Heteronuclear Spin-Spin Coupling Constants Between Directly Bonded Atoms as a Probe of Configuration at Phosphorus Atom Involved in Diastereoisomeric 4-Methyl-1,3,2-dioxaphosphorinans

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Dioxaphosphorinans, conformation, J_{PH}, J_{PSe}

The J_{PH} and J_{PSe} absolute values showed a clear dependence on the orientation of the substituents at 2-P in several pairs of substituted diastereoisomeric 2-X-2-Y-1,3,2-dioxaphosphorinans (X = H, Se; Y = O, S, OR) and may therefore provide information about conformation and configuration at phosphorus atom.

Although several 2-X-2-Y-1,3,2-dioxaphosphorinans have been studied by NMR and IR spectroscopy and a limited number of several solid-state 1,3,2-dioxaphosphorinans were analysed by the X-ray technique, the preferred stereochemical disposition of phosphorus substituents in 2-X-2-Y-1,3,2-dioxaphosphorinans is still not known with certainty and in several instances it is not possible to assign unambiguously the phosphorus stereochemistries of the conformers.

Now we report the evidence that for diastereoisomeric pairs 1-10 where in form A (see Table)

\[
\begin{align*}
X &= \text{O}, \text{S}, \text{Se}; & Y &= \text{H} \\
X &= \text{O}; & Y &= \text{SeAlk} \\
X &= \text{OAlk}; & Y &= \text{Se} \\
\text{and in form B} & \\
X &= \text{H}; & Y &= \text{O, S, Se} \\
X &= \text{SeAlk}; & Y &= \text{O} \\
X &= \text{Se}; & Y &= \text{OAlk}
\end{align*}
\]

the determination of stereochemistry at P atom is possible on the basis of measurements of spin-spin coupling constants between directly bonded phosphorus and hydrogen or selenium nuclei respectively. For six pairs of diastereoisomeric 4-methyl-1,3,2-dioxaphosphorinans, the conformation of which is firmly established ([3], [24], [4, 6, 7, 9]) it has been noted that absolute values of J_{PH} or J_{PSe} are higher when hydrogen or selenium nucleus occupies the equatorial position. All the available data are collected in Table I.

Inspection of the Table reveals that the chemical shift difference can not be used for prediction of cis-trans geometry. Spin-spin coupling constants, however, are regularly higher when magnetically active nuclei bonded to phosphorus are in the equatorial position. This suggested to us that diastereoisomeric pairs of compounds 3, 5, 8, and 10 follow this pattern, and those, with higher absolute values of J have equatorially oriented hydrogen or selenium substituents attached to phosphorus atom.

Although IR spectroscopy demonstrates the very well known dependence of stretching frequency of exocyclic substituent on its axial-equatorial relationship, to our knowledge such general observation of the differences of J between cis and trans isomers has been reported only recently for phosphetanes and phospholenes with respect to 31P-1H spin-spin couplings. However, our observation does not allow us to predict the configuration around phosphorus in compounds 11, 12, 13, and 14. Undoubtedly in acid 13 the selenono-
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<th>R⁵</th>
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a) NMR data presented in this paper were obtained on a Jeol C-60H instrument operating at 24.3 MHz observing frequency on samples in 8 mm glass-tubes and are listed in ppm relative to 85% H₃PO₄ contained in a concentric capillary in a nmr tube. Heteronuclear Spin Decoupler JNX-SD-HC was used for δP and J₁₈O determinations. A positive shift is taken to occur at an applied magnetic field greater than that of the standard. Standard deviation ± 6 Hz.

b) Ar = p-N0₂C₆H₄-CH₂-

c) Corresponds to J₃P₂

d) The conformation of 7A and B has been determined by M. MIKOŁAJCZYK. Both A and B have equatorial 5methyl group. Additional proof was obtained from the lanthanide-d induced PMR shift of R₁ and R₃ protons. In isomer 7A they showed a greater downfield shift than in 7B when Eu(fod), was added to samples A and B in CDCl₃ solution, which suggests that the oxygen atom of the phosphorvl group occupies the axial position in A and the equatorial one in B.

e) Both 8A and B were obtained by alkylation of corresponding tetramethylammonium salts of cis- and trans-selenocaineids with p-nitrobenzylbromide. A m.p. 75 °C; B m.p. 81 °C; correct elemental analysis.

f) Transesterification of trimethyl phosphate with 2-methyl-2,4-pentadiol gave 2-methoxy-4,4,6-trimethyl-1,3,2-dioxaphosphorinan, b.p. 50–53 °C/5 mmHg, δ31P = 1.4435, δδ31P = –2.75 ppm (13°C) and –1.75 ppm (87°C) (PhO)₃P as external standard). Addition of elemental selenium in benzene solution gave a semi-solid product, δ31P = –64.0 ppm (78°C) and –62.5 ppm (22°C) (H₃PO₄). After crystallization from ether-petrol ether m.p. 62–63 °C (93°C/7°C).

g) 11 was obtained by addition of selenium to 2-methoxy-1,3,2-dioxaphosphorinan. Attempts of distillation caused P phosphorus rearrangement.

h) 12 was prepared by addition of selenium to 2-methoxy-5,5-dimethyl-1,3,2-dioxaphosphorinan, m.p. 91–92 °C (petrol ether 60–80 °C). Correct elemental analysis.

i) Addition of selenium to 2-hydroxy-5,5-dimethyl-1,3,2-dioxaphosphorinan in the presence of NEt₃ gave triethylammonium salt of 13. Free acid 13 was obtained by acidification of triethylammonium salt.

j) Obtained by methylation of triethylammonium salt of acid 13 with CH₃I, m.p. 90.5–91.5 °C (petrol ether 60–80 °C). Correct elemental analysis.
form dominates in its tautomeric selenolo-selenono equilibrium. It has to be mentioned that in five-membered ring-systems (compounds 16 and 17) the differences between \( \delta J \) in both diastereoisomers are negligible. Explanation of the observed facts is of great interest. First, depending on axial or equatorial orientation of substituents on phosphorus atom the different overlapping of phosphorus orbitals and lone electron pairs on the ring oxygen atoms can cause the observed differences \( \Delta J \). In phosphetanes, as well as in phospholenes and their oxides, \( \Delta J \) were observed, however this type of effect does not exist in these systems. Only recently it has been fully appreciated that attractive nonbonded interactions can have an important influence on conformational preference around several heteroatoms.

For phosphonates 1 and 2 two models of attractive intramolecular interactions can be considered: 1. Hydrogen-bond like interactions between 4,6-diaxial hydrogens and axial phosphoryl oxygen atom or 2. Hydrogen-hydrogen non-bonded attractions between 4,6-diaxial hydrogens and P-hydrogen. If 1 were operative, owing to change of s-character of equatorial P-H bond an increase of its absolute value would be explainable. But in such case compound 4 would possess only a very small difference \( \Delta \delta J \) with respect to low ability of thio-phosphoryl sulphur atom involved in hydrogen bonding.

Since 100 \( \Delta J / \Delta \) min for phosphonothio- and selenoates 4 and 6 are of the same order as that of 1 and 2, through-space attractive interactions between axial 4,6-hydrogens and P-axial hydrogen are more probable. A similar explanation seems to be applicable to diastereoisomeric pairs of compounds (7-10). It should be remembered that lengthening of bonds (1 \( \delta P = 989 \text{ Hz} \) and 2 \( \delta P = 989 \text{ Hz} \) may make the above interactions even more attractive by further descent into the Morse-like potential well, or less attractive if the optimal distance has already been reached. Compounds 3, 5 and 10 support the presented idea about attractive interactions between axial P-X (X = H,Se,SeAlk) and 4,6-hydrogens. The introduction of methyl group into 4-axial position in the place of the hydrogen atom caused the dramatic decrease of differences between axial and equatorial \( \delta J \), expressed by 100 \( \Delta J / \Delta \) min. The lack of the considered differences in dioxaphospholanes 16 and 17, where steric interactions seem to be less pronounced, also supports the presented explanation.

Attractive interactions between axial substituents X on phosphorus atom and 4,6-hydrogens may cause a change in P-X bond order in this different kind of bonding situation and, as a result, in O-P-X angles and P-X bond length, and consequently they may influence \( \delta J \) and \( \delta J \) values. It has been demonstrated that bond-lengths strongly influence coupling constants. Electron diffraction measurements on methyltetrafluorophosphorane together with \( ^{19} \text{F NMR} \) have shown that to apical P-F bond (\( l = 1.577 \text{ A} \)) corresponds \( \delta J_{PF} = 772 \text{ Hz} \) and to equatorial one (\( l = 1.534 \text{ A} \)) \( \delta J_{PF} = 960 \text{ Hz} \). The synthesis of both solid diastereoisomers made it possible for us to determine their structures by the X-ray method.

Undoubtedly, the differences in bond lengths and/or bond angles between both diastereoisomers can be close to the experimental error. Moreover, the X-ray method gives no information on the intermolecular interactions in these compounds in solution.

The sign of \( \delta J \) requires special attention. It is known that \( \delta J_{PF} \) is positive and \( \delta J_{PC} \) is negative. So the trend of enhancement of \( | \delta J_{PF} | \) and \( | \delta J_{PC} | \) for equatorially oriented hydrogen and selenium is independent of the sign of \( \delta J \). An interpretation of observed facts entirely in terms of syn-axial inter-
actions is a considerable oversimplification of a complicated situation. Although these interactions may be dominant, other H-H and C-H interactions as well as angle deformations certainly contribute to the final conformational result.

Further work on explanation of the reported facts as well as investigation of $^1$J$\text{PF}$ and $^1$J$\text{P}$-$^1$C are in progress.

Author thanks to Professor J. Michalski for his interest in this work and Professor E. Fluck for reading the manuscript and stimulating comment.

6b. M. Mikolajczyk, private information.
7. Both 9A and B were obtained by addition of selenium to trans- and cis-2-methoxy-4-methyl-1,3,2-dioxaphosphorinans. It is supposed that stereochemistry of this process is the same as that of addition of sulphur, C. L. Bodkin and P. Simpson, J. chem. Soc. [London], Ser. B, 1971, 1136.
23. Obtained by addition of selenium to 2-methoxy-1,3,2-dioxaphospholane, m. p. 62–63 °C.
24. Condensation of 2-chloro-4-methyl-1,3,2-dioxaphospholane with MeOH in the presence of NEt₃ gave the diastereomeric mixture of 2-methoxy-4-methyl-1,3,2-dioxaphospholanes (41:59). After addition of selenium 16 was obtained as a higboiling liquid characterized by $^{31}$P NMR and elemental analysis.