A Half Sandwich Ruthenium(II) Complex with *N*-4,6-Dimethyl-2-pyrimidinylimidazole: Synthesis, Crystal Structure and Application in *N*-Alkylation of Amines with Alcohols

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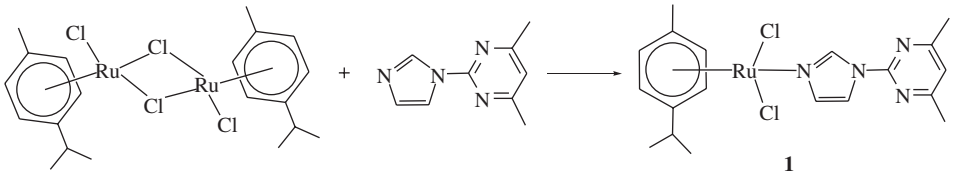
The metal-catalyzed C—N bond forming reaction is one of the most important transformations in organic synthesis and plays a vital role in chemical and biological systems.[1] The *N*-alkylation of amines with electrophiles such as alkyl halides is the conventional method to form C—N bonds.[2] However, this method is undesirable from an environmental point of view. Alcohols are of great importance as cheap and readily available organic materials for the preparation of many pharmaceutical products and fine chemicals.[3] The use of alcohols as electrophiles instead of alkyl halides in C—N bond forming reactions is particularly attractive because the process produces only water as byproduct,[4] and great progress has been obtained for the metal-catalyzed hydrogen autotransfer process by alcohols as the greener alkylating reagents.[5] A number of reports have shown that Ru[6] and Ir[7] complexes are effective catalysts for this transformation. We have also found cyclometallated iridium(III) complexes were very efficient catalysts for α-alkylation using the hydrogen-borrowing strategy.[8] As a continuation of our interest in metal-catalyzed hydrogen autotransfer processes, we have prepared a new half sandwich Ru(II) complex with imidazole (Scheme 1) and examined its activity in the *N*-alkylation of amines with alcohols.

Complex **1** is air- and moisture-stable, both in solid state and in solution. It was characterized by HRMS, ^{1}H, and ^{13}C NMR. These spectra were well consistent with the title complex. Moreover, the molecular structure of **1** has been ascertained by means of single-crystal X-ray studies. The molecule of **1** together with selected bond distances and angles is shown in Figure 1. The complex has an essentially octahedral coordination geometry comprising the *p*-cymene ring carbons occupying one face of the octahedron leaving the other three sites to be coordinated by two chloride atoms and monodentate (*N*-4,6-dimethyl-2-pyrimidinylimidazole) ligand. The Ru—N bond length 2.113(3) Å of **1** is similar to those of the related arene Ru(II) complexes.[9] The imidazole ring and the pyrimidine ring are approximately coplanar (dihedral angle of 9.0°). The dihedral angle between the imidazole ring and *p*-cymene ring is 38.5°. In the crystal, there exist intermolecular C—H···Cl hydrogen bonds (H···Cl=2.828 Å) between chlorine atom and the adjacent C—H of *p*-cymene ring, which construct the 1D chain structure.

In 2014, Özdemir *et al*. reported the first examples of half sandwich Ru(II) complexes bearing benzimidazole moiety for the *N*-alkylation of amines.[6c] However, the catalytic system required a high temperature (150 °C). Initially, the *N*-alkylation of *m*-toluidine with (4-methoxyphenyl)methanol was carried out with various solvents and bases in the presence of 1 mol% of **1** at 120 °C for 12 h. The results from this study are summarized in Table 1. Among the tested solvents, xylene was much better than toluene and dioxane (entries 1–3). After screening a variety of bases (entries 4–7), KOH was found to be the most effective base (96%, entry 5) and KO^{t}Bu as well as CsOH also showed comparable results.

Under the optimized reaction conditions, the *N*-alkylations of *m*-toluidine with a variety of electronically and structurally diverse aryl methanols were carried out to explore the scope of this system (Table 2). Similar to the result of (4-methoxyphenyl)methanol, the coupled products **2b–2d** were obtained in excellent yields. Good yields were also obtained with electron-deficient aryl methanols. For *ortho*-substituents with methyl, chloride and bromine groups, the yields of **2i–2j** decreased slightly. In the following experiments, the *N*-alkylations of a variety of amines were investigated (Table 3). Complex **1** also showed high catalytic activity for the *N*-alkylation of (pyridin-2-yl)- methanol. Similar to the results of varying aryl methanol part, reaction with *para*-, *ortho*-, and



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Scheme 1. Synthesis of **1**.

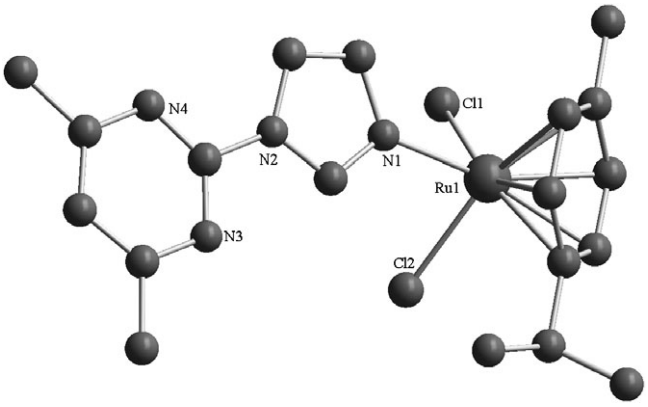
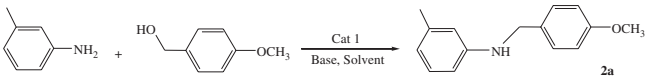


Figure 1. Molecular structure of complex **1**. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Ru1–Cl1 2.4099 (10), Ru1–Cl2 2.4197(9), Ru1–N1 2.113(3), and Cl1–Ru1–Cl2 88.88(4), N1–Ru1–Cl1 85.31(9), N1–Ru1–Cl2 85.71(9).

Table 1. Influence of solvent and base on the *N*-alkylation of *m*-toluidine with (4-methoxyphenyl)methanol.[a]



Entry	Base	Solvent	Yield (%)[b]
1	KO^{t}Bu	Dioxane	78
2	KO^{t}Bu	Toluene	82
3	KO^{t}Bu	Xylene	95
4	NaOH	Xylene	65
5	KOH	Xylene	96
6	CsOH	Xylene	93
7	K_2CO_3	Xylene	21

[a] Reaction conditions: *m*-toluidine (1 mmol), (4-methoxy- phenyl) methanol (1.1 mmol), base (1 mmol), solvent (3 mL), 120 °C, 12 h.
[b] Isolated yields.

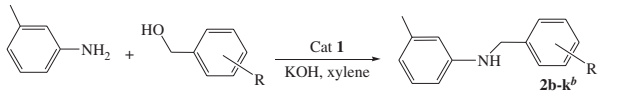
meta-amines proceeded efficiently to from the expected products **3a–3i** in good to excellent yields. Finally, the coupling of (pyridin-2-yl)- methanol with 2-aminopyridine also gave excellent yield.

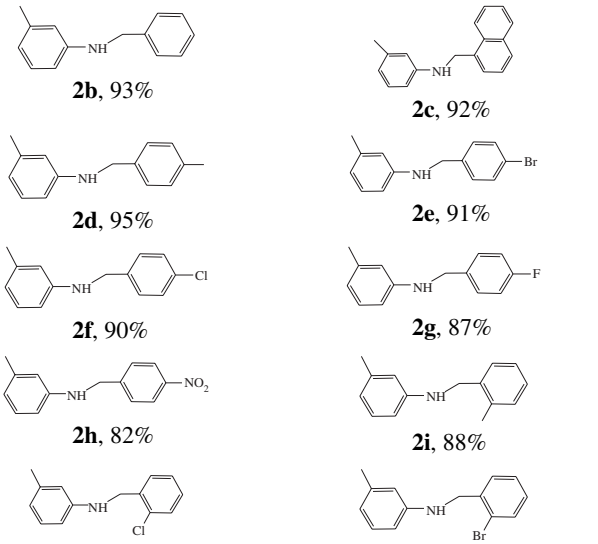
In conclusion, a new half sandwich Ru(II) complex bearing imidazole moiety has been synthesized and characterized. It was an efficient catalyst for the *N*-alkylation of amines with alcohols.

Experimental

Materials and Measurement. Solvents were dried and freshly distilled prior to use. All other chemicals were commercially available expect for the *N*-4,6-dimethyl-2-pyrimidinylimidazole was prepared according to published procedure.[10] High-resolution mass spectra were measured on a Waters Q-Tof Micro™ spectrometer (Waters, Manchester, UK). NMR spectra were recorded on a Bruker DPX-400 spectrometer (Billerica, MA< USA) in $CDCl_3$ with TMS as an internal standard. Crystallographic data were collected on a Xcalibur, Eos, Gemini diffractometer (Agilent, Oxford, UK). CCDC reference number 1402502 for **1**.

Table 2. The *N*-alkylation of *m*-toluidine with aryl meth-anols catalyzed by 1.[a]



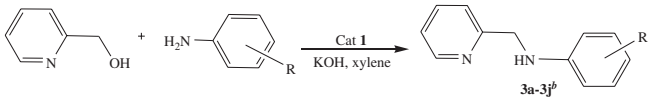


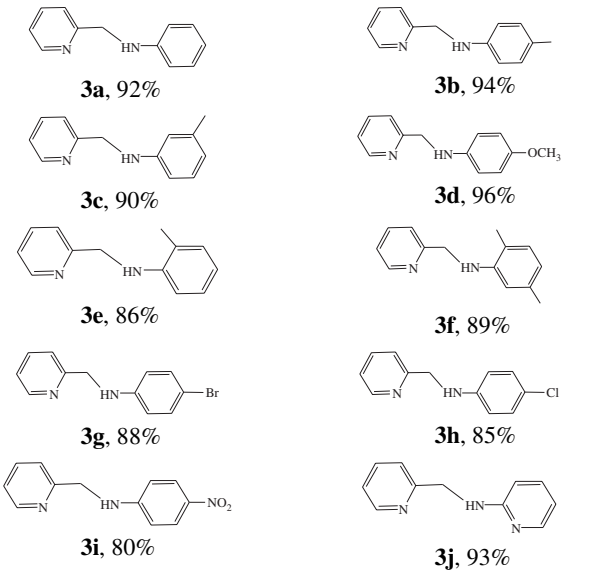
[a] Reaction conditions: *m*-toluidine (1 mmol), aryl methanol (1.1 mmol), KOH (1 mmol), xylene (3 mL), 120 °C, 12 h.
[b] Isolated yields.

Dichloro-(*N*-4,6-dimethyl-2-pyrimidinylimidazole)(*p*-cymene)ruthenium(II) (1). A solution of *N*-4,6-dimethyl-2-pyrimidinylimidazole (0.5 mmol) and $[RuCl_2(p\text{-cymene})]_2$ (0.5 mmol) in toluene (10 mL) was refluxed for 3 h and then cooled to room temperature. The product **1** was filtered off, washed with diethyl ether, and dried in air. Red solid, 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.97 (s, 1H), 7.89 (s, 1H), 7.44 (s, 1H), 6.95 (s, 1H), 5.49 (d, J = 5.8 Hz, 2H), 5.30 (d, J = 5.8 Hz, 2H), 3.00 (hept, 1H), 2.48 (s, 6H), 2.20 (s, 3H), 1.31 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): 169.2, 152.9, 139.1, 132.6, 118.9, 117.0, 102.8, 97.4, 82.9, 81.5, 30.7, 23.9, 22.3, 18.6. HRMS (ESI) calcd for $C_{19}H_{24}Cl_2N_4Ru$: 480.0422, found: 480.0422; Calcd for $[M\text{-}Cl]^+$: 445.0733, found: 445.0733.

General Procedure for the *N*-alkylation. A reaction tube was charged with amines (1 mmol), alcohols (1.1 mmol) catalyst **1** (0.01 mmol), the selected base (1.0 mmol), and solvent (3 mL) under the nitrogen gas. The reaction mixture was heated at 120 °C for 12 h. After being cooled, the solvent was evaporated and the product was separated by passing through a silica gel column. The products **2a**[11a], **2b**[11b],

Table 3. The *N*-alkylation of (pyridin-2-yl)methanol with amines catalyzed by 1.[a]





[a] Reaction conditions: amines (1 mmol), (pyridin-2-yl)- methanol (1.1 mmol), KOH (1 mmol), xylene (3 mL), 120 °C, 12 h.
[b] Isolated yields.

2d[11a], **2f**[11c], **2g**[11d], **2h**[11e], **2k–j**[11f] and **3a–b**[12a], **3d–g**[12b], **3h**[5b], **3i**[12c], **3j**[6a] were characterized by comparison of data with those in the literature. Other products were determined by HRMS, ^{1}H and ^{13}C NMR.

3-Methyl-*N*-[(naphthalen-1-yl)methyl]benzenamine (2c). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 5.6 Hz, 1H), 7.86 (d, *J* = 5.6 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 6.0 Hz, 3H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 7.2 Hz, 1H), 6.48 (s, 2H), 4.68 (s, 2H), 3.88 (br, 1H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 148.4, 139.2, 134.6, 134.0, 131.7, 129.3, 128.9, 128.3, 126.4, 126.2, 125.9, 125.7, 123.8, 118.7, 113.6, 110.0, 46.6, 21.8. HRMS (ESI) calcd for $C_{18}H_{17}N$: 247.1361, found: 247.1361.

***N*-(4-Bromobenzyl)-3-methylbenzenamine (2e).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (t, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.54 (d, *J* = 7.2 Hz, 1H), 4.25 (s, 2H), 3.98 (br, 1H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 151.7, 147.9, 139.1, 132.5, 131.0, 129.2, 127.6, 125.8, 118.8, 110.0, 47.7, 21.7. HRMS (ESI) calcd for $C_{14}H_{14}BrN$: 275.0310, found: 275.0310.

***N*-(2-Methylbenzyl)-3-methylbenzenamine (2i).** ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, *J* = 7.2 Hz, 1H), 7.14–7.18 (m, 3H), 7.06 (t, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.4 Hz, 1H), 6.41–6.45 (m, 2H), 4.23 (s, 2H), 3.65 (br, 1H), 2.35 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 148.4, 139.1, 137.2, 136.4, 130.5, 129.2, 128.4, 127.5, 126.2, 118.58, 113.5, 109.9, 46.5, 21.7, 19.0. HRMS (ESI) calcd for $C_{15}H_{17}N$: 211.1361, found: 211.1361.

3-Methyl-*N*-[(pyridin-2-yl)methyl]benzenamine (3c). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 4.0 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.13 (t, *J* = 6.0 Hz, 1H), 7.04 (t, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.2 Hz, 1H), 6.47 (m, 2H), 4.42 (br, 3H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.7, 149.2, 148.0, 139.0, 136.7, 129.2, 122.1, 121.6, 118.6, 113.9, 110.2, 49.3, 21.7. HRMS (ESI) calcd for $C_{13}H_{14}N_2$: 198.1157, found: 198.1157.

2-Methyl-*N*-[(pyridin-2-yl)methyl]benzenamine (3e). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 4.2 Hz, 1H), 7.60 (t, *J* = 7.2 Hz, 1H), 7.29 (d, *J* = 7.8 Hz, 1H), 7.14 (t, *J* = 5.6 Hz, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.66 (t, *J* = 7.2 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 2H), 4.71 (br, 1H), 4.48 (s, 2H), 2.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.8, 149.3, 148.2, 139.1, 136.9, 129.5, 122.2, 121.7, 118.8, 114.0, 110.3, 49.4, 21.9. HRMS (ESI) calcd for $C_{13}H_{14}N_2$: 198.1157, found: 198.1157.

2,5-Dimethyl-*N*-[(pyridin-2-yl)methyl]benzenamine (3f). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (d, *J* = 4.2 Hz, 1H), 7.59 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.14 (t, *J* = 6.0 Hz, 1H), 6.94 (d, *J* = 7.2 Hz, 1H), 6.47 (d, *J* = 7.2 Hz, 1H), 6.39 (s, 1H), 4.64 (br, 1H), 4.47 (s, 2H), 2.36 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 158.6, 149.2, 145.8, 136.6, 129.9, 122.0, 121.6, 119.3, 117.8, 110.1, 100.0, 25.0, 21.5. HRMS (ESI) calcd for $C_{14}H_{16}N_2$: 212.1314, found: 212.1314.

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