

# Epoxidation of 1-Substituted 3-Cyclohexenes. Theoretical and Experimental Investigation

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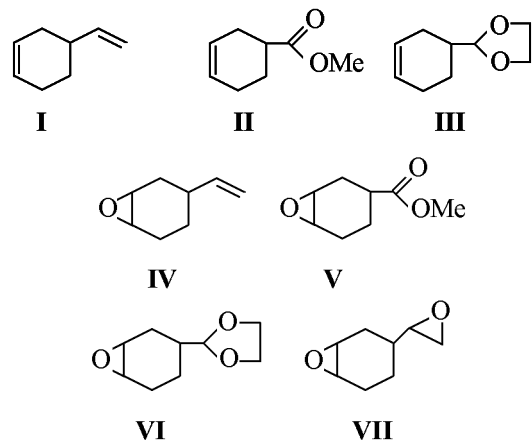
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**Abstract**—Epoxidation of 1-substituted 3-cyclohexenes was investigated. The stereoisomeric composition of the forming epoxides mixture was established by means of GLC and  $^1\text{H}$  NMR spectroscopy. The spectral parameters of the epoxides are considered. The thermodynamical stability of *cis*- and *trans*-epoxides was evaluated by molecular mechanics method. For the epoxidation of 1-substituted 3-cyclohexenes with peracetic acid a quantum-chemical calculation of the potential energy surface by PM3 method was carried out.

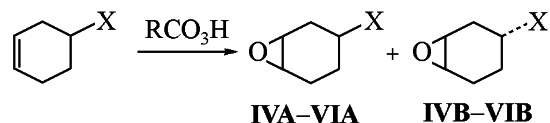
Among the products of butadiene transformations especially interesting are those that contain a cyclohexene moiety: 1-vinyl-3-cyclohexene (**I**), 1-methoxycarbonyl-3-cyclohexene (**II**), and 2-(3-cyclohexenyl)-1,3-dioxolane (**III**) [1]. Vinylcyclohexene is a product forming in a number of industrial processes, and it is easily converted into epoxy derivatives, mono- (**IV**) and diepoxide (**VII**). Preparation of the latter compounds was developed both on laboratory and industrial scale [2]. The aqueous solutions of peracetic acid were successfully used for epoxidation of olefins **I–III** as well as for the kinetic study of these compounds oxidation resulting in epoxy derivatives [3].

Various methods for preparation of epoxide **IV** (by reaction with peroxyacids and their analogs, with hydroperoxides, and with oxygen) were analyzed in a review [4]. Various peracids were applied to the synthesis of epoxide **V**, and for epoxydioxolane **VI** preparation was used only peracetic acid.



Inasmuch as the cycloaliphatic epoxy compounds are widely used in the chemistry of polymer epoxides [6] as binders, the study of oxidation methods and rates, and also of the regio- and stereochemical features of the process presents a fairly urgent problem.

Beside the epoxide samples **IV–VI** obtained with the use of peracetic acid that were in our possession we also prepared epoxide **IV** in 90% yield by treating vinylcyclohexene with peroxyphthalic acid *in situ* nascendi produced from phthalic anhydride and 50% solution of hydrogen peroxide. The analysis of both samples of epoxide **IV** demonstrated the identical stereoisomeric composition.



The composition of stereoisomers mixture of epoxides was studied by GLC with the use of highly efficient capillary columns and by  $^1\text{H}$  NMR spectroscopy. According to GLC data the ratio of *cis*-**IVA–VIA**-isomers to *trans*-**IVB–VIB**-epoxides was respectively 44:56, 38:62, and 45:55.

The published data are well consistent with our results. For instance, the ratio of epoxides **IVA:IVB** produced from vinylcyclohexene was 50:50 at oxidation with hydrogen peroxide in the presence of arene-seleninic acids [7] and at the use of *tert*-butylhydroperoxide with a molybdenum catalyst [8]. The ratio of isomers **VA, VB** after epoxidation of ester **II** with *m*-chloroperoxybenzoic acid was 31:69 according to the preparative GLC [9]. Similar ratio was obtained

**Table 1.** Formation enthalpy and contributions from various strains and interactions into the total steric energy of epoxides **IV–VI** calculated by molecular mechanics method, kJ mol<sup>-1</sup>

Parameter	IVA (e)	IVB (e)	VA (e)	VA (a)	VB (e)	VB (a)	VIA (e)	VIB (e)
Total steric energy	54.74	57.95	59.41	66.86	57.36	60.04	113.01	112.26
Distortion of bond lengths	2.05	2.05	2.34	2.59	2.38	2.43	3.40	3.43
Distortion of bond angles	9.04	9.08	11.38	15.94	11.46	11.55	16.28	16.61
Cross-term (bonds–angles)	0.04	0.00	0.21	0.50	0.21	0.29	0.13	0.13
Torsional strains	32.43	32.30	25.69	29.12	25.44	29.79	66.69	66.90
Van der Waals interactions	17.53	17.57	21.46	21.67	21.67	20.96	29.00	29.29
Dipole-dipole interactions	-3.22	-3.01	-1.67	-3.05	-3.81	-4.98	-5.48	-3.97
Formation enthalpy $H_f$	-46.11	-45.94	-467.27	-459.82	-469.28	-466.68	-428.48	-429.19
Strain energy $E_s$	116.61	116.73	104.56	112.01	102.55	105.19	112.88	114.27

at oxidation with *p*-nitroperoxybenzoic acid [10]. The considerably higher content of the *trans*-isomer in 1-methoxycarbonyl-3,4-epoxycyclohexane (**V**) as compared with epoxide **IV** was ascribed [10] to the steric hindrances arising at the *cis*-attack of peroxy-acid from the side of the methoxycarbonyl group.

The calculations of epoxides **VA**, **VB** by the molecular mechanics method [11] showed that for the *trans*-isomer in one of the conformations the protons of the epoxy ring are spatially near the substituent and apparently should be affected by its magnetically anisotropic influence to different extent. Therefore in the <sup>1</sup>H NMR spectrum of this isomer as also in those of the other *trans*-forms (**IVB**, **VIB**) the protons of the epoxy ring should be magnetically nonequivalent. Actually the prevailing component of the **VA**, **VB** mixture is characterized by considerable nonequivalence of protons attached to the epoxy ring (3.20 and 3.16 ppm) whereas similar protons of the minor isomer appear as a single peak (3.15 ppm). A similar situation is observed with the <sup>1</sup>H NMR spectra of epoxides **IV**, **VI**. The *cis-trans* ratio of isomers determined from the areas of signals belonging to the protons from the epoxy rings amounts for compounds **IV–VI** 45:55, 32:68, and 46:56 respectively. In the assignment of signals in the <sup>1</sup>H NMR spectra to *cis*- and *trans*-isomers were also used the known data on downfield shift of a proton signal from substituent in the spectrum of the *trans*-isomer as compared to that of the *cis*-isomer [12]. The analysis of <sup>1</sup>H NMR spectra is competitive with respect to the other methods of estimation of stereoisomers ratio in products under study.

The signals from substituent protons are present in the <sup>1</sup>H NMR spectra of epoxides. To the 1,3-dioxolane fragment in the spectrum of isomers of epoxides **VI** correspond doublets at 4.56 and 4.65 ppm from

the protons of methine groups linked to two oxygens of the ring. The signals of the other dioxolane protons are present in the region 3.80–3.90 ppm. In the spectrum of epoxide **IV** are observed the proton signals from vinyl group (5.68–5.70 and 4.88–5.02 ppm), and in the spectrum of epoxide **V** are seen the proton signals of the methoxycarbonyl group (3.66, 3.67 ppm).

Absorption bands assigned to vibrations of the C–O bonds of the epoxy ring (1260–1250, 920–914, and 798–792 cm<sup>-1</sup>) are present in the IR spectra of epoxides **IV–VI**. The absorption bands of the carbonyl

**Table 2.** Calculated geometrical parameters (Å, deg) of *syn*-transition states in epoxidation of substituted cyclohexenes **I–III**, and the values of the corresponding activation barriers ( $\Delta H^\ddagger$ )

Parameter	IVA	IVB	VA	VB	VIA	VIB
C <sup>1</sup> –O <sup>1</sup>	1.870	1.886	1.850	1.878	1.870	1.885
C <sup>2</sup> –O <sup>1</sup>	1.890	1.875	1.870	1.863	1.880	1.872
O <sup>1</sup> –O <sup>2</sup>	1.729	1.730	1.732	1.732	1.730	1.730
C <sup>1</sup> –C <sup>2</sup>	1.384	1.385	1.387	1.387	1.385	1.385
C <sup>1</sup> O <sup>1</sup> C <sup>2</sup>	43.10	43.20	43.60	43.50	43.30	43.20
C <sup>1</sup> O <sup>1</sup> O <sup>2</sup>	151.1	151.0	151.5	151.4	151.4	151.3
C <sup>2</sup> O <sup>1</sup> O <sup>2</sup>	152.5	152.5	150.4	152.0	151.0	150.8
C <sup>3</sup> C <sup>2</sup> C <sup>1</sup>	123.1	121.9	122.5	122.0	122.5	122.5
C <sup>3</sup> C <sup>2</sup> O <sup>1</sup>	110.7	110.1	112.3	110.3	112.1	112.2
C <sup>3</sup> C <sup>6</sup> C <sup>1</sup> O <sup>1</sup>	54.80	-85.7	63.40	-85.8	62.80	-94.0
C <sup>4</sup> C <sup>3</sup> C <sup>2</sup> O <sup>1</sup>	-88.1	55.40	-94.0	55.80	-93.0	63.90
$\eta$	36.4	36.1	27.4	35.0	28.9	27.7
$\omega$	38.2	38.1	29.3	37.4	30.4	29.5
$\Delta H^\ddagger$ , kJ mol <sup>-1</sup>	55.27	55.03	62.00	59.87	56.36	56.63
	59.83 <sup>a</sup>	59.45 <sup>a</sup>	61.22 <sup>a</sup>	61.72 <sup>a</sup>	62.59 <sup>a</sup>	60.52 <sup>a</sup>

<sup>a</sup> Values of activation barriers for reactions proceeding through anti-transition states.

group in compound **V** and the cyclic acetal fragment in epoxide **VI** are observed respectively at 1720 and 1200–1140  $\text{cm}^{-1}$  [13].

The calculation results for the structures of *cis*- and *trans*-isomers of epoxides **IV**–**VI** by molecular mechanics method are presented in Table 1.

Conformations of epoxides **VA**, **VB** were investigated distinguished by equatorial (e) or axial (a) orientation of the methoxycarbonyl group with respect to the six-membered ring in semichair conformation. The equatorial conformers were found to be more stable than axial for both configurations studied. The stability of *cis*- or *trans*-form of the epoxide depends on the character of the substituent. In the series under study the more stable form turned out to be the *cis*-one for epoxide **VI** and the *trans*-one for epoxide **V**; therewith a significant contribution into the stability of the isomers make the dipole-dipole interactions. In the epoxy derivative of vinylcyclohexene **IV** both forms possess similar values of formation enthalpy  $H_f$ .

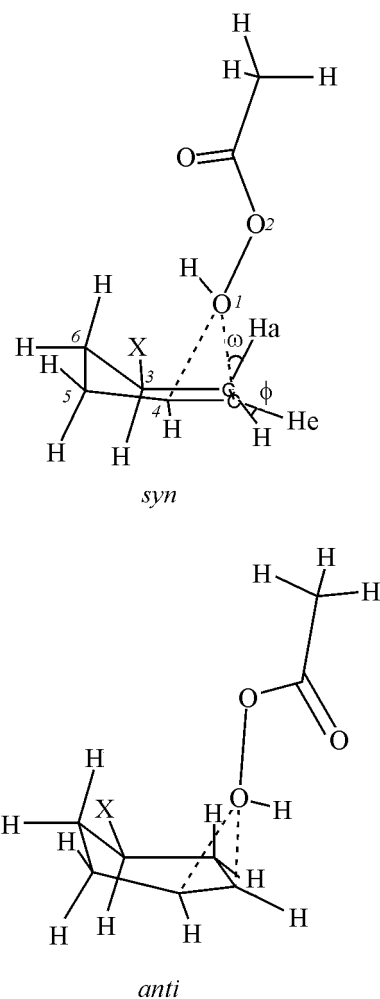
The strain decreases in the epoxide series **IV** > **VI** > **V**. In both stereoisomers of the most strained epoxide **IV** important contributions are made by torsion strain as well as by van der Waals interactions; torsion strains are especially pronounced in the tricyclic structure of epoxide **VI**, and van der Waals interactions are the most significant in molecules of stereoisomeric epoxyesters **V**.

We carried out a more detailed theoretical investigation of stereochemical features of substituted cyclohexenes epoxidation by quantum-chemical calculations of the potential energy surface (PES) at cycloalkenes **I**–**III** epoxidation with peracetic acid. We used PM3 method [14] that among semiempirical procedures best describes the specific features of epoxidation mechanism [15]. The activation barriers were calculated with respect to pre-reaction complexes, for all the stationary points were calculated the vibration frequencies. According to the calculations all the transition states were characterized by one imaginary frequency, and all frequencies of structures corresponding to the minima on PES were positive.

As a result of calculations on PES were localized first order critical points that were transition states in formation of *cis*-(**IVA**–**VIA**) and *trans*-(**IVB**–**VIB**) epoxides respectively. Therewith for each epoxide two transition states are possible that are distinguish-

ed by the spatial orientation of the peracid with respect to the olefin molecule.

The calculated activation enthalpy values and some geometrical parameters of the transition states are given in Table 2. The comparison of the calculated activation barriers for the most favorable reaction routes through syn-transition states evidences that the reactivity of cycloalkenes decreases in the series **I** > **III** > **II** in agreement with kinetic data of Batog *et al.* [3] who determined a significant reduction in the epoxidation rate on introduction to the cyclohexene ring of an electron-withdrawing ester group. As seen from Table 2, for cycloalkenes **I**, **III** the formation of *cis*- and *trans*-epoxides is characterized by close values of the calculated activation barriers that correspond to the isomers ratio 48:53 and 53:47 for compounds **IV** and **VI** respectively. According to



Structure of *syn*- and *anti*-transition states in epoxidation of 1-substituted 3-cyclohexenes.

the calculation the epoxidation of 1-methoxycarbonyl-3-cyclohexene (**II**) should provide *cis*- and *trans*-epoxides **VA** and **VB** at a ratio 30:70 in good agreement with experimentally established *trans*-stereoselectivity of this reaction. The analysis of geometrical parameters of the transition states that we localized evidences that epoxidation stereochemistry of unsaturated ester **II** to a significant measure depends on the structural deformations arising in the course of the reaction. The most informative in this respect are the values of torsional angles  $\eta$  and  $\omega$  (the angles  $\text{HC}^3\text{C}^2\text{H}^e$  and  $\text{O}^1\text{C}^3\text{C}^2\text{H}^a$  for *cis*-transition state and  $\text{HC}^4\text{C}^5\text{H}^e$  and  $\text{O}^1\text{C}^4\text{C}^5\text{H}^a$  for *trans*-transition state respectively, see figure).

To the transition state for *cis*-epoxide **VA** formation correspond smaller values of above-mentioned angles resulting in higher torsional strain due to eclipsed position of the corresponding bonds than in the case of *trans*-isomer.

#### EXPERIMENTAL

IR spectra were recorded on spectrometer Specord 75IR from thin films.  $^1\text{H}$  NMR spectra were registered on spectrometers Bruker CXP and Varian-200 at operating frequency 200 MHz from solutions in  $\text{CDCl}_3$ , internal reference HMDS. The course of reactions was monitored and the purity of products obtained was checked by TLC on Silufol UV-254 plates, development in iodine vapor, and also by GLC on chromatograph Tsvet-5 equipped with a flame-ionization detector, glass capillary column 60 m long, stationary phase SE-30, carrier gas helium, flow rate  $1 \mu\text{l min}^{-1}$ , vaporizer temperature  $280^\circ\text{C}$ . Calculation was carried out by area normalization with the use of Multichrom routine.

**4-Vinyl-1,2-epoxycyclohexane (IV)**. To a mixture of 0.109 mol of vinylcyclohexene (**I**), 0.052 mol of urea, 0.109 mol of 50% solution of hydrogen peroxide in 80 ml of chloroform was added 0.109 mol of phthalic anhydride. The end of reaction was determined by TLC. The reaction mixture was treated with a saturated solution of sodium hydrogen carbonate, the organic layer was separated, and the water layer was extracted with chloroform. The combined organic solutions were dried with magnesium sulfate. On removing the solvent and vacuum-distillation the yield of epoxide **IV** was 12.2 g (90%), bp  $72\text{--}74^\circ\text{C}$  (24 mm Hg),  $n_D^{20}$  1.4695 {bp  $61\text{--}63^\circ\text{C}$  (15 mm Hg),  $n_D^{30}$  1.4660–1.4670 [16]}. IR spectrum,  $\text{cm}^{-1}$ : 3060, 1636, 908, 848, 792.

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