Electronic supplementary information

for the manuscript

A regioselective step-by-step C₆₀Cl₆ functionalization approach affords a novel family of C₆₀Ar₅Th'Th''H fullerene derivatives with promising antiviral properties

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General information

Reagents and solvents were purchased from Sigma-Aldrich, Acros, Chimmed and used without purification unless noted otherwise. Arylation reactions were monitored by analytical HPLC (Shimadzu, Japan) using ULTREMEX 5 C18 150*4.60 mm or Orbit C18 5u 150*4.60 mm (MZ-Analysentechnik, Germany) columns and toluene/acetonitrile mixtures as eluent. Preparative HPLC (Shimadzu, Japan) was performed using Reprosil-Pur Basic C18 250*20 mm (Dr. Maisch, Germany) columns and toluene/acetonitrile mixtures as eluent. ¹H NMR, ¹³C NMR, ¹⁹F NMR, ¹H-¹H COSY, ¹H-¹³C HSQC and ¹H-¹³C HMBC, ¹H-¹H ROESY spectra were recorded on Bruker AVANCE 600 [600 MHz (¹H), 151 MHz (¹³C)] and Bruker AVANCE-III 500 [500 MHz (¹H), 126 MHz (¹³C)] spectrometers. MALDI mass spectra (negative ion mode) were acquired using a Bruker AutoFlex reflector time-of-flight device (N₂ laser, 337 nm, 2.5 ns pulse). Trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB, \geq 98%, Sigma-Aldrich) was used as a matrix, the matrix-to-analyte molar ratio being 1000–4000.

Synthetic procedures

Synthesis of fullerene derivatives 2-3

Compounds 2-3 were synthesized for the first time using the approach described in our previous paper (Org. Lett., 2021, 23, 18, 7226).

Fullerene derivative C₆₀Ar₅Cl with five residues of methyl 2-(2-fluoro-[1,1'-biphenyl]-4vl)propanoate (methyl ester of flurbiprofen) and one chlorine atom attached to the cage (200 mg, 1 eg.) was dissolved in 40 mL of 1,2-dichlorobenzene in a three-necked round bottom flask equipped with condenser, thermometer, stopper, and teflon-coated magnetic stirring bar. The system was degassed and filled with argon. Then thiophene derivative (methyl 2-(thiophen-2-yl)acetate or methyl 3-(thiophen-2-yl)propanoate, 20 eq.), distilled water (100 μ L), and SnCl₄ (100 μ L) were added to the reaction mixture. The reaction mixture was heated to 80°C and stirred at this temperature until HPLC profile demonstrated full conversion of C₆₀Ar₅Cl. Reaction mixture was allowed to cool down to the room temperature, diluted with toluene, and poured on the top of silica gel column. Reaction mixture was eluted using toluene and toluene/methanol mixtures (up to 80%/20% v/v). The toluene/methanol solution was concentrated at the rotary evaporator, residue was washed with acetonitrile or methanol, dried in air, dissolved in toluene/acetonitrile mixture (80%/20% v/v), filtered through the 450 µm PTFE syringe filter. Preparative HPLC was used to purify compounds 2-3. Conditions: Reprosil-Pur Basic C18 250*20 mm (Dr. Maisch, Germany) column, toluene/acetonitrile mixture (20%/80% v/v), 5 mL/min, 40°C, detector - 290 nm and 350 nm. Compounds 2-3 were obtained with 35-63% yields and appeared as brown powders.



Synthesis of fullerene derivatives 4-8

Fullerene derivative 1, 2 or 3 (200 mg, 1 eq.) was dissolved in 10 mL of 1,2dichlorobenzene, the reaction system was degassed and filled with argon. Then a thiophene derivative (2-methylthiophene, methyl 2-(thiophen-2-yl) acetate or methyl 3-(thiophen-2-yl) propanoate) (50 eq.) and $SnCl_4$ (100 μ L) were added to the reaction mixture in one portion. The reaction mixture was heated to 100°C and stirred at this temperature until the peak of the precursor fullerene derivative 1, 2 or 3 disappeared at the HPLC profile (approximately 20-24 h). Then the reaction mixture was cooled to room temperature, diluted with toluene and poured onto the top of the silica gel column. Elution with toluene and then toluene/acetonitrile (up to 80%/20% v/v) mixtures and concentration of the obtained solutions at the rotary evaporator produced brown or red solid. The obtained solid residue was washed with acetonitrile, dried in air, dissolved in toluene/acetonitrile mixture (80%/20% v/v), filtered through the 0.45 µm PTFE syringe filter and processed using preparative HPLC (Reprosil-Pur Basic C18 250*20 mm, Dr. Maisch, Germany) column, toluene/acetonitrile mixture (20%/80% v/v) as eluent, flow 5 mL/min, temperature 40°C, detection at 290 nm and 350 nm. Pure fractions were concentrated in vacuum and the resulting residue was washed with methanol and acetonitrile. Compounds 4-8 were obtained with 40-52% yields and appeared as orange or red powders.

Synthesis of fullerene derivatives A2-A7

Fullerene derivative **2-7** (50-100 mg) was placed into a double-necked round bottom 100 mL flask equipped with a stirring bar, condenser, and thermometer and dissolved in toluene (30 mL). Acetic acid (30 mL) and hydrochloric acid (5 mL) were added. The reaction mixture was heated to 60-70°C and stirred at this temperature for 4-5 days. Finally, the obtained solution was concentrated at the rotary evaporator, solid residue was washed with acetonitrile and dried to produce brown (**A2, A3**) or orange-red (**A4-A8**) powders with an almost quantitative (95-100%) yield. The obtained powders were soluble in methyl sulfoxide, tetrahydrofuran, insoluble in toluene, methanol, and acetonitrile.

Synthesis of water-soluble fullerene derivatives K2-K7

The solution of anhydrous K_2CO_3 (3.0 eq. for **A2-A3**, **A5**, 3.5 eq. for **A4**, **A6-A7**) in distilled water (15 mL) was prepared. Then a fullerene-based polycarboxylic acid (**A2-A7**) (1 eq.) was added and the reaction mixture was stirred at room temperature until complete material dissolution. Obtained solution was filtered through PES syringe filter

(pore size 0.45 $\mu m)$ and freeze-dried. Water-soluble salts K2-K7 were obtained with quantitative yields.

Spectroscopic data

Compound 1. Compound 1 was synthesized and characterized previously (*Org. Lett.*, 2021, 23, 18, 7226).

Compound 2 (yield 63%).¹H NMR (600 MHz, CDCl₃, δ , ppm): 1.48-1.57 (m, 12H, CHC<u>H</u>₃), 1.59 (d, J = 7.2 Hz, 3H, CHC<u>H</u>₃), 3.48 – 3.86 (m, 25H, C<u>H</u>CH₃+OC<u>H</u>₃+C<u>H</u>₂), 6.50 (d, J = 3.4 Hz, 1H, C<u>H</u>), 6.65 (d, J = 3.5 Hz, 1H, C<u>H</u>), 6.94-7.26 (m, 19H, C<u>H</u>), 7.30-7.65 (m, 11H, C<u>H</u>), 7.66-8.13 (m, 5H, C<u>H</u>).

¹³C NMR (151 MHz, CDCl₃, δ, ppm): 18.47 (CH<u>C</u>H₃), 18.55 (CH<u>C</u>H₃), 35.37 (<u>C</u>H₂), 44.86 (<u>C</u>HCH₃), 44.90 (<u>C</u>HCH₃), 44.95 (<u>C</u>HCH₃), 52.14 (COO<u>C</u>H₃), 52.24 (COO<u>C</u>H₃), 52.28 (COO<u>C</u>H₃), 52.30 (COO<u>C</u>H₃), 58.12 (<u>C</u>sp³_{cage}), 58.63 (<u>C</u>sp³_{cage}), 59.80 (<u>C</u>sp³_{cage}), 61.91 (<u>C</u>sp³_{cage}), 62.00 (<u>C</u>sp³_{cage}), 67.71 (<u>C</u>sp³_{cage}), 115.04, 115.17, 115.25, 115.33, 115.40, 123.36, 123.39, 123.41, 123.57, 123.61, 123.63, 123.66, 126.31, 126.67, 127.00, 127.07, 127.16, 127.85, 127.93, 128.03, 128.51, 128.52, 129.17, 129.19, 129.47, 129.48, 129.95, 129.97, 130.74, 130.76, 130.87, 130.89, 133.59, 134.19, 134.66, 134.94, 135.12, 135.43, 135.90, 136.23, 136.88, 138.41, 139.03, 139.75, 141.41, 141.62, 141.68, 142.03, 142.05, 142.07, 142.29, 142.81, 142.87, 143.20, 143.29, 143.44, 143.68, 143.87, 143.97, 144.10, 144.33, 144.48, 144.64, 144.88, 145.25, 145.50, 145.53, 145.74, 145.76, 146.07, 146.26, 146.81, 146.84, 147.04, 147.23, 147.27, 147.44, 147.47, 147.49, 148.05, 148.30, 148.48, 149.23, 149.25, 149.40, 149.43, 149.45, 149.64, 149.92, 150.39, 150.92, 151.32, 151.93, 151.96, 151.97, 152.73, 153.07, 155.18, 156.10, 156.79, 158.70, 158.77, 158.85, 158.89, 158.91, 160.42, 160.50, 160.54, 160.55, 170.52 (<u>C</u>OOCH₃), 174.43 (<u>C</u>OOCH₃), 174.44 (<u>C</u>OOCH₃).

MALDI MS (DCTB): found m/z = 2161.6 (main isotomer); calcd. for $C_{147}H_{77}F_5O_{12}S$ ([M]⁻, second isotomer) m/z= 2161.5.

Compound 3 (yield 35%). ¹H NMR (600 MHz, CDCl₃, δ , ppm): 1.47-1.61 (m, 15H, CHC<u>H₃</u>), 2.35-2.46 (m, 2H, C<u>H</u>₂), 2.88 (t, J = 6.2 Hz, 2H, C<u>H</u>₂), 3.56 (s, 3H, OC<u>H</u>₃), 3.66-3.83 (m, 20H, C<u>H</u>+OC<u>H</u>₃), 6.39 (d, J = 3.4 Hz, 1H, C<u>H</u>), 6.65 (d, J = 3.5 Hz, 1H, C<u>H</u>), 6.94-7.27 (m, 18H, C<u>H</u>), 7.30-8.16 (m, 17H, C<u>H</u>).

¹³C NMR (151 MHz, CDCl₃, δ, ppm): 18.47 (CH<u>C</u>H₃), 18.49 (CH<u>C</u>H₃), 18.56 (CH<u>C</u>H₃), 25.18 (<u>C</u>H₂), 35.82 (<u>C</u>H₂), 44.86 (<u>C</u>HCH₃), 44.91 (<u>C</u>HCH₃), 44.96 (<u>C</u>HCH₃), 51.61 (COO<u>C</u>H₃), 52.24 (COO<u>C</u>H₃), 52.28 (COO<u>C</u>H₃), 52.30 (COO<u>C</u>H₃), 58.11 (<u>C</u>sp³_{cage}), 58.63 (<u>C</u>sp³_{cage}), 59.79 (<u>C</u>sp³_{cage}), 61.90 (<u>C</u>sp³_{cage}), 62.08 (<u>C</u>sp³_{cage}), 67.67 (<u>C</u>sp³_{cage}), 115.16, 115.18, 115.24, 115.33, 115.40, 123.36, 123.64, 124.14, 126.55, 127.01, 127.08, 127.17, 127.31, 127.39, 127.48, 127.85, 127.93, 128.04, 128.51, 128.53, 129.17, 129.19, 129.47, 129.48, 129.97, 130.67, 130.70, 130.74, 130.77, 130.88, 130.90, 133.56, 134.18, 134.65, 134.94, 135.11, 135.80,

136.23, 136.88, 138.43, 139.04, 139.76, 141.39, 141.63, 141.66, 141.83, 141.88, 142.02, 142.05, 142.34, 142.81, 142.85, 143.23, 143.43, 143.69, 143.87, 143.95, 143.96, 144.04, 144.10, 144.32, 144.46, 144.66, 144.86, 145.25, 145.47, 145.73, 145.88, 146.09, 146.26, 146.79, 146.86, 147.03, 147.22, 147.25, 147.28, 147.44, 147.48, 148.03, 148.30, 148.47, 148.73, 148.75, 149.25, 149.26, 149.39, 149.43, 149.45, 149.63, 149.92, 150.39, 150.88, 151.30, 151.97, 152.78, 153.07, 155.41, 156.10, 156.81, 158.70, 158.79, 158.85, 158.89, 158.92, 160.35, 160.44, 160.50, 160.54, 160.57, 172.73 (\underline{COOCH}_3), 174.44 (\underline{COOCH}_3), 174.47 (\underline{COOCH}_3).

MALDI MS (DCTB): found m/z= 2175.6 (main isotopomer); calcd. for $C_{148}H_{79}F_5O_{12}S$ ([M]⁻, second isotopomer) m/z= 2175.5.

Compound 4 (yield 43%). ¹H NMR (500 MHz, CDCl₃, δ , ppm): 2.36-2.48 (m, 4H, C<u>H</u>₂), 2.52-2.61 (m, 4H, C<u>H</u>₂), 2.61-2.76 (m, 6H, C<u>H</u>₂), 2.83-3.02 (m, 6H, C<u>H</u>₂), 3.57 (s, 2H, C<u>H</u>₂), 3.62-3.72 (m, 18H, OC<u>H</u>₃), 3.75 (s, 3H, OC<u>H</u>₃), 3.77 (s, 2H, C<u>H</u>₂), 5.08 (s, 1H, Csp³_{cage}-<u>H</u>), 5.80-6.34 (m, 2H, C<u>H</u>), 6.41-6.49 (m, 1H, C<u>H</u>), 6.49-6.57 (m, 1H, C<u>H</u>), 6.62 (d, *J* = 7.9 Hz, 2H, C<u>H</u>), 6.65 (d, *J* = 3.3 Hz, 1H, C<u>H</u>), 6.73 (d, *J* = 2.6 Hz, 1H, C<u>H</u>), 6.82 (d, *J* = 7.9 Hz, 2H, C<u>H</u>), 6.91 (d, *J* = 7.9 Hz, 2H, C<u>H</u>), 6.93-7.00 (m, 1H, C<u>H</u>), 7.05 (d, *J* = 7.6 Hz, 4H, C<u>H</u>), 7.08-7.13 (m, 1H, C<u>H</u>), 7.16 (d, *J* = 7.8 Hz, 2H, C<u>H</u>), 7.20-7.27 (m, 1H, C<u>H</u>), 7.49 (d, *J* = 7.8 Hz, 2H, C<u>H</u>), 7.52-7.74 (m, 1H, C<u>H</u>).

¹³C NMR (126 MHz, CDCl₃, δ, ppm): 30.28 (<u>C</u>H₂), 30.36 (<u>C</u>H₂), 30.42 (<u>C</u>H₂), 30.53 (<u>C</u>H₂), 30.55 (<u>C</u>H₂), 35.20 (<u>C</u>H₂), 35.32 (<u>C</u>H₂), 35.54 (<u>C</u>H₂), 35.64 (<u>C</u>H₂), 35.88 (<u>C</u>H₂), 36.06 (<u>C</u>H₂), 51.59 (COO<u>C</u>H₃), 51.64 (COO<u>C</u>H₃), 51.67 (COO<u>C</u>H₃), 52.17 (COO<u>C</u>H₃), 52.31 (COO<u>C</u>H₃), 57.48 (<u>C</u>sp³cage), 57.97 (<u>C</u>sp³cage), 58.46 (<u>C</u>sp³cage), 59.03 (<u>C</u>sp³cage), 59.17 (<u>C</u>sp³cage), 60.58 (<u>C</u>sp³cage), 60.92 (<u>C</u>sp³cage), 67.77 (<u>C</u>sp³cage), 124.85, 126.69, 126.90, 127.50, 127.83, 127.87, 127.88, 128.30, 128.62, 128.74, 130.93, 133.44, 133.58, 134.79, 135.84, 136.91, 138.50, 138.70, 138.75, 139.44, 139.72, 139.93, 141.02, 141.89, 141.94, 142.32, 143.63, 144.47, 144.84, 145.31, 145.78, 145.86, 146.23, 146.30, 146.36, 146.44, 146.60, 146.63, 146.71, 146.87, 149.32, 147.43, 147.72, 147.75, 147.81, 147.90, 148.57, 148.83, 149.09, 149.20, 149.32, 149.39, 149.51, 149.55, 149.59, 149.63, 150.16, 150.95, 151.27, 152.07, 152.15, 153.26, 153.47, 154.85, 155.14, 155.79, 157.19, 157.46, 170.52 (<u>C</u>OOCH₃), 170.81 (<u>C</u>OOCH₃), 173.27 (<u>C</u>OOCH₃).

MALDI MS (DCTB): found m/z = 1847.4, 1692.3 (main isotopomers); calcd. for $C_{124}H_{70}O_{14}S_2$ ([M]⁻, second isotopomer) m/z = 1847.4, $C_{117}H_{63}O_{12}S$ ([M– $C_4H_2SCH_2COOCH_3$]⁻, second isotopomer) m/z =1692.4.

Compound 5 (yield 41%).¹H NMR (600 MHz, CDCl₃, δ , ppm): 2.43 (s, 3H, C<u>H₃</u>), 2.39 – 2.46 (m, 4H, C<u>H₂</u>), 2.53 – 2.60 (m, 4H, C<u>H₂</u>), 2.63 – 2.67 (m, 2H, C<u>H₂</u>), 2.68 – 2.71 (m, 2H, C<u>H₂</u>),

2.71 – 2.74 (m, 2H, C<u>H</u>₂), 2.84 – 2.88 (m, 2H, C<u>H</u>₂), 2.88 – 2.92 (m, 2H, C<u>H</u>₂), 2.93 – 2.98 (m, 2H, C<u>H</u>₂), 3.55 (s, 2H, C<u>H</u>₂), 3.64 (s, 3H, OC<u>H</u>₃), 3.66 (s, 6H, OC<u>H</u>₃), 3.68 (s, 3H, OC<u>H</u>₃), 3.69 (s, 3H, OC<u>H</u>₃), 3.70 (s, 3H, OC<u>H</u>₃), 5.06 (s, 1H, Csp³_{cage}-<u>H</u>), 6.22 – 6.34 (m, 1H, C<u>H</u>), 6.46 (d, J = 3.3 Hz, 1H, C<u>H</u>), 6.51 (s, 1H, C<u>H</u>), 6.53 (d, J = 2.6 Hz, 1H, C<u>H</u>), 6.60 (d, J = 3.4 Hz, 1H, C<u>H</u>), 6.62 (d, J = 8.1 Hz, 2H, C<u>H</u>), 6.66 – 6.77 (m, 2H, C<u>H</u>), 6.82 (d, J = 8.0 Hz, 2H, C<u>H</u>), 6.90 (d, J = 8.1 Hz, 2H, C<u>H</u>), 7.04 (d, J = 7.9 Hz, 4H, C<u>H</u>), 7.07 – 7.12 (m, 2H, C<u>H</u>), 7.15 (d, J = 8.0 Hz, 2H, C<u>H</u>), 7.48 (d, J = 7.9 Hz, 2H, C<u>H</u>), 7.51 – 7.62 (m, 1H).

¹³C NMR (126 MHz, CDCl₃, δ, ppm): 15.32 (<u>C</u>H₃), 30.27 (<u>C</u>H₂), 30.36 (<u>C</u>H₂), 30.42 (<u>C</u>H₂), 30.52 (<u>C</u>H₂), 35.28 (<u>C</u>H₂), 35.56 (<u>C</u>H₂), 35.66 (<u>C</u>H₂), 35.90 (<u>C</u>H₂), 36.08 (<u>C</u>H₂), 51.62 (COO<u>C</u>H₃), 51.67 (COO<u>C</u>H₃), 51.70 (COO<u>C</u>H₃), 52.19 (COO<u>C</u>H₃), 57.46 (<u>C</u>sp³_{cage}), 58.03 (<u>C</u>sp³_{cage}), 58.44 (<u>C</u>sp³_{cage}), 59.00 (<u>C</u>sp³_{cage}), 59.15 (<u>C</u>sp³_{cage}), 60.57 (<u>C</u>sp³_{cage}), 60.88 (<u>C</u>sp³_{cage}), 67.76 (<u>C</u>sp³_{cage}), 124.88, 125.09, 126.69, 126.73, 126.85, 126.94, 127.50, 127.86, 128.30, 128.62, 128.73, 133.34, 135.81, 135.85, 136.94, 138.47, 138.68, 138.76, 139.42, 139.70, 139.73, 139.75, 139.92, 141.95, 141.98, 143.70, 144.46, 144.87, 145.31, 145.76, 145.86, 146.22, 146.28, 146.41, 146.47, 146.63, 146.70, 146.91, 146.96, 147.42, 147.70, 147.75, 147.89, 148.04, 148.56, 148.82, 149.07, 149.20, 149.25, 149.36, 149.51, 149.59, 152.08, 153.83, 154.91, 155.14, 155.79, 157.19, 170.50 (<u>C</u>OOCH₃), 173.20 (<u>C</u>OOCH₃), 173.26 (<u>C</u>OOCH₃).

MALDI MS (DCTB): found m/z= 1789.4, 1692.4 (main isotopomers); calcd. for $C_{122}H_{68}O_{12}S_2$ ([M]⁻, second isotopomer) m/z= 1789.4, $C_{122}H_{68}O_{12}S_2$ ([M– $C_4H_2SCH_3$]⁻, second isotopomer) m/z= 1692.4.

Compound 6 (yield 40%). ¹H NMR (500 MHz, CDCl₃, δ , ppm): 2.38-2.47 (m, 4H, C<u>H</u>₂), 2.50-2.61 (m, 4H, C<u>H</u>₂), 2.65 (t, J = 7.7 Hz, 4H, C<u>H</u>₂), 2.68-2.77 (m, 4H, C<u>H</u>₂), 2.84-2.99 (m, 6H, C<u>H</u>₂), 3.08 (t, J = 7.7 Hz, 2H, C<u>H</u>₂), 3.57 (s, 2H, C<u>H</u>₂), 3.64 (s, 3H, OC<u>H</u>₃), 3.67 (s, 3H, OC<u>H</u>₃), 3.67 (s, 3H, OC<u>H</u>₃), 3.68 (s, 3H, OC<u>H</u>₃), 3.69 (s, 3H, OC<u>H</u>₃), 3.71 (s, 3H, OC<u>H</u>₃), 3.71 (s, 3H, OC<u>H</u>₃), 5.06 (s, 1H, Csp³_{cage}-<u>H</u>), 5.70-6.36 (m, 2H, C<u>H</u>), 6.46 (d, J = 3.4 Hz, 1H), 6.50-6.55 (m, 1H), 6.58-6.64 (m, 3H), 6.66 (d, J = 3.5 Hz, 1H), 6.67-6.78 (m, 1H), 6.82 (d, J = 8.2 Hz, 2H, C<u>H</u>), 6.91 (d, J = 8.2 Hz, 2H, C<u>H</u>), 7.05 (d, J = 8.0 Hz, 4H, C<u>H</u>), 7.07-7.14 (m, 1H, C<u>H</u>), 7.16 (d, J = 8.1 Hz, 2H, C<u>H</u>), 7.18-7.26 (m, 1H, C<u>H</u>), 7.30-7.45 (m, 1H, C<u>H</u>), 7.49 (d, J = 8.1 Hz, 2H, C<u>H</u>).

¹³C NMR (126 MHz, CDCl₃, δ, ppm): 25.34 (<u>C</u>H₂), 29.71 (<u>C</u>H₂), 30.27 (<u>C</u>H₂), 30.35 (<u>C</u>H₂), 30.41 (<u>C</u>H₂), 30.51 (<u>C</u>H₂), 30.54 (<u>C</u>H₂), 35.16 (<u>C</u>H₂), 35.53 (<u>C</u>H₂), 35.63 (<u>C</u>H₂), 35.65 (<u>C</u>H₂), 35.87 (<u>C</u>H₂), 36.04 (<u>C</u>H₂), 51.57 (COO<u>C</u>H₃), 51.62 (COO<u>C</u>H₃), 51.65 (COO<u>C</u>H₃), 51.77 (COO<u>C</u>H₃), 52.14 (COO<u>C</u>H₃), 57.48 (<u>C</u>sp³_{cage}), 58.03 (<u>C</u>sp³_{cage}), 58.45 (<u>C</u>sp³_{cage}), 59.02 (<u>C</u>sp³_{cage}), 59.17 (<u>C</u>sp³_{cage}), 60.59 (<u>C</u>sp³_{cage}), 60.93 (<u>C</u>sp³_{cage}), 67.79 (<u>C</u>sp³_{cage}), 124.61, 124.85, 126.68, 126.88, 127.49, 127.83, 127.86, 127.88, 128.28, 128.60, 128.71, 133.42, 133.57, 135.85, 136.91, 138.50, 138.70, 138.75, 139.44, 139.71, 139.84, 139.93, 139.95, 141.03, 141.92, 141.95,

142.33, 143.04, 143.68, 144.46, 144.86, 145.31, 145.78, 145.86, 146.23, 146.30, 146.37, 146.43, 146.53, 146.63, 146.71, 146.90, 146.97, 147.24, 147.43, 147.72, 147.75, 147.81, 147.90, 148.57, 148.61, 148.83, 149.09, 149.20, 149.31, 149.38, 149.39, 149.49, 149.54, 149.59, 149.64, 150.95, 151.26, 152.07, 152.14, 153.40, 153.62, 154.88, 155.15, 155.79, 157.20, 157.49, 170.47 ($\underline{C}OOCH_3$), 172.81 ($\underline{C}OOCH_3$), 173.14 ($\underline{C}OOCH_3$), 173.16 ($\underline{C}OOCH_3$), 173.22 ($\underline{C}OOCH_3$).

MALDI MS (DCTB): found m/z = 1861.3, 1692.4, 1691.4 (main isotopomers); calcd. for $C_{125}H_{72}O_{14}S_2$ ([M]⁻, second isotopomer) m/z = 1861.4, $C_{117}H_{63}O_{12}S$ ([M– $C_4H_2SCH_2CH_2COOCH_3$ second isotopomer) m/z = 1692.4, $C_{117}H_{62}O_{12}S$ ([M– $C_4H_2SCH_2CH_2COOCH_3-H^{-}$, second isotopomer) m/z = 1691.4.

Compound 7 (yield 42%). ¹H NMR (600 MHz, CDCl₃, δ , ppm): 1.39-1.65 (m, 15H, CHC<u>H</u>₃), 3.47-3.86 (m, 30H, C<u>H</u>CH₃+OC<u>H</u>₃+C<u>H</u>₂), 5.17 (s, 1H, Csp³_{cage}-<u>H</u>), 6.46-6.53 (m, 1H, C<u>H</u>), 6.59-6.68 (m, 1H, C<u>H</u>), 6.68-6.73 (m, 1H, C<u>H</u>), 6.74-6.79 (m, 1H, C<u>H</u>), 6.85-7.26 (m, 21H, C<u>H</u>), 7.29 – 7.54 (m, 12H, C<u>H</u>), 7.73 (d, J = 7.7 Hz, 2H, C<u>H</u>).

¹³C NMR (151 MHz, CDCl₃, δ, ppm): 18.46 (CH<u>C</u>H₃), 18.53 (CH<u>C</u>H₃), 35.29 (<u>C</u>H₂), 35.35 (<u>C</u>H₂), 44.85 (<u>C</u>HCH₃), 44.88 (<u>C</u>HCH₃), 44.92 (<u>C</u>HCH₃), 52.16 (COO<u>C</u>H₃), 52.25 (COO<u>C</u>H₃), 52.29 (COO<u>C</u>H₃), 52.41 (COO<u>C</u>H₃), 57.66 (<u>C</u>sp³_{cage}), 58.06 (<u>C</u>sp³_{cage}), 58.67 (<u>C</u>sp³_{cage}), 59.17 (<u>C</u>sp³_{cage}), 59.32 (<u>C</u>sp³_{cage}), 60.77 (<u>C</u>sp³_{cage}), 61.05 (<u>C</u>sp³_{cage}), 67.98 (<u>C</u>sp³_{cage}), 114.97, 115.01, 115.10, 115.15, 115.17, 115.22, 115.25, 115.31, 115.38, 123.36, 123.53, 123.61, 124.96, 127.01, 127.16, 127.25, 127.81, 127.83, 127.90, 128.31, 128.32, 129.09, 129.37, 129.39, 129.63, 130.72, 130.74, 130.80, 130.83, 133.31, 133.43, 133.86, 134.51, 134.76, 134.87, 137.05, 138.26, 139.94, 140.00, 140.02, 141.56, 141.60, 141.74, 141.92, 141.97, 142.13, 142.30, 143.67, 144.84, 144.93, 145.44, 145.81, 145.99, 146.23, 146.45, 146.58, 146.70, 146.77, 146.97, 147.13, 147.30, 147.48, 147.59, 147.77, 147.82, 147.97, 148.03, 148.64, 148.89, 148.92, 149.07, 149.14, 149.27, 149.41, 149.47, 149.56, 149.59, 149.69, 150.10, 151.33, 152.07, 152.17, 152.18, 153.47, 153.55, 153.57, 154.91, 154.92, 154.94, 154.95, 156.18, 157.16, 157.65, 157.71, 157.76, 158.67, 158.74, 158.82, 158.84, 158.88, 160.32, 160.39, 160.47, 160.48, 160.52, 170.64 (<u>C</u>OOCH₃), 170.94 (<u>C</u>OOCH₃), 174.49 (<u>C</u>OOCH₃), 174.50 (<u>C</u>OOCH₃), 174.52 (<u>C</u>OOCH₃).

MALDI MS (DCTB): found m/z = 2318.6, 2162.5 (main isotopomers); calcd. for $C_{154}H_{85}F_5O_{14}S_2$ ([M]⁻, third isotopomer) m/z = 2318.5, $C_{147}H_{78}F_5O_{12}S$ ([M– $C_4H_2SCH_2COOCH_3$]⁻, second isotopomer) m/z = 2162.5.

Compound 8 (yield 52%). ¹H NMR (600 MHz, CDCl₃, δ , ppm): 1.47-1.60 (m, 15H, CHC<u>H</u>₃), 2.35-2.42 (m, 2H, C<u>H</u>₂), 2.66 (t, *J* = 7.6 Hz, 2H, C<u>H</u>₂), 2.89 (t, *J* = 7.2 Hz, 2H, C<u>H</u>₂), 3.09 (t, *J* = 7.5 Hz, 2H, C<u>H</u>₂), 3.56 (s, 3H, OC<u>H</u>₃), 3.68 (s, 3H, OC<u>H</u>₃), 3.69-3.71 (m, 9H, OC<u>H</u>₃), 3.72 (s, 3H,

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OC<u>H₃</u>), 3.73 (s, 3H, OC<u>H₃</u>), 3.73-3.81 (m, 5H, C<u>H</u>CH₃), 5.13 (s, 1H, Csp³_{cage}-<u>H</u>), 6.38 (d, *J* = 3.1 Hz, 1H, C<u>H</u>), 6.53-6.60 (m, 1H, C<u>H</u>), 6.63 (d, *J* = 3.0 Hz, 1H, C<u>H</u>), 6.68 (d, *J* = 3.4 Hz, 1H, C<u>H</u>), 6.92-7.25 (m, 21H, C<u>H</u>), 7.29-7.65 (m, 12H, C<u>H</u>), 7.73 (d, *J* = 7.9 Hz, 2H, C<u>H</u>).

¹³C NMR (151 MHz, CDCl₃, δ, ppm): 18.44 (CH<u>C</u>H₃), 18.46 (CH<u>C</u>H₃), 18.53 (CH<u>C</u>H₃), 25.15 (<u>C</u>H₂), 25.37 (<u>C</u>H₂), 35.62 (<u>C</u>H₂), 36.10 (<u>C</u>H₂), 44.84 (<u>C</u>HCH₃), 44.88 (<u>C</u>HCH₃), 44.92 (<u>C</u>HCH₃), 51.61 (COO<u>C</u>H₃), 51.85 (COO<u>C</u>H₃), 52.22 (COO<u>C</u>H₃), 52.25 (COO<u>C</u>H₃), 52.27 (COO<u>C</u>H₃), 57.65 (<u>C</u>sp³_{cage}), 58.07 (<u>C</u>sp³_{cage}), 58.67 (<u>C</u>sp³_{cage}), 59.16 (<u>C</u>sp³_{cage}), 59.32 (<u>C</u>sp³_{cage}), 60.87 (<u>C</u>sp³_{cage}), 61.07 (<u>C</u>sp³_{cage}), 68.00 (<u>C</u>sp³_{cage}), 114.94, 114.96, 115.04, 115.09, 115.11, 115.15, 115.20, 115.25, 115.30, 115.37, 123.39, 123.52, 124.66, 124.89, 127.07, 127.12, 127.15, 127.21, 127.25, 127.49, 127.80, 127.85, 127.90, 128.29, 128.31, 129.07, 129.09, 129.37, 129.39, 129.62, 130.64, 130.66, 130.72, 130.74, 130.77, 130.80, 130.81, 133.10, 133.40, 133.84, 134.49, 134.76, 134.85, 137.07, 138.29, 139.89, 139.94, 140.00, 141.55, 141.59, 141.75, 141.80, 141.92, 141.98, 142.12, 143.05, 143.71, 144.87, 144.92, 145.43, 145.83, 145.99, 146.23, 146.44, 146.59, 146.72, 146.76, 147.00, 147.12, 147.34, 147.59, 147.77, 147.80, 147.82, 148.03, 148.44, 148.57, 148.64, 148.89, 148.91, 148.98, 148.99, 149.13, 149.26, 149.41, 149.47, 149.48, 149.51, 149.59, 149.68, 152.18, 153.75, 154.92, 157.13, 158.66, 158.76, 158.84, 158.88, 160.31, 160.40, 160.48, 160.53, 172.64 (<u>C</u>OOCH₃), 172.78 (<u>COOCH₃), 174.42 (<u>COOCH₃), 174.45 (<u>COOCH₃), 174.48 (<u>COOCH₃).</u></u></u></u>

¹⁹F NMR (282 MHz, CDCl₃, δ, ppm): -117.00, -117.13, -117.17, -117.19, -117.25.

MALDI MS (DCTB): found m/z = 2345.6, 2176.5 (main isotopomers); calcd. for $C_{156}H_{89}F_5O_{14}S_2$ ([M]⁻, second isotopomer) m/z = 2345.6, $C_{148}H_{80}F_5O_{12}S$ ([M– $C_4H_2SCH_2CH_2COOCH_3$]⁻, second isotopomer) m/z = 2176.5.

Compound A2.¹H NMR (500 MHz, $(CD_3)_2SO$, δ , ppm): 1.31 – 1.46 (m, 15H, $CHC\underline{H}_3$), 3.51 (s, J = 4.7 Hz, 2H, C \underline{H}_2), 3.66 – 3.82 (m, 5H, C $\underline{H}CH_3$), 6.55 (d, J = 2.8 Hz, 1H, C \underline{H}), 6.72 (d, J = 2.8 Hz, 1H, C \underline{H}), 6.95 – 7.34 (m, 24H, C \underline{H}), 7.38 – 7.49 (m, 5H, C \underline{H}), 7.55 (d, J = 7.6 Hz, 2H, C \underline{H}), 7.70 (d, J = 7.5 Hz, 2H, C \underline{H}), 7.84 (d, J = 8.0 Hz, 2H, C \underline{H}), 12.44 (br s, 6H, COO \underline{H}).

¹³C NMR (126 MHz, (CD₃)₂SO, δ, ppm): 18.72 (CH<u>C</u>H₃), 18.82 (CH<u>C</u>H₃), 35.31 (<u>C</u>H₂), 44.53 (<u>C</u>HCH₃), 44.56 (<u>C</u>HCH₃), 44.60 (<u>C</u>HCH₃), 58.00 (<u>C</u>sp³_{cage}), 58.45 (<u>C</u>sp³_{cage}), 59.79 (<u>C</u>sp³_{cage}), 62.04 (<u>C</u>sp³_{cage} (2C)), 67.61 (<u>C</u>sp³_{cage}), 115.44, 115.59, 115.63, 115.77, 124.28, 124.34, 124.41, 124.53, 124.55, 125.92, 126.02, 126.07, 126.39, 126.49, 126.81, 128.00, 128.08, 128.14, 128.80, 128.81, 129.37, 129.40, 129.42, 130.02, 130.03, 130.76, 130.91, 130.94, 131.03, 131.06, 131.16, 131.18, 133.69, 134.27, 134.75, 135.10, 135.28, 135.61, 135.78, 136.62, 137.50, 138.07, 138.78, 139.14, 141.24, 141.80, 141.87, 141.96, 142.07, 142.75, 142.88, 142.90, 143.24, 143.49, 143.55, 143.71, 143.86, 143.88, 144.01, 144.28, 144.52, 144.67, 144.79, 145.27, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.27, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.27, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.89, 144.59, 145.55, 145.75, 145.75, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.89, 145.27, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.27, 145.74, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.75, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 145.75, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.76, 145.76, 146.08, 146.18, 146.61, 146.97, 147.07, 147.12, 147.24, 144.79, 145.76, 145.76, 146.76, 146.76, 145.

147.38, 147.43, 147.55, 147.86, 148.14, 148.38, 149.11, 149.20, 149.30, 149.34, 149.56, 149.57, 149.93, 150.22, 150.94, 151.19, 152.35, 153.22, 156.54, 156.71, 158.17, 158.23, 158.38, 158.41, 160.19, 160.25, 160.34, 160.37, 171.64 (<u>C</u>OOH), 175.28 (<u>C</u>OOH), 175.32 (<u>C</u>OOH), 175.35 (<u>C</u>OOH).

Compound A3.¹H NMR (500 MHz, (CD₃)₂SO, δ, ppm): 1.28 – 1.50 (m, 15H, CHC<u>H</u>₃), 2.27 (t, *J* = 8.3 Hz, 1H, C<u>H</u>₂), 2.72 (t, *J* = 8.1 Hz, 1H, C<u>H</u>₂), 3.63 – 3.84 (m, 5H, C<u>H</u>CH₃), 6.47 (s, 1H, C<u>H</u>), 6.71 (s, 1H, C<u>H</u>), 6.96 – 7.35 (m, 20H, C<u>H</u>), 7.40 – 7.49 (m, 4H, C<u>H</u>), 7.51 – 7.58 (m, 3H, C<u>H</u>), 7.58 – 7.64 (m, 1H, C<u>H</u>), 7.70 (d, *J* = 7.3 Hz, 2H, C<u>H</u>), 7.83 (d, *J* = 7.2 Hz, 2H, C<u>H</u>), 7.86 – 8.15 (m, 3H, C<u>H</u>), 12.41 (br s, 6H, COO<u>H</u>).

¹³C NMR (126 MHz, (CD₃)₂SO, δ, ppm): 18.72 (CH<u>C</u>H₃), 18.82 (CH<u>C</u>H₃), 25.10 (<u>C</u>H₂), 35.82 (<u>C</u>H₂), 44.53 (<u>C</u>HCH₃), 44.56 (<u>C</u>HCH₃), 58.00 (<u>C</u>sp³_{cage}), 58.44 (<u>C</u>sp³_{cage}), 59.78 (<u>C</u>sp³_{cage}), 62.01 (<u>C</u>sp³_{cage}), 62.07 (<u>C</u>sp³_{cage}), 67.61 (<u>C</u>sp³_{cage}), 115.45, 115.59, 115.62, 115.77, 124.29, 124.33, 124.41, 124.52, 124.63, 125.92, 126.03, 126.06, 126.17, 126.26, 126.36, 126.47, 126.77, 127.88, 128.00, 128.07, 128.14, 128.80, 128.85, 129.41, 130.01, 130.25, 130.48, 130.77, 130.90, 131.03, 131.06, 131.14, 131.22, 133.68, 134.26, 134.52, 134.58, 134.74, 135.09, 135.35, 135.65, 135.78, 136.63, 138.07, 138.79, 139.15, 141.23, 141.80, 141.84, 141.92, 142.10, 142.88, 143.06, 143.24, 143.70, 143.79, 143.85, 143.88, 143.99, 144.24, 144.51, 144.66, 144.77, 145.15, 145.25, 145.27, 145.73, 145.76, 146.07, 146.19, 146.60, 146.96, 147.00, 147.06, 147.21, 147.38, 147.41, 147.55, 147.85, 148.11, 148.35, 148.54, 148.82, 149.10, 149.28, 149.34, 149.53, 149.88, 149.90, 149.92, 150.23, 150.89, 151.19, 152.32, 152.36, 152.99, 153.14, 153.92, 156.54, 156.68, 158.17, 158.24, 158.38, 158.41, 160.20, 160.25, 160.34, 160.37, 173.52 (<u>C</u>OOH), 175.27 (<u>C</u>OOH), 175.34 (<u>C</u>OOH).

Compound A4. ¹H NMR (600 MHz, $(CD_3)_2SO$, δ , ppm): 2.26 – 2.35 (m, 4H, $C\underline{H}_2$), 2.41 – 2.49 (m, 4H, $C\underline{H}_2$), 2.52 – 2.60 (m, 6H, $C\underline{H}_2$), 2.68 – 2.72 (m, 2H, $C\underline{H}_2$), 2.72 – 2.84 (m, 4H, $C\underline{H}_2$), 3.49 – 3.59 (m, 2H, $C\underline{H}_2$), 3.74 (s, 2H, $C\underline{H}_2$), 5.20 (s, 1H, Csp^3_{cage} -<u>H</u>), 6.17 – 6.33 (m, 1H, $C\underline{H}$), 6.40 (d, J = 3.4 Hz, 1H, $C\underline{H}$), 6.52 (d, J = 3.4 Hz, 1H, $C\underline{H}$), 6.67 (d, J = 8.2 Hz, 2H, $C\underline{H}$), 6.69 (d, J = 4.4 Hz, 1H, $C\underline{H}$), 6.71 – 6.79 (m, 2H, $C\underline{H}$), 6.79 – 6.89 (m, 4H, $C\underline{H}$), 6.90 – 7.03 (m, 2H, $C\underline{H}$), 7.07 (d, J = 8.1 Hz, 2H, $C\underline{H}$), 7.12 (d, J = 8.1 Hz, 2H, $C\underline{H}$), 7.15 (d, J = 6.6 Hz, 2H, $C\underline{H}$), 7.22 – 7.38 (m, 2H, $C\underline{H}$), 7.44 (d, J = 8.0 Hz, 2H, $C\underline{H}$), 12.22 (br s, 7H, COO<u>H</u>).

¹³C NMR (151 MHz, $(CD_3)_2SO$, δ , ppm): 30.06 ($\underline{C}H_2$), 30.15 ($\underline{C}H_2$), 30.19 ($\underline{C}H_2$), 30.32 ($\underline{C}H_2$), 30.38 ($\underline{C}H_2$), 35.42 ($\underline{C}H_2$), 35.44 ($\underline{C}H_2$), 35.50 ($\underline{C}H_2$), 35.97 ($\underline{C}H_2$), 36.03 ($\underline{C}H_2$), 57.52 ($\underline{C}sp^3_{cage}$), 57.89 ($\underline{C}sp^3_{cage}$), 58.40 ($\underline{C}sp^3_{cage}$), 59.18 ($\underline{C}sp^3_{cage}$), 59.41 ($\underline{C}sp^3_{cage}$), 60.82 ($\underline{C}sp^3_{cage}$), 60.95 ($\underline{C}sp^3_{cage}$), 67.60 ($\underline{C}sp^3_{cage}$), 124.97, 127.21, 127.54, 127.58, 127.59, 127.69, 128.12, 128.91, 129.31, 129.37, 133.27, 135.23, 136.21, 136.48, 137.87, 139.54, 139.68, 139.88, 139.97, 140.40, 140.67, 140.97, 141.14, 142.00, 142.46, 143.73, 144.65, 145.21, 145.68, 145.93, 146.08, 146.10, 146.21, 146.34, 146.54, 146.61, 146.82, 146.90, 147.19, 147.33, 147.49, 147.53, 147.68, 147.77, 147.88, 148.43, 148.46, 148.70, 149.07, 149.48, 149.60, 149.66, 150.05, 151.66, 151.67, 151.91, 152.26, 153.54, 154.24, 155.44, 156.30, 158.03, 158.21, 171.76 (<u>C</u>OOH), 171.99 (<u>C</u>OOH), 174.05 (<u>C</u>OOH), 174.12 (<u>C</u>OOH), 174.16 (<u>C</u>OOH).

Compound A5. ¹H NMR (600 MHz, $(CD_3)_2SO$, δ , ppm): 2.24 – 2.39 (m, 7H, $C\underline{H}_2+C\underline{H}_3$), 2.39 – 2.50 (m, 4H, $C\underline{H}_2$), 2.52 – 2.66 (m, 6H, $C\underline{H}_2$), 2.66 – 2.94 (m, 6H, $C\underline{H}_2$), 3.52 (s, 2H, $C\underline{H}_2$), 5.18 (s, 1H, Csp^3_{cage} -<u>H</u>), 6.50 (d, J = 3.2 Hz, 1H, $C\underline{H}$), 6.53 (d, J = 3.2 Hz, 1H, $C\underline{H}$), 6.57 (d, J = 2.6 Hz, 1H, $C\underline{H}$), 6.68 (d, J = 8.2 Hz, 2H, $C\underline{H}$), 6.73 – 6.90 (m, 6H, $C\underline{H}$), 6.91 – 7.37 (m, 10H, $C\underline{H}$), 7.45 (d, J = 7.9 Hz, 2H, $C\underline{H}$), 7.49 – 7.63 (m, 1H, $C\underline{H}$), 12.14 (br s, 6H, COO<u>H</u>).

¹³C NMR (126 MHz, (CD₃)₂SO, δ, ppm):15.35 (<u>C</u>H₃), 30.07 (<u>C</u>H₂), 30.16 (<u>C</u>H₂), 30.20 (<u>C</u>H₂), 30.33 (<u>C</u>H₂), 30.39 (<u>C</u>H₂), 35.44 (<u>C</u>H₂), 35.46 (<u>C</u>H₂), 35.49 (<u>C</u>H₂), 35.51 (<u>C</u>H₂), 35.99 (<u>C</u>H₂), 36.04 (<u>C</u>H₂), 57.53 (<u>C</u>sp³_{cage}), 57.96 (<u>C</u>sp³_{cage}), 58.40 (<u>C</u>sp³_{cage}), 59.17 (<u>C</u>sp³_{cage}), 59.41 (<u>C</u>sp³_{cage}), 60.83 (<u>C</u>sp³_{cage}), 60.97 (<u>C</u>sp³_{cage}), 67.62 (<u>C</u>sp³_{cage}), 125.43, 126.00, 127.21, 127.60, 127.71, 128.12, 128.91, 129.32, 133.25, 135.26, 136.23, 137.91, 139.54, 139.68, 139.88, 139.91, 140.68, 140.99, 141.13, 141.21, 142.00, 142.43, 143.51, 143.81, 144.65, 145.21, 145.70, 145.95, 146.10, 146.33, 146.56, 146.83, 146.91, 147.32, 147.49, 147.68, 147.70, 147.89, 148.47, 148.70, 149.07, 149.48, 149.58, 149.68, 150.04, 151.67, 151.91, 152.25, 153.72, 154.39, 155.41, 155.48, 156.29, 158.25, 171.72 (<u>C</u>OOH), 174.03 (<u>C</u>OOH), 174.05 (<u>C</u>OOH), 174.13 (<u>C</u>OOH), 174.16 (<u>C</u>OOH).

Compound A6. ¹H NMR (500 MHz, $(CD_3)_2SO$, δ , ppm): 2.25 – 2.38 (m, 4H, $C\underline{H}_2$), 2.40 – 2.48 (m, 4H, $C\underline{H}_2$), 2.52 – 2.64 (m, 8H, $C\underline{H}_2$), 2.66 – 2.75 (m, 2H, $C\underline{H}_2$), 2.75 – 2.87 (m, 4H, $C\underline{H}_2$), 2.94 (t, J = 7.0 Hz, 2H, $C\underline{H}_2$), 3.50 – 3.62 (m, 2H, $C\underline{H}_2$), 5.18 (s, 1H, Csp^3_{cage} -<u>H</u>), 6.14 – 6.37 (m, 1H, C<u>H</u>), 6.44 (d, J = 3.4 Hz, 1H, C<u>H</u>), 6.53 (d, J = 3.3 Hz, 1H, C<u>H</u>), 6.63 (d, J = 3.1 Hz, 1H, C<u>H</u>), 6.64 – 6.78 (m, 4H, C<u>H</u>), 6.79 – 6.88 (m, 4H, C<u>H</u>), 6.89 – 7.00 (m, 2H, C<u>H</u>), 7.06 (d, J = 8.0 Hz, 2H, C<u>H</u>), 7.12 (d, J = 8.2 Hz, 2H, C<u>H</u>), 7.13 – 7.33 (m, 4H, C<u>H</u>),7.44 (d, J = 8.1 Hz, 2H, C<u>H</u>), 12.11 (br s, 7H, COO<u>H</u>).

¹³C NMR (126 MHz, (CD₃)₂SO, δ, ppm): 25.26 (C<u>H</u>₂), 30.06 (C<u>H</u>₂), 30.15 (C<u>H</u>₂), 30.19 (C<u>H</u>₂), 30.32 (C<u>H</u>₂), 30.38 (C<u>H</u>₂), 35.42 (C<u>H</u>₂), 35.44 (C<u>H</u>₂), 35.49 (C<u>H</u>₂), 35.57 (C<u>H</u>₂), 35.97 (C<u>H</u>₂), 36.03 (C<u>H</u>₂), 57.51 (Csp³_{cage}), 57.91 (Csp³_{cage}), 58.39 (Csp³_{cage}), 59.16 (Csp³_{cage}), 59.40 (Csp³_{cage}), 60.81 (Csp³_{cage}), 61.01 (Csp³_{cage}), 67.59 (Csp³_{cage}), 125.27, 125.48, 127.20, 127.59, 127.70, 128.11, 128.91, 129.31, 133.04, 133.26, 135.23, 136.22, 137.88, 139.52, 139.67, 139.86, 139.99, 140.40, 140.66, 140.96, 141.11, 141.17, 142.00, 142.44, 143.75, 143.83, 144.64, 145.20, 145.68, 145.92, 146.07, 146.09, 146.19, 146.32, 146.53, 146.60, 146.82, 146.91, 147.20, 147.32, 147.41, 147.50, 147.67, 147.70, 147.86, 148.39, 148.45, 148.69, 149.06, 149.46, 149.50, 149.60, 149.73, 150.03, 151.65, 151.89, 152.23, 153.65, 154.23, 155.38, 155.46, 156.27, 171.73 (COOH), 173.79 (COOH), 174.06 (COOH), 174.14 (COOH), 174.17 (COOH).

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Compound A7.¹H NMR (500 MHz, $(CD_3)_2SO$, δ , ppm): 1.30 – 1.44 (m, 15H, C<u>H</u>CH₃), 3.43 – 3.82 (m, 9H, C<u>H</u>CH₃+ C<u>H</u>₂), 5.31 (s, 1H, Csp³_{cage}-<u>H</u>), 5.96 – 6.35 (m, 1H, C<u>H</u>), 6.53 (d, *J* = 3.3 Hz, 1H, C<u>H</u>), 6.56 (d, *J* = 2.9 Hz, 1H, C<u>H</u>), 6.74 (d, *J* = 3.3 Hz, 1H, C<u>H</u>), 6.78 – 6.94 (m, 2H, C<u>H</u>), 6.96 – 7.25 (m, 20H, C<u>H</u>), 7.25 – 7.47 (m, 6H, C<u>H</u>), 7.51 (d, *J* = 7.3 Hz, 4H, C<u>H</u>), 7.56 – 7.71 (m, 1H, C<u>H</u>), 7.78 (d, *J* = 7.9 Hz, 2H, C<u>H</u>), 12.44 (br s, 7H, COO<u>H</u>).

¹³C NMR (126 MHz, (CD₃)₂SO, δ, ppm): 18.72 (CH<u>C</u>H₃), 18.78 (CH<u>C</u>H₃), 35.33 (<u>C</u>H₂), 35.46 (<u>C</u>H₂), 44.52 (<u>C</u>HCH₃), 44.56 (<u>C</u>HCH₃), 57.57 (<u>C</u>sp³_{cage}), 57.99 (<u>C</u>sp³_{cage}), 58.48 (<u>C</u>sp³_{cage}), 59.18 (<u>C</u>sp³_{cage}), 59.51 (<u>C</u>sp³_{cage}), 60.99 (<u>C</u>sp³_{cage}), 61.08 (<u>C</u>sp³_{cage}), 67.75 (<u>C</u>sp³_{cage}), 115.40, 115.45, 115.58, 115.76, 124.23, 124.27, 124.30, 124.34, 124.52, 125.04, 125.97, 125.99, 126.07, 126.10, 126.20, 126.36, 126.42, 126.46, 126.52, 127.52, 127.95, 128.03, 128.56, 129.31, 129.91, 130.05, 130.17, 130.72, 130.75, 130.87, 130.90, 131.03, 131.05, 132.94, 133.50, 133.95, 134.59, 134.94, 135.00, 136.68, 136.85, 137.95, 139.37, 139.76, 139.99, 141.38, 142.03, 143.41, 143.47, 143.56, 143.62, 143.74, 143.77, 143.79, 143.84, 143.91, 144.76, 145.31, 145.83, 145.97, 146.17, 146.21, 146.28, 146.50, 146.61, 146.72, 146.93, 147.00, 147.29, 147.36, 147.47, 147.59, 147.63, 147.67, 147.71, 147.82, 148.55, 148.60, 148.65, 148.75, 148.78, 148.83, 149.11, 149.16, 149.50, 149.57, 149.61, 149.83, 151.78, 151.89, 152.01, 154.37, 156.08, 156.34, 158.14, 158.19, 158.28, 158.36, 160.10, 160.15, 160.23, 160.32, 171.68 (<u>C</u>OOH), 171.99 (<u>C</u>OOH), 175.26 (<u>C</u>OOH), 175.28 (<u>C</u>OOH), 175.32 (<u>C</u>OOH).





Figure S1. ¹H NMR spectrum of compound **2**



Figure S3. ¹H-¹H COSY NMR spectrum of compound **2**



Figure S5. ¹H-¹³C HMBC NMR spectrum of compound **2**







Figure S8. ¹H-¹H COSY NMR spectrum of compound **3**







Figure S10. ¹H-¹³C HMBC NMR spectrum of compound **3**



Figure S11. ¹H NMR spectrum of compound **4**



Figure S12. ¹³C NMR spectrum of compound **4**



Figure S13. ¹H-¹H COSY NMR spectrum of compound **4**



Figure S14. ¹H-¹³C HSQC NMR spectrum of compound **4**



Figure S15. ¹H-¹³C HMBC NMR spectrum of compound **4**



Figure S16. ¹H NMR spectrum of compound **5**







Figure S18. ¹H-¹H COSY NMR spectrum of compound **5**



Figure S20. ¹H-¹³C HSQC NMR spectrum of compound **5**



Figure S21. ¹H-¹³C HMBC NMR spectrum of compound **5**















Figure S27. ¹H-¹³C HMBC NMR spectrum of compound **6**







Figure S30. ¹H-¹H COSY NMR spectrum of compound **7**



Figure S32. ¹H-¹³C HMBC NMR spectrum of compound **7**











Figure S37. ¹H-¹H ROESY NMR spectrum of compound 8



Figure S39. ¹H-¹³C HMBC NMR spectrum of compound **8**



Figure S40. Negative ion MALDI mass spectrum of compound 2



Figure S41. Negative ion MALDI mass spectrum of compound 3







Figure S43. Negative ion MALDI mass spectrum of compound 5



Figure S45. Negative ion MALDI mass spectrum of compound 7

Figure S46. Negative ion MALDI mass spectrum of compound 8

Quantum-chemical calculations

The structures of isomers of C_{60} with 8 addends (compound 8) were modelled using the non-empirical Perdew-Burke-Erzernhof (PBE) exchange-correlation functional (*Phys. Rev. Lett.*, 1996, **77**, 3865) with the extended basis H [5s1p/2s1p], C, O, F, S [5s5p2d/3s3p2d] for valence electrons and SBK pseudopotential (*J. Chem. Phys.*, 1984, **81**, 6026). To take into account the effects of the van der Waals interaction the effective Hamiltonian method was used for optimization as well (*J. Chem. Phys.*, 2011, **135**, 134120). Chemical shifts for optimized structures were calculated using the A2 basis set of cc-pVTZ quality (*Chem. Phys. Lett.*, 2005, **416**, 116). All calculations were carried out at the Joint Supercomputer Center of the Russian Academy of Sciences using Priroda software package (*Chem. Phys. Lett.*, 1997, **281**, 151).

To additionally prove the structure of novel fullerene derivatives with C_1 symmetry, we compared the relative energies of the possible isomers of **8**. Relative energies of isomers generally depend on two factors: disturbance of the system of conjugated bonds of fullerene cage, and the effects of the interaction of bulky addends. To evaluate the first factor, we compared the relative energies of 5 C_1 - $C_{60}H_8$ isomers with identical addends of the smallest size (Fig. S47). The obtained values are shown in the Table S1.

Figure S47. Structures of 5 different isomers (**A-E**) of C_1 - C_{60} H₈.

Isomer	Relative energy, kcal/mol
Α	0
В	3.3
C	10.7
D	5.7
E	4.0

Table S1. Relative energies of isomers A-E.

The structures **A**, **B** and **E** have the lowest energy. Taking into account these results, the set of structures **F**-**K** can be proposed for further consideration, among which only structures **F** and **H** meet criteria imposed by COSY and ROESY NMR spectra (Fig. S48). Quantum-chemical calculations showed that the second structure (**H**) is by 14.6 kcal/mol lower in energy than **F** due to steric effects. Structures **G**, **I**, **J** and **K** also have higher energy, by 19.7 and 11.5 kcal/mol respectively, than structure H.

Figure S48. Structures of isomers F-K.

When calculating the theoretical values of the ¹³C magnetic shielding constants, due to the large number of single C–C bonds in the system, there is the problem arises in the necessity of taking into account a significant number of rotational isomers with similar energies. To simplify this task, only the four most important rotamers, which differ in the orientation of the thiophene rings relative to the H atom, were taken into account. In the interaction of neighboring addends, not only steric hindrance but also dispersion forces

play an important role. To adequately take into account both of these effects, we optimized of the structures of various rotamers using the effective Hamiltonian method, which includes van der Waals interaction energies. In this case, the average value of chemical shifts for ${}^{13}C_{sp}{}^{3}$ atoms was 66.7 ppm, which is in better agreement with the experimental data(60.4 ppm), than the value of 74.5 ppm calculated without taking into account van der Waals interaction.

In order to reproduce exactly the average value of 13 C chemical shifts (*A*) and in the maximal spread (the difference between the maximum and minimum chemical shift values) (*D*) the following 2-parameter correction function was used:

$$\tilde{\delta_i} = A_{exp} + \frac{D_{exp}}{D_{theor}} (\delta_i - A_{theor})$$

where $\tilde{\delta}_i$ is the corrected chemical shift for the *i*-th nucleus, and δ_i is the calculated chemical shift (Table S2).

The agreement is rather good, except for line 63.56. This is probably because only one type of spatial arrangement is used for phenyl addends, while there are a lot of internal rotation isomers. At the same time, from comparison of different theoretical approaches it follows the maximal error for this line.

Most importantly, the structure of the theoretical and experimental spectra is very similar – in both spectra the first 5 lines occupy approximately 20% of the width of the full region.

Quite a different situation is observed for structure F, where this value is 40%, which is not in reasonable agreement with the experiment. For example, using the correction function the predicted maximal and minimal ¹³C chemical shifts, 54.96 and 65.31 ppm, are far from the experimental ones.

Corrected theoretical		
chemical s	Experimental	
van der Waals van der Waals		Chemical shifts,
interaction	interaction not	ppm
included	included	
56.98	57.06	57.65
58.08	57.45	58.07
58.31	57.45	58.67
58.50	58.25	59.16
59.46	58.74	59.32
60.63	58.98	60.87
63.51	66.47	61.07
67.33	67.41	68.00

Table S2. Calculated and experimental chemical shifts for isomer H.

Previously reported fullerene derivatives with eight addends

Figure S49. Examples of the C_{60} fullerene derivatives with eight addends and their addition patterns presented using Schlegel diagrams.

Figure S50. ¹H NMR spectrum of compound **A2**

Figure S52. ¹H-¹H COSY NMR spectrum of compound **A2**

Figure S54. ¹H-¹³C HMBC NMR spectrum of compound **A2**

Figure S55. ¹H NMR spectrum of compound A3

Figure S57. ¹H-¹H COSY NMR spectrum of compound A3

Figure S59. ¹H-¹³C HMBC NMR spectrum of compound A3

Figure S63. ¹H-¹³C HSQC NMR spectrum of compound **A4**

Figure S64. ¹H-¹³C HMBC NMR spectrum of compound **A4**

Figure S68. ¹H-¹³C HSQC NMR spectrum of compound **A5**

Figure S69. ¹H-¹³C HMBC NMR spectrum of compound **A5**

Figure S70. ¹H NMR spectrum of compound **A6**

Figure S72. ¹H-¹H COSY NMR spectrum of compound **A6**

Figure S74. ¹H-¹³C HMBC NMR spectrum of compound **A6**

Figure S75. ¹H NMR spectrum of compound **A7**

Figure S77. ¹H-¹H COSY NMR spectrum of compound **A7**

Figure S79. ¹H-¹³C HMBC NMR spectrum of compound **A7**

Biological assays

Investigation of cytotoxicity and antiviral activity of compounds K2-K7 against HIV-1 NL4.3, HIV-2 ROD

Cytotoxicity and antiviral activity assays were performed as described previously (*Org. Lett.*, 2021, **23**, 18, 7226).

Investigation of antioxidant activity of compounds K1 and K4

Cultivation of HELF

Human embryonic lung fibroblasts (HELF) were obtained from the collection of cell cultures of the Research Centre for Medical Genetics. Cells were seeded with 3*10⁴/well density, cultivated at 37°C in serum-free medium "Hybris" (Paneco, Moscow, Russia) enriched with 2% serum.

MTT assay

To determine the cytotoxicity of compounds, MTT test (methyl tetrazolium test) was performed using tablet reader (EnSpire, PerkinElmer). Cells were seeded in a 96-well plate with $1*10^{5}$ /well density. The compounds were added to the cells at a concentration of 4.2 ng/mL - 2.3 mg/mL, the cultivation time was 24 hours. After 24 hours, the medium was decanted from the plate, 100 µL of MTT solution (5 mg/mL in sterile water) was added to each well. Cells were incubated for 1-1.5 h at 37°C in an atmosphere of 7.5% CO₂, washed with PBS. 100 µL of DMSO was added to each well, incubated for 15 min. Optical density was measured on a plate spectrophotometer (EnSpire, PerkinElmer) at a wavelength of 540 nm. Cell survival was calculated using the formula: (OD of experimental wells – OD of the medium / OD of the control wells – OD of the medium) × 100%, where OD is optical density. Obtained results are summarized in Figure S80.

Figure S80. MTT-test results for compounds K1 (A) and K4 (B)

Detection of fullerenes in cells

The penetration of compounds **K1** and **K4** into cells was detected by fluorescence microscopy (Axio Vert, Carl Zeiss Microscopy, Germany). Figure 6: 575–645 nm excitation filter and a 530–555 nm emission filter were used.

Flow cytometry

Flow cytometry were performed as described in our previous paper (*Oxygen,* 2023, **3**, 1-19). Obtained results for compounds **K1** and **K4** are presented in Figure S81.

Figure S81. Fluorescence of compounds **K4** (A) and **K1** (B) (28 μg/mL), excitation by 375 nm: (1) data obtained on a CytoFLEX S flow cytometer (Beckman Coulter); (2) Fluorescence distribution histogram (with a maximum excitation of 675 nm) 1, 3 and 24 hours after addition of **K4** (A) and **K1** (B) to HELF.

Reactive oxygen species assays

The dye 2,7-dichlorodihydrofluorescein diacetate (DCFH-DA) (Molecular Probes/Invitrogen, CA, USA) was added to the cells, the cells were incubated for a predetermined time, washed with a Versen solution (PanEco, Russia) and 0.25% trypsin (PanEco, Russia), 199 medium (PanEco, Russia), then the cells were precipitated, the analysis was performed in PBS (PanEco, Russia). The ROS analysis was performed using a tablet reader (EnSpire, Finland).

Table S3. Dependences of the ratio of the rate constants of DCF synthesis in cells (k_i/k_o) during incubation with fullerenes **K4** and **K1** at a concentration of 18 ng/mL and 122 µg/mL to the control (cells cultured without fullerene derivatives) from cultivation time (1, 3, 24 hours of incubation).

		<i>k_i/k_o</i> , 18 ng/mL	<i>k_i∕k_o</i> , 122 µg/mL
K4	Control	1 ± 0.08	1 ± 0.08
	1 hour	0.8± 0.07	0.56 ± 0. 04 *
	3 hours	$0.72 \pm 0.06^*$	0.53 ± 0.04 *
	24 hours	1.23 ± 0.09	0.75 ± 0.05 *
K1	Control	1 ± 0.08	1 ± 0.07
	1 hour	0.73 ± 0. 05 *	0.51 ± 0.04 *
	3 hours	0.75 ± 0.06 *	0.62 ± 0.04 *
	24 hours	1.3 ± 0.09	1.44 ± 0.09 *

*- the differences are significant according to the Mann–Whitney U test (p<0.01).

Statistical analysis of the results

Statistical analysis was carried out using Microsoft Office Excel, Statistica 6.0, StatGraph. The figures show the mean and standard deviation (SD). The significance of the observed differences was analyzed with nonparametric Mann-Whitney U tests. P values < 0.01 were considered statistically significant.