Chem. Chem. Technol., 2020,
Vol. 14, No. 4, pp. 439–447

Chemistry

SYNTHESIS OF EPOXYPEROXIDES AND PEROXIDE DERIVATIVES OF α-D-GALACTOPYRANOSE BASED THEREON

Roman Fleychuk[1, ✉], Lidiya Vuytsyk[1], Ananiy Kohut[1], Orest Hevus[1]

https://doi.org/10.23939/chcht14.04.439

Abstract. New epoxide-containing peroxides have been synthesized *via* the interaction between epichlorohydrin and ditertiary ω-hydroxyalkyl peroxides. The effect of reaction conditions on both the yield and composition of the reaction products has been established. Through the reactions of either the synthesized epoxide-containing peroxides with 1,2;3,4-di-O-isopropylidene-α-D-galactopyranose or 6-O-glycidyl-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose with the ω-hydroxyalkyl peroxides, new peroxide derivatives with ditertiary and primary-tertiary peroxide groups have been synthesized successfully. The decomposition of the developed substances has been studied by complex thermal analysis and the kinetic parameters of the thermolysis have been determined.

Keywords: hydroxy-containing peroxides, epoxyalkyl peroxides, saccharides with peroxide groups, thermogravimetric analysis.

1. Introduction

A series of requirements with regard to polymers for biomedical applications has to be fulfilled for solving issues of contemporary medicine and pharmacy. The polymers must be biocompatible with living tissues and able to cross cell membranes whereas the metabolism products are needed to be bioinert and non-toxic. To this end, hybrid materials based on natural polymers, particularly polysaccharides, have recently attracted much attention. Such hybrid materials are synthesized by grafting functional monomers, usually acrylic acid and chloromethyl styrene or functional polyperoxides to poly- and oligosaccharides followed by polymer reactions. The hybrid materials have successfully proven themselves in binding biomolecules and drugs, developing diagnostic kits and systems of targeted drug delivery into pathogen cells [1]. Introduction of saccharide moieties into the molecules of various substances imparts a number of useful properties to them including enhanced water solubility, improved biodegradation under natural conditions [2], diminished non-specific interactions with biomaterials, particularly with proteins [3, 4].

Therefore, the synthesis of saccharide-containing modifiers which are capable of chemical grafting onto various surfaces including those of polyolefins with low surface energy, so the formation of hydrophilic layers thereon is of great interest. We believe that the synthesis of saccharide derivatives with peroxide groups in their molecules is a promising way to solve this issue. Due to the decomposition of the peroxide moieties, such peroxide-containing substances would generate saccharide-containing free radicals which are able to initiate radical polymerization and polymer reactions. This allows to prepare hybrid natural-synthetic polymers and to form saccharide-containing layers on the surface of various substrates [5].

In the literature, a couple of papers on the substances simultaneously containing the saccharide and peroxide moieties in the molecules are currently available [6-8] and there is no data on peroxide-containing saccharides with ditertiary peroxide groups, although it is generally recognized that, namely, such type of peroxides is the most efficient for the generation of macroradicals from polyolefins [9]. The application of epoxide-containing peroxides as reactants, in our opinion, could be successfully used for the introduction of peroxide groups into the oligo- and polysaccharide molecules.

For instance, peroxide-functionalized oligomers have been synthesized *via* the reactions of aliphatic diols and oligoethers with the epoxide group of epoxyperoxides and oligomers have been used for the formation of films based on epoxyoligomeric mixtures [10, 11]. Saturated peroxide-functionalized heterochain oligomers prepared through cationic polymerization of epoxyperoxides [12] have been applied for the synthesis of copolymers with improved film-forming, electric and thermomechanical properties [13]. Epoxyperoxides are also precious cross-linking agents for the development of rubber mixtures with enhanced physical, mechanical and adhesive characteristics [14, 15]. Polymers with terminal reactive epoxide groups have been synthesized by using

[1] Lviv Polytechnic National University
12, S. Bandery St., 79013 Lviv, Ukraine
✉ romanfleych@gmail.com

epoxyperoxides for the initiation of polymerization of vinyl monomers [16].

In the literature, the synthesis of epoxyperoxides with primary-tertiary peroxide groups has been reported [12, 17] although ditertiary epoxyperoxides may be of a greater practical interest in the above-mentioned applications. Upon the development of convenient synthetic routes towards ditertiary peroxides with primary hydroxy groups [18-20], new opportunities for the preparation of corresponding peroxide-containing glycidyl ethers has opened up.

This study was aimed to synthesize glycidyl ethers of hydroxyperoxides by reacting the hydroxyperoxides with epichlorohydrin, to modify saccharides with the glycidyl ethers for the development of new saccharide-containing initiators, as well as to study the thermal characteristics of the synthesized substances.

2. Experimental

The solvents (acetone, hexane, dichloromethane, benzene) were used of the chemically pure grade; they were dried over molecular sieves 4 Å and distilled through a Vigreux column 1 m long prior to use. Epichlorohydrin was used of the chemically pure grade and distilled (b.p. 389 K; d_4^{20} 1.181; n_D^{20} 1.4381 [21]). α-D-galactose ("Aldrich") was used without further purification. CTAB from "Merck" and TEBAC from "Aldrich" were of the chemically pure grade.

The starting 2-*tert*-butylperoxy-3-methyl-1-butanol (**1**), 3-*tert*-butylperoxy-2-phenyl-1-butanol (**2**), 4-*tert*-butylperoxy-4-methyl-1-pentanol (**3**), 3-*tert*-butylperoxy-3,3-diphenyl-butan-1-ol (**4**) and 2-*tert*-butylperoxy-2-methyl-1-propanol (**5**) were prepared according to the procedures described in [18-20].

The preparative separation of peroxides by column chromatography was accomplished in glass columns with 20 mm bore and 450 mm long; an adsorbent was aluminium oxide, the II degree of activity of the qualification "for chromatography" (0.15–0.25 mm granularity) from "Merck". Molecular weights were determined by cryoscopy in benzene according to procedures [22, 23].

The ^{1}H NMR spectra were recorded by a Varian VXR-300 NMR and a Joel ECA 400 MHz NMR spectrometer using chloroform-d as a solvent (the concentration of samples was 5 –10%). The spectra were referenced to the TMS signal as an internal standard. The individuality of the synthesized compounds and the course of the reactions were controlled by TLC at the silica gel 60 F_{254} plates ("Merck"). The complex thermogravimetric and differential thermal analyses of the peroxide saccharides were carried out by a derivatograph Q-1500 D (system: F. Paulik, J. Paulik, L Erdey, Hungary) operating in a dynamic mode with a heating rate of 1.25 K/min in argon. The sample weight was 200 mg and aluminium oxide was a reference compound as well. The kinetic parameters of the thermolysis were computed using the method [24, 25] using "Mathcad 2001 Professional" software. The epoxide number (e.n.) was determined by direct titration with 0.1N solution of perchloric acid in glacial acetic acid in the presence of tetraethylammonium bromide [26].

1-[2-(tert-Butylperoxy)-2-methylpropoxy]-3-chloropropan-2-ol (**6**). To the mixture 1.76 g (0.01 mol) of hydroxyperoxide (**5**) and 0.93 g (0.01 mol) of epichlorohydrin in 10 ml of dichloromethane 0.02 ml (0.0001 mol) of $BF_3{\cdot}OEt_2$ were added. The reaction mixture was kept at 313 K and intensively stirred for 6 h. After neutralization with the saturated solution of sodium carbonate and following CO_2 inflation the precipitate was filtered away and the solvent was evaporated. The remainder was distilled on a short path. The yield of the purposive product was 1.55 g (61 %). Found, %: C 51.80; H 8.98; Cl 13.88. Calcl. for $C_{11}H_{23}O_4$, %: C 51.86; H 9.10; Cl 13.92.

2-{[3-(tert-Butylperoxy)-3-methylbutoxy]methyl} oxirane (**7**). To the mixture 6.16 g (0.035 mol) of hydroxyperoxide (**1**) and 12.95 g (0.14 mol) of epichlorohydrin whilst stirring and cooling 2.79 g (0.07 mol) of powdered sodium hydroxide and 0.25 g (0.0007 mol) of CTAB were added. The reaction mixture was kept at 313–318 K while intensively stirring for 6 h. The sodium hydroxide and formed sodium chloride were filtered away and the epichlorohydrin was evaporated *in vacuo*. The purposive epoxyperoxide was purified by chromatography through aluminium oxide (the eluent was hexane). The yield was 5.32 g (64 %); d_4^{20} 0.9574; n_D^{20} 1.4334; MR_D 63.14 (calcl. 63.318); e.n. 18.49 % (calcl. 18.51 %); $O_{act.}$ 6.84 % (calcl. 6.89 %); molecular weight 238 (calcl. 232.31). Found, %: C 62.08; H 10.10. Calcl. for $C_{12}H_{24}O_4$, %: C 62.04; H 10.41. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 3.68 (m, J = 12.7 Hz, 1H, CH_2O glycidyl), 3.47 (t, J = 5.7 Hz, 2H, O–C<u>H</u>$_2$CH$_2$–), 3.38 (m, J = 12.7 Hz, 1H, CH_2O glycidyl), 3.13 (m, J_1 = 5.3 Hz, J_2 = 2.9 Hz, 1H, CH oxirane ring), 2.79 (m, J = 4.5 Hz, 1H, CH_2 oxirane ring), 2.61 (m, J = 2.7 Hz, 1H, CH_2 oxirane ring), 1.85 (t, J = 6.1 Hz, 2H, –C<u>H</u>$_2$–C(CH$_3$)$_2$–), 1.26 (s, 6H, –C(CH$_3$)$_2$), 1.22 (s, 9H, –C(CH$_3$)$_3$).

2-{[3-(tert-Butylperoxy)-3-phenylbutoxy]methyl} oxirane (**8**) was prepared from 1.70 g (0.025 mol) hydroxyperoxide (**2**), 9.25 g (0.1 mol) epichlorohydrin and 20.0 g (0.5 mol) powdered sodium hydroxide in the presence of 0.09 g (0.00025 mol) of CTAB by the procedure similar to compound (7). The yield was 5.1 g (69 %); e.n. 14.550 % (calcl. 14.60 %); $O_{act.}$ 5.41 % (calcl. 5.43 %); molecular weight 289 (calcl. 294.38). Found, %: C 69.31; H 8.88. Calcl. for $C_{17}H_{26}O_4$ %: C 69.36; H 8.90.

2-({[4-(tert-Butylperoxy)-4-methylpentyl]oxy} methyl)oxirane (**9**). To the mixture 5.8 g (0.025 mol) of hydroxyperoxide (**3**) and 18.5 g (0.2 mol) of epichlorohydrin whilst stirring and cooling 4.0 g (0.1 mol) of powdered sodium hydroxide and 0.18 g (0.0005 mol) of CTAB were added. The reaction mixture was kept at 313 K while intensively stirring for 12 h. After cooling, 10 ml of petroleum ether were added, and the reaction mixture was left in a fridge for 14 h. The sodium hydroxide and formed sodium chloride were filtered away. The filtrate was chromatographed through aluminium oxide (the eluent was petroleum ether). The epichlorohydrin and petroleum ether were evaporated *in vacuo*. The yield of the epoxyperoxide was 4.74 g (77 %); d_4^{20} 0.9732; n_D^{20} 1.4491; MR_D 67.90 (calcl. 67.96); e.n. 17.40 % (calcl. 17.40 %); O_{act}. 6.42 % (calcl. 6.49); molecular weight 239 (calcl. 246.34). Found, %: C 63.34; H 10.60. Calcl. for $C_{13}H_{26}O_4$, %: C 63.38; H 10.64. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 3.69 (d, J = = 12.5 Hz, 1H, CH_2O glycidyl), 3.47 (t, J = 5.8 Hz, $OC\underline{H}_2–CH_2$), 3.33 (m, J_1 = 11.5 Hz, J_2 = 5.8 Hz, 1 H, CH_2O glycidyl), 3.13 (m, J_1 = 5.3 Hz, J_2= 2.9 Hz, 1H, CH oxirane ring), 2.78 (m, J = 4.5 Hz, 1H, CH_2 oxirane ring), 2.59 (m, J = 2.7 Hz, 1H, CH_2 oxirane ring), 1.63 (m, J_1 = = 5.8 Hz, J_2 = 5. 7 Hz, 2H, $–C\underline{H}_2–CH_2–C(CH_3)_2$), 1.53 (d t, J = 5.7 Hz, 2H, $–CH_2–C\underline{H}_2–C(CH_3)_2$), 1.18 (s, 9H, $C(CH_3)_3$), 1.16 (s, 6H, $–C(CH_3)_2$).

2-[({4-[(1,1-Diphenylethyl)peroxy]-4-methylpentyl} oxy)methyl]oxirane (**10**). To the mixture 4.7 g (0.0015 mol) of hydroxyperoxide (**4**) in 10 ml of benzene and 11.04 g (0.12 mol) of epichlorohydrin whilst stirring and cooling 2.34 g (0.06 mol) of powdered sodium hydroxide and 0.43 g (0.0006 mol) of CTAB were added. The reaction mixture was kept at 313 K in space for 12 h. The settled sodium hydroxide and sodium chloride after cooling were filtered away. The epichlorohydrin and benzene were evaporated *in vacuo*. The yield of the epoxyperoxide was 5.04 g (90.8 %); m.p. 299 K; e.n. 11.41 % (calcl. 11.60 %); O_{act}. 4.29 % (calcl. 4.31); molecular weight 357 (calcl. 370.48). Found, %: C 74.41; H 8.23. Calcl. for $C_{23}H_{30}O_4$, %: C 74.56; H 8.16.

2-{[2-(tert-Butylperoxy)-2-methylpropoxy] methyl}oxirane (**11**). To the mixture 2.5 g (0.01 mol) of chlorohydrin (**6**) and 0.1 g (0.00027 mol) of CTAB in 10 ml of dichloromethane at 291–295 K whilst effective stirring 0.5 g (0.012 mol) of powdered sodium hydroxide were added. The mixture was stirred for 2.5 h and the precipitate was filtered away. The filtrate was neutralized by passing carbon dioxide. The solvent was evaporated, and the residue was chromatographed through aluminium oxide (the eluent was hexane). The yield of epoxyperoxide was 1.79 g (82 %); d_4^{20} 0.98402; n_D^{20} 1.4412; e.n. 19.24 % (calcl. 19.69 %); O_{act}. 7.30 % (calcl. 7.33); MR_D 58.60 (calcl. 58.67); molecular weight 209 (calcl. 218.28). Found, %: C 60.48; H 10.10. Calcl. for $C_{11}H_{22}O_4$, %: C 60.52; H 10.16. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 3.71 (m, J = 12.1 Hz, 1H, CH_2O glycidyl), 3.61 (s, 2H, $C\underline{H}_2–C(CH_3)_2$), 3.34 (m, J = 12.1 Hz, 1H, CH_2O glycidyl), 3.18 (m, J_1 = 5.3 Hz, J_2 = 2.9 Hz, 1H, CH oxirane ring), 2.80 (m, J = 5.1 Hz, 1H, CH_2 oxirane ring), 2.62 (m, J = 2.7 Hz, 1H, CH_2 oxirane ring), 1.26 (s, 6H, $–C(CH_3)_2$), 1.19 (s, 9H, $C(CH_3)_3$).

2-[(tert-Butylperoxy)methyl]oxirane (**12**) was prepared from 2.30 g (0.025 mol) TBHP and 2.31 g (0.025 mol) of epichlorohydrin in the presence of 2.5 g (0.025 mol) of sodium hydroxide (40% solution in water) and 0.36 g (0.001 mol) of CTAB according to the procedure described in [27]. The yield was 3.2 g (88.5 %); b.p. 313 K/1330 Pa; n_D^{20} 1.4810 (in literature 1.4810 [27]); e.n. 29.4 % (calcl. 29.45 %); O_{act}. 10.7 % (calcl. 10.9 %); molecular weight 142.4 (calcl. 146.184). Found, %: C 57.49; H 9.6. Calcl. for $C_7H_{14}O_3$, %: C 57.51; H 9.65.

1,2;3,4-Di-O-isopropylidene-α-D-galactopyranose (DIPG) (**13**) was prepared from 225 ml (3.07 mol) of acetone and 18.0 g (0.1 mol) of α-D-galactose in the presence of 21.6 g (0.16 mol) anhydrous zinc chloride and 0.72 ml of concentrated sulphuric acid at 293 K for 4 h according to the procedure [28]. After the isolation and distillation *in vacuo* (6.65 Pa) 17.5 g (67 % yield) of the purposive product was received with n_D^{20} 1.4660. Found, %: C 55.16; H 7.80. Calcl. for $C_{12}H_{20}O_6$, %: C 55.37; H 7.74. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 5.57 (d, J = 4.9 Hz, 1H, H-1), 4.61 (dd, J = 7.9, 2.4 Hz, 1H, H-3), 4.34 (dd, J = 5.0, 2.4 Hz, 1H, H-2), 4.28 (dd, J = 7.9, 2.3 Hz, 1H, H-4), 3.88–3.84 (m, 2H, H-6), 3.78–3.71 (m, 1H, H-5), 2.43 (br s, 1H, OH), 1.54 (s, 3H, $C(CH_3)$), 1.46 (s, 3H, $C(CH_3)$), 1.34 (s, 6H, $C(CH_3)_2$).

6-O-[3-(3-(tert-Butylperoxy)-3-methylbutoxy-2-hydroxypropil]-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose (**14**).

Method A. To the solution 1.16 g (0.005 mol) of epoxyperoxide (**7**) in dioxane 1.3 g (0.005 mol) of DIPG (**13**), 0.1 g of powdered sodium hydroxide and 0.1 g of TEBAC were added consecutively. The reaction mixture was stirred at 333–353 K for 6 h and neutralized by passing CO_2; afterwards, it was filtered through a thin layer of aluminium oxide. The solvent was evaporated *in vacuo* to give 0.64 g of the substance (practically quantitative) with the 96 % yield of the purposive product. After the reaction mixture was additionally purified by chromatography through aluminium oxide (the eluent was a combination of dichloromethane and 2-propanone, 10:3) to give 2.06 g (85 % yield). Molecular weight 485 (calcl.

492.6). Found, %: C 58.31; H 8.9. Calcl. for $C_{24}H_{44}O_{10}$, %: C 58.52; H 9.0. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 5.57 (d, J = 4.9 Hz, 1H, H-1), 4.60 (dd, J = 8.1, 2.3 Hz, 1H, H-3), 4.34 (dd, J = 5.0, 2.4 Hz, 1H, H-2), 4.28 (dd, J = = 8.1, 2.3 Hz, 1H, H-4), 3.99-3.93 (m, 1H, C<u>H</u>(OH)), 3.89–3.86 (m, 2H, H-6), 3.85–3.66 (m, 5H, O–CH_2 pyranose ring, t-Bu–$OOCH_2$, H-5), 3.78 (t, J = 5.8 Hz, 2 H, O–C<u>H</u>$_2$–CH_2–), 3.58–3.46 (m, 2H, C<u>H</u>$_2$–CH–OH), 2.63 (br s, 1H, OH), 1.84 (t, J = 5.8 Hz, 2H, C<u>H</u>$_2$–$C(CH_3)_2$), 1.54 (s, 3H, $C(CH_3)$), 1.44 (s, 3H, $C(CH_3)$), 1.34 (s, 6H, $C(CH_3)_2$), 1.23 (s, 6H, $C(CH_3)_2$), 1.18 (s, 9H, $C(CH_3)_3$).

<u>*Method B.*</u> To the solution 1.58 g (0.005 mol) of epoxysaccharide (**16**) in dichloromethane 0.88 g (0.005 mol) of hydroxyperoxide (**1**), 0.1 g of powdered sodium hydroxide and 0.1 g of TEBAC were added consecutively. The reaction mixture was stirred at 343 K for 5 h. The purposive product was purified by chromatography through aluminium oxide (dichloromethane as the eluent) and the solvent was evaporated *in vacuo*. The yield was 2.1 g (85.3 %).

*6-O-[3-(tert-Butylperoxy)-2-hydroxypropil]-1,2;3,4-di-O-*isopropylidene-*α-D-galactopyranose* (15).

<u>*Method A.*</u> To the solution 3.12 g (0.012 mol) of DIPG (**13**) in 20 ml of dichloromethane 0.02 ml (0.0001 mol) of $BF_3{\cdot}(C_2H_5)_2O$ as a catalyst were added and kept at 313 K whilst stirring for 0.25 h; the solution 1.75 g (0.012 mol) of epoxyperoxide (**12**) in 10 ml of dichloromethane was dripped for 1.5 h. The mixture was stirred for 2 h at 303–313 K. Thereafter, the catalyst was neutralized with a solution of sodium carbonate. The precipitate was filtered away and the solvent evaporated. The yield was 2.8 g (57 %); n_D^{20} 1.4624; molecular weight 400.25 (calcl. 406.46). Found, %: C 54.76; H 8.06. Calcl. for $C_{19}H_{34}O_9$, %: C 56.14; H 8.43. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 5.55 (d, J = 5.0 Hz, 1H, H-1), 4.59 (dd, J = 7.9, 2.3 Hz, 1H, H-3), 4.34 (dd, J = 5.0, 2.4 Hz, 1H, H-2), 4.28 (dd, J = 7.9, 2.3 Hz, 1H, H-4), 3.99–3.93 (m, C<u>H</u>(OH),1H), 3.89–3.86 (m, 2H, H-6), 3.85–3.66 (m, 5H, OCH_2 pyranose ring, t-BuOO–CH_2, H-5), 3.58–3.46 (m, 2H, C<u>H</u>$_2$–CH–OH), 2.43 (br s, 1H, OH), 1.22 (s, 6H, $C(CH_3)_2$ pyranose ring), 1.19 (s, 9H, $C(CH_3)_3$).

<u>*Method B.*</u> To the solution 0.63 ml (0.006 mol) of TBHP in 10 ml of dichloromethane at 313 K for 0.25 h 0.012 ml (0.0001 mol) of $BF_3{\cdot}(C_2H_5)_2O$ as a catalyst were added and the solution 1.9 g (0.006 mol) of GDIPG (16) in dichloromethane was dripped for 1.0–1.5 h. The mixture was additionally stirred for 2 h at 303–313 K, the catalyst was neutralized with a solution of sodium carbonate. The precipitate was filtered away and the solvent evaporated. The yield was 1.36 g (56 %).

6-O-Glycidyl-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose (GDIPG) (**16**). To the solution 5.2 g (0.02 mol) of DIPG (**13**) in 13.0 g (0.14 mol) of epichlorohydrin TEBAC were added. The mixture was heated to 333–353 K and 2.4 g (0.06 mol) of sodium hydroxide were added while stirring. The mixture was stirred for 6 h at this temperature, cooled, dissolved in dichloromethane and filtered through an aluminium oxide layer. The solvent and excessive epichlorohydrin were evaporated. The product was purified by recrystallization from a mixture of benzene and hexane. The yield was 5.4 g (86 %); m.p. 347–348 K; molecular weight 305 (calcl. 316.36). Found, %: C 56.17; H 7.68. Calcl. for $C_{15}H_{24}O_7$, %: C 56.95; H 7.65. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 5.55 (d, J = 5.0 Hz, 1H, H-1), 4.59 (dd, J = 7.9, 2.3 Hz, 1H, H-3), 4.34 (dd, J = 5.0, 2.4 Hz, 1H, H-2), 4.28 (dd, J = 7.9, 2.3 Hz, 1H, H-4), 3.89–3.86 (m, 2H, H-6), 3.78–3.69 (m, 1H, H-5), 3.67 (d, J = 12.5 Hz, 1H, CH_2O glycidyl), 3.33 (m, J_1 = 11.5 Hz, J_2 = 5.8 Hz, 1H, CH_2O glycidyl), 3.13 (m, J_1 = 5.3 Hz, J_2 = 2.9 Hz, 1H, CH oxirane ring), 2.78 (m, J = 4.5 Hz, 1H, CH_2 oxirane ring), 2.59 (m, J = 2.7 Hz, 1H, CH_2 oxirane ring), 1.54 (s, 3H, $C(CH_3)$), 1.44 (s, 3H, $C(CH_3)$), 1.32 (s, 6H, $C(CH_3)_2$).

3. Results and Discussion

3.1. Synthesis of Epoxide-Containing Peroxides

Synthetic pathways to peroxides with primary hydroxy groups in the β-, γ-, and δ-positions have been recently developed in our team. The reactive primary hydroxy group of these substances reacts similarly to that of aliphatic alcohols. Typical reactions of the hydroxyperoxides include esterification, transesterification, acylation with unsaturated carboxylic acid anhydrides and acyl chlorides [20, 29, 30]. Hence, the O-alkylation of the hydroxyperoxides with epichlorohydrin has been considered as a reasonable approach to epoxyperoxides (Fig. 1). Sodium hydroxide has been used as a hydrogen chloride scavenger. To conduct the reaction, the technique for the O-alkylation of alcohols in a two-phase system “liquid – powdered NaOH” has been utilized with phase-transfer catalysts. The need to use the system “liquid – solid (NaOH)” has been due to the sensitivity of the glycidyl moiety to hydrolysis by alkaline aqueous solutions. Quaternary ammonium salts (namely, benzyltriethylammonium chloride, cetyltrimethylammonium bromide (CTAB) and tetrabutylammonium iodide) have been applied as phase-transfer catalysts. CTAB has revealed the best results among the studied ones.

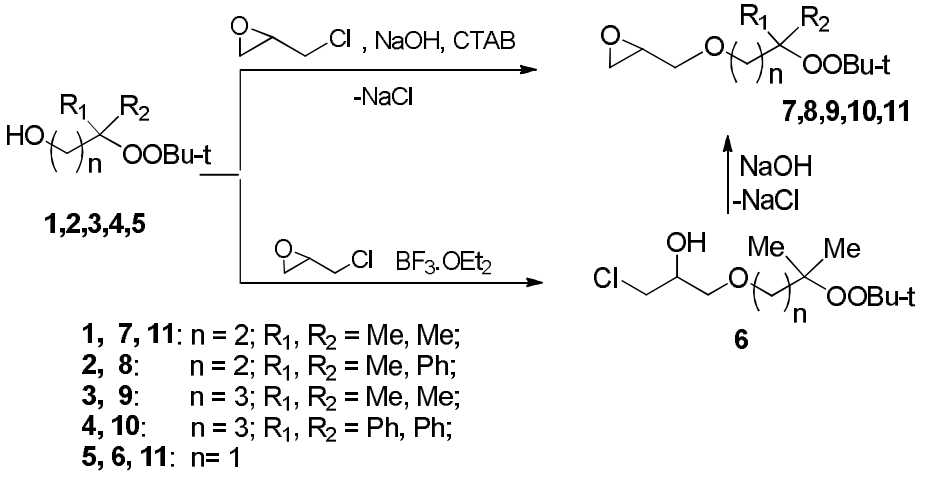

Fig. 1. Scheme of the synthesis of epoxide-containing peroxides based on hydroxyperoxides

Epoxyperoxide (**7**) has been synthesized *via* the interaction of 3-*tert*-butylperoxy-3-methyl-1-butanol (**1**) with epichlorohydrin at 313–318 K in the presence of powdered sodium hydroxide and CTAB as a phase-transfer catalyst (the molar ratio hydroxyperoxide:epichlorohydrin:sodium hydroxide:CTAB was 1:4:2:0.01). The large excess of epichlorohydrin has been used to reduce the contribution of the side reaction of the desired epoxyperoxide with the initial hydroxyperoxide. The double excess of sodium hydroxide has been added because the epoxyperoxide yield decreases with decreasing amount of NaOH. A plausible explanation is shielding the sodium hydroxide surface with NaCl which is generated during the reaction. Under these conditions, almost complete conversion of the hydroxyperoxides has been achieved in 6 h as evidenced by thin-layer and gas-liquid chromatographies. The main side reactions, which decrease the epoxyperoxide yield, are the polymerization of both the epichlorohydrine and the desired epoxyperoxide under the reaction conditions along with the interaction between the initial hydroxyperoxide and the epoxyperoxide. Increasing the reaction temperature to 323–333 K elevates the reactant consumption rate; however, it has not resulted in a higher yield of the desired epoxyperoxide. In this event, the content of side-products (*e.g.*, resin-like substances) in the reaction mixture has increased due to the polymerization of the epichlorohydrin and the desired epoxyperoxide.

Following this technique, epoxyperoxide (**8**) has been synthesized (69 % yield) through the reaction of 3-*tert*-butylperoxy-3-phenyl-1-butanol (**2**) with epichlorohydrin in the presence of sodium hydroxide. However, the conversion of 4-*tert*-butylperoxy-4-methyl-1-pentanol (**3**) and 3-*tert*-butylperoxy-3,3-diphenyl-butan-1-ol (**4**) during their interaction with epichlorohydrin in the presence of sodium hydroxide under this approach has not exceeded 65-72% in 6 hours (the molar ratio hydroxyperoxide:epichlorohydrin:sodium hydroxide equal to 1:4:2). Increasing the amount of epichlorohydrin and sodium hydroxide in the reaction mixture to 8 and 4 mol/mol of the hydroxyperoxide along with extending the reaction time to 12 h has allowed for reaching an almost quantitative conversion of the hydroxyperoxides. The yield of the desired peroxide-containing glycidyl ethers (**9**, **10**) has accounted for 77–90 %.

This technique has nevertheless revealed itself to be inappropriate for the synthesis of glycidyl ether (**11**) from *β*-hydroxyperoxide. The reason for this is that *β*-hydroxyperoxides, unlike *γ*- and *δ*-hydroxyperoxides, are not alkali-resistant and thus undergo fragmentation to give non-peroxide reaction products [31]. However, *β*-hydroxyperoxide derivatives with a substituted OH-group (*e.g.*, ethers) are relatively stable in an alkaline medium. To this end, a different synthetic pathway has been suggested to prepare epoxyperoxide (**11**). First, peroxide-containing chlorohydrin (**6**) has been synthesized by the addition of the hydroxyperoxide to epichlorohydrin under acid catalysis. Then chlorohydrin (**6**) has been transformed into oxirane (**11**). As a catalyst for the addition reaction, $BF_3{\cdot}OEt_2$ has been used (0.01 mol/mol of the hydroxyperoxide) since the hydroxyperoxide is resistant to Lewis acids.

Dehydrochlorination of chlorohydrin (**6**) has been conducted in a dichloromethane solution at 293 K by adding powdered NaOH (1.2 mol/mol of the substrate) (Fig. 1). The yield of this stage has accounted for 82 %. However, we have not succeeded in achieving an appropriate general yield of desired epoxyperoxide (**11**). In our opinion, this was due to low yield of chlorohydrin (**6**) at the first stage owing to the steric effect of the neopentyl-like structure of the initial *β*-hydroxyperoxide. Furthermore, the particular addition of the hydroxyperoxide to the C_2 atom of epichlorohydrin has been observed, which

has resulted in the formation of 1,3-chlorohydrin. The latter cannot form an oxirane ring.

tert-Butyl glycidyl peroxide (**12**) has been prepared by the interaction between epichlorohydrin and *tert*-butyl hydroperoxide (TBHP) using the technique described elsewhere [27].

Synthesized epoxyalkyl peroxides (**7-11**), which could be considered as derivatives of the functional ditertiary peroxides, are of low sensitivity to impact and friction. They have a significant shelf life at room temperature with insignificant loss of active oxygen content. Upon thermolysis, the epoxyalkyl peroxides generate epoxide-containing free radicals and hence can be applied as initiators for the synthesis of polymers with terminal epoxide groups [16]. These peroxides are promising precursors for introducing peroxide groups into various substrates having reactive functional groups (hydroxy, carboxyl, amine, *etc.*), particularly for the modification of saccharides with peroxides.

3.2. Synthesis of Peroxide-Containing Saccharides

The major problem when regioselectively modifying saccharides arises owing to the presence of five hydroxy groups in their molecules; four of which have almost equal reactivity. The glycoside hydroxy group is primarily involved in almost all chemical transformations. However, the formed glycosides are not stable in an acidic medium and the substituent is easily cleaved. Therefore, the preliminary protection of hydroxy groups is widely used for the regioselective introduction of substituents into other positions of a saccharide molecule. The required reaction centre should be left free. Glycidyl ethers are known to relatively easily conjugate with primary alcohols alcohols under alkaline catalysis, whereas their interaction with secondary alcohols is hindered due to the steric effect. Polymerization of an epoxide ring is often observed under the reaction conditions. Hence, for the introduction of peroxyalkyl moieties into saccharide molecules, their derivatives with the free primary hydroxy group and the protected remaining OH groups should be used. 1,2,3,4-di-O-isopropylidene-α-D-galactopyranose (DIPG) (13) meets these requirements. It can be easily synthesized by the reaction of α-D-galactopyranose with either acetone or isopropylidene methyl ether [28]. Owing to the presence of a primary hydroxy group, 1,2,3,4-di-O-isopropylidene-α-D-galactopyranose is able to react with the epoxyperoxides under alkaline catalysis to give peroxide-containing saccharides (**14**, **15**) as major reaction products.

The interaction between saccharide (**13**) and epoxyperoxide (**7**) has been conducted in benzene at 333–353 K in the presence of powdered NaOH and benzyltriethylammonium chloride (TEBAC) as a catalyst (Fig. 2, method A). The reactants have been almost completely consumed within 6 h as determined by thin-layer chromatography. Following this technique for the modification of saccharide (**13**) with *tert*-butyl glycidyl peroxide (**12**) has led to the partial decomposition of desired saccharide-containing peroxide (**15**), which is also typical of β-hydroxyperoxides. Therefore, in this case, the reaction has been carried out in dichloromethane using $BF_3{\cdot}OEt_2$ as a catalyst. The latter provides a sufficient reaction rate at 313 K and does not cause the decomposition of the peroxide groups in both the initial and desired peroxides. The reactants have been almost completely consumed within 3.5 h whereas the yield of desired peroxide (**15**) has counted for 57 %.

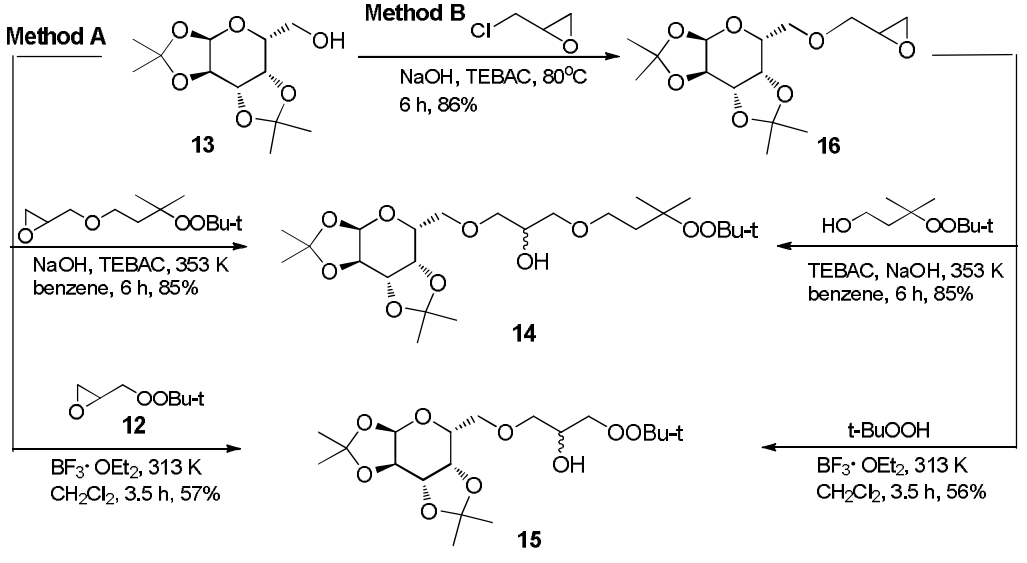

Fig. 2. Scheme of the synthesis of peroxide-containing saccharides

As an alternative method for the synthesis of peroxide-containing saccharides (**14**, **15**), the interaction between epoxide-containing saccharide (**16**) and either *tert*-butyl hydroperoxide or *ω*-*tert*-butylperoxyalkanols (Fig. 2, method B) has been suggested. The interaction between primary alcohols and epichlorohydrin in the presence of a powdered alkali and phase-transfer catalysts undergoes smoothly resulting in a high yield of the desired reaction product, whereas secondary alcohols virtually do not react under these conditions. Thus, the interaction between DIPG (**13**) and epichlorohydrin has been conducted in order to prepare epoxide-containing saccharide 6-O-glycidyl-1,2;3,4-di-O-isopropylidene-*α*-D-galactopyranose (GDIPG) (**16**) (Fig. 2).

The reaction has been carried out at a molar ratio DIPG : epichlorohydrin:NaOH equal to 1:7:3 at 333–353 K in the presence of TEBAC for 6 h until almost complete conversion of DIPG. In this system, epichlorohydrin has served as both a solvent and reactant. The sevenfold excess of epichlorohydrin has been used to decrease the viscosity of the reaction mixture and to minimize the side alkylation reaction of the initial saccharide with the desired epoxysaccharide. The internal standard yield of the epoxide-containing saccharide has been close to quantitative, whereas the isolated yield has accounted for over 80 % after recrystallization.

In the next stage, galactose derivative having the ditertiary peroxide group (**14**) has been synthesized through the interaction between GDIPG (**16**) and *γ*-hydroxyperoxide (**1**). The reaction has been carried out in benzene at the stoichiometric ratio of the reactants and catalytic amount of powdered sodium hydroxide with TEBAC as being a phase-transfer catalyst at 333–353 K for 5–7 h. In this event, the alkali does not cause decomposition of the desired reaction product since the O–O bond is hampered from the hydroxy group by several methylene groups.

Galactose derivative with a primary-tertiary peroxide group (**15**) has been prepared *via* the interaction between GDIPG (**16**) and TBHP in dichloromethane at 303–313 K. Boron trifluoride diethyl etherate has been utilized as a reaction catalyst since it provides a fair yield of 56 % and a sufficient purity of the reaction product. The main side-products are oligosaccharides of an unidentified structure. When NaOH has been used as a catalyst in the form of either an aqueous solution or a very fine powder along with phase-transfer catalysts, the yield of the desired peroxide has decreased to below 40 %. In this event, 2-methyl-2-propanol, formaldehyde and substituted DIPG without a peroxide group have been found in the reaction mixture using thin-layer and gas-liquid chromatographies. Meanwhile, this reaction product gives qualitative reactions typical of aldehydes according to the thin-layer chromatography data. In our opinion, the formation of these products could be explained by the alkali-catalyzed fragmentation of the *β*-hydroxyalkylperoxide moiety.

Noteworthy, both the methods (*i.e.*, the reaction of hydroxyperoxide (**1**) with GDIPG (**16**) and the reaction of epoxyperoxide (**7**) with saccharide (**13**)) are almost equal for the synthesis of peroxide-containing saccharide (**14**). The reaction of GDIPG (**16**) with TBHP is more preferable to the preparation of peroxide-containing saccharide (**15**).

3.3. Investigation of Thermal Stability for Peroxide Saccharides

For the rational application of peroxide initiators, the knowledge concerned with the peculiarities of thermolysis and decomposition rate for those compounds at different temperatures is very important. Thermogravimetric and differential-thermal analyses are the most effective contemporary analytical methods for the investigation of the O-O bond reactivity [24, 25]. The mathematical treatment of thermogravimetric (TG), differential-thermal (DTA) and differential-thermogravimetric (DTG) curves permits to calculate kinetic parameters of decomposition activation energy, the order of a reaction and reaction rate constants.

According to the thermogravimetric analysis data (TG) in the intense weight loss region by the modified kinetic equation [32] (Eq. (1)) and applying the least square procedure the kinetic parameters of thermolysis are computed, which is represented in Table 1.

$$\frac{dW}{W_k dt} = \ln\frac{z}{q} - \frac{E}{RT} + n\ln(1-\frac{W}{W_k}) \qquad (1)$$

where W *is* the sample weight loss at temperature T, mg; W_k is the total sample weight loss in the given stage, mg; z is a pre-exponential factor; q is the sample heating rate, K/s; E is activation energy, kJ/mol; R is the universal gas constant, R = 8.314 J/mol·K; n is the reaction order; T is the absolute temperature, K.

Having compared these curves, it was determined that the most intensive sample weight loss is observed in 383–473 K range due to peroxide fragment destruction. The decomposition of the *tert*-butyl peroxide fragment goes through volatile product formation and is accompanied by the sample weight decrease (TG curve), which strongly pronounced exothermic effect in the DTA curve corresponds to. It is worth drawing attention that both the DTA and DTG maxima coincide. This is a fair indication that the maximal rate of the sample weight loss corresponds to maximal heat release due to peroxide group thermolysis. The complex thermal analysis curves are in Figs. 3 and 4 while the calculated kinetic parameters of thermolysis are in theTable.

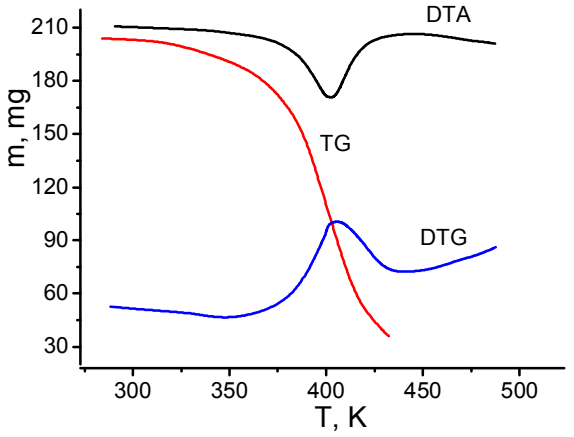

Fig. 3. Thermogravimetric analysis of peroxide (**14**)

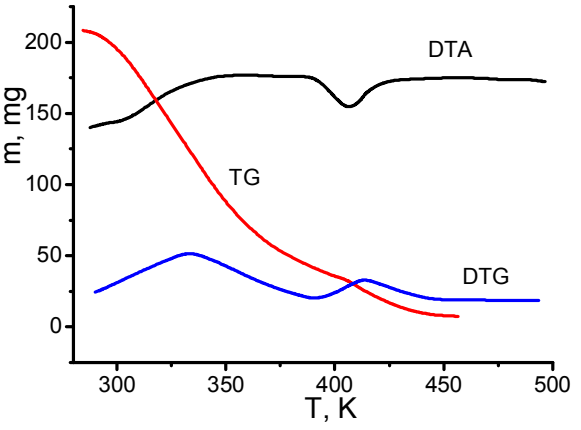

Fig. 4. Thermogravimetric analysis of peroxide (**15**)

Table

Kinetic parameters of the destruction for the synthesized peroxide saccharides

No.	Temperature range, K	E, kJ/mol	n	z	$K \cdot 10^4$	T_{max}, K	Δm, %
14	391–469	128	1.49	$6.08 \cdot 10^{12}$	6.14	438	32
15	359–443	38	1.01	$2.5 \cdot 10^3$	7.37	413	17

All investigated peroxides have the principal thermolysis products, as determined by gas-chromatography: methane, acetone, 2-methyl-2-propanol, and a little amount of 1,1-dimethyloxirane. It is obvious from the given derivatograms that the majority of compounds have the most intensive weight loss in 383–473 K range because of peroxide fragment destruction. Primary-tertiary peroxide (**15**) has the lowest thermal stability among the investigated compounds and begins to decompose already at 353 K. Activation energy is anomalously low for the primary-tertiary peroxides and equals to 38 kJ/mol.

4. Conclusions

Ditertiary epoxyperoxides, *i.e.* glycidyl ethers have been first synthesized *via* the interaction between peroxide-containing primary alcohols and epichlorohydrin. The developed epoxyperoxides are promising enough precursors for introducing peroxide groups into various substrates. New peroxide-containing derivatives of galactose have been prepared using the reactions of the epoxide-containing peroxides with 1,2;3,4-di-O-isopropylidene-α-D-galactopyranose. The structure of the substances has been proven by the counter synthesis, *viz.* the reaction of the initial hydroxyperoxides with 6-O-glycidyl-1,2;3,4-di-O-isopropylidene-α-D-galactopyranose. The kinetic characteristics for thermolysis of the synthesized peroxide derivatives of saccharides have been determined by the method of complex thermal analysis.

Acknowledgements

Thanks are due to D.Sc. V. Vostres, for a fruitful discussion while the interpretation of the experimental data and English text editing.

References

[1] Samaryk V., Varvarenko S., Tarnavchyk I. *et al.*: Macromol. Symp., 2008, **267**, 113. https://doi.org/10.1002/masy.200850721
[2] Samaryk V., Voronov A., Tarnavchyk I. *et al.*: Prog. Org. Coat., 2012, **74**, 687. https://doi.org/10.1016/j.porgcoat.2011.07.015
[3] Revilla J., Elaissari A., Carriere P. *et al.*: J Colloid Interf. Sci., 1996, **180**, 405. https://doi.org/10.1006/jcis.1996.0319
[4] Tirrelli M., Kokkoli E., Biesalski M.: Surf. Sci., 2002, **500**, 61. https://doi.org/10.1016/S0039-6028(01)01548-5
[5] Basinska T.: Macromol. Biosci., 2005, **5**, 1145. htpps://doi.org/10.1002/mabi.200500138
[6] Voronov S., Donchak V., Harhai H. *et al.*: Polym. Int., 2001, **50**, 688. htpps://doi.org/10.1002/pi.683
[7] Solomko N., Dron I., Budishevskaya O., Voronov S.: Procedia Chem., 2009, **1**, 1567. https://doi.org/10.1016/j.proche.2009.11.005
[8] Chobit M.: Chem. Technol. Appl. Substance, 2019, **1**, 139. https://doi.org/10.23939/ctas2018.01
[9] Nudelman Z.: Khimiia Organicheskikh Peroksidov. Izd-vo Volhohradskogo Politech. Inst., Volhohrad 1982.
[10] Bratychak M., Ivashkiv O., Astakhova O.: Dopovidi Nats. Akad. Nauk Ukrainy, 2015, **5**, 119.
[11] Ivashkiv O., Namiesnik J., Astakhova O. *et al.*: Chem. Chem. Technol., 2015, **9**, 313. https://doi.org/10.23939/chcht09.03.313
[12] Puchyn V., Schevchuk V., Jelahin H. *et al.*: UdSSR, A.s. 481631, Publ. Aug. 25, 1975.

[13] Hetmanchuk Yu., Hrebeniuk I., Sembai E. *et al*.: UdSSR, A.s. 443890, Publ. Sep. 25, 1974.
[14] Onyshchenko Z., Krasnobrytaia R., Blokh H. *et al*.: UdSSR, A.s. 414273 Publ. Nov. 05, 1974.
[15] Bazyliak L., Bratychak M., Brostow W. *et al*. Int. Conf. on Polymer Characterization (POLYCHAR-6). USA, Denton 1998, 09.
[16] Sembai E., Yelahin H., Yurzhenko T. *et al*.: UdSSR, A.s. 382649 Publ. May 23, 1973.
[17] Antonovskii V. *et al*: Sintez Perekisei Cyklicheskikh Ketonov i Ocenka ikh Iniciiruiushchikh Sposobnostei [in:] Emanuelia N. *et al.* (Eds.) Uspekhi Khimii. Khimia, Moskva 1969, 100-106.
[18] Bobrova K., Fleychuk R., Hevus O.: Visnyk Lviv Polytechnic National University, 2018, **886**, 52.
[19] Fleichuk R., Gevus' O., Voronov S.: Russ. J. Org. Chem., 2003, **39**, 1799. https://doi.org/10.1023/B:RUJO.0000019748.73690.d2
[20] Fleychuk R.: PhD thesis, Lviv Plytechnic National University, Lviv 2004.
[21] Nikolskii B.: Spravochnik Khimika, T.2. Khimia, Moskva-Leningrad 1964.
[22] Belcher R.: Submicro Methods of Organic Analysis. Elsevier, Amsterdam 1966.
[23] Isaacs N.: Experiments in Physical Organic Chemistry. Macmillan, London 1969.
[24] Uendland U.: Termicheskiie Metody Analiza. Mir, Moskva 1978.
[25] Berg L.: Vvedeniie v Termohrafiiu. Nauka, Moskva 1969.
[26] Siggia S., Hanna J.: Quantitative Organic Analysis via Functional Groups. Wiley, New York 1979.
[27] Gagin M., Bratychak M., Brostow W. *et al*.: Mater. Res. Innovat., 2003, **7**, 291. https://doi.org/10.1007/s10019-003-0266-y
[28] Weygand-Hilgetag: Organisch-Chemische Experimentierkunst. Johann Ambrosius Barth Verlag, Leipzig 1964.
[29] Fleychuk R., Kohut A., Hevus O. *et al*.: Macromol. Symp., 2004, **210**, 85. https://doi.org/10.1002/masy.200450610
[30] Vostres V., Fleichuk R., Voronov S. *et al.*: Russ. J. Org. Chem. 2013, **49,** 1270. https://doi.org/10.1134/S1070428013090042
[31] Kropf H., Ball M., Schroder H. *et al*.: Tetrahedron, 1974, **30**, 2943. https://doi.org/10.1016/S0040-4020(01)97470-8
[32] Semenishin D., Kochubei V., Borova O. *et al*.: Russ. J. Coord. Chem., 2003, **29**, 196. https://doi.org/10.1023/A:1022883731123

Received: November 19, 2019 / Revised: December 12, 2019 / Accepted: February 02, 2020

СИНТЕЗ НОВИХ ЕПОКСИПЕРОКСИДІВ ТА ПЕРОКСИДОВМІСНИХ ПОХІДНИХ α-D-ГАЛАКТОПІРАНОЗИ НА ЇХ ОСНОВІ

Анотація. *Реакцією епіхлоргідрину з дитретинними ω-гідроксиалкілпероксидами синтезовано нові епоксидовмісні пероксиди. З'ясовано вплив умов проведення реакцій на вихід та склад продуктів взаємодії. Реакціями отриманих пероксидовмісних гліцидилових етерів з 1,2;3,4-діізопропіліден-α-D-галактопіранозою або 6-гліцидил-1,2;3,4-діізопропіліден-α-D-галактопіранози з ω-гідроксиалкілпероксидами синтезовано нові пероксидні похідні з дитретинними та первинно-третинними пероксидними групами. Методом комплексного термічного аналізу досліджено розклад синтезованих сполук та визначено кінетичні параметри термолізу.*

Ключові слова: *гідроксилвмісні пероксиди, епоксиалкілпероксиди, сахариди з пероксидними групами, термогравіметричний аналіз.*