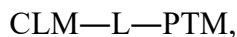


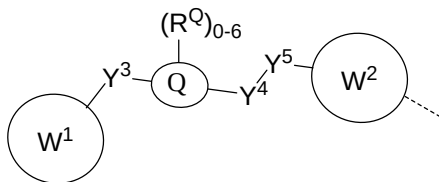
## REIVINDICACIONES

1. Un compuesto bifuncional que tiene la estructura química:



o una de sus sales, enantiómeros, o estereoisómeros aceptables farmacéuticamente,  
en donde:

- (a) la PTM es una porción de unión (ABM) al receptor de andrógenos (AR) que comprende



la estructura

ABM-b

;

en donde:

$W^1$  es arilo, heteroarilo, bicíclico, o biheterocíclico, cada uno independientemente sustituido con 1 o más H, halo, hidroxilo, nitro, CN,  $C\equiv CH$ ,  $C_{1-6}$  alquilo (lineal, ramificado, opcionalmente sustituido; por ejemplo, opcionalmente sustituido con 1 o más halo,  $C_{1-6}$  alcoxilo),  $C_{1-6}$  alcoxilo (lineal, ramificado, opcionalmente sustituido; por ejemplo, opcionalmente sustituido con 1 o más halo),  $C_{2-6}$  alquenilo,  $C_{2-6}$  alquinilo, o  $CF_3$ ;

$Y^3$ ,  $Y^4$ ,  $Y^5$  son cada uno independientemente un enlace, O,  $NR^{Y2}$ ,  $CR^{Y1}R^{Y2}$ ,  $C=O$ ,  $C=S$ , SO,  $SO_2$ , heteroarilo o arilo;

Q es un anillo de 3-6 miembros con 0-4 heteroátomos, opcionalmente sustituido con 0-6  $R^Q$ , en donde cada  $R^Q$ , es independientemente H,  $C_{1-6}$  alquilo (lineal, ramificado, opcionalmente sustituido, por ejemplo, opcionalmente sustituido con 1 o más halo,  $C_{1-6}$  alcoxilo), halógeno, o  $C_{1-6}$  alcoxi, o 2 grupos  $R^Q$  tomados junto con el átomo al que se unen, forman un sistema de anillo de 3-8 miembros que contiene 0-2 heteroátomos);

$R^{Y1}$ ,  $R^{Y2}$  son cada uno independientemente H,  $C_{1-6}$  alquilo (lineal, ramificado, opcionalmente sustituido; por ejemplo, opcionalmente sustituido con 1 o más halo,  $C_{1-6}$  alcoxilo), halógeno,  $C_{1-6}$  alcoxi, cíclico, o heterocíclico;

$W^2$  es un enlace,  $C_{1-6}$  alquilo,  $C_{1-6}$  heteroalquilo, O, arilo, heteroarilo, alicíclico, heterocíclico, biheterocíclico, biarilo, o biheteroarilo, cada uno opcionalmente sustituido con 1-10  $R^{W2}$ ;

cada  $R^{W2}$  es independientemente H, halo,  $C_{1-6}$  alquilo (lineal o ramificado opcionalmente sustituido; por ejemplo, opcionalmente sustituido con 1 o más F), - $OR^{W2A}$ ,  $C_{3-6}$  cicloalquilo,  $C_{4-6}$  cicloheteroalquilo,  $C_{1-6}$  alquilo (opcionalmente sustituido), heterocíclico (opcionalmente sustituido), arilo (opcionalmente sustituido), o heteroarilo (opcionalmente sustituido), heteroarilo bicíclico, o arilo  $OC_{1-3}$ alquilo (opcionalmente sustituido; por ejemplo, opcionalmente sustituido con 1 o más -F), OH,  $NH_2$ ,  $NR^{Y1}R^{Y2}CN$ ;

$R^{W2A}$  es H,  $C_{1-6}$  alquilo (lineal, ramificado), o  $C_{1-6}$  heteroalquilo (lineal, ramificado), cada uno opcionalmente sustituido con un cicloalquilo, cicloheteroalquilo, arilo, heterocíclico, heteroarilo, halo, u  $OC_{1-3}$ alquilo; y

la línea discontinua indica el sitio de unión del enlazador;

(b) el L es una porción de enlace químico que une covalentemente la CLM y la PTM, y comprende una unidad estructural química representada por la Fórmula  $-(A^L)_q$ - en donde:

$(A^L)_q$  se conecta a la CLM y la PTM;

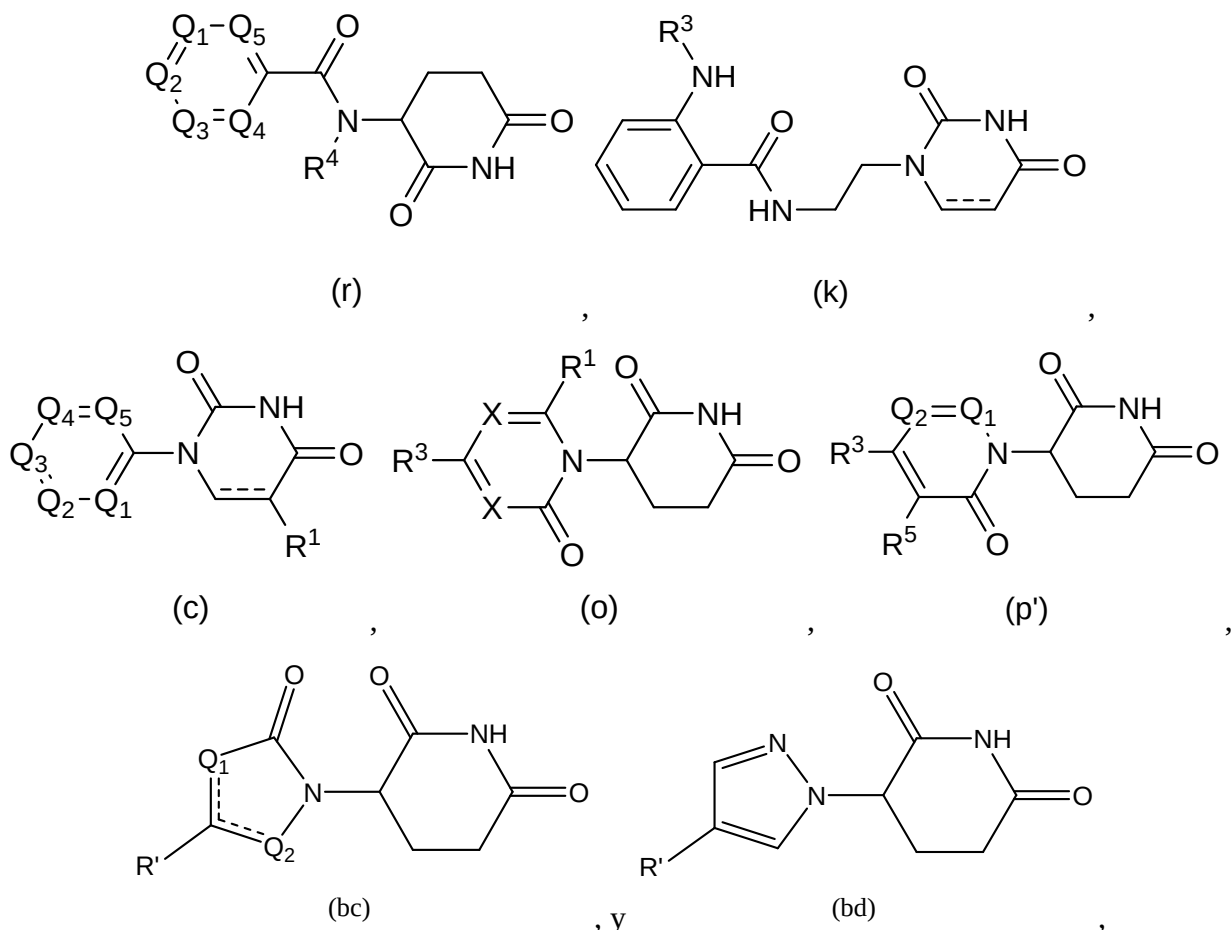
q es un número mayor que o igual a 1;

cada  $A^L$  se selecciona independientemente del grupo que consiste en, un enlace,  $CR^{L1}R^{L2}$ , O, S, SO,  $SO_2$ ,  $NR^{L3}$ ,  $SO_2NR^{L3}$ ,  $SONR^{L3}$ ,  $CONR^{L3}$ ,  $NR^{L3}CONR^{L4}$ ,  $NR^{L3}SO_2NR^{L4}$ , CO,  $CR^{L1}=CR^{L2}$ ,  $C\equiv C$ ,  $SiR^{L1}R^{L2}$ ,  $P(O)R^{L1}$ ,  $P(O)OR^{L1}$ ,  $NR^{L3}C(=NCN)NR^{L4}$ ,  $NR^{L3}C(=NCN)$ ,  $NR^{L3}C(=CNO_2)NR^{L4}$ ,  $C_{3-11}$ cicloalquilo opcionalmente sustituido con 0-6  $R^{L1}$  y/o grupos  $R^{L2}$ ,  $C_{3-11}$ heterociclilo opcionalmente sustituido con 0-6  $R^{L1}$  y/o grupos  $R^{L2}$ , arilo opcionalmente sustituido con 0-6  $R^{L1}$  y/o grupos  $R^{L2}$ , heteroarilo opcionalmente sustituido con 0-6  $R^{L1}$  y/o grupos  $R^{L2}$ , donde  $R^{L1}$  o  $R^{L2}$ , cada uno independientemente se unen opcionalmente a otros grupos para formar porciones cicloalquilo y/o heterociclilo, opcionalmente sustituido con 0-4 grupos  $R^{L5}$ ; y

$R^{L1}$ ,  $R^{L2}$ ,  $R^{L3}$ ,  $R^{L4}$  y  $R^{L5}$  son, cada uno independientemente, H, halo,  $C_{1-8}$  alquilo,  $OC_{1-8}$ alquilo,  $SC_{1-8}$ alquilo,  $NHC_{1-8}$ alquilo,  $N(C_{1-8}alquilo)_2$ ,  $C_{3-11}$ cicloalquilo, arilo, heteroarilo,  $C_{3-11}$ heterociclilo,  $OC_{1-8}$ cicloalquilo,  $SC_{1-8}$ cicloalquilo,  $NHC_{1-8}$ cicloalquilo,  $N(C_{1-8}$

$_8$ cicloalquilo) $_2$ , N(C $_{1-8}$ cicloalquilo)(C $_{1-8}$ alquilo), OH, NH $_2$ , SH, SO $_2$ C $_{1-8}$ alquilo, P(O)(OC $_{1-8}$ alquilo)(C $_{1-8}$ alquilo), P(O)(OC $_{1-8}$ alquilo) $_2$ , CC-C $_{1-8}$ alquilo, CCH, CH=CH(C $_{1-8}$ alquilo), C(C $_{1-8}$ alquilo)=CH(C $_{1-8}$ alquilo), C(C $_{1-8}$ alquilo)=C(C $_{1-8}$ alquilo) $_2$ , Si(OH) $_3$ , Si(C $_{1-8}$ alquilo) $_3$ , Si(OH)(C $_{1-8}$ alquilo) $_2$ , COC $_{1-8}$ alquilo, CO $_2$ H, halógeno, CN, CF $_3$ , CHF $_2$ , CH $_2$ F, NO $_2$ , SF $_5$ , SO $_2$ NHC $_{1-8}$ alquilo, SO $_2$ N(C $_{1-8}$ alquilo) $_2$ , SONHC $_{1-8}$ alquilo, SON(C $_{1-8}$ alquilo) $_2$ , CONHC $_{1-8}$ alquilo, CON(C $_{1-8}$ alquilo) $_2$ , N(C $_{1-8}$ alquilo)CONH(C $_{1-8}$ alquilo), N(C $_{1-8}$ alquilo)CON(C $_{1-8}$ alquilo) $_2$ , NHCONH(C $_{1-8}$ alquilo), NHCON(C $_{1-8}$ alquilo) $_2$ , NHCONH $_2$ , N(C $_{1-8}$ alquilo)SO $_2$ NH(C $_{1-8}$ alquilo), N(C $_{1-8}$ alquilo) SO $_2$ N(C $_{1-8}$ alquilo) $_2$ , NH SO $_2$ NH(C $_{1-8}$ alquilo), NH SO $_2$ N(C $_{1-8}$ alquilo) $_2$ , NH SO $_2$ NH $_2$  y

(c) la CLM es una porción de unión a la ligasa de ubiquitinaE3 cereblon de molécula pequeña que se une o se dirige a una ligasa de ubiquitina E3 cereblon y tiene una estructura química seleccionada del grupo que consiste en:



en donde:

Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub>, Q<sub>4</sub>, Q<sub>5</sub> representan cada uno independientemente un C o N sustituido con un grupo seleccionado independientemente de R', N o N-óxido;

R<sup>1</sup> es ausente, H, OH, CN, C1-C3 alquilo, o C=O;

R<sup>2</sup> es ausente, H, OH, CN, C1-3 alquilo, CHF<sub>2</sub>, CF<sub>3</sub>, CHO, C(=O)NH<sub>2</sub>;

R<sup>3</sup> es ausente, H, alquilo (preferiblemente un C1-C6 o C1-C3 alquilo), alquilo sustituido (preferiblemente C1-C6 o C1-C3 alquilo sustituido), alcoxi (preferiblemente un C1-C6 o C1-C3 alcoxilo), alcoxi sustituido (por ejemplo, C1-C6 o C1-C3 alcoxilo sustituido);

R<sup>4</sup> se selecciona de H, alquilo, alquilo sustituido;

R<sup>5</sup> es H, halógeno, C(=O)R'; CN, OH, o CF<sub>3</sub> ;

X es C, CH, C=O, o N; R' se selecciona de H, halógeno, amina, alquilo (preferiblemente C1-C3 alquilo), alquilo sustituido (preferiblemente un C1-C3 alquilo sustituido), alcoxi (preferiblemente un C1-C3 alcoxilo), alcoxi sustituido (preferiblemente un C1-C3 alcoxilo sustituido), NR<sup>2</sup>R<sup>3</sup>, C(=O)OR<sup>2</sup>, fenilo opcionalmente sustituido; y

∕ es un enlace simple o doble.

2. El compuesto bifuncional de conformidad con la reivindicación 1, en donde la CLM se une al grupo enlazador químico (L) a través de X, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R', Q<sub>1</sub>, Q<sub>2</sub>, Q<sub>3</sub>, Q<sub>4</sub>, o Q<sub>5</sub>.

3. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1 o 2, en donde:

W<sup>1</sup> es arilo, o heteroarilo, cada uno independientemente sustituido con 1 o más H, halo, hidroxilo, nitro, CN, C≡CH, C<sub>1-6</sub> alquilo (lineal, ramificado, opcionalmente sustituido con 1 o más halo, C<sub>1-6</sub> alcoxilo), C<sub>1-6</sub> alcoxilo (lineal, ramificado, opcionalmente sustituido con 1 o más halo), C<sub>2-6</sub> alquenilo, C<sub>2-6</sub> alquinilo, o CF<sub>3</sub>;

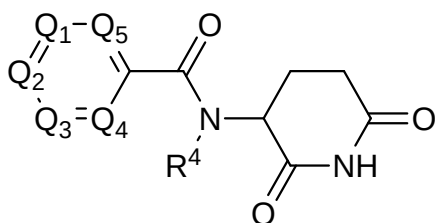
Q es un anillo alicíclico de 4 miembros con 0-2 heteroátomos, opcionalmente sustituido con 0-6 R<sup>Q</sup>, cada R<sup>Q</sup> es independientemente H, C<sub>1-6</sub> alquilo (lineal, ramificado, opcionalmente sustituido con 1 o más halo, C<sub>1-6</sub> alcoxilo), o 2 grupos R<sup>Q</sup> tomados junto con el átomo al que se unen, forman un sistema de anillo de 3-8 miembros que contiene 0-2 heteroátomos);

$R^{Y1}$ ,  $R^{Y2}$  son cada uno independientemente H,  $C_{1-6}$  alquilo (lineal, ramificado, opcionalmente sustituido con 1 o más halo,  $C_{1-6}$  alcoxilo);

$W^2$  es un enlace,  $C_{1-6}$  alquilo,  $C_{1-6}$  heteroalquilo, O,  $C_{1-6}$  alicíclico, heterocíclico, arilo, biheterocíclico, biarilo, o biheteroarilo, o heteroarilo, cada uno opcionalmente sustituido con 1, 2 o 3  $R^{W2}$ ; y

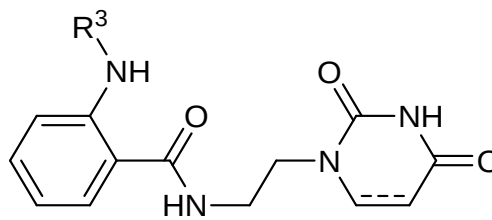
cada  $R^{W2}$  es independientemente H, halo,  $C_{1-6}$  alquilo (lineal, ramificado, opcionalmente sustituido con 1 o más F),  $C_{1-6}$  heteroalquilo (lineal, ramificado, opcionalmente sustituido), - $OR^{W2A}$   $OC_{1-3}$ alquilo (opcionalmente sustituido con 1 o más -F),  $C_{3-6}$  cicloalquilo,  $C_{4-6}$  cicloheteroalquilo (opcionalmente sustituido), heterocíclico (opcionalmente sustituido), arilo (opcionalmente sustituido), heteroarilo (opcionalmente sustituido), heteroarilo bicíclico (opcionalmente sustituido), arilo bicíclico, OH,  $NH_2$ ,  $NR^{Y1}R^{Y2}$ , o CN.

4. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-3, en donde el CLM tiene la estructura



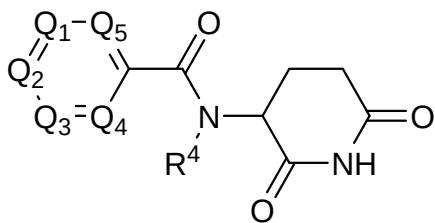
(r)

o



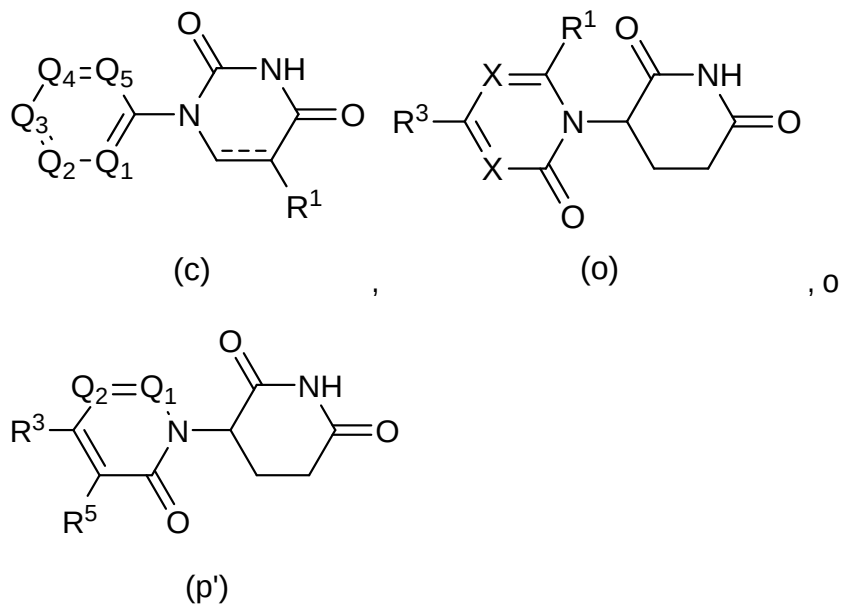
(k)

5. El compuesto bifuncional de conformidad con la reivindicación 4, en donde la CLM tiene la estructura

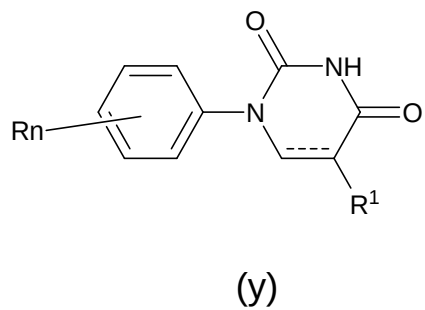


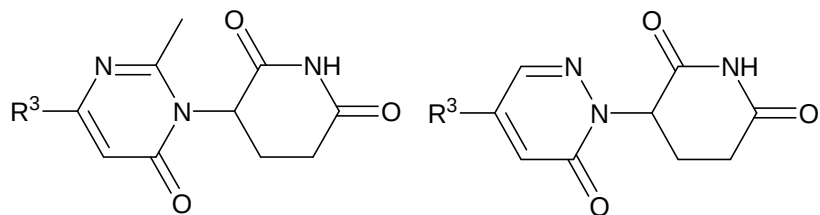
(r)

6. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-3, en donde la CLM tiene la estructura



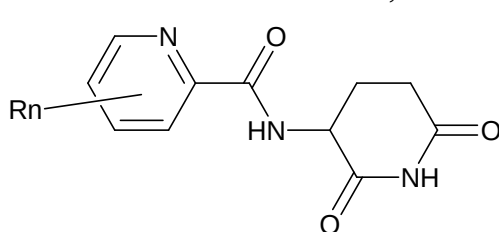
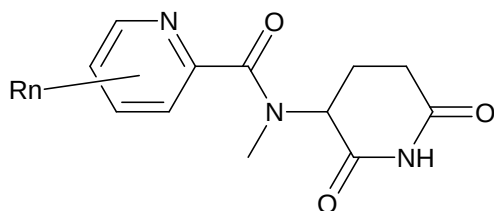
7. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-6, en donde la CLM se representa por una estructura química seleccionada del grupo que consiste en:





(ad)

(ae)

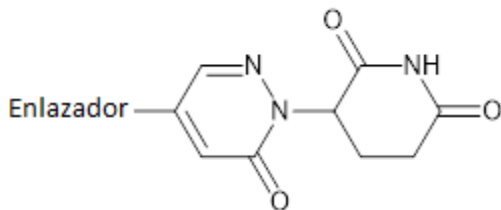
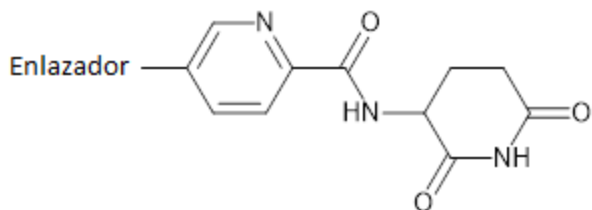
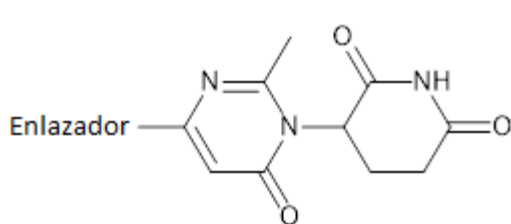


(af)

(ag)

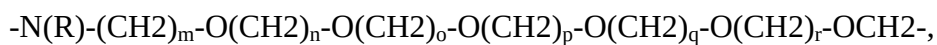
, y  
en donde Rn comprende un grupo funcional o un átomo.

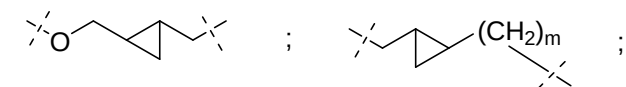
8. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-7, en donde la CLM se representa por una estructura química seleccionada por:

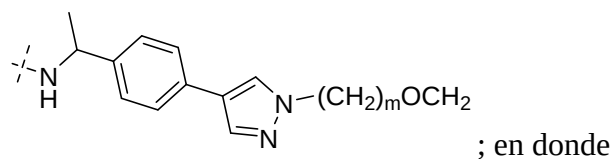
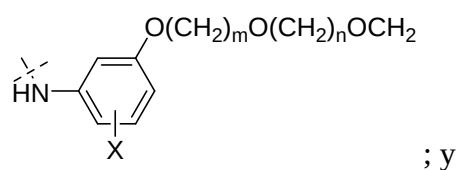
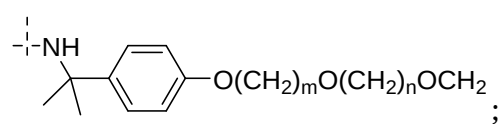
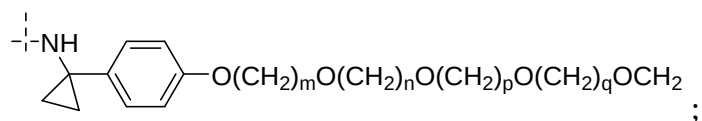
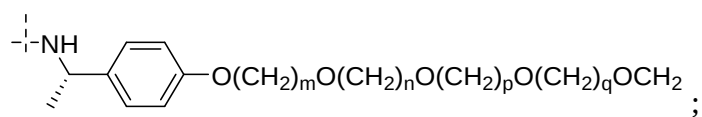
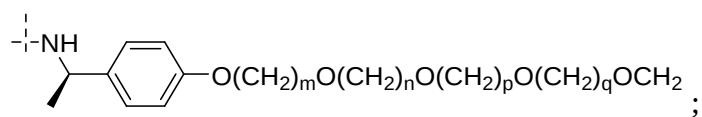
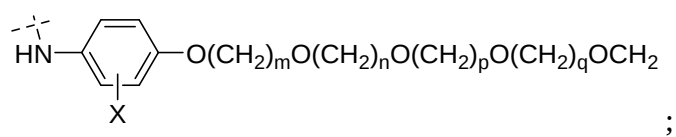
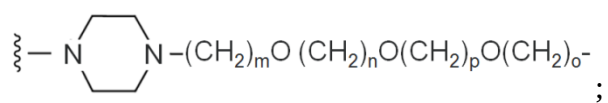
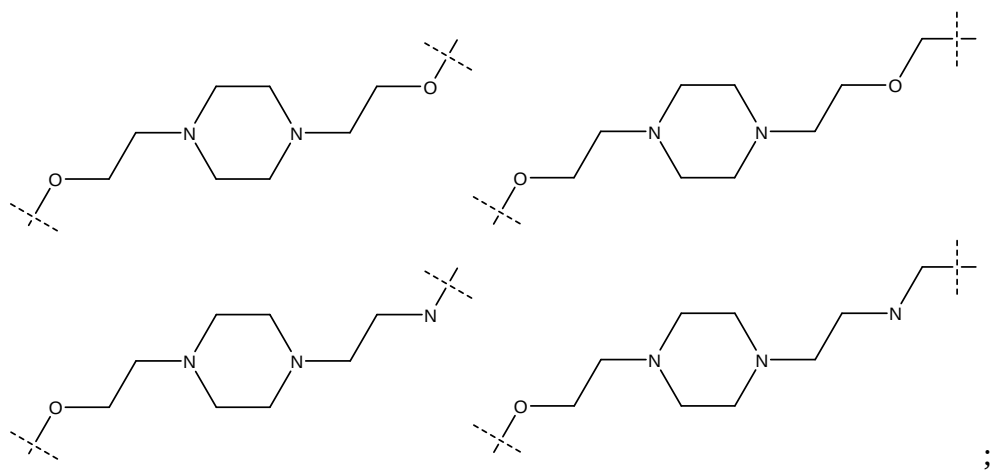


y

9. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-8, en donde L se selecciona del grupo que consiste en:







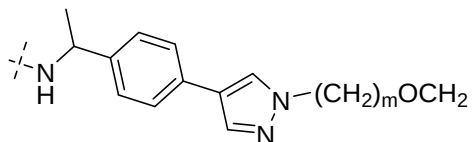
; en donde

m, n, o, p, q, y r del enlazador son independientemente 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13,  
14, 15, 16, 17, 18, 19, 20;

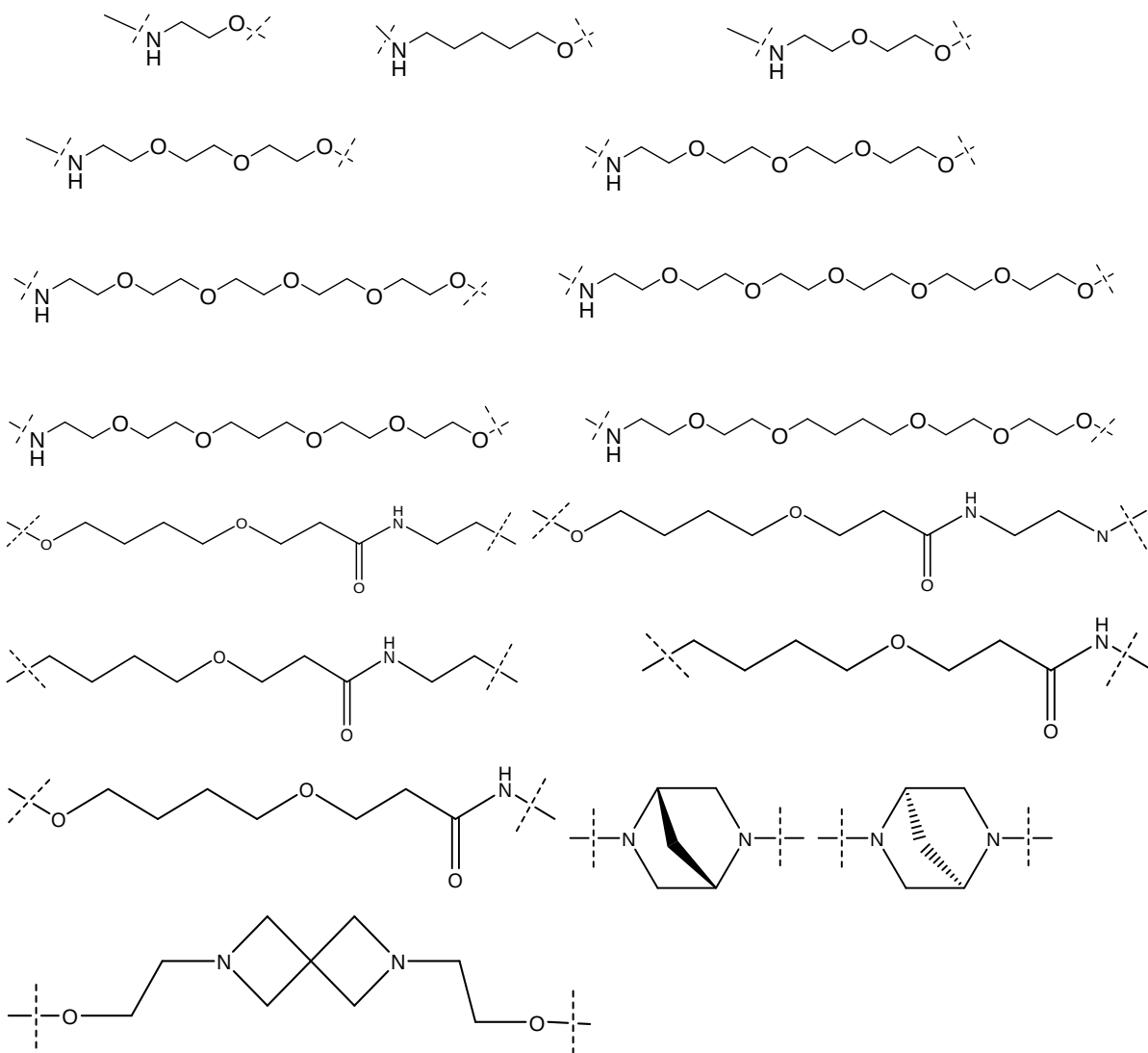
cuando el número es cero, no hay enlace N-O u O-O

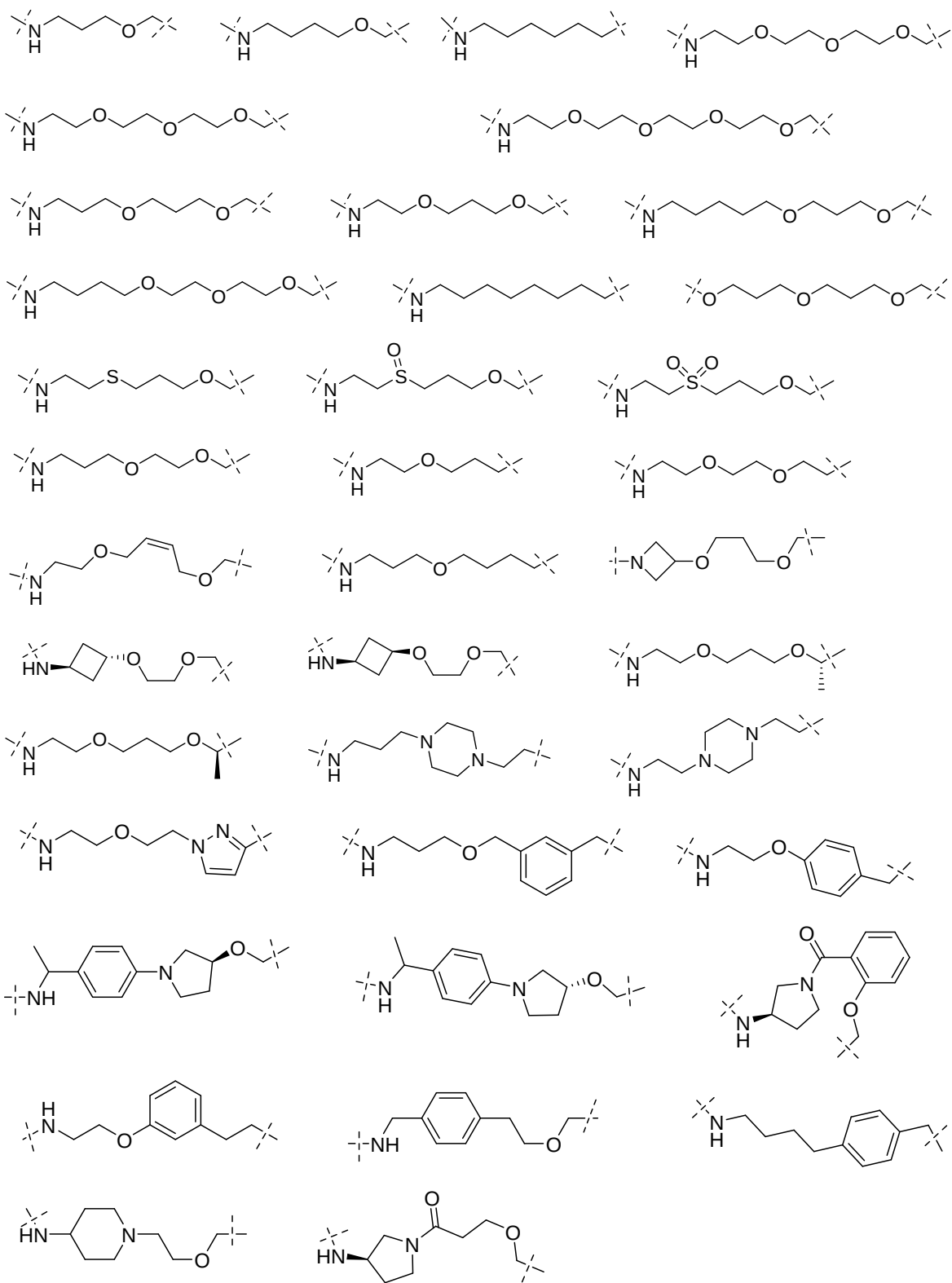
R del enlazador es H, metilo y etilo;

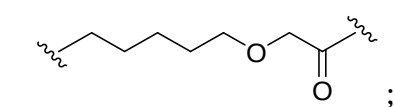
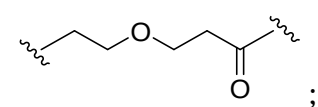
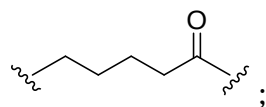
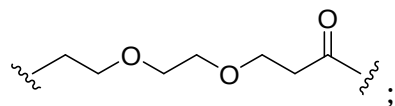
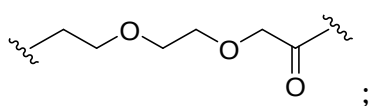
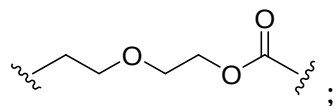
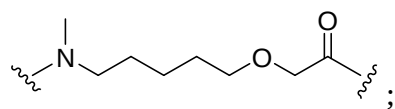
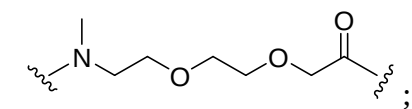
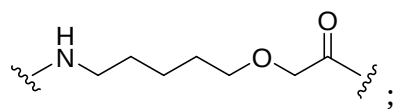
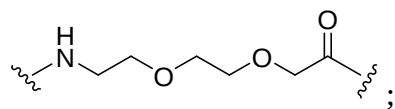
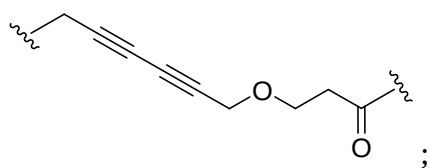
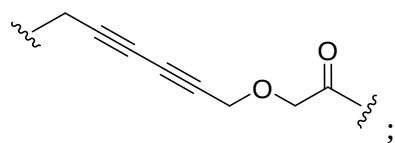
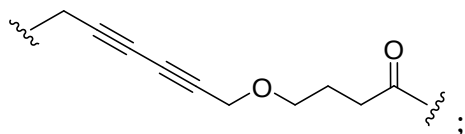
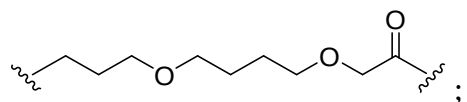
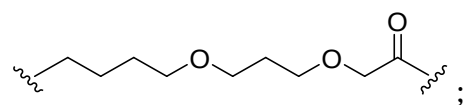
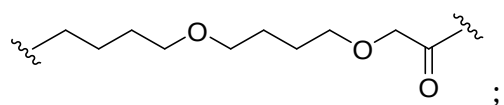
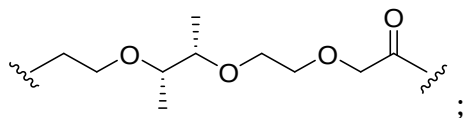
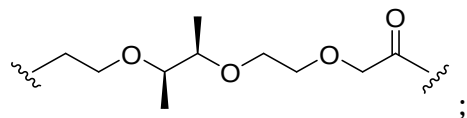
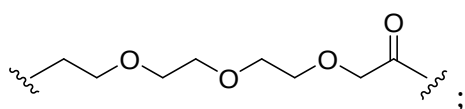
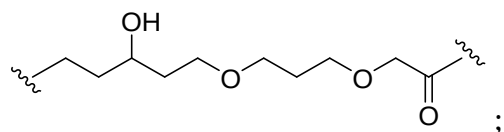
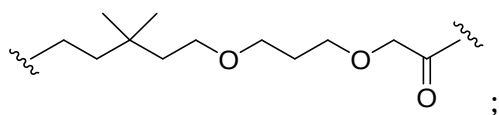
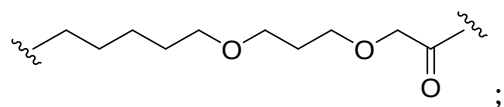
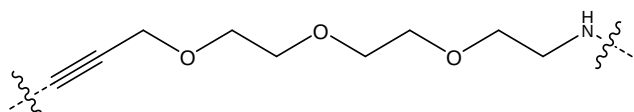
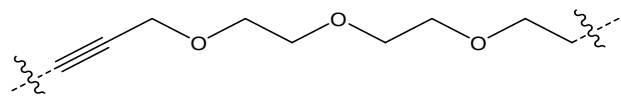
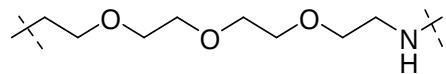
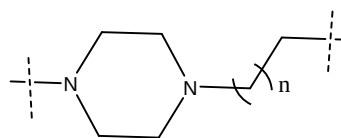
X del enlazador es H y F

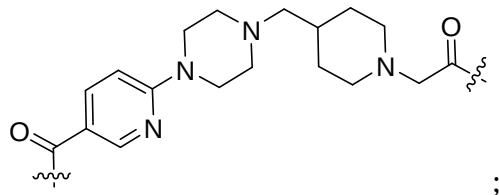
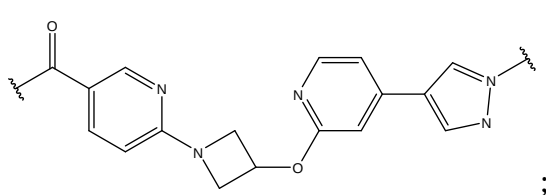
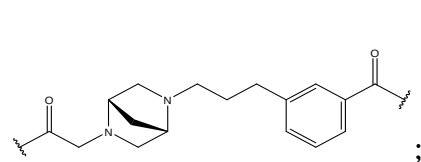
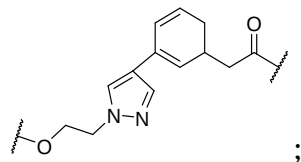
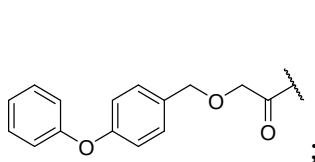
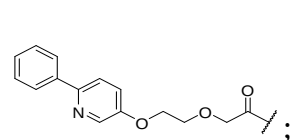
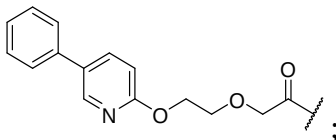
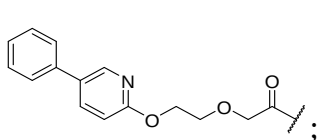
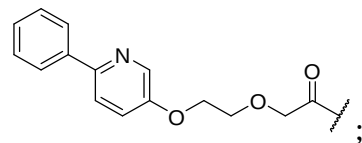
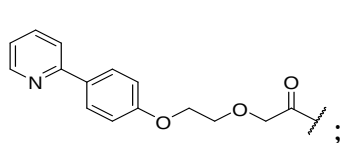
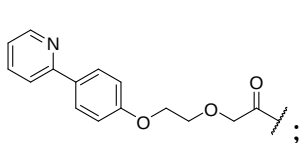
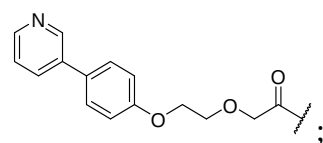
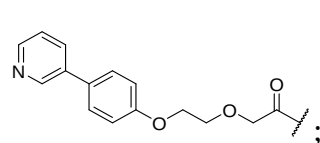
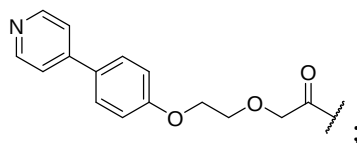
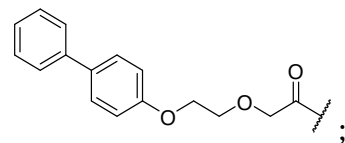
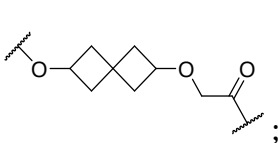
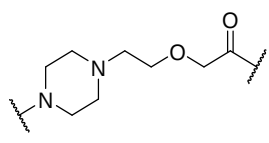
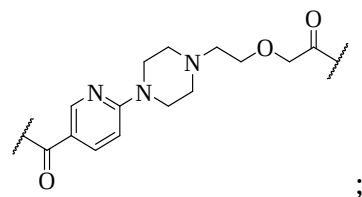
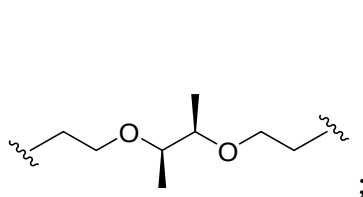
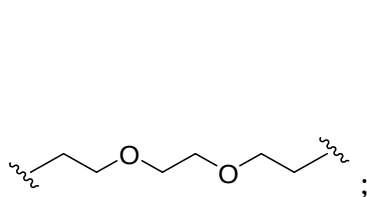
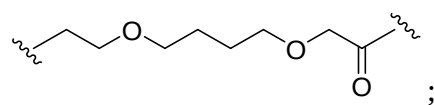
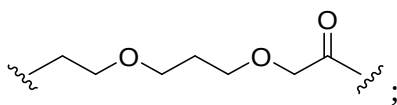
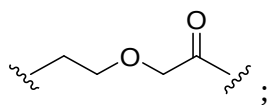
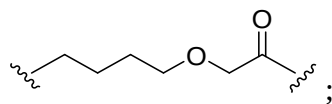
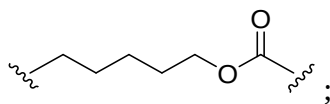
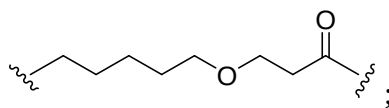


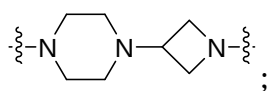
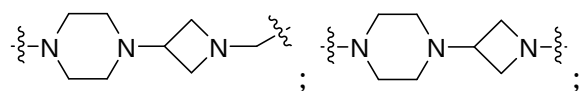
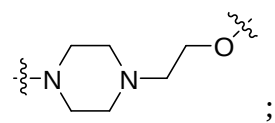
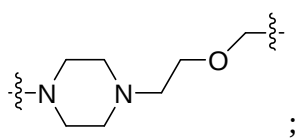
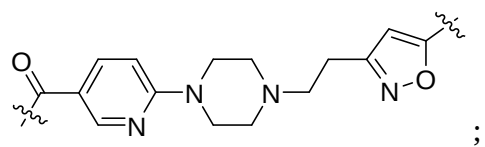
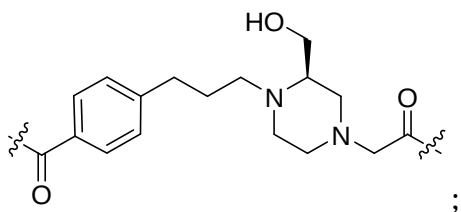
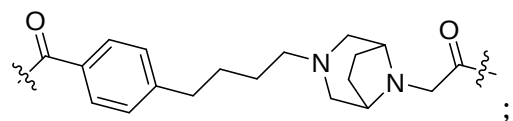
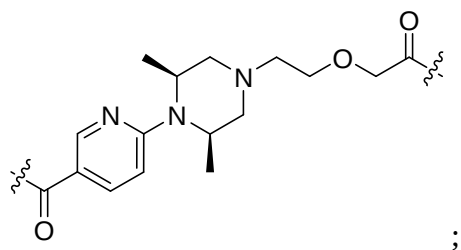
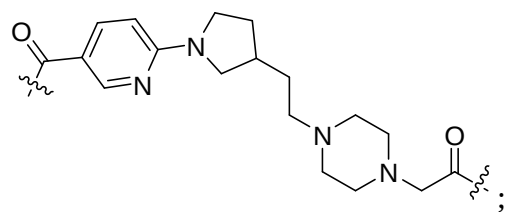
donde m del enlazador puede ser 2, 3, 4, 5

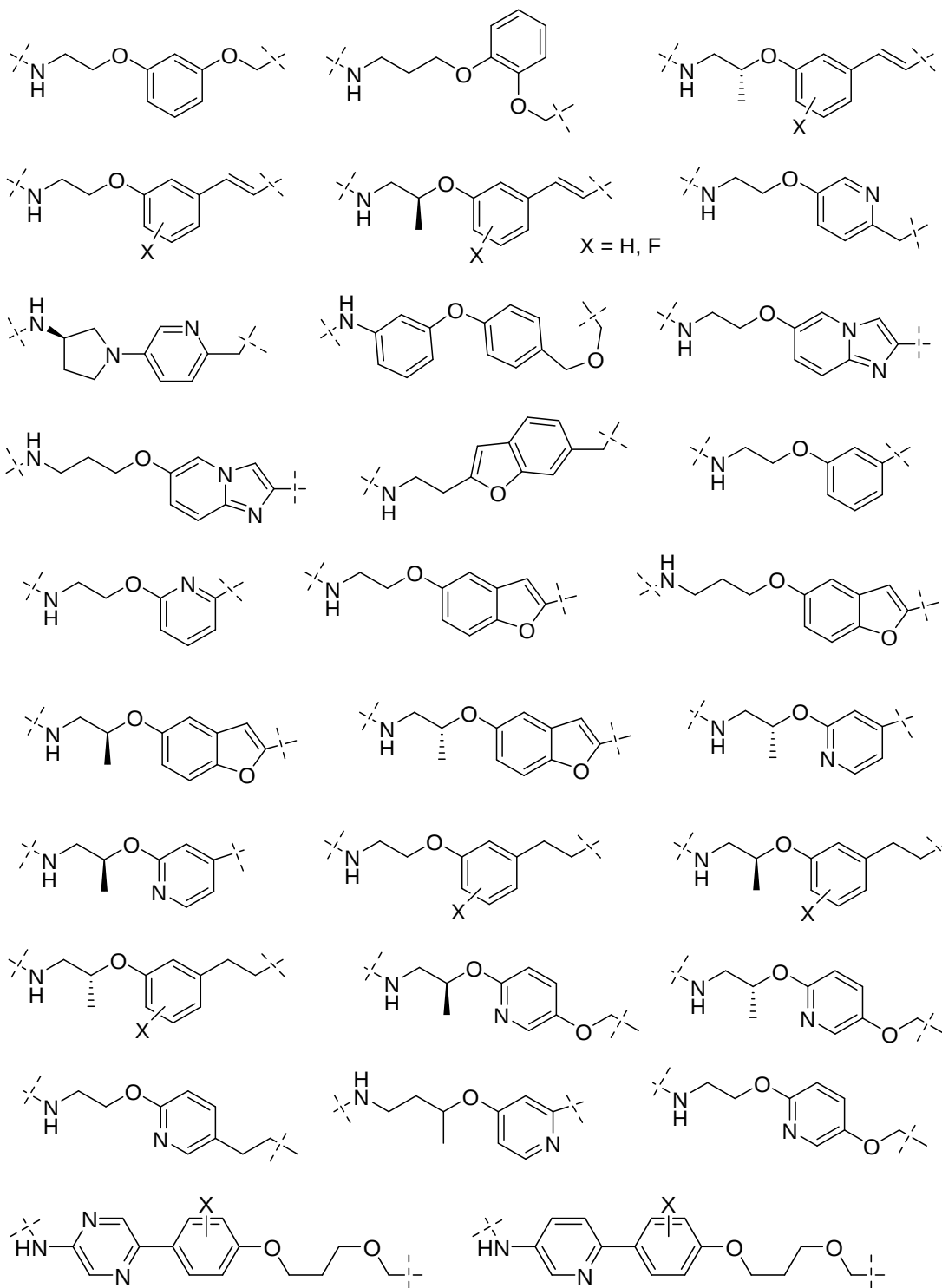


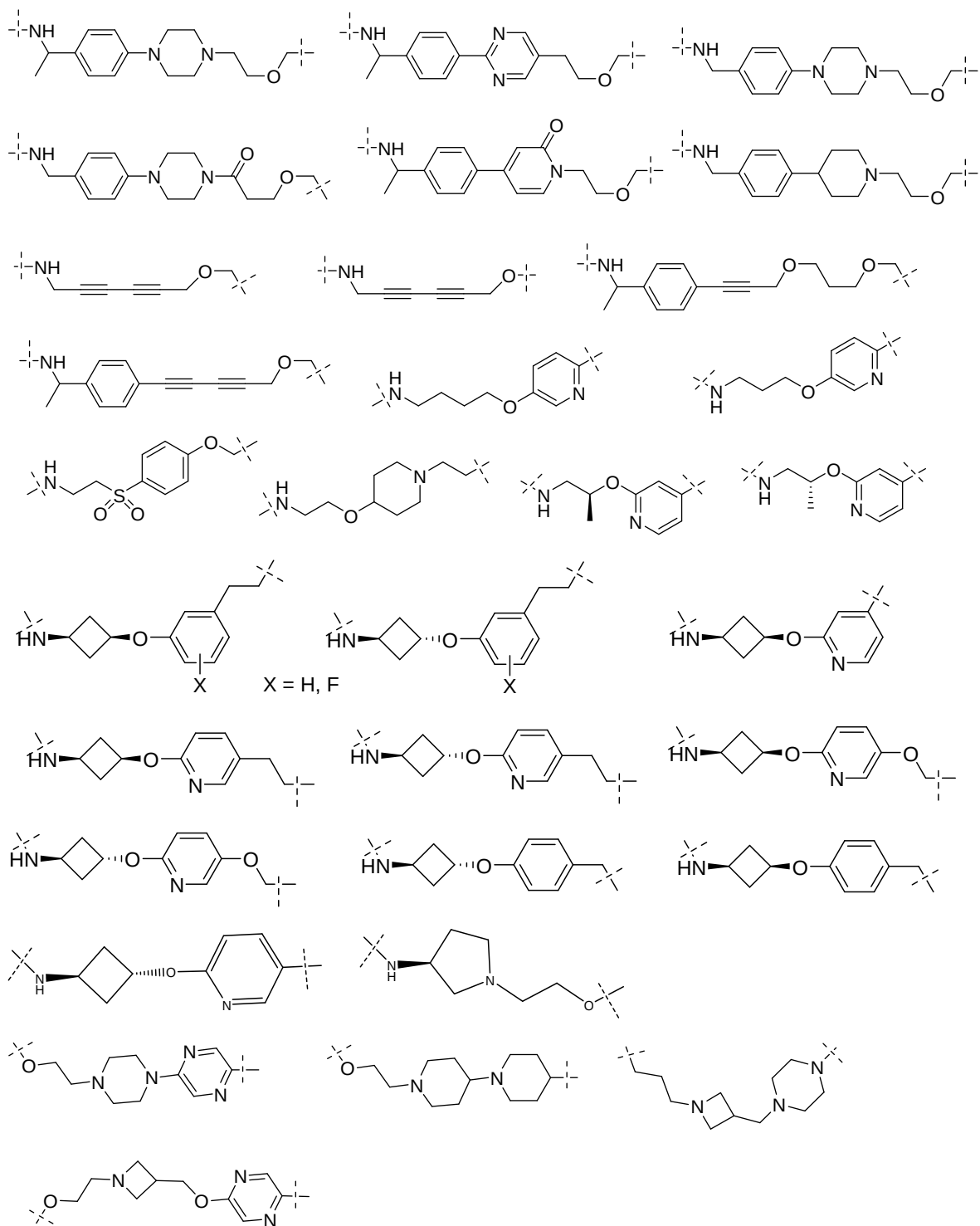


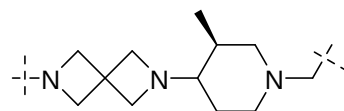
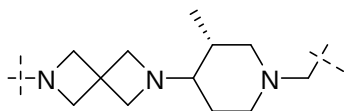
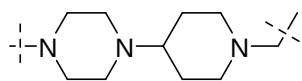
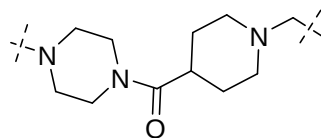
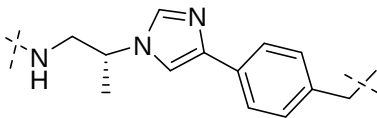
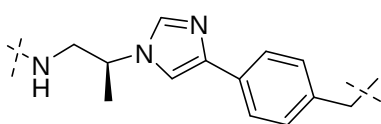
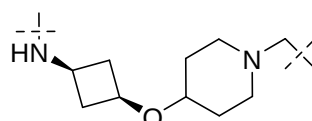
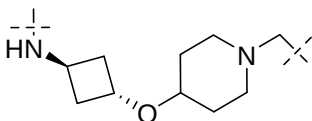
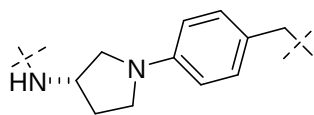
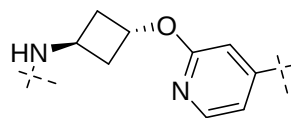
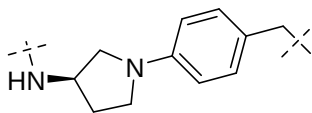
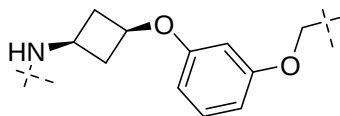
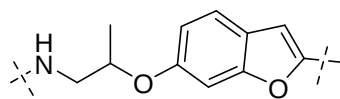
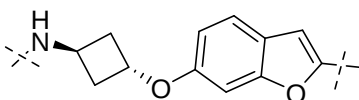
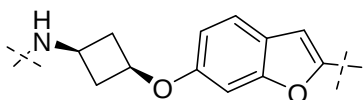
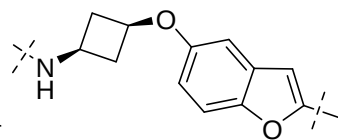
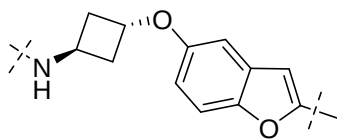
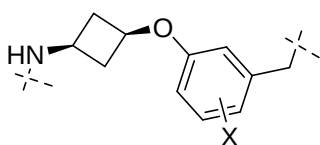
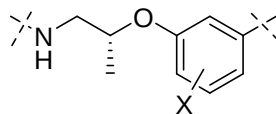
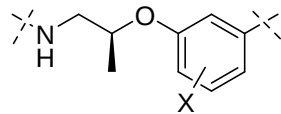
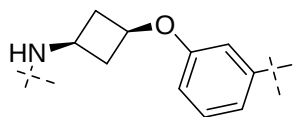
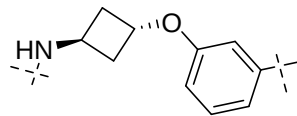
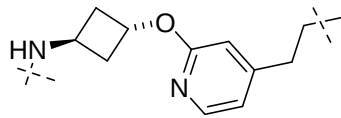
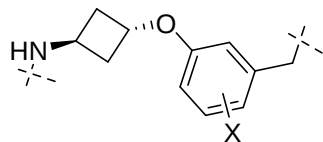
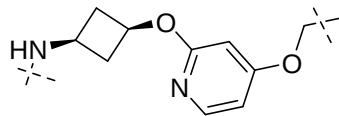
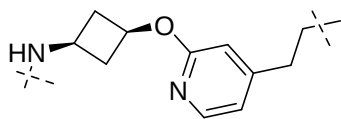
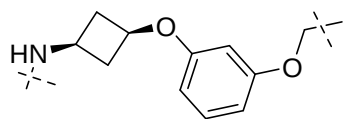


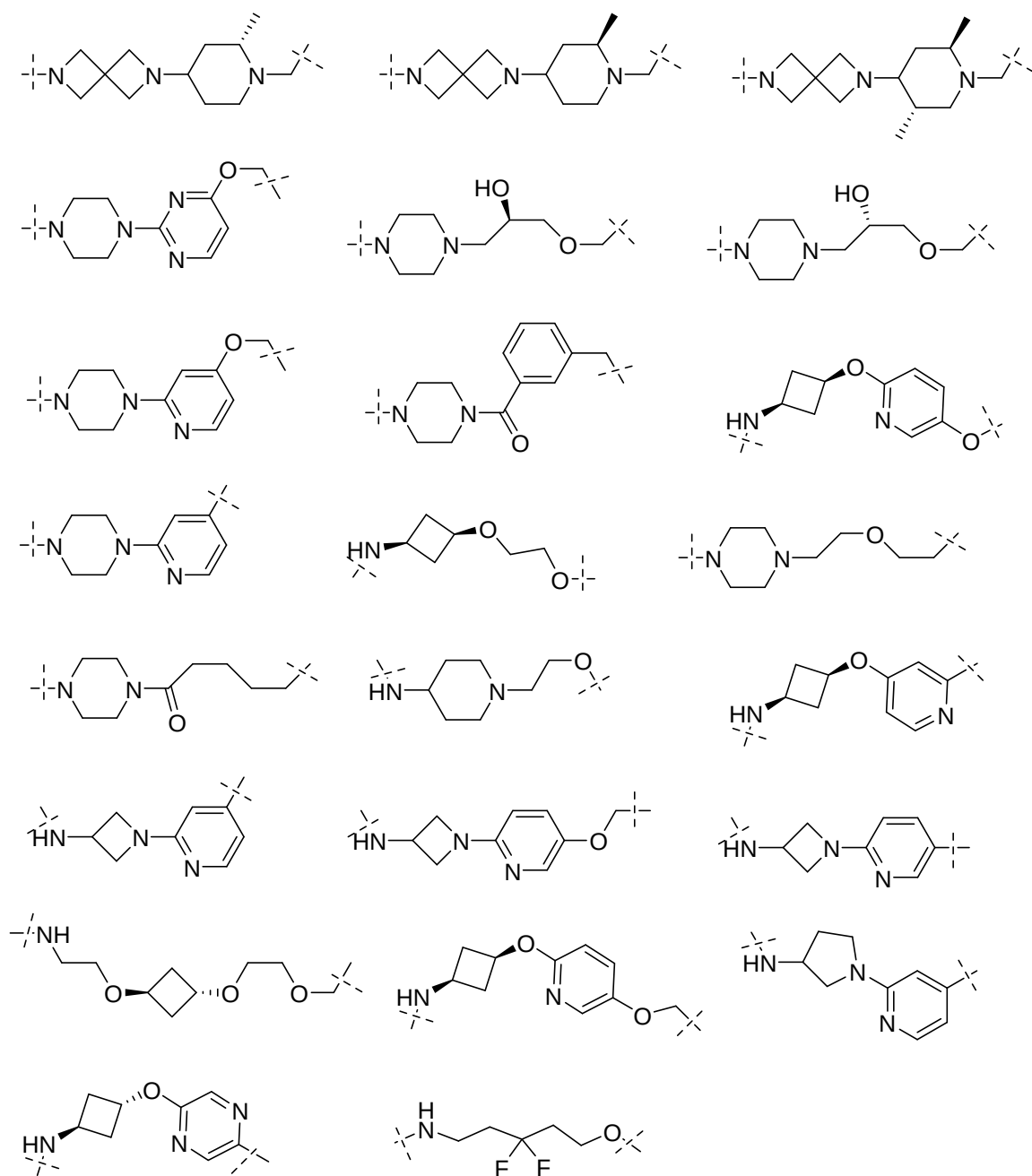






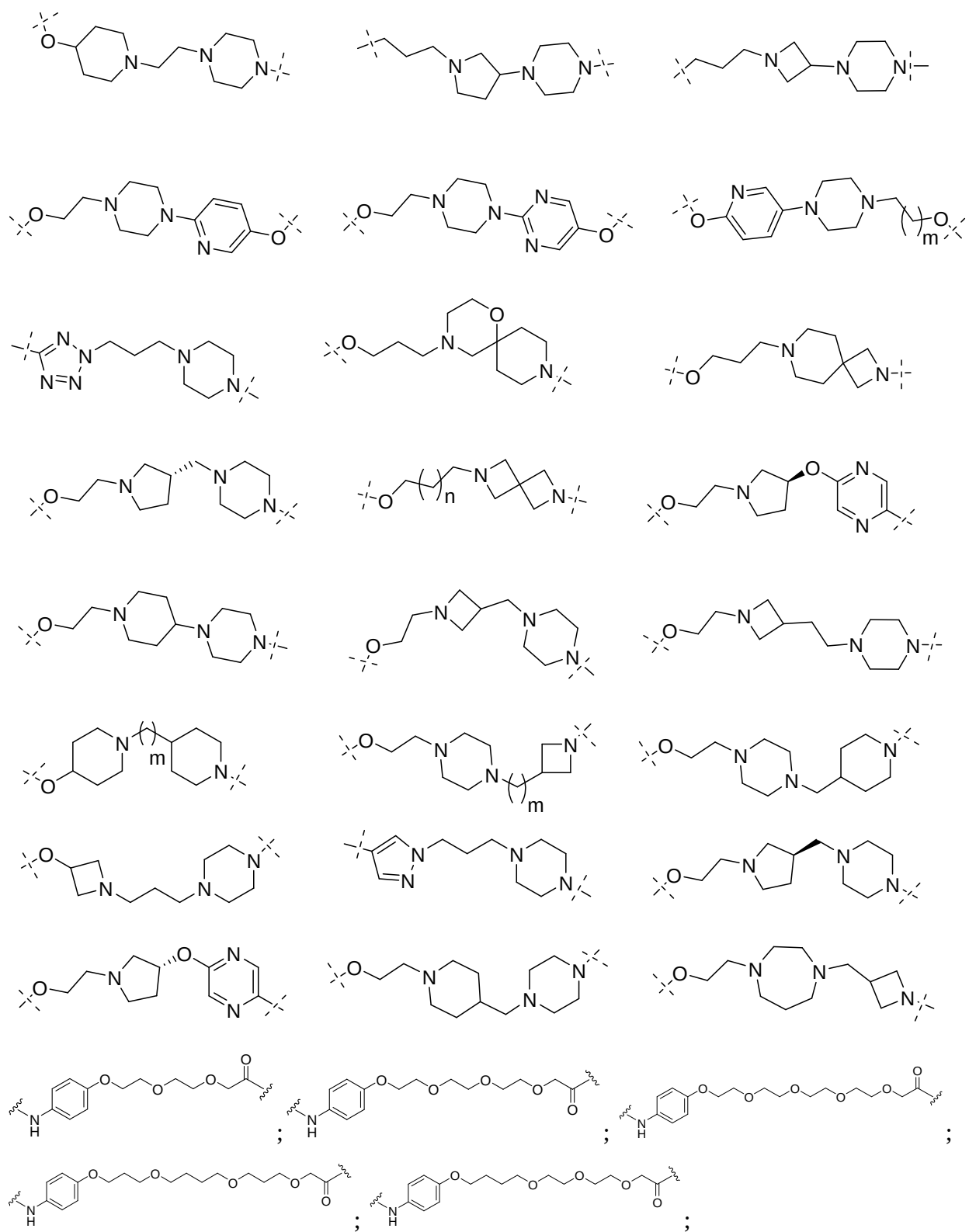


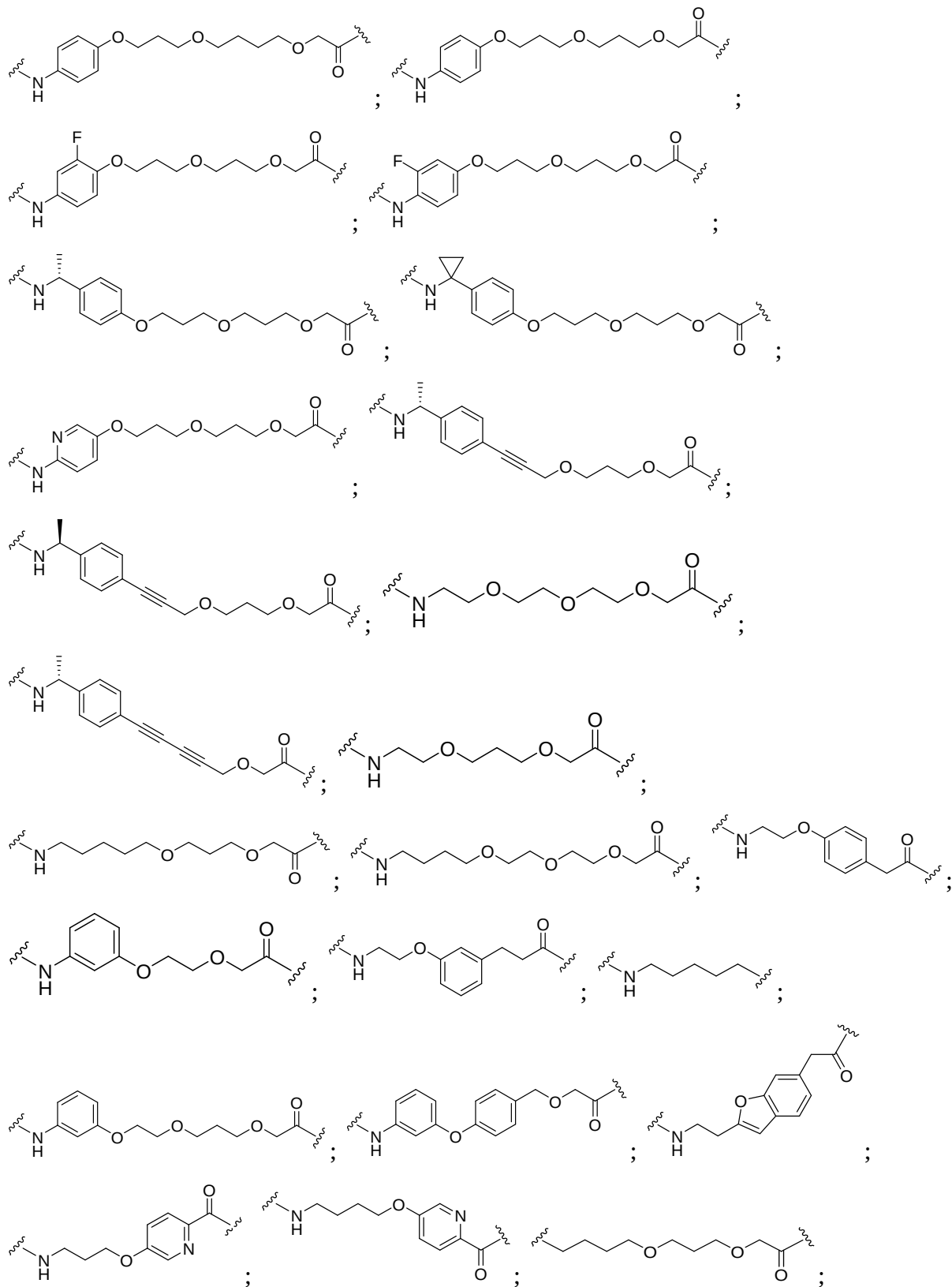


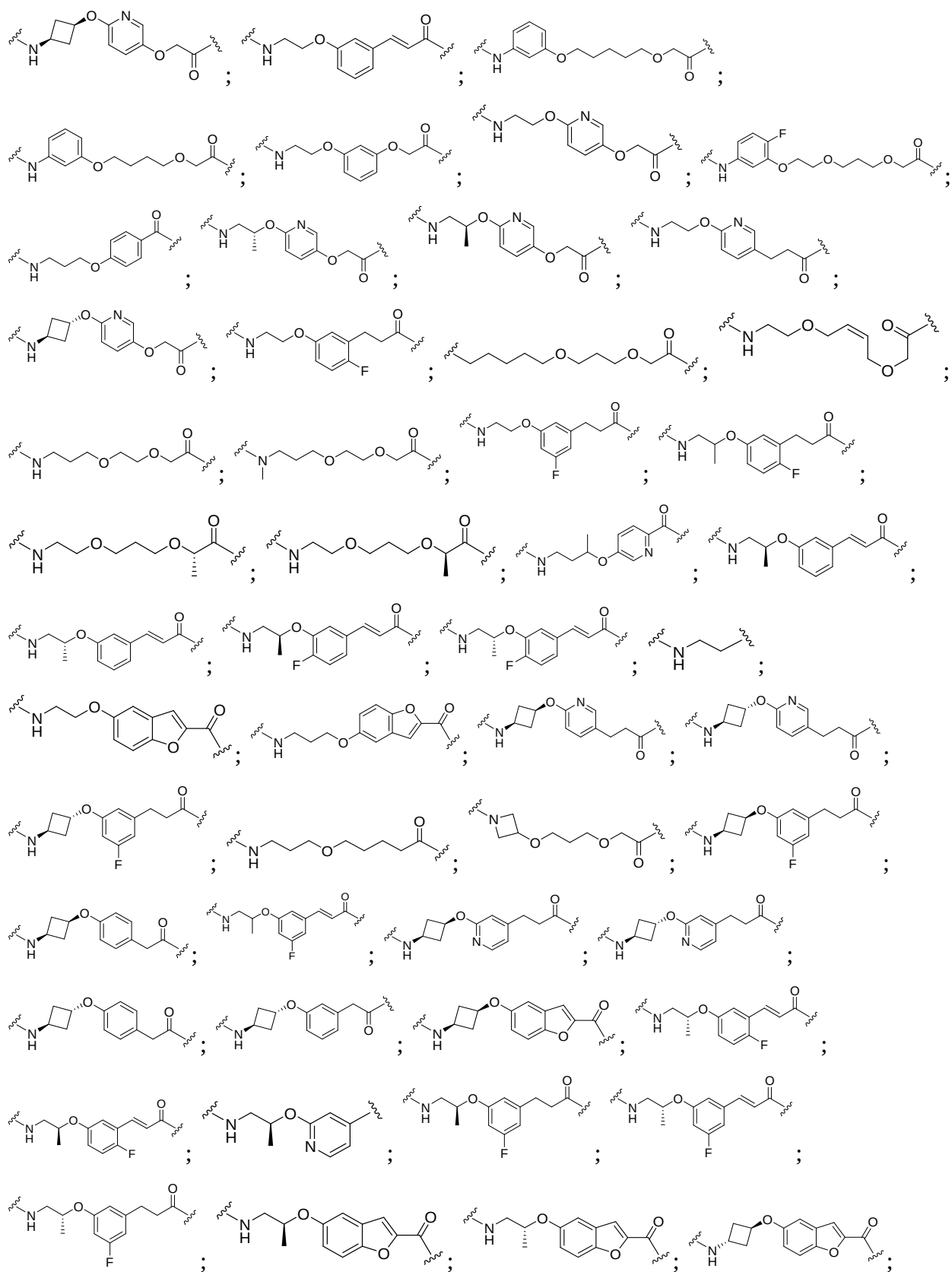


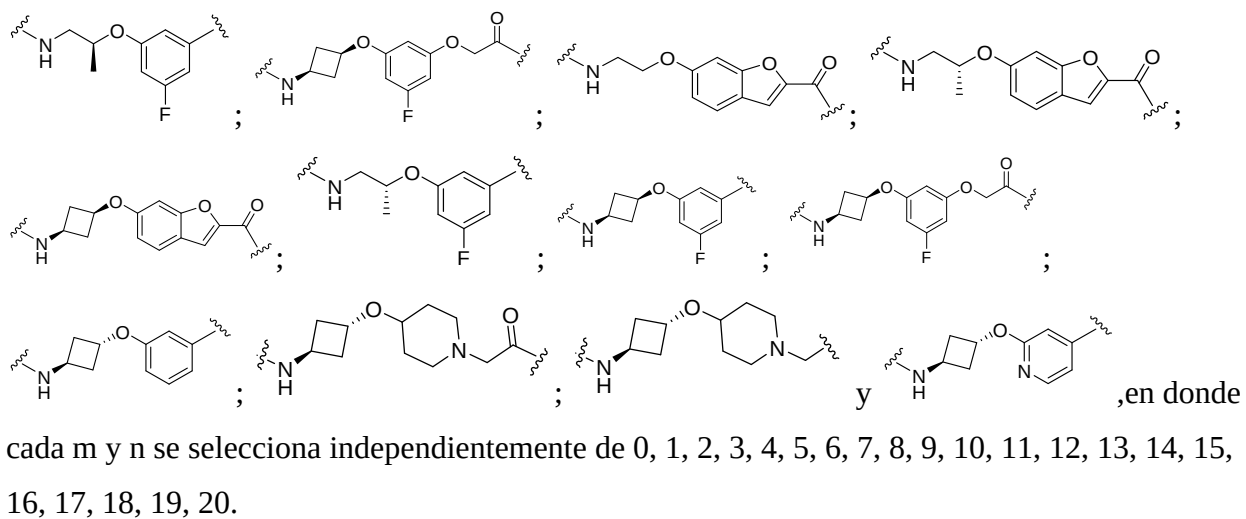
donde cada n y m del enlazador puede ser independientemente 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 20. 1.

10. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-9, en donde L se selecciona del grupo que consiste en:

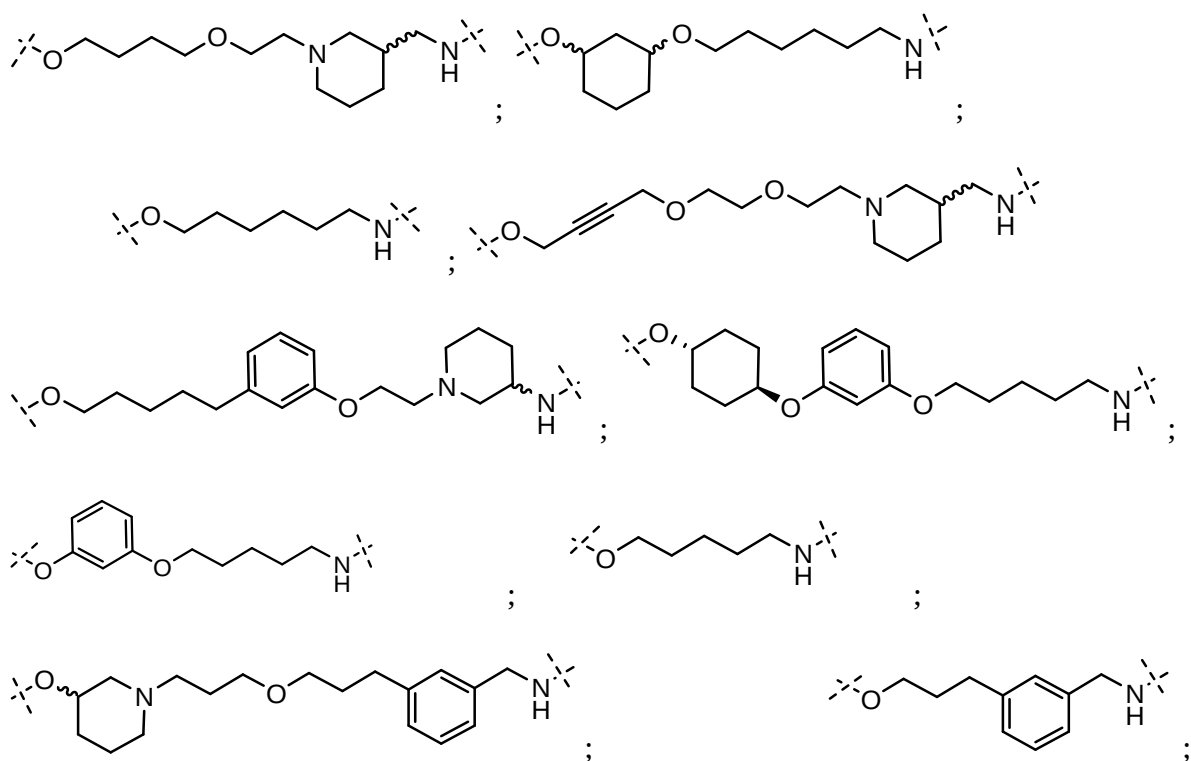


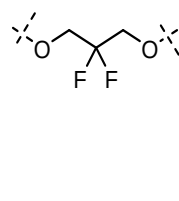
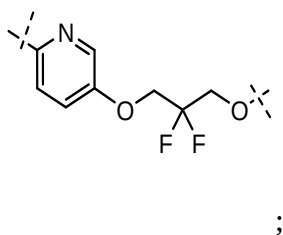
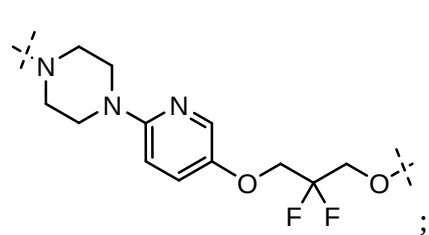
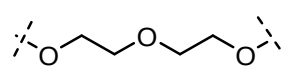
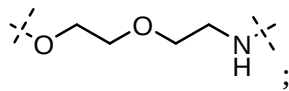
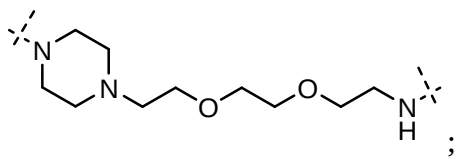
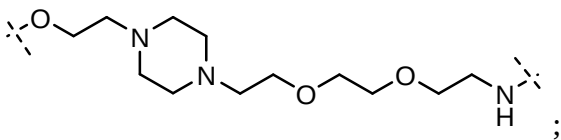
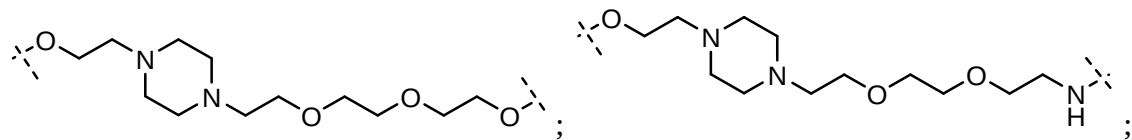
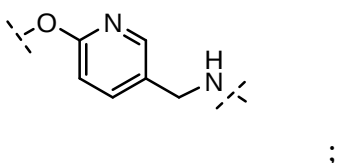
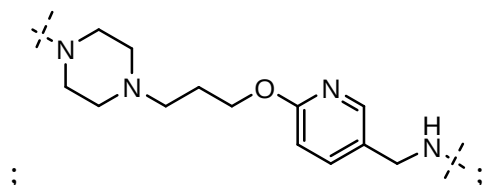
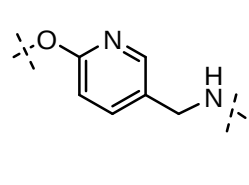
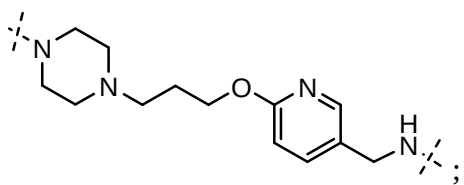
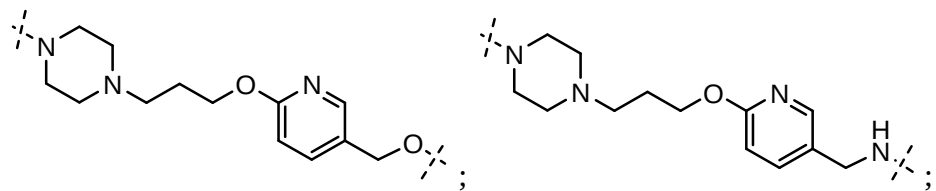
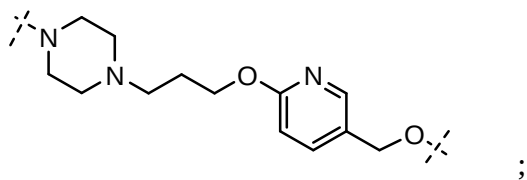
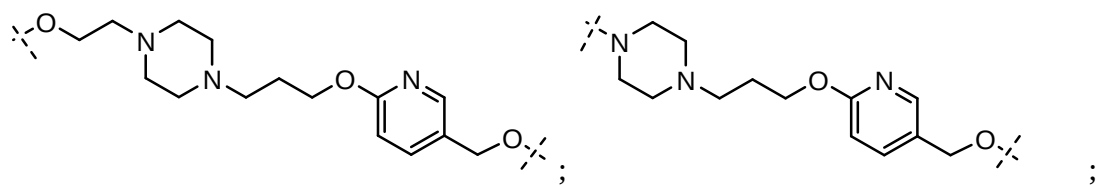
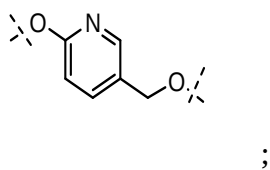
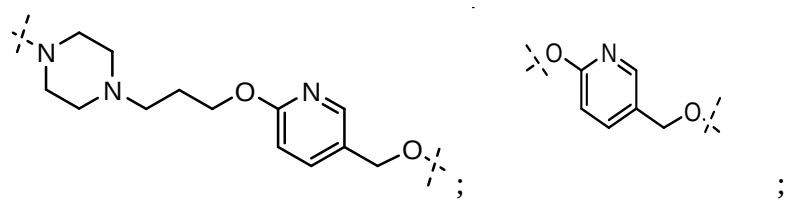




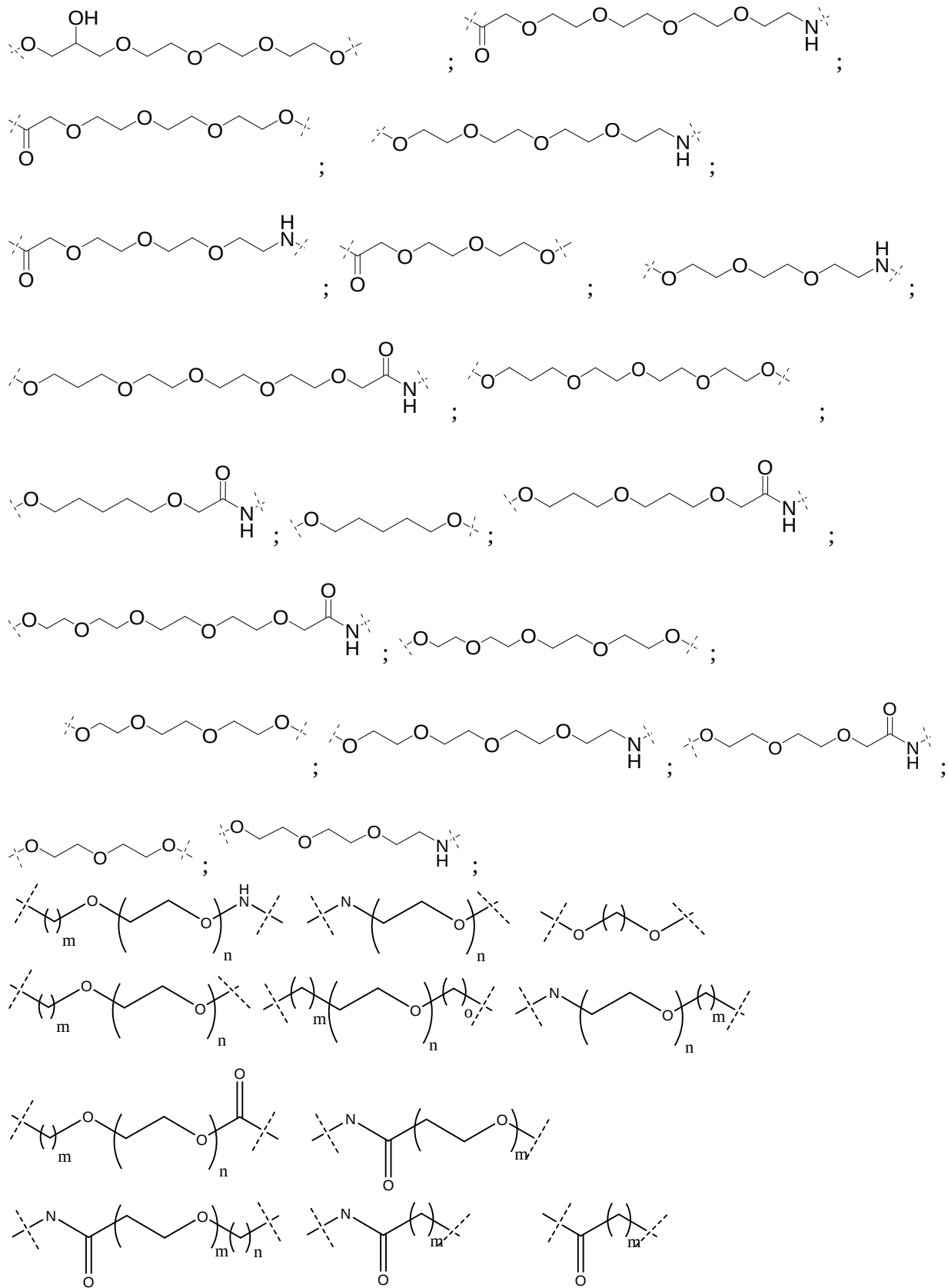


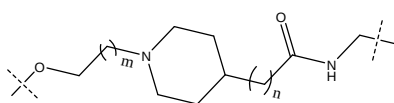
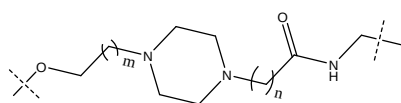
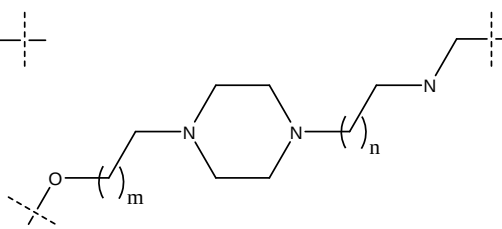
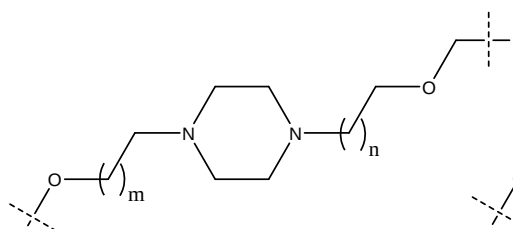
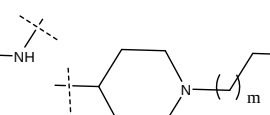
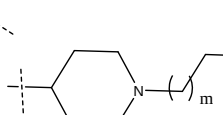
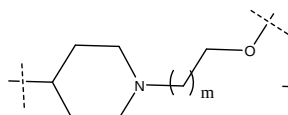
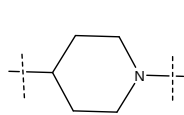
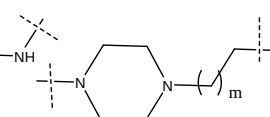
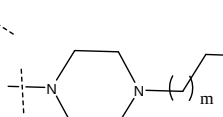
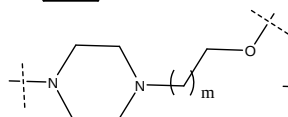
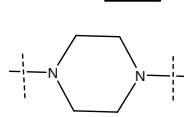
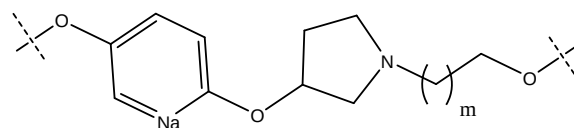
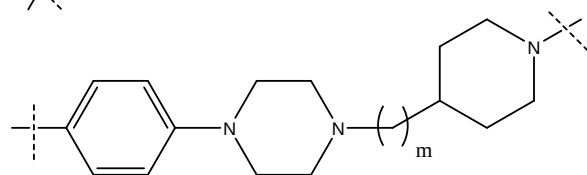
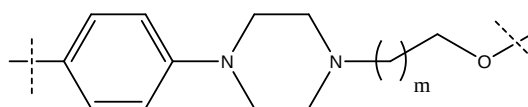
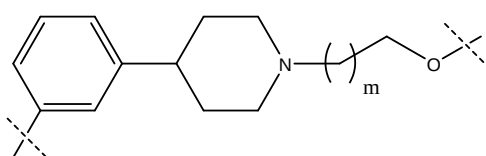
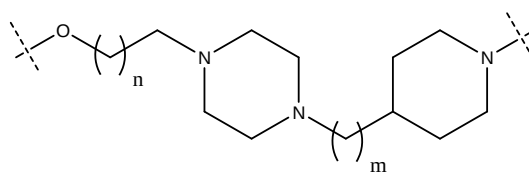
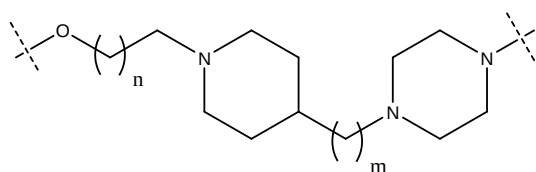
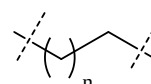
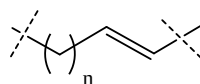
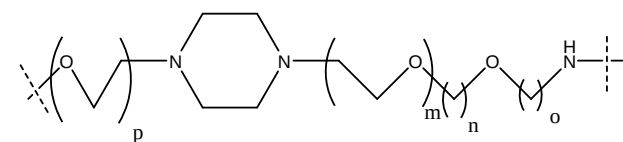
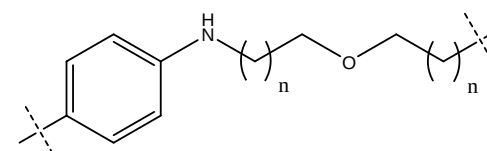
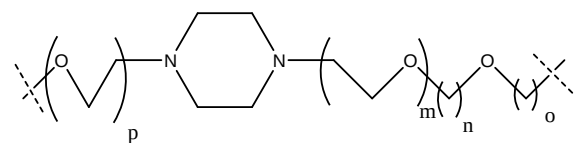
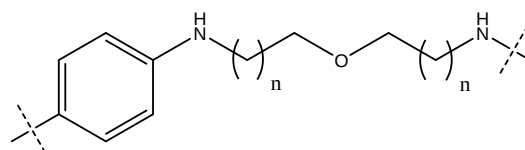
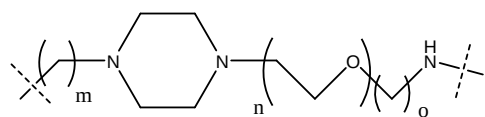
11. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-9, en donde el enlazador (L) se selecciona del grupo que consiste en:

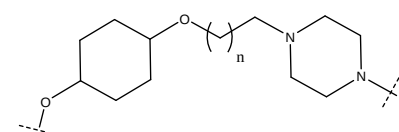
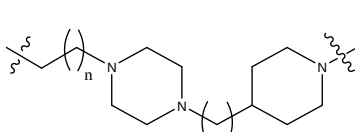
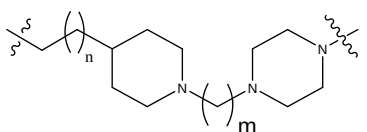
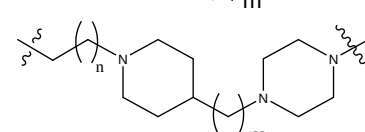
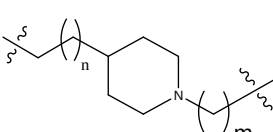
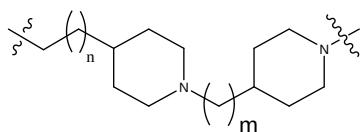
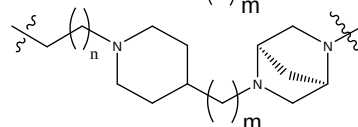
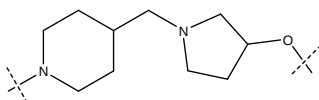
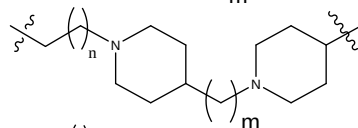
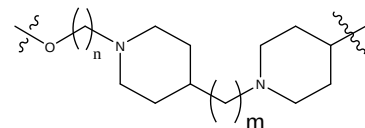
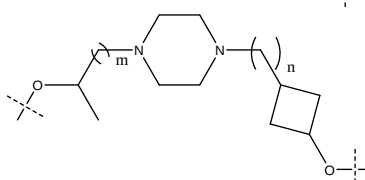
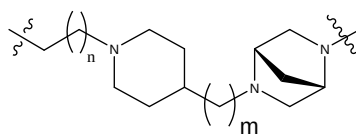
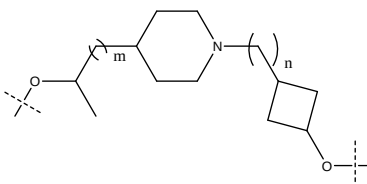
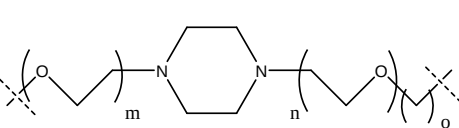
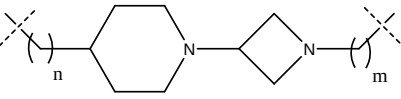
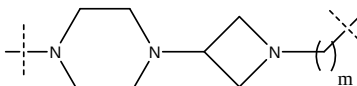
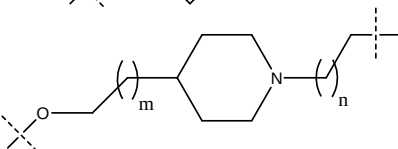
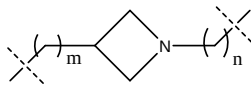
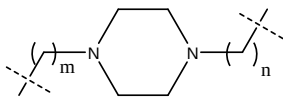


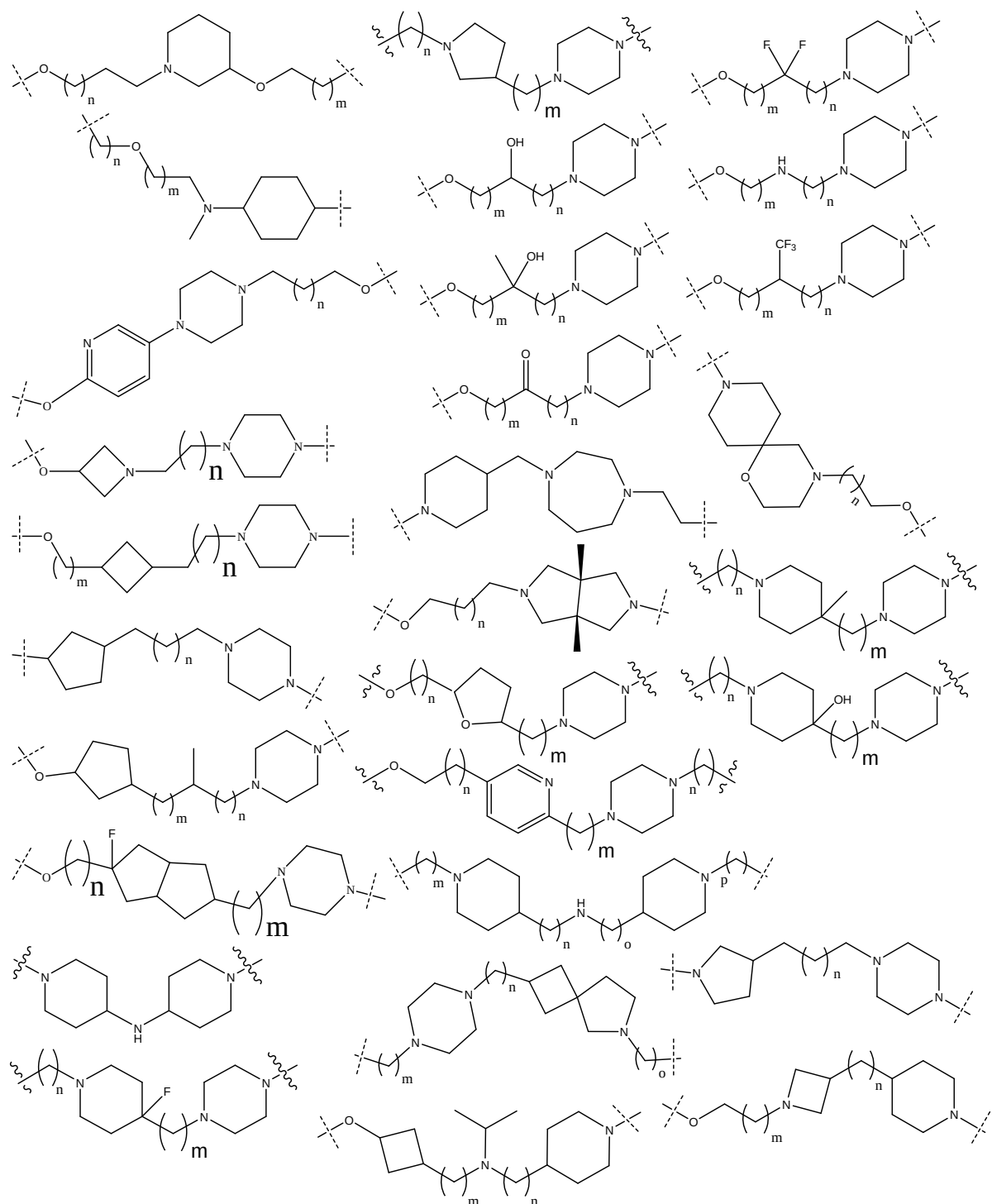


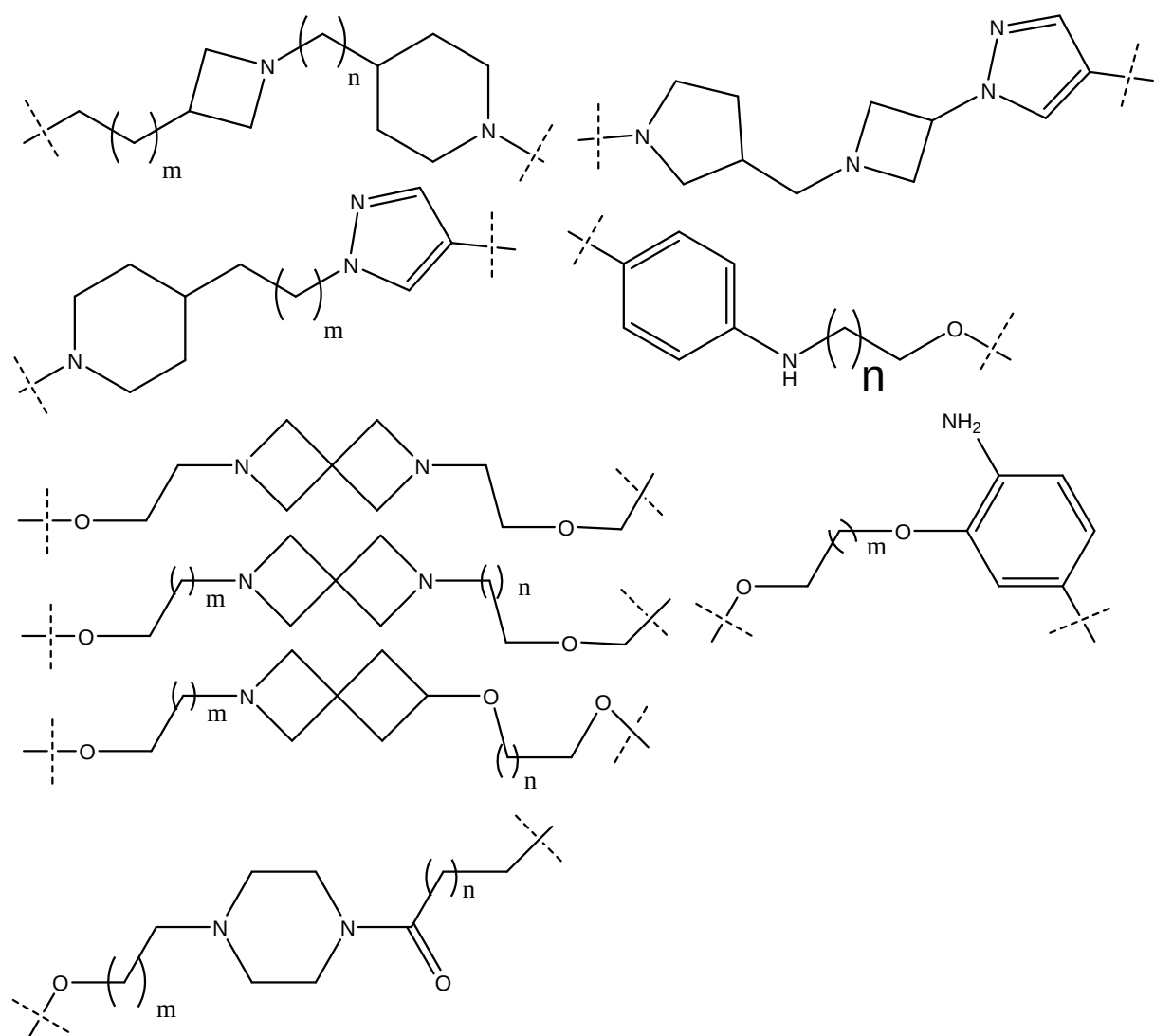


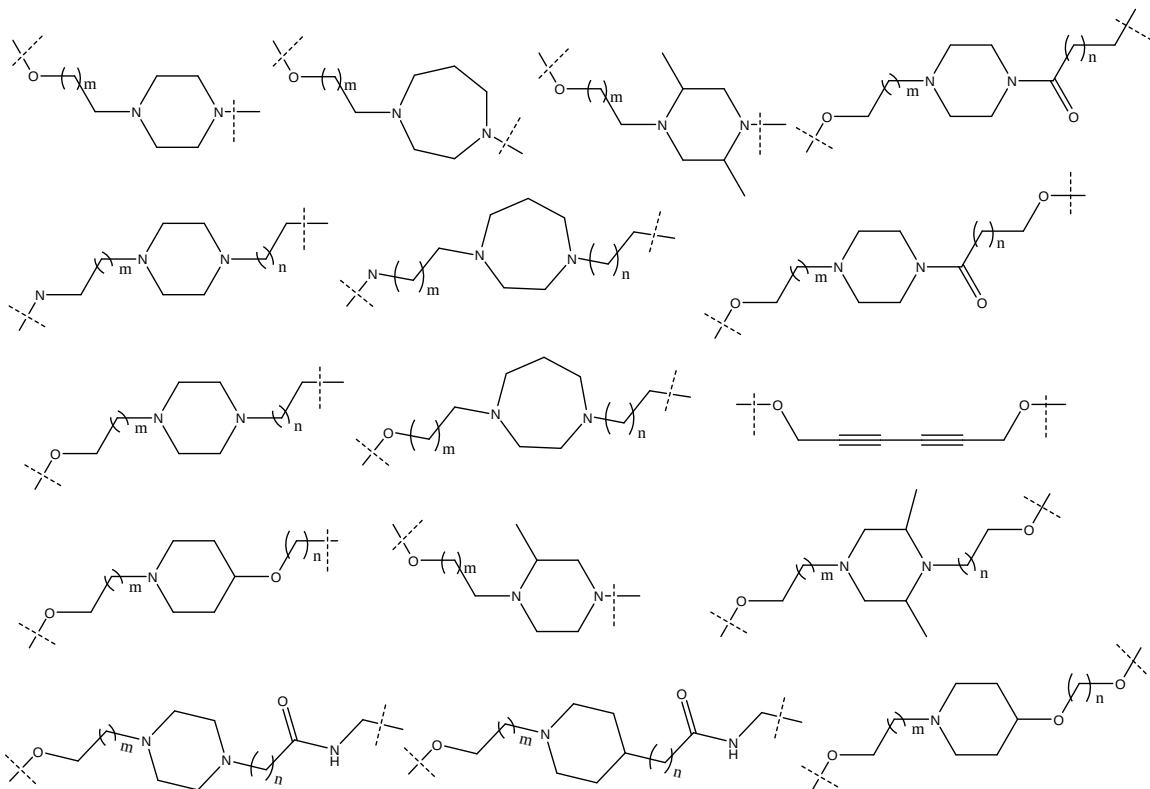
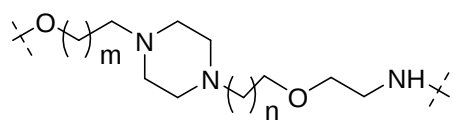
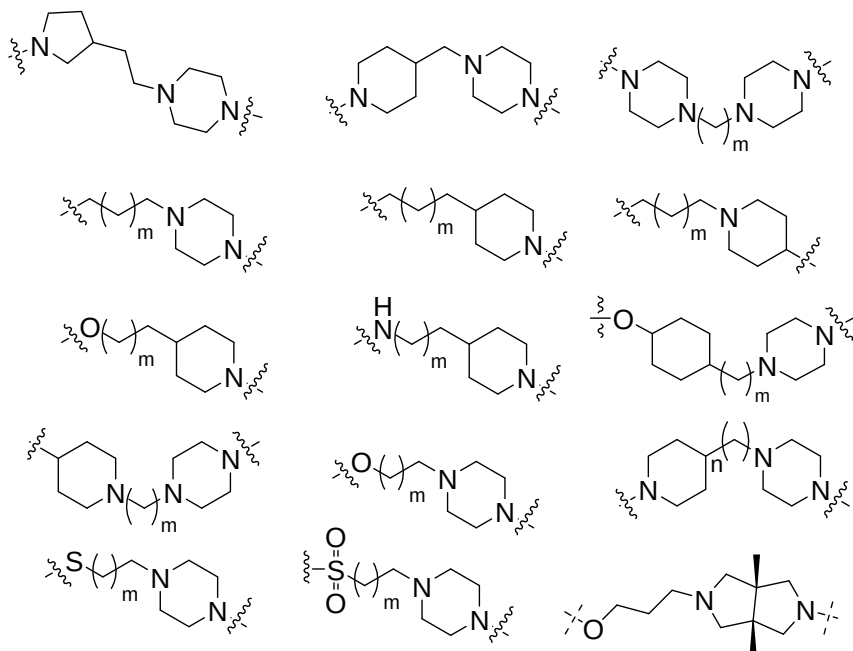


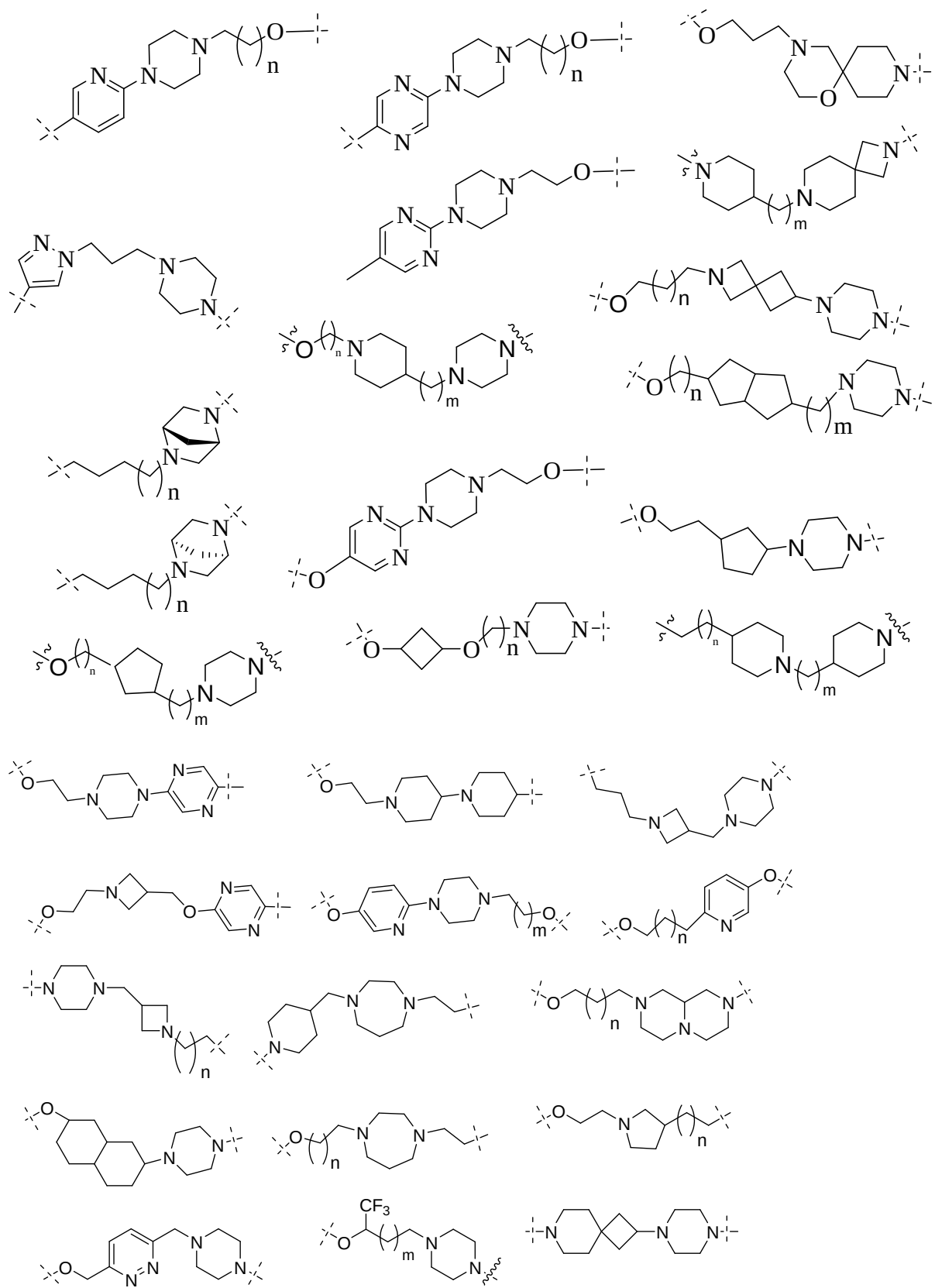


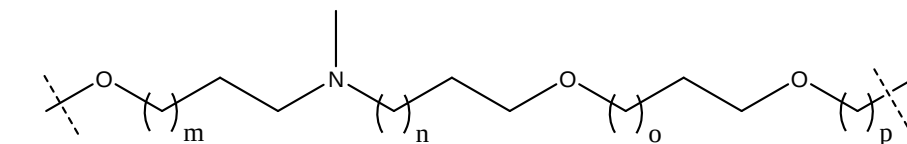


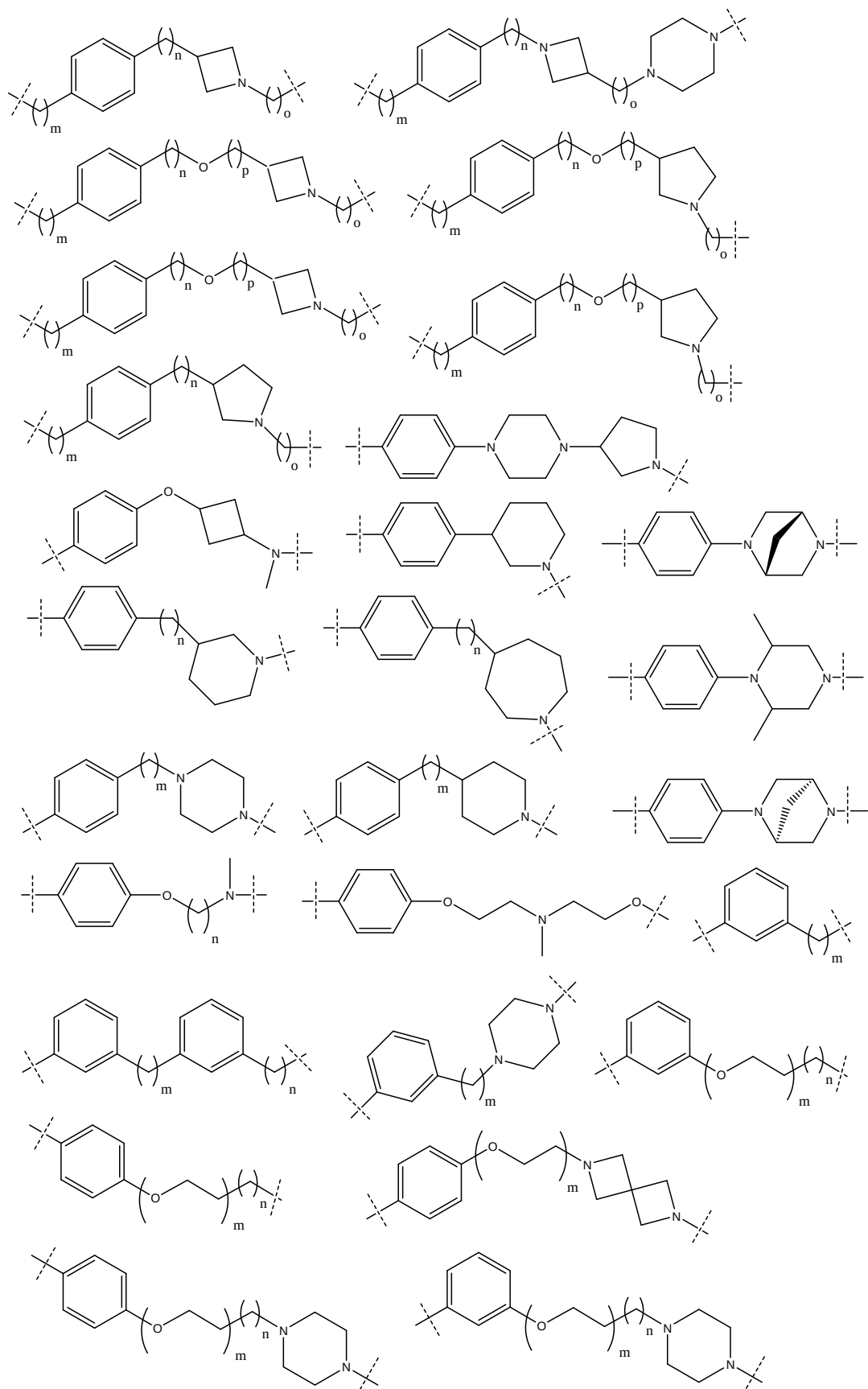


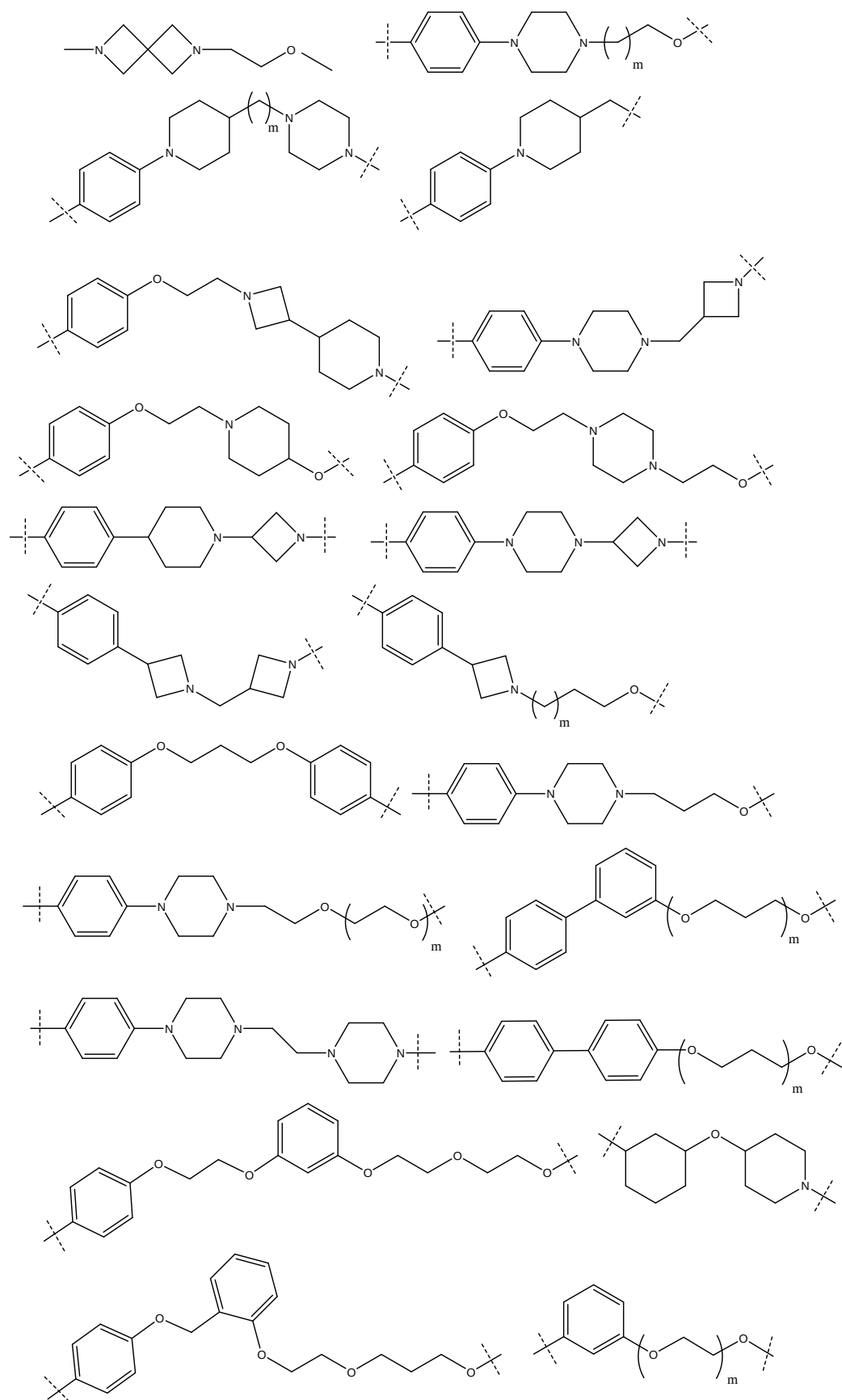


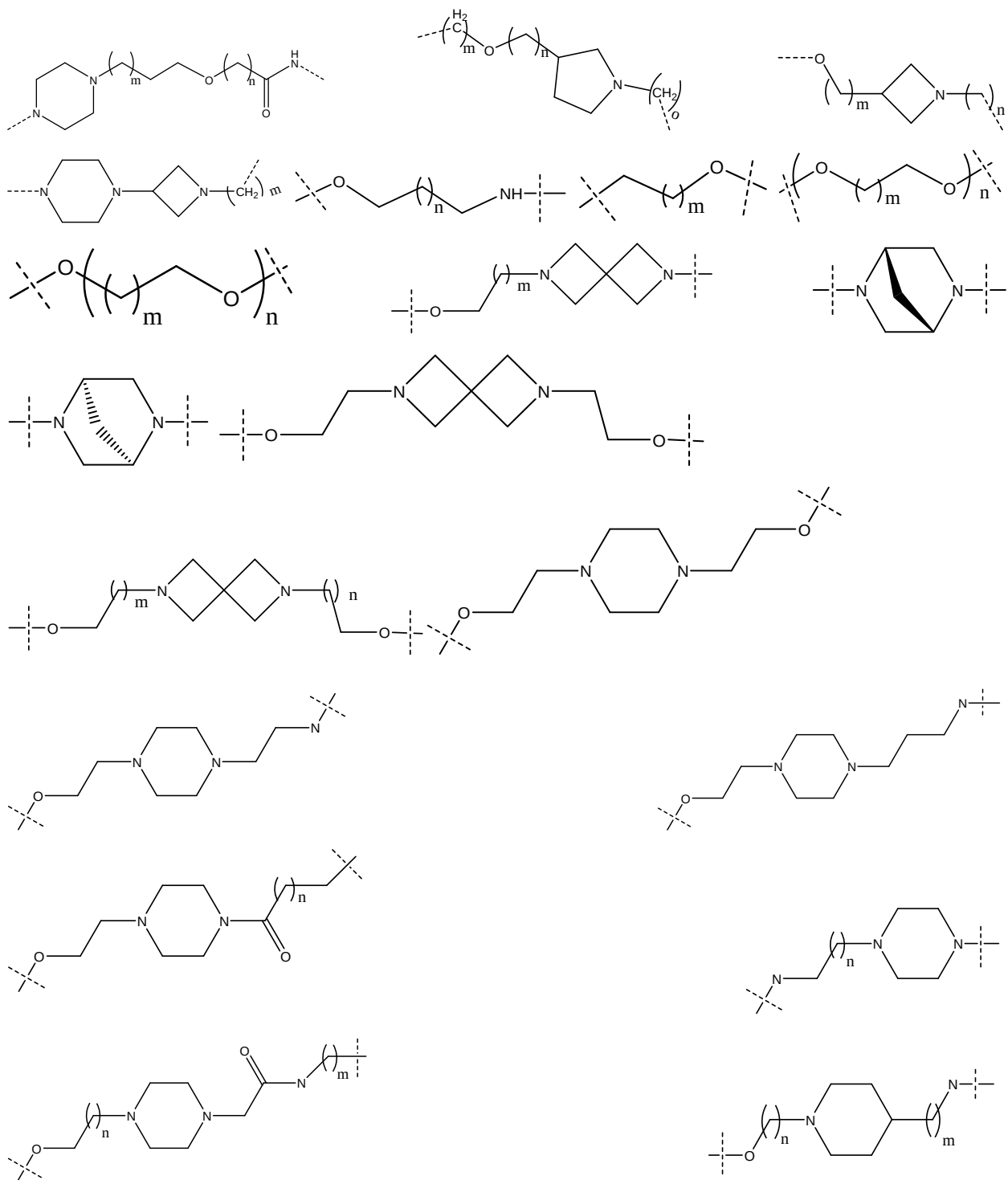


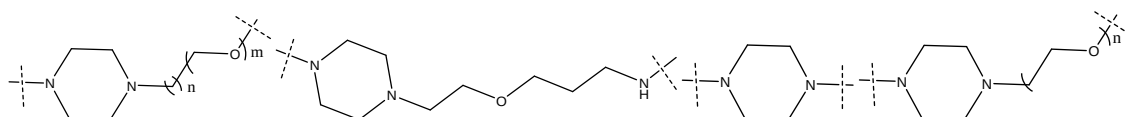
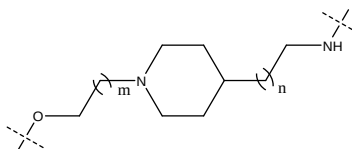
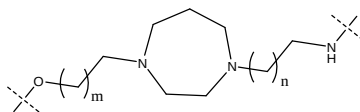
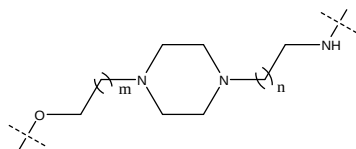
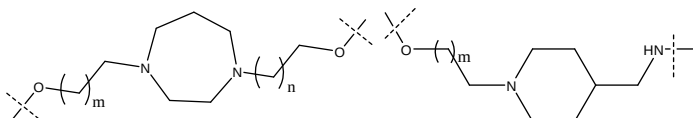
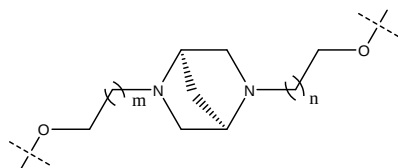
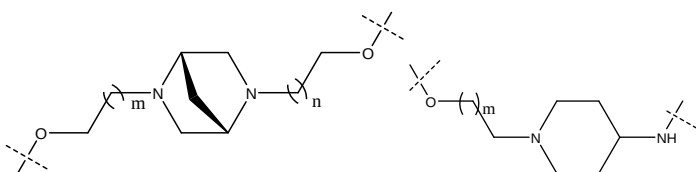
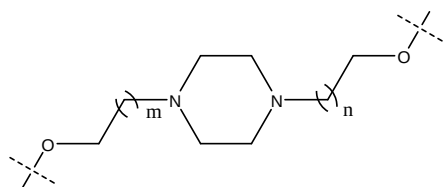
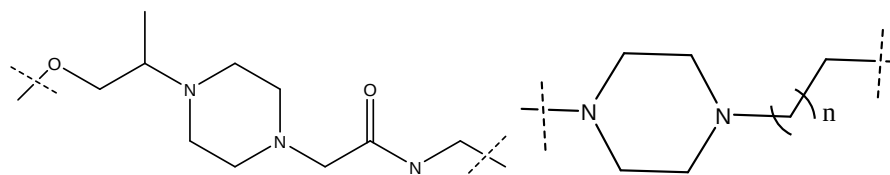
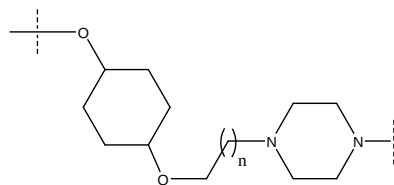
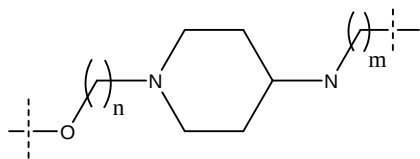


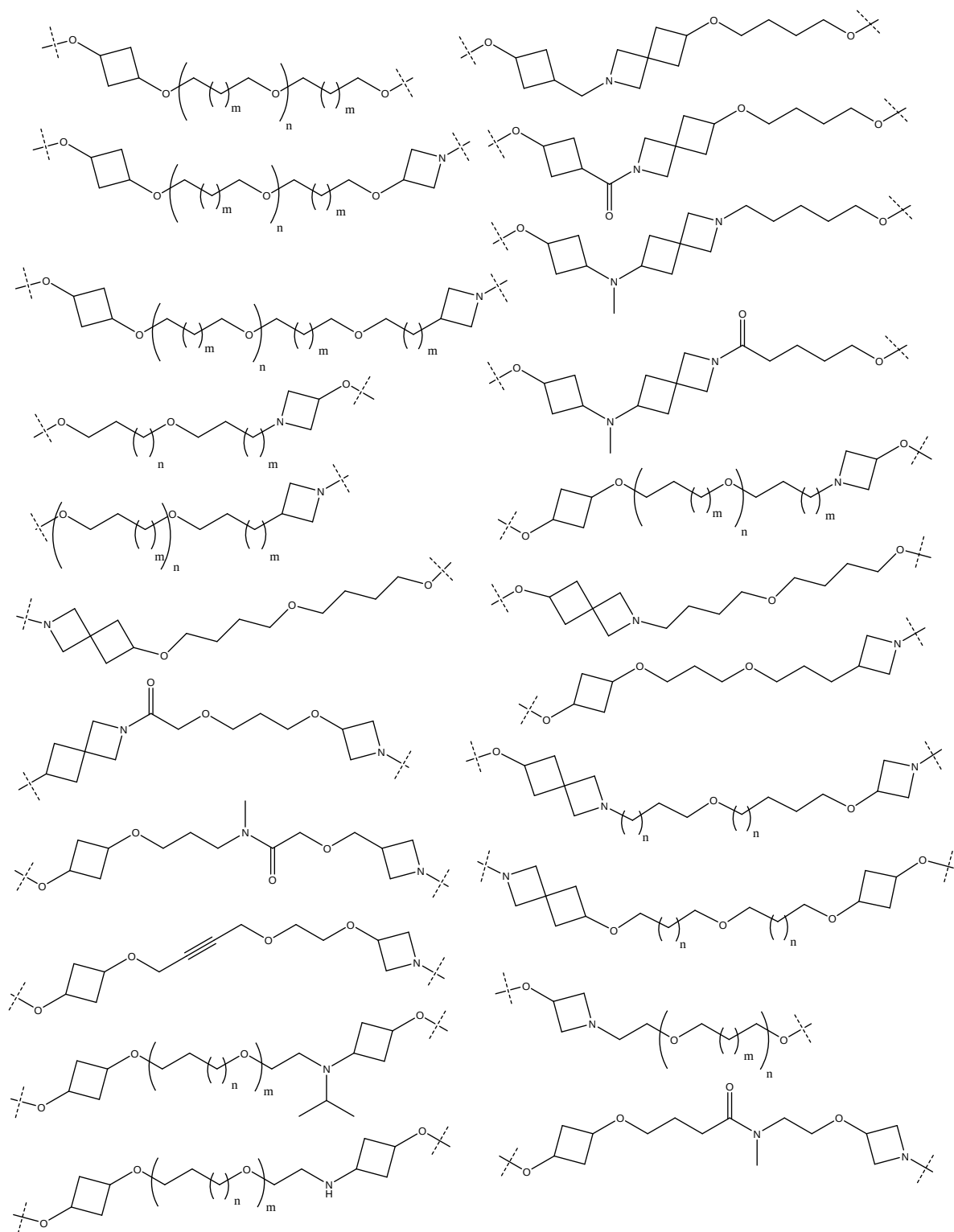


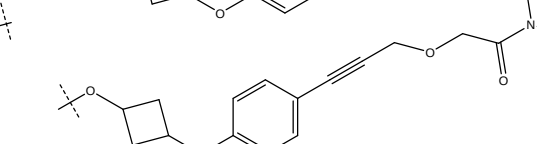
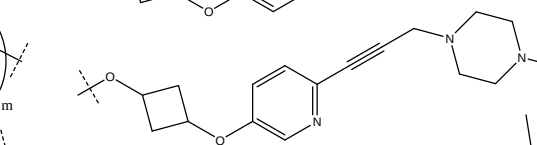
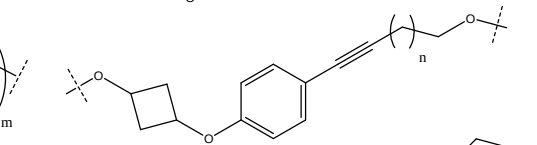
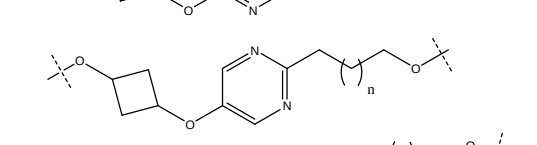
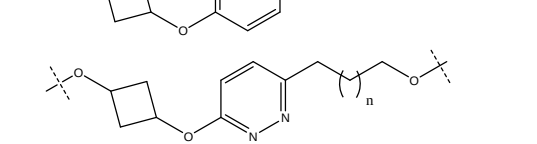
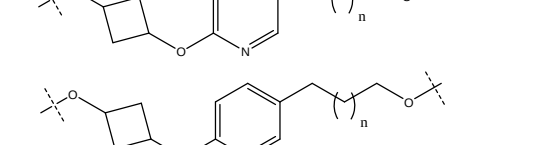
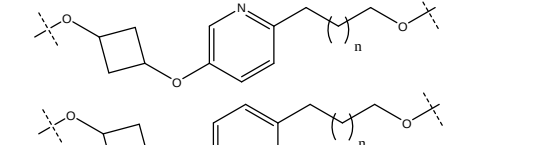
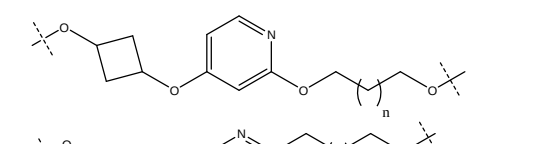
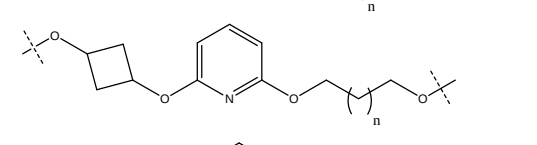
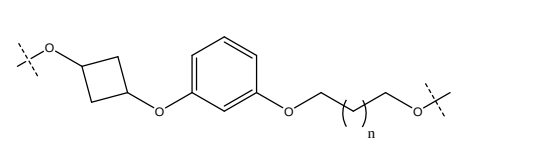
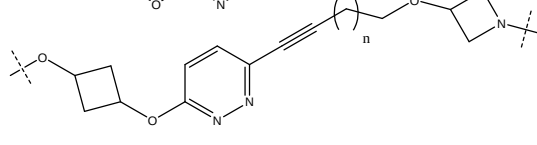
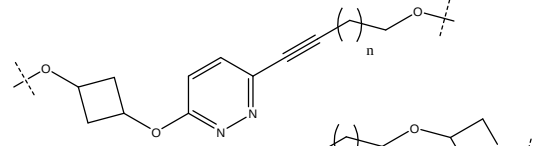
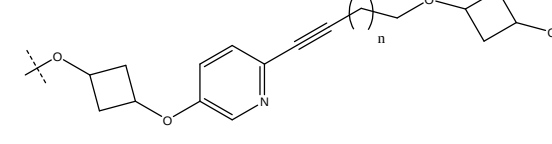
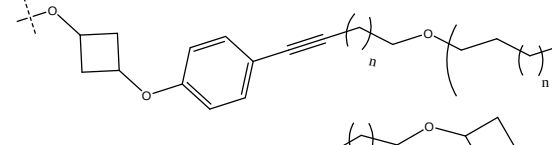
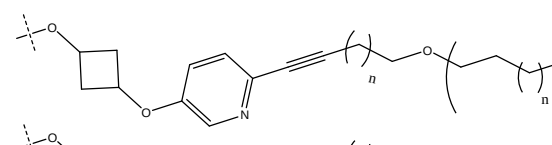
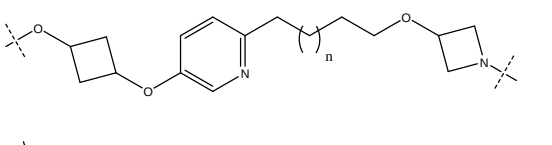
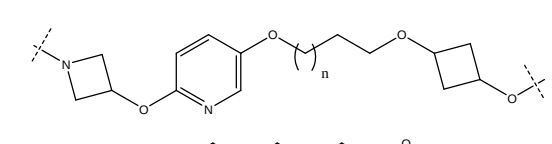
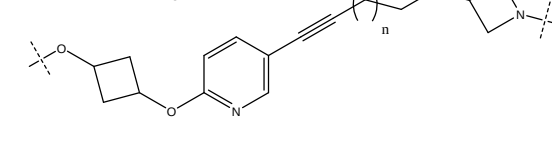
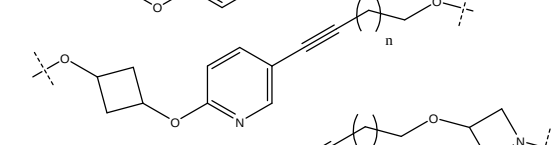
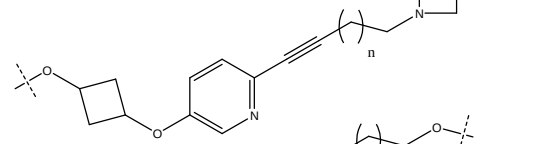
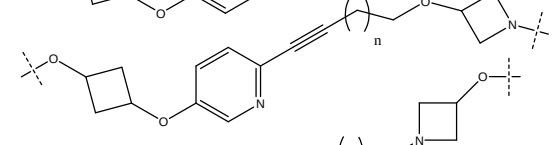
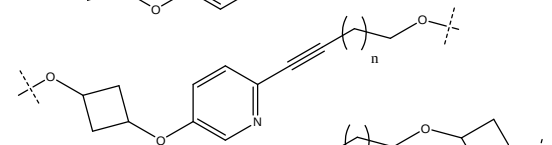
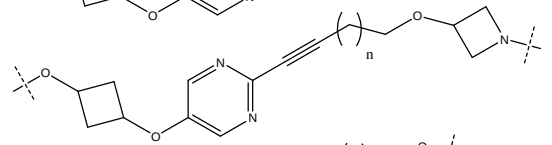
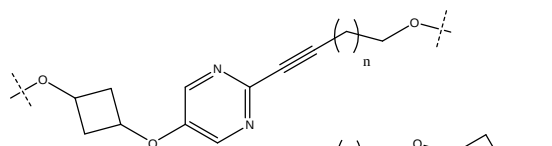


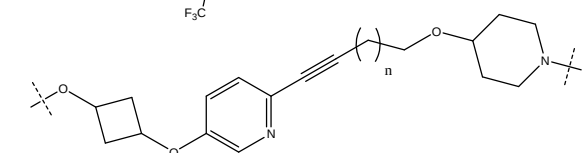
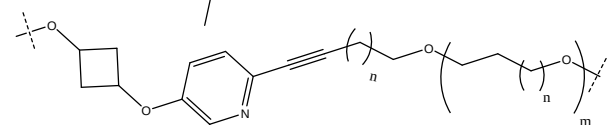
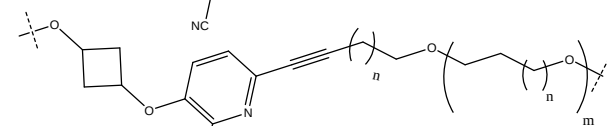
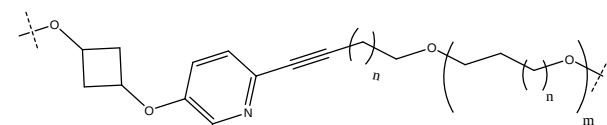
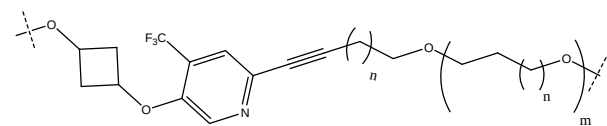
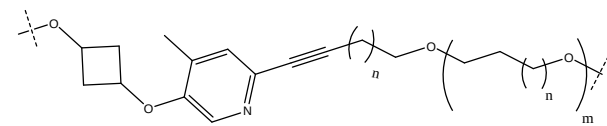
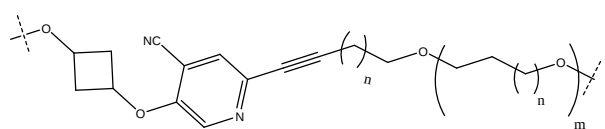
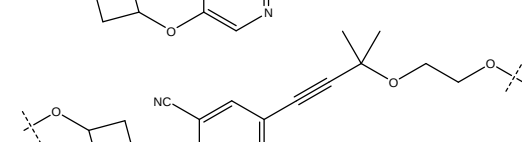
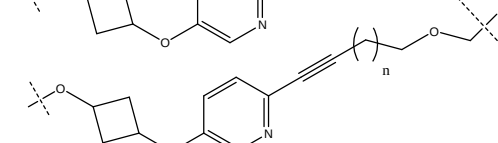
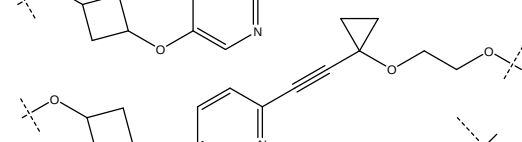
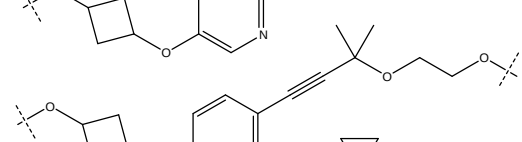
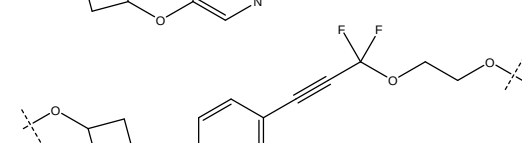
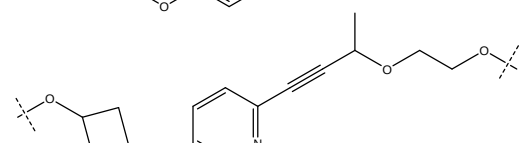
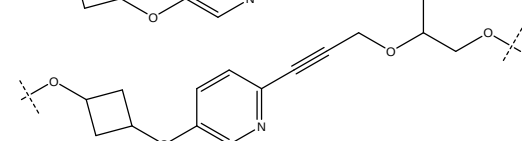
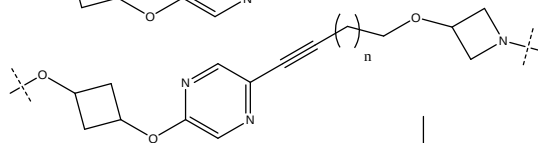
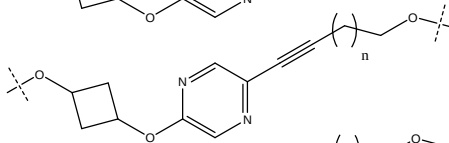
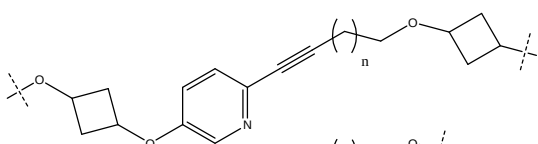




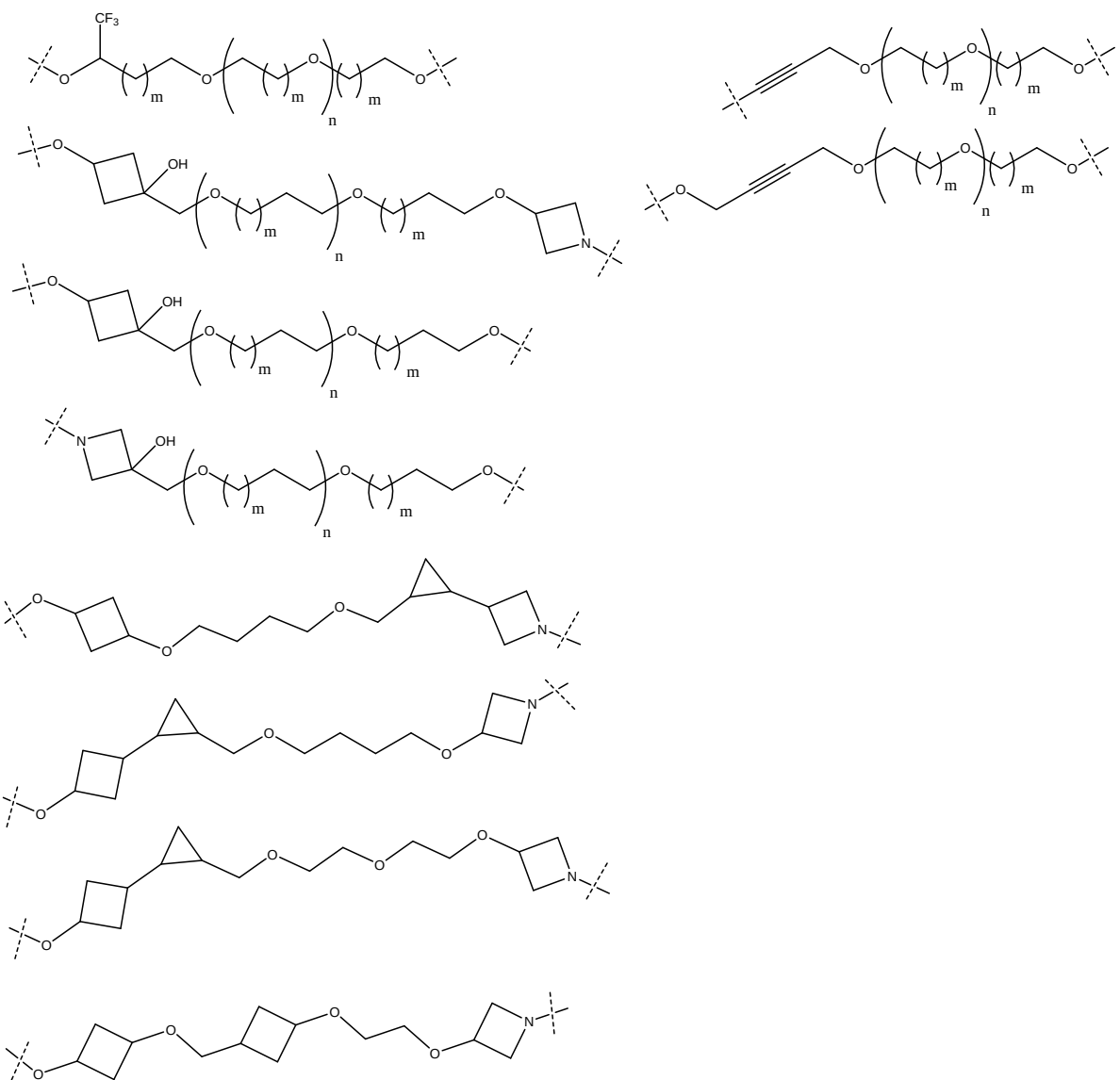


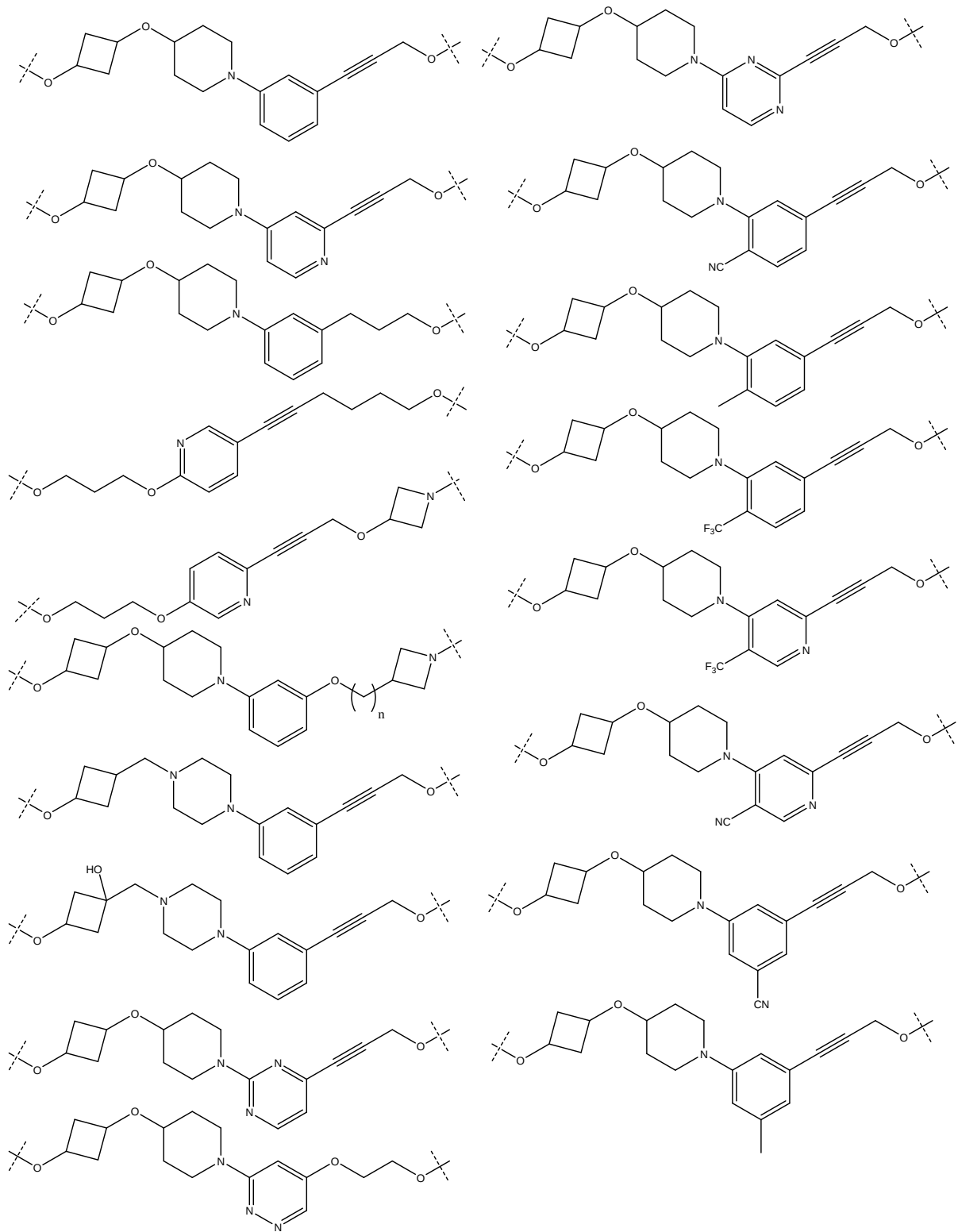


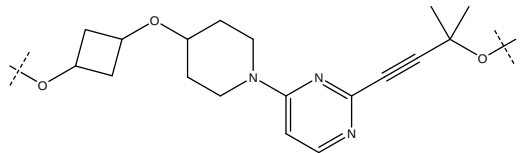
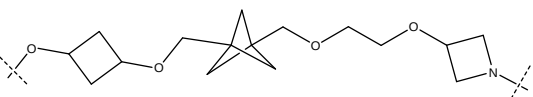
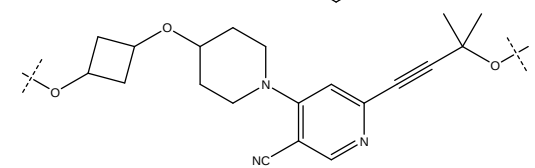
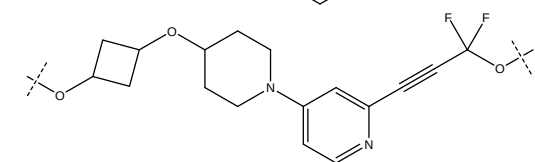
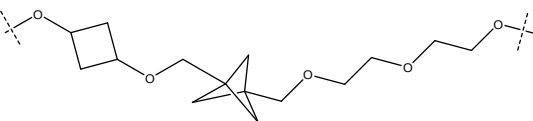
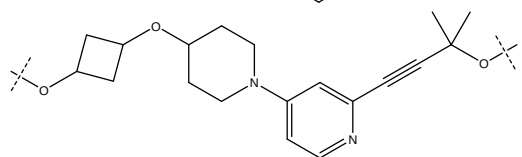
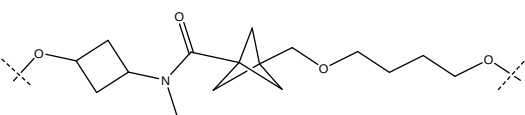
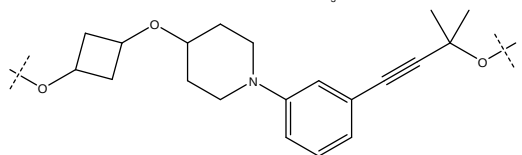
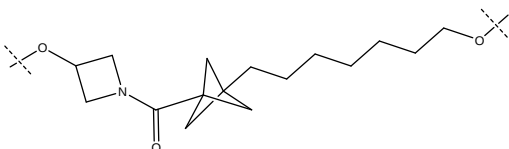
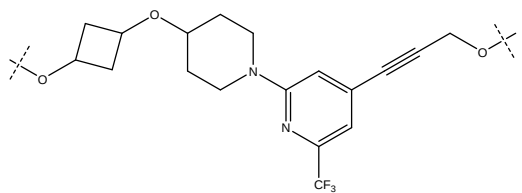
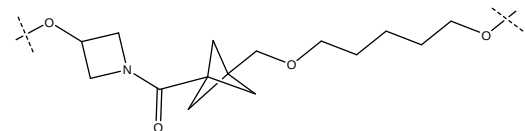
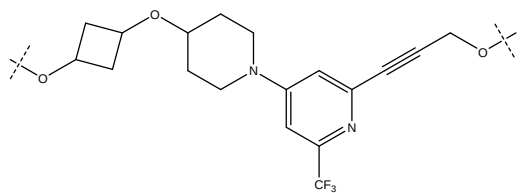
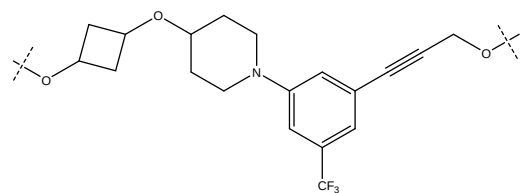


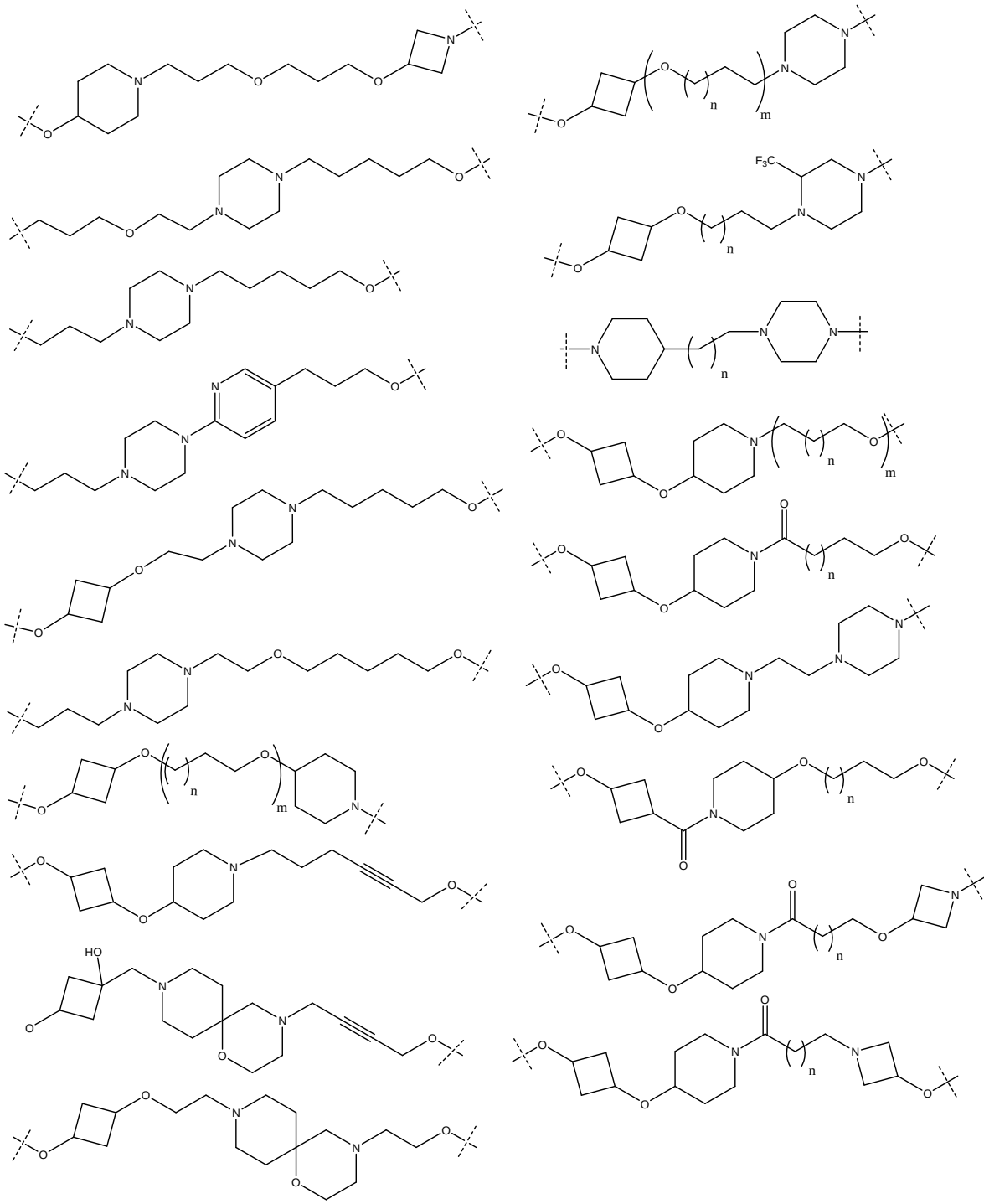


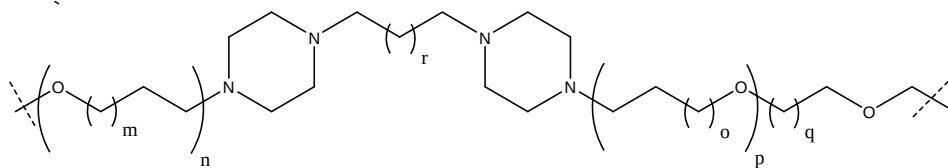
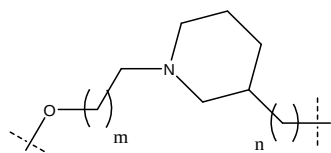
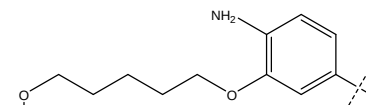
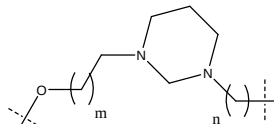
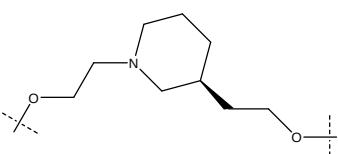
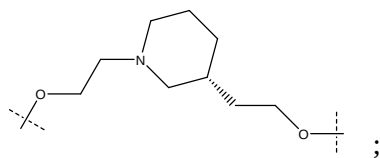
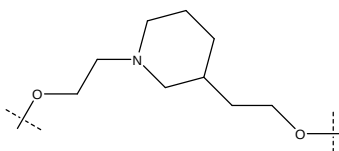
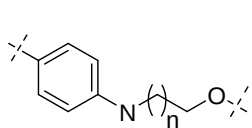
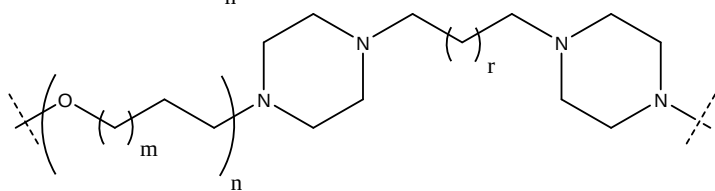
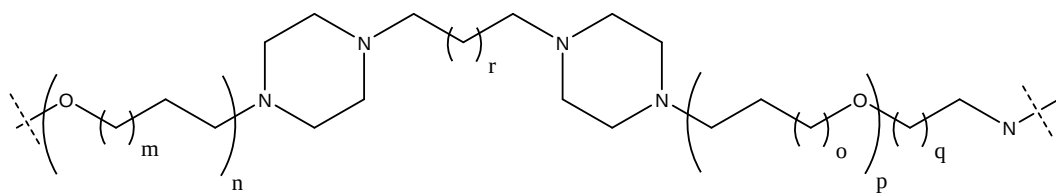
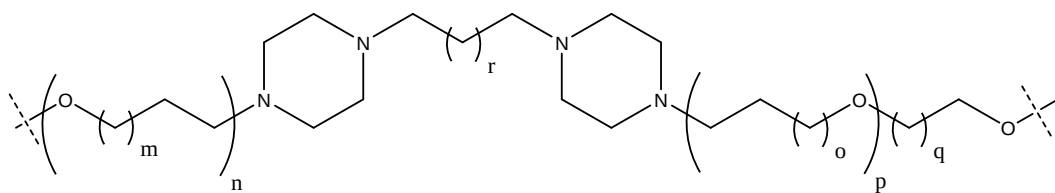


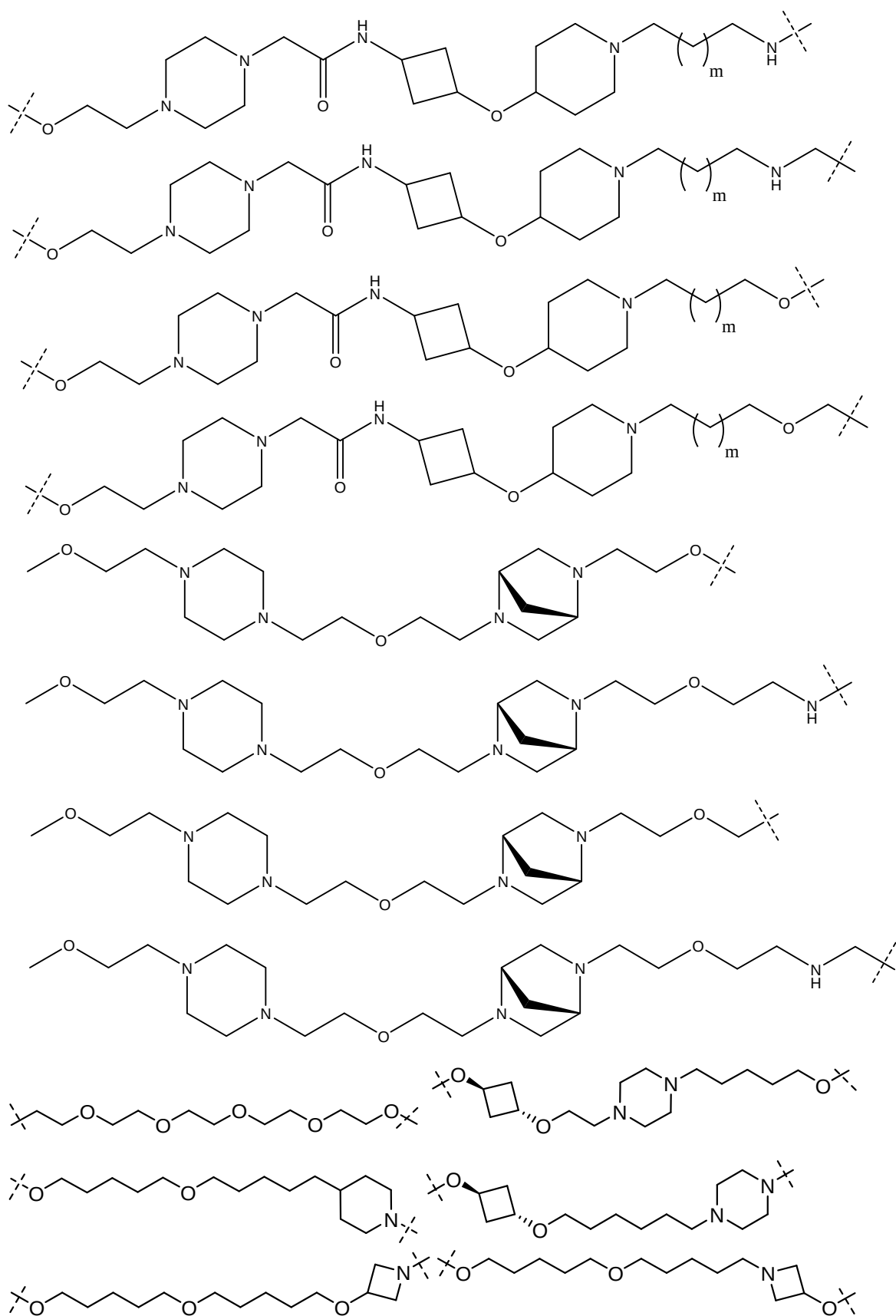


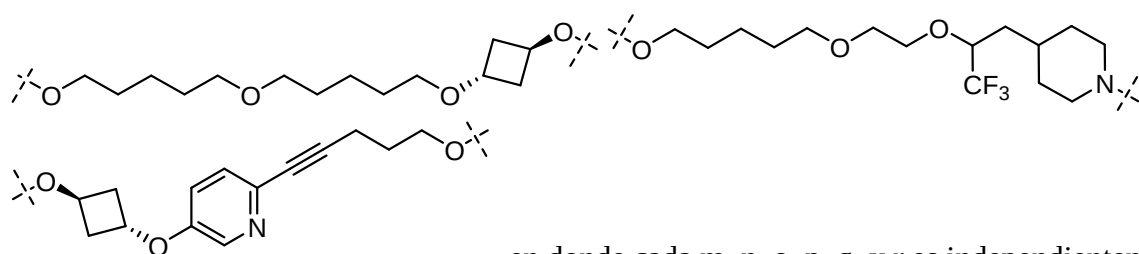






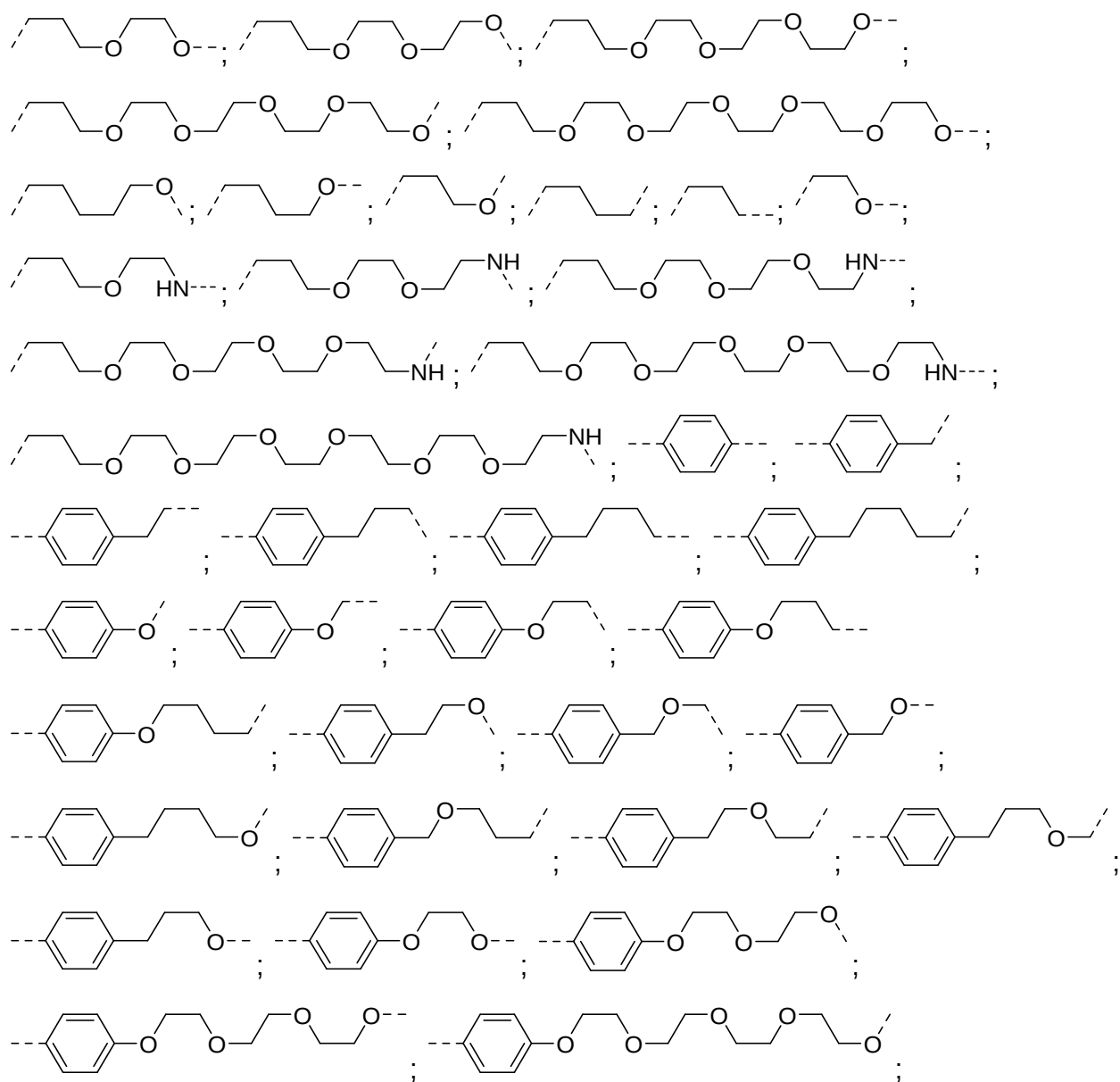


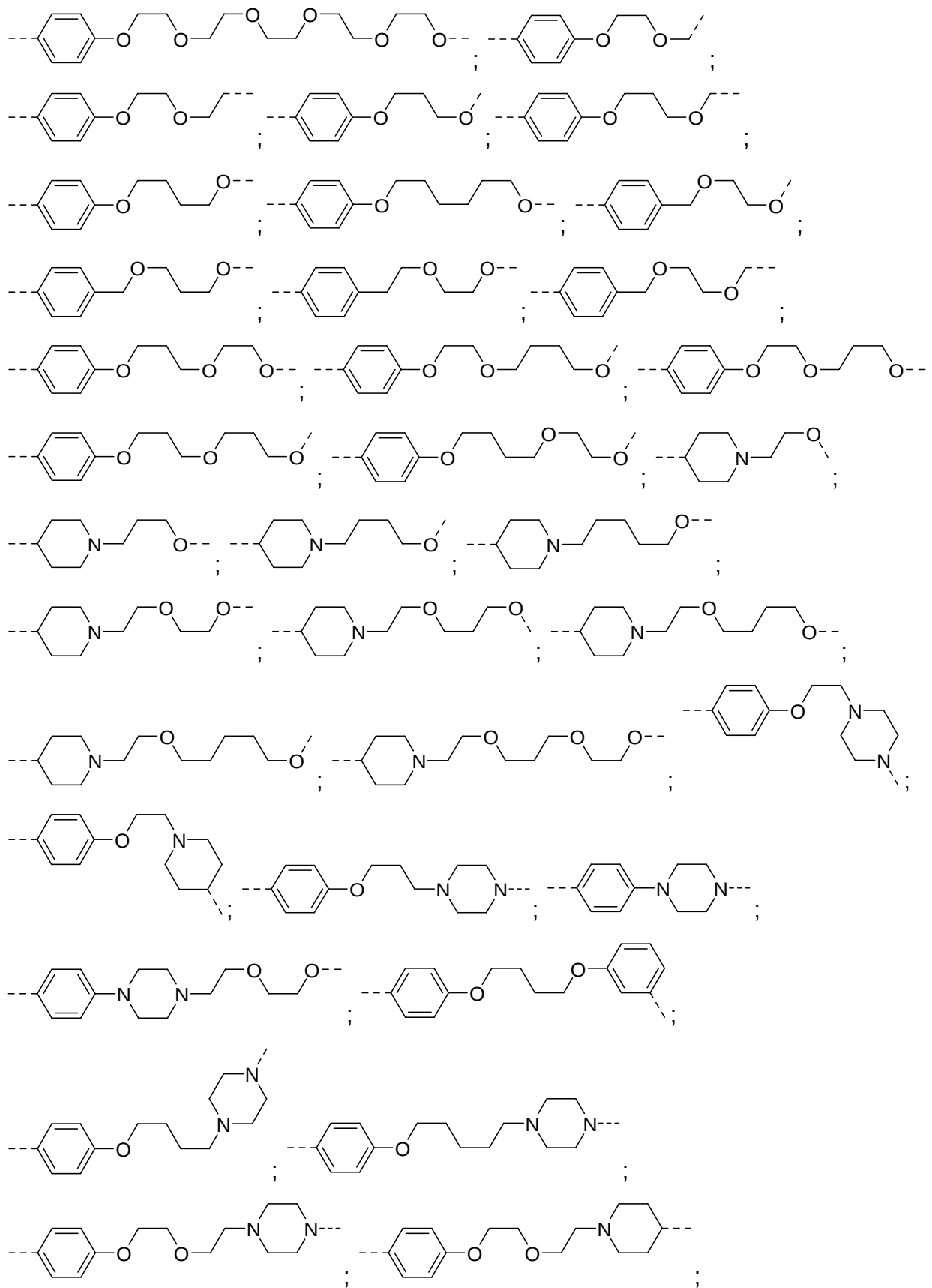


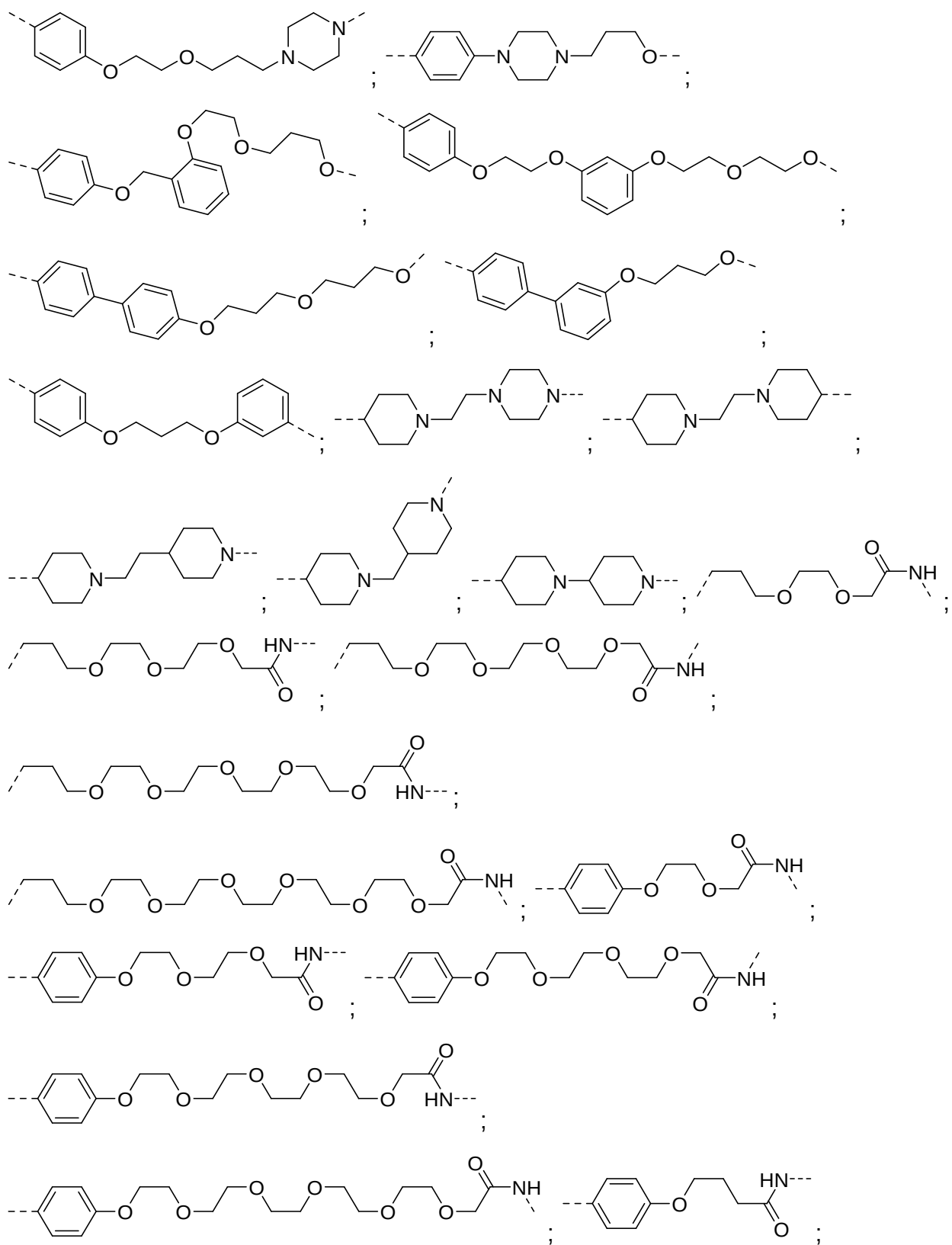


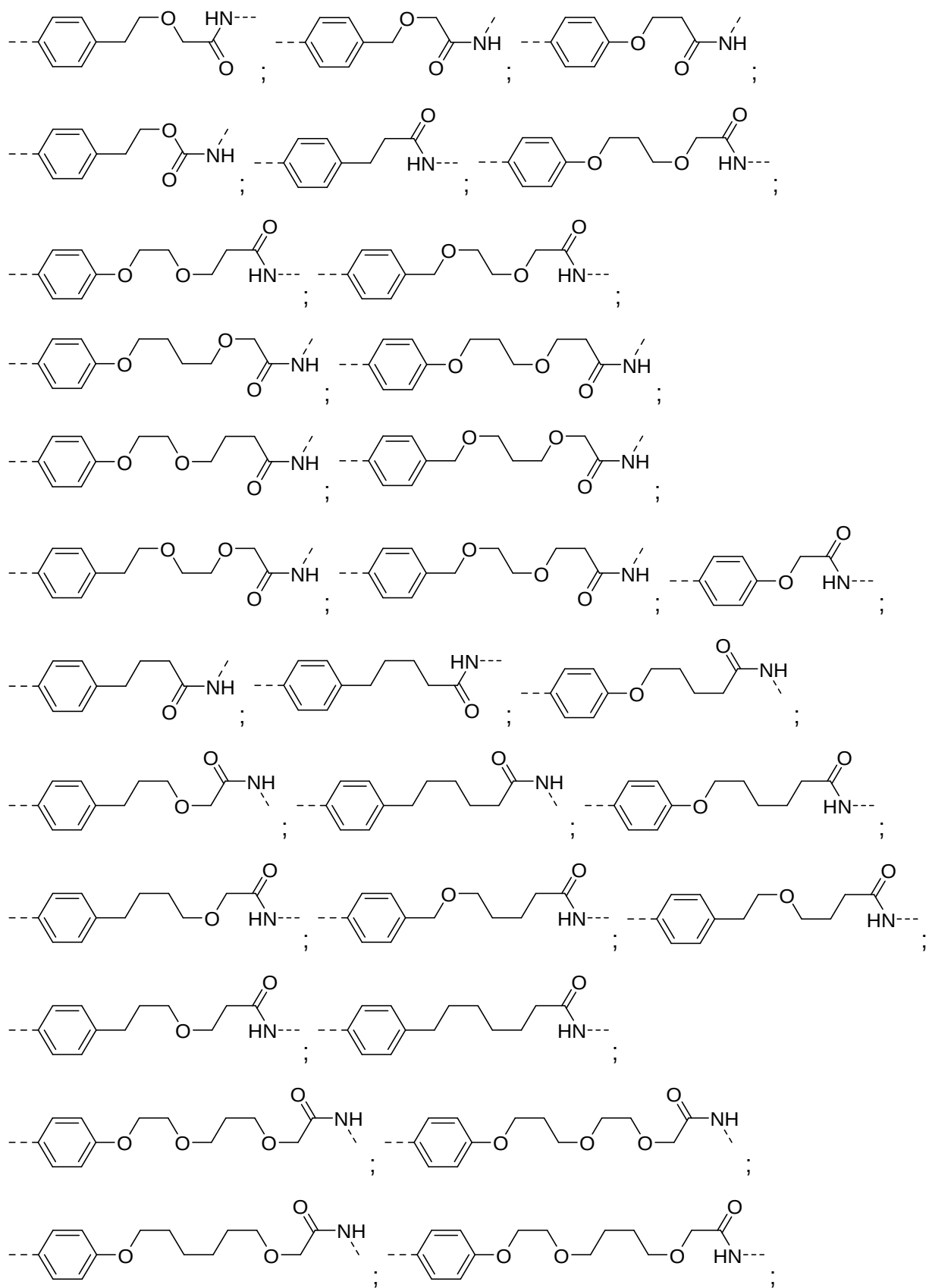
, en donde cada m, n, o, p, q, y r es independientemente 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, o 20.

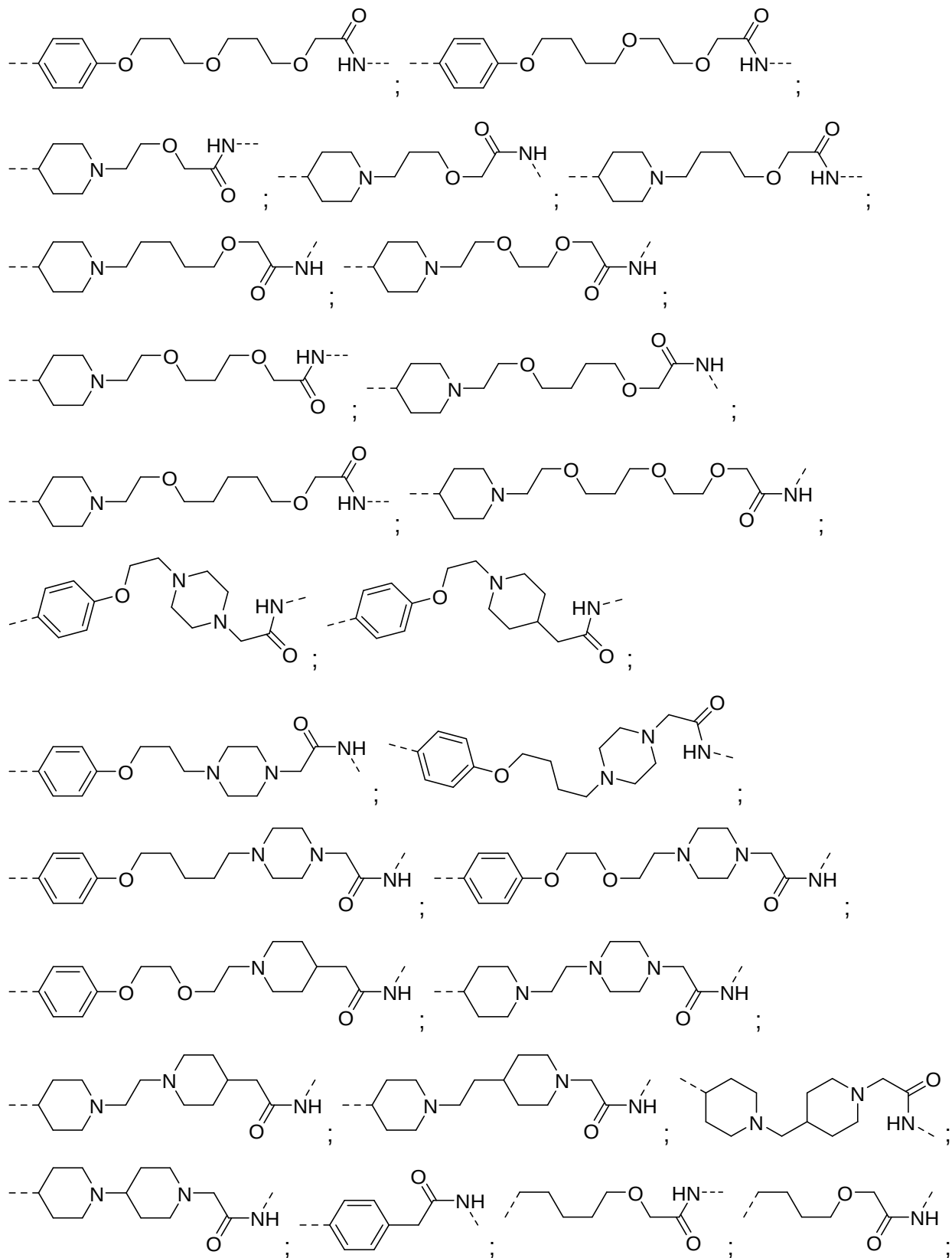
12. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-9, en donde el enlazador (L) se selecciona del grupo que consiste en:

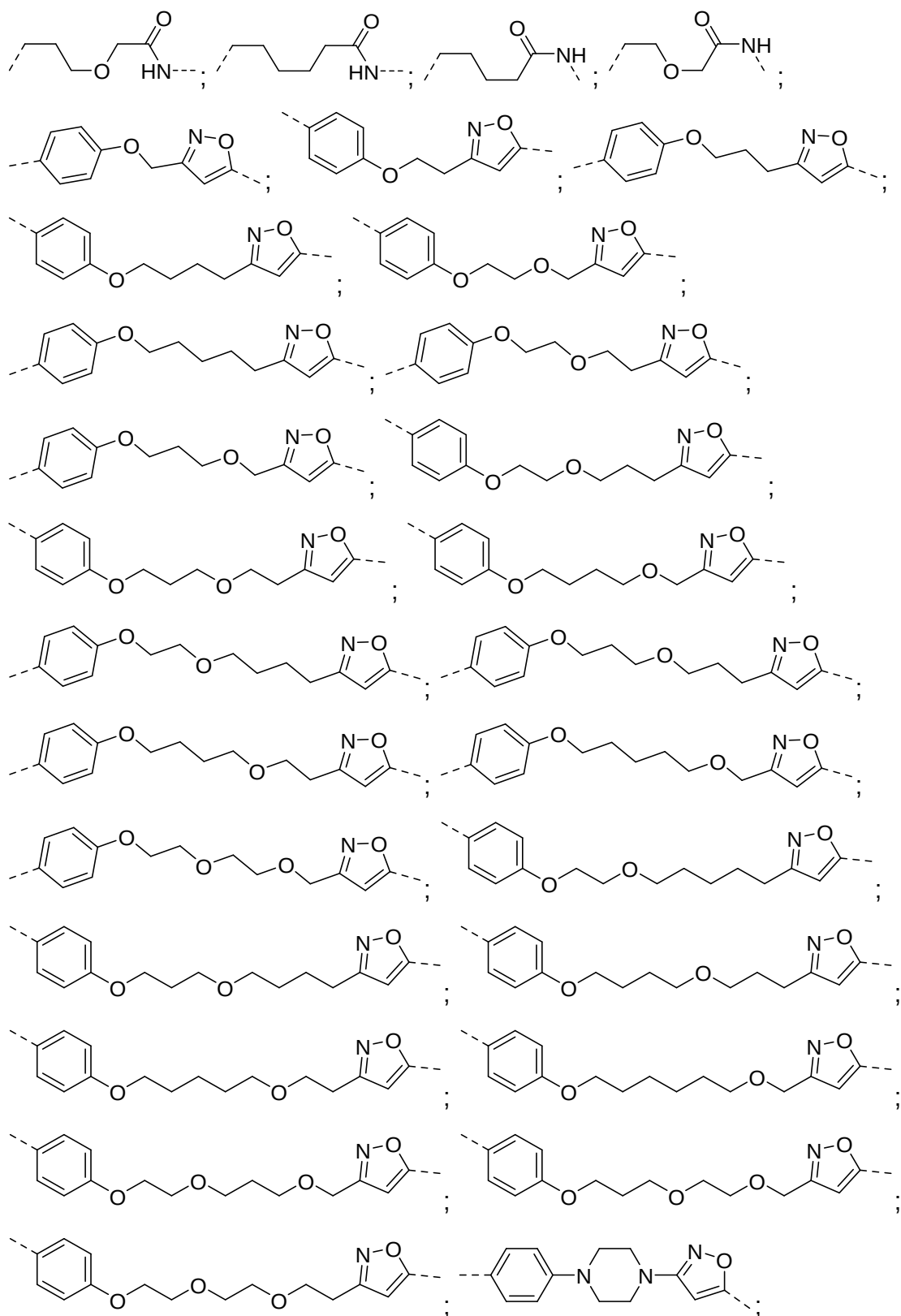


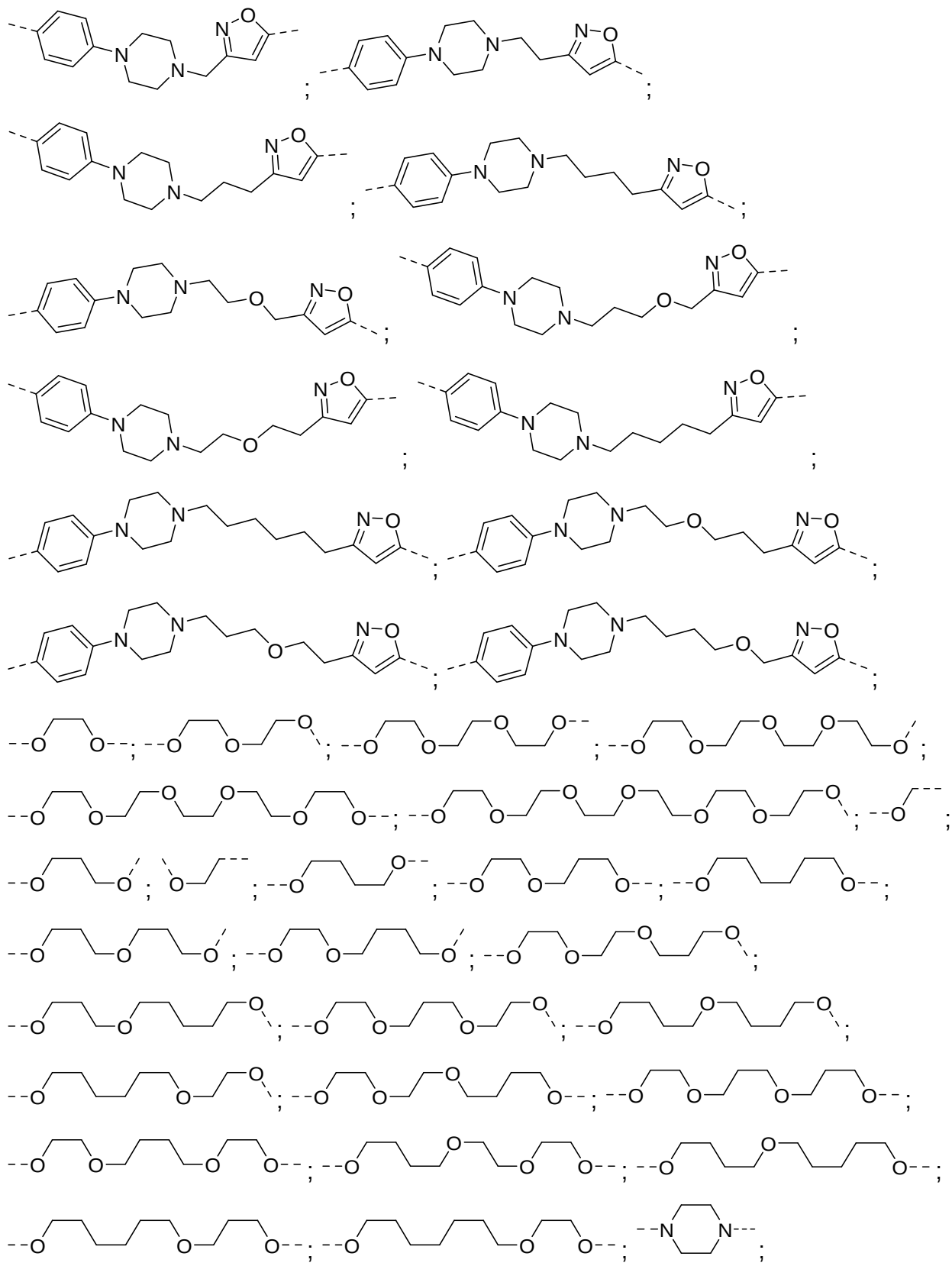


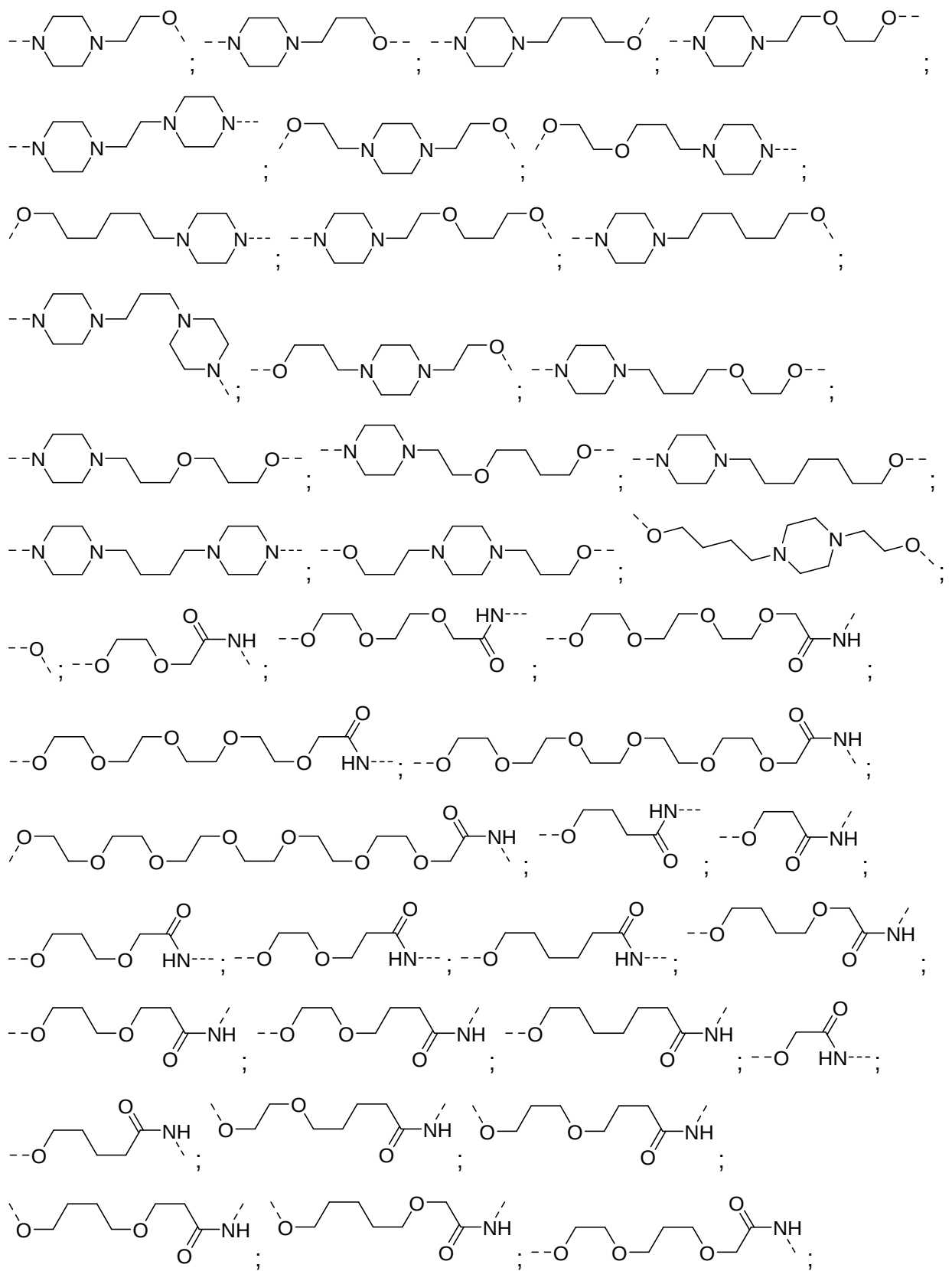


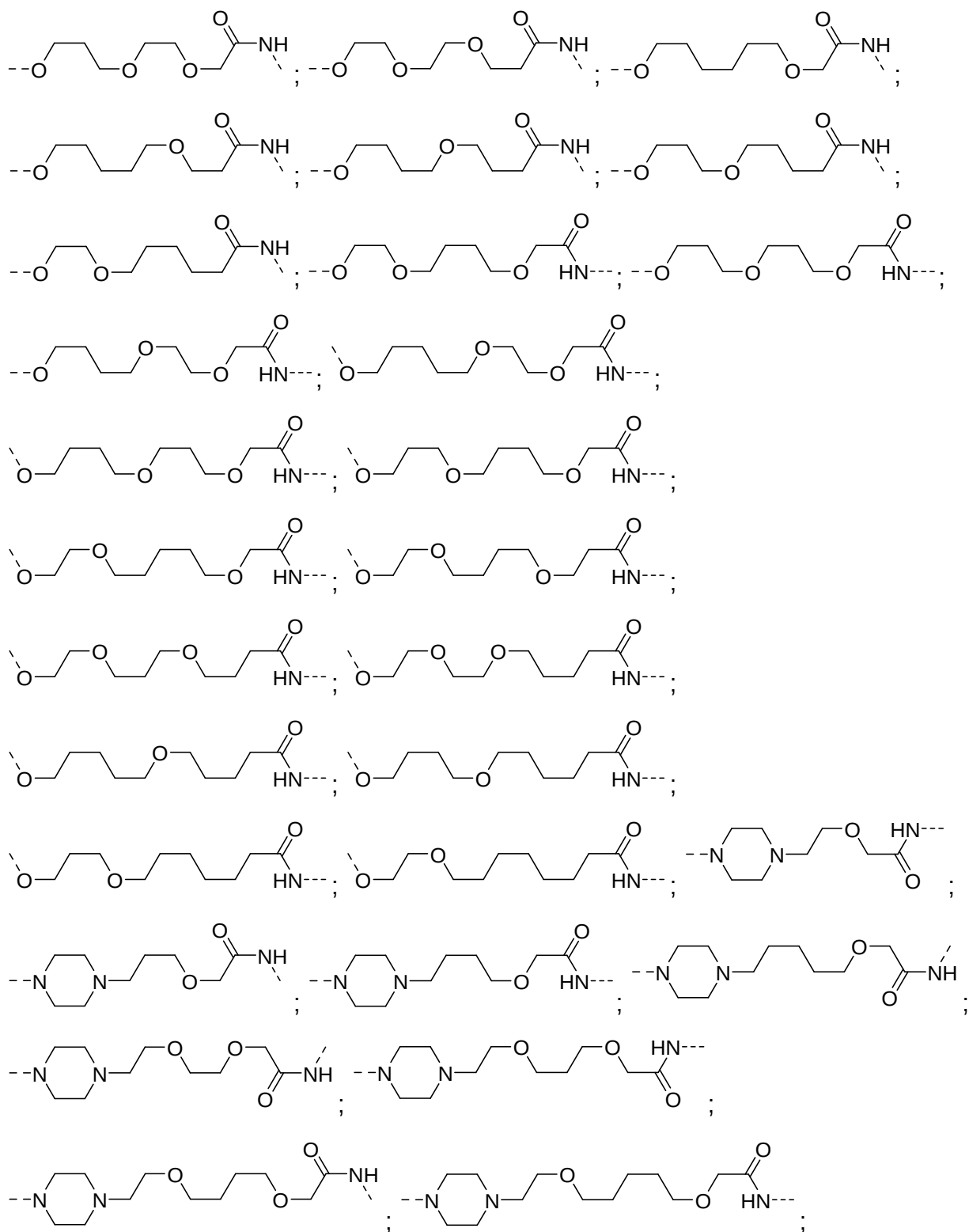


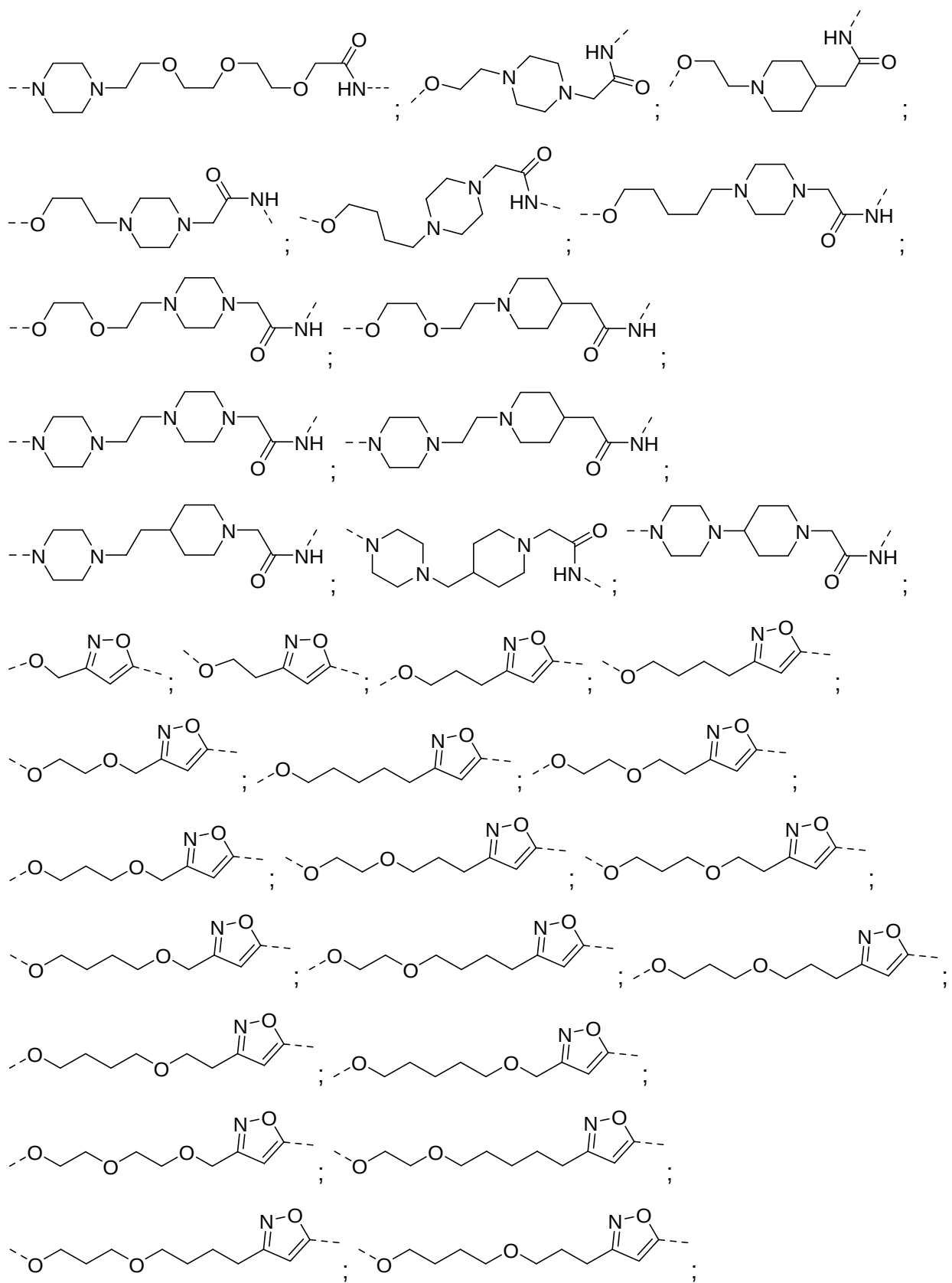


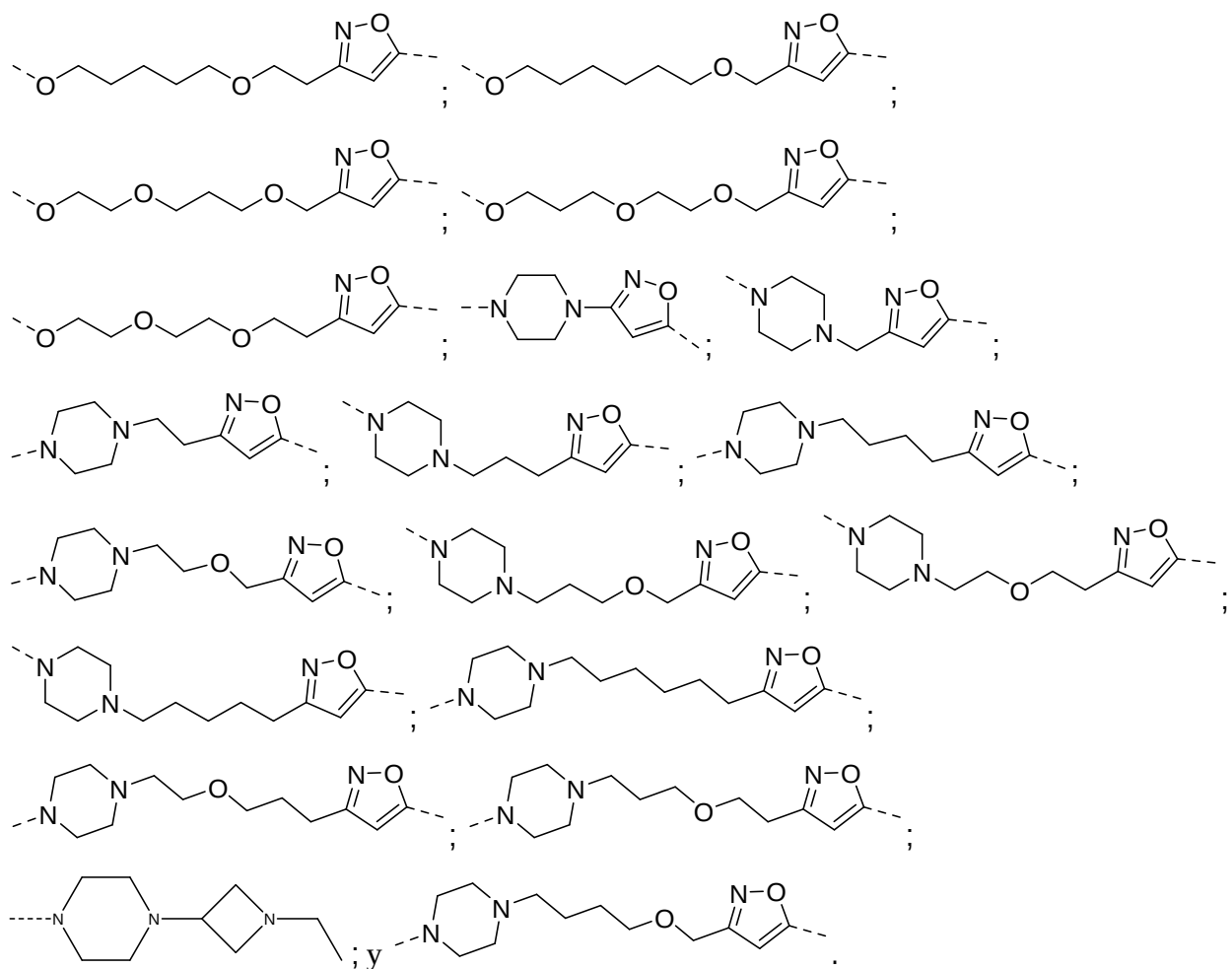




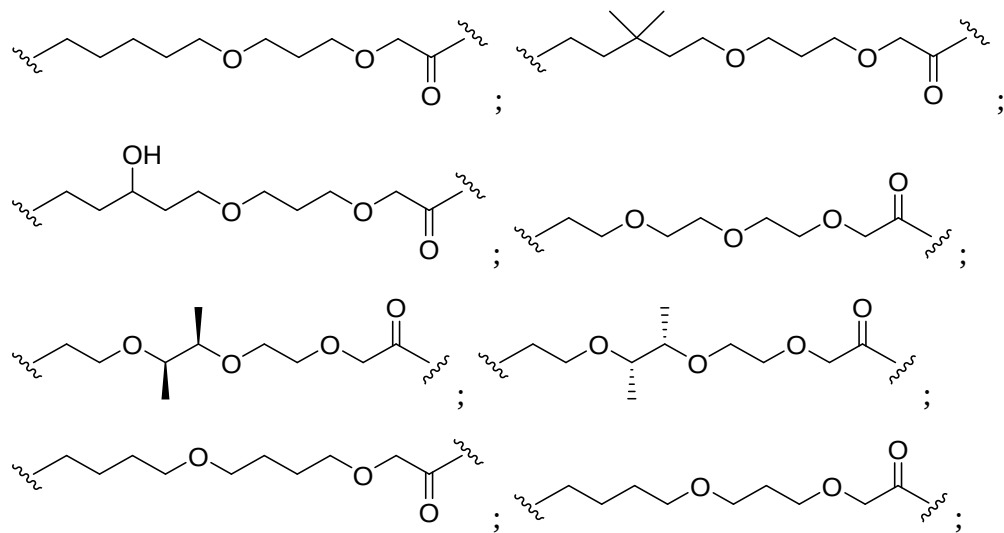


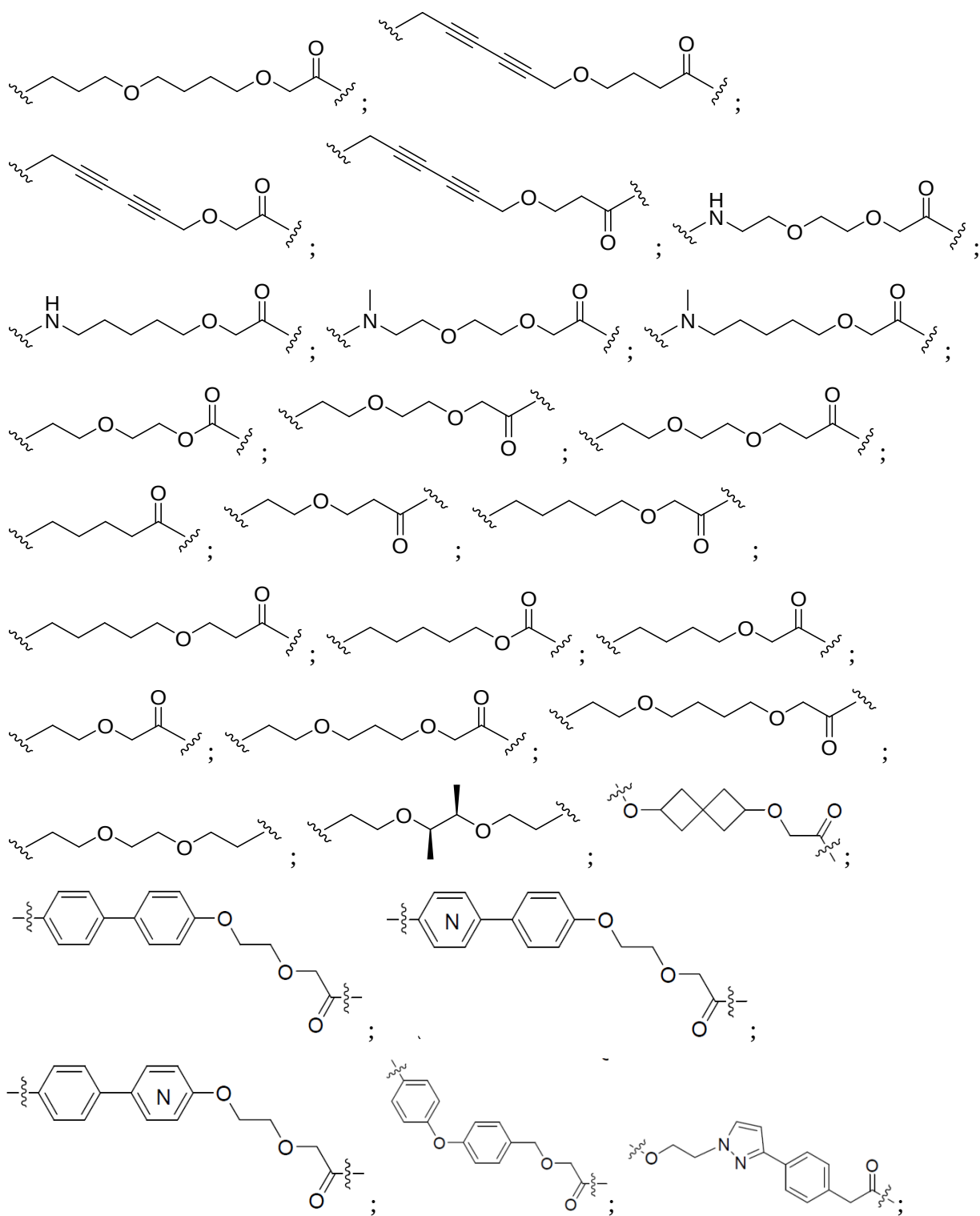


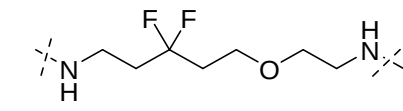
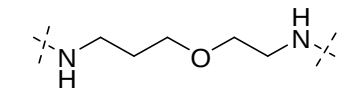
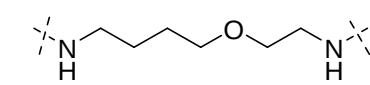
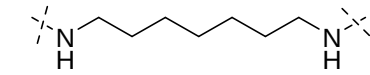
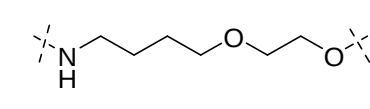
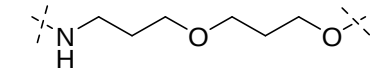
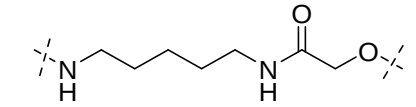
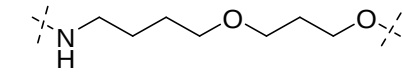
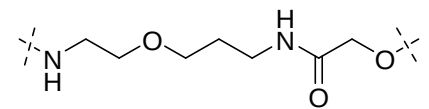
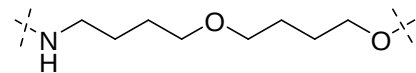
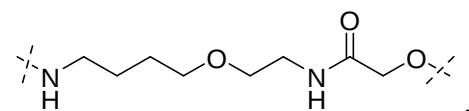
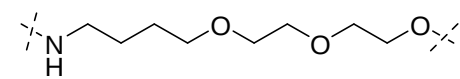
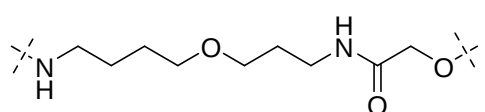
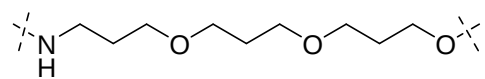
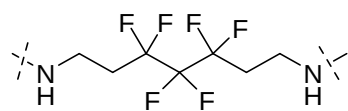
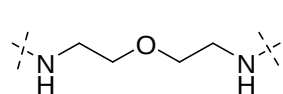
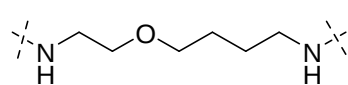
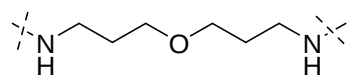
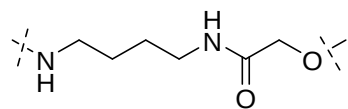
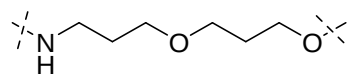
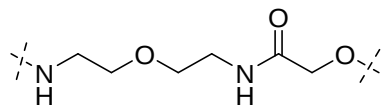
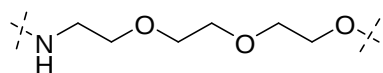
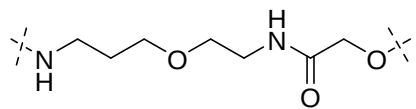
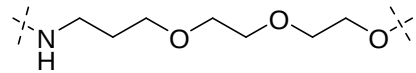
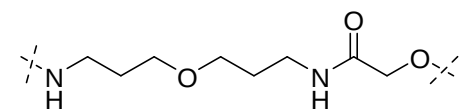
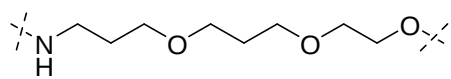
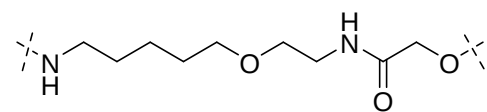
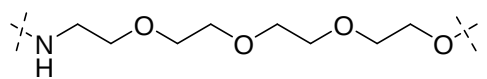


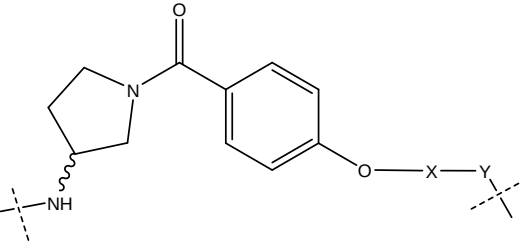
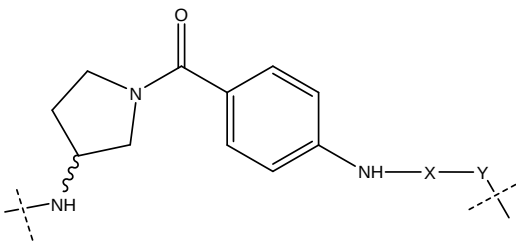
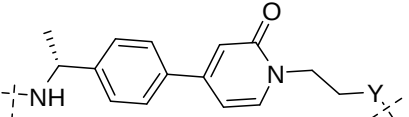
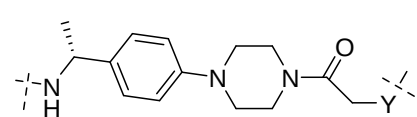
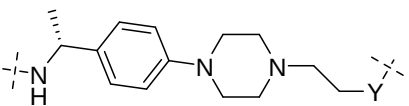
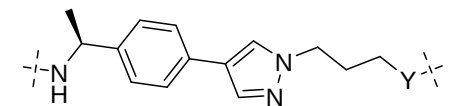
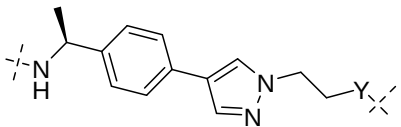
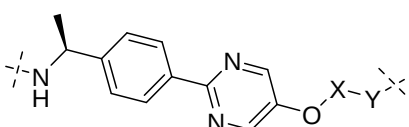
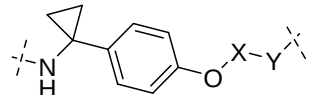
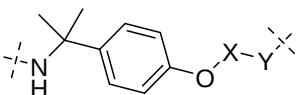
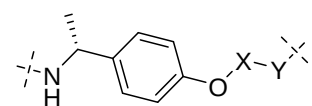
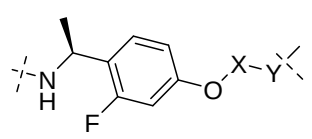
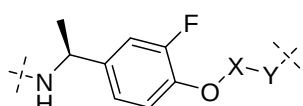
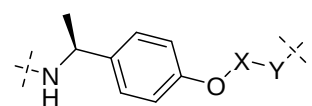
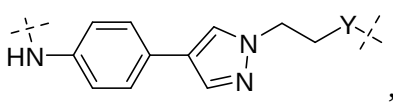
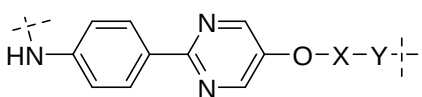
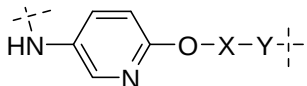
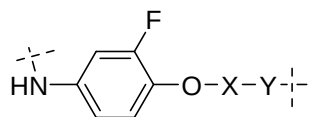
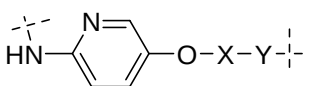
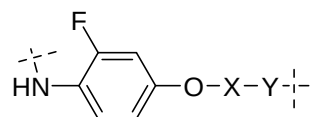
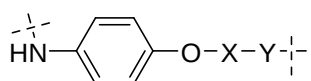
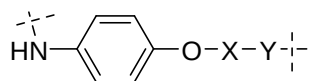


13. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-9, en donde el enlazador (L) se selecciona de:





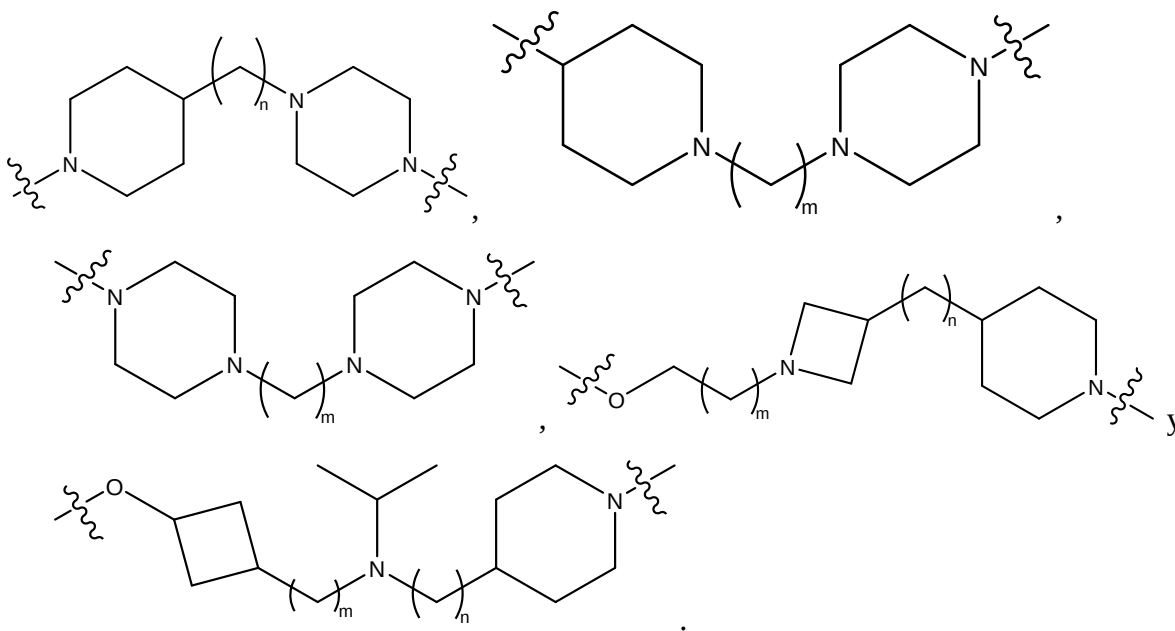




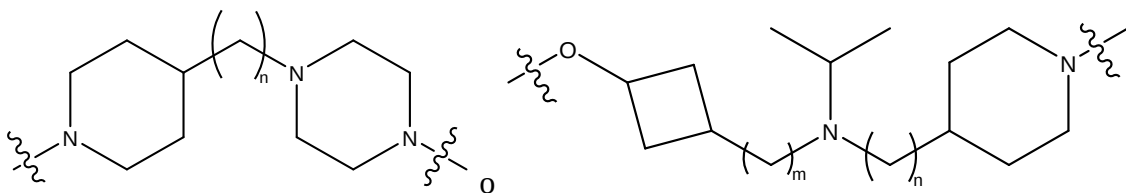
en donde:

"X" en las estructuras anteriores puede ser una cadena lineal con átomos que varían de 2 a 14,  
y la cadena mencionada puede contener heteroátomos tales como oxígeno; y  
"Y" en las estructuras anteriores puede ser O, N, S(O)<sub>n</sub> (n = 0, 1, 2).

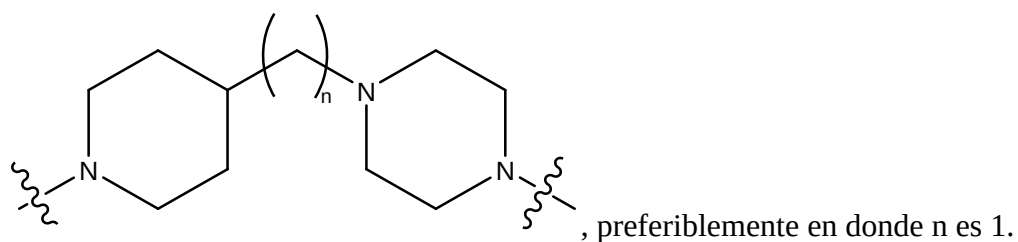
14. El compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-8, en donde el enlazador (L) se selecciona de



15. El compuesto bifuncional de conformidad con la reivindicación 14, en donde el enlazador (L) es

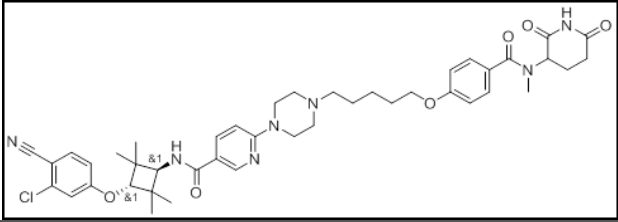
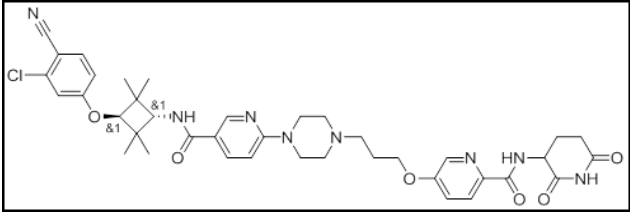
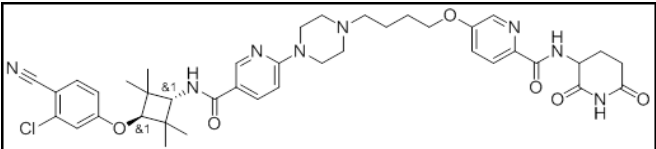
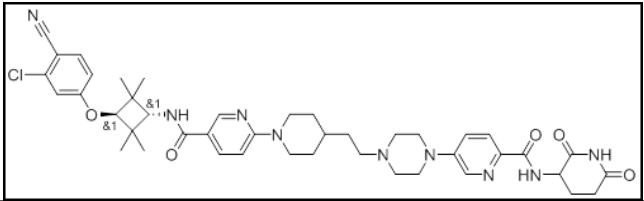
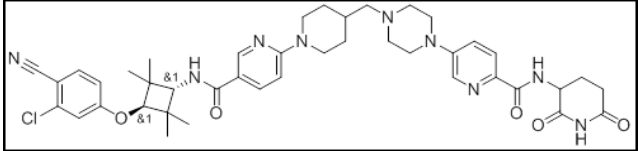
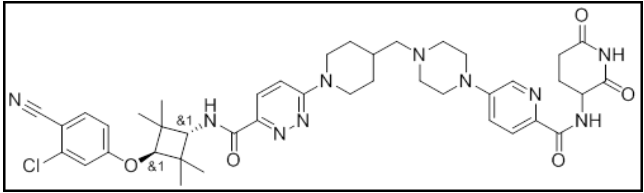
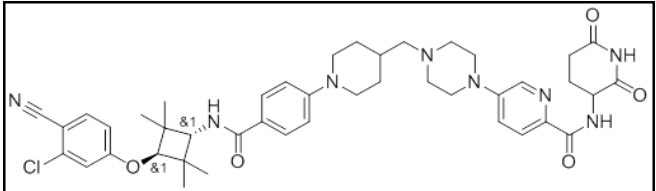


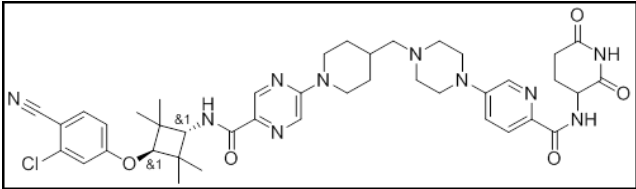
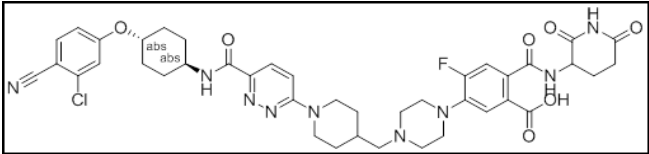
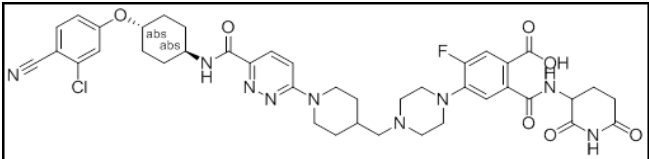
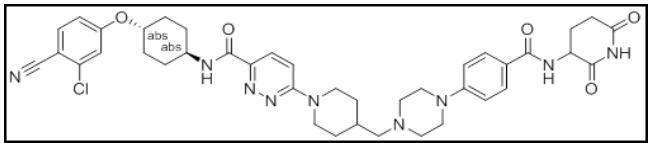
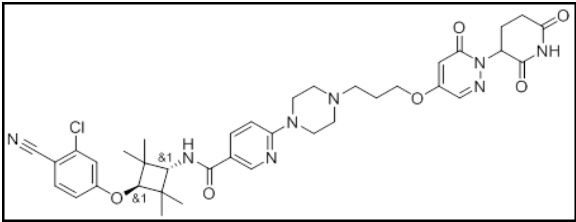
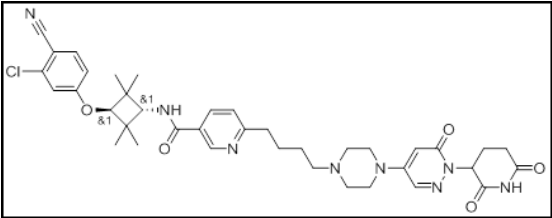
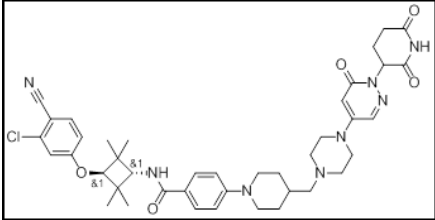
16. El compuesto bifuncional de conformidad con la reivindicación 15, en donde el enlazador (L) es

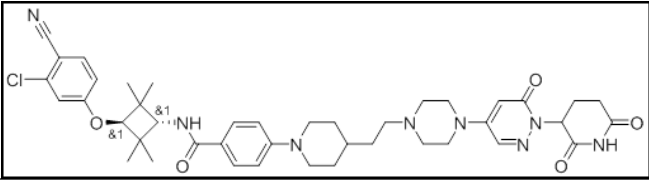
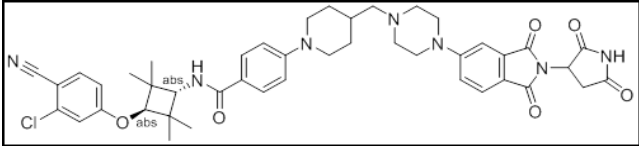
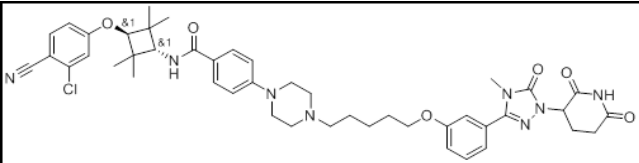
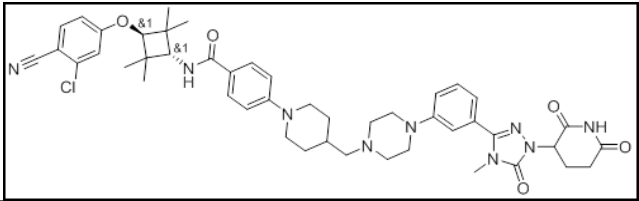
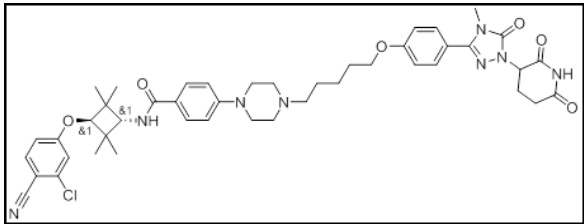
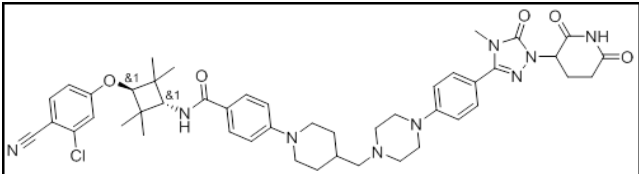


17. El compuesto bifuncional de conformidad con la reivindicación 1, en donde el compuesto se selecciona del grupo que consiste en el PROTAC-27 hasta el PROTAC-29, el PROTAC-48 hasta el PROTAC-63, y el PROTAC-66 hasta el PROTAC-70:

|           |  |
|-----------|--|
| PROTAC-27 |  |
| PROTAC-28 |  |
| PROTAC-29 |  |
| PROTAC-48 |  |

|           |                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PROTAC-49 |  <p>Chemical structure of PROTAC-49: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)phenyl group.</p>         |
| PROTAC-50 |  <p>Chemical structure of PROTAC-50: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p>   |
| PROTAC-51 |  <p>Chemical structure of PROTAC-51: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p>   |
| PROTAC-52 |  <p>Chemical structure of PROTAC-52: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p>  |
| PROTAC-53 |  <p>Chemical structure of PROTAC-53: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p> |
| PROTAC-54 |  <p>Chemical structure of PROTAC-54: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p> |
| PROTAC-55 |  <p>Chemical structure of PROTAC-55: A molecule featuring a 4-chloro-3-cyanophenyl group linked via an ether to a spirocyclic core. This core is connected to a pyridine ring, which is further linked to a piperazine ring. The piperazine ring is connected to a 4-((4-oxo-4,5,6,7-tetrahydro-2H-pyridin-2-yl)amino)pyridin-2-yl group.</p> |

|           |                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PROTAC-56 |  <p>Chemical structure of PROTAC-56, featuring a 4-chloro-3-cyanophenoxy group linked to a spirocyclic core, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p>   |
| PROTAC-57 |  <p>Chemical structure of PROTAC-57, featuring a 4-chloro-3-cyanophenoxy group linked to a cyclohexane ring, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p>   |
| PROTAC-58 |  <p>Chemical structure of PROTAC-58, featuring a 4-chloro-3-cyanophenoxy group linked to a cyclohexane ring, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p>   |
| PROTAC-59 |  <p>Chemical structure of PROTAC-59, featuring a 4-chloro-3-cyanophenoxy group linked to a cyclohexane ring, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p> |
| PROTAC-60 |  <p>Chemical structure of PROTAC-60, featuring a 4-chloro-3-cyanophenoxy group linked to a spirocyclic core, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p> |
| PROTAC-61 |  <p>Chemical structure of PROTAC-61, featuring a 4-chloro-3-cyanophenoxy group linked to a spirocyclic core, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p> |
| PROTAC-62 |  <p>Chemical structure of PROTAC-62, featuring a 4-chloro-3-cyanophenoxy group linked to a spirocyclic core, which is connected via an amide to a pyridine ring. This pyridine is further linked through a piperazine bridge to another pyridine ring, which is finally connected to a glutarimide moiety.</p> |

|           |                                                                                      |
|-----------|--------------------------------------------------------------------------------------|
| PROTAC-63 |    |
| PROTAC-66 |    |
| PROTAC-67 |    |
| PROTAC-68 |   |
| PROTAC-69 |  |
| PROTAC-70 |  |

18. Un compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1- 17, para uso en un método de tratamiento de un estado de enfermedad o de mejoramiento de los

síntomas de una enfermedad o afección en un sujeto que lo necesite, el método comprende administrar a dicho sujeto una cantidad del compuesto.

19. El compuesto bifuncional para uso de la reivindicación 18, en donde el compuesto es administrado en combinación con un agente bioactivo adicional.

20. El compuesto bifuncional para uso de la reivindicación 18 o 19, en donde la enfermedad o afección es cáncer.

21. Una composición que comprende una cantidad de un compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-17, y un portador aceptable farmacéuticamente.

22. La composición de conformidad con la reivindicación 21, en donde la composición comprende, además, al menos uno de un agente bioactivo adicional u otro compuesto bifuncional de conformidad con cualquiera de las reivindicaciones 1-17.

23. La composición de conformidad con la reivindicación 22, en donde el agente bioactivo adicional es un agente anticancerígeno.

24. Una composición para tratar o mejorar al menos un síntoma de una enfermedad o trastorno, caracterizado porque comprende una cantidad de al menos un compuesto de conformidad con cualquiera de las reivindicaciones 1-17 y un portador, aditivo y/o excipiente aceptable farmacéuticamente.

25. La composición para uso de conformidad con la reivindicación 24, en donde la enfermedad o trastorno se asocia con la acumulación y/o agregación de la proteína diana.

26. La composición para uso de conformidad con la reivindicación 24 o 25, en donde la enfermedad o trastorno es atrofia Bulbospinal muscular (enfermedad de Kennedy).

27. La composición de conformidad con cualquiera de las reivindicaciones 24-26, que comprende, además, un agente bioactivo adicional.

28. La composición de conformidad con la reivindicación 27, en donde el agente bioactivo adicional es un agente anticancerígeno.

29. La composición para uso de conformidad con la reivindicación 28, en donde dicho agente anticancerígeno se selecciona del grupo que consiste en everolimus, trabectedin, abraxano, TLK 286, AV-299, DN-101, pazopanib, GSK690693, RTA 744, ON 0910.Na, AZD 6244 (ARRY-142886), AMN-107, TKI-258, GSK461364, AZD 1152, enzastaurin, vandetanib, ARQ-197, MK-0457, MLN8054, PHA-739358, R-763, AT-9263, un inhibidor de FLT-3, un inhibidor de VEGFR, un inhibidor de EGFR TK, un inhibidor de aurora quinasa, un modulador de PIK-1, un inhibidor de Bcl-2, un inhibidor de HDAC, un inhibidor de c-MET, un inhibidor de PARP, un inhibidor de Cdk, un inhibidor de IGFR-TK, un anticuerpo anti-HGF, un inhibidor de PI3 quinasa, un inhibidor de AKT, un inhibidor de mTORC1/2, un inhibidor de JAK/STAT, un inhibidor del punto de control-1 o 2, un inhibidor de la quinasa de adhesión focal, un inhibidor de Map quinasa quinasa (mek), un anticuerpo atrapador de VEGF, pemetrexed, erlotinib, dasatanib, nilotinib, decatanib, panitumumab, amrubicin, oregovomab, Lep-etu, nolatrexed, azd2171, batabulin, ofatumumab, zanolimumab, edotecarin, tetrandrine, rubitecan, tesmilifene, oblimersen, ticilimumab, ipilimumab, gossypol, Bio 111, 131-I-TM-601, ALT-110, BIO 140, CC 8490, cilengitida, gimatecan, IL13-PE38QQR, INO 1001, IPdR<sub>1</sub> KRX-0402, lucanthone, LY317615, neuradiab, vitespan, Rta 744, Sdx 102, talampanel, atrasentan, Xr 311, romidepsin, ADS-100380, sunitinib, 5-fluorouracil, vorinostat, etoposido, gemcitabina, doxorubicina, doxorubicina liposomal, 5'-deoxi-5-fluorouridina, vincristina, temozolomida, ZK-304709, seliciclib; PD0325901, AZD-6244, capecitabina, ácido L-Glutámico, N-[4-[2-(2-amino-4,7-dihidro-4-oxo-1H-pirrol[2,3-d]pirimidin-5-il)etil]benzoil]-, sal disódica, heptahidrato, camptothecin, irinotecan marcado con PEG, tamoxifeno, citrato de toremifeno, anastrozol, exemestano, letrozol, DES(dietilstilbestrol), estradiol, estrógeno, estrógeno conjugado, bevacizumab, IMC-1C11, CHIR-258); 3-[5-(metilsulfonilpiperadinametil)-indolil-quinolona, vatalanib, AG-013736, AVE-0005, acetato de goserelina, acetato de leuprolido, pamoato de triptorelina, acetato de medroxiprogesterona, caproato de hidroxiprogesterona, acetato de megestrol, raloxifeno, bicalutamida, flutamida,

nilutamida, CP-724714; TAK-165, HKI-272, erlotinib, lapatanib, canertinib, anticuerpo ABX-EGF, erbitux, EKB-569, PKI-166, GW-572016, Ionafarnib, BMS-214662, tipifarnib; amifostina, NVP-LAQ824, ácido hidroxámico suberoil analida, ácido valproico, tricostatin A, FK-228, SU11248, sorafenib, KRN951, aminoglutetimida, arnsacrina, anagrelida, L-asparaginasa, vacuna del Bacillus Calmette-Guerin (BCG), adriamicina, bleomicina, buserelina, busulfán, carboplatino, carmustina, clorambucil, cisplatino, cladribina, clodronato, ciproterona, citarabina, dacarbazina, dactinomicina, daunorubicina, epirubicina, fludarabina, fludrocortisona, fluoximesterona, gleevec, hidroxiurea, idarubicina, ifosfamida, imatinib, leuprolida, levamisol, lomustina, mecloretamina, melfalán, 6-mercaptopurina, mesna, metotrexato, mitomicina, mitotano, mitoxantrona, nilutamida, octreotido, oxaliplatino, pamidronato, pentostatina, plicamicina, porfimer, procarbazina, raltitrexed, rituximab, estreptozotocina, teniposido, testosterona, talidomida, tioguanina, tiotepa, tretinoin, vindesina, ácido 13-cis-retinoico, mostaza fenilalanina, mostaza uracilo, estramustina, altretaminae, floxuridinae, 5-deoxiuridina, citosina arabinosido, 6-mercaptopurina, deoxicoformicina, calcitriol, valrubicina, mitramicina, vinblastina, vinorelbina, topotecan, razoxin, marimastat, COL-3, neovastat, BMS-275291, squalamina, endostatina, SU5416, SU6668, EMD121974, interleucina-12, IM862, angiostatina, vitaxin, droloxifeno, idoxifeno, espironolactona, finasterida, cimetidina, trastuzumab, denileukin diftotox, gefitinib, bortezomib, paclitaxel, paclitaxel libre de cremóforo, docetaxel, epitolona B, BMS- 247550, BMS-310705, droloxifeno, 4-hidroxitamoxifeno, pipendoxifeno, ERA-923, arzoxifeno, fulvestrant, acolbifeno, lasofoxifeno, idoxifeno, TSE-424, HMR- 3339, ZK186619, topotecan, PTK787/ZK 222584, VX-745, PD 184352, rapamicina, 40-O-(2-hidroxietil)-rapamicina, temsirolimus, AP-23573, RAD001, ABT-578, BC-210, LY294002, LY292223, LY292696, LY293684, LY293646, wortmannin, ZM336372, L-779,450, PEG-filgrastim, darbepoetin, eritropoietina, factor estimulador de colonia de granulocitos, zolendronato, prednisona, cetuximab, factor estimulador de colonias de granulocitos macrófagos, histrelin, interferón alfa-2a pegilado, interferón alfa-2a, interferón alfa-2b pegilado, interferón alfa-2b, azacitidina, PEG-L-asparaginasa, lenalidomida, gemtuzumab, hidrocloridato, interleucina-11, dexrazoxano, alemtuzumab, ácido retinoico todo-trans, ketoconazol, interleucina-2, megestrol, inmuno globulina, mostaza nitrógeno, metilprednisolona, ibritumomab tiuxetan, andrógenos, decitabina, hexametilmelamina, bexaroteno, tositumomab, trióxido de arsénico, cortisona, editronato, mitotano, ciclosporina, daunorubicina liposomal, Edwina-asparaginasa, estroncio 89, casopitant, netupitant, un antagonista del receptor NK-1,

palonosetron, aprepitant, difenhidramina, hidroxizina, metoclopramida, lorazepam, alprazolam, haloperidol, droperidol, dronabinol, dexametasona, proclorperazina, granisetron, ondansetron, dolasetron, tropisetron, pegfilgrastim, eritropoietina, epoetin alfa, darbepoetin alfa y mezclas de estos.

30. Un compuesto para inducir la degradación de una proteína diana en una célula caracterizada porque es de conformidad con la reivindicación 1.

31. Una composición para tratar cáncer caracterizada porque comprende una cantidad del compuesto de conformidad con la reivindicación 1.

32. La composición para uso de conformidad con la reivindicación 31, en donde el cáncer es carcinomas hepatocelulares, carcinomas de células renales, cáncer de mama, cáncer de próstata, cáncer de cuello uterino, cáncer uterino, o cáncer de ovario.