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Thermodynamics and Mechanism of the Reversible Tin-to-Palladium Transmetalation of the Furyl Group

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Transmetalation, the transfer of an organic moiety from one metal center to another, is an elementary organometallic process of importance in organic cross-coupling reactions, notably the palladium-catalyzed coupling of organostannanes with organic halides or triflates (Stille coupling).[1] We report here the first direct observation and spectroscopic characterization of an intermediate en route to transmetalation, using a cationic catalyst model. We also demonstrate that the transfer is reversible and report, for the first time, thermodynamic parameters relating the starting materials, products, and a key intermediate in a carbon transmetalation reaction.

Square planar complexes of the 2,6-bis(diphenylphosphino)-methylphenyl ligand[2] (**1**; see Scheme 1) are useful in the study of processes involving cationic palladium intermediates. The tridentate ligand inhibits both phosphine dissociation and reductive elimination of the aryl ring. The benzylic methylene protons resonate in an unobstructed region of the ^{1}H NMR spectrum ($\delta \approx 4.0$ ppm), and when the ligand is coordinated to palladium, they appear as a diagnostic virtual triplet.[3]

1 and the triflatopalladium complex **2** were prepared according to literature methods.[2] Treatment of **2** with excess tributylstannylfuran in cold, anhydrous acetone leads to rapid, quantitative precipitation of the furyl complex **3** (Scheme 1).[4] The structure of **3** was determined by X-ray analysis of crystals grown by vapor diffusion of pentane into a methylene chloride solution (Figure 1),[5] confirming the transmetalation of the furyl group. Formation of **3** is reversible.[6] Treatment of **3** with tributylstannyl triflate in CD_2Cl_2 leads to rapid regeneration of tributylstannylfuran and **2**.[7]

Transmetalation is preceded by coordination of 2-tributylstannylfuran to palladium via the tin-substituted double bond. Thus, when **2** is treated with 2-tributylstannylfuran in CD_2Cl_2 and observed in a cold (205−230 K) NMR probe, a small amount of **3** accumulates along with a larger amount of the furan adduct **4**.[7]

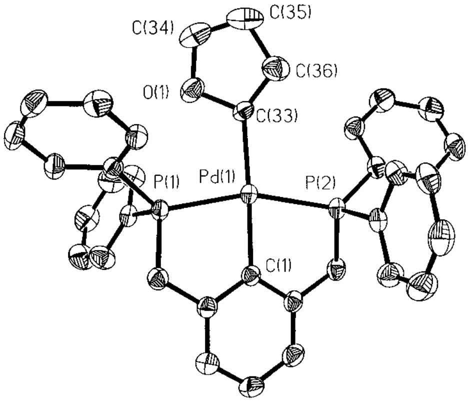
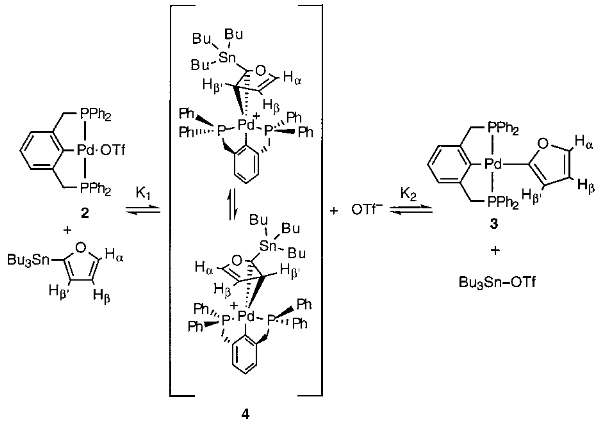


Figure 1. ORTEP drawing of **3**. Thermal ellipsoids are drawn at 50%. Hydrogen atoms are omitted for clarity.

Scheme 1



Formation of **3** and **4** is reversible upon warming the sample. The molecular identity of **4** was established by a series of ^{1}H, ^{31}P, and ^{119}Sn NMR experiments.[4] The furyl H_β signals[8] (see Scheme 1) are similar to those of the only structurally characterized η^2-furan complex, $[Os(NH_3)_5(C_4H_4O)]^{2+}$.[9] The strong upfield shift of $H_{\beta'}$ indicates dihapto coordination of the furan moiety.[10] A series of magnetization-transfer experiments unambiguously connects each of the furyl protons in **3** and **4** to a corresponding resonance in 2-tributylstannylfuran, confirming the regiochemistry of **4**. Thus, saturation of the H_β or $H_{\beta'}$ signal in 2-tributylstannylfuran leads to suppression of the corresponding resonance in **3** and **4**.[11]

The ^{119}Sn signal in **4** is, at +102 ppm, shifted strongly downfield from 2-tributylstannylfuran (δ −52 ppm). The ^{119}Sn chemical shift of tetrahedral R_3SnX molecules is a sensitive indicator of the polarization in the Sn−X bond (cf. Bu_3SnOTf, δ 172;[12] Me_3SnCl, δ 160; Me_3SnBr, δ 128; Me_3SnI, δ 39).[13] The Sn−C bond in **4** is polarized by complexation of the cationic

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[1] (a) Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *98*, 504. (b) Mitchell, T. N. *Chem. Soc. Rev.* **1992**, 803.

[2] (a) Rimml, H.; Venanzi, L. M. *J. Organomet. Chem.* **1983**, *259*, C6. (b) Rimml, H.; Venanzi, L. M. *J. Organomet. Chem.* **1984**, *260*, C52. (c) Rimml, H. Dissertation, ETH No. 7562, 1984. (d) Rimml, H.; Venanzi, L. M. *Phosphorus Sulfur* **1987**, *30*, 297.

[3] Verkade, J. G. *Coord. Chem. Rev.* **1972**, *9*, 1.

[4] Selected NMR data for **3** at 293 K. H_α: δ 7.52, d, $J_{\alpha\beta} = 1.7$ Hz, 1 ^{1}H.; H_β: δ 6.17, d of d, 1 ^{1}H $H_{\beta'}$ δ 5.79, d, $J_{\beta\beta'} = 2.9$ Hz, 1 ^{1}H −CH_2−: δ 4.12, t, $^{2}J_{PH} = 9.0$ Hz, 4 ^{1}H. ^{31}P: δ 33.1 (vs 85% H_3PO_4). Selected NMR data for **4** at 220 K. H_β: δ 6.19, br, 1 ^{1}H $H_{\beta'}$: δ 4.38, d, $J = 2.1$ Hz, 1 ^{1}H −CH_2−: δ 3.8 − 3.9, v br. ^{31}P: δ 34 (vs 85% H_3PO_4), v br. ^{119}Sn: δ 102 (vs $SnMe_4$), br.

[5] Selected bond lengths (Å): Pd(1)−C(33), 2.089(2); Pd(1)−C(1), 2.073(2); Pd(1)−P(1), 2.2709(5); Pd(1)−P(2), 2.2921(5); C(33)−C(36), 1.331(3); C(35)−C(36), 1.446(4); C(34)−C(35), 1.341(4); C(34)−O(1), 1.367(3); C(33)−O(1), 1.433(3). Selected angles and dihedrals (deg): P(1)−Pd(1)−P(2), 160.58(2); C(1)−Pd(1)−C(33), 176.91; O(1)−C(33)−Pd(1)−C(1), −54.85(1.53); C(33)−Pd(1)−C(1)−C(2), 15.87(1.55). Sum of angles about Pd, 359.95°.

[6] Reversible transfer of alkynyl groups among Pd(II), Pt(II), and Cu(I) centers has recently been described: Osakada, K.; Sakata, R.; Yamamoto, T. *J. Chem. Soc., Dalton Trans.* **1997**, 1265.

[7] A small amount of another, unidentified organopalladium species is also formed, the concentration of which is temperature invariant and which does not contain a furyl moiety.

[8] The H_α signal is lost in the crowded aryl region.

[9] (a) Cordone, R.; Harman, W. D.; Taube, H. *J. Am. Chem. Soc.* **1989**, *111*, 5969. (b) Chen, H.; Hodges, M.; Liu, R.; Stevens, W. C., Jr.; Sabat, M.; Harman, W. D. *J. Am. Chem. Soc.* **1994**, *116*, 5499.

[10] Transition metal complexes of furan oxygen are unknown, except where the furan ring is part of a macrocyclic ligand. See: (a) Crescenzi, R.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Inorg. Chem.* **1996**, *35*, 2413. (b) Chmielewski, P. J.; Latos-Grazynski, L.; Olmstead, M. M.; Balch, A. L. *Chem. Eur. J.* **1997**, *3*, 268.

[11] A reviewer has suggested an alternative structure for **4**, in which the furan moiety adopts a zwitterionic, allyl(C_α−C_β−$C_{\beta'}$)/oxonium structure. We currently disfavor this alternative because of the very weak perturbation of the H_β resonance in **4** relative to **3** and free 2-tributylstannylfuran.

[12] Arshadi, M.; Johnels, D.; Edlund, U. *Chem. Commun. (Cambridge)* **1996**, 1279.

10.1021/ja980901w CCC: $15.00

palladium fragment, with the tin atom acquiring substantial positive charge. The ability of tin to stabilize adjacent charge is well-known,[14] and it undoubtedly contributes to the stability of the Pd(olefin) bond in **4**. Coordination of Pd to the more hindered double bond is surprising, but as Scheme 1 illustrates, this produces a sterically favorable isomer. Coordination of the unsubstituted double bond would bring the tributyltin moiety into closer contact with the phosphine phenyl groups.

Complex **4** is unsymmetrical, with inequivalent ^{31}P and methylene resonances expected from the two sides of the ligand. These diastereotopic sites undergo rapid exchange, even at low temperatures. Thus, both the ^{1}H methylene and the ^{31}P resonances for **4** at 205 K are very broad, while the same signals for **2** are sharp. Loss of furan followed by coordination of the opposite face provides the most obvious means of exchange. Exchange must occur without diffusion of the furan away from the palladium center and regeneration of **2**.[15]

The observation of **4** in equilibrium with **2** and **3** does not demonstrate that **4** is a true intermediate. Better evidence is found in a further magnetization-transfer experiment. In an equilibrating mixture at 205 K, saturation of $H_{\beta'}$ in **4** leads to suppression of $H_{\beta'}$ in **3**. Transfer of magnetization between the two minor components of the system, in the presence of a ~10-fold excess of 2-tributylstannylfuran (with respect to **4**), strongly suggests that **4** is indeed an immediate precursor to **3**. Decoordination of the furan ligand in **4** prior to formation of **3** would result in loss of magnetization in **3**.

The temperature regime in which **2**, **3**, and **4** can be simultaneously observed by NMR is narrow.[16] Despite this limitation, a quantitative treatment of the equilibria connecting these species is informative.[17] The thermodynamic parameters for the two processes are significantly different. Substrate binding to **2** is exothermic ($\Delta H_1 = -5(1)$ kcal/mol); subsequent transfer of the furyl group to palladium is endothermic ($\Delta H_2 = +3(1)$ kcal/mol). Substrate binding requires a substantial loss of entropy ($\Delta S_1 = -28(4)$ eu) as would be expected for an associative event. Some entropy is regained after transmetalation ($\Delta S_2 = +12(5)$ eu). The overall reaction is weakly endothermic ($\Delta H_{\mathrm{rxn}} = -1.6(0.2)$ kcal/mol) and proceeds with a modest loss of entropy ($\Delta S_{\mathrm{rxn}} = -16(1)$ eu), rendering it somewhat endergonic at room temperature ($K_{298,\mathrm{calc}} \approx 10^{-3}$). Although these values must be interpreted with caution, they draw a clear distinction between the thermodynamic requirements of the reaction steps.

These results constitute the most detailed sketch presently available for a carbon transmetalation pathway.[18] The observation of **4** establishes that substrate precoordination is an important activating step when transmetalation occurs to an electrophilic Pd fragment and that reversible η^2 coordination is viable for aromatic heterocycles. These experiments do not reveal the process by which the adduct **4** collapses to product. We are continuing our investigations into the details of cationically promoted transmetalation.

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Supporting Information Available: Details of the preparation and crystallographic study of **3**, procedures for spectroscopic experiments and representative spectra, and equilibrium constant data (16 pages, print/PDF). This material is contained in many libraries on microfiche, immediately follows the article in the microfilm version of the journal, and can be ordered from the ACS. See any current masthead page for ordering information. See any current masthead page for ordering information and Web access instructions.

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[13] Many ^{119}Sn chemical shifts and a discussion of chemical shift correlations in compounds of group 14 elements appear in: Mitchell, T. N. *J. Organomet. Chem.* **1983**, *255*, 279.

[14] Lambert, J. B.; Wang, G.-t.; Teramura, D. H. *J. Org. Chem.* **1988**, *53*, 5422.

[15] Other mechanisms are possible, for example, formation of an η^1-allyl/oxonium intermediate (see ref 11) and rotation about Pd−C.

[16] Below 205 K, precipitation within the sample tube results in loss of signal.

[17] Concentrations of palladium species were determined from integration of the appropriate methylene and/or furyl signals relative to an internal toluene standard. Concentrations of the tin reagents were calculated stoichiometrically.

[18] Hartwig recently described a mechanism for the activation of tin−sulfur bonds by neutral palladium intermediates (Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11598). In that case, the stannane clearly behaves as an electrophile, and the palladium center proceeds partly toward oxidative addition in a concerted process.