SYNTHESIS OF FURO[3,2-b]PYRROLE-5-CARBOXYHYDRAZIDES AND THEIR Cu, Co AND Ni COMPLEXES

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Abstract: Carboxhydrazides 3 were synthesized by reaction of substituted furo[3,2-b]pyrrole-5-carboxhydrazides 1 with 4-oxo-4H-chromene-2-carboxaldehyde 2 in the presence of 3-methyl-benzenesulfonic acid in ethanol. Carboxhydrazides 3 were used as ligands for synthesis of Cu, Co and Ni complexes 4.

Keywords: furo[3,2-b]pyrrole, chromene, carboxhydrazide, complex

1. Introduction

Carboxhydrazides and their derivatives represent an interesting class of compounds which exhibits antitumor [1], antimicrobial [2], analgesic and anti-inflammatory [3] activities. Complexes of carbohydrazides are also known for their biological activity. La (I) and Sm (II) complexes of 6-hydroxy chromone-3-carbaldehyde benzoyl hydrazone were tested against tumor cell lines including human promyelocytic leukemia cell line HL-60 and lung adenocarinoma epithelial cell line A-549 [4]. Zn(II) complex of 4-oxo-4H-chromene-3-carbaldehyde thiosemicarbazone binds to DNA and possess significant antioxidant activity [5]. The present study is a follow-up paper to our previous research dealing with the synthesis and reactions of furo[3,2-b]pyrrole system [6,7] and the study of its biological activity. E.g. the effect of N′-{[5-(R-Phenyl)furan-2-yl]methylene}-2-[3-(trifluoromethyl)phenyl]-4H-furo[3,2-b]pyrrole-5-carboxhydrazides on inhibition of photosynthetic electron transport in spinach chloroplasts and chlorophyll content in the antialgal suspensions of Chlorella vulgaris were investigated [8].

2. Experimental

Melting points of products were determined on a Kofler hot plate apparatus and are uncorrected. All solvents were predistilled and dried appropriately prior to use. 1H NMR spectra were obtained on a 300 MHz spectrometer VARIAN GEMINI 2000 in CDCl₃ or DMSO-d₆ with tetramethylsilane as an internal standard. Elemental analyses were measured on EAGER 300 apparatus. Electronic spectra were measured in nujol mull on Specord 200 (Analytical Jena) in the range 50,000 – 9,000 cm⁻¹.
2.1 Synthesis of ligands

A mixture of furo[3,2-b]pyrrole-5-carboxyhydrazide 1 (10 mmol) and 4-oxochromene-3-carboxaldehyde 2 (10 mmol) was heated for 1–4 h at 50–60 °C in ethanol (20 cm³) in the presence of 4-methylbenzenesulphonic acid. The solid products were filtered off, dried and crystallized from ethanol.

2.1.1 N'-[(4-Oxo-4H-chromen-3-yl)methylene]-2,3,4-trimethyl-furo[3,2-b]pyrrole-5-carboxyhydrazide (tmfupy) 3a

For C₂₀H₁₇N₃O₄ (363.4): Mp 251-255 °C; react. time 2.5h; yield: 81%; ¹H NMR (CDCl₃): 10.98 (1H, brs, NH); 8.93 (1H, s, H-2); 8.69 (1H, s, H-9); 8.20 (1H, d, J = 2.5 Hz, H-5); 7.95 (1H, d, J = 7.2 Hz, H-6); 7.68 (1H, ddd, J = 8.1, 7.3, 1.6 Hz, H-7); 7.50 (1H, d, J = 8.4 Hz, H-8); 6.57 (1H, s, H-6'); 4.05 (3H, s, CH₃); 2.36 (3H, s, CH₃); 2.21 (3H, s, CH₃).

2.1.2 N'-[(4-Oxo-4H-chromen-3-yl)methylene]-4-methyl-[1]benzofuro[3,2-b]pyrrole-5-carboxyhydrazide (mbfupy) 3b

For C₂₂H₁₅N₃O₄ (385.4): Mp 241-245 °C; react. time 1h; yield 85%; ¹H NMR (CDCl₃): 11.71 (1H, brs, NH); 8.83 (1H, s, H-2); 8.55 (1H, s, H-9); 8.16-7.72 (4H, m, H-2', H-3', H-4', H-5'); 7.36-7.22 (4H, m, H-5, H-6, H-7, H-8); 7.15 (1H, s, H-6'); 4.31 (3H, s, CH₃).

2.1.3 N'-[(4-Oxo-4H-chromen-3-yl)methylene]-4-benzyl-[1]benzofuro[3,2-b]pyrrole-5-carboxyhydrazide (bzbfupy) 3c

For C₂₈H₁₉N₃O₄ (461.5): Mp 263-266 °C; react. time 4h; yield 82%; ¹H NMR (CDCl₃): 11.69 (1H, brs, NH); 8.81 (1H, s, H-2); 8.56 (1H, s, H-9); 8.17-7.75 (4H, m, H-2', H-3', H-4', H-5'); 7.39-7.29 (4H, m, H-5, H-6, H-7, H-8); 7.27-7.16 (5H, m, Ph); 7.13 (1H, s, H-6'); 5.65 (2H, s, CH₂).

2.1.4 2-Methyl-N'-[(4-oxo-4H-chromen-3-yl)methylene]-4H-furo[3,2-b]pyrrole-5-carboxyhydrazide (mefupy) 3d

For C₁₈H₁₃N₃O₄ (335.3): Mp 253-256 °C; react. time 2.5h; yield 60%; ¹H NMR (DMSO-d₆): 11.53 (1H, s, NH); 11.46 (1H, brs, NH); 8.84 (1H, s, H-2); 8.19-8.16 (2H, m, H-5, H-9); 7.87 (1H, ddd, J = 7.2, 6.9, 1.5 Hz, H-7); 7.75 (1H, d, J = 7.8 Hz, H-8); 7.57 (1H, ddd, J = 8.1, 6.9, 1.2 Hz, H-6); 7.01 (1H, s, H-6'); 6.27 (1H, s, H-3').
2.2 Synthesis of complexes 4

Ligand 3 (0.5 mmol) was dissolved in acetone (10 cm$^3$) at 70 °C. A solution of metal (M$^{2+}$) nitrate or chloride [Ni(NO$_3$)$_2$.6H$_2$O, Co(NO$_3$)$_2$.6H$_2$O, CoCl$_2$.6H$_2$O, CuCl$_2$.2H$_2$O] (0.5 mmol) was added dropwise. Precipitate which was formed immediately, was filtered off, washed with acetone (3 x 15 cm$^3$) and dried.

2.2.1 [Ni(tmfupy)NO$_3$]NO$_3$.H$_2$O 4a

Yield: 80%; Anal. Calcd. for C$_{20}$H$_{19}$N$_5$NiO$_{11}$ (564.1); C, 42.58; H, 3.40; N, 12.42; Ni, 10.41. Found: C, 42.97; H, 3.21; N, 12.57; Ni, 11.69 %.

2.2.2 [Co(mefupy)NO$_3$]NO$_3$.H$_2$O 4b

Yield: 88%; Anal. Calcd. for C$_{22}$H$_{17}$CoN$_5$O$_{11}$ (586.3); C, 45.07; H, 2.92; N, 11.94; Co, 10.05. Found: C, 46.96; H, 2.71; N, 12.07; Co, 11.54 %.

2.2.3 [Co(mefupy)NO$_3$]NO$_3$.H$_2$O 4c

Yield: 78%; Anal. Calcd. for C$_{28}$H$_{21}$CoN$_3$O$_5$ (515.8); C, 46.57; H, 3.71; N, 8.15; Cu, 12.32. Found: C, 45.45; H, 3.62; N, 7.79; Cu, 11.95 %.

2.2.4 [Cu(tmfupy)Cl$_2$]H$_2$O 4d

Yield: 81%; Anal. Calcd. for C$_{20}$H$_{19}$Cl$_2$CuN$_3$O$_5$ (515.8); C, 46.57; H, 3.71; N, 8.15; Cu, 12.32. Found: C, 45.45; H, 3.62; N, 7.79; Cu, 11.95 %.

2.2.5 [Cu(bzbfupy)Cl$_2$]H$_2$O 4e

Yield: 93%; Anal. Calcd. for C$_{28}$H$_{21}$Cl$_2$CuN$_3$O$_5$ (613.9); C, 54.78; H, 3.45; N, 6.84; Cu, 10.35. Found: C, 52.03; H, 3.02; N, 6.48; Cu, 10.84 %.

2.2.6 [Cu(mefupy)Cl$_2$]H$_2$O 4f

Yield: 77%; Anal. Calcd. for C$_{18}$H$_{15}$Cl$_2$CoN$_3$O$_5$ (483.2); C, 44.74; H, 3.13; N, 8.70; Co, 12.20. Found: C, 45.06; H, 3.24; N, 9.30; Cu, 11.45 %.

2.2.7 [Cu(mefupy)Cl$_2$]H$_2$O 4g

Yield: 84%; Anal. Calcd. for C$_{18}$H$_{15}$Cl$_2$CuN$_3$O$_5$ (487.8); C, 44.32; H, 3.10; N, 8.61; Cu, 13.03. Found: C, 45.16; H, 3.07; N, 9.04; Cu, 12.88 %.

3. Results and discussion

$N'-$[4-Oxo-4H-chromen-3-yl)methyene]-2-R$^1$-3-R$^2$-4-R-furo[3,2-b]pyrrole-5-carboxhydrazides 3a-3d were synthesized in 60 – 85% yields by reaction of 1 with 2 in ethanol in the presence of 4-methylbenzenesulphonic acid by heating at 50 - 60° C for 1 - 4h (Scheme 1).

The $^1$H NMR spectra of compounds 3a – 3d displayed signals of H-2 pyran protons in the 8.81-8.93 ppm range, H-6 pyrrole protons in the 7.36 – 7.95 ppm range and signals due to CH=N bonded protons in the 8.19 – 8.69 ppm range. The chemical shifts and the multiplicity confirmed the proposed structures.

Carboxhydrazides 3 were subsequently used as ligands in complexation reactions with solutions of metal (M$^{2+}$) chlorides or nitrates [Ni(NO$_3$)$_2$.6H$_2$O, Co(NO$_3$)$_2$.6H$_2$O, CoCl$_2$.6H$_2$O, CuCl$_2$.2H$_2$O] in acetone at 70 °C. Complexes 4 were obtained in high yields (78-93%).

Structures of 4 were determined by the elemental analyses and electronic spectra. Electronic spectrum of hexacoordinated Ni (II) ion shows transitions at 10000 ($^3$A$_{2g}$ → $^3$T$_{2g}$)
and 16000 cm$^{-1}$ ($^3A_{2g} \rightarrow ^3T_{1g}$). The third transition ($^3A_{2g} \rightarrow ^3T_{1g}$), which is probably overlapped, should be at about 26000 cm$^{-1}$ (Fig. 1).

Electronic spectra of hexacoordinated Co(II) shows weak transitions at 15000 cm$^{-1}$ ($^4T_{1g} \rightarrow ^4A_{2g}$) and transitions at 19000 cm$^{-1}$ ($^4T_{1g} \rightarrow ^4T_{1g}$). Next transitions over 20000 cm$^{-1}$ could be overlapped by strong charge-transfer transitions (Fig. 2).

Hexacoordinated Cu(II) ion has tetragonal symmetry with transitions up to 10000 cm$^{-1}$ ($^2B_{1g} \rightarrow ^2A_{1g}$) and 16000 cm$^{-1}$ ($^2B_{1g} \rightarrow ^2B_{2g}$) (Fig. 3).

Electronic spectrum of tetracoordinated Co(II) ion shows characteristic transitions in the area of 15000 – 16000 cm$^{-1}$ ($^4A_{2} \rightarrow ^4T_{1}(P)$) (Fig. 4).

4. Conclusion

Furo[3,2-b]pyrrole-5-carboxhydrazides 1 reacted with substituted with 4-oxo-4\textit{H}-chromene-2-carboxaldehyde 2 to give $N'$-[(4-oxo-4\textit{H}-chromen-3-yl)methylene]-2-R$^1$-3-R$^2$-4-

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References


