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Chiral pyrophosphites—synthesis and application as ligands in Rh(I)-catalyzed asymmetric hydrogenation

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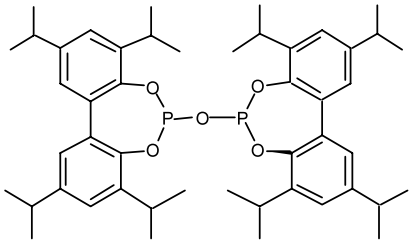
Abstract—Enantiopure pyrophosphites have been prepared for the first time based upon two independent synthetic pathways. The new ligands based on binaphthols, which are remarkably stable towards oxidation, were tested in the Rh(I)-catalyzed asymmetric hydrogenation of functionalized olefins, where up to 70% ee could be achieved.

1. Introduction

Pyrophosphites represent an interesting class of organophosphorus compounds, which has been known for many decades.[1] They have been used in organic chemistry as reagents for peptide syntheses[2] and found to be useful as ligands for the construction of polynuclear metal complexes.[3,4] Surprisingly, with only the exception of their application in a Rh(I)-catalyzed hydrosilylation reaction,[5] they have never been employed as ligands for other transition metal promoted catalytic reactions. Also remarkable is the absence of any optically active pyrophosphites in the literature. Although a few compounds bearing stereogenic carbon atoms have been reported, all of them were obtained from racemic precursors.[6] Recently, Pastor et al. synthesized the sterically congested pyrophosphite **1**, but its diastereoisomers could be detected by ^{31}P NMR only at low temperatures, due to a low ring inversion barrier.[7]



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Herein, we report for the first time the synthesis of optically active pyrophosphites and some preliminary results of their application as chiral ligands in Rh(I)-catalyzed asymmetric hydrogenation.

2. Results and discussion

As chiral building blocks for the synthesis of chiral pyrophosphites, we have chosen binaphthols (*R*)-**2a–d** (Scheme 1). These diols represent a well established source of highly efficient phosphorus ligands used for many important asymmetric catalytic reactions.[8,9] The synthesis of the new pyrophosphites proceeds in two simple steps and commences with the solvent-free reaction of the corresponding diol with PCl_3, followed by treatment of the resulted chlorophosphite with half an equivalent of water in the presence of triethylamine. Flash chromatography of the crude products affords pure pyrophosphites **4a–d** as white crystalline solids.

Our employed method is less common than the standard reaction between dialkyl phosphite and chlorophosphite,[2,6a,10] but represents a convenient pathway for the synthesis of symmetric pyrophos-

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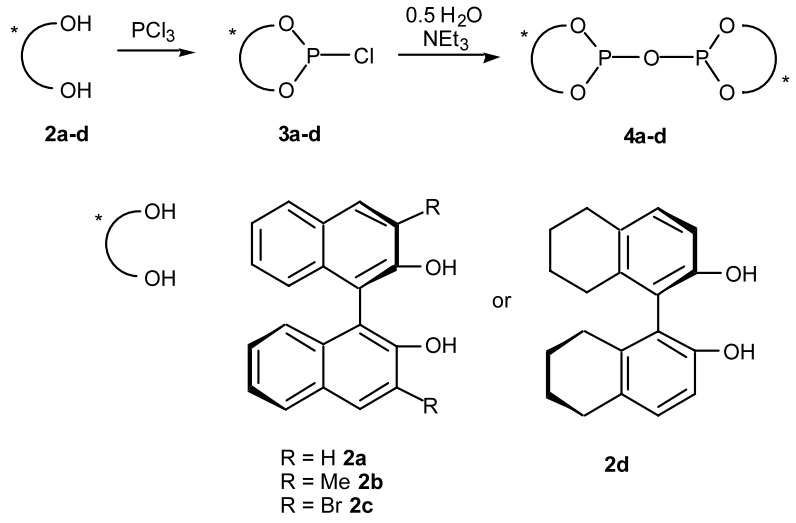


Scheme 1.

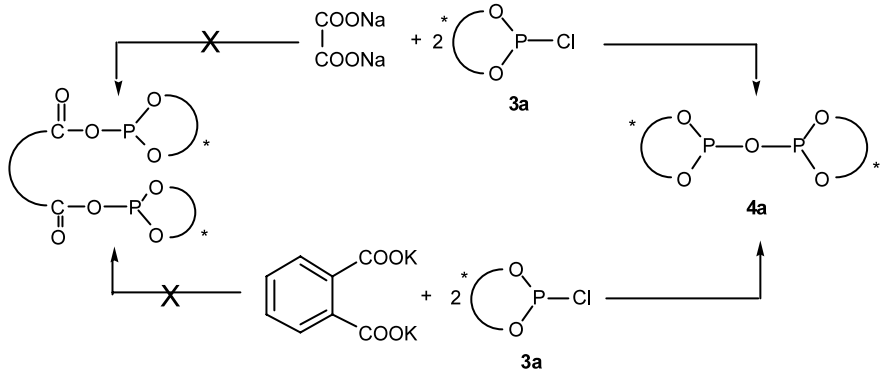
phites.[2,6a,11] In our case, this method allowed us to perform the synthesis in one pot without the isolation of any intermediates. Pyrophosphites **4a**–**c** were found to be remarkably air- and water-resistant. No products of decomposition have been detected by ^{31}P NMR spectroscopy even after exposing the samples to air for several weeks. In contrast, compound **4d** is more sensitive to hydrolysis, which may be the reason for the low yield in its synthesis. Remarkably, all attempts to obtain analogous pyrophosphites with bulky 3,3′-substituents (R = Ph, $SiMe_3$) were unsuccessful. Probably, the desired pyrophosphites are too sterically overcrowded and not stable.

Another, hitherto unknown method of pyrophosphite synthesis, was found by us accidentally during our work on chiral acylphosphite ligands.[12] Thus, instead of the desired diacylphosphite, the reaction of dicarboxylic acid metal salts with chlorophosphite **3a** in THF afforded pyrophosphite **4a** as a main product (Scheme 2).

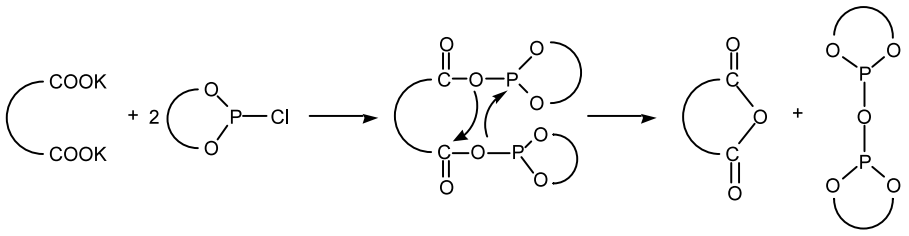
We suggest that the pyrophosphite derives from the rearrangement of an originally formed diacylphosphite (Scheme 3).

The proposed mechanism is supported by the finding that the reaction of dipotassium phthalate with **3a** afforded phthalic anhydride as a by-product. Remarkably, diacylphosphites derived from 1,3-benzene-dicarboxylic acid, with two remote carboxylic groups, can be isolated and turned out to be rather stable.[13] This observation additionally supports our assumption that the reaction proceeds via the intermediate formation of a diacylphosphite.

Pyrophosphites have never been used as ligands in asymmetric homogeneous catalysis. Thus their catalytic potential is absolutely undisclosed, so far. We have tested chiral pyrophosphites **4a**–**d** as chiral ligands in the Rh(I)-catalyzed hydrogenation of functionalized olefins. Precatalysts were generated in situ by reaction of $[Rh(COD)_2]BF_4$ with 1 equiv. of the relevant ligand.



Scheme 2.



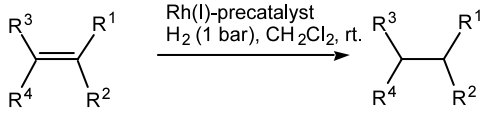
Scheme 3.

Investigations of the precatalyst solutions showed the presence of several complexes of unknown structure. Unfortunately, all attempts to isolate individual compounds failed.

Two standard substrates were employed as a benchmark test, namely methyl α-acetylaminocinnamate (AMe) and dimethyl itaconate ($ItMe_2$). Results are summarized in Table 1. The hydrogenation of AMe in mild conditions proceeded in 100% yield, but with low enantioselectivity (18–48% ee). Interestingly, catalysts based upon ligands **4b** and **4c** derived from 3,3′-disubstituted binaphthols afforded predominantly the (*R*)-product, while ligands **4a** and **4d** favored the (*S*)-enantiomer. The reason for this different behavior is not clear at the moment.

Enantioselectivities achieved in the hydrogenation of $ItMe_2$ are significantly higher. Substituents at the 3,3′-positions of the BINOL framework did not improve the stereodiscriminating ability, but resulted in much lower activity of the relevant catalysts. H_8-BINOL derived phosphorus ligands are often superior to their BINOL analogues in several hydrogenation reactions,[14] but in our case H_8-BINOL derived **4d** and BINOL based **4a** gave nearly identical results.

Table 1. Rh(I)-catalyzed hydrogenation of prochiral olefins[a]



AMe: R^1=COOMe, R^2= NHAc, R^3= H, R^4= Ph
ItMe 2: R^1=COOMe, R^2= CH_2COOMe, R^3= H, R^4= H

Run	Substrate	L*	Time (min)	ee (%)
1	AMe	**4a**	130	30 (*S*)[b]
2	AMe	**4b**	200	18 (*R*)[b]
3	AMe	**4c**	260	30 (*R*)[b]
4	AMe	**4d**	180	48 (*S*)[b]
5	$ItMe_2$	**4a**	12	63 (*R*)[c]
6	$ItMe_2$	**4b**	200	66 (*R*)[c]
7	$ItMe_2$	**4c**	200	14 (*R*)[c]
8	$ItMe_2$	**4d**	15	70 (*R*)[c]

[a] Conditions: The experiments were performed with 0.01 mmol Rh(I)-precatalyst (preformed) and 1.0 mmol of prochiral olefin in 15 ml of CH_2Cl_2 at 25°C.
[b] Determined by chiral GC (Lipodex E, 25 m×0.25 mm, 145°C, 1 ml/min).
[c] Determined by chiral GC (Lipodex E, 25 m×0.25 mm, 80°C, 1 ml/min).

In conclusion, chiral pyrophosphites have been synthesized for the first time by a simple one-pot synthesis starting from easily available starting material. Additionally a previously unknown synthetic route to pyrophosphites, namely the reaction of chlorophosphites with dicarboxylates was discovered. Chiral pyrophosphites obtained were used as ligands in Rh-catalyzed hydrogenations where up to 70% ee were achieved in the benchmark test with $ItMe_2$ (ligand **4a**). Other possible catalytic applications of chiral pyrophosphite ligands are under investigation in our group.

3. Experimental

3.1. General methods

All reactions were carried out under argon in dry solvents. Compounds **2b–d** were obtained starting from (*R*)-(+)-1,1′-bi(2-naphthol) (Fluka) using literature procedures.[15,16] NMR spectra were recorded on a Bruker AMX-400 instrument at 400.13 (^{1}H), 100.63 (^{13}C) or 161.98 MHz (^{31}P). Chemical shifts (ppm) are quoted relative to TMS (^{13}C and ^{1}H NMR) and 85% H_3PO_4 (^{31}P NMR). Mass spectra were recorded on an AMD 402 spectrometer. Elemental analyses were performed at a Leco CHNS-932. Melting points are not corrected. Optical rotations were measured on a Gyromat-HP polarimeter. Hydrogenation experiments have been carried out under normal pressure and isobaric conditions with an automatically registrating gas measuring device (1.0 atm overall pressure over the solution). The experiments were performed with 0.01 mmol Rh(I)-precatalyst (preformed by reaction of 1 equiv. $[Rh(COD)_2]BF_4$ and 1 equiv. pyrophosphite) and 1.0 mmol of prochiral olefin in 15 ml of CH_2Cl_2 at 25°C. The conversion of the prochiral substrates and the ees were determined by GC.

3.2. Bis(1,1′-binaphthyl-2,2′-ene)-pyrophosphite 4a

A suspension of freshly dried (azeotrope with toluene) (*R*)-1,1′-bi(2-naphthol) (2.0 g, 7.0 mmol) and 1-methyl-2-pyrrolidinone (one drop) in freshly distilled PCl_3 (10 ml) was warmed to 75–80°C and stirred for 15 min, then the excess PCl_3 was removed in vacuum followed by azeotropic distillation with toluene (2×7 ml) in vac-

uum. The white solid obtained represented pure chlorophosphite **3a** (^{31}P NMR: δ 178.7) and was used in the second step without further purification.

A solution of degassed water (0.065 ml, 3.5 mmol) in THF (10 ml) was slowly added to a vigorously stirred solution of the chlorophosphite **3a** (7.0 mmol) and triethylamine (1.2 ml, 8.6 mmol) in THF (40 ml). After the mixture had been stirred for additional 2 h, a white precipitate was filtered off and washed with THF (15 ml). The combined filtrates were concentrated in vacuum to give a beige amorphous solid, which was purified by flash chromatography (silica gel, CH_2Cl_2). White solid, 1.72 g (72% yield). Mp 170°C. EI-MS (70 eV): 646 (100%) $[M]^+$. $[\alpha]_D^{23} = -456.7$ (*c* 0.79, CH_2Cl_2). ^{31}P NMR ($CDCl_3$): δ 137.1. ^{13}C NMR ($CDCl_3$): δ 121.8 (CH), 122.0 (CH), 123.2 (C), 124.5 (C), 125.1, 125.4, 126.3, 126.5, 127.1, 127.2, 128.5, 128.6, 130.0, 130.6, 131.4, 131.8, 132.6, 132.9 (CH), 147.1 (C), 147.4 (C). ^{1}H NMR ($CDCl_3$): δ 7.27 (m, 6H), 7.41 (m, 10H), 7.55 (d, $J = 8.8$ Hz, 2H), 7.89 (m, 6H). Found: C, 73.60; H, 3.50. Calcd for $C_{40}H_{24}O_5P_2$: C, 74.29; H, 3.74.

3.3. Bis(3,3′-dimethyl-1,1′-binaphthyl-2,2′-ene)-pyrophosphite 4b

Application of the same method as detailed above for the synthesis of **4a**, starting from 0.63 g (2.0 mmol) of (*R*)-3,3′-dimethyl-2,2′-dihydroxy-1,1′-binaphthyl **2b**. For the intermediate chlorophosphite **3b**: ^{31}P NMR ($CDCl_3$): δ 174.8. White solid, 0.49 g (70% yield). Mp 244–245°C. EI-MS (70 eV): 702 (100%) $[M]^+$. $[\alpha]_D^{22} = -421.1$ (*c* 0.45, CH_2Cl_2). ^{31}P NMR ($CDCl_3$): δ 137.7. ^{1}H NMR ($CDCl_3$): δ 7.83 (m, 6H), 7.42 (m, 6H), 7.22 (m, 8H), 2.51 (s, 6H, CH_3), 2.12 (s, 6H, CH_3). EI-HRMS (70 eV): 702.1766 (calcd for $C_{44}H_{32}O_5P_2$: 702.1725). Found: C, 73.93; H, 4.66. Calcd for $C_{44}H_{32}O_5P_2$: C, 75.20; H, 4.59.

3.4. Bis(3,3′-dibromo-1,1′-binaphthyl-2,2′-ene)-pyrophosphite 4c

Application of the same method as detailed above for the synthesis of **4a**, starting from 0.66 g (1.5 mmol) of (*R*)-3,3′-dibromo-2,2′-dihydroxy-1,1′-dinaphthyl **2c**. For the intermediate chlorophosphite **3c**: ^{31}P NMR ($CDCl_3$): δ 181.1. White solid, 0.49 g (69% yield). Mp 150°C. EI–MS (70 eV): 958 (25%) $[M]^+$, 879 (100%) $[M-Br]^+$. $[\alpha]_D^{23} = -509.4$ (*c* 0.57, CH_2Cl_2). ^{31}P NMR ($CDCl_3$): δ 138.7. ^{1}H NMR ($CDCl_3$): δ 8.21 (s, 2H), 8.07 (s, 2H), 7.79 (m, 4H), 7.43 (m, 4H), 7.21 (m, 8H). Found: C, 50.25; H, 2.48. Calcd for $C_{40}H_{20}Br_4O_5P_2$: C, 50.12; H, 2.10.

3.5. Bis(5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-binaphthyl-2,2′-ene)-pyrophosphite 4d

Application of the same method as detailed above for the synthesis of **4a**, starting from 0.59 g (2.0 mmol) of (*R*)-H_8-BINOL **2d**. For the intermediate chlorophosphite **3d**: ^{31}P NMR ($CDCl_3$): δ 169.2. White solid, 0.15 g (22% yield). Mp 150°C. EI–MS (70 eV): 662 (100%) $[M]^+$. $[\alpha]_D^{22} = -198.8$ (*c* 0.5, CH_2Cl_2). ^{31}P NMR ($CDCl_3$): δ 129.05. ^{1}H NMR ($CDCl_3$): δ 7.05 (m, 4H), 6.96 (m, 4H), 2.80 (m, 8H), 2.64 (m, 4H), 2.27 (m, 4H), 1.77 (m, 12H), 1.55 (m, 4H). EI-HRMS (70 eV): 662.2336 (calcd for $C_{40}H_{40}O_5P_2$: 662.2351).

3.6. Preparation of Rh complexes with ligands 4a–d (general procedure)

A solution of a corresponding ligand (0.18 mmol) in CH_2Cl_2 (10 ml) was added dropwise to a stirred solution of $[Rh(COD)_2]BF_4$ (0.073 g, 0.18 mmol) in CH_2Cl_2 (20 ml) at 20°C. The reaction mixture was stirred for 30 min, concentrated in vacuum, and 10 ml of hexane was added to the residue. The obtained solid rhodium complex was washed with hexane (2×10 ml) and dried in vacuum.

3.7. Catalytic hydrogenations (general procedure)

The prochiral olefin (1 mmol) was dissolved in CH_2Cl_2 (13 ml) under hydrogen atmosphere. A rhodium precatalyst (0.01 mmol) was subsequently added and the reaction mixture vigorously stirred under hydrogen (1 atm) at 25°C until the calculated amount of H_2 had been consumed. Both conversion and enantioselectivity of hydrogenation were then determined by GC.

Acknowledgements

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References

1. *Organic Phosphorus Compounds*; Kosolapoff, G. M.; Maier, L., Eds.; John Wiley: New York, 1973; Vol. 5; p. 196.
2. Anderson, G. W.; Blodinger, J.; Welcher, A. D. *J. Am. Chem. Soc.* **1952**, *74*, 5309–5312.
3. Alvarez, M. A.; Alvarez, C.; Garcia, M. E.; Riera, V.; Ruiz, M. A.; Bois, C. *Organometallics* **1997**, *16*, 2581–2589.
4. Carreno, R; Riera, V; Ruiz, M. A.; Tiripicchio, A.; Tiripicchio-Camellini, M. *Organometallics* **1994**, *13*, 993–1004.
5. Smith, A. R.; Pastor, S. D. (Ciba Specialty Chemicals Corp.), US 5,858,905 (12.01.1999).
6. (a) Arbuzov, B. A.; Nikonorov, K. V.; Vinokurova, G. M.; Fedorova, O. N.; Shishova, Z. G. *Izvest. Kazan. Filiala Akad. Nauk S.S.S.R., Ser. Khim. Nauk* **1955**, *2*, 3–17 (*C. A.* **1958**, 241); (b) Mikolajczyk, M.; Ziemnicka, B.; Karolak-Wojciechowska, J.; Wieczorek, M. *J. Chem. Soc., Perkin Trans. 2* **1983**, 501–514; (c) Grachev, M. K.; Iorish, V. Y.; Bekker, A. R.; Nifant'ev, E. E. *J. Gen. Chem. USSR (Engl. Transl.)* **1990**, *60*, 57–62 (*Zh. Obshch. Khim.* **1990**, *60*, 66–71).
7. DeBellis, A. D.; Pastor, S. D.; Rihs, G.; Rodebaugh, R. K.; Smith, A. R. *Inorg. Chem.* **2001**, *40*, 2156–2160.

8. Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346–353.
9. Ansell, J.; Wills, M. *Chem. Soc. Rev.* **2002**, *31*, 259–268.
10. Anderson, G. W.; McGregor, A. C. *J. Am. Chem. Soc.* **1957**, *79*, 6180–6183.
11. Karlstedt, N. B.; Kudryavtseva, T. N.; Proskurnina, M. V.; Lutsenko, I. F. *J. Gen. Chem. USSR (Engl. Transl.)* **1982**, *52*, 1754–1758 (*Zh. Obshch. Khim.* **1982**, *52*, 1974–1979).
12. Selent, D.; Hess, D.; Wiese, K.-D.; Röttger, D.; Kunze, C.; Börner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1696–1697.
13. Selent, D., Borgmann, C.; Börner, A. unpublished results.
14. (a) Zhang, F.-Y.; Kwok, W. H.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2337–2342; (b) Zeng, Q.; Liu, H.; Cui, X.; Mi, A.; Jiang, Y.; Li, X.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 115–117.
15. Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865–2878.
16. Cram, D. J.; Helgeson, R. C.; Peacock, S. C.; Kaplan, L. J.; Domeier, L. A.; Moreau, P.; Koga, K.; Mayer, J. M.; Chao, Y.; Siegel, M. G.; Hoffman, D. H.; Sogah, G. D. Y. *J. Org. Chem.* **1978**, *43*, 1930–1946.