CONFORMATIONAL ANALYSIS OF METHYLENECYCLOHEXANE OXIDE
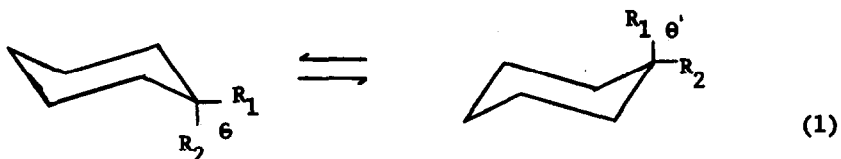
J. J. Uebel

Department of Chemistry, The University of New Hampshire
Durham, New Hampshire

Virtually no experimental evidence has been obtained on the extent to which a conformational equilibrium can be influenced by variations in the external angle θ (See below).

$$(1)$$

However, calculations of the type done by Hendrickson[1] for example, indicate that bond angle readjustments play an important role in conformational equilibria. This communication reports our initial studies on spiro compounds of type I where n=1. These spiranes are unique in that they possess a geminal substitution pattern in which the intergroup angle θ can be varied. This makes it possible to systematically make large changes in the angle θ and study the effects these changes have on conformational equilibria.
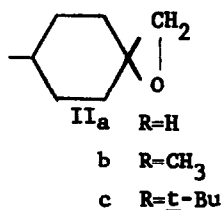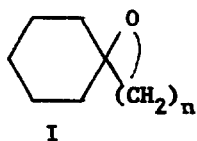

I

IIa   R=H

b   R=CH$_3$

c   R=t-Bu

TABLE I

Rates of Thiosulfate Displacement on Epoxides at 25° [a]

Compound	$k \times 10^2 min^{-1}$	k rel.
cis-II$_c$(cis-t-Bu/CH$_2$)	0.90±0.04	1.00
cis-II$_b$(cis-CH$_3$/CH$_2$)	0.97±0.02	1.08
II$_a$	1.79±0.02	1.99
trans-II$_c$(trans-t-Bu/CH$_2$)	2.47±0.04	2.74
trans-II$_b$(trans-CH$_3$/CH$_2$)	2.62±0.04	2.91

[a] Rates are pseudo first order in 50% (v/v) aqueous methanol at 0.10M sodium thiosulfate.

___

Table I reports the rate data obtained under pseudo first-order conditions for thiosulfate displacement on compounds II$_a$, II$_b$ and II$_c$. The kinetic procedure was essentially that of Fuchs,[2] and was obtained using a Copenhagen Radiometer which automatically titrated the liberated base so as to maintain a constant pH. For the runs reported in Table I, the reference end-point was more acidic by about one pH unit than the initial methanolic thiosulfate solution. The total base liberated during the reaction was, within experimental error, equal to the theoretical maximum. Therefore, under the slightly basic conditions of the kinetic runs, glycol formation is unimportant.

These rate data can be used to estimate -ΔG° for equilibrium (2)--
-ΔG $\left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix} \right)$.

$$\text{(2)}$$
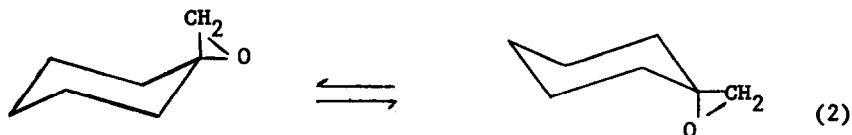
Using the conventional model compounds, cis and trans-4-t-butylmethyl-enecyclohexane oxide, a value of 0.14 kcal/mole is obtained for -ΔG $\left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix} \right)$. Since any model must necessarily be imperfect, a check was sought on this result using another model system. The 4-methyl system was chosen. It was felt that the smaller methyl group would be less likely to cause

added ring distortions which might affect the displacement rates. The methyl group shows a preference for the equatorial position of about 1.7 kcal/mole. This value is not large enough to insure that both cis-II_b(cis-CH_3/CH_2) and trans-II_b(trans-CH_3/CH_2) are conformationally homogeneous. It is, however, large enough to insure that the equatorial methyl conformations of cis and trans-II_b will greatly predominate if $-\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ is small. For example, if $-\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ is about 0.14 kcal/mole, one estimates that $-\Delta G°$ for equilibria (3) and (4) are 1.84 and 1.55 kcal/mole respectively. These free energies correspond to the conformer populations shown below.

(3)

(4)

---
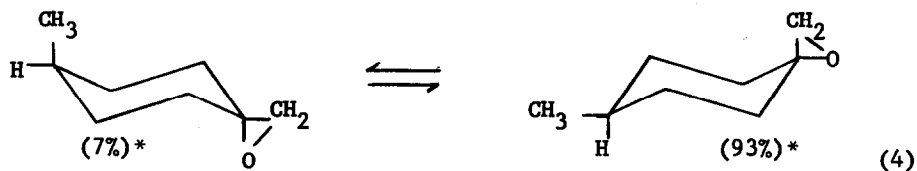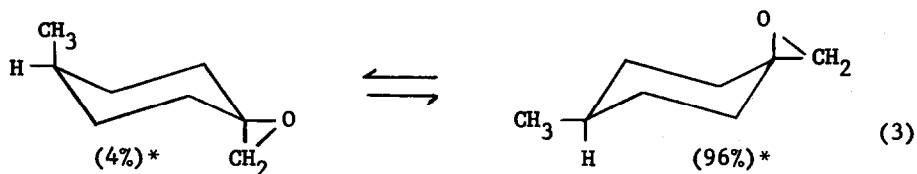
*estimated values--see text.

Therefore, if $-\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ is small, the equatorial methyl conformations for both cis and trans-II_b will dominate, and the rate constants measured for cis-II_b should be close to that for cis-II_c and for trans-II_b to trans-II_c. These expectations are borne out by the data. Furthermore, the rate of cis-II_b is slightly larger than for cis-II_c, as expected. One would also expect that the rate for trans-II_b should be slightly slower than that for trans-II_c; however, this is not the case. The trans-4-methyl oxide (II_b) slightly faster than the trans-4-$\underline{t}$-butyl oxide (II_c). This discrepancy, probably the result of the imperfection in the model, changes the calculated $-\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ slightly. Using the rate constant for the trans-4-methyl oxide (or a slightly larger one to correct for the presence of the axial-methyl conformation) together with that for cis-II_c, alters $\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ by about 0.1 kcal/mole, bringing it to a value of about 0.03 kcal/mole. It appears then that a reasonable estimate for $-\Delta G \left(\begin{smallmatrix} O \\ CH_2 \end{smallmatrix}\right)$ would be in the order of

0.15$\pm$0.1 kcal/mole.

The value for $\Delta G \left(\underset{CH_2}{\overset{O}{|}} \right)$ shows quite clearly that a sharp reduction in the intergroup angle θ can cause an appreciable change in the degree to which a substituent favors an equatorial position. In this case the axial-methylene hydrogens point toward the syn-diaxial hydrogens and, therefore, in the absence of any bending away, this portion of the $O-CH_2$ group should strongly favor an equatorial conformation. This preference would be expected to be significantly greater than 1.7 kcal/mole, the $-\Delta G°$ for methylcyclo-hexane.[3,4] On the other hand, the preference of the oxygen atom of the $O-CH_2$ group for the equatorial position, in the absence of any distortions, should be much smaller. It might reasonably be expected to be similar to those of a halogen atom or an OR group - 0.4-0.7 kcal/mole.[3] Thus, if the intergroup angle θ were "normal", $-\Delta G°$ for equilibrium (3) would be much greater than 1.0 kcal/mole. However, since $-\Delta G°(3)$ is much smaller than 1.0 kcal/mole, it is clear that the reduction of θ has had a significant effect on the equilibrium. A more precise measurement of the magnitude of this effect will have to await further data on the members of the spiro series-I, especially where n=2 and 3. This work is in progress.

REFERENCES

1. J. B. Hendrickson, J. Am. Chem. Soc., 84, 3355 (1962).

2. R. Fuchs, J. Org. Chem., 23, 902 (1958).

3. E. I. Eliel, N. L. Allinger, S. J. Angyal and G. A. Morrison, Conformational Analysis, John Wiley & Sons, New York, 1962, Chapter 7.

4. J. J. Uebel and J. C. Martin, J. Am. Chem. Soc., 86, 4618 (1964).