β-Aryl Elimination

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Rhodium-Catalyzed Aryl Transfer from Trisubstituted Aryl Methanols to α,β-Unsaturated Carbonyl Compounds**

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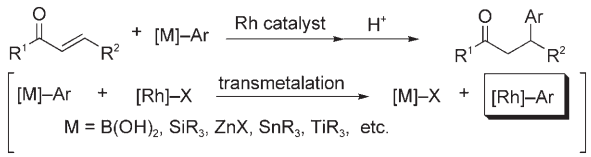
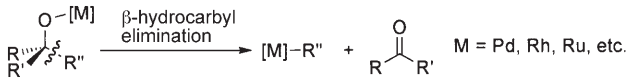
In transition-metal-catalyzed organic reactions involving carbon–carbon bond formation, a carbon–metal catalyst bond is often generated by transmetalation of the organic group in an organometallic reagents. For example, in the rhodium-catalyzed conjugate arylation of electron-deficient alkenes, a wide variety of arylating reagents composed of B, Si, Zn, Sn, and Ti have been used for the formation of aryl rhodium intermediates by transmetalation (Scheme 1).[1] On the other hand, it has been recently reported that organo-transition-metal species can be generated from metal alkoxides through β-hydrocarbyl elimination (Scheme 2) in some catalytic organic transformations.[2–7]

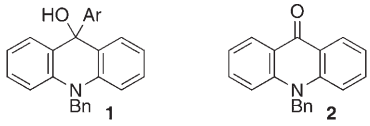


Scheme 1. Rhodium-catalyzed 1,4-addition of aryl organometallic reagents.

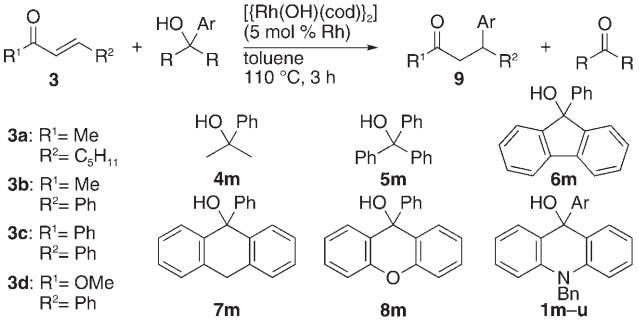


Scheme 2. β-Hydrocarbyl elimination.

As for β-aryl group elimination, Miura and co-workers disclosed that the palladium-catalyzed cross-coupling of aryl halides to give biaryls proceeds with trisubstituted aryl methanols as coupling partners.[3] They also reported the palladium-catalyzed hydroarylation of enones with trisubstituted aryl methanols, although the reaction requires severe reaction conditions (xylene, 160 °C).[3c] Recently, stoichiometric β-phenyl elimination on rhodium was reported by Hartwig and co-workers, in which rhodium *tert*-alkoxide complexes $[Rh(OCR_2Ph)(PEt_3)_3]$ generate the phenylrhodium complex $[RhPh(PEt_3)_3]$ and the corresponding ketones under mild conditions.[8] During our efforts to realize catalytic organic transformations utilizing the β-hydrocarbyl elimination process on transition-metal alkoxides,[5b,6a–d] we found that the acridinols **1** (Bn = benzyl), which are readily obtained by Grignard addition to 10-benzylacridin-9(10*H*)-one (**2**), are highly reactive towards β-aryl elimination on their alkoxide complexes. Herein, we describe the rhodium-catalyzed conjugate arylation of α,β-unsaturated carbonyl compounds with the trisubstituted aryl methanols **1** as aryl transfer reagents.



In the first set of experiments, several types of α,α-substituted benzylalcohols were examined for their reactivity in the rhodium-catalyzed 1,4-addition to 3-nonen-2-one (**3a**; Scheme 3, Table 1). In the presence of $[\{Rh(OH)(cod)\}_2]$ (cod = cycloocta-1,5-diene) as a catalyst in toluene at 110 °C for 3 h, the starting enone **3a** was recovered intact with 2-phenyl-2-propanol (**4m**), triphenylmethanol (**5m**), and cyclic alcohols **6m** and **7m**.[9] The reaction of xanthenol **8m**, which has been reported to be a good phenyl donor in the palladium-catalyzed cross-coupling with aryl halides,[3a] gave the 1,4-addition product **9am**, but its yield was low (22%; Table 1, entry 1). Acridinol **1m** was found to be much more reactive than the others towards the present rhodium-catalyzed 1,4-addition to give **9am** in quantitative yield (Table 1, entry 2). The eliminated ketone, acridinone **2**, was recovered in high yield (86%).



Scheme 3. Rhodium-catalyzed conjugate arylation of α,β-unsaturated carbonyl compounds through β-aryl elimination.

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Table 1: Rhodium-catalyzed hydroarylation of α,β-unsaturated carbonyl compounds through β-aryl elimination.[a]

Entry	Alkene	Ar	Product	Yield[b]
1	**3a**	Ph (**8m**)	**9am**	– (22)
2	**3a**	Ph (**1m**)	**9am**	96 (99)
3	**3a**	2-MeC_6H_4 (**1n**)	**9an**	99
4	**3a**	3-MeC_6H_4 (**1o**)	**9ao**	99
5	**3a**	4-MeC_6H_4 (**1p**)	**9ap**	94
6	**3a**	4-$MeOC_6H_4$ (**1q**)	**9aq**	94
7	**3a**	3,4-$(OCH_2O)C_6H_3$ (**1r**)	**9ar**	98
8	**3a**	1-naphthyl (**1s**)	**9as**	91
9[c]	**3a**	4-ClC_6H_4 (**1t**)	**9at**	91[d]
10[c]	**3a**	4-$CF_3C_6H_4$ (**1u**)	**9au**	96[e]
11	**3b**	4-MeC_6H_4 (**1p**)	**9bp**	99
12	**3c**	4-MeC_6H_4 (**1p**)	**9cp**	99
13[f]	**3c**	4-MeC_6H_4 (**1p**)	**9cp**	99
14	**3d**	Ph (**1m**)	**9dm**	94

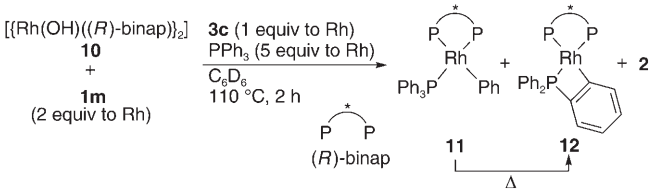
[a] Reaction conditions: alkene **3** (0.20 mmol), alcohol (0.22 mmol), $[\{Rh(OH)(cod)\}_2]$ (5 mol% Rh), and toluene (1.0 mL) at 110°C for 3 h. [b] Yield of isolated product. Values in parentheses are NMR yields. [c] For 10 h. [d] 87% yield of **9at** for 3 h. [e] 48% yield of **9au** for 3 h. [f] Performed with 1 mol% Rh for 6 h.

Several trisubstituted aryl methanols[10] **1n**–**1u**, which bear different substituents on the benzene ring, were successfully applied to the conjugate arylation of enone **3a** to give the corresponding ketones **9an**–**9au** in high yields (91–99%; Table 1, entries 3–10). Although the transfer of aryl groups with electron-withdrawing substituents (Cl and CF_3) was slower, high yields of the arylation products were obtained by carrying out the reaction for a prolonged period of time (Table 1, entries 9 and 10). The addition to α,β-unsaturated ketones **3b** and **3c** and ester **3d** also proceeded smoothly to give the 1,4-addition products **9bp** (99%), **9cp** (99%), and **9dm** (94%), respectively (Table 1, entries 11–14).

On the basis of the high catalytic activity of cod complex $[\{Rh(OH)(cod)\}_2]$, as demonstrated in Table 1, chiral diene ligands were tested for the asymmetric arylation by using the present aryl transfer from acridinols. The use of (*S*,*S*)-Bn-bod*[11] enabled the arylation to proceed with high enantioselectivity. Thus, the reaction of enone **3a** with acridinol **1p** in the presence of Cs_2CO_3 and a chiral diene–rhodium catalyst, generated in situ from $[\{RhCl(C_2H_4)_2\}_2]$ and (*S*,*S*)-Bn-bod*, at 90°C for 24 h gave the 1,4-addition product **9ap** in 95% yield and with an enantiomeric excess (*ee*) of 94% (Scheme 4).

The asymmetric aryl transfer reaction was also catalyzed by bisphosphine–rhodium complex $[\{Rh(OH)((R)\text{-binap})\}_2]$ (**10**; binap = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl), which is known to be one of the best chiral catalysts for the asymmetric 1,4-addition,[12] although its catalytic activity is lower than that of the diene–rhodium complexes. For example, the reaction of enone **3b** with acridinol **1p** (5 mol% Rh of **10**, in toluene at 110°C for 3 h) gave the corresponding β-aryl ketone **9bp** (68% yield, 77% *ee*).

The formation of a phenylrhodium species by phenyl transfer from the acridinol was confirmed by ^{31}P NMR studies of a stoichiometric reaction of complex **10**. Thus, treatment of complex **10** with acridinol **1m** in the presence of enone **3c** and PPh_3 brought about the formation of two rhodium complexes in a ratio of 6:4 (Scheme 5). The major complex, which shows

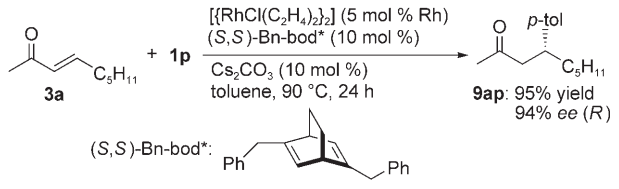


Scheme 5. Reaction of rhodium complex **10** with acridinol **1m**.

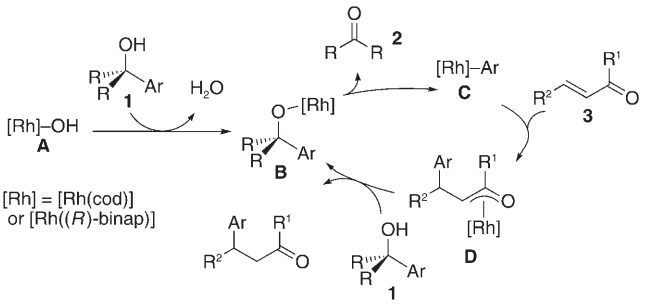
three ddd multiplets at $\delta = 29.5$, 32.8, and 35.4 ppm,[13] was assigned to be complex **11**.[12] The minor complex, which was formed as a sole product on heating complex **11** at 110°C for 24 h, was assigned to be the cyclometalated rhodium complex **12** by the similarity of its ^{31}P NMR spectrum[14] to that of $[Rh(o\text{-}C_6H_4PPh_2)(PPh_3)_2]$.[15] The formation of phenylrhodium complex **11** was not observed with the trisubstituted phenylmethanols **7m** or **8m** under the same conditions (at 110°C for 2 h), which indicates that an efficient β-aryl elimination that generates an aryl rhodium species is characteristic of the alkoxorhodium intermediate derived from acridinol **1**.

A catalytic cycle of this process is illustrated in Scheme 6. β-Aryl elimination of an alkoxorhodium intermediate **B**, generated from the rhodium complex **A** and an acridinol **1**, results in an aryl rhodium species **C**. Insertion of the alkene moiety into the aryl–rhodium bond in **C**, followed by ligand exchange between the resulting oxa-π-allylrhodium intermediate **D**[12] and the alcohol **1**, gives the 1,4-addition product and alkoxorhodium **B**, which carries the catalytic cycle further.

In summary, we have developed a rhodium-catalyzed conjugate arylation of α,β-unsaturated carbonyl compounds by use of trisubstituted aryl methanols derived from acridinone **2**. The β-aryl elimination on an alkoxorhodium intermediate, which is involved as a key step in the catalytic cycle,



Scheme 4. Asymmetric 1,4-addition to enone **3a**.



Scheme 6. Proposed catalytic cycle of the rhodium-catalyzed 1,4-addition of acridinols **1** to enones **3**.

was strongly dependent on the structure of the backbone of the tertiary alcohol bearing the aryl group. Studies on some other catalytic arylation reactions utilizing the trisubstituted aryl methanols are under way.

Experimental Section

3-Nonen-2-one (**3a**; 28.0 mg, 0.20 mmol) was added to a mixture of acridinol **1m** (79.9 mg, 0.22 mmol) and [{Rh(OH)(cod)}$_2$] (2.3 mg, 0.005 mmol) in toluene (1.0 mL), and the mixture was stirred at 110 °C for 3 h under a N_2 atmosphere. After cooling to room temperature, the reaction mixture was passed through a short column of silica gel with diethyl ether as eluent. After evaporation of the solvent, the residue was subjected to preparative thin-layer chromatography (hexane/ethyl acetate 10:1) to give 4-phenylnonan-2-one (**9am**; 96% yield).

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[10] The X-ray crystal structure of **1o** is shown in Figure S1 in the Supporting Information.

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[13] Complex **11**: ^{31}P NMR (C_6D_6): $\delta = 29.5$ (ddd, $J_{P,P,trans} = 324$, $J_{Rh,P} = 178$, $J_{P,P,cis} = 39$ Hz), 32.8 (ddd, $J_{P,P,trans} = 324$, $J_{Rh,P} = 170$, $J_{P,P,cis} = 30$ Hz), 35.4 ppm (ddd, $J_{Rh,P} = 121$, $J_{P,P,cis} = 39$, $J_{P,P,cis} = 30$ Hz).

[14] Complex **12**: ^{31}P NMR (C_6D_6): $\delta = -50.0$ (ddd, $J_{P,P,trans} = 320$, $J_{Rh,P} = 113$, $J_{P,P,cis} = 25$ Hz), 38.4 (ddd, $J_{Rh,P} = 118$, $J_{P,P,cis} = 32$, $J_{P,P,cis} = 25$ Hz), 44.5 ppm (ddd, $J_{P,P,trans} = 320$, $J_{Rh,P} = 185$, $J_{P,P,cis} = 32$ Hz).

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