Room-temperature aqueous Suzuki-Miyaura cross-coupling reactions catalyzed via recyclable palladium@halloysite nanocomposite

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Supporting Information

Materials and Methods. All reactions were carried out in oven-dried glassware under a N_2 atmosphere unless indicated otherwise. Halloysite clay was purchased from Sigma Aldrich. All other chemicals were purchased from Alfa Aesar, Sigma Aldrich and VWR. Halloysite was purchased from Sigma Aldrich. All chemicals were used as received without further purification. ^{1}H and ^{13}C NMR spectra were recorded at r.t. in DMSO-d_6 on a Bruker 400 MHz instrument operating at a frequency of 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR. ^{1}H chemical shifts were referenced to the DMSO solvent signal (2.50 ppm). ^{13}C chemical shifts were referenced to the DMSO solvent signal (39.51 ppm). Pd_{NP} size was determined from TEM images that were obtained on a JEOL 2010 equipped with an EDAX genesis energy dispersive spectroscopy (EDS) system, operated at an accelerating voltage of 200 kV and an emission current of 109 µA. ICP-AES analysis of the Pd@Hal was performed by Galbraith Laboratories, Inc., Knoxville, TN.

Synthesis of 4% Pd@Hal.

A solution of $Pd(OAc)_2$ (60 mg, 0.26 mmol) in deionized water (10 mL) was prepared in a 50 mL Erlenmeyer flask. A solution of L-sodium ascorbate (1400 mg, 7.0 mmol) in deionized water (15 mL) was added to the palladium acetate solution followed by addition of a solution of trisodium citrate (570 mg, 2.7 mmol) in deionized water (10 mL). The combined solution was allowed to stir for 15 min at room temperature. During the first 10 minutes, the initial light orange color of the palladium acetate solution mixture turned black, indicating the formation of Pd nanoparticles. After 15 min, no more color changes were observed, and the solution was left to rest at room temperature, open to air for 80 min. Halloysite (600 mg, 2.0 mmol) was added to the Pd nanoparticle solution and the colloid mixture was stirred for 15 min. The mixture was then allowed to rest at room temperature for 10 min. The mixture was centrifuged (6000 rpm) and the liquid was decanted away from the solid residue. The residue was washed with deionized water (3 x 15 mL) and isopropyl alcohol (3 x 15 mL). The resultant powder was dried at room temperature for 24 h in a desiccator ($CaSO_4$) to afford 4% Pd@Hal as a gray powder (620 mg).

Synthesis of 25% Pd@Hal.

A solution of $Pd(OAc)_2$ (140 mg, 0.60 mmol) in deionized water (10 mL) was prepared in a 50 mL Erlenmeyer flask. A solution of L-sodium ascorbate (1900 mg, 10 mmol) in deionized water (15 mL) was added to the palladium acetate solution followed by addition of a solution of trisodium citrate (180 mg, 0.60 mmol) in deionized water (10 mL). The combined solution was allowed to stir for 15 min at room temperature. During the first 10 minutes, the initial light orange color of the palladium acetate solution mixture turned black, indicating the formation of Pd_{NP}. After 15 min, no more color changes were observed, and the solution was left to rest at room temperature open to air for 80 min. Halloysite (180 mg, 0.60 mmol) was added to the Pd_{NP} solution and the colloid mixture was stirred for 15 min. The mixture was then allowed to rest at room temperature for 10 min. The mixture was centrifuged (6000 rpm) and the liquid was decanted away from the solid residue. The residue was washed with deionized water (3 x 15 mL) and isopropyl alcohol (2 x 15 mL). The resultant powder was dried at room temperature for 24 h in a desiccator ($CaSO_4$) to afford 25% Pd@Hal as a gray powder (310 mg).

General Procedure: Suzuki-Miyaura cross-coupling reaction

To a 50 mL round bottom flask equipped with a magnetic stir bar and a nitrogen inlet balloon, the aryl halide (1.0, mmol 1.2 equiv.) and the aryl boronic acid (1.2 mmol 1.2 equiv.) was added. The reaction mixture was flushed with nitrogen followed by the addition of *n*-propanol (10.0 mL) via syringe. The reaction mixture was allowed to stir the for 5 min allowing complete dissolution of all solids. Cs_2CO_3 (652 mg, 2.0 mmol) was dissolved in (2.0 mL) of DI water, then added to the reaction mixture via syringe. The 4% Pd@Hal (5% wt/wt) catalyst was dissolved in (2.0 mL) of DI water; the solution was sonicated (10 min) to ensure dispersion, then added to the reaction mixture via syringe. The reaction flask was sonicated for 10 mins then allowed to stir at room temperature. The reaction progress was monitored by TLC. Typically, after 1 h the catalyst was recovered by vacuum filtration. The Pd@Hal was rinsed with ethyl acetate (20 mL) followed by DI water (20 mL) and dried in a desiccator ($CaSO_4$). The diluted reaction mixture was transferred to a separatory funnel and the organic phase was removed and filtered through a 2 cm bed of silica gel. The silica gel was rinsed with several portions of hexanes:ethyl acetate (9:1). The organic portions were combined and the solvent was removed under vacuum to afford **6**. Purity was established by TLC and NMR. All products are known compounds unless otherwise indicated and spectral data were identical to those reported in the literature.

Large-scale procedure: Suzuki-Miyarua cross-coupling reaction

To a 200 mL round bottom flask equipped with a magnetic stir bar and a nitrogen inlet balloon, the 4-bromtoluene (2.05 g 12.0 mmol, 1.0 equiv.) and the 4-methoxyphenylboronic acid (1.85 g, 12.2 mmol 1.2 equiv.) was added. The reaction mixture was flushed with nitrogen followed by the addition of 1-propanol (100 mL) via syringe. The reaction mixture was stirred the for 10 min allowing complete dissolution of all solids. Cs_2CO_3 (4.20g, 13.0 mmol) was dissolved in (20 mL) of DI water, then added to the reaction mixture via syringe. The Pd@Hal catalyst (0.100 g, 5 %wt/wt) was dissolved in (20 mL) of DI water; the solution was sonicated (10 min) to ensure dispersion, then added to the reaction mixture via syringe. The reaction flask was sonicated for 10 mins then allowed to stir at room temperature. The reaction progress was monitored by TLC (9:1, hexanes: ethyl acetate). The reaction was determined to be complete by the consumption of the bromotoluene and the catalyst was recovered by vacuum filtration. The Pd@Hal was rinsed with ethyl acetate (40 mL) followed by DI water (40 mL) and dried in a desiccator ($CaSO_4$). The diluted reaction mixture was transferred to a separatory funnel and the organic phase was removed and filtered through a 2 cm bed of silica gel. The silica gel was rinsed with several portions of (9:1, hexanes: ethyl acetate). The organic portions were combined, and the solvent was removed under vacuum to afford **3**. (2.29g, 98%). Purity was established by TLC, melting point and NMR. The product 3 is a known compound and spectral data were identical to those reported in the literature.[1,2]

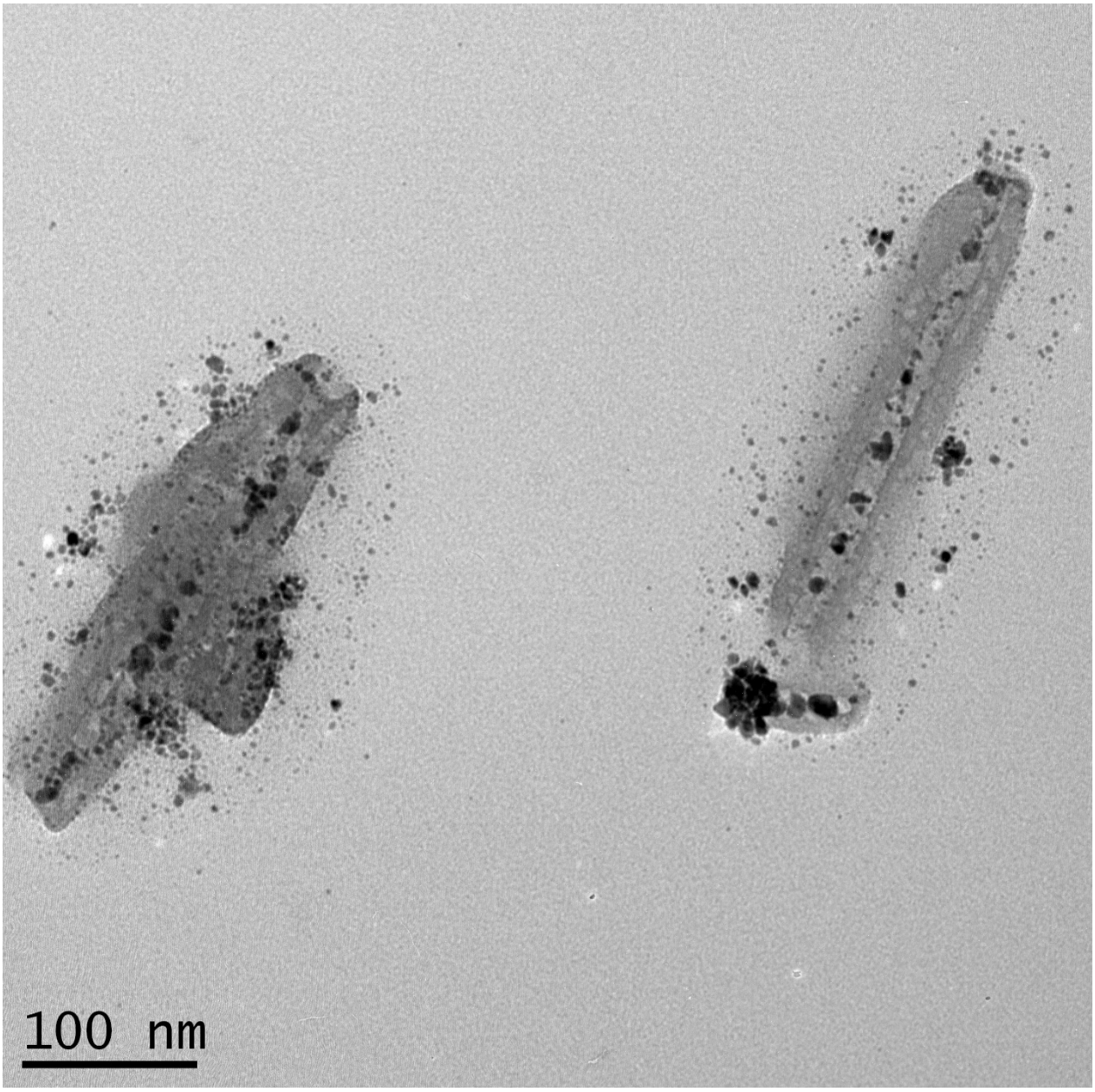
Recycling Studies
The Large-scale procedure was used for the Cycle 1.

Pd@Hal recovery procedure: The Pd@Hal was removed from the filter paper and added to a beaker with EtOH (20 mL) then sonicated for 10 mins. The solid was then centrifuged down and the washed again with (15 mL) DI water followed by (15 mL) isopropyl alcohol. The solid was dried in a desiccator ($CaSO_4$) overnight or in an oven at 120° for 20 mins before each subsequent cycle.

Cycles 2-11. Due to loss of material during the recovery procedure for each cylce, it was necessary to adjust the reagent amounts such that a consistent catalyst loading of 5% (wt/wt) Pd@Hal/4-bromotolune was maintained.

Cycle	Yield , %
1	98
2	99
3	99
4	99
5	98
6	97
7	98
8	96
9	92
10	85
11	52

Table 1, Entry 1



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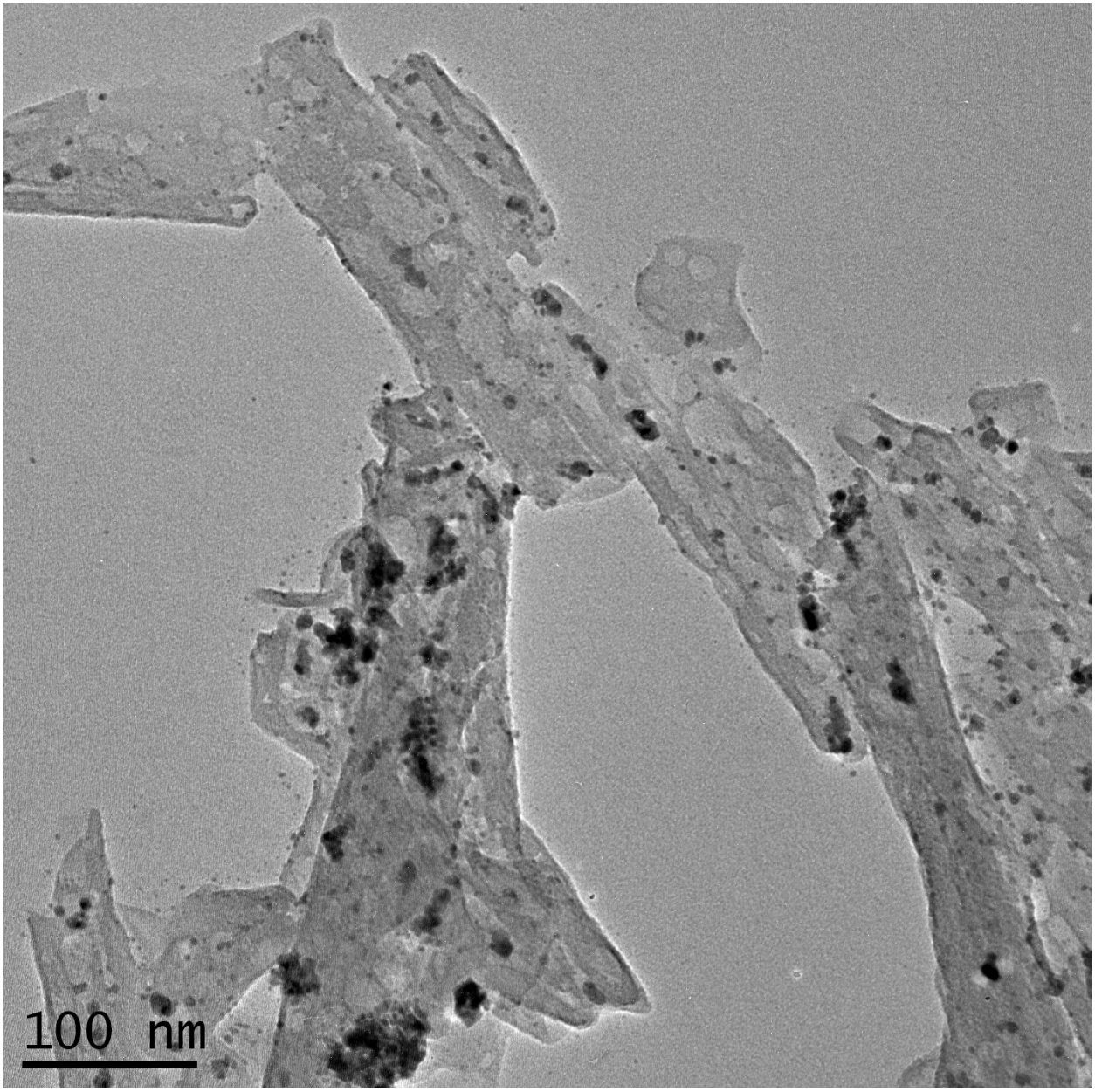
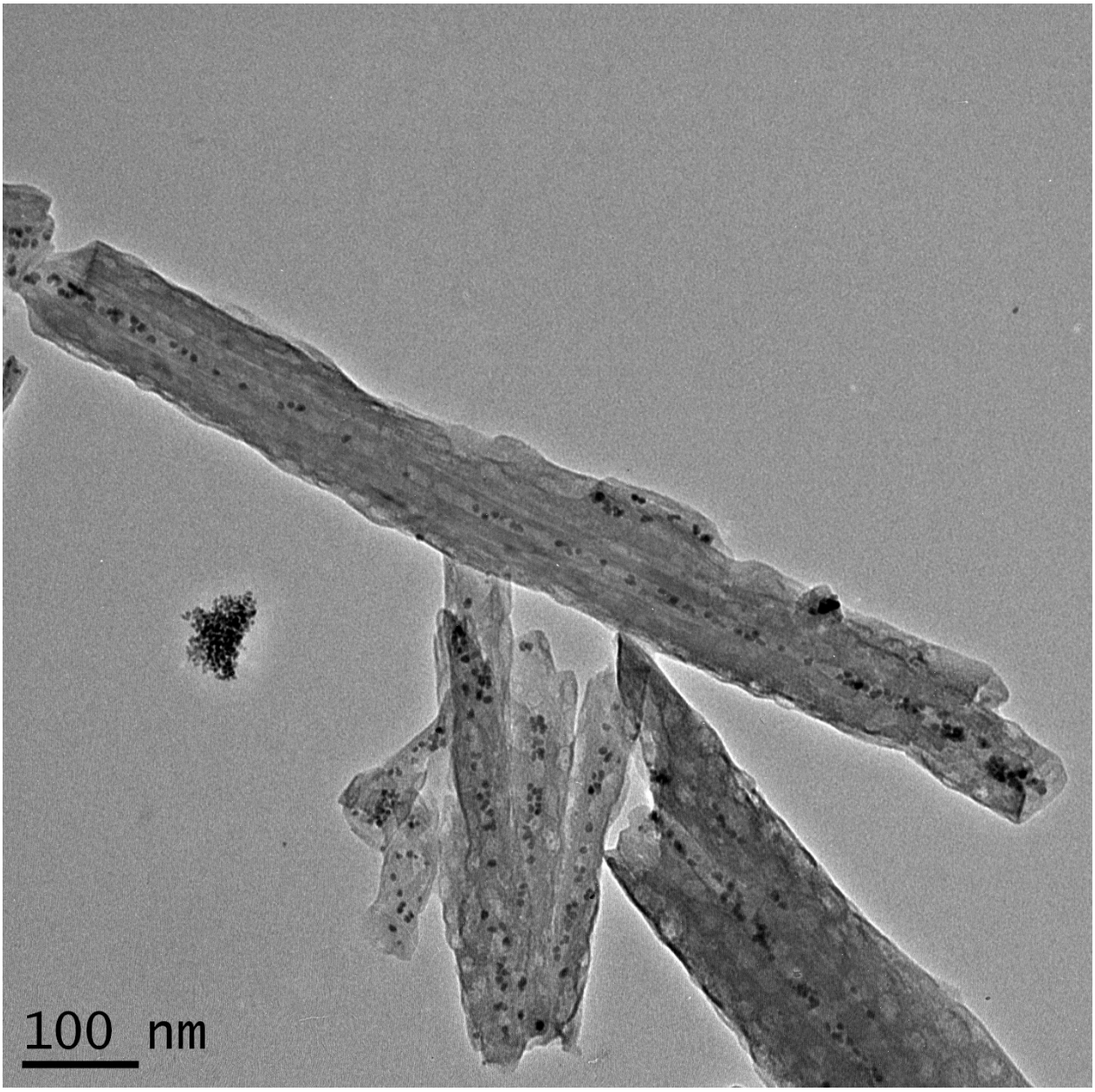


Table 1, Entry 3



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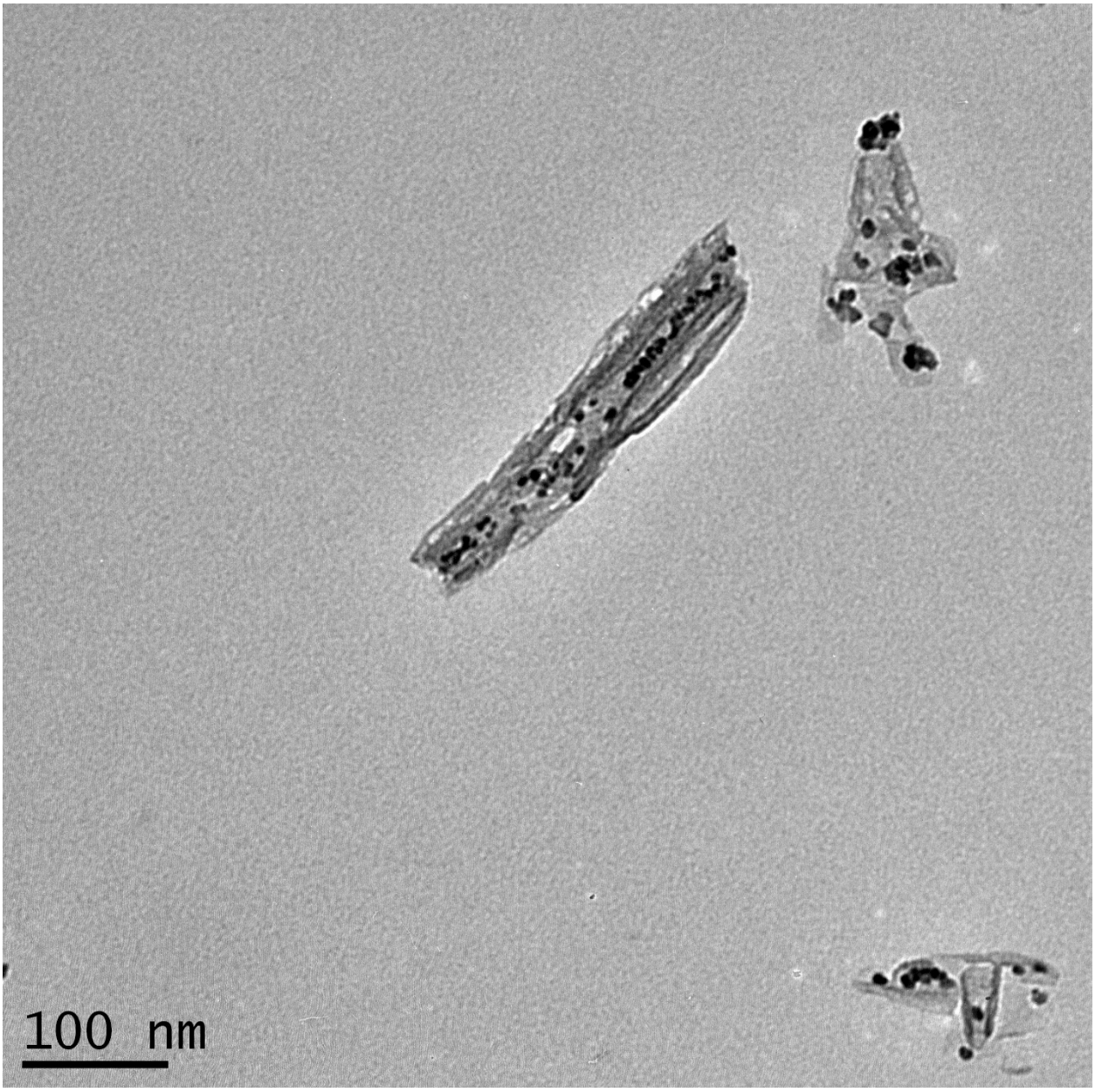

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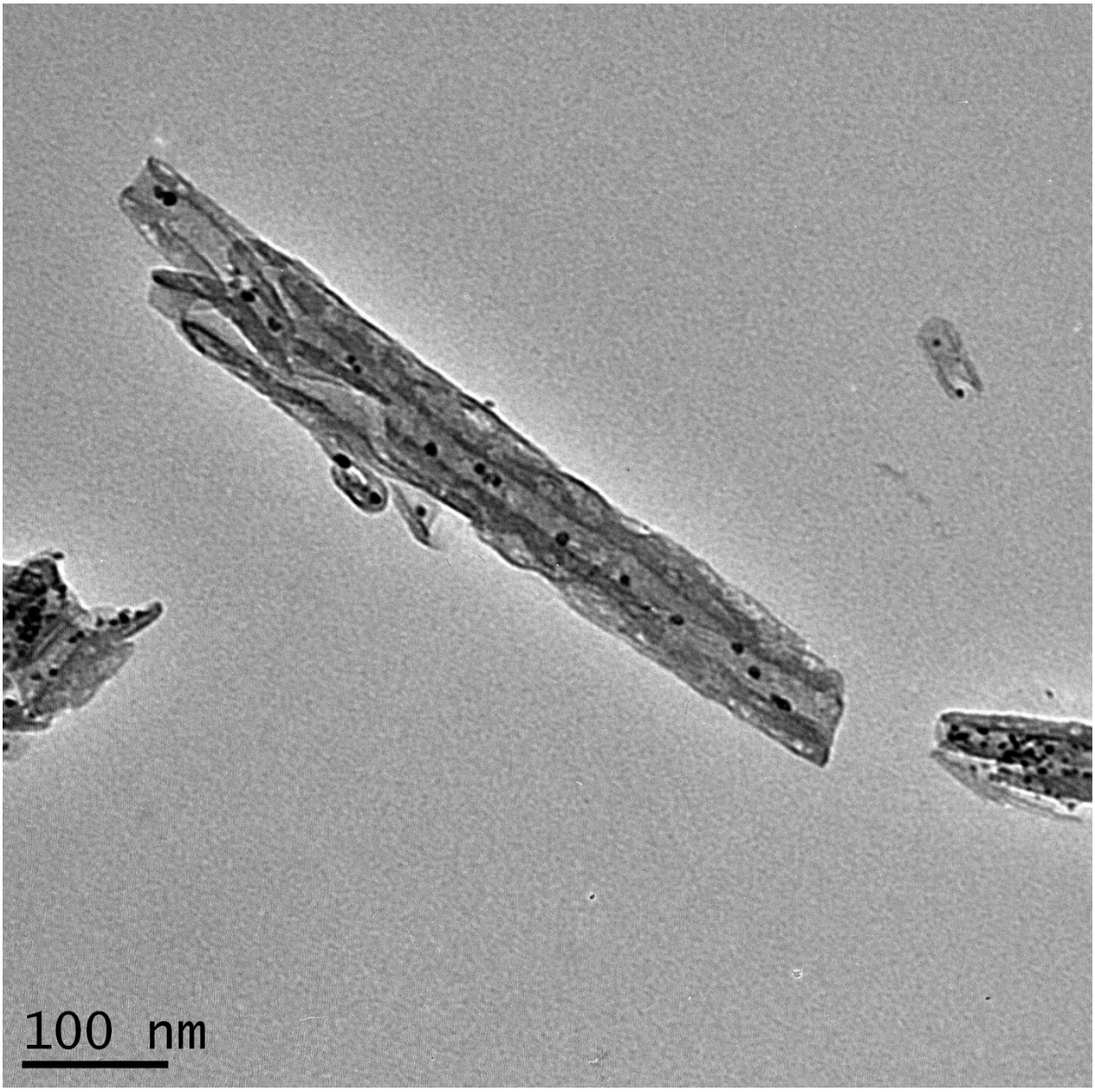
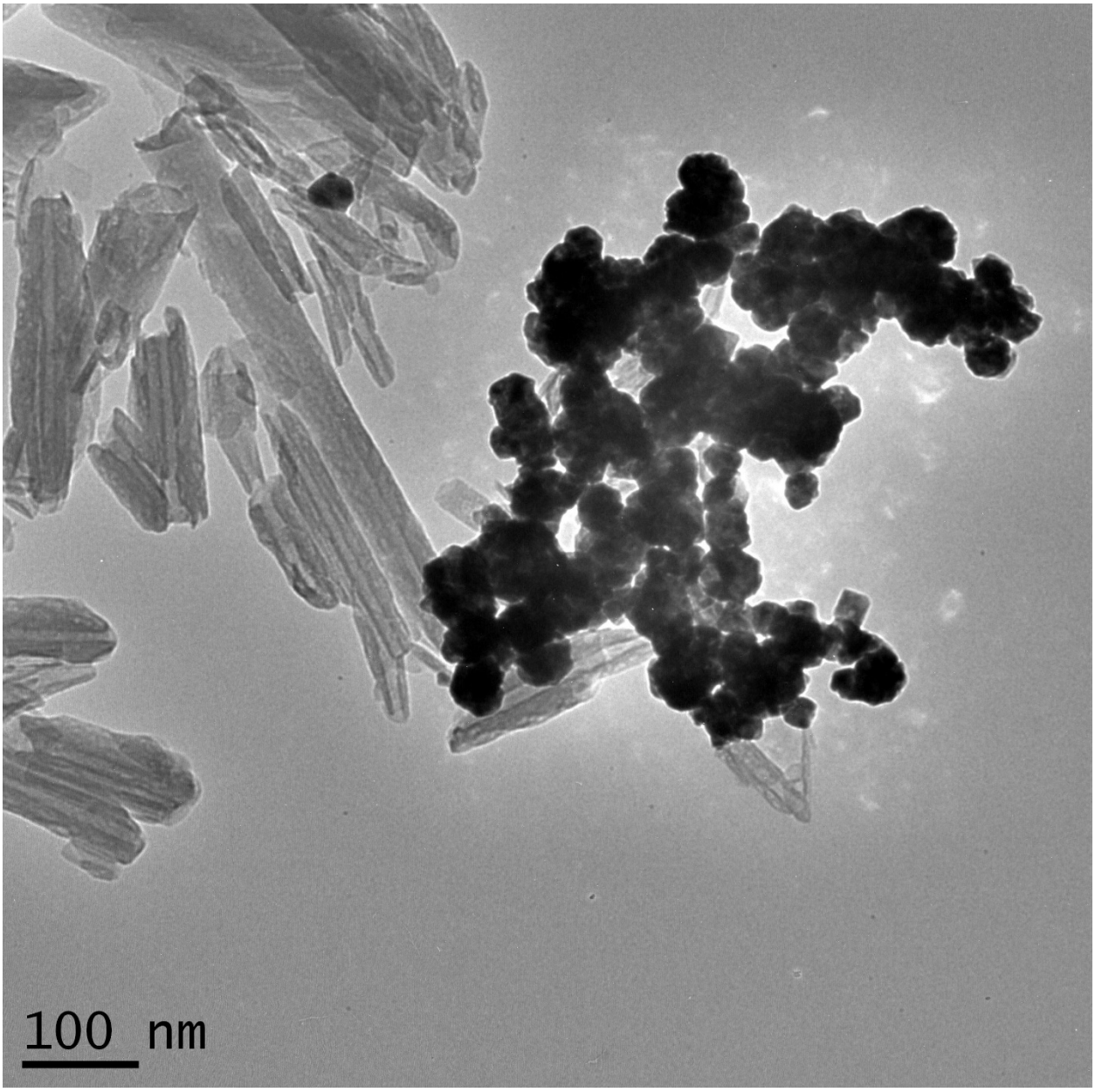


Table 1, Entry 6



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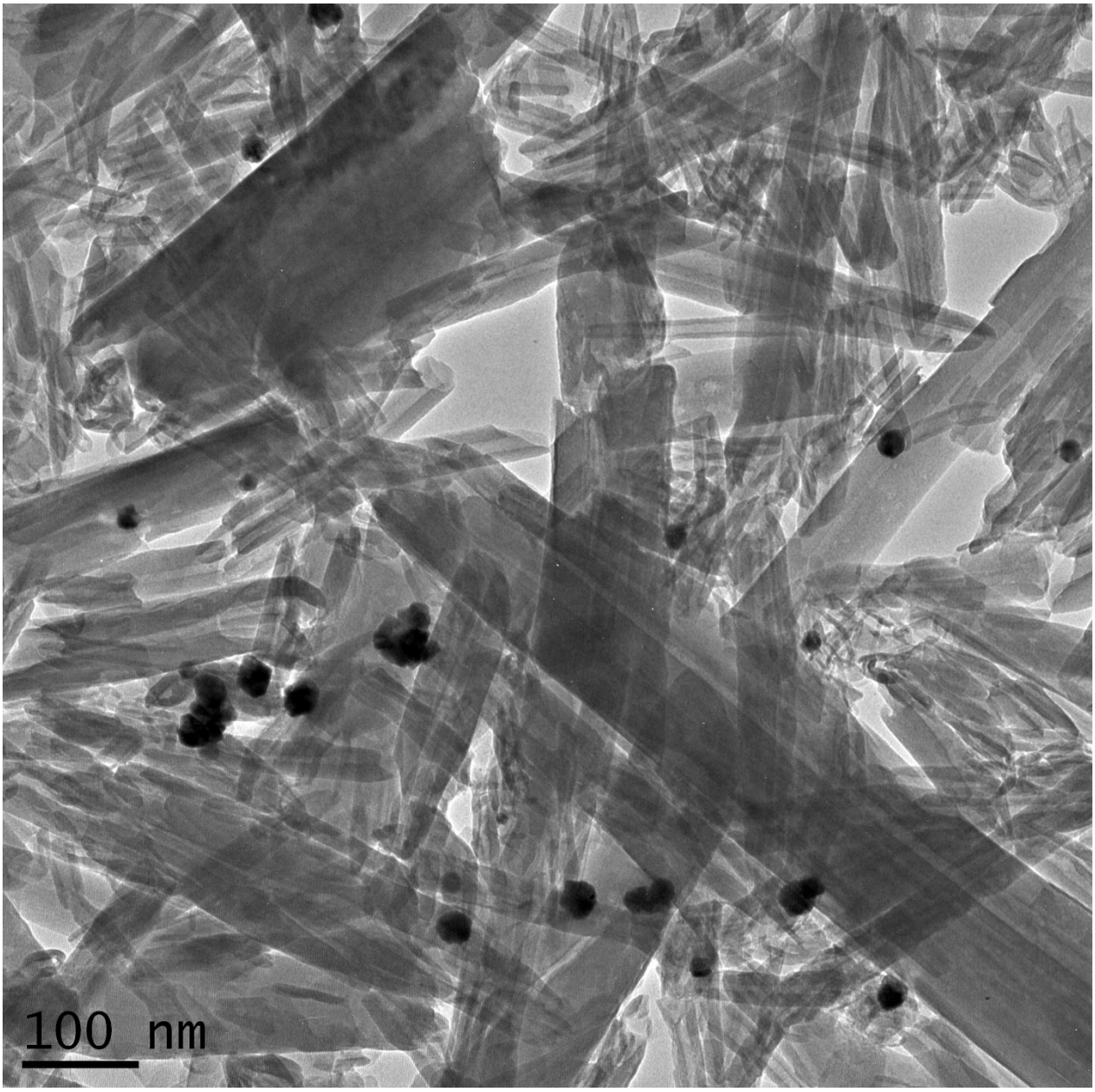

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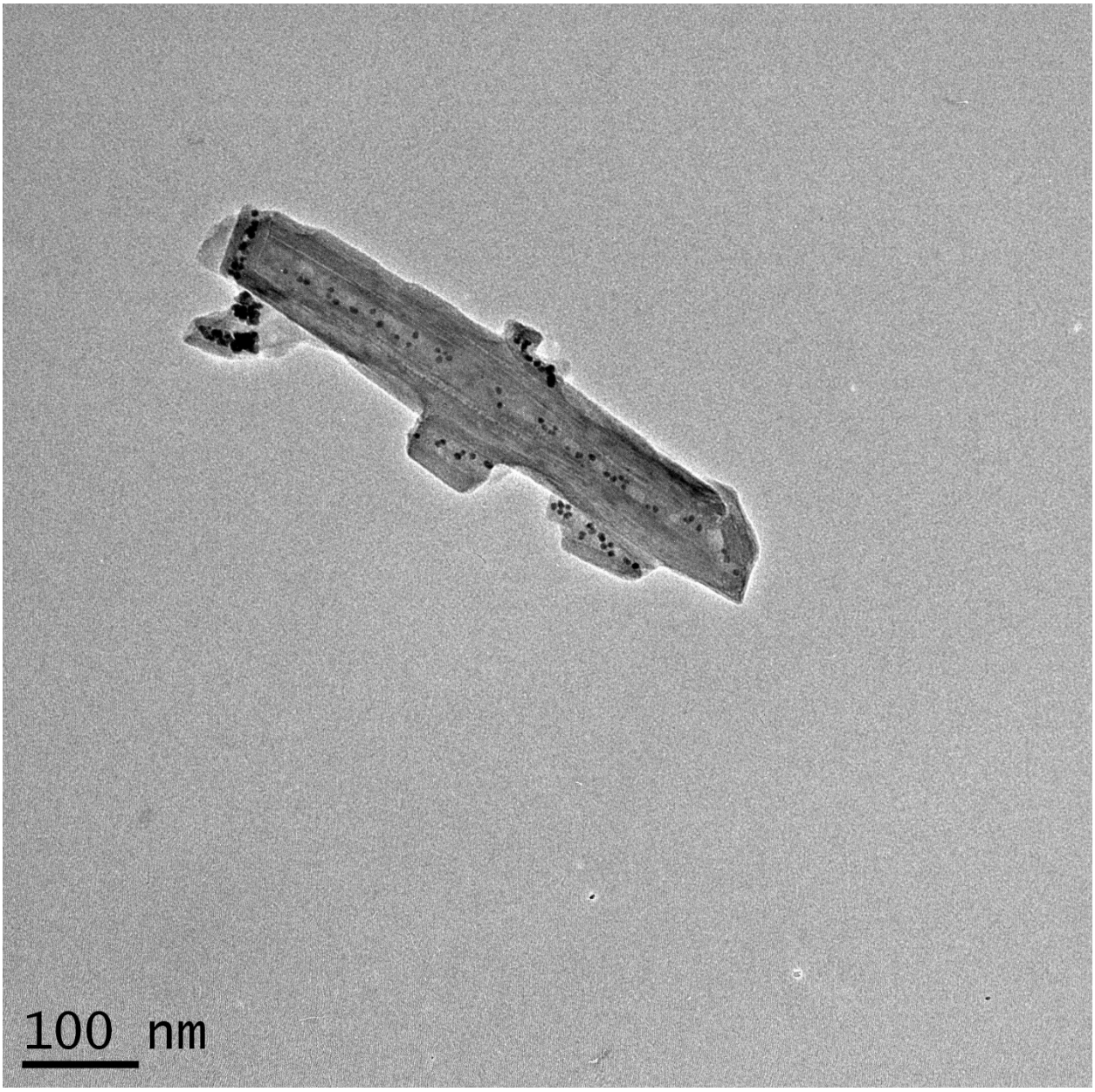

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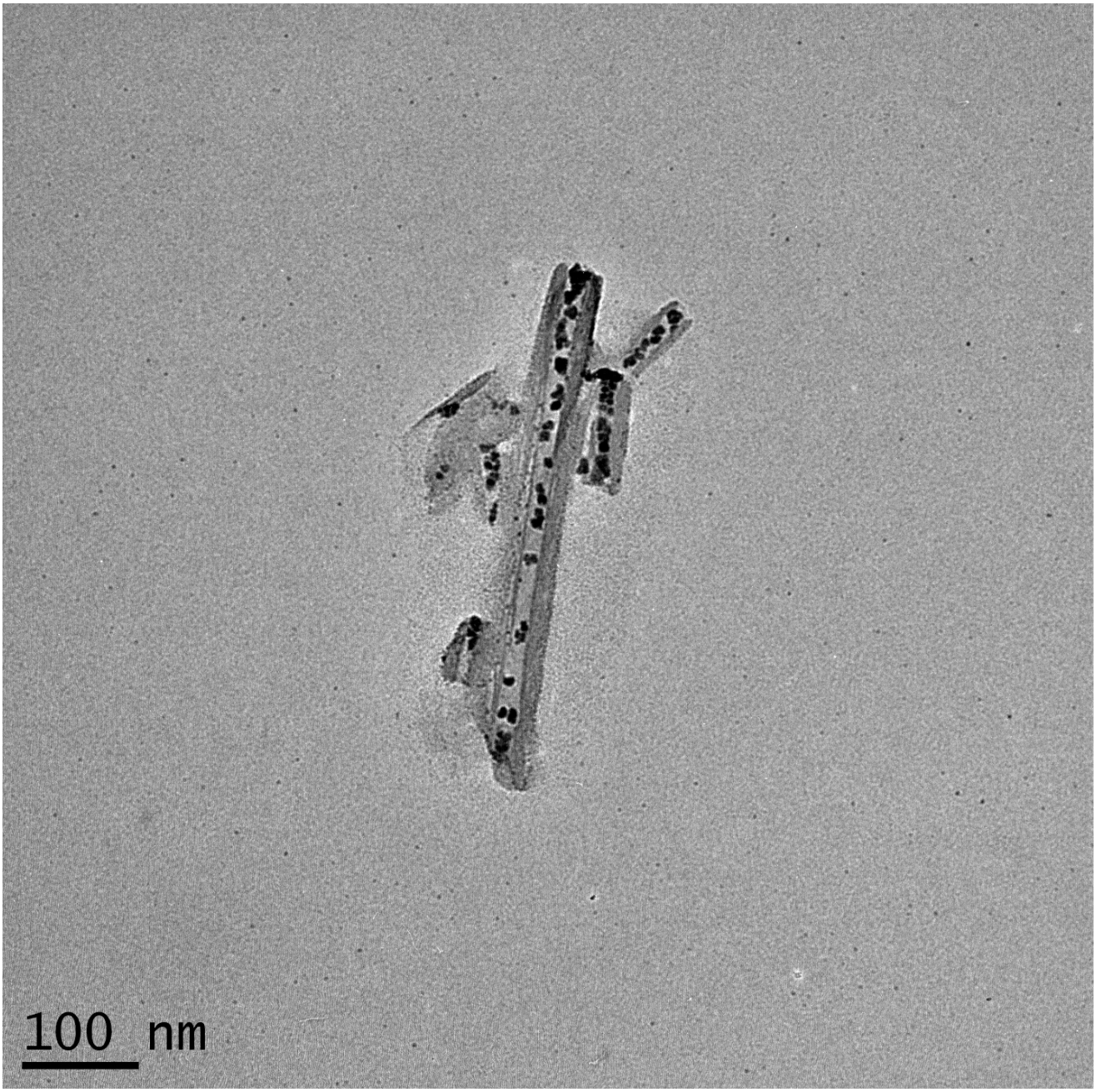

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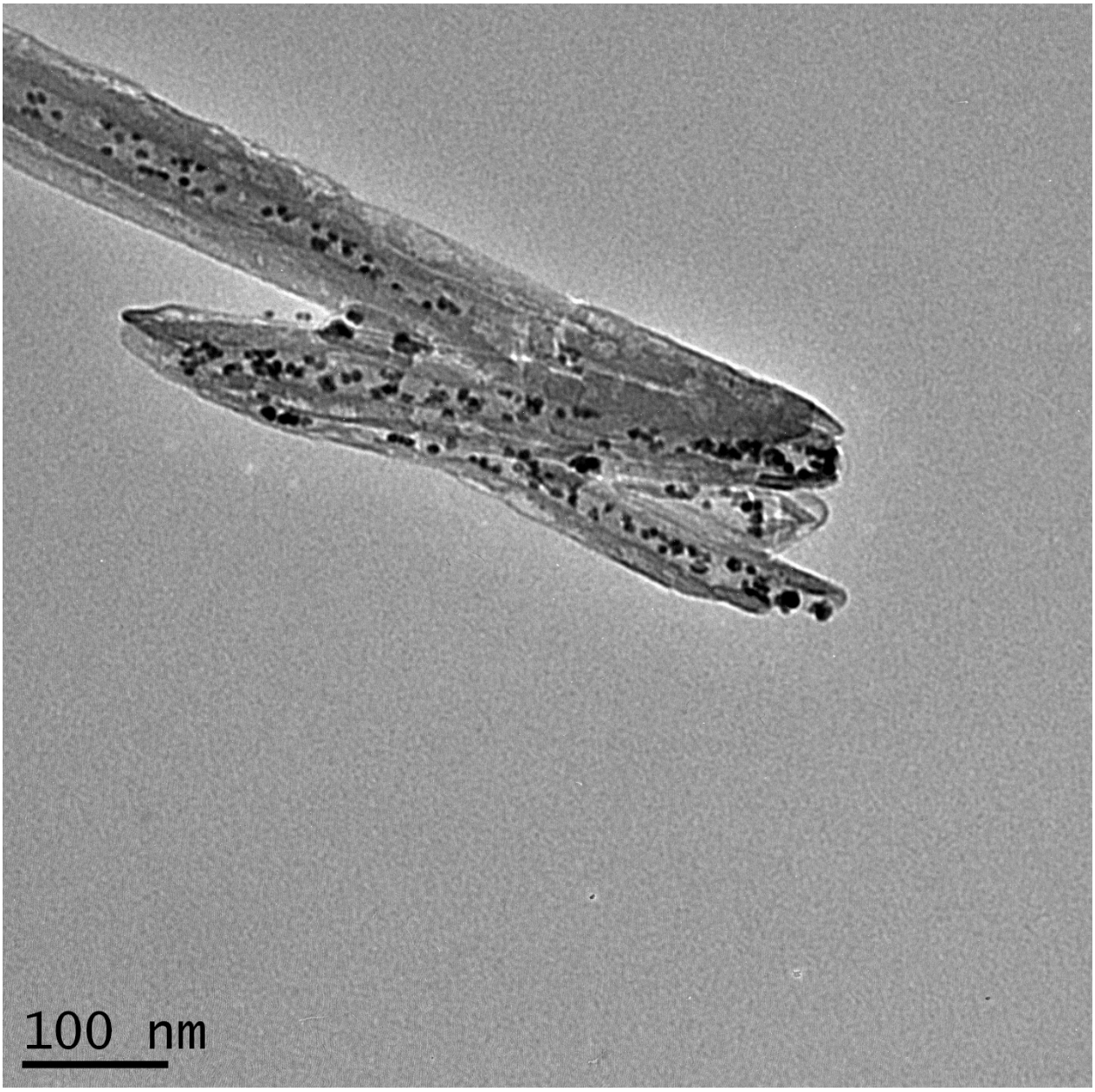
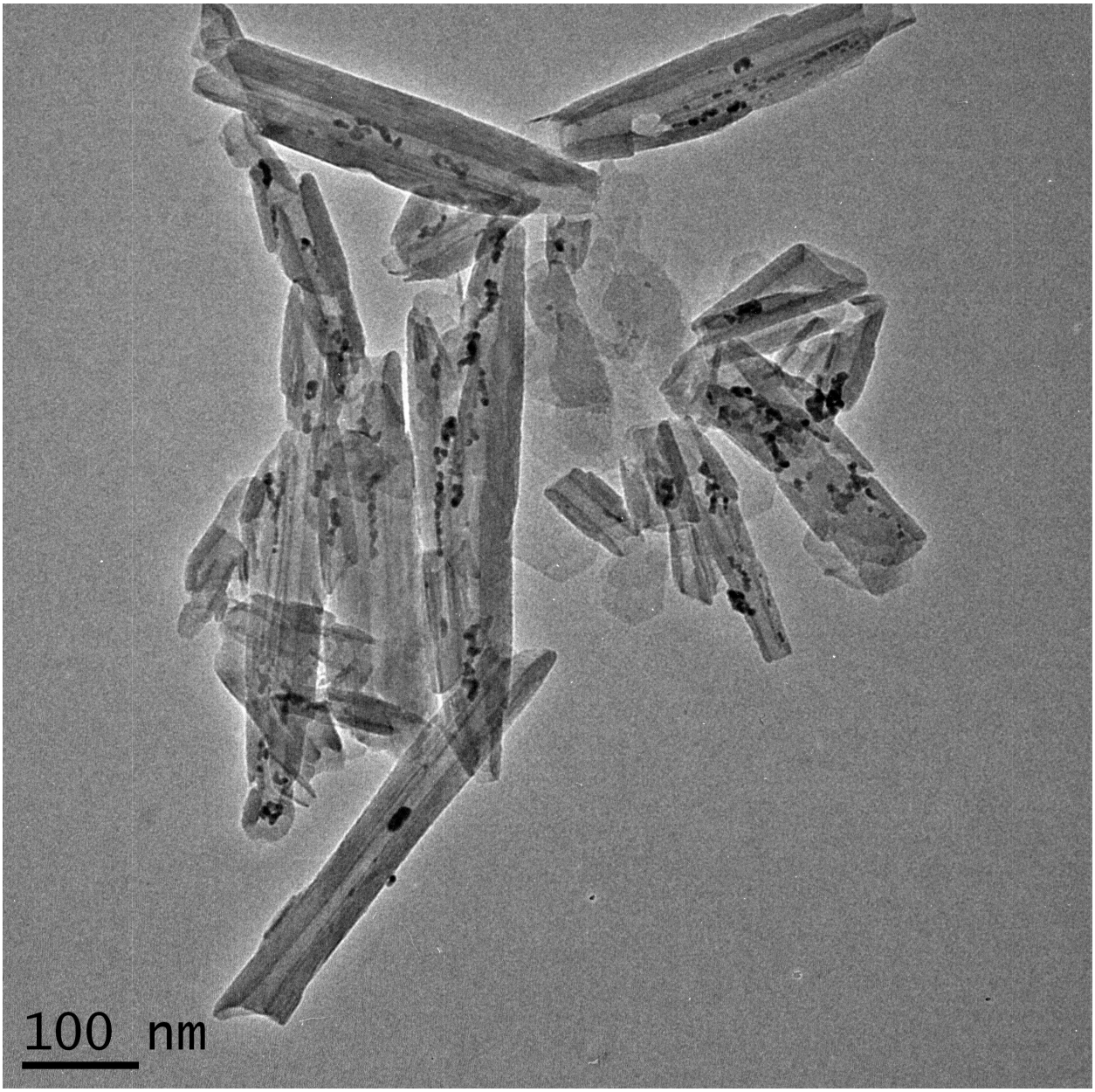
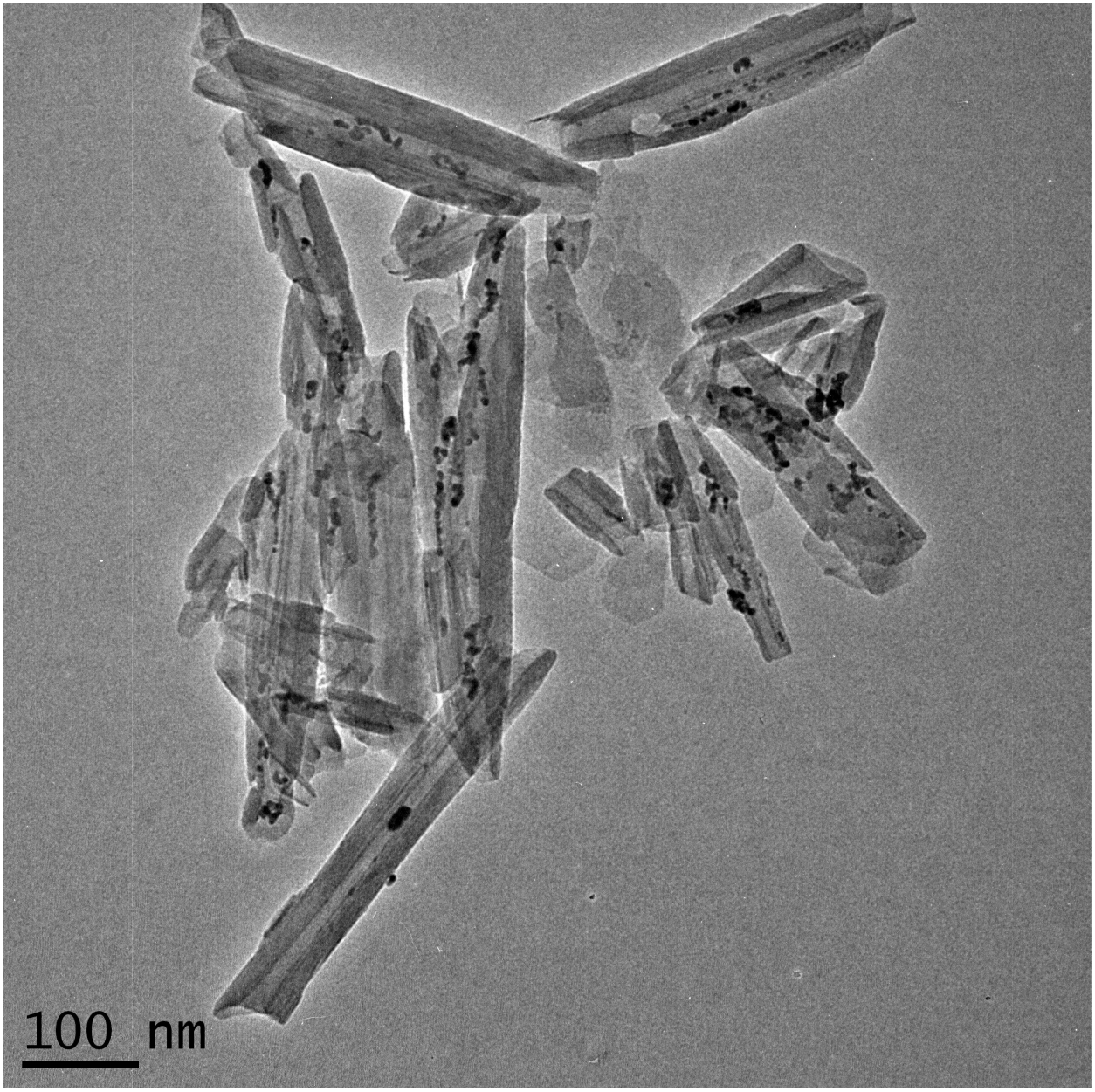


Recycling Studies

Pd@Hal (Cycle 1)



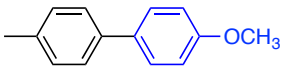
Pd@Hal (after three uses)



Characterization of Coupling Products (6, Scheme 1)

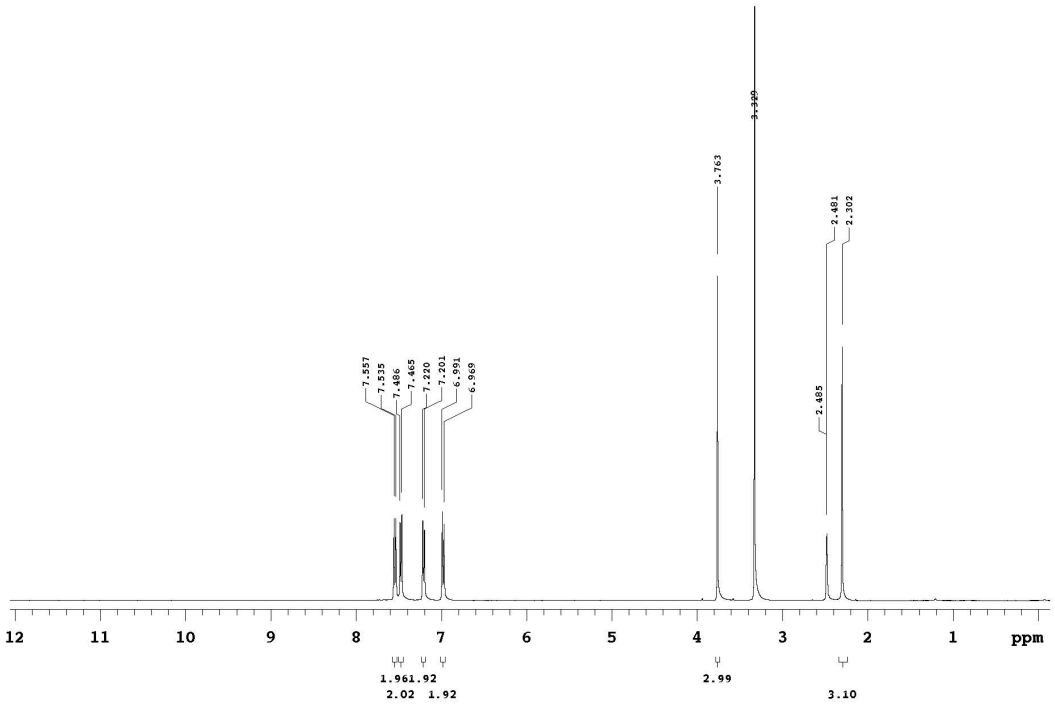
All the products are known compounds and the spectral data and melting points were identical to those reported in the literature. ^{1}H NMR are shown below each entry to illustrate the purity of the sample.

4-methoxy-4'-methyl-1,1'-biphenyl (6a)

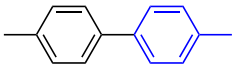


White solid (0.195 g, 98%); mp 109-110 °C. [Lit. mp 107.9-108.1 °C][1]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.55 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 7.6 Hz, 2H, 6.98 (d, J = 8.4 Hz, 2H), 3.76 (s, 3H), 2.30 (s, 3H). Identical to ^{1}H NMR reported in the literature.[2]

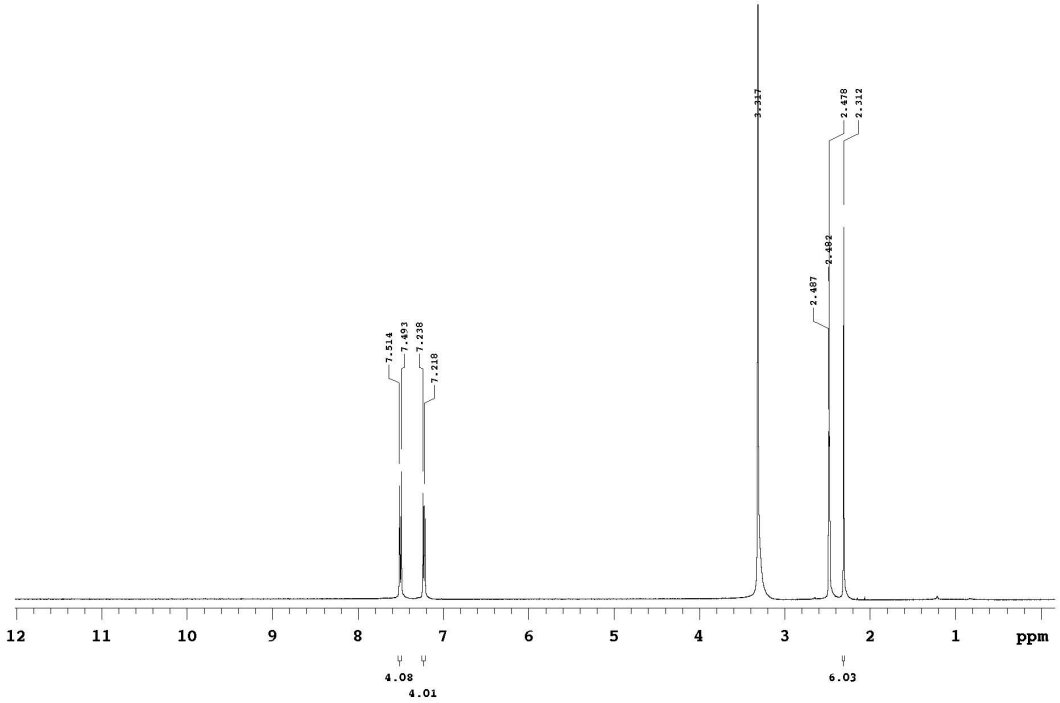


4,4'-dimethyl-1,1'-biphenyl (6b)

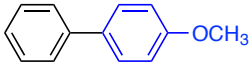


White solid (0.168 g, 92%); mp 118-119.5 °C. [Lit. mp 121.5-122.0 °C][3]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.50 (d, J = 8.4 Hz, 4H), 7.23 (d, J = 8.0 Hz, 4H), 2.31 (s, 6H). Identical to ^{1}H NMR reported in the literature.[3]

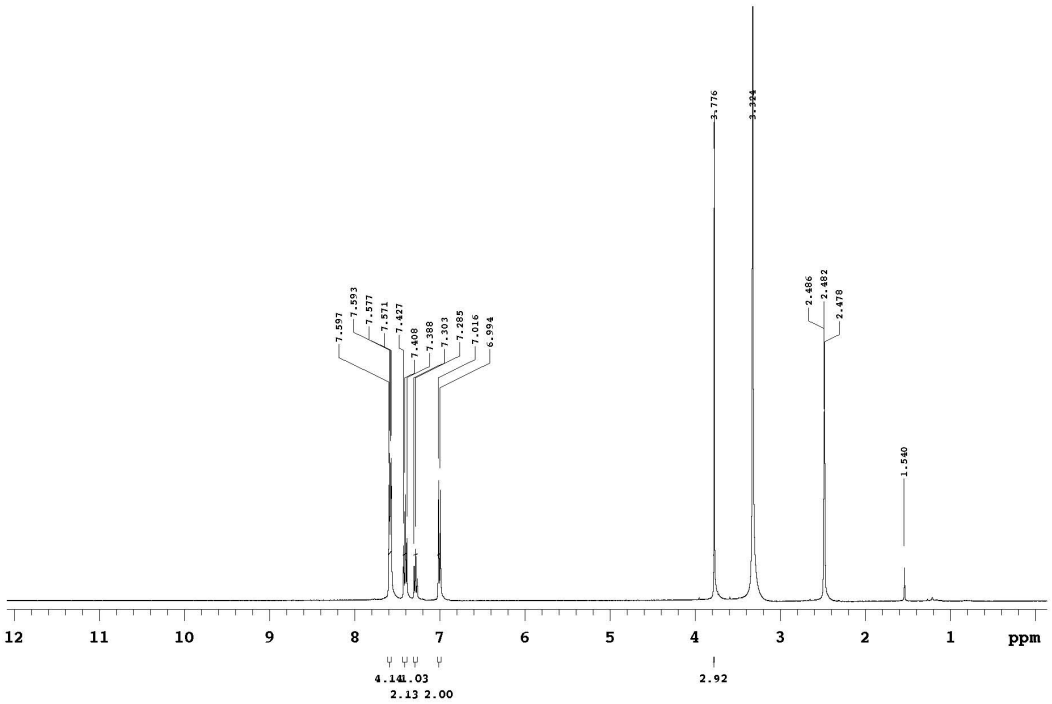


4-methoxy-1,1'-biphenyl (**6c/6d**)

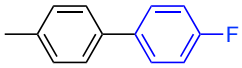


White solid (0.178 g/0.180, 97%/98%); mp 89.2-91.1 °C. [Lit. mp 85.3-85.7°C][1.]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.58 (dd, J = 8.4, 1.6 Hz, 4H), 7.41 (t, J = 7.6 Hz, 2H), 7.29 (t, J = 7.2 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 3.78 (s, 3H). Identical to ^{1}H NMR reported in the literature.[4]

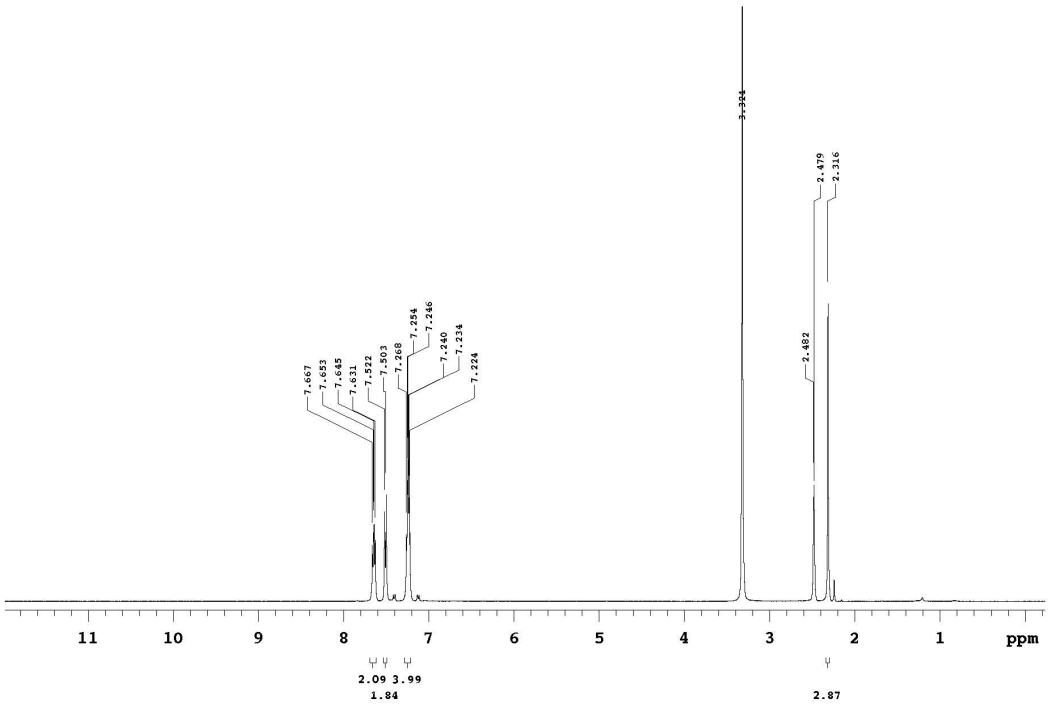


4-fluoro-4'-methyl-1,1'-biphenyl (6e)

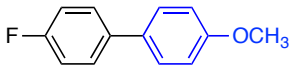


White solid (0.178 g, 96%); mp 76.5-77.1°C {Lit. mp 78-79][5]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.65 (dd, J = 8.8, 5,6 Hz, 2H), 7.51 (d, J = 7.6 Hz, 2H), 7.27- 7.22 (m, 4H), 2.48 (s, 3H). Identical to ^{1}H NMR reported in the literature.[6]

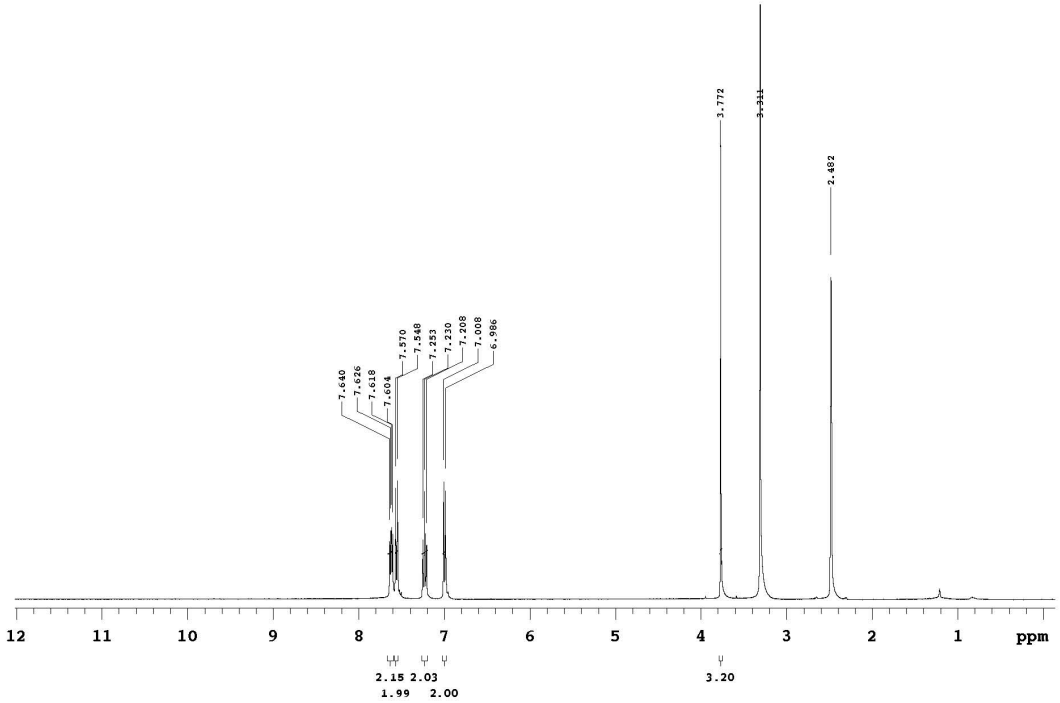


4-fluoro-4'-methoxy-1,1'-biphenyl (6f)

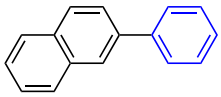


White solid (0.198 g, 98%); mp 88.6-89.5 °C [Lit. mp: 87.3-87.8 °C][1]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.64-7.60 (m, 2H), 7.56 (d, J = 8.8 Hz, 2H), 7.23 (t, J = 8.8 Hz, 2 H), 7.00 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H). Identical to ^{1}H NMR reported in the literature.[7]

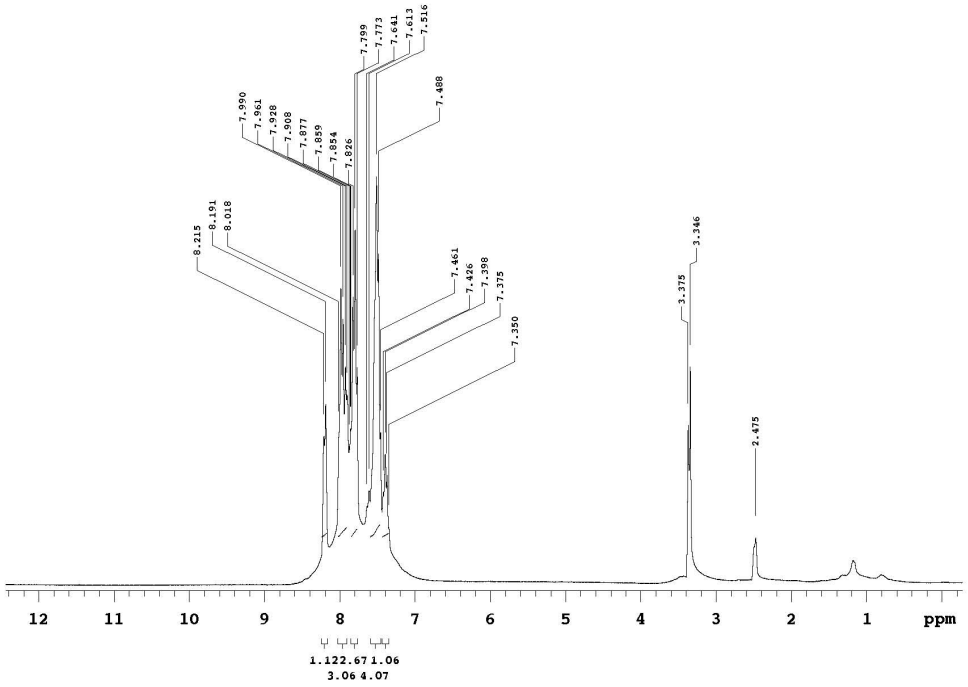


2-phenyl-naphthalene (6g)



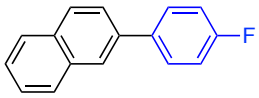
White solid (0.197 g, 96%); mp 102.5-103. 8°C [Lit. mp 101 °C].[8]

^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.19 (d, J = 7.2Hz, 1 H), 7.99-7.91 (m, 3 H), 7.88-7.77 (m, 3 H), 7.64-7.49 (m, 4 H), 7.40-7.35 (m, 1 H). Identical to ^{1}H NMR reported in the literature.[9]

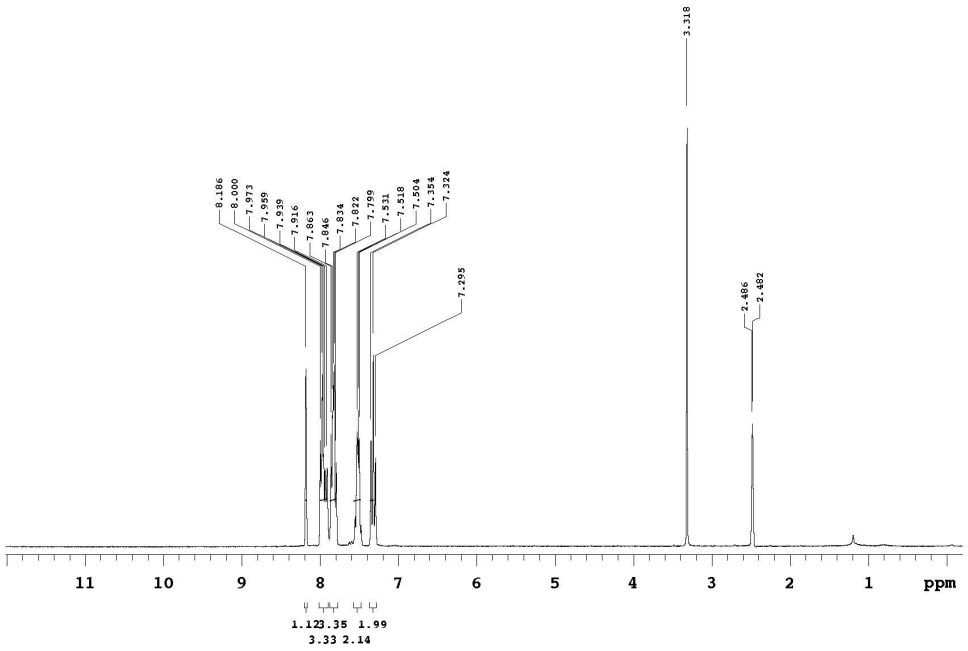


2-(4-fluorophenyl)naphthalene (6h)

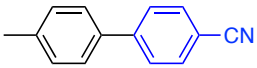
White solid (0.202 g, 91%); mp 101.1-103.2



^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.19 (s, 1H), 8.00-7.92 (m, 3H), 7.86-7.80 (m, 3H), 7.53-7.50 (m, 2H), 7.39 (t, J = 8.7 Hz, 2H). Identical to ^{1}H NMR reported in the literature.[9]

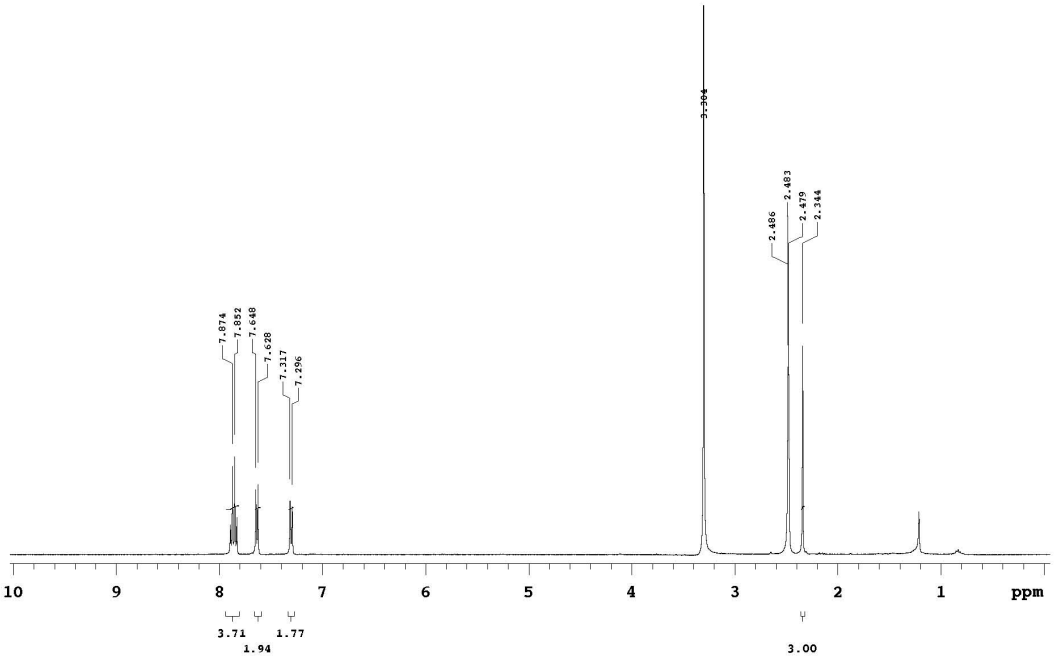


4'-methyl-biphenyl-4-carbonitrile (6i)



White solid (0.182 g, 94%); mp 110.6-111.8°C [Lit. mp 110-111 °C][10]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.89 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 7.6 Hz, 2H), 2.34 (s, 3H). Identical to ^{1}H NMR reported in the literature.[11]



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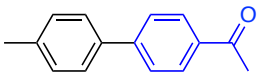
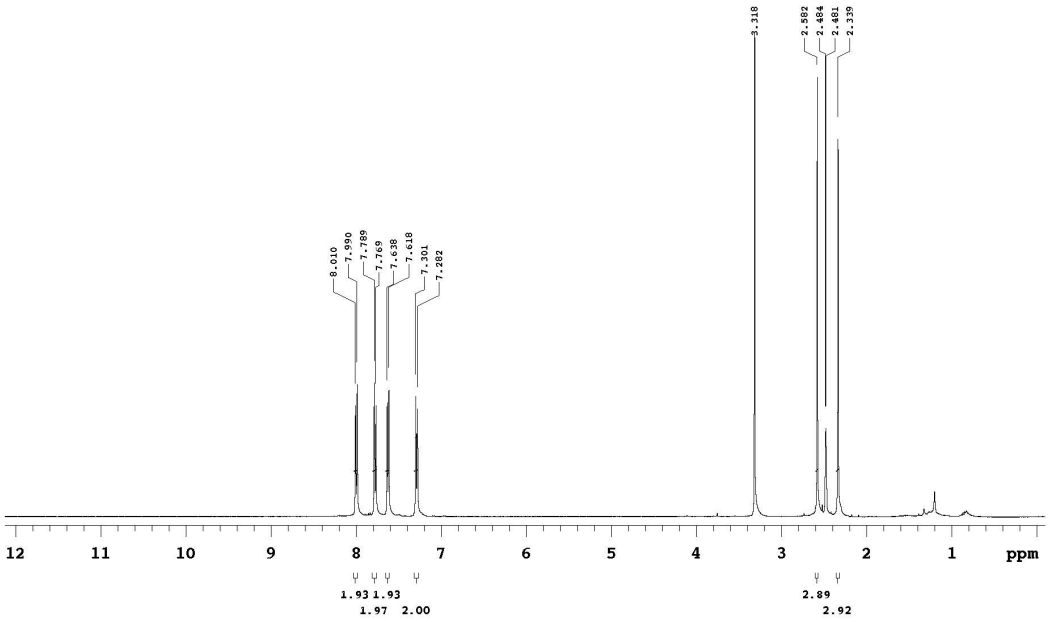
1-(4'-Methyl[1,1'-biphenyl]-4-yl)ethanone (6j)

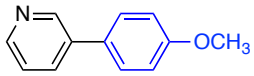


White solid (0.194 g, 92%); mp 120.3-122.1 °C [Lit. mp 122-124 °C][12]

^{1}H NMR (300 MHz, DMSO-d_6) δ: 8.00 (d, J = 6.0 Hz, 2H), 7.78 (d, J = 6.0 Hz, 2H), 7.63 (d, J = 6.0 Hz, 2H), 7.29 (d, J = 5.7 Hz, 2H), 2.58 (s, 3H), 2.34 (s, 3H). Identical to ^{1}H NMR reported in the literature.[12]

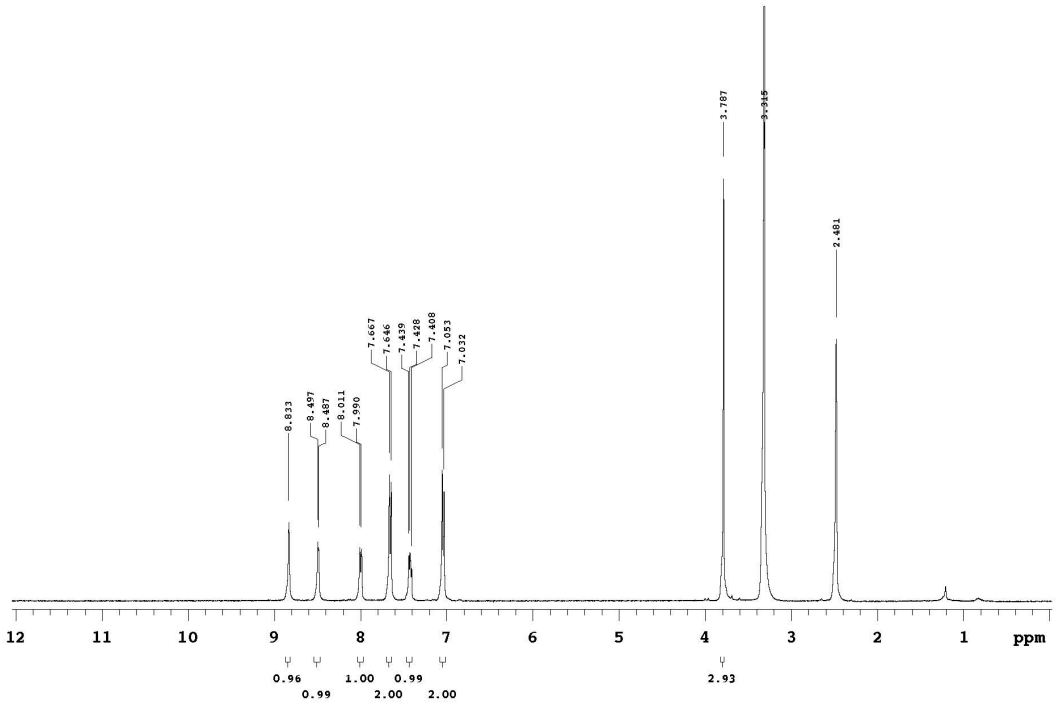


3-(4-methoxyphenyl)pyridine (6k)

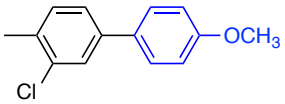


Light yellow solid (0.178 g, 97%); mp 61.5-63.1 °C [Lit. mp 62-63 °C].[13]

^{1}H NMR (400 MHz, DMSO-d_6) δ: 8.83 (s, 1H), 8.49 (d, J = 4.0 Hz, 1H), 8.00 (d, J = 8.4 Hz, 1H), 7.66 (d, J = 8.4 Hz, 2H), 7.43 (m, 1H), 7.04 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H). Identical to ^{1}H NMR reported in the literature.[13]



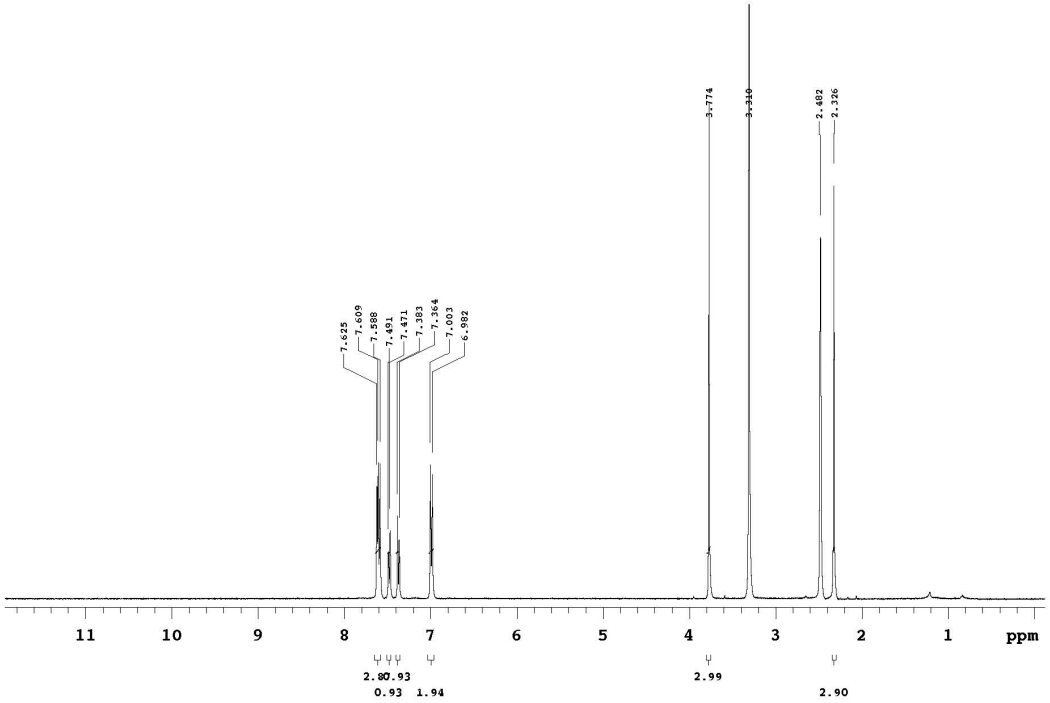
3-chloro-4'-methoxy-4-methyl-1,1'-biphenyl (6l)



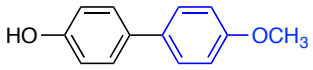
Colorless oil (0.223 g, 96%)

^{1}H NMR (400 MHz, DMSO-d_6) δ: 7.63-7.59 (m, 3H), 7.48 (d, J = 8.0 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 6.99 (d, J = 8.4 Hz, 2H), 3.77 (s, 3H), 2.33 (s, 3H).

Anal. Calcd for $C_{14}H_{13}ClO$: C, 72.26; H, 5.63. Found: 72.18; H, 5.70.

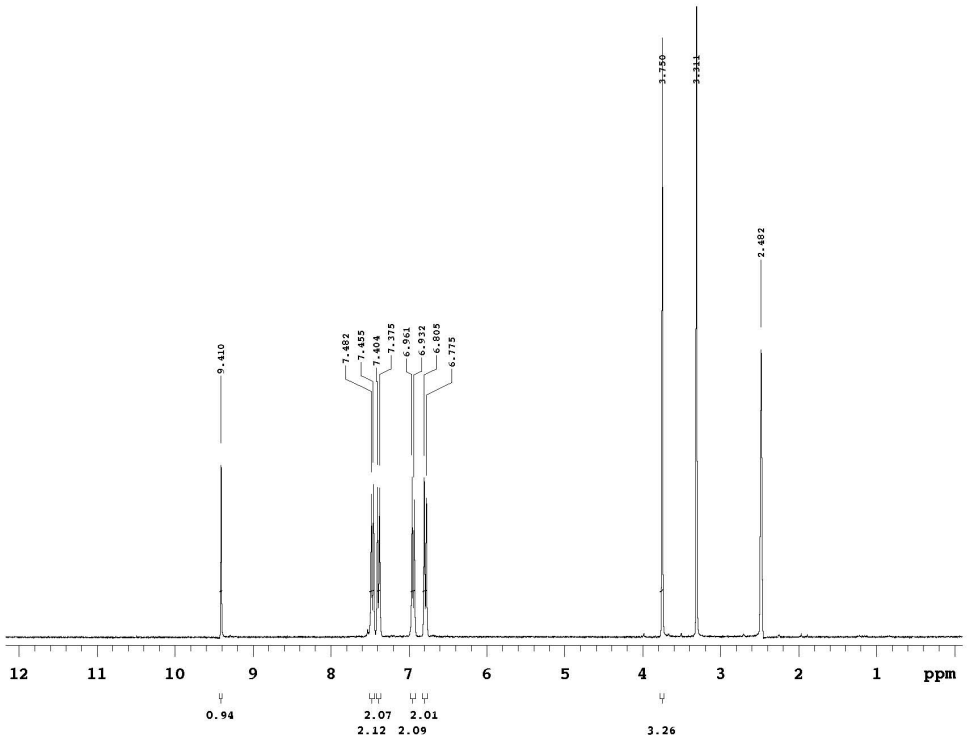


4-(4’-Methoxyphenyl)phenol (**6m**):

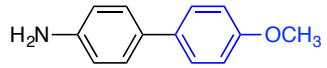


White solid (0.194 g, 97%); mp 181.5-182.2 °C [Lit. mp 180-181°C].[14]

^{1}H NMR (300 MHz, DMSO-d_6) δ: 9.41 (s, 1H), 7.47 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.7, 2H), 6.95 (d, J = 8.7 Hz, 2H), 6.79 (d, J = 9.0 Hz, 2H), 3.75 (s, 3H). Identical to ^{1}H NMR reported in the literature.[15]

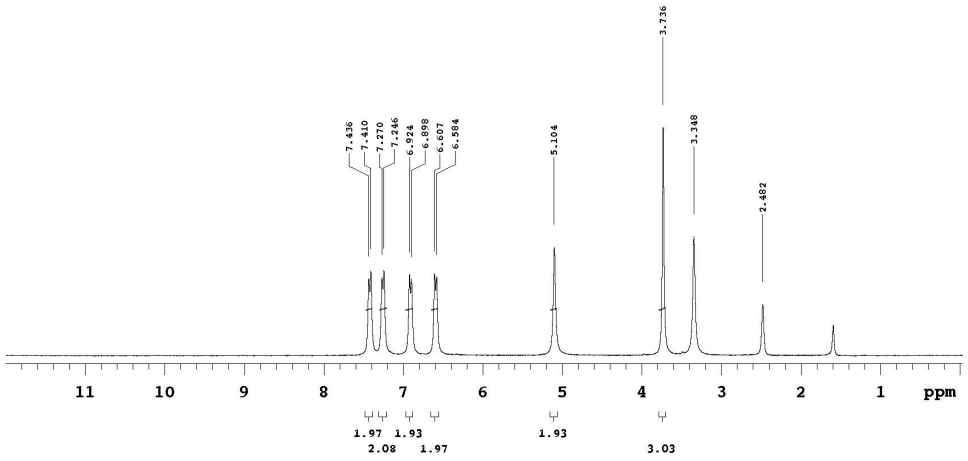


(4-methoxyphenyl)aniline (6n)



Light yellow solid (0.184 g, 92%); mp 144.8-145.2 °C [Lit. mp 147°C][15]

^{1}H NMR (300 MHz, DMSO-d_6) δ: 7.42 (d, J = 7.8 Hz, 2H), 7.26 (d, J = 7.2 Hz, 2H) 6.91 (d, J = 7.8 Hz, 2H), 6.60 (d, J = 6.9 Hz, 2H), 5.10 (s, 2H), 3.74 (s, 3H). Identical to ^{1}H NMR reported in the literature.[16]



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