Stereochemistry of the P–C Bond Formation in an Oxazaphospholidine Borane Complex

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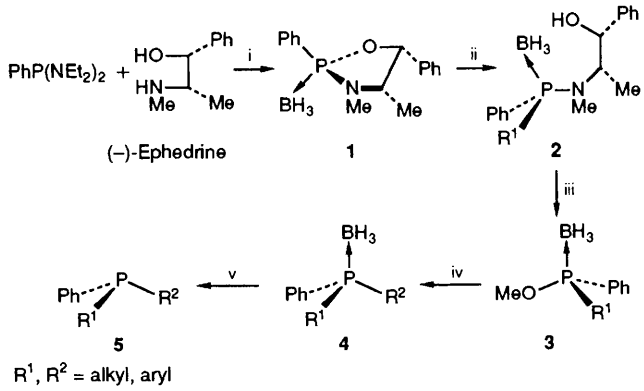
The reaction of the 3,4-dimethyl-2,5-diphenyl-1,3,2-oxazaphospholidine borane complex **1** with organometallic reagents involves a stereoselective P–O bond cleavage; the X-ray structures of the starting complex **1** and of the aminophosphine boranes **2a, b**, reveal a stereochemistry of the P–C bond formation with a retention of the configuration which is explained by a nucleophilic attack on the less hindered side-face of the pyramidal phosphorus atom.

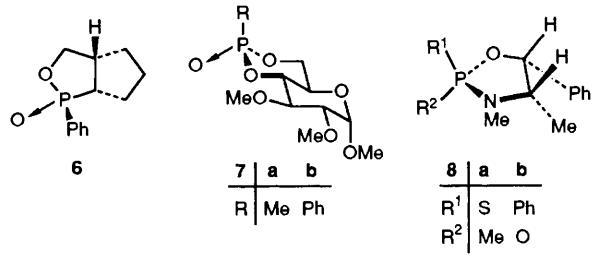
Chiral phosphine ligands are of key importance in catalytic transition metal mediated processes, which attract considerable attention in asymmetric synthesis and industrial applications thereof.[1] The characteristic features of the asymmetric organometallic catalyses are their high stereo- and chemoselectivity applicable to various hydrophobic and water soluble substrates, easy access to the *R* and *S* enantiomers, high substrate concentration and easy work-up applicable to a large-scale production. Several hundreds of chiral phosphine ligands have been tested but their preparations are often difficult and give low overall yields. We have recently described a general and efficient asymmetric synthesis of optically pure tertiary mono- and di-phosphine ligands based on the regio- and stereo-selectivity of the ring opening of the oxazaphospholidine borane complex **1**[2] (Scheme 1).

Up to now, the stereochemistry described for the reaction of a chiral acyclic phosphorus compound,[3] oxazaphospholidine **6**[4] and dioxaphosphorinane **7a**[5a] with an organometallic reagent, has predominantly been with inversion of configuration. In the case of the dioxaphosphorinane **7b**[5b] and the oxazaphospholidines **8a,b** prepared from ephedrine,[5a,6] the reaction occurs with retention of configuration. In order to attribute the absolute configuration of the new organophosphorus borane complexes (**2–5**), we have examined the stereochemistry of the nucleophilic attack on the starting complex **1**, and we report here the X-ray crystal structures of an alkyl and an aryl ring opened product **2a,b**.

The starting borane complex **1** was prepared in one step from bis(diethylamino)phenyl phosphine, (−)-ephedrine and



Scheme 1 *Reagents and conditions*: i, toluene, 105 °C; ii, R^1Li; iii, MeOH, H^+; iv, R^2Li; v, Et_2NH



BH_3·$(Me)_2S$, and its X-ray structure has been established recently.[7] Methyllithium cleanly reacted with **1** at low temperature (−78 to 0 °C) in tetrahydrofuran (THF) to give the corresponding diastereomerically pure aminophosphine borane (**2a**, Scheme 1, R^1 = Me),† which was recrystallized from PriOH–hexane (1 : 9). The aminophosphine borane **2b**† was obtained under the same conditions from the antipodal complex of **1** prepared from (+)-ephedrine, and the *o*-anisyllithium reagent. The compounds **2a,b** could be obtained from the reaction of **1** with the corresponding methyl and *o*-anisylmagnesium reagents, respectively, at higher temperatures.‡ The structures of **2a,b** have been determinated by X-ray crystallography,§ and the main purpose was to determine the absolute configurations of the phosphorus atoms which are shown in Figs. 1 and 2. The imaginary part of the phosphorus anomalous scattering is too small to detect significant differences between intensities of Friedel reflections. Therefore the only way to proceed is to consider the asymmetric atoms C(12) and C(11) of the compound **2a** and C(1) and C(2) of compound **2b**, to choose the right enantiomer, their absolute configurations being known.

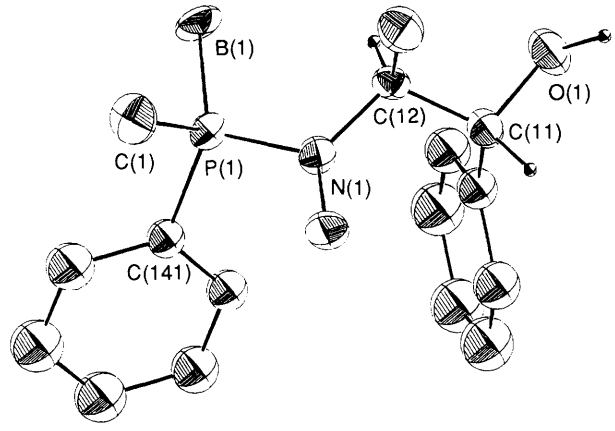


Fig. 1 ORTEP projection of **2a** at the 30% probability level. Selected distances (Å) and angles (°): P(1)–C(1) 1.81(1); P(1)–B(1) 1.90(1); P(1)–N(1) 1.652(8); P(1)–C(141) 1.809(6); B(1)–P(1)–C(1) 110.2(6); N(1)–P(1)–C(1) 109.0(5); N(1)–P(1)–B(1) 114.5(4); C(141)–P(1)–C(1) 104.4(5); C(141)–P(1)–B(1) 112.2(5); C(141)–P(1)–N(1) 105.8(4).

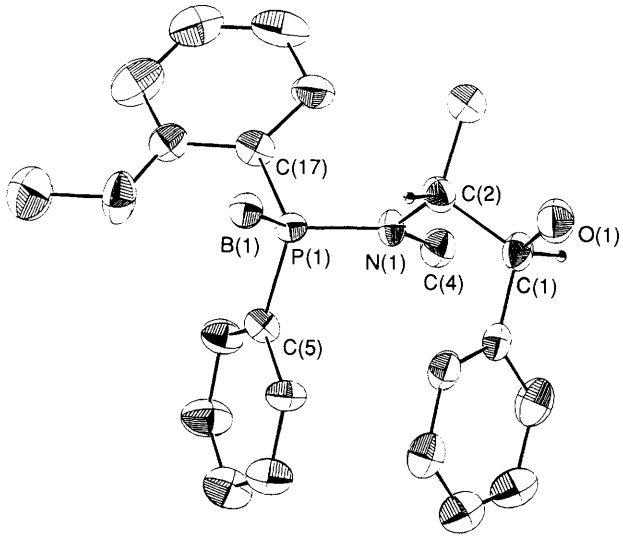


Fig. 2 ORTEP projection of **2b** at the 30% probability level. Selected distances (Å) and angles (°); P(1)–C(5) 1.812(9); P(1)–B(1) 1.93(1); P(1)–N(1) 1.648(7); P(1)–C(17) 1.818(9); B(1)–P(1)–C(5) 111.7(5); N(1)–P(1)–C(5) 107.3(4); N(1)–P(1)–B(1) 110.9(5); C(17)–P(1)–C(5) 107.3(4); C(17)–P(1)–B(1) 110.9(5); C(17)–P(1)–N(1) 110.8(4).

In compound **2a**, the absolute configurations are respectively *R* and *S* for C(11) and C(12), and it may be seen in Fig. 1 that the absolute configuration of the phosphorus atom is *R*. Torsion angles calculated for P(1), C(12) and C(11) environments confirm these results.

In the same way the known absolute configurations of the compound **2b** are *S* for C(1) and *R* for C(2), and Fig. 2 shows that the absolute configuration of the phosphorus atom is *R*. The bond distances and angles around the phosphorus atoms were in good agreement with known values,[7] and torsion angles have also been calculated.

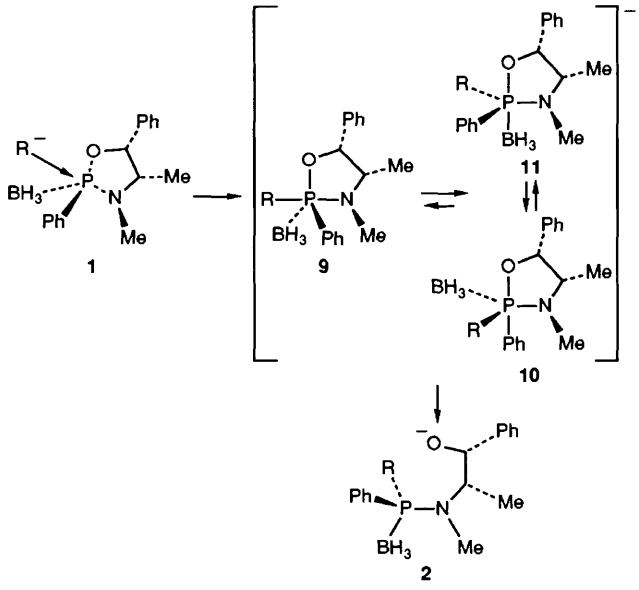
The absolute configuration of the phosphorus atom proves that the P–C bond formation proceeds with a retention of configuration, as for the oxo or thio analogues **8**.[5a,6] Previous explanations of the stereoselectivity of the organometallic attack in these chiral cyclophosphorus compounds, have been proposed by Inch *et al.*[5] and Brown *et al.*[6] From experimental

† *Physical and spectroscopic data* for **2a**: m.p. 67 °C; $[\alpha]_D$ −12.8 (*c* 1, CH_2Cl_2); IR(KBr) ν/cm^{-1} 3354 (OH), 2376 (BH); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.0–1.6 (q, *J* 83 Hz, 3H, BH_3), 1.20 (d, *J* 6.7 Hz, 3H, MeCH), 1.49 (d, *J* 9 Hz, 3H, MeP), 2.1 (s, 1H, OH), 2.4 (d, *J* 8.6 Hz, 3H, MeN), 4.0 (m, J_{HH} 6.9, J_{PH} 7.4 Hz, NCH), 4.7 (d, *J* 7.2 Hz, 1H, OCH), 7–7.1 (m, 3H), 7.2–7.4 (m, 8H); ^{13}C NMR ($CDCl_3$, 62.8 MHz) δ 11.2 (d, J_{PC} 42 Hz, MeP), 13.8 (s, MeCH), 28.9 (s, NCH), 59 (d, J_{PC} 7.6 Hz, MeN), 77.6 (d, J_{PC} 6 Hz, OCH), 126.6–142.5 (aromatic C_{10}); ^{31}P NMR ($CDCl_3$, 100 MHz) δ + 66.5. For **2b**: m.p. 111 °C; $[\alpha]_D$ −38.3 (*c* 1, CH_2Cl_2); IR(KBr) ν/cm^{-1} 3500 (OH), 2381 (BH); ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.2–2 (q, 3H, BH_3), 1.20 (d, *J* 7.8 Hz, 3H, MeCH), 2.1 (s, 1H, OH), 2.5 (d, *J* 8.1 Hz, 3H, MeN), 3.5 (s, 3H, MeO), 4.3 (m, J_{HH} 6, J_{PH} 12 Hz, NCH), 4.85 (d, *J* 5.6 Hz, 1H, OCH), 6.86–6.91 (m, 1H), 6.96–7.02 (m, 1H), 7.15–7.36 (m, 8H), 7.36–7.6 (m, 4H); ^{13}C NMR ($CDCl_3$, 62.8 MHz) δ 12.4 (s, MeCH), 30.9 (s, NCH), 55 (s, MeO), 58.1 (d, J_{PC} 11 Hz, MeN), 78.7 (d, J_{PC} 5 Hz, OCH), 111.6 (d, *J* 5 Hz), 120.8 (d, *J* 11 Hz), 126.5–161.1 (aromatic C_{13}); ^{31}P NMR ($CDCl_3$, 100 MHz) δ + 69.5.

‡ Complex **1** reacted with methyl and *o*-anisylmagnesium reagents respectively at 25 and 80 °C, to give compound **2a** and a mixture of epimeric **2b** in a ratio of 6 : 4.

§ *Crystal data* for **2a**: $C_{17}H_{25}PBON$, colourless crystals. *M* = 301.2, monoclinic system space group $P2_1$, *a* = 20.949(3), *b* = 9.965(1), *c* = 26.497(3) Å, β = 100.79(1)°, *V* = 5434(3) Å^3, D_c = 1.10 g cm^{-3} with *Z* = 12, μ(Mo-Kα) = 1.45 cm^{-1}. For **2b**: $C_{23}H_{29}PBO_2N$, colourless crystals, *M* = 393.2, monoclinic group $P2_1$, *a* = 20.170(7), *b* = 9.616(7), *c* = 11.948(3) Å, β = 101.33(1)°, *V* = 2279(2) Å^3, D_c = 1.17 with *Z* = 4. For both structures, intensity data were measured at 20 °C with Mo-Kα radiation (graphite crystal monochromator) using an Enraf-Nonius CAD4 automatic diffractometer, with the ω–2θ scan method. The structures were solved using direct methods and successive Fourier synthesis. They were refined using a blocked least-squares procedure with the CRYSTALS program[8] with anisotropic thermal parameters for all atoms except in compound **2a**, carbon atoms of phenyl groups which were considered as rigid groups with isotropic thermal parameters. Almost all hydrogen atoms were located on different maps, the other ones being placed theoretically. They were refined with an overall isotropic thermal parameter. Absorption corrections were made with DIFABS.[9]

The structures were refined to *R* (R_w) of 0.069 (0.064) for 5471 reflections for compound **2a**, and 0.052 (0.052) for 1837 reflections for **2b** [intensities used with $I > 3\sigma(I)$], with a weighting scheme of unity. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.



Scheme 2

data, we observe the loss of the stereoselectivity at higher temperature‡ and we have described recently the X-ray structure of the starting complex **1**,[7] showing the distorted oxazaphospholidine ring and the methyl substituent of the nitrogen on the back side of the O-leaving group. Consequently, we think that the stereochemistry of the P–C bond formation is under kinetic control and the nucleophilic attack occurs on the less hindered side-face of the P–O bond which is opposite nitrogen (Scheme 2). The mechanism proposed must require the formation of a pentacoordinate intermediate **9** which stereopermutes into another one (**10** or **11**) having the substituents on the phosphorus atom in a staggered position with the *N*-methyl group (Scheme 2). The presence of the oxygen group in the apical position of the intermediate (**10** or **11**) permits the cleavage of the P–O bond and the formation of the compound **2** with retention of the configuration (Scheme 2). In the case of compound **6**, the prolinol skeleton forms a bicyclic compound with a *cis* junction between the oxazaphospholidine and the pyrrolidine ring, which is probably more favourable to a nucleophilic approach at the position opposite to the leaving group. Finally, the stereochemistry of the organometallic attack on a chiral phosphorus centre could be explained by the steric hindrance of the back side of the leaving group. In cyclic species, the relative configurations and the conformation of the heterocycle, depends on the substituents of the ring.

We thank Dr J. A. Laffitte and the ELF Aquitaine Company for their kind interest in this work.

Received, 20th July 1992; Com. 2/03865J¶

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¶ Received in revised form: 4th January 1993.