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Acid Dissociation and Activation Parameters for Ring Inversion of Diaminocalix[4]arene

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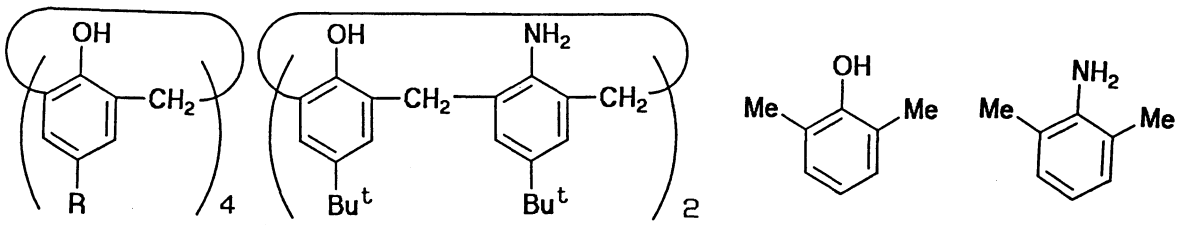
pK_a Values and activation parameters for ring inversion of 25,27-diamino-5,11,17,23-tetra-t-butylcalix[4]arene-26,28-diol were estimated. It was found that in the OH groups of this compound the "super-acidic" proton, observed for conventional calix[4]arene-25,26,27,28-tetrols, no longer exists and ring inversion occurs more easily.

Calix[4]arene-25,26,27,28-tetrols (**1**) adopt a cone conformation because of strong intramolecular hydrogen-bonding interactions.[1] However, ring inversion between mirror-image cone-cone conformers is still allowed, which occurs in a speed comparable with the NMR time-scale.[1-3] Thus, the coalescence temperature T_c exists at intermediary temperature. We previously determined the activation parameters for **1** by computer-assisted simulation of the temperature-dependent ^1H NMR spectra.[2,4] It was found that (i) the $\Delta G^{\ddagger}_{298}$ is about 15 kcal mol^{-1}, (ii) it decreases in polar solvents which can serve as hydrogen-bond acceptors, and (iii) reflecting the unimolecular process, it is mainly governed by the enthalpy term.[2] More recently, we developed a new synthetic method by which the OH groups in **1** can be substituted with the NH_2 groups.[5] It is extremely interesting to estimate how these substituted NH_2 groups affect the activation parameters for ring inversion. In this paper, we report the activation parameters for a 25,27-diamino analogue(**2**) of **1** determined by the complete line shape analysis method.[6] Comparison of these activation parameters provide important insights into the relation lying between ring inversion and intramolecular hydrogen-bonding interactions.



1 2 3 4

a :R=H b :R=t-Butyl

In IR, the ν_{OH} vibration band of **1b** appeared at 3170 cm^{-1} (Table 1). In ^1H NMR, the δ_{OH} of **1b** appeared at low magnetic field (10.34 ppm in $CDCl_3$). These unusual shifts are rationalized in terms of strong intramolecular hydrogen-bonding interactions.[7,8] In **2**, in contrast, ν_{OH} and ν_{NH} appeared at 3270 and 3340 cm^{-1} and δ_{OH} at 7.90 ppm (integral intensity 6H). These spectral data suggest that the "super-acidic" proton arising from unusually strong intramolecular hydrogen-bonding interactions no longer exists in **2**.

Since compounds **1** and **2** are insoluble in water, we estimated their apparent "pK_a" in THF.[8] We titrated the phenol group (PH) in **1**, **2**, and **3** by tetraethylammonium salts of 4-nitrophenolate or picrate (T^-) by following the decrease in the absorption band (422 nm for 4-nitrophenolate and 371 nm for picrate). In the equilibria, the equilibrium constants are defined as $K_e=[P^-][TH]/[PH]/[T^-]$.[8] Thus, the apparent acid dissociation constants are defined as $K_{app}=K_e \cdot K_a$, where K_a denotes the coherent acid dissociation constant in water. On the other hand, the first protonation of the amino group in **2** and **4** was monitored by the titration with picric acid. The results are summarized in Table 1. It is seen from this table

Table 1. Spectral and physical properties (25 °C)

Compound	ν_{OH} or ν_{NH} in IR(nujol)/cm^{-1}	δ_{OH} or δ_{NH} in ^1H NMR/ppm[a]	pK_a	
			Water[b]	THF
1b	3170	10.34	c)	4.11[d]
2	3270, 3340	7.90	c)	9.17(OH),[e] 4.82(NH_2)[f]
3	3600	4.35	10.59	11.85[e]
4	3375, 3480	3.50	3.95	5.67[f]

a)$CDCl_3$. b)μ=0.1. c)Insoluble in water. d)Titrated with tetraethylammonium picrate. e)Titrated with tetraethylammonium 4-nitrophenolate. f)Titrated with picric acid.

that the acidity of the OH groups in **2** is not so peculiar as that observed for **1** (pK_a 4.11, a shift of ca. 6 pK units)[8]: it is more acidic only by 2.68 pK units than **3**. Similarly, the basicity of the NH_2 group in **2** is not so peculiar: it is less basic only by 0.85 pK units than **4**.

Table 2. Activation parameters for ring inversion of **1** and **2**

Compound	Solvent	T_c / °C	$\Delta G^{\ddagger}_{298}$ / kcal mol^{-1}	$\Delta H^{\ddagger}$ / kcal mol^{-1}	$\Delta S^{\ddagger}$ / e.u.
1a	$CDCl_3$	44	15.7	14.2	-5.0
1b	$CDCl_3$	>55	16.4	15.9	-1.7
1b	Toluene-d_8	70	16.1	15.8	-1.0
1b	Pyridine-d_5	19	14.3	11.3	-10
2	$CDCl_3$	13	13.9	13.5	-1.4
2	Toluene-d_8	27	14.9	14.2	-2.1
2	Acetone-d_6	50	16.0	15.8	-0.7
2	Pyridine-d_5	35	14.9	10.9	-13.6

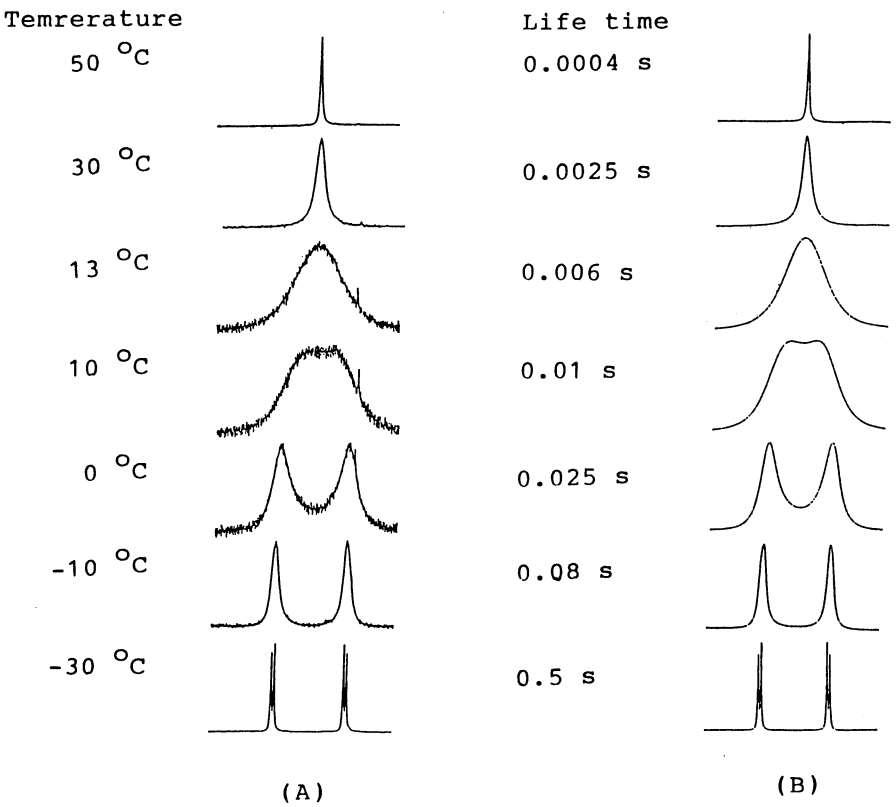


Fig. 1. Observed (A) and simulated spectra (B) of **2** (1.3 x 10^{-2} mol dm^{-3}) in $CDCl_3$.

^{1}H NMR spectra were measured by a JEOL GSX-400 (400 MHz) apparatus. In $CDCl_3$ at -30 °C, for example, **2** gave a pair of doublets for the $ArCH_2Ar$ protons at 3.55 and 4.32 ppm with J_{gem}=13.50 Hz (A in Fig. 1). This indicates that **2** adopts a regular cone conformation. With rising temperature the peaks were broadened and finally coalesced into one peak at 13 °C. This temperature-dependent spectral change was simulated assuming the life time (τ) for each temperature (B in Fig. 1). Excellent agreement is seen between the observed and the simulated spectra. The reliability of the present simulation is further guaranteed by the excellent linear relationship in the Arrhenius plots (ln k vs. T^{-1} where $k=\tau^{-1}$: $r > 0.99$). From the plots we computed $\Delta G^{\ddagger}_{298}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ and summarized them in Table 2. It is seen from this table that (i) the $\Delta G^{\ddagger}_{298}$ values for **2** are less dependent upon the solvent and generally smaller (except for pyridine-d_5) than those for **1b**, (ii) $\Delta G^{\ddagger}_{298}$ is primarily governed by $\Delta H^{\ddagger}$ and the contribution of $\Delta S^{\ddagger}$ is relatively small, and (iii) pyridine-d_5 is exceptional in two points: firstly, the $\Delta S^{\ddagger}$ terms are explicitly smaller than those in other solvents and secondly, the $\Delta G^{\ddagger}_{298}$ for **2** is greater, although slightly, than that for **1b**.

In conclusion, the present study displays that the "super-acidic" proton in **1** results from the very specific, complementary hydrogen-bonding network and insersion of the amino groups rather destroys this network.

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