Highly Selective Insertion of Arynes into a C(sp)–O(sp^3) Sigma Bond

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Org. Lett.

SUPPORTING INFORMATION

CONTENTS

1. Experimental details and spectroscopic data

General methods

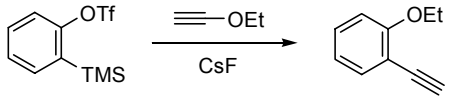
All reactions were carried out under argon using oven-dried glassware. Solvents were dried by distillation from a drying agent: THF from Na/benzophenone; CH_3CN and CH_2Cl_2 from CaH_2. *t*-$BuNH_2$ was distilled from CaH_2 prior to use. TLC was performed on Merck silica gel 60 F_{254}; chromatograms were visualized with UV light (254 and 360 nm). Flash column chromatography was performed on Merck silica gel 60 (ASTM 230-400 mesh). ^1H and ^{13}C NMR spectra were recorded at 250.13 and 62.83 MHz (Bruker DPX-250 instrument) or 300 and 75 MHz (Varian Mercury-300 instrument), respectively. Low-resolution electron impact mass spectra were determined at 70 eV on a HP-5988A instrument. High-resolution mass spectra (HRMS) and FAB (positive FAB in 3-nitrobenzyl alcohol) were obtained on a Micromass Autospec spectrometer.

Aryne precursors **1a-f** were prepared following a published procedure.[1] Ethoxyacetylene and Bu_4NF (TBAF) were used in solution in hexane (40 wt. %, 0.732 g / mL) and THF (1 M), respectively. Commercial reagents were purchased from ABCR GmbH, Aldrich Chemical Co., or Strem Chemicals Inc., and were used without further purification.

Reaction of arynes with ethoxyacetylene

General procedure. Ethoxyacetylene (2 equiv) and CsF (2 equiv) were added to a solution of an aryne precursor **1a-f** (1 equiv) in acetonitrile, and the solution was stirred vigorously for 12 h at room temperature. After addition of water the product was extracted twice with Et_2O and the combined organic phase was dried over anhydrous Na_2SO_4. The solvent was evaporated under reduce pressure and the crude product was purified by column chromatography (SiO_2) with *n*-hexane / Et_2O.

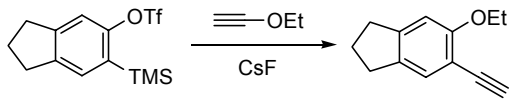
1-Ethoxy-2-ethynylbenzene (3a).[2]



1a **3a**

Compound **3a** (26 mg, 51%) was obtained from aryne precursor **1a** (104 mg, 0.35 mmol), ethoxyacetylene (0.17 mL, 0.70 mmol) and CsF (107 mg, 0.70 mmol) in acetonitrile (8 mL). ^1H NMR (250 MHz, $CDCl_3$), δ: 1.47 (t, *J* = 6.9 Hz, 3H), 3.28 (s, 1H), 4.13 (q, *J* = 6.9 Hz, 2H), 6.89 (dd, *J* = 7.9 Hz, 2H), 7.31 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.46 (dd, *J* = 7.4, 1.4 Hz, 1H) ppm. MS (EI), *m/z* (%): 146 (100), 118 (99).

5-Ethoxy-6-ethynyl-2,3-dihydro-1H-indene (3b).

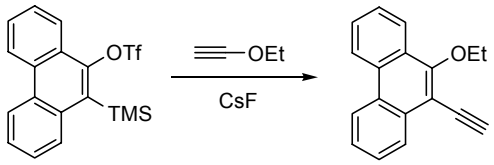


1b **3b**

Compound **3b** (40 mg, 73%) was obtained from aryne precursor **1b**[3] (100 mg, 0.295 mmol), ethoxyacetylene (0.14 mL, 0.59 mmol) and CsF (90 mg, 0.59 mmol) in acetonitrile (8 mL). ^1H NMR (300 MHz, $CDCl_3$), δ: 1.45 (t, *J* = 6.9 Hz, 3H), 2.07 (quin, *J* = 7.6 Hz, 2H), 2.83 (t, *J* = 9.9 Hz, 2H), 2.88 (t, *J* = 9.9 Hz, 2H), 3.22 (s, 1H), 4.10 (q, *J* = 6.9 Hz, 2H), 6.77 (s, 1H), 7.29 (s, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 14.8 (CH_3), 25.6 (CH_2), 31.8 (CH_2), 33.5 (CH_2), 64.5 (CH_2), 79.9 (CH), 81.1 (C), 108.6 (CH), 109.3 (C), 129.4 (CH), 135.8 (C), 147.0 (C), 159.2 (C) ppm. MS (EI), *m/z* (%): 186 (100), 158 (83). HRMS (EI) $C_{13}H_{14}O$, calculated: 186.1045, found: 186.1050.

[1] Peña, D.; Cobas, A.; Pérez, D.; Guitián, E. *Synthesis* **2002**, 1454.
[2] (a) Taber, D. F.; Bai, S.; Guo, P. *Tetrahedron Lett.* **2008**, *49*, 6904. (b) Stiles, M.; Burkhardt, U.; Haag, A. *J. Org. Chem.* **1962**, *27*, 4715.
[3] Yoshida, H.; Sugiura, S.; Kunai, A. *Org. Lett.* **2002**, *4*, 2767.

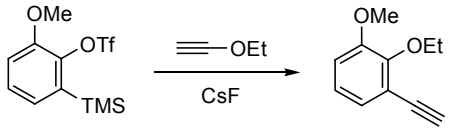
9-Ethoxy-10-ethynylphenanthrene (3c).



1c **3c**

Compound **3c** (90 mg, 67%) was obtained from aryne precursor **1c**[4] (217 mg, 0.54 mmol), ethoxyacetylene (0.26 mL, 1.09 mmol) and CsF (167 mg, 1.09 mmol) in acetonitrile (10 mL). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.60 (t, *J* = 7.0 Hz, 3H), 3.78 (s, 1H), 4.47 (q, *J* = 7.0 Hz, 2H), 7.54-7.80 (m, 4H), 8.32 (dd, *J* = 7.7, 1.4 Hz, 1H), 8.44 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.63 (d, *J* = 7.7 Hz, 1H), 8.65 (d, *J* = 7.8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 15.9 (CH_3), 70.4 (CH_2), 78.6 (C), 86.8 (CH), 108.3 (C), 122.5 (CH), 122.7 (CH), 123.2 (CH), 125.9 (CH), 126.1 (CH), 126.2 (C), 126.8 (CH), 127.3 (CH), 127.5 (C), 127.8 (C), 128.0 (CH), 131.8 (C), 158.0 (C) ppm. MS (EI), *m/z* (%): 246 (100). HRMS (EI), $C_{18}H_{14}O$, calculated: 246.1045, found: 246.1045.

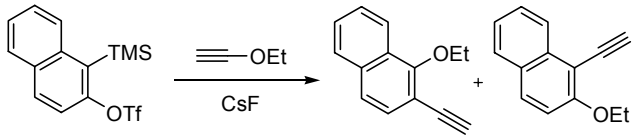
2-Ethoxy-1-ethynyl-3-methoxybenzene (3d).



1d **3d**

Compound **3d** (30 mg, 54%) was obtained from aryne precursor **1d** (109 mg, 0.35 mmol), ethoxyacetylene (0.17 mL, 0.70 mmol) and CsF (107 mg, 0.70 mmol) in acetonitrile (8 mL). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.40 (t, *J* = 7.0 Hz, 3H), 3.23 (s, 1H), 3.84 (s, 3H), 4.16 (q, *J* = 7.0 Hz, 2H), 6.90 (dd, *J* = 8.1, 1.8 Hz, 1H), 6.97 (dd, *J* = 7.6 Hz, 1H), 7.05 (dd, *J* = 7.6, 1.8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 15.6 (CH_3), 55.9 (CH_3), 69.4 (CH_2), 80.0 (C), 80.8 (CH), 113.3 (CH), 117.3 (C), 123.6 (CH), 125.4 (CH), 150.1 (C), 152.9 (C) ppm. MS (CI), *m/z* (%): 177 (M^++1, 100). HRMS (EI), $C_{11}H_{12}O_2$, calculated: 176.0837, found: 176.0839.

1-Ethoxy-2-ethynylnaphthalene (3e) and 2-ethoxy-1-ethynylnaphthalene (3e').

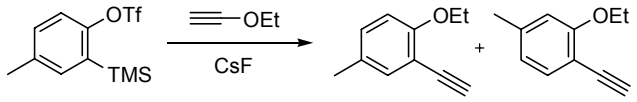


1e **3e** **3e'**

A mixture of compounds **3e** and **3e'** (46 mg, 43%, ratio 7:3) was obtained from aryne precursor **1e**[4] (188 mg, 0.54 mmol), ethoxyacetylene (0.26 mL, 1.08 mmol) and CsF (167 mg, 1.08 mmol) in acetonitrile (10 mL). Data for **3e**: ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.56 (t, *J* = 7.0 Hz, 3H), 3.42 (s, 1H), 4.43 (q, *J* = 7.0 Hz, 2H), 7.42-7.63 (m, 4H), 7.81 (m, 1H), 8.23 (m, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 7.0 (CH_3), 70.3 (CH_2), 80.9 (C), 82.0 (CH), 110.4 (C), 122.5 (CH), 123.1 (CH), 126.2 (CH), 127.1 (CH), 127.7 (CH), 128.2 (C), 129.5 (CH), 134.6 (C), 158.3 (C) ppm. MS (EI), *m/z* (%): 196 (68), 139 (100). HRMS (CI), (M^++1), $C_{14}H_{13}O$, calculated: 197.0966, found: 197.0965. Data for **3e'**: ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.52 (t, *J* = 7.0 Hz, 3H), 3.76 (s, 1H), 4.28 (q, *J* = 6.9 Hz, 2H), 7.21 (d, *J* = 9.1 Hz, 1H), 7.40 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.57 (ddd, *J* = 8.3, 6.8, 1.3 Hz, 1H), 7.79 (dd, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 8.32 (dd, *J* = 8.4, 1.2, Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 14.9 (CH_3), 65.1 (CH_2), 78.2 (C), 86.3 (CH), 105.6 (C), 114.0 (CH), 124.1 (CH), 125.0 (CH), 127.3 (CH), 127.9 (CH), 128.3 (C), 130.4 (CH), 134.7 (C), 159.2 (C) ppm. MS (CI), *m/z* (%): 197 (M^++1, 100). HRMS (CI), (M^++1), $C_{14}H_{13}O$, calculated: 197.0966, found: 197.0965.

[4] Peña, D.; Pérez, D.; Guitián, E.; Castedo, L. *Org. Lett.* **1999**, *1*, 1555.

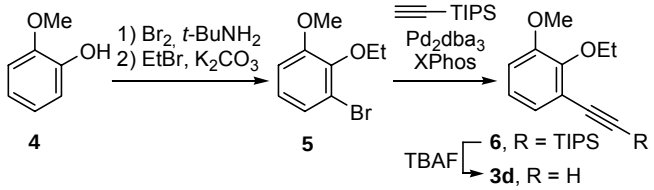
2-Ethoxy-1-ethynyl-4-methylbenzene (3f) and 1-ethoxy-2-ethynyl-4-methylbenzene (3f').



1f **3f** **3f'**

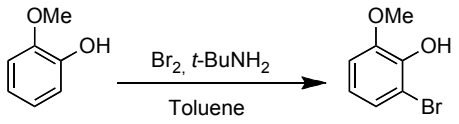
A mixture of compounds **3f** and **3f'** (30 mg, 54%, ratio 1:1) was obtained from aryne precursor **1f**[5] (169 mg, 0.54 mmol), ethoxyacetylene (0.26 mL, 1.08 mmol) and CsF (167 mg, 1.08 mmol) in acetonitrile (10 mL). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.44 (t, *J* = 7.0 Hz, 3H), 1.46 (t, *J* = 7.0 Hz, 3H), 2.26 (s, 3H), 2.34 (s, 3H), 3.24 (s, 1H), 3.25 (s, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 4.11 (q, *J* = 7.0 Hz, 2H), 6.69-6.73 (m, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 7.09 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.27 (d, *J* = 2.2 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 14.7 ($2CH_3$), 20.1 (CH_3), 21.8 (CH_3), 64.1 (CH_2), 64.4 (CH_2), 80.2 (CH), 80.33(C), 80.34 (C), 80.6 (CH), 108.5 (C), 111.3 (C), 112.0 (CH), 112.8 (CH), 121.1 (CH), 129.6 (C), 130.6 (CH), 133.8 (CH), 134.4 (CH), 140.6 (C), 157.9 (C), 159.9 (C) ppm. MS (EI), *m/z* (%): 160 (100). HRMS (CI), (M^++1), $C_{11}H_{13}O$, calculated: 161.0966, found: 161.0969.

Alternative synthesis of compound 3d



4 **5**

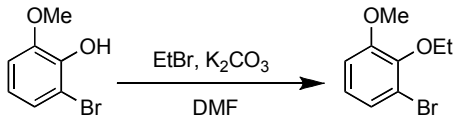
2-Bromo-6-methoxyphenol (4')[6]



4 **4'**

Br_2 (258 mg, 1.61 mmol) was added dropwise to a solution of *tert*-butylamine (338 μL, 3.22 mmol) in toluene (3.0 mL) at -30 ºC. After being stirred for 0.5 h, the reaction mixture was cooled to -60 ºC. A solution of 2-methoxyphenol (**4**, 200 mg, 1.61 mmol) in CH_2Cl_2 (0.2 mL) was added dropwise to the reaction mixture, and the mixture was warmed to rt over a period of 5 h. The reaction mixture was treated with 10% $Na_2S_2O_3$, washed with brine, and the organic phase was dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was separated by column chromatography on silica gel with 40% CH_2Cl_2 in hexane to afford **4'** (250 mg, 76 %) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.88 (s, 3H), 5.96 (s, 1H), 6.82-6.70 (m, 2H), 7.09 (dd, *J* = 7.9, 1.6 Hz, 1H) ppm.

1-Bromo-2-ethoxy-3-methoxybenzene (5)



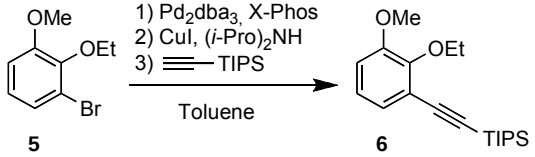
4' **5**

A solution of 2-bromo-6-methoxyphenol (**4'**, 766 mg, 3.79 mmol), K_2CO_3 (2.09 g, 15.2 mmol) and EtBr (826 mg, 7.58 mmol) in DMF (8.5 mL) was stirred at 90ºC for 12 h. The mixture was filter over Al_2O_3 with CH_2Cl_2, washed with water and the organic phase was dried over Na_2SO_4. The solvent was evaporated under reduced pressure and the residue was purified by column chromatography (SiO_2, 30% CH_2Cl_2 in hexane) to afford **5** (633 mg, 73 %) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.40 (t,

[5] Yoshikawa, E.; Radhakrishnan, K. V.; Yamamoto, Y. *Tetrahedron Lett.* **2000**, *41*, 729.
[6] Ishizaki, M.; Ozaki, K.; Kanematsu, A.; Isoda, T.; Hoshino, O. *J. Org. Chem.* **1993**, *58*, 3877.

J = 7.0 Hz, 3H), 3.80 (s, 3H), 4.05 (q, *J* = 7.0 Hz, 2H), 6.91-6.77 (m, 2H), 7.09 (dd, *J* = 7.8, 1.5 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 15.3 (CH_3), 55.7 (CH_3), 68.7 (CH_2), 111.3 (CH), 117.9 (C), 124.4 (CH), 124.5 (CH), 145.4 (C), 153.7 (C) ppm. MS (EI), *m/z* (%): 232 (48), 230 (49), 204 (98), 202 (100).

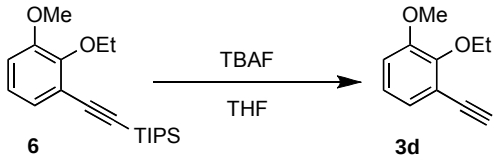
(2-(2-Ethoxy-3-methoxyphenyl)ethynyl)triisopropylsilane (6)



5 **6**

A mixture of 1-bromo-2-ethoxy-3-methoxybenzene (**5**, 65 mg, 0.28 mmol), tris(dibenzylideneacetone)dipalladium (15 mg, 0.014 mmol) and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos, 27 mg, 0.056 mmol) in toluene (2.4 mL) was stirred for 5 min at room temperature. CuI (3.0 mg, 0.015 mmol) and diisopropylamine (183 μL, 1.29 mmol) was added and the reaction mixture was stirred 10 min. Then, ethynyltriisopropilsilane (64 μL, 0.28 mmol) was added dropwise and the mixture was refluxed for 12 h. The solvent was evaporated under reduced pressure, and the residue was separated by column chromatography on silica gel with 40% CH_2Cl_2 in hexane to afford **6** (75 mg, 80 %) as a colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.15 (s, 21H), 1.38 (t, *J* = 7.0 Hz, 3H), 3.83 (s, 3H), 4.17 (q, *J* = 7.0 Hz, 2H), 6.86 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.95 (t, *J* = 7.9 Hz, 1H), 7.05 (dd, *J* = 7.6, 1.7 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 11.3 (3 CH), 15.5 (CH_3), 18.6 (6 CH_3), 55.9 (CH_3), 69.0 (CH_2), 94.6 (C), 103.1 (C), 112.9 (CH), 118.7 (C), 123.4 (CH), 125.6 (CH), 149.8 (C), 152.9 (C) ppm. MS (EI), *m/z* (%): 332 (50), 289 (100). HRMS (CI), (M^++1), $C_{20}H_{33}O_2Si$, calculated: 333.2250, found: 333.2249.

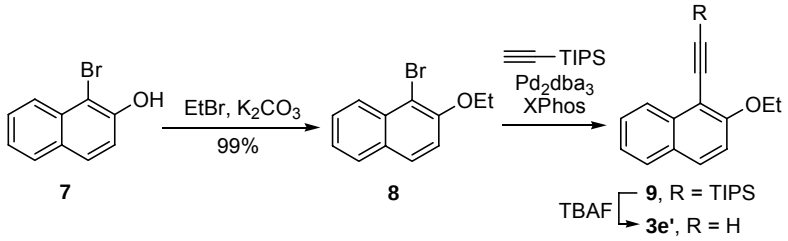
2-Ethoxy-1-ethynyl-3-methoxybenzene (3d)



6 **3d**

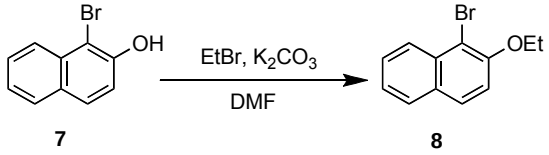
To a 10 mL round bottom flask with a stirring bar was added (2-(2-ethoxy-3-methoxyphenyl)ethynyl)triisopropylsilane (**6**, 26 mg, 0.080 mmol) and THF (1.5 mL). The solution was degassed 5 min with argon, followed by the addition of TBAF (1M in THF, 117 μL, 0.12 mmol). The reaction was stirred at room temperature for 1 h. The solution was diluted with Et_2O, washed with water and brine and the organic phase was dried over Na_2SO_4. The residue was purified by column chromatography (SiO_2, 30% CH_2Cl_2 in hexane) to afford **3d** (11 mg, 80 %) as a colourless oil. For data see page S3.

Alternative synthesis of compound 3e'



7 **8**

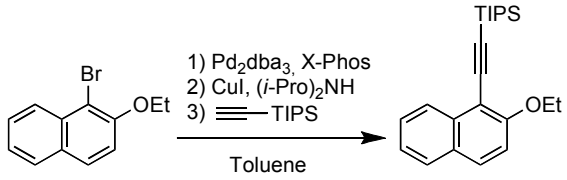
1-Bromo-2-ethoxynaphthalene (8)[7]



7 **8**

In a round bottom flask of 25 mL a solution of 1-bromo-2-naphthol (**7**, 200 mg, 0.90 mmol), K_2CO_3 (495 mg, 3.60 mmol) and EtBr (135 μL, 1.80 mmol) in DMF (2.0 mL) was stirred at 90ºC for 12 h. The mixture was filtered over Al_2O_3 with CH_2Cl_2, washed with water and the organic phase was dried over Na_2SO_4. The solvent was evaporated under reduced pressure. The residue was purified by column chromatography (SiO_2, 30% CH_2Cl_2 in hexane) to afford **8** (224 mg, 99 %) as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.54 (t, *J* = 6.9 Hz, 3H), 4.23 (q, *J* = 6.9 Hz, 2H), 7.22 (d, *J* = 8.9 Hz, 1H), 7.42 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.59 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 8.29 (d, *J* = 8.6 Hz, 1H) ppm. MS (CI), *m/z* (%): 252 (44), 250 (43), 172 (100).

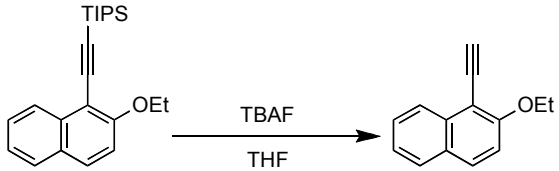
((2-Ethoxynaphthalen-1-yl)ethynyl)triisopropylsilane (9)



8 **9**

A mixture of 1-bromo-2-ethoxynaphthalene (**8**, 220 mg, 0.88 mmol), tris(dibenzylideneacetone)dipalladium (45.0 mg, 0.044 mmol) and 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (X-Phos, 83.0 mg, 0.170 mmol) in toluene (7.5 mL) was stirred for 5 min at room temperature. CuI (8.50 mg, 0.044 mmol) and diisopropylamine (570 μL, 4.00 mmol) were added and the reaction mixture was stirred 10 min. Then, ethynyltriisopropilsilane (196 μL, 0.88 mmol) was added dropwise and the mixture was refluxed for 12 h. The solvent was evaporated under reduced pressure, and the residue was separated by column chromatography on silica gel with 40% CH_2Cl_2 in hexane to afford **9** (296 mg, 94 %) as a brown oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 1.25 (s, 21H), 1.50 (t, *J* = 6.9 Hz, 3H), 4.24 (q, *J* = 6.9 Hz, 2H), 7.20 (d, *J* = 9.1 Hz, 1H), 7.38 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.56 (ddd, *J* = 8.2, 6.8, 1.1 Hz, 1H), 7.77 (d, *J* = 8.7 Hz, 2H), 8.35 (d, *J* = 8.3 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$), δ: 11.4 (3CH), 15.0 (CH), 18.8 ($6CH_3$), 65.1 (CH_2), 100.4 (C), 101.1 (C), 107.3 (C), 114.2 (CH), 124.0 (CH), 125.3 (CH), 127.1 (CH), 127.9 (CH), 128.4 (C), 129.8 (CH), 134.7 (C), 159.3 (C) ppm. MS (EI), *m/z* (%): 352 (81), 309 (100). HRMS (CI), (M^++1), $C_{23}H_{33}OSi$, calculated: 353.2301, found: 353.2317.

2-Ethoxy-1-ethynylnaphthalene (3e')



9 **3e'**

To a 100 mL round bottom flask with a stirring bar was added ((2-ethoxynaphthalen-1-yl)ethynyl)triisopropylsilane (**9**, 290 mg, 0.82 mmol) and THF (16 mL). The solution was degassed 5 min with argon, followed by the addition of TBAF (1M in THF, 1.25 mL, 1.25 mmol). The reaction was stirred at room temperature for 1 h. The solution was diluted with Et_2O, washed with water and brine and

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the organic phase was dried over Na_2SO_4. The residue was purified by column chromatography (SiO_2, 30% CH_2Cl_2 in hexane) to afford **3e'** (130 mg, 80 %) as a yellow solid. For data see page S3.

2. Computational calculations

All DFT calculations were performed with GAUSSIAN03.[9] Structures were first optimized at B3LYP/6-31G(d) level of theory.[10,11] Frequency analyses were used to characterize each stationary point. Intrinsic reaction coordinate (IRC) calculations were also performed at this level to establish the correct connections between the reaction intermediates.[12,13] These structures were reoptimized using the 6-31++G(d,p) basis set and frequency calculations were performed at this level to obtain the thermal and entropic contributions to the free energy.

Cartesian Coordinates, absolute electronic energies, enthalpies and free energies at 289 K in Hartrees/particle for the b3lyp/6-31++G(d,p) calculated geometries,

TS1a	E=-462,06891	H=-461,891942	G=-461,940415
C	-3.04083400	0.22747600	0.28867100
C	-2.15873800	1.29811700	0.50925100
C	-0.78301800	1.17053100	0.21894700
C	-0.48050500	-0.03286600	-0.27213200
C	-1.22800300	-1.15679000	-0.56205500
C	-2.58572100	-0.98993600	-0.24353200
H	-4.09685700	0.33681300	0.52605800
H	-2.55839200	2.22870800	0.91094100
H	-0.85459900	-2.07837400	-0.99855100
H	-3.27957100	-1.80619700	-0.42148100
O	1.10565300	-0.03431300	-0.62534000
C	1.59319800	1.21350200	-0.28240100
C	1.98570100	-1.21270100	-0.31045700
H	2.92644400	-0.98322700	-0.80958300
H	1.48313300	-2.03164400	-0.82507800
C	2.12655800	-1.43536100	1.17860400
H	1.15754800	-1.62447000	1.64662400
H	2.76569600	-2.31109200	1.33723600
H	2.59528800	-0.57518300	1.66212100
C	2.54663800	1.96841600	-0.19473000
H	3.16442900	2.81684300	-0.00656800

TS2a	E= -462,104841	H= -461,927420	G= -461,979850
C	3.40405300	0.54461800	-0.48364300
C	2.90270900	-0.73205400	-0.79767400
C	1.66000500	-1.17292900	-0.30069100
C	1.06898900	-0.20580000	0.49006700
C	1.45167600	0.97173200	0.81211600
C	2.68907600	1.43471900	0.33965800

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H	4.36656200	0.84808300	-0.89033700
H	3.48250500	-1.39721800	-1.43267200
H	1.25472200	-2.15486200	-0.51999500
H	3.09465800	2.41711400	0.57088300
C	-1.67429200	-0.95857600	0.54201500
C	-0.78635200	-0.98707100	1.39440200
H	-0.46135800	-1.13512700	2.40148100
O	-2.41974700	-0.87015500	-0.50444700
C	-2.77673500	0.49802500	-0.94158100
C	-3.80280700	1.12293800	-0.01793600
H	-3.16559700	0.33939600	-1.94820300
H	-1.84958800	1.07447400	-0.99069100
H	-4.06171200	2.11949900	-0.39165700
H	-4.71527000	0.52101200	0.02153600
H	-3.40487400	1.23525400	0.99483200

IVa E= -462,201822 H= -462,021528 G= -462,069357

C	-2.14330800	-1.59596700	0.00006800
C	-0.74389600	-1.51834300	-0.00069900
C	-0.14325500	-0.26014000	-0.00081900
C	-0.91594700	0.91917500	-0.00007400
C	-2.30986500	0.81804300	0.00058100
C	-2.92415200	-0.43844500	0.00065800
H	-2.61853700	-2.57234500	0.00015100
H	-0.66204100	3.13225900	0.00055000
C	-0.15164200	2.16396900	0.00004000
C	1.16554500	2.30374700	-0.00024800
O	1.19495400	-0.00550700	-0.00176900
C	2.15078600	-1.07924900	0.00067900
H	1.98412100	-1.69602800	0.89314900
H	1.98578000	-1.69857000	-0.89034100
C	3.54032400	-0.47016600	0.00092600
H	3.68995300	0.15360700	0.88593100
H	4.28868600	-1.26950000	0.00238500
H	3.69117300	0.15143500	-0.88541400
H	-0.14761600	-2.42349400	-0.00124900
H	-4.00707200	-0.51141100	0.00121100
H	-2.91162100	1.72235200	0.00110900

TS4a E= -462,195007 H= -462,018754 G= -462,067013

C	-1.85313200	-1.87920600	0.00958100
C	-0.47911300	-1.62003100	0.00390600
C	-0.01379800	-0.29996700	-0.00339100
C	-0.94556000	0.76811400	-0.01331100
C	-2.31920200	0.48447700	-0.01671600
C	-2.77642900	-0.83300900	0.00118200
H	-2.19650800	-2.90934700	0.01831000
H	-3.84194400	-1.03716500	0.00334000
H	-1.12679300	3.16227800	0.33434200
C	-0.44782900	2.11887900	-0.01642200
C	0.08259300	3.27040300	-0.02074900
O	1.29339900	0.06201100	-0.01045400
C	2.30788800	-0.95214400	0.00572300
H	2.18696600	-1.57315100	0.90345000
H	2.19492900	-1.59390600	-0.87833000
C	3.65442800	-0.25183100	0.00326200
H	3.75946200	0.38884900	0.88325500
H	4.45757000	-0.99590600	0.01538600

H	3.76724100	0.36768100	-0.89086400
H	0.22023900	-2.44690100	0.00917400
H	-3.02743200	1.30737600	-0.03282300

3a E= -462,267974 H= -462,086565 G= -462,133936

C	-2.75641200	-0.89463700	0.00051400
C	-2.32184200	0.43061700	-0.00007600
C	-0.95307900	0.74872300	-0.00045000
C	-0.00507400	-0.30766000	-0.00062700
C	-0.44483000	-1.63712800	-0.00006200
C	-1.81361900	-1.92332200	0.00055200
H	-3.81808600	-1.11936800	0.00091900
H	-2.13649100	-2.96042600	0.00095900
O	1.30166100	0.06583900	-0.00145100
C	-0.52657200	2.11139000	-0.00092300
C	2.31921100	-0.94061000	-0.00004300
H	2.21040500	-1.57585700	-0.88987700
H	2.20873900	-1.57501400	0.89018300
C	3.66324500	-0.23410500	0.00085400
H	3.76751200	0.39750600	0.88774300
H	4.47116800	-0.97318400	0.00210300
H	3.76927400	0.39641600	-0.88660200
C	-0.19771000	3.27836000	0.00121600
H	0.10472100	4.30038700	0.00071400
H	-3.03896500	1.24511800	-0.00011700
H	0.26853500	-2.45206200	-0.00015600

TS1d E= -576,597199 H= -576,384805 G= -576,438835

C	-2.18501500	1.96186500	0.40807700
C	-0.92100600	2.55957200	0.35095200
C	0.21404000	1.77112600	0.06523300
C	-0.05385500	0.48064600	-0.12941000
C	-1.25465900	-0.21999900	-0.13559000
C	-2.36276300	0.58601500	0.16679100
H	-3.06443500	2.56196300	0.63493500
H	-3.35839000	0.15927400	0.20389200
O	1.30243900	-0.28059500	-0.53480000
C	2.27929000	0.69567700	-0.62293300
C	1.72131800	-1.57141800	0.14509700
H	2.59753700	-1.88350000	-0.42155700
H	0.87232700	-2.22000000	-0.05816200
C	1.99064600	-1.36860500	1.61828700
H	1.10125500	-1.00751600	2.14021700
H	2.27356500	-2.33660900	2.04756800
H	2.81122400	-0.66642700	1.78319000
C	3.43958200	0.98973900	-0.85209600
H	4.35449500	1.52212700	-0.97942500
H	-0.83398600	3.63050300	0.52597300
O	-1.29081900	-1.56305500	-0.42210400
C	-2.56730000	-2.19776500	-0.47250000
H	-2.37232000	-3.23791800	-0.73701400
H	-3.07065000	-2.15524600	0.50071400
H	-3.20523200	-1.73857200	-1.23654900

TS2d E= -576,637376 H= -576,424813 G= -576,483718

C	-2.63100400	-0.74572000	-0.54853000
C	-2.15257300	0.36914700	0.17710200

C	-0.84824500	0.28486700	0.67739600
C	-0.20877700	-0.79783400	0.45476900
C	-0.51686700	-1.96328600	-0.22584700
C	-1.82292400	-1.88343500	-0.73884900
H	-3.62842100	-0.74796900	-0.97535500
H	0.12203400	-2.82857900	-0.35088600
H	-2.22356100	-2.72593400	-1.29765900
O	-2.87733300	1.50669200	0.40289700
C	-4.20315600	1.57683200	-0.10394000
H	-4.83821500	0.78890300	0.32143300
H	-4.58751300	2.55224400	0.19803400
H	-4.21985500	1.50363700	-1.19930300
H	1.47251200	-1.21382800	2.44676100
C	1.77331600	-1.01967800	1.44049600
C	2.60886000	-0.76879900	0.57476100
O	3.30710300	-0.50921300	-0.47504700
C	3.25421100	0.88736200	-0.96599500
H	3.67498400	0.80917200	-1.96921200
H	2.20011800	1.16834500	-1.02795500
C	4.05348800	1.81587600	-0.07440900
H	5.10105000	1.50564000	-0.02079600
H	4.01350600	2.83007200	-0.48630700
H	3.63722500	1.84647800	0.93672800

IVd E= -576,726831 H= -576,510712 G= -576,563198

C	-2.35890200	0.00829900	0.11754400
C	-1.07959300	0.56365000	-0.03842200
C	0.01010900	-0.31535000	-0.08170200
C	-0.15270700	-1.70204800	-0.02549400
C	-1.43603900	-2.24775900	0.11468900
C	-2.52474500	-1.38136400	0.19337000
H	-3.22970300	0.65037000	0.16803000
H	-1.57467800	-3.32308000	0.15802100
H	-3.52716200	-1.78274300	0.30832200
O	-0.81340100	1.89908200	-0.15957100
C	-1.91000600	2.80897700	-0.18331000
H	-2.46855100	2.78580500	0.76017800
H	-1.46968600	3.79712100	-0.32076800
H	-2.58653200	2.59094600	-1.01800900
H	1.22035000	-3.46645600	-0.10626500
C	1.13173100	-2.38203900	-0.14867700
C	2.26917100	-1.69223100	-0.31051700
O	1.33220000	0.03980700	-0.29945600
C	1.97942300	0.96863200	0.63807300
H	1.28551200	1.79388800	0.80031100
H	2.13942000	0.42416700	1.57380500
C	3.27981700	1.43148000	0.01566800
H	3.09208300	1.97334500	-0.91602000
H	3.79097100	2.10559600	0.71199000
H	3.92802800	0.57845100	-0.19471000

TS4d E= -576,716563 H= -576,505367 G= -576,559978

C	-2.07781900	-1.07515000	0.14935600
C	-1.25618600	0.03599200	-0.06685700
C	0.14415800	-0.13392800	-0.15984300
C	0.69107100	-1.42393500	-0.05517000
C	-0.14524100	-2.53971300	0.14676100
C	-1.51671000	-2.35384100	0.25563000

H	-3.15206000	-0.95766800	0.22364200
H	0.28590200	-3.53283600	0.21638000
H	-2.16677500	-3.20794300	0.41680300
O	-1.70498500	1.31560600	-0.20644900
C	-3.10882400	1.55200000	-0.17022500
H	-3.53696700	1.26924700	0.79936200
H	-3.23059100	2.62491900	-0.32187000
H	-3.62361200	1.00973000	-0.97246700
H	2.79261200	-2.60347500	0.19694800
C	2.12204700	-1.55874900	-0.16357300
C	3.38516900	-1.58530300	-0.26592800
O	0.97633300	0.91147800	-0.43884400
C	1.19534200	1.87255200	0.62302200
H	0.23493900	2.30763200	0.91808100
H	1.62949200	1.34672400	1.48320700
C	2.14284300	2.93121100	0.09238300
H	1.70519000	3.44332400	-0.76977900
H	2.34340300	3.67352600	0.87237300
H	3.09257600	2.48332600	-0.21367900

3d E= -576,789135 H= -576,572883 G= -576,627103

C	1.226982	-2.512357	-0.265089
C	-0.157202	-2.525337	-0.166024
C	-0.860520	-1.319825	0.047398
C	-0.151069	-0.109959	0.165505
C	1.259429	-0.112072	0.069717
C	1.941248	-1.312559	-0.149764
O	-0.827232	1.043114	0.450887
C	-2.286967	-1.327225	0.147086
C	-0.967119	1.987464	-0.633007
C	-1.713601	3.195018	-0.097901
C	-3.496020	-1.372265	0.220716
O	1.861868	1.105553	0.211339
C	3.282751	1.166097	0.182161
H	1.767859	-3.438899	-0.431209
H	-0.714210	-3.451724	-0.251803
H	3.022062	-1.326159	-0.223209
H	0.026284	2.267171	-1.001128
H	-1.524977	1.506033	-1.447423
H	-2.696460	2.904169	0.284635
H	-1.854668	3.930747	-0.897094
H	-1.151719	3.667198	0.713657
H	-4.558959	-1.402052	0.294736
H	3.536880	2.215352	0.337214
H	3.679272	0.834502	-0.785822
H	3.724082	0.562453	0.984833

TS1d' E= -576,601316 H= -576,389172 G= -576,443263

C	-2.19641000	-1.12181400	-0.05355600
C	-1.78446500	0.22512600	0.02466400
C	-0.43025700	0.57093900	-0.13875300
C	0.34185700	-0.48658500	-0.37716000
C	0.09409400	-1.84446600	-0.50489100
C	-1.26202300	-2.13808100	-0.31823100
H	-3.23479400	-1.40460200	0.08161500
H	0.82418200	-2.61224200	-0.73676100
H	-1.60050000	-3.16789000	-0.38744000

O	1.83397700	0.06158400	-0.60875700
C	1.76362700	1.44041300	-0.47155700
C	3.02457100	-0.62033100	0.00851400
H	3.87912900	-0.12107800	-0.44640500
H	2.94194200	-1.63802500	-0.37278000
C	3.00641500	-0.54075000	1.51839100
H	2.11673200	-1.02146100	1.93198800
H	3.89186700	-1.06076000	1.90067000
H	3.04279600	0.49699200	1.85762500
C	2.36243100	2.50377000	-0.46913000
H	2.58144600	3.54521100	-0.40048400
O	-2.65513100	1.25689500	0.26367600
C	-4.03368200	0.96337600	0.43144900
H	-4.20626000	0.31166900	1.29851400
H	-4.52537600	1.92285800	0.60029900
H	-4.45888400	0.49191400	-0.46463700

TS2d' E= -576,632986 H= -576,420259 G= -576,479458

C	2.87941800	-1.61695100	-0.49377100
C	1.90831900	-2.49071100	0.02132000
C	0.78393900	-1.83710100	0.53815300
C	0.66152800	-0.57058300	0.55305700
C	1.55493000	0.37762400	0.07005500
C	2.71617800	-0.21743400	-0.47341900
H	3.79123900	-2.02318900	-0.92821600
H	3.50385800	0.40554000	-0.88336100
H	-0.74671200	0.23830600	2.60362100
C	-1.06975300	0.37370800	1.59491700
C	-1.90378700	0.69840500	0.75219600
O	-2.60532200	0.98497100	-0.29130600
C	-3.17176000	-0.16099900	-1.03136500
H	-3.48293600	0.28577400	-1.97671100
H	-2.35789100	-0.86849500	-1.20917800
C	-4.33138900	-0.78741600	-0.28227400
H	-5.12704300	-0.05726400	-0.10782900
H	-4.74129600	-1.61045300	-0.87769700
H	-4.00500700	-1.19551300	0.67878300
H	2.04665500	-3.56752900	-0.00133700
O	1.30525800	1.71233200	0.14156700
C	2.29246300	2.60725700	-0.35834800
H	2.46551800	2.45168600	-1.43059800
H	1.89362500	3.60941100	-0.19657000
H	3.23999100	2.49851400	0.18388100

IVd' E= -576,731190 H= -576,515832 G= -576,569640

C	0.88176700	2.26649600	-0.00004000
C	-0.44066200	1.81625800	-0.00008300
C	-0.66647100	0.43679900	-0.00008700
C	0.39590400	-0.48339100	-0.00003200
C	1.71747100	-0.00192600	0.00000000
C	1.96103900	1.37868000	-0.00000500
H	1.07750200	3.33457000	-0.00003900
H	0.82979600	-2.65561600	0.00000600
C	0.04070700	-1.89664200	0.00001100
C	-1.16048900	-2.44621600	-0.00013500
O	-1.88421200	-0.17111500	-0.00016000
C	-3.09042900	0.60919000	0.00017200
H	-3.09812700	1.24943200	0.89181400

H	-3.09834700	1.24987800	-0.89115000
C	-4.26576900	-0.35052000	0.00008400
H	-4.24277700	-0.99140800	0.88538500
H	-5.20190800	0.21757200	0.00086800
H	-4.24360500	-0.99032000	-0.88602100
H	-1.26115100	2.52289800	-0.00012200
H	2.97211300	1.76579800	0.00002400
O	2.69282500	-0.95730800	0.00004300
C	4.05507900	-0.54444200	0.00009200
H	4.29314000	0.04111400	0.89633900
H	4.64236000	-1.46334100	0.00012700
H	4.29321100	0.04109100	-0.89615200

TS4d' E= -576,725955 H= -576,514556 G= -576,569318

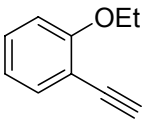
C	0.65219800	-2.33772900	-0.00000100
C	-0.63148200	-1.79071100	-0.00000200
C	-0.78335000	-0.39802000	-0.00000300
C	0.35548500	0.43639800	-0.00000200
C	1.64143900	-0.14255000	0.00000000
C	1.79307100	-1.53291600	0.00000000
H	0.76690800	-3.41742400	0.00000000
H	2.77570400	-1.98656100	0.00000100
H	1.20971100	2.73356800	-0.00000400
C	0.20114200	1.86206100	-0.00000200
C	0.03375200	3.11509800	-0.00000200
O	-1.97327700	0.25369900	-0.00000500
C	-3.19150900	-0.50355700	0.00000100
H	-3.22081400	-1.14515800	-0.89082600
H	-3.22080600	-1.14515900	0.89082700
C	-4.34337100	0.48475100	0.00000700
H	-4.30578100	1.12338600	-0.88699200
H	-5.29503300	-0.05676500	0.00002100
H	-4.30576100	1.12339700	0.88699700
H	-1.49547700	-2.44240100	-0.00000300
O	2.67236300	0.75074000	0.00000100
C	4.01044900	0.25902000	0.00000500
H	4.64831700	1.14310600	0.00000600
H	4.21169900	-0.33828300	0.89686700
H	4.21170500	-0.33828300	-0.89685500

3d' E= -576,795020 H= -576,578529 G= -576,631882

C	1.80547700	-1.52650400	-0.00025400
C	1.65260200	-0.13417100	0.00027700
C	0.36371300	0.45197400	0.00036400
C	-0.76931400	-0.39790100	0.00014900
C	-0.61590300	-1.79099500	-0.00039200
C	0.66848700	-2.33483700	-0.00058200
H	2.78830900	-1.97960200	-0.00035900
H	0.78623900	-3.41456400	-0.00097500
O	-1.97235100	0.23329800	0.00044000
C	0.21031800	1.86794500	0.00070000
C	-3.17330100	-0.54539700	-0.00002400
H	-3.19483200	-1.18906600	0.89000600
H	-3.19462200	-1.18832000	-0.89059600
C	-4.34467700	0.42068200	0.00024900
H	-4.31890200	1.06042500	-0.88657800
H	-5.28637500	-0.13818600	-0.00020200
H	-4.31923600	1.05953900	0.88772500

C	0.08057200	3.07321400	-0.00156000
H	-0.03247700	4.13280700	-0.00143700
H	-1.47695300	-2.44641600	-0.00062500
O	2.69163900	0.74295900	0.00072000
C	4.02004000	0.23485400	0.00007500
H	4.21857100	-0.36536200	-0.89642600
H	4.66869100	1.11152300	0.00018700
H	4.21919700	-0.36603400	0.89599000

3. ^{1}H and ^{13}C NMR spectra



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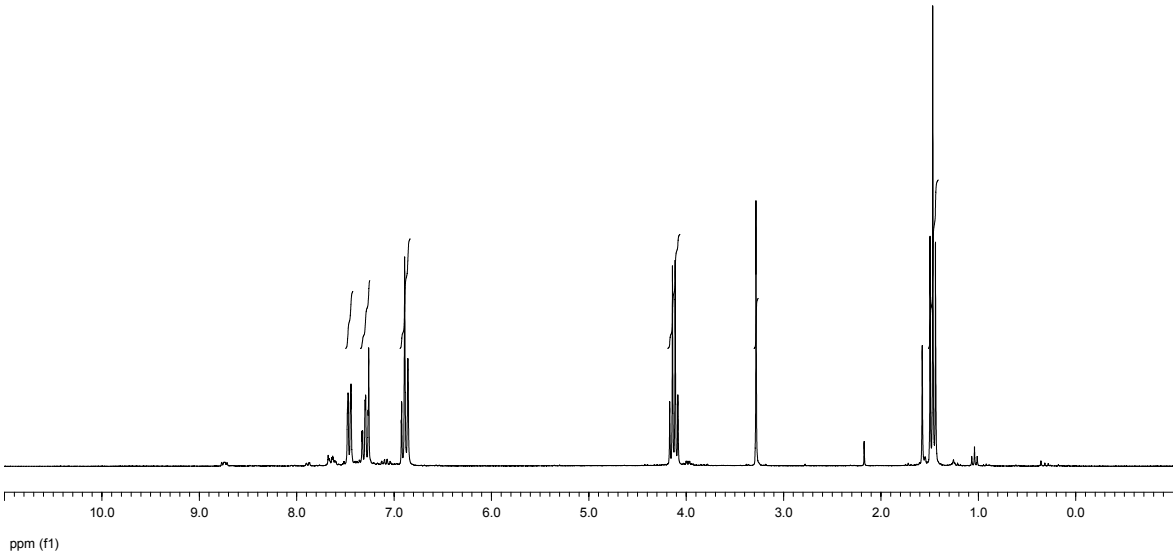
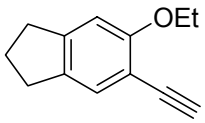
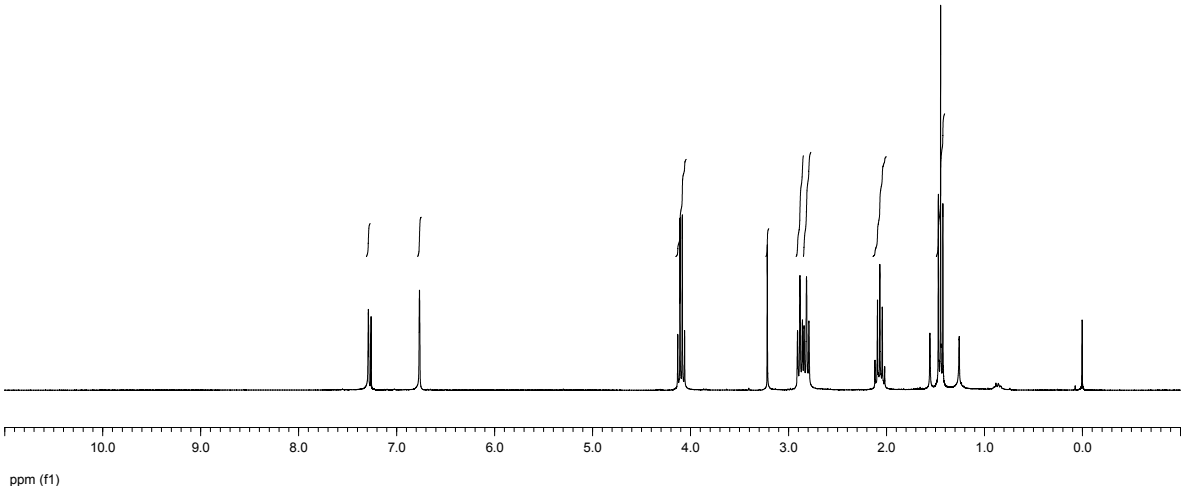
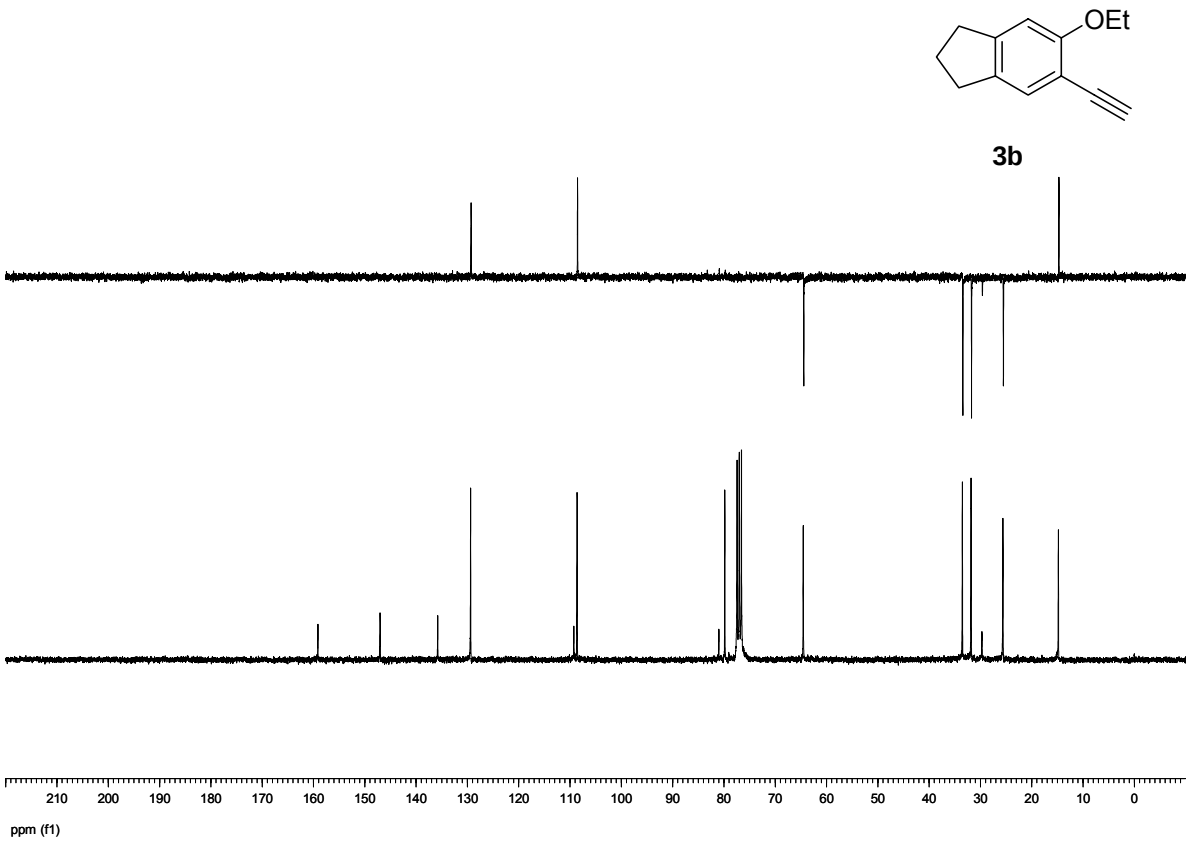




3b




OEt
3b
210
200
190
180
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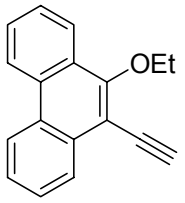
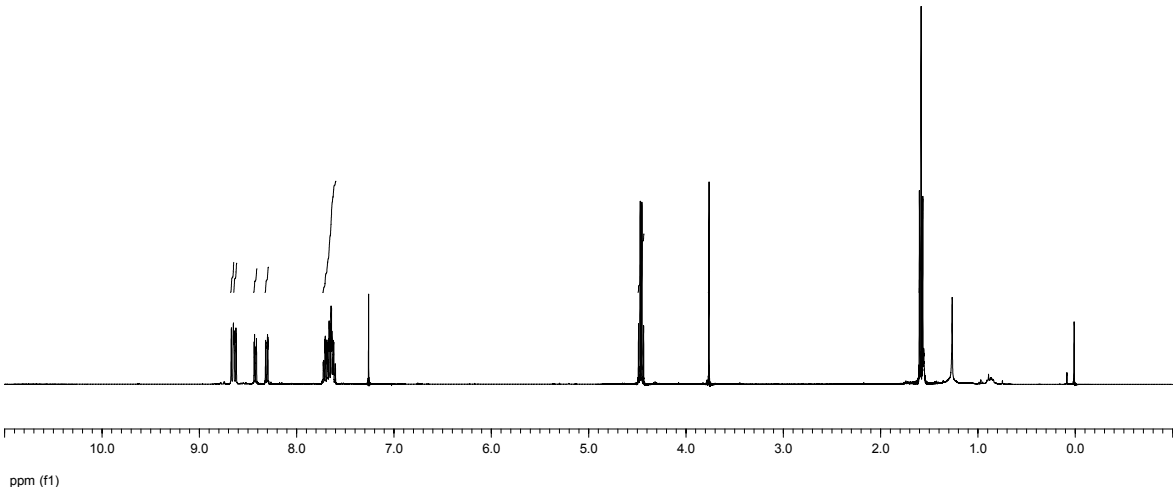
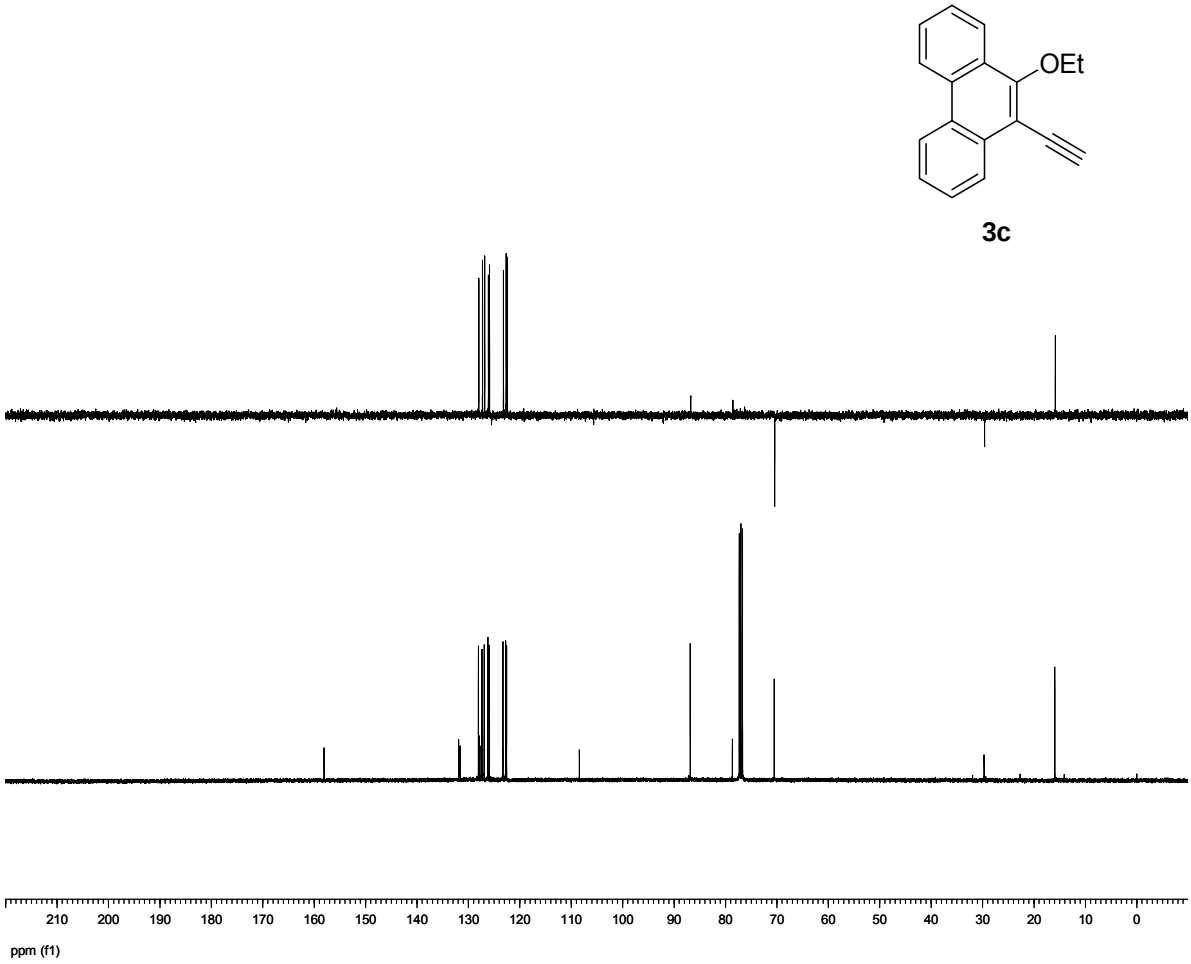
10
0
ppm (f1)

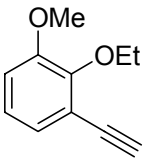


3c

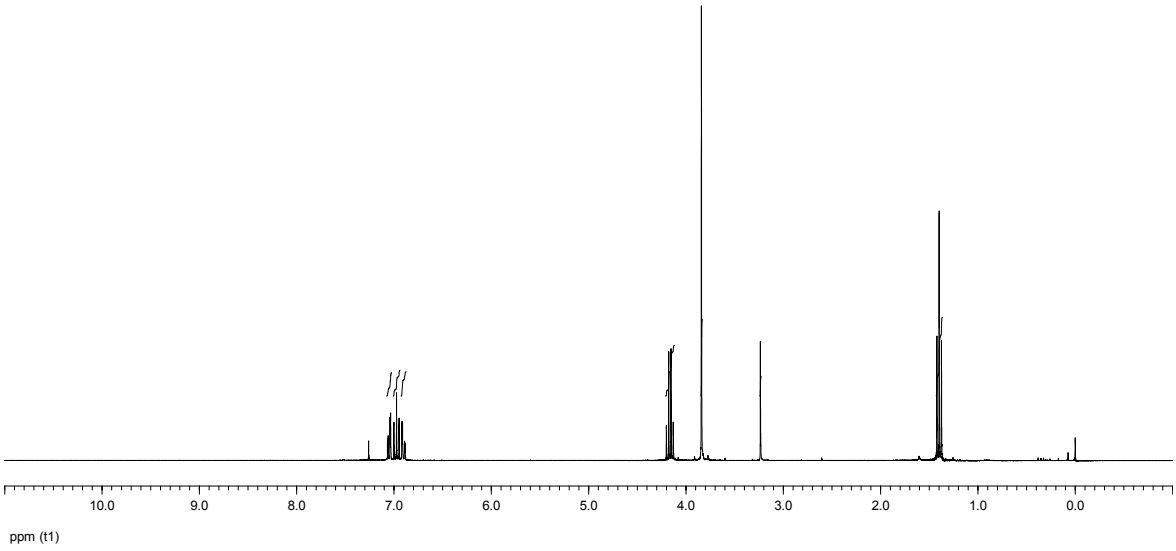


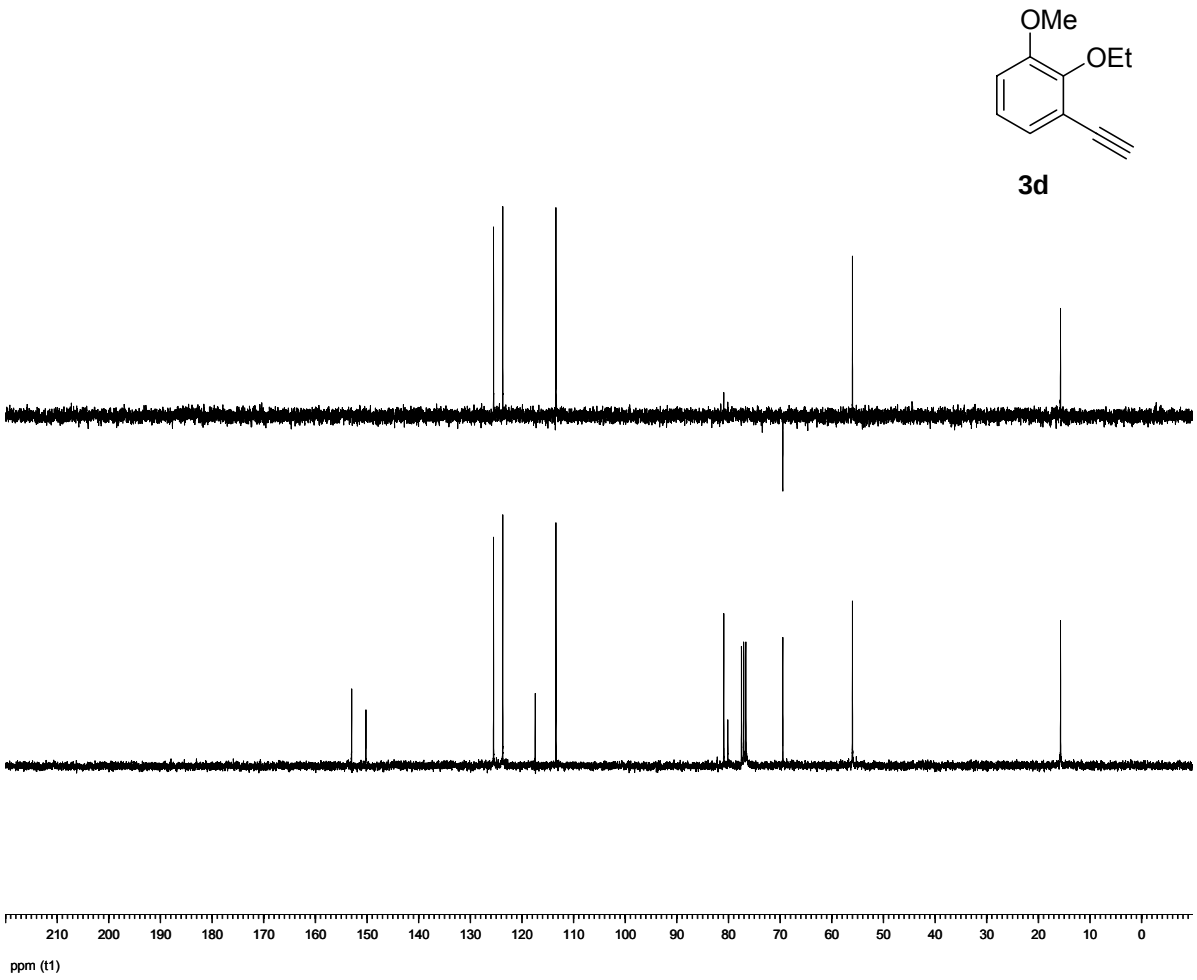

OEt
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (f1)

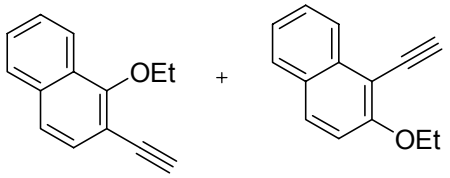
3c



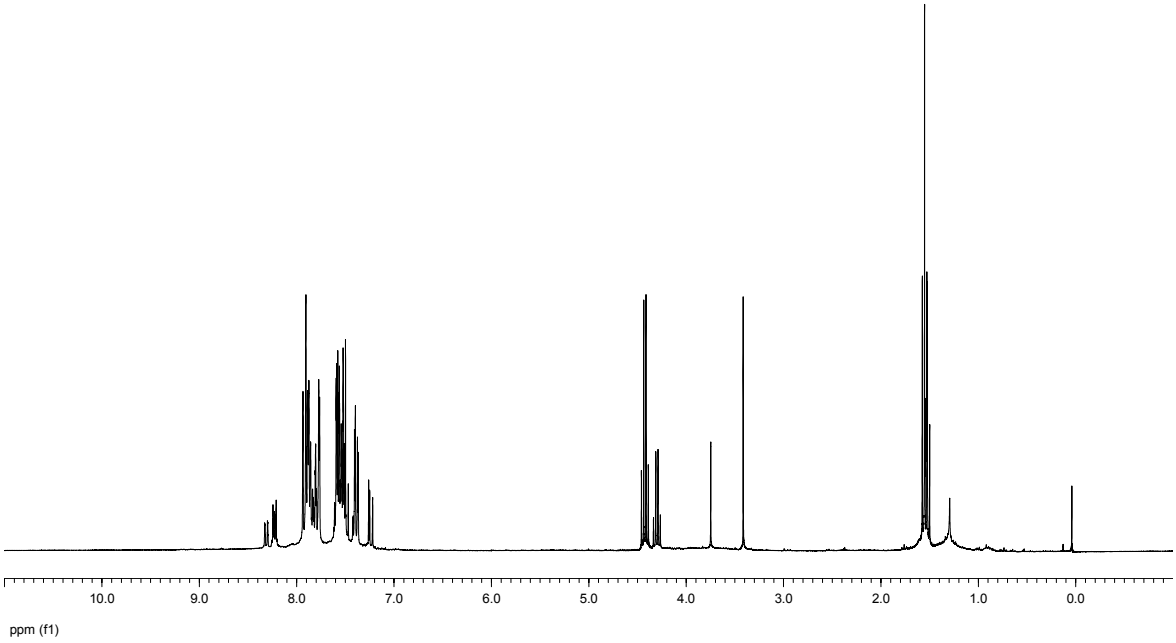
3d

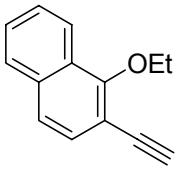



OMe
OEt
3d
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (t1)



3e **3e'**





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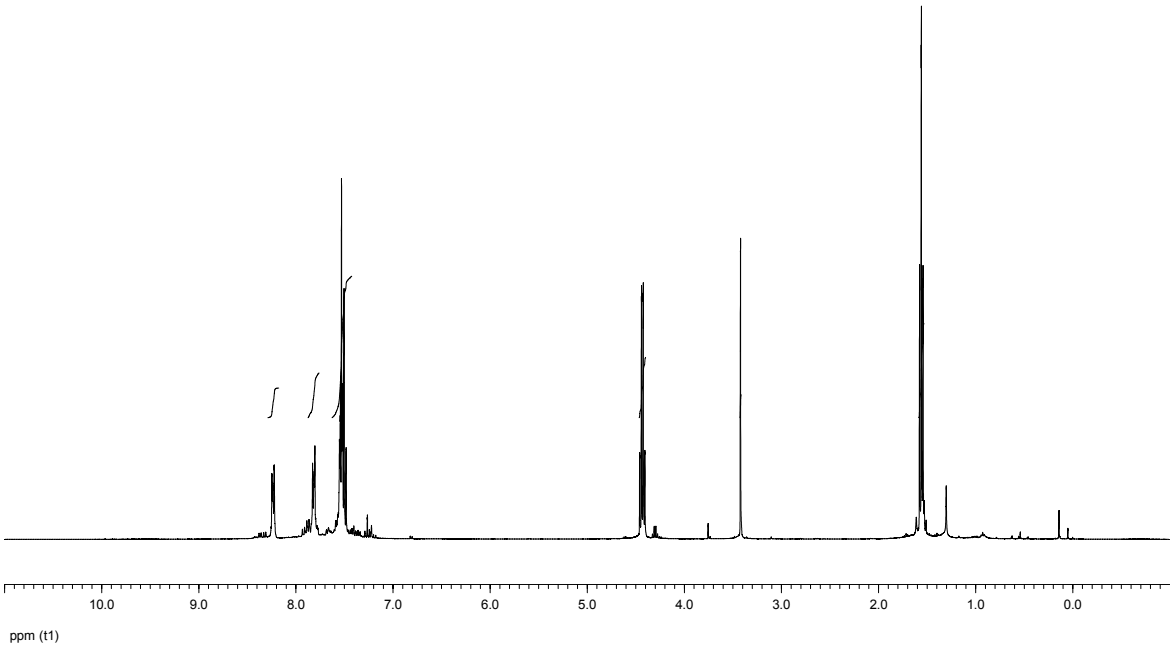
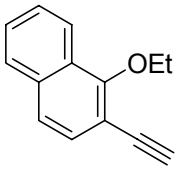
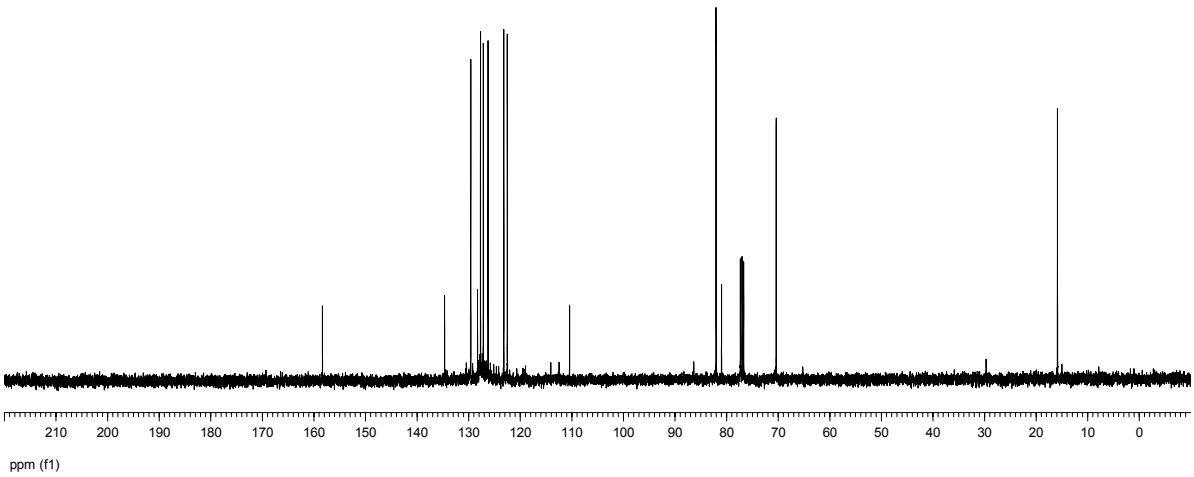



OEt

3e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30
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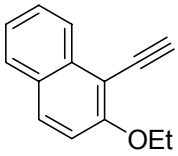
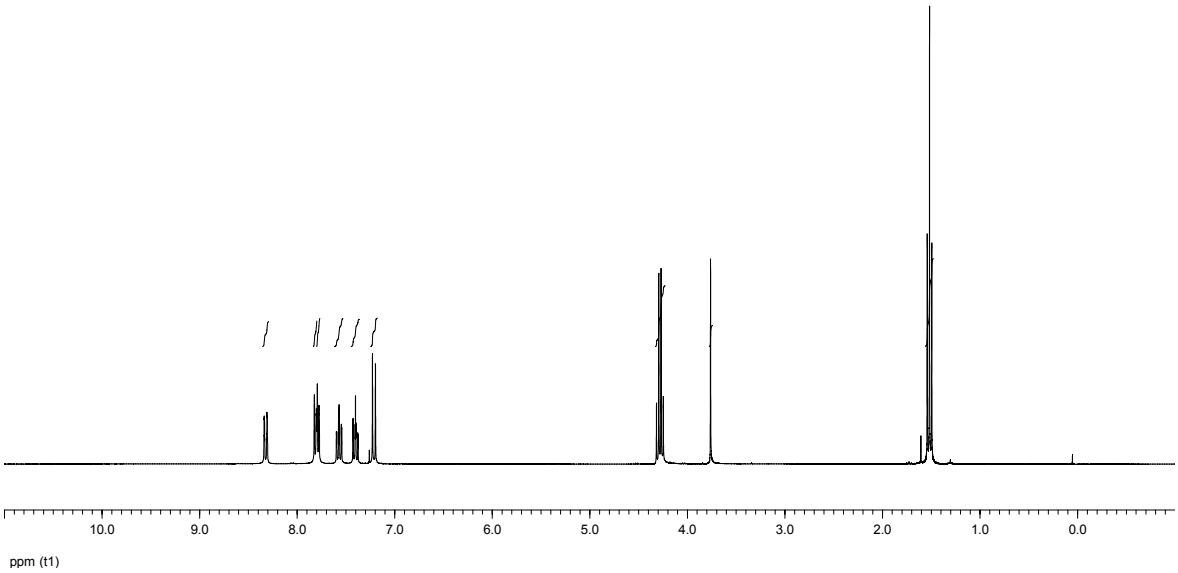
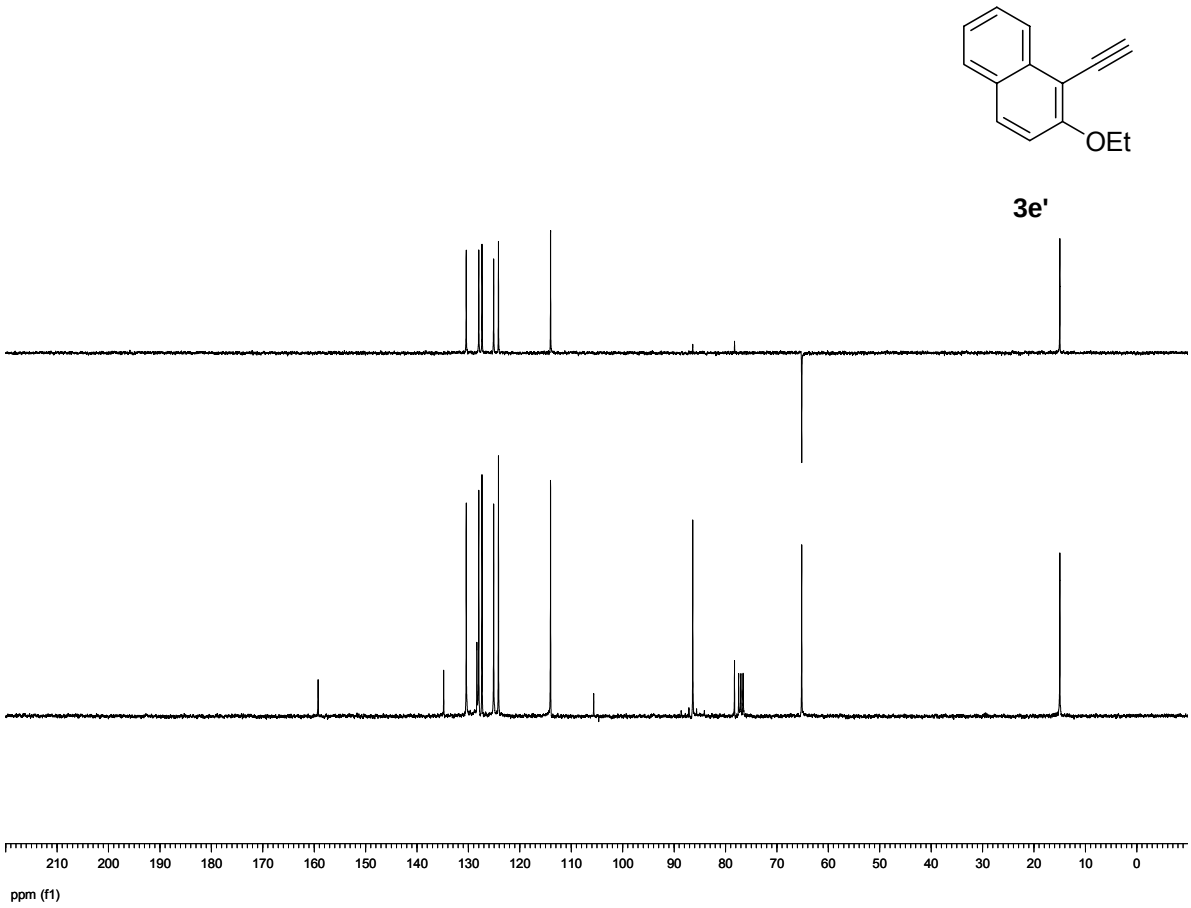
10
0
ppm (f1)



3e'




OEt
3e'
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180
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30
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10
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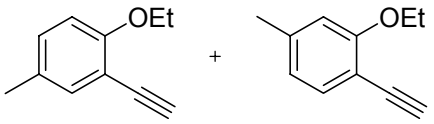
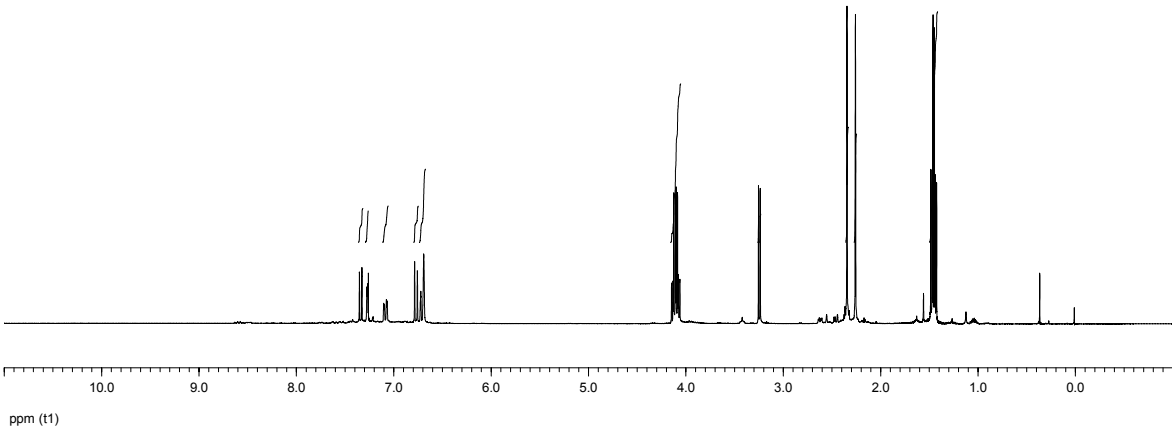
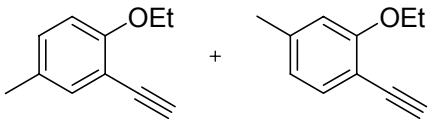
ppm (f1)

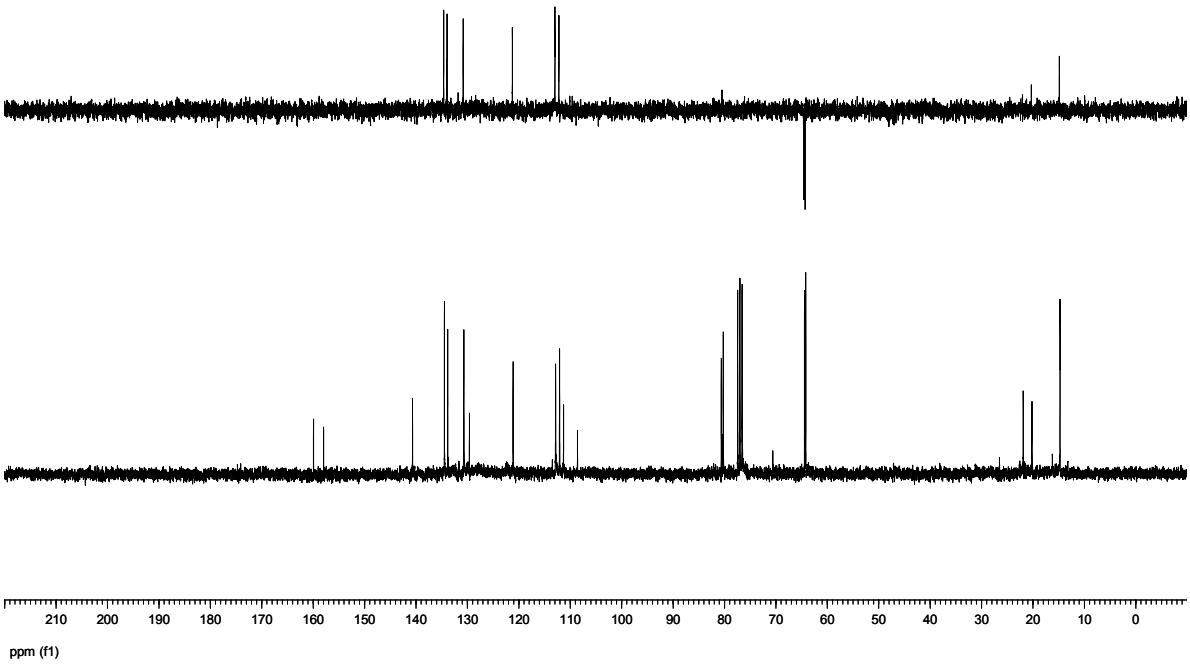


3f **3f'**




OEt
+
OEt

3f **3f'**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10
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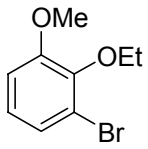
ppm (f1)



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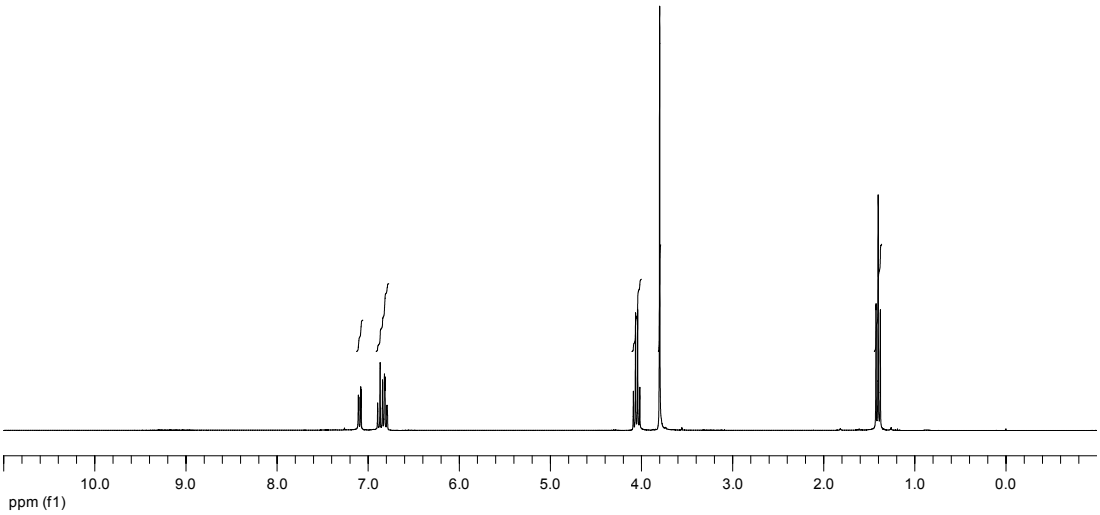

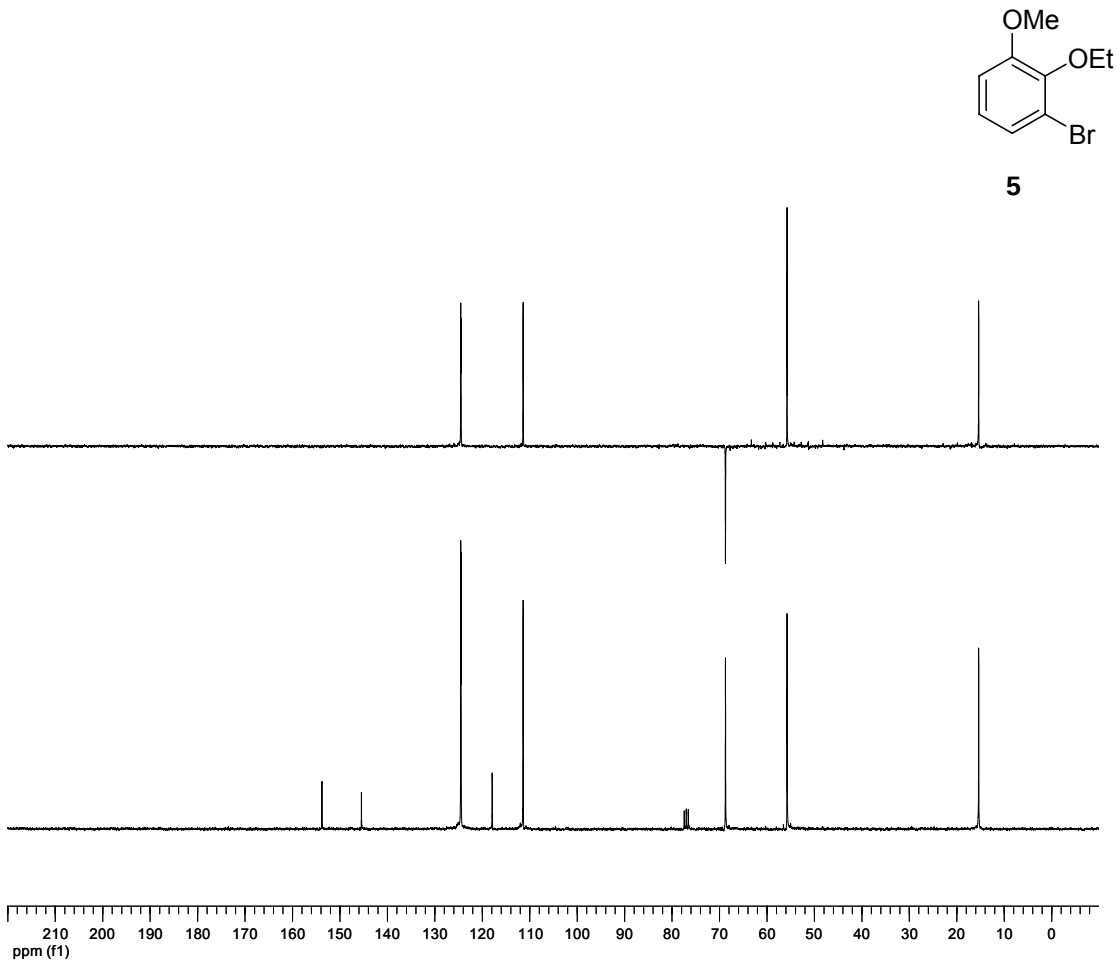
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OEt
Br
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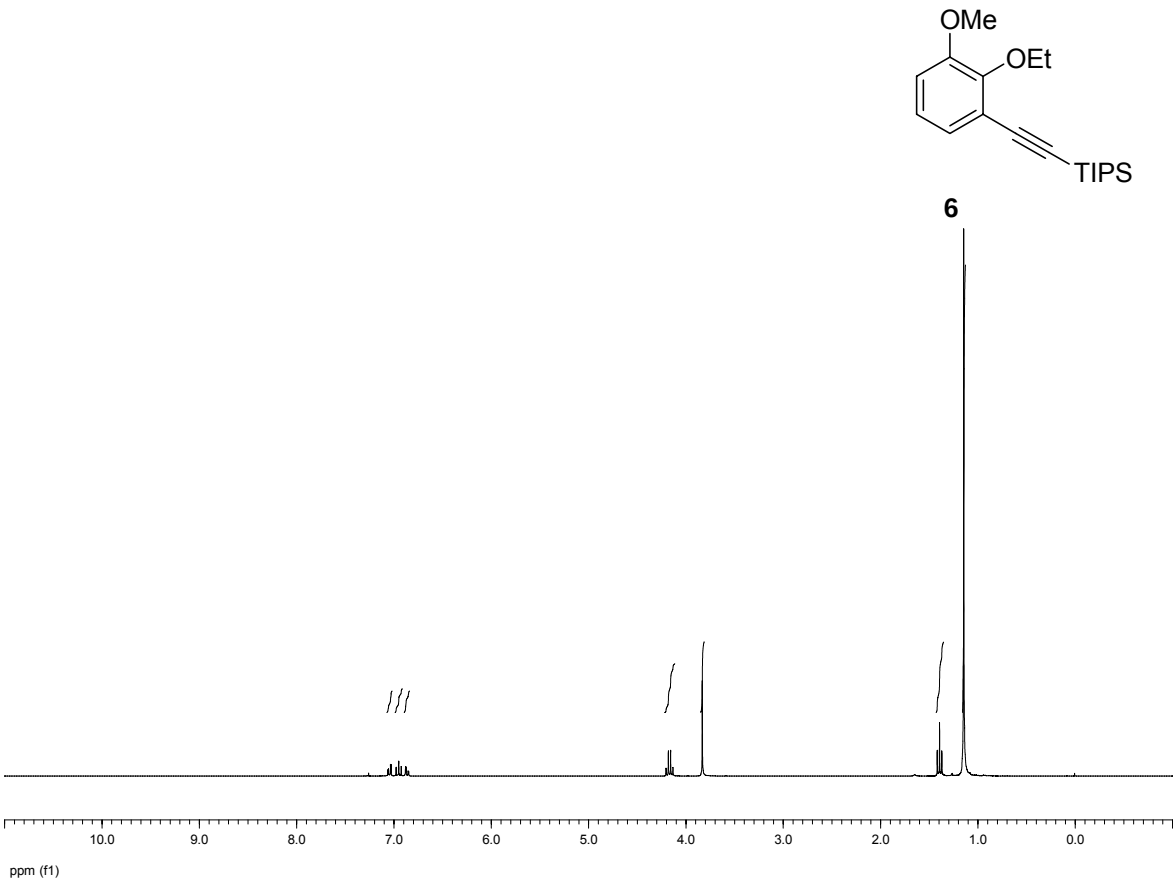
ppm (f1)

5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OEt
TIPS
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2.0
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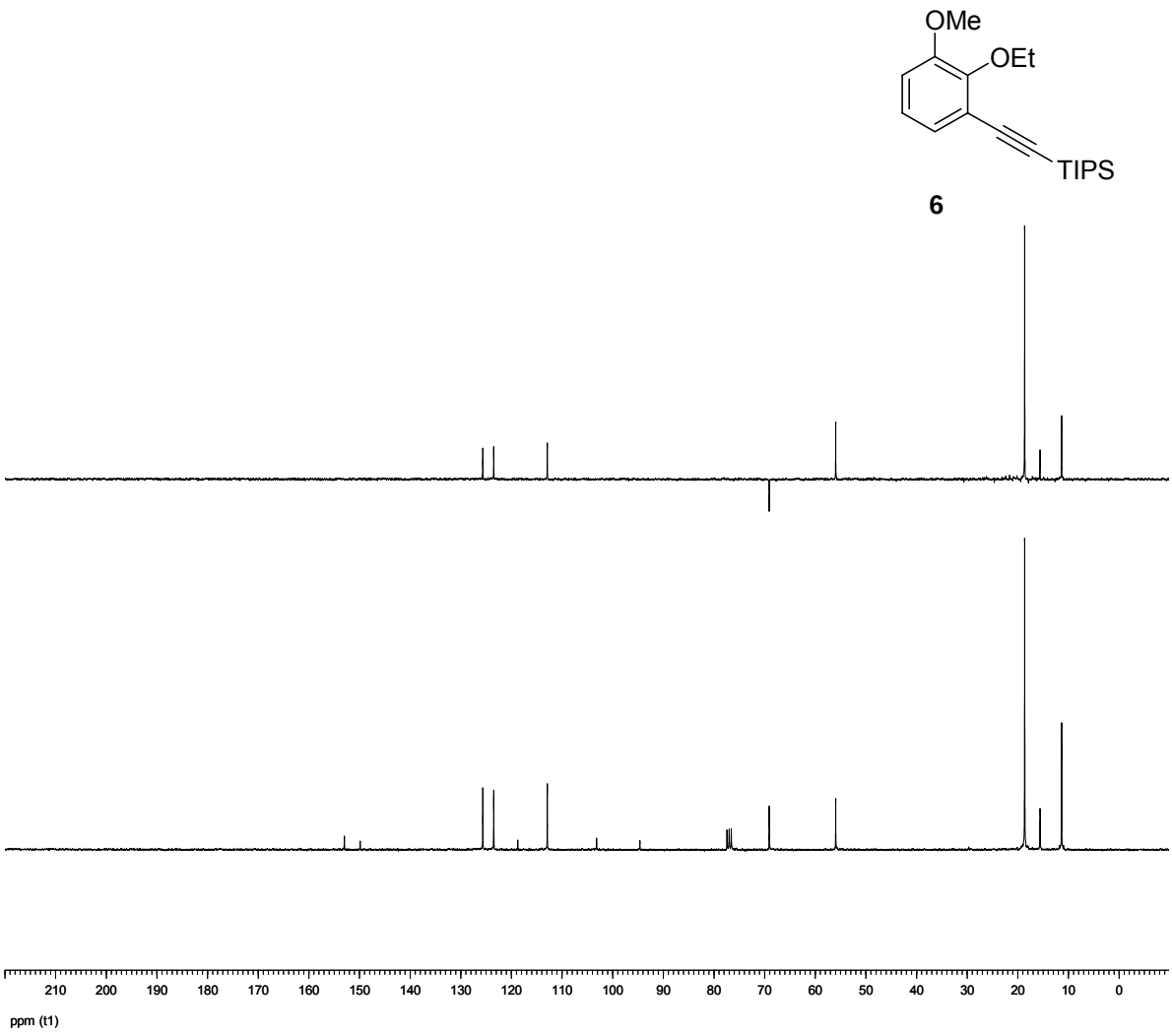
0.0
ppm (f1)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TIPS
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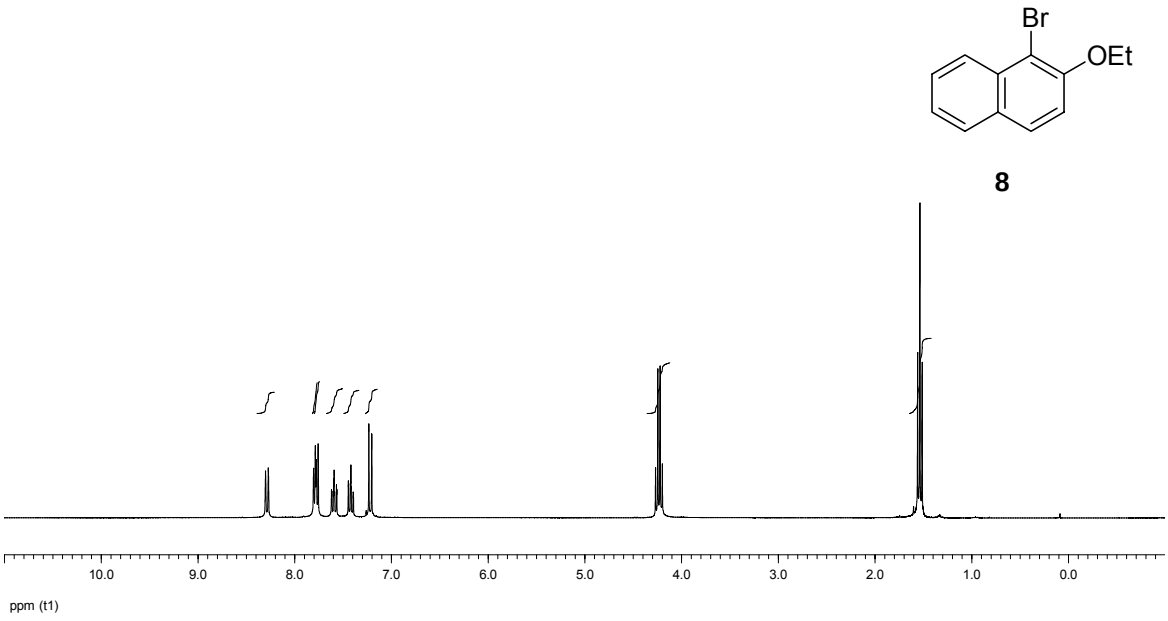
ppm (t1)



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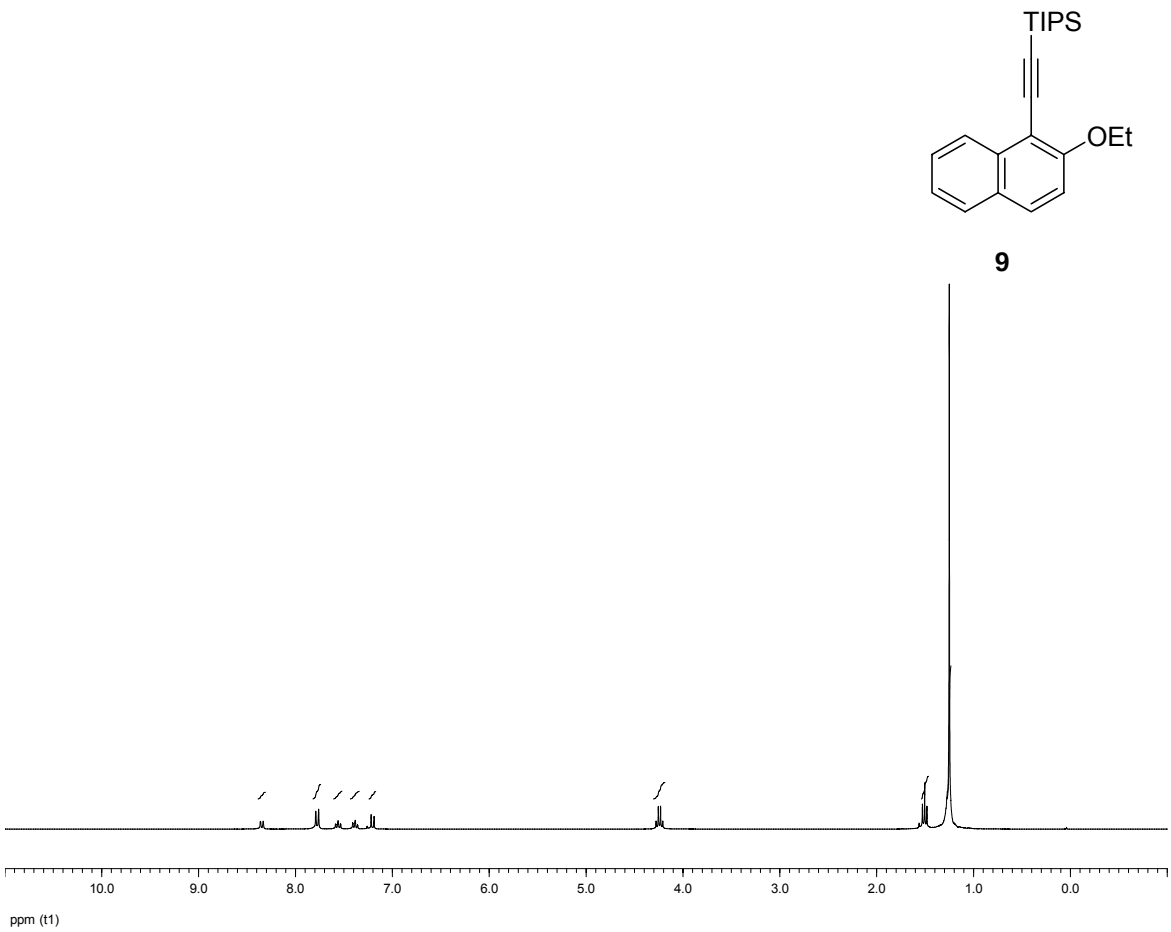
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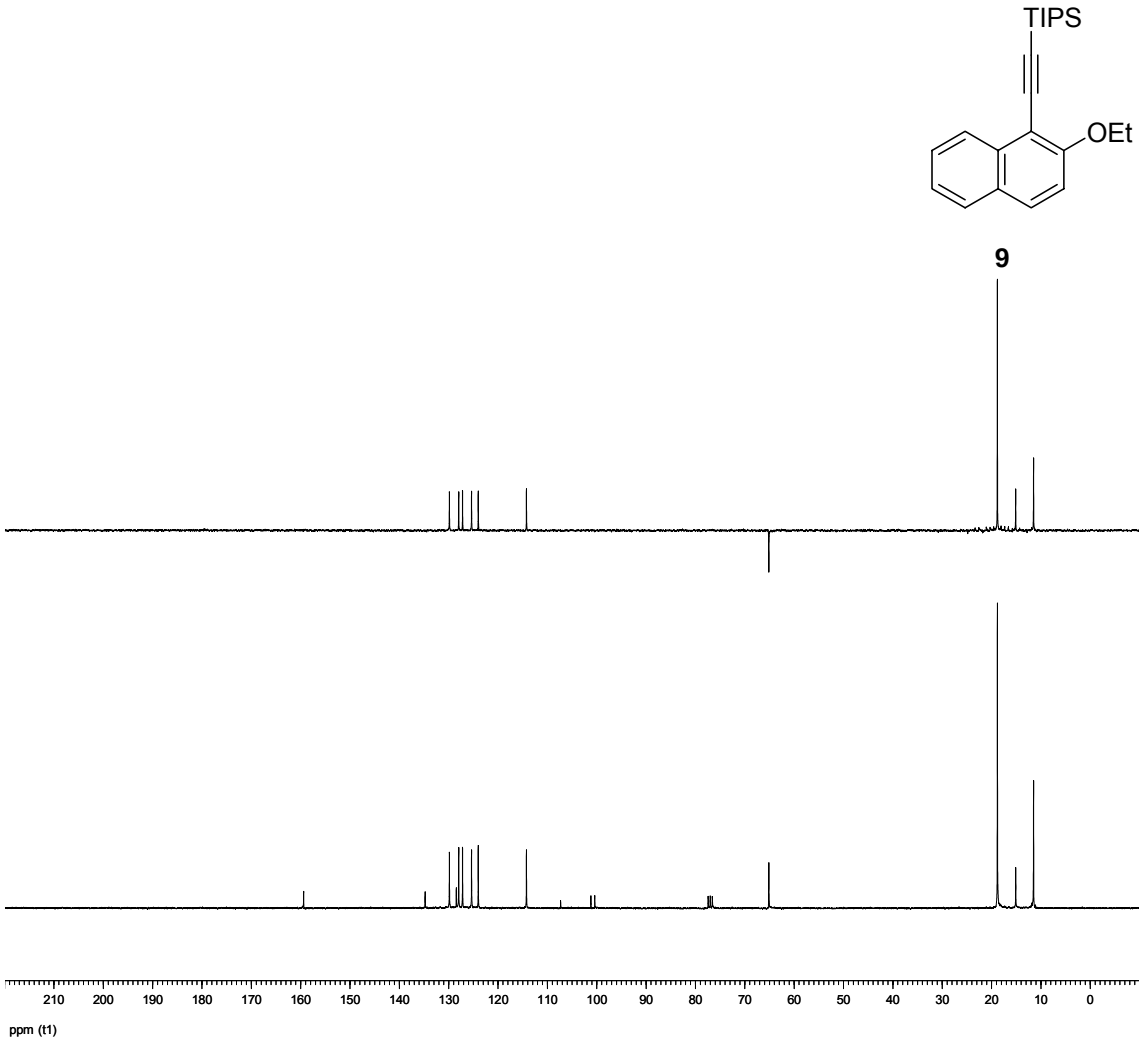
0.0
ppm (t1)


TIPS
OEt
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100
90
80
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50
40
30
20
10
0
ppm (t1)