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Ruthenium(II)-NHC-catalyzed (NHC = perhydrobenzimidazol-2-ylidene) alkylation of amines using the hydrogen borrowing methodology under solvent-free conditions

Murat Yiğit[1] · Emine Özge Karaca[2] · Beyhan Yiğit[1] · Nevin Gürbüz[2,3] · İsmail Özdemir[2,3]

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Abstract
New ruthenium(II) complexes with *N*-heterocyclic carbene ligand were synthesized by transmetalation reactions between silver(I) *N*-heterocyclic carbene complexes and $[RuCl_2(p\text{-cymene})]_2$. The complexes were characterized by physicochemical and spectroscopic methods. These ruthenium complexes were applied to the *N*-monoalkylation of aromatic amines with a wide range of primary alcohols under solvent-free conditions using the hydrogen borrowing strategy. The catalytic reactions using all ruthenium complexes resulted in *N*-monoalkylated products with high selectivities using furfuryl alcohol as the alkylating agent.

Introduction

Alkylation of amines has received much attention by synthetic chemists, as alkylated amines are important compounds widely found in natural products, pharmaceuticals, bulk and fine chemicals [1]. Traditional methods for alkylation of amines involve substitution reactions with alkyl halides [2] or reductive aminations using stoichiometric reducing agents [3]. However, these reactions have significant drawbacks, such as toxicity of alkylating and reducing agents, the formation of large amounts of waste, acidic reaction conditions and undesired side products. Due to the importance of arylated and alkylated amines in the chemical industry, during the last decades, several catalytic methods have been developed for the arylation and alkylation of amines, including Buchwald–Hartwig amination [4], hydroamination [5], hydroaminomethylation [6] and hydrogen borrowing methodology [7]. Among the carbon–nitrogen bond-forming reactions, the hydrogen borrowing methodology also called hydrogen auto-transfer constitutes one of the most important synthetic methods for the preparation of alkylated amines, which involves a simple operation process and mild conditions [8]. This process involves three steps but carried out in one pot. In the initial step, hydrogen is temporarily removed from alcohol with a transition metal catalyst to form a carbonyl compound, and then, the carbonyl compound reacts with a nucleophile to form an unsaturated intermediate. In the last step, the unsaturated molecule is reduced by the metal hydride complex to obtain the final product (Scheme 1). Particularly, the use of alcohols instead of alkyl halides as alkylating agents in the alkylation of amines is highly attractive, because they are readily available, relatively cheap and less toxic than the corresponding alkyl halide, and water is the only by-product in the overall process [9]. Besides alcohols, amines can also be used as alkylating agents in this process, but the use of amines for the alkylation of amines is much more limited [10].

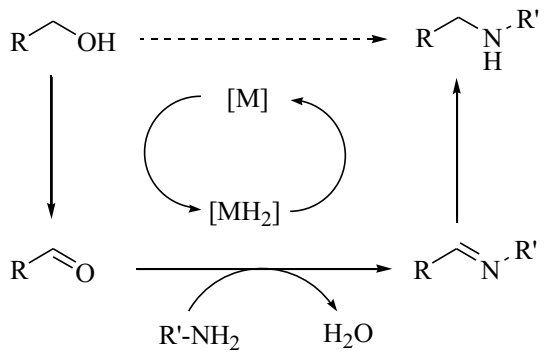
The hydrogen borrowing methodology has been successfully applied for the formation of new carbon–heteroatom and carbon–carbon bonds under catalytic conditions [11]. The first *N*-alkylation of amines with alcohols was described independently by Grigg [12] and Watanabe [13] using rhodium- and ruthenium-phosphine complexes as catalysts, respectively, in 1981. Since then, a number of homogeneous and heterogeneous catalytic systems based on ruthenium [14], iridium [15], palladium [16], silver [17], cobalt [18], copper [19] and rhodium [20] have been developed

✉ Murat Yiğit
myigit@adiyaman.edu.tr

[1] Department of Chemistry, Faculty of Science and Art, Adıyaman University, 02040 Adıyaman, Turkey

[2] Catalysis Research and Application Center, Inönü University, 44280 Malatya, Turkey

[3] Department of Chemistry, Faculty of Science and Art, Inönü University, 44280 Malatya, Turkey



Scheme 1 Hydrogen borrowing strategy for the alkylation of amines with alcohols using a metal complex

by Williams and other groups for alkylation of amines with alcohols. The most important results for the preparation of the secondary amines have largely been achieved using ruthenium and iridium complexes. Recently, important progress in hydrogen borrowing reactions was achieved with Au and Zr as the catalysts with excellent results [21]. In addition, alkylation of amines with alcohols has been performed using biocatalysts for the preparation of enantiopure amines via biocatalytic hydrogen methodology [22].

N-Heterocyclic carbenes (NHC) are an important class of widely used and investigated ligands in organometallic chemistry and catalysis because of their readily tunable steric and electronic properties, and their ease of synthesis [23]. Generally, NHCs have good σ-donor and weak π-acceptor properties and are very strong nucleophiles. The strong electron-donating property of *N*-heterocyclic carbene ligands leads to the formation of stable metal–NHC complexes with strong covalent bonds [24]. This strong metal–carbon bond avoids the decomposition of NHC complexes during the course of catalytic reactions. A variety of NHC complexes have been successfully synthesized and used as antimicrobial, antitumor and anticancer agents [25], photoluminescent materials [26] and catalysts for various transformations [27]. In recent years, NHC complexes have been widely used as catalysts in hydrogen borrowing reactions [28–31]. In particular, NHC complexes of iridium and ruthenium have demonstrated good activity for these transformations [32–35]. However, the use of ruthenium(II)-NHC complexes in the alkylation of amines with alcohols is rare [36, 37]. To the best of our knowledge, ruthenium(II) complexes bearing a perhydrobenzimidazol-2-ylidene ligand for *N*-alkylation reactions have not been reported to date.

In this study, the new $[RuCl_2(NHC)(p\text{-cymene})]$ (NHC = perhydrobenzimidazol-2-ylidene) complexes were readily synthesized by treating the $[RuCl_2(p\text{-cymene})]_2$ dimer directly with the corresponding Ag(I)-NHC complexes, which was prepared in situ by reaction of Ag_2O with symmetrical 1,3-dialkylperhydrobenzimidazolium salts in dichloromethane. The catalytic activity of these complexes was evaluated in *N*-alkylation reactions of aniline with arylmethyl alcohols.

Experimental

All reactions for the preparation of the ruthenium(II)-NHC complexes were carried out under argon in flame-dried glassware using standard Schlenk techniques. The solvents were purified by distillation over the drying agents indicated and were transferred under Ar: THF, Et_2O (Na/K alloy), CH_2Cl_2 (P_4O_{10}), hexane, toluene (Na). All reagents were purchased from Sigma-Aldrich, Merck and Fluka. ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Varian AS 400 Merkur spectrometer operating at 400 MHz (^{1}H), 100 MHz (^{13}C) in $CDCl_3$ with tetramethylsilane as an internal reference. Coupling constants (*J* values) are given in Hertz. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet and m = multiplet signal. FTIR spectra were recorded on ATR unit in the range 400–4000 cm^{-1} on PerkinElmer Spectrum 100. GC was measured by GC-FID on an Agilent 6890 N gas chromatograph equipped with an HP-5 column of 30 m length, 0.32 mm diameter and 0.25 µm film thickness. Melting points were measured in open capillary tubes with an Electrothermal-9200 melting point apparatus and uncorrected. Elemental analyses were performed at Inönü University research center.

Synthesis of perhydrobenzimidazolium salts 1

A mixture of *N*,*N*′-dialkyl-1,2-diaminocyclohexane (4.0 mmol), NH_4Cl (4.0 mmol) and triethyl orthoformate (10 mL) was heated for 12 h at 110 °C. Upon cooling to room temperature, colorless crystals were obtained. These were filtered off, washed with diethyl ether (3 × 15 mL) and dried under vacuum. The crude product was recrystallized from EtOH/Et_2O.

1,3-Bis(4-diethylaminobenzyl)perhydrobenzimidazolium chloride 1c Yield: 1.79 g, 93%, m.p. 172–174 °C. IR, *υ*: 1521 cm^{-1} (NCN). ^{1}H NMR ($CDCl_3$) *δ*: 1.15 (t, 12H, *J* = 6.9 Hz, $N(CH_2CH_3)_2$), 1.17–1.36 (m, 4H, $NCHCH_2CH_2CH_2CH_2CHN$), 1.80–2.25 (m, 4H, $NCHCH_2CH_2CH_2CH_2CHN$), 3.10–3.12 (m, 2H, $NCHCH_2CH_2CH_2CH_2CHN$), 3.36 (d, 8H, *J* = 7.2 Hz, $N(CH_2CH_3)_2$), 4.45 and 5.05 (d, 4H, *J* = 14.4 Hz, NCH_2Ar), 6.61 and 7.22 (d, 8H, *J* = 8.7 Hz, $CH_2C_6H_4N(CH_2CH_3)_2$-4), 10.75 (s, 1H, NCHN). ^{13}C NMR ($CDCl_3$) *δ*: 12.5 ($N(CH_2CH_3)_2$), 23.6, 27.3 and 50.3 ($NCH(CH_2)_4CHN$), 44.2 ($N(CH_2CH_3)_2$), 66.0 (NCH_2Ar), 111.7, 118.8, 129.9 and 147.9

($CH_2C_6H_4N(CH_2CH_3)_2$-4), 161.5 (N*C*HN); Anal. Calcd. for $C_{29}H_{43}N_4CI$: C, 72.12; H, 8.91; N, 11.60. Found C, 72.16; H, 8.87; N, 11.62%.

Synthesis of ruthenium(II)-NHC complexes 2

Ag_2O (0.54 mmol) was added to a solution of the appropriate perhydrobenzimidazolium chloride (1.08 mmol) in dichloromethane (25 mL). The mixture was stirred for 24 h at room temperature in the dark conditions, covered with aluminum foil under argon and then filtered through Celite to remove the AgCl formed. $[RuCl_2(p\text{-cymene})]_2$ (0.43 mmol) was added to the colorless solution, and the reaction mixture was stirred for 24 h at room temperature. The resulting mixture was filtered through Celite, and the solvent was removed under vacuum to afford the product. The crude product was recrystallized from dichloromethane/diethyl ether (1:2) at room temperature. The orange-brown crystals were filtered off, washed with diethyl ether (3 × 10 mL) and dried under vacuum.

Dichloro-[1,3-bis(4-phenylbenzyl)perhydrobenzimidazol-2-ylidene](*p*-cymene)ruthenium(II) 2a Yield: 0.13 g, 81%, m.p = 257–258 °C. IR, *υ*: 1516 cm^{-1} (NCN). ^1H NMR ($CDCI_3$) *δ*: 0.95–1.20 (m, 4H, NCHCH$_2$C*H*$_2$C*H*$_2$CH$_2$CHN), 1.22 and 1.29 (d, 6H, *J* = 4 Hz, *p*-$CH_3C_6H_4CH(CH_3)_2$), 1.57–1.79 (m, 4H, NCHC*H*$_2$CH$_2$CH$_2$C*H*$_2$CHN), 2.14 (s, 3H, *p*-C*H*$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 2.88 (sept, 1H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$C*H*(CH$_3$)$_2$), 3.20–3.35 (m, 2H, NC*H*CH$_2$CH$_2$CH$_2$CH$_2$C*H*N), 4.64, 4.90, 5.79 and 6.00 (d, 4H, *J* = 16 Hz, *p*-CH$_3$C$_6$*H*$_4$CH(CH$_3$)$_2$), 5.10, 5.18, 5.34 and 5.49 (d, 4H, *J* = 8 Hz, NC*H*$_2$Ar), 7.26–7.61 (m, 18H, CH$_2$C$_6$*H*$_4$C$_6$*H*$_5$-4). ^{13}C NMR ($CDCI_3$) *δ*: 18.7 (*p*-CH$_3$C$_6$H$_4$CH(*C*H$_3$)$_2$), 21.8 (*p*-*C*H$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 30.6 (*p*-CH$_3$C$_6$H$_4$*C*H(CH$_3$)$_2$), 23.4, 24.1, 29.7, 54.1 and 55.7 (N*C*H(*C*H$_2$)$_4$*C*HN), 68.0 and 69.8 (N*C*H$_2$Ar), 83.0, 84.4, 85.9, 86.3, 97.6 and 108.4 (*p*-CH$_3$*C*$_6$H$_4$CH(CH$_3$)$_2$), 126.7, 126.9, 127.1, 127.3, 128.3, 128.7, 128.8, 137.5, 138.0, 140.0, 140.5 and 140.8 (CH$_2$*C*$_6$H$_4$*C*$_6$H$_5$-4), 215.2 (Ru-C_{carb}). Anal. Calc. for $C_{43}H_{46}N_2RuCl_2$: C, 67.71; H, 6.04; N, 3.67. Found: C, 67.74; H, 6.06; N, 3.66%.

Dichloro-[1,3-bis(4-benzyloxybenzyl)perhydrobenzimidazol-2-ylidene](*p*-cymene)ruthenium(II) 2b Yield: 0.14 g, 79%, m.p = 214–216 °C. IR, *υ*: 1511 cm^{-1} (NCN). ^1H NMR ($CDCI_3$) *δ*: 0.90–1.19 (m, 4H, NCHCH$_2$C*H*$_2$C*H*$_2$CH$_2$CHN), 1.21 and 1.27 (d, 6H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$CH(C*H*$_3$)$_2$), 1.57–1.75 (m, 4H, NCHC*H*$_2$CH$_2$CH$_2$C*H*$_2$CHN), 2.10 (s, 3H, *p*-C*H*$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 2.85 (sept, 1H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$C*H*(CH$_3$)$_2$), 3.10–3.27 (m, 2H, NC*H*CH$_2$CH$_2$CH$_2$CH$_2$C*H*N), 4.49, 4.83, 5.57 and 5.88 (d, 4H, *J* = 16 Hz, *p*-CH$_3$C$_6$*H*$_4$CH(CH$_3$)$_2$), 5.04, 5.12, 5.30 and 5.44 (d, 4H, *J* = 8 Hz, NC*H*$_2$Ar), 5.05 and 5.06 (s, 4H, OC*H*$_2$Ar), 6.90–6.99 and 7.26–7.43 (m, 18H, CH$_2$C$_6$*H*$_4$OCH$_2$C$_6$*H*$_5$-4). ^{13}C NMR ($CDCI_3$) *δ*: 18.6 (*p*-CH$_3$C$_6$H$_4$CH(*C*H$_3$)$_2$), 21.8 (*p*-*C*H$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 30.6 (*p*-CH$_3$C$_6$H$_4$*C*H(CH$_3$)$_2$), 23.2, 24.2, 29.6, 53.7 and 55.4 (N*C*H(*C*H$_2$)$_4$*C*HN), 67.8 and 69.7 (N*C*H$_2$Ar), 70.0 (O*C*H$_2$Ar), 82.9, 84.2, 85.8, 86.3, 97.5 and 108.4 (*p*-CH$_3$*C*$_6$H$_4$CH(CH$_3$)$_2$), 114.4, 114.8, 127.5, 127.8, 128.0, 128.5, 129.1, 131.0, 136.9 and 158.0 (CH$_2$*C*$_6$H$_4$OCH$_2$*C*$_6$H$_5$-4), 214.5 (Ru-C_{carb}). Anal. Calc. for $C_{45}H_{50}N_2O_2RuCl_2$: C, 65.69; H, 6.08; N, 3.41. Found: C, 65.66; H, 6.05; N, 3.43%.

Dichloro-[1,3-bis(4-diethylaminobenzyl)perhydrobenzimidazol-2-ylidene](*p*-cymene)ruthenium(II) 2c Yield: 0.12 g, 75%, m.p = 223–224 °C. IR, *υ*: 1519 cm^{-1} (NCN). ^1H NMR ($CDCI_3$) *δ*: 0.95–1.06 (m, 4H, NCHCH$_2$C*H*$_2$C*H*$_2$CH$_2$CHN), 1.16–1.18 (m, 12H, N(CH$_2$C*H*$_3$)$_2$), 1.19 and 1.22 (d, 6H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$CH(C*H*$_3$)$_2$), 1.55–1.77 (m, 4H, NCHC*H*$_2$CH$_2$CH$_2$C*H*$_2$CHN), 2.06 (s, 3H, *p*-C*H*$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 2.80 (sept, 1H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$C*H*(CH$_3$)$_2$), 3.13–3.25 (m, 2H, NC*H*CH$_2$CH$_2$CH$_2$CH$_2$C*H*N), 3.33–3.35 (m, 8H, N(C*H*$_2$CH$_3$)$_2$), 4.52, 4.81, 5.40 and 5.64 (d, 4H, *J* = 16 Hz, *p*-CH$_3$C$_6$*H*$_4$CH(CH$_3$)$_2$), 5.10, 5.20, 5.31 and 5.44 (d, 4H, *J* = 8 Hz, NC*H*$_2$Ar), 6.65, 6.70 and 7.19 (d, 8H, *J* = 8 Hz, CH$_2$C$_6$*H*$_4$N(CH$_2$CH$_3$)$_2$-4). ^{13}C NMR ($CDCI_3$) *δ*: 12.6 (N(CH$_2$*C*H$_3$)$_2$), 18.4 (*p*-CH$_3$C$_6$H$_4$CH(*C*H$_3$)$_2$), 21.9 (*p*-*C*H$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 30.5 (*p*-CH$_3$C$_6$H$_4$*C*H(CH$_3$)$_2$), 23.2, 24.2, 29.2, 29.8, 53.7 and 54.8 (N*C*H(*C*H$_2$)$_4$*C*HN), 44.2 (N(*C*H$_2$CH$_3$)$_2$), 68.2 and 68.5 (N*C*H$_2$Ar), 83.4, 84.9, 85.5, 85.6, 96.7 and 107.4 (*p*-CH$_3$*C*$_6$H$_4$CH(CH$_3$)$_2$), 111.9 124.7, 126.0, 127.3, 128.8 and 147.0 (CH$_2$*C*$_6$H$_4$N(CH$_2$CH$_3$)$_2$-4), 213.7 (Ru-C_{carb}). Anal. Calc. for $C_{39}H_{56}N_4RuCl_2$: C, 62.23; H, 7.45; N, 7.45. Found: C, 62.20; H, 7.43; N, 7.49%.

Dichloro-[1,3-bis(2,4,6-trimethoxybenzyl)perhydrobenzimidazol-2-ylidene](*p*-cymene)ruthenium(II) 2d Yield: 0.14 g, 83%, m.p = 200–2001 °C. IR, *υ*: 1591 cm^{-1} (NCN). ^1H NMR ($CDCI_3$) *δ*: 0.67–1.05 (m, 4H, NCHCH$_2$C*H*$_2$C*H*$_2$CH$_2$CHN), 1.24 and 1.28 (d, 6H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$CH(C*H*$_3$)$_2$), 1.39–1.56 (m, 4H, NCHC*H*$_2$CH$_2$CH$_2$C*H*$_2$CHN), 2.08 (s, 3H, *p*-C*H*$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 2.62–2.68 (m, 1H, *J* = 8 Hz, *p*-CH$_3$C$_6$H$_4$C*H*(CH$_3$)$_2$), 2.78–3.09 (m, 2H, NC*H*CH$_2$CH$_2$CH$_2$CH$_2$C*H*N), 3.83 and 3.85 (s, 18H, CH$_2$C$_6$H$_2$(OC*H*$_3$)$_2$-2,4,6), 4.98–5.05 (m, 4H, *p*-CH$_3$C$_6$*H*$_4$CH(CH$_3$)$_2$), 5.65 and 5.69 (d, 4H, *J* = 4 Hz, NC*H*$_2$Ar), 6.13 (s, 4H, CH$_2$C$_6$*H*$_2$(OCH$_3$)$_2$-2,4,6). ^{13}C NMR ($CDCI_3$) *δ*: 18.8 (*p*-CH$_3$C$_6$H$_4$CH(*C*H$_3$)$_2$), 22.3 (*p*-*C*H$_3$C$_6$H$_4$CH(CH$_3$)$_2$), 30.4 (*p*-CH$_3$C$_6$H$_4$*C*H(CH$_3$)$_2$), 23.2, 24.5, 29.2, 30.2, 44.7 and 45.5 (N*C*H(*C*H$_2$)$_4$*C*HN), 55.3, 55.8 (CH$_2$C$_6$H$_2$(O*C*H$_3$)$_2$-2,4,6), 65.8 and 66.3 (N*C*H$_2$Ar), 83.5, 84.1, 87.9, 90.6, 92.9 and 104.8 (*p*-CH$_3$*C*$_6$H$_4$CH(CH$_3$)$_2$), 159.8, 160.0, 160.7 and 160.8 (CH$_2$*C*$_6$H$_2$(OCH$_3$)$_2$-2,4,6), 213.9 (Ru-C_{carb}). Anal. Calc. for $C_{37}H_{50}N_2O_6RuCl_2$: C, 56.20; H, 6.33; N, 3.54. Found: C, 56.24; H, 6.30; N, 3.56%.

General procedure for the *N*-alkylation of amines with alcohols

Under an inert atmosphere, $KOBu^t$ (1 mmol), aromatic amine (1 mmol), alcohol derivative (1.5 mmol) and Ru-NHC complex (2.5 mol%) were added to Schlenk tube. The sealed Schlenk tube was stirred at 120 °C for 24 h. At the end of the reaction, the reaction mixture was cooled to room temperature, and CH_2Cl_2 (2 ml) was added and filtered through a short pad of SiO_2. The filtrate was analyzed by GC–MS with the calibrations based on dodecane.

Results and discussion

Synthesis of perhydrobenzimidazolium salts

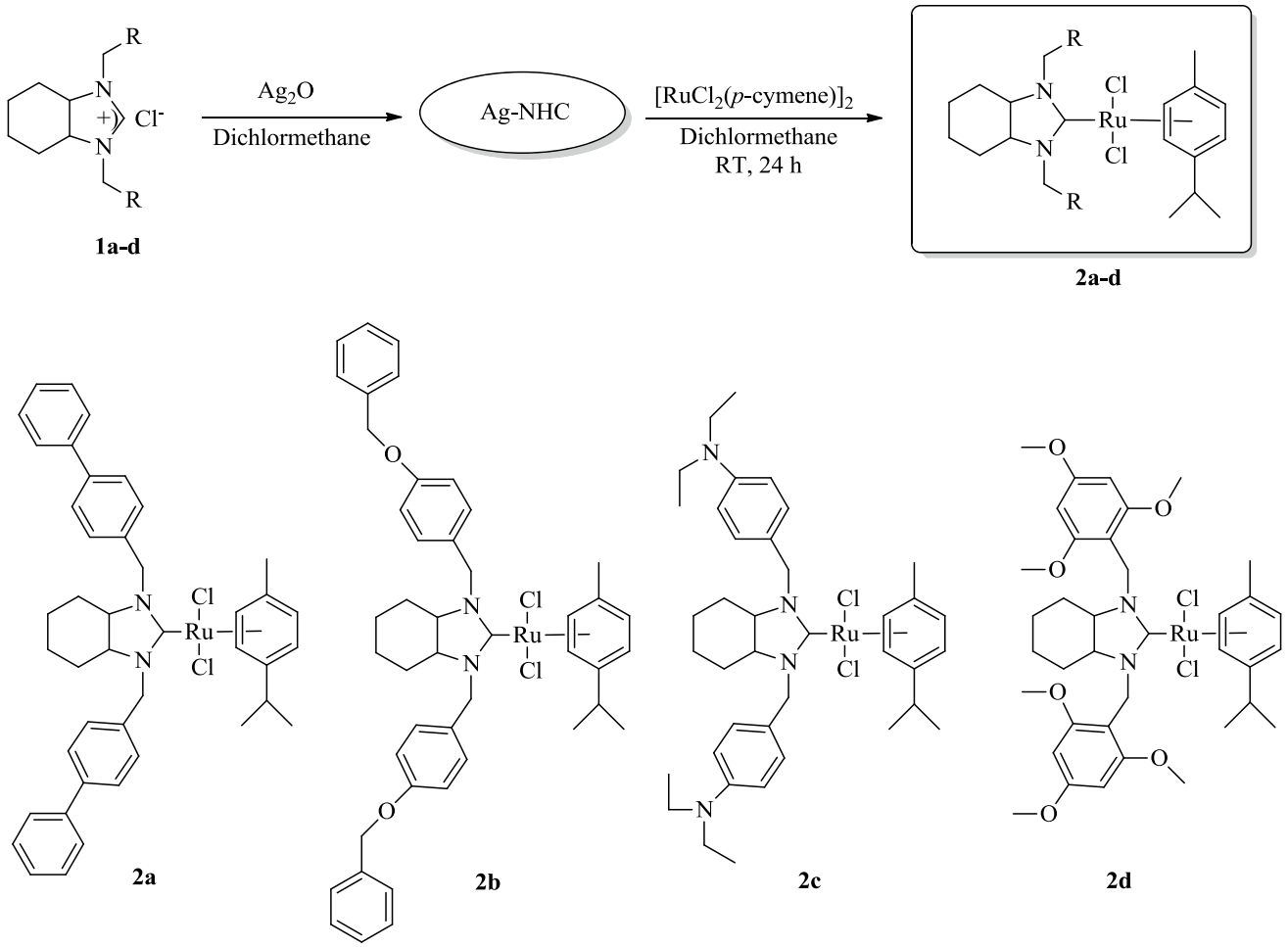
The symmetrical 1,3-dialkylperhydrobenzimidazolium salts **1** as NHC precursors were synthesized from the *N*,*N*′-dialkylcyclohexan-1,2-diamines, triethyl orthoformate and ammonium chloride. Perhydrobenzimidazolium salts are colorless solids and were obtained in good yields. The salts were characterized by ^{1}H and ^{13}C NMR spectroscopy, FTIR and elemental analysis. The spectral properties of **1c** are similar to those of other reported perhydrobenzimidazolium salts. In the ^{1}H NMR spectra of **1c**, NC*H*N proton appeared as a singlet at 10.75 ppm and benzylic protons appeared as two doublets at 4.45 and 5.05 ppm. The N*C*HN carbon resonance of **1c** was observed at 161.5 ppm in the ^{13}C NMR spectra. The appearances of these downfield signals indicate the formation of **1c**. The other perhydrobenzimidazolium salts used in this study (**1a**, **1b** and **1d**) were previously reported by our group [38–40].

Synthesis of Ru(II)-NHC complexes

There are several methods in the literature that describe the synthesis of Ru(II)-NHC complexes. One of these is the generation of silver(I)-NHC complex, followed by transfer of the carbene unit to ruthenium metal. The new [$RuCl_2$(NHC)(*p*-cymene)] complexes were prepared by transmetalation from the corresponding silver *N*-heterocyclic carbene complexes in two steps (Scheme 2). In the first step, the Ag(I)-NHC complexes were synthesized according to the general method described by Wang and Lin [41] by reaction of Ag_2O with 2 equiv. of 1,3-dialkylperhydrobenzimidazolium salts in dichloromethane at ambient temperature in the dark. In the second step, in situ prepared Ag(I)-NHC complexes were converted into the orange-brown monocarbene Ru(II)-NHC complexes at ambient temperature. Ruthenium(II)-NHC complexes were purified by crystallization. The air- and moisture-stable ruthenium–carbene complexes in the solid state were soluble in solvents such as dichloromethane, chloroform and toluene and insoluble in non-polar solvents. Single crystals of these complexes suitable for X-ray diffraction studies could not be obtained. Therefore, all of the Ru(II)-NHC complexes were characterized by ^{1}H NMR, ^{13}C NMR, IR spectroscopy and elemental analysis, which all supported the proposed structures. They exhibit characteristic υ(C=N) band typically at 1516, 1511, 1519 and 1591 cm^{-1}, respectively, for **2a**–**d**. In the NMR spectrum of ruthenium complexes **2a**–**d**, the characteristic downfield NC*H*N proton and N*C*HN carbon resonances of perhydrobenzimidazolium salts **1a**–**d** were disappeared upon complexation with ruthenium. The ^{13}C chemical shifts provide a useful diagnostic tool for this type of metal–carbene complexes and show that $C_{carbene}$ is substantially deshielded. The chemical shifts for the carbene carbon atom of **2a**–**d** complexes were observed at 215.2, 214.5, 213.7 and 213.9 ppm, respectively, for 2**a**–**d**, and these values were similar to those found for other (*p*-cymene)-ruthenium(II)-NHC complexes. These new complexes show typical spectroscopic signatures which are in line with those recently reported for other [$RuCl_2$(NHC)(*p*-cymene)] complexes [42]. The results obtained from the elemental analysis of complexes **2a**–**d** are in agreement with the theoretical requirements of their structures.

Catalytic studies

The catalytic activities of new ruthenium complexes **2a**–**d** for the *N*-alkylation of aromatic amines with arylmethyl alcohols were evaluated. Initially, the reaction of aniline with benzyl alcohol was selected as a model reaction to determine the optimal catalytic conditions with **2c** as a catalyst. The effect of the base, reaction time, solvent and catalyst loading was examined. The results are summarized in Table 1. The bases were crucial to the efficiency of this reaction. Cs_2CO_3, K_2CO_3, KOH and $KOBu^t$ were tested as the base. Among the tested bases, $KOBu^t$ displayed the highest reactivity (entry 3). KOH was less effective (entry 2), while alkali metal carbonates Cs_2CO_3 and K_2CO_3 stopped the reaction completely at the dehydrogenation step. It is noteworthy that, in the absence of base and ruthenium complex, no reaction was observed (entry 11). Toluene and dioxane often used these reactions and gave excellent or poor conversions (entries 2 and 5). However, in the absence of a solvent, an excellent conversion was also observed. Reducing the catalyst loading to 1 mol% decreased the conversion (entry 9). Excellent conversion and selectivity were obtained by the use of 2.5 mol% of **2c** (entry 10). Lower temperature (100 °C) or shorter time (15 h) reduced the conversion (entries 2 and 1), whereas full conversion was observed at 120 °C for 24 h (entry 7). The catalytic experiments were carried out using 1 mmol aromatic amine, 1.5 mmol arylmethyl alcohol, 0.01 mmol $KOBu^t$ and 0.025 mmol **2a**–**d** at 120 °C for 24 h under argon



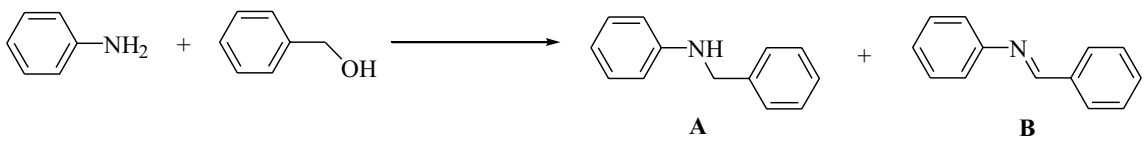
Scheme 2 The synthesis of (*p*-cymene)-ruthenium(II)-NHC complexes

without any solvent or additive. Under these reaction conditions, the ruthenium-catalyzed *N*-alkylation of aromatic amines (aniline, 2,4-dimethylaniline and 2-aminopyridine) with arylmethyl alcohols (benzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol and furfuryl alcohol) was examined. In all cases, only monoalkylated amines and imines were formed, and no bis-alkylated products were detected. The reaction products were characterized by NMR. The conversions and selectivity were screened by GC and GC–MS analysis.

With the determined optimal conditions in hand, we first investigated complexes **2a–d** as catalysts the *N*-alkylation of aniline with benzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol and furfuryl alcohol. In all reactions, alkylation of aniline with high selectivity was achieved. The reaction of aniline with benzyl alcohol gave the *N*-benzylaniline in 96–99% conversions (Table 2, entry 1). The formation of *N*-benzylamine with high selectivity was obtained with complex **2c** (Table 2, entry 1). The treatment of aniline with 4-methylbenzyl alcohol and 4-methoxybenzyl alcohol using complexes **2a–d** as catalysts gave also corresponding monoalkylated amines in conversions between 95–100% and 85–91%, respectively, under these conditions. 4-Methoxybenzyl alcohol afforded the corresponding monoalkylated product *N*-(4-methoxybenzyl)aniline with excellent selectivities for all complexes **2a–d** (Table 2, entry 3). Complete selectivity was achieved with catalysts **2b–d** (Table 2, entry 2). High yields were obtained with complexes **2c** and **2d** (Table 2, entry 1–4). These results show that the electron-donating substituent (4-methyl and 4-methoxy) on benzyl alcohol gave higher selectivity when compared to benzyl alcohol itself. When using furfuryl alcohol as the alkylating agent, *N*-(furan-2-ylmethyl)aniline with 100% selectivity was obtained for all complexes **2a–d**, but conversions of reactions were slightly lower than others (Table 2, entry 4).

We next examined the reactions of 2,4-dimethylaniline with benzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol and furfuryl alcohol in the presence of complexes **2a–d** as catalysts under the same reaction conditions (Table 2, entries 5–8). Thus, 2,4-dimethylaniline was treated

Table 1 Determination of reaction conditions for alkylation of aniline with benzyl alcohol[a–d]



Entry	2c (mol%)	Base	Time (h)	Temp. (°C)	Conversion (%)	A/B (%)
1	1	KOH	15	100	52	37/63
2	1	KOH	24	100	71	43/57
3	1	KOBu^t	24	100	82	57/43
4	1	KOH	24	150	86	48/52
5	1	KOH	24	100	12	13/87[b]
6	1	KOBu^t	24	120	91	78/22
7	2.5	KOBu^t	24	120	100	89/11
8	2.5	KOBu^t	24	120	97	52/48[c]
9	1	KOBu^t	24	120	84	60/40[d]
10	2.5	KOBu^t	24	120	100	88/12[d]
11	–	–	24	120	No reaction	–/–

[a]Reaction Conditions: Aniline (1 mmol), benzylalcohol (1 mmol), base (0.5 mmol), toluene (3 mL)

[b]Dioxane

[c]Base (0.025 mmol)

[d]Solvent free

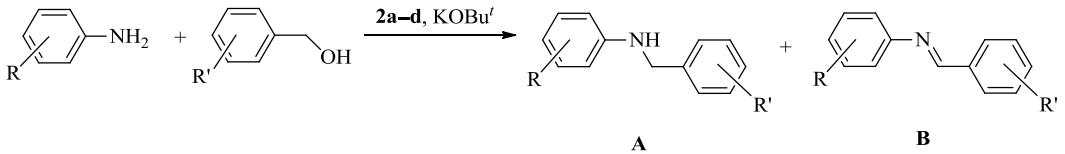
Yields are determined by GC and GC–MS

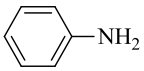
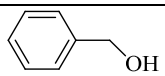
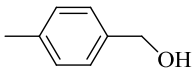
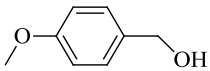
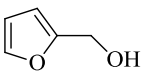
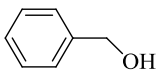
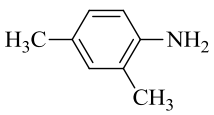
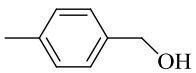
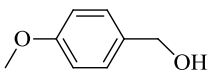
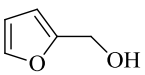
with benzyl alcohol for all complexes **2a**–**d** under optimized reaction conditions to obtain the corresponding *N*-benzyl-2,4-dimethylaniline in 70–84% conversions with 74–87% selectivity (Table 2, entry 5). The reaction of 2,4-dimethylaniline with 4-methylbenzyl alcohol and 4-methoxybenzyl alcohol also afforded corresponding monoalkylated amines in conversions between 75–92% and 70–87% with 80–100% and 55–77% selectivity, respectively. The above results show that the electron-donating substituents such as Me and OMe on both benzyl alcohol and aniline slightly increased the selectivity of monoalkylated amine products under the same conditions (Table 2, entries 1–3, and Table 2, entries 5–7). Similar trends have been observed for the other Ru(II) systems bearing NHC ligands [36]. When the furfuryl alcohol was used as an alkylating agent, only the corresponding monoalkylated amine was obtained with 100% selectivity for all complexes **2a**–**d** (Table 2, entry 8). No imine or bis-alkylated products were detected.

Finally, we also investigated the *N*-alkylation of 2-aminopyridine with the same alcohols (benzyl alcohol, 4-methylbenzyl alcohol, 4-methoxybenzyl alcohol and furfuryl alcohol) by using ruthenium(II)-NHC **2a**–**d** catalysts in order to obtain *N*-alkylated amines under the same reaction conditions. 2-(*N*-alkylamino)pyridines were obtained in good-to-excellent selectivities in the presence of 2.5 mol% catalysts. Moreover, the heteroaromatic moiety in 2-aminopyridine was also well tolerated under this catalytic system. In all reactions, only the nitrogen atom of the amino group of 2-aminopyridine was alkylated; the products with *N*-alkylpyridine were not detected. 2-Aminopyridine was efficiently arylated with benzyl alcohol and furfuryl alcohol for all complexes **2a**–**d** with 100% selectivity (Table 3, entries 1 and 4). The reaction of 2-aminopyridine with 4-methylbenzyl alcohol and 4-methoxybenzyl alcohol also gave corresponding products in conversions between 98–100% and 98–99% with 71–100% and 96–98% selectivity, respectively. As shown in Tables 2 and 3, ruthenium complexes (**2c, 2 d**) bearing NHC ligands with diethylamino or methoxy substituents on benzyl group exhibited better catalytic activity in some cases than the others for the *N*-alkylation of aromatic amines with arylmethyl alcohols.

To the best of our knowledge, studies of Ru-NHC complexes for the alkylation of amines with alcohols are rare in the literature. Recently, our group has investigated ruthenium–carbene complexes in the alkylation of amines with alcohols [37]. In this work, we described the synthesis and characterization of benzimidazole–ruthenium(II) complexes of the general formula [$RuCl_2$(NHC)(η^6-*p*-cymene)]. These complexes were tested as catalysts for the *N*-alkylation of aniline with arylmethyl alcohols. In

Table 2 *N*-alkylation of anilines with benzyl alcohols



Entry	Amine	Alcohol	[Ru]			
			Conversion (Yield A:B%)			
			2a	2b	2c	2d
1			98 (79/21)	96 (63/37)	100 (81/19)	98 (66/34)
2			95 (76/24)	98 (71/29)	100 (77/33)	98 (100/0)
3			84 (98/2)	89 (100/0)	79 (100/0)	87 (100/0)
4			85 (100/0)	97 (100/0)	79 (100/0)	87 (100/0)
5			79 (87/13)	81 (85/15)	84 (75/25)	70 (74/26)
6			92 (86/14)	83 (100/0)	75 (97/3)	78 (80/20)
7			79 (72/28)	70 (77/23)	81 (55/45)	87 (77/23)
8			87 (100/0)	78 (100/0)	82 (100/0)	83 (100/0)

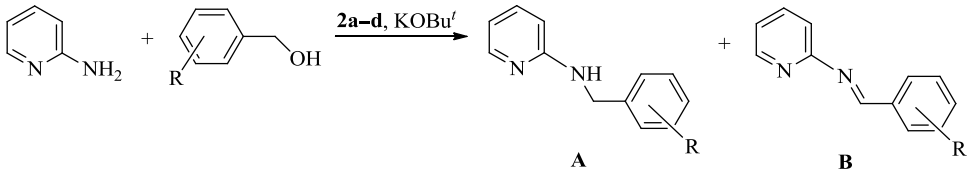
Reaction conditions: Complexes **2a–d** (0.025 mmol, 2.5 mol%), arylmethyl alcohol (1.5 mmol), heterocyclic amine (1 mmol), $KOBu^t$ (1 mmol), 120 °C, 24 h. The conversions and the selectivity determined by GC and GC–MS analysis with the calibrations were based on dodecane

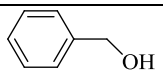
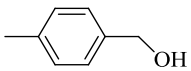
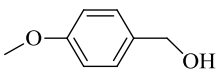
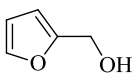
this work we described the synthesis and characterization of perhydrobenzimidazole-ruthenium(II) complexes of the general formula $[RuC_{12}(NHC)(\eta^6\text{-}p\text{-cymene})]$. By comparison, reported for related Ru catalysts such as N-heterocyclic carbene ruthenium(II) complexes, similar results were obtained. The present catalytic system using NHC–ruthenium(II) complexes is particularly effective and selective for amines formation (**A**) despite low-temperature and solvent-free condition [37]. For example in the case of furfuryl alcohol, the amine product (A) was obtained in 84–93% when benzimidazole–ruthenium(II) complexes were employed, whereas the perhydrobenzimidazole–ruthenium(II) complexes (2a–d) afforded full conversion and the amine product (A) was favored (Table 2, entry 4).

Conclusion

In summary, ruthenium(II)-NHC complexes **2a–d** have been easily prepared by the reaction of silver(I)-NHC complexes as a carbene transfer reagent with $[RuCl_2(p\text{-cymene})]_2$ in dichloromethane at room temperature in good yields. The catalytic activity of these complexes was investigated in

Table 3 *N*-alkylation of 2-pyridyl amine with arylmethyl alcohols



Entry	Alcohol	[Ru] Conversion (Yield A:B%)			
		2a	2b	2c	2d
1		96 (100/0)	97 (100/0)	100 (100/0)	98 (100/0)
2		98 (76/24)	98 (71/29)	100 (100/0)	100 (100/0)
3		99 (97/3)	98 (96/4)	99 (98/2)	99 (98/2)
4		98 (100/0)	99 (100/0)	96 (100/0)	97 (100/0)

Reaction conditions: aniline (1 mmol), alcohol (1.5 mmol), Ru-NHC (0.025 mmol), $KOBu^t$ (1 mmol), 120 °C, 24 h. The conversions and the selectivity determined by GC and GC–MS analysis with the calibrations were based on dodecane

N-alkylation reactions of aniline, 2,4-dimethylaniline and 2-aminopyridine with arylmethyl alcohols including benzyl alcohol, 4-methyl benzyl alcohol, 4-methoxybenzyl alcohol and furfuryl alcohol. The *N*-alkylation of amines was performed in solvent-free conditions for 24 h at 120 °C using 2.5 mol% of complexes **2a**–**d**. All of these complexes were found to be suitable for *N*-alkylation of aromatic amines with arylmethyl alcohols via hydrogen borrowing reactions. In this study, high selectivity was obtained. In all cases only monoalkylated amines were formed and no bis-alkylated products were detected.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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