Monatsh Chem (2010) 141:19–22
DOI 10.1007/s00706-009-0218-3

ORIGINAL PAPER

Protonation of electroneutral *p-tert*-butylcalix[4]arenetetraacetic acid

Jaroslav Kříž · Jiří Dybal · Emanuel Makrlík · Jan Budka · Petr Vaňura

Received: 4 September 2009 / Accepted: 22 October 2009 / Published online: 20 November 2009

Abstract Using ^{1}H NMR spectroscopy together with density functional theoretical calculations, it is shown that electroneutral *p-tert*-butylcalix[4]arenetetraacetic acid forms an equimolar complex with a proton in the form of the H_3O^+ ion in nitrobenzene-d_5. Protons were offered by hydrogen bis(1,2-dicarbollyl)cobaltate and converted to hydroxonium ions by traces of water. In the resulting complex, the H_3O^+ cation is bound by strong hydrogen bonds to two phenoxy oxygen atoms of the parent calix[4]arene ligand and to one carbonyl oxygen of the corresponding COOH group of this ligand.

Keywords Calixarenes · Macrocycles · Protonation · Ab initio calculations · Complex structure

Introduction

Calix[*n*]arenes are a well-known family of macrocyclic molecules with many potential applications in various branches of chemistry. Because of their simple one-pot preparation, easy derivatization, and unique complexation abilities, calix[*n*]arenes are widely used as building blocks for the construction of more sophisticated molecular systems. Their unique three-dimensional pre-organization make them very attractive as the receptors for the complexation of cations, anions, and even neutral molecules. Calix[*n*]arenes find applications as selective binders and carriers, as analytical sensors, as catalysts, and as model structures for biomimetic studies [1, 2]. In the field of host–guest chemistry, many studies have focussed on the binding ability of calixarene derivatives with carbonyl groups at their lower rims toward metal ions, predominantly alkali and alkaline-earth, but also transition and heavy metal cations [3–11], and even toward H_3O^+ [12–19].

Recently, deprotonation of calix[*n*]arenes in which $n = 4$, 6, and 8 has been studied using acetonitrile as the solvent [20]. In this communication, on the basis of ^{1}H NMR spectroscopy and DFT quantum mechanical calculations, we suggest the most probable structure of protonated *p-tert*-butylcalix[4]arenetetraacetic acid.

Results and discussion

NMR measurements

Similarly to our previous studies on protonation of valinomycin [21, 22], we used hydrogen bis(1,2-dicarbollyl)cobaltate (HDCC) as a versatile proton source [23]. The protons were converted to hydroxonium ions H_3O^+ by traces of water in the system under study. In order to ensure full ionization of HDCC we had to use a solvent with a rather high dielectric constant, e.g. nitrobenzene ($\varepsilon = 35.6$), acetonitrile ($\varepsilon = 36.6$), or dimethylformamide ($\varepsilon = 38.3$). Among these, nitrobenzene-d_5 proved to give least equivocal results in our previous works as it does not form inclusion complexes with calixarenes and does not

J. Kříž · J. Dybal
Institute of Macromolecular Chemistry,
Academy of Sciences of the Czech Republic,
Prague, Czech Republic

E. Makrlík (✉)
Faculty of Applied Sciences, University of West Bohemia,
Pilsen, Czech Republic
e-mail: makrlik@centrum.cz

J. Budka · P. Vaňura
Institute of Chemical Technology, Prague, Czech Republic
e-mail: petr.vanura@vscht.cz

compete perceptibly with their proton binding. We therefore chose this solvent for use in the present study.

^{1}H NMR spectra of free electroneutral ligand **1** (Scheme 1) and its different mixtures with HDCC in nitrobenzene-d_5 are depicted in Fig. 1. The spin-echo technique was used in order to remove obscuring broad signals of HDCC,which was present in large excess. In Fig. 1, Ar means aromatic protons, CH_a and CH_e are axial and equatorial protons of the macrocycle CH_2 groups, CH_2 is the signal of carboxyl-bearing CH_2 groups, and *t*-Bu denotes *p*-*tert*-butyl protons. The signal marked by the asterisk corresponds to the protons involved in fast proton exchange between free and bound hydrated protons, water molecules, and protons of COOH groups.

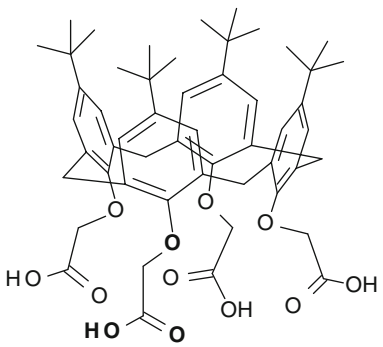
It is necessary to emphasize that the formation of a complex of **1** with the hydrated proton, H_3O^+, leads to a relative chemical shift of virtually all the signals, indicating a slight change in the conformation of the parent calix[4]arene ligand **1**. In particular, the mutual nearing of the signals of the axial and equatorial protons in the macrocyclic CH_2 groups indicates slight opening of the calix[4]arene cup [24], probably because of the shorter distance of the coordinating groups at the lower rim. The increase of the individual shifts between $\beta = 1$ and 10 ($\beta = [H_3O^+]_0/[\mathbf{1}]_0$) shows, however, that the equilibrium $\mathbf{1} + H_3O^+ \rightleftarrows \mathbf{1} \cdot H_3O^+$ is not entirely on the side of the $\mathbf{1}{\cdot}H_3O^+$ complex. Assuming that the resulting complex is equimolecular ($\mathbf{1}{\cdot}H_3O^+$), the considered equilibrium should follow the usual relationship (Eq. 1):

$$K = \frac{[\mathbf{1} \cdot H_3O^+]}{[\mathbf{1}][H_3O^+]} \tag{1}$$

Under conditions of fast exchange between free and coordinated **1**, the actual chemical shift of any signal is a weighted average of the shifts corresponding to the exchanging sites. Thus, the actual relative shift is $\Delta\delta = \alpha\Delta\delta_{max}$, where $\alpha = [\mathbf{1}{\cdot}H_3O^+]/[\mathbf{1}]_0$ and $\Delta\delta_{max}$, obtained by extrapolation, is the maximum relative shift corresponding to the pure complex. Using Eq. (1), $\Delta\delta$ can be expressed by means of Eq. (2), where β was already defined above:

$$\Delta\delta = \Delta\delta_{max} \times \frac{1 + K[\mathbf{1}]_0(1+\beta) - \sqrt{\{1 + K[\mathbf{1}]_0(1+\beta)\}^2 - 4K^2[\mathbf{1}]_0^2\beta}}{2K[\mathbf{1}]_0} \tag{2}$$

It is evident that both K and $\Delta\delta_{max}$ can be obtained by fitting Eq. (2) to the experimental values of $\Delta\delta$. Moreover, Fig. 2 presents $\Delta\delta$ of individual signals in the proton spectra of **1**/HDCC mixtures and the fitting curves. As one can see, the fitting is quite good and offers values of K in a relatively narrow range. Thus, the average value of K is 113.6 ± 0.8 M^{-1}.



Scheme 1

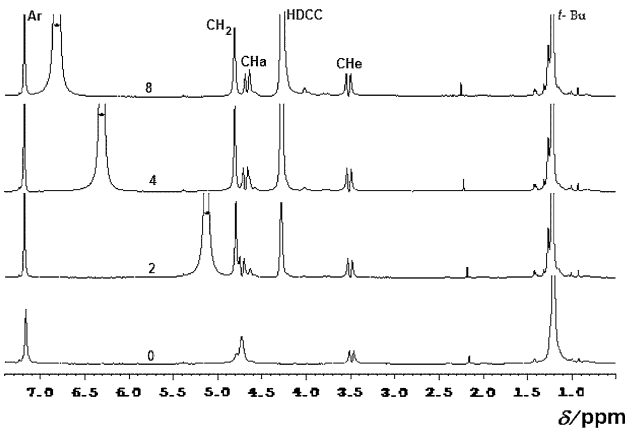


Fig. 1 300.13 MHz ^{1}H NMR spin-echo spectra of **1** (5×10^{-3} M) and its mixtures with the indicated number of equivalents of HDCC (nitrobenzene-d_5, 294 K)

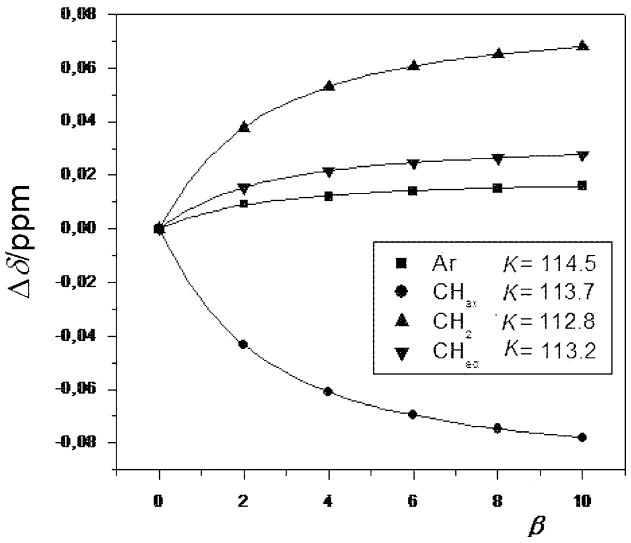


Fig. 2 Experimental relative shifts $\Delta\delta$ of individual signals of **1** in its mixtures with HDCC and the fits obtained using Eq. (2) (the fitted values of K in the graph)

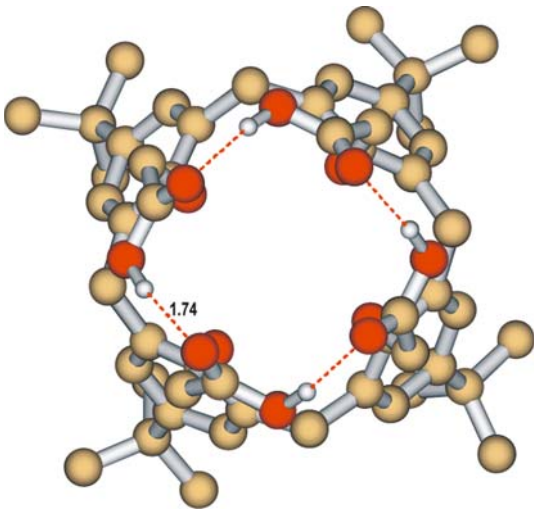


Fig. 3 DFT optimized structure of free ligand **1** (B3LYP/6-31G(d)) (hydrogen atoms omitted for clarity except the four hydrogens taking part in four internal hydrogen bonds between the nearest COOH groups)

Quantum mechanical calculations

The quantum mechanical calculations were carried out at the density functional level of theory (DFT, B3LYP functional) using the Gaussian 03 suite of programs [25]. The 6-31G(d) basis set was used and the optimizations were unconstrained. Although a possible effect of the polar solvent on the detailed structures of **1** and **1**·H_3O^+ could be imagined, our quantum calculations in similar cases, performed analogously, showed very good agreement of experiment with theory [21, 26–30].

In the model calculations, we optimized the molecular geometry of the parent calix[4]arene ligand **1** and its complex with H_3O^+. The optimized structure of **1** is depicted in Fig. 3. From this figure it follows that the most stable conformation of the mentioned ligand **1** is a *cone* structure with C_4 symmetry. It is necessary to emphasize that this structure is supported by four strong internal hydrogen bonds between the nearest COOH groups of free ligand **1**.

In Fig. 4, two projections of the **1**·H_3O^+ complex obtained by the full DFT optimization are illustrated together with the lengths of the corresponding hydrogen bonds (in Å). It is evident that the *cone* structure of the parent calix[4]arene ligand **1** in the cationic complex species **1**·H_3O^+ is preserved; however, the four internal hydrogen bonds between the nearest COOH groups are broken in the resulting **1**·H_3O^+ complex. In this complex, the H_3O^+ ion is bound by strong hydrogen bonds to two phenoxy oxygen atoms of **1** (1.76 and 1.59 Å) and to one carbonyl oxygen of the respective COOH group of **1** (1.67 Å).

Finally, the calculated binding energy of the **1**·H_3O^+ cationic species is −368.3 kJ mol^{-1}, which confirms formation of the complex.

Experimental

The electroneutral macrocyclic compound *p-tert*-butylcalix[4]arenetetraacetic acid (**1**, Scheme 1) was kindly supplied by Prof. V. I. Kalchenko, Institute of Organic Chemistry, NASU, Kiev, Ukraine. Nitrobenzene-d_5 was purchased from Fluka, Buchs, Switzerland. Preparation of hydrogen bis(1,2-dicarbollyl)cobaltate (HDCC) [23] was described elsewhere [21].

^{1}H NMR spectra in nitrobenzene-d_5 were measured in a quadrature detection mode at 300.13 MHz with an upgraded Bruker Avance DPX300 spectrometer collecting 32 kpoints in 128 scans. All NMR measurements were carried out at a temperature of 294 K.

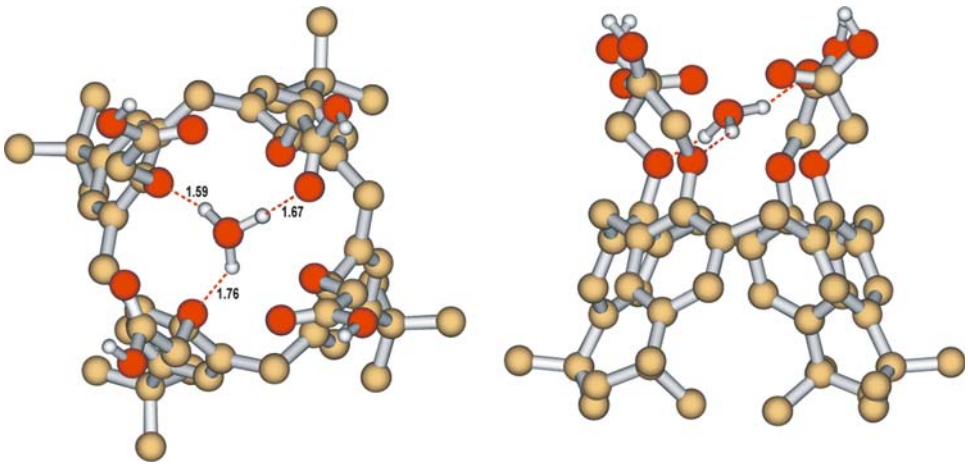


Fig. 4 Two projections of DFT optimized structure of the **1**·H_3O^+ complex (B3LYP/6-31G(d)) (hydrogen atoms omitted for clarity except the four hydrogens of the corresponding COOH groups and those of H_3O^+). H-bond lengths of H_3O^+ to phenoxy oxygens of **1**: 1.76 and 1.59 Å; H-bond length of H_3O^+ to carbonyl oxygen of **1**: 1.67 Å

Acknowledgments This work was supported by the Academy of Sciences of the Czech Republic, project T 400500402, and by the Czech Ministry of Education, Youth, and Sports, projects MSM 4977751303, MSM 6046137301, and MSM 6046137307.

References

1. Gutsche CD (1998) Calixarenes Revisited. The Royal Society of Chemistry, Cambridge
2. Böhmer V (1995) Angew Chem Int Ed 34:713
3. Arduini A, Pochini A, Reverberi S, Ungaro R (1986) Tetrahedron 42:2089
4. Arduini A, Ghidini E, Pochini A, Ungaro R, Andreetti GD, Calestani G, Ugozzoli F (1988) J Inclusion Phenom Macrocyclic Chem 6:119
5. Arnaud-Neu F, Collins EM, Deasy M, Ferguson G, Harris SJ, Kaitner B, Lough AJ, McKervey MA, Marques E, Ruhl BL, Schwing-Weill MJ, Seward EM (1989) J Am Chem Soc 111:8681
6. Arnaud-Neu F, Barrett G, Harris SJ, Owens M, McKervey MA, Schwing-Weill MJ, Schwinté P (1993) Inorg Chem 32:2644
7. Ohto K, Murakami E, Shinohara T, Shiratsuchi K, Inoue K, Iwasaki M (1997) Anal Chim Acta 341:275
8. Ye Z, He W, Shi X, Zhu L (2001) J Coord Chem 54:105
9. Danil de Namor AF, Chahine S, Kowalska D, Castellano EE, Piro OE (2002) J Am Chem Soc 124:12824
10. Marcos PM, Ascenso JR, Segurado MAP, Pereira JLC (2002) J Inclusion Phenom Macrocyclic Chem 42:281
11. Marcos PM, Félix S, Ascenso JR, Segurado MAP, Pereira JLC, Khazaeli-Parsa P, Hubscher-Bruder V, Arnaud-Neu F (2004) New J Chem 28:748
12. Makrlík E, Vaňura P (2006) Monatsh Chem 137:1185
13. Dybal J, Makrlík E, Vaňura P (2007) Monatsh Chem 138:541
14. Kříž J, Dybal J, Makrlík E, Budka J, Vaňura P (2007) Monatsh Chem 138:735
15. Dybal J, Makrlík E, Vaňura P, Budka J (2007) Monatsh Chem 138:1239
16. Dybal J, Makrlík E, Vaňura P, Selucký P (2008) Monatsh Chem 139:1175
17. Dybal J, Makrlík E, Budka J, Vaňura P (2008) Monatsh Chem 139:1353
18. Makrlík E, Dybal J, Vaňura P (2009) Monatsh Chem 140:29
19. Makrlík E, Dybal J, Budka J, Vaňura P (2009) Monatsh Chem 140:1155
20. Cunningham IA, Woolfall M (2005) J Org Chem 70:9248
21. Kříž J, Dybal J, Makrlík E (2006) Biopolymers 82:536
22. Kříž J, Makrlík E, Vaňura P (2006) Biopolymers 81:104
23. Makrlík E, Vaňura P (1985) Talanta 32:423
24. Gutsche CD (1995) Aldrichimica Acta 28:3
25. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Montgomery JA, Vreven T, Kudin KN, Burant JC, Millam JM, Iyengar SS, Tomasi J, Barone V, Mennucci B, Cossi M, Scalmani G, Rega N, Petersson GA, Nakatsuji H, Hada M, Ehara M, Toyota K, Fukuda R, Hasegawa J, Ishida M, Nakajima T, Honda Y, Kitao O, Nakai H, Klene M, Li X, Knox JE, Hratchian HP, Cross JB, Bakken V, Adamo C, Jaramillo J, Gomperts R, Stratmann RE, Yazyev O, Austin AJ, Cammi R, Pomelli C, Ochterski JW, Ayala PY, Morokuma K, Voth GA, Salvador P, Dannenberg JJ, Zakrzewski VG, Dapprich S, Daniels AD, Strain MC, Farkas O, Malick DK, Rabuck AD, Raghavachari K, Foresman JB, Ortiz JV, Cui Q, Baboul AG, Clifford S, Cioslowski J, Stefanov BB, Liu G, Liashenko A, Piskorz P, Komaromi I, Martin RL, Fox DJ, Keith T, Al-Laham MA, Peng CY, Nanayakkara A, Challacombe M, Gill PMW, Johnson B, Chen W, Wong MW, Gonzalez C, Pople JA (2004) Gaussian 03, Revision C.02. Gaussian, Inc, Wallingford, CT
26. Kříž J, Dybal J, Makrlík E, Vaňura P, Lang J (2007) Supramol Chem 19:419
27. Kříž J, Dybal J, Makrlík E, Vaňura P (2008) Supramol Chem 20:387
28. Kříž J, Dybal J, Makrlík E, Budka J, Vaňura P (2008) Supramol Chem 20:487
29. Kříž J, Dybal J, Makrlík E, Budka J (2008) J Phys Chem A 112:10236
30. Kříž J, Dybal J, Makrlík E, Budka J, Vaňura P (2009) J Phys Chem A 113:5896