Electronic Supplementary Material (ESI) for Chemical Communications

Interfacial Strain-Promoted Azide-Alkyne Cycloaddition (I-SPAAC) for the Synthesis of Nanomaterial Hybrids

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Supporting Information

General Materials and Methods

The following reagents were used for the synthesis of the compounds in this article. Sodium azide, potassium thioacetate, triethylene glycol monomethylether, tetraethylene glycol, 4-dimethylaminopyridine (DMAP), sodium borohydride, p-toluenesulfonyl chloride, Gold(III) chloride trihydrate, single wall carbon nanotubes (carbon >90 %, ≥70% carbon as SWCNT, 0.7-1.3 nm diameter) and deuterated chloroform ($CDCl_3$) were purchased from Aldrich. All common solvents, dry methanol, hydrochloric acid, sodium hydroxide, triethylamine, and magnesium sulfate were purchased from Caledon. Glacial acetic acid (99.7%, ACS grade) was purchased from BDH. Celite was purchased from Fisher Scientific. Ethanol was purchased from Commercial Alcohols and Deuterated water (D_2O) was purchased from Cambridge Isotope Laboratories. Dialysis membranes (MWCO 6000-8000) were purchased from Spectra/Por. Dibenzocyclooctyne-amine (DBCO) was purchased from Click Chemistry Tools.

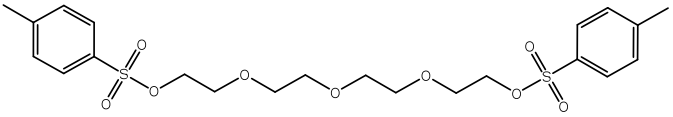
^{1}H and ^{13}C NMR spectra were recorded using a Mercury 400 spectrometer; $CDCl_3$, CD_3CN, and D_2O were the solvents and the residual solvent was used as reference. Thermogravimetric analysis (TGA) was recorded by placing the sample into a 70 μL ceramic crucible and heating it from 25 – 750 $^{\circ}C$ at a rate of 10 ºC min^{-1}. The TGA was run under a flow of nitrogen of 70 mL min^{-1} in a Mettler Toledo TGA/SDTA 851 instrument.

Transmission electron microscopy (TEM) images were recorded from a TEM Philips CM10. Infrared spectra were recorded using a Bruker Vector33 spectrometer and making a thin film of the sample onto a KBr disk.

The XPS analyses were carried out with a Kratos Axis Ultra spectrometer using a monochromatic Al K(alpha) source (15mA, 14kV). XPS can detect all elements except hydrogen and helium, probes the surface of the sample to a depth of 5-7 nanometres, and has detection limits ranging from 0.1 to 0.5 atomic percent depending on the element. The instrument work function was calibrated to give a binding energy (BE) of 83.96 eV for the Au 4f7/2 line for metallic gold and the spectrometer dispersion was adjusted to give a BE of 932.62 eV for the Cu 2p3/2 line of metallic copper. Specimens were mounted on a double side adhesive and the Kratos charge neutralizer system was used on all specimens. Survey scan analyses were carried out with an analysis area of 300 x 700 microns and a pass energy of 160 eV. High resolution analyses were carried out with an analysis area of 300 x 700

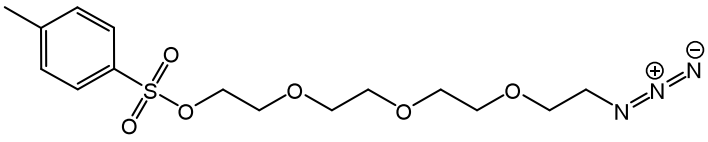
microns and a pass energy of 20 eV. Spectra have been charge corrected to the main line of the carbon 1s spectrum set to 284.5 eV for graphitic/nanotube type species. Spectra were analyzed using CasaXPS software (version 2.3.14).

Synthesis of Compound 1 (Ts-EG$_4$-Ts)



The synthesis of this compound was carried out following the previously established procedure.[1] Briefly, **compound 1** was made by dissolving tetraethylene glycol in DCM and adding triethylamine and DMAP. The reaction was brought down to 0ºC and then 4-toluenesulfonyl chloride was added. The reaction was then left at room temperature for four hours, and the product washed with water, dried with $MgSO_4$ and purified by column chromatography. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 2.45 (singlet, 6H), 3.57 (multiplet, 8H), 3.68 (triplet, 4H, J=8Hz), 4.16 (triplet, 4H, J=8 Hz), 7.34 (multiplet, 4H), 7.80 (multiplet, 4H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 21.6, 68.7, 69.2, 70.5, 70.7, 127.9, 129.8, 133.0,144.8. IR (KBr disk, cm^{-1}) 3643, 3666, 2909, 2864, 2589, 2520, 1927, 1598, 1443, 1349, 1292. HRMS: EI ($C_{22}H_{30}O_9S_2$) calc: 502.133, found 502.138.

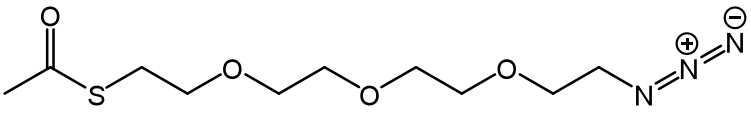
Synthesis of Compound 2 (Ts-EG$_4$-N$_3$)



19 mmol of **compound 1** was dissolved in 50 mL of acetonitrile. To this solution, 6.3 mmol of sodium azide were added, and the reaction mixture was brought to reflux. The solution was clear and colourless, and the sodium azide salt was present as a precipitate. The reaction was left over three nights. Gravity filtration was then used to remove the salt. The salt was washed with DCM. The filtrate was then collected and the solvent was evaporated off. The crude product was then purified by using column chromatography. The eluent used in order to separate **compound 2** from unreacted **compound 1** and the biproduct N_3-$(EG)_4$-N_3 was 1:3 acetone:hexane and the reaction product was the first compound to be eluted. **Compound 2** was obtained as a light yellow oil with a 43% yield. ^{1}HNMR

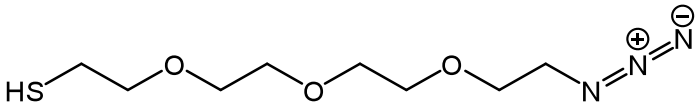
($CDCl_3$, 400 MHz): δ_H (ppm): 2.44 (s, 3H), 3.38 (t, J = 4 Hz, 2H), 3.65 (m, 12H), 4.15 (t, J = 4 Hz, 2H), 7.34 (d, J = 8Hz, 2 H), 7.79 (d, J = 8 Hz, 2H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 21.5, 50.6, 68.59, 69.2, 70.00, 70.5, 70.6, 70.7, 127.9, 129.8, 132.9, 144.75. IR (KBr disk, cm^{-1}) 2909, 2864, 2101, 1927, 1598, 1443, 1349, 1292, 1176. HRMS: CI ($C_{15}H_{23}N_3O_6S$) $(M + H)^+$ calc: 374.140; found 374.140.

Synthesis of Compound 3 (AcS-EG$_4$-N$_3$)



1.3 mmol of **compound 2** were dissolved in 10 mL of acetone. The solution became light yellow. This mixture was stirred, and then 1.6 mmol of potassium thioacetate were added. The solution became milky yellow. This reaction mixture was warmed up to 50 ºC and left overnight. The acetone was evaporated off, and the product was redissolved in DCM. Celite was then used to filter off the insoluble salt. The filtrate was then collected and the DCM was evaporated off. **Compound 3** was obtained as a light yellow oil with an 85% yield. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 2.34 (s, 3H), 3.09 (t, J = 4 Hz, 2H), 3.39 (t, J = 8 Hz, 2H), 3.64 (m, 12H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 28.8, 30.5, 50.7, 69.7, 70.00, 70.28, 70.59, 70.67, 195.5. IR (KBr disk, cm^{-1}) 2909, 2864, 2101, 1692, 1443, 1349, 1292, 1119. HRMS: CI ($C_{10}H_{19}N_3O_4S$) $(M + H)^+$ calc: 278.118; found 278.118.

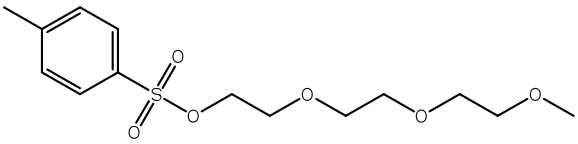
Synthesis of Compound 4 (HS-EG$_4$-N$_3$)



0.24 mmol of **compound 3** was dissolved into 5 mL of dry methanol and the solution was purged with argon for 15 minutes. An NaOH/EtOH 1M solution was purged with argon for 15 minutes in a second flask. Then, 237 µmL of the NaOH/EtOH 1M solution were transferred by the use of a microsyringe to the methanol mixture. This was left for 40 minutes under Argon. While the reaction was taking place, an HCl/H_2O 1M solution was purged with Argon. Then, after the 40 minutes, 474 µmL of 1 M HCl aqueous solution were transferred to the reaction mixture by the use of a microsyringe. The acid base reaction was left for 15 minutes under Ar. The solution was clear and

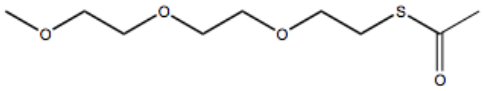
colourless. Once the reaction was finished, the thiol was extracted with DCM. The organic phase was then dried with $MgSO_4$, and the thiol was obtained as a very light yellow liquid, with a yield of 86%. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 1.60 (t, J = 8 Hz, 1 H), 2.70 (m, 2H), 3.40 (t, J = 4 Hz, 2H), 3.65 (m, 12H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 24.2, 50.6, 72.8, 70.01, 70.19, 70.58, 70.64, 70.68. IR (KBr disk, cm^{-1}) 2909, 2864, 2559, 2101, 1443, 1349, 1292, 1119, 936, 851. HRMS: CI ($C_8H_{17}N_3O_3S$) $(M + H)^+$ calc: 237.115; found 237.115.

Synthesis of Compound 5 (Ts-EG$_3$-Me)



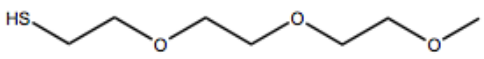
The synthesis for this compound was carried out using an improved procedure from our previous work.[1] Briefly, a solution of 61 mmol of triethylene glycol monomethyl ether, 0.1525 mol of triethylamine, 14.3 mmol 4-dimethylaminopyridine (DMAP), and 400 mL of DCM was brought down to 0^{o}C and stirred. Then 60.39 mmol of 4-toluenesulfonyl chloride was added and the ice bath was removed. At first the solution was clear and colourless, but as soon as the 4-toluenesulfonyl chloride was put in the solution became light yellow and, as the reaction went to completion, the solution darkened. The reaction was left for four hours. The mixture was then washed three times with 1 M NaOH, three times with 1M HCl, and dried with $MgSO_4$. **Compound 5** was obtained with a yield of 86% with no need of further purification as shown by NMR spectroscopies and mass spectrometry. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 2.41 (s, 3H), 3.34 (s, 3H), 3.51 (m, 2H), 3.56 (m, 6H), 3.65 (m, 2H), 4.41 (m, 2H), 7.33 (m,2H), 7.77 (m, 2H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 21.6, 59.0, 68.6, 69.3, 70.5, 70.7, 71.9, 127.9, 129.8, 133.0, 144.7, 175.1. HRMS: EI ($C_{14}H_{22}O_6S$) calc: 318.114; found 318.111.

Synthesis of Compound 6 (AcS-EG$_3$-Me)



The synthesis of this compound is the same as that reported in our previous work.[1] Briefly, a solution of compound 4 was dissolved in acetone. Then potassium thioacetate was added, the reaction was brought to reflux and left overnight. The acetone was then removed, replaced with DCM, and washed with water. Magnesium sulfate was then used to dry the organic phases, and the triethyleneglycolthioacetate product was obtained. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 2.33 (s, 3H), 3.09 (t, 2H, J=4 Hz), 3.38 (s, 3H), 3.55 (m, 2H), 3.60 (t, 2H, J=8Hz), 3.63 (m, 6H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 28.1, 30.5, 59.0, 69.7, 70.2, 70.5, 71.7, 77.0, 77.3, 195.5. HRMS: CI ($C_9H_{18}O_4S$) $(M + H)^+$ calc: 223.100; found 223.100.

Synthesis of Compound 7 (HS-EG$_3$-Me)



A solution of dry MeOH and **compound 6** was purged with argon, and the appropriate amount of NaOH/EtOH 1M and HCl/H2O 1M solutions were also purged in separate flasks. After 15 minutes of purging, the appropriate amount of NaOH 1M solution was transferred into the reaction flask and the reaction was left for 40 minutes under inert gas. Then the appropriate amounts of 1M HCl aqueous solution were transferred into the reaction flask and left purging for 15 minutes. **Compound 7** was then extracted with DCM and dried with $MgSO_4$. ^{1}HNMR ($CDCl_3$, 400 MHz): δ_H (ppm): 1.59 (triplet, 1H, J=8 Hz), 2.70 (quartet, 2H, J=8Hz), 3.38 (singlet, 3H), 3.55 (multiplet, 2H), 3.63 (multiplet, 8H). ^{13}CNMR ($CDCl_3$, 400 MHz) δ_C (ppm): 24.2, 59.0, 70.2, 70.5, 71.9, 72.9, 110.0. HRMS: CI ($C_7H_{16}O_3S$) $(M + H)^+$ calc: 181.090; found 181.090.

Synthesis of Me-EG$_3$-AuNP

The synthesis of the triethylene glycol monomethyl etherAuNP is the same as that done previously by our group.[1] Briefly, a solution of acetic acid, methanol, $HAuCl_4 \bullet 3H_2O$ and **compound**

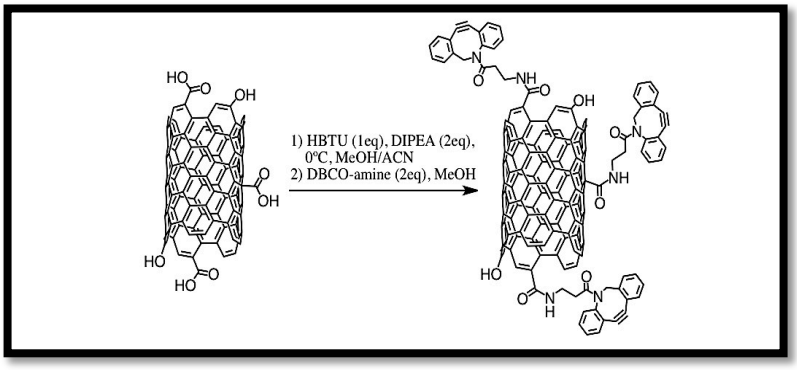
7 was made and left to react for one hour. Then, the appropriate amounts of $NaBH_4$ in milliQH_2O was added dropwise to the reaction mixture, and the reaction was left overnight. The nanoparticles were extracted with toluene and cyclohexane was used to remove excess thiol. Dialysis was then used to further purify the nanoparticles. ^{1}HNMR (D_2O, 400 MHz): δ_H (ppm): 3.34 (broad), 3.58 (broad), 3.66 (broad). IR (KBr disk, cm^{-1}): 2921, 2871, 1443, 1349, 1292, 1244, 1198, 1119, 1033.

Synthesis of N_3-EG_4-AuNP

In a typical synthesis, 50.0 mg of Me-EG_3-AuNP were transferred into a clean 25 mL round bottom flask. This compound was dissolved in 10 mL of acetone. Then 10.0 mg (42.5 µmol) of **compound 4** were transferred into this solution. The reaction was stirred vigorously for 20 minutes. After this time, the acetone was immediately evaporated off. The thin film of nanoparticles was washed first with hexanes (in which AuNP are not soluble) leaving the flask spinning attached to the rotavap and in a 30ºC water bath. Subsequently the film was quickly rinsed with isopropanol three times. This entire washing procedure was repeated three times. until the smell of the thiol was gone. 44.9 mg of nanoparticles were obtained. The nanoparticles were redissolvable readily in H_2O, acetone, acetonitrile, methanol, ethanol, DMF, DMSO and DCM with little to no aggregation. ^{1}HNMR (CD_3CN, 400 MHz): δ_H (ppm): 3.60, 3.49, 3.39, 3.31. ^{1}HNMR (D_2O, 400 MHz): δ_H (ppm): 3.66, 3.57, 3.43, 3.32. IR (KBr disk, cm^{-1}): 2921, 2871, 2101, 1443, 1349, 1292, 1244, 1198, 1119, 1033.

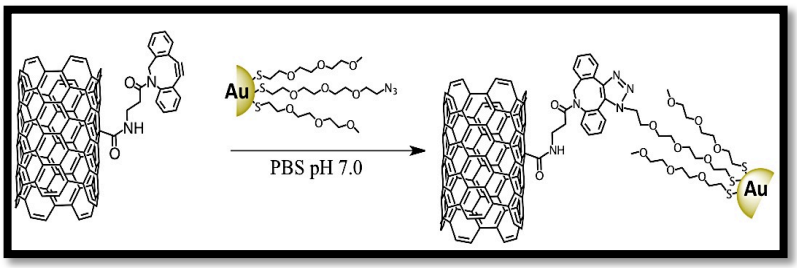
Synthesis of SWCNT-DBCO

In a typical synthesis, 10 mg of SWCNT were dispersed in 5 ml of dry MeOH in a round bottom flask. The system was cooled down to 0ºC, and the solution was purged with argon for 10 minutes. 20 mg of O-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluoro-phosphate (HBTU) (53 µmol) and 19 µl of N,N-Diisopropylethylamine (DIPEA) (106 µmol) were dissolved in a separate round bottom flask in 5 ml of a MeOH/ Acetonitrile (2:1) mixture and they were purged with argon for 10 min. Once the two solutions were purged, HBTU and DIPEA were transferred using a glass syringe into the ice-cold solution of CNT. The reaction was left for 15 min at 0ºC. In a clean round bottom flask, a solution of DBCO-amine (8.2 mg, 106 µmol) in 2 ml of dry methanol was purged with argon. After 15 minutes the solution of DBCO-amine was injected into the ice-cold solution of CNT, HBTU and DIPEA. The ice-bath was removed and the reaction mixture was left overnight under vigorous stirring. The solution was

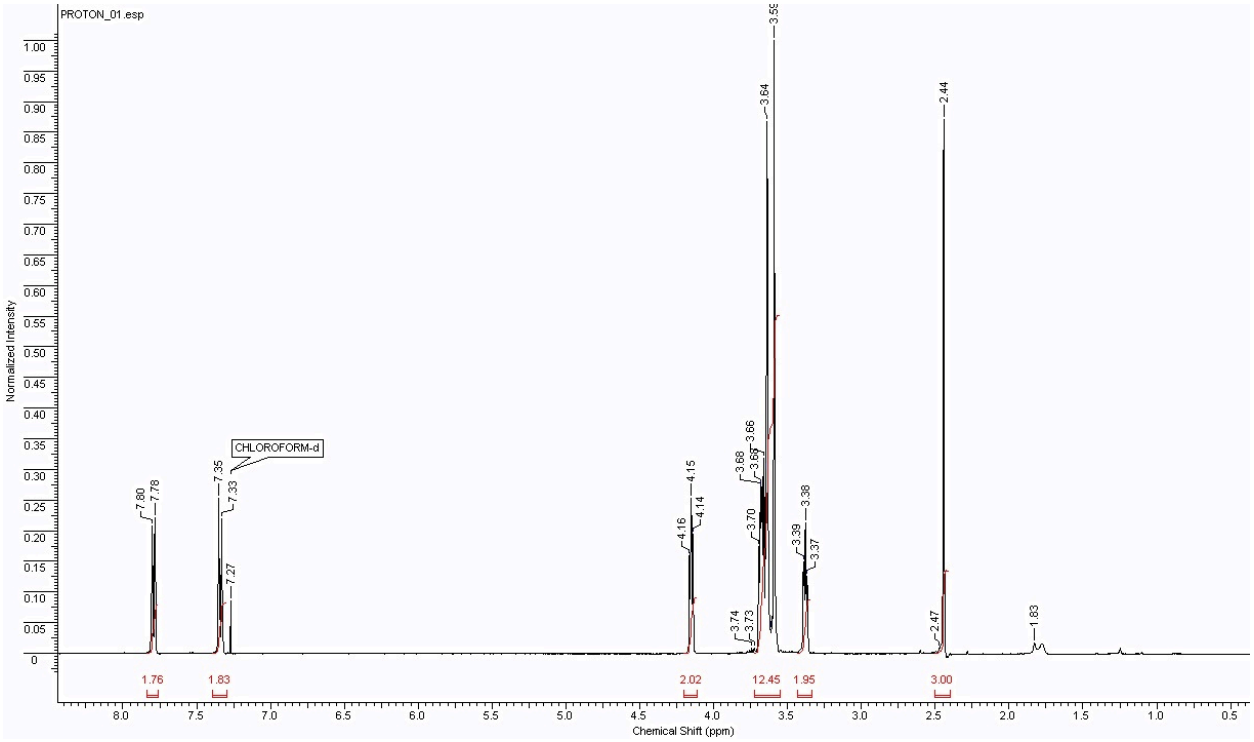


then centrifuged (10 min, 6000 rpm) and the supernatant removed. The resulting SWCNT-DBCO was re-dispersed in acetonitrile, sonicated for 10 min, centrifuged again, and the solvent was decanted. This washing protocol was repeated once more, then acetonitrile was substituted with water and the SWCNT-DBCO were washed and centrifuged twice. This ensured that there was no unreacted DBCO-amine. Finally, the solvent was evaporated and the SWCNT-DBCO was dispersed in a phosphate buffer solution (PBS) pH 7.0 to obtain a concentration of 2 mg/ml. This mother solution was stored in the freezer.

I-SPAAC reaction between N_3-EG_4-AuNP and SWCNT-DBCO



In a typical synthesis, to a 1 ml of the SWCNT-DBCO mother solution 4 mg of N_3-EG_4-AuNP were added, and the reaction's volume was diluted to 4 ml with PBS pH 7.0. The system was stirred for 1 hour at room temperature and then the SWCNT-AuNPs were centrifuged in a Pyrex centrifuge test tube. The supernatant was removed, and the decorated CNT were dispersed in water, sonicated for 10 minutes and centrifuged. Subsequently, water was substituted first with acetone, then with dichloromethane (DCM), and the washing procedure (sonication in DCM and centrifugation) was repeated four more times. This protocol was to ensure removal of any non-covalently bound AuNP.



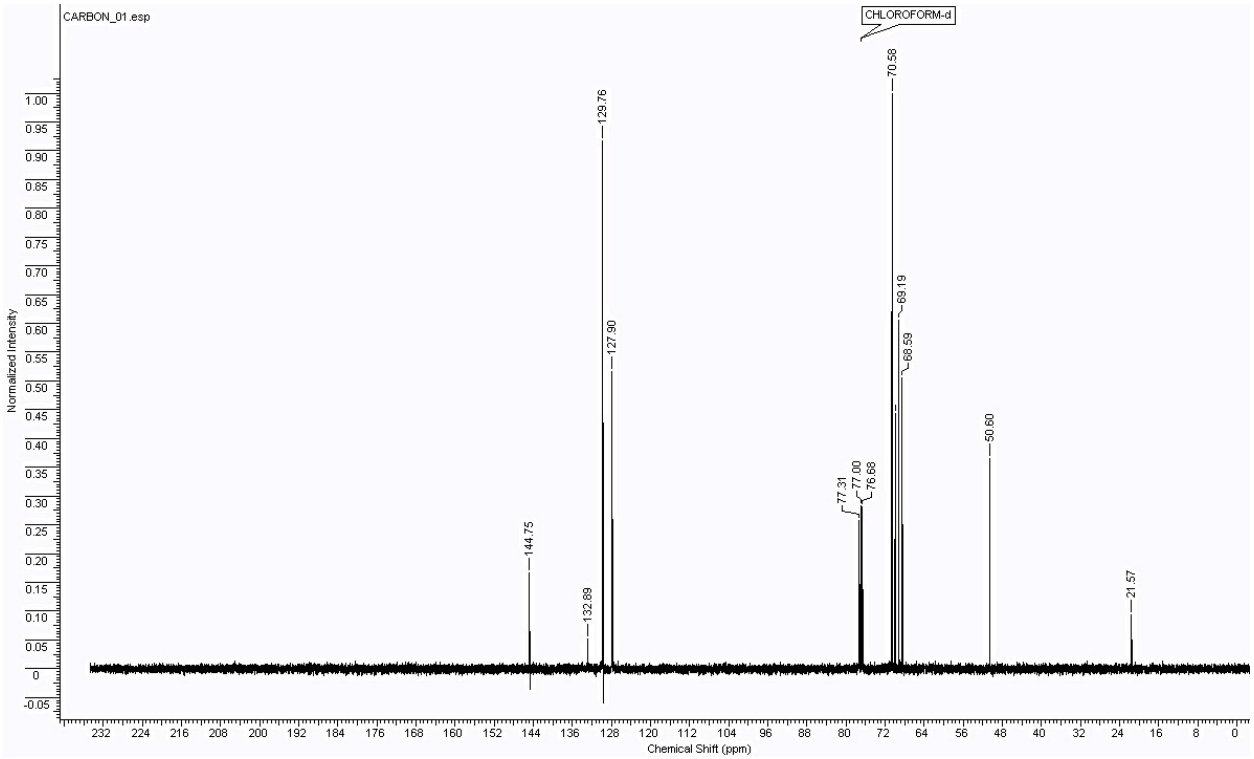


Figure SI 1. ^{1}H and ^{13}C NMR spectra for compound Ts-EG_4-N_3 recorded in $CDCl_3$ and calibrated against $CDCl_3$ or residual chloroform.

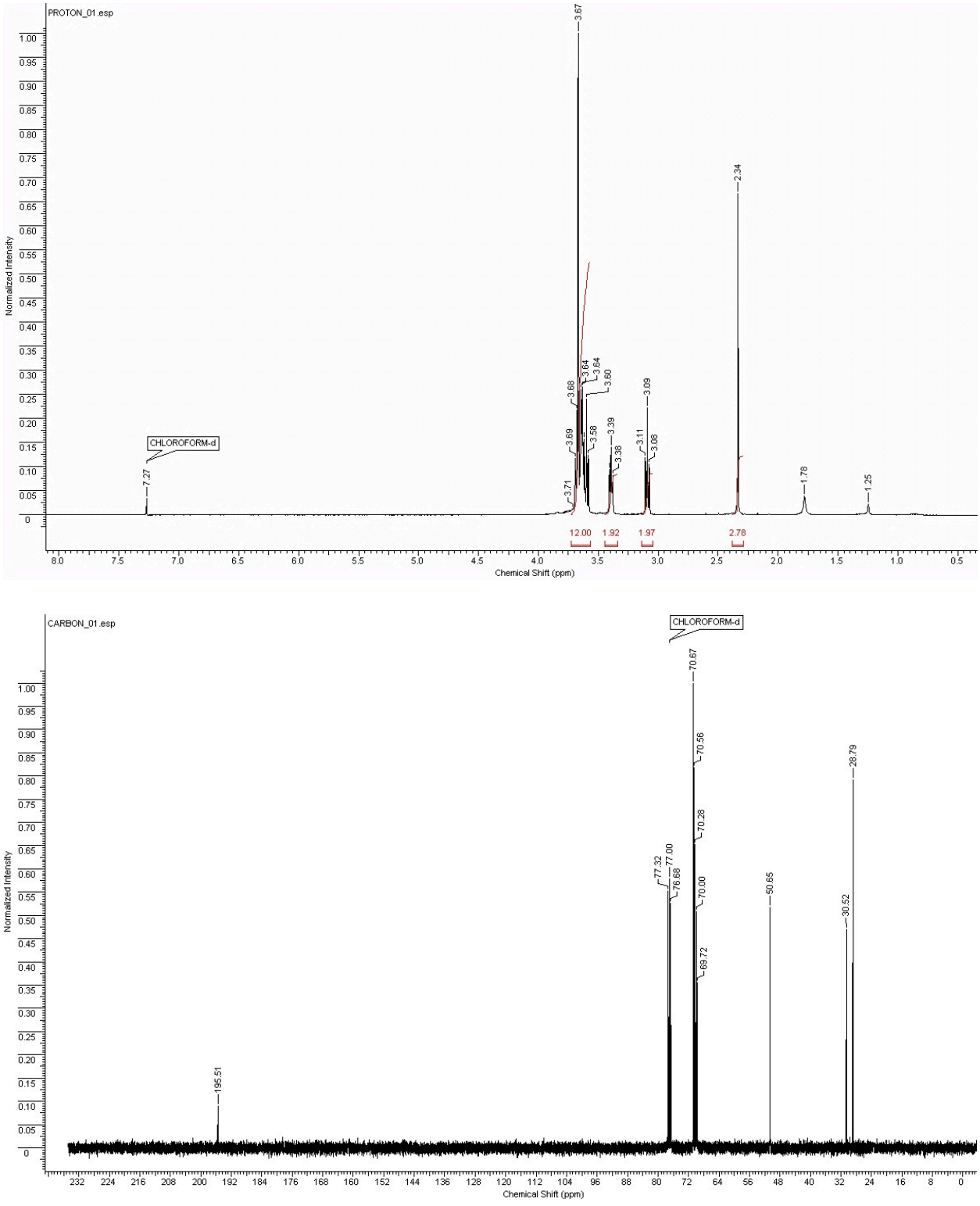


Figure SI 2. ^{1}H and ^{13}C NMR spectra of AcS-EG$_4$-N$_3$ recorded in $CDCl_3$ and calibrated against $CDCl_3$ or residual chloroform.

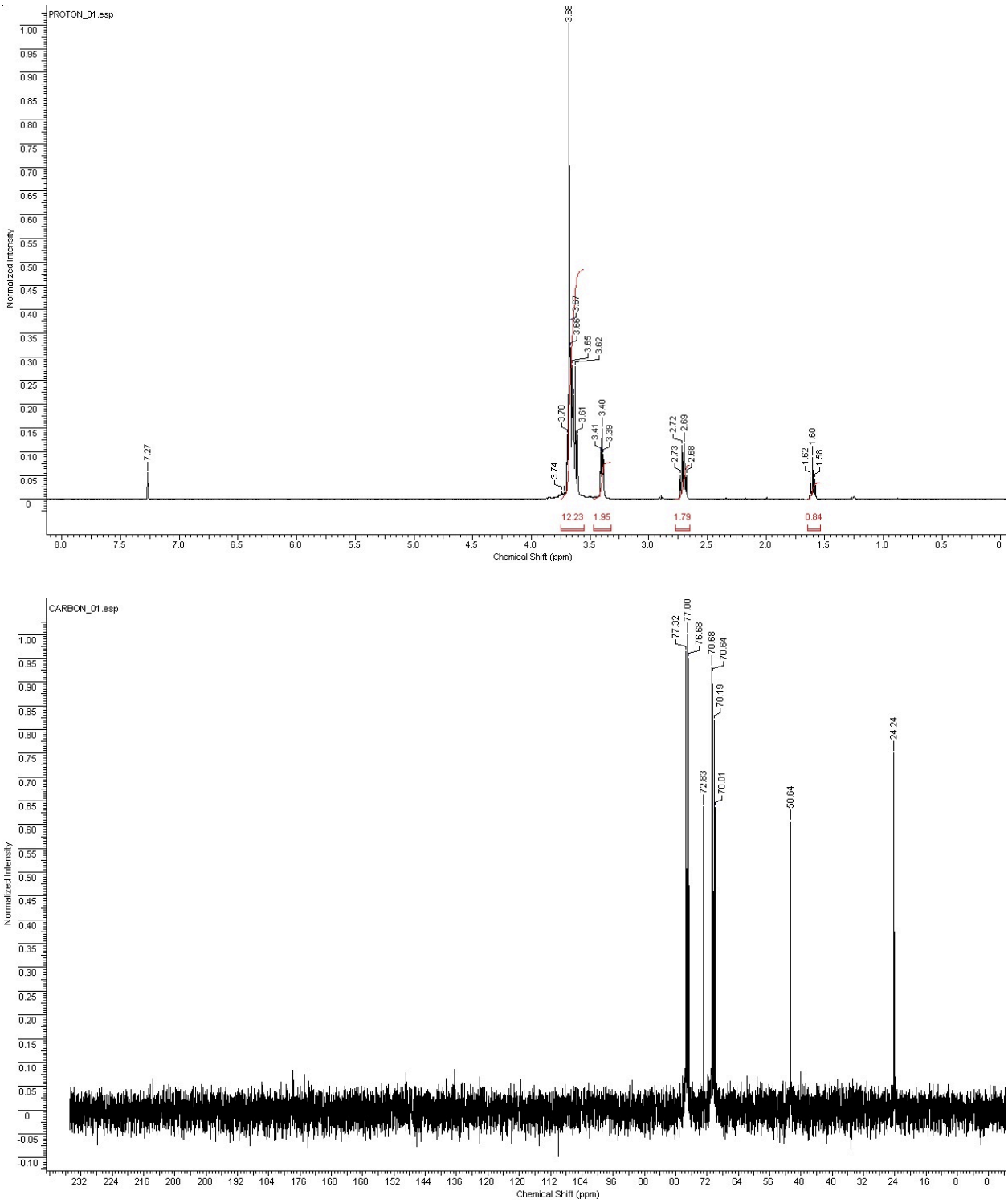


Figure SI 3. ^{1}H and ^{13}C NMR spectra of HS-EG_4-N_3 recorded in $CDCl_3$ and calibrated against $CDCl_3$ or residual chloroform.

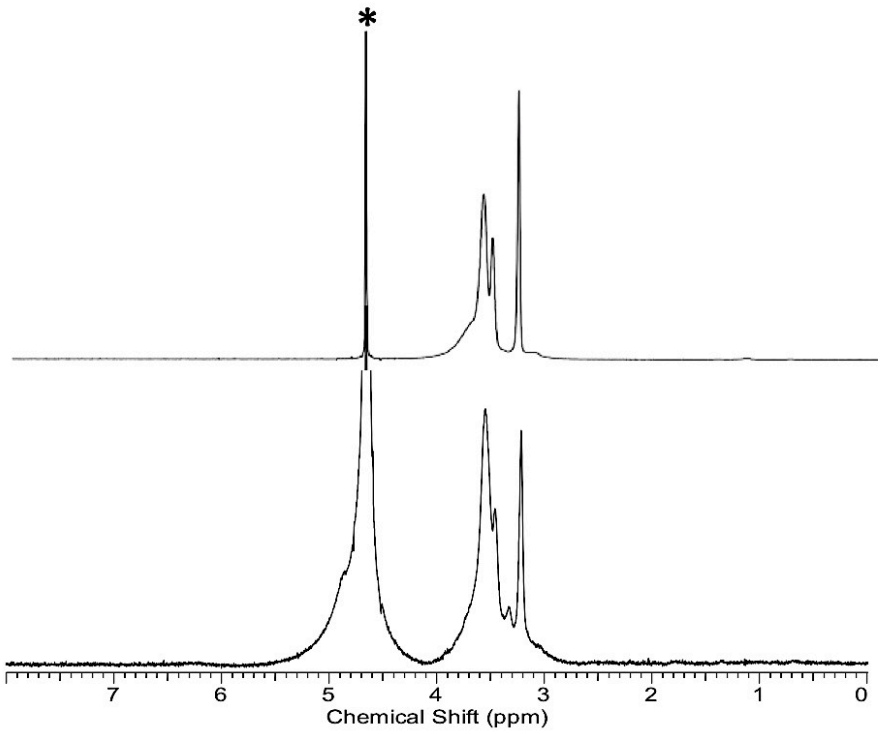


Figure SI 4. ^{1}H NMR spectra of Me-EG$_3$-AuNP (top) and of N$_3$-EG$_4$-AuNP (bottom) recorded in D$_2$O and calibrated against residual water (*).

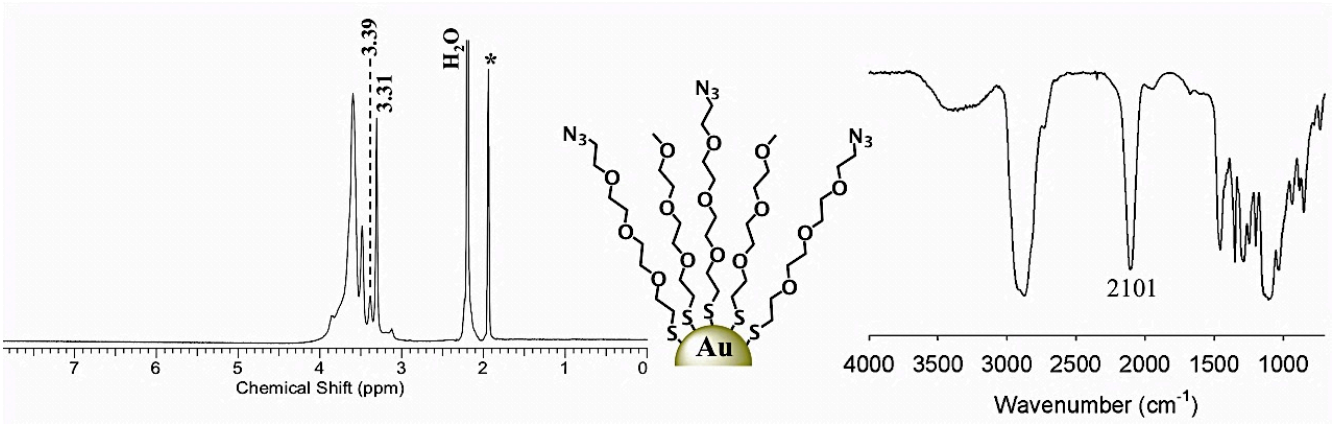


Figure SI 5. ^{1}H NMR spectra of N$_3$-EG$_4$-AuNP recorded in *d3*-acetonitrile and calibrated against residual acetonitrile (*) (left); IR spectra of N$_3$-EG$_4$-AuNP, recorded making a thin film of AuNP on a KBr disk (right).

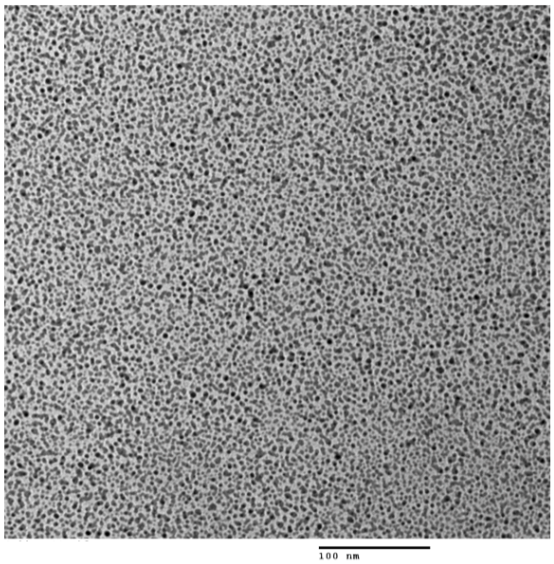


Figure SI 6: TEM images of N_3-EG_4-AuNP.

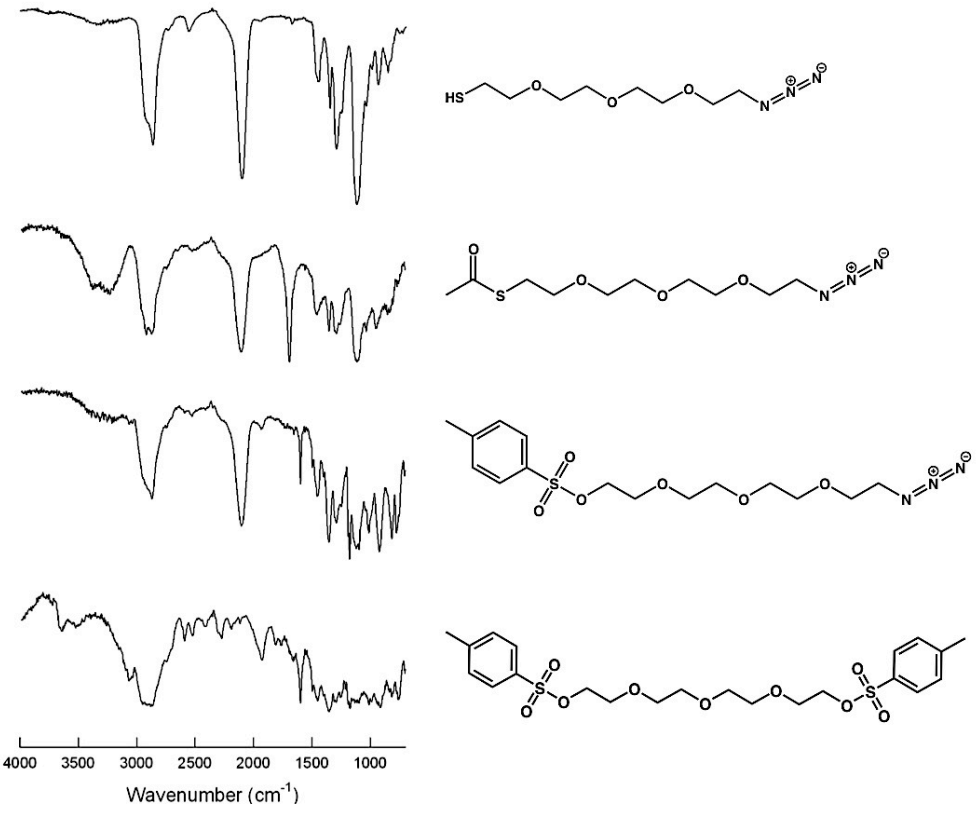


Figure SI 7: IR spectra of intermediates of the synthetic path leading to HS-EG_4-N_3 ligand. Spectra recorded making a thin film of compound onto a KBr disk.

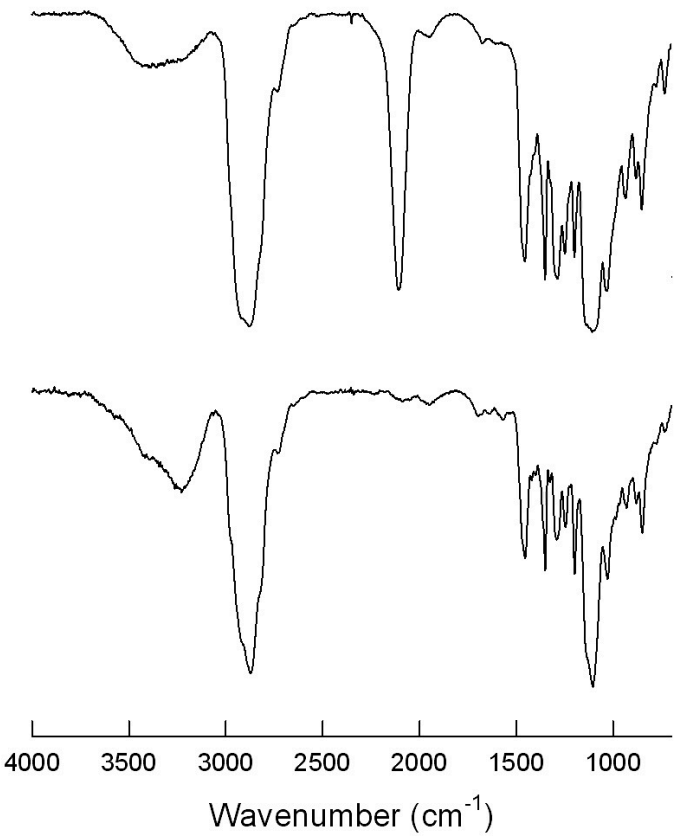


Figure SI 8: IR spectra of the basic Me-EG_3-AuNP (bottom), and of the N_3-EG_4-AuNP (top) Spectra recorded making a thin film of compound onto a KBr disk.

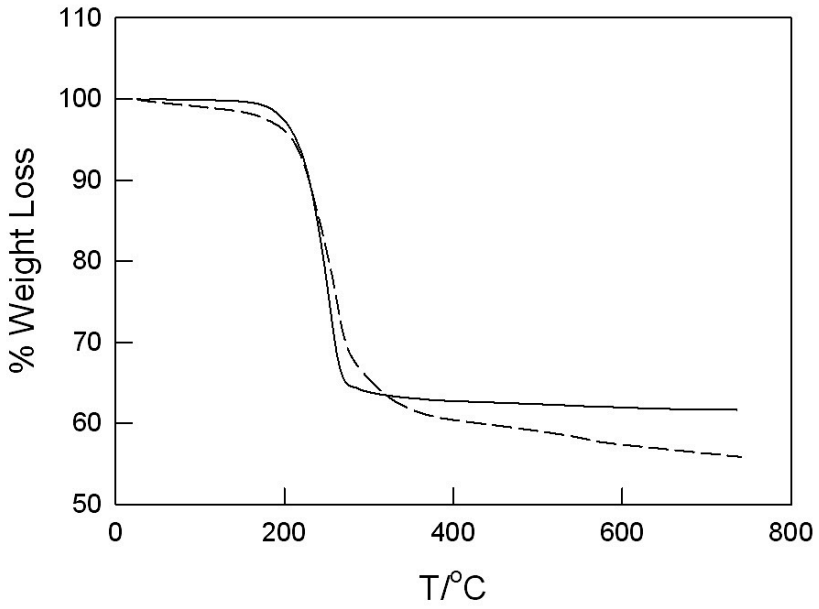


Figure SI 9: TGA of basic Me-EG_3-AuNP (solid line) and of N_3-EG_4-AuNP (dashed line).

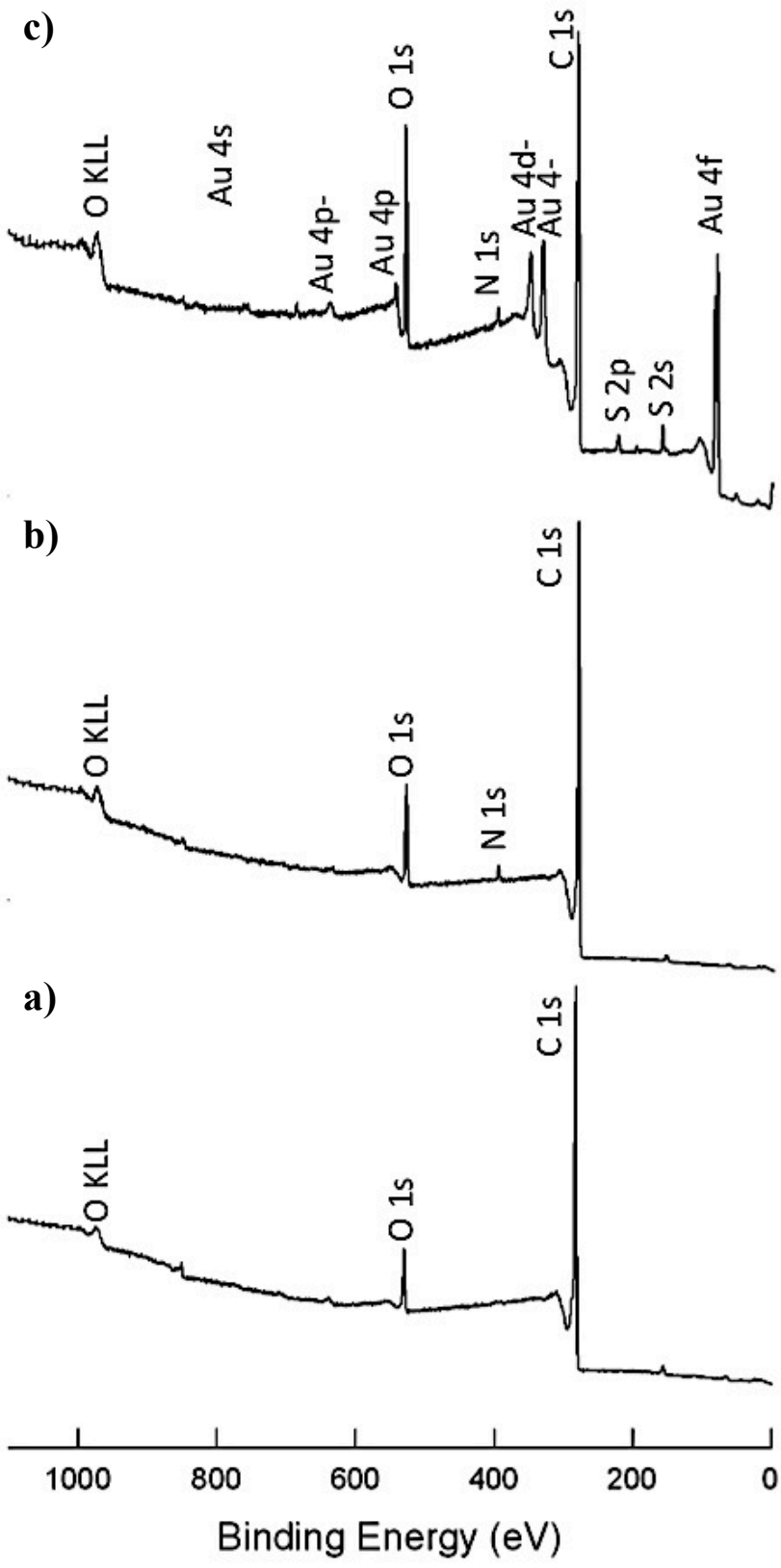


Figure SI 10: XPS survey for a) SWCNT starting material; b)SWCNT-DBCO; c) SWCNT-AuNP hybrid.

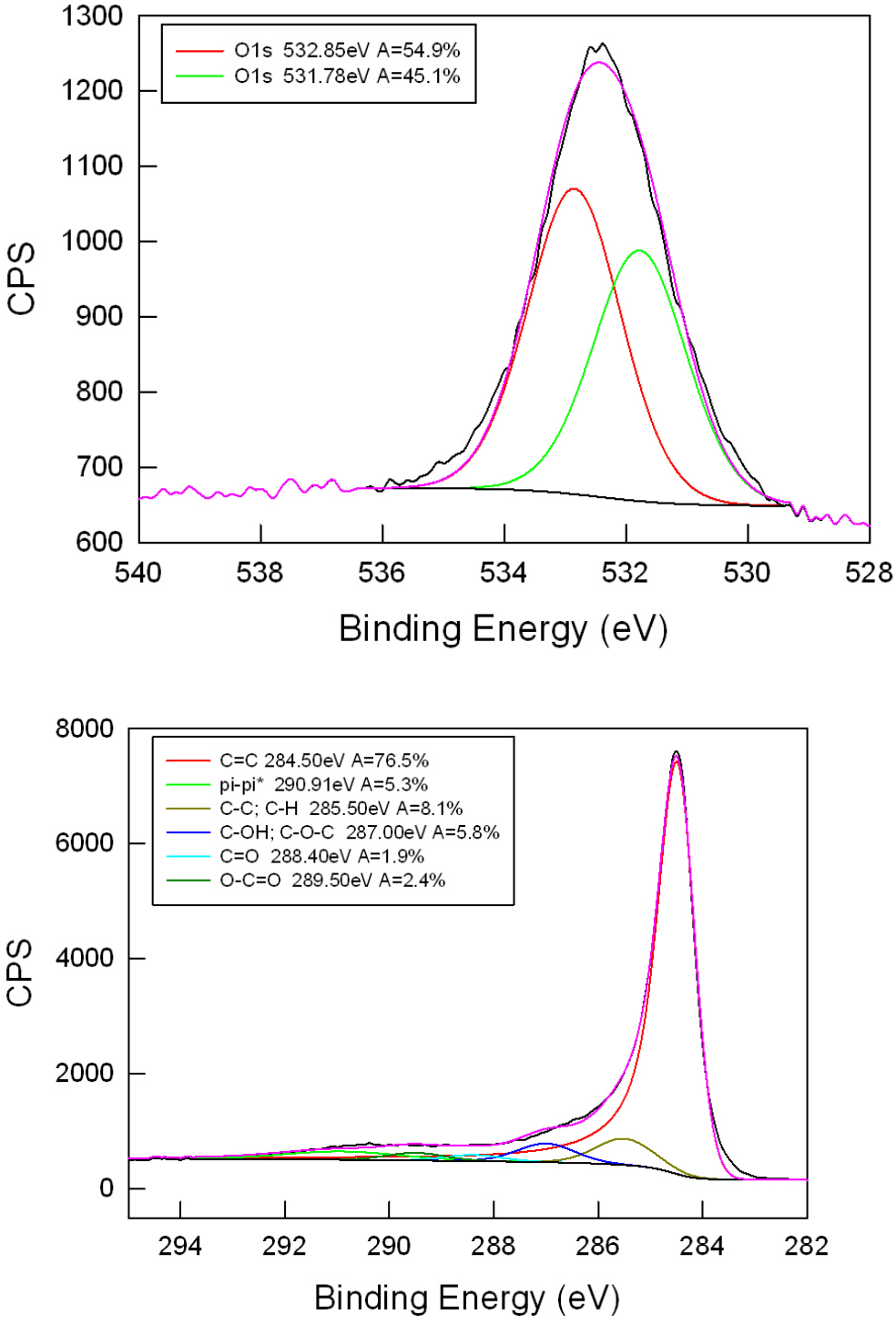


Figure SI 11: High resolution XPS spectra for SWCNT starting material.

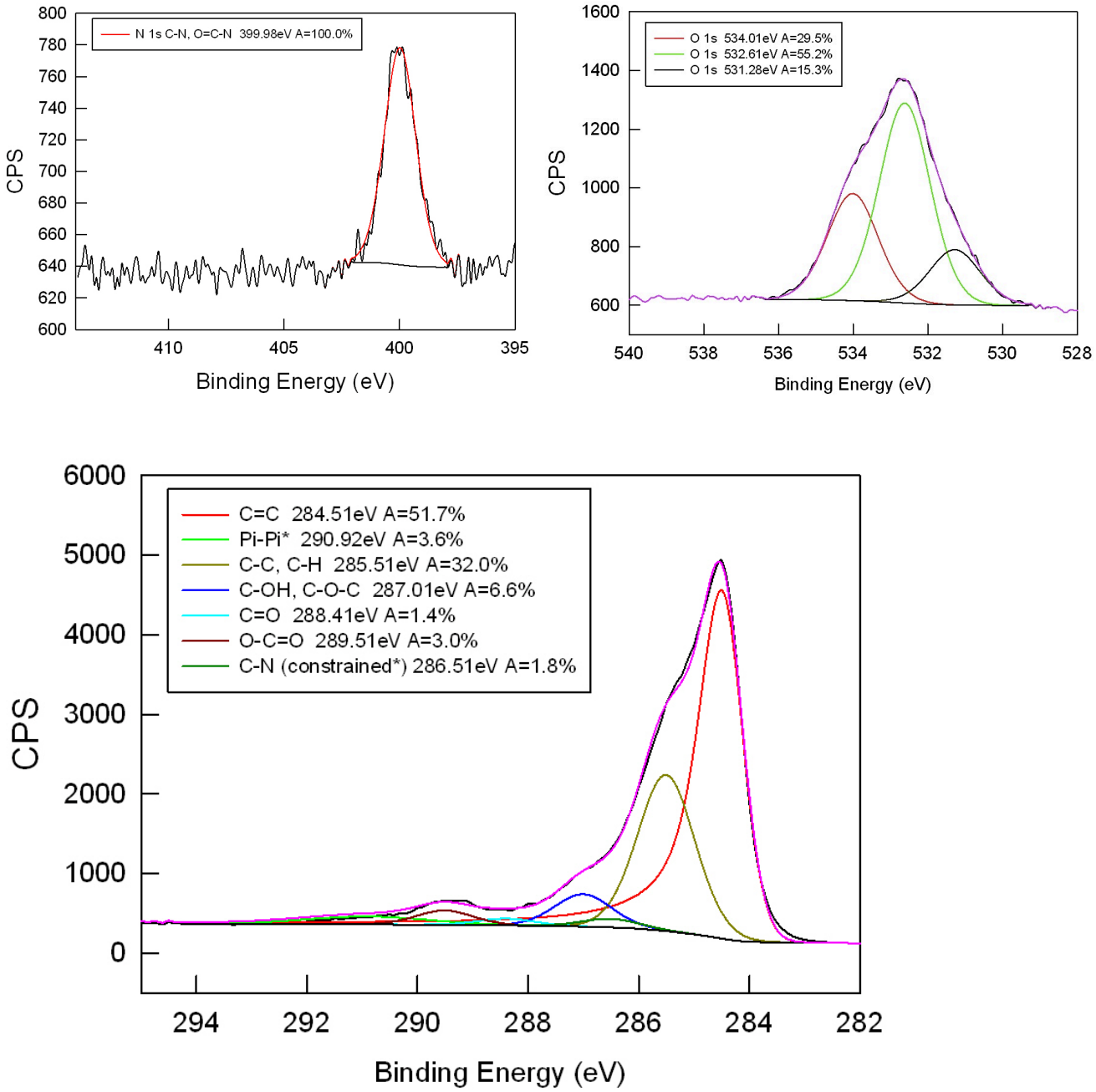


Figure SI 12: High resolution XPS spectra for SWCNT-DBCO. The peak for C-N has been constrained in this peak-fitting to 1.8% of total carbon based on atomic percentages from XPS survey scan results.

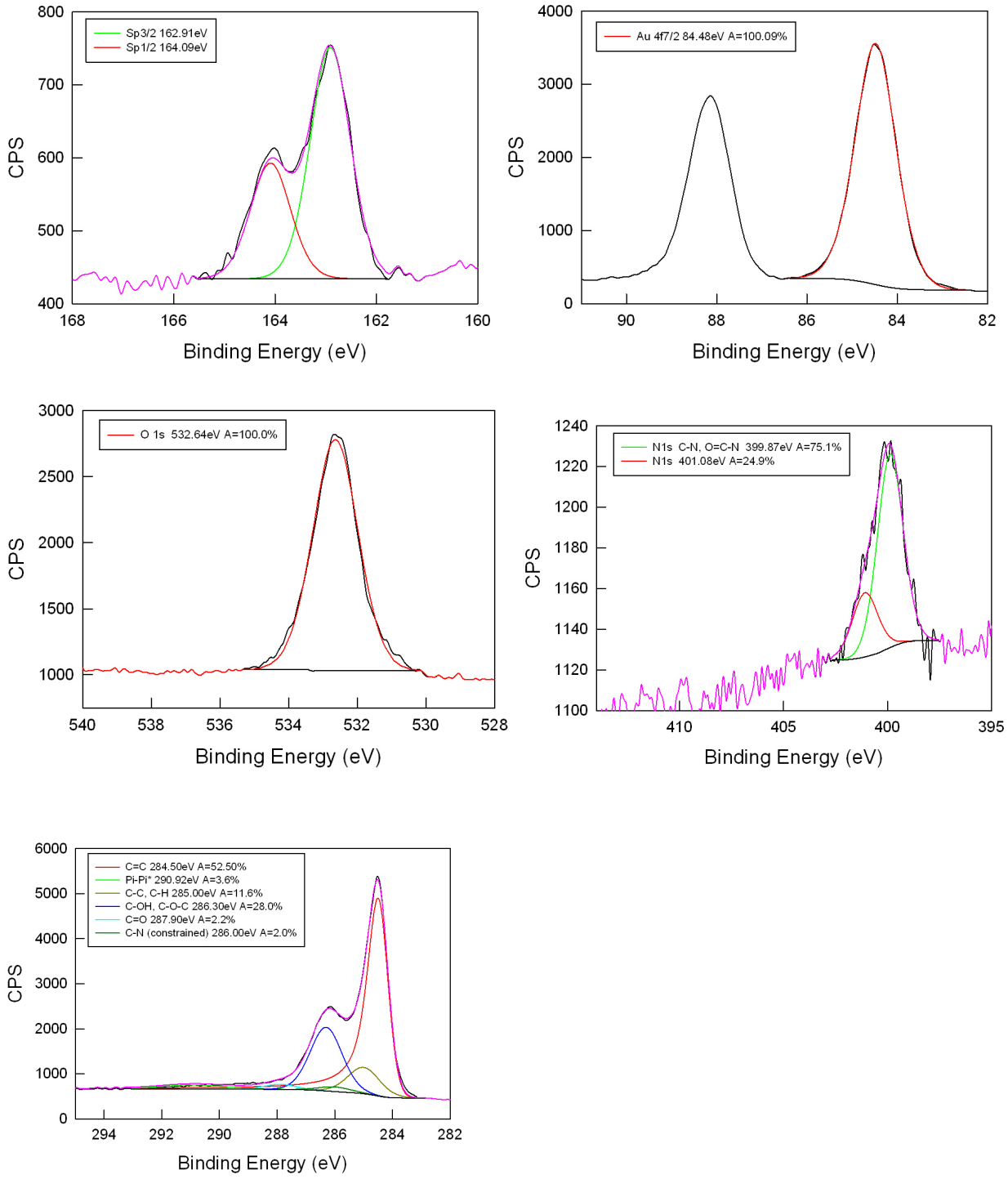


Figure SI 13: High resolution XPS spectra for SWCNT-AuNP hybrid material. The peak for C-N has been constrained in this peak-fitting to 2.0 % of total carbon based on atomic percentages from XPS survey scan results.

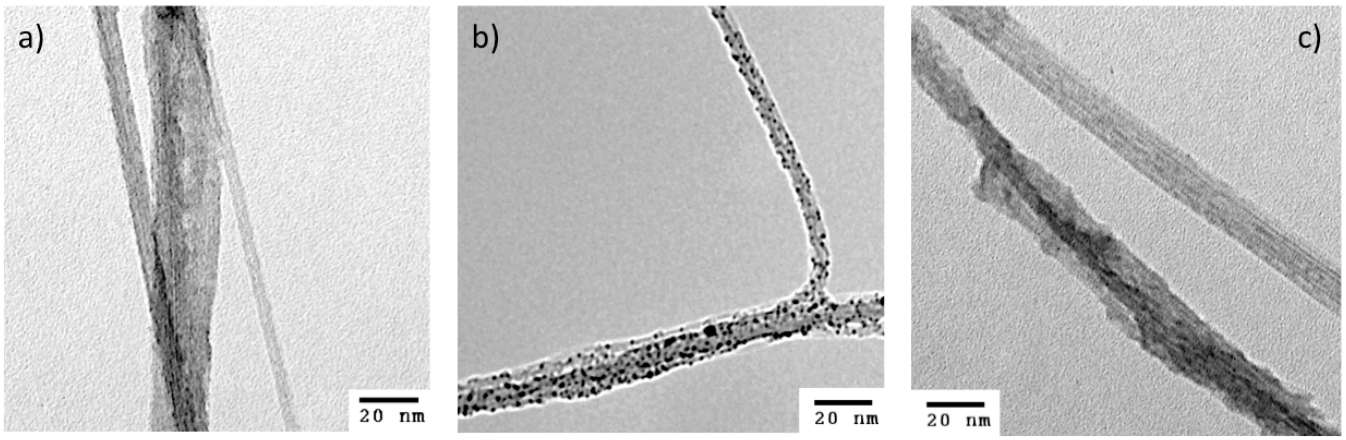


Figure SI 14: TEM images of a) SWCNT-DBCO; b) SWCNT-AuNP hybrid material; c) Control experiment (SWCNT-DBCO + Me-EG3-AuNP).

References

1) P. Gobbo, M. S. Workentin, *Langmuir* **2012**, *28*, 12357−12363.