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P-Chirogenic phosphonium salts: preparation and use in Rh-catalyzed asymmetric hydrogenation of enamides

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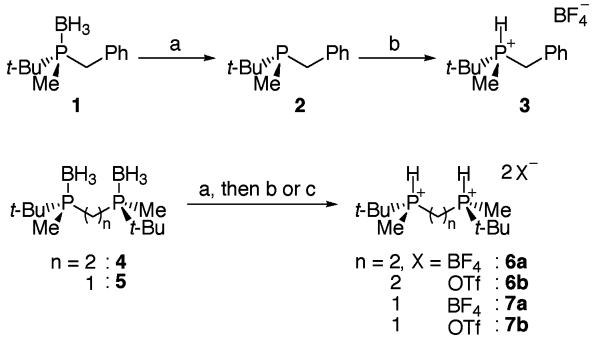
Abstract—P-Chirogenic trialkylphosphonium salts were prepared from the corresponding free phosphines by treatment with a strong acid (HBF_4 or HOTf). No racemization of the phosphonium salts occurred in methanol or water even at considerably high temperature. The salts were conveniently used in rhodium-catalyzed asymmetric hydrogenation of enamides.

During our continuing studies on development of new chiral phosphine ligands, we previously described ethylene- or methylene-bridged P-chirogenic trialkyldiphosphines, 1,2-bis(alkylmethylphosphino)ethanes (abbreviated as BisP*) and bis(alkylmethylphosphino)-methanes (MiniPHOS).[1] These phosphine ligands exhibit high enantioselectivity in some transition metal-catalyzed asymmetric reactions, especially when *t*-Bu-BisP* or *t*-Bu-MiniPHOS are used. However, they are air-sensitive owing to high electron density at phosphorus and are readily oxidized on contact with air. In order to overcome the difficulty of storing them in inert atmosphere, they are usually isolated as air-stable borane complexes and the protecting boranato group is removed prior to use.

Recently, Fu and his co-worker found that tetrafluoroboric acid acts as a good protecting agent for air-sensitive trialkylphosphines such as tributylphosphine and tri-*tert*-butylphosphine.[2] The resulting salts are air-stable and easily liberate the trialkylphosphines on contact with a weak Brønsted base. The authors demonstrated that the salts can be conveniently used as catalyst/reagent precursors in phosphine-catalyzed or -mediated organic transformations without loss of reactivity. Their report intrigued us to develop a convenient protocol for P-chirogenic phosphine mediated process. Herein we wish to describe preparation of P-chirogenic trialkylphosphonium salts and their use as chiral ligands in rhodium-catalyzed asymmetric hydrogenation.

Several P-chirogenic trialkylphosphonium salts were prepared from phosphine–boranes (Scheme 1). Thus, (*S*)-*tert*-butylbenzylmethylphosphine–borane (**1**) was deboranated by treatment with trifluoromethanesulfonic acid followed by potassium hydroxide to give (*S*)-*tert*-butylbenzylmethylphosphine (**2**).[3] Protonation of free phosphine **2** was easily carried out by the use of aqueous tetrafluoroboric acid to provide phosphonium salt **3**. In a similar manner, diphosphonium salts **6a**,**b** and **7a**,**b** were prepared from the corresponding diphosphine–boranes **4** and **5**, respectively, using tetrafluoroboric acid or trifluoromethanesulfonic acid.[4] The phosphonium salts **6a**,**b** were air-stable white powder and remained unchanged upon storing at room temperature for at least several months. In contrast, salts **7a**,**b** proved difficult to be isolated pure, most likely due to their greater lability.

It has been reported that racemization of P-chirogenic phosphine was promoted by various reagents including



Scheme 1. *Reagents and conditions*: (a) i. TfOH, toluene, 0°C to rt, 30 min, ii. KOH, EtOH/H_2O, 60°C, 3 h; (b) HBF_4 aq., Et_2O, rt, 10 min; (c) TfOH, Et_2O, rt, 10 min.

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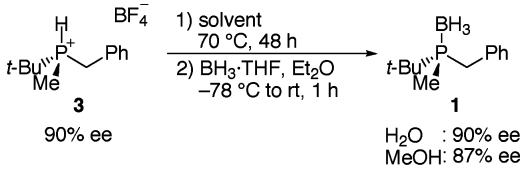
acids.[5] In particular, the acid-catalyzed racemization of phosphine was strongly affected by the nature of its conjugate base: for example, aqueous HBr induces complete racemization of methylphenylpropylphosphine in methanol at 90°C within 5 h, whereas the stereochemical integrity of the same phosphine remains intact in aqueous HCl.

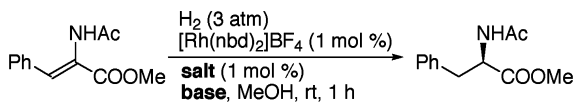
In our hands, no significant decrease in the enantiomeric purity of salt **3** was observed upon heating in water or methanol in a sealed tube at 70°C up to 2 days. The enantiomeric excess of the corresponding borane–adduct revealed to be identical (87–90% ee, Scheme 2) to the one of the starting salt (90% ee).[6]



Scheme 2.

The optically active P-chirogenic phosphonium salts were used in rhodium-catalyzed asymmetric hydrogenation of methyl 2-acetamidocinnamate.[7] The rhodium–diphosphine complex was generated in situ by mixing 1 mol% of $[Rh(nbd)_2]BF_4$ with 1 mol% of diphosphonium salt **6** or **7** in the presence or absence of a Brønsted base. Hydrogenation was carried out in methanol under 3 atm of H_2 at room temperature for 1 h. The results are summarized in Table 1. In the case of tetrafluoroboric acid salt **6a**, the reaction in the presence of diisopropylethylamine proceeded smoothly and gave the hydrogenation product with 99% ee (entries 1 and 2). However, addition of potassium carbonate retarded the reaction (entry 3). It should be noted that the hydrogenation proceeded rapidly even in the absence of base (entry 4). Although this fact is not fully understood, we suppose that, under our reaction conditions, the tetrafluoroboric acid salt enters in equilibrium with free diphosphine (*t*-Bu-BisP*) which reacts with $[Rh(nbd)_2]BF_4$ to form the thermodynamically more stable complex [Rh(*t*-Bu-BisP*)(nbd)]BF_4. On the other hand, addition of a base was essential to promote the hydrogenation with trifluoromethanesulfonic acid salt **6b**. Thus, both excellent yield and enantioselectivity were observed when **6b** was used in the presence of diisopropylethylamine (entry 5), whereas an abrupt decrease of conversion and enantioselectivity was observed in the absence of base (entry 6). Similar results were obtained in the cases of MiniPHOS salts **7a** and **7b** (entries 7–10).

Table 1. Rh-catalyzed asymmetric hydrogenation of methyl acetamidocinnamate with P-chirogenic diphosphonium salts **6** and **7**[a]



Entry	Salt	Base	Conv. (%)[b]	ee (%)[c]
1	**6a**	*i*-Pr_2NEt (2 mol%)	>99	94
2	**6a**	*i*-Pr_2NEt (20 mol%)	>99	99
3	**6a**	K_2CO_3 (10 mol%)	Trace	–
4	**6a**	None	>99	>99
5	**6b**	*i*-Pr_2NEt (2 mol%)	>99	95
6	**6b**	None	13	34
7	**7a**	*i*-Pr_2NEt (2 mol%)	>99	97
8	**7a**	None	>99	>99
9	**7b**	*i*-Pr_2NEt (2 mol%)	>99	99
10	**7b**	None	9	16

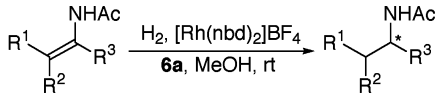
[a] All reactions were carried out in methanol with 1 mol% of $[Rh(nbd)_2]BF_4$, 1 mol% of salt and base under 3 atm of H_2 pressure at room temperature unless otherwise noted.
[b] Determined by ^1H NMR.
[c] Determined by chiral GC or HPLC analysis.

Finally, in sharp contrast to the reaction using the tetrafluoroboric acid salt without a base (entries 4 and 8), use of the trifluoromethanesulfonic acid salt caused sluggish reaction under the same reaction conditions (entries 6 and 10). The remarkable difference in activity may be ascribed to respective acid strength. Thus, trifluoromethanesulfonic acid exhibits stronger acidity than tetrafluoroboric acid and may form a more stable phosphonium salt that does not readily liberate the free phosphine necessary for the formation of the reactive rhodium–diphosphine complex.

Encouraged by these results, we next tried to use phosphonium salt **6a** in the hydrogenation of various olefinic compounds having acetylamino group at the α-position under base-free conditions. Representative results are summarized in Table 2. In all the cases examined, the same sense of enantioselection was observed in comparison with the results obtained by the use of preformed [(*S*,*S*)-*t*-Bu-BisP*-Rh(nbd)]BF_4 as a precatalyst.[1a] It is worthy to note that hydrogenation of methyl acetamidocinnamate went to completion even under atmospheric pressure of H_2 (entry 2). Excellent yield and enantioselectivity were also obtained in the case of dehydroamino acids without substituents at β-position (dehydroalanine derivative, entry 3), whereas hydrogenation of β,β-disubstituted dehydroamino acids afforded lower stereoselectivity (entry 4). This protocol also proved successful to hydrogenation of enamides and dehydro β-amino acid derivatives (entries 6–9). It is also noted that a (*Z*)-dehydro β-amino acid derivative was reduced rapidly under these conditions (entry 9), in contrast to the reduction catalyzed by isolated *t*-Bu-BisP*–Rh complex (18 h at 20 atm of H_2).[8,9]

In conclusion, P-chirogenic trialkylphosphonium salts have been prepared from free phosphines and strong Brønsted acids. No appreciable stereomutation of these chiral phosphonium salts occurs even upon heating in protic solvent. The diphosphonium salts were conveniently used in rhodium-catalyzed asymmetric hydrogenation of various enamides to provide excellent yields and enantioselectivities in most cases.

Table 2. Rh-catalyzed asymmetric hydrogenation of various enamides with diphosphonium salt **6a**[a]



Entry	R^1	R^2	R^3	Time (h)	Conv. (%)[b]	ee (%)[c]	(Config.)
1	Ph	H	CO_2Me	1	>99	>99	(*R*)
2[d]	Ph	H	CO_2Me	1.5	94	>99	(*R*)
3	H	H	CO_2Me	2	98	96	(*R*)
4	-$(CH_2)_5$-		CO_2Me	1	>99	70	(*R*)
5[d]	H	H	Ph	6	98	94	(*R*)
6	H	H	4-$MeOC_6H_4$	1	>99	>99	(*R*)
7	H	H	4-$O_2NC_6H_4$	1	>99	97	(*R*)
8	H	CO_2Me	Me	1	>99	>99	(*R*)
9	CO_2Me	H	Me	1	89	64	(*R*)

[a] All reactions were carried out in methanol with 1 mol% of $[Rh(nbd)_2]BF_4$ and 1 mol% of **6a** under 3 atm of H_2 pressure at room temperature unless otherwise noted.
[b] Determined by ^1H NMR.
[c] Determined by chiral GC or HPLC analysis.
[d] The reaction was carried out under 1 atm of H_2 pressure.

References

1. (a) Imamoto, T.; Watanabe, J.; Wada, Y.; Masuda, H.; Yamada, H.; Tsuruta, H.; Matsukawa, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 1635–1636; (b) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1999**, *64*, 2988–2989; (c) Gridnev, I. D.; Yamanoi, Y.; Higashi, N.; Tsuruta, H.; Yasutake, M.; Imamoto, T. *Adv. Synth. Catal.* **2001**, *343*, 118–136.
2. Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 2988–2989.
3. (a) McKinstry, L.; Livinghouse, T. *Tetrahedron Lett.* **1994**, *35*, 9319–9322; (b) McKinstry, L.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 7655–7666.
4. *Preparation of diphosphonium salt **6a**; a typical procedure*: To a dry toluene solution (10 mL) of (*S*,*S*)-1,2-bis(borano-to(*tert*-butyl)methylphosphino)ethane (260 mg, 1.0 mmol) was added trifluoromethanesulfonic acid (880 μL, 10 mmol) dropwise at 0°C under an Ar atmosphere. After 30 min, the mixture was allowed to warm to ambient temperature and stirred, while monitoring the reaction by TLC, until the starting phosphine–borane disappeared. The volatiles were removed under reduced pressure, and a solution of KOH (1.2 g, 20 mmol) in degassed EtOH–H_2O (10:1, 12 mL) was slowly added to the residue with stirring. The mixture was stirred at 60°C for 2 h then cooled to room temperature. Degassed Et_2O (10 mL) was added, and the mixture was dried over Na_2SO_4. The solution was passed through a column (2 cm diameter) of basic alumina (20 g) eluting with degassed Et_2O (ca. 20 mL). To the filtrate was added aqueous HBF_4 (2.0 mL, 10 mmol) at room temperature with vigorous stirring. After 30 min, the precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give diphosphonium salt **6a** as white powder (374 mg, 91% yield): mp 272–274°C; $[\alpha]_D^{24}$ 23.9 (*c* 0.1, H_2O); ^1H NMR (500 MHz, D_2O) δ 2.68 (m, 2H), 2.51 (m, 2H), 1.89 (d, $^2J_{HP}=7.0$ Hz, 6H), 1.30 (d, $^3J_{HP}=9.5$ Hz, 18H); ^{13}C NMR (126 MHz, D_2O) δ −2.1 (d, $J_{CP}=47.2$ Hz), 10.6 (d, $J_{CP}=42.2$ Hz), 28.2 (d, $J_{CP}=45.2$ Hz); ^{31}P NMR (200 MHz, D_2O) δ 27.7; IR (KBr) ν_{max} 2970, 2360, 1375, 1330, 1080, 780 cm^{-1}: MS (FAB) *m*/*z* 235 (M^+-2BF_4-H).
5. Luckenbach, R. *Dynamic Stereochemistry of Pentaco-ordinated Phosphorus and Related Elements*; Georg Thieme Publishers: Stuttgart, 1973.
6. The conditions for the determination of the enantiomeric purities of **1** with chiral stationary column: DAICEL CHIRALCEL OD-H; hexane/2-propanol=9/1; flow rate=0.5 mL/min.
7. *General procedure for asymmetric hydrogenation*: A 50 mL Fisher–Porter tube was charged with substrate (1 mmol), $[Rh(nbd)_2]BF_4$ (10 μmol), and diphosphonium salt (10 μmol). The tube was connected to the hydrogen tank via stainless steel tubing. The vessel was evacuated and filled with hydrogen gas to a pressure of 3 atm. This operation was repeated and the upper cock of the bottle was opened to allow quick addition of anhydrous, degassed MeOH (4–5 mL) and base (20 μmol) using a syringe. After four vacuum/H_2 cycles, the tube was pressurized to an initial pressure of 3 atm. The tube was closed off and the mixture was stirred at ambient temperature. After stirring for 1 h, the mixture was passed through a silica gel column with eluting EtOAc, and the filtrate was concentrated under reduced pressure. The residue was submitted to HPLC or GC analysis.
8. Yasutake, M.; Gridnev, I. D.; Higashi, N.; Imamoto, T. *Org. Lett.* **2001**, *3*, 1701–1704.
9. Recently, it has been reported that (*Z*)-β-(acylamino)acrylates were reduced under relatively mild conditions in excellent enantioselectivity: (a) Lee, S.; Zhang, Y. J. *Org. Lett.* **2002**, *4*, 2429–2431; (b) Tang, W.; Zhang, X. *Org. Lett.* **2002**, *4*, 4159–4161; (c) Peña, D.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. *J. Am. Chem. Soc.* **2002**, *124*, 14552–14553.