



UNIVERSITÀ  
DEGLI STUDI  
DI UDINE

Università degli studi di Udine

Mild N-Alkylation of Amines with Alcohols Catalyzed by the Acetate  
Ru(OAc)<sub>2</sub>(CO)(DiPPF) Complex

*Original*

*Availability:*

This version is available <http://hdl.handle.net/11390/1121051> since 2017-11-20T16:03:43Z

*Publisher:*

*Published*

DOI:10.1002/chem.201702996

*Terms of use:*

The institutional repository of the University of Udine (<http://air.uniud.it>) is provided by ARIC services. The aim is to enable open access to all the world.

*Publisher copyright*

(Article begins on next page)

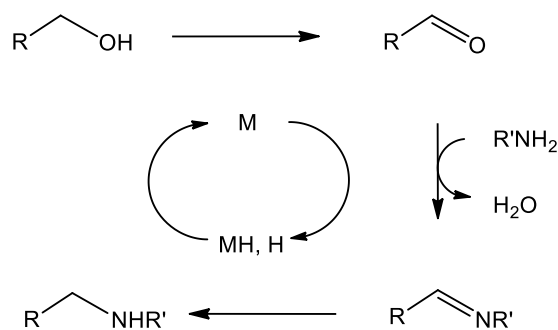
# Mild *N*-Alkylation of Amines with Alcohols Catalyzed by the Acetate Ru(OAc)<sub>2</sub>(CO)(DiPPF) Complex

Rosario Figliolia,<sup>[a]</sup> Salvatore Baldino,<sup>[a]</sup> Hans Günter Nedden,<sup>[b]</sup> Antonio Zanolli-Gerosa,<sup>[b]</sup> and Walter Baratta\*<sup>[a]</sup>

**Abstract:** The acetate complex Ru(OAc)<sub>2</sub>(DiPPF) (**2**) obtained from Ru(OAc)<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> (**1**) and 1,1'-bis(diisopropylphosphino)ferrocene (DiPPF) reacts cleanly with formaldehyde affording Ru(OAc)<sub>2</sub>(CO)(DiPPF) (**3**) in high yield. The monocarbonyl complex **3** (0.4-2 mol %) efficiently catalyzes the *N*-alkylation of primary and secondary alkyl and aromatic amines using primary alcohols ROH (R = Et, *n*Pr, *n*Bu, PhCH<sub>2</sub>) under mild reaction conditions (30 - 100 °C) with an alcohol / amine molar ratio of 10-100. Formation of the monohydride RuH(OAc)(CO)(DiPPF) (**4**) has been observed by reaction of **3** with *i*PrOH in the presence of NEt<sub>3</sub> at RT through an equilibrium reaction.

**Keywords:** *N*-alkylation • amines • alcohols • borrowing hydrogen • ruthenium

The selective formation of C-N bonds is a reaction of high relevance for the synthesis of amine and heterocycle compounds for fine and pharma chemicals.<sup>[1]</sup> As a matter of fact, the preparation of several drug molecules involves *N*-substitution transformations, which are usually performed by reaction of amines with alkylating agents or via reductive amination. In this context, the catalytic *N*-alkylation of amines using environmentally friendly alcohols as alkylating reagents and affording water as only byproduct, is an attractive atom-economic way for the C-N bond formation, widely studied in academia and of great interest for industrial applications.<sup>[2]</sup> It is generally accepted that this reaction may occur through a catalytic borrowing hydrogen approach, in which primary alcohols are dehydrogenated to carbonyl compounds which react with amines, affording imines that are hydrogenated to *N*-alkylated amines (Scheme 1).



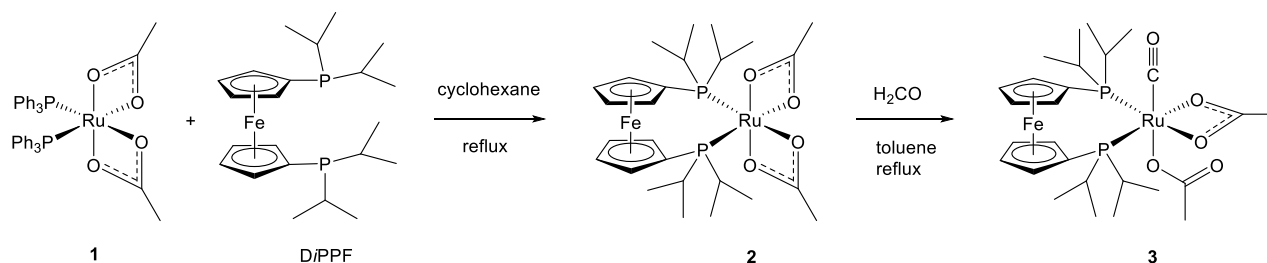
**Scheme 1.** *N*-alkylation of amines with alcohols via borrowing hydrogen

Main group metal hydroxides and alkoxides were found to catalyze the *N*-alkylation of amines with alcohols under harsh conditions, resulting in low yield and selectivity.<sup>[3]</sup> In the last decades, iridium and ruthenium have attracted a great deal of attention for *N*-alkylation via borrowing hydrogen.<sup>[2]</sup> Examples of ruthenium catalysts generated *in situ* entails the use of the precursors RuCl<sub>3</sub>·*n*H<sub>2</sub>O,<sup>[4]</sup> Ru<sub>3</sub>(CO)<sub>12</sub>,<sup>[5]</sup> [RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub>,<sup>[6]</sup> [Ru(COD)Cl<sub>2</sub>]<sub>*n*</sub>,<sup>[7]</sup> RuHCl(CO)(PPh<sub>3</sub>)<sub>3</sub>,<sup>[8]</sup> and RuH<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>3</sub>,<sup>[9]</sup> in combination with phosphanes, phosphates and nitrogen ligands. Conversely, well-defined catalysts are RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>3</sub>,<sup>[10]</sup> RuH<sub>2</sub>(PPh<sub>3</sub>)<sub>4</sub>,<sup>[11]</sup> RuCl(η<sup>5</sup>-C<sub>5</sub>H<sub>5</sub>)(PPh<sub>3</sub>)<sub>2</sub>,<sup>[12]</sup> [RuCl(*p*-cymene)(phosphinooxazoline)]Cl,<sup>[13]</sup> RuHCl(CO)(PNY) (Y = N, P)<sup>[14]</sup> and RuCl(CNN)(dppb).<sup>[15]</sup> *N*-alkylation is generally performed at high temperature (typically 120 or 180 °C), primary alcohols are generally more reactive than secondary and long reaction times are required. Therefore, the development of selective catalysts which can work at low temperature is of crucial importance for the application of this relevant sustainable transformation. Mono carbonyl Ru complexes, namely the Dobson catalyst Ru(OCOCF<sub>3</sub>)<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>2</sub>,<sup>[16]</sup> and [Ru(μ-OCOC<sub>2</sub>F<sub>4</sub>OCO)(CO)(PP)]<sub>2</sub>,<sup>[17]</sup> (PP = diphosphane), are active catalysts for alcohol dehydrogenation, which is the first step of the catalytic *N*-alkylation. Recently, the *in situ* generated complex Ru(OCOCF<sub>3</sub>)<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>2</sub> / (*R*)-BINAP has been found active in the asymmetric C-C coupling between olefin and primary alcohols.<sup>[18]</sup> It is worth pointing out that the coordination properties of carboxylate ligands, which display moderate stability with relatively high lability, are particularly attracting for catalytic reactions, but no examples of carboxylate Ru complexes have been reported in the *N*-alkylation reaction.

We describe here the straightforward preparation of the acetate complexes Ru(OAc)<sub>2</sub>(CO)<sub>*n*</sub>(DiPPF) (*n* = 0, 1), bearing the bulky ferrocene diphosphane DiPPF.<sup>[19]</sup> The monocarbonyl acetate complex has

been found highly active in the alkylation of primary and secondary amines with primary alcohols under mild reaction conditions. Evidence has been provided for the formation of the monohydride species  $\text{RuH}(\text{OAc})(\text{CO})(\text{DiPPF})$  in the alcohol / amine media.

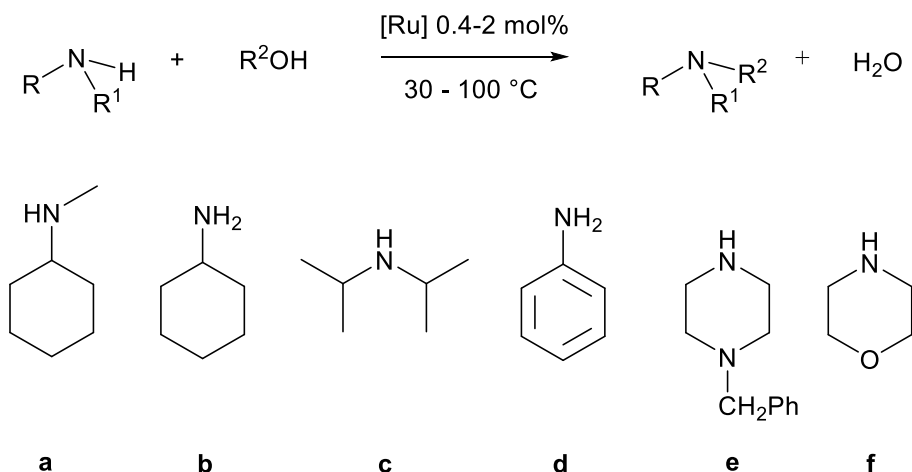
The ruthenium diphosphane compound  $\text{Ru}(\text{OAc})_2(\text{DiPPF})$  (**2**) was easily prepared by treatment of the acetate precursor  $\text{Ru}(\text{OAc})_2(\text{PPh}_3)_2$  (**1**) with one equivalent of DiPPF in cyclohexane at reflux (4 h, 87% yield) (Scheme 2).



**Scheme 2.** Synthesis of  $\text{Ru}(\text{OAc})_2(\text{DiPPF})$  (**2**) and  $\text{Ru}(\text{OAc})_2(\text{CO})(\text{DiPPF})$  (**3**).

The  $^1\text{H}$  and  $^{13}\text{C}\{^1\text{H}\}$  NMR spectra of **2** at RT show two signals for the ferrocene CH moieties, consistent with a rapid displacement of the Ru-O acetate bond *trans* to the P atom. Complex **2** reacts cleanly with formaldehyde (5 equiv) in toluene at reflux within 2 h, affording the monocarbonyl acetate complex **3** in 78 % yield. Alternatively, complex **3** can also be prepared by reaction of **2** with paraformaldehyde in toluene. At RT the  $^{31}\text{P}\{^1\text{H}\}$  NMR spectrum of **3** in  $\text{CD}_2\text{Cl}_2$  shows a broad singlet at  $\delta = 61.7$  ppm ( $\Delta\nu_{1/2} = 110$  Hz), while the  $^1\text{H}$  NMR spectrum exhibits four C-H signals for the ferrocene  $\text{C}_5\text{H}_4$  moiety and a singlet at  $\delta = 1.92$  ppm for the two acetate ligands, indicating an exchange of the  $\text{OAc}^-$  groups on the NMR time scale at RT. Upon cooling at  $-75^\circ\text{C}$  both the  $^{31}\text{P}$  and  $^1\text{H}$  NMR spectra become more complex, possibly due to the formation of conformers with the bulky isopropyl ferrocene ligand and the different coordination mode of the two acetates (see Supporting Information). The CO stretching of **3** is at relatively low wavelength ( $1939\text{ cm}^{-1}$ ), in agreement with the presence of the electron-rich diphosphane.

The carboxylates complexes **1-3** (1-2 mol %) were found active in the *N*-ethylation of *N*-methylcyclohexylamine (**a**) using commercially grade ethanol under mild reaction conditions (Scheme 3). With the diacetate derivative **1**, the tertiary amine  $\text{NMeEtCy}$  is formed in 25 % at  $78^\circ\text{C}$  (20 h), with a  $\text{EtOH}/\text{NHMeCy} = 100$  (entry 1, Table 1).



**Scheme 3.** *N*-alkylation of amines with alcohols catalyzed by **1-3**

**Table 1.** *N*-ethylation of methylcyclohexylamine (**a**) with EtOH catalyzed by ruthenium acetate complexes (1 mol %).

Entry	Complex	Ligand or additive (equiv)	EtOH/NHMeCy	T [°C]	Time [h]	Conv <sup>[a]</sup> [%]	Byproducts <sup>[a]</sup> [%]
1	<b>1</b>		100	78	30	25	3
2	<b>2</b>		10	65	15	80	
3	<b>2</b>	TFA (15)	10	65	15	96	1
4	Ru(OAc) <sub>2</sub> (DPPF)		100	78	16	6	< 1
5	Ru(OAc) <sub>2</sub> (CO)(PPh <sub>3</sub> ) <sub>2</sub>		10	78	29	0	0
6	Ru(OAc) <sub>2</sub> (CO)(PPh <sub>3</sub> ) <sub>2</sub>	DiPPF (1.5)	10	78	25	51	5
7	Ru(OAc) <sub>2</sub> (CO)(PPh <sub>3</sub> ) <sub>2</sub>	DPPF (1.5)	10	78	25	1	5
8	<b>3</b>		100	78	6	97	< 1
9	<b>3</b>		10	65	24	92	1
10	<b>3</b>	TFA (10)	10	65	6	98	< 1
11	<b>3</b> <sup>[b]</sup>		10	30	40	68	1
12	<b>3</b> <sup>[b]</sup>	TFA (10)	10	30	40	97	< 1
13	no catalyst		10	78	22	0	-

[a] The conversion was determined by GC analysis. [b] Catalyst loading 2 mol%.

By employment of **2** bearing DiPPF 80 % conversion was achieved in 15 h at 65 °C with a lower EtOH/NHMeCy = 10 (entry 2). Interestingly, an increase of rate is observed by addition of CF<sub>3</sub>COOH (TFA) (15 equiv, with respect to Ru) to **2**, affording 96 % of the ethylated amine (entry 3). The use of the corresponding DPPF<sup>[1919]</sup> complex Ru(OAc)<sub>2</sub>(DPPF) leads to poor conversion (6 %) (entry 4). The monocarbonyl derivative Ru(OAc)<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>2</sub> gives no conversion under these catalytic conditions

(entry 5). Addition of DiPPF (1.5 equiv) to the latter derivative affords 51% of NMeEtCy at 78 °C in 25 h, whereas with DPPF poor conversion is achieved (1 %), indicating that the more basic DiPPF leads to a more active catalytic species, with respect to DPPF (entries 6, 7). Employment of the isolated monocarbonyl DiPPF complex **3** results in 97 % conversion in 6 h at 78 °C, whereas at 65 °C 92 % of product is achieved in 24 h, with EtOH/NHMeCy = 100 and 10 respectively (entries 8, 9). The higher catalytic activity of **3** with respect to the in situ generated catalyst Ru(OAc)<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>2</sub> / DiPPF can be ascribed to the incomplete diphosphane substitution. Similar to **2**, addition of TFA (10 equiv) to **3** at 65 °C results in an acceleration effect, affording 98 % of product in 6 h (entry 10). Interestingly, by performing the reaction at 30 °C with **3** (2 mol %), 67 % of NMeEtCy is attained in 40 h (entry 11), whereas addition of TFA, resulted in 97% of product (entry 12), indicating that quantitative *N*-alkylation can be achieved *at low temperature*. An increase of rate by addition of acids has previously been reported for the RuH<sub>2</sub>(CO)(PPh<sub>3</sub>)<sub>3</sub> / xantophos system.<sup>[99]</sup> By carrying out the reaction without Ru catalysts no *N*-ethylation is observed after 22 h (entry 13). In addition, no formation of ethyl acetate was observed during the *N*-ethylation of **a** with **3**, suggesting that the in situ generated acetaldehyde undergoes a faster attack of the amine with respect to ethanol.

Complex **3** (0.4-1 mol%) shows catalytic activity for the *N*-alkylation of primary and secondary amines with primary alcohols (Scheme 3). Cyclohexylamine (**b**) reacts with EtOH affording quantitatively the tertiary amine NEt<sub>2</sub>Cy in 21 h at 78 °C (entry 1, Table 2), via the NHEtCy intermediate detected by GC analysis.

**Table 2.** *N*-alkylation of amines with alcohols catalyzed by **3** (1 mol %).

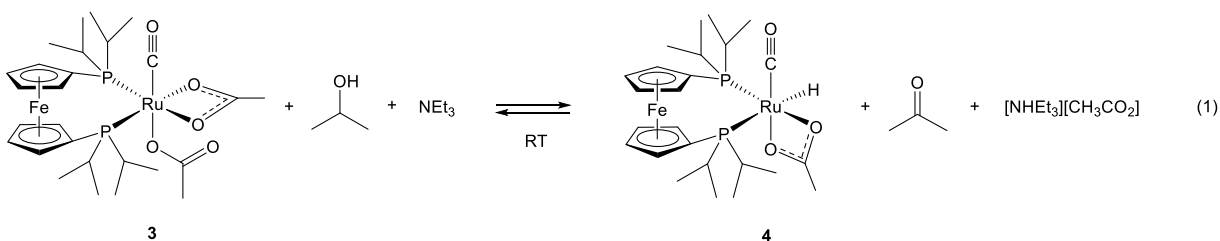
Entry	Amine	Alcohol	Alcohol/ Amine	T [°C]	Time [h]	Conv. <sup>[a]</sup> [%]	Byproducts <sup>[a]</sup> [%]
1	<b>b</b>	EtOH	100	78	21	96 <sup>[b]</sup>	3
2	<b>c</b>	EtOH	100	78	24	15	1
3	<b>d</b>	EtOH	10	65	24	70 <sup>[b]</sup>	2
4	<b>e</b>	EtOH	10	65	5	100	-
5	<b>f</b>	EtOH	10	65	6.5	100	-
6	<b>a</b>	MeOH	10	65	24	10	1
7	<b>a</b>	<i>n</i> PrOH	10	65	27	68	1
8	<b>a</b>	<i>n</i> BuOH	10	65	30	60	7
9	<b>a</b>	PhCH <sub>2</sub> OH	5	100	48	87	1
10	<b>a</b>	<i>i</i> PrOH	10	65	36	0	1
11	<b>e</b> <sup>[c]</sup>	EtOH	10	78	15	100	-

<sup>[a]</sup> The conversion was determined by GC analysis and assessed by <sup>1</sup>H NMR spectroscopy.

<sup>[b]</sup> Dialkylated product. <sup>[c]</sup> Catalyst loading 0.4 mol%.

The bulky amine  $\text{NH}i\text{Pr}_2$  (**c**) leads to  $\text{NE}ti\text{Pr}_2$  in poor conversion (15 %) (entry 2), whereas aniline (**d**) gives  $\text{NE}t_2\text{Ph}$  (70 %) at 65 °C after 24 h (entry 3). Conversely, *N*-benzylpiperazine (**e**) and morpholine (**f**) were quantitatively ethylated at 65 °C to the corresponding amines in 5 and 6.5 h, respectively (entries 4 and 5), indicating that more basic and less sterically hindered amines undergo faster alkylation with **3**. Experiments carried out with **a** and using different primary alcohols show that while with MeOH poor conversion (10 %) is attained at 65 °C (entry 6), *n*PrOH and *n*BuOH afforded the corresponding amines  $\text{NMeRCy}$  ( $\text{R} = \text{Pr}, \text{Bu}$ ) in 68 and 60 % yield in 27 and 30 h (entries 7 and 8). With benzyl alcohol  $\text{NMe}(\text{CH}_2\text{Ph})\text{Cy}$  is formed in 87 % yield at 100 °C after 48 h (entry 9), whereas the use of the secondary alcohol *i*PrOH gave no conversion at 65 °C (entry 10). Although the dehydrogenation step is thermodynamically easier for secondary alcohol compared to primary ones,<sup>[20]</sup> it is likely that the higher reactivity of the primary ones is due to easier formation or hydrogenation of the corresponding aldimines with respect to ketimines. To show the practical potential of catalyst **3**, the amine 1-benzyl-4-ethylpiperazine (1.87 g, 81%) was obtained from **e** (1.98 g) and ethanol (5.70 mL) using 30 mg of **3** (0.4 mol%) at 78 °C in 15 h (entry 11, see SI).

In the catalytic *N*-alkylation reaction the formation of a Ru hydride species is expected during the alcohol dehydrogenation (Scheme 1).<sup>[21]</sup> Complex **3** is soluble in alcohols (EtOH, *i*PrOH) affording a broad  $^{31}\text{P}$  NMR singlet rather similar to that observed for **3** in  $\text{CD}_2\text{Cl}_2$ . Interestingly, addition to **3** of the weakly coordinating  $\text{NEt}_3$  amine (20 equiv) at RT in 2-propanol leads quickly to the monohydride  $\text{RuH}(\text{OAc})(\text{CO})(\text{DiPPF})$  (**4**), which equilibrates with the dicarboxylate **3** (**4** / **3** = 1 / 9 molar ratio) (Eq. 1).



The  $^{31}\text{P}\{^1\text{H}\}$  NMR spectrum of **4** shows two doublets at  $\delta = 80.0$  and 24.6 ppm (external  $\text{CDCl}_3$  lock) with a small  $^2J(\text{P},\text{P})$  of about 7.7 Hz, the high field resonance being attributed to the P *trans* to the H, displaying a  $^2J(\text{H},\text{P})$  of 135 Hz (see SI). Complex **4** also forms by reacting **3** with dihydrogen (4 atm) in  $[\text{D}_8]\text{toluene}$  through an equilibrium reaction, affording in the  $^1\text{H}$  NMR spectrum a doublet of doublets at  $\delta = -5.98$  ppm for the Ru-H with  $^2J(\text{H},\text{P})$  of 31.3 and 133 Hz for the *cis* and *trans* P atoms, respectively,

likewise the RuH(CNN)(dppb) system.<sup>[22]</sup> It is worth pointing out that, while the dinuclear hydride complex [Ru( $\mu$ -H)(CO)(BINAP)]<sub>2</sub>(OCOC<sub>2</sub>F<sub>4</sub>OCO) has been described as resting state in the alcohol dehydrogenation,<sup>[17]</sup> the mononuclear species RuHX(CO)(PP) (X = Cl, carboxylate) have been postulated to play a key role in the catalytic cycles of alcohol dehydrogenation<sup>[17,17]</sup> and C-C coupling reactions.<sup>[23]</sup>

As regards the mechanism of the *N*-alkylation by **3**, it is likely that the monohydride **4** is formed by substitution of one acetate with the alkoxide, generated in the alcohol / amine media, followed by  $\beta$ -H-elimination. The resulting aldehyde reacts with the amine, affording the imine (and water) which gives insertion into the Ru-H bond. Protonation with alcohol leads to the alkylated amine and formation of the Ru-alkoxide which closes the cycle.

In summary, we have shown that the easily accessible carboxylate Ru(OAc)<sub>2</sub>(CO)(DiPPF), containing the bulky DiPPF diphosphane, displays high activity in the *N*-alkylation of amines with primary alcohols under mild reaction conditions. A monohydride species forms promptly at RT in alcohol in the presence of NEt<sub>3</sub> via an equilibrium reaction. Studies are undergoing to rationalize the acceleration effect of CF<sub>3</sub>COOH and give new insights on the mechanism of the *N*-alkylation reaction, as well as to extend this protocol for other C-X coupling reactions, including the use of chiral diphosphanes for asymmetric catalysis.

### Acknowledgments

We thank Dr. P. Martinuzzi (Università di Udine) for NMR assistance and Mr. P. Polese for carrying out the elemental analyses.

[a] Dr. R. Figliolia, Dr. S. Baldino, Prof. W. Baratta

Dipartimento DI4A, Università di Udine

Via Cotonificio 108, 33100 Udine, Italy

Fax: +39-0432-558803

E-mail: walter.baratta@uniud.it

[b] Dr. A. Zanotti-Gerosa, Dr. H. G. Nedden

Johnson Matthey Fine Chemicals Division

28 Cambridge Science Park, Milton Road

Cambridge, CB4 0FP, United Kingdom



- [1] a) S. A. Lawrence, *Amines: Synthesis, Properties and Applications*, Cambridge University Press 2004; b) J. S. Carey, D. Laffan, C. Thomson, M. T. Williams, *Org. Biomol. Chem.* **2006**, 4, 2337.
- [2] a) X. Ma, C. Su, Q. Xu, *Top. Curr. Chem. (Z)* **2016**, 374, 27; b) Q. Yang, Q. Wang, Z. Yu, *Chem. Soc. Rev.* **2015**, 44, 2305; c) J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland, R. Newton, *Org. Process Res. Dev.* **2015**, 19, 1400; d) C. Gunanathan, D. Milstein, *Science* **2013**, 341, 249; e) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, 110, 681; f) G. Guillena, D. J. Ramón, M. Yus, *Chem. Rev.* **2010**, 110, 1611.
- [3] a) J. U. Nef, *Liebigs Ann. Chem.* **1901**, 318, 137; b) W. A. Lazier, H. Adkins, *J. Am. Chem. Soc.* **1924**, 46, 741; c) Y. Sprinzak, *J. Am. Chem. Soc.* **1956**, 78, 3207.
- [4] a) K.-T. Huh, Y. Tsuji, M. Kobayashi, F. Okuda, Y. Watanabe, *Chem. Lett.* **1988**, 449; b) G. Bitsi, E. Schleiffer, F. Antoni, G. J. Jenner, *Organomet. Chem.* **1989**, 373, 343.
- [5] a) A. Tillack, D. Hollman, D. Michalik, M. Beller, *Tetrahedron Lett.* **2006**, 47, 8881; b) D. Hollman, A. Tillack, D. Michalik, R. Jackstell, M. Beller, *Chem. Asian J.* **2007**, 2, 403.
- [6] a) A. B. Enyong, B. Moasser, *J. Org. Chem.* **2014**, 79, 7553; b) M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson, J. M. J. Williams, *J. Am. Chem. Soc.* **2009**, 131, 1766; c) M. H. S. A. Hamid, J. M. J. Williams, *Tetrahedron Lett.* **2007**, 48, 8263; d) M. H. S. A. Hamid, J. M. J. Williams, *Chem. Commun.* **2007**, 725.
- [7] V. R. Jumde, L. Gonsalvi, A. Guerriero, M. Peruzzini, M. Tadde, *Eur. J. Org. Chem.* **2015**, 1829.
- [8] N. Nakagawa, E. J. Derrah, M. Schelwies, F. Rominger, O. Trapp, T. Schaub, *Dalton Trans.* **2016**, 45, 6856.
- [9] A. J. Blacker, M. M. Farah, M. I. Hall, S. P. Marsden, O. Saidi, J. M. J. Williams, *Org. Lett.* **2009**, 11, 2039.
- [10] a) Y. Watanabe, Y. Tsuji, Y. Ohsugi, *Tetrahedron Lett.* **1981**, 22, 2667; b) Y. Watanabe, Y. Tsuji, H. Ige, Y. Ohsugi, T. J. Ohta, *Org. Chem.* **1984**, 49, 3359; c) A. Arcelli, B.-T. Khai, G. Porzi, *J. Organomet. Chem.* **1982**, 235, 93; d) S. Ganguly, F. L. Joslin, D. M. Roundhill, *Inorg. Chem.* **1989**, 28, 4562; e) J. A. J. Marsella, *Org. Chem.* **1987**, 52, 467.
- [11] a) S.-I. Murahashi, K. Kondo, T. Hakata, *Tetrahedron Lett.* **1982**, 23, 229; b) C. S. Cho, J. H. Kim, T.-J. Kim, S. C. Shim, *Tetrahedron* **2001**, 57, 3321.
- [12] A. Del Zotto, W. Baratta, M. Sandri, G. Verardo, P. Rigo, *Eur. J. Inorg. Chem.* **2004**, 524.
- [13] K. O. Marichev, J. M. Takacs *JACS Catal.* **2016**, 6, 2205.

- 
- [14] a) E. Balaraman, D. Srimani, Y. Diskin-Posner, D. Milstein, *Catal. Lett.* **2015**, *145*, 139; b) B. Gnanaprakasam, E. Balaraman, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2011**, *50*, 12240; c) B. Gnanaprakasam, D. Milstein, *Angew. Chem. Int. Ed.* **2008**, *47*, 8661.
- [15] S. Agrawal, M. Lenormand, B. Martin-Matute, *Org. Lett.* **2012**, *14*, 1456.
- [16] a) A. Dobson, S. D. Robinson, *Inorg. Chem.* **1977**, *16*, 137; b) C. J. Creswell, A. Dobson, D. S. Moore, S. D. Robinson, *Inorg. Chem.* **1979**, *18*, 2055.
- [17] J. van Buijtenen, J. Meuldijk, J. A. J. M. Vekemans, L. A. Hulshof, H. Koojiman, A. L. Spek, *Organometallics* **2006**, *25*, 873.
- [18] K. D. Nguyen, D. Herkommer, M. J. Krische, *J. Am. Chem. Soc.* **2016**, *138*, 5238.
- [19] DiPPF = 1,1'-bis(diisopropylphosphino)ferrocene; DPPF = 1,1'-bis(diphenylphosphino)ferrocene.
- [20] H. Adkins, R. M. Eloffson, A. G. Rossow, C. C. Robinson, *J. Am. Chem. Soc.* **1949**, *71*, 3622.
- [21] a) S. E. Clapham, A. Hadzovic, R. H. Morris, *Coord. Chem. Rev.* **2004**, *248*, 2201; b) P. Espinet, A. C. Albéniz *Fundamentals of Molecular Catalysis, Current Methods in Inorganic Chemistry*, Vol. 3 (Eds. H. Kurosawa, A. Yamamoto) Elsevier: Amsterdam, 2003, Chap. 6, p 328.
- [22] a) W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando, P. Rigo, *Angew. Chem. Int. Ed.* **2005**, *44*, 6214; b) W. Baratta, S. Baldino, M. J. Calhorda, P. J. Costa, G. Esposito, E. Herdtweck, S. Magnolia, C. Mealli, A. Messaoudi, S. A. Mason, L. F. Veiros, *Chem. Eur. J.* **2014**, *20*, 13603.
- [23] S. Oda, J. Franke, M. J. Krische, *Chem. Sci.* **2016**, *7*, 136.

---

*Graphical abstract*

**Mild N-Alkylation of Amines with Alcohols Catalyzed by the Acetate  $\text{Ru}(\text{OAc})_2(\text{CO})(\text{DiPPF})$  Complex**

Rosario Figliolia, Salvatore Baldino, Hans Günter Nedden, Antonio Zanotti-Gerosa, and Walter Baratta

The novel complex  $\text{Ru}(\text{OAc})_2(\text{CO})(\text{DiPPF})$  easily prepared by carbonylation of  $\text{Ru}(\text{OAc})_2(\text{DiPPF})$  with  $\text{H}_2\text{CO}$  efficiently catalyzes the alkylation of primary and secondary amines with alcohols under mild reaction conditions. Evidence of the formation of the monohydride  $\text{RuH}(\text{OAc})(\text{CO})(\text{DiPPF})$  species is provided.

