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Synthesis of Chiral Phosphetanes

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Abstract. Reactions of lithium phosphides with the mesylate, or the cyclic sulfate, of (*R,R*)-2,4-pentanediol afford a general access to new chiral ligands based on the phosphetane moiety. Amongst others, the four membered ring analogue of Me-DuPHOS has been obtained by this method.
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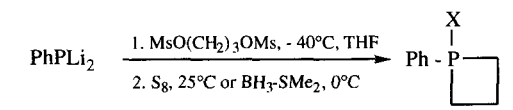
Chiral phosphines based on the *trans*-2,5-disubstituted phospholane moiety[1] have emerged as a valuable class of ligands for transition metal catalysed asymmetric synthesis. Especially high enantiomeric excesses have been obtained by Burk and co-workers[2] in DuPHOS-assisted rhodium and ruthenium catalyzed asymmetric hydrogenations of various unsaturated substrates (DuPHOS = 1,2-bis(phospholano)benzene derivatives). Bearing in mind the impressive results obtained with these five-membered cyclic phosphines, it seems worthwhile to explore the potential of analogous phosphorus heterocycles having different ring sizes. In this context, we have examined and report here the first synthesis of *trans*-2,4-symmetrically disubstituted chiral phosphetanes.

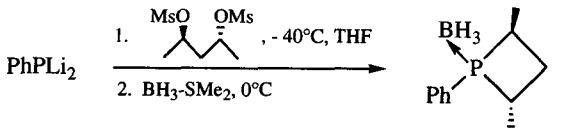
The most general synthetic approach for the preparation of chiral phospholanes[1] involves the reactions between lithium phosphides and bis-mesylates or cyclic sulfates of optically active 1,4-diols. Recently, a similar method has been successfully applied to the synthesis of chiral phosphiranes[3], and such a synthesis would be also very attractive for the preparation of four membered cyclic phosphines from optically active 1,3-diol derivatives.

Earlier preparations of 1-phenylphosphetane from dilithium phenylphosphide and 1,3-dichloropropane gave the desired product, but only as the minor product (13% yield) in a 1:3 mixture with poly(phenylphosphino)propane[4]. In our hands, reversing the order of addition of the reagents in the analogous reaction of dilithium phenylphosphide with the dimesylate of 1,3-propanediol afforded 1-phenylphosphetane much more cleanly. 1-Phenylphosphetane was isolated in good yield as its sulfide or its borane adduct (eq. 1)[5].



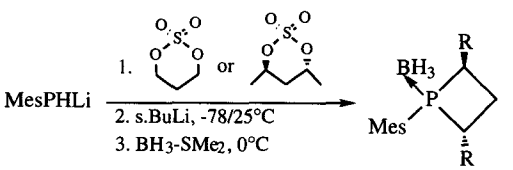
1 X = S 58%
2 X = BH_3 67% (1)

The same experimental procedure allows conversion of the (*R,R*)-2,4-pentanediol dimesylate into the corresponding optically active 2,4-dimethyl-1-phenylphosphetane-borane complex on a 2 mmol scale, in 68% isolated yield, with assumed inversion of the carbon configuration (eq. 2)[6].



3 68% (2)

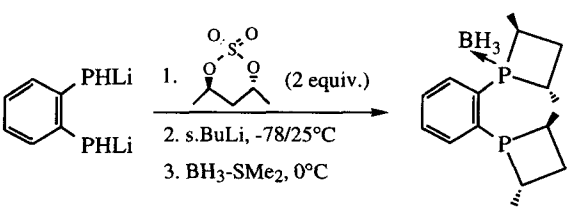
Application of the synthetic approach above to the synthesis of P-mesityl-substituted phosphetanes required an optimization of the experimental protocol. Dilithium mesitylphosphide[7] failed to react cleanly with 1,3-propanediol dimesylate: only a 30% yield of the desired phosphetane was recovered. Thus, a two step synthesis, starting from lithium mesitylphosphide and the cyclic sulfates of 1,3-diols, has been explored. The use of cyclic sulfates in the two-step synthesis[2a] generates an intermediate 3-phosphino-sulfate which is not susceptible to the intermolecular phosphide attacks which could lead to 1,3-bis(phosphino)alkanes or oligomers. Lithium mesitylphosphide addition to a THF solution (4.10^{-2} mmol/mL) of the cyclic sulfates of 1,3-propanediol or (*R,R*)-2,4-pentanediol[8] at -78°C afforded the phosphorus-alkylation products selectively (^{31}P NMR δ = -88.0 ($^{1}J_{H-P}$ = 214 Hz) and -61.8 ($^{1}J_{H-P}$ = 211 Hz), -67.1 ($^{1}J_{H-P}$ = 211 Hz) ppm respectively). The cyclization step, which was performed using *s*-BuLi, afforded phosphetane as essentially the only phosphorus-containing product. The borane adducts of 1-mesitylphosphetane, **4**, and (*S,S*)-1-mesityl-2,4-dimethylphosphetane, **5**, were obtained in 65% and 62% yield respectively after column chromatography on neutral alumina (eq. 3)[9].



4 R = H 65%
5 R = Me 62% (3)

Mes = 2,4,6-trimethylphenyl

When 1,2-diphosphinobenzene[10] and the (*R,R*)-2,4-pentanediol cyclic sulfate were used as starting materials, the same preparative protocol afforded the 1,2-bis((*S,S*)-2,4-dimethylphosphetano)benzene borane mono-adduct, **6**, in 20% yield (eq. 4)[11].

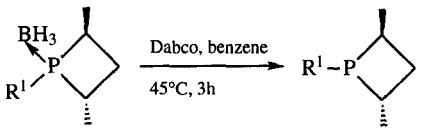


6 20% (4)

The second phosphorus atom does not react with BH_3, probably because of significant sterical hindrance in this *ortho*-disubstituted species. The bis-phosphetane was the only well defined species observed in the

reaction solution by ^{31}P NMR spectroscopy. Insoluble polymeric phosphorus derivatives, which precipitate from the reaction mixture, are also possibly formed as side products. Optimization of the cyclization step by the use of bases other than *s*.BuLi will be necessary in order to achieve preparative-scale synthesis of **6**. Studies of this crucial point are in progress.

Trivalent phosphetanes **7-9** have been obtained quantitatively by reacting the borane adducts with one equivalent of 1,4-diazabicyclo[2.2.2]octane (dabco) (eq.5)[12], according to the well known phosphine-amine exchange procedure[13].



7 R^1 = Ph
8 R^1 = Mes
9 R^1 = o-phenylene (5)

Phosphetane **7** is moderately stable, while **8** and **9** are stable under an inert atmosphere, either in solution or in the pure state. Evaluation of the catalytic potential of the chiral phosphetanes **7-9** is in progress[14].

In summary, this work develops a new general access to chiral ligands based on phosphetane moieties. Optically active mono- and bidentate ligands have been prepared which should find application in organometallic catalysis.

References and Notes

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5. A suspension of $PhPLi_2$ in THF was added to a THF solution of 1,3-propanediol dimesylate at -40°C. Selected data. **1**: ^{31}P NMR ($CDCl_3$) δ 55.7; ^{13}C NMR ($CDCl_3$) δ 14.6 ($^2J_{C-P}$ = 22.8 Hz), 36.4 ($^1J_{C-P}$ = 49.9 Hz). **2**: ^{31}P NMR ($CDCl_3$) δ 42.2 (J_{P-B} = 51.4 Hz); ^{13}C NMR ($CDCl_3$) δ 19.0 ($^2J_{C-P}$ = 19.9 Hz), 23.8 ($^1J_{C-P}$ = 41.1 Hz).
6. (R,R)-(-)-2,4-pentanediol ($[\alpha]_D$ = -41 ± 2 (c = 10, $CHCl_3$)) was purchased from Fluka.

(*S,S*)-**3**: ^{31}P NMR ($CDCl_3$) δ 51.4 (J_{P-B} = 57.8 Hz); ^{1}H NMR ($CDCl_3$) δ 0.99 (dd, $^{3}J_{H-P}$ = 15.7, $^{3}J_{H-H}$ = 7.3 Hz, Me), 1.41 (dd, $^{3}J_{H-P}$ = 18.6, $^{3}J_{H-H}$ = 7.3 Hz, Me); ^{13}C NMR ($CDCl_3$) δ 15.3 (Me), 15.8 ($^{2}J_{C-P}$ = 7.3 Hz, Me), 25.9 ($^{1}J_{C-P}$ = 41.1 Hz, CH), 29.1 ($^{1}J_{C-P}$ = 39.7 Hz, CH), 35.9 ($^{2}J_{C-P}$ = 15.4 Hz, CH_2); $[\alpha]_D$ = + 103 (c = 1, $CHCl_3$).

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9. **4**: ^{31}P NMR ($CDCl_3$) δ 38.8 (J_{P-B} = 53.3 Hz); ^{13}C NMR ($CDCl_3$) δ 19.2 ($^{2}J_{C-P}$= 16.2 Hz, CH_2), 20.7 ($^{3}J_{C-P}$ = 7.6 Hz, Me), 20.9 (Me), 26.3 ($^{1}J_{C-P}$ = 40.5 Hz, CH_2). (*S,S*)-**5**: ^{31}P NMR ($CDCl_3$) δ 50.5; ^{1}H NMR ($CDCl_3$) δ 1.20 (dd, $^{3}J_{H-P}$ = 14.4, $^{3}J_{H-H}$ = 7.4 Hz, Me), 1.40 (dd, $^{3}J_{H-P}$ = 18.3, $^{3}J_{H-H}$ = 6.8 Hz, Me), 2.27 (2 Me), 2.31 (Me), 6.85, 6.86 (CH); ^{13}C NMR ($CDCl_3$) δ 14.2 (Me), 16.7 ($^{2}J_{C-P}$ = 7.7 Hz, Me), 20.6 (br, Me), 20.9 (Me), 22.3 (br, Me), 30.3 ($^{1}J_{C-P}$ = 39.0 Hz, CH), 31.0 ($^{1}J_{C-P}$ = 38.1 Hz, CH), 34.6 ($^{2}J_{C-P}$ = 11.8 Hz, CH_2); $[\alpha]_D$ = + 123 (c = 1, $CHCl_3$).
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11. (*S,S*)-**6**: ^{31}P NMR ($CDCl_3$) δ 49.1, 16.9 ($^{3}J_{P-P}$ = 36.1 Hz); ^{1}H NMR ($CDCl_3$) δ 0.90 (dd, $^{3}J_{H-P}$ = 8.6, $^{3}J_{H-H}$ = 7.2 Hz, Me), 1.13 (dd, $^{3}J_{H-P}$ = 15.3, $^{3}J_{H-H}$ = 7.5 Hz, Me), 1.33 (dd, $^{3}J_{H-P}$ = 18.2, $^{3}J_{H-H}$ = 7.2 Hz, Me), 1.40 (dd, $^{3}J_{H-P}$ = 17.5, $^{3}J_{H-H}$ = 7.0 Hz, Me); ^{13}C NMR ($CDCl_3$) δ 14.5 (Me), 16.9 ($^{2}J_{C-P}$ = 7.7 Hz, Me), 17.1 ($^{2}J_{C-P}$ = 4.7 Hz, Me), 20.2 ($^{2}J_{C-P}$ = 23.9 Hz, Me), 24.1 ($^{1}J_{C-P}$ = 9.0 Hz, CH), 25.4 ($^{1}J_{C-P}$ = 7.4 Hz, CH), 28.9 (dd, $^{1}J_{C-P}$ = 39.6 Hz, $^{4}J_{C-P}$ = 4.4 Hz, CH), 31.4 (dd, $^{1}J_{C-P}$ = 40.8 Hz, $^{4}J_{C-P}$ = 10.4 Hz, CH), 34.1 ($^{2}J_{C-P}$ = 11.9 Hz, CH_2), 37.8 (CH_2), 129.0 (J_{C-P} = 8.7 Hz, CH), 129.9 (CH), 130.4 (t, J_{C-P} = 9.0 Hz, CH), 132.7 (J_{C-P} = 7.4 Hz, CH), 138.6 (t, J_{C-P} = 33.2 Hz, C), 139.9 (dd, J_{C-P} = 37.0 Hz, J_{C-P} = 10.2 Hz, C); $[\alpha]_D$ = + 354 (c = 1, $CHCl_3$).
12. (*S,S*)-**7**: ^{31}P NMR (C_6D_6) δ 25.8; ^{1}H NMR (C_6D_6) δ 0.78 (dd, $^{3}J_{H-P}$ = 8.0, $^{3}J_{H-H}$ = 7.1 Hz, Me), 1.31 (dd, $^{3}J_{H-P}$ = 17.3, $^{3}J_{H-H}$ = 7.1 Hz, Me); ^{13}C NMR (C_6D_6) δ 17.5 (d, $^{2}J_{C-P}$ = 4.6 Hz, Me), 20.2 ($^{2}J_{C-P}$ = 22.9 Hz, Me), 24.0 ($^{1}J_{C-P}$ = 2.9 Hz, CH), 24.8 ($^{1}J_{C-P}$ = 9.0 Hz, CH), 38.8 (CH_2). (*S,S*)-**8**: ^{31}P NMR (C_6D_6) δ 21.0; ^{1}H NMR (C_6D_6) δ 0.97 (t, $^{3}J_{H-P}$ = $^{3}J_{H-H}$ = 6.8 Hz, Me), 1.30 (dd, $^{3}J_{H-P}$ = 16.6, $^{3}J_{H-H}$ = 6.7 Hz, Me), 2.12, 2.13 (3 Me); ^{13}C NMR (C_6D_6) δ 17.7 (d, $^{2}J_{C-P}$ = 6.0 Hz, Me), 20.1 ($^{2}J_{C-P}$ = 19.8 Hz, Me), 20.9 (Me), 21.7 (Me), 21.9 (Me), 25.9 ($^{1}J_{C-P}$ = 3.0 Hz, CH), 29.0 ($^{1}J_{C-P}$ = 3.0 Hz, CH), 35.9 ($^{2}J_{C-P}$ = 3.2 Hz, CH_2). (*S,S*)-**9**: ^{31}P NMR (C_6D_6) δ 18.3; ^{1}H NMR (C_6D_6) δ 1.03 (m, 6H), 1.28 (m, 6H), 1.9-2.3 (m, 4H), 2.6-2.8 (m, 4H), 7.1-7.4 (m, 4H); ^{13}C NMR (C_6D_6) δ 16.8 (Me), 19.3 (t, J_{C-P} = 10.8 Hz, Me), 24.0 (t, J_{C-P} = 4.6 Hz, CH), 25.5 (t, J_{C-P} = 7.6 Hz, CH), 36.3 (CH_2), 126.8 (CH), 128.7 (t, J_{C-P} = 3.5 Hz, CH), 142.5 (t, J_{C-P} = 4.8 Hz, C); $[\alpha]_D$ = + 429 (c = 1, CH_2Cl_2).
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