Supplementary data

Regioselective synthesis and zone selective deprotection of [60]fullerene trisadducts with an $e,e,e$ addition pattern

Florian Beuerle, Nikos Chronakis and Andreas Hirsch*

Institut für Organische Chemie der Universität Erlangen, Henkestrasse 42, D-91054 Erlangen, Germany.
E-mail: andreas.hirsch@chemie.uni-erlangen.de


1,3,5-Tris(hydroxymethyl)benzene 2: The synthesis was performed according to the literature: M. Nakazaki, K. Yamamoto, T. Toya, J. Org. Chem., 1981, 46, 1611.


1,3,5-Tris-(2’-methylmalonyl)ethoxymethyl)benzene 5: A solution of 3-chloro-3-oxopropionate (0.76 ml, 7.1 mmol) in 5 ml of dry CH$_2$Cl$_2$ was added dropwise to a solution of 4 (430 mg, 1.4 mmol) and dry pyridine (0.58 ml, 7.1 mmol) in 25 ml of dry CH$_2$Cl$_2$ under N$_2$, at 0ºC. The reaction mixture was stirred at room temperature for 65 hours. After evaporation of the solvent under vacuum, the crude product was separated by flash column chromatography on SiO$_2$ using a mixture of CH$_2$Cl$_2$/MeOH = 97:3 as eluent to give 5 as a pale
yellow high viscous oil (620 mg, 1.0 mmol, 72%). \( \delta \text{H(CDCl}_3, 300 \text{ MHz)} 3.42 (s, 6H), 3.70 (t, J = 4.8 \text{ Hz}, 6H), 3.73 (s, 9H), 4.33 (t, J = 4.8 \text{ Hz}, 6H), 4.55 (s, 6H), 7.23 (s, 3H). \delta \text{C(CDCl}_3, 75 \text{ MHz)} 41.13, 52.48, 64.50, 67.81, 72.87, 126.28, 138.33, 166.46, 166.82. FT-IR (NaCl, r.t.): \nu_{\text{max}}/\text{cm}^{-1} 2957, 2854, 2363, 1734, 1734, 1608, 1439, 1412, 1338, 1278, 1208, 1155, 1038, 959, 852, 770, 684, 666, 489. MS (FAB, NBA), \text{m/z}: 602 ([M]^{+} + \text{H}), 624 ([M]^{+} + \text{Na}], 40\%).


Malonic acid mono-3-(tert-butoxycarbonyl)propyl ester 9: A solution of malonic acid (4.1 g, 39 mmol) and 8 (6.3 g, 39 mmol) in 75 ml of dry CH\textsubscript{2}Cl\textsubscript{2} was cooled at 0°C, under N\textsubscript{2}. Subsequently, a solution of DCC (8.0 g, 39 mmol) in 40 ml of dry CH\textsubscript{2}Cl\textsubscript{2} was added dropwise over a period of two hours and the reaction mixture was stirred at room temperature for 18 hours. The solution was filtered and the solvent was evaporated under vacuum. The residue was dissolved in diethylether and washed with a saturated solution of NaHCO\textsubscript{3} (4 x 50 ml). The combined aqueous layers were acidified with 1M HCl and extracted with diethylether (3 x 100 ml). The combined organic layers were dried over MgSO\textsubscript{4} and the solvent was evaporated under vacuum to yield 9 as a colourless oil (4.3 g, 17 mmol, 45%). \( \delta \text{H(CDCl}_3, 400 \text{ MHz)} 1.42 (s, 9H), 1.93 (m, 2H), 2.30 (t, J = 7.4 \text{ Hz}, 2H), 3.41 (s, 2H), 4.18 (t, J = 6.4 \text{ Hz}, 2H), 10.16 (s, 1H). \delta \text{C(CDCl}_3, 100.5 \text{ MHz)} 23.59, 27.74, 31.50, 40.59, 64.76, 80.79, 167.20, 171.22, 172.77. FT-IR (NaCl, r.t.): \nu_{\text{max}}/\text{cm}^{-1} 3492, 3227, 2980, 2937, 2576, 1732, 1560, 1458, 1417, 1394, 1370, 1328, 1257, 1154, 1094, 1035, 955, 882, 846, 753, 665. MS (FAB, NBA): \text{m/z} 247
([M⁺], 100%), 191 ([M⁺ - t-Bu], 10%).

1,3,5-Tris-(2-(3-(t-butoxycarbonyl)propylmalonyl)ethoxymethyl)benzene 10: N,N'-Dimethyl-4-aminopyridine (100 mg, 0.82 mmol) and DCC (1.7 g, 8.1 mmol) were added to a solution of 4 (700 mg, 2.3 mmol) and 9 (2.0 g, 8.1 mmol) in 100 ml of dry CH₂Cl₂ at 0 °C, under N₂ atmosphere and the reaction mixture was stirred for 65 hours at room temperature. The solution was filtered and after evaporation of the solvent under vacuum the residue was dissolved in ethyl acetate and filtered again to remove the remaining DCU. After evaporation of the solvent the resulting crude product was separated by flash column chromatography on SiO₂ using a mixture of CH₂Cl₂/EtOAc = 80:20 and then CH₂Cl₂/EtOAc = 50:50 as eluent to give 10 as a pale yellow high viscous oil (2.2 g, 2.2 mmol, 95%). δ_H(CDCl₃, 400 MHz) 1.43 (s, 27H), 1.92 (m, 6H), 2.28 (t, J = 7.4 Hz, 6H), 3.41 (s, 6H), 3.69 (t, J = 4.7 Hz, 6H), 4.16 (t, J = 6.4 Hz, 6H), 4.32 (t, J = 4.7 Hz, 6H), 4.56 (s, 6H), 7.23 (s, 3H). δ_C(CDCl₃, 100.5 MHz) 23.88, 27.98, 31.66, 41.25, 64.45, 64.54, 67.79, 72.87, 80.48, 126.37, 138.43, 166.44, 166.59, 172.07. FT-IR (NaCl, r.t.): ν_max/cm⁻¹ 2977, 2934, 2860, 1731, 1640, 1615, 1560, 1455, 1418, 1392, 1368, 1331, 1258, 1153, 1037, 957, 882, 847, 769, 754, 666. MS (FAB, NBA): m/z 817 ([M⁺ - 3·t-Bu], 50%), 951 ([M⁺ - t-Bu], 20%), 983 ([M⁺], 15%), 1007 ([M⁺ + Na], 100%).


1,3,5-Tris-(2-(3-(t-butoxycarbonyl)propylmalonyl)ethoxy)benzene 12: N,N'-Dimethyl-4-aminopyridine (100 mg, 0.82 mmol) and DCC (1.7 g, 8.1 mmol) were added to a solution of 11 (600 mg, 2.3 mmol) and 9 (2.0 g, 8.1 mmol) in 120 ml of dry THF at 0 °C under N₂ atmosphere and the reaction mixture was stirred for 65 hours at room temperature. The solution was filtered and after evaporation of the solvent under vacuum the residue was dissolved in ethyl acetate and filtered again to remove the remaining DCU. After evaporation of the solvent the resulting crude product was separated by flash column chromatography on SiO₂ using a mixture of CH₂Cl₂/EtOAc = 80:20 as eluent to give 12 as a pale yellow high viscous oil (2.0 g, 2.0 mmol, 85%). δ_H(CDCl₃, 400 MHz) 1.43 (s, 27H), 1.91 (m, 6H), 2.28 (t, J = 7.4 Hz, 6H), 3.42 (s, 6H), 4.13 (m, 12H), 4.57 (t, J = 4.5 Hz, 6H), 6.09 (s, 3H). δ_C(CDCl₃, 100.5 MHz) 23.88, 27.98, 31.66, 41.21, 63.53, 64.61, 65.63, 80.51, 94.57, 160.29,
166.54, 166.54, 172.07. FT-IR (NaCl, r.t.): \( \nu_{\text{max}}/\text{cm}^{-1} \) 2977, 2925, 2362, 1734, 1599, 1457, 1418, 1393, 1368, 1331, 1259, 1153, 1083, 1032, 957, 846, 752, 682, 666. MS (FAB, NBA): \( m/z \) 775 ([M\(^+\) - 3-t-Bu], 100%), 942 ([M\(^+\)], 25%), 965 ([M\(^+\) + Na], 10%).

**Trisadduct 13**: In a dry 1000 ml two-necked round-bottomed flask equipped with a gas inlet and a dropping funnel, \( \text{C}_{60} \) (200 mg, 0.28 mmol) was dissolved in 300 ml of dry toluene under argon atmosphere. Subsequently, 5 (160 mg, 0.27 mmol) and iodine (220 mg, 0.87 mmol) were added, followed by the dropwise addition of a solution of DBU (310 \( \mu \)l, 2.1 mmol) in 150 ml of dry toluene over a period of three hours. The reaction mixture was stirred for 20 hours at room temperature, filtered through a paper filter and subjected to flash column chromatography on SiO\( _2 \). Elution with toluene afforded traces of unreacted \( \text{C}_{60} \) and then the eluent was changed to toluene/EtOAc = 70:30 to elute a fraction consisted of a mixture of trisadducts followed by the elution of trisadduct 13. Reprecipitation from CHCl\( _3 \)/pentane and drying under high vacuum yielded pure 13 as a cherry-red solid (85 mg, 0.063 mmol, 25%). \( \delta_{\text{H}}(\text{CDCl}_3, 400 \text{ MHz}) \) 3.69 (m, 6H), 3.94 (s, 9H), 4.23 (ddd, \( \text{J} = 11.5, 4.3, 4.3 \) Hz, 3H), 4.43 (d, \( \text{J} = 11.7 \) Hz, 3H), 4.50 (d, \( \text{J} = 11.7 \) Hz, 3H), 4.76 (ddd, \( \text{J} = 11.5, 6.8, 4.5 \) Hz, 3H), 7.08 (s, 3H). \( \delta_{\text{C}}(\text{CDCl}_3, 100.5 \text{ MHz}) \) 52.56, 53.79, 65.25, 67.41, 69.72, 70.65, 72.37, 125.85, 137.68, 140.88, 141.25, 141.79, 142.24, 142.55, 143.33, 144.19, 144.53, 144.84, 145.61, 145.81, 146.22, 146.28, 146.39, 146.64, 146.84, 147.10, 163.20, 163.82. FT-IR (KBr, r.t.): \( \nu_{\text{max}}/\text{cm}^{-1} \) 2970, 2928, 2850, 1747, 1728, 1455, 1391, 1366, 1280, 1248, 1212, 1154, 1103, 1065, 1026, 847, 735, 705, 670, 527, 476. UV/Vis (CHCl\( _3 \)): \( \lambda_{\text{max}}/\text{nm} \) (\( \epsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1} \)) 285 (38 000), 308 (27 000), 380 (9 800), 350 (9 800), 480 (3 500), 570 (950). MS (FAB, NBA): \( m/z \) 720 ([C\( _{60} \)^+], 100%), 1315 ([M\(^+\)], 50%).

**Trisadduct 14**: In a dry 2000 ml two-necked round-bottomed flask equipped with a gas inlet and a dropping funnel, \( \text{C}_{60} \) (500 mg, 0.69 mmol) was dissolved in 1000 ml of dry toluene under an argon atmosphere. Subsequently, 10 (650 mg, 0.66 mmol) and iodine (620 mg, 2.4 mmol) were added, followed by the dropwise addition of a solution of DBU (830 \( \mu \)l, 5.6 mmol) in 250 ml of dry toluene over a period of four hours. The solution was stirred for 40 hours at room temperature, filtered through a paper filter to remove the DBU salts and subjected to flash column chromatography on SiO\( _2 \). Elution with toluene afforded traces of unreacted \( \text{C}_{60} \) and then the eluent was changed to toluene/EtOAc = 70:30 to elute a fraction consisted of a mixture of
trisadducts followed by the elution of trisadduct 14. Reprecipitation from CHCl₃/pentane and drying under high vacuum yielded pure 14 as a cherry-red solid (280 mg, 0.16 mmol, 25%). δ_H(CDCl₃, 400 MHz) 1.46 (s, 27H), 2.03 (m, 6H), 2.36 (t, J = 7.4 Hz, 6H), 3.71 (m, 6H), 4.25 (ddd, J = 11.5, 4.3, 4.3 Hz, 3H), 4.38 (m, 6H), 4.43 (d, J = 11.6 Hz, 3H), 4.47 (d, J = 11.6 Hz, 3H), 4.75 (ddd, J = 11.5, 6.8, 4.5 Hz, 3H), 7.08 (s, 3H).

δ_C(CDCl₃, 100.5 MHz) 23.97, 28.06, 31.63, 52.48, 65.04, 65.98, 67.40, 69.71, 70.62, 72.22, 80.69, 125.87, 137.75, 140.85, 141.38, 141.98, 142.42, 142.54, 143.34, 144.26, 144.63, 144.87, 145.66, 145.91, 146.26, 146.35, 146.47, 146.73, 146.91, 147.06, 163.24, 163.33, 171.93. FT-IR (KBr, r.t.): ν_max/cm⁻¹ 2972, 2926, 2842, 1747, 1728, 1456, 1391, 1367, 1358, 1248, 1213, 1154, 1104, 1064, 846, 737, 705, 527, 476. UV/Vis (CHCl₃): λ_max/nm (ε/dm³mol⁻¹cm⁻¹) 250 (72 000), 280 (45 000), 308 (30 000), 380 (4 6000), 480 (3 8000), 570 (1 000). MS (FAB, NBA): m/z 720 ([C₆₀⁺], 100%), 1699 ([M⁺], 10%).

**Trisadduct 15:** In a dry 2000 ml two-necked round-bottomed flask equipped with a gas inlet and a dropping funnel, C₆₀ (500 mg, 0.69 mmol) was dissolved in 1000 ml of dry toluene under an argon atmosphere. Subsequently, 12 (625 mg, 0.66 mmol) and iodine (620 mg, 2.4 mmol) were added, followed by the dropwise addition of a solution of DBU (830 µl, 5.6 mmol) in 250 ml of dry and toluene over a period of four hours. The solution was stirred for 40 hours at room temperature, filtered through a paper filter and subjected to flash column chromatography on SiO₂. Elution with toluene afforded traces of unreacted C₆₀ and then the eluent was changed to toluene/EtOAc = 80:20 to elute trisadduct 15. Reprecipitation from CHCl₃/pentane and drying under high vacuum yielded pure 15 as a cherry-red solid (370 mg, 0.22 mmol, 35%). δ_H(CDCl₃, 400 MHz) 1.45 (s, 27H), 2.02 (m, 6H), 2.34 (t, J = 6.8 Hz, 6H), 4.07 (d, J = 11.4 Hz, 3H), 4.25 (m, 3H), 4.34 (m, 3H), 4.45 (m, 8H), 4.81 (d, J = 11.4 Hz, 3H), 5.82 (s, 3H). δ_C(CDCl₃, 100.5 MHz) 23.96, 28.04, 31.54, 52.49, 65.74, 66.01, 66.08, 69.35, 70.66, 80.71, 94.11, 140.89, 141.02, 141.84, 142.03, 142.54, 143.24, 143.62, 144.14, 145.11, 145.75, 145.98, 146.20, 146.43, 146.55, 146.65, 146.77, 146.92, 147.00, 160.31, 162.74, 163.01, 171.85. FT-IR (KBr, r.t.): ν_max/cm⁻¹ 2972, 2926, 2361, 1748, 1729, 1604, 1456, 1392, 1367, 1248, 1213, 1156, 1103, 1062, 1023, 877, 815, 737, 705, 670, 526, 458. UV/Vis (CHCl₃): λ_max/nm (ε/dm³mol⁻¹cm⁻¹) 250 (57 000), 285 (30 000), 308 (21 000), 380 (2 9000), 480 (2 7000), 570 (730). MS (FAB, NBA): m/z 720 ([C₆₀⁺], 100%), 1489 ([M⁺-3·t-Bu], 10%), 1699 ([M⁺], 20%).
**Trisadduct 16**: A solution of 13 (57 mg, 0.043 mmol) in 30 ml of dry CH$_2$Cl$_2$ was cooled to -78 °C, followed by the dropwise addition of a solution of BBr$_3$ (37 µl, 0.39 mmol) in 15 ml of dry CH$_2$Cl$_2$ over a period of two hours. The reaction mixture was allowed to reach room temperature and stirred overnight. After the addition of 10 ml water the reaction mixture was stirred for 15 more minutes, the phases were separated and the organic layer was dried over MgSO$_4$. After evaporation of the solvent, 16 was purified by flash column chromatography on SiO$_2$ using a mixture of CH$_2$Cl$_2$/MeOH = 95:5 as eluent (11 mg, 0.0092 mmol, 21%). UV/Vis (CH$_2$Cl$_2$): $\lambda_{\text{max}}$/nm 251, 281, 308, 350, 380, 480, 565. MS (FAB, NBA): $m/z$ 720 ([C$_{60}^+$], 100%), 1201 ([M$^+$], 10%).

**Trisadduct 17**: A solution of 14 (210 mg, 0.12 mmol) in 15 ml of formic acid (99%) was stirred for four days at room temperature, under an argon atmosphere. The reaction was monitored by TLC (SiO$_2$, toluene/EtOAc = 80:20) and after completion the acid was removed under reduced pressure. The residue was dissolved in THF and distilled under vacuum for several times to remove traces of formic acid. Drying under high vacuum yielded 17 (180 mg, 0.12 mmol, 97%). UV/Vis (DMSO): $\lambda_{\text{max}}$/nm 285, 308, 350, 380, 480, 570. MS (FAB, NBA): $m/z$ 720 ([C$_{60}^+$], 100%), 1531 ([M$^+$], 5%).

**Trisadduct 18**: A solution of 15 (320 mg, 0.19 mmol) in 15 ml of formic acid (99%) was stirred for three days at room temperature, under an argon atmosphere. The reaction was monitored by TLC (SiO$_2$, toluene/EtOAc = 80:20) and after completion the acid was removed under reduced pressure. The residue was dissolved in THF and distilled under vacuum for several times to remove traces of formic acid. Drying under high vacuum yielded 18 (273 mg, 0.18 mmol, 95%). UV/Vis (DMSO): $\lambda_{\text{max}}$/nm 285, 308, 350, 380, 480, 570. MS (FAB, NBA): $m/z$ 720 ([C$_{60}^+$], 100%), 1489 ([M$^+$], 5%).