Amphiphilic [5:1]- and [3:3]-Hexakisadducts of C_{60}

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We have synthesized and characterized a variety of new amphiphilic hexakisadducts of C_{60} involving mixed octahedral [5:1]- and [3:3]-addition patterns. The [5:1]-adducts **3** and **13** contain five pairs of didodecyl or diethyl malonates as nonpolar addends and, as their polar part, an extended bis(malonate) involving C_{14} and ethylene glycol chains and two biotin termini. For the first time, amphiphilic [3:3]-hexakisadducts have been prepared using the *e*,*e*,*e*-trisadduct **18**, which contains a *cyclo*-[3]-octyl malonate addend, as the precursor. As polar groups, we used malonates featuring carboxy, amino, or peptide termini. The charge on the termini, which can range from zero up to sixfold positive or sixfold negative, can be built up by protonation or deprotonation. All the amphiphilic [3:3]-hexakisadducts are very soluble in water in their completely charged forms. Initial investigations on the aggregation properties of the amphiphilic [3:3]-hexakisadducts, conducted using transmission electron microscopy (TEM) and pulse-gradient spin echo (PGSE) NMR spectroscopy, reveal the pH-dependent formation of aggregates.

Introduction

Recently, we introduced two examples, **1**[1,2] and **2**,[3−5] of amphiphilic [5:1]-hexakisadducts of C_{60} that involve an octahedral addition pattern.[6] The remarkably facile access to these stereochemically defined multiple adducts required control over the regioselectivity of the subsequent additions to the [6,6]-bonds in *equatorial* sites. This control was achieved using the template mediation strategy that we introduced previously[7] in which 9,10-dimethylanthracene (DMA) units act as reversible-binding precursor addends.

The globular amphiphile **1** readily dissolves in water at physiological pH, forming unilamellar vesicles (buckysomes) having diameters typically between 100 and 400 nm, and has a very small critical micelle concentration (CMC).[1] Stable monolayers of **1** at the air/water interface were prepared by the Langmuir technique.[2] Because of the presence of 18 carboxylic groups, which can be deprotonated successively, electrostatic interactions between the globular amphiphiles can be modified systematically, making them interesting vehicles for the delivery of nonpolar drug molecules. Amphifullerene **1** is expected to offer several advantages over conventional lipid-based drug-delivery systems.[8] First, a higher loading capacity for lipophilic guest molecules located between the bilayers can be expected because the radially arranged alkyl chains prevent dense packing within the unloaded vesicle. Secondly, the aggregation properties of the buckysomes can be modulated readily by variations in pH. Thirdly, the presence of the 18 carboxylic groups of **1** enables further functionalization, such as targeting with labels or antibodies, without losing the aggregation properties.

The biofunctional amphifullerene **2** can intercalate into a dipalmitoyl-*sn*-*glycero*-3-phosphatidylcholine (DPPC) bilayer and serve as a transmembrane anchor for proteins located outside the membrane.[3−5] The biotin anchor in **2** is able to bind proteins such as avidin and streptavidin. As a consequence, the possibility of biocompatibilization of liposomes is provided. The amphiphilic behavior of **2** was demonstrated by Langmuir−Blodgett (LB) investigations.[5]

Since the investigation of the supramolecular properties of these first examples of amphiphilic hexakisadducts of C_{60} was very encouraging, we decided to synthesize a whole range of amphifullerenes[9] by systematically changing the nature of the hydrophilic and lipophilic addends and the nature of the hexaaddition pattern itself. In this contribution, we introduce the syntheses of three new types of amphifullerenes involving [5:1]- and [3:3]-addition patterns that feature neutral as well as cationic and anionic polar groups. These new amphifullerenes are now available for the systematic investigation of their aggregation and encapsulation properties.

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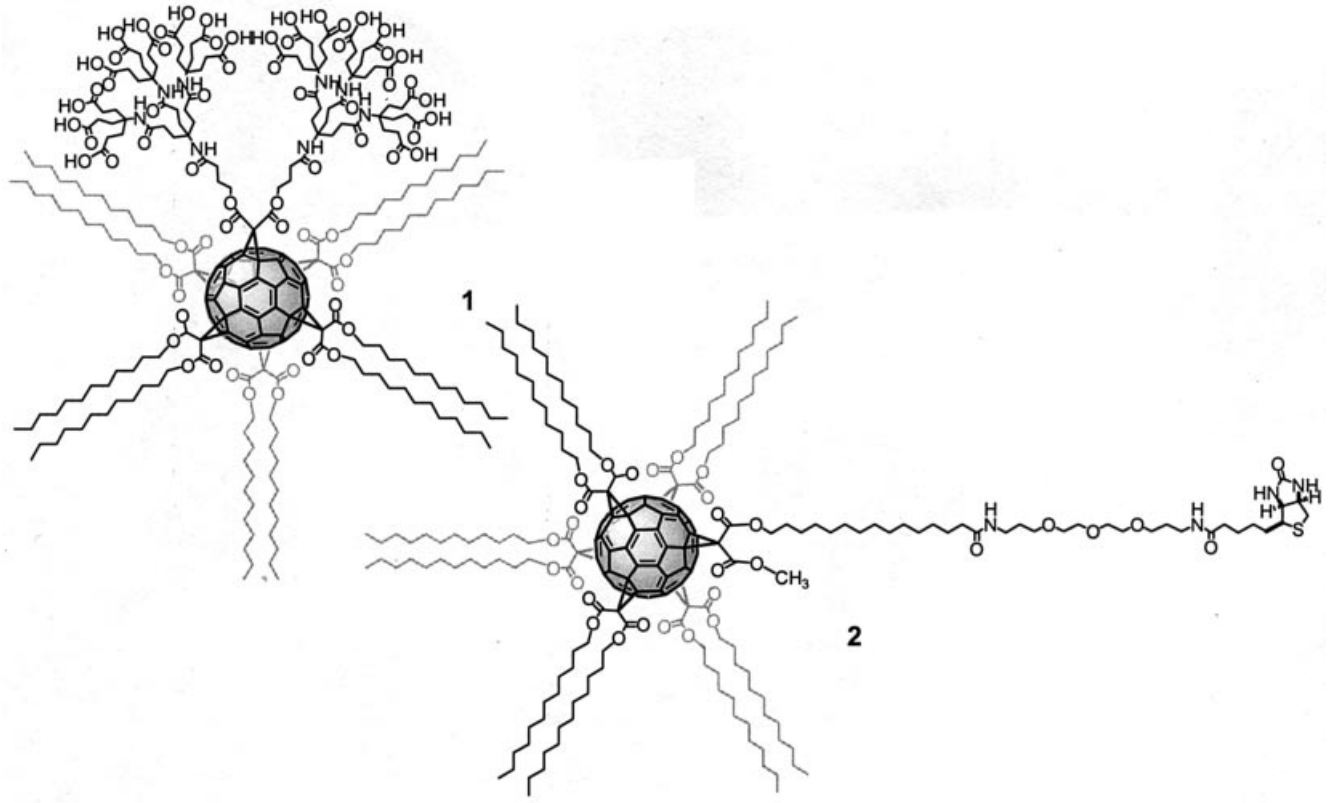


Results and Discussion

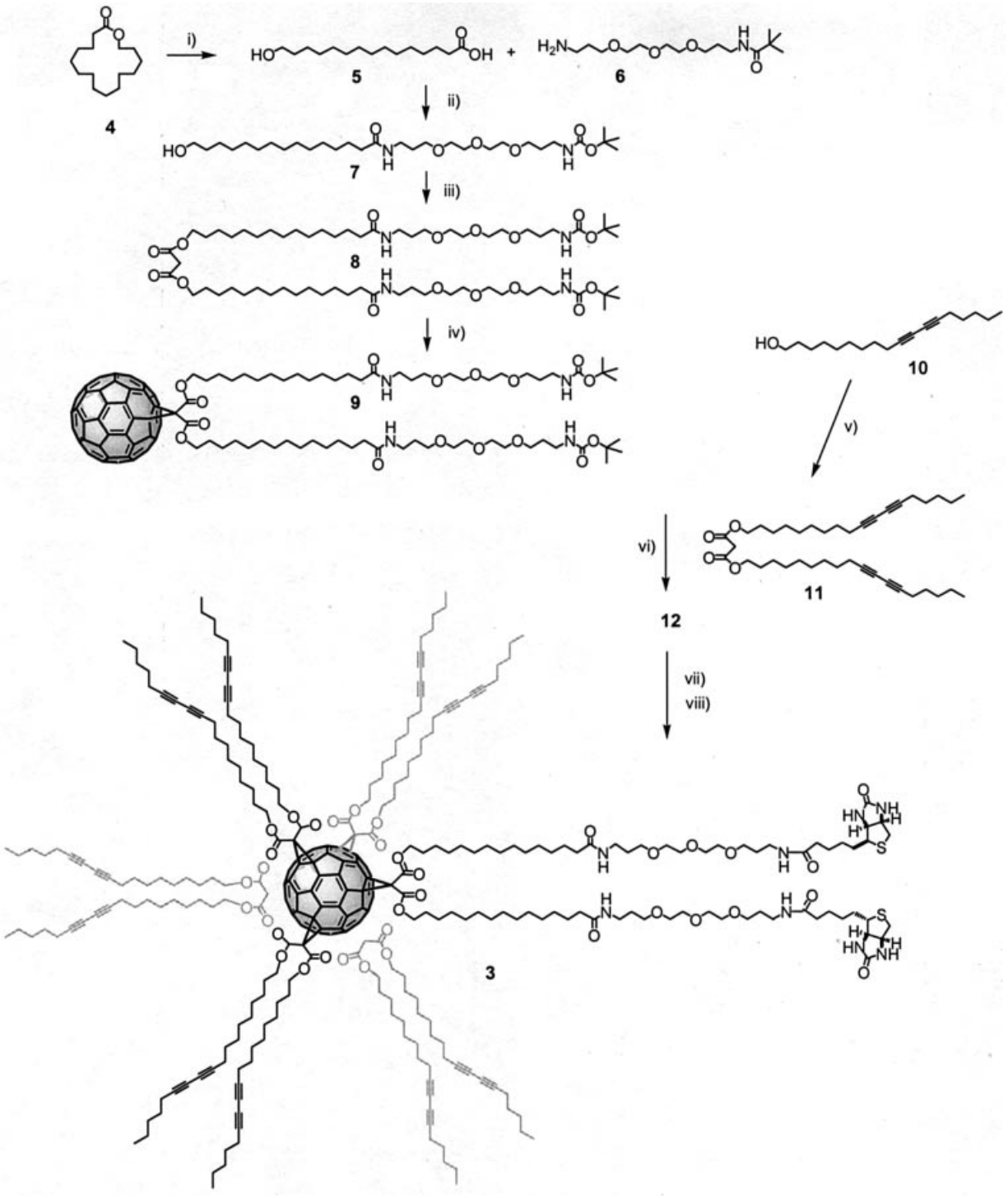
Biotinylated [5:1]-Amphifullerenes

We intended to synthesize a second-generation biotinylated [5:1]-amphiphile having the following structural properties: (i) One of the malonate addends should carry two biotin groups instead of one attached to spacer units that are long enough to protrude through a lecithin layer. We expected that, compared to **2**, the amphiphilic character is more pronounced and that the ability to form micelles or vesicles is increased. (ii) Nonpolar building blocks, C_{18}-alkyl chains containing butadiyne units instead of saturated C_{12} chains, should be used to allow subsequent 1,4-addition-type polymerization to occur in the same manner as that which we reported for comparable lipofullerenes.[10] In contrast to the polymerization of these lipofullerenes, where we observed the formation of perfectly spherical polymer beads and destroyed lipid vesicles,[10] now it is conceivable for polymerization to occur inside the intact bilayer membrane.

All these structural features are represented in the target molecule **3**. The synthesis of **3** is shown in Scheme 1. The new biotin linker **7**, which involves an extended polar part when compared with **2**, was obtained by carbonyldiimidazole (CDI) activated coupling[11] of 15-hydroxypentadecanoic acid (**5**), which was derived from commercially available pentadecanolide (**4**), with the *N*-Boc-protected glycol **6**. Subsequently, the corresponding malonate **8** was synthesized. Cyclopropanation[12] of **8** with C_{60} led to the methanofullerene **9**. The synthesis of bis(10,12-octadecadiynyl) malonate (**11**) was achieved by coupling of the corresponding alcohol **10** with malonyl chloride.[13] The mixed [5:1]-hexakisadduct **12** having a C_{2v}-symmetrical octahedral addition pattern[6] was obtained by exhaustive DMA-mediated cyclopropanation[6,7,14] of **9** with malonate **11**. Subsequently, the two Boc protecting groups were removed using TFA/CH_2Cl_2. The final coupling with CDI-activated D-(+)-biotin resulted in the isolation of target molecule **3**.

All reaction intermediates and products were fully characterized by means of ^1H and ^{13}C NMR spectroscopy, IR or UV/Vis spectroscopy, mass spectrometry, and elemental analysis. The ^{13}C NMR spectrum of **3** perfectly displays the expected signals for the terminal biotin groups and the two resonances of the C_{60} unit's sp^2-hybridized carbon atoms, clearly demonstrating local T_h symmetry around the fullerene nucleus (Figure 1).

The interactions of the bifunctional amphifullerene **3** with lipid membranes, as well as polymerization reactions within the corresponding composites, are currently under investigation. Because of the "*trans*" orientation of the two biotinylated transmembrane side chains of amphifullerene **3**, bolaamphiphilic character can be expected. Two characteristic low-energy orientations (**a** and **b** in Figure 2) of the amphiphilic side chains were obtained according to semiempirical calculations. The possible intercalation into a DPPC lipid membrane segment is shown in Figure 2. After intercalation of **3** into the membrane, the biotin units may act as transmembrane anchors and molecular recognition signals and the ten polymerizable malonate chains may allow photopolymerization to occur.[15]



Scheme 1. Synthesis of the biotinylated amphiphilic mixed [5:1]-hexakisadduct **3** having a C_{2v}-symmetrical addition pattern around the C_{60} core (i: NaOH; ii: CDI; iii: malonic acid, CDI; iv: C_{60}, CBr_4, DBU, toluene, room temp.; v: malonyl dichloride, pyridine; vi: DMA, CBr_4, DBU, toluene, room temp.; vii: TFA, CH_2Cl_2; viii: CDI, biotin)

Hexakisadduct **3** did not meet our expectations regarding its solubility and aggregation properties in water. Acceptable solubility was found only in organic solvents such as $CHCl_3$, CH_2Cl_2, and DMF. In water, **3** is soluble only in the presence of a co-solvent, such as methanol. Thus, we have not investigated the self-aggregation behavior of **3**. To increase the polar character and to improve the water solubility of such a bis(biotinylated) derivative, we synthesized the [5:1]-hexakisadduct **13** having five ethyl malonate addends rather than five octadecadiynyl malonate units (Scheme 2). In this case, to overcome the general problem of separating the desired hexakisadducts from other ad-

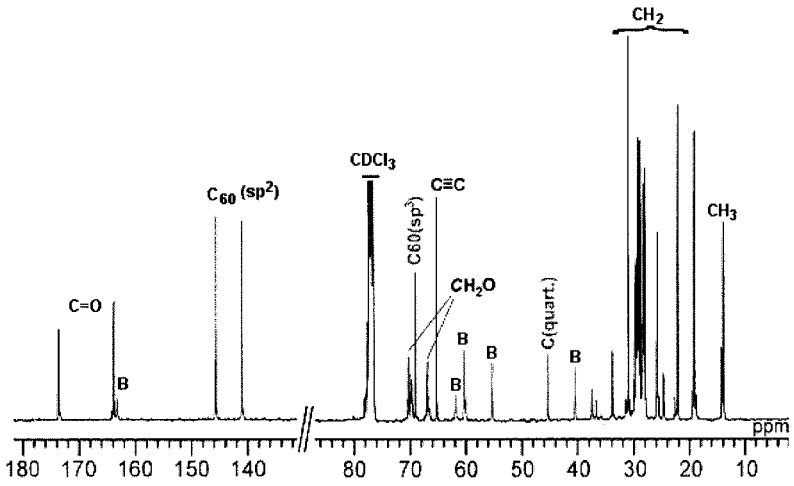


Figure 1. ^{13}C NMR spectrum (100.5 MHz, room temp., $CDCl_3$) of hexakisadduct **3**; the resonances at δ = 37 and 70 ppm belong to the carbon atoms of the diethyl ether moiety of the spacer; B = biotin

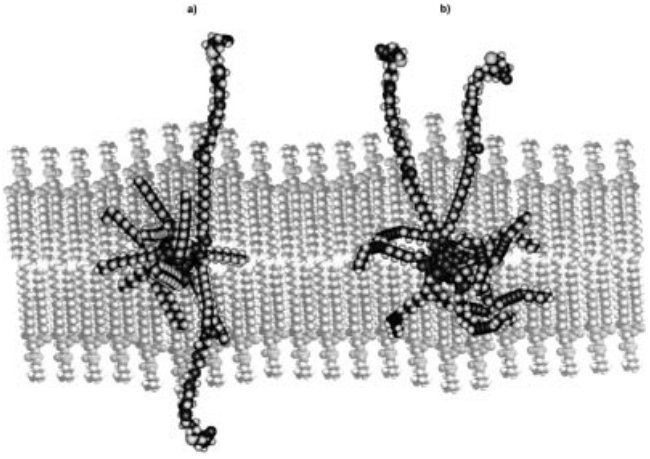


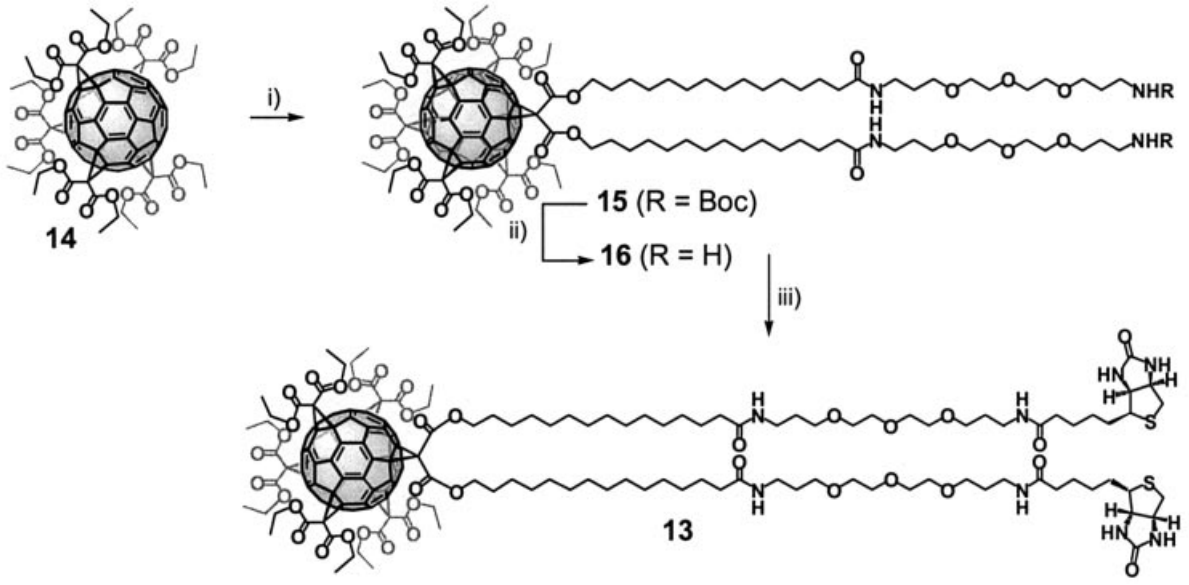
Figure 2. CPK model of a DPPC lipid bilayer with amphifullerene **3** in "*trans*" (left) and "*cis*" (right) orientations of its biotinylated transmembrane side chains, obtained by optimization from semi-empirical PM3 geometries (HyperChem 6.01)

ducts formed simultaneously during the exhaustive cyclopropanation step, we reversed the sequence of addition steps. For this purpose, we prepared the cherry-red, C_{2v}-symmetrical [5:0]-pentakisadduct **14**[14] and used it as our starting material. The subsequent cyclopropanation reaction with the Boc-protected spacer malonate **8**, to complete the C_{2v}-symmetrical octahedral addition pattern, afforded the bright-yellow *N*-Boc-protected [5:1]-hexakisadduct **15** in 63% yield after purification by flash chromatography (FC) and high-performance liquid chromatography (HPLC). After cleavage of the Boc protecting groups using TFA/CH_2Cl_2, the bis(amino)amphifullerene **16** was obtained in quantitative yield. The final coupling of two (+)-biotin moieties, by CDI activation, to the amino termini resulted in the formation of target molecule **13**.

All reaction intermediates and products were fully characterized by means of ^1H and ^{13}C NMR, IR, and UV/Vis spectroscopy, elemental analysis, and mass spectrometry. Again, we found that appreciable solubility of the short-chain bis(amino)amphifullerene **16** and its biotinylated derivative **13** exists only in organic solvents, e.g., $CHCl_3$ and CH_2Cl_2; relative to their corresponding octadecadiynyl analogues, **12** and **3**, they display enhanced solubility in methanol.

Water-Soluble [3:3]-Amphifullerenes

The water-insoluble amphifullerenes **3** and **13** exhibit demixing properties and do not self-assemble in water, probably because they possess insufficiently low numbers of polar moieties. To improve their amphiphilic character, either larger polar addends are necessary, as exemplified by the dendrofullerene **1**, or a more balanced ratio of polar and nonpolar addends should be considered. For this purpose, we chose [3:3]-hexakisadducts containing three pairs of non-dendritic polar chains as target systems. To guarantee easy access to amphiphilic [3:3]-hexakisadducts in satisfactory yields, we used macrocyclic *cyclo*-[3]-octyl malonate (**17**)[16] for the initial addition to C_{60} (Scheme 3). Recently, we reported that multiple adducts of C_{60} having specific addition patterns are accessible in good yields with remarkable, and, in many cases, complete regioselectivity in one synthetic step when flexible *cyclo*-[*n*] malonates are used as addends.[16] The high regioselectivities are a result of the nearly balanced distribution of strain energy within the flexible alkyl chains of the *cyclo*-[*n*] malonates. For example, the *e*,*e*,*e*-trisadduct **18** (Scheme 3), in which the cyclic malonate is attached to three adjacent octahedral [6,6]-binding sites, can be obtained with very pronounced regioselectivity and an isolated (HPLC) 64% yield upon reaction of C_{60} with **17**. In the context of amphiphilic fullerenes, the tris(malonate) addend in **18**, which comprises three C_{12} chains, serves as the non-polar unit of the amphiphile. The remaining octahedral binding sites within **18** are free for the addition of three polar malonates. A very favorable observation that supports this purpose is the fact that completing an octahedral addition pattern proceeds with very good regioselec-



Scheme 2. Synthesis of amphiphilic bis(amino) hexakisadduct **16** and its biotinylated derivative **13** [i: malonate **8**, CBr_4, DBU; ii: TFA, CH_2Cl_2; iii: CDI, D-(+)-biotin]

tivity both when using or not using the template mediation strategy.[6] Both cationic or anionic end groups can be used to increase the water solubility and enable pH-dependent aggregation.

Cationic Water-Soluble [3:3]-Amphifullerenes

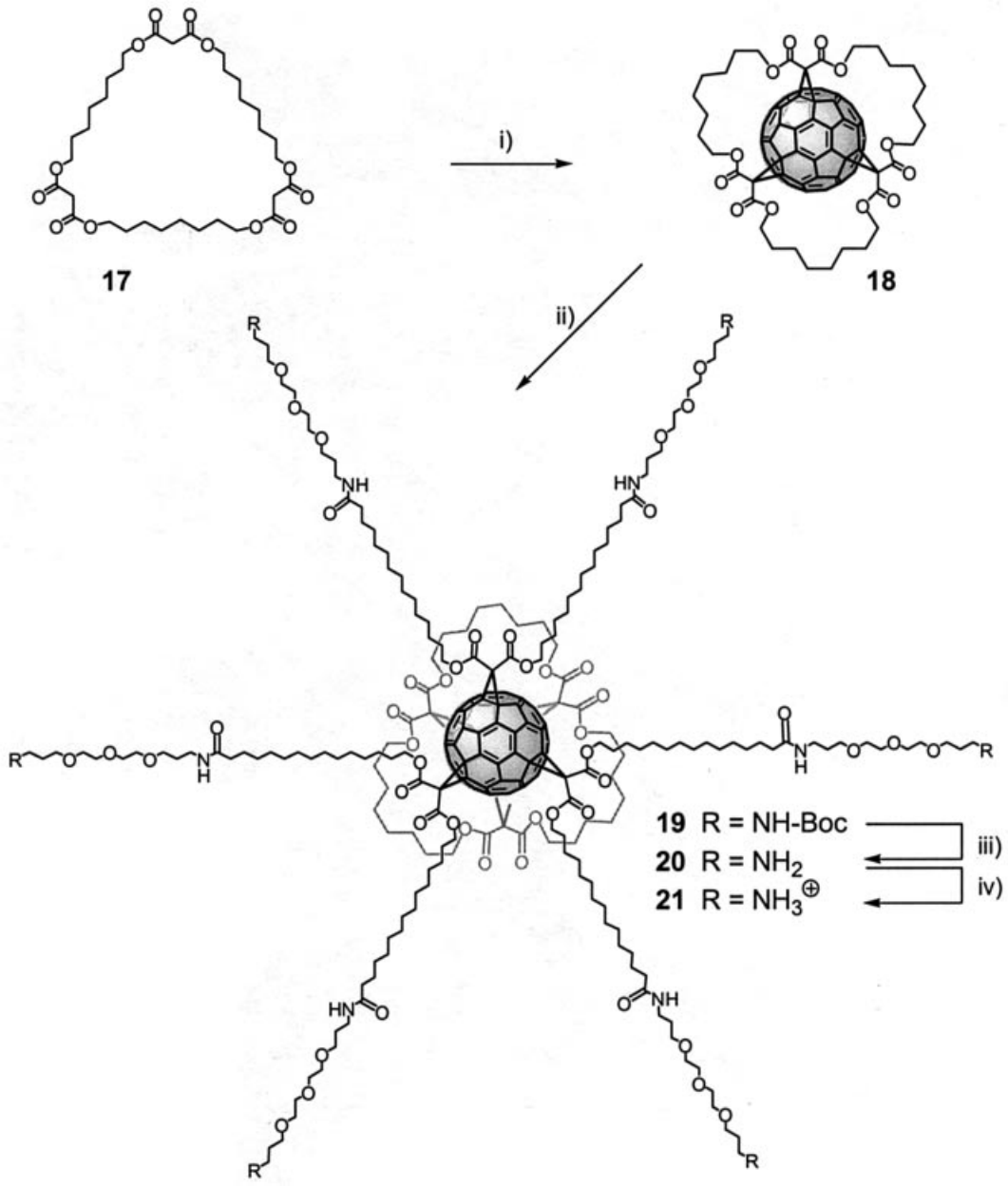
As a first example of a cationic [3:3]-amphifullerene, we undertook the synthesis of compound **21** (Scheme 3). To provide the lipophilic *e*,*e*,*e*-trisadduct **18** with polar moieties, the octahedral addition pattern was completed by DMA-templated cyclopropanation[7] using an excess of the spacer malonate **8**. The Boc-protected, C_3-symmetrical [3:3]-hexakisadduct **19** was obtained in 55% yield after separation using HPLC. The cleavage of the Boc protection groups was achieved using TFA. The resulting amphifullerene **20** was protonated to give target molecule **21** (Scheme 3). All reaction intermediates and products were fully characterized by ^{1}H and ^{13}C NMR, IR or UV/Vis spectroscopy, elemental analysis, and mass spectrometry.

The pH-dependent solubility of **20** in water was demonstrated by UV/Vis spectroscopic investigations. Very low solubility of **20** occurs at neutral pH (buffered) and in weakly acidic solution. The saturated aqueous solutions were almost colorless because of the low concentration and the hexakisadduct bands in the UV/Vis spectra were very weak because of low solubility (Figure 3). Upon lowering the pH to 5, water solubility increases, which causes a slight increase in the absorption. Finally, at pH = 3, a value at which all of the amino groups are completely protonated to give the cationic amphiphile **21**, all of the material dissolved to form a yellow solution from which all of the absorption bands characteristic of a hexakisadduct with an octahedral addition pattern exhibited high intensities.

Preliminary TEM investigations on the aggregation properties of **20** revealed the formation of thin aggregates in basic solutions at pH = 9−10. Similar to carbon nanotubes, the self-assemblies possess diameters of ca. 70 Å and are very long (Figure 4). The diameters are similar to those of micelles formed from structurally related dendritic polycarboxylic fullerene derivatives.[1] We observed no aggregates by TEM at neutral or acidic values of pH, which is due possibly to electrostatic repulsion between individual highly charged molecules and the fact that the addends carrying amino termini are very long and so can wrap around the whole molecule to shield its apolar moieties from the aqueous phase (monomolecular micelles).

Using the same synthetic pathway, we prepared the Boc-protected hexakisadduct **22** and the sixfold-protonated amphifullerene **23** having shorter hydrophilic malonate branches by reaction of *e*,*e*,*e*-trisadduct **18** with an excess of malonate **24**. The isolated yield of **22**, after chromatographic purification, was 55%. The cleavage of the protection groups was achieved using TFA and the protonated amphifullerene **23** was isolated as yellow solid in quantitative yield. All reaction intermediates and products were fully characterized by ^{1}H and ^{13}C NMR spectroscopy, IR or UV/Vis spectroscopy, and mass spectrometry.

In a similar manner, we synthesized a number of related amphiphilic mixed [3:3]-hexakisadducts, **25**−**32**, by cyclopropanation of the *e*,*e*,*e*-trisadduct **18** with a variety of malonate and malonamide addends, **33**−**36**, containing either alkyl or oligoethylene glycol chains. Relative to the previous example, all these chains are considerably shorter and match the size of the nonpolar *cyclo*-[3]-octyl malonate moiety of the resulting amphiphiles. The *N*-Boc-protected malonate **33** was obtained in 72% yield by condensation of malonic acid with an excess of commercially available *N*-Boc-protected 6-aminohexan-1-ol in the presence of DMAP and DCC. The corresponding conversion of the mono-*N*-protected α,ω-diamines hexamethylenediamine, 3,6-dioxa-



Scheme 3. Synthesis of the amphiphilic [3:3]-hexakisadduct **20** having a C_3-symmetrical addition pattern (i: 1.5 equiv. C_{60}, CBr_4, DBU; ii: DMA, malonate **8**, CBr_4, DBU; iii: TFA, CH_2Cl_2; vi: H_3O^+/TFA)

1,8-octanediamine, and 4,7,10-trioxa-1,13-tridecanediamine with malonic acid, by applying the same reaction conditions, afforded the Boc-protected malonamides **34**, **35** and **36**, respectively, in comparable yields.

The subsequent cyclopropanation of **18** with an excess of the malonyl derivatives **33**−**36** in the presence of DMA, CBr_4, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[12] yielded, after chromatographic purifications, the *N*-Boc-protected, mixed [3:3]-hexakisadducts **25**−**28** in 50, 28, 45, and 49% yields, respectively. The protecting groups were removed using TFA in CH_2Cl_2 and the hexaammonium trifluoroacetates **29**−**32** were isolated as yellow solids, each in quantitative yield.

The malonate and malonamide spacers, as well as the *N*-protected [3:3]-hexakisadducts and the corresponding hexaammonium trifluoroacetates, were fully characterized. The fast-atom bombardment (FAB) mass spectra of the Boc-protected [3:3]-hexakisadducts **25**, **26**, **27**, and **28** revealed, in each case, signals for the molecular ion [M^+] and the [M − 6 Boc]$^+$ fragment. The fullerene portion of the sp^2 region of the ^{13}C NMR spectra of each of the new hexakisadducts **25**−**32** consists of 16 resonances grouped into two characteristic sets of signals[6] for the fullerene's sp^2-hybridized carbon atoms at δ = 141 and 145 ppm. This display clearly reflects the expected C_3 symmetry within an octahedral addition pattern. The UV/Vis spectra of **25**−**32** show the characteristic

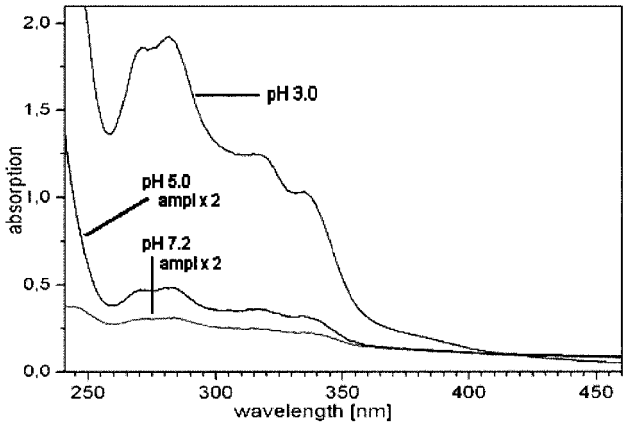


Figure 3. UV/Vis spectra of aqueous solutions of hexakisadduct **20** at different pH values (Shimadzu UV-3102 PC)

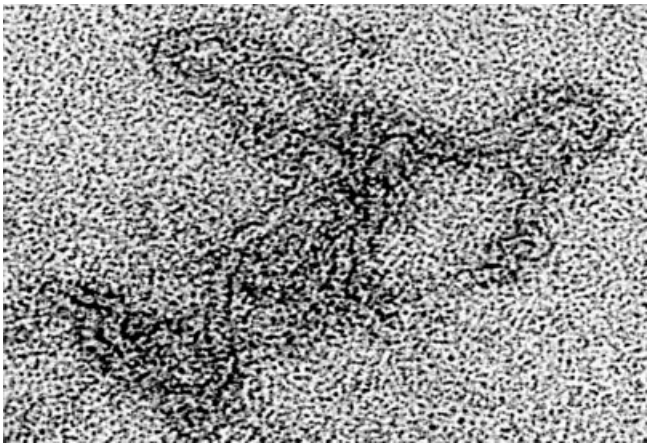
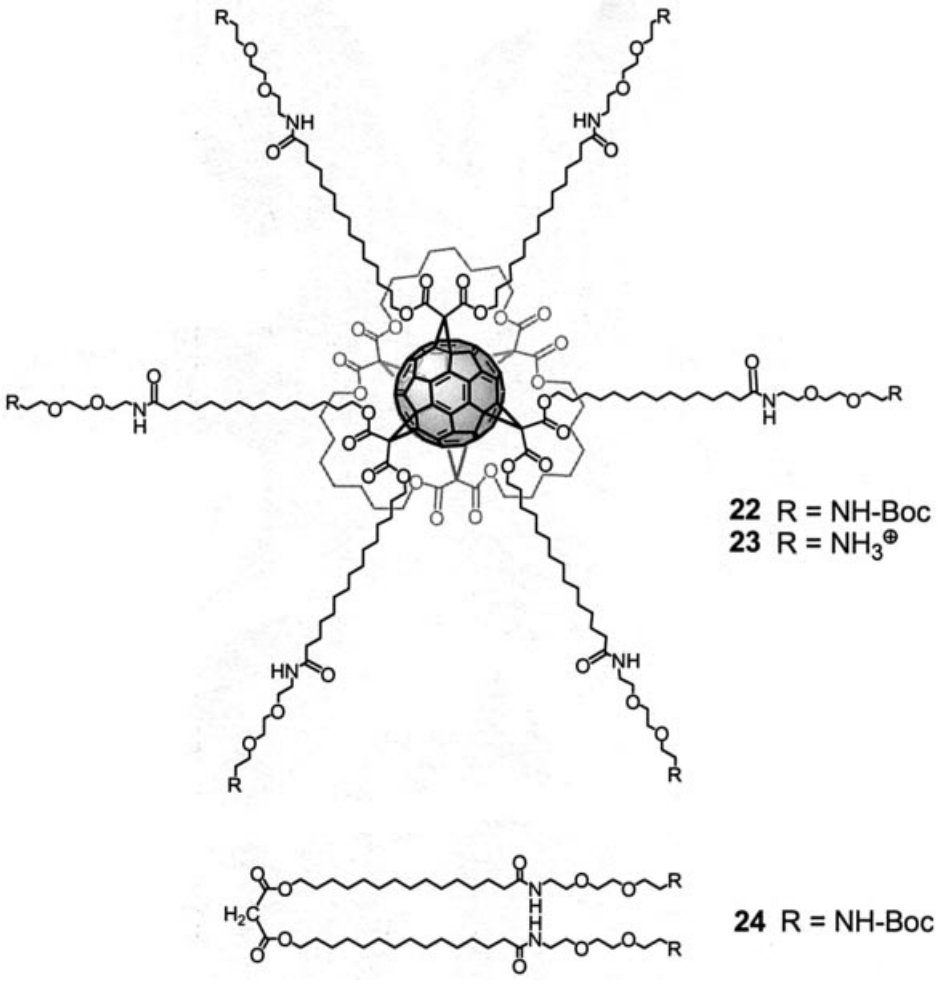
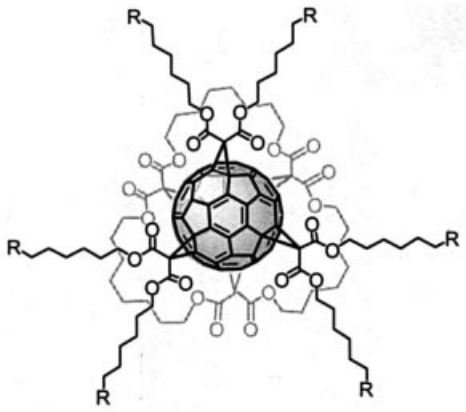


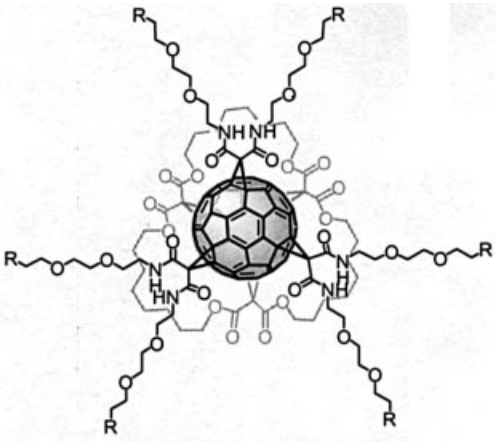
Figure 4. Transmission electron micrograph of micellar structures formed by the self-assembly of **20** in aqueous solution at pH = 9−10 (diameter ≈ 70 Å); sample droplets (5 μL) were applied to hydrophilized copper grids (400 mesh); imaging performed using a Philips CM 12 TEM at an accelerating voltage of100 kV



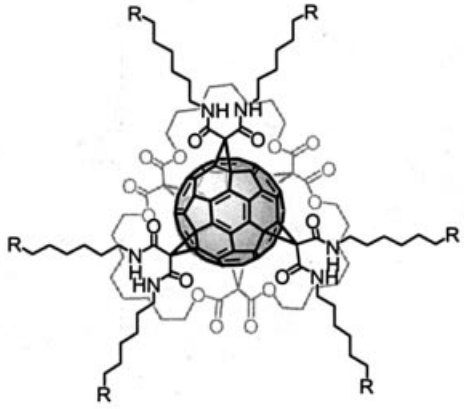
features of octahedral malonate adducts of C_{60}.[6] Microscopic studies on self-assembling properties and aggregation behavior of the synthesized compounds are currently in progress. Pulse-field gradient spin echo nuclear magnetic resonance (^{1}H-PGSE NMR) spectroscopy provides a powerful tool for determining diffusion constants *D* and hydrodynamic



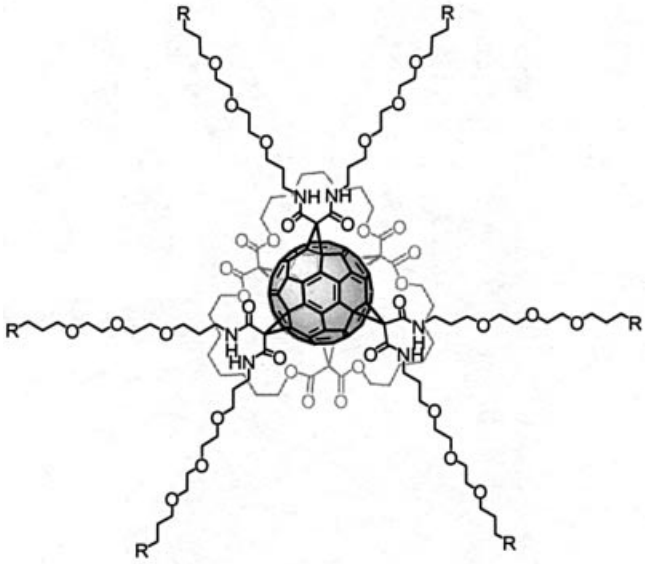
25 R = -NH-Boc
29 R = $-NH_3^{\oplus}$



27 R = -NH-Boc
31 R = $-NH_3^{\oplus}$



26 R = -NH-Boc
30 R = $-NH_3^{\oplus}$



28 R = -NH-Boc
32 R = $-NH_3^{\oplus}$

radii of particles in translational motion in solution, and as a consequence allows molecular and particle dimensions to be determined.[17] From these measurements, we obtained particles of 11.0 and 3.5 nm diameter for the hexammonium triflates **30** and **31**, respectively, in D_2O solution.

Anionic [3:3]-Mixed Hexaadduct Amphifullerene 37

Extending this concept of mixed [3:3]-hexakisadducts containing a *cyclo*-[3]-octyl malonate addend as a lipophilic moiety, we designed the amphifullerene **37** that, after deprotonation of its carboxylic termini, can be transferred readily into an anionic amphiphile. The synthesis of **37** is depicted in Scheme 4. For the introduction of the corresponding hydrophilic addends, bis[3-(*tert*-butyloxycarbonyl)propyl] malonate **38** was treated with the trisadduct **18** by means of the DMA-template mediation technique[7] to give the precursor hexakisadduct **39**. Only very small amounts of tetra- and pentakisadducts were formed as side products. The separation of these lower adducts was achieved by FC, which resulted in analytically pure **39** being isolated in 69.8% yield. The cleavage of the protecting *tert*-butyl ester groups using TFA in CH_2Cl_2 afforded the water-soluble hexaacid hexakisadduct **37** in quantitative yield. Complete structural characterization of the reaction products was carried out by ^1H and ^{13}C NMR, IR, and UV/Vis spectroscopy, elemental analysis, and mass spectrometry.

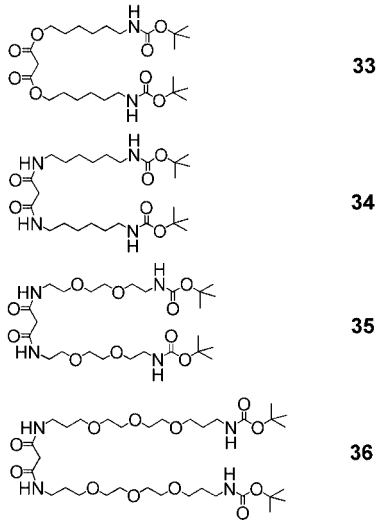
The UV/Vis spectrum of **37** was measured in phosphate-buffered H_2O at pH = 7.2 and is shown in Figure 5. The use of water as the solvent allows for the detection of all the absorption bands characteristic for the octahedral hexa-

kismalonate of C_{60},[6] including the high-energy absorption at 210 nm. This absorption is usually obscured when organic solvents are used.

In phosphate buffer at pH = 7.2, we determined the solubility of hexaacid **37** to be 2.1 mg/mL (1 mM). For comparison, under the same conditions, the solubility of dendrofullerene hexakisadduct **1**, which has a considerably higher molecular weight, is 2.5 mg/mL (0.5 mM).[18] The yellow solution of **37** at neutral pH appears opalescent, which indicates the formation of aggregates. Cryo-TEM investigations are in progress to elucidate the structure of these aggregates.

[3:3]-Amphifullerenes Having Short Peptide Sequences

The hexaacid **37** not only represents an example of a water-soluble amphifullerene whose degree of negative charge, and, therefore, its aggregation properties, can be switched by changes in pH, but it is also susceptible for further functionalization. For example, it is conceivable to couple its carboxy termini with peptides or other biomolecules. As a consequence, not only can the supramolecular behavior of the corresponding amphifullerenes be further influenced, but also additional molecular recognition phenomena, as well as a bio-compatibilization of micelles or liposomes, can be introduced. As a first example, we carried out the synthesis of the hexakis(L-alanine)-decorated [3:3]-amphifullerene **40**. For this purpose, hexaacid **37** was first treated (Scheme 5) with enantiomerically pure L-alanine *tert*-butyl ester (**41**) in the presence of DCC and *N*-hydroxysuccinimide (NHS) to afford the coupling product **42** in 62% yield after FC purification (SiO_2; CH_2Cl_2/MeOH, 97:3). The *tert*-butyl protecting groups were removed using TFA in CH_2Cl_2 and the hexakis(L-alanine) amphifullerene **40** was obtained almost quantitatively as a dark-yellow solid. Compound **40** and its *tert*-butyl-protected precursor **42** were fully characterized by IR, UV/Vis, and ^1H and ^{13}C NMR spectroscopy and by FAB mass spectrometry. Because of the chirality of the amino acid, as well as the inherent chirality of mixed [3:3]-hexakisadducts of C_{60}, the formation of mixtures of diastereoisomers is expected. As a consequence, all signals in NMR spectra should, in principle, split into at least two sets of signals, but we did not observe multiple signals in any case. This finding is probably due to the fact that the chiral centers within the polar addends are located in a fairly remote positions relative to the chiral fullerene core. In addition, it was not possible to separate the diastereoisomers using either



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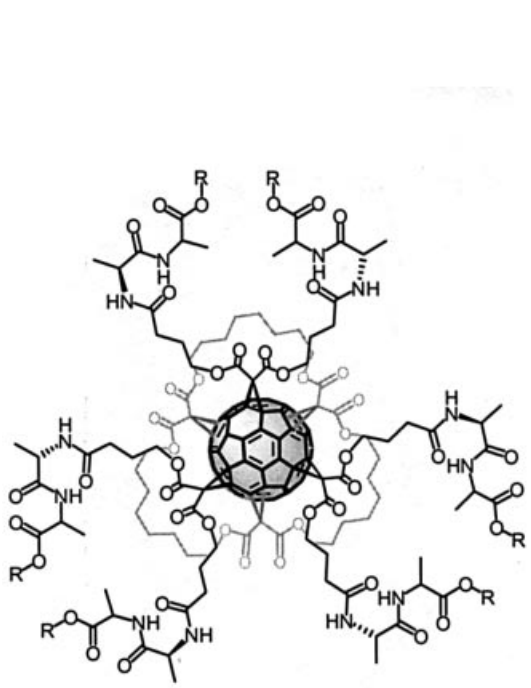
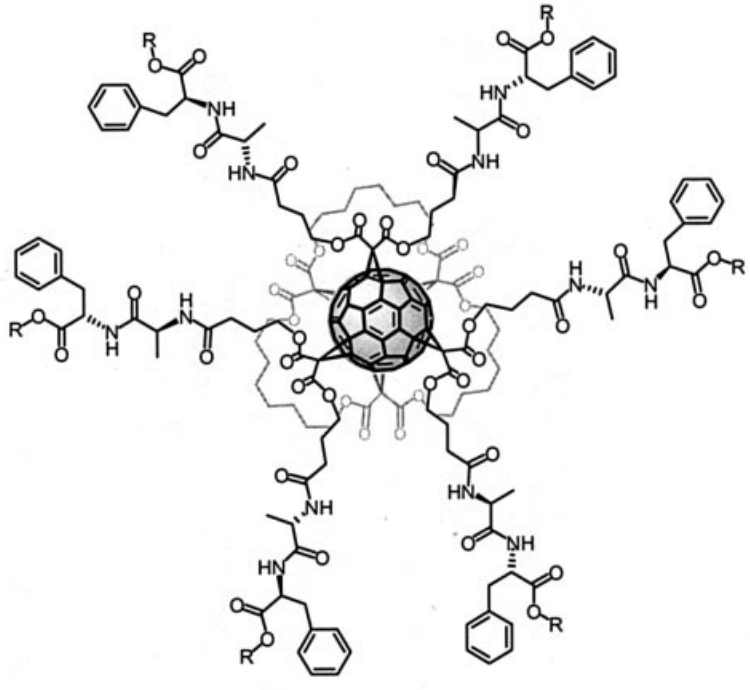
34

35

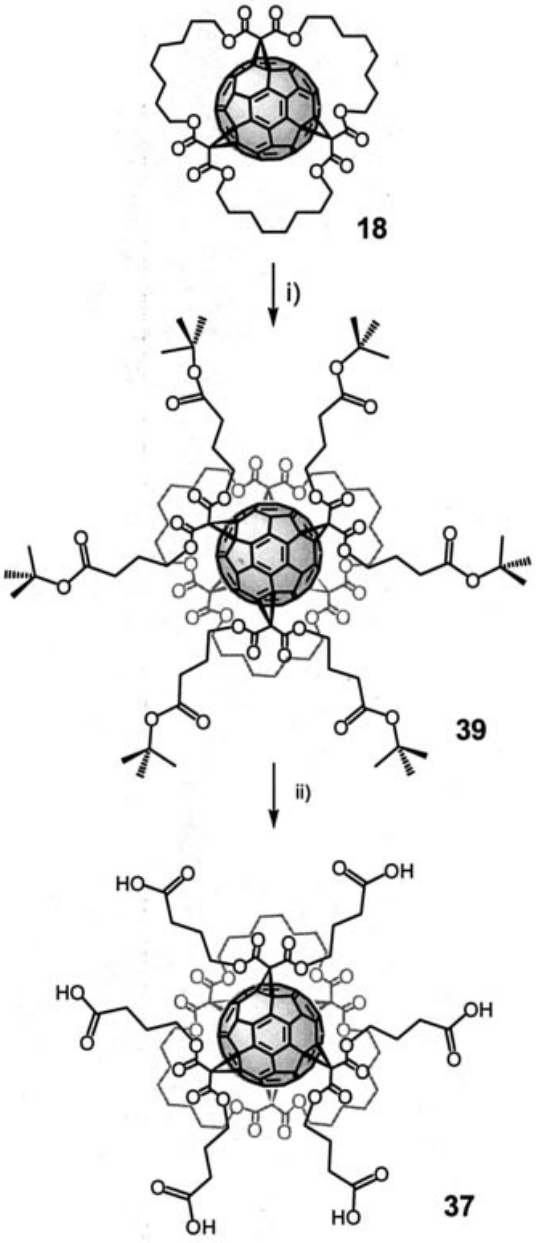
36



45 R = *t*Bu
47 R = H



46 R = *t*Bu
48 R = H



Scheme 4. Synthesis of the amphiphilic [3:3]-hexakisadduct **37** (i: DMA, malonate **38**, CBr_4, DBU; ii: TFA, CH_2Cl_2)

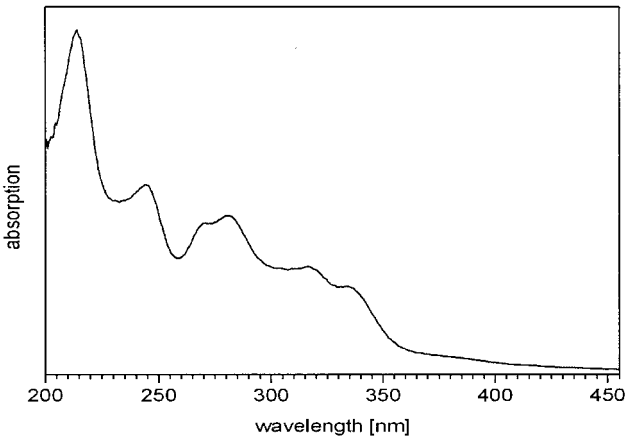
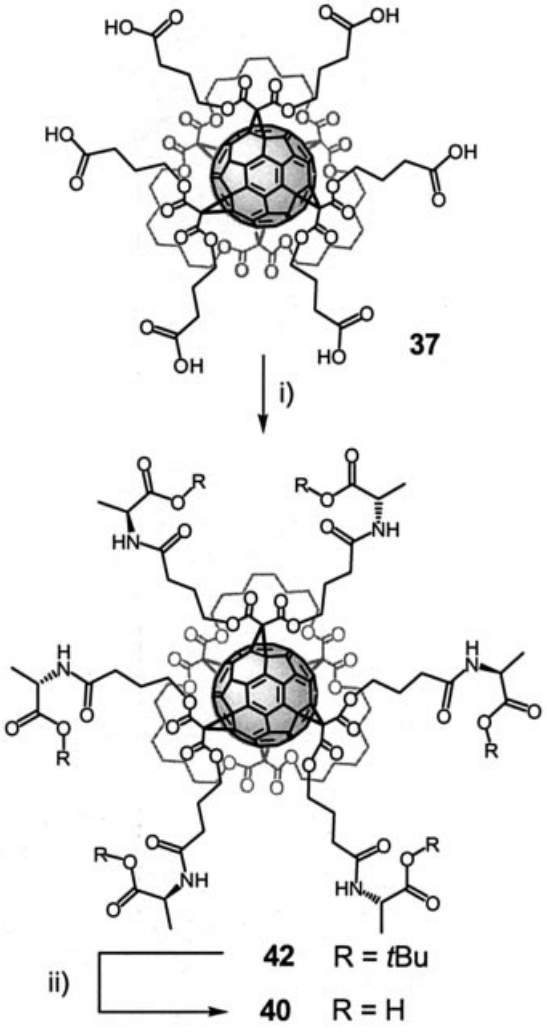


Figure 5. The UV/Vis spectrum of **34** in phosphate-buffered H_2O at pH = 7.2 (Shimadzu UV-3102 PC)



Scheme 5. Synthesis of the amphiphilic [3:3]-hexakisadduct **40** [i: DCC, NHS, L-alanine *tert*-butyl ester (**41**), THF, 14 h; ii: TFA, CH_2Cl_2]; only one of the possible diastereoisomers is represented

thin-layer chromatography (TLC) or HPLC. The deprotected amphifullerene **40** is very soluble in THF, DMSO, and water at pH = 7.2, but is completely insoluble in organic solvents such as CH_2Cl_2 and $CHCl_3$.

The corresponding coupling of **37** with *N*-(L-alanyl)-L-alanine *tert*-butyl ester (**43**) and *N*-(L-alanyl)-L-phenylalanine *tert*-butyl ester (**44**) afforded the *tert*-butyl-protected hexakis-dipeptides **45** and **46**, respectively, in 64 and 48% yield, respectively. After deprotection in TFA/CH_2Cl_2 at room temp., the C_3-symmetrical amphifullerenes **47** and **48** were obtained as mixtures of diastereoisomers, each in quantitative yield.

The characterization of the protected dipeptide hexakisadduct precursors **45** and **46**, as well as the free dipeptide hexakisadducts **47** and **48**, was performed using IR, UV, and ^1H and ^{13}C NMR spectroscopy, C,H,N-elemental analysis, and FAB mass spectrometry. The deprotected peptido-amphifullerenes **47** and **48** exhibit solubility behavior similar to that of **40**.

In a search for self-aggregation, we examined freshly prepared buffered D_2O solutions of the alanineamphifullerene **40** and the alanylphenylalanineamphifullerene **48** at pH = 7.2 and 9.0 by ^1H-PGSE NMR spectroscopy experiments; the parameters of the assembly particles are summarized in Table 1. The average diffusion coefficients (D) and particle diameters ($d = 2R_H$, the hydrodynamic radii) are based on the most distinct signals in the ^1H NMR spectra of the two amphiphiles **40** and **48**.

Table 1. Molecular dimensions of self-assembled aggregates of amphiphiles **40** and **48** in buffered D_2O solutions as determined by ^1H-PGSE NMR spectroscopy experiments

Compound	pH	D [m^2/s]	$d = 2\ R_H$ [nm]
40	7.2	1.07×10^{-10}	5.15−5.28
48	7.2	1.09×10^{-10}	4.91−5.26
40	9.0	9.47×10^{-11}	5.80−5.94
48	9.0	9.36×10^{-11}	5.44−6.44

Both amphiphilic molecules, **40** and **48**, tend to self-aggregate in neutral and basic solutions; the average diameter of the aggregates is 5 nm, with an average volume of 65 nm^3 and a surface area of 78 nm^2. It is interesting to note that the self-assemblies formed at pH = 9.0 were slightly larger than those prepared in neutral solution. This feature can be attributed to a higher degree of solvation of the multiple negatively charged carboxylic amphiphiles by surrounding water molecules.

Conclusion and Outlook

We present here the synthesis of a series of mixed amphiphilic hexakisadducts of C_{60} that have an octahedral addition pattern. The new [5:1]-hexakisadduct **3**, which features five nonpolar long-chain malonate addends and one polar addend having two biotin termini, is insoluble in water. As a consequence, it cannot be used to investigate its superstructures that form in aqueous solution, but it represents an attractive building block for a potential co-surfactant-aided assembly to mixed micelles or liposomes. The spacer carrying the biotin termini was designed in a way that it can protrude through a layer of assembled lipid molecules, such as DPPC. This feature, in principle, makes it available for targeting of micelles and liposomes by avidin-mediated binding of label molecules. Progress in this direction will be reported in due course. For the first time, we report the synthesis of amphiphilic [3:3]-hexakisadducts of C_{60}. The key for the very facile access to these aesthetically pleasing molecules is the simple synthesis of the *e*,*e*,*e*-trisadduct **18**, which can be prepared in one step from the highly regioselective addition of *cyclo*-[3]-octyl malonate **17**. The remaining three octahedral sites are available for the attachment of three ionic or neutral polar addends. For termini, we used carboxy, amino, and peptide moieties. This design allows for the introduction of a number of tuneable positive or negative charges within the polar groups by variations in pH. In some cases, we have undertaken preliminary investigations on the self-assembly processes using cryo-TEM and PGSE NMR spectroscopy. We have shown that the solubility and self-assembly properties depend on the number of ionic charges and, therefore, the value of pH. These structures provide very favorable opportunities for the controlled encapsulation and release of nonpolar guest molecules, which makes such amphiphilic fullerenes interesting candidates for drug delivery systems. Extensive investigations on the aggregation and inclusion properties of amphiphilic [3:3]-hexakisadducts of C_{60} are currently under way.

Experimental Section

General Remarks

Chemicals: C_{60} was obtained from Hoechst AG/Aventis and separated from higher fullerenes by a plug filtration process.[19,20] All analytical and reagent grade solvents were purified by distillation. Dry solvents were prepared using customary literature procedures.[21]

Thin-Layer Chromatography (TLC): Riedel−de Haën silica gel F_{254} and Merck silica gel 60 F_{254}. Detection: UV lamp, $H_3[P(Mo_3O_{10})_4]$/$Ce(SO_4)_2/H_2SO_4/H_2O$ bath, $KMnO_4/H_2O$, and iodine chamber.

Flash Chromatography (FC): ICN Silica 32−63, 60 Å; typical parameters for column diameter, loading, optimum eluent mixtures, and eluent flow rate were selected from the literature.[22]

High-Performance Liquid Chromatography (HPLC): Shimadzu Liquid Chromatograph LC-10AT equipped with an SCL-10AVP system controller, LC-8A preparative liquid chromatographs, a diode array detector, an auto injector, a refractive index detector, a UV/Vis detector, a selection valve, and a fraction collector. Analytical columns: Nucleosil 5 μm, 200 × 4 mm, Macherey−Nagel; Gromsil 100 Si, NP1, 5 μm, 200 × 4 mm; Rexchrom Buckyclutcher 10 × 250 mm, Regis; and Nucleogel GFC 500-5, Macherey−Nagel. Preparative columns: Nucleosil 5 μm, 250 × 21 mm, Macherey−Nagel; Grom-Sil 100 Si, NP1, 5 μm, 250 × 20 mm; Nucleogel GFC 500-10, Macherey−Nagel; Buckyclutcher 250 × 21 mm. The purity of the synthesis products was determined by analytical HPLC (peak integration).

NMR Spectra: JEOL JNM EX 400 and JEOL JNM GX 400 (^1H: 400 MHz; ^{13}C: 100.5 MHz), Bruker AVANCE 300 (^1H: 300 MHz; ^{13}C: 75.4 MHz), Bruker AVANCE 400 (^1H: 400 MHz; ^{13}C: 100.5 MHz). The chemical shifts are given in ppm relative to $SiMe_4$ (TMS). The resonance multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quadruplet), and m (multiplet); broad resonances as br. Pulsed-field gradient measurements (^1H-PGSE NMR) were carried out at 303 K, with an actively shielded gradient probehead ($g_{max.}$ = 1.8 T/m) and a BPP-LED pulse sequence with δ = 1 ms and Δ = 100 ms at pH = 7.2 and Δ = 150 ms at pH = 9.0.

UV/Vis Spectra: Shimadzu UV-3102 PC, UV/Vis/NIR scanning spectrophotometer; absorption maxima $\lambda_{max.}$ are given in nm.

IR Spectra: Bruker FT-IR Vector 22, KBr pellets or thin film (NaCl plates), $\tilde{\nu}$ values in cm^{-1}.

Mass Spectra: Micromass Zabspec, FAB (liquid secondary ion mass spectroscopy LSIMS) mode (3-nitrobenzyl alcohol) and ESI mode; Varian MAT 311A EI mode.

Elemental Analyses: C, H, and N we measured by combustion and gas chromatographical analysis using an EA 1110 CHNS analyzer (CE Instruments).

Transmission Electron Microscopy: Sample preparation: Droplets of the samples (5 μL) were applied to hydrophilized (glow-discharged in a BALTEC MED 020, BAL-TEC AG, Liechtenstein, for 60 s at 8 W) carbon-covered microscopical copper grids (400 mesh). The supernatant fluid was removed using a filter paper until an ultrathin layer of the sample was obtained. A droplet of contrasting material (1% uranyl acetate) was added, blotted again, and air-dried. Imaging was performed using a Philips CM 12 TEM (FEI Company, Oregon) at a 100-kV accelerating voltage under low-dose conditions at a primary magnification of 58300×. The defocus value was chosen to correspond to a first zero of the CTF at ca. 15 Å.

15-Hydroxypentadecanoic Acid (5): Pentadecanolide (**4**; 2.56 g, 10.7 mmol) was dissolved in ethanol (25 mL) at 50 °C. An aqueous 1 M NaOH solution (11.75 mL, 11.80 mmol) was added and stirred at 50 °C, until TLC control [SiO_2; CH_2Cl_2/EtOAc, 95:5; R_f(**5**) = 0.28] showed the complete hydrolysis of the lactone. The ethanol was evaporated and the remaining alkaline solution was washed with CH_2Cl_2. After neutralization with 1 M HCl, the product was dissolved in CH_2Cl_2, the aqueous layer was removed, and the solvent CH_2Cl_2 was evaporated. Drying in vacuo gave a white powder (2.64 g, 96%). ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 5.99 (br., 2 H; in [D_6]DMSO at δ = 4.34 and 11.97 ppm, respectively), 3.64 (t, ^3J = 6.6 Hz, 2 H), 2.33 (t, ^3J = 7.40 Hz, 2 H), 1.53−1.67 (m, 4 H), 1.22−1.40 (m, 20 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 178.89 (1 C), 63.12 (1 C), 34.04 (1 C), 32.82 (1 C), 29.54, 29.49, 29.43, 29.34, 29.12, 29.01 (9 C), 25.70 (1 C), 24.72 (1 C) ppm. IR (KBr): $\tilde{\nu}$ = 3455, 3305, 2918, 2850, 2616, 1712, 1472, 1406, 1294, 1269, 1248, 1226, 1204, 1186, 1059, 1021, 926, 719, 596, 494 cm^{-1}.

Monoprotected 1-*N*-Boc-1,13-diamino-4,7,10-trioxatridecane (6): Bis(3-aminopropyl)diethylene glycol (26.85 g, 26.7 mL, 122 mmol) was dissolved in 1,4-dioxane (50 mL) and a solution of Boc-anhydride (4.37 g, 23.5 mmol) in dioxane (30 mL) was added dropwise at room temperature within 5 h.[23] The mixture was stirred for additional 5 h and then the solvent was evaporated. The resulting yellowish oil was dissolved in water (50 mL) and extracted with CH_2Cl_2 (4 × 50 mL). The organic phases were pooled and washed with saturated aqueous NaCl (4 × 30 mL). The extraction procedure and the subsequent washing were repeated. The resulting organic solution was dried ($MgSO_4$), which subsequently was filtered off to give an almost colorless oil after evaporation and drying in vacuo (6.70 g, 89% rel. to $BocO_2$). TLC control (SiO_2; CH_2Cl_2/EtOH, 9:1) indicated only traces of doubly protected diamine (R_f = 0.95) and no starting material. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 5.12 (br., 1 H), 3.64−3.60 (m, 4 H), 3.60−3.55 (m, 4 H), 3.55−3.49 (m, 4 H), 3.20 (dt, $^3J_1$ = $^3J_2$ = 6.1 Hz, 2 H), 2.81 (app. dt, $^3J_1$ = 6.7, $^3J_2$ = 1.7 Hz, 2 H), 2.06 (br., 2 H), 1.78−1.69 (m, 4 H), 1.41 (s, 9 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 155.80 (1 C), 78.40 (1 C), 70.32, 70.28, 69.93, 69.90, 69.15 (6 C), 39.31 (1 C), 38.14 (1 C), 33.05 (1 C), 29.36 (1 C), 28.17 (3 C) ppm. IR (film/KBr): $\tilde{\nu}$ = 3362, 2930, 2868, 1708, 1524, 1456, 1391, 1365, 1252, 1173, 1113, 1043, 944, 865 cm^{-1}. MS (EI, 40 °C): *m*/*z* = 320 $[M]^+$, 247, 177, 164, 146, 102, 89, 74, 57, 44. $C_{15}H_{32}N_2O_5$ (320.43): calcd. C 56.23 H 10.07 N 8.74; found C 55.81 H 10.00 N 8.53.

***N*-[13-(Boc-amino)-4,7,10-trioxatridecyl]-15-hydroxypentadecanoylamide (7):** The hydroxy acid **5** (440 mg, 1.70 mmol) was dissolved in dry DMF (25 mL) and then CDI (290 mg, 1.79 mmol) was added under N_2 at room temp. The imidazolide formation was complete after several minutes. A solution of the amine **6** (545 mg, 1.70 mmol) in dry CH_2Cl_2 (5 mL) was prepared, and the imidazolide solution was added through a dry syringe/septum under nitrogen. The combined solutions were stirred for 2 h, washed with saturated aqueous NaCl solution (3 × 5 mL), and dried ($MgSO_4$). Purification by FC (SiO_2; CH_2Cl_2/EtOH, 95:5) gave **7** as a white solid (675 mg, 70%). ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.25, 4.98 (2 br., 2 H), 3.66−3.48 (m, 14 H), 3.34 (dt, 2 H), 3.20 (dt, 2 H), 2.12 (t, ^3J = 7.7 Hz, 2 H), 1.98 (br., 1 H), 1.74 (m, 4 H) 1.64−1.49 (m, 4 H), 1.41 (s, 9 H), 1.36−1.18 (m, 20 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.1 (1 C), 156.0 (1 C), 78.9 (1 C), 70.5, 70.1, 70.1, 69.5 (6 C), 62.9 (1 C), 38.4, 37.8 (2 C), 36.8 (1 C), 32.7 (1 C), 29.6, 29.5, 29.5, 29.4, 29.3, 29.3, 28.9 (9 C), 28.4 (3 C), 25.7, 25.7 (2 C) ppm. IR (film/KBr): $\tilde{\nu}$ = 3321, 3064, 2921, 2850, 1686, 1636, 1535, 1471, 1421, 1366, 1277, 1250, 1179, 1139, 1061, 997, 867, 783, 721, 632, 578 cm^{-1}. MS (FAB): *m*/*z* = 693 $[M + Cs]^+$, 583 $[M + Na]^+$, 561 $[M]^+$, 461 $[M - Boc]^+$, 298. $C_{30}H_{60}N_2O_7$ (560.81): calcd. C 64.25 H 10.78 N 5.00; found C 63.92 H 10.66 N 5.12.

Bis[29-(Boc-amino)-15-oxo-20,23,26-trioxa-16-azanonacosyl] Malonate (8): Malonic acid (104 mg, 1 mmol) and alcohol **7** (1.23 g, 2.2 mmol) were dissolved in dry CH_2Cl_2 under N_2 and the solution was cooled in an ice bath. DMAP (41.0 mg, 0.20 mmol, 10 mol%) and DCC (454 mg, 2.20 mmol) were then added. After stirring under N_2 at 0 °C for 15 min and then at room temp. for 2 h, TLC indicated complete conversion of the starting material. Dicyclohexylurea precipitated during the reaction and was filtered off. Traces of urea were subsequently removed by repeated precipitation from EtOAc. After evaporation of the solvent and purification by FC (SiO_2; CH_2Cl_2/EtOH, 94:6), a white solid was obtained (714 mg, 60%). ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.22, 4.97 (2br., 4 H), 4.11 (t, ^3J = 6.8 Hz, 4 H), 3.66−3.48 (m, 12 H), 3.34 (s, 2 H), 3.33 (dt, 4 H), 3.20 (dt, 4 H), 2.11 (t, ^3J = 7.6 Hz, 4 H), 1.74 (m, 4 H), 1.60 (m, 4 H), 1.41 (s, 18 H), 1.35−1.19 (m, 40 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 172.9 (2 C), 166.4 (2 C), 155.8 (2 C), 78.9 (2 C), 70.5, 70.5, 70.2, 70.1, 70.1, 69.5 (12 C), 65.6 (2 C), 41.7 (1 C), 38.6, 37.9 (4 C), 36.9 (2 C), 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1 (20 C), 28.5 (6 C), 25.9, 25.8 (4 C) ppm. IR (film/KBr): $\tilde{\nu}$ = 3312, 3082, 2919, 2851, 1747, 1719, 1685, 1640, 1543, 1468, 1390, 1366, 1347, 1251, 1182, 1127, 1021, 997, 867, 720, 694, 603 cm^{-1}. MS (FAB): *m*/*z* = 1322 $[M + Cs]^+$, 1212 $[M + Na]^+$, 1190 $[M]^+$, 1190, 990, 443. $C_{63}H_{120}N_4O_{16}$ (1189.64): calcd. C 63.61 H 10.17 N 4.71; found C 63.64 H 10.09 N 4.91.

1,2-[Bis(14-{[3-(2-{2-[3-(Boc-amino)propoxy]ethoxy}ethoxy)propyl]-carbamoyl}tetradecyloxycarbonyl)methano]-1,2-dihydro[60]fullerene (9): C_{60} (255 mg, 0.35 mmol) was dissolved in dry toluene (150 mL) under vigorous stirring and then CBr_4 (64.0 mg, 0.193 mmol) and malonate **8** (208 mg, 0.175 mmol) were added. DBU (29.3 mg, 0.193 mmol), dissolved in toluene (20 mL), was added dropwise at room temp. over a period of 1 h. After 2 h of additional stirring and monitoring by TLC, the reaction mixture was separated by FC

(SiO_2; toluene). The unchanged C_{60} eluted first [toluene/EtOH, 9:1; R_f(**9**) = 0.25]; **9** (137 mg, 41%) was obtained as a brown solid after drying under high vacuum [purity (HPLC) = 99%]. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.38, 4.94 (2 br., 2 H), 4.48 (t, ^3J = 6.6 Hz, 4 H), 3.66−3.49 (m, 24 H), 3.35 (dt, 4 H), 3.21 (dt, 4 H), 2.15 (t, ^3J = 7.7 Hz, 4 H), 1.88−1.70 (2m, 12 H), 1.65−1.55 (m, 4 H), 1.43 (s, 18 H), 1.38−1.16 (m, 20 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.3 (2 C), 163.6 (2 C), 156.0 (2 C), 145.3, 145.2, 145.1, 144.8, 144.6, 144.6, 144.5, 143.8, 143.0, 142.9, 142.2, 141.9, 140.9, 138.9 (58 C, C_{60} sp^2), 79.0 (2 C), 71.6 (2 C), 70.5, 70.5, 70.2, 70.1, 70.0, 69.5 (12 C), 67.5 (2 C), 52.4 (1 C), 38.6, 37.9 (4 C), 36.7 (2 C), 29.6, 29.6, 29.6, 29.4, 29.4, 29.2, 28.9, 28.6 (14 C), 28.4 (6 C), 26.0, 25.8 (4 C) ppm. IR (KBr): $\tilde{\nu}$ = 3319, 2921, 2851, 1747, 1714, 1686, 1637, 1540, 1471, 1383, 1366, 1254, 1175, 1118, 798, 526 cm^{-1}. UV−Vis (CH_2Cl_2): $\lambda_{max.}$ = 256, 320, 425 nm. MS (FAB): *m*/*z* = 1907 $[M]^+$, 1807, 1709, 1652, 720. $C_{123}H_{118}N_4O_{16}$ (1908.27): calcd. C 77.42, H 6.23, N 2.96; found C 76.97, H 6.21, N 2.66.

1,2-[Bis(14-{[3-(2-{2-[3-(Boc-amino)propoxy]ethoxy}ethoxy)propyl]-carbamoyl}tetradecyloxycarbonyl)methano]-18,36:22,23:27,45:31,32:55,60-pentakis[bis(10,12-octadecadiynyloxycarbonyl)methano]-1,2:18,36:22,23:27,45:31,32:55,60-dihydro[60]fullerene (12): Similar to the procedure for the preparation of C_{60} hexakisadducts,[6,7,14] monoadduct **9** (53.0 mg, 34 μmol, 1 equiv.) was dissolved in dry, degassed toluene (50 mL) under N_2. An excess of DMA (70.0 mg, 10 equiv.) was added to the solution, which was then stirred at ambient temperature for 2 h. The diyne malonate **11**[13] (65.0 mg, 10 equiv.) and CBr_4 (113 mg, 10 equiv.) were subsequently added. After a few minutes of stirring to allow complete dissolution to occur, DBU (102 μL, 20 equiv.), diluted in dry toluene (10 mL), was added dropwise over a period of 1 h. The reaction mixture was stirred under N_2 until TLC indicated that the reaction remained unchanged (1−3 d). The separation from DMA and side products was accomplished by FC (SiO_2; CH_2Cl_2/EtOH, 95:5). A subsequent purification by HPLC (nucleosil; CH_2Cl_2/EtOH, 96:4) gave **12** as a yellow solid (34.0 mg, 21%) [purity (HPLC) = 100%]. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.62, 4.96 (2br., 4 H), 4.23 (t, ^3J = 6.7 Hz, 24 H), 3.68−3.50 (m, 24 H), 3.37 (m, 4 H), 3.21 (m, 4 H), 2.23 (t, ^3J = 6.9 Hz, 44 H), 1.84−1.58 (m, 36 H), 1.56−1.46 (tt, 40 H), 1.43 (s, 18 H), 1.41−1.20 (m, 180 H), 0.89 (t, ^3J = 6.7 Hz, 30 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.7 (2 C), 163.8 (12 C), 156.1 (2 C), 145.7, 141.1 (48 C, C_{60} sp^2), 79.0 (2 C), 77.5, 77.4 (20 C), 70.5, 70.2, 70.1, 70.0, 69.5, 69.0 (24 C), 66.9 (12 C), 65.3, 65.2 (20 C), 45.3 (6 C), 38.9, 38.1 (4 C), 36.6 (2 C), 31.0, 29.7, 29.6, 29.5, 29.4, 29.4, 29.2, 29.0, 28.8, 28.4, 28.4, 28.0 (108 C), 25.8 (12 C), 22.1 (10 C), 19.2, 19.1 (20 C), 13.9 (10 C) ppm. IR (film/KBr): $\tilde{\nu}$ = 3416, 2929, 2856, 2258, 2153, 1746, 1652, 1520, 1466, 1365, 1264, 1218, 1123, 1082, 716, 530 cm^{-1}. UV−Vis (CH_2Cl_2): $\lambda_{max.}$ = 271, 280, 316 (sh), 333 (sh) nm. MS (FAB): *m*/*z* = 4862 $[M]^+$, 4761, 4659, 720. $C_{318}H_{408}N_4O_{36}$ (4862.65): calcd. C 78.55, H 8.46, N 1.15; found C 77.82, H 8.03, N 1.11.

1,2-[Bis(14-{[3-[2-(2-[3-(Biotinylamino)propoxy]ethoxy}ethoxy)-propyl]carbamoyl}tetradecyloxycarbonyl)methano]-18,36:22,23:27,45:31,32:55,60-pentakis[bis(10,12-octadecadiynyloxycarbonyl)-methano]-1,2:18,36:22,23:27,45:31,32:55,60-dihydro[60]fullerene (3): D-(+)-Biotin (15.6 mg, 65 μmol) was dissolved in dry DMF (2 mL) and then DCI (6.20 mg, 38.5 μmol, 6 equiv.) was added under N_2 at room temp. After several minutes, a solution of the hexakisadduct **12** (31.0 mg, 6.4 μmol, 1 equiv.) in dry DMF (40 mL) was prepared and the biotin/imidazolide reaction mixture was added under N_2 through a syringe/septum. The reaction mixture was stirred at room temp. for 2 h and subsequently washed with saturated aqueous NaCl (3 × 5 mL). Purification by FC (SiO_2; CH_2Cl_2/EtOH, 9:1) and HPLC gave **3** as a yellow wax-like solid (27.0 mg, 82%) [purity (HPLC) = 99%]. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.68, 6.61, 5.45, 5.30 (4 br., 8 H), 4.52 (m, 2 H), 4.32 (m, 2 H), 4.23 (t, ^3J = 6.6 Hz, 24 H), 3.66−3.50 (m, 24 H), 3.32 (m, 4 H), 3.15 (m, 4 H), 2.91 (dd, $^3J_1$ = 4.8, $^3J_2$ = 12.8 Hz, *exo*-H), 2.75 (d, ^3J = 12.9 Hz, *endo*-H), 2.32 (t, ^3J = 7.4 Hz), 2.24 (t, ^3J = 7.0 Hz), 2.16 (m), 1.81−1.56 (m), 1.56−1.43 (m), 1.41−1.20 (m), 0.89 (t, ^3J = 7.1 Hz) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.6 (4 C), 163.8 (12 C), 163.5 (2 C), 145.7, 141.1 (48 C, C_{60} sp^2), 77.5, 77.4 (20 C), 70.3, 69.9, 69.7, 69.6, 69.0 (24 C), 66.9 (12 C), 65.2 (20 C), 62.0 (2 C), 60.4 (2 C), 55.3 (2 C), 45.3 (6 C), 40.5 (2 C), 37.4, 36.8 (4 C), 36.1 (2 C), 33.8, 31.0 (14 C), 29.7, 29.4, 29.2, 29.0, 28.8, 28.4, 28.4, 28.3, 28.0 (98 C), 25.8, 24.7 (14 C), 22.1 (10 C), 19.2, 19.1 (20 C), 13.9 (10 C) ppm. IR (film/KBr): $\tilde{\nu}$ = 3272, 3153, 3086, 2927, 2855, 2258, 2156, 1743, 1695, 1652, 1558, 1464, 1378, 1262, 1214, 1080, 1037, 801, 761, 715, 634 cm^{-1}. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 270, 281, 317 (sh), 333 (sh) nm. $C_{328}H_{420}N_8O_{36}S_2$ (5115.01): calcd. C 77.02, H 8.28, N 2.19; found C 76.41, H 8.02, N 2.01.

***N*-Boc-Protected [5:1]-Hexakisadduct 15 and Diaminoamphifullerene [5:1]-Hexakisadduct 16:** The synthesis of the [5:0]-pentakisadduct **14** was performed according to a literature protocol.[12] **14** (32.6 mg, 21.6 μmol, 1.0 equiv.) was dissolved in dry toluene (15 mL). CBr_4 (16.0 mg, 48.2 μmol, 2.2 equiv.) and malonate **8** (56.4 mg, 48.2 μmol, 2.2 equiv.), each dissolved in toluene (50 mL), were added. DBU (10 μL, 3.1 equiv.) in toluene (1 mL) was added dropwise over a period of 1 h to the stirred solution at room temp. After additional stirring for 2 h and monitoring by TLC, the [5:1]-hexakisadduct **15** was obtained as a bright-yellow solid (36.7 mg, 63%) after purification by HPLC (nucleosil; toluene/EtOH, 92:8) [purity (HPLC) = 98%]. The cleavage of the Boc protecting groups of **15** (32.0 mg, 11.9 μmol) was achieved in TFA/CH_2Cl_2 (5 mL/5 mL) during a reaction time of 30 min. Subsequently, the solvents were evaporated and the deprotected hexakisadduct **16** was dissolved in CH_2Cl_2 and washed with saturated $NaHCO_3$. The separated organic phase was dried ($MgSO_4$) and the solvent evaporated to give diaminoamphiphile **16** [30.3 mg, 89%; purity (HPLC) = 99%].

15: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.24, 4.97 (2 br., 4 H), 4.32 (q, ^3J = 7.1 Hz, 20 H), 4.23 (t, ^3J = 6.8 Hz, 4 H), 3.66−3.50 (m, 24 H), 3.34 (dt, 4 H), 3.21 (dt, 4 H), 2.13 (t, ^3J = 7.6 Hz, 4 H), 1.80−1.54 (m, 16 H) 1.42 (s, 18 H), 1.32 (t, ^3J = 7.1 Hz, 30 H) 1.28−1.21 (m, 40 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.1 (2 C), 163.9, 163.8 (12 C), 156.0 (2 C), 145.7, 141.1 (48 C, C_{60} sp^2), 78.9 (2 C), 70.5, 70.2, 70.1, 70.0, 69.5, 69.1, 69.0 (24 C), 67.0 (2 C), 62.8 (10 C), 45.3 (6 C), 38.5, 37.8 (4 C), 36.8 (2 C), 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.2, 29.0 (24 C), 28.4 (6 C), 25.8 (4 C), 14.0 (10 C). UV−Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 272, 281, 316, 334 nm. MS (FAB): *m*/*z* = 2698 $[M]^+$, 2599 $[M - Boc]^+$, 2498 $[M - 2\ Boc]^+$, 1510, 1352, 1194, 1036, 720 $[C_{60}]^+$. $C_{158}H_{168}N_4O_{36}$ (2699.03): calcd. C 70.31, H 6.27, N 2.08; found C 69.62, H 6.22, N 2.01.

16: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.54 (br., 2 H), 4.33 (q, ^3J = 7.1 Hz, 20 H), 4.24 (t, ^3J = 6.7 Hz, 4 H), 3.67−3.51 (m, 24 H), 3.33 (dt, 4 H), 2.85 (t, ^3J = 6.6 Hz, 4 H), 2.14 (t, 4 H), 1.98 (br., 4 H), 1.82−1.52 (m, 16 H), 1.32 (t, ^3J = 7.1 Hz, 30 H) 1.28−1.20 (m, 40 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.7 (2 C), 164.3, 164.2 (12 C), 146.2, 141.5 (48 C, C_{60} sp^2), 70.9, 70.8, 70.5, 70.3, 70.1, 69.5, 69.4 (24 C), 67.4 (2 C),

63.2 (10 C), 45.7 (6 C), 40.1, 38.0 (4 C), 37.2 (2 C), 30.1, 30.0, 29.9, 29.8, 29.7, 29.4 (24 C), 28.8 (6 C), 26.3 (4 C), 14.4 (10 C) ppm.

Biotinylated [5:1]-Hexakisadduct 13: An excess of D-(+)-biotin (58.0 mg, 0.24 mmol) was activated with CDI (38.5 mg, 0.24 mmol) in dry DMF (2 mL). After stirring for 30 min, the coupling was performed in dry CH_2Cl_2 by adding the activated biotin to the solution of **16**. FC (SiO_2; CH_2Cl_2/EtOH, 85:15) and HPLC (CH_2Cl_2/EtOH, 92:8) gave **13** as a yellow solid [20.3 mg, 60%; purity (HPLC) = 99%]. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.41, 5.12, 4.87 (3 br., 8 H), 4.51 (m, 2 H), 4.32 (q, ^3J = 7.1 Hz, 22 H), 4.23 (t, ^3J = 6.8 Hz), 3.70−3.42 (m, 24 H), 3.30 (m, 4 H), 3.17 (m, 4 H), 2.92 (dd, $^3J_1$ = 4.9, $^3J_2$ = 12.9 Hz, *exo*), 2.73 (d, ^3J = 12.6 Hz, *endo*), 2.32 (t, 4 H), 2.14 (t, ^3J = 7.6 Hz, 4 H), 1.90−1.53 (m, 24 H), 1.45 (m, 4 H), 1.32 (t, ^3J = 7.1 Hz, 30 H), 1.29−1.21 (m, 40 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.5, 173.4, 163.9, 163.8, 162.8, 145.7, 141.1, 70.6, 70.3, 70.3, 70.1, 70.1, 69.8, 69.5, 69.1, 69.0, 67.0, 62.8, 61.8, 60.3, 60.0, 55.2, 45.3, 40.5, 40.1, 37.4, 36.8, 33.8, 29.7, 29.6, 29.4, 29.4, 29.2, 29.1, 28.4, 28.4, 28.2, 28.2, 25.8, 24.7, 14.0 (168 C) ppm. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 270, 281, 316, 334 nm. $C_{168}H_{180}N_8O_{38}S_2$ (2983.39): calcd. C 67.63, H 6.08, N 3.76; found C 66.94, H 6.00, N 3.55.

***N*-Boc-Protected [3:3]-Hexakisadduct 19 and Hexaaminoamphiphile 20:** *e*,*e*,*e*-Trisadduct **18** (59.0 mg, 43.5 μmol)[16,19] was dissolved in dry toluene (50 mL) and treated with an excess of DMA (54.0 mg, 260 μmol). After stirring at room temp. for 2 h, malonate **8** (310 mg, 260 μmol) and CBr_4 (87.0 mg, 260 μmol) were added subsequently and the reaction mixture was stirred for some minutes to allow complete dissolution. DBU (79.0 mg, 520 μmol, 78 μL) in dry toluene (5 mL) was added dropwise over 1 h and the solution was stirred at room temp. and under N_2 for one more day. Purification by FC [SiO_2; CH_2Cl_2/EtOH, 95:5 to 9:1; R_f(**19**) = 0.2 at 95:5] gave **19** as a yellow solid [118 mg, 55% yield; purity (HPLC) = 99%]. The cleavage of the Boc protection groups was performed in CH_2Cl_2 (5 mL) using TFA (3 mL); after washing, the clear, yellow solid **20** was obtained in almost quantitative yield.

19: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.27, 4.99 (2br., 12 H), 4.67 (m, 6 H), 4.30−4.10 (m, 15 H), 4.00 (m, 3 H), 3.67−3.50 (m, 72 H), 3.35 (dt, 12 H), 3.22 (dt, 12 H), 2.14 (t, ^3J = 7.7 Hz, 12 H), 1.84−1.43 (m, 63 H), 1.43 (s, 54 H), 1.39−1.21 (m, 120 H), 1.17 (m, 18 H), 0.82 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.1 (6 C), 163.8, 163.7, 163.6, 163.1 (12 C), 156.0 (6 C), 146.4, 145.9, 145.6, 145.6, 145.3, 144.9, 144.8, 142.0, 141.8, 141.8, 140.9, 140.8, 140.7, 140.6 (48 C, C_{60} sp^2), 78.9 (6 C), 70.5, 70.2, 70.1, 70.0, 69.5, 69.2., 69.1 (48 C), 67.0, 66.9 (12 C), 46.7, 45.6 (6 C), 38.5, 37.7 (12 C), 36.8 (6 C), 29.7, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 29.0, 29.0 (90 C), 28.4 (18 C), 25.8 (12 C) ppm. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 271, 282, 315, 334 nm. MS (FAB): *m*/*z* = 4943 [M + Na]$^+$, 4920 [M]$^+$, 4820, 4621, 4316, 4096, 720. $C_{282}H_{402}N_{12}O_{60}$ (4920.25): calcd. C 68.84, H 8.24, N 3.42; found C 68.34, H 8.07, N 3.23.

20: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 4.64 (m, 6 H), 4.32−4.07 (2m, 15 H), 4.01 (m, 3 H), 3.73−3.47 (m, 72 H), 3.31 (dt, 12 H), 3.17 (dt, 12 H), 2.55 (very br., 18 H), 2.21 (m, 12 H), 2.02 (m, 2 H), 1.84−1.44 (m, 61 H), 1.41−1.21 (m, 120 H), 1.18 (m, 18 H), 0.87 (m, 3 H) ppm. IR (KBr): $\tilde{\nu}$ = 3417, 3302, 3084, 2926, 2855, 1747, 1682, 1645, 1551, 1465, 1434, 1384, 1354, 1264, 1204, 1131, 1084, 874, 833, 800, 759, 721, 670, 528 cm^{-1}. UV/Vis (H_2O/pH = 7.2): $\lambda_{max.}$ = 214, 244, 271, 280, 316, 334 nm. MS (FAB): *m*/*z* = 4320 [M]$^+$, 3332 [M − diaminomalonate]$^+$, 2349 [M − 2 diaminomalonates]$^+$, 720 [C_{60}]$^+$.

Bis[24-(Boc-amino)-15-oxo-19,22-dioxa-16-azatetracosyl] Malonate (24): According to the procedure for the synthesis of **6**, an excess of bis(2-aminoethyl)ethylene glycol (18.0 g, 122 mmol) was mono-Boc-protected with Boc-anhydride (4.37 g) in dioxane. In a manner analogous to that for the preparation of **7**, the resulting Boc derivative was condensed with an equimolar amount of hydroxy acid **5** in the presence of CDI in DMF/CH_2Cl_2. The thus prepared amido alcohol (2.00 g, 4.09 mmol) and malonic acid (192.2 mg, 1.85 mmol) were allowed to react in the presence of DMAP (70 mg, 0.537 mmol) and DCC (0.84 g, 4.09 mmol) as described for the synthesis of **8**. After FC chromatographic purification (SiO_2; EtOAc/EtOH, 95:5) the malonate **24** was isolated in 48% yield. ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.00 (br., 2 H), 4.99 (br., 2 H), 4.09 (t, ^3J = 6.7 Hz, 4 H), 3.55 (m, 8 H), 3.51 (m, 8 H), 3.42 (dt, 4 H), 3.33 (s, 2 H), 3.29 (dt, 4 H), 2.14 (t, ^3J = 7.4 Hz, 4 H), 1.60 (m, 8 H), 1.41 (s, 18 H), 1.22 (m, 40 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.26 (2 C), 166.68 (2 C), 155.95 (2 C), 79.34 (2 C), 70.17, 69.99 (8 C), 65.65 (2 C), 41.66 (1 C), 40.29, 39.09 (4 C), 36.72 (2 C), 29.60, 29.54, 29.48, 29.37, 29.30, 29.18, 29.05, 28.43 (20 C), 28.37 (6 C), 25.75 (4 C) ppm. MS (FAB): *m*/*z* = 1069 [M + Na]$^+$, 1046 [M]$^+$, 945 [M − Boc]$^+$, 845 [M − 2 Boc]$^+$. $C_{55}H_{104}N_4O_{14}$ (1045.43): calcd. C 63.19 H 10.03 N 5.36; found C 62.92, H 9.94, N 5.27.

***N*-Boc-Protected [3:3]-Hexakisadduct 22 and Sixfold-Protonated Hexaaminoamphifullerene 23:** *e*,*e*,*e*-Trisadduct **18** (75.0 mg, 55.2 μmol) was dissolved in dry CH_2Cl_2 (25 mL) and treated with an excess of DMA (68.35 mg, 0.331 mmol). After stirring at room temp. for 2 h, the malonate **24** (346.7 mg, 0.331 mmol) and CBr_4 (111.25 mg, 0.331 mmol) were added and the reaction mixture was stirred for some minutes to allow complete dissolution. DBU (100.5 mg, 0.663 mmol, 99 μL) in dry CH_2Cl_2 (15 mL) was added dropwise over 1 h. The solution was stirred at room temp. under N_2 for one more day. Purification by FC [SiO_2; CH_2Cl_2/EtOH, 95:5 to 9:1; R_f(**22**) = 0.2 at 95:5] gave **22** as a yellow solid [95.0 mg, 55% yield; purity (HPLC) = 97.5%]. Cleavage of the Boc protection groups was performed in CH_2Cl_2 (5 mL) and TFA (3 mL) to yield a clear, yellow solid **23** almost quantitatively.

22: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.98 (br., 6 H), 5.00 (br., 6 H), 4.65 (m, 6 H), 4.22 (m, 12 H), 4.14 (m, 3 H), 3.98 (m, 3 H), 3.63−3.50 (m, 48 H), 3.43 (dt, 12 H), 3.29 (m, 12 H), 2.15 (t, ^3J = 7.6 Hz, 12 H), 2.00−1.51 (m, 39 H), 1.41 (s, 54 H), 1.35−1.21 (m, 120 H), 1.14 (m, 18 H), 0.82 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 173.27 (6 C), 163.83, 163.69, 163.64, 163.15 (12 C), 155.96 (6 C), 146.39, 145.89, 145.66, 145.60, 145.31, 144.89, 144.84, 141.97, 141.85, 141.78. 140.96, 140.81, 140.69, 140.65, (48 C, C_{60} sp^2), 79.32 (6 C), 70.22, 70.00, 69.25, 69.21, 69.11 (28 C, C_{60} sp^3), 67.03, 66.92, 66.23 (12 C), 46.66, 45.63 (6 C), 40.30, 39.10 (12 C), 36.70 (6 C), 29.96, 29.70, 29.66, 29.57, 29.50, 29.42, 29.36, 29.26, 29.17, 28.77 (78 C), 28.38 (18 C), 26.33, 25.81, 25.75, 25.60 (12 C) ppm. IR (KBr): $\tilde{\nu}$ = 3423, 2926, 2854, 1747, 1716, 1652, 1541, 1457, 1385, 1366, 1263, 1218, 1171, 1101, 804, 757, 715, 540, 528, 457 cm^{-1}. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 243, 271, 281, 316, 334 nm. MS (FAB): *m*/*z* = 4510 [M + Na]$^+$, 4487 [M]$^+$, 4388 [M − Boc]$^+$, 3885 [M − 6 Boc]$^+$. $C_{258}H_{354}N_{12}O_{54}$ (4487.62): calcd. C 69.05, H 7.95, N 3.75; found C 68.33, H 7.79, N 3.64.

23: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 8.00 (m, 6 H), 4.64 (m, 6 H), 4.28 (m, 12 H), 4.10 (m, 3 H), 4.03 (m, 3 H), 3.72−3.51 (m, 48 H), 3.30 (dt, 12 H), 3.11 (m, 12 H), 2.18 (t, ^3J = 7.5 Hz), 1.88−1.45 (m, 39 H), 1.40−1.23 (m, 120 H), 1.20 (m, 18 H), 0.89 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 176.51, 176.41 (6 C), 164.84, 164.82, 164.52, 163.95

(12 C), 147.17, 147.09, 146.76, 146.59, 146.30, 145.80, 143.51, 143.40, 143.06, 142.98, 142.56, 142.46, 142.19 (48 C, C_{60} sp^2), 71.32, 71.25, 70.84, 70.78, 70.65, 69.54 (28 C, C_{60} sp^3), 68.28, 67.87, 67.33, 66.44 (12 C), 47.71 (6 C), 40.62, 40.24, 40.12 (12 C), 37.12, 37.07 (6 C), 30.89, 30.84, 30.76, 30.71, 30.67, 30.58, 30.56, 30.41, 30.26, 30.10, 30.03, 29.71, 29.65, 29.54, 29.15 (78 C), 27.14, 27.04, 26.99, 26.91 (12 C) ppm. IR (KBr): $\tilde{\nu}$ = 3423, 2925, 2854, 1747, 1682, 1648, 1543, 1465, 1431, 1384, 1354, 1264, 1206, 1133, 836, 801, 722, 528 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 246.5, 272, 284, 321, 339.5 nm. MS (FAB): *m*/*z* = 1944 $[M]^{2+}$, 3887 $[M]^+$, 3910 $[M + Na]^+$.

Bis[(6-(Boc-amino)hexyl] Malonate (33): Malonic acid (104 mg, 1.00 mmol) was treated with *N*-Boc-protected 6-aminohexan-1-ol (477.5 mg, 2.20 mmol, 1.1 equiv.) in the presence of DMAP and DCC according to the procedure for preparing malonate **8**. **33** was isolated (167 mg, 72%) as a colorless oil. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 4.59 (br., 2 H), 4.09 (t, ^3J = 6.8 Hz, 4 H), 3.32 (s, 2 H), 3.06 (m, 4 H), 1.59 (q, ^3J = 7.0 Hz), 1.50−1.39 (m, 4 H), 1.39 (s, 18 H), 1.25−1.34 (m, 8 H) ppm. ^{13}C NMR(100.5 MHz, room temp., $CDCl_3$): δ = 166.62 (2 C), 155.95 (2 C), 78.98 (2 C), 65.40 (2 C), 41.56 (1 C), 40.38 (2 C), 33.81 (2 C), 29.89 (2 C), 28.36 (6 C), 26.30, 25.43 (4 C) ppm. MS (FAB): *m*/*z* = 503 $[M^+]$, 403 $[M^+ - Boc]$, 347 $[M^+ - Boc - tBu]$, 303 $[M^+ - 2 Boc]$. $C_{25}H_{46}N_2O_8$ (502.64): calcd. C 59.74, H 9.22, N 5.57; found C 59.71, H 8.98, N 5.54.

Bis[6-(Boc-amino)hexyl] Malonamide (34), Bis[8-(Boc-amino)-3,6-dioxaoctyl] Malonamide (35) and Bis[13-(Boc-amino)-4,7,10-trioxatridecyl] Malonamide (36): By procedures similar to that for the synthesis of **8**, condensation of malonic acid (104 mg, 1 mmol, 1.0 equiv.) with *N*-Boc-hexamethylenediamine, *N*-Boc-8-amino-3,6-dioxaoctylamine, and *N*-Boc-13-amino-4,7,10-trioxatridecylamine (each 2.20 mmol, 2.2 equiv.), respectively, in the presence of DMAP and DCC gave **34** (61%), **35** (67%), and **36** (58%).

34: ^1H NMR (300 MHz, room temp., $CDCl_3$): δ = 6.97 (br., 2 H), 4.54 (br., 2 H), 3.22 (q, ^3J = 6.9 Hz, 4 H), 3.13 (s, 2 H), 3.01 (q, ^3J = 6.8 Hz, 4 H), 1.54−1.42 (m, 8 H), 1.42 (s, 18 H), 1.36−1.27 (m, 8 H) ppm. ^{13}C NMR (75 MHz, room temp., $CDCl_3$): δ = 169.34 (2 C), 158.12 (2 C), 81.15 (2 C), 45.07, 42.26 (4 C), 41.36 (1 C), 32.01, 31.21 (4 C), 30.48 (6 C), 28.30, 28.16 (4 C) ppm. MS (FAB): *m*/*z* = 501 $[M^+]$, 401 $[M^+ - Boc]$, 345 $[M^+ - Boc - tBu]$, 301 $[M^+ - 2 Boc]$. $C_{25}H_{48}N_4O_6$ (500.67): calcd. C 59.97, H 9.66, N 11.19; found C 59.81, H 9.53, N 10.96.

35: ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 7.34 (br., 2 H), 5.26 (br., 2 H), 3.57 (m, 8 H), 3.52 (t, ^3J = 5.1 Hz, 8 H), 3.43 (m, 4 H), 3.27 (m, 4 H), 1.40 (s, 18 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 167.19 (2 C), 155.93 (2 C), 79.24 (2 C), 70.29, 70.18 (8 C), 42.76 (1 C), 40.49 (2 C), 39.41 (2 C), 28.48 (6 C) ppm. MS (FAB): *m*/*z* = 565 $[M^+]$, 465 $[M^+ - Boc]$, 365 $[M^+ - 2 Boc]$. $C_{25}H_{48}N_4O_{10}$ (564.67): calcd. C 53.18, H 8.57, N 9.92; found C 53.06, H 8.52, N 9.94.

36: ^1H NMR (300 MHz, room temp., $CDCl_3$): δ = 7.39 (br., 2 H), 5.02 (br., 2 H), 3.65−3.47 (m, 12 H), 3.33 (q, ^3J = 6.1 Hz, 4 H), 3.18 (q, ^3J = 6.1 Hz, 4 H), 3.09 (s, 2 H), 1.82−1.66 (m, 8 H), 1.40 (s, 18 H) ppm. ^{13}C NMR (75 MHz, room temp., $CDCl_3$): δ = 167.73 (2 C), 156.47 (2 C), 79.27 (2 C), 70.94, 70.91, 70.58, 70.11, 69.91 (12 C), 43.17 (1 C), 38.87 (2 C), 38.13 (2 C), 30.02 (2 C), 29.22 (2 C), 28.85 (6 C) ppm. MS (FAB): *m*/*z* = 709 $[M^+]$, 610 $[M^+ - Boc]$, 510 $[M^+ - 2 Boc]$. $C_{33}H_{64}N_4O_{12}$ (708.88): calcd. C 55.91, H 9.10, N 7.90; found C 55.75, H 8.98, N 7.78.

***N*-Boc-Protected Bis(6-aminohexyl) Malonate [3:3]-Hexakisadduct 25:** The title compound was prepared under the same reaction conditions outlined for the preparation of hexakisadduct **19**, by treating *e*,*e*,*e*-trisadduct **18** (100 mg, 73.6 μmol, 1.0 equiv.) with an excess of DMA (91.1 mg, 0.442 mmol, 6.0 equiv.) and *N*-protected aminohexyl malonate **33** (221.8 mg, 0.442 mmol, 6.0 equiv.) in the presence of CBr_4 (146.6 mg, 0.442 mmol, 6.0 equiv.), dissolved in CH_2Cl_2 (40 mL), and DBU (134.6 mg, 132.2 μL, 0.884 mmol, 12.0 equiv.) in CH_2Cl_2 (15 mL) under stirring for 2 d. After liquid chromatographic purification (CH_2Cl_2/EtOAc, 93:7), **25** was isolated [106 mg, 50%; purity (HPLC) = 98%]. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 4.74 (br., 6 H), 4.63 (m, 6 H), 4.25 (m, 12 H), 4.12 (m, 3 H), 3.98 (m, 3 H), 3.05 (m, 12 H), 1.69−1.40 (m, 39 H), 1.40 (s, 54 H), 1.31 (m, 24 H), 1.16 (m, 18 H), 0.85 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 163.81, 163.73, 163.55, 163.13 (12 C), 155.98 (6 C), 146.23, 145.74, 145.68, 145.21, 144.89, 144.85, 142.03, 141.82, 141.75, 141.64, 140.85, 140.72 (48 C, C_{60} sp^2), 78.87 (6 C), 69.22, 69.18, 69.11 (12 C), 67.00, 66.86, 66.79, 66.27 (12 C), 46.66, 45.66 (6 C), 40.46 (6 C), 29.89, 29.17, 28.78, 28.73, 28.30, 26.40, 26.34, 25.59, 25.54 (42 C), 28.40 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3422, 2930, 2857, 1746, 1716, 1634, 1517, 1458, 1385, 1366, 1385, 1366, 1263, 1218, 1170, 1080, 759, 714, 540, 528 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 245, 273 (sh), 282 (sh), 320, 336 nm. MS (FAB): *m*/*z* = 2859 $[M]^+$, 2802 $[M - tBu]^+$, 2759 $[M - Boc]^+$, 2704 $[M - Boc - tBu]^+$, 2560, $[M - 3 Boc]^+$, 2459 $[M - 4 Boc]^+$, 2359 $[M - 5 Boc]^+$, 2259 $[M - 6 Boc]^+$. $C_{168}H_{180}N_6O_{34}$ (2859.25): calcd. C 70.57, H 6.35, N 2.94; found C 69.98, H 6.33, N 2.84.

Hexaammonium Trifluoroacetate Amphifullerene 29: The cleavage of the Boc protection groups of **25** (100 mg) in CH_2Cl_2 (5 mL) and TFA (3 mL) resulted in the formation of the hexaammonium trifluoroacetate salt **29** as a clear, yellow solid in quantitative yield [purity (HPLC) = 99%]. ^1H NMR (300 MHz, room temp., CD_3OH): δ = 7.85 (br., 18 H), 4.69 (m, 6 H), 4.35 (m, 12 H), 4.14 (m, 3 H), 4.02 (m, 3 H), 2.92 (t, ^3J = 6.7 Hz, 12 H), 1.95−1.51 (m, 39 H), 1.35 (m, 24 H), 1.34−1.11 (m, 18 H), 0.83 (m, 3 H) ppm. ^{13}C NMR (75 MHz, room temp., CD_3OH): δ = 165.29, 165.23, 164.69, 164.47 (12 C), 147.71, 147.50, 147.25, 146.82, 146.76, 146.50, 146.29, 144.09, 143.91, 143.33, 143.22, 142.99, 142.84, 142.66 (48 C, C_{60} sp^2), 71.29, 71.26, 71.21, 70.99 (12 C, C_{60} sp^3), 68.87, 68.61, 67.81 (12 C), 48.25 (6 C), 41.05 (6 C), 31.20, 30.85, 30.57, 30.41, 29.85, 29.82, 28.90, 28.87, 28.01, 27.43, 27.38, 27.34, 27.00, 26.95 (42 C) ppm. IR (KBr): $\tilde{\nu}$ = 3443, 30.95, 2935, 2859, 1745, 1681, 1539, 1463, 1433, 1385, 1355, 1264, 1206, 1136, 1082, 993, 838, 801, 759, 723, 669, 540, 527 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 214.5, 245.5, 271, 282.5, 319, 337 nm. MS (FAB): *m*/*z* = 720 $[C_{60}]^+$,1131 $[M]^{2+}$, 2259 $[M]^+$, 2281 $[M + Na]^+$.

***N*-Boc-Protected Bis(6-aminohexyl) Malonamide [3:3]-Hexakisadduct 26:** By the same procedure as described for **25**, the title compound was prepared from the reaction of *e*,*e*,*e*-trisadduct **18** (100 mg, 73.6 μmol, 1.0 equiv.), DMA (91.1 mg, 0.442 mmol, 6.0 equiv.), bis[6-(Boc-amino)hexyl] malonamide (**34**; 221.3 mg, 0.442 mmol, 6 equiv.), CBr_4 (146.6 mg, 0.442 mmol, 6.0 equiv.) and DBU (134.6 mg, 132.2 μL, 0.884 mmol, 12 equiv.) in CH_2Cl_2. After chromatographic purification (toluene/EtOAc, 70:30), **26** was obtained [135 mg, 28%; purity (HPLC) = 98.5%]. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.92 (br., 3 H), 6.60 (br., 3 H), 4.92 (br., 3 H), 4.75 (br., 3 H), 4.61 (m, 6 H), 4.13 (m, 3 H), 3.99 (m, 3 H), 3.45−3.10 (m, 12 H), 3.05−3.20 (m, 12 H), 3.01 (m, 12 H), 1.70−1.40 (m, 39 H), 1.39 (s, 54 H), 1.26 (m, 24 H), 1.15 (m, 18 H), 0.84 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 163.54, 163.07 (12 C), 156.08, 155.99 (6 C), 145.51, 145.17, 144.70, 144.48, 144.14, 142.27, 142.06, 141.76, 140.96, 140.82, (48 C, C_{60} sp^2), 78.84 (6 C), 71.14, 70.97, 69.48 (12 C),

66.99, 66.38 (6 C), 52.25 (3 C), 46.86 (3 C), 40.49, 40.28 (12 C), 29.86, 29.63, 29.31, 29.18, 28.81, 26.57, 26.44, 26.35, 25.58 (42 C), 28.44, 28.42 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3418, 2931, 2857, 1747, 1632, 1523, 1548, 1392, 1366, 1261, 1223, 1172, 1138, 1106, 1075, 865, 802, 752, 710, 539, 524. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 273.5 (sh), 282.5 (sh), 320, 337 nm. MS (FAB): *m*/*z* = 2852 $[M]^+$, 2753 $[M - Boc]^+$, 2697 $[M - Boc - tBu]^+$, 2653 $[M - 2\ Boc]^+$, 2553 $[M - 3\ Boc]^+$, 2453 $[M - 4\ Boc]^+$, 2353 $[M - 5\ Boc]^+$, 2252 $[M - 6\ Boc]^+$, 720 $[C_{60}]^+$. $C_{168}H_{186}N_{12}O_{28}$ (2853.34): calcd. C 70.72, H 6.57, N 5.89; found C 70.09, H 6.34, N 5.86.

Hexaammonium Trifluoroacetate Amphiphile 30: The stable hexaammonium triflate **30** (75.1 mg, 95%) was obtained from the deprotection of **26** (100 mg) using an excess of TFA in CH_2Cl_2. ^1H NMR (400 MHz, room temp., CD_3OD): δ = 8.83 (m, 3 H),8.72 (m, 3 H), 7.82 (br., 18 H), 4.80 (m, 3 H), 4.64 (m, 3 H), 4.15 (m, 3 H), 4.01 (m, 3 H), 3.38−3.20 (m, 12 H), 2.89 (m, 12 H), 1.83−1.45 (m, 39 H) 1.36 (m, 24 H), 1.20 (m, 18 H), 0.89 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., CD_3OD): δ = 165.06, 164.83, 164.60, 164.21 (12 C), 146.84, 146.75, 146.25, 145.97, 145.85, 145.50, 144.70, 144.51, 144.25, 143.94, 143.71, 143.58, 143.28, 142, 13, 142.05 (48 C, C_{60} sp^2), 73.52, 72.88, 71.12, 71.10 (12 C), 68.35, 67.44 (6 C), 54.87 (3 C), 48.65 (3 C), 41.00, 40.94, 40.75, 40.70 (12 C), 30.66, 30.56, 30.33, 30.30, 29.87, 28.63, 28.53, 27.67, 27.57, 27.37, 27.02, 26.95 (42 C) ppm. IR (KBr): $\tilde{\nu}$ = 3424, 2935, 2859, 1744, 1678, 1541, 1460, 1385, 1275, 1204, 1179, 1135, 836, 800, 722, 539, 522 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 215, 242.5 (sh), 272 (sh), 281 (sh), 317.5, 336 nm. MS (FAB): *m*/*z* = 2253 $[M]^+$, 1440 $[C_{60}$ dimer$]^+$, 720 $[C_{60}]^+$.

***N*-Boc-Protected Bis[8-(Boc-amino)-3,6-dioxaoctyl] Malonamide [3:3]-Hexakisadduct 27:** The title compound was obtained from the reaction of the *e*,*e*,*e*-trisadduct **18** (100 mg, 73.6 μmol, 1.0 equiv.), DMA (91.1 mg, 0.442 mmol, 6.0 equiv.), bis[8-(Boc-amino)-3,6-dioxaoctyl) malonamide (**35**; 249.5 mg, 0.442 mmol, 6 equiv.), CBr_4 (146.6 mg, 0.442 mmol, 6.0 equiv.), and DBU (134.6 mg, 132.2 μL, 0.884 mmol, 12 equiv.) in CH_2Cl_2 (25 mL). After chromatographic purification [LC: CH_2Cl_2/EtOH, 95:5; HPLC: toluene/MeOH, 93:7), **27** was obtained [100 mg, 45%; purity (HPLC) = 98%]. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 7.40 (br., 6 H), 5.29 (br., 3 H), 5.17 (br., 3 H), 4.59 (m, 6 H), 4.13 (m, 3 H), 3.98 (m, 3 H), 3.51 (m, 60 H), 3.27 (m, 12 H), 1.75−1.45 (m, 15 H), 1.40 (s, 54 H), 1.20 (m, 18 H), 0.90 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 163.74, 163.13, 163.03, 162.97 (12 C), 156.07, 156.03 (6 C), 145.50, 145.34, 145.11, 144.83, 144.56, 144.35, 144.21, 141.88, 141.76, 141.00, 140.88 (48 C, C_{60} sp^2), 79.08 (6 C), 71.16, 70.72 (6 C), 70.33, 70.16, 70.13, 69.47, 69.44, (30 C), 66.96, 66.48 (6 C), 51.89 (3 C), 46.79 (3 C), 40.29 (12 C), 29.27, 29.06, 28.80, 28.59, 26.44, 25.61 (12 C), 28.44 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3420, 2926, 2857, 1746, 1694, 1521, 1456, 1385, 1367, 1258, 1172, 1105, 710, 524 cm^{-1}. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 243.5, 273 (sh), 284 (sh), 320.5, 336.5 nm. MS (FAB): *m*/*z* = 3068 $[M^+ + Na]$, 2946 $[M^+ - Boc]$, 2889 $[M - Boc - tBu]^+$, 2845 $[M^+ - 2\ Boc]$, 2745 $[M^+ - 3\ Boc]$, 2645 $[M^+ - 4\ Boc]$, 2545 $[M^+ - 5\ Boc]$, 2445 $[M^+ - 6\ Boc]$. $C_{168}H_{186}N_{12}O_{42}$ (3045.33): calcd. C 66.26, H 6.16, N 5.52; found C 65.65, H 6.02, N 5.43.

Hexaammonium Trifluoroacetate Amphiphile 31: The hexaammonium trifluoroacetate **31** was obtained (76.25 mg, 95% yield) from the deprotection of **27** (100 mg) using an excess of TFA in CH_2Cl_2. ^1H NMR (400 MHz, room temp., CD_3OD): δ = 4.78 (m, 3 H), 4.60 (m, 3 H), 4.14 (m, 3 H), 3.99 (m, 3 H), 3.86 (m), 3.73−3.40 (m, 60 H), 3.15 (m, 12 H), 1.80−1.20 (m, 33 H),), 0.90 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., CD_3OD): δ = 165.03, 164.82, 164.56, 164.01 (12 C), 146.81, 146.40, 145.92, 145.78, 145.61, 145.55, 145.02, 144.17, 143.97, 143.85, 143.61, 143.49, 143.28, 142.09, 142.02 (48 C, C_{60} sp^2), 73.15, 72.69 (6 C), 71.50, 71.45, 71.37, 71.00, 70.66, 70.31 (30 C), 68.25, 67.90 (6 C), 54.37 (3 C), 44.58 (3 C), 41.18, 40.65 (12C), 30.65, 30.54, 30.24, 29.81, 27.67, 26.93 (12 C) ppm. IR (KBr): $\tilde{\nu}$ = 3442, 2927, 2857, 1742, 1682, 1541, 1458, 1432, 1385, 1275, 1206, 1180, 1132, 837, 802, 723, 539, 522 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 214, 244 (sh), 272 (sh), 283 (sh), 319, 335.5 nm. MS (FAB): *m*/*z* = 2467 $[M + Na]^+$, 2445 $[M]^+$, 1440, 720 $[C_{60}]^+$.

***N*-Boc-Protected Bis[13-(Boc-amino)-4,7,10-trioxatridecyl] Malonamide [3:3]-Hexakisadduct 28:** A mixture of *e*,*e*,*e*-trisadduct **18** (100 mg, 73.6 μmol, 1.0 equiv.), DMA (91.1 mg, 0.442 mmol, 6.0 equiv.), bis[13-(Boc-amino)-4,7,10-trioxatridecyl] malonamide (**36**; 313.4 mg, 0.442 mmol, 6 equiv.), CBr_4 (146.6 mg, 0.442 mmol, 6.0 equiv.), and DBU (134.6 mg, 132.2 μL, 0.884 mmol, 12 equiv.) was stirred for 3 d; after chromatographic purification (LC: EtOAc/EtOH, 92:8; HPLC: toluene/MeOH, 91:9), **28** was obtained [121.9 mg, 49%; purity (HPLC) = 98.5%]. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 7.50−6.90 (br., 6 H), 5.00 (m, 6 H), 4.59 (m, 6 H), 4.10 (m, 3 H), 3.97 (m, 3 H), 3.70−3.35 (m, 84 H), 3.17 (m, 12 H), 1.80−1.40 (m, 39 H), 1.40 (s, 54 H), 1.17 (m, 18 H), 0.85 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 164.45, 163.66, 163.03, 162.92 (12 C), 156.02 (6 C), 145.49, 145.31, 145.07, 144.80, 144.66, 144.58, 144.38, 144.14, 142.26, 141.73, 141.00, 140.81 (48 C, C_{60} sp^2), 78.81 (12 C), 71.37, 71.15 (6 C), 70.86, 70.47, 70.35, 70.25, 70.17, 69.76, 69.49, 69.01, 68.75 (42 C), 66.81, 66.27 (6 C), 52.33 (3 C), 46.78 (3 C), 39.21, 38.49, 38.23, 38.02 (12 C), 29.61, 29.21, 20.00, 28.79, 28.73, 26.42, 25.54 (30 C), 28.44 (6 C) ppm. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 270.5, 281, 318, 336 nm. MS (FAB): *m*/*z* = 3381 $[M]^+$, 3323 $[M - tBu]^+$, 3277 $[M - Boc]^+$, 3177 $[M - 2\ Boc]^+$, 3077 $[M - 3\ Boc]^+$, 2977 $[M - 4\ Boc]^+$, 2877 $[M - 5\ Boc]^+$. $C_{192}H_{234}N_{12}O_{48}$ (3477.96): calcd. C 66.30, H 6.78, N 4.83; found C 65.67, H 6.64, N 4.85.

Hexaammonium Trifluroacetate Amphiphile 32: The trifluoroacetate **32** was obtained (85.0 mg, 94% yield) by deprotection of **28** (100 mg) using an excess of TFA in CH_2Cl_2. ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 9.18 (m, 3 H), 9.07 (m, 3 H), 7.79 (m, 18 H), 4.55 (m, 6 H), 4.15 (m, 3 H), 3.97 (m, 3 H), 3.70−3.25 (m, 82 H), 3.03 (m, 12 H), 1.97−1.47 (m, 39 H), 1.20 (m, 18 H), 0.88 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 163.96, 163.90, 163.84, 163.06 (12 C), 145.47, 145.28, 144.91, 144.69, 144.47, 144.26, 144.03, 143.41, 142.90, 142.60, 142.50, 142.43, 142.16, 141.64, 140.94, 140.88 (48 C, C_{60} sp^2), 71.69, 71.55 (6 C), 70.31, 70.24, 70.02, 69.90, 69.80, 69.66, 69.55, 69.46, 69.41, 68.35, 68.13, 67.96 (42 C), 67.00, 66.56 (8 C), 53.21 (3 C), 46.92 (3 C), 39.90, 39.74 (6 C), 37.21, 37.15 (6 C), 29.67, 29.28, 29.24, 28.91, 28.79, 28.43, 26.31, 26.10, 25.69 (30 C) ppm. IR (KBr): $\tilde{\nu}$ = 3442, 2926, 1741, 1682, 1558, 1541, 1523, 1458, 1434, 1385, 1275, 1206, 1179, 1131, 837, 802, 723, 538, 522 cm^{-1}. UV/Vis (H_2O, pH = 7.2): $\lambda_{max.}$ = 214.5, 245.5, 271, 282.5, 319, 337 nm. MS (FAB): *m*/*z* = 2878 $[M^+]$, 2371, 1440, 720 $[C_{60}^+]$.

***tert*-Butyl Ester [3:3]-Hexakisadduct 39 and [3:3]-Hexakisadduct Amphiphile 37:** Trisadduct **18** (49.90 mg, 0.037 mmol, 1.0 equiv.) was treated in degassed dry toluene (20 mL) with DMA (45.60 mg, 6 equiv.), malonate **38** (74.70 mg, 6 equiv.), CBr_4 (73.20 mg, 6 equiv.) and DBU (66 ςL, 12 equiv., diluted in 7 mL of toluene). After purification by FC {SiO_2; toluene/ethyl acetate, 9:1 [R_f(**39**) = 0.15] to 8:2 [R_f(**39**) = 0.45]}, a bright yellow solid (**39**) was obtained and dried in high vacuum (64.70 mg, 69.8%). The cleavage of the *tert*-butyl esters was carried out in toluene (15 mL) with TFA (3 mL) at room temp. After stirring for 6 h, the solvent was evapo-

rated and the completeness of the deprotection confirmed by ^1H NMR (quantitative yield of **37**).

39: ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 4.67 (m, 6 H), 4.40−4.20 (m, 12 H), 4.15 (m, 3 H), 4.00 (m, 3 H), 2.31 (m, 12 H), 1.98 (m, 12 H), 1.78 (m, 3 H), 1.60 (m, 6 H), 1.49 (m, 6 H), 1.44 (s, 54 H), 1.16 (m, 18 H), 0.81 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 171.70 (6 C), 163.62, 163.61, 163.43, 163.13 (12 C), 146.51, 145.93, 145.75, 145.71, 145.32, 144.94, 144.91, 142.01, 141.90, 141.64, 141.61, 141.02, 140.80, 140.60, 140.52 (48 C, C_{60}, sp^2), 80.61 (6 C), 69.21, 69.12 (12 C), 66.90, 66.21 (6 C), 66.03, 65.92 (6 C), 46.71, 45.33 (6 C), 31.73 (6 C), 29.34, 29.22, 28.82, 28.20 (12 C), 28.13 (18 C), 26.33, 25.62 (6 C), 23.91 (6 C) ppm. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 245, 270, 281, 316, 334 nm. MS (FAB): *m/z* = 2516 $[M]^+$, 2460 $[M - t\text{Bu}]^+$, 2181, 2077, 720 $[C60]^+$. C150H138O36 (2516.60): calcd. C 71.58 H 5.53; found C 70.72 H 5.21.

37: ^1H NMR (400 MHz, room temp., $[D_8]$THF): δ = 10.92 (br., 12 H), 4.70 (m, 3 H), 4.63 (m, 3 H), 4.38−4.22 (m, 12 H), 4.07 (m, 3 H), 3.96 (m, 3 H), 2.35 (m, 12 H), 1.96 (m, 12 H), 1.78 (m, 6 H), 1.53 (m, 9 H), 1.40 (m, 3 H), 1.21 (m, 18 H), 0.85 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $[D_8]$THF): δ = 174.01, 173.92 (6 C), 164.02, 163.91, 163.82, 163.33 (12 C), 147.31, 146.80, 146.61, 146.40, 145.94, 145.91, 145.71, 143.02, 142.73, 142.11, 141.90, 141.81, 141.64 (48 C, C_{60}, sp^2), 70.44, 70.34, 70.23 (12 C), 66.81, 66.71, 66.38 (12 C), 47.89, 46.69 (6 C), 30.64, 30.55, 30.44, 30.24, 29.78, 29.73, 27.52, 26.61, 26.42, 25.79, 25.65, 25.61, 25.46, 25.41, 24.84, 24.79 (24 C), 23.60 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3418, 2931, 2857, 1743, 1629, 1572, 1459, 1405, 1355, 1260, 1219, 1178, 1117, 1075, 997, 955, 802, 713, 540, 525 cm^{-1}. UV/Vis (H_2O): $\lambda_{max.}$ = 214, 246, 272, 281, 316, 334 nm. MS (FAB): *m/z* = 2319 $[M + 6\ Na]^+$, 2250 $[M + 3\ Na]^+$, 2202 $[M + Na]^+$, 2179 $[M]^+$, 2076, 720 $[C_{60}]^+$.

L-Alanine *tert*-Butyl Ester [3+3]-Hexakisadduct 42 and L-Alanine [3+3]-Hexakisadduct 40: Hexaacid **37** (351.9 mg, 0.161 mmol, 1 equiv.), L-alanine *tert*-butyl ester (**41**) hydrochloride (361.3 mg, 1.99 mmol, 12 equiv.), Et_3N (270 μL), and NHS (223.2 mg, 12 equiv.) were dissolved in a mixture of dry THF (50 mL) and dry DMF (20 mL) and the resulting solution was cooled to 0 °C. DCC (371.8 mg, 12 equiv.) in dry THF (15 mL) was slowly added and the mixture was stirred at room temp. for 3 d. The dicyclohexylurea that formed was filtered off and the filtrate was concentrated in vacuo. The remaining residue was dissolved in EtOAc (100 mL) and washed with 10% aqueous citric acid, 0.5 N aqueous $KHCO_3$, and brine. The organic layer was dried ($MgSO_4$) and the EtOAc was removed in vacuo. Flash chromatography (SiO_2; CH_2Cl_2/MeOH, 97:3) afforded **42** as a dark-yellow solid [307.5 mg, 73%; purity (HPLC) = 99%]. The cleavage of the *tert*-butyl groups of the [3+3]-hexakisadduct **42** (100 mg, 0.034 mmol) was achieved using TFA (1.5 mL) in CH_2Cl_2 (20 mL). The mixture was stirred at room temp. for 8 h before the solvent and TFA were removed in vacuo; the alanino amphifullerene **40** (88.5 mg, 0.034 mmol) was obtained as a yellow solid in quantitative yield.

42: ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 6.68 (m, 6 H), 4.64 (m, 6 H), 4.44 (m, 6 H), 4.33 (m, 12 H), 4.10 (m, 3 H), 3.96 (m, 3 H), 2.33 (m, 12 H), 2.03 (m, 12 H), 1.73 (m, 3 H), 1.57 (m, 6 H), 1.50 (m, 6 H), 1.42 (s, 54 H), 1.33 (d, ^2J = 7.08 Hz, 18 H), 1.13 (m, 18 H), 0.78 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 172.10 (6 C), 171.05 (6 C), 163.48, 163.26, 162.86 (12 C), 146.07, 146.0, 145.74, 145.67, 145.57, 145.52, 145.47, 144.94, 144.70, 141.96, 141.75, 141.37, 141.28, 141.22, 140.82, 140.70, 140.56, 140.51 (48 C, C_{60} sp^2), 81.64 (6 C), 69.20, 69.16 (12 C), 67.05, 66.32 (12 C), 48.65 (6 C), 46.86, 46.81, 45.51 (6 C), 32.16 (6 C), 29.36, 29.27, 28.89 (12 C), 28.04 (18 C), 26.46, 25.68 (6 C), 24.32, 24.22, 24.15 (6 C), 18.42 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3406, 2976, 2933, 2857, 1743, 1677, 1655, 1526, 1458, 1384, 1369, 1263, 1218, 1153, 1079, 1017, 994, 847, 759, 714, 540, 528 cm^{-1}. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 242, 271, 282, 317, 335 nm. MS (FAB): *m/z* = 2942 $[M]^+$, 2886 $[M - t\text{Bu}]^+$, 2607 $[M - 6\ t\text{Bu}]^+$, 720 $[C_{60}]^+$. $C_{168}H_{168}N_6O_{42}$ (2943.15): calcd. C 68.56, H 5.75, N 2.86; found C 68.12, H 5.79, N 2.79.

40: ^1H NMR (300 MHz, room temp., $[D_8]$THF): δ = 8.41 (s br., 6 H), 7.53 (m, 6 H), 4.69 (m, 6 H), 4.66 (m, 6 H), 4.45 (t, ^3J = 6.05 Hz, 6 H), 4.30 (m, 12 H), 4.05 (m, 3 H), 3.93 (m, 3 H), 2.29 (t, ^3J = 6.10 Hz, 12 H), 1.99 (m, 12 H), 1.76 (m, 3 H), 1.54 (m, 6 H), 1.51 (m, 6 H), 1.32 (d, ^2J = 7.15 Hz, 18 H), 1.19 (m, 18 H), 0.80 (m, 3 H) ppm. ^{13}C NMR (75 MHz, room temp., $[D_8]$THF): δ = 174.58 (6 C), 172.26, 171.98 (6 C), 164.08, 164.00, 163.76, 163.76, 163.31 (12 C), 147.24, 146.85, 146.71, 146.57, 146.28, 145.88, 145.80, 145.70, 145.68, 143.08, 142.99, 142.65, 142.59, 141.97, 141.86, 141.64 (48 C, C_{60} sp^2), 70.36, 70.27 (12 C), 68.21, 66.36 (12 C), 48.51, 48.45 (6 C), 47.94, 46.77 (6 C), 32.41 (6 C), 30.44, 30.21, 29.75 (12 C), 27.48, 26.51 (6 C), 18.23, 18.18 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3382, 3074, 2934, 2857, 2556, 1745, 1635, 1541, 1458, 1384, 1354, 1263, 1217, 1167, 1079, 1042, 1020, 898, 806, 754, 713, 667, 538, 527 cm^{-1}. MS (FAB): *m/z* = 2607 $[M + H]^+$, 2562 $[M - CO_2]^+$, 2477, 720 $[C_{60}]^+$. UV/Vis (H_2O): $\lambda_{max.}$ = 212.5, 244, 271.5, 280, 316, 337 nm.

***N*-(L-Alanyl)-L-alanine *tert*-Butyl Ester [3+3]-Hexakisadduct 45 and *N*-(L-Alanyl)-L-alanine [3+3]-Hexakisadduct 47:** The coupling of *N*-(L-alanyl)-L-alanine *tert*-butyl ester (346.2 mg, 12 equiv.) with the hexaacid **37** (273.9 mg, 1 equiv.) was carried out according to the procedure for the synthesis of **42** by activation with DCC (12 equiv.) and NHS (12 equiv.). Purification by flash chromatography (SiO_2; CH_2Cl_2/MeOH, 96:4) gave the [3+3]-hexakisadduct **45** as a dark-yellow solid [326.7 mg, 77%; purity (HPLC) = 99%]. The cleavage of the *tert*-butyl groups of the [3+3]-hexakisadduct **45** (175.1 mg, 0.052 mmol) was achieved in CH_2Cl_2 (20 mL) using TFA (1.5 mL). The mixture was stirred overnight at room temp. before the solvent and TFA were evaporated in vacuo; the peptido amphifullerene hexakisadduct **47** was obtained (157.6 mg, 0.052 mmol) as a yellow solid in quantitative yield.

45: ^1H NMR (400 MHz, room temp., $CDCl_3$): δ = 7.52 (br. d, 3 H), 7.33 (br. d, 3 H), 4.67 (m, 12 H), 4.36 (m, 12 H), 4.13 (m, 3 H), 3.98 (m, 3 H), 2.66, 2.35 (m, 12 H), 2.04 (m, 12 H), 1.77 (m, 3 H), 1.52 (m, 12 H), 1.45 (s, 54 H), 1.39 (d, ^2J = 7.15 Hz, 18 H), 1.36 (d, ^2J = 7.05 Hz, 18 H), 1.15 (m, 18 H), 0.81 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 172.38, 172.27 (12 C), 171.95, 171.66 (6 C), 163.75, 163.51, 163.48, 163.12 (12 C), 146.32, 145.78, 145.72, 145.19, 145.10, 144.92, 142.13, 141.90, 141.58, 141.39, 140.95, 140.86, 140.74, 140.57 (48 C, C_{60} sp^2), 81.73 (6 C), 69.24, 69.15 (12 C), 67.05, 66.31 (12 C), 48.80, 48.54 (12 C), 46.77, 45.31 (6 C), 31.76 (6 C), 29.18, 28.81 (12 C), 27.94 (18 C), 26.35, 25.60 (6 C), 24.13, 23.96, 23.87 (6 C), 18.29, 18.15, 18.09, 18.04 (12 C) ppm. IR (KBr): $\tilde{\nu}$ = 3388, 3315, 3071, 2977, 2934, 2858, 1744, 1655, 1527, 1456, 1383, 1369, 1263, 1218, 1157, 1079, 1017, 993, 847, 759, 714, 540, 528 cm^{-1}. MS (FAB): *m/z* = 3370 $[M]^+$, 3314 $[M - t\text{Bu}]^+$, 3113, 720 $[C_{60}]^+$. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 246, 271.5, 281.5, 317.5, 336.5 nm. $C_{186}H_{198}N_{12}O_{48}$ (3369.61): calcd. C 66.30, H 5.92, N 5.92; found C 65.77, H 5.74, N 5.85.

47: ^1H NMR (300 MHz, room temp., $[D_6]$DMSO): δ = 8.12 (d, ^2J = 7.69 Hz, 6 H), 8.03 (d, ^2J = 7.68 Hz, 6 H), 4.75 (m, 6 H),

4.64 (m, 6 H), 4.30 (m, 12 H), 4.18 (m, 6 H), 3.99 (m, 6 H), 2.19 (m, 12 H), 1.82 (m, 6 H), 1.52 (m, 9 H), 1.25 (d, ^2J = 7.04 Hz, 18 H), 1.17 (d, ^2J = 7.06 Hz, 18 H), 1.06 (m, 18 H), 0.50 (m, 3 H) ppm. ^{13}C NMR (75 MHz, room temp., [D$_6$]DMSO): δ = 173.95 (6 C), 172.10 (6 C), 170.79, 170.66 (6 C), 162.63, 162.13, 161.79 (12 C), 145.74, 145.67, 144.88, 144.43, 144.01, 143.96, 143.80, 141.66, 141.52, 141.46, 141.27, 140.47, 140.32, 140.13 (48 C, C_{60} sp^2), 69.04, 68.85 (12 C), 66.72, 66.65, 65.76 (12 C), 47.64, 47.29 (12 C), 46.88, 45.57 (6 C), 30.97 (6 C), 29.23, 28.59, 28.12 (12 C), 26.08 (6 C), 24.84, 24.03 (6 C), 18.10, 16.99 (12 C) ppm. IR (KBr): $\tilde{\nu}$ = 3306, 3064, 3030, 2934, 2858, 2548, 1744, 1649, 1532, 1455, 1384, 1352, 1264, 1217, 1170, 1079, 1019, 992, 901, 810, 755, 738, 713, 701, 669, 539, 527 cm^{-1}. UV/Vis (H_2O): $\lambda_{max.}$ = 212, 243.5, 272, 281, 318, 336 nm. MS (FAB): *m*/*z* = 3512 [M + Na]$^+$, 3489 [M + H]$^+$, 3213, 720 [C_{60}]$^+$.

***N*-(L-Alanyl)-L-phenylalanine *tert*-Butyl Ester [3+3]-Hexakisadduct 46 and *N*-(L-Alanyl)-L-phenylalanine [3+3]-Hexakisadduct 48:** The coupling of *N*-(L-alanyl)-L-phenylalanine *tert*-butyl ester (459.3 mg, 12 equiv.) with the [3+3]-hexakisadduct hexaacid **37** (285.3 mg, 1 equiv.) was carried out according to the procedure described for the [3+3]-hexakisadduct **53** by activation with DCC (12 equiv.) and NHS (12 equiv.). Purification by flash chromatography (SiO_2; CH_2Cl_2/MeOH, 97:3 to 96:4) gave the *tert*-butyl-protected [3+3]-hexakisadduct **46** as a dark-yellow solid [382.6 mg, 0.100 mmol, 76.3%; purity (HPLC) = 100%]. The *tert*-butyl protecting groups of **46** (172.1 mg, 0.045 mmol) were cleaved off with THF/CH_2Cl_2 as described in the cases above and the [3+3]-hexakisadduct peptido derivative **48** was obtained as a yellow solid in quantitative yield (157.0 mg, 0.045 mmol).

46: ^{1}H NMR (400 MHz, room temp., $CDCl_3$): δ = 7.21 (m, 18 H), 7.14 (m, 18 H), 7.06 (br. d, 6 H), 4.68 (m, 6 H), 4.60 (m, 12 H), 4.28 (m, 12 H), 4.12 (m, 3 H), 3.96 (m, 3 H), 3.03 (m, 12 H), 2.28 (m, 12 H), 2.00 (m, 12 H), 1.77 (m, 6 H), 1.53 (m, 9 H), 1.35 (d, ^2J = 7.01 Hz, 18 H), 1.15 (m, 18 H), 0.78 (m, 3 H) ppm. ^{13}C NMR (100.5 MHz, room temp., $CDCl_3$): δ = 172.28, 172.20 (12 C), 171.75, 171.61, 171.54 (6 C), 163.68, 163.53, 163.47, 163.44, 163.08 (12 C), 146.27, 146.25, 145.81, 145.79, 145.74, 145.69, 145.16, 145.12, 144.89, 144.86, 142.12, 141.88, 141.86, 141.58, 141.52, 141.39, 141.35, 140.94, 140.92, 140.87, 140.75, 140.63, 140.61 (48 C, C_{60} sp^2), 136.12 (6 C), 129.38 (12 C), 128.29 (12 C), 126.88 (6 C), 82.10 (6 C), 69.25, 69.17 (12 C), 67.05, 66.39, 66.30 (12 C), 48.59 (12 C), 46.77, 45.36 (6 C), 37.93, 37.90 (6 C), 31.79, 31.76 (6 C), 29.23, 29.16, 28.78, 27.89 (12 C), 26.33, 25.57 (6 C), 24.06, 23.95, 23.87 (6 C), 18.16, 17.96 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3388, 3309, 3062, 3029, 2976, 2933, 2857, 1744, 1652, 1524, 1455, 1369, 1263, 1219, 1156, 1079, 1044, 1017, 992, 844, 738, 714, 702, 539, 528 cm^{-1}. UV/Vis (CH_2Cl_2): $\lambda_{max.}$ = 244, 270.5, 281.5, 318, 337.5 nm. MS (FAB): *m*/*z* = 3826 [M + H]$^+$, 3770 [M − *t*Bu]$^+$, 3495 [M − 6 *t*Bu]$^+$, 720 [C_{60}]$^+$. $C_{222}H_{222}N_{12}O_{48}$ (3826.19): calcd. C 69.69, H 5.85, N 4.39; found C 69.31, H 5.81, N 4.18.

48: ^{1}H NMR (300 MHz, room temp., [D$_8$]THF): δ = 7.61 (m, 12 H), 7.18 (m, 30 H), 4.68 (m, 6 H), 4.52 (m, 12 H), 4.25 (m, 12 H), 4.06 (m, 3 H), 3.92 (m, 3 H), 3.13 (dd, ^2J = 12.5, ^2J = 6.30 Hz, 6 H), 2.97 (dd, ^2J = 12.5, ^2J = 6.30 Hz, 6 H), 2.22 (m, 12 H), 1.92 (m, 12 H), 1.73 (m, 6 H), 1.51 (m, 9 H), 1.38 (m, 3 H), 1.23 (m, 36 H), 0.85 (m, 3 H) ppm. ^{13}C NMR (75 MHz, room temp., [D$_8$]THF): δ = 173.36, 173.24, 173.06 (6 C), 172.39, 172.36, 172.14 (12 C), 164.08, 164.00, 163.83, 163.79, 163.34, 163.31 (12 C), 147.23, 147.21, 146.92, 146.90, 146.70, 146.67, 146.59, 146.32, 146.30, 145.99, 145.92, 145.84, 145.72, 145.69, 143.11, 143.01, 142.99, 142.70, 142.62, 142.55, 142.57, 142.00, 141.91, 141.85, 141.72 (48 C, C_{60} sp^2), 138.17 (6 C), 130.36 (12 C), 128.96 (12 C), 127.32 (6 C), 70.30 (12 C), 66.40 (12 C), 49.27 (12 C), 47.94, 46.75 (6 C), 38.23 (6 C), 32.35, 30.22, 29.75, 27.46, 26.54 (24 C), 18.58 (6 C) ppm. IR (KBr): $\tilde{\nu}$ = 3383, 3074, 2936, 2858, 1742, 1647, 1541, 1458, 1384, 1265, 1218, 1169, 1080, 1045, 1017, 992, 904, 810, 758, 714, 668, 540, 528 cm^{-1}. UV/Vis (H_2O): $\lambda_{max.}$ = 212.5, 244, 271.5, 282, 320, 337 nm. MS (FAB): *m*/*z* = 3055 [M + Na]$^+$, 3033 [M + H]$^+$, 2854, 2833, 720 [C_{60}]$^+$.

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