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Thiacalix[4]arene–porphyrin conjugates with high selectivity towards fullerene C_{70}

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Abstract—Molecular tweezers based on calix[4]arene- or thiacalix[4]arene–porphyrin conjugates have been prepared starting from tetraformyl calixarenes and aminoporphyrin moieties. As proven by NMR and UV/vis titration experiments, these compounds form 1:1 complexes with C_{60} and C_{70} fullerenes in solution while possessing a high selectivity towards fullerene C_{70}.

The unique three-dimensional shapes of calix[4]arenes[1] and thiacalix[4]arenes[2] together with their simple preparation make these compounds ideal candidates for application in supramolecular chemistry. Since the seminal work of Atwood[3a] and Shinkai[3b] on calix[8]arene–C_{60} inclusion complexes, many examples showing that the concave cavities of these compounds can serve for the recognition of spherical fullerenes have been reported.[4] Recent studies have revealed that the curved fullerene surfaces can interact with planar porphyrins or metalloporphyrins by attractive interactions.[5] While these interactions were originally studied in the solid state, it was soon discovered that suitably designed multi-porphyrin systems can also recognize fullerenes on the basis of their size in solution.[6] As we have shown in our previous studies, the combination of porphyrin and calixarene motifs can give rise to novel receptors with many interesting complexation properties.[7] It was demonstrated, that the calixarene core can serve as an efficient molecular scaffold enabling appropriate mutual arrangement of porphyrin units in space with recognition potential for fullerenes. In this Letter, we report the synthesis and binding ability of novel molecular tweezers designed for effective fullerene binding.[8]

The synthesis of target thiacalixarene-based receptor **7a** is depicted in Scheme 1. The starting thiacalix[4]arene was brominated with NBS in acetone[9] to give 5,11,17,23-tetrabromo derivative **2** in 68% yield. Subsequent alkylation using propyl iodide/K_2CO_3 in refluxing acetone gave, stereoselectively, the corresponding tetrapropoxy derivative **3** immobilized in the *1,3-alternate* conformation.[10] The generation of a tetralithium derivative using the described procedure[11] (*n*-BuLi/toluene, rt) failed. In contrast, reaction with *tert*-butyllithium in THF (conditions used in classical calixarene chemistry) and the subsequent addition of *N*-formylpiperidine led to the tetraaldehyde **4**[12] smoothly in 51% yield. The Schiff-base derivative **7a**[13] was then obtained in 62% yield by condensation of **4** with aminoporphyrin **5** in CH_2Cl_2. To gain a deeper insight into the role of calixarene preorganization on recognition process, the double bond (imine) of **7a** was reduced to a single bond (amine) **8a**[14] by $NaBH_3CN$ in THF. Similar reactions were also carried out with tetraaldehyde **6**[15] to yield the analogous receptors **7b**[16] and **8b**[17] representing derivatives with a classical calix[4]arene core moiety.

The complexation ability of the receptors towards fullerenes C_{60} and C_{70} was studied by ^{1}H NMR titrations in

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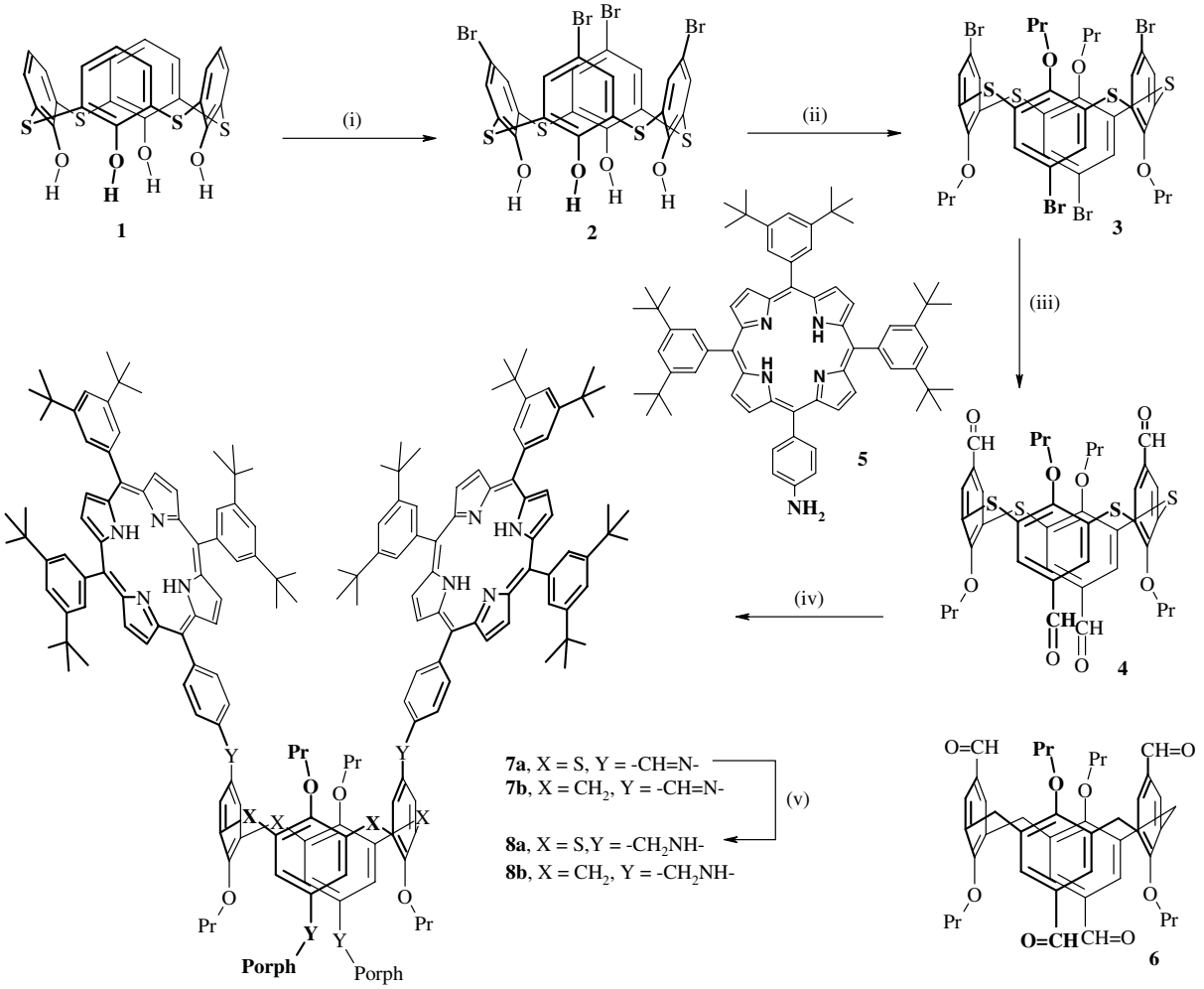

Scheme 1. Reagents and conditions: (i) NBS, acetone, rt (68%); (ii) K_2CO_3, PrI, acetone, reflux (62%); (iii) (a) *t*-BuLi, THF, −78 °C; (b) *N*-formylpiperidine (51%); (iv) **5**, mol sieves (4 Å), DCM (62% for **7a**, 72% for **7b**); (v) $NaBH_3CN$, THF–EtOH, rt (11% for **8a**, 70% for **8b**).

toluene-d_8 and benzene-d_6. Upon addition of excess (up to 15 equiv) of C_{70}, the proton resonances of the porphyrin NH shifted upfield (0.98 ppm **7a**/C_7D_8 and 0.75 ppm for **7a**/C_6D_6, 298 K, 300 MHz). Similar upfield shifts, albeit not so pronounced (0.22–0.28 ppm), were observed upon addition of C_{60}. The porphyrin aromatic resonances are subjected to minor complexation induced chemical shifts only (CIS < 0.1 ppm). Due to difficulties with following these shifts in the overcrowded aromatic region of the spectra, only the NH resonances of the porphyrin moieties were used for the construction of the corresponding titration curves and Job plots.

The 1:1 stoichiometry of binding of C_{60} and C_{70} to receptors **7** and **8** was established by Job plot analysis (Fig. 1). The only exception is represented by receptor **8a** in benzene, where the Job plot indicated the presumable presence of both 1:1 and 1:2 receptor–fullerene complexes. Assuming the 1:1 stoichiometry, the binding isotherms constructed from induced chemical shifts of the NH resonances were analyzed by a nonlinear least-squares method.[18] The corresponding binding constants are summarized in Table 1.

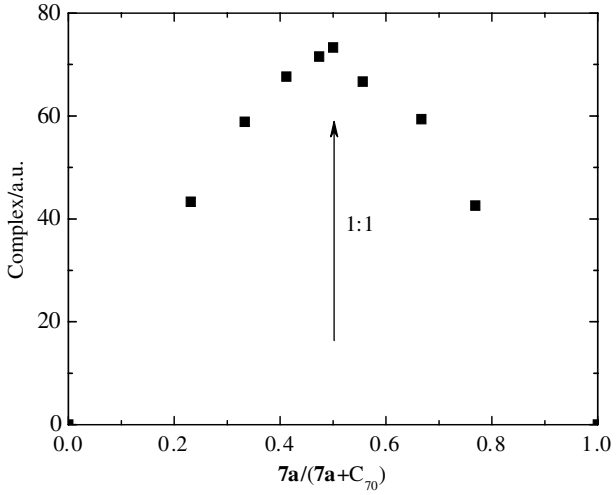

Figure 1. Job plot for the **7a** + C_{70} system in toluene-d_8 at 298 K (^{1}H NMR titration, 300 MHz).

NMR spectroscopy is optimally suitable for estimation of lower K_b values (<10^4 mol^{-1} L). As the K_b constants in benzene exceeded the limit value, reliable titration

Table 1. Binding constants K_b of **7a**–**8b** towards C_{60} and C_{70} fullerenes (^{1}H NMR titrations, 25 °C, 300 MHz)

	K_b [mol^{-1} L]			
	Benzene-d_6		Toluene-d_8	
	C_{60}	C_{70}	C_{60}	C_{70}
7a	2300	3.6×10^4	2000	2.0×10^4
	2000 ± 200[a]	$(3.3 \pm 0.2) \times 10^4$[a]	900 ± 100[a]	
7b	3600	4.9×10^4	2200	1.0×10^4
	3000 ± 300[a]	$(5.5 \pm 0.4) \times 10^4$[a]		
8a	[b]	[b]	6000	6200
8b	4400	5.2×10^4	3000	1.9×10^4

Experimental error less than 20%.
[a] Results from UV/vis titrations.
[b] Unclear stoichiometry.

curves were obtained using extremely dilute solutions ($c \approx 10^{-5}$ mol L^{-1}). To check our results independently we verified them through UV/vis titration experiments. The absorption spectra of the receptors were not affected by sulfur or methylene calixarene bridges and showed characteristic porphyrin absorption bands: the Soret band occurred at 423 nm and the Q-bands appeared at 518, 553, 594 and 650 nm. Three main features were noticed after the addition of C_{60} or C_{70}: (i) the original Soret band was red-shifted by several nm with significant hypochromicity indicating the formation of a host–guest complex between both components. (ii) Well-defined isosbestic points appeared which are typical of the presence of two spectroscopically distinguishable components. (iii) The appearance of very weak and broad absorption bands above 700 nm can be attributed to ground-state porphyrin-to-fullerene charge transfer interactions.[8b] The Soret band of the 1:1 complex retrieved from the global fit is shown in Figure 2 including the binding isotherm recorded at 423 nm.[19] Evidently, the K_b values are comparable with those obtained from the ^{1}H NMR titrations (Table 1). This demonstrates the compatibility of both methods and the absence of concentration-dependent effects on the function of the receptors.

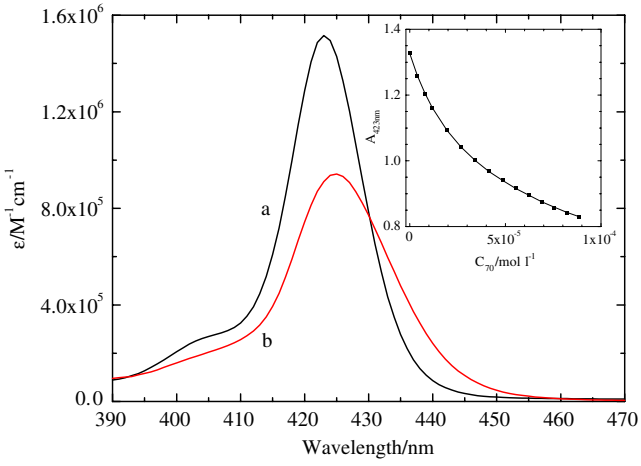

Figure 2. Absorption spectra of **7a** (a) and 1:1 complex **7a**–C_{70} (b). Inset: Binding isotherm at 423 nm, the solid line represents the least-squares fit to the experimental data.

It is worth noting that the binding constants are larger in benzene than in toluene, a feature that is more pronounced for binding of C_{70}. For example, the K_b values of **7b** increased from 1.0×10^4 to 4.9×10^4 mol^{-1} L in toluene and benzene, respectively. The fact that the binding constants are inversely proportional to the solubility of fullerenes (toluene is a better solvent than benzene)[20] was described recently[8b] indicating that solvation effects[8a] play an important role in fullerene recognition. In all cases, the receptors have substantially stronger affinity towards fullerene C_{70} than fullerene C_{60}. The resulting selectivity factor $K_b(C_{70})/K_b(C_{60})$ is solvent-dependent with larger values in benzene where the factor is above 10.

In conclusion, we have shown that calix[4]arenes and thiacalix[4]arenes in the *1,3-alternate* conformation bearing four porphyrin units behave as monodentate receptors with high C_{70}/C_{60} binding selectivity.

Acknowledgement

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References and notes

1. For books on calixarenes, see: (a) *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic: Dordrecht, 2001; (b) Mandolini, L.; Ungaro, R. *Calixarenes in Action*; Imperial College Press: London, 2000; (c) Gutsche, C. D. In *Calixarenes Revisited: Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; The Royal Society of Chemistry: Cambridge, 1998; Vol. 6.
2. For recent reviews on thiacalixarenes see: (a) Lhoták, P. *Eur. J. Org. Chem.* **2004**, 1675; (b) Morohashi, N.; Narumi, F.; Iki, N.; Hattori, T.; Miyano, S. *Chem. Rev.* **2006**, *106*, 5291.
3. (a) Atwood, J. L.; Koutsantonis, G. A.; Raston, C. L. *Nature* **1994**, *368*, 229–231; (b) Suzuki, T.; Nakashima, K.; Shinkai, S. *Chem. Lett.* **1994**, 699–702.
4. For selected papers, see: (a) Qin, D.; Zeng, X.; Li, Q.; Xu, F.; Song, H.; Zhang, Z. Z. *Chem. Commun.* **2007**, 147–149; (b) Haino, T.; Fukunaga, C.; Fukazava, Y. *Org. Lett.* **2006**, *8*, 3545–3548; (c) Iglesias-Sanches, J. C.; Fragoso, A.; de Mendosa, J. *Org. Lett.* **2006**, *8*, 2571–2574; (d) Zhang, S.; Eschegoyen, L. *J. Org. Chem.* **2005**, *70*, 9874–9881; (e) Makha, M.; Raston, C. L.; Sobolev, A. N.; Turner, P. *Crys. Growth Des.* **2005**, *6*, 224–228; (f) Kunsagi-Mate, S.; Szabo, K.; Bitter, I.; Nagy, G.; Kollar, L. *Tetrahedron Lett.* **2004**, *45*, 1387–1390; (g) Atwood, J. L.; Barbour, L. J.; Heaven, M. W.; Raston, C. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 3254–3257; (h) Atwood, J. L.; Barbour, L. J.; Heaven, M. W.; Raston, C. L. *Chem. Commun.* **2003**, 2270–2271.
5. For a review on fullerene–porphyrin interactions, see: Boyd, P. D. W.; Reed, C. A. *Acc. Chem. Res.* **2005**, *38*, 235–242.
6. For some recent examples, see: (a) Shoji, Y.; Tashiro, K.; Aida, T. *J. Am. Chem. Soc.* **2006**, *128*, 10690–10691; (b) Ouchi, A.; Tashiro, K.; Yamaguchi, K.; Tsuchiya, T.; Akasaka, T.; Aida, T. *Angew. Chem., Int. Ed.* **2006**, *45*,

3542–3546; (c) Wu, Z. Q.; Shao, X. B.; Li, C.; Hou, J. L.; Wang, K.; Jiang, X. K.; Li, Z. T. *J. Am. Chem. Soc.* **2005**, *127*, 17460–17468; (d) Iwamoto, H.; Yamaguchi, M.; Hiura, S.; Fukazawa, Y. *Heterocycles* **2004**, *63*, 2005–2011; (e) Yamaguchi, T.; Ishii, N.; Tashiro, K.; Aida, T. *J. Am. Chem. Soc.* **2003**, *125*, 13934–13935.

7. (a) Dudič, M.; Lhoták, P.; Stibor, I.; Dvořáková, H.; Lang, K. *Tetrahedron* **2002**, *58*, 5475–5482; (b) Dudič, M.; Lhoták, P.; Stibor, I.; Lang, K.; Prošková, P. *Org. Lett.* **2003**, *5*, 149–152; (c) Dudič, M.; Lhoták, P.; Petříčková, H.; Stibor, I.; Lang, K.; Sýkora, J. *Tetrahedron* **2003**, *59*, 2409–2415.
8. (a) Káš, M.; Lang, K.; Stibor, I.; Lhoták, P. *Tetrahedron Lett.* **2007**, *48*, 477–481; (b) Hosseini, A.; Taylor, S.; Accorsi, G.; Armaroli, N.; Reed, C. A.; Boyd, P. D. W. *J. Am. Chem. Soc.* **2006**, *128*, 15903–15913; (c) Dudič, M.; Lhoták, P.; Stibor, I.; Petříčková, H.; Lang, K. *New. J. Chem.* **2004**, *28*, 85–90; (d) Arimura, T.; Nishioka, T.; Suga, Y.; Murata, S.; Tachiya, M. *Mol. Cryst. Liq. Cryst.* **2002**, *379*, 413–418.
9. Kasyan, O.; Swierczynski, D.; Drapailo, A.; Suwinska, K.; Lipkowski, J.; Kalchenko, V. *Tetrahedron Lett.* **2003**, *44*, 7167–7170.
10. Desroches, C.; Lopes, C.; Kessler, V.; Parola, S. *Dalton Trans.* **2003**, 2085–2092.
11. Desroches, C.; Kessler, V. G.; Parola, S. *Tetrahedron Lett.* **2004**, *45*, 6329–6331.
12. *Preparation of 5,11,17,23-tetraformyl-25,26,27,28-tetrapropoxythiacalix[4]arene* **4**: A solution of 5,11,17,23-tetrabromo-25,26,27,28-tetrapropoxythiacalix[4]arene **3** (707 mg, 0.72 mmol) in dry THF (50 mL) was cooled to −78 °C under argon and *tert*-butyllithium (1.4 M in pentane, 28.9 mmol) was added and the reaction stirred for 2 h. *N*-Formylpiperidine (5.6 mL, 50.5 mmol) was added to the solution at −78 °C and the mixture was slowly warmed to room temperature. Next, 1 M aqueous HCl (10 mL) was added and the crude was extracted with diethyl ether (3 × 50 mL). The organic phase was dried over $MgSO_4$ and evaporated to dryness. Product **4** was obtained as a white powder after column chromatography on silica gel using petroleum ether/ethyl acetate = 3:1 as eluent (283 mg, yield 51%). Mp: 251–256 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ: 9.78 (s, 4H, –CH=O), 7.89 (s, 8H, ArH), 3.94 (t, $J = 7.1$ Hz, 8H, –OCH_2), 1.20–1.32 (m, 8H, CH_2), 0.61 (t, $J = 7.4$ Hz, 12H, –CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 189.8 (Ar–*C*H=O), 165.4 (Ar–C), 134.9 (Ar–C), 131.8 (Ar–C), 129.9 (Ar–C), 86.9 (–O–*C*H_2–), 23.0 (–O–CH_2–*C*H_2–), 10.1 (–CH_2–*C*H_3). TOF MS ES+ calcd for $C_{40}H_{40}O_8S_4$ [M+Na^+]: 799.1504. Found: 799.233 [M+Na^+]. IR (KBr): 1727 cm^{-1}.
13. *Preparation of derivative* **7a**: A mixture of derivative **4** (27 mg, 0.035 mmol) and aminoporphyrin **5** (220 mg, 0.23 mmol) in dry dichloromethane (15 mL) was refluxed over 4 Å molecular sieves under a nitrogen atmosphere for 7 days. The solvent was removed and the product was purified by column chromatography on aluminium oxide with petroleum ether/ethyl acetate = 3:1 as eluent (98 mg of a purple solid, yield 62%). Mp > 300 °C. ^{1}H NMR (C_6D_6, 300 MHz, 298 K) δ: 9.05–9.30 (m, 32H, porph-H), 8.15–8.55 (m, 32H, porph-ArH), 8.02 (s, 12H, porph-ArH), 7.85 (s, 8H, ArH), 7.58 (d, $J = 7.7$ Hz, 8H, porph-ArH), 4.36 (s, 4H, –CH=N–), 3.96 (t, $J = 7.1$ Hz, 8H, –OCH_2), 1.20–1.74 (m, 224H, –$C(CH_3)_3$ and CH_2), 0.94 (t, $J = 6.6$ Hz, 12H, –CH_3), −1.81 (s, 8H, NH). IR (KBr): 1627 cm^{-1}. UV–vis (benzene) λ_{max} (nm), ε (M^{-1} cm^{-1}) in parentheses: 423 (1.56×10^6), 518 (6.6×10^4), 553 (4.0×10^4), 594 (1.9×10^4), 650 (1.9×10^4). Elemental Anal. Calcd for $C_{312}H_{348}N_{20}O_4S_4$: C, 81.99; H, 7.67; N, 6.13. Found C, 81.68; H, 7.67; N, 6.08. MALDI MS calcd for [M^+]: 4570.55. Found: 4571.04.
14. *Preparation of derivative* **8a**: A mixture of **7a** (50 mg, 0.011 mmol) and $NaBH_3CN$ (14 mg, 0.220 mmol) was stirred in 10 mL of THF/ethanol mixture (1:1) at room temperature for 3 days under a nitrogen atmosphere. The reaction was quenched with 1 M aqueous HCl (1 mL) and the reaction mixture was then neutralized with aqueous NaOH. The crude product was extracted into dichloromethane (3 × 20 mL). The organic phase was dried over $MgSO_4$ and evaporated to dryness. Product **8a** (purple powder, 5 mg, 11% yield) was obtained by preparative TLC on aluminium oxide using petroleum ether/ethyl acetate (4:1) as eluent. Mp > 300 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ: 8.86–8.94 (m, 32H, porph-H), 8.01–8.07 (m, 32H, porph-ArH), 7.75 (s, 12H, porph-ArH), 7.68 (s, 8H, ArH), 6.96 (d, $J = 8.1$ Hz, 8H, porph-ArH), 4.46 (s, 8H, Ar–CH_2–N), 4.22 (s, 4H, –NH–), 4.13 (t, $J = 7.3$ Hz, 8H, –OCH_2), 1.20–1.74 (m, 224H, –$C(CH_3)_3$ and CH_2), 0.91 (t, $J = 6.3$ Hz, 12H, –CH_3), –2.68 (s, 8H, NH). EA calcd for $C_{312}H_{356}N_{20}O_4S_4$: C, 81.85; H, 7.84; N, 6.12. Found C, 81.48; H, 7.57; N, 5.98. MALDI MS calc. for [M^+]: 4578.61. Found: 4579.187. IR (KBr): 3435 cm^{-1}.
15. Lhotak, P.; Shinaki, S. *Tetrahedron Lett.* **1996**, *37*, 645–648.
16. *Preparation of derivative* **7b**: This compound was obtained analogously to **7a** using **6** as the starting material. Purple powder, 72% yield, mp > 300 °C. ^{1}H NMR (C_6D_6, 300 MHz, 298 K) δ: 9.11–9.30 (m, 32H, porph-H), 8.21–8.42 (m, 32H, porph-ArH), 8.03 (s, 12H, porph-ArH), 7.91 (s, 8H, ArH), 7.60 (d, 8H, $J = 7.7$ Hz, porph-ArH), 4.31 (s, 4H, –CH=N–), 3.95 (t, $J = 7.3$ Hz, 8H, –OCH_2), 3.70 (s, 8H, Ar–CH_2–Ar), 0.98–1.82 (m, 236H, –$C(CH_3)_3$ and CH_2 and –CH_3), −1.84 (s, 8H, NH). IR (KBr): 1628 cm^{-1}. UV–vis (benzene) λ_{max} (nm), ε ($M^{-1}cm^{-1}$) in parentheses: 423 (1.72×10^6), 518 (6.9×10^4), 553 (4.2×10^4), 594 (1.9×10^4), 650 (2.0×10^4). EA calcd for $C_{316}H_{356}N_{20}O_4$: C, 84.37; H, 7.98; N, 6.23. Found C, 84.49; H, 8.04; N, 6.01. MALDI MS calcd for [M^+]: 4498.39. Found: 4500.15.
17. *Preparation of derivative* **8b**: Prepared analogously to **8a** using **7b** as the starting material. Purple powder with mp > 300 °C, 70% yield. ^{1}H NMR ($CDCl_3$, 300 MHz, 298 K) δ: 8.86–8.98 (m, 32H, porph-H), 8.50 (s, 8H, ArH), 8.08–8.13 (m, 32H, porph-ArH), 7.80 (s, 12H, porph-ArH), 7.14 (d, $J = 8.4$ Hz, 8H, porph-ArH), 4.26 (s, 8H, Ar–CH_2–N), 4.10 (s, 4H, –NH–), 3.94 (t, $J = 7.1$ Hz, 8H, –OCH_2), 3.68 (s,8H, Ar–CH_2–Ar), 1.02–1.80 (m, 236H, –$C(CH_3)_3$ and CH_2 and –CH_3), −2.66 (s, 8H, NH). IR (KBr): 3443 cm^{-1}. EA calcd for $C_{316}H_{364}N_{20}O_4$: C, 84.22; H, 8.14; N, 6.22. Found: C, 83.89; H, 7.89; N, 6.03. MALDI MS calcd for [M^+]: 4506.45. Found: 4529.069 [M+Na^+].
18. The binding constants were calculated using the computer program OPIUM (Kyvala M.) freely available at: http://www.natur.cuni.cz/~kyvala/opium.html.
19. *Binding experiments*: All UV/vis experiments were performed in benzene or toluene at 295 K by adding aliquots of a fullerene stock solution to a receptor solution of micromolar concentration and to the solvent. The latter solution was used as a reference sample. The recorded sets of absorption spectra were globally analyzed using the SPECFIT program (v. 3.0, Spectrum Software Associates) to obtain the corresponding absorption spectra of complexes and binding constants.
20. Sivaraman, N.; Dhamodaran, R.; Kaliappan, I.; Srinivasan, T. G.; Vasudeva Rao, P. R.; Mathews, C. K. *Fullerene Sci. Technol.* **1994**, *2*, 233–246.