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New chiral phosphine-phosphonites derived from (2*R*,3*R*)-dimethyl tartrate, (*S*)-binaphthol and (1*R*,2*S*)-ephedrine

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Abstract

The reaction of 2-lithiophenyldiphenylphosphine with phosphorus trichloride afforded the new unsymmetric phosphine, dichloro(2-diphenylphosphinophenyl)phosphine (**4**). Condensation of **4** with (a) (2*R*,3*R*)-dimethyl tartrate or (b) (*S*)-binaphthol in the presence of triethylamine gave new chiral phosphine-phosphonite ligands, (2*R*,3*R*)-[2-(2′-(diphenylphosphino)phenyl)-4,5-bis(carbomethoxy)-1,3,2-dioxaphospholane] ((2*R*,3*R*)-**5**) and (*S*)-[2-(diphenylphosphino)benzene][1,1′-binaphthalen-2,2′-diyl]phosphonite] ((*S*)-**6**). The analogous reaction of **4** with (1*R*,2*S*)-ephedrine using *N*-methylmorpholine as the base, gave [2-(2′-(diphenylphosphino)phenyl)-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidine] (**7**) as a 95:5 mixture of diastereoisomers.

Non-C_2 symmetric bidentate organophosphorus ligands have been the focus of attention of late, in transition metal catalyzed asymmetric synthesis.[1] Notable examples are the use of phosphine-phosphite ligands such as (*S*,*R*)-BINAPHOS[2] and (*S*,*R*)-BIPHEMPHOS,[3] and phosphine-phosphinite ligands such as (*R*,*S*)-EPHOS,[4] in the rhodium catalyzed hydroformylation of olefins, and bisphosphinites in the nickel catalyzed hydrocyanation of olefins.[5] Their success has been attributed to the highly asymmetric environment around the metal center that such ligands provide. It is surprising therefore, that alternative bidentate chelating ligands based on phosphine-phosphonites **1** (Fig. 1) have not been the subject of investigation, particularly as monodentate TADDOL-type phosphonite ligands have been used with success in the asymmetric rhodium catalyzed hydrosilylation of ketones.[6] The rhodium catalyzed asymmetric hydrogenation of olefins has also been studied using a chiral bisphosphonite ligand based on a ferrocene backbone.[7] Various chiral bidentate, chelating ligands based on *ortho*-substituted triphenylphosphine such as **2** and **3** have recently been applied to enantioselective catalytic reactions including the ruthenium mediated hydrosilylation of ketones and imines[8] and palladium catalyzed Heck reactions.[9,10] To the best of our knowledge there are no reported examples of phosphonite functionalized phosphine ligands. In addition to exploring the coordination chemistry of a new ligand class, several additional features of chiral

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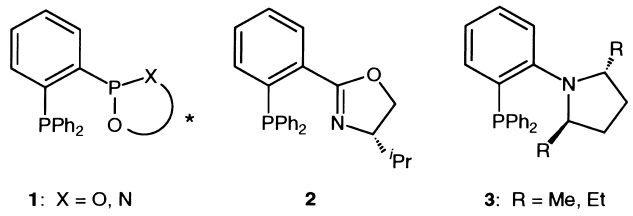
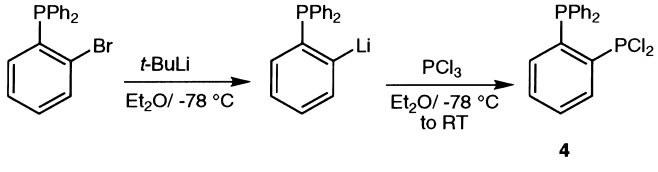


Figure 1.

phosphine-phosphonites were attractive to us: (1) the chelating ligands have non-C_2 symmetry which has recently been shown to be an important consideration for certain classes of transition metal catalyzed asymmetric carbon–carbon bond formation; and (2) a wide variety of inexpensive, readily available chiral diols, amino alcohols and diamines of both antipodes would allow us to investigate a large number of optically active ligands in enantioselective catalytic reactions. This communication describes the first synthesis of optically active phosphine-phosphonite ligands derived from the chiral vicinal diols, (2*R*,3*R*)-dimethyl tartrate and (*S*)-binaphthol, and the chiral amino alcohol (1*R*,2*S*)-ephedrine. Representative transition metal complexes are also described.

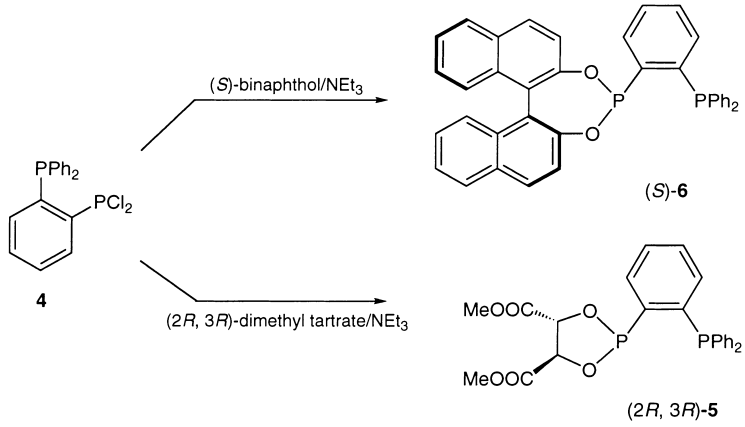
Cyclic phosphonites and 1,3,2-oxazaphospholidines may be prepared readily via the nucleophilic attack of mono and bi-functional diols or 1,2-amino alcohols on phosphorus dichlorides,[11] and one of the initial problems associated with this strategy was the lack of synthetic accessibility of unsymmetric dichlorophosphino-phosphines. While symmetric dichlorophosphines have been known for some time,[12] there are no reports on the synthesis of phosphines of the type *o*-$Cl_2PC_6H_4PR_2$. The synthetic methods available for the synthesis of arylphosphonous dichlorides include chlorination of primary phosphines using phosgene or thionyl chloride;[12] decomposition of pentavalent dichlorides;[13] the reaction of PCl_3 with diarylmercury compounds;[11] and the Friedel–Crafts reaction.[13] The use of either Grignard reagents or organolithium precursors is often deliberately avoided due to facile formation of mixtures of monoaryl-, diaryl- and triarylphosphines, even at low temperatures.[14] The reaction of phosphorus trichloride with *o*-lithiophenyldiphenyl phosphine generated from *o*-bromophenyldiphenylphosphine[15] and two equivalents of *t*-butyllithium in THF at −78°C resulted in the clean conversion to the desired dichlorophosphine **4** as evidenced by ^{31}P NMR and mass spectral data (Scheme 1). It seemed reasonable to suggest that the steric bulk of the diphenylphosphino-substituted aryllithium suppresses additional substitution reactions and subsequent formation of the diaryl and triaryl derivatives. The ^{31}P NMR spectrum of **4** in THF contained two sets of doublets at −20.7 and 156.7 ppm typical of a triarylphosphine and an arylphosphonous dichloride, respectively, with a coupling constant of 347 Hz. Compound **4** was isolated as a viscous, air sensitive, yellow oil which could not be distilled or crystallized without extensive decomposition, and further condensation reactions were performed using **4** in situ.



Scheme 1. Synthesis of dichlorophosphine **4**

Compound **4** was then reacted with either (2*R*,3*R*)-dimethyl tartrate, (*S*)-binaphthol, or (1*R*,2*S*)-ephedrine in the presence of base or in CH_2Cl_2 to give the new mixed phosphine-phosphonites (2*R*,3*R*)-**5** and (*S*)-**6**, respectively (Scheme 2).

After removal of hydrochloride salts by filtration, solvent removal and column chromatography of the resulting residues, the diastereomerically pure binaphthol and dimethyl tartrate derivatives (2*R*,3*R*)-**5** and



Scheme 2. Synthesis of chiral phosphine-phosphonites (2*R*,3*R*)-**5** and (*S*)-**6**

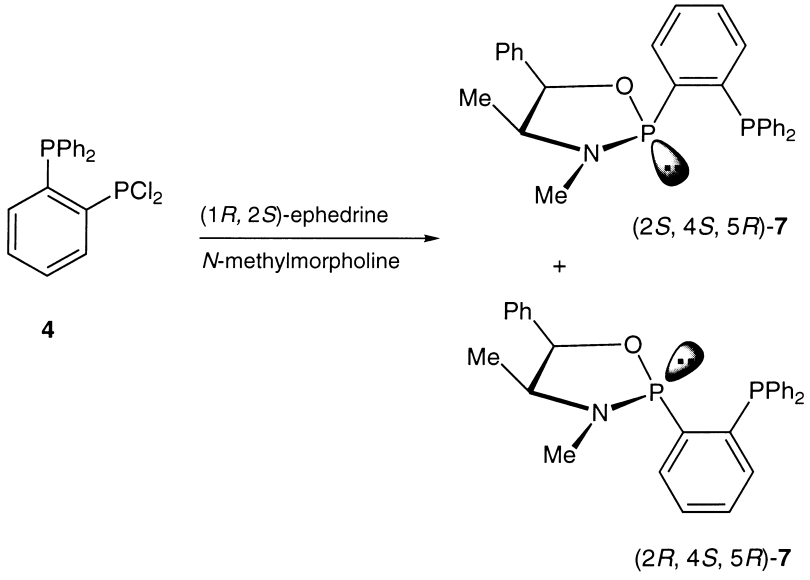
(*S*)-**6** were isolated as white solids in good yield. The phosphonites are particularly sensitive to hydrolysis and oxidation, and all attempts to obtain analytically pure samples of (2*R*,3*R*)-**5** and (*S*)-**6** using repeated column chromatography or crystallization were unsuccessful.[16] The sensitivity of phosphonite ligands to hydrolysis has been previously documented.[7] The ^{31}P NMR spectra of (2*R*,3*R*)-**5** and (*S*)-**6** show typical chemical shift values for triarylphosphines[14] and arylphosphonites.[17]

Using the same methodology but with *N*-methylmorpholine as the base, the 1,3,2-oxazaphospholidine **7** was formed as a mixture of diastereomers (Scheme 3).[18] Attempts to separate the diastereomers using chromatography or fractional crystallization led to varying degrees of oxidation. However, the formation of **7** was followed in situ using ^{31}P NMR and the initial spectrum contained two doublets at 142.6 and −17.0 ppm ($^2J_{PP}$=119 Hz), and 154.2 and −18.6 ppm ($^2J_{PP}$=115 Hz), in a 95:5 ratio which have been assigned to the major and minor diastereomers (2*R*,4*S*,5*R*)-**7** and (2*S*,4*S*,5*R*)-**7** respectively (90% de). The stereochemical assignment of individual diastereomers was made on the basis of ^{1}H and ^{31}P NMR chemical shifts.[17] In addition, the formation of the major isomer (2*R*,4*S*,5*R*)-**7**, which contains the diphenylphosphino and phenyl groups in the *trans* disposition, would be favored on steric grounds.

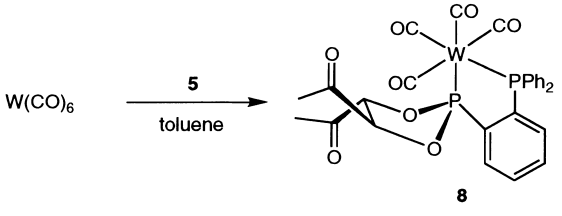
The new phosphine-phosphonites form metal complexes in which the ligands are coordinated via a bidentate chelate ring as expected. The thermal displacement of carbon monoxide from $W(CO)_6$ with (2*R*,3*R*)-**5** in refluxing toluene for 36 hours yielded a new yellow complex *cis*-[$W(CO)_4$(L–L′)] **8** for which the IR and ^{31}P NMR spectra are consistent with a structure in which the phosphine-phosphonite ligand is binding in bidentate, chelating mode as shown in Scheme 4.[19]

Other phosphine-phosphonite complexes have been prepared in situ and show similar binding properties. For example, the, slow, controlled addition of a pre-cooled THF solution of (*S*)-**6** to $[RhCl(cod)]_2$ in THF at −78°C resulted in a color change from yellow to orange and a ^{31}P NMR spectrum of the solution contained two sets of doublets of doublets at 182.9 ppm (J_{RhP}=346 Hz, J_{PP}=47 Hz) and 78.0 ppm (J_{RhP}=197 Hz, J_{PP}=47 Hz) which we have tentatively assigned to the phosphine-phosphonite complex [RhCl(L–L′)(cod)].[20]

In conclusion, we have prepared the first examples of chiral phosphine-phosphonite ligands and representative organometallic derivatives. The application of these new ligands in enantioselective catalytic reactions will be presented in future publications.



Scheme 3. Synthesis of (1*R*,2*S*)-ephedrine-derived phosphine-phosphonite **7**



Scheme 4. Synthesis of tungsten complex **8**

Acknowledgements

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16. The following synthetic procedure is representative: A Schlenk flask was charged with 2-bromophenyldiphenylphosphine (0.413 g, 1.14 mmol), ether (15 mL), and a stirrer bar and cooled to −78°C (2-propanol/CO_2). Then *t*-BuLi (1.5 mL, 2.3 mmol, 1.5 M in pentane) was added dropwise with stirring. The resulting suspension was stirred for 10 mins and transferred slowly via catheter to a stirred solution of PCl_3 (1.0 mL, 11 mmol) in ether (20 mL) cooled to −78°C (2-propanol/CO_2). The cold-bath was removed and the reaction mixture allowed to warm to room temperature. The resulting pale-yellow suspension was filtered and the solvent was removed under oil-pump vacuum to give a yellow oil (**4**) which was taken up in CH_2Cl_2 (10 mL). Then NEt_3 (0.42 mL, 3.0 mmol) and (*S*)-binaphthol (0.143 g, 0.499 mmol) were added and the solution stirred overnight. The solvent was removed under oil-pump vacuum and the residue was taken up in benzene (15 mL). The solution was chromatographed on a 12 mm diameter silica gel column (10 g, benzene). The solvent was removed from the eluate under oil-pump vacuum to give (*S*)-**6** as a white foam (0.257 g, 90%). ^{1}H NMR ($CDCl_3$): δ 7.94 (d, *J*=8.8 Hz, 1H), 7.87 (d, *J*=8.1 Hz, 1H), 7.74 (d, *J*=8.1 Hz, 1H), 7.56–6.95 (m, 22H), 6.14 (d, *J*=8.8 Hz, 1H). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −19.1 (d, ^2J=207 Hz, PAr_2), 175.3 (d, ^2J=207 Hz, PO_2). MS: *m/e* 577 (M+1). Spectroscopic data for (2*R*,3*R*)-**5**: ^{1}H NMR ($CDCl_3$): δ 7.86–6.64 (m, $2C_6H_5$, C_6H_4), 5.51 (d, 1H, $^3J_{HH}$=6.6 Hz, CH), 5.32 (dd, 1H, $^3J_{HH}$=6.7 Hz, $^3J_{PH}$=13.6 Hz, CH), 3.72 (s, 3H of $2CH_3O$), 3.41 (s, 3H of $2CH_3O$). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −19.8 (d, ^2J=140 Hz, PAr_2), 180.1 (d, ^2J=140 Hz, PO_2).
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18. Spectroscopic data for (2*R*,4*S*,5*R*)-**7**: ^{1}H NMR ($CDCl_3$): δ 7.95–6.78 (m, $3C_6H_5$, C_6H_4), 5.20 (d, *J*=6.7 Hz, $C(C_6H_5)H$), 3.17 (m, $C(CH_3)H$), 2.66 (d, *J*=14.2 Hz, NCH_3), 0.40 (d, *J*=6.7 Hz, CCH_3). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −17.0 (d, ^2J=119 Hz, PAr_2), 142.6 (d, ^2J=119 Hz, PO_2). Spectroscopic data for (2*S*,4*S*,5*R*)-**7**: ^{1}H NMR ($CDCl_3$): δ 2.91 (d, *J*=15.3 Hz, NCH_3), 0.65 (d, *J*=6.1 Hz, CCH_3) (aromatic, and methine protons not observed). ^{31}P{^{1}H} NMR ($CDCl_3$): δ −18.6 (d, ^2J=115 Hz, PAr_2), 154.2 (d, ^2J=115 Hz, PO_2).
19. Spectroscopic data for **8**: IR (CH_2Cl_2, 0.051 M): ν(CO) 2031 (s), 1991 (sh), 1944 (sh), 1919 (s) cm^{-1}. ^{31}P{^{1}H} NMR ($CDCl_3$): δ 43.9 (^2J=20 Hz, PAr_2, J_{WP}=242 Hz), 220.5 (^2J=20 Hz, J_{WP}=345 Hz, PO_2).
20. The ^{31}P NMR spectrum also contained minor, unidentified rhodium–phosphine species.