[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY[1]]

# Esters of Lactyllactic Acid

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The reaction of α-acetoxypropionyl chloride (I) with alkyl lactates (II) was used recently[2] to prepare certain esters (III) of dimeric lactic acid (lactyllactic acid). The reaction of I with lactic esters has now been used to make additional esters (III) of lactyllactic acid. The yields were high (80 to 90%), and therefore this method appears to be generally suitable for synthesizing acyl derivatives of lactyllactic esters[3] (Table I).

$$\underset{\text{I}}{CH_3COOCH(CH_3)COCl} + \underset{\text{II}}{HOCH(CH_3)COOR} \longrightarrow \underset{\text{III}}{CH_3COOCH(CH_3)COOCH(CH_3)COOR}$$

TABLE I

PROPERTIES OF $CH_3COOCH(CH_3)COOCH(CH_3)COOR$

| R | B. p., °C. 10 mm. | B. p., °C. 1 mm. | $n^{20}_D$ | $d^{20}_4$ | $M^{20}_D$ Calcd. | $M^{20}_D$ Obs. | C, %[a] Calcd. | C, %[a] Found | H, % Calcd. | H, % Found | Sapon. equiv. Calcd. | Sapon. equiv. Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $—CH_2CH_2O(CH_2)_4H$ | 156 | 129 | 1.4340 | 1.0705 | 73.46 | 74.04 | 55.25 | 54.93 | 7.95 | 7.94 | 101.4 | 101.7 |
| $—CH_2CH_2OCH_2CH_2O(CH_2)_4H$ | 200 | 167 | 1.4383 | 1.0785 | 84.34 | 84.84 | 55.16 | 55.07 | 8.10 | 7.97 | 116.1 | 115.6 |
| $—CH_2\underbrace{CHCH_2CH_2CH_2}_{O}$ | 170 | 138 | 1.4488 | 1.1556 | 66.64 | 66.88 | 54.16 | 53.94 | 6.99 | 6.93 | 96.1 | 96.3 |
| $—CH_2CH_2OCH_2CH_2Cl$[b] | 194 | 161 | 1.4480 | 1.2008 | 69.09 | 69.04 | ... | ... | .. | .. | ... | ... |
| $—CH_2CH_2OCOCH(CH_3)OCOCH_3$[c] | 175–180 at 0.4 mm. | | 1.4416 | 1.1963 | 79.69 | 80.07 | 49.72 | 49.64 | 6.12 | 6.25 | 72.5 | 73.1 |

[a] The authors are indebted to Mary J. Welsh, Mildred H. Selvecki and C. O. Willits for analytical data. [b] Chlorine content, 11.21% (calcd., 11.45%). [c] Viscosity at 20°; 937.1 centipoises; solubility in water at 29°; 0.57 g. per 100 ml.

Because of their relatively low vapor pressures[4] and their solubilizing ester groups, the compounds of Table I might be suitable as plasticizers and high-boiling solvents. On the basis of earlier work,[2] it would be anticipated that only low yields of the corresponding acrylates ($CH_2{=}CHCO-OCH(CH_3)COOR$) would result from the pyrolysis of the esters of Table I.

## Experimental

α-Acetoxypropionic acid,[5] α-acetoxypropionyl chloride,[2,5] tetrahydrofurfuryl lactate,[6,7] and β-*n*-butoxyethyl lactate[6] were made by previously described methods. Acetoxypropionic acid was made also by the interaction of methyl lactate and acetic acid as described below. Methyl lactate is advantageous as a raw material for making α-acetoxypropionic acid in that it (unlike lactic acid) can be readily purified by distillation. Vigreux columns approximately 20 in. high were used in most of the distillations.

**α-Acetoxypropionic Acid.**—A mixture of 728 g. of methyl lactate, 2520 g. of acetic acid, 1000 ml. of benzene, and 4 ml. of concentrated sulfuric acid was refluxed in a 5-liter flask attached to a column (50 × 3.8 cm.) packed with short pieces of Pyrex glass tubing; a modified Barrett tube (cooled by passing water through its jacket) was attached to the top of the packed column. The aqueous layer and low-boiling material, collected in the Barrett tube, was drained periodically (total of 130 ml. of aqueous layer plus 1500 ml. of low-boiling material). The Barrett tube was then replaced by a still head, and the mixture was distilled at atmospheric pressure (1000 ml. of distillate, principally benzene, collected). The acetic acid was then distilled under reduced pressure (water aspirator). The distillation was continued (oil pump); acetoxypropionic acid (68% of the theoretical) was collected at about 101° (1.8 mm.).

Acetoxypropionic acid was converted into its acid chloride by treatment with thionyl chloride.[2,5]

**Lactate of Diethylene Glycol Mono-*n*-butyl Ether.**—This ester was obtained by direct esterification[6] (63% yield) and by alcoholysis[6] (81% yield) of ethyl lactate; b. p. at 2.2 mm., 138°; $d^{20}_4$ 1.0333; $n^{20}_D$ 1.4397; $M^{20}_D$ 59.72 (calcd., 59.46). *Anal.* Calcd. for $C_{11}H_{22}O_5$: C, 56.39; H, 9.47; sapn. equiv., 234.3. Found: C, 56.15; H, 9.40; sapn. equiv., 235.1.

**Lactate of Glycol Mono-β-chloroethyl Ether.**—This compound was made by alcoholysis[6] (79% yield) of ethyl lactate and by direct esterification[6] (96% yield) of lactic acid (82% edible grade) and β-(chloroethoxy)-ethanol[8]; b. p. at 1.6 mm., 111°; $d^{20}_4$ 1.2088; $n^{20}_D$ 1.4565; $M^{20}_D$ 44.26 (calcd., 44.21). *Anal.* Calcd. for $C_7H_{13}O_4Cl$: C, 42.75; H, 6.66; Cl, 18.03; sapn. equiv., 98.3. Found: C, 42.60; H, 6.27; Cl, 18.15; sapn. equiv., 98.9.

**Ethylene Glycol Monolactate.**—Two moles of methyl lactate, 6 moles of ethylene glycol, and 2 g. of aluminum *i*-propoxide were refluxed gently under a 50-cm. Vigreux column. Methanol was distilled slowly as formed. When the distillation of methanol was complete, the excess glycol was distilled under vacuum, a modified alembic flask[9] being used. The product (82% yield) distilled over a 20° range. It was redistilled and the following data were obtained with the middle fraction (b. r. 105–111° at approx. 0.1 mm.): $n^{20}_D$ 1.4495; $d^{20}_4$ 1.1996; $M^{20}_D$ 30.02 (obs.), 29.99 (calcd.). *Anal.* Calcd. for $C_5H_{10}O_4$: C, 44.77; H, 7:52; sapn. equiv., 134.1. Found: C, 44.87; H, 7.73; sapn. equiv., 134.9.

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[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, United States Department of Agriculture.

[2] E. M. Filachione, J. H. Lengel and C. H. Fisher, THIS JOURNAL, **68**, 330 (1946).

[3] Acetyl derivatives of alkyl lactyllactates have been made by acetylating lactyllactates, which had been prepared by the reaction of lactide with methanol, ethanol and *n*-butanol (H. V. Claborn, U. S. Patent 2,350,388, June 6, 1944).

[4] *n*-Butyl phthalate, a widely used plasticizer, boils at 195 and 149° at 10 and 1 mm., respectively [K. C. D. Hickman, *J. Franklin Inst.*, **221**, 383 (1936); some of the esters of the present work (Table I) have comparable or lower vapor pressures].

[5] E. M. Filachione, J. H. Lengel, and C. H. Fisher, THIS JOURNAL, **66**, 494 (1944).

[6] M. L. Fein, W. P. Ratchford and C. H. Fisher, *ibid.*, **66**, 1201 (1944).

[7] H. V. Claborn, U. S. Patent 2,222,363, Nov. 19, 1940, and U. S. Patent 2,229,997, Jan. 28, 1941.

[8] This alcohol (diglycol chlorohydrin), butyl Cellosolve, and butyl Carbitol were kindly supplied by the Carbide and Carbon Chemicals Corporation.

[9] Similar to that described by J. C. Cowan, L. B. Falkenburg and H. M. Teeter, *Ind. Eng. Chem., Anal. Ed.*, **16**, 90 (1944).

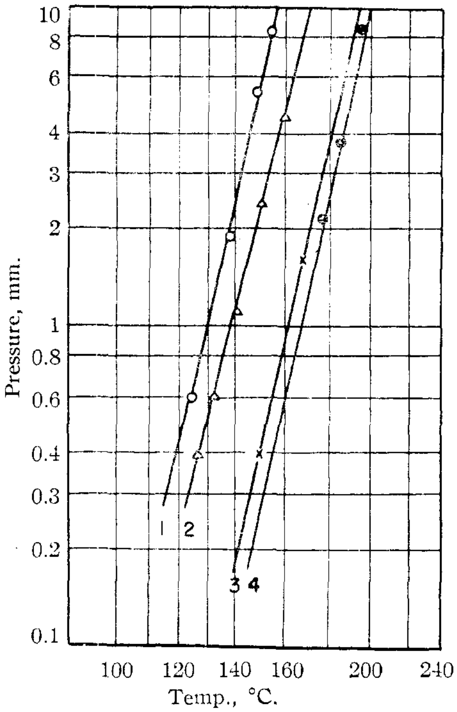

Fig. 1.—Boiling points of $CH_3COOCH(CH_3)COOCH(CH_3)COOR$: 1, R is $—CH_2CH_2O(CH_2)_4H$; 2, R is $—CH_2CHCH_2CH_2CH_2$; 3, R is $—CH_2CH_2OCH_2CH_2Cl$;
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4, R is $—CH_2CH_2OCH_2CH_2O(CH_2)_4H$.

The following boiling points were determined with a narrow-boiling fraction of glycol monolactate: 100° (0.4 mm.), 109° (1.2 mm.), 124° (4.2 mm.) and 139–140° (10.4 mm.).

Other possible products are ethylene glycol dilactate, methyl lactyllactate, the methyl ester of higher polylactic acids and lactide. From the results of several preparations in which various ratios of glycol to methyl lactate were used, it appears that glycol monolactate is the favored product.

Smith and Claborn[10] and Evdokimov[11] prepared glycol monolactate by direct esterification. The following physical constants were given: b. r. 285–287[11]; 140° (10 mm.)[10]; $d^{25}_{25}$ 1.1967[10]; and $n^{25}_D$ 1.4452.[10]

**Reaction of α-Acetoxypropionyl Chloride with Lactic Esters.**—The previously described method[2] was used. It was found important to keep the temperature below approximately 20° during the addition of acid chloride to the lactic ester; at higher temperatures the corresponding acetoxypropionates ($CH_3COOCH(CH_3)COOR$) were formed to some extent. particularly in the case of the tetrahydrofurfuryl ester.

**Compatibilities.**—The di-α-acetoxypropionate of glycol monolactate was compatible with commercially available samples of cellulose acetate (80% acetate–20% lactic ester), cellulose acetate butyrate (80% cellulose derivative–20% lactic ester) and ethyl cellulose (50% ethyl cellulose–50% lactic ester). The di-acetoxypropionate of glycol monolactate was only slightly compatible with polyvinyl chloride.

*Vapor pressures* of four of the esters of Table I were determined by careful distillation either through a Vigreux column or in an alembic flask.[9] The data thus obtained (Fig. 1) gave straight lines when plotted on a Cox chart.[12,13] Results (168 and 185° at 3 and 7.5 mm., respectively) obtained by distilling *n*-butyl phthalate in a similar manner agreed with the data of Hickman.[4]

## Summary

Several esters ($CH_3COOCH(CH_3)COOCH(CH_3)COOR$) of dimeric lactic acid (lactyllactic acid) were made in high yields by treating certain lactic esters ($HOCH(CH_3)COOR$: R = $—CH_2CH_2O(CH_2)_4H$, $—CH_2CH_2OCH_2CH_2O(CH_2)_4H$, $—CH_2CHCH_2CH_2CH_2$, $—CH_2CH_2OCH_2CH_2Cl$,
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and $—CH_2CH_2OH$) with α-acetoxypropionyl chloride. It is considered that this method is generally suitable for the preparation of acyl derivatives of alkyl lactyllactates. The satisfactory preparation of the intermediate lactic esters and of α-acetoxypropionyl chloride (from the interaction of methyl lactate and acetic acid followed by treatment with thionyl chloride) is described.

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[10] Lee T. Smith and H. V. Claborn, *Ind. Eng. Chem.*, **32**, 692 (1940).

[11] A. G. Evdokimov, *Priroda*, No. 11, 68 (1940); *C. A.*, **38**, 717 (1944).

[12] E. R. Cox, *Ind. Eng. Chem.*, **15**, 592 (1923).

[13] G. Calingaert and D. S. Davis, *ibid.*, **17**, 1287 (1925).