0.95 [d, 6 H, $-CH_2CH(CH_3)_2$]; mass spectrum (70 eV) *m/e* (rel intensity) 289 (M + 1, 0.7), 288 (M, 0.3), 229 (42) 215 (15), 173 (100), 158 (77), 155 (60), 113 (23), 102 (94), 99 (23), 73 (1.7), 57 (47). Anal. Calcd for $C_{14}H_{29}N_2O_4Cl$: N, 8.62. Found: N, 8.40.

***N*-[2-[(Benzyloxycarbonyl)amino]ethyl]-L-leucine Methyl Ester Hydrochloride (2b).** Z-Gly-Leu-OMe (10 mmol, 3.38 g) was treated with 20 ml of 1 M BH_3 in THF according to the procedure for **2a** except that the reaction was stopped after 5 h by the addition of 15 ml of 2 N HCl in MeOH. Work-up gave 1.4 g of starting material and 0.94 g of **2b** after recrystallization from MeOH–Et_2O: yield 26% (44% on basis of recovered **2a**); mp 160–162.5 °C; $[\alpha]^{25}D$ +15.9° (*c* 1, MeOH); TLC (EAE) R_f 0.46; ^1H NMR ($CDCl_3$, Me_4Si) δ 7.33 (5 H, C_6H_5), 5.13 (s, 2 H, $C_6H_5CH_2$), 3.77 (s, 3 H, $COOCH_3$), 0.95 [d, 6 H, $CH_2CH(CH_3)_2$]; mass spectrum (70 eV) *m/e* (rel intensity) 323 (M + 1, 1.9), 322 (M, 1), 263 (100), 215 (1.2), 158 (76), 155 (88), 113 (52), 107 (28), 102 (77), 99 (47), 91 (80). Anal. Calcd for $C_{17}H_{27}N_2O_4Cl$: N, 7.83. Found: N, 7.71.

***N*-[L-2-[(Benzyloxycarbonyl)amino]-4-methylpentyl]-L-leucine Methyl Ester Hydrochloride (2c).** Z-Leu-Leu-OMe (10 mmol, 3.92 g) was treated with 20 mmol of BH_3 according to the procedure for **2b**. The ether extracts gave 3.1 g of starting material **1c**. Chromatography of the residue from the aqueous layer by the usual method gave **2c**, 0.30 g after recrystallization from MeOH–Et_2O: yield 7% (35% based on **1c** recovered); mp 162–164 °C; $[\alpha]^{25}D$ +2.0° (*c* 1, MeOH); TLC (EAE) R_f 0.74; ^1H NMR ($CDCl_3$, Me_4Si) δ 7.33 (5 H, C_6H_5), 5.10 (s, 2 H, $C_6H_5CH_2$), 3.75 (s, 3 H, $COOCH_3$), 0.93 [broad, 12 H, $CH_2CH(CH_3)_2$]; mass spectrum (70 eV) *m/e* (rel intensity) 379 (M + 1, 0.6), 378 (M, 0.4), 319 (37), 271 (1.2), 211 (100), 169 (22), 158 (58), 155 (29), 107 (27), 102 (55), 91 (56). Anal. Calcd for $C_{21}H_{35}N_2O_4Cl$: N, 6.75. Found: N, 6.35.

***N*-[2-(*tert*-Butyloxycarbonyl)amino]ethyl]-L-leucine (4a).** A solution of 1.62 g of **3a** in 30 ml of MeOH and 11.0 ml of 1 N NaOH was allowed to stand at room temperature for 6 h, then concentrated under vacuum to a syrup, diluted with water, and adjusted to pH 6.5 with HCl. The precipitate was collected and washed with a little cold water, wt 1.00 g (73%). Anal. Calcd for $C_{13}H_{26}N_2O_4$: N, 10.21. Found: N, 9.97.

Registry No.—**1a**, 7535-69-5; **1b**, 17331-93-0; **1c**, 3504-37-8; **2a** HCl, 57901-23-2; **2b** HCl, 57901-24-3; **2c** HCl, 57901-25-4; **3a**, 57901-26-5; **4a**, 57901-27-6; BH_3, 13283-31-3.

References and Notes

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A Selective Phosphorylation by Means of Bis(*O*-thiocarbonyl) Disulfides and Triphenylphosphine

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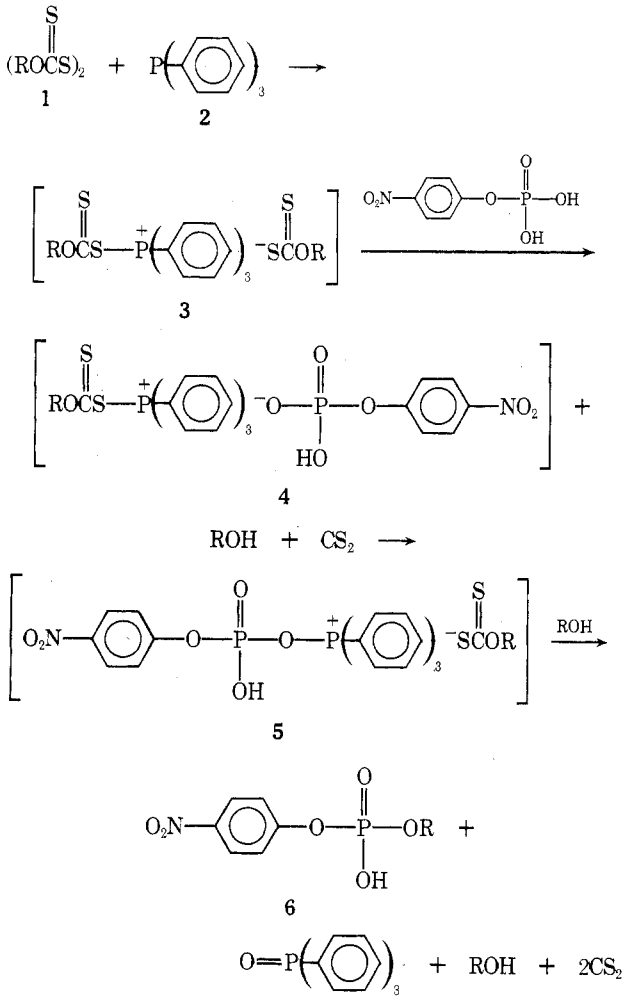
A number of phosphorylating systems have been devised with a view to preparing mixed diesters of phosphoric acid by intermolecular dehydration between monophosphates and alcohols. In order to bring the phosphate into reaction with an alcohol most systems employed initial activation of monophosphates by coupling reagents such as dicyclohexylcarbodiimide,[1] trichloroacetonitrile,[2] or 2,2′-dipyridyl disulfide and triphenylphosphine.[3] In these cases, mixed diesters of phosphoric acid, monophosphate, and pyrophosphate were formed so that the isolation of the expected mixed diesters of phosphoric acid became more difficult.



Recently, it has been demonstrated in this laboratory that phosphorylation of alcohols, phosphates, and nucleosides by the use of 8-quinolyl phosphates gave the corresponding mixed diesters of phosphoric acid, pyrophosphates, and nucleotides in good yields.[4]

The present paper describes a new method for the preparation of mixed diesters of phosphoric acid from monophosphate by the use of bis(*O*-thiocarbonyl) disulfides (**1**) and triphenylphosphine (**2**). The reaction seems to proceed through a phosphonium salt (**3**) which in turn reacts with monophosphate to form an intermediate (**4**), alcohol, and carbon disulfide. The intermediate (**4**) is further converted to phosphoryloxyphosphonium salt (**5**) by intramolecular oxidation–reduction reaction. The intermediate (**5**) reacts with alcohol to give mixed diester of phosphoric acid and triphenylphosphine oxide.

It is known that xanthic acid decomposes under acidic condition to give the corresponding alcohol and carbon disulfide.[5]

When *p*-nitrophenyl phosphate was treated with **1** and **2** at room temperature for 2 h, mixed diesters of phosphoric acid (**6**) were obtained in high yields without the formation of by-product such as symmetrical P^1,P^2-bis(*p*-nitrophenyl) pyrophosphate.

When *p*-nitrophenyl phosphate was treated with 5 equiv each of bis(*n*-butyl) dithiobis(thioformate) (**1c**) and **2** in dry tetrahydrofuran, *n*-butyl *p*-nitrophenyl phosphate (**6c**) was obtained in 85% yield.

Table I. Phosphorylation by Means of Bis(*O*-thiocarbonyl) Disulfides and Triphenylphosphine

Compd	Alkyl	Yield, %, of 6	R_f value[a]
6a	Ethyl	84	0.82
6b	*n*-Propyl	82	0.84
6c	*n*-Butyl	85	0.86
6c	*n*-Butyl	83[b]	0.85
6c	*n*-Butyl	63[c]	0.86
6d	*n*-Pentyl	83	0.87
6e	Benzyl	76	0.86

[a] Paper chromatography was performed by the desending technique using Toyo Roshi No. 51 paper. Solvent system used was 2-propanol–concentrated ammonia–water, 7:1:2 (A). [b] Three equivalents each of reagents, bis(*n*-butyl) dithiobis(thioformate) and triphenylphosphine, were used. [c] One equivalent each of reagents, bis (*n*-butyl) dithioformate and triphenylphosphine.

Table II. Solvent Effects in Phosphorylation by Means of Bis(*n*-butyl)dithiobis(thioformate) and Triphenylphosphine

Solvent	Yield, %, of 6c	Solvent	Yield, %, of 6c
THF	85	Dioxane	76
Pyridine	85	CH_2Cl_2	80
DMF	67	$CHCl_3$	78
CH_3CN	70		

In a similar manner, various mixed diesters of phosphoric acid (6) were obtained in high yields (see Table I).

The effect of the solvent was examined in order to find a suitable condition for the preparation of **6c**. Of various solvents examined, it was found that the yield of **6c** decreased when dimethylformamide (DMF) is used as the solvent (see Table II).

In the above reactions, it was shown that the yields of **6** depend on the amount of **1** and **2**. As an example, when *p*-nitrophenyl phosphate was treated with 3 equiv each of **1c** and **2**, the result was almost the same as those obtained when 5 equiv each of **1c** and **2** were used. However, when 1 equiv each of **1c** and **2** were used, the yield of **6c** remarkably decreased (see Table I).

Finally, the synthesis of 3′-*O*-acetylthymidine 5′-ethyl phosphate was attempted. When 3′-O-acetylthymidine 5′-phosphate was treated with 3 equiv each of bis(ethyl) dithiobis(thioformate) (**1a**) and **2** in dry pyridine at room temperature for 8 h, the corresponding 3′-*O*-acetylthymidine 5′-ethyl phosphate was obtained in 98% yield.

In conclusion, it was noted that this type of phosphorylation was found to be effective for the preparation of pure mixed diesters of phosphoric acid in good yield under mild condition. Differing from the case of the phosphorylation with the use of dicyclohexylcarbodiimide, trichloroacetonitrile, or 2,2′-dipyridyl disulfide and triphenylphosphine, this reaction proceeds without the formation of by-product such as symmetrical pyrophosphate to afford the phosphorylated products in high yields.

Further studies on the synthesis of carboxylic esters are now in progress.

Experimental Section

Descending paper chromatography was performed on Toyo Roshi No. 51 or 51A paper using the solvent system 2-propanol–concentrated ammonia–water, 7:1:2 (solvent A), or 1-butanol–water–concentrated ammonia, 84:16:1 (solvent B). The R_f values of different compounds are given in Table I. Paper electrophoresis was performed in a high-voltage apparatus using Toyo Roshi No. 51A paper and 0.05 M phosphate buffer at pH 7 or 8. The phosphorus compounds were detected by means of a spray of Hanes–Isherwood reagent[6] on paper. Bis(ethyl) (**1a**), bis(*n*-propyl) (**1b**), bis(*n*-butyl) (**1c**), bis(*n*-pentyl) (**1d**), and bis(benzyl) dithiobis(thioformate) (**1e**) were prepared by the procedures in the literature.[7,8] *p*-Nitrophenyl phosphate was prepared by the method of Hata.[9] Triphenylphosphine was obtained from a commercial source and purified by recrystallization. 3′-O-Acetylthimidine 5′-phosphate was prepared by acetylation of thymidine 5′-phosphate with acetic anhydride in dry pyridine.

General Method. Reaction of *p*-Nitrophenyl Phosphate with Bis(*O*-thiocarbonyl) Disulfide and Triphenylphosphine. To a solution of *p*-nitrophenyl phosphate (21.9 mg, 0.1 mmol) and bis(*O*-thiocarbonyl) disulfide (**1**, 0.5 mmol) in dry tetrahydrofuran (1 ml), triphenylphosphine (**2**, 131 mg, 0.5 mmol) was added with vigorous stirring at room temperature for 2 h. To the reaction mixture, 1 ml of water was added and then the mixture was stirred at room temperature for several minutes. The mixture was then concentrated to dryness and the residue was dissolved in water (10 ml). Chromatography was performed on paper using solvent A and B for development. Yield of the compound **6** was determined spectrophotometrically using λ_{max} (H_2O) 291 nm (ϵ 10 000) (pH 7) for alkyl *p*-nitrophenyl phosphate (**6**). The results are summarized in Tables I and II.

3′-*O*-Acetylthymidine 5′-Ethyl Phosphate. To a solution of 3′-*O*-acetylthymidine 5′-phosphate (d-pTOAc, 0.5 mmol) and bis(ethyl) dithiobis(thioformate) (**1a**, 363 mg, 1.5 mmol) in dry pyridine (2.5 ml), triphenylphosphine (**2**, 393 mg, 1.5 mmol) was added and the mixture was kept standing at room temperature. After 8 h, water (5 ml) was added and then the solution was stirred at room temperature for several minutes. The mixture was then concentrated to dryness and the residue was dissolved in water (25 ml) and extracted with ether (three 20-ml portions). The aqueous layer was evaporated to dryness, and the residue was dissolved in water, converted into the sodium form, evaporated to dryness, and dissolved in dry methanol (10 ml). Addition of dry ether (200 ml) gave a precipitate which was collected and dried in vacuo to give 252 mg (98%) of 3′-*O*-acetylthymidine 5′-ethyl phosphate as a white solid: uv (pH 7) λ_{max} (H_2O) 268 nm (ϵ 9600). Paper chromatography (solvent A) R_f 0.72. Paper electrophoresis (0.05 M phosphate, pH 8) Rd-pT 0.54. Anal. Calcd for $C_{14}H_{20}PO_9N_2Na\cdot1.5H_2O$: C, 31.08; H, 4.29; N, 5.18. Found: C, 31.17; H, 4.35; N, 5.23.

Registry No.—**1a**, 502-55-6; **1b**, 3750-28-5; **1c**, 105-77-1; **1d**, 869-91-0; **1e**, 23363-97-5; **2**, 603-35-0; **6a**, 17659-67-5; **6b**, 18123-85-8; **6c**, 18123-87-0; **6d**, 29690-44-6; **6e**, 18123-91-6; d-pTOAc, 4304-30-7; *p*-nitrophenyl phosphate, 330-13-2; sodium 3′-*O*-acetylthymidine 5′-ethyl phosphate, 57821-08-6.

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Phosphorus Tribromide Promoted Allylic Rearrangement of a Tertiary Vinyl Carbinol. Stereochemistry of the Reaction Product and Application to the Synthesis of JH-25, a Potent Juvenile Hormone Mimic

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In recent years considerable attention[1] has been given to the possibility of controlling insect pests by interfering with the action of certain hormones that regulate normal