Cycloisomerization of Aromatic Homo- and bis-Homopropargylic Alcohols via Catalytic Ru-Vinylidenes: Formation of Benzofuranes and Isochromenes

Alejandro Varela-Fernández, Carlos González-Rodríguez, Jesús A. Varela, Luis Castedo and Carlos Saá*

Departamento de Química Orgánica, Facultad de Química, Universidad de Santiago de Compostela, 15782 Santiago de Compostela, Spain

Supporting Information

Index

I. General

Solvents THF, Et_3N, $^iPr_2NH$ and MeOH were used after distillation. All other reagents were used as received without further purification, unless otherwise noted. All reactions were carried out under argon atmosphere in flame-dried glassware with magnetic stirring, unless otherwise indicated.

II. Preparation of starting materials and catalysts

- Aromatic alkynols **1a**,[1] **1d**,[1] **9b**,[1] **9d**[1] were prepared following published procedures or with appropriate modifications.

- Aromatic alkynols **1b** and **1c** were prepared in three steps in 71% and 61% overall yields, respectively: a) Sonogashira coupling of methyl-2-bromo-5-chlorobenzoate and methyl-2-bromo-5-methoxybenzoate with trimethylsilylacetylene (1.5 equiv) using $Pd(OAc)_2$ (0.02 equiv), Ph_3P (0.05 equiv) and CuI (0.03 equiv) in Et_3N at 90ºC; b) reduction with $LiAlH_4$ (1.4 equiv) in THF; c) desilylation with TBAF (1.25 equiv) in THF.

- Aromatic alkynol **1e** was prepared in three steps in 86% overall yield: a) Sonogashira coupling of 1-(2-iodophenyl)ethanone with trimethylsilylacetylene (1.5 equiv) using $Pd(PPh_3)_2Cl_2$ (0.02 equiv) and CuI (0.03 equiv) in THF/Et_3N at rt; b) reduction with $NaBH_4$ (1 equiv) in MeOH; c) desilylation with TBAF (1.25 equiv) in THF.

- Aromatic alkynols **1f** and **1g** were prepared in three steps in 48% and 86% overall yields, respectively: a) Sonogashira coupling of 2-iodobenzaldehyde and 1-(2-iodophenyl)ethanone with trimethylsilylacetylene (1.5 equiv) using $Pd(PPh_3)_2Cl_2$ (0.02 equiv) and CuI (0.03 equiv) in THF/Et_3N at rt; b) desilylation with TBAF (1.25 equiv) in THF; c) addition of allylmagnesium chloride (1.5 equiv) and methylmagnesium iodide (2 equiv) in THF, respectively.

- 2-Ethynylbenzoic acid **3** was prepared in three steps in 20% overall yield: a) esterification of 2-iodobenzoic acid in MeOH with H_2SO_4; b) Sonogashira coupling of the ester obtained with trimethylsilylacetylene (1.5 equiv) using $Pd(PPh_3)_2Cl_2$ (0.02 equiv) and CuI (0.03 equiv) in THF/Et_3N at rt; c) ester saponification and desilylation with NaOH in MeOH.

- Alkynol **5** was prepared in three steps in 32% overall yield: a) silylation of pent-4-yn-1-ol by treatment with n-BuLi (2.1 equiv) and TMSCl (2.2 equiv) in THF; b) Swern oxidation of the resulting alcohol; c) addition of hexylmagnesium chloride (1 equiv) in THF.

- 2,2-Di(prop-2-ynyl)propane-1,3-diol **7** was prepared in 70% overall yield by reduction of dimethyl 2,2-di(prop-2-ynyl)malonate[2] with $LiAlH_4$ (2.8 equiv) in THF.

---

[1] Kabalka, G. W.; Wang, L.; Pagni, R. M. *Tetrahedron* **2001**, *57*, 8017.
[2] Trost, B. M.; Rudd, M. T. *J. Am. Chem. Soc.* **2005**, *127*, 4763.

- Phenol **9a** was prepared in three steps in 34% overall yield: a) Sonogashira coupling of 3-hydroxy-2-iodo-4-methoxybenzaldehyde with trimethylsilylacetylene (1.5 equiv) using $Pd(PPh_3)_2Cl_2$ (0.10 equiv) and CuI (0.10 equiv) in THF/$^{i}Pr_2NH$ at 40ºC; b) reduction with $NaBH_4$ (1.5 equiv) in MeOH; c) desilylation with TBAF (1.25 equiv) in THF.

- Phenol **9c** was prepared in three steps in 50% overall yield: a) iodination of 4-hydroxybenzonitrile with KI (2 equiv), I_2 (1 equiv), NH_4OH (1 equiv) in H_2O;[3] b) Sonogashira of the resulting aryl iodide with trimethylsilylacetylene (1.5 equiv) using $Pd(PPh_3)_2Cl_2$ (0.02 equiv) and CuI (0.03 equiv) in THF/Et_3N at rt; c) desilylation with TBAF (1.25 equiv) in THF.

- $CpRuCl(PPh_3)_2$,[4] $CpRuCl(dppm)$[5] and $[Cp^*Ru(CH_3CN)_3]PF_6$[6] were prepared following literature procedures. $Cp^*RuCl(PPh_3)_2$, (η^5-indenyl)$RuCl(PPh_3)_2$ and $TpRuCl(PPh_3)_2$ were used as received from commercial suppliers.

III. Optimization of the Ru-catalyzed cycloisomerization conditions

- *Catalyst*: Ru-catalyzed reaction of bis-homopropargylic alcohol **1a** using 10% of $Cp^*RuCl(PPh_3)_2$, $TpRuCl(PPh_3)_2$, $CpRuCl(dppm)$ or $[Cp^*Ru(CH_3CN)_3]PF_6$ failed to give the cycloisomerized product, with recovery of **1a** unaltered. When η^5-(indenyl)$RuCl(PPh_3)_2$ was used as catalyst, isochromene **2a** was obtained in a low 15% yield.
- *Amines*: Ru-catalyzed cycloisomerization of **1a** in $iPrNH_2$ gave a low 25% yield of **2a**. Secondary amines like iPr_2NH and pirrolidine, tertiary amines like Et_3N and 2,2'-bipyridine failed to afford **2a**, with recovery of **1a** unaltered.

IV. General conditions for the Ru-catalyzed reaction

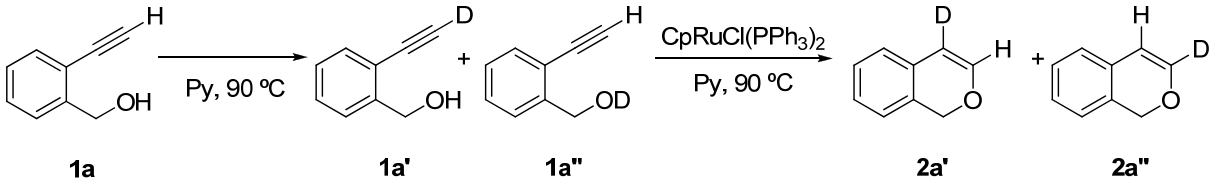
Aromatic alkynols were added to a suspension of the Ru catalyst (10% mmol) in the solvent (0.15 M) and the mixture heated in an oil-bath at 90-130ºC until disappearance of the starting alkynol (GC and TLC monitoring). After reaching rt, the mixture was concentrated and the resulting residue was chromatographed on silica gel using Et_2O/hexane as eluents to afford the final cycloisomerized products.

V. Isotopic labeling experiments

Deuterated alkyne **1a'** (obtained by reaction of **1a** with NaH in THF followed by sequential quenching with D_2O and MeOH) was heated in pyridine for 30 min at 90 ºC until a stationary mixture of **1a'** and deuterated alcohol **1a''** was obtained in 3:7 ratio (Scheme 1). Then, $CpRuCl(PPh_3)_2$ was added to the reaction mixture to give a 3:7 mixture of isochromenes **2a'** and **2a''** (Scheme 1).

---

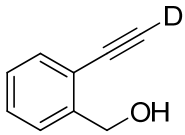
[3] Sun, M.; Cowart, M. *J. Med. Chem*. **2005**, *48*, 6482.
[4] Bruce, M. I.; Windsor, N. J. *Aust. J. Chem*. **1977**, *30*, 1601.
[5] Ashby, G. S.; M. I. Tomkins, I. B.; Wallis, R. C. *Aust. J. Chem*. **1979**, *32*, 1003.
[6] a) Trost, B. M.; Older, C. M. *Organometallics* **2002**, *21*, 2544. b) Schrenk, J. L.; McNair, A. M.; McCormick, F. B. Mann, K. R. *Inorg. Chem.* **1986**, *25*, 3501.



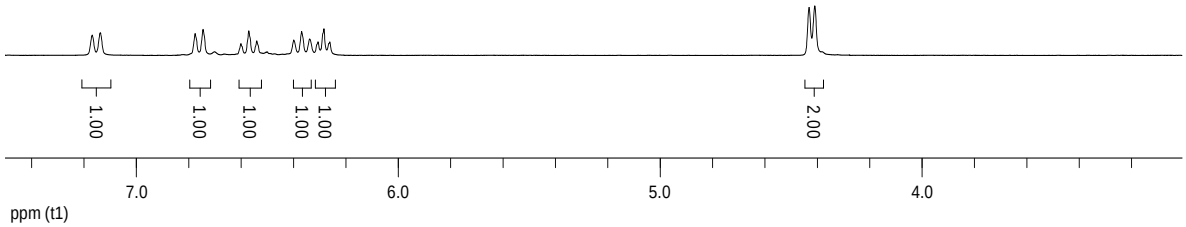
1a **1a'** **1a"** **2a'** **2a"**

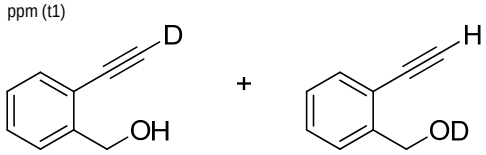
30:70 30:70

Scheme 1



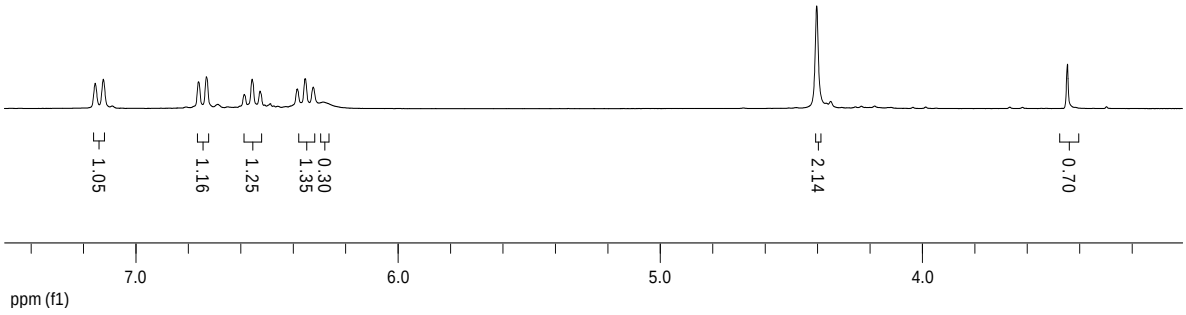
1a'

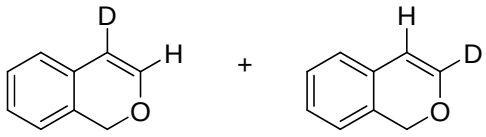




1a' **1a"**

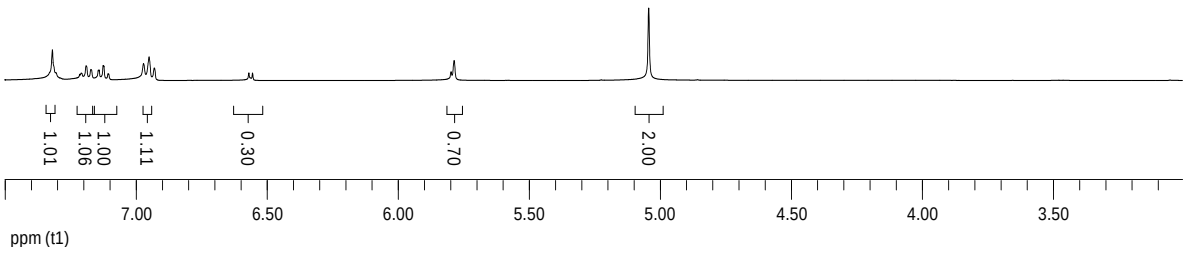
30:70



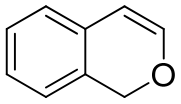


2a' **2a"**

30:70



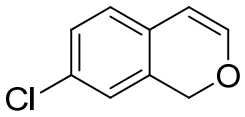
VI. Spectral data



2a

1H-isochromene (2a)

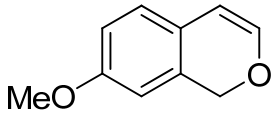
Brown oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.28-7.09 (m, 2H), 6.96 (t, *J* = 7.6 Hz, 2H), 6.57 (d, *J* = 5.7 Hz, 1H), 5.80 (d, *J* = 5.7 Hz, 1H), 5.05 (s, 2H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.2 (CH), 130.4 (C), 128.1 (CH), 128.0 (C), 126.6 (CH), 123.9 (CH), 122.8 (CH), 105.4 (CH), 68.1 (CH_2). MS, m/z (% relative intensity): 133 (M^++1, 100), 132 (16), 105 (39). HRMS (CI) calculated for C_9H_9O [M^++1]: 133.0653; found: 133.0653.



2b

7-chloro-1H-isochromene (2b)

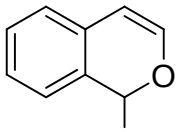
Yellow solid (mp: 48-50ºC). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.17 (dd, *J* = 7.9, 1.9 Hz, 1H), 6.98 (s, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 6.57 (d, *J* = 5.7 Hz, 1H), 5.77 (d, *J* = 5.7 Hz, 1H), 5.01 (s, 2H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.4 (CH), 131.7 (C), 129.5 (C), 128.9 (C), 128.1 (CH), 124.2 (CH), 124.0 (CH), 104.7 (CH), 67.5 (CH_2). MS, m/z (% relative intensity): 167 (M^++1, 100), 166 (39), 139 (38), 141 (12), 131 (32). HRMS (CI) calculated for C_9H_8ClO [M^++1]: 167.0264; found: 167.0264.



2c

7-methoxy-1H-isochromene (2c)

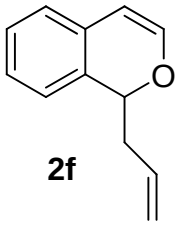
White solid (mp: 52-54ºC). ^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.91 (d, *J* = 8.3 Hz, 1H), 6.76 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.58 (s, 1H), 6.51 (d, *J* = 5.7 Hz, 1H), 5.78 (d, *J* = 5.7 Hz, 1H), 5.03 (s, 2H), 3.79 (s, 3H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 158.6 (C), 144.1 (CH), 129.7 (C), 124.0 (CH), 123,2 (C), 112.9 (CH), 110.2 (CH), 105.0 (CH), 68.0 (CH_2), 55.3 (CH_3). MS, m/z (% relative intensity): 163 (M^++1, 27), 149 (22), 137 (31), 123 (46), 109 (61), 95 (74), 83 (100). HRMS (ESI) calculated for $C_{10}H_{11}O_2$ [M^++1]: 163.0756; found: 163.0754.



2e

1-methyl-1H-isochromene (2e)

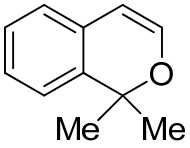
Yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$), δ ppm 7.25-7.09 (m, 2H), 7.04-6.89 (m, 2H), 6.51 (d, *J* = 5.7 Hz, 1H), 5.76 (d, *J* = 5.7 Hz, 1H), 5.21 (q, *J* = 6.5 Hz, 1H), 1.59 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$) δ (ppm): 144.8 (CH), 132.4 (C), 129.7 (C), 127.8 (CH), 126.6 (CH), 123.3 (CH), 123.0 (CH), 104.7 (CH), 73.5 (CH), 19.7 (CH_3). MS, m/z (% relative intensity): 147 (M^++1, 100), 146 (24), 131 (13), 129 (15), 119 (35). HRMS (EI) calculated for $C_{10}H_{10}O$ [M^+]: 146.0732; found: 146.0732.



2f

1-allyl-1H-isochromene (2f)

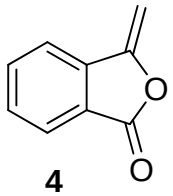
Yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$), δ (ppm): 7.23-7.10 (m, 2H), 6.96 (d, *J* = 7.0 Hz, 2H), 6.49 (d, *J* = 5.7 Hz, 1H), 5.99-5.80 (m, 1H), 5.75 (d, *J* = 5.7 Hz, 1H), 5.21-5.06 (m, 3H), 2.87-2.71 (m, 1H), 2.56-2.44 (m, 1H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 144.1 (CH), 134.1 (CH), 130.8 (C), 129.6 (C), 127.9 (CH), 126.4 (CH), 124.2 (CH), 123.3 (CH), 117.6 (CH_2), 104.6 (CH), 76.9 (CH), 38.5 (CH_2). MS, m/z (% relative intensity): 173 (M^++1, 18), 159 (13), 155 (11), 145 (26), 131 (100), 129 (5), 117 (5). HRMS (EI) calculated for $C_{12}H_{12}O$ [M^+]: 172.0888; found: 172.0888.



2g

1,1-dimethyl-1H-isochromene (2g)

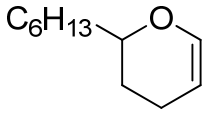
Yellowish oil. ^{1}H NMR (250 MHz, $CDCl_3$), δ (ppm): 7.19-7.12 (m, 2H), 7.08-7.03 (m, 1H), 6.93 (dd, *J* = 6.1, 2.7 Hz, 1H), 6.45 (d, *J* = 5.7 Hz, 1H), 5.72 (d, *J* = 5.7 Hz, 1H), 1.61 (s, 6H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 143.4 (CH), 137.0 (C), 136.0 (C), 127.4 (CH), 126.8 (CH), 123.4 (CH), 122.6 (CH), 104.0 (CH), 77.9 (C), 27.3 (2xCH_3). MS, m/z (% relative intensity): 161 (M^++1, 100), 160 (42), 145 (29), 143 (86), 133 (21). HRMS (EI) calculated for $C_{11}H_{12}O$ [M^+]: 160.0888; found: 160.0888.



4

3-methyleneisobenzofuran-1(3H)-one (4)

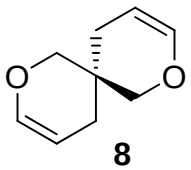
Brown oil.[1]H NMR (300 MHz, $CDCl_3$), δ (ppm): 7.92 (d, *J* = 7.6 Hz, 1H), 7.73 (d, *J* = 3.7 Hz, 2H), 7.63-7.54 (m, 1H), 5.24 (s, 2H). [13]C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 169.6 (C), 166.8 (C), 151.8 (C), 139.1 (C), 134.4 (CH), 130.4 (CH), 125.4 (CH), 120.6 (CH), 91.2 (CH_2). MS, m/z (% relative intensity): 147 (M^++1, 100), 131 (1), 103 (2). IR (KBr), cm^{-1}: 2924, 1774, 1657. HRMS (CI) calculated for $C_9H_7O_2$ [M^++1]: 147.0446; found: 147.0446.



6

2-hexyl-3,4-dihydro-2H-pyran (6)

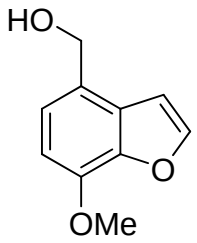
Dark brown oil.[1]H NMR (250 MHz, $CDCl_3$), δ (ppm): 6.33 (d, *J* = 6.2 Hz, 1H), 4.66-4.56 (m, 1H), 3.78-3.65 (m, 1H), 2.05-1.20 (m, 14H), 0.84 (t, *J* = 6.7 Hz, 3H). [13]C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 143.8 (CH), 100.4 (CH), 75.2 (CH), 35.3 (CH_2), 31.9 (CH_2), 29.3 (CH_2), 27.8 (CH_2), 25.3 (CH_2), 22.6 (CH_2), 19.9 (CH_2), 14.1 (CH_3). MS, m/z (% relative intensity): 169 (M^++1, 100), 151 (45), 141 (31), 137 (25), 123 (35), 109 (43), 97 (50), 83 (78), 71 (91). HRMS (CI) calculated for $C_{11}H_{21}O$ [M^++1]: 169.1592; found: 169.1592



8

(±)-2,8-dioxaspiro[5.5]undeca-3,9-diene (8)

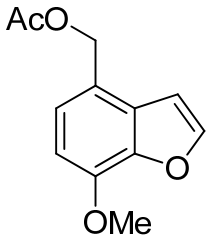
Brown oil. [1]H NMR (300 MHz, $CDCl_3$), δ (ppm): 6.36 (td, *J* = 6.1, 2.0 Hz, 2H), 4.67 (td, *J* = 6.1, 3.7 Hz, 2H), 3.82 (d, *J* = 10.7 Hz, 2H), 3.62 (d, *J* = 10.7 Hz, 2H), 1.82 (bs, 4H). [13]C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 143.3 (CH), 98.6 (CH), 69.2 (CH_2), 30.0 (C), 29.2 (CH_2). MS, m/z (% relative intensity): 153 (M^++1, 91), 175 (68), 123 (19), 107 (79), 97 (100). HRMS (CI) calculated for $C_9H_{13}O_2$ [M^++1]: 153.0916; found: 153.0916.



10a

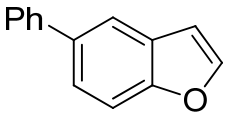
(7-methoxybenzofuran-4-yl)methanol (10a)

Yellowish solid (mp: 61-63ºC). ^{1}H NMR (250 MHz, $CDCl_3$), δ (ppm): 7.60 (d, *J* = 2.1 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.86 (d, *J* = 2.1 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 4.78 (s, 2H), 3.96 (s, 3H), 1.94 (s, 1H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 145.2 (C), 145.1 (CH), 144.3 (C), 127.7 (C), 125.8 (C), 122.3 (CH), 105.8 (CH), 105.5 (CH), 63.3 (CH_2), 56.0 (CH_3). MS, m/z (% relative intensity): 179 (M^++1, 45), 177 (37), 163 (93), 161 (100), 149 (35). HRMS (EI) calculated for $C_{10}H_{10}O_3$ [M^+]: 178.0630; found: 178.0630.



(7-methoxybenzofuran-4-yl)methyl acetate

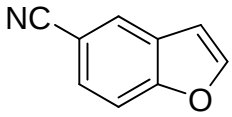
^{1}H NMR (250 MHz, $CDCl_3$), δ (ppm): 7.67 (d, *J* = 2.1 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 6.87 (d, *J* = 2.1 Hz, 1H), 6.78 (d, *J* = 8.1 Hz, 1H), 5.29 (s, 2H), 4.02 (s, 3H), 2.09 (s, 3H).



10b

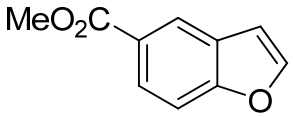
5-phenylbenzofuran (10b)

White solid (mp: 58-60ºC). ^{1}H NMR (400 MHz, *$CDCl_3$*), δ (ppm): 7.81-7.79 (bs, 1H), 7.66 (d, *J* = 2.2 Hz, 1H), 7.64 (t, *J* = 1.6 Hz, 1H), 7.62 (d, *J* = 0.9 Hz, 1H), 7.59-7.52 (m, *J* = 8.55, 2H), 7.48-7.43 (m, 2H), 7.36 (dd, *J* = 4.84, 3.60 Hz, 1H), 6.83 (dd, *J* = 2.17, 0.88 Hz, 1H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$) ,δ (ppm): 154.5 (C), 145.5 (CH), 141.6 (C), 136.5 (C), 128.7 (2xCH), 128.0 (C), 127.4 (2xCH), 126.8 (CH), 123.9 (CH), 119.7 (CH), 111.5 (CH), 106.8 (CH). MS, m/z (% relative intensity): 195 (M^++1, 100), 194 (9). HRMS (CI) calculated for $C_{14}H_{11}O$ [M^++1]: 195.0810; found: 195.0810.



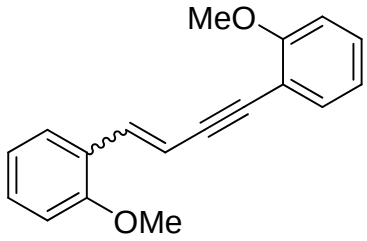
10c

1-benzofuran-5-carbonitrile (10c)
White solid (mp: 81-82ºC). ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.95 (s, 1H), 7.74 (d, *J* = 2.2 Hz, 1H), 7.65-7.47 (bs, 2H), 6.84 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 156.4 (C), 147.1 (CH), 128.0 (C), 127.9 (CH), 126.3 (CH), 119.4 (C), 112.6 (CH), 106.7 (C), 106.6 (CH). MS, m/z (% relative intensity): 144 (M^++1, 100), 137 (30), 123 (46), 109 (62), 95 (74), 83 (98). HRMS (CI) calculated for C_9H_6NO [M^++1]: 144.0449; found: 144.0449.



10d

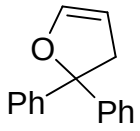
Methyl benzofuran-5-carboxylate (10d)
Yellow solid (mp: 69-70ºC). ^{1}H NMR (250 MHz, $CDCl_3$), δ (ppm): 8.35 (d, *J* = 1.3 Hz, 1H), 8.03 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.68 (d, *J* = 2.1 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 6.84 (d, *J* = 1.3 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 167.2 (CO), 157.4 (C), 146.2 (CH), 127.5 (C), 126.0 (CH), 125.1 (C), 123.7 (CH), 111.2 (CH), 107.1 (CH), 52.1 (CH_3). MS, m/z, (% relative intensity): 177 (M^++1, 100), 145 (7), 133 (5), 105 (5). HRMS (ESI) calculated for $C_{10}H_9O_3$ [M^++1]: 177.0552; found: 177.0552.



12

1,1'-but-1-en-3-yne-1,4-diylbis(2-methoxybenzene) (12)[7]
Dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.44 (td, *J* = 7.6, 1.5 Hz), 7.36 (d, *J* = 16.4 Hz), 7.29-7.22 (m), 7.16 (dd, *J* = 13.4, 6.2 Hz), 7.06 (t, *J* = 7.31), 6.97-6.84 (m), 6.53 (d, *J* = 16.4 Hz), 5.98 (d, *J* = 12.1 Hz), 3.90 (s), 3.86 (s). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 159.7 (C), 157.0 (C), 136.3 (CH), 133.5 (CH), 133.4 (CH), 129.5 (CH), 129.4 (CH), 128.2 (CH), 126.8 (CH), 125.5 (C), 120.7 (CH), 120.5 (CH), 120.2 (CH), 112.8 (C), 111.0 (CH), 110.6 (CH), 109.0 (CH), 93.8 (C), 87.5 (C), 85.1 (CH), 55.8 (CH_3), 55.4 (CH_3). MS, m/z (% relative intensity): 265 (M^++1, 100), 250 (7), 135 (5), 121 (10'), 109 (6).

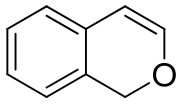
[7] Bassetti, M.; Pasquini, C.; Raneri, A.; Rosato, D. *J. Org. Chem*. **2007**, *72*, 4558



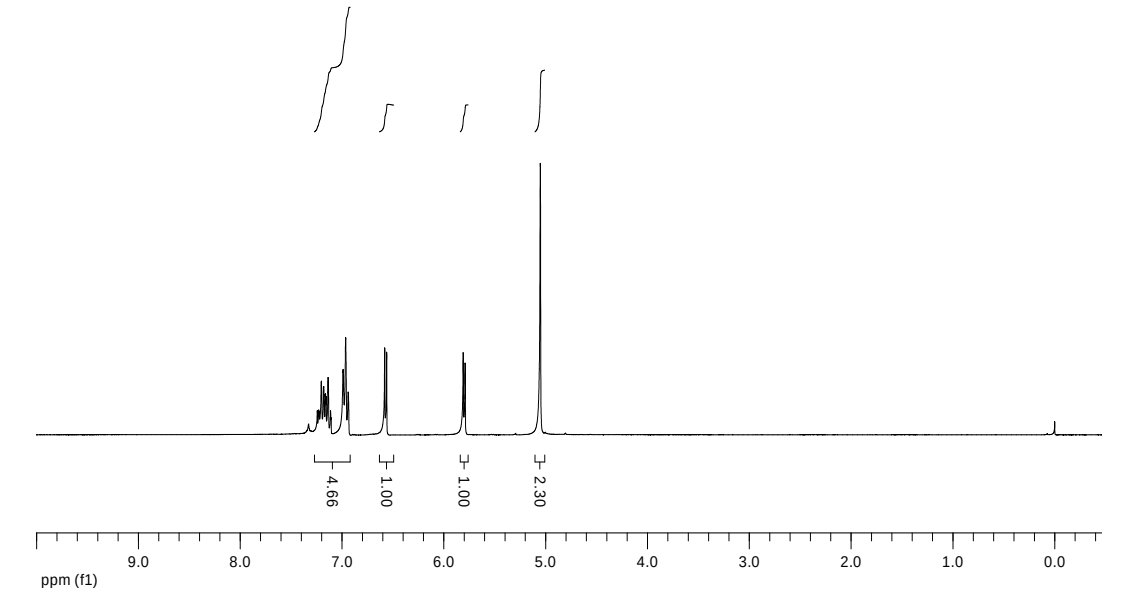
2,2-diphenyl-2,3-dihydrofuran

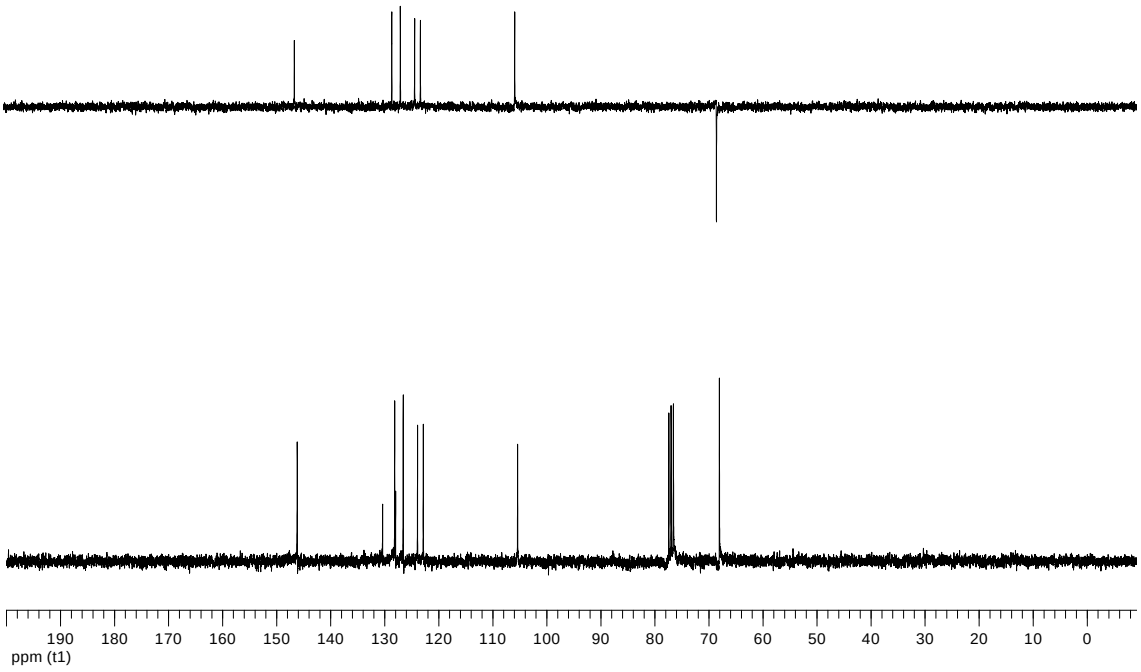
White oil. ^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.60-7.08 (m, 10H), 6.51 (d, *J* = 2.8 Hz, 1H), 5.00-4.89 (m, 1H), 3.33 (t, *J* = 2.4, 2H). ^{13}C NMR, DEPT (75 MHz, $CDCl_3$), δ (ppm): 146.2 (CH), 144.2 (2xC), 128.2 (4xCH), 127.1 (2xCH), 125.8 (4xCH), 99.0 (CH), 90.8 (C), 43.8 (CH_2). MS, m/z (% relative intensity): 223 (M^++1, 94), 205 (83), 193 (15), 145 (100), 105 (40). HRMS (ESI) calculated for $C_{16}H_{15}O$ [M^++1]: 223.1113; found: 223.1117.

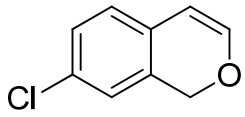
VII. Spectra



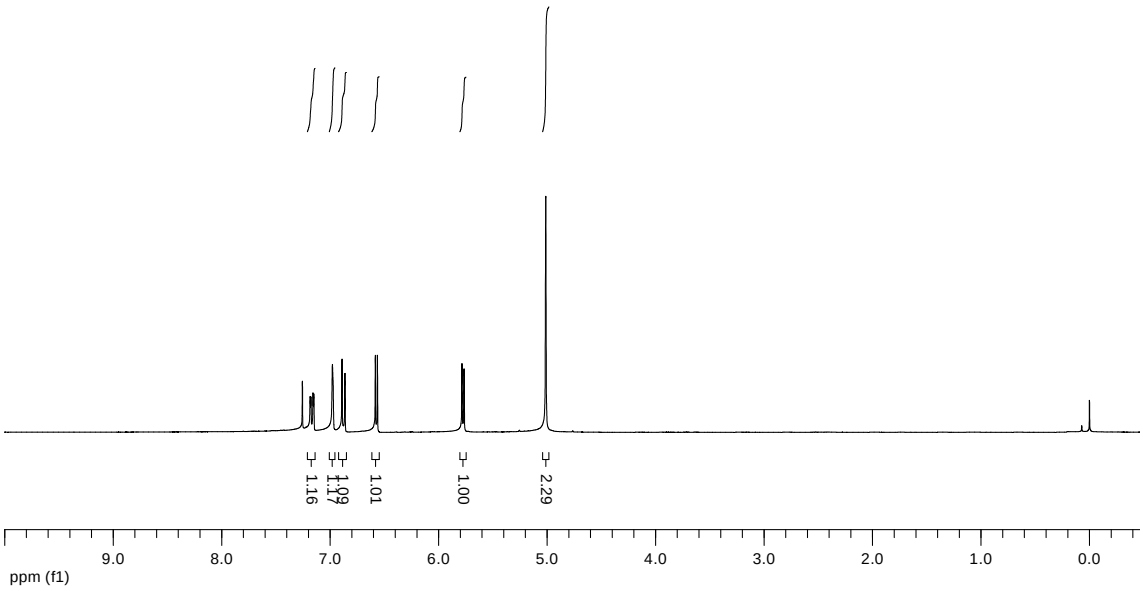
2a

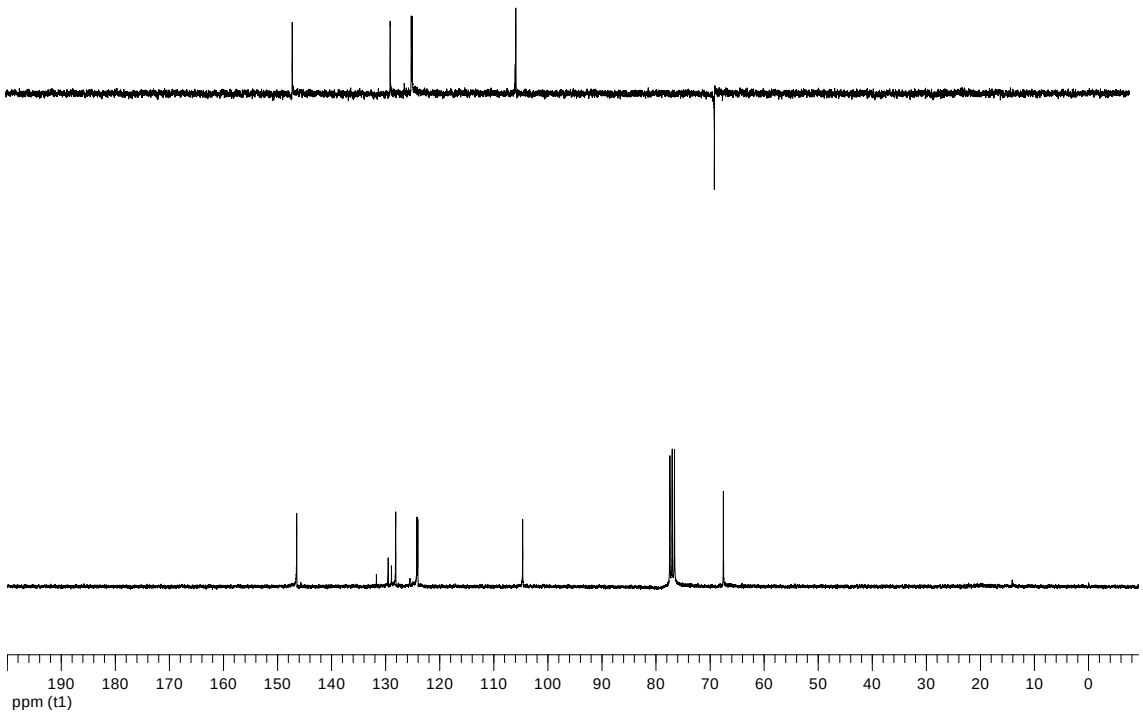


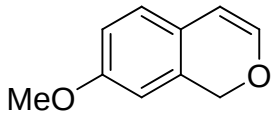



Cl
O

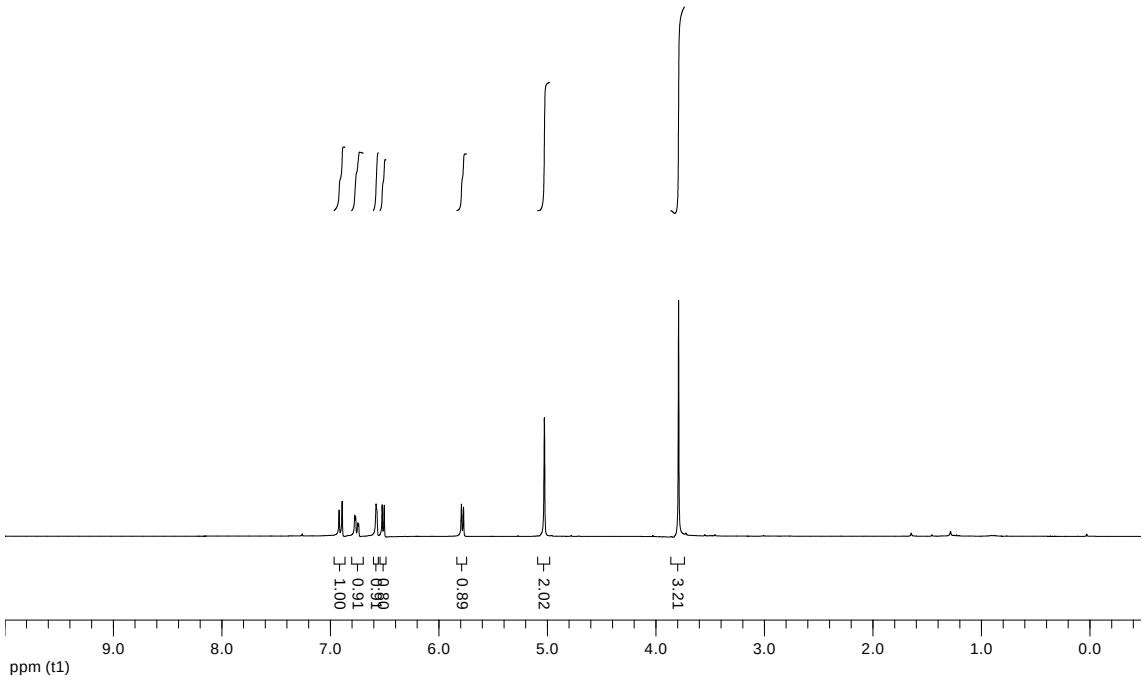
2b

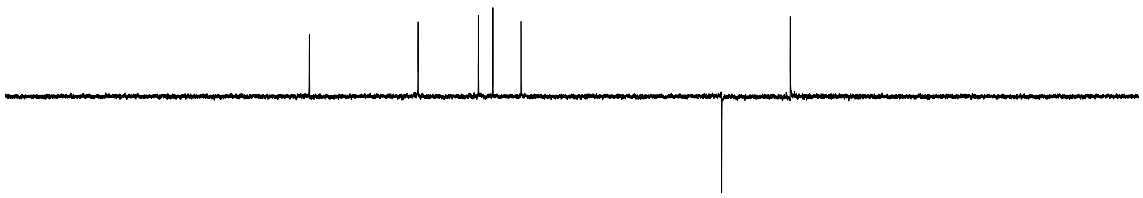

1.16
1.17
1.09
1.01
1.00
2.29
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

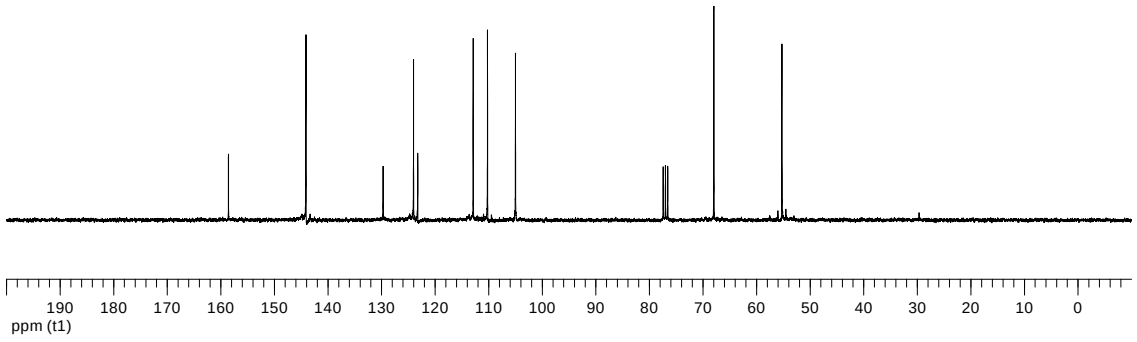

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

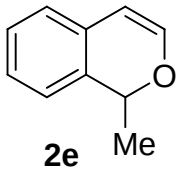

MeO
O

2c

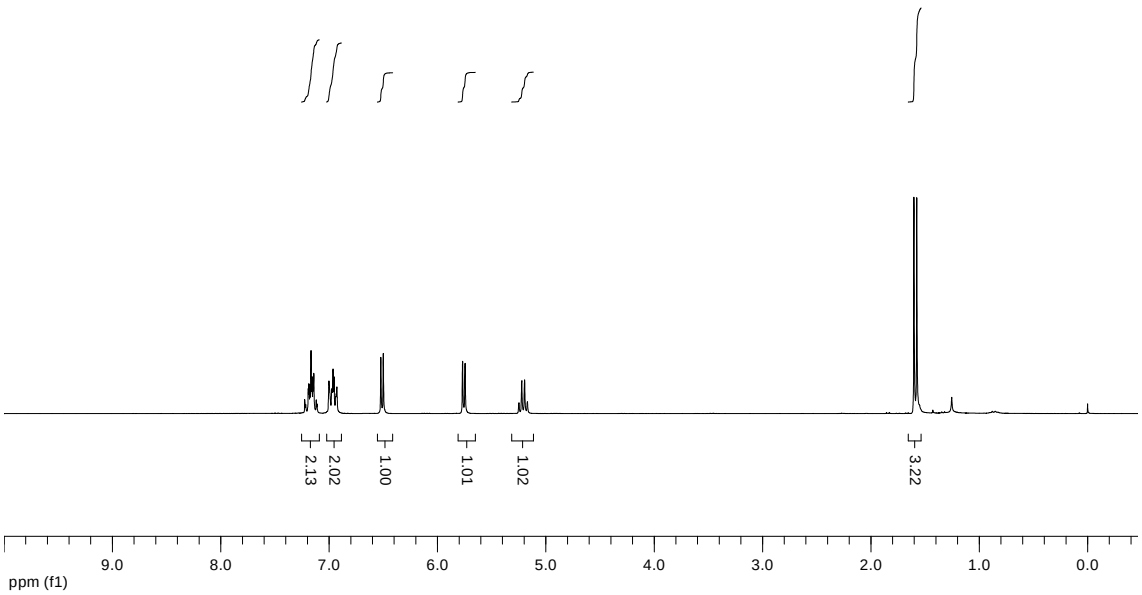

1.00
0.91
0.89
2.02
3.21
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

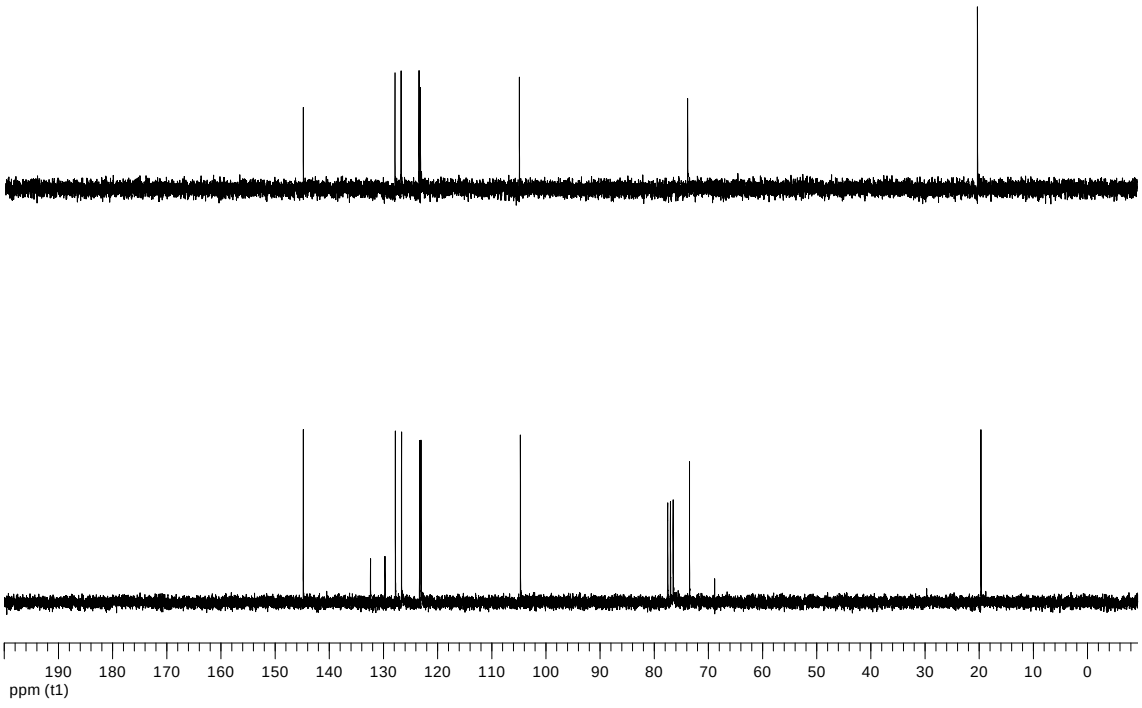


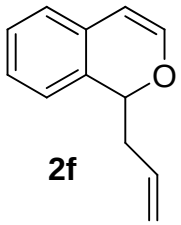

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)


O
Me

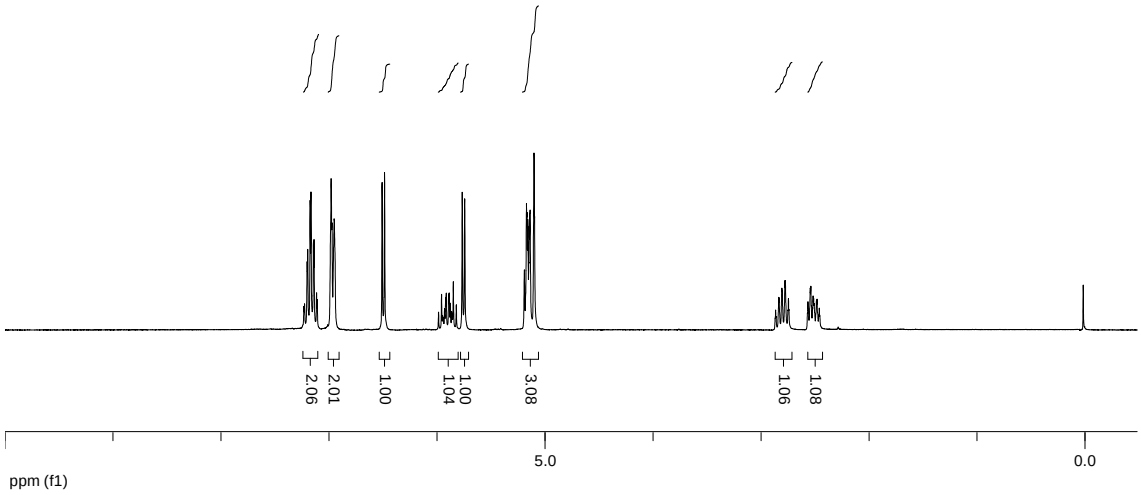
2e

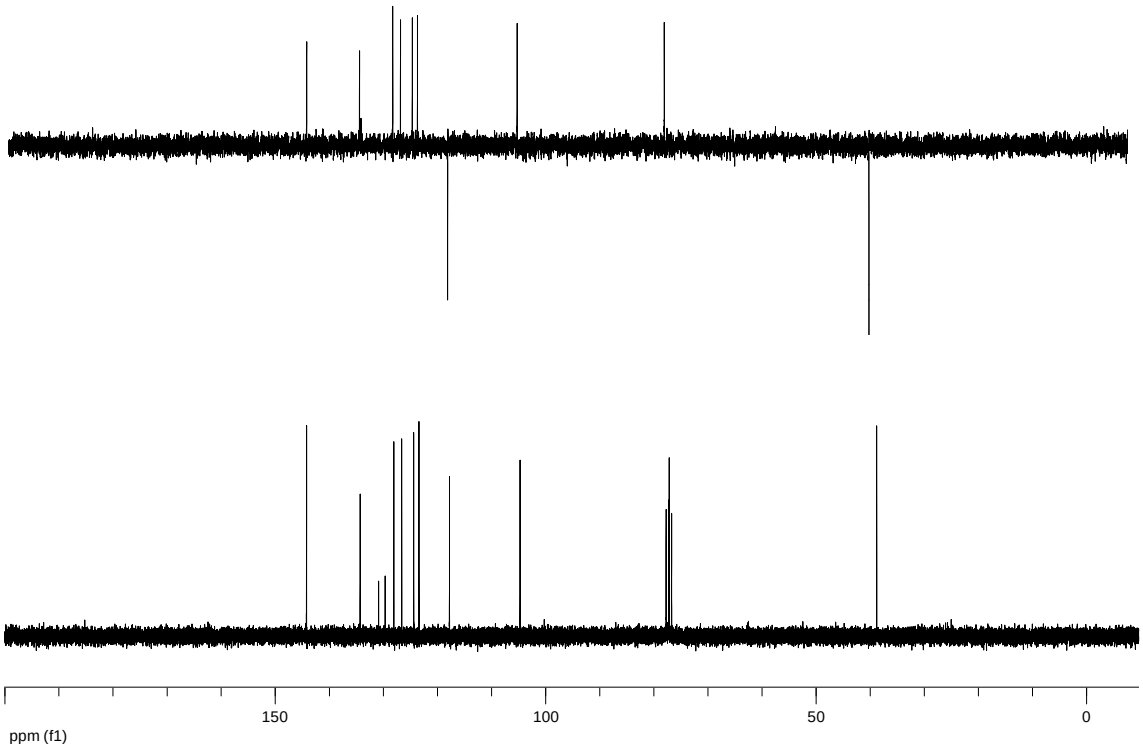

2.13
2.02
1.00
1.01
1.02
3.22
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

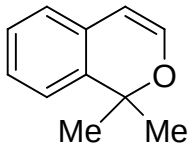

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)



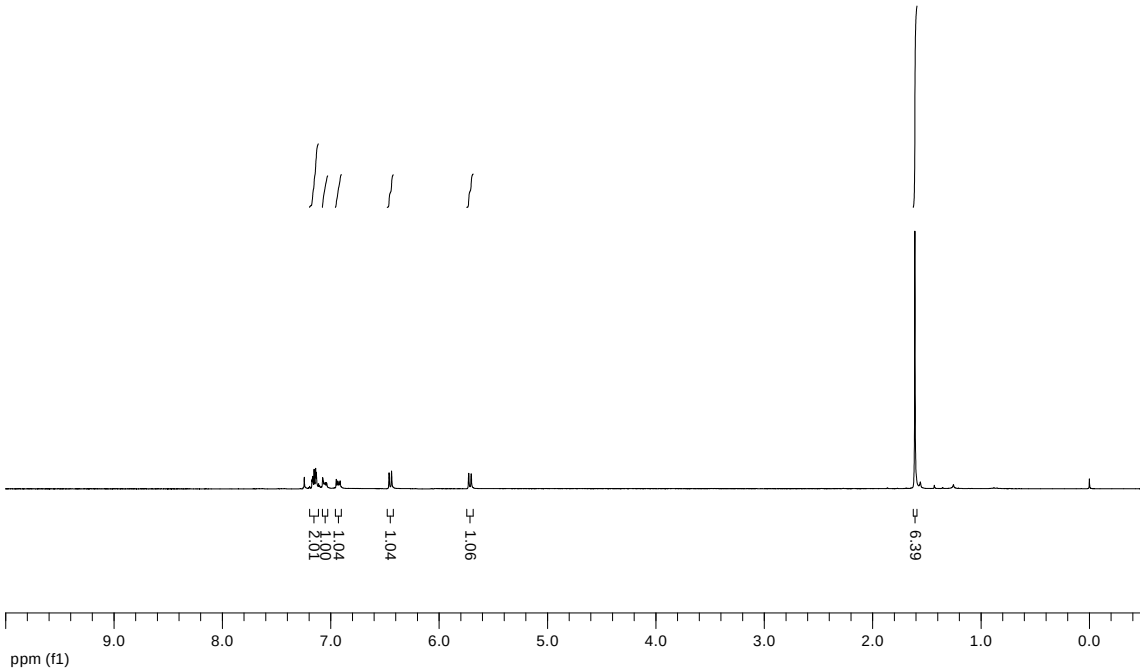
2f

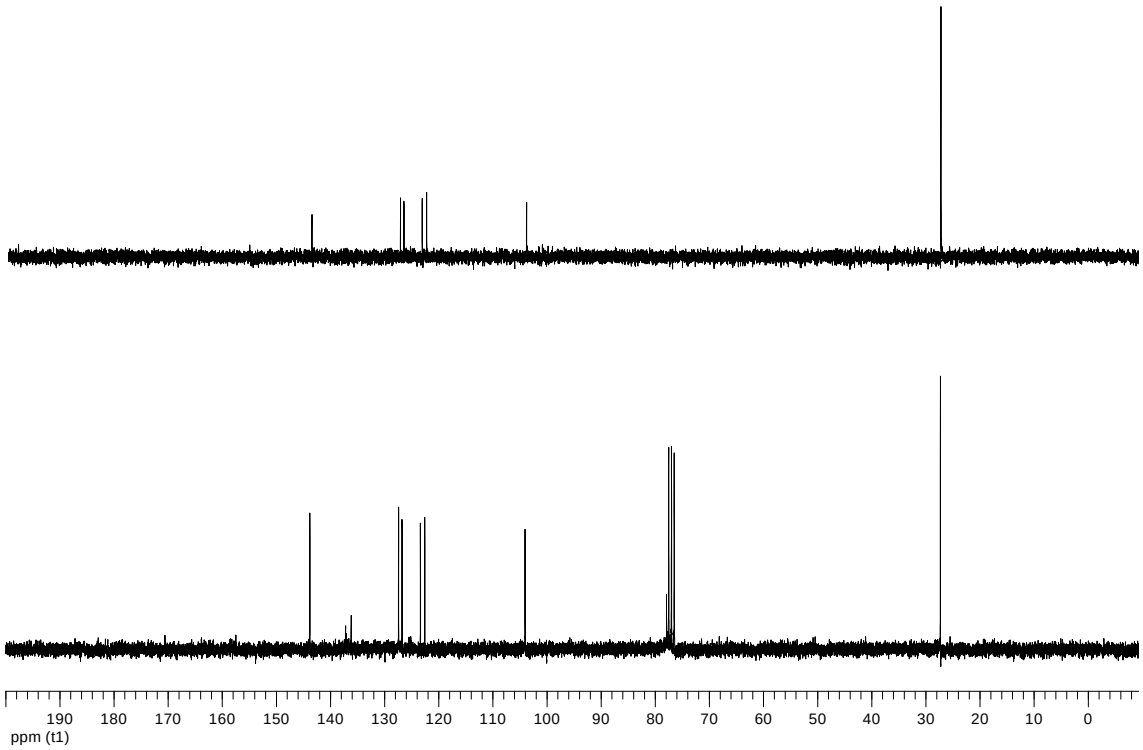


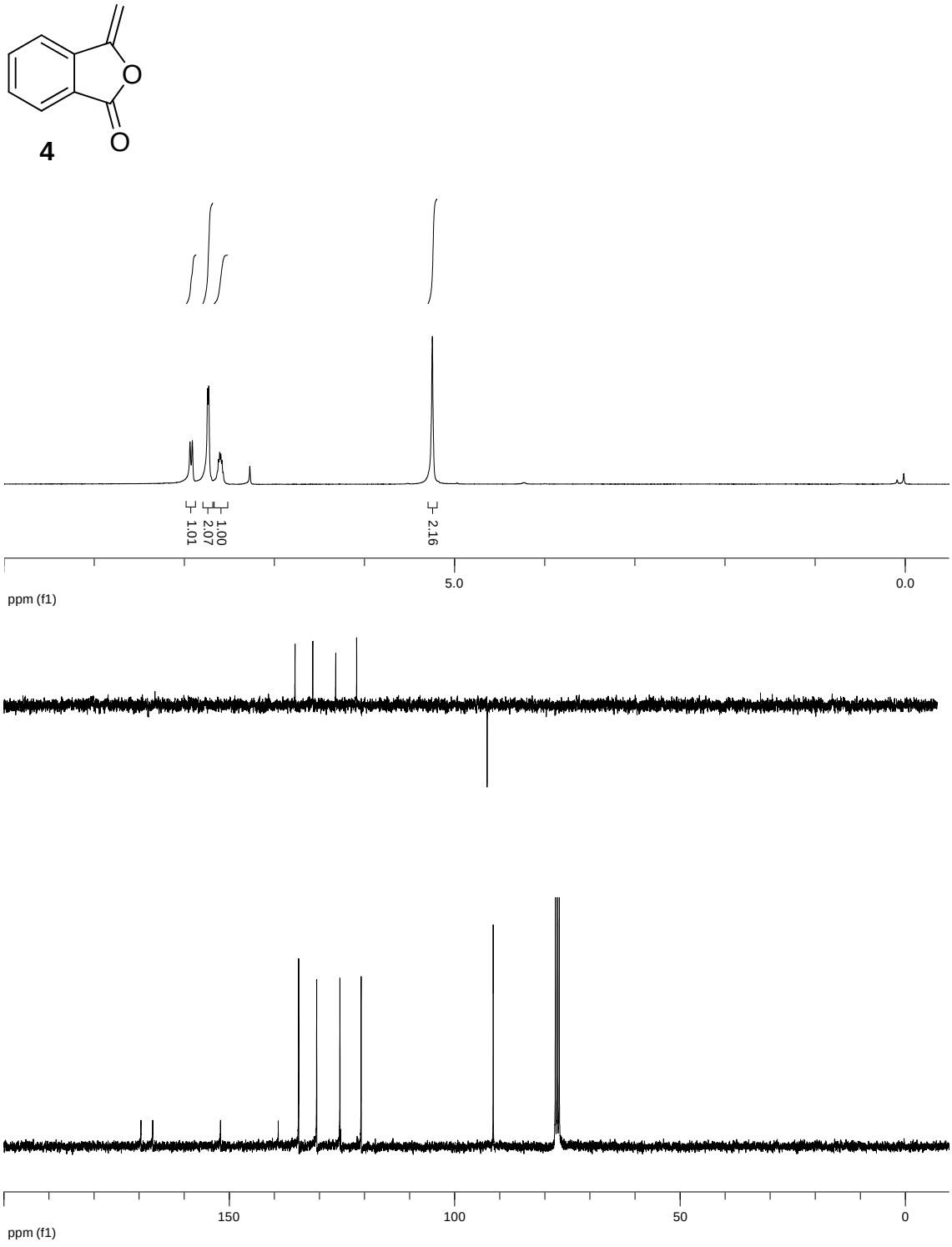


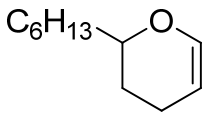

O
Me
Me

2g

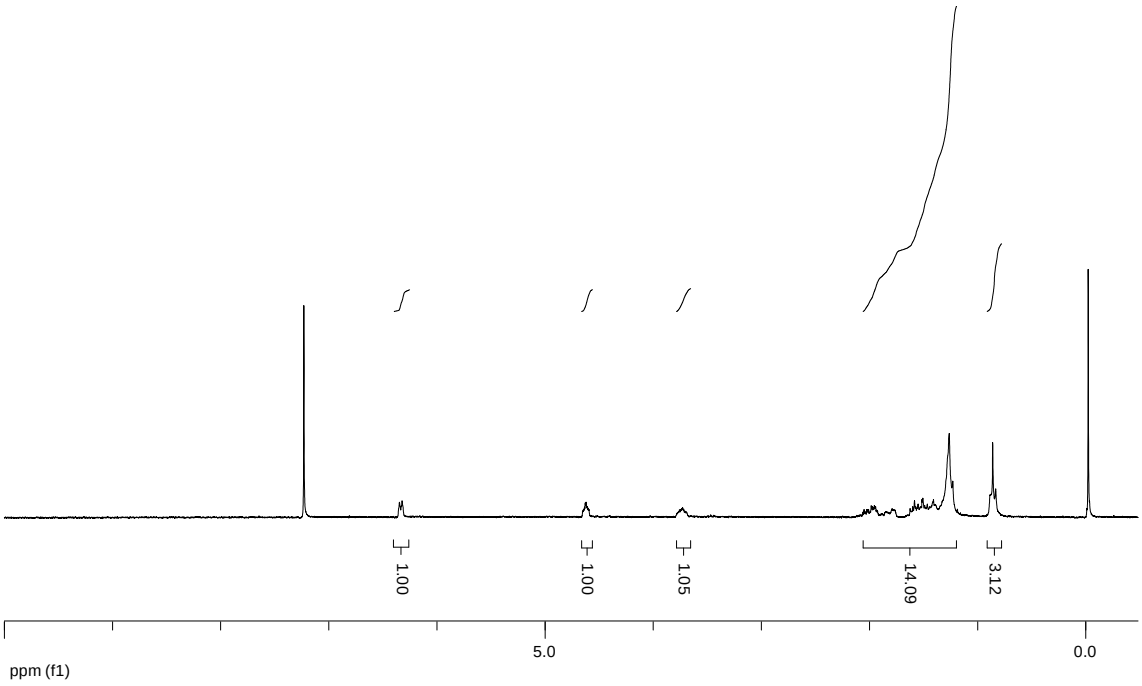

2.01
1.00
1.04
1.04
1.06
6.39
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)

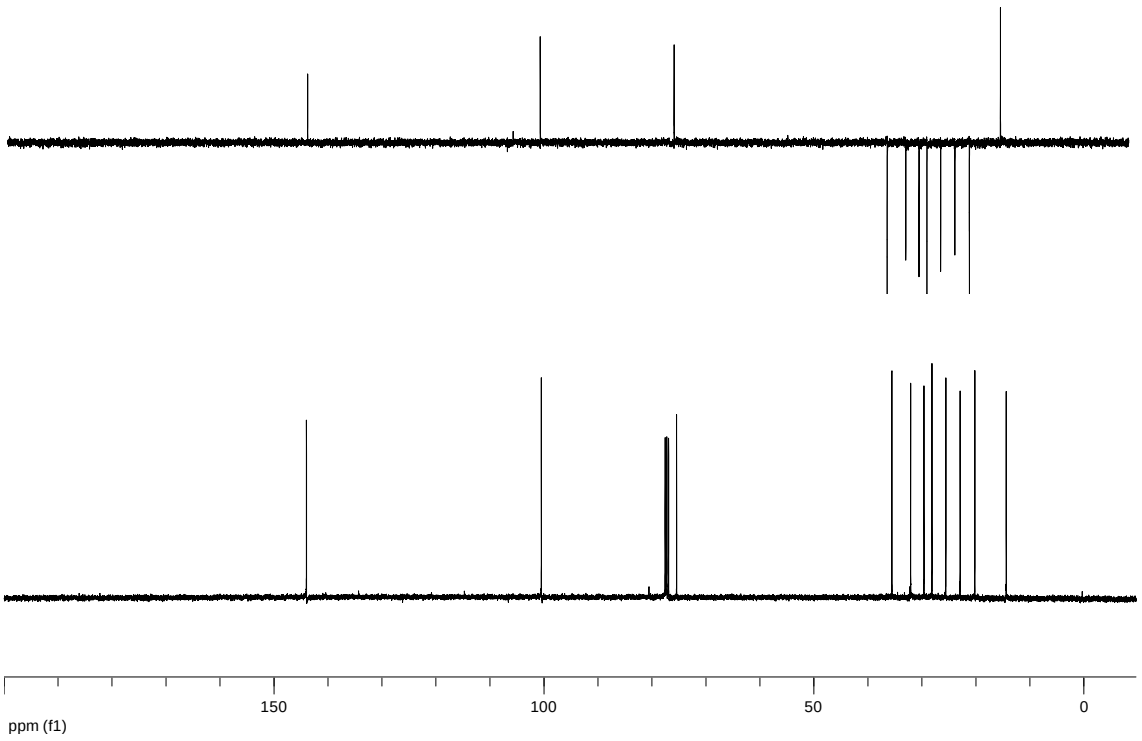

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

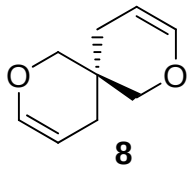

O
O
4
1.01
2.07
1.00
2.16
5.0
0.0
ppm (f1)
150
100
50
0
ppm (f1)



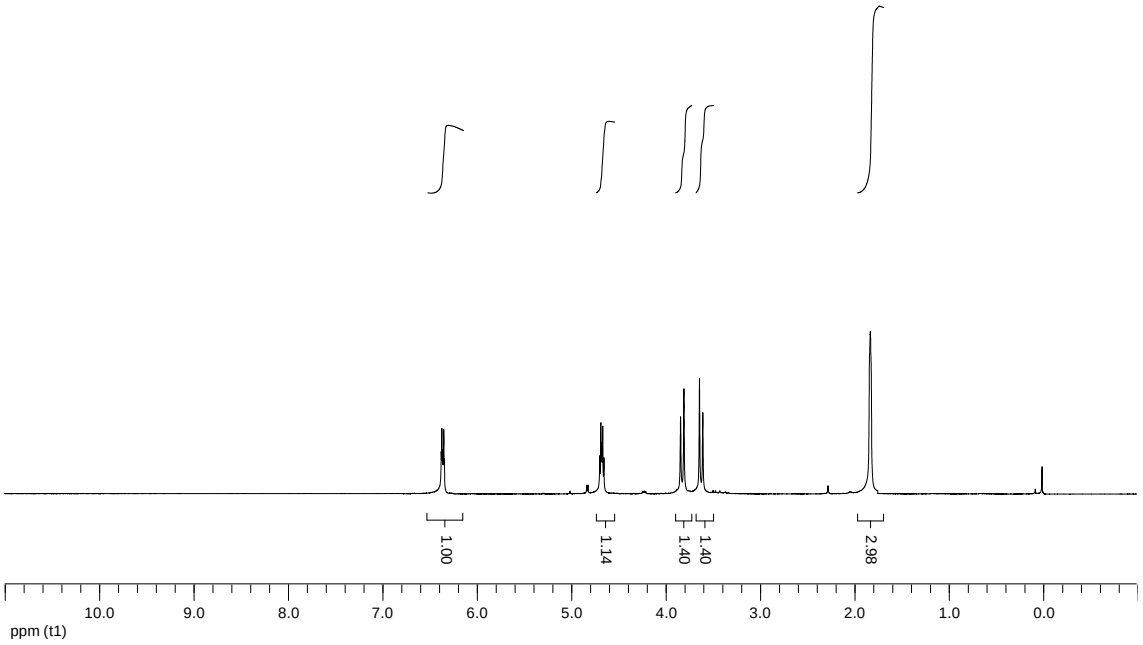
6

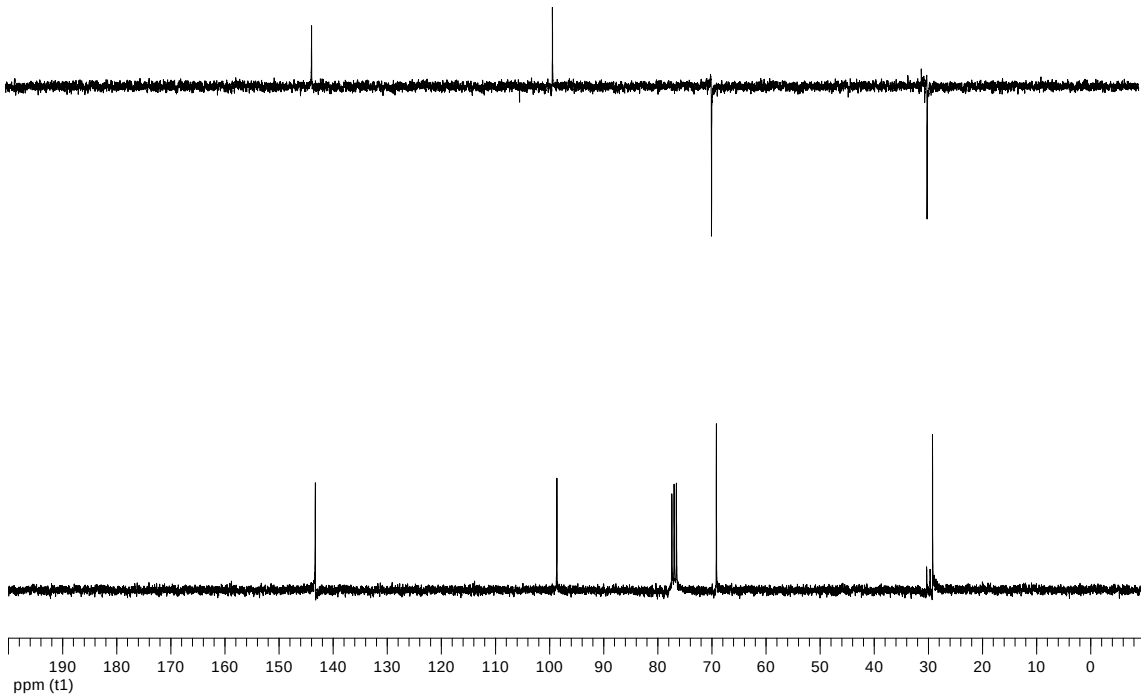


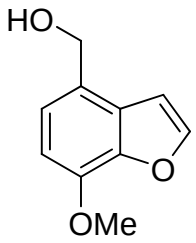



O
O

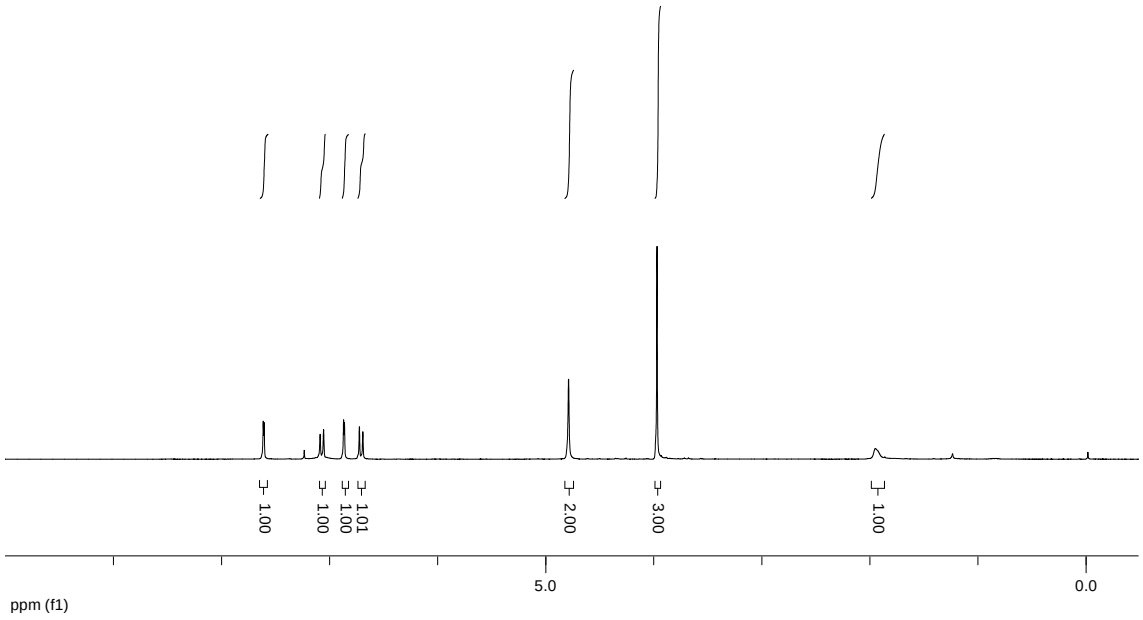
8

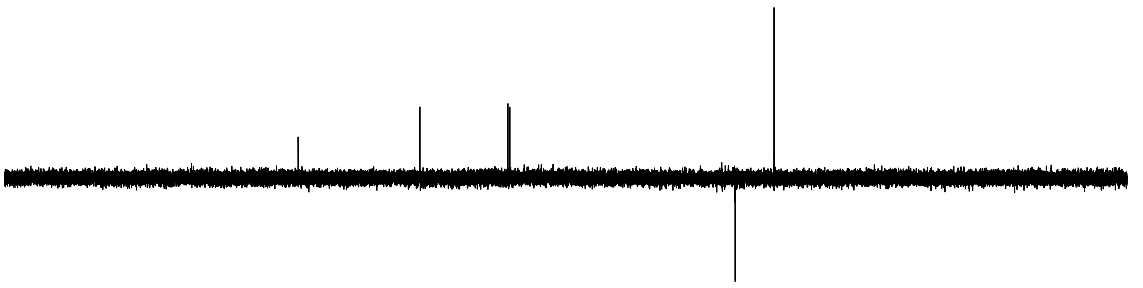

1.00
1.14
1.40
1.40
2.98
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

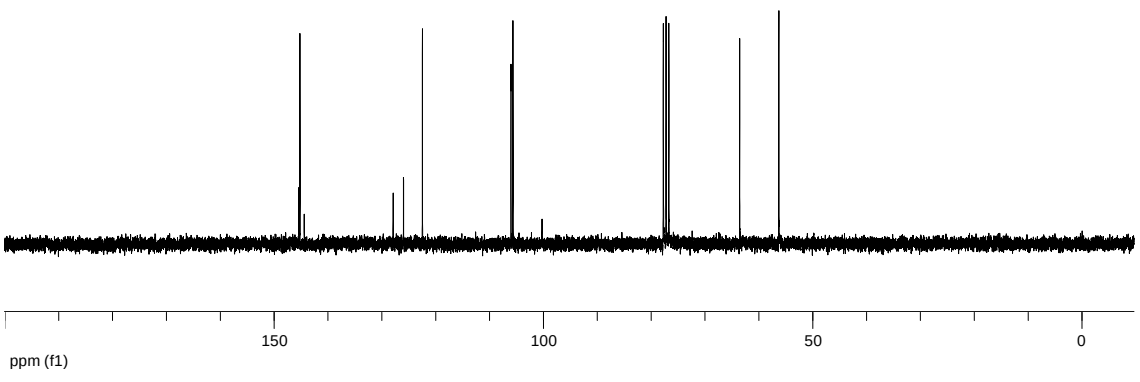

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

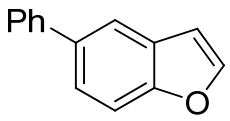

HO
O
OMe

10a

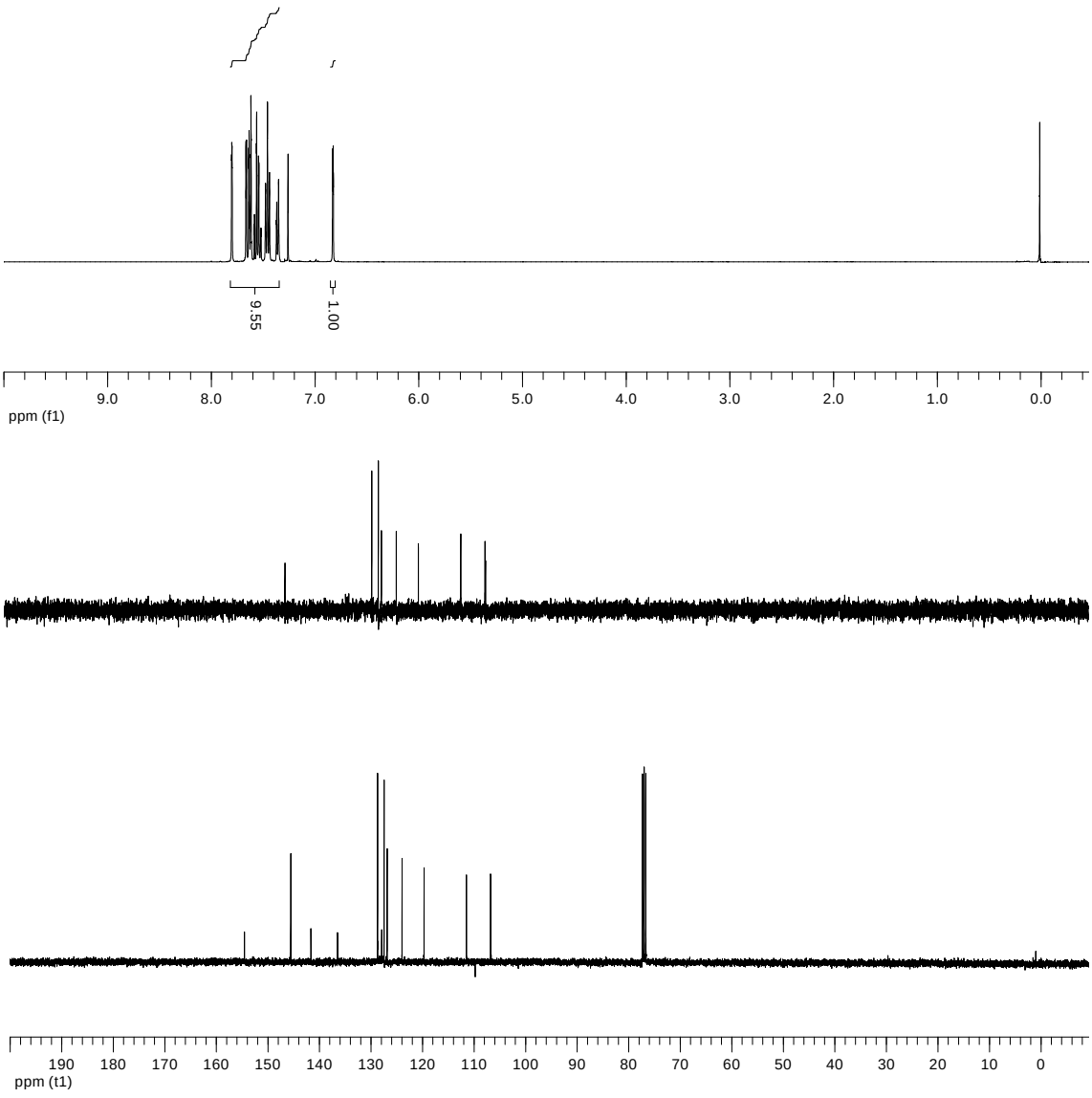

1.00
1.00
1.00
1.01
2.00
3.00
1.00
5.0
0.0
ppm (f1)

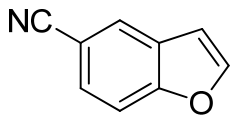



150
100
50
0
ppm (f1)

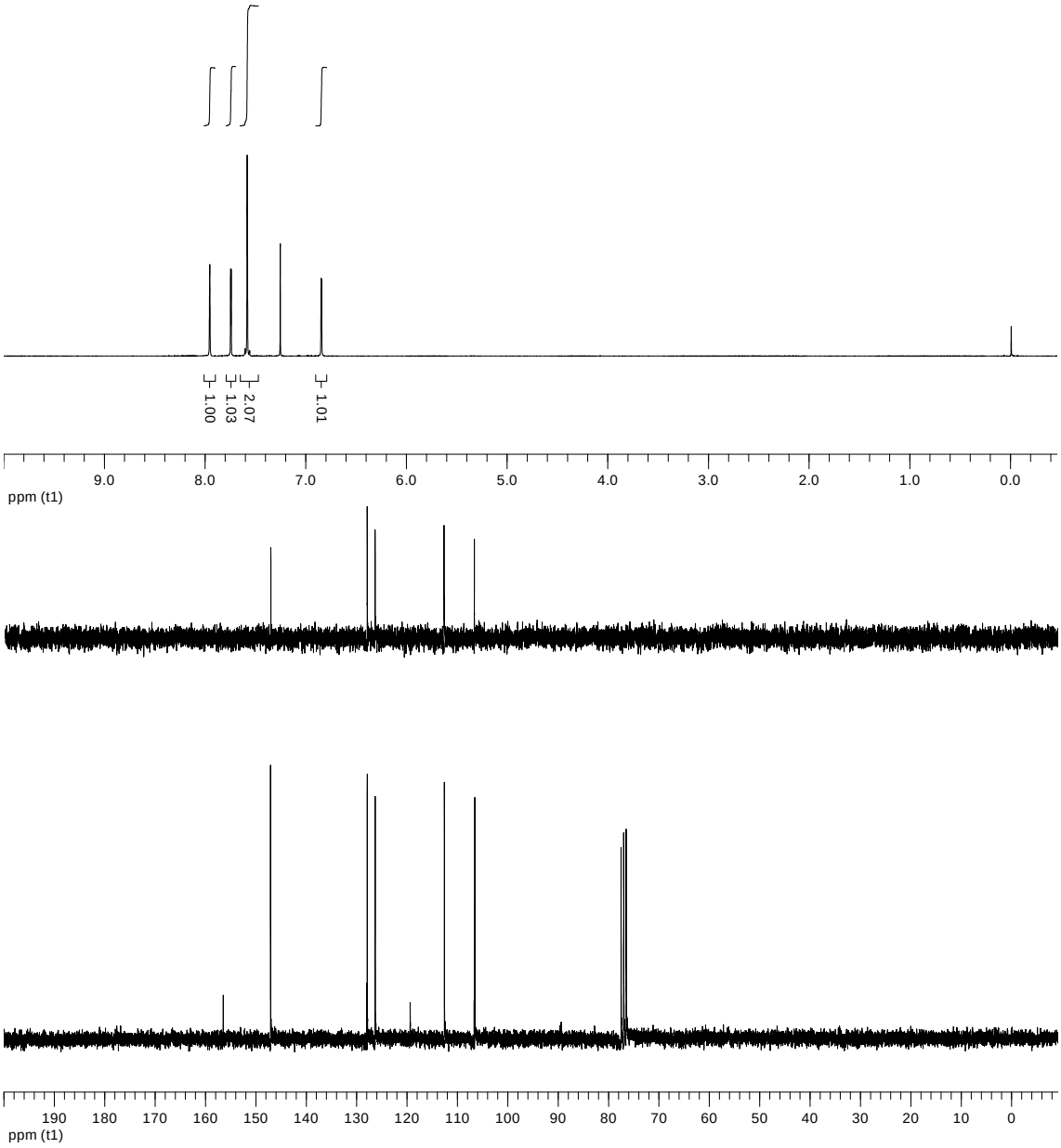

Ph
O

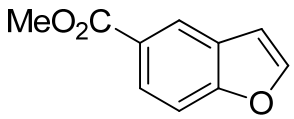
10b


9.55
1.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

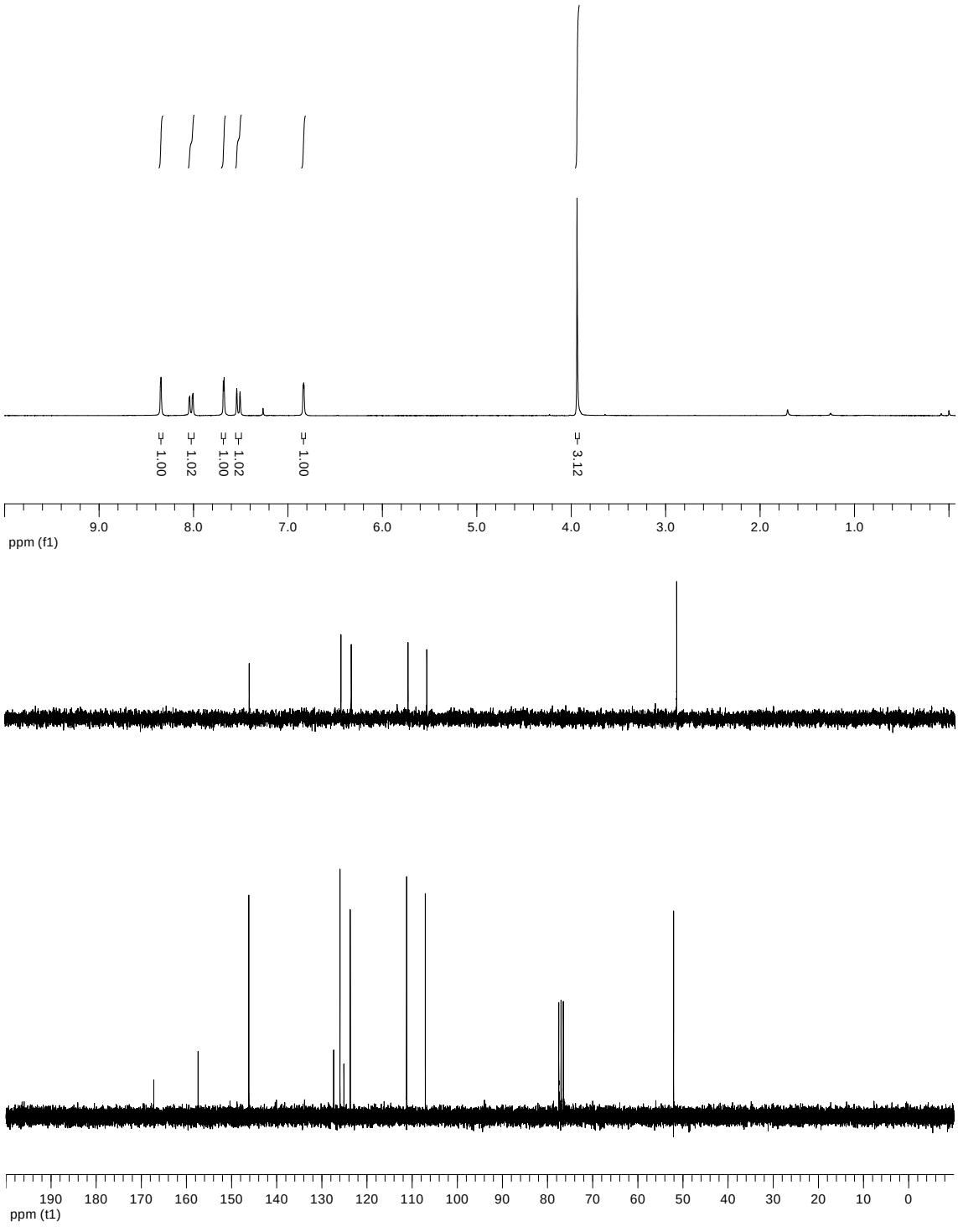

NC
O

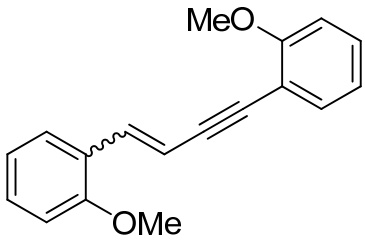
10c


1.00
1.03
2.07
1.01
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

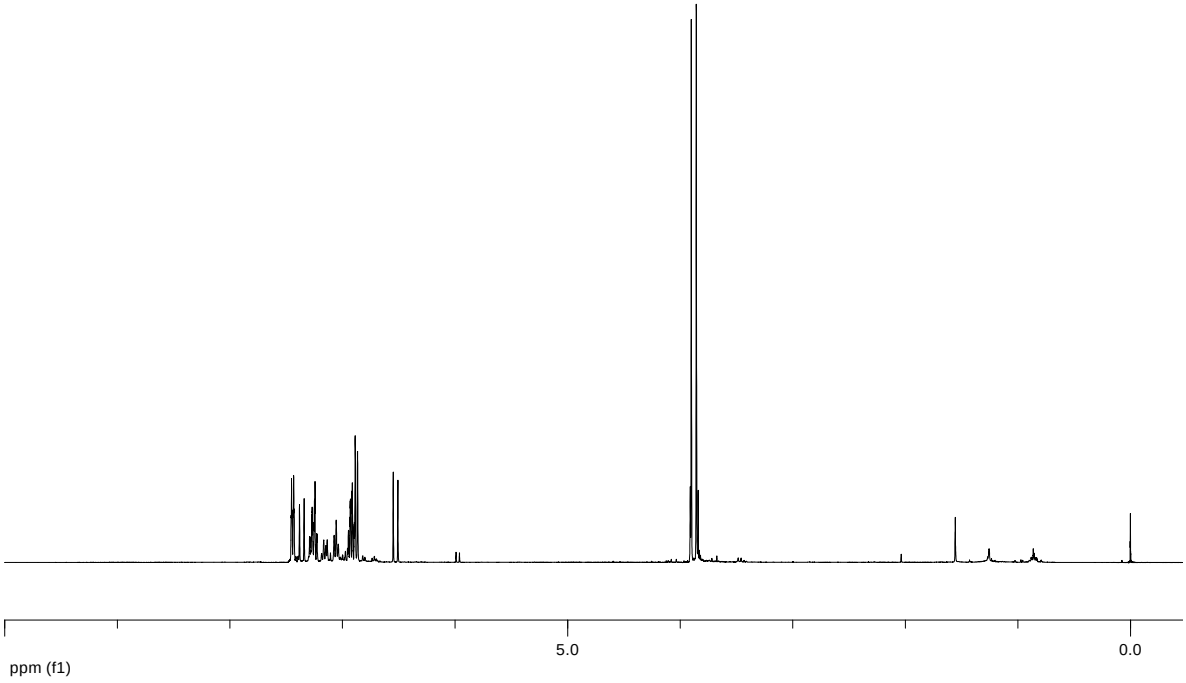

MeO2C
O

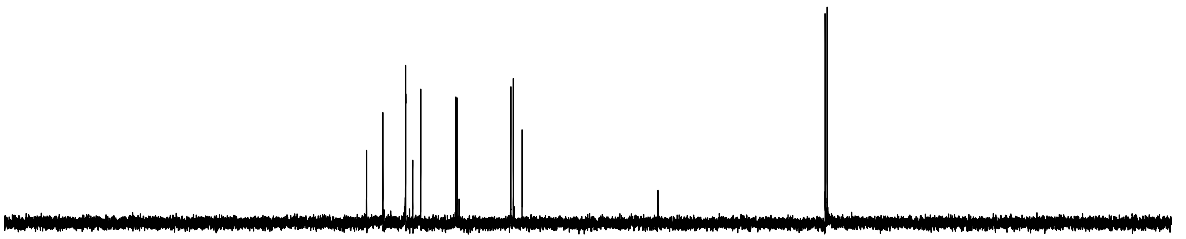
10d

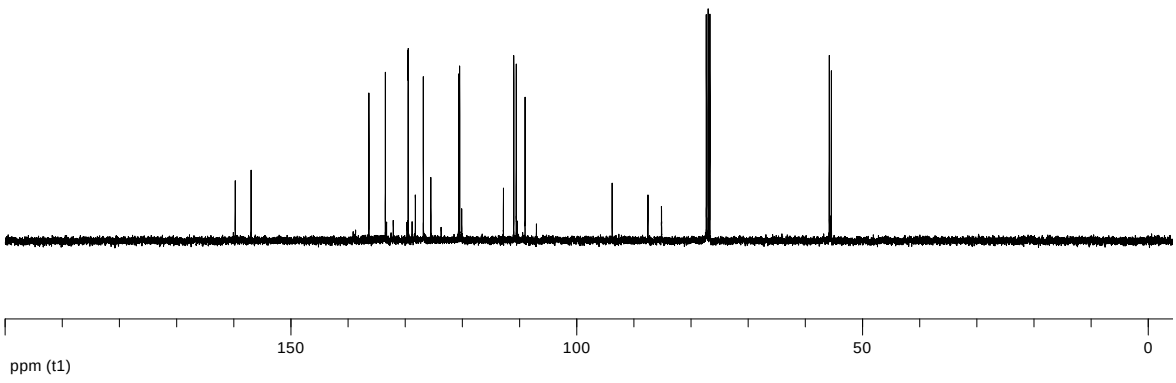

1.00
1.02
1.00
1.02
1.00
3.12
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)

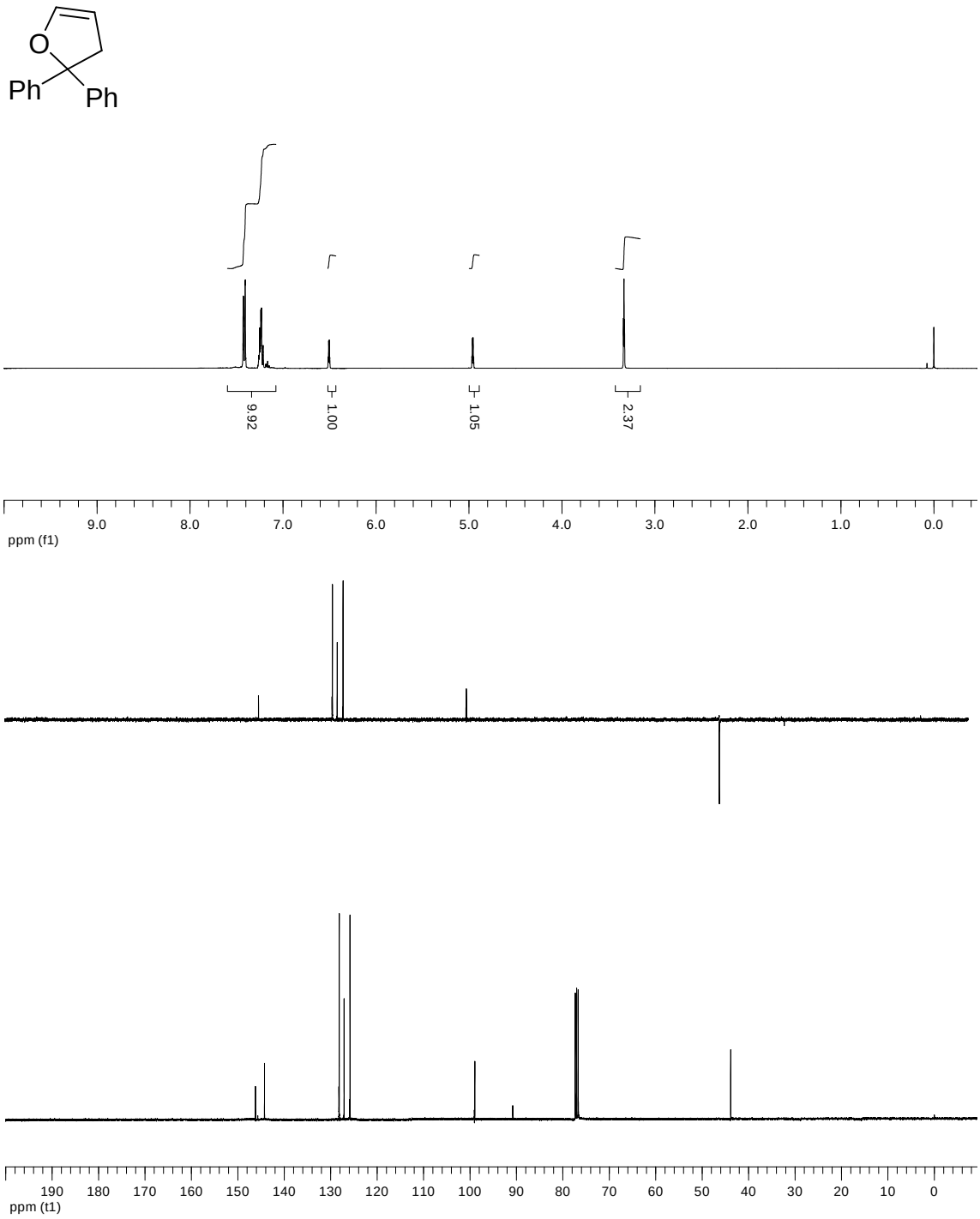


12 (E/Z: 9/1)








O
Ph
Ph
9.92
1.00
1.05
2.37
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm (t1)