Fourth International Electronic Conference on Synthetic Organic Chemistry (ECSOC-4), www.mdpi.org/ecsoc-4.htm, September 1-30, 2000

[A0048]

X-Ray Structures of Bicyclic Organophosphates

Illustrating the Anomeric Effect

S. Furegati, A. Linden and P. Rüedi*

Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland
E-mail: sfuregati@hotmail.com , peru@oci.unizh.ch

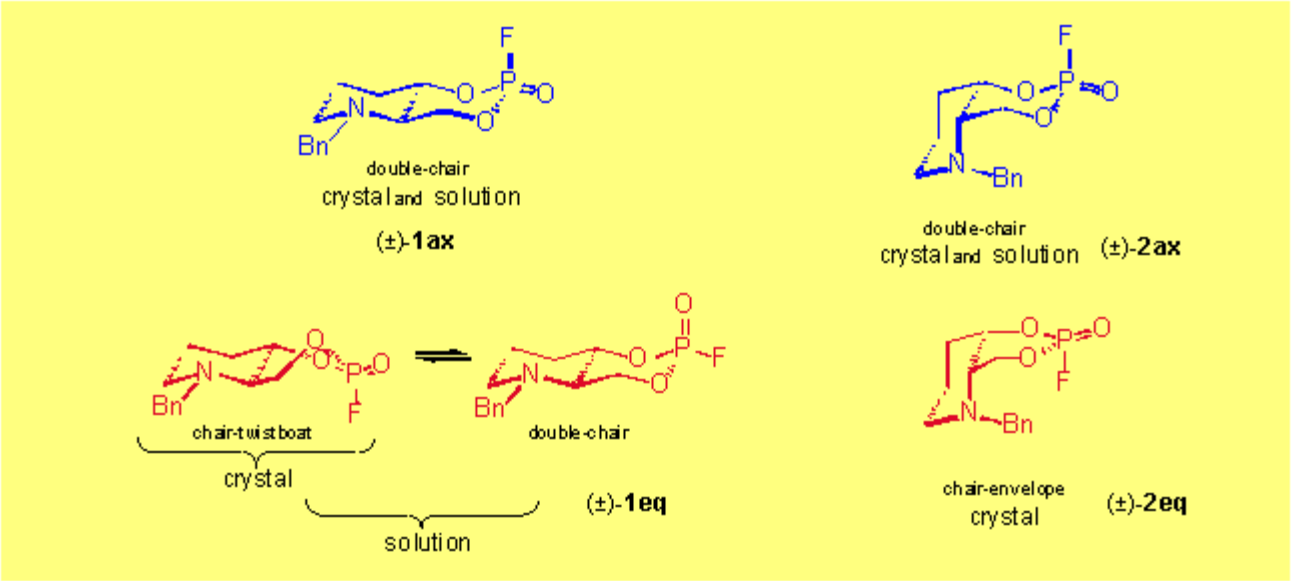
Received: 21 July 2000 / Uploaded: 30 July 2000

Introduction

The influence of the anomeric effect on bicyclic organophosphates could be shown for the first time by means of X-ray analysis.

In the course of our syntheses of bicyclic organophosphates as inhibitors of acetylcholinesterase we have been able to crystallize a series of four isomeric compounds: (±)-7-aza-7-benzyl-3-fluoro-2,4-dioxa-3l^5-phosphabicyclo[4.4.0]decan-3-ones (±)-**1ax**,**eq** and (±)-**2ax**,**eq**, *cis*- and *trans*-decaline-type congeners with the F-substituent in the *axial* and *equatorial* position.

The syntheses of the mentioned and of some related compounds as well as their inhibitory effects on acetylcholinesterase are described on a separate Poster A0047.



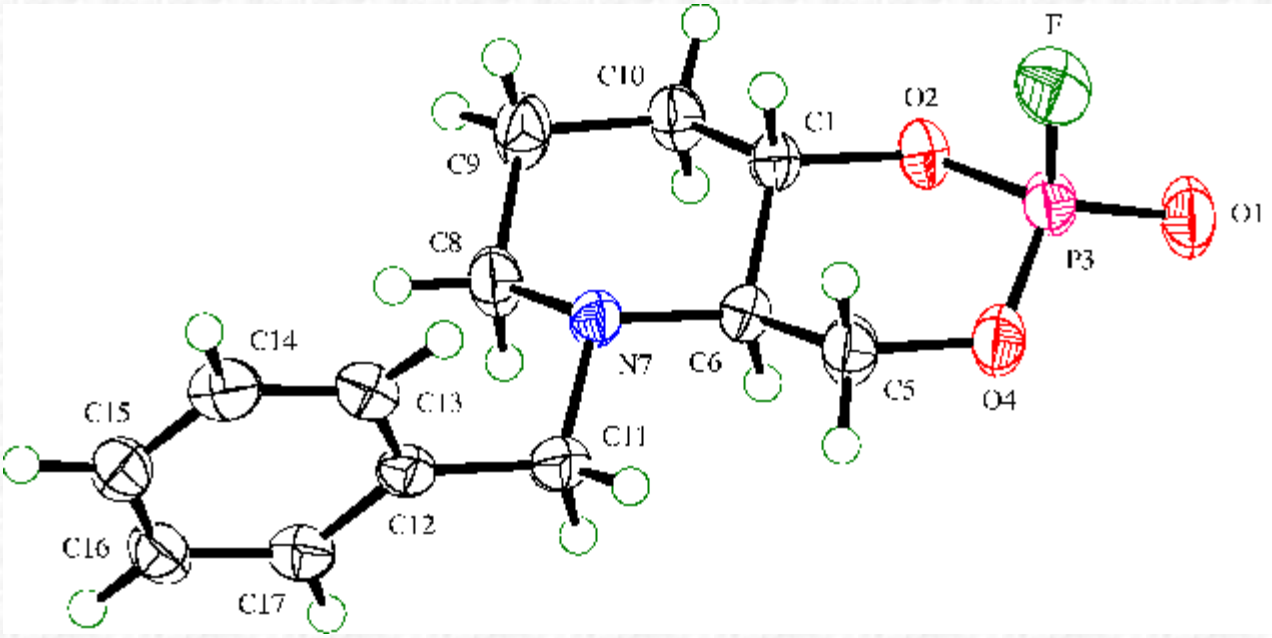
X-Ray Structures

(±)-**1ax**,**eq** and (±)-**2ax**,**eq** had been crystallized and submitted to X-ray analysis. As expected, both axially substituted

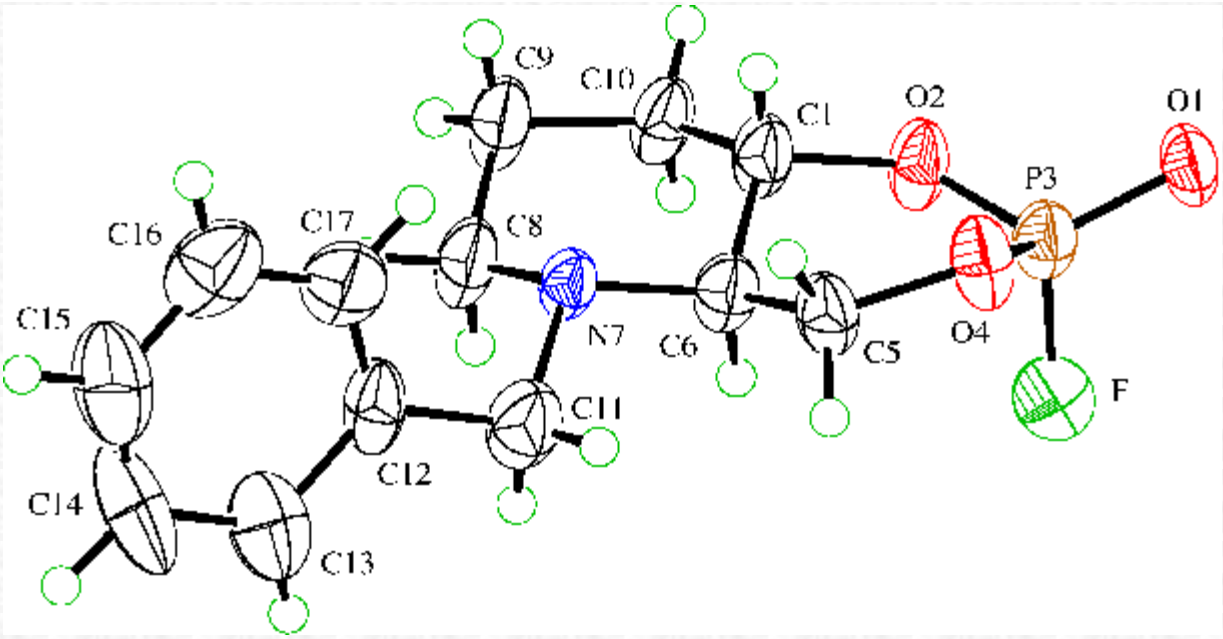
isomers adopt the sterically and stereoelectronically favoured double-chair conformation in the crystals (as well as in solution).

For the two equatorially substituted compounds the electronegative substituent (F) tends to occupy the sterically unfavoured *pseudo-axial* position according to the anomeric effect [1]. This results *e.g.* in a chair-twistboat conformation. Although we showed by means of NMR-spectroscopy that in solution (±)-**1eq** and (±)-**2eq** exist in a mixture of double-chair and chair-twistboat conformations ((±)-**1eq** in CD_2Cl_2: 33:67 at 293 K, 21:79 at 213 K) we obtained crystals of a chair-twistboat form ((±)-**1eq**) and a chair-envelope form ((±)-**2eq**) as they seem to have a slightly lower DG than the double-chair forms. The envelope conformation is highly surprising, it represents a middle position between the two possible twistboat conformations with five ring-atoms in plane, only C(6) laying outside.

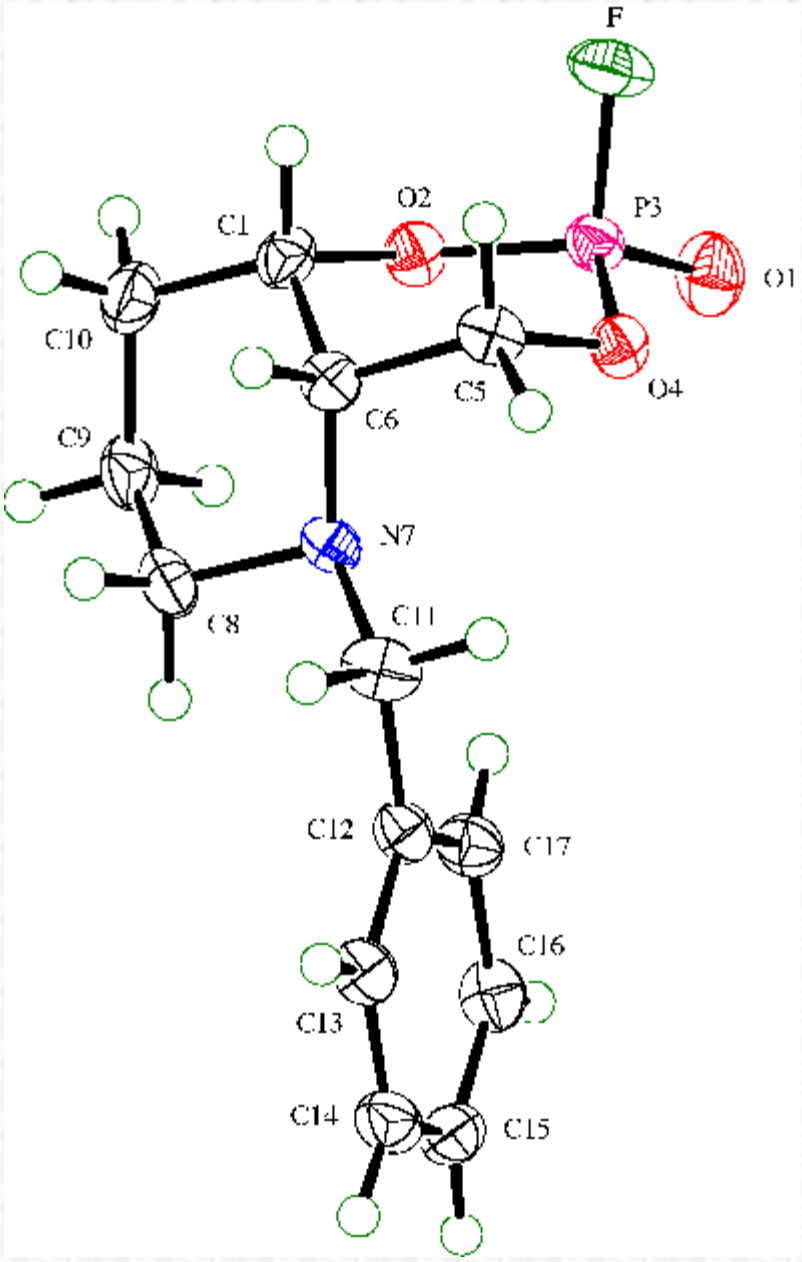
This is the first time the anomeric effect could be illustrated by X-ray analysis of such bicylic phosphates. Former attempts to crystallize related compounds lead to X-ray structures only with double-chair conformations, the electronegative substituent (*O*-phenyl, *O*-4-methoxyphenyl, $N(CH_2CH_2Cl)_2$, resp.) being located in the *axial* resp. *equatorial* position [2], see also poster. However, a 1,4-*bis*-*t*-butyl substituted monocylic organophosphate yielded an X-ray structure showing a boat conformation [3].



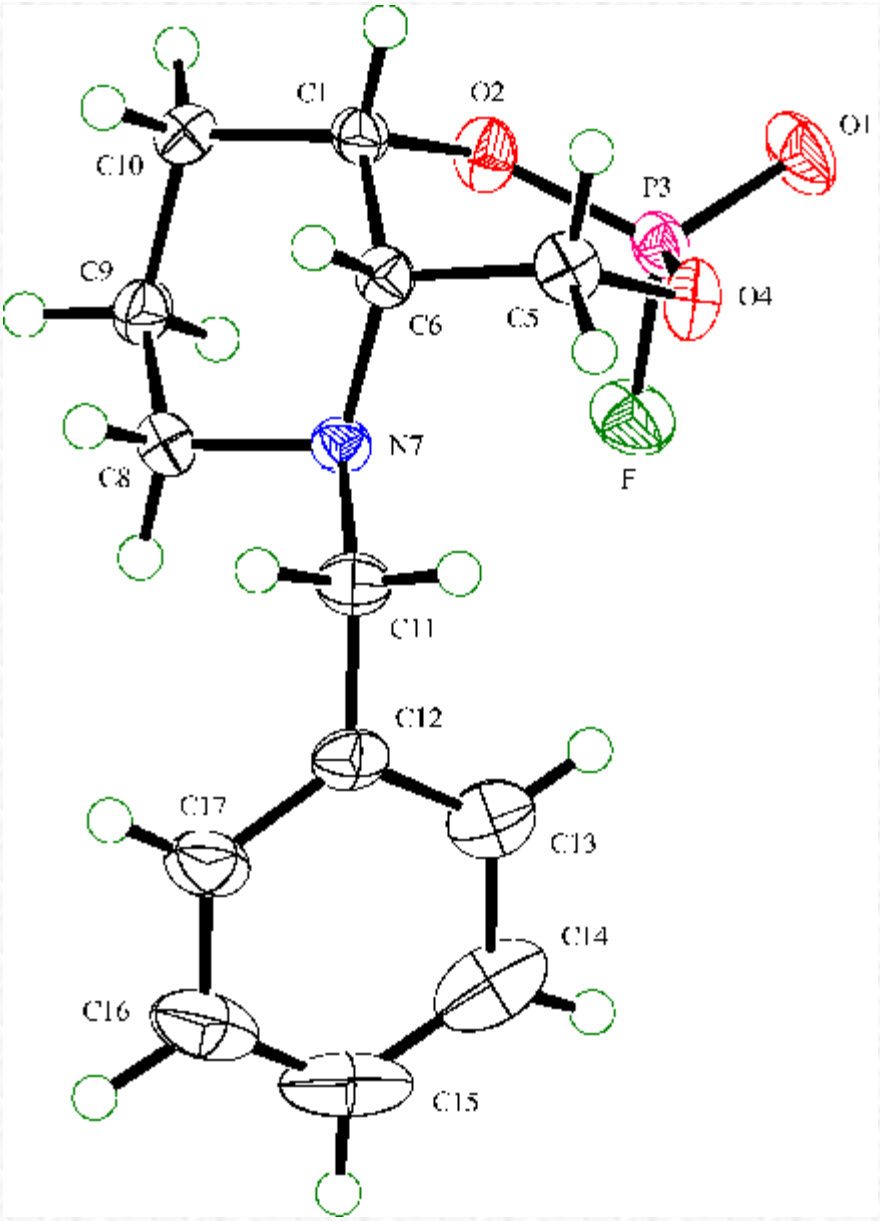
(±)-**1ax** (double-chair)



(±)-**1eq** (chair-twistboat)



(±)-**2ax** (double-chair)



(±)-**2eq** (chair-envelope)

Conformation analysis in solution ($CDCl_3$) was carried out by means of ^{31}P- and ^{1}H-NMR-spectroscopy using the $^{3}J_{PH}$-coupling constants. According to the *Karplus*-equation a torsion angle between P–O–C–H of 180° leads to a maximal $^{3}J_{PH}$ *ca.* 25 Hz, while a 90° angle corresponds with zero. The characteristic pattern of the three $^{3}J_{PH}$-coupling constants in each compound gives information about the conformations ocurring in solution [4].

References

[1] D.G. Gorenstein, R. Rowell, J. Findlay, *J. Am. Chem. Soc.* **1979**, *102*, 5077.

[2] R.O. Day, D.G. Gorenstein, R.R. Holmes, *Inorg. Chem.* **1983**, *22*, 2192; P. Van Nuffel, A.T.H. Lenstra, H.J. Geise, *Bull. Soc. Chim. Belg.* **1982**, *91*; J.-C. Yang, D.O. Shah, N.U.M. Rao, W.A. Freeman, G. Sosnovsky, D.G. Gorenstein, *Tetrahedron* **1988**, *44*, 6305.

[3] R.O. Day, W.G. Bentrude, K.C. Yee, W.N. Setzer, J.A. Deiters, R.R. Holmes, *J. Am. Chem. Soc.* **1984**, *106*, 103.

[4] S. Furegati, PhD Thesis, University of Zurich, in preparation.

All comments on this poster should be sent by e-mail to (mailto:ecsoc@listserv.ariz ona.edu) ecsoc@listserv.arizona.edu with **A0048** as the message subject of your e-mail.
