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Platinum(II)-Coordinated Phosphinous Acid-Catalyzed Alkylidenecyclopropanation of Bicyclic Alkenes with Terminal Alkynes

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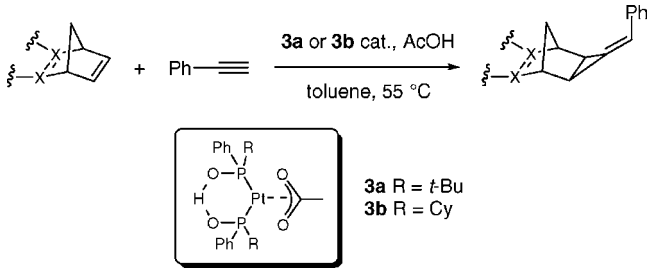
ABSTRACT

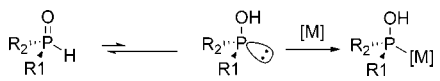


New Pt(η^2-acetato){[(R)(Ph)PO]$_2$H} complexes 3 prepared from $PtCl_2(CH_3CN)_2$ and secondary phosphine oxides (SPOs) catalyzed the [2 + 1] cycloaddition of phenylethyne (5a) with norbornene derivatives 4 to afford benzylidenecyclopropanes.

Secondary phophine oxides (SPOs) are weak acids[1] characterized by an equilibrium between a P(V) and a P(III) form.[2]

The latter is more appropriate for the coordination of metal centers through the phosphorus atom, affording air-stable complexes resistant to moisture and high temperature (Scheme 1).[3] In 2001, Li showed that phosphinous acid−palladium complexes were able to catalyze the cross-coupling reactions of electronically deactivated aryl chlorides.[4] Since this pioneering work, a new class of complexes have emerged as powerful catalysts in various transformations.[5] Moreover, chiral phosphine oxides are promising preligands in enantioselective catalysis.[5c] In a few cases, platinum−SPO complexes have been used in stoichiometric amounts to

Scheme 1. Coordinating Behavior of SPOs



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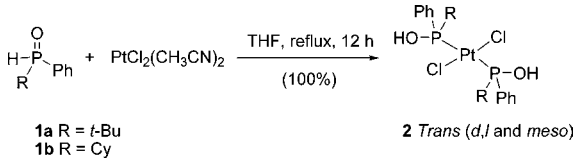
elucidate the mechanism of reactions such as hydrophosphinylation[6] and hydrophosphorylation.[7] Regarding these complexes, only addition processes such as chemoselective hydrolysis of nitrile to amide[8] or hydroformylation[9] have been reported to date. However, no catalytic effect on carbon−carbon bond formation has ever been mentioned involving platinum−SPO complexes. Recently, we disclosed an unusual [2 + 1] cycloaddition of terminal alkynes with norbornene derivatives catalyzed by phosphinous acid−palladium complexes.[10,11] In connection with these studies, we decided to examine the catalytic activity of platinum−SPO complexes in the coupling reaction of norbornadienes with alkynes. The extension of this method to platinum would be the first example of carbon−carbon bond formation catalyzed by this class of complex. In this letter, we report the synthesis of a novel Pt(η^2-acetato){[(R)(Ph)PO]$_2$H} complex **3** and its application to the benzylidenecyclopropanation of norbornene derivatives. First, we studied the formation reaction of this complex involving $PtCl_2(CH_3CN)_2$ and 2 equiv of (*R*)-(+)-*tert*-butylphenylphosphine oxide (*R*)-(+)-**1a**.[12] Complete conversion was achieved after 12 h in THF at 60 °C. The ^{31}P NMR spectrum of the crude mixture was consistent with the structure $PtCl_2$[(*t*-Bu)(Ph)P(OH)]$_2$ **2a**, in which the metal is coordinated by two SPOs **1a** in the *trans* configuration (Scheme 2).[13] Noteworthy in this case

Scheme 2. Synthesis of Platinum Complex **2** from Pt(II) and SPOs **1**



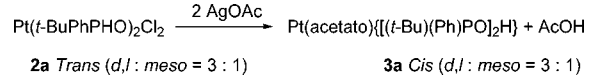
1a R = *t*-Bu
1b R = Cy

2 *Trans* (*d*,*l* and *meso*)

is that the coordination of chiral SPO (*R*)-(+)-**1a** to the metal proceeded with partial racemization.[14] Interestingly, when the reaction was carried out at room temperature for 12 h in CH_2Cl_2, with $PtCl_2$(COD) (more soluble than $PtCl_2(CH_3CN)_2$), a mixture of *cis*- and *trans*-**2a** isomers was obtained in a 1:1 ratio but with almost no racemization.[15]

Exchange of chloride to acetate using 2 equiv of AgOAc resulted in irreversible formation of a neutral Pt(acetato) complex **3a** in 65% yield accompanied by a loss of acetic acid. Indeed, ^{31}P NMR only reveals the exclusive formation of a *cis* complex, and mass spectrometry data are in agreement with a monomeric structure containing one acetate ligand (Scheme 3).

Scheme 3. Synthesis of **3a** from $PtCl_2$(*t*-BuPhPHO)$_2$ **2a**



2a *Trans* (*d*,*l* : *meso* = 3 : 1)

3a *Cis* (*d*,*l* : *meso* = 3 : 1)

Finally, X-ray analysis of the *meso* complex[16] confirmed a Pt(η^2-acetato){[(*t*-Bu)(Ph)PO]$_2$H} structure for **3a**. The planar geometry around the platinum atom and the distance between the two oxygen atoms O1 and O2 (2.391 Å) suggest a symmetrical O−H−O hydrogen bonding (Figure 1).[17] The

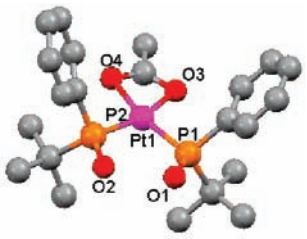


Figure 1. X-ray structure of (*meso*)-**3a**. Selected bond lengths [Å] and angles [°]: Pt1−P1 2.2298 (9), Pt1−P2 2.2267 (9), P1−O1 1.540 (3), P2−O2 1.553 (3), O4−Pt1−O3 60.34 (10), O4−Pt1−P2 103.21 (7), 03−Pt1−P1 104.08 (7), P2−Pt1−P1 92.38 (3).

reaction was extended to other SPO ligands. For example, **1b** could be converted to complex **3b** with an overall yield of 70%.

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(11) For recent examples of transition metal catalyzed vinylcyclopropanation of norbornene derivatives, see: (a) Trépanier, V. E.; Fillion, E. *Organometallics* **2007**, *26*, 30−32. (b) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338−5339. (c) Miura, T.; Sasaki, T.; Harumashi, T.; Murakami, M. *J. Am. Chem. Soc.* **2006**, *128*, 2516−2517. (d) Tenaglia, A.; Marc, S. *J. Org. Chem.* **2006**, *71*, 3569−3575 and references therein.

(12) NMR analyses became easier by monitoring the reaction with enantiopure **1**. For the enantioselective synthesis of SPOs, see: (a) Leyris, A.; Nuel, D.; Giordano, L.; Achard, M.; Buono, G. *Tetrahedron Lett.* **2005**, *46*, 8673−8676. (b) Leyris, A.; Bigeault, J.; Nuel, D.; Giordano, L.; Buono, G. *Tetrahedron Lett.* **2007**, *48*, 5247−5250.

(13) The structures of complexes were deduced from coupling constants between platinum and phosphorus atoms. For the *cis* isomer, the $^1J_{^{195}Pt-P}$ coupling constant is larger (≈3700 Hz) than that for the *trans* isomer (≈2500 Hz). For ^{31}P NMR study of tertiary phosphine complexes of platinum(II), see: (a) Grim, S. O.; Keiter, R. L.; McFarlane, W. *Inorg. Chem.* **1967**, *6*, 1133−1137. (b) Cobley, C. J.; Pringle, P. G. *Inorg. Chim. Acta.* **1997**, *265*, 107−115.

(14) The observation in the NMR spectrum of two doublets for the *trans*, *meso*, and D,L isomers of **2a** revealed a racemization process during the conversion of $PtCl_2(CH_3CN)_2$ to **2a**. The racemization of (*R*)-(+)-*t*-BuPhP(O)H in the presence of $PtCl_2$ was recently reported: ref 8c.

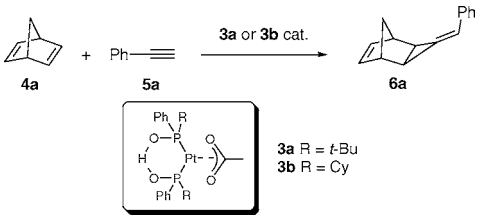
(15) For similar observations, see: Jiang, X.-B. Ph.D. Thesis, University of Groningen, 2004.

(16) The crystallographic data for complex **3a** have been deposited with the Cambridge Crystallographic Data Centre (CCDC 644335). These data can be obtained free of charge at www.ccdc.cam.ac.uk/data_request/cif.

(17) Naik, D. V.; Palenik, G. J.; Jacobson, S.; Carty, A. J. *J. Am. Chem. Soc.* **1974**, *96*, 2286−2288.

Second, the reaction of phenylethyne (**5a**) and norbornadiene **4a** in the presence of 5 mol % of platinum complexes in toluene at 55 °C was examined (Table 1). No reaction

Table 1. Pt/SPOs-Catalyzed [2 + 1] Cycloaddition of **4a** with **5**[a]



entry	catalytic system (ratio)	yield (%)[b]
1	$PtCl_2(CH_3CN)_2$	–
2	$PtCl_2(CH_3CN)_2$/AgOAc (1:2)	–
3	$PtCl_2(CH_3CN)_2$/AgOAc/AcOH (1:2:2)	–
4	**2a**	–
5	$PtCl_2(PPh_3)_2$/AgOAc (1:2)	–
6	**2a**/AgOAc (1:2)	65[c]
7	**3a**	52[d]
8	**3a**/AcOH (1:2)	68[c]
9	**3a**/AcOH (1:20)	80[c]
10	**3a**/AcOH (1:20)	81[e]

[a] All reactions were carried out with 1 mmol of **4a** at 55 °C for 20 h in toluene. **4a**/**5a**/**Pt-cat**. = 2:1:0.05. [b] Isolated yield. Cycloadduct **6a** was always contaminated by unidentified and inseparable byproducts. [c] Purity 90%. [d] Purity 55%. [e] Reaction carried out with **4a**/**5a**/**3a** = 1:2:0.05 as the molar ratio afforded a pure adduct.

was observed with halide complexes including SPOs or not (Table 1, entries 1−4). However, the addition of 2 equiv of AgOAc to catalyst **2a** proved to be beneficial. Indeed, in this case, the [2 + 1] cycloadduct **6a** was obtained in 65% isolated yield (entry 6).[10,18]

Interestingly, cyclopropanations are usually observed in an intramolecular fashion from $PtCl_2$ (without ligands) and 1,6- and 1,5-enynes.[19] In the present case, the formation of benzylidenecyclopropane **6a** occurred in intermolecular fashion via a Pt(II)−SPOs catalytic process. To our knowledge, this represents the first intermolecular alkylidenecyclopropanation of an alkene with a terminal alkyne catalyzed by platinum. It is worth mentioning that when carried out with $Pt(PPh_3)_2Cl_2$/AgOAc (1:2 molar ratio) the reaction did not proceed at all (entry 5). These experiments reveal that acetate and SPO ligands are crucial for the achievement of the cycloaddition. Finally, one of the most promising results was observed with **3a**/AcOH (1:2) as a catalytic system (entry 8). The yield raised to 80% when increasing amounts of AcOH were used (entry 9). Moreover, reversing the molar ratio of **4**/**5a** to (1:2) resulted in the suppression of byproducts (entry 10).[20] Note that the palladium complex with two SPOs **1a** afforded **6a** in lower yield (42%) compared to platinum complex **3a** (81%).[10] Moreover, the catalyst **3b** proved to be the most active for the alkylidenecyclopropanation. Under similar conditions, a 3:2 mixture of dicycloadduct **7** and monocycloadduct **6a** was isolated (Figure 2).

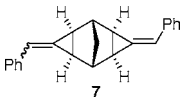
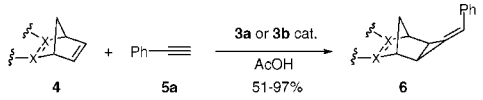


Figure 2. Structure of dicycloadduct **7**.

These promising results prompted us to test other strained alkenes using the optimized conditions. We were pleased to observe that this platinum(II)-catalyzed [2 + 1] cycloaddition tolerated a broad range of norbornene derivatives (Table 2).[21] Norbornene (**4b**) and benzonorbornene (**4c**) afforded the expected benzylidenecyclopropanes **6b** and **6c** in fair yields

Table 2. Pt/SPOs-Catalyzed [2 + 1] Cycloaddition of **4** with **5a**[a]



entry	alkene	time (h)	product	yield (%)[b]
1	**4a**	20	**6a**	81
2	**4b**	14	**6b**	51[c]
3	**4c**	36	**6c**	68
4	**4d**	36	**6d**	82 (88)[c]
5	**4e**	60	**6e**	86
6	**4f**	60	**6f**	85
7	**4g**	14	**6g**	97[c]
8	**4h**	38	**6h**	75[c,d]

[a] All reactions were carried out with 0.5 mmol of **4** at 55 °C in toluene. **4**/**5a**/**AcOH**/**3a** = 0.5:1:0.5:0.025. [b] Isolated yield. [c] Yield obtained using **3b** as catalyst. [d] **6h** was obtained as a 1:1 mixture of diastereomers.

(18) The *exo*-selectivity for reactions of [2.2.1] bicyclic alkenes is well established. See: Koga, N.; Ozawa, T.; Morokuma, K. *J. Phys. Org. Chem.* **1990**, *3*, 519−533.

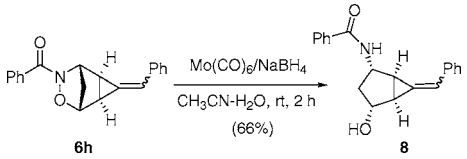
(19) For recent reviews, see: (a) Fürstner, A.; Davies, P. W. *Angew. Chem. Int. Ed.* **2007**, *46*, 3410−3449. (b) Zhang, L.; Sun, J.; Kozmin, S. A. *Adv. Synth. Catal.* **2006**, *348*, 2271−2296. (c) Bruneau, C. *Angew. Chem. Int. Ed.* **2005**, *44*, 2328−2334.

(Table 2, entries 2 and 3) which could not be improved with prolonged reaction times. However, functionalized norbornadienes **4d**−**f** reacted chemoselectively at the less-substituted double bond with superior yields (Table 2, entries 4−6). Interestingly, the presence of heteroatoms such as nitrogen and oxygen in the bicyclic alkenes was well tolerated. Diaza- and oxazabicyclic alkenes **4g** and **4h** afforded the expected cycloadducts **6g** and **6h** in 97% and 75% yields, respectively (Table 2, entries 7 and 8).

In contrast, the presence of heteroatoms in the bicyclic alkenes was detrimental for the reaction catalyzed with $Pd(OAc)_2$/SPOs **1b** affording the expected adduct **6g** (57%) and **6h** (27%) in lower yields.

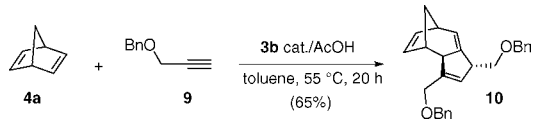
Compounds **6g** and **6h** appeared to be very attractive for synthetic purposes because the reductive cleavage of N−N or N−O bonds offers an entry to *cis*-2,4-diamido- or 2,4-hydroxyamido-6-methylenebicyclo[3.1.0]hexane.[22] As a proof-of-principle, the N−O bond of **6h** was easily reduced with $Mo(CO)_6/NaBH_4$, affording **8** in 66% yield (Scheme 4). A

Scheme 4. Synthesis of Amidoalcohol **8**



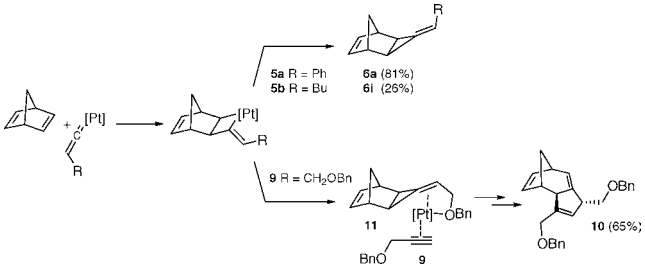
notable difference in selectivity compared to the palladium catalyst[10] was observed when the reaction was carried out with prop-2-ynyloxymethyl-benzene (**9**). In this case, only a tricyclic compound **10** was obtained as a single regio- and stereoisomer in 65% yield (Scheme 5). The regio- and stereochemistry were established by 2D NMR experiments.

Scheme 5. Synthesis of the Tricyclic Compound **10**



A possible pathway for the metal-catalyzed [2 + 1] cycloaddition of norbornadiene (**4a**) and phenylethyne (**5a**) was proposed in our previous work.[10] Due to the intramolecular coordination of the metal with the oxygen atom, tricyclic compound **10** could be formed by insertion of the alkyne moiety into the carbon−carbon bond of alkylidenecyclopropane. Indeed, with phenylethyne (**5a**) or hex-1-yne (**5b**), the reaction stopped at the alkylidenecyclopropanation step (Scheme 6).

Scheme 6. Proposed Reaction Pathways for **6a** and **10**



This proposal is supported by the reaction of **11**[23] and alkyne **9** in the presence of **3b**-cat which afforded **10** as a single adduct. The whole transformation can be viewed as an unprecedented [4 + 2] cycloaddition involving alkylidenecyclopropanes and terminal alkynes.

In conclusion, we have shown that new Pt(η^2-acetato)-{[(R)(Ph)PO]$_2$H} complexes **3** are able to catalyze a benzylidenecyclopropanation of **4** with phenylethyne (**5a**). This cycloaddition represents the first example of carbon−carbon bond formation catalyzed by platinum/SPO complexes. Like palladium, platinum(II) complexes coordinated by SPOs may involve a metal vinylidene complex as a key intermediate. Moreover, this new class of complexes proves to be useful as catalysts for an unusual [4 + 2] intermolecular cycloaddition of an alkylidenecyclopropane with a terminal alkyne. Platinum−SPO-catalyzed reactions of alkylidenecyclopropanes and insights into the mechanism of this reaction are in progress in our laboratories.

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Supporting Information Available: Experimental procedures and characterization data of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) An excess of phenylethyne (**5a**) leads to a well-known mixture of linear and branched enynes which could be removed by chromatography. Without the presence of alkene, the homocoupling did not proceed. For examples of terminal alkyne−alkyne couplings catalyzed by palladium, see: Trost, B. M.; Sorum, M. T.; Chan, C.; Harms, A. E.; Rühter, G. *J. Am. Chem. Soc.* **1997**, *119*, 698−708.

(21) The same reaction carried out with cyclopentene in place of strained alkenes did not work.

(22) For the reductive cleavage of a cyclic N−N or N−O bond, see: (a) Pérez Luna, A.; Ceschi, M.-A.; Bonin, M.; Micouin, L.; Husson, H.-P.; Gougeon, S.; Estenne-Bouhtou, G.; Marabout, B.; Sevrin, M.; George, P. *J. Org. Chem.* **2002**, *67*, 3522−3524. (b) Zhang, D.; Süling, C.; Miller. M. J. *J. Org. Chem.* **1998**, *63*, 885−888.

(23) Obtained through our previous Pd-catalyzed alkylidenecyclopropanation: see ref 10.