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Nazan Kaloğlu, Mathieu Achard, Christian Bruneau, İsmail Özdemir. Ruthenium(II)-(Arene)-N-Heterocyclic Carbene Complexes: Efficient and Selective Catalysts for the N -Alkylation of Aromatic Amines with Alcohols. European Journal of Inorganic Chemistry, 2019, 2019 (21), pp.2598-2606. 10.1002/ejic.201900191 . hal-02169359

HAL Id: hal-02169359

https://univ-rennes.hal.science/hal-02169359v1

Submitted on 1 Jul 2019

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Ruthenium(II)-(arene)-*N*-Heterocyclic Carbene Complexes: Efficient and Selective Catalysts for the *N*-Alkylation of Aromatic Amines with Alcohols

Nazan Kaloğlu,[a,b] Mathieu Achard,[c] Christian Bruneau[c] and İsmail Özdemir*[a,b]

Abstract: A series of unsymmetrical 1,3-disubstituted benzimidazolium chlorides were synthesized as *N*-heterocyclic carbene (NHC) precursors. These compounds were used for synthesis of the new ruthenium(II) complexes of the type [$RuCl_2$(arene)(NHC)], (arene = η^6-*p*-cymene). The structures of all compounds were characterized by ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopy techniques. The catalytic activity of the ruthenium complexes has been evaluated with respect to the mono-*N*-alkylation reactions of aromatic amines with various alcohol derivatives under solvent-free conditions at 120 °C using the borrowing hydrogen strategy.

Introduction

Amines are an important class of compounds that are widely found in bioactive molecules, pharmaceuticals and natural products, due to their diverse biological and pharmacological properties [1-3]. Considering structural diversity and biological properties of amines, it is clear that they are an important component in medicinal applications [4]. As selected examples of benzyl-substituted amines, Tripelennamine (marketed as Pyribenzamine®) is a drug that is used as an antipruritic and first-generation antihistamine, Bepridil (marketed as Vascor®) is is an amine calcium channel blocker once used to treat angina and Zafuleptine (proposed brand name Thymeon) is an antidepressant drug, developed in the 1970s but never marketed (Figure 1).

Conventional methods to access amines include the nucleophilic substitution of halides [5] as well as reductive alkylation processes [6]. However, these conventional methods suffer disadvantages as follows; (1) the use of alkyl halides or strong reducing reagents is undesirable from an environmental point of view and (2) these reactions generate equimolar amounts of wasteful salts as co-products [7-9]. Therefore, the development of improved synthetic methodologies for the preparation of the alkylated amines continue to be of significant interest to organic chemists.

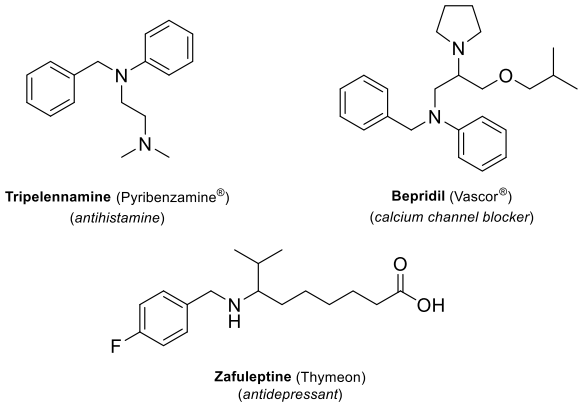

Figure 1. Examples of biologically active benzyl-substituted amines.

Recently, several papers briefly reported the transition metal-catalyzed *N*-alkylation of amines with alcohols following the so-called "hydrogen borrowing" or "hydrogen auto-transfer" methodology, has attracted much attention (Figure 2) [10-12]. It is a new, efficient and alternative method for the synthesis of alkylamines. The use of alcohols instead of alkyl halides to achieve the alkylated amines is an attractive method, because, it does not generate any harmful and/or wasteful by-products (only H_2O as by-product). In addition, alcohols are more readily available than alkyl halides and related alkylating agents in many cases, and if the reaction proceeds efficiently by the employment of equimolar amounts of starting materials, extremely high atom economical system can be realized [13]. In borrowing hydrogen strategy, firstly, metal takes the hydrogen from the alcohol. The short-term removal of the hydrogen in the alcohol converts it into the aldehyde and forms a metal hydride. Then, aldehyde can react with an amine to to give the imine upon removal of water, and finally, the transition-metal catalyst returns the borrowed hydrogen to the imine to form the secondary amine, (tertiary amine if the starting material is a secondary amine) [14].

[a] Dr. Nazan Kaloğlu and Prof. Dr. İsmail Özdemir,
Department of Chemistry, Faculty of Science and Art, İnönü University, 44280 Malatya, Turkey
E-mail: ismail.ozdemir@inonu.edu.tr
https://www.inonu.edu.tr/
[b] Dr. Nazan Kaloğlu and Prof. Dr. İsmail Özdemir,
Catalysis Research and Application Center, İnönü University. 44280 Malatya, Turkey
[c] Dr. Mathieu Achard and Dr. Christian Bruneau,
Rennes University, CNRS, ISCR (Institut des Sciences Chimiques de Rennes) - UMR6226, 35000 Rennes, France

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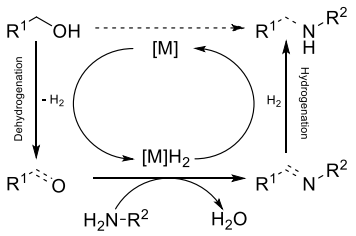
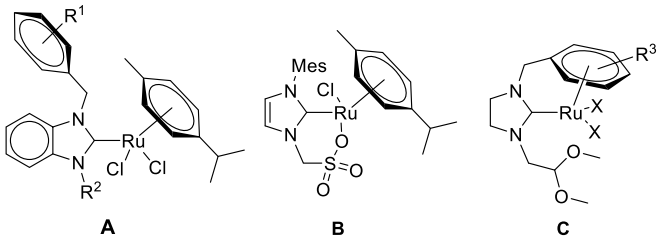


Figure 2. General mechanism of the "borrowing hydrogen" strategy.

Pioneering works in this field have been done independently by the groups of Grigg [15], Watanabe [16] and Murahashi [17] in the presence of rhodium and ruthenium catalysts at the beginning of the 1980s. These first reports demonstrated that noble metals such as rhodium and ruthenium could catalyse borrowing hydrogen reactions. But due to the lack of selectivity, both secondary and tertiary amines were formed, due to the harsh catalytic conditions. Then, new catalysts were developed to carry out this reaction under milder conditions [18]. Recently, great contributions have also been made the groups of Beller [19], Williams [20], Milstein [21], Zhao [22], Fujita [23] and Bruneau [24]. In most of the cases, ruthenium or iridium complexes have been used as catalysts to achieve efficient *N*-alkylation of a variety of amines with alcohols. Recently, important progress in borrowing hydrogen strategy was achieved with Au and Zr as the catalysts with excellent results [25]. In addition, these strategy has been performed using biocatalysts for the preparation of enantiopure amines via biocatalytic hydrogen methodology [26].

Over the last two decades, *N*-heterocyclic carbenes (NHCs) have emerged as a highly versatile class of ligands for a broad range of transition metals. Transition-metal complexes of NHCs have been widely used in organometallic chemistry as an alternative to well-known phosphine ligands for the synthesis of homogeneous catalysts. Many types of *N*-alkyl, *N*-aryl and *N*-benzyl (benz)imidazolylidene carbene ligands have been used in transition-metal catalysis and medical applications, and many research groups have provided a large number of NHC-based complexes [27,28]. To date, NHC complexes of ruthenium and iridium have been reported to be active catalysts for the hydrogen borrowing reactions involving alcohols. In particular, *N*-alkylation of primary amines with alcohols via hydrogen borrowing processes have been carried out with (arene)ruthenium- and (Cp*)iridium-carbene complexes. As an early example, Cp*-functionalized iridium-carbene complexes have been reported by Peris for the *N*-alkylation of aniline and *β*-alkylation of secondary alcohols [29]. Crabtree have reported the use of [IrCp*] complex as a catalyst for the *N*-alkylation of amines [30]. Valerga reported the *N*-alkylation of both aromatic and non-aromatic amines using ruthenium(II)-picolyl-NHC complex as a catalyst [31]. Recently, Huynh and Seayad have reported the *N*-alkylation of amines with alcohols and diols using [$RuCl_2$(*p*-cymene)(NHC)] complex [32]. More recently, our research group [$RuCl_2$(arene)(NHC)] complexes (Figure 3, **A**) have also been used for the formation of tertiary amines from cyclic secondary amines and primary benzylic alcohols (or aldehydes) [33a, 34b,c,e]. We have also previously shown that the half-sandwich ruthenium complexes (Figure 3, **B**), bearing a chelating NHC-sulfonate ligand [33b], and the chelating ruthenium-NHC-arene complexes (Figure 3, **C**) were efficient catalysts for the *N*-alkylation of aniline and secondary cyclic amines by benzylic and aliphatic alcohols, and the regioselective C3-alkylation of *N*-protected secondary amines by aldehydes [34].



A **B** **C**

R^1 = alkyl; R^2 = benzyl Mes = 2,4,6-trimethylphenyl X = Cl, Br; R^3 = alkyl

Figure 3. Our previously published ruthenium-NHC complexes for the hydrogen borrowing reactions.

Herein, we now describe the synthesis and characterization of the five novel ruthenium(II) complexes of the general formula [$RuCl_2$(η^6-*p*-cymene)(NHC)] (NHC = benzimidazol-2-ylidene), **2a**-**2e**. These complexes were characterized by ^{1}H NMR, ^{13}C NMR, FT-IR spectroscopy techniques. Next, we examined the catalytic activity of all ruthenium complexes in the *N*-alkylation of aromatic amines with different alcohol derivatives under solvent-free conditions using the borrowing hydrogen strategy.

Results and Discussion

Preparation of Benzimidazolium Chlorides

The all benzimidazolium chlorides (**1a**-**1e**) were synthesized as we previously described in the literature [28g,m] by the reaction of *N*-(3-methoxybenzyl)benzimidazole with alkyl chlorides in dimethylformamide (DMF) at 80 ^{o}C for 36 h (Scheme 1). These

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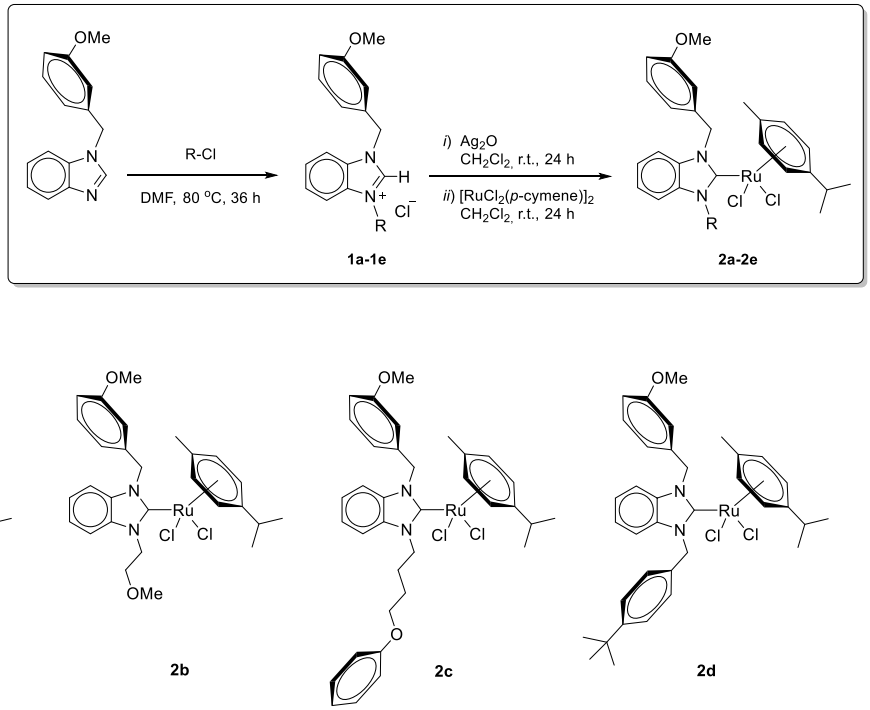
unsymmetrical benzimidazolium chlorides were isolated as white solids soluble in water and protic solvents, and were fully characterized by ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopy. FT-IR data clearly indicated that all benzimidazolium chlorides exhibit a characteristic $\nu_{(NCN)}$ band typically between 1557-1567 cm^{-1}. The resonances for C(2)-*H* were observed as sharp singlets at δ 11.48-12.00 ppm. The ^{13}C NMR values of N*C*HN resonances in the all benzimidazolium chlorides appear at the range 143.7-143.9 ppm as single signal. These spectroscopic values are in line with those found for other benzimidazolium chlorides of the literature [28d-m, 33b,c]. For the ^{1}H NMR, ^{13}C NMR and FT-IR spectrums of the all benzimidazolium chlorides (**1a**-**1e**) see SI, pp. S1-S10.

Preparation of Ruthenium-(arene)-NHC Complexes

The new ruthenium complexes **2a-2e** were obtained in 54-82% yields by transmetalation of the corresponding silver-NHC adducts and $[RuCl_2(p\text{-cymene})]_2$. The air and moisture-stable ruthenium complexes are brown in colour and soluble in common chlorinated organic solvents such as chloroform and dichloromethane. They are found to be diamagnetic and they were fully characterised by ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopy. Their FT-IR data each show a band at 1453-1480 cm^{-1} ($\nu_{(NCN)}$) and their ^{13}C NMR spectra each display a singlet in the range 188.8-191.5 ppm (Ru-$C_{carbene}$), two evidences of the formation of a Ru-carbene bond. These spectroscopic values are in line with those found for other $[RuCl_2(p\text{-cymene})(NHC)]$ complexes of the literature [33a,b,d]. For the ^{1}H NMR, ^{13}C NMR and FT-IR spectrums of the new ruthenium complexes **2a-2e** see SI, pp. S11-S20.

All compounds were prepared according to general reaction pathway depicted in Scheme 1. The analytical data are in good agreement with the compositions proposed for all the new ruthenium complexes we prepared, and are summarized in Table 1.



Scheme 1. Synthesis of benzimidazolium chlorides (**1a-1e**) and their ruthenium(II) complexes (**2a-2e**).

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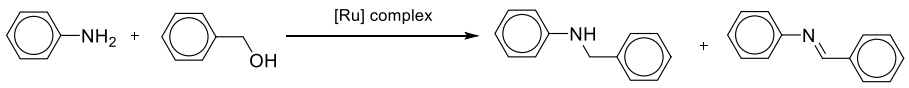
Table 1. Physical and spectroscopic properties of new ruthenium complexes (**2a**-**2e**).

Compound	Molecular formula	Isolated yield (%)	M.p. (°C)	$\nu_{(CN)}$ (cm^{-1})	C(2) ^{13}C NMR (ppm)
2a	$C_{26}H_{30}Cl_2N_2ORu$	82	115-116	1458	190.3
2b	$C_{28}H_{34}Cl_2N_2O_2Ru$	75	148-149	1453	191.5
2c	$C_{35}H_{40}Cl_2N_2O_2Ru$	78	190-191	1465	188.8
2d	$C_{36}H_{42}Cl_2N_2ORu$	65	201-202	1480	191.5
2e	$C_{37}H_{44}Cl_2N_2ORu$	54	153-154	1454	190.3

Optimization of the Reaction Conditions for *N*-Alkylation of Aniline with Benzyl Alcohol

The catalytic activity of the ruthenium complexes **2a-2e** for alcohol activation towards *N*-alkylation was investigated by taking the coupling between benzyl alcohol and aniline as a standard reaction (Table 2). Catalyst **2a** was selected for initial optimization of the reaction conditions. To find the best base, different bases (^{t}BuOK, Cs_2CO_3, K_2CO_3, KOH) were tested under solvent-free conditions at 120 °C for 24 h (Table 2, entries 1-4).

Table 2. Optimization of the reaction conditions for ruthenium catalyzed *N*-alkylation of aniline with benzyl alcohol.[a]



3aa **3ba**

Entry	Ru-complex **2a** [mol%]	Base	Time [h]	Temp. [°C]	Yield[b] [%]	Selectivity[c] [%]	
						3aa	**3ba**
1	4	^{t}BuOK	24	120	100	96	4
2	4	Cs_2CO_3	24	120	45	81	19
3	4	K_2CO_3	24	120	50	75	25
4	4	KOH	24	120	55	70	30
5	2.0	^{t}BuOK	24	120	100	95	5
6	1.5	^{t}BuOK	24	120	99	94	6
7	1	^{t}BuOK	24	120	74	65	35
8	1.5	^{t}BuOK	24	100	75	75	25
9	**1.5**	**^{t}BuOK**	**20**	**120**	**97**	**94**	**6**
10	1.5	^{t}BuOK	16	120	50	64	36
11[d]	1.5	^{t}BuOK	20	120	15	75	25
12[e]	-	^{t}BuOK	20	120	-	-	-
13[f]	1.5	^{t}BuOK	20	120	59	70	30

[a] Reaction conditions: Aniline (1.0 mmol), benzyl alcohol (1.5 mmol), base (1.5 mmol).
[b] Yields (%) were calculated according to aniline by GC-MS analysis using dodecane as an internal standard.
[c] Selectivities (%) of **3aa** and **3ba** were calculated by GC and GC-MS analysis.
[d] Only $[RuCl_2(p\text{-cymene})]_2$ complex was used as catalyst.
[e] Without any ruthenium catalyst.
[f] *In situ* generated catalytic system with **1a** carbene precursor and $[RuCl_2(p\text{-cymene})]_2$ was used.

When a base of ^{t}BuOK was used, a good yield of *N*-benzylaniline (**3aa**) was obtained (Table 2, entry 1). When the amount of catalyst is reduced from 4 mol% to 2 mol% and from 2 mol% to 1.5 mol%, no noticeable effect on the yield and selectivity was observed (Table 2, entries 5,6), but when the amount of catalyst was reduced from 1.5 mol% to 1 mol%, the yield dropped to 74% and the selectivity of **3aa** decreased from 94% to 65%. (Table 2, entry 7). Thus, the most suitable amount of catalyst was determined as 1.5 mol% in this reaction. Decreasing the reaction temperature from 120 °C to 100 °C had detrimental effect on the yield (Table 2, entry 8). When the reaction time was reduced from 24 h to 20 h at 120 °C, no noticeable effect on the yield was observed (Table 2, entry 9), but when the reaction time was reduced from 20 h to 16 h, the yield and selectivity dropped (Table 2, entry 10). As a result of the optimization experiments, a very good yield (97%) and selectivity (**3aa**/**3ba,** 94/6) was obtained with ^{t}BuOK as base and under solvent-free conditions, at 120 °C for 20 h (Table 2, entry 9). It is known that in the absence of any additional ligand, $[RuCl_2(p\text{-cymene})]_2$ alone does not catalyze efficiently the *N*-alkylation by primary alcohols even in refluxing toluene [20b]. Indeed, in the absence of any ligand only 15% yield was

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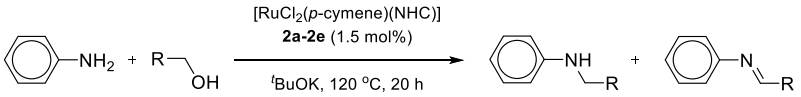
observed (Table 2, entry 11), and we checked that without any ruthenium precursor no reaction took place (Table 2, entry 12). When *in situ* generated catalytic system with 3 mol% of **1a** carbene precursor and 1.5 mol% of $[RuCl_2(p\text{-cymene})]_2$ was used, 59% yield was observed (Table 2, entry 13).

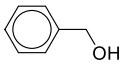
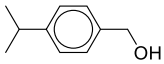
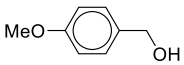
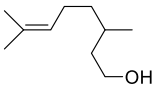
N-Alkylation of Aromatic Amines with Various Alcohols

The optimized conditions were applied to *N*-alkylation of aniline with benzyl alcohol using the ruthenium complexes (**2a-2e**) under solvent-free conditions at 120 °C for 20 h (Table 2). As shown in Table 3-6, aromatic amine derivatives were selectively *N*-mono-alkylated with different alcohols bearing both electron-donating and electron-withdrawing substituents on the aryl ring in good yields (typically 63-100%). Under the determined reaction conditions, benzyl alcohol, *p*-isopropylbenzyl alcohol, *p*-methoxybenzyl alcohol and citronellol reacted very cleanly with aniline and produced the *N*-alkylation products with high selectivity (Table 3, entries 1-20). The selectivity was in high ratio toward to amine. Among the tested complexes, **2a** is highly efficient in the *N*-alkylation of aniline (Table 3, entries 1,6,11,16). When the reaction of aniline with benzyl alcohol was performed by the complexes **2a-2e**, *N*-benzylaniline (**3aa**) was obtained as a major product (selectivity of **3aa**, 90-94%), (Table 3, entries 1-5). *p*-Isopropylbenzyl alcohol was also good alkylating reagents, *N*-(*p*-isopropylbenzyl)aniline (**3ab**) was obtained in excellent yields (selectivity of **3ab**, 92-98%), (Table 3, entries 6-10). All of the reactions using 4-methoxybenzyl alcohol resulted in the selective formation of *N*-(4-methoxybenzyl)aniline (**3ac**) in high to excellent yields (selectivity of **3ac**, 90-99%) (Table 3, entries 11-15). With Citronellol, which was used as the aliphatic alcohol derivative in this reaction, were obtained as a major product *N*-(3,7-dimethyloct-6-en-1-yl)aniline (**3ad**), (selectivity of **3ad**, 90-100%) (Table 3, entries 16-20).

Table 3. Ruthenium-catalyzed *N*-alkylation of aniline with alcohols.[a]



3a **3b**

Entry	Ru-complex	Alcohols	Yield[b] [%]	Selectivity[c] [%]	
				3a	**3b**
1	**2a**		97	94	6
2	**2b**		98	91	9
3	**2c**		95	93	7
4	**2d**		97	92	8
5	**2e**		89	90	10
6	**2a**		100	98	2
7	**2b**		95	95	5
8	**2c**		97	97	3
9	**2d**		91	96	4
10	**2e**		90	92	8
11	**2a**		100	99	1
12	**2b**		97	97	3
13	**2c**		98	98	2
14	**2d**		95	95	5
15	**2e**		88	90	10
16	**2a**		90	100	-
17	**2b**		85	95	5
18	**2c**		86	100	-
19	**2d**		80	96	4
20	**2e**		75	90	10

[a] Reaction conditions: [Ru] (**2a-2e**) (0.015 mmol, 1.5 mol%), aniline (1.0 mmol), alcohol (1.5 mmol), ^{t}BuOK (1.5 mmol), 120 °C, 20 h.
[b] Yields (%) were calculated according to aniline by GC-MS analysis using dodecane as an internal standard.
[c] Selectivities (%) of **3a** and **3b** were calculated by GC and GC-MS analysis.

When the reaction of *p*-methylaniline with alcohol derivatives such as benzyl alcohol, *p*-isopropylbenzyl alcohol and citronellol was investigated, the yields were at between 80-90%, 75-85% and 63-75%, respectively (Table 4, entries 1-15). *N*-(Benzyl)-*p*-methylaniline (**4aa**) and *N*-(*p*-isopropylbenzyl)-*p*-methylaniline (**4ab**) were obtained in excellent yields (selectivity

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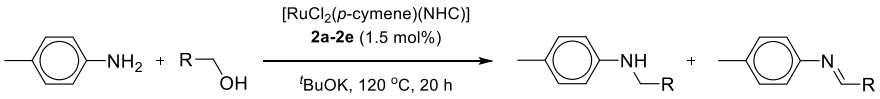
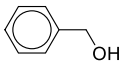
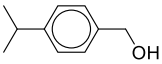
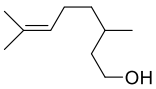
of **4aa**, 95-100% and selectivity of **4ab**, 93-100%), (Table 4, entries 6-10). The *N*-alkylation of citronellol with *p*-methylaniline proceeds nicely. The citronellol was also a good substrate to afford the corresponding products *N*-(3,7-dimethyloct-6-en-1-yl)-*p*-methylaniline (**4ac**) with high yields (Table 4, entries 6-10). In general, *N*-alkylation of benzyl alcohol and *p*-isopropylbenzyl exhibited more good yields than the citronellol with *p*-methylaniline. Also, because of similar nature of **2a**-**2e** complexes, they had a no significant effect on the overall yield of the reaction.

Table 4. Ruthenium-catalyzed *N*-alkylation of *p*-methylaniline with alcohols.[a]



4a **4b**

Entry	Ru-complex	Alcohols	Yield[b] [%]	Selectivity[c] [%]	
				4a	**4b**
1	**2a**		90	100	-
2	**2b**		88	98	2
3	**2c**		83	95	5
4	**2d**		85	99	1
5	**2e**		80	96	4
6	**2a**		85	99	1
7	**2b**		83	94	6
8	**2c**		80	100	-
9	**2d**		78	97	3
10	**2e**		75	93	7
11	**2a**		75	100	-
12	**2b**		74	96	4
13	**2c**		70	97	3
14	**2d**		69	95	5
15	**2e**		63	91	9

[a] Reaction conditions: [Ru] (**2a-2e**) (0.015 mmol, 1.5 mol%), *p*-methylaniline (1.0 mmol), alcohol (1.5 mmol), ^{t}BuOK (1.5 mmol), 120 °C, 20 h.
[b] Yields (%) were calculated according to *p*-methylaniline by GC-MS analysis using dodecane as an internal standard.
[c] Selectivities (%) of **4a** and **4b** were calculated by GC and GC-MS analysis.

When 2,4-dimethylaniline was used as substrate, the reaction became more difficult and yields of *N*-(benzyl)-2,4-dimethylaniline (**5aa**) 69-77% only could be obtained with benzyl alcohol as respective partners after 20 h (Table 5, entries 1-5). 2,4-Dimethylaniline reacted also with 4-methoxybenzyl alcohol to give the *N*-(4-methoxybenzyl)-2,4-dimethylaniline (**5ab**) in 73-80% yields (Table 5, entries 6-10). The results obtained show that the steric hindrance in the *ortho*-position of the aniline substrate partially inhibits the reaction.

With ruthenium catalysts, only a few examples of alkylation of 2-aminopyridine with alcohols have been recently reported with ruthenium complexes featuring tridentate (C,N,N) ligand [35], and cationic ruthenium(arene) complex equipped with a chelating pyridine-carbene ligand [36]. In the presence of our optimized catalytic systembased on **2a**-**2e** catalysts, the primary heteroaromatic 2-aminopyridine reacted readily with various alcohols to selectively give the *N*-mono-alkylated secondary amines (**6a**), (Table 6). Benzyl alcohol and *p*-isopropylbenzyl alcohol gave excellent yields of *N*-alkylated 2-aminopyridines (**6aa** and **6ab**) (Table 6, entries 1-10). Alkylation with the purely aliphatic alcohol derivative 1-hexanol was also possible in satisfactory yield (**6ac**) (Table 6, entries 11-15). When Table 6 is examined, it is observed that alcohols with aromatic rings give higher yields of *N*-alkylated product than 1-hexanol. Only the amine products (**6a**) were observed in all reactions.

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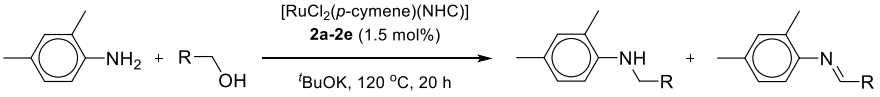
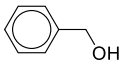
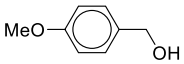
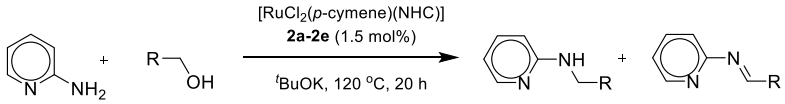
Table 5. Ruthenium-catalyzed *N*-alkylation of 2,4-dimethylaniline with alcohols.[a]

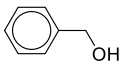
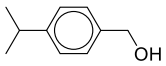
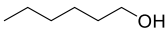


Entry	Ru-complex	Alcohols	Yield[b] [%]	Selectivity[c] [%]	
				5a	**5b**
1	**2a**		77	86	14
2	**2b**		73	84	16
3	**2c**		70	89	11
4	**2d**		71	85	15
5	**2e**		69	83	17
6	**2a**		80	95	5
7	**2b**		78	93	7
8	**2c**		79	90	10
9	**2d**		75	91	9
10	**2e**		73	90	10

[a] Reaction conditions: [Ru] (**2a-2e**) (0.015 mmol, 1.5 mol%), 2,4-dimethylaniline (1.0 mmol), alcohol (1.5 mmol), ^{t}BuOK (1.5 mmol), 120 °C, 20 h.
[b] Yields (%) were calculated according to 2,4-dimethylaniline by GC-MS analysis using dodecane as an internal standard.
[c] Selectivities (%) of **5a** and **5b** were calculated by GC and GC-MS analysis.

Table 6. Ruthenium-catalyzed *N*-alkylation of 2-aminopyridine with alcohols.[a]



Entry	Ru-complex	Alcohols	Yield[b] [%]	Selectivity[c] [%]	
				6a	**6b**
1	**2a**		96	100	-
2	**2b**		91	100	-
3	**2c**		90	100	-
4	**2d**		85	100	-
5	**2e**		88	100	-
6	**2a**		92	100	-
7	**2b**		90	100	-
8	**2c**		87	100	-
9	**2d**		84	100	-
10	**2e**		85	100	-
11	**2a**		82	100	-
12	**2b**		79	100	-
13	**2c**		75	100	-
14	**2d**		70	100	-
15	**2e**		69	100	-

[a] Reaction conditions: [Ru] (**2a-2e**) (0.015 mmol, 1.5 mol%), 2-aminopyridine (1.0 mmol), alcohol (1.5 mmol), ^{t}BuOK (1.5 mmol), 120 °C, 20 h.
[b] Yields (%) were calculated according to 2-aminopyridine by GC-MS analysis using dodecane as an internal standard.
[c] Selectivities (%) of **6a** and **6b** were calculated by GC and GC-MS analysis.

The ruthenium complex [$RuCl_2$(*p*-cymene)(*N,N'*-bis(mesityl)imidazolylidene)] featuring aryl substituents directly connected to the nitrogen atoms of the carbene is known to catalyze the formation of amides from alcohols and primary aliphatic amines including aniline at a lower extend, in the presence of 15 mol% of ^{t}BuOK [37]. Recently, ruthenium complexes such as (*N,N*-bis(benzyl)benzimidazolylidene)- and (*N,N*-bis(isopropyl)benzimidazolylidene)-$RuCl_2$(*p*-cymene) equipped with *N*-alkyl or/and *N*-benzyl NHC ligands with no chelating or hemilabile group on the NHC have revealed good catalytic properties for the alkylation of anilines with various alcohols under neat conditions at 130 °C with 5 mol% catalyst loading without additional base [32]. The presence of the functionalized benzyl and alkyl group in our NHC precursors does not seem to be essential in terms of reactivity, but contributes to promote the formation of amines rather than imines or amides. This is very important in terms of selectivity. All these results show that the nature of the NHC ligand is crucial for the ruthenium-catalyzed selective alkylation of anilines by alcohols with hydrogen borrowing processes.

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However, at the moment, the most efficient catalytic systems for alkylation of aromatic amines operating under really mild conditions are based on iridium catalysts. They include reactions carried out in diglyme at 70 °C in the presence of ^{t}BuOK [38], a few examples at 50 °C in toluene/CH_2Cl_2 as solvent in the absence of an extra base [39], and even some scarce examples at room temperature in the presence of ^{t}BuOK under solvent-free conditions with 1 mol% catalyst loading [40].

Conclusions

In summary, we prepared a library of five new well-defined *N*-heterocyclic carbene based ruthenium(*p*-cymene) complexes. These complexes were characterized using different spectroscopic and analytical techniques. Ruthenium complexes were used as the efficient and selective catalysts in the synthesis of *N*-alkylaromatic amines using *N*-alkylation reaction between the aromatic amines and alcohol derivatives under solvent-free conditions and mild conditions. When the catalytic studies were evaluated, it was found that all of the ruthenium complexes were suitable for the *N*-alkylation reaction of aromatic amines with alcohols by borrowing hydrogen strategy. Since the ruthenium complexes are structurally similar, it is clear that, there is no significant difference between the complexes on the catalytic activity of *N*-alkylation of aromatic amines with alcohols, and the selectivity of the reaction strongly depends on the nature of the alcohols.

Experimental Section

General Methods: The synthesis of NHC precursors and their ruthenium complexes were carried out under argon using standard Schlenk line techniques. Melting points were measures in open capillary tubes with an Electrothermal-9200 melting points apparatus. FT-IR spectra were recorded on ATR unit in the range of 450-4000 cm^{-1} with a Perkin Elmer Spectrum 100 Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded using a Bruker Avance AMX and a Bruker Avance III spectrometer operating at 300, 400 and 500 MHz (^{1}H NMR) and at 75, 100 and 125 MHz (^{13}C NMR) in $CDCl_3$. The NMR studies were carried out in high-quality 5 mm NMR tubes. The chemical shifts (δ) are reported in ppm relative to $CDCl_3$. Coupling constants (J values) are given in hertz. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, pent = pentet, hext = hextet, m = multiplet. ^{1}H NMR spectra are referenced to residual protiated solvents (δ = 7.26 ppm for $CDCl_3$), ^{13}C chemical shifts are reported relative to deuterated solvents (δ = 77.16 ppm for $CDCl_3$). All catalytic reactions were monitored on an Agilent 6890N GC and a Schimadzu 2010 Plus GC-MS system by GC-FID with an HP-5 column of 30 m length, 0.32 mm diameter, and 0.25 μm film thickness.

General Procedure for the Preparation of Benzimidazolium Chlorides (1a-1e): *N*-(3-Methoxybenzyl)benzimidazole (1.0 g; 4.2 mmol) was dissolved in degassed DMF (3 mL) and alkyl chloride (4.2 mmol) was added at room temperature. The reaction mixture was stirred at 80 °C for 36 h under argon. After completion of the reaction, the solvent was removed by vacuum and diethyl ether (15 mL) was added to obtain a white crystalline solid, which was filtered off. The solid was washed with diethyl ether (3×10 mL) and dried under vacuum. The crude product was recrystallized from ethanol/diethyl ether mixture (1:3, *v/v*) at room temperature and, completely dried under vacuum. All benzimidazolium chlorides (**1a-1e**) were isolated as air- and moisture-stable white solids in accordance with the literature [28g,m].

General Procedure for the Preparation of Ruthenium-(arene)-NHC Complexes (2a-2e): For the preparation of ruthenium complexes, a solution of benzimidazolium chloride (1.0 mmol), Ag_2O (0.5 mmol) and activated 4 Å molecular sieves in anhydrous dichloromethane (10 mL) was stirred at room temperature for 24 h in the dark conditions. The reaction mixture was then filtered through Celite and the solvent was removed under reduced pressure. The prepared crude silver-NHC complex was reacted with $[RuCl_2(p\text{-cymene})]_2$ dimer (0.5 mmol) in anhydrous dichloromethane (10 mL), and the mixture was allowed to stirred for 24 h at room temperature. The solution was filtered through Celite and the solvent was removed under reduced vacuum to afford the product as a red-brown powder. The crude product was recrystallized from CH_2Cl_2/*n*-pentane (1:3, *v/v*).

Dichloro-[1-(3-methoxybenzyl)-3-(methyl)benzimidazole-2-ylidene] (*p*-cymene)ruthenium(II), (2a): (0.458 g, yield 82%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.25 (d, J = 6.9 Hz, 6H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.03 (s, 3H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.96 (h, J = 6.8 Hz, 1H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 3.75 (s, 3H, $CH_2C_6H_4(OCH_3)$-3); 4.27 (s, 3H, CH_3); 5.30 (s, 2H, $CH_2C_6H_4(OCH_3)$-3); 4.93, 5.09, 5.48 and 5.59 (m, 4H, arom. *CH*s, $CH_3C_6H_4(CH(CH_3)_2)$-4); 6.59-6.66, 6.80-6.82 and 7.06-7.39 (m, 8H, arom. *CH*s, NC_6H_4N and $CH_2C_6H_4(OCH_3)$-3). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ (ppm) = 18.7 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 22.3 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 30.7 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 36.9 (CH_3); 52.1 ($CH_2C_6H_4(OCH_3)$-3); 55.3 ($CH_2C_6H_4(OCH_3)$-3); 81.8, 83.4, 85.2, 87.1 (arom. *C*s of $CH_3C_6H_4(CH(CH_3)_2)$-4); 99.1, 109.5, 110.0, 111.2, 111.9, 112.4, 118.0, 123.1, 123.3, 130.0, 135.3, 135.9, 139.5, 160.0. (arom. *C*s, NC_6H_4N and $CH_2C_6H_4(OCH_3)$-3); Ru-$C_{carbene}$: 190.3.

Dichloro-[1-(3-methoxybenzyl)-3-(2-methoxyethyl)benzimidazole-2-ylidene](*p*-cymene)ruthenium(II), (2b): (0.452 g, yield 75%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.25 (d, J = 6.9 Hz, 6H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.01 (s, 3H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.92 (h, J = 7.0 Hz, 1H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 3.75 (s, 3H, $CH_2C_6H_4(OCH_3)$-3); 3.94 (t, 2H, J = 4.2 Hz, $CH_2CH_2OCH_3$); 5.13 (t, 2H, J = 4.3 Hz, $CH_2CH_2OCH_3$); 5.34 (s, 2H, $CH_2C_6H_4(OCH_3)$-3); 4.78, 5.10, 5.34 and 5.52 (m, 4H, arom. *CH*s, $CH_3C_6H_4(CH(CH_3)_2)$-4); 6.59-6.64, 6.81-6.82, 7.05-7.25 and 7.66-7.68 (m, 8H, arom. *CH*s, NC_6H_4N and $CH_2C_6H_4(OCH_3)$-3); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ (ppm) = 18.3 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 22.5 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 30.6 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 50.4 ($CH_2CH_2OCH_3$); 52.5 ($CH_2C_6H_4(OCH_3)$-3); 55.3 ($CH_2C_6H_4(OCH_3)$-3);

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58.9 ($CH_2CH_2OCH_3$); 72.0 ($CH_2CH_2OCH_3$); 83.4, 84.7, 85.3, 86.5 (arom. *C*s of $CH_3C_6H_4(CH(CH_3)_2)$-4); 98.1, 108.4, 111.3, 111.6, 111.7, 111.9, 112.4, 118.0, 123.1, 123.2, 130.0, 135.2, 135.5, 139.2, 139.3, 160.1 (arom. *C*s of NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3); Ru-$C_{carbene}$: 191.5.

Dichloro-[1-(3-methoxybenzyl)-3-(4-phenoxybutyl)benzimidazole-2-ylidene](*p*-cymene)ruthenium(II), (2c): (0.540 g, yield 78%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.16 (d, J = 6.9 Hz, 6H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 1.59-2.29 (m, 4H, $CH_2CH_2CH_2CH_2OC_6H_5$ and $CH_2CH_2CH_2CH_2OC_6H_5$); 1.92 (s, 3H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.84 (h, J = 7.0 Hz, 1H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 3.68 (s, 3H, $CH_2C_6H_4(OCH_3)$-3); 3.94 (m, 2H, $CH_2CH_2CH_2CH_2OC_6H_5$); 4.92 (m, 2H, $CH_2CH_2CH_2CH_2OC_6H_5$); 5.22-5.33 (m, 2H, $CH_2C_6H_4(OCH_3)$-3); 4.11, 4.44, 5.60 and 6.53 (m, 4H, arom. CH, $CH_3C_6H_4(CH(CH_3)_2)$-4); 6.88 and 7.44 (d, J = 8.0 Hz, 4H, arom. CH, $CH_2CH_2CH_2CH_2OC_6H_5$); 7.07 (t, J = 7.7 Hz, 1H, arom. CH, $CH_2CH_2CH_2CH_2OC_6H_5$); 6.80 (s, 1H, arom. CH, $CH_2C_6H_4(OCH_3)$-3); 6.72-6.74, 6.98-7.00 and 7.15-7.24 (m 7H, arom. CH, NC_6H_4N and $CH_2C_6H_4(OCH_3)$-3). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ (ppm) = 17.6 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 22.4 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 25.6 ($CH_2CH_2CH_2CH_2OC_6H_5$); 26.3 ($CH_2CH_2CH_2CH_2OC_6H_5$); 29.6 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 48.9 ($CH_2CH_2CH_2CH_2OC_6H_5$); 51.4 ($CH_2C_6H_4(OCH_3)$-3); 54.3 ($CH_2C_6H_4(OCH_3)$-3); 66.3 ($CH_2CH_2CH_2CH_2OC_6H_5$); 81.1, 82.8, 84.8, 86.2 (arom. *C*s of $CH_3C_6H_4(CH(CH_3)_2)$-4); 98.1, 107.7, 109.9, 110.6, 111.0, 111.5, 113.5, 117.1, 119.7, 122.0, 122.1, 128.5, 128.9, 134.0, 134.8, 138.3, 157.9, 159.0 (arom. *C*s of NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3 and $CH_2CH_2CH_2CH_2OC_6H_5$); Ru-$C_{carbene}$: 188.9.

Dichloro-[1-(3-methoxybenzyl)-3-(4-tert-butylbenzyl)benzimidazole-2-ylidene](*p*-cymene)ruthenium(II), (2d): (0.449 g, yield 65%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.16 (d, J = 7.0 Hz, 6H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 1.31 (s, 9H, $CH_2C_6H_4(C(CH_3)_3)$-4); 1.89 (s, 3H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.67 (h, J = 6.8 Hz, 1H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 3.79 (s, 3H, $CH_2C_6H_4(OCH_3)$-3); 5.09-5.12 and 5.33-5.38 (m, 4H, arom. CHs, $CH_3C_6H_4(CH(CH_3)_2)$-4); 5.70-5.75 (m, 2H, $CH_2C_6H_4(OCH_3)$-3); 6.60-6.64 (m, 2H, $CH_2C_6H_4(C(CH_3)_3)$-4); 6.66-6.71, 6.82-6.84 and 7.01-7.37 (m, 12H, arom. CHs, NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3 and $CH_2C_6H_4(C(CH_3)_3)$-4). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ (ppm) = 18.2 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 22.6 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 30.5 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 31.3 ($CH_2C_6H_4(C(CH_3)_3)$-4); 34.5 ($CH_2C_6H_4(C(CH_3)_3)$-4); 52.5 $CH_2C_6H_4(C(CH_3)_3)$-4); 52.9 ($CH_2C_6H_4(OCH_3)$-3); 55.3 ($CH_2C_6H_4(OCH_3)$-3); 84.5, 85.1, 85.2, 85.6 (arom. *C*s of $CH_3C_6H_4(CH(CH_3)_2)$-4); 97.0, 107.6, 111.6, 111.7, 111.8, 112.7, 118.0, 123.1, 125.5, 125.8, 130.1, 134.4, 135.5, 135.6, 139.2, 150.5, 160.1 (arom. *C*s of NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3 and $CH_2C_6H_4(C(CH_3)_3)$-4); Ru-$C_{carbene}$: 191.5.

Dichloro-[1-(3-methoxybenzyl)-3-(2,3,4,5,6-pentamethylbenzyl)benz-imidazole-2-ylidene](*p*-cymene)ruthenium (II), (2e): (0.380 g, yield 54%); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ (ppm) = 1.21 (d, J = 4.8 Hz, 6H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.01 (s, 3H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 2.17 and 2.24 (s, 15H, $CH_2C_6(CH_3)_5$-2,3,4,5,6); 2.83 (h, J = 6.9 Hz, 1H, $CH_3C_6H_4(CH(CH_3)_2)$-4); 3.69 (s, 3H, $CH_2C_6H_4(OCH_3)$-3); 5.23 (s, 2H, $CH_2C_6H_4(OCH_3)$-3); 5.43 (s, 2H, $CH_2C_6(CH_3)_5$-2,3,4,5,6); 5.51-6.56 (m, 4H, arom. CH, $CH_3C_6H_4(CH(CH_3)_2)$-4); 6.68-7.19 (m, 8H, arom. CH, NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ (ppm) = 14.1, 17.3 and 18.5 ($CH_2C_6(CH_3)_5$-2,3,4,5,6); 22.4 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 22.7 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 31,0 ($CH_3C_6H_4(CH(CH_3)_2)$-4); 52.6 ($CH_2C_6(CH_3)_5$-2,3,4,5,6); 53.0 ($CH_2C_6H_4(OCH_3)$-3); 55.3 ($CH_2C_6H_4(OCH_3)$-3); 84.6, 85.1, 85.5, 86.6 (arom. *C*s of $CH_3C_6H_4(CH(CH_3)_2)$-4); 96.2, 107.4, 111.1, 111.7, 112.0, 112.5, 112.8, 122.4, 122.6, 129.3, 130.0, 135.4, 135.5, 135.6, 139.5, 160.2 (arom. *C*s of NC_6H_4N, $CH_2C_6H_4(OCH_3)$-3 and $CH_2C_6(CH_3)_5$-2,3,4,5,6); Ru-$C_{carbene}$: 190.3.

General Procedure for the *N*-Alkylation of Aromatic Amines with Alcohols: Aromatic amine derivative (1.0 mmol), alcohol derivative (1.5 mmol), ^{t}BuOK (1.5 mmol), ruthenium complex (**2a-2e**) (0.015 mmol, 1.5 mol%) were added to a 10 mL Schlenk tube under argon atmosphere. The mixture was stirred at 120 °C for 20 h. The reaction was cooled room temperature and filtered through a short pad of SiO_2. CH_2Cl_2 (2 mL) was then added to the crude mixture. This solution was used for GC and GC-MS analysis, and the resulting *N*-alkylated amines were purified and isolated by column chromatography (eluent: $CHCl_3$/MeOH). Yields (%) were calculated according to aromatic amine derivative using dodecane as an internal standard. The chemical characterizations of the catalytic products were made by NMR spectroscopy.

The catalytic products *N*-benzylaniline (**3aa**) [32c, 18p,v], *N*-(*p*-isopropylbenzyl)aniline (**3ab**) [32c, 18y], *N*-(4methoxybenzyl)aniline (**3ac**) [32c, 18v], *N*-(3,7-dimethyloct-6-en-1-yl)aniline (**3ad**) [32c, 24c], *N*-(benzyl)-*p*-methylaniline (**4aa**) [32c, 18v], *N*-(*p*-isopropylbenzyl)-*p*-methylaniline (**4ab**) [32c, 18z], *N*-(3,7-dimethyloct-6-en-1-yl)-*p*-methylaniline (**4ac**) [32c], *N*-(benzyl)-2,4-dimethylaniline (**5aa**) [32c], *N*-(4-methoxybenzyl)-2,4-dimethylaniline (**5ab**) [32c], *N*-(benzyl)-2-aminopyridine (**6aa**) [32c, 18v], *N*-(*p*-isopropylbenzyl)-2-aminopyridine (**6ab**) [32c] and *N*-(hexan-1-yl)-2-aminopyridine (**6ac**) [32c] are known in the literature. For the ^{1}H NMR and ^{13}C NMR spectrums of the all catalytic products see SI, pp. S21-S32.

Supporting Information (see footnote on the first page of this article): Full ^{1}H NMR, ^{13}C NMR and FT-IR spectra for the benzimidazolium chlorides (**1a-1e**), ruthenium-(arene)-NHC complexes (**2a-2e**) and all catalytic products (**3a-6a**).

Keywords: *N*-Heterocyclic carbene • ruthenium catalyst • aromatic amines • *N*-alkylation • borrowing hydrogen strategy

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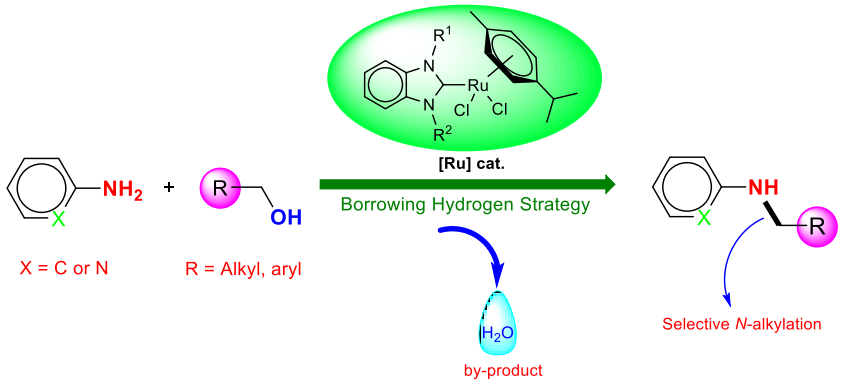

Five new ruthenium(II) complexes with the general molecular formula [$RuCl_2$(NHC)(η^6-*p*-cymene)], (NHC = *N*-heterocyclic carbene) were synthesized. The obtained complexes were fully characterized by ^{1}H NMR, ^{13}C NMR and FT-IR spectroscopy techniques. The catalytic activity of the all ruthenium complexes have been evaluated in the *N*-alkylation of anilines with alcohol derivatives using the borrowing hydrogen strategy.

Ruthenium(II)-(arene)-*N*-Heterocyclic Carbene Complexes: Efficient and Selective Catalysts for the *N*-Alkylation of Anilines with Alcohols

*N. Kaloğlu, M. Achard, C. Bruneau, İ. Özdemir**

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Ruthenium(II)-(arene)-*N*-Heterocyclic Carbene Complexes for the *N*-Alkylation of Anilines with Alcohol Derivatives Using the Borrowing Hydrogen strategy

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