

Supporting information for:

Grignard Reagent Functionalization of Weinreb Amide Modified Au Nanoparticles

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Instrumentation:

^1H NMR spectra were acquired using a Bruker AV 360 MHz spectrometer. FTIR spectra of particle samples and compounds were obtained on a Varian FTS 7000 spectrophotometer operating in diffuse reflectance or transmission mode respectively, over a range of 4000 to 500 cm^{-1} with a resolution of 2 cm^{-1} . Particle samples were deposited on KBr powder as solutions in tetrahydrofuran (THF) and allowed to dry overnight, then ground prior to data collection. Transmission Electron Microscopy (TEM) images were collected with a JEOL JEM 1200 EXII electron microscope with an accelerating voltage of 80 keV. Digital images were taken using a Tietz 224 digital camera and samples were prepared by drop-casting dilute samples of particles in THF onto Cu grids precoated with a layer of amorphous carbon. Fluorescence spectra were taken with a Photon Technology International (PTI) fluorimeter.

Chemicals:

Grignard reagents were purchased from Aldrich, with the exceptions of phenylmagnesium bromide and phenyl lithium, which were purchased from Acros Organics. THF was purified under nitrogen using activated alumina columns. Mg ribbon was purchased from Aldrich chemical and kept under a

nitrogen atmosphere prior to use. All other chemicals were purchased from commercial sources and used as received.

Synthesis:

11-mercapto-N-methoxy-N-methyl undecanamide (ω-terminated Weinreb amide thiol ligand): A solution of 0.99 g (4.5 mmol) of 11-mercaptopundecanoic acid in DCM (50 mL) was cooled to 0 °C. A 1.0 g (4.9 mmol) amount of dicyclohexylcarbodiimide (DCC) and 82.5 mg (0.675 mmol) of 4-dimethylamino pyridine (4-DMAP) were added and the solution stirred for 15 min at 0 °C. Next 5.0 mL (45 mmol) of N-methylmorpholine (NMM) was added and the reaction solution stirred for an additional 10 min. N,O-dimethylhydroxylamine hydrochloride (0.94 g, 9.6 mmol) was added and the reaction was allowed to warm to room temperature overnight and continued to react for an additional 24 h. Following reaction, the remaining DCC was quenched with 1 mL of acetic acid (17 mmol) and the DCM removed under reduced pressure. The white residue was subsequently resuspended in ~50 mL of ether, filtered to remove dicyclohexylurea (DCU), and washed with an additional ~25 mL of diethyl ether. The combined filtrates were then washed with three ~50 mL portions of 10% HCl (emulsions take several minutes to separate), dried over Na₂SO₄ and concentrated, resulting in a cloudy, colorless solution with some suspended DCU. The crude product was purified on silica gel in 50% hexanes/2% triethylamine/48% ethyl acetate, to yield 0.42 g (1.59 mmol, 35%^{S1}) of pure (**10**) as a clear oil. (note: in some cases DCC/DCU can streak through the column and is seen as a white solid precipitating in the collection vials. In these cases the fractions were concentrated and the product dissolved in a small amount of ethyl acetate. The ethyl acetate solution was subsequently cooled to 0 °C and filtered to remove this impurity). ¹H NMR (CDCl₃, 360 MHz): 3.60 (3H, s), 3.09 (3H, s), 2.43 (2H, q), 2.33 (2H, t), 1.51 (4H, m), 1.30-1.19 (14H, broad sloping multiplet); IR (KBr, cm⁻¹): 2927 (C-H), 2853 (C-H), 2555 (S-H), 1668 (C=O), 1464, 1414, 1384, 1177, 1116, 999, 722.

Au MPCs with mixed monolayers of octanethiol and Weinreb amide alkane thiol: Au MPCs were prepared by the method of Brust *et al.* with 2 equivalents of tetra-N-octyl-ammonium bromide, 3 equivalents of octanethiol and 40 equivalents of NaBH₄.^{S2} Subsequent ligand exchange in toluene with Weinreb amide alkyl thiol afforded Au MPCs bearing a mixed monolayer of methyl and N-methoxy-N-methyl-amide termini.¹⁰ The majority of particles were precipitated in hexanes at 0 °C overnight and recovered by centrifugation. The recovered particles were then placed through 5 more cycles of dispersion in a minimal amount of THF, followed by precipitation in hexanes at room temperature. Following the wash cycles the particles were redispersed in THF and centrifuged to remove any insoluble material. A stock solution of the recovered particles in THF was then used for all experiments.

General Addition of Grignards and Organo Lithiums to Au MPCs: A 4 mL amount of a 7.15 mg/mL Au MPC stock solution in THF was concentrated *in vacuo* to relative dryness and placed under N₂. A 10 mL amount of fresh anhydrous THF was then added, followed by a solution of the desired organometallic reagent in THF (see below for specific particle and organometallic concentrations). The solution was stirred for between 1 to 48 h (paper, Table 1). Addition of the organometallic reagent caused an apparent aggregation of the particles followed by a slow and incomplete return to solution with time. Subsequently the reaction was quenched with 1 mL of water and the entire solution was poured into 100 mL of a basic EDTA solution (~180 mg EDTA, ~200 mg NaOH). A cloudy dark suspension formed and was extracted 3 times with ~30 - 50 mL portions of EtOAc or until the water layer was colorless. In some cases a thin layer of particle aggregates formed at the phase boundary and these were collected along with the organic layer (Figure S1). The organic layers were combined and washed once with 100 mL of 5% acetic acid, which caused most of the agglomerated particles to return to solution (Figure S1). The organic layer was dried briefly over Na₂SO₄ to avoid any possible adsorption, filtered and concentrated. The particles were dissolved in a minimal amount of EtOAc and precipitated in hexanes and isolated by centrifugation. These were then redispersed in THF and

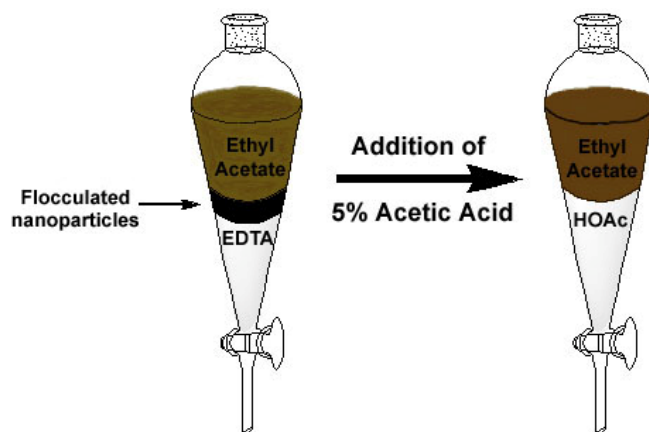
precipitated in cycles repeated 3 times for small very volatile compounds (ethyl, isopropyl, ethynyl) and 6 times for all others. After a thorough washing, the particles were dissolved in THF and centrifuged to remove any insoluble aggregates.

Table S1: Commercially available organometallics

Organometallic Reagent	Concentration (M) ^b	mmol added	mg of particles
Ethynyl MgBr	0.5	0.250	28.6
Ethyl MgBr	0.5	0.125	15.2
Isopropenyl MgBr	0.5	0.250	28.6
Isopropyl MgCl	0.226	0.113	8.5
Phenyl Li	1.46	0.365	28.6
Phenyl MgBr	0.67	0.362	28.6
3-Methyl-2-thiophenyl MgBr	0.5	0.250	28.6
9-Phenanthrenyl MgBr	0.33	0.165	28.6

a) All concentrations were determined by titration with diphenylacetic acid in dry THF at RT. b) ethylmagnesium bromide and isopropylmagnesium chloride were diluted to the values listed from their as-purchased concentrations under N₂.

Figure S1



Addition of 9-pyrenylmagnesium bromide to Au MPCs: 62.8 mg of magnesium ribbon (0.3 mm thickness) was roughened with sand paper and cut into small pieces (about 2 mm x 3.5 mm). The Mg was placed under N₂ and to it was added 0.292 (1.04 mmol) of 9-bromopyrene in 5 mL of anhydrous THF.^{S3} The solution was refluxed for 2 h and subsequently cooled to room temperature. Meanwhile, 2 mL of a 7.6 mg/mL stock solution of Weinreb Amide particles were dried in vacuo and placed under N₂. 5 mL of fresh anhydrous THF was added to the particles followed by 1 mL of the cooled 9-pyrenylmagnesium bromide solution. The solution was stirred for 3 h, followed by quenching with 1 mL of water. At this point the reaction followed the standard work up outlined above.

Figure S2: ^1H NMR, IR and TEM data for Au MPCs with a mixed monolayer of methyl and Weinreb amide termini

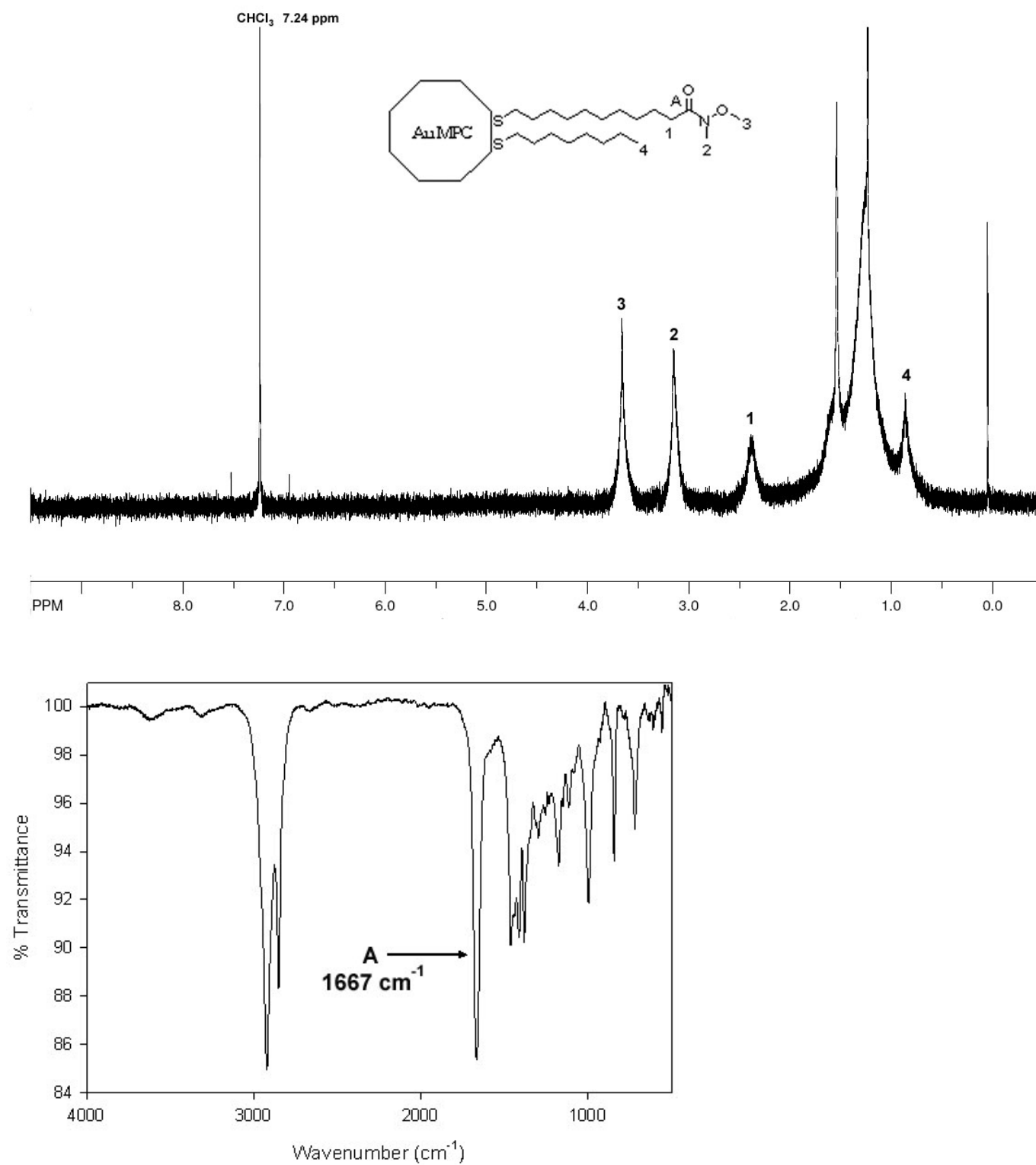


Figure S3: IR and TEM data for Au particle post reaction with ethynylmagnesium bromide (13-mercapto-tridec-1-yn-3-one, **1**):

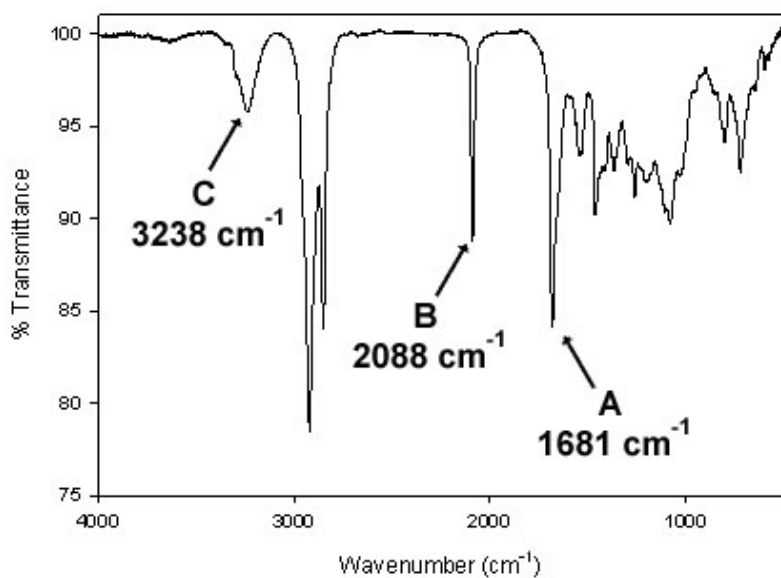
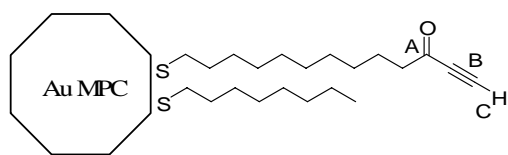
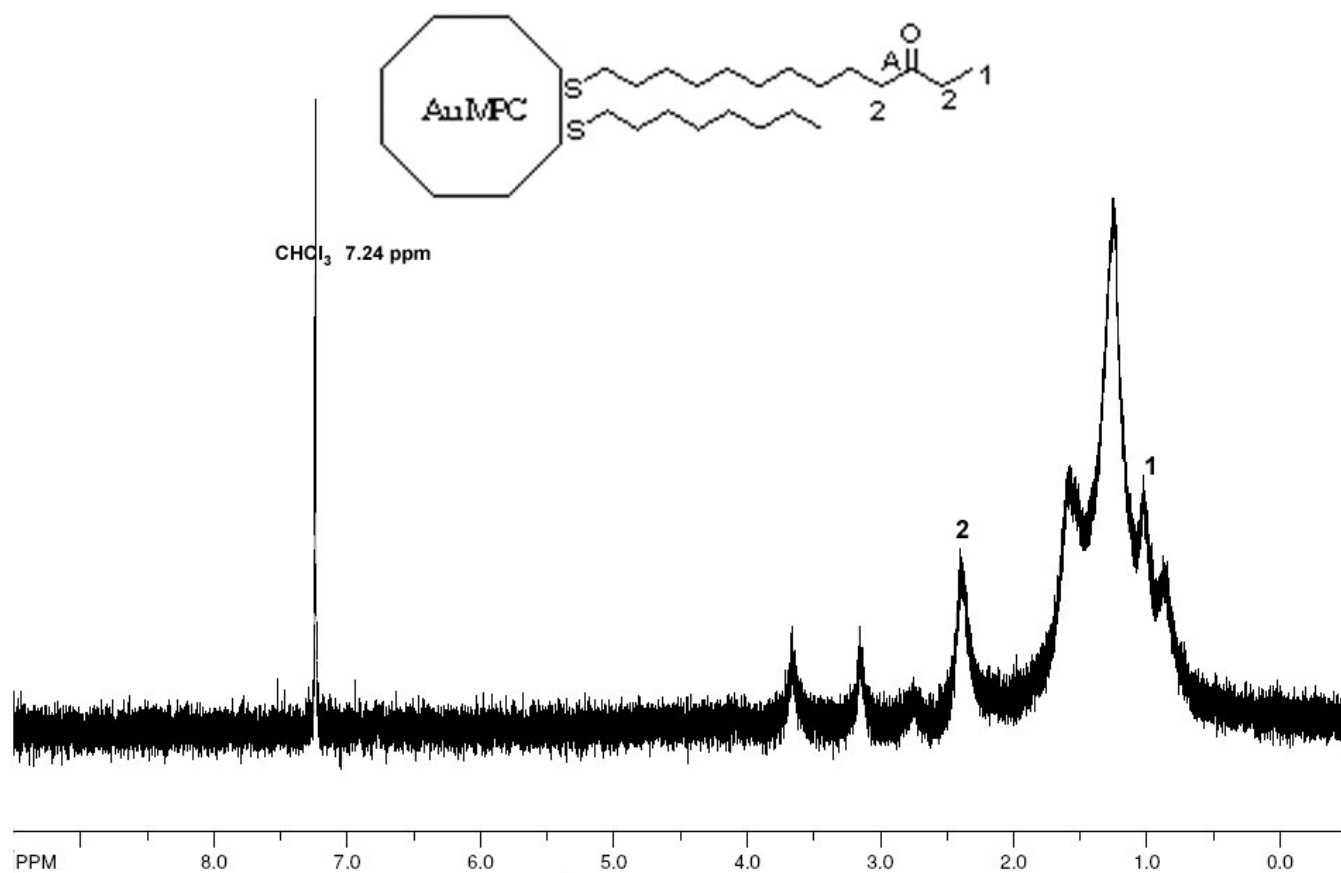


Figure S4: ^1H NMR, IR, and TEM data for Au particles post reaction with ethylmagnesiumbromide



(13-mercapto-tridecan-3-one, 2):

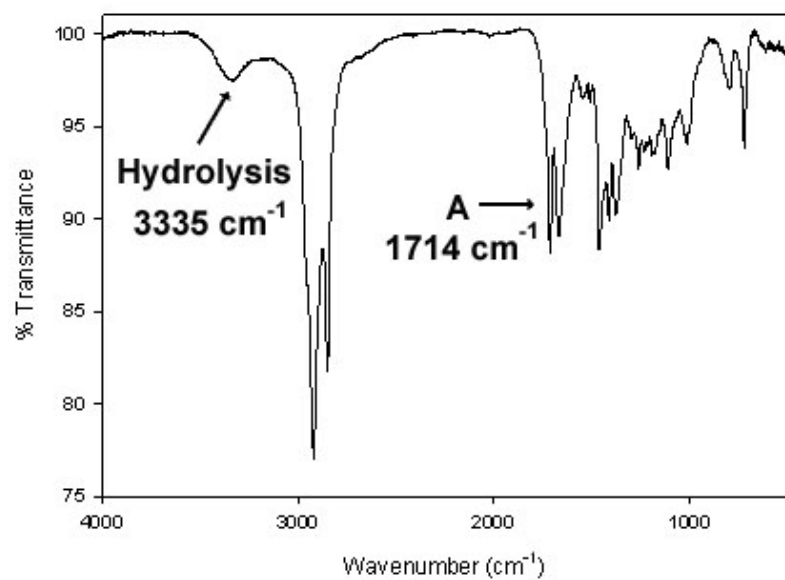
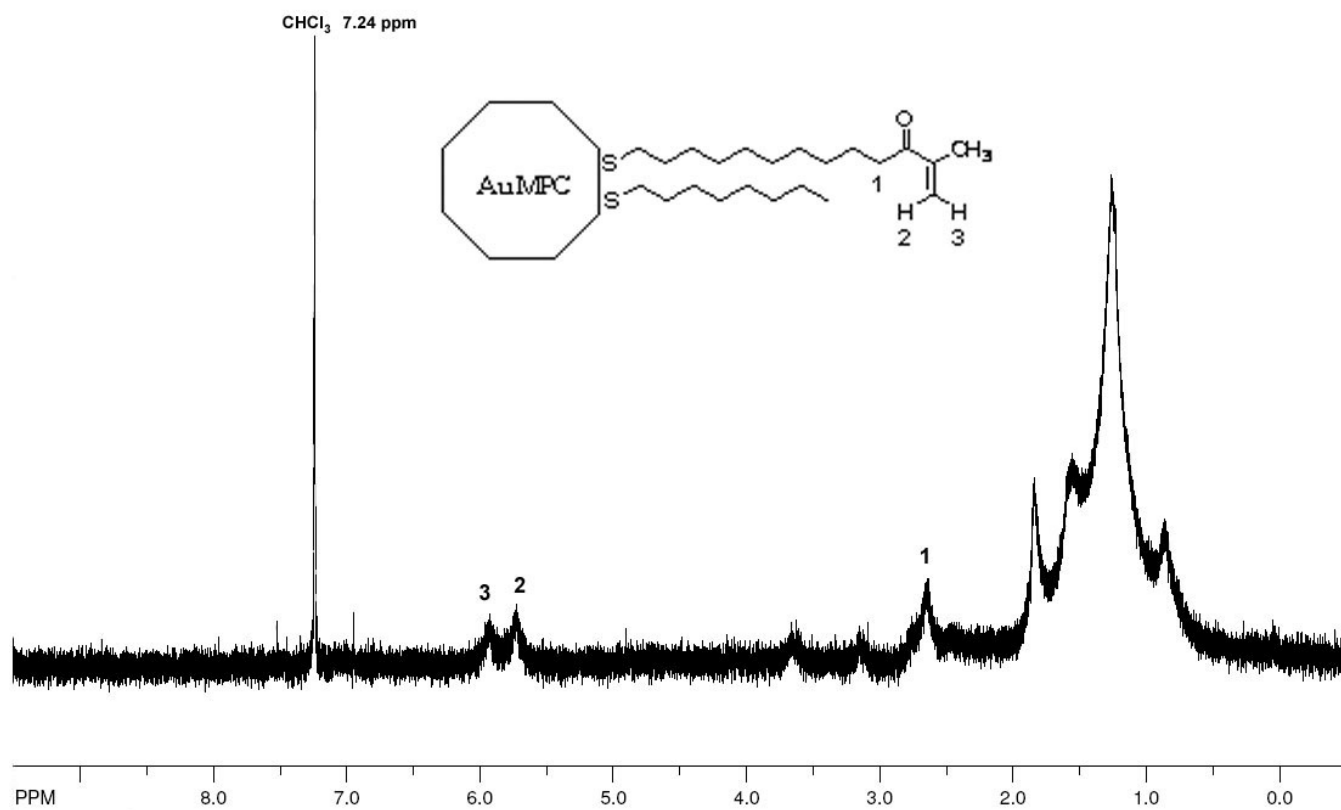
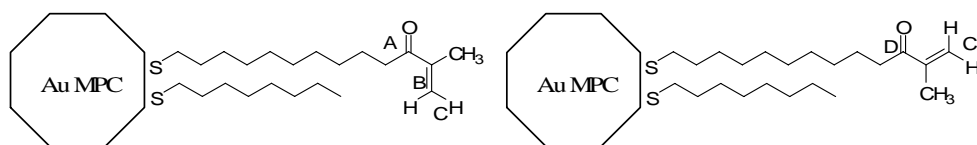
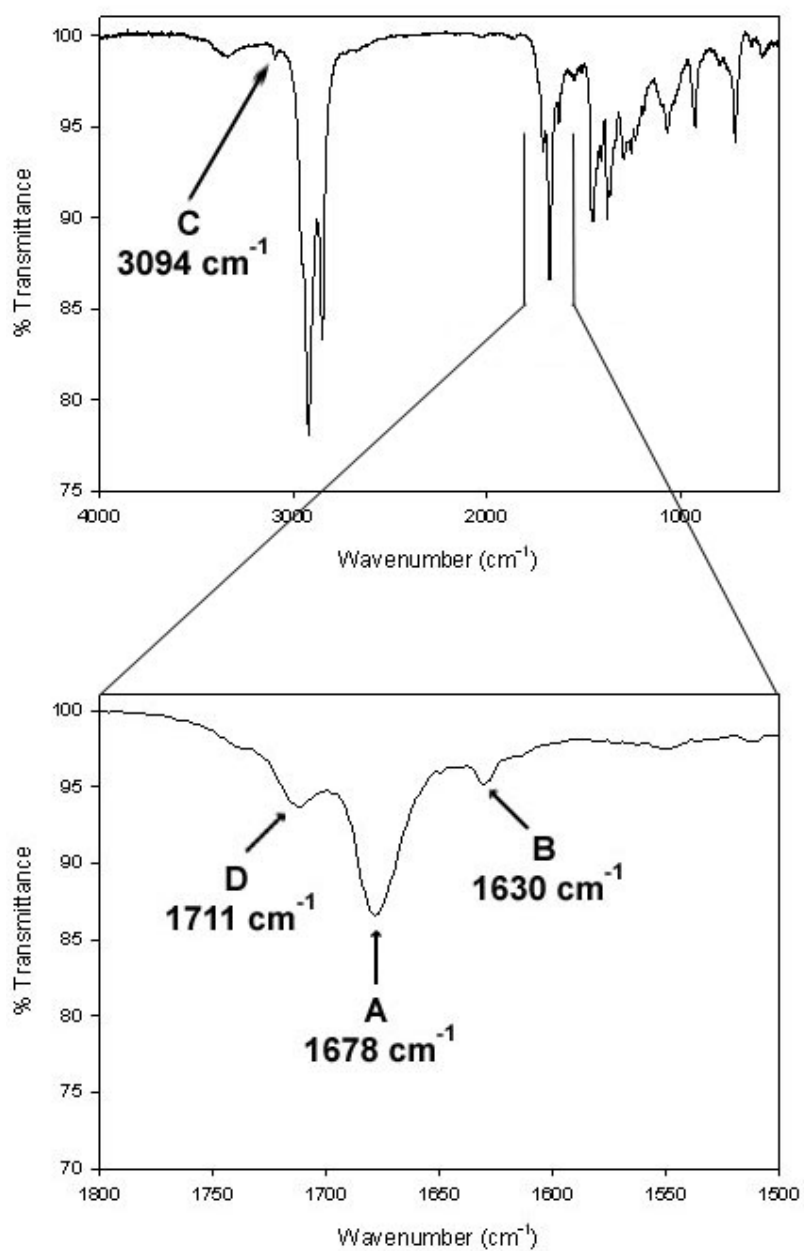


Figure S5: ^1H NMR, IR, and TEM data for Au particle post reaction with isopropenylmagnesium



bromide (13-mercapto-2-methyl-tridec-1-en-3-one, **3**):





See reference S4 and S5 for details on these peak assignments.

Figure S6: ^1H NMR and IR data for Au particle post reaction with isopropylmagnesium chloride (13-mercapto-2-methyl-tridecan-3-one, **4**):

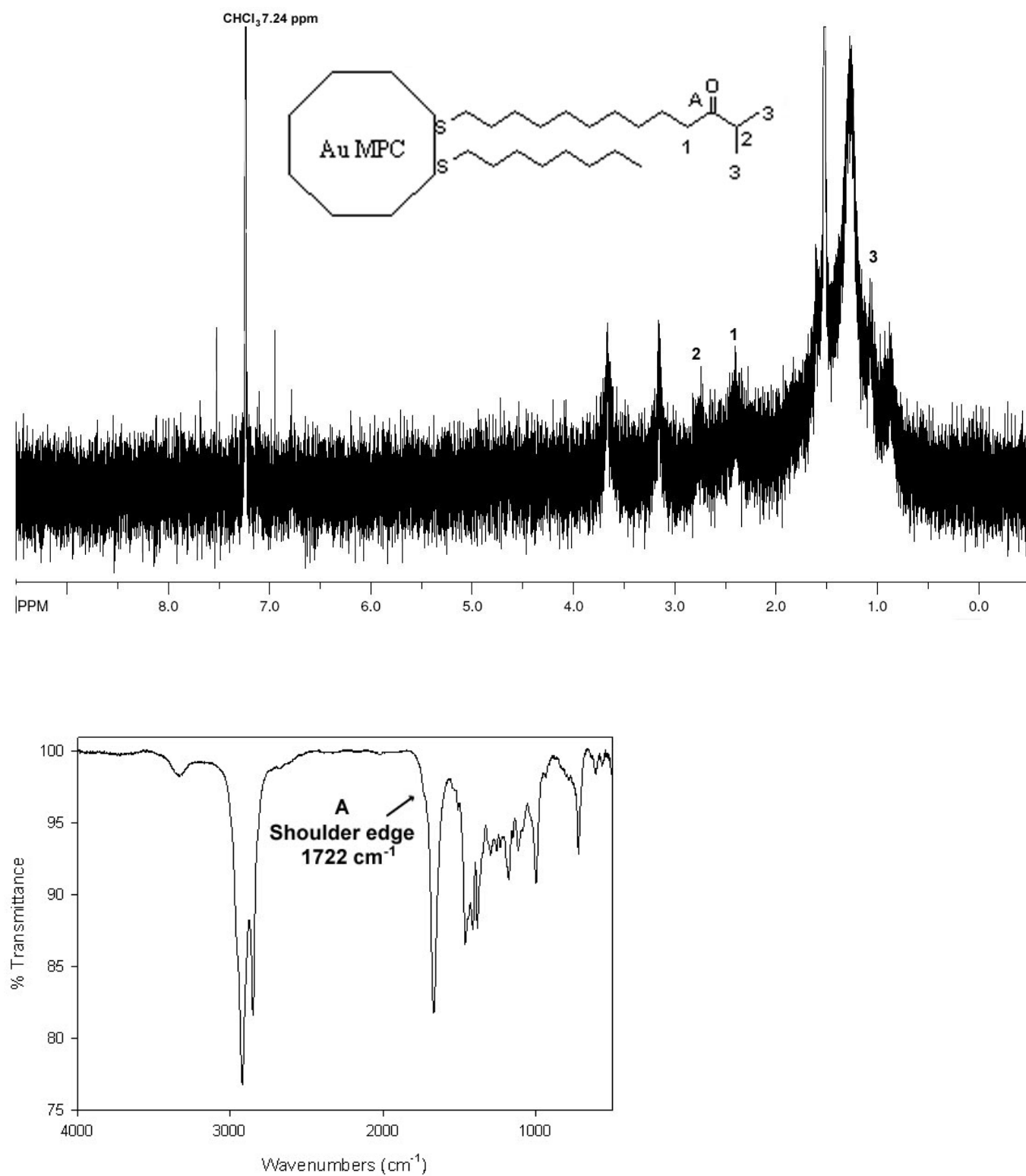
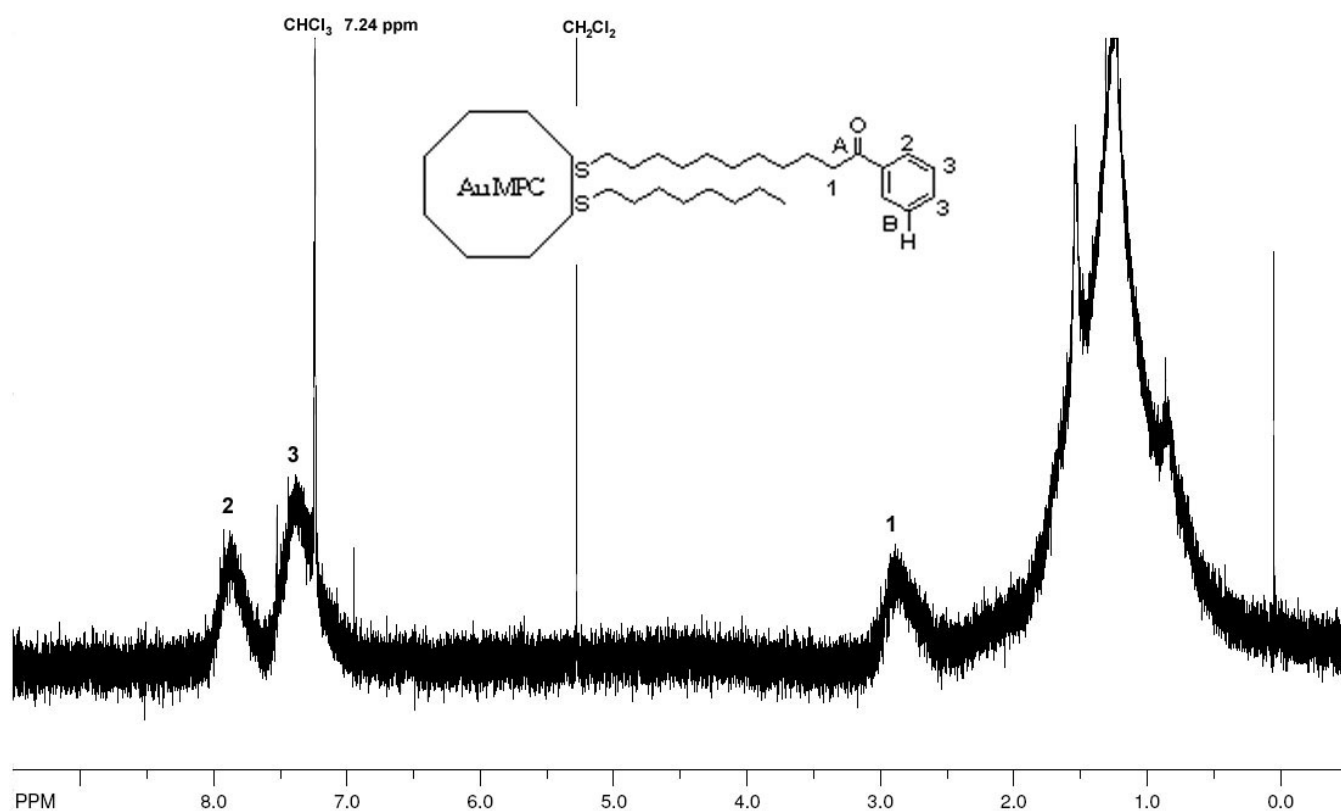


Figure S7: ^1H NMR and IR data for Au particle post reaction with phenyl lithium (11-mercapto-1-



phenyl-undecan-1-one, **5**):

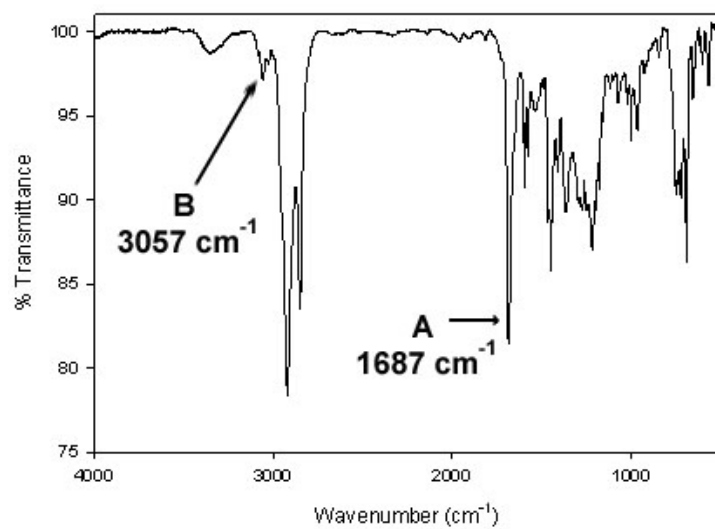


Figure S8: ^1H NMR, IR, and TEM data for Au particle post reaction with phenylmagnesium bromide (11-mercapto-1-phenyl-undecan-1-one, **6**):

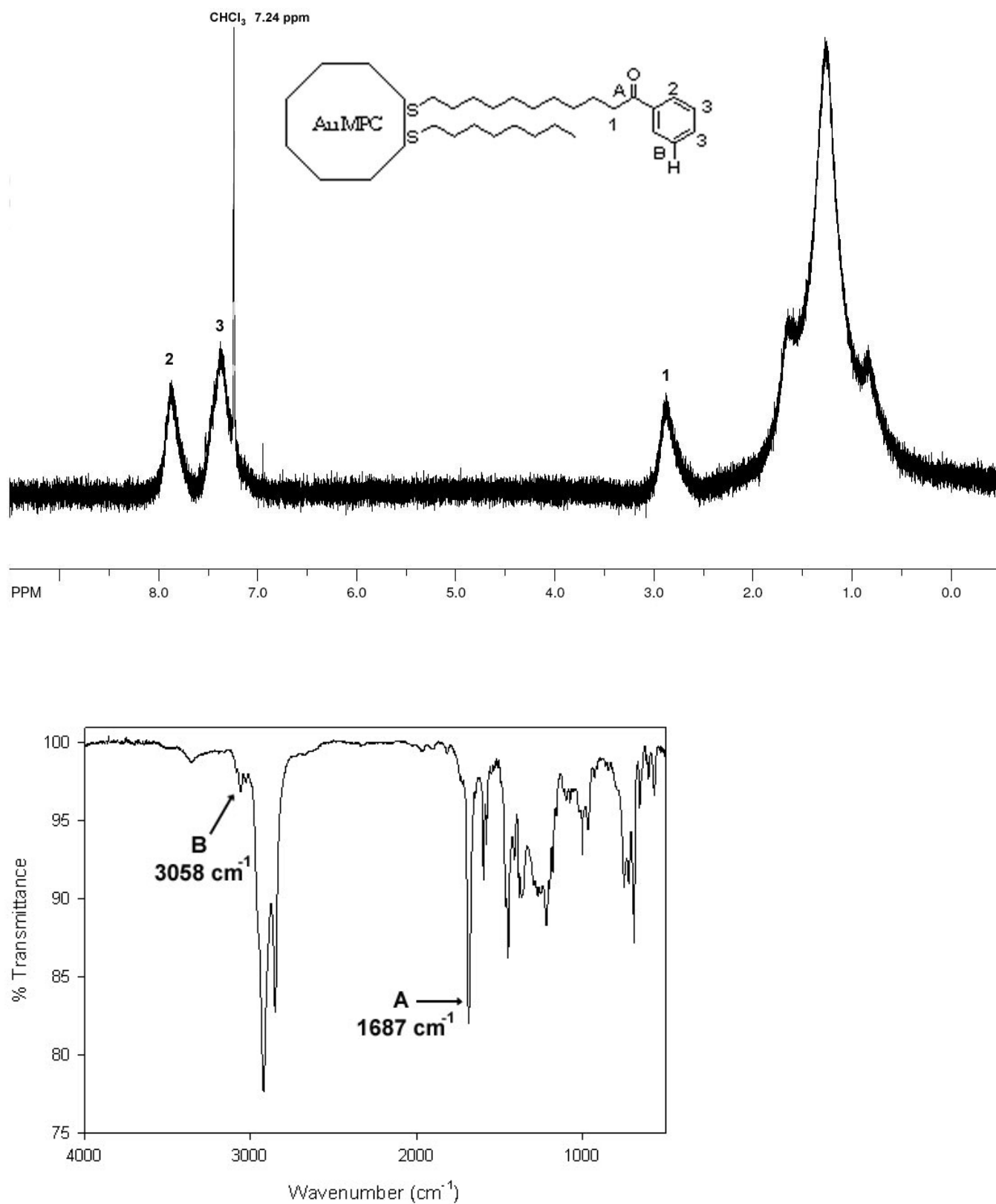


Figure S9: ^1H NMR, IR and TEM data for Au particle post reaction with 1-pyrenylmagnesium bromide(11-mercapto-1-pyren-1-yl-undecan-1-one, **8**):

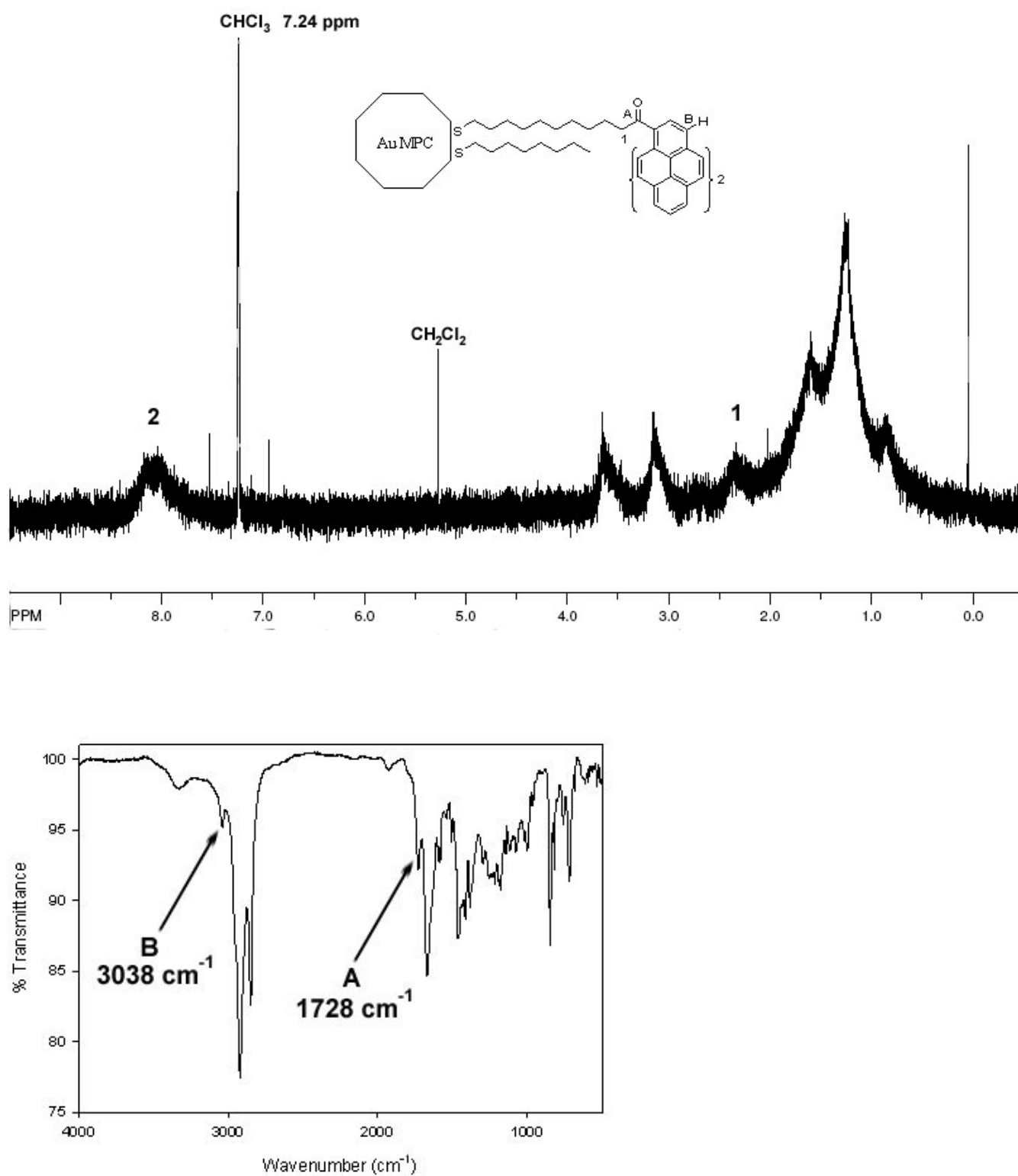


Figure S10: ^1H NMR, IR and TEM data for Au particle post reaction with 9-phenanthrenylmagnesium bromide (11-mercapto-1-phenanthren-9-yl-undecan-1-one, **9**):

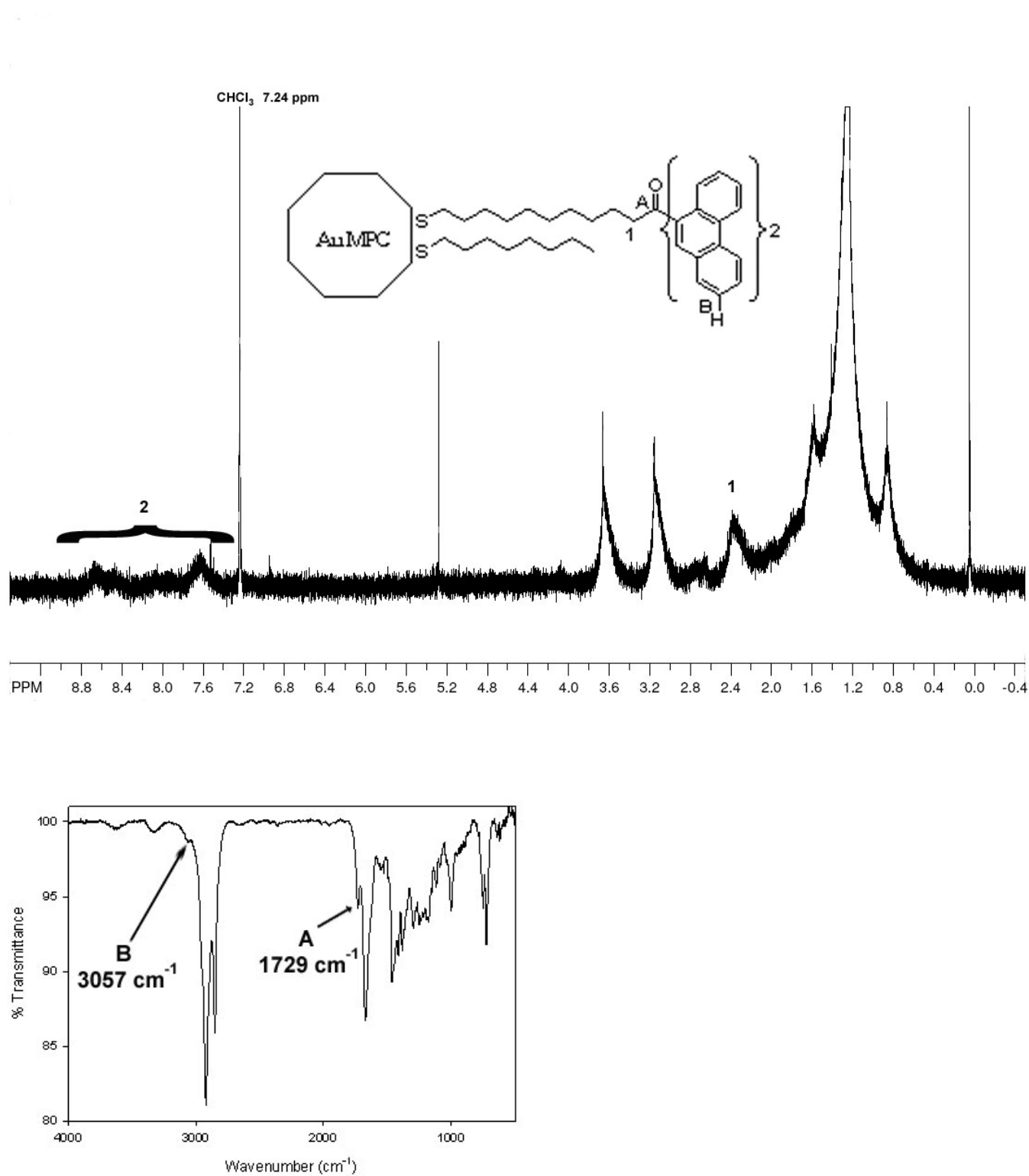
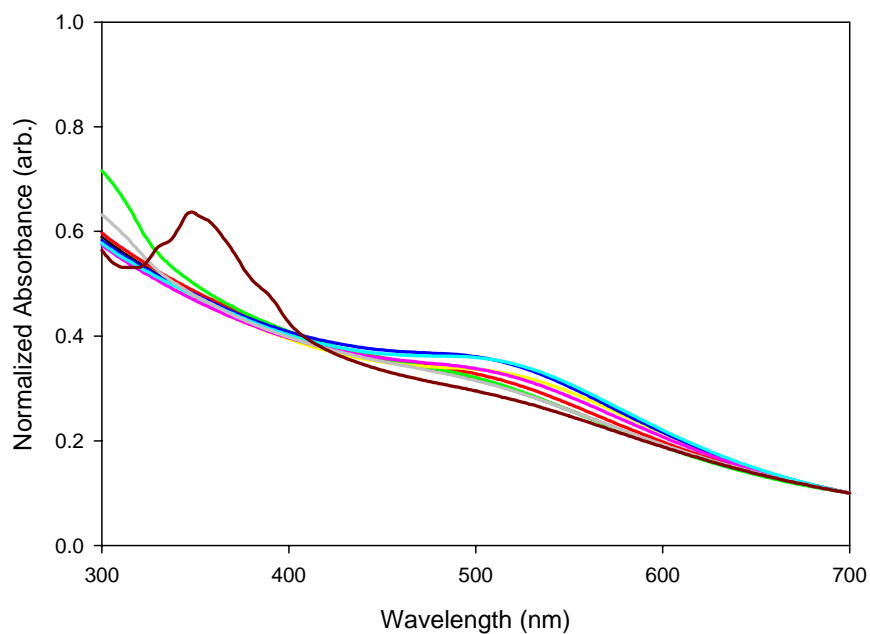


Figure S11: UV-Visible spectroscopy



The spectra have been normalized to 0.1 at 700nm where the absorbance is considered to be due solely to scattering. Surface functionalities are as follows: (■) Weinreb amide, (■, 1) ethyl, (■, 2) ethynyl, (■, 4) isopropyl, (■, 3) isopropenyl, (■, 6) phenyl from MgBr, (■, 5) phenyl from Li, (■, 9) 9-phenanthrenyl, (■, 8) 1-pyrenyl

Table S2: Particle Return Yields

Surface Functionality	vs. Control	vs. Stock Solution
Alkyne	49%	33%
Ethyl	88%	58%
Isopropenyl	95%	63%
Isopropyl	51%	27%
Phenyl (from Li)	78%	52%
Phenyl (from MgBr)	100%	79%
Pyrene	100%	67%
9-Phenanthrene	100%	72%

Particle return yields were calculated by comparing the solvent free mass of the total recovered sample from 2 mL of stock solution with the solvent free mass of either 2 mL of the stock solution or control experiment involving full workup.

References

- S1. While a thiol protection scheme was not used for this proof of concept study, it is expected that the yield will be much higher if a protecting group is used.
- S2. Brust, M.; Walker, M.; Bethell, D.; Schiffrin, D. J.; Whyman, R. *J. Chem. Soc., Chem. Commun.* **1994**, 7, 801- 802.
- S3. Gerard, B.; Sangji, S.; O'Leary, D. J.; Porco, J. A. Jr. *J. Am. Chem. Soc.* **2006**, 128, 7754-7755.
- S4. Nyquist, R. A. *Interpreting Infrared, Raman, and Nuclear Magnetic Resonance Spectra*; Academic Press: San Diego, CA, 2001; Vol. 1, pp 291-294, 319.
- S5. Lin-Vien, D.; Colthup, N. B.; Fateley, W. G.; Grasselli, J. G. *The Handbook of Infrared and Raman Characteristic Frequencies of Organic Compounds*; Academic Press: San Diego, CA, 1991; pp 88-90,130-132.