ORGANIC LETTERS

2006
Vol. 8, No. 25
5725–5728

Palladium-Catalyzed Regiocontrolled α-Arylation of Trimethylsilyl Enol Ethers with Aryl Halides

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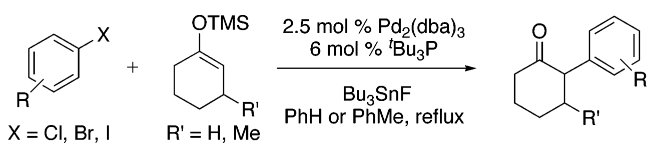
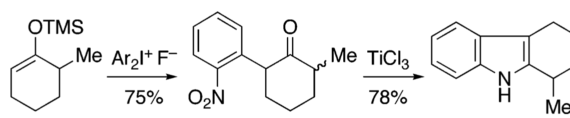
Received August 24, 2006

ABSTRACT

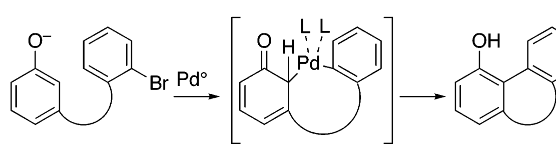


Inter- and intramolecular arylations of trimethylsilyl enol ethers with aryl halides are accomplished regiospecifically in the presence of a palladium catalyst and tributyltin fluoride in refluxing benzene or toluene. The optimal catalyst system called for the use of $Pd_2(dba)_3$ and tri-*tert*-butylphosphine in ca. 1:2 ratio. Aryl iodides, bromides, and chlorides are all effective arylation partners in this reaction.

The direct introduction of an aryl unit at a nucleophilic carbon is a transformation of central importance to complex molecule synthesis.[1] A synthetically useful subset of this class of reactions is the arylation of ketones at the α-position.[2] Such transformations are even more valuable in instances where the arylating agent is adorned with substitutents. For example, in connection with a route to *Aspidosperma* alkaloids,[3] we developed a diaryliodonium reagent for the regiospecific *o*-nitrophenylation of an silyl enol ether, wherein subsequent reduction of the nitro group yielded indoles (e.g., eq 1).[4] Our long-standing interest in transition metal catalyzed arylation and vinylation of phenolates (eq 2)[5] prompted us to examine procedures for the palladium-catalyzed arylations of silyl enol ethers with aryl halides, and we report our results below.[6,7]



(1)



(2)

In pioneering work, Kuwajima and Urabe[8] reported the palladium-catalyzed α-arylation of silyl enol ethers of ketones with aryl halides in the presence of Bu_3SnF.[9−11] The advantage of this method over the palladium-catalyzed arylation of ketones under basic conditions is that it enables *regiocontrol of the arylation* rather than have it be controlled by the inherent kinetic or, more commonly, thermodynamic

(1) Abramovitch, R. A.; Barton, D. H. R.; Finet, J. P. *Tetrahedron* **1988**, *44*, 3039−3071.

(2) Selected examples of α-arylation of ketones that do not involve Pd catalysis: (a) Semmelhack, M. F.; Chong, B. P.; Stauffer, R. D.; Rogerson, T. D.; Chong, A.; Jones, L. D. *J. Am. Chem. Soc.* **1975**, *97*, 2507−2516. (b) Sakakura, T.; Hara, M.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1985**, 1545−1546. (c) Rathke, M. W.; Vogiazoglou, D. *J. Org. Chem.* **1987**, *52*, 3697−3698. (d) Negishi, E. I.; Akiyoshi, K. *Chem. Lett.* **1987**, 1007−1010. (e) Finet, J. P. *Chem. Rev.* **1989**, *89*, 1487−1501. (f) Chen, K.; Koser, G. F. *J. Org. Chem.* **1991**, *56*, 5764−5767. (g) Morgan, J.; Pinhey, J. T.; Rowe, B. A. *J. Chem. Soc., Perkin Trans. 3* **1997**, 1005−1008. (h) Mino, T.; Matsuda, T.; Maruhashi, K.; Yamashita, M. *Organometallics* **1997**, *16*, 3241−3242. (i) Ryan, J. H.; Stang, P. J. *Tetrahedron Lett.* **1997**, *38*, 5061−5064. (j) Oxidative arylation of ketone enolate: Bhowmik, D. R.; Venkateswaran, R. V. *Tetrahedron Lett.* **1999**, *40*, 7431−7433. (k) Deng, H.; Konopelski, J. P. *Org. Lett.* **2001**, *3*, 3001−3004. (l) Ooi, T.; Maruoka, K. *J. Am. Chem. Soc.* **2003**, *125*, 10494−10495. (m) Koech, P. K.; Krische, M. J. *J. Am. Chem. Soc.* **2004**, *126*, 5350−5351. For a comprehensive listing of methods for α-arylation of ketones, see ref 13d.

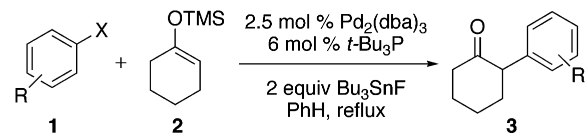
(3) (a) Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **1998**, *120*, 13523−13524. (b) Kozmin, S. A.; Iwama, T.; Huang, Y.; Rawal, V. H. *J. Am. Chem. Soc.* **2002**, *124*, 4628−4641.

10.1021/ol062093g CCC: $33.50
Published on Web 11/08/2006

reactivity of the ketone.[12−15] Furthermore, one can hope to exploit the rich chemistry of regioselective enolate formation and parlay it into a regioselective arylation procedure.[16] Unfortunately, as originally reported, the scope of this reaction was rather limited, primarily to the arylation of the kinetic enol silyl ethers of methyl ketones.[8] Even the arylation of cyclohexanone enol ether was reported to give <15% yield of the α-arylation product. We examined modern variations of this process and developed a general procedure for the regiospecific inter- and intramolecular arylation of various ketone enol silyl ethers.[6,7]

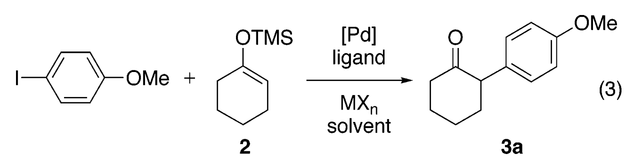
In considering the results and probable mechanism of the Kuwajima−Urabe arylation, the problematic steps appeared to be either the transmetalation of the putative tin enolate to the arylpalladium enolate or its reductive elimination to the arylated ketone. Assuming the latter was the issue, the expectation was that this step could be accelerated through the use of the bulky ligand *t*-Bu_3P.[17] Numerous reaction conditions were examined for the arylation of cyclohexanone trimethylsilyl enol ether (**2**) with *p*-iodoanisole (eq 3).[18,19] Of the reaction parameters examined, the combination that afforded the cleanest reaction involved the use of 2.5 mol % of $Pd_2(dba)_3$, 6 mol % of *t*-Bu_3P, and 1 equiv of Bu_3SnF in refluxing benzene. However, the reaction was slow under these conditions and reached only ~50% completion after 20 h. On the other hand, it progressed well when the silyl enol ether and tin fluoride were used in excess (2 equiv each), and afforded arylated product **3a** in 82% isolated yield (Table 1, entry 1).

Table 1. Pd-Catalyzed Arylation of Trimethylsilyl Enol Ether of Cyclohexanone with Various Aryl Halides[a]



entry	R	X	time (h)	product	% yield[a]
1	4-MeO	I	19	**3a**	82
2	4-MeO	Br	19	**3a**	78
3[b]	4-MeO	Br	20	**3a**	64
4[c]	4-MeO	Cl	20	**3a**	64
5	4-NMe_2	Br	9	**3b**	54
6	H	I	21	**3c**	75
7	4-NO_2	I	8	**3d**	70
8	4-NO_2	Br	8	**3d**	71
9	4-NO_2	Cl	5	**3d**	61
10	4-MeO_2C	Br	21	**3e**	62
11	3-MeO	I	20	**3f**	53
12	2-MeO	I	21	**3g**	71
13	2-Me	Br	21	**3h**	70
14	2-Me	Cl	20	**3h**	55
15	2-NO_2	Cl	3.5	**3i**	25

[a] Reactions were conducted with 1 equiv of the aryl halide **1** (0.25 M) and 2 equiv of TMS enol ether **2.** Yield is based on the aryl halide. [b] 2-(Di-*tert*-butylphosphino)biphenyl (6 mol %) was used instead of *t*-Bu_3P. [c] Carried out in refluxing toluene.



(3)

The standard conditions described above were utilized to perform the arylation of **2** with various aryl halides, and the results are summarized in Table 1.[20,21] The arylation of **2** with *p*-bromoanisole under the same conditions afforded cyclohexanone **3a** in 78% yield (entry 2). Arylation product **3a** was obtained in slightly lower yield when the bulky ligand 2-(di-*tert*-butylphosphino)biphenyl was used (entry 3). Even the corresponding aryl chloride gave the arylated product in good yield, provided the reaction was carried out at a slightly higher temperature, in refluxing toluene (entry 4). By contrast, the corresponding triflate was unreactive and was recovered cleanly (by ^{1}H NMR) after 18 h. Other electron-rich aryl halides were also effective coupling partners (entries

(4) (a) Iwama, T.; Birman, V. B.; Kozmin, S. A.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 673−676. (b) The direct *o*-nitroarylation of enolates with aryliodonium salts has also been reported: Rawal, V. H.; Takenaka, N.; Iwama, T. *Abstracts of Papers*; 222nd National Meeting of the American Chemical Society, Chicago, IL, August 26−30, 2001; American Chemical Society: Washington, DC, 2001; ORGN-007 (for a detailed abstract, see *Chem. Abstr.* AN 2001:640370). For a full discussion of this work, see: Takenaka, N. Ph.D. Dissertation, University of Chicago, Chicago, IL, 2002. For a related report, see: (c) Aggarwal, V. K.; Olofsson, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 5516−5519.

(5) (a) Hennings, D. D.; Iwasa, S.; Rawal, V. H. *J. Org. Chem.* **1997**, *62*, 2−3. (b) Hennings, D. D.; Iwasa, S.; Rawal, V. H. *Tetrahedron Lett.* **1997**, *38*, 6379−6382. (c) Hennings, D. D.; Iwama, T.; Rawal, V. H. *Org. Lett.* **1999**, *1*, 1205−1208. For application to complex molecule synthesis see: (d) MacKay, J. A.; Bishop, R. L.; Rawal, V. H. *Org. Lett.* **2005**, *7*, 3421−3424.

(6) The contents of this paper were presented at the 222nd National Meeting of the American Chemical Society: Rawal, V. H.; Iwama, T. *Abstracts of Papers*; 222nd National Meeting of the American Chemical Society, Chicago, IL, August 26−30, 2001; American Chemical Society: Washington, DC, ORGN-606 (for a detailed abstract, see *Chem. Abstr.* AN 2001:640969). This work was also presented at the 33rd Great Lakes/Central Regional Meeting of the American Chemical Society, Grand Rapids, MI, June 11−13, 2001.

(7) A recent publication by Verkade, Hartwig, and co-workers, describing the use of similar conditions, that appeared on the web prompts us to present fully our previously reported work (ref 6) in this area. See: Su, W.; Raders, S.; Verkade, J. G.; Liao, X.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2006**, *45*, 5852−5855.

(8) Kuwajima, I.; Urabe, H. *J. Am. Chem. Soc.* **1982**, *104*, 6831−6833.

(9) Other early examples of Pd-catalyzed α-arylation that go through stannyl enolates: (a) Kosugi, M.; Sizuki, M.; Hagiwara, I.; Goto, K.; Saitho, K.; Migita, T. *Chem. Lett.* **1982**, 939−940. (b) Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *J. Chem. Soc., Chem. Commun.* **1983**, 344−345. (c) Kosugi, M.; Hagiwara, I.; Sumiya, T.; Migita, T. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 242−246. (d) Sakakura, T.; Hara, M.; Tanaka, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 283−288. Antimony enolate: (e) Kang, S. K.; Ryu, H. C.; Hong, Y. T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3350−3351.

(10) Pd-catalyzed arylations of silyl ketene acetals: (a) Carfagna, C.; Musco, A.; Sallese, G.; Santi, R.; Fiorani, T. *J. Org. Chem.* **1991**, *56*, 261−263. (b) Galarini, R.; Musco, A.; Pontellini, R.; Santi, R. *J. Mol. Catal.* **1992**, *72*, L11−L13. (c) Sakamoto, T.; Kondo, Y.; Masumoto, K.; Yamanaka, H. *Heterocycles* **1993**, *36*, 2509−2512. (d) Sakamoto, T.; Kondo, Y.; Masumoto, K.; Yamanaka, H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 235−236. (e) Agnelli, F.; Sulikowski, G. A. *Tetrahedon Lett.* **1998**, *39*, 8807−8810. (f) Lee, S.; Lee, W.-M.; Sulikowski, G. A. *J. Org. Chem.* **1999**, *64*, 4224−4225. (g) Liu, X.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 5182−5192.

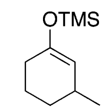
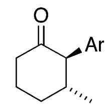
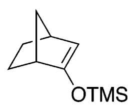
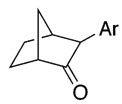
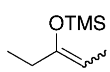
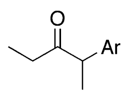
(11) For recent developments on Pd-catalyzed arylation of silyl enol ethers or related species, see: (a) Hama, T.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 4976−4985,and references cited therein. (b) Chae, J.; Yun, J.; Buchwald, S. L. *Org. Lett.* **2004**, *6*, 4809−4812 and references cited therein.

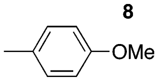
(12) Early examples of Ni-catalyzed α-arylation of enolates: (a) Reference 2a. (b) Millard, A. A.; Rathke, M. W. *J. Am. Chem. Soc.* **1977**, *99*, 4833−4835.

6, 11−14). The successful use of *o*-chlorotoluene, in particular, is noteworthy, since it is both electron-rich and sterically encumbered. Aryl halides possessing an electron-withdrawing group at the para position gave the respective arylated products in good yields (entries 7−10). By comparison, *o*-nitro-substituted aryl halides (Cl, Br, I) were poor arylating agents, and only *o*-chloronitrobenzene gave any of the arylation product (entry 15). Some of the above arylations were also carried out successfully in toluene at 80 °C instead of refluxing benzene.

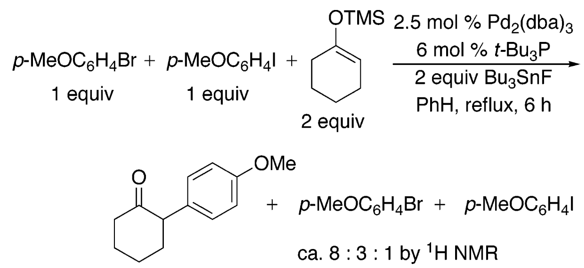
To explore the generality of the arylation protocol, additional TMS enol ethers were prepared and subjected to standard arylation protocol (Table 2).[16] Entry 1 highlights an important feature of the silyl enol ether arylation method: arylations take place regiospecifically. Thus, arylation of enol ether **4,** prepared easily and regiospecifically by methylcuprate addition to 2-cyclohexenone,[22] with *p*-iodoanisole gave arylated product **5** as a single regio- and stereoisomer in 72% yield.[23] Evidently, the putative tin and palladium enolate intermediates do not equilibrate to the regioisomeric, less-hindered enolates. Norbornanone-derived enol ether **6** reacted slowly with *p*-iodoanisole to produce the expected arylation product (**7**) in 58% yield together with recovered *p*-iodoanisole (entry 2). Also slow to react was the acyclic enol ether **8**.[8] This reaction was carried out in refluxing benzene, using *p*-bromoanisole as the arylating agent, and examination of the reaction mixture by ^{1}H NMR after 9 h showed the presence of primarily unreacted **8**. In refluxing toluene, however, this arylation proceeded well and afforded **9** in 70% yield (entry 3). When this reaction was carried out with *p*-iodoanisole, it proceeded in low yield and produced unindentified byproducts. A competition experiment (eq 4) showed that the aryl iodide is consumed faster

Table 2. Intermolecular Pd-Catalyzed Arylation of Different TMS Enol Ether Substrates[a]

entry	ArX	TMS-ether	solvent	time (h)	product	% yield
1	ArI	 **4**	benzene	21	 **5**	72
2	ArI	 **6**	benzene	21	 **7**	58
3	ArBr	 **8**	toluene	26	 **9**	70

Ar: 

[a] Reactions were conducted with 1 equiv of the aryl halide (0.25 M), 2 equiv of TMS-enol ether, 2.5 mol % of $Pd_2(dba)_3$, 6 mol % of *t*-Bu_3P, 2 equiv of Bu_3SnF, PhH, reflux.



(4)

than the bromide, consistent with the expected relative rates of oxidative addition of Pd^0 to aryl halides. These observations indicate that oxidative addition of Pd^0 onto the aryl halide is not the rate determining step in the reaction and suggest that the Pd-intermediate formed from the aryl iodide is less competent, due to either poor reactivity or stability, than that from the aryl bromide at proceeding to the product.

(13) For the Pd-catalyzed intermolecular arylation of carbonyl compounds, see: (a) Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 11108−11109. (b) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 12382−12383. (c) Kawatsura, M; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473−1478. (d) Fox, J. M.; Huang, X.; Chieffi, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 1360−1370. (e) Ehrentraut, A.; Zapf, A.; Beller, M. *Adv. Synth. Catal.* **2002**, *344*, 209−217. (f) Marion, N.; Ecarnot, E. C.; Navarro, O.; Amoroso, D.; Bell, A.; Nolan, S. P. *J. Org. Chem.* **2006**, *71*, 3816−3821 and references cited therein. (g) Review: Culkin, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *36*, 234−245.

(14) Intramolecular α-arylation of enolates: (a) Muratake, H.; Natsume, M.; Nakai, H. *Tetrahedron* **2004**, *60*, 11783−11803 and references cited therein. (b) Shaughnessy, K. H.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1998**, *63*, 6546−6553. (c) Sole, D.; Vallverdu, L.; Solans, X.; Font-Bardia, M.; Bonjoch, J. *J. Am. Chem. Soc.* **2003**, *125*, 1587−1594. (d) Honda, T.; Sakamaki, Y. *Tetrahedron Lett.* **2005**, *46*, 6823−6825. (e) Reference 5d.

(15) For early reports on Pd-catalyzed alkenylation of enolates, see: (a) Piers, E.; Marais, P. C. *J. Org. Chem.* **1990**, *55*, 3454−3455. (b) Piers, E.; Renaud, J. *J. Org. Chem.* **1993**, *58*, 11−13. See also: (c) Yu, J. M.; Wang, T.; Liu, X. X.; Deschamps, J.; Flippen-Anderson, J.; Liao, X. B.; Cook, J. M. *J. Org. Chem.* **2003**, *68*, 7565−7581 and references cited therein. (d) Sole, D.; Urbaneja, X.; Bonjoch, J. *Adv. Synth. Catal.* **2004**, *346*, 1646−1650 and references cited therein. (e) Chieffi, A.; Kamikawa, K.; Ahman, J.; Fox, J. M.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 1897−1900.

(16) (a) Heathcock, C. H. *Mod. Synth. Methods* **1992**, *6*, 1−102. (b) Kobayashi, S.; Manabe, K.; Ishitani, H.; Matsuo, J. I. In *Science of Synthesis*; Bellus, D., et al., Eds.; Georg Thieme: Stuttgart, Germany, 2002; Vol. 9, pp 317−369.

(17) (a) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617−620. (b) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 2367−2370. (c) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387−3388. (d) Shaughnessy, K. H.; Kim, P.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 2123−2132. See also ref 13g.

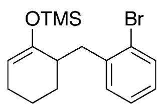
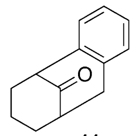
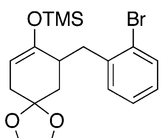
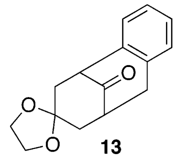
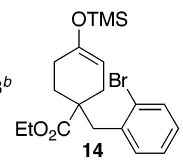
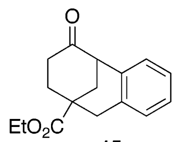
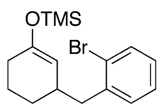
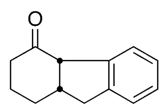
(18) This combination was selected as it was expected to be a challenging arylation, since not only is the phenylation cyclohexanone reported to be low yielding (ref 8), but the oxidative addition to the electron-rich *p*-iodoanisole was expected to be slow.

(19) An extensive screening of reaction conditions was carried out. Pd sources examined: $PdCl_2(Ph_3P)_2$, $PdCl_2(o\text{-}Tol_3P)_2$, $PdCl_2$, $Pd_2(dba)_3$, $Pd(OAc)_2$, or $PtCl_2(PhCN)_2$. Phosphine ligands: BINAP, Tol-BINAP, *t*- Bu_3P, $(t\text{-}BuCH_2)_3P$, 2-(di-*tert*-butylphosphino)biphenyl, ^{c}Hex$_3$P, Ph_3P, $(o\text{-}Tol)_3As$, Ph_3As, and $(i\text{-}PrO)_3P$. Fluoride sources: Bu_3SnF, LiF, NaF, CsF, CuF_2, ZnF_2, ZrF_4, KF, $ZnCl_2$, $SnCl_4$, or Me_4NF. Solvents: benzene, toluene, DMF, or THF. Additives: LiCl, NaOAc and *t*-BuOK.

(20) General procedure for Pd-catalyzed arylation: A mixture containing TMS enol ether (1 mmol), aryl halide (0.5 mmol), 2.5 mol % of $Pd_2(dba)_3$ (11.4 mg), and Bu_3SnF (309 mg, 1 mmol) under a nitrogen atmosphere was treated with a solution of ^{t}Bu$_3$P (7.5 μL) in benzene (2 mL) at room temperature. The resulting mixture was heated to reflux. After cooling to room temperature, the reaction mixture was diluted with ether (20 mL) (when the precipitate of tin residue was formed, it was removed by decantation with ether), washed with 1 N aqueous NaOH twice (5 mL each) followed by brine (2 × 5 mL), dried ($MgSO_4$), and concentrated. The residue was purified by flash column chromatography on silica gel.

The synthetic utility of this method was further developed through the examination of substrates in which the arylation would take place intramolecularly (Table 3).[14] Treatment of TMS enol ether **10** with 1 equiv of Bu_3SnF, 5 mol % of $Pd_2(dba)_3$, and 12 mol % of t-Bu_3P in benzene furnished [3.3.1] bicyclic product **11** in 62% yield together with 12% of the uncyclized ketone, corresponding to the hydrolysis product of **11.** The arylative cyclization of **12** required higher temperature (refluxing toluene) and gave **13** in 66% yield, accompanied by the uncyclized ketone (12%). In both cases, lower loadings of $Pd_2(dba)_3$ (2.5 mol %) and t-Bu_3P (6 mol %) resulted in slower reactions and increased amounts of the ketone arising from hydrolysis of the starting material. On the other hand, the reaction of **14** with 2.5 mol % of $Pd_2(dba)_3$ and 6 mol % of t-Bu_3P in refluxing benzene afforded arylation product **15** high yield (entry 3). All three of the entries are noteworthy in that they produce a [3.3.1]-bicyclic array. The final entry shows the construction of tetrahydrofluorenone **17** through the intramolecular arylation method. In this case the arylated product (**17**), assumed to be cis, was formed in 46% yield along with 24% of the recovered ketone.

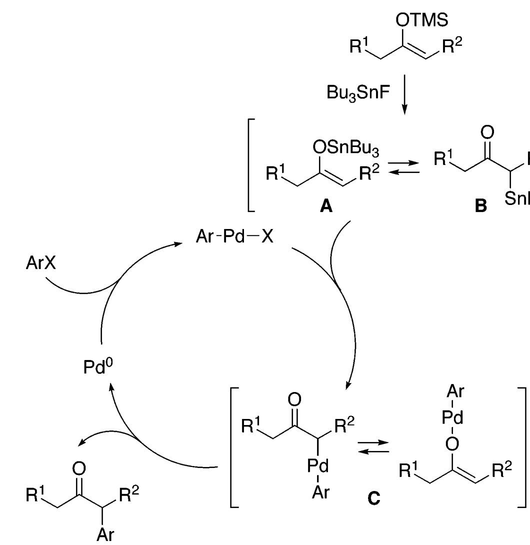
Table 3. Intramolecular Pd-Catalyzed Arylation

entry	TMS-ether	solvent	time (h)	product[a]	% yield
1	 **10**	benzene	21	 **11**	62[c]
2	 **12**	toluene	21	 **13**	66[c]
3[b]	 **14**	benzene	17	 **15**	84
4	 **16**	benzene	21	 **17**	46[d]

[a] Standard conditions: 0.25 M of TMS enol ether, 5 mol % of $Pd_2(dba)_3$, 12 mol % of t-Bu_3P, 1 equiv of Bu_3SnF, reflux. [b] 2.5 mol % of $Pd_2(dba)_3$ and 6 mol % of t-Bu_3P were used. [c] Uncyclized ketone was isolated in 12% yield. [d] Uncyclized ketone was isolated in 24% yield.

A plausible mechanism for the Pd-catalyzed arylation of TMS enol ethers is shown in Scheme 1. The starting TMS enol ether is expected to react with Bu_3SnF to generate tin enolate **A**, which is under equilibrium with α-stannyl ketone **B**.[8,24] The reaction of the tin enolate with Ar−Pd−X would produce the transmetalation product, Pd-enolates **C**.[9−11] Reductive elimination of **C** to give a C−C bond then gives the arylation product and regenerates Pd^0.

Scheme 1



In summary, Pd-catalyzed arylation of TMS enol ethers was achieved in both inter- and intramolecular manner by use of $Pd_2(dba)_3$ and t-Bu_3P in the presence of Bu_3SnF. Electron-poor and electron-rich aryl halides, including iodides, bromides, and chlorides, participated in the present arylation. The arylations proceeded regiospecificity and with a range of substrates.

Acknowledgment. We thank the National Institutes of Health for financial suport of this work. We also thank Merck & Co. for additional support.

Supporting Information Available: Experimental procedures and ^1H and ^{13}C NMR spectra of arylated compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) The success of this reaction is dependent on the quality of t-Bu_3P. Irreproducible results were obtained with one, newly purchased bottle of t-Bu_3P.

(22) (a) Binkley, E. S.; Heathcock, C. H. *J. Org. Chem.* **1975**, *40*, 2156−2160. (b) Dieter, R. K.; Dieter, J. W. *J. Chem. Soc., Chem. Commun.* **1983**, 1378−1380.

(23) The product arising from the regioisomeric enolate was not detected in the ^1H NMR of the crude reaction mixture. Product **5** was assigned the trans stereochemistry based on the coupling constant of the 2,3-vicinal protons (J = 11.5 Hz).

(24) Shibata, I.; Baba, A. *Org. Prep. Proced. Int.* **1994**, *26*, 85−100.