Oxidation of Tertiary Phosphines by Hydroxylamine[1]

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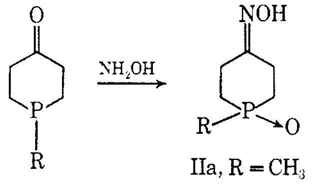
The oximes of phosphorinanones **1a** and **1b** were required as intermediates in the synthesis of the corresponding 4-aminophosphorinanes. However, the usual procedure[3] of treating ketone **1b** with hydroxylamine hydrochloride in aqueous sodium hydroxide or ethanol–pyridine (under nitrogen) failed to give the expected water-insoluble product. Since Ib had readily formed a thiosemicarbazone, no difficulty in oxime formation had been anticipated. The water-soluble, hygroscopic residue from evaporation of the ethanol–pyridine reaction medium was therefore further examined and found to be crystallizable from acetonitrile. The product proved to be the oxime of 1-ethyl-4-phosphorinanone-1-oxide (IIb), obtained in 65% yield. Its structure was evident from its elemental analysis as well as its spectral properties. Of particular significance was the ^{31}P nmr spectrum; this consisted of a broad singlet at −54 ppm (85% H_3PO_4 standard). This chemical shift is in the range characteristic of tertiary phosphine oxides;[4] the phosphines have positive values. Similar results were obtained with ketone Ia; only the oxime (IIa) of its 1-oxide could be isolated (25% yield).



Ia, R = CH_3
b, R = C_2H_5

IIa, R = CH_3
b, R = C_2H_5

Since considerable care had been exercised to prevent air oxidation of the phosphines, it appeared that hydroxylamine had been acting as the oxidizing agent, although to our knowledge it has not been previously used for this purpose. This possibility was explored by examining the behavior of two nonketonic tertiary phosphines toward hydroxylamine. Tri-*n*-butylphosphine was converted to its oxide in 66% yield after 2-hr reflux in ethanol, using conditions similar to those employed for oxime formation. Triphenylphosphine was less reactive, but after 16 hr of reflux in pyridine, a 75% yield of its oxide resulted. Presumably, the hydroxylamine is reduced to ammonia, although no effort was made to detect this product.

Many reagents are known to oxidize tertiary phosphines,[5] and the use of hydroxylamine for this purpose would appear to offer no special advantage. However, the occurrence of this reaction is worthy of note for two reasons. As in our experience, it can be a complication where trivalent phosphorous is present in a molecule undergoing reaction with hydroxylamine. Also, the transfer of oxygen from a system of general structure N–O–R to trivalent phosphorus is not common; one other example (conversion of a cyclic hydroxamide to a lactam) has very recently been reported.[6]

Experimental Section[7]

1-Ethyl-4-phosphorinanone Thiosemicarbazone.—To a mixture of 3.0 g (0.033 mol) of thiosemicarbazide and 3.0 g (0.021 mol) of 1-ethyl-4-phosphorinanone[8] (Ib) was added a solution of 6.0 g of sodium acetate in 30 ml of distilled water. The mixture was heated at 64–68° for 1.75 hr. After several hours, the crystalline material was filtered, washed three times with distilled water, and dried in a vacuum desiccator over solid potassium hydroxide and phosphorus pentoxide. The yield was 4.97 g (69.1%) of crude 1-ethyl-4-phosphorinanone thiosemicarbazone, mp 145–153° dec. After three recrystallizations, a sample had mp 153.5–154.5° dec.

Anal. Calcd for $C_8H_{16}N_3PS$: C, 44.22; H, 7.42; P, 14.50; S, 14.76. Found: C, 44.32; H, 7.56; P, 14.26; S, 15.02.

1-Ethyl-4-phosphorinanone 1-Oxide Oxime (IIb).—A mixture of 10.0 g (0.070 mol) of 1-ethyl-4-phosphorinanone (Ib), 10.0 g (0.14 mol) of hydroxylamine hydrochloride, 27 ml of pyridine, and 33 ml of absolute ethanol was refluxed under nitrogen for 1.75 hr. Most of the solvent was then removed on a rotary evaporator. The residue was extracted (under nitrogen) with 130 ml of boiling acetonitrile. The extract was concentrated to *ca.* 30 ml. Allowing the concentrate to stand at 7° for 1 day, and −10° for 1 day, yielded a crop of 6.06 g of oxime IIb, mp 180–182°. A second crop (1.86 g, mp 182–187°) was obtained from the mother liquor. The total yield was 7.92 g (65%). The oxime had ir bands (Nujol) at 3.15 (strong) and 3.25 μ (strong) for OH, 6.05 μ (weak) for C=N, 8.35 (medium) and 8.6 μ (strong, probably for free and hydrogen-bonded P$\rightarrow$O). The ^{1}H nmr spectrum ($CDCl_3$) had a singlet (1 H) at δ 9.0 ppm, which exchanged with D_2O, and an envelope (13 H) at δ 0.96–3.3. The ^{31}P nmr (2 *M* D_2O) signal was located at −54 ppm. Two recrystallizations of a portion of IIb from acetonitrile gave an analytical sample, mp 190–193°.

Anal. Calcd for $C_7H_{14}NO_2P$: C, 48.00; H, 8.06; N, 7.99; P, 17.68. Found: C, 48.03; H, 8.03; N, 8.05; P, 17.70.

1-Methyl-4-phosphorinanone 1-Oxide Oxime (IIa).—A mixture of 5.00 g (0.038 mol) of 1-methyl-4-phosphorinanone[9] (Ia), 6.00 g (0.084 mol) of hydroxylamine hydrochloride, 14 ml of pyridine, and 14 ml of absolute ethanol was refluxed under nitrogen for 1.7 hr. Most of the solvent mixture was evaporated on a rotary evaporator. The residue was extracted with four 35-ml portions of boiling acetonitrile and two 25-ml portions of boiling 2-propanol. The filtered extracts were combined and the solvents were removed. The oily white residue was dried *in vacuo* over phosphorus pentoxide. This was dissolved in 95% ethanol; on addition of ethyl acetate a small amount of an oily solid precipitated and was discarded. The solvents of the filtrate were evaporated and the residue was dried in a vacuum oven at 70° to give 2.87 g of a brown solid. Recrystallization from acetonitrile yielded 1.54 g (25%) of 1-methyl-4-phosphorinanone 1-oxide oxime (IIa), mp 145–160°. Its ir spectrum (nujol) had peaks at

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[2] To whom inquiries may be addressed.

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[4] V. Mark, C. H. Dungan, M. M. Crutchfield, and J. R. Van Wazer in "Topics in Phosphorus Chemistry," Vol. 5, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, Inc., New York, N. Y., 1967, p 284.

[5] (a) J. I. G. Cadogan, *Quart. Rev.* (London), **16**, 208 (1962); (b) K. Sasse in "Methoden der Organischen Chemie (Houben-Weyl)," Vol. 12, Part 1, Georg Thieme Verlag, Stuttgart, Germany, 1963, p 140.

[6] D. Döpp, *Chem. Commun*, 1284 (1968).

[7] All reactions were performed in a nitrogen atmosphere. Solvents were degassed with nitrogen before use. Melting points were taken with a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded with a Perkin-Elmer Model 137 spectrophotometer. Proton nmr spectra were recorded with a Varian Associates Model A-60 spectrometer using TMS as an internal standard in $CDCl_3$, and as an external standard in D_2O. ^{31}P nmr spectra were obtained with a Varian Associates Model HR-60 spectrometer using 85% H_3PO_4 as an external standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

[8] R. P. Welcher, G. A. Johnson, and V. P. Wystrach, *J. Amer. Chem. Soc.*, **82**, 4437 (1960).

[9] H. E. Shook, Jr., and L. D. Quin, *ibid.*, **89**, 1841 (1967).

6.05 μ (weak, C=N) and 8.35 and 8.85 μ. Five recrystallizations from acetonitrile gave an analytical sample, mp 175–183°, whose ^{1}H nmr spectrum (D_2O) contained peaks at δ 2.3–3.6 (m, 8 H, CH_2) and 2.15 (d, 3 H, J_{PH} = 13 Hz, $P\text{-}CH_3$).

Anal. Calcd for $C_6H_{12}NO_2P$: C, 44.72; H, 7.60; N, 8.69; P, 19.22. Found: C, 44.56; H, 7.43; N, 8.52; P, 18.96.

Reaction of Tri-*n*-butylphosphine with Hydroxylamine.—A mixture of 10 ml of absolute ethanol, 1.0 g (0.014 mol) of hydroxylamine hydrochloride, and 1.3 ml (1.1 g, 0.0055 mol) of tri-*n*-butylphosphine was refluxed for 2 hr. The mixture was filtered under nitrogen and the filtrate was poured into saturated ammonium chloride solution. The mixture was extracted with two 25-ml portions of tetrahydrofuran. The combined extracts were washed with saturated sodium chloride solution and dried over sodium sulfate under nitrogen. The solvent was evaporated and the residue was dried *in vacuo* over phosphorus pentoxide to give 0.78 g (66%) of tri-*n*-butylphosphine oxide. The sample contained an ir peak (Nujol) at 8.65 μ for $P \rightarrow O$; its ^{31}P nmr peak (5 *M* in tetrahydrofuran) was at −42.7 ppm (lit.[4] −43.2, −45.8 ppm).

This reaction was repeated using a 1:1 (*v/v*) pyridine–absolute ethanol solution. Work-up afforded a 50% yield, bp 126–130° (0.8 mm) [lit.[10] bp 300° (760 mm)].

Reaction of Triphenylphosphine with Hydroxylamine.—A mixture of 10.0 g (0.038 mol) of triphenylphosphine, 2.72 g (0.038 mol) of hydroxylamine hydrochloride, and 60 ml of pyridine was refluxed under nitrogen for 16 hr. The mixture was cooled and poured into 125 ml of saturated ammonium chloride solution. The two-phase mixture that formed was extracted with two 60-ml portions of benzene. The aqueous layer was filtered and extracted with a third 60-ml portion of benzene. The combined extracts were dried over sodium sulfate, and the solvent was removed to give 8.0 g (75%) of crude triphenylphosphine oxide, mp 151–159°, ^{31}P nmr signal (5.5 *M* in $CDCl_3$) at −27.6 ppm (lit.[4] −23.0 to −27.0 ppm). After recrystallization from benzene–cyclohexane, it melted at 158–161° (lit.[11] mp 156°).

Registry No.—Hydroxylamine, 7803-49-8; Ib thiosemicarbazone, 20817-03-2; IIa, 20797-90-4; IIb, 20797-91-5; tri-*n*-butylphosphine, 998-40-3; triphenylphosphine, 603-35-0.

Acknowledgment.—We are indebted to Stephen W. Dale for the ^{31}P nmr spectra.

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(11) "Handbook of Chemistry and Physics," 45th ed, Chemical Rubber Co., Cleveland, Ohio, 1964, p C-473.

A Study of Some Substituted Cycloheptatrienecarboxylic Acids by Nuclear Magnetic Resonance Spectroscopy

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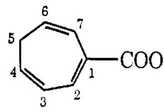
The thermal decomposition of ethyl diazoacetate in the presence of aromatic hydrocarbons, originally reported in 1885 by Buchner and Curtius,[3,4] constitutes one of the more direct preparative routes to cycloheptatriene derivatives. Since the pioneering work of Doering and his coworkers,[5,6] who were the first to recognize the existence of the cycloheptatrienyl (tropylium) cation in organic chemistry, there has been a sustained interest in this class of nonbenzenoid "aromatic" hydrocarbons. An added incentive has been the recognition that the thermal reaction of ethyl diazoacetate with aromatic hydrocarbons proceeds by a carbene mechanism.[7] Although the chemistry of cycloheptatriene has been adequately discussed in the literature,[4,8] the synthesis of substituted cycloheptatrienecarboxylic acids seems to have been confined to those members which are derived from methyl and methoxyl benzenes. Thus, in a series of papers following the initial discovery of the reaction, Buchner prepared alkylcycloheptatrienecarboxylic acids from the reaction of ethyl diazoacetate with toluene,[9] 1,3-dimethylbenzene,[10] and mesitylene.[11] In their extensive work, Johnson and coworkers described the preparation of alkoxycycloheptatrienecarboxylic acids resulting from the reaction of ethyl diazoacetate with anisole,[12] 1,3-dimethoxybenzene,[13,14] 1,4-dimethoxybenzene,[15] and 1,2,4-trimethoxybenzene.[14] Although the positions of the substituents in these products were established by chemical means, in few cases were the positions of the double bonds located. The lability[16] of the triene system under acidic conditions and also heat would preclude any definitive assignments based on chemical transformations.

We have recently had the occasion to prepare several of these known acids in connection with another problem,[17] and it became desirable to reinvestigate the structural assignments by nmr spectroscopic techniques. The monocyclic seven-membered-ring structure of the simplest member, β-cycloheptatrienecarboxylic acid **1**,[18,19] had been unambiguously established in 1956 by the same technique.



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The acids were prepared by published procedures with some minor modifications in some cases. Their melting points and nmr parameters are listed in Table I. Nearly all of the compounds gave first-order spectra with some long-range coupling being observed in certain cases. Their interpretation was based on the observations made on β-cycloheptatrienecarboxylic acid as well

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[2] Geigy Research Laboratories, Switzerland.

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