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SYNTHESIS OF [60]FULLERENE DERIVATIVES WITH AN OCTAHEDRAL ADDITION PATTERN

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Abstract: Regioselective formations of [60]fullerene derivatives with octahedral addition patterns are described. Via template activation with 9,10-dimethylanthracene T_h-symmetric as well as mixed C_{2v}-symmetric hexaadducts are obtained in one step starting from C_{60} or C_{2v}-symmetric monoadducts in comparatively high yields. The thermally induced cycloreversion of azide from fullerotriazolines with five methano bridges in octahedral positions allows also the synthesis of the C_{2v}-symmetric pentaadduct $C_{65}(COOEt)_{10}$ in large quantities, which shows that azides can be used as protecting groups for 6-6 double bonds. The remaining octahedral double bond in $C_{65}(COOEt)_{12}$ is by far the most reactive in the molecule, which also allows an extremely regioselective synthesis of hexaadducts with an octahedral addition pattern. The specific oxidation of the reactive octahedral double bond of $C_{65}(COOEt)_{10}$ leads to an unusual dioxetane formation.

Introduction

The exohedral chemistry of C_{60} has been dominated thus far by investigations of its reactivity and the isolation and characterization of monoaddition products[1]. The regioselectivity observed for the formation of dihydro[60]fullerene derivatives (monoadducts) is determined by the structure of the fairly electronegative and strained molecule C_{60}, in which the bonds between the six-membered rings (6-6 double bonds) are shorter than the bonds between a six-membered and a five membered ring (5-5 single bonds). As a consequence, dihydro[60]fullerene derivatives are predominantly formed by 1,2-additions to a 6-6 double bond and only for additions of sterically demanding segregated addends also 1,4-additions have been observed. In these cases the number of energetically unfavourable 5-6 double bonds is minimized (none for a 1,2-adduct and one for a 1,4-adduct). Since the spherical workspace of C_{60} contains 30 reactive 6-6 double bonds a huge number of regioisomeric multiple addition products are in principle possible. The facile access to stable and highly symmetrical oligoadducts of C_{60} in high yields plays an important role, for example, for material science and biological applications of fullerene derivatives and is still one of the major synthetic challenges in fullerene chemistry. We have shown recently that multiple additions to the fullerene core

show a remarkably high regioselectivity[2,3,4,5] because addends already bound provide a directing influence for further additions. Among the possible sites (Figure 1) for a subsequent attack of a 6-6 double bond *e* positions followed by *trans-3* positions are significantly preferred[2,3,4,6,7,8]. A special situation is accompanied with the *e* relationship. As we already pointed out[3], the two *e* double bonds on the mirror plane perpendicular to the bond carrying the first addend are more reactive than the other two *e* bonds. Therefore, it is useful to distinguish between *e'* and *e''* sites (Figure 1), although a second attack of identical addends into these positions leads to identical products. The observed regioselectivity of multiple additions to C_{60} can be explained by a combined consideration of the thermodynamic stability of the corresponding adducts as well as by enhanced frontier orbital coefficients in the preferred positions[3]. The regioselectivity of attacks into remaining *e* positions (octahedral sites, Figure 1) becomes even more pronounced as the number of addends already bound in *e* positions increases. This is expressed, for example, by further enhanced frontier orbital coefficients at the preferred sites as well as by an increasing thermodynamic stability of adducts with a more completed octahedral addition pattern[3].

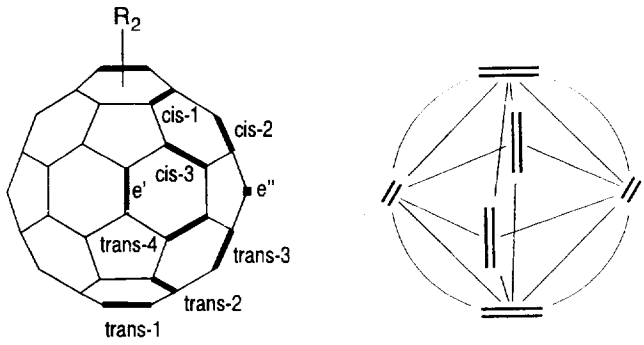


Figure 1. Positional relationships of the double bonds in a C_{60} monoadduct relative to the 6-6 bond carrying the first addend R_2 (for identical addends a second attack into e' or e" positions leads to identical products) and schematic representation of an octahedral fashion of 6-6 double bonds in C_{60}

Following these rules we synthesized the hexaaduct $C_{66}(COOEt)_{12}$ (**1**), by successive cyclopropanations of C_{60} with diethyl bromomalonate in the presence of a base into *e* positions[3]. However, the overall yield of **1** is very low, if the additions are carried out stepwise with the isolation of each adduct with the right addition pattern prior to a subsequent cyclopropanation. On the other hand, aesthetically pleasing compounds like **1** exhibit the extremely rare cases of organic molecules with a T_h-symmetrical structure and can be used as precursors for further side chain chemistry[4]. This encouraged us to improve the yield of **1**. Applying a reversible template activation of C_{60} with 9,10-dimethylanthracene (DMA) allows

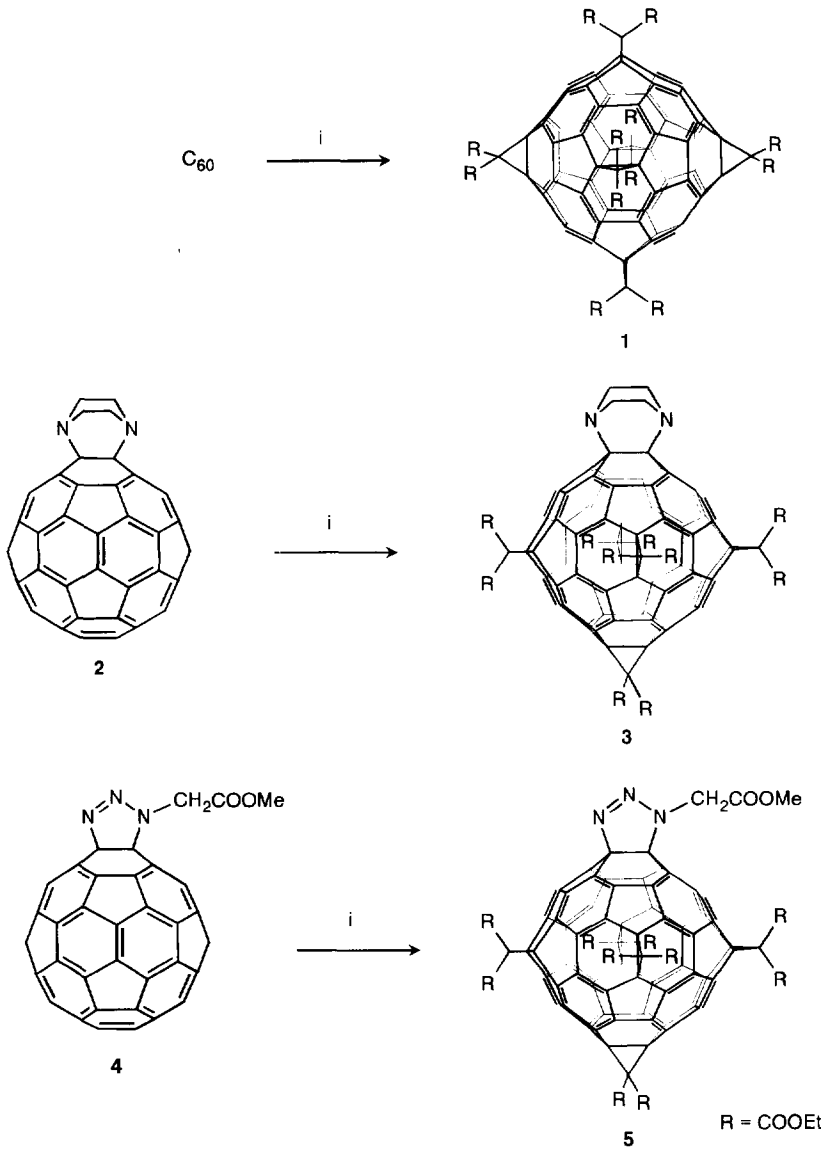
the synthesis of **1** in almost 50% yield starting from C_{60}[4]. In this paper we report the synthesis of C_{60} derivatives with a mixed octahedral addition pattern by using this template activation method. Moreover, we show that a high yield access to these compounds is also possible starting from pentaadduct precursors in which the remaining octahedral 6-6 double bond is by far the most reactive.

Results and Discussion

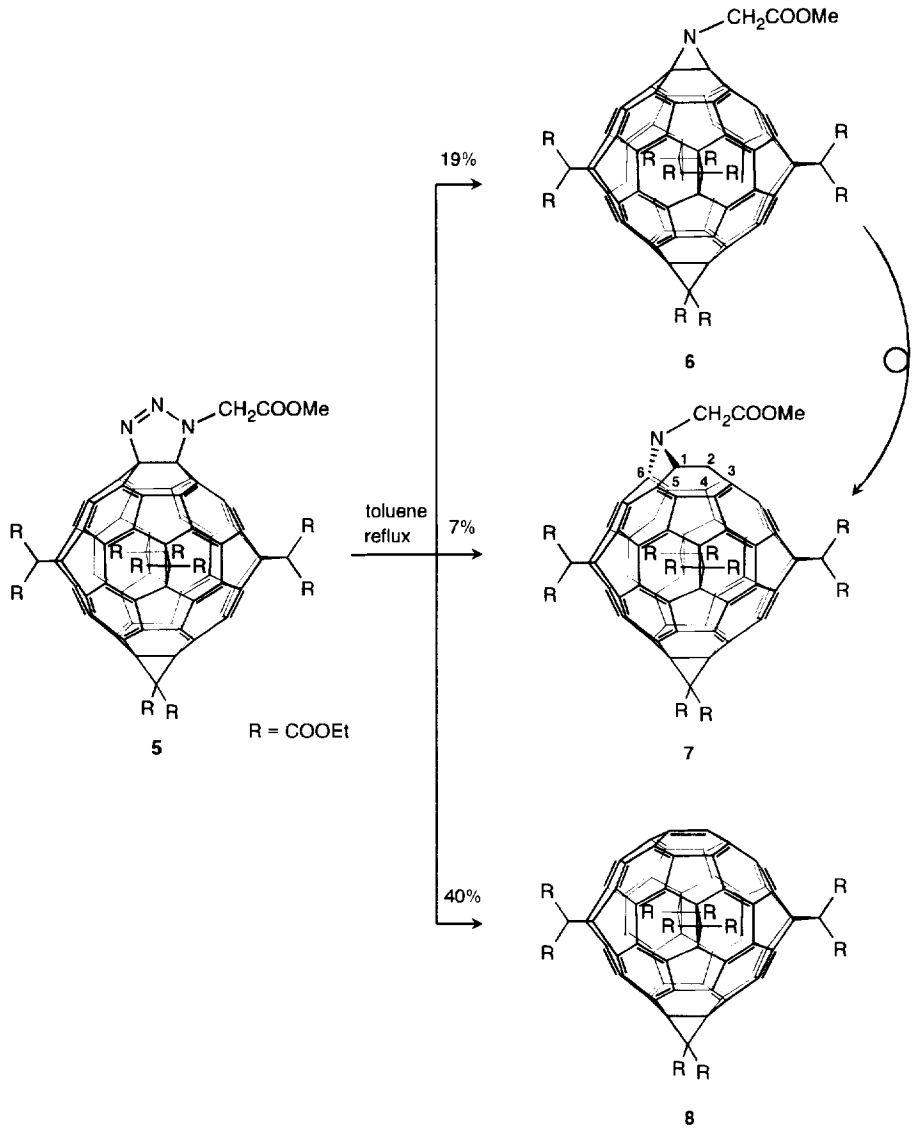
The key process for the high yield synthesis of C_{60} derivatives with an octahedral addition pattern is the *in situ* formation of templates with reversibly bound addends. Looking for suitable template intermediates, we found that the Diels-Alder reaction of C_{60} with DMA is reversible already at room temperature[4]. An increasing amount of DMA causes a shift of the equilibrium towards higher addition products. DMA can be removed from the equilibrium, for example by the reaction with air in laboratory light under formation of the 9,10-endoperoxide of DMA and free C_{60}. By using a tenfold excess of DMA, $C_{60}(DMA)_2$ and $C_{60}(DMA)_3$ are formed predominantly (HPLC) as mixtures of regioisomers. Since these adduct formations are reversible the thermodynamic control of the adduct distribution gains additional importance. Therefore, among the various regioisomers of $C_{60}(DMA)_3$, the C_3-symmetrical *e,e,e*-isomer with an uncompleted octahedral addition pattern is by far the most abundant (UV/Vis). In *e,e,e*-$C_{60}(DMA)_3$ the remaining unsaturated octahedral bonds are significantly preferred for subsequent attacks, for example of addends, which bind irreversibly to C_{60}. Subsequently or alternatively the DMA addends can be substituted. Furthermore if, for example, *e,e,e*-$C_{60}(DMA)_3$ is attacked into a position other than *e* the DMA addends can rearrange to an isomer with a complete octahedral addition pattern.

The irreversible cyclopropanation of such a mixture of template activated C_{60} (10 equiv. DMA) with 10 equiv. of diethyl bromomalonate with DBU as base leads to **1** in a total yield up to 48% (Scheme 1)[4]. **1** can be easily isolated from the reaction mixture simply by flash chromatography followed by recrystallization from $CHCl_3$/bromobenzene (1:1) as yellow rhombic crystals suitable for X-ray single crystal structure analysis[4]. The major amount of free DMA can be recovered. In addition to **1**, we analogously synthesized the mixed hexaadducts **3** and **5** in one step by using the fulleropiperazine **2**[4] and the triazoline **3**[5] instead of C_{60} (Scheme I). The triazoline **4** was obtained by the treatment of a concentrated solution of C_{60} in 1-chloronaphthalene with one equiv. of methyl azidoacetate at 60°C. We have shown previously that the thermal treatment of **4** after extrusion of N_2 leads to the formation of the corresponding azafulleroid (24%), the corresponding fulleroaziridine (4%) and of two regioisomeric bisazafulleroids (16%) as well as of free C_{60} (22%) upon cycloreversion[5]. The same heating experiment with **5** leads to a significantly different and very interesting result. In this case the cycloreversion to the pentadduct **8**, which is formed in 40% yield, is the main

reaction and extrusion of N_2 leads preferably to the aziridine **6** rather than the fulleroid **7** (Scheme II). Adducts with two azabridges are formed only in traces. Moreover, in contrast to the non-cyclopropanated analogue **7** rearranges slowly already at room temperature to **6**.



Scheme I (i: 10 equiv. DMA, 10 equiv. diethyl bromomalonate/DBU, toluene, RT, N_2, 8-104 h)



Scheme II

The reasons for the latter behaviour are very likely unfavourable steric interactions between the ester groups of the aza-brigde with those of a nearby methano-bridge in **7**, which can be released upon rearrangement to **6**. In addition, a complete octahedral addition pattern itself, which is present in **6** but not in **7** is the thermodynamically most favourable situation[3]. The

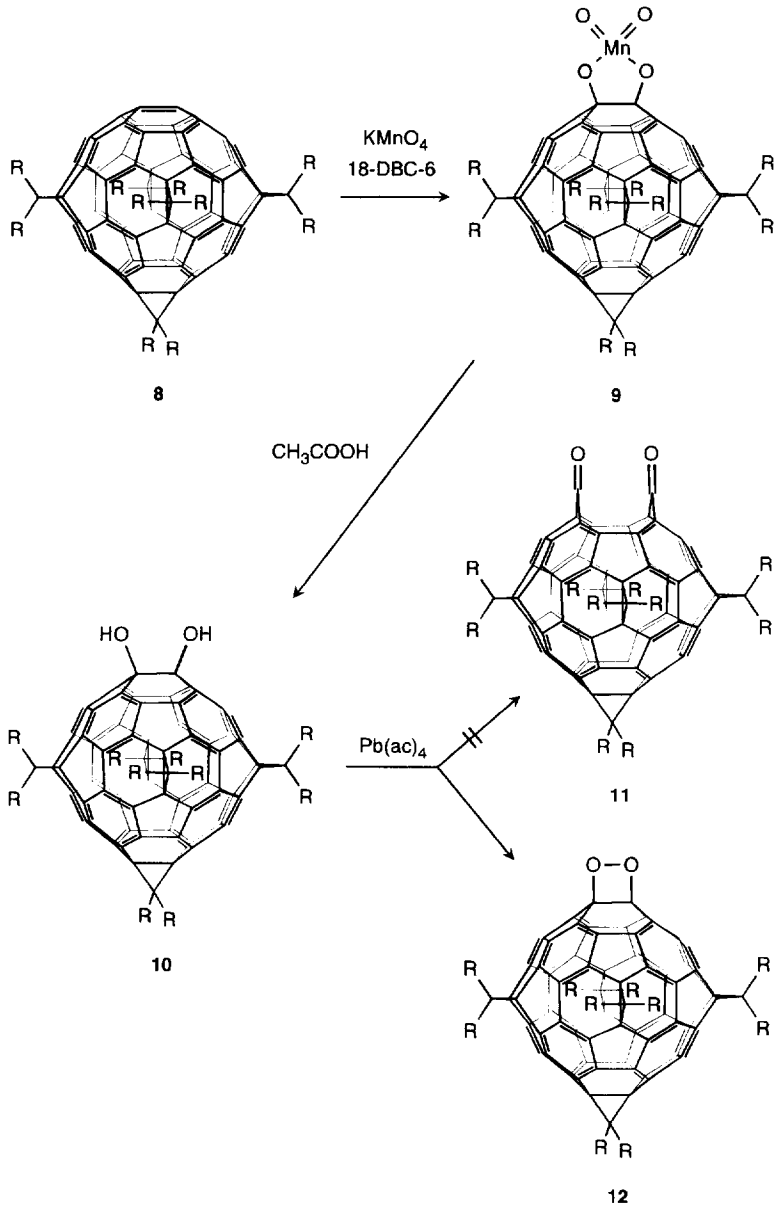
present case is the first example for a rearrangement from an azafulleroid to a fulleroaziridine. In the case of the methano analogues it is well known that the ring-opened fulleroids rearrange thermally to the ring-closed 6-6 bridged derivatives[9], with the exception of the parent $C_{61}H_2$[10]. In general, methanofullerenes are thermodynamically more stable than the fulleroids. Like in the case of the methano fullerenes the rearrangement from the azafulleroid **7** (kinetic product) to the fulleroaziridine **6** might proceed via electrocyclic reactions coupled to sigmatropic shifts[11]. An alternative mechanism would be a homolytic bond cleavage of one N-C_{60} bond followed by a recombination in position 2.

Since the triazoline group in **4** undergoes a facile cycloreversion, azides can be used as protecting groups for octahedral 6-6 double bonds, which, for example, allows the synthesis of pentaaducts like **8** in comparatively high yields. This is of importance, since a direct synthesis of pentaaducts of C_{60} with di(ethoxycarbonyl)methylene yields mixtures of regioisomers with similar or identical R_f-values on various stationary phases using toluene or mixtures of toluene and ethyl acetate as eluents. On the other hand, pentaadducts like **8** are very interesting reagents, since further additions are expected to occur almost exclusively at the remaining octahedral 6-6 double bond, because all the other double bonds are shielded by the addends and exhibit considerably less enhanced coefficients in the frontier orbitals.

We have proven this hypothesis already by cyclopropanating **8**, where we obtained **1** as the only hexaadduct[3]. The accessibility of a double bond in a fullerene, whose reactivity is much higher than those of all the others prompted us also to look, whether it is possible to specifically oxidize and maybe open up the fullerene framework, which has been shown to be a very difficult task for C_{60} itself, since, due to the polyfunctionality, uncharacterizable mixtures of products are obtained. The treatment of **8** with one equiv. of $KMnO_4$ in the presence of cis-dicyclohexano-18-crown-6 indeed, after hydrolysis with acetic acid, leads to the formation of the diol **10**, which is the first example of a completely characterized fullerenol. Surprisingly, the oxidation of **10** with $Pb(ac)_4$ does not give the diketone **11** but the dioxetane **12**, in which the fullerene cage structure is retained. So far, it is not clear, whether **12** is formed directly or via **11** as an intermediate. Molecular modelling studies on **11** showed, that the carbonyl groups are arranged in an almost parallel eclipsed fashion and are still in van-der-Waals contact. This could be the reason for a possible, so far unobserved cyclization from a diketone to a dioxetane.

The C_{2v}- or C_s-symmetry of the compounds **3**, **5**, **6**, **10** and **12** can easily be determined from their ^{13}C NMR spectra. For **5** 28 of the expected 32 signals for the fullerene C-atoms are clearly resolved. A very interesting phenomenon can be observed upon comparing the NMR spectra of the compounds **1**, **3**, **6**, **10** and **12**. Whereas for **3**, **5**, **10** and **12** 12 signals for the sp^2-C-atoms and the 5 signals for the sp^3-C-atoms of the fullerene framework are clearly

resolved and spread out, the ^{13}C NMR spectrum of **6** nearly approaches the features observed for the T_h-symmetric compound **1**[3].



Scheme III

In **1** only three resonances for the fullerene C-atoms appear at δ = 145, 141 (sp^2-C-atoms) and 69 (sp^3-C-atoms). The various characteristically overlapping signals of the fullerene C-atoms of **6** are gathered as groups in the same very distinct ppm areas of the spectrum as those of **1**, with the exception of the sp^3-C-atoms carrying the aza-bridge, which resonate at δ = 82. A very similar behavior is reflected in the corresponding ^1H NMR spectra. Whereas for **3**, **5**, **10** and **12** the protons of the 10 ethyl side chains appear as complex multiplets at δ = 4.3 and 1.3 those of **6**, in analogy to **1**, appear as one almost complete resolved quartet for the methylene groups and one triplet for the methyl groups. In contrast to **3**, **5**, **10** and **12** the sixth addend in **6** forms also a three membered ring (aziridine ring) with the fullerene framework. As a consequence and in contrast to the other mixed hexadducts synthesized, the local symmetry of the fullerene core in **6** seems to be almost T_h (pseudo-octahedral). The sp^3-C-atoms carrying the sixth addend, being either an O- or N-group appear between δ = 75 and 104. This also shows that the compound obtained by the oxidation of diol **10** with $Pb(ac)_4$ cannot be the diketone **11**, whose carbonyl groups should resonate at around δ = 180.

The UV/Vis spectra of all the yellow mixed hexadducts **3**, **5**, **6**, **10** and **12** exhibit very similar features, which are closely related to the spectrum of **1**, where the two absorptions at about 280 and 325 nm appear in general as double bands. Moreover, the extinction coefficients in the visible part of the spectrum are very small for all pseudooctahedral hexadducts **1**, **3**, **5**, **6**, **10** and **12**. This points to an enhanced aromatic behaviour of the remaining π-electron system in these hexaadducts compared to other fullerene derivatives. In the corresponding π-electron systems of the fullerene core eight benzenoid rings are arranged in a cubic fashion. The X-ray structure analysis of **1** shows, that indeed the bond length alternation of 5-6 and 6-6 bonds is reduced to only 0.03 Å in the sp^2 substructure[4], which independently demonstrates more aromatic character compared to C_{60}.

The synthesis of further mixed hexadducts with octahedral addition patterns, where, for example, more than two different addends or two addends in different ratios are bound to the fullerene framework as well as their use as building blocks for new materials with technological importance are subjects for further investigations.

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Experimental Part

The purity of the new compounds **3**, **5**, **6**, **10** and **12** is higher than 98% as determined by HPLC.

3: To a solution of 70 mg (79 μmol) fulleropiperazine **2** in 50 mL toluene 163 mg (790 μmol) of DMA were added. After allowing this mixture to stirr for 2 h at room temperature 135 μL (790 μmol) diethylbromomalonate and 117 μL (790 μmol) of DBU were added. After stirring for 24 h at room temperature the reaction mixture was separated by preparative HPLC on a nitrophenyl phase with ethylacetate as eluent to yield 27% of yellow-orange **3** as the most polar fraction.

M = 1595.55; MS (FAB): *m/z* 1595 (M^+, 59 %), 1510 (M^+-$C_4H_8N_2$, 100 %); UV/VIS (CH_2Cl_2): λ_{max} [nm] = 245, 268, 286, 312, 334 sh; IR (KBr): ν [cm^{-1}] = 2939, 2874, 1738, 1585, 1493, 1452, 1407, 1390, 1327, 1313, 690, 561, 507; ^{1}H-NMR (250 MHz, $CDCl_3$, 25° C): δ = 4.30 (m, 20 H; CH_2), 3.89 (m, 4 H; CH_2), 3.11 (m, 4 H; CH_2), 1.30 (m, 30 H; CH_3); ^{13}C-NMR (62.9 MHz, $CDCl_3$, 25° C): δ = 164.15, 163.92, 163.68, 163.36, 150.16 (4 C), 146.42 (4 C), 146.36 (4 C), 146.19 (4 C), 145.45 (4 C), 145.15 (4 C), 144.86 (4 C), 142.13 (4 C), 142.02 (4 C), 140.04 (4 C), 138.81 (4 C), 138.11 (4 C), 75.38, 69.86, 69.51, 68.95, 67.37, 62.91, 62.82, 62.73, 62.67, 45.96, 45.59, 44.81, 40.05, 14.01.

5: To a solution of 157 mg (188 μmol) of triazoline **4** in 100 mL toluene 310 mg (8 equiv.) DMA were added. After allowing this mixture to stirr for 2 h at room temperature 10 equiv. of each diethyl bromomalonate an DBU were added. After stirring for 4 days at room temperature the reaction mixture was separated by flash-chromatography on silica gel with toluene/ethylacetate (1:1) to yield 60% of the yellow hexaadduct **5** as the most polar fraction.

M = 1626.52; MS (FAB): *m/z* 1627 (M^+); UV/VIS (CH_2Cl_2): λ_{max} [nm] = 243 sh, 269,282 sh, 315, 334 sh; IR (KBr): ν [cm^{-1}] = 3448, 2982, 2938, 2905, 1746, 1635, 1465, 1445, 1394, 1368, 1267, 1222, 1095, 1072, 1040, 1017, 932, 858, 822, 757, 714, 679, 531, 510, 437, 416, 406; ^{1}H-NMR (250 MHz, $CDCl_3$, 25°C): δ = 4.81 (s, 2 H, CH_2),4.29 (m, 20 H, CH_2), 3.70 (s, 3 H, CH_3), 1.28 (m, 30 H, CH_3); ^{13}C-NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 169.14, 163.90, 163.79, 163.66, 163.59, 163.53, 163.43, 163.36, 147.13 (2 C), 146.47 (2 C), 146.40 (2 C), 145.86 (4 C), 145.45 (2 C), 145.36 (2 C), 145.31 (2 C), 145.19 (2 C), 145.02 (2 C), 144.09 (2 C), 144.05 (2 C), 143.43 (2 C), 142.10 (2 C), 142.02 (2 C), 141.60 (2 C), 141.55 (2 C), 140.89 (2 C), 140.70 (2 C), 140.45 (2 C), 139.98 (2 C), 139.91 (2 C), 139.54 (2 C), 139.32 (2 C), 103.38 (2 C), 69.66 (2 C), 69.64 (2 C), 68.89 (2 C), 67.98 (2 C), 67.67 (2 C), 63.00, 62.93, 62.74, 52.60, 47.84, 45.52, 45.29, 45.12, 41.82, 14.05, 13.99.

6 and **8**: A solution of 270 mg of **5** in 50 mL toluene was heated under reflux for 2 hours, whereupon the color of the solution changed from orange to red. The reaction mixture was separated by preparative HPLC (silica gel; toluene/ethylacetate 95:5) to give in the order of

elution: 40% **8**, 7% **7** and 19% **6**. Azafulleroid **7** rearranges slowly already at room temperature to **6**.

6: M = 1598.51; MS (FAB): m/z = 1598 (M^+); UV/VIS (CH_2Cl_2): λ_{max} [nm] = 243, 280, 318, 336; IR (KBr): ν [cm^{-1}] = 3449, 2982, 1745, 1445, 1391, 1368, 1263, 1223, 1096, 1079, 1018, 855, 716, 666, 529; ^{1}H-NMR (250 MHz, $CDCl_3$, 25°C): δ = 4.29 (q, 20 H, CH_2), 3.93 (s, 2 H, CH_2), 3.76 (s, 3 H, CH_3), 1.30 (t, 30 H, CH_3); ^{13}C-NMR (62.9 MHz, $CDCl_3$, 25°C): δ = 169.08, 163.68, 145.94 (8 C), 145.79 (8 C), 145,63 (8 C), 141.69 (4 C), 141.43 (4 C), 141.21 (4 C), 140.96 (12 C), 81.94 (2 C), 69.18, 69.12, 69.03, 62.87, 52.26, 51.92, 45.52, 45.47, 45.23, 13.98.

10: To a solution of 34,7 mg (23 µmol) of the pentaadduct **8** in 20 mL CH_2Cl_2 3 mL of a 0.01 n solution of $KMnO_4$ (30 µmol) containing 30 µmol of cis-dicyclohexano-18-crown-6 were added. After stirring for two hours at room temperature 2 mL of acetic acid were added and the reaction mixture was stirred for another 2 hours. The yellow diol **10** was isolated in almost quantitative yield by column chromatography on silica gel with ethyl acetate as eluent.

M = 1545.44; MS (FAB): m/z 1545 (M^-, 93 %), 1527 (M^--H_20, 54 %), 1510 (M^+-2 OH, 33 %), 720 (C_{60}, 100 %); UV/VIS (CH_2Cl_2): λ_{max} [nm] = 269, 284, 313, 371 sh, 393 sh, 419 sh; IR (KBr): ν [cm^{-1}] = 2982, 2937, 1745, 1466, 1445, 1296, 1256, 1020, 714, 530; ^{1}H-NMR (250 MHz, $CDCl_3$, 25° C): δ = 5.13 (OH), 4.44 (m, 20 H; CH_2), 1.31 (m, 30 H; CH_3); ^{13}C-NMR (62.9 MHz, $CDCl_3$, 25° C): δ = 164.09, 163.78, 163.56, 163.52, 149.28 (4 C), 146.67 (4 C), 146.42 (4 C), 145.51 (4 C), 145.28 (4 C), 144.99 (4 C), 144.03 (4 C), 142.23 (4 C), 142.03 (4 C), 140.30 (4 C), 138.85 (4 C), 138.21 (4 C), 81.62, 69.95, 69.77, 69.08, 67.30, 63.00, 62.84, 45.57, 44.76, 39.65, 14.07, 13.98.

12: To a solution of 30 mg (19 µmol) of **10** in 15 mL CH_2Cl_2 43 mg (96 µmol) of $Pb(ac)_4$ were added. After stirring for 20 h at room temperature the yellow dioxetane **12** was isolated by column chromatography on silica gel with toluene/ethylacetate (1:1) in almost quantitative yield.

M = 1543.43; MS (FAB): m/z 1542 (M^-, 45 %), 720 (C_{60}, 100 %); UV/VIS (CH_2Cl_2): λ_{max} [nm] = 271, 287, 325 sh, 375 sh; IR (KBr): ν [cm^{-1}] = 2982, 2937, 1746, 1466, 1447, 1391, 1369, 1227, 1094, 1078, 1022, 858, 812, 708, 532; ^{1}H-NMR (250 MHz, $CDCl_3$, 25° C): δ = 4.32 (m, 20 H; CH_2), 1.31 (m, 30 H; CH_3); ^{13}C-NMR (62.9 MHz, $CDCl_3$, 25° C): δ = 164.22, 163.69, 163.28, 163.14, 149.68 (4 C), 147.02 (4 C), 146.45 (4 C), 145.54 (4 C), 144.67 (4 C), 144.07 (4 C), 142.32 (4 C), 141.71 (4 C), 140.65 (4 C), 138.89 (4 C), 137.83 (4 C), 134.48 (4 C), 104.05, 71.94, 70.86, 70.30, 67.17, 63.06, 62.94, 62.85, 46.20, 44.61, 39.47, 14.10, 14.00.

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