

Snapshots of a Stille reaction

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Received (in Liverpool, UK) 1st November 2000, Accepted 12th January 2001

First published as an Advance Article on the web 31st January 2001

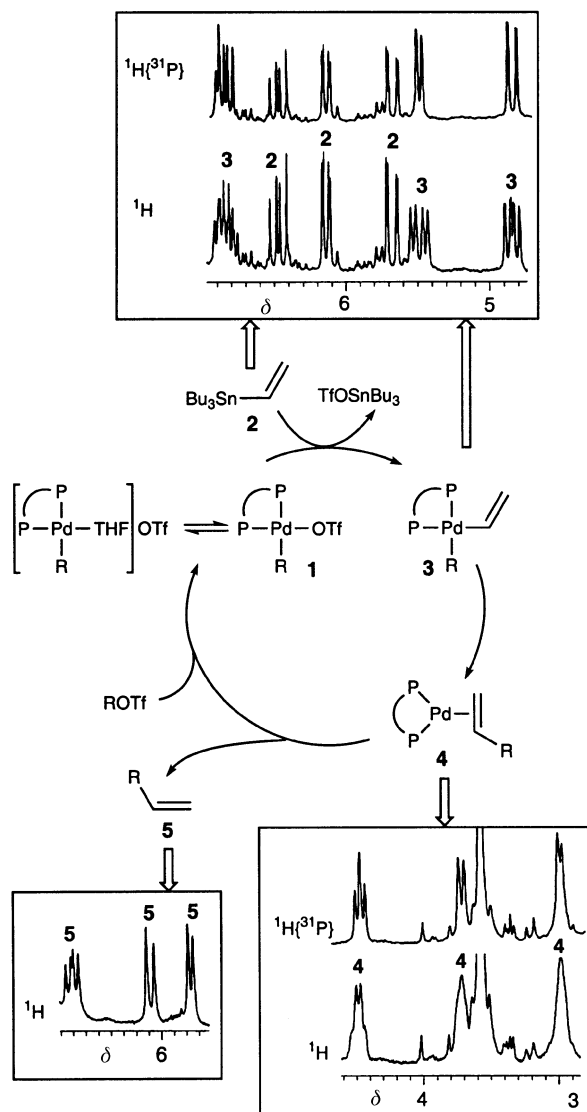
The main sequential intermediates involved in a real catalytic cycle of the Stille reaction (the coupling of ROTf with $\text{CH}_2=\text{CHSnBu}_3$ catalyzed by $[\text{PdR}(\text{OTf})(\text{dppe})]$; R = aryl) are observed and characterized unequivocally before the coupling product is released.

Only in rare occasions can real intermediates in a catalytic cycle be observed and unambiguously identified. The Stille reaction (palladium-catalyzed coupling of organotin reagents with carbon electrophiles) is nowadays one of the most powerful synthetic methods for the formation of carbon-carbon bonds.¹ Its catalytic cycle involves a number of intermediates, but evidence for these only comes from model reactions outside a real cycle. Echavarren and coworkers have synthesized oxo- and aza-palladacycles using the oxidative addition of haloaryl-stannanes to Pd(0) complexes, followed by an intramolecular transmetalation, thus the products can be considered intermediates of a frustrated Stille cycle, which do not undergo coupling because of the high energy of the coupling product.² We have shown that the coupling of halides R^1I with SnR^2Bu_3 (R^2 = vinyl or phenyl) follows a $\text{S}_{\text{E}}2$ mechanism involving an associative L-for- R^2 substitution on *trans*- $[\text{PdR}^1\text{IL}_2]$. This Pd(II) complex, which can be prepared separately, was actually observed as involved in the catalytic cycle.³ More recently we have observed the formation and fading out of *trans*- $[\text{PdR}^1\text{R}^2\text{L}_2]$ in the coupling of triflates R^1OTf with $\text{Sn}(\text{vinyl})\text{Bu}_3$.⁴ Here we present a catalytic Stille coupling in which all the main intermediates involved are observed, as they are formed and disappear, using ^1H , ^{19}F and ^{31}P NMR spectroscopy.

$[\text{Pd}(\text{C}_6\text{F}_5)(\text{OTf})(\text{dppe})]$ **1a** [dppe = 1,2-bis(diphenylphosphino)ethane] is a poor catalyst for the coupling, in THF at 50 °C (Pd:Sn = 1:20), of $\text{C}_6\text{F}_5\text{OTf}$ and $\text{CH}_2=\text{CHSnBu}_3$ **2** to give $\text{CH}_2=\text{CHC}_6\text{F}_5$. When the reaction was carried out in THF- d^8 at low temperature, starting with $[\text{Pd}(\text{C}_6\text{F}_5)(\text{OTf})(\text{dppe})]$ and $\text{CH}_2=\text{CHSnBu}_3$ in 1:1 molar ratio, several intermediate species could be detected and identified until the coupling product was formed. For an easier monitoring of the cycle the studies were repeated on $[\text{Pd}(\text{C}_6\text{Cl}_2\text{F}_3)(\text{OTf})(\text{dppe})]$ **1b** ($\text{C}_6\text{Cl}_2\text{F}_3$ = 3,5-dichlorotrifluorophenyl), which behaves identically to **1a** and shows the same intermediates, but has more simple ^{19}F NMR spectra, facilitating a more accurate integration of the signals.⁵ Scheme 1 shows, step by step, the mechanism of the catalytic cycle and the ^1H NMR spectra of the intermediates identified in the stoichiometric cycle for **1b** while Fig. 1 shows the evolution of the reaction, as monitored by ^{19}F NMR.

The first intermediate in the cycle is **1a** (or **1b**). Under catalytic conditions **1a** is formed very slowly by oxidative addition of $\text{C}_6\text{F}_5\text{OTf}$ to $[\text{Pd}(0)]$, but stoichiometrically these compounds are better prepared from $[\text{PdRCl}(\text{dppe})]$ (R = C_6F_5 , $\text{C}_6\text{Cl}_2\text{F}_3$) and AgOTf . Complexes **1a** and **1b** are stable in the solid state and have been isolated and fully characterized.⁶ In solution in dry THF they give the ionic species $[\text{PdR}(\text{dppe})(\text{THF})](\text{OTf})$ (specific molar conductivity, $\Lambda_{\text{m}} = 4.66 \text{ S cm}^{-1} \text{ mol}^{-1}$ for **1a**),⁷ on which the transmetalation occurs.⁴

The next step is the transmetalation on **1b** leading to a σ -vinyl complex $[\text{Pd}(\text{C}_6\text{Cl}_2\text{F}_3)(\text{CH}=\text{CH}_2)(\text{dppe})]$ **3**, characterized by NMR. Its ^{19}F NMR spectrum shows the characteristic resonances expected for a $\text{C}_6\text{Cl}_2\text{F}_3$ group linked to Pd(II), with the



Scheme 1 Catalytic cycle showing the ^1H NMR spectra of the products detected in the range of vinylic protons.

F_{ortho} coupled to the *trans* phosphorus atom (coupling to the *cis* phosphorus is not observed). In the $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum two signals are observed: one for the *P trans* to $\text{C}_6\text{Cl}_2\text{F}_3$, which appears as an overlapped doublet of triplets, and one for the *cis* phosphorus which appears as a doublet. The ^1H NMR spectrum (Scheme 1) shows three resonances for the three vinylic protons, coupled to phosphorus (see changes upon ^{31}P irradiation in the corresponding $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum).

Complex **3** is unstable and can be observed only at low temperature.⁸ In spite of the *cis* configuration of this complex, the reductive elimination step takes place less easily than with PPh_3 because of the small bite angle chelating ligand,⁹ and this stabilizes the compound sufficiently for it to be observed.¹⁰ The

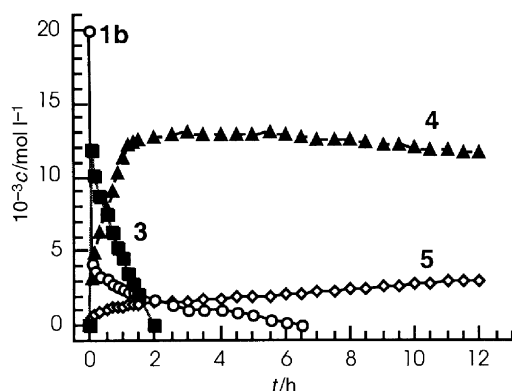


Fig. 1 Profiles of the reaction between $[\text{Pd}(\text{C}_6\text{Cl}_2\text{F}_3)(\text{OTf})(\text{dppe})]$ **1b** and $\text{CH}_2=\text{CHSnBu}_3$ **2** in THF at 243 K. Concentrations were obtained by integration in the ^{19}F NMR spectra. Starting concentration: 0.02 mol L^{-1} in **1b**.

coupling product remains coordinated stabilizing a Pd^0 complex $[\text{Pd}(\text{dppe})(\eta^2\text{-CH}_2=\text{CHC}_6\text{Cl}_2\text{F}_3)]$ **4**. Its ^1H NMR spectrum (Scheme 1) shows three broadened signals, at higher field than in the σ -vinyl complex **3** due to the bigger shielding produced by the metallic center. They are coupled to each other (as seen by ^1H COSY) and also coupled with the phosphorus nuclei of the dppe ligand. In the $^1\text{H}\{^{31}\text{P}\}$ NMR spectrum (Scheme 1) only the coupling between protons is observed. The ^{31}P NMR spectrum of **4** shows an AB system. This chemical inequivalence of the two P atoms is consistent with a trigonal-planar coordination of the palladium, with the double bond of the asymmetric olefin lying in the plane containing the palladium atom and two phosphorus atoms. Similar complexes have been reported in the literature.¹¹ This compound is again rather stable and can be observed even at room temperature in the stoichiometric reaction. Upon decomposition (or when it undergoes oxidative addition) the olefin $\text{CH}_2=\text{CHC}_6\text{Cl}_2\text{F}_3$ **5** is released.

In catalytic conditions the cycle should close upon oxidative addition to **4** or to a low coordinated $[\text{Pd}(0)]$ complex formed by decoordination of **5**. This oxidative addition is extremely slow and decomposition pathways compete, causing the low efficiency of the catalyst.^{11a} However, four to five turnovers are observed showing that the cycle is actually catalytic. Alternatively, the oxidative addition step can be accelerated very efficiently by adding LiCl once **4** has been formed [the accelerating effect of LiCl on some Stille catalytic cycles is well documented in ref. 1(a), and is discussed in ref. 11(a)]. This leads to the easy formation of $[\text{PdRCl}(\text{dppe})]$ on which, however, transmetalation is extremely slow. A thorough discussion of these observations will be made in a forthcoming full paper.

This article is dedicated to Professor Rafael Usón on occasion of his 75th birthday. The work was supported by the Dirección General de Investigación Científica y Técnica (Project No. PB96-0363) and the Junta de Castilla y León (Project No. VA80-99). A. M. G. is grateful for a grant from the Dirección General de Enseñanza Superior (Spain).

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- 1a** and **1b** were prepared from their corresponding precursors,¹² by treatment of $[\text{PdRCl}(\text{dppe})]$ with AgOTf, removal of the AgCl led to crystallisation. **1a**: yield: 89%; calc. for $\text{C}_{33}\text{H}_{24}\text{F}_6\text{O}_3\text{P}_2\text{PdS}$: C, 48.28; H, 2.95; found: C, 48.62, H 3.17%; ^{19}F NMR (ref. CFCl_3 , CDCl_3 -THF), δ -78.22/-74.71 (s, CF₃), -118.52/-113.70 (m, *o*-CF), -158.88/-157.76 (t, $^3J_{\text{FF}}$ 19.5 Hz, *p*-CF), -162.50/-160.43 (m, *m*-CF); $^{31}\text{P}\{^1\text{H}\}$ NMR (ref. 85% H_3PO_4 , CDCl_3 -THF), δ 61.9/67.9 (m, *P*_{cis}), 46.3/52.6 (m, *P*_{trans}); ^1H NMR (300 MHz, ref. TMS, CDCl_3), δ 7.85-7.40 (m, arom-CH), 2.57 (m, CH₂), 2.19 (m, CH₂). **1b**: yield: 87%; calc. for $\text{C}_{33}\text{H}_{24}\text{Cl}_2\text{F}_6\text{O}_3\text{P}_2\text{PdS}$: C, 46.42, H, 2.83%; found: C 46.28, H, 2.83%; ^{19}F NMR (CDCl_3 -THF), δ -78.19/-74.72 (s, CF₃), -92.46/-87.43 (dd, $^4J_{\text{FP}(\text{trans})}$ 13.5, $^4J_{\text{FP}(\text{cis})}$ 7.5 Hz, *o*-CF), -117.26/-115.14 (s, *p*-CF); $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 -THF), δ 61.6/67.5 (dt, $^2J_{\text{PP}}$ 15.5, $^4J_{\text{FP}}$ 7.5 Hz, *P*_{cis}), 46.0/51.7 (dt, $^2J_{\text{PP}}$ 15.5, $^4J_{\text{FP}}$ 13.5 Hz, *P*_{trans}); ^1H NMR (CDCl_3), δ 7.85-7.43 (m, arom-CH), 2.55 (m, CH₂), 2.18 (m, CH₂).
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- NMR characterization of the intermediates*: **3**: ^{19}F NMR (THF, 243 K), δ -85.41 (d, $^4J_{\text{FP}}$ 10.8 Hz, *o*-CF), -119.11 (s, *p*-CF); $^{31}\text{P}\{^1\text{H}\}$ NMR (THF, 243 K), δ 47.2 (dt, $^2J_{\text{PP}}$ 21.3, $^4J_{\text{FP}}$ 10.8 Hz, *P*_{trans}), 44.0 (d, $^2J_{\text{PP}}$ 21.3 Hz, *P*_{cis}); ^1H NMR ($[\text{D}_8]\text{THF}$, 243 K), δ 8.00-6.88 (m, arom-CH), 6.83 (m, *trans*- J_{HH} 18.3, *cis*- J_{HH} 10.9, $^3J_{\text{HP}(\text{trans})}$ 10.9, $^3J_{\text{HP}(\text{cis})}$ 8.3 Hz, CH), 5.49 (dddd, *cis*- J_{HH} 10.9, *gem*- J_{HH} 2.2, *trans*- $J_{\text{HP}(\text{trans})}$ 25.1, $^4J_{\text{HP}(\text{cis})}$ 2 Hz, CH), 4.84 (ddd, *trans*- J_{HH} 18.3, *gem*- J_{HH} 2.2, *cis*- $J_{\text{HP}(\text{trans})}$ 11.7 Hz, CH), 3.00 (br, CH₂), 2.40 (br, CH₂). **4**: ^{19}F NMR (THF, 243 K), δ -114.64 (s, *o*-CF), -123.24 (s, *p*-CF); $^{31}\text{P}\{^1\text{H}\}$ NMR (THF, 243 K), δ 42.5 (d, $^2J_{\text{PP}}$ 48.4 Hz, P), 38.7 (d, $^2J_{\text{PP}}$ 48.4 Hz, P); ^1H NMR ($[\text{D}_8]\text{THF}$, 243 K), δ 7.85-6.80 (m, arom-CH), 4.49 (br. m, *trans*- J_{HH} 12.5, *cis*- J_{HH} 9.6, $^3J_{\text{HP}(\text{trans})}$ 9.5 Hz, CH), 3.72 (br, *trans*- J_{HH} 12.5 Hz, CH), 2.98 (br, *cis*- J_{HH} 9.6 Hz, CH), 2.50 (br, CH₂), 2.10 (br, CH₂).
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