Glycerolipids. III.[1] Stereospecific Syntheses of D- and L-1,2-Diglycerides *via* Glycerol Carbonates[2]

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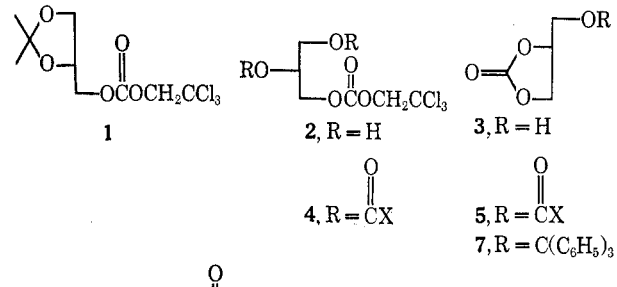
Stereospecific syntheses of acyclic and cyclic glycerol carbonates are described. These carbonates were used to prepare optically active, unsaturated 1,2-diglycerides. From the common precursor, 1,2-isopropylidene-*sn*-glycerol-3-β,β,β-trichloroethylcarbonate (**1**), both D- and L-1,2-diglycerides were obtained.

The specific role of phospholipids in biological systems is not currently well understood. They are known to be necessary for the functioning of cell membranes, are involved in the blood-clotting processes, are associated with the transmission of nerve impulses and cations, have a function in the mobilization of lipids in the serum, and are essential for many biological oxidation systems.[3-9] Phospholipids have been shown to be substrates for a cyclopropane synthetase system[10] and necessary for the reconstitution of lipid depleted cell particles,[11] and have been implicated as inhibitors of the renin–angiotensin system.[12] Exciting physicochemical studies of model membranes based on phospholipid bilayers and liquid crystals give promise of leading to a more detailed understanding of their role in membrane function[13] and their effects on associated bound protein.[14] In these investigations, the availability of reasonable quantities of specific molecular species of phospholipids, especially those with polyunsaturated fatty acyl groups, has been limited by the available synthetic procedures.[15-21]

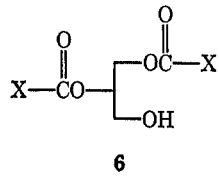
Our interest in obtaining a variety of unique unsaturated phospholipids for biochemical studies has led us to a new and expeditious preparation of the 1,2-diglycerides required for the synthesis of most types of phospholipid moieties. This paper describes the adaptation of a new protecting group into a facile synthesis of optically active, unsaturated 1,2-diglycerides.

Treatment of 1,2-isopropylidene-*sn*-glycerol[22] with β,β,β-trichloroethylchloroformate[23-26] in the presence of pyridine gave 1,2-isopropylidene-*sn*-glycerol-3-β,β,β-trichloroethylcarbonate (**1**) which was isolated in 85% by vacuum distillation. The nmr spectrum of **1** showed a sharp singlet at δ 4.81 which is characteristic for the methylene protons of the CCl_3 CH_2OCO group. Hydrolysis of **1** with 1 *N* HCl in methanol–ether gave a mixture of 94% of *sn*-glycerol-3-β,β,β-trichloroethylcarbonate (**2**) and 6% of *sn*-glycerol-2,3-carbonate (**3**) as determined by glpc analysis of the derived trifluoroacetates.[27] Alternatively, cleavage of the isopropylidene group of **1** with boric acid in refluxing trimethylborate afforded a mixture of 74% of **2** and 26% of **3**.[28] Attempted separation of the mixture on silicic



1 **2**, R = H **3**, R = H

4, R = CX **5**, R = CX **7**, R = $C(C_6H_5)_3$



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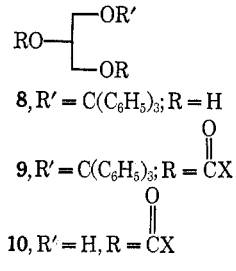


8, R′ = $C(C_6H_5)_3$; R = H

9, R′ = $C(C_6H_5)_3$; R = CX

10, R′ = H, R = CX

a, X = $C_{17}H_{35}$ (stearyl)
b, X = $C_{17}H_{33}$ (oleyl)
c, X = $C_{17}H_{33}$ (elaidyl)
d, X = $C_{17}H_{31}$ (linoleyl)
e, X = $C_{10}H_{39}$ (10-undecenyl)

(1) Glycerolipids. II: F. R. Pfeiffer, S. R. Cohen, and J. A. Weisbach, *J. Org. Chem.*, **34**, 2795 (1969).

(2) For a preliminary report regarding a portion of the present work, see F. R. Pfeiffer, S. R. Cohen, K. R. Williams, and J. A. Weisbach, *Tetrahedron Lett.*, 3549 (1968).

(3) L. L. M. van Deenen and G. H. de Haas, *Ann. Rev. Biochem.*, **35**, 157 (1966).

(4) R. M. C. Dawson and D. N. Rhodes, "Metabolism and Physiological Significance of Lipids," John Wiley & Sons, Inc., New York, N. Y., 1964.

(5) G. B. Ansell and J. N. Hawthorne, "Phospholipids," Elsevier Publishing Co., Amsterdam, 1964.

(6) E. J. Masuro, "Physiological Chemistry of Lipids in Mammals," W. B. Saunders Co., Philadelphia, Pa., 1968.

(7) J. L. Moore, T. Richardson, and H. F. Deluca, *Chem. Phys. Lipids*, **3**, 39 (1969), and references cited therein.

(8) See *Brit. Med. Bull.*, **24**, 99 (1968).

(9) A. Kuksis, L. Marai, W. C. Breckenridge, D. A. Gornall, and O. Stachnyk, *Can. J. Physiol. Pharmacol.*, **46**, 511 (1968).

(10) A. E. Chung and J. H. Law, *Biochemistry*, **3**, 1989 (1964).

(11) S. Fleischer, G. Brierly, H. Klouwen, and D. B. Slautterback, *J. Biol. Chem.*, **237**, 3264 (1962).

(12) S. Sen, R. R. Smeby, and F. M. Bumpus, *Biochemistry*, **6**, 1572 (1967).

(13) R. Pagano and T. E. Thompson, *J. Mol. Biol.*, **38**, 41 (1968), and references cited therein.

(14) G. G. Shipley, R. B. Leslie, and D. Chapman, *Biochim. Biophys. Acta*, **173**, 1 (1969), and references cited therein.

(15) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463 (1939).

(16) J. C. Sowden and H. O. L. Fischer, *J. Amer. Chem. Soc.*, **63**, 3244 (1941).

(17) E. Baer, *J. Amer. Oil Chem. Soc.*, **42**, 257 (1965).

(18) F. H. Mattson and R. A. Volpenhein, *J. Lipid Res.*, **3**, 281 (1962).

(19) W. E. M. Lands and A. Zschocke, *ibid.*, **6**, 324 (1965).

(20) L. Krabisch and B. Borgström, *ibid.*, **6**, 156 (1965).

(21) L. J. Stegerhoek and P. E. Verkade, *Rec. Trav. Chim. Pays-Bas*, **74**, 143 (1955).

(22) E. Baer, *Biochem. Prep.*, **2**, 31 (1952).

(23) The β,β,β-trichloroethoxylcarbonyl group was introduced in the total synthesis of cephalosporin C by R. B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbrüggen, *J. Amer. Chem. Soc.*, **88**, 852 (1966).

(24) For other examples of the use and removal of the β,β,β-trichloroethoxycarbonyl group, see T. B. Windholz and D. B. R. Johnston, *Tetrahedron Lett.*, 2555 (1967).

(25) A. F. Cook [*J. Org. Chem.*, **33**, 3589 (1968)] has reported on the use of the closely related β,β,β-tribromoethoxycarbonyl group for the protection of nucleoside hydroxyl groups.

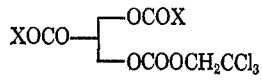
(26) β,β,β-Trichloroethyl chloroformate is available from the Aldrich Chemical Co.

(27) R. Wood and F. Snyder, *Lipids*, **1**, 62 (1966).

(28) L. Hartman, *J. Chem. Soc.*, 4134 (1959).

TABLE I

1,2-DIACYL-*sn*-GLYCEROL-3-(β,β,β-TRICHLOROETHYL)CARBONATES

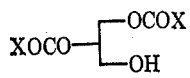


Compd[a]	X	Yield, %	$[\alpha]^{25}D$ (*c*, %)[b]	Anal., % Calcd C	Calcd H	Calcd Cl	Found C	Found H	Found Cl
4a	$CH_3(-CH_2-)_{16}$	75	−1.7° (1.05)	63.02	9.70	13.29	63.23	9.66	13.43
4b	$CH_3(-CH_2-)_7C{=}C(-CH_2-)_7$ (*cis*)	66	−1.4° (0.88)	63.34	9.24	13.36	63.30	9.21	13.29
4c	$CH_3(-CH_2-)_7C{=}C(-CH_2-)_7$ (*trans*)	58	−1.5° (1.08)	63.34	9.24	13.36	63.10	9.17	12.98
4d	$CH_3(-CH_2-)_3(-CH_2C{=}C)_2(-CH_2-)_7$ (*cis*)	49	−1.8° (1.49)	63.66	8.78	13.42	63.35	8.77	13.60
4e	$CH_2{=}CH(-CH_2-)_8$	68	−0.6° (1.05)	56.05	7.56	17.73	56.10	7.67	17.72

[a] Compounds are oils except **4a**, mp 56–57° (from EtOAc–MeOH). [b] Optical rotations determined in $CHCl_3$.

TABLE II

sn-GLYCEROL-1,2-DIACYLATES



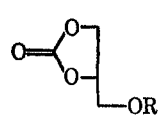
Compd[a]	X	Yield,[b] %	$[\alpha]^{25}D$ (*c*, %)[c]	Anal., % Calcd C	Calcd H	Found C	Found H
6a	Stearyl[d]	87	−2.6° (1.0)				
6b	Oleyl	75	−1.91°[e] (6.2)				
6c	Elaidyl[f]	69	−1.85° (1.0)	75.43	11.69	75.33	11.59
6d	Linoleyl	51	−2.2° (1.0)	75.92	11.11	75.61	11.17
6e	10-Undecenyl	60	−2.0° (1.1)	70.82	10.46	70.62	10.40

[a] Compounds are oils except where indicated. [b] Yields reported are for the chromatographed products. Conversions of **4** to **6** were essentially quantitative as judged by tlc. [c] Optical rotations determined in $CHCl_3$. [d] Compound **6a** has mp 73–74.5° [lit.[16] mp 74–74.5°; $[\alpha]D$ −2.7° (*c* 6.18, $CHCl_3$)]. [e] Lit. $[\alpha]^{20}D$ −2.8° (*c* 10, $CHCl_3$); E. Baer and D. Buchnea, *J. Biol. Chem.*, **230**, 447 (1958). [f] Compound **6c** had mp *ca.* 25°.

acid columns led to partial conversion of **2** to **3**; neutral alumina (Woelm Activity III) likewise caused cyclization of **2** to **3** with concomitant cleavage of the base-sensitive carbonate bonds. Compounds **2** and **3** were cleanly separated on acid-washed Florisil impregnated with 10% boric acid.[29] The crude diol **2**, which was obtained from **1** by HCl hydrolysis, was adequate for the preparation of the *sn*-glycerol-1,2-diacylates **6a–6e**. It was treated with 2 mol of the appropriate acid chloride[30] to afford the 1,2-diacyl-*sn*-glycerol-3-β,β,β-trichloroethylcarbonates **4a–4e** in addition to trace amounts of the 1-acyl-*sn*-glycerol-2,3-carbonates **5a–5e**. Compounds **5** can also be formed by cyclization of the monoacylated diol, since more hindered branched-chain fatty acids have been shown[31] to give a higher proportion of the cyclic carbonates **5** than straight-chain acids. Compounds **4** were separated efficiently from **5** on Florisil columns with petroleum ether–ether mixtures (see Table I for yields). Treatment of purified **4** with activated zinc in acetic acid for 1–2 hr at room temperature gave the *sn*-glycerol-1,2-diacylates **6a–6e**. After separation of the inorganics by filtration and removal of acetic acid *in vacuo* or with a bicarbonate wash, the isolated 1,2-diglycerides were sufficiently pure to carry on without further purification. Only trace amounts of the 1,3 isomers could be detected in the crude reaction mixtures in an appropriate, sensitive thin layer chromatography system.[32] Analytical samples (see Table II) were prepared by column chromatography on acid-washed Florisil impregnated with 10% boric acid or on thick layer plates of 10–15% boric acid in silica gel G. Nmr spectra of **6a–6e** showed the characteristic chemical shifts for 1,2-disubstituted glycerols.[33]

Hydrolysis of **1** with boric acid followed by tritylation of the crude product with triphenylmethyl chloride in pyridine at 60° gave a 65% yield of 1-trityl-*sn*-glycerol-2,3-carbonate (**7**).[34] Alkaline hydrolysis of **7** led to the diol **8**.[35] Compound **8** was acylated to afford the 1-trityl-*sn*-glycerol-2,3-diacylates **9a** and **9b** and then converted to the 2,3-diacyl-*sn*-glycerols **10a** and **10b** by mild boric acid hydrolysis. The utility of boric acid for detritylation of **9** as well as its use in chromatographic separations is dependent on the formation of borate esters, which effectively prevent acyl migration.[18]

Treatment of **2** with phosgene afforded *sn*-glycerol 1,2-carbonate-3-β,β,β-trichloroethylcarbonate (**11**) in

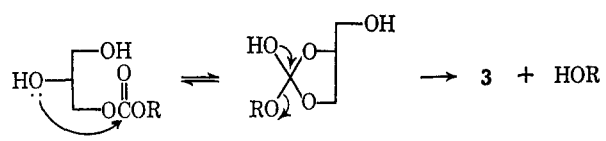


11, R = $COOCH_2CCl_3$
12, R = H
13, R = $C(C_6H_5)_3$

(29) B. Serdarevich and K. K. Carroll, *J. Lipid Res.*, **7**, 277 (1966).
(30) The acid chlorides were prepared with oxalyl chloride; see ref 18.
(31) Unpublished results.
(32) A. E. Thomas, III, J. E. Scharoun, and H. Ralston, *J. Amer. Oil Chem. Soc.*, **42**, 789 (1965), and references cited therein.
(33) B. Serdarevich, *ibid.*, **44**, 381 (1967).
(34) Compound **7** was prepared by J. Gigg and R. Gigg [*J. Chem. Soc.*, 1865 (1967)] by degradation of 1,3:2,5:4,6-tri-*O*-methylene-D-mannitol.
(35) J. Gigg and R. Gigg, *ibid.*, 431 (1967).

75% yield. The acyclic carbonate group of **11** was removed with zinc in acetic acid to give *sn*-glycerol-1,2-carbonate (**12**) which was isolated as the trityl derivative **13** in about 70% yield.[36] Thus, from the common intermediate **2**, both *sn*-glycerol-1- and 3-trityl ethers are readily obtained. Application of known methods of syntheses to these easily accessible optically active trityl glycerols provide direct access to all combinations of 1,2-diglycerides.[18]

Since the acyclic carbonate **2** readily eliminated β,β,β-trichloroethanol with the formation of the cyclic carbonate **3**, it was of interest to survey the relative effectiveness of different leaving groups on the formation of **3**. The diol carbonates **2a–2c** were stirred in pyridine at 60° for 18 hr and treated with trifluoroacetic anhydride, and the derived trifluoroacetates were analyzed by glpc. Under these specific conditions, cyclization of the trichloroethyl **2a**, *p*-nitrobenzyl **2b**, and benzyl **2c** derivatives to the cyclic carbonate **3** were



2a, R = CH_2CCl_3
b, R = $CH_2C_6H_4NO_2$-*p*
c, R = $CH_2C_6H_5$

100%, 31%, and 9%, respectively. It thus appears that the trichloroethyl ethyl group represents a particularly excellent leaving group for this synthetic sequence. Under these relatively mild conditions, the optical integrity of the heat-sensitive **3** is assured.

Experimental Section[37]

1,2-Isopropylidene-*sn*-glycerol-3-β,β,β-trichloroethylcarbonate (1).—A solution of 200 g (0.943 mol) of β,β,β-trichloroethyl chloroformate[26] in 100 ml of $CHCl_3$ (distilled from P_2O_5) was added dropwise to an ice-cold mixture of 124.6 g (0.942 mol) of 1,2-isopropylidene-*sn*-glycerol,[22] 50 ml of dry pyridine, and 100 ml of $CHCl_3$. The solution was stirred at room temperature for 18 hr, diluted with Et_2O (800 ml), and washed successively with dilute HCl, H_2O, 5% $NaHCO_3$, and H_2O. The dried (Na_2SO_4) organic extract was concentrated and distilled to give 252 g (87%) of the colorless, syrupy **1**: bp 140–145° (0.25 mm); $[\alpha]^{25}D$ −1.5° (*c* 0.87, $CHCl_3$); nmr ($CDCl_3$) δ 4.81 (s, 2, CH_2CCl_3).

Anal. Calcd for $C_9H_{13}Cl_3O_5$: C, 35.15; H, 4.26; Cl, 34.58. Found: C, 35.35; H, 4.39; Cl, 34.80.

***sn*-Glycerol-3-β,β,β-trichloroethylcarbonate (2). Method A. Hydrolysis of 1 with HCl.**—A mixture of 126 g (0.41 mol) of **1**, 150 ml of Et_2O, 40 ml of MeOH, and 40 ml of 3 *N* HCl was stirred at room temperature overnight. The solvents were evaporated at 40° at H_2O aspirator pressure, the residue was extracted with EtOAc, and the organic phase was washed with brine five times. After being dried (Na_2SO_4), the solvent was evaporated and the residue was azeotroped several times with C_6H_6 at 40°. The yield was quantitative. Analysis of the crude product as the derived trifluoroacetate[27] showed a mixture of 94% of **2** and 6% of *sn*-glycerol-2,3-carbonate (**3**). This mixture was used without further purification in the acylation reactions described below, and can be stored at 0° for several months. An analytical specimen of **2** was prepared by chromatographing 1 g of the crude material on 60 g of acid-washed Florisil impregnated with 10% of H_3BO_3[29] with 1:1 cyclohexane–EtOAc as the eluent. Pure **2** is a colorless oil: $[\alpha]^{25}D$ −1.31° (*c* 1.0, $CHCl_3$); nmr ($CDCl_3$) δ 4.79 (s, 2, CH_2CCl_3); R_f 0.48 on silica gel G plates (0.25 mm) with 1:1 EtOAc–cyclohexane.

Anal. Calcd for $C_6H_9Cl_3O_5$: C, 26.94; H, 3.39; Cl, 39.76. Found: C, 27.20; H, 3.54; Cl, 39.48.

Method B. Hydrolysis of 1 with H_3BO_3.—A solution of 30.7 g of **1**, 22 g of finely ground H_3BO_3, and 200 ml of trimethylborate was refluxed on the steam bath for 40 min. The solution was concentrated *in vacuo* at 75°. The residue was partitioned between 300 ml of EtOAc and enough brine to dissolve all of the solids. After being dried, the organic layer was evaporated to give a mixture of 74% of **2** and 26% of **3** as determined by glpc.[27]

1,2-Diacyl-*sn*-glycerol-3-(β,β,β-trichloroethyl)carbonates 4 (Table I).—The appropriate acid chloride[30] (0.12 mol) in $CHCl_3$ (75 ml, distilled from P_2O_5) was added dropwise with stirring to a cold (0°) solution of **2** (0.06 mol, crude **2** obtained from HCl hydrolysis of **1**), 14 ml of anhydrous pyridine, and 75 ml of $CHCl_3$. The reaction mixture was then stirred at 25° for 24 hr, diluted with Et_2O (500 ml), and washed with dilute HCl, H_2O, 5% $NaHCO_3$, and H_2O. The dried (Na_2SO_4) solution was concentrated, dissolved in a minimum amount of 8:1 Et_2O–petroleum ether (bp 30–60°), and applied to a column (65 × 6.5 cm) packed with 800 g of Florisil (100–200 mesh). The column was developed with increasing concentrations of Et_2O in petroleum ether, and was monitored by tlc; compounds **4** had R_f of *ca.* 0.75–0.85 on silica gel G (0.25 mm) using a system of 3:1 cyclohexane–EtOAc. Elution with Et_2O–$CHCl_3$ mixtures afforded the cyclic carbonate **5**, which was isolated in trace to small amounts. Compounds **5** had R_f of 0.15–0.20 in the above system and showed a characteristic doublet in the carbonyl region of the ir spectrum at 5.59 (carbonate) and 5.77 μ (ester).

1-Stearoyl-*sn*-glycerol-2,3-carbonate (5a).—A solution of 6.34 g (0.0237 mol) of **2** in 15 ml of anhydrous pyridine was stirred at 60° for 18 hr. The mixture of **3** and β,β,β-trichloroethanol was cooled to 0° and a solution of 7.35 g (0.0237 mol) of stearoyl chloride in 15 ml of dry $CHCl_3$ was added dropwise. Then the solution was stirred overnight at room temperature, diluted with $CHCl_3$, and washed with dilute HCl, H_2O, 5% $NaHCO_3$, and H_2O. Evaporation of the dried solvent gave white crystals which were a mixture of **5a** and a faster moving component (tlc) which was not identified, but was probably stearoylated β,β,β-trichloroethanol. Crystallization from acetone–hexane (1:5) gave 5.75 g (63%) of pure **5a**, mp 79–80°. An analytical specimen melted at 82–82.5°: $[\alpha]^{25}D$ +6.9° (*c* 1.08, $CHCl_3$); infrared absorption at 5.59 and 5.77 μ.

Anal. Calcd for $C_{22}H_{40}O_5$: C, 68.71; H, 10.48. Found: C, 68.96; H, 10.50.

***sn*-Glycerol-1,2-diacylates 6 (Table II).**—Compounds **4** (0.03 mol) were dissolved in a mixture of HOAc (30 ml) and Et_2O (20 ml) and cooled in an ice bath, and 25 g of activated zinc[38] were added. The suspension was stirred at 20–25° for 1–2 hr or until tlc indicated complete conversion of **4** to **6**. After dilution with 4:1 Et_2O–$CHCl_3$ (300 ml), the inorganics were filtered and the filter cake was washed with additional solvents. The filtrate was washed with H_2O three times, 5% $NaHCO_3$, and brine. After being dried (Na_2SO_4), the solvents were evaporated at 30°. Tlc of the isolated diglycerides on silica gel G impregnated with 10% H_3BO_3[32] with hexane–Et_2O (3:2) or $CHCl_3$–Me_2CO (96:4) showed little or no 1,3-diglyceride in the crude products. The analytical specimens were prepared by column chromatography over acid-washed Florisil containing 10% of H_3BO_3[29] and elution with hexane–ether mixture, or by thick layer chromatography on plates coated with 1 mm of silica gel G mixed with 10–15% of H_3BO_3 and using $CHCl_3$–Me_2CO (96:4) as the moving phase.

1-Trityl-*sn*-glycerol-2,3-carbonate (7). Method A.—A mixture of 2.67 g (0.01 mol) of crude **2**, obtained from HCl hydrolysis of **1**, 2.78 g (0.01 mol) of triphenylmethyl chloride, 10 ml of dry pyridine, and 15 ml of dry $CHCl_3$ was stirred at 60° for 18 hr. The mixture was diluted with EtOAc and washed with dilute HCl, H_2O, 5% $NaHCO_3$, and H_2O. After being dried, the solvent was evaporated and the residue was crystallized from acetone–petroleum ether to give 2.27 g (63%) of **7**, mp 216–217°. Two recrystallizations from acetone afforded analytically pure **7**: mp 218–220° (lit.[34] mp 221–223°); $[\alpha]^{25}D$ +18.9° (*c* 1.67, $CHCl_3$) [lit.[34] $[\alpha]^{25}D$ +19.6° (*c* 0.85, $CHCl_3$)].

Anal. Calcd for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59. Found: C, 76.58; H, 5.66.

(36) Compound **12** had been prepared (see ref 35) from *sn*-glycerol-3-benzyl ether.

(37) Melting points were determined using a Thomas–Hoover apparatus and are corrected. Infrared spectra were determined as Nujol mulls on a Perkin-Elmer Infracord and nmr spectra were recorded on a Varian Associates A-60 spectrometer in $CDCl_3$ (TMS). Optical rotations were determined on a Perkin-Elmer 141 polarimeter.

(38) E. Baer and D. Buchnea, *J. Biol. Chem.*, **230**, 447 (1958).

Method B.—A solution of 30.76 g (0.1 mol) of **1**, 22 g of finely ground boric acid, and 200 ml of trimethylborate was refluxed for 30 min and worked up as described for the preparation of **2**. The crude product was dissolved in 50 ml of $CHCl_3$ and 10 ml of pyridine, and 27.8 g (0.1 mol) of triphenylmethyl chloride was added dropwise at 0°. After being stirred overnight, the reaction mixture was worked up as in method A. The isolated product was chromatographed on 700 g of Woelm neutral alumina (activity III). After some impurities were eluted with Et_2O–petroleum ether mixtures, compound **7** was eluted with $CHCl_3$ to give 23.4 g (65%), mp 217–219°.

1-Trityl-*sn*-glycerol-2,3-diacylates 9. (Procedure Exemplified by the Dioleoyl Derivative 9b).—Compound **7** was converted to the diol **8** as previously described[34]: mp 89–90°; $[\alpha]^{25}D$ −15.7° (*c* 1.38, pyridine) [lit.[34] mp 94°; $[\alpha]D$ −16.8° (*c* 1.05, pyridine)]. A solution of 3.34 g (0.01 mol) of **8**, 5.6 ml of pyridine, and 15 ml of $CHCl_3$ was stirred under N_2 at 0°. Oleoyl chloride (6.01 g, 0.02 mol) in $CHCl_3$ (25 ml) was added dropwise and then the solution was stirrred for 48 hr at 25°. After being diluted with ether, the reaction mixture was washed with cold 1 *N* HCl, H_2O, 5% $NaHCO_3$, and H_2O and dried over Na_2SO_4. The resulting orange oil was chromatographed on 175 g of Florisil and eluted with Et_2O–petroleum ether mixtures. The homogenous fractions were combined to give 5.7 g (67%) of oily 1-trityl-*sn*-glycerol-2,3-dioleate (**9b**): $[\alpha]^{25}D$ −9.4° (*c* 1.23, $CHCl_3$).

Anal. Calcd for $C_{58}H_{86}O_5$: C, 80.69; H, 10.04. Found: C, 80.56; H, 9.77.

The distearoyl derivative **9a** was prepared in 73% yield as described above: mp 52.5–53.5° (from petroleum ether) (lit.[39] mp 65–66°); $[\alpha]^{25}D$ −12.2° (*c* 0.97, $CHCl_3$).

Anal. Calcd for $C_{58}H_{90}O_5$: C, 80.32; H, 10.46. Found: C, 80.60; H, 10.55.

***sn*-Glycerol 2,3-diacylates 10. (Procedure Exemplified by the Dioleoyl Derivative 10b).**—A mixture of 1.6 g of **9b**, 1.6 g of finely ground H_3BO_3, and 25 ml of trimethylborate was refluxed on the steam bath ($CaCl_2$ drying tube) for 2.5 hr. The solvent was evaporated at 75° with H_2O aspirator pressure. The orange residue was partitioned between cold H_2O and Et_2O with vigorous shaking in a separatory funnel; the Et_2O layer was washed with 5% $NaHCO_3$ and H_2O and then dried over Na_2SO_4. A tlc of the crude product showed a small amount of trityl derivative **9b**, triphenylmethyl methyl ether, triphenylmethylcarbinol, a small amount of the 1,3-diglyceride, and, the major product, *sn*-glycerol 2,3-dioleate (**10b**). This mixture was chromatographed on 150 g of acid-washed Florisil mixed with 10% H_3BO_3. Elution with hexane–Et_2O mixtures readily separated the reaction products to give about 0.5 g (43%) of homogeneous,[32] oily **10b**;[40] $[\alpha]^{25}D$ +2.14° (*c* 5.62, $CHCl_3$) [lit.[38] $[\alpha]^{25}D$ +2.7° (*c* 10, $CHCl_3$)]. *sn*-Glycerol 2,3-distearate was prepared as described above: mp 73–74°; $[\alpha]^{25}D$ +2.5° (*c* 1.2, $CHCl_3$) (lit.[38] mp 74–74.5°; $[\alpha]^{25}D$ +2.7°).

***sn*-Glycerol-1,2-carbonate-3-(β,β,β-trichloroethyl)carbonate (11).**—A solution of 10 g of crude **2** in 50 ml of anhydrous pyridine was cooled to −10° and vigorously stirred as phosgene was introduced over the surface of the solution. The voluminous precipitate which appeared in a few minutes precluded continued stirring. After 30 min the mixture was cooled to −50° and small pieces of ice were added cautiously. When the initial reaction had subsided, ice–H_2O and EtOAc were added and the layers were separated. The EtOAc was washed with dilute HCl, H_2O, 5% $NaHCO_3$, and H_2O. After being dried (Na_2SO_4), the solvent was evaporated and the residual oily solid was crystallized from Et_2O to yield 8.2 g (75%) of **11**, mp 77–79°. Additional crystallization from Et_2O gave pure **11** as white crystals: mp 80–82°; $[\alpha]^{25}D$ −10.5° (*c* 1.16, $CHCl_3$); infrared absorption at 5.60–5.82 μ (broad).

Anal. Calcd for $C_7H_7Cl_3O_6$: C, 28.65; H, 2.40; Cl, 36.24. Found: C, 28.89; H, 2.44; Cl, 36.45.

3-Trityl-*sn*-glycerol-1,2-carbonate (13).—Compound **11** (4 g, 0.0136 mol) was dissolved in 15 ml of HOAc; zinc dust (4 g) was added and the suspension was stirred at room temperature for 3 hr. Ether (50 ml) was added, and the mixture was chilled and filtered. Evaporation of the Et_2O followed by removal of the HOAc at 40° under high vacuum afforded the crude *sn*-glycerol-1,2-carbonate (**12**). This product was dissolved in 10 ml of pyridine and 20 ml of $CHCl_3$, and 3.8 g (0.0136 mol) of triphenylmethyl chloride in 15 ml of anhydrous $CHCl_3$ was added at 0°. After being stirred overnight at room temperature, the reaction was worked up by the procedure used for the enantiomer **7**. The crude product was crystallized from Me_2CO–petroleum ether to give 3.4 g (69%) of white **13**, mp 214–216°. Several recrystallizations from Me_2CO gave a product: mp 217–219°; $[\alpha]^{25}D$ −17.5° (*c* 4, $CHCl_3$) [lit.[35] mp 219–222°; $[\alpha]^{23}D$ −17.5° (*c* 4, $CHCl_3$)].

Anal. Calcd for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59. Found: C, 76.83; H, 5.60.

Registry No.—**1**, 20473-89-6; **2**, 22202-35-3; **4a**, 22202-36-4; **4b**, 22202-37-5; **4c**, 22202-38-6; **4d**, 22202-39-7; **4e**, 22202-40-0; **5a**, 22202-41-1; **6c**, 22202-42-2; **6d**, 22202-44-4; **6e**, 22202-43-3; **7**, 17327-06-9; **9b**, 22202-46-6; **11**, 22202-47-7.

(39) N. B. Karpova, M. A. Grum-Grzhimailv, L. V. Volkova, L. M. Vernikova, and N. A. Preobrazhenskii, *Zh. Org. Khim.*, **2**, 789 (1966); *Chem. Abstr.*, **65**, 12103c (1966).

(40) *sn*-Glycerol-2,3-dioleate was prepared previously (see ref 38) by zinc debromination of *sn*-glycerol-2,3-(bis-9,10-*cis*-dibromo)distearate.