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THE CONFORMATION OF THE ALKYL GROUPS IN N, N'-DIALKYL-1, 3-DIAZANES

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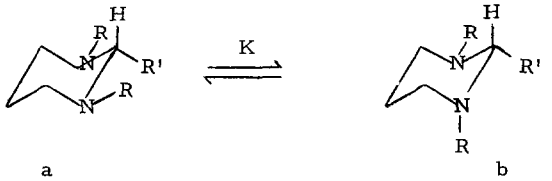
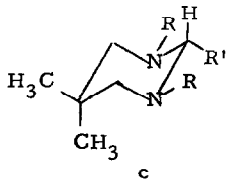
In a previous publication[1] we had indicated, on the basis of proton NMR data, that the equilibrium (a⇌b) shown in Scheme 1 lay to the right for I, R = CH_3, R' = CH_3. The conclusion was based on a comparison of the chemical shift of the C-2 proton with the corresponding proton in the 5, 5-dimethyl analog Ic in which it was assumed that the N-alkyl groups must be equatorial. No model was then available for an axial N-alkyl group and the original conclusion was therefore qualitative.



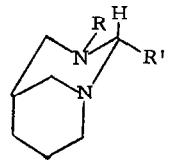
a ⇌ b

Scheme 1

I, R = CH_3, R' = CH_3
II, R = CH_3, R' = H
III, R = C_2H_5, R' = H
IV, R = $(CH_3)_2CH$, R' = H
V, R = $(CH_3)_3C$, R' = H
VI, R = $(CH_3)_2C_2H_5C$, R' = H



c



d

In the interim, Katritzky and coworkers have published[2] dipole moment data for the compounds II - V, which are devoid of substituents at C-2, and have concluded that equilibrium is somewhat on the side of the N, N'-diequatorial conformation even when the N-substituent is methyl or ethyl, and almost completely so when it is isopropyl or t-butyl. The contrast between the two sets of results is of importance, since our postulation of a "rabbit-ear effect" - i.e. a repulsion, presumably caused by dipole interaction, in that conformation in which the unshared electron pairs on nitrogen are parallel - rested on the greater stability of isomer Ib compared to Ia. We estimated the magnitude of the effect to be 1 - 1.5 kcal/mol whereas on the basis of Katritzky's data it could not be much more than 0.5 kcal/mol, perhaps less.[3]

Since conformational equilibrium positons derived from dipole moment measurements

may be quite sensitive to the exact value of the calculated dipoles of the extreme conformers (a and b in Scheme 1) which, in turn, would be affected by deviations of the molecule from the assumed ideal chair form, we felt confirmation of Katritzky's findings by an alternative method would be desirable, as would be placing our own data on a quantitative footing. To this end, and following Riddell's precedent in the oxazane series,[4] we synthesized model compounds d as well as c in Scheme 1 for compounds I - IV and VI[5] and derived the equilibrium constant K for the a $\rightleftharpoons$ b equilibrium from the position of the C-2 axial proton in a/b, c and d using the relations[6] $K = N_b/N_a$ and $\nu_{a/b} = N_a\nu_c + N_b\nu_d$. Here $\nu_{a/b}$, ν_c and ν_d stand for the shifts of H-2(axial) in a/b, c and d, respectively and N_a, N_b are the mole fractions of a and b in the conformational equilibrium mixture a/b. It is assumed, in this derivation, that the chemical shift for H-2(axial) is the same in a as in c and in b as in d. After this work was completed, we learned that Riddell had undertaken a similar study for compound II.[7]

Our measured chemical shifts are shown in Table I. For Compounds II - IV and VI which undergo rapid inversion at room temperature it was necessary to operate in the vicinity of -80°C; the same temperature was used for the conformationally rigid model d as for the mobile systems a/b and c so as to eliminate errors due to temperature dependence of chemical shift. The derived ΔG° data are shown in Table II. Since b is a dl-pair but a a meso form a correction of -RT ln 2 has been applied in Table II (last column) to show the equatorial - axial equilibrium of the N-alkyl group independent of the entropy-of-mixing advantage of conformer b.

Table I[a]

Compound	R	R'	T(°K)	ν_{H2-a}	ν_{H2-3}	J_2
Ia/b	CH_3	CH_3	303	283.8	-	-
Ic	CH_3	CH_3	303	221.0	-	-
Id	CH_3	CH_3	303	308.9	-	-[b]
II a/b	CH_3	H	200	224.6	355.9	9.0[c]
IIc	CH_3	H	201	189.6	360.0	8.6[c]
IId	CH_3	H	192	313.0	369.8	11.0[b]
III a/b	C_2H_5	H	196	228.5	376.1	9.1[c]
IIIc	C_2H_5	H	189	194.1	376.7	8.7[c]
IIId	C_2H_5	H	189	314.5	378.9	10.8[b]
IV a/b	i-C_3H_7	H	200	285	373.6	8.2[c]
IVc	i-C_3H_7	H	200	267.9	362.7	7.0[c]
IVd	i-C_3H_7	H	200	353.3	373.5	10.6[c]
VI a/b	t-C_5H_{11}	H	200	259.2	397.6	8.1[c]
VIc	t-C_5H_{11}	H	200	244.5	390.1	~7.6[c]
VId	t-C_5H_{11}	H	200	355.5	380.5	10.6[b]

[a] Shifts in Hz from TMS at 100 MHz. [b] Analyzed mass spectrometrically, m/e within 0.009 mass unit of calculated value. [c] C, H analysis within 0.35% of calculated value.

Table II

R	R'	T (°K)	Solvent	ΔG^o	ΔG^o(corr.)[a]	ref.
CH_3	CH_3	303	$CHCl{=}CCl_2$	-0.55	-0.13	b
CH_3	H	298	C_6H_{12}	0.13	0.54	2
CH_3	H	200	CH_2Cl_2, etc.	0.0	0.4	6
CH_3	H	200	$CHCl{=}CCl_2$	0.37	0.65	b
C_2H_5	H	298	C_6H_{12}	0.21	0.62	2
C_2H_5	H	196	$CHCl{=}CCl_2$	0.36	0.63	b
i-C_3H_7	H	298	C_6H_{12}	>1.4	>1.8	2
i-C_3H_7	H	200	$CHCl{=}CCl_2$	0.55	0.83	b
t-C_5H_{11}	H	200	$CHCl{=}CCl_2$	0.75	1.03	b

[a] ΔG^o + RTln 2, in kcal/mol [b] This work

Our data for the N-methyl compounds ($II_{a/b}$) are in good agreement with Katritzky's and Riddell's and those for N-ethyl ($III_{a/b}$) are in good agreement with Katritzky's, suggesting that both the dipole and NMR methods are valid in these cases and the results probably dependable. Our data for isopropyl ($IV_{a/b}$) are in less good agreement with Katritzky's showing that either of the two methods gives poor results. Although our ΔG^o value for i-Pr is close to the values for Me and Et, which seems intuitively correct, by comparison with alkylcyclohexane values,[8] we had some difficulty in positioning the H-2a signal for IIIa/b due to signal overlap in the NMR spectrum;[9] moreover the ΔG^o value for t-amyl is smaller than expected, which raises questions as to the validity of the rigid model d for the isopropyl and t-amyl compounds. It is therefore not certain which of the two divergent values for N,N'-diisopropyl-1,3-diazane is the better one.

In accordance with earlier reports[10] we find that the geminal coupling constant J_2 for the C-2 protons is smallest for the N,N'-diequatorial isomers c, largest for the equatorial-axial isomer d and intermediate for the mobile system a/b, However, the range of J-values is too small to warrant calculation of accurate ΔG^o's from J_2.

Our results with N,N'-2-trimethyl-1,3-diazane (Ia/b) confirm the earlier suggestion[1] that its equilibrium lies considerably to the right (Ib), i.e. that one of the N-methyl groups is largely axial. However, the large difference between Ia/b and IIa/b indicates that the "rabbit-ear effect"[11] contributes only in small measure to the predominance of Ib at equilibrium. It would appear that steric interference of three equatorial methyl groups in Ia, partially relieved in conformation Ib must be in considerable part responsible for the predominance of Ib. This point is under further investigation.

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