Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Binding Studies on the Control of the Conformation and Self-assembly of a Calix[4]arenedicarboxylic Acid through Hydrogen Bonding Interactions

Hidekazu Miyaji[a]; Miroslav Dudic[b]; James H. R. Tucker[a]; Ivan Prokes[a]; Mark E. Light[c]; Thomas Gelbrich[c]; Michael B. Hursthouse[c]; Ivan Stibor[b]; Pavel Lhoták[b]; Lee brammer[d]
[a] School of Chemistry, University of Exeter, Stocker Road, UK [b] Department of Organic Chemistry, Institute of Chemical Technology, Prague, Czech Republic [c] Department of Chemistry, University of Southampton, Highfield, UK [d] Department of Chemistry, University of Sheffield, Brook Hill, UK

Online publication date: 13 May 2010

To cite this Article Miyaji, Hidekazu , Dudic, Miroslav , Tucker, James H. R. , Prokes, Ivan , Light, Mark E. , Gelbrich, Thomas , Hursthouse, Michael B. , Stibor, Ivan , Lhoták, Pavel and brammer, Lee(2003) 'Binding Studies on the Control of the Conformation and Self-assembly of a Calix[4]arenedicarboxylic Acid through Hydrogen Bonding Interactions', Supramolecular Chemistry, 15: 5, 385 — 390
To link to this Article: DOI: 10.1080/1061027031000115994
URL: http://dx.doi.org/10.1080/1061027031000115994

Supramolecular Chemistry, 2003 Vol. 15 (5), pp. 385–390

Binding Studies on the Control of the Conformation and Self-assembly of a Calix[4]arenedicarboxylic Acid through Hydrogen Bonding Interactions

HIDEKAZU MIYAJI[a], MIROSLAV DUDIC[a,b], JAMES H. R. TUCKER[a,*], IVAN PROKES[a], MARK E. LIGHT[c], THOMAS GELBRICH[c], MICHAEL B. HURSTHOUSE[c], IVAN STIBOR[b], PAVEL LHOTÁK[b] and LEE BRAMMER[d]

[a]*School of Chemistry, University of Exeter, Stocker Road, Exeter, EX4 4QD, UK;* [b]*Department of Organic Chemistry, Institute of Chemical Technology, Technicka 5, 166 28, Prague 6, Czech Republic;* [c]*Department of Chemistry, University of Southampton, Highfield, Southampton, SO17 1BJ, UK;* [d]*Department of Chemistry, University of Sheffield, Brook Hill, Sheffield, S3 7HF, UK*

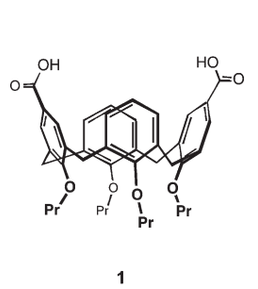
Received (in Southampton, UK) 11 February 2003; Accepted 12 March 2003

A convenient method for measuring the dimerisation constant in solution of a calix[4]arenedicarboxylic acid is reported. This compound also co-crystallises with a bis(amidopyridyl)calix[4]arene as independent tubular calixarene stacks that are cross-linked via carboxyl–amidopyridyl hydrogen bonding and π-stacking of the amidopyridyl arms.

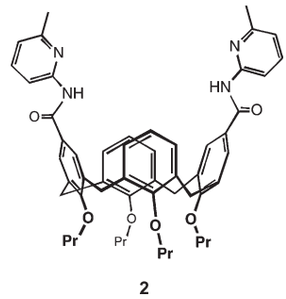
Keywords: Calix[4]arene; Hydrogen bonds; Carboxylic acid; Amidopyridine; Crystal engineering

INTRODUCTION

Self-organisation and self-assembly through hydrogen bonds has enabled large, highly-ordered structures to be synthesized with the minimum of synthetic effort [1]. Calix[4]arenes are attractive molecules in this respect since these bowl-shaped molecules can provide appropriate molecular recognition sites through self-organisation. For example, calix[4]resorcinarenes are known to form capsule-like dimers [2–5] and higher aggregates [6–8] through hydrogen bonds involving their OH groups. Such structures can then encapsulate neutral and/or charged guests in the cavities. Calix[4]arenes containing urea groups are also known to form dimers through the formation of intermolecular hydrogen bonds between the urea NH protons and the carbonyl group [9,10]. Recently, calix[4]arenes derivatives containing two [11–15] or four [16] carboxylic acid groups on the upper rim have been shown to form self-assembled dimers in organic solvents. However, attempts at quantifying the strength of these assemblies have been hampered by the high stability of the dimer with respect to the monomer in non-protic organic solvents [13]. Here we report a convenient method for measuring dimerisation constants for these assemblies in a competitive solvent mixture using the parent structure, calix[4]-arenedicarboxylic acid **1** [11,12]. We also report its interaction with bis(amidopyridyl)calix[4]arene **2** [17] to yield a 1:1 co-crystal that comprises tubular calixarene stacks linked via hydrogen bonds between carboxylic acid and amidopyridine moieties and π-stacking of the amidopyridyl arms.



1



2

RESULTS AND DISCUSSION

Compound **1** was prepared as described previously [11]. Crystals of **1** suitable for X-ray diffraction were grown from methanol and reveal the formation of a symmetrical dimer $\mathbf{1}_2$, as a result of hydrogen bonds

*Corresponding author. E-mail: j.h.r.tucker@exeter.ac.uk

ISSN 1061-0278 print/ISSN 1029-0478 online © 2003 Taylor & Francis Ltd
DOI: 10.1080/1061027031000115994

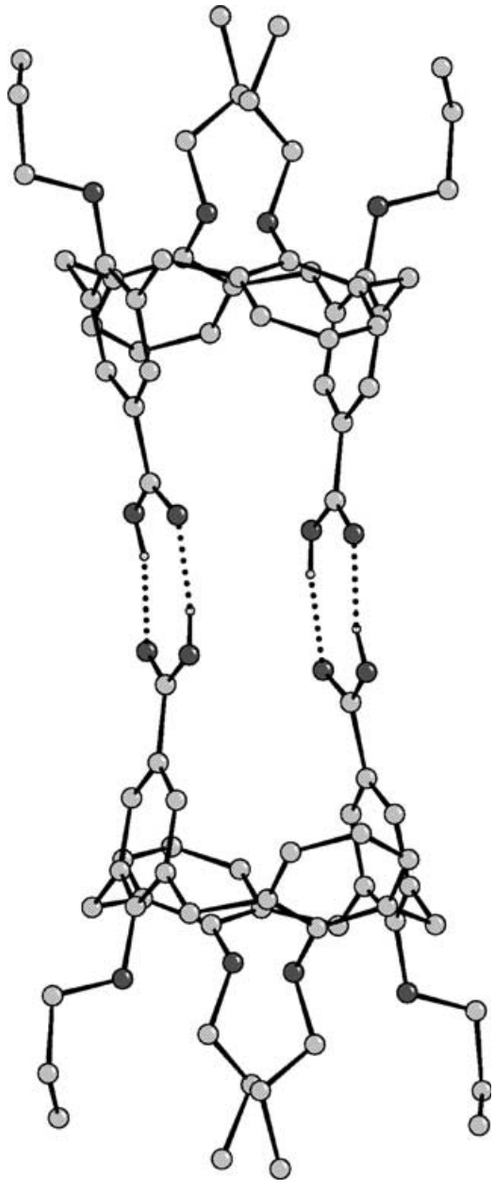


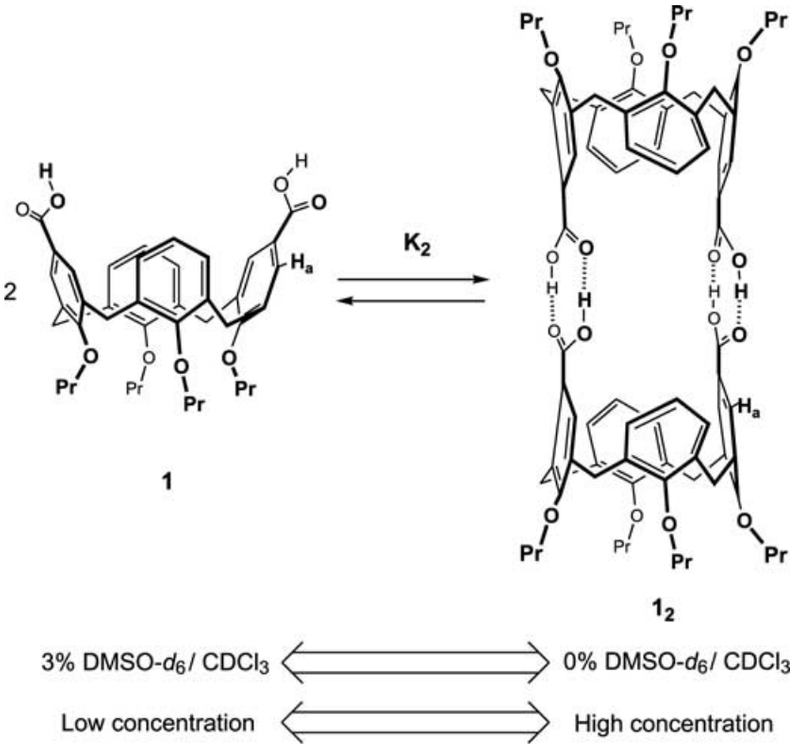
FIGURE 1 Crystal structure of the calix[4]arene pinched cone dimer $\mathbf{1}_2$.

between the carboxylic acid groups [O6···O7 = 2.647(4) Å, (O6)H6···O7 = 1.83 Å, O6–H6···O7 = 162.4°; O8···O5 = 2.621(4) Å, (O8)H8···O5 = 1.80 Å, O8–H8···O5 = 165.5°] (Fig. 1). These distances are very similar to those reported from a crystal structure of a related calix[4]arenedicarboxylic acid dimer containing two nitro groups [13]. The presence of these intermolecular hydrogen bonds results in the structure adopting a pinched cone conformation, where two of the phenyl rings are turned in towards one another [dihedral angle = 21.06(16)°], whereas the unsubstituted rings point away from one another in an open conformation [dihedral angle = 75.51(11)°].

The ^{1}H-NMR spectrum of **1** (2.5 mM) at 25°C (after heating to 40–50°C to effect dissolution) in $CDCl_3$ reveals that this dimeric structure also exists in solution, in agreement with previous studies on this and related compounds [11–15]. Specifically, the signal for the four equivalent protons (H_a) on the two substituted phenyl rings is shifted upfield ($\delta = 6.76$ ppm) relative to the expected chemical shift for these protons in a bis-substituted calixarene containing a symmetrical cone of C_{4v} symmetry (usually >7.0 ppm, e.g. 7.62 ppm for the signal for these protons in compound **2**).[†] However, the addition of DMSO-d_6 resulted in a downfield shift in this signal; in $CDCl_3$ solutions of **1** (2.5 mM) containing 0.5%, 1% and 3% DMSO-d_6, the H_a signal was observed at 6.78 ppm, 7.26 ppm and 7.42 ppm, respectively. These changes, along with the signals for the six protons on the other two aromatic rings of **1** undergoing upfield shifts upon addition of DMSO-d_6 (up to 3% DMSO in $CDCl_3$), show that DMSO competes effectively for solvation of the carboxylic acid groups. This causes the equilibrium to shift towards a monomer, resulting in the calixarene ring adopting the usual symmetrical cone conformation (Scheme 1).

In solutions containing higher amounts (>3%) of DMSO-d_6, no further changes to the NMR spectra were observed. Therefore the signal for H_a at 7.42 ppm is a limiting value and corresponds to the presence of only monomeric **1** in solution. These results gave us the opportunity to measure the dimerisation constant, K_2, where $K_2 = [\text{dimer}]/[\text{monomer}]^2$, via a NMR dilution method. An appropriate solvent ratio (1% DMSO-d_6-$CDCl_3$) was chosen to enable appreciable amounts of monomer and dimer to be observed over a millimolar concentration range. The resulting data were fitted to the Spurr and Byers equation (see the Experimental section) [18], giving $K_2 = 35\,\text{M}^{-1}$ at 298 K (error <5%) from a linear plot (Fig. 2). In this solvent system, the H_a signal moved from 7.00 ppm at 10 mM to the limiting value of 7.42 ppm at 0.65 mM. In accordance with other studies [13], in $CDCl_3$ alone, no downfield shift in the H_a signal was observed in this concentration range, which indicates that the pinched cone dimer $\mathbf{1_2}$ is by far the predominant species in solution in the absence of DMSO.

[†]The apparent C_{4v} symmetry of the symmetrical cone of calix[4]arenes is in fact a result of fast interconversion on the NMR timescale between two pinched cone conformers of C_{2v} symmetry [13].



SCHEME 1 Equilibrium between calix[4]arene monomer **1** and dimer $\mathbf{1}_2$ (3–0% DMSO-d_6-$CDCl_3$, concentration of **1**: 0.65 mM–10 mM).

Previously, we reported the bis(amidopyridyl) calix[4]arene **2** as a receptor for various dicarboxylic acids in 0.5–3% DMSO-d_6–$CDCl_3$ solutions [17]. Therefore a complexation study between **2** and calix[4]arene dicarboxylic acid **1** was attempted in the same way. As expected, downfield shifts in the signal corresponding to the two NH protons of **2** (ca. + 0.6 ppm, [**2**] = 0.2 mM, [**1**] = 1.8 mM) were observed in 0.5% DMSO-d_6–$CDCl_3$ solution. Unfortunately, a Job plot [19] could not establish with any certainty the binding stoichiometry, due in part to competition from the $\mathbf{1}$–$\mathbf{1}_2$ equilibrium in solution. However, the shape of the curve (Fig. 3) indicated a preference for a 2:1 (acid:amide) stoichiometry, which implies that a [**1**–**2**–**1**] trimer may exist in the solution phase. This result is consistent with previous binding studies on **2** with aliphatic diacids ($HOOC–(CH_2)_n–COOH$) that also show a preference for this stoichiometry for guests with larger (e.g. $n = 12$) spacer units [17]. Crystals suitable for X-ray diffraction were obtained by slow evaporation of a 0.5% DMSO-d_6–$CDCl_3$ solution containing equimolar amounts of **1** and **2**. The crystal structure was revealed to be a 1:1 co-crystal of the two compounds comprising parallel tube-like stacks each containing a single type of calixarene. Neighbouring tubes of **1** and **2** are linked in a 'zig-zag' arrangement via hydrogen bonds between carboxylic acids and amidopyridine units (Fig. 4). Additionally, neighbouring antiparallel tubes containing amidopyridyl-calixarenes are mutually intercalated via π-stacking of the planar amidopyridyl arms (Fig. 5). Other examples of tubular arrangements involving calixarenes and resorcarenes have been observed in the solid state [20,21]. The hydrogen bond lengths in **1·2** are similar to those found in related amidopyridine–carboxylic acid complexes [O6···N2 = 2.684(7) Å, (O6)H6···N2 = 1.86 Å, O6–H6···N2 = 167.2°; N1···O7 = 3.046(7) Å, (N1)H1···O7 = 2.25 Å, N1–H1···O7 = 149.8°] [22,23].

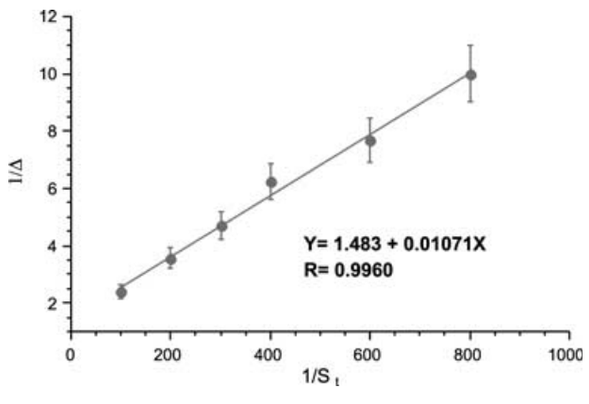


FIGURE 2 Spurr and Byers plot for **1** at 298 K in 1% DMSO-d_6-$CDCl_3$.

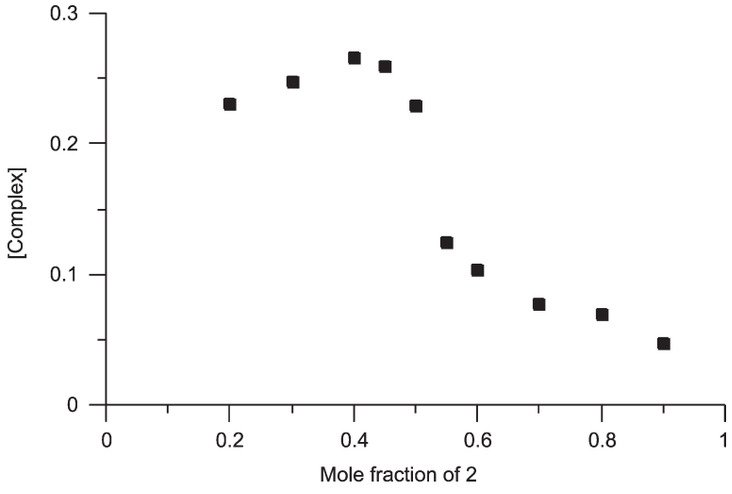


FIGURE 3 Job plot of **2** with **1** in 0.5% DMSO-d_6–$CDCl_3$ solution.

CONCLUSIONS

These studies confirm that the calix[4]pyrrole dicarboxylic acid **1** forms a pinched cone dimer, $\mathbf{1_2}$ both in the solid state and in solution, with the extent of the monomer(**1**)–dimer($\mathbf{1_2}$) equilibrium in solution dependent upon the extent of intermolecular hydrogen bonding. As well as demonstrating that this compound associates through hydrogen bonding interactions with a bis(amidopyridyl)-calix[4]arene both in solution and in the solid state, we have utilised a convenient spectroscopic method for measuring the dimerisation constant of **1** in solution that may be applied to a range of related self-assembling calixarene systems.

EXPERIMENTAL

General

All reagents were used as received from chemical suppliers. CH_2Cl_2 was distilled from calcium hydride under inert gas. THF was distilled from sodium under inert gas. ^1H and ^{13}C NMR spectra were recorded on either a Bruker AC 300 or a Bruker Avance DRX 400 spectrometer. Chemical shifts are

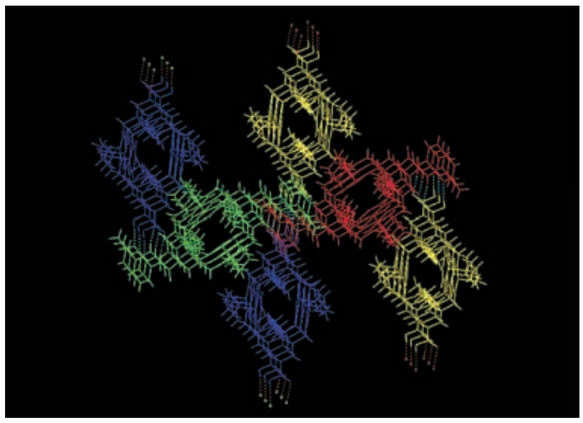


FIGURE 4 View of **1·2** down the tubular calixarene stacks. Molecules of dicarboxylic acid **1** are shown in blue and yellow; molecules of bis(amidopyridyl)calix[4]arene **2** are shown in green and blue. Dashed lines indicate hydrogen bonding between carboxylic acids and amidopyridyl groups that propagates a zigzag chain orthogonal to the tube axes (*viz.* yellow–red–yellow and blue–green–blue).

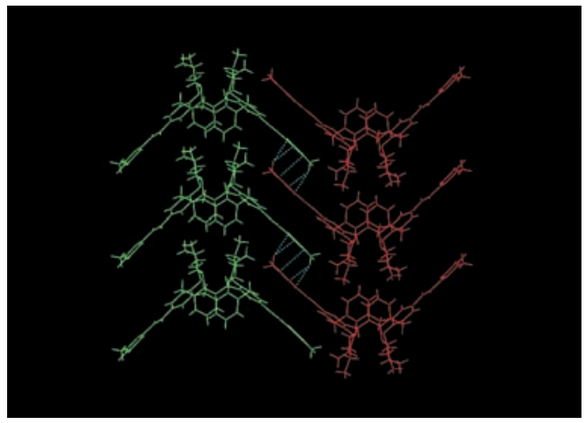


FIGURE 5 View of neighbouring antiparallel tubes comprising bis(amidopyridyl)calix[4]arene molecules **2**. Mutual intercalation of amidopyridyl arms is observed. All contacts that lie within the sum of van der Waals radii are indicated with dashed lines. Note that it is not appropriate to discuss the geometry of any C—H···π contacts involving the tolyl groups since methyl hydrogen atoms were not refined without constraints.

reported in ppm (δ). J_H values are given in Hz. 25,26,27,28-Tetrakis(1-propoxy)calix[4]arene-5,17-dicarboxylic acid **1** was prepared according to literature procedures [11].

5,17-Bis(amidopyridyl)-25,26,27,28-tetrakis (1-propoxy)calix[4]arene 2

25,26,27,28-Tetrakis(1-propoxy)calix[4]arene-5,17-dicarboxylic acid **1** (200 mg, 0.294 mmol) was dissolved in dry CH_2Cl_2 (5 ml) and $(COCl)_2$ (0.51 ml, 5.87 mmol) was added to the solution. The reaction mixture was refluxed for 3 hours. Then, the CH_2Cl_2 was distilled off and the residue was dried *in vacuo* for 1 hour. The obtained acyl chloride was dissolved in THF (25 ml), and the solution was added to solution of 2-amino-6-picoline (127 mg, 1.175 mmol) and Et_3N (0.245 ml, 1.175 mmol) dissolved in THF (10 ml). The reaction mixture was stirred for 1 hour. Then, the THF was distilled off, the residue was dissolved in $CHCl_3$ (30 ml) and washed with water (20 ml). The water layer was extracted with $CHCl_3$ (10 ml) and the organic layer was dried over $MgSO_4$. Following evaporation, the resulting yellow oil was purified by column chromatography on silica gel using hexane–ethyl acetate (3:1) as eluent. Yield 180 mg (71%), mp = 268–269°C (ethanol). ^{1}H NMR (400 MHz, $CDCl_3$): 0.94 (t, $J = 7.4$, 6H, $OCH_2CH_2CH_3$), 1.10 (t, $J = 7.5$, 6H, $OCH_2CH_2CH_3$), 1.97 (m, 8H, $OCH_2CH_2CH_3$), 2.49 (s, 6H, NHpyCH_3), 3.25 (d, $J = 13.6$, 4H, ArCH_2Ar), 3.74 (t, $J = 7.0$, 4H, $OCH_2CH_2CH_3$), 4.08 (t, $J = 8.0$, 4H, $OCH_2CH_2CH_3$), 4.49 (d, $J = 13.5$, 4H, ArCH_2Ar), 6.24 (d, $J = 7.4$, 4H, Ar*H*), 6.32 (m, 2H, Ar*H*), 6.91 (d, $J = 7.5$, 2H, Arpy*H*), 7.61 (t, $J = 7.8$, 2H, Arpy*H*), 7.62 (s, 4H, Ar*H*), 8.41(s, 2H, ArCO*NH*); ^{13}C NMR (300 MHz,$CDCl_3$): 10.00, 10.67, 23.20, 23.46, 23.99, 31.01, 76.79, 111.00, 119.07, 122.49, 127.95, 127.99, 132.91, 136.96, 138.75, 149.48, 151.14, 155.40, 156.62, 161.35, 165.65, 221.78; MS (EI) m/z 860.45 (M^+); Elemental analysis, found: C, 74.79; H, 7.02; N, 6.27%. Calcd. for ($C_{54}H_{60}O_6N_4$): C, 75.32; H, 7.02; N, 6.51%.

X-ray Crystallography

The crystal of **1** was grown by slow evaporation from methanol after full dissolution by heating. Co-crystal [**1·2**] was grown by slow evaporation from the 0.5% DMSO-d_6–$CDCl_3$ solution that was used in the NMR study.

Crystallographic data for **1**. $C_{42}H_{48}O_8$, $M = 680.80$, $T = 120(2)$ K, monoclinic, space group $P2_1/n$, $a = 11.7592(4)$ Å, $b = 25.9714(9)$ Å, $c = 12.6411(5)$ Å, $\beta = 96.581(2)°$, $V = 3835.2(2)$ Å^3, $Z = 4$, $\rho_{calc} = 1.179$ Mg/m^3. Reflections collected: 16713, independent: 6625 ($R_{int} = 0.0817$). Final R indices [$I > 2\sigma I$] : $R_1 = 0.0696$, $wR_2 = 0.1509$; R indices (all data): $R_1 = 0.1549$. $wR_2 = 0.1839$. All hydrogen atoms were located from the difference map and refined using a riding model. CCDC number: 183225.

Crystallographic data for [**1·2**]: $C_{96}H_{108}N_4O_{14}$, $M = 1541.86$, $T = 120$ K, monoclinic, space group $P2/n$, $a = 19.6710(6)$ Å, $b = 9.3321(4)$ Å, $c = 27.5985(11)$ Å, $\beta = 101.504(2)°$, $V = 4964.5(3)$ Å^3, $Z = 2$, $\rho_{calc} = 1.031$ Mg/m^3. Colourless block, crystal size $0.10 \times 0.07 \times 0.07$ mm. Reflections collected: 26307, independent: 8595 ($R_{int} = 0.142$). Final R indices [$I > 2\sigma I$] : $R_1 = 0.1141$, $wR_2 = 0.1753$; R indices (all data): $R_1 = 0.2802$. $wR_2 = 0.2185$. All hydrogen atoms were located from the difference map and refined using a riding model. CCDC number: 183226

Determination of the Dimerisation Constant of 1

The dimerisation constant (K_2) of **1** in 1% DMSO-d_6–$CDCl_3$ was determined by ^{1}H NMR spectroscopy using a dilution technique. The data were analyzed by a linear graphical method for dimerisation developed by Spurr and Byers [18]. The experiment started with the most concentrated solution ($S_t = 10$ mM) of compound **1**, which was then diluted gradually until the detection limit was reached. The ^{1}H NMR spectrum (δ_{obs} = the chemical shift of the H_a proton of **1**) was recorded for each of these concentrations. The chemical shift of this proton in the most dilute solution was taken to be that of the monomer, $\delta_{monomer}$. The dimerisation constant (K_2) of **1** was then calculated according to $\Delta = 2\Delta_2 K_2 S_t/(1 + 4K_2 S_t)$ (Spurr and Byers equation), where $\Delta = \delta_{obs.} - \delta_{monomer}$, $\Delta_2 = \delta_{dimer} - \delta_{monomer}$, S_t = total concentration, and $1/\Delta = (1/S_t)(1/2\Delta_2 K_2) + 2/\Delta_2$ (linear form), where the slope = $1/2\Delta_2 K_2$, intercept = $2/\Delta_2$. Intercept/slope = $4K_2$, $4K_2 = 1.483/0.01071$, $K_2 = 34.6$ M^{-1}.

Acknowledgements

We thank the EPSRC for the award of a PDRA grant (H.M.), the EU for the award of a Marie-Curie Training Grant (M.D.) and the Czech Grant Agency (Grant No.: 203/00/1011).

References

[1] Prins, L. J.; Reinhoudt, D. N.; Timmerman, P. *Angew. Chem. Int. Ed.* **2001**, *40*, 2382.
[2] Rose, K. N.; Barbour, L. J.; Orr, G. W.; Atwood, J. L. *Chem. Commun.* **1998**, 407.
[3] Murayama, K.; Aoki, K. *Chem. Commun.* **1998**, 607.
[4] Shivanyuk, A.; Rissanen, K.; Kolehmainen, E. *Chem. Commun.* **2000**, 1107.
[5] Shivanyuk, A.; Rebek, J. Jr. *Chem. Commun.* **2001**, 2374.
[6] MacGillivray, L. R.; Atwood, J. L. *Nature* **1997**, *389*, 469.

[7] Atwood, J. L.; Barbour, L. J.; Jerga, A. *Chem. Commun.* **2001**, 2376.
[8] Shivanyuk, A.; Rebek, J. Jr. *Chem. Commun.* **2001**, 2424.
[9] Rebek, J. Jr. *Chem. Commun.* **2000**, 641 and references cited therein.
[10] Rincon, A. M.; Prados, P.; de Mendoza, J. *J. Am. Chem. Soc.* **2001**, *123* 3493 and references cited therein.
[11] Arduini, A.; Fabbi, M.; Mantovani, M.; Mirone, L.; Pochini, A.; Secchi, A.; Ungaro, R. *J. Org. Chem.* **1995**, *60*, 1454.
[12] Larsen, M.; Jørgensen, M. *J. Org. Chem.* **1996**, *61*, 6651.
[13] Struck, O.; Verboom, W.; Smeets, W. J. J.; Spek, A. L.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 2* **1997**, 223.
[14] Jørgensen, M.; Krebs, F. C. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1929.
[15] Krebs, F. C.; Jørgensen, M. *J. Chem. Soc., Perkin Trans. 2* **2000**, 1935.
[16] Kobayashi, K.; Shirasaka, T.; Yamaguchi, K.; Sakamoto, S.; Horn, E.; Furukawa, N. *Chem. Commun.* **2000**, 41.
[17] Miyaji, H.; Dudic, M.; Tucker, J. H. R.; Prokes, I.; Light, M. E.; Hursthouse, M. B.; Stibor, I.; Lhotak, P. *Tetrahedron Lett.* **2002**, *43*, 873.
[18] Spurr, R. A.; Byers, H. F. *J. Phys. Chem.* **1958**, *62*, 425.
[19] Conners, K. A. *Binding Constants*; John Wiley & Sons: New York, 1987.
[20] For examples, see: Hosseini, M. W.; Cian, A. D. *Chem. Commun.* **1998**, 727.
[21] For examples, see: MacGillivary, L. R.; Atwood, J. L. *Chem. Commun.* **1999**, 181.
[22] Garcia-Tellado, F.; Goswami, S.; Chang, S. K.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1990**, *112*, 7393, and references cited therein.
[23] Goswami, S.; Ghosh, K.; Dasgupta, S. *J. Org Chem.* **2000**, *65*, 1907 and references cited therein.