PERKIN 2

Pyridine-appended 5,6-open-aza[60]fulleroid can act as a unique host for alcohols

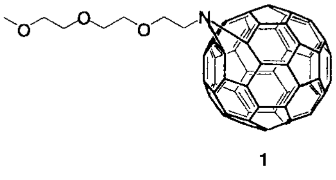
Atsushi Ikeda,[a] Chie Fukuhara,[a] Masaru Kawaguchi,[a] Munenori Numata,[a] Seiji Shinkai,*[a] Sheng-Gao Liu[b] and Luis Echegoyen[b]

[a] *Department of Chemistry & Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka 812-8581, Japan*
[b] *Department of Chemistry, University of Miami, Coral Gables, FL 33124, USA*

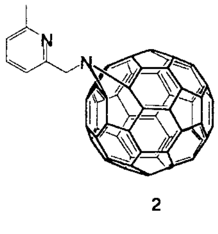
Received (in Cambridge, UK) 20th August 1999, Accepted 25th November 1999

Pyridine-appended 5,6-open-aza[60]fulleroid (**2**) and 6,6-closed-aza[60]fullerene (**3**) were synthesised for the first time. It was found that **2**, in which the aza group conjugates with the [60]fulleroid π-system, can bind certain alcohols *via* a hydrogen-bonding interaction and shows high selectivity towards methanol. In contrast, **3**, in which the aza group does not conjugate with the [60]fullerene π-system, scarcely shows such an alcohol affinity. The results indicate that a slight difference in the arrangement of the nitrogens results in a drastic change in the guest affinity. The guest-binding processes were thoroughly investigated by UV–Vis absorption and NMR spectroscopic methods and electrochemical methods. This is a unique neutral guest recognition system utilising the [60]fullerene surface.

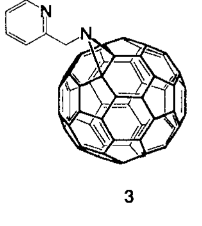
The ready availability of [60]fullerene and its homologues offers a unique opportunity for exploration of the outstanding new physical and chemical properties of fullerene derivatives. Among them, one of the most attractive research topics is the superconductivity observed for certain exohedral [60]fullerene–metal complexes:[1] that is, the metal cation immobilised onto the [60]fullerene surface should facilitate the electron injection into the [60]fullerene moiety and stabilise the C_{60}–M^+ complexes. Such [60]fullerene derivatives with ionophoric functional groups have been synthesised by several groups[2–8] but spectroscopic evidence for direct [60]fullerene–metal ion interaction was obtained only in a few systems.[4,6,8] With this object in mind we and Hawker *et al.* previously synthesised **1** (5,6-open-[60]fulleroid),[7] **2** (5,6-open-[60]fulleroid) and **3** (6,6-closed-[60]fullerene).[8] In the course of spectral examination of metal–fullerene interactions, we unexpectedly found that the absorption spectra and cyclic voltammogram of **2** changed significantly upon addition of methanol. This implies that [60]fullerene derivatives bearing basic functional groups are useful not only for the formation of exohedral metal complexes but also for the molecular recognition of neutral molecules utilising hydrogen-bonding interactions. This paper reports why methanol is bound so efficiently to a pyridine-appended [60]fulleroid surface and why only **2** can exhibit such a binding ability among the three compounds. In addition, we discuss the possible future applications of this unexpected finding to [60]fullerene-based molecular recognition.



1



2



3

Experimental

^1H NMR and UV–Vis spectroscopic measurements were carried out with a Bruker DRX 600 spectrometer and a Shimazu UV-2500PC spectrometer, respectively.

Materials

The syntheses of compounds **1**, **2** and **3** were described previously.[7,8]

Electrochemical studies

Cyclic voltammetry (CV) and Osteryoung square wave voltammetry (OSWV) were performed on a Windows-driven BAS 100W electrochemical analyser (Bioanalytical Systems, West Lafayette, IN) at room temperature with a three-electrode configuration in *o*-dichlorobenzene solution containing the substrate (0.1–0.5 mmol dm^{-3}) and supporting electrolyte (*n*-Bu_4NPF_6, 0.05 mol dm^{-3}). A platinum disc (ϕ 1 mm) was used as a working electrode, the counter electrode being a platinum wire (ϕ 1 mm). An Ag/AgCl electrode was used as the reference electrode. Both the counter and the reference electrodes were directly immersed in the electrolyte solution. The scan rate was 100 mV s^{-1} unless otherwise specified. All potentials were referenced to the ferrocene/ferrocenium couple (Fc/Fc^+) as the internal standard. OSWV experiments were performed with parameters of step potential: 4 mV, S. W. amplitude: 25 mV, frequency: 15 Hz, and quiet time: 2 s.

Results and discussion

UV–Vis absorption spectroscopy

As shown in Fig. 1A, the addition of a trace amount of methanol (0–8.00 mmol dm^{-3}) to a dilute toluene solution of **2** (2.00×10^{-2} mmol dm^{-3}) with the 5,6-open structure (λ_{max} 337 nm) induced a clear spectral change with a new λ_{max} at 326 nm and isosbestic points at 330 and 374 nm. In addition, a new broad absorption band appeared in the 400–500 nm region. A similar spectral change was also observed in tetrachloroethane (TCE: λ_{max} 331 nm, new λ_{max} 323 nm). Plots of A_{337} (in toluene) or A_{331} (in TCE) *vs.* [MeOH] satisfied the Benesi–Hildebrand equation[9] assuming the formation of a 1 : 1 complex. The 1 : 1

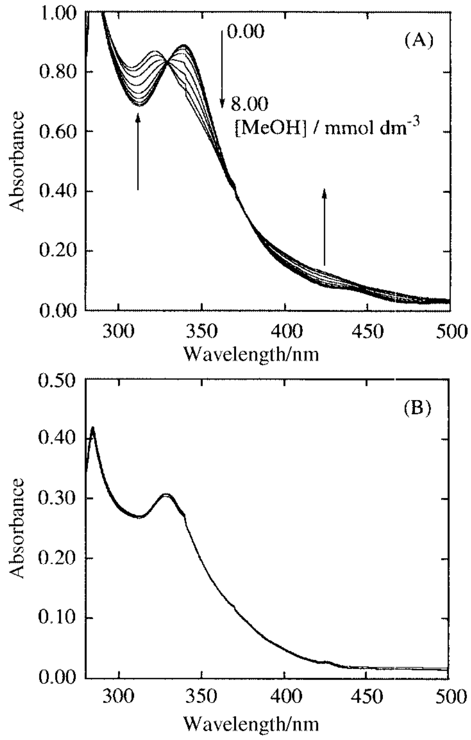


Fig. 1 Absorption spectral change of (A) **2** (2.00×10^{-5} mol dm^{-3}) and (B) **3** (2.00×10^{-5} mol dm^{-3}) in toluene at 25 °C: [MeOH] = 0–8.00 mmol dm^{-3}.

stoichiometry was also supported by the ^{1}H NMR spectroscopic data (*vide post*). The association constants (K_{ass}) were estimated to be 6.6×10^2 dm^3 mol^{-1} (in toluene) and 1.2×10^3 dm^3 mol^{-1} (in TCE). In contrast, a methanol-dependent spectral change was scarcely observed for **3** with the 6,6-closed structure, indicating that the 5,6-open structure can provide more basic nitrogens than the 6,6-closed structure (Fig. 1B).[8] This may be related to the structural difference between **2** and **3**: that is, the aza group of **2** conjugates with the [60]fulleroid π-system whereas that of **3** does not. The spectral change was not observed for **1** with a similar 5,6-open structure. This difference supports the idea that the pyridine moiety in **2**, which can cooperatively act with the NCH_2 pyridine as a hydrogen-bond acceptor site, plays a crucial role in the methanol binding.

Here, we examined the influence of other hydroxy-containing compounds on the spectral properties of **2** (Fig. 2). As guest compounds, ethanol and *tert*-butyl alcohol (*t*-BuOH) were chosen to estimate the steric effect whereas 2,2,2-trifluoroethanol (TFE) and phenol were chosen to estimate the OH group's acidity effect. The addition of a small amount of ethanol (0–8.00 mmol dm^{-3}) to the toluene solution again induced a clear spectral change, giving rise to a new λ_{max} at 328 nm, although the magnitude of the spectral change is smaller than that induced by methanol. The K_{ass} (1.4×10^2 dm^3 mol^{-1}) was smaller by 4.7-fold than that for methanol. The addition of *t*-BuOH did not induce any spectral changes. The results indicate that the **2**–alcohol interaction is significantly suppressed by steric bulkiness in the guest compounds. Meanwhile, the spectral changes induced by the addition of TFE (new λ_{max} at 335 nm) were smaller than those induced by the addition of ethanol. However, the K_{ass} (1.4×10^3 dm^3 mol^{-1}) determined from a plot of A_{337} *vs.* [TFE] was greater by 2.2-fold than that for methanol. The addition of phenol did not induce any spectral changes. The results show that as long as the steric bulkiness does not interfere with the complexation, the more acidic OH group is bound more favourably to **2**.

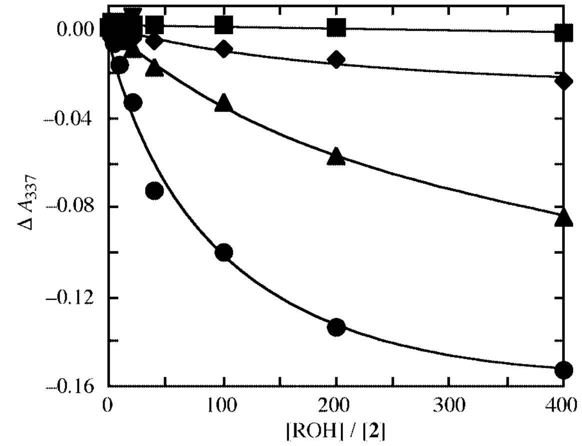


Fig. 2 ΔA_{337} *vs.* [ROH]/[**2**] plots in toluene at 25 °C: [**2**] = 2.00×10^{-5} mol, ●: methanol, ▲: ethanol, ■: *tert*-butyl alcohol, ◆: 2,2,2-trifluoroethanol, ▼: phenol.

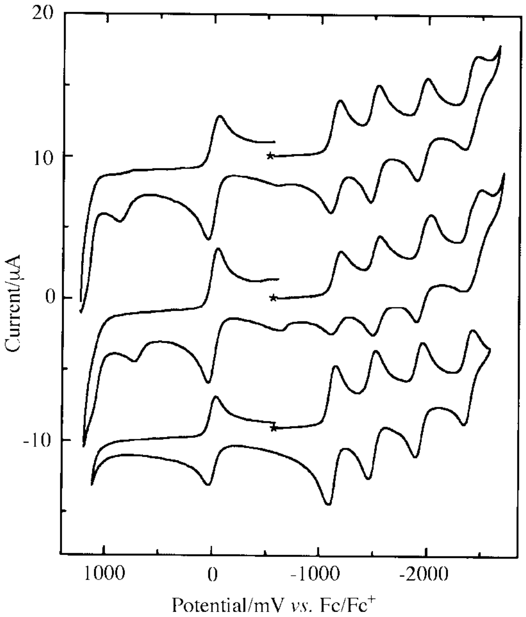


Fig. 3 CVs of **2** (upper), **3** (middle) and [60]fullerene (bottom) in *o*-dichlorobenzene solution containing 5.0×10^{-2} mol dm^{-3} Bu_4NPF_6, scan rate 100 mV s^{-1}. *: starting point.

Electrochemical studies

Several features of the CVs reported in Fig. 3 can be considered. First of all, both **2** and **3** exhibit four well-separated reduction peaks together with four corresponding re-oxidation peaks in the cathodic direction and two irreversible oxidation peaks in the anodic part within the scan range. Sequential electron-transfer processes are clearly observed for the four reversible reduction steps, which have been already described as an EEEE mechanism by Hirsch *et al.*[10] Compared to the CV of [60]fullerene, the irreversible oxidation peaks should be originating from oxidation of the substituted addend of [60]fullerene. The cathodic redox half-wave potentials ($E_{1/2}$) and the potential differences between reduction and the corresponding re-oxidation peak potentials (ΔE) are listed in Table 1. For the reductions, both the two [60]fullerene derivatives essentially retain the electronic properties of [60]fullerene and the observed reduction potentials of both species are slightly shifted to more negative values when compared to those of pure [60]fullerene. This is the same behaviour observed for most [60]fullerene derivatives, whose cyclic voltammograms are typically characterised by a small shift to more negative values of the reduction potentials due to partial loss of

Table 1 $E_{1/2}{}^{a}$ or E_{ox} values (mV *vs.* Fc/Fc$^+$) of [60]fullerene, **2** and **3** detected by CV or OSWV in ODCB at room temperature. Errors for $E_{1/2}$ or E_{ox} values are estimated to be ±5 mV

	$E_{1/2}{}^{1}$ (ΔE)	$E_{1/2}{}^{2}$ (ΔE)	$E_{1/2}{}^{3}$ (ΔE)	$E_{1/2}{}^{4}$ (ΔE)	$E_{ox}{}^{1\,b}$	$E_{ox}{}^{2\,b,c}$
[60]Fullerene	−1122 (52)	−1493 (66)	−1928 (60)	−2390 (60)		
2	−1142 (81)	−1520 (51)	−1946 (85)	−2425 (94)	728[b]	1084[b,c]
3	−1132 (76)	−1499 (64)	−1945 (85)	−2400 (99)	874[b]	1124[b,c]

[a] $E_{1/2} = (E_{red} + E_{ox})/2$, E_{red} or E_{ox}: peak potentials, $\Delta E = E_{ox} + E_{red}$. [b] Peak potentials reported, due to chemical irreversibility. [c] Determined by OSWV technique.

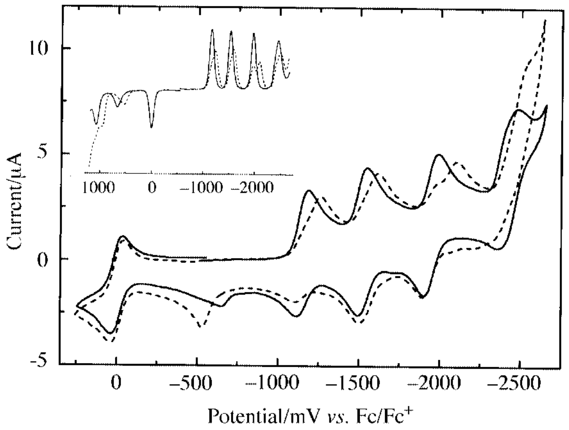


Fig. 4 CVs of **2** in *o*-dichlorobenzene solution containing 5.0×10^{-2} mol dm^{-3} Bu_4NPF_6 in the absence (——) and the presence (– – –) of methanol (5.0×10^{-2} mol dm^{-3}). Scan rate 100 mV s^{-1}. Insert: OSWV in the absence (——) and the presence (– – –) of methanol.

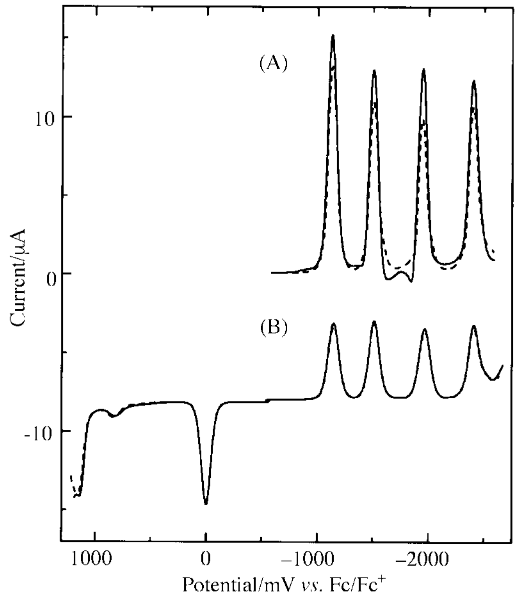


Fig. 5 OSWVs of (A) [60]fullerene and (B) **3** in *o*-dichlorobenzene solution in the absence (——) and the presence (– – –) of methanol (5.0×10^{-2} mol dm^{-3}), showing that there is no effect of added methanol on the electrochemistry of either of these compounds.

'conjugation'.[11] To our surprise, as we can see from Table 1, the cathodic reduction peak potentials of **2** are slightly but significantly more negative than those of **3**, which indicates that reduction of the [60]fullerene moiety in **2** is more difficult than for **3**. However, oxidation of the *N*-bridged addend in **2** is easier than for **3**. These observations may be due to the structural difference between these two compounds, which is in agreement with the strong differences in hydrogen-bonding effects between these two molecules, as detailed below.

It is known that hydrogen bonds, by virtue of their strength and directionality, are found extensively in biological systems controlling both intra- and intermolecular structure. In recent years, chemists have begun to exploit hydrogen bonds for similar reasons. Indeed, receptors that utilise directed hydrogen bonds to bind substrates are of major importance in molecular recognition research.[12] Fig. 4 presents the CVs in *o*-dichlorobenzene (ODCB) solution of **2** in the presence and absence of methanol. As we can see from Fig. 4, the CV in the presence of methanol is very different from that in the absence of methanol. The four reduction peaks in the presence of methanol became broader, the peak potentials are cathodically shifted, and the peak currents become smaller than those of the corresponding peaks observed in the absence of methanol. More dramatically, the third reduction peak splits into two clearly separated peaks, with each of the peak currents being almost half of the corresponding one for the third reduction peak in the absence of methanol, as clearly shown by the OSWVs of the compound (see inset of Fig. 4). Thus, the hydrogen-bonding interaction between methanol and **2** results in two different species, in good agreement with the UV–Vis spectral analysis, and also in good agreement with additional control experiments. Both pure [60]fullerene and **3** did not show any detectable hydrogen-bonding effect with methanol by either CV or OSWV (Fig. 5).

In addition, it is interesting to note that after the addition of methanol, the anodic oxidation peak potentials are less positive by about 120–130 mV indicating that oxidation of the *N*-bridged addend became easier in the presence of methanol. This can be easily explained as an electrostatic effect of the hydrogen bonds, since hydrogen bonds are in fact substantially electrostatic in nature. However, the main cathodic reduction peak potentials for the possible new structural species are more negative by about 50–110 mV, indicating that the reduction of the [60]fullerene moiety for the new structural species became more difficult. This may be explained by the conformational change after the addition of methanol due to the formation of hydrogen bonds, which is in good agreement with the ^{1}H-NMR analysis. Finally, it should be mentioned that all of our efforts to separate the first, second and fourth broad reductions into two peaks, as does the third reduction, by lowering the temperature after the addition of methanol were not successful because the freezing point of ODCB is rather high.

^{1}H NMR spectroscopy

What is the origin of the spectral changes? We tried to find a rationale by performing ^{1}H NMR spectroscopic measurements. As shown in Fig. 6A, the NCH_2 methylene protons appeared as a singlet peak at 4.94 ppm in toluene-d_8, indicating that the pyridine moiety is free to rotate with a speed faster than the ^{1}H NMR time-scale. When methanol-d_4 was added, the intensity of this singlet peak decreased with an appearance of a pair of doublets at 5.95 and 6.32 ppm (Figs. 6B and 6C). To confirm that these new peaks are not due to decomposition, the solution was once evaporated to dryness and the residue was dissolved again in toluene-d_8. The ^{1}H NMR spectrum thus obtained was identical to that in Fig. 6A. This result supports the view that the methanol-induced new spectrum in Figs. 6B and 6C is ascribed to some conformational change in **2**. The splitting pattern implies that the NCH_2 methylene protons become

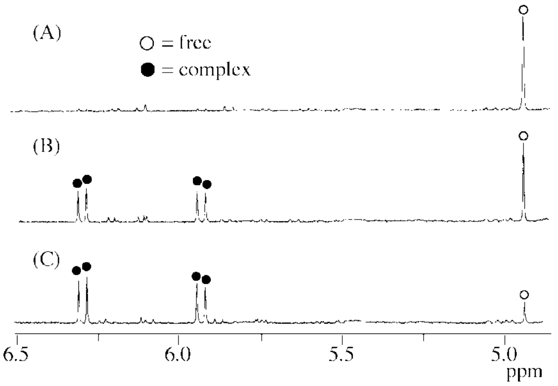


Fig. 6 ^{1}H NMR spectra of **2** (1.00×10^{-3} mol dm^{-3}) in (A) the absence of methanol and (B) and (C) the presence of methanol (1.20×10^{-3} and 3.00×10^{-3} mol dm^{-3}, respectively): 25 °C, toluene-d_8, 600 MHz.

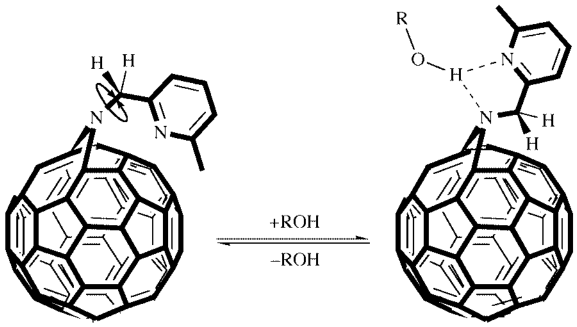


Fig. 7 Schematic representation of an alcohol-induced conformational change in **2**.

inequivalent to each other and the rotational speed becomes slower than the ^{1}H NMR time-scale. It is known that the five-membered ring has a deshielding effect whereas the six-membered ring has a shielding effect.[13] The large down-field shift of the new peaks suggests that the NCH_2 methylene protons are approaching the five-membered ring or detached from the six-membered. Since the rotational speed of the pyridine moiety is more suppressed, the latter conformational change, which is more affected by steric crowding, is more likely.

As a summary of the foregoing findings, one may propose a methanol-induced conformational change as illustrated in Fig. 7. It is not clear from a survey of past references which hybrid orbital (sp^2 or sp^3) the azafulleroid nitrogen adopts. It seems more reasonable to consider that it is sp^2-hybridised because it conjugates with the C=C double bonds. To reduce the steric crowding the NCH_2 methylene protons should be directed toward the opposite side of the [60]fulleroid surface. In this conformation, the space between the [60]fulleroid surface and the NCH_2 chain is too narrow to accept a guest alcohol. When the two nitrogens cooperatively interact with a guest alcohol, the NCH_2 methylene protons should be directed toward the [60]fulleroid surface (Fig. 7). Because of complex formation, the rotation of the NCH_2 group becomes more difficult and the NCH_2 methylene protons exactly exist on the five-membered ring.

Conclusions

In conclusion, the present study demonstrated that the [60]fullerene π-system can serve as a potential scaffold to design not only a selective metal-binding site but also a unique neutral molecular recognition site and these guest-binding events can be readily monitored by the absorption spectral change of the fullerene chromophore. Electrochemical studies of compounds **2** and **3** show that the electrochemical properties of these two [60]fullerene derivatives mainly retain the electronic properties of [60]fullerene and a hydrogen bond has a significant effect on the electrochemical behaviour of the 5,6-bridged structure, but not so on the 6,6-bridged isomer. The findings have important implications since molecular recognition could be coupled with the control of various chemical and physical functions inherent to the fullerene π-system such as electrochemical redox reactions, sensitisation of singlet dioxygen, photochemical electron or energy transfer, *etc.* The applications of these systems are continuously studied in these laboratories.

Acknowledgements

This work was partially supported by Shorai Foundation for Science and Technology and a Grant-in-Aid for Scientific Research from the Ministry of Education, Japan (No. 11750749). L. E. and S. G. L. wish to thank the US National Science Foundation (grant CHE-9816503) for generous financial support.

References

1 A. F. Hebard, M. J. Rosseinsky, R. C. Haddon, D. M. Murphy, S. H. Glarum, T. T. M. Palstra, A. P. Ramirez and A. R. Kortan, *Nature*, 1991, **350**, 600.
2 A. Gügel, A. Kraus, J. Spickermann, P. Belik and K. Müllen, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 559; A. Kraus, A. Gügel, P. Belik, M. Walter and K. Müllen, *Tetrahedron*, 1995, **51**, 9927.
3 S. N. Davey, D. A. Leigh, A. E. Moody, L. W. Tetler and F. A. Wade, *J. Chem. Soc., Chem. Commun.*, 1994, 397.
4 J. Osterodt, M. Nieger, P.-M. Windscheif and F. Vögtle, *Chem. Ber.*, 1993, **126**, 2331; J. Osterodt, A. Zett and F. Vögtle, *Tetrahedron*, 1996, **52**, 4949.
5 F. Diederich, U. Jonas, V. Gramilich, A. Herrmann, H. Ringsdorf and C. Thilgen, *Helv. Chim. Acta*, 1993, **76**, 2445; U. Jonas, F. Cardullo, P. Belik, F. Diederich, A. Gügel, E. Harth, A. Herrmann, L. Isaacs, K. Müllen, H. Ringsdorf, C. Thilgen, P. Uhlmann, A. Vasella, C. A. A. Waldraff and M. Walter, *Chem. Eur. J.*, 1995, **1**, 243; J. P. Bourgeois, L. Echegoyen, M. Fibbioli, E. Pretsch and F. Diederich, *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 2118.
6 A. Ikeda, C. Fukuhara and S. Shinkai, *Chem. Lett.*, 1997, 407.
7 C. J. Hawker, P. M. Saville and J. W. White, *J. Org. Chem.*, 1994, **59**, 3503.
8 Preliminary communication: A. Ikeda, C. Fukuhara and S. Shinkai, *Tetrahedron Lett.*, 1996, **37**, 7091.
9 H. A. Benesi and H. Hildebrand, *J. Am. Chem. Soc.*, 1949, **71**, 2703.
10 J. K. Zhou, A. Rieker, T. Grösser, A. Skiebe and A. Hirsch, *J. Chem. Soc., Perkin Trans. 2*, 1997, 1.
11 For a recent review, see: M. Prato, *J. Mater. Chem.*, 1997, **7**, 1097; L. Echegoyen and L. E. Echegoyen, *Acc. Chem. Res.*, 1998, **31**, 593.
12 Y. Ge, R. R. Lilienthal and D. K. Smith, *J. Am. Chem. Soc.*, 1996, **118**, 3976.
13 L. Isaacs, A. Wehrig and F. Diederich, *Helv. Chim. Acta*, 1993, **76**, 1231; A. Pasquarello, M. Schlcüter and R. C. Haddon, *Science*, 1992, **257**, 1660.

Paper a906772h