A new synthon for the incorporation of [60]fullerene in macrocycles

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A bis(methano)fullerenedicarboxylic acid was obtained in four steps from C_{60} as a new synthon for incorporation of the carbon sphere into macrocycles; the preparation of the target compound involves the tether-directed synthesis of a macrocyclic *cis*-2 bis(malonic acid diester) adduct of C_{60}, followed by selective ester deprotection, decarboxylation of the formed bis(malonic acid monoester) and removal of the tether.

Since their discovery, fullerenes and their covalent derivatives[1] have attracted increasing attention, due to their original structure and unusual optical and electronic properties which make them powerful tools in molecular construction and engineering. For instance, the preparation of macrocycles incorporating C_{60} is of substantial interest in the fields of functional supramolecular architecture[2] and advanced materials.[3] Cyclophane-type C_{60} crown ether conjugates as electrochemical ion sensors,[4] C_{60} porphyrin conjugates as photochemical molecular devices,[5] fullerene-containing catenanes[6] and C_{60} nesting on the concave surface of a covalently attached cyclotriveratrylene cap[7] represent some recent examples of macrocyclic fullerene derivatives. For further developments, a general synthon for incorporation of the carbon sphere into macrocyclic structures was highly desirable. Here we report the preparation of *cis*-2 bis(methano)fullerenedicarboxylic acid **1** (Fig. 1) in which the bis(methano)fullerene scaffold functions as the backbone of a U-type motif at the ends of which two precisely positioned COOH groups point in the same direction. This convergent orientation of the two functional groups is ideal for the formation of macrocyclic diesters, diamides or other constructs. The synthesis of **1** takes advantage of our tether-directed remote functionalization strategy[8,9] and proceeds not only regioselectively, yielding predominantly the *cis*-2 adduct, but also stereoselectively, thereby discriminating between the possible **in-in** (**1**), **in-out** and **out-out** diastereoisomers (Fig. 1). The length of the tether was selected to provide a *cis*-2 rather than the regioisomeric *cis*-3 bis-adduct, in order to avoid additional stereoisomerism resulting from the intrinsically chiral addition pattern in the latter.

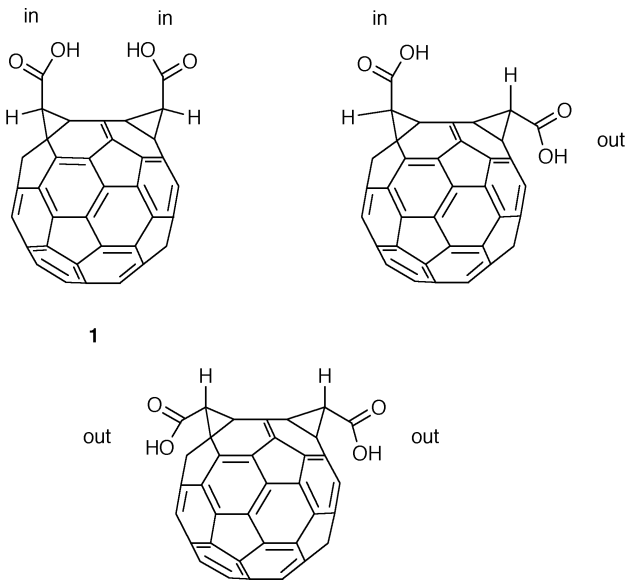


Fig. 1 The novel **in-in** *cis*-2 bis-adduct **1** and its two **in-out** and **out-out** stereoisomers.

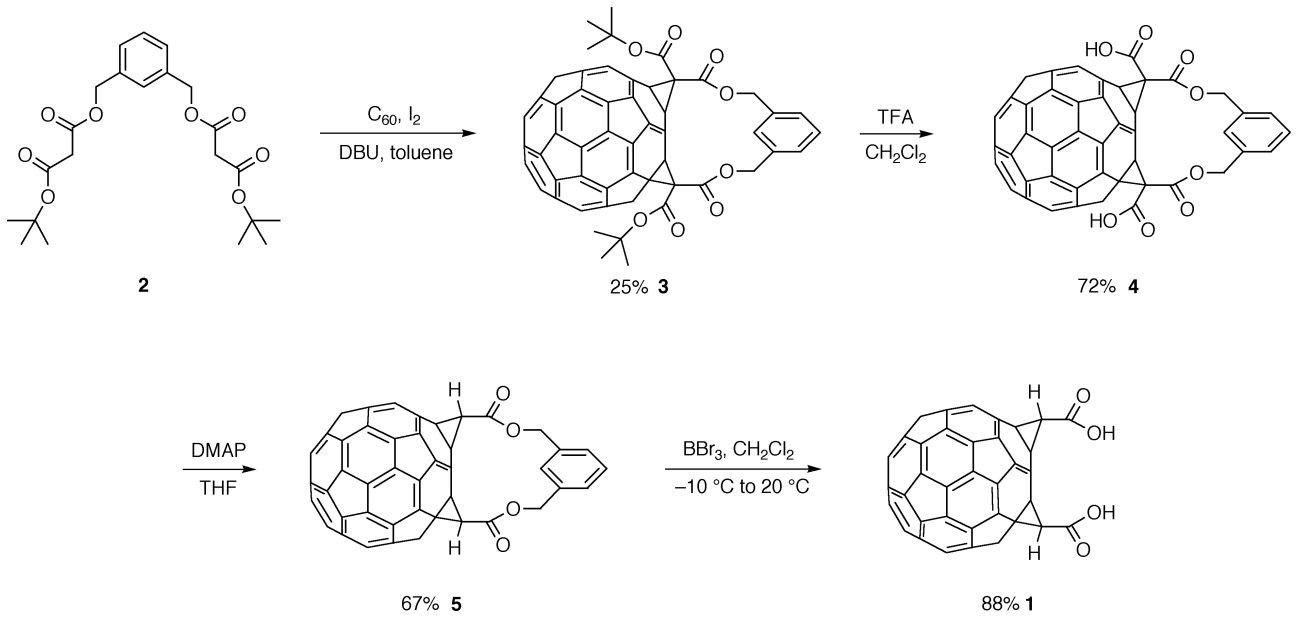
For the synthesis of **1** (Scheme 1), bis(malonate) **2** was prepared by heating Meldrum's acid in Bu^{t}OH (90 °C, 4 h) to give *tert*-butyl malonate (Bu^{t}O$_2$CCH$_2$CO$_2$H) in 74% yield. Two equivalents of this ester reacted with benzene-1,3-dimethanol in the presence of dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (DMAP) in THF to afford **2** in 80% yield. The Bingel macrocyclization[10] of **2** with C_{60} was carried out in the presence of I_2 and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give the *cis*-2 bis-adduct **3** in 25% yield together with a minor amount of e bis-adduct (4% yield).[11] This reaction proceeded with a slightly decreased yield and regioselectivity compared to the conversion of the diethyl ester analog of **2** with C_{60} which provided the corresponding *cis*-2 bis-adduct in 33% yield with only traces of other regioisomers.[9] For both regioisomers, UV/Vis and NMR spectral comparisons provided a clear assignment of the addition patterns.[9b,11] Selective hydrolysis of the *tert*-butyl ester residues with trifluoroacetic acid (TFA) in CH_2Cl_2[12] afforded the dicarboxylic acid **4** (72% yield) which precipitated out of solution. This bis(malonic acid monoester) was readily decarboxylated in basic solution. Stirring a mixture of **4** with DMAP in THF[13] under Ar for 20 h at 20 °C gave **5** in 67% yield. Finally, cleavage of the tether using BBr_3 in CH_2Cl_2 produced **1** in high yield (88%). Using this route, gram quantities of **1** can be readily prepared.

The spectroscopic data were in full agreement with the proposed structures of the C_s-symmetrical C_{60} bis-adducts **1** and **3**–**5**. Mass spectra (FAB, MALDI-TOF, ESI) showed the molecular ions which appeared as the parent ions in the spectra of **3** and **5**. The ^{1}H NMR spectrum of **3** ($CDCl_3$, 300 MHz) featured a characteristic AB quartet for the benzylic CH_2 protons. The ^{13}C NMR spectra displayed the correct number of C-atom resonances expected for C_s-symmetrical bis-adducts. Purification and characterization of the two dicarboxylic acids **1** and **4** proved quite difficult due to solubility problems; nevertheless, a full characterization of the pure target compound **1** was obtained. We are currently investigating the construction of various macrocycles using **1** as a synthon to incorporate C_{60} in their backbone.

Experimental

General

See ref. 14.



2 25% **3** 72% **4**

67% **5** 88% **1**

Scheme 1 Synthesis of bis(methano)fullerenedicarboxylic acid **1**.

Syntheses

61,62-Di(*tert*-butyl)-*endo*,*endo*-61,62-(*m*-phenylenedimethylene)-1,2 : 7,21-bis(methano)[60]fullerene-61,61,62,62-tetracarboxylate 3. DBU (2 ml, 13.2 mmol) was added under N_2 at 20 °C to a well-degassed solution of C_{60} (1.44 g, 2 mmol), I_2 (1.22 g, 4.8 mmol) and **2** (844 mg, 2.2 mmol) in toluene (1.5 l), and the mixture was stirred for 4 h. The crude material was filtered through a short plug (SiO_2), first eluting with toluene to remove unreacted C_{60} and then with CH_2Cl_2–MeOH (98 : 2). Column chromatography (SiO_2;hexane–CH_2Cl_2 (8 : 2 → 4 : 6) yielded **3** (565 mg, 25%) besides the corresponding e bis-adduct (78 mg, 4%). Orange solid (mp > 280 °C); υ_{max}(KBr)/cm^{-1} 1750 (C=O); λ_{max}(THF)/nm (ε/dm^3 mol^{-1}) 258 (106 300), 324 (sh, 29 900), 377 (sh, 9630), 437 (2960), 468 (2610); δ_H(300 MHz, $CDCl_3$) 7.55 (1 H, s), 7.41 (1 H, t, *J* 6.9), 7.29 (2 H, d, *J* 6.9), 5.88 (2 H, d, *J* 12.9), 5.19 (2 H, d, *J* 12.9 Hz), 1.55 (18 H, s, CH_3); δ_C(125 MHz, $CDCl_3$) 163.30, 161.63, 148.83, 147.43, 147.38, 147.21, 146.15, 145.97, 145.71, 145.64, 145.53, 145.26, 145.09 (2 ×), 145.02, 144.46, 144.43, 144.15, 144.07, 143.85, 143.62, 143.48, 143.21, 143.07, 142.24, 141.17, 140.92, 139.77, 137.15, 136.58, 136.18, 135.75, 135.22, 128.53, 126.17, 123.14, 84.82, 70.85, 67.21, 67.12, 50.11, 27.74; *m*/*z* (MALDI-TOF-MS) 1138.5 (M^+, 100%; calc. 1138.1).

61,62-Dihydrogen-*endo*,*endo*-61,62-(*m*-phenylenedimethylene)-1,2 : 7,21-bis(methano)[60]fullerene-61,61,62,62-tetracarboxylate 4. TFA (50 ml) was added *via* syringe under Ar at 20 °C to a solution of **3** (625 mg, 0.54 mmol) in freshly distilled and degassed CH_2Cl_2 (100 ml). After stirring for 4 h the precipitate thus formed was filtered off, washed with CH_2Cl_2 and dried under high vacuum (10^{-2} Torr) to give **4** (405 mg, 72%) which was used without further purification in the subsequent conversion. Burgundy-red solid (mp > 280 °C); λ_{max}(THF)/nm (ε/dm^3 mol^{-1}) 326 (sh, 40 600), 382 (sh, 14 520), 442 (5220); *m*/*z* (FAB$^+$-MS) 1027.0 (M^+, calc. 1026.9).

***endo*,*endo*-(*m*-Phenylenedimethylene)-1,2 : 7,21-bis(methano)-[60]fullerene-61,62-dicarboxylate 5.** DMAP (8 mg, 0.06 mmol) in freshly distilled and degassed THF (5 ml) was added under Ar at 20 °C *via* syringe to a solution of **4** (307 mg, 0.3 mmol) in freshly distilled and degassed THF (500 ml), and the mixture was stirred at 20 °C for 20 h. After dilution with CH_2Cl_2 (500 ml), filtration over SiO_2 and elution with CH_2Cl_2 gave pure **5** (190 mg, 67%). Burgundy-red solid (mp > 280 °C); υ_{max}(KBr)/cm^{-1} 1739 (C=O); λ_{max}(THF)/nm (ε/dm^3 mol^{-1}) 258 (80 400), 322 (sh, 25 700), 379 (sh, 9130), 441 (2820), 470 (sh, 2390), 620 (293); δ_H(200 MHz, $CDCl_3$) 7.53 (1 H, s), 7.41 (1 H, t, *J* 7.4), 7.36 (2 H, 4, *J* 7.4), 5.89 (2 H, d, *J* 12.8), 5.20 (2 H, d, *J* 12.8 Hz), 4.30 (2 H, s); δ_C(125 MHz, $CDCl_3$) 165.21, 149.70, 149.51, 147.38 (2 ×), 146.33, 146.18 (2 ×), 145.77, 145.67, 145.64, 145.24, 145.13, 145.01, 144.95, 144.49, 144.48, 144.20, 144.15, 144.07, 143.92, 143.77, 143.66 (2 ×), 142.72, 141.57, 141.46, 140.50, 137.19, 134.15, 128.64, 127.21, 124.76, 70.13, 67.97, 66.47, 38.37; *m*/*z* (FAB$^+$-MS) 939.0 (M^+, calc. 938.9).

***endo*,*endo*-1,2 : 7,21-Bis(methano)[60]fullerene-61,62-dicarboxylic acid 1.** BBr_3 (960 mg, 3.84 mmol) was added dropwise *via* syringe under Ar at − 10 °C to a vigorously stirred solution of **5** (240 mg, 0.26 mmol) in freshly distilled and degassed CH_2Cl_2 (500 ml). After the addition, the mixture was left for 15 h at 20 °C, then H_2O was added very slowly to quench the excess reactant. The solid thus formed was collected by filtration and dried at 10^{-2} Torr to give **1** (187 mg, 88%). Burgundy-red solid (mp > 280 °C); υ_{max}(KBr)/cm^{-1} 3211 (OH), 1706 (C=O); λ_{max}(THF)/nm (ε/dm^3 mol^{-1}) 263 (97 300), 328 (sh, 33 700), 383 (sh, 13 600), 442 (5650); δ_H (200 MHz, d_8-THF) 4.48 (2 H, s); δ_C(125 MHz, d_8-THF) 166.74, 152.56, 151.35, 150.42, 147.93, 147.49, 147.19, 146.83, 146.36, 146.30, 146.14, 145.86, 145.78, 145.64, 145.58, 144.93, 144.75 (2 ×), 144.68, 144.49, 144.36, 143.90, 143.52, 142.36, 142.33, 142.13, 138.06, 134.92, 134.73, 128.73, 125.78, 71.95, 68.64, 39.49; *m*/*z* (HR-ESI-MS, THF/MeOH, negative ion mode) 835.004 ([M − H]$^-$, 85%; calc. 835.003), 417.6 (M^{2-}, 100%).

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