# The Self-assembly of Branched [*n*]Rotaxanes—the First Step Towards Dendritic Rotaxanes

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The self-assembly, by means of a slippage procedure, of three novel rotaxanes incorporating, respectively, one, two and three bisparaphenylene-34-crown-10 macrocyclic components and a single branched component, consisting of three bipyridinium units attached covalently to a 1,3,5-trisubstituted benzene central core and each bearing at its other end a substituted tetraarylmethane blocking group, is described.

Since the first mention in the literature[1] of the idea of a molecule comprising a linear dumbbell component encircled by a macrocyclic one, the synthesis of the so-called rotaxanes[2–6] and polyrotaxanes[7–9] has been achieved and carried out successfully exploiting either statistical methods or template-directed syntheses. Most of the rotaxanes and polyrotaxanes [Fig. 1(*a*)] reported to present are composed of one or more macrocycles encircling one dumbbell component, bearing at both ends of a linear thread, two large blocking groups or stoppers in order to prevent the macrocycles slipping off the end of the thread.

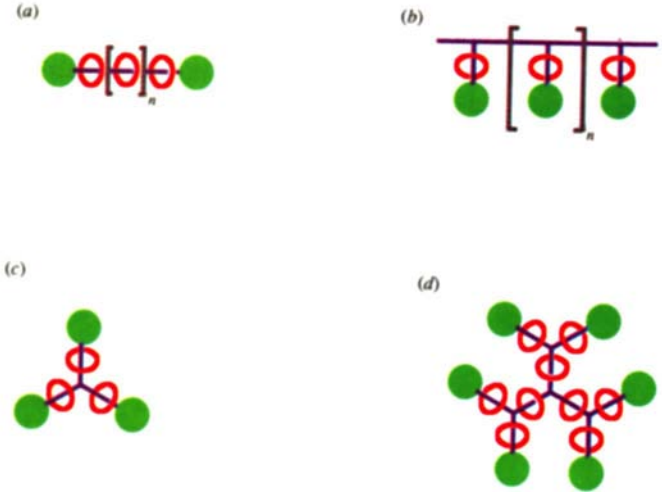
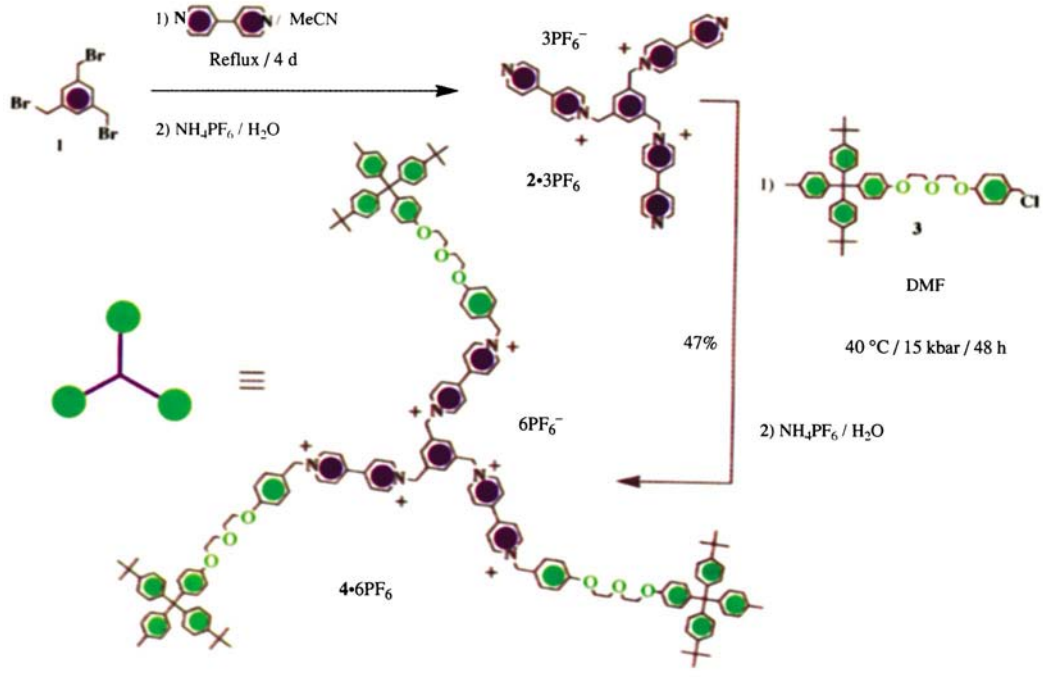



**Fig. 1** (*a*) A linear [*n* + 3]rotaxane. (*b*) A side-chain [*n* + 3]rotaxane. (*c*) A branched [4]rotaxane. (*d*) A highly branched [10]rotaxane.

Recently, the synthesis of side-chain polyrotaxanes[10,11] has also been reported. In these novel macromolecules, the rotaxane portions are attached covalently to a linear polymeric backbone, affording a comb-like structure [Fig. 1(*b*)]. Here, we report the self-assembly[12–14] of a new type of rotaxane, in which three side-chains are linked directly to a single central core, producing a dendritic-type[15–19] structure. In previously reported investigations,[20–22] using the so-called slipping approach, we have self-assembled rotaxanes comprised of dumbbell-shaped components incorporating one or two bipyridinium units encircled by one or two macrocyclic polyethers, namely bisparaphenylene-34-crown-10 (**BPP34C10**) and/or 1,5-dinaphtho-38-crown-10. We reasoned that, by using the same approach and the appropriate building blocks, but, by altering the nature and the substitution pattern associated with the spacers linking the recognition sites located within the linear stoppered components, we should be able to generate branched rotaxanes [Fig. 1(*c*)] that possess dendritic-type [Fig. 1(*d*)] characteristics.

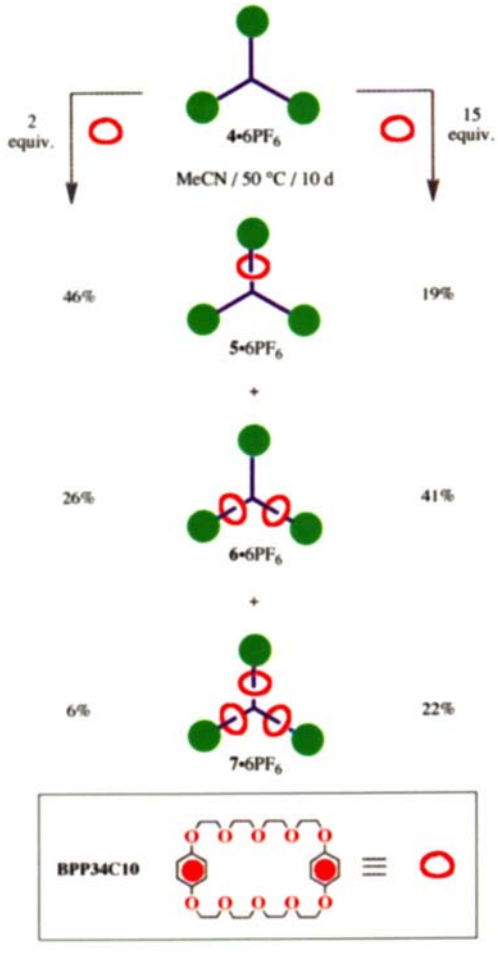
The triply-branched tris(bipyridinium) derivative **4**·6$PF_6$ was prepared (Scheme 1) *via* a two-step synthesis starting from the tribromide **1**.[23] Reaction of **1** with an excess of bipyridine in MeCN afforded **2**·$PF_6$,† after counterion exchange ($NH_4PF_6$/$H_2O$). This intermediate trication was then reacted with an excess of the freshly prepared[20] chloride **3** in DMF under ultra high pressure reaction conditions to give **4**·6$PF_6$,† again following counterion exchange. The end of each side-chain of **4**·6$PF_6$ is terminated with a stopper over which—given the right amount of thermal energy—**BPP34C10** can just slip.[18] Indeed, after heating **4**·6$PF_6$ at 50 °C in MeCN for 10 d in the presence of **BPP34C10** (2 equiv.), the [2]- **5**·6$PF_6$,† the [3]- **6**·6$PF_6$,† and [4]-rotaxanes **7**·6$PF_6$† were isolated (Scheme 2), after column




**Scheme 1** Two-step synthesis of the branched derivative **4**·6$PF_6$

chromatography, in yields of 46, 26 and 6%, respectively. When the experiment was repeated employing 15 equiv. of **BPP34C10**, under otherwise identical conditions, **5**·6$PF_6$, **6**·6$PF_6$, and **7**·6$PF_6$ were obtained in yields of 19, 41 and 22%, respectively. Interestingly, even when a large excess of macrocycle was employed the major product of the reaction was not the fully-occupied [4]rotaxane **7**·6$PF_6$, but rather the [3]rotaxane **6**·6$PF_6$. The reason for this result could be a consequence of the steric crowding around the central core, which inhibits the slipping on of the third macrocycle. Also, the third bipyridinium unit may have its recognition characteristics satisfied partially by the hydroquinone rings present in the two **BPP34C10** macrocycles already present in the [3]rotaxane **6**·6$PF_6$.

The branched compound **4**·6$PF_6$ and the rotaxanes **5**·6$PF_6$, **6**·6$PF_6$, and **7**·6$PF_6$ were fully characterised by electrospray mass spectrometry, and by $^1H$ and $^{13}C$ NMR spectroscopies. The electrospray mass spectra showed (Table 1), for all these compounds, peaks corresponding to the loss of two counterions, giving rise to signals with *m/z* values for $(M - 2PF_6)^{2+}$. In the case of the rotaxanes **6**·6$PF_6$ and **7**·6$PF_6$, the spectra also revealed the peaks corresponding to the loss of three counterions, affording signals with *m/z* values for $(M - 3PF_6)^{3+}$. Furthermore, for the compounds **4**·6$PF_6$, **5**·6$PF_6$ and **6**·6$PF_6$, we observed signals with *m/z* values for $(2M - 3PF_6)^{3+}$. These peaks correspond to the loss of three counterions from dimeric species.[24] Intermolecular π–π stacking interactions could be the origin of these dimers. The evidence for the formation of the rotaxanes was confirmed by the $^1H$ NMR spectrum recorded in $CD_3COCD_3$ at room temperature. The chemical shifts for the protons α and β to the nitrogen atoms in the bipyridinium units incorporated within the branched backbone of **4**·6$PF_6$ and of the rotaxanes **5**·6$PF_6$, **6**·6$PF_6$ and **7**·6$PF_6$, are listed in Table 2. The $^1H$ NMR spectrum of the branched derivative **4**·6$PF_6$ shows two pairs of doublets (δ 9.42, 9.26 and δ 8.69, 8.64) for the α and β protons. After the slipping on of one **BPP34C10** macrocycle to afford the [2]rotaxane **5**·6$PF_6$, the $^1H$ NMR spectrum shows four doublets (δ 9.37, 9.29, 9.09 and 9.02) for the four pairs of α protons and two doublets (δ 8.59 and 8.54) and one multiplet (δ 8.17–8.09) for the four pairs of β protons. The slipping on of a second **BPP34C10** macrocycle, to yield the [3]rotaxane **6**·6$PF_6$, does not change the symmetry of the system. Therefore, the $^1H$ NMR spectrum still shows four doublets (δ 9.32, 9.24, 9.15, and 9.12) for the α protons and two doublets (δ 8.52 and 8.36) and one multiplet (δ 8.28–8.19) for the β protons. After the slipping on of the third **BPP34C10** macrocycle to give the [4]rotaxane **7**·6$PF_6$, the original $C_3$ symmetry is restored. In fact, the $^1H$ NMR spectrum of **7**·6$PF_6$ shows only two doublets (δ 9.20 and 9.11) for the α protons and two doublets (δ 8.31 and 8.29) for the β protons. Interestingly, on going from the *free* compound **4**·6$PF_6$ to the fully occupied [4]rotaxane **7**·6$PF_6$, the resonances of both α and β protons shift to higher fields. The cause of this movement is thought to be the shielding effect exerted by the hydroquinone rings incorporated within the **BPP34C10** macrocycle. This result is confirmed by the up-field shift (Table 2) of the resonances of the protons directly attached to the hydroquinone rings. Nevertheless, the highest up-field shift for the protons of the hydroquinone rings is observed for the [2]rotaxane **5**·6$PF_6$. In this case, the hydroquinone rings incorporated within the **BPP34C10** can interact, not only with the bipyridinium unit threaded within the cavity of the macrocycle, but also with the two unoccupied bipyridinium units residing alongside. These additional interactions clearly result in a higher shielding effect being experienced by the hydroquinone protons.




**Scheme 2** Synthesis of the rotaxanes **5**·6$PF_6$, **6**·6$PF_6$ and **7**·6$PF_6$ *via* the slipping of **BPP34C10** over the stoppers of **4**·6$PF_6$

**Table 1** Electrospray mass spectrometry data[a] for the branched derivative **4**·6$PF_6$ and the rotaxanes **5**·6$PF_6$, **6**·6$PF_6$ and **7**·6$PF_6$

| Compound | M[b] | $(2M - 3PF_6)^{3+}$ | $(M - 2PF_6)^{2+}$ | $(M - 3PF_6)^{3+}$ |
|---|---|---|---|---|
| **4**·6$PF_6$ | (3373) | 2106 | 1543 | — |
| **5**·6$PF_6$ | (3909) | 2464 | 1811 | — |
| **6**·6$PF_6$ | (4446) | 2821 | 2080 | 1338 |
| **7**·6$PF_6$ | (4982) | — | 2348 | 1517 |

[a] ESMS spectra were obtained using a VG Prospec triple-focusing magnetic sector instrument operating at 4 kV accelerating voltage and fitted with an electrospray ion source. Solvent delivery to the spraying capillary employed a Jasco HPLC pump operating at a flow rate of 40 μl $min^{-1}$. Solutions of samples (5–10 pmol $\mu l^{-1}$ in MeCN) were introduced into the solvent flow *via* a Rheodyne model 7125 injection valve with a 20 μl loop. [b] The peaks corresponding to the molecular ions and $(M - PF_6)^+$ species were outside the mass range scanned. The molecular weights (M) are listed in parentheses. The measured masses correspond to the centroids of the unresolved isotopic distributions for each species.

**Table 2** Chemical shifts[a] for the protons α and β to nitrogen in the bipyridinium units and for the hydrogen atoms directly attached to the hydroquinol rings of the **BPP34C10** macrocycle

| Compound | α(δ) | β(δ) | ArH |
|---|---|---|---|
| **BPP34C10** | — | — | 6.77 |
| **4**·6$PF_6$[b] | 9.42, 9.26 | 8.69, 8.64 | — |
| **5**·6$PF_6$[c] | 9.37, 9.29, 9.09, 9.02 | 8.59, 8.54, 8.17–8.09 | 5.96 |
| **6**·6$PF_6$[c] | 9.32, 9.24, 9.15, 9.12 | 8.52, 8.36, 8.28–8.19 | 6.05 |
| **7**·6$PF_6$[b] | 9.20, 9.11 | 8.31, 8.27 | 6.15 |

[a] The $^1H$ NMR spectra were recorded at room temperature in $CD_3COCD_3$ on a Bruker AC300 (300 MHz) spectrometer. [b] The $^1H$ NMR spectrum of the compound shows two pairs of doublets for the α and β protons. [c] The $^1H$ NMR spectrum of the compound shows four doublets for the α protons and two doublets and one multiplet for the β protons.

The efficiency and the relative simplicity of the self-assembly approach leading to these novel rotaxanes suggests strongly the possibility of being able to generate more complex molecular assemblies. The synthesis of highly branched macromolecular skeletons, incorporating appropriate recognition sites for macrocycles can, in principle, lead to the construction of dendritic rotaxanes provided the macrocyclic components can be introduced efficiently by the slippage procedure.

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## Footnotes

† *Spectroscopic data* for **2**·6$PF_6$: mp 240 °C (decomp.); FABMS 875 (M − $PF_6$)$^+$, 729 (M − 2$PF_6$)$^+$; $^1$H NMR ($CD_3COCD_3$) δ 9.25 (6H, d, *J* = 7 Hz), 8.87–8.82 (6H, m), 8.60 (6H, d, *J* = 7 Hz), 8.09 (3H, s), 7.95–7.90 (6H, m), 6.17 (6H, m); $^{13}$C NMR ($CD_3CN$) δ 155.69, 152.07, 146.02, 141.76, 136.13, 131.92, 127.08, 122.60, 63.89.

For **4**·6$PF_6$: mp 225 °C (decomp.); ESMS 2106 (2M − 3$PF_6$)$^{3+}$, 1543 (M − 2$PF_6$)$^{2+}$; $^1$H NMR ($CD_3COCD_3$) δ 9.42 (6H, d, *J* = 7 Hz), 9.26 (6H, d, *J* = 7 Hz), 8.69 (6H, d, *J* = 7 Hz), 8.64 (6H, d, *J* = 7 Hz), 8.04 (3H, s), 7.63 (6H, d, *J* = 9 Hz), 7.30 (12H, d, *J* = 9 Hz), 7.15–7.04 (36H, m), 6.83 (6H, d, *J* = 9 Hz), 6.14 (6H, s), 6.09 (6H, s), 4.23–4.17 (6H, m), 4.16–4.09 (6H, m), 3.93–3.64 (12H, m), 2.28 (9H, s), 1.29 (54H, s); $^{13}$C NMR ($CD_3CN$) δ 161.18, 157.71, 151.47, 151.22, 149.09, 146.72, 146.41, 145.30, 145.16, 140.27, 136.31, 135.89, 132.72, 132.05, 131.55, 131.32, 128.78, 128.37, 128.23, 125.69, 124.95, 116.28, 114.01, 70.42, 70.20, 68.53, 68.14, 65.35, 64.61, 63.88, 34.74, 31.55, 20.77.

For **5**·6$PF_6$: mp 207 °C (decomp.); ESMS 2464 (2M − 3$PF_6$)$^{3+}$, 1811 (M − 2$PF_6$)$^{2+}$; $^1$H NMR ($CD_3COCD_3$) δ 9.37 (4H, d, *J* = 7 Hz), 9.29 (4H, d, *J* = 7 Hz), 9.09 (2H, d, *J* = 7 Hz), 9.02 (2H, d, *J* = 7 Hz), 8.59 (4H, d, *J* = 7 Hz), 8.54 (4H, d, *J* = 7 Hz), 8.17–8.09 (7H, m), 7.69 (2H, d, *J* = 9 Hz), 7.62 (4H, d, *J* = 9 Hz), 7.32–7.27 (12H, m), 7.15–7.05 (36H, m), 6.87–6.76 (6H, m), 6.22 (4H, s), 6.16 (2H, s), 6.05 (4H, s), 5.99 (2H, s), 5.96 (8H, s), 4.25–4.17 (6H, m), 4.16–4.08 (6H, m), 3.93–3.85 (32H, m), 3.84–3.55 (32H, m), 2.28 (9H, s), 1.29 (54H, s); $^{13}$C NMR ($CD_3CN$) δ 161.25, 157.69, 152.84, 151.40, 149.52, 146.80, 146.65, 146.19, 145.60, 145.52, 140.73, 136.37, 135.93, 132.78, 132.48, 132.32, 131.54, 131.29, 129.18, 128.38, 128.14, 125.43, 116.49, 116.38, 115.69, 114.37, 71.33, 71.19, 70.64, 70.51, 70.29, 68.75, 68.37, 65.40, 64.90, 64.10, 34.96, 31.62, 29.74, 20.90.

For **6**·6$PF_6$: mp 189 °C (decomp.); ESMS 2821 (2M − 3$PF_6$)$^{3+}$, 2080 (M − 2$PF_6$)$^{2+}$, 1338 (M − 3$PF_6$)$^{3+}$; $^1$H NMR ($CD_3COCD_3$) δ 9.32 (2H, d, *J* = 7 Hz), 9.24 (2H, d, *J* = 7 Hz), 9.15 (4H, d, *J* = 7 Hz), 9.12 (4H, d, *J* = 7 Hz), 8.52 (2H, d, *J* = 7 Hz), 8.36 (2H, d, *J* = 7 Hz), 8.28–8.19 (8H, m), 8.11 (3H, s), 7.71 (4H, d, *J* = 9 Hz), 7.60 (2H, d, *J* = 9 Hz), 7.30 (12H, d, *J* = 9 Hz), 7.15–7.05 (36H, m), 6.82 (6H, d, *J* = 9 Hz), 6.27 (6H, s), 6.05 (16H, s), 6.02 (4H, s), 6.01 (2H, s), 4.25–4.17 (6H, m), 4.15–4.07 (6H, m), 3.92–3.84 (12H, m), 3.83–3.60 (64H, m), 2.28 (9H, s), 1.29 (54H, s); $^{13}$C NMR ($CD_3CN$) δ 161.29, 157.81, 153.06, 149.64, 147.74, 146.84, 146.52, 146.18, 145.71, 145.63, 140.85, 136.73, 136.48, 132.88, 132.63, 132.38, 131.65, 131.40, 129.29, 128.35, 128.05, 126.41, 126.14, 125.54, 116.61, 116.52, 115.86, 114.47, 71.45, 71.32, 70.79, 70.62, 70.45, 68.90, 68.62, 68.49, 65.12, 64.40, 64.22, 35.08, 31.73, 21.01.

For **7**·6$PF_6$: mp 168 °C (decomp.); ESMS 2348 (M − 2$PF_6$)$^{2+}$, 1517 (M − 3$PF_6$)$^{3+}$; $^1$H NMR ($CD_3COCD_3$) δ 9.20 (6H, d, *J* = 7 Hz), 9.11 (6H, d, *J* = 7 Hz), 8.31 (6H, d, *J* = 7 Hz), 8.27 (6H, d, *J* = 7 Hz), 8.12 (3H, s), 7.74 (6H, d, *J* = 9 Hz), 7.29 (12H, d, *J* = 9 Hz), 7.16–7.04 (36H, m), 6.82 (6H, d, *J* = 9 Hz), 6.33 (6H, s), 6.15 (24H, s), 6.06 (6H, s), 4.21 (6H, t, *J* = 5 Hz), 4.11 (6H, t, *J* = 5 Hz), 3.93–3.63 (108H, m), 2.28 (9H, s), 1.28 (54H, s); $^{13}$C NMR ($CD_3CN$) δ 161.19, 157.69, 153.04, 149.53, 146.83, 146.47, 145.59, 145.51, 140.74, 136.37, 132.75, 132.57, 131.52, 131.27, 129.17, 126.44, 126.09, 126.01, 125.59, 125.42, 116.42, 116.31, 115.80, 114.35, 71.33, 71.21, 70.70, 70.49, 70.30, 68.79, 68.58, 68.37, 65.07, 64.31, 64.09, 34.96, 31.60, 20.88.

## References

1 H. L. Frisch and E. Wasserman, *J. Am. Chem. Soc.*, 1961, **83**, 3789.
2 G. Schill, *Catenanes, Rotaxanes and Knots*, Academic Press, New York, 1971.
3 D. M. Walba, *Tetrahedron*, 1985, **41**, 3161.
4 C. O. Dietrich-Buchecker and J. P. Sauvage, *Chem. Rev.*, 1987, **87**, 795.
5 J. F. Stoddart, *Chem. Aust.*, 1992, **59**, 576.
6 G. Wenz, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 803.
7 H. W. Gibson and H. Marand, *Adv. Mater.*, 1993, **5**, 11.
8 X. Sun, D. B. Amabilino, P. R. Ashton, I. W. Parsons and J. F. Stoddart, *Macromol. Symp.*, 1994, **77**, 191.
9 D. B. Amabilino, I. W. Parsons and J. F. Stoddart, *Trends Polym. Sci.*, 1994, **2**, 146.
10 M. Born and H. Ritter, *Makromol. Chem., Rapid Commun.*, 1991, **12**, 471.
11 H. Ritter, *Makromol. Symp.*, 1994, **77**, 73.
12 J. S. Lindsey, *New J. Chem.*, 1991, **15**, 153.
13 D. B. Amabilino and J. F. Stoddart, *Pure Appl. Chem.*, 1993, **65**, 2351.
14 D. B. Amabilino and J. F. Stoddart, *New Scientist*, 1994, **1913**, 25.
15 D. A. Tomalia, A. M. Naylor and W. A. Goddard III, *Angew. Chem., Int. Ed. Engl.*, 1990, **29**, 138.
16 D. A. Tomalia and H. Dupont-Durst, *Top. Curr. Chem.*, 1993, **165**, 193.
17 E. M. M. deBrabander-van der Berg and E. W. Meijer, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1308.
18 G. R. Newkome, C. N. Moorefield, J. M. Keith, G. R. Baker and G. H. Escamilla, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 666.
19 J. L. J. Fréchet, *Science*, 1994, **263**, 1710
20 P. R. Ashton, M. Bělohradský, D. Philp and J. F. Stoddart, *J. Chem. Soc., Chem. Commun.*, 1993, 1269.
21 P. R. Ashton, M. Bělohradský, D. Philp, N. Spencer and J. F. Stoddart, *J. Chem. Soc., Chem. Commun.*, 1993, 1274.
22 D. B. Amabilino, P. R. Ashton, M. Bělohradský, F. M. Raymo and J. F. Stoddart, Preceding Communication.
23 F. Vögtle, M. Zuber and R. G. Lichtenthaler, *Chem. Ber.*, 1973, **106**, 717.
24 P. R. Ashton, C. L. Brown, J. R. Chapman, R. T. Gallagher and J. F. Stoddart, *Tetrahedron Lett.*, 1992, **33**, 7771.