Tetrahedron Letters,Vol.27,No.16,pp 1755-1756,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

THE SIMPLE CONVERSION OF A PHOSPHOROCHLORIDATE INTO ONE OF OPPOSITE CONFIGURATION

Alagappan Thenappan and William S. Wadsworth, Jr.*

Department of Chemistry, South Dakota State University, Brookings, S.D. 57007

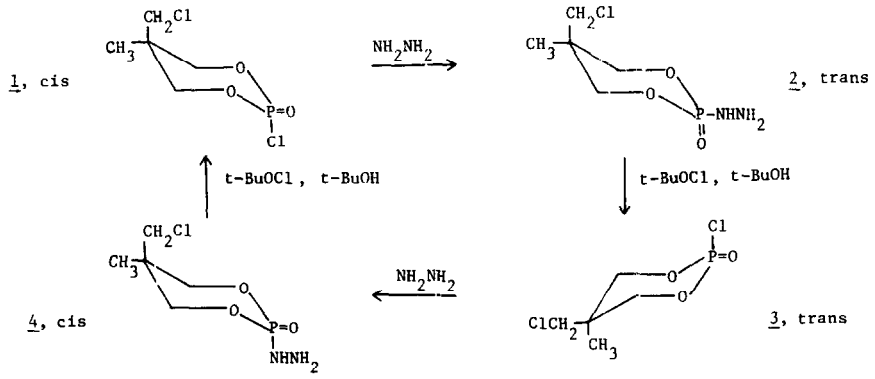
Abstract: Conversion of a phosphorochloridate with known configuration at phosphorus to a hydrazide followed by oxidation by means of t-butyl hypochlorite gives the phosphorochloridate of opposite configuration.

Addition of cis-2-chloro-5-chloromethyl-5-methyl-2-oxo-1,3,2- dioxaphosphorinan, 1, to an equivalent of hydrazine dissolved in acetonitrile gives, after filtration and solvent removal, a N-phosphorylhydrazide, 2. The inversion process is not unlike that found upon treatment of the same phosphorochloridate with other primary and also secondary amines.[1] As reported in previous articles, the 2-substituent in cyclic phosphoramidates normally assume an equatorial position.[1,2,3] As a consequence of conformational immobility, the stereochemistry of substitution can be easily determined by ^{1}H NMR analysis.[1,4] The chemical shift of the hydrogens of the 5-chloromethyl group is downfield when the group is fixed in an axial position compared to their chemical shift when the group is equatorial. The same is true for the chemical shift of the hydrogens of the 5-methyl group. For the hydrazide, 2, the chemical shifts of the hydrogens in these groups are typical of an axial chloromethyl group, 1.00 ppm, and equatorial methyl group, 3.90 ppm, measured from tetramethylsilane as an internal standard, and are similar to those observed for the starting phosphorochloridate, 1.10 ppm and 3.90 ppm.[1] For the latter, as is the case for esters, the ring conformation is fixed by the strong preference for the phosphoryl oxygen to be equatorial.[5]

With t-butyl alcohol as solvent, addition of two equivalents of t-butyl hypochlorite dropwise to a solution containing one equivalent of the hydrazide, 2, (mp 156°) gives an immediate evolution of nitrogen, one equivalent. After removal of solvent and the by-products, t-butyl chloride and water (the presence of both was confirmed by gas chromatography) under reduced pressure, there is obtained a liquid product whose ^{1}H NMR spectrum shows the presence of one product, the trans phosphorochloridate, 3, 5-CH_3 axial, 1.40 ppm (3H) and 5-$ClCH_2$ equatorial, 3.46 ppm (2H). The product was further identified by conversion with piperidine via inversion to the known cis-2-piperidino-5-chloromethyl-5-methyl-2-oxo-1,3,2-dioxaphosphorinan obtained by a different route.[1] The conversion of the hydrazide to the chloridate via retention is not unlike the reported conversion of 2-phenylamino-4-methyl-2-

oxo-1,3,2-dioxaphosphorinan to the 2-hydroxy derivative, also by retention.[6]

Additional evidence for the retention process was obtained by completing the cycle. Under conditions identical for those described for the preparation of 2, the phosphorochloridate, 3, was added to hydrazine to give the cis hydrazide, 4. The latter, (mp 177-8°), ^{1}H NMR: 5-CH_3 equatorial, 0.91 ppm (3H) and 5-$ClCH_2$ axial, 3.77 ppm (2H), apparently has its 2-substituent axial instead of equatorial, an unusual but not unknown phenomenon.[5] That it does have the assigned configuration is proved by its conversion to the original phosphorochloridate, 1, which in order to complete the cycle and conform to the conversion of 2 to 3 must be a retention process. That the starting cis phosphorochloridate is obtained exclusively was proved by comparison of the spectrum of the product with an authentic sample, with which it is identical, and its conversion, by inversion, into the known trans phosphoramidate upon treatment with piperidine.[1]



The phosphorochloridates are, like all acid chlorides, reactive species. They can, under controlled conditions, be converted into esters and amides of known configuration. Thus, the simple scheme described herein for the conversion of one reactive isomer into another of opposite configuration should prove useful.

References and Notes

1. Wadsworth, W.S., Jr., Larsen, S., Horton, H.L., J. Org. Chem. 1973, 38, 256.
2. Wadsworth, W.S., Jr., J. Org. Chem., 1973, 38, 2921.
3. W.J. Stec, A. Okruszek, J. Chem. Soc., Perkin I, 1975, 1828 and references cited therein.
4. Wadsworth, W.G., Wadsworth, W.S., Jr., J. Am. Chem. Soc., 1983, 105, 1631.
5. R.R. Holmes, R.O Day, W.N. Setzer, A.E. Sopehik, W.G. Bentrude, J. Am. Chem. Soc., 1984, 106, 2353 and references cited therein.
6. P. Gugz, A. Wilk, W.J. Stec, Tetrahedron Lett., 1985, 3279.

Acknowledgement: Acknowledgement is made to the donors of The Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(Received in USA 29 October 1985)