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Palladium-Catalyzed Dehydroarylation of Triarylmethanols and Their Coupling with Unsaturated Compounds Accompanied by C−C Bond Cleavage

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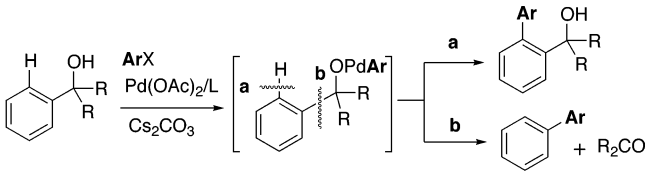
Abstract: Triarylmethanols are effectively dehydroarylated and reacted with some unsaturated compounds by using an appropriate palladium catalyst system such as $Pd(OAc)_2$-$P(1\text{-}Nap)_3$ (1-Nap = 1-naphthyl) to give the corresponding arenes and hydroarylation products, respectively, along with diaryl ketones.

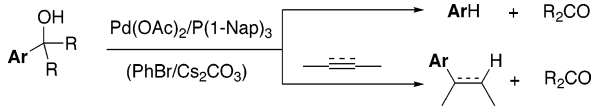
Transition metal catalyzed organic reactions involving the cleavage of C−C single bonds have recently attracted much attention.[1] Although the cleavage is energetically unfavorable, various unique catalytic transformations including ring-expansion or ring-contraction, fragmentation, and coupling with another molecule can be realized when appropriately designed. Among the most promising strategies of C−C bond activation is to utilize the proximate effect by coordination of a functional group in a given substrate to the metal center of a catalyst. As such an example, we recently reported that a number of α,α-disubstituted arylmethanols react with aryl chlorides and bromides to give biaryls via cleavage of the sp^2-sp^3 C−C bond (Scheme 1, path b),[2] in which *β*-carbon elimination in a Pd(II) alcoholate intermediate is involved as the key step.[3,4]

While this reaction occurs in competition with the coupling via cleavage of the *o*-C−H bond (path a), it can proceed selectively when a relatively bulky ligand such as PCy_3 (Cy = cyclohexyl) is employed. In the course of a further investigation into the reaction, it has been found that using one of the most bulky aromatic phosphines, $P(1\text{-}Nap)_3$ (1-Nap = 1-naphthyl),[5,6] triarylmethanols selectively undergo dehydroarylation to give arenes together with diaryl ketones (Scheme 2).

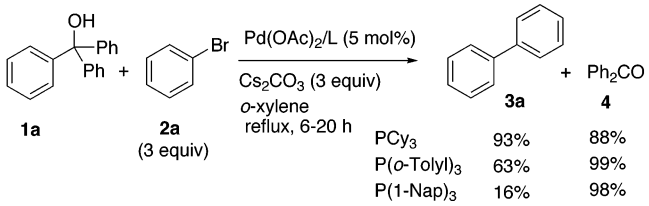
SCHEME 1



SCHEME 2



SCHEME 3



In this case, the aryl−aryl coupling hardly occurs even in the presence of excess aryl halides. Thus, a new mechanistic aspect appears to be involved in the catalytic C−C cleavage. Furthermore, it has been revealed that the hydroarylation of some unsaturated compounds occurs by addition of them to the reaction system. These new findings are reported herein.

As reported previously, treatment of triphenylmethanol (**1a**) with bromobenzene (**2a**) (3 equiv) in the presence of $Pd(OAc)_2$-$4PCy_3$ (5 mol %) and Cs_2CO_3 (3 equiv) as catalyst and base, respectively, in refluxing *o*-xylene gave biphenyl (**3a**) and benzophenone (**4**) in good yields (Scheme 3).

Using $P(o\text{-}Tolyl)_3$ in place of PCy_3 as ligand gave a reduced yield of **3a**, while **4** was formed in a quantitative yield. The coupling product **3a** was formed in only 16% yield, when $P(1\text{-}Nap)_3$ was employed. In the latter two reactions, no other coupling products derived from **1a** and **2a** were observed, although a considerable amount of the ligand phenylated was detected in the case of $P(o\text{-}Tolyl)_3$.[2b] Thus, it was conceived that dehydroarylation to give benzene along with **4** predominantly took place, especially when $P(1\text{-}Nap)_3$ was used.

Consequently, the reaction of (1-naphthyl)diphenylmethanol (**1b**) was examined with $P(1\text{-}Nap)_3$ as ligand (Table 1). When **1b** was treated with **2a** (1.2 equiv),

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(5) Bartik, T.; Himmler, T. *J. Organomet. Chem.* **1985**, *293*, 343.

(6) Application of $P(1\text{-}Nap)_3$ in the palladium-catalyzed reaction of organic halides: (a) Shaw, B. L.; Perera, S. D.; Staley, E. A. *Chem. Commun.* **1998**, 1361. (b) Goossen, L. J. *Chem. Commun.* **2001**, 669. (c) Ziegler, C. B., Jr.; Heck R. F. *J. Org. Chem.* **1978**, *43*, 2941. (d) Wagaw, S.; Rennels, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 8451. For the reaction of allyl compounds see: (e) Friess, B.; Cazes, B.; Gore, J. *Bull. Soc. Chim. Fr.* **1992**, *129*, 273. (f) Ollivier, J.; Dorizon, P.; Priras, P. P.; de Meijere, A.; Salaün, J. *Inorg. Chim. Acta* **1994**, *222*, 37. (g) Bienaymé H. *Tetrahedron Lett.* **1994**, *35*, 7383.

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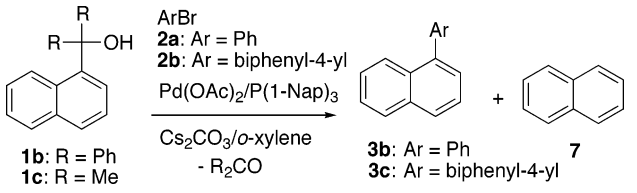
TABLE 1. Reaction of (1-Naphthyl)Methanols with or without Aryl Bromides[a]



entry	alcohol	bromide (equiv)	time (h)	% yield[b] 3	% yield[b] 7
1[c]	**1b**	**2a** (1.2)	3	6	88
2	**1b**	**2a** (0.2)	3	0	98
3	**1b**		36		98
4	**1b**	**2b** (1)	2	0[d]	94
5[e]	**1b**	**2b** (1)	2	95	0
6	**1c**		24		90
7	**1c**	**2a** (0.2)	24	0	94

[a] Reaction conditions: [**1**]:[Pd(OAc)$_2$]:[P(1-Nap)$_3$] = 0.5:0.05:0.1 (in mmol), [ArBr] = [Cs_2CO_3], in refluxing *o*-xylene (2.5 mL) under N_2. [b] GLC yield based on the amount of **1** used. Benzophenone (**4**) was formed quantitatively in entries 1−5. [c] [**1**]:[Pd(OAc)$_2$] = 0.5:0.025 (in mmol). [d] Biphenyl (6%) was formed. [e] PCy_3 was used in place of P(1-Nap)$_3$.

naphthalene (**7**) (88%) was produced along with 1-phenylnaphthalene (**3b**) (6%) and **4** (>98%), indicating that dehydroarylation occurred preferentially as expected (entry 1).

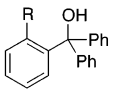
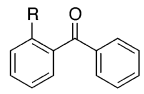
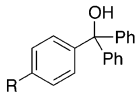
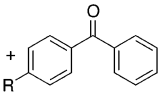
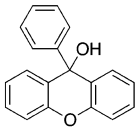
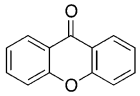
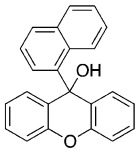
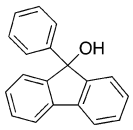
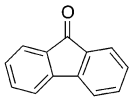
Arene **7** was obtained exclusively with a reduced amount of **2a** (0.2 equiv) (entry 2). While the reaction proceeded without addition of **2a** and the base, a longer reaction time was required to obtain a high yield of **7** (entry 3). In the reaction with 4-bromobiphenyl (**2b**) (1 equiv) in place of **2a**, 1-(biphenyl-4-yl)naphthalene (**3c**) was not detected and a minor amount of biphenyl (6%) was formed (entry 4). This indicates that a part of the bromide was reduced during the reaction. The role of aryl bromides for the acceleration of dehydroarylation is discussed later. In harmony with the results in Scheme 3, **3b** was obtained selectively in good yield by using PCy_3 in the reaction with **1b** (entry 5). 2-(1-Naphthyl)-2-propanol (**1c**) could also afford **7** by using P(1-Nap)$_3$ (entries 6 and 7).

Various triarylmethanols **1d**−**j** were also subjected to the dehydroarylation. The results are summarized in Table 2. As can be seen, the selectivity with respect to which C−C bond is broken in each substrate is consistent with that in the aryl−aryl coupling with use of PCy_3 with the exception of **1j**.[2b] Thus, the aryl groups having an ortho substituent in the alcohols are selectively eliminated (entries 1 and 2). From 9-arylxanthen-9-ols **1h** and **1i** were produced only xanthone (**12**) (entries 5−7). The reaction of 9-phenylfluoren-9-ol (**1j**) unexpectedly gave fluorenone (**13**) as the single product. This contrasts with the reaction with use of PCy_3, in which ring-opening aryl−aryl coupling took place.

It seems to be reasonable to consider that the above dehydroarylation procceds via β-carbon elimination in Pd(II) alcoholate intermediate **A**, which is formed by the reaction of **1** with Pd(II) species in the medium, to give ArPd(II) intermediate **B** (Scheme 4).[7]

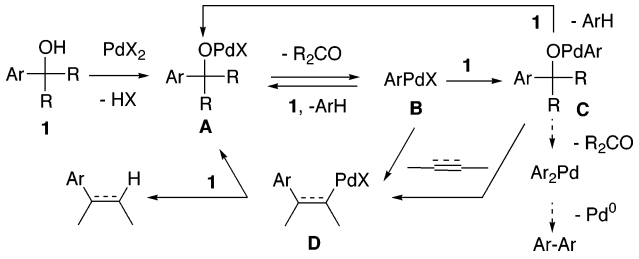
This reacts with **1** to give arene with the regeneration of **A** according to the reverse arrow.[8] Alternatively, the

TABLE 2. Dehydroarylation of Triarylmethanols 1d−j

entry	alcohol	conditions[a]	time (h)	ketone, % yield[b]
				 4 +
1	**1d**: R = OMe	A	24	93 (**4**/**8** = 100:0) **8**: R = OMe
2	**1e**: R = CF_3	A	5	>98 (**4**/**9** = 98:2) **9**: R = CF_3
				 4 +
3	**1f**: R = OMe	A	24	>98 (**4**/**10** = 52:48) **10**: R = OMe
4	**1g**: R = CF_3	A	24	98 (**4**/**11** = 45:55) **11**: R = CF_3
				
5	**1h**	B[c]	24	**12**, 19
6		B	4	>98
				
7	**1i**	B[c]	2	**12**, >98 [d]
				
8	**1j**	B	48	**13**, 81

[a] Condition A: [**1**]:[Pd(OAc)$_2$]:[P(1-Nap)$_3$]:[PhBr]:[Cs_2CO_3] = 0.5:0.05:0.1:0.1:0.1, in refluxing *o*-xylene (2.5 mL) under N_2. Condition B: [**1**]:[Pd(OAc)$_2$]:[P(1-Nap)$_3$]:[PhBr]:[Cs_2CO_3] = 0.5:0.025:0.05:0.05:0.05, in refluxing *o*-xylene (2.5 mL) under N_2. [b] GLC yield based on the amount of **1** used. [c] Without addition of PhBr and Cs_2CO_3. [d] Naphthalene (**7**) was also formed quantitatively.

SCHEME 4



reaction of **B** with **1** may give ArPd(II) alcoholate **C**, which may lead to homocoupling of the aryl group. However, the formation of biaryl was not detected or negligible in each reaction. Thus, alcoholate **C**, if formed, undergoes mainly protonolysis to give **A** before β-carbon

(7) P(1-Nap)$_3$ may form a palladacycle with Pd(II) species accompanied by cleavage of a peri C−H bond of the naphthyl groups.[6a] The cyclization process is considered to be reversible under the present conditions.

(8) A reviewer has kindly suggested a possibility that intermediate **B** reversibly reacts with the ketone moiety liberated to regenerate **A**. Such a nucleophilic arylation of ketones with ArPd(II) species is known to occur intramolecularly: (a) Quan, L. G.; Lamrani, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4827. (b) Solé, D.; Vallverdú, L.; Solans, X.; Font-Bardía, M.; Bonjoch, J. *J. Am. Chem. Soc.* **2003**, *125*, 1587. Thus, the selective formation of **13** as well as **12** under the present conditions (Table 2) could be attributed to the reversibility.

elimination occurs to form Ar_2Pd. Anyway, the steric bulkiness of the ligand seems to make the protonolysis of **B** and/or **C** to **A** favorable. Added aryl bromide appears to oxidize adventitiously formed Pd(0) species to form ArPd(II)Br (**B**, X = Br), which then undergoes protonolysis directly or via **C** (see entry 4 in Table 1).

It may be expected that intermediate **B** or **C** reacts with unsaturated compounds, which allows hydroarylation of them via intermediate **D**. Thus, we next undertook the hydroarylation. It was found that diphenylacetylene (**14a**) and 1-substituted 3-phenyl-2-propen-1-ones **14b** and **14c** are suitable substrates for the reaction as described below.

The reaction of **1a** with **14a** (1.5 equiv) under the conditions employed for the dehydroarylation of aryldiphenylmethanols gave 1,1,2-triphenylethene (**15**) in 73% yield (Table 3, entry 1). (*E*)-1-(1-Naphthyl)-1,2-diphenylethene (**16**) was produced in good yields by using **1b**, **1c**, and **1i**. (entries 2−6). Especially, xanthenol **1i** afforded the best yield of **16** within 1.5 h with use of 5 mol % of Pd (entry 6). The exclusive formation of the (*E*)-isomer is consistent with the mechanism shown in Scheme 4. As expected, 9-(4-methoxyphenyl)- and 9-(4-trifluoromethylphenyl)xanthen-9-ols (**1k** and **1l**) afforded the corresponding (*E*)-1-aryl-1,2-diphenylethenes (**17** and **18**) selectively (entries 9 and 10). While the reaction of **1k** with 4-octyne gave a low yield of coupling product (ca. 15% by GC-MS), the alcohol efficiently reacted with benzylideneacetophenone (**14b**) to afford the corresponding conjugate addition product **19** (entry 11). Benzylideneacetone (**14c**) could also be used, although the product yield was moderate (entry 12). The reaction of **1i** with **14b** gave compound **21** in good yield (entry 13).

It should be noted that in the above hydroarylation reactions, the contamination of phenyl group in bromide **2a** was, if any, negligible. One of the possible reasons for this is that ArPd(II)Br is relatively less reactive toward **14** compared with the corresponding oxygen-coordinated species under the conditions and preferentially undergoes protonolysis. While further studies are required to reveal the detailed mechanism, the consideration may be partly supported by the fact that in the reaction of **1h** with **14a** in the presence of 1-bromonaphthalene (**1c**) (Table 3, entry 8), the naphthyl group was transformed to naphthalene and did not couple with **14a**.

In summary, we have demonstrated that the palladium-catalyzed dehydroarylation of triarylmethanols effectively occurs by using the bulky ligand P(1-Nap)$_3$. This reaction may be utilized as a method for the deprotection of diaryl ketones, especially with an ortho-substituted phenyl group as the sacrifice. It has also been shown that the hydroarylation of some unsaturated compounds with the alcohols is possible. While the hydroarylation of alkynes and α,β-unsaturated compounds under palladium catalysis has been carried out with arylmetal reagents and proton sources[9−11] or aryl halides and hydrogen sources,[12] the present reaction represents the first example of that involving β-carbon elimination.

TABLE 3. Hydroarylation of Unsaturated Compounds 14a−c with Alcohols 1a−c,h,i,k,*l*

entry	1	14	conditions [a]	time (h)	ptoduct, % yield[b]
1	**1a**		A	24	**15**, 73
2 [c]	**1b**	**14a**	A	24	**16**, 84
3	**1b**		A	8	89 (65)
4 [c]	**1c**		A	24	79
5	**1c**		A	10	89
6	**1i**		B	1.5	90 (68)
7	**1h**: R = H	**14a**	B	24	**15**: R = H, 87 (63)
8 [d]	**1h**: R = H		B	2	**15**: R = H, 81
9	**1k**: R = OMe		B	10	**17**: R = OMe, 88 (71)
10	**1l**: R = CF_3		B	10	**18**: R = CF_3, 74 (54)
11	**1k**	**14b**: R = Ph	B	24	**19**: R = Ph, 96 (63)
12	**1k**	**14c**: R = Me	B	24	**20**: R = Me, 35
13	**1i**	**14b**	B	2	**21**, 72 (57)

[a] Condition A: [**1**]:[Pd(OAc)$_2$]:[P(1-Nap)$_3$]:[PhBr]:[Cs_2CO_3] = 0.5:0.05:0.1:0.1:0.1, in refluxing *o*-xylene (2.5 mL) under N_2. Condition B: [**1**]:[Pd(OAc)$_2$]:[P(1-Nap)$_3$]:[PhBr]:[Cs_2CO_3] = 0.5:0.025:0.05:0.05:0.05, in refluxing *o*-xylene (2.5 mL) under N_2. [b] GLC yield based on the amount of **1** used. Value in parentheses is the yield after chromatographic purification. [c] Without addition of PhBr and Cs_2CO_3. [d] 1-Bromonaphthalene was used in place of PhBr.

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Supporting Information Available: Standard experimental procedure and characterization data of products. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049031T

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