

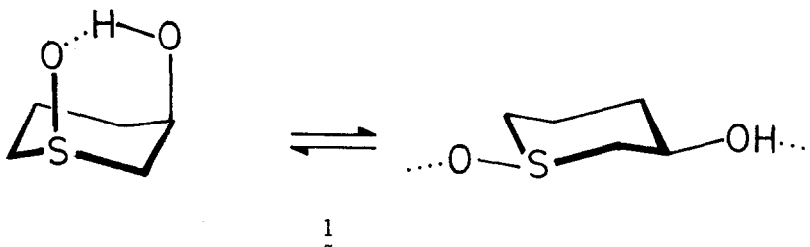
## LARGE CONCENTRATION EFFECTS ON CONFORMATIONAL EQUILIBRIA

Ernest L. Eliel\* and Ernesto Brunet

William R. Kenan, Jr. Laboratories of Chemistry  
University of North Carolina, Chapel Hill, NC 27514 USA

**Summary.** The conformational equilibrium in *cis*-3-Hydroxythiane S-oxide (Scheme 1) is strongly concentration dependent, being affected by intermolecular hydrogen bonding at high concentration.

In a previous paper<sup>1</sup> we reported large solvent and temperature effects on conformational equilibria in a heterosubstituted cyclohexane. The present report deals with a large concentration effect on such equilibria, specifically on the conformational equilibrium in *cis*-3-hydroxythiane S-oxide (**1**, Scheme 1).



Scheme 1

The variation of  $-\Delta G^\circ$  for the equilibrium shown in Scheme 1 with concentration in solvent  $\text{CD}_2\text{Cl}_2$  is shown in Fig. 1. The data at high concentration (black dots) were obtained by low-temperature C-13 nmr spectroscopy; at the highest concentration investigated (ca. 3M)  $-\Delta G^\circ$  is approximately 1.0 kcal/mol and even so has not yet come to a plateau (i.e. it might be even larger at still higher concentrations which were not accessible to measurement). At the lowest concentration accessible by C-13 nmr (ca. 0.1M)  $-\Delta G^\circ$  was near zero. Yet much lower concentrations could be studied by proton nmr by observation of the carbonyl (C-3) proton at low temperature in the 2,2,4,4-tetradeuterated analog (Fig. 1, circles). At the lowest concentration thus reached, 0.0023M,  $+\Delta G^\circ$  exceeds 1.3 kcal/mol and becomes too large to be measured. Thus, over the concentration range from 3M to 0.0023M, the equilibrium shown in Scheme 1 changes from lying almost entirely on the right to lying almost entirely on the left.<sup>2</sup>

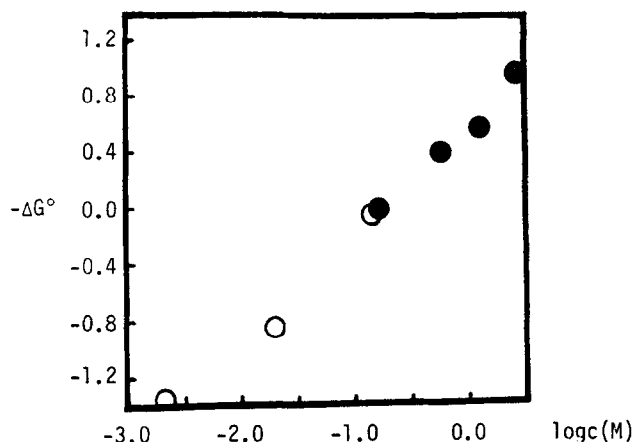


Figure 1

The reason for this remarkable change undoubtedly lies in the counterplay of intermolecular and intramolecular hydrogen bonding. The S-O...H-O hydrogen bond is a strongly stabilizing factor. At high concentrations, this bond is principally intermolecular and since equatorial S-O and equatorial O-H are better disposed to hydrogen bonding than their axial counterparts, the diequatorial conformation is preferred by far. On the other hand, at low concentration intermolecular hydrogen bonding is no longer predominant (for reasons of unfavorable entropy) and stabilization is now by intramolecular hydrogen bonding which demands the diaxial conformation.

This result may be of some general interest in the conformational analysis of compounds capable of both inter- and intramolecular hydrogen bonding.

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#### References and Notes

1. M. Manoharan, E.L. Eliel and F.I. Carroll, *Tetrahedron Lett.*, **1983**, 1855.
2. The C-13 shifts used in the analysis were (ppm from TMS, in CD<sub>2</sub>Cl<sub>2</sub>, at -90°C): e,e Conformer, C(2), 64.0; C(3), 66.4; C(4), 32.0; C(5), 17.1; C(6), 44.2. a,a Conformer, C(2), 49.3; C(3), 57.4; C(4), 30.7; C(5), 8.8; C(6), 44.0. The carbinol proton shifts were e,e, 3.64, a,a, 4.28 ppm.

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