Communications

A Protic Additive Suppresses Formation of Byproducts in Platinum-Catalyzed Hydrophosphination of Activated Olefins. Evidence for P−C and C−C Bond Formation by Michael Addition

Corina Scriban, Ivan Kovacik, and David S. Glueck*

6128 Burke Laboratory, Department of Chemistry, Dartmouth College, Hanover, New Hampshire, 03755

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Summary: Platinum-catalyzed hydrophosphination of activated olefins yields byproducts derived from more than one alkene. Formation of byproducts is suppressed by adding tert-butyl alcohol, consistent with a mechanism in which Michael addition of a nucleophilic Pt-PR_2 group to the alkene yields a zwitterionic intermediate, which can undergo further conjugate additions.

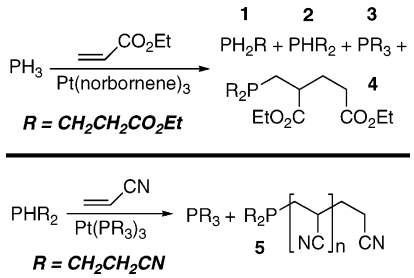
Platinum-catalyzed hydrophosphination of activated olefins (acrylonitrile and acrylate derivatives) is an atom-economical route to functionalized phosphines.[1] Unfortunately, this reaction commonly yields higher molecular weight byproducts, which are believed to be derived from more than one olefin. For example, Pt-catalyzed reaction of phosphine with ethyl acrylate yielded telomer **4** (∼10%) in addition to the phosphines **1**−**3**.[2] Similarly, addition of $PH(CH_2CH_2CN)_2$ to acrylonitrile also gave byproducts (5% in MeCN, 20% in acetone, and 60% in DMSO), which were tentatively identified as **5** by ^{13}C NMR spectroscopy (Scheme 1).[3]

We report here independent synthesis and characterization of the byproducts in related reactions and propose a new mechanism for their formation, which suggested a successful method to improve the selectivity in Pt-catalyzed hydrophosphination.

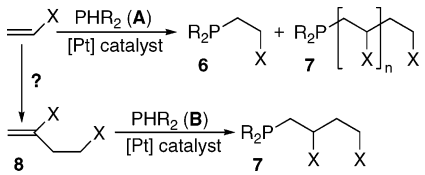
As reported earlier, Pt((*R*,*R*)-Me-Duphos)-catalyzed addition of PHPh(*i*-Bu) to *tert*-butyl acrylate selectively gave the expected hydrophosphination product **6a** along with minor phosphine byproducts (Scheme 2).[4] The amount of byproducts increased at low temperature and/or when an excess of acrylate was used.[5] The major byproduct **7a** ($n = 1$) was prepared independently by Pt-catalyzed addition of PHPh(*i*-Bu) to *tert*-butyl acrylate dimer **8**.[6] Mass spectroscopy showed that the other byproducts contained more acrylates ($n = 2$−6). The major byproducts (**7b**−**d**) formed from related substrates were identified similarly.[5]

Nucleophilic phosphines catalyze dimerization and polymerization of Michael acceptor olefins,[7] and M-PR_2 complexes contain nucleophilic phosphido groups,[8] so byproduct formation might occur by dimerization of the alkene substrate and its subsequent hydrophosphination. If this occurred, then phosphines **7** would be formed with the same selectivity (diastereomeric ratio

Scheme 1



Scheme 2[a]



[a] [Pt] = Pt((*R*,*R*)-Me-Duphos)(*trans*-stilbene); for X = CO_2t-Bu, PR_2 = PPh(*i*-Bu) (**6a**, **7a**), PPh_2 (**6b**, **7b**), PMeIs (Is = 2,4,6-(*i*-Pr)$_3C_6H_2$) (**6c**, **7c**); for X = CN, PR_2 = PPh(Cy) (**6d**, **7d**, Cy = *cyclo*-C_6H_{11}). In reaction **A**, phosphine **6** was the major product and byproducts **7** with $n \geq 1$ were observed; in reaction **B**, phosphines **7** were the major products.

* To whom correspondence should be addressed. E-mail: glueck@dartmouth.edu.

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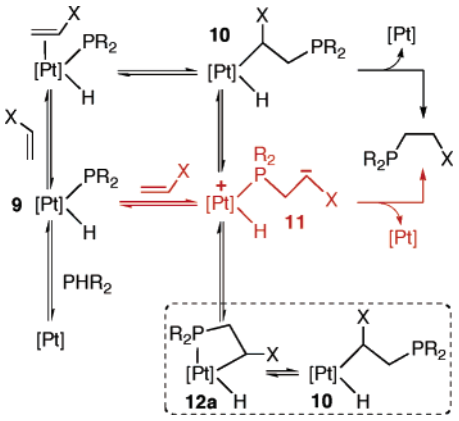
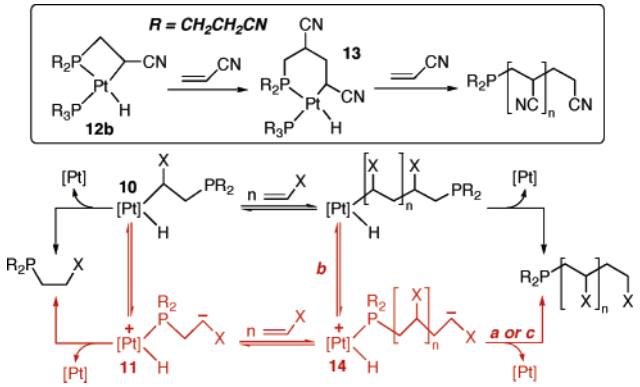
Scheme 3[a]



[a] [Pt] = Pt(diphos); X = CO_2R or CN.

Scheme 4[a]



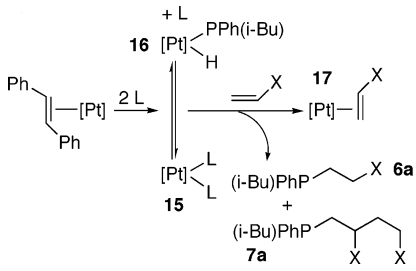
[a] [Pt] = Pt(diphos); X = CO_2R or CN. Step **a** refers to deprotonation of the Pt−H by the carbanionic ligand, **b** to carbanion attack at Pt, and **c** to carbanion attack on another alkene, eventually followed by steps **a** or **b** to yield the product.

= dr) in path **A** (as the byproducts) as in path **B** (as the major products). However, the dr was significantly different in these two syntheses, ruling out this mechanism.[9]

How else might the byproducts form, and how is this side reaction related to formation of the desired product? We previously reported direct observation of P−H oxidative addition to Pt(0), followed by selective insertion of the olefin into the Pt−P (not the Pt−H) bond of **9** and reductive elimination from **10** to form the product and regenerate Pt(0).[4,10] Instead of this "organometallic" mechanism, an ionic/Michael addition process might occur. Scheme 3 compares these pathways and shows how they are related. From phosphido hydride **9**, P−C bond formation could occur by a classical coordination/migratory insertion process, shown in black, as proposed for insertions of CO or tetrafluoroethylene into the Pt−O bond of Pt(dppe)(Me)(OMe).[11]

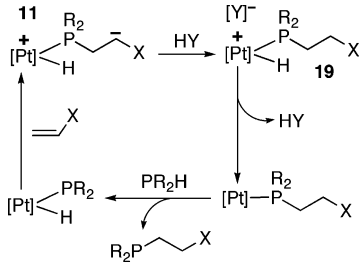
Alternatively, Michael addition (in red) of the nucleophilic Pt-PR_2 ligand to the alkene could yield zwitterionic **11**. Such a process is well precedented both for metal phosphido complexes[12] and in the reactions of phosphines with Michael acceptors.[13] Attack of the stabilized carbanion at the electrophilic Pt center and Pt−P bond dissociation would then yield **10**, perhaps via five-coordinate **12a**. Product formation could occur either via C−H reductive elimination from **10** or by intramolecular proton transfer between the carbanion (base) and the cationic Pt-hydride (acid) in zwitterion **11**.

Scheme 5[a]



[a] [Pt] = Pt(Me-Duphos), L = PHPh(*i*-Bu), X = CO_2t-Bu.

Scheme 6[a]



[a] [Pt] = Pt(diphos), X = CO_2R or CN.

Byproduct formation could also occur via organometallic (black) or Michael (red) pathways (Scheme 4). With monodentate phosphine ligands, Pringle suggested that insertion of acrylonitrile into the Pt−C bond in **12b** (or analogous dinuclear species), driven by release of strain, would give **13**. Reductive elimination would then yield a byproduct with $n = 1$,[3] or further Pt−C insertions and reductive elimination would give higher oligomers. With catalysts bearing bidentate diphosphines, similar reactions could occur, perhaps via **12a** and a five-coordinate analogue of intermediate **13**.

Alternatively, Michael addition of the zwitterion **11** to another alkene would yield a new zwitterion (**14**, $n = 1$), which could (a) yield a byproduct containing two olefin-derived fragments by the acid−base chemistry described above; (b) intersect the organometallic pathway by carbanion attack at Pt; or (c) attack another alkene to eventually yield byproducts derived from three or more olefins. It is not clear how the strong solvent effects on byproduct formation in Scheme 1 can be rationalized by the insertion pathway, but stabilization

(9) The dr values for path **A** and path **B** are as follows: for PPh(*i*-Bu), 1:1.3 vs 2:1; for PMe(Is), 1:1.6 vs 7:1; for PPh(Cy), 1:1.6 vs 1.2:1.

(10) For related observations, see: (a) Wicht, D. K.; Kourkine, I. V.; Lew, B. M.; Nthenge, J. M.; Glueck, D. S. *J. Am. Chem. Soc.* **1997**, *119*, 5039−5040. (b) Wicht, D. K.; Kourkine, I. V.; Kovacik, I.; Glueck, D. S.; Concolino, T. E.; Yap, G. P. A.; Incarvito, C. D.; Rheingold, A. L. *Organometallics* **1999**, *18*, 5381−5394.

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Table 1. Effect of Protic Additives on Pt-Catalyzed Hydrophosphination of Activated Olefins CH_2=CH(X)[a]

entry	catalyst precursor[b]	PHR_2	X	alkene/ PHR_2	equiv of additive[c]	time (min)[d]	selectivity (%)[e]	ee (%)[f]
1	A	PHPh(*i*-Bu)	CO_2t-Bu	1	none	20	97	25
2	A	PHPh(*i*-Bu)	CO_2t-Bu	1	20	5	99	6
3	A	PHPh(*i*-Bu)	CO_2t-Bu	10	20	5	76	ND[g]
4	A	$PHPh_2$	CO_2t-Bu	1	none	20	99.5	
5	A	$PHPh_2$	CO_2t-Bu	1	5	5	99.9	
6	A	$PHPh_2$	CO_2t-Bu	1	20	5	100	
7	A	$PHPh_2$	CO_2t-Bu	10	none	5	97.8	
8	B	$PHPh_2$	CO_2t-Bu	1	none	> 30 d	100	
9	B	$PHPh_2$	CO_2t-Bu	1	20	5 d	100	
10	A	PHMe(Is)	CO_2t-Bu	1	none	5 d	99.2	28
11	A	PHMe(Is)	CO_2t-Bu	1	20	2 d	100	56
12	B	PHMe(Is)	CO_2t-Bu	1	none	>30 d	100	
13	B	PHMe(Is)	CO_2t-Bu	1	20	7 d	100	
14	A	PHPh(Cy)	CN	2[h]	none	5 d	66	11
15	A	PHPh(Cy)	CN	1	20	60	96.5	8
16[i]	A	PHPh(Cy)	CN	2[h]	none	5 d	62	9
17[i]	A	PHPh(Cy)	CN	1	20[j]	20	96.5	5

[a] Catalytic reactions were carried out in toluene (except for entries 16, 17, in THF) with 0.24 mmol of the phosphine substrate and 5 mol % catalyst. [b] A = Pt((R,R)-Me-Duphos)(*trans*-stilbene); B = Pt(norbornene)$_3$. [c] Additive = *t*-BuOH in entries 1−16, H_2O in entry 17. [d] Time for completion of the reaction, from ^{31}P NMR monitoring. [e] Selectivity = [major product]/([major product] + [byproducts]), from ^{31}P NMR integration of crude reaction mixtures. [f] Enantiomeric excess was determined by NMR after complexation of the phosphine to a chiral Pd complex (Supporting Information). [g] ND = not determined. [h] It was necessary to use 2 equiv of alkene to ensure complete conversion of the secondary phosphine. [i] In THF. [j] Additive = water.

of the ionic intermediates in this Michael route by the polar solvents is plausible.

In experiments designed to enable direct observation of some of the proposed catalytic intermediates, treatment of Pt(Me-Duphos)(*trans*-stilbene) with phenyl(isobutyl)phosphine gave a mixture of Pt(0) complex **15** (mixture of four diastereomers) and the phosphido hydride **16** (Scheme 5).[5] As observed for Pt(Me-Duphos)(PPhIs)(H) (Is = 2,4,6-(*i*-Pr)$_3$C$_6$H$_2$), only one set of signals for **16** was observed by NMR spectroscopy, even at low temperature, presumably because of rapid (on the NMR time scale) interconversion of the two expected diastereomers by phosphorus inversion.[4] Treatment of this mixture with *tert*-butyl acrylate at low temperature gave phosphines **6a** and **7a** and acrylate complex **17**; no intermediates were observed.[14]

These observations led us to develop an indirect probe for proposed zwitterionic intermediate **11** (Scheme 6). If it were trapped by another, added electrophile before it could undergo further reaction with the alkene, formation of byproducts by the Michael addition pathway would be prevented. An acid HY, for example, would protonate **11** and yield cationic phosphine hydride complex **19**, whose deprotonation by the conjugate base Y^- would form Pt(0) and a functionalized phosphine. This process would be catalytic in acid, but might require higher HY concentrations for efficient trapping of **11**.[15]

To test this hypothesis, we carried out catalytic hydrophosphinations under identical conditions in the presence or absence of varied amounts of *tert*-butyl alcohol (Table 1).[7] Formation of byproducts was indeed suppressed. This effect was most striking for addition of PHPh(Cy) to acrylonitrile (entries 14−17), but also evident in cases where selectivity was already high, and it was difficult to quantify changes in product ratios, such as entries 1, 2, and 4−6. As expected from Scheme 4, adding more alkene reduced the selectivity (entries 3 and 7), even in the presence of *t*-BuOH. The additive also increased reaction rate and affected the enantioselectivity (entries 1 and 2, 10 and 11). Water (entry 17) was as effective as *tert*-butyl alcohol, and the rate effects were similar for two different catalyst precursors, Pt(Me-Duphos)(*trans*-stilbene) and Pt(norbornene)$_3$, although the latter was more selective.

If byproducts were formed by insertion into a Pt−C bond, as in Scheme 4, such behavior would not be expected. Instead, these observations are consistent with the hypothesis that the Michael addition mechanism of Scheme 4 is responsible for the byproduct formation in this system.[16] The additive-induced changes in rate and enantioselection also suggest that conjugate addition is important in product formation. If nucleophilic attack on the alkene is reversible,[7,13] irreversible trapping of zwitterionic intermediate **11** by *tert*-butyl alcohol might increase the rate and also affect ee by freezing in any initial kinetic selectivity in formation of diastereomers of **11**.

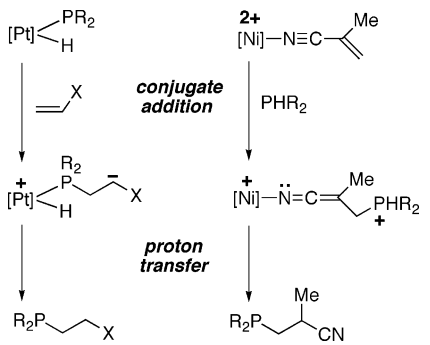
We cannot tell if the formation of functionalized β-phosphino-alkyl groups (Pt-CH(X)CH_2PR_2) in catalysis (**10**) and in related model compounds also occurs via **11** by carbanion attack at Pt (Scheme 4, path b) or/and by the coordination/insertion mechanism of Scheme 3.[4,10,17] However, contribution from a Michael addition pathway, and hence byproduct formation, should be favored for smaller, more nucleophilic Pt-PR_2 groups and for

(14) Complex **17** was also observed after Pt-catalyzed reaction of *tert*-butyl acrylate with PHPh(*i*-Bu).

(15) Under catalytic conditions, the secondary phosphine substrate might act as the acid HY or be deprotonated by Y^-.

(16) Scheme 6 predicts that the deuterium-labeled acid DY would yield $R_2PCH_2CH(D)X$. In contrast, unlabeled product would be formed by a coordination/insertion mechanism (Scheme 3). However, attempts to test these predictions were thwarted by rapid P-H/O-D exchange between secondary phosphines R_2PH and added D_2O (or *t*-BuOD) in the presence of the catalyst Pt(Me-Duphos)(*trans*-stilbene). When an alkene was added to these mixtures, ca. 50−90% deuterium was incorporated into the hydrophosphination product, depending on the substrates and the additive. Since P−D oxidative addition followed by insertion and C−D reductive elimination (Scheme 3), as well as zwitterion protonation (Scheme 6), could yield deuterated product, these results did not provide the desired mechanistic information. See the Supporting Information for experimental details.

Scheme 7[a]



[a] [Pt] = Pt(diphos), X = CO_2R or CN. [Ni] = Ni(Pigiphos).[1c]

alkenes more susceptible to nucleophilic attack,[18] consistent with the data in Table 1.

In summary, we have provided evidence that P−C and C−C bond formation in Pt-catalyzed hydrophosphination proceeds via Michael addition, although contribution from coordination/insertion mechanisms cannot be ruled out. A similar conjugate addition/proton-transfer mechanism was proposed for hydrophosphination catalyzed by a cationic nickel complex,[1c] but with some significant differences (Scheme 7). For Pt, the Pt-PR_2 group attacks the free alkene, while for Ni, the phosphine attacks complexed methacrylonitrile. Thus, the Pt catalyst activates the nucleophile, and the Ni one the electrophile.

We are currently investigating the mechanism in more detail, the generality of these additive effects in improving the selectivity in Pt-catalyzed hydrophosphination, and the possibility of intercepting putative zwitterionic intermediates **11** with other electrophiles.[19]

Acknowledgment. We thank the National Science Foundation and the American Chemical Society Petroleum Research Fund for support, Cytec Canada for a gift of PHPh(*i*-Bu), and Professor H. Amri for advice on synthesis of **8**.

Note Added after ASAP Publication. Due to a production error, the version of this paper posted on the Web on September 13, 2005, had atom labels missing in Schemes 1 and 2. The version that now appears is correct.

Supporting Information Available: Details of synthesis and characterization and of the catalytic experiments. This information is available free of charge via the Internet at http://pubs.acs.org.

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