New Derivatives of Levulinic Acid. I.[1] Synthesis of 2,3-Epoxy-3-Methyladipic Esters

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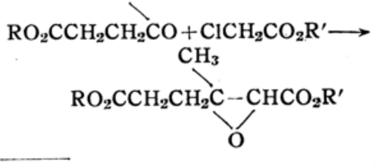
Glycidic esters, namely 2, 3-epoxy esters, are easily obtained by the condensation of carbonyl compounds with α-halo esters[2]. Many types of ketones have been reported to give good yields smoothly. Nevertheless, previous investigations of analogous reactions of keto-esters have not been extended beyond the synthesis of γ-lactones by zinc from ethyl levulinate[3] and 3, 3-dimethyllevulinate[4] with ethyl monobromoacetate.

This investigation was undertaken to synthesize glycidic esters, viz. 2, 3-epoxy-3-methyladipic esters, from levulinic and monochloroacetic esters as represented in the following equation:



$$RO_2CCH_2CH_2\overset{CH_3}{C}O + ClCH_2CO_2R' \longrightarrow RO_2CCH_2CH_2\overset{CH_3}{C}\underset{O}{-}CHCO_2R'$$

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[1] Presented at the 7th Annual Meeting of the Chemical Society of Japan, Tokyo, April 2, 1954.

[2] M. S. Newman, *Org. Reactions*, **5**, 413 (1949), a review.

[3] H. E. Baumgarten, *J. Am. Chem. Soc.*, **75**, 979 (1953).

[4] H. E. Baumgarten and W. P. Schneider, *J. Org. Chem.*, **16**, 1658 (1951).

n-Butyl (I), 2-ethylhexyl and lauryl levulinates were used as a carbonyl component, *n*-butyl (I′), 2-ethylhexyl and lauryl monochloroacetates as halo ester, and sodium methoxide, sodium ethoxide, potassium *tert.*-butoxide⁵⁾ and sodium amide as a condensing agent. The synthesis of these glycidic esters was conducted by a slightly modified procedure of the standard Darzens glycidic synthesis.

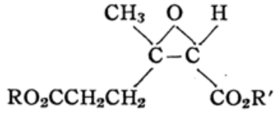
The results are presented in Table I. On the basis of the saponification value and quantitative elemental analysis, it seems reasonable to assume that the products, obtained by the use of potassium *tert.*-butoxide and sodium amide as the condensing agent, are the desired 2, 3-epoxy-3-methyladipic esters, which have not yet been reported in literature. In the case of these two di-*n*-butyl esters, the observed values of molecular refraction are higher by about 0.7 than the calculated value. From consideration of the case of cyclopropane (exaltation is known as +0.7) this exaltation seems to be attributed to the existence of a three-membered oxirane ring neighbouring a carboxyl group.

The epoxy contents of these glycidic esters were determined by Swern's method⁶⁾. The observed epoxy contents of these epoxy esters, however, were about one third of the calculated values, while the observed epoxy content of 2, 3-epoxylauric acid⁷⁾ and the observed iodine values for 2, 3-unsaturated acids show also similar results. Therefore the low observed values are probably due to some effect of the neighbouring carboxyl group.

Slight differences are observed between the properties of the two di-*n*-butyl esters, obtained by potassium *tert.*-butoxide and sodium amide respectively, while the esters obtained by sodium amide have a tendency to turn yellow if kept. Therefore these differences may be due to some impurities.

TABLE I

2, 3-Epoxy-3-methyladipates



R	R′	Condensing agent	Yield %	b. p.	S. V. Calcd.	S. V. Found	n_D^{20}	Analytical C% Calcd.	Analytical C% Found	Analytical H% Calcd.	Analytical H% Found
n-Butyl	*n*-Butyl	$NaNH_2$	17	148-149°/1.5 mmHg	391.8	395.9	1.4478	62.91	62.80	9.15	9.20
"	"	*tert.*-BuOK	48	189-191°/15 mmHg	"	389.1	1.4458	"	62.56	"	9.25
"	2-Ethylhexyl	$NaNH_2$	(11)	163-165°/1 mmHg	327.6	322.2	1.4537	66.63	66.50	10.01	10.10
2-Ethylhexyl	*n*-Butyl	"	(10)	159°/1 mmHg	327.6	322.5	1.4532	66.63	66.80	10.01	10.15
"	2-Ethylhexyl	"	(8)	ca. 160°/0.1 mmHg	281.5	285.0	1.4599	69.31	69.01	10.62	10.66
n-Butyl	Lauryl	"	(24)	ca. 190°/0.1 mmHg	281.5	288.2	1.4602	69.31	69.27	10.62	10.73
Lauryl	*n*-Butyl	"	(23)	ca. 195°/0.1 mmHg	281.5	273.1	1.4595	69.31	69.20	10.62	10.55
2-Ethylhexyl	Lauryl	"	(25)	ca. 200°/0.1 mmHg	246.8	246.2	1.4650	71.32	71.09	11.09	11.25
Lauryl	2-Ethylhexyl	"	(23)	ca. 200°/0.1 mmHg	246.8	243.0	1.4642	71.32	71.38	11.09	11.30
"	Lauryl	"	(28)	ca. 220°/0.1 mmHg	219.5	225.0	1.4708	72.89	72.75	11.45	11.68
"	"	*tert.*-BuOK	(34)	ca. 220°/0.1 mmHg	"	221.5	1.4695	"	72.70	"	11.58

Yields in parentheses show those of the crude ester.

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[5] W. S. Johnson, J. S. Beloew, L. J. Chinn and R. H. Hunt, *J. Am. Chem. Soc.*, **75**, 4995 (1953).

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[6] D. Swern, T. W. Findley, G. N. Billen and J. T. Scanlan, *Anal. Chem.*, **19**, 414 (1947).

[7] Unpublished data, 2, 3-epoxylauric acid was obtained by epoxidation of *trans*-2-dodecenoic acid with hydrogen peroxide and acetic acid, m.p. 48—48.5°C.

which must be included in the esters by sodium amide[8].

Only a few drops of the pure esters were obtained from the combinations of the higher starting esters, because of their higher boiling points and greater tendency to decompose at elevated temperatures. Also, as commercial sodium amide from different stock was used in each reaction, it is impossible to compare the reactions in regard to yield. But combinations of the lower starting esters gave generally lower yields, which is perhaps due to hydrolysis of the keto-esters. While it was reported that cyclohexanone and monochloroacetic esters gave as high as 90% of the desired products by the use of potassium *tert.*-butoxide[5], only 48% of the desired di-*n*-butyl 2, 3-epoxy-3-methyladipate was obtained from (I) and (I′) under similar conditions. But this yield is still higher than those obtained in the case when sodium amide was used. Sodium ethoxide and methoxide were not suitable as condensing agent, because they probably caused transesterification and gave no desired results. Calculated saponification values are 391.8 for di-*n*-butyl 2, 3-epoxy-3-methyladipate, 488 for the diethyl ester and 555 for the dimethyl ester, while the observed values were 554 for the ester obtained by sodium ethoxide and 585 for the ester obtained by sodium methoxide. Therefore it is deduced that these fractions suffered transesterification and some hydrolysis, and that they were also contaminated by some by-products.

As they are the esters of a dibasic acid and have an epoxy ring, these esters would be able to be utilized as a plasticizer and simultaneously as a stabilizer for polyvinyl chloride (PVC). In fact they showed more excellent results than dioctyl phthalate in our preliminary examinations. For example, the testing sheets, obtained by adding 30, 40 and 50 parts of di-*n*-butyl 2, 3-epoxy-3-methyladipate to 100 parts of polyvinyl chloride, were put to the Shopper tensile strength test at 25°C, and the values of tensile strength, elongation, elongation at 100 kg./cm² load, 100% modulus,tear resistance and permanent set are listed in Table II. Also it was shown that they were heat-proof stabilizers.

TABLE II

SHOPPER TENSILE STRENGTH TEST (at 25°C)

Proportion of the di-*n*-butyl ester (Parts to 100 parts of PVC)	30	40	50
Elongation %	175	245	283
Tensile strength kg./cm²	324	209	206
Elongation at 100 kg./cm² load	5	105	165
100 % Modulus kg./cm²	246	98	68
Tear resistance kg./cm²	161	100	70
Permanent set %	65	12.5	10

Experimental

Reagents. *Levulinic acid.*—This material was obtained by courtesy of the Aji-no-moto Co. Ltd., and was used without purification.

Monochloroacetic acid and sodium amide.—Commercial products were used without purification.

2-Ethylhexyl alcohol.—A commercial product, obtained by courtesy of the Shin-Nihon-Chisso-Hiryo K. K., was distilled under diminished pressure, b. p. 94°C/27 mm Hg.

Lauryl alcohol.—Commercial fatty alcohol, obtained by hydrogenation of coconut oil, was rectified repeatedly in vacuo, b. p. 140–141°C/15mm Hg, hydroxyl value 296.5 (calcd. for $C_{12}H_{25}OH$ 301.1), S. V. 2.5.

tert-Butyl alcohol.—Commercial *tert.*-butyl alcohol was dried by refluxing with sodium and then by distilling in the presence of the free metal[9].

Sodium alcoholates.—Eighteen grams (0.8 mol.) of fresh sodium was dissolved in 450 ml. of anhydrous ethyl or methyl alcohol. Upon removal of the excess alcohol under diminished pressure on a water bath the alcoholate was obtained in the form of yellow or white powder.

Potassium tert-butoxide.—Fresh potassium (5.88 g., 0.15 mol.) was dissolved in 125 ml. of dry *tert.*-butyl alcohol by refluxing in an atmosphere of dry nitrogen[9].

Monochloroacetic and levulinic esters.—*n*-Butyl, 2-ethylhexyl and lauryl esters of these two acids were prepared by refluxing a mixture of an appropriate alcohol, acid and concentrated sulfuric acid with azeotropic removal of water. For the preparation of both the lauryl esters and 2-ethylhexyl levulinate benzene was added to the refluxing mixture. Some properties of these six esters are listed in Table III.

TABLE III

STARTING ESTERS

Ester	b. p.	n_D^{25}	S. V.	
			Calcd.	Found
Butyl levulinate	125–126°/20 mmHg	1.4257	327.9	325.8
2-Ethylhexyl levulinate	157–159°/15 mmHg	1.4372	245.8	247.6
Lauryl levulinate	190–195°/18 mmHg	1.4437	204.8	201.9
Butyl monochloroactate	178–180°	1.4271	745.4	749.8
2-Ethylhexyl monochloroacetate	123–124°/16 mmHg	1.4395	542.9	545.1
Lauryl monochloroacetate	158–160°/5 mmHg	1.4468	443.9	445.0

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[8] C. F. H. Allen and J. Van Allan, *Org. Synth.*, **24**, 82.

[9] W. S. Johnson and W. P. Schneider, *Org. Synth.*, **30**, 20.

Syhntheses of 2, 3-epoxy-3-methyladipic esters. Synthesis of the di-*n*-butyl esters (*a*) *Use of sodium amide as condensing agent.*—To a mixture of 86 g. (0.5 mol.) of *n*-butyl levulinate, 75 g. (0.5 mol.) of *n*-butyl monochloroacetate and 100 ml. of dry benzene in a 500-ml. three-necked round-bottomed flask was added 25 g. (0.6 mol.) of pulverized sodium amide over a period of 2 hrs. with mechanical stirring. The temperature was kept at 15–20°C in a water bath. After addition had been completed, the mixture was stirred for 2 hrs. more at room temperature. The mixture was poured upon 350 g. of cracked ice with hand stirring. The organic layer was separated and the aqueous layer was extracted with 100 ml. of benzene. The combined benzene solution was washed with three 100-ml. portions of water, dried with anhydrous sodium sulfate, and benzene was removed under diminished pressure. The product (90 g.) was distilled in vacuo to give 25 g. of the desired ester, b. p. 148–149°C/1.5 mm Hg, n_D^{20} 1.4478, d_4^{20}1.023, S. V. 395.9 (calcd.for the dibutyl ester 391.8).

Found: C 62.80% ; H 9.20%. Calcd. for $C_{15}H_{23}O_5$: C 62.91% ; H9.15%.

Other experiments were conducted in exactly the same way as the above, but the temperature was kept at 5°C. Only a few grams of the di-*n*-butyl ester were obtained.

(*b*) *Use of potassium tert-butoxide as condensing agent.*—A mixture of 25.5 g. (0.15 mol.) of *n*-butyl levulinate, 22.5 g. (0.15 mol.) of *n*-butyl monochloroacetate was placed in a 500-ml. four-necked round-bottomed flask, fitted with a stirrer, thermometer and dropping funnel containing *tert.*-butyl alcohol solution of potassium *tert.*-butoxide (from 5.88 g. of the metal). The reaction was carried out with mechanical stirring in an atmosphere of dry nitrogen. The alcoholate was added during one hour, and then the mixture was stirred for one hour. The temperature was kept at 25–30°C. From the reaction mixture *tert.*-butyl alcohol was removed as much as possible under diminished pressure on a steam bath. After addition of water the product was extracted successively with three 100-ml. portions of ether. The combined ether solution was washed with 50 ml. of water and dried with anhydrous sodium sulfate. The product (35.8 g.) was distilled in vacuo to give 20.5 g. (48% yield) of colorless fraction, b.p. 189–191°C/15 mm Hg, n_D^{20} 1.4458, d_4^{20} 1.021, S. V. 389.1 (calcd. for the dibutyl ester 391.8).

Found: C 62.56% ; H 9.25%. Calcd. for $C_{15}H_{26}O_5$: C 62.91% ; 9.15%.

Other experiments were conducted in exactly the same way as the above, but the temperature was kept at 5–10°C, and 30–38% yields were procured.

(*c*) *Attempted use of sodium ethoxide as condensing agent.*—To a mixture of 86 g. (0.5 mol.) of *n*-butyl levulinate and 75 g. (0.5 mol.) of *n*-monochloroacetate, cooled in an ice-salt bath, 40 g. (about 0.5 mol.) of freshly prepared sodium ethoxide was added over a period of 4 hrs. The mixture was then stirred for 9 hrs. with cooling, 2 hrs. at room temperature, and finally 6 hrs. with warming on a water bath, and then poured on ice water. The mixture was acidified with acetic acid, and the product was extracted with ether. The ether layer was dried with anhydrous sodium sulfate, and the ether was removed under diminished pressure. The product (60 g.) was distilled in vacuo, b.p 150°C/2.5 mm Hg, n_D^{20} 1.4688, S. V. 554.1 (calcd. for the dibutyl ester 391.8).

(*d*) *Attempted use of sodium methoxide as condensing agent.*—The synthesis was conducted similarly to the above. To a mixture of *n*-butyl monochloroacetate (0.5 mol.), *n*-butyl levulinate (0.5 mol.) and 200 ml. of dry benzene was added 54 g. (0.8 mol.) of sodium methoxide. The product (60 g.) was distilled in vacuo to give 24 g. of yellow fraction, b.p. 128–130°C/3 mmHg, n_D^{20} 1.4701, S. V. 584.6 (calcd. for the dibutyl ester 391.8).

Syntheses of the 2-ethylhexyl-(1)-*n*-butyl-(6), *n*-Butyl-(1)-2-ethylhexyl-(6), Di-2-ethylhexyl, Lauryl-(1)-*n*-butyl-(6), *n*-Butyl-(1)-lauryl-(6), Lauryl-(1)-2-ethylhexyl-(6), and 2-Ethylhexyl-(1)-lauryl-(6) esters.—These seven 2, 3-epoxy-3-methyladipates were synthesized from 0.5 mol. of the monochloroacetate and 0.5 mol. of the levulinate by 0.6 mol. of sodium amide in a way exactly similar to the method of synthesis of the di-*n*-butyl ester using sodium amide, and are represented in Table I.

Synthesis of the Di-lauryl ester (*a*) *Use of sodium amide as condensing agent.*—A mixture of 137 g. (0.5 mol.) of lauryl levulinate, 126 g. (0.5 mol.)of lauryl monochloroacetate and 100 ml. of dry benzene was used with 25 g. (0.6 mol.) of sodium amide. The properties of the ester are recorded in Table I.

(*b*) *Use of potassium tert-butoxide as condensing agent.*—To a mixture of 41.0 g. (0.15 mol.) of lauryl levulinate and 37.8 g. (0.15 mol.) of lauryl monochloroacetate was added potassium *tert.*-butoxide prepared from 5.88 g. (0.15 mol.) of potassium. The method of synthesis was exactly similar to that of the di-*n*-butylester. As a residue of the first vacuum distillation (over 150°C/i2 mm Hg), the crude desired ester was obtained n 34% yield, S. V. 221.5 (calcd. for the dilauryl ester 219.7).

Summary

Levulinic and monochloroacetic esters are condensed by sodium amide or potassium *tert.*-butoxide to give the corresponding 2, 3-epoxy-3-methyladipic esters. *n*-Butyl (B), 2-ethylhexyl (O), and lauryl (L) alcohols were used as alcoholic components of these starting esters. Although the yields were poor, nine new esters, namely the B-B, B-O, O-B, B-L, L-B, O-O, O-L, L-O,and L-L 2, 3-epoxy-3-methyladipates were obtained.

As for condensing agents, potassium *tert.*-

butoxide was the most excellent, and sodium amide gave also good results, while sodium ethoxide and methoxide gave no desired ester.

These new esters would be able to be utilized as a stabilizing plasticizer for polyvinyl chloride.

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