N–H activation *vs.* C–H activation: ruthenium-catalysed regioselective hydroamination of alkynes and hydroarylation of an alkene with *N*-methylaniline

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Phenylacetylene and its derivatives undergo regioselective insertion into the N–H bond of *N*-methylaniline in the presence of $Ru_3(CO)_{12}$ catalyst to afford *N*-methyl-*N*-(α-styryl)anilines in high yields, whereas styrene reacts with the *ortho* C–H bond of *N*-methylaniline giving 2-(1-phenylethyl)-*N*-methylaniline.

Transition metal complex-catalysed hydroamination of carbon–carbon double or triple bonds with non-tertiary amines is an attractive method for carbon–nitrogen bond formation. Indeed, various *intramolecular* hydroamination reactions of aminoalkenes and aminoalkynes have been reported to date.[1,2a] Although several examples of *intermolecular* reactions[2–5] have been also reported, the substrates for these reactions are usually limited to highly reactive or strained carbon unsaturated compounds.[4] We have found that ordinary alkynes undergo hydroamination with aromatic amines in the presence of a catalytic amount of $Ru_3(CO)_{12}$. This is the first example of ruthenium-catalysed *intermolecular* hydroamination. In addition, the same ruthenium complex catalyses regioselective hydroarylation reaction of an alkene with an aromatic amine *via ortho* C–H bond activation. We report here these ruthenium complex-catalysed reactions.

A mixture of phenylacetylene (**1a**, 0.25 mmol), *N*-methylaniline (**2a**, 2.5 mmol), and $Ru_3(CO)_{12}$ (0.0125 mmol Ru) was heated at 70 °C in a sealed glass tube under nitrogen. After 18 h, **1a** was completely consumed and *N*-methyl-*N*-(α-styryl)aniline (**3a**) was regioselectively formed in 85% GLC yield (based on the amount of **1a** charged) (Table 1, run 1). GLC and GC-MS analyses indicated that isomers of **3a** were less than 2% yield.† A similar result was obtained under milder conditions (50 °C, 3 d). In a separate four-fold scale reaction, **3a** was isolated in 61% yield by Kugelrohr distillation and was fully characterised by ^1H and ^{13}C NMR, IR and GC-MS analyses.‡

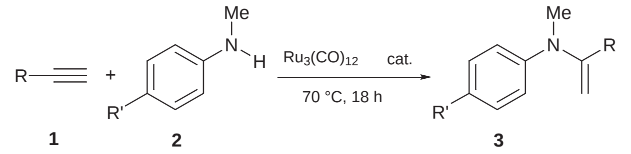
The catalytic activity of several transition metal complexes was also examined for the present reaction (**1a** : **2a** : catalyst = 1 : 10 : 0.05 mol ratio, 70 °C, 18 h). A ruthenium complex $[RuCl_2(CO)_3]_2$ was found to promote the reaction. However, the catalyst $Ru_3(CO)_{12}$ was more effective; 85% yield of **3a** with $Ru_3(CO)_{12}$, 69% with $[RuCl_2(CO)_3]_2$. In addition, the amine **2a** was more selectively transformed to **3a** with $Ru_3(CO)_{12}$ (96% selectivity based on the amount of **2a** consumed) than with $[RuCl_2(CO)_3]_2$ (74%). Other transition metal complexes such as $[RuCl_2(p\text{-cymene})]_2$, $RuCl_2(PPh_3)_3$, $[RuCl_2(cod)]_n$ $[CpRu(CO)_2]_2$, $Fe(CO)_5$, $Co_2(CO)_8$, $Co_4(CO)_{12}$, $PdCl_2(PPh_3)_2$ and Cp_2ZrMe_2 were ineffective. Thus, $Ru_3(CO)_{12}$ was the most effective among the complexes examined.

Table 1 summarises the results of the reactions of alkynes **1a**–**d** with *p*-substituted *N*-methylanilines **2a**,**b**. In all cases, the corresponding enamines **3a–e** were obtained in high yields. The results of *p*-substituted phenylacetylenes **1a**–**c** (runs 1–3) suggest that an electron-withdrawing substituent at the *para*-position increases the yield of **3**. The tendency was more clearly observed when the reactions were carried out under the retarded reaction conditions (**1** : **2a** = 1 : 1 mol/mol, in toluene, 70 °C, 18 h); the yields of products: **3c** (26%) > **3a** (13%) > **3b** (4%).§ A conjugated enyne, 1-ethynylcyclohexene (**1d**) also underwent hydroamination with **2a** to give enamine **3e** under similar conditions (run 5).

Surprisingly, when styrene (**4**) was used instead of alkynes, the reaction course was completely different. As shown in Scheme 1, the hydroarylation product, 2-(1-phenylethyl)-*N*-methylaniline (**5**), was selectively obtained in 83% yield after heating a mixture of **4** (0.25 mmol), **2a** (0.25 mmol), $Ru_3(CO)_{12}$ (0.0125 mmol Ru) and toluene (0.2 ml) at 150 °C for 19 h.‡ The hydroamination product was not detected at all. Treatment of the same mixture at 70–100 °C reaction temperature resulted in complete recovery of both starting materials **2a** and **4**. Previously a $[RhCl(PEt_3)_2]_2$–lithium amide system was reported to promote hydroarylation of norbornene with aniline.[4d] In this system, however, not only hydroarylation, but also hydroamination proceeded at the same time, and the combined yields for both reactions were not high. Therefore we believe that our present reaction is the first successful example of transition-metal complex-catalysed hydroarylation of an alkene with an aromatic amine.[6]

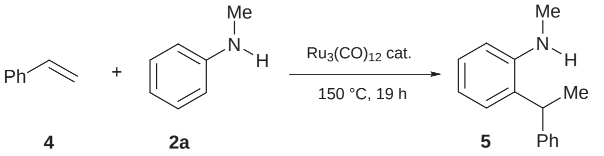
A plausible mechanism for hydroamination of alkyne is shown in Scheme 2, which involves (i) oxidative addition of the N–H bond of amine **2** to a coordinatively unsaturated ruthenium(0) centre giving the (amido)ruthenium hydride **6**,[7,8] (ii) coordination of alkyne **1** to the ruthenium centre to form complex **7**, followed by (iii) intramolecular nucleophilic attack of the nitrogen lone pair of **7** on the coordinated carbon–carbon triple bond,[4a,d] and (iv) reductive elimination of enamine **3** from the vinyl ruthenium species **8** to reproduce the coordinatively unsaturated ruthenium(0) centre.¶ The trend of the relative

Table 1 Hydroamination of alkynes catalysed by $Ru_3(CO)_{12}$[a]

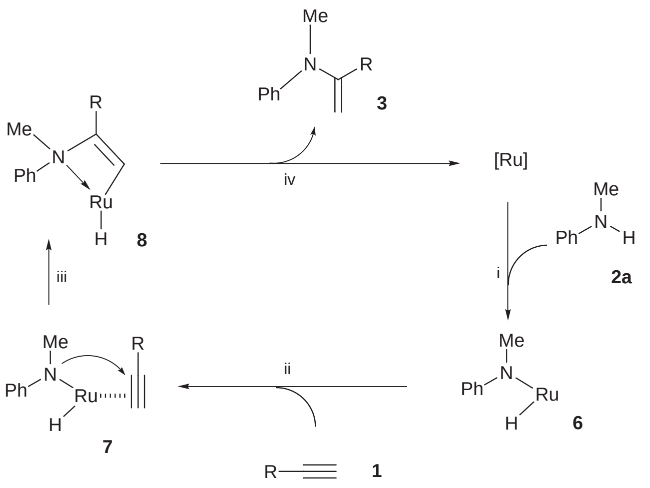


Run	1	R	2	R′	3	Yield (%)[b]
1	**1a**	Ph	**2a**	H	**3a**	85
2	**1b**	p-MeC_6H_4	**2a**	H	**3b**	78
3	**1c**	p-FC_6H_4	**2a**	H	**3c**	88
4	**1a**	Ph	**2b**	Me	**3d**	76
5	**1d**	Cyclohex-1-enyl	**2a**	H	**3e**	77

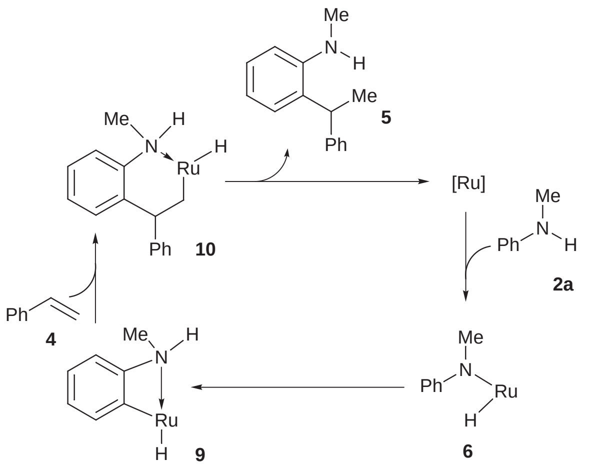
[a] **1** 0.25 mmol; **2** 2.5 mmol; $Ru_3(CO)_{12}$ 0.0125 mmol/Ru; 70 °C for 18 h. [b] GLC yields based on the charged amount of alkyne **1**.‡



Scheme 1



Scheme 2



Scheme 3

reactivities of *para*-substituted phenylacetylenes **1a**–**c** toward **2a** (*vide supra*) is consistent with step (iii). On the other hand, the striking difference in the reaction course for styrene (hydroarylation) may be explained by a mechanism depicted in Scheme 3. Probably because of the lower coordination ability of the carbon–carbon double bond to the metal centre,[8] the styrene analogue of complex **7** might not be produced from the (amido)ruthenium hydride complex **6**. Instead, if *ortho* C–H bond activation[9] takes place to form complex **9**, hydroarylation product **5** could be formed *via* a ring expansion reaction of the strained four-membered ruthenacycle **9** with styrene followed by reductive elimination from the resulting six-membered ruthenacycle **10**.

To summarize, we have found the first examples of ruthenium-complex catalysed regioselective hydroamination and hydroarylation of carbon–carbon multiple bonds with *N*-methylaniline. The reaction course depends on the structure of the unsaturated substrate. Studies on other substrates and the mechanism are in progress.

Notes and references

† Trimers of **1a**, such as 1,2,4-triphenylbenzene and 1,3,5-triphenylbenzene, were detected in 5 and 2% yields, respectively.

‡ All the products in this study were known and were identified by ^{1}H and ^{13}C NMR, IR and GC-MS analyses or by comparison with authentic samples. For synthesis of authentic samples of the enamines, see J. Barluenga, F. Aznar, R. Liz and R. Rodes, *J. Chem. Soc., Perkin Trans. 1,* 1980, 2732. For an authentic sample of 2-(1-phenylethyl)-*N*-methylaniline, see M. M. Aly, M. Z. Badr, A. M. Fahmy and S. A. Mahgoub, *Acta Chim. Hung.,* 1985, **120**, 15.

§ Recoveries of the starting materials are as follows; for the reaction of **1c** (**1c** 69%, **2a** 72%), for the reaction of **1a** (**1a** 85%, **2a** 86%), for the reaction of **1b** (**1b** 94%, **2a** 96%).

¶ Since activation of an N–H bond of aniline by $Ru_3(CO)_{12}$ was reported to take place under reaction conditions similar to those in the present reaction [see ref. 7(*a*)], we propose a mechanism with the (amido)ruthenium hydride **6** involved as an intermediate [step (i)]. However, because of the relatively high coordination ability of the carbon–carbon triple bond with the metal centre, we cannot completely exclude the possibility of another mechanism which includes alkyne coordination to the Ru metal centre followed by nucleophilic attack of an amine nitrogen at the activated carbon–carbon triple bond.

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