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SYNTHESIS OF 1,3-DIGLYCIDYLIMIDAZOLIUM SALTS

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For the first time, 1,3-diglycidylimidazolium salts were obtained. Their synthesis was accomplished by two routes: the reaction of imidazole with epichlorohydrin in the presence of sodium perchlorate with the subsequent dehydrochlorination of the reaction products with alkalis, and the quaternization of 1-glycidylimidazoles with epichlorohydrin in the presence of salts of strong acids.

In the works [1, 2], we first obtained stable glycidylazolium and glycidylazinium salts by the recyclization of the oxirane ring of epichlorohydrin by the action of azoles and azines in the presence of sodium perchlorate. However, the isolation of difunctional oxirane-containing salts remained problematic in connection with the probability of oligomerization, which is higher by comparison with monofunctional systems, as well as the high sensitivity of the N,N′-disubstituted imidazolium cation obtained to alkaline agents.

We previously established that the reaction of imidazole (Ia) with epichlorohydrin in an alcoholic medium leads to the formation of the chlorohydrin derivative of imidazole (II), the further exposure of which results in conversion to ionic oligomers [3]. However, the character of the reaction changes in the presence of sodium perchlorate: 1-glycidylimidazolium hydroperchlorates (III) are formed initially, and these undergo the further addition of a second molecule of epichlorohydrin to give the mixed glycidylchlorohydrin salt (IV) (see Scheme 1, route 1). The last is not isolated in the crystalline form, but its formation is confirmed by the analysis of the resin-forming reaction product for the content of epoxide groups (CEG) and the content of readily hydrolyzed chlorine.

The formation of the intermediate imidazolium salt (IV) may also proceed by another route — via the chlorohydrin derivative (II) with its subsequent quaternization by epichlorohydrin in the presence of sodium perchlorate. The role of the last consists in the removal of the nucleophilic chloride ion, able to initiate the chain of polymerization of the oxirane rings in solution, from the sphere of reaction (in the form of sodium chloride precipitated from the epichlorohydrin), as well as the stabilization of the final glycidylimidazolium salt (Va).

By analogy with the reaction of hydroperchlorates of pyridines described in the work [4], as well as the conversion of hydroperchlorates of 2-methylbenzimidazole (Id). $HClO_4$ and 3,5-dimethylpyrazole by the action of epichlorohydrin, presented here, to the bischlorohydrin salts (VII) and (VIII), the addition of epichlorohydrin to salts of the type (III) is also evidently characteristic of hydrosalts of azaaromatic rings. The synthesis of compound (VII) evidently also proceeds via the intermediate hydroperchlorate (VI).

The action of equimolar amounts of alkalis on the intermediate (IV) allows the isolation of the diglycidylimidazolium salt (Va) in the form of a colorless crystalline substance, which is very stable on storage (the period of storage without significant change of the CEG is not less than 1 year when the Δ CEG/CEG $\leq$ 10%), and crystallizes from polar solvents (alcohols, without the noticeable opening of the epoxide groups).

The isolation of the aromatic substituted imidazolium salts (Vb,c) was found to be effective by the route 2 (see Scheme 1) based on the quaternization of the 1-glycidylimidazoles (IXa,b) with epichlorohydrin, previously described [5], in the presence of sodium perchlorate. The reaction proceeds exclusively readily even at room temperature for (IXb), or with moderate heating at 50-60°C, for (Xa). The salt (Vb) is isolated in the crystalline form, and (Vc) is isolated in the form of a colorless luminescing oil-forming product with the CEG close to the calculated value.

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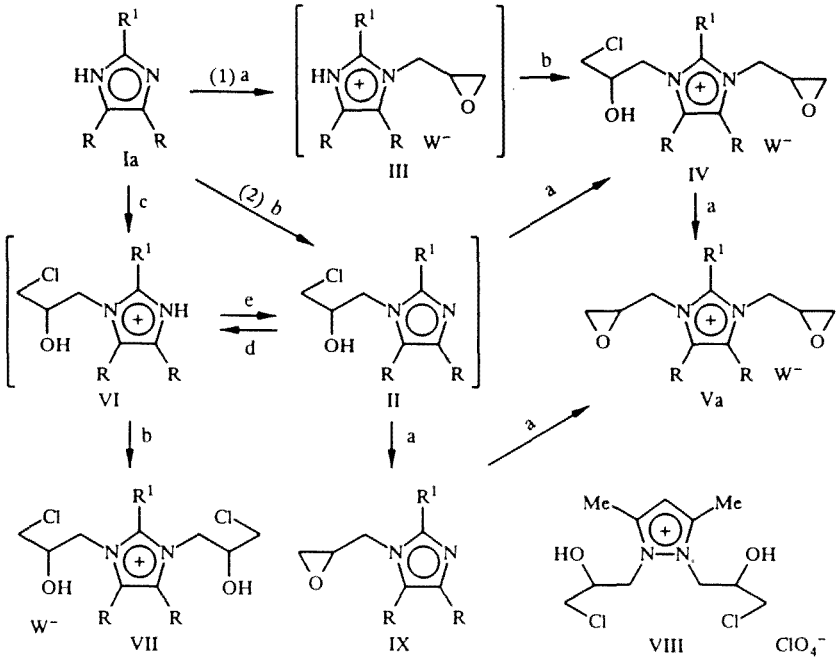
Scheme 1



Reagents: a) epichlorohydrin, $NaClO_4$; b) epichlorohydrin;
c) 1. $HClO_4$ 2. epichlorohydrin; d) $HClO_4$; e) NaOH.
I, V.a R = R^1 = H; I, Vb, IXa R = R^1 = Ph; I, Vc, IXb R = Ph, R^1 = H;
Id. VII R,R = $(CH{=}CH)_2$, R^1 = Me; Va,b, VII W = ClO_4; Vc W = ClO_4, BF_4

The exchange of anions in the salts obtained can be performed by the method of [2], described for glycidylazinium salts, using potassium salts of inorganic and organic acids in methanol or water. However, a disadvantage of the approach indicated is that this case requires the good solubility of both salts in the solvents indicated and the precipitation of one of the exchange products in the residue; this is not always practicable. Moreover, the separation of oxirane-containing salts from water is not always expedient due to the hydrolysis of three-membered rings.

Taking into account the simplicity and ease in performing the quaternization of the glycidylimidazole (IXb), we attempted to synthesize salts with weakly nucleophilic counterions (BF_4, ClO_4) using the reaction in the diphasic system of epichlorohydrin — the aqueous solution of the inorganic salt. Thus, when the 1-glycidylimidazole (IXb) reacts with epichlorohydrin in the presence of a saturated solution of sodium tetrafluoroborate, the salt (Vc) (W = BF_4) is isolated from the organic phase in the form of a colorless luminescing oil-forming product with a high CEG close to the calculated value. By analogy, the perchlorate (Vc) (W = ClO_4) is also obtained. It can be seen that the diphasic approach of the method can be extended to the synthesis of glycidylimidazolium salts with other counterions, which are however more strongly nucleophilic, as well as proton-containing anions (Cl^-, CH_3COO^-, $H_2PO_4^-$, etc.) which are not inert to epoxide groups, and we could not isolate the pure salts in this case.

It is interesting that the salts (Vc) (W = BF_4, ClO_4), especially the tetrafluoroborate, undergo ready self-hardening on heating at 100-130°C for 0.5-1 h to form luminophore polymers. This property is not characteristic of the salt (Vb); this is probably associated with the absence of the sufficiently acidic mesoproton C^2H in its structure which can be cleaved on heating to form the borohydrofluoric or perchloric acids correspondingly and the corresponding heteroaromatic carbene, catalytically strengthening the monomer (Vc).

The attempt to carry out the analogous reaction of epichlorohydrin with azines (pyridines, acridine) in a diphasic system leads to the hydrolysis of the epoxide groups and the formation of N-(2,3-dihydroxypropyl)azinium salts, in contrast to the smooth conversion in the dry medium according to [2].

Therefore, we developed two new approaches to the synthesis of previously unknown diglycidylimidazolium salts, based on the reaction of the corresponding N-unsubstituted imidazoles and N-glycidylimidazoles with epichlorohydrin in the presence of anions of strong acids.

TABLE 1. Main Constants and the Data of the Elemental Analysis of the Diglycidylimidazolium Salts (Va-c) and Bis(2-hydroxy-3-chloropropyl)azolium Salts (VII), (VIII)

Compound	Empirical formula	Found, % / Calculated, %					mp,* °C	Yield, %
		C	H	Cl	N	CEG		
Va	$C_9H_{13}ClN_2O_6$	38.8 38,5	4.6 4,6	12.8 12,7	10.4 10,0	30.3 30,7	84...86	70
Vb	$C_{27}H_{25}ClN_2O_6$	63.6 63,7	5.0 4,9	7.2 7,0	5.7 5,5	16.5 16,9	248...250	68
Ve	$C_{21}H_{21}ClN_2O_6$	58.4 58,3	4.7 4,9	8.0 8,2	6.5 6,5	19.4 19,9	Resin-forming product	95
VII	$C_{14}H_{19}Cl_3N_2O_6$	40.4 40,1	4.6 4,5	25.0 25,4	7.0 6,7	—	118...120	74
VIII	$C_{11}H_{19}Cl_3N_2O_6$	34.6 34,6	5.1 5,0	27.7 27,9	7.5 7,3	—	134...137	77

*Apart from compound (Vc), the solvent for crystallization is methanol.

The composition and structure of the resulting dioxiranes (Va-c) and the chlorohydrins (VII) and (VIII) were confirmed by data of the elemental analysis (Table 1), IR and PMR spectroscopy, and measurement of the content of epoxide groups (Table 2), and the discreteness was confirmed using the method of thin layer chromatography.

The PMR spectra of the salts (Va-c) contain signals of the cyclic CH_2O protons in the form of two multiplets (δ 2.47-2.51, 2.65-2.82 ppm), multiplets of the CHO protons (δ 3.25-3.36 ppm), the acyclic CH_2N protons (δ 3.89-4.45 ppm), and signals specific for each of the heterocyclic nuclei (CH im., Ar). The signals of the protons of the chlorohydrin groups in the salts (VII) and (VIII) appear in the region of δ 3.47-3.78 ppm (CH_2Cl), 3.84-4.08 ppm (CHO), 4.19-4.58 ppm (CH_2N), and 5.11-5.37 ppm (OH).

The most characteristic absorption bands in the IR spectra of compounds (Va-c) are those of the C–O groups in the region of 865-980 cm^{-1} and the CH_2 groups of the oxirane rings in the region of ν 3030-3120 cm^{-1}. The most characteristic bands for the salts (Va-c) and (VIII) are those of the cyclic CH groups of the imidazole and pyrazole rings (ν 3115-3170 cm^{-1}). The most characteristic absorption bands of the chlorohydrin salts (VII) and (VIII) are those of the OH groups (ν 3165-3510 cm^{-1}), the $C=N^+$ groups (ν 1530-1568 cm^{-1}), and the C-Cl (ν 650-660 cm^{-1}).

EXPERIMENTAL

The PMR spectra were taken on the Gemini 200 (200 MHz) spectrometer of the firm Varian in DMSO-D_6. The IR spectra were taken on the UR-20 instrument using the program 4 with the registration rate of 160 cm^{-1}/min. The content of epoxide groups was determined by means of treating the samples of oxiranes with the solution of hydrogen chloride in acetone with the subsequent argentometric back titration of the excess acid according to the GOST 12497–78 standard. The discreteness of the substances was evaluated by the method of thin layer chromatography on silica gel Silufol, with the 10:1 mixture of chloroform—methanol as the eluent.

1,3-Diglycidylimidazolium Perchlorate (Va). The mixture of 6.8 g (0.1 mole) of imidazole (Ia) and 15 g (0.122 mole) of anhydrous sodium perchlorate is stirred at room temperature in 78 ml (1 mole) of epichlorohydrin for 1 h. Then 4 g (0.1 mole) of sodium hydroxide are added in portions with stirring for 3 h. After 1 h, the residue is filtered off, and the filtrate is concentrated *in vacuo*. The residual resin-forming product is dissolved in 70-100 ml of acetone, prior to bubbling in carbon dioxide gas to remove the possible residue of sodium hydroxide. The precipitated residue is filtered off, and the acetone is distilled off *in vacuo*. The residue is primed with 10 ml of dry methanol, and is left for crystallization for 5-10 days. The resulting crystals are pressed out on the filter, washed with 10 ml of cold methanol at 0°C, and recrystallized.

General Method for the Isolation of the 1,3-Diglycidylimidazolium Salts (Vb,c) in a Dry Medium. The mixture of 10 mmole of the imidazole (Ib,c), 0.44 g (11 mmole) of sodium hydroxide, 2 ml of methanol, and 7.8 ml (0.1 mole) of

TABLE 2. Spectral Characteristics of the Diglycidylimidazolium Salts (Va-c) and Bis(2-hydroxy-3-chloropropyl)azolium Salts (VII), (VIII)

Compound	PMR spectra, δ, ppm*	IR spectra, ν, cm⁻¹
Va	2,47 (2H, m), 2,65 (2H, m, CH_2O), 3,25 (2H, m, CHO), 3,95...4,45 (4H, m, CH_2N), 7,15 (1H, s, C_4HN), 8,45 (1H, s, C_2HN)	3170 medium (CH im.), 3120 medium (CH_2 ox.), 1575 medium (C=C im.), 1100 s (ClO_4^-), 980 medium 915 medium (C—O ox.)
Vb	2,49 (2H, m), 2,82 (2H, m, CH_2O), 3,28 (2H, m, CHO), 3,89 (2H, m), 4,20 (2H, m, CH_2N), 7,43 (5H, m), 7,71 (5H, m), 7,84 (5H, m, CH arom.)	3070 weak 3030 weak (CH arom. CH_2 ox.), 1590 weak, 1490 medium (C=C arom.), 1080 s (ClO_4^-), 970 medium 923 medium, 865 medium (C—O ox.)
Vc	2,51 (2H, m), 2,76 (2H, m, CH_2O), 3,36 (2H, m, CHO), 4,29 (4H, m, CH_2N)	3140 weak (CH im), 3035 weak (CH_2O, CH arom.), 1105 s (ClO_4^-), 975 weak, 920 weak (C—O ox.)
VII	2,60 (3H, s CH_3), 3,47 (4H, m, CH_2Cl), 3,84 (2H, m, CHO), 4,19 (4H, m, CH_2N), 5,37 (1H, s, OH), 7,26 (2H, m), 7,59 (2H, m, CH arom.)	3470 s, 3200 weak (OH), 1615 weak (C=C arom.), 1530 s (C=N⁺), 650 s (C—Cl)
VIII	2,48 (3H, s, CH_3), 3,78 (4H, m, CH_2Cl), 4,08 (2H, m, CHO), 4,58 (4H, m, CH_2N), 5,11 (1H, s CHC), 6,63 (2H, s, OH)	3510 medium, 3165 weak (OH), 3115 weak (CH pyr), 1568 medium (C=N⁺), 660 s (C—Cl)

*PMR spectra of compounds (Va,b), (VII), and (VIII) were taken in DMSO-D_6. PMR spectrum of (Vc) was taken in chloroform.

epichlorohydrin is stirred at room temperature for 2-3 h until the completion of the conversion of the imidazole, using monitoring by TLC. To the mixture are then added 1.83 g (15 mmole) of anhydrous sodium perchlorate. The mixture is stirred for 1 h, and is then left at 20°C for 7 days, in the case of (Ic), or heated for 7-8 h at 50°C, in the case of (Ib), until the completion of the conversion of the intermediate 1-glycidylimidazoles (IXa,b). The residue of sodium chloride is filtered off, and the mother solution is concentrated *in vacuo*. The salt (Vb) is crystallized on trituration with 5-10 ml of methanol, and (Vc) is isolated in the form of a colorless luminescing viscous resin-forming product.

General Method for the Isolation of the 1,3-Diglycidylimidazolium Salts (Vb,c) Using the Diphasic Approach. To the solution of 10 mmole of the 1-glycidylimidazole (IXb,c) in 7.8 ml (0.1 mole) of epichlorohydrin are added 20 mmole of sodium perchlorate or sodium tetrafluoroborate and 0.2-0.3 ml of water. The mixture is stirred intensively for 1 h, and is then left for 7 days at room temperature, in the case of (IXa), or heated at 50-60°C for 2-3 h, in the case of (IXb). The organic layer is separated from the dispersion of inorganic salts in water, washed with 2-3 ml of water, dried with anhydrous sodium sulfate, and concentrated *in vacuo*. The residue affords the diglycidylimidazolium salts (Vb,c): the perchlorate (Vc) (W = ClO_4) or tetrafluoroborate (W = BF_4) in the form of colorless luminescing viscous resin-forming products, and the perchlorate (Vb) in crystalline form.

General Method for the Isolation of the N,N'-Bischlorohydrin Salts (VII), (VIII). To the suspension of 10 mmole of the corresponding azole in 2 ml of isopropyl alcohol at room temperature are added, with stirring, 0.83 ml (10 mmole) of 70% perchloric acid and then 2.36 ml (30 mmole) of epichlorohydrin. The stirring is continued for 1 h, and the mixture is left for 2-3 days under the same conditions. The reaction mixture is then boiled for 2-3 min and cooled. The residue obtained is filtered off, washed with ether, dried, and recrystallized.

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