

Chelation-assisted alkylation of benzylamine derivatives by Ru⁰ catalyst

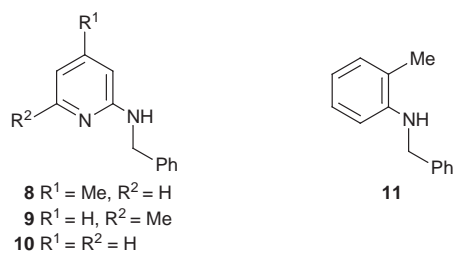
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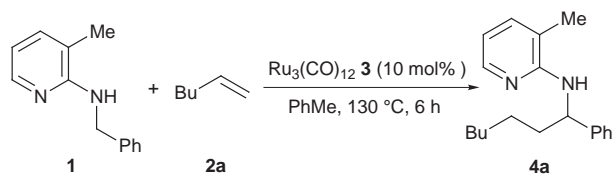
N-Benzyl-*N*-(3-methyl-2-pyridyl)amine **1** reacts with various alkenes via sp³ C–H bond cleavage by catalytic Ru₃(CO)₁₂ to give the corresponding alkylated products.

C–H bond activation is currently of interest in organometallic chemistry.¹ In particular, its application to organic synthesis has been under intensive development in recent years.² One useful method by which to achieve C–H bond activation by transition metal complexes is cyclometallation utilizing nearby heteroatoms.³ Stoichiometric cleavage of a C–H bond of a methyl group through cyclopalladation has been applied to functionalization of organic molecules.⁴ Vinyl,⁵ imine,⁶ aldehyde⁷ and aromatic groups⁸ were catalytically alkylated through chelation-assisted C–H bond cleavage by a transition metal catalyst and subsequent cross coupling with an alkene. Many chelation-assisted alkylations are centered on the sp² C–H bond, and not on the sp³ C–H bond, probably due to the better thermodynamic stability of the metal–sp² carbon bond compared to that of the metal–sp³ carbon bond.⁹ Here we report the catalytic addition of a benzylic sp³ C–H bond to an alkene to give alkylated products.

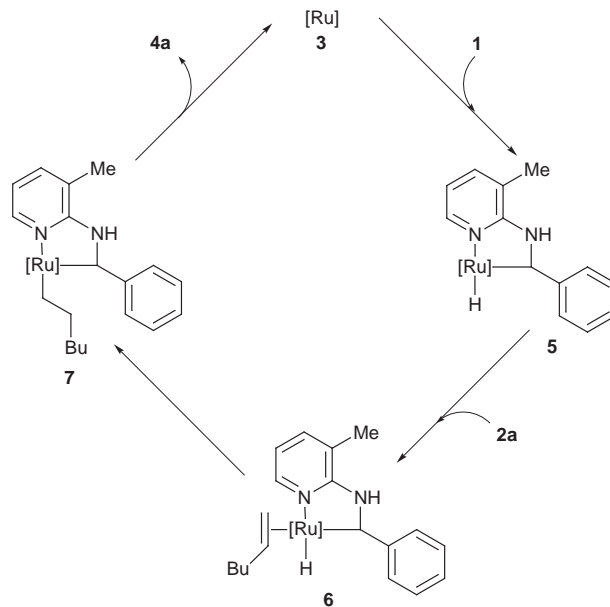
N-Benzyl-*N*-(3-methyl-2-pyridyl)amine **1** reacted with 500 mol% of hex-1-ene **2a** in toluene at 130 °C for 6 h under 10 mol% of Ru₃(CO)₁₂ **3** based on **1**. After the reaction, the corresponding alkylated product **4a** was isolated in 95% yield by column chromatography (Scheme 1). The reaction mechanism is shown in Scheme 2. The first step is likely to be the oxidative addition of a Ru⁰ catalyst to the benzylic C–H bond in **1** to generate **5**, a stable 5-membered ring metallacycle complex. The coordination of **2a** to **5**, hydride-insertion into **2a** and the subsequent reductive elimination of the resulting metal–hexyl complex **7** produces **4a** with the regeneration of catalyst **3**. Alkylations of various amine substrates with **2a** were carried out. In this reaction, it was found that the geometrical structure of **1**, in which the methyl group is placed in the 3-position of the pyridyl group, is prerequisite. When **8–10**, in which the methyl



group is either placed in the 4- or 6-position or is replaced by hydrogen, trace amounts of alkylated products were obtained under identical reaction conditions (1–2% GC yield). These

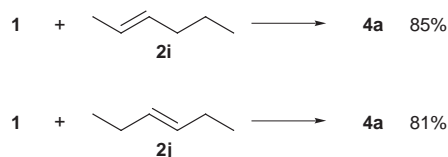


Scheme 1

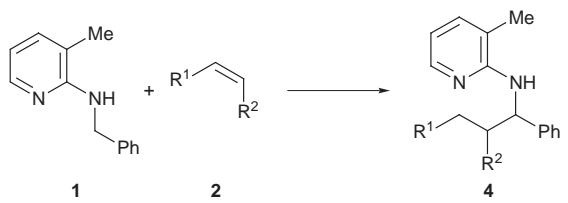


Scheme 2

results demonstrate that the 3-methyl group in **1** may retard the free rotation of the benzyl group around the amine group, and help the benzylic C–H bond to approach the Ru catalyst after the coordination of the nitrogen atom in the pyridyl group to the Ru catalyst. Also, precoordination of the metal complex is a very important requirement for cleaving the C–H bond since **11** bearing no coordination site gave no alkylated product and was fully recovered. The reactions between **1** and various alkenes were examined, and the results are shown in Table 1. For terminal olefins (entries 1–6), linear alkylated products were obtained. Sterically hindered alkenes such as **2c** and **2d** reacted with **1** to give the alkylated products **4c** and **4d** in a lower yield (72 and 75%) than unhindered alkenes such as **2a** and **2b**. Styrene **2e** was also formed in a low yield (70%) due to a side reaction, polymerization (entry 5). When internal olefins such as **2i** and **2j** were used, the linear alkylated product **4a** was isolated in 85 and 81% yield respectively (Scheme 3). No branched alkylated product was detected. The reason must be that the 2- or 3-hexyl–metal complex initially generated from hydride insertion into **2i** or **2j**, may isomerize to the 1-hexyl–metal complex due to the steric congestion of the secondary alkyl group. This type of isomerization has already been studied.¹⁰ However, for cyclic alkenes such as **2g** and **2h**, the corresponding cycloalkyl compounds, **4g** and **4h**, were isolated in 70 and 60% yield, respectively. To examine the effect of phenyl substituents, competitive alkylation between benzyl-



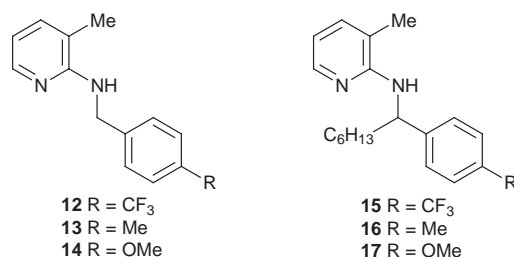
Scheme 3

Table 1 Alkylation of **1** with various alkenes **2^a** in the presence of **3**


Entry	Alkene	R ¹	R ²	Product	Isolated yield (%)
1	2a	Bu	H	4a	95
2	2b	C ₈ H ₁₇	H	4b	93
3	2c	Bu ^t	H	4c	72
4	2d	Cyclohexyl	H	4d	75
5	2e	Ph	H	4e	70
6	2f	Bn	H	4f	85
7	2g	-(CH ₂) ₃ -		4g	70
8	2h	-(CH ₂) ₄		4h	60

^a 500 mol% based on **1**.

amines bearing electron-donating and electron-withdrawing groups was carried out. When a mixture of **12** and **13** was



allowed to react with **2a** under 20 mol% of catalyst **3** at 130 °C for 1.2 h, 39 and 70% yield of **15** and **16** (**15** : **16** = 1 : 1.8) were determined by GC, indicating that the electron-donating group activates benzylic C–H bond cleavage better than the electron-withdrawing group. For the competitive reaction of **12** and **14** with **2a**, a mixture of **15** and **17** was obtained in 26 and 60% yield (**15** : **17** = 1 : 2.3). The higher ratio of 1 : 2.3 for **15** : **17** compared with that of 1 : 1.8 for **15** : **16** can be rationalised by a more electron-donating substituent such as the methoxy group

in **14** showing higher activity for C–H bond activation than the moderately electron-donating methyl group in **13**.

In conclusion, the sp³ C–H bond of benzylamine bearing the 3-methyl-2-pyridyl group was readily alkylated with various alkenes *via* cyclometallation by a Ru₃(CO)₁₂ catalyst.

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Notes and References

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