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Published on Web 03/20/2002

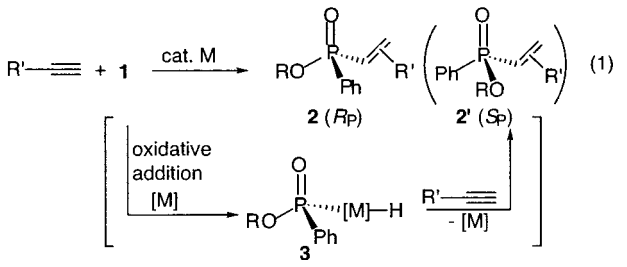
Retention of Configuration on the Oxidative Addition of P−H Bond to Platinum (0) Complexes: The First Straightforward Synthesis of Enantiomerically Pure P-Chiral Alkenylphosphinates via Palladium-Catalyzed Stereospecific Hydrophosphinylation of Alkynes

Li-Biao Han,* Chang-Qiu Zhao, Shun-ya Onozawa, Midori Goto, and Masato Tanaka*

National Institute of Advanced Industrial Science and Technology, AIST Tsukuba Central 5, Tsukuba, Ibaraki 305-8565, Japan

Received February 5, 2002

P-chiral organophosphorus compounds are of great importance in biological chemistry, organic synthesis, and asymmetric catalysis.[1] However, their preparations usually require tedious steps.[2] We have reported a series of metal-catalyzed addition reactions of P(V)−H bonds to carbon−carbon unsaturated bonds (hydrophosphinylation), which cleanly and efficiently furnish a wide variety of organophosphorus compounds in high yields and selectivities.[3] On the other hand, (R_P)-phenylphosphinate **1**, a white solid easy to prepare and handle, has been known for more than 30 years.[4] With these in mind, we commenced our study on a new synthetic strategy for P-chiral phosphorus compounds via metal-catalyzed stereospecific hydrophosphinylation (eq 1). Since the metal-catalyzed hydrophosphinylation of alkynes is triggered by the oxidative addition of the P−H bond as illustrated in eq 1, stereospecific oxidative addition to the metal (either complete retention or inversion) is one of the preconditions. Although oxidative additions of P−H bonds to metal-complexes have been documented previously, nothing is known about its stereochemistry.[3] Herein reported are (1) the first investigation on the stereochemistry of the oxidative addition of the P(V)−H bond to metal complexes, revealing retention of configuration at the phosphorus center in the reaction of **1** with platinum (0) complexes, and (2) the first straightforward synthesis of **2** by a novel palladium-catalyzed stereospecific hydrophosphinylation of alkynes with **1**. Compound **2** is a versatile intermediate, which can be readily converted to other P-chiral compounds by simple operations.[2]



When an equimolar mixture of **1** and $Pt(PEt_3)_4$ was mixed in toluene at room temperature for 1 h, the starting materials completely disappeared to afford white hydrido platinum complex **3a** in 87% isolated yield as single stereoisomer.[5] On the other hand, a similar treatment of a 50/50 mixture of **1**/**1′** resulted in the formation of a 50/50 mixture of two isomeric complexes, **3a** and **3a′**, which are readily distinguishable in NMR spectroscopies[5](see

* Author for correspondence. E-mail: libiao-han@aist.go.jp.

Chart 1

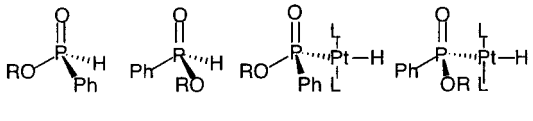


Chart 1). The oxidative addition of the P−H bond to platinum (0), therefore, proceeds stereospecifically.

Although complex **3a** failed to give crystals suitable for X-ray analysis, the structure of a similar complex **3b**, generated via the reaction of **1** with Pt(dcpe)(cod) (dcpe = 1,2-bis(dicyclohexylphosphino)ethane; cod = 1,5-cyclooctadiene) has been unambiguously determined (Figure 1).[6] The absolute configuration at P(O) in **3b** is *S*, conclusively showing that *the oxidative addition of **1** to platinum (0) proceeds with retention of configuration.*

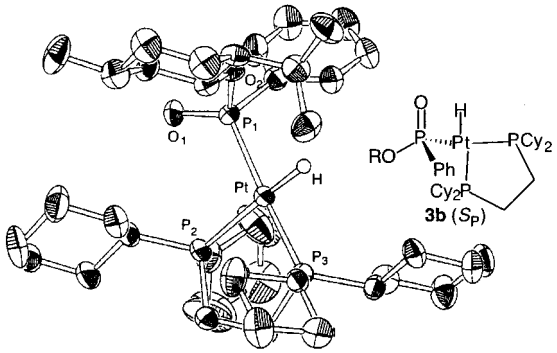
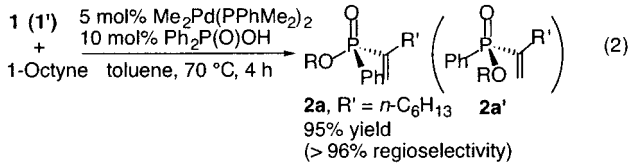


Figure 1. Molecular structure of complex **3b**.

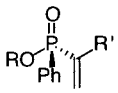
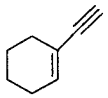
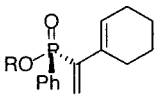
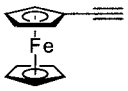
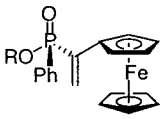
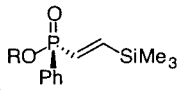
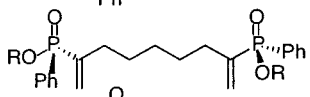
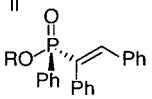
On the basis of this finding, the metal-catalyzed stereospecific hydrophosphinylation of **1** with alkynes is successfully developed.[7] Thus, extensive screening of the reaction procedure has revealed that $Me_2Pd(PPhMe_2)_2/Ph_2P(O)OH$ is the right catalyst[8] for the addition of **1** to 1-octyne to produce α-adduct **2a** in a high yield and regioselectivity (eq 2).[9]



While **2a′** was not found in this particular reaction of **1**, a 50/50 mixture of **2a**/**2a′** was generated by using a 50/50 mixture of **1**/**1′**.[10]

10.1021/ja025816+ CCC: $22.00

Table 1. Stereospecific Hydrophosphinylation of Alkynes[a]

run	alkyne	adduct **2**[b]	% isolated yield
	R'—		
1		R' = *n*-C_6H_{13}	96
2		R' = H	93[c]
3		R' = $Cl(CH_2)_3$	85
4		R' = $NC(CH_2)_3$	82
5		R' = *t*-$BuCO_2(CH_2)_2$	60
6		R' = Ph	91
7		R' = 2,4,6-$Me_3C_6H_2$	83
8		R' = 4-$MeOC_6H_4$	64
9		R' = 4-ClC_6H_4	86
10		R' = 1-naphthyl	81
11			89
12			60[d]
13	Me_3Si—		89[e]
14	—$(CH_2)_5$—		65[d]
15	Ph— —Ph		85[f]

[a] R = (−)-menthyl. Conditions: equimolar **1** and an alkyne in toluene (0.4 M), 3 mol % $Me_2Pd(PPhMe_2)_2$, 5 mol % $Ph_2P(O)OH$, 70 °C, 4.5 h. Regioselectivity to the adduct shown is ca. 95∼98%. [b] The absolute configuration at phosphorus is R_P. ($R_P/S_P \geq 99$). [c] 1 atm acetylene gas, THF, 67 °C, 15 h. [d] 2.1 equiv of **1** was used. [e] *trans* isomer only. [f] THF, 67 °C, 16 h.

Since **2a** was an oil, we were unable to determine the absolute configuration by X-ray analysis. However, its analogue adduct obtained from the reaction of **1** with 2,4,6-trimethylphenylacetylene afforded a crystalline material, X-ray analysis of which revealed that the configuration was *R*,[10] showing that *the palladium-catalyzed hydrophospinylation also proceeds with retention of configuration at phosphorus.*

The palladium-catalyzed stereospecific hydrophosphinylation has a wide generality. As shown in Table 1, acetylene gas can also be employed as the substrate and the novel synthetically versatile (R_P)-vinylphosphinate[2] was obtained in 93% yield. With the exception of trimethylsilylacetylene[3a] which gave the *β-trans*-adduct, other alkynes of both aliphatic and aromatic ones, including those bearing functionalities such as chloro, cyano, carbonylalkoxy, olefinic, and alkoxy groups were all able to react in a efficient way under similar reaction conditions to afford the corresponding (R_P)-vinylphosphinates in high yields and selectivities. Note that ethynylferrocene was also successfully hydrophosphinylated to give a good yield of the corresponding ferrocene, which can be readily applicable in the synthesis of novel optically active ferreocenyl phosphines of great applications in modern asymmetric catalysis.[11] As exemplified by run 14, two phosphinyl groups were easily introduced into diynes such as nona-1,8-diyne. Although a relatively prolonged heating was needed, an internal alkyne tolane was also successfully hydrophosphinylated to give the corresponding *trans*-adduct selectively.

In conclusion, both the oxidative additionof the P(V)−H bond to platinum (0) complexes and the palladium-catalyzed hydrophosphinylation of alkynes proceed stereospecifically with retention of configurations at phosphorus, and the latter provides a convenient and general synthetic route to enantiomerically pure P-chiral alkenylphosphinates.[12] Further studies on the applications of this finding are now in progress.

Acknowledgment. Partial financial support from the Japan Science and Technology Corporation (JST) through the CREST (Core Research for Evolutional Science and Technology) program and a STA fellowship to C.-Q.Z.

Supporting Information Available: Spectral and analytical data of products (PDF) and X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) Pure (R_P)-**1** (**1**/**1′** ≥ 99/1) was readily prepared in a large scale by adopting a modified method of Mislow. Farnham, W. B.; Murray, R. K.; Mislow, K. *J. Am. Chem. Soc.* **1970**, *92*, 5809. See Supporting Information for its characterization.

(5) Characteristic signals of **3a** and **3a′** in ^{1}H and ^{31}P NMR spectroscopies: **3a**, δ −5.23 (Pt−H, J_{HPt} = 720.4 Hz); δ 100.1 (P(O), $J_{P(O)Pt}$ = 2803.1 Hz). **3a′**, δ −5.53 (Pt−H, J_{HPt} = 714.9 Hz); δ 104.2 (P(O), $J_{P(O)Pt}$ = 2800.4 Hz). See Supporting Information for details.

(6) Selected bond lengths (Å) and angles (deg) of **3b**: O(1)−P(1) = 1.508(5), O(2)−P(1) = 1.628(6), P(1)−Pt = 2.299(2), P(2)−Pt = 2.304(2), P(3)−Pt = 2.286(2); P(1)−Pt−P(2) = 97.29(7), P(1)−Pt−P(3) = 175.31(8), P(2)−Pt−P(3) = 86.94(7). See Supporting Information for details.

(7) Although metal-catalyzed hydrophosphinylations have been studied with $(RO)_2P(O)H$ and $Ph_2P(O)H$, which showed different reactivity (ref 3), similar reactions have not been performed with (RO)R′P(O)H yet.

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(9) Adduct **2a** and its minor *β*-regioisomer were isolated in pure form and fully characterized. See Supporting Information.

(10) Adducts **2a** and **2a′** were readily distinguished in ^{1}H NMR spectroscopy. **2a** (=CH_2): δ 5.71 (d, J_{HP} = 44.1 Hz), 5.91 (d, J_{HP} = 21.3 Hz); **2a′** (=CH_2) δ 5.58 (d, J_{HP} = 42.2 Hz), 6.18 (d, J_{HP} = 20.0 Hz). See Supporting Information.

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(12) In the presence of a base, palladium-catalyzed couplings of diastereomerically pure P−H compounds with halides have been reported to give highly pure P-chiral compounds. See (a) Xu, Y.; Wei, H.; Zhang, J.; Huang, G. *Tetrahedron Lett.* **1989**, *30*, 949. (b) Oshiki, T.; Imamoto, T. *J. Am. Chem. Soc.* **1992**, *114*, 3975. However, an investigation on the scope and limitations of these methods seem to be necessary considering the results of a recent report. (c) Al-Masum, M.; Kumaraswamy, G.; Livinghouse, T. *J. Org. Chem.* **2000**, *65*, 4776.

JA025816+