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SYNTHESIS AND SOME CHEMICAL CONVERSIONS OF EPOXY ALCOHOLS OF THE CYCLOHEXANONE

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The unsaturated epoxyketones of the aliphatic and alicyclic series – 2-methyl-1,2-epoxy-4-hexene-3-one and 2-methyl-5-(cyclohex-3-enyl)-1,2-epoxy-4-hexene-3-one in the presence of sodium ethylate easily undergo the addition reaction with β-diketone – acetylacetone, acetoacetic and malonic esters with formation of primary Michael adducts – functionally substituted ketoepoxides. Their further conversions by intramolecular aldol condensation lead to the formation of epoxy alcohols of the cyclohexanone series. The hydrobromination, bromination and amination of cyclohexanone epoxy alcohols proceeds with the participation of an oxirane and cyclohexene ring, which leads to the formation of new bromo- and amino derivatives of cyclohexanones.

Keywords: *α,β-unsaturated epoxy ketone, β-diketone, Michael reaction, functionally substituted ketoepoxide, intramolecular aldol condensation, epoxy alcohol of the cyclohexanone series.*

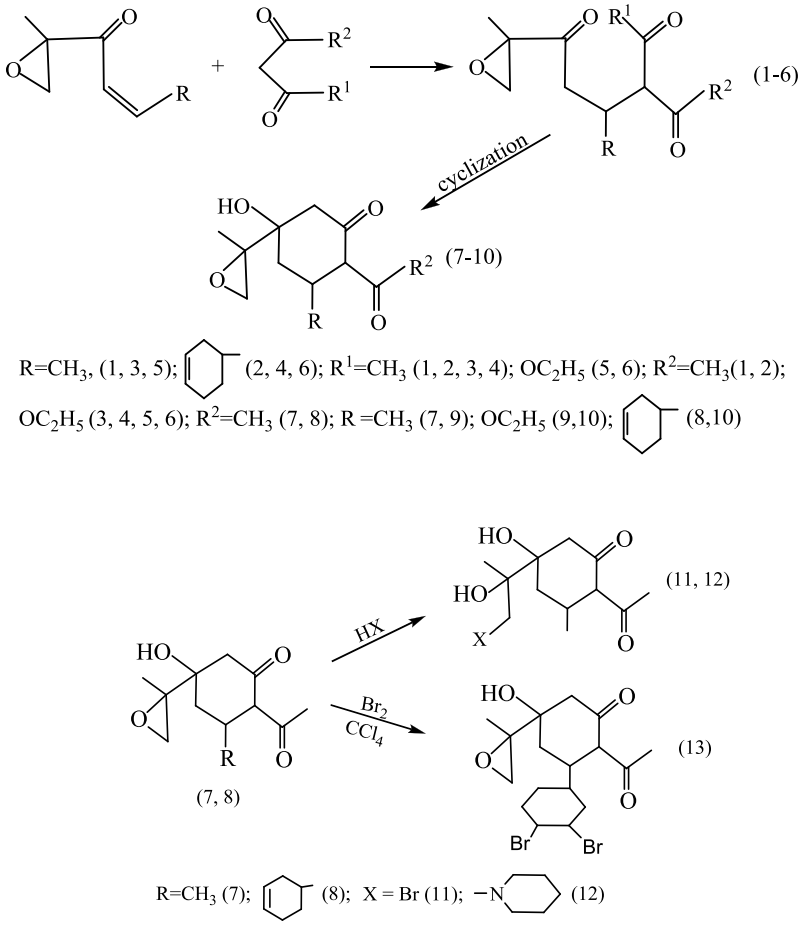
Introduction

It was known that α,β-unsaturated ketones due to the availability of an activated double C=C bond in the molecule easily undergo the Michael addition reaction with various C- and N-nucleophilic reagents, 1,3-diketones, with the formation of various classes of organic compounds, including functionally substituted cyclohexanones. The cyclohexanones and their derivatives, due to their polyfunctionality (carbonyl, hydroxyl, ester groups) and favorable mutual location of functional groups in the molecule, undergo the reaction with various nucleophilic reagents, forming structurally complex carbo- and heterocyclic derivatives possessing practically useful properties, including biological activity (antimicrobial, antioxidant, antiphage activity, analgetic, antipyretic) [1–8]. Therefore, the synthesis, the study of physical, chemical and biological properties, and also the establishment of the practical value of cyclohexanones indicate the actuality of their investigation not only in the theoretical but also in the applied aspect.

Results and discussion

We have previously reported that α,β-unsaturated epoxy ketones of the aliphatic (UEKA) and alicyclic (cyclohexene) series (UEKC) are highly reactive compounds that easily undergo the reaction with nucleophilic and electrophilic reagents [9–13] with the formation of carbo- and heterocyclic compounds. Considering the above-mentioned fact and that the structure of UEKA (UEKC) contains an activated double bond, we have tried to involve them in the Michael reaction and to carry out the synthesis of new functionally substituted derivatives of cyclohexanones, which considerably expand the synthetic possibilities of the latter ones. This paper shows the results of studying the interaction reactions of UEKA (UEKC) with β-diketones (DK) – acetylacetone (AA), acetoacetic (AAE) and malonic esters (ME). As a result of investigations it has been established that the unsaturated epoxy ketones – 2-methyl-1,2-epoxy-4-hexen-3-one and 2-methyl-5-(cyclohex-3-enyl)-1,2-epoxy-4-hexen-3-one – in the presence of sodium ethylate (at 25 °C for 2 h), easily undergo the Michael addition reaction with DK. According to the approved mechanism, under the action of the base, β-diketones – $R^1COCH_2COR^2$ are deprotonated with the formation of carbanions of the $R^1CO\bar{C}HCOR^2$ type, which then are added to β-carbon atom as nucleophilic agents, activated with double C=C-bond of unsaturated epoxy ketone, as a result of which the primary Michael adducts, i.e. alkylation products of linear structure – functionally substituted ketoepoxides **1**–**6** are formed. It should be noted that at the temperature rise to 40 °C and increase of the interaction reaction behavior time of the of unsaturated epoxyketones with β-diketones up to 8 h, the forming intermediate ketoepoxides **1,2** and carboethoxyketoepoxides **3,4** are subjected to the intramolecular aldol condensation, which as a result leads to formation of epoxy alcohols of the cyclohexanone series **7**–**10**, which is a convenient method of synthesis of such compounds [14]. Unlike **1**–**4**, the dicarboethoxyketoepoxides **5,6** are not changed in such conditions, evidently due to essential steric obstacles of intramolecular cyclization.

The cyclohexanone fragment is the main structural peculiarity of a number of widely used natural and synthetic drugs [15–16], which allows synthesizing of new representatives of functionally substituted cyclohexanones and, in the future, using them as biologically active substances. Taking into account the availability of active reactive centers in the synthesized cyclohexanone **7, 8**, they were subjected to various chemical conversions with the formation of new cyclohexanone derivatives. For this purpose, some chemical reactions have been carried out: the oxirane ring opening in epoxy alcohol **7** with 47% HBr leads to the formation of bromdiol **11**, with piperidines – amino alcohol **12**, and the bromination of epoxyalcohol **8** leads to the formation of cyclohexanone dibromide **13**.



The structure of the synthesized compounds **1**–**13** has been confirmed with data of IR, NMR ^{1}H and NMR ^{13}C spectroscopy. In the IR spectra of compounds **1**–**10** there are the following characteristic frequencies (v, cm^{-1}): 1704–1725 (C=O), 1735–1753 ($C=O_{ether}$), 830–870, 1240–1263 (epox), 1610–1630 ($C=C_{cyclohex}$), 3430–3560 cm^{-1} (OH-group). The reaction of the oxirane ring opening in epoxy alcohol **9** with 47% HBr and piperidines follows the Krasusky's rule. The bromination of the cyclohexene ring has been confirmed by absence of the absorption bands characteristic for methylene group of end epoxy rings (3060 cm^{-1}) and asymmetric valence vibration of the oxirane ring (915 cm^{-1}) and the appearance of bands in the field of 1220–1200, 660–680 cm^{-1} characteristic for valence vibrations of C-N and C-Br bonds, respectively, and also by disappearance of the valence vibration of the double bond (1620 cm^{-1}) in cyclohexanone dibromide **13** in the IR spectra of compounds **11, 12**. In the NMR ^{1}H spectra of compounds **1**–**10, 13**, the proton signals of CH_2 group of the oxirane cycle are appeared as two doublets in the field of 2.60–3.06 ppm., there are signals as a singlet of protons of methyl groups on the epoxide ring in the field of 1.26–1.48 ppm. (3H, 2-$CH_{3\ epox}$), in compounds **1, 2, 7, 8, 11**–**13**, the signals of CH_3 of acetyl group (CH_3CO-) as a singlet in the field of 1.90–2.23 ppm are observed. In compounds **1, 2, 7**–**10, 13,** the multiplets at 2.15–2.45 ppm characterize the protons of CH_2 and CH group in the fragment -CH_2CHCH-. In compounds **2, 4, 6, 8, 10**, the singlet at 5.52–5.68 ppm refers to the vinyl proton of the cyclohexene ring (2H,CH=CH), and its methylene and methine protons in the fragment (7H, $CH_2CH_2CHCH_2$) give signals as a multiplet in the field of 1.5–2.50 ppm. In compounds **7**–**10, 13,** there are signals as a singlet in the field of 3.62–4.10 ppm, referred to hydroxyl groups, connected with the cyclohexane ring, and in the spectrum of amino alcohol **12** in the field of 2.98 ppm, the signals as a multiplet of protons of methylene groups (CH_2-N-CH_2) of the piperidine fragment are detected.

In the NMR ^{1}H spectrum of dibromide **13**, the signals of vinyl protons of the cyclohexene ring are absent, the signals of CH_2 and CH groups in the fragment (7H, $CH_2CH_2CHCH_2$) of the dibromocyclohexane ring, as well as the cyclohexene ring, are observed in almost the same interval as a multiplet in the field of 1.25–2.50 ppm. In the spectra of compounds **3**–**6, 9, 10**, the signals as a triplet with δ = 1.10–1.35 ppm and a quadruplet with δ = 3.94–4.4 ppm belong to protons of CH_3- and CH_2 -carbethoxy of ($C_2H_5CO_2$-, $J_{CH_3\text{-}CH_2}$ = 6.7–7.0 Hz) group. In the spectrum of compounds **7, 9, 11, 12**, the protons of methyl group in C^3 position of the cyclohexane fragment give a signal at 0.91–1.10 ppm as a doublet (J = 6.9 Hz), the protons of methylene groups in C^4 position of alicycle are observed as a doublet and triplet in the

fields 1.81–1.92 and 2.16–2.31 ppm, respectively, and the signals of methylene groups in C^6 position of alicycle – as two doublets at 2.30–2.80 ppm.

Thus, we have established that α,β-unsaturated epoxy ketones easily undergo the Michael addition reaction with β-dicarbonyl compounds containing a reactive methylene group in their composition, with the formation of functionally substituted ketoepoxides, which, by further conversions by intramolecular aldol condensation are converted into epoxy alcohols of the cyclohexanone series, being polyfunctional alicyclic compounds and providing possibilities for their wide use in synthetic organic chemistry.

Experimental part

IR spectra have been recorded on IR Fourier-spectrometer Alpha FT-IR Bruker on a ZnSe crystal in the wave number range 600–4000 $см^{-1}$. NMR ^1H and ^{13}C have been recorded on spectrometer Bruker FT-300 (300.13 and 75.45 MHz). The chemical shifts have been determined relative to TMS; deuterochloroform has been used as a solvent. The purity of the initial compounds and individuality of the obtained substances were controlled by TLC on plates "Silufol UV-254" (eluent – benzene-diethyl ether 3:1) and gas chromatography on the chromatograph LKhM-8MD-5 (column 200×0.4 cm, immobile phase SE-30, Chromaton-W (3%), gas-carrier rate (helium) – 30 ml/min).

The initial unsaturated epoxy ketones were synthesized by the method described in [9–10].

General methodology of addition of β-dicarbonyl compounds (acetyl acetone, acetoacetic ether, malonic ester) to unsaturated epoxy ketones (UEKA and UEKC) on Michael condensation. 0.06 mol of DK was added to a solution of 0.05 mol of UEKA (UEKC) in 25 ml of ethyl alcohol at 5–10 °C and with intensive stirring for 20 min. Then 5 ml of 10% alcohol solution of NaOH was added, while adding the solution the temperature of the reaction mixture was maintained at 20–25 °C. After the addition, the stirring was continued at the same temperature for another 30 min., the alkali was neutralized with 10% acetic acid. After corresponding treatment and vacuum distillation of the initial substances, the compounds **1**–**6** were isolated.

1,2-Epoxy-6-acetyl-2,5-dimethyl-3,7-octane dion (1). Yield – 67.8%, b.p. 125–126 °C (1 mm merc.c.), n_D^{20} 1.4450, d_4^{20} 1.0435. IR spectrum, ν, cm^{-1}: 1720 (C=O), 1710 ($C=O_{acetyl}$), 860, 1260 (epox.). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.07 d and 1.12d (3H, CHC$\underline{H}_3$, *J* = 6.8 Hz), 1.33s (3H, CH_{3epox}), 1.90s (6H, $2CH_3CO$-), 2.20–2.51m (4H, CH_2CHCH), 2.60d, 2.74d (2H, CH_{2epox} *J* = 5.6 Hz). Found, %: C 63.49; H 8.08. $C_{12}H_{18}O_4$. Calculated, %: C 63.72; H 7.96.

1,2-Epoxy-6-acetyl-2-methyl-5-(cyclohexen-3-yl)-3,7-octane dion (2). Yield – 73.1%, b.p. 160–161 °C (1 mm merc. c.), n_D^{20} 1.5080, d_4^{20} 1.1052. IR spectrum, ν, cm^{-1}: 1725 (C=O), 1712 ($C=O_{acetyl}$), 865, 1255 (epoxy), 1620 ($C=C_{cyclohex}$). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.26s (3H, $CH_{3epox.}$), 1.50–2.16 m (7H, $CH_2CHCH_2CH_2$ $_{cyclohex}$), 2.20s (6H, $2CH_3CO$), 2.30–2.56 m (4 H, CH_2CHCH), 2.75d, 2.88d (2H, CH_{2epox}, *J* = 5.2 Hz), 5.46-5.58 m (2H, HC=CH). Found, %: C 70.02; H 8.01. C_{17} $H_{24}O_4$. Calculated, %: C 69.86; H 8.22.

1,2-Epoxy-6-carboethoxy-2,5-dimethyl-3,7-octane dion (3). Yield **–** 72.9%, b.p. 135–136 °C (1 mm merc. c.), n_D^{20}1.4380, d_4^{20}1.0695. IR spectrum, ν, cm^{-1}: 1715 (C=O), 1735 ($C=O_{ether}$), 870, 1250 (epoxy). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.10d, 1.14d (3H, CHC$\underline{H}_3$, *J* = 6.8 Hz), 1.20t (3H, C$\underline{H}_3CH_2CO$, *J* = 7.2 Hz), 1.35s (3H, CH_{3epox}), 1.86s (3H, CH_3CO), 2.24–2.57m (4 H, CH_2CHCH), 2.74d, 2.84d (2H, *J* = 5.2 Hz, CH_{2epox}), 3.94q (2H, C$\underline{H}_2CO$, *J* = 7.2 Hz**)**. Found, %: C 60.71; H 7.98. $C_{13}H_{20}O_5$. Calculated, %: C 60.94; H 7.81.

1,2-Epoxy-6-carboethoxy-2-methyl-5-(cyclohexen-3-yl)-3,7-octane dion (4). Yield – 78.2%, b.p. 170–171 °C (1 mm merc.c.), n_D^{20} 1.4940, d_4^{20}1.1073. IR spectrum, ν, cm^{-1}: 1712 (C=O), 1740 ($C=O_{ether}$), 850, 920, 1250 (epox), 1630 ($C=C_{cyclohex}$). NMR ^1H spectrum, δ, ppm. (J, Hz): 1.13t (3H, C$\underline{H}_3CH_2CO$, *J* = 7.1 Hz), 1.34s (3H, CH_3 $_{epox}$), 1.50c (3H, CH_3CO-), 1.65–2.28м (7H, $CH_2CHCH_2CH_2$ $_{cyclohex}$), 2.36–2.60 m (4 H, CH_2CHCH), 2.76d, 2.88d (2H, CH_{2epox}, *J* = 5.3 Hz), 5.37–5.56m (2H, HC=CH), 4.0q (2H, C$\underline{H}_2CO$, *J* = 7.1 Hz**)**. Found, %: C 67.35; H 7.98. $C_{18}H_{26}O_5$. Calculated, %: C 67.08; H 8.07.

1,1-Dicarboethoxy-5,6-epoxy-2,5-dimethylhexan-3-one (5). Yield – 76.7%, b.p. 145–146 °C (1 mm merc.c.), n_D^{20} 1.4320, d_4^{20} 1.0557. IR spectrum, ν, cm^{-1}: 1710 (C=O), 1745 ($C=O_{ether}$), 848, 1245 (epox). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.11t (6H, $2C\underline{H}_3CH_2CO$, *J* = 7.0 Hz), 1.19d, 1.26d (3H, CHC$\underline{H}_3$, *J* = 6.2 Hz), 1.42s (3H, CH_{3epox}), 2.30-2.56m (4 H, CH_2CHCH), 2.68d, 276d (2H, CH_{2epox}, *J* = 5.5 Hz), 4.10q (4H, $2C\underline{H}_2CO$, *J* = 7.0 Hz**)**. Found, %: C 58.43; H 7.87. $C_{14}H_{22}O_6$. Calculated, %: C 58.74; H 7.69.

1,1-Dicarboethoxy-5,6-epoxy-2-methyl-5-(cyclohexen-3-yl)hexan-3-one (6). Yield – 81.9%, b.p. 180–181°C (1mm merc.c.), n_D^{20} 1.4870, d_4^{20} 1.1109. IR spectrum, ν, cm^{-1}: 1708(C=O), 1738 ($C=O_{ether}$), 865, 1250 (epox), 1625 ($C=C_{cyclohex}$). NMR^1H spectrum, δ, ppm. (*J*, Hz): 1.20t (6H, $2C\underline{H}_3CH_2CO$, *J* = 6.9 Hz), 1.45s (3H, CH_{3epox}), 1.52–2.48m (7H, $CH_2CHCH_2CH_{2cyclohex}$), 2.52–2.67m (4H, CH_2CHCH), 2.78d, 2.92d (2H, CH_{2epox}, *J* = 5.5 Hz), 5.44–5.60m (2H, HC=CH), 4.15q (4H, $2CH_2CO$, *J* = 6.9 Hz**)**. (Found, %: C 64.89; H 7.61. $C_{19}H_{28}O_6$. Calculated, %: C 64.77; H 7.95.

General methodology of synthesis of epoxy alcohols of the cyclohexanone series. 0.06 mol of DC was added to a solution of 0.05 mol of UEKA (UEKC) in 25 ml of ethyl alcohol at 5–10 °C and with intensive stirring, 5 mol of 10% alcohol solution of NaOH was added for 30 min., maintaining the same temperature of the reaction mixture. After the

addition, the temperature of the reaction mixture was raised to 40 °C and stirred for another 8 h. After cooling the reaction mixture to 0 °C, the precipitated crystals were filtered, washed with 10% acetic acid and recrystallized from ethanol with the isolation of compounds **7**–**10.**

2-Acetyl-5-(2-methyloxiran-2-yl)-5-hydroxy-3-methyl-1-cyclohexanone (7). Yield – 66.6%, b.p. 54–55 °C. IR spectrum, ν, cm^{-1}: 1722 (C=O), 1713 ($C=O_{acetyl}$), 830, 1240 (epox), 3450 (OH). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.95 s (3H, CH_3CO-), 1.19 d, 1.27 d (3H, CH_{3cycl}, *J* = 5.8 Hz), 1.46 s (3H, CH_{3epox}), 2.29 s (2H, CH_2), 2.40–2.64 m (4H, CH_2CHCH), 2.80 d, 2.90 d (2H, CH_{2epox}, *J* = 5.3 Hz), 3.82 s (1H, OH). NMR ^{13}C spectrum, δ_C, ppm.: 22.4 (CH_3), 24.8 (CH_3), 26.2 ($CO\underline{C}H_3$), 27.3 (CH_2), 30.1 (CH), 31.4 (CH_2), 54.3 ($\underline{C}HCO$), 68.7 (CH_2O), 98.8 (C-O), 70.3 (C-OH), 198.3 (C=O), 207.6 ($\underline{C}OCH_3$). Found, %: C 63.49; H 8.08. $C_{12}H_{18}O_4$. Calculated, %: C 63.72; H 7.96.

2-Acetyl-5-(2-methyloxiran-2-yl)-5-hydroxy-3-(cyclohexen-3-yl)-1-cyclohexanone (8). Yield – 62.5%, b.p. 105–106 °C. IR spectrum, ν, cm^{-1}: 1720 (C=O), 1708 ($C=O_{acetyl}$), 850, 1250 (epox), 3475 (OH), 1615 ($C=C_{cyclohex}$). NMR ^1H spectrum, δ, ppm (*J*, Hz): 1.34 s (3H, CH_{3epox}), 1.50–2.06 m (7H, $CH_2CH_2CHCH_{2cyclohex}$), 2.15c (3H, CH_3CO), 2.26–2.63 m (5H, CH_2CH, CH_2), 2.88 d, 2.95 d (1H, CH_{2epox}, *J* = 5.6 Hz), 3.73 s (1H, OH), 5.40–5.60 m (2H, CH=CH). NMR ^{13}C spectrum, δ_C, ppm.: 23.9 (CH_3), 26.0 (CH_2), 26.9 (CH_2), 27.7 ($CO\underline{C}H_3$), 28.1 (CH), 29.3(CH), 30.7 (CH_2), 32.4 (CH_2), 55.0 ($\underline{C}H_3CO$), 65.7 (CH_2O), 99.1 (C-O), 69.8 (C-OH), 129.4 (CH=), 130.1 (CH=), 199.1 (C=O), 205.6 ($\underline{C}OCH_3$). Found, %: C 70.05; H 8.04. $C_{17}H_{24}O_4$. Calculated, %: C 69.86; H 8.22.

5-(2-Methyloxiran-2-yl)-5-hydroxy-3-methyl-2-ethoxycarbonyl-1-cyclohexanone (9). Yield – 58.7%, b.p. 66–67 °C. IR spectrum, ν, cm^{-1}: 1714 (C=O), 1750 ($C=O_{ether}$), 840, 1248 (epox), 3430 (OH). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.18 d, 1.25 d (3H, *J* = 5.7 Hz, CH_{3cycl}), 1.30 t (3H, $C\underline{H}_3CH_2CO$, *J* = 6.8 Hz), 1.48 s (3H, CH_{3epox}), 2.14–2.62 m (6H, CH_2CHCH, CH_2), 2.90 d, 2.97 d (1H, CH_{2epox}, *J* = 5.6 Hz), 3.86 s (1H, OH), 4.23 q (2H, $2C\underline{H}_2CO$, *J* = 6.8 Hz). NMR^{13}C spectrum, δ_C, ppm.: 13.8 (CH_3), 21.9 (CH_3), 25.8 (CH_2), 29.2 (CH), 30.8 (CH_2), 53.7 ($\underline{C}HCO$), 61.8 (OCH_2), 69.1 (CH_2O), 97.9 (C-O), 71.7 (C-OH), 174.8 (COO), 197.6 (C=O). Found, %: C 60.71; H 7.98. $C_{13}H_{20}O_5$. Calculated, %: C 60.94; H 7.81.

5-(2-Methyloxiran-2-yl)-5-hydroxy-3-(cyclohexen-3-yl)-2-ethoxycarbonyl-1- cyclohexanone (10). Yield – 53.4%, b.p. 126–128 °C. IR-spectrum, ν, cm^{-1}: 1720 (C=O), 1753 ($C=O_{ether}$), 830, 1240, 915 (epox), 3560 (OH), 1610 (C=C in cycle). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.21 t (3H, $C\underline{H}_3CH_2CO$, *J* = 6.9 Hz), 1.33 s (3H, CH_{3epox}), 1.40–2.35 m (7H, $CH_2CHCH_2CH_{2cyclohex}$), 2.44–2.76 m (6H, CH_2CHCH, CH_2), 2.98 d, 3.06 d (2H, CH_{2epox}, *J* = 5.6 Hz), 3.92 s (1H, OH), 4.33 q (2H, $C\underline{H}_2CO$, *J* = 6.9 Hz), 5.56–5.68 m (2H, CH=CH). NMR ^{13}C spectrum, δ_C, ppm.: 14.4 (CH_3), 24.9 (CH_3), 25.8 (CH_2), 26.2 (CH_2), 28.4 (CH_2), 29.1 (CH), 30.0 (CH), 31.6 (CH_2), 32.4 (CH_2), 54.4 ($\underline{C}HCO$), 60.7 (OCH_2), 68.4 (CH_2O), 69.8 (C-OH), 99.1 (C-O), 132.4 (CH=), 133.1 (CH=), 173.6 (COO), 200.4 (C=O). Found, %: C 67.38; H 7.94. $C_{18}H_{26}O_5$. Calculated, %: C 67.08; H 8.07.

5-(2-methyl-1-bromo-2-hydroxyethyl)-5-hydroxy-3-methyl-2-acetyl-1-cyclohexanone (11). 25 ml of 47% HBr was added to a solution of 0.05 mol of compound **7** in 40 ml of acetic acid at 20–25 °C; after 30 min., the reaction mixture was poured on ice. The isolated product **11** was filtered, washed with water and recrystallized from ethanol. Yield – 54%, b.p. 107 °C. IR spectrum, ν, cm^{-1}: 1718 (C=O), 1704($C=O_{acetyl}$), 3490 (OH), 660 (C-Br). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.14 d, 1.20 d (3H, $CHC\underline{H}_3$, *J* = 6.3 Hz), 1.45 s (3H, CCH_3), 1.98 s (3H, CH_3CO-), 2.18–2.32 m (6H, CH_2CHCH, $CH_{2cyclohex}$), 3.41–3.60 m (2H, CH_2Br), 2.56 s, 3.45 s (2H, 2OH). NMR ^{13}C spectrum, δ_C, ppm.: 24.2 (CH_3), 25.3 (CH_3), 26.2 (CH_2), 27.6 (CH), 28.1 ($CO\underline{C}H_3$), 31.7 (CH_2), 35.6 (CH_2Br), 56.3 ($\underline{C}HCO$), 69.9 (C-OH), 199.6 (C=O), 206.9 ($\underline{C}OCH_3$). Found, %: C 46.99; H 6.02. $C_{12}H_{19}BrO_4$. Calculated, %: C 46.91; H 6.19.

5-(2-methyl-1-piperidino-2-hydroxyethyl)-5-hydroxy-3-methyl-2-acetyl-1-cyclohexanone (12). 0.06 mol of piperidine was added to a solution of 0.05 mol of oxirane **7** in 50 ml of absolute isopropyl alcohol at 5–10 °C. The reaction mixture was heated to 70 °C and stirred for 5 h. The solvent was distilled out, and the residue was crystallized from mixture of hexane and ether (5:1). Yield – 89%, b.p. 71 °C. IR spectrum, ν, cm^{-1}: 1722 (C=O), 1710 ($C=O_{acetyl}$), 3480 (OH), 1200–1220 (C-N). NMR ^1H spectrum, δ, ppm. (*J*, Hz): 1.15 d, 1.22 d (3H, $CHC\underline{H}_3$, *J* = 6.4 Hz), 1,43 s (3H, CH_3), 1.51–1.74 m (6H, $3CH_{2piper}$), 2.02 s (3H, CH_3CO-), 2.18-2.32 m (6H, CH_2CHCH, $CH_{2cyclohex}$), 2.48 s (H, OH), 2.74–2.98 m [6H, $N(CH_2)_3$], 3.60 s (1H, OH). NMR^{13}C spectrum, δ_C, ppm.: 23.2 (CH_3), 24.1 (CH_3), 25.3 (CH_2), 26.4 (CH), 28.6 ($CO\underline{C}H_3$), 29.4 (CH_2), 30.2 (CH_2), 51.2 (CH_2N), 55.1 ($\underline{C}HCO$), 57.1 (CH_2N), 66.3 (C-OH), 70.2 (C-OH), 197.8 (C=O), 209.0 ($\underline{C}OCH_3$). Found, %: C 65.27; H 9.55. $C_{17}H_{29}NO_4$. Calculated, %: C 65.59; H 9.32.

2-Acetyl-5-(2-methyloxiran-2-yl)-5-hydroxy-3-(3,4-dibromocyclohexane)-1-cyclohexanone (13). The solution of 0.06 mol of bromine in 10 ml of CCl_4 was added dropwise to the solution of 0.05 mol of compound **8** in 50 ml of CCl_4 at -10÷-5 °C with stirring. The reaction mass was stirred for another 1.5–2 h at 10–15 °C. On completion of the reaction (decoloration), the solvent was removed, the reaction mixture was cooled to -5 °C, the isolated product was filtered, washed with water and crystallized from ethanol. Yield – 56%, b.p. 145 °C. IR spectrum, ν, cm^{-1}: 1723 (C=O), 1710 ($C=O_{acetyl}$), 855, 1263, 930 (epox), 3485 (OH), 670 (C-Br). NMR ^1H spectrum, δ, ppm. (J, Hz): 1.38 s (3H, CH_{3epox}), 1.49–2.04 m (7H, $CH_2CH_2CHCH_2$), 2.10 s (3H, CH_3CO-), 2.16-2.30 m (6H, CH_2CHCH, CH_2), 2.72 d, 2.86 d (1H, CH_{2epox}, J = 5.6 Hz), 3.50 s (1H, OH), 3.91-4.60 m (2H, 2CHBr). NMR ^{13}C, δ_C, ppm.: 23.4 (CH_3), 25.8 (CH_2), 26.1 (CH), 26.9 (CH), 27.8 ($CO\underline{C}H_3$), 28.8 (CH_2), 29.6 (CH_2), 30.2 (CH_2), 31.1 (CH_2), 32.1 (CHBr), 33.0 (CHBr), 54.2 ($\underline{C}HCO$), 67.9 (CH_2O), 69.2 (C-OH), 98.6 (C-O), 198.1 (C=O), 208.9 ($\underline{C}OCH_3$). Found, %: C 45.02; H 5.26. $C_{17}H_{24}Br_2O_4$. Calculated, %: C 45.13; H 5.31.

Conclusions

1. We have established that α,β-unsaturated epoxyketones of the aliphatic and alicyclic series easily undergo the Michael addition reaction with β-dicarbonyl compoundscontaining reactive methylene group in its composition. As a result, the functionally substituted cyclohexanones with epoxide fragments are formed.

2. The availability of the synthesized functionally substituted cyclohexanones of carbonyl, hydroxyl and also ester groups in the molecule gives wide possibilities to carry out the reaction with nucleophilic and electrophilic reagents, as a result of which, the prospects are opened for the synthesis of a wide range of compounds, including biologically active ones, which indicates the actuality of our investigations not only in the theoretical, but also in the applied aspect.

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