Homocoupling of aryl Grignard reagents to form biaryls using ruthenium(III) complex, [RuCl(C$_3$S$_5$)(H$_2$O)(PPh$_3$)$_2$]

P.I. Aparna, Badekai Ramachandra Bhat[*]

Catalysis and Materials Laboratory, Department of Chemistry, National Institute of Technology Karnataka, Surathkal, Srinivasanagar 575025, India

ARTICLE INFO

ABSTRACT

Ruthenium(III) complex, [RuCl(C$_3$S$_5$)(H$_2$O)(PPh$_3$)$_2$] is an effective catalyst for the homocoupling of the aryl-Grignard reagents (ArMgX) to form biaryl derivatives. The catalytic methodology involves an *in situ* generation of the Grignard reagents. The method is simpler, economical and of great synthetic utility. The reaction will be environmental friendly due to the involvement of molecular oxygen as oxidant.

© 2012 Elsevier B.V. All rights reserved.

1. Introduction

The potential applications of the symmetrical di- or pol-yaromatic, olefinic or acetylenic conjugated compounds in pharmaceuticals, optical materials, conductive polymers and liquid crystals are well recognized [1,2]. Homocoupling reactions of aryl, alkenyl and alkynyl Grignard reagents provide an easy and efficient access for the synthesis of such compounds. The transition metal catalyzed coupling reactions are the popular choice for biaryl synthesis, holding the synthetic advantages such as high selectivity, broad substrate scopes and mild reaction conditions [3]. Several kinds of transition metal precursors, CoCl$_2$ [4], MnCl$_2$ [5], FeCl$_3$ [6], TiCl$_4$ [7], VO(OEt)Cl$_2$ [8], Cu(OAc)$_2$ [9], *etc.* were used in stoichiometric amount or catalytical amount in the presence of a reoxidant to carry out the oxidative coupling process. Recently iron [10], palladium [11], *etc.* catalyzed aerobic homocoupling reactions of aryl magnesium derivatives have been achieved successfully. Although transition metal free homocoupling of ArMgX has been reported [12–15], their urge in stoichiometric amount of organic oxidant limits its use for large scale applications. The exploration of the catalytic systems which are greener and more efficient approaches for this transformation is still challenging. Nevertheless, palladium and nickel complexes have been the dominant choice to catalyze the coupling of the Grignard reagents with aryl bromides, iodides and chlorides [16,17], the ability of ruthenium complexes to assume

a wide range of oxidation states, coordination geometries, tolerance towards functional groups, ease of synthesis and versatility provides unique opportunities for catalysis [18,19].

As a part of our ongoing research towards synthesis of biaryls, herein, we report the efficient catalytic system for the coupling of Grignard reagents using new ruthenium(III) complex, containing C$_3$S$_5$ and triphenylphosphine ligands, to afford biaryls in good to high yields. We have synthesized Grignard reagent *in situ* and atmospheric molecular oxygen being used as the oxidant, renders the reaction greener. This procedure is simple, mild and works efficiently without any external oxidants and additives.

2. Experimental

2.1. Materials and methods

All chemicals used were of analytical grade. Solvents were purified and dried according to the standard procedures [20]. [RuCl$_2$(PPh$_3$)$_2$] was synthesized as per the reported procedure [21]. The C, H, O and S contents of the complex were determined by Thermoflash EA1112 series elemental analyzer. Magnetic susceptibility measurement was recorded on a Sherwood Scientific instrument (UK). Thermal analysis was carried out (EXSTAR-6000) from room temperature to 700 °C at a heating rate of 10 °C/min. The electronic spectrum of the complex was measured on a GBC Cintra 101 UV–Vis double beam spectrophotometer using DMF in the 200–800 nm range. FT-IR spectrum was recorded on a Thermo Nicolet Avatar FT-IR spectrometer in the frequency range 400–4000 cm^{-1}. ^{1}H NMR and ^{31}P NMR spectra were recorded in Bruker AV 400 instrument

* Corresponding author. Tel.: +91 824 2474000x3204; fax: +91 824 2474033.
  E-mail address: chandpoorna@yahoo.com (B.R. Bhat).
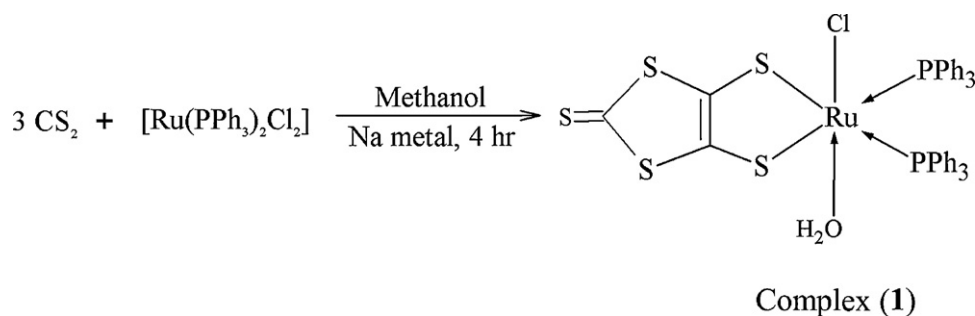
Fig. 1. Schematic representation of synthesis of complex (1).

Table 1
FT-IR and UV–Vis spectral results of complex (1).

FT-IR				UV–Vis	
Wave number (cm^{-1})	Assignment	Wave number (cm^{-1})	Assignment	λ_{max} (nm)	Assignment
1431, 1226	ν(C=C)	619	ν(SC=CS)	418	LM CT
1053	ν(C=S)	3383.6	ν(O—H)		
972.9	ν(C—S)	747, 691.7, 511	Bands due to triphenylphosphine	367, 358, 275	ILCT

LMCT, ligand to metal charge transfer transition.
ILCT, intra ligand charge transfer transition.

using TMS and H_3PO_4 as internal standards respectively. Electrochemical study was performed using Versa STAT-3 in 0.005 M dichloromethane solutions of [(n-C_4H_9)$_4$N]ClO$_4$ (TBAP) as a supporting electrolyte. Coupling reactions were monitored by gas chromatography, Shimadzu 2014.

2.2. Preparation of complex [RuCl(C$_3$S$_5$)(H$_2$O)(PPh$_3$)$_2$] (1)

Complex (1) was prepared under strictly anhydrous conditions (Fig. 1). To a methanol (20 ml) solution containing CS_2 (0.2 ml, 3 mmol) and sodium metal, was added ruthenium complex, [RuCl$_2$(PPh$_3$)$_2$] (695 mg, 1 mmol) with constant stirring. The mixture was refluxed for 4 h. The dark brown precipitate obtained was filtered, washed with methanol, petroleum ether (60–80 °C) and dried in *vacuo*. Yield: 72%. M.P: 235 °C.

Anal. Calc. for $C_{39}H_{32}ClOP_2RuS_5$, Found (calculated) (%): C, 52.86 (53.50); H, 3.62 (3.68); O, 1.89 (1.83); S, 18.26 (18.31).

2.3. Aryl–aryl coupling reaction

Coupling reaction was carried out according to the reported procedure [22] with slight modification. Present catalytic reaction was performed in the presence of atmospheric molecular oxygen. Magnesium turnings (0.320 g, 0.013 g atom) were placed in a two necked round bottom flask with a calcium chloride guard tube. A crystal of iodine was added. Aryl halide (Ar-X, X = Br or Cl) (2 mmol of total 10 mmol) in 5 ml of anhydrous diethyl ether was added with stirring at room temperature. The appearance of turbidity after 5 min indicated the initiation of the reaction. The remaining Ar-X in 5 ml of ether was added drop wise and the reaction mixture was stirred for 40 min at room temperature. To this reaction mixture, ruthenium(III) catalyst chosen for investigation was added and stirring was continued for 6 h. The reaction mixture was cooled and hydrolyzed with a saturated solution of aqueous ammonium chloride. The ether extract on evaporation of the solvent gave the crude product which compared well with authentic samples of biphenyl using gas chromatography.

3. Results and discussion

3.1. Characterization

The elemental analyses (C, H, O, S) are in good agreement with the molecular formula proposed for the complex (1). Selected IR bands and electronic spectral results are listed in Table 1. ^{1}H NMR spectra showed resonance at δ 7.08–7.23 ppm which has been assigned to the protons of two coordinated triphenylphosphine groups present in the complex (1). ^{31}P{^{1}H} NMR spectrum exhibits a sharp singlet at 50.28 ppm supporting the presence of the magnetically equivalent triphenylphosphine groups [23]. The room temperature magnetic moment 1.81 BM shows that the complex (1) is one- electron paramagnetic, which confirms its octahedral geometry [24]. From TG analysis (Fig. 2), the weight loss of the complex (1) was observed at temperature around 150–190, 190–215, 215–305 and 305–371 °C which corresponds to the loss of coordinated water, chloride, triphenylphosphine and carbon disulphide respectively. This further supports the assumed structure of the ruthenium(III) complex. Cyclic voltammogram of the complex (1)
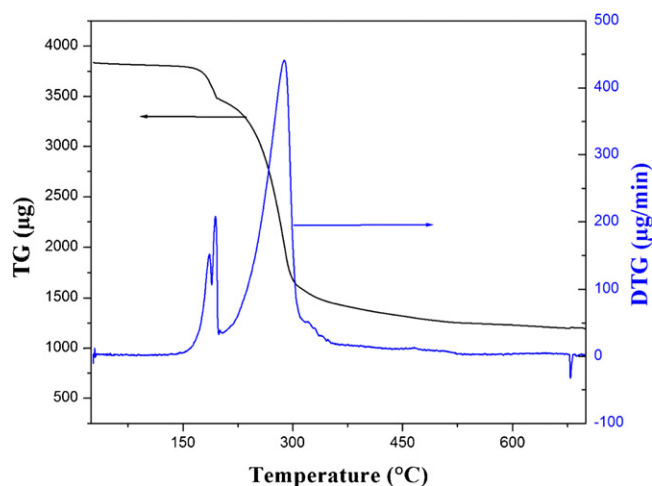
Fig. 2. TG and DTG curves of complex (1).

Table 2
Electrochemical data of complex (**1**).

Ru^{III}/Ru^{IV}				Ru^{III}/Ru^{II}
E_{pa} (V)	E_{pc} (V)	$E_{1/2}$ (V)	ΔE_p (mV)	E_{pc} (V)
0.85	0.92	0.88	70	−0.59

Supporting electrolyte, $[(NBu_4)ClO_4]$ (0.005 M); complex, 0.001 M in dichloromethane.
$E_{1/2} = 0.5(E_{pa} + E_{pc})$.
$\Delta E_p = E_{pa} - E_{pc}$.

exhibits reversible oxidation couple Ru^{III}/Ru^{IV} at $E_{1/2}$ = +0.88 V with a peak-to-peak separation ΔE_p = 70 mV with respect to Ag/AgCl, which does not change with a change in the scan rates, supporting reversibility (Table 2). Further, the complex exhibits an irreversible reduction in the range −0.59 V. The reason for the irreversibility observed for the reductive response of the complex may be due to a short lived reduced state of the metal ion [25] or due to oxidative degradation of ligands [26].

3.2. Catalytic activity

In the present methodology, the Grignard reagent which was synthesized *in situ* on reaction with a catalytic amount of complex (**1**) yields respective biaryl. In order to activate the surface of the commercial magnesium turnings, iodine was added. Formation of Grignard reagent was carried out with careful control of the rate of addition of aryl halide to avoid coupling side products. The reaction was carried out in the presence of the atmospheric molecular oxygen, which is considered as the greenest and most environmentally benign protocol [27], without addition of any external oxidants. The reaction conditions for the coupling of phenylmagnesium bromide (**1e**) were optimized with respect to solvent, time and catalyst concentration.

3.2.1. Solvent effect

Solvents play a crucial role in the coupling reactions. The activity of the complex (**1**) was checked in different solvents, tetrahydrofuran, diethyl ether, benzene, *etc.*, with molecular oxygen as oxidant (Table 3). The best conversion was observed in diethyl ether as ether molecules actually coordinate with and thus helps in stabilizing the Grignard reagent (entry 2). The least conversion was observed in benzene, since the formation of polar Grignard reagent stops in most non-polar organic solvents as it forms an insoluble deposit at the metallic surface. The order of increasing percentage yield in tested solvents follows, benzene < tetrahydrofuran < diethyl ether.

3.2.2. Effect of reaction time

The dependence of product yield on reaction time for the coupling of **1e** was studied by analyzing the reaction mixture at
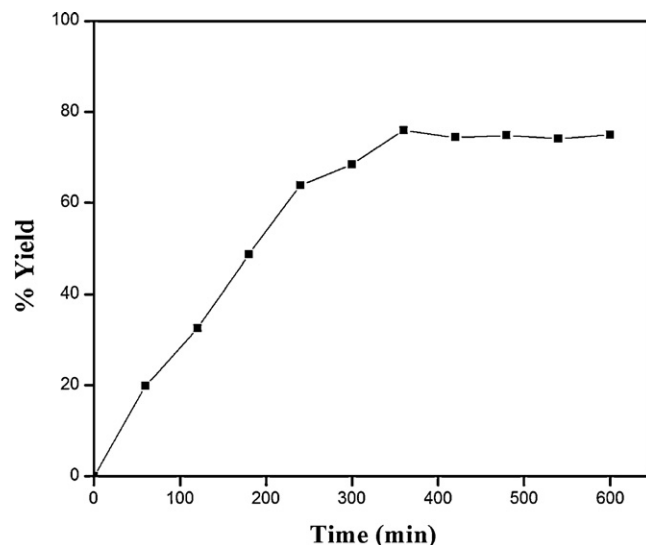
Fig. 3. Effect of reaction time on the yield of bromobenzene to biphenyl.

Table 4
Effect of catalyst concentration on the yield of coupling product.[a]

Entry	Amount of complex (**1**) (mmol)	Yield (%)[b]
1	No catalyst	01.12
2	0.01	19.72
3	0.015	32.36
4	0.02	47.36
5	0.025	61.23
6	0.03	75.96
7	0.04	75.62
8	0.05	74.97
9[c]	0.03	75.88
10[d]	0.03	04.23
11[e]	0.15	74.02

[a] Reactions were carried out with 10 mmol of bromobenzene in the presence of atmospheric molecular oxygen.
[b] GC yield based on the amount of bromobenzene.
[c] In the presence of pure oxygen.
[d] Inert atmosphere (argon).
[e] With 50.0 mmol of bromobenzene in the presence of 0.15 mmol catalyst for 10 h.

regular intervals of time under similar reaction conditions. The yield increased with reaction time (Fig. 3) and total reaction time of 6 h at room temperature gave a constant conversion of 76%.

3.2.3. Effect of catalyst loading and influence of air on the reaction

To study the effect of catalyst concentration on the reaction, substrate to catalyst ratio was varied from total catalyst amount 0.01 mmol to 0.05 mmol (Table 4). It can be observed that even at very low catalyst loading of 0.025 mmol (entry 5), the moderate

Table 3
Optimization of ruthenium-catalyzed homocoupling of phenylmagnesium bromide (**1e**)[a] in different solvents.
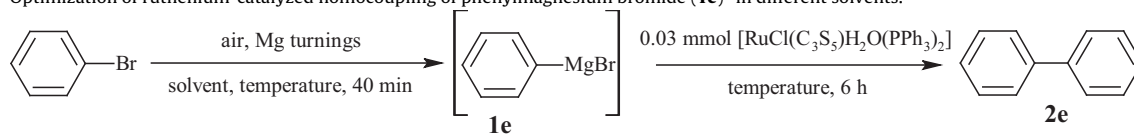
Entry	Solvent	Temperature (°C)	Yield (%)[b]
1	Tetrahydrofuran	60	62
2	Diethyl ether	r.t.[c]	75
3	Benzene	40	36

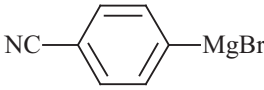[a] Reaction conditions: Mg turnings (0.320 g), bromobenzene (10 mmol), catalyst (0.03 mmol), Et_2O (10 ml).
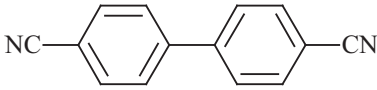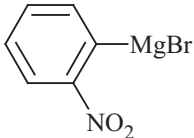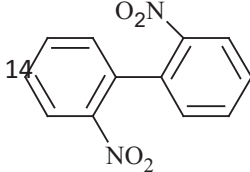[b] GC yield based on the amount of bromobenzene.
[c] r.t., room temperature.

Table 5

Ruthenium-catalyzed homocoupling of Grignard reagents with atmospheric oxygen as an oxidant.[a] $Ar-Mg-Br \xrightarrow[\text{Et}_2\text{O, r.t., 6 h}]{\text{air, 0.03 mmol [RuCl(C}_3\text{S}_5\text{)(H}_2\text{O)(PPh}_3\text{)}_2\text{]}} Ar-Ar$.

Entry	RMgBr	Product	Yield (%)[b]
1	**1a**	**2a**	83
2	**1b**	**2b**	74
3	**1c**	**2c**	89
4	**1d**	**2d**	72
5	**1e**	**2e**	76
6	**1f**	**2f**	71
7	**1g**	**2g**	70
8[c]	**1h**	**2h**	65

Table 5 (*Continued*)

Entry	RMgBr	Product	Yield (%)[b]
9	NC—⟨⟩—MgBr **1i**	NC—⟨⟩—⟨⟩—CN **2i**	62
10	⟨⟩—MgBr NO₂ **1j**	O₂N—⟨⟩—⟨⟩ NO₂ **2j**	64

[a] Reaction conditions: Mg turnings (0.320 g), aryl halide (10 mmol), catalyst (0.03 mmol), Et$_2$O (10 ml).
[b] GC yield based on the amount of aryl halide.
[c] In THF, 60 °C, 10 h.

yield was obtained. The yield increased with increase in catalyst loading and reaches to the highest value of 76% with 0.03 mmol of catalyst (entry 6). It is noteworthy that the use of pure oxygen instead of atmospheric oxygen has no significant influence on the yields (entry 9). Also the absence of air results lower yield may be due to the lack of formation of peroxo-ruthenium(IV) active species (entry 10). The present coupling can be readily scaled up to the reaction of 50.0 mmol of the aryl halide using 0.15 mmol of the catalyst, which yields 74% of biaryl with negligible amount of byproducts (entry 11). The efficiency of the complex (**1**) should be underlined since, in the absence of ruthenium(III) complex, Grignard reagents generally react very quickly with oxygen to give various products (mainly ROH and RH) but only traces of coupling product.This promising result encouraged us to extend the scope of the reaction to various aryl Grignard reagents (Table 5). Thus, simple and functionalized biaryl compounds were synthesized in good yields (entries 1–10). Introduction of methyl group at the ortho-position of the aryl Grignard reagent **1b** resulted in somewhat lower yield of the homocoupling product (entry 2). 4-Methoxy- and 2-methoxyphenylmagnesium bromide can be efficiently converted into the corresponding biaryls **2c** and **2d**, respectively, under similar conditions (entries 3 and 4).It is noteworthy that the present reaction system is tolerant of aryl chloride functionality (entry 6). Also it allows the coupling of heteroaryl Grignard reagent 1 g successfully (entry 7). Although sterically demanding substrate 1 h required higher reaction temperature and longer reaction time, it gave the corresponding biaryl 2 h in moderate to good yield (entry 8). The reaction is chemoselective; thus, nitrile, or nitro groups are tolerated (entries 9 and 10). It is observed that electron donating group on Grignard reagent enhances the yield of coupling product compared to that of electron withdrawing group (entries 1 and 6). In all these experiments, formations of cross-coupling products were very less.

3.3. Proposed mechanism

The proposed mechanism is depicted in Fig. 4 for complex (**1**) catalyzed reaction. The oxidative addition of the molecular oxygen to a low valent ruthenium complex (**a**) forms peroxo-ruthenium(IV) intermediate (**b**) which is the key step of this catalytic cycle [28,29]. It is then reacts with two equivalents of RMgX to give biarylruthenium(IV) intermediate (**c**) and XMgOOMgX [30]. Thus formed biarylruthenium(IV) intermediate (**c**) undergoes rapid reductive elimination which eventually yields

homocoupling product Ar–Ar and Ru(II) is regenerated. In fact, the best way to favor the reductive elimination is to increase the oxidation state of the metal. Thus, it is very reasonable to think that the formation of an unstable ruthenium(IV) species (**c**) is required to achieve a very quick reductive elimination that gives (**d**). The formation of peroxo-ruthenium(IV) intermediate was confirmed by the UV–Vis spectrophotometer analysis. The absorption peak of the catalytic reaction mixture appeared at 398 nm that can be attributed for peroxo-ruthenium(IV) intermediate [31] and its absence in the reaction mixture carried out under inert condition further confirms the necessity of molecular oxygen for the present catalytic system. The formation of such a peroxo complex as catalytic intermediate is very well established for various manganese, iron and palladium-catalyzed reactions [30,32,33].
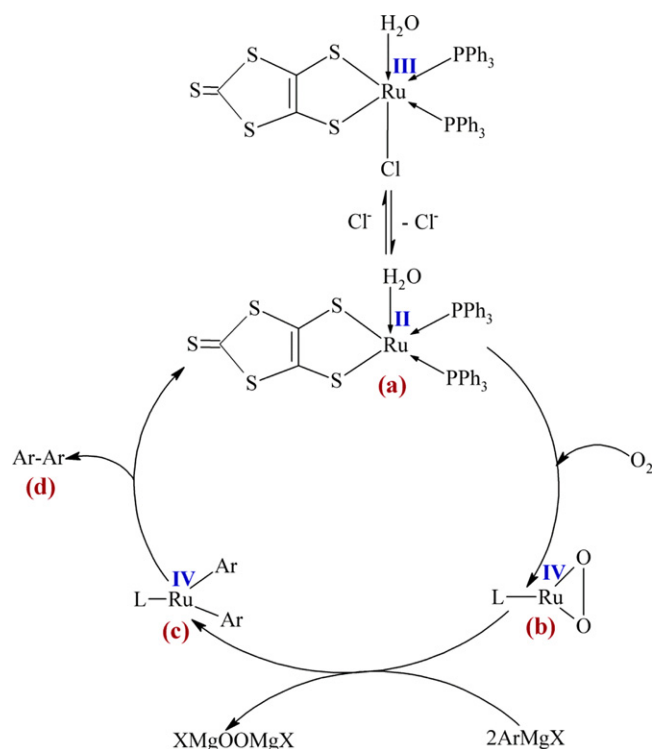

Fig. 4. Proposed mechanism for the complex (**1**) catalyzed coupling reaction.

4. Conclusions

In conclusion, newly synthesized octahedral ruthenium(III) complex has been effectively applied for the catalytic transformation of various aryl halides to the corresponding symmetric biaryl in good to high yields. Present catalytic procedure of an *in situ* formation of the Grignard reagent makes the biaryl synthesis route much simpler, energy efficient, economical and of great synthetic utility. The oxidant atmospheric molecular oxygen makes the coupling reaction environmental friendly and cost effective. Peroxo-ruthenium(IV) active species is responsible for the efficiency of present catalytic system. The small amount of catalyst, chemoselectivity and eco-friendly procedures makes the reaction system readily amenable to a large-scale synthesis of biaryl compounds.

Acknowledgments

References

[1] J.P. Corbet, G. Mignani, Chem. Rev. 106 (2006) 2651–2710.
[2] S.S. Zhu, T.M. Swager, Adv. Mater. 8 (1996) 497–500.
[3] D. Alberico, M.E. Scott, M. Lautens, Chem. Rev. 107 (2007) 174–238.
[4] G. Cahiez, A. Moyeux, Chem. Rev. 110 (2010) 1435–1462.
[5] G. Cahiez, O. Gager, F. Lecomte, Org. Lett. 10 (2008) 5255–5256.
[6] M. Nakamura, K. Matsuo, S. Ito, E. Nakamura, J. Am. Chem. Soc. 126 (2004) 3686–3687.
[7] A. Inoue, K. Kitagawa, H. Shinokubo, K. Oshima, Tetrahedron 56 (2000) 9601–9605.
[8] T. Ishikawa, A. Ogawa, T. Hirao, Organometallics 17 (1998) 5713–5716.
[9] A.S. Demir, O. Reis, M. Emrullahoglu, J. Org. Chem. 68 (2003) 10130–10134.
[10] W. Liu, A. Lei, Tetrahedron Lett. 49 (2008) 610–613.
[11] H. Yoshida, Y. Yamaryo, J. Ohshita, A. Kunai, Tetrahedron Lett. 44 (2003) 1541–1544.
[12] A. Krasovskiy, A. Tishkov, V. Amo, H. Mayr, P. Knochel, Angew. Chem. Int. Ed. 45 (2006) 5010–5014.
[13] M.S. Maji, A. Studer, Synthesis 14 (2009) 2467–2470.
[14] M.S. Maji, T. Pfeifer, A. Studer, Chem. Eur. J. 16 (2010) 5872–5875.
[15] M.S. Maji, T. Pfeifer, A. Studer, Angew. Chem. Int. Ed. 47 (2008) 9547–9550.
[16] S.Y.W. Lau, G. Hughes, P.D. O'Shea, I.W. Davies, Org. Lett. 9 (2007) 2239–2242.
[17] T. Hatakeyama, S. Hashimoto, K. Ishizuka, M. Nakamura, J. Am. Chem. Soc. 131 (2009) 11949–21196.
[18] V.K. Srivastava, R.S. Shukla, H.C. Bajaj, R.V. Jasra, Appl. Catal. A: Gen. 282 (2005) 31–38.
[19] N. Mizuno, K. Yamaguchi, Catal. Today 132 (2008) 18–26.
[20] A.I. Vogel, Textbook of Practical Organic Chemistry, fifth ed., Longman, London, 1989.
[21] T.A. Stephenson, G. Wilkinson, J. Inorg. Nucl. Chem. 28 (1966) 945–956.
[22] N.P. Priya, S. Arunachalam, A. Manimaran, D. Muthupriya, C. Jayabalakrishnan, Spectrochim. Acta A 72 (2009) 670–676.
[23] M.W. Schoonover, C.P. Kubiak, R. Eisenberg, Inorg. Chem. 17 (1978) 3050–3055.
[24] R. Raveendran, S. Pal, Polyhedron 27 (2008) 655–662.
[25] A.M. Bond, R. Colton, D.R. Mann, Inorg. Chem. 29 (1990) 4665–4671.
[26] A. Basu, T.G. Kasar, N.Y. Sapre, Inorg. Chem. 27 (1988) 4539–4542.
[27] C. Liu, H. Zhang, W. Shi, A. Lei, Chem. Rev. 111 (2011) 1780–1824.
[28] A. Hussain, R.S. Shukla, R.B. Thorat, H.J. Padhiyar, K.N. Bhatt, J. Mol. Catal. A: Chem. 193 (2003) 1–12.
[29] A. Ourari, M. Khelafi, D. Aggoun, G. Bouet, M.A. Khan, Adv. Phys. Chem. 2011 (2011) 1–11.
[30] G. Cahiez, A. Moyeux, J. Buendia, C. Duplais, J. Am. Chem. Soc. 129 (2007) 13788–13789.
[31] T. Joseph, D.P. Sawant, C.S. Gopinath, S.B. Halligudi, J. Mol. Catal. A: Chem. 184 (2002) 289–299.
[32] B.S. Lane, K. Burgess, Chem. Rev. 103 (2003) 2457–2474.
[33] C. Adamo, C. Amatore, I. Ciofini, A. Jutand, H. Lakmini, J. Am. Chem. 128 (2006) 6829–6836.