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Preparation and Characterization of Fulleroid and Methanofullerene Derivatives

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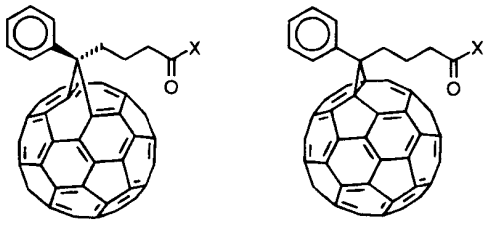
We describe the synthesis and complete characterization of soluble derivatives of C_{60} for applications to physics and biology. The goal of the strategy was to have a "modular" approach in order to be able to easily vary a functional group attached indirectly to the cluster. The functionality could be hydrophilic (e.g., histamide) or hydrophobic (e.g., cholestanoxy). The former was prepared for biological studies and the latter for photophysical studies toward improvement of photoinduced electron transfer efficiencies in the fabrication of photodetectors and photodiodes. An important intermediate, a carboxylic acid, was found to be recalcitrant to characterization by the usual mass spectroscopic and elemental analysis techniques. This problem was solved by the use of MALDI-MS. The carboxylic acid was easily converted to the key intermediate acid chloride, which in turn was convertible to a large variety of derivatives. Both isomeric forms ([5,6], fulleroid and [6,6], methanofullerene) of the C_{61} clusters were prepared. The fulleroid formation could have given rise to a 50:50 mixture of phenyl-over-former pentagon phenyl-over-former hexagon isomers but, remarkably, afforded a 95:5 mixture of these isomers, respectively. The fulleroid and methanofullerene gave different cyclic voltammograms, with the former being reduced at 34 mV more positive potential than the latter.

Introduction

There exist a large number of reactions for the functionalization of C_{60}.[1-13] Of these, the addition of diazoalkanes is the one we have exploited in our group. The discovery of biological properties[14-18] as well as materials properties[19] of some of these adducts prompted us to devise a general strategy for the preparation of C_{61} derivatives which would have the versatility of being useful for a large variety of studies in both fields. A methanofullerene for a specific function, namely electrospray mass spectroscopy, has been described.[20]

The approach consists of the preparation of a stable diazo compound which could be generated in situ and which would have a functional group, compatible with C_{60} chemistry, for attachment of a large variety of moieties ("handle").[21] After some thought, we settled on both isomers ([5,6] fulleroid **F** and [6,6] methanofullerene **M**) of structure **1**, below. To the best of our knowledge,[1]



F1 [5.6] **M1** [6.6]

the addition of unsymmetrically substituted diazoalkanes is the only approach which will produce a fulleroid. Carbene additions produce only methanofullerenes.[1]

The phenyl ring is just for synthetic convenience; a phenyl ketone is easier to obtain and is more robust, and its hydrazone is more stable than the corresponding alkane aldehyde hydrazone. We settled on the trimeth-

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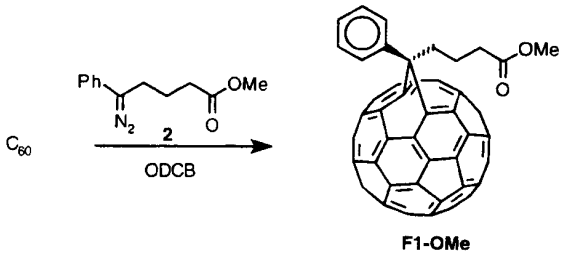
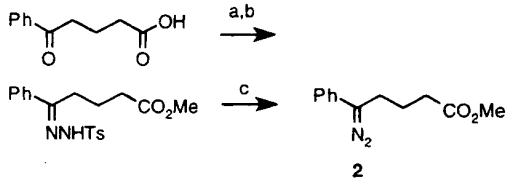
Scheme 1



F1-OMe

Scheme 2[a]



2

[a] Key: (a) methanol/HCl (g);[23] (b) $TsNHNH_2$/methanol reflux; (c) pyridine/NaOMe.

ylene tether because we assumed it was long enough to provide solubility and act as a flexible and inert spacer between the ball and the handle (COX in **1**); it was also part of a commercially available compound. The carboxy functional group is among the most versatile and one of the few which is compatible with the electrophilic nature of C_{60}.

Here we describe initial results of *in situ* trapping of a diazo compound which gave considerably improved yields. We present full experimental details on the preparation of methanofullerenes and fulleroids and give a brief description of some of their properties. We also show, for the first time, that a fulleroid with two different substituents on the bridge carbon preferentially forms only one isomer and is stable toward isomerization to the methanofullerene at 65°.

Results

Scheme 1 describes the preparation of **F1-OMe** by a typical diazo addition route.[7,22]

The diazo compound **2** was prepared from commercial 4-benzoylbutyric acid in three steps as shown in Scheme 2.

In the past, the diazo compound was isolated, purified, and then added to C_{60}. The dipole was usually generated by oxidation of a hydrazone with silver oxide, nickel peroxide, mercuric oxide, or lead dioxide. In the case of relatively unstable diazo compounds (for example, those derived from aldehyde hydrazones) or derivatives which were sensitive to oxidative conditions, the reaction failed or produced unacceptably low yields. Another method for the generation of diazoalkanes is the base-induced decomposition of tosylhydrazones.[24-26] The latter procedure allows the *in situ* generation of the diazo compound without the requirement of its purification prior to addition to C_{60}. Since they are rapidly trapped by C_{60}, even unstable diazo compounds can be successfully coaxed to undergo the 1,3-dipolar addition by the above one-pot reaction procedure. In order to efficiently generate **2** from the tosylhydrazone anion, a temperature of about 70 °C is required.

Remarkably, addition of **2** to C_{60} gives, of the two possible [5,6] isomers, essentially only the isomer with the phenyl ring over the former pentagon. This is likely due to stereoelectronic effects which remain to be studied in detail.[27] No difference in product isomer distribution was observed when **2** was generated in situ. Conversion of the [5,6] to the [6,6] isomer was accomplished by heating. Unlike previous cases,[7,28] higher temperature and prolonged heating was required in the case of **F1-OMe** (180 °C, 2-7 h). From our experience with diaryl, arylalkyl, and dialkyl C_{61} fulleroids, it became clear that the ease of thermal isomerization to the corresponding methanofullerene decreases in that order. A simple kinetic study indicated that the rate of conversion of **F1-OMe** to **M1-OMe** is independent of the substrate concentration; a zero order reaction. A classic interpretation of such a result is that the reaction is dependent on the adsorption onto a surface, as in the case of the decomposition of HI on a gold surface.[29] It is possible that in this case the vessel wall is participating in the reaction. The isomerization reaction is also mediated by acid[30] as well as by photoexcitation.[31]

Electrochemical Properties of F1-OMe and **M1-OMe**. The cyclic voltammograms of both the [5,6] and [6,6] isomers of the methyl ester **1-OMe** are shown in Figure 2. In *o*-dichlorobenzene,[32] each isomer exhibits three well-defined, single-electron, quasireversible waves.[33] The half-cell potentials (defined as $E_1 = 0.5[E_{p,c} + E_{p,a}]$) for the reduction of the [5,6] and [6,6] isomers of **1-OMe** relative to Fc/Fc^+ were -1135, -1525, -2000 mV and -1169, -1549, -2050 mV, respectively. Under the same conditions, the E_1 values for C_{60} were -1056, -1451, and -1906 mV.

The first two reduction waves of the [5,6] isomer occur at almost the same potential as in the parent C_{60}. This is not unexpected, since fulleroids and C_{60} are isoelectronic.[28] It is interesting to note that the reduction potentials of the [6,6] isomer are all shifted significantly toward more negative values than in C_{60} itself. This suggests that the removal of only one double bond from C_{60} significantly alters its electron-accepting ability.

In order to test the scope of our strategy, we prepared a few derivatives of **M1**. In order to convert the methyl ester **M1-OMe** to any other derivative, it had to be converted, in a relatively straightforward fashion, to the key intermediate, the acid chloride (**M1-Cl**). This is shown in Scheme 3.

The acid **M1-OH** was found to be insoluble in most organic solvents, most likely due to the combination of intermolecular hydrogen bonding and C_{60}-C_{60} interac-

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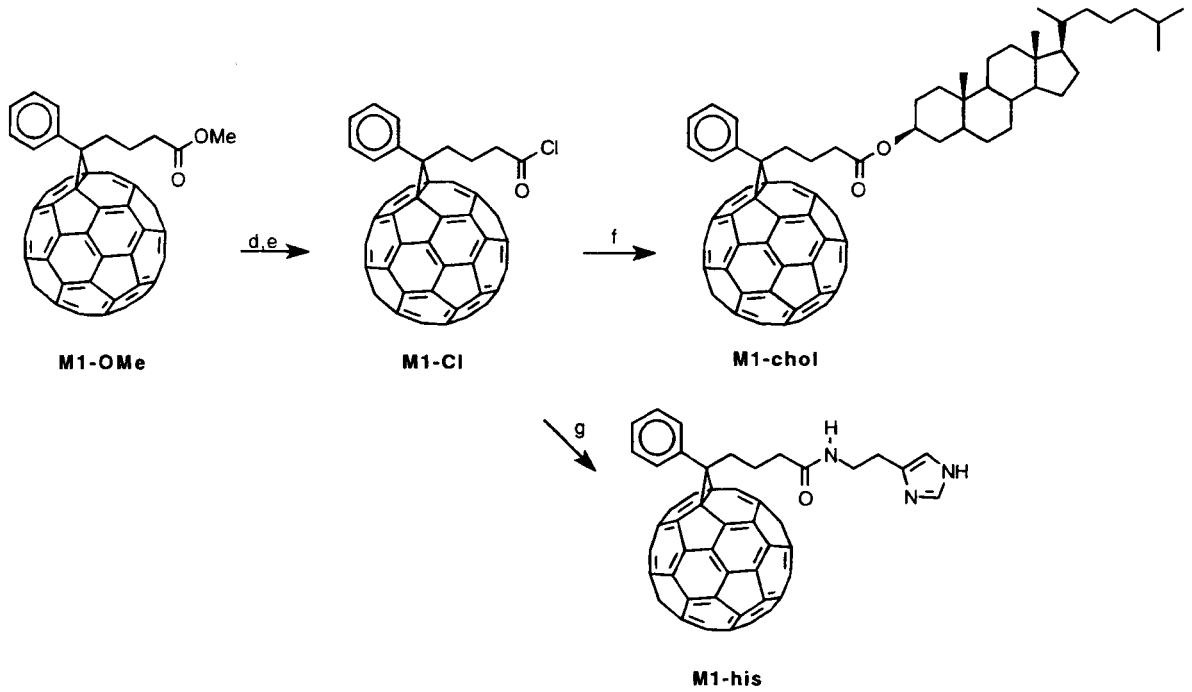
Scheme 3[a]



[a] Key: (d) aqueous HCl/AcOH/1,2-dichlorobenzene; (e) $SOCl_2/CS_2$; (f) cholestanol/pyr/toluene; (g) histamine/pyr.

tions. It is only slightly soluble in carbon disulfide, pyridine, and CS_2/formic acid. In contrast to the acid, the acid chloride appeared to be a relatively soluble derivative, especially in aromatic solvents and CS_2. Most important for further transformations is its solubility in pyridine. It can be kept as a powder under an atmosphere of nitrogen for a few days without significant decomposition. The recalcitrant insolubility and attendant low volatility of **M1-OH** and **F1-OH**[30] prevented mass spectral analysis by the usual FAB-MS techniques, frequently used in fullerene research. As in a previous case,[16] we had to resort to MALDI-FTMS (matrix-assisted laser desorption/ionization Fourier transform mass spectra) as a method for the molecular mass determination.

Molecular Ion Mass Determination. Figure 1 contains the high-resolution MALDI-FTMS negative ion spectra of compounds **F1-OH**[30] and **M1-OH** using 2,5-dihydroxybenzoic acid as matrix. The most abundant ion is the molecular ion $[M]^-$, with *m / z* 896.08 The second most abundant ions correspond to loss of the 61st carbon with its attached groups, i.e., to C_{60}. In the case of **F1-OH**[30] the next most abundant ion corresponds to loss of CO_2. Mass resolution of approximately 5000 is obtained for the **M1-OH** ion spectrum and resolution of about 12 000 for the **F1-OH** ion spectrum.

In another set of measurements, with the appropriate internal calibrants added, an average mass measurement difference of 0.7 and 3.3 ppm for **M1-OH** and **F1-OH**, respectively, from the calculated mass of the all-^{12}C molecular ion species, $[M]^-$, was measured for four separate spectra, each obtained by averaging the spectra resulting from 9 laser shots. Figure 1a and b (insets of Figure 1) shows typical mass measurement accuracy results for the molecular ion region of the negative ion spectra. Unlike the case of the HIV-inhibiting diacid,[16] peaks attributable to C_{60} ions are seen in negative ion MALDI spectra.

From the mass spectral experiments done in the past, it was clear that fulleroid and methanofullerene derivatives are readily converted to C_{60} under FAB-MS or direct laser desorption conditions but that use of MALDI-FTMS suppressed this undesired decomposition and provided analytical data on the unchanged analyte. In this case, however, FAB-MS did not afford spectra at all and the MALDI-FTMS technique showed some decomposition to C_{60}. Thus, it is extremely important to use the appropriate mass spectral technique if reliable conclusions are to be drawn regarding structures of putative fulleroids and methanofullerene.

The acid chloride **M1-Cl** was converted to a number of carboxy derivatives. Here we describe only two: histamide **M1-his** and cholestanyl ester **M1-chol**.

The histamide **M1-his** was produced by reaction of **M1-Cl** with freshly distilled histamine in anhydrous pyridine. The histamide was only sparingly soluble in DMF, formic acid, and DMSO; its hydrochloride was sparingly soluble in methanol. The methanolic solution could be diluted with water. This compound was submitted to Prof. Schinazi's group for virucidal activity testing; preliminary tests indicate that it is as active as the original, more complex[14-16] methanofullerene.

The cholestanyl ester **M1-chol** was prepared from **M1-Cl** and cholestanol in toluene/pyridine. It is one of the most soluble methanofullerenes prepared to date. It forms composites with conjugated polymers such as MEH-PPV and BeCHA-PPV (bis(epicholestanoxy)-PPV).[34]

Hydrolyzed **M1-Cl**, together with traces of **M1-Cl**, and the anhydride of **M1-OH**, formed during the reaction with alcohols or amines, can be recycled by hydrolysis and subsequent chromatography over silica gel using toluene/CS_2/HOAc (10:2:1) as the eluent, yielding pure **M1-OH**.

It was shown in the past that the methanofullerenes exhibit diagnostic, sharp bands at 430 and 700 nm.[28,35] We found that all derivatives of **M1** also show a diag-

(34) Janssen, R. A. J.; Hummelen, J, C,; Wudl, F. Unpublished results.

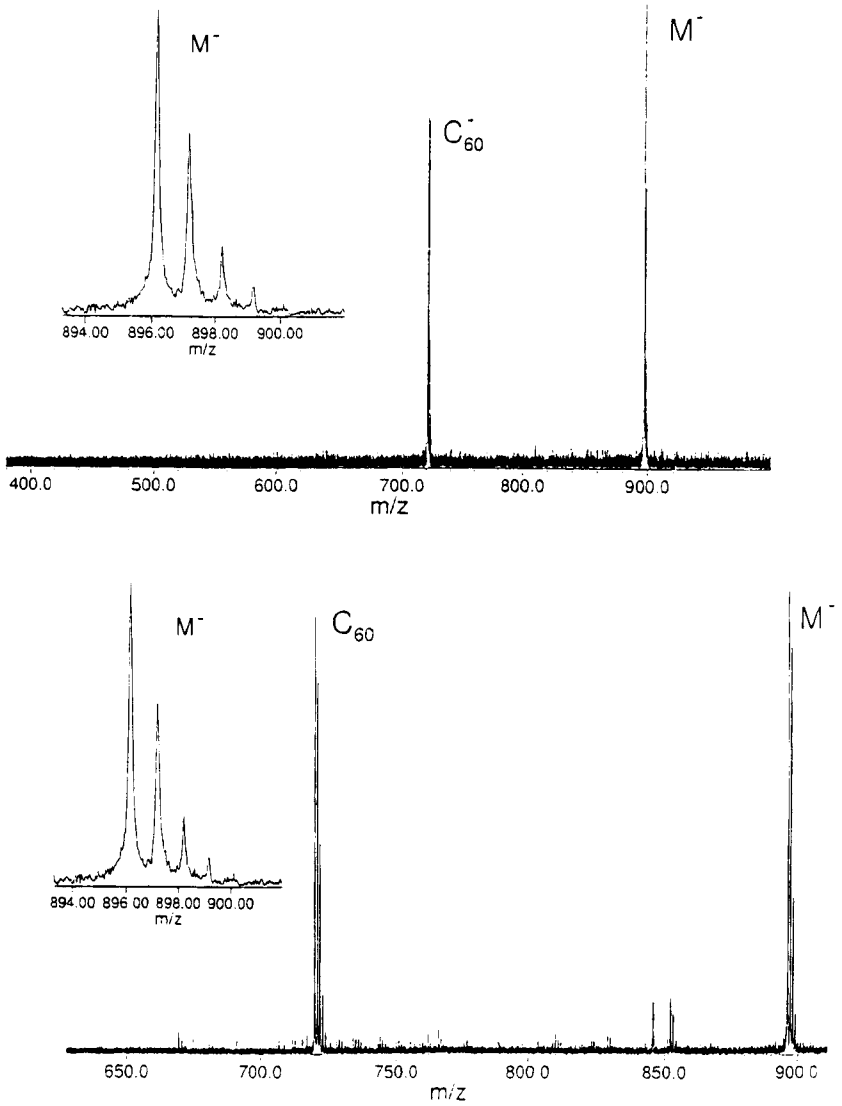


Figure 1. (Top) High-resolution negative ion MALDI Fourier transform mass spectrum of **M1-OH**. (Bottom) high-resolution negative ion MALDI Fourier transform mass spectrum of **F1-OH**. Insets: accurate mass molecular ion measurements of **M1-OH** and **F1-OH**. M^-: using C_{60} as internal calibrant.

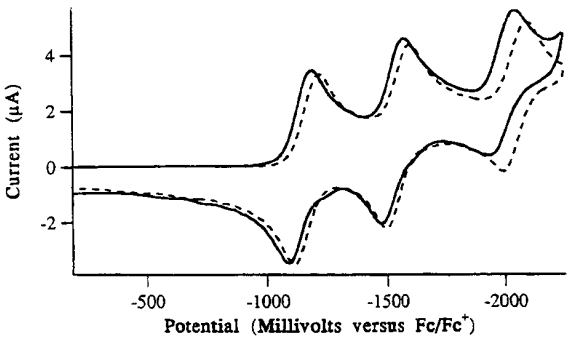


Figure 2. Full line, cyclic voltammogram of **F1-OH** (10^{-3} M) at 100 mV/s, ODCB/0.1 M TBAF vs $Ag/AgNO_2$ (0.01 M, 0.09 M $TBAPF_6$): dotted line, cyclic voltammogram of **M1-OH** (10^{-3} M) at 100 mV/s, ODCB/0.1 M TBAF vs $Ag/AgNO_2$ (0.01 M, 0.09 M $TBAPF_6$).

nostic set of FTIR bands at 585 (m), 572 (m), 564 (w), 559 (w), 550 (m), and 527 (s) cm^{-1}, which are perhaps more useful for structure assignment. Derivatives of **F1** show a different diagnostic pattern, consisting of 16 peaks between 500 and 600 cm^{-1}. The assignment of the protons of the trimethylene group in all derivatives **1** in the 500 MHz ^1H NMR was facilitated by the observation that, consistently, the α-methylene protons appear as a triplet, while the *b*-methylene protons appear as a multiplet and the *g*-methylene protons appear as a multiplet. The chemical shift values of the *g*-methylene protons in the isomeric derivatives of **F1** and in derivatives of **M1** are in agreement with those previously observed for [5,6] and [6,6] 1-methyl-1-(*p*-methoxyphenyl)-C_{61}.[28] Although for **F1** and **M1** compounds, respectively, 36 and 35 different sp^2 carbon resonances (including those for the phenyl ring) could be expected in ^{13}C NMR, not all are resolved at 125 MHz. Instead, 28 (**F1**) and 24-26 (**M1**) line patterns are observed between 127 and 150 ppm. The assignment of the resonances observed for **M1-chol** was based in part on the values reported for cholestanyl acetate.[36,37] Typical [5,6] and

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[6.6] adduct absorption maxima in UV-vis spectroscopy were found for all compounds **F1** and **M1**, respectively.

In the meantime, many other derivatives of **1** with various different X handles were prepared in our group and will be reported in due course. The fullerene functionalization reactions described above are simple, and most of the products have suitable solubilities for further studies such as fullerene and fulleroid thin film-forming derivatives for exploitation of electro-optical properties and polar solvent/water solubility for biological studies.

Experimental Section

Electrochemistry. All electrochemical measurements were performed using a Bioanalytical Systems 100A electrochemical workstation inside an inert atmosphere drybox. Solutions consisted of approximately 1 mM analyte in *o*-dichlorobenzene with 0.1 M tetrabutylammonium tetrafluoroborate. All experiments were done in the presence of 0.5 mM ferrocene added as an internal reference. The experimental setup consisted of a single-compartment cell with a Pt disk working electrode and a Pt wire counter electrode. A silver wire immersed in a solution of 0.01 M $AgNO_3$ and 0.09 M tetrabutylammonium hexafluorophosphate, which was separated from the remainder of the cell by a ceramic tip, served as the reference electrode. The working electrode was polished using a 0.1 *m*m alumina slurry prior to each experiment. Anhydrous *o*-dichlorobenzene was obtained from Aldrich and used as received. Tetrabutylammonium tetrafluoroborate (Aldrich) was recrystallized three times from water/ethanol and dried *in vacuo* at 70 °C. Ferrocene (Aldrich) was sublimed prior to use.

Fourier Transform Mass Spectral Measurements. Instrumental Conditions. Matrix-assisted laser desorption/ionization (MALDI) Fourier transform mass spectra (FTMS) were obtained using a Waters-Extrel (Madison, WI) FTMS-2000 Fourier transform mass spectrometer at a magnetic field strength of 6.2 T. For MALDI negative ion spectra, a Lambda Physik EMG 201-MSC excimer laser using XeCl producing 308 nm light pulses which were attenuated to 7-8 mJ/28 ns pulse. Spectra were obtained using a gated trapping sequence, employing a -9 V decelerating potential for 60 *m*s following the laser pulse, before trapping the desorbed ions with a -2 V trapping potential. For spectral observations, a 200 V peak-to-peak excitation sweep from 50 Hz to 500 kHz at a 300 Hz/ms sweep rate was employed, with detection occurring in the source cell of the dual cell system. Molecular mass determinations were made with reference to the C_{60} peak, which served as internal calibrant. Each spectrum is the result of one laser shot, where 65536 data points were acquired, augmented by an equal number of zeroes and base line corrected prior to magnitude mode Fourier transformation. No apodization was used.

Sample Preparation. A matrix solution consisting of 50 mM 2,5-dihydroxybenzoic acid (DHB) and 0.1% trifluoroacetic acid in methanol was added to sample solutions to maintain a matrix/analyte ratio of 5000:1. A weighed amount of **M1-OH** was dissolved in 3:4 by volume toluene/acetic acid solution and a weighed amount of **F1-OH** in a 1:1 by volume of *o*-dichlorobenzene/acetic acid solution prior to making up with the appropriate volume of DHB matrix solution. For spectral measurements, the matrix/sample solutions were aerosprayed onto a stainless steel probe tip and solvents evaporated, prior to insertion into the vacuum system.

Methyl 4-Benzoylbutyrate. This compound was prepared on 25 g scale from 4-benzoylbutyric acid and MeOH using HCl gas according to a literature procedure.[23] Yield: 92% of a colorless oil. Bp: 132-4 °C/2 mmHg (lit.[23] bp 147-8 °C/8 Torr). FTIR (neat): 1735, 1686 cm^{-1}.

Methyl 4-Benzoylbutyrate *p*-Tosylhydrazone. A mixture of methyl 4-benzoylbutyrate (20.6 g, 0.1 mole), *p*-toluenesulfonyl hydrazide (22.3 g, 1.2 equiv), and MeOH (70 mL) was stirred and refluxed during 5.5 h. The mixture was left without heating during 1 day and then cooled to -15 °C. The product was collected by filtration, washed with a little cold MeOH, and dried in a desiccator to yield 35.9 g (96%) tosylhydrazone as white crystals, mp 122-3 °C. ^{1}H NMR ($CDCl_3$): 9.3 (s, 1H, NH), 7.93 (d, J = 8.5 Hz, 2H; ortho $HArSO_2$-), 7.66 (m, 2H; ortho HPh), 7.34 (m, 3H), 7.28 (d, J = 8.5 Hz, 2H; meta $HArSO_2$), 3.79 (s, 3H, OCH_3), 2.64 (m, 2H, N=CCH_2-), 2.40 (s, 3H, ArCH_3), 2.33 (t, J = 6Hz, -CH_2CO_2R), 1.69 (m, 2H, -$CH_2CH_2CO_2R$). ^{13}C-NMR ($CDCl_3$; d ($CDCl_3$ = 77.00 ppm)) (chemical shifts for (*E*)-isomer with possibly corresponding values for (*Z*)-isomer in parentheses): 174.51 (C=O; 173.43), 153.90 (C=N; 156.98), 143.63 (Ts C_1; 143.95), 136.01 (Ph C_1; 132.45), 135.77 (Ts C_4; 135.08), 129.46 (Ph C_4), 129.36 (Ts $C_{2,3}$; 129.40), 128.25 (Ts $C_{2,3}$; 128.35), 127.73 (Ph $C_{2,3}$; 127.91), 126.06 (Ph $C_{2,3}$; 126.21), 52.00 (OCH_3; 51.35), 32.01 (CCO_2; 32.75), 25.70 (CH_2C=N; 36.98), 21.38 (Ts CH_3), 20.77 (CH_2CCO_2; 20.92). FTIR (KBr): 3113, 1712, 1369, 1228, 1171 cm^{-1}. HRMS (EI) m / z: calcd for $C_{19}H_{23}N_2O_4S$ ($(M + 1)^+$) 375.1349, found 375.1378. Anal. Calcd for $C_{19}H_{22}N_2O_4S$: C, 60.94;H, 5.92; N, 7.48; S, 8.56. Found: C, 61.18; H, 5.91; N, 7.57; S, 8.47.

1-Phenyl-1-(3-(methoxycarbonyl)propyl)diazomethane (2). A solution of 10 g (0.0267 mol) of *p*-tosylhydrazone in dry pyridine (100 mL) was stirred under N_2 at 61-64 °C. Sodium methoxide (0.0278 mol, 1.04 equiv) was added, and the mixture was stirred at about 63 °C during 2 h. The rose-colored mixture was poured onto pentane (200 mL)/ice-water (500 mL). After separation of the layers, the aqueous phase was extracted with pentane (2 × 100 mL). The combined organic phases were washed with ice-water (4 × 200 mL), dried with $MgSO_4$/Na_2SO_4, filtered, and concentrated *in vacuo* at 30 °C to yield the diazo compound as a red oil. TLC (Al_2O_3/toluene): R_f 0.8. The product was stored at -15 °C. Yield: 570 mg (10%). FTIR (neat): 2951, 2037(s), 1737(s), 1596, 1497, 1451, 1163, 751, 693 cm^{-1}.

{6}-1-(3-(Methoxycarbonyl)propyl)-{5}-1-phenyl[5.6]C61 (F1-OMe). Method A. One-Pot Procedure. Methyl 4-benzoylbutyrate *p*-tosylhydrazone (1.50 g, 4 mmol) was dissolved in 30 mL of dry pyridine in a dried three-necked flask provided with N_2 inlet, a thermometer, and a magnetic stirring bar. Then, NaOMe (225 mg, 4.16 mmol) was added, and the mixture was stirred during 15 min. A solution of 1.44 g (2 mmol) of C_{60} in 100 mL of HPLC grade 1,2-dichlorobenzene was added, and the homogeneous reaction mixture was stirred at 65-70 °C during 22 h. (The course of the reaction was followed by TLC (SiO_2/toluene).) The reaction mixture was transferred to a round bottom flask and concentrated to 70 mL at about 0.1 mmHg. The solution was poured on a silica gel/toluene column (40 × 10 cm), pre-eluted with 100 mL of chlorobenzene. The mixture was eluted with 200 mL of chlorobenzene and then with toluene. The first fraction, containing unreacted C_{60}, was collected, concentrated *in vacuo* to about 20 mL, and transferred to a 150 mL centrifuge tube. Et_2O (120 mL) was added, the mixture was immersed in an ultrasound bath for 1 min, the suspension was centrifuged, the supernatant was decanted, and the residue was treated with Et_2O (100 mL) twice in the same manner. The pellet was dried *in vacuo* at 70 °C. Yield: 837.4 mg (58.1%).

After an intermediate fraction, containing a trace of an unknown brown compound, the fraction containing **F1-OMe** was collected. The product was obtained and purified in the above-described manner for C_{60}, using MeOH instead of Et_2O. Yield: 634.2 mg (35%; or 83% based on converted C_{60}). ^{1}H NMR (CS_2) major isomer (95%): 7.87 (d, J = 7.5 Hz, 2H; *o*-H arom), 7.50 (m, 2H; *m*-H arom), 7.37 (m, 1H; *p*-H arom), 3.50 (s, 3H; OCH_3), 2.01 (t, J = 7.5 Hz, 2H; CH_2CO_2Me), 1.58 (m, 2H; $PhCCH_2$), 1.37 (m, 2H; $CH_2CH_2CO_2Me$). Minor isomer (about 5%): 7.19 (m, 2H, *m*-H arom), 7.10 (m, 1H; *p*-H arom), 7.01 (d, J = 9 Hz, 2H; *o*-H arom), 3.78 (m, 2H; $PHCCH_2$), 3.53 (s, 3H; OCH_3), 2.35 (t, J = 8 Hz, 2H; CH_2CO_2Me), 1.90 (m, 2H; $CH_2CH_2CO_2Me$). ^{13}C NMR (CS_2; 125 MHz; d (CS_2) = 192.50 ppm): 171.94 (CO_2), 147.39, 146.21, 145.19, 144.81,

(37) Iida, T.: Tamura, T.; Matsumoto, T. *Magn. Res. Chem.* **1987**, *25*, 558.

144.51, 144.25, 143.98, 143.78, 143.68, 143.63, 143.04, 142.75, 142.47, 142.17, 141.95, 141.35, 141.03, 140.52, 139.70, 139.65, 138.83, 138.21, 137.93, 136.59, 135.02, 130.67, 128.86 (Ph $C_{2,3}$), 127.83 (Ph $C_{2,3}$), 60.94 (Ph*C*), 51.04 (OCH_3), 35.58 (PhC*C*), 33.67 (*C*CO_2), 20.14 (*C*CCO_2). FTIR (KBr): 1735 (m), 1432 (m), 1171 (m), 698 (m), 644 (w), 589 (w), 583 (w), 572 (w), 559 (w), 546 (w), 542 (w), 526 (s) cm^{-1}. UV-vis (hexane) l_{max} (nm): 222, 262, 336, 424, 542. FABMS (NBA) *m / z*: 910 (M^+), 720 (C_{60}^+). Anal. Calcd for $C_{72}H_{14}O_2$: C, 94.94; H, 1.55. Found: C, 94.66; H, 1.69.

Upon elution with CH_2Cl_2, the fraction containing a mixture of isomeric bis-adducts was collected. Workup as described above (using MeOH) yielded 111.2 mg (5%; or 12% based on converted C_{60}). ^{1}H NMR (CS_2): 8.1-7.6 (m, 2H; *o*-H Ar), 7.6-7.0 (m, 3H; *m*- and *p*-H Ar), 3.7-3.35 (3H, >20 peaks for O*CH*$_3$), 2.9-2.6 (m, 1H; [6.6]PhCC*H*$_2$), 2.6-2.25 (m,1H; [6.6]C*H*$_2$CO$_2$), 2.25-1.8 (m, 2H; [5.6]C*H*$_2$CO$_2$ + [6.6]C*H*$_2$CH$_2$-CO$_2$), 1.8-1.0 (m, 2H; [5.6]PhCC*H*$_2$ + [5.6]C*H*$_2$CH$_2$CO$_2$). FTIR (KBr): 1736 (s), 1446(m), 1433 (m), 1252 (m), 1201, 1159, 702, 527 cm^{-1}. FABMS (NBA) *m / z*: 1101 ((M + 1)$^+$), 720 (C_{60}^+). Anal. Calcd for $C_{84}H_{28}O_4$: C, 91.63; H, 2.56. Found: C, 90.90; H, 2.61.

Method B. To a stirred solution of C_{60} (360 mg, 0.5 mmol) in HPLC grade 1,2-dichlorobenzene (20 mL) was added 3 mL of a stock solution of 570 mg of diazoester **2** in 10 mL of 1,2-dichlorobenzene (1.5 equiv). After 24 h, another 3 mL aliquot of the stock solution was added, and further reaction was allowed to proceed during 1 h. The mixture was chromatographed (silica/chlorobenzene), and the three fractions containing C_{60}, **F1-OMe**, and the bis[5.6]ester, respectively, were worked up as described above. Yield: C_{60}, 106 mg (29%); **F1-OMe**, 227 mg (50%); bis[5.6]ester, 96 mg (17%).

1-(3-(Methoxycarbonyl)propyl)-1-phenyl[6.6]C61 (M1-OMe). General Procedure. Purple solutions of **F1-OMe** in HPLC grade 1,2-dichlorobenzene (1-10 mg/mL) were stirred and heated to reflux during 2-7 h. The isomerization was monitored by HPLC (analytical reversed-phase C_{18} column (Vydac, 25 cm), UV detection at 350 nm, eluent MeOH/$CHCl_3$ 3:1, flow rate 1.5-2 mL/min, injection volume 1-5 *m*L). The resulting brown solution was concentrated *in vacuo* to 5-20 mL and transferred to a centrifuge tube. The product was precipitated with 50-100 mL of MeOH and purified as described for **F1-OMe**. Yield: 98%. ^{1}H NMR (CS_2): 7.83 (d, *J* = 8 Hz, 2H; *o*-H arom), 7.47 (m, 2H; *m*-H arom), 7.40 (m, 1H; *p*-H arom), 3.56 (s, 3H; O*CH*$_3$), 2.84 (m, 2H; PhCC*H*$_2$), 2.40 (t, *J* = 7.5 Hz, 2H; C*H*$_2$CO$_2$R), 2.10 (m, 2H; C*H*$_2$CH$_2$CO$_2$R). ^{13}C NMR (CS_2; 125 MHz): 171.0 (*C*O$_2$Me), 148.2, 147.2, 145.4, 144.8, 144.7, 144.4, 144.3, 144.1, 143.7, 143.4, 142.8, 142.7, 142.6, 141.83, 141.77, 141.67, 140.7, 140.4, 137.8, 137.3, 136.3, 131.7, 128.2 (Ph $C_{2,3}$), 128.0 (Ph $C_{2,3}$), 79.3 (bridgehead C), 51.5 (OCH_3), 50.7 (PhC*C*H$_2$), 33.4, 33.3 (PhC*C*H$_2$ and *C*H$_2$CO$_2$Me), 22.3 (*C*H$_2$CCO$_2$Me). FTIR (KBr): 1737 (s), 1445 (m), 1428 (m), 1187 (m), 689 (m), 585 (m), 572 (m), 564 (w), 559 (w), 550 (m), 527 (s). UV-vis (hexane) l_{max} (nm): 210, 258, 328, 430, 492, 696. FABMS (NBA) *m*/z: 910 (M^+). Anal. Calcd for $C_{72}H_{14}O_2$: C, 94.94; H, 1.55. Found: C, 94.66; H, 1.65.

1-(3-Carboxypropyl)-1-phenyl[6.6]C$_{61}$ M1-OH). Either to 50-100 mL of a solution of **M1-OMe** in 1,2-dichlorobenzene (8 mg/mL), chlorobenzene (6 mg/mL), or toluene (6 mg/mL) or directly to the 1,2-dichlorobenzene solution obtained after isomerization of the [5.6] isomer was added glacial HOAc (50 mL) and concd HCl (20 mL). The mixture was stirred and refluxed during 4.5-22 h. The course of the reaction was followed by TLC (silica/toluene): ester, R_f 0.6; acid R_f 0.0. All volatile components were removed *in vacuo*, and the residue was transferred to a centrifuge bottle as a suspension in Et_2O or MeOH, centrifuged, decanted, resuspended in Et_2O, centrifuged, decanted, resuspended in toluene, centrifuged, decanted, and treated twice with Et_2O in the same manner. The residue was dried *in vacuo* at 70 °C during 16 h. Yield: 97-99% (or overall yield from [5.6] isomer: 96-98%). The acid is sparingly soluble in CS_2 and pyridine and more readily in mixtures of either CS_2, 1,2-dichlorobenzene, chlorobenzene, or toluene with HOAc. ^{1}H NMR (CS_2; 500 MHz): 7.83 (d, *J* = 8 Hz, 2H; *o*-H arom), 7.47 (m, 2H; *m*-H arom), 7.40 (m, 2H; *p*-H arom), 2.87 (m, 2H; PhCC*H*$_2$), 2.47 (t, *J* = 7 Hz, 2H; C*H*$_2$CO$_2$), 2.13 (m, 2H; C*H*$_2$CH$_2$CO$_2$). ^{13}C NMR (CS_2/CDOOD; 125 MHz; *d* (CS_2) = 192.5): 179.2 (*C*O$_2$H), 148.4, 147.5, 145.8, 145.2, 145.1, 145.0, 144.8, 144.7, 144.5, 144.2, 143.8, 143.14, 143.10, 143.03, 142.97, 142.2, 142.1, 142.06, 141.1, 140.9, 138.1, 137.7, 136.5, 132.0, 128.6 (Ph $C_{2,3}$), 128.4 (Ph $C_{2,3}$), 79.97 (bridgehead C), 52.06 (Ph*C*), 34.23, 34.11 (*C*CO_2H and PhC*C*), 22.82 (*C*CCO_2H). FTIR (KBr): 1704 (s), 1428 (m), 1187 (m), 755 (m), 698 (m), 585 (m), 572 (m), 564 (w), 559 (w), 550 (m), 527 (s) cm^{-1}. UV-vis (toluene/HOAc 4:1) l_{max} (nm): 332, 432, 498, 696. FABMS (NBA): only matrix observed. MALDI *m / z*: 896.08127 (M^-). Anal. Calcd for $C_{71}H_{12}O_2$: C, 95.08; H, 1.35. Found: C, 92.40; H, 1.55.

1-(3-(Chlorocarbonyl)propyl)-1-phenyl[6.6]C$_{61}$ (M1-Cl). Acid **M1-OH** (300 mg, 0.335 mmol) was dissolved in 100 mL of dry CS_2 under an atmosphere of N_2. Thionyl chloride (20 mL) was added via a syringe, and the mixture was stirred at reflux temperature during 18 h. The volatile components were removed *in vacuo*. The residue was suspended in 80 mL of dry ether, using an ultrasound bath, the suspension was centrifuged at 3500 rpm, and the supernatant was decanted. This procedure was repeated twice with 50 mL of dry ether. The brown powder was dried *in vacuo* at 70 °C during 18 h and stored under N_2. Yield: 268 mg (88%). FTIR (KBr): 1793 (m), 1445 (m), 1428 (m), 1398 (m), 1187 (m), 765 (m), 755 (m) 715 (m), 698 (s), 585 (m), 572 (m), 564 (w), 559 (w), 550 (m), 527 (s) cm^{-1}. ^{1}H NMR (200 MHz; CS_2): 7.85 (m, 2H; *o*-H arom), 7.48 (m, 3H; *m*- and *p*-H arom), 3.05 (t, *J* = 8 Hz, 2H; C*H*$_2$COCl), 2.87 (m, 2H; PhCC*H*$_2$), 2.22 (m, 2H; C*H*$_2$CH$_2$COCl). UV-vis (toluene) l_{max} (nm): 332, 432, 492, 696.

1-(3-(*w*-*N*-Histaminocarbonyl)propyl)-1-phenyl[6.6]C$_{61}$ (M1-his). A solution of distilled histamine (60 mg, 0.54 mmol) in anhydrous pyridine was added via a syringe to acid chloride **M1-Cl** (40 mg, 0.044 mmol) in a dry flask under an atmosphere of N_2. The homogeneous mixture was stirred for 18 h at ambient temperature. The solvent was removed *in vacuo*. The residue was suspended in 50 mL of CS_2 using an ultrasound bath, the suspension was centrifuged (3500 rpm), and the supernatant was decanted. This procedure was repeated with 50 mL of CS_2 (1×), with MeOH (3 × 50 mL), with distilled ether (2 × 50 mL), with toluene (2 × 50 mL), and finally with CS_2 (2 × 50 mL). The brown product was dried *in vacuo* at 60 °C during 24 h. Yield: 29.4 mg (68%). The amid is slightly soluble in DMF, DMSO, and CS_2/MeOH 1:1. The corresponding HCl salt (from a suspension of the amide in 1 N HCl) is slightly soluble in MeOH. ^{1}H NMR (too insoluble to record a spectrum). FTIR (KBr): 3430 (m), 1652 (s), 1632 (sh), 1428 (s), 1188 (m), 712 (m), 585 (w), 572 (w), 565 (w), 559 (w), 550 (w), 527 (s). UV-vis (DMSO) l_{max} (nm): 332, 434, 490 (very weak). FABMS (NBA) *m / z:* 989 (M^+).

1-(3-Carboxypropyl)-1-phenyl[6.6]C$_{61}$ Cholestanyl Ester (M1-chol). To a stirred solution of **M1-Cl** (220 mg, 0.24 mmol) in 50 mL freshly distilled toluene under an atmosphere of N_2 was added 2 mL of dry pyridine and then 5α-cholestan-3*b*-ol (225 mg, 2.4 equiv). The resulting mixture was stirred at ambient temperature for 18 h. The volatile components were removed *in vacuo*, and the product was extracted from the resulting mixture of solids with 3 × 50 mL of toluene using the centrifuge method. The toluene extracts were combined and concentrated. The residue was chromatographed over a silica gel column using toluene as the eluent. The fast running fraction containing the product was concentrated to 10 mL and transferred to a centrifuge bottle. The ester was precipitated with MeOH, the suspension was centrifuged, and the resulting clear supernatant was decanted. The brown powder was washed with 2 × 100 mL of MeOH using the centrifuge method and dried *in vacuo* overnight at 60 °C. Yield: 53 mg (18%). Mp: 296-299 °C. ^{1}H NMR (CS_2, TMS; 500 MHz): 7.82 (d, *J* = 7.5 Hz, 2H; *o*-H Ph), 7.46 (t, *J* = 7.5 Hz, 2H; m-H Ph), 7.40 (t, *J* = 7.5 Hz, 1H; *p*-H Ph), 4.52 (m, seven lines at 5 Hz distance, 1H; CO$_2$C*H*), 2.82 (m, 2H; PhCC*H*$_2$), 2.33 (t, *J* = 7 Hz, 2H; C*H*$_2$CO$_2$), 2.06 (m, 2H; C*H*$_2$CH$_2$CO$_2$), 1.95-0.5 (m), with peaks at 0.86 (d, *J* = 6.5 Hz; Me-21), 0.84 (d, *J* = 6.6 Hz; Me-26), 0.837 (d, *J* = 6.6 Hz; Me-27), 0.77 (s; Me-19), 0.61 (s; Me-18). ^{13}C NMR (CS_2; *d* (CS_2) = 192.5; 125 MHz): 170.1 (*C*O$_2$R), 148.2, 147.3, 145.4, 144.8, 144.7, 144.4, 144.3, 144.1, 143.7, 143.4, 142.73, 142.67, 142.6, 141.9, 141.76, 141.67,

140.7, 140.4, 137.8, 137.3, 136.3, 131.7, 128.2 (Ph $C_{2,3}$), 127.9 (Ph $C_{2,3}$), 79.39 (bridgehead C), 72.97 (CO_2CH), 56.31 ($C_{14,17}$), 56.17 ($C_{14,17}$), 54.09 (C_9), 51.62 (Ph*C*), 44.6 (C_5), 42.35 (C_{13}), 40.06 (C_{12}), 39.50 (C_{24}), 36.88 ($C_{1,22}$), 36.2 (C_{20}), 35.76 ($C_{8,10}$), 35.28 ($C_{8,10}$), 34.02 (C_4), 33.90 (CCO_2), 33.46 ($PhCCH_2$), 32.20 (C_7), 28.88 (C_6), 28.48 (C16), 28.14 (C_{25}), 27.54 (C_2), 24.44 (C_{15}), 23.95 (C_{23}), 22.84 (C_{27}), 22.59 (C_{26}), 22.35 ($CCCO_2$), 21.28 (C_{11}), 18.71 (C_{21}), 12.26 ($C_{18,19}$), 12.07 ($C_{18,19}$). FTIR (KBr): 2929 (s), 2865 (m), 2851 (m), 1731 (s), 1465 (m), 1456 (m), 1445 (m), 1428 (m), 1257 (m), 1187 (m), 1150 (m), 585 (m), 573 (m), 564 (w), 559 (w), 554 (w), 551 (m), 527 (s), 524 (m) cm^{-1}. UV-vis (hexanes) l_{max} (nm): 212, 258, 328, 430, 498, 696. FABMS (NBA/toluene) *m / z:* 1267 (MH^+), 720 (C_{60}^+). Anal. Calcd for $C_{98}H_{58}O_2$: C, 92.86; H, 4.61. Found: C, 91.95; H, 4.70.

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