

# First totally diastereoselective opening of chiral triquinphosphoranes. A new access to enantiopure oxazaphospholidines†

Caroline Marchi, Guillaume Delapierre, Frédéric Fotiadu and Gérard Buono\*

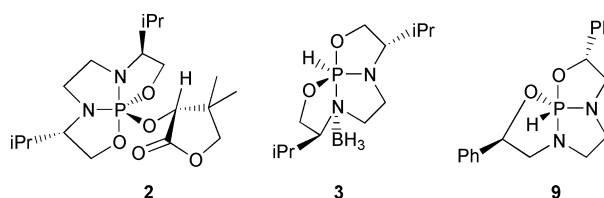
Laboratoire de Synthèse Asymétrique, UMR 6516, ENSSPICAM, Avenue Escardrille Normandie-Niemen, 13397 Marseille cedex 20, France. E-mail: buono@spi-chim.u-3mrs.fr; Fax: +33 4 91 28 82 47

Received (in Liverpool, UK) 18th July 2000, Accepted 3rd October 2000

First published as an Advance Article on the web

Asymmetric addition of isocyanate compounds on chiral triquinphosphoranes, tricyclic hydridophosphoranes, led by a total diastereoselective opening of the diazaphospholidine ring. This provides chiral bicyclic oxazaphospholidines in which an eight-membered ring is fused to the oxazaphospholidine ring by the P–N bond.

Chiral tricoordinated organophosphorus compounds containing an oxazaphospholidine ring have been applied with success in enantioselective catalysis<sup>1</sup> and in asymmetric synthesis.<sup>2</sup> We wish to report herein an original synthesis of new enantiopure bicyclic oxazaphospholidines based on the reaction between isocyanate compounds and chiral triquinphosphoranes.† This new class of chiral tricyclic phosphoranes was synthesized from enantiopure diaminodiols having a  $C_2$  symmetry axis.<sup>3</sup> Those phosphoranes exist as two trigonal bipyramidal structures (TBP) with opposite absolute configuration at the phosphorus atom,  $R_P$  and  $S_P$ , in fast equilibrium by a Berry pseudorotation process via a SP transition state (Scheme 1).<sup>3,4</sup> We have described the first asymmetric addition of chiral triquinphosphorane **1c** to ketopantolactone and to  $BH_3 \cdot SMe_2$  complex leading to chiral alkoxyphosphorane<sup>3c</sup> **2** and chiral triquinphosphorane–borane<sup>3b</sup> adduct **3**, respectively. The X-ray diffraction structure of **3** revealed that the borane group coordinated to the axial nitrogen atom of the TBP structure is in the *syn* position with respect to the P–H bond and in the *anti* position with respect to the



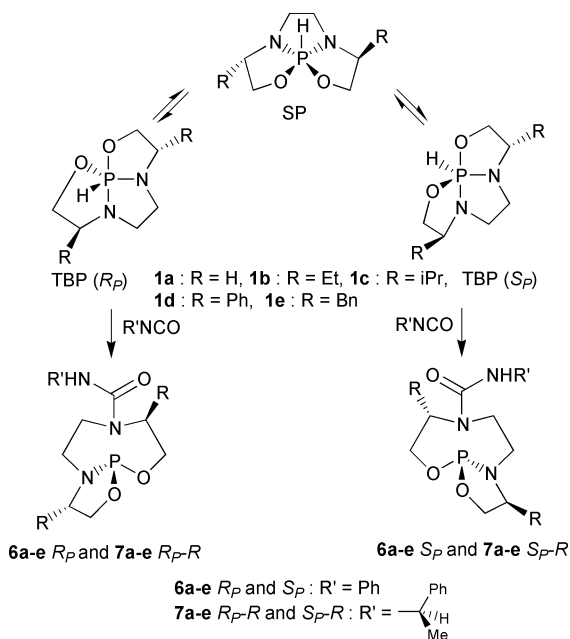
adjacent pseudoaxial isopropyl substituent.<sup>3b,5</sup> Phenyl isocyanate **4** and (*R*)-phenylethyl isocyanate **5** reacted readily with the triquinphosphoranes **1a–e**<sup>6</sup> to afford chiral bicyclic oxazaphospholidines **6a–e** and **7a–e**, respectively, in which an eight-membered ring is fused to the oxazaphospholidine ring by the P–N bond (Scheme 1).

Oxazaphospholidines **6a** and **7a** were formed in quantitative yield by direct reaction of the parent triquinphosphorane **1a** with isocyanates **4** and **5**, respectively, in toluene solution at  $-30^\circ C$ . The exclusive formation of these new compounds could be monitored by  $^{31}P$  NMR spectroscopy showing only one downfield singlet at 130.1 ppm for racemic **6a** and two signals at 130.70 and 130.77 ppm for **7a** in a 1:1 ratio corresponding to the diastereomers **7a- $R_P$**  and **7a- $S_P$** . Due to the high energy barrier for the epimerization of the tricoordinated phosphorus atom ( $30\text{--}35\text{ kcal mol}^{-1}$ ),<sup>7</sup> this result shows that no dynamic chiral discrimination occurred during the attack of chiral isocyanate **5** on the two enantiomeric structures **1a- $R_P$**  and **1a- $S_P$**  in fast equilibrium.

In the case of chiral triquinphosphoranes **1b–e**,  $^{31}P$  NMR monitoring showed that condensation of isocyanates **4** and **5** occurred with a total diastereoselective opening of the diazaphospholidine ring, to afford a single diastereomer as shown by the  $^{13}C$  and  $^{31}P$  NMR spectra. Compound **7e** reacted with  $BH_3 \cdot SMe_2$  complex in toluene solution to give the borane adduct **8** in which the borane is coordinated to the phosphorus atom ( $\delta^{31}P$ : 120.3 ppm). The structure of adduct **8** and the absolute configuration of the phosphorus atom were determined by single X-ray diffraction (Fig. 1).<sup>8</sup> The nitrogen, oxygen, and boron atoms around the phosphorus center adopt a slightly distorted tetrahedral arrangement with bond angles between  $95.0$  and  $119.8^\circ$ . Because the complexation of borane occurs with retention of configuration at the phosphorus atom, the borane adduct shows that the diastereoselective opening of the diazaphospholidine ring led to a tricoordinated compound with the  $S_P$  absolute configuration. The shortness of the P1–N6 bond [ $1.637(5)\text{ \AA}$  instead of  $1.67\text{--}1.70\text{ \AA}$  usually]<sup>9</sup> can in part be assigned to negative hyperconjugation, due to electron donation from  $\pi_N$  to  $\sigma_{P-B}^*$  orbitals.<sup>10</sup> In fact the N6 nitrogen exhibits a planar configuration [sum of bond angles  $359.8(4)^\circ$ ].

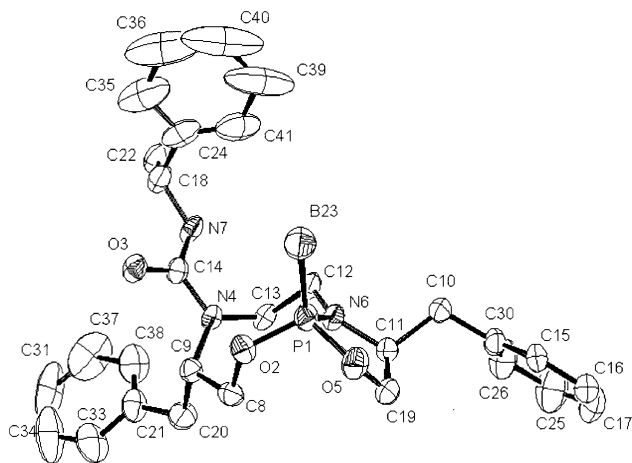
The newly formed eight-membered ring adopts a twist–boat–chair conformation and the five-membered ring a slightly flattened envelope conformation with the C19 atom as the tip. The benzyl group bound to the C11 carbon of the oxazaphospholidine ring is in the *syn* position with respect to the boron atom whereas the benzyl group bound to the C9 carbon of the eight-membered ring is in the *anti* position.

Taken together, these results suggest that just like borane,<sup>3b</sup> isocyanates attack preferentially the least hindered axial nitrogen atom of the  $S_P$  phosphorane diastereomer (Scheme 2).

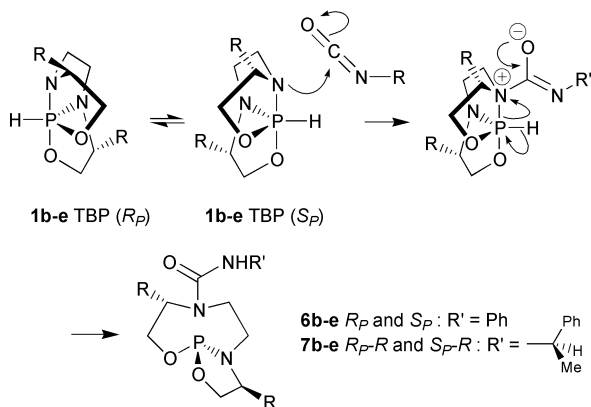


**Scheme 1** Pseudorotation process and addition of isocyanates **4** and **5** on triquinphosphoranes.

† Electronic supplementary information (ESI) available: experimental procedures and characterization of compounds **6a–e**, **7a–e**, **8**. See <http://www.rsc.org/suppdata/cc/b0/b005884j>



**Fig. 1** ORTEP drawing of **8**. For more clarity, we omitted hydrogen atoms and used 30% probability ellipsoids. Selected bond lengths [Å]: O2–P1, 1.581(4); O5–P1, 1.592(4); N6–P1, 1.637(5); N4...P, 3.472(4); B23–P1, 1.888(7). Bond angles [°]: B23–P1–O2, 109.3(3); B23–P1–O5, 113.9(3); B23–P1–N6, 119.8(4); N6–P1–O5, 95.0(2); N6–P1–O2, 108.9(2); O2–P1–O5, 109.0(2); P1–N6–C11, 113.6(3); P1–N6–C12, 125.0(3); C8–O2–P1, 122.4(3); C19–O5–P1, 112.3(3); C11–N6–C12, 121.2(3); C9–N4–C13, 119.1(4); C9–N4–C14, 118.2(4); C13–N4–C14, 122.8(5).



**Scheme 2** Addition mechanism of isocyanates **4** and **5** on triquinphosphoranes **1b-e**.

In fact, the TBP- $S_P$ , the pseudoaxial substituent is in an *anti* position with respect to the lone pair of the axial nitrogen atom whereas it is in a *syn* position in TBP- $R_P$ . The diastereoselectivity observed can thus be rationalized in terms of a kinetically controlled process in which the minor triquinphosphorane diastereomer (29%) reacts faster than the major one (71%) to afford only one diastereomeric oxazaphospholidine.<sup>4</sup>

The importance of steric factors was further confirmed by the fact that the diastereoselectivity of the isocyanate addition depends on the position of the substituents. Indeed, in the case of triquinphosphorane **9**,<sup>11</sup> in which the phenyl substituents are

$\beta$  to the nitrogen atom, the diastereoselectivity of the addition of isocyanates **4** and **5** decrease to 77 and 93%, respectively.

In summary, we disclose for the first time the formation of enantiomerically pure  $P^{III}$  oxazaphospholidines from chiral pentacoordinated phosphoranes. These new compounds feature an eight-membered ring, difficult to synthesize with classical methods.<sup>12</sup> Research to evaluate the efficiency of these new compounds in asymmetric catalysis either as ligands or as catalysts is in progress.

We gratefully acknowledge financial support from the CNRS and fellowships from the MNRT (C. M. and G. D.). We thank Dr M. Giorgi and Professor M. Pierrot from the 'Université d'Aix-Marseille' for the X-ray structure determinations.

## Notes and references

‡ The IUPAC name for triquinphosphorane is hexahydro-11  $\lambda^5$ -[1,3,2]oxazaphospholo[2',3':2,3][1,3,2]diazaphospholo[2,1-b][1,3,2]oxazaphosphole.

- G. Buono, O. Chiodi, M. Gamble and M. Wills, *Synlett*, 1999, **4**, 377.
- O. I. Kolodiazny, *Tetrahedron: Asymmetry*, 1998, **9**, 1279.
- (a) Y. Vannoorenberghe and G. Buono, *J. Am. Chem. Soc.*, 1990, **112**, 6142; (b) C. Marchi, F. Fotiadu and G. Buono, *Organometallics*, 1999, **18**, 915; (c) C. Marchi and G. Buono, *Tetrahedron Lett.*, 1999, **40**, 9251.
- Semi empirical AM1 MO calculations predict that the TBP ( $R_P$ ) and TBP ( $S_P$ ) ground-state species are in equilibrium through a SP transition state, the activation barrier being about 5 kcal mol<sup>-1</sup>. Calculations predict a marked predominance of the ( $R_P$ ) form [71 : 29 for **1e**], see ref. 3b.
- Compounds **2** and **3** have been studied by X-ray diffraction. They exhibit a percentage of deformation from the ideal TBP structure along the Berry pseudorotation pathway of 66 and 6.9%, respectively.
- Triquinphosphoranes **1b-e** were prepared from *N,N'*-bis[(1*S*)-1-alkyl-2-hydroxyethyl]ethylenediamine. See ref. 3(b).
- (a) K. Mislow, *Pyramidal Inversion Barriers of Phosphines and Arsenes in Organophosphorus Stereochemistry part I: Origin and P(III and IV) Compounds*, eds. W. E. McEwen and K. D. Berlin, Dowden, Hutchinson and Ross, Inc., Stroudsburg, Pennsylvania, 1975, p. 195–210; (b) D. G. Gilheany, *Structure and Bonding in Organophosphorous (III) Compounds in The Chemistry of Organophosphorous Compounds vol. 1*, eds. F. R. Hartley and S. Patai, J. Wiley & Sons Publication, New York, 1990, p. 9–49.
- Crystal data for **8**:  $C_{29}H_{37}BN_3O_8P$ ,  $M_r = 517.42$ , hexagonal, space group  $P6_1$ ,  $a = 13.0505(5)$ ,  $c = 29.9705(7)$  Å,  $Z = 6$ ,  $V = 4420.3(3)$  Å<sup>3</sup>,  $\rho_{\text{calcd}} = 1.166$  g cm<sup>-3</sup>,  $\mu(\text{MoK}\alpha) = 0.126$  cm<sup>-1</sup>, final  $R1$  and  $wR2$  are 0.0734 and 0.1745 for 368 parameters and 3328 unique observed reflections with  $I > 2.0\sigma(I)$ . CCDC 182/1811. See <http://www.rsc.org/suppdata/cc/b0/b005884j/> for crystallographic files in .cif format.
- J. M. Dupart, A. Grand, S. Pace and J. G. Riess, *Inorg. Chem.*, 1984, **23**, 3776.
- (a) D. G. Gilheany, *Chem. Rev.*, 1994, **94**(5), 1339; (b) P. von R. Schleyer and A. J. Kos, *Tetrahedron*, 1983, **39**, 1141.
- Triquinphosphorane **9** was prepared from *N,N'*-bis[2(*S*)-2-phenyl-2-hydroxyethyl]ethylenediamine.
- L. D. Quin, in *Conformational Analysis of Medium-Sized Heterocycles*, ed. R. S. Glass, VCH, 1988, chap. 5, p. 181–216.