# MNDO CONFORMATIONS OF CHLOROMETHYLOXIRANE AND SOLVENT EFFECT

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Structure of chloromethyloxirane during rotation around the C—C single bond connecting oxirane ring and chloromethyl group has been studied theoretically in twelve solvents. Molecular characteristics and energy of the isolated molecule have been calculated by the semi-empirical MNDO method of molecular orbitals. The MNDO calculation predicts the existence of only two synclinal conformers $G-1$ and $G-2$, the more stable being the less polar $G-2$, $\mu = 2 \cdot 39 \cdot 10^{-30}$ mC. However, the calculation carried out for dilute solutions including the solvation energy by the method of continuum reveals the presence of a third, antiperiplanar conformer $T$, $\mu = 9 \cdot 26 \cdot 10^{-30}$ mC. Populations of the individual conformers depend considerably on solvent, the most stable in ethanol being $G-1$, $\mu = 11 \cdot 06 \cdot 10^{-30}$ mC. The results obtained are compared with experimental data and also discussed from the point of view of the gauche effect.

Chloromethyloxirane (epichlorohydrine), $\overset{\frown}{CH_2-O-CH}-CH_2Cl$ is used in chemical industry as intermediate in spite of being considered carcinogenic and mutagenic compound[1]. Its applications are based on the presence of two reactive groups — epoxide ring and chloromethyl group — which determine its chemical reactivity and conformational properties. Structure of chloromethyloxirane was studied experimentally in gaseous, liquid and solid states[2-8]. Four conformers (Fig. 1) were suggested to be present, their ratio being dependent on the phase and the method used. Although structure and reactivity of oxirane and its derivatives were paid considerable attention by theoretical chemists[9,10], analogous studies about chloromethyloxirane are not available. Within a broader context of studies of cross-linking reactions of polysaccharide chains with chloromethyloxirane[11], we present in this communication results of study of structure and effect of medium on conformational properties of chloromethyloxirane.

## METHOD AND CALCULATIONS

Energy of the individual chloromethyloxirane conformations formed by rotation around the C—C bond (angle $\Phi = \Phi[Cl-C(7)-C(1)]-H(6)]$, $\Phi = 0°$ for the synclinal arrangement) in the interval of 10° (Fig. 1) in isolated state was calculated by the semi-empirical method of the SCF molecular orbitals of the MNDO type[12]. The published parameters[14] for Si, P, S, Cl were

included in the original program[13]. In the calculation of the individual conformations of the isolated molecule we optimized all the bond lengths, bond angles and dihedral angles except for the dihedral angle $\Phi$ which determined the given conformation. The solvent effect was included by the method[15] in which the total Gibbs energy $G_T$ is given by the sum of the Gibbs energy of the isolated molecule ($G_u$) and that of solvation ($G_{solv}$),

$$G_T = G_u + G_{solv} . \tag{1}$$

$G_{solv}$ is composed of three contributions: cavity term, electrostatic interactions and dispersion interactions.

$$G_{solv} = G_{cav} + G_{elst} + G_{disp} . \tag{2}$$

Identification of the MNDO energy of the individual conformations of the isolated chloromethyloxirane molecule with the Gibbs energy presumes implicitly that differences of entropy contributions and zero point vibrational energy contribution between the individual conforma-
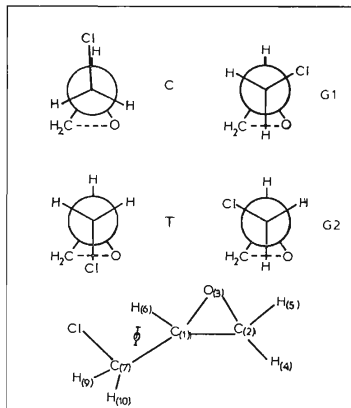


Fig. 1

Newman projection of the four conformations of chloromethyloxirane and denotation of the individual atoms
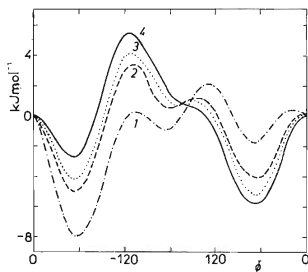
Fig. 2

Changes of total Gibbs energy of chloromethyloxirane during rotation around the C(1)—C(7) bond in the isolated molecule (solid line), in chloroform (dotted line), in acetonitrile (dashed line) and in water (dot and dash line)

tions are insignificant. Calculation of these contributions requires calculation of normal vibrational frequencies of the molecule. Expressions for calculation of the individual contributions to $G_{solv}$ as well as physico-chemical parameters characterizing the individual solvents are given in our previous works[15,16].

## RESULTS AND DISCUSSION

*Rotation around* C—C *bond.* The energy changes during rotation around the C—C bond are represented in Fig. 2. The solid line describing the course of the MNDO energy at various rotational positions of chloromethyl group and oxirane ring ($\Phi$ angle) in the isolated molecule involves two minima in synclinal regions. One minimum belongs to the $G-1$ conformer ($\Phi = -58°$), the other is $G-2$ ($\Phi = 60°$). The $G-2$ conformer has a smaller dipole moment $\mu = 2·39 . 10^{-30}$ mC and is more stable by $2·87$ kJ mol$^{-1}$ than the $G-1$ conformer whose dipole moment is $\mu = 11·06 . 10^{-30}$ mC. The course of the MNDO energy of rotation shows no other $C$ or $T$ conformer. The same conclusion follows from analysis of infrared spectra[4,5] indicating the presence of two conformers with different polarities, the less polar conformer being predominant. Charles and coworkers[5] assigned structures to the $G-1$ and $G-2$ conformers. Equilibrium of these conformers can also contribute to explanation of results of electron diffraction which were interpreted by Igarashi[2] — probably incorrectly — as being due to the presence of the C form only.

The course of energy of rotation in dilute solution, which was calculated by the method of continuum including the solvation energy, has a different form. Influence of solvation energy is manifested in two ways. An important change consists in that (already in dioxane) there appears a further minimum at the energy curve in antiperiplanar region ($T$) whose dipole moment is $\mu = 9·26 . 10^{-30}$ mC. The $T$ conformer is further stabilized with increasing polarity of solvent. Also population of two synclinal conformers depends considerably on solvent polarity: its increasing results in increased proportion of $G-1$ conformer and, on the contrary, decreased proportion of $G-2$. In ethanol and in solvents with still higher values of dielectric constant $\varepsilon$, the $G-1$ conformer is even dominating. The relative Gibbs energies (related to $G-2$) and proportions of the individual conformers are given in Table I along with mean values of dipole moments. Experimental value of dipole moment of chloromethyloxirane in benzene[7] is $7·63 . 10^{-30}$ mC, *i.e.* somewhat higher than the calculated value. The reversed stability order of the conformers in polar solvents (as compared with their order in vapour state) agrees with the NMR and infrared data[3,4] which predict the following stability order in solution: $G-1 > G-2 > T$. However, it must be mentioned that Charles and coworkers[5] found, in contrast to our results, that the $G-1$ conformer predominates in CS$_2$ solution, too.

*Geometry of the conformers.* Table II compares the calculated MNDO geometry parameters of the three chloromethyloxirane conformers with the values suggested

TABLE I

The calculated relative (with respect to $G-2$) Gibbs energies $\Delta G_i$ (in kJ mol$^{-1}$) and molar fractions $x_i$ of chloromethyloxirane conformers at 298.2 K with mean dipole moment (in mC . $10^{30}$) in isolated state and in solution

| Solvent | $\Delta G_i$ | | $x_i$ | | | $\langle \mu \rangle$ |
|---|---|---|---|---|---|---|
| | $G-1$ | $T$ | $G-1$ | $T$ | $G-2$ | |
| Isolated molecule | 2.87 | — | 23.92 | — | 76.08 | 5.79 |
| 1,4-Dioxane | 1.98 | 6.41 | 31.04 | 4.95 | 68.96 | 6.49 |
| Benzene | 2.33 | — | 28.10 | — | 71.90 | 6.19 |
| Chloroform | 0.85 | 5.65 | 39.17 | 5.66 | 55.18 | 7.49 |
| Tert-Butylamine | 1.83 | 6.30 | 30.71 | 5.07 | 64.22 | 6.76 |
| Tetrahydrofuran | 0.96 | 5.73 | 38.19 | 5.58 | 56.23 | 7.39 |
| Octanol | 1.79 | 6.31 | 31.06 | 5.02 | 63.92 | 6.79 |
| Isobutyl alcohol | 0.85 | 5.66 | 39.18 | 5.64 | 55.19. | 7.49 |
| Acetone | 0.34 | 5.30 | 43.82 | 5.93 | 50.25 | 7.86 |
| Ethanol | −0.32 | 4.82 | 49.88 | 6.28 | 43.84 | 8.29 |
| Acetonitrile | −0.81 | 4.52 | 54.41 | 6.36 | 39.25 | 8.62 |
| Dimethyl sulphoxide | −0.19 | 4.95 | 48.73 | 6.14 | 45.14 | 8.23 |
| Water | −6.22 | 0.72 | 87.53 | 5.34 | 7.13 | 10.59 |

TABLE II

Comparison of the calculated and experimental geometry parameters (angles in degrees, lengths in pm), dipole moment (in mC . $10^{30}$) and ionisation potential $I$ (in eV) of stable conformers of chloromethyloxirane

| Parameter | $G-1$ | | $T$ | | $G-2$ | |
|---|---|---|---|---|---|---|
| | MNDO | exp | MNDO | exp | MNDO | exp |
| $C_{(1)}-C_{(2)}$ | 152.28 | 147.1 | 152.11 | 147.1 | 152.12 | 147.1 |
| $C_{(1)}-O_{(3)}$ | 142.06 | 143.6 | 141.96 | 143.5 | 142.19 | 143.6 |
| $C_{(2)}-O_{(3)}$ | 141.31 | 143.6 | 141.52 | 143.6 | 141.46 | 143.6 |
| $C_{(1)}-H_{(6)}$ | 110.2 | 108.2 | 110.3 | 108.2 | 110.2 | 108.2 |
| $C_{(1)}-C_{(7)}$ | 152.0 | 151.3 | 152.0 | 152.2 | 152.16 | 152.2 |
| $C_{(7)}-H$ | 110.7 | 109.2 | 111.1 | 109.2 | 110.8 | 109.2 |
| $C_{(1)}-C_{(7)}-H$ | 113.8 | 109.45 | 110.8 | 109.45 | 111.2 | 109.45 |
| $C_{(1)}-C_{(7)}-Cl$ | 111.7 | 109.45 | 116.0 | 110.94 | 124.7 | 110.97 |
| $C_{(1)}-O_{(3)}-C_{(3)}$ | 65.0 | — | 64.9 | — | 64.9 | — |
| $O_{(3)}-C_{(2)}-C_{(1)}-Cl$ | 80.6 | — | −44.6 | — | 162.8 | — |
| $\Phi$ | −58.1 | −54.02 | 178.0 | 173.22 | 60.3 | 70.21 |
| $C_{(7)}-Cl$ | 180.1 | 176.0 | 180.07 | 179.4 | 180.36 | 176.7 |
| $\mu$ | 11.06 | 11.32 | 9.26 | 7.99 | 2.39 | 2.66 |
| $I$ | 11.731 | — | 11.61 | — | 11.767 | — |

on the basis of microwave spectra[7,8]. When comparing the structures it must not be forgotten that the experimental models were obtained by fitting of three parameters only, *viz.* the C(7)—Cl bond length, the C(1)—C(7)—Cl bond angle and dihedral angle $\Phi$, whereas all geometry parameters were optimized in the MNDO structure calculation. Therefore, agreement between the two sets can be considered relatively good. Larger differences only are in the case of the C(7)—Cl bond length and the C(1)—C(7)—Cl bond angle whose MNDO-calculated values are more conformational-dependent than the experimental data. They reflect to a greater extent the tendency of the molecule to remove unfavourable repulsive interactions between chloromethyl group and oxirane ring.

*Conformational dependence of solvation energy contributions.* Analysis of the conformational dependence of solvation energy and its individual contributions makes it possible to explain the reasons of considerable dependence of conformational behaviour of chloromethyloxirane on medium. For illustration Table III gives values of the individual terms and total solvation energy for four solvents. Among the

TABLE III
Solvation Gibbs energy (in kJ $mol^{-1}$) of the stable conformers of chloromethyloxirane in four solvents at 298·2 K and the corresponding contributions of the individual terms

| Solvent | Energy | $G-1$ | $T$ | $G-2$ |
|---|---|---|---|---|
| $CH_3Cl$ | $G_{elst}$ | − 2·684 | − 1·936 | − 0·299 |
| | $G_{cav}$ | 11·187 | 11·176 | 11·185 |
| | $G_{disp}$ | −16·263 | −16·189 | −16·287 |
| | $G_{solv}$ | − 7·760 | − 6·949 | − 5·400 |
| Pyridine | $G_{elst}$ | − 3·367 | − 2·434 | − 0·385 |
| | $G_{cav}$ | 17·511 | 17·493 | 17·508 |
| | $G_{disp}$ | −22·142 | −22·050 | −22·171 |
| | $G_{solv}$ | − 7·998 | − 6·991 | − 5·052 |
| $CH_3CN$ | $G_{elst}$ | − 4·742 | − 3·474 | − 0·675 |
| | $G_{cav}$ | 37·620 | 37·578 | 37·613 |
| | $G_{disp}$ | −25·599 | −25·478 | −25·639 |
| | $G_{solv}$ | 7·279 | 8·626 | 11·300 |
| $H_2O$ | $G_{elst}$ | −12·446 | − 9·546 | − 2·966 |
| | $G_{cav}$ | 48·519 | 48·462 | 48·509 |
| | $G_{disp}$ | −24·700 | −24·587 | −24·739 |
| | $G_{solv}$ | 11·373 | 14·329 | 20·804 |

contributions to solvation energy the greatest are the dispersion interactions and the cavity term, but they both are practically conformation-independent. The analysis shows that the reason consists in the negligible change of size of the molecule (and, hence, of the cavity radius) during rotation around the C—C bond. The distinct conformational dependence of solvation energy is thus determined by the conformational dependence of electrostatic interactions. Although absolute magnitude of the electrostatic interactions is smaller than that of the previous two terms, their conformational changes are dominant. The large conformational dependence of the electrostatic interactions is due to conformational dependence of dipole moment (Table II). The dipole moment of chloromethyloxirane is mostly determined by mutual orientation of the dipole moment of C(7)—Cl bond and that of the C(1)—O(3)—C(2) segment of oxirane ring. As the other variables involved in the expression for electrostatic interactions are only little changed with conformation of chloromethyloxirane, the course of electrostatic interactions (and, hence, solvation energy) will follow the conformational dependence of the dipole moment whose square appears in numerator of the expression for calculation of $G_{elst}$ (ref[15,16]).

*Gauche effect.* Rotation around the C—C bond connected with electronegative heteroatoms at the both ends exhibits anomalous conformational behaviour: gauche orientations are preferred to trans orientations (gauche effect)[17]. Chloromethyloxirane belongs to these types of molecules, since it carries chlorine atom at one carbon atom of the rotating C—C bond, the other carbon atom being connected with oxygen atom of oxirane ring. According to the gauche effect, synclinal arrangement of C(7)—Cl and C(1)—O(3) bonds (*i.e.* $G-1$ and $T$ conformers) should be the most stable in chloromethyloxirane, though it is also important that one of the carbon atoms is a part of three-membered ring. It is just steric interaction of chlorine atom with oxirane ring which result in destabilization of one of these two conformers, *viz.* the $T$ conformer. Equilibrium of the remaining two conformers ($G-1$ and $G-2$) in isolated state and in non-polar solvents is, however, shifted in opposite direction than that dictated by the gauche effect. The $G-2$ conformer with antiperiplanar arrangements of C(7)—Cl and C(1)—O(3) bonds is more stable. Only in polar solvents the $G-1$ conformer predominates in accordance with the gauche effect. Thus it can be stated that solvent effect acts in this case in the direction of gauche effect and stabilizes synclinal arrangement of the two bonds. So the influence of solvent on conformational stability of chloromethyloxirane conformers is opposite to that observed with one of other conformational effect — anomeric or exoanomeric effect — which expresses unusual stabilization of synclinal arrangement as compared with the antiperiplanar one in C—X—C—Y—C segments (X, Y are atoms with lone electron pairs)[15,18]. The more stable arrangement of *e.g.* acetal segment in non-polar solvent is the synclinal one, this preference being decreased with increased solvent polarity, and in very polar solvents the antiperiplanar arrangements can predominate. Hence the solvent acts against the anomeric and exoanomeric effects.

Again the obtained results stress the inevitability to involve solvent effect in calculations of conformational energies, especially so in molecules carrying heteroatoms with lone electron pairs at the atoms forming the rotation axis.

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