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Investigation of Reaction of Dimedone and Ethyl Acetoacetate with 1,2-Epoxy-3-chloropropane

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Abstract—Reactions of dimedone and ethyl acetoacetate with 1,2-epoxy-3-chloropropane in the presence of K_2CO_3 in DMSO medium were investigated. The reaction of 1,2-epoxy-3-chloropropane with ethyl acetoacetate afforded ethyl 5-hydroxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate, with dimedone, 3-(1',2'-epoxypropyloxy)-5,5-dimethyl-cyclohex-2-en-1-one.

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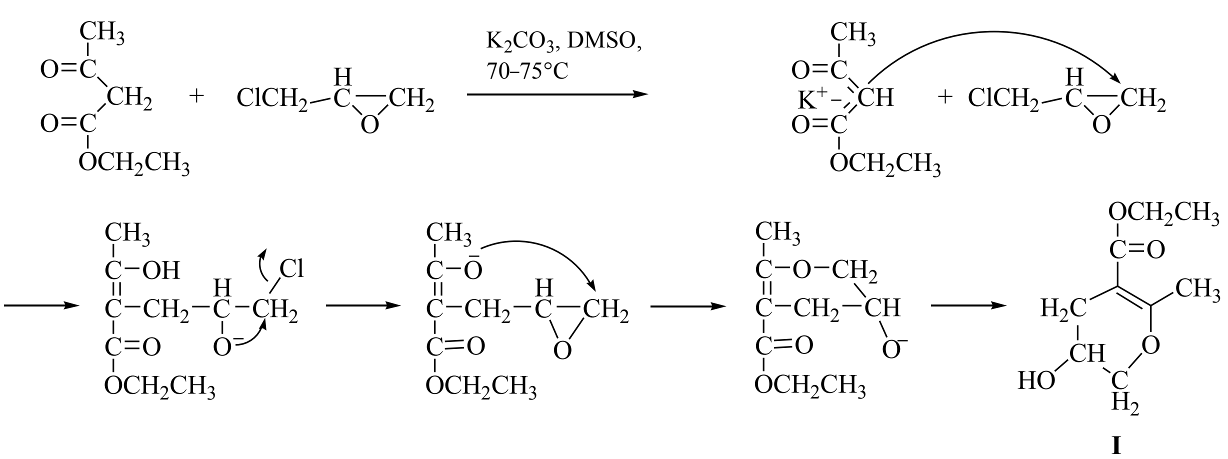
In reactions of some haloderivatives with β-dicarbonyl compounds and their derivatives in the presence of K_2CO_3 in different phases may form products of C- and O-alkylation [1–7]. We showed that in the reaction of ethyl acetoacetate with 1,2-epoxy-3-chloropropane formed ethyl 5-hydroxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate (**I**) (Scheme 1).

The structure of compound I was established from the data of elemental analysis, the IR, ^{1}H and ^{13}C NMR spectroscopy, in particular, with the use of DEPT, COSY, and HMQC spectra.

The DEPT-135 spectrum showed the presence in the pyran **I** molecule of two methyl, three methylene, and one methine group. In the COSY ^{1}H–^{1}H spectrum the presence of cross-peak 1.18 (CH_3)/4.05 ppm (OCH_2) confirms the spin-spin coupling between the protons of the ethyl group. The cross-peaks at 2.56/2.77 and 2.56, 2.77/4.61 ppm prove the geminal coupling between the protons of the CH_2 contiguous to the double bond, and also the coupling between the protons of this CH_2 and CH groups. In the ^{1}H NMR spectrum the signal of the hydroxy proton appeared as a triplet in agreement with the COSY spectrum where a cross-peak was present between the protons of groups OCH_2 (3.46 ppm) and OH (4.89 ppm). The HMQC spectrum is characterized by the lack of the corresponding carbon atom proving the

Scheme 1.



I

assignment of this signal to the hydroxy group. Besides the spectrum contained cross-peaks between the protons OCH_2 (3.46 ppm) and CH (4.61 ppm).

The IR spectrum of the synthesized compound **I** is characterized by the strong absorption bands of the stretching vibrations of groups OH (3420 cm^{-1}) and C=O (1685 cm^{-1}) of the ester moiety.

The presence in the molecule of the hydroxy group was also confirmed in a chemical way. To this end ethyl 5-hydroxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate was reacted with acetyl chloride to obtain ethyl 5-acetyloxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate (**II**) (Scheme 2).

The lack in the ^1H NMR spectrum of the OH group signal at 4.89 ppm, the singlet at 2.21 ppm belonging to CH_3 group and also the appearance in the ^{13}C NMR spectrum of the signal from the carbonyl carbon atom at 169.03 ppm confirm the structure **II**.

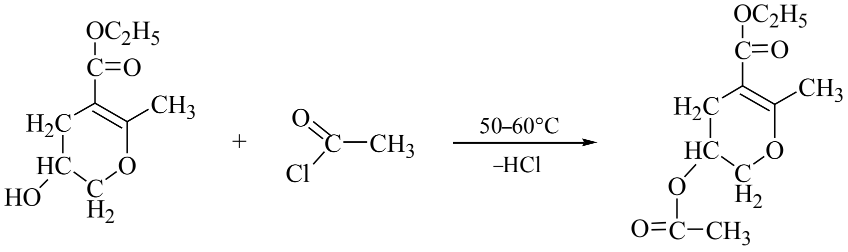
The product of the reaction of the enol form of dimedone with 1,2-epoxy-3-chloropropane is 3-(1',2'-epoxypropyloxy)-5,5-dimethylcyclohex-2-en-1-one (**III**) (Scheme 3).

The ^1H NMR spectrum of compound **III** contains singlets at 0.92, 2.05, 2.18, 5.18 ppm characteristic of methyl, methylene, and =CH groups of dimedone respectively; the multiplets observed at 2.57–2.73 and 3.16 ppm are assigned to CH_2 and CH groups of the epoxide respectively, and the doublets at 3.56 and 4.01 ppm, belong to the protons of OCH_2 group. The structure of compound **III** was also confirmed by IR and ^{13}C NMR spectra (see EXPERIMENTAL).

The reaction of compound **III** with *o*-toluidine gave the corresponding aminoalcohol, 1-(N-2'-methylphenylamino-)-3-O-(4',4'-dimethylcyclohex-1-en-6-on-2-yl) propanol (**IV**) (Scheme 4).

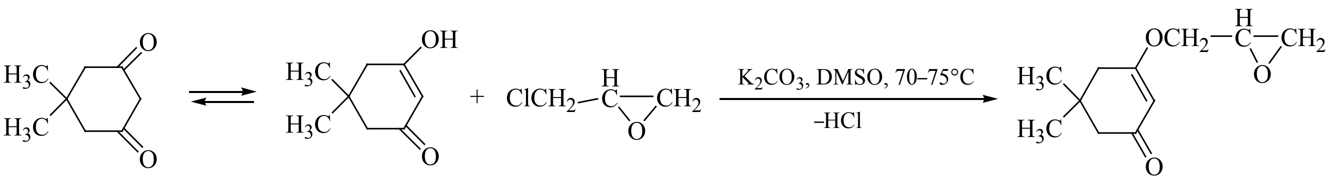
In the ^1H NMR spectrum of compound **IV** the proton signals of the CH and CH_2 groups are shifted downfield compared to these groups in the epoxy ring of compound **III** (from 3.16 to 4.79 ppm and from 2.57–2.73 to 3.18 ppm respectively) proving the involvement in the reaction with the nucleophile of the oxirane fragment. In

Scheme 2.



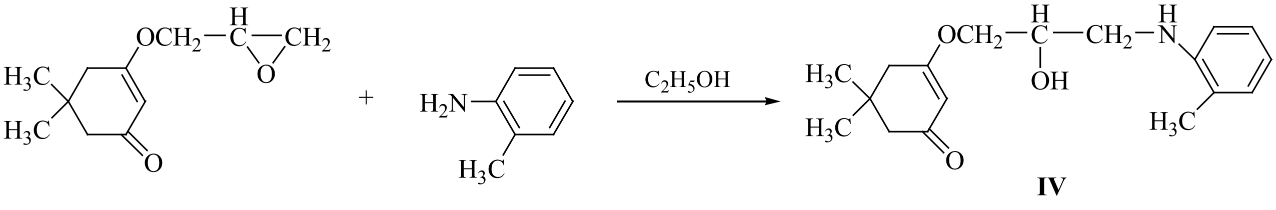
II

Scheme 3.



III

Scheme 4.



IV

the ^{1}H NMR spectrum of the reaction product alongside the characteristic signals of the protons of the aryl fragment and dimedone the singlets are present at 3.42 (OH), 3.81 (NH), and a doublet at 3.99 ppm (OCH_2).

EXPERIMENTAL

IR spectra were registered on a spectrophotometer Varian 3600 FT-IR from liquid films, ^{1}H and ^{13}C NMR spectra were recorded on a spectrometer Bruker Avance-300 at operating frequencies 300 and 75 MHz. Elemental analyses were performed on a CHN analyzer Hewlett Packard 185. The purity of compounds was proved by TLC on Silufol UV-254 plates.

Ethyl 5-hydroxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate (I). To 55 ml of DMSO was added 35 g of K_2CO_3, and the mixture was stirred for 20 min. Then to the reaction mixture 39.06 g (0.30 mol) of ethyl acetoacetate was added, and the stirring was continued for 30 min. The temperature in this interval increased to 35°C. Then 27.75 g (0.30 mol) of 1,2-epoxy-3-chloropropane was added, and the reaction mixture was stirred for 1 h at 20°C. The mixture heated to 70–75°C and was stirred at this temperature for 25 h. Then the mixture was diluted with distilled water and extracted with ether. The extract obtained was dried with Na_2SO_4, ether was distilled off, the residue was distilled in a vacuum. Yield 29 g (52%), bp 144°C (1 mm Hg), n_D^{20} 1.4930, R_f 0.18 (eluent heptane–2-propanol, 3:2). IR spectrum, ν, cm^{-1}: 3420, 1685. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.18 t (3H, CH_3, ^{3}J 6.89 Hz), 2.09 s (3H, CH_3), 2.56 and 2.77 m (2H, CH_2), 3.46 m (2H, OCH_2), 4.05 q (2H, OCH_2, ^{3}J 6.89 Hz), 4.61 m (1H, CH), 4.89 t (1H, OH, ^{3}J 5.52 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 14.96 ($\underline{CH_3}CH_2$), 14.98 (CH_3), 32.25 (CH_2), 59.95 ($O\underline{CH_2}CH_3$), 64.77 (OCH_2), 83.89 (OCH), 102.93 (C^3), 165.91 (C^2), 167.93 (COO). Found, %: C 58.27; H 7.35. $C_9H_{14}O_4$. Calculated, %: C 58.05; H 7.58.

Ethyl 5-acetoxy-2-methyl-5,6-dihydro-4*H*-pyran-3-carboxylate (II). A mixture of 3 g (16 mmol) of compound **I** and 2.5 g (32 mol) of acetyl chloride was stirred for 20 min at 50–60°C, then it was left standing for 24 h and afterwards it was distilled. Yield 2.4 g (65%), bp 59°C (1 mm Hg), n_D^{20} 1.4712, R_f 0.29 (eluent heptane–2-propanol, 3 : 2). ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.34 t (3H, CH_3), 2.13 s (3H, CH_3), 2.21 s (3H, CH_3), 2.65 and 2.99 m (2H, CH_2), 4.15 m (4H, $2CH_2$), 4.82 m (1H, CH). ^{13}C NMR spectrum (CCl_4), δ, ppm: 13.98 ($\underline{CH_3}CH_2$), 14.55 (CH_3), 20.09 ($\underline{CH_3}COO$), 32.25 (CH_2), 59.01 ($O\underline{CH_2}CH_3$), 65.54 (OCH_2), 78.98 (CH), 102.05 (C^3), 164.65 (C^2), 167.20 (COO), 169.03 (COO). Found, %: C 57.63; H 6.84. $C_{11}H_{16}O_5$. Calculated, %: C 57.89; H 7.07.

5,5-Dimethyl-3-(2-oxiranylmethoxy)-2-cyclohexen-1-one (III). To 60 ml of DMSO was added 35 g of K_2CO_3, and the mixture was stirred for 15 min. To the mixture 42.06 g (0.30 mol) of dimedone was added, and the stirring was continued for 30 min, then 27.75 g (0.30 mol) of 1,2-epoxy-3-chloropropane was added, and the stirring at 50–60°C was performed for 20 h. The reaction mixture was diluted with distilled water and extracted with ether. The extract obtained was dried with Na_2SO_4, ether was distilled off, the residue was distilled in a vacuum. Yield 22 g (37%), bp 143°C (1 mm Hg), n_D^{20} 1.5050, R_f 0.57 (eluent heptane–2-propanol, 3:2). IR spectrum, ν, cm^{-1}: 1710, 1230, 1015. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 s (6H, $2CH_3$), 2.05 s (2H, CH_2), 2.18 s (2H, CH_2), 2.57 and 2.73 m (2H, CH_2), 3.16 m (1H, CH), 3.56 d and 4.01 d (2H, OCH_2), 5.18 s (1H, =CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 27.81 ($2CH_3$), 33.12 (C^5), 41.91 (CH_2), 43.89 (CH_2), 48.94 (CHO in the ring), 51.05 (CH_2O in the ring), 69.21 (CH_2O), 102.79 (=CH), 175.74 (C^3), 199.96 (CO). Found, %: C 67.12; H 8.47. $_{11}H_{16}O_3$. Calculated, %: C 67.32; H 8.22.

3-[2-Hydroxy-3-(2-toluidino)propoxy]-5,5-dimethyl-2-cyclohexen-1-one (IV). To a mixture of 2 g (0.01 mol) of compound **III** and 2.5 g (0.023 mol) of *o*-toluidine was poured 15 ml of C_2H_5OH, and the mixture was stirred for 15 h at 65–70°C. Then ethanol was distilled off from the reaction mixture. The liquid residue crystallized at standing. The crystals obtained were washed with CCl_4. Yield 1.95 g (63%), mp 145°C, R_f 0.38 (eluent heptane–2-propanol, 5:1). IR spectrum, ν, cm^{-1}: 3315, 3440, 1700. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.0 s (6H, $2CH_3$), 2.19 s (4H, $2CH_2$), 2.28 s (3H, CH_3–C_{arom}), 3.18 d (2H, CH_2N), 3.42 s (1H, OH), 3.81 s (1H, NH), 3.99 d (2H, CH_2O), 4.79 m (1H, HCO), 5.32 s (1H, =CH), 6.48–6.99 ($4H_{arom}$). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 18.72 (CH_3), 28.41 ($2CH_3$), 31.87 (C^5), 42.85 (CH_2), 46.78 (CH_2), 51.93 (CH_2N), 67.21 (CHO), 71.73 (CH_2O), 102.11 (=CH), 109.98 (CH_{arom}), 117.12 (CH_{arom}), 122.84 (C_{arom}), 127.14 (CH_{arom}), 130.04 (CH_{arom}), 147.21 (C_{arom}), 177.18 (C^3), 198.81 (CO). Found, %: C 71.47; H 8.07; N 4.83. $C_{18}H_{25}NO_3$. Calculated, %: C 71.26; H 8.30; N 4.62.

REFERENCES

1. Nagiev, F.N., Magerramov, A.M., Mamedov, I.G., Kurbanov, A.V., and Allakhverdiev, M.A., *Zhurnal Khimicheskikh Problem*, 2006, vol. 1, p. 99.
2. Muthusamy, S. and Gnanaprakasam, B., *Tetrahedron*, 2005, vol. 46, p. 635.
3. Marchetti, P., *Tetrahedron*, 2003, vol. 46, p. 4121.
4. Zhu, J., You, L., Zhao, S.X., White, B., Chenb, J.G., and Skonezny, P.M., *Tetrahedron*, 2002, vol. 43, p. 7585.
5. Song, Z., Reiner, J., and Zhao, K., *Tetrahedron*, 2004, vol. 45, p. 3953.
6. Trabelsi, H., Szonyi, F., and Geribaldi, S., *J. Fluor. Chem.*, 2001, vol. 107, p. 177.
7. Meciarova, M., Kiripolsky, M., and Toma, S., *Ultrasonics Sono-Chemistry*, 2005, vol. 12, p. 401.