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Article

Synthesis, Spectral Studies and Catalytic Activity of Ruthenium(II) Complexes with Organic Amide Ligands

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Doze novos complexos hexacoordenados de rutênio(II) com amidas, $[RuH(CO)(PPh_3)_2(L_2)]$, foram sintetizados a partir do precursor $[RuH_2(CO)(PPh_3)_3]$. Esses complexos foram caracterizados por análise elementar e por espectroscopias no UV-vis, no infravermelho e RMN de ^1H, ^{13}C e ^{31}P. Fórmulas moleculares e estruturas octaédricas foram propostas para os produtos. Os complexos mostraram-se eficientes na redução catalítica do grupo nitro em drogas do tipo cloranfenicol e metronidazol. Os rendimentos dos produtos de redução foram determinados espectrofotometricamente.

Twelve new hexacoordinated ruthenium(II) complexes with organic amides, $[RuH(CO)(PPh_3)_2(L_2)]$, have been synthesized by treating the precursor, $[RuH_2(CO)(PPh_3)_3]$, with twelve different amide proligands separately. These complexes were characterized by elemental analysis and by UV-vis, IR, ^1H, ^{13}C and ^{31}P NMR spectroscopies. Molecular formulae and octahedral structures have been tentatively proposed for the products. These complexes were found to be efficient in the catalytic reduction of NO_2-containing drugs such as chloramphenicol and metronidazole to their amino derivatives. The percent yields of the reduction products were determined spectrophotometrically.

Keywords: synthesis, ruthenium complexes, spectroscopic analysis, catalysis, organic amide ligand

Introduction

Ruthenium(II) complexes are known for their structural novelty.[1-5] The increasing catalytic applications of triphenylphosphine derivatives of ruthenium[6] insist the importance of convenient synthetic methods for these compounds. Ruthenium complexes containing organic amide ligands[7-8] are found to exhibit diverse coordinating behavior and interesting structural features. Literature survey reveals that amide complexes of the $[RuH_2(CO)(PPh_3)_3]$[9-17] precursor have not been synthesized so far. Our continuous efforts to develop catalytically active[18-19] amide complexes of ruthenium[20-21] resulted in the synthesis of the present complexes, $RuH(CO)(PPh_3)_2(L_2)$ (complexes **1** to **12**), using this precursor with organic amide ligands.

The development of simple synthetic routes to amines from readily available nitro compounds and their derivatives using metals is one important goal in pharmaceutical industry. The reduction reactions of nitro compounds using ruthenium complexes were rarely published. Hence, in the course of exploring the reduction characteristics of ruthenium complexes, two drug molecules containing nitro group, *viz.* chloramphenicol (CP) and metronidazole (MZ), were selected. Literature survey reveals that chloramphenicol is reduced by metal-containing combinations such as Zn–HCl[22] and titanium(III) chloride–glacial acetic acid[23] to produce reduced chloramphenicol (RCP). Similarly, metronidazole is reduced by Zn-HCl[24] and Pd-C(10%)-formic acid[25] to produce reduced metronidazole (RMZ). As the nitro group of these drugs has not been tested for reduction with ruthenium compounds, an alternative reduction method was developed using ruthenium(II) complexes as catalysts. The reduction products were allowed to react with nitrous acid to give diazotized products, which were then treated with β-naphthol (NL) to get azodyes. These were employed in the spectrophotometric determination of the percent yields of the reduced products of these drugs.

Experimental

Instruments

The melting points of all proligands and complexes were obtained on a Buchi 510 melting point apparatus. The

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percentages of carbon, hydrogen and nitrogen in the ruthenium complexes were determined at the Technical University of Berlin, Germany, using a Perkin-Elmer 240C CHN analyzer. UV-visible spectra were recorded with a Shimadzu UV-160A, a UV-visible double beam spectrophotometer with matched quartz cells of path length 1 cm at the National Institute of Technology, Warangal. The IR spectra were recorded in KBr pellets on a Perkin Elmer-283 spectrophotometer at Kakatiya University, Warangal. The scanning rate was 6 min in the range of 4000-200 cm^{-1}. A Jeol 100 MHz FT NMR spectrometer was used for recording ^{1}H NMR spectra at the Indian Institute of Chemical Technology, Hyderabad. A Bruker WH 270 spectrometer was used for recording ^{13}C NMR (67.93 MHz) and ^{31}P NMR (109.29 MHz) spectra at the Technical University of Berlin, Germany. A Gouy balance calibrated with $Hg[Co(NCS)_4]$ was used to determine the magnetic susceptibilities of complexes in solid state at room temperature. A vibrating sample magnetometer at RSIC, Indian Institute of Technology Madras, Chennai, was also employed for the above purpose. When small amounts of complexes were available, diamagnetic corrections were made using Pascal's constants. Conductance measurements were done in 10^{-3} mol L^{-1} solutions of compounds in dichloromethane at room temperature, using Digison Digital conductivity meter model DL-909.

Materials

$RuCl_3 \cdot 3H_2O$ (Johnson Matthey & Co.), acetone (Qualigens) and diethyl ether (Qualigens) were used as such. The precursor, $[RuH_2(CO)(PPh_3)_3]$,[9] and the twelve amide proligands, *viz.* 2-(anilinocarbonyl)benzoic acid (ACBA); 4-anilino-4-oxobut–2-enoic acid (AOBEA); 4-anilino-4-oxobutanoic acid (AOBA); 2-[(1-naphthylamino)carbonyl]benzoic acid (NACBA); 4-(1–naphthylamino)4-oxobut-2-enoic acid (NAOBEA); 4-(1-naphthyl amino)4-oxobutanoic acid (NAOBA); (2-[(1H-benzimidazol-2-ylamino)carbonyl]benzoic acid (BACBA); 4-(1H-benzimidazol-2-ylamino)-4-oxobut-2-enoic acid (BAOBEA); 4-(1H-benzimidazol-2-ylamino)-4-oxobutanoic acid (BAOBA); 2-[(2-phenylhydrazino)carbonyl] benzoic acid (PHCBA); 4-oxo-4-(2-phenylhydrazino)but-2-enoic acid (OPHBEA); 4-oxo-4-(2-phenyl hydrazino)butanoic acid (OPHBA), were prepared as previously reported.[26,27]

Drug solutions

Standard stock solutions of chloramphenicol and metronidazole (1 mg mL^{-1}) were prepared by dissolving 100 mg of pure chloramphenicol or metronidazole in 100 mL of methanol. These stock solutions were diluted with the same solvent to get the working pure drug solutions of 100 μg mL^{-1}.

An accurately weighed amount of tablet powder equivalent to 100 mg of chloramphenicol or metronidazole was extracted separately with isopropanol (4 × 20 mL) and filtered. The filtrate was evaporated to dryness and the residue was dissolved in 100 mL of methanol to achieve a concentration of 1 mg mL^{-1}. This solution was diluted with the same solvent to get the working pharmaceutical solutions of 100 μg mL^{-1}.

Reagents

0.1 mol L^{-1} acetic acid solution (Qualigens) was prepared by diluting 6.3 mL of glacial acetic acid to 1000 mL with double distilled water. 0.1 mol L^{-1} of $NaNO_2$ solution (Merck) was prepared by dissolving 0.699 g in 100 mL of double distilled water. 0.2 mol L^{-1} sulfamic acid solution (Merck) was prepared by dissolving 1.941 g in 100 mL of double distilled water. 0.1 mol L^{-1} of β-naphthol solution (Merck) was prepared by dissolving 1.441 g in 100 mL of double distilled water. 10 % NaOH solution (Merck) was prepared by dissolving 25 g in 250 mL of double distilled water.

Synthesis of the ruthenium(II) complexes

In a 100 mL round bottom flask, 20 mL of $[RuH_2(CO)(PPh_3)_3]$ solution (0.4 mmol, 0.366 g in acetone) and 20 mL of proligand solution (0.4 mmol in acetone as above) were mixed and the reaction mixture was stirred magnetically for 3 h. The resulting solution was concentrated to 5 mL under reduced pressure and few mL of diethylether were added to initiate crystallization. The resulting precipitate was separated by suction filtration, washed with diethylether, vacuum dried to get a crystalline compound and recrystallised using a mixture of dichloromethane and diethylether.

Catalytic reductions

In a 100 mL round bottom flask, 5 mL of chloramphenicol or metronidazole solution, 2 mL of acetic acid and 0.01 mmol of $[RuH(CO)(PPh_3)_2(ACBA)]$ (complex **1**) were mixed and stirred for 5 min at room temperature. The reduced drug and the catalyst were separated by using a column, and the reduced drug was then dissolved in 10 mL of methanol and transferred to 20 mL calibrated tubes. 1 mL of 0.1 mmol L^{-1} $NaNO_2$

solution was added and the mixture was stirred for 2 min; 1 mL of 0.2 mol L^{-1} sulfamic acid solution was added and stirred again for 1 min. Finally, 1 mL of β-naphthol solution was added and the mixture was kept aside for 2 min; the solution was then made up to 100 mL with NaOH solution. The absorbances of the colored solutions were measured at 520 nm (Figure 1) against their reagent blanks. The amounts of RCP and RMZ formed during the reduction process were estimated from their respective calibrated curves. The procedure was repeated by changing the ruthenium(II) catalysts (2 to 12), one by one. This procedure was also applied for pharmaceutical solutions. The separated catalyst was dissolved in 20 mL of methanol and, after addition of CaH_2 (0.01 mmol), the mixture was heated for 30 min to recover the original catalyst, which was recrystallized using dichloromethane.

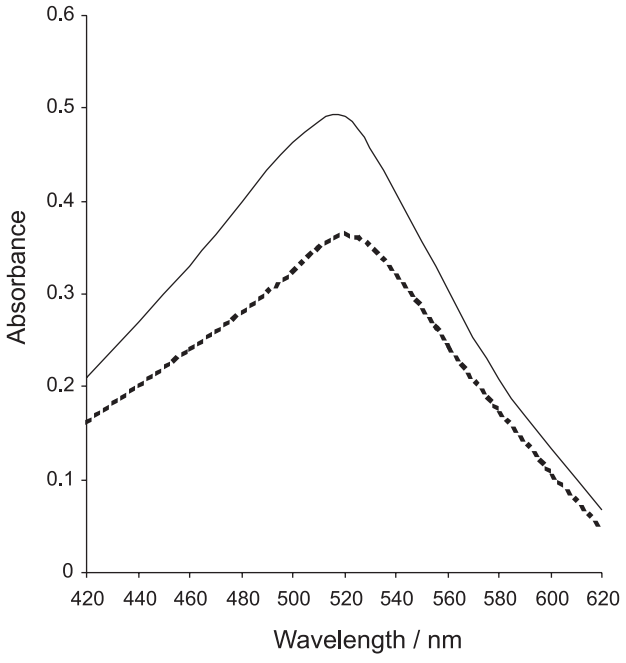


Figure 1. Absorption spectra of RCP (—) and RMZ (----), [RCP] or [RMZ]=20 μg mL^{-1}.

Results and Discussion

Characterization of the ruthenium(II) complexes with organic amides

The percentages of carbon, hydrogen and nitrogen were determined experimentally using a CHN analyzer. The percentage of ruthenium in the complexes was determined by a literature method.[28] The physical and analytical data (Table 1) is in good agreement with the proposed $[RuH(CO)(PPh_3)_2(L_2)]$ molecular formulae.

Infrared spectroscopy

The infrared spectra of the precursor and free amides were compared with those of the new ruthenium(II) complexes to access the coordination of the amides to ruthenium. The stretching frequencies of amide nitrogen and oxygen are found in the ranges of 3367-3252 and 1672-1631 cm^{-1}, respectively, in the free amides. In the spectra of the new ruthenium(II) complexes, negative shifts by 30-40 cm^{-1} are observed in the range of 1625-1608 cm^{-1},[26,27] indicating the coordination of the amide oxygen to ruthenium. There is no appreciable change in the ν_{N-H} region, indicating the non-participation of the amide nitrogen in chelation.[21] However, in the IR spectra of complexes having ligands derived from benzimidazoles, *viz.* BACBA, BAOBEA and BOABA, N-H bands (benzimidazole) are observed at 3261, 3244 and 3251 cm^{-1}, respectively. Similarly, in the IR spectra of complexes having ligands derived from phenylhydrazine, *viz.* PHCBA, OPHBEA and OPHBA, N-H bands (phenylhydrazine) are observed at 3285, 3274 and 3283 cm^{-1}, respectively. In the free amides, strong absorption bands are observed around 1710 and 1340 cm^{-1}, due to $\nu_{C=O}$ stretching and δ_{O-H} deformations of carboxylic acid, respectively. These bands are replaced with new bands in the ranges of 1553-1540 and 1388-1372 cm^{-1} corresponding to ν_{COO^-} (asymmetric) and ν_{COO^-} (symmetric) vibrations in the spectra of the complexes, supporting the fact that the oxygen atom of the carboxylic acid is participating in chelation.[21] The coordination of the oxygen atom of the ligand to ruthenium is also indicated by the presence of a band in the range of 460-400 cm^{-1}. In the precursor spectrum, the Ru-H bond is observed at 1960 cm^{-1}, while in the ruthenium(II) complexes these peaks appear as medium bands[29] with a slight negative shift of 10-20 cm^{-1} in the range of 1959-1942 cm^{-1}, indicating the presence of the Ru-H bond. Similarly, the existence of strong bands in the range of 1919-1910 cm^{-1} in the spectra of the complexes reveals the presence of the carbonyl ligand.[29] All other characteristic bands due to triphenylphosphine are observed in the expected regions in the spectra of the precursor and the complexes (Table 2). [30]

NMR spectroscopy

In order to confirm the presence of amide ligands in the ruthenium(II) complexes, ^1H NMR spectra of the precursors, amide proligands and of the new ruthenium(II) complexes were recorded. The integral intensities of each signal in the ^1H NMR spectra of the

proligands and of the corresponding complexes were found to agree with the number of different types of hydrogens present. The presence of the carboxylic hydrogen in the proligands is indicated by the appearance of a sharp signal in the δ 10.0-12.1 range. However, in the spectra of the complexes these signals were not found, thereby confirming the deprotonation of the carboxylic group, followed by chelation through the oxygen atom.[21,31] In the spectra of the proligands, a broad signal attributed to the amide hydrogen is observed in the δ 5.0-10.0 range. Appreciable change in this region is not observed in the spectra of the complexes, confirming the non-participation of this group in chelation. However, in the spectra of complexes containing ligands derived from benzimidazoles, *viz.* BACBA, BAOBEA and BOABA, medium intensity signals corresponding to the NH hydrogen of benzimidazololes are observed at δ 9.19, 7.12 and 7.09, respectively. Similarly, in the spectra of the complexes with ligands derived from phenylhydrazines, *viz*. PHCBA, OPHBEA and OPHBA, medium intensity signals corresponding to the phenylhydrazine NH hydrogen are observed at δ 9.49, 7.41 and 7.19, respectively. A sharp signal is present around δ -12.75 in the spectra of the precursor, indicating the presence of a hydride attached to the ruthenium. In the spectra of the complexes, these peaks are observed in the δ -11.21 to -12.87 range. The spectra of the proligands AOBEA, NAOBEA, BOABEA and OPHBEA contain a doublet of doublets in the δ 5.42-6.69 range, indicating the presence of a CH=CH unit and these signals remain almost unshifted in the complexes. Similarly, the spectra of the proligands AOBA, NAOBA, BOABA and OPHBA contain a triplet of triplets in the δ 2.26-2.74 range, indicating the presence of a CH_2-CH_2 unit, and these signals also remain almost unshifted in the complexes. Multiplets observed in the spectra of the complexes in the δ 6.16-8.13 range have been assigned to the aromatic hydrogens of the ligands and triphenylphosphines[32] (Table 3).

^{13}C NMR spectra of free amides were compared with the ^{13}C NMR spectra of the corresponding ruthenium(II) complexes. The two carboxylic carbons exhibit signals in a similar range, δ 170.92-179.21, in the free amides.[33] However, ^{13}C signals are observed in the high frequency regions at δ 187.21-191.52 and δ 178.01-185.11 in the spectra of the complexes, indicating coordination of the carboxylic carbon and carbonyl carbon of the amide, respectively. The spectra of the proligands AOBEA, NAOBEA, BOABEA and OPHBEA and those of their corresponding complexes contain a signal around ä 115.17 confirming the presence of doubly bonded carbon. Similarly, the spectra of the proligands AOBA, NAOBA, BOABA and OPHBA and those of their

Table 1. Physical and analytical data for ruthenium(II) complexes with organic amides

Complex No.	Ruthenium(II) complex formed	mp (°C)	Color	Yield (g)	Analyses Found (Calculated) (%)			
					C	H	N	Ru
1	$RuH(CO)(PPh_3)_2(ACBA)$	225	Dark	0.278	68.37	4.61	1.57	11.33
	$C_{51}H_{41}NO_4P_2Ru$		brown	(78%)	(68.45)	(4.58)	(1.56)	(11.29)
2	$RuH(CO)(PPh_3)_2(AOBEA)$	218	Brown	0.259	66.75	4.60	1.66	11.94
	$C_{47}H_{39}NO_4P_2Ru$			(77%)	(66.82)	(4.62)	(1.65)	(11.96)
3	$RuH(CO)(PPh_3)_2(AOBA)$	212	Light	0.256	66.56	4.86	1.63	11.97
	$C_{47}H_{41}NO_4P_2Ru$		brown	(76%)	(66.66)	(4.84)	(1.65)	(11.93)
4	$RuH(CO)(NACBA)$	229	Green	0.286	69.97	4.56	1.47	10.67
	$(PPh_3)_2C_{55}H_{43}NO_4P_2Ru$			(76%)	(69.91)	(4.55)	(1.48)	(10.69)
5	$RuH(CO)(NAOBEA)$	226	Light	0.267	68.51	4.60	1.57	11.27
	$(PPh_3)_2C_{51}H_{41}NO_4P_2Ru$		green	(75%)	(68.45)	(4.58)	(1.56)	(11.29)
6	$RuH(CO)(PPh_3)_2(NAOBA)$	225	Light	0.261	68.24	4.81	1.58	11.24
	$C_{51}H_{43}NO_4P_2Ru$		green	(73%)	(68.30)	(4.79)	(1.56)	(11.27)
7	$RuH(CO)(PPh_3)_2(BACBA)$	259	Brown	0.268	66.7	4.40	4.48	10.79
	$C_{52}H_{41}N_3O_4P_2Ru$			(72%)	(66.80)	(4.38)	(4.49)	(10.81)
8	$RuH(CO)(PPh_3)_2(BAOBEA)$	257	Brown	0.275	65.22	4.43	4.76	11.44
	$C_{48}H_{39}N_3O_4P_2Ru$			(78%)	(65.15)	(4.41)	(4.75)	(11.42)
9	$RuH(CO)(PPh_3)_2(BAOBA)$	251	Brown	0.265	64.94	4.65	4.77	11.38
	$C_{48}H_{41}N_3O_4P_2Ru$			(75%)	(65.01)	(4.62)	(4.74)	(11.39)
10	$RuH(CO)(PPh_3)_2(PHCBA)$	222	Light	0.279	67.23	4.65	3.10	11.08
	$C_{51}H_{42}N_2O_4P_2Ru$		brown	(77%)	(67.32)	(4.62)	(3.08)	(11.11)
11	$RuH(CO)(PPh_3)_2(OPHBEA)$	216	Light	0.263	65.71	4.61	3.27	11.73
	$C_{47}H_{40}N_2O_4P_2Ru$		brown	(77%)	(65.65)	(4.65)	(3.25)	(11.75)
12	$RuH(CO)(PPh_3)_2(OPHBA)$	213	Light brown	0.254	65.42	4.84	3.27	11.72
	$C_{47}H_{42}N_2O_4P_2Ru$			(74%)	(65.50)	(4.87)	(3.25)	(11.73)

Table 2. Infrared spectral data for ruthenium(II) complexes with organic amides

Complex No.	Complex / Formula	Selected IR bands (cm^{-1})						
		$\nu_{C=O}$(Amide)	ν_{Ru-H}	$\nu_{C=O}$(Carbonyl)	ν_{N-H}(Amide)	ν_{COO^-}(asy)	ν_{COO^-}(sy)	ν_{Ru-P}
1	$RuH(CO)(PPh_3)_2$(ACBA)	3350	1950	1910	1608	1540	1375	517
2	$RuH(CO)(PPh_3)_2$ (AOBEA)	3361	1953	1913	1612	1542	1380	519
3	$RuH(CO)(PPh_3)_2$(AOBA)	3365	1948	1918	1610	1545	1384	521
4	$RuH(CO)(PPh_3)_2$(NACBA)	3257	1942	1915	1619	1542	1383	522
5	$RuH(CO)(PPh_3)_2$(NAOBEA)	3251	1956	1917	1617	1552	1382	529
6	$RuH(CO)(PPh_3)_2$(NAOBA)	3273	1959	1916	1612	1553	1373	528
7	$RuH(CO)(Ph_3)_2$(BACBA)	3361	1951	1910	1623	1545	1388	527
8	$RuH(CO)(PPh_3)_2(BAOBEA)_2$	3363	1955	1916	1625	1547	1386	528
9	$RuH(CO)(PPh_3)_2$(BAOBA)	3365	1955	1919	1611	1542	1372	520
10	$RuH(CO)(PPh_3)_2$(PHCBA)	3362	1957	1917	1612	1553	1386	521
11	$RuH(CO)(PPh_3)_2$(OPHBEA)	3369	1955	1918	1611	1548	1388	522
12	$RuH(CO)(PPh_3)_2$(OPHBA)	3364	1942	1915	1614	1543	1379	529

corresponding complexes contain a signal around δ 33.3 confirming the presence of a singly bonded carbon. The aryl carbons are found to resonate in the δ 119.11-137.21 range.[32]

^{31}P NMR spectra of these complexes show singlets in the δ 32.76-34.91 range, suggesting that the triphenylphosphine groups are *trans* to each other around the ruthenium(II) centre.[34] In the process of complexation, the leaving hydride and triphenylphosphine ligands, which are in *cis* position in the precursor, are eliminated and the bidentate amide group is coordinated. As the precursor contains the eliminated hydride ion in *trans* position relative to CO, the COO^- ion of the amide occupies a *trans* position to CO in the complex.

Electronic, magnetic and conductance studies

The ground state of ruthenium(II) (t_{2g}^6 configuration) is $^1A_{1g}$. For a hexacoordinate ruthenium(II) complex, four transitions corresponding to $^1A_{1g} \rightarrow {}^3T_{1g}$; $^1A_{1g} \rightarrow {}^3T_{2g}$; $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ are possible.[35] The electronic spectra of the complexes showed high intensity charge transfer bands in the 270-320 nm range (ε_{max} range = 21320-15200 L mol^{-1} cm^{-1}), $n \rightarrow \pi^*$ band in the 420-455 nm range (ε_{max} range = 11330-6150 L mol^{-1} cm^{-1}) and ruthenium(II) $d \rightarrow \pi^*$ MLCT in the 520-580 nm range (ε_{max} range = 5117-2894 L mol^{-1} cm^{-1}). Sometimes the higher energy transition is totally obscured by intense charge transfer bands. This data suggests octahedral geometry for all ruthenium(II) complexes.[36]

All these complexes are found to be diamagnetic in nature, thereby assigning a +II oxidation state to ruthenium.

The molar conductance values of ruthenium(II) complexes determined in dichloromethane are found to be low, indicating their non-electrolytic behavior.

On the basis of analytical and spectral data, octahedral structures (Scheme 1) have been tentatively proposed for all ruthenium(II) complexes reported in the present work.

Catalytic reduction

Optimum conditions

The experimental parameters were optimized to obtain maximum yields and absorbance in the reduction

Table 3. ^1H NMR spectral data for ruthenium(II) complexes with organic amides

Complex No.	Complex / Fomula	^1H peak position (ppm)				
		Hydride	Amide	CH=CH	CH_2-CH_2	Aromatic
1	$RuH(CO)(PPh_3)_2$(ACBA)	–12.41	8.53	-	-	7.2-8.04
2	$RuH(CO)(PPh_3)_2$ (AOBEA)	–12.39	5.86	6.63	-	6.85-7.68
3	$RuH(CO)(PPh_3)_2$(AOBA)	–12.35	5.08	-	2.24	6.28-7.92
4	$RuH(CO)(PPh_3)_2$(NACBA)	–11.89	8.83	-	-	6.27-8.65
5	$RuH(CO)(PPh_3)_2$(NAOBEA)	–11.21	5.75	6.55	-	6.29-8.09
6	$RuH(CO)(PPh_3)_2$(NAOBA)	–12.17	5.62	-	2.34	6.25-7.82
7	$RuH(CO)(Ph_3)_2$(BACBA)	–12.87	9.64	-	-	6.36-7.82
8	$RuH(CO)(PPh_3)_2$(BAOBEA)	–12.71	7.43	6.49	-	6.28-8.13
9	$RuH(CO)(PPh_3)_2$(BAOBA)	–12.68	7.29	-	2.51	6.26-7.75
10	$RuH(CO)(PPh_3)_2$(PHCBA)	–11.45	9.85	-	-	6.16-8.08
11	$RuH(CO)(PPh_3)_2$(OPHBEA)	–11.31	7.88	6.32	-	6.32-7.76
12	$RuH(CO)(PPh_3)_2$(OPHBA)	–11.23	7.57	-	2.69	6.34-7.67

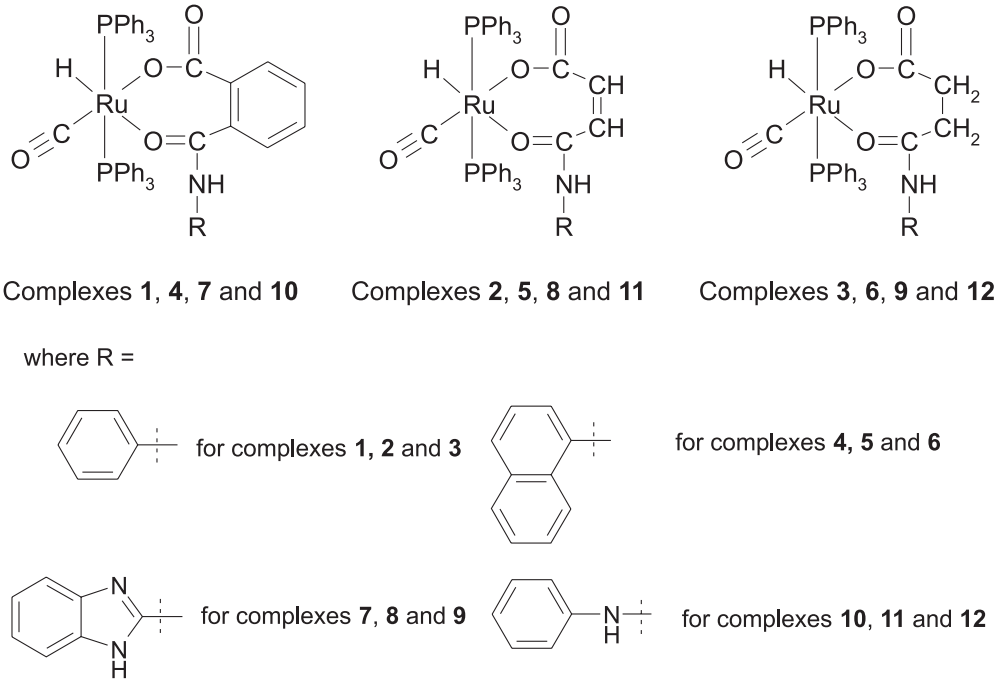
and spectrophotometric procedures. In the preliminary investigations, reducing agents such as Zn–HCl, titanium(III) chloride–glacial acetic acid and Pd-C(10%)-formic acid were used along with $[RuH(CO)(PPh_3)_2(ACBA)]$ (complex **1**) to reduce the nitro group of drug molecules to amino group. The percent yields of amino derivatives of these drugs, *viz.* RCP and RMZ, were found to be high when $[RuH(CO)(PPh_3)_2(ACBA)]$ was used as catalyst (Table 4). Similar tendencies were observed with the remaining eleven ruthenium(II) catalysts (complexes **2** - **12**). 0.01 mmol of ruthenium catalyst was found to be sufficient for the reaction. Acetic acid is preferred over HCl and formic acid because of better yields. In addition, the formed amino derivatives were determined by diazotization reaction with β-naphthol,[24] along with other color reagents such as trisodium pentacyanoaminoferrate,[22] P-benzoquinone[37] and 1,2-naphthaquinone-4-sulfonate.[25] As β-naphthol produces a high molar absorptivity value, it was preferred for color development (Table 5). The factors affecting color development, reproducibility, sensitivity, and conformity with Beer's law were also investigated. It was found that 1-3 mL of acetic acid, 1-3 mL of $NaNO_2$ solution and 0.5-1.5 mL of β-naphthol solution were necessary to achieve maximum color intensity. The excess of sodium nitrite was removed by addition of 1 mL of sulfamic acid solution. Addition of an excess of sulfamic acid has no effect on the color intensity of the product formed. λ_{max} values of both colored products were found to be 520 nm. The color products were stable up to one hour.

Table 4. Percent yields of RCP and RMZ with various reduction systems

Sample number	Reduction system	Yield (%) RCP	RMZ
1	$RuH(CO)(PPh_3)_2(ACBA)$-CH_3COOH	98.23	96.18
2	Zn-HCl	85.34	81.74
3	Titanium(III)chloride-CH_3COOH	80.45	76.15
4	Pd-C- HCOOH	72.14	69.01

Table 5. λ_{max} and ε_{max} values of RCP and RMZ with various color reagents

Sample number	Color reagent	RCP		RMZ	
		λ_{max}(nm)	ε_{max}(L mol^{-1} cm^{-1})	λ_{max}(nm)	ε_{max}(L mol^{-1} cm^{-1})
1	β-naphthol	520	7.20×10^3	520	2.56×10^3
2	Trisodiumpentacyanoaminoferrate	510	3.65×10^3	510	1.13×10^3
3	p-benzoquinone	520	5.62×10^3	520	2.02×10^3
4	1,2-naphthaquinone-4-sulfonate	510	6.12×10^3	510	2.25×10^3



Scheme 1. Structures of ruthenium(II) complexes derived from $[RuH_2(CO)(PPh_3)_3]$.

Interference studies

The extent of interference by additives such as talc, starch, boric acid, stearic acid, magnesium stearate, kaolin, sodiumlaurylsulfate and gelatin, used in the preparation of pharmaceuticals, were determined by measuring the absorbance of a solution containing 5 mL of chloramphenicol or metronidazole and various amounts of additives.[37] The majority of them do not interfere with the reduction nor with the determination. A 2% error in the absorbance readings was considered a tolerable limit.

Product analysis

The infrared spectra of chloramphenicol and metronidazole show a broad band around 1360 cm^{-1} due to the stretching of the nitro group. They do not show any sharp band around 3300 cm^{-1}, indicating the absence of aromatic primary amino group. The appearance of a strong absorption band around 3300 cm^{-1} in RCP and RMZ indicates the N-H stretching of aromatic primary amino group. Similarly, the disappearance of the broad peak at 1360 cm^{-1} indicates the absence of nitro group in RCP and RMZ.

Reduction of aromatic nitro groups to aromatic primary amino groups is further confirmed by NMR spectral analysis. The NMR spectra of CP and MZ do not show a peak at δ 4.13, whereas their reduction products show one additional broad peak at δ 4.10, confirming the presence of aromatic primary amino groups in them.

Table 6. Percent yields of RCP and RMZ formed with CP and MZ using ruthenium(II) catalysts of the type $[RuH(CO)(PPh_3)_2(L_2)]$

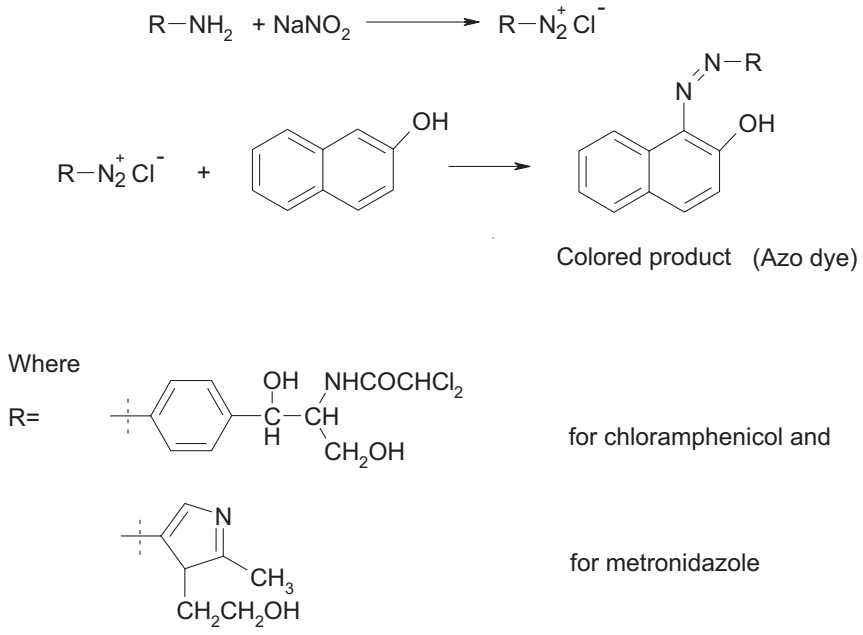
Complex No.	Complex	Yield (%)	
		RCP	RMZ
1	$RuH(CO)(PPh_3)_2$(ACBA)	98.23	96.18
2	$RuH(CO)(PPh_3)_2$(AOBEA)	98.54	97.15
3	$RuH(CO)(PPh_3)_2$(AOBA)	98.02	96.71
4	$RuH(CO)(PPh_3)_2$(NACBA)	99.65	98.23
5	$RuH(CO)(PPh_3)_2$(NAOBEA)	99.42	98.51
6	$RuH(CO)(PPh_3)_2$(NAOBA)	97.34	96.64
7	$RuH(CO)(PPh_3)_2$(BACBA)	98.35	97.28
8	$RuH(CO)(PPh_3)_2$(BAOBEA)	98.65	98.14
9	$RuH(CO)(PPh_3)_2$(BAOBA)	98.15	97.85
10	$RuH(CO)(PPh_3)_2$(PHCBA)	97.94	97.70
11	$RuH(CO)(PPh_3)_2$(OPHBEA)	98.81	96.46
12	$RuH(CO)(PPh_3)_2$(OPHBA)	97.98	97.64

The red colored azo dyes were formed with RCP and RMZ by the diazotization with nitrous acid and coupling with β-naphthol (Scheme 2). [24]

The percent yields of RCP and RMZ with all twelve ruthenium(II) catalysts were determined spectrophotometrically. The percent yields of RCP were high when compared to RMZ (Table 6).

Conclusions

Ruthenium(II) complexes with organic amide ligands were prepared from $[RuH_2(CO)(PPh_3)_3]$. Octahedral structures have been assigned to these complexes by analyzing elemental and spectral data. These complexes



Scheme 2. Colored products formed between RCP or RMZ and NL.

were used as catalysts in the reduction of nitro group containing drugs. This catalytic reduction method is based on the reduction of the nitro group of CP and MZ using the ruthenium(II) catalyst-glacial acetic acid system. The reduction method is simpler and more economical than most of the existing reduction methods. Analysis of authentic pharmaceuticals containing these drugs showed that there are no interferences from the common additives. Hence, this is an alternative approach for the reduction of drugs in quality control laboratories.

Supplementary Information

Spectra data are available free of charge at http://jbcs.sbq.org.br, as PDF file.

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Synthesis, Spectral Studies and Catalytic Activity of Ruthenium(II) Complexes with Organic Amides Ligands

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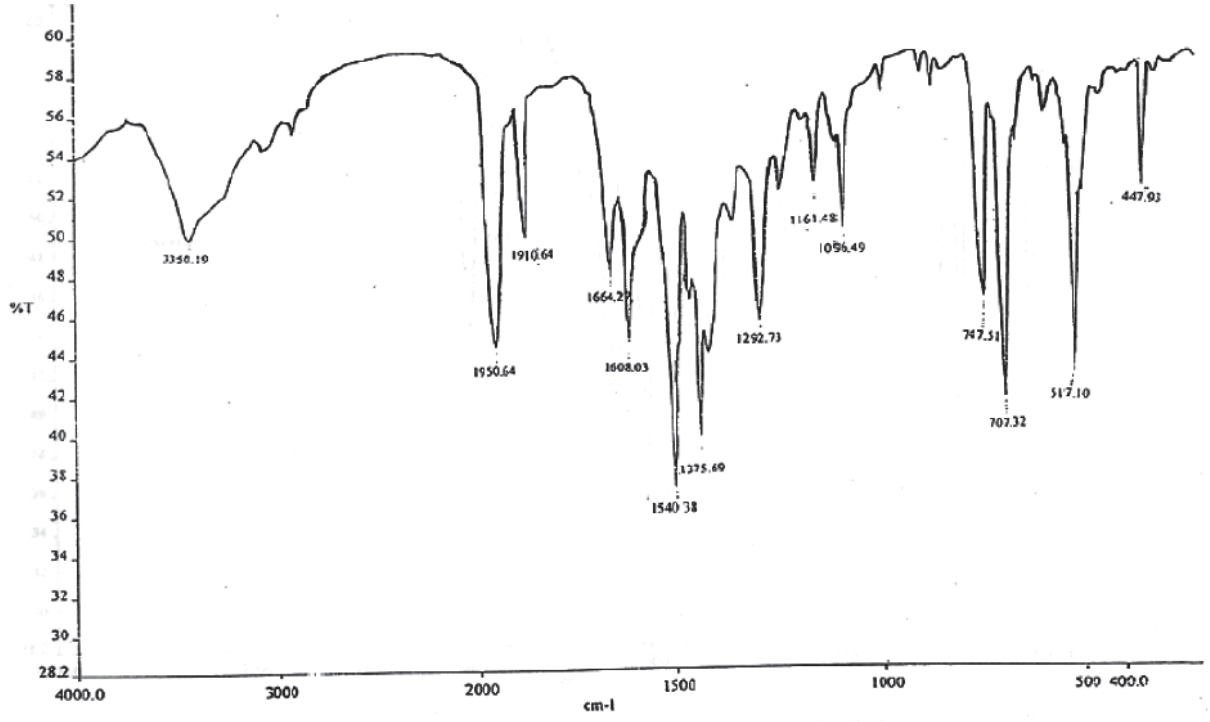

Figure S1. IR spectrum of [RuH(CO)(PPh_3)$_2$(ACBA)]

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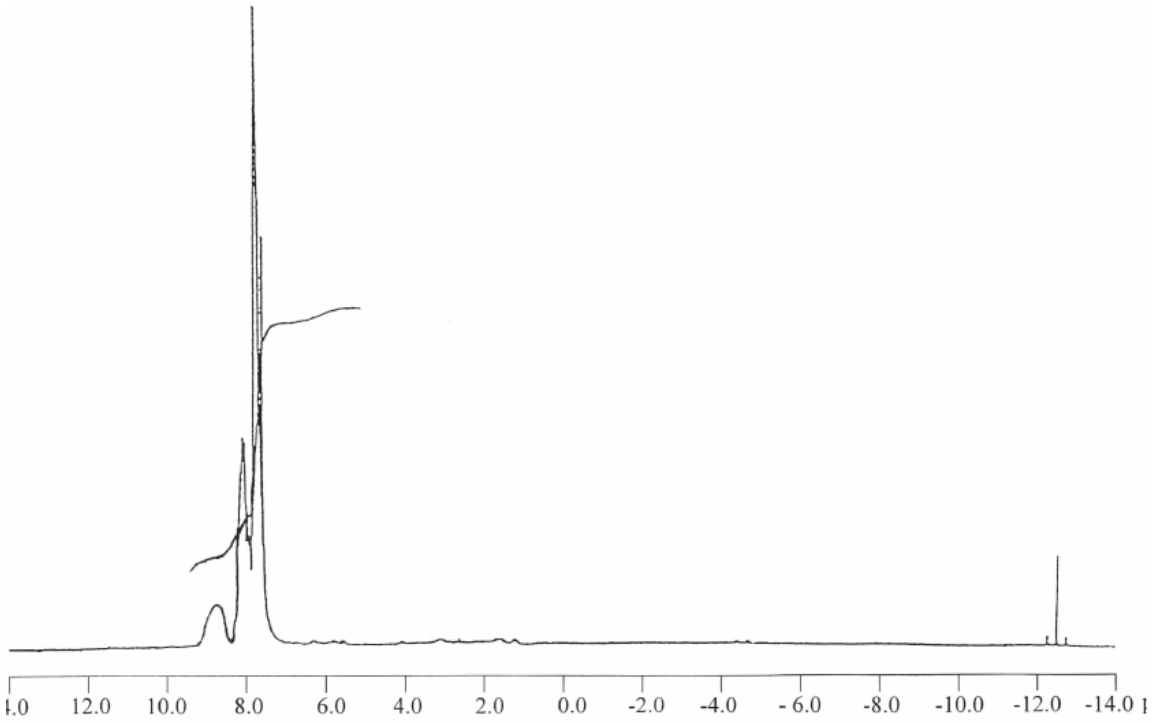

Figure S2. ^{1}H NMR spectrum of $[RuH(CO)(PPh_3)_2(ACBA)]$

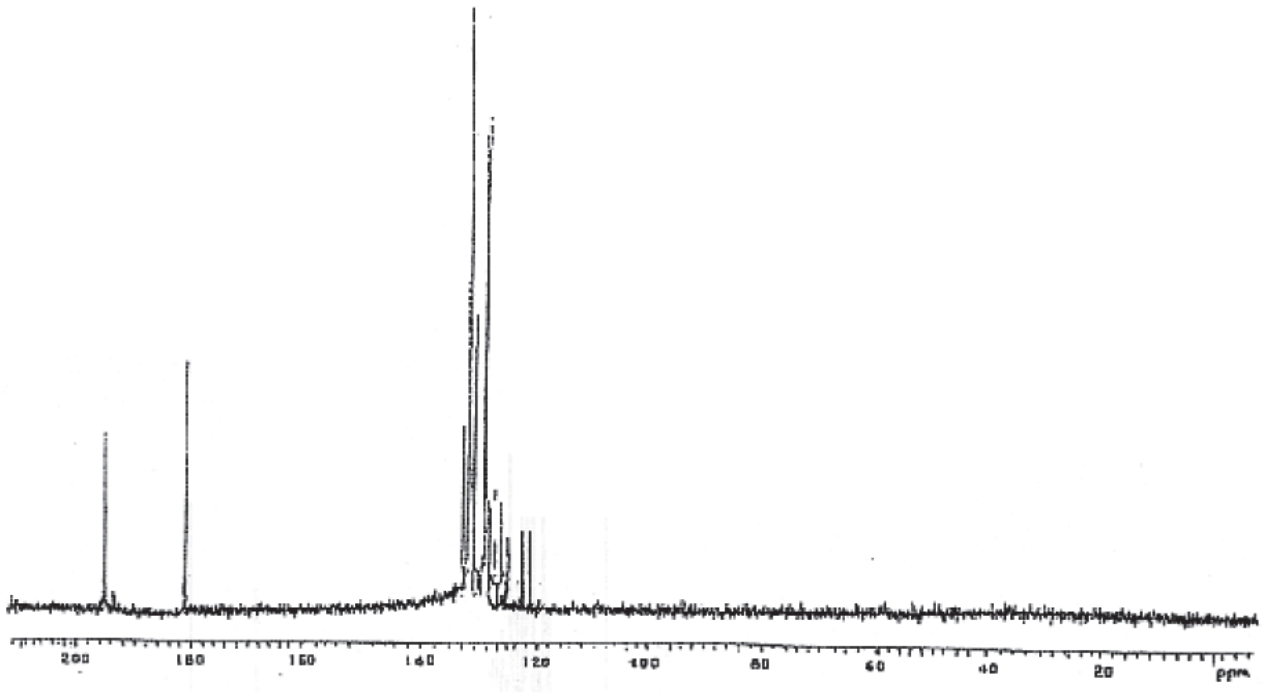

Figure S3. ^{13}C NMR spectrum of $[RuH(CO)(PPh_3)_2(ACBA)]$