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Mapping the Reaction Pathway in Palladium-Catalyzed Cross-Coupling Reactions[†]

John M. Brown* and Neil A. Cooley

Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, U.K.

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The formation of the cyclooctatetraene (COT) complex Pd(dppf)(COT) (dppf = 1,1'-bis(diphenylphosphino)ferrocene) from Pd(dppf)X_2 (X = Cl, Br, I) and dilithium cyclooctatetraenide in situ affords an entry into the cross-coupling chemistry of this system. The reaction of Pd(dppf)(COT) with an alkenyl bromide or iodide results in the formation of the appropriate (η^1-alkenyl)palladium halide via an oxidative addition of a η^2-coordinated alkene species. The η^1-2-alkenyl complexes react with norbornene to give insertion products, while Grignard reagents give the products of nucleophilic attack and carbon–carbon coupling. The full characterization of the intermediate Pd(dppf)(CH=CHC$_6$H$_4$OCH$_3$)Br (9) and the norbornene insertion product Pd(dppf)(C$_7$H$_{10}$CH=CHC$_6$H$_4$OCH$_3$) (15) is reported. A set of putative intermediates for the coupling of alkenyl and benzyl moieties by palladium complexes is demonstrated spectroscopically. The cross-coupling cycle for the case of alkenyl–aryl coupling is delineated by an analysis of cross-coupling reactions employing ^{13}C-labeled catalysts and unlabeled substrates (and vice versa). Platinum analogues of all the intermediates in this cross-coupling catalytic cycle have been observed.

Introduction

The reaction of an alkenyl halide with an organometallic nucleophile under palladium complex catalysis is a well-established procedure in organic synthesis.[1] Tetrakis-(triphenylphosphine)palladium is often employed as a catalyst in such transformations due to its ready availability and proven utility. Improvements in yield and substrate tolerance can be achieved however by the use of catalysts containing chelating biphosphines with a large "bite" angle. The ligand 1,1'-bis(diphenylphosphino)-ferrocene (1) (Chart I) fulfills these criteria and is particularly successful in cross-coupling systems in which β-elimination of alkyl substituents could lead to byproducts.[2]

Despite the wide utilization of these catalysts, scant information concerning their mechanism of action is available. It is generally accepted that the catalytic cycle involves the sequence oxidative addition–transmetalation–reductive elimination. Mechanistic studies of related model systems have, however, revealed a number of potential complicating factors; for example, when bis(triphenylphosphine)dimethylpalladium is treated with methyl iodide, the rate of ethane formation is increased.[3] An explanation of this observation involves an oxidative fragmentation via a palladium(IV) intermediate. Alternatively, an associative mechanism, with fragmentation of a bimetallic complex, similar to those studied by Yamamoto and co-workers could be invoked.[4]

The results reported here concern the reactions of palladium complexes of ligand 1, which have been used to define intermediates in the cross-coupling catalytic cycle. The structure of these intermediates and their interconversion routes have been defined by ^{31}P NMR spectroscopy. The use of ^{13}C-labeled alkenyl iodide provided further information.

Results and Discussion

The Overall Catalytic Reaction. The identification of reaction intermediates required the use of reactants that were readily available, stereoisomerically pure, and efficient in cross-coupling. For this reason (*E*)-2-bromo-1-(4-methoxyphenyl)ethene (2a),[5] which can easily be syn-

Chart I

1

2 a X=Br
  b X=Cl
  c X=I
  d X=I,1'-^{13}C

3
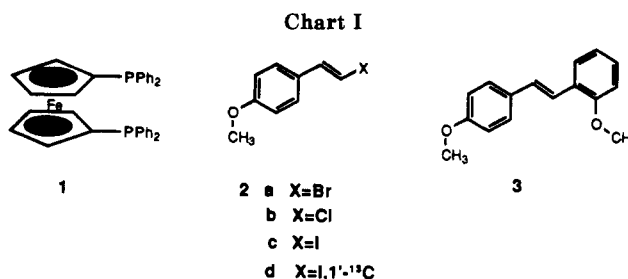
thesized in crystalline form from the corresponding cinnamic acid, was employed. At least initially, aromatic Grignard reagents were utilized as the nucleophilic component. Substrate 2a reacts with (2-methoxyphenyl)-magnesium bromide and 4b (2 mol %) in tetrahydrofuran at 0 °C over 16 h to give the cross-coupled product 3 exclusively. Under similar conditions in the absence of catalyst, no 3 is produced. The reaction is therefore genuinely catalytic and clean.

Preparation of Zerovalent Olefin Complexes. It has been generally assumed that the first step of the cross-coupling catalytic cycle involves the addition of the electrophile to a palladium(0) complex. When the catalyst precursor is a palladium(II) species, as is often the case, the true catalytic species is produced in situ by addition of 2 mol of the nucleophile followed by reductive elimination.[6]

For mechanistic studies, it was decided that the use of dilithium cyclooctatetraenide as a reducing agent[7] seemed promising. Accordingly, the reaction of this reagent with any of the halide complexes 4a–c at 70 °C suspended in THF led to dissolution and formation of a single labile species, considered to be complex 5 (δ_P = 10.6 ppm (s)). Attempted isolation of this species proved unsuccessful,

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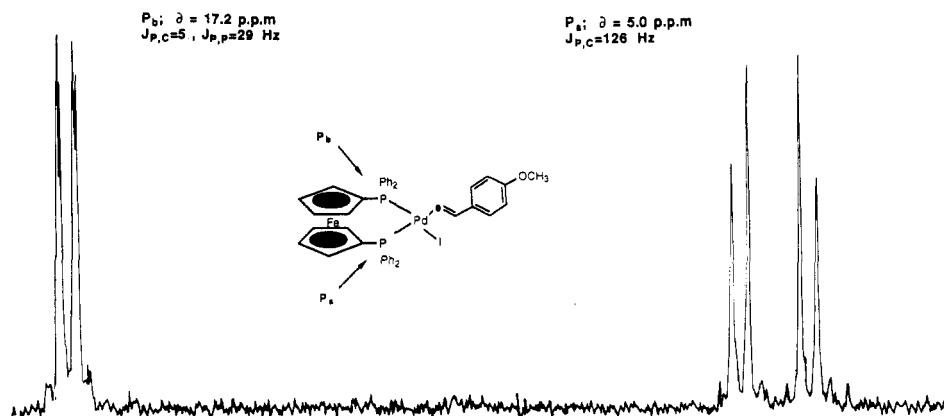
Figure 1. ^{31}P NMR spectrum (THF) of ^{13}C-labeled complex **12b**.

Scheme I

Table I. Phosphorus-31 NMR Data

(a) Pd Complexes[a]

complex	δ, ppm	J_{P-P}, Hz	T, °C
4a	28.5		30
4b	25.2		30
4c	19.33		30
5	10.6		-70
6	12.0		-70
7	11.5		-70
8	11.2, 11.7	15	-60
9	6.3, 24.9[b]	29	-80
10	11.2, 11.6	17	-70
11	7.0, 17.7[b]	28	-70
12a	5.0, 17.2[b]	29	-70
13	3.5, 30.7[b]	53	30
14	10.9, 11.6	29	-70
15a	13.0, 13.4	20	-60
15b	12.5		-80
15c	11.7, 12.5	24	-80
15d	12.9		-80
17a	10.4, 16.1	24	-60
18	7.0, 28.7[b]	51	-60
19	12.4		30

(b) Pt Complexes[c]

	δ, ppm	J_{P-P}, Hz	J_{P-Pt}, Hz	
20	25.1		2704	
21	23.1		3736	
22	20.3, 21.6	30	3499	3421
23	12.5, 12.8	10	4346	1712
24	15.0, 18.8	16	1748	1900
25	22.1, 22.1		3730	3730
26	12.2, 16.2	16	1965	1912
27	21.1, 22.6	43	3780	3780

[a] Recorded in THF solution with an external CD$_3$OD lock. [b] Nucleus trans to halogen. [c] Recorded in THF solution at ambient temperature with an external D$_2$O lock.

although other Pd(0) olefin complexes have been prepared and characterized by X-ray analysis,[8] but cyclooctaetraene was readily displaced by other alkenes, giving, for example, the η^2-olefin complexes **6** and **7** from ethylene and norbornene, respectively (Scheme I).

Reactions with Alkenyl Halides. The reactions of complex **5** are summarized in Scheme I. Displacement of cyclooctatetraene from **5** by alkene **2** at -70 °C gives the η^2 complex **8**, evident as a tight AB quartet in the ^{31}P NMR spectrum centered at δ_P = 11.4 ppm, in equilibrium with its organometallic precursor. This equilibrium was moderately favorable toward **5** such that the reaction never proceeded to completion, even in the presence of excess alkenyl halide, although at -60 °C **5** and **8** were the only Pd species present in solution. When the tetrahydrofuran solution was warmed to -40 °C, rearrangement occurred, giving the fully characterized palladium(II) compound **9**, which drove the equilibrium between the η^2-olefin complexes **5** and **8** to completion. The reaction of complex **5**

with the chloride **2b** promotes its equilibrium with the η^2 complex **10** (K = 0.3), which, as expected, has a ^{31}P NMR spectrum very similar to that of complex **8** (Table I) but is stable to oxidative addition at 25 °C. The expected product of such an oxidative addition, **11**, is formed with bromide **9** is allowed to react with excess lithium chloride in THF. In contrast to these observations the iodide **2c** adds rapidly to complex **5** at -70 °C, giving the η^1-alkenyl iodide complex **12a** without intervention of observable intermediates. The assignment of this structure is confirmed by the ^{13}C-labeled species **12b** (Figure 1), which has ^{31}P-^{13}C coupling constants of 125 Hz (trans) and 5 Hz (cis).

When complex **7** was generated in situ and then reacted with the alkenyl bromide **2a**, displacement was observed as before. The ultimate product **13**, which was isolated and characterized, is derived by insertion of norbornene.[9]

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Table II. Data from the Isotope Partitioning Experiments[a]

| | init conditions | | | | | | % ^{13}C in products | | | | | |
| | catal | | substrate | | Grignard | obsd | | calcd Pd(II) | | calc Pd(IV) | |
run no.	concn[b]	% ^{13}C	concn[b]	% ^{13}C	concn[b,c]	catal	stilbene	catal	stilbene	catal	stilbene
1	1	99	3.53	1	1.86	15.8	45.2	16.7	46.0	40.3	33.1
2	1	1	3.53	99	1.34	66.0	50.7	72.7	44.5	48.2	63.1
3	1	1	1.50	99	0.375	36.7	<10	31.0	16.9	17.4	54.8
4	1	14	1.30	99	0.429	42.2	35.0	43.1	50.0	30.6	60.9
5	1	69	1.20	1	0.478	42.3	55.7	43.2	55.1	54.5	31.2

[a] See experimental Section for typical reaction conditions. [b] Concentration relative to [catalyst], derived from the number of turnovers observed after complete reaction. [c] Turnover number.

Scheme II
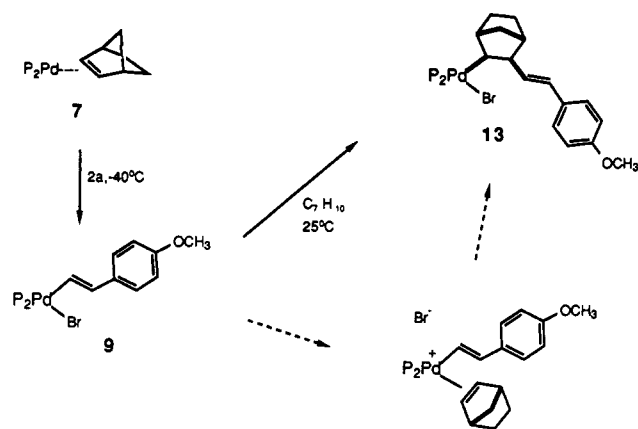
Scheme III

A likely mechanism outlined in Scheme II involves a cationic coordinated norbornene, with alkenyl migration therein. This reaction pathway is not observed when either the η^2-ethylene or η^2-cyclooctatetraene complex is employed and indicates that the η^2-norbornene complex 7 is not suitable for mechanistic studies of this nature.

Transmetalation. Tetrahydrofuran solutions of complex 9 react rapidly with a variety of aromatic Grignard reagents at -80 °C. In all cases the η^2-coordinated products 14 and 15a–d are first observed (Scheme III). The evidence for these structures is the similarity of the chemical shift to that of other η^2-olefin complexes (Table I). In addition, complex 14 was generated separately by direct reaction of the cyclooctatetraene complex 5 with olefin 3. Presumably the elimination step from intermediates such as 16 is fast at -80 °C, precluding their observation.

If benzylmagnesium chloride is added to a solution of complex 9 at -80 °C, however, the (η^1-alkenyl)benzyl-palladium species 17a is formed first. Confirmation of the structure is available from analysis of the product of the reaction of 9 and [α-^{13}C]benzylmagnesium chloride, 17b, which exhibits a trans CP coupling of 87 Hz. Further support for the identity of this intermediate was obtained by oxidative addition of benzyl bromide to complex 5, giving 18. This was reacted with [(E)-2-(4-methoxy-phenyl)ethenyl]magnesium bromide to form the *same* unstable intermediate 17a. From either sequence the olefin complex 19 began to form above -30 °C. The reaction was clean and followed to completion at -15 °C, where the half-life is approximately 4 min. The reactivity is comparable to that of cis-PhCH=CH(Me)Pd(PPh$_2$Me)$_2$, whose thermolysis (in admixture with its trans isomer) has been studied by Stille and Loar.[10]

All of these η^2-olefin complexes formed by addition of Grignard reagents to the alkenyl halide complex 9 reacted
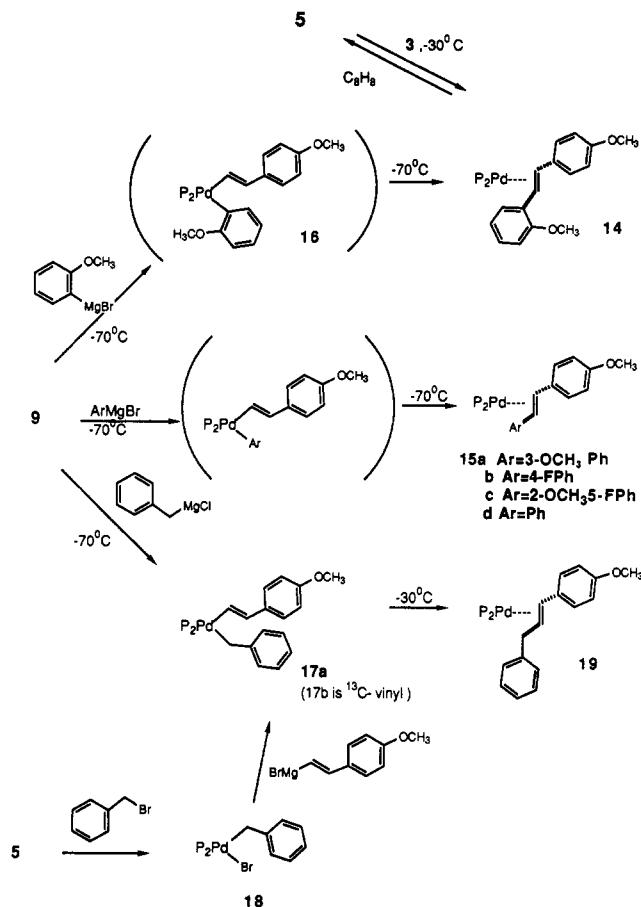
subsequently with excess of the halide 2a, thereby regenerating 9.

Isotope Partitioning Experiments. Taken together, the reactions detailed above provide a plausible set of intermediates for catalytic cross-coupling. Indeed, the organic products of such stepwise transformations are solely those derived by cross-coupling. Evidence for the participation of these as true intermediates in cross-coupling reactions is obtained from the following isotope partitioning experiments, details of which are summarized in Table II.

The basic principle of the experiment is as follows.[11] A putative catalytic intermediate carries an isotopic label and is employed to promote the reaction of substrate(s) for a limited number of turnovers. At the end of that period, the isotope label should be distributed between the product and catalytic intermediate, if it is involved. Further, the extent of labeling may distinguish between different catalytic mechanisms. Conversely the experiment may be

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Scheme IV

Figure 2. ^{31}P NMR spectra (THF) spectra of Pt complexes 22–25.
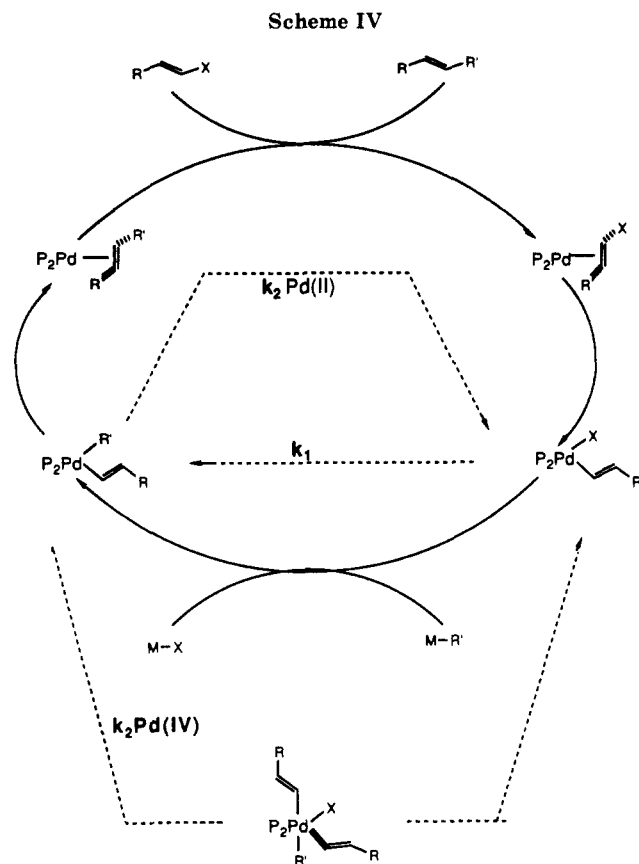
conducted with the reactant carrying the isotopic label, which is diluted by an unlabeled catalyst on conversion into the product.

In the present case, both types of experiments were carried out, employing the ^{13}C-labeled alkenyl iodide **2d**[12] or alternatively the palladium iodide **12b**. Samples of complex **12a** or **12b** were prepared in THF and mixed with, respectively, iodide **2d** or **2c**. A deficit of *o*-anisyl-magnesium bromide, relative to the electrophile, was added at 0 °C. At the end of the experiment the solution contained only **12** and the product **3**, both partly labeled with ^{13}C, together with excess alkenyl iodide. The ^{13}C content of complex **12** was derived directly from the ^{31}P spectrum, by analyzing the higher field signal; this consisted of a doublet corresponding to the labeled complex with a singlet corresponding to the unlabeled complex at its midpoint. For product **3**, integration of the alkene proton signal at 7.14 ppm afforded an accurate measure because of the clear separation of the standard ^{1}H signal from its ^{13}C satellites. In a control experiment, it was established that unreacted alkenyl iodide had the same proportion of ^{13}C label at the end of the experiment as at its commencement. Thus, there is no alkenyl exchange between iodide **2d** and palladium complex **12**.

The isotope partitioning experiments were computer-simulated by using numerical integration techniques on an HP 85B microcomputer. Two model reactions were constructed; in each two relative rate constants were required (Scheme IV). The first of these, k_1, described the reaction of complex **12a** or **12b** with the nucleophile; the second, k_2, encompassed the regeneration of **12b** or **12a**. The ratio $k_1:k_2$ in all simulations was 1:200, although the results were found to be relatively insensitive to these values. The two models differed in that $k_2(\text{Pd(IV)})$ in-
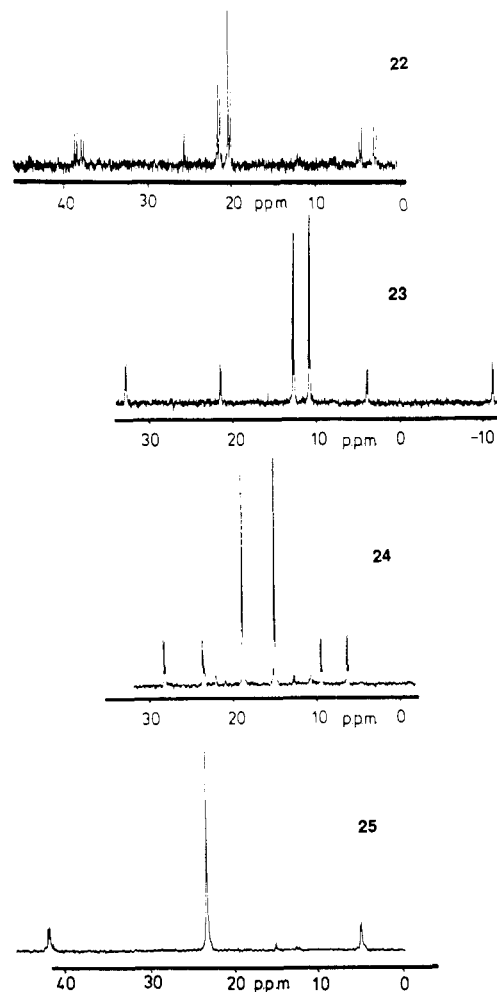
cluded a "scrambling" factor to mimic the formation of a palladium(IV) intermediate, formed by addition of a molecule of **2** *prior* to an elimination step in which the alkenyl groups are indistinguishable.

Table II shows tht the simulation in which this scrambling factor is absent, involving only Pd(II) intermediates, is in excellent agreement with experiment. The simulation of the palladium(IV) pathway mitigates against the involvement of such intermediates, since results are in discord with experiment. The distributions obtained from an associative or crossover pathway[4] would also differ from the observed results. Therefore, the C–C bond-forming step in catalytic cross-coupling is simply a cis elimination of the alkenyl and aryl groups, giving the olefin complex **14**.

The isotope partitioning experiments confirm the direct involvement of species **12** in the cross-coupling cycle, so that it is not merely functioning by, for example, an electron-transfer mechanism.[13]

Platinum Analogues of Reaction Intermediates. It is generally thought that C–C elimination from platinum-(II) complexes is very unfavorable, when compared with that for palladium(II) or nickel(II) analogues.[14] The most widely studied case involves diarylplatinum complexes,

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Chart II
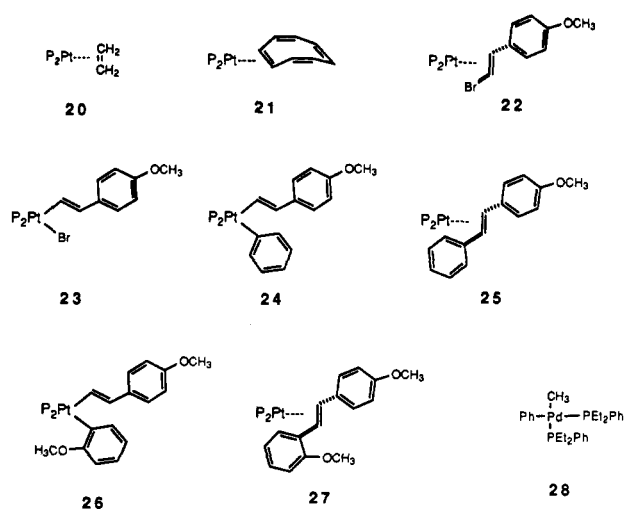
which normally require heating above 80 °C before appreciable elimination occurs. For this reason the (supposedly stable) platinum analogues of complexes described above have been examined. It transpires that all the intermediates in a potential catalytic cycle may be observed readily (Figure 2).

(Diphosphine)platinum olefin complexes have been prepared previously and are much more stable than their palladium counterparts.[15] The first approach involved synthesis of (dppf)(η^2-ethene)platinum(0) (20) (Chart II) by the standard method. Alternatively, the corresonding η^2-cyclooctatetraene complex 21 was prepared and used in situ. From either precursor, the η^2-alkenyl bromide complex 22 was prepared by olefin displacement, normally by employing an excess of the precursor 2a. For ethylene displacement, the reaction was complete within 10 minutes in THF at room temperature. For cyclooctatetraene displacement, reaction was a factor of 5 slower, but the equilibrium was completely displaced toward product formation, unlike the palladium case.

The η^2-olefin complex 22 proved to be stable in THF solution at room temperature. Over the course of 1 week, the ^{31}P spectrum changed entirely to that of a new species, which was characterized as the stable bromo η^1-alkenyl complex 23. In CH_2Cl_2 solution this rearrangement proceeded very rapidly, being complete within 10 min. This appeared to be too large a difference to be ascribed to simple solvent effects, and we suspected involvement of dichloromethane in electron-transfer catalysis. This was reinforced by further examination of the rearrangement in THF in the presence of $Ag^+BF_4^-$, a known electron-transfer catalyst for organometallic reactions.[16] The presence of ca. 10^{-5} M $Ag^+BF_4^-$ in THF caused a dramatic acceleration of the rearrangement, shortening the half-life from days to a few minutes. This observation will be subjected to a more detailed study, to be reported in a future publication.

Addition of PhMgBr to the THF solution of compound 23 caused instantaneous conversion into the alkenyl aryl complex 24 at 30 °C. This clean transformation was followed by ^{31}P NMR spectroscopy (Figure 2). It was demonstrated that the olefin precursor complex 22 was inert

to these reaction conditions.

Surprisingly the product 24 was thermolabile and rearranged at room temperature or above to form the coordinated olefin complex 25. In the presence of excess halide 2a olefin/olefin displacement is evident before the elimination is complete. The spectrum of compound 25 in Figure 2 was obtained by carrying out the rearrangement over 1 h at 65 °C in the presence of excess (E)-4-methoxystilbene.

When o-$(CH_3O)C_6H_4MgBr$ was employed in place of PhMgBr, the initial adduct 26 rearranged with a half-life of <1 h at 30 °C, giving the olefin complex 27 cleanly. This same species was formed by displacement of cyclooctatetraene from 21 with use of the olefin 3.

When they are taken together, these observations represent a complete cycle for platinum-catalyzed cross-coupling, which has been realized in practice.[17] All of the intermediates can be defined spectroscopically, and they are relatively stable.

Summary and Conclusions

The experiments described herein demonstrate the sequence of cross-coupling in a true catalytic system. When one starts with a palladium(0) olefin complex, displacement by alkenyl halides occurs readily. The easy rearrangement of the η^2-halide complex is strongly dependent on the nature of the halogen (I $\gg$ Br $\gg$ Cl), suggesting an electron-transfer component to the transition state.[19] Only for the alkenyl bromide are both intermediates observable.

It proved impossible to observe the alkenyl aryl complex formed by the addition of Grignard reagents to complex 9, even at low temperatures. This implies that the putative intermediate (e.g. 16) is unstable to rearrangement at −70 °C. This surprising lability may be in accord with a low-energy pathway that does not involve fragmentation. Calculations on an alternative pathway whereby the aryl group migrates to coordinated vinyl have been carried out.[18] When the corresponding benzyl complex 17 is prepared, then the thermal lability is much lower, and decomposition may be followed at −15 °C. It is of interest that Ph migration to coordinated CO is much faster than alkyl migration in the respective CpRhCO(I)R complexes;[19] if the cross-coupling elimination step is regarded as R migration to the vinyl group, this establishes a precedent for the higher reactivity of Ar over that of CH_2Ph.

There has been much speculation about the precise mechanistic pathway followed in palladium-catalyzed cross-coupling. The C–C elimination step has been subject to many model experiments, and precedents exist for its promotion by ligand or substrate association,[20] oxidative addition,[21] or ligand dissociation.[22] At least in the present case, the first two postulates are unnecessary: the isotope distribution observed in experiments described above is fully consistent with a simple unassisted pathway. Ligand dissociation is possible but unlikely in the case of a chelate diphosphine. We believe that the experimental results are in best accord with the catalytic cycle summarized in Scheme V. Support for this is derived from the observation of homologous platinum intermediates and their

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interrelationships. The simple catalytic cycle proposed, with reductive elimination via an unassisted pathway, is in accord with recent observations by Yamamoto and co-workers.[23] They find that the cis phenyl methyl complex 28 eliminates toluene under mild conditions without prior phosphine dissociation, while its trans stereoisomer shows more complex thermal behavior.

Experimental Section

Reactions were carried out under an argon atmosphere with solvents that were dried and distilled under anaerobic conditions immediately before use.

The starting materials [1,1'-(diphenylphosphino)ferrocene]-palladium dibromide,[2] (*E*)-2-bromo-1-(4-methoxyphenyl)ethene,[6] (*E*)-2-iodo-1-(4-methoxyphenyl)ethene,[12,24] (*E*)-2-iodo-1-(4-methoxyphenyl)[2-^{13}C]ethene,[12] and [α-^{13}C]benzyl chloride[25] were prepared by literature methods.

Dilithium cyclooctatetraenide was prepared from finely divided lithium, thereby reducing the reported reaction time from 3 days to 2 h.[7] Benzylic Grignard reagents were prepared in ether at -5 °C, in concentrations ranging from 0.02 to 0.4 M. Aldrich "Gold Label" magnesium, preactivated with 1,2-dibromoethane (ca. 10 μL), was employed in all cases. Small quantities of aryl Grignard reagents (ca. 0.4 M) were prepared in THF (3–5 cm³) by the addition of the appropriate aryl bromide to magnesium activated as above.

^{31}P NMR spectra (101.2 ppm) and ^{13}C NMR spectra (62.86 ppm) were recorded on a Bruker AM250 machine.

(*E*)-2-Chloro-1-(4-methoxyphenyl)ethene (2c). Anisaldehyde (0.113 cm³, 0.93 mmol) and chloroform (0.100 cm³, 1.24 mmol) were added to a suspension of CrCl₂ (Aldrich, 0.687 g, 5.59 mmol) in THF (10 cm³). The mixture was refluxed for 2 h to give a purple solution. After addition of H₂O (20 cm³), the crude product was extracted with Et₂O (2 × 20 cm³). The solvent was removed by rotary evaporation, and the resulting colorless oil was chromatographed on 60-μm silica, with hexane as eluant. (*E*)-2-chloro-1-(4-methoxyphenyl)ethene (2b) (0.985, 63%) was obtained as a colorless liquid that was identified by its ^{1}H NMR spectrum.[26]

(*E*)-1,4'-Dimethoxystilbene (3). A 10 cm³ solution of 2a (0.2004 g, 0.94 mmol) and catalyst 4b (0.0160 g, 0.02 mmol, 2 mol %) in THF was cooled to 0 °C, and (*o*-methoxyphenyl)magnesium bromide (3.0 cm³, 0.4 M, 1.2 mmol) was added by syringe. Upon addition of the Grignard reagent the orange solution momentarily become red and then changed to pale lemon yellow. The reaction mixture was stirred overnight (16 h) at 0 °C. The catalyst was quenched with hydrochloric acid (10 cm³, 0.1 M), and the crude product was extracted with Et₂O (3 × 20 cm³). Recrystallization from boiling hexane (30 cm³) gave (*E*)-1,4'-dimethoxystilbene (3) as colorless needles (0.175 g, 78%), mp 85–86 °C. Anal. Calcd for C₁₆H₁₆O₂: C, 53.70; H, 3.88. Found: C, 53.70; H, 3.83. ^{1}H NMR (δ, CDCl₃): 6.85–7.60 (anisyl); 7.37 (d) and 7.08 (-CH=CH-, d, *J* = 14 Hz); 3.90 (s) and 3.84 (OCH₃, s).

Bromo[1,1'-bis(diphenylphosphino)ferrocene][(*E*)-2-(4-methoxyphenyl)ethenyl]palladium (9). A suspension of bromide 4b (0.100 g, 0.12 mmol) in Et₂O (10 cm³) was stirred with dilithium cyclooctatetraenide (0.50 cm³, 0.24 M, 0.12 mmol) at -30 °C for 30 min. Approximately 10 equiv of 2a was added, and the mixture was stirred at -20 °C for 1 h. Petroleum ether (bp 30–40 °C, 70 cm³) was added, and the product was collected by filtration. After it was washed with petroleum ether (4 × 40 cm³) and H₂O (2 × 20 cm³) and again with petroleum ether (40 cm³), the product was dried to afford bromo[1,1'-bis(diphenyl-phosphino)ferrocene][(*E*)-2-(4-methoxyphenyl)ethenyl]palladium as a pale yellow powder (0.0769 g, 72%), mp 156–157 °C dec. Anal. Calcd for C₄₃H₃₇BrFeOP₂Pd: C, 59.09; H, 4.28. Found: C, 58.68; H, 4.69. ^{1}H NMR (δ, CD₂Cl₂): 7.95–7.35 (Ph, m); 6.00 (C*H*-Pd, m); 4.53 (s), 4.39 (s), 4.19 (s), and 3.89 (Cp, s); 3.68 (OCH₃, s). ^{13}C

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NMR (δ, THF): 147.0 (Pd–CH, d, J_{P-C} = 128 Hz).

Bromo[1,1'-bis(diphenylphosphino)ferrocene][*exo*,*exo*-3-((*E*)-2-(4-methoxyphenyl)ethenyl)-2-bicyclo[2.2.1]hepta-nyl]palladium (13). A solution of dilithium cyclooctatetraenide (0.78 cm³, 0.30 M in THF, 0.24 mmol) was added over a period of 5 min to a stirred suspension of 4b (0.200 g, 0.24 mmol) in tetrahydrofuran containing norbornene (0.30 g, 3.2 mmol), at -78 °C. The resulting clear yellow solution was treated with 2a (0.50 g, 0.24 mmol) and warmed to room temperature. The mixture was stirred for 2 h, and the solvent was evaporated. The residue was redissolved in CH₂Cl₂ (10 cm³) and filtered. A layer of Et₂O (40 cm³) was added, and the solution was placed in the freezer overnight. The product, bromo[1,1'-bis(diphenylphosphino)-ferrocene][*exo*,*exo*-3-((*E*)-2-(4-methoxyphenyl)ethenyl)-2-bicy-clo[2.2.1]heptanyl]palladium (13), was obtained as orange prisms (0.043 g, 18%), mp 177–179 °C dec. Anal. Calcd for C₅₀H₄₇BrFeOP₂Pd: C, 62.03; H, 4.90. Found: C, 61.85; H, 5.01. ^{1}H NMR (δ, CDCl₃): δ 6.89–8.11 (Ar); 5.84 (=C*H*CHCHPd, d, *J* = 16 Hz); 3.98–4.70 (Cp); 3.91 (OCH₃, s); 3.21 and 3.12 (C*H*C-H₂C*H*); 2.95 (s), 2.70 (d), 1.60 (s), 1.07 (d, *J* = (Hz) (C*H₂*C*H₂*); 2.33 (Pd—C*H*, m); 0.87 (Pd—CH—C*H*CH=); 0.71 (CHC*H₂*CH, syn); 0.42 (CHC*H₂*CH, anti).

Preparation of Samples for NMR Studies of Intermediates. Preparation of Olefin Complexes. Complex 4b (0.030 g, 0.037 mmol) was suspended in THF (1.5 cm³) and degassed by three freeze/thaw cycles. The suspension was recooled to -70 °C, and a solution of dilithium cyclooctatetraenide (0.17 cm³, 0.14 M in Et₂O, 0.04 mmol) was added, dropwise, over a period of 5 min. This solution was transferred via a steel cannula to a degassed, cooled NMR tube. The ^{31}P NMR spectrum of the cy-clooctatetraene complex 5 was recorded.

Ethylene was bubbled through a solution of the cyclo-octatetraene complex 5, prepared as above, for 5 min at -70 °C, affording the ethylene complex 6.

The complex Pd(dppf)(norbornene) (7) was prepared as for 5 in the presence of 10 equiv of norbornene. Attempts to isolate the olefin complexes 5–7 led to decomposition.

Addition of 5 equiv of (*E*)-2-bromo-1-(4-methoxyphenyl)ethene (0.040 g, 0.19 mmol) to a solution of the cyclooctatetraene complex 5, prepared as above, at -70 °C gave a solution containing the η²-olefin complex 8.

Observation of Intermediate 17a. (*E*)-2-bromo-1-(4-meth-oxyphenyl)ethene (0.008 g, 0.038 mmol) was added to a solution of the cyclooctatetraene complex 5, prepared as above, at -40 °C. The solution was cooled to -70 °C, and a solution of benzyl-magnesium chloride (0.150 cm³, 0.38 M in Et₂O, 0.057 mmol) was added by syringe. The ^{31}P NMR spectrum of this solution showed both complex 17a and its elimination product 19.

Alternative Preparation of 17a. Benzyl bromide (0.004 cm³, 0.033 mmol) was added at -70 °C to a solution of complex 5 prepared as above. This solution of the benzylpalladium bromide complex 18 was treated with [(*E*)-2-(4-methoxyphenyl)-ethenyl]magnesium bromide (0.409 cm³, 0.4 M in Et₂O, 0.16 mmol) to give a yellow solution containing the alkenyl benzyl complex 17a.

Isotope Partitioning Experiments. The following experiment, entry 1 in Table II, is representative of the procedures employed in all such experiments.
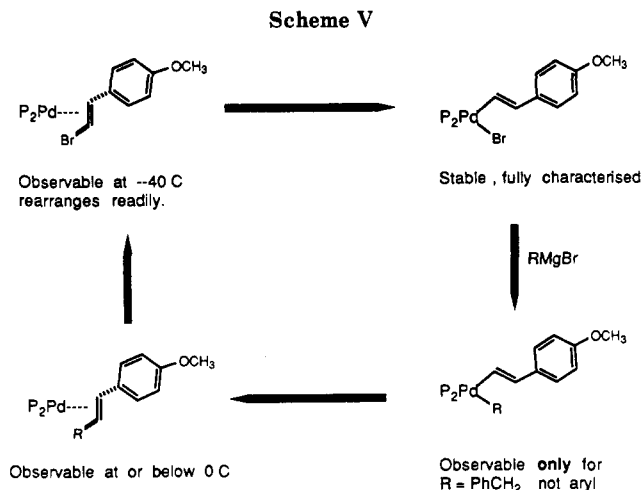
Complex 4c (0.0500 g, 0.055 mmol) was suspended in THF (1.6 cm³), and the solution was degassed by three freeze/thaw cycles. The suspension was recooled to -78 °C, and a solution of dilithium cyclooctatetraenide (0.171 cm³, 0.32 M, 0.055 mmol) was added dropwise, with stirring. Solid ^{13}C-labeled iodide 2d (0.0142 g, 0.055 mmol) was added to the yellow solution of complex 5, and the solution was transferred via a steel cannula to an NMR tube. The sample was warmed to -20 °C, and a solution of iodide 4c (0.050 g, 0.19 mmol) in THF (0.150 cm³) was added. The ^{31}P and ^{13}C spectra of the sample at -20 °C were recorded. The sample was transferred to a cold bath at -20 °C, and a solution of *o*-anisyl-magnesium bromide (0.205 cm³, 0.77 M, 0.16 mmol) was injected. After incubation at 0 °C for 25 min the ^{31}P NMR spectrum was recorded. This spectrum showed only 12a and 12b. The reaction was quenched with HCl (1 cm³, 0.1 M), and the products were extracted into ether (2 × 5 cm³). The ^{1}H NMR spectrum of the crude products showed no 2d; therefore, no crossover between 12 and 2 had occurred. The products 3 and its ^{13}C-labeled

Scheme V

Observable at --40 C
rearranges readily.

Stable , fully characterised

RMgBr

Observable at or below 0 C

Observable only for
R = PhCH₂ , not aryl

analogue were isolated by flash chromatography, with petroleum ether (bp 30–40 °C) as eluant. The 500-MHz NMR spectrum of the products was recorded, and the ratio of unlabeled to labeled product was determined to be 55.45. The turnover number for the experiment was determined from the ¹H and ³¹P NMR spectra, assuming that all of the complex **12b** that was consumed resulted in stilbene formation.

The reaction was simulated by using the parameters derived from experiment (entry 1, Table II). It proved necessary to allow for a small amount of adventitious quenching of the Grignard reagent to derive the correct turnover number.

The simulation was carried out by using simple numerical integration techniques based on the reaction sequence of Scheme IV on a program written for an HP85 microcomputer. The alkenylalkylpalladium complex of Scheme IV partitions in two ways: via the simple reductive-elimination pathway with formation of 1 mol of hydrocarbon product and assumed rapid regeneration of the alkenyliodopalladium complex by reaction with iodoalkene substrate. Alternatively, the alkenylalkylpalladium complex reacts with a molecule of iodoalkene; the resulting Pd(IV) intermediate breaks down to product and the alkenyliodopalladium complex. These two pathways give very different isotopic label distributions in both product and residual complex. It was assumed that ¹³C isotope effects could be ignored.

The input to the program is a set of molar concentrations for labeled and unlabeled complex, labeled and unlabeled substrate, and Grignard reagent. The last was derived from the observed turnovers in each experiment to avoid corrections for the effect of adventitious quenching. The results obtained are insensitive to the ratio of rate constants k_1 and k_2, but for the results recorded in Table II a value of 1:200 was employed.

[1,1'-Bis(diphenylphosphino)ferrocene](η²-ethene)platinum (20).[27] A stirred suspension of Pt(dppf)Cl₂ (0.200 g, 0.244 mmol), in CH₂Cl₂ (5 cm³) and EtOH (5 cm³), was cooled to –70 °c and purged with a stream of ethylene. Sodium borohydride (0.040 g, 1.05 mmol) was added, and the resulting solution was warmed to 0 °C over a period of 30 min, with a steady flow of ethylene being maintained. Ethanol (75 cm³) was added, and stirring was continued, under ethylene, for 1 h at ambient temperature. The resulting precipitate was collected by filtration and washed with water (20 cm³), ethanol (20 cm³), and petroleum ether (bp 30–40 °C, 20 cm³). The product was dried in vacuo to afford [1,1'-bis(diphenylphosphino)ferrocene](η²-ethene)platinum (0.149 g, 0.192 mmol) as a pale yellow powder: yield 78%; mp 198–200 °C dec. Anal. Calcd for C₃₆H₃₂FeP₂Pt: C, 55.60; H, 4.12. Found: C, 55.58; H, 4.12. ¹H NMR (δ, CDCl₃): 7.32–7.78 (m, Ph); 4.23 (s) and 4.17 (s, Cp); 2.15 (t, ethene, J_{Pt-H} = 29 Hz).

[1,1'-Bis(diphenylphosphino)ferrocene][η²-(E)-2-bromo-1-(4-methoxyphenyl)ethene]platinum (22). The alkenyl bromide **2a** (0.100 g, 0.470 mmol) was added to a solution of complex **20** (0.100 g, 0.129 mmol) in THF (5 cm³). The solution was stirred for 5 min, and petroleum ether (bp 30–40 °C, 80 cm³) was added. The product was collected by filtration and dried in

vacuo. [1,1'-Bis(diphenylphosphino)ferrocene][η²-(E)-2-bromo-1-(4-methoxyphenyl)ethene]platinum (0.078 g, 0.081 mmol) was obtained as an off-white powder: yield 63%; mp 215–216 °C dec. Anal. Calcd for C₄₃H₃₇BrFeOP₂Pt: C, 53.64; H, 3.88. Found: C, 53.13; H, 3.88.

[1,1'-Bis(diphenylphosphino)ferrocene]bromo[(E)-2-(4-methoxyphenyl)vinyl]platinum (23). A suspension of Pt-(dppf)Cl₂ (0.250 g, 0.305 mmol) in CH₂Cl₂ (2.5 cm³) and ethanol (2.5 cm³) with norbornene (0.150 g, 1.59 mmol) was treated with sodium borohydride (0.0540 g, 1.32 mmol). This mixture was stirred, under argon, for 30 min and filtered. The solid was redissolved in CH₂Cl₂ (5 cm³), and alkenyl bromide **2a** (0.080 g, 0.375 mmol) was added. Et₂O (70 cm³) was added, and the product was crystallized at –20 °C. [1,1'-Bis(diphenylphosphino)-ferrocene]bromo[(E)-2-(4-methoxyphenyl)vinyl]platinum (0.232 g, 0.240 mmol) was obtained as yellow prisms: yield 79%; mp 228–229 °C dec. Anal. Calcd for C₄₃H₃₇BrFeOP₂Pt: C, 54.64; H, 3.88. Found: C, 53.70; H, 3.83. ¹H NMR (δ, CDCl₃): 7.27–8.02 (m, Ph); 6.60 (s, anisyl); 6.54 (m) and 6.28 (dd, vinyl); 4.65 (m), 4.44 (m), 4.19 (m), and 3.82 (m, Cp); 3.70 (s, OCH₃).

In Situ Studies of Platinum Complexes. A suspension of Pt(dppf)Br₂ (0.030 g, 0.033 mmol) in THF (1.6 cm³) was treated with dilithium cyclooctatetraenide (0.150 cm³, 0.24 M in Et₂O 0.036 mmol) to give a clear, yellow solution of the cyclooctatatetraene complex **21**. The solution was transferred to an NMR tube, via a steel cannula, and the ³¹P NMR spectrum was recorded. A solution of the alkenyl bromide **2a** (0.007 g, 0.0329 mmol) in THF (0.100 cm³) was added, and the olefin-exchange reaction was monitored by ³¹P NMR spectroscopy. The resulting solution of complex **22** was stored in the dark, at ambient temperature, for 1 week. The ³¹P NMR spectrum of this solution was recorded at regular intervals during this period to observe the formation of the η¹-alkenyl bromide complex **23**. An excess of (o-methoxyphenyl)magnesium bromide (0.5 cm³, 0.40 M in THF, 0.200 mmol) was injected, and the rearrangement of the η¹-alkenyl aryl complex **26** to the η²-stilbene complex **27** was followed, at 30 °C, by ³¹P NMR spectroscopy over 1 h.

Isolation of Samples of Complexes 26 and 27. (a) To a suspension of complex **23** (0.200 g) in THF (5 cm³) was added 1 equiv of (o-methoxyphenyl)magnesium bromide in THF (5 cm³). The reaction mixture became clear after stirring at room temperature for 10 min, and stirring was continued for a further 20 min. Solvent was removed in vacuo below ambient temperature, and the residual yellow-brown solid was used without further purification. Examination by ³¹P NMR spectroscopy showed the desired product **26** contaminated by its rearrangement product **27** (cf. Table Ib).

(b) Dichloro[1,1'-bis(diphenylphosphino)ferrocene]platinum (0.100 g, 0.12 mmol) was dissolved in CH₂Cl₂/EtOH (50:50; 5 cm³) together with olefin **3** (0.100 g, 0.4 mmol) and cooled to –5 °C. NaBH₄ (0.03 g, excess) was added in one portion, giving an orange solution. The reaction mixture was warmed to room temperature, and a bright yellow precipitate formed over the course of 30 min. EtOH (25 cm³) was added, and stirring continued for 20 min. The solid was thenn collected by filtration and washed successively with H₂O, EtOH, and hexane, giving the *product* **27** (0.082 g) as a bright yellow solid, with a ³¹P NMR spectrum identical with that prepared by rearrangement of **26**.

Supplementary Material Available: Program for isotopic analysis (1 page). Ordering information is given on any current masthead page.

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(27) We thank D. W. Price for this experiment.