A chiral dumbbell shaped bis(fullerene) oligoelectrolyte†

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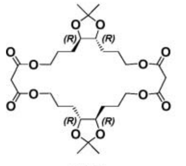
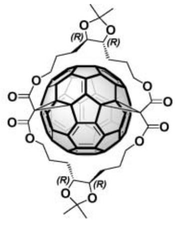
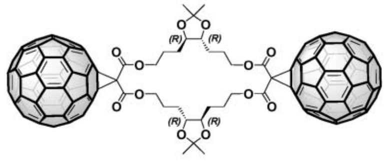
The first icosacationic bis(fullerene) whose water solubility is provided by twenty peripheral ammonium groups has a rigid, almost cylindrical shape and was synthesized by connecting two fullerene cores with a chiral cyclo-bis(malonate), followed by the regioselective addition of ten amino-terminated malonates into the octahedral positions of the fullerene moieties and subsequent cleavage of the Boc-protecting groups.

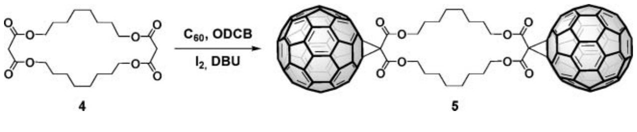
Dumbbell shaped bis(fullerenes) where two C$_{60}$ cages[1,2] or a C$_{60}$- and a C$_{59}$N-cage[3] are covalently[4] connected by bridging organic addends have recently attracted considerable attention not only because of their remarkable and aesthetically pleasing architectures including new molecular carbon allotropy[5] but also because of their potential applications in various fields such as molecular electronics.[2] These bridged molecular architectures can be prepared by coupling of fullerene adducts *via* their functional addends, by the attachment of a suitably functionalized fullerenes with a parent C$_{60}$ molecule or by the direct bridging of two fullerene with a bis(functional) addend. In the latter approach the formation of bis-adducts, which can be highly regioselective, is a competitive reaction pathway.[6,7] The relative yield of bridged adducts (dimeric and polymeric) *versus* bis-adducts depends on the ability of the difunctional addend to allow for a strain free bis-binding to one fullerene cage, as well as, on the C$_{60}$/addend molar ratio used. Thus, it is to be expected that using an excess of C$_{60}$ allows for the predominant formation of bis(fullerenes). We have recently used macrocyclic oligo-malonates containing flexible alkyl linkers for the highly regioselective bis- and oligo-functionalization of C$_{60}$.[7,8] We realized that, depending on the length of the bridge linking, the malonates either preferred oligo-functionalization or the formation of polymeric material is observed, if C$_{60}$ and the oligo-functional groups are used in equal amounts. We have also used chiral tris-malonates for the tris-functionalization of C$_{60}$ and isolated enatiomerically pure tris-adducts with an inherently chiral addition pattern.[8] When using the corresponding bis(malonate) (+)-**1** we obtained, in addition to the bis-adduct *ent*-**2** with a *cis*-2 addition pattern (34.5% isolated yield), the chiral D_2-symmetrical bis(fullerene) *ent*-**3** as the minor component.[8]

We report here on the efficient synthesis of a related chiral bis(fullerene) by using a shorter and more rigid cyclo-bis(malonate). This dumbbell served as a very suitable platform for the generation of the first water soluble bis(fullerene) icosacation by the regioselective addition of ten polar malonate addends into the octahedral sites of the fullerene cores. Prior to the synthesis of the actual target compounds we wanted to explore reaction conditions leading to a preferred formation of bis(fullerenes) *versus* bis-adducts. For this purpose, we investigated the formation of the bis(fullerene) **5** as a model case (Scheme 1). Like (+)-**1** the corresponding *cyclo*-[2]-octylmalonate **4** bears C$_8$ linkers. According to our previous results,[7] the *cyclo*-[2]-octylmalonate **4** was not suitable for the preferred formation of bis-adducts of C$_{60}$. The major part of the reaction mixture consisted of oligomeric- and insoluble polymeric material. We have now systematically increased the molar ratio of C$_{60}$ relative to **4** for the Bingel cyclopropanation in *o*-dichlorobenzene (ODCB) solvent. When the reaction was carried out with a five-fold molar excess of C$_{60}$, bis(fullerene) **5** was the major product in the reaction mixture. Purification was achieved by flash column chromatography and repeated preparative TLC by using toluene as an eluent. Once the purified product **5** was isolated as a dry powder it was hard to redissolve in toluene. It showed little solubility in CS$_2$/ODCB mixtures only. Structural characterization was accomplished by ^{1}H–, ^{13}C NMR, UV/Vis spectroscopies and by FAB MS. The sp^2 fullerene carbon region in the ^{13}C NMR spectra reflects clearly the D_{2h} symmetry of the whole molecule, while the UV/Vis spectrum reveals the features of a Bingel mono-adduct, notably the weak characteristic absorption at 425 nm.


(+)-**1**


ent-**2**, *cis*-**2**


ent-**3**



Scheme 1 Synthesis of the dumbbell shaped bis(fullerene) **5**.

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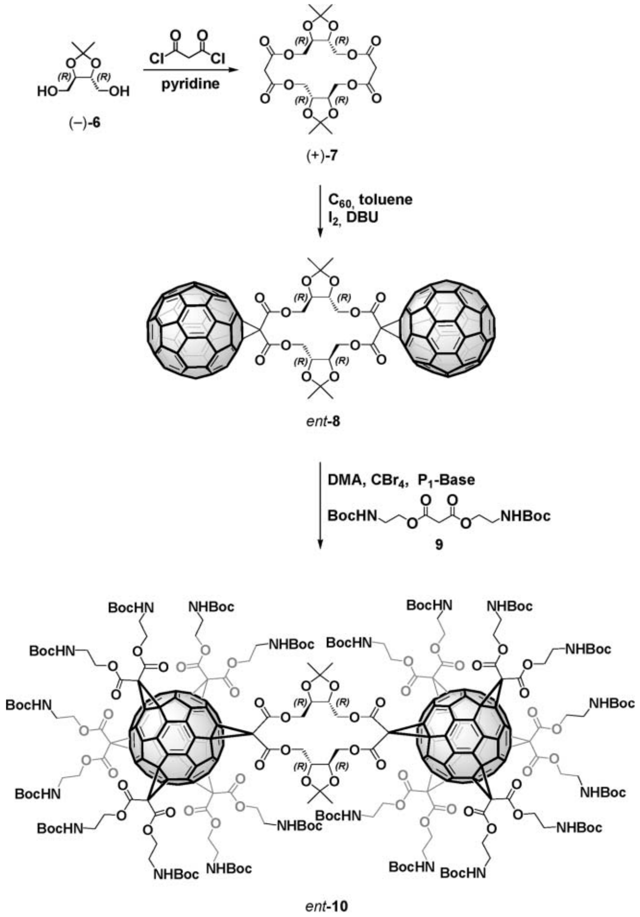
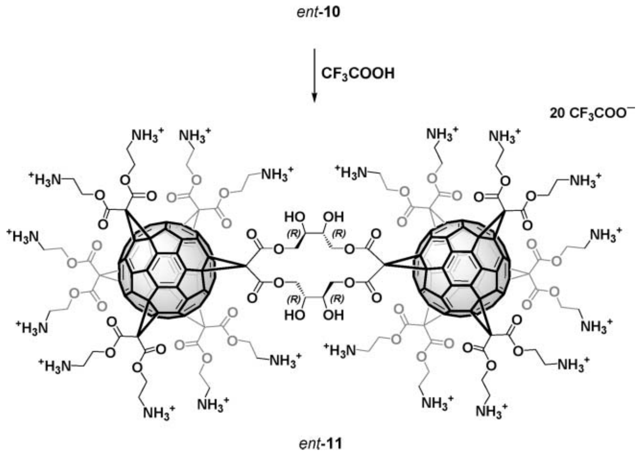
For the synthesis of the chiral target products we used shorter C_4 spacers which was expected to facilitate the formation of bis(fullerenes) and to make the corresponding dumbbells more rigid. For this purpose, the optically pure cyclo-bis(malonate) (+)-**7** was synthesized *via* the cyclization reaction of the commercially available (4*R*,5*R*)-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol (−)-**6** with malonyl dichloride, under the experimental conditions reported before (Scheme 2).[9] First, we evaluated the propensity of (+)-**7** to form bis-adducts with C_{60}.[10] Significantly, by using equimolar amounts of C_{60} and the cyclo-malonate tether and a fullerene concentration of 10^{-4} M in toluene, the reaction afforded no bis-adducts, but only a small amount of the bis(fullerene) *ent*-**8** together with unreacted C_{60}. After purification by flash column chromatography (SiO_2, toluene then toluene–EtOAc 90 : 10), *ent*-**8** was isolated in 4.2% yield. The Bingel bis-functionalization of C_{60} with the D_2-symmetrical tether (+)-**7** was also attempted under high dilution conditions ($\approx 10^{-6}$ M for C_{60}) showing identical behaviour. Those results revealed that the C_4-spacers connecting the malonate reactive groups within the tether are inappropriate for achieving a bis-addition on the same fullerene sphere.

In order to increase the yield of the bis(fullerene) *ent*-**8** we used a molar ratio of C_{60} : tether (+)-**7** = 2 : 1 and a fullerene concentration 1.2×10^{-3} M in toluene. Purification was achieved by flash column chromatography (SiO_2, toluene then toluene–EtOAc 90 : 10) where *ent*-**8** eluted as a red-wine coloured fraction, which is characteristic for cyclopropanated monoadducts of C_{60}. After precipitation from $CHCl_3$/pentane, the product was isolated in 26% yield and its structural assignment was accomplished by ^1H and ^{13}C NMR spectroscopies, and by mass spectrometry. Compared to the bis(fullerene) **5**, the solubility of *ent*-**8** in organic solvents such as toluene or $CHCl_3$ is considerably higher. The FAB-MS of *ent*-**8** shows the expected M^+ molecular ion at 1898 *m*/*z* confirming that the covalent attachment of two C_{60} molecules on the tether was successful. The ^{13}C NMR spectrum of the bis(fullerene) adduct is in complete agreement with the proposed structure indicating a D_2 molecular symmetry. In the fullerene spectral region between 139 and 145 ppm, 14 signals for the sp^2 C atoms of the fullerene are observed reflecting a local C_{2v} symmetry of each fullerene sphere. In addition, one signal for the fullerene sp^3 C carbons at 71.03 ppm, and one signal for the bridgehead sp^3 C atoms at 50.87 ppm are present in the spectrum, while the four carbonyl C atoms show one resonance at 162.63 ppm. The methylene carbon atoms of the tether show one peak at 66.35 ppm, while the stereogenic methine carbons appear at 76.68 ppm. Finally, the methyl carbons of the isopropylidene moieties resonate at 26.93 ppm and the quaternary carbons appear at 110.89 ppm. For the conversion of *ent*-**8** into a defined water soluble oligoelectrolyte we decided to attach five polar malonate addends each to the octahedral sites of *ent*-**8** (Scheme 2). In previous investigations water solubility of hexakis adducts of C_{60} has been achieved, for example, by addends with terminal carboxylates or ammonium groups.[11] In the present case we synthesized the Boc-protected malonate **9** as precursor addend, which was obtained by the treatment of Boc-protected aminoethanol with malonyl dichloride. Subsequently, the synthesis of the dodecakis adduct *ent*-**10** was accomplished by template activation of the bis(fullerene) *ent*-**8** using an excess of 9,10-dimethylanthracene (DMA)[12] and treatment with malonate **9** in the presence of CBr_4 and phosphazene base P_1-*t*-Bu. The usual use of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base turned out to be not suitable since the conversion to *ent*-**10** proceeded much less efficiently. The dodecakis adduct *ent*-**10** is the most polar compound in the reaction mixture, which facilitates its chromatographic separation. It eluted as the last component from silica gel columns. However, since side products with an incomplete octahedral addition pattern are also very polar and cause broad elution bands, successive chromatographic separation steps are required. Finally, after repeated precipitation from CH_2Cl_2 solutions by adding pentane, *ent*-**10** was obtained in very pure form as a pale-orange powder. Despite these purification problems the overall yield was 38%. The local octahedral environment of each fullerene moiety within *ent*-**10** is nicely reflected in the ^{13}C NMR spectrum, where only two signals for the sp^2 C atoms of the fullerene sphere appear at the expected spectral region (146 and 141 ppm).[12] The unambiguous structural characterization of *ent*-**10** was completed by ^1H NMR and UV/Vis spectroscopies, showing the expected characteristics[12] for mixed octahedral [5 : 1] adducts with an octahedral addition pattern as well as by mass spectrometry (see supplementary material†).



Scheme 2 Synthesis of the enantiomerically pure polyfunctionalized bis(fullerene) *ent*-**10**.

In order to achieve water solubility, the deprotection of the Boc-groups was carried out by treatment of *ent*-**10** with TFA in CH_2Cl_2 solvent (Scheme 3). Next to the quantitative deprotection



Scheme 3 Synthesis of the water soluble *ent*-**11** by deprotection of the Boc and acetonide groups.

of the Boc-groups the simultaneous cleavage of the acetonide residues within the chiral malonate bridge took place as demonstrated by the absence of any signals for methyl groups in the ^{1}H– and ^{13}C NMR spectrum of *ent*-**11**. Next to water the chiral dumbbell shaped bis(fullerene) *ent*-**11** is very soluble in methanol.

The molecular topology of *ent*-**11** without counterions as determined by a molecular dynamic simulation is depicted in Fig. 1. First a geometry optimization was carried out using the MM+ force field followed by a semiempirical PM3 calculation. This geometry was then imbedded in a waterbox (40 × 40 × 40 Å^3) containing 2100 water molecules which represented the starting situation for the MD simulation (supplementary material†). The ammonium groups are evenly distributed in the three dimensions around the two fullerene moieties. The electrostatic interactions between the charged groups are expected to introduce significant rigidity. Structural rigidity of defined negatively charged oligoelectrolytes has already been demonstrated with the observation of shape persistent micelles formed out of amphiphilic polycarboxy-fullerenes and -calixarenes in water.[13,14] Compared to an open chain addend the bridging macrocycle *ent*-**11** introduces additional restrictions concerning the possible relative orientation of the two fullerene units. Indeed, during the course of the entire MD simulation the dumbbell and the almost cylindrical shape of the icosacation *ent*-**11** stayed remarkably persistent. With the exception of some movements of the addends, no significant bending or other types of major distortions were observed.

This icosacationic building block has potential for the development of tailor made layer-by-layer assemblies of oppositely charged monodisperse oligoelectrolytes.[15] If *ent*-**11** serves as the outermost layer in addition to an ordered arrangement of closely packed cylindrical objects surface chirality can be provided. Another interesting subject for further investigations is the electrostatic hybridization of *ent*-**11** with polyanions such as oligomeric DNA in homogeneous solution. Work along these lines is currently underway in our laboratories.

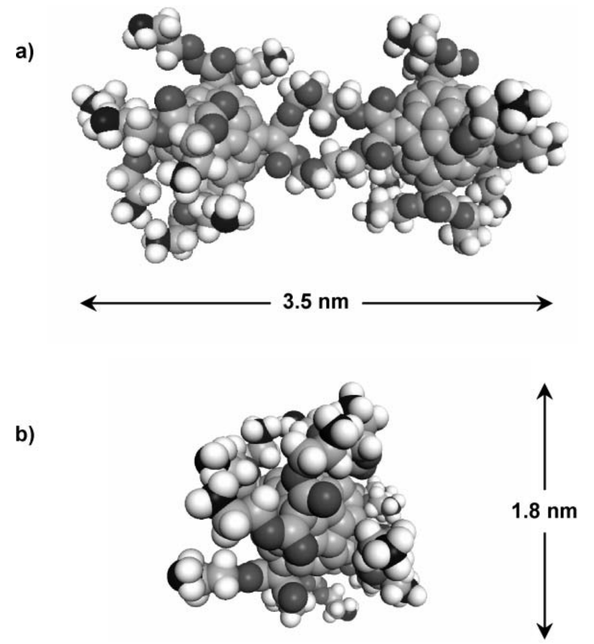


Fig. 1 Space filling representation of the icosacation of *ent*-**11** obtained after an MD simulation in a water box. The water molecules are omitted for clarity. Side view (a) and front view (b).

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Notes and references

1 J. L. Segura and N. Martin, *Chem. Soc. Rev.*, 2000, **29**, 13.
2 L. Sánchez, M. Á. Herranz and N. Martin, *J. Mater. Chem.*, 2005, **15**, 1409.
3 F. Hauke, M. Á. Herranz, L. Echegoyen, D. Guldi, A. Hirsch and S. Atalik, *Chem. Commun.*, 2004, 600.
4 For non-covalently linked fullerene dyads see: L. Sánchez, N. Martin and D. Guldi, *Angew. Chem., Int. Ed.*, 2005, **44**, 5374.
5 A. L. Anderson, R. Faust, Y. Rubin and F. Diederich, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 1366.
6 (*a*) L. Isaacs, F. Diederich and R. F. Haldimann, *Helv. Chim. Acta*, 1997, **80**, 317; (*b*) F. Diederich and R. Kessinger, *Acc. Chem. Res.*, 1999, **32**, 537.
7 U. Reuther, T. Brandmüller, W. Donaubauer, F. Hampel and A. Hirsch, *Chem. Eur. J.*, 2002, **6**, 2261.
8 N. Chronakis and A. Hirsch, *Chem. Commun.*, 2005, 3709.
9 N. Chronakis, T. Brandmüller, C. Kovacs, U. Reuther, W. Donaubauer, F. Hampel, F. Fischer, F. Diederich and A. Hirsch, *Eur. J. Org. Chem.*, 2006, 2296.
10 C. Thilgen and F. Diederich, *Top. Stereochem.*, 2003, **23**, 1.
11 M. Braun, U. Hartnagel, E. Ravanelli, B. Shade, C. Böttcher, O. Vostrowsky and A. Hirsch, *Eur. J. Org. Chem.*, 2004, 1983.
12 A. Hirsch and O. Vostrowsky, *Eur. J. Org. Chem.*, 2001, **5**, 829.
13 M. Kellermann, W. Bauer, A. Hirsch, B. Schade, K. Ludwig and C. Böttcher, *Angew. Chem.*, 2004, **116**, 3019, (*Angew. Chem., Int. Ed.*, 2004, **43**, 2959).
14 S. Burghardt, A. Hirsch, B. Schade, K. Ludwig and C. Böttcher, *Angew. Chem.*, 2005, **117**, 3036, (*Angew. Chem., Int. Ed.*, 2005, **44**, 2976).
15 D. M. Guldi, I. Zilbermann, G. Anderson, A. Li, D. Balbinot, N. Jux, M. Hatzimarinaki, A. Hirsch and M. Prato, *Chem. Commun.*, 2004, 726.