Synthesis of functionalized, dispersible carbon coated cobalt nanoparticles for potential biomedical applications

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Supporting Information

All reactions were carried out in oven-dried glassware under an atmosphere of dry nitrogen unless stated otherwise. All commercially available reagents were used as received. Carbon coated cobalt nanoparticles were purchased from Turbobeads Llc (Co/C, 20.5 m^2/g, mean particle size ≈25 nm). Prior to use, they were washed in a concentrated HCl (Merck, puriss)/deionized water (Millipore) mixture (1:1) 5 times for 24 h. Acid residuals were removed by washing with Millipore water (5x) and the particles were dried at 50 _C in a vacuum oven. Carbon coated cobalt nanoparticles were purchased from Turbobeads Llc (Co/C, 20.5 m^2/g, mean particle size ≈25 nm). Prior to use, they were washed in a concentrated HCl (Merck, puriss)/deionized water (Millipore) mixture (1:1) 5 times for 24 h. Acid residuals were removed by washing with Millipore water (5x) and the particles were dried at 50 °C in a vacuum oven. Pent-4-ynoic acid andhydride,[1] azide functionalized Co/C nanoparticles (loading: 0.14 mmol/g),[2] propargyl-[G3]-$(OH)_8$ **2**,[3] propargyl-[G3]-$(NH_3^+TFA\_)_8$ **3**,[4] Co/C-[G3]-$(OH)_8$ **4**,[5] Co/C-[G3]-$(NH3^+TFA\_)_8$ **5**,[5] 2-azidoethyl-*β*-D-gluco-pyranoside,[6] pyrene-[G3]-$(OH)_8$ **7a**,[7]pyrene-[G3]-$(alkyne)_8$ **7b**,[7] phenylethylamine functionalized carbon coated cobalt nanoparticles **21**,[8] aziridine (**22**)[9] were prepared according to literature procedures. Magnetic nanobeads were dispersed using an ultrasound bath (Sonorex RK 255 H-R, Bandelin) and recovered with the aid of a neodymium based magnet (N48, W-12-N, Webcraft GmbH, side length 12 mm) unless indicated otherwise.
Microwave reactions were carried out using a CEM Discover S-Class microwave reactor and appropriate glass tubes. ATR-IR spectroscopy was carried out on a Biorad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. Diffuse reflectance infrared fourier transform spectroscopy (DRIFTS) was performed on an JASCO FT/IR-610 spectrometer using a PIKE Reflectance Analysis Kit. Thermogravimetric analysis was performed using a Perkin Elmer TGA7 apparatus. For TEM measurements, sample suspension drops were placed on a cupper grid (400 mesh) and subsequently blotted dry with a filter paper. The samples were examined in a LEO912AB electron microscope (Zeiss, Oberkochen/Germany) operating at 100 kV, equipped with a side-mounted CCD-camera capable of recording images with 1k x1k pixels. High-resolution transmission electron microscopy was carried out using a Philips CM30 ST equipped with a LaB6 cathode and operated at 300kV point resolution (~ 4 Å) at the ETH Zürich.

Pyrene-[G3]-$(NH_3^+TFA^-)_8$ 7c: 248 mg (0.20 mmol) of pyrene tagged dendrimer **7a,** 86 mg (0.74 mmol) DMAP and 48 µL absolute pyridine were dissolved in 5 mL of dry CH_2Cl_2. A solution of 1.44 g (4.00 mmol) 3-((*tert*-butoxycarbonyl)amino)-propanoic anhydride in 8 mL of dry CH_2Cl_2 was added dropwise and the resulting mixture was stirred for 24 h at room temperature. Water (10 mL) was added and the mixture stirred for further 3 hours. After dilution with 50 mL of CH_2Cl_2 the organic layer was successively washed with 10% HCl (3 x 20 mL), 10% Na_2CO_3 (3 x 20 mL) and brine (20 mL). The organic phase was dried over MgSO4, filtered and concentrated under reduced pressure. Purification by column chromatography eluting with PE:EE 8:2 and gradually increasing polarity to 100% ethyl acetate yielded 435 mg (0.17 mmol, 85%) of **pyrene-[G3]-$(NHBoc_3)_8$** as a yellow waxy solid. ^{1}H-NMR (400 MHz, CDCl3): δ = 8.20 (d, *J*=9.3, 1H), 8.06 (dd, *J*=7.6, 2.2, 2H), 8.03-7.98 (m, 2H), 7.93-7.87 (m, 3H), 7.77 (d, *J*=7.8, 1H), 7.74 (s, 1H), 6.53-6.40 (bs, 1H),5.44-5.06 (m, 10H), 4.31 (t, *J*=6.7, 2H), 4.22-4.06 (m, 28H), 3.28 (d, *J*=5.4, 16H), 3.17 (dd, *J*=12.3, 6.2, 2H), 2.45 (t, *J*=6.0, 16H), 2.23 (t, *J*=7.1, 2H), 2.12 (dt, *J*=14.3,7.2, 2H), 2.05-1.96 (m, 2H), 1.34 (s, 72H), 1.19 (s, 3H), 1.14 (s, 12H), 1.12 (s, 6H). ^{13}C-NMR (100.6 MHz, CDCl3) δ = 173.3, 172.0, 171.7, 171.4, 155.8, 141.8, 135.8, 131.3, 130.8, 129.9, 128.7, 127.4, 127.3, 127.3, 126.7, 125.8, 125.0, 124.9, 124.9, 124.8, 124.7, 124.6, 123.3, 79.2, 77.4, 66.1, 65.2, 64.9, 58.4, 47.8, 46.6(0), 46.5(5), 46.4, 36.3, 36.1, 35.8, 34.4, 32.8, 30.3, 28.5, 28.3, 28.1, 27.4, 17.7, 17.5, 17.4; m.p. 48 °C; IR (ν/cm^{-1}): 3374, 2977, 1737, 1696, 1513, 1366, 1245, 1160, 1127, 966, 848, 757; MS (ESI): m/z = 2610.8 (MH^+).

430 mg (0.16 mmol) of **pyrene-[G3]-(NHBoc$_3$)$_8$** was dissolved in 1 mL of CH_2Cl_2. 1 mL of TFA (13.9 mmol, 99%) was added and the solution stirred for 3 h at ambient temperature. The solvents were distilled off at reduced pressure affording 422 mg (0.16 mmol, 100%) **7c** as a light brown waxy solid. ^{1}H-NMR (400 MHz, MeOD): δ = 8.35 (d, *J*=9.3, 1H), 8.19 (dd, *J*=7.5, 3.5, 2H), 8.16-8.09 (m, 3H), 8.05 (s, 2H), 8.00 (t, *J*=7.7, 1H), 7.91 (d, *J*=7.8, 1H), 5.27 (s, 2H), 4.45 (t, *J*=6.9, 2H), 4.33-4.18 (m, 28H), 3.42-3.37 (m, 2H), 3.22 (t, *J*=6.7, 16H), 3.20-3.16 (m, 2H), 2.79 (t, *J*=6.6, 16H), 2.38 (t, *J*=7.3, 2H), 2.21-2.07 (m, 4H), 1.29 (s, 3H), 1.25 (s, 12H), 1.20 (s, 6H); 13C NMR (100.6 MHz, MeOD): δ = 176.1, 174.8, 173.6, 173.5, 173.2, 172.0, 171.8, 163.2, 162.9, 162.5, 143.4, 137.3, 132.8, 132.3, 131.4, 129.9, 128.6, 128.4, 127.8, 127.1, 126.5, 126.2, 126.1, 126.0(2), 125.9(8), 125.9, 124.4, 119.7, 116.8, 113.8, 67.4, 66.8, 66.6, 59.1, 49.9, 48.0, 47.6, 37.4, 37.0, 36.8, 36.4, 36.3, 33.8, 32.1, 32.0, 31.1, 29.0, 18.0(2), 17.9(5), 17.9, 17.7. IR (*ν*/cm^{-1}): 2936, 1736, 1672, 1469, 1406, 1176, 1123, 1004, 835, 798, 721, 650; MALDI-MS: m/z = 1805.7 (calc. 1806.83).

Propargyl-PEG$_{2000}$-OMe 11: To a stirred suspension of NaH (60% in mineral oil, 144 mg, 6 mmol) in dry DMF (10 mL) PEG2000-OMe (4 g, 2 mmol) was added in portions at ambient temperature and stirred for 30 min. Propargylbromide (420 µL, 3.9 mmol) was added dropwise and the reaction mixture was heated to 80 °C for 24 h. After quenching with 3 mL of water under vigorous stirring the solvents were evaporated under reduced pressure. The resulting slurry was diluted with CH_2Cl_2 (30 mL) and washed with water (3 x 40 mL). The organic phase was dried over MgSO4, filtrated and concentrated under reduced pressure to about 10 mL solvent. This solution was poured into cold Et_2O (150 mL) and cooled to –5 °C for 30 min to complete crystallization. The precipitate was filtered off and washed thoroughly with cold Et_2O. This purification process was repeated once. 3.6 g (1.8 mmol, 90%) of **11** were obtained as a slightly brown solid. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 4.02 (d, *J*=1.7, 2H), 3.54-3.40 (m, 191H), 3.20 (s, 3H), 2.36 (s, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$): δ = 79.3, 77.6, 77.2, 76.7, 74.5, 71.5, 70.2, 70.0, 68.7, 58.6, 58.0; m.p. 49 °C; IR (*ν*/cm^{-1}): 2882, 1981, 1467, 1341, 1279, 1241, 1096, 960, 841, 683; MS (ESI): m/z = 2245.9 (MNH_4^+, n=48), 2202.0 (MNH_4^+, n=47), 2158.8 (MNH_4^+, n=46), 2114.7 (MNH_4^+, n=45), 2070.5 (MNH_4^+, n=44), 2026.9 (MNH_4^+, n=43), 1982.9 (MNH_4^+, n=42), 1937.7 (MNH_4^+, n=41), 1894.3 (MNH_4^+, n=40), 1893.4 (MNH_4^+, n=39).

Pyrene-PEG2000-OMe 15: To a stirred suspension of NaH (60% in mineral oil, 151 mg, 3.9 mmol) in dry DMF (30 mL) 4-(pyren-1-yl)butan-1-ol (**13**) (823 mg, 3 mmol) was added in portions at 0°C and stirred for 30 min. After dropwise addition of propargylbromide (420 µL, 3.9 mmol) at 0°C the resulting mixture was allowed to warm to room temperature while stirring continued for a further 6 h. Water (30 mL) was added and the resulting mixture extracted with EtOAc (5 x 20 mL). The combined organic phases were washed with water (5 x 20 ml), dried over MgSO4, filtered and concentrated under reduced pressure. Purification by column chromatography eluting with PE:EE (9:1) and increasing polarity gradually to PE:EE (1:1) yielded 490 mg (1.57 mmol, 52%) 1-(4-(prop-2-yn-1-yloxy)butyl)pyrene as a slightly yellow solid. ^{1}H-NMR (400 MHz, CDCl3): δ = 8.31 (d, *J*=9.3, 1H), 8.20 (dd, *J*=7.6, 2.5, 2H), 8.13 (dd, *J*=8.5, 3.6, 2H), 8.06 (d, *J*=1.9, 3H), 7.88 (d, *J*=7.8, 1H), 4.21 (d, *J*=2.3, 2H), 3.61 (t, *J*=6.4, 2H), 3.41-3.35 (m, 2H), 2.53 (s, 1H), 1.99 (s, 2H), 1.84 (d, *J*=8.3, 2H); ^{13}CNMR (100.6 MHz, CDCl3): δ = 136.7, 131.4, 130.9, 129.8, 128.6, 127.5, 127.2(1), 127.1(6), 126.5, 125.8, 125.1, 125.0, 124.8, 124.8, 124.7, 123.4, 80.1, 74.3, 69.9, 58.1, 33.2, 29.6, 28.3; m.p. 54 °C; IR (*ν*/cm^{-1}): 3280, 3234, 2941, 2856, 2116, 1600, 1479, 1437, 1351, 1186, 1089, 838, 762, 686, 655, 586; HRMS (EI, 70 eV): m/z = 312.1515 (calc. 312.1514).
100 mg (0.32 mmol) of 1-(4-(prop-2-yn-1-yloxy)butyl)pyrene and 668 mg (0.33 mmol) of PEG2000-OMe azide **14** were dissolved in degassed CH_2Cl_2 (20 mL). After adding Et_3N (44 µL, 0.32 mmol) and CuI (3 mg, 16 µmol), the reaction mixture was stirred at room temperature for 42 h. After 24 h a second portion of CuI (3 mg, 16 µmol) was added. The reaction mixture was washed four times with 20 mL of an aqueous EDTA-solution (0.02 mol/L) and then two times with 20 mL of water. The organic phase was dried over MgSO4, filtrated and concentrated under reduced pressure. Purification by column chromatography eluting with CH2Cl2 and increasing polarity by addition of MeOH to a final composition of 20% yielded 688 mg (0.29 mmol, 92%) of **15** as a brown solid. ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.18 (d, *J*=9.2, 1H), 8.11-7.98 (m, 4H), 7.95-7.87 (m, 3H), 7.77 (d, *J*=7.8, 1H), 7.62 (s, 2H), 4.55 (s, 2H), 4.41 (t, *J*=4.9, 2H), 3.76-3.70 (m, 2H), 3.62-3.48 (m, 192H), 3.30 (s, 3H), 1.91-1.79 (m, 2H), 1.77-1.66 (d, *J*=6.9, 2H). ^{13}C-NMR (75.5 MHz, CDCl3): δ = 145.1, 136.8, 131.4, 130.9, 129.7, 128.6, 127.5, 127.3, 127.2, 126.5, 125.8, 125.0, 124.8, 124.6, 123.6, 123.4, 71.9, 70.5, 70.4, 69.4, 64.3, 59.0, 50.2, 33.3, 29.7, 28.4.; m.p. 49 °C; IR (*ν*/cm^{-1}): 2885, 1466, 1342, 1280, 1242, 1107, 964, 843, 634, 537, 500; MS (ESI): m/z = 2370.4 (MNH_4^+, n=44), 2281.3 (MNH_4^+, n=42), 2238.7 (MNH_4^+, n=41), 2195.2 (MNH_4^+, n=40), 2149.1 (MNH_4^+, n=39), 2106.6 (MNH_4^+, n=38), 2061.8 (MNH_4^+, n=37), 1972.2 (MNH_4^+, n=35).

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