[CONTRIBUTION FROM THE MALLINCKRODT LABORATORIES OF HARVARD UNIVERSITY]

The Oxidation of Trisubstituted Phosphites by Dinitrogen Tetroxide

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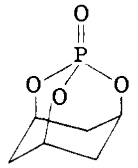
Dinitrogen tetroxide oxidizes trisubstituted phosphites to the corresponding phosphates in methylene chloride solution at the temperature of Dry Ice; the oxidant is reduced to a mixture of N_2O and N_2. The method allows the preparation of tri-*t*-butyl phosphate, and of other phosphates which are solvolyzed easily, and which had not been synthesized previously.

Introduction

The oxidation of phosphites to phosphates is of growing preparative importance. Ayres and Rydon[2] have used mercuric oxide to oxidize triesters of phosphorous acid to the corresponding triesters of phosphoric acid. Stetter and Steinacker[3] report an essentially quantitative yield of I by oxidation of the corresponding phosphite with aqueous H_2O_2. However, in our hands the oxidation of triethyl phosphite, under similar conditions, produced significant amounts of side reaction. Todd and his collaborators[4] have successfully halogenated diesters of phosphorous acid with chlorine, with N-chlorosuccinimide and with carbon tetrachloride, to obtain acid halides at the phosphate level of oxidation. These methods, however, do not serve to produce triesters of phosphoric acid. Dimroth and Ploch[5] have oxidized phosphites to phosphates with aqueous permanganate, but the reaction generally leads to the hydrolysis of triphosphates to diphosphates; in particular, the oxidation is accompanied by the opening of cyclic esters. The use of alkyl hypochlorites[6] is subject to complications, and the intriguing "oxidation" of phosphites by epoxides[7] does not appear to be of preparative value. The air oxidation of trialkyl phosphites to the corresponding phosphates is successful in some instances,[8] but the reaction, with triethyl phosphite, was unsuccessful in our hands. Dinitrogen tetroxide has been used successfully to oxidize diethyl sulfide to diethyl sulfoxide,[9] to oxidize trialkylphosphines to the phosphine oxides,[9] and to oxidize triphenylphosphine to triphenylphosphine oxide.[10] We now have investigated the reaction of N_2O_4 with a variety of phosphites, and found it to be a valuable reagent for converting triesters of phosphorous acid to the corresponding phosphates.



(I)

Results

Triethyl phosphite is oxidized by dinitrogen tetroxide in methylene chloride at −78° or in carbon tetrachloride at 0°; a major part of the reaction proceeds according to equations 1 and 2.

$$3(C_2H_5O)_3P + N_2O_4 \longrightarrow 3(C_2H_5O)_3PO + N_2O \quad (1)$$

$$4(C_2H_5O)_3P + N_2O_4 \longrightarrow 4(C_2H_5O)_3PO + N_2 \quad (2)$$

The organic product was identified by comparing its infrared spectrum with that of an authentic sample. The fact that N_2O and N_2 (rather than NO) may be the principal inorganic reaction products was first inferred from the following evidence: NO itself does not oxidize triethyl phosphite to the phosphate, and furthermore N_2O_4 fails to catalyze the oxidation of triethyl phosphite by oxygen. Had the product been NO, it would have been reoxidized to NO_2, and a small amount of dinitrogen tetroxide would have sufficed to catalyze the formation of considerable phosphate. The inference was later confirmed by identifying N_2O by its infrared spectrum as the principal oxide of nitrogen produced in the reaction. Nitrogen was detected in the mass spectrum of the gaseous products. Incidentally, in the earlier work[10] on the oxidation of triphenylphosphine to triphenylphosphine oxide with N_2O_4, the product was identified as NO; reinvestigation has shown that here, too, the major product is N_2O. In both oxidations, some NO is found, and the amount varies somewhat with the experimental conditions. The mechanism for these oxidation–reduction reactions, and in particular for the formation of N_2O and N_2 as the nitrogenous reduction products, has not yet been established.

Not only triethyl phosphate but tributyl, triisopropyl and triphenyl phosphates have been prepared by this method, and identified by comparison of their infrared spectra with those of authentic samples. Further, the method has proved useful in the preparation of phosphates which are sensitive to acid and base. Tri-*t*-butyl phosphate has been prepared by the oxidation of the corresponding phosphite. Our interest in cyclic phosphates[11] led us to the preparation of ethylene phosphorochloridate by the oxidation of ethylene chlorophosphite, and of benzyl ethylene phosphate by the oxidation of benzyl ethylene phosphite. Both of these triesters are very sensitive to hydrolysis.

Further, the method should provide a convenient pathway to esters of phosphoric acid labeled with O^{18} in the phosphonyl group.

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(1) Predoctoral Fellow, National Institutes of Health, 1957–1958.

(2) D. C. Ayres and H. N. Rydon, *J. Chem. Soc.*, 1109 (1957).

(3) H. Stetter and K. H. Steinacker, *Ber.*, **85**, 451 (1952).

(4) F. R. Atherton, H. T. Openshaw and A. R. Todd, *J. Chem. Soc.*, 382, 660 (1945); G. W. Kenner, A. R. Todd and F. J. Weymouth, *ibid.*, 3675 (1952).

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(6) K. A. Petrov and G. A. Sokol'skii, *J. Gen. Chem.* (*U.S.S.R.*), **26**, 3377 (1956).

(7) C. B. Scott, *J. Org. Chem.*, **22**, 1118 (1957).

(8) E. V. Kuznetsov and R. K. Valetdinov, *C. A.*, **51**, 11985f (1957).

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(10) L. Horner and W. Jurgeleit, *Ann.*, **591**, 138 (1955).

(11) J. Kumamoto, J. R. Cox, Jr., and F. H. Westheimer, THIS JOURNAL, **78**, 4858 (1956).

Although the oxidation therefore appears useful for the preparation of a wide variety of stable and unstable trisubstituted phosphates, the method does not serve for the oxidation of diesters of phosphorous acid to the corresponding diesters of phosphoric acid. This latter oxidation, and the properties of some of the more unusual phosphates here reported, remain for further investigation.

Experimental

Dinitrogen Tetroxide.—N_2O_4 (Matheson) was purified by oxidation at 0° in a stream of oxygen until the blue color changed to red-brown. After distillation from P_2O_5, it solidified on cooling in a deep-freeze to nearly colorless crystals.

Oxidation Method A.—Ten grams of the phosphite was dissolved in 50 ml. of CH_2Cl_2 or CCl_4 and cooled either in a Dry Ice–acetone-bath (CH_2Cl_2) or in an ice–salt-bath (CCl_4). A solution of N_2O_4 in the same solvent was added at such a rate that the temperature did not fluctuate greatly from 0 or −78°, depending on coolant, and boiling due to evolution of gas was not excessive. The end-point was determined by the appearance of a permanent faint green color in the previously colorless solution.

Oxidation Method B.—The desired quantity of the phosphite was cooled in an ice–salt-bath and N_2O_4 was passed in, in a stream of dry nitrogen. The liquid N_2O_4 was contained over P_2O_5 in a flask in an ice-bath, and prepurified nitrogen was bubbled through it and then through the phosphite. This method was slower than method A, but more convenient when large quantities were desired.

Isolation of the Gaseous Reaction Products.—Dinitrogen tetroxide was frozen in one arm of a U-tube, provided with a stop-cock, and an excess of triethyl phosphite was placed in the other arm. The system was degassed on a vacuum line, the stopcock was closed, and the reaction carried out as follows: The arm of the U-tube containing the phosphite was immersed in an ice-bath, and that containing the N_2O_4 was allowed to warm to room temperature. When all of the N_2O_4 had vaporized, the tube was shaken to ensure complete mixing and complete reaction. The U-tube was connected to the vacuum line, and cooled in ice; the gases were then transferred, by vacuum line techniques, either to an infrared gas-cell or to a mass-spectrometer bulb. An authentic sample of N_2O for comparison was prepared by the thermal decomposition of ammonium nitrate, and purified by passing it through concentrated sodium hydroxide solution, and then through a Dry Ice trap.

The infrared spectra of the gases obtained by the oxidation of both triethyl phosphite and triphenylphosphine were almost identical with that of pure N_2O. When air was admitted to the infrared cell, a faint brown color was produced, showing that the original gas was contaminated with a small amount of NO. The infrared spectrum of the resulting mixture was complex, presumably in part because of reaction between the gases produced and the rock-salt windows of the cell.[12] The amount of NO (judged by the color of the gas when air was admitted) varied considerably in various preparations; probably the exact ratio of gaseous products depends on the excess of reducing agent and perhaps on other experimental conditions.

We are indebted to Professor K. B. Wiberg, who used a Consolidated model 21 mass spectrometer to analyze a sample of gas prepared by the reduction of N_2O_4 in the presence of excess triethyl phosphite. Comparison of this mass spectrum with those of pure gases showed that the reduction product consisted principally of N_2O and N_2 (with a predominance of the former); a small amount of NO and traces of hydrocarbons were also present; no oxygen or NO_2 was found.

Alkyl Phosphates.—Triethyl, triisopropyl and tri-*n*-butyl phosphites (Eastman Chemical Co., practical grade) were oxidized without purification. The reaction products could be vacuum distilled directly from the reaction mixture (method B) or could be distilled after prior evaporation of the solvent (method A). The infrared spectrum of each oxidation product was identical with that of an authentic sample of the corresponding phosphate. The yields and boiling points of the products were as shown: triethyl phosphate, 75%, 69–71° (3.5 mm.); triisopropyl phosphate 76%, 49–51° (0.5 mm.), (triisopropyl phosphate from distilled phosphite, 87%, 46.5° (0.45 mm.); tri-*n*-butyl phosphate, 70%, 47° (0.45 mm.).

Tri-*t*-butyl Phosphate.—The procedure given by Kosolapoff[13] for the preparation of tri-*t*-butyl phosphite has been shown[14] to yield largely di-*t*-butyl phosphite. However, when triethylamine was used as the base, phosphorus trichloride reacted with *t*-butyl alcohol in ligroin as solvent at 5°, under the conditions described by Kosolapoff,[13] to yield a mixture of phosphites. The solvent was removed under vacuum, and the product distilled at 60–62° (4.0 mm.). The analysis for phosphorus (13.92%) corresponded to a mixture of di- and tri-*t*-butyl phosphite; the same conclusion was reached from the carbon and hydrogen analyses. The infrared spectrum showed the P═O and P—H bands of the dialkyl phosphite. This mixture of phosphites was oxidized by method A. After removal of the solvent, the product partially solidified. The solid was pressed between soft filter paper, and sublimed at room temperature at 10^{-4}–10^{-5} mm. The mixture of di- and tri-*t*-butyl phosphite (2.82 g.) yielded 0.63 g. of tri-*t*-butyl phosphate, m.p. 68–72°. After two sublimations, the large colorless crystals melted at 71–75°. The analysis was performed by Elek Microanalytical Laboratories, Los Angeles, Calif.

Anal. Calcd. for $C_{12}H_{27}O_4P$: C, 54.11; H, 10.22; P, 11.59. Found: C, 54.27; H, 10.39; P, 11.77.

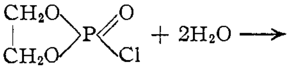
The tri-*t*-butyl phosphate was insoluble in water or aqueous alkali or acid, but dissolved readily in organic solvents. A solution in aqueous acetone was initially neutral, but became acid on standing. The infrared spectrum of the ester was similar to that of the mixed phosphites, although typical of phosphates; the compound showed no absorption in the region of 4.1 μ (P–H stretching). Principal infrared bands were located at 3.34, 7.17, 7.30, 7.91, 8.51, 9.63, 10.08 and 10.90 μ in CCl_4 solution.

The proton magnetic resonance spectrum of the ester was determined with a Varian Associates n.m.r. spectrometer equipped with superstabilizer. Even under high resolution, the compound exhibited only a single peak, which presumably represented all twenty-seven equivalent hydrogen atoms.

Ethylene Phosphorochloridate.—Ethylene chlorophosphite was prepared by the method of Lucas[15] and oxidized by method B, to give ethylene chlorophosphate in 30% yield. The low yield is due to polymerization during distillation of the product. The phosphorochloridate boiled at 89–91° (0.8 mm.). Principal infrared absorption bands occurred at 3.32, 3.41, 6.77, 7.32, 7.55, 7.73, 9.62, 10.82 and 11.65, broad μ.

Anal. Calcd. for $C_2H_4O_3PCl$: Cl, 25.24. Found: Cl, 25.20.

The compound (0.63 g.) was dissolved in 75 cc. of water and heated for 30 minutes on the steam-bath. The solution was then neutralized with barium hydroxide, and a volume of ethanol added equal to that of the solution. The barium salt of hydroxyethyl phosphate precipitated in 94% yield; it was identified by its infrared spectrum. Presumably the hydrolysis of the chloride was accompanied by opening of the ring,[11] according to the equation



$$\text{(CH}_2\text{O)}_2\text{P(O)Cl} + 2H_2O \longrightarrow HOCH_2CH_2OPO_3H_2 + HCl \quad (3)$$

Benzyl Ethylene Phosphate.—Benzyl ethylene phosphite was prepared from ethylene chlorophosphite, benzyl alcohol and triethylamine, following the general procedure of Lucas.[15] The product, obtained in 53% yield, boiled at 106–108° (1.5 mm.). Principal infrared bands occurred at 3.34, 3.42, 3.49, 6.69, 6.89, 7.30, 9.65, 10.03 and 10.84 μ in CCl_4 solution. The analysis was performed by Elek Microanalytical Laboratories, Los Angeles, Calif.

Anal. Calcd. for $C_9H_{11}PO_3$: C, 54.57; H, 5.59; P, 15.64. Found: C, 54.39, H, 5.71; P, 15.46.

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(12) J. H. Wise and J. T. Elmer, *J. Chem. Phys.*, **18**, 1411 (1950).

(13) G. Kosolapoff, This Journal, **74**, 4953 (1952).

(14) H. Goldwhite and B. C. Saunders, *J. Chem. Soc.*, 2409 (1957); R. W. Young, This Journal, **75**, 4620 (1953); W. Gerrard, M. J. D. Isaacs, G. Machell, K. B. Smith and P. L. Wyvill, *J. Chem. Soc.*, 1920 (1953).

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The phosphite was oxidized by method B, and the product subjected to molecular distillation at 10^{-5} mm. and a bath temperature of 65°. The product crystallized on the cold finger of the distillation apparatus; the yield was 61%. The highest melting point obtained was 49–51°. However, the solid rapidly deliquesced on exposure to the atmosphere, and dissolved in water to give an acidic solution; the material is thus extraordinarily unstable to moisture. The principal infrared bands were located at 3.31, 3.40, 3.46, 6.68, 6.79, 6.88, 7.25, 7.32, 7.69, 8.25, 9.45(shoulder), 9.67, 9.83, 10.79, 11.48(broad) and 11.90(broad) μ. A sample was resublimed for analysis, performed by S. M. Nagy, M. I. T.

Anal. Calcd. for $C_9H_{11}PO_4$: C, 50.23; H, 5.42; P, 14.47. Found: C, 50.00; H, 5.46; P, 14.56.

Triphenyl Phosphate.—Triphenyl phosphite was oxidized by method A. The excess N_2O_4 was removed under vacuum, and the product, dissolved in methylene chloride, was filtered through a short column of activated alumina in order to remove a colored impurity. The yield of triphenyl phosphate, melting at 49–51°, was 84%.

Triphenyl Phosphine Oxide.—Triphenyl phosphine (Eastman Kodak Co.) was oxidized by method A. Removal of the solvent gave 99% of triphenylphosphine oxide, m.p. 155–156° (reported[16] 153°); N_2O was identified in the gaseous product by infrared measurements, as reported above.

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[16] G. Kosolapoff, THIS JOURNAL, **64**, 2982 (1942).

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORIES OF HARVARD UNIVERSITY]

The Structure and Chemistry of Ferrocene. III. Evidence Pertaining to the Ring Rotational Barrier

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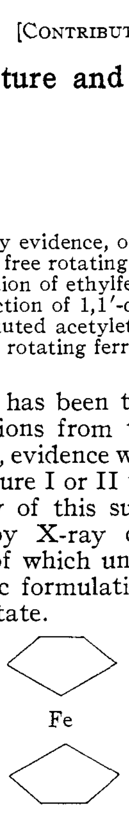
Certain early evidence, on the basis of which it had been concluded that the carbocyclic rings in the ferrocene molecule are essentially free rotating, is summarized. Both the number and structural type of acetylethylferrocene isomers formed in the acetylation of ethylferrocene are shown to be inconsistent with the assumption of a rigid ferrocene system. Partial catalytic reduction of 1,1′-diacetylferrocene leads to the formation of an acetylethylferrocene identical with the heteroannularly substituted acetylethylferrocene derived from acetylation of ethylferrocene. This result is interpretable only in terms of a free rotating ferrocene model.

Ferrocene has been the subject of two previous communications from this Laboratory.[3,4] In the first of these, evidence was presented on the basis of which structure I or II was advanced for ferrocene. The validity of this suggestion subsequently was confirmed by X-ray crystallographic studies,[5–7] the results of which unequivocally established the antiprismatic formulation (I) for ferrocene in the crystalline state.



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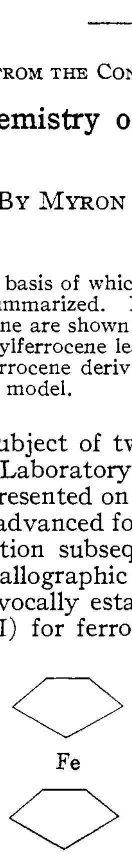

II

Notwithstanding the high degree of formal unsaturation implied by such a structure, ferrocene does not exhibit properties characteristic of polyolefinic substances. Thus, its failure to undergo a Diels–Alder addition with maleic anhydride and its resistance to catalytic reduction led to the view that the substance must possess a high order of resonance stabilization. The subsequent demonstration that ferrocene entered into a normal Friedel–Crafts substitution reaction with a variety of acyl halides not only accorded well with this hypothesis, but opened up an entirely new field of research, the fertility of which is attested by the ever growing number and variety of ferrocene derivatives which have since taken their place in chemical literature.[8] Some early observations concerning the preparation and properties of several acylated ferrocenes and of substances derived from these were recorded briefly in our second communication.[4] In the present report, evidence pertaining to the question of the ring rotational barrier in ferrocene is adduced.

It must be noted that the conclusions regarding the rotational barrier in ferrocene, derived some time ago[2] and reported herein, have in the intervening years been amply confirmed in the synthetic work of Pauson[9] and in the dipole moment studies of Richmond and Freiser.[10] They are, moreover,

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[2] Abstracted in part from the Ph.D. thesis of M. Rosenblum, Harvard University, August, 1953. In 1955, Pauson (*Quart. Revs.*, **9**, 391 (1955), briefly outlined our experimental results and the conclusions derived therefrom. More recently, Struchkov (*Zhur. Obshch. Khim.*, **27**, 2039 (1957) has discussed in some detail the question of the rotational barrier in ferrocene and the effect of ring substitution on this potential barrier, citing the chemical evidence referred to by Pauson for certain of the conclusions deduced.

[3] G. Wilkinson, M. Rosenblum, M. C. Whiting and R. B. Woodward, THIS JOURNAL, **74**, 2125 (1952).

[4] R. B. Woodward, M. Rosenblum and M. C. Whiting, *ibid.*, **74**, 3458 (1952).

[5] J. D. Dunitz and L. E. Orgel, *Nature*, **171**, 121 (1953).

[6] P. F. Eiland and R. Pepinsky, THIS JOURNAL, **74**, 4971 (1952).

[7] E. O. Fischer and W. Pfab, *Z. Naturforschung*, **7B**, 377 (1952).

[8] The number of such publication is so large and their present proliferation so great that it is impossible to summarize these here. The interested reader is, however, referred to the very excellent review article by Pauson (ref. 2) for an early account of progress in this field.

[9] P. L. Pauson, THIS JOURNAL, **76**, 2187 (1954); *cf.* also P. L. Pauson, ref. 2, p. 400.

[10] H. H. Richmond and H. Freiser, THIS JOURNAL, **77**, 2022 (1955).