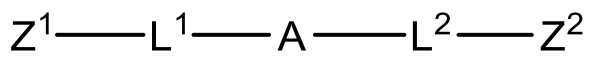
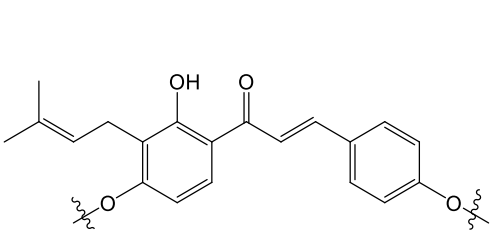
Claims

1. A compound having the following formula (I):

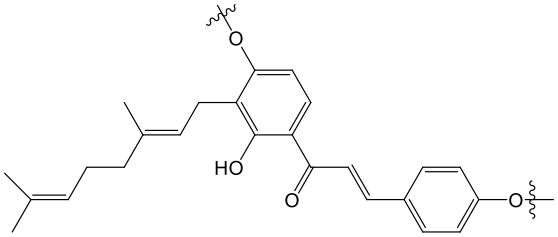


formula (I)

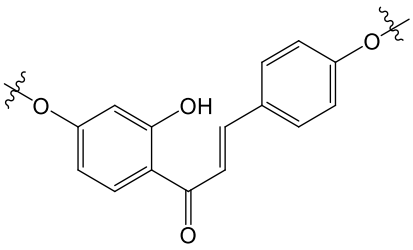
wherein A is selected from the group consisting of



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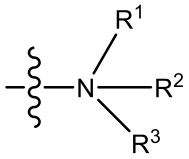
, and any mixture thereof, wherein the broken bond represents where the structure attaches to the remainder of formula (I);

L^1 and L^2 are independently a linker; and

Z^1 and Z^2 are independently an N-containing moiety.

2. The compound according to claim 1, wherein Z^1 and Z^2 independently have a pKa value greater than 9.

3. The compound according to claim 1 or 2, wherein Z^1 and Z^2 independently have the following structure:



wherein the broken bond represents where the structure attaches to the remainder of formula (I);

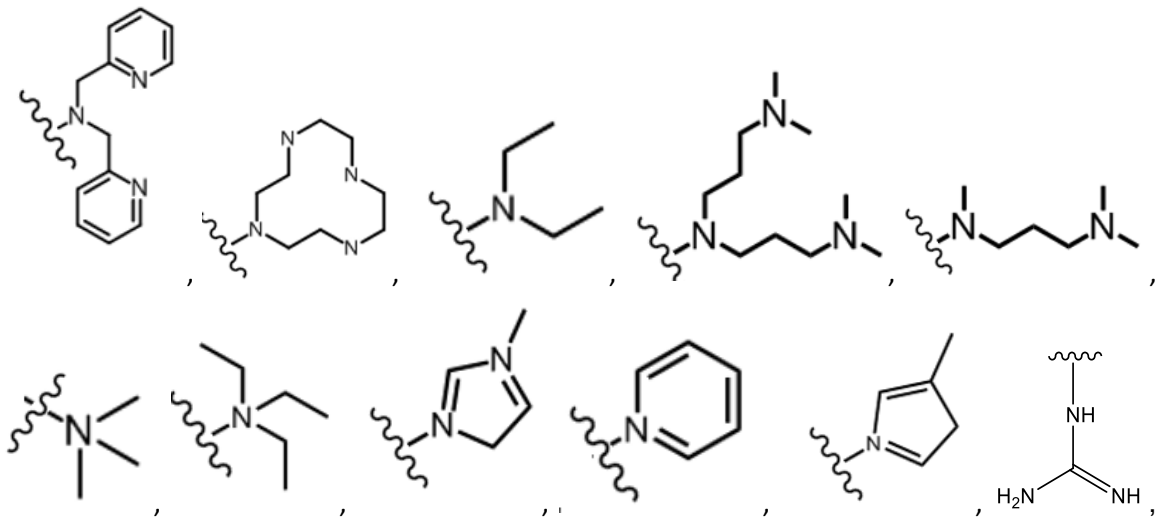
R^1 and R^2 are independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aminoalkyl, guanidine, substituted or unsubstituted guanidylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, amino acid or peptide, or R^1 and R^2 are taken

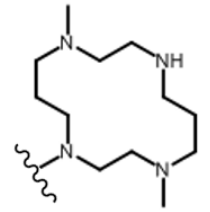
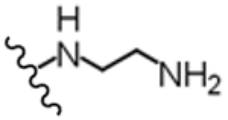
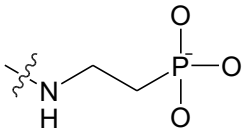
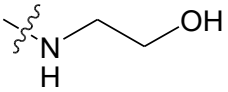
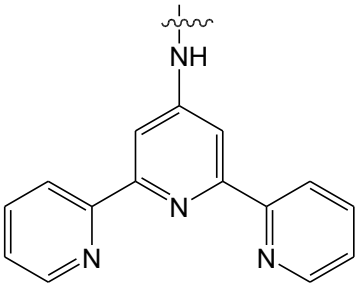
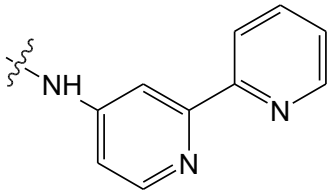
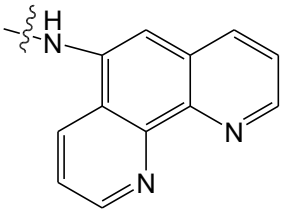
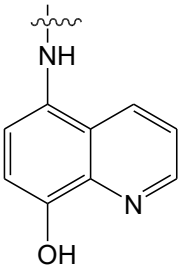
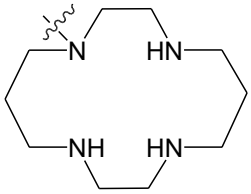
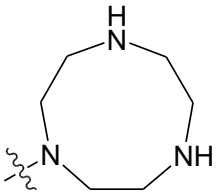
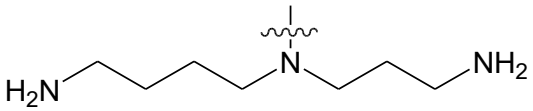
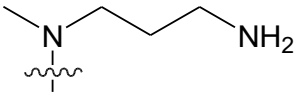
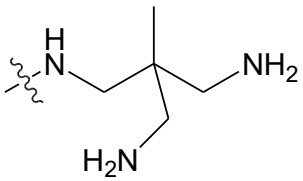
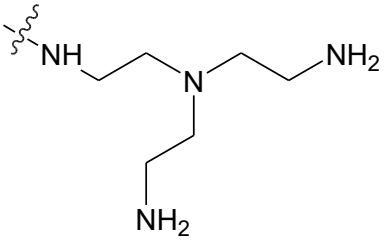
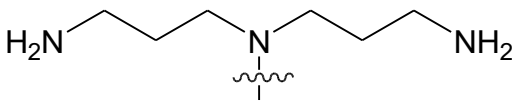
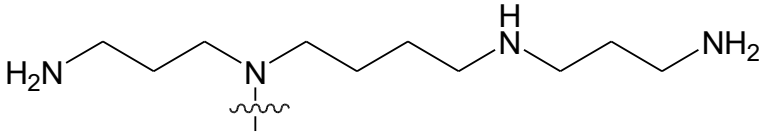
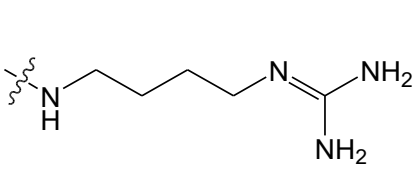
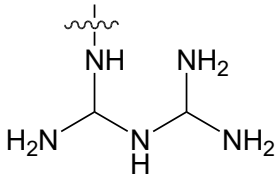
together to form a saturated or unsaturated, substituted or unsubstituted heterocyclic ring; and

R^3 is absent or hydrogen, or substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aminoalkyl, guanidine, substituted or unsubstituted guanidylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, amino acid or peptide,

wherein when R^3 is present, the nitrogen atom is a cationic quaternary nitrogen.

4. The compound according to claim 3, wherein R^1, R^2 and R^3 independently comprise a functional group selected from the group consisting of amine, guanidine, pyrrolidine, pyrrole, imidazolidine, pyrazolidine, imidazole, pyrazole, triazole, piperidine, pyridine, piperazine, diazine, hydroxamic acid, hydrazine, N-hydroxyurea, squaric acid, carbamolyphosphonate, oxazoline, pyrimidinetrione, 1-hydroxy-2(1H)-pyridinone (1,2-HOPO) and any combination thereof; and/or wherein R^1, R^2 and R^3 are independently selected from the group consisting of methyl, ethyl, propyl, butyl, $-(CH_2)_xNR'R''$, $-(CH_2)_xOH$, $-(CH_2)_xPO_3$, $-(CH_2)_xCR'R''R'''$, $-(C(NH_2)NHC(NH_2))x-NH_2$, guanidine, 2-methylpyridine, 1-methylimidazole, pyridine, bipyridine, terpyridine, phenanthroline, 3-methylpyrrole, cyclen (1,4,7,10-tetraazacyclododecane), cyclam (1,4,8,11-tetraazacyclotetradecane), 1,8-dimethyl-1,4,8,11-tetraazacyclotetradecane, 1,4,7-triazacyclononane, arginine, polyarginine, lysine, polylysine, poly-epsilon lysine and any mixture thereof, wherein x is any integer from 1 to 10, and R', R'' and R''' are independently hydrogen or substituted or unsubstituted alkyl; and/or wherein Z^1 and Z^2 are independently selected from the group consisting of:

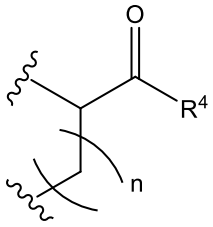


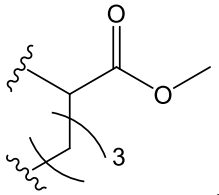



















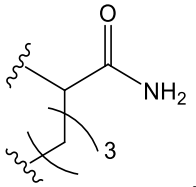
and any combination thereof.

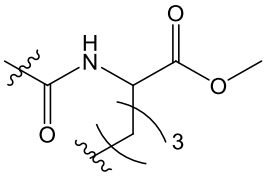
5. The compound according to any one of the preceding claims, wherein L^1 and L^2 are independently a substituted or unsubstituted alkyl, substituted or unsubstituted

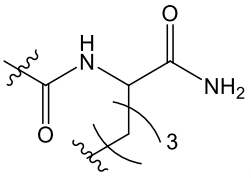
alkenyl, substituted or unsubstituted alkynyl, ester, amide, ether, -(O-CH_2-CH_2-O)$_n$-, L^3 or any combination thereof, wherein L^3 has the following structure:



wherein n is an integer from 1 to 10 and R^4 is an amino or a heteroalkyl and the broken bond represents where the structure attaches to the remainder of formula (I); preferably wherein L^1 and L^2 are independently selected from the group consisting of -(CH_2)$_4$-, amide, 

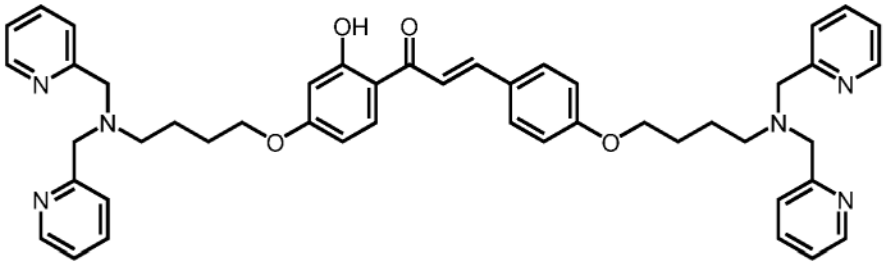
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, and any combination thereof, or 

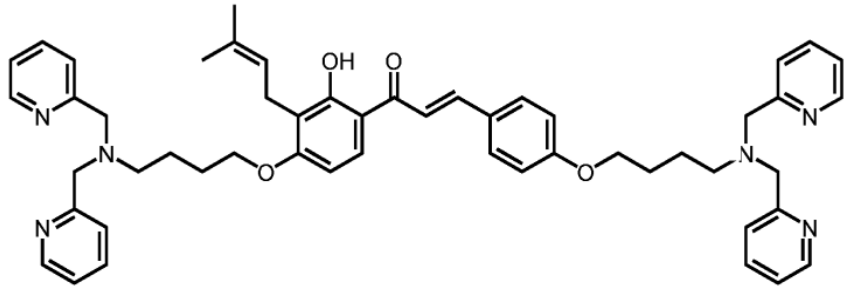
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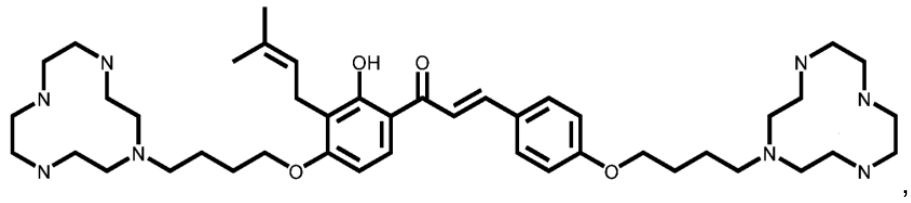
6. The compound according to any one of the preceding claims, wherein the compound of formula (I) has a logP value greater than 4; and/or wherein the compound of formula (I) has the following structure:



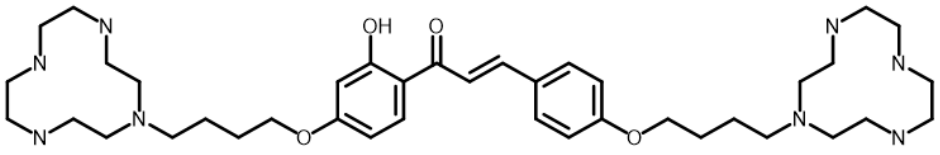
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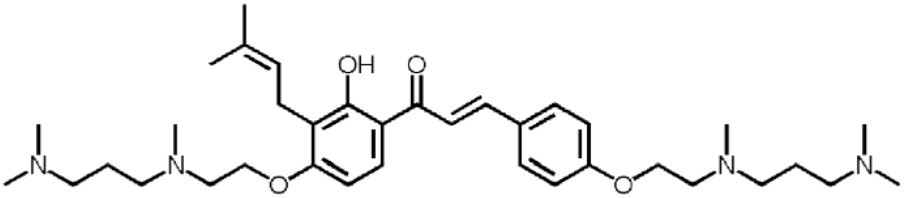


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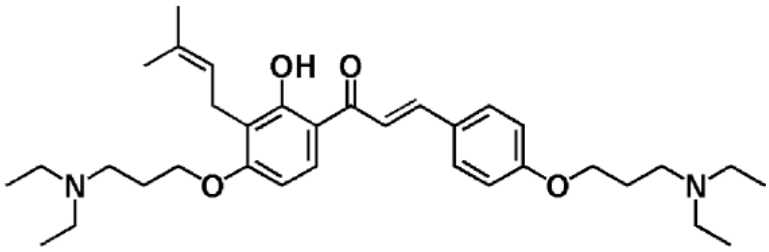


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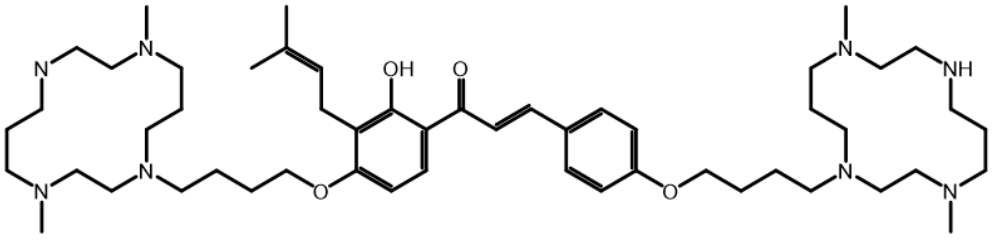




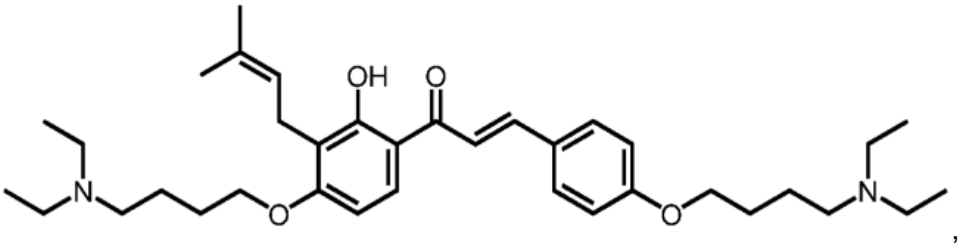
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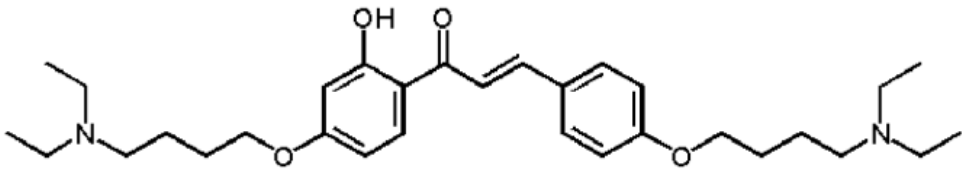
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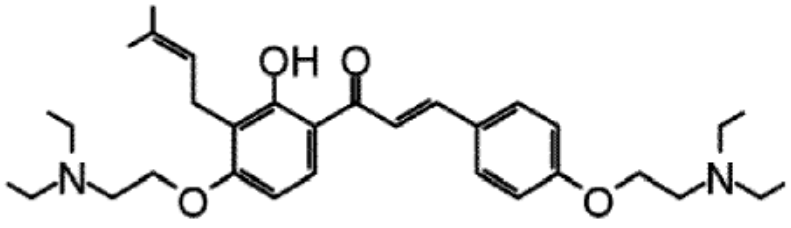
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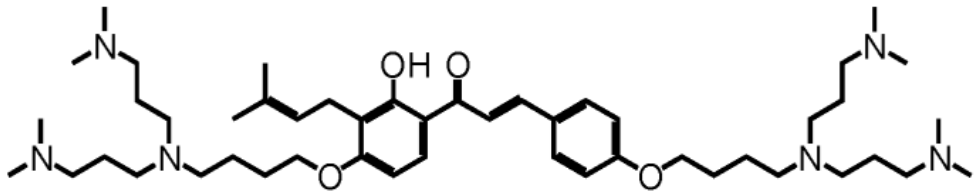
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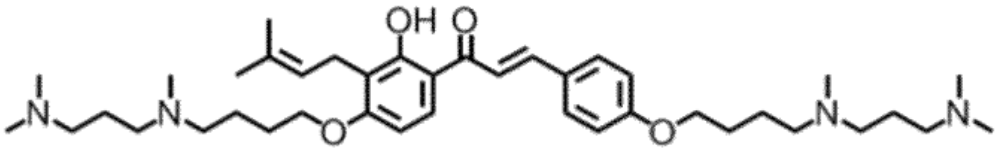
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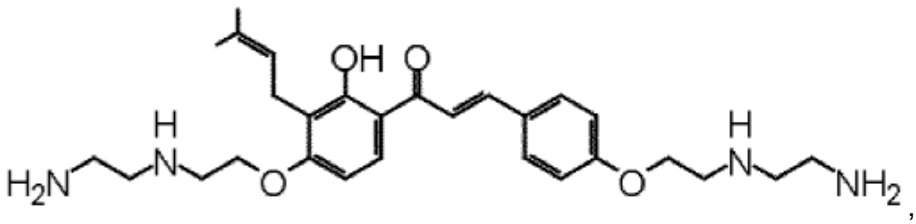
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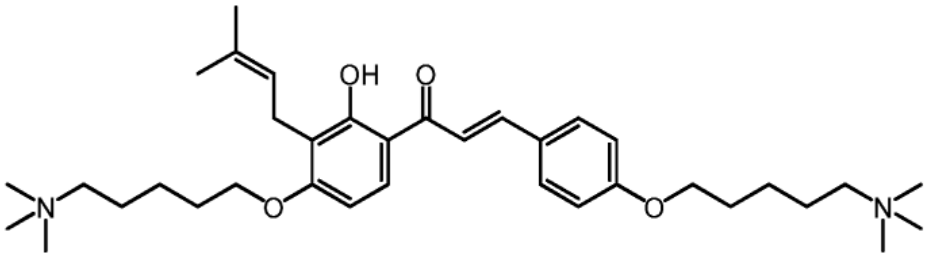
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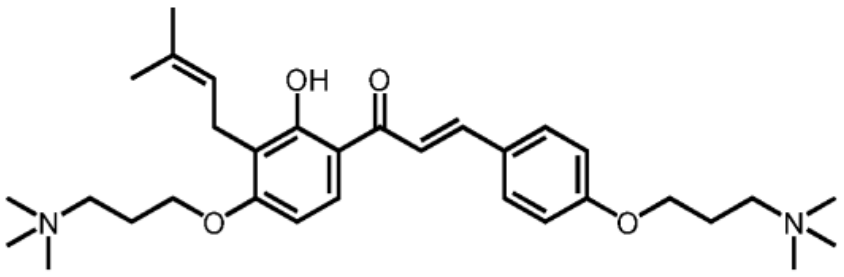
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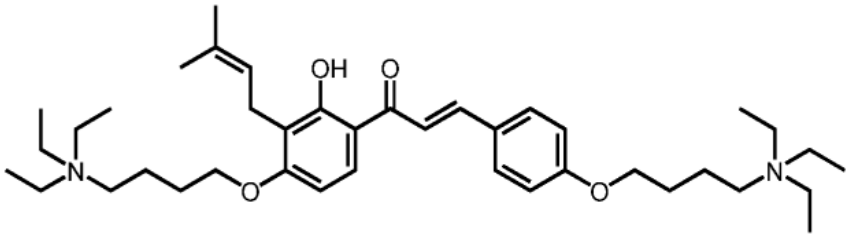
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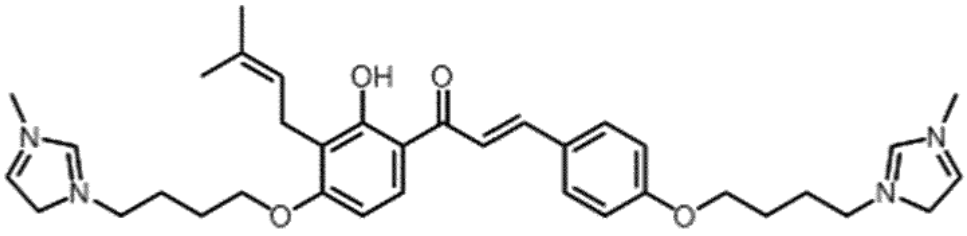
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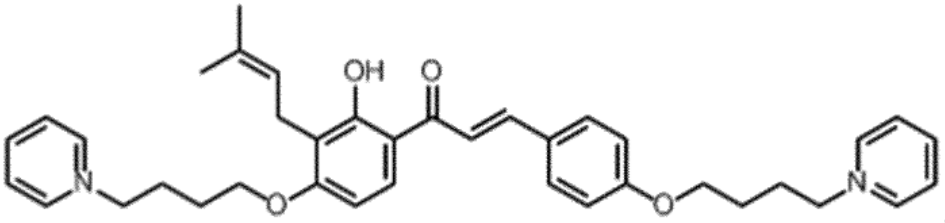
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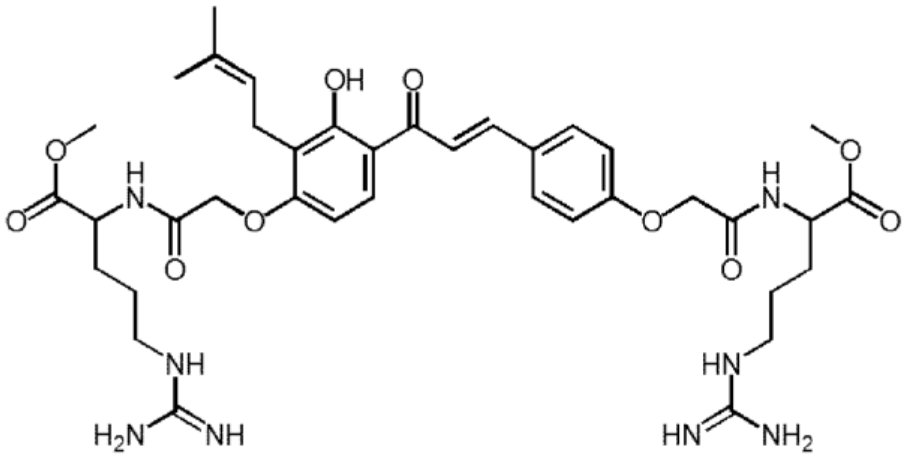
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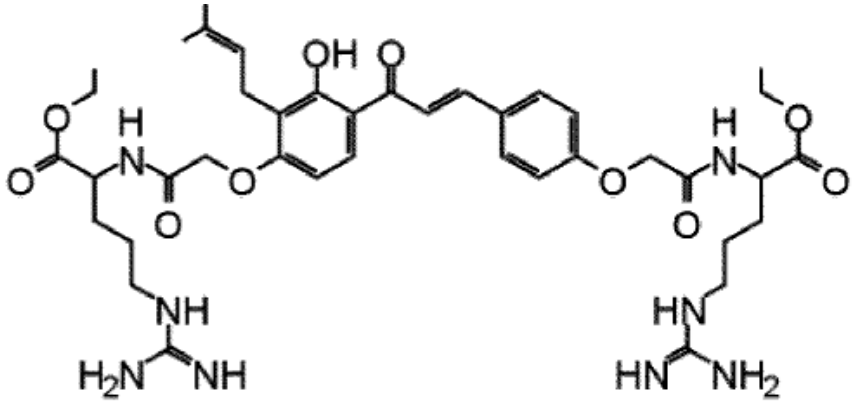
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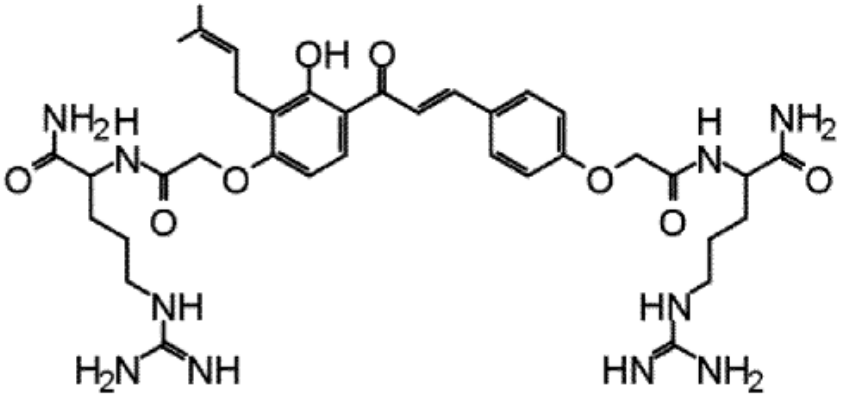
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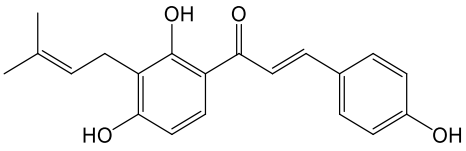
;

and/or wherein each N-containing moiety is independently chelated to zinc; and/or wherein each N-containing moiety independently has a positive charge.

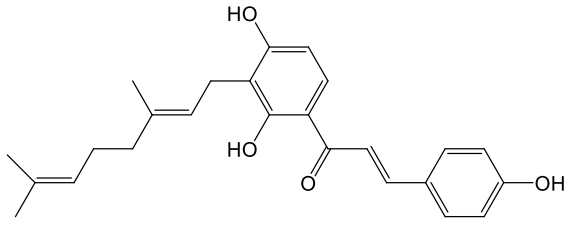
7. A pharmaceutical composition comprising a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt or hydrate thereof, in association with a pharmaceutically acceptable carrier.

8. A process for preparing a compound according to any one of claims 1 to 6, comprising the steps of:

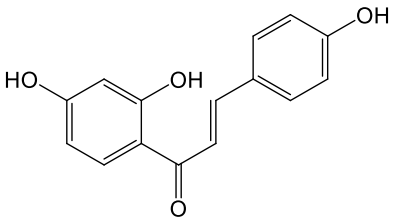
   1) contacting a hydrophobic moiety selected from the group consisting of:



,



,



, with a linker under reaction conditions; and

   2) contacting the linker with an N-containing moiety under reaction conditions.

9. The process according to claim 8, wherein a covalent bond is formed between the hydrophobic moiety and the linker or the linker and the N-containing moiety; and/or wherein the linker is selected from the group consisting of 1,4-dibromobutane, 1,3-diiodobutane, ethyl iodoacetate, hydroxybenzotriazole, 1,2-dibromoethane, 1,3-dibromopropane, methyl iodoacetate, methyl bromoacetate, 1,4-diiodobutane and any combination thereof; and/or wherein the N-containing moiety is selected from the group consisting of dipicolylamine, cyclen, 1,8-dimethyl,1,4,8,11-tetracyclotetradecane, diethylamine, -NH[$(CH_2)_3N(CH_3)]_2$, -$NH_2(CH_2)_3N(CH_3)_2$, 5-

bromopentyltrimethylammonium bromide, 3-bromopentyl trimethylammonium bromide, 4-bromobutyl triethylammonium bromide, 3-(4-Bromobutyl)-1-methylimidazole bromide, 1-(4-Bromobutyl)pyridine bromide, 1-(4-Bromobutyl)pyridine bromide and any combination thereof, and/or wherein the process comprises the step of adding zinc after the N-containing moiety is covalently bonded to the linker or hydrophobic moiety; and/or wherein the contacting is done in a solvent selected from the group consisting of acetone, methanol, ethanol, propanol, butanol, N,N-dimethylformamide, dimethylsulfoxide, tetrahydrofuran, dichloromethane, pyridine, water and any mixture thereof; and/or wherein the contacting step is performed at a temperature in the range of about 21 °C to about 160 °C; and/or wherein the contacting step is performed for a duration in the range of about 2 hours to about 36 hours.

10. Use of the compound according to any one of claims 1 to 6 or the pharmaceutical composition according to claim 7, to kill or inhibit the growth of a microorganism in vitro; preferably wherein the compound according to any one of claims 1 to 6 is used in conjunction with colistin.

11. A compound according to any one of claims 1 to 6 for use in therapy.

12. Use of a compound according to any one of claims 1 to 6 in the manufacture of a medicament for the treatment of a bacterial infection; preferably wherein the compound according to any one of claims 1 to 6 is administered in conjunction with colistin.

13. The use according to claim 12, wherein the compound according to any one of claims 1 to 6 is present at an amount in the range of about 2 μg/mL to about 75 μg/mL; and/or wherein the compound according to any one of claims 1 to 6 and colistin are present at an equal amount by weight, or the compound according to claim 1 to 6 is present in excess of about 1.5 to about 6 times of colistin by weight, preferably wherein colistin is present at a range of about 1 mg/kg to about 10 mg/kg and the compound according to any one of claims 1 to 6 is present at a range of 10 mg/kg to about 50 mg/kg.

14. The use according to claim 12 and 13, wherein the compound according to claims 1 to 6 is to be administered intramuscularly, intraperitoneally, topically, subcutaneously or intravenously.