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Communications

Isolation of the Transmetalation Step in the Hiyama Cross-Coupling Reaction of Organosilanes

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Summary: The oxidative addition of o-(Me_2RSiCH_2O)-C_6H_4I *(*$R = Me, Ph, F$*) to palladium(0) complexes leads to the corresponding complexes o-*(Me_2RCH_2O)C_6H_4Pd-(L_2)I *(*$L = PPh_3, AsPh_3; L_2 =$ *dppf). The intramolecular Pd/Si transmetalation proceeds smoothly with fluorides and carbonates as the promoters.*

Transmetalation of organosilanes with organopalladium(II) complexes is a key step in the synthetically useful Hiyama cross-coupling reaction (eq 1),[1] an attractive alternative to the Stille coupling reaction of organostannanes.[2] However, although organosilanes

$$R^1\text{–}X + R^2\text{–}SiY_3 \xrightarrow[F^-]{[Pd]} R^1\text{–}R^2 + SiXY_3 \qquad (1)$$

are more convenient reagents than organostannanes in organic synthesis from the point of view of their toxicity and ecological impact, silanes are considerably less reactive toward transmetalation with the *in situ* generated organopalladium complexes.[3,4] In practice, palladium-catalyzed coupling of alkenyl or aryl halides with alkenyl-, allyl-, and alkynylsilanes (Hiyama reaction) is only possible in the presence of stoichiometric amounts of a fluoride salt as the activating agent.[5] The best results are usually obtained by using less readily available fluorosilanes as the nucleophilic partners,[1,5] although the presence of the fluoride ion (TASF or TBAF)[6] as a promoter is still necessary. Probably, the acceleration observed in the presence of fluoride is a consequence of the formation of a pentacoordinated fluorosilane intermediate, more nucleophilic toward the organopalladium in the rate-determining transmetalation step.[1,5,7,8] Fluoride salts have also been found to enhance the reactivity of alkenyl- and arylboronic acids in their cross-coupling with organic electrophiles (Suzuki reaction) by the likely formation of a reactive fluoroborate.[9,10] Alternatively, fluoride also promotes

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[⊗] Abstract published in *Advance ACS Abstracts*, April 15, 1997.

[1] Reviews: (a) Hatanaka, Y.; Hiyama, T. *Synlett* **1991**, 845. (b) Hiyama, T.; Hatanaka, Y. *Pure Appl. Chem.* **1994**, *66*, 1471.

[2] Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508.

[3] (a) For a review on the transmetalation of allyl-, alkenyl-, alkynyl-, and arylsilanes with Pd(II) salts, see: Akhrem, I. S.; Chistovalova, N. M.; Vol'pin, M. E. *Russ. Chem. Rev.* **1983**, *52*, 542. (b) Weber, W. P.; Felix, R. A.; Willard, A. K.; Koenig, K. E. *Tetrahedron Lett.* **1971**, 4701. (c) Yamamoto, K.; Shinohara, K.; Ohuchi, T.; Kumada, M. *Tetrahedron Lett.* **1974**, 1153.

[4] Allylsilanes are several orders of magnitude less reactive than allylstannanes toward electrophiles, see: Mayr, H.; Patz, M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 938.

[5] For additional references, not included in ref 1, see: (a) Takahashi, K.; Minami, T.; Ohara, Y.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2649. (b) Gouda, K.; Hagiwara, E.; Hatanaka, Y.; Hiyama, T. *J. Org. Chem.* **1996**, *61*, 7232. (c) Hiyama, T.; Matsuhashi, H.; Fujita, A.; Tanaka, M.; Hirabayashi, K.; Shimizu, M.; Mori, A. *Organometallics* **1996**, *15*, 5762.

[6] (a) TASF = tris(dimethylamino)sulfonium difluorotrimethylsilicate. (b) TBAF = tetrabutylammonium fluoride. (c) dba = dibenzylideneacetone. (d) dppf = 1,1′-bis(diphenylphosphino)ethane.

[7] The stereochemistry of the transmetalation step has been examined by using optically active benzylic trifluorosilanes leading to retention or inversion of configuration as a function of temperature and solvent polarity, see: Hatanaka, Y.; Hiyama, T. *J. Am. Chem. Soc.* **1990**, *112*, 7793.

[8] See also: (a) Chuit, C.; Corriu, R. J. P.; Reye, C.; Young, J. C. *Chem. Rev.* **1993**, *93*, 1371. (b) The driving force is the formation of a strong Si−F bond, see: Walsh; R. In *The Chemistry of Organic Silicon Compounds*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1989.

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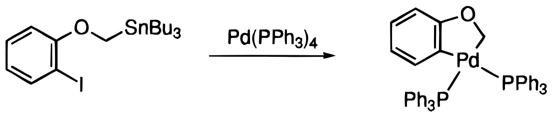
the reduction of phosphine palladium(II) complexes to palladium(0), probably by nucleophilic attack on the coordinated phosphine.[11]

We have recently reported that iodoaryl stannane **1** reacts with $Pd(PPh_3)_4$ to afford palladacycle **2**, as a result of an intramolecular Pd/Sn transmetalation of the intermediate oxidative addition arylpalladium(II) complex (eq 2).[12] We have now found that by using silanes instead of stannanes the intermediate complexes can be obtained as stable compounds, allowing one to systematically study the transmetalation step of an important cross-coupling reaction, isolated from the oxidative-addition and reductive-elimination steps. Importantly, the Pd/Si transmetalation can be promoted by the formation of a transient Pd−O bond.



1 **2** (2)

Silanes **3**, **4**, and **5**[13] reacted smoothly with $Pd(PPh_3)_4$ (toluene, 40 °C) or $Pd(dba)(AsPh_3)_2$[6c,14] (acetone, 23 °C) to give the oxidative-addition complexes **6**−**10** (Scheme 1). Similarly, reaction of **3** and **5** with Pd(dba)(dppf)[6d,15] (toluene, 23 °C) afforded **11** and **12**, respectively.[16]

Palladium(II) complexes **6**−**12** are stable compounds and did not suffer intramolecular Pd/Si transmetalation after being heated at 50 °C for 17 h ($CDCl_3$ or CD_3CN solutions). Furthermore, trimethylsilyl derivatives **6** and **11** failed to undergo transmetalation in the presence of fluoride anion as the promoter. We envisioned that the desired transmetalation could be achieved by using the less strongly coordinating ligand triphenylarsine,[17] which could facilitate the formation of a coordinatively unsaturated 14-electron complex, which would be more reactive in the transmetalation reaction.[18] This was shown to be the case. Thus, once TBAF was added to a solution of complex **7** in acetonitrile at 23 °C, transmetalation ensued to give palladacycle **13**[12b] (Table 1, entry 4). Addition of TASF led to only 22% conversion of **7** into **13** under these conditions (entry 3). Among the fluoride sources examined with **8**, only TBAF led to a significant conversion into **13** (entry 8). The more favorable cleavage of the alkyl−Si bond in the presence of a phenyl−Si bond in **8** is another example

Scheme 1

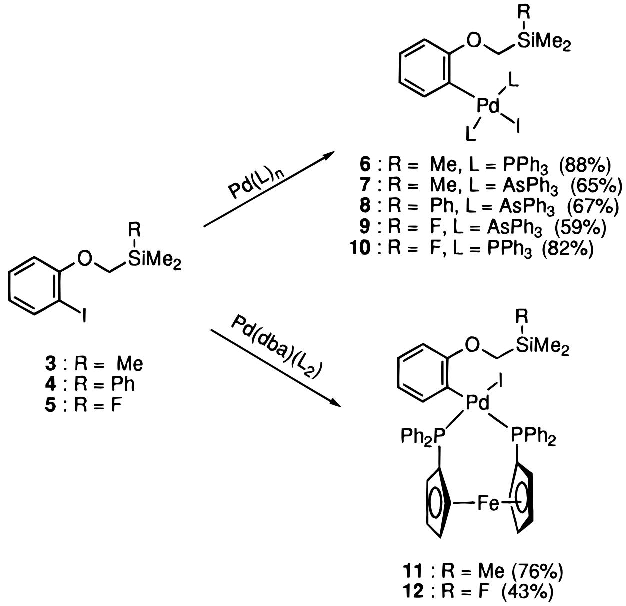
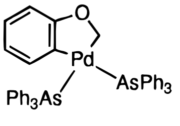


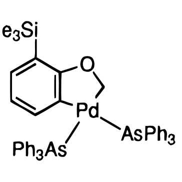
Table 1. Transmetalation of Complexes $Ar-Pd(L)_2-I$ (6−12) to Palladacycles 2, 13−15

entry no.	Ar−Pd−I	reagent[a]	*T* (°C)	reaction time (h)	palladacycle	yield (%)[b]
1	**6**	TBAF[c]	23			*d*
2	**6**	Ag_2CO_3	50			*d*
3	**7**	TASF	23	51	**13**	(22)
4	**7**	TBAF	23	51	**13**	(80)
5	**7**	Ag_2CO_3	23		**13** + **14**	95[e]
6	**7**	K_2CO_3	50	5	**13**	100
7	**8**	TASF	23			*d*
8	**8**	TBAF	23	51	**13**	(67)
9	**8**	Ag_2CO_3	23	51	**13**	(100)
10	**8**	K_2CO_3	50	44	**13**	(20)
11	**9**	TASF	23	1	**13**	(100)
12	**9**	TBAF	23	1	**13**	(100)
13	**9**	KF	23	51	**13**	(25)
14	**9**	Ag_2CO_3	23	2	**13**	70 (100)
15	**9**	K_2CO_3	23		**13**	(27)
16	**10**	Ag_2CO_3	23	1	**2**	94
17	**11**	Ag_2CO_3	50			*d*
18	**12**	Ag_2CO_3	23	1	**15**	100

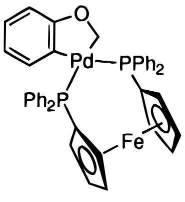
[a] Two molar equivalents of additive was used. Unless otherwise stated, the reactions were carried out in MeCN. [b] Isolated yields. Numbers in parentheses are for yields determined by ^1H NMR. [c] MeOH as the solvent. [d] No reaction was observed after 24−48 h. [e] A 1:1 mixture of **13** and **14**.



13



14



15

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(9) Wright, S. W.; Hageman, D. L.; McClure, L. D. *J. Org. Chem.* **1994**, *59*, 6095.

(10) For a recent review, see: Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(11) Mason, M. R.; Verkade, J. G. *Organometallics* **1992**, *11*, 2212.

(12) (a) Cárdenas, D. J.; Mateo, C.; Echavarren, A. M. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2445. (b) Mateo, C.; Cárdenas, D. J.; Fernández-Rivas, C.; Echavarren, A. M. *Chem. Eur. J.* **1996**, *2*, 1596.

(13) (a) Silane **3** was prepared by alkylation of *o*-iodophenol with (iodomethyl)trimethylsilane (92% yield). (b) Silane **4** was prepared similarly by using (chloromethyl)dimethylphenylsilane (81% yield). (c) Fluorosilane **5** was prepared from **4** by reaction with HBF_4 in CH_2Cl_2 at 23 °C (82% yield) (cf. Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29).

(14) This complex was prepared *in situ* by reaction of $Pd_2(dba)_3 \cdot dba$ with 2 equiv of $AsPh_3$. For the preparation of similar complexes, see: (a) Takahashi, Y.; Ito, T.; Sakai, S.; Ishii, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 1065. (b) Ukai, T.; Kawazura, H.; Ishii, Y.; Bonnet, J. J.; Ibers, J. A. *J. Organomet. Chem.* **1974**, *65*, 253. (c) Amatore, C.; Jutand, A.; Khalil, F.; M'Barki, M. A.; Mottier, L. *Organometallics* **1993**, *12*, 3168.

(15) (a) Xi, Z.; Yang, R.; Jin, D. *Chin. Chem. Lett.* **1991**, *2*, 331. (b) For the synthesis of related $PdL_2(dba)$ complexes (L_2 = dppe, dppp), see: Herrmann, W. A.; Thiel, W. R.; Brossmer, C.; Öfele, K.; Priermeier, T.; Scherer, W. *J. Organomet. Chem.* **1993**, *461*, 51.

(16) The isolation of a moderately stable stannane analogue of **12** with dppf as a ligand, which undergoes rapid transmetalation, has been recently achieved.[12b]

(17) (a) Farina, V.; Krishnan, B.; Marshall, D. R.; Roth, G. *J. Org. Chem.* **1993**, *58*, 5434. (b) Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585. (c) For a review, see: Farina, V. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 12, Chapter 3.4.

(18) Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11598.

of endocyclic restriction[19] in the intramolecular transmetalation reaction.[12] (Fluorosilyl)palladium(II) complex **9** was the most reactive, leading to **13** in almost quantitative yield in the presence of 1 equiv of TASF or TBAF (entries 11 and 12). Treatment of a solution of **9** in acetonitrile with potassium fluoride, which was a very poor promoter for the transmetalation of **7** and **8**, led to 33% conversion into **13** after 51 h at 23 °C (entry 13).[20]

Interestingly, an alternative procedure for the transmetalation was uncovered by using Ag_2CO_3 as the additive in the absence of fluoride anion. Thus, (dimethylphenylsilyl)palladium complex **8** led to **13** after being treated with Ag_2CO_3 (Table 1, entry 9). The fluorosilyl derivative **9** reacted very rapidly under these conditions (entry 14). However, trimethylsilyl derivatives **6** and **11** with phosphines as the donor ligand for palladium were also unreactive under these conditions. In contrast, (fluorosilyl)palladium complex **10** readily reacted in the presence of Ag_2CO_3 to afford palladacycle **2** (entry 16). Complex **7** reacted with Ag_2CO_3 in acetonitrile at 50 °C to give palladacycle **13**. Surprisingly, complex **13** was accompanied by an equimolar amount of the silyl-substituted complex **14** (entry 5). Formation of the last complex was unexpected, but it could be envisaged as taking place by cleavage of palladacycle **13** by a trimethylsilyl electrophile followed by aromatic palladation.[21] A similar result was obtained by using Ag_2O as the additive.[22] Significantly, the presence of silver ion was not essential for these reactions since the transmetalation of **7** could be cleanly achieved with K_2CO_3 in acetonitrile to give exclusively palladacycle **13** (entry 6). Furthermore, the use of silver salts like AgOTf, $AgBF_4$, or AgOTs gave negative results (either no reaction or extensive decomposition of **7**) under different reaction conditions. Reaction of **8** with K_2CO_3 also led to **13**, albeit in low yield (entry 10). Fluorodimethylsilyl complex **12** with a bidentate dppf ligand underwent smooth transmetalation in the presence of Ag_2CO_3 to give to oxapalladacycle **15** in quantitative yield (entry 18).

These experiments are in accord with the formation of an arylpalladium carbonato complex,[23,24] which may lead to a reactive arylpalladium oxo intermediate by decarboxylation. This proposal is in agreement with the activation promoted by Ag_2O. Therefore, these results suggest that formation of an intermediate palladium(II) complex with a Pd−O bond is key for the success of the Pd/Si transmetalation reaction. Interestingly, formation of complexes with a Pd−O bond has been proposed to accelerate the Pd/B transmetalation, which occurs in the Suzuki coupling reaction.[10,25,26]

In summary, we have achieved the intramolecular transmetalation of alkylsilanes with arylpalladium complexes, the key step in the Hiyama coupling reaction. The developed system allows one to study the effect of ligands and additives on the rate of the transmetalation step, isolated from the oxidative-addition and reductive-elimination steps. The preliminary results shown here demonstrate that the Pd/Si transmetalation can be promoted by the formation of a Pd−O bond. Additionally, the use of $AsPh_3$ as the ligand for palladium, which has been demonstrated to facilitate the transmetalation in the Stille reaction,[17] substantially accelerates the Pd/Si transmetalation step. The study of the effect of additional ligands and additives on the transmetalation and the application of these findings for the development of new coupling reactions are in progress.

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Supporting Information Available: Text giving the experimental details and characterization data for new compounds (7 pages). Ordering information is given on any current masthead page.

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[19] Beak, P. *Acc. Chem. Res.* **1992**, *25*, 215.

[20] The reduced reactivity of KF may be due, at least in part, to its low solubility in organic solvents. Similar results were obtained with CsF.

[21] Alternatively, complex **14** may arise by an oxidative-addition−reductive-elimination pathway. Studies on this subject are in progress.

[22] (a) As expected,[18] the addition of excess $AsPh_3$ slows down the transmetalation reaction. (b) Complex **7** also afforded palladacycle **13** in low yield in the presence of NaOH or Na_2HPO_4 as the additives (MeCN, 23 °C).

[23] For the formation of bis(triphenylphosphino)(carbonato)palladium(II), see: Nyman, C. J.; Wymore, C. E.; Wilkinson, G. *J. Chem. Soc. A* **1968**, 561.

[24] Reaction of Ag_2CO_3 with dichloro(diphosphine)platinum(II) complexes leads to (diphosphine)(carbonato)platinum(II) complexes, see: (a) Andrews, M. A.; Gould, G. L.; Voss, E. J. *Inorg. Chem.* **1996**, *35*, 5740. (b) Andrews, M. A.; Gould, G. L:, Klooster, W. T.; Koenig, K. S.; Voss, E. J. *Inorg. Chem.* **1996**, *35*, 5478 and references cited therein.

[25] The palladium-catalyzed coupling of allyl carbonates with alkenyl fluorosilanes proceeds in the absence of added fluoride. Presumably, the alkoxide leaving group promotes the transmetalation reaction, see: Matsuhashi, H.; Hatanaka, Y.; Kuroboshi, M.; Hiyama, T. *Tetrahedron Lett.* **1995**, *36*, 1539.

[26] Very recently, NaOH has been shown to promote the cross-coupling of organosilicon compounds with organic halides, see: Hagiwara, E.; Gouda, K.; Hatanaka, Y.; Hiyama, T. *Tetrahedron Lett.* **1997**, *38*, 439.