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CONFORMATIONAL DATA IN BICYCLIC 1,3-DIOXANES.

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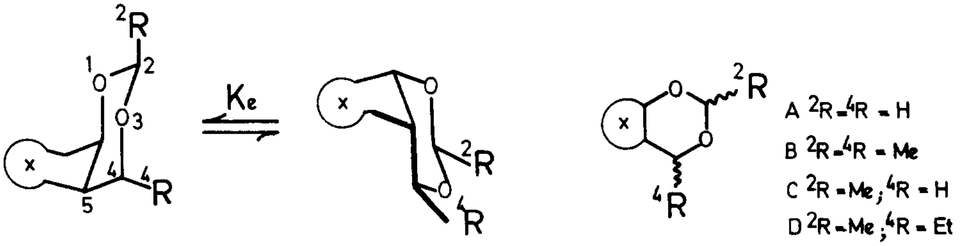
We have previously estimated, and found from ^{1}H-NMR studies (1) and chemical equilibrations (2) of suitable derivatives, that the O-inside conformer for x = 6 is the more stable form by ca. 2.2 Kcal/mole in the equilibrium IA ⇆ IIA.



I O-inside II O-outside III

Equilibria have now been assessed for different ring sizes of the carbocyclic moieties (x = 5,7,8). To strengthen some findings, the equilibrium has also been determined for IC ⇆ IIC (x = 7), where it is now found that, in contrast to the case where x = 6 (1), the system is not biased in favour of O-in. Eight different isomers may exist for the bicyclic dioxanes having the basic structure IIIB (^{2}R = ^{4}R = Me). Not all of them are formed during synthesis (3) but fortunatedly both desirable epimerisable isomers are, so that chemical equilibrations could be done. The different isomers were separated by GC and their structures assigned by ^{1}H-NMR 300 MHz spectroscopy (3). Equilibria between the isomeric pairs IB ⇆ IIB were obtained for 0.5 molar solutions in CCl_4 using 0.1 equivalent CF_3COOH as the catalyst. The equilibria (at four different temperatures for five different samples of each pure isomer IB and IIB) were quenched by crashing a small tube enclosed in the reaction vessel, containing sodium carbonate.

Quantitation was performed by GC and electronic integration. Capillary glass columns (1 = 50-70 mm; Ø = 0.5 mm; PTMO on Carbowax) and flame ionisation detection were used. Reproducible results (± 0.2 %) were obtained with on-column injections, avoiding the use of a splitter[x].

The results of all equilibria are gathered in Tables I and II. It is difficult to assess the contributions for ΔΔS° changes. For different periods of analyses or by using different GC columns, one finds wide differences in ΔΔH° and ΔΔS° data, but the ΔΔG° values remain in excellent mutual agreement. The actual results were obtained as much as possible in standardised conditions. Nevertheless, for comparison it is wise to rely only upon ΔΔG° values, and not on ΔΔH° and ΔΔS° data. We have however the impression that, replacing a Me-4 group by an Et-4, the relative changes in stabilities of O-in/O-out may be influenced by entropy changes. The most striking results are, that for x = 7 and x = 8 the O-out isomer is preferred to the O-in. It is also found that changes of ΔΔG° with temperature, are the largest observed in these members.

The main reason why for x = 5 and x = 6 the O-in conformer is preferred, is the intrinsic behaviour of this form (1). The difference between O-in and O-out may be evaluated (2) to 2.2 Kcal/mole for x = 5 and x = 6, counterbalanced (a) by the presence of a Me-4ax group in IB (O-in) [which may be estimated in 1,3-dioxanes at 2.9-3.1 Kcal/mole (4)], (b) but reinforced in IIB (O-out) by a gauche interaction (depicted by the heavy lines) and estimated at some 900 cal/mole (5). The fact that O-out becomes more stable for IIB, x = 7 and x = 8, in contrast to the case for x = 5 and x = 6, must point to either a lowering of the gauche interaction in IIB, or alternatively to still other alterations of interactions in either the O-out or O-in forms. Coupling values (3) indicate some specific ring shape alterations, when x = 7 and x = 8, but the results are not always coherent and contain some ambiguities. It is sensible therefore to compare the results obtained for ΔΔG° in IB ⇄ IIB (x = 7) with those in IC ⇄ IIC (x = 7). Thus, when a Me-4 is omitted from the basic structure IB, an overall change in energy of about 2.4 Kcal/mole is noticed.

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[x] Actual results for IB ⇄ IIB (x=6) show a higher degree of conformity with the data obtained from previous ^{1}H-NMR studies, e.g. $\Delta\Delta G^\circ_{275}$ = 678 cal/mole (^{1}H-NMR 654 cal/mole (1); splitter method (2) : 475 cal/mole).

Table I.

Epimerization (O-in ⇄ O-out) in *cis*-bicyclic dioxanes

I ⇄ II (x=5,7,8)

Temp.(K)	%(O-out)	K_e=(O-in)/(O-out)	ΔΔG°[(a)] cal/mole	
IB ⇄ IIB; x=5				
274.0	31.67	2.15	417	$\Delta\Delta G^\circ_{298}$ = 483 cal/mole
310.0	30.24	2.32	517	ΔΔH° =-340 cal/mole
333.0	29.40	2.40	579	ΔΔS° =-2.8e.u.
351.5	23.73	2.48	631	r = 1.0
IB ⇄ IIB; x=6				
293.0	23.4	3.27	690	Ref.(2): 500 cal/mole
IB ⇄ IIB; x=7				
276.8	85.0	0.174	-961	$\Delta\Delta G^\circ_{298}$ =-886 cal/mole
298.0	81.6	0.22_5	-889	ΔΔH° =-1964 cal/mole
310.0	79.6	0.25_5	-842	ΔΔS° =-3.6 e.u.
327.0	77.1	0.29_8	-780	r = 1.0
IC ⇄ IIC; x=7				
291.0	6.9	13.5	1500	
IB ⇄ IIB; x=8				
273.0	68.4	0.45_8	-422	$\Delta\Delta G^\circ_{298}$ =-243 cal/mole
305.0	57.8	0.73_0	$-189._5$	ΔΔH° =-2378 cal/mole
312.5	55.5	0.80_0	-137	ΔΔS° =-7.1 e.u.
324.0	52.3	0.91_7	-57.5	r = 1.0

Table II.

Epimerization (O-in ⇄ O-out) in *cis*-bicyclic dioxanes

I ⇄ II (x=5, ^{2}R=Me, ^{4}R=Et)

Temp.(°K)	%(O-out)	K_e = (O-in)/(O-out)	ΔΔG°[(a)] cal/mole	
ID ⇄ IID; x=5				
272.5	22.7	3.38	659	ΔΔH° =+542 cal/mole
304.5	24.8	3.02	672	ΔΔS° =-0.4 e.u.
313.0	25.2	2.98	677	r = 1.0
324.0	25.9	2.88	681	$\Delta\Delta G^\circ_{298}$ = + 670 cal/mole
ID ⇄ IID; x=6				$\Delta\Delta G^\circ_{298}$ = +1431 cal/mole
272.0	7.5_2	12.3	1355	ΔΔH° =+588 cal/mole
304.0	8.40	11.0	1488	ΔΔS° =-2.9 e.u.
313.5	8.54	10.7	1475	r = 1.0
325.5	8.77	10.4	1513	

(a) Positive values when in favour of the O-inside isomer.

This comes from the fact that ΔG° for a Me-4 in 1,3-dioxanes (2.9-3.1 Kcal/mole) and the gauche interaction (heavy lines shown in IIB) are left out. For the dioxa-bicycloundecane derivatives (x = 7), this gauche interaction seems therefore to amount to ca. 500 cal/mole, instead of the normal value of 850-900 cal/mole observed for x = 6 (1)(2). However the total difference between the systems x = 6 and x = 7 amounts to about 1600 cal/mole, and there must be other contributing factors for ca. 1100 cal/mole. Inspection of Dreiding models shows, that in the O-out isomer the CH_2-4ax moiety does not necessarily point one of its C-H bonds above the dioxane ring, e.g. approaching the syn-axial C_2-H bond. Lastly, the specific conformations and the overall flexibility of the higher membered carbocyclic rings, may be at the basis of both the above mentioned contributions (gauche interaction and syn-axial strain).

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