REACTIONS INVOLVING ADDITIONS TO THE DOUBLE BOND IN 4,5-EPOXY-2-HEXENOIC ACID ESTERS

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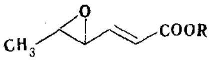
4,5-Epoxy-2-hexenoic acid esters add alcohols (in the presence of the alkoxide) and diazomethane to the double bond with retention of the oxirane ring; alkoxylation products and Δ^2-pyrazolines are formed. The alkoxide anion and diazomethane add to the positively polarized β-carbon atom of the conjugated ether. The structures of the synthesized compounds were proved by their IR, UV, and PMR spectra.

Derivatives of unsaturated aliphatic acids that contain an epoxide ring have recently attracted the attention of researchers since they may be intermediates for the synthesis of diverse polyfunctional compounds and may have the activity of juvenile hormones [1-3].

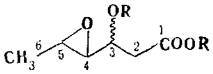
We have previously shown that opening of the epoxide ring in 4,5-epoxy-2-hexenoic acid esters by alcohols in the presence of acid catalysts [4] is the primary process and leads to the formation of 4-alkoxy-5-hydroxy-2-hexenoic acid esters.

It seemed of interest to us to find processes in which the multiple bond would undergo attack without involvement of the epoxide ring. In the present research we studied the reaction of 4,5-epoxy-2-hexenoic acid esters with alcohols in the presence of alkoxides and the 1,3-dipolar addition of diazomethane, which, as will be seen below, take place at the double bond without involvement of the other functional groups.

We found that alkoxylation products III and IV are formed in the reaction of esters I and II with methanol and ethanol in the presence of the corresponding alkoxide:



I, II



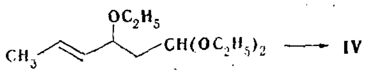
III, IV

I, III R=CH$_3$; II, IV R=C$_2$H$_5$

The IR spectra of III and IV did not contain absorption bands at 1650 (C=C) and 3450 cm^{-1} (OH) but did contain a band at 1730 cm^{-1} (C=O) and bands at 860 and 1255 cm^{-1}, which are characteristic for the epoxide ring. In the PMR spectrum of methyl 3-methoxy-4,5-epoxyhexanoate (III) the signal of the 5-H proton shows up in the form of a quartet with J_{56} = 5 Hz at 2.76 ppm; the signal of the 4-H proton is a doublet at 2.9 ppm. Each component of the doublet and quartet has further doublet splitting with a lower but identical J_{45} content of 2 Hz. Two signals of a methoxy group at 3.36-3.42 ppm, one signal of an ester methoxy group at 3.67 ppm, and two doublets of nonequivalent methyl groups at 1.25-1.34 ppm are present in the spectrum of III. The multiplet at 2.39-2.65 ppm is related to the 2-H and 3-H protons.

These data show that the addition of a methoxy group proceeds nonstereospecifically and gives a mixture of two diastereomers with different configurations at the C_3 atom.

To obtain additional proof for the structure of IV we realized its alternative synthesis via the scheme



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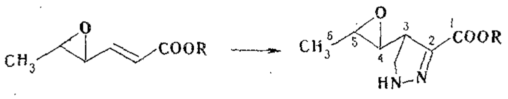
Epoxidation of 1,1,3-triethoxy-4-hexene (V) with permaleic acid, obtained from concentrated hydrogen peroxide and maleic acid in the presence of urea, leads to simultaneous oxidation of the double bond to an epoxide and of the acetal group to an ester group to give IV, the identity of which with the compound that we previously obtained was proved by gas-liquid chromatography (GLC) and the set of spectral data.

The reaction of 4,5-epoxy-2-hexenoic acid esters with diazomethane gives the corresponding pyrazolines. Considering the direction of polarization in the reagents, we assigned 3-carbalkoxy-4-(1,2-epoxypropyl)-Δ^2-pyrazoline structures (VIa-c) to them.



VI a-c

VIa R=CH_3; b R=C_2H_5; c R=C_3H_7

The IR spectra of pyrazolines VIa-c contain bands of stretching vibrations of an NH group (3100-3350 cm^{-1}) and a C=N bond (1520-1560 cm^{-1}) of a heteroring. The shift of the band of a carbonyl group to 1690-1700 cm^{-1} and the UV spectra indicate conjugation of this group with the C=N bond of the pyrazoline ring. The following signals are observed in the PMR spectrum of 3-carbethoxy-4-(1,2-epoxypropyl)-Δ^2-pyrazoline (VIb): 2.6-3.0 (5-H and 4-H, q and d, J_{56} = 5.0, J_{45} = 2.0, J_{34} = 6.3 Hz), 1.08 (3H, t, $OCH_2\mathbf{CH}_3$), 4.1 (2H, q, $O\mathbf{CH}_2CH_3$), and 1.11 ppm (3H, d, $\mathbf{CH}_3\underset{O}{CH}CH$, J_{65} = 5 Hz). The signals of the protons of the pyrazoline ring are overlapped by the signals of the protons of the epoxide ring (at ~3.0 ppm).

Thus the double bond in 4,5-epoxy-2-hexenoic acid esters undergoes normal 1,3 cycloaddition. The reaction with alkoxide ions is also directed to the double bond, and nucleophilic addition to the polarized double bond is observed.

EXPERIMENTAL

The IR spectra of mineral oil suspensions and solutions of the compounds in CCl_4 were recorded with a UR-10 spectrometer. The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of solutions of the compounds in CCl_4 and $CDCl_3$ were obtained with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard. The course of the reactions was monitored and the individuality of the substances was determined by thin-layer chromatography (TLC) on Silufol UV-vis plates and on plates with activity II (Brockmann) aluminum oxide [elution with ether-hexane (2:1)].

Methyl 3-Methoxy-4,5-epoxyhexanoate (III). A 7.1-g (0.05 mole) sample of methyl 4,5-epoxy-2-hexenoate (I) was added dropwise with stirring to a solution of sodium methoxide obtained from 0.15 g (0.006 mole) of sodium in 26 ml of methanol, and the reaction mixture was stirred at 60-70°C for 10-12 h. The alcohol was removed by distillation, water was added, and the mixture was extracted with ether. The solvent was removed, and the residue was distilled in vacuo to give 4.5 g (52%) of III with bp 68-70°C (1 mm) and n_D^{20} 1.4294. PMR spectrum (CCl_4): 1.25-1.34 (3H, dd, CH_3 attached to the oxide ring), 2.39-2.65 (3H, m, $-CHCH_2-$), 2.76 (1H, q, J = 5 Hz, $\underset{O}{\mathbf{CH}-CH}$), 2.90 (1H, d, $\underset{O}{CH-\mathbf{CH}}$), 3.36-3.42 (3H, d, $CHOCH_2$), and 3.67 ppm (3H, s, $COOCH_3$). Found: C 55.5; H 8.2%. $C_8H_{14}O_4$. Calculated: C 55.2; H 8.0%.

Ethyl 3-Ethoxy-4,5-epoxyhexanoate (IV). A) This compound was similarly obtained from 6 g (0.038 mole) of ester II and 0.13 g (0.005 mole) of sodium in 20 ml of ethanol. Workup gave 4.95 g (64%) of IV with bp 70-72°C (1 mm) and n_D^{20} 1.4359. PMR spectrum (CCl_4): 1.0-1.33 (9H, m, $3CH_3$), 2.36-2.53 (2H, m, CH_2), 2.53-3.03 (2H, m, $\underset{O}{CH-CH}$), 3.46 (3H, m, $\mathbf{CH}O\mathbf{CH}_2CH_3$), and 4.0 ppm (2H, m, J = 7 Hz, $COO\mathbf{CH}_2CH_3$).

B) A 2.04-ml sample of 87-90% hydrogen peroxide was added dropwise with stirring to a mixture of 4.32 g (0.02 mole) of 1,1,3-triethoxyhexene (V), 5.88 g (0.06 mole) of maleic anhydride, and 1.2 g (0.02 mole) of urea in 10 ml of absolute ether while maintaining the temperature at no higher than 25°C. The precipitated maleic acid was washed with ether, and the ether extracts were treated with $NaHCO_3$ solution and water and dried to give 1.70 g (42%) of IV with bp 70-75°C (1 mm) and n_D^{20} 1.4338.

TABLE 1. Constants of 3-Carbalkoxy-4-(1,2-epoxypropyl)-Δ^2-pyrazolines (VIa-c)

Compound	R	mp, °C	Found, %			Empirical formula	Calc., %			UV spectrum, λ_{max}, nm (log ε)	Yield, %
			C	H	N		C	H	N		
VIa	CH_3	62—63	53,5	6,5	15,0	$C_8H_{12}N_2O_3$	52,2	6,5	15,2	300 (4,00)	45
VIb	C_2H_5	116—117	54,6	7,2	13,9	$C_9H_{14}N_2O_3$	54,5	7,1	14,1	298 (4,04)	80
VIc	C_3H_7	91—92	56,0	5,8	13,0	$C_{10}H_{16}N_2O_3$	56,6	6,5	13,2	300 (4,04)	48

3-Carbalkoxy-4-(1,2-epoxypropyl)-Δ^2-pyrazolines (VIa-c). A 10-g (0.07 mole) sample of 4,5-epoxy-2-hexenoic acid ester was added with stirring to an ether solution of 0.14 mole of diazomethane obtained from nitrosomethylurea, and the solution was maintained at 0-5°C for 48 h. The precipitated crystals were recrystallized from alcohol. The constants of the corresponding pyrazolines are presented in Table 1.

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POLAROGRAPHY OF FURAN-2-CARBOXYLIC ACID ESTERS

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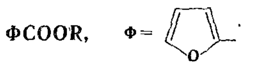
The polarographic reduction of furan-2-carboxylic acid esters in dimethylformamide was studied. The $E_{1/2}$ values correlate with the σ* constants for the substituents in the alcohol part of the 2-furoates.

We have previously shown that the electrophilicity of the carbonyl group of furan-2-carboxylic acid esters in processes involving the formation of an intermolecular hydrogen bond depends on the character of the substituent in both the 5 position of the furan ring and in the alcohol part of the molecule [1, 2]. It is also known that the rate-determining step in nucleophilic substitution reactions of the $B_{Ac}2$ type is attack by the nucleophile at the carbonyl carbon atom [3]. In this connection it is of interest to evaluate the electron-acceptor capacity of the C=O group by polarography.

The results of polarographic reduction in dimethylformamide (DMF) of some furan-2-carboxylic acid esters are presented in this paper.



$R = CH_3, C_2H_5, C_3H_7, C_4H_9, CH_2{-}CH{=}CH_2, CH_2{-}C{\equiv}CH; CH_2{-}C_6H_5, CH_2{-}\Phi$

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