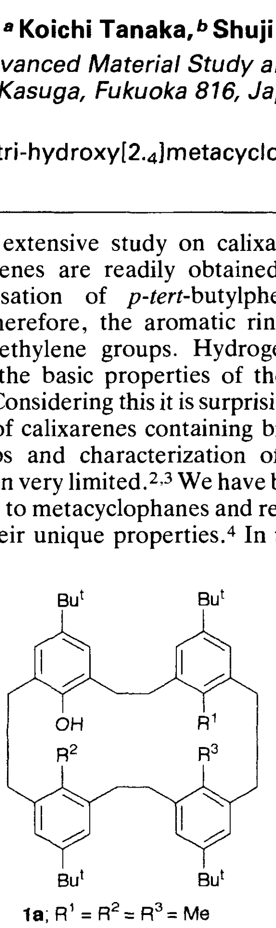
Partially Hydroxy Depleted Calixarene-like Compounds

Akihiko Tsuge,[a] Koichi Tanaka,[b] Shuji Sonda,[b] Shuntaro Mataka[a] and Masashi Tashiro*[a]

[a] *Institute of Advanced Material Study and* [b] *Graduate School of Engineering Sciences, Kyushu University, Kasuga-kohen, Kasuga, Fukuoka 816, Japan*

Mono-, di- and tri-hydroxy[$2._4$]metacyclophanes **1** have been prepared and their modes of hydrogen bonding characterized.

There has been extensive study on calixarenes in the last decade.[1] Calixarenes are readily obtained from the base-induced condensation of *p*-*tert*-butylphenol and formaldehyde, and therefore, the aromatic rings are invariably connected by methylene groups. Hydrogen bonds play a decisive role in the basic properties of the [$1._n$]metacyclophane skeleton. Considering this it is surprising that reports on the preparation of calixarenes containing bridges other than methylene groups and characterization of their hydrogen bonding have been very limited.[2,3] We have been developing a preparative route to metacyclophanes and related compounds and disclosing their unique properties.[4] In the course of our study we also have been interested in metacyclophanes[5,6] consisting of four aromatic rings, which can be considered as analogues of calix[4]arenes. Here we report the synthesis of four different hydroxy-methylmetacyclophanes **1** and their ways of hydrogen bonding.



1a; $R^1 = R^2 = R^3 = Me$
1b; $R^1 = R^2 = Me, R^3 = OH$
1c; $R^1 = R^3 = Me, R^2 = OH$
1d; $R^1 = R^2 = OH, R^3 = Me$
1e; $R^1 = R^2 = R^3 = OH$

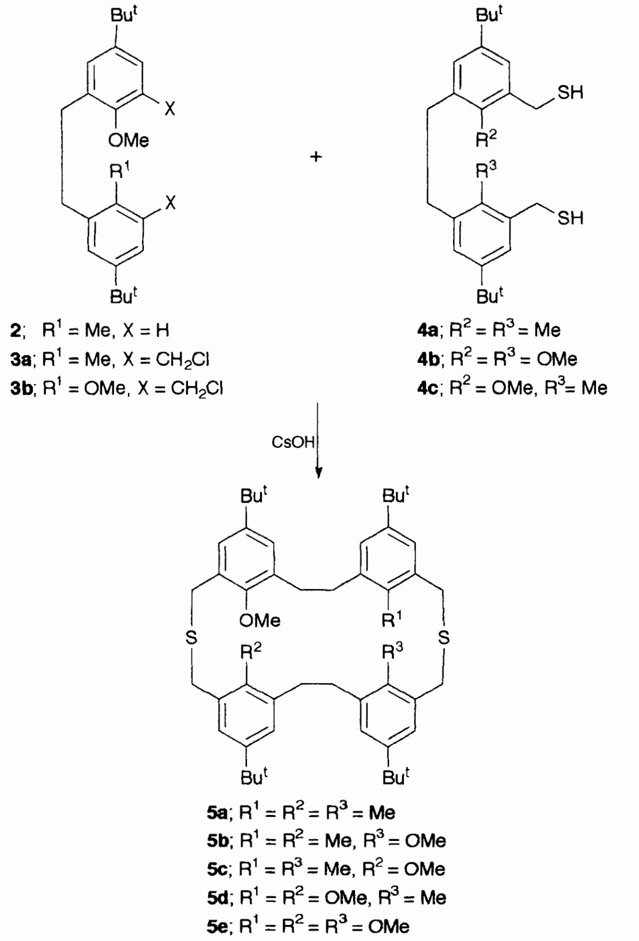
Metacyclophanes **1** were prepared according to our reported method,[6] which can be applied to a large scale synthesis. Grignard coupling of 2-chloromethyl-4-*tert*-butyltoluene and 2-chloromethyl-4-*tert*-butylanisole afforded **2a**. Compounds **2** and **3** were coupled under a high dilution condition. The reaction of **3a** and **4c** gave a mixture of **5b** and **5c**, which was easily separated. **1a–e** were obtained by employing the sulphone extrusion method for **5a–e**, followed by BBr_3-induced demethylation of the corresponding methyl ether cyclophanes.

The results of IR and ^1H NMR spectroscopy of **1a–e** are summarized in Table 1. For calixarenes it is known that the stretching vibration of OH groups at low frequency and the resonance for protons of OH groups at low field can be attributed to circular hydrogen bonding. The ν_{OH} and δ_{OH}

Table 1 Values of ν_{OH} in IR and δ_{OH} in ^1H NMR spectra of **1a–e**

Compound	$\nu_{OH}/cm^{-1\,a}$	$\delta_{OH}{}^b$
1a	3528	3.15
1b	3512	3.17
1c	3480	4.20
1d	3458, 3384	6.20, 8.71
1e	3220	10.4

[a] In KBr. [b] In $CDCl_3$ at 27 °C, 270 MHz.



2; R^1 = Me, X = H
3a; R^1 = Me, X = CH_2Cl
3b; R^1 = OMe, X = CH_2Cl

4a; R^2 = R^3 = Me
4b; R^2 = R^3 = OMe
4c; R^2 = OMe, R^3 = Me

5a; R^1 = R^2 = R^3 = Me
5b; R^1 = R^2 = Me, R^3 = OMe
5c; R^1 = R^3 = Me, R^2 = OMe
5d; R^1 = R^2 = OMe, R^3 = Me
5e; R^1 = R^2 = R^3 = OMe

values in **1b** are almost same as those in **1a**, suggesting that there is no appreciable intramolecular hydrogen bonding. However, **1c** in which two hydroxy groups are located in neighbouring positions, shows a slightly lower-frequency and down-field shift, which implies that a weak hydrogen bond might exist. Compound **1d** gives two peaks at δ 6.20 and 8.71 with the integral intensity of 2H and 1H, respectively. The peak at δ 8.71 can probably be assigned to the proton of the central phenol unit, to which the band at 3384 cm^{-1} could be ascribed. Thus, the other peaks (δ 6.20; 3458 cm^{-1}) are assigned to the external phenol unit. Similar results for partially methylated calix[4]arenes were reported by Shinkai *et al.*[7] In the mono methylated calix[4]arene which corresponds to **1d** two peaks at δ 9.54 and 10.13 for the protons of the hydroxy groups and two ν_{OH} bands (3150 and 3280 cm^{-1}) are observed. They assign the peak at lower magnetic field to the proton of the inner phenol unit which is 'fully' hydrogen bonded, whereas the external phenol units form 'half' hydrogen bonds. **1d** seems to assume two such types of hydrogen bonding, however, the extent of down-field shift is smaller, indicating that hydrogen bonding is weakened in the [2.$_4$]metacyclophane skeleton. The flexible structure of **1** would be expected to destabilize the hydrogen bonding somewhat, however, **1e**[6] shows surprisingly strong hydrogen bonding, judging from the peak at δ 10.40 and the band at 3220 cm^{-1} for the hydroxy groups of **1e**. In conclusion, hydrogen bonding in hydroxy[2.$_4$]metacyclophanes **1a–e**, namely ethylene-bridged calix[4]arenes, was found to be similar to that of calixarenes.

Received, 8th July 1991; Com. 1/03442A

References

1 C. D. Gutsche, *Calixarenes*; *Monographs in Supramolecular Chemistry*, ed. J. F. Stoddart, Royal Society of Chemistry, Cambridge, 1989.
2 B. Dhawan and C. D. Gutsche, *J. Org. Chem.*, 1983, **48**, 1536.
3 C. D. Gutsche, B. Dhawan, K. H. No and R. Muthukrishnan, *J. Am. Chem. Soc.*, 1981, **103**, 3782.
4 M. Tashiro, K. Koya and T. Yamato, *J. Am. Chem. Soc.*, 1982, **104**, 3707; M. Tashiro and T. Yamato, *J. Am. Chem. Soc.*, 1982, **104**, 3701; M. Tashiro and T. Yamato, *J. Chem. Soc., Chem. Commun.*, 1983, 617; M. Tashiro, K. Koya and T. Yamato, *J. Am. Chem. Soc.*, 1983, **105**, 6650; M. Tashiro, T. Yamato and K. Kobayashi, *J. Org. Chem.*, 1984, **49**, 3380; M. Tashiro and T. Yamato, *J. Chem. Soc., Perkin Trans. 1*, 1984, 2165; M. Tashiro, S. Mataka, Y. Takezaki, M. Takeshita, T. Arimura, A. Tsuge and T. Yamato, *J. Org. Chem.*, 1989, **54**, 451; M. Tashiro, H. Fujimoto, A. Tsuge, S. Mataka and H. Kobayashi, *J. Org. Chem.*, 1989, **54**, 2012.
5 M. Tashiro, T. Watanabe, A. Tsuge, T. Sawada and S. Mataka, *J. Org. Chem.*, 1989, **54**, 2632; A. Tsuge, S. Sonda, S. Mataka and M. Tashiro, *Chem. Lett.*, 1990, 1173.
6 M. Tashiro, A. Tsuge, T. Sawada, T. Makishima, S. Horie, T. Arimura, S. Mataka and T. Yamato, *J. Org. Chem.*, 1990, **55**, 2404.
7 K. Araki, K. Iwamoto, S. Shinkai and T. Matsuda, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 3480.