

Supplementary Materials:

Computational Study of Bis-(1-(benzoyl)-3-methyl thiourea) Platinum (II) Complex Derivatives as Anticancer Candidates

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Table S1. The docking results of the platinum complex against the 3ERT receptor.

Compound	3ERT (breast cancer)					
	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)
Native ligand	4.21 nM	-11.43 kcal/mol	4.17 nM	-11.43 kcal/mol	4.16 nM	-11.43 kcal/mol
Cisplatin	15.19 μM	-6.57 kcal/mol	15.31 μM	-6.57 kcal/mol	15.19 μM	-6.57 kcal/mol
Bis-(1-(2,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	2.23 μM	-7.71 kcal/mol	2.23 μM	-7.71 kcal/mol	2.24 μM	-7.71 kcal/mol
Bis-(1-(2-chlorobenzoyl)-3-methylthiourea) Platinum (II)	174.28 nM	-9.22 kcal/mol	182.64 nM	-9.19 kcal/mol	176.38 nM	-9.21 kcal/mol
Bis-(1-(3,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	1.7 μM	-7.87 kcal/mol	1.71 μM	-7.87 kcal/mol	1.76 μM	-7.85 kcal/mol
Bis-(1-(3,5-dinitrobenzoyl)-3-methylthiourea) Platinum (II)	257.23 μM	-4.90 kcal/mol	260.37 μM	-4.89 kcal/mol	250.62 μM	-4.91 kcal/mol
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)	174.23 nM	-9.22 kcal/mol	174.71 nM	-9.22 kcal/mol	175.44 nM	-9.22 kcal/mol
Bis-(1-(4-bromobenzoyl)-3-methylthiourea) Platinum (II)	5.69 μM	-7.16 kcal/mol	3.75 μM	-7.40 kcal/mol	4.18 μM	-7.34 kcal/mol
Bis-(1-(4-chlorobenzoyl)-3-methylthiourea) Platinum (II)	6.87 μM	-7.04 kcal/mol	6.86 μM	-7.04 kcal/mol	5.93 μM	-7.13 kcal/mol
Bis-(1-(4-decylbenzoyl)-3-methylthiourea) Platinum (II)	3.09 μM	-7.52 kcal/mol	315.68 μM	-4.78 kcal/mol	554.73 nM	-8.53 kcal/mol
Bis-(1-(4-fluorobenzoyl)-3-methylthiourea) Platinum (II)	1.27 μM	-8.05 kcal/mol	1.26 μM	-8.05 kcal/mol	1.29 μM	-8.03 kcal/mol
Bis-(1-(4-heptylbenzoyl)-3-methylthiourea) Platinum (II)	499.46 nM	-8.60 kcal/mol	342.43 nM	-8.82 kcal/mol	492.35 nM	-8.61 kcal/mol
Bis-(1-(4-hexylbenzoyl)-3-methylthiourea) Platinum (II)	667.43 nM	-8.42 kcal/mol	125.62 nM	-9.41 kcal/mol	369.35 nM	-8.78 kcal/mol
Bis-(1-(4-methoxybenzoyl)-3-methylthiourea) Platinum (II)	18.48 μM	-6.46 kcal/mol	12.35 μM	-6.70 kcal/mol	10.29 μM	-6.80 kcal/mol
Bis-(1-(4-tert-butylbenzoyl)-3-methylthiourea) Platinum (II)	219.75 nM	-9.08 kcal/mol	209.89 nM	-9.11 kcal/mol	251.14 nM	-9.00 kcal/mol
Bis-(1-benzoyl-3methylthiourea) Platinum (II)	411.78 nM	-8.71 kcal/mol	416.19 nM	-8.70 kcal/mol	414.03 nM	-8.71 kcal/mol
Bis-(3-methyl-1-(3-nitrobenzoyl)thiourea) Platinum (II)	1.21 μM	-8.07 kcal/mol	1.19 μM	-8.08 kcal/mol	1.15 μM	-8.10 kcal/mol
Bis-(3-methyl-1-(4-nitrobenzoyl)thiourea) Platinum (II)	2.5 mM	-3.55 kcal/mol	32.11 μM	-6.13 kcal/mol	22.01 μM	-6.35 kcal/mol
Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea) Platinum (II)	207.57 pM	-13.21 kcal/mol	207.86 pM	-13.21 kcal/mol	207.99 pM	-13.21 kcal/mol
Bis-(3-methyl-1-[4-(trifluoromethyl)benzoyl]thiourea) Platinum (II)	321.31 nM	-8.86 kcal/mol	385.01 nM	-8.75 kcal/mol	342 nM	-8.82 kcal/mol

Table S2. The docking results of the platinum complex against the 2ITO receptor.

Compound	2ITO (lungs cancer)					
	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)
Native ligand	8.19 μM	-6.94 kcal/mol	8.08 μM	-6.95 kcal/mol	7.8 μM	-6.97 kcal/mol
Cisplatin	16.53 μM	-6.52 kcal/mol	16.52 μM	-6.52 kcal/mol	16.58 μM	-6.52 kcal/mol
Bis-(1-(2,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	30.92 nM	-10.25 kcal/mol	30.66 nM	-10.25 kcal/mol	30.52 nM	-10.25 kcal/mol
Bis-(1-(2-chlorobenzoyl)-3-methylthiourea) Platinum (II)	53.87 nM	-9.92 kcal/mol	51.65 nM	-9.94 kcal/mol	52.06 nM	-9.94 kcal/mol
Bis-(1-(3,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	14.74 nM	-10.68 kcal/mol	14.57 nM	-10.69 kcal/mol	14.61 nM	-10.69 kcal/mol
Bis-(1-(3,5-dinitrobenzoyl)-3-methylthiourea) Platinum (II)	522.52 nM	-8.57 kcal/mol	522.21 nM	-8.57 kcal/mol	542.13 nM	-8.55 kcal/mol
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)	21.2 nM	-10.47 kcal/mol	21.04 nM	-10.47 kcal/mol	21.05 nM	-10.47 kcal/mol
Bis-(1-(4-bromobenzoyl)-3-methylthiourea) Platinum (II)	35.28 nM	-10.17 kcal/mol	35.36 nM	-10.17 kcal/mol	35.96 nM	-10.16 kcal/mol
Bis-(1-(4-chlorobenzoyl)-3-methylthiourea) Platinum (II)	45.58 nM	-10.02 kcal/mol	46.3 nM	-10.01 kcal/mol	45.54 nM	-10.02 kcal/mol
Bis-(1-(4-decylbenzoyl)-3-methylthiourea) Platinum (II)	56.99 nM	-9.88 kcal/mol	42.88 nM	-10.05 kcal/mol	119 nM	-9.45 kcal/mol
Bis-(1-(4-fluorobenzoyl)-3-methylthiourea) Platinum (II)	157.79 nM	-9.28 kcal/mol	158.24 nM	-9.28 kcal/mol	158.14 nM	-9.28 kcal/mol
Bis-(1-(4-heptylbenzoyl)-3-methylthiourea) Platinum (II)	36.66 nM	-10.14 kcal/mol	35.75 nM	-10.16 kcal/mol	28.99 nM	-10.28 kcal/mol
Bis-(1-(4-hexylbenzoyl)-3-methylthiourea) Platinum (II)	44.32 nM	-10.03 kcal/mol	57.34 nM	-9.88 kcal/mol	51.63 nM	-9.94 kcal/mol
Bis-(1-(4-methoxybenzoyl)-3-methylthiourea) Platinum (II)	1.31 μM	-8.02 kcal/mol	1.35 μM	-8.01 kcal/mol	1.32 μM	-8.02 kcal/mol
Bis-(1-(4-tert-butylbenzoyl)-3-methylthiourea) Platinum (II)	285.12 nM	-8.93 kcal/mol	245.77 nM	-9.02 kcal/mol	248.96 nM	-9.01 kcal/mol
Bis-(1-benzoyl-3methylthiourea) Platinum (II)	66.84 nM	-9.79 kcal/mol	66.68 nM	-9.79 kcal/mol	66.9 nM	-9.79 kcal/mol
Bis-(3-methyl-1-(3-nitrobenzoyl)thiourea) Platinum (II)	68.57 nM	-9.77 kcal/mol	69.34 nM	-9.77 kcal/mol	69.09 nM	-9.77 kcal/mol
Bis-(3-methyl-1-(4-nitrobenzoyl)thiourea) Platinum (II)	310.19 nM	-8.88 kcal/mol	311.97 nM	-8.88 kcal/mol	218.78 nM	-9.09 kcal/mol
Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea) Platinum (II)	1.42 nM	-12.07 kcal/mol	2.47 nM	-11.74 kcal/mol	1.43 nM	-12.07 kcal/mol
Bis-(3-methyl-1-[4-(trifluoromethyl)benzoyl]thiourea) Platinum (II)	213.95 nM	-9.10 kcal/mol	212.06 nM	-9.10 kcal/mol	215.3 nM	-9.10 kcal/mol

Table S3. The docking results of the platinum complex against the 1Z95 receptor.

Compound	1Z95 (Prostate cancer)					
	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)	KI	Binding Affinity (ΔG)
Native ligand	645.25 nM	-8.45 kcal/mol	570.85 nM	-8.52 kcal/mol	573.75 nM	-8.51 kcal/mol
Cisplatin	628.37 μ M	-4.33 kcal/mol	628.37 μ M	-4.37 kcal/mol	639.9 μ M	-4.36 kcal/mol
Bis-(1-(2,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	400.22 nM	-8.73 kcal/mol	406.95 nM	-8.72 kcal/mol	392.34 nM	-8.74 kcal/mol
Bis-(1-(2-chlorobenzoyl)-3-methylthiourea) Platinum (II)	59.39 nM	-9.86 kcal/mol	58.81 nM	-9.86 kcal/mol	58.59 nM	-9.87 kcal/mol
Bis-(1-(3,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)	1.52 μ M	-7.94 kcal/mol	1.51 μ M	-7.94 kcal/mol	1.51 μ M	-7.94 kcal/mol
Bis-(1-(3,5-dinitrobenzoyl)-3-methylthiourea) Platinum (II)	304.9 mM	-0.70 kcal/mol	267.89 mM	-0.78 kcal/mol	268.38 mM	-0.78 kcal/mol
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)	53.74 nM	-9.92 kcal/mol	53.78 nM	-9.92 kcal/mol	54.04 nM	-9.91 kcal/mol
Bis-(1-(4-bromobenzoyl)-3-methylthiourea) Platinum (II)	570.15 nM	-8.52 kcal/mol	561.47 nM	-8.53 kcal/mol	563.88 nM	-8.52 kcal/mol
Bis-(1-(4-chlorobenzoyl)-3-methylthiourea) Platinum (II)	571.87 nM	-8.52 kcal/mol	588.14 nM	-8.50 kcal/mol	560.73 nM	-8.53 kcal/mol
Bis-(1-(4-decylbenzoyl)-3-methylthiourea) Platinum (II)	-	+12.28 kcal/mol	-	+11.87 kcal/mol	-	+13.46 kcal/mol
Bis-(1-(4-fluorobenzoyl)-3-methylthiourea) Platinum (II)	365.41 nM	-8.78 kcal/mol	362.54 nM	-8.79 kcal/mol	360.49 nM	-8.79 kcal/mol
Bis-(1-(4-heptylbenzoyl)-3-methylthiourea) Platinum (II)	93.7 mM	-1.40 kcal/mol	892.36 mM	-0.07 kcal/mol	66.95 mM	-1.60 kcal/mol
Bis-(1-(4-hexylbenzoyl)-3-methylthiourea) Platinum (II)	6.68 mM	-2.97 kcal/mol	29.95 mM	-2.08 kcal/mol	22.36 mM	-2.25 kcal/mol
Bis-(1-(4-methoxybenzoyl)-3-methylthiourea) Platinum (II)	88.29 μ M	-5.53 kcal/mol	88.24 μ M	-5.53 kcal/mol	86.51 μ M	-5.54 kcal/mol
Bis-(1-(4-tert-butylbenzoyl)-3-methylthiourea) Platinum (II)	-	+8.27 kcal/mol	-	+8.19 kcal/mol	-	+8.14 kcal/mol
Bis-(1-benzoyl-3methylthiourea) Platinum (II)	257.25 nM	-8.99 kcal/mol	253.06 nM	-9.00 kcal/mol	249.99 nM	-9.01 kcal/mol
Bis-(3-methyl-1-(3-nitrobenzoyl)thiourea) Platinum (II)	1.04 mM	-4.07 kcal/mol	1.11 mM	-4.03 kcal/mol	1.12 mM	-4.02 kcal/mol
Bis-(3-methyl-1-(4-nitrobenzoyl)thiourea) Platinum (II)	84.16 mM	-1.47 kcal/mol	79.63 mM	-1.50 kcal/mol	83.57 mM	-1.47 kcal/mol
Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea) Platinum (II)	1.39 μ M	-7.99 kcal/mol	1.42 μ M	-7.98 kcal/mol	1.41 μ M	-7.98 kcal/mol
Bis-(3-methyl-1-[4-(trifluoromethyl)benzoyl]thiourea) Platinum (II)	51.72 μ M	-5.85 kcal/mol	51.72 μ M	-5.85 kcal/mol	54.46 μ M	-5.82 kcal/mol

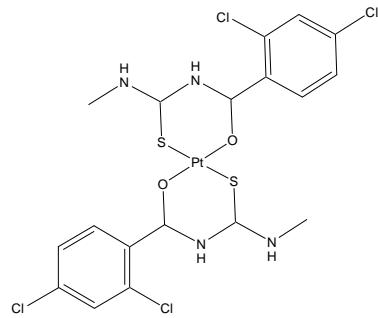
Table S4. the average, minimum and maximum values of RMSD during the 50 ns simulation of each ligand-3ERT complex

System Kompleks	Average	Minimum	Maximum
Native ligand-3ERT	3.316	1.255	4.195
Cisplatin-3ERT	3.462	1.193	4.204
Bis-(1-(2-chlorobenzoyl)-3-methylthiourea) Platinum (II)- 3ERT	3.424	1.211	4.312
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)-3ERT	3.281	1.488	4.025
Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea-Platinum (II)-3ERT	3.332	1.243	4.574

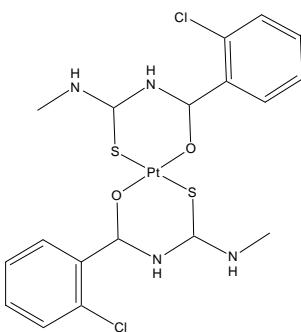
Table S4. the average, minimum and maximum values of RMSD during the 50 ns simulation of each ligand-2ITO complex

System Kompleks	Average	Minimum	Maximum
Native ligand-2ITO	2.368	0.976	3.135
Cisplatin-2ITO	2.967	1.173	4.168
Bis-(1-(3,4-dichlorobenzoyl)-3-methylthiourea) Platinum (II)-2ITO	2.288	1.205	3.025
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)-2ITO	2.847	1.078	4.292
Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea-Platinum (II)-2ITO	2.563	1.247	3.224

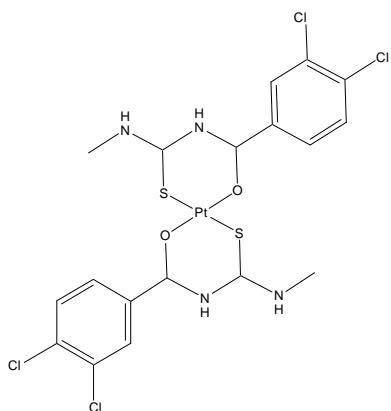
Figure S1. The structure of the platinum complexes



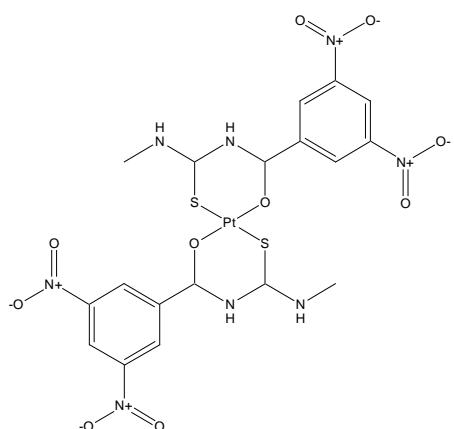
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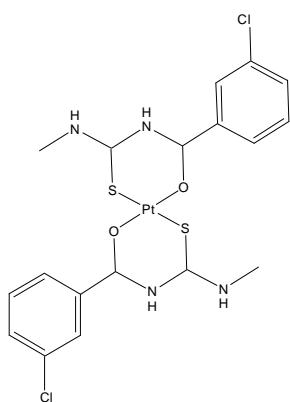
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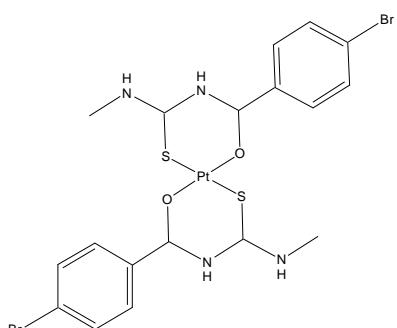
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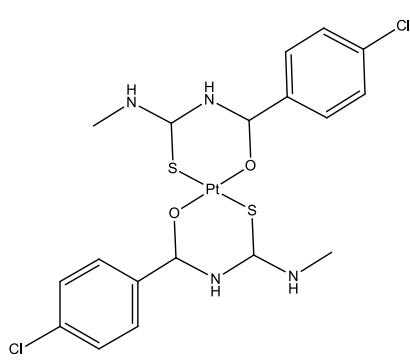
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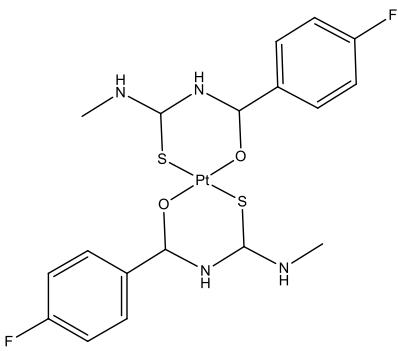
Bis-(1-(3-chlorobenzoyl)-3-methylthiourea) Platinum (II)



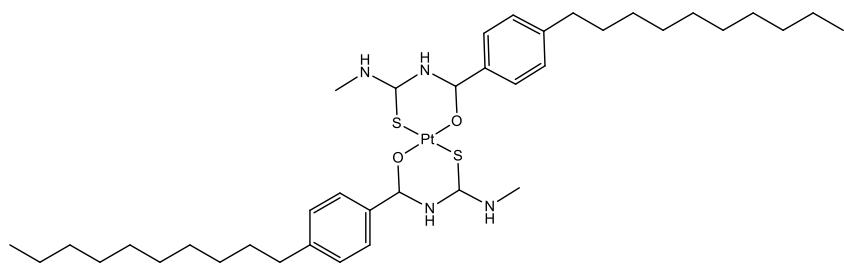
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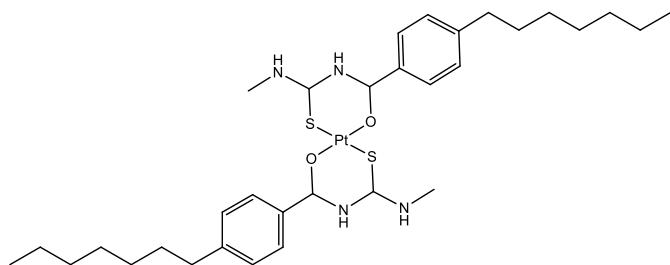
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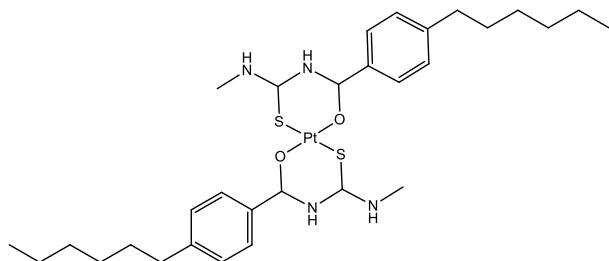
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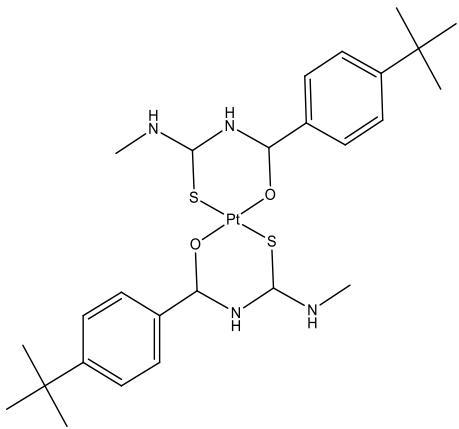
Bis-(1-(4-decylbenzoyl)-3-methylthiourea) Platinum (II)



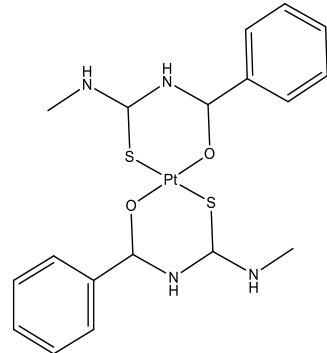
Bis-(1-(4-heptylbenzoyl)-3-methylthiourea) Platinum (II)



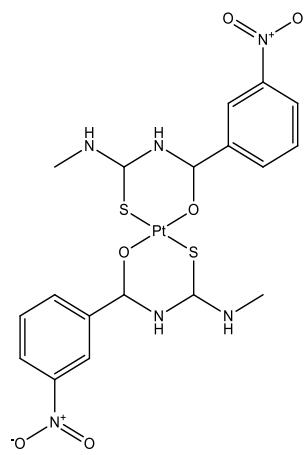
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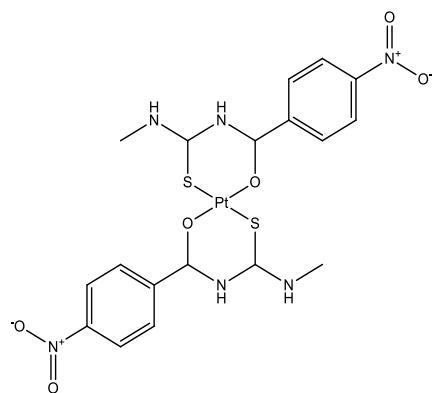
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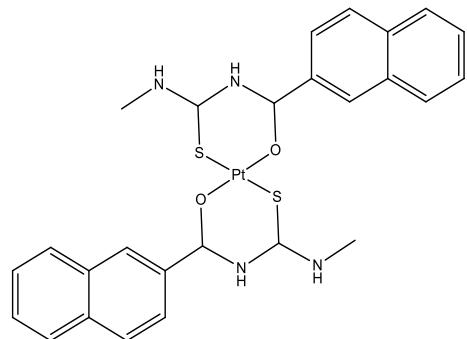
Bis-(1-benzoyl-3methylthiourea) Platinum (II)



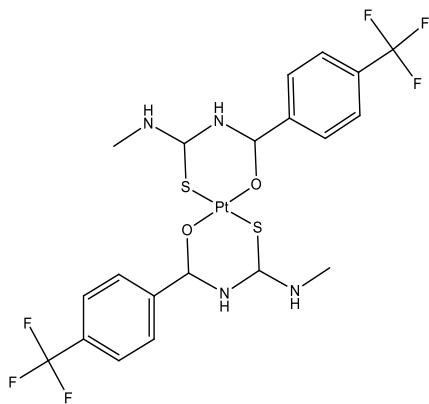
Bis-(3-methyl-1-(3-nitrobenzoyl)thiourea) Platinum (II)



Bis-(3-methyl-1-(4-nitrobenzoyl)thiourea) Platinum (II)



Bis-(3-methyl-1-(naphthalene-2-carbonyl)thiourea) Platinum (II)



Bis-(3-methyl-1-[4-(trifluoromethyl)benzoyl]thiourea) Platinum (II)