Conversion of Diarylphosphine Oxides to Phosphinous Chlorides with Phosphorus Trichloride[1]

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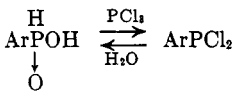
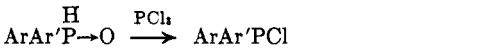
Treatment of diarylphosphine oxides with excess phosphorus trichloride at room temperature effects their conversion to diarylphosphinous chlorides. Three examples are reported with yields in the 60–80% range. The reaction is of interest as an example of the rare change from tetra- to tricovalent phosphorus; it also has practical value in the synthesis of certain symmetrical diarylphosphinous chlorides.

It has been reported,[3] and we have now confirmed, that arylphosphinic acids may be easily converted to arylphosphonous dichlorides by phosphorus trichloride. Since the dichlorides are readily hydrolyzed to the phosphinic acids, these changes represent an interconversion of tri- and tetracovalent phosphorus.



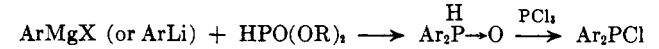
This behavior is not common for phosphorus, which exhibits a pronounced preference for tetracovalency. Attempts to prepare a phosphinous chloride in an analogous reaction from a secondary phosphine oxide [bis(2,3,5,6-tetramethylphenyl)phosphine oxide] were unsuccessful, but the possibility remains that a less highly substituted oxide might respond.[3] Because of our interest in the chemistry of diarylphosphinous chlorides[4-6] and diarylphosphine oxides,[4] we reinvestigated this reaction, particularly since it held promise of providing a new route to the reactive phosphinous chlorides. We have indeed found that certain



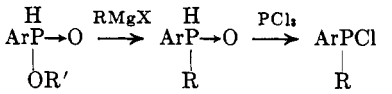
Ia, Ar = Ar′ = C_6H_5
b, Ar = C_6H_5; Ar′ = *p*-ClC_6H_4
c, Ar = Ar′ = *p*-$CH_3C_6H_4$

diarylphosphine oxides may be converted to phosphinous chlorides by phosphorus trichloride. Three chlorides (Ia, b, and c) have been prepared by this reaction; yields were 59, 80, and 71%, respectively. Conditions similar to those developed by Frank[3] for the phosphonous dichloride synthesis were effective. This involved treating the oxide with a tenfold excess of phosphorus trichloride at room temperature for several hours. After decantation from gummy solids, the liquid is freed of phosphorus trichloride by distillation. The product may be obtained directly by continued distillation, or by extracting it with cyclohexane from residual solids, followed by distillation of the extract.

This new reaction of diarylphosphine oxides is of particular synthetic value when coupled with the preparation of the requisite oxides from organometallic reagents.[7,8] Thus, a two-step synthesis of symmetrical diarylphosphinous chlorides, using a commercially available phosphorus compound as starting material, may be visualized. The reaction may also find use in

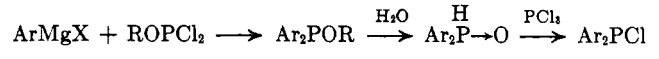


the synthesis of the difficultly accessible alkylarylphosphinous chlorides. The requisite mixed secondary



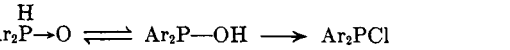
phosphine oxides are not presently known, but might be attainable from monoalkyl arylphosphinates as shown. Dialkylphosphine oxides[9] may also respond to the reaction, making dialkylphosphinous chlorides more readily available.

Another application is seen in the following sequence.



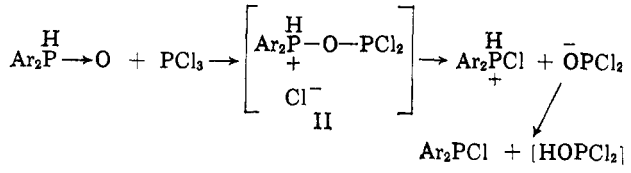
These reactions were used in the present work to prepare bis(*p*-tolyl)phosphinous chloride, using methyl phosphorodichloridite as starting material. Sander,[10] who first described the arylation of dichloridites, commented that tri- rather than disubstitution predominated with the alkyl esters and that an aryl ester was required for satisfactory control at disubstitution. However, in the single case studied, we observed diarylation of methyl phosphorodichloridite to be practical. In agreement with Sander, we found a distinct preference for the Grignard chloride rather than the bromide in this reaction. Sander isolated several phosphinites by direct distillation of the Grignard reaction mixtures, and was able to convert them directly to the phosphinous chlorides with phosphorus trichloride. We experienced difficulty with the distillation of this complex reaction mixture, and preferred to hydrolyze the ester to the solid isolable oxide. The phosphinous chloride synthesis was then completed with the phosphorus trichloride reaction on the oxide.

Except for the present case, all known reactions of secondary phosphine oxides proceed with preservation of tetracovalency of phosphorus. On encountering the formation of a tricovalent product, one is tempted to believe that a tautomeric shift to the phosphinous acid form is indicated as a preliminary step. This may

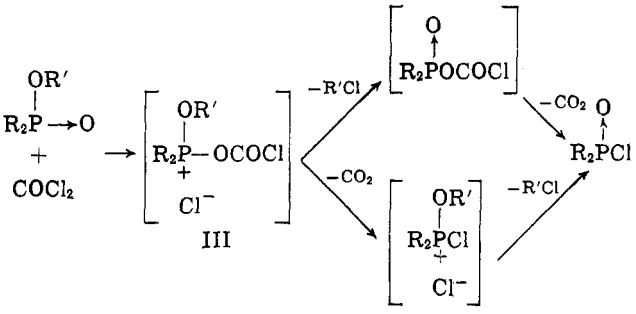


(1) Supported by Research Grant CA-05507-3 from the National Cancer Institute, U .S. Public Health Service.
(2) To whom inquiries may be addressed.
(3) A. Frank, *J. Org. Chem.*, **26**, 850 (1961).
(4) L. D. Quin and R. E. Montgomery, *ibid.*, **28**, 3315 (1963).
(5) L. D. Quin and H. G. Anderson, *J. Am. Chem. Soc.*, **86**, 2090 (1964).
(6) L. D. Quin and H. G. Anderson, *J. Org. Chem.*, **29**, 1859 (1964).
(7) B. B. Hunt and B. C. Saunders, *J. Chem. Soc.*, 2413 (1957).
(8) J. L. Willans, *Chem. Ind.* (London), 235 (1957).
(9) First prepared by R. H. Williams and L. A. Hamilton [*J. Am. Chem. Soc.*, **74**, 5418 (1952)] by the Grignard method. Newer methods are reviewed by K. Sasse in "Methoden der organischen Chemie," Vol. XII, Part 1, E. Muller, Ed., 4th Ed., Georg Thieme Verlag, Stuttgart, 1963, p. 193.
(10) M. Sander, *Ber.*, **93**, 1220 (1960).

indeed be the case. However, another mechanism may be advanced which adequately explains the formation of a tricovalent derivative. This mechanism depends on nucleophilicity of the phosphoryl group of the secondary oxide, and involves displacement of chloride from phosphorus trichloride to give intermediate II. This intermediate may be visualized as producing the phosphinous chloride by a process involving chloride ion attack on the original oxide phosphorus, and then proton loss. The inorganic product

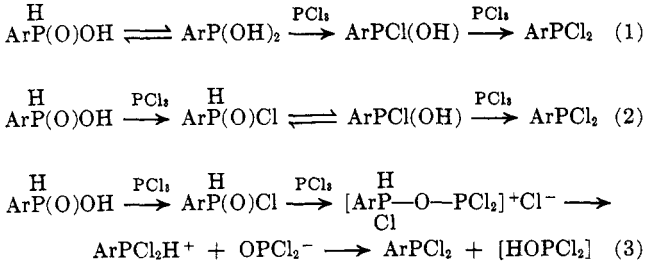


is represented as $HOPCl_2$ in the absence of any knowledge of its structure. Nucleophilicity in the phosphoryl group in other organophosphorus compounds is currently receiving due attention in the establishment of reaction mechanisms. A recent example, which is not unrelated to the proposal above, is seen in the phosphinate–phosgene reaction described by Green and Hudson.[11] It is felt, therefore, that the oxide–



phosphinous chloride conversion should not be construed at this time as providing proof that the oxides are involved in a tautomeric equilibrium. Further experimental work is required to establish the mechanism of this reaction.

The same reasoning is applicable to the phosphinic acid–phosphonous dichloride conversion. The course of this reaction may be visualized in three ways.



Frank,[3] who suggested path 1, proposed that the reaction provided evidence for tautomerism between the phosphinic and phosphonous acid forms. Path 2 is an alternative pointed out by Quin and Dysart[12] primarily to show that the reaction did not *necessarily* depend on the preliminary tautomeric shift from the phosphinic to the phosphonous acid form. Path 3 is now presented as yet another possibility, in which nucleophilicity of the phosphoryl group is involved and no tautomeric shift is required. No experimental evidence is available at present to discriminate between these possible reaction paths.[13]

(11) M. Green and R. F. Hudson, *J. Chem. Soc.*, 1004 (1963).
(12) L. D. Quin and M. R. Dysart, *J. Org. Chem.*, **27**, 1012 (1962).

Experimental

General.—Melting points were obtained with a Mel-Temp apparatus and are corrected; boiling points are uncorrected. Infrared spectra were obtained with a Perkin-Elmer Model 137 spectrophotometer. Diphenylphosphine oxide and (*p*-chlorophenyl)phenylphosphine oxide were prepared as described previously.[4] Methyl phosphorodichloridite was prepared by the method of Martin and Pizzolato.[14] Reactions were conducted in a nitrogen atmosphere. Analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Phenylphosphonous Dichloride from Phenylphosphinic Acid.[3]—To 62 ml. of phosphorus trichloride was added in small portions 10.0 g. (0.0704 mole) of phenylphosphinic acid. A heavy oil separated, and after 1 hr. the liquid was decanted and distilled. There was obtained 11.2 g. (89%) of phenylphosphonous dichloride, b.p. 46–47° (0.7 mm.).

Diphenylphosphinous Chloride from Diphenylphosphine Oxide.—A mixture of 3.2 g. (0.016 mole) of diphenylphosphine oxide and 15 ml. of phosphorus trichloride was stirred for 1 hr. The liquid was decanted and then distilled. Diphenylphosphinous chloride (2.2 g., 59%) was collected at 117–119° (0.8 mm.). It was identified by hydrolysis[4] to diphenylphosphine oxide.

(*p*-Chlorophenyl)phenylphosphinous Chloride.—Phosphorus trichloride (18 ml.) and (*p*-chlorophenyl)phenylphosphine oxide (4.8 g., 0.020 mole) were stirred for 2 hr. The mixture was distilled directly, giving 4.0 g. (80%) of the phosphinous chloride boiling at 140–145° (0.95–1.0 mm.), in agreement with a reported value of 134–136° (0.77–0.81 mm.).[4] It formed (*p*-chlorophenyl)phenylphosphine oxide on hydrolysis.[4]

Preparation of Bis(*p*-tolyl)phosphine Oxide.—*p*-Tolylmagnesium chloride was prepared in 125 ml. of tetrahydrofuran from 36.0 g. (0.284 mole) of *p*-chlorotoluene and 12 g. (0.50 g.-atom) of magnesium. The chilled suspension was treated slowly with 30.0 g. (0.226 mole) of methyl phosphorodichloridite. The mixture was then brought to reflux; after 0.5 hr. the mixture had so thickened as to require dilution with 300 ml. of ether. Reflux was continued for 2 hr., and then, with cooling, the mixture was treated with 200 ml. of 6 *N* hydrochloric acid to hydrolyze the phosphinite. Extraction with ether removed 4.5 g. of solid, 1 g. of which was soluble in pentane and was identified as *p,p'*-bitolyl, m.p. 119–121°. The remainder was crude diarylphosphine oxide. Extraction of the hydrolysate next with benzene removed an oil which was induced by mixing with ether to give 11.5 g. of solid bis(*p*-tolyl)phosphine oxide, m.p. 94–96°. The ether filtrate was evaporated to leave an oil, which after washing with pentane weighed 9.7 g. This oil did not crystallize, but its infrared spectrum was identical with that of the solid bis(*p*-tolyl)-phosphine oxide. The pentane washings contained 2.8 g. of an oil which was chromatographed on alumina. Elution with pentane removed 1.7 g. of crude tris(*p*-tolyl)phosphine; elution with ether–pentane removed an additional 0.5 g. of the secondary phosphine oxide. The total yield of crude bis(*p*-tolyl)phosphine oxide was 25.2 g. (49%).

The tris(*p*-tolyl)phosphine, recrystallized from aqueous ethanol, had m.p. 147–148.5° (lit.[15] m.p. 146°). It formed an ethiodide, m.p. 190–192° (lit.[15] m.p. 185°).

Bis(*p*-tolyl)phosphinous Chloride.—A mixture of 4.05 g. (0.0176 mole) of bis(*p*-tolyl)phosphine oxide and 16 ml. of phosphorus trichloride was stirred for 2 hr. and then filtered and dis-

(13) G. P. Sollott and E. Howard, Jr. [*ibid.*, **29**, 2451 (1964)] claim that since ferrocenylphosphinic acid undergoes Frank's reaction a preference for path 1 over path 2 is at hand. Their observation (qualitative only) seems to have no real mechanistic significance. The argument that the strong electron-releasing effect of ferrocenyl should retard a path such as 2 but still permit a path such as 1 seems to overlook the fact that *both* mechanisms involve the same basic operations on phosphorus, and differ only in sequence. Thus, if electron release is assumed to be capable of retarding the tautomeric shift in 2, therefore retarding the over-all reaction, it should for the same reason retard path 1. That electron release fails to retard the reaction (if substantiated quantitatively) might suggest a lack of involvement of tautomerism.
(14) D. R. Martin and P. J. Pizzolato, *J. Am. Chem. Soc.*, **72**, 4584 (1950).
(15) A. Michaelis, *Ann.*, **315**, 43 (1901).

tilled. There was obtained 3.12 g. (71.4%) of bis(*p*-tolyl)phosphinous chloride boiling at 125–128° (0.21 mm.). This value agrees on extrapolation with a previously reported[15] boiling point (345–350°).

Hydrolysis of Bis(*p*-tolyl)phosphinous Chloride.—A sample of bis(*p*-tolyl)phosphine oxide was obtained for analysis by hydrolyzing the phosphinous chloride prepared above. To 25 ml. of water was slowly added 2.66 g. (0.0107 mole) of bis(*p*-tolyl)phosphinous chloride. After stirring for 2 hr., the mixture was extracted with benzene. The benzene extract was washed with 5% sodium bicarbonate and then water, dried over magnesium sulfate, and evaporated to leave 2.30 g. (94%) of bis(*p*-tolyl)phosphine oxide, m.p. 98.5–100.5°.

Anal. Calcd. for $C_{14}H_{15}OP$: P, 13.45. Found: P, 13.41.

The infrared spectrum possessed PH (2340 cm.$^{-1}$), and P(O) (1180 cm.$^{-1}$) stretching bands.

Studies on the Tetrazole–Azidoazomethine–Tetrazole Equilibrium. III. 2-Azidopyrimidines[1]

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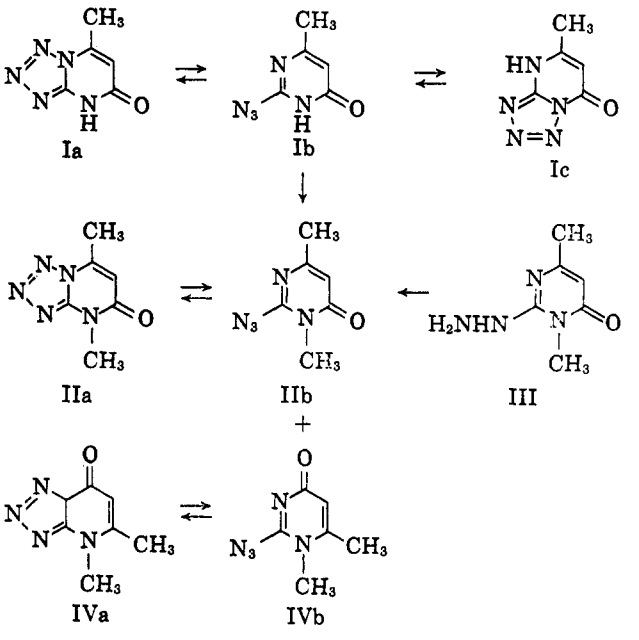
The rate of tautomerization as a function of temperature of 7-methyltetrazolo[1,5-*a*]pyrimidin-5(4H)-one (Ia) to 5-methyltetrazolo[1,5-*a*]pyrimidin-7(4H)-one (Ic) through 2-azido-4-methylpyrimidin-6(1H)-one (Ib) has been determined from data derived from infrared and proton magnetic resonance spectrometry. Activation parameters indicate that the rate-determining step is opening of the tetrazole ring of Ia to give the 2-azidopyrimidine intermediate Ib. The structure of I in the solid state is determined by the solvent from which it is isolated.

The azidoazomethine–tetrazole equilibrium[2] and the related isomerization of substituted 5-aminotetrazoles[3a] at elevated temperatures has been demonstrated. The existence of an equilibrium at room temperature between a bicyclic tetrazole and a tautomeric bicyclic tetrazole through an azido intermediate, however, has not been reported heretofore.[3b] This type of equilibrium is involved in solutions of I, which previously was considered by some to have the structure of 5-methyltetrazolo[1,5-*a*]pyrimidin-7(4H)-one (Ic).[4,5] We have found that I exists mainly as 7-methyltetrazolo-[1,5-*a*]pyrimidin-5(4H)-one (Ia)[4] in the solid state, and mainly as a mixture of Ia and Ic in most solutions.

Although three structures (Ia, b, and c) might result from the methods[6] used to prepare I, the product was assigned structure Ic in one case[5] and apparently structure Ia in another.[7] 2-Azido-4-methylpyrimidin-6(1H)-one (Ib) was eliminated from consideration as the product by the transparency of the azido absorption region of the infrared spectrum of I in the solid state (KBr disk) and in pyridine and dimethyl sulfoxide (DMSO) solutions.[8] Both Ia and Ic were detected in the proton magnetic resonance (p.m.r.) spectra of pyridine and DMSO-d_6 solutions of I. The spectrum of I in DMSO-d_6 initially indicates the presence of only one compound; however, after about 10 min. the absorption of an additional but similar compound appears. The compound first detected, which corresponds to the structure of I in the solid state, was identified as Ia by comparison of its chemical shifts and apparent coupling constants with those of 4,7-dimethyltetrazolo[1,5-*a*]pyrimidin-5(4H)-one (IIa)[7] in DMSO-d_6 (see Table I).[9] The new compound that appears



in the DMSO-d_6 solution must be Ic, which is formed from Ia through the intermediate 2-azidopyrimidine Ib. The possibility that we were observing the keto–enol equilibration of I was dismissed by infrared spectral data. Initially a solution of I in DMSO shows a band at 1690 cm.$^{-1}$ (Ia), but after 24 hr. the solution

(1) This investigation was supported by funds from the C. F. Kettering Foundation and the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Contract No. PH-43-64-51.

(2) C. Temple, Jr., and J. A. Montgomery, *J. Org. Chem.*, **30**, 829 (1965), and references therein.

(3) (a) R. A. Henry, W. G. Finnegan, and E. Lieber, *J. Am. Chem. Soc.*, **77**, 2264 (1955), and prior references. (b) The existence of such an equilibrium has been considered by I. N. Goncharova and I. Ya. Postovskii [*J. Gen. Chem. USSR*, **33**, 2413 (1963)].

(4) A. M. Patterson, L. T. Capell, and D. F. Walker, "The Ring Index," American Chemical Society, Washington, D. C., 1960.

(5) (a) C. F. H. Allen, H. R. Beilfuss, D. M. Burness, G. A. Reynolds, J. F. Tinker, and J. A. VanAllan, *J. Org. Chem.*, **24**, 779 (1959); (b) C. Bulow, *Ber.*, **42**, 284 (1909).

(6) One method involved the nitrosation of 2-hydrazino-4-methylpyrimidin-6-ol[7] and another the interaction of 5-aminotetrazole either with ethyl acetoacetate or with ethyl β-aminocrotonate.[5]

(7) K. Shirakawa, Japanese Patent 777 (February 6, 1957); *Chem. Abstr.*, **52**, 4699*h* (1958).

(8) The infrared spectra of solutions were determined in an Irtran-2, fixed-thickness cell.

(9) II[7] is obtained by nitrosation of III,[10] which is prepared by hydrazinolysis of 1,6-dihydro-1,4-dimethyl-2-methylthiopyrimidin-6(1H)-one, a compound of proven structure.[11,12] Further, we have prepared 1,6-dihydro-1,4-dimethylpyrimidin-6(1H)-one[12] by oxidation of II, which proved the structure of III.

(10) C. F. H. Allen, G. A. Reynolds, J. F. Tinker, and L. A. Williams, *J. Org. Chem.*, **25**, 361 (1960).

(11) H. L. Wheeler and D. F. McFarland, *Am. Chem. J.*, **42**, 106 (1909)

(12) F. H. S. Curd and D. N. Richardson, *J. Chem. Soc.*, 1857 (1955).