylpropyl]karbamoyl]-2-metyl-propyl]-
 metylkarbamoyl]oksymetyl]fenyl]metansulfonsyre;
 - [4-[[[(2S)-2-[[[(2S)-2-[3-[2-(2,5-dioksopyrrol-1-yl)etoksy]propanoylamino]-
 3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-sulfo-fenyl]metyl-
 [(1S)-1-[[[(1S)-1-[[[(1S,2R)-4-[(2S)-2-[(1R,2R)-3-[(1R,2S)-2-hydroksy-1-
 metyl-2-fenyl-etyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-
 yl]-2-metoksy-1-[(1S)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-
 metyl-propyl]karbamoyl]-2-metyl-propyl]-dimetyl-ammonium; 2,2,2-
 trifluoracetat;
 - *N*-({[4-({*N*-[6-(2,5-diokso-2,5-dihydro-1*H*-pyrrol-1-yl)heksanoyl]-L-valyl-
 L-alanyl]amino)-2-sulfofenyl]metoksy}karbonyl)-*N*-metyl-L-valyl-

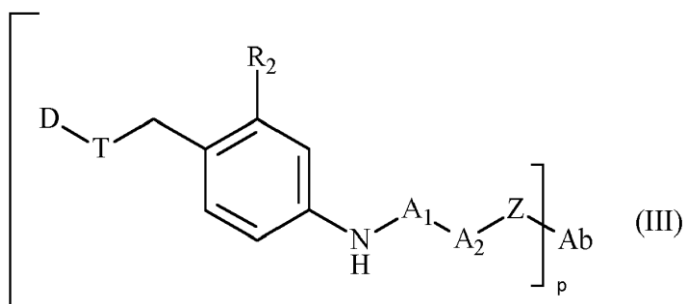
N [(3*R*,4*S*,5*S*)-1-{(2*S*)-2-[(1*R*,2*R*)-3-[(1*S*,2*R*)-1-hydroksy-1-fenylpropan-2-yl]amino}-1-metoksy-2-metyl-3-oksopropyl]pyrrolidin-1-yl}-3-metoksy-5-metyl-1-oksoheptan-4-yl]-*N*-metyl-L-valinamid;

- *N*-[6-(2,5-diokso-2,5-dihydro-1*H*-pyrrol-1-yl)heksanoyl]-L-valyl-*N*⁵-karbamoyl-*N*-(4-{[[(4*S*)-4,11-dietyl-9-hydroksy-3,14-diokso-3,4,12,14-tetrahydro-1*H*-pyrano[3',4':6,7]indolizino[1,2-*b*]kinolin-4-yl]oksy}karbonyl)oksy]metyl}-3-sulfofenyl)-L-ornitinamid;

- (1*S*,3*S*)-3,5,12-trihydroksy-3-(hydroksyacetyl)-10-metoksy-6,11-diokso-1,2,3,4,6,11-heksahydrotetracen-1-yl-2,3,6-trideoksy-3-[(4-{*N*-[6-(2,5-diokso-2,5-dihydro-1*H*-pyrrol-1-yl)heksanoyl]-L-valyl-*N*⁵-karbamoyl-L-ornityl]amino)-2-sulfofenyl]metoksy}karbonyl)amino]-α-L-lykso-heksopyranosid;

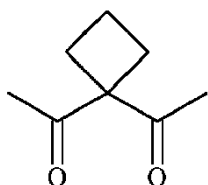
- *N*-{3-[2-(2,5-diokso-2,5-dihydro-1*H*-pyrrol-1-yl)etoksy]propanoyl]-L-valyl-*N*-{4-[(5*S*,8*S*,11*S*,12*R*)-11-[(2*S*)-butan-2-yl]-12-(2-{(2*S*)-2-[(1*R*,2*R*)-3-[(1*S*,2*R*)-1-hydroksy-1-fenylpropan-2-yl]amino}-1-metoksy-2-metyl-3-oksopropyl]pyrrolidin-1-yl}-2-oksoetyl)-4,10-dimetyl-3,6,9-triokso-5,8-di(propan-2-yl)-2,13-dioksa-4,7,10-triazatetradekan-1-yl]-3-(2-sulfoetyl)fenyl]-*N*⁵-karbamoyl-L-ornitinamid;

- 5-[(2*S*)-2-[(2*S*)-2-[6-(3,4-dibrom-2,5-diokso-pyrrol-1-yl)heksanoylamino]-3-metyl-butanoyl]amino]-5-ureido-pentanoyl]amino]-2-[[[(1*S*)-1-[(1*S*)-1-[(1*S*,2*R*)-4-[(2*S*)-2-[(1*R*,2*R*)-3-[(1*R*,2*S*)-2-hydroksy-1-metyl-2-fenyletyl]amino]-1-metoksy-2-metyl-3-okso-propyl]pyrrolidin-1-yl]-2-metoksy-1-[(1*S*)-1-metylpropyl]-4-okso-butyl]-metyl-karbamoyl]-2-metylpropyl]karbamoyl]-2-metyl-propyl]-metylkarbamoyl]oksymetyl]benzensulfonsyre.

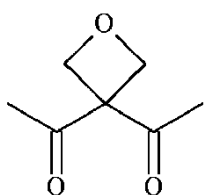
17. Antistoff-legemiddelkonjugat av formel (III):

hvor

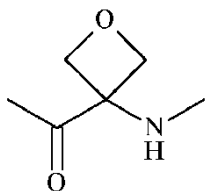
- Ab representerer et antistoff eller et antigenbindende fragment derav;
- D er en legemiddeldel;
- T er en binding, $-\text{O}-\text{C}(\text{O})-\text{N}(\text{CH}_3)-\text{CH}_2-\text{CH}_2-\text{N}(\text{CH}_3)-\text{C}(\text{O})-\text{*}$, $-\text{O}-\text{*}$, $-\text{NR}_5-\text{*}$, $-\text{NR}_5-\text{C}(\text{O})-\text{*}$ eller $-\text{O}-\text{C}(\text{O})-\text{*}$, hvor * indikerer festepunktet til D;
- Z representerer en avstandsenhet;
- A_1 representerer en $-\text{C}(\text{O})-\text{CH}(\text{R}_3)-\text{NH}$ -gruppe;
- A_2 representerer en $-\text{C}(\text{O})-\text{CH}(\text{R}_4)-\text{NH}$ -gruppe, en



-gruppe, en



-gruppe, eller en



-gruppe;

- R_2 representerer en $-\text{S}(\text{O})_2(\text{OH})$ -gruppe, en $-\text{S}(\text{O})_2(\text{O}^-\text{M}^+)$ -gruppe, en lineær eller forgrenet $-(\text{C}_1-\text{C}_4)\text{alkyl}-\text{S}(\text{O})_2(\text{OH})$ -gruppe, en lineær eller

forgrenet $-(C_1-C_4)alkyl-S(O)_2(O^-M^+)$ -gruppe, en lineær eller forgrenet -halogen $(C_1-C_4)alkyl-S(O)_2(OH)$ -gruppe, eller en lineær eller forgrenet -halogen $(C_1-C_4)alkyl-S(O)_2(O^-M^+)$ -gruppe;

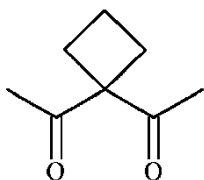
- R_3 og R_4 , uafhængig af hverandre, repræsenterer sidekæden til en aminosyre;
- R_5 repræsenterer en (C_1-C_4) -alkylgruppe;
- M^+ repræsenterer et farmasøytisk akseptabelt enverdig kation; og
- p er et heltal fra 1 til 8.

18. Antistoff-legemiddelkonjugatet ifølge krav 17, hvori T er en binding eller $-O-C(O)-*$, hvori $*$ indikerer festepunktet til D .

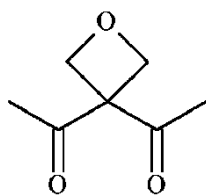
19. Antistoff-legemiddelkonjugatet ifølge krav 17, hvori R_2 repræsenterer en $-S(O)_2(OH)$ -gruppe, en $-S(O)_2(O^-M^+)$ -gruppe, en $-CH_2-S(O)_2(OH)$ -gruppe, en $-CH_2-S(O)_2(O^-M^+)$ -gruppe, en $-CH_2-CH_2-S(O)_2(OH)$ -gruppe, en $-CH_2-CH_2-S(O)_2(O^-M^+)$ -gruppe, en $-CH_2-CH_2-CH_2-S(O)_2(OH)$ -gruppe eller en $-CH_2-CH_2-CH_2-S(O)_2(O^-M^+)$ -gruppe.

20. Antistoff-legemiddelkonjugatet ifølge krav 17, hvori A_1 repræsenterer en $-C(O)-CH(R_3)-NH$ -gruppe hvor R_3 repræsenterer en $-(CH_2)_3-NH-CO-NH_2$ -gruppe eller en metylgruppe.

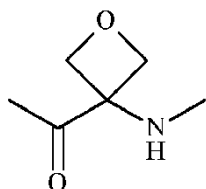
21. Antistoff-legemiddelkonjugatet ifølge krav 17, hvori A_2 repræsenterer en $-C(O)-CH(R_4)-NH$ -gruppe hvor R_4 repræsenterer en isopropylgruppe; en



-gruppe; en

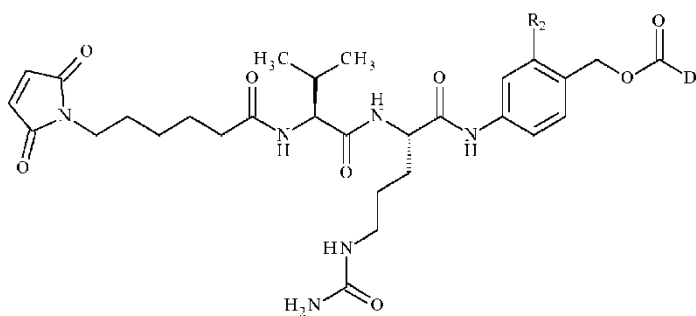
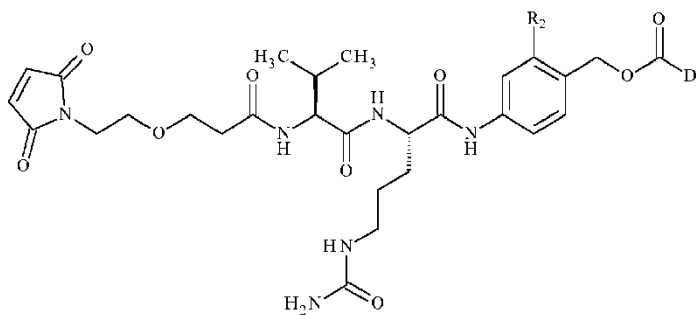


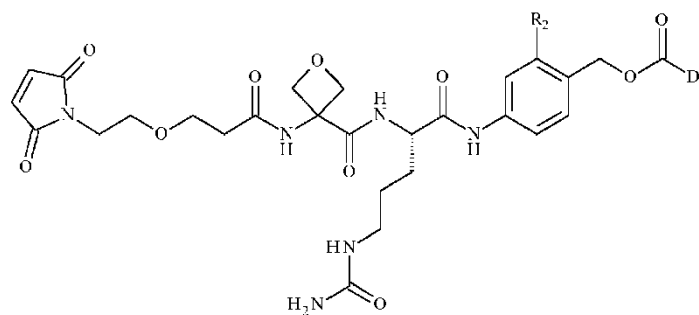
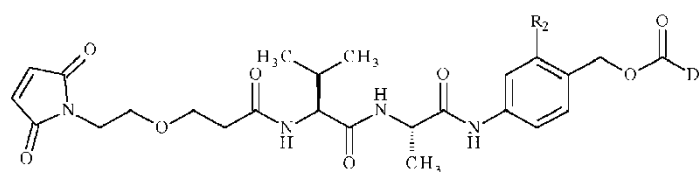
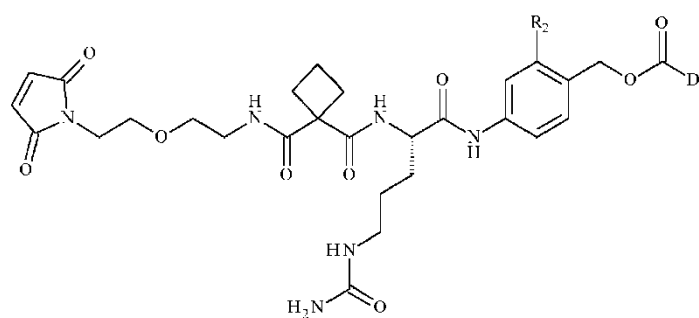
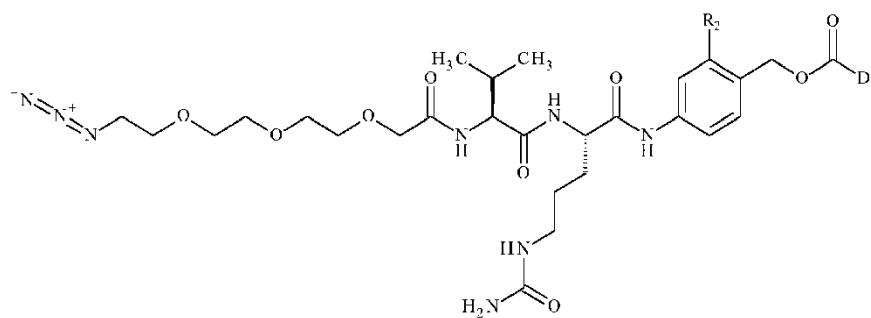
-gruppe; eller en

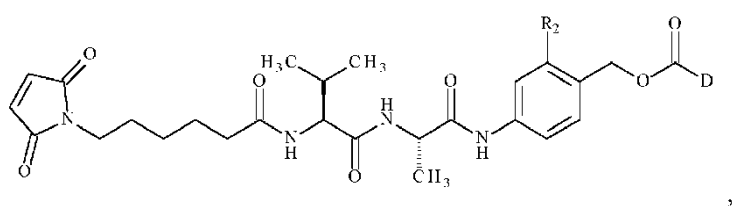
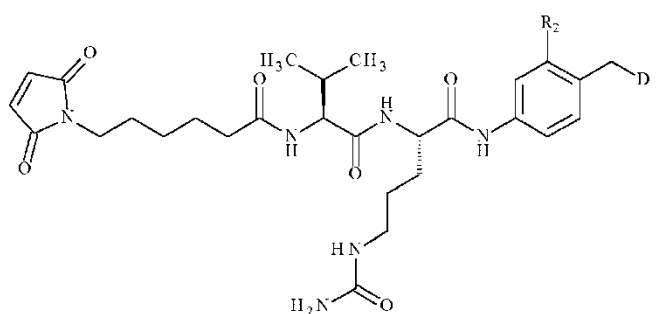
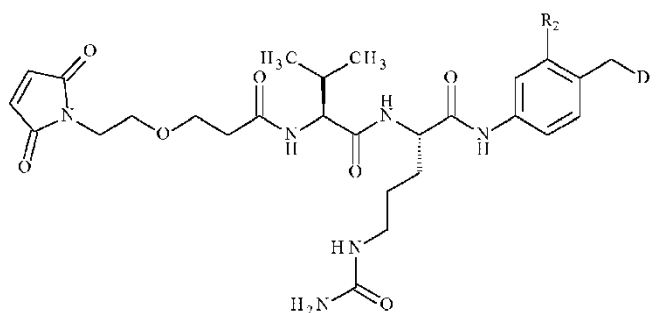


-gruppe.

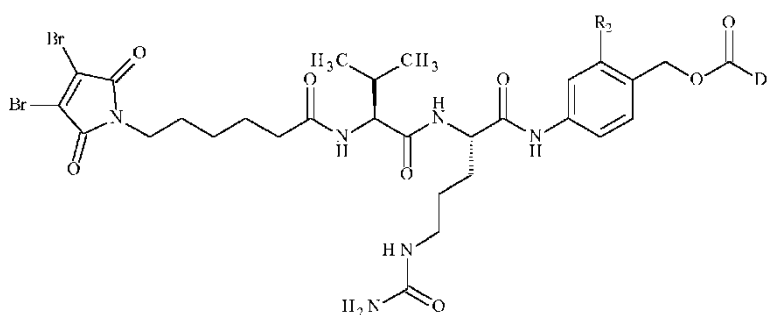
22. Antistoff-legemiddelkonjugatet ifølge krav 17, hvori antistoff-legemiddelkonjugatet dannes fra en bindeledd-legemiddelforbindelse av formel (II) valgt fra:





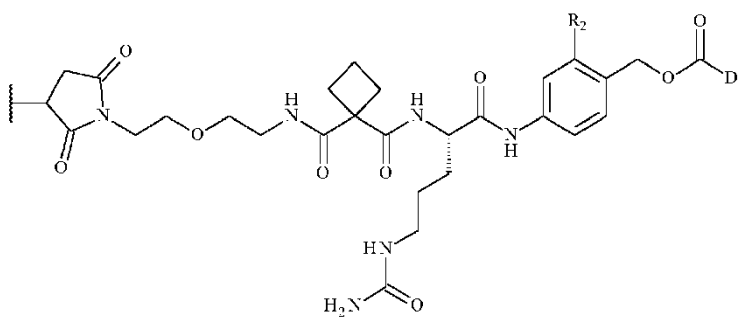
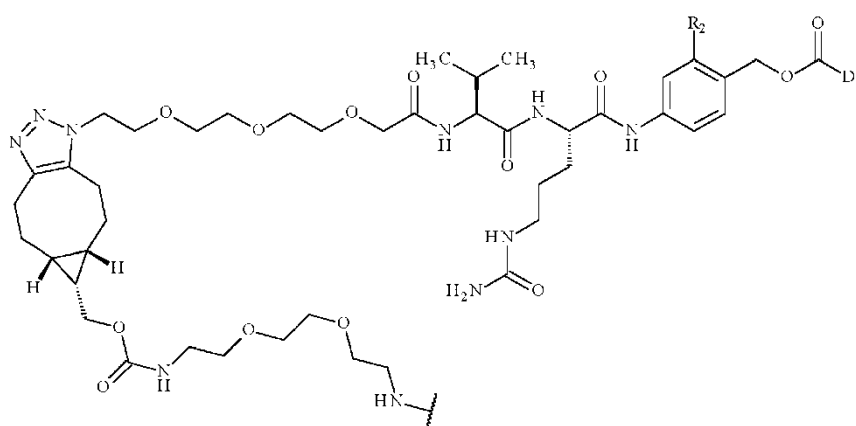
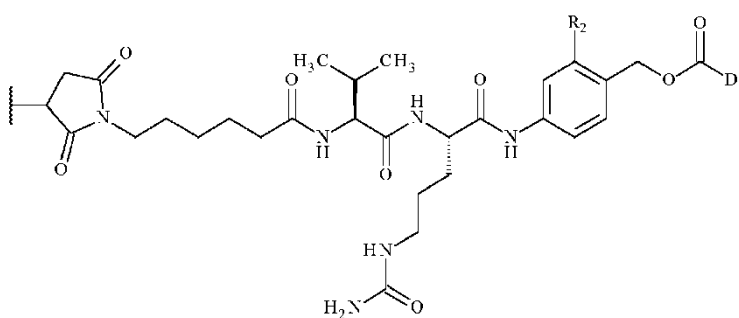
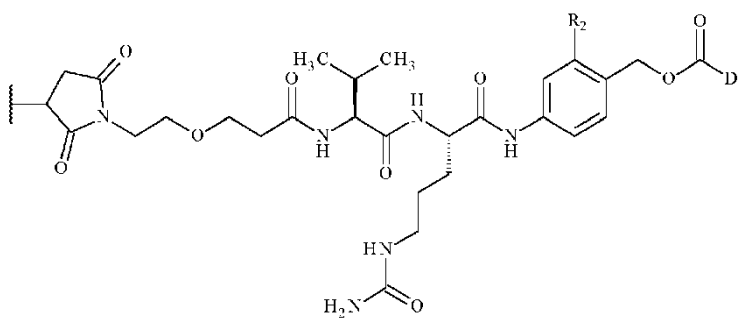


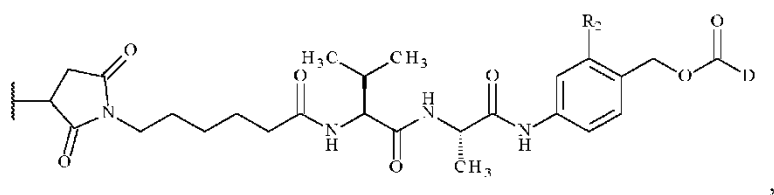
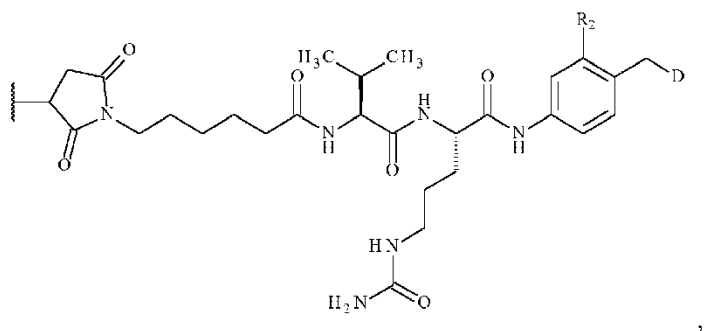
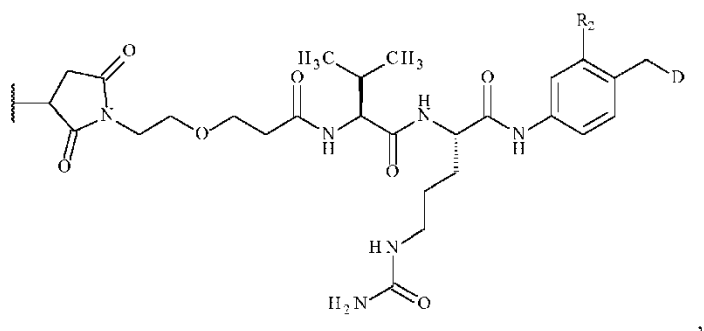
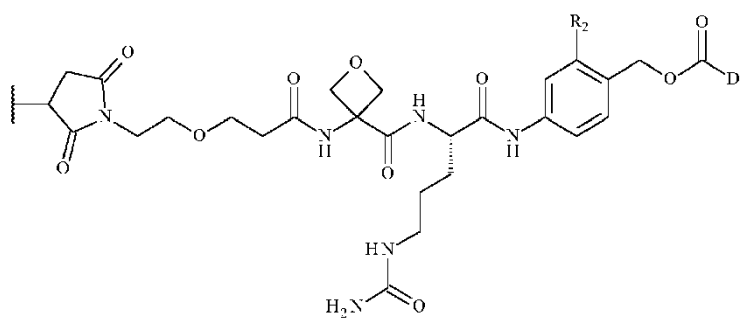
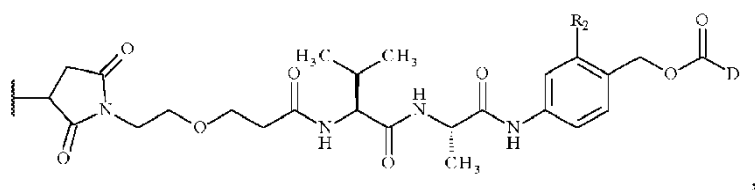
og



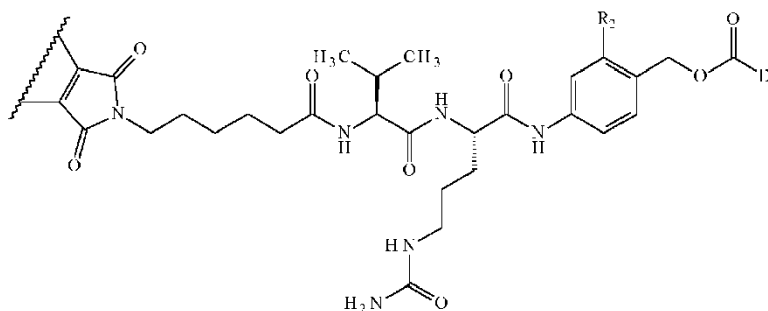
hvor R_2 og D er som defineret i krav 17.

23. Antistoff-legemiddelkonjugatet ifølge krav 17, hvor antistoff-legemiddelkonjugatet omfatter en formel valgt fra:





og



hvor den bølgede linjen indikerer det kovalente festestedet til antistoffet eller det antigenbindende fragmentet derav, og D og R₂ er som defineret i krav 17.

24. Farmasøytisk sammensetning omfattende antistoff-legemiddelkonjugatet ifølge et hvilket som helst av kravene 17 til 23, og en farmasøytisk bærer.

25. Antistoff-legemiddelkonjugatet ifølge et hvilket som helst av kravene 17 til 23, for anvendelse i behandlingen av et pattedyr som har behov derav.