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Supplementary Information

Self-assembled cage as a non-covalent protective group: regioselectivity control in the nucleophilic substitution of aryl-substituted allylic chlorides

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Table of Contents

Materials and Instrumentations

^{1}H, ^{13}C, and 2D NMR spectra were obtained on a Bruker Avance 500 equipped with CP-TCI cryoprobe. All NMR spectral data were collected at 300 K and the chemical shift values reported here are with respect to an internal TMS standard for $CDCl_3$ and to a residual solvent signal for D_2O. GC-MS spectra were obtained on an Agilent 5973 inert Mass selective Detector equipped with a 6890N Network GC system and an EI source. High-resolution ESI-TOF mass spectra were measured on a Bruker maXis®. Melting points were determined with a Yanaco MF-500 V micro melting point apparatus. IR measurements were carried out using a DIGILAB FTS-7000 instrument. Column chromatography was performed on Wakogel® C-400HG or Wakogel® C-500HG purchased from WAKO Pure Chemical Industries, Ltd. Solvents and reagents were purchased from TCI Co., Ltd., WAKO Pure Chemical Industries, Ltd., KANTO Chemical Co., Inc., or Sigma-Aldrich, Inc. Deuterated solvents were acquired from Cambridge Isotope Laboratories, Inc. All the chemicals were of reagent grade and used without further purification.

Experimental procedure and spectroscopic data

Typical procedure for nucleophilic substitution of allylic chloride 2a within cage 1.

A solution of cage **1** (2.5 mM, 6.0 mL, 1.5×10^{-2} mmol) in D_2O was added to allylic chloride **2a** (6.45 mg, 2.98×10^{-2} mmol) in a screw tube, and the mixture was stirred for 5 min at room temperature to give protected allylic chloride **1**•(**2a**)$_2$. Silver nitrate (6.13 mg, 3.61×10^{-2} mmol) was added to the solution and the mixture was stirred at 70 ºC in dark for 24 h. The cage protection was removed from the products by extraction with $CDCl_3$. NMR spectroscopy revealed that allylic chloride **2a** was completely converted to allylic alcohols **3a** and **4a** in the $CDCl_3$ layer and that empty cage **1** remained in the aqueous layer. The ratio of terminal product **3a** to internal product **4a** was calculated to be 2.4 from the NMR integral ratio. After concentration in vacuo, the product mixture was separated by flash column chromatography on silica gel (hexane/AcOEt = 4:1) to give **3a** (4.35 mg, 74%) as a colorless oil and **4a** (1.53 mg, 26%) as a colorless oil. The product structures were identified by comparison with the authentic samples.

Nucleophilic substitution of allylic chloride 2a within cage 1 in H_2O.

The nucleophilic substitution of **2a** in H_2O was carried out in a similar way to that in D_2O. The product ratio within cage **1** in H_2O and D_2O were **3a**:**4a** = 76:24 and 71:29, respectively. Without cage **1**, the product ratio in H_2O and D_2O were **3a**:**4a** = 58:42 and 57:43, respectively.

Physical data of 1•(2a)$_2$:

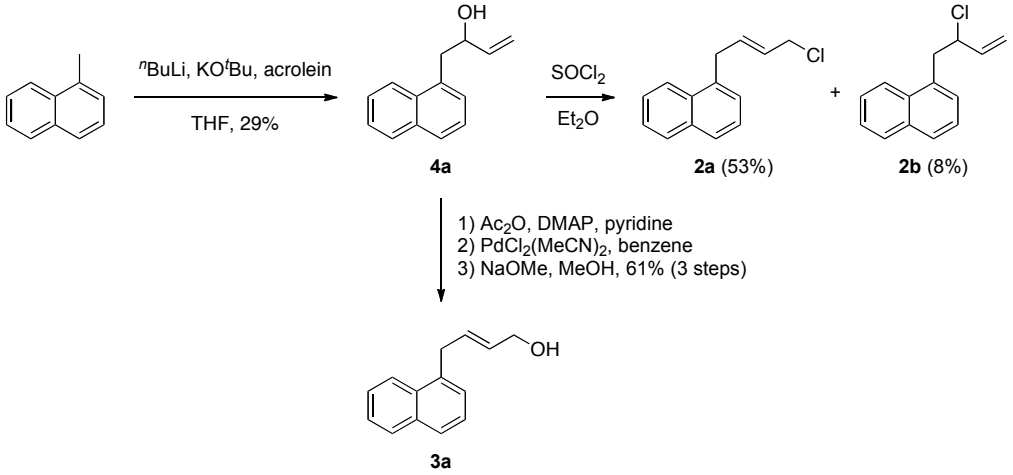
^{1}H NMR (500 MHz, D_2O) δ = 9.63 (24H, br s, **1**), 8.91 (24H, d, *J* = 6.2 Hz, **1**), 8.52 (12H, d, *J* = 8.2 Hz, **1**), 8.41 (12H, dd, *J* = 8.2, 7.6 Hz, **1**), 7.70 (12H, d, *J* = 5.7 Hz, **1**), 7.62 (12H, dd, *J* = 7.6, 5.7 Hz, **1**), 6.11 (1H, br s, Ar, **2a**), 6.03 (1H, br d, *J* = 7.5 Hz, Ar, **2a**), 5.90 (1H, br s, Ar, **2a**), 5.79 (1H, br s, Ar, **2a**), 5.41 (1H, br s, Ar, **2a**), 5.32 (1H, br s, Ar, **2a**), 4.66 (1H, br s, Ar, **2a**), 4.30–4.19 (1H, m, H_c, **2a**), 3.65 (1H, br s, H_b, **2a**), 2.45 (2H, br s, H_a, **2a**), 1.37 (2H, br s, H_d, **2a**).

Nucleophilic substitution of allylic chloride 2a with inclusion complex 1•(1-adamantanol)$_4$.

To a D_2O solution of cage **1** (2.5 mM, 3.0 mL, 7.5 μmol) was added 1-adamantanol (13.81 mg, 90.71 μmol), and the suspension was stirred at room temperature for 30 min and filtered. Part of the filtered solution of inclusion complex **1**•(1-adamantanol)$_4$ (2.5 mM, 1.0 mL, 2.5 μmol) was added to allylic chloride **2a** (1.11 mg, 5.12 μmol) in a screw tube, and the mixture was stirred for 5 min. Silver nitrate (1.06 mg, 6.02 μmol) was added to the solution, and the mixture was stirred at 70 ºC in dark for 24 h.

The resulting mixture was extracted with $CDCl_3$. The ratio of terminal product **3a** to internal product **4a** was calculated to be 1.6 from the NMR integral ratio.

Preparation of allylic chlorides 2a and 2b, and allylic alcohol 3a and 4a.



1-(Naphthalen-1-yl)but-3-en-2-ol (4a):[1]

To a cooled (–75 ºC) suspension of KO^{t}Bu (2.050 g, 16.77 mmol) in anhydrous THF (35 mL) was slowly added a solution of ^{n}BuLi in hexane (1.65 M, 11.1 mL, 18.3 mmol) via syringe under argon atmosphere, and the mixture was stirred at the same temperature for 5 min. To the cooled (–75 ºC) mixture was slowly added a solution of 1-methylnaphthalene (2.10 mL, 15.2 mmol) in anhydrous THF (15 mL) via cannula, and the resulting solution was warmed slowly to 0 ºC with stirring over 2 h. The dark purple mixture was cooled to –75 ºC and acrolein (2.20 mL, 3.29 mmol) was added dropwise via syringe. The light green mixture was allowed to warm to room temperature over 1 h and stirred over night. After dilution with saturated aqueous NH_4Cl solution, the organics was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 6:1) to give **4a** (886.1 mg, 29%) as a colorless oil. IR (thin film, ν_{max}/cm^{-1}) 3383 (br), 3047, 2932, 1595, 1510, 1022, 992, 924, 791, 776; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.07 (1H, d, *J* = 8.3 Hz), 7.87 (1H, d, *J* = 8.1 Hz), 7.77 (1H, d, *J* = 8.0 Hz), 7.56–7.47 (2H, m), 7.43 (1H, dd, *J* = 8.0, 6.8 Hz), 7.38 (1H, d, *J* = 6.8 Hz), 6.02 (1H, ddd, *J* = 17.1, 10.5, 5.9 Hz), 5.30 (1H, d, *J* = 17.1 Hz), 5.16 (1H, d, *J* = 10.5 Hz), 4.56–4.49 (1H, m), 3.38 (1H, dd, *J* = 13.9, 5.0 Hz), 3.22 (1H, dd, *J* = 13.9, 8.2 Hz), 1.63 (1H, d, *J* = 3.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 140.3 (CH), 134.0 (C), 133.8 (C), 132.1 (C), 128.9 (CH), 127.9 (CH), 127.5 (CH), 126.0 (CH), 125.6

[1] For the preparation of Schlosser's base, see: M. Schlosser, *Pure Appl. Chem.,* 1988, **60**, 1627.

(CH), 125.4 (CH), 123.8 (CH), 115.0 (CH_2), 73.0 (CH), 41.0 (CH_2); HRMS (ESI TOF) *m/z* calcd for $C_{14}H_{14}NaO$ ($[M+Na]^+$) 221.0937, found 221.0926.

(*E*)-4-(Naphthalen-1-yl)but-2-en-1-ol (3a):

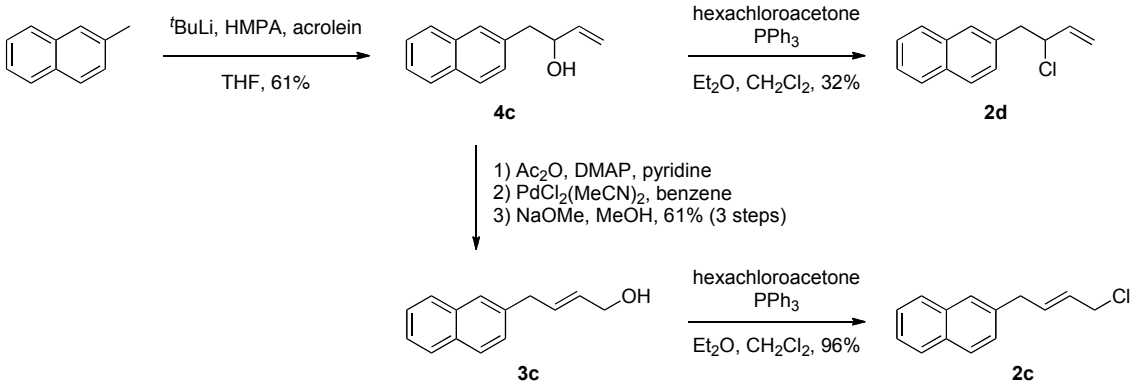
Allylic alcohol **3a** was prepared according to the procedure reported by Crilley.[2] To a solution of **4a** (369.3 mg, 1.863 mmol) and DMAP (11.5 mg, 94.1 μmol) in anhydrous pyridine (2.5 mL) was slowly added acetic anhydride (0.23 mL, 2.4 mmol) via syringe. The mixture was stirred at room temperature for 40 min. After dilution with CH_2Cl_2 and hydrochloric acid (1 M), the reaction mixture was extracted with CH_2Cl_2. The combined organic layer was washed with hydrochloric acid (1 M), saturated aqueous $NaHCO_3$ solution, water, and brine, then dried over Na_2SO_4 and concentrated in vacuo to yield an unpurified acetate (423.2 mg) as a yellow-tinged oil. The oil was diluted with anhydrous benzene (9.5 mL) followed by addition of $PdCl_2(MeCN)_2$ (31.4 mg, 0.121 mmol). The solution was stirred at room temperature for 18 h and concentrated in vacuo. The residue was passed through a plug of silica gel (hexane/AcOEt = 5:1) and concentrated in vacuo to give a mixture of allylic isomers of an acetate (361.5 mg) as a colorless oil. To a solution of the mixture in anhydrous MeOH (5.5 mL) was added NaOMe (6.10 mg, 0.113 mmol) and the mixture was stirred at room temperature for 15 h. The solution was diluted with water and neutralized with saturated aqueous NH_4Cl solution. After removing MeOH in vacuo, the orgnics was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4:1) to recover starting material **4a** (43.5 mg, 20% over three steps) as a colorless oil and give **3a** (155.0 mg, 71% over three steps) as a colorless oil. IR (thin film, ν_{max}/cm^{-1}) 3339 (br), 3044, 2920, 1595, 1510, 1092, 972, 792, 779; ^1H NMR (500 MHz, $CDCl_3$) δ = 8.03 (1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 8.2 Hz), 7.74 (1H, d, *J* = 8.0 Hz), 7.53–7.46 (2H, m), 7.41 (1H, dd, *J* = 8.0, 7.0 Hz), 7.34 (1H, d, *J* = 7.0 Hz), 6.01 (1H, dt, *J* = 15.4, 6.2 Hz), 5.72 (1H, dt, *J* = 15.4, 5.6 Hz), 4.11 (2H, d, *J* = 5.6 Hz), 3.84 (2H, d, *J* = 6.2 Hz), 1.25 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.1 (C), 133.8 (C), 131.9 (C), 131.0 (CH), 130.6 (CH), 128.7 (CH), 127.0 (CH), 126.3 (CH), 125.9 (CH), 125.61 (CH), 125.56 (CH), 123.9 (CH), 63.6 (CH_2), 35.7 (CH_2); HRMS (ESI TOF) *m/z* calcd for $C_{14}H_{14}NaO$ ($[M+Na]^+$) 221.0937, found 221.0926.

[2] M. M. L. Crilley, B. T. Golding and C. Pierpoint, *J. Chem. Soc., Perkin Trans. 1,* 1988, 2061.

(*E*)-1-(4-Chlorobut-2-en-1-yl)naphthalene (2a) and 1-(2-Chlorobut-3-en-1-yl)naphthalene (2b):

To a cooled (0 ºC) solution of **4a** (441.1 mg, 2.225 mmol) in anhydrous Et_2O (4.5 mL) was added thionyl chloride (0.32 mL, 4.4 mmol) dropwise via syringe under argon atmosphere, and the solution was stirred at the same temperature for 5 h. After dilution with saturated aqueous $NaHCO_3$ solution, the organics was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 30:1) to give **2a** (40.3 mg, 8%) as a colorless liquid and **2b** (256.8 mg, 53%) as a colorless liquid. **2a**: IR (thin film, ν_{max}/cm^{-1}) 3044, 2953, 1595, 1511, 1249, 968, 792, 778, 677; 2a: ^1H NMR (500 MHz, $CDCl_3$) δ = 7.98 (1H, d, *J* = 8.1 Hz), 7.86 (1H, d, *J* = 7.5 Hz), 7.75 (1H, d, *J* = 8.1 Hz), 7.54–7.46 (2H, m), 7.42 (1H, dd, *J* = 8.1, 6.8 Hz), 7.33 (1H, d, *J* = 6.8 Hz), 6.08 (1H, dt, *J* = 15.2, 6.4 Hz), 5.69 (1H, dt, *J* = 15.2, 7.1 Hz), 4.04 (2H, d, *J* = 7.1 Hz), 3.86 (2H, d, *J* = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 135.4 (C), 133.9 (CH), 133.8 (C), 131.8 (C), 128.7 (CH), 127.5 (CH), 127.2 (CH), 126.4 (CH), 126.0 (CH), 125.6 (2C, CH), 123.8 (CH), 45.0 (CH_2), 35.6 (CH_2); LRMS (EI) *m/z*: 216 (M^+), 181, 167, 141, 89. **2b**: IR (thin film, ν_{max}/cm^{-1}) 3064, 2935, 1641, 1597, 1511, 985, 930, 778, 702; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.99 (1 H, d, *J* = 8.4 Hz), 7.87 (1 H, d, *J* = 8.3 Hz), 7.78 (1 H, d, *J* = 8.0 Hz), 7.57–7.47 (2 H, m), 7.42 (1 H, dd, *J* = 8.0, 7.0 Hz), 7.36 (1 H, d, *J* = 7.0 Hz), 5.99 (1 H, ddd, *J* = 16.9, 10.2, 8.0 Hz), 5.16 (1 H, d, *J* = 16.9 Hz), 5.10 (1 H, d, *J* = 10.2 Hz), 4.73 (1 H, ddd, *J* = 8.0, 7.3, 7.2 Hz), 3.63 (1 H, d, *J* = 14.3, 7.2 Hz), 3.54 (1 H, dd, *J* = 14.3, 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 138.0 (CH), 133.9 (C), 133.2 (C), 131.8 (C), 129.0 (CH), 128.2 (CH), 127.8 (CH), 126.2 (CH), 125.6 (CH), 125.3 (CH), 123.3 (CH), 117.1 (CH_2), 62.3 (CH), 42.0 (CH_2); LRMS (EI) *m/z*: 216 (M^+), 181, 141, 89.

Preparation of allylic chlorides 2c and 2d and allylic alcohol 3c and 4c.



1-(Naphthalen-2-yl)but-3-en-2-ol (4c):[3]

To a cooled (–100 °C) solution of 2-methylnaphthalene (792.1 mg, 5.570 mmol) and HMPA (100 μL, 0.575 mmol) in anhydrous THF (15 mL) was slowly added a solution of ^{t}BuLi in pentane (1.6 M, 4.5 mL, 7.2 mmol) via syringe under argon atmosphere. The mixture was warmed slowly to 0 ºC with stirring over 2 h. To the cooled (–80 ºC) mixture was slowly added acrolein (520 μL, 7.79 mmol), and the mixture was allowed to warm to room temperature over 2 h and stirred overnight. After dilution with saturated aqueous NH_4Cl solution, the reaction mixture was extracted with AcOEt. The combined organic layer was washed with saturated aqueous LiCl solution and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 6:1) to give **4c** (669.3 mg, 61%) as a colorless oil. IR (thin film, ν_{max}/cm^{-1}) 3385 (br), 3054, 2919, 1636, 1599, 1508, 1024, 993, 924, 859, 814, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.84–7.78 (3H, m), 7.69 (1H, s), 7.49–7.42 (2H, m), 7.38 (1H, d, *J* = 8.3 Hz), 5.98 (1H, ddd, *J* = 17.2, 10.5, 5.9 Hz), 5.28 (1H, d, *J* = 17.2 Hz), 5.15 (1H, d, *J* = 10.5 Hz), 4.46 (1H, ddd, *J* = 5.9, 5.1, 8.0 Hz), 3.05 (1H, dd, *J* = 13.6, 5.1 Hz), 2.96 (1H, dd, *J* = 13.6, 8.0 Hz), 1.65 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 140.1 (CH), 135.2 (C), 133.5 (C), 132.3 (C), 128.11 (CH), 128.07 (CH), 127.8 (CH), 127.6 (CH), 127.5 (CH), 126.1 (CH), 125.5 (CH), 115.1 (CH_2), 73.6 (CH), 44.0 (CH_2); HRMS (ESI TOF) *m/z* calcd for $C_{14}H_{14}NaO$ ($[M+Na]^+$) 221.0937, found 221.0930.

(*E*)-2-(4-Chlorobut-2-en-1-yl)naphthalene (2d):

Allylic chloride **2c** was prepared according to the procedure reported by Winkler.[4] To a cooled (0 ºC) solution of **4c** (397.1 mg, 2.003 mmol) and PPh_3 (685.0 mg, 2.612 mmol) in anhydrous CH_2Cl_2 (10 mL) and anhydrous Et_2O (7.0 mL) was added hexachloroacetone (480 μL, 2.62 mmol) under argon atmosphere, and the mixture was stirred at 0 ºC for 1.5 h. After dilution with saturated aqueous $NaHCO_3$ solution, the organics was extracted with AcOEt. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 40:1) to give **2d** (140.5 mg, 32%) as a colorless liquid. IR (thin film, ν_{max}/cm^{-1}) 3055, 2927, 1638, 1601, 1508, 986, 930, 856, 818, 742, 696; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.84–7.77 (3H, m), 7.67 (1H, s), 7.50–7.43 (2H, m), 7.34 (1H, dd, *J* = 8.4, 1.2 Hz), 5.97 (1H,

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[3] Schlosser's base is also applicable to preparation of **4c** instead of the combination of ^{t}BuLi and HMPA (see the preparation of **4a**).

[4] J. D. Winkler, M. B. Rouse, M. F. Greaney, S. J. Harrison and Y. T. Jeon, *J. Am. Chem. Soc.*, 2002, **124**, 9726.

ddd, *J* = 16.8, 10.1, 8.2 Hz), 5.23 (1H, d, *J* = 16.8 Hz), 5.13 (1H, d, *J* = 10.1 Hz), 4.65 (1H, dt, *J* = 8.2, 7.2 Hz), 3.33–3.24 (2H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 137.9 (CH), 134.7 (C), 133.4 (C), 132.4 (C), 128.2 (CH), 128.0 (CH), 127.6 (3C, CH), 126.1 (CH), 125.7 (CH), 117.2 (CH_2), 63.0 (CH), 45.0 (CH_2); LRMS (EI) *m/z*: 216 (M^+), 181, 141, 127, 89.

(*E*)-4-(Naphthalen-2-yl)but-2-en-1-ol (3c):

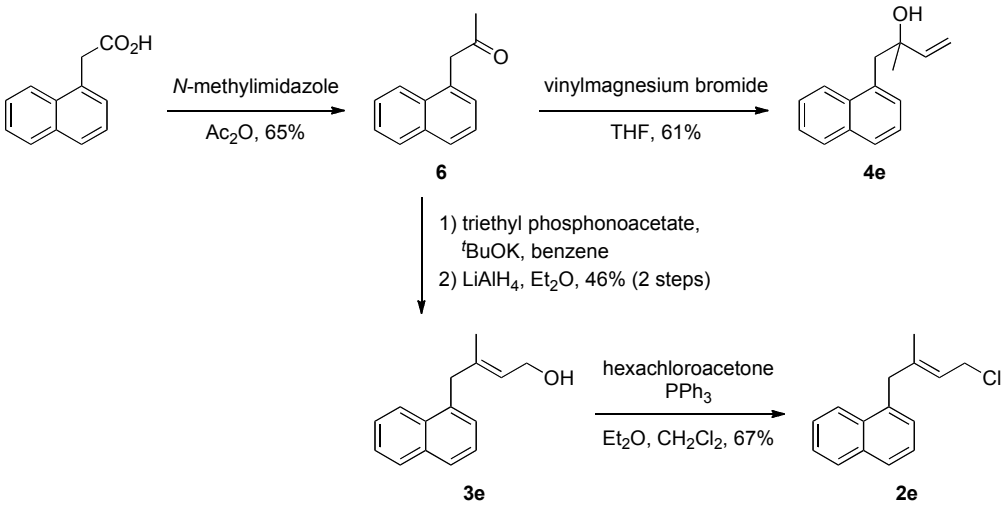
Allylic alcohol **3c** was prepared similarly to the synthesis of **3a** from **4a**. To a solution of **4c** (219.8 mg, 1.108 mmol) and DMAP (6.8 mg, 0.056 mmol) in anhydrous pyridine (1.5 mL) was slowly added acetic anhydride (0.13 mL, 1.4 mmol) via syrinde. The mixture was stirred at room temperature for 0.5 h. After dilution with CH_2Cl_2 and hydrochloric acid (1 M), the reaction mixture was extracted with CH_2Cl_2. The combined organic layer was washed with hydrochloric acid (1 M), saturated aqueous $NaHCO_3$ solution, water, and brine, then dried over Na_2SO_4 and concentrated in vacuo to yield an unpurified acetate (219.9 mg) as a yellow oil. The oil was diluted with anhydrous benzene (5.5 mL) followed by addition of $PdCl_2(MeCN)_2$ (14.4 mg, 55.5 μmol). The solution was stirred at room temperature for 15 h and concentrated in vacuo. The residue was passed through a plug of silica gel (hexane/AcOEt = 5:1) and concentrated in vacuo to give a mixture of allylic isomers of acetate (245.6 mg) as a colorless oil. To a solution of the mixture in anhydrous MeOH (5.5 mL) was added NaOMe (6.10 mg, 0.113 mmol) and the mixture was stirred at room temperature for 15 h. The solution was diluted with water and neutralized with saturated aqueous NH_4Cl solution. After removing MeOH in vacuo, the organics was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4:1) to recover starting material **4c** (43.5 mg, 20% over three steps) as a colorless oil and give **3c** (155.0 mg, 71% over three steps) as a white solid. mp 32.1–32.9 ºC; IR (thin film, ν_{max}/cm^{-1}) 3333 (br), 3052, 1601, 1506, 1092, 972, 854, 817, 745; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.82–7.76 (3H, m), 7.62 (1H, s), 7.48–7.40 (2H, m), 7.32 (1H, d, *J* = 8.3 Hz), 5.94 (1H, dt, *J* = 15.4, 6.7 Hz), 5.76 (1H, dt, *J* = 15.4, 5.8 Hz), 4.16 (2H, s), 3.56 (2H, d, *J* = 6.7 Hz), 1.30 (1H, t, *J* = 5.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 137.5 (C), 133.6 (C), 132.1 (C), 131.4 (CH), 130.6 (CH), 128.0 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 126.6 (CH), 126.0 (CH), 125.3 (CH), 63.6 (CH_2), 38.8 (CH_2); LRMS (EI) *m/z*: 198 (M^+), 167, 141.

(*E*)-2-(4-Chlorobut-2-en-1-yl)naphthalene (2c):

Allylic chloride **2c** was prepared similarly to the synthesis of **2d** from **4c**. To a cooled (0 ºC) solution of **3c** (128.8 mg, 0.650 mmol) and PPh_3 (188.6 mg, 0.719 mmol) in anhydrous CH_2Cl_2 (2.0 mL) and

anhydrous Et_2O (2.0 mL) was added hexachloroacetone (145 μL, 0.791 mmol) under argon atmosphere, and the mixture was stirred at 0 ºC for 12 h. After dilution with saturated aqueous $NaHCO_3$ solution, the organics was extracted with AcOEt. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 40:1) to give **2c** (148.3 mg, 96%) as a colorless liquid. IR (thin film, ν_{max}/cm^{-1}) 3051, 2954, 1601, 1506, 1248, 968, 855, 817, 747, 672; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.83–7.77 (3H, m), 7.61 (1H, s), 7.48–7.41 (2H, m), 7.31 (1H, d, *J* = 8.4 Hz), 6.01 (1H, dt, *J* = 15.1, 6.7 Hz), 5.73 (1H, dt, *J* = 15.1, 7.0 Hz), 4.08 (2H, d, *J* = 7.0 Hz), 3.56 (2H, d, *J* = 6.7 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 136.8 (C), 134.2 (CH), 133.6 (C), 132.2 (C), 128.1 (CH), 127.6 (CH), 127.5 (2C, CH), 127.2 (CH), 126.7 (CH), 126.0 (CH), 125.4 (CH), 45.0 (CH_2), 38.5 (CH_2); LRMS (EI) *m/z*: 216 (M^+), 181, 167, 141, 89.

Preparation of allylic chlorides 2e and allylic alcohol 4e.



1-(Naphthalen-1-yl)propan-2-one (6):

Ketone **6** was prepared according to the procedure reported by Tran[5] and the structure was confirmed by comparing the spectral data with the reported value.[6] 1-Naphthaleneacetic acid (2.170 g, 11.65 mmol) was dissolved in acetic anhydride (5.5 mL, 58 mmol) at room temperature, and the solution was stirred and purged with argon for 5 minutes. The reaction was initiated by the addition of *N*-methylimidazole (0.46 mL, 5.8 mmol), and the reaction was continuously purged with a slow flow of argon over the course of the reaction. After stirring at room temperature for 13 h, water was added to hydrolyze acetic

[5] K.-V. Tran and D. Bickar, *J. Org. Chem.*, 2006, **71**, 6640.
[6] K. Jozwiak, C. Khalid, M. J. Tanga, I. Berzetei-Gurske, L. Jimenez, J.A. Kozocas, A. Woo, W. Zhu, R.-P. Xiao, D. R. Abernethy and I. W. Wainer, *J. Med. Chem.*, 2007, **50**, 2903.

anhydride. The reaction mixture was extracted with AcOEt, and the combined organic layer was washed with saturated aqueous Na_2CO_3 solution and water, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 8:1) to give **6** (1.401 g, 65%) as a yellow-tinged oil.

2-Methyl-1-(naphthalen-1-yl)but-3-en-2-ol (4e):

To a cooled (–90 ºC) solution of **6** (168.6 mg, 0.9152 mmol) in anhydrous THF (5.2 mL) was added a solution of vinylmagnesium bromide (1.2 mL, 1 M, 1.2 mmol) in THF dropwise via syringe under argon atmosphere, and the lemon yellow solution was allowed to warm to room temperature over 3 h and stirred additional 3 h at room temperature. After dilution with saturated aqueous NH_4Cl solution, the organics was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 9:1) to give **4e** (118.6 mg, 61%) as a colorless oil. IR (thin film, ν_{max}/cm^{-1}) 3448 (br), 3047, 2976, 2930, 1596, 1511, 1016, 997, 923, 800, 781; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.16 (1H, d, *J* = 8.3 Hz), 7.84 (1H, d, *J* = 7.9 Hz), 7.76 (1H, d, *J* = 8.1 Hz), 7.53–7.40 (3H, m), 7.37 (1H, d, *J* = 6.8 Hz), 6.04 (1H, dd, *J* = 17.3, 10.8 Hz), 5.17 (1H, d, *J* = 17.3 Hz), 5.00 (1H, d, *J* = 10.8 Hz), 3.36 (1H, d, *J* = 13.9 Hz), 3.34 (1H, d, *J* = 13.9 Hz), 1.37 (1H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 144.9 (CH), 134.0 (C), 133.3 (C), 133.1 (C), 129.3 (CH), 128.6 (CH), 127.5 (CH), 125.7 (CH), 125.5 (CH), 125.11 (CH), 125.10 (CH), 111.8 (CH_2), 73.9 (C), 44.3 (CH_2), 27.9 (CH_3); LRMS (EI) *m/z*: 212 (M^+), 141, 71.

(*E*)-3-Methyl-4-(naphthalen-1-yl)but-2-en-1-ol (3e):

Allylic alcohol **3e** was prepared according to the procedure reported by Mirzabekova[7] and the structure was confirmed by comparing the spectral data with the reported value.[8] To a solution of **6** (1.075 g, 5.835 mmol) in anhydrous benzene (7.3 mL) was added triethyl phosphonoacetate (1.23 mL, 6.14 mmol) and ^{t}BuOK (790.0 mg, 7.040 mmol), and the resulting solution was stirred at room temperature for 43 h. The mixture was poured into a beaker containing crushed ice and the organics was extracted with AcOEt. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was roughly purified by short column chromatography on silica gel (hexane/AcOEt = 20:1) to yield an unpurified ester (974.7 mg) as a yellow oil. To a suspension of $LiAlH_4$ (190.0 mg, 5.006 mmol) in anhydrous Et_2O (15 mL) was added a solution of the unpurified ester

[7] N. S. Mirzabekova, N. E. Kuz'mina, O. I. Lukashov, N. A. Sokolova, S. N. Golosov, P. V. Kazakov, T. G. Perlova, V. V. Potapova, V. A. Kheinman and G. B. Ivanova, *Russ. J. Org. Chem.*, 2008, **44**, 1139.
[8] M. F. Mechelke and D. F. Wiemer, *J. Org. Chem.*, 1999, **64**, 4821.

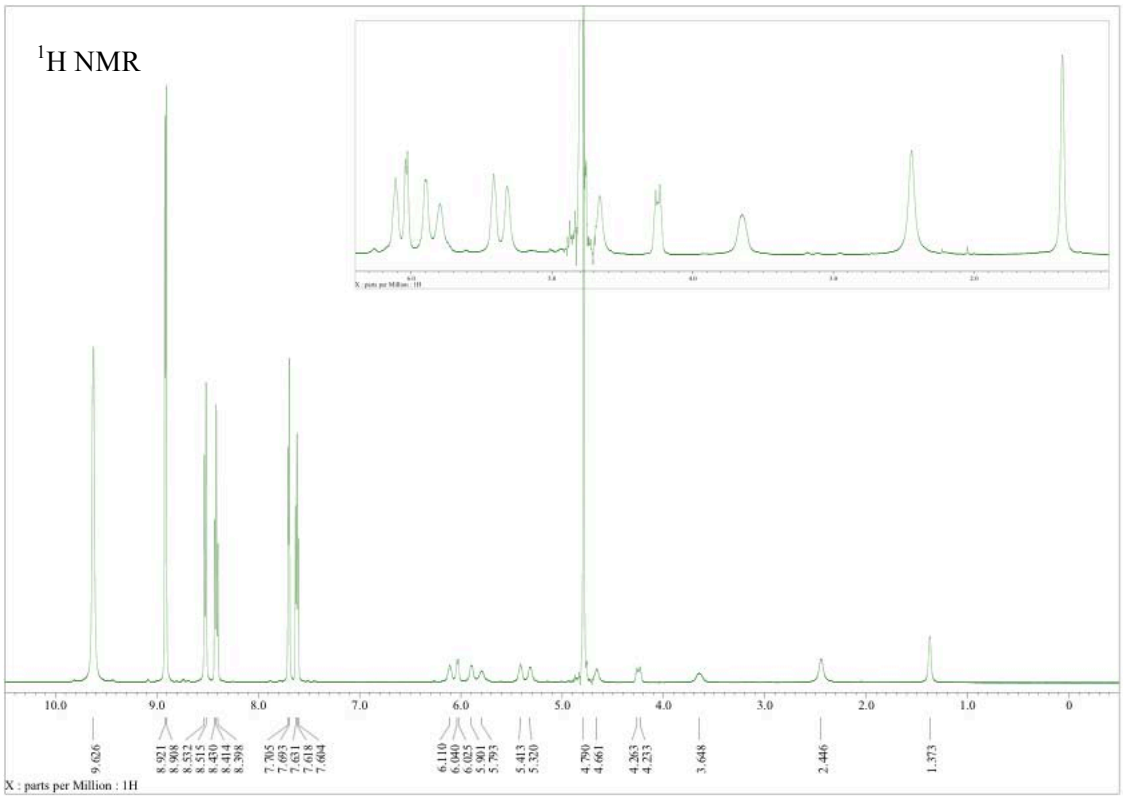
in anhydrous Et_2O slowly via syringe under argon atmosphere. After stirring at room temperature for 17 h, the mixture was cooled (0 ºC) and saturated aqueous Rochelle's salt solution (15 mL) was added dropwise by syringe. The mixture was stirred at room temperature over night and extracted with AcOEt. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 4:1) to give **3e** (568.0 mg, 70% over two steps) as a yellow-tinged oil.

(*E*)-1-(4-Chloro-2-methylbut-2-en-1-yl)naphthalene (2e):

Allylic chloride **2e** was prepared similarly to the synthesis of **2d** from **4c**. To a cooled (0 ºC) solution of **3e** (230.9 mg, 1.088 mmol) and PPh_3 (317.7 mg, 1.211 mmol) in anhydrous CH_2Cl_2 (3.0 mL) and anhydrous Et_2O (3.0 mL) was added hexachloroacetone (0.24 mL, 1.3 mmol) and stirred at 0 ºC for 8 h. After dilution with saturated aqueous $NaHCO_3$ solution, the organics was extracted with AcOEt. The combined organic layer was washed with water and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (hexane/AcOEt = 40:1) to give **2e** (168.0 mg, 67%) as a colorless liquid. IR (thin film, ν_{max}/cm^{-1}) 3045, 2976, 2913, 1663, 1595, 1510, 1254, 783, 665; ^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.96 (1H, d, *J* = 8.0 Hz), 7.85 (1H, d, *J* = 8.1 Hz), 7.75 (1H, d, *J* = 8.3 Hz), 7.51–7.45 (2H, m), 7.42 (1H, dd, *J* = 8.3, 6.7 Hz), 7.31 (1H, d, *J* = 6.7 Hz), 5.45 (1H, t, *J* = 8.0 Hz), 4.10 (2H, d, *J* = 8.0 Hz), 3.82 (2H, s), 1.77 (3H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 141.5 (C), 134.7 (C), 133.8 (C), 132.3 (C), 128.7 (CH), 127.3 (CH), 127.2 (CH), 125.9 (CH), 125.6 (CH), 125.5 (CH), 124.1 (CH), 122.3 (CH), 42.6 (CH_2), 40.9 (CH_2), 16.6 (CH_3); LRMS (EI) *m/z*: 230 (M^+), 215, 195, 181, 141, 89.

^{1}H, ^{13}C, and 2D NMR spectra

inclusion complex 1•(2a)$_2$



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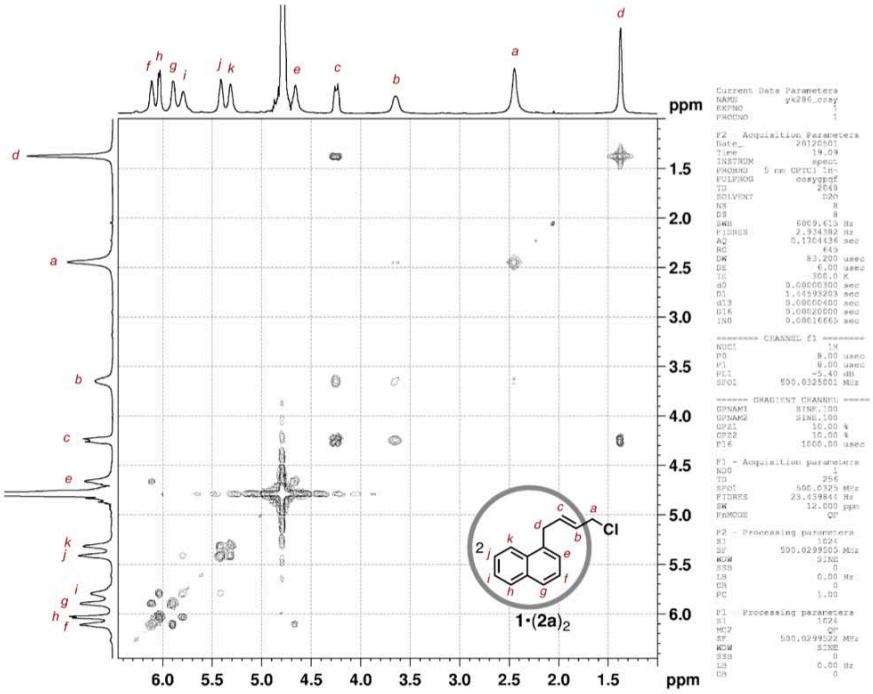

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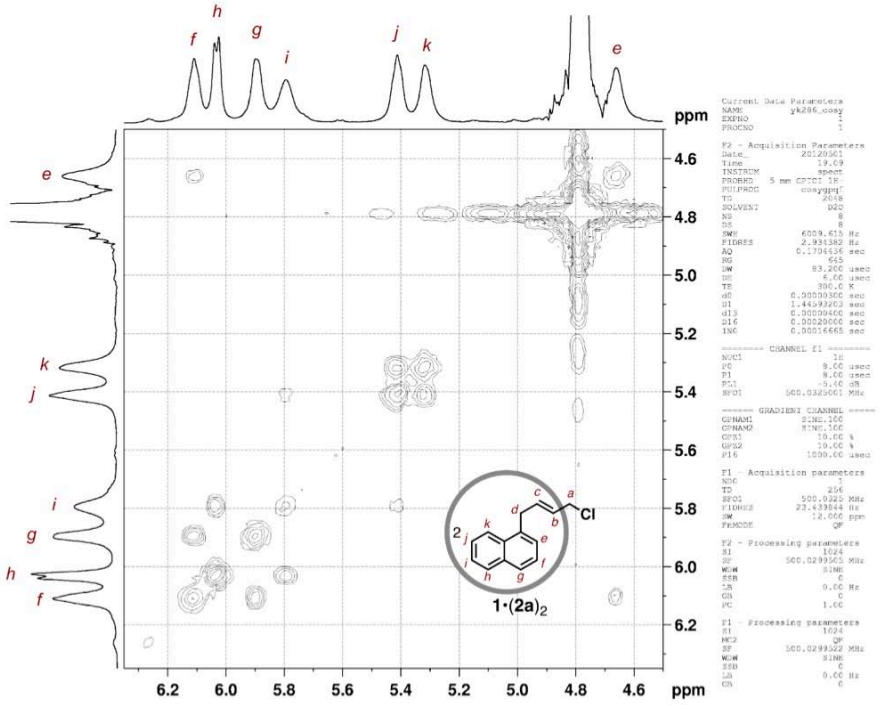

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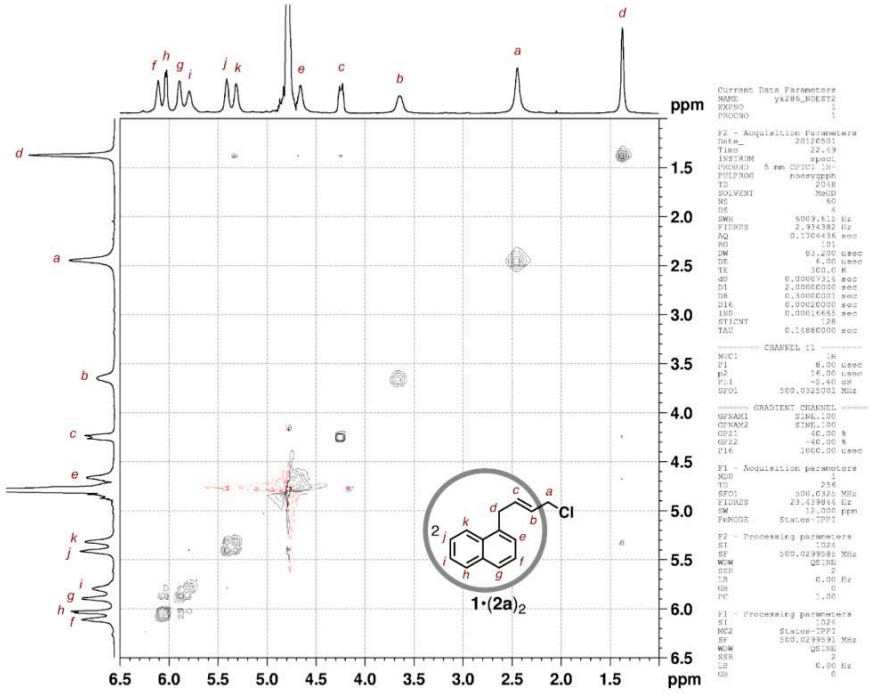

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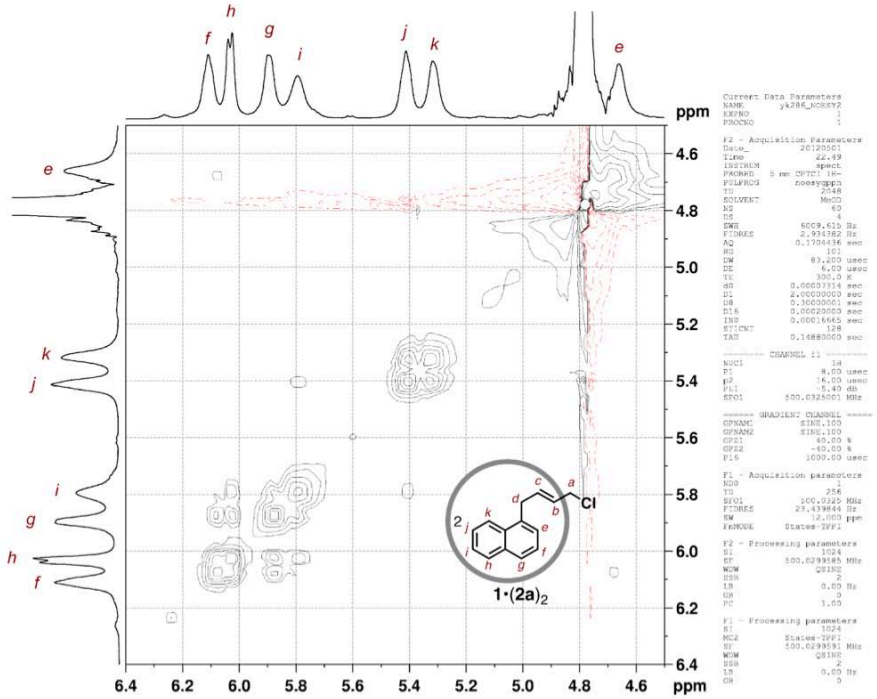
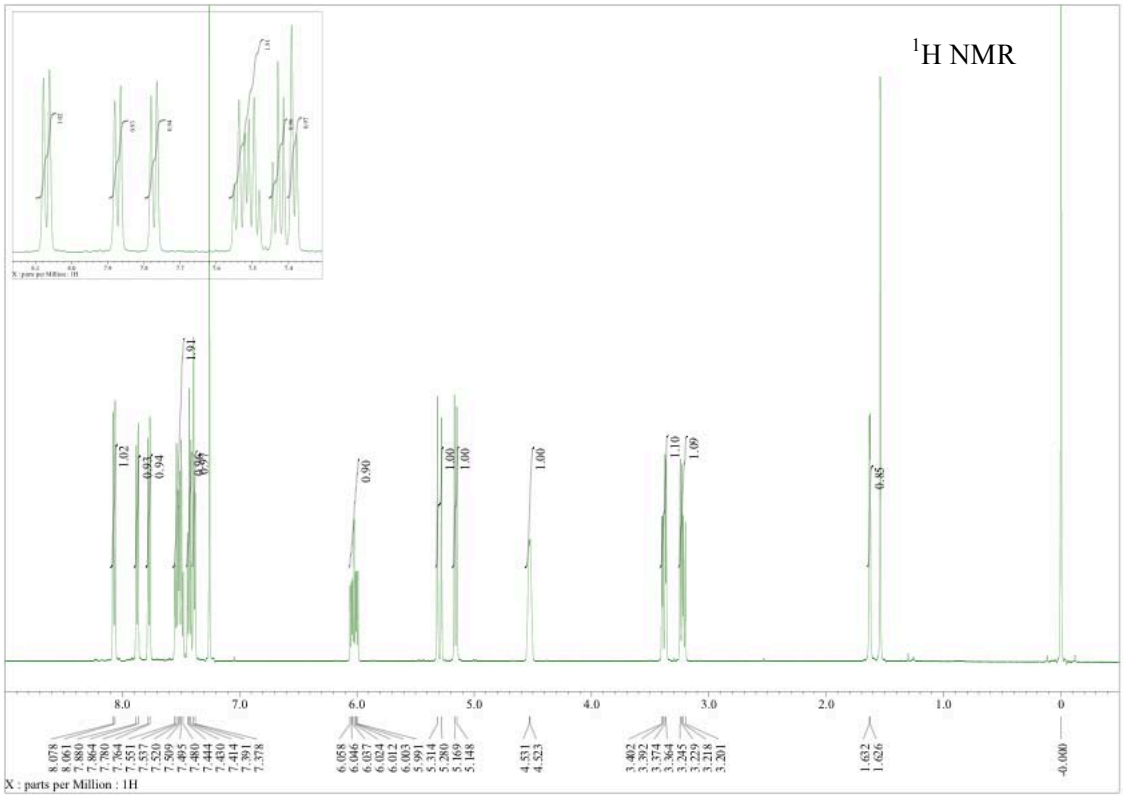
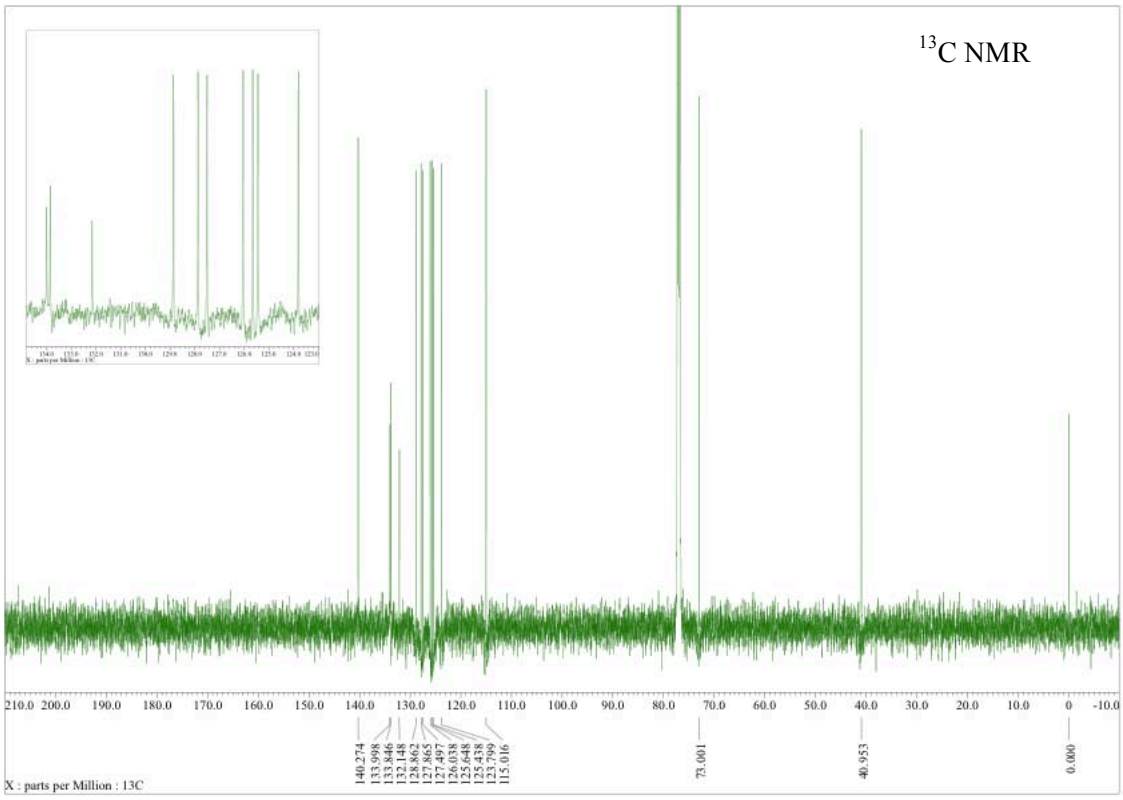
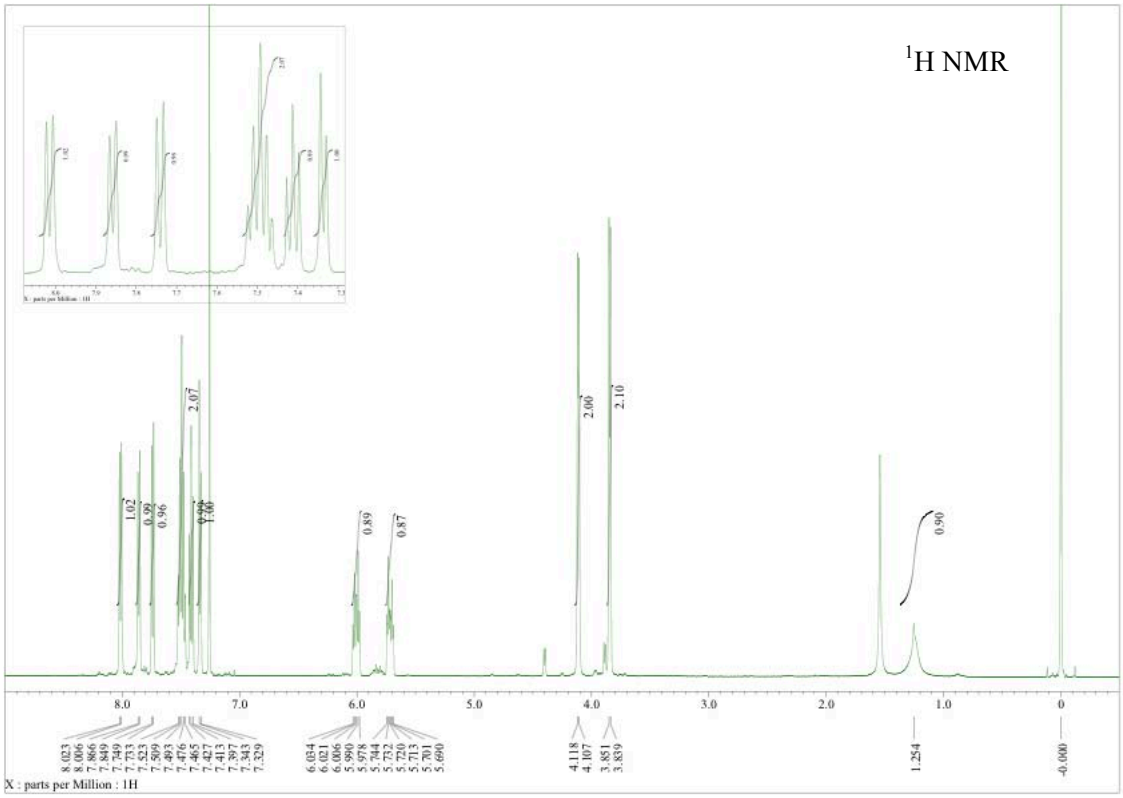


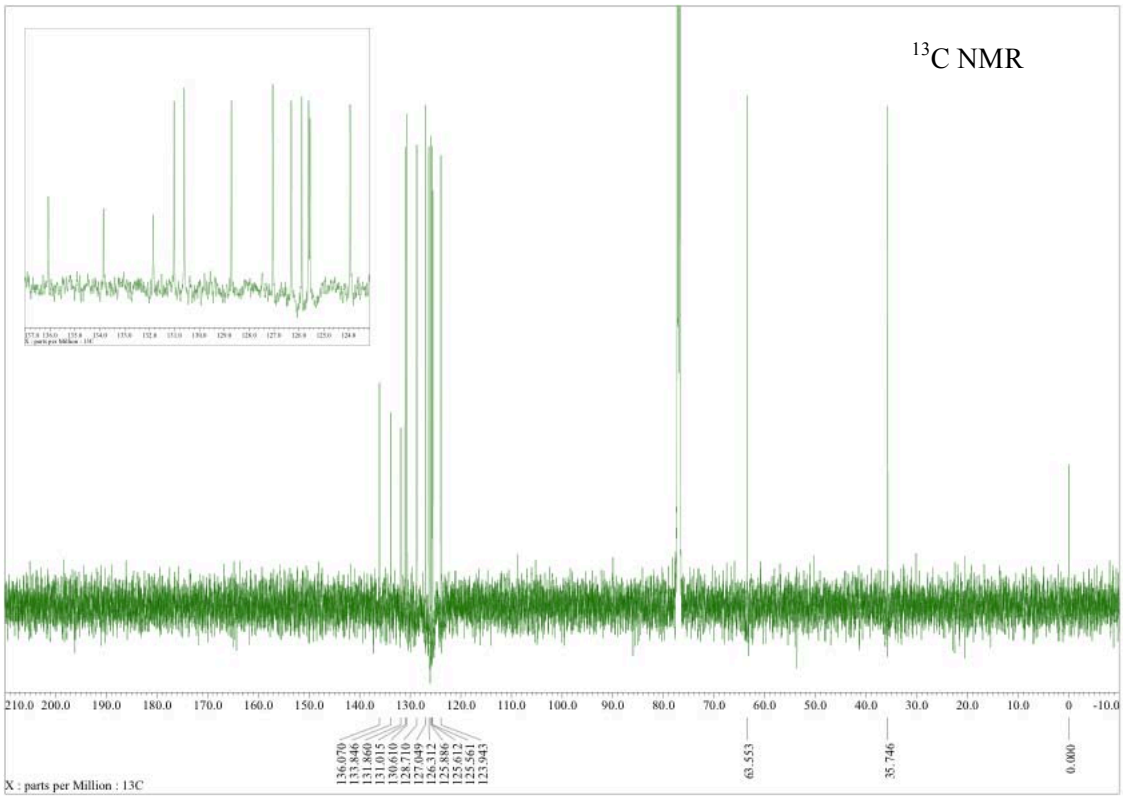
1-(Naphthalen-1-yl)but-3-en-2-ol (4a)





(*E*)-4-(Naphthalen-1-yl)but-2-en-1-ol (3a)





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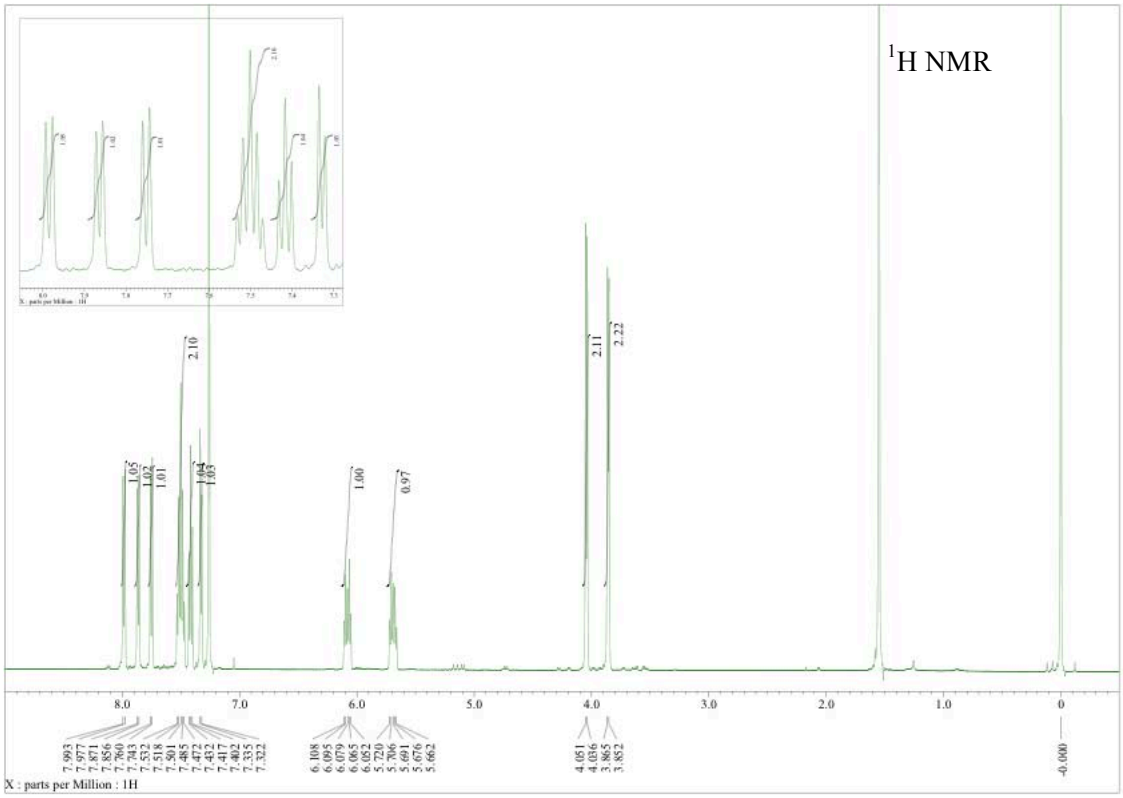
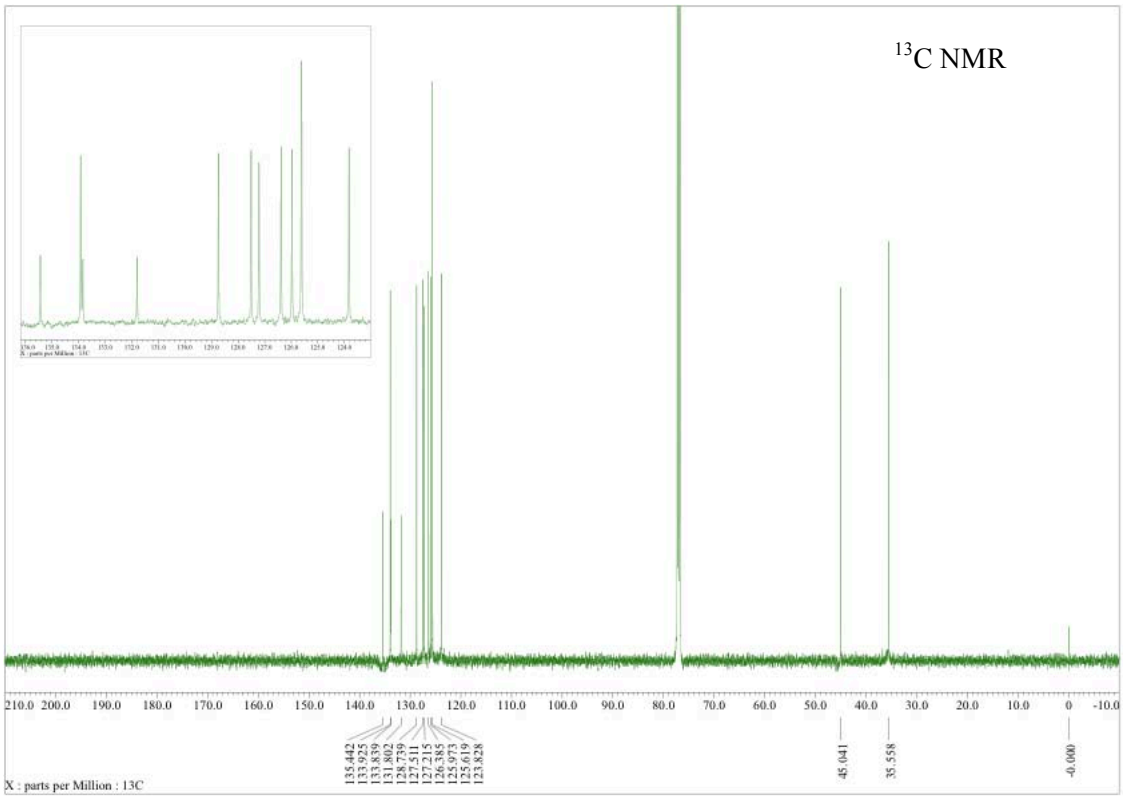
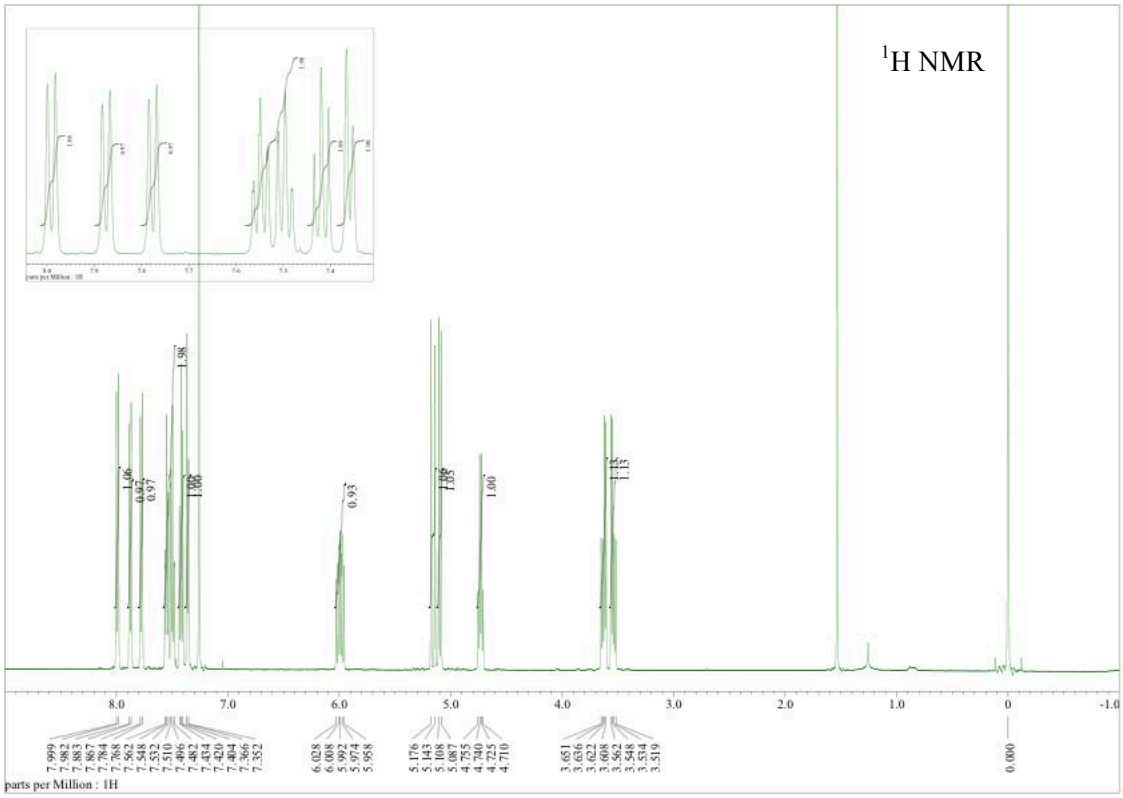
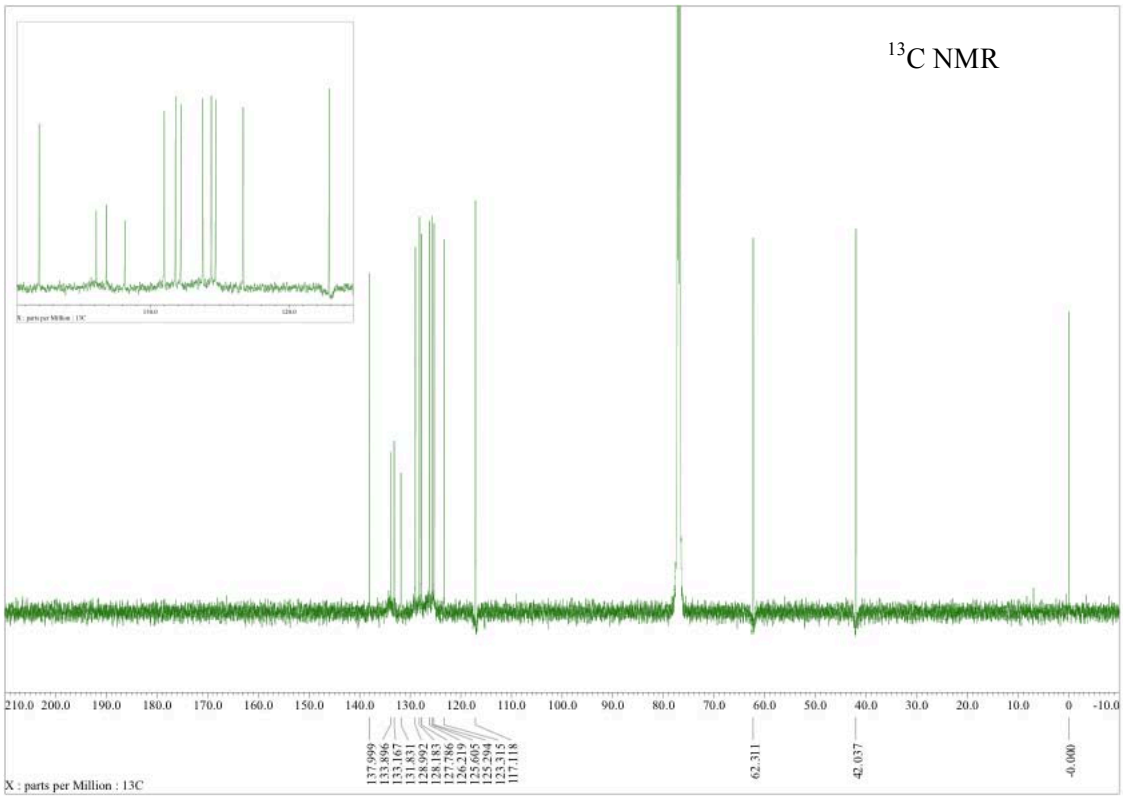


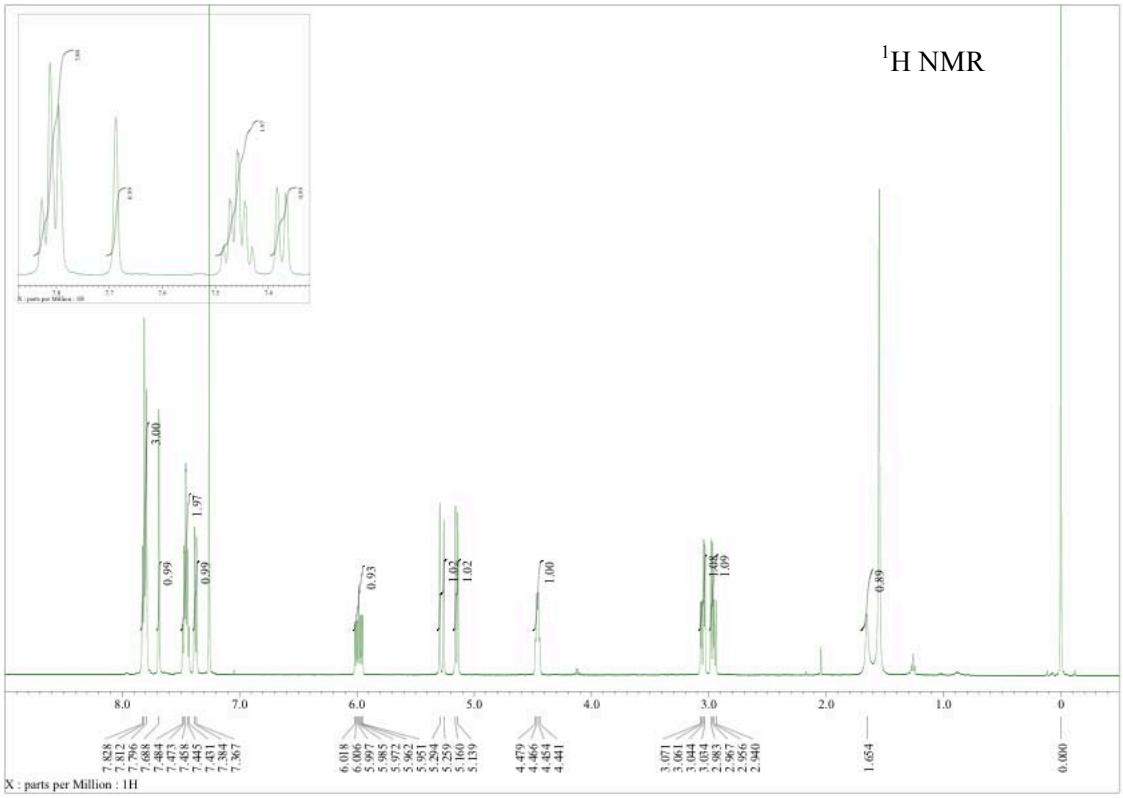


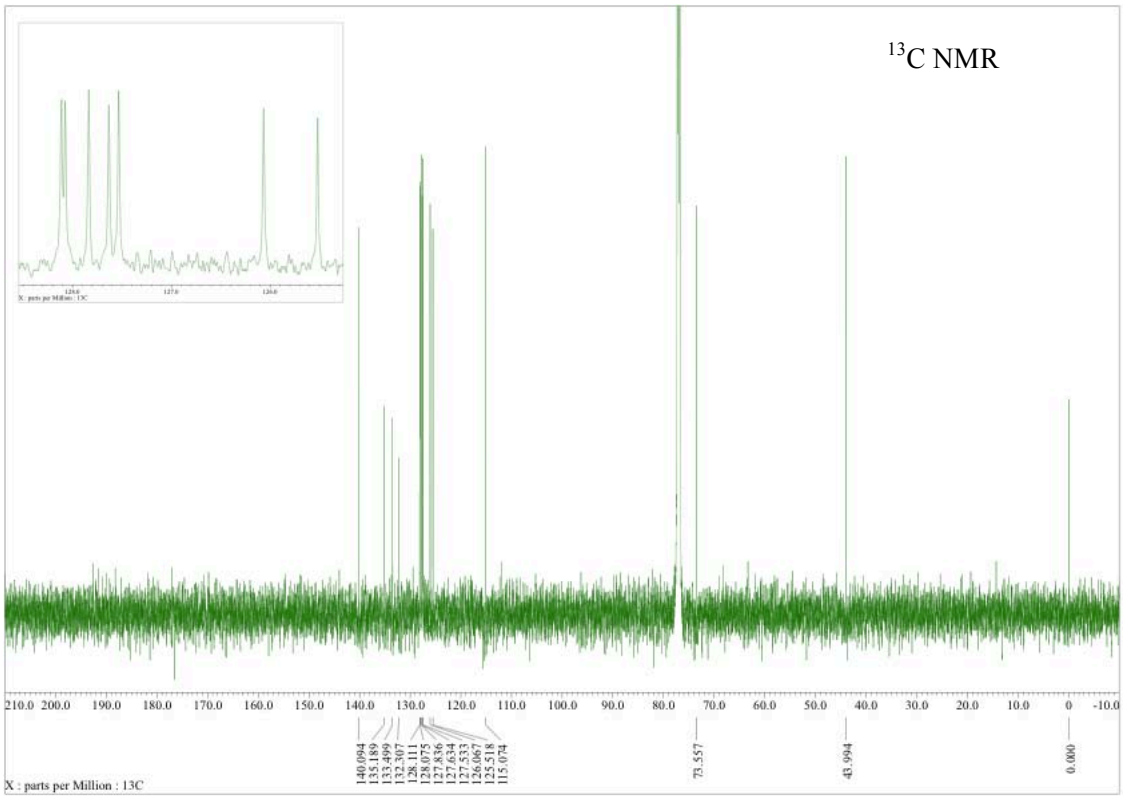
1-(2-Chlorobut-3-en-1-yl)naphthalene (2b)



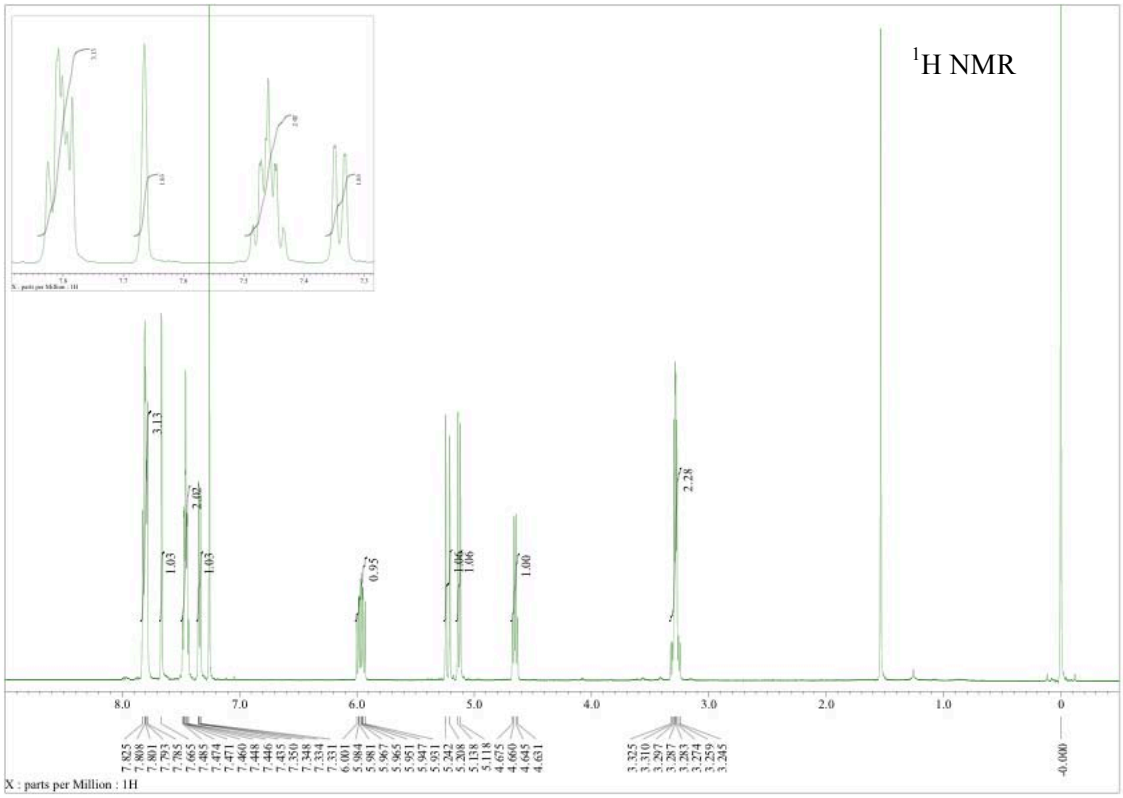


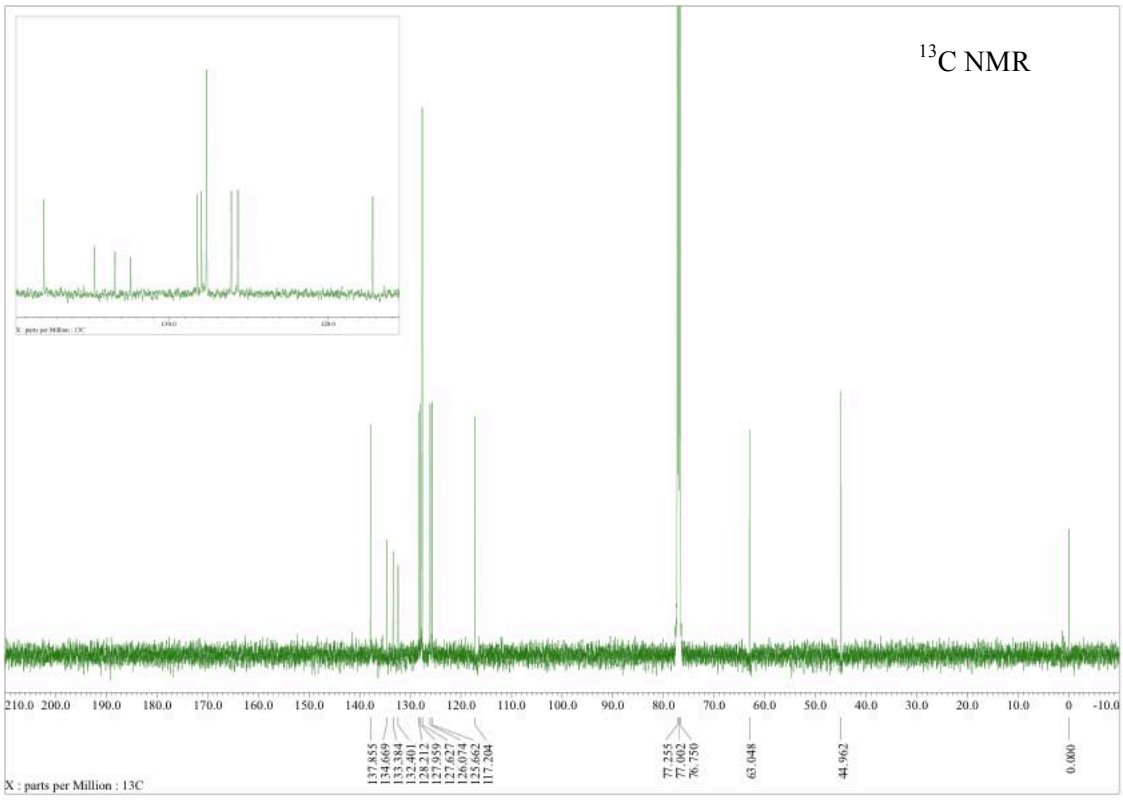
1-(Naphthalen-2-yl)but-3-en-2-ol (4c)



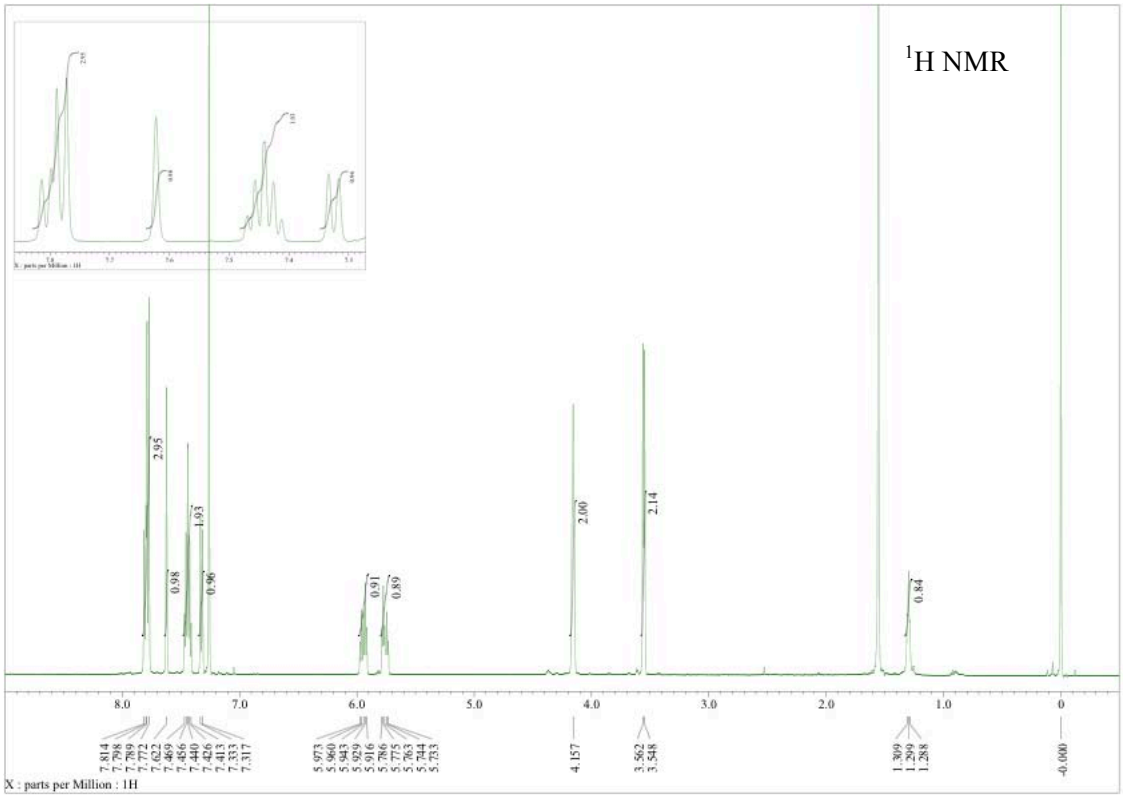


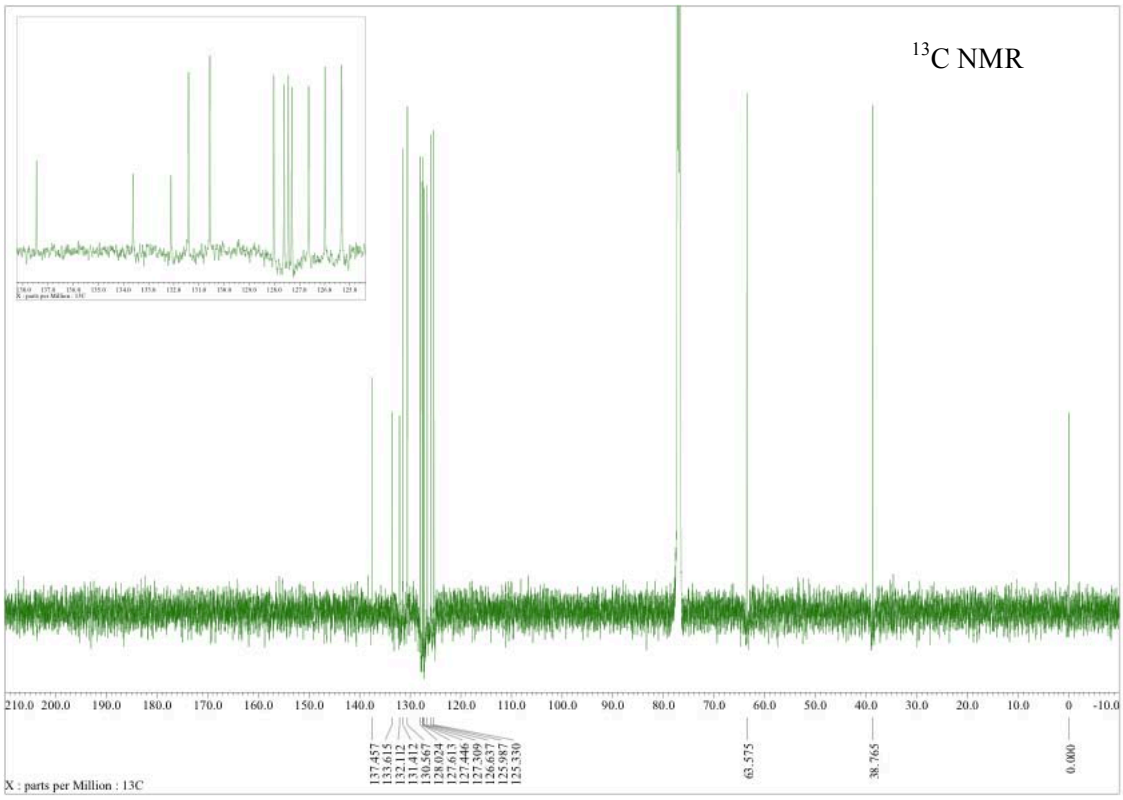
2-(2-Chlorobut-3-en-1-yl)naphthalene (2d)



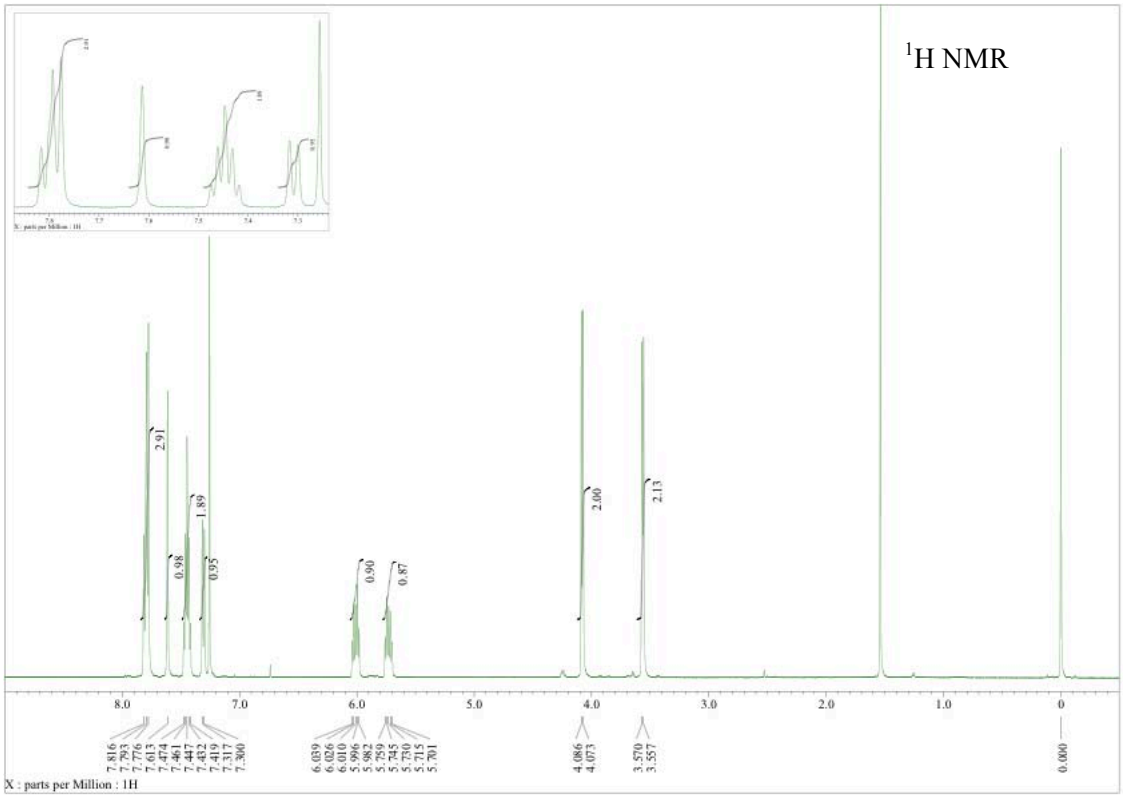


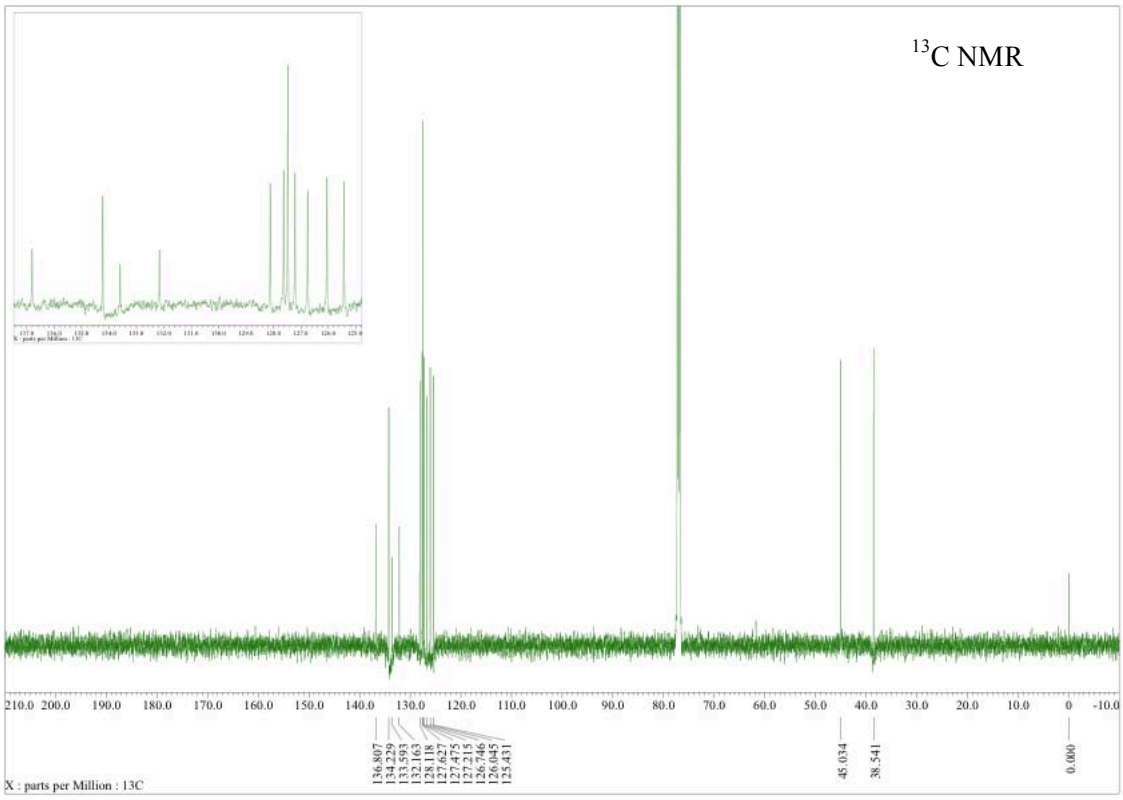
(*E*)-4-(Naphthalen-2-yl)but-2-en-1-ol (3c)



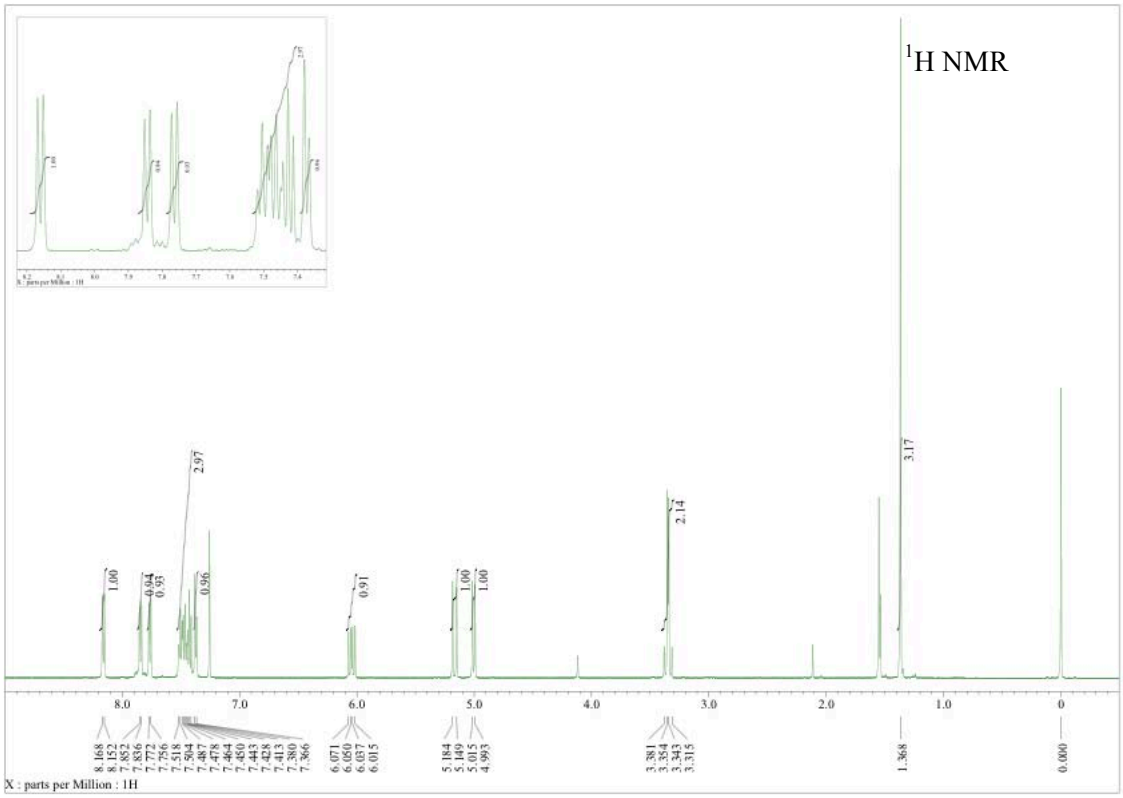


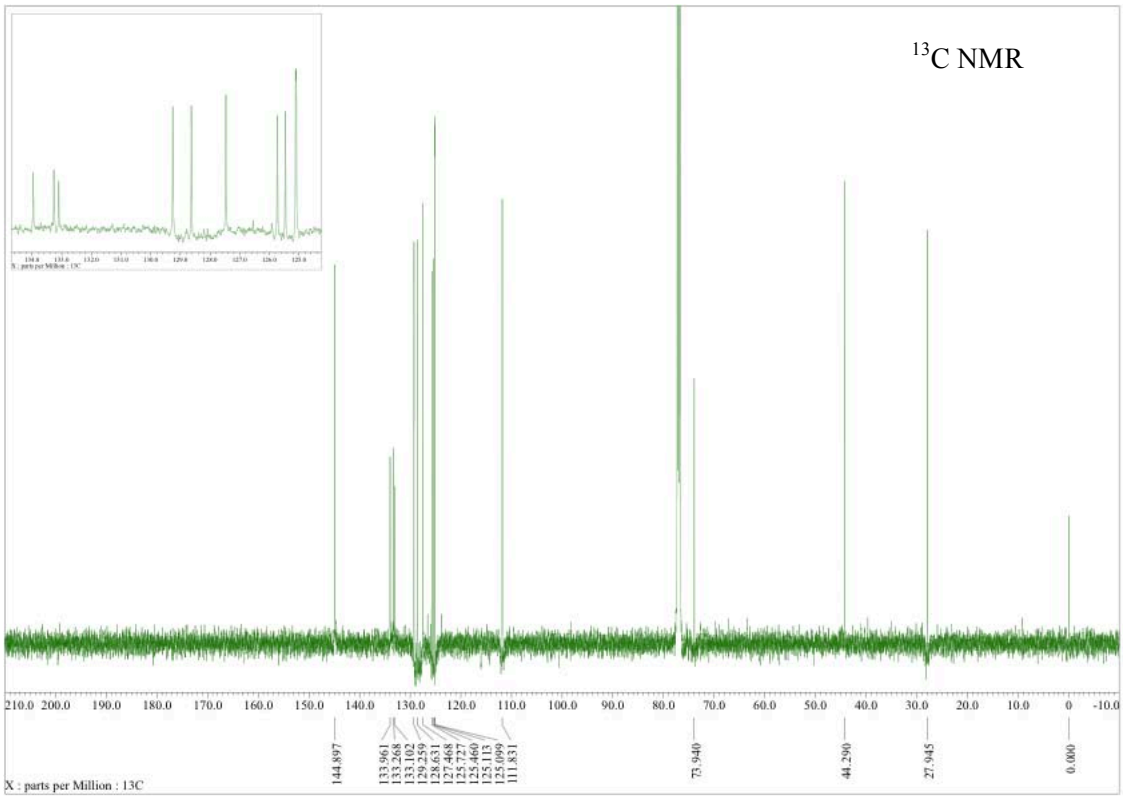
(*E*)-2-(4-Chlorobut-2-en-1-yl)naphthalene (2c)





2-Methyl-1-(naphthalen-1-yl)but-3-en-2-ol (4e)





(*E*)-1-(4-Chloro-2-methylbut-2-en-1-yl)naphthalene (2e)