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Sugar Balls: Synthesis and Supramolecular Assembly of [60]Fullerene Glycoconjugates

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The synthesis and characterization of fully deprotected C_{60} glycoconjugates **4** and **17** is reported. Bis(α-D-mannopyranosyl)malonamide **4** was obtained by using nucleophilic cyclopropanation chemistry, which in general is a very versatile method for fullerene functionalization. Fullerene sugar **17** contains two dendritic α-D-mannopyranosides that are connected through two adjacent imino bridges to the all-carbon framework. In this adduct-type of C_{60}, which represents a 1,9-dihydro-1a-aza-1(2)a-homo(C_{60}-I_h)[5,6]fullerene derivative, the entire 60-π-electron system of the fullerene core is retained. This architecture allows the basic cleavage of the acetyl protection groups of precursor adduct **16** without destruction of the core structure of the fullerene sugar. Dendritic glycoconjugate **17** containing six deprotected sugar building blocks is very soluble in water. The amphiphilic nature of **17** with its cone-shaped structure forces the formation of small supramolecular aggregates in aqueous solutions to shield the hydrophobic fullerene units from the water subphase. DOSY NMR spectroscopy and TEM investigation reveal micellar sugar balls with an extremely narrow size distribution of around 4 nm.

Introduction

Since the synthesis of the first fullerene sugars in both the fully protected and deprotected forms by Vasella and Diederich,[1] various families of fullerene glycoconjugates have been designed and characterized.[2] Fullerene sugars have potential in biomedical and materials applications. For example, amphiphilic [60]fullerene-sugar-conjugates with one and two fully protected glycodendron headgroups, form stable, ordered monomolecular Langmuir layers at the air–water interface.[3] The monolayers were transferred successfully as X-type Langmuir–Blodgett films onto quartz slides. In contrast, mono- and bis(α-D-mannopyranosyl)[60]fullerene adducts displayed marked activity in blocking lectin-induced hemagglutination by concanavaline A.[4] The corresponding bis(α-D-mannopyranosyl)[60]fullerene was found to form large aggregates during sugar deprotection as determined by dynamic light scattering (DLS) and atomic force microscopy (AFM).[5] Thiolate/alkyl halide coupling in aqueous media provided a facile one-step synthesis of fullerene glycoconjugates bearing five carbohydrate groups.[2f] Apart from monosaccharide binding, a synthetic route for the attachment of oligosaccharides to C_{60} by the cycloaddition of azido sugars to the fullerene core, followed by deacetylation, was reported.[6] All fullerene sugars reported so far show, if at all, only very limited solubility in water.

We have now developed the fullerene glycoconjugate **17** where two dendritic branches terminated by six deprotected α-D-mannopyranosyl building blocks are connected through two adjacent imino bridges to the all-carbon framework. In this bis(imino)homofullerene, the entire 60-π-electron system of the fullerene core is retained (Figure 1). Fullerene sugar **17** represents the first very water soluble glycoconjugate of C_{60}. To also exploit nucleophilic cyclopropanation chemistry,[7] which represents one of most versatile functionalization methods of fullerenes, we also synthesized and characterized bis(α-D-mannopyranosyl)fullerene **4** (Scheme 1).

Figure 1. Schematical representation of a diazabishomo[60]fullerene.

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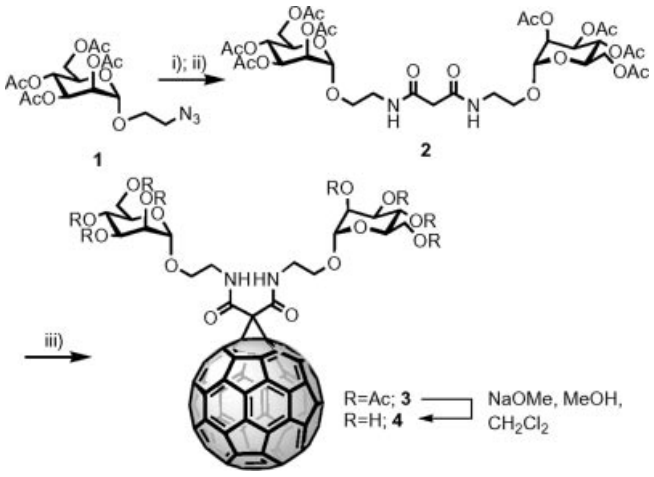


Scheme 1. Synthesis of bis(α-D-mannopyranosyl)malonamide-[60]fullerene-conjugate **4**: i) PPh_3, H_2O, THF; ii) malonic acid, HBTU, DIPEA, DMF; iii) C_{60}, CBr_4, DBU, toluene.

Results and Discussion

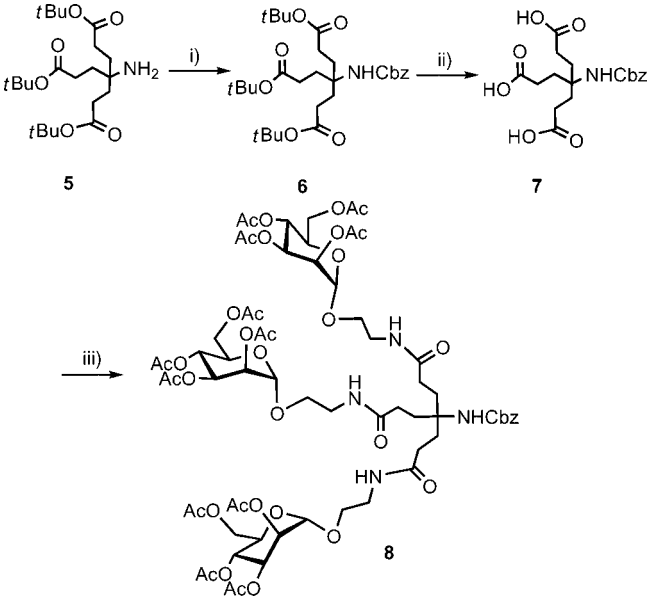
Syntheses

For the synthesis of fullerene sugar **4**, fully acetyl-protected bis(α-D-mannopyranose)malonamide **2** was first synthesized (Scheme 1). This was achieved by the reduction of 2-azidoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**1**)[2b] to the corresponding amine. Upon hydrogenation [H_2/Pd or $Pd(OH)_2$],[8] significant amounts of the dimeric secondary amines were formed, as confirmed by ^{13}C NMR spectroscopy and FAB mass spectrometry. However, clean and quantitative reduction of **1** was obtained with the use of triphenylphosphane (Staudinger reduction)[9] in THF. The chromatographically purified amine was then allowed to undergo a coupling reaction with malonic acid in the presence of *O*-(benzotriazole-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HBTU) and diisopropylethylamine (DIPEA) in DMF. After purification, desired malonamide **2** was isolated in 56% yield. The subsequent nucleophilic cyclopropanation of C_{60} with malonamide **2** was carried out in toluene with CBr_4 as the bromine transfer reagent and DBU as the base. Unreacted C_{60} was removed from the crude mixture by flash chromatography (SiO_2, toluene to 10% MeOH in toluene) upon which also a fraction containing a mixture of fullerene glycoconjugates eluted. Mono adduct **3** was isolated from higher adducts by an additional chromatographic separation (SiO_2, 1% MeOH in $CHCl_3$). The overall isolated yield of **3** was 6%.

The UV/Vis spectrum of **3** gives a sharp absorption at 426 nm, which corresponds to the typical spectrum of a [6,6]-monoadduct of C_{60}. The ^1H NMR spectrum of **3** revealed two equivalent 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside units. The ^{13}C NMR spectrum of **3** clearly reveals the expected C_2-symmetry and shows the fullerene sp^3 carbon atom at δ = 73.61 ppm and 27 signals for the fullerene sp^2 carbon atoms, where one signal, which is attributed to three closely overlapping resonances, is three times as high as the remaining 26 lines and attributed to two magnetically equivalent carbon atoms.

Treatment of **3** with MeONa in a mixture of CH_2Cl_2 and MeOH led to the quantitative removal of all acetyl protecting groups and the deposition of a brown precipitate of **4**. Unprotected sugar **4** is soluble in DMSO, DMF and mixtures of water and DMSO. However, it is insoluble in pure water, MeOH, EtOH, acetone, THF, CH_2Cl_2 and $CHCl_3$. The ^1H NMR spectrum of **4** in [D_6]DMSO revealed very broadened signals, which suggests that **4** forms aggregates in DMSO. The poor solubility of **4** in most solvents is probably due to its pronounced propensity to form large aggregates. It was observed before that many deprotected sugar conjugates of C_{60} are only sparingly soluble in DMF, DMSO and mixtures of DMSO and water and give very broad signals in their NMR spectra.[1a,2c,4–6]

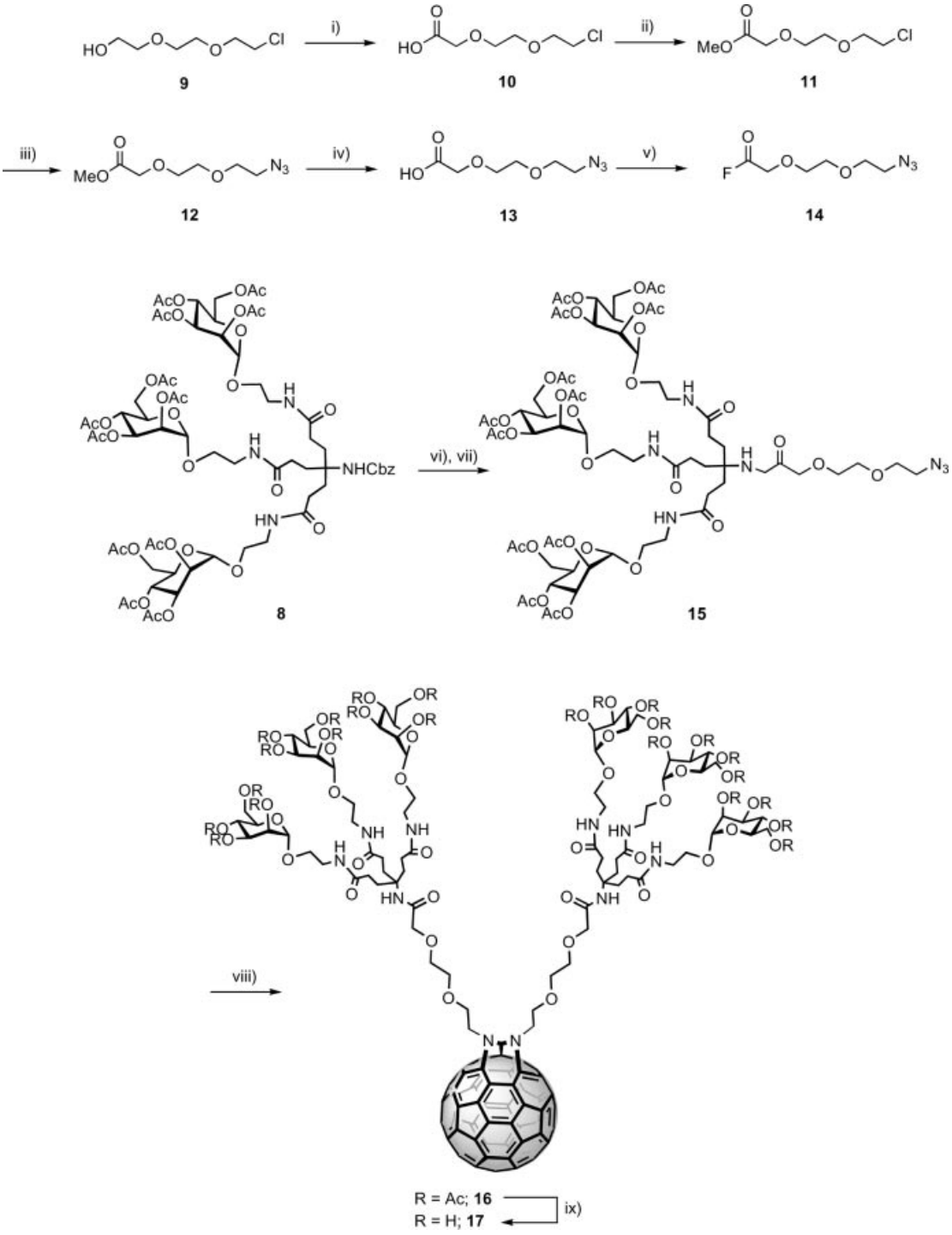
For the synthesis of target compound **17**, the dendritic mannosyl building blocks first needed to be assembled. For this purpose, Newkome dendron **5**[10] was protected with benzyl chloroformate (CbzCl) *prior* to the coupling reaction with 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside[2b] (Scheme 2). Treatment of tris(ester) **6** with formic acid led to quantitative deprotection and the formation of corresponding tris(acid) **7**. The subsequent coupling reaction of tris(acid) **7** with 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside was carried out in the presence of DCC/HOBT as the coupling reagent in a mixture of dichloromethane and DMF (2:1) to give mannosyl glycodendron **8** in 83% yield.



Scheme 2. Syntheses of glycosyl dendron **8**: i) ZCl, $NaHCO_3$, acetone/water, 9:1; ii) formic acid; iii) 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside, DCC, HOBT, DMF, CH_2Cl_2.

We decided to couple dendritic building **8** with C_{60} by using the very regioselective bisaddition of azides to give a twofold cluster-opened diazabishomofullerene adduct,[11] whose general structure is schematically depicted in Figure 1. For this purpose, a suitable linker molecule bearing

a terminal azide group was required. The best results were obtained with the hitherto unknown 2-[2-(2-azidoethoxy)-ethoxy]acetyl fluoride (**14**). It was obtained by the oxidation of commercially available glycol derivative **9**, followed by conversion into ester **11** and introduction of the azide group to give compound **12** (Scheme 3). The final steps of the synthetic sequence were the hydrolysis to acid **13** and conversion to fluoride **14**, which was used for the subsequent coupling reactions without further work up. For the coupling reaction, the Cbz protecting group of **8** was first removed by hydrogenolysis (10% of Pd on C) in a mixture of EtOH and ethyl acetate (1:2) to give the corresponding amine in quantitative yield. The obtained amine was treated without further work up with an excess amount of **14** in



Scheme 3. Syntheses of water-soluble dendritic fullerene sugar **17**: i) TEMPO, trichlorocyanuric acid, $NaHCO_3$, water/acetone; ii) NaOMe, methanol, MeI, DMF; iii) NaN_3, DMF, 60 °C; iv) NaOH, H_2O, MeOH; v) HFPDA, CH_2Cl_2; vi) Pd/C, aqueous HCl, H_2, ethyl acetate/ethanol, 2:1; vii) **14**, DMAP, CH_2Cl_2; viii) C_{60}, toluene, reflux; ix) NaOMe, MeOH.

the presence of DMAP as the base in CH_2Cl_2 to provide azido oligo(ethylene glycol)-terminated glycodendron **15** in 94% yield. The thermal coupling reaction between **15** and C_{60} in toluene afforded a mixture of mono- and bisglycodendron adducts (silica gel TLC, R_f = 0.67 and R_f = 0.61, $CHCl_3$/MeOH, 10:1). After removal of C_{60} by column chromatography, an additional chromatographic separation step (SiO_2, 10% MeOH in $CHCl_3$) allowed the separation of the product from the monoadduct to give targeted bisglycodendron **16** in 8% overall yield. The UV/Vis spectrum of **16** shows broad absorptions at 256 nm and 324 nm, which are characteristic for a diazabishomofullerene possessing two opened and adjacent [5,6]-bonds.[11] The ^{1}H NMR spectrum of **16** reveals two equivalent glycodendron addends. The ^{13}C NMR spectrum displays 31 lines for the fullerene sp^2 C atoms, 1 with fourfold intensity, 26 with twofold intensity and 3 with single intensity, which implies a C_2-symmetric structure. This finding is surprising at first glance because, owing to the chirality of the mannosyl groups, the overall symmetry of **17** is lowered to C_1 relative to a corresponding bisadduct containing two achiral substituents.[2b,6] Obviously, the conformationally very flexible and long spacer linking of the fullerene part with the sugar subunits causes a high amount of flexibility. As a consequence, the fullerene core experiences a local C_s symmetry on the NMR timescale. The most characteristic signal in the ^{13}C NMR spectrum is that of the bridgehead atom C^1 (Figure 1), which appears as expected[11] at about 163 ppm.

The quantitative deprotection of **16** to generate desired fullerene sugar **17** was accomplished by treatment with MeONa in methanol. Significantly, sugar **17** very easily dissolves in water; the water solubility is higher than 40 mg mL^{-1}. The ^{1}H NMR spectrum of **17** in D_2O displays rather broad signals, which implies that aggregates are formed from this new sugar amphiphile. The aggregation of amphiphilic fullerene derivatives to micelles, liposomes and nanorods[12] as well as to Langmuir–Blodgett films,[3,13] was documented for a variety of cases. It can be expected that the corresponding aggregates of **17** are very small micelles because the aqueous solutions are clear to the eye even when they are fairly concentrated. Indeed, determination of the particle size by using DOSY NMR spectroscopy revealed a diameter of the micelles of 4.2 nm. Considering that amphiphilic fullerene sugar **17** exhibits a rather cone shaped architecture in which the hydrophilic part is much larger than the hydrophobic fullerene subunit, it is unlikely that large liposomal aggregates are easily generated.[14] The conical shape of **17** obviously favours the formation of highly curved micelles in water where the smaller fullerene moieties are located in the centre of the aggregates, whereas the more extended hydrophilic sugar parts are exposed to the water subphase. Only in this way can close-packing of the amphiphiles within the aggregated be achieved. Along the same lines, we have recently demonstrated that amphiphilic fullerenes and calixarenes that exhibit a comparatively rigid cone- or T-shape form small shape-persistent micelles, whose supramolecular arrangement could be determined with molecular precision by using transmission electron microscopy (TEM).[15] To corroborate the observations on the aggregation of **17** described above, we also carried out TEM investigations with aqueous solutions of fullerene sugar **17**. We were very pleased to see that indeed very uniform micelles were formed whose diameter is below 5 nm (Figure 2). These supramolecular structures represent a new arrangement of sugars and can be considered as micellar sugar balls.

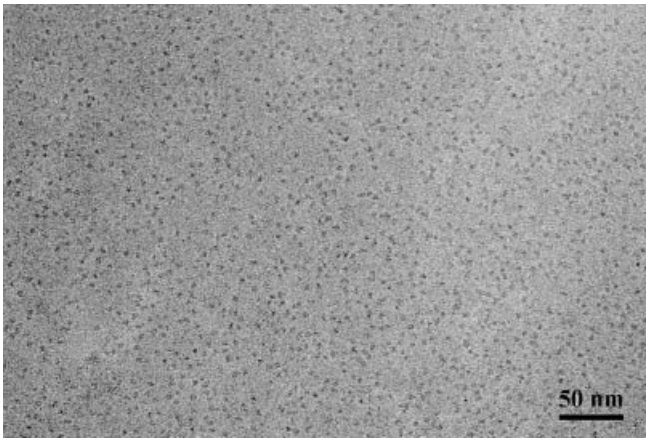


Figure 2. Transmission electron micrograph of the micellar sugar balls composed of amphiphiles **17**. Thin layers of the aqueous solution of **17** were created on the surface of carbon-coated grids by blotting droplets with a filter paper. After subsequent addition of a contrasting solution (phosphotungstic acid at pH 7) and blotting, the grids were dried in air. Microscopy was carried out by using a Philips CM12 TEM (FEI Company, Oregon, USA) at an accelerating voltage of 100 kV and a defocus of 600 nm corresponding to a first zero of the contrast transfer function at 1.5 nm. The microscope's low dose protocol was used to avoid unnecessary radiation damage in the sample. The image shows a monodisperse population of spherical particles with a diameter in the order of 4 ± 0.5 nm. Very rarely larger agglomerates were found. The contrast of the negative was not inverted for better visibility of the small objects.

Conclusions

We synthesized fullerene glycoconjugate **17** where two dendritic α-D-mannopyranosides are connected through two adjacent imino bridges to the all-carbon framework. In this adduct-type of C_{60}, which represents a 1,9-dihydro-1a-aza-1(2)a-homo(C_{60}-I_h)[5,6]fullerene derivative, the entire 60-π-electron system of the fullerene core is retained, which allows the basic cleavage of the acetyl protection groups of precursor adduct **16** without destruction of the core structure of the fullerene sugar. In general, nucleophilic cyclopropanation chemistry is a very versatile method for the functionalization of fullerenes. However, it turned out that basic deprotection of acetylated glycosides terminating malonates attached to C_{60} is accompanied by the cleavage of the malonate anchor points. However, to overcome this problem, we introduced for the first time a nucleophilic cyclopropanation of C_{60} for the synthesis of deprotected fullerene sugars by using a bis(α-D-mannopyranosyl)malon-

amide as a precursor addend. The amide linkages tolerate the basic deprotection conditions as demonstrated with the synthesis of glycoconjugate **4**. In contrast to **4**, which contains two α-D-mannopyranosyl moieties only, dendritic glycoconjugate **17** containing six deprotected sugar building blocks is very soluble in water. To the best of our knowledge, **17** is by far the most water-soluble fullerene sugar known to date. The amphiphilic nature of **17** with its cone-shaped structure forces the formation of small supramolecular aggregates in aqueous solutions to shield the hydrophobic fullerene units from the water subphase. DOSY NMR spectroscopy reveals a very small particle size of about 4 nm. This was corroborated by TEM investigations, which showed that spherical micelles with an extremely narrow size distribution are formed. These small micelles represent supramolecular sugar balls, which have potential for biomedical applications such as neuroprotection due to superoxide-dismutation.[16] So far, water-soluble fullerene derivatives that were successfully studied in this regard contain ionic groups such as carboxylates for the promotion of water solubility. Fullerene sugars like **17** have neutral components only. This may improve the bioavailability and pharmacokinetic properties of such bioactive fullerenes considerably. Investigations along these lines are currently underway in our laboratory.

Experimental Section

General: All chemicals were obtained from Sigma–Aldrich, Acros Organics or Merck, or they were prepared according to known literature procedures. All reactions were performed by using standard glassware under a nitrogen atmosphere. The solvents were purified by distillation. Dry solvents were prepared by using customary literature procedures. Reactions were monitored by thin-layer chromatography (TLC) using Riedel-de-Haën silica gel 60 F_{254} aluminium foils, detection by UV lamp. ^1H and ^{13}C NMR spectra were recorded with Bruker Avance 300 or JEOL JNM EX 400 instruments. The chemical shifts are given in ppm relative to TMS or the solvent peak as a standard reference. The ^1H NMR and ^{13}C NMR of **17** in D_2O were calibrated with HOD as 4.75 ppm at 300 K, and with C=O of **17** as 175.78 ppm that was determined with C=O of added [D_6]acetone as 215.94 ppm, respectively. The resonance multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet), unresolved signals as br. The atoms of the sugar moieties are numbered according to standard numbering for sugars. Mass spectra were measured with a Micromass Lab Spec (FAB) with the use of a Finnigan MAT 900 spectrometer with 3-nitrobenzylalcohol as the matrix. MALDI-TOF (Matrix-assisted laser desorption/ionisation time-of-flight) mass spectra were acquired with an AXIMA-CFR plus instrument (Kratos Analytical, Manchester, UK) equipped with a 1.2-m drift tube. MALDI was produced by pulses of UV light (337 nm, 3-ns pulse width) generated by a nitrogen laser with a maximum pulse rate of 10 Hz. The laser was operated between 5.0 and 17 μJ. The ion source was held at 1×10^{-4} Pa. For the reflectron mode, the delayed extraction was optimized according to the molecular mass of the analyte. IR spectra were recorded with a React IR-1000 ASI Applied Systems (ATR-DiComp-Detector) on a diamond crystal. UV/Vis spectroscopy was performed by using a Shimadzu UV-3102 spectrophotometer. Elementary analysis succeeded by combustion and gas chromatographical analysis with an EA 1110 CHNS analyser (CEInstruments). Products were isolated by flash column chromatography (FC) (silica gel 60, particle size 0.04–0.063 nm, Merck).

Bis[2-(2,3,4,6-tetra-*O*-acetyl α-D-mannopyranosyl)ethyl] Malonamide (2): Ph_3P (1.38 g, 5.5 g) and water (1.8 mL, 100 mmol) were added to a THF solution (35 mL) of 2-azidoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (2.09 g, 5.0 mmol). The mixture was stirred at room temperature for 16 h. The reaction mixture was concentrated in vacuo, and the residue was separated by FC ($CHCl_3$/MeOH, 100:1–5:1) to give 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (1.66 g). The obtained amine was used for the next step. A DMF solution (2.0 mL) of malonic acid (0.208 g, 2.00 mmol), HBTU (1.70 g, 4.40 mmol), HOBt (hydroxybenzotriazole) (674 mg, 4.40 mmol) and DIPEA (0.568 g, 4.40 mmol) was stirred for 20 min at 0 °C under a N_2 stream. A DMF solution (2.0 mL) of 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (1.66 g, 4.22 mmol) was added to the solution, and the mixture was stirred for 13 h at room temp. under a N_2 stream. The solvent was removed in vacuo, and the residue was dissolved in $CHCl_3$ (200 mL) and washed with 1 M HCl, a saturated solution of $NaHCO_3$ and a saturated solution of NaCl. The organic layer was dried with $MgSO_4$. After evaporation of the solvent, the resulting crude product was separated by FC ($CHCl_3$/MeOH, 100:2)to give **12** as a colourless solid. Yield: 946 mg (56%) based on malonic acid. ^1H NMR (300 MHz, $CDCl_3$, 300 K) 2.00 (s, 6 H, Ac), 2.06 (s, 6 H, Ac), 2.11 (s, 6 H, Ac), 2.16 (s, 6 H, Ac), 3.25 (s, 2 H, COCH_2CO), 3.45–3.63 (m, 4 H, OCH$_2$CH_2N), 3.50–3.63 (m, 2 H, OCH_2CH$_2$N), 3.76–3.82 (m, 2 H, OCH_2CH$_2$N), 4.01 (ddd, J = 2.5, 5.5, 9.5 Hz, 2 H, 5-H), 4.12 (dd, J = 2.4, 12.2 Hz, 2 H, 6-H), 4.28 (dd, J = 5.4, 12.2 Hz, 2 H, 6′-H), 4.84 (d, J = 1.2 Hz, 2 H, 1-H), 5.26 (dd, J = 1.7, 3.1 Hz, 2 H, 2-H), 5.27 (dd, J = 10.0, 9.7 Hz, 2 H, 4-H), 5.34 (dd, J = 3.2, 10.0 Hz, 2 H, 3-H), 7.25 (*t*, J = 5.2 Hz, 2 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 20.29 (2 C), 20.31 (2 C), 20.35 (2 C), 20.46 (2 C), 38.57 (2 C), 42.05 (1 C), 62.02 (2 C), 65.62 (2 C), 66.46 (2 C), 68.16 (2 C), 68.65 (2 C), 68.93 (2 C), 97.23 (2 C), 167.32 (2 C), 169.32 (2 C), 169.54 (2 C), 169.58 (2 C), 170.30 (2 C) ppm. IR (ATR): $\tilde{\nu}$ = 2945, 1741, 1671, 1532, 1432, 1370, 1216, 1135, 1081, 1042, 977, 899, 687 cm^{-1}. MS (FAB, NBA): m/z = 850 $[M]^+$, 808 $[M - Ac]^+$. $C_{35}H_{50}N_2O_{22}$·1/3CH_2Cl_2 (850.29): calcd. C 48.28, H 5.81, N 3.19; found C 48.29, H 5.80, N 3.20.

1,2-{Bis[2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethylaminocarbonyl]methano}-1,2-dihydro(C_{60}-I_h)[5,6]fullerene (3): C_{60} (72 mg, 0.10 mmol) was dissolved in dry toluene (50 mL) under an atmosphere of N_2. Subsequently, malonamide **2** (85 mg, 0.10 mmol) and CBr_4 (33 mg, 0.11 mmol) were added, followed by the dropwise addition of a solution of DBU (16 mg, 0.11 mmol) in toluene (20 mL) over a period of 20 min. The solution was stirred at room temperature for 1 d. The crude reaction mixture was separated by FC. The remaining C_{60} and other impurities were eluted with toluene, and then the eluent was changed to a mixture of $CHCl_3$/MeOH = 100:1 to give **3** as a brown solid. Yield: 10 mg (6%). ^1H NMR (300 MHz, $CDCl_3$, 300 K): δ = 1.97 (s, 6 H, Ac), 2.04 (s, 6 H, Ac), 2.12 (s, 6 H, Ac), 2.14 (s, 6 H, Ac), 3.69–3.96 (m, 8 H, OCH_2CH_2N), 4.03 (ddd, J = 2.4, 5.5, 9.1 Hz, 2 H, 5-H), 4.13 (dd, J = 2.4, 12.2 Hz, 2 H, 6-H), 4.29 (dd, J = 5.5, 12.2 Hz, 2 H, 6′-H), 4.82 (d, J = 1.4 Hz, 2 H, 1-H), 5.23 (dd, J = 1.7, 3.0 Hz, 2 H, 2-H), 5.26 (dd, J = 9.5, 9.5 Hz, 2 H, 4-H), 5.27 (dd, J = 3.2, 9.8 Hz, 2 H, 3-H), 8.00 (t, J = 5.5 Hz, 2 H, NH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 20.68 (2 C), 20.74 (2 C), 20.82 (2 C),

20.90 (2 C), 40.23 (2 C), 58.25 (1 C), 62.55 (2 C), 66.00 (2 C), 67.47 (2 C), 68.82 (2 C), 69.10 (2 C), 69.32 (2 C), 73.61 (2 C), 98.03 (2 C), 137.80 (2 C), 137.90 (2 C), 141.00 (2 C), 141.01 (2 C), 141.97 (2 C), 142.12 (6 C), 142.88 (2 C), 142.92 (2 C), 143.00 (2 C), 143.02 (2 C), 143.06 (2 C), 143.69 (2 C), 143.74 (2 C), 144.45 (2 C), 144.52 (2 C), 144.65 (2 C), 144.67 (2 C), 144.69 (2 C), 144.74 (2 C), 145.17 (2 C), 145.20 (2 C), 145.22 (2 C), 145.26 (2 C), 145.28 (2 C), 145.38 (2 C), 145.81 (2 C), 146.23 (2 C), 163.12 (2 C), 169.66 (2 C), 169.89 (2 C), 170.08 (2 C), 170.80 (2 C) ppm. IR (ATR): $\tilde{\nu}$ = 2945, 1741, 1687, 1529, 1428, 1366, 1216, 1135, 1081, 1042, 977, 896, 799, 687 cm^{-1}. UV/Vis (CH_2Cl_2): λ = 257, 323, 425 nm. MS (FAB, NBA): *m/z* = 3139 $[2M + H]^+$, 1569 $[M]^+$, 720 $[C_{60}]^+$. $C_{95}H_{48}N_2O_{22}$ (1569.40): calcd. C 72.70, H 3.08, N 1.78; found C 70.92, H 3.36, N 1.66.

1,2-{Bis[2-(α-D-mannopyranosyloxy)ethylaminocarbonyl]methano}-1,2-dihydro(C_{60}-I_h)[5,6]fullerene (4): Sugar deprotection of **3** was carried out under Zemplén conditions.[17] To a solution of **3** (8 mg, 5.1 μmol) in dry dichloromethane (10 mL) was added MeOH (1.0 mL) containing a catalytic amount of MeONa (1.0 mg, 19 μmol), and this mixture was stirred for 1 h. The resulting precipitate was collected and washed with MeOH to give **4** as a brown solid. Yield: 6 mg (95%). ^{1}H NMR (300 MHz, [D_6]DMSO, 300 K): δ = 2.5–4.8 (br) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO, 300 K) no signal. IR (ATR): $\tilde{\nu}$ = 3350, 2930, 1710, 1544, 1417, 1131, 1058, 977, 810, 679 cm^{-1}. MS (FAB, NBA): *m/z* = 1255 $[M + Na]^+$.

Benzyl *N*-[Tris(2-*tert*-butoxycarbonylethyl)methyl]carbamate (6): A solution of benzyl chloroformate (CbzCl) (8.63 g, 50.6 mol) in acetone (40 mL) was added dropwise to a cooled solution (0 °C) of amino dendron **5** (10.5 g, 25.3 mol) and $NaHCO_3$ (4.25 g, 50.6 mmol) in 90% aqueous acetone (400 mL). The mixture was stirred for 18 h at room temperature. The precipitates were removed by filtration, and the filtrates were then concentrated in vacuo. The residue was diluted with $CHCl_3$ and washed with 1 N HCl, satd. $NaHCO_3$, satd. NaCl and dried with $MgSO_4$. After evaporation of the solvents, the resulting crude product was separated by FC (hexane/ethyl acetate, 4:1) to give **6** as a colourless solid. Yield: 12.0 g (91%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 1.43 (s, 9 H, *t*Bu), 1.93 (t, *J* = 8.7 Hz, 6 H, CH_2CH_2), 2.21 (t, *J* = 8.7 Hz, 2 H, CH_2CH_2), 4.83 (br. s, 1 H, NH), 5.04 (s, 2 H, CH_2Ph), 7.45–7.25 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 28.00 (9 C), 29.62 (3 C), 30.04 (3 C), 56.52 (1 C), 66.15 (1 C), 80.53 (9 C), 127.92 (2 C), 127.99 (1 C), 128.44 (2 C), 136.52 (1 C), 154.11 (1 C), 172.46 (3 C) ppm. IR (KBr): $\tilde{\nu}$ = 3333, 2979, 2942, 2885, 1726, 1535, 1461, 1417, 1393, 1368, 1330, 1258, 1226, 1154, 1086, 1043, 951, 847, 773, 773, 699 cm^{-1}. MS (FAB, NBA): *m/z* = 550 $[M]^+$, 494 [M – isobutene]$^+$, 438 [M – 2 × isobutene]$^+$, 382 [M – 3 × isobutene]$^+$, 416 [M – Cbz]$^+$. $C_{30}H_{47}NO_8$ (549.70): calcd. C 65.55, H 8.62, N 2.55; found C 65.52, H 8.60, N 2.57.

Benzyl *N*-[Tris(2-carboxyethyl)methyl]carbamate (7): Formic acid (30 mL) was added to **6** (8.15 g, 14.8 mmol). The mixture was then stirred for 24 h at room temperature. Evaporation of formic acid gave tricarboxylic acid **7** as a colourless solid. Yield: 5.18 g (92%). ^{1}H NMR (300 MHz, CD_3OD, 300 K): δ = 1.43 (s, 9 H, *t*Bu), 1.93 (m, 6 H, CH_2CH_2), 2.21 (m, 6 H, CH_2CH_2), 5.02 (s, 2 H, CH_2Ph), 7.34–7.21 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, CD_3OD, 300 K): δ = 29.17 (3 C), 30.66 (3 C), 57.52 (1 C), 66.89 (1 C), 128.70 (1 C), 128.89 (1 C), 129.46 (3 C), 136.62 (1 C), 156.66 (1 C), 177.11 (3 C) ppm. IR (KBr): $\tilde{\nu}$ = 3063, 2958, 1710, 1531, 1457, 1417, 1256, 1075, 915, 740, 698 cm^{-1}. MS (FAB, NBA): *m/z* = 1144 $[3M + H]^+$, 763 $[2M + H]^+$, 382 $[M + H]^+$. $C_{18}H_{23}NO_8$ (381.38): calcd. C 56.69, H 6.08, N 3.67; found C 56.10, H 5.71, N 3.72.

Benzyl *N*-(Tris{2-[2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)carbamate (8): A solution of 2-aminoethyl-2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (1.25 g, 3.20 mmol) in dry dichloromethane (10 mL) was added to a stirred solution of benzyl *N*-[tris(3-propanoic acid) methyl]carbamate (339 mg, 0.89 mmol), *N*,*N*′-dicyclohexylcarboxydiimide (DCC) (766 mg, 3.74 mmol) and 1-hydroxybenzotriazole (HOBT) (407 mg, 2.55 mmol) in dry DMF at 0 °C. The solution was stirred at ambient temperature for 16 h. After removal of the solvent under reduced pressure, the residue was dissolved in $CHCl_3$ and washed with 1 N HCl, $NaHCO_3$ and brine. The $CHCl_3$ layer was then dried ($MgSO_4$), the solvent was removed in vacuo, and the residue was purified by FC ($CHCl_3$/MeOH, 100:2) to give **8** as a colourless solid. Yield: 1.10 g (83%) based on **7**. ^{1}H NMR: δ = (300 MHz, $CDCl_3$, 300 K) 1.97 (s, 9 H, Ac), 1.95–2.05 (m, 6 H, CH_2-dendron), 2.04 (s, 9 H, Ac), 2.10 (s, 9 H, Ac), 2.15 (s, 9 H, Ac), 2.22 (t, *J* = 7.5 Hz, 6 H, CH_2-dendron), 3.33–3.43 (m, 3 H, OCH_2CH_2N), 3.48–3.56 (m, 6 H, OCH_2CH_2N), 3.70–3.80 (m, 3 H, OCH_2CH_2N), 3.95–4.02 (m, 3 H, 5-H), 4.13 (dd, *J* = 2.3, 12.2 Hz, 3 H, 6-H), 4.26 (dd, *J* = 5.4, 12.2 Hz, 3 H, 6′-H), 4.83 (d, *J* = 1.3 Hz, 3 H, 3 H, 1-H), 5.04 (s, 2 H, CH_2Ph), 5.25 (dd, *J* = 1.8, 3.1 Hz, 3 H, 2-H), 5.26 (dd, *J* = 9.9, 9.9 Hz, 3 H, 4-H), 5.25 (dd, *J* = 3.1, 9.6 Hz, 3 H, 3-H), 5.74 (br. s, 1 H, NH), 6.47 (br. s, 3 H, NH), 7.24–7.38 (m, 5 H, Ph) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 20.51 (3 C), 20.55 (3 C), 20.62 (3 C), 20.73 (3 C), 30.51 (3 C), 31.05 (3 C), 38.78 (3 C), 57.04 (1 C), 62.33 (3 C), 65.91 (3 C), 66.83 (3 C), 68.54 (3 C), 69.00 (3 C), 69.23 (3 C), 97.47 (3 C), 127.79 (2 C), 128.31 (1 C), 136.85 (2 C), 154.60 (1 C), 169.59 (3 C), 170.00 (6 C), 170.61 (3 C), 173.14 (3 C) ppm. IR (ATR): $\tilde{\nu}$ = 1745, 1652, 1536, 1436, 1370, 1220, 1135, 1081, 1046, 977, 896, 741, 691 cm^{-1}. MS (FAB, NBA): *m/z* = 6005 $[4M]^+$, 4503 $[3M]^+$, 3002 $[2M]^+$, 1501 $[M]^+$. $C_{66}H_{92}N_4O_{35}$ (1501.44): calcd. C 52.80, H 6.18, N 3.73; found C 51.66, H 6.08, N 3.71.

2-[2-(2-Chloroethoxy)ethoxy]acetic Acid (10): An aqueous 15 wt.-% solution of $NaHCO_3$ (80 mL) was added to a stirred solution of alcohol **9** (4.4 g, 26.1 mmol) in acetone (260 mL) and maintained at 0 °C. Subsequently, solid KBr (0.626 g, 5.25 mmol) and TEMPO (2,2,6,6-tetramethylpiperidine-*N*-oxide) (0.080 g, 0.8 mmol) were added. Trichlorocyanuric acid (12.20 g, 52.5 mmol) was then slowly added to the mixture within 20 min at 0 °C. After the addition, the mixture was warmed to room temperature and stirred for the required time until completion and then 2-propanol (50 mL) was added. The mixture was filtered through Celite, concentrated under vacuum and treated with a saturated solution of Na_2CO_3. The aqueous phase was washed with portions of ethyl acetate, treated with 1 N HCl and extracted twice with ethyl acetate. The organic layer was dried ($MgSO_4$), and the solvent was evaporated to yield **10** as a colourless liquid without further purification. Yield: 3.94 g (83%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.65 (t, *J* = 5.7 Hz, 2 H, CH_2), 3.71–3.75 (m, 2 H, CH_2), 3.76–3.80 (m, 2 H, CH_2), 3.76 (t, *J* = 5.7 Hz, 2 H, CH_2), 4.14 (s, 2 H, CH_2), 10.77 (s, 1 H, COOH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 42.44, 68.09, 70.29, 70.79, 71.14, 174.63 ppm. MS (FAB, glycerol): *m/z* = 365 $[2M]^+$, 183 $[M]^+$.

Methyl 2-[2-(2-Chloroethoxy)ethoxy]acetate (11): To a methanol (20 mL) solution of carboxylic acid **10** (3.94 g, 21.6 mmol) was added sodium methoxide (1.19 g, 22.0 mmol) while stirring. After stirring for 20 min, the solvent was removed from the reaction mixture in vacuo. To the residue, MeI (6.13 g, 43.2 mmol) was added and the mixture was stirred for 24 h. The resulting reaction mixture was concentrated in vacuo. The residue was dissolved in $CHCl_3$, washed with 1 N HCl, saturated $NaHCO_3$ and saturated NaCl. The organic phase was dried with $MgSO_4$, concentrated, and the resi-

due was purified by FC ($CHCl_3$/MeOH, 1:0–5:1) to give **11** as a colourless liquid. Yield: 3.73 g, (63%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.65 (t, J = 5.4 Hz, 2 H, CH_2), 3.60–3.72 (m, 6 H, CH_2), 3.65 (s, 3 H, CH_3), 4.09 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 42.44, 51.43, 68.28, 70.37, 70.57, 71.01, 170.49 ppm. MS (FAB, glycerol): m/z = 297 $[M]^+$.

Methyl 2-[2-(2-Azidoethoxy)ethoxy]acetate (12): To a DMF (70 mL) solution of **11** (3.73 g, 18.9 mmol) was added NaN_3 (6.15 g, 94.6 mmol), and the mixture was stirred at 70 °C for 22 h. The reaction mixture was filtered and concentrated in vacuo. The residue was dissolved in $CHCl_3$, washed with 1 N HCl, saturated $NaHCO_3$ and saturated NaCl. The organic layer was dried ($MgSO_4$), and the solvent was evaporated to yield **12** as a liquid without further purification. Yield: 3.28 g (85%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.40 (t, J = 5.0 Hz, 2 H, CH_2), 3.69 (t, J = 5.2 Hz, 2 H, CH_2), 3.69–3.73 (m, 2 H, CH_2), 3.74–3.78 (m, 2 H, CH_2), 3.76 (s, 3 H, CH_3), 4.19 (s, 2 H, CH_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 50.55, 51.74, 68.58, 69.98, 70.64, 70.90, 170.78 ppm. MS (FAB, glycerol): m/z = 204 $[M + H]^+$.

2-[2-(2-Azidoethoxy)ethoxy]acetic Acid (13): NaOH (0.520 g, 13.0 mmol) was added to a 50% aqueous methanol solution (40 mL) of **12** (2.20 g, 10.8 mmol), and the mixture was stirred at room temperature for 18 h. The mixture was then neutralized with 1 N HCl, and the neutralized solution was concentrated in vacuo. The residue was dissolved in $CHCl_3$, and washed with 1 N HCl, saturated $NaHCO_3$, and saturated aqueous NaCl. The organic layers were dried with $MgSO_4$, and the solvent was evaporated to yield **13** as a liquid. Yield: 0.828 g (41%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 3.42 (t, J = 5.0 Hz, 2 H, CH_2), 3.70 (t, J = 5.0 Hz, 2 H, CH_2), 3.71–3.73 (m, 2 H, CH_2), 3.77–3.80 (m, 2 H, CH_2), 4.22 (s, 2 H, CH_2), 10.16 (br. s, 1 H, COOH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 50.07, 67.74, 69.52, 70.01, 70.50, 174.29 ppm. MS (FAB, glycerol): m/z = 379 $[2M + H]^+$, 190 $[M + H]^+$.

2-[2-(2-Azidoethoxy)ethoxy]acetyl Fluoride (14): Hexafluoropropene diethylamine (3.6 g, 8.4 mmol) was added to a solution of [2-(2-azidoethoxy)ethoxy]acetic acid (529 mg, 2.8 mmol) in dry dichloromethane (8 mL). After the mixture was stirred at room temperature for 4 h, triethylamine (1.13 g, 11.2 mmol) was added. The mixture was used for the coupling reaction with the deprotected amine of **8** without further treatment.

2-[2-(2-Azidoethoxy)ethoxy]-*N*-(tris{2-[2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)acetamide (15): A mixture of palladium and carbon (400 mg) and conc. HCl (5 drops) was added to a solution of **8** (1.05 g, 0.70 mmol) in ethyl acetate/EtOH (1:1; 120 mL). The mixture was stirred under a hydrogen atmosphere at room temperature for 2.5 h. Pd/C was removed by filtration through Celite. The filtrate was concentrated in vacuo and used in the next step without further purification. A solution of **14** (8.4 mmol) in dichloromethane was added to a solution of the deprotected glycosyl dendron and DMAP (171 mg, 1.4 mmol) in dry dichloromethane (10 mL). The solution was stirred at ambient temperature for 48 h. Subsequently, the solution was diluted with $CHCl_3$ and washed twice with 1 N HCl, $NaHCO_3$ and brine. The $CHCl_3$ layer was then dried ($MgSO_4$), the solvent was removed in vacuo, and the residue was purified by FC ($CHCl_3$/MeOH, 100:0–100:3)to give a colourless solid. Yield: 1.01 g (94%). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 2.00 (s, 9 H, Ac), 2.06 (s, 9 H, Ac), 2.05–2.11 (m, 6 H, CH_2-dendron), 2.11 (s, 9 H, Ac), 2.16 (s, 9 H, Ac), 2.05–2.12 (m, 6 H, CH_2-dendron), 3.36–3.44 (m, 3 H, OCH_2CH_2N), 3.45 (t, J = 5.0 Hz, 2 H, CH_2-EG), 3.49–3.57 (m, 6 H, OCH_2CH_2N), 3.66–3.72 (m, 4 H, CH_2-EG), 3.72 (t, J = 4.8 Hz, 2 H, CH_2-EG), 3.74–3.80 (m, 3 H, OCH_2CH_2N), 3.91 (s, 2 H, OCH_2CO), 3.98–4.02 (m, 3 H, 5-H), 4.13 (dd, J = 2.1, 12.1 Hz, 3 H, 6-H), 4.27 (dd, J = 5.4, 12.3 Hz, 3 H, 6′-H), 4.84 (d, ^3J = 1.3 Hz, 3 H, 1-H), 5.23–5.30 (m, 3 H, 2-H), 5.27 (dd, J = 10.0, 10.0 Hz, 3 H, 4-H), 5.34 (dd, J = 3.3, 10.4 Hz, 3 H, 3-H), 6.57 (t, J = 5.1 Hz, 3 H, N*H*), 6.68 (br. s, 1 H, N*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 20.53 (6 C), 20.58 (3 C), (3 C), 20.70 (3 C), 30.42 (3 C), 31.14 (3 C), 38.80 (3 C), 50.29 (1 C), 58.01 (1 C), 62.29 (3 C), 65.92 (3 C), 66.97 (3 C), 68.48 (3 C), 68.93 (3 C), 69.20 (3 C), 69.86 (1 C), 69.96 (1 C), 70.0 (1 C), 70.44 (1 C), 70.83 (1 C), 97.52 (3 C), 169.20 (1 C), 169.56 (3 C), 169.83 (3 C), 169.89 (3 C), 170.53 (3 C), 172.76 (3 C) ppm. IR (ATR): $\tilde{\nu}$ = 2104, 1741, 1656, 1532, 1432, 1370, 1370, 1220, 1135, 1081, 1042, 977, 907, 971 cm^{-1}. MS (FAB, NBA): m/z = 1538 $[M]^+$. $C_{64}H_{95}N_7O_{36}$ (1538.46): calcd. C 49.96, H 6.22, N 6.37; found C 49.38, H 6.24, N 6.53.

1a*H*-1,9-[(2-{2-[(Tris{2-[2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)carbamoylmethoxy]ethyl}ethyl)imino]-1a-(2-{2-[(tris{2-[2-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)carbamoylmethoxy]ethyl}ethyl)-1,9-dihydro-1a-aza-1(2)a-homo(C_{60}-I_h)[5,6]fullerene (16): A solution of C_{60} (96 mg, 0.13 mmol) and azide **15** (245 mg, 0.16 mmol) in dry toluene (100 mL) was heated at reflux for 24 h under a N_2 stream. The crude reaction mixture was separated by FC. Unreacted C_{60} and other impurities were eluted with toluene. After evaporation of the solvent, the remaining solid was dissolved in $CHCl_3$/MeOH (100:5) and purified by FC (toluene/MeOH, 100:10). Bisadduct **15** eluted as the second fraction. After evaporation of the solvent and recrystallization from CH_2Cl_2, **16** was isolated in 8% yield (38 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = 1.99 (s, 18 H, Ac), 2.05 (s, 18 H, Ac), 2.05–2.11 (m, 12 H, CH_2-dendron), 2.10 (s, 18 H, Ac), 2.15 (s, 18 H, Ac), 2.18–2.26 (m, 12 H, CH_2-dendron), 3.33–3.43 (m, 6 H, OCH_2CH_2N), 3.45–3.58 (m, 12 H, OCH_2CH_2N), 3.72–3.80 (m, 10 H, OCH_2CH_2N + CH_2-EG), 3.83–3.88 (m, 4 H, CH_2-EG), 3.97 (s, 4 H, OCH_2CO), 3.95–4.03 (m, 6 H, 5-H), 4.06–4.15 (m, 4 H, CH_2-EG), 4.12 (dd, J = 2.1, 12.1 Hz, 6 H, 6-H), 4.27 (dd, J = 5.3, 12.2 Hz, 6 H, 6′-H), 4.35–4.38 (m, 4 H, CH_2-EG), 4.83 (d, J = 1.0 Hz, 6 H, 1-H), 5.25 (dd, J = 1.5, 2.8 Hz, 6 H, 2-H), 5.27 (dd, J = 10.0, 10.0 Hz, 6 H, 4-H), 5.31 (dd, ^3J = 3.0, 10.2 Hz, 6 H, 3-H), 6.75 (t, J = 5.4 Hz, 6 H, N*H*), 6.78 (s, 2 H, N*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 20.67 (12 C), 20.72 (6 C), 20.84 (6 C), 30.59 (6 C), 31.35 (6 C), 38.93 (6 C), 51.26 (2 C), 58.11 (2 C), 62.39 (6 C), 66.00 (6 C), 67.00 (6 C), 68.60 (6 C), 69.11 (6 C), 69.31 (6 C), 70.20 (2 C), 70.27 (2 C), 70.74 (2 C), 71.09 (2 C), 97.60 (6 C), 130.56 (2 C), 131.31 (1 C), 132.70 (2 C), 134.55 (2 C), 135.15 (2 C), 137.15 (2 C), 138.86 (2 C), 139.02 (2 C), 139.34 (2 C), 139.53 (2 C), 141.03 (2 C), 141.50 (2 C), 141.58 (2 C), 141.99 (2 C), 142.61 (2 C), 143.33 (2 C), 143.49 (2 C), 143.73 (2 C), 143.89 (2 C), 144.03 (1 C), 144.11 (4 C), 144.19 (2 C), 144.57 (2 C), 144.60 (2 C), 144.85 (2 C), 144.97 (2 C), 145.12 (2 C), 145.48 (1 C), 146.78 (2 C), 147.53 (2 C), 163.04 (1 C), 169.42 (2 C), 169.67 (6 C), 170.03 (6 C), 170.04 (6 C), 170.67 (6 C), 172.97 (6 C) ppm. IR (ATR): $\tilde{\nu}$ = 2937, 1745, 1660, 1532, 1432, 1370, 1220, 1135, 1081, 1042, 977, 896, 753, 687 cm^{-1}. UV/Vis (CH_2Cl_2): λ = 256, 324 nm. MS (FAB, NBA): m/z = 3740 $[M + H]^+$, 1512 $[M - 1\times\text{adduct-}C_{60}]^+$, 720 $[C_{60}]^+$. $C_{188}H_{190}N_{10}O_{72}\cdot 2.5CH_2Cl_2$ (3739.15): calcd. C 57.87, H 4.97, N. 3.54; found C 57.42, H 5.09, N 3.65.

1a*H*-1,9-[(2-{2-[(Tris{2-[2-(α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)carbamomethoxy]ethoxy}ethyl)imino]-1a-(2-{2-[(tris{2-[2-(α-D-mannopyranosyloxy)ethylcarbamoyl]ethyl}methyl)carbamoylmethoxy]ethoxy}ethyl)-1,9-dihydro-1a-aza-1(2)a-homo(C_{60}-I_h)[5,6]fullerene (17): Sugar deprotection of **16** was carried out under Zemplén conditions.[17] To a solution of **16** (33 mg 14.8 μmol) in MeOH (7 mL) was added MeOH (1.0 mL) contain-

ing a catalytic amount of MeONa (1.0 mg, 19 μmol), and this mixture was stirred for 2 h. The resulting precipitate was collected and washed with MeOH to give **11** as a brown solid. Yield: 20 mg (quant). ^{1}H NMR (300 MHz, D_2O, 300 K): δ = 1.70–2.30 (br., 24 H, CH_2-dendron), 3.2–3.9 (br., 80 H, mannose + CH_2-EG + NHCH_2CH_2O) ppm. ^{13}C NMR (75 MHz, D_2O, 300 K): δ = 30.3 (br., 12 C), 39.4 (br., 6 C), 61.3 (br., 6 C), 66.1 (br., 6 C), 66.4 (br., 6 C), 70.4 (br., 6 C), 70.9 (br., 6 C), 73.2 (br., 6 C), 100.0 (br., 6 C), 127–153 (br., 59 C), 171.3 (br., 2 C), 175.8 (br., 6 C) ppm. IR (ATR): $\tilde{\nu}$ = 3358, 2934, 1640, 1544, 1455, 1420, 1135, 1092, 1058, 969, 807, 730, 683 cm^{-1}. UV/Vis (CH_2Cl_2): λ = 217, 256 nm. MS (MALDI, CHCA): *m/z* = 2758 [M + 4Li]$^+$. $C_{140}H_{142}N_{10}O_{48}$·11$H_2O$ (2930.83): calcd. C 57.37, H 5.64, N 4.78; found C 57.20, H 5.64, N 4.78.

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