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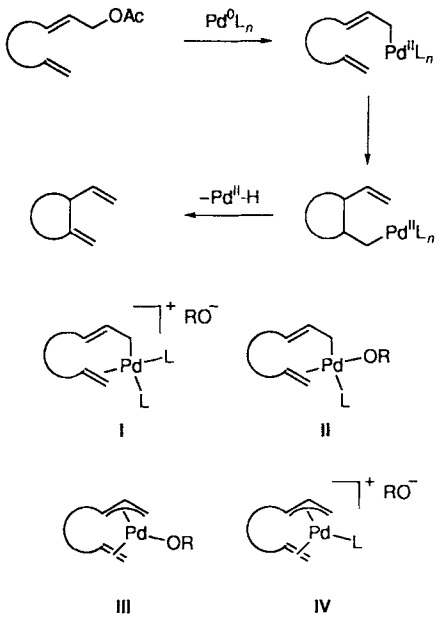

Scheme 1. Palladium–ene reaction with possible intermediates.

Cationic Intermediates in the Intramolecular Insertion of Alkenes into (η^3-Allyl)palladium(II) Complexes**

Enrique Gómez-Bengoa, Juan Manuel Cuerva, Antonio M. Echavarren,* and Gabriel Martorell

In memory of Wolfgang Oppolzer

The palladium-catalyzed intramolecular carbocyclization of allyl acetates with alkenes is a powerful method for the formation of five- and six-membered rings.[1, 2] Most of these reactions only proceed satisfactorily in polar solvents such as HOAc at 70–100 °C in the presence of a palladium(0) catalyst with PPh_3 ligation.[1–3] Oppolzer et al. have hypothesized that carbopalladation may proceed by a pericyclic-type reaction of a (η^1-allyl)palladium(II) complex (palladium–ene reaction, Scheme 1).[1, 2] Although the coordination at the metal center is undetermined in most mechanistic proposals, it seems likely that, in the presence of excess ligand, the key intermediate is coordinated with two donor phosphane ligands, for example as in **I**, which could be in equilibrium with neutral (η^1-allyl)-palladium(II) complex **II** (R = Ac). Alternatively, the insertion may proceed via (η^3-allyl)palladium(II) complexes **III** or **IV**.[4]

It would be desirable to perform the cyclization of allylic substrates bearing sensitive functionalities under milder and/or neutral reaction conditions. In addition, we have observed that the usual reaction conditions[5] are not satisfactory for the cyclization of the more highly substituted allyl substrates. We therefore decided to examine the reaction under stoichiometric conditions. An important motivation for studying the mechanism of this cyclization in more detail was the prospect of rationally developing asymmetric versions with appropriate mono- or bidentate chiral ligands. Here we report that the reaction proceeds through cationic complexes of type **IV**, in which the palladium atom is coordinated with only one phosphane ligand.

The (η^3-allyl)palladium(II) complexes were prepared from the allyl trifluoroacetates.[6, 7] Thus, **1** was treated with $[Pd_2(dba)_3]\cdot$dba (dba = dibenzylideneacetone)[8] in THF/MeCN (3/1) at 25 °C to afford **2** in quantitative yield (Scheme 2). The ^{13}C NMR spectrum of **2** showed resonances for the η^3-allyl carbon atoms at δ = 93.3, 80.6, and 75.0. The alkene group gave rise to signals at δ = 115.4 and 107.2, which is in agreement with the expected values for an η^2-coordinated olefin (Table 1).[9–11] Treatment of **2** with excess NaOAc (acetone, 25 °C) led to complex **3**, which on attempted isolation underwent reductive elimination to furnish the allylic acetate **4**.[7a, 12, 13] Trifluoracetato complexes **5** and **6** were prepared from **2** with one equivalent of 1,10-phenanthroline (phen; Et_2O, 25 °C, 10 min, 95%)[14] or 1,2-bis(diphenylphosphane)ethane (dppe; Et_2O, 25 °C, 45 min, 73%). Complex **7** was prepared in almost quantitative yield from **2** with two equivalents of PPh_3 ($CDCl_3$, 25 °C). Reaction of **2** with one equivalent of PPh_3 afforded **8**. The NMR spectra of **5**–**8** clearly showed a noncoordinated alkene.[15]

The trifluoroacetato complex **2** was very stable and failed to cyclize after being heated at reflux in [D_6]benzene, [D_6]acetone, or $CDCl_3$. In contrast, the acetato complex **3** yielded **4** and metallic palladium after being heated at 60–70 °C in [D_6]benzene or $CDCl_3$. Complexes **5**–**7**, which are likely precursors to complexes of type **I**, also failed to cyclize under the usual conditions (0.2–0.02 M solutions).[16]

Complex **8**, which was stable in solution at 25 °C for several days, underwent smooth cyclization in [D_6]benzene or $CDCl_3$ at reflux to yield **11** and **12** (1:1) in almost quantitative yield. The alkene of **8** can presumably displace the trifluoroacetate ligand to give cationic **9**, which undergoes insertion and β-hydrogen

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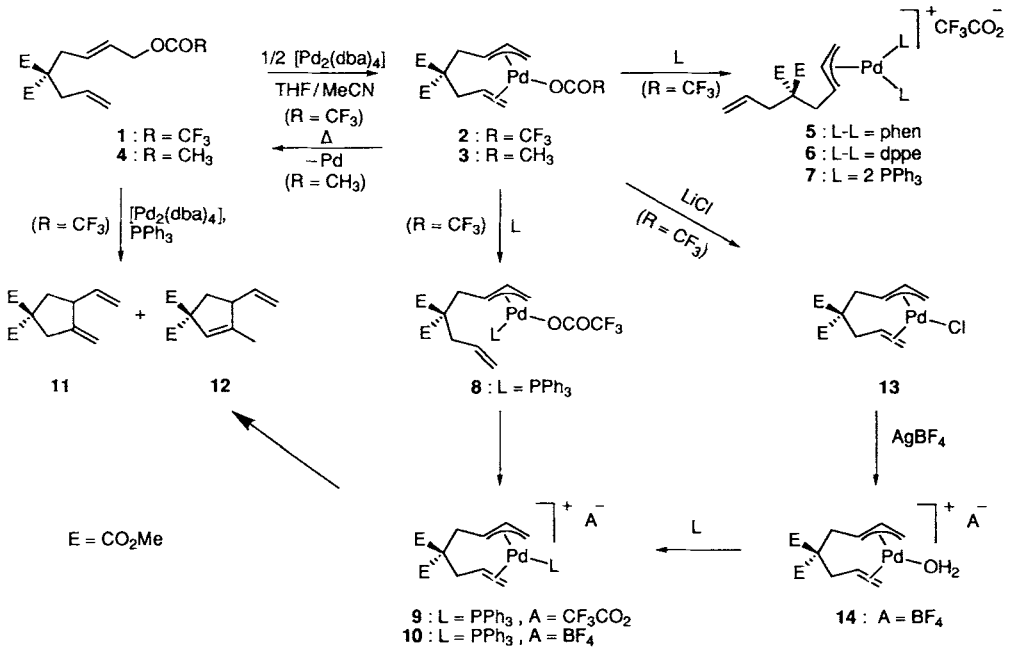

Scheme 2.

elimination to yield **11**[1] and a palladium hydride. The more stable endocyclic alkene **12** originates from the reaction of the palladium hydride with **11** followed by elimination. An increase in the cone angle of the phosphane[17] has a detrimental effect on the cyclization rate. Thus, addition of one equivalent of a bulky ligand such as PCy_3 or $P(o\text{-}MeC_6H_4)_3$ led to slower cyclizations in $CDCl_3$.[18] On the other hand, poorer donor ligands (for example $P(OMe)_3$, $P(OPh)_3$, or $AsPh_3$) led to incomplete conversions into **11** and **12**. The best results were obtained by treatment of **8** with $NaBF_4$ in CH_2Cl_2: the cyclization of **8**, presumably proceeding via **10**, at 30 °C gave pure **11** in 62% yield (24 h, 82% conversion by ^1H NMR spectroscopy).[19]

Isolation of the key cationic intermediates **9** or **10** could not be achieved from **8**, since the cyclization proceeded at a rate similar to that of ligand substitution. An alternative synthesis of **10** was realized from **13** (Table 1), which was readily prepared in quantitative yield from **2** and excess LiCl in acetone (Scheme 2). Complex **13**[20] showed no propensity to cyclize after being heated in $CDCl_3$. Treatment of **13** with $AgBF_4$ gave cationic **14**, in which the metal is coordinated with one water molecule (Table 1).[21] Addition of one equivalent of PPh_3 led quantitatively to **10**, whose structure was confirmed by NMR spectroscopy. $^1H-^{13}P$ HOESY correlation demonstrated that the palladium center is coordinated with the phosphane, alkene, and allyl group (η^3, Figure 1).[22] In contrast with **14**, which failed to undergo cyclization, a smooth reaction was observed for **10** (CH_2Cl_2, 30 °C), giving a mixture of five-membered ring carbocycles.[23]

The results summarized in Scheme 2 suggested that the cyclization of **1** could be effected under neutral conditions with a palladium catalyst containing just one equivalent of phosphane as ligand. Indeed, **1** was converted into **11** (75–79% yield, contaminated with about 5% of **12**) in the presence of 5 mol% $[Pd_2(dba)_3]\cdot dba$ and 10 mol% PPh_3 or PCy_3 in toluene at 100 °C for 24 h.[24] The inertness of complexes with bidentate ligands (for example **5** and **6**) towards insertion was also demonstrated under catalytic conditions.[25]

These results indicate that formation of intermediates of type **IV** is the key to successful cyclization. When allyl acetates are used as the starting materials under catalytic conditions, both oxidative addition and formation of cationic **IV** are unfavorable processes. In these cases, the acidic solvent probably promotes the reaction by protonation of the acetate ligand, thereby facilitating formation of **IV**. Although this study does not exclude the involvement of internal η^1-allyl species as intermediates in the catalytic cycle,[26, 27] the results are in accordance with direct insertion of the η^3-allyl group into the alkene. Our conclusions are supported by the recent, independent work of Keim et al. and Brookhart et al.,[28] which demonstrate that insertion of ethylene proceeds smoothly on cationic (η^3-allyl)palladium complexes.

We have found that cyclization of substrates such as **1** may proceed under neutral conditions. Cationic complexes, which are key intermediates in the palladium-catalyzed reactions of

Table 1. Selected physical and spectroscopic data for complexes **2**, **8**, **10**, **13**, and **14** [a].

2: ^1H NMR (300 MHz, $CDCl_3$) [b]: δ = 5.43 (ddd, J = 13.0, 10.6, 7.7 Hz, 1H), 5.24 (dtd, J = 14.5, 10.8, 2.4 Hz, 1H), 4.97 (d, J = 7.4 Hz, 1H), 4.82 (d, J = 9.1 Hz, 1H), 4.46 (br. d, J = 5.4 Hz, 1H), 4.03 (d, J = 13.3 Hz, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.78–3.60 (m, 1H), 3.19 (br. d, J = 14.1 Hz, 1H) 2.67 (dd, J = 14.9, 2.9 Hz, 1H), 1.70–1.40 (m, 1H), 1.43 (dd, J = 8.8, 2.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$): δ = 170.41, 169.64, 162.18 (q, $^2J(C,F)$ = 34.4 Hz), 116.08 (q, $^1J(C,P)$ = 291.4 Hz), 115.36, 107.20, 93.34, 80.65, 74.97, 61.64, 53.39, 53.24, 35.30, 33.71; elemental analysis calcd for $C_{14}H_{17}F_3O_6Pd$: C 37.81, H 3.85; found: C 37.99, H 3.91.

8: ^1H NMR (200 MHz, $CDCl_3$) [c]: δ = 7.50–7.30 (m, 15H), 5.70–5.40 (m, 1H), 5.60–5.40 (m, 1H), 5.10–4.95 (m, 2H), 4.75–4.55 (m, 1H), 3.71 (s, 6H), 3.20–3.05 (m, 1H), 2.75–2.40 (m, 5H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$): δ = 170.70, 133.63 (d, $^2J(C,P)$ = 11.7 Hz), 131.15 (d, $J(C,P)$ = 41.5 Hz), 130.72, 128.74 (d, $^3J(C,P)$ = 10.0 Hz), 118.23, 96.24 (d, $^2J(C,P)$ = 25 Hz), 58.01, 52.51, 51.50, 37.85, 35.47 (signals for two C atoms not observed).

10 [21]: ^1H NMR (200 MHz, $CDCl_3$) [d]: δ = 7.55–7.40 (m, 15H), 5.60–5.40 (m, 1H), 5.10–4.80 (m, 1H), 4.75–4.50 (m, 1H), 4.29 (br. d, J = 6.9 Hz, 1H), 4.13 (br. t, J = 8.6 Hz, 1H), 3.84 (s, 3H), 3.75 (s, 3H), 3.50–3.15 (m, 3H), 2.70–2.40 (m, 1H), 2.00–1.80 (m, 1H), 1.70–1.50 (m, 1H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$): δ = 170.53, 169.67, 133.52 (d, $^2J(C,P)$ = 11.2 Hz), 131.30 (br. s), 130.36 (d, $^1J(C,P)$ = 45.0 Hz), 129.19 (d, $^3J(C,P)$ = 10.0 Hz), 117.61 (d, $^2J(C,P)$ = 4.7 Hz), 105.65 (br. s), 95.56 (br. s), 82.09, 78.74, 63.94, 53.37, 53.20, 33.22; $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): δ = 22.3.

13: ^1H NMR (200 MHz, $CDCl_3$): δ = 5.45–5.20 (m, 1H), 5.15–4.90 (m, 3H), 4.31 (br. d, J = 15.5 Hz, 1H), 3.92 (d, J = 9.2 Hz, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.80–3.75 (m, 1H), 3.20 (br. d, J = 16.0 Hz, 1H), 2.83 (dd, J = 14.7, 3.0 Hz, 1H), 1.60–1.35 (m, 2H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$): δ = 170.05, 169.90, 114.07, 102.21, 92.28, 80.05, 77.18, 62.48, 53.31, 53.16, 34.91, 33.97; elemental analysis calcd for $C_{12}H_{17}ClO_4Pd$: C 39.26, H 4.67; found: C 39.64, H 4.62.

14: ^1H NMR (200 MHz, $CDCl_3$) [e]: δ = 5.70–5.52 (m, 1H), 5.52–5.33 (m, 1H), 5.18 (d, J = 7.5 Hz, 1H), 4.83 (d, J = 9.3 Hz, 1H), 4.55 (d, J = 16.5 Hz, 1H), 4.51 (br. s, 2H, H_2O), 4.10 (d, J = 13.3 Hz, 1H), 3.91 (td, J = 11.4, 2.5 Hz, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 3.09 (br. d, J = 15.4 Hz, 1H), 2.51 (dd, J = 15.2, 2.7 Hz, 1H), 1.80–1.5 (m, 1H), 1.54 (dd, J = 14.8, 12.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (50 MHz, $CDCl_3$): δ = 170.53, 169.68, 116.96, 111.69, 94.49, 84.45, 76.81, 60.92, 53.40, 35.27, 33.56.

[a] NMR spectra obtained at 25 °C. Confirmed by [b] a COSY ($CDCl_3$, 25 °C) spectrum. [c] COSY and NOESY ($CDCl_3$, 25 °C) spectra. [d] COSY and HMQC ([D$_6$]acetone, 0 °C) spectra. [e] a NOESY ($CDCl_3$, 25 °C) spectrum.

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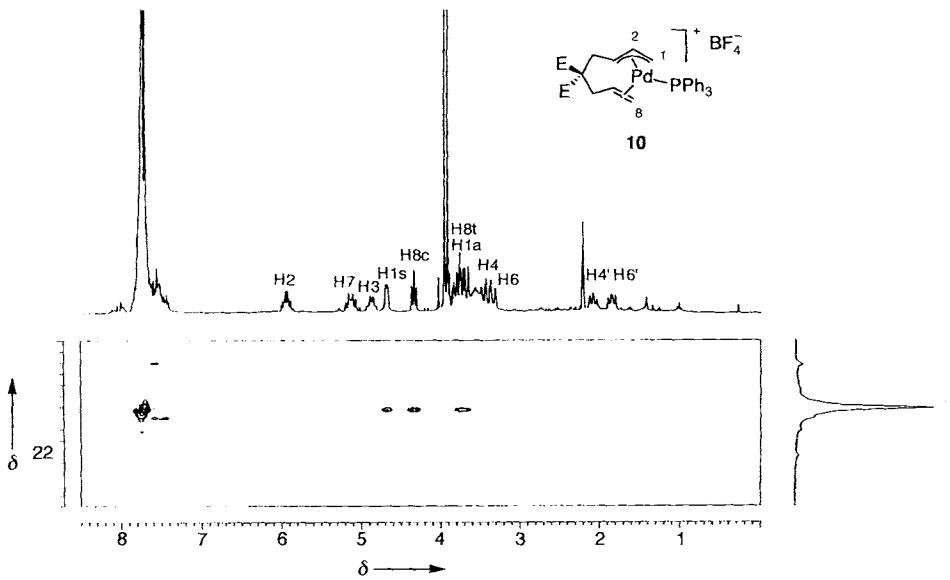

Figure 1. $^1H-^{31}P$ HOESY spectrum of **10** ([D$_6$]acetone, 0 °C) showing correlations between the phosphorous atom and H1-*syn*, H8-*cis*, H8-*trans*, and H1-*anti*. Assignments are based on a COSY spectrum.

allyl substrates,[29] are also involved in the insertion of alkenes into (η^3-allyl)palladium complexes. Development of a chiral version of this palladium-catalyzed cyclization is underway.

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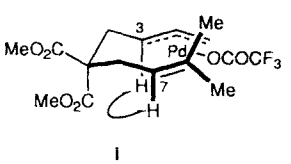

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[25] No cyclization was observed when **4** was heated in HOAc with catalysts prepared from [$Pd_2(dba)_3$]·dba and 1,4-bis(diphenylphosphane)butane or 1,1′-bis(diphenylphosphane)ferrocene. 1,1-bis(diphenylphosphane)methane, which probably acts as a monodentate ligand, led to a 1.2:1 mixture of **11** and **12** (44% yield).

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