tion was separated, washed with water, and evaporated to give a yellow crystalline residue. The residue was recrystallized by dissolution in the minimum amount of boiling water and cooling to 0–5° to give 5.25 g. (18.4%) of VI, m.p. 113.5–114°.

Anal. Calcd. for $C_{12}H_9O_4P$: C, 58.15; H, 3.63; P, 12.49. Found: C, 58.21; H, 3.80; P, 12.36.

The ultraviolet spectrum of VI showed a maximum at 238 mμ (ε 33,600). The infrared spectrum showed bands at the following frequencies (cm.$^{-1}$): 3009 w, 1555 m, 1210 s, 1179 m, 1164 m, 1131 s, 1123 m, 1059 w, 1021 s, 1007 s, 914 s, 905 w, 878 m, 831 w, 792 w, 778 m, 753 s, 722 s (Nujol mull); and 2960 m, 1590 w, 1459 s, 1369 m, 1228 w, 1203 w ($CHCl_3$ solution).

Oxidation of Phosphites and Phosphines *via* Quaternary Phosphonium Salts

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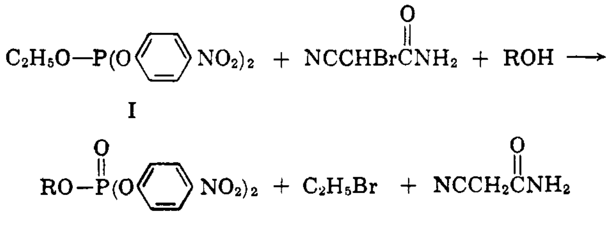
When phosphorylation of *n*-propyl alcohol by means of ethyl di-*p*-nitrophenyl phosphite (I) and monobromocyanoacetamide was tried, *n*-propyl di-*p*-nitrophenyl phosphate (IIa) and, unexpectedly, ethyl di-*p*-nitrophenyl phosphate (IIb) were obtained. The result can be best explained by assuming an initial formation of a quaternary phosphonium salt (IV) as an intermediate, from which the phosphates are formed by elimination of the alkyl bromides. The direction of the reaction may depend on the stability of the alkyl cation eliminated. This hypothesis was confirmed by the formation of triethyl phosphate in a 72% yield from the reaction of triethyl phosphite with monobromocyanoacetamide and benzyl alcohol. In view of this result, several alkyl and aryl phosphites were successfully oxidized by means of monobromocyanoacetamide with either benzyl alcohol or allyl alcohol, as were phosphines. Similarly, some cyclic phosphites, such as ethyl ethylene phosphite and ethyl propylene phosphite, were oxidized and gave the corresponding cyclic phosphates in good yields. The reaction was further extended to oxidation of diethyl phosphite, and diethyl phosphate was obtained in quantitative yield.

The preceding papers[1,2] describe a selective phosphorylation of alcohols and phosphates by means of monobromocyanoacetamide or monobromomalonamide with trialkyl phosphites, forming mixed esters of phosphoric acid and unsymmetrical pyrophosphates.

Further, the methods were successfully applied to the synthesis of some naturally occurring phosphorus derivatives.[3] In those experiments, tribenzyl phosphite was employed since the benzyl group can be readily removed from the resulting phosphates by catalytic hydrogenation after phosphorylation has been performed.

Another phosphite, ethyl di-*p*-nitrophenyl phosphite, was prepared and treated with monobromocyanoacetamide and alcohols in order to determine if it too would be effective in the reactions described above. The ethyl group of the phosphite would be expected to be split off as ethyl bromide in the first stage of the reaction, and the *p*-nitrophenyl group would be readily removed by the subsequent alkaline hydrolysis of the resulting phosphates under mild conditions[4] to yield the expected alkyl dihydrogen phosphates.

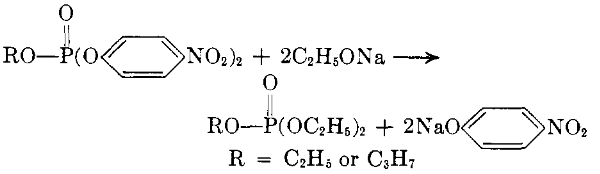
When ethyl alcohol was added to a suspension of equimolar amounts of ethyl di-*p*-nitrophenyl phosphite (I) and monobromocyanoacetamide in ether, ethyl di-*p*-nitrophenyl phosphate (IIa) was obtained in a 73% yield as expected (eq. 1).



$$C_2H_5O{-}P(OC_6H_4NO_2)_2 + NCCHBrC(=O)NH_2 + ROH \longrightarrow RO{-}P(=O)(OC_6H_4NO_2)_2 + C_2H_5Br + NCCH_2C(=O)NH_2 \quad (1)$$

IIa, R = C_2H_5
b, R = C_3H_7

However, when phosphorylation of *n*-propyl alcohol was attempted in the same manner, there was obtained a colorless crystalline compound which could not be purified by recrystallization. When this product (A was allowed to react with sodium ethoxide under the assumption that the *p*-nitrophenyl group might be replaced by the ethyl group according to eq. 2, a liquid with b.p. 107–108° at 15 mm. was obtained. This substance showed two peaks by gas chromatography, one of which was identified as *n*-propyl diethyl phosphate and the other as triethyl phosphate. The ratio of the amounts of *n*-propyl diethyl phosphate and triethyl phosphate was about 2:3. The result shows that the unpurified product (A) consists of *n*-propyl di-*p*-nitrophenyl phosphate and ethyl di-*p*-nitrophenyl phosphate.



$$RO{-}P(=O)(OC_6H_4NO_2)_2 + 2C_2H_5ONa \longrightarrow RO{-}P(=O)(OC_2H_5)_2 + 2NaOC_6H_4NO_2 \quad (2)$$

$$R = C_2H_5 \text{ or } C_3H_7$$

The formation of ethyl di-*p*-nitrophenyl phosphate can be explained by assuming an initial formation of quaternary phosphonium salt III from the phosphite and monobromocyanoacetamide. The intermediate III is then converted to IV by the reaction with an alcohol (eq. 3). The intermediate IV thus formed has two possible paths for decomposition: (1) the formation of *n*-propyl di-*p*-nitrophenyl phosphate by the elimination of ethyl bromide (phosphorylation of *n*-propyl alcohol) and (2) the formation of ethyl di-*p*-nitrophenyl phosphate by the elimination of *n*-propyl bromide (oxidation of ethyl di-*p*-nitrophenyl phosphite) as shown in eq. 4. The direction of the reaction may depend on the stability of the alkyl cation eliminated.

For the purpose of elucidating the proposed mechanism and of oxidizing only the phosphite, benzyl alcohol was employed in the place of *n*-propyl alcohol in the above experiment. When monobromocyano-

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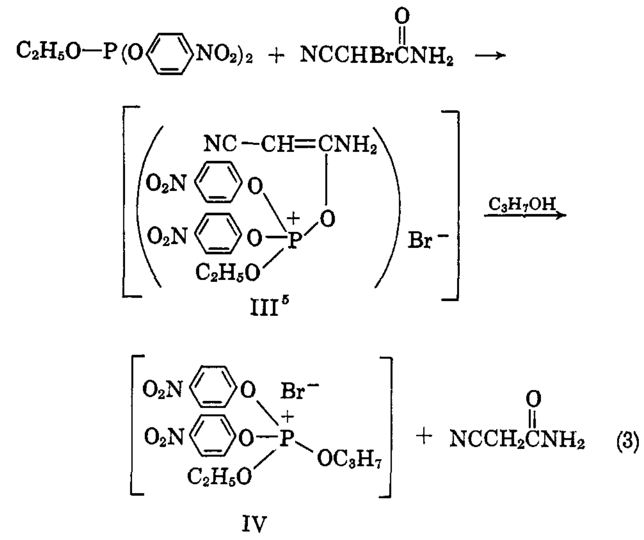
[1] T. Hata and T. Mukaiyama, *Bull. Chem. Soc. Japan*, **35**, 1106 (1962).

[2] T. Mukaiyama, T. Hata, and K. Tasaka, *J. Org. Chem.*, **28**, 481 (1963).

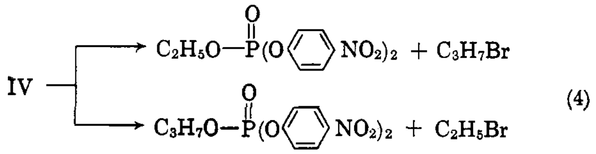
[3] T. Hata and T. Mukaiyama, *Bull. Chem. Soc. Japan*, **37**, 103 (1964).

[4] J. G. Moffatt and H. G. Khorana, *J. Am. Chem. Soc.*, **79**, 3741 (1957).

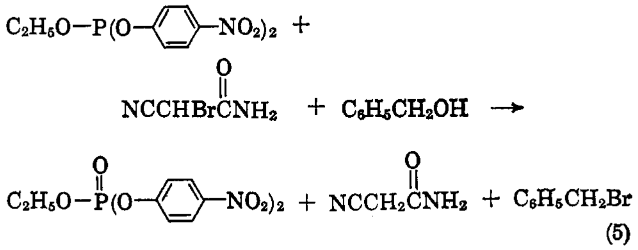

III[5]

IV

(3)


(4)

acetamide and ethyl di-*p*-nitrophenyl phosphite were treated with benzyl alcohol at room temperature, ethyl di-*p*-nitrophenyl phosphate and benzyl bromide were obtained in 76 and 52% yields, respectively, as expected (eq. 5).


(5)

Further, the reaction was extended to the preparation of other alkyl phosphates and aryl phosphates from the corresponding phosphites.

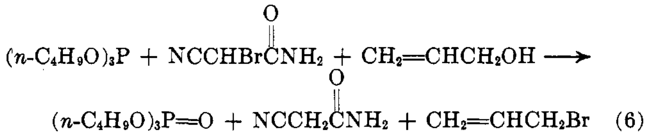
Triethyl phosphite was added to a suspension of equimolar amounts of monobromocyanoacetamide and benzyl alcohol in ether at room temperature. After the solution was kept standing overnight, triethyl phosphate (47%) and benzyl bromide (52%) were obtained by fractionation. At the same time, a higher boiling material was obtained, whose infrared spectrum suggests benzyl diethyl phosphate. In the course of this reaction, an oily product always clung to the flask, but disappeared soon. This may suggest the existence of the said intermediate, quaternary phosphonium salt. However, when the above reaction was carried out at −60°, the yield of triethyl phosphate increased to 72%, and no benzyl diethyl phosphate was isolated.

When triphenyl phosphite was treated with monobromocyanoacetamide and benzyl alcohol at room temperature, a 90% yield of triphenyl phosphate and a 73% yield of benzyl bromide were obtained. On the other hand, only about a 50% yield of ethyl diphenyl phosphate was obtained by oxidation of ethyl diphenyl phosphite under the same condition.

In addition, it was confirmed that the reaction of triphenylphosphine or tri-*n*-butylphosphine with monobromocyanoacetamide and benzyl alcohol gave triphenylphosphine oxide or tri-*n*-butylphosphine oxide in good yield.

Table I shows the results of oxidation of various phosphites and phosphines by means of monobromocyanoacetamide and benzyl alcohol. From these results it can be concluded that phosphites having more than one alkyl group are better oxidized at a low temperature (−60°), while phosphites, having no alkyl groups, which can not undergo the Perkow and Arbuzov-type reactions, are oxidized exclusively at room temperature by the present method as are phosphines.

Next, an attempt was made to use allyl alcohol in place of benzyl alcohol in oxidation of tri-*n*-butyl phosphite. A 72% yield of tri-*n*-butyl phosphate, along with a 55% yield of allyl bromide, was obtained. Similarly, triethyl phosphate, ethyl diphenyl phosphate, triphenyl phosphate, and triphenylphosphine oxide were obtained in 76, 65, 85, and 80% yields each from the corresponding phosphites or phosphine (Table II).



$$(n\text{-}C_4H_9O)_3P + NCCHBr\overset{O}{\overset{\|}{C}}NH_2 + CH_2{=}CHCH_2OH \longrightarrow$$
$$(n\text{-}C_4H_9O)_3P{=}O + NCCH_2\overset{O}{\overset{\|}{C}}NH_2 + CH_2{=}CHCH_2Br \quad (6)$$

It is noted that the use of allyl alcohol is preferable to that of benzyl alcohol, because the allyl bromide formed can be much more readily removed from the reaction mixture than benzyl bromide.

Though many attempts[6–8] have been made recently to oxidize cyclic phosphites, particular attention is called to the oxidation of these compounds by the methods described here. When ethyl propylene phosphite (V, R = C_2H_5), propyl propylene phosphite (V, R = C_3H_7), or butyl propylene phosphite (V, R = C_4H_9) were treated with monobromocyanoacetamide and benzyl alcohol in ether, there was initially formed a viscous oily product which soon dissolved and cyanoacetamide was precipitated. After removal of the cyanoacetamide, the corresponding cyclic phosphates were obtained in fairly good yields by fractionation (eq. 7). The results are summarized in Table III.

When ethyl ethylene phosphite was treated in the same manner, a large amount of viscous, oily product initially formed remained unchanged. Then tetra-

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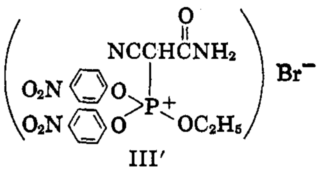
[5] Concerning the structure of the intermediate, two alternative structures are conceivable, the enol phosphonium and keto phosphonium salts (III and III′). The latter was omitted in the reaction mechanism because it has been shown by Trippet and Borowitz that enol phosphonium salts, formed from α-halo ketones and trivalent phosphorus compounds, react with alcohols but keto phosphonium salts do not: S. Trippet, *J. Chem. Soc.*, 2337 (1962); I. J. Borowitz and R. Virkhaus, *J. Am. Chem. Soc.*, **85**, 2183 (1963).


III′

[6] K. Dimroth and R. Ploch, *Chem. Ber.*, **90**, 801 (1957).

[7] J. R. Cox, Jr., and F. H. Westheimer, *J. Am. Chem. Soc.*, **80**, 5441 (1958).

[8] L. Keay and E. M. Crook, *J. Chem. Soc.*, 710 (1961).

Table I

Oxidation of Phosphites or Phosphines by Means of Monobromocyanoacetamide and Benzyl Alcohol[a]

Phosphite or phosphine	Product				
	Phosphate or phosphine oxide	Yield, %	B.p., °C. (mm.)	Benzyl bromide, %	Cyanoacetamide, %
$(C_2H_5O)_3P$	$(C_2H_5O)_3P{=}O$	44	104–110 (13)	52	83
		72[b]	101–104 (12)	98	73
$(C_4H_9O)_3P$	$(C_4H_9O)_3P{=}O$	50	92–99 (0.25–0.40)	100	49
		55[b]	91–93 (0.15)	90	
$(C_6H_5O)_2POC_2H_5$	$(C_6H_5O)_2P(O)OC_2H_5$[c]	50	146–148 (0.20)	58	64
		62[b]	138–143 (0.20)	56	
$(p\text{-}O_2NC_6H_4O)_2POC_2H_5$	$(p\text{-}O_2NC_6H_4O)_2P(O)OC_2H_5$	76	M.p. 127–133	52	45
$(C_6H_5O)_3P$	$(C_6H_5O)_3P{=}O$	90	175–176 (0.21)	73	96
$(C_4H_9)_3P$	$(C_4H_9)_3P{=}O$	98	120–126 (0.25)	87	93
$(C_6H_5)_3P$	$(C_6H_5)_3P{=}O$	88	M.p. 148–154	98	74

[a] At room temperature. [b] The reaction was carried out at −60°. [c] *Anal.* Calcd. for $C_{14}H_{15}O_4P$: C, 60.50; H, 5.95. Found: C, 60.43; H, 5.41.

Table II

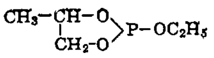
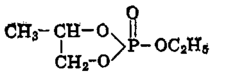
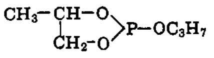
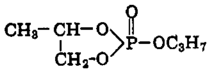
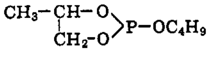
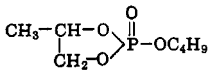
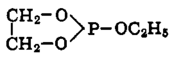
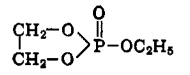
Oxidation of Phosphites or Phosphines by Means of Monobromocyanoacetamide and Allyl Alcohol[a]

Phosphite or phosphine	Product				
	Phosphate or phosphine oxide	Yield, %	B.p., °C. (mm.)	Allyl bromide, %	Cyanoacetamide, %
$(C_2H_5O)_3P$	$(C_2H_5O)_3P{=}O$	76	104–105 (11.5)		58
$(C_4H_9O)_3P$	$(C_4H_9O_3)P{=}O$	72	110–112 (0.45–0.50)	55	61
$(C_6H_5O)_2POC_2H_5$	$(C_6H_5O)_2P(O)OC_2H_5$	65	135–140 (0.15)	48	69
		62[b]	138–143 (0.20)	56	75
$(C_6H_5O)_3P$	$(C_6H_5O)_3P{=}O$	85	187–188 (0.55)	10	98
$(C_6H_5)_3P$	$(C_6H_5)_3P{=}O$	81	M.p. 149–152	10	87

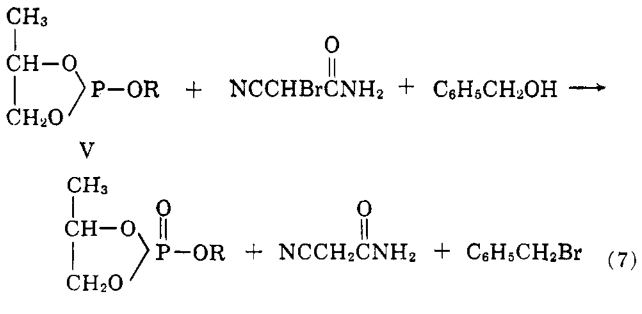
[a] At room temperature. [b] The reaction was carried out at −60°.

Table III

Oxidation of Alkyl Propylene Phosphites or Ethyl Ethylene Phosphite by Means of Monobromocyanoacetamide and Benzyl Alcohol

Phosphite	Product				
	Phosphate	Yield, %	B.p., °C. (mm.)	Benzyl bromide, %	Cyanoacetamide, %
		68	120–128 (4–5)	90	94
		60[a]	102–108 (1.2–1.3)	61[b]	97
		84	110–120 (1.2)	78	89
		37	115–120 (0.25)	54	56
		36	72–75 (0.04)		95

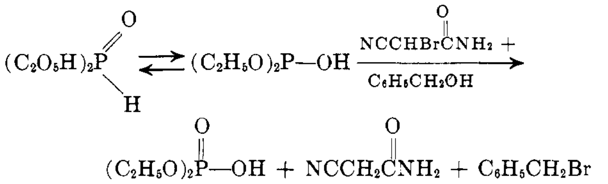
[a] Allyl alcohol was used in the place of benzyl alcohol. [b] The yield of allyl bromide.


(7)

hydrofuran was added to dissolve it, and, after the solution was kept standing overnight, ethyl ethylene phosphate was obtained in 36% yield. The poor yield of ethyl ethylene phosphate compared with that of ethyl propylene phosphate is presumably due to the instability of the ethylene ring which may have caused undesirable side reactions.

Finally, it is noteworthy that dialkyl phosphites are also successfully oxidized by this method. When diethyl phosphite was treated with monobromocyanoacetamide and benzyl alcohol at room temperature, a 96% yield of diethyl phosphate and a quantitative yield of benzyl bromide were obtained. Diethyl phosphate was identified by paper chromatography (eq. 8).

This result suggests that dialkyl phosphite such as dibenzyl phosphite can be used in the phosphorylation of alcohols by the analogous process mentioned earlier[1] to give the mixed secondary phosphate directly.



$$(C_2O_5H)_2\overset{\overset{\displaystyle O}{/\!/}}{\underset{\underset{\displaystyle H}{\diagdown}}{P}} \rightleftharpoons (C_2H_5O)_2P{-}OH \xrightarrow[C_6H_5CH_2OH]{NCCHBr\overset{\overset{\displaystyle O}{\|}}{C}NH_2\ +} (C_2H_5O)_2\overset{\overset{\displaystyle O}{\|}}{P}{-}OH + NCCH_2\overset{\overset{\displaystyle O}{\|}}{C}NH_2 + C_6H_5CH_2Br \quad (8)$$

Further studies on oxidation of diesters and monoesters of phosphorous acid and their application to the phosphorylation of naturally occurring compounds are now in progress.

Experimental

Melting points and boiling points are uncorrected.

Reagents.—Monobromocyanoacetamide,[1] triethyl phosphite,[9] tri-*n*-butylphosphine,[10] diethyl phosphite,[11] ethyl ethylene phosphite,[8] and alkyl propylene phosphites[12] were prepared by literature procedures. Triphenyl phosphite, tri-*n*-butyl phosphite, and triphenylphosphine were obtained from a commercial source and purified by distillation or recrystallization. The solvents and alcohols were purified and dried by ordinary procedures.

Preparation of Ethyl Di-*p*-nitrophenyl Phosphite.—A solution of ethyl phosphorodichloridite (7.4 g., 0.05 mole) in 25 ml. of ether was added dropwise over a period of 15 min. to sodium *p*-nitrophenoxide (16.0 g., 0.1 mole) suspended in 100 ml. of ether at −5° with vigorous stirring. Then, a further 100 ml. of ether was added to the mixture and it was gently refluxed for an additional 30 min. After separation of sodium chloride, about 100 ml. of ether was removed from the filtrate under reduced pressure. The precipitate of ethyl di-*p*-nitrophenyl phosphite was filtered, washed twice with ether (10 ml.), and dried over P_2O_5, m.p. 65°, 5.7 g., 32%.

Anal. Calcd. for $C_{14}H_{13}N_2O_7P$: N, 7.95. Found: N, 7.92.

Ethyl di-*p*-nitrophenyl phosphite is a very hygroscopic, unstable, crystalline compound which turns brownish when stored for more than 2 weeks.

Reaction of Ethyl Di-*p*-nitrophenyl Phosphite with Monobromocyanoacetamide and Ethanol.—To a solution of monobromocyanoacetamide (0.81 g., 0.005 mole) and ethanol (0.30 g.) in 20 ml. of tetrahydrofuran (THF) was added dropwise a solution of ethyl di-*p*-nitrophenyl phosphite (1.76 g., 0.005 mole) in 10 ml. of THF at −40° with exclusion of moisture. After the mixture was kept standing overnight at room temperature, it was evaporated to dryness under reduced pressure and the residue was treated with 5 ml. of water to dissolve cyanoacetamide. The remaining crystalline compound was dried over P_2O_5 giving 1.38 g. (73%) of crude ethyl di-*p*-nitrophenyl phosphate, m.p. 128–136°; one recrystallization from ethyl acetate raised this to 134–137°. A mixture melting point with an authentic sample was not depressed. From the aqueous solution, crude cyanoacetamide (0.75 g.) was isolated after evaporation of water. Recrystallization from ethanol gave 0.21 g. (52%) of pure cyanoacetamide, m.p. 116–119°.

Reaction of Ethyl Di-*p*-nitrophenyl Phosphite with Monobromocyanoacetamide and *n*-Propyl Alcohol.—A solution of ethyl di-*p*-nitrophenyl phosphite (7.32 g., 0.021 mole) in 20 ml. of THF was added to a solution of *n*-propyl alcohol (4 ml.) and monobromocyanoacetamide (3.36 g., 0.021 mole) in 50 ml. of THF over a period of 15 min. at room temperature. After the mixture was kept standing overnight at room temperature, the solvent was removed under reduced pressure. The residue was washed with 30 ml. of water to dissolve cyanoacetamide. This left 1.80 g. of product A, m.p. 116–118°. When this product A was treated with sodium ethoxide in the same manner as shown below, 0.52 g. of an unknown compound (b.p. 107–108° at 15 mm.) was obtained. This was compared with authentic specimens by gas chromatography and proved to be a mixture of triethyl phosphate and *n*-propyl diethyl phosphate (the ratio was about 3:2).

Preparation of *n*-Propyl Di-*p*-nitrophenyl Phosphate.—A solution of *n*-propyl phosphorodichlorodate (4.4 g., 0.025 mole) in 30 ml. of ether was added dropwise to a suspension of sodium *p*-nitrophenoxide (8.0 g., 0.05 mole) in 50 ml. of ether at room temperature. The mixture was gently refluxed for 2 hr. and sodium chloride was separated. After the mixture was kept standing overnight at room temperature, white needles precipitated, which were recrystallized from ether giving 3.25 g. (34%) of *n*-propyl di-*p*-nitrophenyl phosphate, m.p. 72–73°.

Anal. Calcd. for $C_{15}H_{15}N_2O_8P$: N, 7.33. Found: N, 7.32.

Reaction of *n*-Propyl Di-*p*-nitrophenyl Phosphate with Sodium Ethoxide.—Sodium (0.23 g., 0.01 g.-atom) was dissolved in 10 ml. of ethanol and the solution which resulted was added dropwise to a solution of *n*-propyl di-*p*-nitrophenyl phosphate (1.91 g., 0.005 mole) in 20 ml. of ethanol with stirring at −70°. After the mixture was kept standing overnight at room temperature, ethanol was removed under reduced pressure and 10 ml. of ether was added to the residue. The mixture was filtered to remove sodium *p*-nitrophenoxide (1.85 g.) and the filtrate was distilled to give *n*-propyl diethyl phosphate (0.64 g., 66%, b.p. 127° at 17 mm.).

Reaction of Ethyl Di-*p*-nitrophenyl Phosphite with Monobromocyanoacetamide and Benzyl Alcohol.—Monobromocyanoacetamide (2.30 g., 0.014 mole) and benzyl alcohol (1.75 g., 0.016 mole) were added to ethyl di-*p*-nitrophenyl phosphite (prepared from 2.93 g., 0.02 mole, of ethyl phosphorodichloridite and 6.44 g., 0.04 mole, of sodium *p*-nitrophenoxide) in 100 ml. of ether at room temperature. After standing overnight, the mixture was filtered to remove a white precipitate (2.87 g.) which was washed with 20 ml. of water to dissolve cyanoacetamide. The undissolved precipitate was dried *in vacuo* over P_2O_5, giving 2.05 g. of ethyl di-*p*-nitrophenyl phosphate, m.p. 127–133°. The aqueous solution was evaporated to dryness under reduced pressure and the solid residue (1.18 g.) was recrystallized from 3 ml. of ethanol giving 0.53 g., 45%, of cyanoacetamide. After removal of ether from the first filtrate, benzyl bromide (1.25 g., 52%, b.p. 53° at 2 mm.) was obtained by fractionation and the residue gave crude ethyl di-*p*-nitrophenyl phosphate (2.25 g., m.p. 118–130°) which was recrystallized from ethyl acetate. The total yield of ethyl di-*p*-nitrophenyl phosphate was 76%.

Oxidation of Triethyl Phosphite by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of triethyl phosphite (1.66 g., 0.01 mole) in 10 ml. of ether was added to a suspension of monobromocyanoacetamide (1.63 g., 0.01 mole) and benzyl alcohol (1.10 g., 0.01 mole) in 20 ml. of ether with vigorous stirring at room temperature. After standing overnight, the mixture was filtered to remove cyanoacetamide (0.53 g., 83%, m.p. 115–117°), and ether was removed from the filtrate. The residue was distilled giving benzyl bromide (0.89 g., 52%, b.p. 88–90° at 16 mm.), triethyl phosphate (0.81 g., 44%, b.p. 106–108° at 16 mm.), and a fraction boiling at 100–125° at 0.14 mm. (1.01 g., redistillation narrowed the boiling point to 100–103° at 0.03 mm.) whose infrared spectrum suggested benzyl diethyl phosphate. When the addition of triethyl phosphite was carried out at −60°, the yield of triethyl phosphate was increased to 72% and no benzyl diethyl phosphate was obtained.

Oxidation of Tri-*n*-Butyl Phosphite, Ethyl Diphenyl Phosphite, or Triphenyl Phosphite by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of triphenyl phosphite (3.10 g., 0.01 mole) in 10 ml. of ether was added dropwise to a suspension of monobromocyanoacetamide (1.63 g., 0.01 mole) and benzyl alcohol (1.10 g., 0.01 mole) in 20 ml. of ether with vigorous stirring at room temperature. A white precipitate, cyanoacetamide, soon appeared. After the mixture was kept standing overnight, it was filtered to remove cyanoacetamide, and ether was removed from the filtrate. The residue was distilled giving benzyl bromide (1.24 g., 73%, b.p. 63–65° at 5 mm.) and triphenyl phosphate (2.88 g., 90%, b.p. 175–176° at 0.21 mm.). Similarly, tri-*n*-butyl phosphate and ethyl diphenyl phosphate were obtained from the corresponding phosphites. The results are summarized in Table I.

Oxidation of Tri-*n*-butylphosphine by Means of Monobromocyanoacetamide and Benzyl Alcohol.—Tri-*n*-butylphosphine was oxidized in a similar manner as mentioned above to give a 98% yield of tri-*n*-butylphosphine oxide. In this case, tetrahydrofuran was used as solvent (Table I).

Oxidation of Triphenylphosphine by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of triphenylphosphine (5.24 g., 0.02 mole) in 30 ml. of chloroform was added dropwise for a period of 20 min. to a suspension of monobromocyanoacetamide (3.26 g., 0.02 mole) and benzyl alcohol (2.2 g., 0.02 mole) in 20 ml. of ether with vigorous stirring at room temperature. After standing overnight, the mixture was fil-

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(9) A. H. Ford-Moore and B. J. Perry, *Org. Syn.*, **31**, 111 (1951). This compound was treated with sodium and distilled.

(10) W. C. Davies and W. J. Jones, *J. Chem. Soc.*, 33 (1929).

(11) H. McCombie, B. C. Saunders, and G. J. Stacey, *ibid.*, 380 (1945).

(12) T. Mukaiyama, T. Hata, and K. Tasaka, unpublished.

tered to remove cyanoacetamide (1.24 g., 74%, m.p. 114–117°, m.m.p. 117–120°). The filtrate was distilled giving benzyl bromide (3.37 g., 98%, b.p. 60° at 3.5 mm.). The residue gave 5.9 g. of crude triphenylphosphine oxide (m.p. 70–120°) which was washed with 5 ml. of ether and with 5 ml. of water giving 4.87 g. of pure triphenyl phosphine oxide, m.p. 149–152°.

Oxidation of Phosphites or Phosphines by Means of Monobromocyanoacetamide and Allyl Alcohol.—To a solution of monobromocyanoacetamide (1.63 g., 0.01 mole) and allyl alcohol (0.6 g., 0.011 mole) in 20 ml. of ether was added dropwise with vigorous stirring a solution of tri-*n*-butyl phosphite (2.60 g., 0.01 mole) in 10 ml. of ether at room temperature. A white precipitate, cyanoacetamide, soon appeared. The mixture was kept standing overnight at room temperature and was filtered to remove cyanoacetamide (0.51 g., 61%). After removal of ether from the filtrate, allyl bromide (0.67 g., 55%, b.p. 72–76°) and tri-*n*-butyl phosphate (1.90 g., 72%, b.p. 110–120° at 0.45 mm.) were obtained by fractionation. Similarly, various phosphates and phosphine oxides were obtained from the corresponding phosphites or phosphines (see Table II).

Oxidation of Triphenyl Phosphine by Means of Monobromocyanoacetamide and Allyl Alcohol.—A solution of triphenyl phosphine (2.62 g., 0.01 mole) in 25 ml. of chloroform was added dropwise to a suspension of monobromocyanoacetamide (1.63 g., 0.01 mole) and allyl alcohol (1.04 g., 0.02 mole) in 15 ml. of chloroform with vigorous stirring at room temperature. The reaction started soon with liberation of heat. After standing overnight, the mixture was filtered to remove cyanoacetamide (0.73 g., 87%, m.p. 107–113°) and from the filtrate, allyl bromide (10%, b.p. 71–72°) was obtained. The residue solidified soon and gave triphenyl phosphine oxide (2.23 g., 80%, m.p. 145–150°).

Oxidation of Alkyl Propylene Phosphites by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of ethyl propylene phosphite (1.50 g., 0.01 mole) in 10 ml. of ether was added dropwise to a suspension of monobromocyanoacetamide (1.63 g., 0.01 mole) and benzyl alcohol (1.10 g., 0.01 mole) in ether with vigorous stirring at room temperature. The reaction proceeded with liberation of heat and a white precipitate, cyanoacetamide, appeared soon. After standing overnight at room temperature, the mixture was filtered to remove cyanoacetamide (0.80 g., 95%). After removal of ether from the filtrate, benzyl bromide (1.54 g., 90%) and ethyl propylene phosphate (1.13 g., 68%, b.p. 120–128° at 4–5 mm., lit.[13] b.p. 105–108° at 3 mm.) were obtained by fractionation.

Anal. Calcd. for $C_5H_{11}O_4P$: C, 36.15; H, 6.67. Found: C, 36.62; H, 7.13.

Similarly, propyl propylene phosphate and butyl propylene phosphate were prepared from the corresponding cyclic phosphites (see Table III).

Oxidation of Ethyl Ethylene Phosphite by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of ethyl ethylene phosphite (1.40 g., 0.01 mole) in 10 ml. of ether was added dropwise to a suspension of monobromocyanoacetamide (1.63 g., 0.01 mole) and benzyl alcohol (1.10 g., 0.01 mole) with vigorous stirring at room temperature. Since a viscous, oily product was formed during the addition of the phosphite, 20 ml. of THF was added to dissolve it. After standing overnight, the solvent was removed and the residue was filtered to remove cyanoacetamide (95%). From the filtrate, benzyl bromide (0.95 g., 56%, b.p. 55–56° at 2.5 mm.) and ethyl ethylene phosphate (0.55 g., 36%, b.p. 72–75° at 0.004 mm.) were obtained by fractionation.

Oxidation of Diethyl Phosphite by Means of Monobromocyanoacetamide and Benzyl Alcohol.—A solution of diethyl phosphite (1.40 g., 0.01 mole) in 10 ml. of THF was added dropwise to a solution of monobromocyanoacetamide (1.63 g., 0.01 mole) and benzyl alcohol (1.10 g., 0.01 mole) in 20 ml. of THF at room temperature. After standing overnight at room temperature, the mixture was filtered to remove cyanoacetamide (0.74 g., 94%). The filtrate was distilled giving benzyl bromide (1.71 g., 100%) and diethyl hydrogen phosphate (1.47 g., 96%, b.p. 113–115° at 0.025 mm.). Diethyl hydrogen phosphate was identified by paper chromatography, R_f 0.70 (solvent system: *n*-propyl alcohol–concentrated NH_4OH–water, 6:3:1).

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Yohimbane Derivatives. I. The Preparation of 3-Substituted Yohimbane Derivatives

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The preparation of 3-cyano-, 3-methyl-, 3-phenyl-, and 3-benzylyohimbanes is described. 3-Dehydroyohimbane salts (II) react with cyanide to give 3-cyanoyohimbanes (I). Compounds I or II treated with methyllithium or phenyllithium gave the corresponding 3-methyl- and 3-phenylyohimbanes (III); benzylmagnesium bromide gave 3-benzylyohimbane. Oppenauer oxidation of 3-methyl-17β-hydroxyyohimbane (IIIc) and 3,16α-dimethyl-17α-hydroxyyohimbane (IIId) gave, respectively, 3-methylyohimbone (IVa) and 3,16α-dimethylyohimbone (IVb). The position of substitution was supported by the n.m.r. spectra and by failure to give 3-dehydroyohimbanes when oxidized with *t*-butyl hypochlorite. The stereochemistry at C-3 was not firmly established since the rotation data tended to support the α-configuration but the infrared data were inconclusive. The infrared spectrum of 3-dehydroyohimbane base (Va) showed a strong NH band which led us to propose a different structure from that reported in the literature.

Of the many investigations in the field of the yohimbanoid[1] alkaloids which have been reported in recent years, a considerable number have concerned themselves with the chemistry of the C-3 position.[2] These studies have included acid-[3,4] and base-catalyzed[4,5] epimerizations, oxidative rearrangements,[6] and spectral correlations.[2a,7] Convenient methods have been devised for the oxidation of yohimbanoids[1] to give 3-dehydroyohimbanoids[8–10] and the latter have been re-

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[1] In this paper, the term "yohimbanoids" refers to the pentacyclic skeleton without regard to the stereochemistry of the ring junctions whereas "yohimbanes" refers to compounds having the normal or all *trans* configuration which is present in yohimbine.

[2] Much of this work is reviewed in the following articles: (a) E. Wenkert and D. K. Roychaudhuri, *J. Am. Chem. Soc.*, **80**, 1613 (1958); (b) P. E. Aldrich, *et al.*, *ibid.*, **81**, 2481 (1959).

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