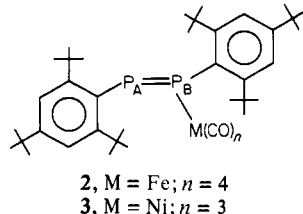


and diarsenes (RAs=AsR)<sup>4</sup> have been isolated, four of which have now been structurally characterized.<sup>2a,m,3,4b</sup> We now report (i) the first indication that compounds with P=P and P=As bonds will react with organometallic reagents, (ii) a new mode of coordination for a diphosphene, and (iii) the first phospharsene complexes.

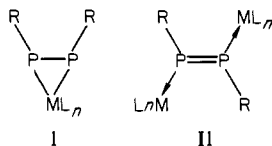
In a typical reaction, 0.563 g (1.02 mmol) of (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)<sub>2</sub>P<sub>2</sub> (1)<sup>2a</sup> was treated with 0.51 g (1.40 mmol) of Fe<sub>2</sub>(CO)<sub>9</sub> in 45 mL of *n*-hexane at 0 °C. The dark-red reaction mixture was allowed to warm to ambient temperature, and stirring was continued for 6 h. After filtration, the solvent and volatiles were removed by pumping in vacuo. Purification was effected by chromatography at -78 °C (*n*-hexane/Florisil). Red-brown crystals of (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)<sub>2</sub>P<sub>2</sub>Fe(CO)<sub>4</sub> (2) (mp 168-170 °C



dec) formed from *n*-hexane solutions held at -20 °C (yield 65%). 2: <sup>31</sup>P{<sup>1</sup>H} NMR (AB pattern) δ<sub>A</sub> +423.6, δ<sub>B</sub> +396.4, <sup>1</sup>J<sub>PP</sub> = 578.0 Hz; IR (*n*-hexane) ν<sub>CO</sub> 1940, 1915, 1895, 1880 cm<sup>-1</sup>; UV-vis (CH<sub>2</sub>Cl<sub>2</sub>) λ<sub>max</sub> 486 (ε = 5200), 288 (ε = 18 700), 244 nm (ε = 26 000).

The X-ray structure of 2<sup>5</sup> (Figure 1) reveals a P(1)-P(2) bond length of 2.050 (1) Å, which is comparable to those reported for other compounds with P=P bonds.<sup>2a,m,8</sup> Furthermore, within experimental error the C<sub>2</sub>P<sub>2</sub>Fe framework is planar. The P-C bond angles in 2 are 6° larger than those in the free ligand, 1.<sup>2a</sup> Steric crowding is also evidenced by the fact that the P(1)-C(1) bond is 0.03 Å longer than the P(2)-C(7) bond.

Compound 2 represents a new mode of coordination for a diphosphene. Previously reported complexes were of type I<sup>9</sup> or II.<sup>8</sup>



Compound 2 is also formed (along with 1) when (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)PCL<sub>2</sub> is treated with Na<sub>2</sub>Fe(CO)<sub>4</sub> in THF solution. The

(3) Cowley, A. H.; Lasch, J. G.; Norman, N. C.; Pakulski, M.; Whittlesey, B. R. *J. Chem. Soc., Chem. Commun.* **1983**, 881.

(4) (a) Couret, C.; Escudie, J.; Madaule, Y.; Ranaivorjatovo, H.; Wolf, J.-G.; *Tetrahedron Lett.* **1983**, 24, 2769. (b) Cowley, A. H.; Lasch, J. G.; Norman, N. C.; Pakulski, M. *J. Am. Chem. Soc.* **1983**, 105, 5506.

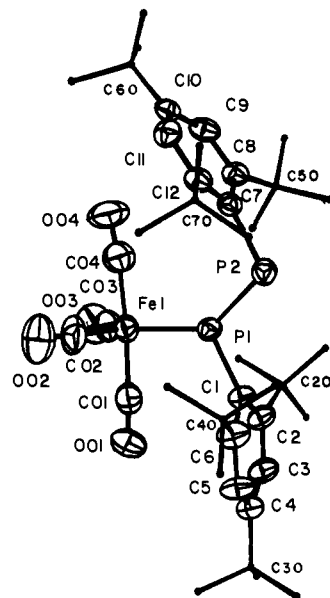
(5) Crystal data for (2): C<sub>40</sub>FeH<sub>58</sub>O<sub>4</sub>P<sub>2</sub>, M = 720.7, monoclinic, space group P2<sub>1</sub>/c (No. 14), a = 21.251 (6) Å, b = 9.793 (2) Å, c = 20.99 (2) Å, β = 108.73 (6)°, U = 4136 (5) Å<sup>3</sup>, D<sub>c</sub> = 1.157 g cm<sup>-3</sup>, Z = 4, λ(Mo Kα) = 0.71069 Å (graphite monochromator), μ(Mo Kα) = 4.7 cm<sup>-1</sup>. From a total of 7504 unique reflections, measured on an Enraf-Nonius CAD-4F diffractometer, 4204 (I > 2.5σ(I)) were used to solve (MULTAN<sup>6</sup> and difference Fourier) and refine (full matrix, least squares) the structure of 2. All non-hydrogen atoms were refined with anisotropic thermal parameters. However, under these conditions, the methyl carbon C(41) did not refine well and in the final cycle was given an isotropic temperature factor. All hydrogen atoms were fixed in idealized geometries 0.95 Å from their respective carbon atom. These were included in the structure factor calculation but not refined due to insufficient data. Refinement with a weighting scheme<sup>7</sup> converged smoothly to give final residuals R = 0.0578, R<sub>w</sub> = 0.0824, GOF = 1.634.

(6) Germain, G.; Main, P.; Woolfson, M. M. *Acta Crystallogr., Sec. A* **1971**, A27, 368. Main, P. MULTAN 82, University of York, York, England, 1982.

(7) The weighting scheme used was of the form w = (4F<sup>2</sup>/σ<sup>2</sup>(F<sup>2</sup>) + P<sup>2</sup>F<sup>4</sup>) with P = 0.08.

(8) Flynn, K. M.; Olmstead, M. M.; Power, P. P. *J. Am. Chem. Soc.* **1983**, 105, 2085.

(9) (a) Elmes, P. S.; Scudder, M. L.; West, B. O. *J. Organomet. Chem.* **1976**, 122, 281. (b) Cannillo, E.; Coda, A.; Prout, K.; Daran, J. C. *Acta Crystallogr., Sect. B* **1977**, B33, 2608. (c) Deppisch, B.; Schäfer, H. *Ibid.* **1982**, B38, 748. (d) Chatt, J.; Hitchcock, P. B.; Pidcock, A.; Warrens, P. W.; Dixon, K. R. *J. Chem. Soc., Chem. Commun.* **1982**, 932.



**Figure 1.** View of the (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)<sub>2</sub>P<sub>2</sub>Fe(CO)<sub>4</sub> (2) molecule showing the atom numbering scheme. Important parameters: P(1)-P(2) 2.050 (1), P(1)-Fe(1) 2.215 (1), P(1)-C(1) 1.893 (4), P(2)-C(7) 1.859 (4) Å; P(1)-P(2)-C(7) 108.4 (1)°, P(2)-P(1)-Fe(1) 135.52 (6)°, P(2)-P(1)-C(1) 109.3 (1)°, C(1)-P(1)-Fe(1) 115.1 (1)°.

fact that only one Fe(CO)<sub>4</sub> attaches is a consequence of steric effects. Likewise, only one Ni(CO)<sub>3</sub> group attaches even when 1 is treated with excess Ni(CO)<sub>4</sub> (in Et<sub>2</sub>O). [2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>]<sub>2</sub>P<sub>2</sub>Ni(CO)<sub>3</sub> (3): <sup>31</sup>P{<sup>1</sup>H} NMR (AB pattern) δ<sub>A</sub> +449.0, δ<sub>B</sub> +422.0, <sup>1</sup>J<sub>PP</sub> = 540.3 Hz; IR (*n*-hexane) ν<sub>CO</sub> 1800, 1860, 1955 cm<sup>-1</sup>. The very bulky diphosphene (Me<sub>3</sub>Si)<sub>3</sub>CP=PC(SiMe<sub>3</sub>)<sub>3</sub><sup>2b,f,m</sup> does not react with Ni(CO)<sub>4</sub> at 25 °C.

The unsymmetrical diphosphene, (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)P=PCH-(SiMe<sub>3</sub>)<sub>2</sub> also reacts with Fe<sub>2</sub>(CO)<sub>9</sub> to afford the corresponding (Me<sub>3</sub>Si)<sub>2</sub>CHP-bound Fe(CO)<sub>4</sub> complex 4 in 63% yield. 4: <sup>31</sup>P NMR (ABX system) δ<sub>A</sub> +424, δ<sub>B</sub> +416, <sup>1</sup>J<sub>PP</sub> = 519.0, <sup>2</sup>J<sub>PH</sub> = 30.0, <sup>3</sup>J<sub>PH</sub> = -3.2 Hz; IR (*n*-hexane) ν<sub>CO</sub> = 1970 (br), 2060 cm<sup>-1</sup>. Preliminary studies of the reaction of the phospharsene (2,4,6-*t*-Bu<sub>3</sub>C<sub>6</sub>H<sub>2</sub>)As=PCH(SiMe<sub>3</sub>)<sub>2</sub><sup>3</sup> indicate the formation of two products, 5a and 5b, in which the Fe(CO)<sub>4</sub> moiety is attached to phosphorus and arsenic atoms, respectively. <sup>31</sup>P NMR: 5a, s +390; 5b, s +429 ppm.

**Acknowledgment.** Generous financial support from the National Science Foundation (Grant CHE-8205871) and the Robert A. Welch Foundation is acknowledged. We are also grateful to Professor Philip P. Power for discussing his work prior to publication.

**Registry No.** 1, 79073-99-7; 2, 87937-39-1; 3, 87937-40-4; 4, 87937-

**Supplementary Material Available:** Tables of bond lengths, bond angles, atomic coordinates, and thermal parameters (8 pages). Ordering information is given on any current masthead page.

### Six-Membered Ring Phosphites in Twist Conformations. The Methyl and Phenyl Trans-3',5'-Cyclic Phosphites of Thymidine

Keith A. Nelson, Alan E. Sopchik, and Wesley G. Bentrude\*

Department of Chemistry, University of Utah  
Salt Lake City, Utah 84112

Received July 11, 1983

The replacement of the ring carbons of cyclohexane with heteroatoms containing electron lone pairs may greatly affect the relative free energies of potentially populated conformations as

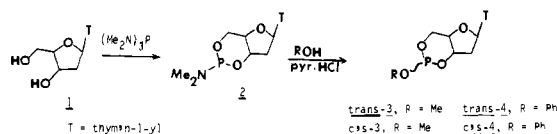
Table I.  $^1\text{H}$  NMR Parameters for **3** and **4** at 300 MHz<sup>a</sup>

compound	solvent	$J$ , Hz							
		5'a5'b	5'a4'	5'aP	5'bP	5'b4'	3'4'	3'P	4'P
<i>cis</i> - <b>3b</b>	acetone- $d_6$	-9.1	10.8	2.4	10.6	4.3	9.5	1.8	c
<i>trans</i> - <b>3d</b>	acetone- $d_6$	-9.6	9.7	7.7	3.0	6.2	9.5	1.1	-0.8
<i>cis</i> - <b>4b</b>	acetone- $d_6$	-9.2	10.7	2.6	10.8	4.4	9.1	~2	c -
<i>trans</i> - <b>4d</b>	acetone- $d_6$	-9.7	9.8	9.2	1.4	6.6	9.7	1.1	-1.0

<sup>a</sup> At  $\sim 25^\circ\text{C}$ . <sup>b</sup> First-order analysis. <sup>c</sup>  $< 0.6$  Hz. <sup>d</sup> Iteratively refined with LAOCN3 program.

well as strongly influence, via stereoelectronic interactions, the orientational preferences of substituents. We report here  $^1\text{H}$  NMR evidence that for certain six-membered ring phosphites<sup>1</sup> (*trans*-**3** and **-4**) the *twist* form, **6**, rather than the chair, **5**, is the more stable conformation. In spite of numerous conformational studies, twist forms have not previously been observed unequivocally for saturated six-membered ring phosphites. The twist conformations found in our studies could be the result of the strong stereoelectronically directed configurational preference of the RO group but also could reflect a relatively low chair–twist free energy difference.

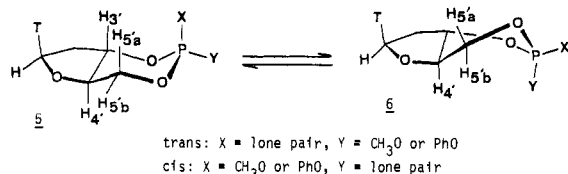
Phosphites **3** and **4**, comprised of at least 80% of the thermodynamically less stable *trans* diastereomer (relationship of RO and T, structures **5** and **6**), were prepared by slow addition of 1.0



equiv of  $\text{CH}_3\text{OH}$  or  $\text{PhOH}$  to **2** in  $\text{CH}_2\text{Cl}_2$  stirred at  $-78^\circ\text{C}$  (for **3**) or  $-10^\circ\text{C}$  (for **4**) in the presence of  $\sim 2.0$  equiv of anhydrous pyridine hydrochloride. Immediate solvent exchange with ethyl acetate to precipitate the amine hydrochloride and rapid chromatography of the supernatant on a short  $\text{SiO}_2$  column eluted with ethyl acetate afforded pure ( $^{31}\text{P}$ ,  $^1\text{H}$  NMR) **3** and **4** in 47% and 67%, respective, yields [ $\delta^{31}\text{P}$  ( $\text{CDCl}_3$ ): *cis*-**3** 123.2; *trans*-**3**, 129.4; *cis*-**4**, 114.5; *trans*-**4**, 120.6]. *Cis* and *trans* geometries were assigned as reported previously for **3**.<sup>2</sup> The diastereomeric excesses of *trans*-**3** and **-4** were quite suitable for  $^1\text{H}$  NMR analysis at 300 MHz.

Diastereomerically pure *cis*-**3** was formed in a parallel procedure in alcohol-free  $\text{CHCl}_3$  solvent, which involved thermal isomerization of the initial mixture of diastereomers. Quantitative amounts were isolated by  $\text{SiO}_2$  column chromatography. *cis*-**4** resulted from **2**, stirred at room temperature in  $\text{CH}_2\text{Cl}_2$  for 24 h under dry  $\text{CO}_2$  in the presence of catalytic  $\text{Me}_2\text{NH}_2^+\text{Cl}^-$  to give the carbamate, which was then reacted for 24 h with 1.1 equiv of phenol. Ethyl acetate elution on  $\text{SiO}_2$  gave pure *cis*-**4** in 36% isolated yield.

Pertinent  $^1\text{H}$  NMR data for **3** and **4** are compiled in Table I. For *cis*-**3** and **-4** (X = MeO, PhO; Y = lone pair), only chair conformation **5** is populated in keeping with the well-known axial



propensities of RO groups of such phosphites.<sup>1</sup> The  $^3J_{\text{HP}}$  values for the equatorial  $\text{H}5'b$  (10.6 and 10.8 Hz) ( $\text{H}5'b$  and P approximately antiperiplanar) and axial  $\text{H}5'a$  protons (2.4 and 2.6 Hz) are very similar to those of other chair-form phosphites.<sup>1</sup> (See

also  $J_{\text{HP}}$ .) The expected relatively large  $^3J_{\text{HH}}$  values for  $\text{H}5'a/\text{H}4'$  (10.8 and 10.7 Hz) also are seen.

Unmistakeably, however, the phosphite rings of *trans*-**3** and **-4** are primarily in nonchair conformations. Most notable and diagnostic for the twist conformation, **6**, is the combination for  $\text{H}5'a$  of a relatively large  $^3J_{\text{HP}}$  (7.7 and 9.5 Hz) along with a large  $^3J_{4'5'a}$  value (9.7 and 9.6 Hz).<sup>3</sup> This unique situation arises from the pseudoequatorial position of  $\text{H}5'a$  (large  $^3J_{\text{HP}}$ ) and relatively unchanged  $\text{H}4'\text{C}4'\text{C}5'\text{H}5'a$  dihedral angle. The somewhat reduced  $\text{H}4'\text{C}4'\text{C}5'\text{H}5'b$  dihedral angle increases  $J_{4'5'b}$  in **6** compared to **5**.

From the observed large difference in  $J_{5'aP}$  and  $J_{5'bP}$ , it is clear that *trans*-**4** is  $>90\%$  in conformation **6**. *trans*-**3** populates a greater portion of chair **5** (perhaps 20–30%) as reflected in the increase in  $J_{5'bP}$  and decrease in  $J_{5'aP}$ .<sup>4</sup> The configurational preference of RO for the axial (**5**) or pseudoaxial (**6**) position is of stereoelectronic origins<sup>5</sup> closely related to the classical anomeric effect ( $n\text{-}\sigma^*$  stabilization). This results in the greater thermodynamic stability of *cis*-**3** and **-4** and the predominant population of the twist conformation, **6**, for the *trans* diastereomers. The larger fraction of twist **6** populated by *trans*-**4** is consistent with the greater electronegativity of the PhO (lower  $\sigma^*$  energy), which should enhance the dominant, stabilizing  $n\text{-}\sigma^*$  interaction between the ring oxygen p-orbital lone pair and the pseudoaxial P–OR  $\sigma^*$  orbital. (This interaction is only possible with RO axial or pseudoaxial.)

Two energetic components are involved in the *trans*-**5**  $\rightleftharpoons$  **-6** equilibrium: the stabilization energy gained by reorientation of X ( $\Delta G^\circ_X$ ) and the increased energy of the twist conformation ( $\Delta G^\circ_{\text{CT}}$ ).

$$\Delta G^\circ(\mathbf{5} \rightarrow \mathbf{6}) = \Delta G^\circ_X + \Delta G^\circ_{\text{CT}}$$

For *trans*-**3** a 75% population of **6** corresponds to  $\Delta G^\circ(\mathbf{5} \rightarrow \mathbf{6})$  of  $-0.5$  kcal/mol. The axial preference of MeO is not known for certain in phosphites although it must be at least 2 kcal/mol,<sup>6</sup> and the twisting of ring **6** will alter the O/P orbital interactions somewhat. Nonetheless,  $\Delta G^\circ_{\text{MeO}}$  is sufficient to overcome  $\Delta G^\circ_{\text{CT}}$ . This may indeed be a result of  $\Delta G^\circ_{\text{CT}}$  being relatively low for such a six-membered ring, as it is for 4-coordinate 2-oxo-1,3,2-dioxo-,<sup>7</sup> 2-oxo-1,3,2-dithia-,<sup>8</sup> and 2-oxo-1,3,2-oxazaphosphorinanes.<sup>3a,7e</sup> Either origin, from  $\Delta G^\circ_{\text{MeO}}$  or  $\Delta G^\circ_{\text{CT}}$ , reflects a major consequence of heteroatom substitution into the cyclohexane ring.

(3) We have noted this combination for the unmistakably twist conformations of (a) *cis*-2-oxo-2-(dimethylamino)-5-*tert*-butyl-1,3,2-oxazaphosphorinane, x ray and  $^1\text{NMR}$  (Bajwa, G. S.; Chandrasekaran, S.; Hargis, J. H.; Sopchik, A. E.; Blatter, D.; Bentrude, W. G. *J. Am. Chem. Soc.* **1982**, *104*, 6385. Bajwa, G. S.; Bentrude, W. G.; Pantaleo, N. S.; Newton, M. G.; Hargis, J. H. *Ibid.* **1979**, *101*, 1602.), and (b) the *cis*-(dimethylamino)-phosphoramidate based on cyclic 3',5'-thymidine monophosphate (Sopchik, A. E.; Bentrude, W. G. *Tetrahedron Lett.* **1980**, 4679).

(4) For *trans*-**3** and **-4** the sums of  $J_{\text{H}5'a\text{P}}$  and  $J_{\text{H}5'b\text{P}}$  are lower than for the *cis* chair structure **5**. This is reasonable since the degree of twist in **6** may not have moved the  $\text{C}_\beta$  protons into completely pseudoequatorial and pseudoaxial positions. It is perhaps surprising that the sum for *trans*-**3** is not intermediate in value since a portion of **5** seems to be populated.

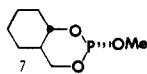
(5) See: (a) Hudson, R. F.; Verkade, J. G. *Tetrahedron Lett.* **1975**, 3231. (b) Bentrude, W. G.; Tan, H. W. Yee, K. C. *J. Am. Chem. Soc.* **1975**, *97*, 573.

(6) *meso*-2-Methoxy-4,6-dimethyl-1,3,2-dioxaphosphorinane at thermodynamic equilibrium failed to show by NMR any (i.e.,  $<5\%$ ) of the *cis* (MeO equatorial) isomer to be present. (a) Haemers, M.; Ottinger, R.; Zimmermann, D.; Reisse, J. *Tetrahedron* **1973**, *29*, 3539. (b) White, D. W.; Bertram, R. D.; McEwen, G. K. Verkade, J. G. *J. Am. Chem. Soc.* **1970**, *92*, 7125. A limit value for  $\Delta G^\circ_{\text{CT}}$  of at least  $-3.1$  kcal/mol also has been estimated.<sup>6b</sup>

(1) For a comprehensive review of the properties of such three- and four-coordinate 1,3,2-dioxaphosphorinanes, see: Maryanoff, B. E.; Hutchins, R. O.; Maryanoff, C. A. *Top. Stereochem.* **1979**, *11*, 187.

(2) Bajwa, G. S.; Bentrude, W. G. *Tetrahedron Lett.* **1978**, 421.  $^{31}\text{P}$  chemical shifts are in ppm downfield from external 85%  $\text{H}_3\text{PO}_4$ .

It appears highly significant that population of a twist conformer was not reported for the *trans*-decalin-like system **7**.<sup>9</sup> This may



reflect an important difference between the relatively strain-free system **7**, which Dreiding models indicate potentially can exist in either of two boat forms (or intermediate twist), and our system for which only the one twist form (**6**) is accessible. This restriction arises from the need for C4'-O and C2'-C3 bonds of the sugar ring to approach coplanarity. A closer comparison of these ring systems will be in order so as to establish firmly their conformational properties. These studies are of special importance, even in trivalent phosphorus systems, because of the central role of cyclic nucleotides, e.g., cAMP and cGMP, in biochemical processes and the desire to thoroughly understand the conformational properties of the phosphorus-containing ring. This includes any influence of the strain associated with the *trans* ring fusion demonstrated for cAMP.<sup>10</sup>

**Acknowledgment.** This work was supported by a grant from the National Cancer Institute of the Public Health Service (CA 11045).

**Registry No.** **2**, 40652-74-2; **2** carbamate, 87970-11-4; *cis*-**3**, 66386-45-6; *trans*-**3**, 66386-46-7; *cis*-**4**, 87970-09-0; *trans*-**4**, 87970-10-3.

(7) See, e.g.: Reference 3b. (a) Hargis, J. H.; Benrude, W. G. *Chem. Commun.* **1969**, 1113. (b) Benrude, W. G.; Tan, H. W. *J. Am. Chem. Soc.* **1973**, *95*, 4666. (c) Mosbo, J. A. *Org. Magn. Reson.* **1978**, *11*, 281. (d) Gerlt, J. A.; Gutterson, N. I.; Drews, R. E.; Sokolow, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 1665. (e) Gorenstein, D. G.; Rowell, R.; Findlay, J. *Ibid.* **1980**, *102*, 5077. Gorenstein, D. G.; Rowell, R. *Ibid.* **1979**, *101*, 4925.

(8) Maryanoff, B. E.; McPhail, A. T.; Hutchins, R. O. *J. Am. Chem. Soc.* **1981**, *103*, 4432.

(9) Haemers, M.; Ottinger, R.; Reisse, J.; Zimmerman, D. *Tetrahedron Lett.* **1971**, 461. Changes of ~2 Hz in the  $^3J_{\text{HP}}$  values of the CH<sub>2</sub> hydrogens of **7** corresponding to 5'a and 5'b of **3** and **4** were reported without comment. These values could mean that a minor depopulation of the chair occurs.

(10) In the phosphate diesters this amounts to about 5 kcal/mol. (Gerlt, J. A.; Gutterson, N. I.; Datta, P.; Belkeau, B.; Penny, C. L. *J. Am. Chem. Soc.* **1980**, *102*, 1655.)

### Chiral 1,4-Dihydropyridine Equivalents: A New Approach to the Asymmetric Synthesis of Alkaloids. The Enantiospecific Synthesis of (+)- and (-)-Coniine and -Dihydropinidine<sup>1</sup>

Luc Guerrier, Jacques Royer, David S. Grierson, and Henri-Philippe Husson\*

*Institut de Chimie des Substances Naturelles du C.N.R.S.*  
91190 Gif s/Yvette, France

Received June 28, 1983

In connection with our work on the synthesis of a number of biologically important 2,6-disubstituted piperidine alkaloids,<sup>2-6</sup> we were prompted to consider the preparation of piperidine

(1) Dedicated to Professor Sir Derek Barton on the occasion of his 65th birthday. Preliminary communication at the 8th Symposium on Heterocyclic Chemistry, Rennes, France, Sept 1982; see: *Bull. Soc. Chim. Belg.* **1982**, *91*, 985.

(2) Grierson, D. S.; Harris, M.; Husson, H.-P. *J. Am. Chem. Soc.* **1980**, *102*, 1064.

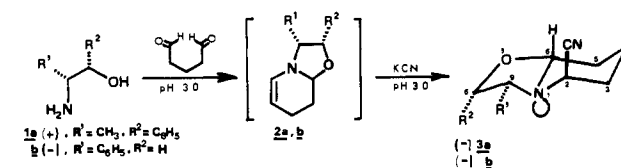
(3) Bonin, M.; Besselièvre, R.; Grierson, D. S.; Husson, H.-P. *Tetrahedron Lett.* **1983**, *24*, 1493.

(4) Harris, M.; Grierson, D. S.; Husson, H.-P. *Tetrahedron Lett.* **1981**, *22*, 1511.

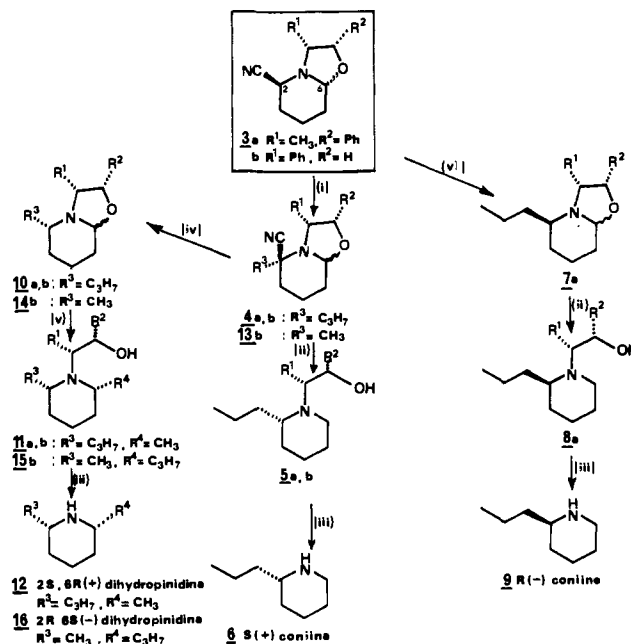
(5) Bonin, M.; Romero, J. R.; Grierson, D. S.; Husson, H.-P. *Tetrahedron Lett.* **1982**, *23*, 3369.

(6) Gnecco Medina, D.; Grierson, D. S.; Husson, H.-P. *Tetrahedron Lett.* **1983**, *24*, 2099.

#### Scheme I

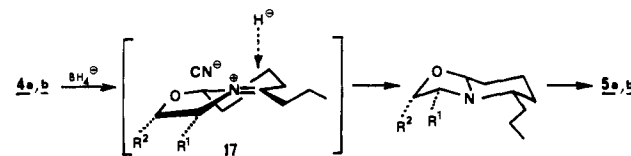


#### Scheme II<sup>a</sup>



<sup>a</sup> Reagents: (i) LDA, THF, -78 °C; R<sup>3</sup>X, 3 h. (ii) NaBH<sub>4</sub>, EtOH, 25-80 °C, 15 h. (iii) for a, H<sub>2</sub>SO<sub>4</sub> 70%, 18 h; for b, H<sub>2</sub>, Pd/C, MeOH, HCl, 15 h. (iv) AgBF<sub>4</sub>, THF; Zn(BH<sub>4</sub>)<sub>2</sub>, -60 °C, 30 min. (v) R<sup>4</sup>MgX, ether, -60 °C, 20 h. (vi) AgBF<sub>4</sub>, THF; *n*-PrMgBr, 0 °C, 1 min.

#### Scheme III



synthons based upon the 1,4-dihydropyridine system. It was felt that such synthons should (i) be readily available, (ii) show nonequivalent reactivities at the 2- and 6-positions (providing control over four carbon centers), and (iii) be chiral.

The Robinson-Schopf type condensation of glutaraldehyde with amino alcohols in the presence of KCN appeared as a particularly attractive route to the type of synthon we were seeking.<sup>7</sup> Thus, the condensation of (+)-norephedrine (0.01-0.2 mol) with glutaraldehyde (1.7 equiv) in H<sub>2</sub>O at pH 3.0 (1 h) followed by the addition of KCN (1.4 equiv) (room temperature, 72 h) led in a "one-pot reaction" to the formation of a single chiral crystalline 2-cyano-6-oxazolopiperidine **3a** [ $\alpha_{\text{D}}^{20}$  -126.5° (CHCl<sub>3</sub>, *c* 2.3)] in 82% yield<sup>8</sup> (Scheme I). Similarly the reaction with (-)-phenylglycinol as the chiral component gave a single product **3b** [ $\alpha_{\text{D}}^{20}$  -278° (CHCl<sub>3</sub>, *c* 1.0)], in 50% yield.<sup>9</sup>

(7) Langdale-Smith, R. A. *J. Org. Chem.* **1971**, *36*, 226.

(8) The spectral data for all compounds were in accord with their proposed structures. Satisfactory microanalyses and/or high-resolution mass spectra were obtained for these products.

(9) The *trans*-H-2<sub>ax</sub>, H-6<sub>ax</sub> relative configuration was determined for both **3a** and **3b** from an analysis of their 400-MHz <sup>1</sup>H NMR spectra. The absolute configurations 2*S*,6*R* were assigned on the basis of NMR arguments and on the results of theoretical energy calculations (to be reported at a later date).