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Der Pharmacia Lettre, 2013, 5 (2):95-100
(http://scholarsresearchlibrary.com/archive.html)

Der Pharmacia Lettre
Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Synthesis, spectral studies, catalytic and antibacterial activity of Ru (II) complexes with biologically active coordinated Amides

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ABSTRACT

Twelve novel catalytic and biologically active Ru(II)complexes with coordinating amides were synthesized and characterized by elemental analysis,IR,^{1}H,^{13}C NMR and mass spectral analysis, Molecular formulae have been tentatively proposed. These complexes were used as catalysts for the hydrolysis of rivastigmine and neostigmine pharmaceuticals and the percent yields of hydrolyzed products of these drugs were determined spectrophotometrically all the ligands and metal complexes were screened for antibacterial activity.

Keywords: synthesis, Ru (II) complexes, coordinated amides catalytic activity, antibacterial activity

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INTRODUCTION

The interest in design and synthesis of ruthenium chemistry stems from its ability to have a wide range of oxidation states(-2 to +8)and various coordination geometries[1] due to their stability and structural novelty [2-3]ruthenium organometallics exhibit versatile electron transfer properties hence a wide range of reactivity's [4].As a result, a large variety of ruthenium organometallics has been utilized as catalysts in the organic synthesis [5] hence there is a continuous pursuit for new ruthenium complexes with diverse types of ligands Literature survey[6-13] on the existing complexes of the precursor $RuHCl(CO)(PPh_3)$ reveals that the amide complexes of this precursor were not synthesized so far.with this in mind Ru(II) complexes with coordinated amide of the type $RuCl(CO)(PPh_3)_2(L_2)$(Complex 1-12)were synthesized and used as catalysts for hydrolysis of rivastigmine and neostigmine. The yields of hydrolyzed rivastigmine (HRS) and neostigmine (HNS) were determined spectro photo metrically [1].

MATERIALS AND METHODS

Analar grade samples of $RuCl_3.3H_2O$ (Johnson Matthey & Co.Ltd), acetone (Qualigens) and diethyl ether (Qualigens) were used as such. The ^{1}H NMR and ^{13}C NMR spectra ESI and FAB MS were used to obtain mass spectra. Hot air oven (Instrument and equipment Pvt.Ltd, Mumbai), incubator (Instrument and equipment Pvt.Ltd, Mumbai), laminar airflow unit (Clas laminar technologies Pvt. Ltd, secunderabad), autoclave (Medical instrument Mfg. Co., Mumbai) were used in the present investigations. Organisms like gram +ve *Bacillus subtilis* (MTCC-619, IMTECH, Chandigarh), *Staphylococcus aureus* (MTCC-96, IMTECH Chandigarh), and gram –ve bacteria *Escherichia coli* (MTCC-722, IMTECH Chandigarh), *Klebsiella pneumonia* (MTCC-109, IMTECH, Chandigarh), *Aspergillus flavus* (A. flavus) (MGM Hospital, Warangal), *Fusarium* (MGM Hospital, Warangal), were used in the present investigations.

The precursor RuHCl(CO)(PPh_3)[9] and twelve amide ligands viz. 2-(anilinocarbonyl) benzoic acid(ACBA); 4-anilino-4-oxobut-2-enoicacid (AOBEA); 4-anilino-4-oxobutanoicacid (AOBA); 2-[(1-napthylamino) carbony1] benzoic acid (NACBA); 4-(1-napthylamino)-4-oxobut-2-enoicacid (NAOBEA); 4-(1-naphthylamino)-4-oxobutanoic acid (NAOBA); (2-[(H-bezimidazol-2-ylamino)carbonyl]benzoic acid (BACBA); 4-(1H-bezimidazol-2-ylamino)-4-oxobut-2-enoicacid (BAOBEA); 4-(1H-bezimidazol-2-ylamino)-4-oxobut-2-enoicacid (BAOBA); 2-[(2-phenylhydrazino)carbonyl] benzoic acid(PHCBA); 4-oxo-4-(2-phenylhydrazino)-but-2-enoicacid (OPHBEA); 4-oxo-4-(2-phenylhydrazino) butanoic acid (OPHBA) were synthesized as previously reported [1].

General procedure for the preparation of compounds 1-12.
In a 100 ml round bottom flask, 20 ml of RuHCl(CO)(PPh_3)$_3$ solution (0.4 mmol, 0.381 g in acetone) and 20 ml of ligand solution (0.4 mmol viz. 0.096 g of ACBA, 0.076 g of AOBEA, 0.076 g of AOBA, 0.116 g of NACBA, 0.096 g of NAOBEA, 0.096 g of NAOBA, 0.112 g of BACBA, 0.092 g of BAOBEA, 0.092 g of BAOBA, 0.102 g of PHCBA, 0.082 g of OPHBEA, or 0.082 g OPHBA in acetone) were taken and the reaction mixture was stirred magnetically for 3 h. The resulting solution was concentrated to 5 ml under reduced pressure and a few ml of diethyl ether was added to initiate the crystallization. The resulting precipitate was separated by suction filtration, washed with diethyl ether, and vacuum dried to get a crystalline compound which was recrystallized using dichloromethane and diethyl ether solvent mixture.

RuCl(CO)(PPh_3)$_2$(ACBA)(1) Brown color solid (0.271g, 79%); IR: 3375, 1934, 1638,1556,1376,537,432,326 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$),(δ_{N-H}) 8.21, (Ar-H) 7.80 ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 170.92-179.21,187.42-195.81, 179.11-186.32,112.2-121.13 δ. Anal found: C, 65.98; H,4.33; N, 1.51; Ru, 10.84%. Calc. for $C_{51,}H_{40}ClNO_4P_2Ru$, C, 65.91; H, 4.30; N 1.50; Ru, 10.87 %.

RuCl(CO)(PPh_3**)$_2$(AOBEA)(2)** Gray color powder (0.266g, 76%); IR: 3378, 1961, 1653,1534,1385,547,420,342 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 5.40, A_{r-H} 6.92,$\delta_{CH=CH}$ 6.25; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 122.12-123.24,123.12-124.17, 125.112-126.32,112.2-121.13 δ. Anal. found: C, 64.11; H,4.35; N, 1.60; Ru, 11.56%; Calc. for $C_{47,}H_{38}ClNO_4P_2Ru$, C,64.20; H, 4.32; N 1.59 ; Ru, 11.49% .

RuCl(CO)(PPh_3)$_2$(AOBA)(3) Light yellow color solid (0.256g, 73%); IR: 3363, 1968, 1610,1525,1384,540,415,321 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 5.01, CH_2-CH_2 2.21, A_{r-H} 7.03-7.81; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 121.58-121.92,122.12-123.45, 123.54-123.86,124.14-125.56.Anal. found: C, 63.98; H,4.55; N, 1.61; Ru, 11.49%; Calc. for $C47_{1,}H_{40}ClNO_4P_2Ru$, C,64.05; H, 4.54; N 1.59 ; Ru, 11.47%;

RuCl(CO)(PPh_3)$_2$(NACBA)(4) Green color solid (0.289g, 74%; IR: 3265, 1955, 1639,1562,1383,542,413,335 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 8.75, A_{r-H} 6.24-7.65 ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 121.12-122.45,122.56-123.12, 123.56-124.85, 124.92-125.36 δ. Anal. found: C, 67.49; H,4.30; N, 1.45; Ru, 10.37%; Calc. for $C_{55,}H_{42}ClNO_4P_2Ru$, C,67.42; H, 4.29; N 1.43 ; Ru, 10.32%.

RuCl(CO)(PPh_3)$_2$(NAOBEA)(5) Light green solid (0.267g, 72%); IR: 3262, 1957, 1637,1560,1382,539,410,338 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 5.72, $\delta_{CH=CH}$ 6.15, A_{r-H} 6.25-7.69 δ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 114.62-114.88, 121.45-122.56,123.13-125.25, 126.15-126.85 δ. Anal found: C, 66.01; H,4.32; N, 1.53; Ru, 10.82; Calc. for $C_{51,}H_{40}ClNO_4P_2Ru$, C,65.91; H, 4.30; N 1.50 ; Ru, 10.87%.

RuCl(CO)(PPh_3)$_2$(NAOBA)(6) Light green solid (0.263g, 71%); IR: 3267, 1956, 1642,1563,1383,538,418,339 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 5.62, CH_2-CH_2 2.54, A_{r-H} 7.7-7.62 δ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ122.34-122.85, 123.18-123.75, 124.32-124.86, 125.12-126.25. Anal. found: C, 65.83; H,4.53; N, 1.53; Ru, 10.83%. Calc. for $C_{51,}H_{42}ClNO_4P_2Ru$, C, 65.77; H, 4.51; N, 1.50; Ru, 10.85%.

RuCl(CO)(PPh_3)$_2$(BACBA)(7) Light pink solid (0.294g, 76%); IR: 3360, 1938, 1623,1545,1388,537,425,341 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 9.68, A_{r-H} 6.34-7.82 δ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ127.32-128.45, 128.56-129.23, 129.50-131.52, 132.85-133.11. Anal. found: C, 64.49; H, 4.14; N, 4.36; Ru, 10.47%. Calc. for $C_{52,}H_{40}ClN_3O_4P_2Ru$, C, 64.42; H, 4.11; N, 4.33; Ru, 10.42%.

RuCl(CO)(PPh_3)$_2$(BAOBEA)(8) Light pink solid (0.275g, 75%); IR: 3368, 1936, 1625,1541,1380,538,412,338 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 7.47, $\delta_{CH=CH}$ 6.09, A_{r-H} 6.26-7.73 δ; ^{13}C NMR(67.3 MH_Z, $CDCl_3$) δ 116.21-117.54, 118.65-119.54, 119.60-121.52, 122.56-123.45 δ. Anal. found: C, 62.77; H,4.13; N, 4.54; Ru, 11.04; Calc. for $C_{48,}H_{38}ClN_3O_4P_2Ru$, C,62.71; H, 4.11; N 4.57 ; Ru, 10.99%.

RuCl(CO)(PPh_3)$_2$(BAOBA)(9) Light pink solid (0.279g, 76%); IR: 3274, 1939, 1631,1542,1382,540,420,337 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ_{N-H} 7.28, CH_2-CH_2 2.56, A_{r-H} 6.28-7.75 δ; ^{13}C NMR(67.93 MH_Z, $CDCl_3$) δ 126.52-

126.89, 127.15-127.82, 128.52-129.15, 130.25-131.35 δ. Anal. found: C, 62.64; H,4.36; N, 4.51; Ru, 11.01; Calc. for $C_{48,}H_{40}ClN_3O_4P_2$Ru, C,62.57; H, 4.34; N 4.56 ; Ru, 10.97%.

RuCl(CO)$(PPh_3)_2$(PHCBA)(10) Light brown powder (0.282g, 75%); IR: 3368, 1947, 16132,1531,1386,541,430,321 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ $_{N-H}$ 9.87, A_{r-H} 7.14-7.88 δ; ^{13}C NMR(67.93 $MH_{Z,}$ $CDCl_{3)}$ δ 125.62-125.85, 126.25-126.80, 127.52-128.55, 129.30-130.54 δ. Anal. found: C, 64.94; H,4.36; N, 3.80; Ru, 10.74; Calc. for $C_{51,}H_{41}ClN_2O_4P_2$Ru, C,64.86; H, 4.34; N 2.96 ; Ru, 10.70%.

RuCl(CO)$(PPh_3)_2$(OPHBEA)(11) Light green powder (0.264g, 74%); IR: 3362, 1948, 1611,1527,1388,542,426,322 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ $_{N-H}$ 7.86, δ $_{CH=CH}$ 5.34, A_{r-H} 6.64-7.67 δ; ^{13}C NMR(67.93 $MH_{Z,}$ $CDCl_{3)}$ δ 121.22-122.58, 122.62-123.54, 123.82-124.50, 124.80-125.12 δ. Anal. found: C, 63.19; H,4.38; N, 3.17; Ru, 11.33; Calc. for $C_{47,}H_{39}ClN_2O_4P_2$Ru, C,63.12; H, 4.36; N 3.13 ; Ru, 11.30%.

RuCl(CO)$(PPh_3)_2$(OPHBA)(12) Light brown powder (0.261g, 73%); IR: 33371, 1945, 1612,1529,1389,539,415,323 cm^{-1} ^{1}H NMR (200 MHz $CDCl_3$), δ $_{N-H}$ 7.58, CH_2-CH_2 2.67, A_{r-H} 6.32-7.66 δ; ^{13}C NMR(67.93 $MH_{Z,}$ $CDCl_{3)}$ δ 126.52-127.85, 128.12-130.54, 131.64-132.56, 133.15-139.72S δ. Anal. found: C, 63.03; H,4.61; N, 3.15; Ru, 11.30; Calc. for $C_{47,}H_{41}ClN_2O_4P_2$Ru, C,62.98; H, 4.58; N 3.12 ; Ru, 11.27%.

Antimicrobial testing by agar diffusion

Antimicrobial testing was done by cup plate method (14). 27 ml of molten agar was added in to sterile petri dishes and allowed to solidify for 1 hr then 50 ml of the 24 hrs culture of a test organism was spread evenly on to the agar plate with the sterile cotton swab. Six mm wide bores were made on the agar using a borer. The solution of the Ru (II) metal compounds were added in to each of the bores using a sterile tip with micro pipette. A similar plate was prepared by replacing Ru (II) metal compound by streptomycin sulphate.This was taken as a standard against bacteria. These dishes were then incubated at 37°C for 24 hrs. The zones of growth inhibition were found the activities of compounds were interpreted either active or inactive. The minimum inhibitory concentration required was also found when a series of dilutions were tested.

Determination of minimum inhibitory concentration (MIC)

The minimum inhibitory concentration [15] was determined by liquid dilution method. Stock solutions of Ru (II) compounds with 2.5 µg/ml, 5 µg/ml, 10µg/ml, 20 µg/ml, 50µg/ml and 100µg/ml concentrations were prepared with appropriate solvent. The solutions of standard drugs like Streptomycin and Ampicillin were also prepared in the same concentrations. Inoculums of the overnight culture were prepared. To a series of tubes containing 1 ml each of Ru (II) compound solution with different concentrations and 0.2 ml of the inoculums was added. Further 3.8 ml of the sterile water was added to each of the test tubes. These test tubes were incubated for 24 hrs and observed for the presence of turbidity. The absorbance of the suspension of the inoculums was detected using a spectrophotometer at 550 nm. This method was repeated by changing macro cyclic compounds with drugs like Streptomycin and Ampicillin for comparison.

Determination of antifungal activity

Ru (II) compounds were tested for their in vitro growth inhibitory activity against the pathogenic fungus, namely *A. flavus* and *Fusarium* species cultured on sabour dextrose agar medium prepared by taking 11 ml of distilled water in a conical flask followed by the addition of following ingredients: mycological peptone, 10 g; dextrose, 30 g; agar, 12 g; and the pH of the solution was adjusted to 5.7 boiling was continued until complete dissolution. After that, the solution was sterilized by autoclaving at 15 lb pressure (120 ^{0}C for 20 min) by diffusion method [16-18] and incubated at 28 0C for 3 days. Several test solutions of different concentration (microgram per liter) were prepared in water-methanol solution. The percentage inhibition of fungal growth was determined on the growth in test plates compared to that of respective control plates, given by the Vincent equation [19]. Percentage inhibition = 100(*C-T)/C,* Where *C* is the diameter of Fungal growth on the control plate, and T is the diameter of fungal growth on the test plate.

RESULTS AND DISCUSSION

In the present investigations twelve Ru (II) oraganometallic compounds by the direct condensation of 1:1 ratio of Ru (II) precursor with amides ligands and the corresponding ruthenium coordinated amides were synthesized.

All these compounds were characterized by elemental IR, 1H, and ^{13}C NMR and Mass spectral analysis. In IR spectral analysis, In order to study the binding mode of the amide ligand to ruthenium in the complexes the infrared spectra of free amide ligands and the precursor were compared with the spectra of Ru (II) complexes In the free amide ligands, the stretching frequencies of amide nitrogen and oxygen are observed in the range 3367–3252 and

1672–1631 cm–1, respectively. In the complexes spectra, negative shifts by 30–40 cm–1 are observed in the range 1653–1610 cm–1, indicating the coordination of amide oxygen to ruthenium [20]. No appreciable change is observed in the N–H region, confirming the non-involvement of amide nitrogen in coordination [21]. However, in the IR spectra of complexes having ligands derived from benzimidazoles viz. BACBA, BAOBEA, and BOABA, N–H (benzimidazole) modes are observed at 3360, 3368, and 3374 cm–1, respectively. Similarly, in the IR spectra of complexes Having ligands derived from phenylhydrazine viz. PHCBA, OPHBEA, and OPHBA, N-H(phenyl hydrazine) modes are observed at 3368, 3362, and 3371 cm–1, respectively. Strong Absorption bands are observed in the spectra of free amide ligands around 1710 and 1340 cm–1 due to C=O stretching and O–H deformations of carboxylic acid, respectively. In the spectra of the complexes, these bands are replaced by new bands in the ranges of 1563–1525 and1389–1376 cm–1 corresponding to COO– (asymmetric) and COO– (symmetric) vibrations [21]. The differences between the asymmetric and symmetric stretching frequencies of the coordinated carboxyl group lie in the 150–180 cm–1 range, which is a clear indication of the mononegative coordination of the carboxyl group of ligands [22]. The above facts support the mononegative bidentate coordination of amide ligands in the complexes through amide oxygen and carboxylic oxygen. In the precursor spectrum, a strong absorption band is present around 2020 cm^{-1}, indicating the presence of Ru–H bond, whereas in the spectra of the complexes, this band is not observed, indicating the replacement of the hydride ligand in the precursor by amide ligands [23]. The existence of a very strong band around 1960 cm^{-1} in the precursor spectrum indicates the presence of a terminally coordinated carbonyl ligand [24]. This peak is observed in the range 1968–1936 cm^{-1} in the spectra of the complexes [25]. In the precursor spectrum a strong absorption band around 540 cm–1 and a sharp peak around 320 cm^{-1} are observed due to the presence of Ru–P and Ru–Cl bonds. The appearance of a strong absorption band in the range 547–537 cm^{-1} in the spectra of the complexes indicates the presence of Ru–P bonds [26]. The coordination of the oxygen atom of the ligand with ruthenium is indicated by the presence of a band in the range 432–410 cm^{-1}. Similarly, the appearance of sharp peaks in the range 342–321 cm^{-1} in the spectra of the complexes indicates the presence of chloride ligands in all the complexes [27]. All the characteristic bands of triphenylphosphine are present in the expected regions in the precursor spectrum and spectra of the complexes [28].

The 1H NMR spectra of the precursor, free amide ligands, and Ru (II) complexes were recorded to confirm the presence of coordinated amide ligands in the new Ru (II) complexes. The integral intensities of each signal in the 1H NMR spectra of the precursor, ligands, and the corresponding complexes are found to agree with the number of different types of protons present. A sharp signal is present in the range (10.02–12.13)□in all the spectra of the ligands, indicating the presence of the carboxylic proton. The disappearance of this signal in the spectra of the complexes confirms the deprotonation of carboxylic acid followed by chelation through the oxygen atom [21]. A broad signal of the amide proton is observed in the range (5.08–9.99)□in the spectra of the ligands. Similar bands are virtually found in the range (5.01–9.87)in the corresponding complexes, confirming the non-participation of this group in chelation [20]. In the spectra of complexes containing ligands derived from benzimidazoles viz. BACBA, BAOBEA, and BOABA, N–H proton peaks in benzimidazolole are observed at 9.68, 7.47, and 7.28, respectively. Similarly, in the spectra of complexes containing ligands derived from phenyl hydrazine viz. PHCBA, OPHBEA and OPHBA, N–H proton peaks of the phenyl hydrazine unit are observed at 9.87, 7.86, and 7.587, respectively. A sharp signal is present at –13.51□in the precursor spectrum, indicating the presence of a proton attached to ruthenium. However, this signal is not observed in the spectra of the complexes, confirming the replacement of the proton attached to ruthenium by amide ligand [29]. The spectra of ligands viz. AOBEA, NAOBEA, BOABEA, and OPHBEA contain doublet of doublets at 6.69, 6.48, 6.45, and 5.42, respectively, and these signals are found in complexes at 6.25, 6.15, 6.09, and 5.34, respectively, indicating the presence of the CH=CH unit in both ligands and complexes. Similarly, the spectra of ligands viz. AOBA, NAOBA, BOABA, and OPHBA contain triplet of triplets at 2.26, 2.67, 2.69, and 2.74, respectively, and these signals are found in the complexes at 2.21, 2.54, 2.56, and 2.67, respectively, indicating the presence of the CH2–CH2 unit in both ligands and complexes [30]. Each complex shows multiplets in the range (6.24–7.88)□due to the presence of aromatic protons of ligands and triphenylphosphines [31]. ^{13}C NMR signals for the new Ru(II) complexes are assigned by comparing the spectra with those of the corresponding free amide ligands. The carboxylic carbon and carbonyl carbon of the amide group exhibit signals in the similar range (170.92–179.21) in free amide ligands. However, in the spectra of the complexes, ^{13}C signals are observed in the downfield regions of (187.42–195.81) and (179.11–186.32), indicating the coordinated carboxylic carbon and carbonyl carbon of the amide group, respectively [32]. The spectra of ligands viz. AOBEA, NAOBEA, BOABEA, OPHBEA and their corresponding complexes contain a signal in the range (112.12–121.22), confirming the presence of doubly bonded carbon. Similarly, the spectra of ligands viz. AOBA, NAOBA, BOABA, OPHBA and their corresponding complexes contain a signal in the range (31.12–34.31)□□ confirming the presence of singly bonded carbon. The aryl carbons are found to resonate in the range (121.58–139.72)□[31]. The 31P NMR spectra were recorded to confirm the presence and geometry of triphenylphosphine groups in the complexes. The appearance of singlets in the range (32.56–34.51)□in the spectra of the complexes confirms the presence of magnetically equivalent. Mass spectrum of RuCl (CO) $(PPh_3)_2$(ACBA). Phosphorous atoms, thereby suggesting that the two triphenylphosphine groups are Trans to each other around the Ru (II) center [33]. The ^{1}H, ^{13}C, and ^{31}P NMR spectra of RuCl (CO) $(PPh_3)_2(L_2)$.

The mass spectra,proposed molecular formula of the Ru (II) complex was confirmed by mass spectral analysis through comparing its formula weight with *m*/*z* values. The mass spectra contain molecular ion peaks at *m*/*z* (M+) of 928.5 (Complex1), 878.0 (**2**), 880.0 (**3**), 978.5 (**4**), 928.0 (**5**), 930.0 (**6**), 968.5 (**7**), 918.5 (**8**), 920.0 (**9**), 943.5 (**10**), 893.0 (**11**), and 895.0 (**12**). These data are in good agreement with the respective molecular formulas for RuCl(CO) $(PPh3)_2(L_2)$

Antibacterial activity: The antibacterial activities of the ligands and their metal complexes have been screened against four different bacteria by cup plate method [34]preliminary screening for all the compounds was performed at fixed concentrations of 2 mg/ml.each of the compounds was found to be acting on two types of gram+ve (Bacillus subtilis(MTCC-619) and Staphylococcus aures (MTCC-96)) and gram-ve bacteria (Escherichia coli (MTCC-722) and Klebsiella pneumonia (MTCC-109)) Out of twelve amide ligands,only three ligands namely BACBA,BAOBEA,and BAOBA (table 5) were found to be very effective based on the obtained values of relative zone of inhibition [35] It has also been observed in the antimicrobial screening studies that the ruthenium complexes showed higher activity than the corresponding free ligands against the same microorganism under identical experimental conditions. It was concluded that the ligands with the N and O donor systems might have inhibited enzyme production.Chelation reduces the polarity of the central ion mainly because of the partial sharing of its positive charge with the door groups and possible pie- electron delocalization within the whole chelating ring; this chelation increases the lipophilic nature of the central atom which favours its permeation through lipid layers of the cell membrane [36]. From the preliminary screening, Ru (II) compounds were found to be active against four different strains of bacteria and their rank order to be as follows: complex 8>7>9>11>10>12>5=4>6>2>1=3.

TABLE 1. Yields of HRS and HNS Obtained with Ru (II) Complexes with Coordinated Amide

Complex No	Ru(II) complex	Yield (%)	
		HRS	HNS
1	$RuCl(CO)(PPh_3)_2$(ACBA)	97.11	98.71
2	$RuCl(CO)(PPh_3)_2$(AOBEA)	97.72	98.76
3	$RuCl(CO)(PPh_3)_2$(AOBA)	96.25	98.45
4	$RuCl(CO)(PPh_3)_2$(APACBA)	97.56	98.78
5	$RuCl(CO)(PPh_3)_2$(APAOBEA)	97.65	98.45
6	$RuCl(CO)(PPh_3)_2$(APAOBA)	97.55	99.25
7	$RuCl(CO)(PPh_3)_2$(CBABA)	96.65	97.23
8	$RuCl(CO)(PPh_3)_2$(CPEABA)	97.47	98.27
9	$RuCl(CO)(PPh_3)_2$(CPABA)	98.47	99.75
10	$RuCl(CO)(PPh_3)_2$(NACBA)	95.28	96.68
11	$RuCl(CO)(PPh_3)_2$(NAOEA)	97.59	98.79
12	$RuCl(CO)(PPh_3)_2$(NAOBA)	97.62	98.55

Table 2. Zones of Inhibition for Ru (II) Complexes with Coordinated Amide against Four Different Bacteria

Complex No.	Ru(II) complex	Zone of inhibition (mm)			
		MTCC–619	MTCC–96	MTCC–722	MTCC–109
1	RuCl(CO)(PPh3)2(ACBA)	01	01	02	02
2	RuCl(CO)(PPh3)2(AOBEA)	03	04	06	08
3	RuCl(CO)(PPh3)2(AOBA)	01	01	01	03
4	RuCl(CO)(PPh3)2(APACBA)	07	06	11	12
5	RuCl(CO)(PPh3)2(APAOBEA)	07	06	10	12
6	RuCl(CO)(PPh3)2(APAOBA)	05	05	08	11
7	RuCl(CO)(PPh3)2(CBABA)	11	12	17	17
8	RuCl(CO)(PPh3)2(CPEABA)	13	13	18	18
9	RuCl(CO)(PPh3)2(CPABA)	10	11	15	16
10	RuCl(CO)(PPh3)2(NACBA)	08	09	13	14
11	RuCl(CO)(PPh3)2(NAOEA)	09	10	14	15
12	RuCl(CO)(PPh3)2(NAOBA)	07	08	13	14

Catalytic Activity. The hydrolysis of rivastigmine tartrate and neostigmine bromide by Ru(II) complexes with coordinated amide in the presence of sodium hydroxide was performed as per the conditions reported in our previous paper; the IR and NMR spectral data for hydrolyzed rivastigmine (HRS) and hydrolyzed neostigmine (HNS) matched exactly those reported earlier [1]. These two drug molecules were hydrolyzed separately in the presence of 0.01 mm of amide complexes of Ru (II) and 4 ml of 10% sodium hydroxide at 60oC. The resultant hydrolyzed products were determined spectrophotometrically by coupling them with 3-methylbenzothiazolinone hydra zone reagent in the presence of sodium metaperiodate. To assess the direct hydrolysis caused by the addition of sodium hydroxide was added to rivastigmine tartrate and neostigmine bromide separately in the absence of ruthenium catalyst at 60oC. The hydrolysis started after about 25 min and was completed 1 hour later. The yields of hydrolyzed products for rivastigmine and neostigmine were found to be 88.63% and 83.17%, respectively. However,

in the presence of $RuCl(CO)(PPh_3)_2$(ACBA) (1), the hydrolysis processes of both drugs were completed within ten min, and the yields of hydrolyzed products for rivastigmine as free base and neostigmine as bromide were found to be 97.11%, and 98.71% respectively. This supports the catalytic behavior of the complexes. The yields of HRS and HNS are presented in Table 1.

CONCLUSION

Twelve Ruthenium amide compounds were synthesized by non-template methods which involves the direct condensation of ruthenium compounds with different amides. The ruthenium amide compounds work has been assigned for these compounds, on the basis of elemental analysis, IR ^{1}H NMR, ^{13}C NMR and mass spectral data. All the compounds showed good antibacterial activity against gram+ve and garm-ve bacteria.

REFERENCES

[1] M Ashok; V Ravinder; A V S S Prasad. *Transition Met. Chem*., **2007,** 32, 23.
[2] J P Collin; D Jourenot; M Koizumi and JP Sauvage. *Inorg. Chem* ., **2005,** 44, 4693
[3] T Koike and T Ikaria. *Organometallics*, **2005,** 24 724.
[4] MJ Clarke. Coord. *Chem Rev*., **2002,** 69, 232.
[5] T Naota; H Takaya; SI Murahashi. *Chem. Rev*., **1998,** 98, 2599.
[6] N Ahmed; JJ Levison; S D Robinson and M F Uttley. *Inorg. Synth*., **1974**. 15, 48.
[7] K. Naresh Kumar; R Ramesh; Y Liu J. *Inorg. Biochem.*, **2006**, 100, 18.
[8] M V Kaveri; R Prabhakaran; ; R Karrembu; K Natarajan. *Spectrochim, Acta.A,*. **2005**, 13, 2915.
[9] S Kanchana devi; KP Balasubramanian; V Chinnu samy; R Karrembu; K Natarajan. *Transition Met. Chem*., **2005**, 30,330.
[10] K.P balasubramaniam; V Chinnu samy; R. Karrembu; K Natarajan, *Transition Met. Chem*., **2004**, 29, 644.
[11] C Jayabalakrishnan; R Karrembu; K Natarajan. *Transition Met. Chem.*, **2002**, 27, 790.
[12] TD Thangadurai; K Natarajan.*Transition Met. Chem.*, **2002**, 27,485.
[13] N Dharmaraj; P Vishvanathamurthi; K Natarajan. *Transition Met. Chem*., **2001**, 26,105.
[14] Alam S. Ind. Acad. Sci., J. *Chem. Sci*., **2004**, 166(6), 325.
[15] S A Salmon; JL watts; Cheryal A J Clin. *Microbial*, **1995**, 2435.
[16] R Cruikshank; JP Duguid; BP Marmion; Swain RHA. *Medical Microbiology*, 12th Edition, vol.II, **1975**, 403.
[17] PM Reddy; YP Ho; K.Shankar; R Rohini; Ravinder V. *Eur. J. Med. Chem.*, **2009**, 44, 2621.
[18] R Rohoni; K. Shankar; PM Reddy; YP Ho; Ravinder V. *Eur. J. Med. Chem.*, **2009**, 44, 3330.
[19] Vincent JM. Nature, **1947**, 189, 850.
[20] F. Elost, J. Sletton, R. Ring, M. Julve, J. Frans, and M. Verdanger, *Inorg. Chem*., **1992**, 31, 798
[21] V. Ravinder, P. Lingaiah, and K. Veera Reddy, *Inorg. Chim. Acta*, **1984**, 87, 35.
[22] S. D. Robinson and M. F. Uttley, *J. Chem. Soc. Dalton Trans*., **1973**, 1912.
[23] N. Dharmaraj, P. Viswanathamurthi, and K. Natarajan, *Transition Met. Chem*., **2001**, 26, 105.
[24] R. K. Poddar, K. P. Sharma, and U. S. Sharma, *Polyhedron*, **1985**,4, 1419.
[25] M. R. Maurya, I. R. Unny, N. A. Alekar, S. Gopinathan, and C. Gopinathan, *Ind. J. Chem*., **1997**,**36A**, 916.
[26] M. M. Taquikhan, Md. K. Nazeemuddin, and H. C. Bajaj, *Inorg. Chim. Acta*, **1988**,143, 177.
[27] P. V. Murthi, N. Dharmaraj, S. Anuradha, and K. Natarajan, *Transition Met. Chem*., **1998**, **23**, 337.
[28] S. Goswami, R. Mukerjee, and A. Chakravorty, *Inorg. Chem*., **1983**, 22, 2825.
[29] S. Gopinathan, I. R. Unny, S. S. Deshpande, and C. Gopinathann, *Ind. J. Chem*., **1986**, 25A, 1015.
[30] G. Balaswamy, B. K. Kumar, V. Ravinder, and S. J. Swamy, *Ind. J. Chem*., **33A**, 136 (**1994**).
[31] T. D. Thangadurai and S. Ihm, *Transition Met. Chem*., **29**, 189 (**2004**).
[32] M. Sarangapani and V. Ravinder, *Ind. J. Chem*., **41A**, 2060 (**2002**).
[33] Y. S. Pandey, H. N. Pandey, and P. Mathur, *Polyhedron*, **13**, 3111 (**1994**).
[34] TPT Cushine; AJ Lamba. Inter J. *Antimicrobial Agents*, **2005**, 26, 343.
[35] P Muralidhar Reddy; AVSS Prasad; V Ravinder. *Transition Met. Chem.*, **2007**, 32, 507.
[36] Maruvada; SC Pal; GB Nair. J. *Micro, Biomethods*, **1994**, 20, 115.