Monatshefte für Chemie 138, 735–740 (2007)
DOI 10.1007/s00706-007-0677-3
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Protonated Tetramethyl *p-tert*-Butylcalix[4]arene Tetraketone: NMR Evidence and Probable Structures

Jaroslav Kříž[1], **Jiří Dybal**[1], **Emanuel Makrlík**[2], **Jan Budka**[3], and **Petr Vaňura**[3,*]

[1] Academy of Sciences of the Czech Republic, Institute of Macromolecular Chemistry, Prague, Czech Republic
[2] Faculty of Applied Sciences, University of West Bohemia, Pilsen, Czech Republic
[3] Institute of Chemical Technology, Prague, Czech Republic

Received February 2, 2007; accepted (revised) March 8, 2007; published online May 31, 2007

Summary. Both NMR spectra in nitrobenzene-d_5 and high-precision quantum mechanical DFT calculations proved that tetramethyl *p-tert*-butylcalix[4]arene tetraketone binds hydroxonium cation H_3O^+ quite strongly to form an equimolar complex. Three different structures of the resulting complex species were indicated by the NMR spectra and the DFT calculations.

Keywords. Calixarenes; Macrocycles; Protonation; NMR; DFT.

Introduction

Calixarenes are macrocyclic compounds, which are not easily available on a large scale, yet offer nearly boundless possibilities for chemical modification [1]. This makes them highly attractive as building blocks for more sophisticated and elaborate host molecules. Calixarenes find applications as selective binders and carriers, as analytical sensors, as catalysts, and model structures for biomimetic studies [2].

Recently, experimental evidence for the *p-tert*-butylcalix[4]arenetetrakis(*N*,*N*-diethylacetamide) $\cdot H_3O^+$ complex species has been advanced [3] and its complex structure has been derived [4]. In the present work, NMR evidence for protonated tetramethyl *p-tert*-butylcalix[4]arene tetraketone (**1** $\cdot H_3O^+$) in nitrobenzene-d_5 is presented.

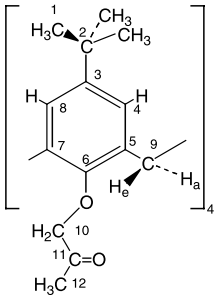
* Corresponding author. E-mail: petr.vanura@vscht.cz

Results and Discussion

NMR Spectra

Similarly as in our previous studies on protonation of some electroneutral ionophores [5–7], we used hydrogen bis(1,2-dicarbollyl) cobaltate (H*DCC*) as a versatile proton source [8]. The protons were converted to the hydroxonium ions H_3O^+ by traces of water in the system under study. In order to ensure full ionization of H*DCC* 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 them, nitrobenzene-d_5 proved to give least equivocal results in our former works as it does not form inclusion complexes with calixarenes and does not compete perceptibly with their proton binding. Therefore, we have chosen this solvent in the present study.

After mixing equimolar amounts of H*DCC* and ligand **1** (*cf.* Scheme 1) in nitrobenzene-d_5 at 296 K, slight changes in the NMR spectra of the mixture set on immediately. They gradually evolved and reached the final equilibrium state in about 48 h. The 300.13 MHz ^{1}H NMR spectra of a 0.01 *M* solution of **1** and of an equimolar mixture of **1** with H*DCC* in the final equilibrium state are compared in Fig. 1, the analogous 75.5 MHz ^{13}C NMR spectra are depicted in Fig. 2. The signal assignment corresponds to Scheme 1, where the protons have



Tetramethyl *p-tert*-butylcalix[4]arene tetraketone (**1**)

Scheme 1

the same numbering as the carbons they are attached to.

Closer inspection of the spectra shown in Figs. 1 and 2 suggests the presence of at least three different structures, each of them differing from that of **1**. Using a combination of 2D ^{1}H N*O*ESY, ^{1}H-^{13}C HSQC, and ^{1}H-^{13}C HMBC spectra, one can assign the signals A + E, B + C, and D to one of three molecular structure types populated approximately in the ratio 1:0.6:0.8. As confirmed by a PFG NMR measurement, all three structure types have almost identical self-diffusion coefficients ($1.96 \pm 0.02\,m^2\,s^{-1}$), *i.e*. they not only have the same molecular weight, but even their overall molecular shape must be similar. In the first (*i.e*. A + E) and second (*i.e*. B + C) structure types, protons 4 and 8 are equivalent in all four aryl groups of the calixarene part, while the two pairs of mutually opposite aryl groups are not. On the other hand, the four aryl groups in the last structure type (signals D) including the attached *t*-butyl groups are apparently equivalent, however, protons 4 and 8 in them are not (as shown, the signals have different chemical shifts and are split by mutual spin coupling). Intuitively, one could conclude that the first two molecular types (in particular A + E) adopt a *pinched cone* conformation [2], in contrast to the considered last type. The *pinched cone* conformation is certainly adopted by free ligand **1**, in which it is rapidly averaged by a fast internal motion [7] so that all four units in this macrocycle appear to be equiva-

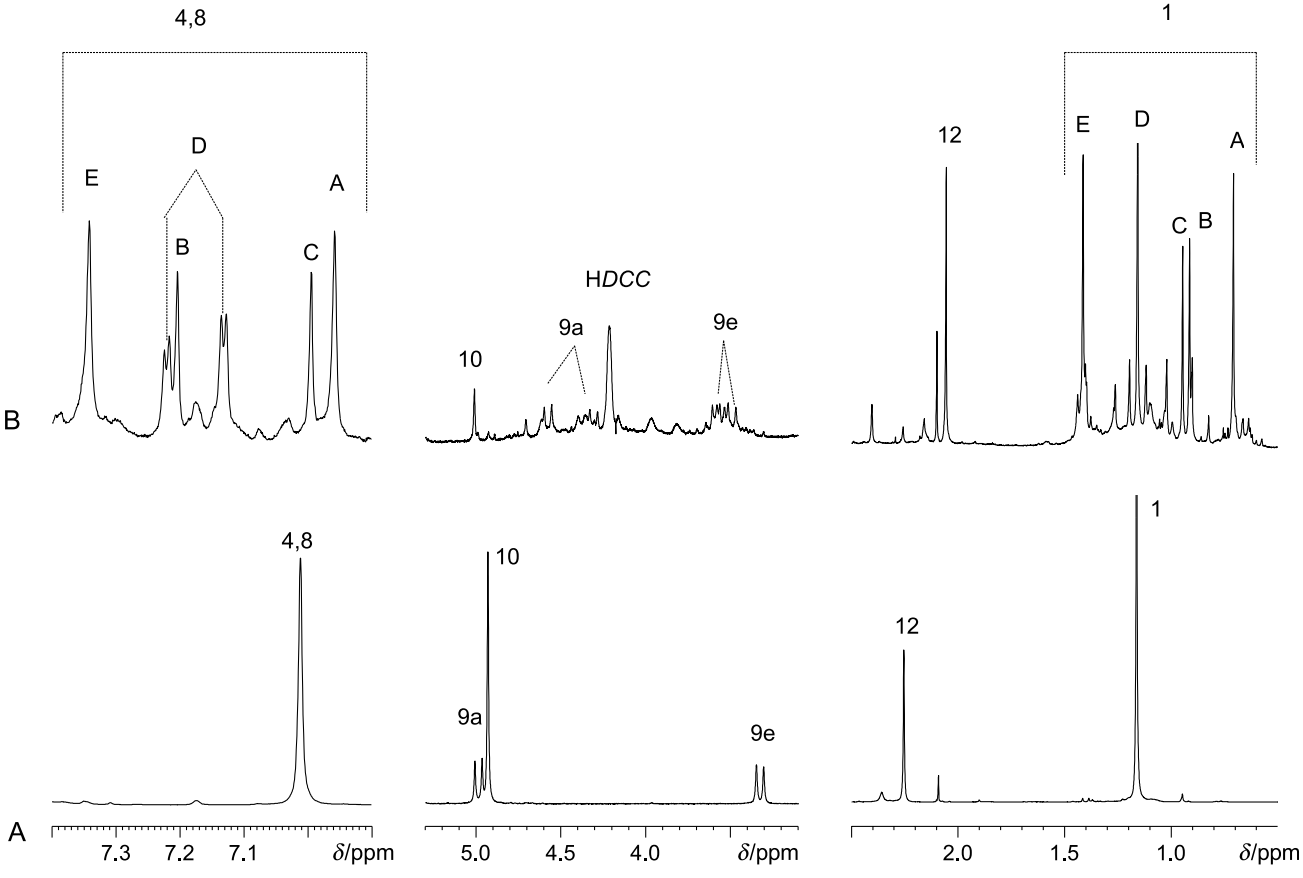


Fig. 1. 300.13 MHz ^{1}H NMR spectra of 0.01 *M* **1** (A) and an equimolar equilibrium mixture of **1** with H*DCC* after 48 h (B) (nitrobenzene-d_5, 296 K)

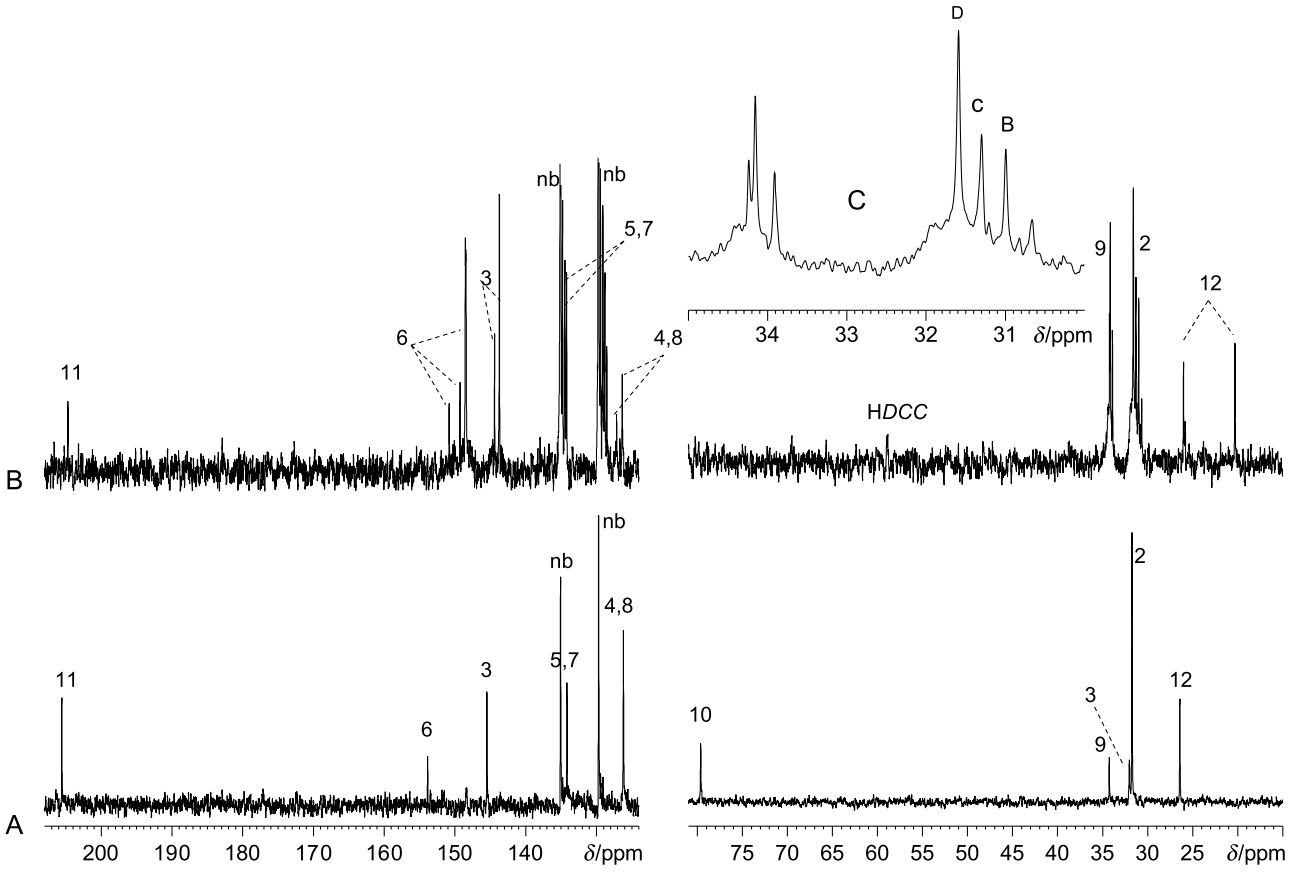


Fig. 2. 75.5 MHz ^{13}C NMR DEPT45 spectra of 0.01 *M* **1** (A) and an equimolar equilibrium mixture of **1** with H*DCC* after 48 h (B, methyl region expanded in C) (nitrobenzene-d_5, 296 K)

lent in both ^{1}H and ^{13}C NMR spectra (*cf.* Figs. 1A and 2A). In the three visible forms of the complex $\mathbf{1} \cdot H_3O^+$, such fast averaging is precluded by the coordination of the groups (C=O and O–Ar) at the lower rim. There is a moderately slow internal motion in these structures as discussed below.

In spite of the *pinched cone* form of two of the visible structures of $\mathbf{1} \cdot H_3O^+$, their aromatic cavity is markedly more open than in **1**. This is clearly documented [7] by the large shifts of signals of equatorial 9e (0.24 and 0.16 ppm) and axial 9a (−0.41 and −0.68 ppm) CH_2 protons. The relative opening of the calixarene cup indicates that a rather strong coordination pulls the polar groups at the lower rim together. This certainly concerns the C=O groups, as shown by the −0.87 ppm shift of the signal 11 in ^{13}C NMR, as well as somewhat surprising shifts of 12, namely −0.20 ppm in ^{1}H NMR or −0.41 and even −6.14 ppm in ^{13}C NMR. In this context it should be emphasized that the phenoxy oxygen atoms of **1** are also included in this coordination as shown by the upfield shifts of signals 6 in the carbon spectrum.

In addition to all these features, there must be substantial slow internal motion in the mentioned $\mathbf{1} \cdot H_3O^+$ structures. Strong broadening is observed both in proton and carbon spectra, obscuring some of the signals. As seen in Fig. 2C, even part of the signals of carbon 1 is severely broadened. Signal 10, entirely missing in the carbon spectrum, is too weak in the proton spectrum of the $\mathbf{1} \cdot H_3O^+$ complex species; the intensity of 11 is also lowered, part of the signal being probably extremely broadened. All this indicates a moderately fast exchange between several H_3O^+ – holding complex structures. The corresponding conformational changes of the aromatic part of the complex $\mathbf{1} \cdot H_3O^+$ apparently lag behind this motion so that we are able to see at least some of the $\mathbf{1} \cdot H_3O^+$ structures in the spectra.

Considering the broadening of signals and the chemical shifts involved, the logarithm of the correlation time of exchange ($\log(\tau_{ex})$) between

individual forms of the $\mathbf{1} \cdot H_3O^+$ complex can be estimated to be in the interval between -2.0 and 3.0 (τ_{ex} being in s), the lower bound applying to the intramolecular motions of the bound H_3O^+, the upper one corresponding to the exchange between free and complexed **1** or different structural forms of the complex under study.

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 [9]. The 6-31G(d) basis set was used and the optimization was unconstrained. The optimizations were done *in vacuo* as no reliable correction for the influence of the solvent is at hand at this precision level. Although possible influence of a polar solvent on the detailed structures of **1** and $\mathbf{1} \cdot H_3O^+$ could be imagined, our quantum calculations in similar cases, performed in analogous way, showed very good agreement of experiment with theory [5–7].

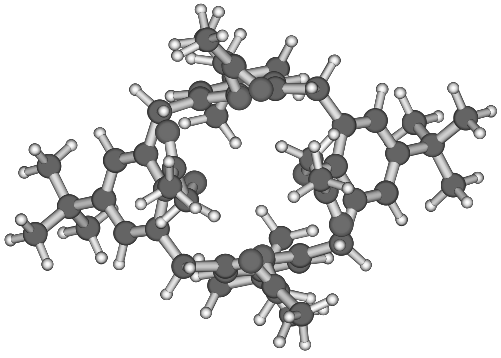


Fig. 3. DFT optimized structure of free **1** (*B3LYP*/6-31G(d))

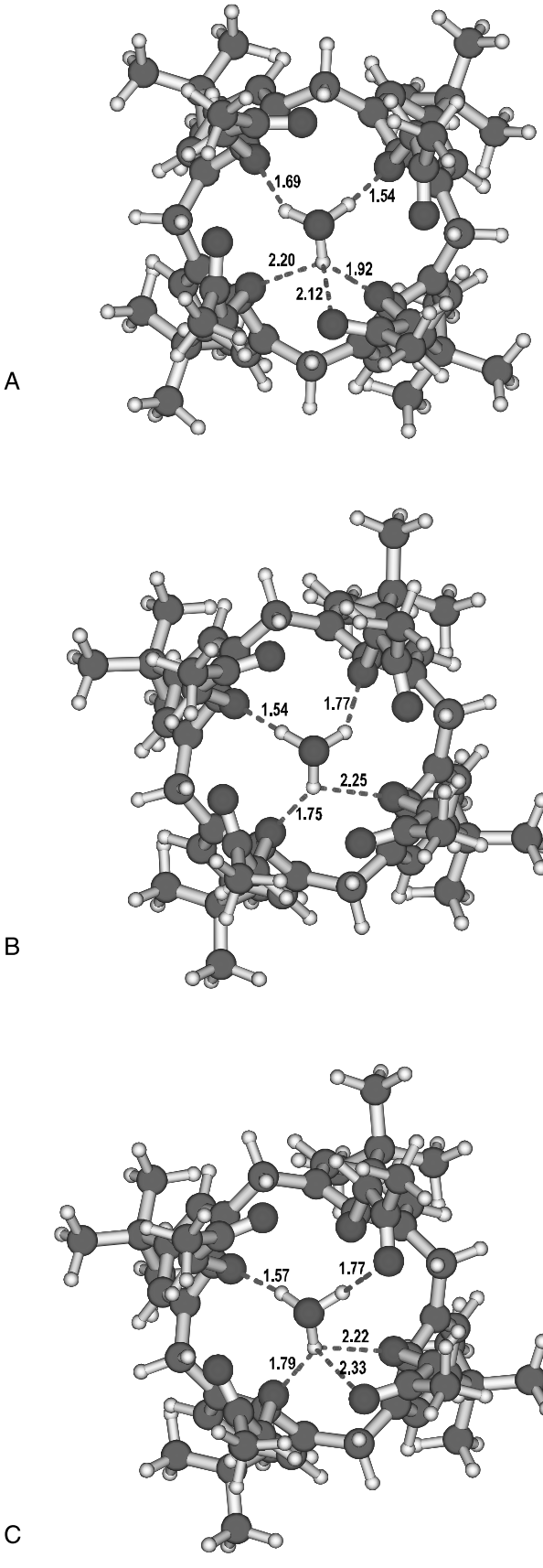


Fig. 4. DFT optimized structures (A, B, C) of the $\mathbf{1} \cdot H_3O^+$ complex (*B3LYP*/6–31G(d)) with the lengths of the corresponding hydrogen bonds. Structure A: the lengths of H-bonds of H_3O^+ to phenoxy oxygens of **1**: 1.69, 1.54, 1.92, and 2.20 Å; the length of H-bond of H_3O^+ to carbonyl oxygen of **1**: 2.12 Å
Structure B: the lengths of H-bonds of H_3O^+ to phenoxy oxygens of **1**: 1.54, 1.77, 2.25, and 1.75 Å
Structure C: the lengths of H-bonds of H_3O^+ to phenoxy oxygens of **1**: 1.57, 2.22, and 1.79 Å; the lengths of H-bonds of H_3O^+ to carbonyl oxygens of **1**: 1.77 and 2.33 Å

In the model calculations, we optimized molecular geometry of the parent calixarene ligand **1** and its complex with H_3O^+. The optimized structure of **1** is shown in Fig. 3. From this figure it follows that the most stable conformation of the calixarene ligand **1** forms a *pinched cone* structure [2] with a C_2 symmetry.

In Fig. 4, the structures A, B, and C of the $\mathbf{1} \cdot H_3O^+$ complex obtained by DFT optimization are illustrated together with the lengths of the corresponding hydrogen bonds (in Å). Compared to free ligand **1** (Fig. 3), the calixarene part of the complex $\mathbf{1} \cdot H_3O^+$ is more open and very close to the C_4 symmetry. The hydroxonium ion H_3O^+, placed in the coordination cavity formed by the calixarene lower-rim groups, is bound by strong hydrogen bonds to the phenoxy oxygen atoms of **1** (structures A, B, and C) and also to one carbonyl oxygen of **1** (structure A) or two carbonyl oxygens of **1** (structure C).

Finally, the calculated stabilization energy of the $\mathbf{1} \cdot H_3O^+$ complex, 406.7 kJ mol^{-1}, is the same for all three optimized structures depicted in Fig. 4 and besides, this value unambiguously confirms the very high stability of the considered complex species.

In conclusion, both NMR spectra and high-precision quantum mechanical DFT calculations confirm that hydroxonium ion H_3O^+ is bound very strongly to the keto-modified calixarene ligand **1** to form the $\mathbf{1} \cdot H_3O^+$ complex. At least three different structures of the resulting complex $\mathbf{1} \cdot H_3O^+$ are indicated by the NMR spectra and the DFT calculations. In very good agreement of experiment with theory, the hydroxonium ion H_3O^+ is bound especially to phenoxy oxygen atoms or carbonyl oxygens of the calixarene ligand **1**, thus forcing the calixarene cup to open into a less *pinched cone* conformation. In a slight contrast to the calculations, the NMR spectra show that the calixarene parts in two of the considered structures of $\mathbf{1} \cdot H_3O^+$ still adopt a slightly *pinched cone* conformation in spite of their wider openness relative to free ligand **1**. The NMR spectra also give evidence for a moderately fast exchange between individual structures of the $\mathbf{1} \cdot H_3O^+$ complex. This motion is faster at the lower rim part of this complex, the conformation changes of the calixarene cup somewhat lagging behind it. This conclusion is in good agreement with the calculations finding all three optimal complex structures to be on the same energy level. Although the large stabilization energy of the $\mathbf{1} \cdot H_3O^+$ complex (406.7 kJ mol^{-1}) precludes easy liberation of the hydroxonium cation H_3O^+ out of the lower rim coordination cavity, this does not hinder concerted motions of H_3O^+ within it.

Experimental

Tetramethyl *p-tert*-butylcalix[4]arene tetraketone (**1**) was synthesized by the procedure described in Ref. [10]. Nitrobenzene-d_5 was supplied by Fluka, Buchs, Switzerland and was used as obtained. Cesium bis(1,2-dicarbollyl) cobaltate (Cs*DCC*) was prepared in the Institute of Inorganic Chemistry, Řež, Czech Republic, using the method published by *Hawthorne et al.* [11]. In order to obtain its hydrogen analogue, H*DCC*, an 0.2 *M* solution of Cs*DCC* in nitrobenzene was twice shaken with equal volumes of 15% *v*/*v* *n*-propanol in 1 *M* H_2SO_4 in distilled H_2O, followed by tenfold equilibrium shaking with equal amounts of 1 *M* H_2SO_4 and two equilibrations with distilled H_2O. After separation of the phases, nitrobenzene was removed by distillation. The product was dried under high vacuum to a constant weight for two weeks.

^{1}H and ^{13}C NMR spectra were measured in a quadrature detection mode at 300.13 and 75.45 MHz with an upgraded Bruker Avance DPX300 spectrometer; 32 and 64 kpoints were carried out for ^{1}H and ^{13}C NMR collecting 64 and 25000 or more scans, respectively. ^{13}C NMR measurements were performed in an inverse-gated (N*O*E uninfluenced) mode, with a $\pi/6$ pulse and 10.8 s repetition time; exponential weighting (lb = 1 Hz) was used before *Fourier* transform. In homonuclear 2D ^{1}H spectra (COSY, LR-COSY, DQF-COSY, N*O*ESY) and heteronuclear ^{1}H–^{13}C 2D (HSQC and HMBC), 1028 points in F2 and 256 increments in F1 dimensions were measured using a *z*-gradient inverse-detection probe.

All NMR measurements were carried out at a temperature of 296 K.

Acknowledgement

The present work was supported by the Academy of Sciences of the Czech Republic, Project T400500402, and the Czech Ministry of Education, Youth, and Sports, Projects MSM 4977751303 and MSM 6046137307.

References

[1] Böhmer V (1995) Angew Chem **34**: 713
[2] Gutsche CD (1998) Calixarenes Revisited, The Royal Society of Chemistry, Cambridge
[3] Makrlík E, Vaňura P (2006) Monatsh Chem **137**: 1185
[4] Dybal J, Makrlík E, Vaňura P (2007) Monatsh Chem **138** (in press)
[5] Kříž J, Makrlík E, Vaňura P (2006) Biopolymers **81**: 104
[6] Kříž J, Dybal J, Makrlík E (2006) Biopolymers **82**: 536
[7] Kříž J, Dybal J, Makrlík E, Vaňura P (2007) Supramol Chem (in press)
[8] Makrlík E, Vaňura P (1985) Talanta **32**: 423
[9] 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

[10] 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

[11] Hawthorne MF, Young DC, Andrews TD, Howe DV, Pilling RL, Pitts AD, Reintjes M, Warren LF, Wegner PA (1968) J Am Chem Soc **90**: 879