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# Ruthenium(II) carbonyl complexes containing pyridine carboxamide ligands and $PPh_3$/$AsPh_3$/Py coligands: Synthesis, spectral characterization, catalytic and antioxidant studies

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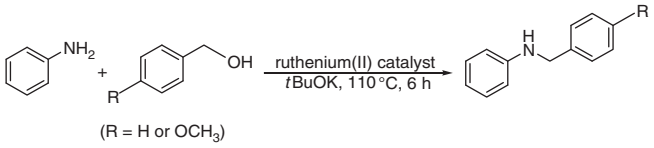
## HIGHLIGHTS

- Ruthenium(II) pyridine carboxamide complexes were synthesized and characterized.
- They have proved to be an efficient catalyst for the transfer hydrogenation of ketones.
- The catalytic efficiency of the complexes in *N*-alkylation of amine was examined.
- Ruthenium(II) complexes also exhibit good antioxidant activity.

## GRAPHICAL ABSTRACT

Ruthenium(II) pyridine carboxamide complexes were synthesized and characterized. They have been assigned an octahedral structure. The new complexes were found to be efficient catalyst for transfer hydrogenation of ketones and *N*-alkylation of amine. The complexes also exhibited excellent antioxidant (DPPH radical, NO radical OH radical and $H_2O_2$ scavengers) activities.

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## ABSTRACT

New ruthenium(II) carbonyl complexes bearing pyridine carboxamide and triphenylphosphine/triphenylarsine/pyridine have been prepared by direct reaction of ruthenium(II) precursors with some pyridine carboxamide ligands, *N*,*N*-bis(2-pyridinecarboxamide)-1,2-ethane ($H_2L^1$), *N*,*N*-bis(2-pyridinecarboxamide)-1,2-benzene ($H_2L^2$) and *N*,*N*-bis(2-pyridinecarboxamide)-trans-1,2-cyclohexane ($H_2L^3$). The organic ligands offering two $N_{amide}$ and two $N_{pyridine}$ donor sites to the metal centre. They have been characterized by elemental analyses, FT-IR, UV–Visible, NMR ($^1H$, $^{13}C$ and $^{31}P$) and ESI-MS techniques. Based on the above data, an octahedral structure has been assigned for all the complexes. The catalytic efficiency of the complexes in transfer hydrogenation of ketones in the presence of *i*PrOH/KOH and *N*-alkylation of amine in the presence of *t*BuOK was examined. Furthermore, the antioxidant activity of the ligands and its ruthenium(II) complexes were determined by DPPH radical, nitric oxide radical, hydroxyl radical and hydrogen peroxide scavenging methods, which indicates that the ruthenium(II) complexes exhibit more effective antioxidant activity than the ligands alone.



## Introduction

In the last few decades pyridine carboxamide ligands have been the subject of intense research in the field of co-ordination chemistry, because of their extraordinary properties they have found access to a great variety of catalytic and biological process, which include asymmetric allylic alkylation [1], epoxidation [2], cyclopropanations [3], norbornene polymerization [4], hydroxylation [5], DNA-binding [6] and the preparation of platinum(II) complexes with antitumor properties [7]. One factor which makes the ligands attractive for catalytic applications is the simplicity whereby the structure of the ligands can be modified by a modular approach. The electronic and steric properties can conveniently be modified by altering the diamine backbone by the introduction of suitable substituent in the pyridine nuclei [8]. Since the pyridine nitrogen atom resembles imidazole nitrogen, metal complexes of bispyridylamides have also been employed as models for metalloenzymes [9].

The transfer hydrogenation of ketones represents an useful means of producing value-added alcohols under relatively benign

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conditions, and many effective systems involving phosphorus- and nitrogen-ligated ruthenium complexes have been developed for this purpose [10]. The *N*-alkylation of amines is an important transformation for the preparation of pharmaceuticals, agrochemicals, polymers, dyes, and other fine chemicals [11]. Traditionally, the alkylation of amines is achieved using conventional alkylating agents, such as alkyl halides. Many alkyl halides have toxic or even mutagenic properties and an alternative to using such reagents is therefore advantageous [12]. In recent years, a number of reports on the hydroamination [13] and hydroamino-methylation of olefins or alkynes [14] for the synthesis of amines have been reported. Compared to the frequently applied *N*-alkylations with alkyl halides and reductive aminations methods, an economically and environmentally attractive method is the *N*-alkylation of amines using primary and secondary alcohols. Since the early 1980, transition metal complexes [15], in particular ruthenium complexes have been shown to be active for this transformation. Recently, Williams, Beller and co-workers [16] were able to obtain good yields in the *N*-alkylation of indoles by using 0.2–0.5 mol% of the dimeric Shvo's ruthenium catalyst (0.4–1 mol% Ru) at 110 °C. Matute also reported that small loadings of ruthenium pincer complex (1 mol% Ru) afford excellent results in the selective alkylation of (hetero) aromatic amines with alcohols [17].

Oxidation is highly important for many living organisms to produce their metabolic energy by using biological processes. However, oxygen-centred free radicals and other reactive oxygen species, that are continuously produced in cell result death and tissue damage. Atherosclerosis, ageing, cancer, diabetes mellitus, inflammation, AIDS, etc. may be related to oxidative damage [18]. So, ascorbic acid and tocopherols or superoxide dismutase and catalase are well known antioxidant compounds or enzymes, respectively, defend the organisms against free radical damage [19]. In the conditions that these defense systems may not be sufficient to prevent the damage, antioxidant supplements or foods containing antioxidants may be used to help the human body to reduce oxidative damage [20]. Transition metals are known to participate in reversible redox reactions. Several metal complexes, especially, ruthenium complexes have been investigated extensively [21]. In connection with our ongoing interest in this field of research, we have already investigated several ruthenium(II) complexes [22]. Herein, we describe the synthesis and characterization of a series of new class of ruthenium(II) pyridine carboxamide complexes along with their catalytic activity towards the transfer hydrogenation of ketones and *N*-alkylation of amine with alcohols in the presence of *t*BuOK. Further, the ligands and their ruthenium(II) complexes were also tested for antioxidant activity.

## Experimental

### *Materials and reagents*

Commercially available $RuCl_3{\cdot}3H_2O$ (Loba) was used without further purification. Solvent were purified and dried according to standard procedure. The pyridine carboxamide ligands [23] ($H_2L^1$, $H_2L^2$ and $H_2L^3$) and the starting complexes [$RuHCl(CO)(PPh_3)_3$] [24], [$RuHCl(CO)(AsPh_3)_3$] [25] and [$RuHCl(CO)(Py)(PPh_3)_2$] [26] were prepared as reported earlier. The structures of the ligands are given Fig. 1.

### *Physical measurements*

Elemental analyses (C, H, N) were performed on Vario EL III Elemental analyzer at SAIF-Cochin, India. IR spectra (4000–400 $cm^{-1}$) for KBr pellets were recorded on a Nicolet Avatar model FT–IR spectrophotometer. The electronic spectra of the complexes have been recorded in dichloromethane using a Shimadzu UV-1650 PC spectrophotometer in 800–200 nm range. $^1H$, $^{13}C$ and $^{31}P$ NMR spectra were recorded in Jeol GSX-400 instrument using DMSO as the solvent. $^1H$ and $^{13}C$ NMR spectra were obtained at room temperature using TMS as the internal standard. $^{31}P$ NMR spectra of the complexes were obtained at room temperature using *o*- phosphoric acid as a reference. The ESI–MS spectra were recorded by using LC–MS Q–ToF Micro-Analyzer (Shimadzu) in the SAIF, Panjab University, Chandigarh. Melting points were recorded on a Technico micro-heating table and are uncorrected. The catalytic yields were determined using ACME 6000 series GC-FID with DP-5 column of 30 m length, 0.53 mm diameter and 5.00 μm film thickness.

### *Synthesis of new ruthenium(II) pyridine carboxamide complexes (**1**–**9**)*

All the new mononuclear ruthenium(II) complexes were prepared by the following general procedure. An ethanolic solution of [$RuHCl(CO)(EPh_3)_2(B)$] ($E$ = P or As; $B$ = $PPh_3$, $AsPh_3$ or Py) and the appropriate ligand in 1:1 mol ratio was heated under reflux for 4–6 h. The solution was filtered while hot, reduced to half of its volume and left for slow evaporation. The resulting solid obtained was filtered, washed with diethyl ether and dried in *vacuo*. The purity of the complexes was checked by TLC.

*[$Ru(CO)(PPh_3)(L^1)$] (**1**)*

Brown solid, yield: 85%, m.p. 201 °C, elemental analysis calcd. (%) for $C_{33}H_{27}N_4PO_3Ru$: C, 60.09; H, 4.13; N, 8.49. Found: C, 60.18; H, 4.18; N, 8.40. IR (KBr Pellets, $cm^{-1}$): 1941 (s, C≡O), 1624 (s, C=O), 1347 (m, C—N), 653 (m, C=N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 219, 244, 347, 493. $^1H$ NMR ($CDCl_3$): (δ ppm): 9.18 (d, 2H, H-1), 8.37 (t, 2H, H-3), 8.18 (d, 2H, H-4), 7.94 (t, 2H, H-2), 7.85–7.19 (m, 15H, H-$PPh_3$), 4.04, 3.93 (m, 4H, H-6 and H-7). $^{13}C$ NMR ($CDCl_3$): (δ ppm): 204.73 (C≡O), 166.51 (C=O), 157.70 (C-5), 152.47 (C-1), 141.41 (C-3), 137.23–128.39 (C—$PPh_3$), 127.74 (C-2), 125.58 (C-4), 51.67 (C-6 and C-7). $^{31}P$ NMR (DMSO): (δ ppm): 28.15 (s, $PPh_3$), ESI–MS (m/z): 659 ($M^+$).

*[$Ru(CO)(PPh_3)(L^2)$] (**2**)*

Green solid, yield: 74%, m.p. 198 °C, elemental analysis calcd. (%) for $C_{37}H_{27}N_4PO_3Ru$: C, 62.80; H, 3.85; N, 7.92. Found: C, 62.75; H, 3.84; N, 7.40. IR (KBr Pellets, $cm^{-1}$): 1937 (s, C≡O), 1637 (s, C=O), 1340 (m, C—N), 651 (w, C=N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 237, 261, 322, 412. $^1H$ NMR ($CDCl_3$): (δ ppm): 9.23 (d, 2H, H-1), 8.54 (m, 2H, H-7), 8.40 (t, 2H, H-3), 8.20 (d, 2H, H-4), 7.94 (t, 2H, H-2) 7.68–7.19 (m, 15H, H—$PPh_3$), 7.09 (m, 2H, H-8). $^{13}C$ NMR ($CDCl_3$): (δ ppm): 204.13 (C≡O), 163.24 (C=O), 158.23 (C-5), 152.46 (C-1), 143.69 (C-6), 141.87 (C-3), 137.67–128.45 (C—$PPh_3$), 128.07 (C-2), 126.43 (C-4), 123.65 (C-8), 121.20 (C-7). $^{31}P$ NMR (DMSO): (δ ppm): 28.75 (s, $PPh_3$). ESI–MS (m/z): 707 ($M^+$).

*[$Ru(CO)(PPh_3)(L^3)$] (**3**)*

Brown solid, yield: 54%, m.p. 272 °C, elemental analysis calcd. (%) for $C_{37}H_{33}N_4PO_3Ru$: C, 62.26; H, 4.66; N, 7.85. Found: C, 62.52; H, 4.60; N, 7.98. IR (KBr Pellets, $cm^{-1}$): 1941 (s, C≡O),

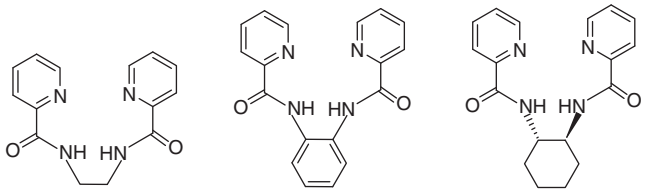


**Fig. 1.** Structure of pyridine carboxamide ligands.

1627 (s, C═O), 1354 (s, C—N), 653 (w, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 233, 247, 371, 457. $^1$H NMR ($CDCl_3$): (δ ppm): 9.27 (d, 2H, H-1), 8.29 (t, 2H, H-3), 8.09 (d, 2H, H-4), 7.94 (t, 2H, H-2), 7.73–7.25 (m, 15H, H-$PPh_3$), 4.26 (m, 2H, H-6), 2.40, 1.83 (m, 8H, H-7 and H-8). $^{13}$C NMR ($CDCl_3$): (δ ppm): 204.42 (C≡O), 164.14 (C═O), 157.81 (C-5), 152.31 (C-1), 141.82 (C-3), 137.67–128.58 (C—$PPh_3$), 127.63 (C-2), 125.31 (C-4), 52.32 (C-6), 32.68, 24.85 (C-7 and C-8). $^{31}$P NMR (DMSO): (δ ppm): 28.51 (s, $PPh_3$).

*[Ru(CO)(AsPh$_3$)(L$^1$)] (**4**)*

Pale brown solid, yield: 78%, mp. 243 °C, elemental analysis calcd. (%) for $C_{33}H_{27}N_4AsO_3Ru$: C, 56.33; H, 3.87; N, 7.96. Found: C, 56.53; H, 4.05; N, 7.64. IR (KBr Pellets, cm$^{-1}$): 1941 (s, C≡O), 1628 (s, C═O), 1352 (m, C—N), 654 (m, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 237, 244, 383, 430. $^1$H NMR ($CDCl_3$): (δ ppm): 9.24 (d, 2H, H-1), 8.35 (t, 2H, H-3), 8.07 (d, 2H, H-4), 7.90 (t, 2H, H-2), 7.88–7.17 (m, 15H, H—$AsPh_3$), 4.05, 3.90 (m, 4H, H-6 and H-7). $^{13}$C NMR ($CDCl_3$): (δ ppm): 205.01 (C≡O), 166.54 (C═O), 157.72 (C-5), 152.41 (C-1), 141.44 (C-3), 137.82–127.87 (C—$AsPh_3$), 127.70 (C-2), 125.51 (C-4), 51.63 (C-6 and C-7).

*[Ru(CO)(AsPh$_3$)(L$^2$)] (**5**)*

Pale brown solid, yield: 69%, m.p. 248 °C, elemental analysis calcd. (%) for $C_{37}H_{27}N_4AsO_3Ru$: C, 59.12; H, 3.62; N, 7.45. Found: C, 59.75; H, 3.64; N, 7.48. IR (KBr Pellets, cm$^{-1}$): 1945 (s, C≡O), 1625 (s, C═O), 1342 (m, C—N), 652 (w, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 207, 245, 352, 447. $^1$H NMR ($CDCl_3$): (δ ppm): 9.26 (d, 2H, H-1), 8.57 (m, 2H, H-7), 8.38 (t, 2H, H-3), 8.19 (d, 2H, H-4), 7.93 (t, 2H, H-2) 7.85–7.20 (m, 15H, H—$AsPh_3$), 7.06 (m, 2H, H-8). $^{13}$C NMR ($CDCl_3$): (δ ppm): 204.17 (C≡O), 163.27 (C═O), 158.27 (C-5), 152.45 (C-1), 143.71 (C-6), 141.88 (C-3), 137.68–128.47 (C—$AsPh_3$), 128.09 (C-2), 126.45 (C-4), 123.63 (C-8), 121.22 (C-7). ESI–MS (m/z): 751 ($M^+$).

*[Ru(CO)(AsPh$_3$)(L$^3$)] (**6**)*

Brown solid, yield: 45%, m.p. 258 °C, elemental analysis calcd. (%) for $C_{37}H_{33}N_4AsO_3Ru$: C, 58.65; H, 4.39; N, 7.39. Found: C, 58.92; H, 4.65; N, 7.98. IR (KBr Pellets, cm$^{-1}$): 1940 (s, C≡O), 1625 (s, C═O), 1354 (s, C—N), 653 (m, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 217, 222, 237, 382, 443. $^1$H NMR ($CDCl_3$): (δ ppm): 9.29 (d, 2H, H-1), 8.28 (t, 2H, H-3), 8.23 (d, 2H, H-4), 7.90 (t, 2H, H-2), 7.83–7.16 (m, 15H, H—$AsPh_3$), 4.21 (m, 2H, H-6), 2.46, 1.87 (m, 8H, H-7 and H-8). $^{13}$C NMR ($CDCl_3$): (δ ppm): 204.47 (C≡O), 164.11 (C═O), 157.79 (C-5), 152.37 (C-1), 141.78 (C-3), 137.41–128.51 (C—$AsPh_3$), 127.61 (C-2), 125.37 (C-4), 53.37 (C-6), 32.72, 24.84 (C-7 and C-8).

*[Ru(CO)(Py)(L$^1$)](**7**)*

Brown solid, yield: 54%, m.p. 185 °C, elemental analysis calcd. (%) for $C_{20}H_{17}N_5O_3Ru$: C, 50.42; H, 3.60; N, 14.70. Found: C, 50.58; H, 3.80; N, 14.72. IR (KBr Pellets, cm$^{-1}$): 1941 (s, C≡O), 1624 (s, C═O), 1347 (s, C—N), 649 (w, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 202, 221, 242, 382, 495. $^1$H NMR ($CDCl_3$): (δ ppm): 9.25 (d, 2H, H-1), 8.60 (d, 2H, Py), 8.38 (t, 2H, H-3), 8.06 (d, 2H, H-4), 7.93 (d, 2H, H-2), 7.84 (t, 2H, H—Py), 7.65 (t, 2H, H—Py), 4.03–3.97 (4H, H-6 and H-7). $^{13}$C NMR ($CDCl_3$): (δ ppm): 205.12 (C≡O), 166.57 (C═O), 157.71 (C-5), 152.47 (C-1), 151.27 (C—Py), 141.43 (C-1), 138.82 (C—Py), 127.77 (C-2), 125.94 (C—Py), 125.53 (C-4), 51.68 (C-6 and C-7).

*[Ru(CO)(Py)(L$^2$)] (**8**)*

Green solid, yield: 64%, m.p. 196 °C, elemental analysis calcd. (%) for $C_{24}H_{17}N_5O_3Ru$: C, 55.96; H, 3.27; N, 13.35. Found: C, 55.98; H, 3.84; N, 13.40. IR (KBr Pellets, cm$^{-1}$): 1941 (s, C≡O), 1618 (s, C═O), 1338 (s, C—N), 652 (m, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 202, 211, 242, 320, 434. $^1$H NMR ($CDCl_3$): (δ ppm): 9.34 (d, 2H, H-1), 8.64 (d, 2H, H—Py), 8.53 (m, 2H, H-7), 8.39 (t, 2H, H-3), 8.21 (d, 2H, H-4), 7.96 (t, 2H, H-2) 7.82 (t, 2H, H—Py), 7.61 (t, 2H, H—Py), 7.02 (m, 2H, H-8). $^{13}$C NMR ($CDCl_3$): (δ ppm): 204.16 (C≡O), 163.25 (C═O), 158.17 (C-5), 152.49 (C-1), 152.33 (C—Py), 143.76 (C-6) 141.83 (C-3), 139.21 (C—Py), 128.01 (C-2), 126.41 (C-4), 126.41 (C-4), 125.91 (C—Py), 123.69 (C-8), 121.28 (C-7).

*[Ru(CO)(Py)(L$^3$)] (**9**)*

Brown solid, yield: 48%, m.p. 205 °C, elemental analysis calcd. (%) for $C_{24}H_{23}N_5O_3Ru$: C, 54.33; H, 4.37; N, 13.20. Found: C, 54.52; H, 4.60; N, 13.98. IR (KBr Pellets, cm$^{-1}$): 1938 (s, C≡O), 1619 (s, C═O), 1341 (s, C—N), 652 (w, C═N). UV–Visible ($CH_2Cl_2$): $\lambda_{max}$ (nm): 233, 247, 350, 457. $^1$H NMR ($CDCl_3$): (δ ppm): 9.24 (d, 2H, H-1), 8.63 (d, 2H, H—Py), 8.24 (t, 2H, H-3), 8.07 (d, 2H, H-4), 7.96 (t, 2H, H-2,2), 7.81 (t, 2H, H—Py), 7.65 (t, 2H, H—Py), 4.44 (m, 2H, H-6), 2.43, 1.92 (m, 8H, H-7 and H-8). $^{13}$C NMR ($CDCl_3$): (δ ppm): 204.51 (C≡O), 164.01 (C═O), 157.80 (C-5), 152.37 (C-1), 152.24 (C—Py), 141.80 (C-3), 139.27 (C—Py), 127.61 (C-2), 125.29 (C-4), 125.09 (C—Py), 54.01 (C-6), 32.71, 24.83 (C-7 and C-8).

*General procedure for the ruthenium-catalyzed transfer hydrogenation of ketones*

The catalytic transfer hydrogenation reactions were conducted at a substrate/catalyst/base(S/C/base) molar ratio of 1:0.005:4. The procedure was described as follows. A mixture containing ketone (1 mmol), the ruthenium complex (**1**–**9**) (0.005 mmol) and KOH (4 mmol) in 10 ml of *i*PrOH was heated to reflux for 2 h. After completion of reaction the catalyst was removed from the reaction mixture by the addition of petroleum ether followed by filtration and subsequent neutralization with 1 M HCl. The ether layer was filtered through a short path of silica gel by column chromatography. The filtrate was subjected to GC analysis and the hydrogenated product was identified and determined with authentic samples.

*General procedure for the ruthenium-catalyzed N-alkylation of amine*

A mixture of amine (0.3 mmol), ruthenium(II) complex (**1**, **2**, **4** and **5**) ($3 \times 10^{-3}$ mmol), *t*BuOK (0.12 mmol) in benzyl alcohol or *p*-methoxybenzyl alcohol (0.9 mmol) was placed in a flask under atmospheric pressure of nitrogen and heated by an oil bath at 110 °C for 6 h. Then brine (3 ml) and $CH_2Cl_2$ (5 ml) were added. The organic layer was separated and the aqueous layer was extracted into $CH_2Cl_2$. The combined organic extracts were dried with magnesium sulfate and concentrated. The compounds were purified by chromatography and characterized by NMR spectroscopy. The product yields were obtained by the $^1$H NMR integration compared to the internal standard.

*N-phenylbenzylamine*

$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.34–7.01 (m, 5H, phenyl), 7.11 (m, 2H, phenyl), 6.72 (t, 1H, phenyl), 6.58 (d, 2H, phenyl), 4.31 (s, 2H, —$CH_2$NH—), 3.92 (br, 1H, —NH—).

*N-phenyl-(p-methoxybenzyl) amine*

$^1$H NMR (300 MHz, $CDCl_3$): δ (ppm): 7.26 (d, 2H, phenyl), 7.17 (m, 2H, phenyl), 6.89 (d, 2H, phenyl), 6.65 (d, 2H, phenyl), 6.21 (d, 1H, phenyl), 4.21 (s, 2H, —$CH_2$NH—), 3.95 (br, 1H, —NH—), 3.83 (s, 3H, —OMe).

*Antioxidant assays*

The ability of ruthenium complexes to act as hydrogen donors or free radical scavengers was explored by conducting a series of

*in vitro* antioxidant assays involving DPPH radical, nitric oxide radical, hydroxyl radical, hydrogen peroxide and comparing the results with standard antioxidants, including the natural antioxidant vitamin C and the synthetic antioxidant BHT.

*DPPH· scavenging assay*

The DPPH radical scavenging activity of the compounds was measured according to the method of Blios [27]. The DPPH radical is a stable free radical. Because of the odd electron, DPPH shows a strong absorption band at 517 nm in the visible spectrum. As this electron becomes paired off in the presence of a free radical scavenger, the absorption vanishes and the resulting decolorization is stoichiometric with respect to the number of electrons taken up. Various concentrations of the experimental complexes were taken and the volume was adjusted to 100 μl with methanol. About 5 ml of a 0.1 mM methanolic solution of DPPH was added to the aliquots of samples and standards (BHT and vitamin C) and shaken vigorously. A negative control was prepared by adding 100 ml of methanol in 5 ml of 0.1 mM methanolic solution DPPH. The tubes were allowed to stand for 20 min at 27 °C. The absorbance of the sample was measured at 517 nm against the blank (methanol).

*NO· scavenging assay*

The assay of nitric oxide (NO·) scavenging activity is based on a method [28] where sodium nitroprusside in aqueous solution at physiological pH spontaneously generates nitric oxide, which interacts with oxygen to produce nitrite ions. These can be estimated using the Greiss reagent. Scavengers of nitric oxide compete with oxygen leading to reduced production of nitrite ions. For the experiment, sodium nitroprusside (10 mM) in phosphate buffered saline was mixed with a fixed concentration of the complex and standards and incubated at room temperature for 150 min. After the incubation period, 0.5 ml of Griess reagent containing 1% sulfanilamide, 2% $H_3PO_4$ and 0.1% *N*-(1-naphthyl) ethylenediamine dihydrochloride was added. The absorbance of the chromophore formed was measured at 546 nm.

*OH· scavenging assay*

The hydroxyl radical scavenging activity of the complex has been investigated by using the Nash method [29]. *In vitro* hydroxyl radicals were generated by an $Fe^{3+}$/ascorbic acid system. The detection of hydroxyl radicals was carried out by measuring the amount of formaldehyde formed from the oxidation reaction with DMSO. The formaldehyde produced was detected spectrophotometrically at 412 nm. A mixture of 1.0 ml of iron-EDTA solution (0.13% ferrous ammonium sulfate and 0.26% EDTA), 0.5 ml of EDTA solution (0.018%), and 1.0 ml of DMSO (0.85% DMSO (v/v) in 0.1 M phosphate buffer, pH 7.4) were sequentially added in the test tubes. The reaction was initiated by adding 0.5 ml of ascorbic acid (0.22%) and was incubated at 80–90 °C for 15 min in a water bath. After incubation, the reaction was terminated by the addition of 1.0 ml of ice-cold trichloroacetic acid (17.5% w/v). Subsequently, 3.0 ml of Nash reagent was added to each tube and left at room temperature for 15 min. The intensity of the color formed was measured spectrophotometrically at 412 nm against reagent blank.

*$H_2O_2$ scavenging assay*

The ability of the complexes to scavenge hydrogen peroxide was determined using the method of Ruch et al. [30]. A solution of hydrogen peroxide (2.0 mM) was prepared in phosphate buffer (0.2 M, pH 7.4) and its concentration was determined spectrophotometrically from absorption at 230 nm with molar absorptivity 81 $M^{-1}$ $cm^{-1}$. The complexes (100 μg $ml^{-1}$), BHT and vitamin C (100 μg $ml^{-1}$) were added to 3.4 ml of phosphate buffer together with hydrogen peroxide solution (0.6 ml). An identical reaction mixture without the sample was taken as negative control. Absorbance of hydrogen peroxide at 230 nm was determined after 10 min against the blank (phosphate buffer).

For the above four assays, all the tests were run in various concentrations of the compounds were used to fix a concentration at which compounds showed in and around 50% of activity. In addition, the percentage of activity was calculated using the formula, % of activity = $[(A_0–A_C)/A_0] \times 100$ ($A_0$ and $A_C$ are the absorbance in the absence and presence of the tested complex respectively). The 50% of activity ($IC_{50}$) can be calculated using the percentage of activity results.

## Results and discussion

Diamagnetic, hexa-coordinated low spin ruthenium(II) pyridine carboxamide complexes of general formula [Ru(CO)(B)(L)] (B = $PPh_3$, $AsPh_3$ or Py; L = pyridine carboxamide ligand) were synthesized in quantitative yield from the reaction of [RuHCl(CO)$(EPh_3)_2$(B)] (E = P or As; B = $PPh_3$, $AsPh_3$ or Py) with pyridine carboxamide ligands in ethanol in 1:1 M ratio. In all these reactions, it was observed that the pyridine carboxamide behave as dianionic tetradentate ligands by replacing two molecules of triphenylphosphine or triphenylarsine, one molecule of hydride and one moles of chlorine from the starting complexes.

The analytical data (C, H, N) of all the pyridine carboxamide ligands and their ruthenium(II) complexes are in good agreement with the calculated values, thus confirming the proposed mononuclear composition for all the complexes. The complexes were obtained in powder form. All the ligands and their complexes are stable at room temperature, non-hygroscopic and insoluble in water and soluble in dichloromethane, chloroform, benzene, acetonitrile, ethanol, methanol, dimethylformamide and dimethylsulfoxide. Various attempts have been made to obtain the single crystals of the complexes but it has been unsuccessful. In order to confirm the composition of the new complexes, ESI–MS spectra were recorded in positive mode. The molecular ion peaks ($M^+$) observed at $m/z$ = 659, 707 and 751 (complexes **1**, **2** and **5**) supporting the molecular formulae. In addition, few representative fragment peaks were seen in the spectra of the three complexes. These fragments indicated the coordination of pyridine carboxamide ligands to the ruthenium metal atom.

*Infrared spectroscopic analysis*

The FT–IR data of the complexes are given in the experimental section. Meaningful information regarding the bonding sites of the ligand molecules can be obtained by comparing the IR spectra of ruthenium(II) complexes with the uncomplexed ligands. The IR spectra of the ligands exhibit a band at 3316–3330 $cm^{-1}$ due to NH group. The absence of $\upsilon_{N\text{-}H}$ in the IR spectra of the complexes confirms that the ligands are coordinated in their deprotonated form [31]. A further indication of the formation of deprotonated complexes is the rather large decrease (red shifted) in the carbonyl (amide I) stretching frequency exhibited by the ligands upon complex formation. A strong band at 1653–1678 $cm^{-1}$ in the free ligands is assigned to C═O stretching. This band shifted to 1618–1637 $cm^{-1}$ in complexes, which is in accordance with the data reported for the related complexes [32]. The medium bands at 1518–1536 $cm^{-1}$ and 1250–1278 $cm^{-1}$ in the free ligands are assigned to amide II and amide III modes. The amide II and amide III bands, combination of $\upsilon_{C–N}$ and $\delta_{N–H}$ modes, are replaced by a medium to strong band at 1338–1354 $cm^{-1}$. This replacement is to be expected, as the removal of an amide proton produces a pure C—N stretch [33]. The band at 618–624 $cm^{-1}$ in the free ligands, attributable to the in-plane deformation of the pyridine ring, shifts to higher frequency at 649–654 $cm^{-1}$ in its ruthenium complexes,

thus indicating ligation of the pyridine nitrogen atoms [34] of the ligands to ruthenium. Further the strong absorption around 1945–1937 $cm^{-1}$ have been assigned to the terminally coordinated carbonyl group in the new ruthenium complexes [35]. In the case of complexes (**7**, **8** and **9**) containing coordinated heterocyclic nitrogen bases, a medium intensity band was observed in the region 1026–1031 $cm^{-1}$. In addition, the other characteristic bands due to triphenylphosphine and triphenylarsine (around 700, 1090 and 1440 $cm^{-1}$) were also present in the spectra of all the complexes [36].

*Electronic spectroscopic analysis*

The electronic spectra of all the new complexes have been recorded in $CH_2Cl_2$ solution. The spectral data are given in the experimental section. The band around 412–495 nm range has been assigned to the spin allowed $^1A_{1g} \rightarrow {}^1T_{1g}$ transition. The other high intensity bands around 320–383 nm have been assigned to charge transfer transitions arising from the metal $t_{2g}$ level to the unfilled molecular orbitals derived from the $\pi^*$ level of the ligands [37] based on their extinction coefficient values. The bands below 300 nm were characterized by intra-ligand charge transfer. The electronic spectra are similar to those observed for other octahedral ruthenium(II) complexes [38].

*$^1$H NMR spectroscopic analysis*

The $^1$H NMR spectra of the ligands and the corresponding ruthenium(II) pyridine carboxamide complexes were recorded in $CDCl_3$ to confirm the presence of coordinated ligand in the complexes. The spectral data and their assignments are given in the experimental section. The spectra of the free ligands showed a signal at 8.6–10.7 ppm characteristics of amide [—C(O)NH—] proton [39], which is absent in the complexes, suggesting that the coordination is through deprotonated amide nitrogen. As expected, the most significant downfield shifts correspond to the protons (H-1), ortho to the pyridyl nitrogen atom, exhibit its peak in the region of 9.18–9.34 ppm [40]. The triplets at 8.24–8.40 ppm for all complexes are assigned to the H-3 protons of ligands, which is shifting to the downfield compared with the free ligands. The signal for H-4 protons was observed as a doublet at 8.06–8.23 ppm region and H-2 protons were appeared as a triplet at 7.90–7.96 ppm for all the complexes. In the spectra of the complexes **2**, **5** and **8**, two multiplets were observed around 8.53–8.57 and 7.02–7.09 ppm due to the H-7 and H-8 protons of the ligands. The spectra of the complexes **1**, **4** and **7**, two multiplets were observed around 3.90–3.97 and 4.03–4.05 ppm due to the H-6 and H-7 protons respectively. The spectrum of the complexes **3**, **6** and **9** exhibited three signals around 1.83–1.92 ppm, 2.40–2.46 ppm and 4.21–4.44 ppm, corresponding to the H-6, H-7 and H-8 protons. The spectra (complexes **7**, **8** and **9**) showed two triplets and a doublet for pyridine protons that appeared in the range 7.61–7.65, 7.81–7.84 and 8.60–8.64 ppm. The multiplets at 7.16–7.73 ppm in the spectra of the complexes **1**–**6** are assigned to $PPh_3$/$AsPh_3$ protons.

*$^{13}$C NMR spectroscopic analysis*

$^{13}$C NMR spectra of complexes were recorded in $CDCl_3$, and their assignments are given in the experimental section. A peak at 204.13–205.12 ppm region is due to C≡O carbon. The signals at 163.24–166.57 ppm and 157.71–158.27 ppm in the spectrum of the complexes are assigned to the carbonyl carbon (C═O) and the pyridyl carbon C-5, respectively [41]. The most significant downfield shifts correspond to the carbons (C-1), ortho to the pyridyl nitrogen atom, exhibit its peak in the region of δ 152.31–152.49 ppm. The peaks at 141.41–141.87 ppm are assigned to C-3 carbon. The appearance of a peak at 127.61–128.09 ppm region in the spectrum arises due to C-2 carbon. The carbons C-4 exhibit its peak in the region of 125.58–126.45 ppm. The signals at 51.63–51.68 (complexes **1**, **4** and **7**) ppm are assigned to C-6 and C-7 respectively. The spectrum of **2**, **5** and **8** showed three peaks around 143.71–143.87, 123.63–123.69, 121.20–121.28 ppm corresponding to the C-6, C-7 and C-8 carbon respectively. The complexes **3**, **6** and **9** exhibited three signals around 24.83–24.85 ppm, 32.68–32.72 and 53.37–54.01 ppm corresponding to the C-6, C-7 and C-8 carbons. The multiplets appear around 127.87–137.23 ppm region are assigned to $PPh_3$/$AsPh_3$ carbons. The data confirm the formation of new ruthenium(II) pyridine carboxamide complexes.

*$^{31}$P NMR spectroscopic analysis*

$^{31}$P NMR spectra of some of the complexes were recorded to confirm the presence of triphenylphosphine group in the complexes. A sharp singlet was observed around 28.15–28.75 ppm due to presence of triphenylphosphine ligand in the complexes.

On the basis of analytical and spectral IR, electronic, $^1$H, $^{13}$C, $^{31}$P NMR and ESI-MS data, an octahedral structure (Fig. 2) has been tentatively proposed for all the new ruthenium(II) pyridine carboxamide complexes.

*Catalytic transfer hydrogenation (TH) of ketones*

TH reaction in which hydrogen is transferred from one organic molecule to another is of great importance in organic synthesis since one can avoid the use of molecular hydrogen [42]. The ruthenium(II) complexes (**1**–**9**) catalyzed the reduction of ketones to the corresponding alcohols *via* hydrogen transfer from *i*PrOH with KOH as the promoter. The reaction was conducted at a substrate, catalyst and base in molar ratio 1:0.005:4 respectively. Complex **5** was selected as a model catalyst for optimization of the reaction conditions. In order to study the effect of time on the activity, the product analysis was done at regular intervals of time under similar reaction conditions (Fig. 3). In order to optimize the reaction conditions, different substrate/catalyst/base (S/C/base) ratios were tested and the results are summarized in Table 1. When increasing

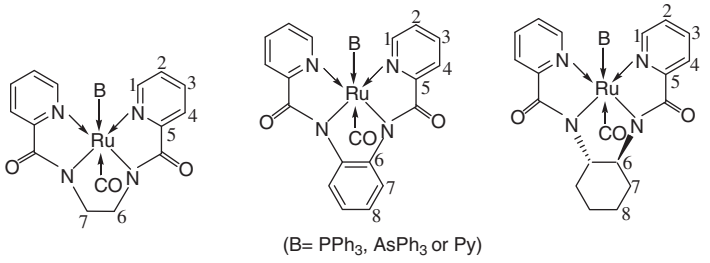



**Fig. 2.** Structure of new ruthenium(II) pyridine carboxamide complexes.

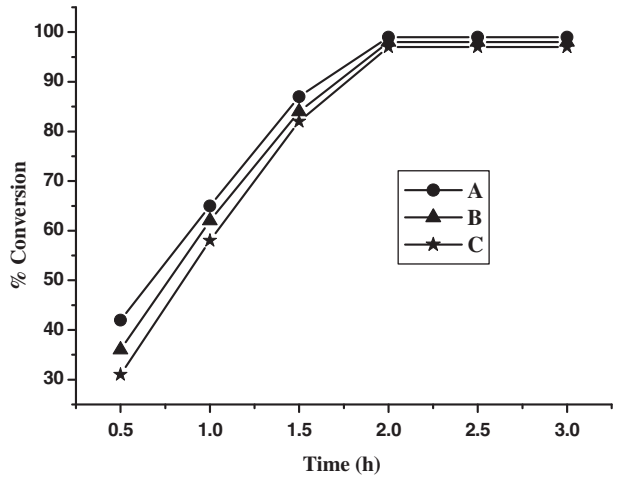



**Fig. 3.** Catalytic transfer hydrogenation of: (A) Acetophenone, (B) benzophenone, (C) cyclohexanone in different time intervals.

**Table 1**
Catalytic transfer hydrogenation of acetophenone by complex (**5**).

| Entry | Substrate/catalyst/base ratios | | | Time (h) | Conversion (%)[a] |
|---|---|---|---|---|---|
| 1 | 1 | 0.1 | 4 | 2 | 64 |
| 2 | 1 | 0.05 | 4 | 2 | 78 |
| 3 | 1 | 0.01 | 4 | 2 | 88 |
| 4 | 1 | 0.005 | 4 | 2 | 99 |
| 5 | 1 | – | 4 | 4 | Not detected |
| 6 | 1 | 0.005 | 2 | 2 | 80 |
| 7 | 1 | 0.005 | – | 2 | Not detected |

[a] Conversion of the product determined by GC.

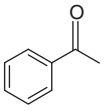
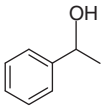
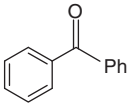
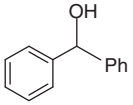
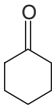
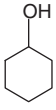
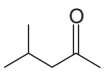
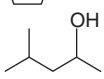
the S/C/base ratio to 1:0.01:4, 1:0.05:4, 1:0.1:4 in (Entry 1, 2 and 3) *i*PrOH, the reaction still proceeds with reasonable conversions. Thus, it was concluded that S/C/base ratio of 1:0.005:4 is the best compromise between optimum reaction rates (Entry 4). A blank experiment carried out in the absence of the catalyst gave no hydrogenation of acetophenone at all (Entry 5). As expected, the conversion of the reaction decreased dramatically by decreasing the base quantity (Entry 6). In the absence of a base no transfer hydrogenation of the ketones was observed (Entry 7).

A variety of ketones were transformed into the corresponding secondary alcohols using the complexes (**1**–**9**) as the catalyst. Typical results are shown in Table 2. The most efficient conversions are found in the case of acetophenone with all catalysts (up to 99%), while in the case of aliphatic secondary ketone the conversions were up to 84%. The catalysts efficiently catalyzed the reduction of benzophenone into benzhydrol up to 84–97% conversions. Interestingly, the catalysts show excellent activity for the conversions of five- and six-membered cyclic ketones to their corresponding alcohols with 67–95% conversions in the case of cyclopentanone and 87–98% conversions in case of cyclohexanone. The catalytic efficiency varies in the order of $—C_6H_4— > —CH_2CH_2— > —C_6H_{10}—$, which may be tailored by a bulky group present on diamine backbone of the pyridine carboxamide ligand. The complex catalysts **2** and **5** are the most efficient catalyst among all, because of the presence of the bulky pyridine carboxamide moiety ($—C_6H_4—$), which appears to lead to an improvement in activity. It is further inferred from the results that the triphenylphosphine, triphenylarsine, pyridine ligands may also influence the catalytic efficiency by their electron donor–acceptor nature. The presence of a catalytic amount of base is necessary for the transfer hydrogenation of ketones. Acetone was identified as only byproduct in all the cases. As the catalyst is stable in all organic solvents and it can be recovered and the work up process is also very simple for this catalytic system. The catalytic activity of the present complex is low when compared to ruthenium complexes containing Schiff base or pincer ligands [43,44]. However, the catalytic efficiency of the complex is better than the other ruthenium complexes in the transfer hydrogenation of ketones with respect to substrate/catalyst ratio (1:0.005) [45,46].

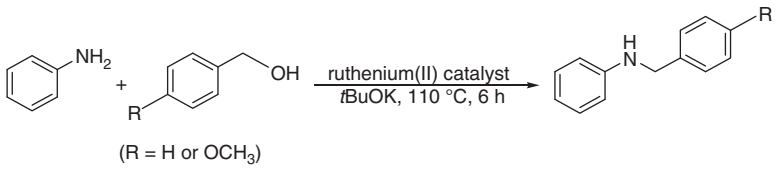
*Catalytic N-alkylation of amine*

The ruthenium(II) complexes **1**, **2**, **4** and **5** catalyzed the *N*-alkylation of amine with alcohols in the presence of *t*BuOK (scheme 1). In a typical experiment, a mixture of aniline, benzyl alcohol or *p*-methoxybenzyl alcohol, *t*BuOK and ruthenium(II) complex

**Table 2**
Catalytic transfer hydrogenation of ketones using complexes (**1**–**9**) as catalyst.[a]

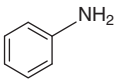
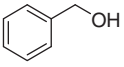
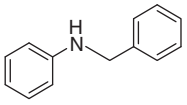
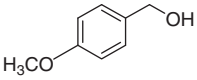
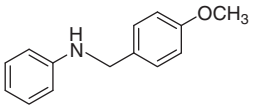
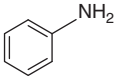
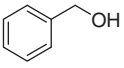
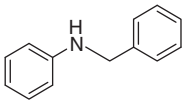
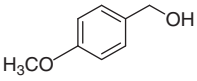
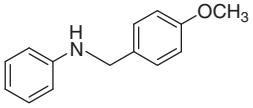
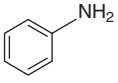
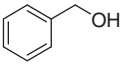
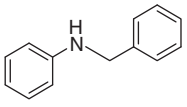
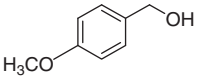
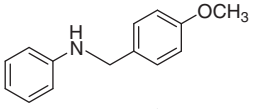
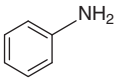
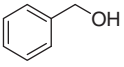
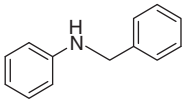
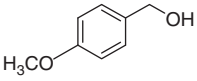
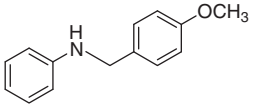
| Substrate | Product | Conversion (%)[b] | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** |
|  |  | 95 | 98 | 94 | 97 | 99 | 96 | 91 | 92 | 89 |
|  |  | 94 | 95 | 87 | 95 | 97 | 92 | 90 | 91 | 84 |
|  |  | 96 | 97 | 93 | 97 | 98 | 91 | 88 | 95 | 87 |
|  |  | 92 | 93 | 87 | 92 | 95 | 88 | 69 | 72 | 67 |
|  |  | 74 | 78 | 72 | 79 | 84 | 73 | 63 | 64 | 61 |

[a] Reaction conditions:1.0 mmol substrate, catalyst (0.005 mmol), base (4 mmol) in *i*PrOH (10 ml) reflux at 80 °C for 2 h.
[b] Conversion of the product determined by GC.




**Scheme 1.** *N*-alkylation of amine.

**Table 3**
*N*-alkylation of amine catalyzed by ruthenium(II) complexes (**1**, **2**, **4** and **5**).[a]

| Complex | Amine | Alcohol | Product | Yield (%)[b] |
|---|---|---|---|---|
| 1 |  |  |  | 81 |
| | |  |  | 62 |
| 2 |  |  |  | 86 |
| | |  |  | 65 |
| 4 |  |  |  | 71 |
| | |  |  | 63 |
| 5 |  |  |  | 88 |
| | |  |  | 71 |

[a] Reaction conditions: amine (0.3 mmol), catalyst ($3 \times 10^{-3}$ mmol), *t*BuOK (0.12 mmol) in benzyl alcohol or *p*-methoxybenzyl alcohol (0.9 mmol) reflux at 110 °C for 6 h.
[b] Yield based on NMR integration.

(1:3:0.4:0.01) was placed in a flask. Excess benzyl alcohol or *p*-methoxybenzyl alcohol was used as the solvent, and the mixture was heated to 110 °C for 6 h. The desired amine product was extracted from the reaction mixture and analyzed by $^1$H NMR spectroscopy. Product yields were obtained by the $^1$H NMR integration compared to the internal standard. As shown in the Table 3, benzyl alcohols reacted smoothly to give the corresponding products in good yields (71–88%) whereas, *p*-methoxybenzyl alcohol gave the corresponding product in moderate yield (up to 71%). As can be seen in Table 3, complex **5** is a significantly better catalyst than other complexes. Comparison with protocols previously developed for this reaction [47], the catalyst loadings are very low and the reaction conditions are very mild in the present catalytic system.

*Antioxidant activity*

The DPPH, NO and OH radicals have been widely used to test the ability of compounds as free radical scavengers to evaluate the antioxidant activity. The scavenging activity may help to arrest the chain of reactions initiated by excess generation of radicals that is detrimental to human health. Among all free radicals, the hydroxyl radical is by far the most potent and therefore the most dangerous oxygen metabolite, elimination of this radical is one of the major aims of antioxidant administration [48]. Hydrogen peroxide itself is not very reactive, but sometimes it is toxic to cells because it may give rise to hydroxyl radicals in the cells [49]. According to relevant reports in the literature [50,51], some transition metal complexes may exhibit antioxidant activity. We therefore conducted an investigation to explore whether the ligands and complexes have the antioxidant activities.

The antioxidant potential of free pyridine carboxamide ligands ($H_2L^1$, $H_2L^2$ and $H_2L^3$) and corresponding ruthenium(II) complexes (**1**, **2**, **3**, **4** and **5**) against DPPH radical, NO radical, OH radical and $H_2O_2$ assay were investigated with respect to different concentrations of the test compounds varying from 0 to 50 μM and the results were shown in Table 4. It was observed that, the 50% inhibitory concentration ($IC_{50}$) value of ligands and complexes varies from 139.8 μM to 182.1 μM and from 24.0 μM to 59.7 μM, respectively,

**Table 4**
Antioxidant activity of the ligands, complexes (**1**–**5**), vitamin C and BHT against various radicals.

| Compound | $IC_{50}$ (μM) | | | |
|---|---|---|---|---|
| | DPPH· | NO· | OH· | $H_2O_2$ |
| $H_2L^1$ | 171.4 | 95.8 | 76.1 | 48 |
| $H_2L^2$ | 139.8 | 88.4 | 72.6 | 31.2 |
| $H_3L^3$ | 182.1 | 104.6 | 89.9 | 54.7 |
| 1 | 43.7 | 11 | 35.4 | 27.8 |
| 2 | 30.8 | 7.8 | 24.9 | 22.4 |
| 3 | 59.7 | 37.8 | 36 | 33.4 |
| 4 | 30.9 | 10 | 25.9 | 25.2 |
| 5 | 24.0 | 6.7 | 22.5 | 19.7 |
| Vitamin C | 147.6 | 215.8 | 232.8 | 238.5 |
| BHT | 86.2 | 154.3 | 163.4 | 149.8 |

against DPPH radical. The ligands showed their $IC_{50}$ values against NO and OH radicals up to 88.4–104.6 μM and 72.6–89.9 μM respectively, whereas, the complexes showed their $IC_{50}$ values up to 6.7–37.8 μM and 22.5–36 μM, respectively. The $IC_{50}$ values against $H_2O_2$ assay varies from 31.2 μM to 54.7 μM for ligands and from 19.7 μM to 33.4 μM for complexes. From the above results, it can be concluded that a much less scavenging activity was exhibited by the free ligands when compared to that of their corresponding ruthenium complexes which is due to the chelation of them with the ruthenium ions. The overall scavenging activity of the tested compounds was found to increase in the order of $H_2L^3 < H_2L^1 < H_2L^2 < 3 < 1 < 4 < 2 < 5$. Moreover, from the results obtained for the ruthenium(II) complexes, it can be inferred that the difference in the nature of the complex and the co-ligands present in the complexes are likely to induce variations in antioxidant activities. The complex **5** showed better activity compared to the other complexes, which may be due to the electron donating effect on diamine backbone of the pyridine carboxamide ligands. Further, the results obtained against the four different methods confirmed that the ruthenium(II) pyridine carboxamide complexes are more effective to arrest the formation of NO radical than the $H_2O_2$, OH radical and DPPH radical and are compared with that of the other metal complexes [52]. The lower $IC_{50}$ values observed in antioxidant assays did demonstrate that these complexes have a strong potential to be applied as scavengers to eliminate the radicals. Further, it is significant to mention that the metal complexes synthesized herein possess superior antioxidant activity against the above said radicals than that of the standard antioxidant Vitamin C and butylated hydroxyl toluene (BHT).

## Conclusions

A new family of carbonyl complexes of ruthenium(II) containing pyridine carboxamide incorporating triphenylphosphine/triphenylarsine/pyridine ligands were synthesized and characterized by analytical and FT–IR, UV–Visible, NMR ($^1H$, $^{13}C$ and $^{31}P$) and ESI–MS techniques. Spectral studies are confirmed the coordination mode of the ligand to the metal through tetradentate donors and reveal the presence of an octahedral geometry around the ruthenium center. The catalytic reaction results demonstrated that this complex is highly efficient in transfer hydrogenation of ketones, even with 0.005 mol% loading, and also for *N*-alkylation of amine with good yields. Additionally, ruthenium(II) pyridine carboxamide complexes also exhibited excellent antioxidant (DPPH radical, NO radical OH radical and $H_2O_2$ scavengers) activities. Therefore, the information obtained from the present work would help in developing new potent antioxidants drugs to eliminate the radicals.

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