temperature, the organic phase was carefully siphoned from the mixture of aqueous phase and unchanged phosphorus. The organic phase was neutralized with 2 drops of concentrated hydrochloric acid, dried over anhydrous sodium sulfate, and distilled under reduced pressure to obtain 12.7 g. (4%) of tris(2-carbethoxyethyl)phosphine, b.p. 160–180° (0.3 mm.) (lit.,[5] b.p. 193–194/1 mm.), identified by comparison of its infrared spectrum with that of an authentic sample, and 28.1 g. (8%) of tris(2-carbethoxyethyl)phosphine oxide, b.p. 205–220° (0.5 mm.). The latter was redistilled to obtain an analytical sample, b.p. 199–203° (0.2 mm.), $n^{25}D$ 1.4682.

Anal. Calcd. for $C_{15}H_{27}O_7P$: C, 51.42; H, 7.77; P, 8.84. Found: C, 51.85; H, 7.58; P, 8.84.

From the aqueous phase was recovered 15.9 g. (51.2%) of white phosphorus.

Reaction of Aqueous Ethanolic Potassium Hydroxide with Phosphorus Followed by Addition of Acrylamide.—To a well stirred mixture of 9.0 g. (0.29 g.-atom) of finely divided white phosphorus and 100 ml. of 2B ethanol was added dropwise during 15 min. 15 ml. (0.15 equivalent) of 10 *N* aqueous potassium hydroxide solution. The temperature was maintained at 5–10° during the addition and for an additional 45 min. Most, but not all, of the phosphorus dissolved leaving a deep red solution. The n.m.r. spectrum of the solution showed only a triplet centered at −2 p.p.m. (relative to 85% phosphoric acid) corresponding to hypophosphite ion.

To the deep red solution, stirred at 5–10°, was added dropwise during 15 min. a solution of 32.0 g. (0.45 mole) of acrylamide in 75 ml. of 2B ethanol. Neither a color change nor an exotherm was observed. The mixture was stirred at 5–10° for an additional 30 min. and allowed to warm to room temperature. The color lightened on standing, and the mixture became colorless after standing overnight. A small amount of oil separated from the reaction mixture and was collected. Treatment with methanol and acetone gave 4.6 g. (6%) of tris(2-carbamoylethyl)phosphine oxide, m.p. 200–204°. Attempts to obtain other products from the main body of the reaction mixture were unsuccessful.

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A Selective Phosphorylation by Means of Dibromomalonamide and Trialkyl Phosphites

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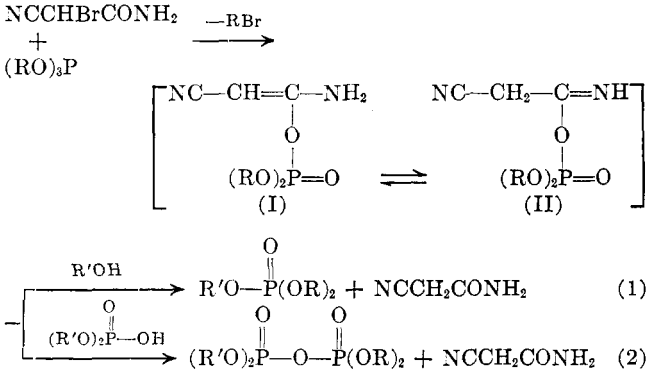
A selective phosphorylation of alcohols and phosphates forming mixed esters of phosphoric acid and unsymmetrical pyrophosphates by the use of one mole of dibromomalonamide and two moles of trialkyl phosphite has been investigated. By this method, various phosphates and pyrophosphates were obtained in high yields under mild conditions.

It has been demonstrated in a previous paper that trialkyl phosphites react with α-bromocyanoacetoamide to give a reactive intermediate, enol- (I) or imidoylphosphate (II), from which either mixed esters of phosphoric acid or unsymmetrical pyrophosphates can be obtained by further reaction with an alcohol or with diethyl hydrogen phosphate.[1]



A selective phosphorylation can be effected successfully by this method without isolating the intermediate, I or II, since it reacts exclusively with nucleophilic reagents such as alcohols, amines, and dialkyl hydrogen phosphates, under mild conditions, but it does not react with trialkyl phosphite.

In the present experiment, a selective phosphorylation of alcohols and phosphates was tried further by the use of dibromomalonamide and trialkyl phosphites.

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

When dibromomalonamide was treated with two molecular equivalents of trialkyl phosphite in a large excess of anhydrous *n*-propyl alcohol at room temperature, an instantaneous reaction took place and *n*-propyl diethyl phosphate was obtained in high yield. A similar result was obtained when two equivalents of *n*-propyl alcohol were used in the above reaction.

$$CBr_2(CONH_2)_2 + (EtO)_3P + n\text{-}PrOH \longrightarrow CHBr(CONH_2)_2 + n\text{-}PrO{-}P(OEt)_2 + EtBr \quad (3)$$

$$CHBr(CONH_2)_2 + (EtO)_3P + n\text{-}PrOH \longrightarrow CH_2(CONH_2)_2 + n\text{-}PrO{-}P(OEt)_2 + EtBr \quad (4)$$

The reaction is considered to involve two steps of phosphorylation (equations 3 and 4). First, one mole of dibromomalonamide and one mole of triethyl phosphite were used for the phosphorylation of one mole of *n*-propyl alcohol, and *n*-propyl diethyl phosphate and monobromomalonamide were obtained in good yields. In a second reaction, one mole of monobromomalonamide and one mole of triethyl phosphite were treated with one mole of *n*-propyl alcohol; *n*-propyl diethyl phosphate was also obtained in good yield along with malonamide. The mechanism of these reactions is believed to be similar to that already discussed for α-bromocyanoacetoamide.

The generality of the technique was established by the preparation of a number of simple alkyl diethyl phosphates (see Table I).

TABLE I

PHOSPHORYLATION OF ALCOHOLS AND PHENOLS BY MEANS OF DIBROMOMALONAMIDE AND TRIETHYL PHOSPHITE

Alcohols and phenols	Phosphates (products)	Yield, %	B.p., °C./mm.
Methanol	Methyl diethyl	78	100–102/24
Ethanol	Triethyl	89	60–63/0.6
Ethanol[a]	Triethyl	74	90–92/12
n-Propyl alcohol	*n*-Propyl diethyl	72	109–114/10.5
n-Propyl alcohol[b]	*n*-Propyl diethyl	72	109/16
n-Propyl alcohol[a]	*n*-Propyl diethyl	77	106–108/8
Isopropyl alcohol	Isopropyl diethyl	73	91/11
n-Butyl alcohol	*n*-Butyl diethyl	94	82–87/3–5
Cyclohexanol	Cyclohexyl diethyl	28	59–60/4
Phenol	Phenyl diethyl	86	90–108/1.0
p-Nitrophenol	*p*-Nitrophenyl diethyl	72	160–165/0.45

[a] Phosphorylation by means of one mole of bromomalonamide and one mole of triethyl phosphite (equation 4). [b] Phosphorylation by means of one mole of dibromomalonamide and one mole of triethyl phosphite (equation 3).

In another reaction, preparation of unsymmetrical pyrophosphates by the reaction of diethyl hydrogen phosphate with dibromomalonamide and trialkyl phosphites, was tried.

When a solution of two moles of diethyl hydrogen phosphate and two moles of trimethyl phosphite was treated with one mole of dibromomalonamide at 0°, the reaction started instantly and malonamide soon separated from the solution; unsymmetrical dimethyl diethyl pyrophosphate was obtained in a 68% yield (equation 5).

$$CBr_2(CONH_2)_2 + 2(MeO)_3P + 2(EtO)_2P(=O)-OH \xrightarrow{-2MeBr} 2(MeO)_2P(=O)-O-P(=O)(OEt)_2 + CH_2(CONH_2)_2 \quad (5)$$

Similarly, tetraethyl pyrophosphate was obtained in a 78% yield by the reaction of diethyl hydrogen phosphate with triethyl phosphite and dibromomalonamide. In this reaction, a very small amount of liquid having a lower boiling point (40–50°/0.5 mm., $n^{24}D$ 1.4039) was obtained, which is probably triethyl phosphate.

The formation of pyrophosphate by the preceding reaction is considered to occur *via* two steps as is shown in the case of phosphorylation of the alcohol. These two steps also occurred separately, and tetraethyl pyrophosphate was obtained in good yield.

The results of phosphorylation of diethyl hydrogen phosphate by means of dibromomalonamide and trialkyl phosphites are summarized in Table II.

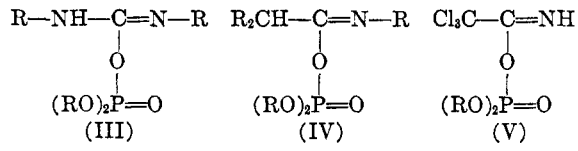
TABLE II

PHOSPHORYLATION OF DIETHYL HYDROGEN PHOSPHATE BY MEANS OF DIBROMOMALONAMIDE AND TRIALKYL PHOSPHITES

Phosphites	Pyrophosphates (products)	Yield, %	B.p., °C./mm.
Trimethyl	*unsym*-Dimethyl diethyl	68	125–128/0.06
Triethyl	Tetraethyl	78	126–131/0.55
Tri-*n*-butyl	*unsym*-Diethyl di-*n*-butyl	62	108–114/0.01
Triethyl[a]	Tetraethyl	78	108–110/0.16
Triethyl[b]	Tetraethyl	69	112–116/0.35

[a] Phosphorylation by means of one mole of dibromomalonamide and one mole of triethyl phosphite. [b] Phosphorylation by means of one mole of bromomalonamide and one mole of triethyl phosphite.

It is interesting that the two intermediate imidoyl-phosphates postulated in this reaction are similar in structure to the phosphates III,[2] IV,[3] and V,[4] which are known to be excellent phosphorylating agents. They are formed by the reaction of dialkyl hydrogen phosphate and organic dehydrating agents, such as carbodiimide, ketenimine, and trichloroacetonitrile.



Attempts to isolate the intermediate by the reaction of either dibromomalonamide or bromomalonamide with triethyl phosphite were unsuccessful. Although an analytically pure imidoyl-phosphate has not been isolated, the presence of the intermediate was supported by the following experiments; the reaction of one mole of dibromomalonamide with one mole of triethyl phosphite led to an oily product, which reacted with *n*-propyl alcohol exothermically to give *n*-propyl diethyl phosphate in 40% yield along with bromomalonamide. A similar result was obtained from bromomalonamide; again *n*-propyl diethyl phosphate was obtained.

In conclusion, it was noted that phosphorylation by means of dibromomalonamide and phosphites (dibromomalonamide method) gives, as with that of α-bromocyanoacetamide and phosphites (cyanoacetamide method) shown in the previous paper, excellent results under mild conditions. Between these two methods of phosphorylation, the bromocyanoacetamide method proved remarkably effective for the synthesis of unsymmetrical pyrophosphates, while the dibromomalonamide method was found to be more effective for the preparation of pure mixed esters of phosphoric acid in excellent yields.

Experimental

All boiling points are uncorrected.

Reagents.—Dibromomalonamide, bromomalonamide,[5] diethyl hydrogen phosphate,[6] and trimethyl phosphite[7] were prepared by literature procedures. Triethyl phosphite and tri-*n*-butyl phosphite were obtained from a commercial source and purified by distillation.

Reaction of n-Propyl Alcohol with Dibromomalonamide (1 mole) and Triethyl Phosphite (2 moles).—To a solution of triethyl phosphite (3.32 g., 0.02 mole) and anhydrous *n*-propyl alcohol (50 ml.), thoroughly pulverized dibromomalonamide (2.60 g., 0.01 mole) was added in portions over a period of 5 min. with vigorous stirring at room temperature. A white precipitate of malonamide soon separated from solution. The solution was allowed to stand overnight at room temperature and was filtered. After removal of ethyl bromide and the excess *n*-propyl alcohol, 2.82 g. (72%) of *n*-propyl diethyl phosphate, b.p. 109–114°/10.5 mm., was obtained. Similarly, methyl diethyl-, isopropyl diethyl-, *n*-butyl diethyl phosphate and triethyl phosphate were prepared from dibromomalonamide, triethyl phosphite, and corresponding alcohols. The properties of these compounds together with the yields obtained are summarized in Table I.

n-Propyl diethyl phosphate was also obtained in 72% yield by the reaction of dibromomalonamide (2.60 g., 0.01 mole) and

(2) H. G. Khorana and A. R. Todd, *J. Chem. Soc.*, 2257 (1953).
(3) R. J. Cremlyn, G. W. Kenner, and Sir A. Todd, *ibid.*, 4511 (1960).
(4) F. Crammer and G. Weimann, *Chem. Ber.*, **94**, 996 (1961).
(5) J. V. Backes, R. W. West, and M. A. Whiteley, *J. Chem. Soc.*, **119**, 364 (1921).
(6) A. D. F. Toy, *J. Am. Chem. Soc.*, **70**, 388 (1948).
(7) A. H. Ford-Moore and B. J. Perry, *Org. Syntheses*, **31**, 111 (1951).

triethyl phosphite (1.66 g., 0.01 mole) with anhydrous *n*-propyl alcohol (50 ml.) *via* the same procedure as in the case of the above reaction. The reaction of bromomalonamide (1.81 g., 0.01 mole) and triethyl phosphite (1.66 g., 0.01 mole) with anhydrous *n*-propyl alcohol (50 ml.) also gave *n*-propyl diethyl phosphate in 77% yield (1.50 g.) by the same procedure.

Reaction of Benzyl Alcohol with Dibromomalonamide (1 mole) and Tribenzyl Phosphite (2 moles).—Dibromomalonamide (1.30 g., 0.005 mole) was added to a solution of tribenzyl phosphite (3.52 g., 0.01 mole) in freshly distilled benzyl alcohol (20 ml.). The mixture was stirred for 3 hr. at 5° and allowed to stand at room temperature overnight. The precipitate of malonamide was removed by filtration and 0.76 g. of thiourea[8] was added to the filtrate. The mixture was stirred for 15 min. at room temperature, after which the precipitate which formed was removed by filtration. Then the filtrate was washed with three 35-ml. portions of water. After the addition of a 35-ml. portion of ether, the solution was washed with one more 35-ml. portion of water. The ether solution was dried over anhydrous sodium sulfate after which the ether and excess benzyl alcohol were removed under reduced pressure (0.5 mm.) at 90° until a thick sirup remained. The sirup was dissolved in 30 ml. of anhydrous acetone containing 1.65 g. of sodium iodide. The solution was refluxed for 20 min. and the solvent was removed. After the addition of ether (40 ml.), the ether solution was extracted with two 40-ml. portions of water. The combined water extracts were acidified with hydrochloric acid; a colorless oil separated and was crystallized. The crystals, dibenzyl hydrogen phosphate (0.58 g., 20%), m.p. 79–80°, were recrystallized from ether.

Reaction of Phenol with Dibromomalonamide (1 mole) and Triethyl Phosphite (2 moles).—To a solution of triethyl phosphite (3.32 g., 0.02 mole) and phenol (1.88 g., 0.02 mole) in 50 ml. of anhydrous acetonitrile, thoroughly pulverized dibromomalonamide (2.60 g., 0.01 mole) was added at one time with vigorous stirring at room temperature. The solution was allowed to stand overnight at room temperature and the precipitate of malonamide was separated by filtration. Ethyl bromide and acetonitrile were removed under reduced pressure and the residual material was fractionated; 4.24 g. (86%) of phenyl diethyl phosphate, b.p. 90–103°/1.0 mm., was obtained and 0.10 g. of phenol was recovered.

(8) Thiourea smoothly reacts with benzyl bromide forming a water soluble salt.[9]

(9) A. Bernthsen and H. Klinger, *Chem. Ber.*, **12**, 574 (1879).

Similarly, *p*-nitrophenyl and cyclohexyl diethyl phosphate were obtained by the reaction of the corresponding alcohols with dibromomalonamide and triethyl phosphite. The properties of these compounds together with the yields obtained are listed in Table I.

Reaction of Diethyl Hydrogen Phosphate (2 moles) with Dibromomalonamide (1 mole) and Trimethyl Phosphite (2 moles).—A solution of trimethyl phosphite (1.24 g., 0.01 mole) in 10 ml. of anhydrous acetonitrile was added slowly with stirring to a solution of diethyl hydrogen phosphate (1.54 g., 0.01 mole) and dibromomalonamide (1.30 g., 0.005 mole) in 40 ml. of anhydrous acetonitrile. The temperature was controlled by cooling in an ice bath. A white precipitate, malonamide, separated soon. After addition was completed, the mixture was stirred at 0° for 4 hr. and it was kept at room temperature overnight. Malonamide was removed by filtration. The filtrate was concentrated under reduced pressure and the resulting oil was treated with dry ether (50 ml.) to remove the residual malonamide. After concentration, the solution was distilled under high vacuum. *unsym*-Dimethyl diethyl pyrophosphate, 125–128°/0.06 mm., was obtained in 68% yield (1.78 g.).

In similar fashion, *unsym*-di-*n*-butyl diethyl pyrophosphate was prepared by the reaction of tri-*n*-butyl phosphite with diethyl hydrogen phosphate and dibromomalanamide. The results are summarized in Table II.

Reaction of Diethyl Hydrogen Phosphate (1 mole) with Dibromomalonamide (1 mole) and Triethyl Phosphite (1 mole).—When a mixture of triethyl phosphite (1.66 g., 0.01 mole), diethyl hydrogen phosphate (1.54 g., 0.01 mole) and dibromomalonamide (2.60 g., 0.01 mole) in acetonitrile was treated in the same manner as above, 2.27 g. (78%) of tetraethyl pyrophosphate, b.p. 108–110°/0.16 mm., and 1.64 g. of bromomalonamide were obtained.

Reaction of Diethyl Hydrogen Phosphate with Bromomalonamide and Triethyl Phosphite.—To a solution of bromomalonamide (0.90 g., 0.005 mole) in 30 ml. of anhydrous acetonitrile a solution of triethyl phosphite (0.83 g., 0.005 mole) in 10 ml. of anhydrous acetonitrile was added dropwise (in 5–10 min.) with stirring. The temperature was controlled by cooling in an ice bath. After the crystal of bromomalonamide was dissolved completely, a solution of diethyl hydrogen phosphate in 10 ml. of anhydrous acetonitrile was immediately dropped into the above mixture, and a white precipitate appeared. Then the mixture was treated in the usual manner and 1.01 g. (70%) of tetraethyl pyrophosphate, b.p. 112–116°/0.35 mm., was obtained.

Synthesis of Some Triphenylphosphinalkylimines and Mono- and Dialkylaminotriphenylphosphonium Halides

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The syntheses of some triphenylphosphinalkylimines and their addition reactions with alkyl halides to yield mono- and dialkylaminotriphenylphosphonium halides are reported. The limitation of alkyl halide addition reactions has been described. Sterically hindered *t*-butylmethylamine and *t*-butylethylamine have been prepared through the hydrolysis of the corresponding dialkylaminotriphenylphosphonium halides.

For other investigations in the field of nitrogen chemistry[1] a method for the preparation of di-*tert*-butylamine (I) in rather large quantities was needed. Though the synthesis of I has been reported previously,[2,3] the duplication of these results was not obtained. I could only be prepared in an impure state and in exceedingly small yields. Consequently, other methods of preparation were examined.

A possible route for the preparation of I was through the use of triphenylphosphinimines as intermediates. Staudinger[4] several decades ago found that triphenylphosphinimines added alkyl halides to yield dialkylaminotriphenylphosphonium halides. These compounds could be hydrolyzed to give triphenylphosphinoxide and dialkylamines.

$$[Ph_3\overset{\oplus}{P}-\overset{\ominus}{N}-R \longleftrightarrow Ph_3P{=}N-R] + R'X \longrightarrow [Ph_3P-NRR']^{\oplus}X^{\ominus} \xrightarrow{H_2O} Ph_3P{=}O + HNRR' \quad (1)$$

Horner[5a,b,c] recently increased the usefulness of this synthesis tremendously by introducing a simple method for the preparation of phosphinimines, according to

(1) H. Zimmer, L. F. Audrieth, R. A. Rowe, and Marlies Zimmer, *J. Am. Chem. Soc.*, **77**, 790 (1955).

(2) F. Klages, G. Nober, F. Kircher, and M. Bock, *Ann.*, **547**, 1 (1941).

(3) F. Klages and H. Sitz, *Ber.*, **92**, 2606 (1959).

(4) H. Staudinger and E. Hauser, *Helv. Chim. Acta*, **4**, 861 (1921).