Effect of Solvent on the Position of Equilibrium of the 2-Methyl-5-t-butyl-1,3-dioxans and on their Nuclear Magnetic Resonance Spectra

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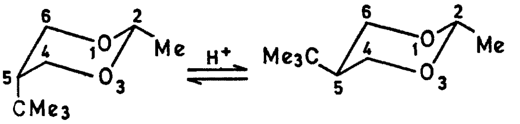
Summary Configurational equilibria of the 2-methyl-5-t-butyl-1,3-dioxans are affected by solvent in a minor way only; in the n.m.r. spectra of the two diastereoisomers, chemical shifts but not coupling constants are solvent dependent.

IN connection with an investigation of the effects of solvent on configurational equilibria in 5-hetero-substituted 1,3-dioxans[1] it became necessary to study, for purposes of comparison, the influence of solvent, if any, on the corresponding equilibria involving non-polar substituents. 2-Methyl-5-t-butyl-1,3-dioxan[2,3] was chosen as an example, since previous investigation[2] had shown that *cis–trans* equilibrium [(I) ⇌ (II)], in this compound involves



(I) *cis* (II) *trans*

movement of the bulky t-butyl group from the equatorial to the axial position. Thus, if solvation of the oxygen atoms by hydrogen-bonding or high-dielectric solvents were a major factor determining the relative stability of the diastereoisomers (I) and (II), the *cis*-isomer (I) should be strongly disfavoured in such solvents, since the t-butyl group screens the axial side of the ring oxygens. Also, since there is a dipolar repulsion between the ring oxygen atoms,[4] and since such repulsion should depend on solvent dielectric constant (provided the solvent can penetrate into the molecular cavity) it was *a priori* conceivable that the exact shape of the ring might be strongly solvent dependent; this, in turn, would presumably affect not only the equilibrium (I) ⇌ (II), but also the n.m.r. coupling constants of the protons in the C-4, -5, -6 region of compounds (I) and (II).

TABLE 1

Equilibration results[a]

Solvent	ϵ_{25}[b]	$-\Delta G^0_{25}$[c]
Cyclohexane	2·015	1·37 ± 0·01
Carbon tetrachloride	2·228	1·53 ± 0·03
Benzene	2·274	1·52 ± 0·01
Ether	4·335	1·47 ± 0·01
Neat	—	1·54 ± 0·01
Dimethoxyethane	3·5	1·57 ± 0·01
Nitrobenzene	34·82	1·66 ± 0·01
Acetonitrile	36·7	1·73 ± 0·01
Chloroform	4·806	1·78 ± 0·01
Methanol	32·63	1·62 ± 0·02
t-Butyl alcohol	—	1·59 ± 0·02
Acetic acid	6·15	*ca.* 1·85
Formic acid	58·5	*ca.* 1·97

[a] All solutions were *ca.* 0·3M; equilibration was effected by a Rohm and Haas Amberlyst-15 (polystyrenesulphonic acid) catalyst; g.l.p.c. analysis was performed on a 6 ft. Carbowax 20M, 20% on Chromosorb W column; the response ratio was 1·042 ± 0·004. In each solvent, two samples, one initially rich in (I) and one rich in (II), were equilibrated. [b] Dielectric constant at 25°. [c] In kcal/mole at 25°.

TABLE 2

Chemical shifts and coupling constants for (I) *and* (II)[a]

Solvent	ν_{H-2}	ν_{H-4e}	ν_{H-4a}	ν_{H-5}	ν_{Me-2}	ν_{But-5}	$J^{vic}_{4a,5}$	$J^{vic}_{4e,5}$	$J^{gem}_{4a,4e}$
				(I)					
CCl_4	274·5	250	224	50	70·5	65	3·75	1·25	−12·25
C_6H_6	273·5	247	213	31	77	61·5	4·0	1·25	−12·5
C_6H_6*[b]	—	247·54	213·87	30·98	—	—	2·93	1·28	−10·98
C_5H_5N	279	250	222	48	74·5	62	4·0	1·50	−12·25
$(CD_3)_2SO$	279·5	251	225	complete overlapping	68·5	61·5	3·75	1·25	−12·25
Neat	276·5	250	224	50	68·5	62	3·75	1·25	−12·25
				(II)					
CCl_4	265·5	240·5	207·0	100·0	69·5	53·0	11·0	4·5	−11·25
CCl_4*[b]	—	240·5	206·8	100·1	—	—	11·1	4·46	−11·26
C_6H_6	267	241·8	203·2	101	71·5	39·0	11·5	4·5	−11·25
$PhNO_2$	268	242·0	208	97·5	74·0	47·5	11·0	4·25	−11·25
C_5H_5N	272·5	247·0	209	102·5	80·5	44·0	11·0	4·50	−11·25
$CHCl_3$	272	246	212	104	75·5	53·0	11·0	4·25	−11·25
CH_2Cl_2	270·5	244	212	101·5	72·5	52·0	11·0	4·25	−11·25
Neat	268·5	242	208	101·5	69·5	51·0	11·0	4·25	−11·0

[a] In Hz, chemical shifts measured downfield from Me_4Si at 60 MHz in 20% solutions. [b] Data calculated by computer analysis. $J_{4e,6e}$ − 2·79 for (I), −1·71 Hz for (II).

In Table 1 are shown the $-\Delta G^0_{25}$ values for the equilibrium (I) ⇌ (II) established in various solvents. The maximum variation in $-\Delta G^0$ is about 0·6 kcal/mole with most of the values comprised in a 0·3 kcal/mole range.

The n.m.r. parameters for (I) and (II) as a function of solvent are shown in Table 2. These parameters were obtained by first-order analysis, except for the asterisked data which were extracted by computer analysis using the Laocoon III program.

The following conclusions may be reached from this investigation: (i) The coupling constants in (I) and (II) are virtually independent of solvent. It appears, then, that the shape of the 1,3-dioxan ring in these isomers is not palpably affected by the polarity of the solvent or its tendency to form hydrogen bonds. (ii) As usual, the chemical shifts are affected by solvent. The largest effect is on the equatorial substituent at C-5: H-5 in (I) and Bu^t in (II); the corresponding axial substituent is affected much less. Sizeable effects are also observed for Me-2 and H-4a; solvent effects on H-2 and H-4e are noticeably smaller. (iii) The equilibrium between (I) and (II) is somewhat affected by the medium in the sense that solvents which might be expected to associate with the ring oxygen atoms favour the equatorial isomer (II) more. However, the effect is much smaller than that seen in 5-hetero-substituted 1,3-dioxans[1] and operates in the opposite direction.

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[3] F. W. Nader and E. L. Eliel, *J. Amer. Chem. Soc.*, in the press.

[4] *cf.* E. L. Eliel, *Kem. Tidskr.*, 1969, **81**, No. 6/7, 22.