Tetrahedron Letters,Vol.22,No.48,pp 4763-4766,1981 0040-4039/81/484763-04$02.00/0
Printed in Great Britain

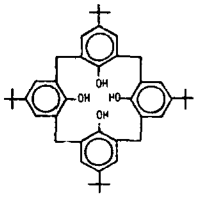
CALIXARENES. 5. DYNAMIC NMR CHARACTERISTICS OF *p-tert*-BUTYLCALIX[4]-ARENE and *p-tert*-BUTYLCALIX[8]ARENE

C. David Gutsche and Lorenz J. Bauer

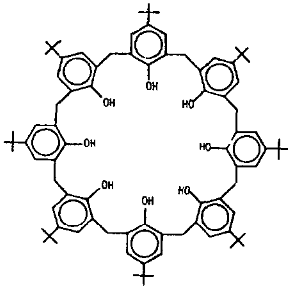
Department of Chemistry, Washington University
St Louis, Missouri 63130

Abstract. The near identity of the temperature dependent ^{1}H-NMR spectra of *p-tert*-butylcalix-[4]- and calix[8]arene in $CDCl_3$ and bromobenzene-d_5 is shown to be drastically altered in pyridine-d_5, attributable to disruption of intramolecular hydrogen bonding.

In a previous paper in this series[1] attention was drawn to the remarkable similarity between the temperature dependent ^{1}H-NMR (DNMR) spectra of *p-tert*-butylcalix[4]arene (1) and *p-tert*-butylcalix[8]arene (2). It has now been shown that the similarity disappears when pyridine is used in place of chloroform, which was the solvent employed in the experiments already reported[2].

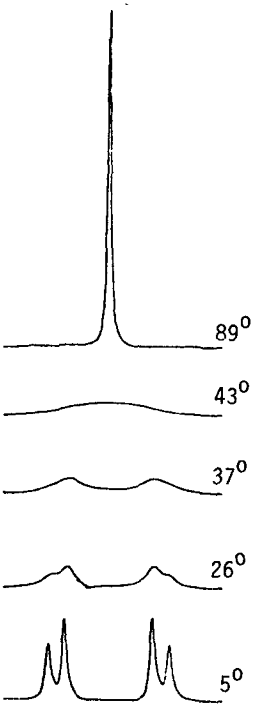


1

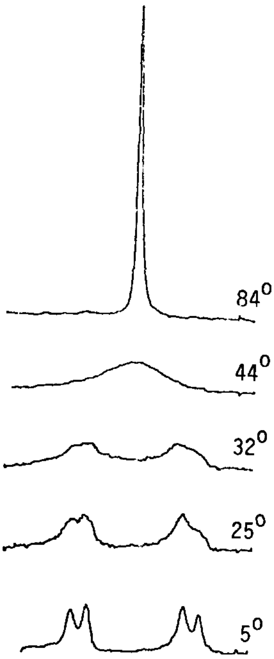


2

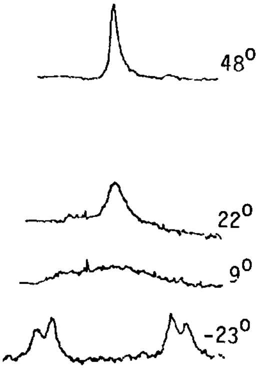
The DNMR behavior of the calixarenes that we have recently reported[1] as well as that published earlier by Kåmmerer[3] and Munch[4] suggest that the cyclic tetramer exists preferentially in a "cone" conformation in which the CH_2 hydrogens are in non-identical environments. If the interconversion between mirror image cone conformations is slow on the NMR time scale the CH_2 resonances appear as a pair of doublets; if it is fast on the NMR time scale they appear as a singlet. In $CDCl_3$ and bromobenzene-d_5 solutions the DNMR behavior of 1 and 2 is so similar that one might believe the two compounds to be identical. However, they are not! The calix[4]arene melts at 344-346°, and its structure has been established, *inter alia,* by x-ray crystallography[5]. The calix[8]-arene melts at 410-412°, and its structure also has been established, *inter alia,* by x-ray crystallography of its octaacetate[6]. Yet, the spectra are almost superimposable, as illustrated by Figs 1-A, 1-B, 1-C, and 1-D, which show the resonances arising from the CH_2 hydrogens. This puzzling result has been responsible for some confusion in the literature and for considerable delay in unravelling the complexities of the product mixtures obtained when *p*-substituted phenols are condensed with paraformaldehyde in the presence of a base. With the discovery that



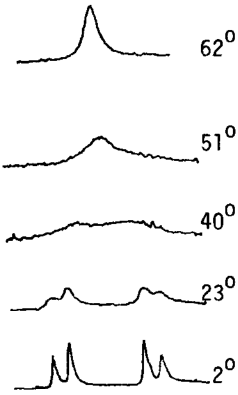
1-A. *p-tert*-butylcalix[4]-arene in bromobenzene-d_5



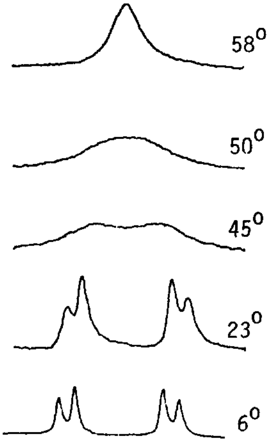
1-B. *p-tert*-butylcalix[8]-arene in bromobenzene-d_5



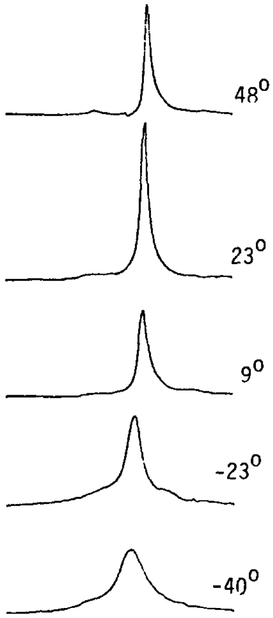
1-E. *p-tert*-butylcalix[4]-arene in pyridine-d_5



1-C. *p-tert*-butylcalix[4]-arene in $CDCl_3$



1-D. *p-tert*-butylcalix[8]-arene in $CDCl_3$



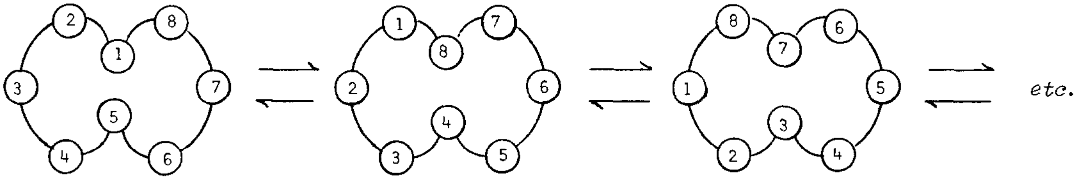
1-F. *p-tert*-butylcalix[8]-arene in pyridine-d_5

Fig. 1. Temperature-dependent ^{1}H-NMR spectra of *p-tert*-butylcalix[4]arene and *p-tert*-butyl calix[8]arene, showing the CH_2 resonance at δ 3.9.

when pyridine-d_5 is used as the solvent the DNMR characteristics of 1 and 2 become entirely different, the reasons for these results become more understandable.

With pyridine-d_5 as the solvent *p-tert*-butylcalix[4]arene (1) manifests DNMR behavior completely analogous to that in $CDCl_3$ or bromobenzene-d_5, except that the coalescence temperature for the CH_2 resonances is lowered from 45-52° to about 15°, as illustrated in Fig 1-E. The spectrum of *p-tert*-butylcalix[8]arene, on the other hand, fails to show any resolution of the CH_2 resonances into doublets down to -53° in pyridine-d_5, as illustrated in Fig. 1-F, and in a mixture of pyridine-d_5 and CS_2 carried to -93° no indication of an impending coalescence point was observed. Clearly, there is a drastic difference in DNMR behavior of 1 and 2 in pyridine-d_5, in contrast to that in $CDCl_3$ and bromobenzene-d_5, and we attribute this to the ability of pyridine to act as a hydrogen bonding solvent. That the calixarenes are very strongly intramolecularly hydrogen bonded is indicated by the OH stretching bands in the IR at 3160 cm^{-1} for 1 and 3230 cm^{-1} for 2 (neat or in $CHCl_3$), and this is in accord with a cone conformation in which intramolecular hydrogen bonding can be maximized. In pyridine, however, it is postulated that the intramolecular hydrogen bonding is disrupted -- to a modest extent in the case of 1 where the cyclic tetrameric structure forces the OH groups to be close whether hydrogen bonded or not, and to a far larger extent in the case of 2 where the cyclic octameric structure does not provide a comparable constraint. The IR spectra in pyridine solution support this contention, showing a single symmetrical envelope with a maximum at 3420 cm^{-1} for 2 and a broader envelope with two maxima for 1, one at 3440 cm^{-1} and the other at 3350 cm^{-1}.

The similarity of the DNMR spectra of 1 and 2 in non-hydrogen bonding solvents, therefore, must be ascribed to an intramolecular hydrogen bonding phenomenon in the cyclic octamer (2) that makes 2 behave, quite fortuitously, as though it were a cyclic tetramer (1) or, as we postulated earlier[1], a transannularly pinched conformation which has the superficial aspect of a pair of cyclic tetramers "stuck" together. A necessary corollary to this postulate is that a pseudorotation is operative which averages the CH_2 *groups* at a rate that is fast on the NMR time scale at the temperatures at which the DNMR studies are conducted, *i.e.*



Otherwise, one would expect to observe more than a single CH_2 resonance at temperatures above the coalescence point.

Employing conventional techniques[7], the τ values were obtained from which the standard free energies of activation were calculated, using the Eyring equation, for the various conformational inversion processes; the results are shown in Table 1. Kammerer and coworkers[3]

Compound	Solvent	ν_{AB}, Hz	τ, sec x 10^3	T_c, ^oC	$\Delta G^\ddagger$, kcal/mole
1	$CDCl_3$	73	6.1	52	15.7
	Bromobenzene-d_5	90	2.4	44	15.2
	Pyridine-d_5	125	3.6	15±4	13.4
2	$CDCl_3$	83	5.4	53	15.7
	Bromobenzene-d_5	85	2.6	43	15.2
	Pyridine-d_5	-	-	-	<9

Table 1. Free energies of activation for conformational inversion of 1 and 2.

obtained a $\Delta G^\ddagger$ value of 15.84 kcal/mole for the conformational inversion of 1, and Munch[4] obtained a $\Delta G^\dagger$ value of 16.03 kcal/mole for the conformational inversion of what was believed to be the *p*-octyl analog of 1 but which we believe to be the *p*-octyl analog of 2. Both values are in reasonably close agreement with those obtained in the present work with 1 and 2. The strength of the intermolecular hydrogen bond for phenol in CCl_4 solution is 4.35 kcal/mole[8], suggesting that the effect of pyridine on the cyclic tetramer is to break approximately half a hydrogen bond (*i.e.* $\Delta\Delta G^\ddagger$ in $CDCl_3$ and pyridine-d_5 is 2.3 kcal/mole) but in the case of the cyclic octamer to break at least a full hydrogen bond (*i.e.* $\Delta\Delta G^\ddagger$ in $CDCl_3$ and pyridine-d_5 is greater than 6.7 kcal/mole).

In a subsequent paper the DNMR behavior of variously substituted calix[4]arenes and calix[8]arenes will be published as well as data on the conformationally more complex calix[6]arenes and bishomooxacalix[4]arenes.

ACKNOWLEDGMENT

We are indebted to the National Institutes of Health for a grant (GM 23534) in support of this research

REFERENCES and FOOTNOTES

1. C.D.Gutsche, B.Dhawan, K.H.No, and R.Muthukrishnan, *J. Am. Chem. Soc.*, *103*, 3782 (1981).
2. The previously reported ^{1}H-NMR spectrum of 2 was stated[1] to be in pyridine-d_5; this is incorrect and should have been stated to be in $CDCl_3$.
3. G.Happel, B.Mathiasch, and H.Kämmerer, *Makromol. Chem.*, *176*, 3317 (1975).
4. J.H.Munch, *Makromol. Chem.*, *178*, 69 (1977).
5. G.D.Andreeti, R.Ungaro, and A.Pochini, *J. Chem. Soc. Chem. Commun.*, 1005 (1979).
6. G.D.Andreeti, R.Ungaro, and A.Pochini, *J. Chem. Soc. Chem. Commun.*, 533 (1981).
7. R.J.Kurland, M.B.Rubin, and W.B.Wise, *J. Chem. Phys.*, *40*, 2426 (1964).
8. G.C.Pimentel and A.I.McClellan, "The Hydrogen Bond", W.H.Freeman and Co., San Francisco, 1960, p. 224, 357.

(Received in USA 3 August 1981)