CONFORMATIONAL STUDIES OF TRIMETHYLENE SULFITE AND RELATED COMPOUNDS III*

THE CONFORMATIONAL ENERGY OF SUBSTITUENTS AT CARBON ATOM 2

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Conformational studies (1,2) of the cyclic sulfites of 2-substituted-propane-1,3-diols have indicated that these esters occupy preferentially a chair form with axial S=O bond. X-ray analyses (3,4) of two compounds have shown that the sulfite group holds the remainder of the ring in an almost ideal staggered conformation, all dihedral angles in the ring being close to 60°.

We now report that cis-trans isomeric sulfites can be equilibrated by acid catalysts. Although isomerisation takes place rather slowly with BF_3-etherate, due to partial decomposition of the catalyst, the equilibrium position may be reached from either side and is independent of the catalyst concentration.

Ten sulfites, all occurring both as cis and trans isomers, have been investigated. From the final cis-trans ratio's, measured in various solvents by NMR or GLC techniques, equilibrium constants K_i were evaluated. The results in terms of the free-energy differences $-\Delta G^{\circ} = RT \ln K_i$ are given in Table 1.

The experimental evidence for the structural and conformational assignments impliedly given in the last column has been (1,2) or will be published (5) elsewhere, together with details about synthetic procedures.

It has previously been observed (2), that the conformational homogeneity of the isomers may be affected seriously in polar solvents, due to the strong interaction between a highly polar conformation and the surrounding dielectric.

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* Part II: H.F. van Woerden, Tetrahedron Letters 2407 (1966).

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The presence of a conformational equilibrium for one isomer (denoted II) has
been detected particularly if X = t-butyl or X = alkyl and Y = electronegative
(group of) atom(s). Presumably the molecules in a destabilised chair IIa
now shift partly to conformation IIb with equatorial S=O bond and relatively
high dipole moment
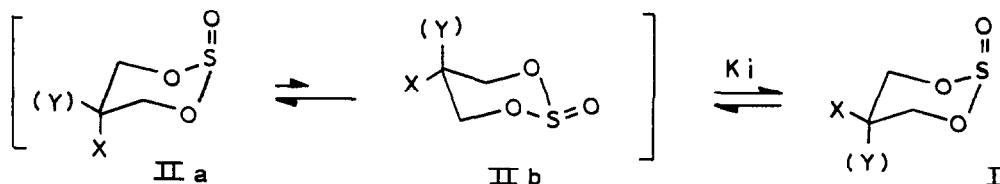
This solvent effect is weakly reflected in the values shown in Table 1, although
more experiments are needed to establish it accurately. The evidence (IR spec-
tral data, dipole moment measurements) available for the compounds listed,

TABLE 1

Free Energy Differences (Kcal./mole) of Isomeric Cyclic Sulfites
of 2-substituted Propane-1,3-diols.

X, Y, C, CH₂-O, SO	$-\Delta G^{o} = RT \ln K_i$ in various solvents			T	Assignments
X	Y	CCl_4	$CHCl_3$	CH_3CN	^{o}C	structure of major isomer
CH_3	H	0.66	0.59	0.75	25 40	CH_3(e);H(a)
Cl	H		0.12*	0.10	25	Cl (e);H(a)
CH_3	Cl			0.60	25	CH_3(e);Cl(a)
NO_2	H	0.43**		0.58	25	NO_2(a);H(e)
CH_3	NO_2	1.30**	1.21		40	CH_3(e);NO_2(a)
C_2H_5	NO_2		1.20	1.20	40	C_2H_5(e);NO_2(a)
CH_3	$COOCH_3$		0.44	0.44	40	CH_3(e);CO_2CH_3(a)
CH_3	n-C_3H_7	0.02			40	CH_3(a);C_3H_7(e)
CH_3	C_6H_5	0.39		0.14	40	CH_3(a);C_6H_5(e)
t-C_4H_9	H	1.56	1.50	1.50		t-C_4H_9(e);H(a)

*determined in diethyl ether   ** ibid., in dioxane

suggests that the fraction x of isomer II that occupies form (a) is at least 0.9 in non-polar solvents. In the pure liquid, however, or in polar solvents it may vary between 0.5 and 0.9. This implies that the conformational energy $-\Delta G_x$ of a substituent X at C-2 (resp. the difference for two substituents X,Y if $Y \neq H$) can be equated to the values given in Table 1, only after allowing for conformational non-homogeneity. The corrected values, given by the equation

$$-\Delta G_x = RT \ln K_i x$$

are shown in Table 2. The possible error, estimated at $\pm$ 0.2 Kcal., is mainly caused by the present uncertainty in the "correction factor" x. In spite of this inaccuracy, some interesting conclusions may already be drawn:

(1) The conformational energy of an alkyl group at C-2 in cyclic sulfites differs hardly from that for the corresponding position (C-5) in 1,3-dioxanes (6,7). The value of 0.7 Kcal. corresponds closely to the interaction energy between a methyl group and two oxygens in gauche relation, as determined from substituted cyclitols (8).

(2) The agreement between measured and calculated values for Cl and NO_2, and

TABLE 2

Conformational Free Energies $-\Delta G_x$ (Kcal./mole)

Substituents	at C-2 in Trimethylene sulfites		at C-5 in 1,3-dioxanes (cf. ref.6,7)	in cyclo-hexanes (cf. ref.8,9,10)
	Observed	calculated from additivity		
CH_3	0.7	-	0.8;0.9	1.7
C_2H_5	-	0.7	0.7;0.8	1.8
$n-C_3H_7$	-	0.7		
Cl	0.1	~0		0.4
NO_2	-0.5	-0.6		0.8;1.3
$COOCH_3$	-	0.2		1.2
C_6H_5	-	1.2	1.0	2.1;3.0
$t-C_4H_9$	1.8	-	1.4;1.7	

the similarity in the values found for the alkyl groups indicate that the free energy difference between conformation I and IIa is -to a first approximation- additively built up from contributions of the two substituents.

(3) The trend found in cyclohexane systems (11) of decreasing conformational energy with increasing electron-acceptor properties (σ_I value) of the substituent, is also observed in cyclic sulfites.

(4) The anomeric effect in 2-halotetrahydropyrans has recently been explained semi-quantitatively (12) in terms of electrostatic interactions of bond moments. A calculation on this basis would predict a considerable <u>disfavouring</u> of the axial position in e.g. 3-halotetrahydropyrans and 2-halotrimethylene sulfites. The presently obtained results suggest that this electrostatic effect is much smaller than one might have expected (13).

REFERENCES

1. H.F. van Woerden, <u>Thesis</u>, Leiden (1964); D.G. Hellier, J.G.Tillett, H.F. van Woerden and R.F.M. White, <u>Chem.Ind.</u>(London), 1965 (1963); D.G. Hellier, PH.D. <u>Thesis</u>, London (1966).

2. H.F. van Woerden and E. Havinga, <u>Rec.Trav.Chim.</u><u>86</u>, 341, 353 (1967).

3. C. Altona, H.J. Geise and C. Romers, <u>Rec.Trav.Chim.</u><u>85</u>, 1197 (1966).

4. H. van Oijen, R. Hasekamp, G. Verschoor and C. Romers, <u>Acta Cryst.</u>, in the press.

5. H.F. van Woerden, C.H. Green and A. de Vries, <u>Rec.Trav.Chim.</u>to be published.

6. E.L. Eliel and M.C. Knoeber, <u>J.Am.Chem.Soc.</u> <u>90</u>, 3444 (1968).

7. F.G. Riddell, and M.J.T. Robinson, <u>Tetrahedron</u> <u>23</u>, 3417 (1967).

8. E.L. Eliel, N.L. Allinger, S.J. Angyal and G.A. Morrison, "<u>Conformational Analysis</u>", Interscience Publ.Inc., New York (1965).

9. W.F. Trager and C. Huitric, <u>J.Org.Chem.</u> <u>30</u>, 3257 (1965).

10. N.C. Franklin and H. Feltkamp, <u>Tetrahedron</u> <u>22</u>, 2801 (1966).

11. M. Charton and B.I. Charton, <u>J.Chem.Soc.</u>(B), 43 (1967).

12. C.B. Anderson and D.T. Sepp, <u>J.Org.Chem.</u> <u>32</u>, 607 (1967).

13. Compare also note (40) in ref. 6.