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Some Reactions of the Glycidyl Esters of Sulfonic Acids

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1-Chloro-2-hydroxypropyl sulfonates are obtained by the reaction of glycidyl sulfonates with hydrochloric acid at room temperature. They are converted into 1, 3-dichloro-2-propanol by the action of hydrochloric acid at 100°C, or into epichlorohydrin by that of bases. The reaction of glycidyl sulfonates and sodium carboxylates affords glycidyl carboxylates. In the preparation of glycidyl carboxylates, glycidyl sulfonates act as a direct alkylation agent for sodium carboxylates. The addition of amines to the epoxide is carried out at first in the reaction of glycidyl sulfonates and amines. The adducts are converted into glycidyl amines by the action of sodium hydroxide, or into *N*-[β-hydroxypropylene(α, γ)]-ammonium sulfonates by the isomerization, by heating them or letting them stand for a long time. The latter is an intermediate used in preparing 1, 4-dioxane derivatives in the presence of sodium hydroxide.

Glycidyl vinylsulfonate, glycidyl allylsulfonate, and glycidyl β-styrenesulfonate have been prepared and copolymerized with acrylonitrile, styrene and methyl methacrylate to obtain reactive polymers containing a glycidyl sulfonate group.[1-3] During our recent study of the reaction of the copolymers with amines, it has been demonstrated that a ring-opening addition of epoxide competes with a carbon-oxygen bond scission of sulfonate. The latter reaction is unfavorable for the purpose of polymer reaction because of the elimination of the reaction site from the polymers.

The present work was undertaken in order to investigate in more detail the reactions of glycidyl sulfonates with hydrochloric acid, sodium carboxylates and amines.

Results and Discussion

The Preparation of Glycidyl Sulfonates and Their Reaction with Hydrochloric Acid.— Glycidyl esters of methane-, allyl-, 2-propane-, butane-, and *p*-toluenesulfonic acid were prepared from glycidol and the corresponding sulfonyl chlorides. The results are shown in Table I.

$$RSO_2Cl + HOCH_2CH(\diagdown O \diagup)CH_2 \rightarrow RSO_2OCH_2CH(\diagdown O \diagup)CH_2$$

Glycidyl sulfonates reacted with hydrochloric acid to give 3-chloro-2-hydroxypropyl sulfonates in a good yield at room temperature. The results are shown in Table II.

$$RSO_2OCH_2CH(\diagdown O \diagup)CH_2 + HCl \rightarrow RSO_2OCH_2CH(OH)CH_2Cl$$

3-Chloro-2-hydroxypropyl sulfonates afforded 1, 3-dichloro-2-propanol in the reaction with hydrochloric acid at 100°C, whereas they formed epichlorohydrin in the presence of sodium hydroxide or triethylamine. This indicates that the scission of the carbon-oxygen bond of sulfonic ester

Table I. Preparations of glycidyl sulfonates

R	Yield %	B. p. °C/mmHg	Anal. $C_{Calcd.}$	$H_{Calcd.}$	C_{Found}	H_{Found}	n_D^{25}
CH_3	74.5	109—110/1 (lit.[4] 115—116/2)					1.4497
$(CH_3)_2CH$	69.2	113—115/2	40.00	6.71	40.00	6.54	1.4493
n-C_4H_9	70.9	122—123/1	43.29	7.27	43.19	7.24	1.4522
p-$CH_3C_6H_4$	45.0	167—172/2 (lit.[4] 162/1)					1.5243

1) Y. Iwakura and N. Nakabayashi, *Makromol. Chem.*, **66**, 142 (1963).
2) Y. Iwakura, N. Nakabayashi and M. H. Lee, Unpublished results.
3) Y. Iwakura, K. Uno, N. Nakabayashi, T. Tani and W. Y. Chiang, *J. Chem. Soc. Japan, Ind. Chem. Sect.* (*Kogyo Kagaku Zasshi*), **68**, 1222 (1965).
4) K. Ichikawa, *Yûki Gôsei Kagaku Kyôkai Shi*, **22**, 553 (1964).

Table II. Addition of hydrochloric acid to glycidyl sulfonates

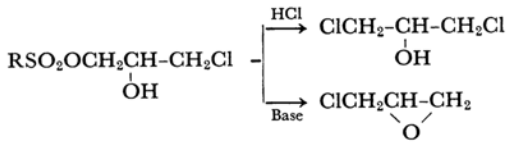
R	Yield %	B. p. °C/mmHg	Anal. $C_{Calcd.}$	$H_{Calcd.}$	C_{Found}	H_{Found}	n_D^{25}
CH_3	67	140—141/1	25.47	4.81	25.00	5.10	1.4711
$(CH_3)_2CH$	91	148—150/1.5	33.26	6.05	33.22	6.09	1.4680
$CH_2=CHCH_2$	86	154—156/1	33.57	5.17	33.25	5.35	1.4667
n-C_4H_9	95	150—152/1	36.44	6.55	36.09	6.50	1.4680

Table III. Preparations of glycidyl acetate (Nos. 1—12) and glycidyl methacrylate (No. 13)

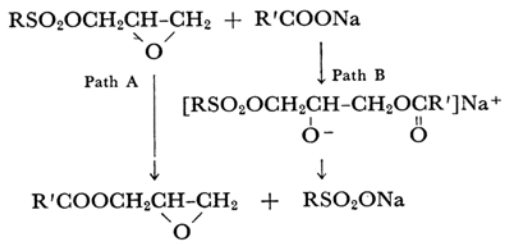
No.	R in $RSO_2OCH_2CH(O)CH_2$	g.	Time hr.	Yield g. (%)	The recovered glycidyl sulfonate g. (%)
1	CH_3	3.0	0.5	1.2 (50)	0.8 (27)
2[1]	CH_3	3.0	0.5	—	2.8 (93)
3[2]	CH_3	15.2	0.5	0.6 (26)	12.5
4[3]	CH_3	3.0	11.5	0.3 (13)	2.0 (67)
5	$(CH_3)_2CH$	3.6	0.5	0.4 (17)	2.1 (57)
6	$CH_2=CHCH_2$	3.6	0.5	0.3 (13)	2.5 (69)
7	n-C_4H_9	3.9	0.5	0.3 (13)	2.5 (64)
8	p-$CH_3C_6H_4$	4.6	0.5	0.2 (8.6)	3.2 (70)
9	p-$CH_3C_6H_4$	4.6	0.5	0.2 (8.6)	3.6 (78)
10	p-$CH_3C_6H_4$	4.6	4	0.3 (13)	2.5 (54)
11[1]	p-$CH_3C_6H_4$	4.6	0.5	—	3.6 (78)
12	ECH[4]	1.9	4	<0.1	—
13	CH_3	3.0	0.5	1.2 (42)	0.8 (37)

1) Triethylbenzylammonium chloride was not used.
2) Excess GMS was used as a reagent and solvent.
3) The solvent was water and the catalyst was not used.
4) ECH indicates epichlorohydrin. It was used in place of glycidyl sulfonates.

predominates over that of the carbon-chlorine bond.



The Reaction of Glycidyl Sulfonates with Sodium Carboxylates.—Next, the preparations of glycidyl carboxylates by the reactions of sodium acetate or sodium methacrylate and glycidyl sulfonates in the presence of a catalytic amount of triethylbenzylammonium chloride[5,6] were studied (Table III).



As is shown in the above scheme, there can be considered to be two alternative pathways for the formation of glycidyl carboxylates; namely, the direct displacement of sulfonate by carboxylate (Path A), or the attack of the carboxylate ion on the terminal carbon of the epoxide, thus giving rise to an intermediate alkoxide ion, which subsequently reforms the epoxide by the displacement of sulfonate (Path B), similar as in the case of the reaction of epichlorohydrin with sodium carboxylate.[6] It was found that the reaction of *n*-propyl methanesulfonate with sodium acetate gave *n*-propyl acetate in the same yield as in the case of glycidyl acetate. In view of this finding, it may be said that the reaction proceeds through Path A.

5) Y. Iwakura, T. Kurosaki and N. Nakabayashi, *Makromol. Chem.*, **44/46**, 570 (1961).
6) O. Maerker, J. F. Carmichael and W. S. Port, *J. Org. Chem.*, **26**, 2681 (1961).

The Reaction of Glycidyl Sulfonates with Amines.—When glycidyl methanesulfonate (GMS) was allowed to stand with morpholine at 25°C for an hour, the formation of 2-hydroxy-3-(4-morpholinyl)-propyl methanesulfonate (I) was observed by means of a study of the infrared spectrum. The treatment of the reaction mixture (hereafter we will call it the "first stage reaction mixture," which might be composed mainly of I) with sodium hydroxide at 25°C for an hour gave 4-(2, 3-epoxypropyl)-morpholine (III) in a 70% yield. III was also obtained by the reaction of GMS with morpholine in the presence of sodium hydroxide at −5°C for 30 min.

The isomerization of I to 4-[β-hydroxypropylene-(α, γ)]-morpholinium methanesulfonate (II)[4] was observed by the change in the infrared spectrum when the first stage reaction mixture was allowed

Table IV. Reactions of glycidyl sulfonates and amines[1]

No.	R	Amine[2]	H_2O g.	Condition of treatments[3] 1st. °C	1st. hr.	NaOH	2nd °C	2nd hr.	Product,[4]	Yield %
1	CH_3	Mo	trace	25	1	B	25	1	III	70
2	CH_3	Mo	5	−5	1/2	A			III	53
3[5]	CH_3	Mo	5	0	1	A			III	39, IV 25
4	CH_3	Mo	5	80	1/3	A			III	17, IV 35
5	CH_3	Mo	5	25	45	B	75	1/3	IV	45
6	CH_3	Mo	5	80	1/3	B	80	1/3	IV	56
7	CH_3	Mo	5	80	1/3	B	25	1		—[6]
8	$(CH_3)_2CH$	Mo	5	80	1/3	B	90	1/3	IV	53
9	p-$CH_3C_6H_4$	Mo	5	80	1/2	B	90	1/4	IV	53
10	CH_3	Py	5	90	1/2	B	90	1/2	V	32
11	CH_3	Pi	5	90	1/2	B	90	1/2	VI	39
12	CH_3	Et	5	25	1	B	25	1	VII	27
13	CH_3	Py	5	0	1/3	B	25	1	VIII	20

1) The reaction was carried out in 0.02 mol. scale.
2) Mo indicates morpholine, Py: pyrrolidine, Pi: piperidine, and Et: diethylamine
3) 1st: First treatment of an aqueous mixture of glycidyl sulfonates and amines.
NaOH: A or B shows that addition of sodium hydroxide to the mixture of glycidyl sulfonates and amines was performed together with 1st or 2nd treatment.
After 1st treatment, 2nd treatment was carried out.
4) III is 1-(2,3-epoxypropyl)-morpholine, IV: 2,5-bis-(4-morpholinylmethyl)-1,4-dioxane, V: 2,5-bis-(1-pyrrolidinylmethyl)-1,4-dioxane, VI: 2,5-bis-(1-piperidinylmethyl)-1,4-dioxane, VII: *N*-(2,3-epoxypropyl)-*N*,*N*-diethylamine, and VIII: 1-(2,3-epoxypropyl)-pyrrolidine.
5) The reaction temperature was raised by the heat of reaction for an instant.
6) A resinous product was obtained.

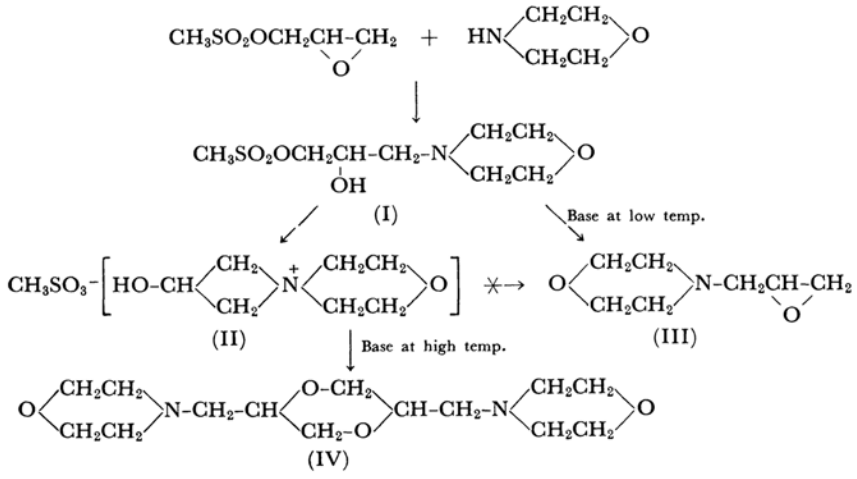


Fig. 1. The process of the reaction of GMS with morpholine.

to stand at 25°C for 45 hr. or at 80°C for 20 min. (we will call the reaction mixture at this stage the "second stage reaction mixture," which might be composed mainly of II). By treating the second stage reaction mixture with sodium hydroxide at 80°C for 20 min., 2, 5-bis-(4-morpholinylmethyl)-1, 4-dioxane (IV) was obtained in a 56% yield. On the other hand, the treatment of the above mixture with sodium hydroxide at 25°C resulted in the formation of a resinous product. The reaction of GMS with morpholine in the presence of sodium hydroxide at 80°C gave a mixture of III (17%) and IV (35%) after 20 min.

Both glycidyl 2-propanesulfonate or glycidyl *p*-toluenesulfonate and morpholine gave IV in a 53% yield when the reaction mixture (after standing at 80°C for 20—30 min.) was treated with sodium hydroxide at 90°C for 15—20 min.

The reaction of piperidine or pyrrolidine with GMS and sodium hydroxide also afforded 2, 5-bis-(1-piperidinylmethyl)-1, 4-dioxane or 1-(2, 3-epoxypropyl)-pyrrolidine and 2, 5-bis-(1-pyrrolidinylmethyl)-1, 4-dioxane, just as in the reaction of piperidine or pyrrolidine with epichlorohydrin.[7,8] By the treatment of GMS with diethylamine and sodium hydroxide, *N*-(2, 3-epoxypropyl)-*N*, *N*-diethylamine was obtained, but no dioxane derivative was detected as was in the reaction of epichlorohydrin with diethylamine and sodium hydroxide.[8,9] The above results are summarized in Table IV.

The process of the reaction of GMS with morpholine may be depicted as Fig. 1.

As the reaction of GMS with morpholine in the presence of sodium hydroxide to give III proceeded faster than that of *n*-propyl methanesulfonate with morpholine to give 4-(*n*-propyl)-morpholine under the same reaction conditions, it seems rational to consider the former reaction to proceed via an intermediate such as I rather than via the direct replacement of the ester group by an amino group. The isomerization of I to II, which was favored in the absence of sodium hydroxide, and the formation of III from I may be considered to be competitive reactions on the basis of the following facts. (1) When the mixture of GMS and morpholine was allowed to stand without sodium hydroxide to afford the second stage reaction mixture, only IV was obtained upon subsequent treatment with sodium hydroxide. (2) On the other hand, when sodium hydroxide was added earlier to the reaction mixture (first stage), III was obtained in a 70% yield. (3) The reaction of GMS with morpholine, carried out in the presence of sodium hydroxide from the beginning at 80°C, gave a mixture of III and IV.

TABLE V. M. P. (B. P.) AND YIELD OF V—VIII

Compound	M. p. (b. p.) °C (°C/mmHg) Found	lit.[8]	Yield %
V	106—108	107.5—109.5	32
VI	102—104	101 —104	39
VII	(58—58.5/19)	(58—60/20)	27
VIII	(61—63/11)	(63—64/12)	20

Experimental

Raw Materials.—Methanesulfonyl chloride, 2-propyl bromide, *n*-butyl bromide, sodium sulfite, phosphorus pentachloride, glycidol and *p*-toluenesulfonyl chloride were commercially available. Sodium 2-propanesulfonate,[10] sodium butanesulfonate, 2-propanesulfonyl chloride (b.p. 83°C/25 mm.; lit.[11] 74.5°C/15 mm.), *n*-butanesulfonyl chloride (b. p. 96°C/16 mm.; lit.[12] 93.5°C/15 mmHg), glycidyl methanesulfonate[4] (GMS) and glycidyl *p*-toluenesulfonate[4] (GTS) were prepared by methods reported previously.

Glycidyl 2-Propanesulfonate (GPS).—To a solution of 22.3 g. (0.301 mol.) of glycidol and 30.3 g. (0.300 mol.) of triethylamine in 200 ml. of dry toluene, there was added, drop by drop, a mixture of 40.7 g. (0.286 mol.) of 2-propanesulfonyl chloride and 20 ml. of dry toluene under cooling in an ice-salt bath. The reaction mixture was then stirred for 3 hr. at room temperature. The triethylamine hydrochloride formed was removed by filtration, and the toluene was distilled off in vacuo. The residue was distilled under reduced pressure to give 35.8 g. of GPS boiling at 114—115°C/1 mmHg. The yield was 69.2%.

2-Hydroxy-3-chloropropyl 2-Propanesulfonate.—A mixture of 7.8 g. of GPS and 20 ml. of concentrated hydrochloric acid was occasionally stirred over a 2 hr. period while being kept at room temperature. The fractionation of the residue after the water had been removed gave 8.5 g. (91%) of 2-hydroxy-3-chloropropyl 2-propanesulfonate boiling at 148—150°C/1.5 mmHg.

Glycidyl Acetate from GMS. — a) A mixture of 3.0 g. (0.02 mol.) of GMS, 1.6 g. (0.02 mol.) of sodium acetate, 0.2 g. of triethylbenzylammonium chloride and 20 ml. of dry toluene was refluxed for 0.5 hr. After the precipitate had been removed by filtration and the toluene had been removed by distillation in vacuo, the fractional distillation of the residue afforded 1.2 g. (50%) of glycidyl acetate (b. p. 71°C/17 mmHg) and 0.8 g. (27%) of GMS.

b) A suspension of 15.2 g. (0.10 mol.) of GMS and 1.6 g. (0.02 mol.) of sodium acetate and 0.2 g. of triethylbenzylammonium chloride was stirred for 0.5 hr. at 110°C. After the precipitate had been removed, the residue was fractionated to give 0.6 g. (26% yield based on the sodium acetate charged) of glycidyl acetate and 12.5 g. of GMS.

c) A suspension of 3.0 g. of GMS and 1.6 g. of sodium acetate in 5.0 g. of water was stirred for 11.5 hr. at

7) R. Rothstein and K. Binovic, *Compt. rend.*, **236**, 1050 (1953).
8) D. L. Heywood and B. Phillips, *J. Am. Chem. Soc.*, **80**, 1257 (1958).
9) J. H. Ross, D. Baker and A. T. Coscia, *J. Org. Chem.*, **29**, 824 (1964).
10) S. Zuffanti, *J. Am. Chem. Soc.*, **62**, 1044 (1940).
11) F. Asinger, W. Schmidt and F. Ebeneder, *Ber.*, **75**, 34 (1942).
12) F. Asinger, F. Ebeneder and E. Bock, ibid., **75**, 42 (1942).

room temperature. The reaction mixture was then extracted with ether. After the ether had been removed, the distillation of the residue gave 0.3 g. (13%) of glycidyl acetate boiling at 57—59°C/11 mmHg and 2.0 g. (67%) of GMS.

Glycidyl Methacrylate from GMS.—Glycidyl methacrylate was prepared exactly as was glycidyl acetate, except that sodium methacrylate was treated with GMS in place of sodium acetate. From 2.2 g. of sodium methacrylate and 3.0 g. of GMS, 1.2 g. (42%) of glycidyl methacrylate (b. p. 84—85°C/15 mmHg) (lit.[5] 85°C/15 mmHg) was obtained and 0.8 g. (37%) of GMS was recovered.

4-(2, 3-Epoxypropyl)-morpholine (III).—a) Under occasional cooling with a dry-ice methanol bath in order to maintain the reaction temperature below 30°C, there were mixed 3.0 g. (0.02 mol.) of GMS and 1.7 g. (0.02 mol.) of morpholine. After the initial exothermic reaction had subsided, the reaction mixture was allowed to stand for an hour at room temperature. The infrared spectrum of the mixture showed a hydroxyl band at 3390 cm.$^{-1}$ and sulfonic ester bands at 1350 and 1170 cm.$^{-1}$, but no epoxide bands. The mixture was then treated, with occasional stirring, with a solution of 0.9 g. (0.023 mol.) of sodium hydroxide in 2 ml. of water for 1 hr. at room temperature. The solution was extracted with ether continuously. After the ether had been removed, the fractionation of the residue afforded 2.0 g. (70%) of III boiling at 93—97°C/12 mmHg (lit.[8] 93—95°C/12 mmHg).

b) Into 3.0 g. (0.02 mol.) of GMS in an ice-salt bath there was stirred a solution of 1.7 g. (0.02 mol.) of morpholine and 1.0 g. (0.025 mol.) of sodium hydroxide in 5.0 ml. of water at −5°C. The reaction mixture was then allowed to stand for 0.5 hr. at this temperature. The other treatment was same as that described above. The yield of III was 1.5 g. (53%).

2, 5-Bis-(4-morpholinylmethyl)-1, 4-dixoane (IV).—a) GMS (3.0 g., 0.02 mol.) was mixed with a solution of 1.7 g. (0.02 mol.) of morpholine in 5 ml. of water under moderate cooling in order to maintain the temperature below 30°C. The mixture was allowed to stand for 20 min. at 80°C. The infrared spectrum of the mixture obtained showed sulfonate ion bands at 1200 and 1030 cm^{-1} and a hydroxyl band at 3220 cm^{-1}; it was essentially identical with that reported by Ichikawa.[4] The above mixture was then treated with 0.9 g. (0.023 mol.) of sodium hydroxide at 80°C for 20 min. and extracted continuously with ether. After the ether had been removed, 1.6 g. (56%) of IV was obtained as a crystalline product. It was recrystallized from ether. The melting point of IV was 107—108°C (lit.[8] 108—110°C).

b) IV was also prepared by the reaction of GPS or GTS with morpholine in a manner similar to that used with GMS (see above). The yield was 53% in both cases.

2, 5-Bis-(1-pyrrolidinylmethyl)-1, 4-dioxane (V), 2, 5-Bis-(1-piperidinylmethyl)-1, 4-dioxane (VI), *N*-(2, 3-Epoxypropyl)-*N*,*N*-diethylamine (VII) and 1-(2, 3-Epoxypropyl)-pyrrolidine (VIII).—The reaction of GMS with the secondary amines was carried out in a manner similar to that used for GMS with morpholine (III and IV).