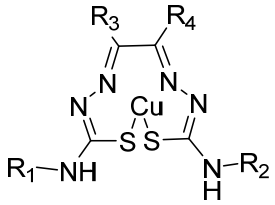
CLAIMS

1. A compound of Formula (V):



(V),

or pharmaceutically acceptable salts thereof, wherein:

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_3 is 4- to 8-membered heterocycle or 5-membered heteroaryl, wherein the 4- to 8-membered heterocycle is optionally substituted one, two, or three times with the group R_{3a}, and wherein the 5-membered heteroaryl is optionally substituted one, two, or three times with the group R_{3b};

R_{3a} independently for each occurrence is C_1-C_6 alkyl, C_1-C_6 alkyl-(C_6-C_{10} aryl), C_1-C_6 alkyl-(5- to 10-membered heteroaryl), $S(O)_2H$, $S(O)_2$-(C_1-C_6 alkyl), $S(O)_2$-(C_3-C_7 cycloalkyl), or $S(O)_2$-(C_6-C_{10} aryl); wherein each heteroaryl is optionally further substituted one to four times with C_1-C_6 alkyl or C_6-C_{10} aryl; and wherein each C_6-C_{10} aryl is optionally further substituted one to four times with C_1-C_6 alkyl;

R_{3b} independently for each occurrence is C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 alkyl-N(R_5)$_2$, (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), halo, nitro, cyano, C_6-C_{10} aryl, C(O)-(4- to 8-membered heterocycle), C_1-C_6 alkyl-(C_6-C_{10} aryl), C_1-C_6 alkyl-(5- to 10-membered heteroaryl), or C_1-C_6 alkyl-(4- to 8-membered heterocycle), wherein each 4- to 8-membered heterocycle, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl are optionally further substituted one to four times with C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, or halo;

R_4 is hydrogen or C_{1-3} alkyl; and

R_5 independently for each occurrence is hydrogen, C_1-C_6 alkyl, or C_1-C_3 alkyl-(C_6-C_{10} aryl).

2. The compound of claim 1, wherein:

R_1 is methyl or ethyl; and

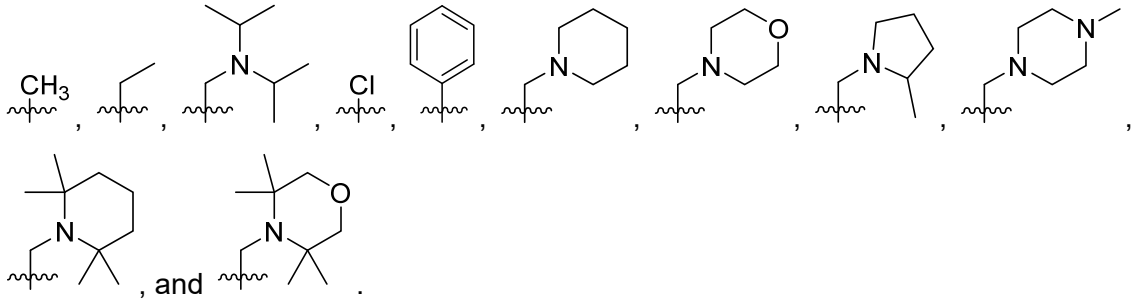
R_2 is methyl or ethyl.

3. The compound of any one of claims 1-2, wherein R_3 is tetrahydrofuranyl, morpholinyl, piperidinyl, furyl, thiophenyl, pyrrolyl, oxazolyl, pyrazolyl, or imidazolyl, wherein the tetrahydrofuranyl, morpholinyl, and piperidinyl are optionally substituted one, two, or three times with the group R_{3a}, and wherein the furyl, thiophenyl, pyrrolyl, oxazolyl, pyrazolyl, and imidazolyl are optionally substituted one, two, or three times with the group R_{3b}.

4. The compound of any one of claims 1-3, wherein R_3 is furyl, thiophenyl, oxazolyl, pyrazolyl, or imidazolyl optionally substituted one, two, or three times with the group R_{3b}.

5. The compound of any one of claims 1-4, wherein when R_1 is not methyl, R_2 is not methyl, and R_4 is not hydrogen, then R_{3b} independently for each occurrence is C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, C_1-C_6 alkyl-N(R_5)$_2$, (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), halo, nitro, cyano, C_6-C_{10} aryl, C(O)-(4- to 8-membered heterocycle), C_1-C_6 alkyl-(C_6-C_{10} aryl), C_1-C_6 alkyl-(5- to 10-membered heteroaryl), or C_1-C_6 alkyl-(4- to 8-membered heterocycle), wherein each 4- to 8-membered heterocycle, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl are optionally further substituted one or two times with C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, or halo.

6. The compound of any one of claims 1-5, wherein R_{3b} is selected from the group consisting of:

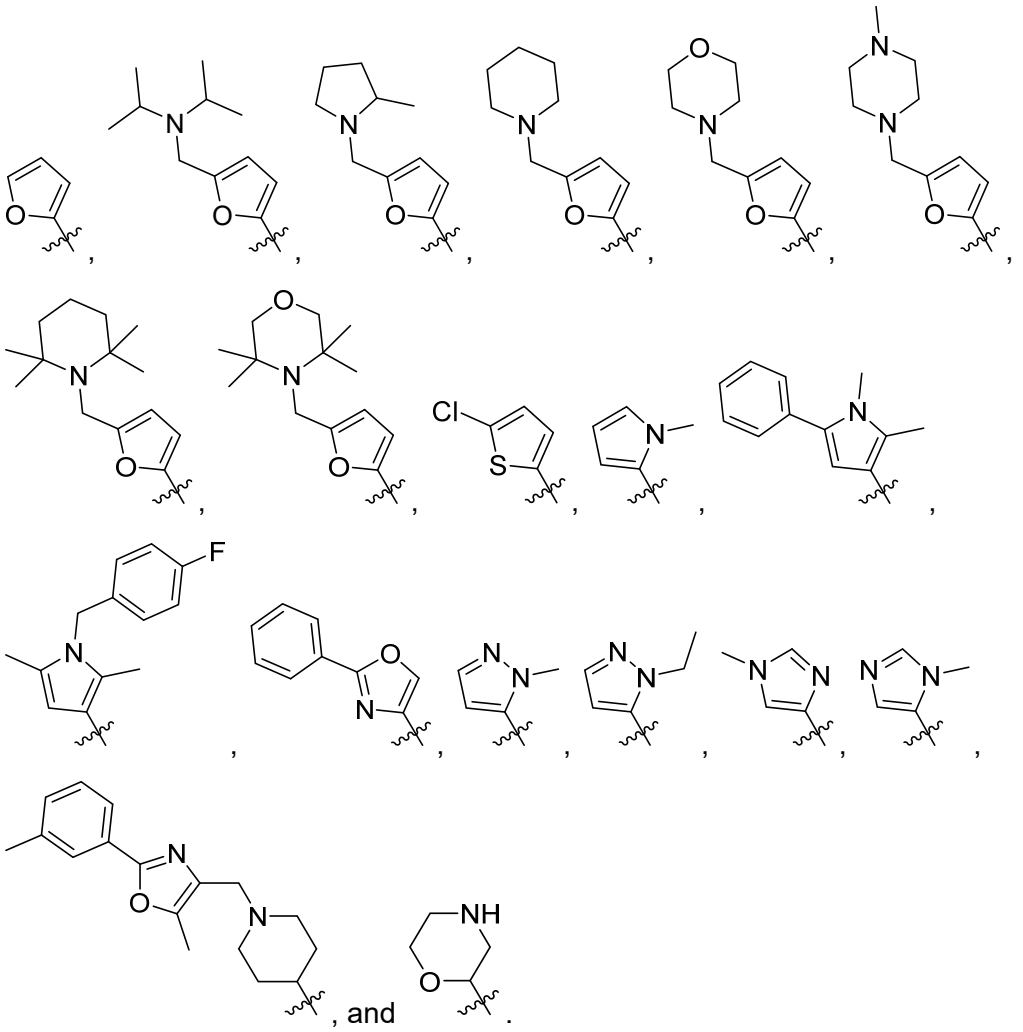


, and .

7. The compound of any one of claims 1-4 or 5, wherein R_3 is furyl optionally substituted one time with C_1-C_3 alkyl-N(C_1-C_4 alkyl)$_2$ or C_1-C_3 alkyl-(5- to 6-membered heterocycle), wherein the 5- to 6-membered heterocycle is optionally further substituted one to four times with C_1-C_3 alkyl.

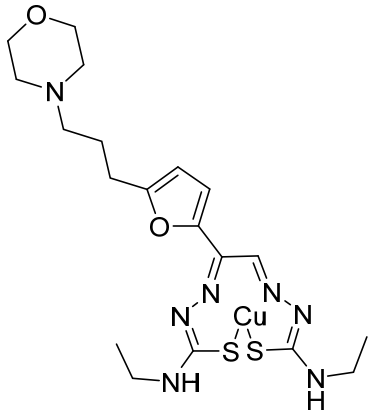
8. The compound of any one of claims 1-5, wherein R_3 is thiophenyl, oxazolyl, pyrazolyl, or imidazolyl, optionally substituted one, two, or three times with C_1-C_6 alkyl, halo, C_6-C_{10} aryl, or C_1-C_6 alkyl-(C_6-C_{10} aryl), wherein each C_6-C_{10} aryl is optionally further substituted one to four times with C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkyl, or halo.

9. The compound of any one of claims 1-3, wherein R_3 is selected from the group consisting of:

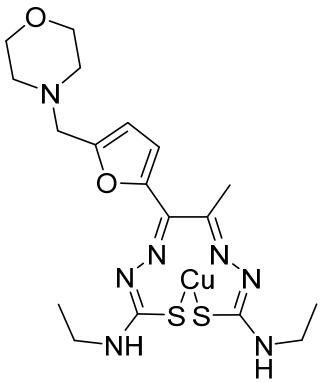


10. The compound of any one of claims 1-9, wherein R_4 is hydrogen or methyl.

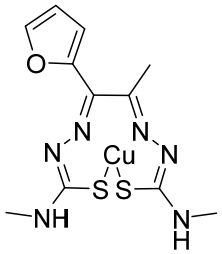
11. The compound of claim 1, selected from the group consisting of:



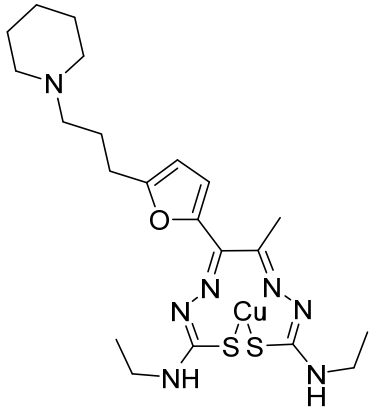
Compound 23



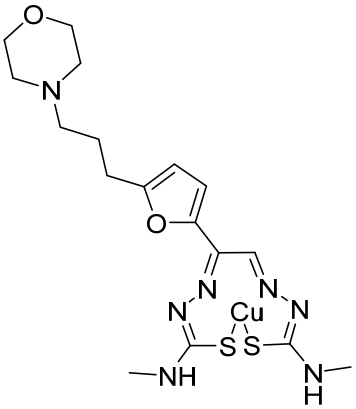
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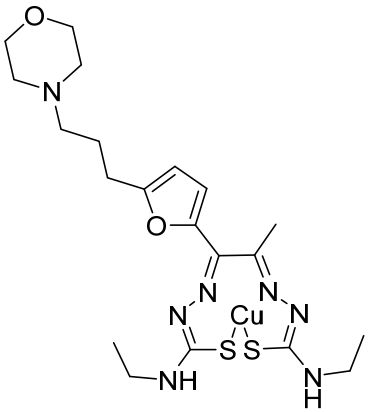
Compound 25



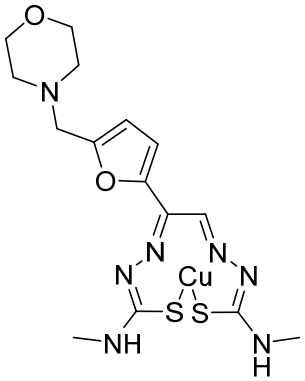
Compound 26



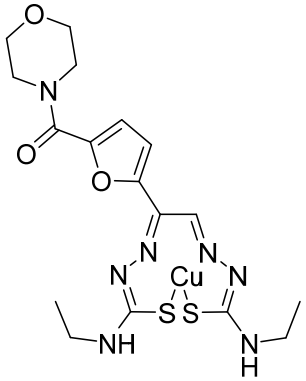
Compound 27



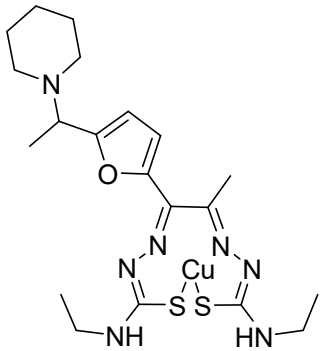
Compound 28



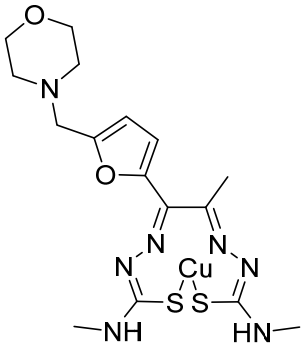
Compound 29



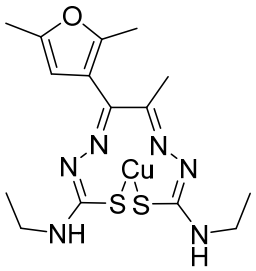
Compound 30



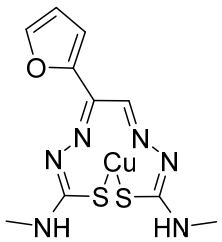
Compound 31



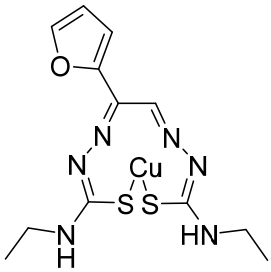
Compound 32



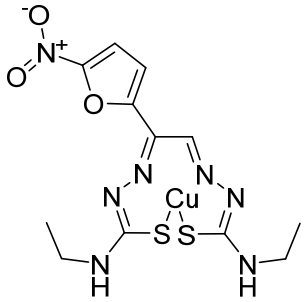
Compound 33



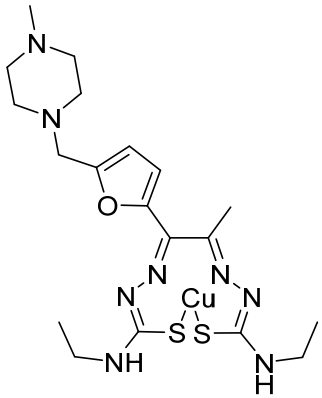
Compound 34



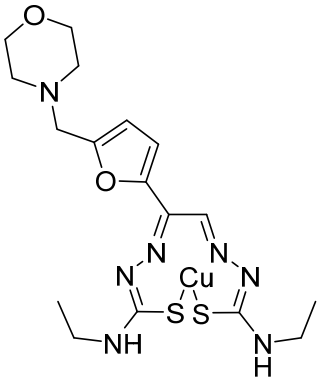
Compound 35



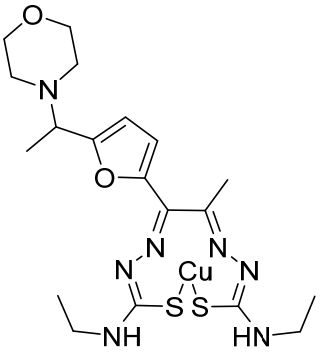
Compound 36



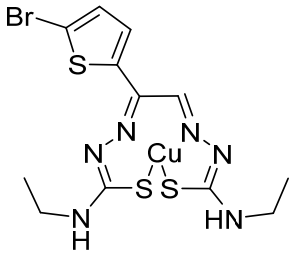
Compound 37



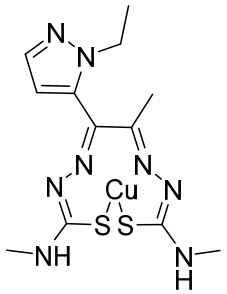
Compound 38



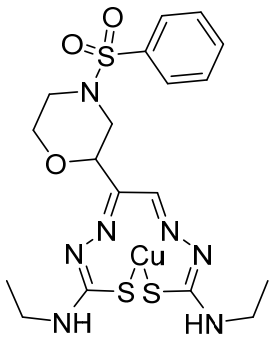
Compound 39



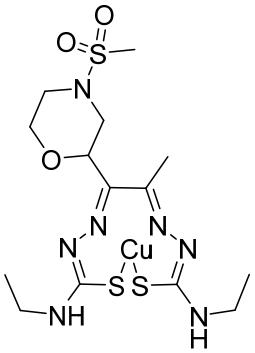
Compound 40



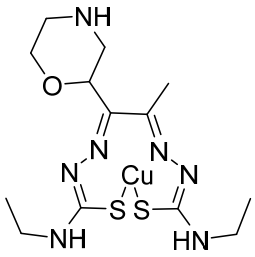
Compound 41



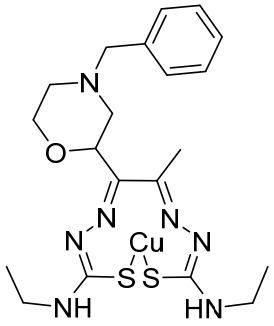
Compound 42



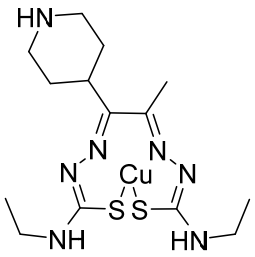
Compound 43



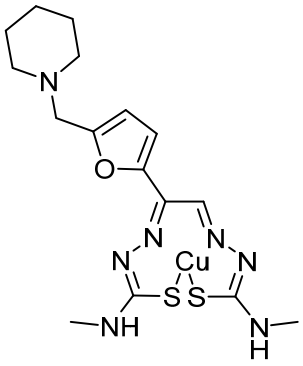
Compound 44



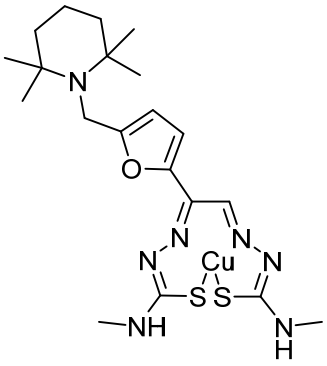
Compound 45



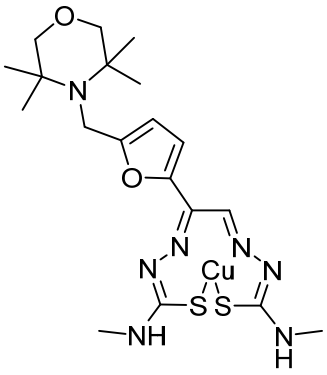
Compound 46.



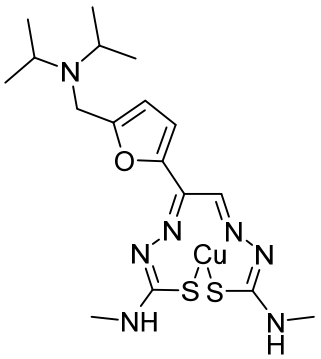
Compound 79



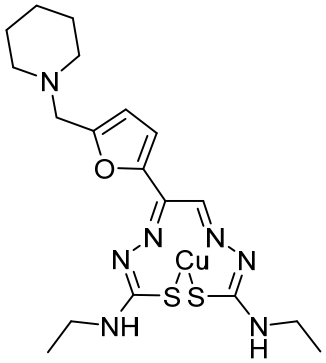
Compound 80



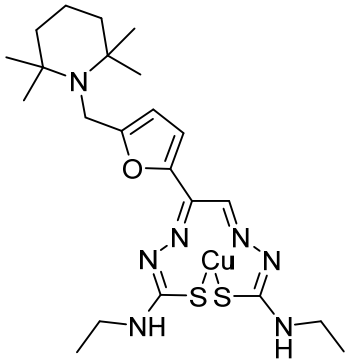
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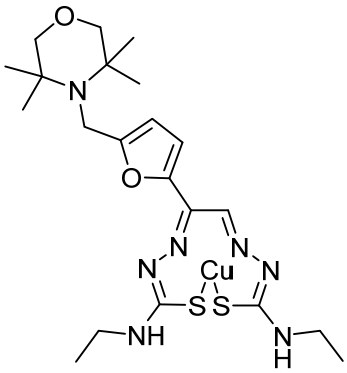
Compound 82



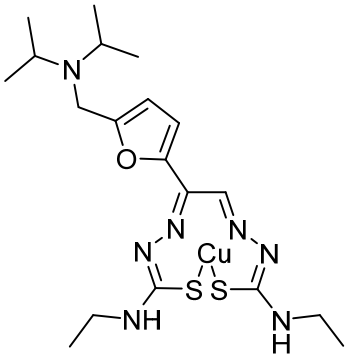
Compound 83



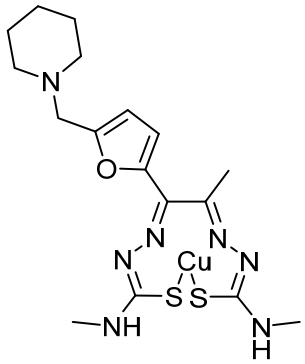
Compound 84



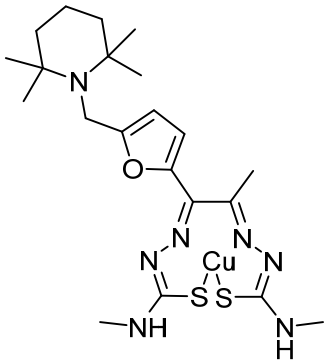
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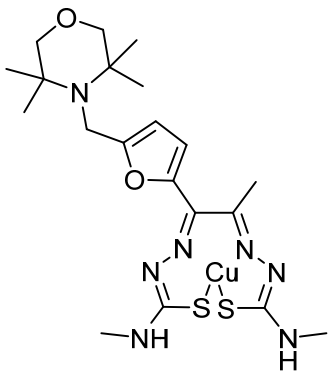
Compound 86



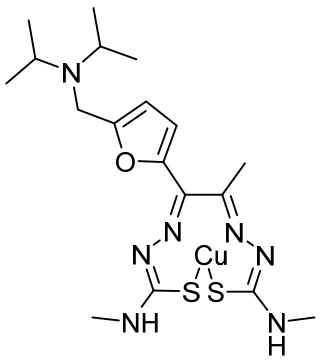
Compound 87



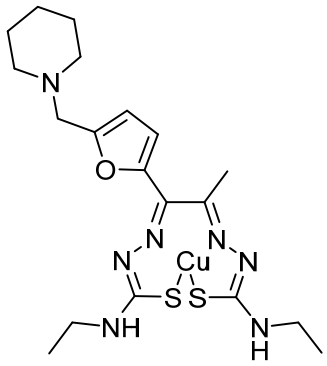
Compound 88



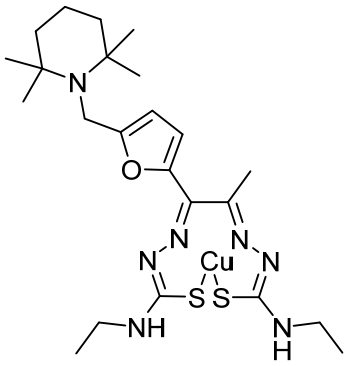
Compound 89



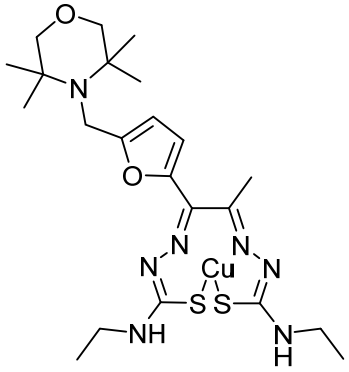
Compound 90



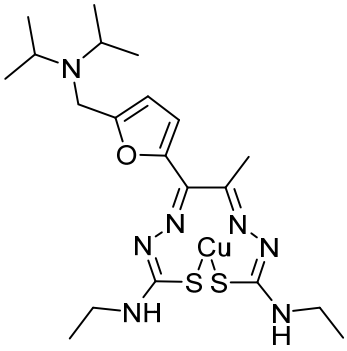
Compound 91



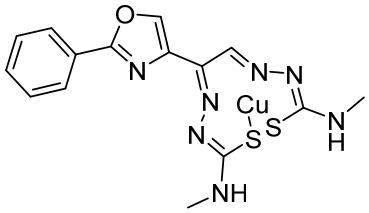
Compound 92



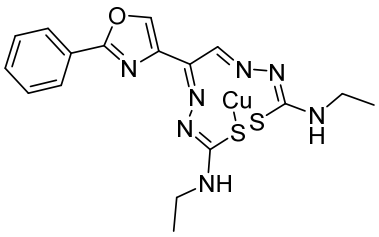
Compound 93



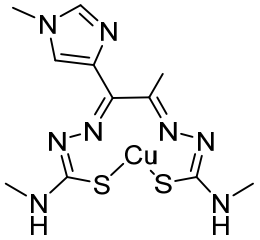
Compound 94



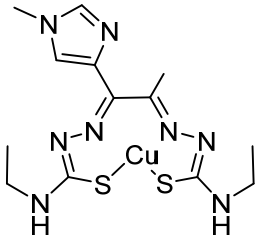
Compound 95



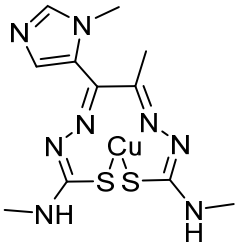
Compound 96



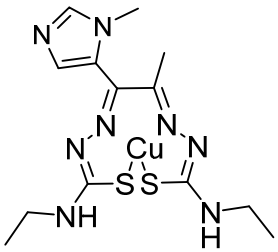
Compound 97



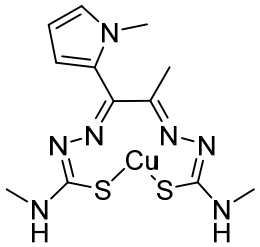
Compound 98



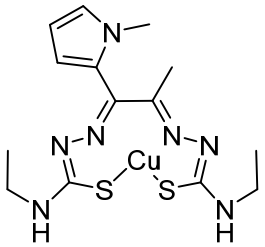
Compound 99



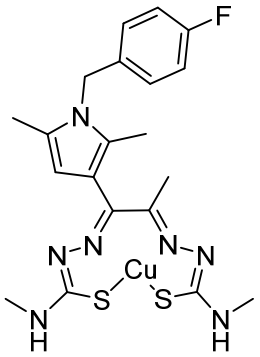
Compound 100



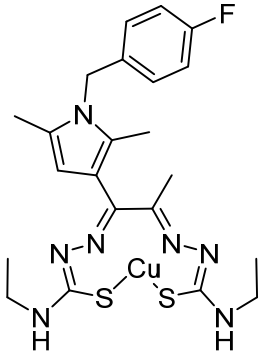
Compound 101



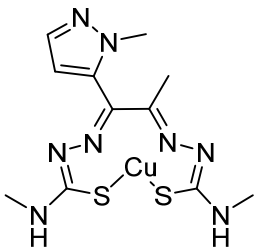
Compound 102



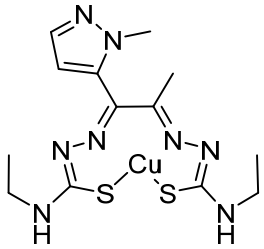
Compound 103



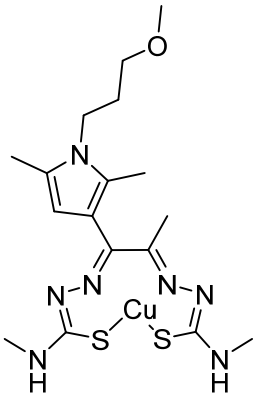
Compound 104



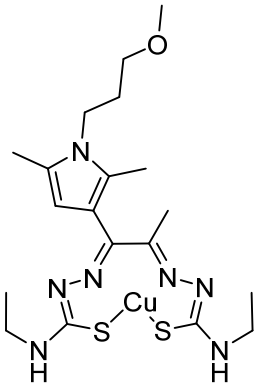
Compound 105



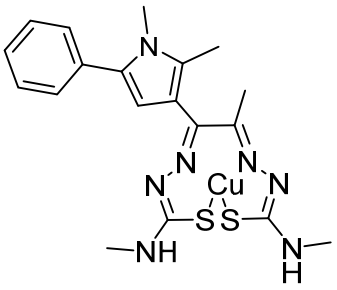
Compound 106



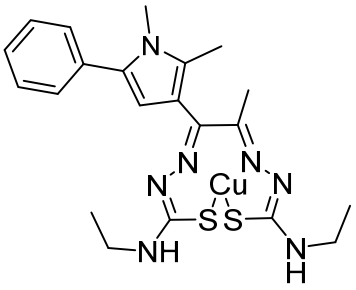
Compound 107



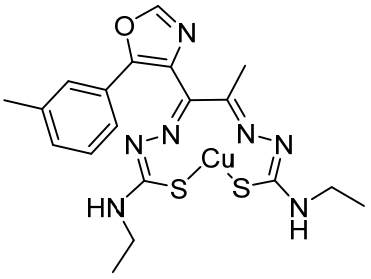
Compound 108



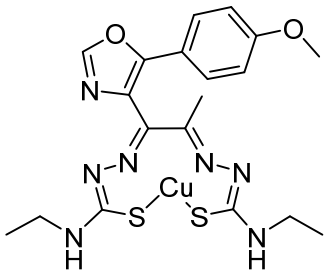
Compound 109

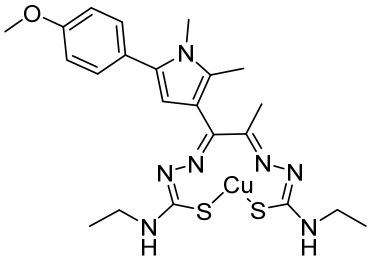


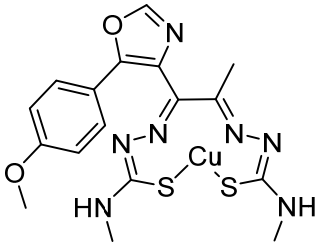
Compound 110



Compound 111



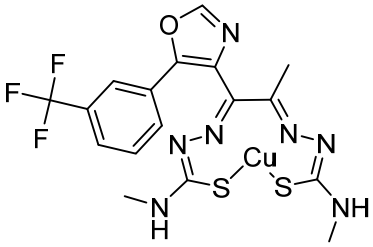


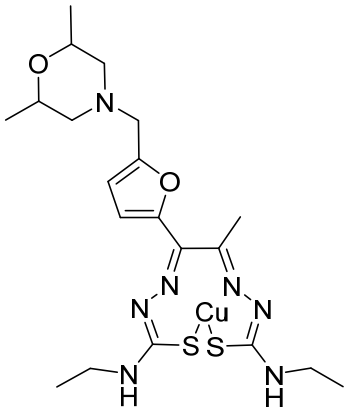


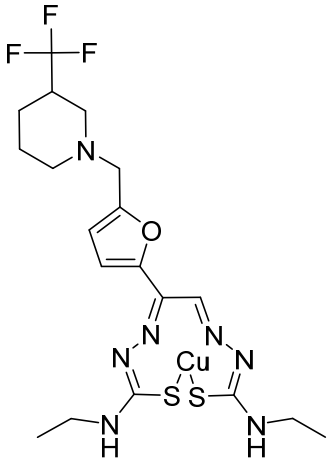
Compound 114

Compound 112

Compound 113



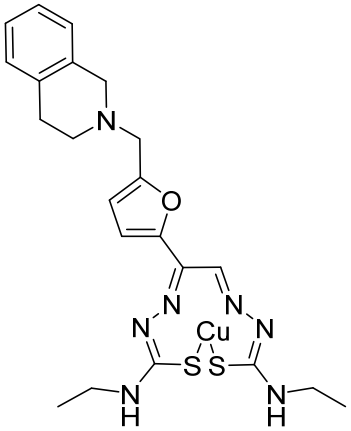


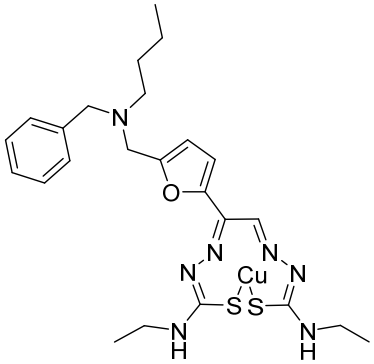


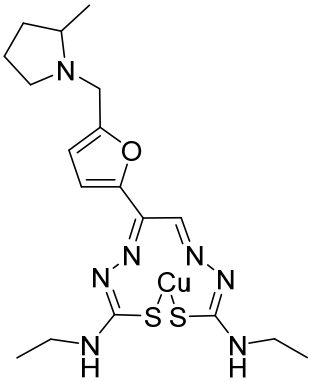
Compound 115

Compound 116

Compound 117



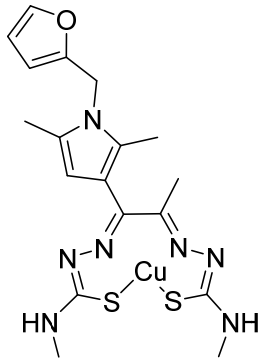


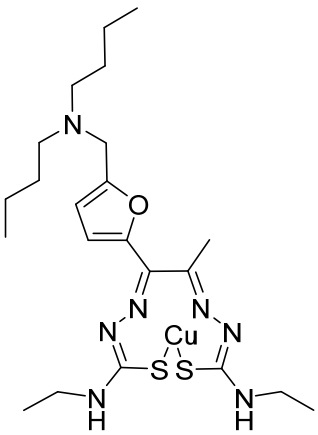


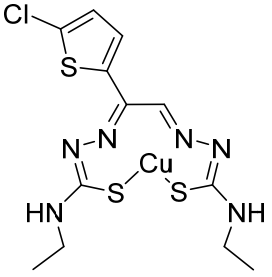
Compound 118

Compound 119

Compound 120



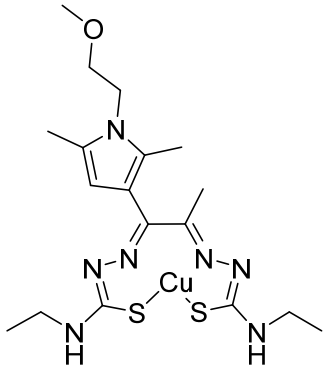




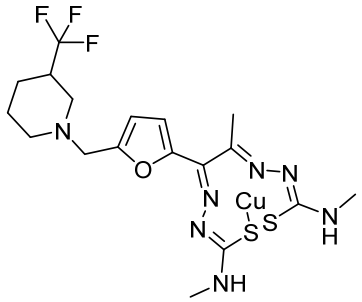
Compound 121

Compound 123

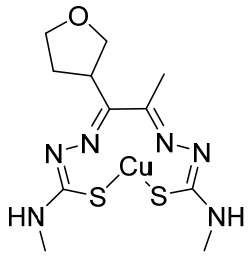
Compound 122



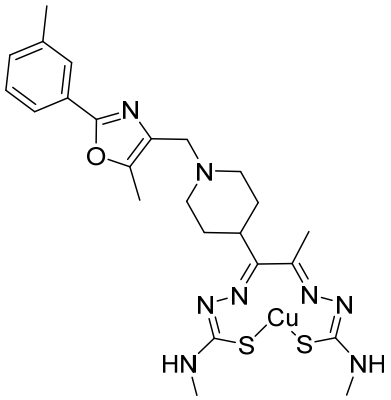
Compound 124



Compound 125



Compound 126

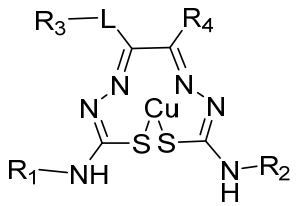


Compound 127

or a pharmaceutically acceptable salt thereof.

12. The compound of claim 11, selected from the group consisting of Compounds 25, 29, 32, 34, 41, 43, 44, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 90, 91, 94, 95, 96, 98, 100, 104, 105, 106, 120, and 123, or a pharmaceutically acceptable salt thereof.

13. A compound of Formula (IV):



(IV),

or pharmaceutically acceptable salts thereof, wherein:

L is C_3-C_7 cycloalkyl, C_1-C_6 alkyl, or absent;

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_3 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, C_3-C_{10} cycloalkyl, C(O)NH-(C_1-C_6 alkyl)-PPh_3, hydroxy, C_1-C_6 alkoxy, or O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), wherein the C_6-C_{10} aryl is substituted one, two, or three times with the group R_{3a}, and wherein the 5- to 10-membered heteroaryl is optionally substituted one, two, or three times with the group R_{3b};

R_{3a} independently for each occurrence is C_3-C_7 cycloalkyl or 4- to 8-membered heterocycle, wherein the 4- to 8-membered heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl;

R_{3b} independently for each occurrence is C_1-C_3 alkyl, C_1-C_3 alkoxy, C_3-C_7 cycloalkyl, or 4- to 8-membered heterocycle, wherein the heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl; and

R_4 is hydrogen, C_1-C_3 alkyl, or C_6-C_{10} aryl;

provided that when L is absent, R_3 is C_6-C_{10} aryl substituted one, two, or three times with the group R_{3a}; or when L is absent, R_3 is 6- to 10-membered heteroaryl substituted one, two, or three times with the group R_{3b}; or when L is absent, R_3 is 6- to 10-membered heteroaryl optionally substituted one, two, or three times with the group R_{3b}, and R_4 is H.

14. The compound of claim 13, wherein:

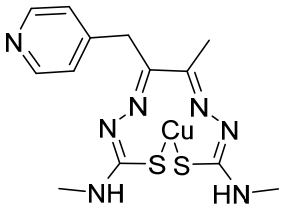
R_1 is methyl or ethyl; and

R_2 is methyl or ethyl.

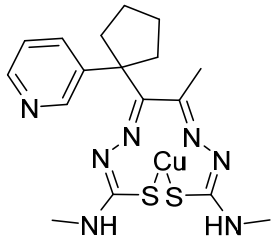
15. The compound of any one of claims 13-14, wherein R_3 is phenyl, pyrazolyl, pyridinyl, benzofuranyl, benzothiazolyl, benzodioxolyl, C_3-C_6 cycloalkyl, adamantyl, C(O)NH-(C_1-C_6 alkyl)-PPh_3, hydroxy, C_1-C_6 alkoxy, or O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), wherein the phenyl is substituted one, two, or three times with the group R_{3a}; and wherein the pyrazolyl, pyridinyl, benzofuranyl, benzothiazolyl, and benzodioxolyl are optionally substituted one, two, or three times with the group R_{3b}.

16. The compound of any one of claims 13-15, wherein when L is absent, R_3 is C_6-C_{10} aryl substituted one, two, or three times with the group R_{3a}; or when L is absent, R_3 is 6- to 10-membered heteroaryl substituted one, two, or three times with the group R_{3b}.

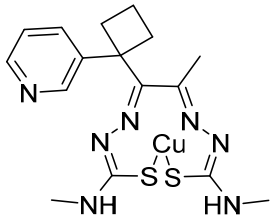
17. The compound of claim 13, selected from the group consisting of:



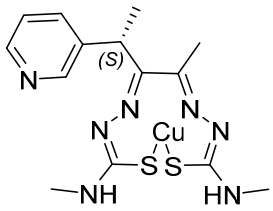
Compound 1



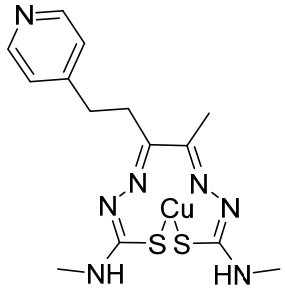
Compound 2



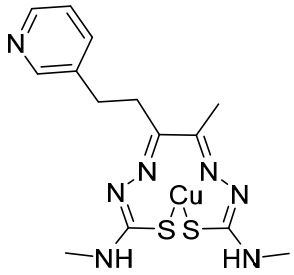
Compound 3



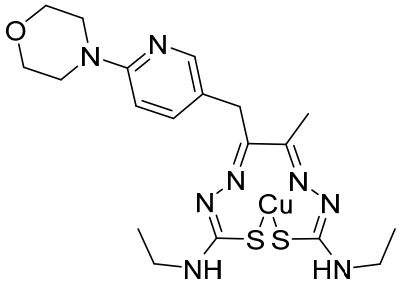
Compound 4



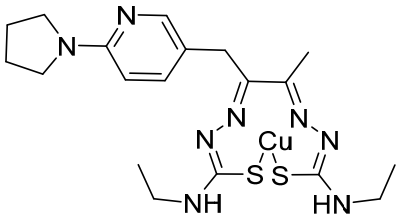
Compound 5



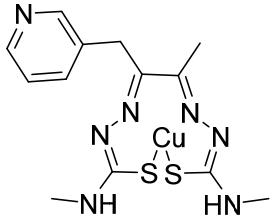
Compound 6



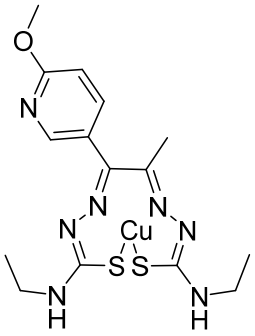
Compound 7



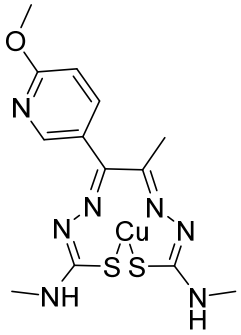
Compound 8



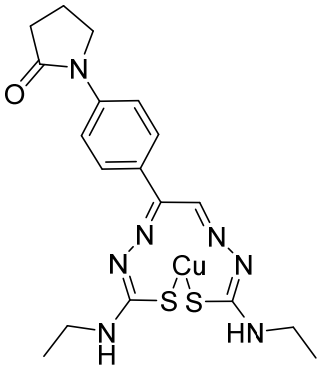
Compound 9



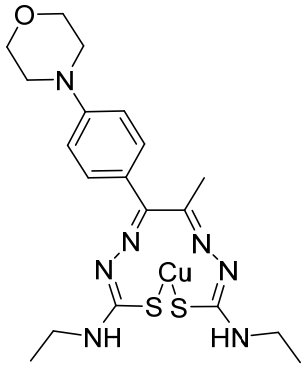
Compound 10



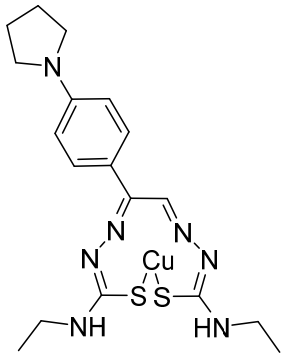
Compound 11



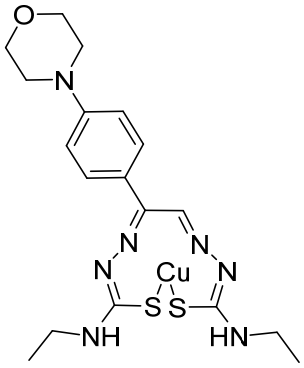
Compound 12



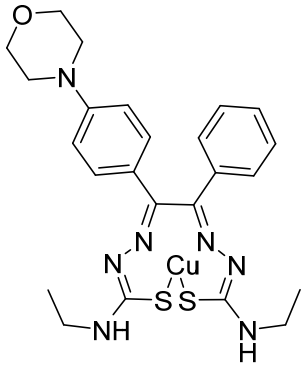
Compound 13



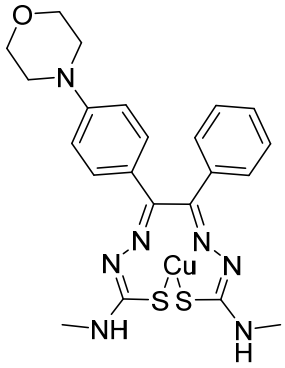
Compound 14



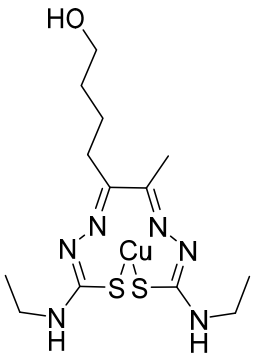
Compound 15



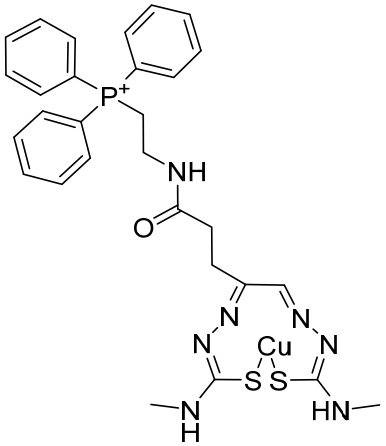
Compound 16



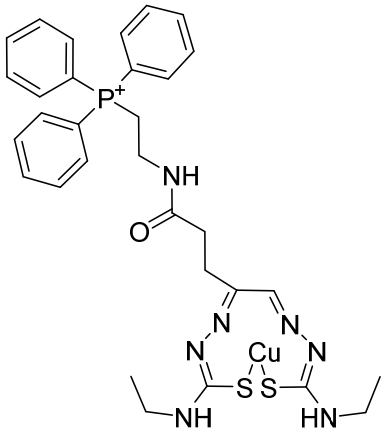
Compound 17



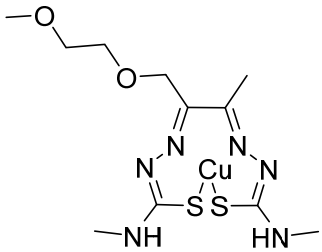
Compound 18



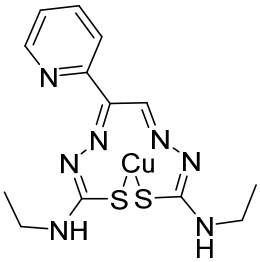
Compound 19



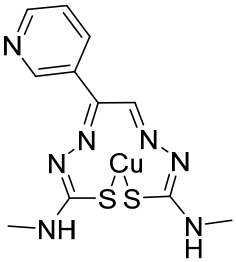
Compound 21



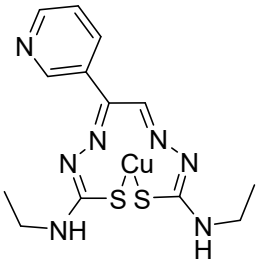
Compound 22



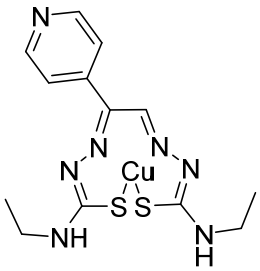
Compound 57



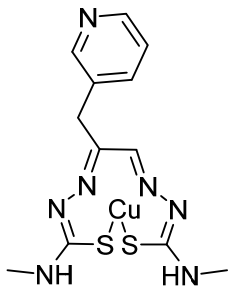
Compound 59



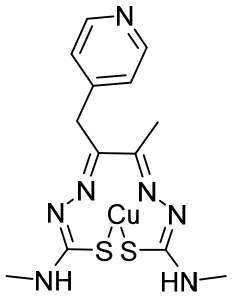
Compound 60



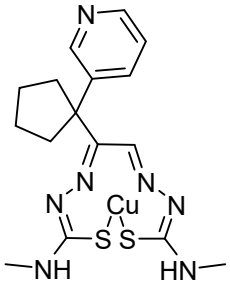
Compound 61



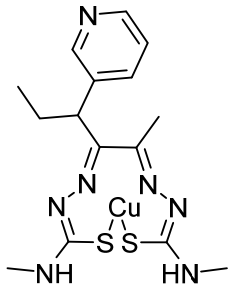
Compound 66



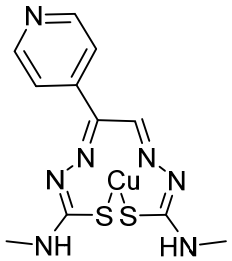
Compound 67



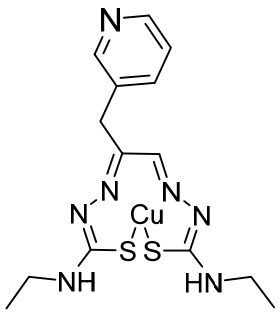
Compound 68



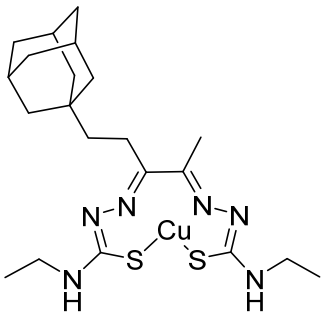
Compound 69



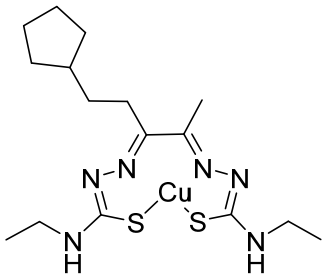
Compound 70



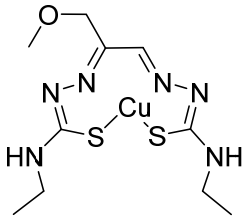
Compound 71



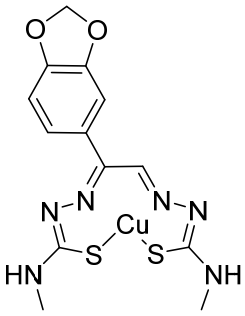
Compound 72



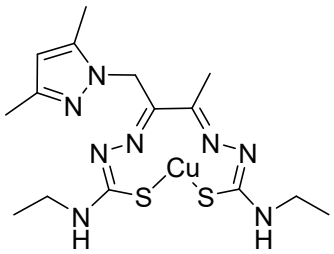
Compound 73



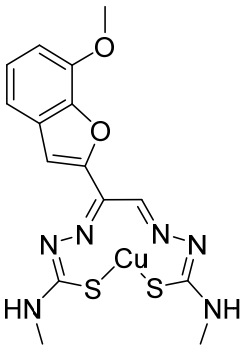
Compound 74



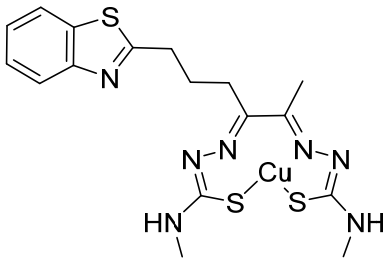
Compound 75



Compound 76



Compound 77

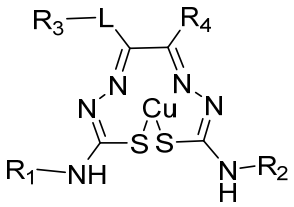


Compound 78

or a pharmaceutically acceptable salt thereof.

18. The compound of claim 17, selected from the group consisting of Compounds 2, 12, 15, 17, 59, 60, 61, 66, 74, and 77, or a pharmaceutically acceptable salt thereof.

19. The compound of claim 13, having a structure according to Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

L is C_3-C_7 cycloalkyl, C_1-C_6 alkyl, or absent

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

R_3 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, C(O)NH-(C_1-C_6 alkyl)-PPh_3, hydroxy, C_1-C_6 alkoxy, or O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), wherein the C_6-C_{10} aryl is substituted one, two, or three times with the group R_{3a}, and wherein the 5- to 10-membered heteroaryl is optionally substituted one, two, or three times with the group R_{3b};

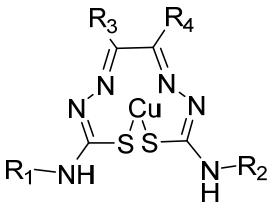
R_{3a} independently for each occurrence is C_3-C_7 cycloalkyl or 4- to 8-membered heterocycle, wherein the 4- to 8-membered heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl;

R_{3b} independently for each occurrence is C_1-C_3 alkoxy, C_3-C_7 cycloalkyl, or 4- to 8-membered heterocycle, wherein the heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl; and

R_4 is hydrogen, C_1-C_3 alkyl, or C_6-C_{10} aryl;

provided that when L is absent, R_3 is C_6-C_{10} aryl substituted one, two, or three times with the group R_{3a}; or when L is absent, R_3 is 6- to 10-membered heteroaryl substituted one, two, or three times with the group R_{3b}.

20. The compound of claim 1, having a structure according to Formula (II):



(II),

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

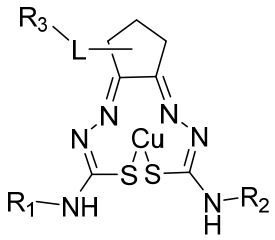
R_3 is 4- to 8-membered heterocycle or 5-membered heteroaryl, wherein the 4- to 8-membered heterocycle is optionally substituted one, two, or three times with the group R_{3a}, and wherein the 5-membered heteroaryl is optionally substituted one, two, or three times with the group R_{3b};

R_{3a} independently for each occurrence is C_1-C_6 alkyl, C_1-C_6 alkyl-(C_6-C_{10} aryl), $S(O)_2H$, $S(O)_2$-(C_1-C_6 alkyl), $S(O)_2$-(C_3-C_7 cycloalkyl), or $S(O)_2$-(C_6-C_{10} aryl);

R_{3b} independently for each occurrence is C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, halo, nitro, cyano, C(O)-(4- to 8-membered heterocycle), or C_1-C_6 alkyl-(4- to 8-membered heterocycle), wherein each 4- to 8-membered heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl; and

R_4 is hydrogen or C_{1-3} alkyl.

21. A compound of Formula (III):



(III),

or a pharmaceutically acceptable salt thereof, wherein:

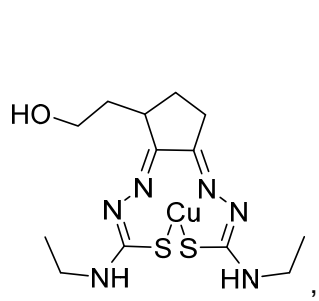
L is C_1-C_6 alkyl or absent

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

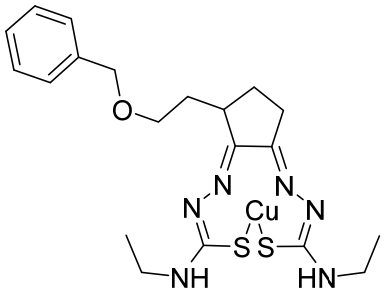
R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, $NH(C_1$-C_6 alkyl), or $N(C_1$-C_6 alkyl$)_2$;

R_3 is C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 haloalkyl, halo, hydroxy, $C(O)NH_2$, $C(O)NH(C_1$-C_6 alkyl), $C(O)N(C_1$-C_6 alkyl$)_2$, or C(O)-(4- to 8-membered heterocycle), wherein the C_1-C_6 alkyl and the C_1-C_6 alkoxy are optionally substituted one, two, or three times with C_6-C_{10} aryl, and wherein the C(O)-(4- to 8-membered heterocycle) is optionally substituted one, two, or three times with C_1-C_3 alkyl.

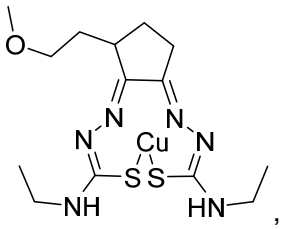
22. The compound of claim 21, selected from the group consisting of:



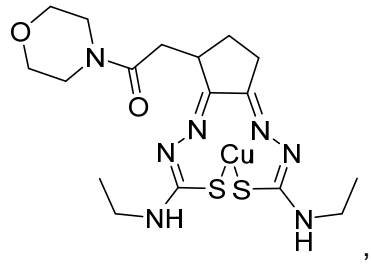
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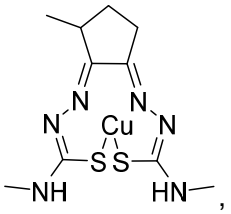
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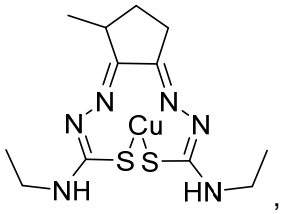
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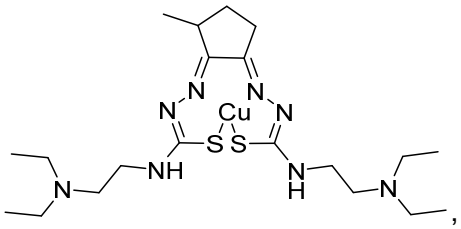
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,



,

and 

,

or a pharmaceutically acceptable salt thereof.

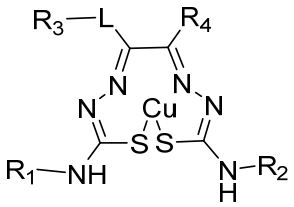
23. A pharmaceutical composition comprising a compound of any one of claims 1-22, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient, diluent, or carrier.

24. The compound of any one of claims 1-22, for use as a medicament.

25. Use of the compound of any one of claims 1-22 in the preparation of a medicament for treating or preventing a neurodegenerative disease in a subject in need thereof.

26. The use of claim 25, wherein the neurodegenerative disease is amyotrophic lateral sclerosis (ALS), frontal temporal dementia (FTD), Parkinson’s disease, Huntington’s disease, and Alzheimer’s disease.

27. A method of making a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt thereof, wherein:

L is C_3-C_7 cycloalkyl, C_1-C_6 alkyl, or absent

R_1 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_2 is C_1-C_6 alkyl optionally substituted with 5- to 10-memebered heteroaryl, NH_2, NH(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)$_2$;

R_3 is C_6-C_{10} aryl, 5- to 10-membered heteroaryl, C(O)NH-(C_1-C_6 alkyl)-PPh_3, hydroxy, C_1-C_6 alkoxy, or O-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl), wherein the C_6-C_{10} aryl is substituted one, two, or three times with the group R_{3a}, and wherein the 5- to 10-membered heteroaryl is optionally substituted one, two, or three times with the group R_{3b};

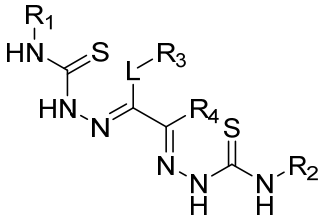
R_{3a} independently for each occurrence is C_3-C_7 cycloalkyl or 4- to 8-membered heterocycle, wherein the 4- to 8-membered heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl;

R_{3b} independently for each occurrence is C_1-C_3 alkoxy, C_3-C_7 cycloalkyl, or 4- to 8-membered heterocycle, wherein the heterocycle is optionally further substituted one, two, or three times with C_1-C_3 alkyl; and

R_4 is hydrogen, C_1-C_3 alkyl, or C_6-C_{10} aryl;

provided that when L is absent, R_3 is C_6-C_{10} aryl substituted one, two, or three times with the group R_{3a}; or when L is absent, R_3 is 6- to 10-membered heteroaryl substituted one, two, or three times with the group R_{3b};

the method comprising mixing a compound of Formula (I-A):



(I-A)

with a copper (II) salt to form the compound of Formula (I).