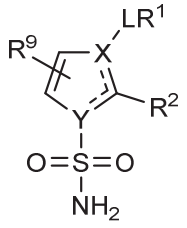
CLAIMS

1. A compound of formula (**I**) or a pharmaceutically acceptable salt thereof:



(I)

wherein

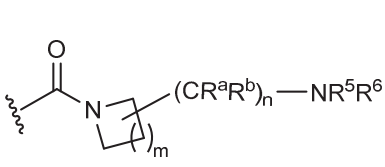
one of X and Y is N and the other is C;

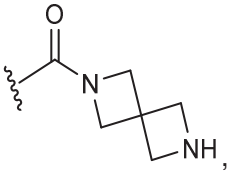
L is a linker group selected from a bond or $-(CH_2)_a-Q-(CH_2)_b-$ in which, Q is selected from the group comprising: O, NH, SO_2, C=C, and C≡C or Q is absent;

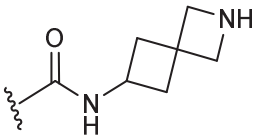
R^1 is a 6 membered monocyclic aromatic, carbocyclic, heteroaromatic or heterocyclic ring substituted by one R^3 group, R^1 may be further substituted with 0 or 1 groups selected from halo, C_{1-6} alkyl, or C_{1-6} haloalkyl;

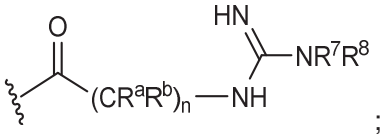
R^2 is -C(O)OH or -C(O)OM; wherein M is a group 1 cation;

R^3 is selected from the group comprising: $-CONR^4(CR^aR^b)_nNR^5R^6$, $-CONR^4(CR^aR^b)_nOSO_2OR^5$, $-CONR^4(CR^aR^b)_nCN$, $-CONR^4(CR^aR^b)_nC(=O)OH$, $-CONR^4(CR^aR^b)_nC(=O)NR^7R^8$, $-NR^4CO(CR^aR^b)_nNR^7R^8$, $-NR^4CO(CR^aR^b)_nOSO_2OR^5$, $-NR^4CO(CR^aR^b)_nCN$, $-NR^4CO(CR^aR^b)_nC(=O)OH$, $-NR^4CO(CR^aR^b)_nC(=O)NR^7R^8$, $-SO_2NR^4(CR^aR^b)_nNR^5R^6$, $-SO_2NR^4(CR^aR^b)_nOSO_2OR^5$, $-SO_2NR^4(CR^aR^b)_nCN$, $-SO_2NR^4(CR^aR^b)_nC(=O)OH$, $-SO_2NR^4(CR^aR^b)_nC(=O)NR^7R^8$,



,


,


and


;

R^4 is selected at each occurrence from the group comprising: H, halo, -OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, $-(CH_2)_f$-aryl, $-(CH_2)_d$-heteroaryl, $-(CH_2)_g$-heterocyclyl; wherein R^4 may be optionally substituted where chemically possible with one, two or three groups independently selected at each occurrence from the group comprising: halo, $-NH_2$, $-N(C_{1-4}\text{ alkyl})_2$, -OH, $-SO_2N(C_{1-4}\text{ alkyl})_2$, $-NHC(=O)OC_{1-6}$ alkyl and $-C(=O)OC_{1-6}$ alkyl;

R^5 and R^6 are each independently H or C_{1-6} alkyl;

wherein at least one of R^4, R^5 or R^6 is C_{1-6} alkyl when each of R^4, R^5 and R^6 are present;

R^7 and R^8 are each independently selected at each occurrence from H or C_{1-4} alkyl;

R^9 is selected from the group comprising: H, C_{1-4} alkyl, and C_{1-4} haloalkyl;

R^a and R^b are each independently selected at each occurrence from: H, halo, $-NH_2$, and C_{1-4} alkyl;

a, b, d, f and g are independently selected as integers from 0 to 3;

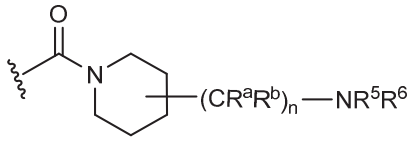
m is an integer selected from 1,2 or 3;

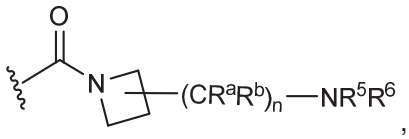
n is an integer selected from 1, 2, 3, 4 or 5; and

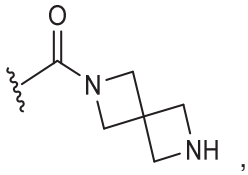
- - -represents a single or a double bond as required to satisfy valence requirements.

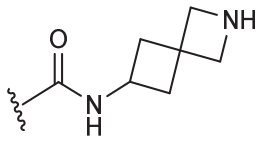
2. A compound according to claim 1, wherein Y is N and X is C.

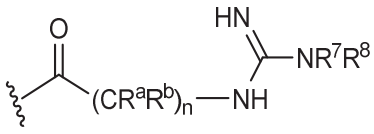
3. A compound according to claim 1 or claim 2, wherein R^3 is selected from the group comprising: : -$CONR^4(CR^aR^b)_nNR^5R^6$, -$CONR^4(CR^aR^b)_nOSO_2OR^5$, -$CONR^4(CR^aR^b)_nCN$, -$CONR^4(CR^aR^b)_nC(=O)OH$, -$CONR^4(CR^aR^b)_nC(=O)NR^7R^8$,



,


,


,


and


4. A compound as claimed in any preceding claim, wherein R^3 is selected from: -$CONH(CH_2)_2NHMe$, -$CON(Me)(CH_2)_2NHMe$, -$CONH(CH_2)_3NHMe$, -$CON(Me)(CH_2)_2NHMe$, -$CONH(CH_2)_3OSO_2OH$, -$CON(Me)(CH_2)_3OSO_2OH$, -$CONH(CH_2)_3OSO_2OMe$, -$CON(Me)(CH_2)_3OSO_2OMe$, -$CONHCH_2CN$, -$CONH(CH_2)_2CN$, -$CON(Me)CH_2CN$, -$CON(Me)(CH_2)_2CN$, -$CONH(CH_2)_2C(=O)OH$, -$CON(Me)(CH_2)_2C(=O)OH$, -$CONHCH_2C(=O)OH$, -$CON(Me)CH_2C(=O)OH$, -$CONHCH_2C(=O)NH_2$, -$CONMeCH_2C(=O)NH_2$, -$CONHCH_2C(=O)NHMe$, -$CONMeCH_2C(=O)NHMe$, -$CONH(CH_2)_2C(=O)NH_2$, -$CONMe(CH_2)_2C(=O)NH_2$, -$CONH(CH_2)_2C(=O)NHMe$, -$CONMe(CH_2)_2C(=O)NHMe$.

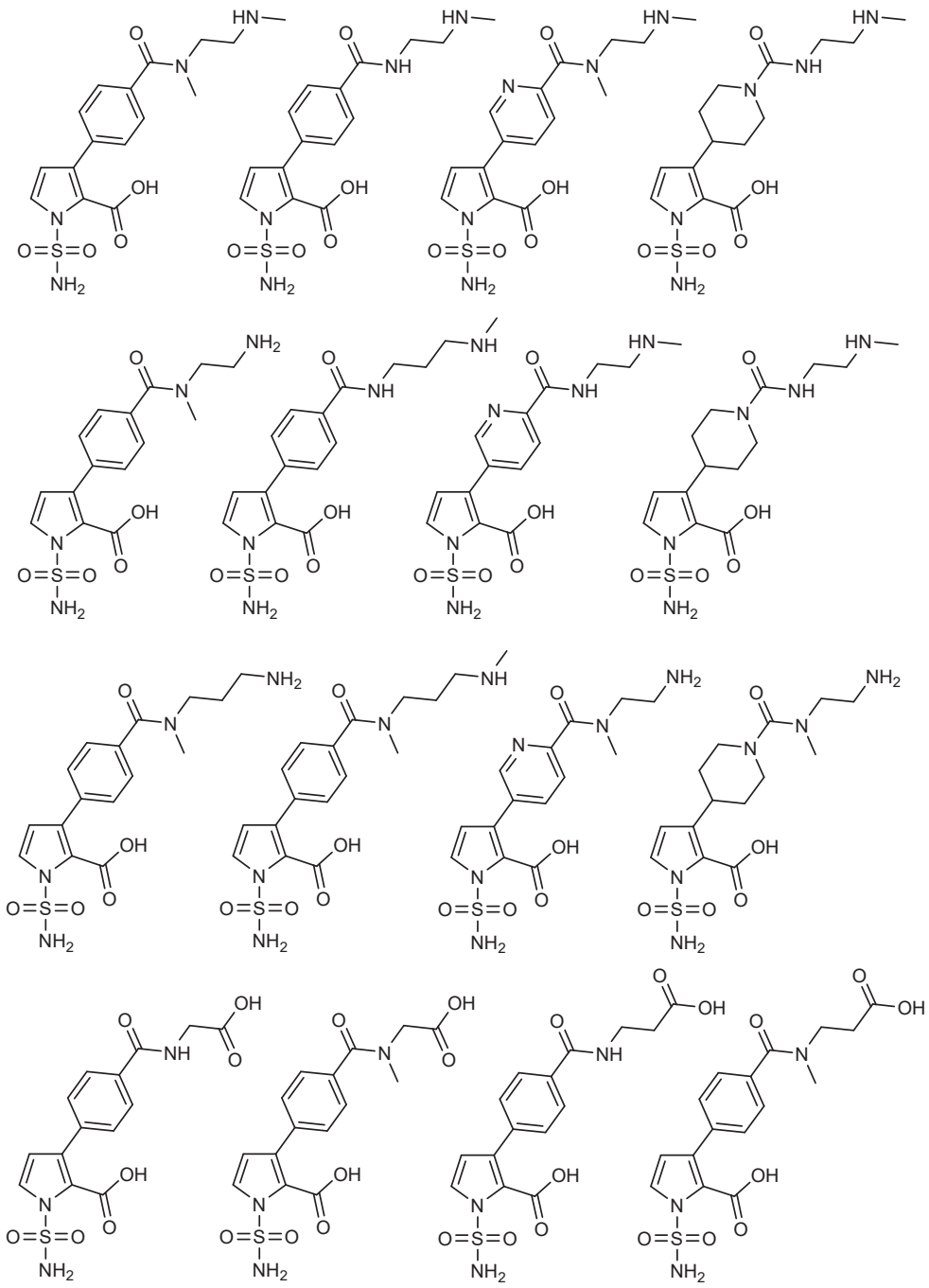
5. A compound as claimed in any preceding claim, wherein R^4 is selected at each occurrence from the group comprising: H, halo, substituted or unsubstituted $C_{1\text{-}6}$ alkyl, and substituted or unsubstituted $C_{3\text{-}8}$ cycloalkyl, optionally ~~.~~

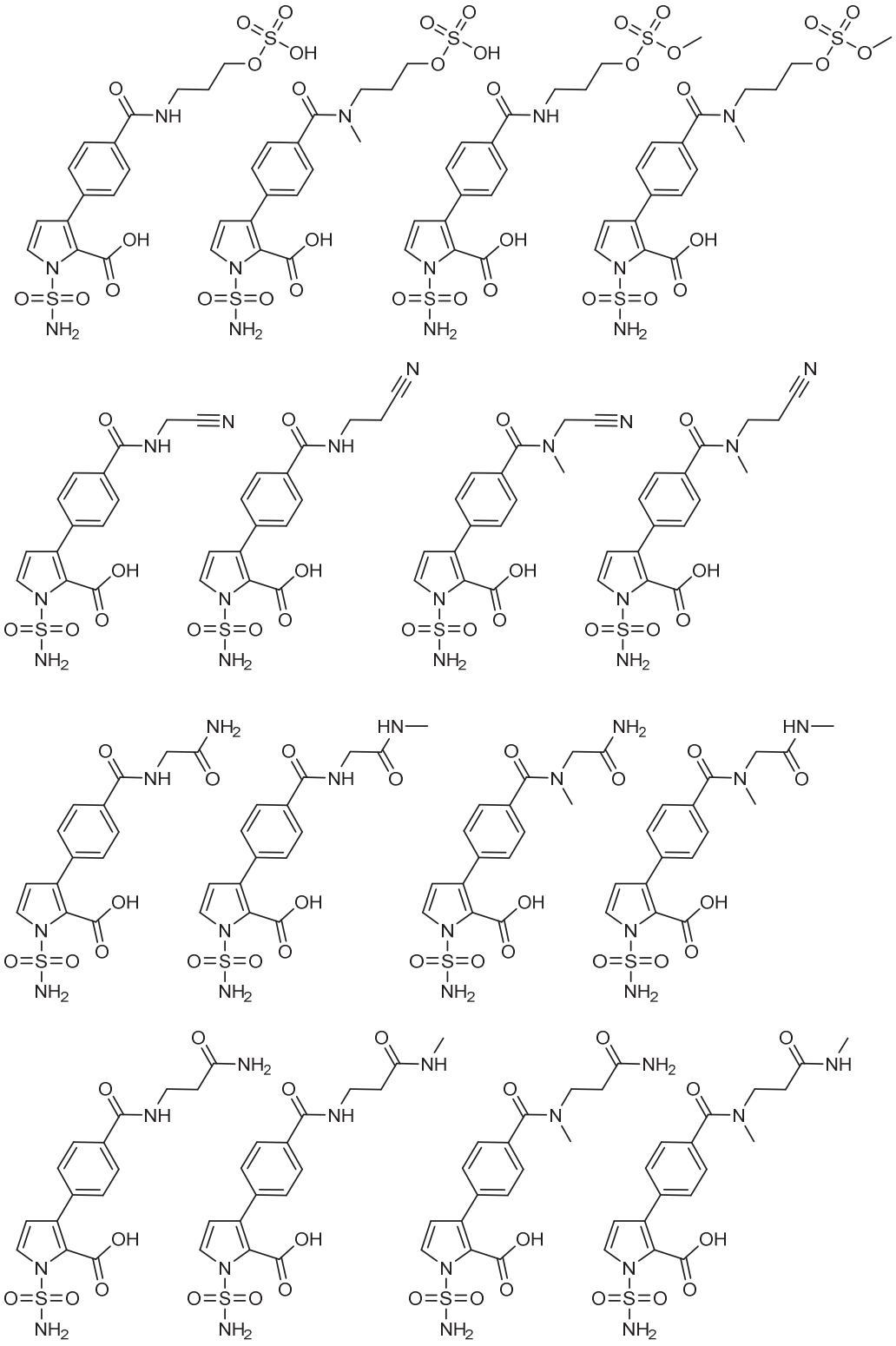
~~6. A compound as claimed in claim 5,~~ wherein R^4 is independently selected at each occurrence from H and Me.

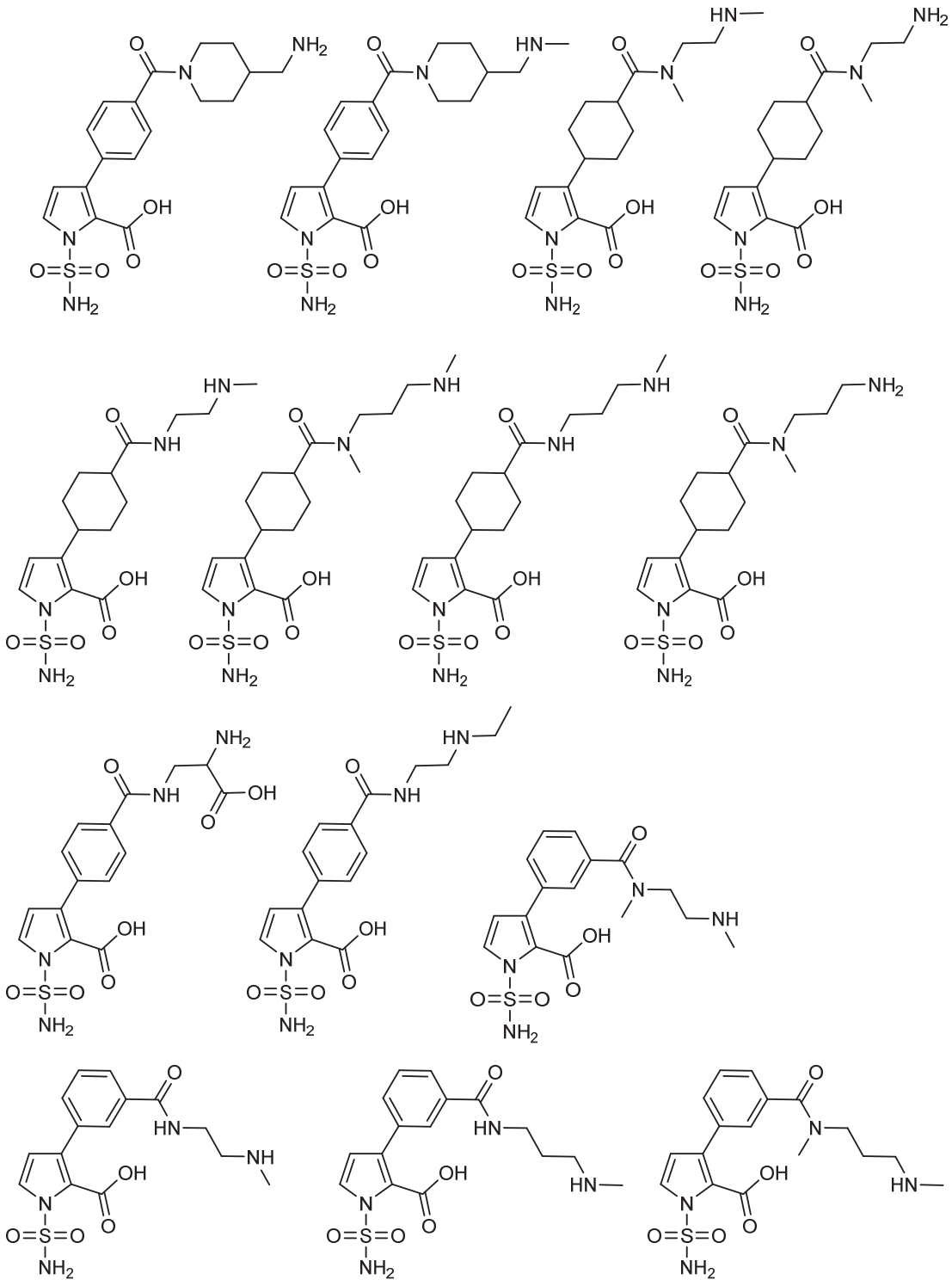
6~~7~~. A compound as claimed in claim 5~~6~~, wherein R^5 and R^6 are each independently selected from the group comprising: H, Me, Et, ^{n}Pr, ^{i}Pr and ^{n}Bu, optionally ~~.~~

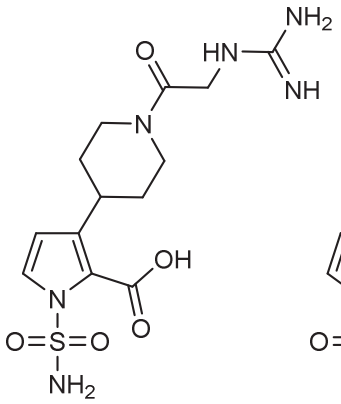
~~8. A compound as claimed in any preceding claim,~~ wherein R^5 and R^6 are each independently H or Me.

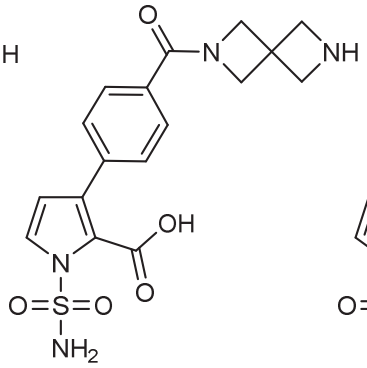
9~~7~~. A compound as claimed in claim 1, wherein the compound is selected from:

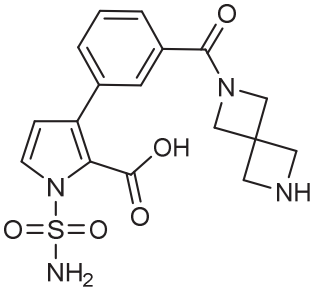


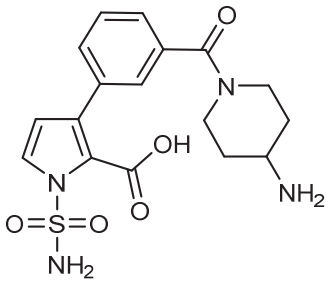


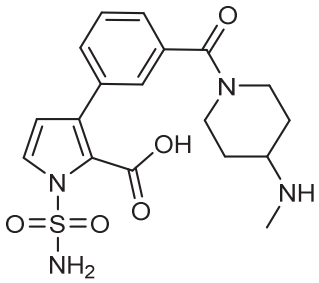


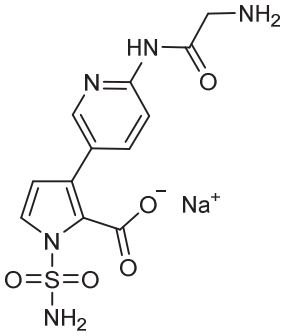


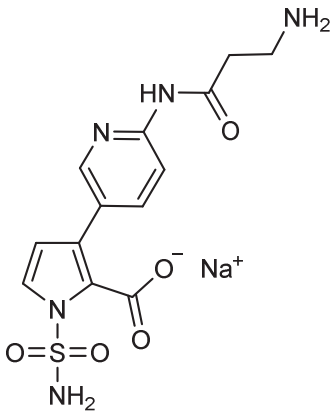


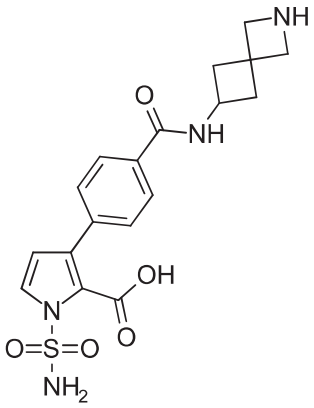


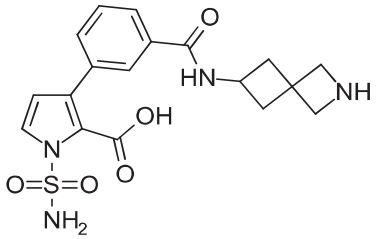


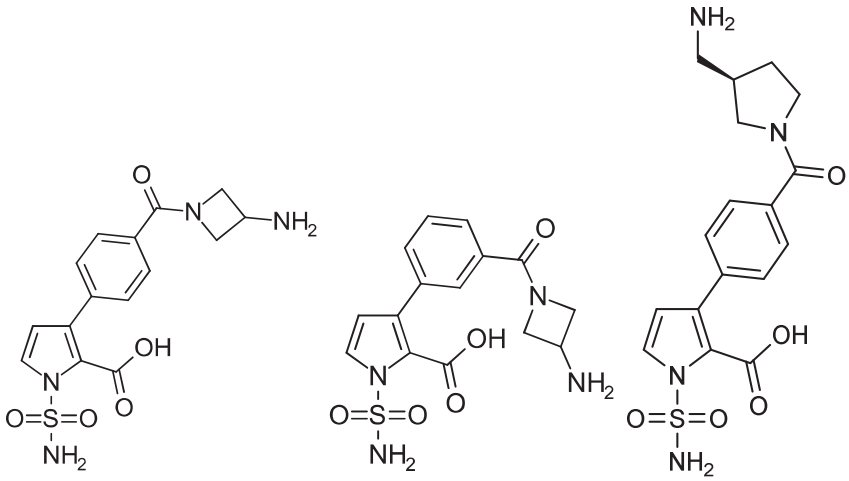




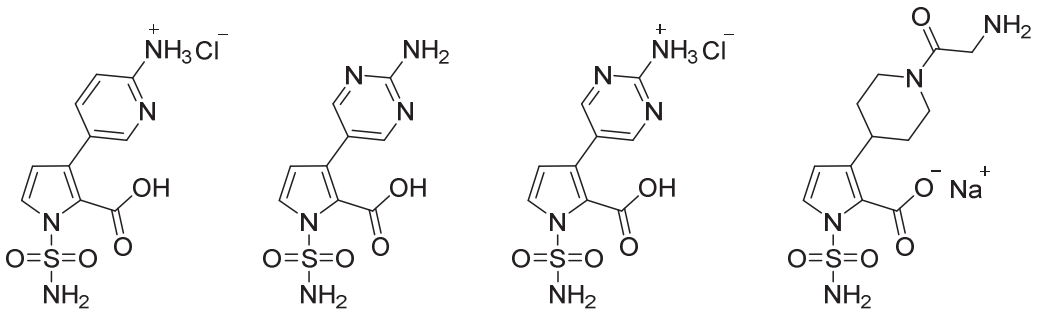


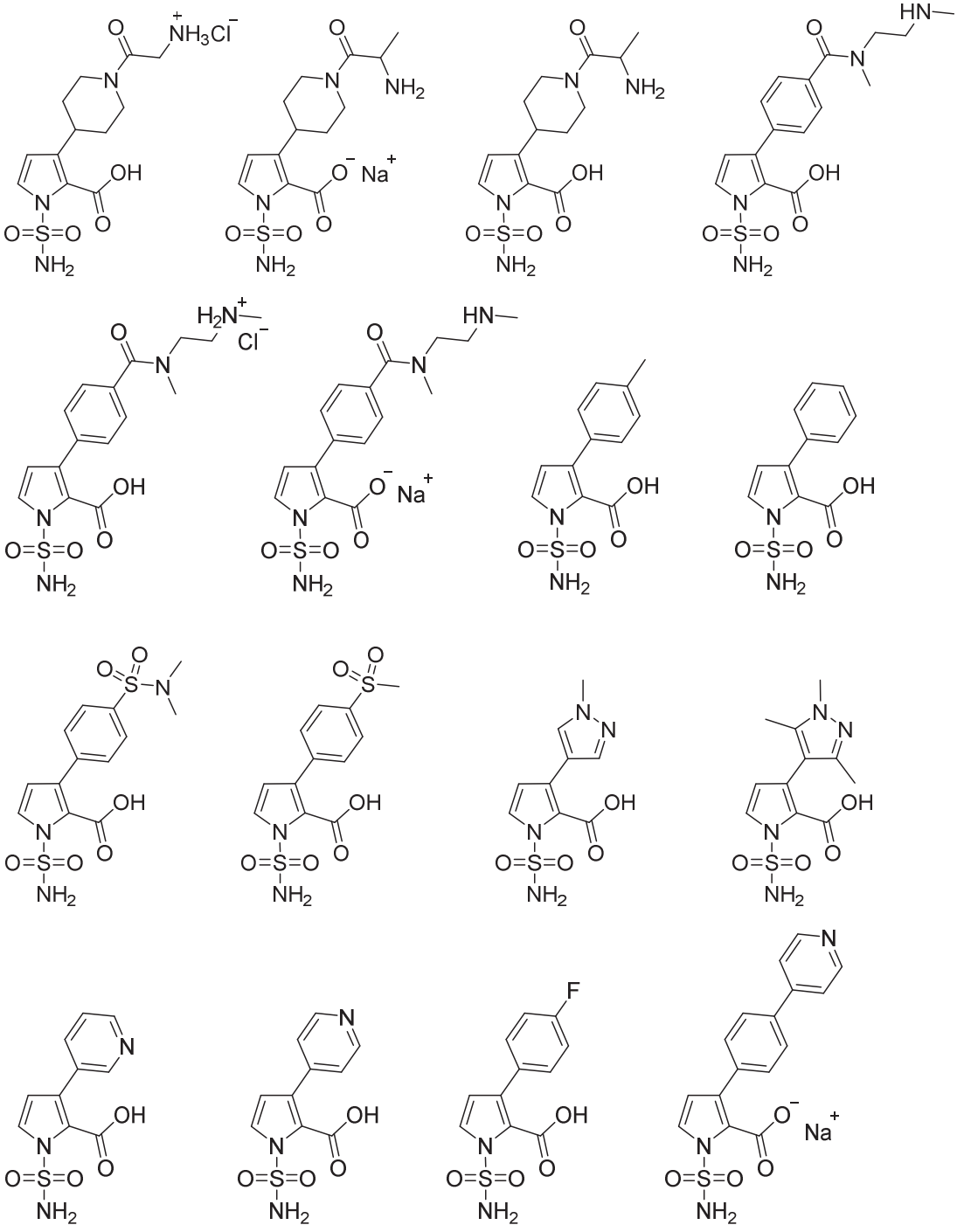


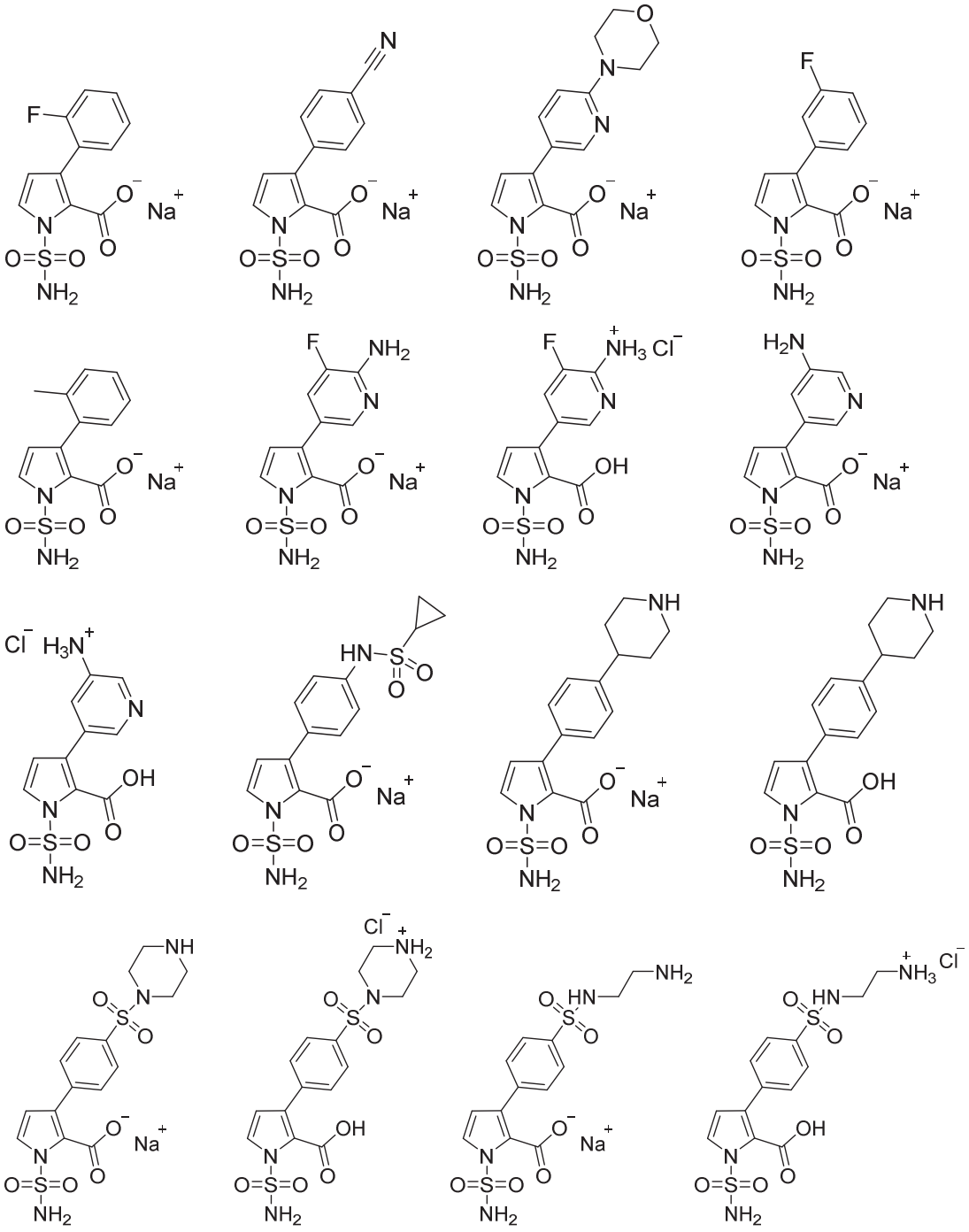


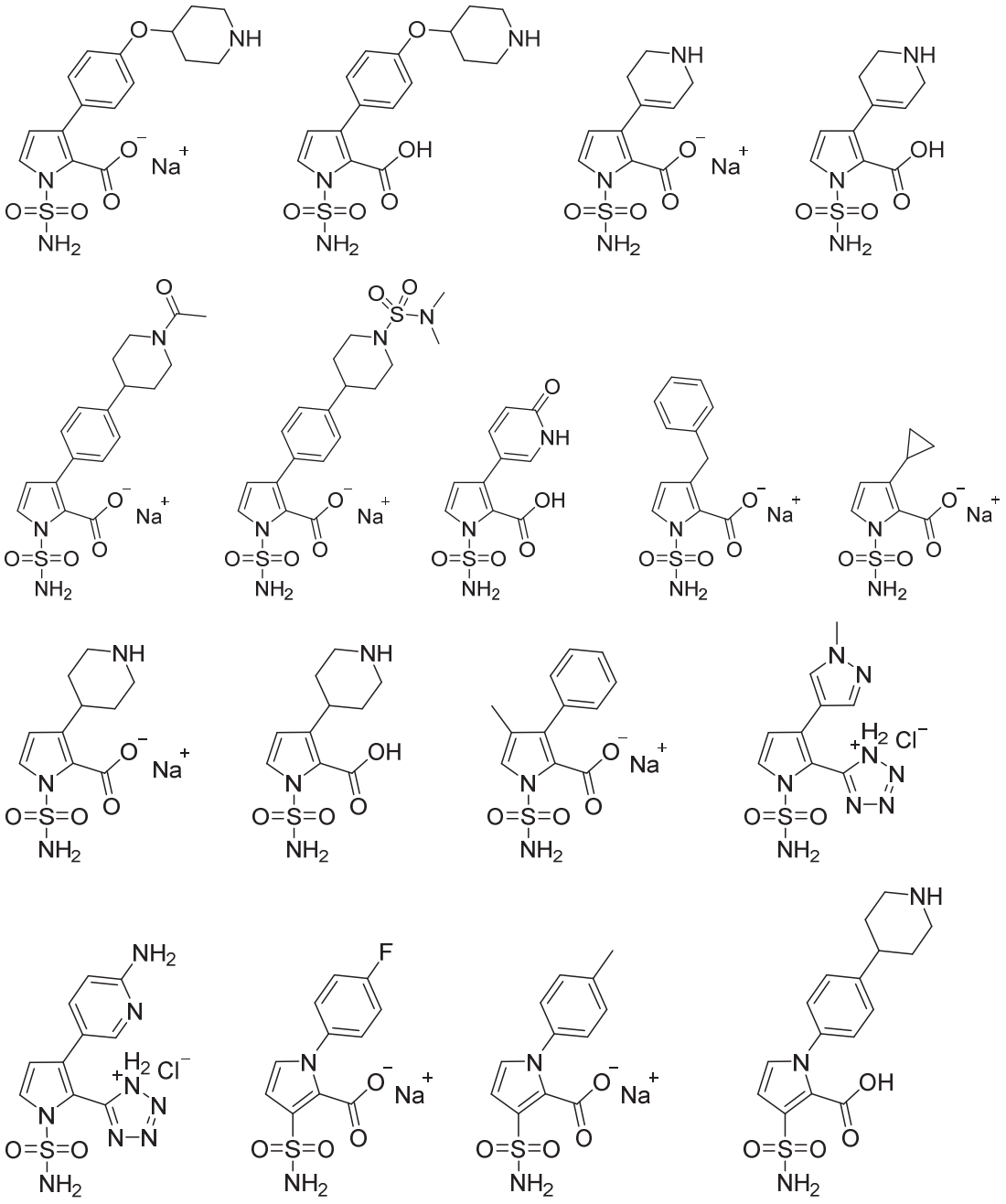


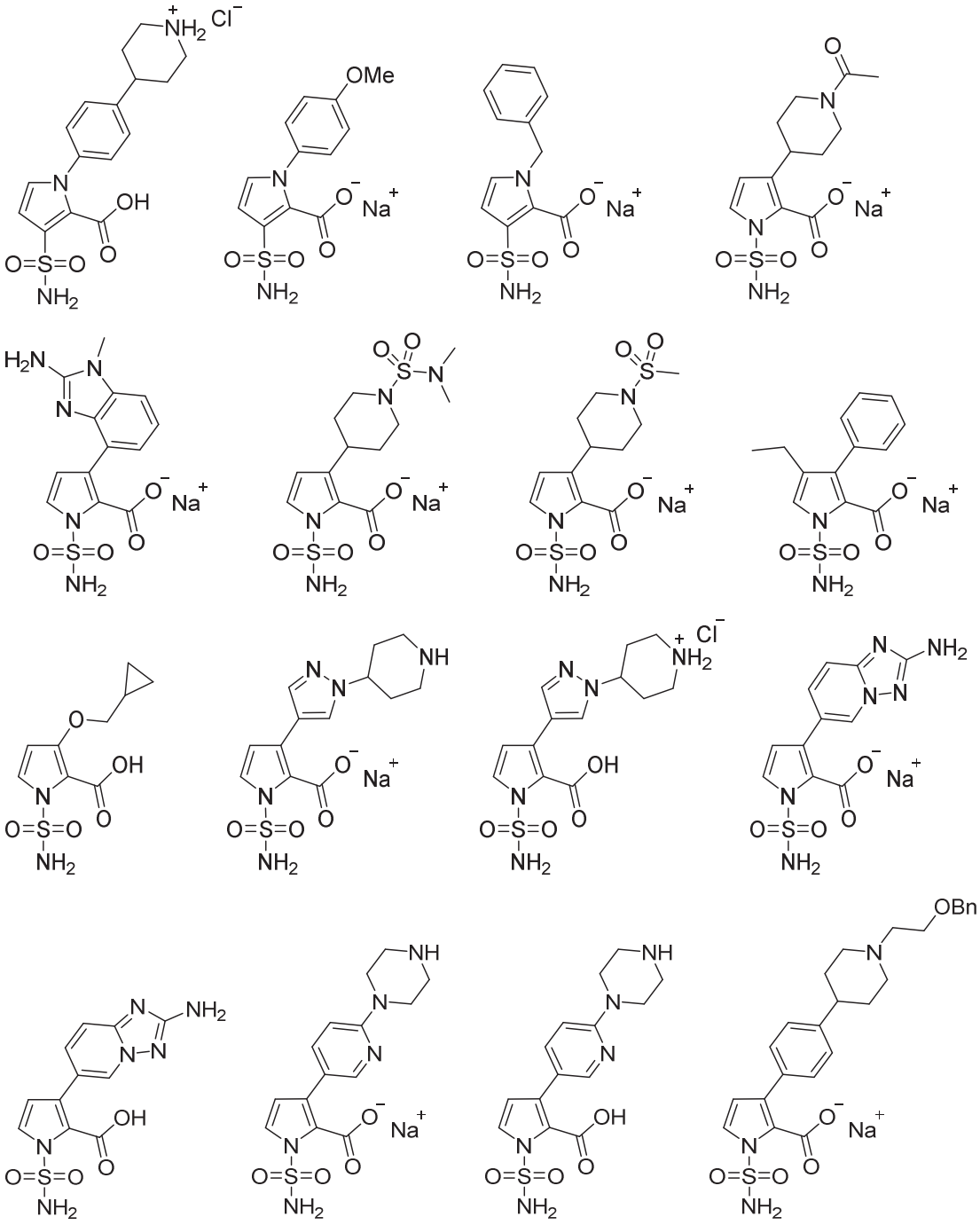
8~~10~~. A compound selected from:

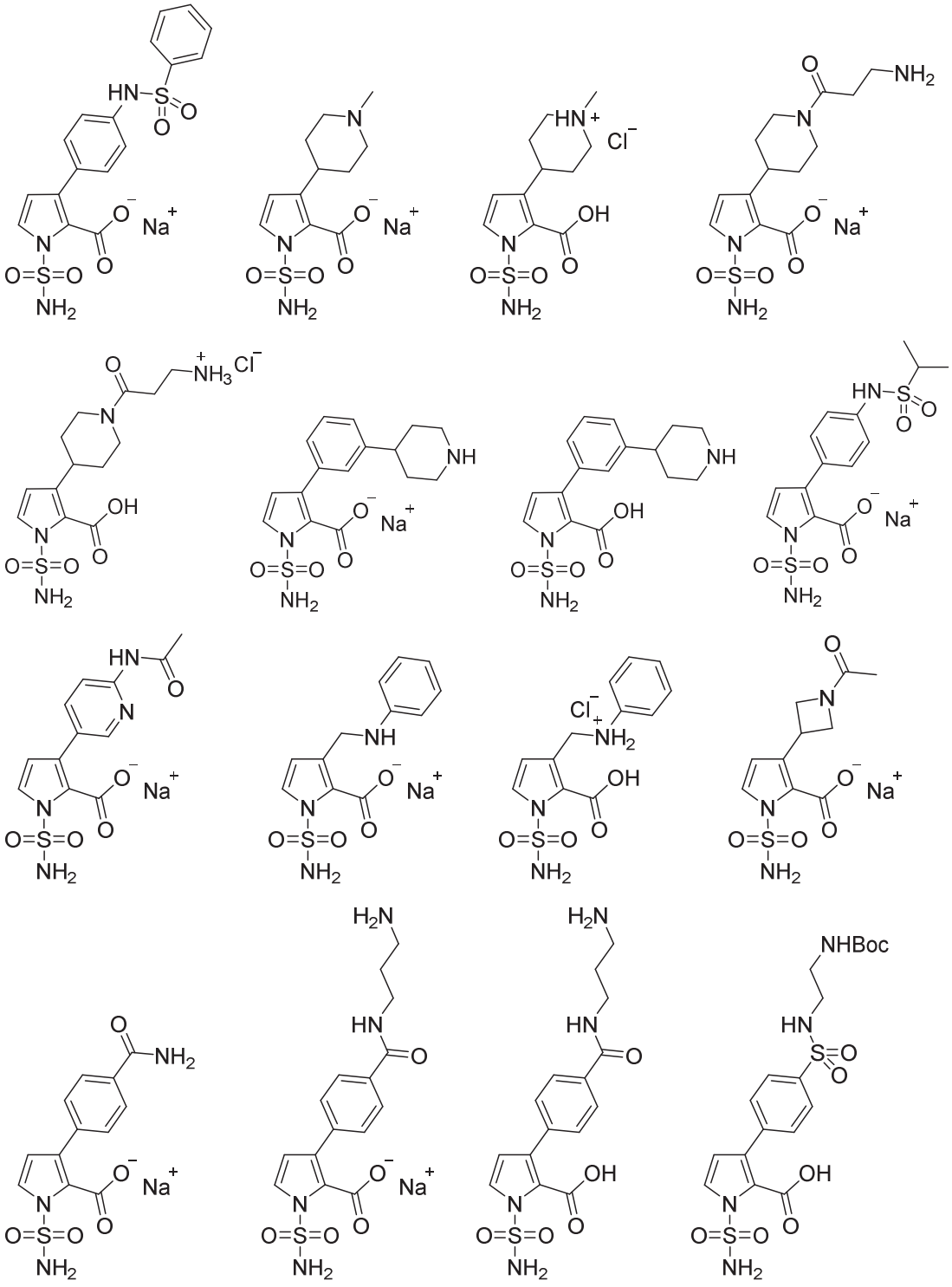


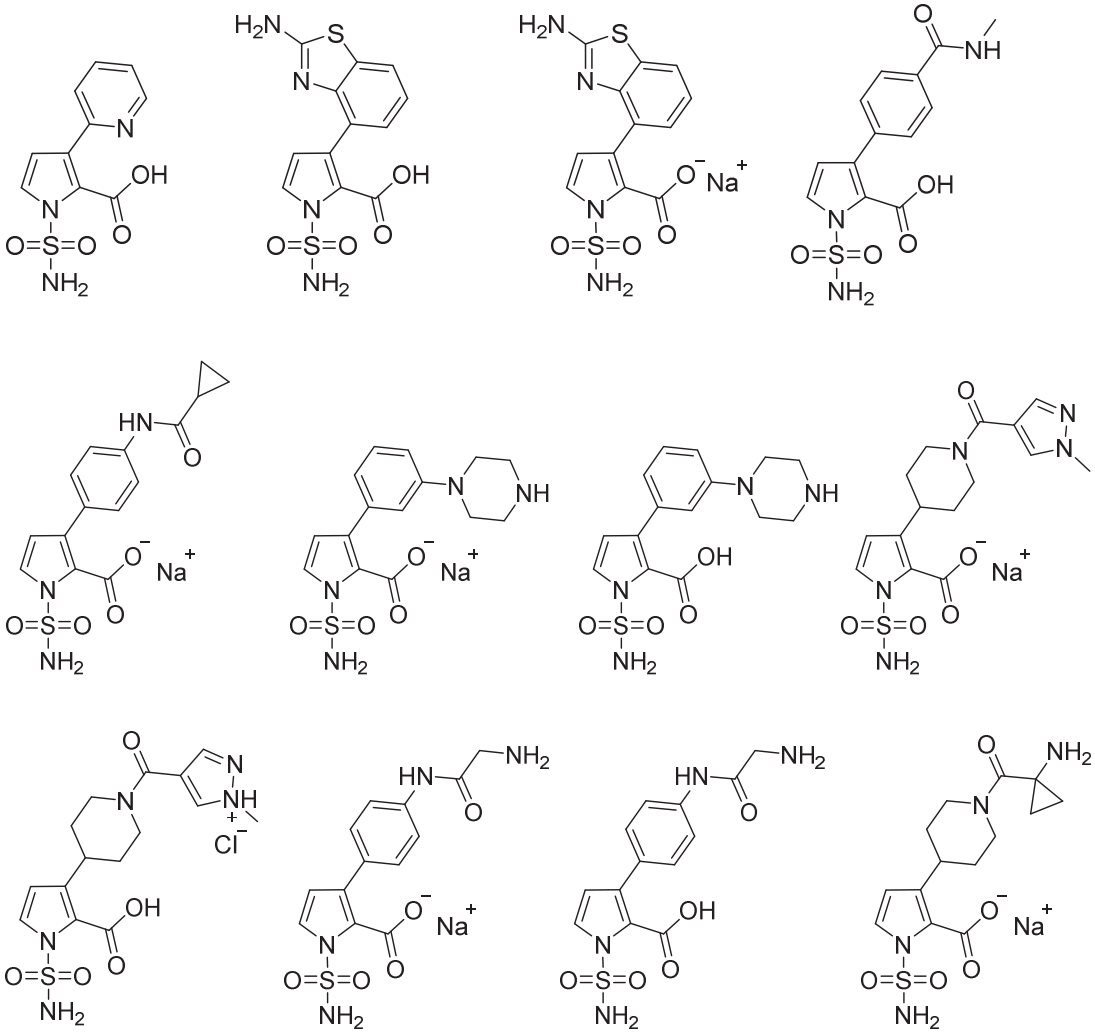


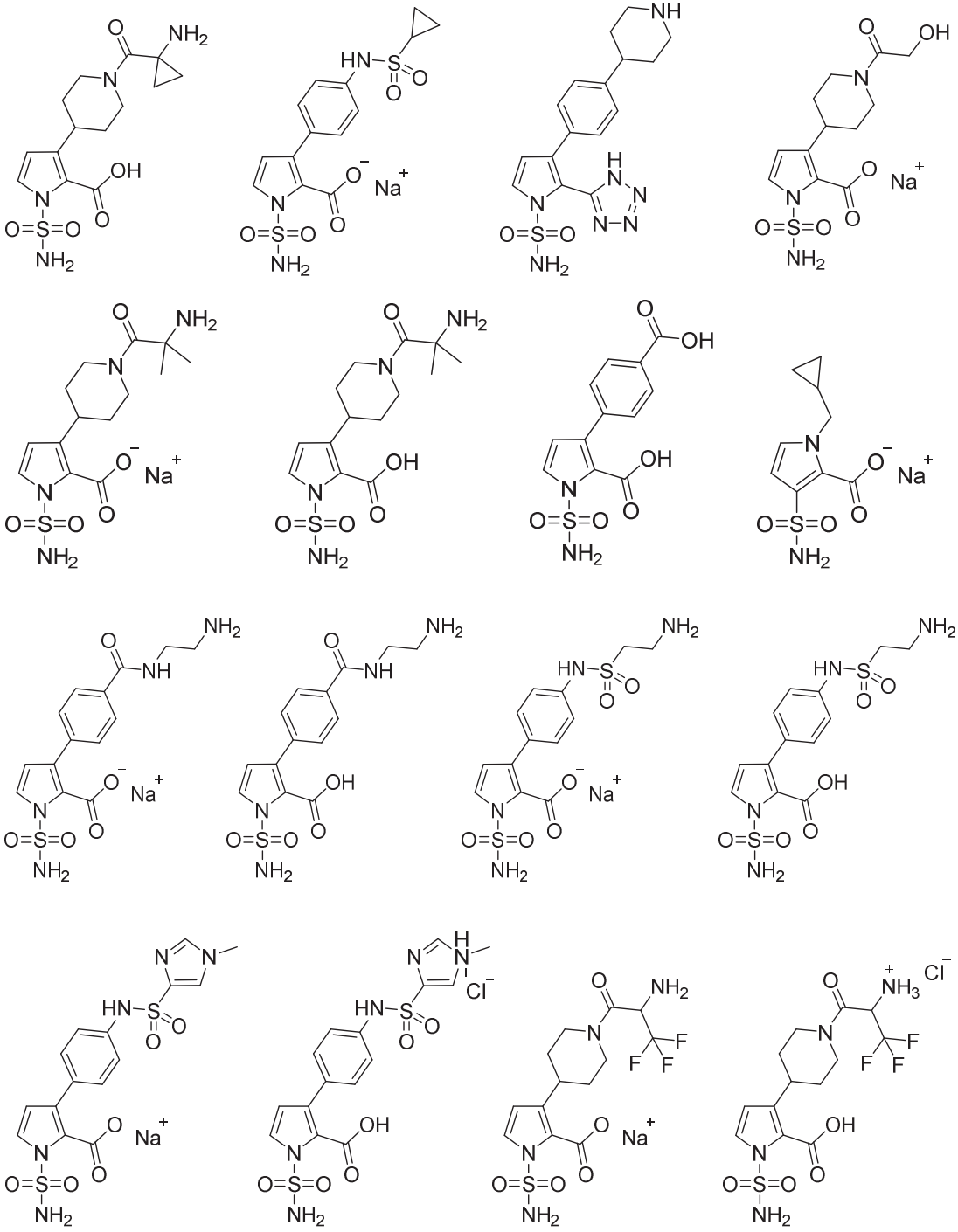


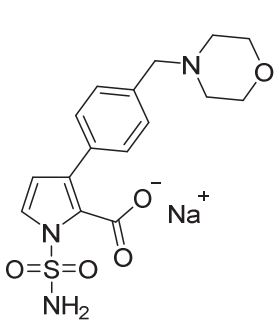


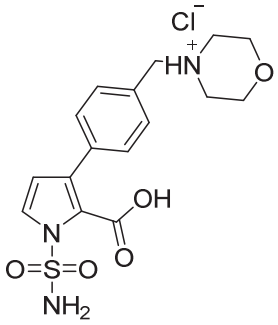




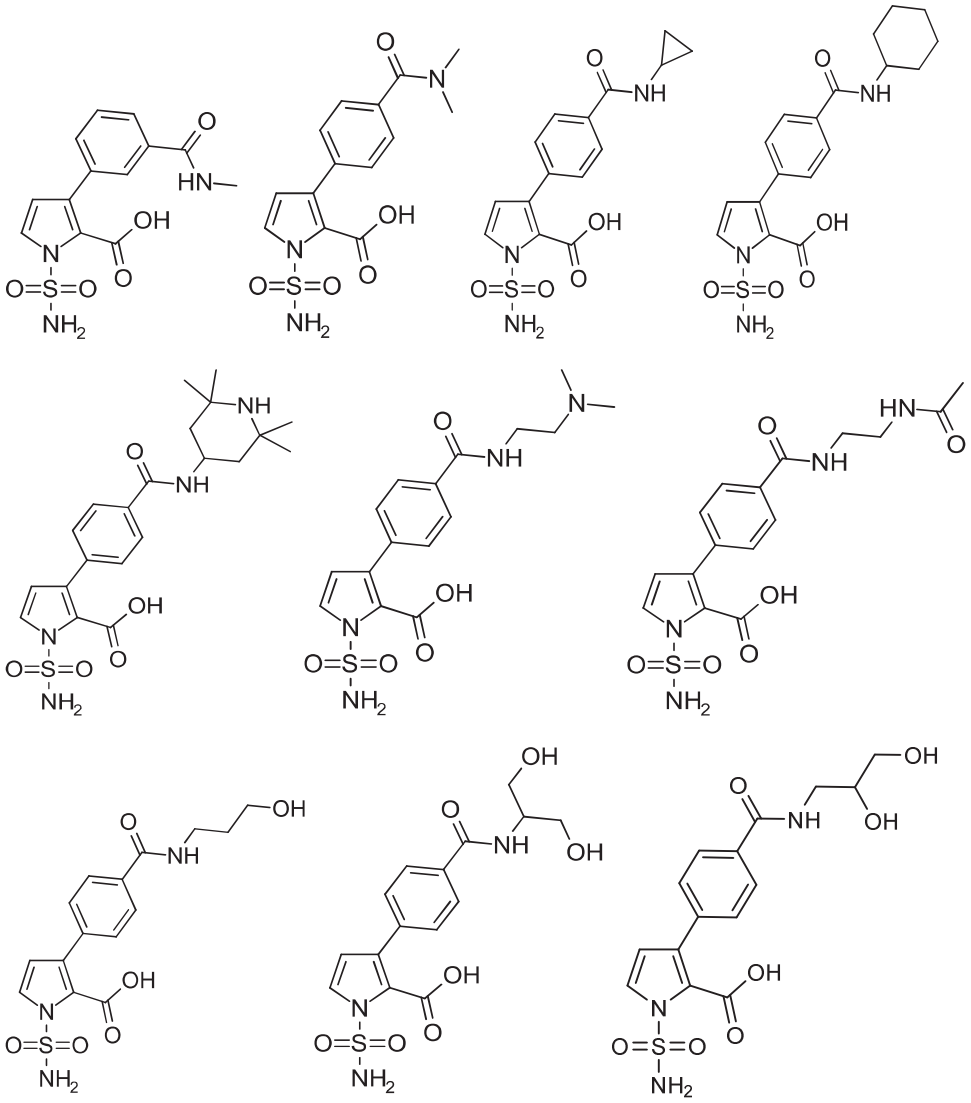


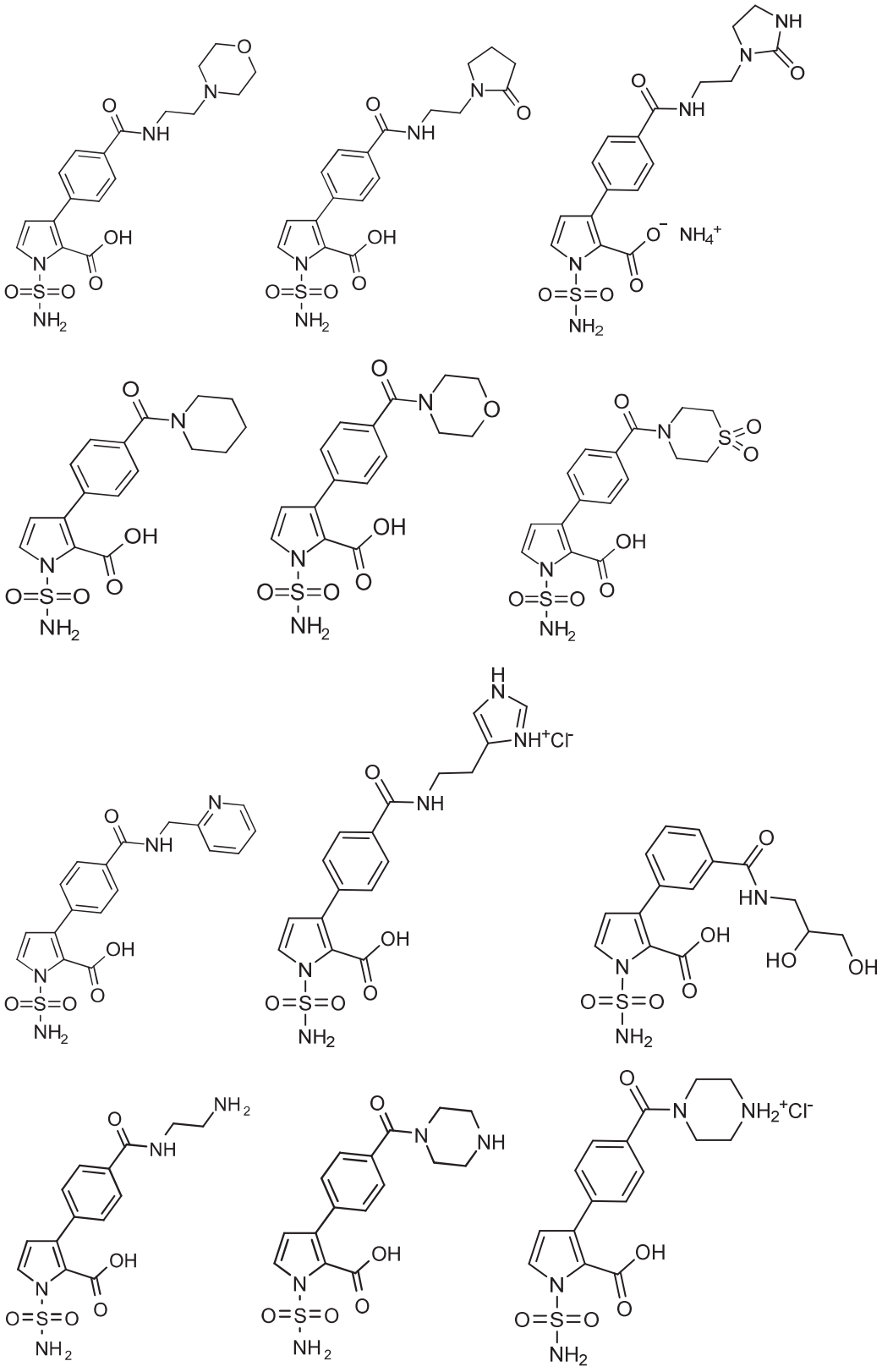


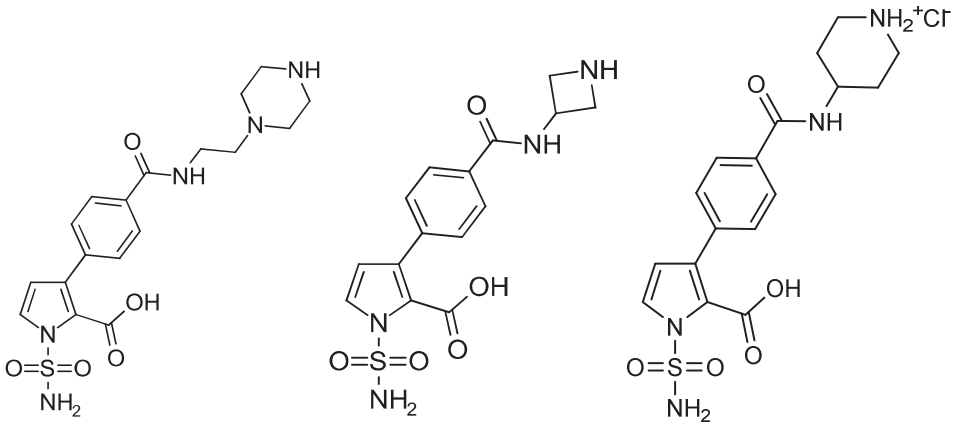


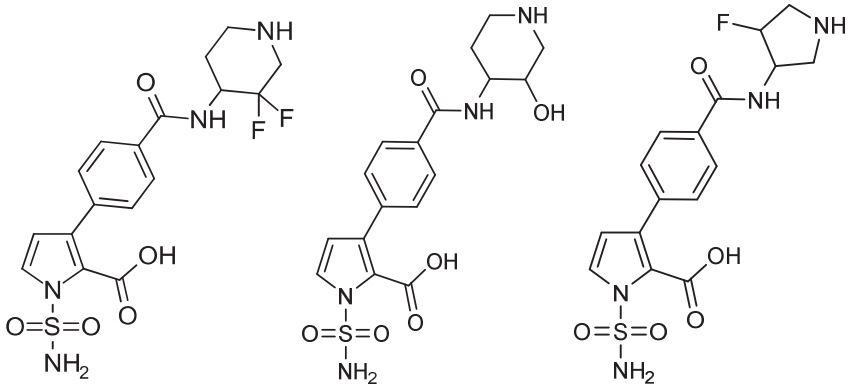


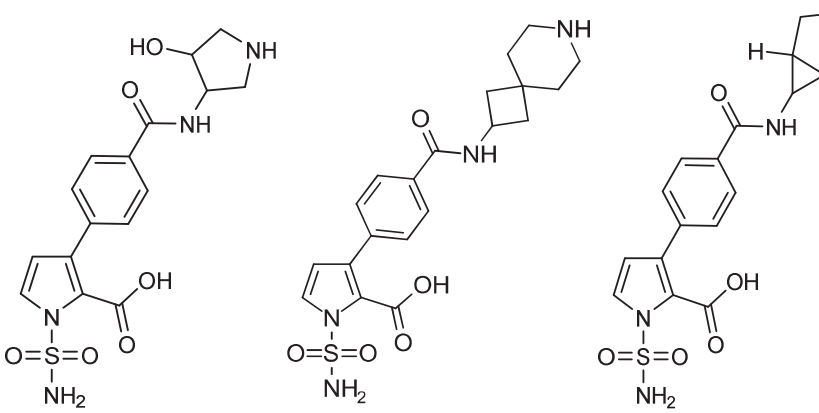
911. A compound selected from:

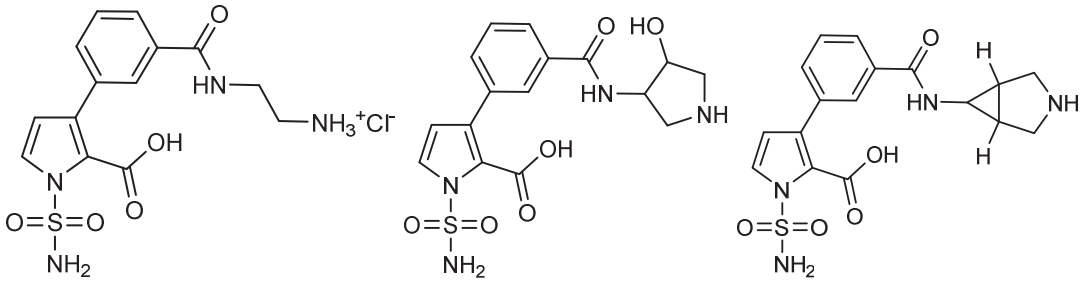


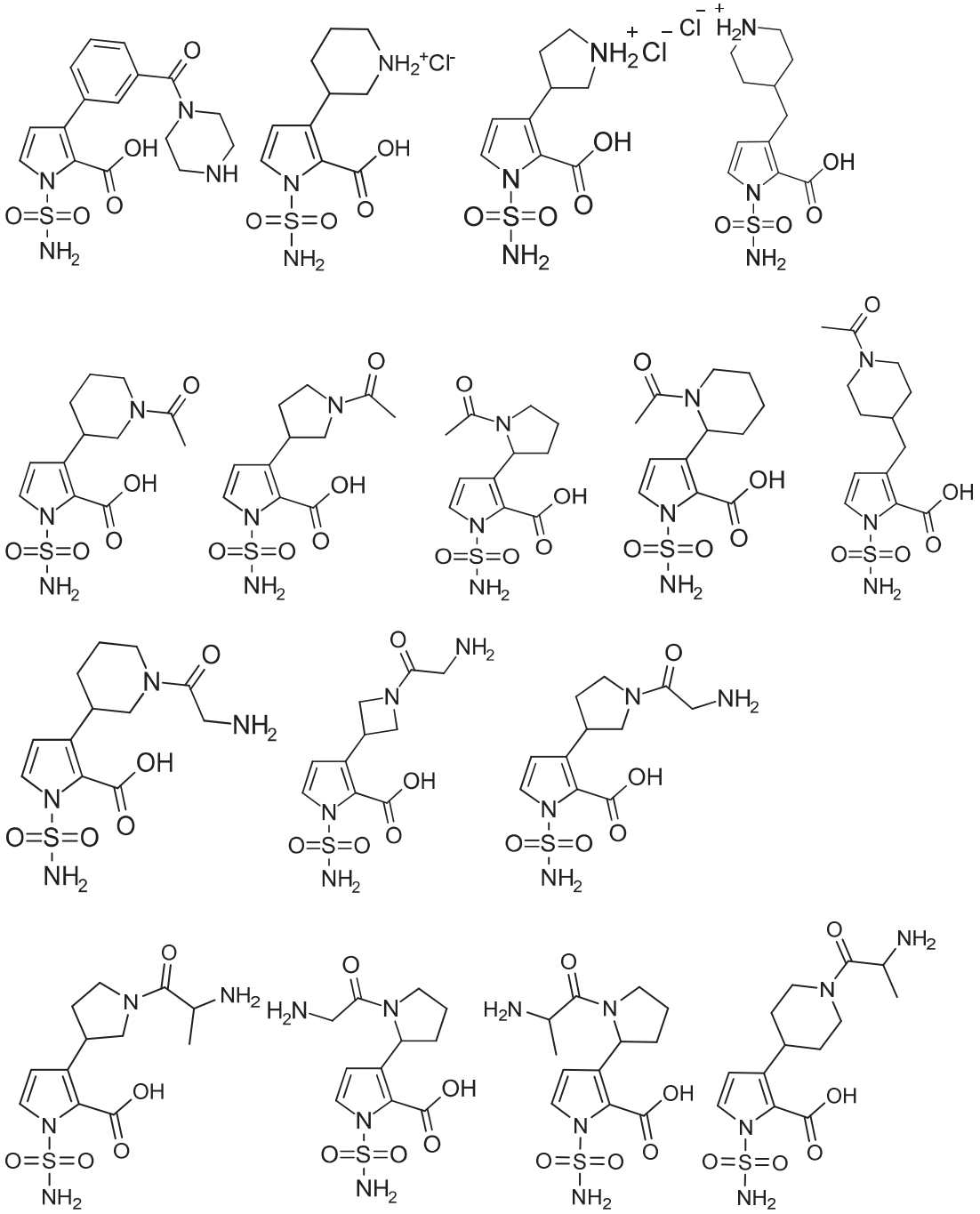


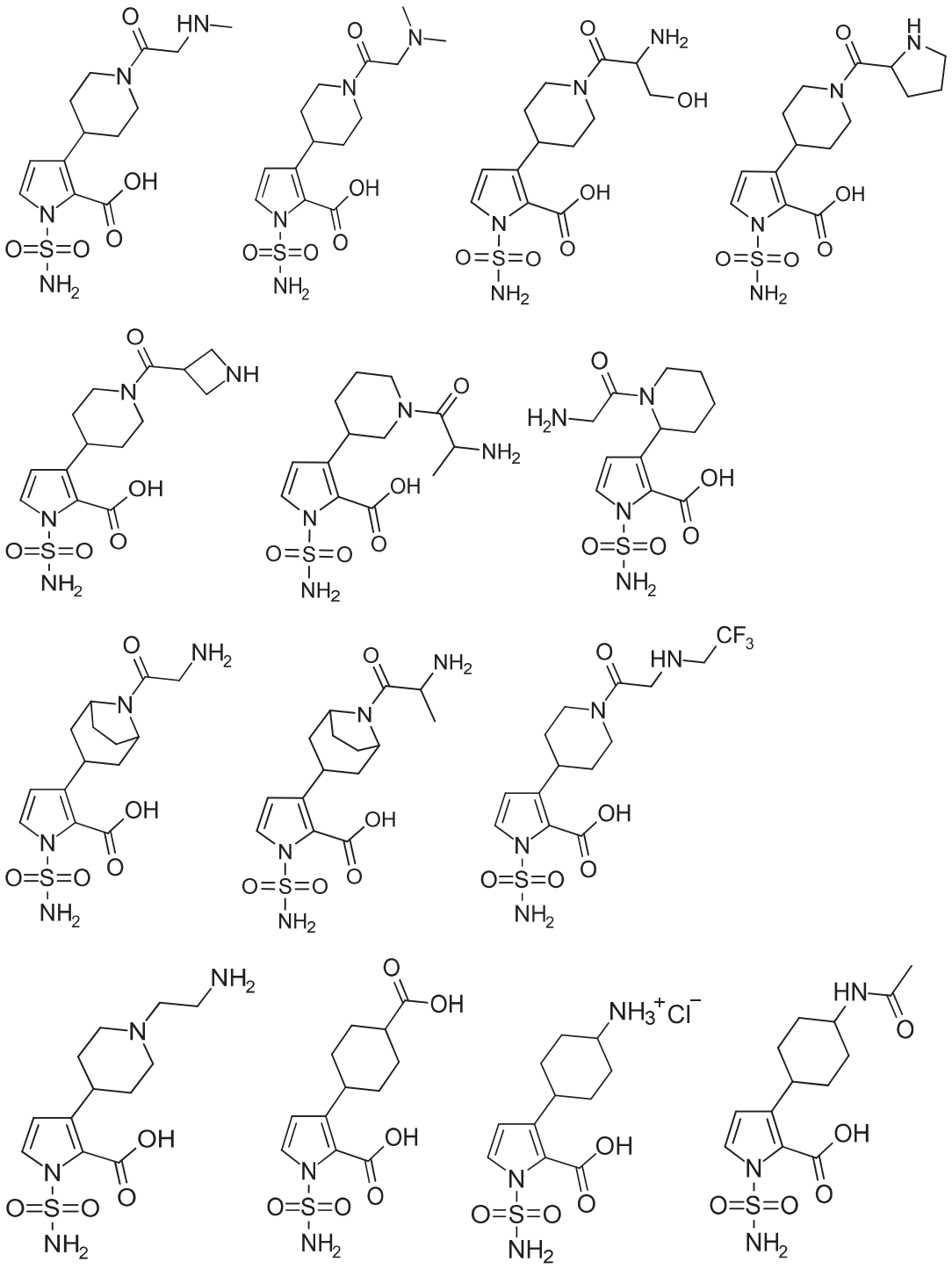


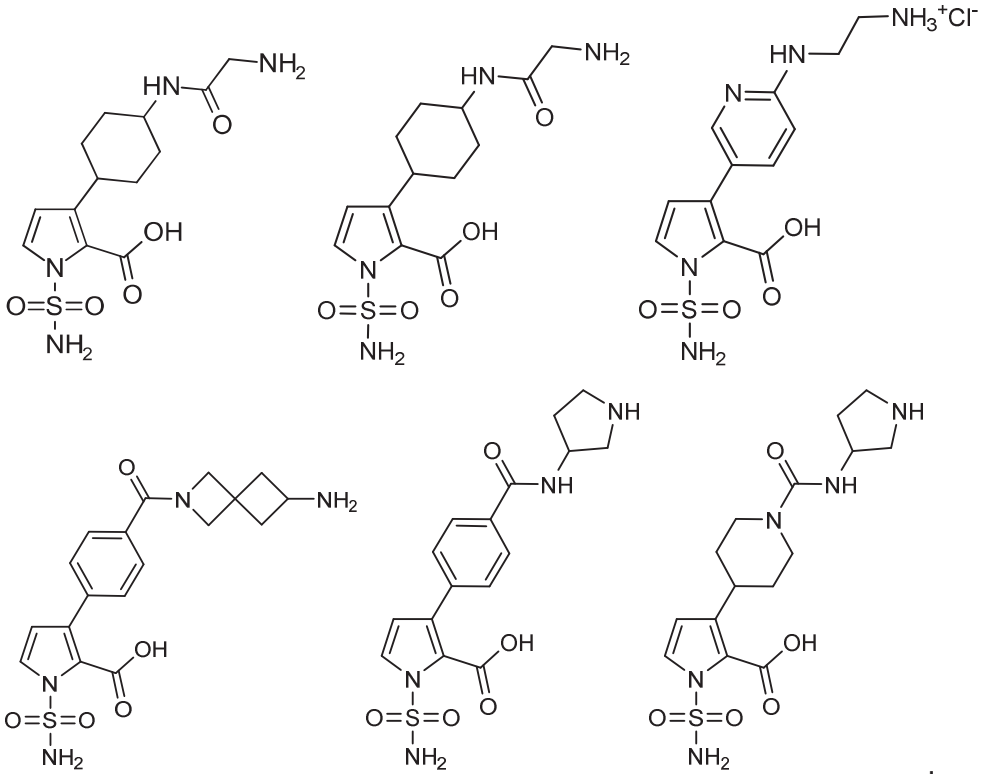












~~12~~10. A pharmaceutical composition which comprises a compound of any preceding claim, or a pharmaceutically acceptable salt, hydrate or solvate thereof, in association with one or more pharmaceutically acceptable excipients.

~~13~~11. A compound of any of claims 1 to ~~9~~11, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a formulation as claimed in claim ~~14~~10, for use in the inhibition of metallo-β-lactamase activity.

~~14~~12. A compound of any of claims 1 to ~~11~~9, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a composition as claimed in claim ~~12~~10, for use in the treatment of a disease or disorder in which metallo-β-lactamase activity is implicated.

~~15~~13. Use of ~~A~~a compound of any of claims 1 to ~~11~~9, or a pharmaceutically acceptable salt, hydrate or solvate thereof, ~~for use in a method of~~in the manufacture of a medicament for treating a disease or disorder caused by aerobic or anaerobic Gram-positive, or aerobic or anaerobic Gram-negative bacteria.

~~16~~14. The ~~compound for~~ use of claim 13~~15~~ wherein the disease or disorder is caused by metallo-β-lactamase producing Gram-positive bacteria.

~~17~~15. The ~~compound for~~ use of claim ~~15~~ 13 or ~~16~~ 14 wherein the disease or disorder is selected from: pneumonia, respiratory tract infections, urinary tract infections, intra-abdominal infections, skin and soft tissue infections, bloodstream infections, septicaemia, intra- and post-partum infections, prosthetic joint infections, endocarditis, acute bacterial meningitis and febrile neutropenia.~~,~~

~~18. The compound for use of claim 17 in the treatment of a~~ optionally wherein the disease or disorder selected from: community acquired pneumonia, nosocomial pneumonia (hospital-acquired/ventilator-acquired), respiratory tract infections associated with cystic fibrosis, non-cystic fibrosis bronchiectasis, COPD, urinary tract infection, intra-abdominal infections, skin and soft tissue infection, bacteraemia, septicaemia, intra- and post-partum infections, prosthetic joint infections, endocarditis, acute bacterial meningitis and febrile neutropenia.~~,~~

~~19. The compound for use of claim 18 in the treatment of a~~ further optionally wherein the disease or disorder selected from: community acquired pneumonia, nosocomial pneumonia (hospital-acquired/ventilator-acquired), respiratory tract infections associated with cystic fibrosis, non-cystic fibrosis bronchiectasis, COPD, urinary tract infection, intra-abdominal infections, skin and soft tissue infection, bacteraemia and septicaemia.

~~20~~16. Use of a~~A~~ compound of any of claims 1 to 9~~11~~, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a formulation as claimed in claim ~~12~~10, in the manufacture of a medicament for ~~use in~~ the treatment of a bacterial infection.

~~21~~17. Use of ~~A~~a compound of any of claims 1 to ~~11~~9, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a formulation as claimed in claim ~~12~~10, in the manufacture of a medicament for use in combinatorial therapy for the treatment of a bacterial infection, wherein said medicament is to be administered in combination with an antibacterial agent~~, for use in the treatment of a bacterial infection~~.

18. Use of a compound of any of claims 1 to 9, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a formulation as claimed in claim 10 and an antibacterial agent in the manufacture of a medicament for combination therapy to treat a bacterial infection

19. Use of a compound of any of claims 1 to 9, or a pharmaceutically acceptable salt, hydrate or solvate thereof, or a formulation as claimed in claim 10 in the manufacture of a first medicament and use of an antibacterial agent in the manufacture of a second medicament, wherein the first and second medicaments are to be used in combination therapy to treat a bacterial infection.

~~22~~20. ~~A~~ The use~~compound~~ as claimed in any one of claims ~~21~~17 to 19, wherein the compound and the antibacterial agent are presented in the same dosage forms.

~~23~~21. ~~A compound~~The use as claimed in any one of claims ~~21~~ 17 to 20~~or 22~~, wherein the antibacterial agent is a carbapenem, and preferably the carbapenems is selected from the group comprising: meropenem, faropenem, imipenem, ertapenem, doripenem, panipenem/betamipron and biapenem, razupenem, tebipenem, lenapenem and tomopenem~~.~~, optionally

~~24. A compound as claimed in claim 23,~~ wherein the antibacterial agent is meropenem.

~~25~~22. ~~A compound~~The use as claimed in any of claims ~~20~~ 16 to ~~21~~24, wherein the bacterial infection is caused by bacteria from one or more of the following families; *Streptococcus, Acinetobacter, Staphylococcus, Clostridioides, Pseudomonas*, *Escherichia, Salmonella, Klebsiella, Legionella, Neisseria, Enterococcus*, *Enterobacter, Serratia, Stenotrophomonas, Aeromonas, Mycobacterium, Morganella, Yersinia, Pasteurella, Haemophilus, Citrobacter, Burkholderia, Brucella, or Moraxella.*

~~26. A method for the prevention or treatment of bacterial infection in a patient in need of such treatment, said method comprising administering to said patient a therapeutically effective amount of a combination of an antibacterial agent with a compound of in any of claims 1 to 11, or a pharmaceutically acceptable salt, hydrate or solvate thereof; or administering to said patient a therapeutically effective amount of an antibacterial agent in combination with a pharmaceutical composition, as claimed in claim 12, containing a compound of Formula (I) or a pharmaceutically acceptable salt, hydrate or solvate thereof.~~

~~27. A method for the prevention or treatment of a disease or disorder, said method comprising administering to a patient in need of such treatment a therapeutically effective amount of a combination of an antibacterial agent with a compound of any of claims 1 to 11, or a pharmaceutically acceptable salt, hydrate or solvate thereof; or administering to said patient a therapeutically effective amount of an antibacterial agent in combination with~~

a pharmaceutical composition as claimed claim 12, containing a compound of or a pharmaceutically acceptable salt, hydrate or solvate thereof.

28. The method of claim 27, wherein the disease or disorder is caused by aerobic or anaerobic Gram-positive, or aerobic or anaerobic Gram-negative bacteria.

29. The method of claim 28, wherein the disease or disorder is caused by metallo-β-lactamase producing Gram-positive bacteria.

30. The method of claim 28 or 29, wherein the disease or disorder is selected from: pneumonia, respiratory tract infections, urinary tract infections, intra-abdominal infections, skin and soft tissue infections, bloodstream infections, septicaemia, intra- and post-partum infections, prosthetic joint infections, endocarditis, acute bacterial meningitis and febrile neutropenia.

31. The method of claim 30, wherein the disease or disorder is selected from: community acquired pneumonia, nosocomial pneumonia (hospital-acquired/ventilator-acquired), respiratory tract infections associated with cystic fibrosis, non-cystic fibrosis bronchiectasis, COPD, urinary tract infection, intra-abdominal infections, skin and soft tissue infection, bacteraemia, septicaemia, intra- and post-partum infections, prosthetic joint infections, endocarditis, acute bacterial meningitis and febrile neutropenia.

32. The method of claim 31, wherein the disease or disorder is selected from: community acquired pneumonia, nosocomial pneumonia (hospital-acquired/ventilator-acquired), respiratory tract infections associated with cystic fibrosis, non-cystic fibrosis bronchiectasis, COPD, urinary tract infection, intra-abdominal infections, skin and soft tissue infection, bacteraemia and septicaemia.