ORGANIC
LETTERS

2010
Vol. 12, No. 21
4724−4727

Arylsilanes: Application to Gold-Catalyzed Oxyarylation of Alkenes

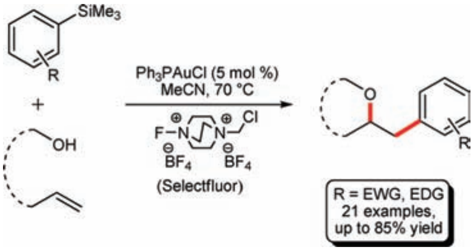
Liam T. Ball, Michael Green, Guy C. Lloyd-Jones,* and Christopher A. Russell*

School of Chemistry, University of Bristol, Cantock's Close, Bristol,
United Kingdom BS8 1TS

guy.lloyd-jones@bristol.ac.uk; chris.russell@bristol.ac.uk

Received August 14, 2010

ABSTRACT



Arylsilanes are efficient reagents for the gold-catalyzed oxyarylation of alkenes (21 examples, up to 85% isolated yield). Using commercially available Ph$_3$PAuCl and readily prepared, benign arylsilanes, these two- and three-component reactions proceed smoothly in air. The oxidant, Selectfluor, not only facilitates entry to the Au(I/III) manifold but also provides a fluoride anion for silane activation, thereby avoiding the need for addition of a stoichiometric base.

While the isolobal relationship between gold and palladium Au(I/III) and Pd(0/II) has been remarked upon,[1] the full potential for development of gold-catalyzed "palladium-like"[2] cross-coupling has not been realized, and there exist only a few reports[3] of gold-mediated Sonogashira[4] and Suzuki[1b,5] couplings. The difficulty in achieving these very powerful transformations stems from the fact that the two-electron redox cycle—analogous to the Au(I/III) cycle central to most cross-coupling reactions[6]—is not facile.[1d,7] However, the Au(I/III) manifold can be accessed through use of an exogenous oxidant, such as *tert*-butylhydroperoxide, PhI(OAc)$_2$, or Selectfluor:[8] this approach has been the subject of significant recent interest, with a number of oxidative transformations, including dimerization,[1a,9,10] arylation,[11] and C−O[12] and C−N[13] bond formation, having been reported.

---

(1) (a) Carretin, S.; Guzman, J.; Corma, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 2242. (b) González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *J. Catal.* **2006**, *238*, 497. (c) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (d) Lauterbach, T.; Livendahl, M.; Rosellón, A.; Espinet, P.; Echavarren, A. M. *Org. Lett.* **2010**, *12*, 3006. (e) Carretin, S.; Corma, A.; Iglesias, M.; Sánchez, F. *Appl. Catal., A* **2005**, *291*, 247.

(2) See, for example: (a) *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E., Ed.; Wiley: New York, 2004; Vol. 1 and 2. (b) Tsuji, J. *Palladium Reagents and Catalysis: New Perspectives for the 21st Century*; Wiley: Chichester, 2004.

(3) For a review, see: Garcia, P.; Malacria, M.; Aubert, C.; Gandon, V.; Fensterbank, L. *ChemCatChem* **2010**, *2*, 493.

(4) Examples of gold-catalyzed Sonogashira coupling: (a) Li, P.; Wang, L.; Wang, M.; You, F. *Eur. J. Org. Chem.* **2008**, 5946. (b) González-Arellano, C.; Abad, A.; Corma, A.; Garcia, H.; Iglesias, M.; Sánchez, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1536. (c) González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *Eur. J. Inorg. Chem.* **2008**, 1107. Echavarren[1d] has recently demonstrated that trace palladium contaminants in gold complexes can induce what appear to be "gold-catalyzed" Sonogashira couplings.

(5) Examples of gold-catalyzed Suzuki coupling: (a) Lin, J. C. Y.; Tang, S. S.; Vasam, C. S.; You, W. C.; Ho, T. W.; Huang, C. H.; Sun, B. J.; Huang, C. Y.; Lee, C. S.; Hwang, W. S.; Chang, A. H. H.; Lin, I. J. B. *Inorg. Chem.* **2008**, *47*, 2543. (b) Corma, A.; Gutiérrez-Puebla, E.; Iglesias, M.; Monge, A.; Pérez-Ferreras, S.; Sánchez, F. *Adv. Synth. Catal.* **2006**, *348*, 1899.

(6) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366.

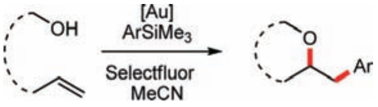
(7) For a computational comparison of reductive elimination from Cu(III), Ag(III), and Au(III) species, see: Nakanishi, W.; Yamanaka, M.; Nakamura, E. *J. Am. Chem. Soc.* **2005**, *127*, 1446.

(8) The mechanism of oxidative fluorination—i.e., electrophilic attack by "F$^+$" vs two single-electron transfer events—continues to be debated. See (and references therein): Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Wiley: Weinheim, 2005; Chapter 2, p 76.

10.1021/ol1019162

Herein we demonstrate the use of arylsilanes in gold-catalyzed oxidative oxyarylation of olefins (Scheme 1).

Scheme 1. Gold-Catalyzed Oxidative Oxyarylation of Alkenes with Arylsilanes in the Presence of Selectfluor

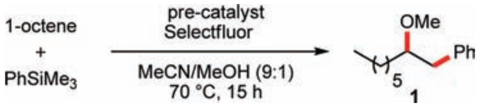


Within the remit of gold chemistry, such reactions are unusual in that they proceed in generally good to excellent yield, despite being three-component systems and requiring activation of an alkenyl, as opposed to the more common alkynyl or allenyl, substrate.

Recently, the groups of Zhang[14] and Toste[15] independently reported the gold-catalyzed amino- and oxyarylation of terminal olefins with arylboronic acids in the presence of Selectfluor as the stoichiometric oxidant. The proposed mechanisms involve oxidative fluorination of Au(I) to furnish a Au(III) species with concomitant generation of a fluoride anion, the latter activating the arylboronic acid and thereby facilitating transmetalation through formation of a B−F bond. The use of organosilanes (the Hiyama[16] reaction) and organosiloxanes (the Tamao−Ito[17] reaction) as the nucleophilic partner in palladium-catalyzed cross-coupling is well established and typically requires a stoichiometric base as an activator.[18] We envisaged that the fluoride formed in situ by oxidation of Au(I) would be similarly capable of activating a silane and thus that an arylsilane could be used in place of the boronic acid for alkene oxyarylation; formation of a strong Si−F bond[19,20] would provide the thermodynamic driving force. This supposition was further supported by the observation[12a] that silyloxyethers are not stable under the conditions of Selectfluor-mediated oxidation of Au(I). Our planned methodology would thus confer the benefits inherent in silanes—namely, ease of preparation and handling, stability, and low toxicity—upon gold catalysis, without the need to employ "more than stoichiometric amounts of expensive additives"[2b] to achieve their activation.

The reaction between 1-octene, methanol, and trimethyl(phenyl)silane in the presence of Selectfluor was used to assay the viability of our proposed methodology and, subsequently, to identify the most efficient gold precatalyst (Table 1) and optimal conditions:[21] it was encouraging to find that, using commercially available Ph$_3$PAuCl (10 mol %, added in two portions) under an atmosphere of air, the expected methoxyphenylated product **1** was obtained in excellent yield (entry 1). This result was not surpassed with other precatalysts, although Cy$_3$PAuCl, (*o*-Tol)$_3$PAuCl, AuCl,[22] and Me$_2$SAuCl (entries 3−6) also exhibited significant activity. It was interesting to note that simple Au(III) salts were able to catalyze the reaction (entries 7 and 8) and that use of tri-*tert*-butylphosphine and XPhos (2-dicyclohexylphosphino-2′,4′,6′-tri-*iso*-propylbiphenyl)—bulky phosphines which are outstanding

Table 1. Screening of Precatalyst for Oxyarylation of Alkenes:[a] Summary of Reaction Optimization[b]



entry	precatalyst	**1**, yield %[c,d]
1	Ph$_3$PAuCl	99
2	*t*-Bu$_3$PAuCl	27
3	Cy$_3$PAuCl	80
4	(*o*-Tol)$_3$PAuCl	79
5	AuCl	98
6	Me$_2$SAuCl	83
7	AuCl$_3$	22
8	HAuCl$_4$·3H$_2$O	6
9	XPhosAuCl	70
10	Ph$_3$PAuCl	86[e]
11	Ph$_3$PAuCl	13[f]
12	**Ph$_3$PauCl**	**96**[g]

[a] Reaction conditions: 1-octene (0.1 mmol), trimethyl(phenyl)silane (0.2 mmol), Selectfluor (0.2 mmol), and precatalyst (10 mol %, added in 2 equal portions at $t = 0$ and $t = 2$ h) were stirred in anhydrous MeCN (0.9 mL) and anhydrous MeOH (0.1 mL) in a 7 mL vial under air at 70 °C. [b] For full details of reaction optimization, see Supporting Information. [c] Yields determined by GC-FID referenced to an internal standard (mesitylene). [d] Yields are averages of at least two repetitions. [e] PhSi(OMe)$_3$ used in place of PhSiMe$_3$. [f] PhSiMe$_2$OH used in place of PhSiMe$_3$. [g] 5 mol % Ph$_3$PAuCl used, added in a single portion at $t = 0$. XPhos is 2-dicyclohexylphosphino-2′,4′,6′-tri-*iso*-propylbiphenyl.

---

(9) See, for example: González-Arellano, C.; Corma, A.; Iglesias, M.; Sánchez, F. *Chem. Commun.* **2005**, 1990.

(10) (a) Kar, A.; Mangu, N.; Kaiser, H. M.; Beller, M.; Tse, M. K. *Chem. Commun.* **2008**, 386. (b) Wegner, H. A.; Ahles, S.; Neuburger, M. *Chem.—Eur. J.* **2008**, *14*, 11310. (c) Cui, L.; Zhang, G.; Zhang, L. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3884. (d) Hopkinson, M. N.; Tessier, A.; Salisbury, A.; Giuffredi, G. T.; Combettes, L. E.; Gee, A. D.; Gouverneur, V. *Chem.—Eur. J.* **2010**, *16*, 4739.

(11) Zhang, G.; Peng, Y.; Cui, L.; Zhang, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 3112.

(12) (a) Peng, Y.; Cui, L.; Zhang, G.; Zhang, L. *J. Am. Chem. Soc.* **2009**, *131*, 5062. (b) Whitman, C. A.; Mauleón, P.; Shapiro, N. D.; Sherry, B. D.; Toste, F. D. *J. Am. Chem. Soc.* **2007**, *129*, 5838.

(13) Iglesias, A.; Muniz, K. *Chem.—Eur. J.* **2010**, *15*, 10563.

(14) Zhang, G.; Cui, L.; Wang, Y.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 1474.

(15) (a) Melhado, A. D.; Brenzovich, W. E., Jr.; Lackner, A. D.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8885. (b) Brenzovich, W. E., Jr.; Benitez, D.; Lackner, A. D.; Shunatona, H. P.; Tkatchouk, E.; Goddard, W. A., III; Toste, F. D. *Angew. Chem., Int. Ed.* **2010**, *49*, 5519.

(16) Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1988**, *53*, 918.

(17) Tamao, K.; Kobayashi, K.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6051.

(18) Denmark, S. E.; Sweiss, R. F. *Acc. Chem. Res.* **2002**, *35*, 835.

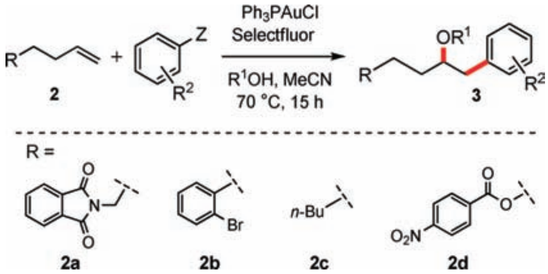
(19) The Me$_3$Si−F bond has a dissociation energy of 807 kJ mol $^{-1}$: Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981; Chapter 2, p 4.

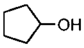
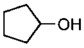
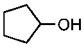
(20) This hypothesis was corroborated by subsequent observation of Me$_3$SiF in the ^{19}F NMR spectrum of a crude reaction mixture (δ_F −157.5 (decet, $^3J_{HF} = 7.6$ Hz)). Myers, E. L.; Butts, C. P.; Aggarwal, V. K. *Chem. Commun.* **2006**, 4434.

(21) The formation of biphenyl—from oxidative homocoupling of the arylsilane—was observed during the optimization process; this is comparable to Zhang's findings when trifluoroborate salts were assayed in oxy- and aminoarylation,[14] as well as Corma's reports that arylboronic acids are efficiently homocoupled by Au(III) complexes.[1b] These observations are the subject of ongoing investigations.

(22) We thank one of the reviewers for suggesting the use of AuCl as a precatalyst. While AuCl is effective as a catalyst, the reaction generates a higher proportion of biphenyl[21] as compared to Ph$_3$PAuCl.

Table 2. Oxyarylation of Terminal Alkenes: Investigation of Scope and Comparison of Arylsilanes[a] and Arylboronic Acids



entry	olefin 2	R^{1}OH	R^2	3, yield%[b]		
					Z = SiMe$_3$	Z = B(OH)$_2$[c]
1	**2a**	MeOH	H	**3a**	71	79
2	**2a**	EtOH	H	**3b**	69	85
3	**2a**	*i*-PrOH	H	**3c**	70 (80)	90
4	**2a**	*t*-BuOH	H	**3d**	-[d]	33
5	**2a**	NpOH	H	**3e**	80	91
6	**2a**	 OH	H	**3f**	57 (76)	85
7	**2a**	AcOH	H	**3g**	79	62
8	**2a**	MeOH	4-Me	**3h**	55 (79)	88
9	**2a**	MeOH	2-Me	**3i**	20 (29)	-
10	**2a**	MeOH	4-Br	**3j**	80	90
11	**2a**	MeOH	3-F	**3k**	63	79
12	**2a**	MeOH	4-MeO$_2$C	**3l**	80	83
13	**2b**	 OH	4-Br	**3m**	51	69
14	**2b**	AcOH	4-Br	**3n**	51	51
15	**2b**	H$_2$O	H	**3o**	76	76
16	**2c**	 OH	4-Br	**3p**	38	76
17	**2c**	NpOH	4-Br	**3q**	85	73
18	**2c**	H$_2$O	H	**3r**	78	73
19	**2d**	H$_2$O	H	**3s**	75	67

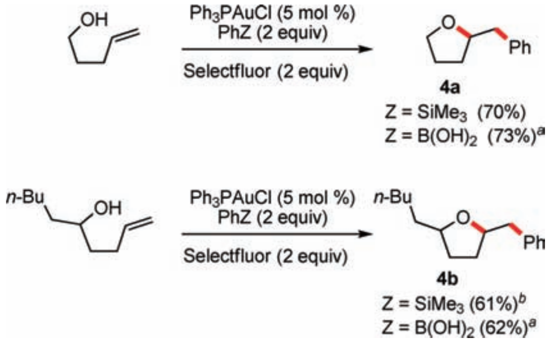
[a] Reaction conditions: olefin **2** (0.5 mmol), arylsilane (1.0 mmol), Selectfluor (1.0 mmol), Ph$_3$PAuCl (5 mol %), and R^{1}OH (0.5 mL for liquids, 5.0 mmol for solids and water) were stirred in anhydrous MeCN (0.1 M concentration of olefin) in a 7 mL vial under air at 70 °C. [b] Isolated yields; values in parentheses are calculated by recovered **2**. [c] Data for boronic acids taken from ref 15a. [d] 27% conversion observed by ^{1}H NMR of crude reaction mixture. Np is *neo*-pentyl (Me$_3$CCH$_2$−).

ligands in palladium[6,23] and Au(I) chemistry[24]—afforded **1** in only poor to moderate yield (entries 2 and 9). Also worthy of note is that excellent yields were obtained when a siloxane was used in place of the silane but that the analogous silanol performed poorly (compare entries 1, 10, and 11). Having identified Ph$_3$PAuCl as the preferred precatalyst, a screen of reaction conditions (Table S1, Supporting Information) indicated that portionwise addition of reagents and use of inert atmosphere was unnecessary, that the precatalyst loading could be lowered to 5 mol % without significant attenuation of yield, and that 2 equiv of both Selectfluor and arylsilane was required for high conversion of the alkene.[25]

Having identified optimal conditions[26] (Table 1, entry 12), we probed the reaction scope with regards to each of the three components (Table 2). Olefins **2** bearing both functionalized (**2a**, **2b**, and **2d**) and simple alkyl (**2c**) substituents proved suitable substrates for oxyarylation, reacting with a range of primary alcohols to afford the expected ethers in good to excellent yield. Use of secondary alcohols, however, resulted in lower yields and/or recovery of starting material **2**, suggesting sensitivity to the steric nature of the alcohol; with *tert*-butanol (entry 4), the expected product **3d** was not isolated.[27] In addition to alcohols, both acetic acid and water proved competent O-nucleophiles, furnishing acetates **3g** and **3n** and alcohols **3o**, **3r**, and **3s** in respectable yield. Variation of the arylsilane indicated that both electron-deficient and electron-rich arenes (compare, e.g., entry 1 with entries 8−12) could be employed in the key C−C bond forming step, with the best results obtained using silane reagents bearing an electron-withdrawing substituent. Again, use of sterically demanding reagents resulted in reduced yields (compare entries 8 and 9). Overall, the oxyarylation process tolerated a diverse range of functionality; that bromide—a versatile synthetic handle for use in further manipulations—could be incorporated in both the arylsilane and the olefin further illustrates the different reactivities of palladium and gold. The combination of arylsilanes with a commercially available precatalyst (5 mol % Ph$_3$PAuCl) afforded the oxyarylation products **3** in yields comparable to those obtained at the higher loadings of more complex precatalyst (dppm(AuBr)$_2$; 10 mol % in Au; dppm = bis(diphenylphosphino)methane) reported by Toste[15a] for arylboronic acids (Table 2).

The two-component reaction also proceeded efficiently under our optimized conditions: intramolecular alkoxycyclization of 4-penten-1-ol and subsequent arylation furnished 2-benzyltetrahydrofuran **4a** in 70% isolated yield (Scheme 2). 2-Benzyl-5-pentyltetrahydrofuran **4b** was similarly prepared in good yield from dec-1-en-5-ol.

Scheme 2. Two-Component Oxyarylation via Intramolecular Alkoxycyclization



[a] Data for boronic acids taken from ref 14. [b] Obtained as a 1:1.13 mixture of diastereomers (determined by ^{1}H NMR).

---

(23) (a) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555. (b) Huang, X.; Anderson, K. W.; Zim, D.; Jiang, L.; Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 6653. (c) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338.

(24) (a) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (b) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351.

(25) While excess silane remained in the crude reaction mixture, lowering the number of equivalents resulted in decreased yield of **1**.

(26) Despite furnishing **1** in marginally lower yield than the conditions outlined in Table 1, entry 1, the conditions in entry 12 were chosen as optimal on the grounds of lower precatalyst loading.

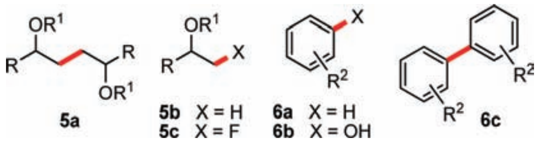


Figure 1. Possible side products of oxyarylation, arising from dimerization **5a**, protodeauration **5b**, or reductive elimination **5c** of an alkylgold fluoride intermediate or protodesilylation **6a** or oxidation **6b** of arylsilane reagents (not observed). Biaryl **6c**, from oxidative homocoupling of the silane reagent, was observed.

We carefully monitored the reaction for formation of potential side products: during the course of our investigations we did not observe the products arising from dimerization **5a**, protodeauration **5b**,[28] or reductive elimination **5c** (Figure 1) of a putative alkylgold fluoride intermediate.[14,15] The protio- **6a** or phenolic **6b** products arising from protodesilylation or oxidation of the arylsilanes also were not detected, although the homocoupled species **6c** was generated in 3−5% isolated yield (up to 7% by GC-FID) based on silane.[21]

In conclusion, we have demonstrated that arylsilanes can be employed in gold-catalyzed oxyarylation reactions, affording the products of two- and three-component coupling in generally good to excellent isolated yields. While the substrate scope—as seen in this preliminary study—is currently limited to terminal olefins, the rapid increase in molecular complexity that can be achieved may lend itself to the synthesis of biologically relevant compounds. The dual role of Selectfluor as both an oxidant and a source of fluoride negates the need for an additional, stoichiometric activator.[29] In addition, the ability to use a commercially available catalyst under air and the ease of preparation and benign nature of arylsilanes/siloxanes make this methodology a potentially important addition to the repertoire of gold-catalyzed oxidative transformations.

Acknowledgment. We thank Umicore AG & Co. KG for the generous donation of $HAuCl_4$. L.T.B. thanks the Bristol Chemical Synthesis Doctoral Training Centre, funded by EPSRC (EP/G036764/1), AstraZeneca, GlaxoSmithKline, Novartis, Pfizer, Syngenta, and the University of Bristol, for the provision of Ph.D. studentship. G.C.L.J. is a Royal Society Wolfson Research Merit Award Holder.

Supporting Information Available: Experimental procedures, characterization data. and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

OL1019162

---

(27) Integration of characteristic peaks[15a] in the ^{1}H NMR spectrum of the crude reaction mixture indicated that ca. 27% of *tert*-butyl ether **3d** had been formed.

(28) Cf. the formation of comparable species, either as the intended product or as a side product, from vinylgold intermediates: refs 10b−d, 11, and 12a.

(29) Use of alternative oxidants (CuF_2, AgF_2, $PhI(OAc)_2$, $[Ph_2I][OTf]$), with or without an external source of fluoride (TBAF, TBAT) under conditions analogous to Table 1, entry 12, gave product **1** in 0−2.8% yield; see Table S2, Supporting Information.