reactants. The following general procedure was used for the kinetic experiments.

Ten individual samples were prepared which consisted of 5.00 ml. of a 1.00 *M* solution of O-ethyl-N,N-ethyleneurethane in anhydrous ethanol and 5.00 ml. of a 2.00 *M* solution of the aniline derivative in anhydrous ethanol. These samples were then placed in a constant-temperature bath held at 50.0 ± 0.1° and this time recorded as "zero" time. At various time intervals samples were removed and analyzed for unreacted O-ethyl-N,N-ethyleneurethane. This analysis was carried out by adding the sample to 20.0 ml. of a solution of concentrated hydrochloric acid in pyridine which was approximately 0.25 *M* HCl. The pyridine solution was then refluxed for 30 min., cooled, diluted with water, and titrated to a phenolphthalein end point with 0.100 *N* NaOH solution. A blank sample (20.0 ml. of pyridine–HCl solution) was treated in the same manner and the difference in titer for the two samples corresponded to the amount of HCl consumed. The HCl consumed corresponds to the amount of O-ethyl-N,N-ethyleneurethane present in the sample. This method of analysis has been shown to be accurate and reproducible for a number of the activated aziridines.[16]

The rate constants, k, given in Table I were determined from the slope of the line obtained by plotting $[1/(a - b)] \ln [a(b - x)/b(a - x)]$ *vs.* time in minutes, where a is the initial concentration of O-ethyl-N,N-ethyleneurethane, b is the initial concentration of aniline derivative, and x is the amount of O-ethyl-N,N-ethyleneurethane consumed in the reaction at each time. The ρ-constant for the reaction was determined by the method of least squares from a plot of the accepted σ-values[14] for the various substituents *vs.* log k. The standard deviation for the points from the line obtained in this plot was 0.10.

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(16) L. Levine, unpublished results.

Reactions of Aliphatic Methanesulfonates. I. Syntheses of Long-Chain Glyceryl-(1) Ethers[1]

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Methanesulfonates of saturated and unsaturated long-chain alcohols were prepared and used for syntheses of alkyl glyceryl-(1) ethers (3-alkoxy-1,2-propanediols) by reaction with 1,2-O-isopropylideneglycerol (2,2-dimethyl-1,3-dioxalane-4-methanol).

The use of halides and *p*-toluenesulfonates (tosylates) of unsaturated, long-chain alcohols as alkylating agents has been limited by great difficulties in their isolation[2,3] and purification and by the formation of *trans* isomers.[4] Esters of methanesulfonic acid (mesylates), as described in the present communication, can be easily synthesized without isomerization of double bonds. The mesylates offer additional advantages over tosylates such as simplicity of preparation, lower tendency to form emulsions, better crystallizing properties, and higher stability which recommend their application as alkylating agents. Mesylates of unsaturated, long-chain alcohols have not been described previously, whereas some saturated analogues are known.[5-7] A simple method for the preparation of saturated and unsaturated long-chain mesylates is presented here. The characteristic data and yields of the crystallized and highly purified products are quoted in Table I.

Alkyl glycerol-(1) ethers are ubiquitous constituents of human,[8] animal,[9] and plant[10] tissues. Hexadecyl,[11] octadecyl,[11] and 9-octadecenyl[12] glyceryl-(1) ethers, the most abundant members of this class of compounds, have been synthesized and so have the short-chain homologs up to C-11.[13] Syntheses of other saturated and unsaturated glyceryl-(1) ethers have not been reported, although it is known that these compounds occur naturally.[14]

Reboul[15] has described the first synthesis of a glyceryl-(1) ether in 1860. The procedure, however, starting from epichlorohydrin and sodium ethoxide, has been found unsuitable for the preparation of long-chain homologues.[11] Therefore, Davis, *et al.*,[11] have developed a method for oxidation of allyl alkyl ethers by means of hydrogen peroxide, which has been improved upon later.[16] In the present study additional methods have been investigated using sodium[17] or potassium salts[3,18] of 1,2-O-isopropylideneglycerol[19] and alkyl halides[18] or tosylates,[3,17] and were compared with results obtained from the reaction of metal alkoxides and various alkylating glycerol derivatives.[12,15]

Thin layer adsorption chromatography (t.l.c.) was employed for analyzing the reaction mixtures of a series of experiments. It was found that the use of 1,2-O-isopropylideneglyceryl tosylate as alkylating agent, as suggested by Baer, *et al.*,[12] for the synthesis of glyceryl-(1) ethers, leads invariably to formation of sub-

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TABLE I

METHANESULFONATES

CH_3SO_3R

No.	R	Formula	Mol. wt.	% yield	M.p., °C.	Sulfur, % Calcd.	Sulfur, % Found
I	Decyl[a]	$C_{11}H_{24}O_3S$	236.4	65	18.5	13.57	13.42
II	Dodecyl[b]	$C_{13}H_{28}O_3S$	264.4	77	32.5–33	12.13	11.72
III	Tetradecyl[b]	$C_{15}H_{32}O_3S$	292.5	71	44–45	10.96	11.02
IV	Hexadecyl[b,c]	$C_{17}H_{36}O_3S$	320.5	77	54–55	10.01	10.20
V	Octadecyl[b]	$C_{19}H_{40}O_3S$	348.6	70	61.5	9.20	8.92
VI	Eicosyl	$C_{21}H_{44}O_3S$	376.7	71	66	8.51	8.51
VII	*cis*-9-Hexadecenyl	$C_{17}H_{34}O_3S$	318.5	55	0.5	10.06	9.72
VIII	*cis*-9-Octadecenyl	$C_{19}H_{38}O_3S$	346.6	85	9	9.25	9.07
IX	*trans*-9-Octadecenyl	$C_{19}H_{38}O_3S$	346.6	92	32	9.25	8.67
X	*cis,cis*-9,12-Octadecadienyl	$C_{19}H_{36}O_3S$	344.6	79	−5	9.31	9.10
XI	*cis,cis,cis*-9,12,15-Octadecatrienyl[d]	$C_{19}H_{34}O_3S$	342.6	43	...	9.36	9.20

[a] See ref. 6. [b] See ref. 7. [c] See ref. 5. [d] Different batches of starting material contained up to 20% of *trans* isomers.

TABLE II

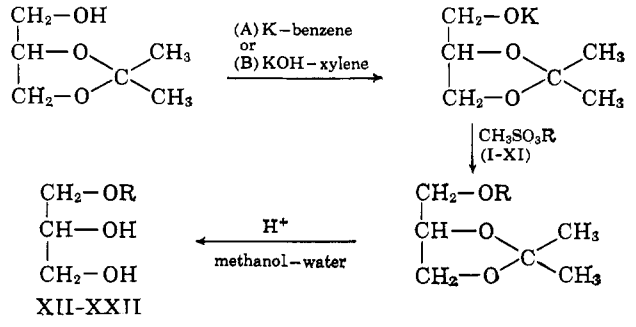
GLYCERYL-(1) ETHERS

No.	R	Formula	Mol. wt.	% yield, method A	% yield, method B	M.p., °C.	CST, °C.[a]	R_f THF–H_2O (1:1)	Calcd., % C	Calcd., % H	Calcd., % O	Found, % C	Found, % H	Found, % O
XII	Decyl[b]	$C_{13}H_{28}O_3$	232.4	89	63	38.5	55	0.86	67.20	12.15	20.65	67.10	12.19	20.68
XIII	Dodecyl	$C_{15}H_{32}O_3$	260.4	73	75	49.5	66.5	0.70	69.18	12.39	18.43	69.35	12.30	18.87
XIV	Tetradecyl	$C_{17}H_{36}O_3$	288.5	80	81	58.5	74	0.55	70.78	12.58	16.64	71.12	12.34	16.81
XV	Hexadecyl[c]	$C_{19}H_{40}O_3$	316.5	69	79	65.5	81	0.44	72.10	12.74	15.16	72.26	12.28	15.29
XVI	Octadecyl[c,d]	$C_{21}H_{44}O_3$	344.6	78	78	71–71.5	87.5	0.34	73.20	12.87	13.93	72.82	12.98	13.71
XVII	Eicosyl	$C_{23}H_{48}O_3$	372.6	85	79	76.5–77	93	0.26	74.14	12.98	12.88	73.95	12.93	12.81
XVIII	*cis*-9-Hexadecenyl	$C_{19}H_{38}O_3$	314.5	57	...	12.5	68	0.51	72.56	12.18	15.26	71.67	12.23	15.79
XIX	*cis*-9-Octadecenyl[e]	$C_{21}H_{42}O_3$	342.6	45	49	18–19	75	0.40	73.63	12.36	14.01	73.80	12.58	13.68
XX	*trans*-9-Octadecenyl[e]	$C_{21}H_{42}O_3$	342.6	81	...	49	77	0.42	73.63	12.36	14.01	73.76	12.00	13.98
XXI	*cis,cis*-9,12-Octadecadienyl	$C_{21}H_{40}O_3$	340.6	68	...	8	62	0.49	74.07	11.84	14.09	73.65	11.81	14.42
XXII	*cis,cis,cis*-9,12,15-Octadecatrienyl[f]	$C_{21}H_{38}O_3$	338.5	66	...	13	52.5	0.58	74.51	11.31	14.18	74.05	11.46	14.04

[a] Critical solution temperatures with nitromethane. [b] See ref. 13. [c] See ref. 11. [d] See ref. 16. [e] See ref. 12. [f] Different batches of starting material contained up to 20% of *trans* isomers.

stantial amounts of dialkyl ethers. Obviously, transalkylation proceeds faster than alkylation of the alkoxides. This was confirmed by isolation of diisopropylideneglyceryl ether and dialkyl ethers by t.l.c. from the reaction mixtures. These side products were identical with reference products (melting point, mixture melting point, R_f values, and infrared spectra), prepared from potassium alkoxides and the corresponding mesylates.

The present communication describes two convenient methods (A and B) for the synthesis of glyceryl-(1) ethers in high yields. Both procedures utilize alkyl methanesulfonates which are treated with 1,2-O-isopropylideneglycerol. Method A uses potassium in absolute benzene, method B uses potassium hydroxide in xylene for condensation. In the latter procedure



(B), the water formed is removed continuously by azeotropic distillation. Hydrolysis of the ketals and recrystallization yield products XII–XXII.

The *n*-alkyl glyceryl-(1) ethers of the saturated alcohols C-10 through C-20 with an even-numbered carbon chain were prepared by both routes. To avoid isomerization, method A is recommended for the synthesis of unsaturated compounds, although the unsaturated ether XIX prepared by method B was free of *trans* isomers.

The infrared spectra of compounds XVIII, XIX, and XXI show bands for *cis*-C—H stretching vibrations at 2985 and for C=C stretching near 1650 cm.$^{-1}$. The latter frequency is not detectable in the case of compound XX, because of the relative symmetry of the *trans* double bond in the long carbon chain.[20] The *trans*-C–H out-of-plane deformation occurs at 965 cm.$^{-1}$.

The spectra of the methyl esters of unsaturated carboxylic acids used as starting materials and those of the end products indicate that no *cis–trans* isomerization of the double bonds occurred in the course of the synthesis of glyceryl ethers. In glyceryl-(1) ethers the ether groups show characteristic C–O frequencies at

(20) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co., Ltd., London, and John Wiley and Sons, Inc., New York, N. Y., 1958, p. 39.

1122–1117 cm.$^{-1}$, and in symmetrical long-chain dialkyl ethers at 1113 cm.$^{-1}$.

The ultraviolet spectrum of XXI does not exhibit absorption near 230 mμ associated with conjugated double bond systems.

Experimental

Critical solution temperatures (CST)[21] with nitromethane (Fisher Scientific Co., No. N 98) and melting points were determined on a Kofler hot stage[22] and are corrected.

Infrared spectra were recorded with the Perkin-Elmer spectrophotometer Model 21 in carbon disulfide solution or potassium bromide pellets.

Elemental analyses were by Mikroanalytisches Laboratorium I. Beetz, 8640 Kronach, Germany.

Saturated and unsaturated alcohols were prepared from the methyl esters of the corresponding carboxylic acids (The Hormel Institute) by reduction with lithium aluminum hydride.[23]

The purity of each of the methyl esters in regard to chain length and degree of unsaturation was established by the supplier through gas–liquid chromatography. The course of reactions and purity of products were checked by ascending thin layer adsorption chromatography[24] on Silica Gel G (Merck). The plates were developed with hexane–diethyl ether (70:30 v./v.) for mesylates in unlined tanks or with hexane–diethyl ether–acetic acid (60:40:1 v./v./v.) for glyceryl ethers in tanks lined with filter paper. After chromatography, the plates were sprayed lightly with a solution, which had been prepared from 15 g. of potassium dichromate, 30 ml. of concentrated sulfuric acid, and 150 ml. of water, and the substances were made visible by charring them at 180°. Thin layer adsorption chromatography of the glyceryl ethers verified their purity in regard to other classes of compounds, and reversed-phase partition chromatography on siliconized Whatman No. 1 paper[25] was employed to assure uniform chain length and degree of unsaturation.

With unsaturated compounds, all procedures were carried out under purified nitrogen using oxygen-free water and freshly distilled solvents for extractions.

A. Preparation of Methanesulfonates I–XI.—The synthesis of X is described in detail. All other methanesulfonates were prepared under similar conditions.

cis,cis-**9,12-Octadecadienyl Methanesulfonate (X).**—In a 500-ml., three-necked flask equipped with a mechanical stirrer, inlet and outlet tubes for purified nitrogen, and a dropping funnel (connected with the nitrogen inlet tube) 23.0 g. (86 mmoles) of *cis,cis*-9,12-octadecadienol is dissolved in 80 ml. of absolute pyridine (kept dry by storing over solid potassium hydroxide). The solution is chilled in an ice bath, and 15.0 g. (130 mmoles) of methanesulfonyl chloride (Eastman No. 5388) is added dropwise during 1 hr. The ice bath is removed and stirring is continued for another 5 hr. at room temperature.

The almost colorless slurry is dissolved by adding 150 ml. of oxygen-free water and 200 ml. of ether with stirring and cooling, and the mixture is transferred to a 1-l. funnel. The yield of methanesulfonate depends greatly upon the rapidity and manner the extraction is done. After separation the water layer is kept in an ice bath. The ether phase is extracted consecutively with 50 ml. of water, 2 *N* sulfuric acid (until acidic), 50 ml. of water, 1% potassium carbonate solution (until neutral or basic), and 50 ml. of water. The organic layer is dried over anhydrous sodium sulfate.

The original water phase and the other *basic* water layers are combined and treated with 200 ml. of ether. After washing the ether extract with 50 ml. of water, it is used to extract the original *acidic* layers (add 2 *N* H_2SO_4, if basic). The organic phase is then treated with 50 ml. of water, 1% potassium carbonate solution, and 50 ml. of water, and is dried with the original extract over sodium sulfate.

After removing the solvent in a rotary evaporator, the residue is dissolved in 120 ml. of absolute ethanol and recrystallized at −50°. The long needles of methanesulfonate X are collected at the same temperature on a chilled Büchner funnel. The product is transferred into a flask and dried first by a nitrogen stream, then under vacuum, yielding 23.7 g. (79%), m.p. −5°.

The methanesulfonate XI is recrystallized and the crystals are separated at −50°; I, II and VII–IX at −30° (freezer); methanesulfonates III–VI are isolated at room temperature after storing in the refrigerator.

B. Preparation of Glyceryl-(1) Ethers XII–XXII. Method A. *cis,cis*-**9,12-Octadecadienyl Glyceryl-(1) Ether (XXI).**—In a 300-ml., three-necked flask fitted with a reflux condenser, magnetic stirrer, nitrogen inlet and outlet tubes, and a dropping funnel (connected with the nitrogen inlet tube) are placed 80 ml. of dry benzene and 1.6 g. (40 mmoles) of clean pieces of potassium. The mixture is refluxed for 2 hr., then 5.3 g. (40 mmoles) of 1,2-*O*-isopropylideneglycerol[26] is added dropwise and refluxing is continued for another 4 hr. *cis,cis*-9,12-Octadecadienyl methanesulfonate (X, 12.2 g., 35 mmoles), dissolved in 20 ml. of dry benzene, is added dropwise and the reaction is continued for 15 hr. The flask is chilled in a water bath, moist ether and oxygen-free water are added, and the extraction is carried out in a 1-l. separatory funnel under nitrogen using approximately 250 ml. of water and 250 ml. of ether. After a second extraction with 150 ml. of ether, the combined ether layers are washed with water and are dried over anhydrous potassium carbonate. The solvent is removed by distillation in a rotary evaporator under vacuum. The residue of almost pure *cis,cis*-9,12-octadecadienyl 2,3-O-isopropylideneglyceryl-(1) ether is hydrolyzed by refluxing in a solution of 5 ml. of concentrated hydrochloric acid in 50 ml. of methanol. After cooling, the resultant product is treated with 100 ml. of water and the solution is extracted with 250 and 150 ml. of ether. The ether extract is washed consecutively with small amounts of water, 1% potassium carbonate solution, and water, and is dried over anhydrous sodium sulfate. Evaporation and recrystallization of the residue from 70 ml. of low-boiling hydrocarbon (Skellysolve F) at −50° and filtration over a chilled Büchner funnel yields 8.2 g. (68%, over two stages, on the basis of X) of glyceryl ether XXI, m.p. 8°.

The glyceryl ethers XII–XXII are prepared under conditions described for XXI; XXII is purified in the same manner as XXI; XVIII–XX are recrystallized and separated under nitrogen at −30°. The saturated ethers XII–XVII are isolated at room temperature after storing their solutions (Skellysolve F) in the refrigerator.

Method B. Tetradecyl Glyceryl-(1) Ether (XIV).—Powdered potassium hydroxide 2.5 g., 80 ml. of xylene, and 2.1 g. (15 mmoles) of 1,2-O-isopropylideneglycerol[26] are placed in a 300-ml., three-necked flask, fitted with water separation head, reflux condenser, dropping funnel, magnetic stirrer, and heating mantle. The mixture is refluxed for 1 hr. to remove water by azeotropic distillation. Tetradecyl methanesulfonate (III, 2.9 g., 10 mmoles), dissolved in 20 ml. of xylene, is added dropwise, and refluxing is continued for another 4–5 hr. After removing 50 ml. of xylene by distillation, cooling, addition of water, and extraction with ether (see method A), the product is saponified and the glyceryl ether is recrystallized yielding 2.3 g. (81%) of tetradecyl glyceryl-(1) ether (XIV), m.p. 58.5°.

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