Ruthenium-Catalysed Murai-Type Couplings at Room Temperature

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In 1993 Murai et al. first reported the regioselective activation of C–H bonds and consecutive C–C bond formation in the *ortho*-position to aromatic keto or imine groups under control of ruthenium catalysts.[1] Since then the Murai reaction[2] and similar ruthenium-catalysed processes[3] have been extended to a wide variety of aromatic and olefinic substrates.

The currently established catalysts for this highly interesting C–C bond forming reaction are ruthenium complexes such as $[RuH_2(CO)(PPh_3)_3]$ **1**. Unfortunately, the application of these first-generation catalysts requires rather forcing conditions (i. e., reaction temperatures at or above 130 °C) to be most effective.

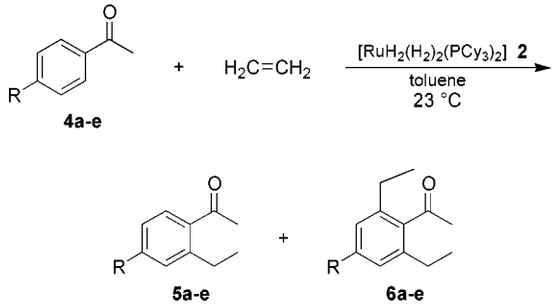
In 1998, Chaudret et al. first observed that the carbonyl-free complex $[RuH_2(H_2)_2(PCy_3)_2]$ **2**[4] containing two dihydrogen ligands is able to catalyse the Murai-type coupling between acetophenone and ethene even at room temperature.[5]

As part of our continuing studies towards the use of low-valent ruthenium complexes in C–H bond activation processes,[6] we have developed a practical method for room temperature Murai-reactions based on this pre-catalyst.[7] We have now extended this protocol to the one-pot generation of **2** in the reaction mixture. In both cases **2** is prepared via hydrogenation of commercially available [Ru(cod)(2-methylallyl)$_2$] **3** in the presence of PCy_3.[7,8] This approach allowed us to study the activity of **2** towards various substrates in detail and to investigate possible catalyst deactivation pathways.

Pre-catalyst **2** was generated from a suspension of **3** and 2 equivalents of PCy_3 in pentane by heating to 60 °C for 18 h in the presence of hydrogen in a pressure vessel. After cooling to room temperature the reactor was vented and a pentane solution of acetophenone **4 a** was added without intermediate purification or work-up. The reaction mixture was then pressurised with ethene and stirred at 23 °C for 24 h. Analysis of the resulting red solution by GC/MS revealed 54 ± 10% conversion of **4 a**. The 1 : 1 coupling product **5 a** was formed almost exclusively and only trace amounts of the 1 : 2-product **6 a** were detected.

If complex **2** was used in isolated and purified form under otherwise identical conditions, yields of **5 a** were in a similar range, but even larger variations were observed.[7] The significant deviation from the average yield may be at least partially associated with the poor solubility of **2** in saturated hydrocarbon solvents and the presence of a suspension during the initial state of reaction. Replacing pentane with toluene gave homogeneous solutions throughout the course of reaction and 63% conversion was obtained for the standard substrate **4 a**. Under these conditions, yields were reproducible within ±5% in two independent runs for all substrates **4 b–e**, respectively.

Table 1 summarises the results obtained with various *para*-substituted acetophenones **4 a–e** in the Murai-coupling with ethene at room temperature using isolated **2** as catalyst in toluene solution (Scheme 1).



Scheme 1.

All substrates gave good to excellent conversion to the alkylated products. The results indicate that the reactivity of the aryl ketones increases with the electron-withdrawing effect of the group R in the *para*-position to the keto group. In particular, the amount

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Table 1. Reactivity of substituted aromatic ketones **4a–e** towards ethene in the presence of **2**[a]

Substrate		Yields (%)[b]	
R	**4**	**5**	**6**
H	**a**	63	1
CH_3	**b**	76	1
OCH_3	**c**	82	2
Cl	**d**	89	7
CF_3	**e**	61	36

[a] **4**: 0.40 mmol, **2**: 0.04 mmol, C_2H_4: 1.0 g (30 bar), toluene: 5 mL, 23 °C.
[b] Determined by GC/MS analysis after 24 h.

of double substitution increased with the –I effect of R, reaching up to 36% in case of **4e** (R = CF_3).

The influence of R on the reactivity of the substrates observed with catalyst **2** is remarkably different to the one reported by Murai et al. for $[RuH_2(CO)(PPh_3)_3]$ **1** as catalyst using triethoxyvinylsilane as the olefinic substrate.[9,10] In the latter case, the reactivity followed the order OCH_3 > F > CF_3. These complementary reactivities may indicate that the rate-determining step of the catalytic cycle is different for the two catalytic systems.

In order to get further insight into the Murai-coupling with **2**, the course of the reactions of **4c–e** with ethene were investigated under slightly elevated temperatures (28 °C) using an online-GC/MS system.[11] The results of typical experiments are illustrated in Figure 1 and Figure 2. Conversion starts immediately with a relatively high initial rate but slows down continuously and reaches a plateau after about 250 min. The amount of double alkylation is small for **4c** (Figure 1) but can be studied in case of **4e** (Figure 2). Double alkylation occurs in a sequential manner. The mono-alkylated product **5e** is formed rapidly from **4e** under standard conditions and subsequently converted to **6e**.

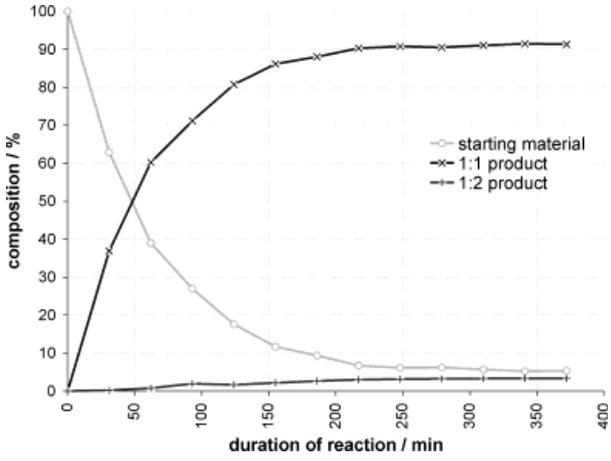

Figure 1. Conversion of **4c** (R = OCH_3) with ethene monitored by online-GC/MS. Conditions: **4c**: 0.40 mmol, **2**: 0.04 mmol, C_2H_4: 30 bar, toluene: 5 ml, 28 °C.

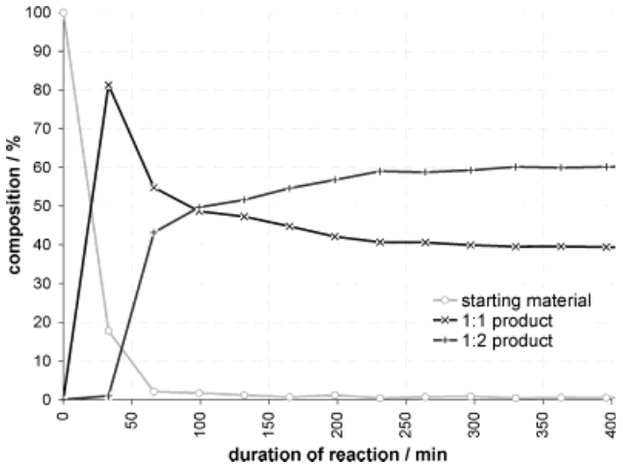

Figure 2. Conversion of **4e** (R = CF_3) with ethene monitored by online-GC/MS. Conditions: **4e**: 0.40 mmol, **2**: 0.04 mmol, C_2H_4: 30 bar, toluene: 5 mL, 28 °C.

Table 2. Maximum rates and catalyst lifetime from online-GC/MS monitoring

Substrate		v^0 [a]	t_{max} [b]
R	**4**	[mmol · min^{-1} · L^{-1}]	[min]
OCH_3	**c**	0.95	253
Cl	**d**	1.34	240
CF_3	**e**	1.94	237

[a] Initial rate of consumption of **4**.
[b] Time after which maximum conversion was first noticed, ± 15 min.

The initial rates reflect the order of reactivity CF_3 > Cl > OCH_3 already discussed earlier in a more quantitative fashion (Table 2). Most notably, the data also reveal that catalytic turnover ceases at around the same time in all experiments independent of the aromatic substrate. This indicates that a common catalyst deactivation pathway limits the conversion in all cases.

The deactivation of the catalyst was further substantiated by the observation that no conversion occurred when additional substrate **4c** was added after the reaction had ceased. In contrast, conversion of **5c** to **6c** started again when fresh catalyst was added to the reaction mixture.

Complex **2** is known to have only a limited stability in aromatic solvents,[4a] but ^{31}P NMR experiments demonstrated that the signal of **2** retains at least 60% of its initial strength after 330 minutes in toluene-d_8 solution. The complex $\{RuH(H_2)[o\text{-}C_6H_4\text{-}C(O)Me](PCy_3)_2\}$ **7**, which is presumably the key intermediate in the Murai-reaction of **4a** catalysed by **2**,[5] shows a similar lifetime. After 230 minutes the original signal at 48.6 ppm had decreased to 75% of its initial intensity with the concomitant formation of a new signal at 46.4 ppm. These experiments demonstrate that de-

composition of **2** or **7** is far too slow to account for the observed deactivation. Furthermore, no indication for formation of free PCy_3 was observed in these experiments. In contrast, ^{31}P NMR spectroscopic investigations of the reaction mixtures revealed the presence of large amounts of free PCy_3 after conversion had ceased. This indicates that ligand dissociation may play an important role in the deactivation process.

In summary, we have developed a practical method for Murai-type couplings at room temperature based on the formation of **2** from air-stable and readily available starting materials. The electronic effects of substrates on the reactivity of **2** were found to be remarkably different from that of classical Murai-catalysts. A substrate-independent deactivation pathway was identified as the major limitation of the catalyst lifetime under these conditions. Structural modification of Chaudret's catalyst seems highly promising to overcome these limitations for controlled alkylation of aromatic compounds.

Experimental Section

General Comments

All manipulations were carried out under an argon atmosphere unless otherwise noted. Experiments involving elevated pressures require appropriate safety precautions and must only be carried out with suitable equipment.

Analytical Techniques

NMR spectra were recorded on a Bruker AMX-300 operating at 121.5 MHz for the ^{31}P nucleus. Chemical shifts are given relative to H_3PO_4 as external standard. Gas chromatographic analyses were performed with a Hewlett-Packard 6890 GC using a 30 m RTX-5 capillary column and flame detector as well as a mass selective detection. Sample injection was carried out manually or with an online-sampling system.[11]

High-Pressure Equipment

Two stainless steel autoclaves of 10 mL and 100 mL volume, respectively, were employed as reactors. Both were equipped with two thick-walled glass windows, internal thermocouple, pressure gauge and a Teflon-coated magnetic stirring bar. The 100 mL autoclave additionally featured a capillary and a second valve in order to allow online-sampling during the reaction.

Materials

All solvents, starting materials and reagents were purified and deoxygenated according to standard procedures. $[RuH_2(H_2)_2(PCy_3)_2]$ **2** was synthesised by hydrogenation of $[Ru(cod)(2\text{-methylallyl})_2]$ **3** in the presence of PCy_3 using *n*-hexane as the reaction medium.[7]

One-Pot Generation of 2 and Consecutive Murai Reaction

In a representative experiment, **3** (0.045 mmol) and PCy_3 (0.090 mmol) were placed in a 10 mL autoclave and pentane (5 mL) was added. The suspension was pressurised with H_2 (10 bar) and heated to 60 °C for 18 h. After cooling to room temperature the reactor was vented and a pentane solution of acetophenone **4a** (0.40 mmol) and an internal standard (eicosane, 0.04 mmol) was added. The reaction mixture was pressurised with ethene (1.0 g, 30 bar) and stirred at 23±2 °C for 24 h. GC/MS analysis revealed the presence of **4a** (42%), **5a** (58%) and **6a** (trace amounts) as the only reaction products.

Murai Reaction Employing Isolated 2

$[RuH_2(H_2)_2(PCy_3)_2]$ **2** (0.04 mmol) was added to a solution of acetophenones **4a–e** (0.40 mmol) and an internal standard (eicosane, 0.04 mmol) in toluene (5 mL). After stirring for 30 minutes the resulting orange-red solution was transferred into the reactor, pressurised with ethene (1.0 g, 30 bar) and stirred at 23±2 °C for 24 h. The reaction mixture was analysed by GC/MS. Results are given in Table 1.

Online Reaction Monitoring

$[RuH_2(H_2)_2(PCy_3)_2]$ **2** (0.04 mmol) was added to a solution of acetophenones **4c–e** (0.40 mmol) and an internal standard (eicosane, 0.04 mmol) in toluene (5 mL). After stirring for 30 minutes the resulting orange-red solution was transferred into the reactor, pressurised with ethene (30 bar) and stirred at 28±2 °C for 10 hours. Samples were taken automatically from the solution for online-GC/MS analysis every 30 min.

Monitoring the Decomposition of the Catalyst Precursor

Catalyst **2** (0.05 mmol) was dissolved in toluene-d_8 (0.5 mL) and the obtained solution transferred into an NMR tube containing a capillary with PPh_3 in C_6D_6 as external standard. The decomposition was monitored by ^{31}P NMR at room temperature. A similar experiment was carried out with a solution of **7**, formed *in situ* from **2** (0.05 mmol) and **4a** (0.50 mmol).

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References and Notes

[1] (a) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Nature* **1993**, *366*, 529–531; (b) S. Murai, F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, *Pure Appl. Chem.*

1994, *66*, 1527; (c) F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, S. Murai, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 62–83.

[2] (a) F. Kakiuchi, Y. Tanaka, T. Sato, N. Chatani, S. Murai, *Chem. Lett.* **1995**, 679–680; (b) F. Kakiuchi, Y. Yamamoto, N. Chatani, S. Murai, *Chem. Lett.* **1995**, 681–682; (c) M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 109–110; (d) F. Kakiuchi, M. Yamauchi, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 111–112; (e) M. Sonoda, F. Kakiuchi, A. Kamatani, N. Chatani, S. Murai, *Chem. Lett.* **1996**, 113–114; (f) S. Murai, N. Chatani, F. Kakiuchi, *Pure Appl. Chem.* **1997**, *69*, 589–594.

[3] (a) B. M. Trost, K. Imi, I. W. Davies, *J. Am. Chem. Soc.* **1995**, *117*, 5371–5372; (b) P. W. R. Harris, P. D. Woodgate, *J. Organomet. Chem.* **1996**, *506*, 339–341; (c) G. Wang, H. Guo, W. P. Weber, *J. Organomet. Chem.* **1996**, *521*, 351–354; (d) P. W. R. Harris, P. D. Woodgate, *J. Organomet. Chem.* **1997**, *530*, 211–223; (e) T. M. Londergan, W. P. Weber, *Macromol. Rapid Commun.* **1997**, *18*, 207–211; (f) M. Mori, Y. Kozawa, M. Nishida, M. Kanamaru, K. Onozuka, M. Takimoto, *Org. Lett.* **2000**, *2*, 3245–3247; (g) T. Matsubara, N. Koga, D. G. Musaev, K. Morokuma, *Organometallics* **2000**, *19*, 2318–2329.

[4] (a) B. Chaudret, R. Poilblanc, *Organometallics* **1985**, *4*, 1722–1726; (b) T. Arliguie, B. Chaudret, R. H. Morris, A. Sella, *Inorg. Chem.* **1988**, *27*, 598–599; (c) A. F. Borowski, B. Donnadieu, J.-C. Daran, S. Sabo-Etienne, B. Chaudret, *Chem. Commun.* **2000**, 543–544.

[5] Y. Guari, S. Sabo-Etienne, B. Chaudret, *J. Am. Chem. Soc.* **1998**, *120*, 4228–4229.

[6] C. Six, B. Gabor, H. Görls, R. Mynott, P. Philipps, W. Leitner, *Organometallics* **1999**, *18*, 3316–3326.

[7] S. Busch, W. Leitner, *Chem Commun.* **1999**, 2305–2306.

[8] R. P. Beatty, R. A. Paciello, (Du Pont) *U.S. Patent* WO 96/23804, **1996**.

[9] M. Sonoda, F. Kakiuchi, N. Chatani, S. Murai, *Bull. Chem. Soc. Jpn.* **1997**, *70*, 3117–3128.

[10] A direct comparison using the same olefinic substrate is impossible, as **2** does not catalyse the coupling of **4** and triethoxyvinylsilane.[5] Other substituted olefins $RCH{=}CH_2$ ($R = Me_3Si$, n-C_4H_9, n-C_6H_{13}) were also unreactive.

[11] The online-sampling system is similar to the setup described in D. Koch, W. Leitner, *J. Am. Chem. Soc.* **1998**, *120*, 13398–13404.