A New Method of Synthesis of Alkyl-Glycidyl Esters of Dicarboxylic Acids in High Yields

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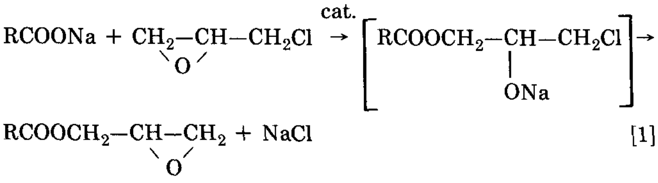
A series of new alkyl-glycidyl esters of dicarboxylic acids which could be used as PVC plasticizers were synthesized. The method adopted is a new synthetic process which can be carried out in two stages. During the first stage, the carboxylic acid anhydride reacts with the salt of the alcohol, and the sodium salt produced reacts with epichlorhydrin in the presence of a catalyst to yield an alkyl-glycidyl ester. The specific reactions give pure products in high yields. The reaction of phthalic acid bisodium salt with epichlorhydrin, as well as the reaction of phthaloyl chloride with glycidol, gave diglycidyl phthalate in 36% and 22% yields, respectively.

KEY WORDS: **Alkyl-glycidyl esters of dicarboxylic acids, cyclic acid anhydrides, dicarboxylic acids, dicarboxylic acid chlorides, dicarboxylic acid disodium salt, dicarboxylic acid sodium salt, diglycidyl esters, epichlorhydrin, monoglycidyl esters, tetraethylammonium iodide.**

In a previous paper (1) a new method was proposed for the preparation of monoglycerides from carboxylic acids and glycidol. The aim was to prepare a new category of glycidyl esters, the alkyl glycidyl esters of dicarboxylic acids, which have a similar structure and properties with monoglycerides (one epoxy ring corresponds to two neighboring hydroxyl groups).

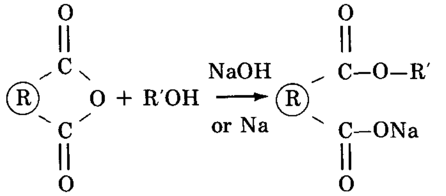
In general, glycidyl esters are prepared from carboxylic acid sodium salts and epichlorhydrine (2-8), according to the reaction:



$$\mathrm{RCOONa} + \underset{\diagdown O \diagup}{\mathrm{CH_2{-}CH{-}CH_2Cl}} \xrightarrow{cat.} \left[\mathrm{RCOOCH_2{-}\underset{ONa}{CH}{-}CH_2Cl}\right] \rightarrow \mathrm{RCOOCH_2{-}\underset{\diagdown O \diagup}{CH{-}CH_2}} + \mathrm{NaCl} \qquad [1]$$

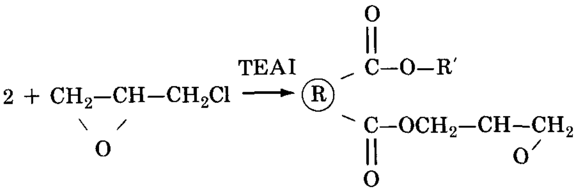
With monocarboxylic acid salts, glycidyl esters are produced in good yields; while with dicarboxylic acid salts only low yields are obtained (9).

Therefore, a study of the reaction between epichlorhydrin and the sodium salts, which are obtained from the reaction of carboxylic acid cyclic anhydrides with a primary alcohol in the presence of sodium hydroxide or metallic sodium is presented in the presence of tetraethylammonium iodide as a catalyst (reactions [2] and [3]).



[2]

2 a-d



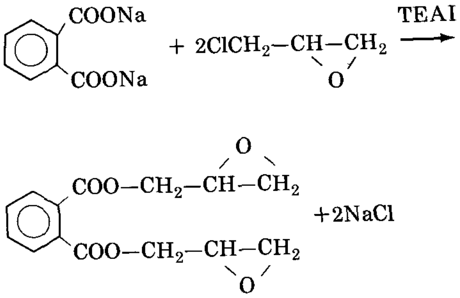
[3]

3 a-d

The anhydrides were selected so that the effect of their electronic structure in the above reaction could be studied.

An attempt was made to synthesize diglycidyl esters, which present special difficulties in their preparation (10-14). The sodium and potassium salts of dicarboxylic acids, which are mainly used for the preparation of diglycidyl esters, have low solubility in epichlorhydrine therefore, the reaction is slow in an anhydrous environment. As a result, the yield is low and the final products contain impurities, which are difficult to eliminate.

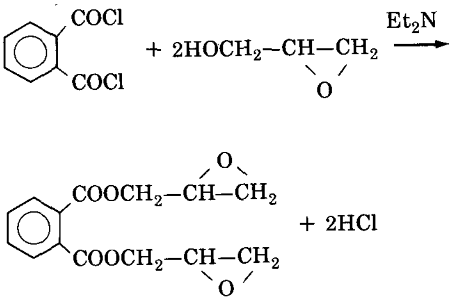
In this study we tried to prepare the diglycidyl esters of phthalic acid in one phase. We proceeded in two ways: i) By reacting the bisodium phthalate and boiling epichlorhydrine in the presence of tetraethylammonium iodide (TEAI) as a catalyst; and



[4]

3 e

ii) by reacting phthaloyl chloride and glycidol at room temperature in the presence of triethylamine as a catalyst.



[5]

The glycidyl and diglycidyl esters present significant industrial applications in the preparation of unsaturated polyester resins (15). They are also new as plasticizers and

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heat stabilizers for chlorine containing polymers (PVC) (16–18), and in the synthesis of high resistance materials for surface coatings (19).

EXPERIMENTAL

The principal starting materials were: Phthalic anhydride, ca. 98% m.p. 130–132°C (Merck, Darmstadt, West Germany); maleic anhydride, ca. 98% m.p. 51–54°C (Merck); succinic anhydride, ca. 98% m.p. 116–119°C (Merck); diacetyl tartaric anhydride, Purum Krist. (Roth, Karlsruhe, West Germany); and bisodium phthalic acid, prepared by titration of a solution of phthalic anhydride-acetone with aqueous 1 NaOH.

Preparation of sodium salts (*reaction* [*2*]). *Sodium salts of monoalkylphthalates.* Sodium hydroxide (40 g, 1 mole) was added to the corresponding alcohol (1 L). The mixture was heated for 2 hr with continuous stirring under N_2. When the mixture dissolved, a slight coloration appeared. Phthalic anhydride (80 g, 0.54 mole) was dissolved in a mixture of benzene (400 mL), and alcohol (400 mL) at 60°C under continuous stirring and a solution of 1N NaOH/alcohol was added to a pH 8.5 (phenolphthalein change).

The solvent and the excess of alcohol were evaporated *in vacuo.* The product was precipitated from acetone, filtered after standing for 3 hr at ca. 3°C, washed with acetone and dried under vacuum over silica-gel. ^1H NMR (D_2O) of $2a_5$ δ:7.45 (m, 4H, aromatic), 5.93(m, 1H, $-CH=$), 5.30 (m, 2H, $=CH_2$), 4.70(d, 2H, $-COOCH_2-$).

Sodium salts of monoalkylmaleates. A solution of maleic anhydride (9.4 g, 0.41 mole) in a mixture of the alcohol (400 mL) and benzene (400 mL) was added to a solution of sodium (0.41 mole) in alcohol (440 mL). The product isolation and purification followed the procedure outlined above. The sodium salts of monoalkylsuccinates and monoalkyl diaketyl tartarates were prepared in a similar way (Table 1).

Preparation of alkyl-glycidyl esters of dicarboxylic acids (*reaction* [3]). A mixture of 0.5 mole of sodium salt 2, 10 mole of epichlorhydrin and 0.01 mole of tetraethylammonium iodide was refluxed under stirring for 45 min at 117°C. The product was filtered at room temperature and the filtrate was isolated from the excess of epichlorhydrin at 120°C under vacuum. The ester was extracted from the residue with ether, washed with water and dried with Na_2SO_4 (Table 2).

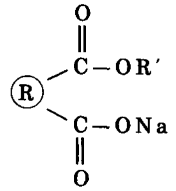
^1H NMR (CD_2Cl_2) of $3a_1$ δ: 7.53 (m, 4H, aromatic), 4.63 (doublet of doublets, 1H, CH_2), 3.98 (doublet of doublets 1H, CH_2), 3.86 (S, 3H, OCH_3), 3.25 (m, 1H, CH oxirane) 2.881 (doublet of doublets, 1H, CH_2 oxirane), 2.65 (doublet of doublets, 1H, CH_2 oxirane).

MS of $3a_1$ $m^+/_z$ (%) 236 (1), 204(12), 164(28), 163(100), 149(29), 146(19), 135(11), 105(9), 104(13), 92(9), 77(30), 57(63).

Preparation of diglycidyl phthalate (*reaction* [*3e*]). The bisodium salt of phthalic acid (80 g, 0.38 mole) was gradually added during 30 min at 130°C to epichlorhydrin (1.4 kg, 15 mole) containing 3.6 g of tetraethylammonium

TABLE 1

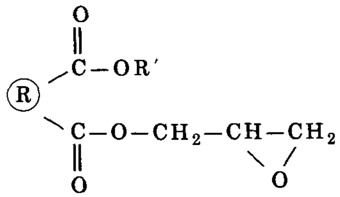
Yields and Analytical Data of the Sodium Salts of Monoalkyl Dicarboxylates



Anhydride	Alcohol	Compd	R	R′	Yield (% Th.)	m.p. (°C)	Acid number	
							exptal	calc
Phthalic	Methanol	$2a_1$	$o-C_6H_4$	CH_3-	97	105-108	310	311
Phthalic	n-Butanol	$2a_2$	$o-C_6H_4$	$n-C_4H_9-$	96	111-114	250,1	252
Phthalic	n-Octanol	$2a_3$	$o=C_6H_4-$	$-n=C_8H_{17}-$	95	120-122	199	201,5
Phthalic	2-Ethyl-1-hexanole (iso-octanol)	$2a_4$	$o=C_6H_4-$	$C_4H_9-\underset{\underset{C_2H_5}{\vert}}{CH}-CH_2-$	96	189-193	201	201,5
Phthalic	Allylalcohol	$2a_5$	$o\text{-}C_6H_4$	$CH_2=CH-CH_2-$	98	310<	257	271
Maleic	Methanol	$2b_1$	$-CH=CH-$	CH_3-	85	85-88	425,5	430,7
Maleic	n-Butanol	$2b_2$	$-CH=CH-$	$n-C_4H_9-$	82	95-97	319,3	325,5
Maleic	n-Octanol	$2b_3$	$-CH=CH-$	$-n=C_8H_{17}-$	80	101-102	237,1	245,8
Succinic	Methanol	$2C_1$	$-CH_2-CH_2-$	CH_3-	83,5	70-71	420,1	424
Succinic	n-Butanol	$2C_2$	$-CH_2\_CH_2-$	$-n=C_4H_9-$	81	91-92	315,4	322
Succinic	n-Octanol	$2C_3$	$-CH_2-CH_2-$	$-n=C_8H_{17}-$	78	110-112	234,7	243,4
Diacetyl tartaric	Methanol	$2d_1$	$CH_3OCO-\underset{\vert}{CH}-\underset{\vert}{CH}-OCOCH_3$	CH_3-	79	237-238	218,2	225,8
Diacetyl tartaric	n-Butanol	$2d_2$	$CH_3OCO-\underset{\vert}{CH}-\underset{\vert}{CH}-OCOCH_3$	$n-C_4H_9-$	76	210-212	181	193
Diacetyl tartaric	n-Octanol	$2d_3$	$CH_3OCO-\underset{\vert}{CH}-\underset{\vert}{CH}-OCOCH_3$	$-n=C_8H_{17}-$	73	125-126	150	162

TABLE 2

Yields and Analytical Data of the Alkyl Glycidyl Dicarboxylates ($3a_1$–$3d_3$) and of the Diglycidyl Phthalate (3e)



Compd	Yield	b.P (°C/mmHg)	n_D^{20}	Acid number[d]		Saponification number		Epoxide number	
				exptl.	calc	exptl.	calc.	exptl.	calc.
$3a_1$	96,5 (92,3)[a]	152–158/0,6	1,5226	0	0	476,3	474,5	6,7	6,8
$3a_2$	96,2 (91,5)[a]	195–200/1	1,5136	0,2	0	405,3	402,8	5,65	5,75
$3a_3$	93,1 (87,9)[a]	240–250/5	1,5025	0,3	0	341	335,5	4,56	4,78
$3a_4$	93,3 (88,3)[a]	175–186/0,1	1,5046	0	0	342	335,5	4,72	4,78
$3a_5$	87,3 (82,8)[a]	154–164/0,3	1,5252	0	0	425	428	5,25	6,09
$3b_1$	96,2 (93,1)[a]	123–127/1,5	1,4686	0	0	602,8	602	8,2	8,6
$3b_2$	95,9 (90,5)[a]	157–162/1	1,4432	0,2	0	492,3	491	6.1	7
$3b_3$	97,6 (91)[a]	180–190/1	1,4629	0	0	395,7	394,6	4,84	5,62
$3C_1$	94,5 (88,7)[a]	128–130/3	1,4489	0	0	596,9	595,7	8,4	8,5
$3C_2$	96,2 (90,7)[a]	144–148/1,5	1,4320	0,2	0	491,2	487	6	6,95
$3C_3$	97,1 (91,2)[a]	173–178/2	1,4511	0,2	0	395,4	391,6	4,2	5,6
$3d_1$	89,6 (83,8)[a]	44–47/1	1,4820	0,2	0	737,8	736,8	5,2	5,26
$3d_2$	90,1 (83,1)[a]	69–72/2	1,4518	0,3	0	652,8	647,4	4,4	4,6
$3d_3$	91,1 (82,7)[a]	184–189/3	1,4438	0,3	0	554,8	557,2	3,7	4
3e	— (36)[b]	—	1,5018	0,35	0	415	403	9,25	11,5
3e[c]	— (22)[b]	—	1,5043	2,7	0	426	403	9,6	11,5

[a] Purified by distillation.

[b] Purified by column chromatography.

[c] Prepared from phthaloyldichloride and glycidole.

[d] Calculated after acidification of the slat by concetrated H_2SO_4 and isolation of the free acid.

iodide as a catalyst. The reaction mixture was well stirred for 45 min at the same temperature. The sodium salt separated out and it was filtered and washed with 150 mL chloroform.

The filtrate was washed with 4 × 500 mL of a saturated solution of Na_2SO_4 and epichlorhydrin and chloroform were removed *in vacuo* to afford the crude diglycidyl phthalates 3e (46.7 g).

A solution of the crude product (12.5 g) in chloroform was eluted through a column packed with Kieselgel (55 cm h, 3 cm d) as follows: Eluant, 350 mL p. ether; eluant, 1500 mL benzene/ether (80:20); eluant, 1500 mL ether; and eluant, 1500 mL methanol.

Fractions of 100 mL are collected. By mixing the fractions 1–20 and evaporation of the solvent 9.1 g of diglycidyl phthalate 3e is obtained, with a 36% yield (Table 2). The above procedure was repeated and yielded a total 18.2 g of the ester.

From phthaloyl chloride and glycidol. A mixture of glycidol (11 g, 0.15 mole), triethylamine (50 g) and benzene (100 mL) was placed in a round-bottom flask, cooled to 0°C, and phthaloychloride (13.7 g, 0.067 mole) was added. After standing for 48 hr at room temperature, the mixture was diluted to three times its volume with chloroform and washed with water. The chloroform layer was dried with Na_2SO_4 and after evaporation of the solvent, 7.4 g of crude glycidyl ester were obtained. The product was purified by means of a Kieselgel column as described previously.

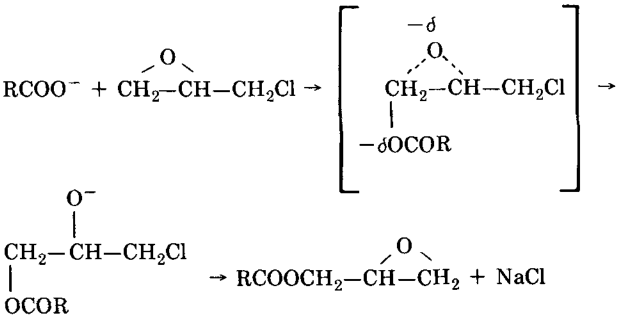
The yield of diglycidyl ester 3e was 4.1 g (22%) (Table 2). ^1H NMR (CD_2Cl_2) of 3e δ:7.5 (m. 4H, aromatic), 4.65 (doublet of doublets, 1H CH_2), 4.06 (doublet of doublets, 1H, CH_2), 3.27 (m. 1H, CH oxirane), 2.78 (doublet of doublets, 1H, CH_2 oxirane), 2.64 (doublet of doublets, 1H, CH_2 oxirane).

RESULTS AND DISCUSSION

Phthalic, maleic, succinic and diacetyl tartaric anhydrides were used as cyclic anhydrides of dicarboxylic acids. By titration of phthalic anhydride with an alcohol-NaOH solution, the sodium salts $2a_1$-a_5, in practically quantitative yield, were prepared (Table 1). The compounds $2b_1$-d_3 were also obtained in high yields (73–85%) with the same reaction.

The reaction of sodium salts 2a-d with excess of epichlorhydrine in the presence of tetraethyl ammonium iodide (reaction [3]) led to the formation of alkyl glycidyl esters of dicarboxylic acids 3a-d (yield 80%) (Table 2).

It can be concluded that due to stereochemistry and polarity, the attack of carboxylic ion occurs in the primary carbon atom of the epoxide. This process may be formulated by an S_N2 mechanism as follows:



[6]

The synthesized glycidyl esters were purified by distillation and their identity checked by nuclear magnetic resonance and mass spectrometry spectroscopy. In addition to that, the acid saponification and epoxide numbers were determined (see Table 2).

The reaction of bisodium phthalate with epichlorhydrine (reaction [4]) gave glycidyl phthalate 3e (36% yield), while the reaction of phthaloyl chloride with glycidol gave the same product in lower yield (reaction [5]). The reaction product was tested by column chromatography, and its structure was identified by the methods used for the glycidyl esters. Our experiments have shown that the electronic structure of the anhydrides used does play some role in the yield of salts 3a-d, which is reduced from phthalate to tartaric: phthalate > maleate > succinate > diacetyl tartarate.

Apparently the phthalate ion is stabilized by the resonance effect, which causes electron shift from π-bonding or atomic orbitals. The ion of sodium salt of maleic monoester is favored for the same reason, but to a lesser extent. On the contrary, when the ion derives from diacetyl tartarate, the negative ion weakens because of the electron acceptor substituents.

It is clear from the above that the synthesis of alkyl glycidyl esters of dicarboxylic acids according to reactions [2] and [3] is a satisfactory new process, and it is proposed for the preparation of such compounds. If the cyclic anhydrides and the primary alcohols are substituted, this process might yield other alkyl glycidyl esters of dicarboxylic acids.

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