actly 74 ml of concentrated HCl was added over 1.5 hr, producing an orange–brown precipitate. The solid was taken up in ether, which was washed with $NaHCO_3$ solution. Acidification of the $NaHCO_3$ solution produced 11.4 g of crude solid, which yielded 8 g (60.3%) of white solid upon recrystallization from methylcyclohexane: mp 130–132°, neut equiv 198, ir ($CHCl_3$) 1700 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.67; H, 9.08. Found: C, 66.60; H, 9.09.

Ethyl ester had bp 115° (2 mm); $n^{22}D$ 1.4982; nmr ($CDCl_3$) 1.1–2.2 (m, 18 H), 3.8 (1 H), 3.9–4.3 (m, 3 H); ir (neat) 1700 (C=O), 3530 cm^{-1} (O–H); mass spectrum, *m/e* (rel intensity) 226 (5), 208 (25), 135 (100), 134 (44), 123 (31), 93 (43), 91 (25), 81 (51), 73 (28), (72).

Cyclononane-1,5-dicarboxylic Acid (VII).—1-Carboxybicyclo[4.3.1]decan-10-one (VIa) (1.0 g) was refluxed with 2 g of sodium amide in 50 ml of xylene for 1 week. The xylene was distilled off, the residue was treated with water, and the mixture was then extracted with ether. Next the water suspension was acidified and again extracted with ether. The ether extract was washed with water and dried (Na_2SO_4). Evaporation gave a small amount of white solid and 0.4 g of crude, sticky solid. Recrystallization from ethyl acetate gave 0.3 g of a clear white solid: mp 138–140°.

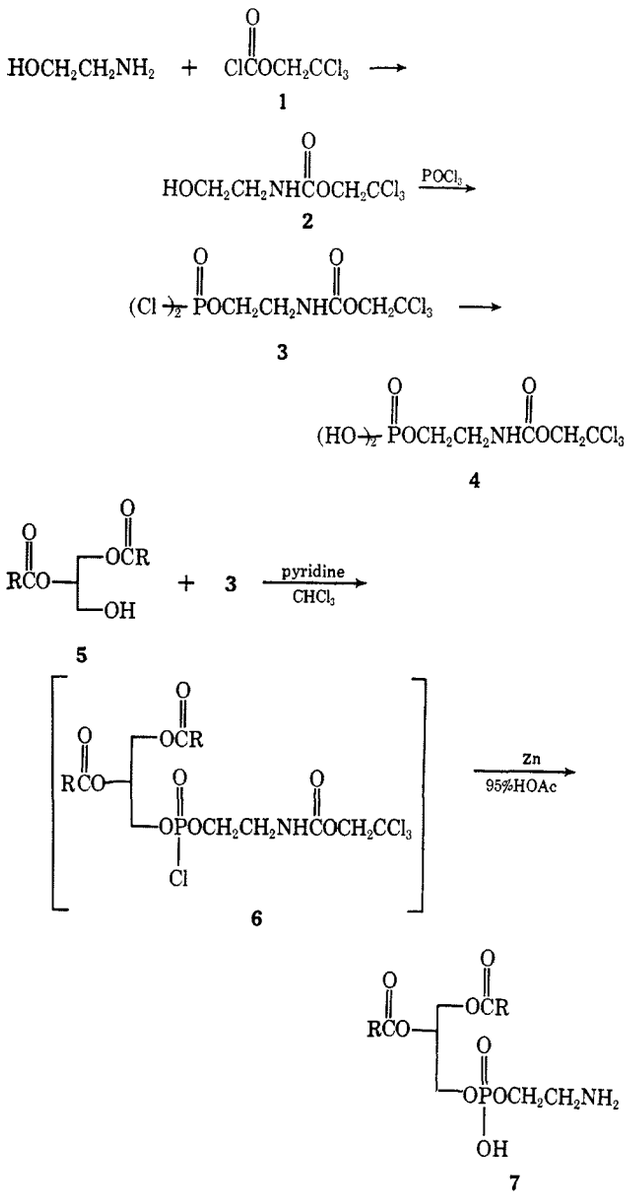
Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.68; H, 8.41. Found: C, 61.36; H, 8.39.

1-Cyclononene-4,8-dicarboxylic Acid (X).—1-Carboxybicyclo[4.3.1]dec-3-en-10-one[4] (IXa) (6.0 g) was refluxed for 1 week with 5 g of sodium amide in 200 ml of xylene. The above work-up, followed by recrystallization from ethyl acetate, produced 0.70 g of a white solid: mp 183–185°.

Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.56. Found: C, 61.89; H, 7.56.

α-(δ-Valeric acid)-γ-vinyl-γ-butyrolactone (XII).—1-Carbethoxybicyclo[4.3.1]dec-3-en-10-one (IXb) (20 g) in a solution of 0.92 g of sodium in 58.3 ml of absolute ethyl alcohol was left at room temperature for 3 days. Treatment with $NaHCO_3$ solution was followed by extraction with ether. From the ether extract, 9.5 g of starting material was recovered. Acidification of the bicarbonate layer, followed by extraction with ether, drying, and evaporation of the ether produced a crude solid. Upon recrystallization from toluene, only about 1 g of pure white solid was recovered. Its infrared spectrum identified it as XII.[5]

Registry No.—VIa, 13348-05-5; VIb, 13348-03-3; VIc, 20440-21-5; VIc (2,4-dinitrophenylhydrazone), 20440-22-6; VII, 20440-24-8; VIII, 20440-23-7; VIII (ethyl ester), 20440-25-9; X, 20440-26-0; XI, 20440-27-1.



Glycerolipids. II.[1] Use of the β,β,β-Trichloroethoxycarbonyl Protecting Group in Phosphatidylethanolamine Synthesis

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Received February 24, 1969

Phosphorylation of 1,2-diacylglycerols with phosphorus oxychloride or with a phosphorylated, protected amine is an approach to phosphatidylethanolamines. This method was limited by (1) the availability of appropriate optically active 1,2-diglycerides and (2) the current use of the carbobenzoxy[2,3] and phthaloyl[2–6] protecting groups, which suffer from complications, including the difficulty of purifying the final products. Our recent facile and direct synthesis of either optical modification of 1,2-diacylglycerols[1] and the use of a new amine protecting group described below, which is removed under reductive, nonhydrolytic conditions, provides renewed impetus for use of this general sequence to phosphatidylethanolamines.

The new protecting group, β,β,β-trichloroethoxycarbonyl, was originally introduced in the total synthesis of cephalosporin C;[7] recently, further demonstrations of its utility,[8] as well as that of the closely related β,β,β-tribromoethoxycarbonyl group,[9] have been reported. Removal of the β,β,β-trichloroethoxycarbonyl group is accomplished with zinc in 90% acetic acid[7] or in refluxing methanol.[8] Under these conditions, phosphatidylethanolamine variants containing mono- or poly-

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unsaturated acyl residues can be expected to be stable. β,β,β-trichloroethylchloroformate (**1**)[10] was allowed to react with ethanolamine in a suspension of dioxane containing magnesium oxide to give the syrupy N-(β,β,β-trichloroethoxycarbonyl)ethanolamine (**2**) in 90–95% yield. Treatment of **2** with excess phosphorus oxychloride in benzene afforded the dichloride **3**. Hydrolysis of **3** gave N-β,β,β-trichloroethoxycarbonyl-2-aminoethylphosphoric acid (**4**), which was isolated as the dicyclohexylamine salt. The purified dicyclohexylamine salt of **4** was converted into the free acid by stirring a solution of the salt with Amberlite IR-120 (H^+) ion-exchange resin.

The synthesis of O-(1,2-dilinoleoyl-*sn*-glycero-3-phosphoryl)ethanolamine (**7**), *i.e.*, 1,2-dilinoleoyl-3-*sn*-phosphatidylethanolamine,[11] is an example of the use of the intermediate **3**. *sn*-Glycerol 1,2-dilinoleate (**5**)[1] was allowed to react in chloroform with a benzene solution of **3** with pyridine as the acid acceptor. The derived diacylglycerophosphate ester chloride **6** was treated without further purification with zinc in 95% acetic acid. Thin layer chromatography of the crude phosphatidylethanolamine **7** showed one ninhydrin positive material and some trace phosphate-containing impurities.[12] Filtration of the crude product through DEAE-cellulose in the acetate form[13] provided 1,2-dilinoleoyl-3-*sn*-phosphatidylethanolamine. The phosphatide was hydrolyzed with boron trifluoride–methanol, and glpc analysis of the derived methyl esters indicated about 98% methyl linoleate.

Experimental Section[14]

N-(β,β,β-Trichloroethoxycarbonyl)ethanolamine (2).—A solution of 100 g (0.47 mol) of β,β,β-trichloroethylchloroformate[10] in 50 ml of dioxane was added at 0° to a mixture of 36.7 g (0.6 mol) of ethanolamine, 40 g of MgO, 125 ml of dioxane, and 125 ml of H_2O. The suspension was warmed to room temperature and stirred for an additional 16 hr. Ether (500 ml) was added, the inorganics were filtered, and the filtrate was washed with dilute HCl, brine, 5% NaHCO, and brine again. After being dried (Na_2SO_4), the solvent was evaporated to yield 112 g of the colorless syrup **2**. An analytical specimen was prepared by chromatography over Florisil, using 1:1 Et_2O–petroleum ether as the eluent: infrared absorption at 3.04, 5.83 and 8.01 μ.

Anal. Calcd for $C_5H_8Cl_3NO_3$: C, 25.39; H, 3.41; Cl, 44.98. Found: C, 25.56; H, 3.55; Cl, 44.48.

The 3,5-dinitrobenzoate derivative of **2** had mp 86–87° after crystallization from acetone–H_2O.

Anal. Calcd for $C_{12}H_{10}Cl_3N_3O_8$: C, 33.47; H, 2.34; N, 9.76. Found: C, 33.37; H, 2.20; N, 9.54.

Dichloro(N-β,β,β-trichloroethoxycarbonyl-2-aminoethyl)phosphate (3).—A solution of 41 g (0.174 mol) of **2** in 100 ml of dry C_6H_6 was added dropwise under N_2 over 4 hr to a cooled, stirred solution of 60 ml (0.64 mol) of freshly distilled $POCl_3$ in 250 ml of dry C_6H_6. After being stirred for 16 hr at room temperature, the reaction mixture was concentrated at H_2O aspirator pressure at 40°. Then the residue was azeotroped with dry C_6H_6 several times and finally concentrated at 1 mm to give about 55 g of crude **3**. The product was dissolved in dry C_6H_6, diluted to volume in a 100-ml volumetric flask, and stored at 0° under N_2. Under these conditions, the compound is stable for several months. Attempted molecular distillation at high vacuum did not give an analytically pure sample of **3**; the material readily polymerized in the distilling flask.

Dicyclohexylammonium Salt of N-β,β,β-Trichloroethoxycarbonyl-2-aminoethylphosphoric Acid (4).—A solution of 5 g of crude **3**, 50 ml of 50% aqueous dioxane, and 100 ml of 0.1 *N* KCl was stirred at room temperature for 2 hr. Solid NaCl was added, and the mixture was extracted several times with EtOAc. The EtOAc extracts were washed with H_2O, dried (Na_2SO_4), and concentrated to a colorless oil. Acetone (150 ml) was added, and the solution was treated with cyclohexylamine until basic. After being cooled, the white solid was filtered to give 5.8 g (80%) of the dicyclohexylammonium salt of **4**, mp 201–203°. Several recrystallizations from a mixture of EtOH–cyclohexylamine–H_2O (90:10:1) gave an analytical sample, mp 204–205°.

Anal. Calcd for $C_{17}H_{35}Cl_3N_3O_6P \cdot 0.5H_2O$: C, 38.98; H, 6.93; N, 8.02; H_2O, 1.72. Found: C, 38.58; H, 6.97; N, 7.69; H_2O, 1.60.[15]

N-β,β,β-Trichloroethoxycarbonyl-2-aminoethylphosphoric Acid (4).—The cyclohexylammonium salt of **4** (1 g) was dissolved in Me_2CO (100 ml) and H_2O and stirred with 10 ml of Amberlite IR-120 (H^+) for 1 hr. The resin was filtered and washed with $CHCl_3$, and the filtrate was concentrated to a viscous syrup. Chromatography on silicic acid with 9:2 $CHCl_3$–MeOH gave pure **4**, a colorless, viscous syrup.

Anal. Calcd for $C_5H_9Cl_3NO_6P$: C, 19.13; H, 2.87; N, 4.43; Cl, 33.61; P, 9.79. Found: C, 19.38; H, 3.11; N, 4.23; Cl, 33.45; P, 9.52.

1,2-Dilinoleoyl-3-*sn*-phosphatidylethanolamine (7).—A solution of 4.0 g (0.00644 mol) of **5**[1] in 35 ml of dry $CHCl_3$ and 3 ml of dry pyridine was added to an ice-cold solution of 4.1 g (0.0116 mol) of **3** in 10 ml of C_6H_6. The addition took about 70 min and, after being stirred 1 hr at 0°, the solution was stirred at room temperature under N_2 for 18 hr longer. Ether (700 ml) was added, and the mixture was washed with H_2O, dilute HCl, brine, 5% $NaHCO_3$, and brine again. The Et_2O layer was evaporated without drying to give the creamy **6**. Tlc showed one major spot which was phosphate positive. This material was dissolved in HOAc (50 ml) and Et_2O (25 ml) and 20 g of activated zinc[16] were added. Then the suspension was stirred at 25° for 16 hr. After being diluted with Et_2O (600 ml), the zinc and inorganics were filtered, and the filtrate was washed with four 200-ml portions of H_2O, then with 5% $NaHCO_3$ (the addition of brine retards emulsification), and finally with brine. Evaporation of the dried (Na_2SO_4) solvent gave 5.8 g of a yellow oil which contained one ninhydrin-positive material and some lesser amounts of phosphate-positive products. Chromatography on 400 g of DEAE-cellulose in the acetate form[13] gave 1.2 g of homogeneous **7** and an additional 0.8 g containing trace impurities (42% yield over-all): $[\alpha]^{25}D$ +6.2° (*c* 1, $CHCl_3$) {lit.[11] $[\alpha]D$ +5.8° (*c* 5, $CHCl_3$)}; R_f 0.67, using the solvent system 65:25:4, $CHCl_3$–MeOH–H_2O, on 0.25-mm silica gel G plates.

Anal. Calcd for $C_{41}H_{74}NO_8P$: C, 66.55; H, 10.08; N, 1.89. Found: C, 66.51; H, 9.94; N, 1.75.

Registry No.—**2**, 20708-12-7; **2** (3,5-dinitrobenzoate derivative), 20708-13-8; **4**, 20728-37-4; **4** (dicyclohexylammonium salt), 20708-11-6; **7**, 20707-71-5.

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The Reaction of β-Keto Esters with 1,3-Diketones

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Received January 14, 1969

The reaction of β-keto esters with 5,5-dimethyl-1,3-cyclohexanedione and 1,3-indanedione in trifluoroacetic acid (TFA) shows an interesting contrast of the action