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CONFORMATION AND CONFIGURATION OF DIASTEREOMERIC PHOSPHINE OXIDES

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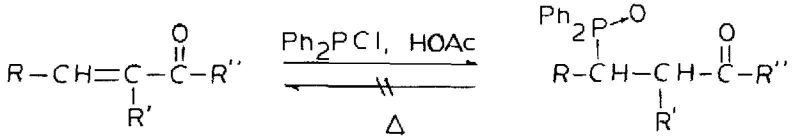
In 1921, Conant, et al. discovered a convenient synthesis of phosphine oxides (eq. 1).[1] This reaction permits the preparation of a variety of diastereomers, 2, which can be separated with extraordinary ease. Attempted proof of configuration of the diastereomers of this study by pyrolytic elimination to reform the alkenes was unsuccessful. Unlike sulfoxides,[2] selenoxides,[3] and amine oxides,[4] these phosphine oxides were resistant to the Ei reaction at temperatures[5] at which 1 would isomerize.



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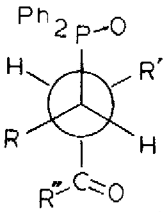
The ^1H and ^{13}C nmr data for the compounds of interest, 3-12, are listed in Table I. The recently postulated Karplus relationship[7] for ^{13}C-C-C-^{31}P was of paramount importance in proving configuration as $^3J_{HH}$ and $^3J_{PH}$ data were insufficient. Thus, the $^3J_{HH}$ values for 3-12 (~10 Hz) indicate a high degree of conformational purity, and a preference for trans vicinal hydrogens in either diastereomer. Some variation in $^3J_{PH}$ is noted (4-11 Hz), but these values fall within the range expected for gauche nuclei. These $^3J_{PH}$ are substantially less than the 40-50 Hz values expected for trans nuclei.[6] Thus, the $^3J_{HH}$ and $^3J_{PH}$ data for a given diastereomer do not distinguish between possibilities 13 and 14.

The literature data regarding the $^3J_{CP}$ values expected for trans and for gauche nuclei remain somewhat unclear. Cremer and Gray found a dependence of $^3J_{CP}$ on PO orientation in phosphetane oxides (e.g. 15).[7a] These and other compounds previously studied are strained and/or involve multiple paths for ^{13}C-C-C-^{31}P coupling. Wetzel and Kenyon interpreted the data on molecules such as 15 in terms of a "$^3J_{PC}$ per coupling path" of 6-14 Hz.[7b] The work of Wiseman and Krabbenhoft[7c] in bicyclic phosphine oxides as well as that of Wetzel and Kenyon suggest "single path $^3J_{CP}$" values of 3-4 Hz for gauche nuclei. The data of Quin, et al. for CO rather than CH_2 can be interpreted similarly.[7d] However, it remains unclear whether a double path for coupling results in ^3J values twice that for a single path, or whether a more complicated relationship pertains. Our work in molecules similar to 3-10 suggests rough values of 14 Hz for trans nuclei and 2 Hz for gauche nuclei, where the ^{13}C in question is part of CO.[8]



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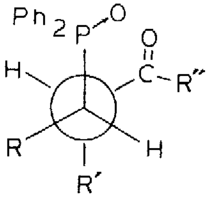

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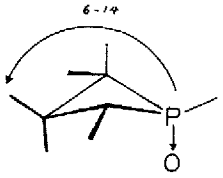

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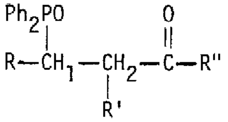
Compounds 4, 5, 8, 11, and 12 show $^3J_{PC}$ values of 13 Hz, indicative of trans nuclei. Thus, 4, 5, and 8 posses the erythro configuration 13. Compounds 3, 7, 9, and 10 show $^3J_{PC} \leq 2$ Hz, and these have the threo configuration 14. The counterparts of 9 and 10 of opposite configuration were not accessible, and their nmr data remain unknown.

In 7 and 8, the $^3J_{PC}$ values for methyl corroborate the above assignments. In 7, methyl is trans to ^{31}P, and a large $^3J_{PC}$ is observed (7.6 Hz). In 8, the $^3J_{PC}$ (≤ 1 Hz) is consistent with gauche nuclei. As with other couplings,[9] $^3J_{PC}$ appears to be smaller for sp^3 hybridized nuclei than for sp^2 nuclei. To the extent that conformation in the solid phase is relevant to that in solution,[10] the x-ray crystallographic data (next communication) indicate that P--C dihedral angles of 83° for CO and 153° for CH_3 pertain in the case of 7. If allowance is made for the fact that these skewed dihedral angles reduce ^3J compared to an idealized molecule having 60° for 180° angles, these data are reasonably close to the "single path" $^3J_{PC}$ values quoted above.

Compounds 11 and 12 prefer the conformer with CO trans to PO, rather than trans to Ph (11) or CH_3 (12). In 11, the different $^3J_{P-H}$ values are suggestive of different average dihedral angles involving H(2) and H(2') and P. One possible contributing conformer is shown as 11a in which the CO-Ph angle has widened to relieve repulsion.

Table I

^1H-^1H, ^{31}P--H, and ^{13}C--^{31}P Coupling Constants[a]

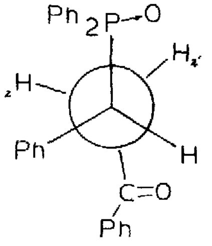


$$R-\overset{Ph_2PO}{\overset{|}{CH_1}}-\underset{R'}{\underset{|}{CH_2}}-\overset{O}{\overset{\|}{C}}-R''$$

cmpd	mp	R	R'	R"	$^3J_{H(1)-H(2)}$[e]	$^3J_{P-H(2)}$[e]	$^2J_{P-H(1)}$[d]	$^3J_{P-CO}$[f]
3	158°	Ph	Ph	CH_3	9.6	13.6	-9.0	2
4	276°	Ph	Ph	CH_3	11.5	6.5	-4.5	12.5
5	285°	Ph	Ph	Ph	11.2	6.7	-4.3	13
6	246°	Ph	Ph	Ph	9.6	12.6	-6.8	<1
7	190°	Ph	CH_3	Ph	8.5	11.2	-6.5	2
8	232°	Ph	CH_3	Ph	10.8	5.5	-4.8	13
9	196°	CH_3	Ph	Ph	9.5	12.6	-5.4	2
10	185°	Ph	Br	Ph	11.8	8.1	-7.8	~1
11	231°	Ph	H(2')	Ph	11.6	4.5	-7.1	13.5
					2.4[b]	11.5[b]		
12[c]	oil	CH_3	H	CH_3		8		14.9

a. As reproduced by LAOCON3 simulation, as appropriate.
b. Couplings to H(2').
c. CH_3 replaces H(1).
d. The sign is assumed to be negative.
e. Verified by heteronuclear decoupling in certain cases.
f. Error ± 1 Hz (solubility prevented a high sample concentration; considerable noise was present in the coupled spectra).

With regard to conformation, the feature of interest is the preference for conformers with trans hydrogens despite various permutations of the substituents on the ethanic skeleton. Similar conformational preferences (termed type II behavior) were evident on phenyl substituted ethanes having Br, SO, SO_2, COR, and COOH groups and lacking vicinal alkyl substituents. A postulate to explain type II behavior was proposed earlier,[11] involving contraction of the angle between large geminal substituents. Alternatively, the distinctive shape of phenyl may be involved. In order to obtain more accurate information, the crystallographic structure of a typical compound 7 was determined. The results are given in the next communication.



11a

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