Characterization of Carbon Nanotube Dispersions in Solutions of Bile Salts and Derivatives Containing Aromatic Substituents

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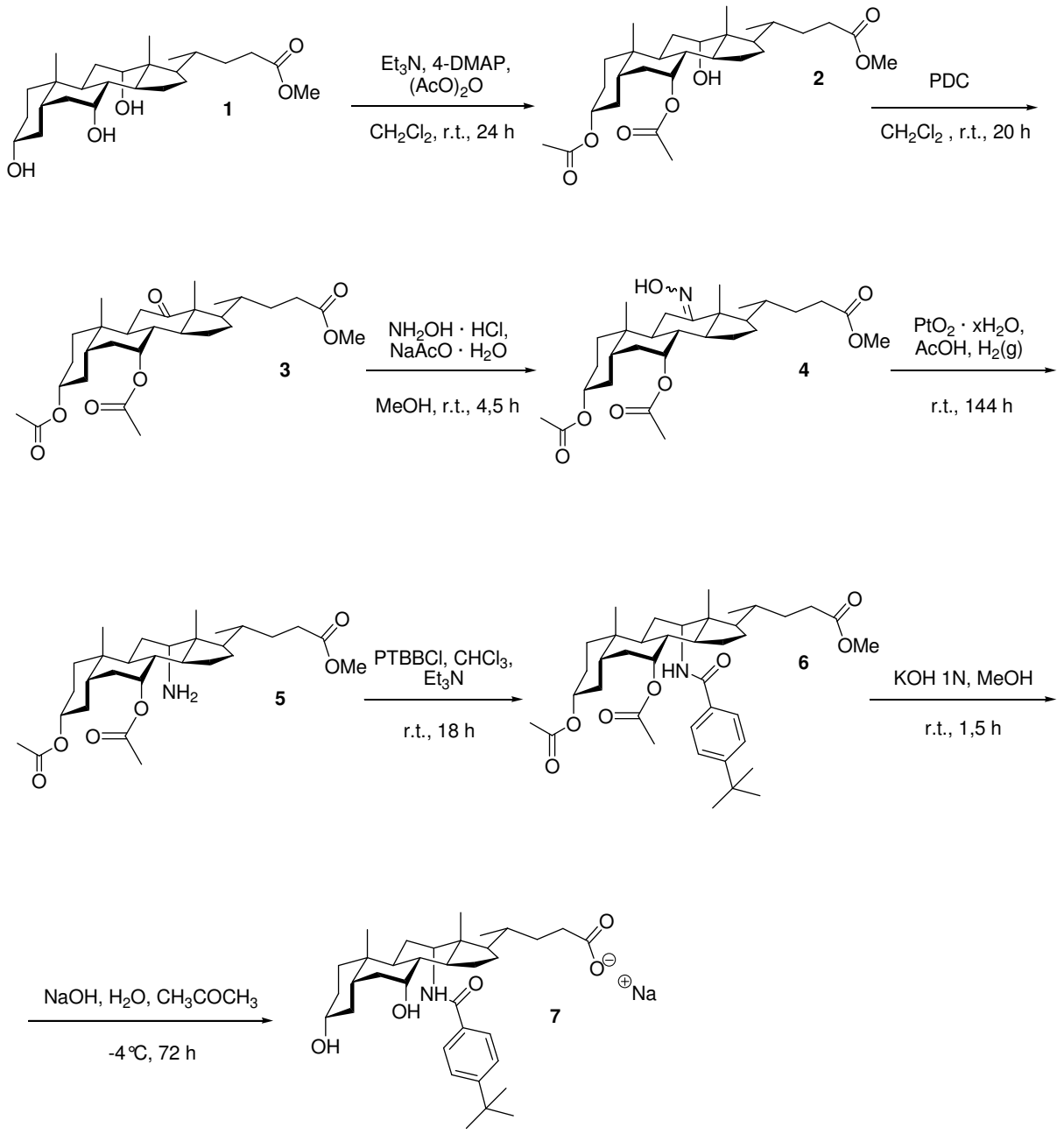
Supporting information

Contents:

Materials

Synthesis of 12-NaTbuBC

Scheme 1 shows the synthetic path related to the preparation of the new derivative 12-NaTbuBC. The methyl ester **1** of cholic acid, obtained as reported in literature,[1] was used as starting material.



Scheme 1. Reaction sequence for the synthesis of 12-NaTbuBC.

Synthesis of Methyl [3α,5β,7α,12α]-3,7-diacetyloxy-12-hydroxycolan-24-oate (2). A mixture of the monoesther **1** (20 g, 39.47 mmol), triethylamine (22 mL, 157.8 mmol), 4-DMAP (0,576 g, 4.71 mmol), dry acetic anhydride (14.3 mL, 151.28 mmol) and 550 mL of CH_2Cl_2 was stirred for 24 h. The solvent was removed under reduced pressure and the product was purified via silica-gel column chromatography (ethyl acetate/hexane 1:2) to afford 17.9 g, 75% of pure diacetylated product **2**. ^{1}H NMR (400 MHz, $CDCl_3$): 4.87 (br, 1H, 12-CH); 4.56 (m, 1H, 3-CH); 3.98 (s, 1H, 7-CH); 3.64 (s, 3H, CH_3OCO), 2.35 (m, 1H, 12-OH); 2.22 (m, 2H); 2.08 (s, 1H); 2.04 (2, 3H, 7- CH_3CO); 2.01 (s, 3H, 3-CH_3CO); 2.00-1.00 (m, 24H, -CH and -CH_2 of steroid skeleton and side chain); 0.97 (d, 3H, 21-CH_3); 0.90 (s, 3H, CH_3); 0.67 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 174.8 (24-CO_2), 170.9, 170.8 (3,7-$\underline{C}OCH_3$), 74.3, 72.9, 71.0 (3,7,12 $\underline{C}$-OAc), 51.7 ($CO_2\underline{C}H_3$), 47.4, 46.8, 42.3, 41.1, 38.3, 35.2, 34.957, 34.7, 34.6, 31.5, 31.2, 31.0, 28.8, 28.4, 27.5, 26.89, 23.2, 22.8, 21.9, 21.7, 17.6, 12.7.
IR (KBr, cm^{-1}): 3554, 3524, 2946, 2875, 1773, 1735, 1708, 1438, 1259, 1232, 1023, 889.

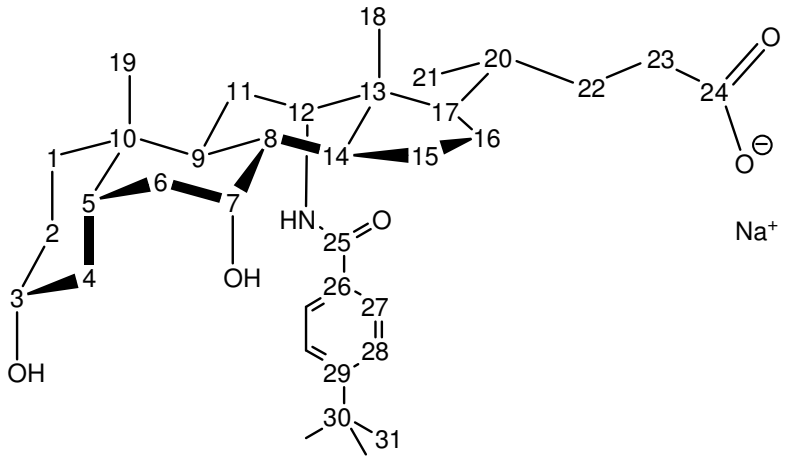
Synthesis of Methyl [3α,5β,7α]-3,7-diacetyloxi-12-oxocolan-24-oate (3). A mixture of 20 g of just dried molecular sieves (4 Å), 475 mL of CH_2Cl_2 and dried pyridine (30.5 mL, 378.9 mmol) and dried CrO_3 (18.96 g, 189.6 mmol) was stirred for 15 minutes using a $CaCl_2$ moisture trap in order to prepare PDC (Pyridinium chromate). To this system a mixture of alcohol **2** (16 g, 31.7 mmol) and 300 mL of CH_2Cl_2 was added, the reaction was stirred overnight at room temperature. The solvent was removed under reduced pressure and the white pure product **3** (15.0 g, y=94%) was isolated using a silica-gel flash chromatography (ethyl acetate/hexane 1:2).
IR (KBr, cm^{-1}): 3446, 2936, 1735, 1701, 1447, 1259, 1024, 967, 802.

Synthesis of Methyl [3α,5β,7α]-3,7-diacetyloxi-12-oximocolan-24-oate (4). A mixture of ketone **3** (15 g, 29.72 mmol), hydroxylamine hydrochloride (3.61 g, 51.21 mmol), trihydrated sodium acetate (13.2 g, 97.00 mmol) and 470 mL of methanol was refluxed during 4.5 h. Solvent was removed under vacuum, the obtained amorphous white crude was redissolved in methylene chloride, washed thrice with brine, the organic layer was dried using anhydrous Na_2SO_4 and the product was crystalized from methanol, obtaining 12.0 g (y=80 %) of white needles of oxime **4**. ^{1}H NMR (400 MHz, $CDCl_3$): 4.93 (d,1H, 7-CH), 4.57 (m,1 H, 3-CH), 3.64 (s, 3H, CH_3OCO), 3.34 (dd, 1H, NOH), 2.03 (s, 3H, 7-CH_3CO), 2.00 (s, 3H, 3-CH_3CO), 0.98-2.40 (m, 28H, -CH and -CH_2 of steroid skeleton and side chain), 1.00 (s, 3H, CH_3), 0.95 (d, 3H, 21-CH_3), 0.94 (s, 3H, CH_3).
IR (KBr, cm^{-1}): 3453, 2948, 2872, 1735, 1646, 1646, 1438, 1249,1062, 1024, 923, 859, 609.

Synthesis of Methyl [3α,5β,7α,12α]-12-amino-3,7-diacetyloxycolan-24-oate (5). A pressurized stainless steel reactor equipped with a suitable glass container in it was loaded with oxime 23 (3.0 g, 5.78 mmol), 150 mg of $PtO_2 \bullet xH_2O$, 5 mL of glacial acetic acid and a magnetic stirring bar, the mixture was put under 4 atm of H_2 pressure during 6 days. The reaction mixture was filtered using a porous glass filter and the isolated hydroxylamine was stirred for 12 h with powdered zinc (3.0 g, 45.86 mmol) in glacial acetic acid, ¾ of the solvent was removed under reduced pressure, the concentrated mixture was then basified with KOH and the amine **5** was extracted with ethyl acetate (3x40 mL), the organic extracts were dried over anhydrous Na_2SO_4 and solvent was removed under reduced pressure again to obtain 12.0 g (y=80%) of chemically pure amine **5**. ^{1}H NMR (400 MHz, $CDCl_3$): 4.84 (br, 1H, 7-CH); 4.54 (m, 1H, 3-CH); 3.84 (b, 2H, N-H); 3.62 (s, 3H, CH_3OCO); 3.13 (s, 1H, 12-CH); 2.03 (2, 3H, 7- CH_3CO); 1.98 (s, 3H, 3-CH_3CO); 2.40-0.91 (m, 23H, -CH and -CH_2 of steroid skeleton and side chain); 0.93 (d, 3H, 21-CH_3); 0.88 (s, 3H, CH_3); 0.68 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 174.0 (24C=O), 170.9 (C=O acetyl), 170.6 (C=O acetyl), 74.0, 71.0, 57.3, 53.5, 51.7, 49.6, 47.0, 40.9, 38.2, 35.6, 35.2, 35.1, 34.7, 34.7, 31.5, 31.5, 30.8, 28.1, 26.8, 23.7, 22.3, 21.8, 21.7, 19.7, 19.3, 12.2. IR (KBr, cm^{-1}): 3448, 2945, 2872, 1735, 1570, 1437, 1377, 1249, 1062, 1024, 936, 800.

Synthesis of Methyl [3α,5β,7α,12α]-3,7-diacetyloxy-12-(4-tert-butilbenzoilamine)colan-24-oate (6). p-(t-butyl)benzoic acid (0.565 g, 3.17 mmol) was refluxed in 3 mL of thionyl chloride for 45 min, the excess of solvent was microdistillated and traces of the former were removed under vacuum; in this way, the obtained p-(*t*-butyl)benzoil chloride (PTBBCl) was dissolved using 5 mL of dried chloroform and dropped slowly over a cold mixture of the amine 6 (1.63 g, 3.22 mmol), dried triethylamine (1.45 mL, 3.23 mmol) and 14.0 mL of chloroform provided with magnetic stirring under N_2. The reaction was stopped after 18 hours and the product **6** (1.78 g, y=83%) was isolated using silica-gel column chromatography (ethyl acetate/hexane 3:7). ^{1}H NMR (400 MHz, $CDCl_3$): 7.65 (dd, 4H), 4.86 (br, 1H, 7-CH); 4.54 (m, 1H, 3-CH); 3.84 (s, 1H, N-H); 3.60 (s, 3H, CH_3OCO); 3.13 (s, 1H, 12-CH); 2.00 (s, 3H, 7- CH_3CO); 1.98 (s, 3H, 3-CH_3CO); 2.48-0.91 (m, 24H, -CH and -CH_2 of steroid skeleton and side chain); 1.28 (s, 9H, t-butyl); 0.95 (d, 3H, 21-CH_3); 0.88 (s, 3H, CH_3); 0.76 (s, 3H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 174.0 (24C=O), 170.9 (C=O acetyl), 170.6 (C=O acetyl), 74.0, 71.0, 57.3, 53.5, 51.7, 49.6, 47.0, 40.9, 38.2, 35.6, 35.2, 35.1, 34.7, 34.7, 31.5, 31.5, 30.7, 28.1, 26.8, 23.7, 22.3, 21.8, 21.7, 19.7, 19.3, 12.2. IR (KBr, cm^{-1}): 3394, 2959, 2872, 1735, 1656, 1610, 1364, 1250, 1188, 1024, 968, 938, 891, 849.

Synthesis of Sodium [3α,5β,7α,12α]-12-(4-tert-butilbenzoilamine)-3,7-dihydroxy-colan-24-oate (7). (12-NaTbuBC). The amide **6** (0.920 g, 1.38 mmol) was refluxed with 25 mL of a methanolic solution of KOH 1M for 1.5 h. The solvent was removed under vacuum, a minimal amount of distilled water was added and the product was isolated acidifying the media dropping concentrated HCl. The amorphous white solid was filtered and dried under vacuum for 1 day. A solid powder was recovered. This carboxylic derivative was dissolved in a minimal amount of distilled water and an equivalent of NaOH was added. The mixture was homogenized and poured on 400 mL of acetone, then was cooled at -4°C during 3 days and the white powder obtained was filtered and dried under vacuum to obtain 12-NaTbuBC (0.488 g, y=58%). IR (KBr, cm^{-1}): 3424, 3055, 1711, 1637, 1508, 1446, 1373, 1239,1077, 982, 735.



Scheme 2. Structure of the new compound 12-NaTbuBC.

The structure elucidation of the new compound 12-NaTbuBC was performed by NMR (^{1}H, ^{13}C)

^{1}H NMR (600 MHz, DMSO) δ 7.69 (NH), 7.68, 7.66 (H_{27} ,$J_{27\text{-}28}$: 8.40 Hz), 7.49, 7.48 (H_{28} ,$J_{28\text{-}27}$: 8.40 Hz), 4.29 (H_{12}), 3.65 (H_7), 3.18 (H_3), 2.11 (H_4) , 2.03 (H_{23}), 1.97 (H_9, H_{14}), 1.90-1.77 (H_6, H_{23}, H_{16}), 1.73-1.57(H_1, H_{15}, H_{17}, H_{22}) , 1.54-1.44 (H_4, H_8, H_{11}), 1.41(H_6), 1.37(H_2), 1.33-1.22 (H_5, H_{16}, H_{20}, H_{31}), 1.06 (H_{15}, H_{22}), 0.97 (H_2), 0.84 (H_1, H_{19}), 0.77 (H_{18}), 0.73 (H_{21}).

^{13}C NMR (151 MHz, DMSO) δ 177.2 (C_{24}), 167.0 (C_{25}), 154.1 (C_{29}), 133.6 (C_{26}), 127.6 (C_{27}), 125.6 (C_{28}), 70.8 (C_3), 67.1 (C_7), 52.51 (C_{12}), 48.8 (C_{17}), 44.5 (C_{13}), 43.4 (C_{14}), 41.7 (C_5), 40.2 (C_4),

39.4 (C_8), 35.5 (C_1), 35.1 (C_6, C_{29}), 35.00 (C_{30}), 33.9 (C_{23}), 32.3 (C_{22}), 31.4 (C_{31}), 30.1(C_2) 27.7 (C_9), 27.6 (C_{16}), 26.7 (C_{11}), 23.3 (C_{15}), 23.0 (C_{19}), 17.8 (C_{29}).

References

1) S. Gouin and X. X. Zhu, Synthesis of 3 alpha- and 3 beta-dimers from selected bile acids, *Steroids*, **1996,** *61*, 664-669.
2) Vogel, A. I.; Smith, P. W.; Furniss, B. S.; Hannaford, A. J. *Vogel's Textbook of Practical Organic Chemistry, 5th edition*; Longman/Wiley, New York, 1989.

Supporting Figures

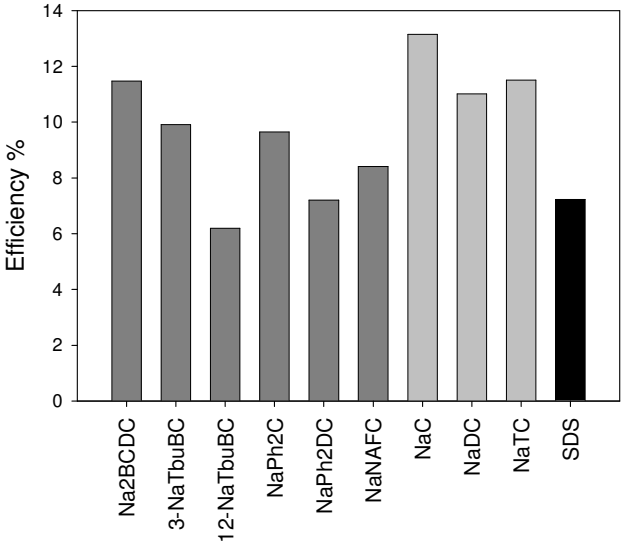


Fig. S1. Efficiency expressed as percent of SWCNT remaining in the supernatant, estimated from the absorbance at 850 nm, after sonication and centrifugation in 0.060 wt% BDSs (dark grey), BSs (grey) and SDS (black) solutions for electric arc SWCNTs. For each bar the error is within ±10% of the bar value.

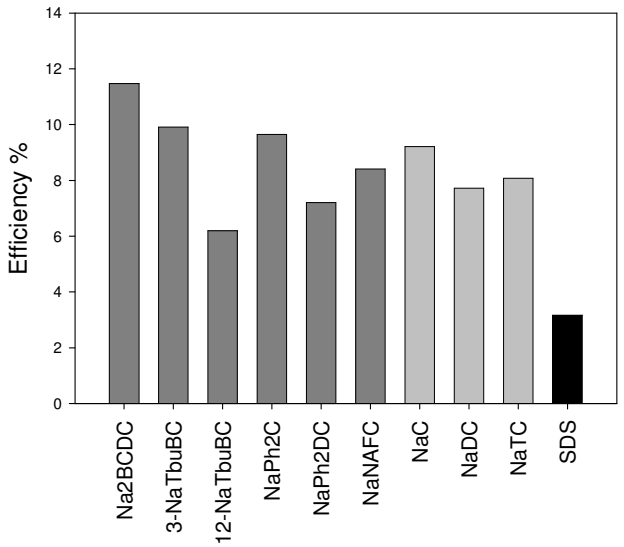


Fig. S2. Efficiency expressed as percent of SWCNT remaining in the supernatant, estimated from the absorbance at 850 nm, after sonication and centrifugation in 1.00 mM BSDs (dark grey), BSs (grey) and SDS (black) solutions for electric arc SWCNTs. For each bar the error is within ±10% of the bar value.

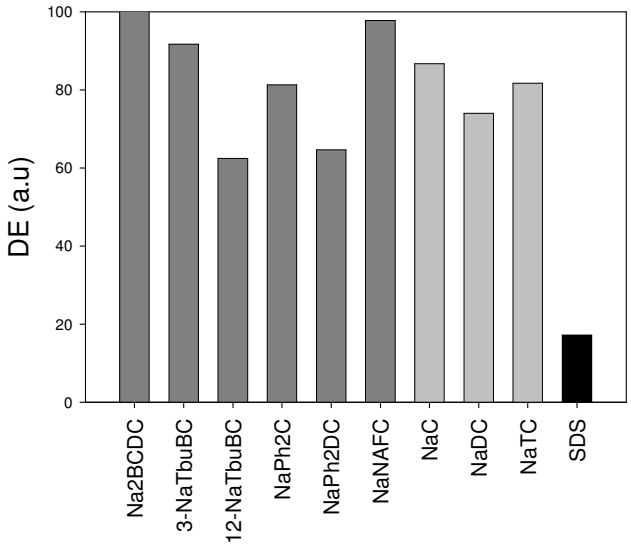


Figure S3. DE values (a.u.), estimated by areal peak integration of electric arc SWCNT dispersions in 1.0 mM solutions of BSDs (dark grey), BSs (grey) and SDS (black). For each bar the error is within ±10% of the bar value.

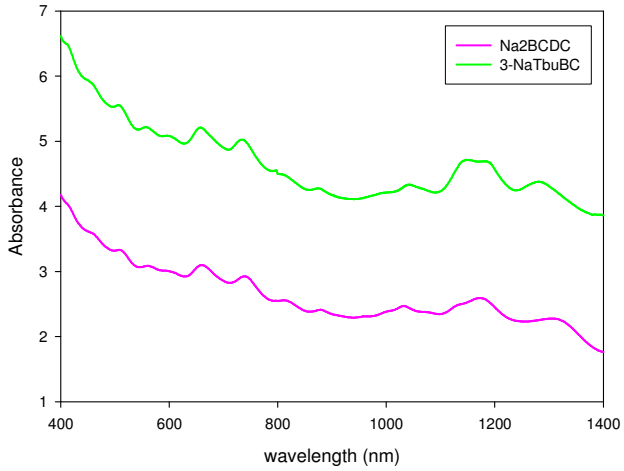


Figure S4. Vis-NIR absorbance spectra of the CoMoCAT SWCNT suspensions in 1.0 wt% 3-NaTbuBC and Na_2BCDC aqueous solutions.

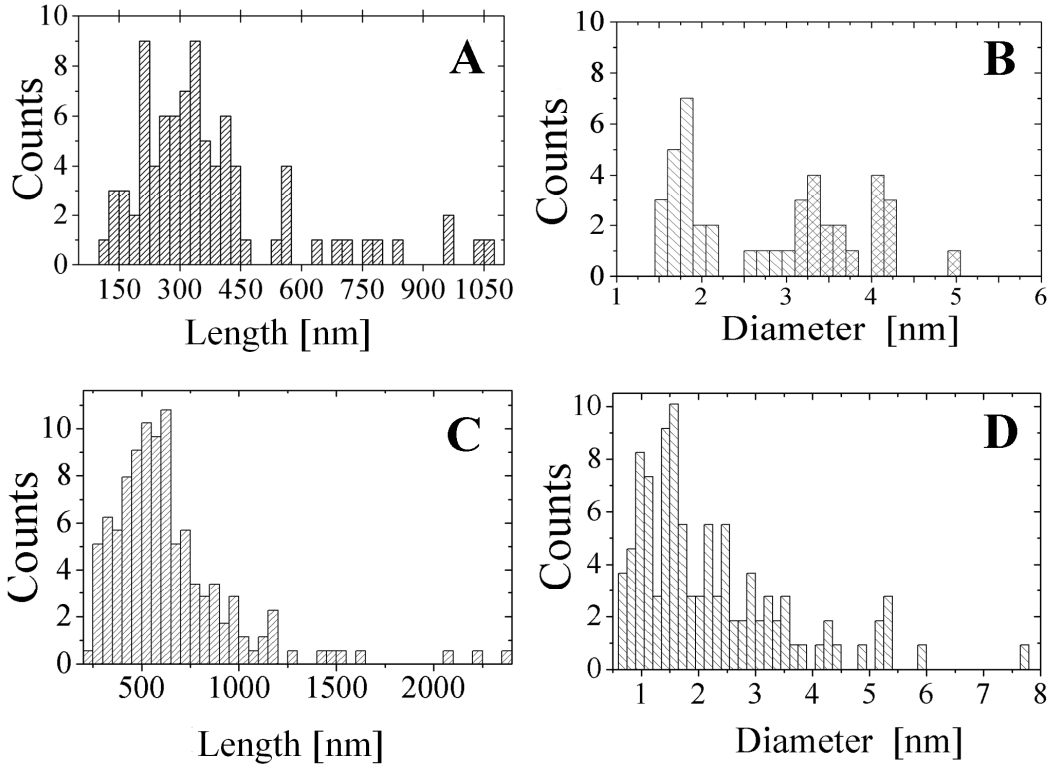


Figure S5. Length and diameter distributions obtained from AFM images for electric arc (A and B) and CoMoCAT (C and D) SWCNT dispersions in 0.06 wt% Na_2BCDC aqueous solutions. The diameters were inferred from the heights of the structures.