

Synthesis, characterization and biological activity of copper (I) and silver (I) complexes of thiosemicarbazone having heterocyclic ring

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Abstract

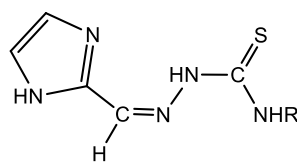
Reaction of 2-imidazolecarboxyaldehyde thiosemicarbazone (H^1L), 2- imidazolecarboxyaldehyde-N-methyl thiosemicarbazone (H^2L) and 2-imidazolecarboxyaldehyde-N-phenyl thiosemicarbazone (H^3L) with copper(I) and silver(I) halides and triphenylphosphine yielded complexes of stoichiometry, $[MX(HL)(Ph_3P)_2]$ (**1-15**). IR spectrum suggested that thio- ligands are binding to metal centre as neutral form thus coordinating via thione sulfur. The expected geometry for complexes is tetrahedral. Thiosemicarbazones and complexes **1-15** were tested for their antibacterial activities. Only complex $[CuCl(H^2L)(PPh_3)_2]$ **6** has shown antibacterial activity in the range 500 ppm (0.66 mm) and 1000 ppm (2.66 mm). Other compounds were found to be inactive.

Keywords: Thiosemicarbazone, 2-imidazolecarboxyaldehyde thiosemicarbazone, copper(I) halides, silver(I) halides, antibacterial activity, NMR spectra.

Introduction

Thiosemicarbazones are versatile ligands with sulphur and nitrogen donor atoms. Presence of N, S- donor ligands enhance their coordination possibilities. Importance of thiosemicarbazones lies in i) bonding ability; ii) variable bonding modes and iii) various biological application [1-Thiosemicarbazones shows a wide range of biological applications. In inorganic chemistry, the stereochemistry of thiosemicarbazones is one of the major interest [1,5]. A number of copper (I) complexes with thiosemicarbazone with single heteroatom are known [6-9], but the coordination chemistry of copper (I) with heterocyclic ring having two hetero-atom at C^2 carbon is still not explored. Moreover, Imidazole ring is an important part of biological system as it exists in the binding site of different metal ions in metalloproteins [11-15]. Thiosemicarbazone containing imidazole ring are potential biologically active molecules. In present paper, synthesis and characterization of 2-imidazole carboxaldehyde thiosemicarbazone (H^1L), 2-imidazole carboxaldehyde-N¹- methyl thiosemicarbazone (H^2L) and 2-imidazolecarboxyaldehyde N¹-Phenyl thiosemicarbazone (H^3L) (chart 1) and their complexes with copper(I) halides (chloride, bromide and iodide)

and silver(I) halides (chloride and bromide) has been reported. All the compounds were tested for their antibacterial activities.



R = H, 2-imidazolecarboxyaldehyde thiosemicarbazone (H^1L)

R = Me, 2-imidazolecarboxyaldehyde-N methyl thiosemicarbazone (H^2L)

R = Ph, 2-imidazolecarboxyaldehyde-N phenyl thiosemicarbazone (H^3L)

Chart 1

Experimental

Chemicals:

Thiosemicarbazide, N-methyl thiosemicarbazide, N-phenyl thiosemicarbazone and 2-imidazolecarboxyaldehyde were purchased from Sigma Aldrich. SHIMADZU FTIR 8400S, Fourier Transform, Infrared spectrophotometer used for Infrared (IR) spectra and BRUCKER ADVAANCE 1.1 400 MHz NMR Spectrophotometer was used to get 1H NMR.

Synthesis:

2-imidazole carboxyaldehyde thiosemicarbazone (H^1L), 2-imidazolecarbaxyaldehyde methyl thiosemicarbazone (H^2L) and 2-imidazolecarboxyaldehyde phenyl thiosemicarbazone (H^3L) was synthesized by condensation of 2-imidazole carboxyaldehyde with respective thiosemicarbazides. Characterization of these ligands is given in Table 1.

Table 1. Characterization of H^1L - H^3L

| S. No. | Compound | Yield | M. P | 1H NMR ($CDCl_3$, δ ppm) |
|--------|----------|-------|-----------|--|
| 1 | H^1L | 82% | 190-194°C | 11.5 s (1H, N^2H), 8.40, 8.32 d (2H, N^1H_2), 7.78 s (1H, C^2H), Ring proton (4H, 7.73-8.00). |
| 2 | H^2L | 85% | 200-205°C | - |
| 3 | H^3L | 87% | 140-145°C | 10.3 s (1H, N^2H), 8.32, 8.89 d (2H, N^1H), 8.21 s (1H, C^2H), Ring proton (4H, 7.73-8.00). |

Synthesis of complexes:

[CuI(H^1L)(Ph_3P) $_2$] **1**. CuI (0.025g, 0.131mmol) was dissolved in 15 ml CH_3CN . To it was added H^1L (0.022g, 0.130mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph_3P were added in the

solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 82%, m. p. 250 - 254°C.

[CuBr(H¹L)(Ph₃P)₂] 2. CuBr (0.025g, 0.174mmol) dissolved in 15 ml CH₃CN. To it was added H¹L (0.029g, 0.171mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole stirred for 6 hours. 2 mole of Ph₃P were added in the Solution and stirred for another 10 minutes. Solution was filtered. Transparent crystals thus obtained were collected after two day. Yield, 67%, m. p. 220-224°C.

[CuCl(H¹L)(Ph₃P)₂] 3. CuCl (0.025g, 0.252mmol) dissolved in 15 ml CH₃CN. To it was added H¹L (0.0426g, 0.2520mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 72%, m. p. 261-263°C).

[CuI(H²L)(Ph₃P)₂] 4. CuI (0.025g, 0.131mmol) dissolved in 15ml CH₃CN. To it was added H²L (0.034g, 0.1857mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 79%, m. p. 240-243°C.

[CuBr(H²L)(Ph₃P)₂] 5. CuBr (0.025g, 0.174mmol) dissolved in 15ml CH₃CN. To it was added H²L (0.0318g, 0.173mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 70%, m. p. 210-214°C.

[CuCl(H²L)(Ph₃P)₂] 6. CuCl (0.025g, 0.252mmol) dissolved in 15 ml acetonitrile. To it was added H²L (0.046g, 0.251mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 79%, m. p. 210-215°C.

[CuI(H³L)(Ph₃P)₂] 7. CuI (0.025g, 0.131mmol) dissolved in 15 ml CH₃CN. To it was added H³L (0.032g, 0.127mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 65%, m. p. 170-175°C.

[CuBr(H³L)(Ph₃P)₂] 8. CuBr (0.025g, 0.174mmol) dissolved in 15ml CH₃CN. To it was added H³L (0.0437g, 0.173mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in

the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 65%, m. p. 180-184°C.

[CuCl(H³L)(Ph₃P)₂] 9. CuCl (0.025g, 0.252mmol) dissolved in 15ml CH₃CN. To it was added H³L (0.063g, 0.250mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days Yield, 65%, m. p. 218-224°C.

[AgBr(H¹L)(Ph₃P)₂] 10. AgBr (0.025g, 0.133mmol) dissolved in 15ml CH₃CN. To it was added H¹L (0.022g, 0.130mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystal were collected after two days. Yield, 65%, m. p. 250-253°C.

Other silver (I) complexes are also synthesized by similar method

[AgCl(H¹L)(Ph₃P)₂] 11. AgCl (0.025g, 0.174mmol) dissolved in 15ml CH₃CN. To it was added H¹L (0.029g, 0.171mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 63%, m. p. 235-240°C.

[AgBr(H²L)(Ph₃P)₂] 12. AgBr (0.025g, 0.133mmol) dissolved in 15ml CH₃CN. To it was added H²L (0.024g, 0.131mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 67%, m. p. 198-202°C.

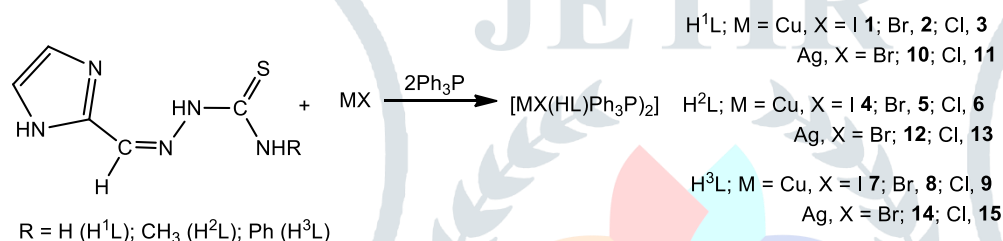
[AgCl(H²L)(Ph₃P)₂] 13. AgCl (0.025g, 0.174mmol) dissolved in 15ml CH₃CN. To it was added H²L (0.031g, 0.173mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 73%, m. p. 220-224°C.

[AgBr(H³L)Ph₃P)₂] **14**. AgBr (0.025g, 0.133mmol) dissolved in 15ml CH₃CN. To it was added H³L (0.033g, 0.131mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 76%, m. p. 195-200°C.

[AgCl(H³L)(Ph₃P)₂] **15**. AgCl (0.025g, 0.174mmol) dissolved in 15ml CH₃CN. To it was added H³L (0.043g, 0.171mmol) and reaction mixture is then stirred for 3-4 hours and 2 mole of Ph₃P were added in the solution. From the reaction mixture, transparent crystals were collected after two days. Yield, 76%, m. p. 234-240°C.

RESULT AND DISCUSSION

Reaction of 2-imidazolecarboxyaldehyde thiosemicarbazone (H¹L), 2- imidazolecarboxyaldehyde-N-methyl thiosemicarbazone (H²L) and 2-imidazolecarboxyaldehyde-N-phenyl thiosemicarbazone (H³L) with Cu(I)X (X = I, Br, Cl) and Ag(I)X (X = Br, Cl) and triphenylphosphine in 1 : 1 : 2 (M : L : PPh₃) ratio yielded complexes of stoichiometry, [MX(HL)(Ph₃P)₂] (HL = H¹L, H²L, H³L; M = Cu, Ag, X = I, Br, Cl).



Discussion on IR:

The IR peaks of ligands 2-imidazolecarboxyaldehyde thiosemicarbazone, 2- imidazolecarboxyaldehyde methyl thiosemicarbazone, 2-imidazolecarboxyaldehyde phenyl thiosemicarbazone are given in Table 2. The ν(N-H) peak found in ligand is divided into two categories; Asymmetric stretching appears in the range of 3577-3463 cm⁻¹ and Symmetric stretching appears in the range of 3284-3223 cm⁻¹. Other important three peaks ν(C=C) + ν(C=N) + δ NH₂ appear in the range of 1634-1539 cm⁻¹. Peak of ν(C=S) also found in the range of 860-810 cm⁻¹. Presence of all these peaks indicate the formation of ligand.

Table 2. Important IR peaks (cm^{-1}) of ligands (H^1L - H^3L) and their complexes are given:

| Compound | vas(N-H) | vs(N-H) | $\nu(\text{C}=\text{C}) + \nu(\text{C}=\text{N}) + \delta\text{NH}_2$. | $\nu(\text{P}-\text{C}_{\text{Ph}})$ | $\nu(\text{C}=\text{S})$ |
|----------------------|----------|---------|---|--------------------------------------|--------------------------|
| H^1L | 3577 | 3274 | 1623,1547,1516 | - | 845 |
| 1. | 3387 | 3275 | 1593,1549,1521 | 1097 | 837 |
| 2. | 3242 | 3175 | 1552,1541,1479 | 1093 | 848 |
| 3. | 3342 | 3254 | 1629,1602,1558 | 1116 | - |
| H^2L | 3241 | 3174 | 1553,1515 | - | 844 |
| 4. | 3263 | 3181 | 1580,1511,1460 | 1106 | 759 |
| 5. | 3352 | 3049 | 1567,1529,1480 | 1094 | 846 |
| 6. | 3435 | 3241 | 1622,1555,1515 | 1113 | 844 |
| H^3L | 3410 | 3156 | 1616,1593,1549 | - | 844 |
| 7. | 3427 | 3268 | 1590,1545,1393 | 1113 | 789 |
| 8. | 3268 | 3152 | 1590,1530,1443 | 1064 | 735 |
| 9. | 3409 | 3265 | 1594,1552,1479 | 1103 | 841 |
| 10. | 3128 | 3050 | 1631,1583,1541 | 1094 | 854 |
| 11. | 3116 | 3050 | 1683,1619,1542 | 1095 | 852 |
| 12. | 3048 | - | 1965,1908,1827 | 1092 | 846 |
| 13. | 3240 | 3159 | 1685,1555,1511 | 1091 | 847 |
| 14. | 3145 | 3051 | 1600,1514,1483 | 1095 | 841 |
| 15. | 3416 | 3217 | 1600,1476,1431 | 1090 | 840 |

Presence of peaks due to N^2H and NH_2 in all the complexes indicates that no deprotonation takes place during complexation and thio- ligand bind to metal (copper and silver) in neutral mode. Shift in $\nu(\text{C}=\text{S})$ band in complexes vis-à-vis free ligands indicate complexation. Appearance of additional band due to $\nu(\text{P}-\text{C}_{\text{Ph}})$ in the range of 1093-1116 cm^{-1} in complexes indicate coordination of Ph_3P to metal center.

Discussion on ^1H NMR:-

^1H NMR spectra of 2-imidazolecarboxyaldehyde thiosemicarbazone (H^1L) (Figure 1) and 2-imidazolecarboxyaldehyde-N-phenyl thiosemicarbazone (H^3L) (Figure 2) were recorded. The value of N^2H proton of both ligands (H^1L) and (H^3L) appeared at δ 11.5 ppm and 10.3 ppm. The chemical environment of amino proton (NH_2) is different because one hydrogen of NH_2 is near nitrogen and form hydrogen bonding. So two different value were appeared as broad singlet at δ 8.40 ppm and 8.32 ppm in H^1L . Similar singlet has been obtained at δ 8.32 ppm and 8.89 ppm in H^3L . Ring protons of both the ligand appear in the range δ 7.73- 8.00 ppm. The value of C^2H proton for both H^1L and H^3L the ligands appeared at δ 7.78 ppm and δ 8.21 ppm. Presence of all these protons in their ^1H NMR spectrum conform the formation of ligands. Due to the poor solubility of complexes, ^1H NMR could not be obtained.

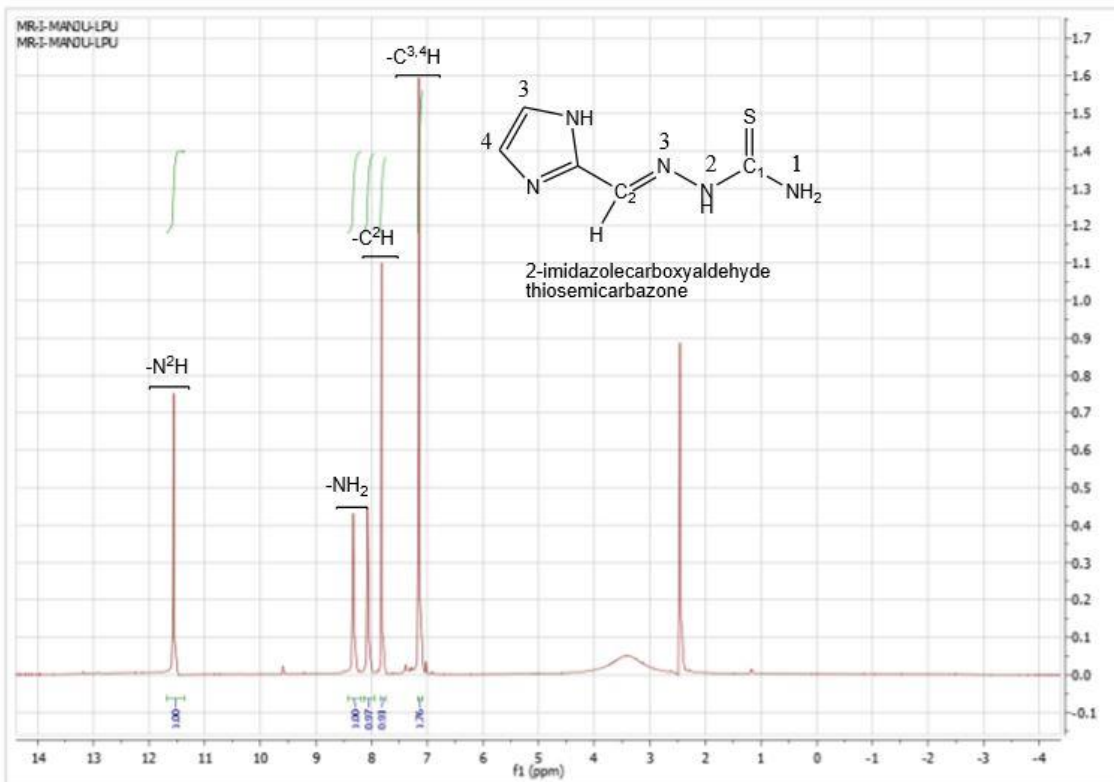


Figure 1. ¹H NMR of 2-imidazolecarboxyaldehyde thiosemicarbazone

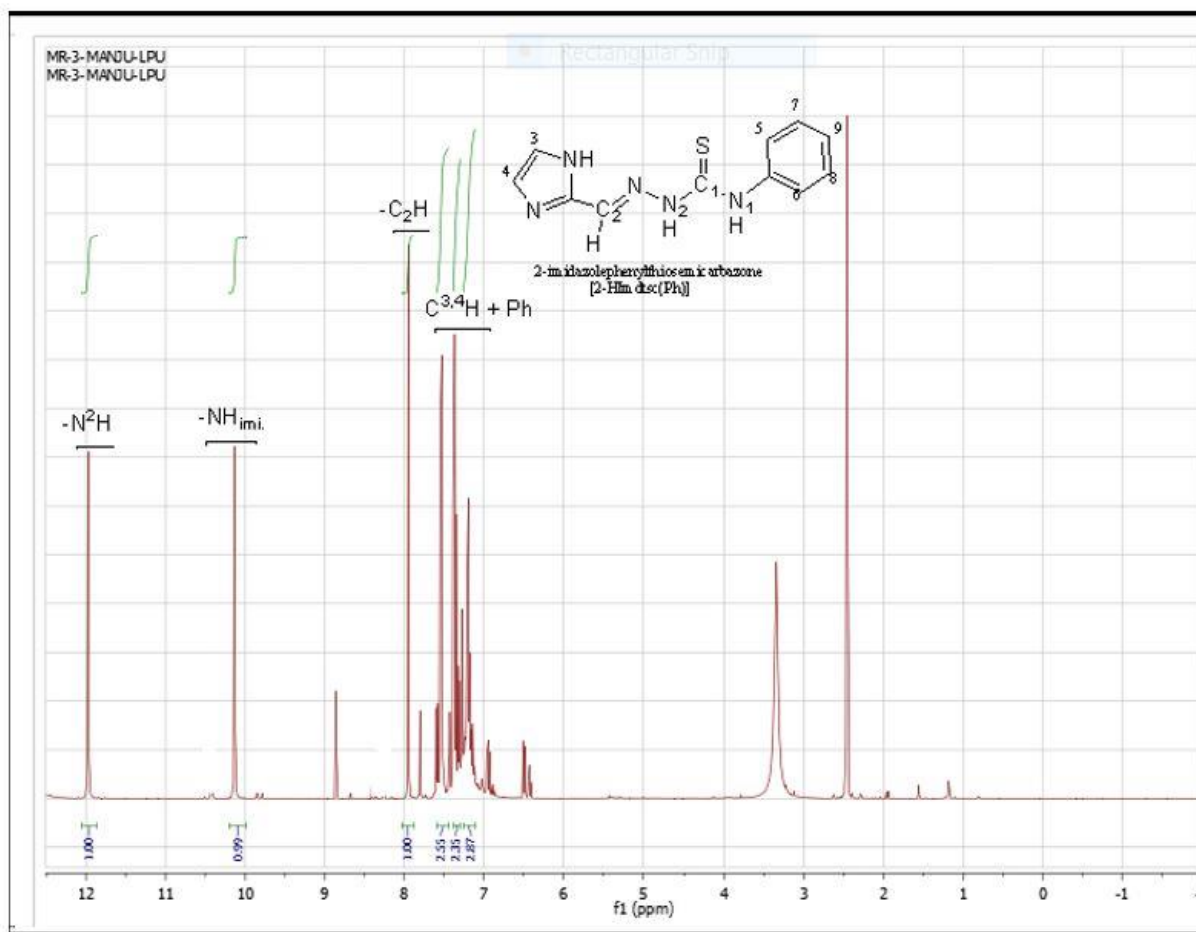


Figure 2. ¹H NMR of 2- imidazolecarboxyaldehyde-N-phenyl thiosemicarbazone

Antibacterial activities

In 300 ml distilled water 8.98 gm. of nutrient agar was added. Then it was mixed properly by placing it in microwave for 15-20 seconds. Then put it in autoclave for autoclaving with the washed petri plates by covering it with brown paper and it was tightly tied with thread. After around 1 hour when the process of autoclaving is completed place it in a laminar to avoid it from contamination. Then the agar solution was poured into petri plates. After pouring the solution into the plates kept it for 15-20 minutes so that it gets solidify. When it will get solidify pour 3-4 ml of *Pseudomonas* bacteria over the solidified agar with the help of a micropipettes. Then spread it with the help of spreader over the agar properly. After spreading the *Pseudomonas* over the agar place discs of different concentration over the agar. Then cover the plates and fix Para film wax on the sides of plates properly. Then place it in incubator for 24 hours then note the zone of clearance. The complex $[\text{CuCl}(\text{H}^2\text{L})(\text{PPh}_3)_2]$ **6** has shown antibacterial activity in the range 500 ppm (0.66 mm) and 1000 ppm (2.66 mm) (Figure 3). In other ligands and complexes no activity was obtained.

Figure 3. Antibacterial activity of complex **6**



Conclusion: 2-imidazolecarboxyaldehyde thiosemicarbazone (H^1L), 2-imidazolecarboxyaldehyde-N-methyl thiosemicarbazone (H^2L) and 2-imidazolecarboxyaldehyde-N-phenyl thiosemicarbazone (H^3L) formed monomeric tetrahedral complexes of formula, $\text{MX}(\text{HL})(\text{Ph}_3\text{P})_2$ with copper(I) and silver(I) halides and triphenylphosphine. IR spectrum suggested that thiosemicarbazones are binding to metal centre as neutral monodentate ligands coordinating via thione sulfur. The expected geometry for complexes is tetrahedral. Both the ligands and complexes were studied for their antibacterial activities. The complex $[\text{CuCl}(\text{H}^2\text{L})(\text{PPh}_3)_2]$ **6** has shown antibacterial activity in the range 500 ppm (0.66 mm) and 1000 ppm (2.66 mm). In other ligands and

complexes no activity was obtained.

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