

Studies of Intramolecular Hydrogen Bonding in Cyclic Acetal Isomers of Glycerol

GUNNAR AKSNES and PER ALBRIKTSSEN

Chemical Institute, University of Bergen, Bergen, Norway

The equilibrium constants between free and intramolecularly hydrogen bonded conformers of *cis* and *trans* 5-hydroxy-2-methyl-1,3-dioxane and *cis* and *trans* 4-hydroxymethyl-2-methyl-1,3-dioxolane have been measured at different temperatures in carbon tetrachloride, and the enthalpy and entropy differences between free and hydrogen bonded conformers of the four acetal isomers have been calculated. The difference in stability of substituents in axial and equatorial positions in 1,3-dioxane and 1,3-dioxolane is discussed in relation to the stability of axial and equatorial substituents in cyclohexane and cyclopentane.

In a previous paper, the isolation and isomerisation of cyclic acetal isomers of glycerol were reported.¹ Four stable isomers were isolated, each of which was an equilibrium mixture of one free and one intramolecularly hydrogen bonded conformer (Figs. 1 and 2). Comparison of the stability of 1,3-dioxane and 1,3-dioxolane isomers of ketals and acetals indicated that an axial methyl group in the 2-position of the 1,3-dioxane ring might give rise to a repulsion energy of approximately 2 kcal towards hydrogen atoms in 4- or 6-positions of the ring, *i.e.* similar to the effect found for a methyl group in axial position in cyclohexane.²

It was hoped that a study of the intramolecular hydrogen bond formation of the different acetal isomers might shed further light on the energetic problem of 1,3-dioxane and 1,3-dioxolane derivatives, since restriction with respect to occupation of axial and equatorial positions is laid upon the substituents on chelate formation. The present paper reports an infrared study of the equilibrium between free and hydrogen bonded conformers of the four cyclic acetal isomers in carbon tetrachloride at several temperatures.

EXPERIMENTAL

Materials. The four cyclic acetal isomers of glycerol were isolated on a preparative gas chromatograph according to earlier descriptions.¹

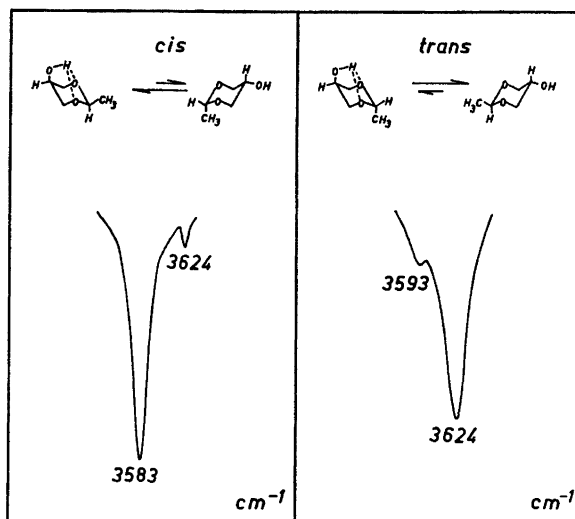


Fig. 1. Infrared bands of free and hydrogen bonded hydroxyl groups of 0.01 M *cis* and *trans* 5-hydroxy-2-methyl-1,3-dioxane in CCl_4 . *Cis*: 59.8°C, *trans*: 28.7°C.

Carbon tetrachloride, spectroscopically graded, was dried over phosphorus pentoxide and distilled over solid potassium hydroxide.

Measurements of equilibrium constants. The intramolecular hydrogen bonding of the four acetals was studied in 0.01 M concentration of the acetals in carbon tetrachloride. At this concentration, only two sharp infrared bands were observed in the O—H stretching region; the free and the intramolecularly hydrogen bonded one (Figs. 1 and 2). A thermostated infrared cell of 2 mm path length was used. The temperature in the cell was measured with a thermocouple with an accuracy of $\pm 0.2^\circ\text{C}$. The optical densities of the free and associated O—H bands were measured at three to six different tempera-

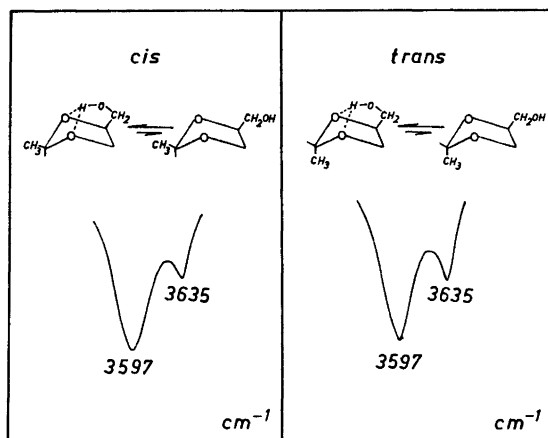
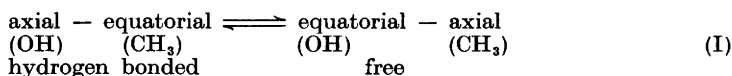


Fig. 2. Infrared bands of free and hydrogen bonded hydroxyl groups of 0.01 M *cis* and *trans* 4-hydroxymethyl-2-methyl-1,3-dioxolane in CCl_4 . *Cis*: 37.7°C, *trans*: 45.1°C.

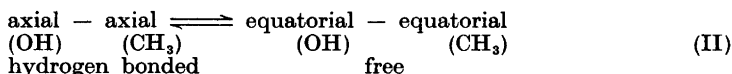
tures in the region between 20 and 60°C. Prior to calculation of the equilibrium constants, the optical densities were corrected for band overlap. The spectra were recorded on a high resolution infrared instrument, Unicam S.P. 100, Mk 2. The experimental data together with the calculated thermodynamic functions are summarized in Tables 1–4.

RESULT AND DISCUSSION

The *cis* and *trans* isomers of the 1,3-dioxanes (Fig. 1) differ with regard to the position of the hydroxyl and methyl group in the ring. Since formation of an intramolecular hydrogen bond with the acetal oxygen in the ring requires an axial position of the hydroxyl group, the transition between the hydrogen bonded and free conformers of *cis* 5-hydroxy-2-methyl-1,3-dioxane must be as follows:



In the same way the two conformers of *trans* 5-hydroxy-2-methyl-1,3-dioxane are:



Studies of methyl substituted cyclohexanes have shown that an axial methyl group is 1.8 kcal/mole less stable than an equatorial one (1.9 kcal/mole in the gas phase, 1.6–1.7 kcal/mole in the liquid phase is reported³). It is reasonable to expect that a corresponding situation might exist also in 1,3-dioxane derivatives. This would mean that the hydrogen bonded conformer of the *cis* 1,3-dioxane acetal of glycerol should be stabilized with respect to the free conformers through hydrogen bonding as well as by the equatorial position of the methyl group (I) (*cf.* Fig. 1). On the other hand, the hydrogen bonded conformer of the *trans* isomer has an axial methyl group, which will oppose the energy gain due to intramolecular hydrogen bonding (II). The calculated enthalpy difference between associated and free conformers must therefore include this contribution of energy due to axial and equatorial position of the methyl group, and we accordingly get:

$$\Delta H_{cis} = \Delta H_{cis(H)} + \Delta H_{e-a} \quad (1)$$

$$\Delta H_{trans} = \Delta H_{trans(H)} - \Delta H_{e-a} \quad (2)$$

where ΔH_{cis} and ΔH_{trans} are the calculated total enthalpy differences between free and hydrogen bonded conformers of *cis* and *trans* 4-hydroxy-2-methyl-1,3-dioxane. $\Delta H_{cis(H)}$ and $\Delta H_{trans(H)}$ are the enthalpies of the hydrogen bond interaction in *cis* and *trans* conformers, and ΔH_{e-a} is the enthalpy difference between equatorial and axial position of the methyl group in the 1,3-dioxane ring.

As a first approximation it seems reasonable to put $\Delta H_{cis(H)} = \Delta H_{trans(H)}$. The experimental data in Tables 1 and 2: $\Delta H_{cis} = -6.4$ kcal/mole and $\Delta H_{trans} = -2.6$ kcal/mole, inserted in eqns. (1) and (2) then give $\Delta H_{e-a} =$

1.9 kcal/mole. The energy difference between equatorial and axial methyl substituents in the 1,3-dioxane ring is therefore very nearly the same as in cyclohexane.

With respect to the intramolecularly hydrogen bonded conformers of the five-membered 1,3-dioxane isomers of glycerol acetal (Fig. 2), it is seen from Tables 3 and 4 that the enthalpy difference between the associated and free conformers of the *cis* and *trans* dioxolane is approximately 0.3 kcal greater for the *trans* isomer. A planar structure of the dioxolane ring would give rise

Table 1. Equilibrium constants and thermodynamic data for the intramolecularly hydrogen bonded *cis* 5-hydroxy-2-methyl-1,3-dioxane in CCl_4 . Conc.: 0.01 M.

Temp. °C	<i>K</i>	ΔG kcal/mole	ΔH kcal/mole	ΔS cal/mole deg.
30.1	18.8	-1.77	-6.4	-15.3
38.8	16.9	-1.75		-14.9
47.0	11.5	-1.55		-15.2
53.8	10.2	-1.51		-15.0
59.8	7.5	-1.34		-15.2

Table 2. Equilibrium constants and thermodynamic data for the intramolecularly hydrogen bonded *trans* 5-hydroxy-2-methyl-1,3-dioxane in CCl_4 . Conc.: 0.01 M.

Temp. °C	<i>K</i>	ΔG kcal/mole	ΔH kcal/mole	ΔS cal/mole deg.
20.3	0.201	0.94	-2.6	-12.2
20.7	0.201	0.94		-12.1
28.7	0.188	1.00		-12.3
31.7	0.197	0.99		-11.9
45.6	0.172	1.12		-11.8
45.8	0.174	1.11		-11.7

Table 3. Equilibrium constants and thermodynamic data for the intramolecularly hydrogen bonded *cis* 4-hydroxymethyl-2-methyl-1,3-dioxolane in CCl_4 . Conc.: 0.01 M.

Temp. °C	<i>K</i>	ΔG kcal/mole	ΔH kcal/mole	ΔS cal/mole deg.
21.9	3.92	-0.80	-3.1	-7.7
29.7	3.43	-0.74		-7.7
37.7	2.95	-0.67		-7.7
44.4	2.66	-0.61		-7.7

Table 4. Equilibrium constants and thermodynamic data for the intramolecularly hydrogen bonded *trans* 4-hydroxymethyl-2-methyl-1,3-dioxolane in CCl₄. Conc. 0.01 M.

Temp. °C	<i>K</i>	ΔG kcal/mole	ΔH kcal/mole	ΔS cal/mole deg.
21.2	3.38	-0.71		-9.2
30.5	3.03	-0.67	-3.4	-9.1
45.1	2.22	-0.50		-9.2

to a repulsion between the methyl group in the 2-position and the methyl group in the 4-position of the *cis* isomer, thus destabilizing the intramolecular hydrogen bonding in the *cis* isomer relative to the *trans* isomer. If the 1,3-dioxolane ring is comparable with the cyclopentane ring, a slight puckering of the ring is to be expected.⁴ The puckering is not fixed, however, but rotates around the ring by an up and down motion of the ring atoms. As an average it is therefore reasonable to expect that the repulsion between *cis* occupied substituents in 2- and 4-positions is present also in five-membered puckered ring system. But since the calculated enthalpy difference of 0.3 kcal/mole between the *cis* and *trans* isomers lies within the experimental error of the present method, no definite conclusion can be reached.

REFERENCES

1. Aksnes, G., Albriktsen, P. and Juvvik, P. *Acta Chem. Scand.* **19** (1965) 920.
2. Eliel, E. L. *Stereochemistry of Carbon Compounds*, McGraw, New York 1962, p. 200.
3. Prosen, E. J., Johnson, W. H. and Rossini, F. D. *J. Res. Natl. Bur. Std.* **39** (1947) 173.
4. Eliel, E. L., Allinger, N. L., Angyal, S. J. and Morrison, G. A. *Conformational Analysis*, Interscience, New York 1965, p. 200.

Received January 18, 1966.