COMMUNICATION

Sandwiching C_{70} between two crown ether-bound cations: regioselective synthesis, electrochemistry and cation binding properties of C_{70} bis-crown ether conjugates

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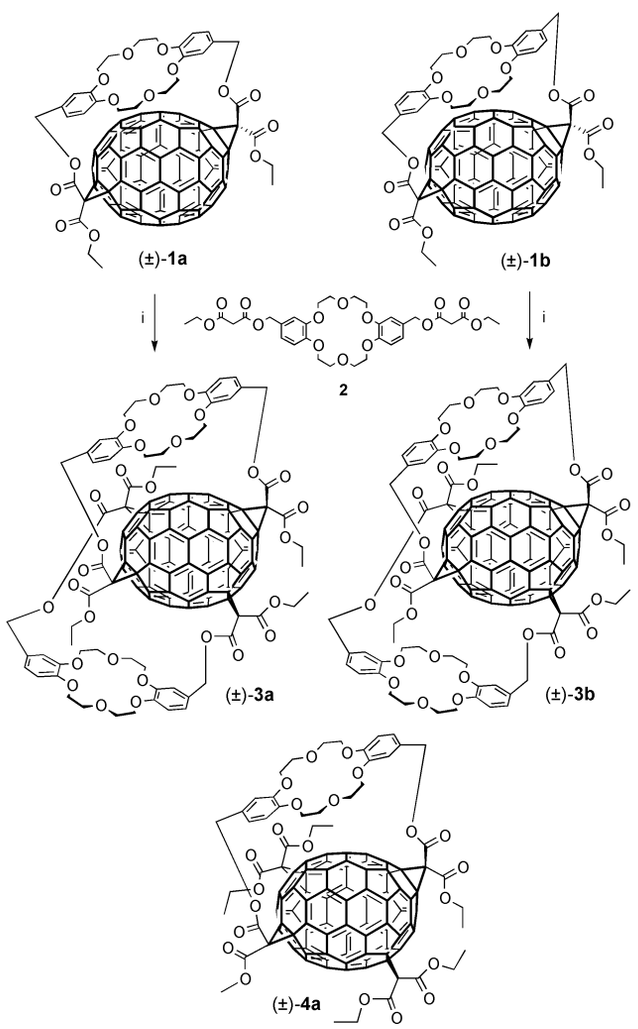
Tetrakis-adducts of C_{70}, featuring two covalently attached crown ethers, form stable 1 : 1 and 1 : 2 host–guest complexes with alkali metal cations. A large influence of cation complexation on the first reduction potential of the fullerene was observed.

Recently, we reported the regioselective synthesis of the two diastereoisomeric C_{70} crown ether conjugates (±)-**1a** and (±)-**1b**.[1] In a Newman-type projection looking down the C_5 axis of the C_{70} core onto the two polar pentagons, the two addends at the C(1)–C(2) and C(67)–C(68) bonds on the carbon sphere adopt a five o'clock geometrical relationship.[2] Third and fourth Bingel additions to bis-cyclopropanated C_{70}[3] also occur regioselectively at the 6–6 bonds C(31)–C(32) and C(42)–C(43) on opposite hemispheres,[2] with the geometric relationship between the two addends at one hemisphere corresponding to the kinetically favoured equatorial (*e*) addition pattern in C_{60}.[4] The distance between the two "*e*-type" 6–6 bonds in (±)-**1a/b** is similar to that between the two bonds already functionalised. Thus, it should be possible to bridge the carbon sphere with a second crown ether by Bingel macrocyclisation, allowing for the first time the study of the electrochemistry of a fullerene sandwiched between two crown ether-bound cations.

When (±)-**1a** was reacted under modified Bingel conditions (I_2, DBU, toluene–Me_2SO 4 : 1) with a bis-malonate containing an *anti*-substituted dibenzo[18]crown-6 (DB18C6) tether,[5] an inseparable mixture of four bis-crown ether conjugates was obtained in 69% yield. On the other hand, when bis-malonate **2**,[6] with a *syn*-substituted DB18C6 tether, was employed under the same conditions, a single bis-crown ether conjugate ((±)-**3a**) was formed regio- and stereoselectively in 31% yield (Scheme 1). The *syn*-tether, advantageously, does not introduce additional planar chirality into the product. Also, with its shorter length, it probably avoids *in–out* isomerism at the methano bridge C-atoms, and bridges the two "*e*-type" 6–6 bonds only in the *out–out* configuration.

Similarly, Bingel macrocyclisation of (±)-**1b** with **2** led to tetrakis-adduct (±)-**3b** in 26% yield. Both (±)-**3a** and (±)-**3b** were fully characterised by ^1H and ^{13}C NMR, IR, UV–Vis and MALDI-TOF MS.† The addition pattern in (±)-**3a/b** is C_2-symmetrical, but the overall symmetry is C_1 (^{13}C NMR) due to the two different types of DB18C6 tethers. To ascertain the C_2-symmetrical addition pattern, compound (±)-**4a** (50% yield) was prepared for comparison by reacting (±)-**1a** with diethyl 2-bromomalonate (2 equiv.) under modified Bingel conditions. From the ^{13}C NMR spectrum, which displays the 31 resonances expected for sp^2-hybridised fullerene C-atoms, the C_2-symmetry of (±)-**4a** was readily deduced. The UV–Vis spectra of (±)-**4a** and (±)-**3a/b** are virtually identical, providing support for the correct structural assignment of the bis-crown ether conjugates. Additional evidence comes from the first reduction potentials, which are also similar for (±)-**3a/b** and (±)-**4a** (*vide infra*).



Scheme 1 Synthesis of the C_{70} bis-crown ether conjugates (±)-**3a/b**. *Reagents and conditions*: i, I_2, DBU, toluene–Me_2SO (4 : 1), 20 °C; 31% ((±)-**3a**); 26% ((±)-**3b**). Also shown is comparison compound (±)-**4a**.

Cation binding properties of (±)-**1a/b**, (±)-**3a/b** and (±)-**4a** were studied with the help of ion-selective electrodes (ISEs), the membrane of which was composed of the respective ionophore, sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaTFPB, ion exchanger), bis(2-ethylhexyl) sebacate (DOS, plasticizer) and poly(vinyl chloride) (PVC) of high molecular weight.[7,8] The ISEs showed theoretical (Nernstian) response to the chloride solutions of the investigated cations. All crown ether conjugates act as ionophores with a selectivity for K^+.

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Table 1 Effective complex formation constants of C_{70} crown ether conjugates, log β, obtained for the organic membrane phase with the sandwich membrane method (for K^+) and from the potentiometric selectivity coefficients (for the other ions)[a]

Ligand	Stoichiometry[b]	K^+	Na^+[c]	NH_4^+[c]	H^+[c]
(±)-**1a**	1 : 1	5.90 ± 0.05	4.28 ± 0.05	4.57 ± 0.05	3.12 ± 0.06
(±)-**1b**	1 : 1	5.90 ± 0.03	4.10 ± 0.03	4.60 ± 0.03	3.17 ± 0.04
(±)-**3a**	1 : 1	5.96 ± 0.04	4.82 ± 0.04	4.39 ± 0.04	2.94 ± 0.06
(±)-**3a**	1 : 2	11.31 ± 0.44			
(±)-**3b**	1 : 1	6.04 ± 0.09	4.45 ± 0.09	4.53 ± 0.10	3.59 ± 0.10
(±)-**3b**	1 : 2	11.36 ± 0.57			
(±)-**4a**	1 : 1	6.04 ± 0.01	4.25 ± 0.05	4.82 ± 0.01	3.86 ± 0.06

[a] Error bounds: standard deviations of five measurements. [b] Assumed host–guest stoichiometries. The values for (±)-**3a** and (±)-**3b** were obtained from two measurements, with a molar excess of the ligand and the ion exchanger, respectively. [c] The ISE membrane conditions do not allow a correct determination of the second step complex formation constant.

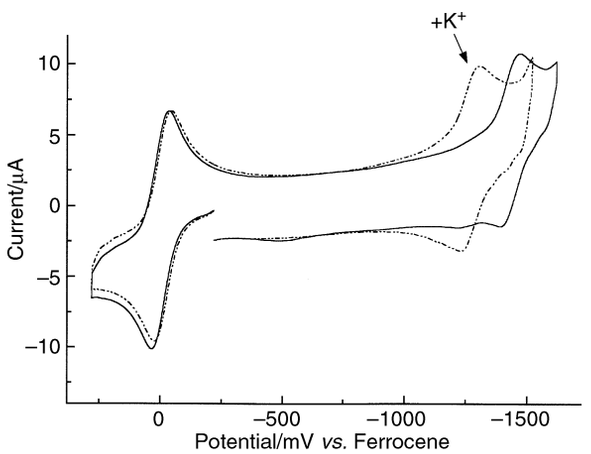

Fig. 1 CV response of (±)-**3b** in the absence (——) and presence (-..-..-) of 2 equivalents of KPF_6 at a scan rate of 100 mV s^{-1}.

Table 2 Redox potentials of C_{70} crown ether conjugates (*vs.* ferrocene–ferricinium couple) in the absence or presence of alkali metal cations. Values in parentheses are the ΔE_{pp} in mV[a]

	E_1/V	E_2/V	+ KPF_6 E_1/V	+ $NaBF_4$ E_1/V
(±)-**1a**	−1.13 (67)	−1.57[b]	−1.05 (65)[c]	−1.06 (68)[e]
(±)-**1b**	−1.14 (68)	−1.58[b]	−1.07 (68)[c]	−1.06 (67)[e]
(±)-**3a**	−1.47[b]	−1.72[b]	−1.31[b,d]	−1.30[b,f]
(±)-**3b**	−1.44 (83)	−1.74[b]	−1.27 (76)[d]	−1.27 (87)[f]
(±)-**4a**	−1.43[b]	−1.71[b]	−1.33[b,c]	−1.34[b,e]

[a] Measurements were performed under Ar in toluene–MeCN (4 : 1) containing 0.1 M Bu_4NPF_6 as the supporting electrolyte. Concentration of ionophores: 0.2–0.3 mM. Salts were dissolved in MeCN and added in μL amounts. Glassy carbon working electrode. Non-aqueous Ag/Ag^+ reference electrode. Pt wire counter electrode. Scan rate 100 mV s^{-1}. [b] Cathodic peak potential. The reversibility of the first reduction of (±)-**3a** and (±)-**4a** was difficult to ascertain due to the presence of a small, yet significant redox couple resulting from a minor fullerene impurity. [c] + 1.0 equiv. of KPF_6. [d] + 2.0 equiv. of KPF_6. [e] + 1.0 equiv. of $NaBF_4$. [f] + 2.0 equiv. of $NaBF_4$.

Effective complex formation constants with K^+ (β) in the organic membrane phase were determined by the sandwich membrane method[9] and found to be the same for all compounds within experimental error ($\beta_1 \approx 10^6$ M^{-1}, Table 1). The same holds true for the 1 : 2 host–guest complexes of (±)-**3a/b** ($\beta_2 \approx 2 \times 10^{11}$ M^{-2}). As no distinction can be made between the two different crown ether sites in (±)-**3a/b** *via* ISE membrane measurements, these numbers represent average binding properties in the 1 : 1 and 1 : 2 complexes. Effective complex formation constants for the other investigated ions were obtained from the potentiometric selectivity coefficients and the K^+ values from sandwich membrane measurements (Table 1).[10]

To determine the effects of cation complexation on the redox properties of the crown ether conjugates, cyclic voltammetric studies were performed in toluene–MeCN (4 : 1) in the absence and presence of KPF_6 and $NaBF_4$ (Table 2). Based on the ΔE_{pp} values, the first fullerene-centered reduction waves of these conjugates appear to be either reversible or quasi-reversible. However, the second reductions are chemically irreversible as judged by the appearance of additional oxidation waves on the reverse scan. Consequently, cation binding effects were only monitored for the first reductions.

Addition of one equivalent of KPF_6 to (±)-**1a/b** caused a shift of the first reduction wave by 70 to 80 mV which was explained by the electrostatic effect of the K^+ ion bound closely to the fullerene core.[1] Similar electrostatic effects have been observed for fulleropyrrolidinium salts which reduce at a potential which is 60 mV less negative with respect to C_{60}.[11] Much larger shifts are measured when the fullerene is sandwiched between two cations. Addition of one equivalent of K^+ ions to tetrakis-adducts **3a/b** produced the appearance of two new, poorly resolved redox couples which must correspond to the 1 : 1 and 1 : 2 host–guest complexes, respectively. Addition of two equivalents of K^+ ions resulted in only one redox couple which is anodically shifted by 170 mV with respect to the corresponding wave in the absence of the salt (Fig. 1). The addition of more K^+ ions caused no further changes in the voltammetric response. This clearly establishes that the redox couple, shifted by 170 mV, corresponds to a complex with two K^+ ions.[12] Similar anodic shifts were observed upon addition of $NaBF_4$.

The magnitude of the cation-induced redox shift in (±)-**3a/b** (170 mV) is about twice that measured for (±)-**1a/b**; accordingly, there is no cooperative effect between the two binding sites. MM2-calculations indicate that the cation in the *anti*-DB18C6 site is located above the midpoint of a hexagon, whereas in the *syn*-DB18C6 site it sits above the midpoint of a pentagon. However, the redox effects resulting from cation binding at both sites are similar. This implies that the potential shifts only depend on the distance and not on the location of the cation with respect to the fullerene surface. Hence it is concluded that the measured anodic shifts are purely caused by electrostatic effects, in contrast to the π-interactions observed for sandwich complexes of C_{60} and C_{70} with zinc(II) porphyrins.[13]

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Notes and references

† *Selected data* for (±)-**3a**: λ_{max} (CH_2Cl_2)/nm 269sh (ε/dm^3 mol^{-1} cm^{-1} 87 910), 314sh (32 230), 375sh (17 310), 422 (18 510), 490sh (9720), 533sh (7340), 579sh (3700), 625sh (2360); δ_H (500 MHz; $CDCl_3$) 7.09 (1 H, d, *J* 7.9), 6.93 (1 H, s), 6.86–6.80 (5 H, m), 6.71 (1 H, d, *J* 7.9), 6.56 (1 H, d, *J* 8.0), 6.39 (1 H, d, *J* 8.5), 6.33 (1 H, d, *J* 8.3), 6.21 (1 H, d, *J* 1.1), 5.79 (1 H, d, *J* 11.6), 5.73 (1 H, d, *J* 11.0), 5.68 (1 H, d, *J* 11.0),

5.54 (1 H, d, *J* 11.0), 4.99 (1 H, d, *J* 11.6), 4.88 (1 H, d, *J* 11.0), 4.82 (1 H, d, *J* 11.0), 4.68 (1 H, d, *J* 11.0), 4.61–3.61 (40 H, m), 1.54 (3 H, t, *J* 7.1), 1.53 (3 H, t, *J* 7.1), 1.49 (3 H, t, *J* 7.1), 1.30 (3 H, t, *J* 7.1); δ_C (125 MHz; $CDCl_3$) 164.62, 163.71, 163.61, 162.96, 162.47, 162.32, 162.08, 162.03, 151.65, 151.49, 151.01, 150.94, 149.42, 149.16, 149.12, 148.87, 148.85, 148.79, 148.66, 148.52, 148.26, 147.99, 147.71, 147.64, 147.48, 147.41 (2×), 147.30, 147.28, 147.06, 146.00, 145.00, 144.40, 144.35, 143.95, 143.90, 143.07, 142.34, 141.68, 141.64, 146.59, 141.51, 141.47, 141.27, 141.16, 141.15, 140.97, 140.96, 140.72, 140.68, 140.35, 139.16, 139.02, 138.98, 138.85 (2×), 138.51, 138.27, 138.06, 137.36, 137.00, 136.75, 135.11, 135.04, 134.79, 134.52, 134.20, 134.00, 133.95, 133.40, 133.24, 133.21, 132.35, 131.85, 131.62, 130.24, 129.27, 128.62, 127.32, 127.23, 126.87, 126.04, 123.64, 123.59, 123.43, 122.09, 115.17, 115.08, 114.20, 112.15, 112.10, 111.97, 111.63 (2×), 70.68, 70.58 (2×), 70.40, 70.21, 70.05, 69.97, 69.92, 69.75, 69.65, 69.44 (2×), 69.38, 69.01, 68.80, 68.73, 68.66, 68.46, 68.10, 67.95, 67.72, 67.67, 66.97, 66.87, 64.07, 64.05, 63.40 (2×), 63.30, 63.28, 63.23, 62.98, 40.24, 40.07, 39.46, 39.11, 14.39, 14.33, 14.12, 14.09; HR-MALDI-FT-MS (2,5-dihydroxybenzoic acid) m/z = 2151.4130 ($[M + Na]^+$, $C_{134}H_{72}O_{28}Na^+$, calcd. 2151.4102).

1 M. J. van Eis, R. J. Alvarado, L. Echegoyen, P. Seiler and F. Diederich, *Chem. Commun.*, 2000, 1859.

2 (*a*) A. Herrmann, M. Rüttimann, C. Thilgen and F. Diederich, *Helv. Chim. Acta*, 1995, **78**, 1673; (*b*) A. Herrmann, M. W. Rüttimann, T. Gibtner, C. Thilgen, F. Diederich, T. Mordasini and W. Thiel, *Helv. Chim. Acta*, 1999, **82**, 261.

3 C. Bingel and H. Schiffer, *Liebigs Ann. Chem.*, 1995, 1551.

4 A. Hirsch, I. Lamparth, T. Grösser and H. R. Karfunkel, *J. Am. Chem. Soc.*, 1994, **116**, 9385.

5 J.-P. Bourgeois, P. Seiler, M. Fibbioli, E. Pretsch, F. Diederich and L. Echegoyen, *Helv. Chim. Acta*, 1999, **82**, 1572.

6 The synthesis of **2** closely follows the one reported for the *anti*-DB18C6 analog[5] and will be published in a subsequent full paper.

7 E. Bakker, P. Bühlmann and E. Pretsch, *Chem. Rev.*, 1997, **97**, 3083.

8 E. Bakker and E. Pretsch, *Anal. Chem.*, 1998, **70**, 295.

9 Y. Mi and E. Bakker, *Anal. Chem.*, 1999, **71**, 5279.

10 A. Ceresa and E. Pretsch, *Anal. Chim. Acta*, 1999, **395**, 41.

11 T. Da Ros, M. Prato, M. Carano, P. Ceroni, F. Paolucci and S. Roffia, *J. Am. Chem. Soc.*, 1998, **120**, 11645.

12 S. R. Miller, D. A. Gustowski, Z. Chen, G. W. Gokel, L. Echegoyen and A. E. Kaifer, *Anal. Chem.*, 1988, **60**, 2021.

13 J. Zheng, K. Tashiro, Y. Hirabayashi, K. Kinbara, K. Saigo, T. Aida, S. Sakamoto and K. Yamaguchi, *Angew. Chem., Int. Ed.*, 2001, **40**, 1857.