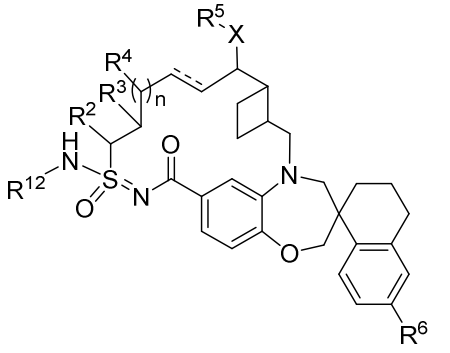
CLAIMS

1. A compound according to Formula (I):



(I)

wherein:

--- is a single or double bond;

X is O or NR^7;

R^{12} is hydrogen or $–C(O)R^1$;

R^1 is C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{6-10}aryl, 3-12 membered heterocyclyl, 5-10 membered heteroaryl, $–OR^7$, or $–NR^8R^9$, wherein

said C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{6-10}aryl, 3-12 membered heterocyclyl, and 5-10 membered heteroaryl are optionally substituted with 1-5 R^{10} groups;

R^2 is hydrogen, C_{1-6}alkyl, C_{3-10}cycloalkyl, or 3-12 membered heterocyclyl, wherein

said C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-10}cycloalkyl, and 3-12 membered heterocyclyl are optionally substituted with 1-5 R^{10} groups;

R^3 and R^4 are independently hydrogen, C_{1-6}alkyl, $–OR^7$, C_{1-6}heteroalkyl, $–NR^8R^9$, $NR^8C(O)R^9$, $–NR^8C(O)OR^9$, C_{6-10}aryl, C_{3-10}cycloalkyl, 5-10 membered heteroaryl, 3-12 membered heterocyclyl, $–C(O)R^7$, $–C(O)OR^7$, $–C(O)NR^8R^9$, $–OC(O)NR^8R^9$, –CN, or $–SO_2R^7$, wherein

said C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, 5-10 membered heteroaryl, and 3-12 membered heterocyclyl are optionally substituted with 1-5 R^{10} groups;

R^5 is hydrogen, C_{1-6}alkyl, $–(CH_2CH_2O)_pR^7$, C_{1-6}heteroalkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, 5-10 membered heteroaryl, or 3-12 membered heterocyclyl, wherein

said C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{6-10}aryl, C_{3-10}cycloalkyl, 5-10 membered heteroaryl, and 3-12 membered heterocyclyl are optionally substituted with 1-5 R^{10} groups;

R^6 is hydrogen or halo;

each R^7 is independently hydrogen, C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, or 5-10 membered heteroaryl, wherein

said C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10} aryl, and 5-10 membered heteroaryl are optionally substituted with from 1-5 R^{10};

each R^8 and R^9 are independently hydrogen, C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, or 5-10 membered heteroaryl, or R^8 and R^9 together with the atoms to which they are attached form a 3-12 membered heterocycle, wherein

said C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, and 5-10 membered heteroaryl are optionally substituted with 1-5 R^{10};

each R^{10} is independently C_{1-6}alkyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, 5-10 membered heteroaryl, halo, oxo, $–OR^a$, $–C(O)R^a$, $–C(O)OR^a$, $–C(O)NR^aR^b$, $–OC(O)NR^aR^b$, $–NR^aR^b$, $–NR^aC(O)R^b$, $–NR^aC(O)OR^b$, $–S(O)_qR^a$, $–S(O)_2NR^aR^b$, $–NR^aS(O)_2R^b$, $–N_3$, –CN, or $–NO_2$, or two R^{10} groups form a fused, spiro, or bridged C_{3-10} cylcloalkyl or 3-12 membered heterocyclyl, wherein

each C_{1-6}alkyl, C_{1-6} heteroalkyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, C_{6-10}aryl, 3-12 membered heterocycle, and 5-10 membered heteroaryl is optionally substituted with 1-5 R^{20} groups;

each R^a and R^b is independently hydrogen, C_{1-6}alkyl, C_{2-6} alkenyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, 5-10 membered heteroaryl, or R^a and R^b together with the atoms to which they are attached form a 3-12 membered heterocyclyl wherein

said C_{1-6}alkyl, C_{2-6} alkenyl, C_{3-10}cycloalkyl, C_{1-6}heteroalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, 5-10 membered heteroaryl is optionally substituted with 1-5 R^{20} groups;

each R^{20} is independently C_{1-6} alkyl, C_{3-10} cycloalkyl, C_{1-6} heteroalkyl, 3-12 membered heterocyclyl, C_6-C_{10} aryl, 5-10 membered heteroaryl, hydroxyl, C_{1-6} alkoxy, amino, -CN, -C(O)H, $-C(O)NH_2$, $-C(O)NH(C_{1-6}$ alkyl), $-C(O)N(C_{1-6}$ alkyl)$_2$, -COOH, $-C(O)C_{1-6}$ alkyl, $-C(O)OC_{1-6}$ alkyl, or halogen;

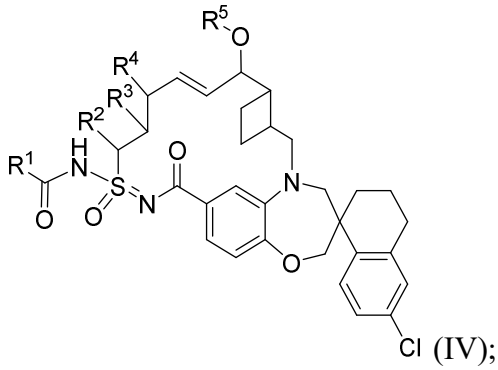
n is 0, 1, or 2;

p is 0, 1, or 2; and

q is 0, 1, or 2;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, according to Formula (IV):



(IV);

wherein: R^1 is C_{3-10}cycloalkyl, 3-12 membered heterocyclyl, C_{6-10}aryl, or 5-10 membered heteroaryl;

wherein R^1 is independently optionally substituted with 1-4 R^{10};

wherein each R^{10} is independently selected from halo, hydroxyl, –CN, C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-10}cycloalkyl, and 3-12 membered heterocyclyl;

wherein C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-10}cycloalkyl and 3-12 membered heterocyclyl of R^{10} are independently optionally substituted with 1-4 substituents independently selected from halo, C_{1-4}alkyl, C_{1-4}haloalkyl, and C_{1-4}heteroalkyl;

R^2 is hydrogen, C_{1-6}alkyl, or C_{1-6}heteroalkyl;

wherein C_{1-6}alkyl and C_{1-6}heteroalkyl of R^2 is optionally substituted with 1-3 substituents independently selected from halo, oxo, and hydroxyl;

R^3 and R^4 are independently hydrogen, C_{1-6}alkyl, C_{1-6}heteroalkyl, -OR^7, or -SO_2R^7;

wherein C_{1-6}alkyl and C_{1-6}heteroalkyl of R^3 and R^4 are independently optionally substituted with 1-3 substituents independently selected from halo, oxo, C_{3-6}cycloalkyl, 4-6 membered heterocyclyl, C_{6-10}aryl, and 5-10 membered heteroaryl;

wherein C_{3-6}cycloalkyl, 4-6 membered heterocyclyl, C_{6-10}aryl, and 5-10 membered heteroaryl are independently optionally substituted with 1-3 substituents independently selected from halo, C_{1-4}alkyl, and C_{1-4}heteroalkyl;

R^5 is hydrogen, C_{1-6}alkyl, or C_{1-6}heteroalkyl;

wherein C_{1-6}alkyl and C_{1-6}heteroalkyl of R^5 are optionally substituted with 1-3 substituents independently selected from halo, oxo, C_{3-6}cycloalkyl, and 4-6 membered heterocyclyl; and

R^7 is independently hydrogen, C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocyclyl, C_{6-10}aryl, or 5-10 membered heteroaryl;

wherein C_{1-6}alkyl, C_{1-6}heteroalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocyclyl, C_{6-10}aryl, and 5-10 membered heteroaryl of R^7 are optionally substituted with 1-4 substituents independently selected from halo, oxo, C_{1-4}alkyl, C_{1-4}haloalkyl, and C_{1-4}heteroalkyl.

3. The compound claim 1 or 2, wherein:

R^2 is hydrogen or C_{1-3}alkyl;

R^3 is hydrogen or C_{1-3}alkyl;

R^4 is hydrogen;

R^5 is C_{1-3}alkyl, wherein

said C_{1-3}alkyl is optionally substituted with a 5-6 membered heterocyclyl;

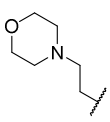
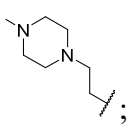
or a pharmaceutically acceptable salt thereof.

4. The compound of any one of claims 1-3, wherein:

R^2 is hydrogen, methyl, or ethyl;

R^3 is hydrogen or methyl;

R^4 is hydrogen; and

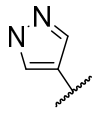
R^5 is hydrogen, methyl, , or ;

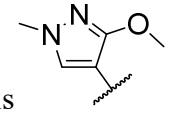
or a pharmaceutically acceptable salt thereof.

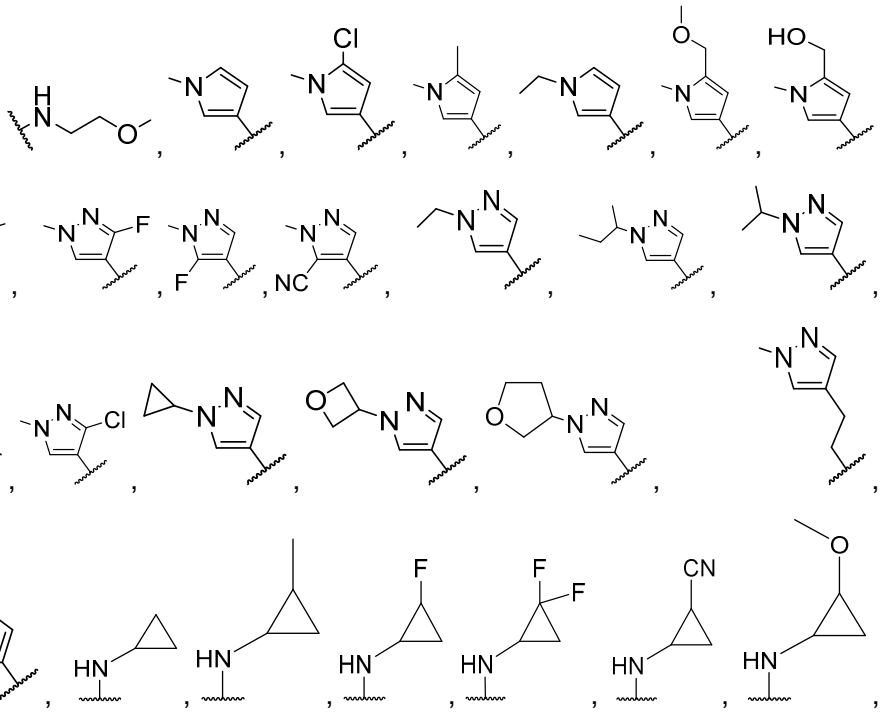
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein R^3 is methyl.

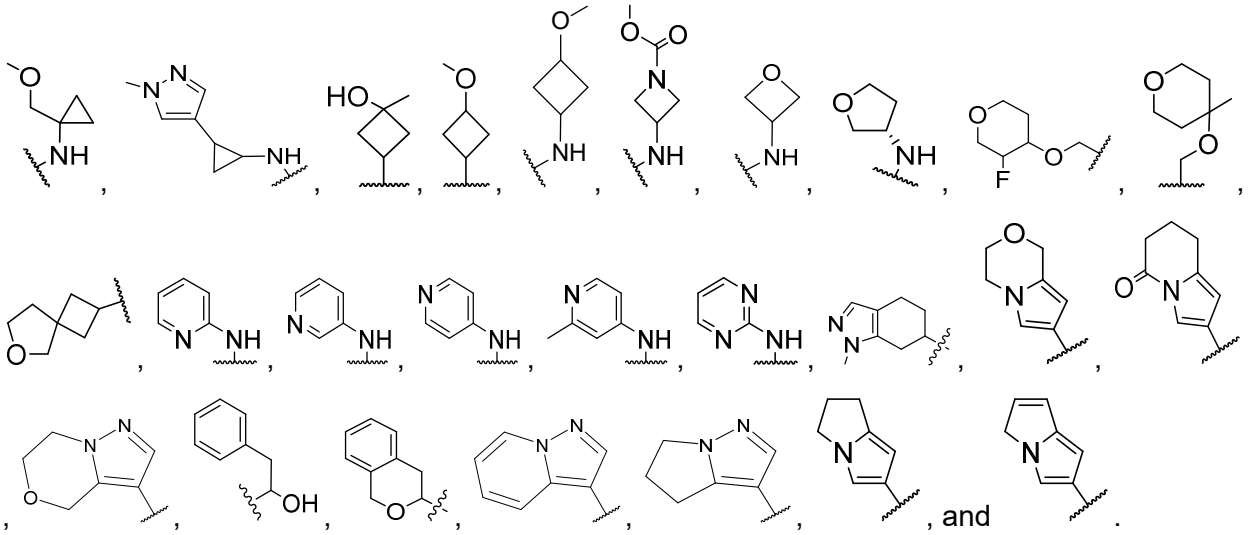
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt thereof, wherein R^4 is hydrogen.

7. The compound of any one of claims 1-6, or a pharmaceutically acceptable salt thereof, wherein R^5 is methyl.

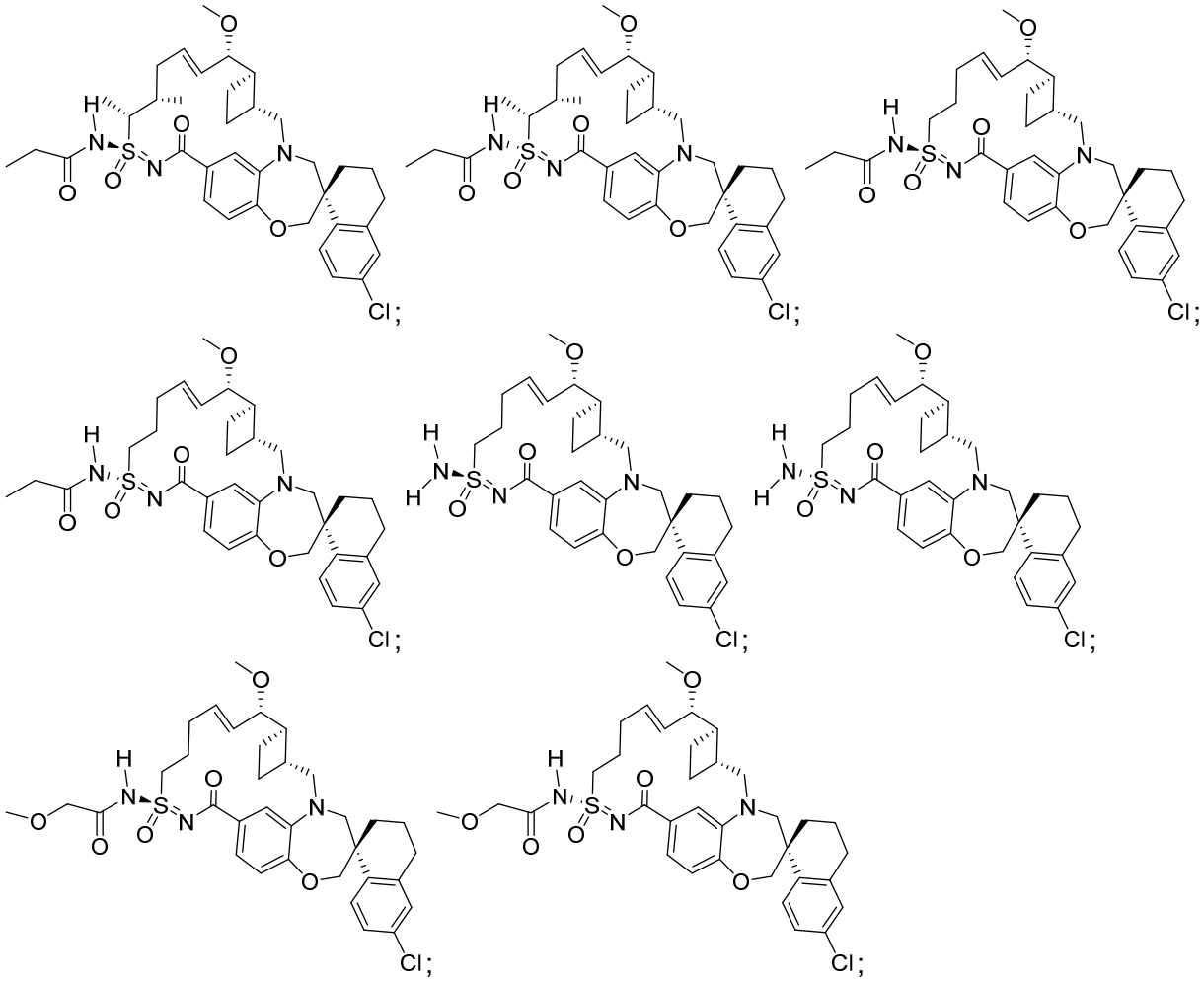
8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein R^1 is  substituted with two groups selected from $C_{1\text{-}4}$alkyl and $C_{1\text{-}4}$alkoxyl.

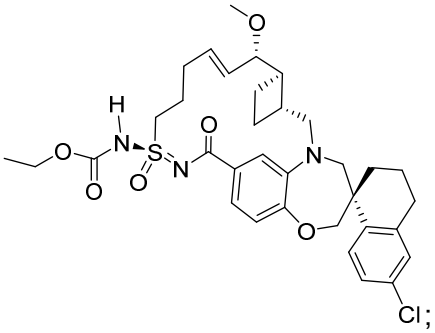
9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, wherein R^1 is .

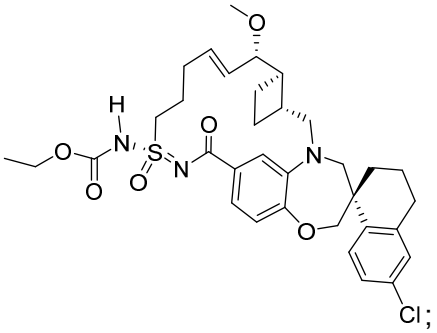
10. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt thereof, wherein R^1 is selected from: 

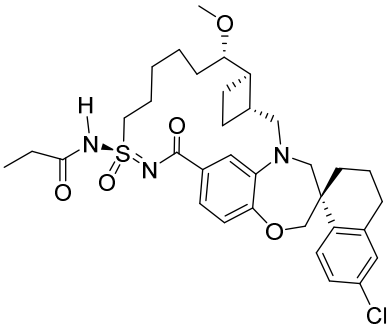


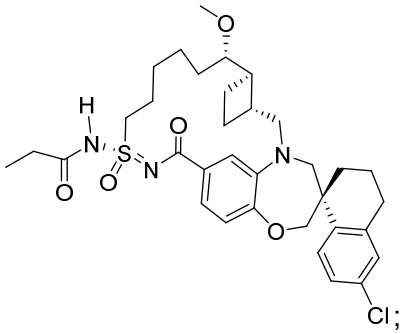
11. A compound, or a pharmaceutically acceptable salt thereof, selected from:

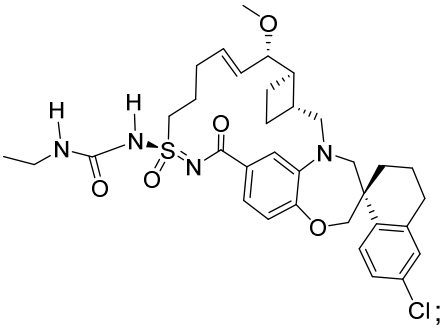


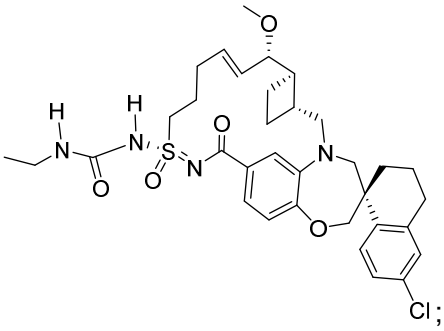


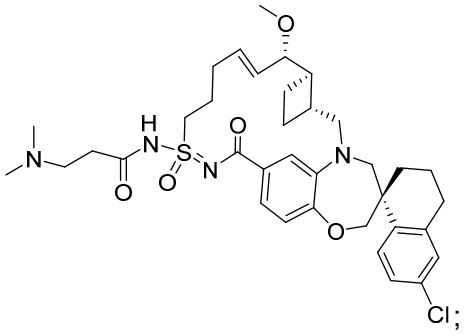


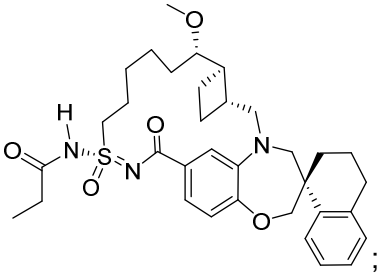


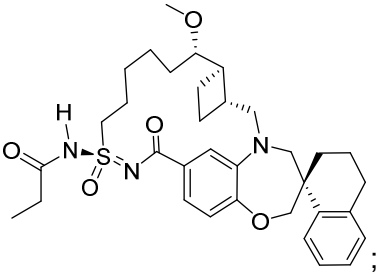


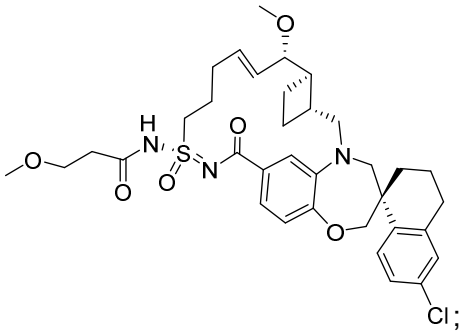


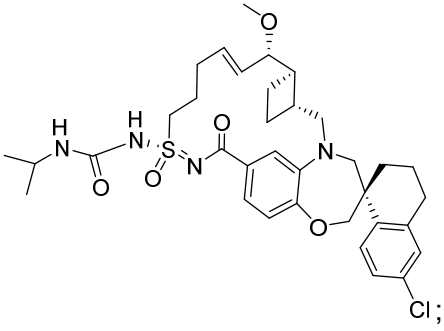


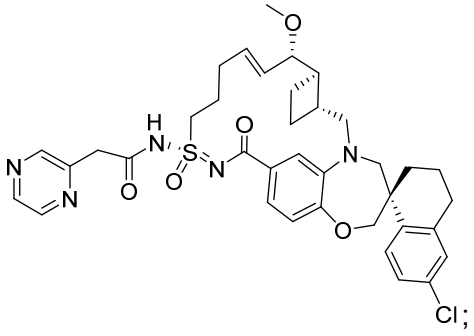


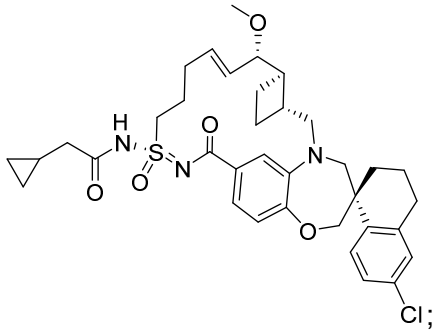


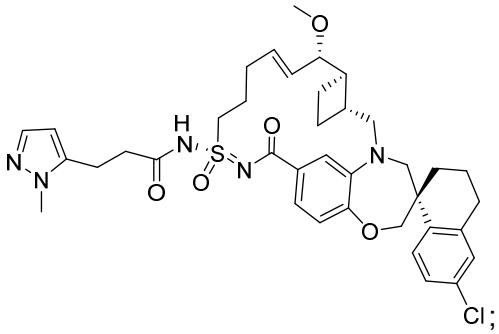


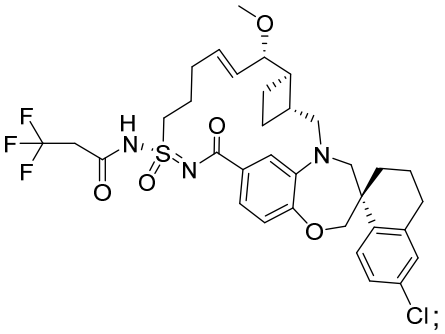


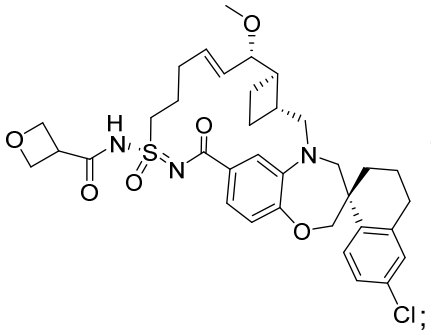


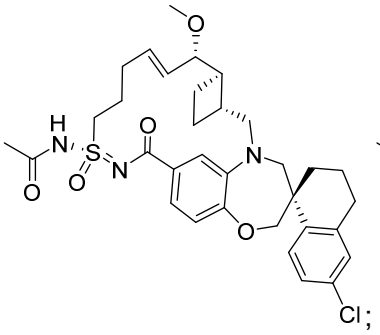


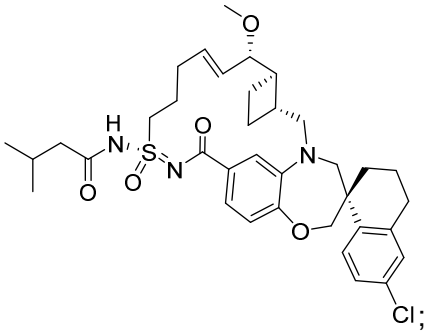


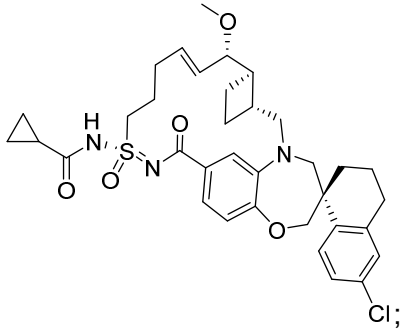


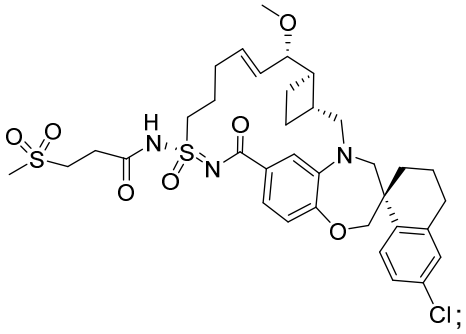


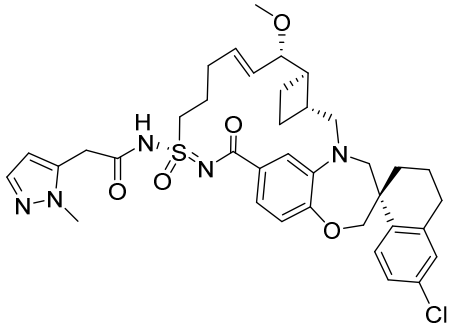


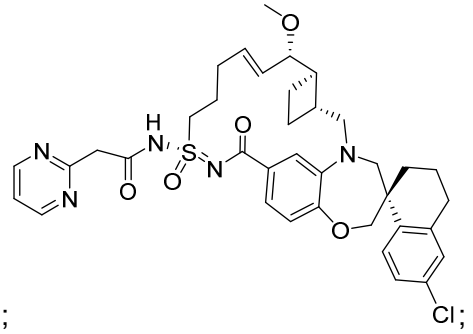


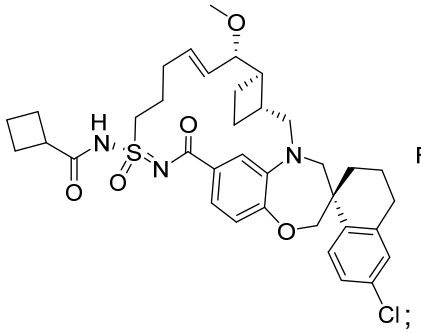


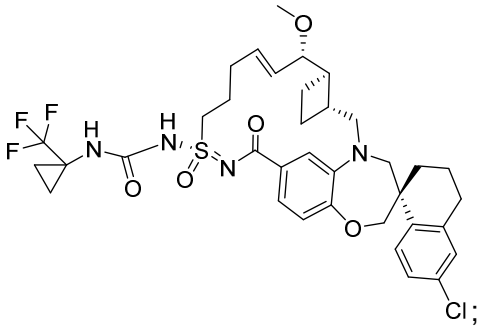


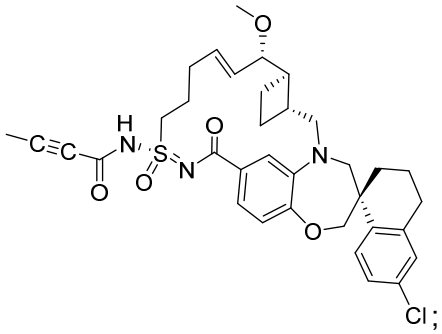


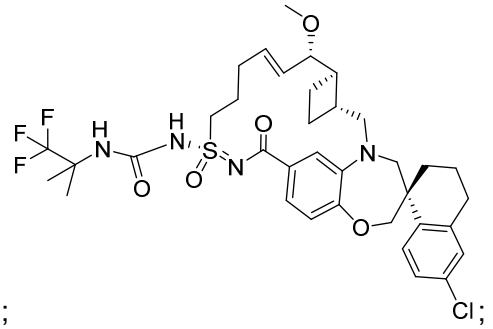


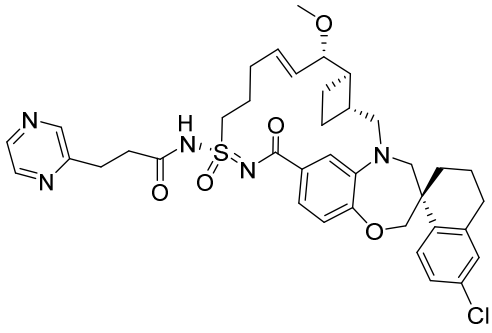


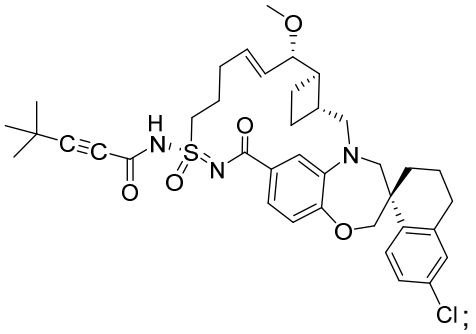


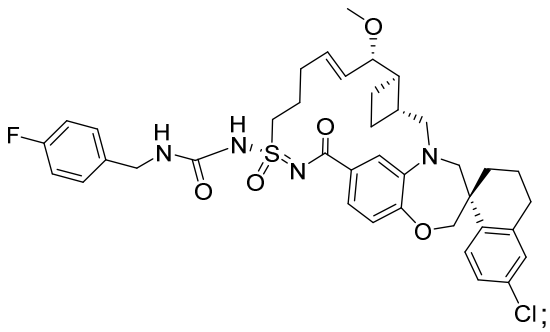


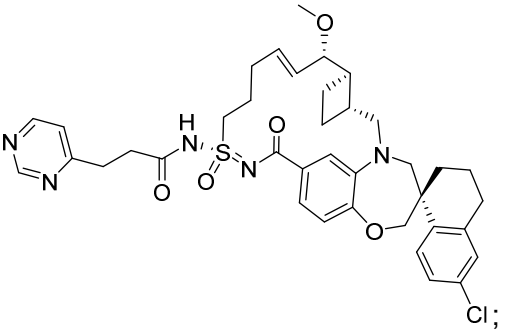


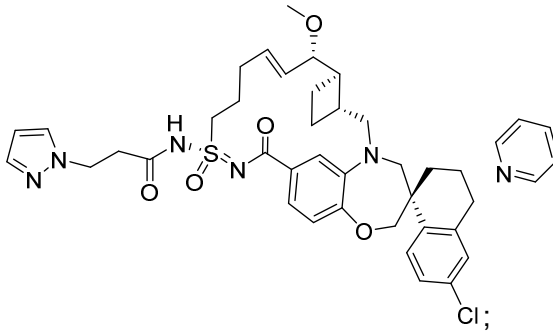




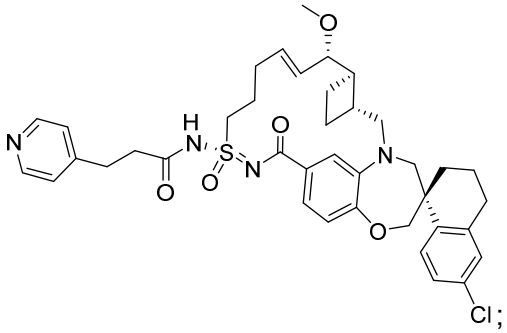


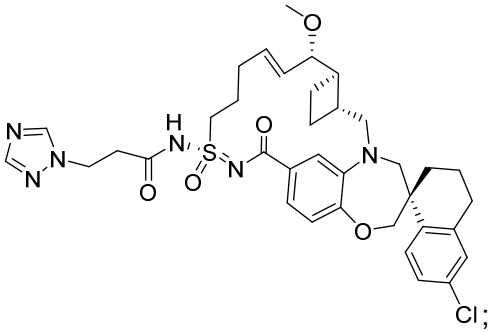


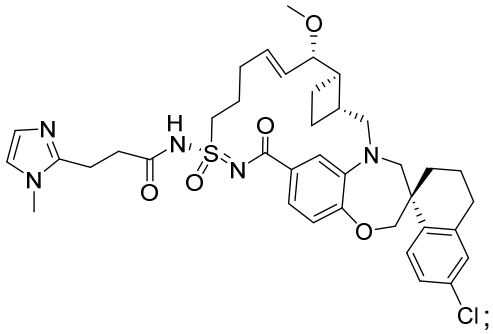


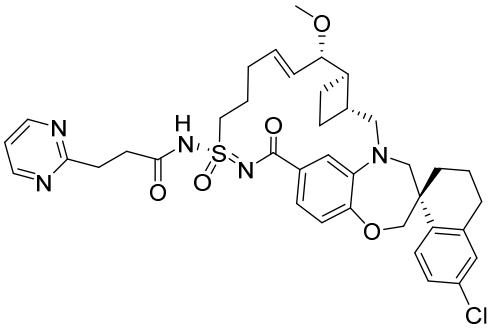


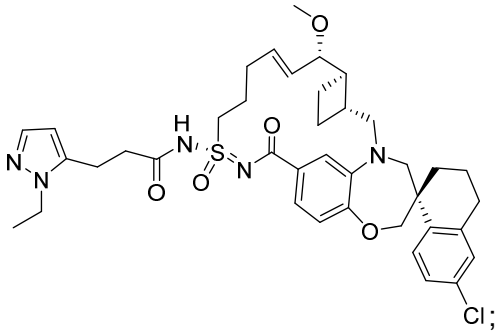


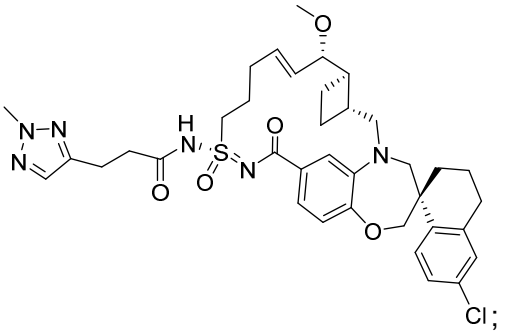


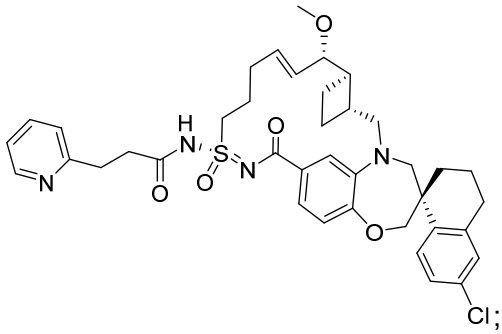


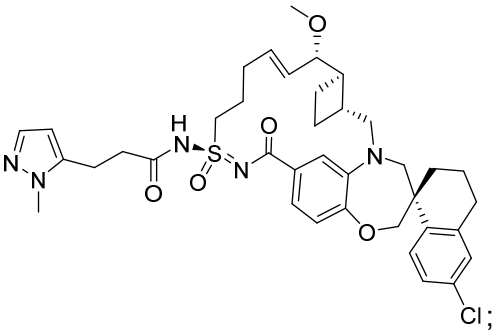


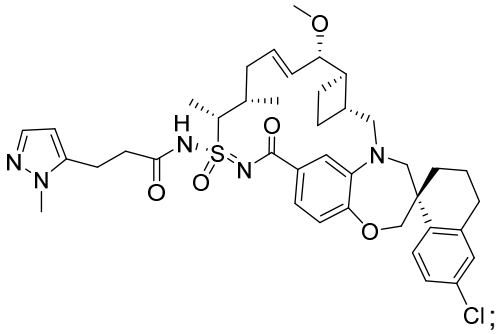


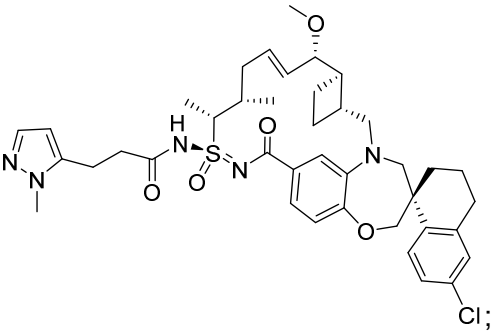


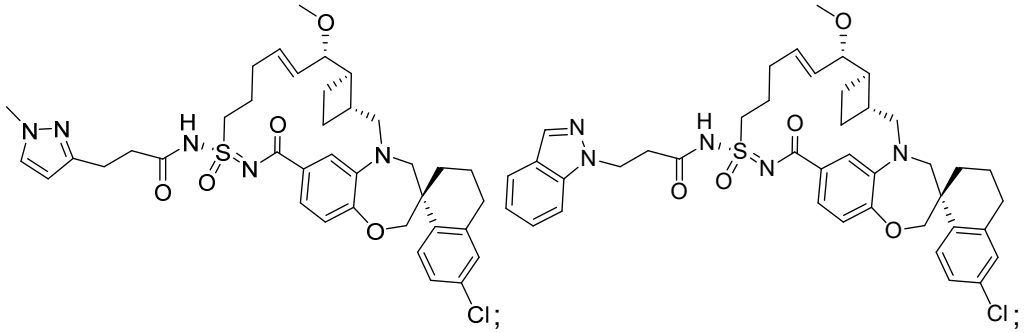


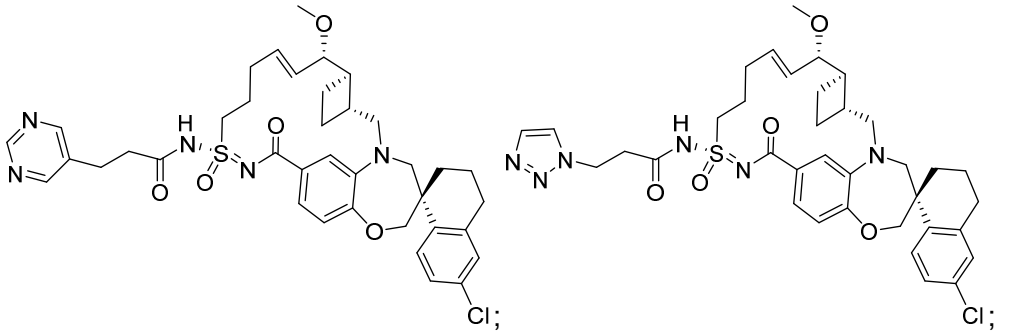


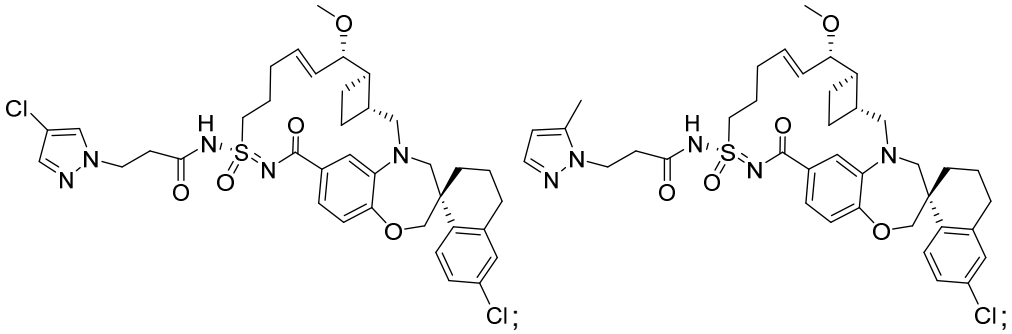


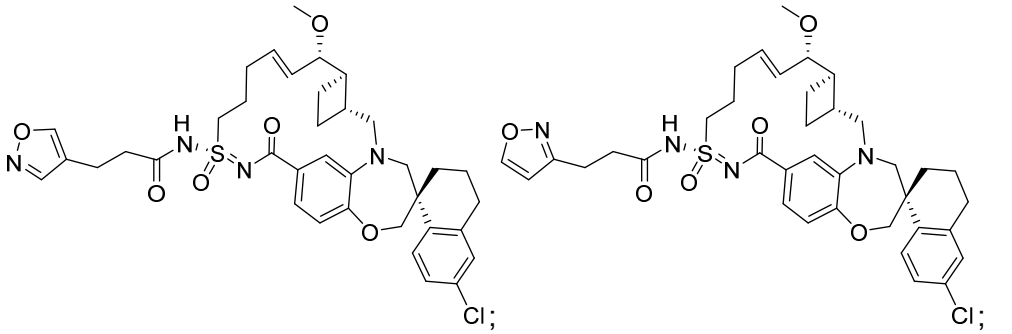


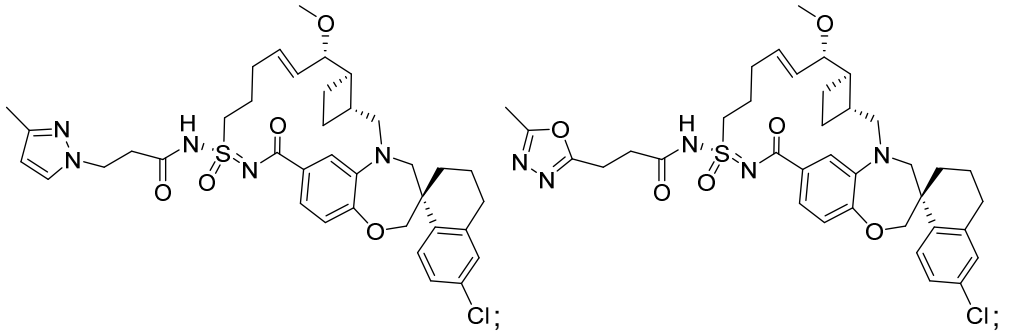


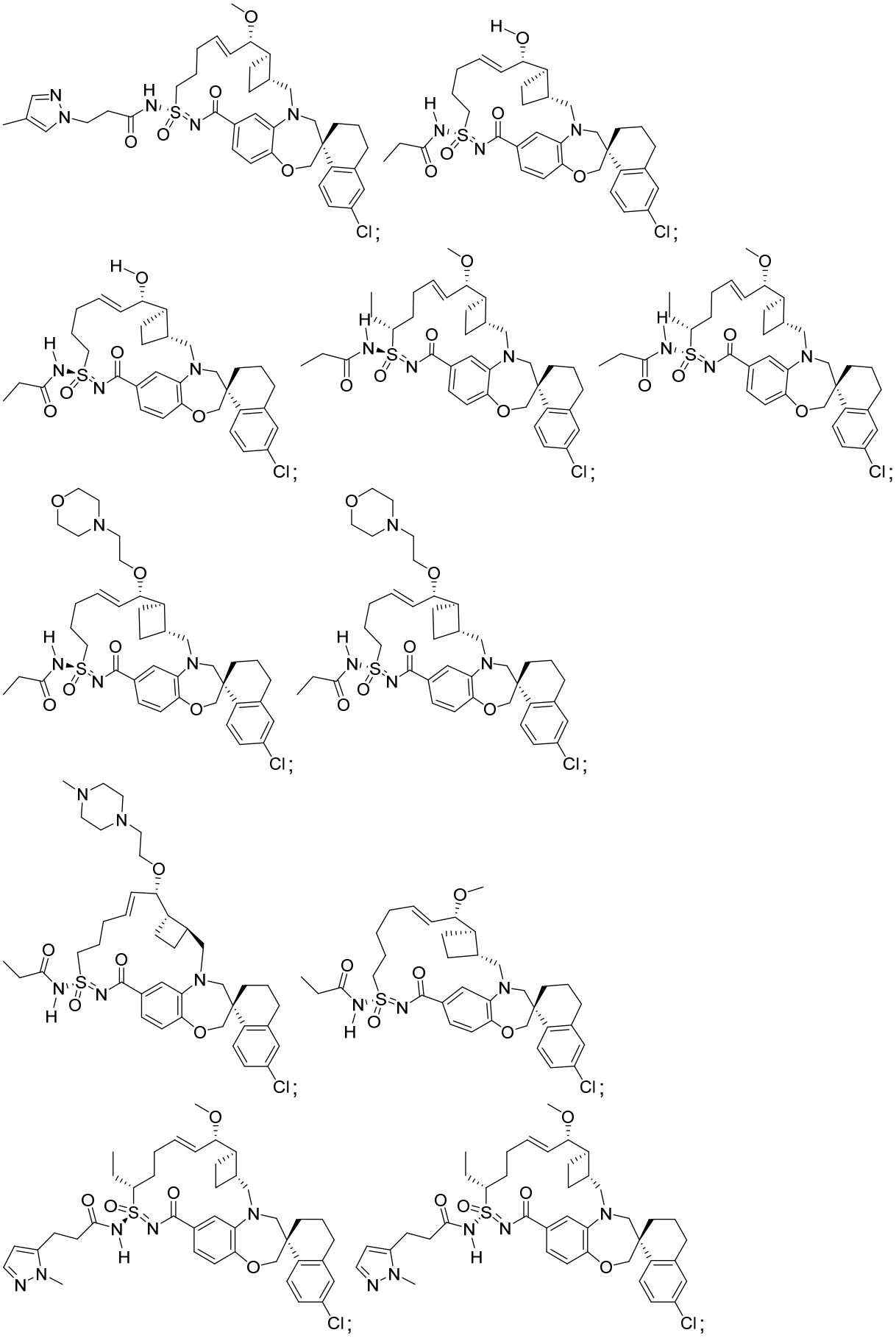


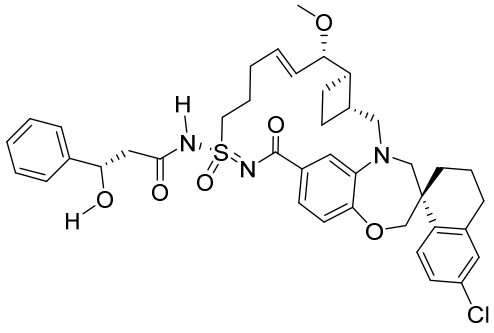


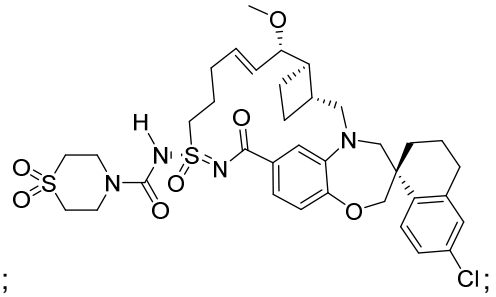


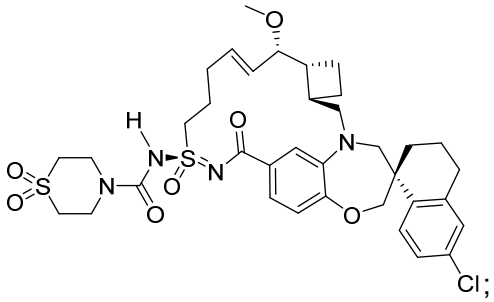


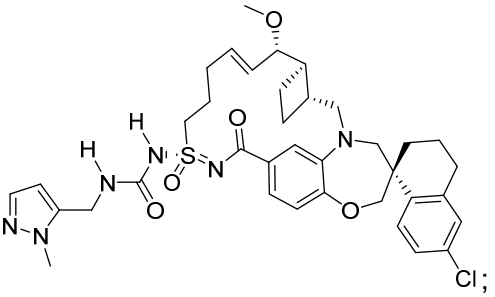


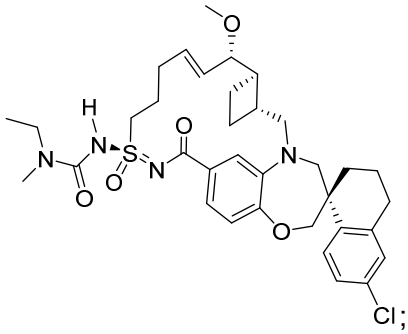


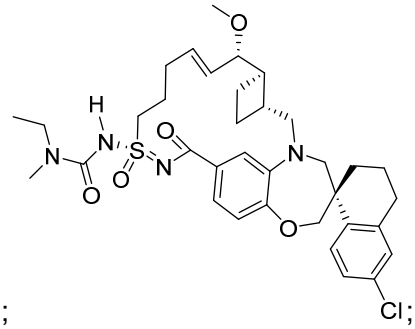


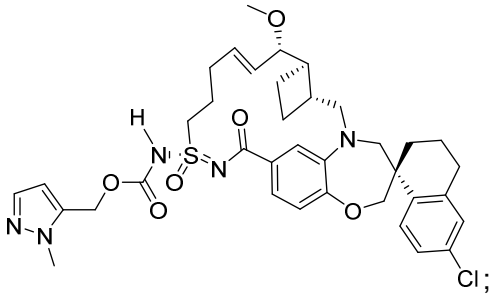


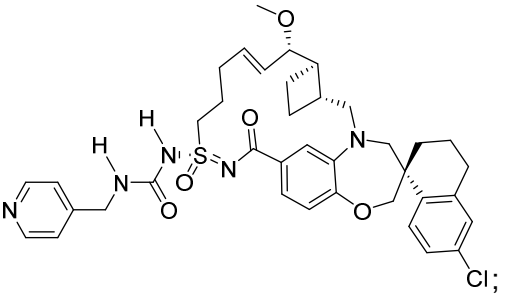


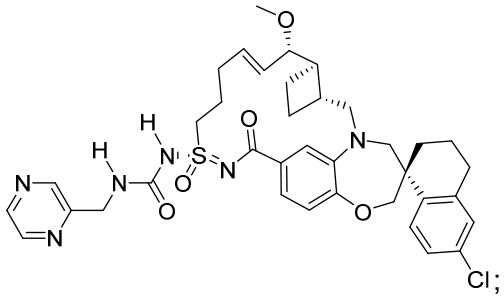


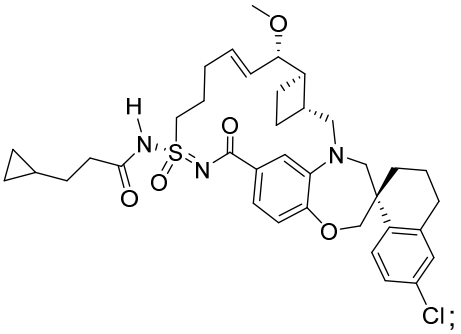


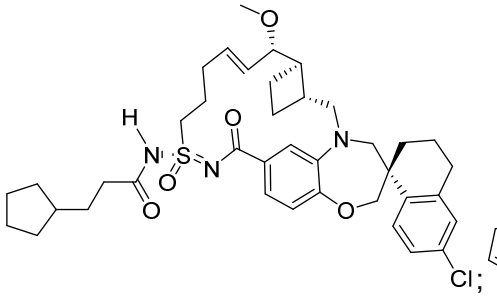


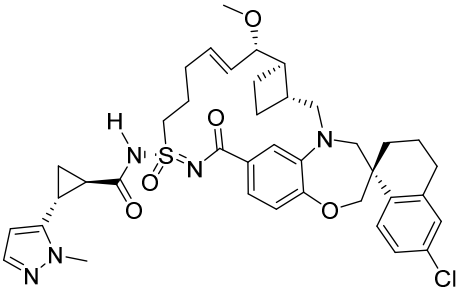


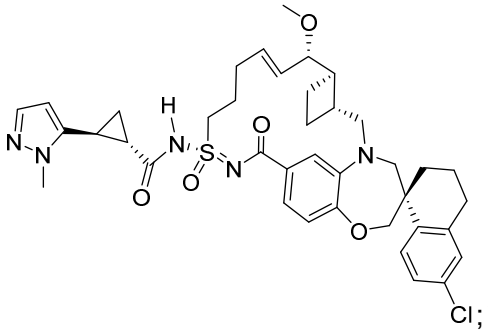


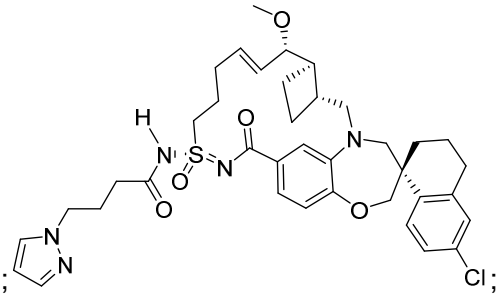


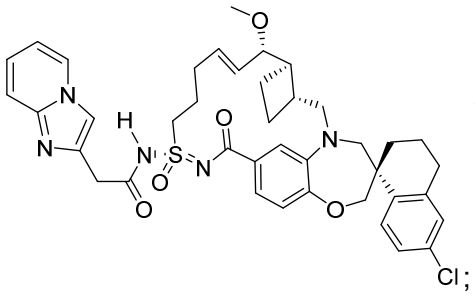


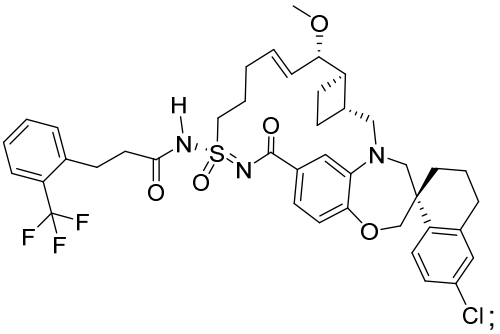


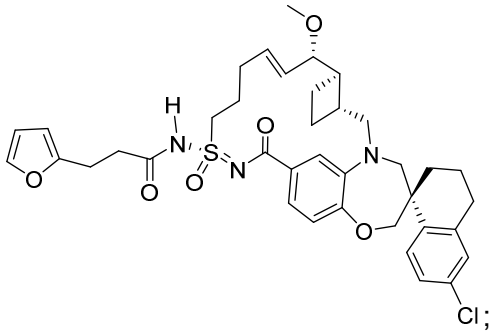


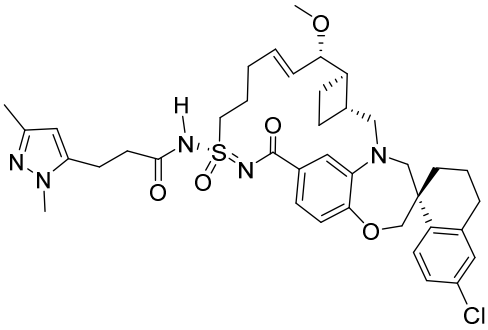


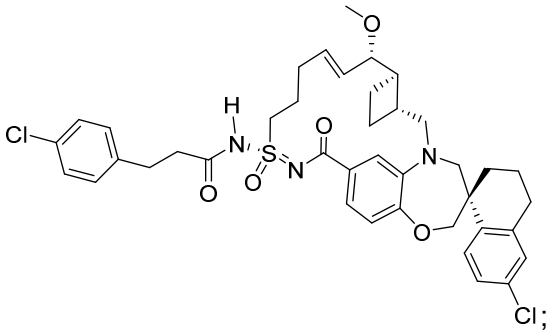


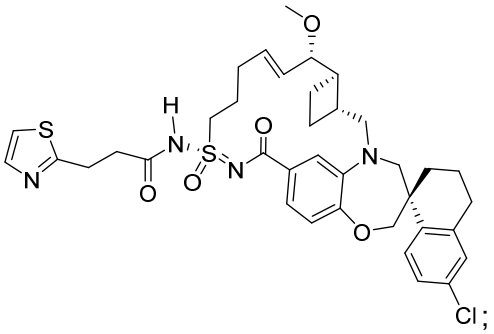


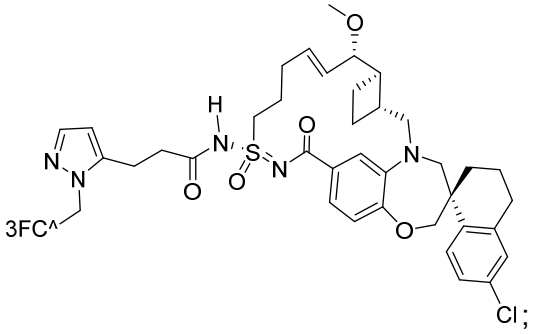


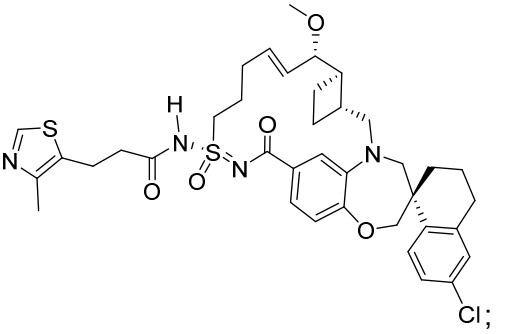


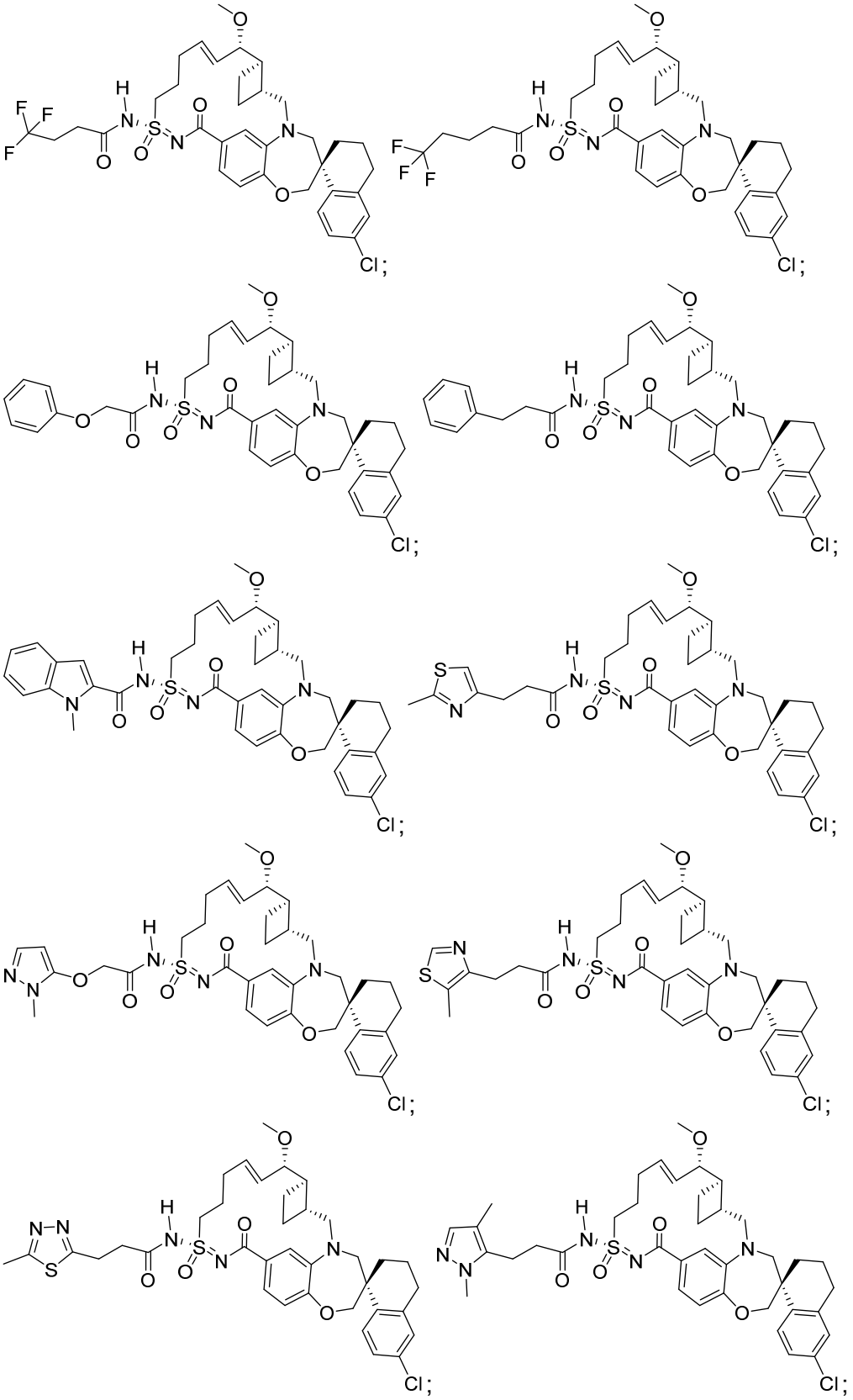


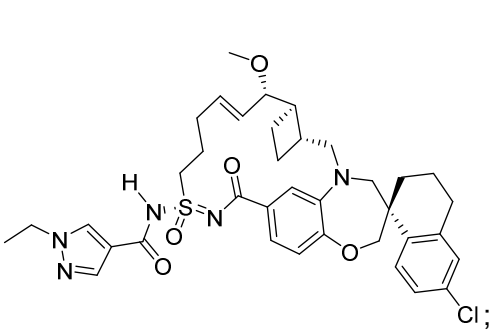


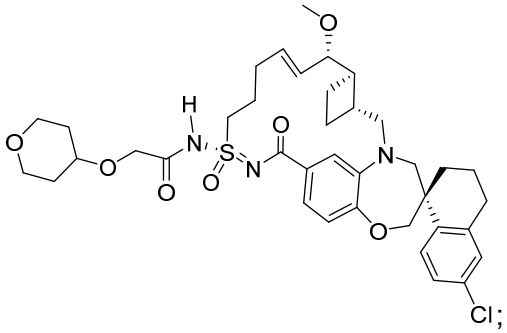


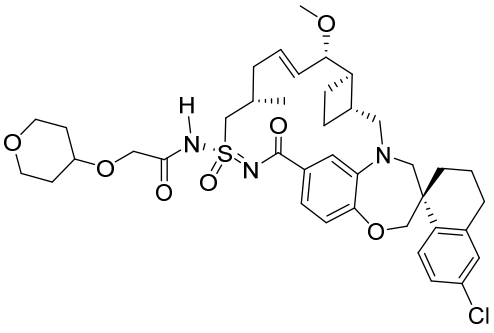


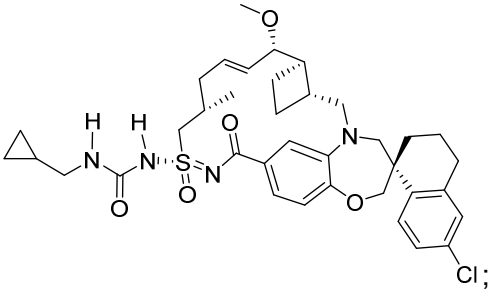


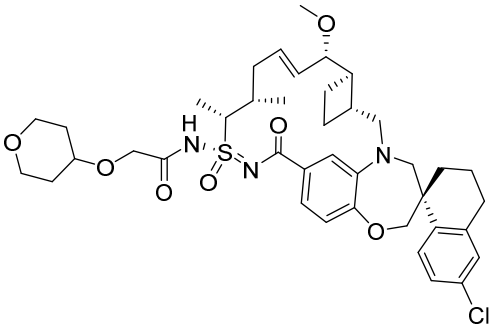


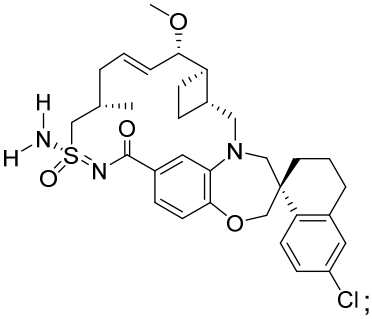


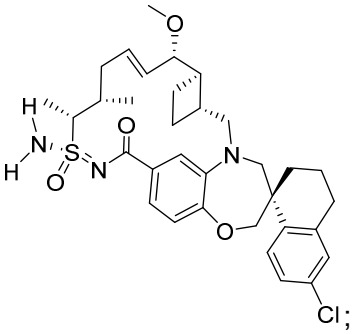


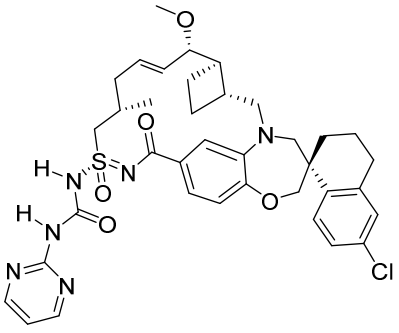


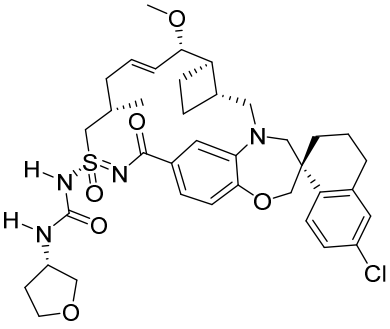


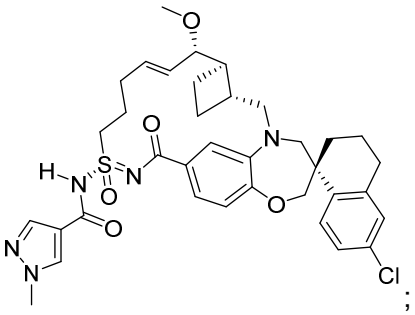


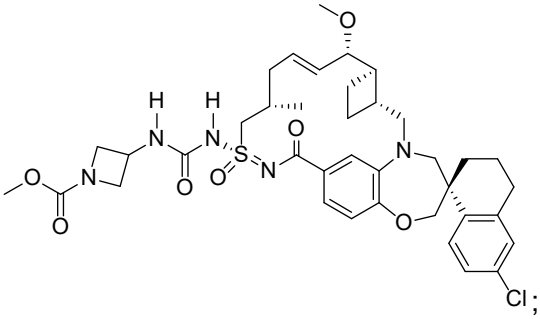


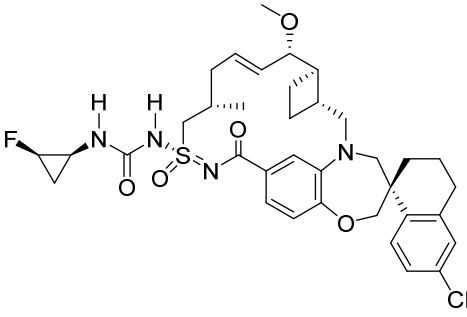


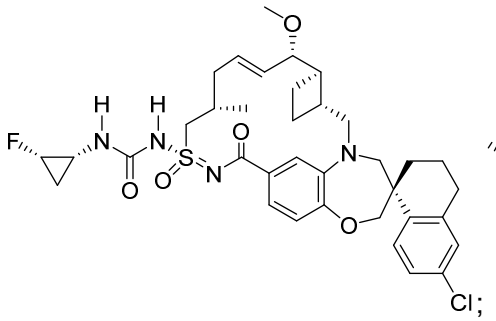


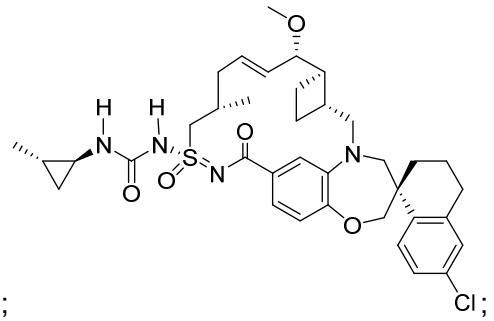


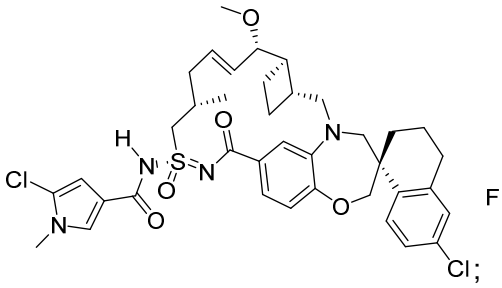


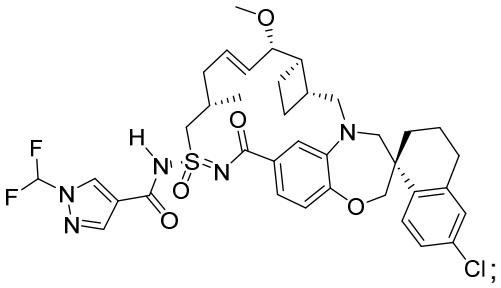


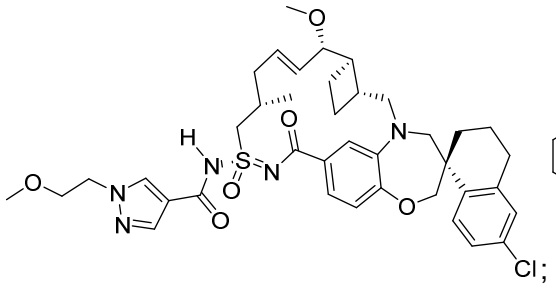


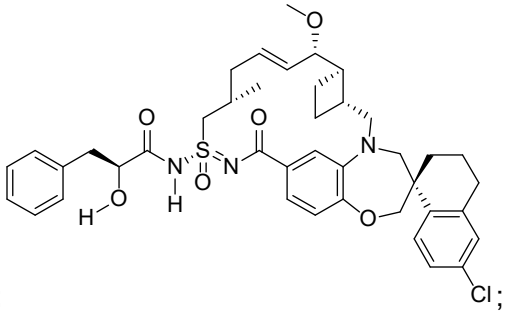


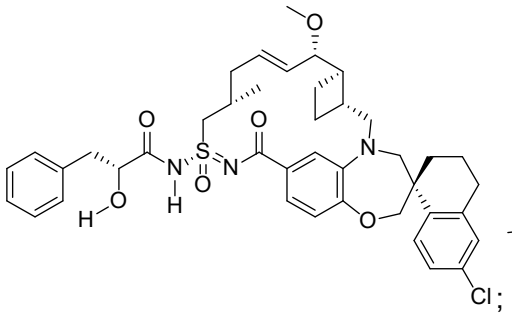


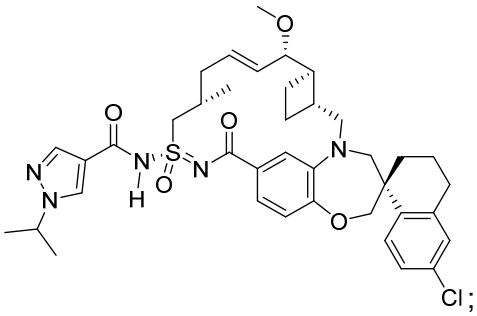


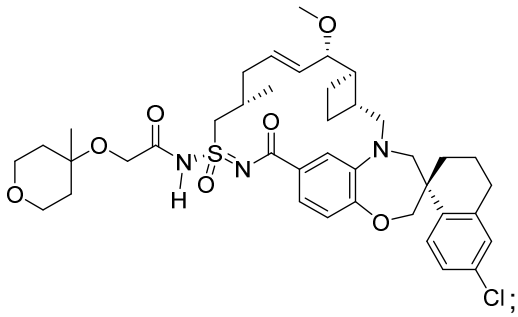


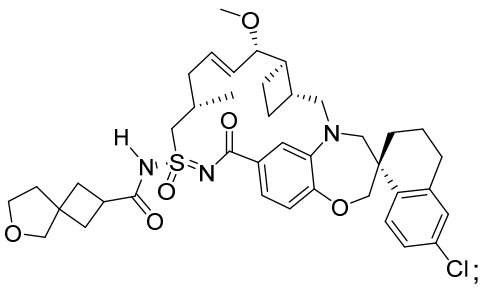


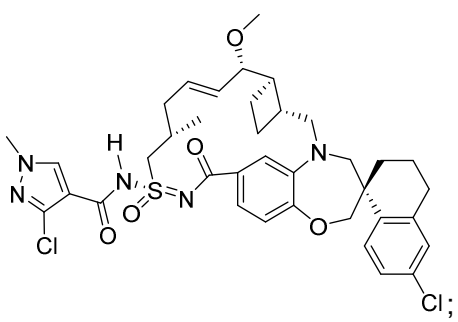


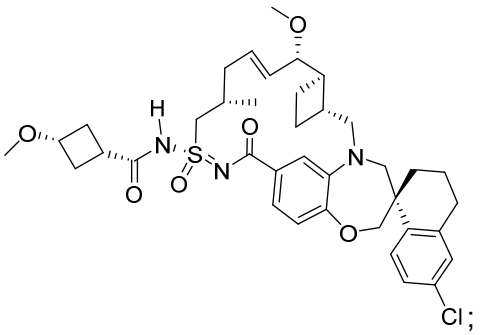


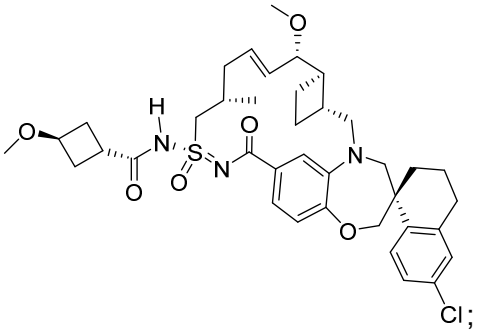


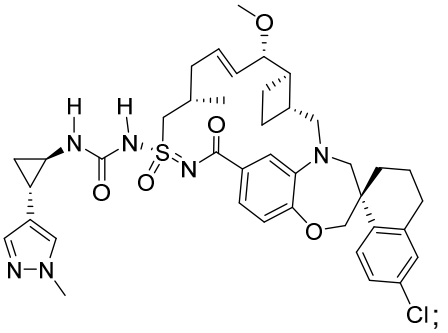


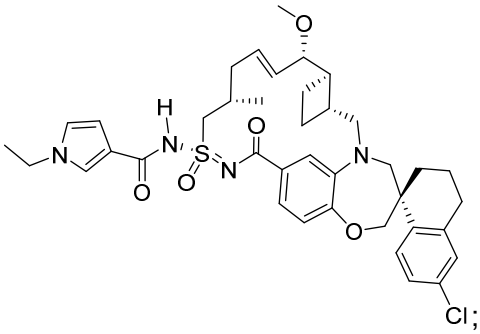


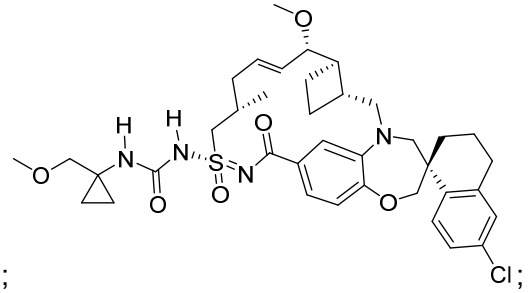


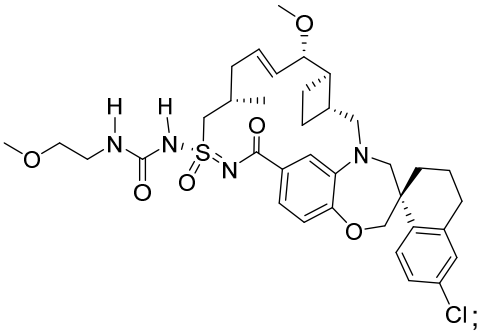


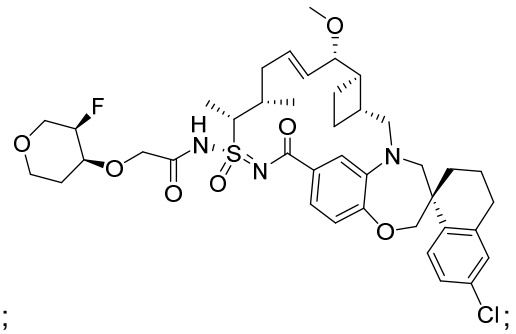


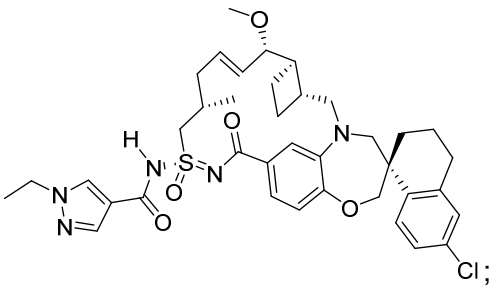


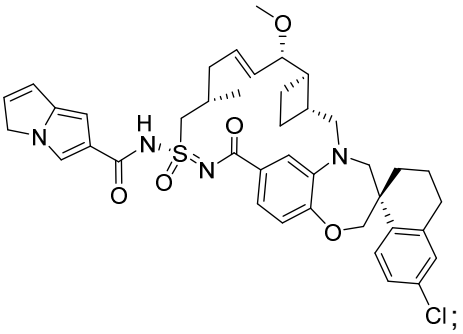


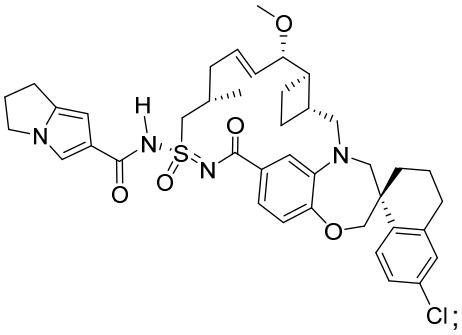


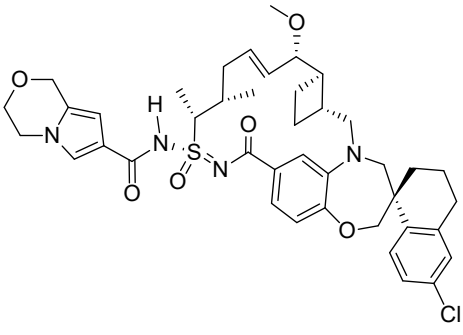


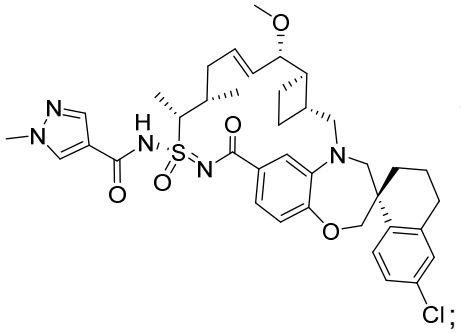


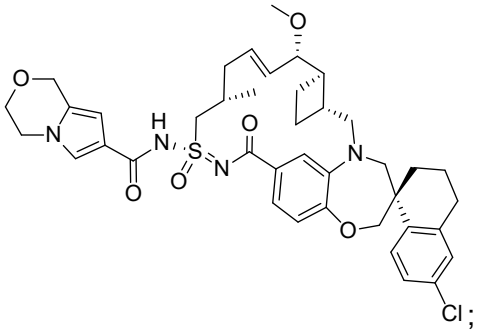


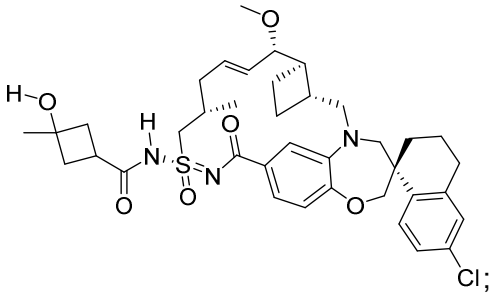


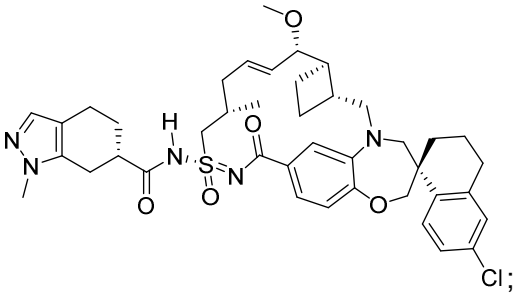


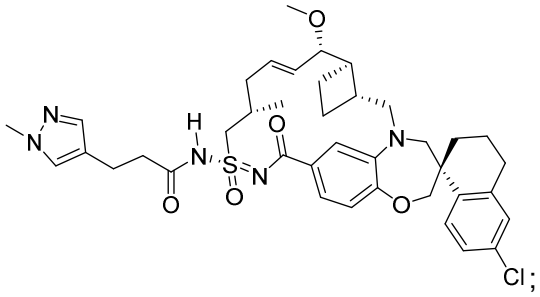


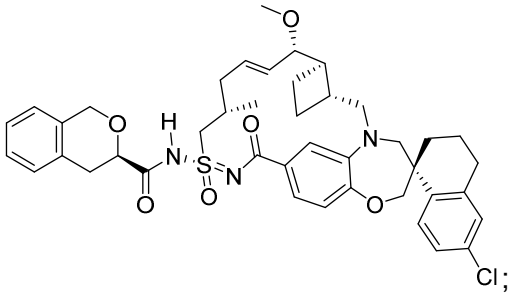


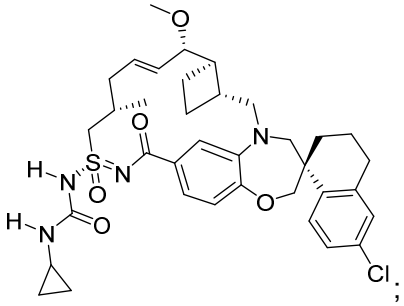


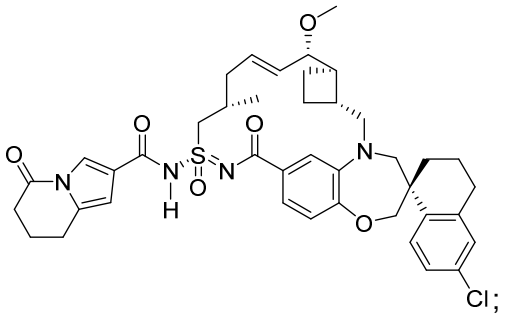


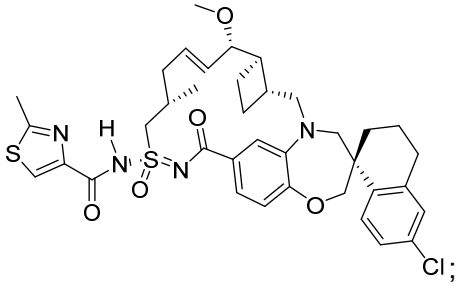


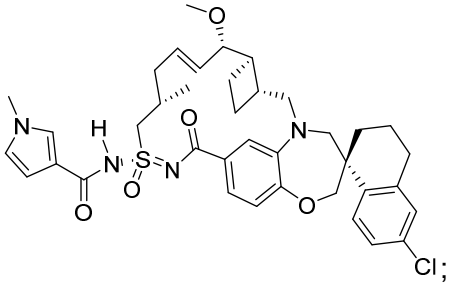


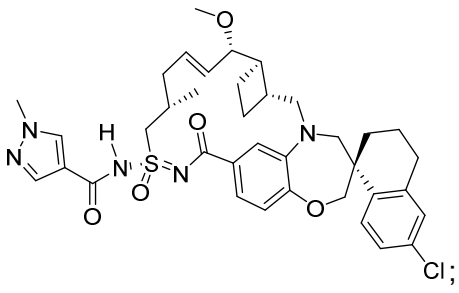


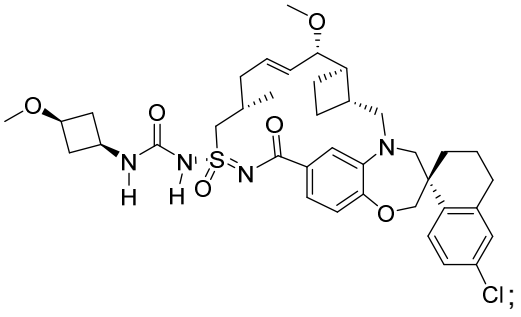


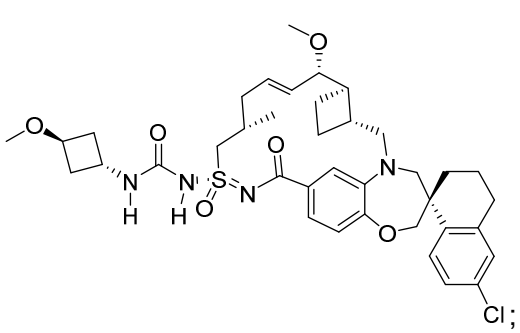


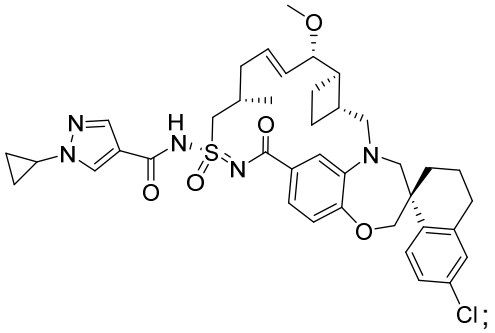


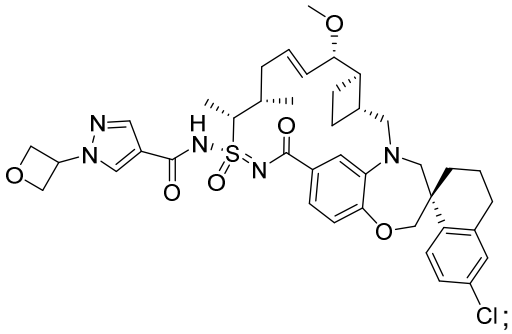


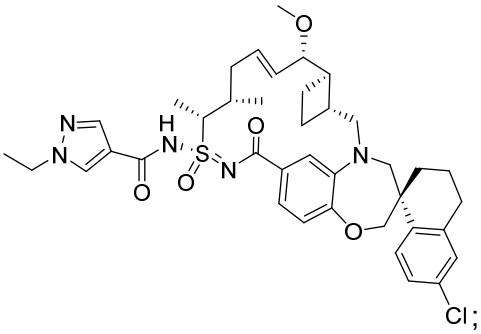


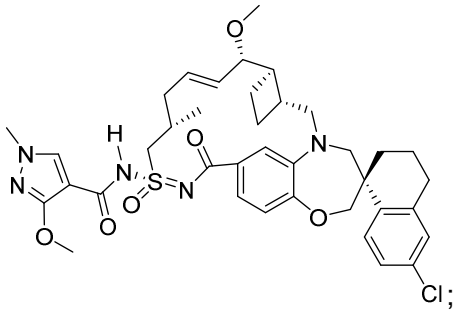


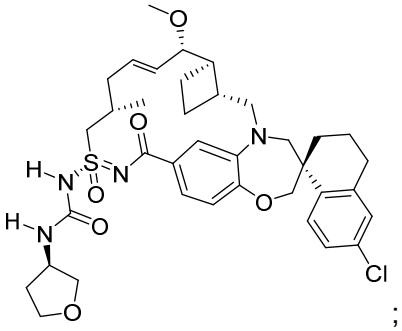


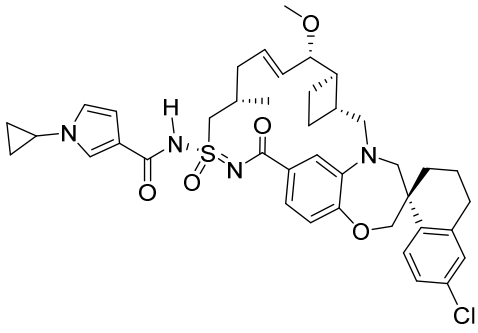


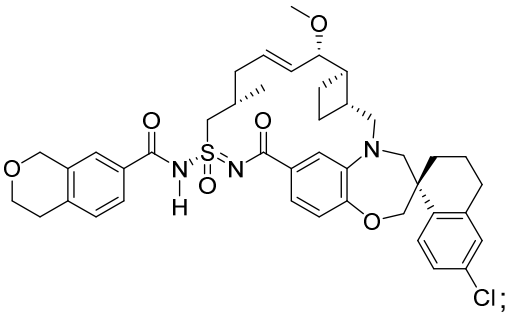


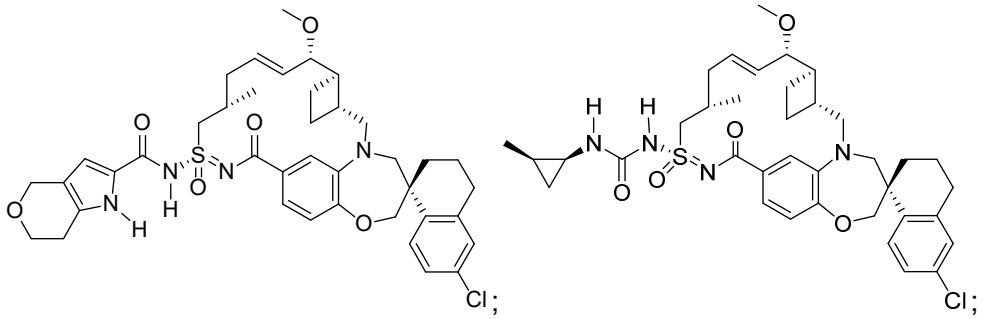


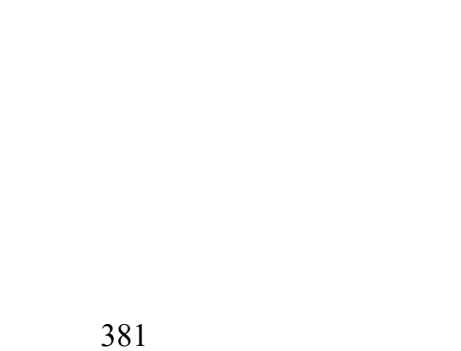


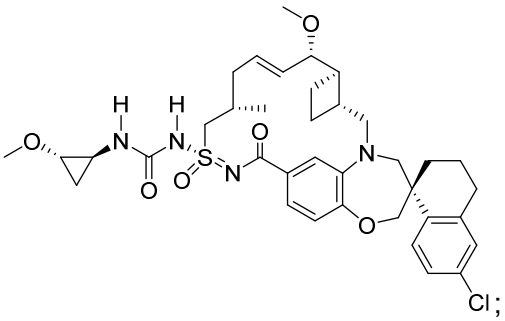


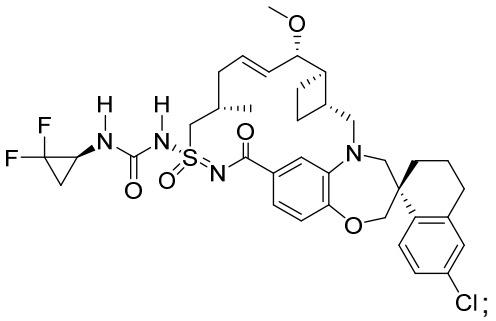


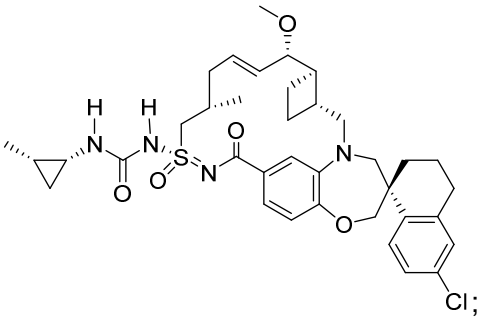


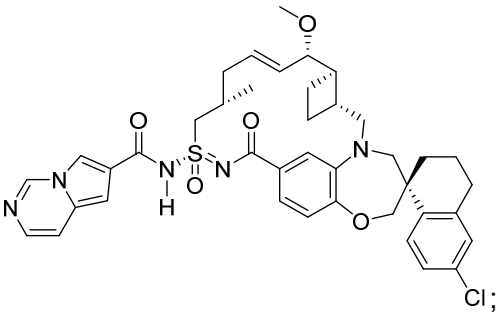


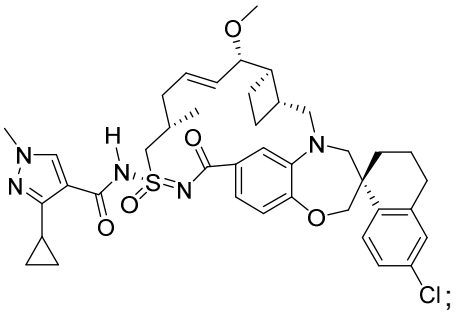


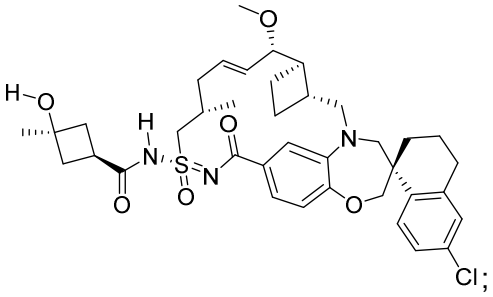


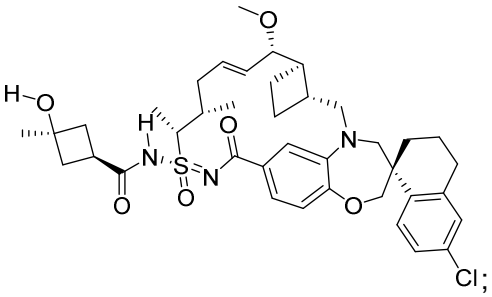


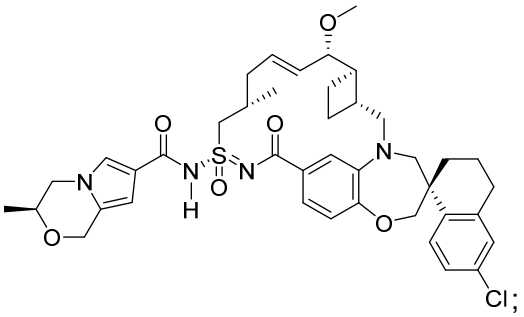


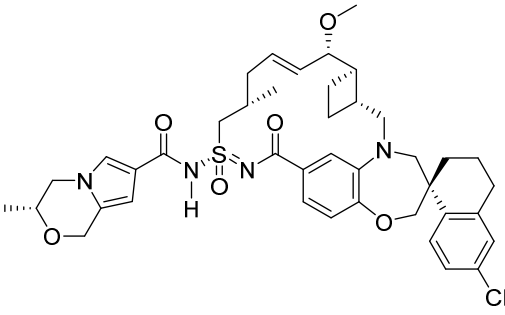


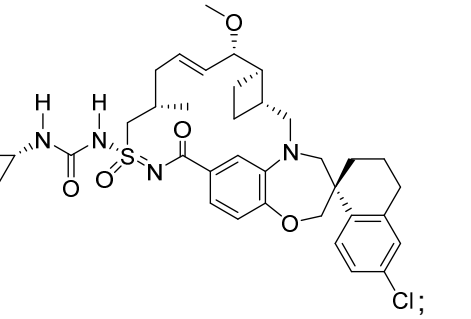


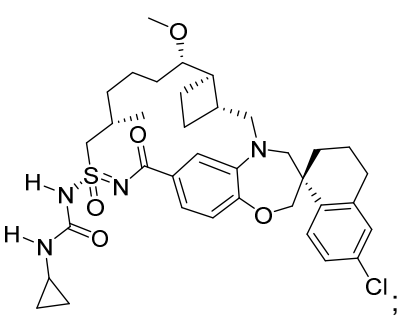


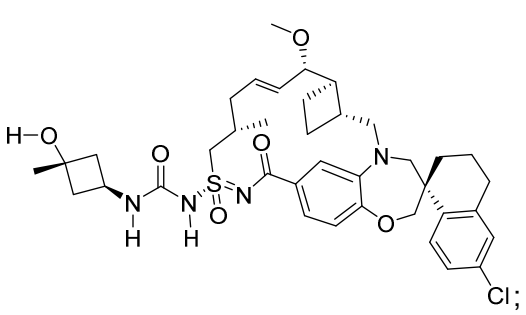


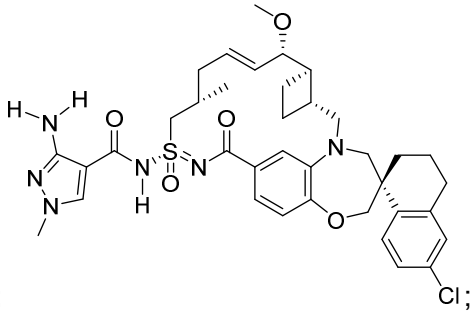


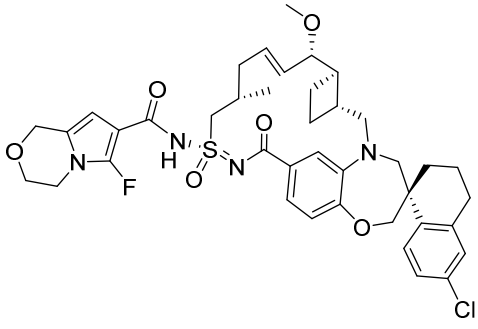


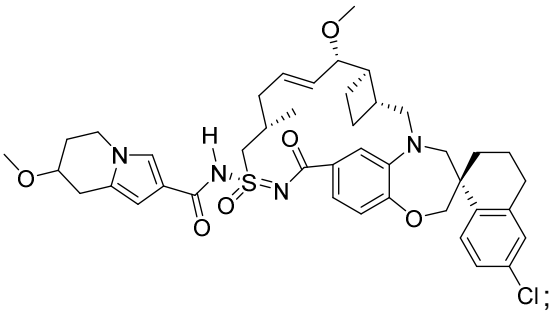


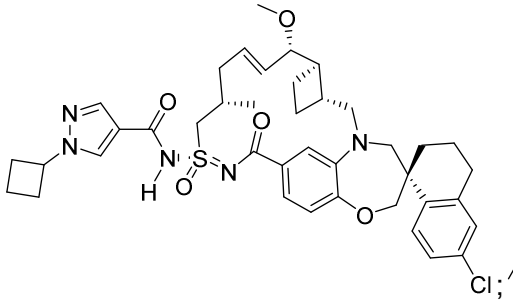


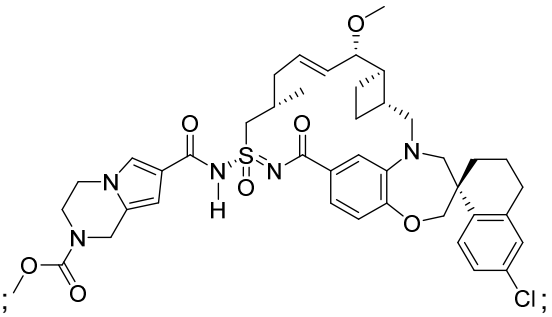


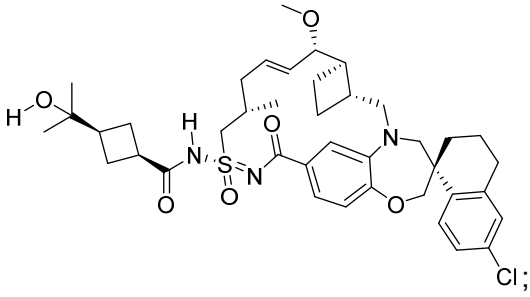


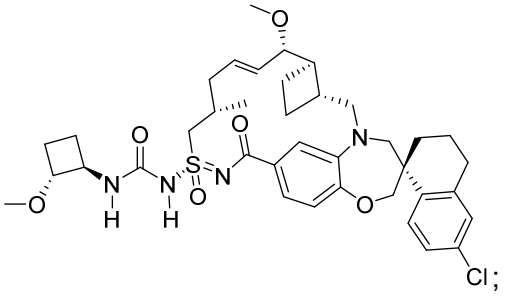


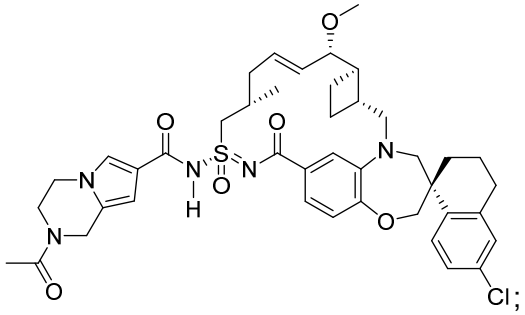


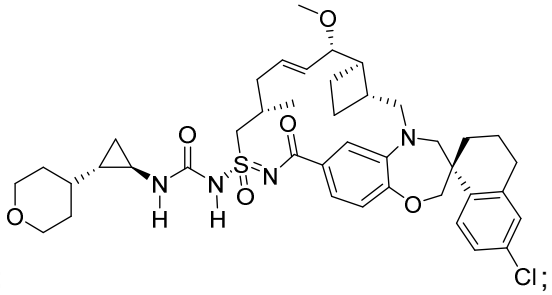


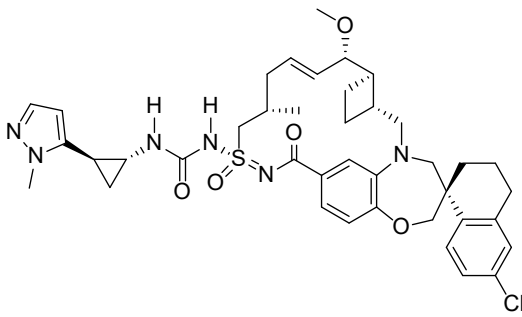


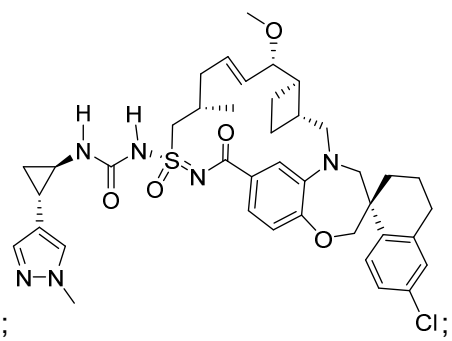


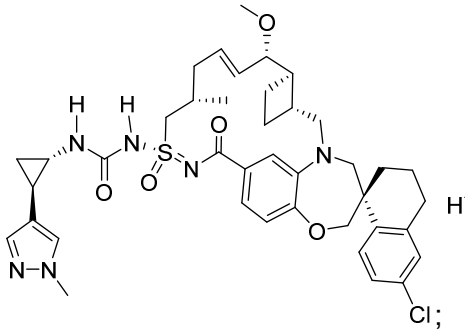


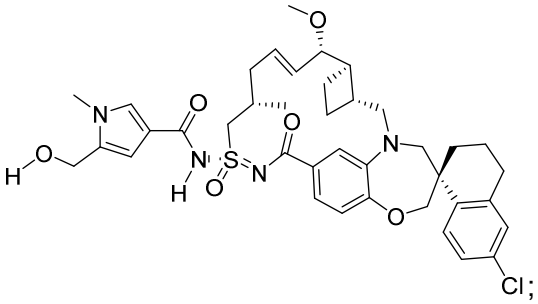


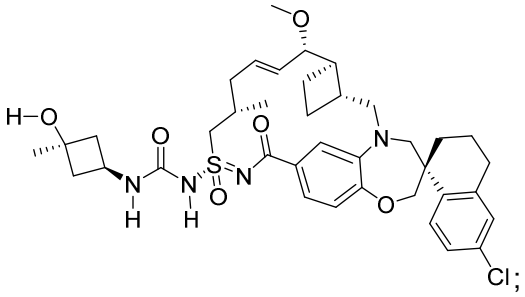


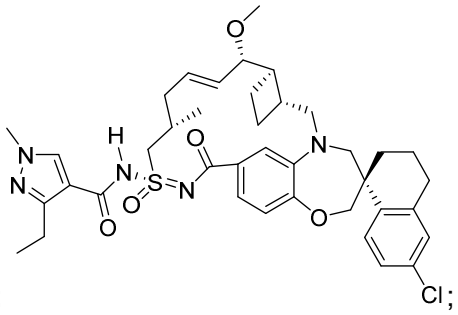


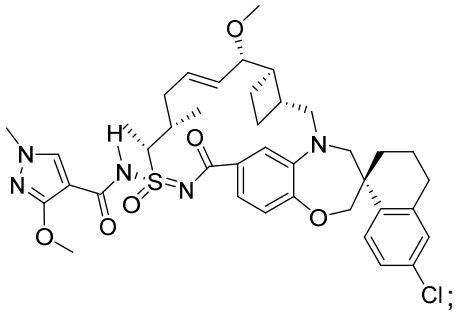


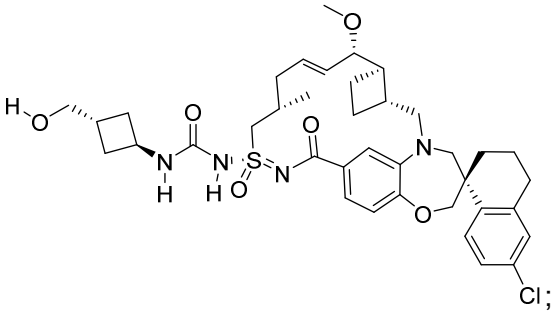


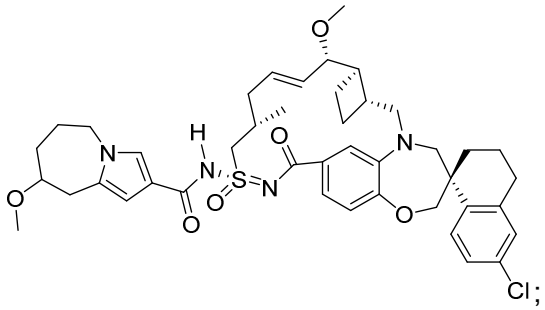


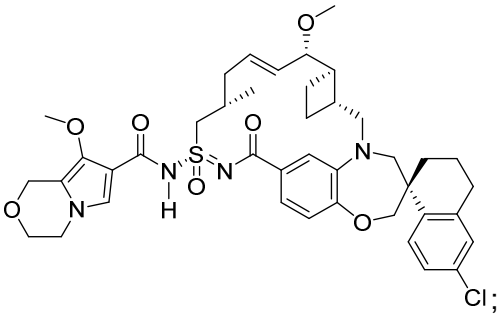


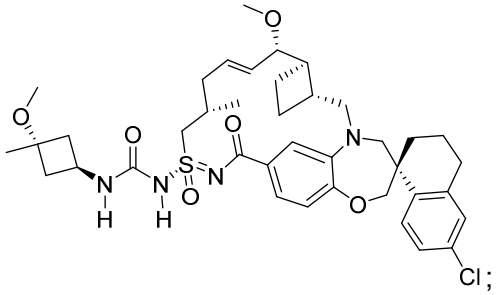


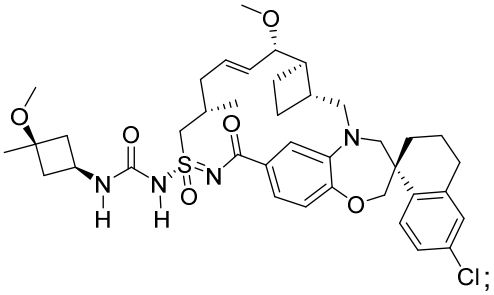


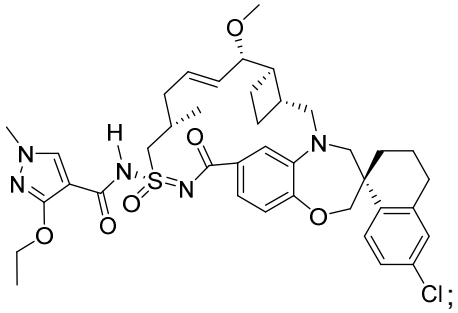


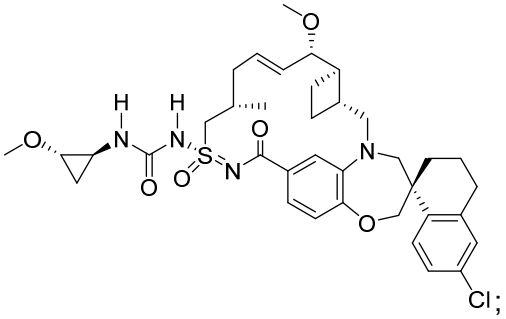


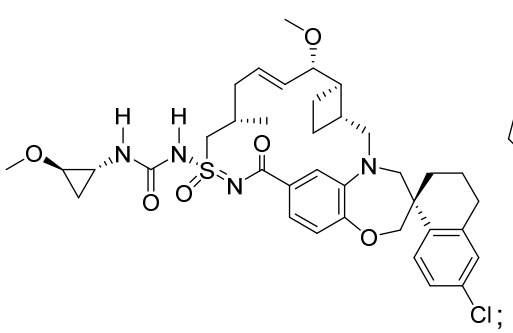


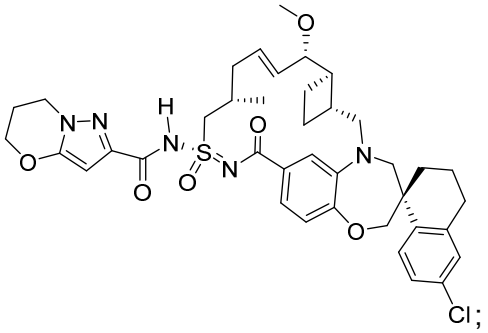


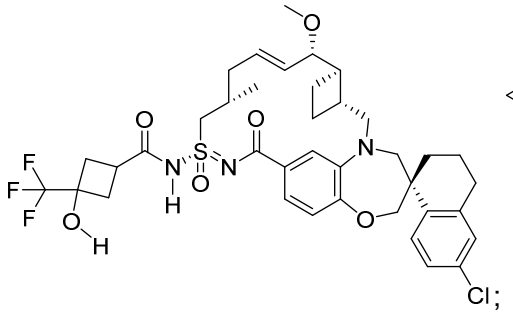


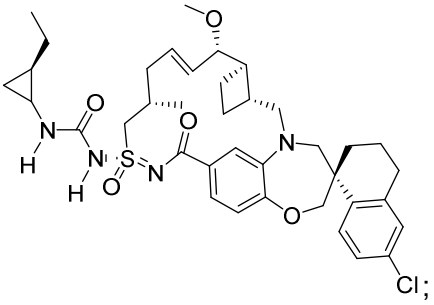


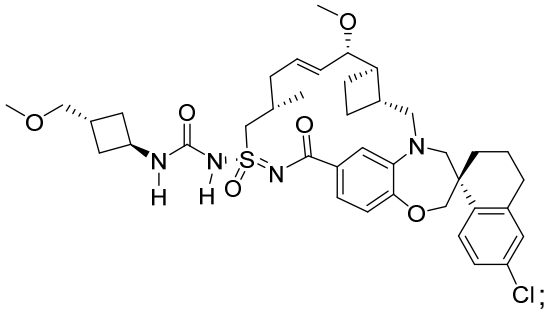


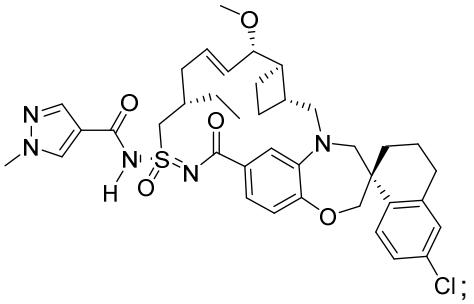


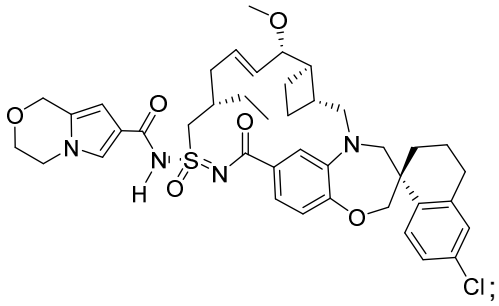


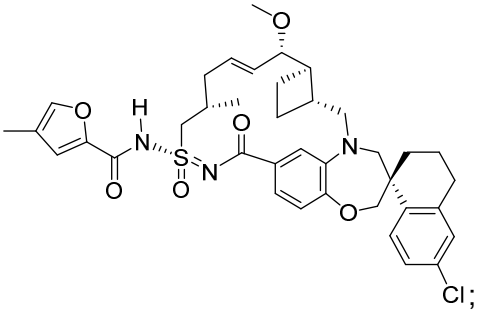


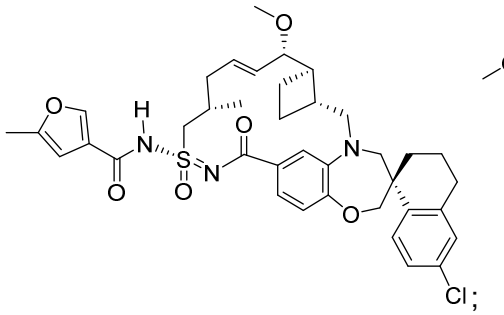


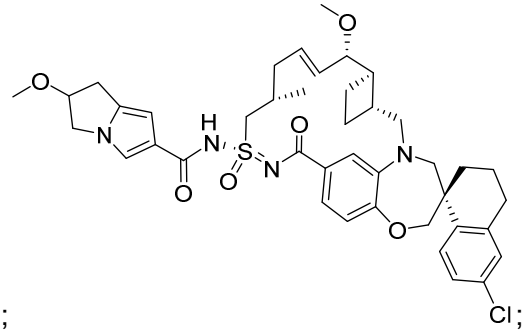


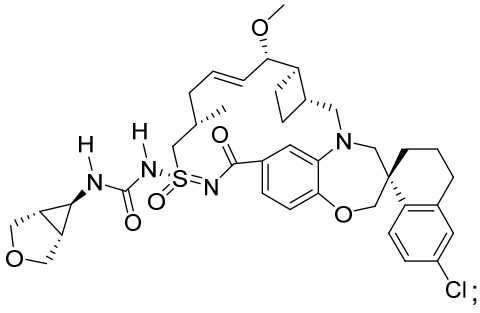


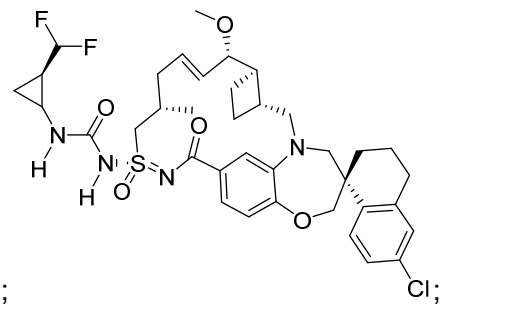


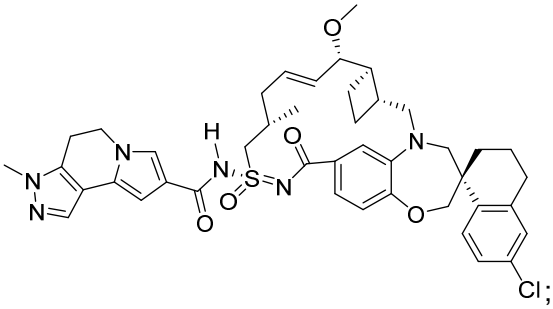


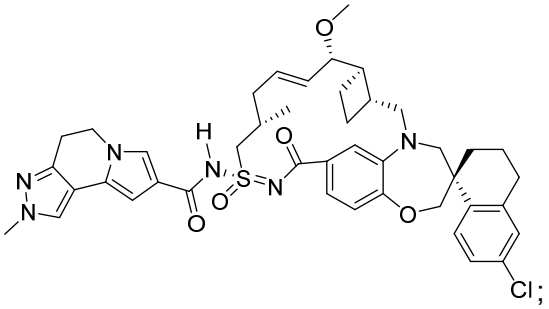


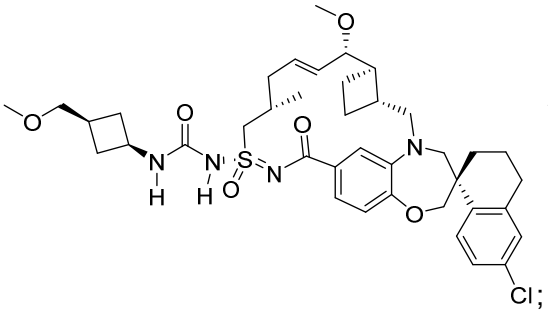


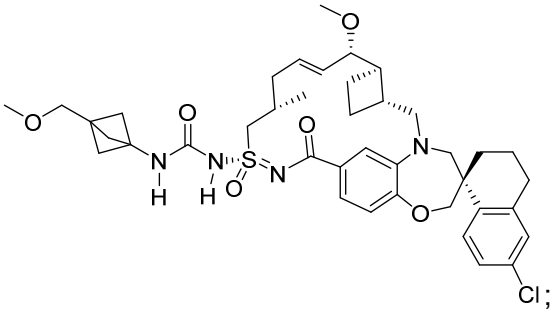


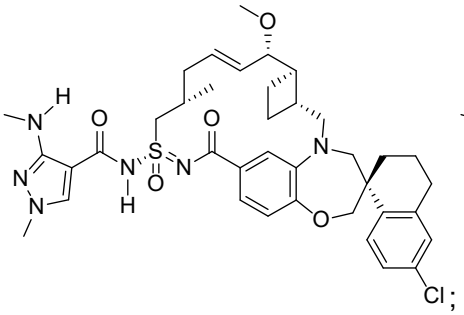


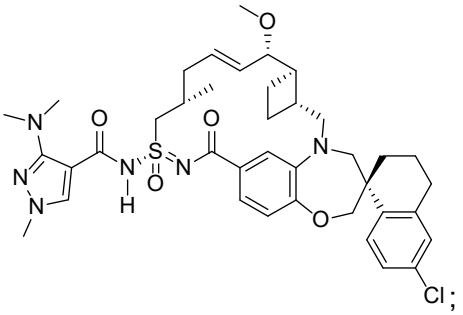


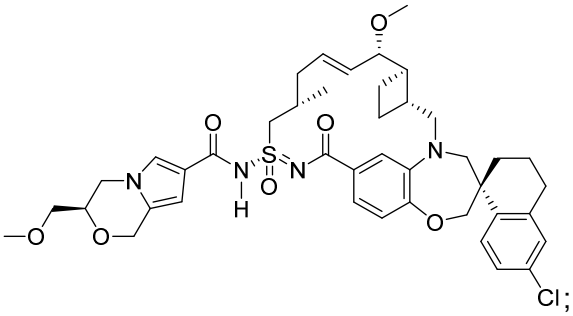


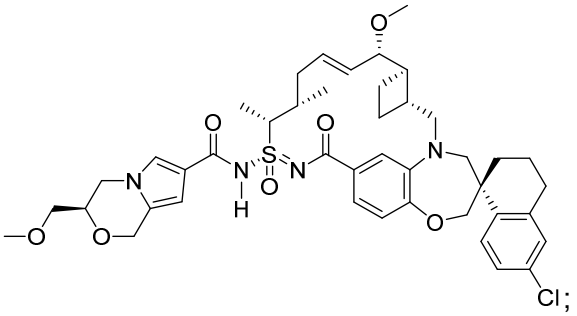


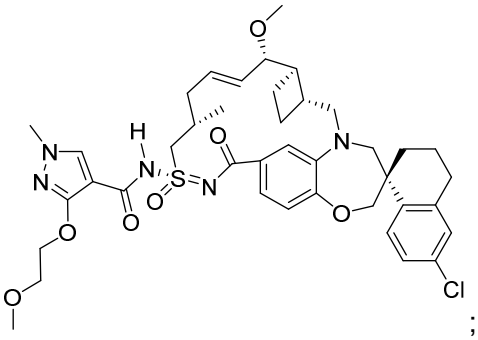


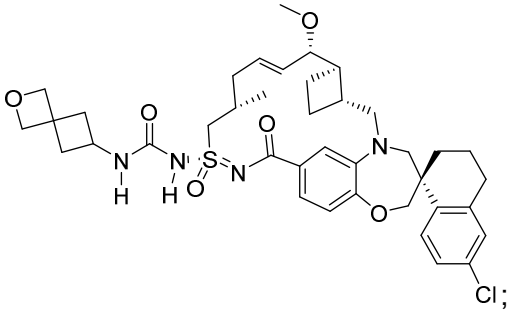


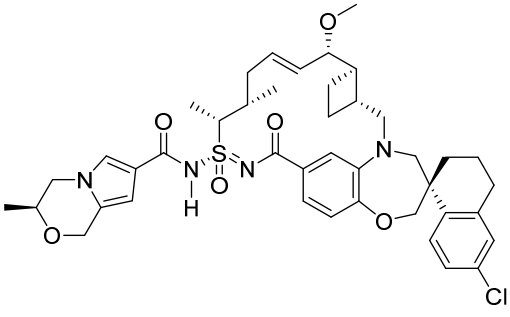


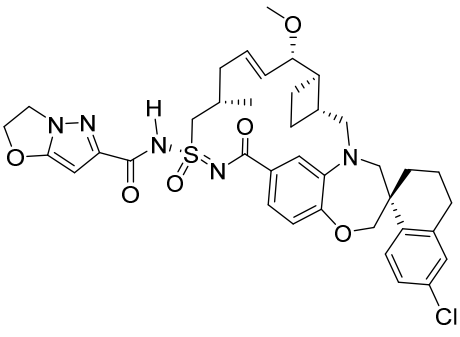


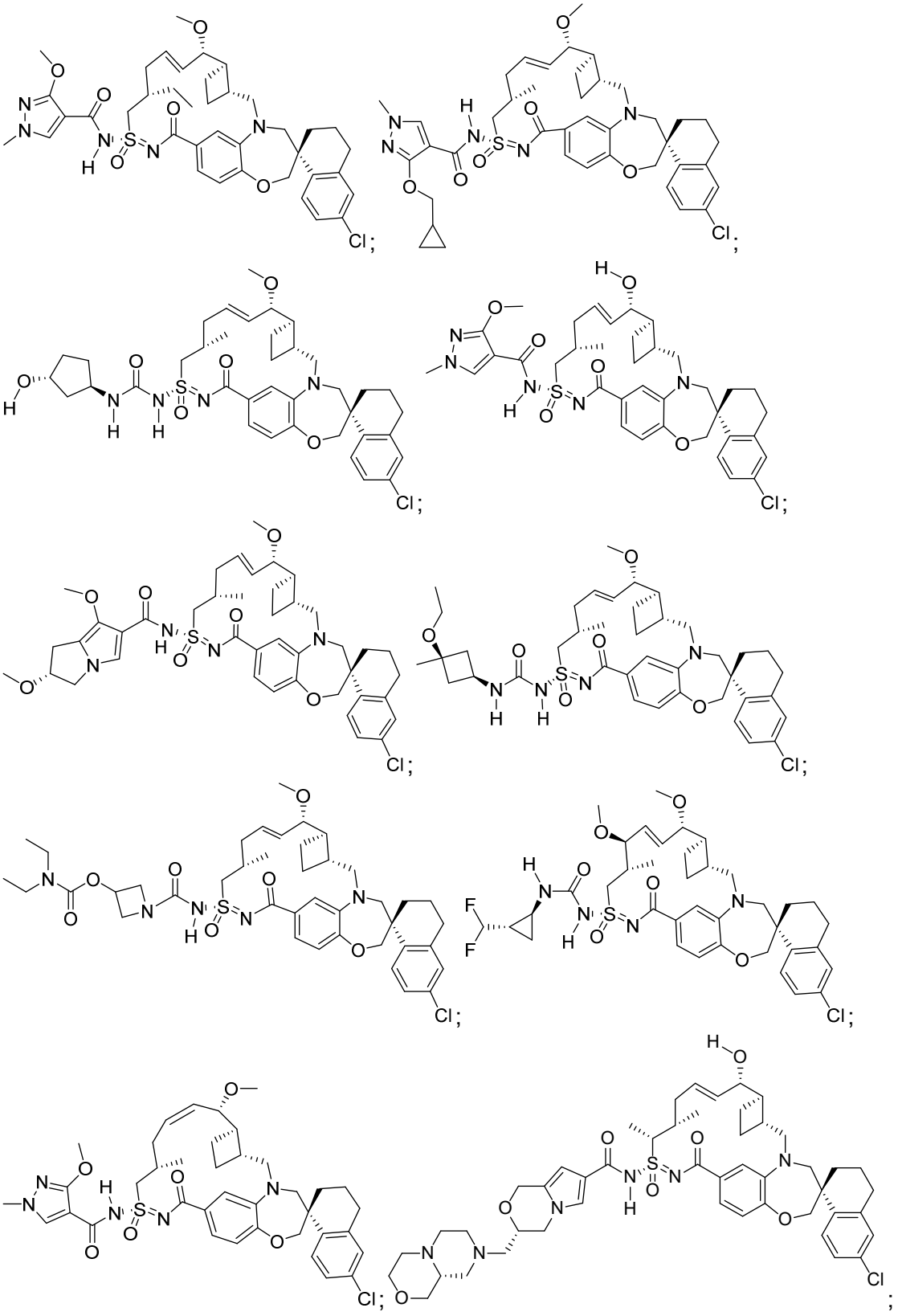


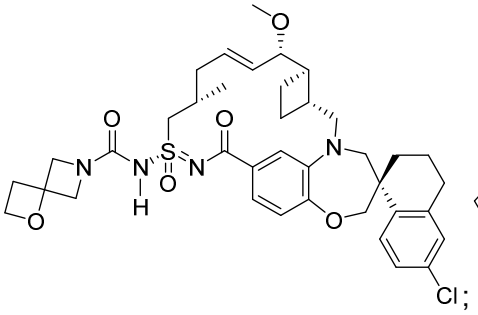


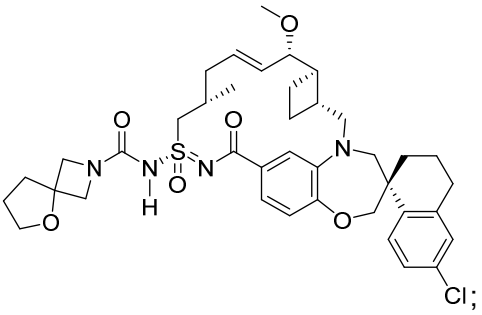


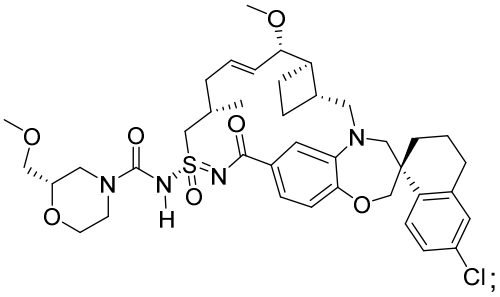


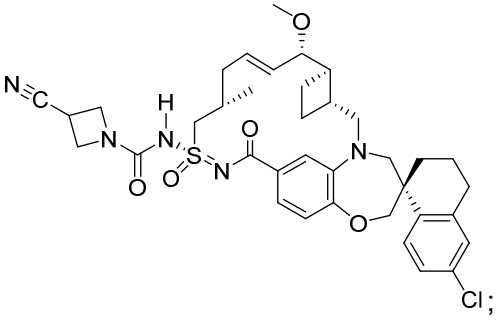


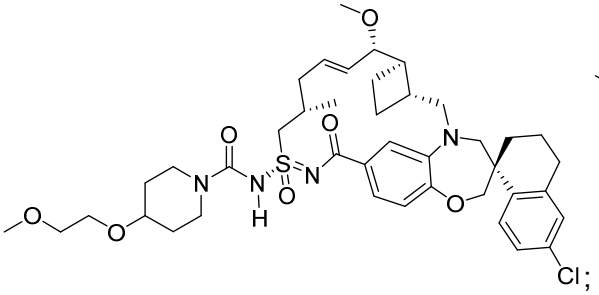


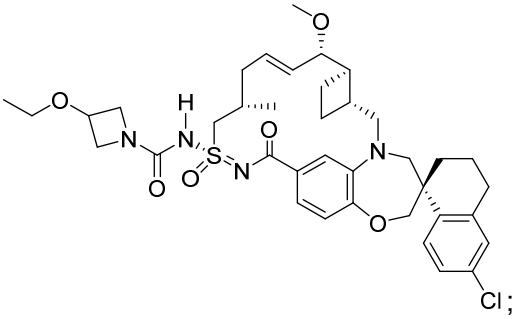


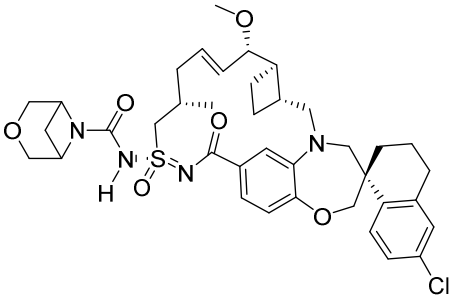


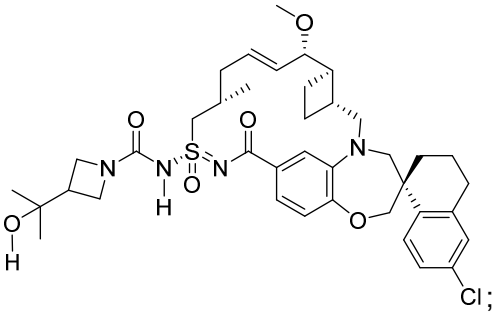


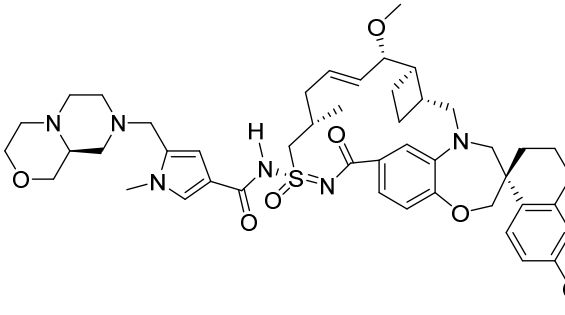


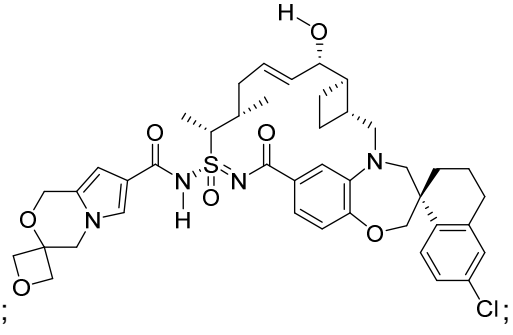


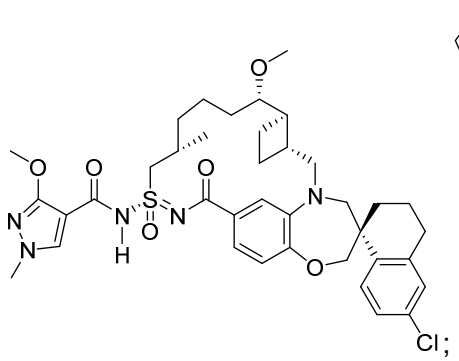


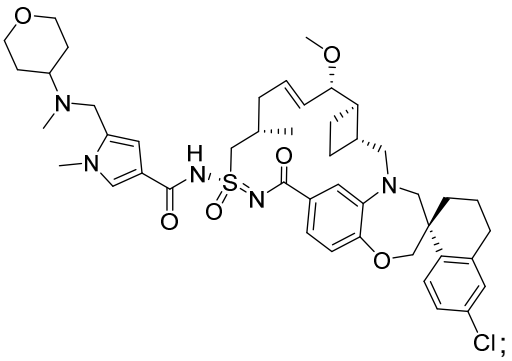


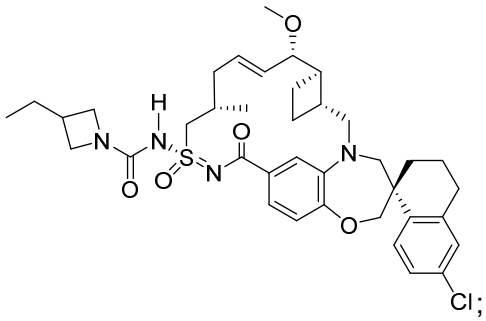


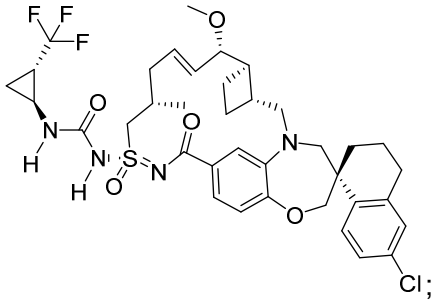


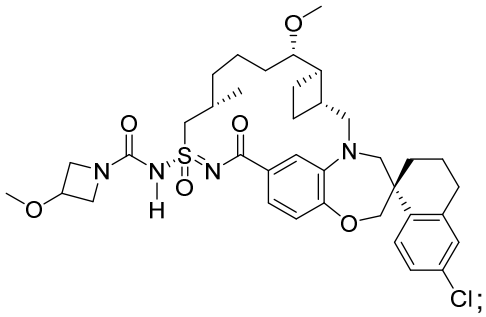


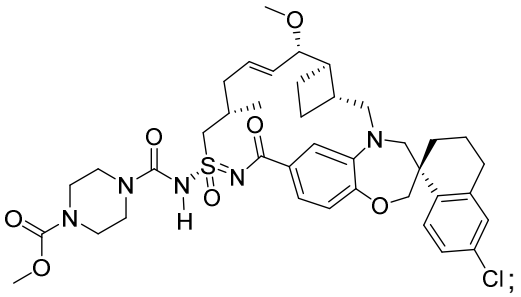


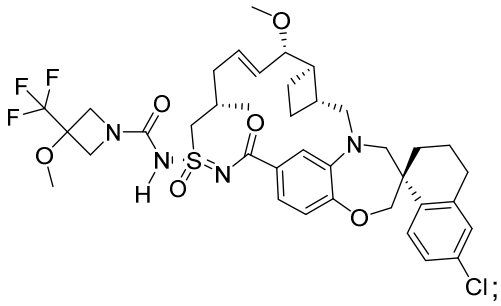


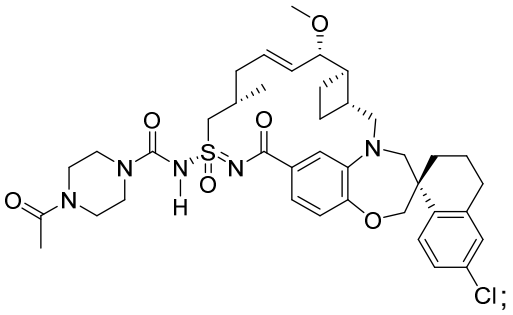


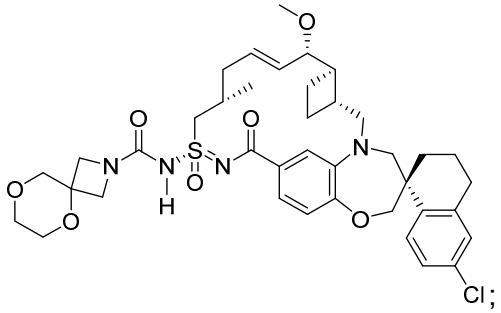


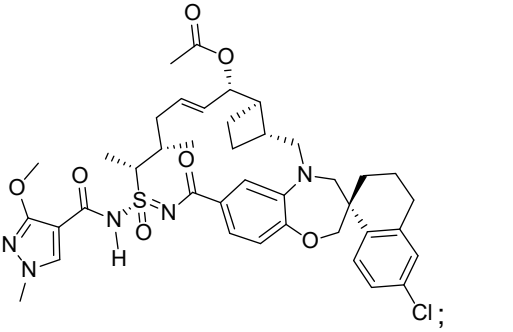


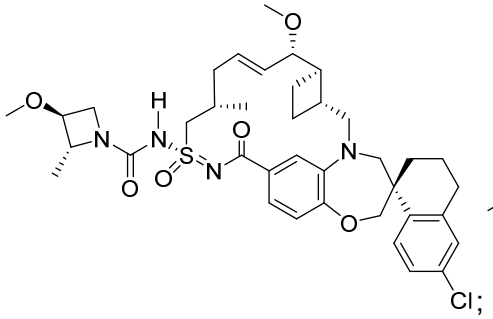


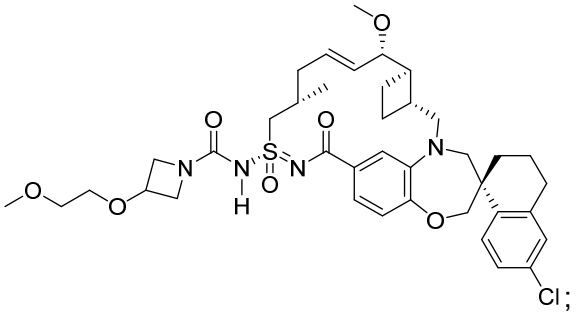


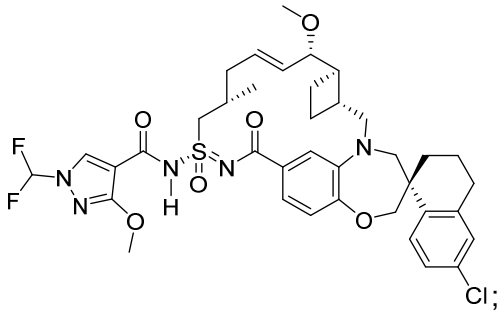


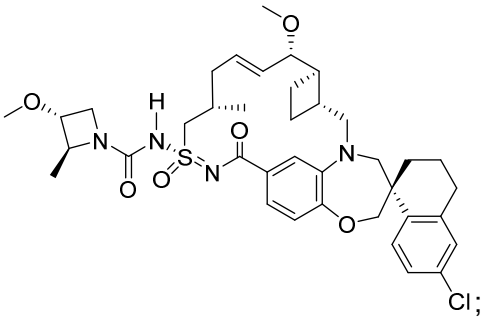


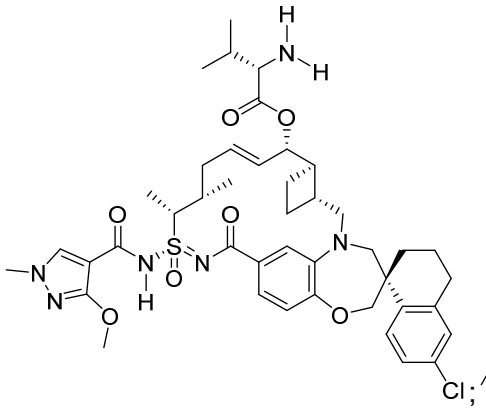


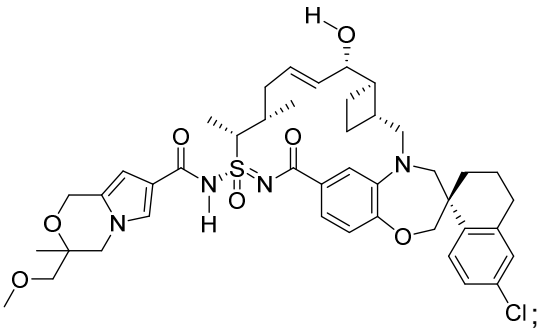


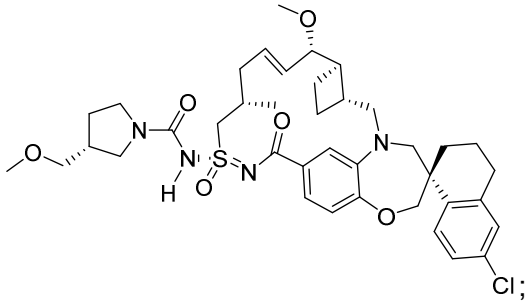


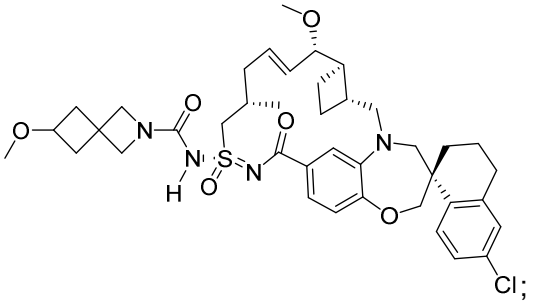


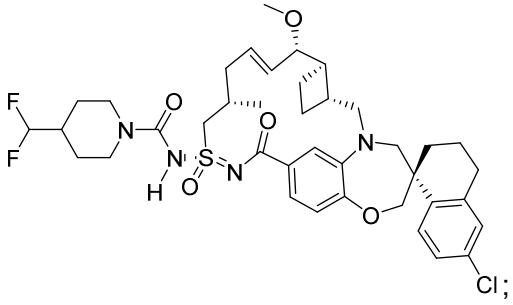


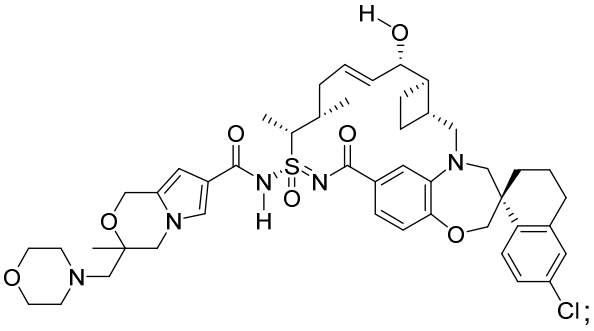


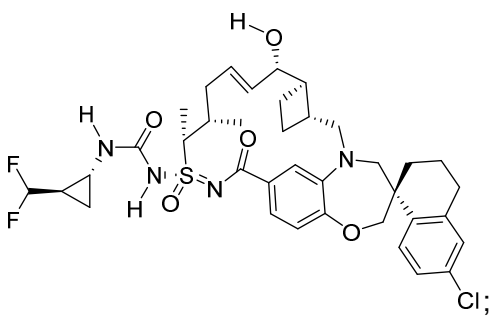


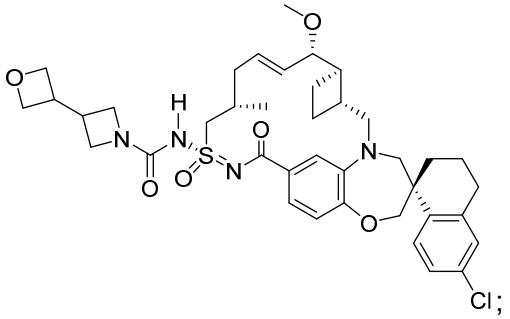


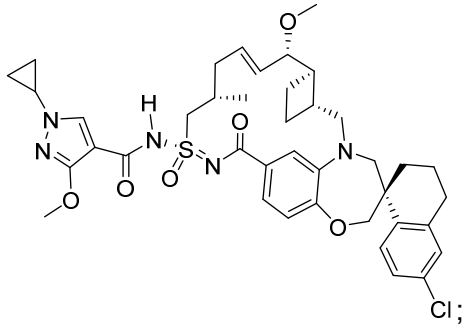


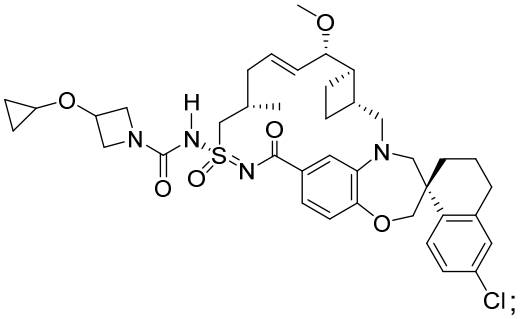


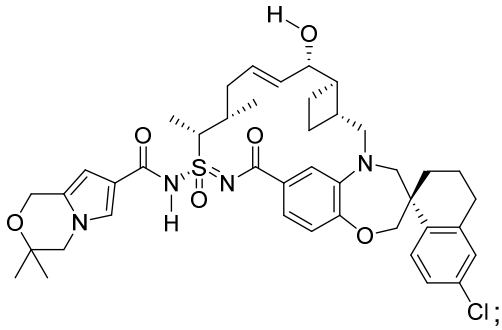


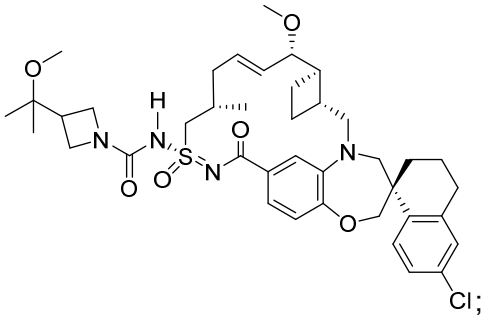


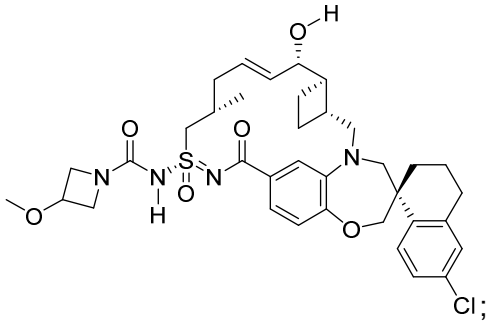


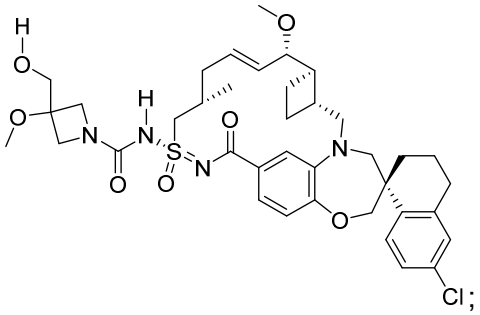


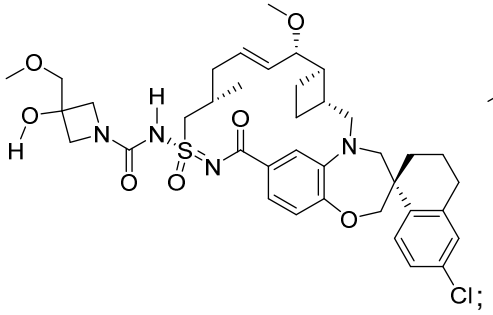


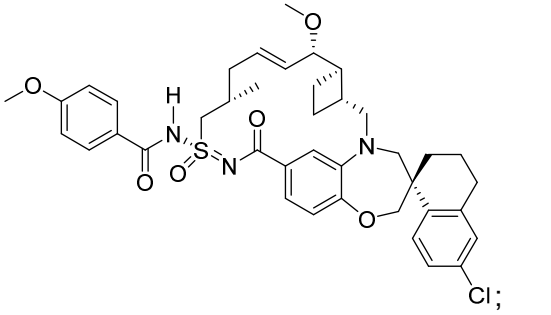


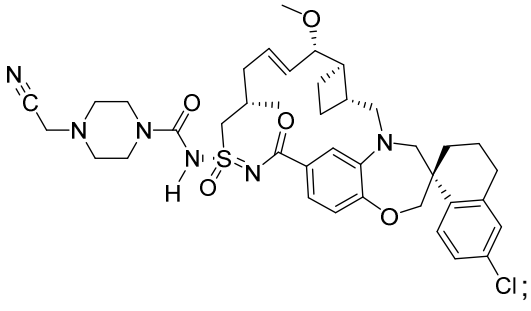


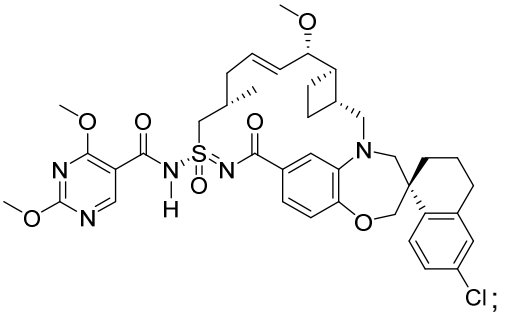


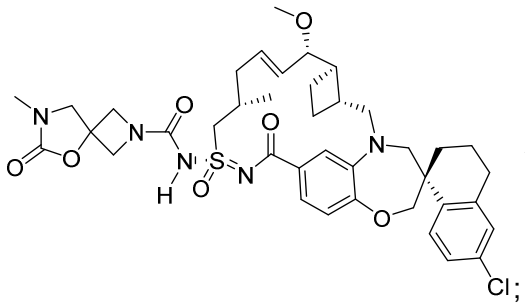


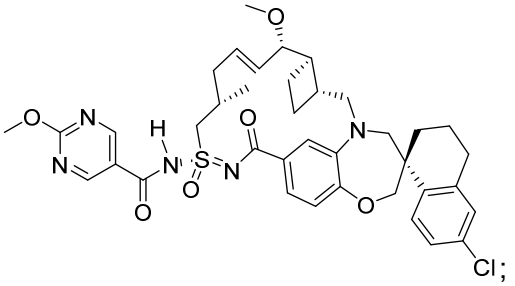


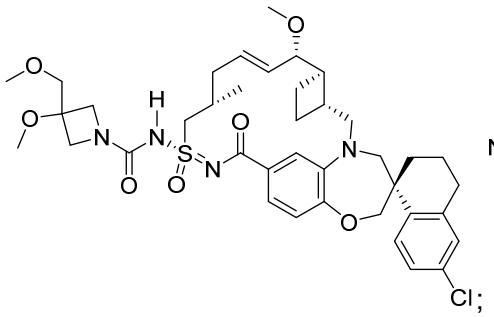


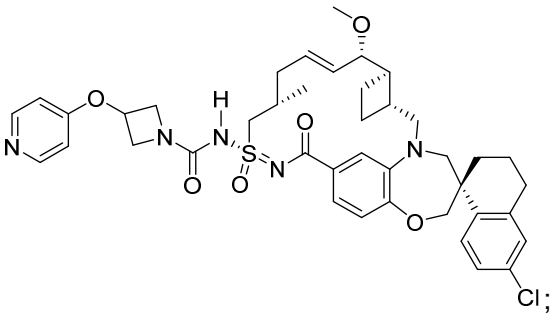


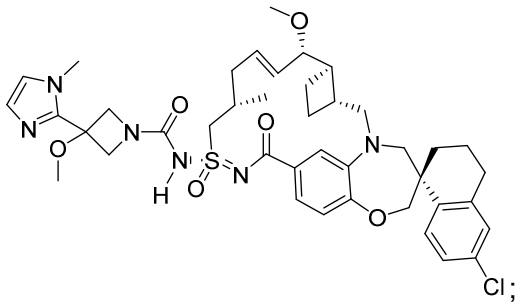


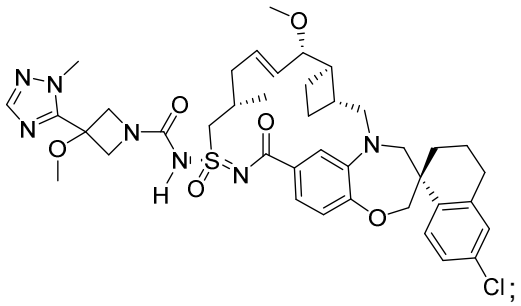


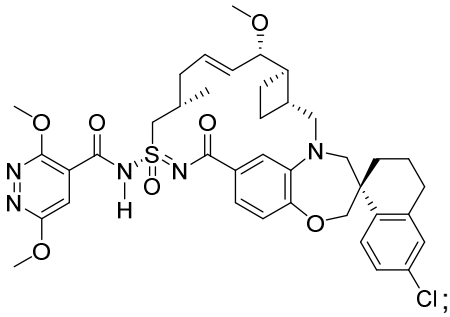


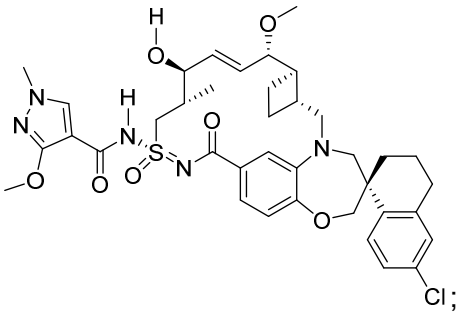


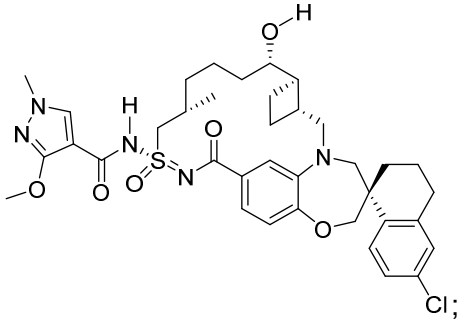


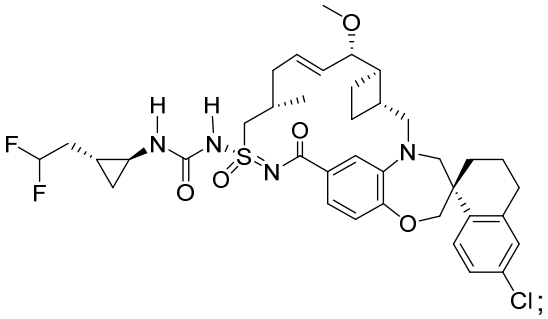


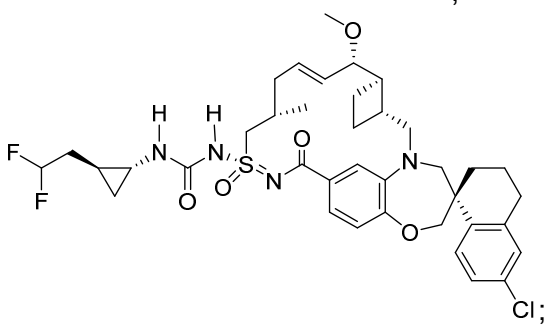


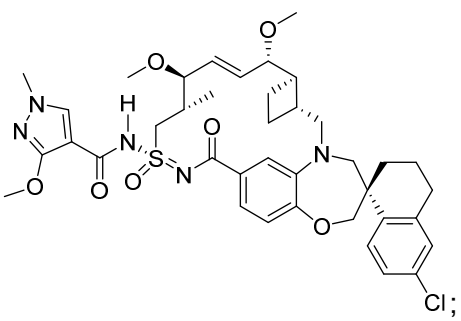


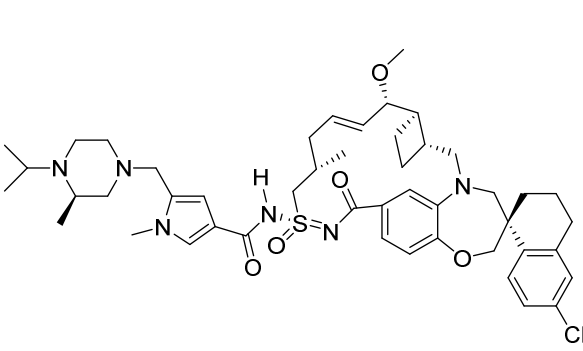


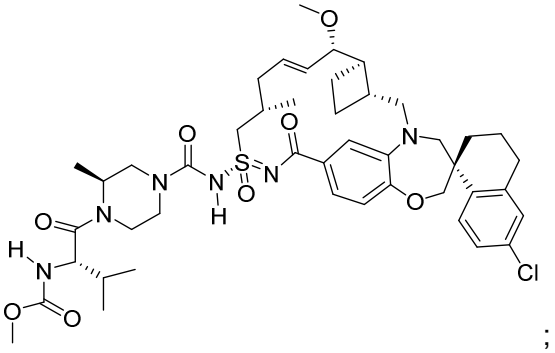




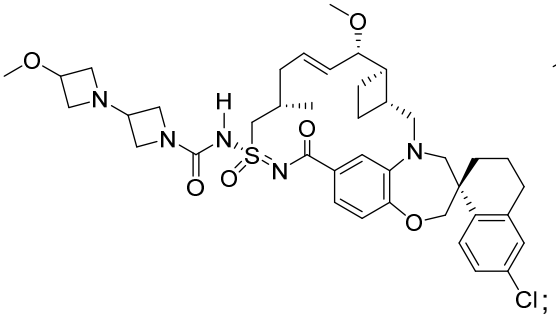


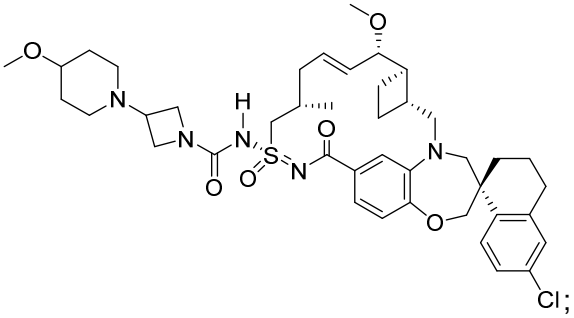


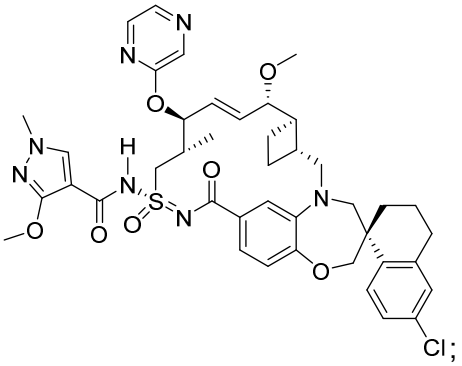


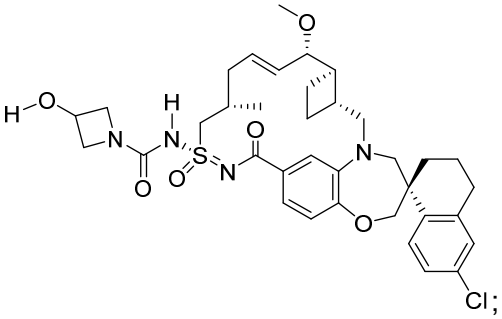


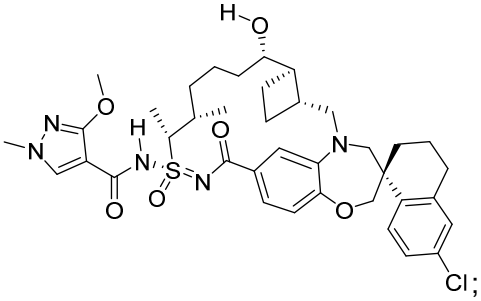
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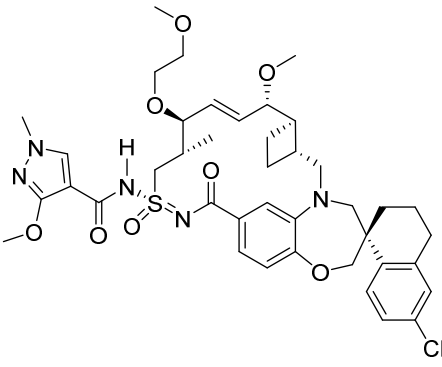


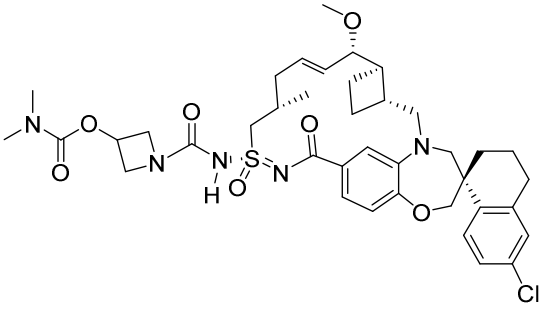


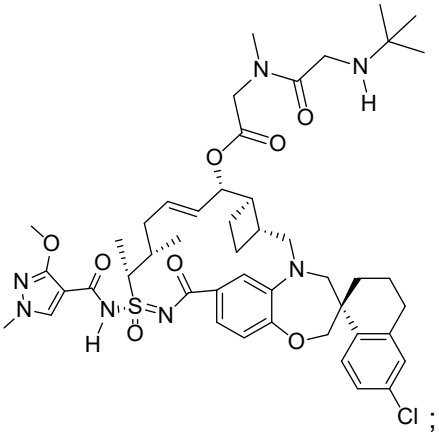


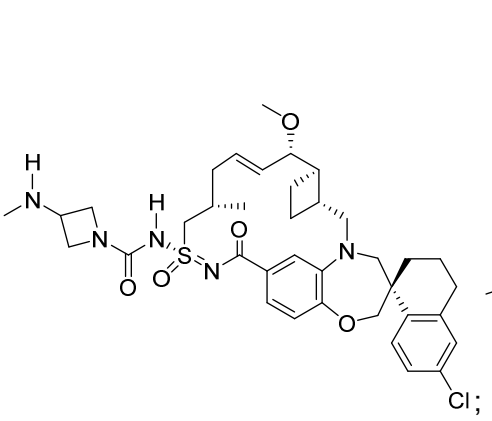


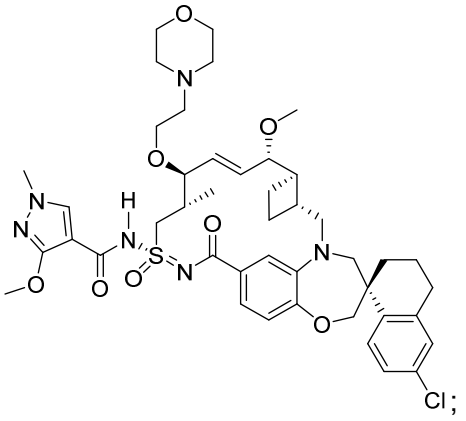


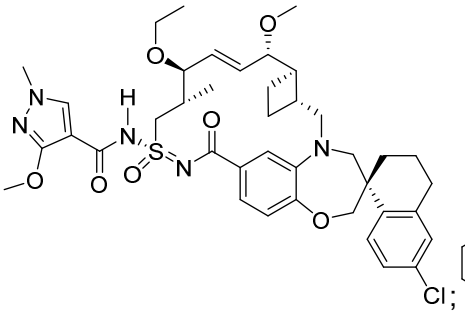


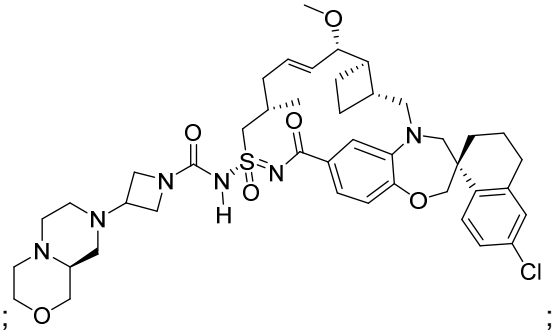




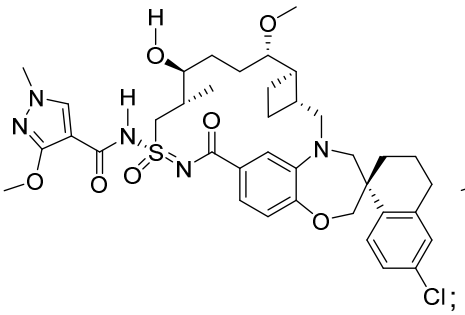


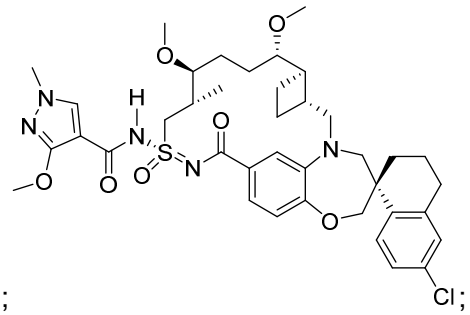


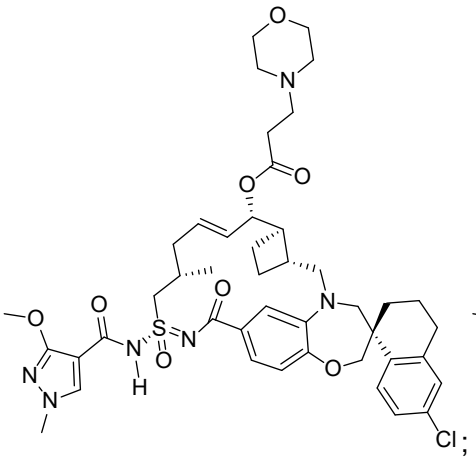


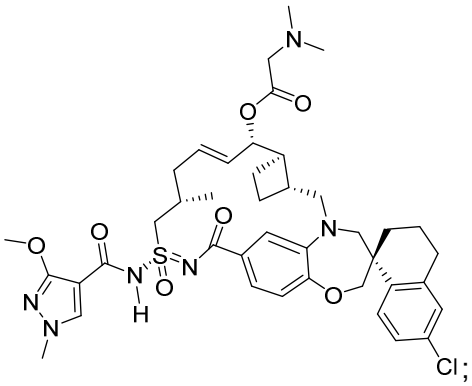


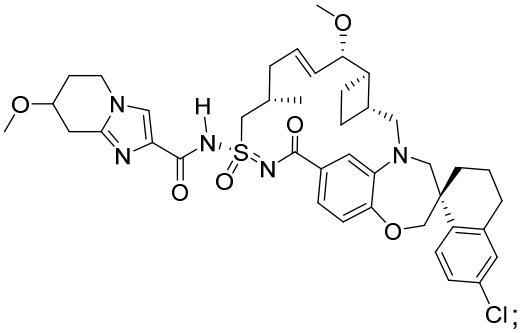
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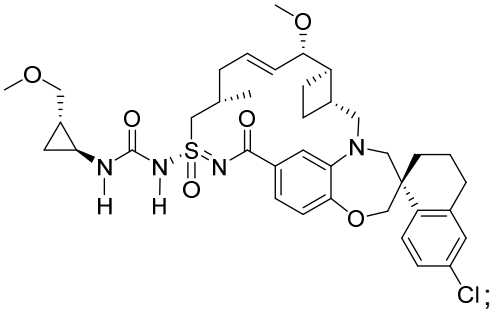


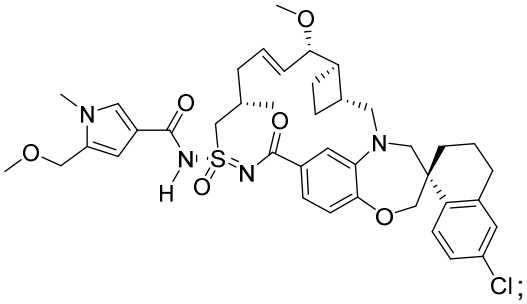


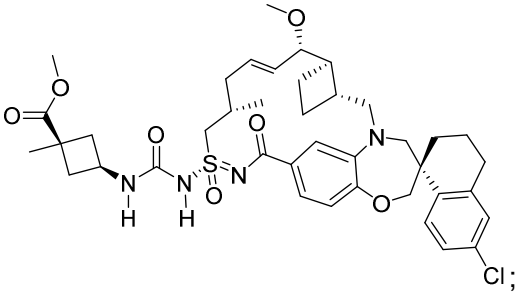


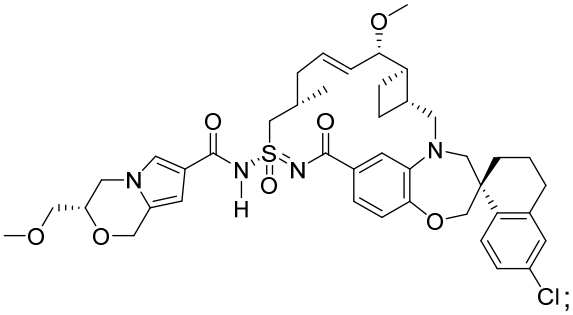


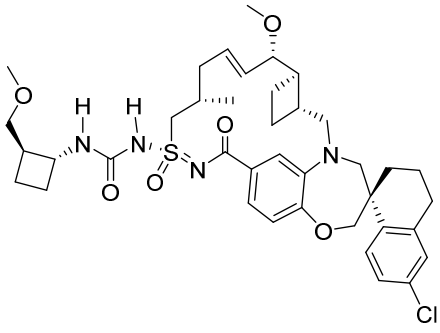


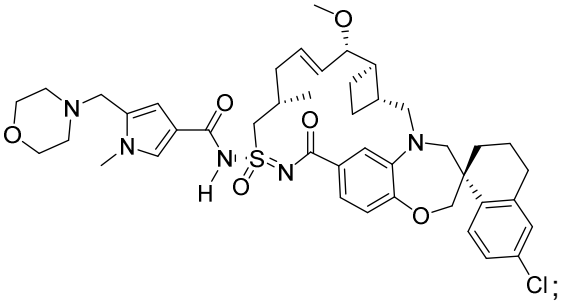


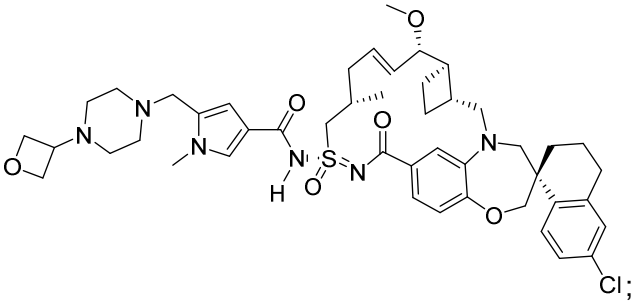


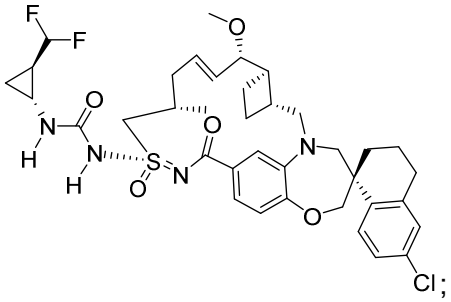


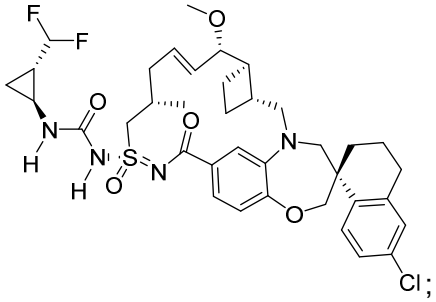


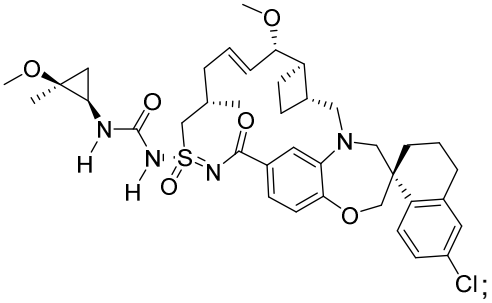


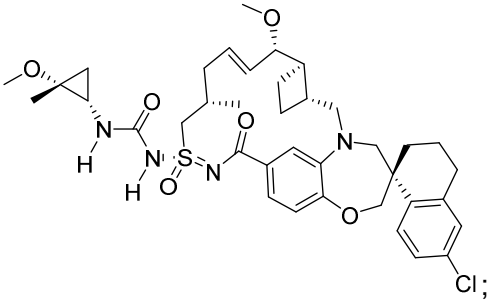


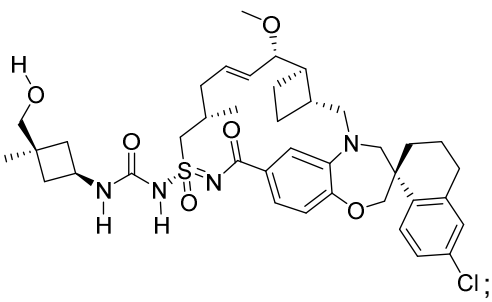


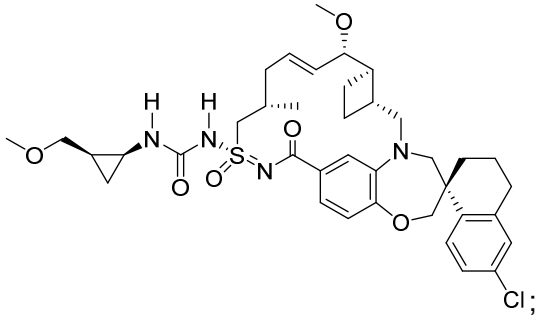


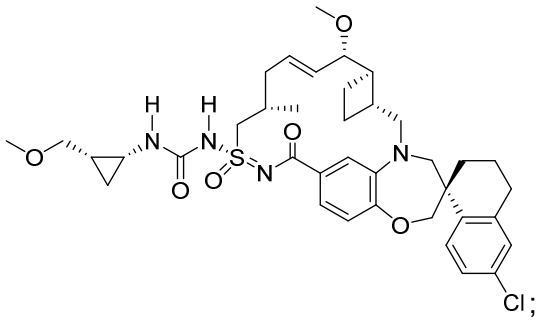


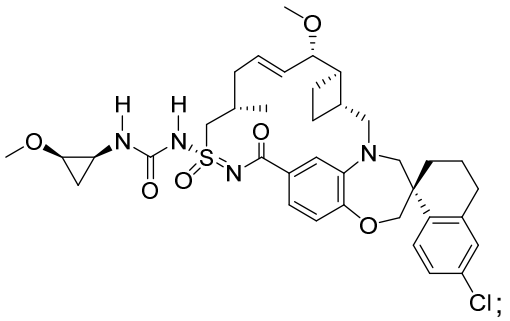


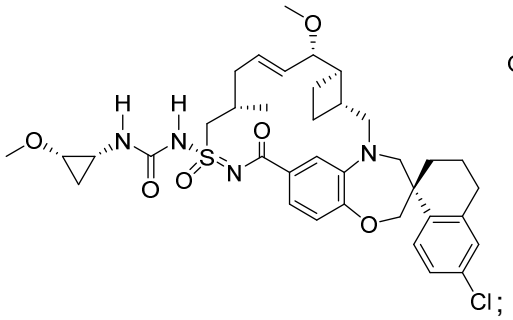


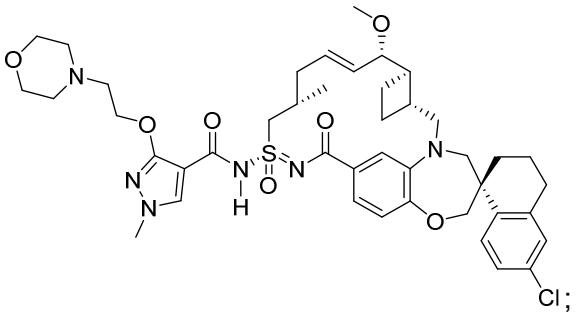


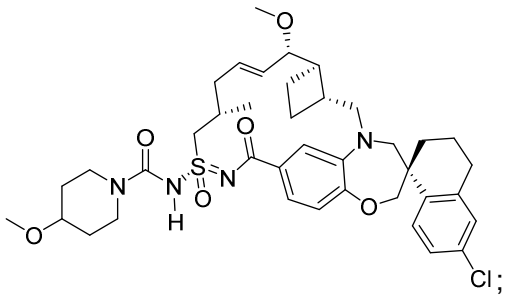


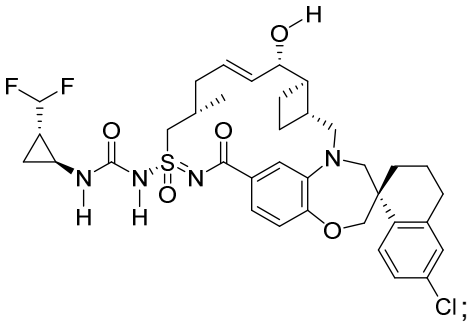


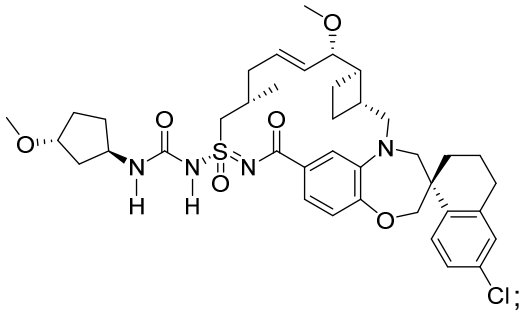


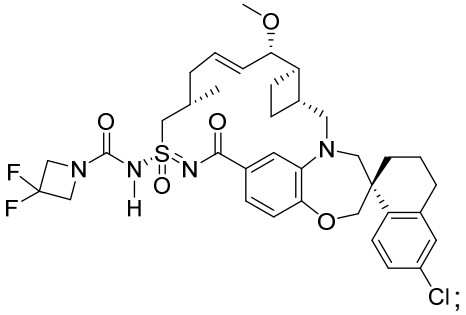


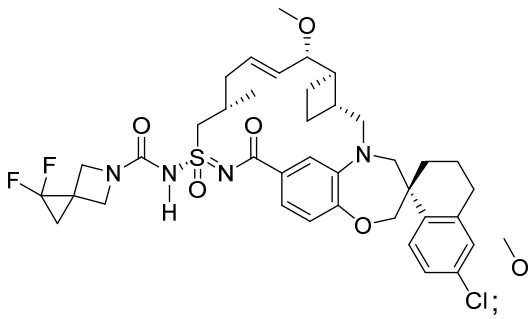


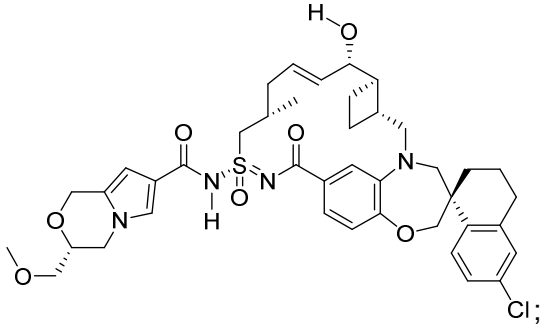


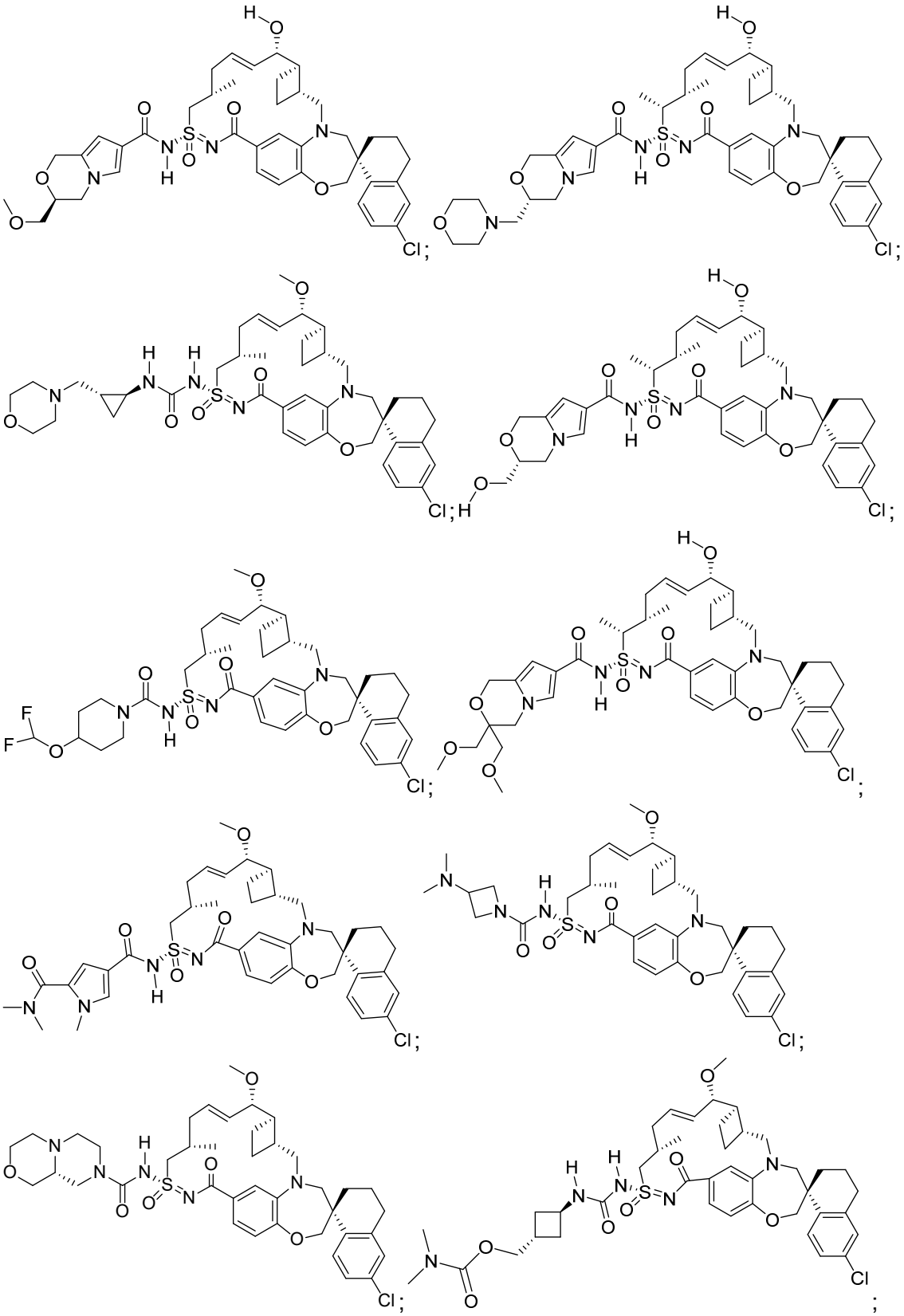


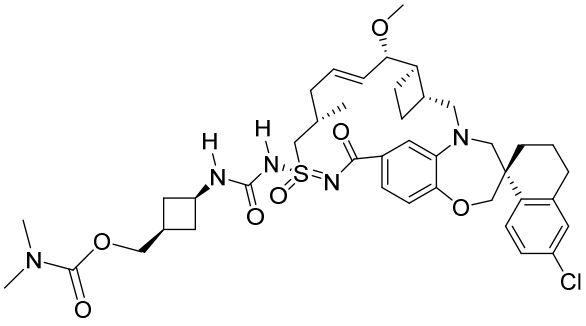
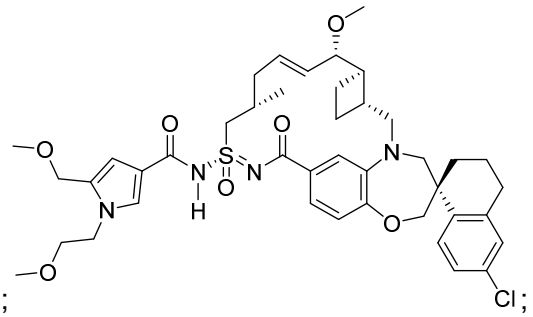
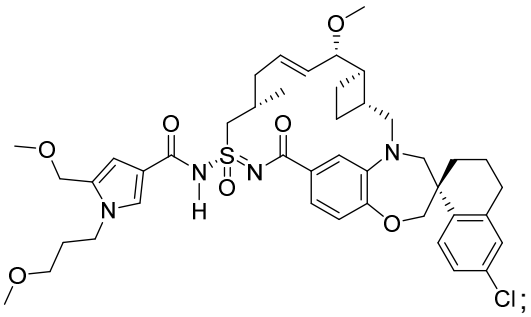
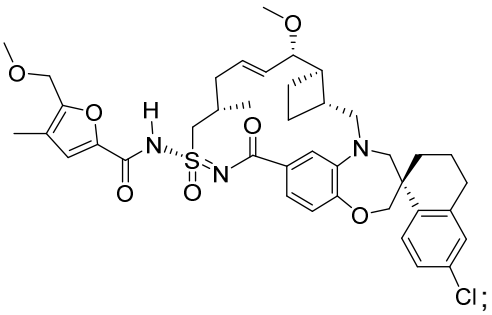
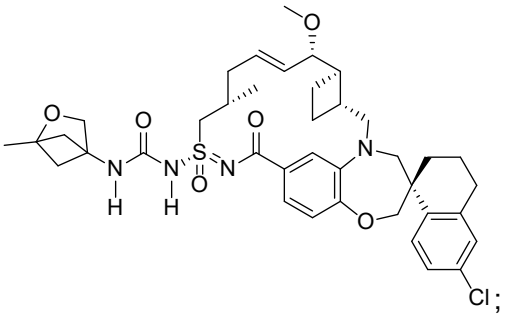
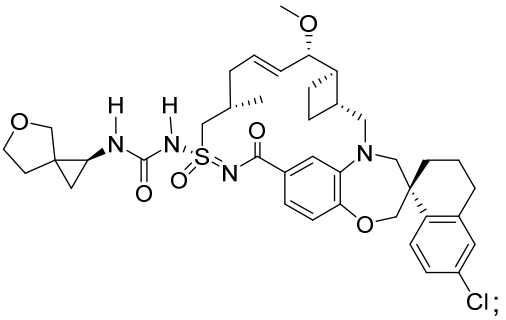
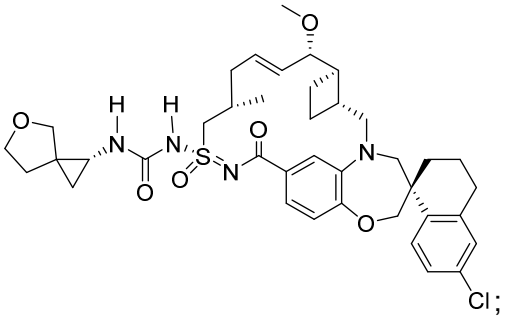
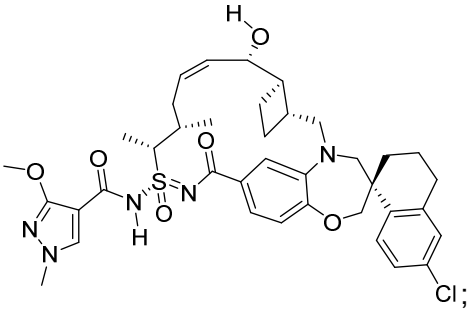
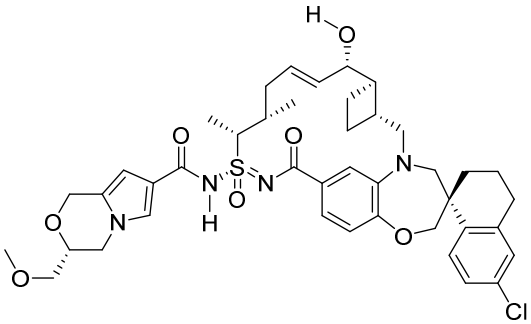
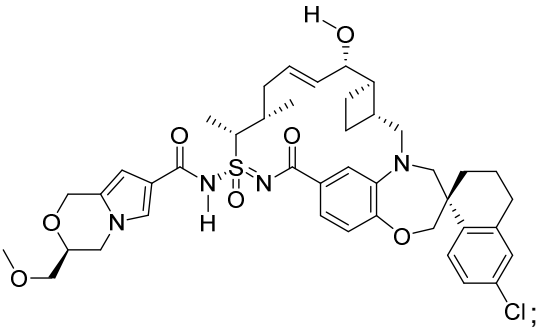
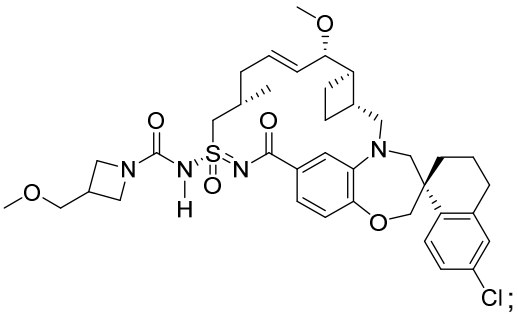
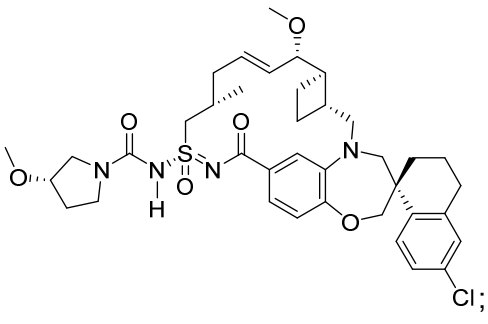


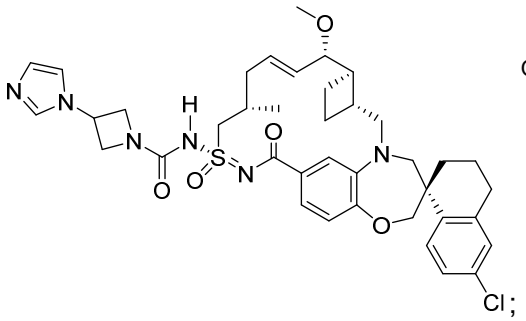


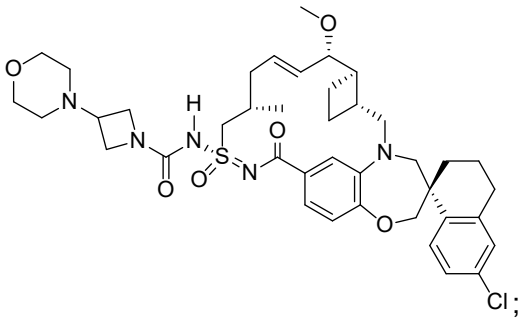


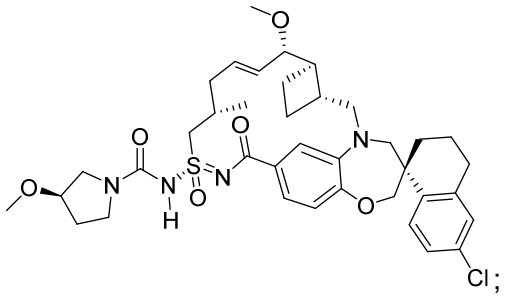


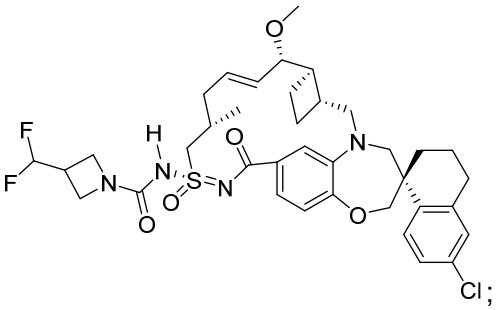


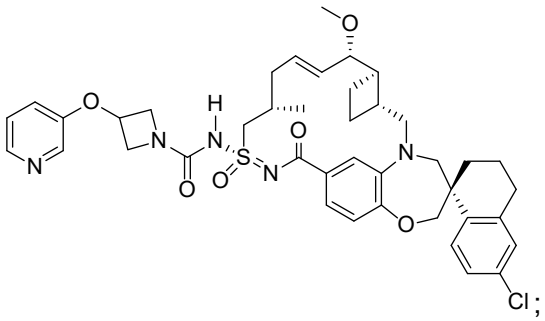

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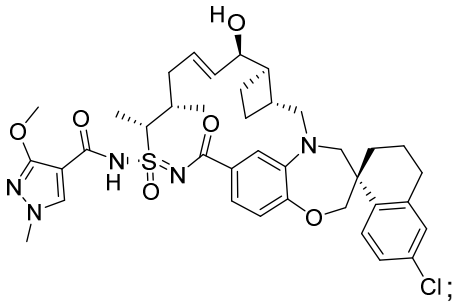


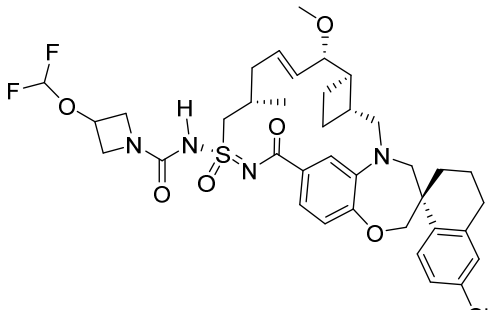


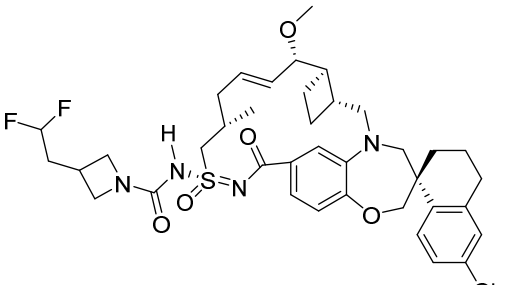


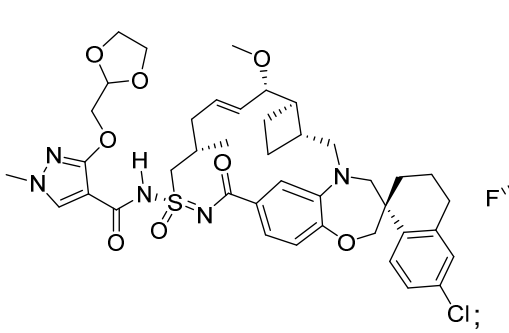


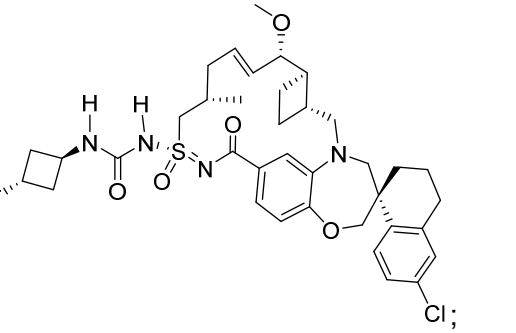






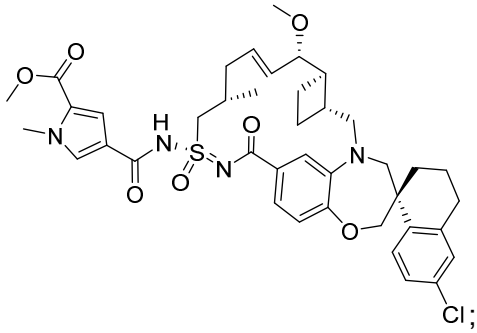


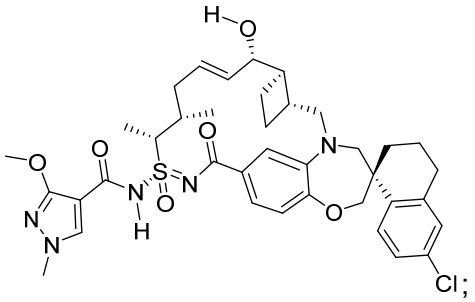


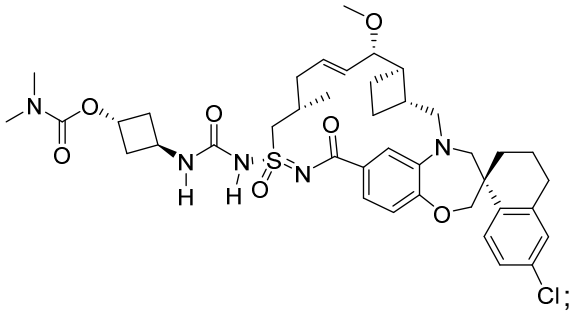


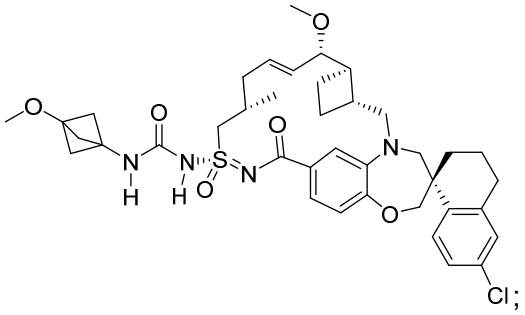


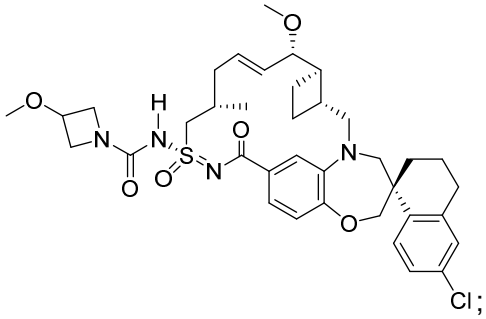


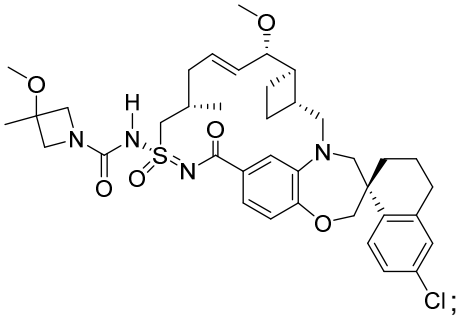


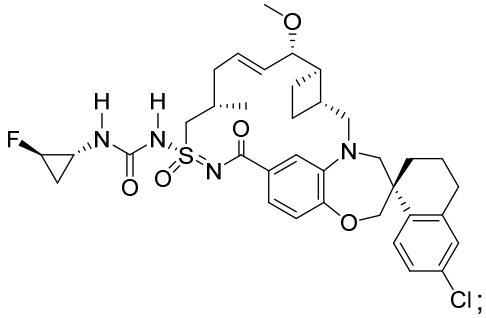


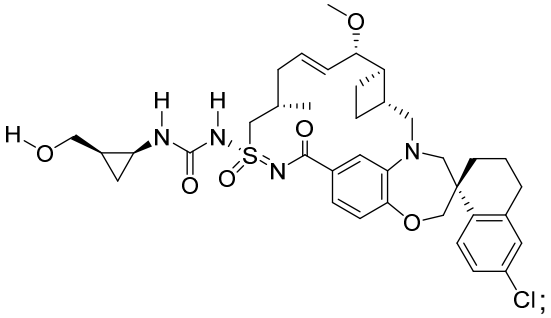


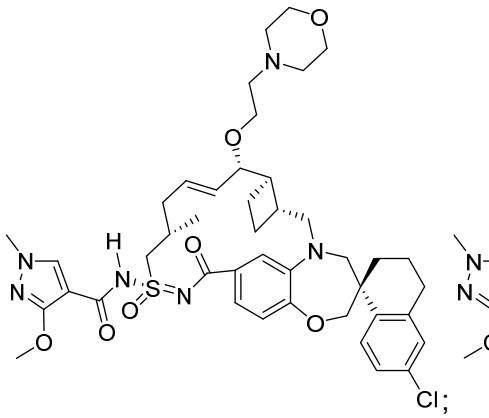


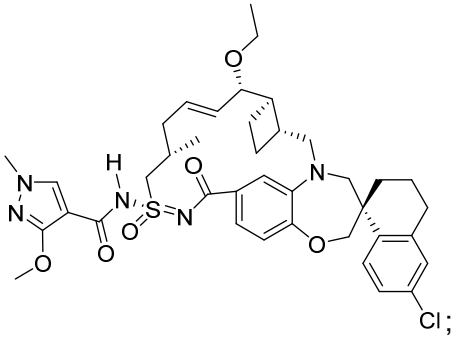


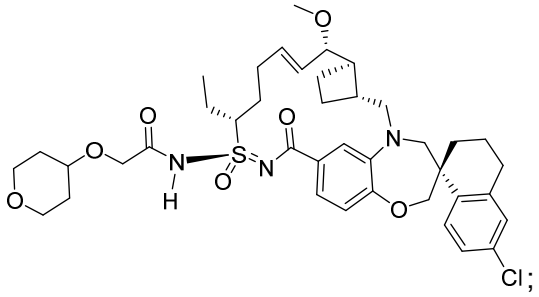


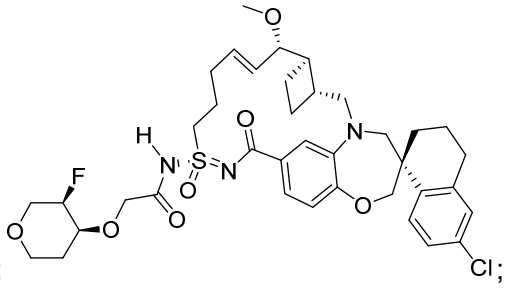


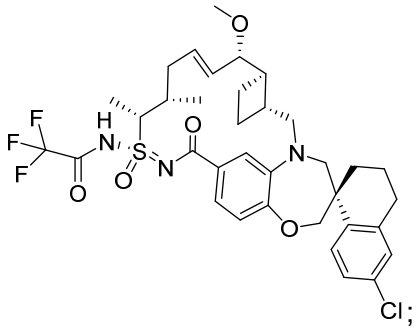


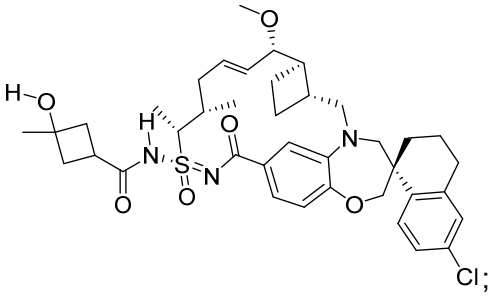


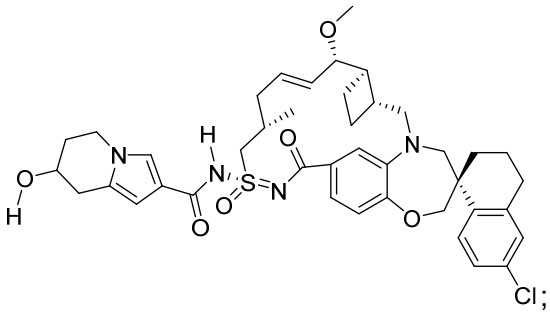


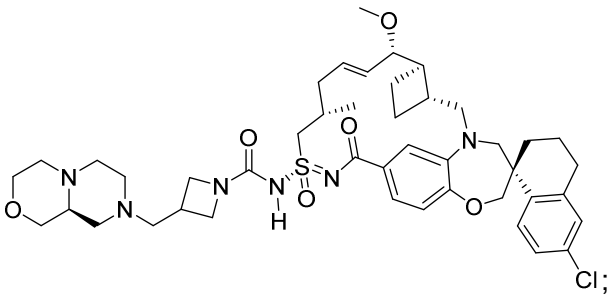


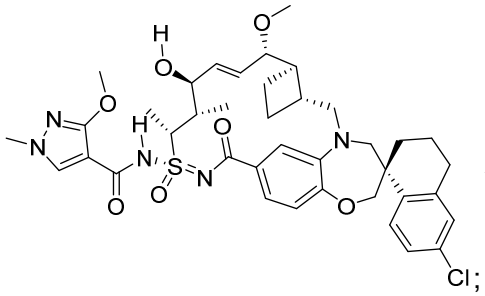


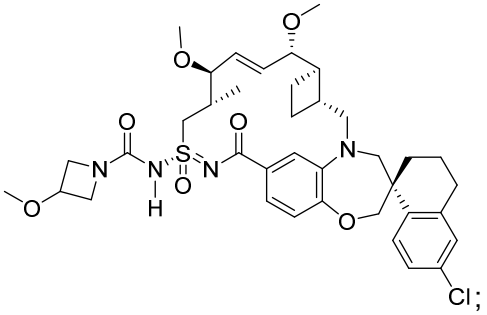


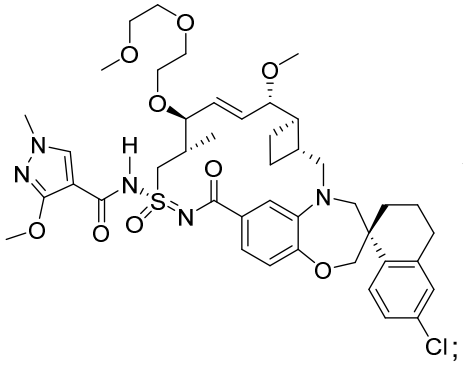


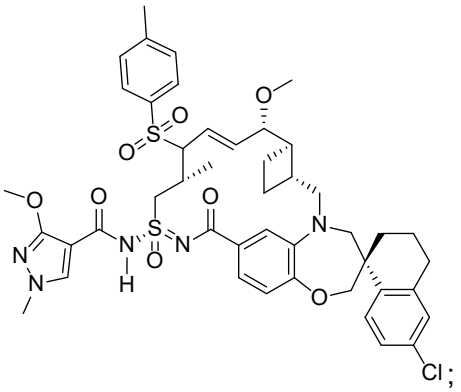


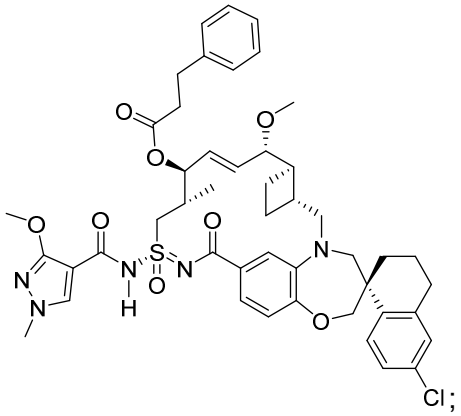


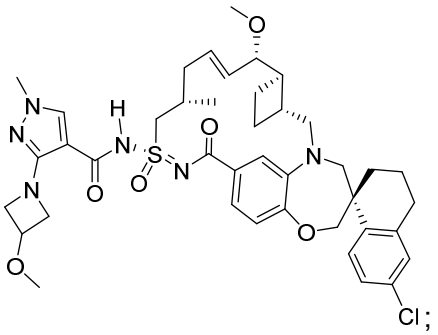


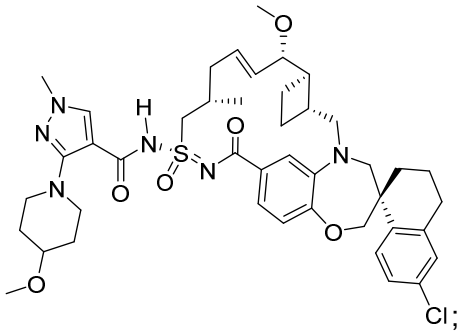


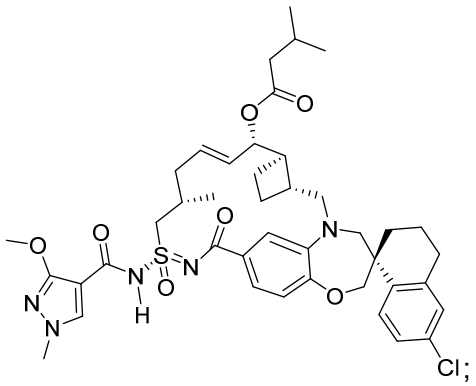


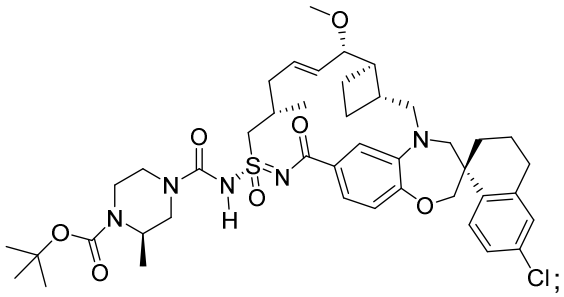


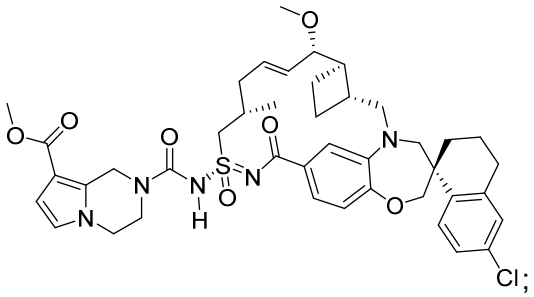


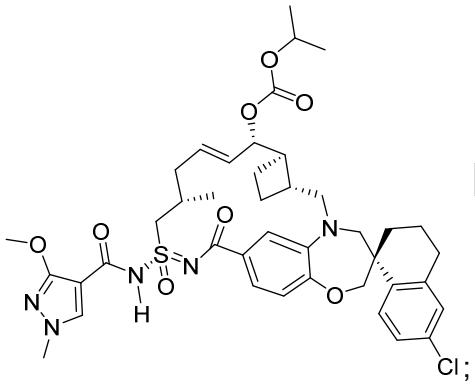


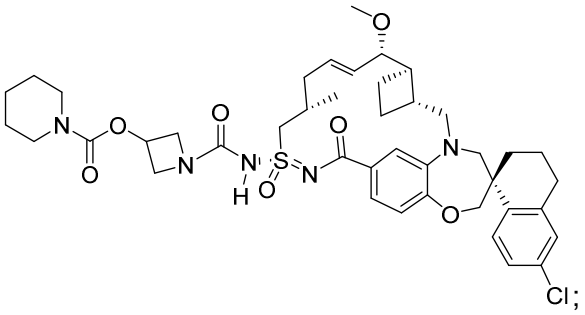


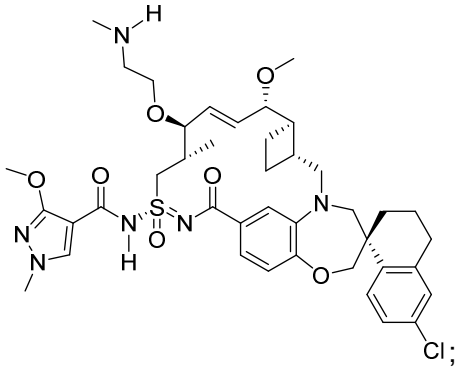


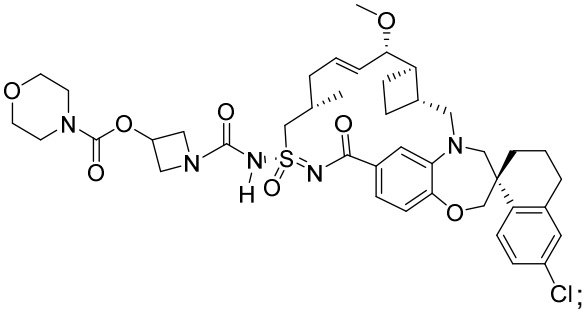


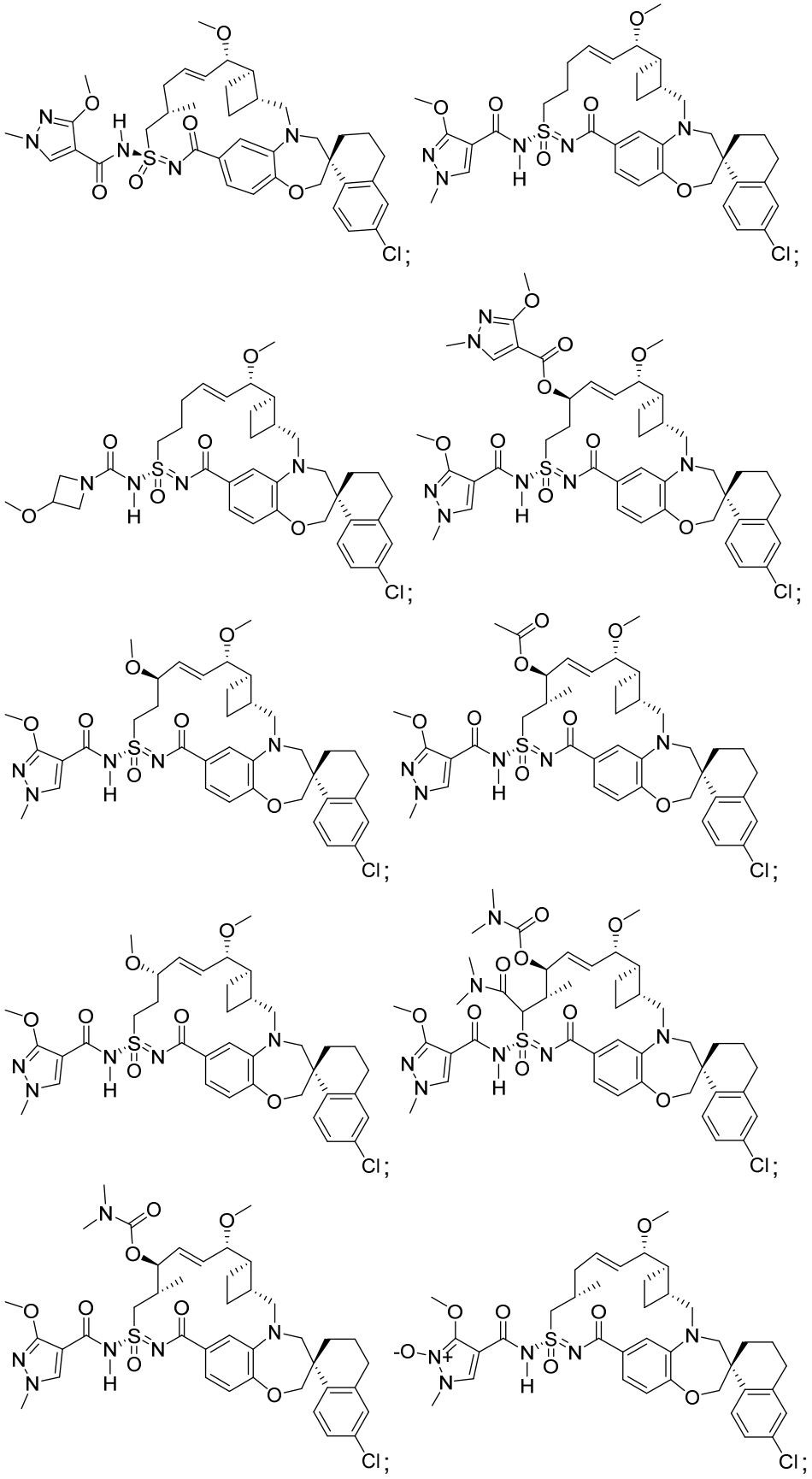


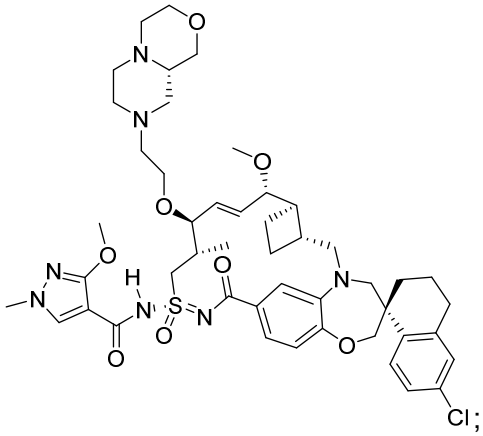


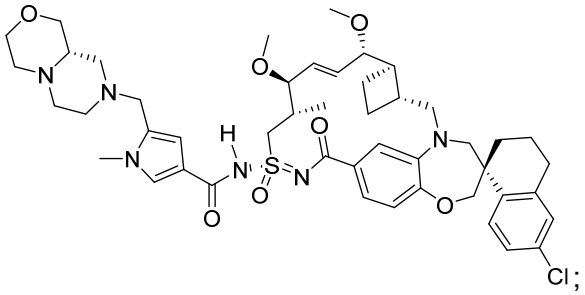


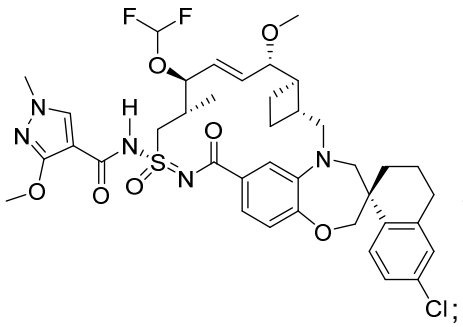


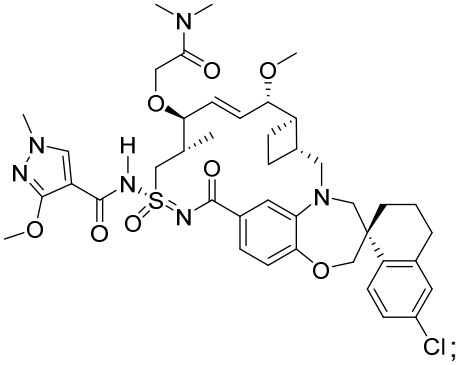


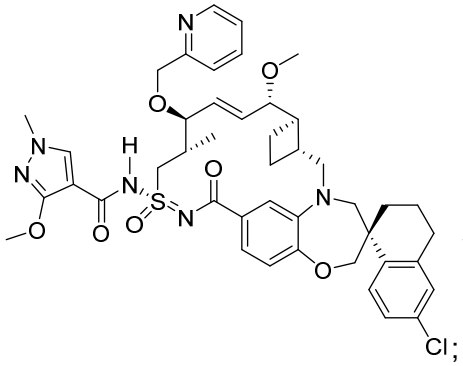


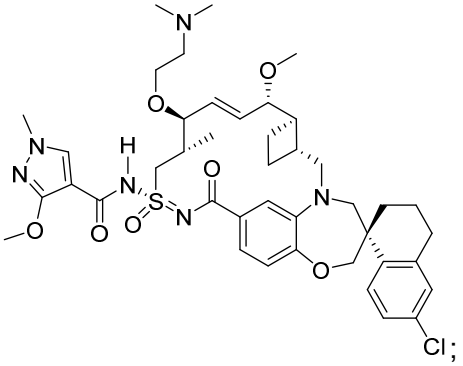


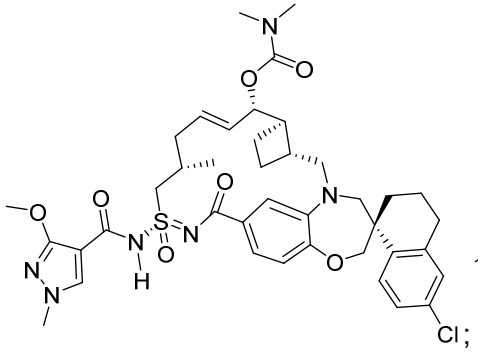


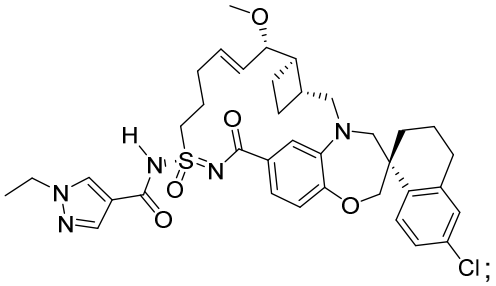


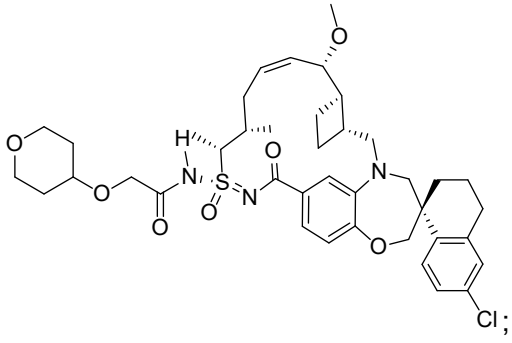


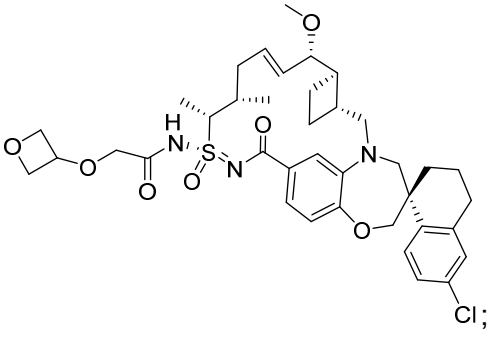


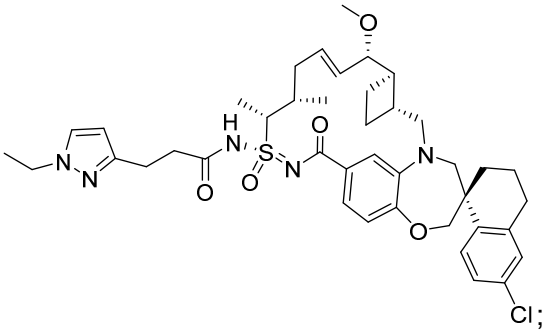


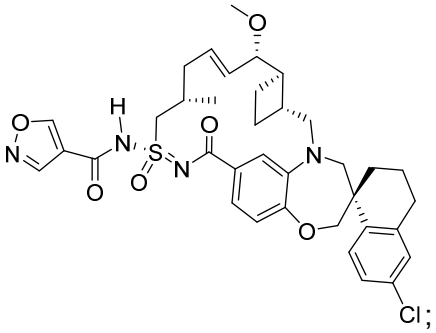


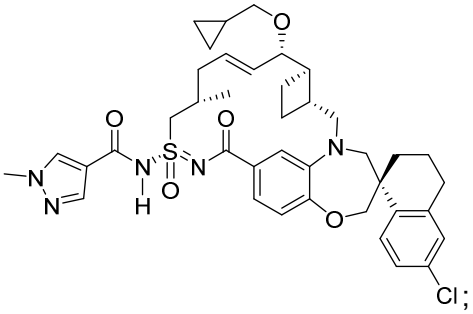


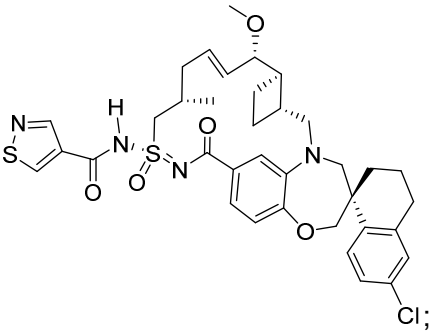


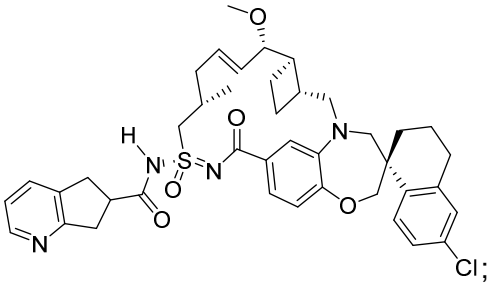


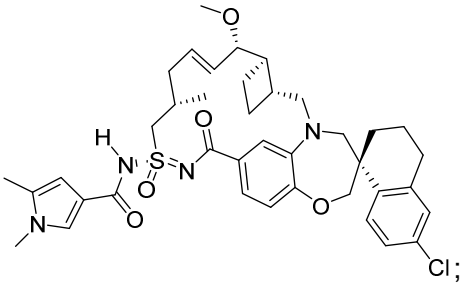


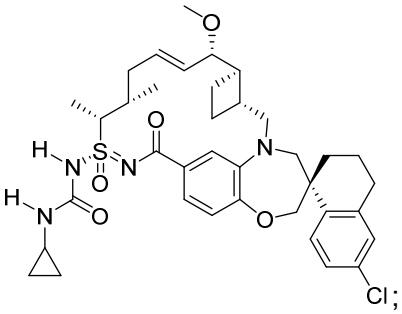


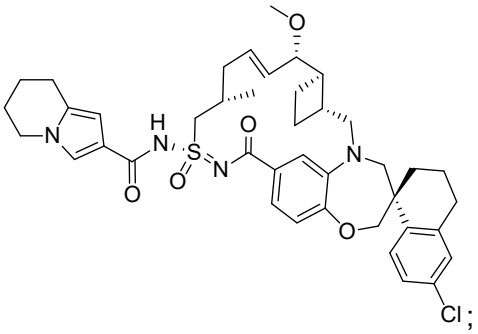


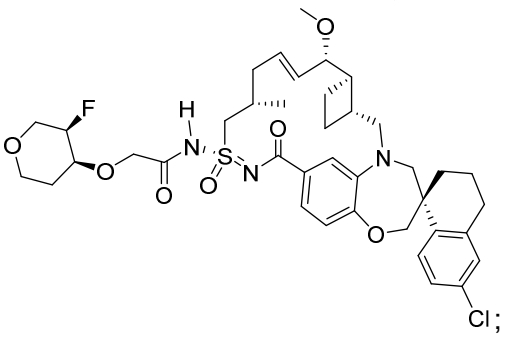


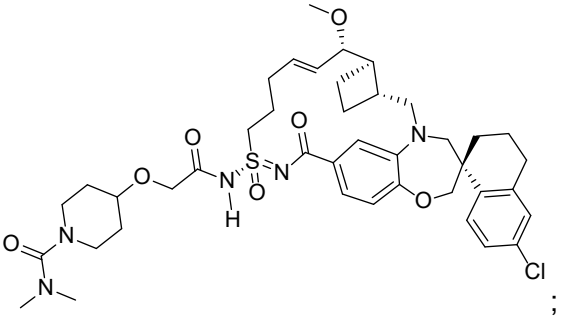


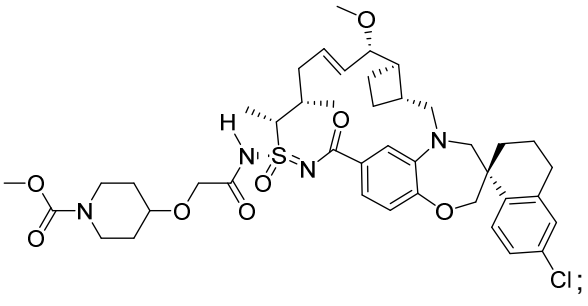


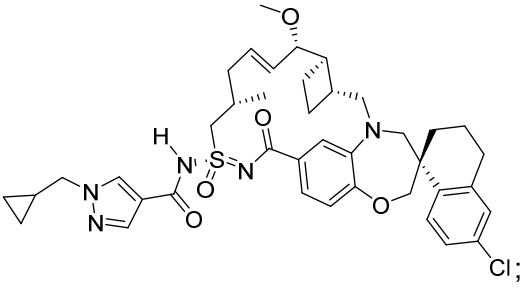


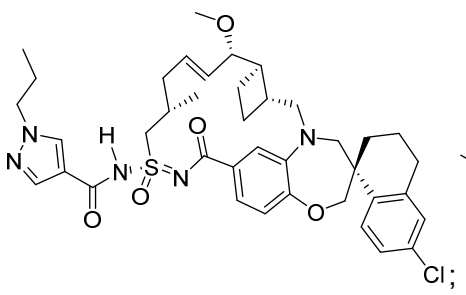


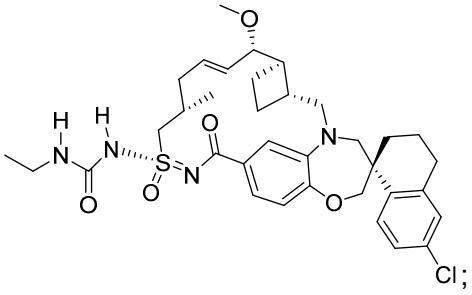


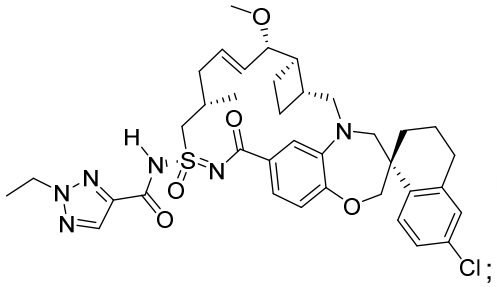


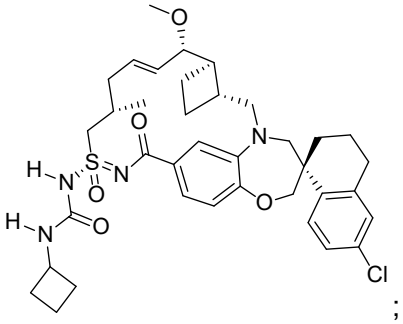


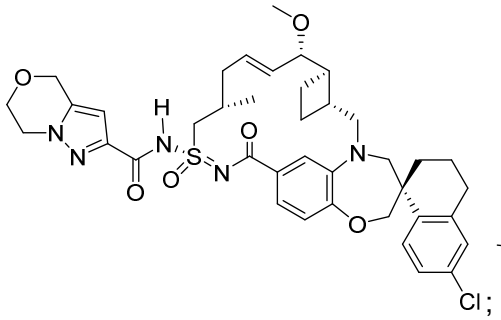


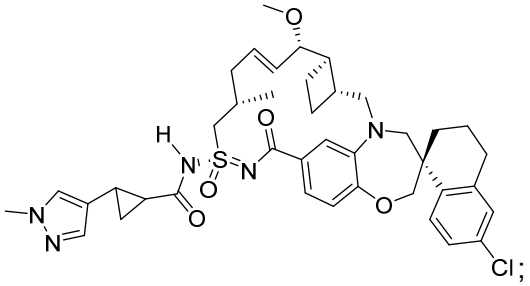


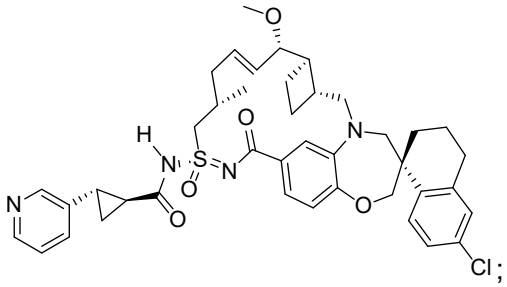


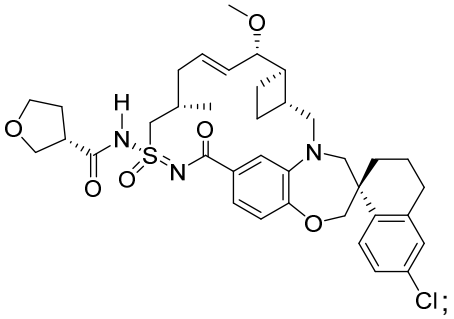


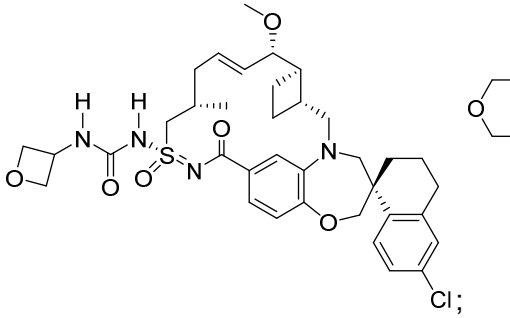


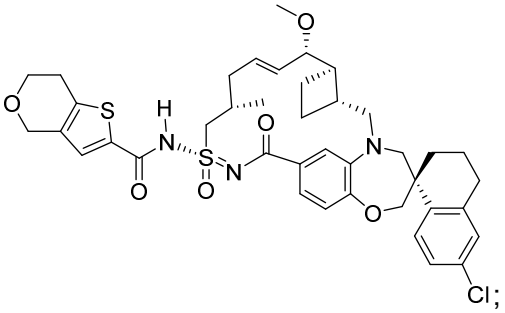


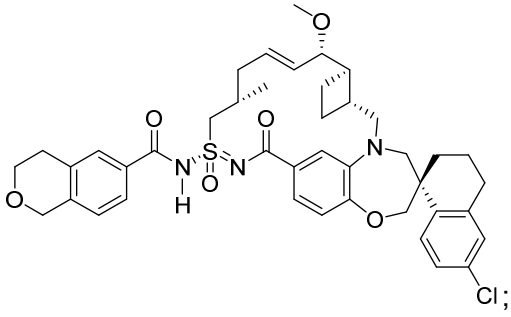


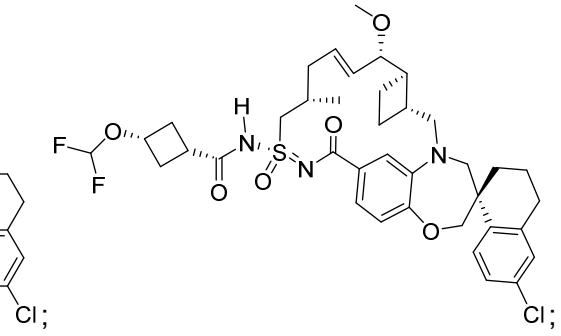


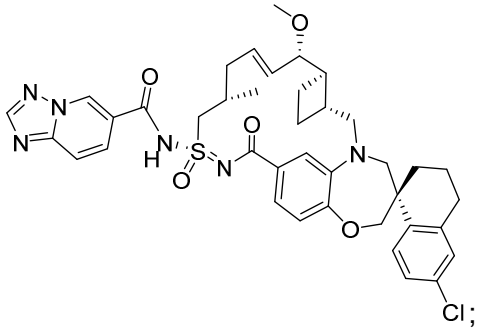


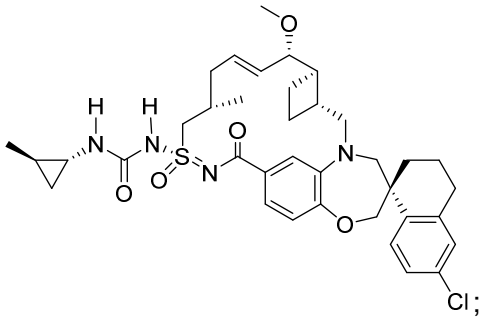


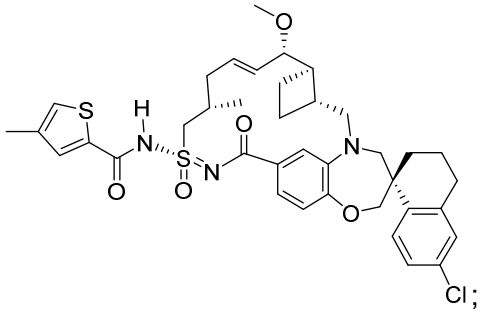


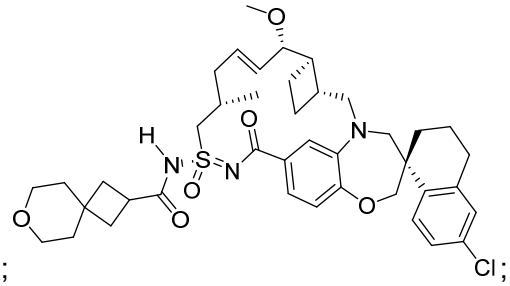


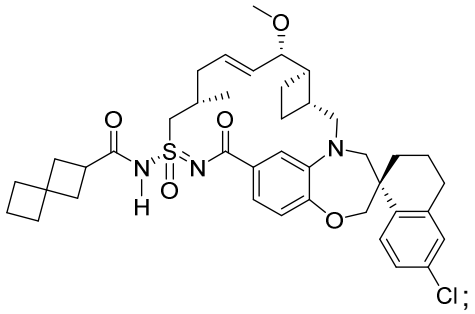


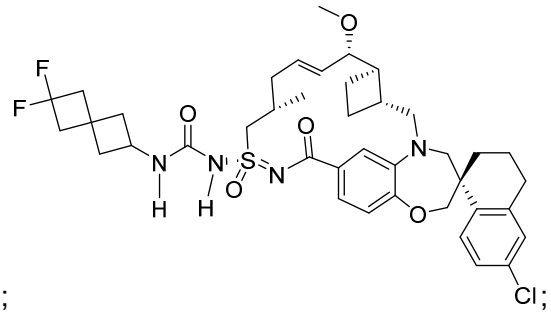


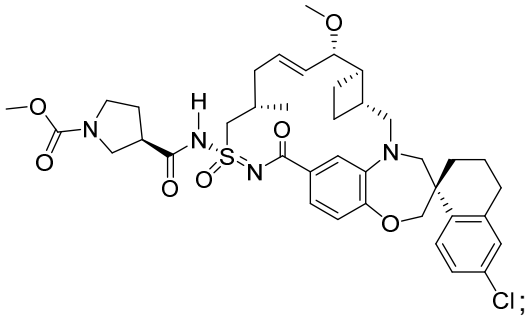


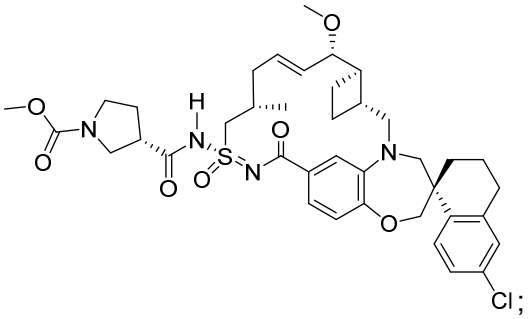


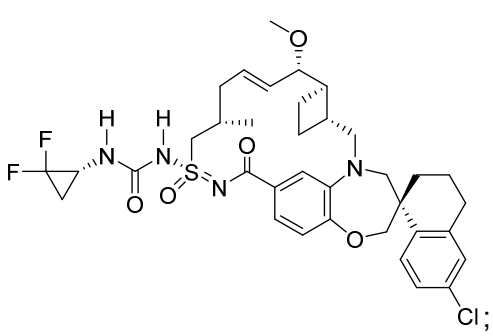


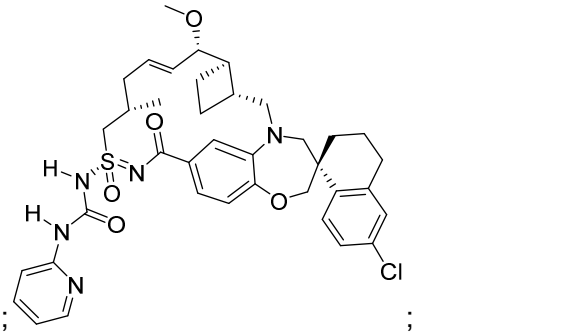


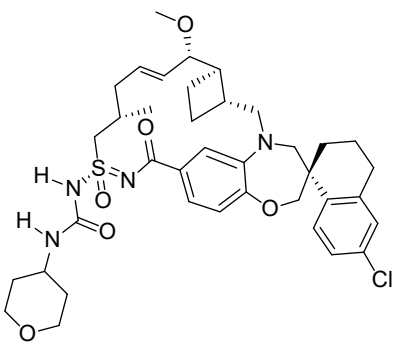
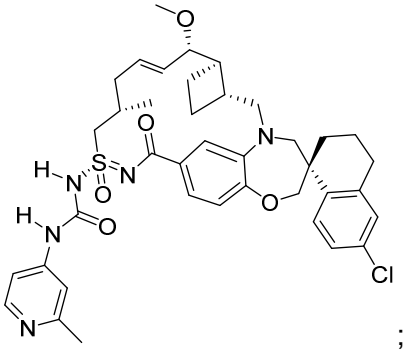
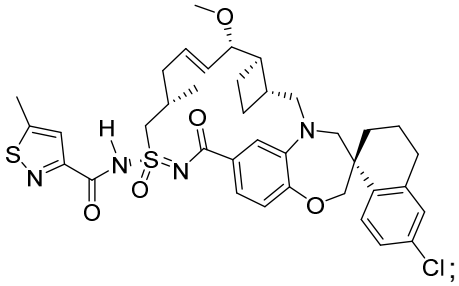
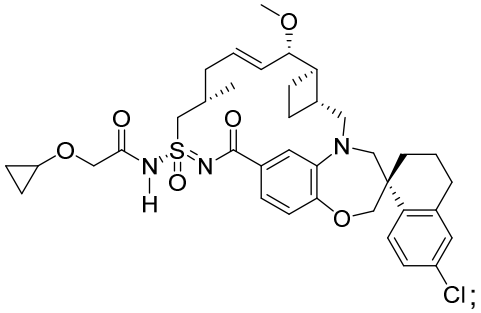
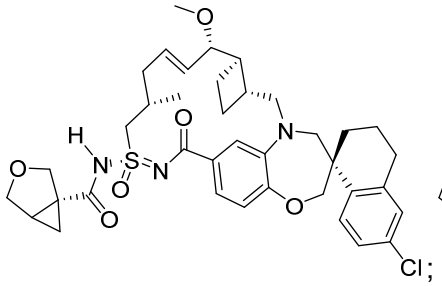
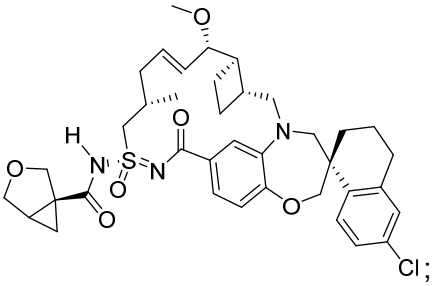
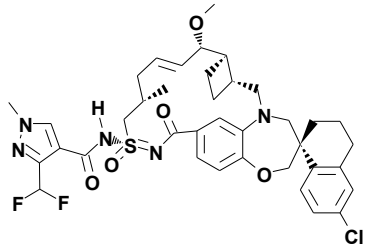
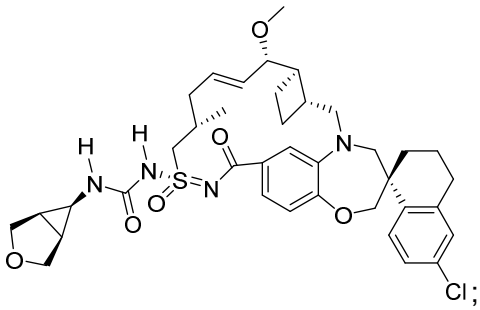
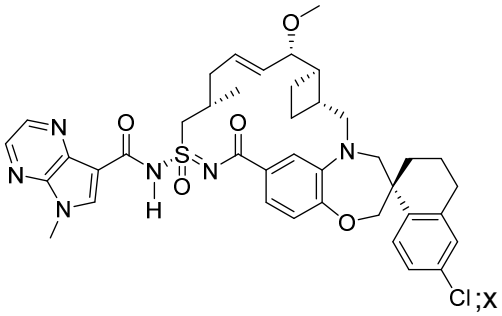


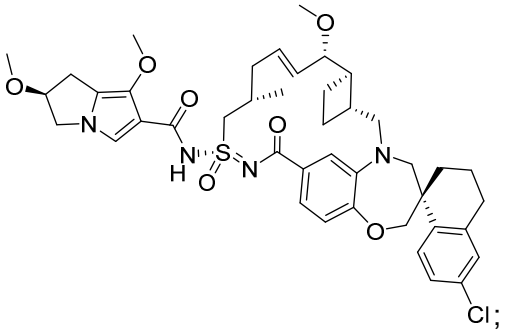


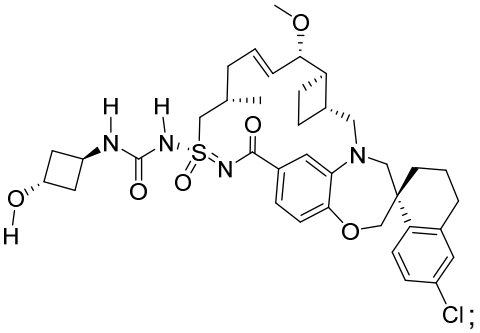


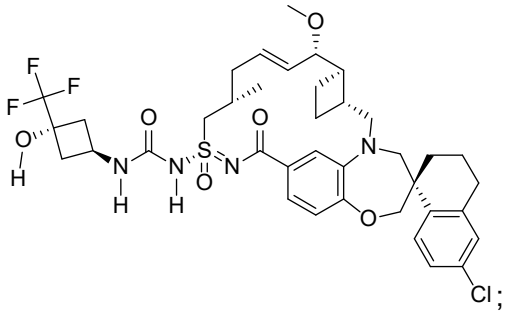


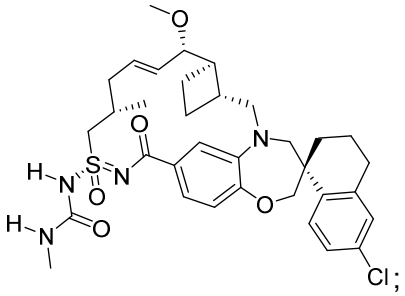


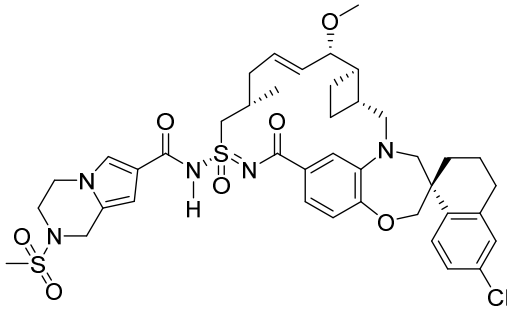

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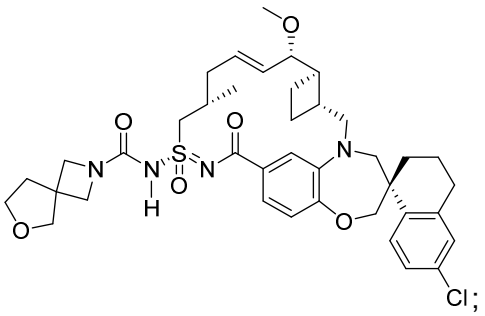


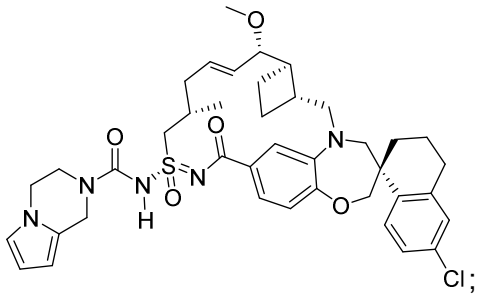


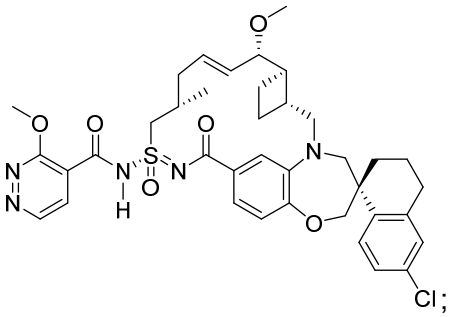


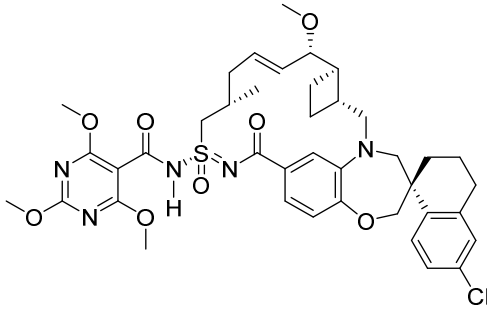


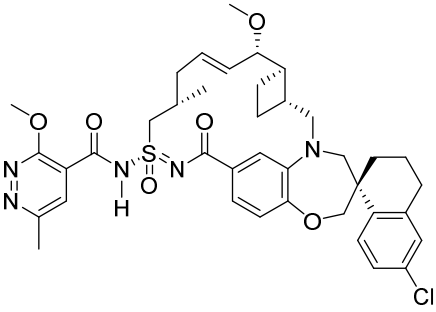


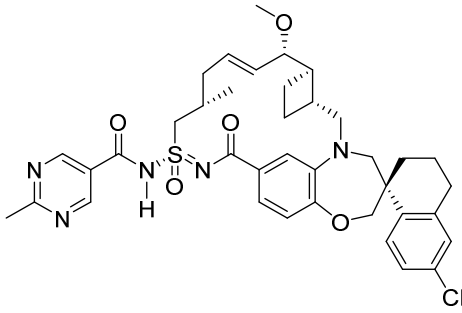


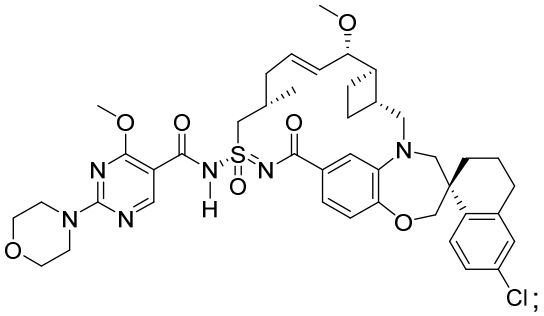


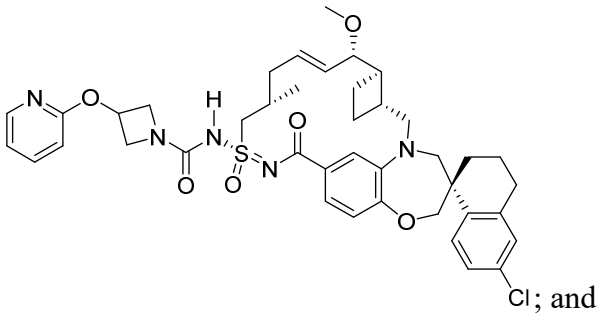
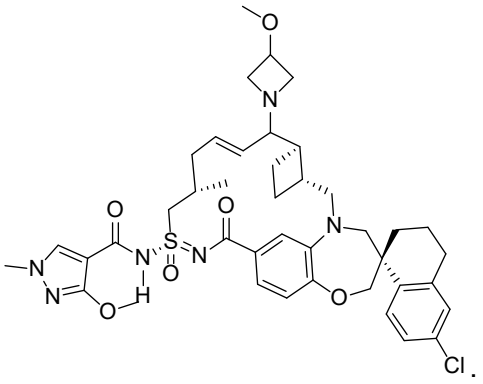




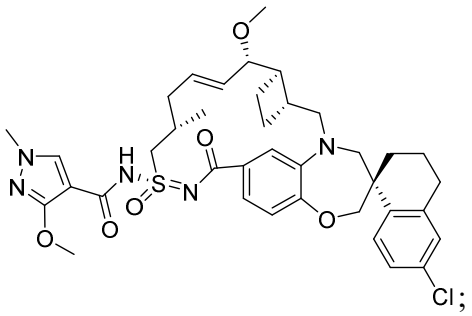






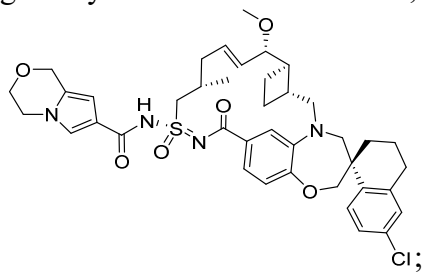

; and

.

12. The compound of any one of claims 1-11, which is:


;

or a pharmaceutically acceptable salt thereof.

13. The compound according to any one of claims 1-7 or 11, which is:


;

or a pharmaceutically acceptable salt thereof.

14. A pharmaceutical composition comprising the compound of claim 1 or claim 11, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

15. Use of a compound of any one of claims 1 - 13, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 14, in the manufacture of a medicament for treating cancer responsive to MCL-1 inhibition.