# One-Carbon Homologation of Primary Alcohols to Carboxylic Acids, Esters, and Amides via Mitsunobu Reactions with MAC Reagents

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## General Information

Reactions were run in oven-dried glassware under a nitrogen atmosphere. Reactions were monitored by thin-layer chromatography (TLC) on EMD Millipore silica gel 60 Å F254 plates or Merck silica gel 60 $F_{254}$ plates, visualized by UV florescence quenching (254 nm), $I_2/SiO_2$, PMA, Seebach's stain, or Hanessian's staining solution. Ambient temperature refers to 18–23 °C. Lower temperatures were maintained using ice/water bath (0 °C) or an EYELA PSL-2500A (−40 to 0 °C) bath. Flash column chromatography (EtOAc/Hexanes, MeOH/$CH_2Cl_2$, or MeOH/$CHCl_3$) was performed on SiliCycle SiliaFlash (40-63 μm) or Cica 60 (spherical/ 63–210 μm) silica gel. Recycling preparative HPLC was performed on a JAI LC-9201 with a JAIGEL-1H and JAIGEL-2H GPC column (600 mm x 20 mm), equipped with a guard column and employing chloroform. NMR spectra were measured on Bruker DRX, DMX, or SMP spectrometers at 500 MHz for $^1$H spectra and 125 MHz for $^{13}$C spectra, or JEOL JNM–ECA600 at 600 MHz for $^1$H spectra and 150 MHz for $^{13}$C spectra. $^1$H spectra were calibrated from internal standard TMS (δ 0.0) or solvent resonance ($CHCl_3$: 7.26). $^{13}$C spectra were calibrated from solvent resonance ($CHCl_3$: 77.0). NMR data are reported as: chemical shift (parts per million, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), and integration. Infrared spectra were recorded on a Jasco FT/IR-4700 spectrometer with Smiths DuraSampl*IR* II (ATR) and reported in frequency of absorption ($cm^{-1}$). High-resolution mass spectral analyses using electrospray ionization (ESI) were measured on an Agilent Technologies 6224 TOF LC/MS or a JEOL JMS-T100 AccuTOF LC-plus. High-resolution mass spectra using fast atom bombardment (FAB) or electron ionization (EI) were reported at Kyoto Institute of Technology, Kyoto, on a JEOL JMS-700 Mstation, or at JEOL Ltd., Tokyo, on a JEOL JMS-700V. Gas chromatography mass spectral analysis was measured on a Varian Saturn 2200 GC-MS-MS. Optical rotations were measured on a Jasco P-2200 polarimeter using 50 mm path-length cell.

## Materials

Tetrahydrofuran (THF) and methylene chloride ($CH_2Cl_2$) were purified by passage over activated alumina, using an Innovative Technology, Inc. Puresolv solvent purification system. Anhydrous THF was also purchased from Wako Pure Chemical Industries, Ltd. Anhydrous MeOH, DME and $CH_2Cl_2$ were purchased from Kanto Chemical Co., Inc. All other solvents were purchased from Fisher Scientific and used as received. All commercially obtained reagents were used as received. Substrate alcohols were acquired commercially. DIAD, DMEAD and $PPh_3$ were purchased from Sigma-Aldrich and Tokyo Chemical Industry Co., Ltd. MOM-MAC **2a** was synthesized according to previously published procedures.[1] Ac-MAC **2b** was both synthesized[2] and commercially available

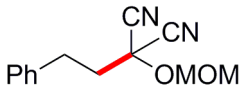
[1] Yang, K. S.; Nibbs, A. E.; Türkmen, Y. E.; Rawal, V. H. *J. Am. Chem. Soc.* **2013**, *135*, 16050-16053
[2] Nemoto, H.; Li, X.; Ma, R.; Suzuki, I.; Shibuya, M. *Tetrahedron. Lett.* **2003**, *44*, 73-75.

from Masuda Chemical Industries Co., Ltd. (*Z*)-2-iodobut-2-en-1-ol [3] and 2-(3',3'-dimethyl-6-nitrospiro[chromene-2,2'-indolin]-1'-yl)ethan-1-ol [4] were prepared according to literature procedure.

**General Procedure for Mitsunobu Homologation Reaction**

To an oven-dried two-neck round bottom flask was added a stir bar, $PPh_3$ (115 mg, 0.44 mmol), and solvent (2 mL). The flask was capped with a septum and connected to a $N_2$ atmosphere. The mixture was cooled with an ice/water bath, and DIAD (0.44 mmol) was added. The mixture was allowed to stir for 30 min, then ROH (0.44 mmol) was added in one portion. After an additional 30 min, the MAC reagent (50 mg, 0.4 mmol) was added. The ice/water bath was allowed to warm to ambient temperature, and the reaction was monitored by TLC. After the MAC reagent was consumed, the reaction mixture was concentrated in vacuo. The residue was purified by flash column chromatography to afford the desired homologated product.

**Mitsunobu Homologation Products**




**3a**

**2-(Methoxymethoxy)-2-phenethylmalononitrile** (**3a**): Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), phenethyl alcohol (53 μL, 0.44 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 24 h. Purification by flash column chromatography ($SiO_2$, 15% EtOAc/Hexanes) afforded **3a** (75 mg, 82%) as a pale yellow (almost-colorless) oil.

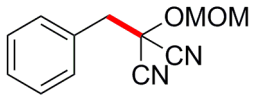
Analytical data for **3a**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.33 (t, *J* = 7.8 Hz, 2H), 7.26 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 5.07 (s, 2H), 3.56 (s, 3H), 2.99 – 2.96 (m, 2H), 2.52 – 2.49 (m, 2H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 138.1, 128.8 (x2), 128.4 (x2), 126.9, 113.1 (x2), 96.2, 65.3, 57.4, 41.7, 29.8

**IR** (ATR): 1455, 1164, 1090, 1031, 985, 925, 754, 699

**HRMS** (FAB) calcd for $(C_{13}H_{14}O_2N_2)^+$ $[M]^+$: 230.1055. Found: 230.1061

[3] Wanner, M. J.; Boots, R. N. A.; Eradus, B.; de Gelder, R.; van Maarseveen, J. H.; Hiemstra, H. *Org. Lett.* **2009**, *11*, 2579-2581.
[4] Raymo, F. M.; Giordani, S. *J. Org. Chem.* **2003**, *68*, 4158-4169.




**3b**

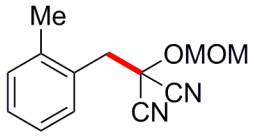
**2-Benzyl-2-(methoxymethoxy)malononitrile** (**3b**): Prepared according to the general procedure using $PPh_3$ (164 mg, 0.63 mmol), THF (2.5 mL), DIAD (123 μL, 0.63 mmol), benzyl alcohol (65 μL, 0.63 mmol), and MOM-MAC (52.7 mg, 0.42 mmol) for 43 h. Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **3b** (81.2 mg, 90%) as a colorless oil.

Analytical data for **3b**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.39 (s, 5H), 5.03 (s, 2H), 3.48 (s, 3H), 3.46 (s, 2H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 130.8 (x2), 130.2, 128.8, 128.7 (x2), 112.9 (x2), 96.2, 66.5, 57.2, 45.7

**IR** (ATR): 1456, 1162, 1071, 1017, 969, 921, 767, 700

**HRMS** (FAB) calcd for $(C_{12}H_{12}O_2N_2Na)^+$ $[M+Na]^+$: 239.0796. Found: 239.0802




**3c**

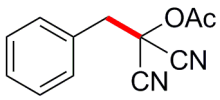
**2-(Methoxymethoxy)-2-(2-methylbenzyl)malononitrile** (**3c**): Prepared according to the general procedure using $PPh_3$ (194 mg, 0.74 mmol), THF (3.5 mL), DIAD (146 μL, 0.74 mmol), 2-methylbenzyl alcohol (91 mg, 0.74 mmol), and MOM-MAC (62.2 mg, 0.49 mmol) for 41 h. Purification by flash column chromatography ($SiO_2$ 10% EtOAc/Hexanes) afforded **3c** (97.5 mg, 86%) as a colorless oil.

Analytical data for **3c**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.39 (d, *J* = 7.2 Hz, 1H), 7.28 – 7.20 (m, 3H) 5.01 (s, 2H), 3.54 (s, 2H), 3.48 (s, 3H), 2 44 (s, 3H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 138.1, 131.6, 131.0, 128.9, 128.8, 126.2, 113.1 (x2), 96.2, 66.3, 57.3, 42.2, 20.0

**IR** (ATR): 1444, 1163, 1069, 1014, 968, 774, 748, 728

**HRMS** (FAB) calcd for $(C_{13}H_{14}O_2N_2Na)^+$ $[M+Na]^+$: 253.0953. Found: 253.0961




**3b'**

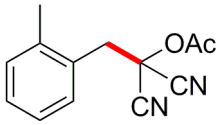
**1,1-Dicyano-2-phenylethyl acetate (3b')**: Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), benzyl alcohol (46 μL, 0.44 mmol), and MOM-MAC (49 mg, 0.4 mmol) for 48 h. Purification by flash column chromatography ($SiO_2$, 25% EtOAc/Hexanes) and recycling preparative HPLC afforded **3b'** (58 mg, 68%) as a colorless oil.

Analytical data for **3b'**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.416 (s, 5H), 3.552 (s, 2H), 2.229 (s, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 169.4, 130.9 (x2), 129.24, 129.21, 128.9 (x2), 111.6 (x2), 62.3, 43.9, 20.0

**IR** (ATR): 1773, 1371, 1197, 1034, 766, 701

**HRMS** (FAB) calcd for ($C_{12}H_{11}O_2N_2$) $[M+H]^+$: 215.0820. Found: 215.0816




**3c'**

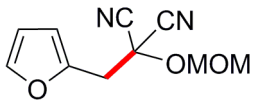
**1,1-Dicyano-2-(o-tolyl)ethyl acetate (3c')**: Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), 2-methylbenzyl alcohol (54 mg, 0.44 mmol), and MOM-MAC (49 mg, 0.4 mmol) for 48 h. Purification by flash column chromatography ($SiO_2$, 25% EtOAc/Hexanes) and recycling preparative HPLC afforded **3c'** (71 mg, 78%) as a colorless oil.

Analytical data for **3c'**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.41 (d, *J* = 7.2, 1H), 7.29 (td, *J* = 7.2 Hz, 1.8 Hz, 1H), 7.26 (d, *J* = 7.8 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 3.63 (s, 2H), 2.46 (s, 3H), 2.22 (s, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 167.3, 138.1, 131.6, 131.2, 129.2, 127.9, 126.4, 111.8 (x2), 62.0, 40.4, 20.1, 19.9

**IR** (ATR): 1775, 1371, 1195, 1091, 1031, 925, 854, 775, 748, 723, 664

**HRMS** (FAB) calcd for ($C_{13}H_{13}O_2N_2$) $[M+H]^+$: 229.0977. Found: 229.0987




**3d**

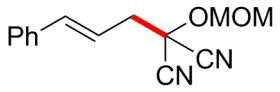
**2-(Furan-2-ylmethyl)-2-(methoxymethoxy)malononitrile** (**3d**): Prepared according to the general procedure using $PPh_3$ (157 mg, 0.60 mmol), THF (2.5 mL), DIAD (118 μL, 0.60 mmol), furfuryl alcohol (52 μL, 0.60 mmol), and MOM-MAC (50.4 mg, 0.40 mmol) for 8 h. Purification by flash column chromatography ($SiO_2$, 14% EtOAc/Hexanes) afforded **3d** (58 mg, 70%) as a colorless oil.

Analytical data for **3d**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 1.9, 0.9 Hz, 1H), 6.48 (d, *J* = 3.3 Hz, 1H), 6.41 (dd, *J* = 3.2, 1.8 Hz, 1H), 5.05 (s, 3H), 3.57 (s, 3H), 3.52 (s, 3H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 144.4, 143.7, 112.6 (x2), 111.3, 110.9, 96.3, 65.1, 57.3, 38.9

**IR** (ATR): 1203, 1163, 1073, 1025, 967, 921, 748

**HRMS** (FAB) calcd for $(C_{10}H_{10}O_3N_2)Na^+$ $[M+Na]^+$: 229.0589. Found: 229.0587




**3e**

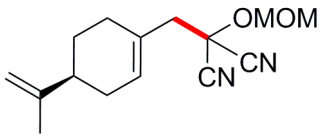
**2-Cinnamyl-2-(methoxymethoxy)malononitrile** (**3e**): Prepared according to the general procedure using $PPh_3$ (157 mg, 0.60 mmol), THF (2.5 mL), DIAD (118 μL, 0.60 mmol), cinnamyl alcohol (87.0 mg, 0.65 mmol), and MOM-MAC (50.4 mg, 0.40 mmol) for 4 h. Purification by flash column chromatography ($SiO_2$, 14% EtOAc/Hexanes) afforded **3e** (80.9 mg, 84%) as a pale yellow (almost-colorless) oil.

Analytical data for **3e**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 7.41 (dd, *J* = 7.2, 1.8 Hz, 2H), 7.34 (td, *J* = 7.2, 1.8 Hz, 2H), 7.29 (tt, *J* = 7.8, 1.8 Hz, 1H), 6.73 (d, *J* = 16 Hz, 1H), 6.19 (dt, *J* = 16, 7.2 Hz, 1H), 5.05 (s, 2H), 3.54 (s, 3H), 3.08 (dd, *J* = 7.8, 1.8 Hz, 2H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 138.5, 135.7, 128.6 (x2), 128.4, 126.7 (x2), 117.3, 113.0 (x2), 96.3, 65.8, 57.3, 43.5

**IR** (ATR): 1449, 1163, 1072, 1032, 965, 749, 694

**HRMS** (FAB) calcd for $(C_{14}H_{14}O_2N_2)^+$ $[M]^+$: 242.1055. Found: 242.1055




**3f**

**(*S*)-2-(Methoxymethoxy)-2-((4-(prop-1-en-2-yl)cyclohex-1-en-1-yl)methyl)malononitrile (3f)**: Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), (*s*)-(−)-perillyl alcohol (70 μL, 0.44 mmol), and MOM-MAC (43 mg, 0.34 mmol) for 18 h. Purification by flash column chromatography ($SiO_2$, 9% EtOAc/Hexanes) afforded **3f** (71 mg, 81%) as a colorless oil.

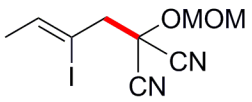
Analytical data for **3f**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 5.90 (d, *J* = 2.4 Hz, 1H), 5.04 (s, 2H), 4.73 (dt, *J* =16, 1.5 Hz, 2H), 3.54 (s, 3H), 2.83 (s, 2H), 2.30 – 2.14 (m, 4H), 2.07 – 1.99 (m, 1H), 1.84 (dtd, *J* = 13, 6.0, 3.0 Hz, 1H), 1.74 (s, 3H), 1.51 (dtd, *J* = 13, 11, 5.4 Hz, 1H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 149.0, 130.9, 128.2, 113.3, 113.2, 108.9, 96.1, 66.2, 57.2, 47.4, 40.1, 30.8, 29.9, 27.5, 20.7

**IR** (ATR): 2921, 1437, 1164, 1069, 1025, 981, 937, 890

**HRMS** (FAB) calcd for ($C_{15}H_{21}O_2N_2$) $[M+H]^+$: 261.1603. Found: 261.1598

**$[\alpha]^{23.8}_D$** = −58.38° (c 1.0, $CHCl_3$)




**3g**

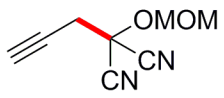
**(*Z*)-2-(2-Iodobut-2-en-1-yl)-2-(methoxymethoxy)malononitrile (3g):** Prepared according to the general procedure using $PPh_3$ (149 mg, 0.57 mmol), THF (2 mL), DIAD (112 μL, 0.57 mmol), (*Z*)-2-iodobut-2-en-1-ol (112 mg, 0.57 mmol), and MOM-MAC (48 mg, 0.38 mmol) for 17 h. Purification by flash column chromatography ($SiO_2$, 5% EtOAc/Hexanes) afforded **3g** (93 mg, 80%) as a colorless oil.

Analytical data for **3g**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 6.10 (q, *J* =6.0 Hz, 1H), 5.06 (s, 2H), 3.55 (s, 3H), 3.42 (s, 2H), 1.85 (d, *J* =6.0 Hz, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 141.0, 112.5 (x2), 96.1, 90.8, 65.8, 57.4, 52.6, 22.9

**IR** (ATR):1215, 1163, 1026, 971, 919, 757, 690, 609

**HRMS** (ESI) calcd for ($C_9H_{11}O_2N_2I_1Na_1$) $[M+Na]^+$: 328.9763. Found: 328.9754




**3h**

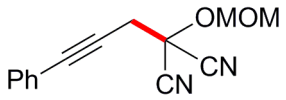
**2-(Methoxymethoxy)-2-(prop-2-yn-1-yl)malononitrile** (**3h**): Prepared according to the general procedure using $PPh_3$ (164 mg, 0.625 mmol), THF (3 mL), DIAD (123 μL, 0.625 mmol), propargyl alcohol (36 μL, 0.63 mmol), and MOM-MAC (52.5 mg, 0.42 mmol) for 18 h. Purification by flash column chromatography ($SiO_2$, 10→15% EtOAc/Hexanes) afforded **3h** (56.0 mg, 82%) as a white crystalline solid.

Analytical data for **3h**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.08 (s, 2H), 3.56 (s, 3H), 3.14 (d, *J* = 2.6 Hz, 2H), 2.40 (t, *J* = 2.7 Hz, 1H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$) $^{13}$C NMR (125 MHz, $CDCl_3$): δ 112.2 (x2), 96.5, 75.3, 73.2, 64.9, 57.4, 31.5

**IR** (ATR): 1164, 1037, 978, 922, 666, 616

**HRMS** (EI) calcd for $(C_8H_7O_2N_2)^+$ $[M-H]^+$: 163.0508. Found: 163.0512




**3i**

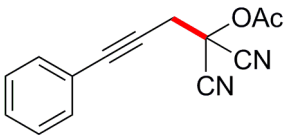
**2-(Methoxymethoxy)-2-(3-phenylprop-2-yn-1-yl)malononitrile** (**3i**): Prepared according to the general procedure using $PPh_3$ (157 mg, 0.60 mmol), THF (2.5 mL), DIAD (118 μL, 0.60 mmol), 3-phenyl-2-propyn-1-ol (75 μL, 0.60 mmol), and MOM-MAC (50.4 mg, 0.40 mmol) for 3 h. Purification by flash column chromatography ($SiO_2$, 14% EtOAc/Hexanes) afforded **3i** (87.2 mg, 91%) as an amber oil.

Analytical data for **3i**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 7.48 (dd, *J* = 8.1, 1.7 Hz, 2H), 7.39 – 7.30 (m, 3H), 5.10 (s, 2H), 3.57 (s, 3H), 3.36 (s, 2H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 131.9 (x2), 128.9, 128.3 (x2), 121.7, 112.5 (x2), 96.4, 86.9, 78.3, 65.3, 57.4, 32.4

**IR** (ATR): 1491, 1443, 1216, 1164, 1084, 1035, 968, 919, 756, 690

**HRMS** (FAB) calcd for $(C_{14}H_{12}O_2N_2Na)^+$ $[M+Na]^+$: 263.0796. Found: 263.0789




**3i'**

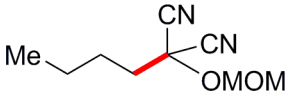
**1,1-Dicyano-4-phenylbut-3-yn-1-yl acetate (3i')**: Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), 3-phenyl-2-propyn-1-ol (55 μL, 0.44 mmol), and MOM-MAC (49 mg, 0.4 mmol) for 48 h. Purification by flash column chromatography ($SiO_2$, 25% EtOAc/Hexanes) and recycling preparative HPLC afforded **3i'** (64 mg, 68%) as a colorless oil.

Analytical data for **3i'**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.50 – 7.47 (m, 2H), 7.39 – 7.31 (m, 3H), 3.46 (s, 2H), 2.27 (s, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 167.3, 131.9 (x2), 129.2, 128.4 (x2), 121.4, 111.2 (x2), 87.5 (x2), 60.9, 30.9, 20.0

**IR** (ATR): 1781, 1491, 1372, 1199, 1050, 758, 691

**HRMS** (FAB) calcd for ($C_{14}H_{11}O_2N_2$) $[M+H]^+$: 239.0820. Found: 239.0828




**3j**

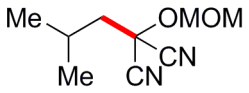
**2-Butyl-2-(methoxymethoxy)malononitrile** (**3j**): Prepared according to modified general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), 1-butanol (40 μL, 0.44 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 7 h. Purification by flash column chromatography ($SiO_2$, 15% EtOAc/Hexanes) afforded **3j** (65 mg, 89%) as a pale yellow (almost colorless) oil.

Analytical data for **3j**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 5.04 (s, 2H), 3.54 (s, 3H), 2.22 – 2.19 (m, 2H), 1.68 – 1.62 (m, 2H), 1.45 (sextet, $J$ = 7.2 Hz, 2H), 0.98 (t, $J$ = 7.2 Hz, 3H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 113.3 (x2), 96.1, 65.8, 57.3, 39.8, 25.6, 21.8, 13.6

**IR** (ATR): 1458, 1166, 1091, 1008, 965, 923

**HRMS** (EI) calcd for $(C_9H_{13}O_2N_2)^+$ $[M-H]^+$: 181.0977. Found: 181.0974




**3k**

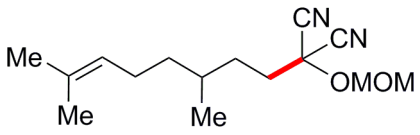
**2-Isobutyl-2-(methoxymethoxy)malononitrile** (**3k**): Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (2 mL), DIAD (87 μL, 0.44 mmol), isobutyl alcohol (41 μL, 0.44 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 2 h. Purification by flash column chromatography ($SiO_2$, 14% EtOAc/Hexanes) afforded **3k** (50 mg, 69%) as a colorless oil.

Analytical data for **3k**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.05 (s, 2H), 3.54 (s, 3H), 2.18 – 2.07 (m, 3H), 1.10 (d, *J* = 6.6 Hz, 6H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 113.5 (x2), 96.1, 65.2, 57.3, 47.8, 25.1, 23.1 (x2)

**IR** (ATR): 2964, 1470, 1165, 1088, 1005, 966, 923

**HRMS** (EI) calcd for ($C_9H_{13}O_2N_2$) $[M-H]^+$: 181.0977. Found: 181.0981




**3l**

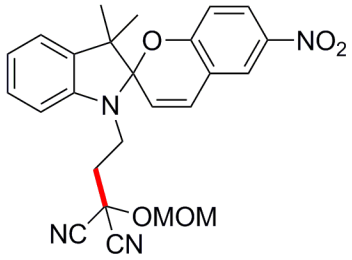
**2-(3,7-Dimethyloct-6-en-1-yl)-2-(methoxymethoxy)malononitrile** (**3l**): Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), β-citronellol (80 μL, 0.44 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 2 h. Purification by flash column chromatography ($SiO_2$, 9% EtOAc/Hexanes) afforded **3l** (81 mg, 77%) as a colorless oil.

Analytical data for **3l**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 5.08 (tt, *J* = 6.6, 1.2 Hz, 1H), 5.04 (s, 2H), 3.54 (s, 3H), 2.24 (td, *J* = 13, 4.8 Hz, 1H), 2.17 (ddd, *J* = 14, 12, 4.8 Hz, 1H), 2.03 (sextet, *J* = 7.2 Hz, 1H), 1.97 (sextet, *J* = 7.2 Hz, 1H), 1.69 (s, 3H), 1.69 – 1.65 (m, 1H), 1.61 (s, 3H), 1.57 – 1.46 (m, 2H), 1.39 – 1.34 (m, 1H), 1.25 – 1.19 (m, 1H), 0.94 (d, *J* = 6 Hz, 3H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 131.7, 124.2, 113.3 (x2), 96.2, 66.0, 57.3, 38.0, 36.5, 31.7, 30.3, 25.7, 25.3, 19.2, 17.6

**IR** (ATR): 2920, 1455, 1165, 1088, 1028, 924

**HRMS** (FAB) calcd for ($C_{15}H_{23}O_2N_2$) $[M-H]^+$: 263.1759. Found: 263.1756




**3m**

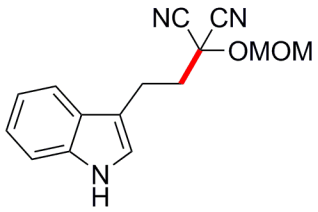
**2-(2-(3',3'-Dimethyl-6-nitrospiro[chromene-2,2'-indolin]-1'-yl)ethyl)-2-(methoxymethoxy)malononitrile (3m):** Prepared according to the general procedure using $PPh_3$ (164 mg, 0.63 mmol), THF (2.3 mL), DIAD (123 μL, 0.63 mmol), 2-(3',3'-dimethyl-6-nitrospiro[chromene-2,2'-indolin]-1'-yl)ethan-1-ol (221 mg, 0.63 mmol), and MOM-MAC (53 mg, 0.42 mmol) for 6 h. Purification by flash column chromatography ($SiO_2$, 20% EtOAc/Hexanes) afforded **3m** (161 mg, 84%) as a purple oil.

Analytical data for **3m**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 8.05 (dd, *J* = 8.4, 3.0 Hz, 1H), 8.03 (d, *J* = 3.0 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 3.6 Hz, 1H), 6.98 (d, *J* = 6.0 Hz, 1H), 6.94 (t, *J* = 7.2 Hz, 1H), 6.77 (d, *J* = 9.0 Hz, 1H), 6.64 (d, *J* = 8.4 Hz, 1H), 5.89 (d, *J* = 11 Hz, 1H), 5.02 (s, 2H), 3.66 (ddd, *J* = 15, 10, 6.0 Hz, 1H), 3.54 (ddd, *J* = 14, 10, 5.4 Hz, 1H), 3.51 (s, 3H), 2.62 (ddd, *J* = 12, 9.6, 4.8 Hz, 1H), 2.46 (ddd, *J* = 15, 10, 6.0 Hz, 1H), 1.29 (s, 3H), 1.19 (s, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 159.0, 145.7, 141.3, 136.0, 128.9, 127.9, 126.1, 122.9, 122.1, 121.4, 120.5, 118.4, 115.5, 112.79, 112.76, 106.6, 106.5, 96.3, 63.6, 57.5, 52.9, 38.3, 38.1, 25.7, 19.9

**IR** (ATR):2966, 1609, 1577, 1518, 1479, 1458, 1335, 1268, 1165, 1087, 993, 955, 919, 809, 743, 680

**HRMS** (EI) calcd for ($C_{25}H_{25}O_5N_4$) $[M+H]^+$: 461.1825. Found: 461.1844




**3n**

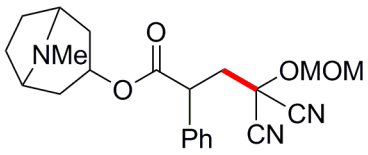
**2-(2-(1*H*-Indol-3-yl)ethyl)-2-(methoxymethoxy)malononitrile** (**3n**): Prepared according to the general procedure using $PPh_3$ (131 mg, 0.50 mmol), THF (1.5 mL), DIAD (98 μL, 0.50 mmol), tryptophol (80 mg, 0.50 mmol), and MOM-MAC (57 mg, 0.45 mmol) for 20 h. Purification by flash column chromatography ($SiO_2$, 20% EtOAc/Hexanes) afforded **3n** (81 mg, 66%) as a white solid.

Analytical data for **3n**:
**$^{1}$H NMR** (600 MHz, $CDCl_3$): δ 8.03 (br s, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.23 (t, *J* = 7.2 Hz, 1H), 7.16 (t, *J* = 7.2 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 5.09 (s, 2H), 3.57 (s, 3H), 3.16 – 3.13 (m, 2H), 2.60 – 2.57 (m, 2H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 136.3, 126.8, 122.4, 121.8, 119.7, 118.3, 113.2(x2), 112.5, 111.3, 96.2, 65.4, 57.4, 40.6, 19.6

**IR** (ATR): 3418, 1456, 1337, 1219, 1163, 1091, 1035, 984, 921, 740, 633, 619, 604

**HRMS** (ESI) calcd for ($C_{15}H_{16}O_2N_3$) $[M+H]^+$: 270.1237. Found: 270.1231




**3o**

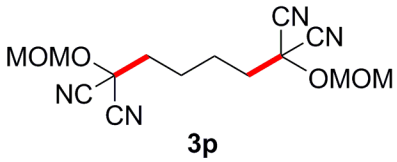
**8-Methyl-8-azabicyclo[3.2.1]octan-3-yl 4,4-dicyano-4-(methoxymethoxy)-2-phenylbutanoate (3o)**: Prepared according to the general procedure using $PPh_3$ (177 mg, 0.68 mmol), THF (2.5 mL), DIAD (133 μL, 0.68 mmol), atropine (195 mg, 0.68 mmol), and MOM-MAC (57 mg, 0.45 mmol) for 16 h. Purification by flash column chromatography ($SiO_2$, 5→20% MeOH/$CH_2Cl_2$) afforded **3o** (155 mg, 86%) as a colorless oil.

Analytical data for **3o**:
**$^{1}$H NMR** (600 MHz; $CDCl_3$): δ 7.38 – 7.30 (m, 5H), 5.02 – 4.98 (m, 3H), 3.90 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.51 (s, 3H), 3.30, (dd, *J* = 14, 8.4 Hz, 1H), 3.05 (t, *J* = 3.6 Hz, 1H), 2.92 (t, *J* = 3.0 Hz, 1H), 2.62 (dd, *J* = 14, 5.4 Hz, 1H), 2.21 (s 3H), 2.11 (dt, *J* = 16, 4.2 Hz, 1H), 2.01 (dt, *J* = 14, 4.2 Hz, 1H), 1.94 – 1.88 (m, 1H), 1.79 – 1.71 (m, 2H), 1.69 (d, *J* = 16 Hz, 1H), 1.43 (d, *J* = 14 Hz, 1H), 1.24 – 1.20 (m, 1H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 170.7, 136.6, 129.2 (x2), 128.4, 127.8 (x2), 112.61, 112.57, 96.2, 69.1, 64.3, 59.6, 59.5, 57.5, 47.1, 42.2, 40.4, 36.4, 36.2, 25.4, 25.0

**IR** (ATR): 2938, 1727, 1201, 1167, 1033, 983, 698

**HRMS** (ESI) calcd for ($C_{22}H_{28}O_4N_3$) $[M+H]^+$: 398.2080. Found: 398.2068




**3p**

**2,4,11,13-Tetraoxatetradecane-5,5,10,10-tetracarbonitrile** (**3p**): Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (2 mL), DIAD (87 μL, 0.44

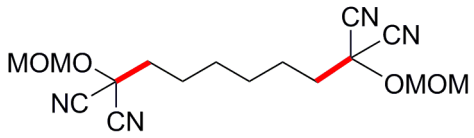
mmol), 1,4-butanediol (20 μL, 0.22 mmol), and MOM-MAC (48.1 mg, 0.38 mmol) for 3 h. Purification by flash column chromatography ($SiO_2$, $CH_2Cl_2$) afforded **3p** (28.1 mg, 48%) as a colorless solid.

Analytical data for **3p**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.05 (s, 4H), 3.55 (s, 6H), 2.35 – 2.21 (m, 4H), 1.81 (quintet, *J* = 3.7 Hz, 4H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 113.0 (x4), 96.3 (x2), 65.3 (x2), 57.4 (x2), 39.6 (x2), 22.8 (x2)

**IR** (ATR): 1469, 1254, 1227, 1199, 1166, 1091, 997, 962, 922, 858, 700

**HRMS** (FAB) calcd for $(C_{14}H_{18}O_4N_4)H^+$ $[M+H]^+$: 307.1401. Found: 307.1396




**3q**

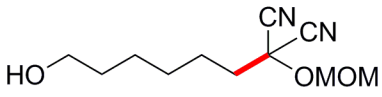
**2,4,13,15-Tetraoxahexadecane-5,5,12,12-tetracarbonitrile** (**3q**): Prepared according to modified general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), 1,6-hexanediol (28 mg, 0.22 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 8 h. Purification by flash column chromatography ($SiO_2$, 15% EtOAc/Hexanes) afforded **3q** (41 mg, 61%) as a white solid and **3q'** (20 mg, 40%) as a pale yellow oil.

Analytical data for **3q**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.04 (s, 4H), 3.54 (s, 6H), 2.27 – 2.16 (m, 4H), 1.73 – 1.67(m, 4H), 1.49 (quintet, *J* = 3.5 Hz, 4H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 113.2 (x4), 96.2 (x2), 65.6 (x2), 57.3 (x2), 39.9 (x2), 28.2 (x2), 23.4 (x2)

**IR** (ATR): 2943, 1219, 1159, 1084, 1019, 988, 917, 666, 616

**HRMS** (FAB) calcd for $(C_{16}H_{22}O_4N_4Na)^+$ $[M+Na]^+$: 357.1539. Found: 357.1529

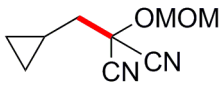



**3q'**

Analytical data for **3q'**:
**$^1$H NMR** (500 MHz, $CDCl_3$): δ 5.03 (s, 2H), 3.66 (t, *J* = 6.5 Hz, 2H), 3.54 (s, 3H), 2.25 – 2.17 (m, 2H), 1.74 – 1.64 (m, 2H), 1.60 (quintet, *J* = 6.7 Hz, 2H), 1.50 – 1.41 (m, 4H)

**$^{13}$C NMR** (125 MHz, $CDCl_3$): δ 113.3 (x2), 96.1, 65.8, 62.6, 57.3, 40.0, 32.3, 28.4, 25.3, 23.6

**GCMS** calcd for $(C_{16}H_{22}O_4N_4)^{\cdot}$ $[M\text{-}MAC]^{\cdot}$: 209. Found: 209




**3r**

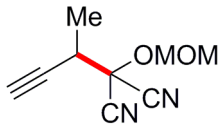
**2-(Cyclopropylmethyl)-2-(methoxymethoxy)malononitrile (3r):** Prepared according to the general procedure using $PPh_3$ (107 mg, 0.41 mmol), THF (2 mL), DIAD (80 μL, 0.41 mmol), cyclopropylmethanol (33 mg, 0.41 mmol), and MOM-MAC (42.9 mg, 0.34 mmol) for 4 h. Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **3r** (49 mg, 80%) as a colorless oil.

Analytical data for **3r**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 5.06 (s, 2H), 3.55 (s, 3H), 2.15 (d, *J* =7.2 Hz, 2H), 1.09 – 1.02 (m, 2H), 0.75 – 0.66 (m, 2H), 0.45 – 0.37 (m, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 113.4 (x2), 96.0, 65.8, 57.2, 44.6, 5.3, 4.3 (x2)

**IR** (ATR):1217, 1162, 1086, 1024, 981, 922, 863, 831, 800, 694

**HRMS** (EI) calcd for $(C_9H_{11}O_2N_2)$ $[M-H]^+$: 179.0821. Found: 179.0828




**3s**

**2-(But-3-yn-2-yl)-2-(methoxymethoxy)malononitrile** (**3s**): Prepared according to the general procedure using $PPh_3$ (115 mg, 0.44 mmol), THF (1 mL), DIAD (87 μL, 0.44 mmol), 3-butyn-2-ol (34 μL, 0.44 mmol), and MOM-MAC (50 mg, 0.4 mmol) for 8 h. Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **3s** (48 mg, 68%) as a colorless oil.

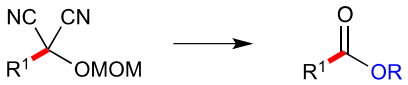
Analytical data for **3s**:
**$^1$H NMR** (600 MHz, $CDCl_3$): δ 5.09 (d, *J* = 7.2 Hz, 1H), 5.08 (d, *J* =7.2 Hz, 1H), 3.56 (s, 3H), 3.25 (qd, *J* = 7.2, 2.4 Hz, 1H), 2.45 (d, *J* = 2.4 Hz, 1H), 1.53 (d, *J* = 7.2 Hz, 3H)

**$^{13}$C NMR** (150 MHz, $CDCl_3$): δ 112.2, 111.8, 96.6, 78.7, 74.8, 69.4, 57.5, 37.1, 15.6

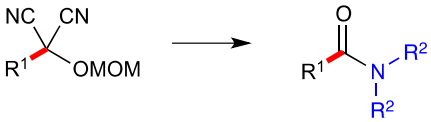
**IR** (ATR): 3295, 1456, 1218, 1165, 1108, 1041, 932, 657

**HRMS** (EI) calcd for $(C_9H_9O_2N_2)^+$ $[M-H]^+$: 177.0664. Found: 177.0672

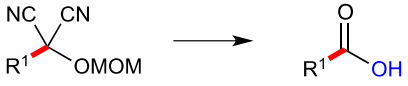
**General Procedure for Unmasking of the Mitsunobu Adducts**




To an oven-dried two-neck round bottom flask was added MAC adduct **3** (1 equiv), 1:1 AcOH/DME (0.5 M), and (*R*)-CSA (0.5-1.1 equiv). The flask was sealed with two glass stoppers and heated to 60 °C for 3-8 h until the conversion to cyanohydrin was complete as determined by TLC. At this point one of the two stoppers was changed to a septum and the other was connected to nitrogen atmosphere. The reaction mixture was cooled to ambient temperature, diluted with anhydrous MeOH (0.5 M), and cooled to –40 °C. A solution of 1:1 MeOH/$Et_3N$ (20.4 equiv. of $Et_3N$) was added dropwise over 10 min. After 2-3 h, the reaction was warmed to 0 °C. After 3-15 h at 0 °C, the reaction was slowly quenched with sat. aq. $NH_4Cl$. The mixture was extracted three times with $CH_2Cl_2$ and the combined organics were washed with brine, dried over anh. $Na_2SO_4$, and concentrated. Purification by flash column chromatography ($SiO_2$, EtOAc/Hexanes) afforded ester **5**.



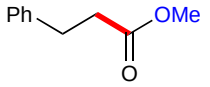

To an oven-dried two-neck round bottom flask was added MAC adduct **3** (1 equiv), 1:1 AcOH/DME (0.5 M), and (*R*)-CSA (1.1 equiv). The flask was sealed with two glass stoppers and heated to 60 °C for 5.5 h until the conversion to cyanohydrin was complete as determined by TLC. At this point one of the two stoppers was changed to a septum and the other was connected to nitrogen atmosphere. The reaction mixture was cooled to ambient temperature, diluted with $CH_2Cl_2$ (0.5 M), and cooled to –40 °C. A solution of 1:1 Amine/$CH_2Cl_2$ (20.4 equiv of amine) was added dropwise over 10 min, then $Et_3N$ (20.4 equiv) was added. After 10 min, the reaction was warmed to 0 °C. After 0.4-2 h at 0 °C, the reaction was slowly quenched with sat. aq. $NH_4Cl$. The mixture was extracted three times with $CH_2Cl_2$ and the combined organics were dried over anh. $Na_2SO_4$ and concentrated. Purification by flash column chromatography ($SiO_2$, EtOAc/Hexanes→MeOH/$CHCl_3$) afforded amide **6**.




To an oven-dried 2-dram vial was added MAC adduct **3** (1 equiv), (*R*)-CSA (0.5-5 equiv) and 1:1 AcOH/$H_2O$ (0.2 M). The vial was sealed with a cap and heated to 60 °C for 15-

19 h. The reaction mixture was cooled to ambient temperature. The mixture was extracted three times with $CH_2Cl_2$ and the combined organics were dried over anh. $Na_2SO_4$ and concentrated. Purification by flash column chromatography ($SiO_2$, MeOH/$CHCl_3$) afforded carboxylic acid **7**.

**Unmasked Esters, Amides, and Carboxylic Acids**




**5a**

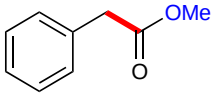
**Methyl 3-phenylpropanoate** (**5a**): Prepared according to the general procedure using MAC adduct **3a** (61 mg, 0.26 mmol), 1:1 AcOH/DME (0.53 mL), and (*R*)-CSA (30 mg, 0.13 mmol) for 3 h, then anhydrous MeOH (0.53 mL) and 1:1 MeOH/$Et_3N$ (1.5 mL, 5.4 mmol of $Et_3N$). Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **5a** (35 mg, 80%) as a colorless oil.

Analytical data for **5a**:

**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.29 (t, *J* = 7.8 Hz, 2H), 7.21 – 7.19 (m, 3H), 3.67 (s, 3H), 2.95 (t, *J* = 7.8 Hz, 2H), 2.63, (t, *J* = 7.8 Hz, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 173.3, 140.5, 128.5, 128.2, 126.2, 51.6, 35.7, 30.9

**CAS Number**: [103-25-3]




**5b**

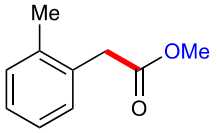
**Methyl 2-phenylacetate** (**5b**): Prepared according to the general procedure using MAC adduct **3b** (25 mg, 0.11 mmol), 1:1 AcOH/DME (0.23 mL), and (*R*)-CSA (29 mg, 0.12 mmol) for 5 h, then anhydrous MeOH (0.23 mL) and 1:1 MeOH/$Et_3N$ (0.65 mL, 2.3 mmol of $Et_3N$). Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **5b** (14 mg, 80%) as a colorless oil.

Analytical data for **5b**:

**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.34 – 7.31 (m, 2H), 7.29 – 7.25 (m, 3H), 3.69 (s, 3H), 3.63 (s, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 172.0, 134.0, 129.2, 128.6, 127.1, 52.0, 41.2

**CAS Number**: [101-41-7]




**5c**

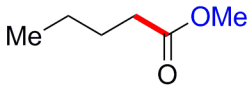
**Methyl 2-(2-methyphenyl)acetate (5c)**: Prepared according to the general procedure using MAC adduct **3b** (25 mg, 0.11 mmol), 1:1 AcOH/DME (0.23 mL), and (*R*)-CSA (29 mg, 0.12 mmol) for 5 h, then anhydrous MeOH (0.23 mL) and 1:1 MeOH/$Et_3N$ (0.65 mL, 2.3 mmol of $Et_3N$). Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **5c** (14 mg, 80%) as a colorless oil.

Analytical data for **5c**:

**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.20 – 7.15 (m, 4H), 3.69 (s, 3H), 3.64 (s, 2H), 2.31 (s, 3H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 171.9, 136.8, 132.7, 130.3, 130.1, 127.4, 126.1, 52.0, 39.0, 19.6

**CAS Number**: [7218-49-7]

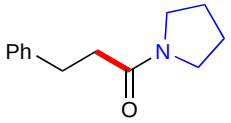



**5j**

**Methyl pentanoate** (**5j**): Prepared according to the general procedure using MAC adduct **3j** (21 mg, 0.12 mmol), 1:1 AcOH/DME (0.23 mL), and (*R*)-CSA (29 mg, 0.13 mmol) for 8 h, then anhydrous MeOH (0.23 mL) and 1:1 MeOH/$Et_3N$ (0.66 mL, 2.4 mmol of $Et_3N$). Purification by flash column chromatography ($SiO_2$, 10% EtOAc/Hexanes) afforded **5j** (12 mg, 87%) as a colorless oil.

Analytical data for **5j**:
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 3.67 (s, 3H), 2.31 (t, $J$ = 7.8 Hz, 2H), 1.61 (quintet, $J$ = 7.8 Hz, 2H), 1.35 (sextet, $J$ = 7.8 Hz, 2H), 0.92 (t, $J$ = 7.8 Hz, 3H)

**CAS Number**: [624-24-8]



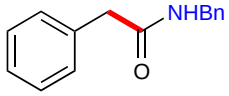

**6a**

**3-Phenyl-1-(pyrrolidin-1-yl)propan-1-one** (**6a**): Prepared according to the general procedure using MAC adduct **3a** (16 mg, 0.071 mmol), 1:1 AcOH/DME (0.14 mL), and (*R*)-CSA (18 mg, 0.078 mmol) for 5.5 h, then anhydrous $CH_2Cl_2$ (0.14 mL), 1:1 pyrrolidine/$CH_2Cl_2$ (0.24 mL, 1.4 mmol of pyrrolidine) and $Et_3N$ (0.20 mL, 1.4 mmol). Purification by flash column chromatography ($SiO_2$, 25% EtOAc/Hexanes→2% MeOH/$CHCl_3$) afforded **6a** (14 mg, 98%) as a white solid.

Analytical data for **6a**:
**$^{1}$H NMR** (600 MHz; $CDCl_3$): δ 7.30 – 7.27 (m, 2H), 7.23 (d, *J* = 6.6 Hz, 2H), 7.20 (t, *J* = 7.2 Hz, 1H), 3.47 (dd, *J* = 6.6, 7.2 Hz, 2H), 3.29 (t, *J* = 6.6 Hz, 2H), 2.99 (dd, *J* = 7.2, 8.4 Hz, 2H), 2.56 (dd, *J* = 7.8, 8.4 Hz, 2H), 1.88 (dt, *J* = 13, 6.6 Hz, 2H), 1.82 (dt, *J* = 14, 7.8 Hz, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 170.7, 141.5, 128.41, 128.37, 126.0, 46.5, 45.6, 36.7, 31.2, 26.0, 24.3

**CAS Number**: [151647-54-0]



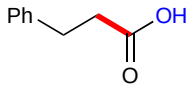
**6b**

***N*-Benzyl-2-phenylacetamide** (**6b**): Prepared according to the general procedure using MAC adduct **3b** (22 mg, 0.10 mmol), 1:1 AcOH/DME (0.20 mL), and (*R*)-CSA (26 mg, 0.11 mmol) for 5.5 h, then anhydrous $CH_2Cl_2$ (0.20 mL), 1:1 benzylamine/$CH_2Cl_2$ (0.46 mL, 2.1 mmol of pyrrolidine) and $Et_3N$ (0.29 mL, 2.1 mmol). Purification by flash column chromatography ($SiO_2$, 67% EtOAc/Hexanes) afforded **6b** (23 mg, 99%) as a white solid.

Analytical data for **6b**:
**$^{1}$H NMR** (600 MHz; $CDCl_3$): δ 7.35 – 7.33 (m, 3H), 7.30 – 7.23 (m, 5H), 7.17 (d, *J* = 7.2 Hz, 2H), 4.40 (d, *J* = 5.4 Hz, 2H), 3.62 (s, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 170.9, 138.1, 134.7, 129.4, 129.0, 128.6, 127.43, 127.38, 127.35, 43.8, 43.5

**CAS Number**: [7500-45-0]



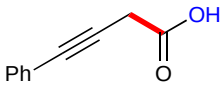
**7a**

**3-Phenylpropanoic acid** (**7a**): Prepared according to the general procedure using MAC adduct **3a** (22 mg, 0.10 mmol), 1:1 AcOH/$H_2O$ (0.48 mL), and (*R*)-CSA (112 mg, 0.48 mmol) for 19 h. Purification by flash column chromatography ($SiO_2$, 0→1% MeOH/$CHCl_3$) afforded **7a** (14 mg, 99%) as a white solid.

Analytical data for **7a**:
**$^{1}$H NMR** (600 MHz; $CDCl_3$): δ 11.51 (br s, 1H), 7.30 (t, *J* = 7.8 Hz, 2H), 7.23 – 7.21 (m, 3H), 2.96 (dd, *J* = 8.4, 7.8 Hz, 2H), 2.69 (dd, *J* = 8.4, 7.2 Hz, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 179.2, 140.1, 128.5, 128.2, 126.4, 35.6, 30.5

**CAS Number**: [501-52-0]




**7i**

**4-Phenylbut-3-ynoic acid** (**7i**): Prepared according to the general procedure using MAC adduct **3i** (25 mg, 0.10 mmol), 1:1 AcOH/$H_2O$ (0.52 mL), and (*R*)-CSA (12 mg, 0.051 mmol) for 15 h. Purification by flash column chromatography ($SiO_2$, 5% MeOH/$CHCl_3$) afforded **7i** (10.4 mg, 63%) as a pale yellow solid, and recovered starting material **3i** (5.1 mg, 21%).

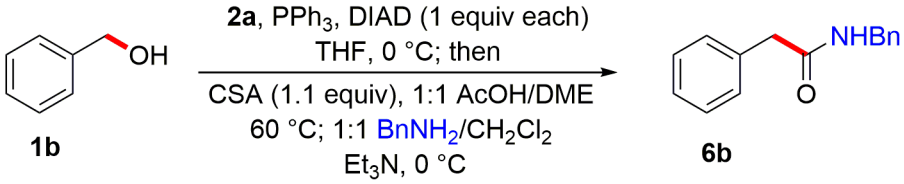
Analytical data for **7i**:

**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.46 – 7.44 (m, 2H), 7.32 – 7.29 (m, 3H), 3.59 (s, 2H)

**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 173.9, 131.8 (x2), 128.4, 128.2 (x2), 122.6, 84.0, 80.1, 26.5

**CAS Number**: [7218-49-7]

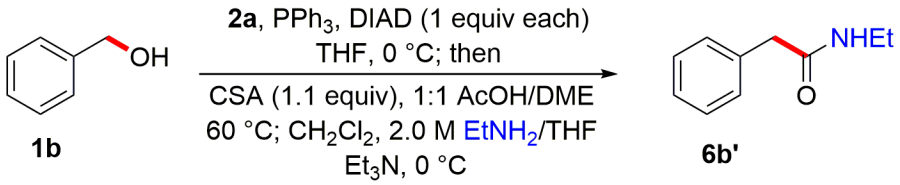
**One-Pot Procedure for Conversion of Benzyl Alcohol to Homologated Amides**




**1b** **6b**

To an oven-dried two-neck round bottom flask was added a stir bar, $PPh_3$ (48 mg, 0.18 mmol), and solvent (2 mL). The flask was capped with a septum and connected to $N_2$ atmosphere. The mixture was cooled with an ice/water bath, and DIAD (36 μL, 0.18 mmol) was added. The mixture was allowed to stir for 30 min, then benzyl alcohol (**1b,** 19 μL, 0.18 mmol) was added. After an additional 30 min, the MAC reagent **2a** (23 mg, 0.18 mmol) was added. The ice/water bath was allowed to warm to ambient temperature, and the reaction was stirred for 15 h and concentrated in vacuo. To the residue was added 1:1 AcOH/DME (0.36 mL), and (*R*)-CSA (46 mg, 0.20 mmol). The flask was sealed with glass-caps and heated to 60 °C for 5.5 h. The reaction mixture was cooled to ambient temperature, diluted with $CH_2Cl_2$ (0.36 mL), and cooled to –40 °C. 1:1 Benzylamine/$CH_2Cl_2$ (0.81 mL, 3.7 mmol of $BnNH_2$) was added dropwise over 10 min, then $Et_3N$ (0.52 mL, 3.7 mmol) was added. After 5 min, the reaction was warmed to 0 °C. After 1 hour at 0 °C, the reaction was slowly quenched with sat. aq. $NH_4Cl$ (5 mL). The mixture was extracted three times with $CH_2Cl_2$ and the combined organics were dried over anh. $Na_2SO_4$ and concentrated to give a crude solid. The crude solid was diluted with EtOAc, filtered through a cotton plug, and concentrated to give a crude oil.

Purification by flash column chromatography ($SiO_2$, 50% EtOAc/Hexanes, then 1:2:1 EtOAc/Hexanes/$CH_2Cl_2$, then 1.0% MeOH/$CHCl_3$) afforded **6b** (39 mg, 96%).




To an oven-dried two-neck round bottom flask was added a stir bar, $PPh_3$ (34 mg, 0.13 mmol), and solvent (1 mL). The flask was capped with a septum and connected to a $N_2$ atmosphere. The mixture was cooled with an ice-water bath, and a solution of DMEAD (30 mg, 0.13 mmol) in THF (0.5 mL) was added using a cannula. The mixture was allowed to stir for 30 min, then benzyl alcohol **1b** (13 µL, 0.13 mmol) was added. After an additional 30 min, the MAC reagent **2a** (16 mg, 0.13 mmol) was added. The ice/water bath was allowed to warm to ambient temperature, and the reaction was stirred for 18 h and concentrated in vacuo. To the residue was added 1:1 AcOH/DME (0.26 mL), and (*R*)-CSA (33 mg, 0.14 mmol). The flask was sealed with glass stoppers and heated to 60 °C for 5 h. The reaction mixture was cooled to ambient temperature, diluted with $CH_2Cl_2$ (0.26 mL), and cooled to –40 °C. A 2.0 M solution of ethylamine in THF (1.3 mL, 2.6 mmol of $EtNH_2$) was added dropwise over 10 min, then $Et_3N$ (0.36 mL, 2.6 mmol) was added. After 5 min, the reaction was warmed to 0 °C. After 1.5 h at 0 °C, the reaction was slowly quenched with sat. aq. $NH_4Cl$ (5 mL). The mixture was extracted three times with $CH_2Cl_2$ and the combined organics were dried over anh. $Na_2SO_4$ and concentrated to give a crude solid. The crude solid was washed with $H_2O$, and dried over anh. $Na_2SO_4$ and concentrated to give a pink crude solid. Purification by flash column chromatography ($SiO_2$, 67% EtOAc/Hexanes) afforded **6b'** (18 mg, 85%).

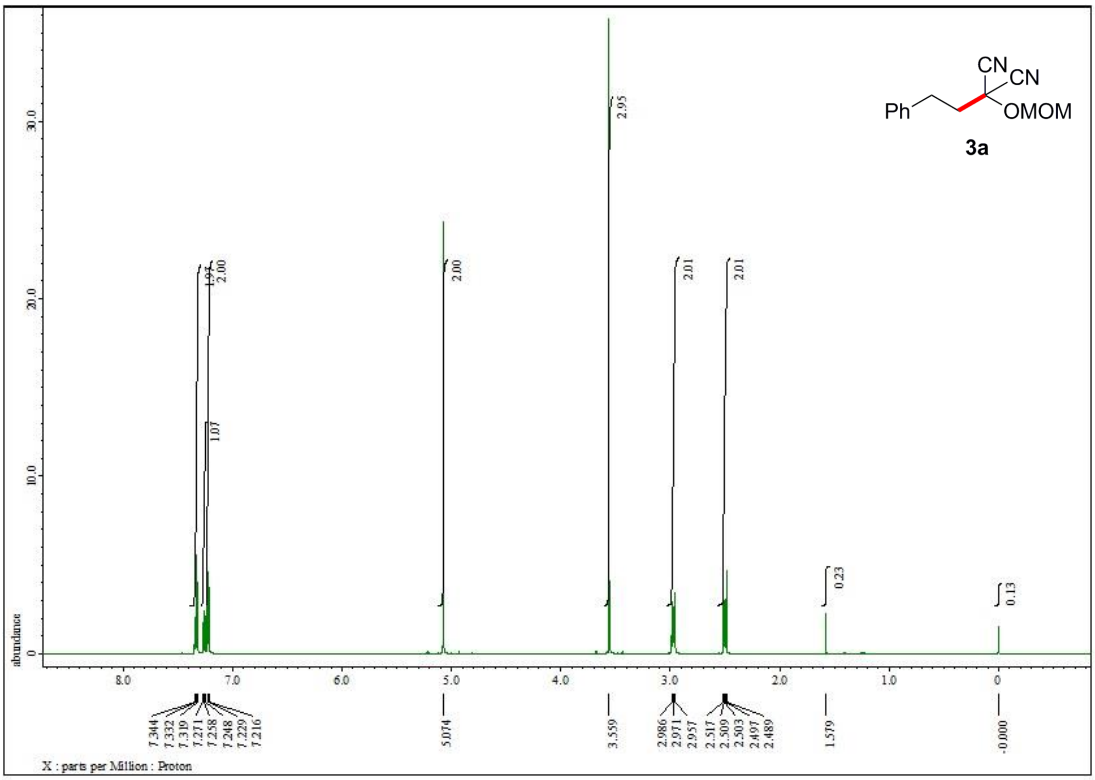
Analytical data for **6b'**:

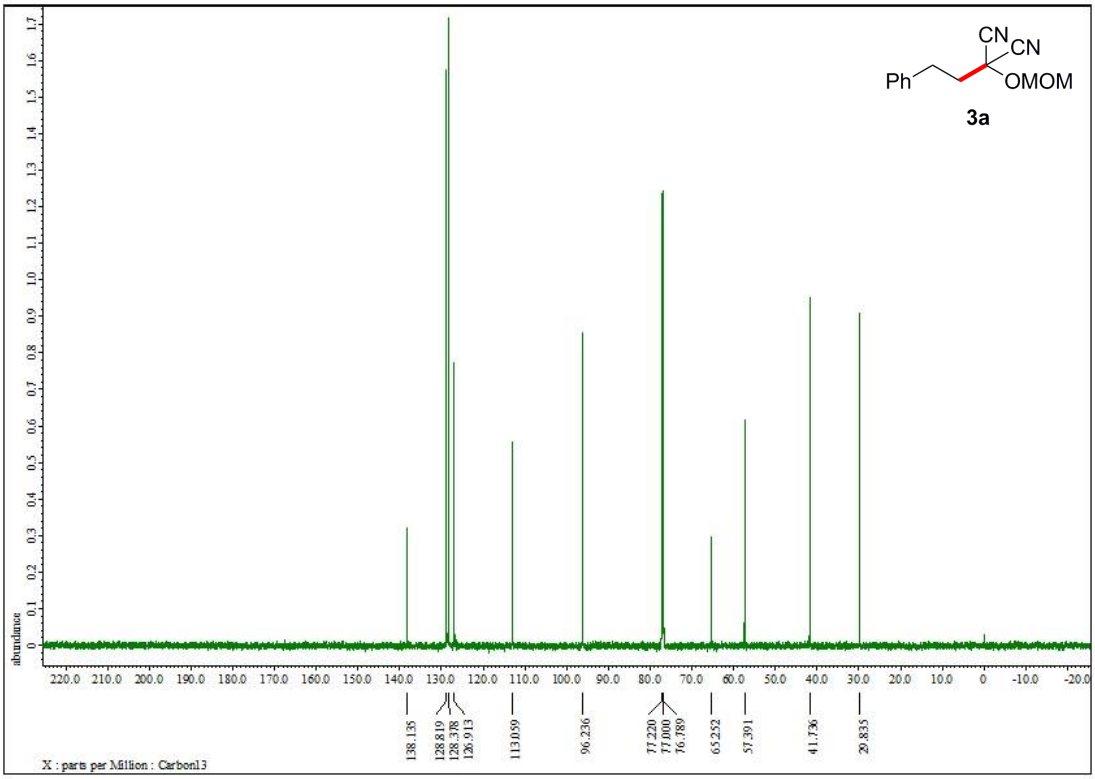
**$^1$H NMR** (600 MHz; $CDCl_3$): δ 7.36 (dd, *J* = 8.4, 7.2 Hz, 2H), 7.30 (dd, *J* = 7.2, 5.4 Hz, 1H), 7.26 (d, *J* = 9.0 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 1H), 3.57 (s, 3H), 3.25 (ddd, *J* = 15, 7.8 5.4 Hz, 2H), 1.06 (t, *J* = 7.2 Hz, 3H)

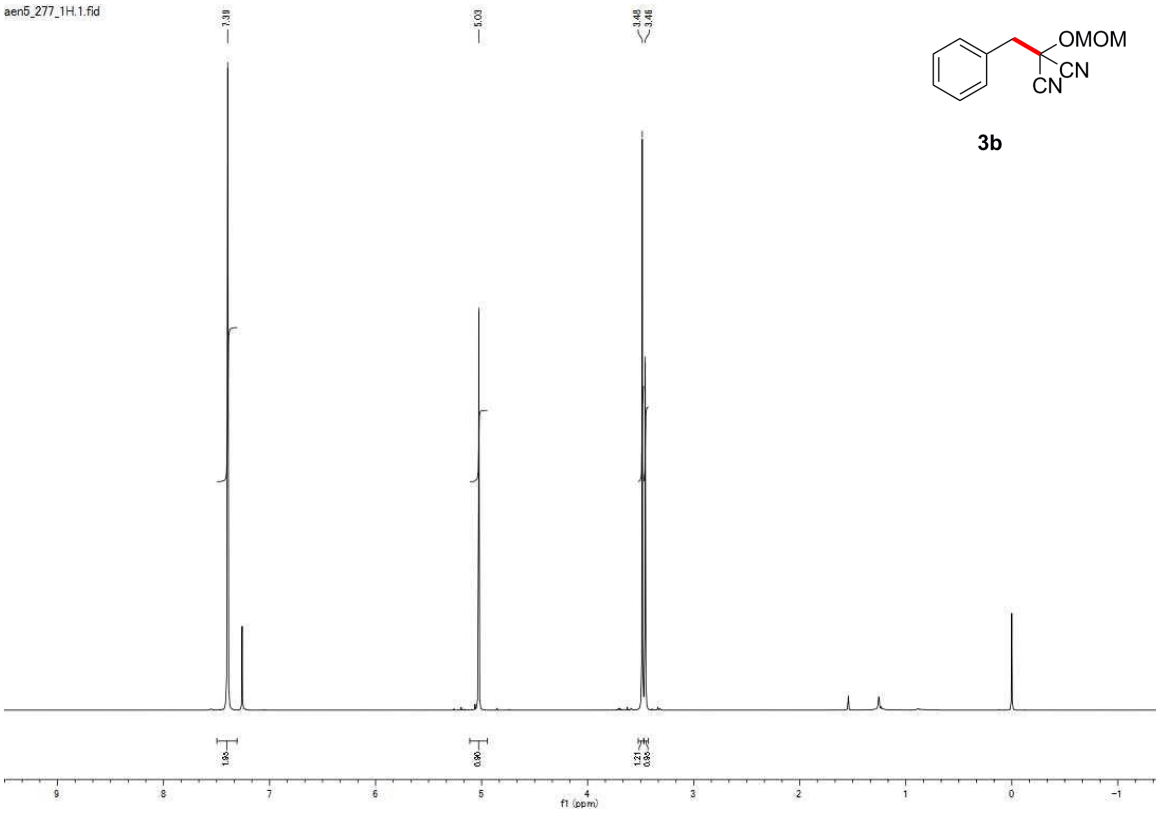
**$^{13}$C NMR** (150 MHz; $CDCl_3$): δ 170.8, 134.9, 129.5, 129.0, 127.3, 43.8, 34.5, 14.7

**CAS Number**: [5465-00-9]

## Selected NMR Spectra

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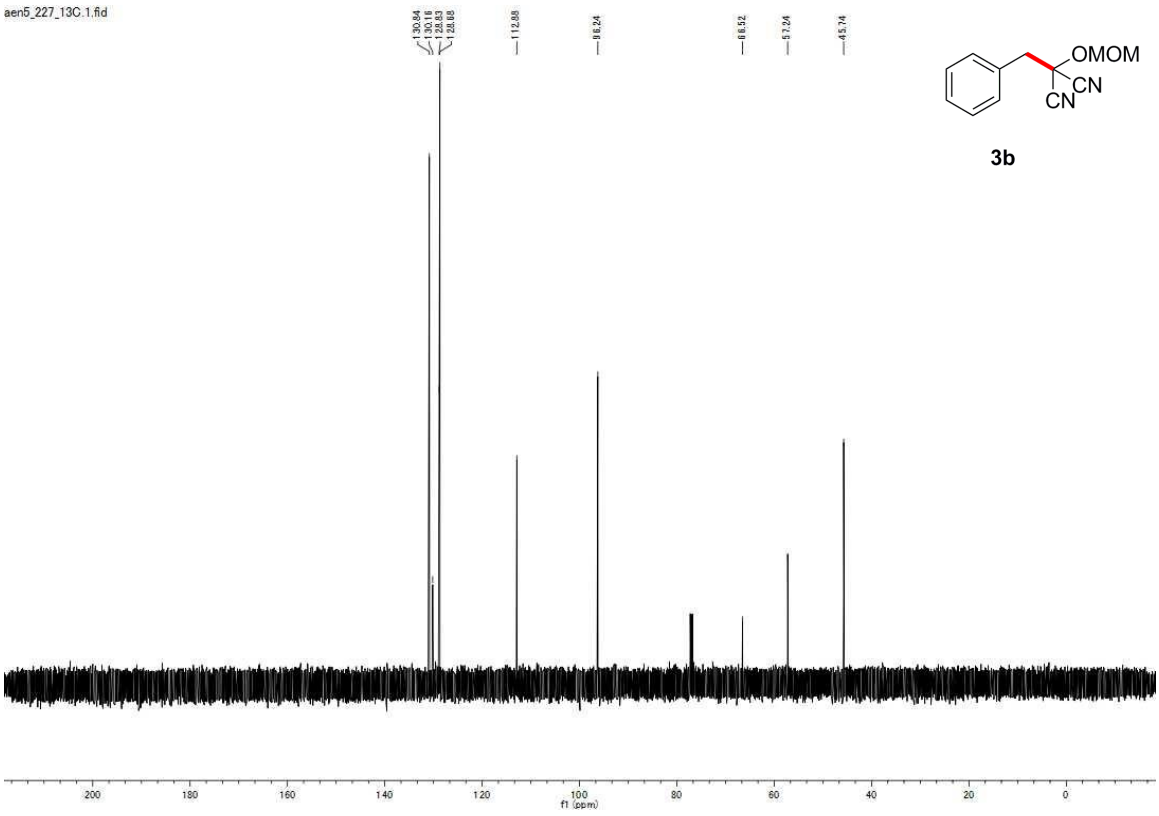
0.93
f1 (ppm)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66.52
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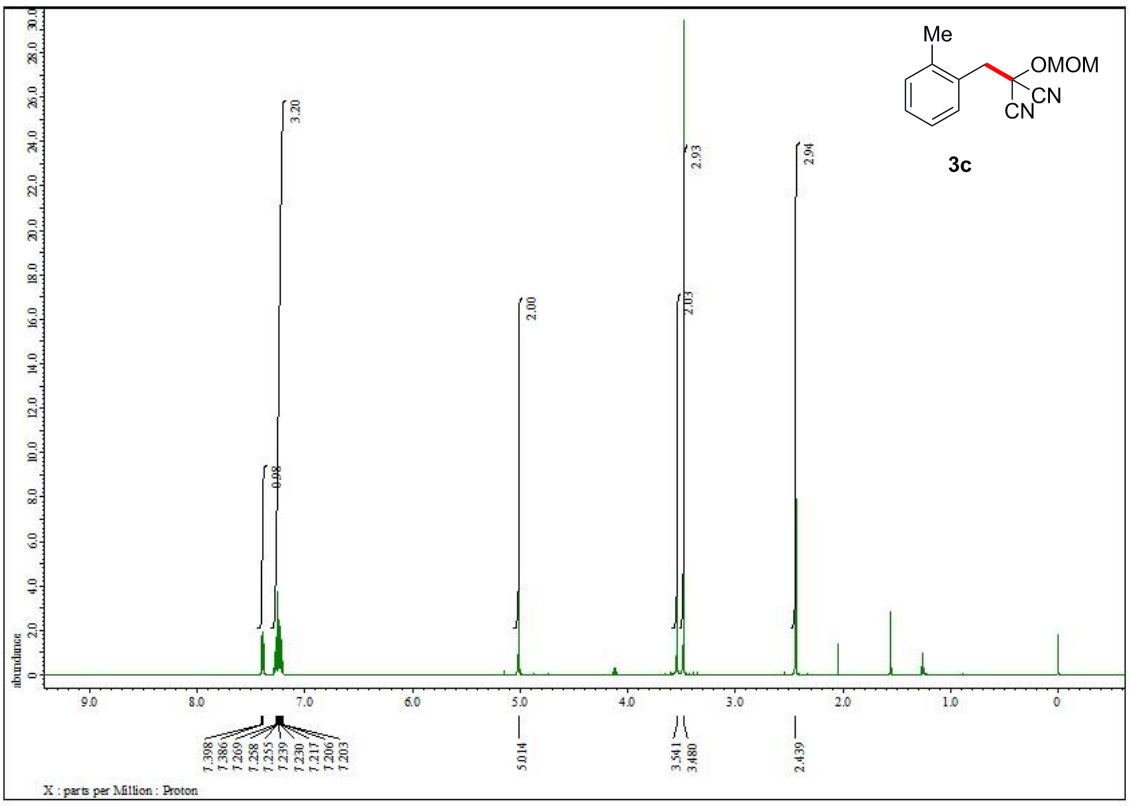
45.14
OMOM
CN
CN
3b
f1 (ppm)


Me
OMOM
CN
CN
3c
3.20
2.93
2.94
2.00
2.03
0.98
abundance
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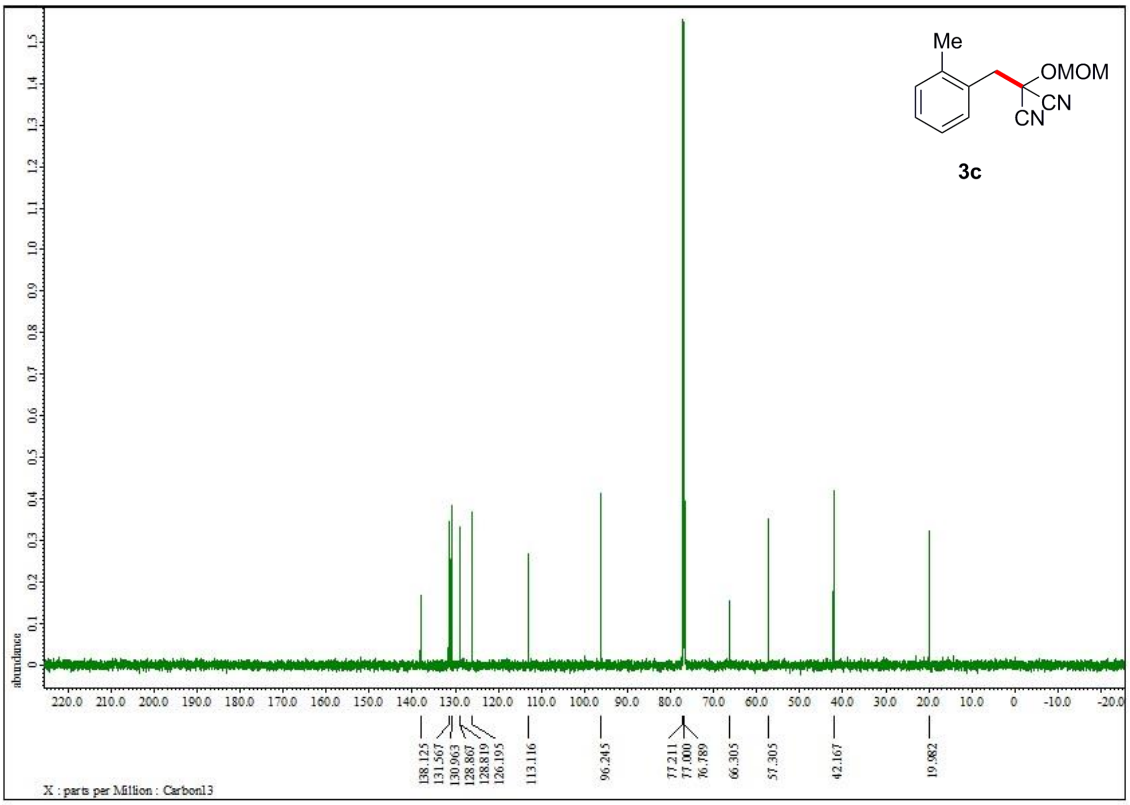
7.386
7.269
7.258
7.255
7.239
7.230
7.217
7.206
7.203
5.014
3.541
3.480
2.439
X : parts per Million : Proton


Me
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CN
CN
3c
abundance
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130.963
128.867
128.819
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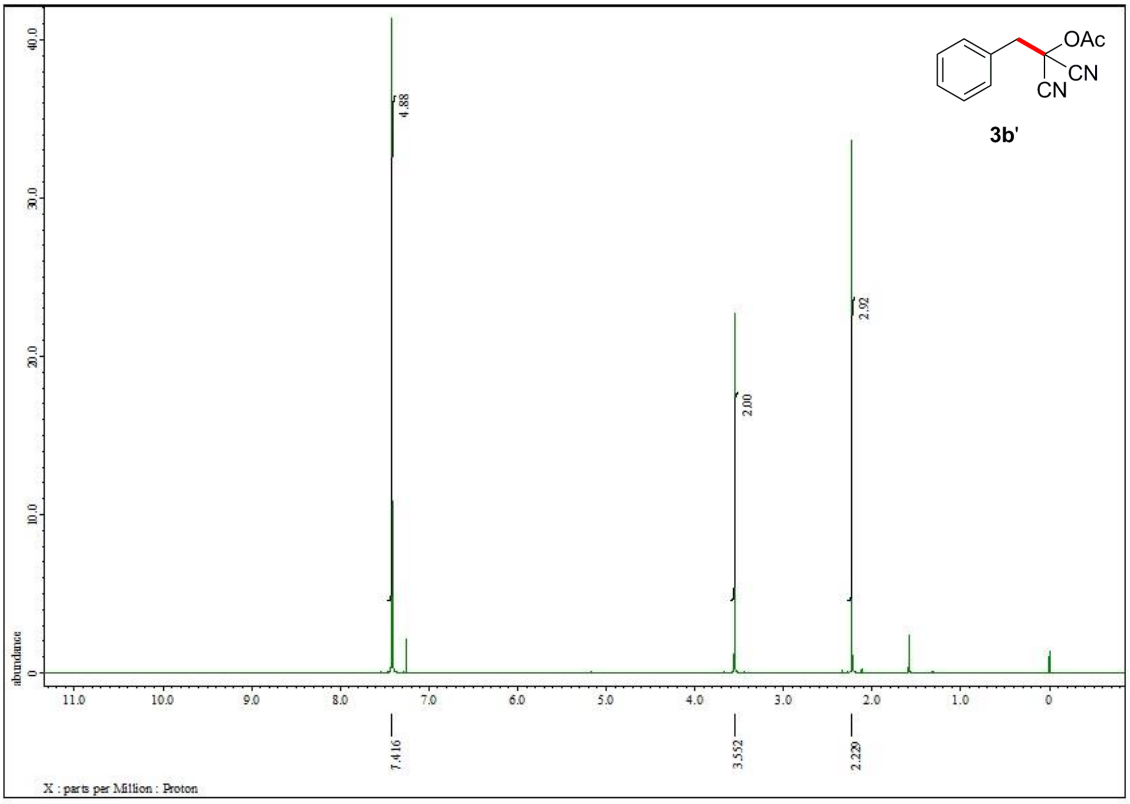
77.211
77.000
76.789
66.305
57.305
42.167
19.982
X : parts per Million : Carbon13


OAc
CN
CN
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2.92
abundance
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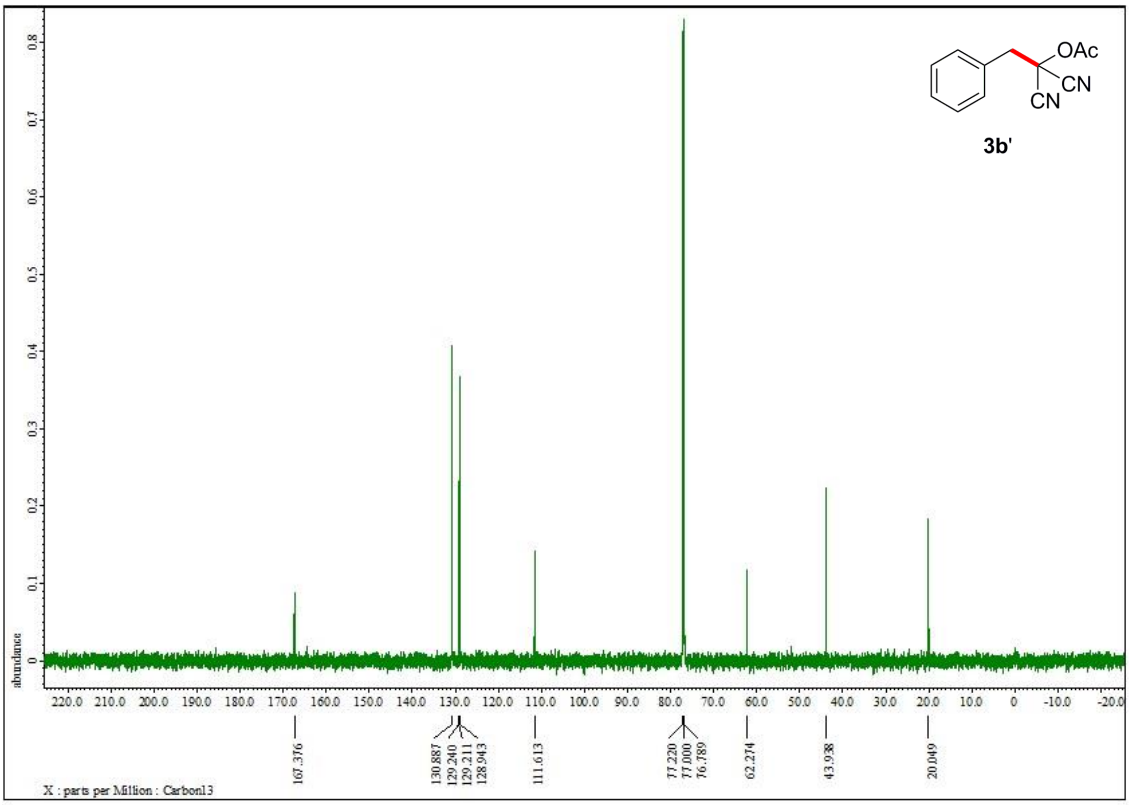
3.552
2.229
X : parts per Million : Proton


OAc
CN
CN
3b'
abundance
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128.943
111.613
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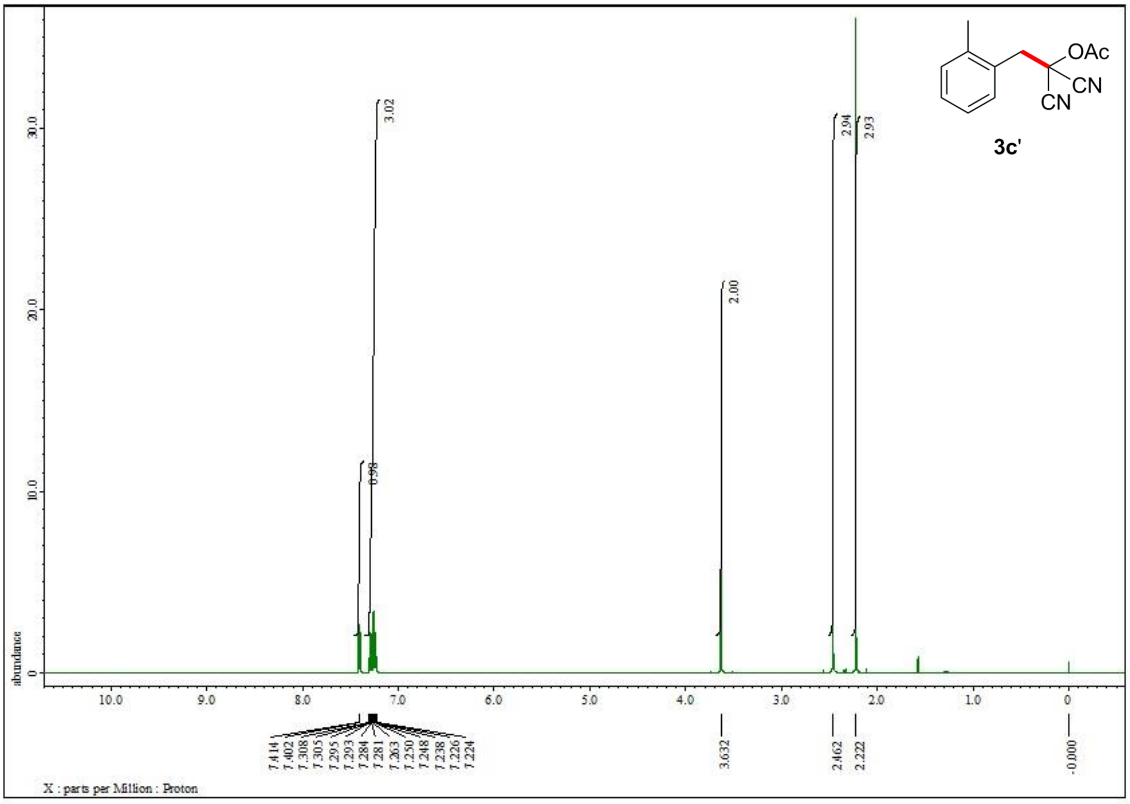
77.000
76.789
62.274
43.938
20.049
X : parts per Million : Carbon13


OAc
CN
CN
3c'
3.02
2.94
2.93
2.00
0.98
abundance
7.414
7.402
7.308
7.305
7.295
7.293
7.284
7.281
7.263
7.250
7.248
7.238
7.226
7.224
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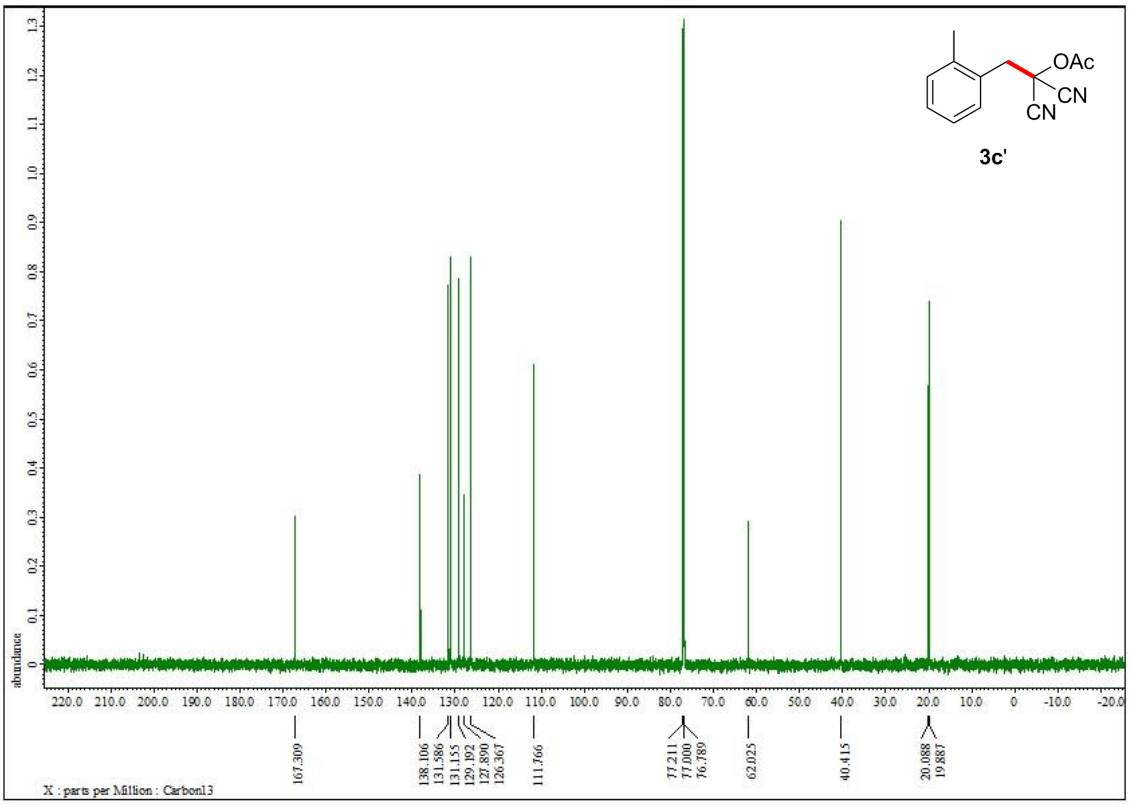
2.462
2.222
-0.000
X : parts per Million : Proton


OAc
CN
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3c'
abundance
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76.789
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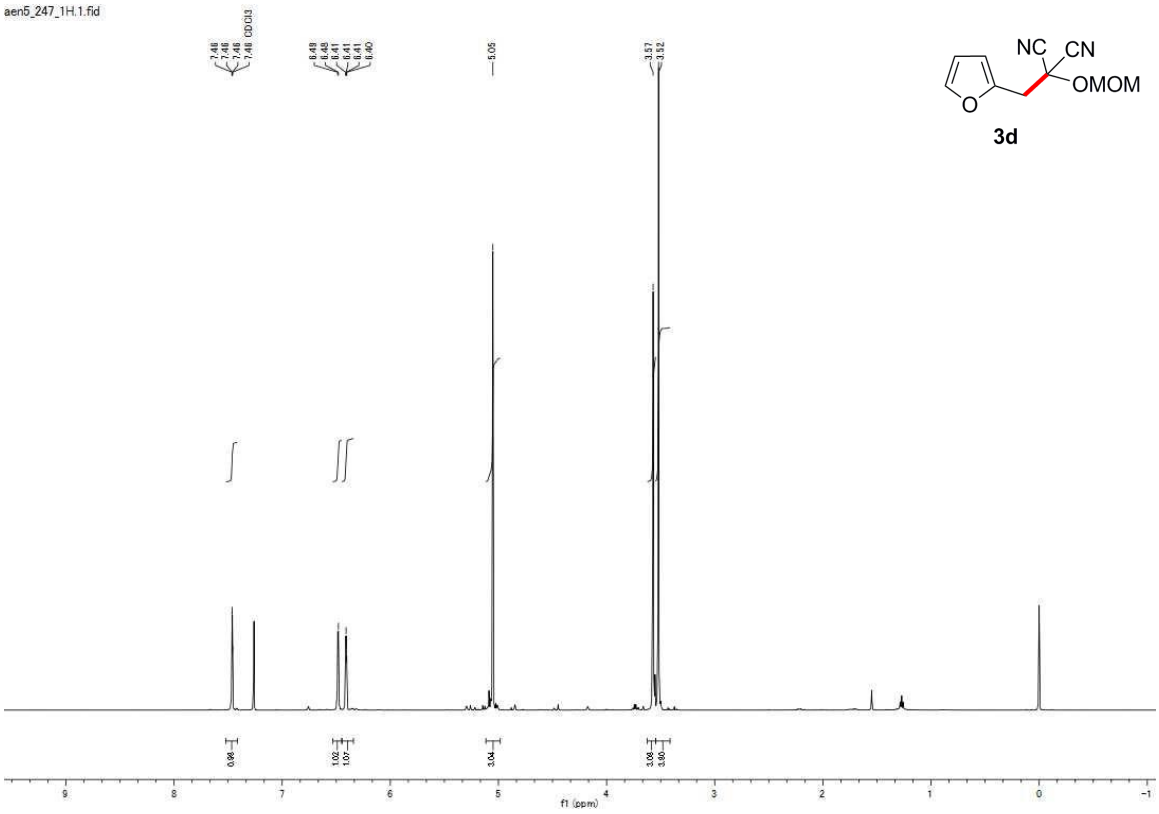
40.415
20.088
19.887
X : parts per Million : Carbon13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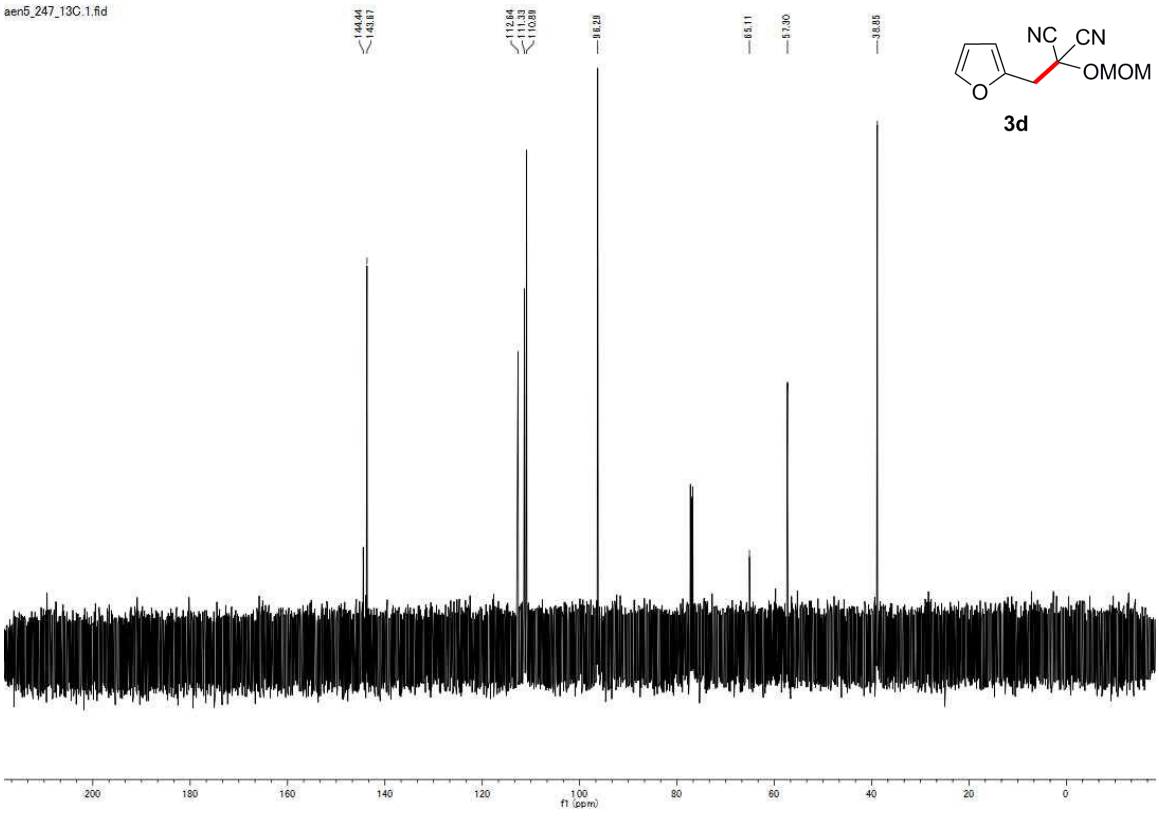
7.46
7.46
7.46 CDCl3
6.49
6.48
6.41
6.41
6.41
6.40
5.05
3.57
3.52
0.98
1.02
1.07
3.04
3.08
3.00
f1 (ppm)
NC
CN
OMOM
O
3d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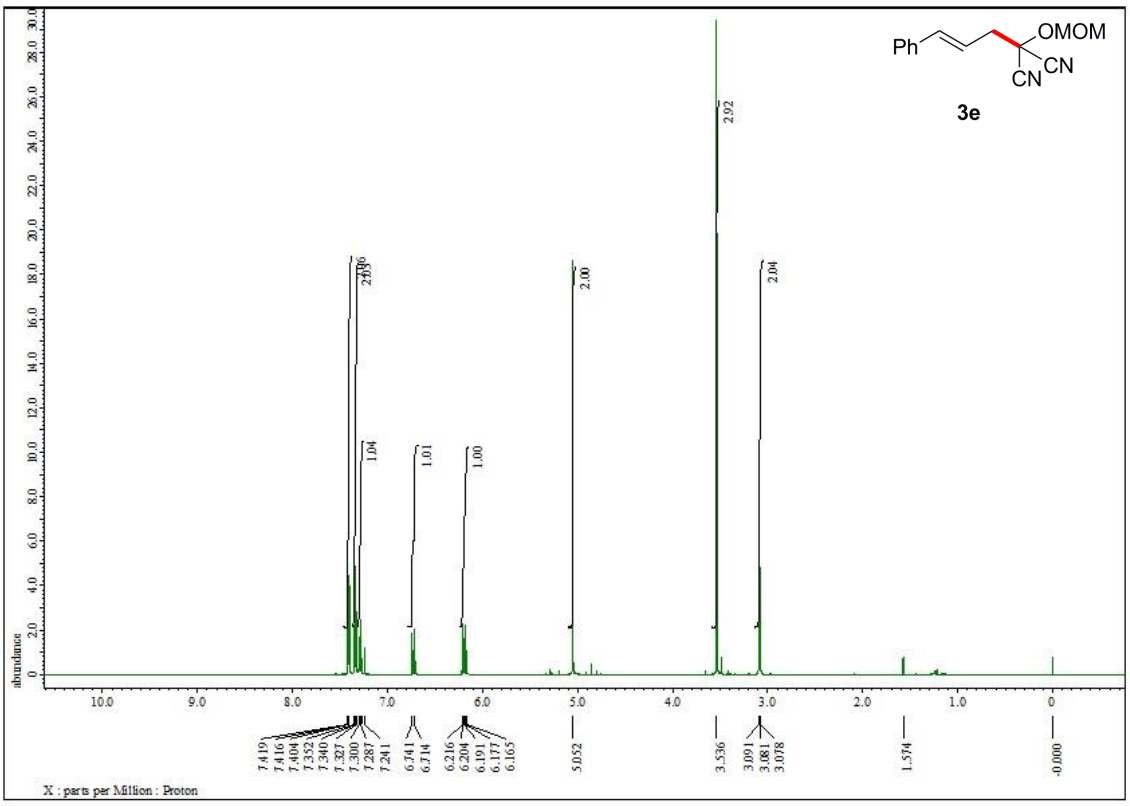
f1 (ppm)
NC
CN
OMOM
O
3d


Ph
OMOM
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CN
3e
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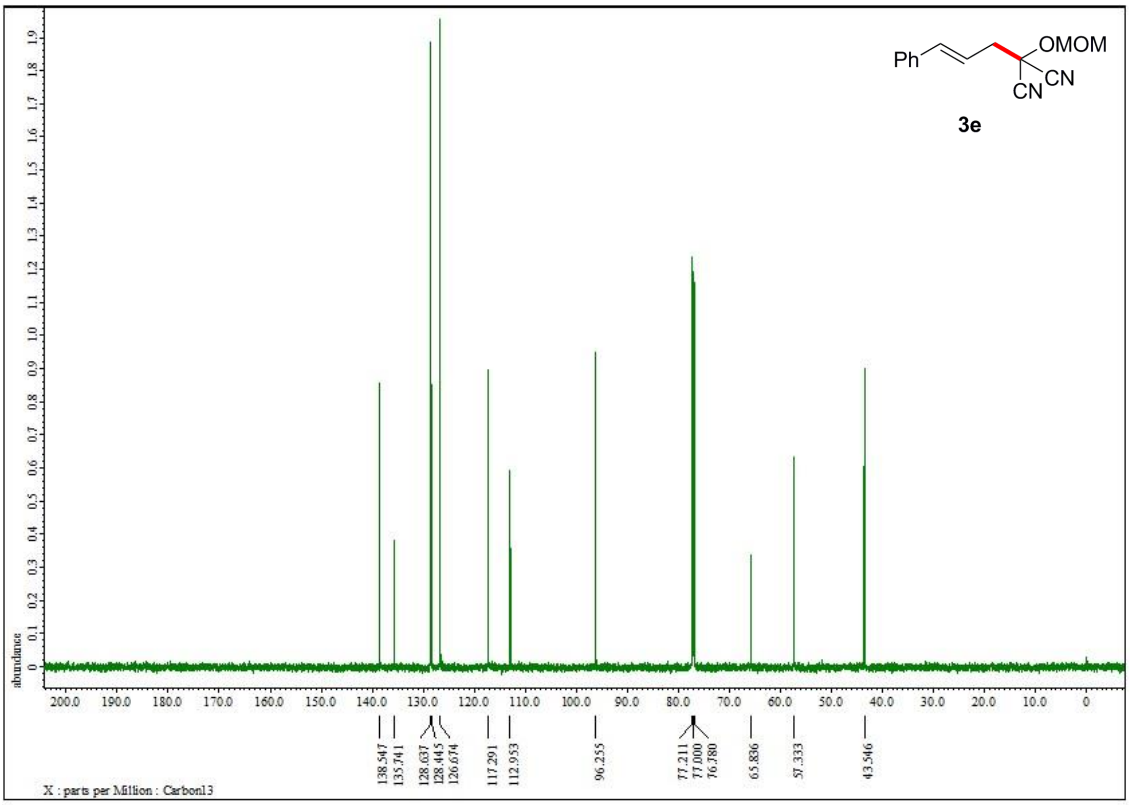
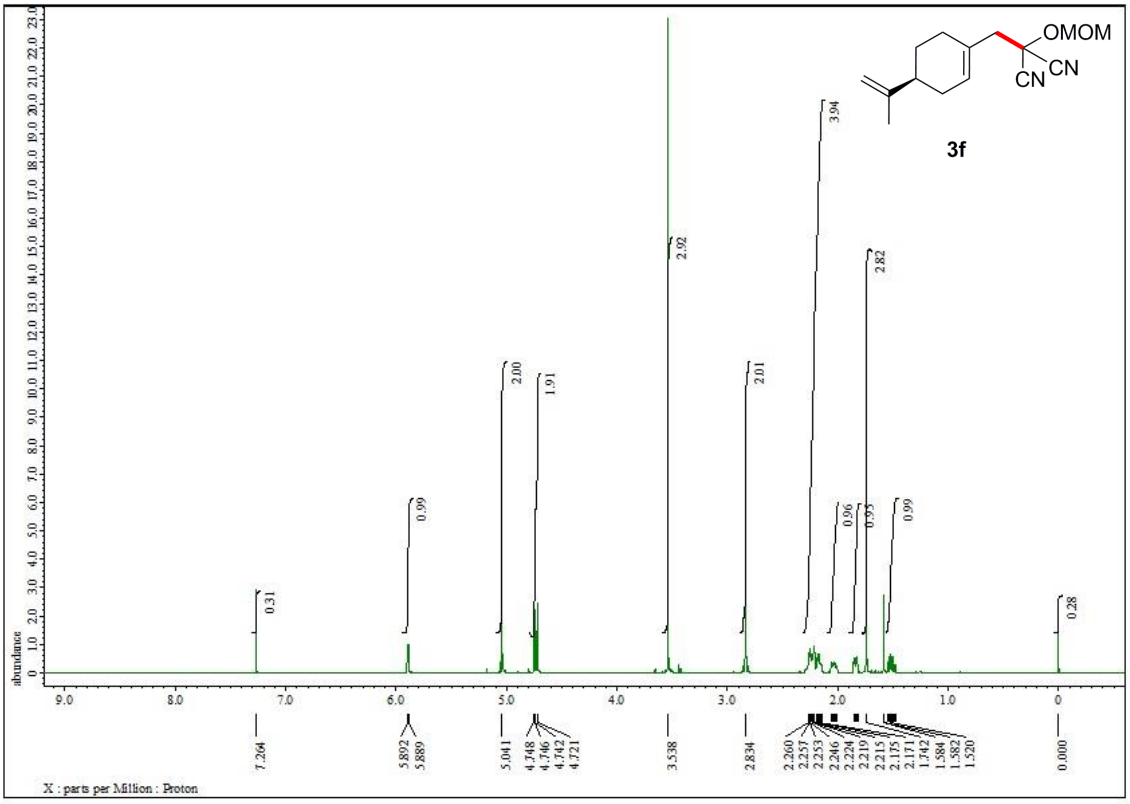
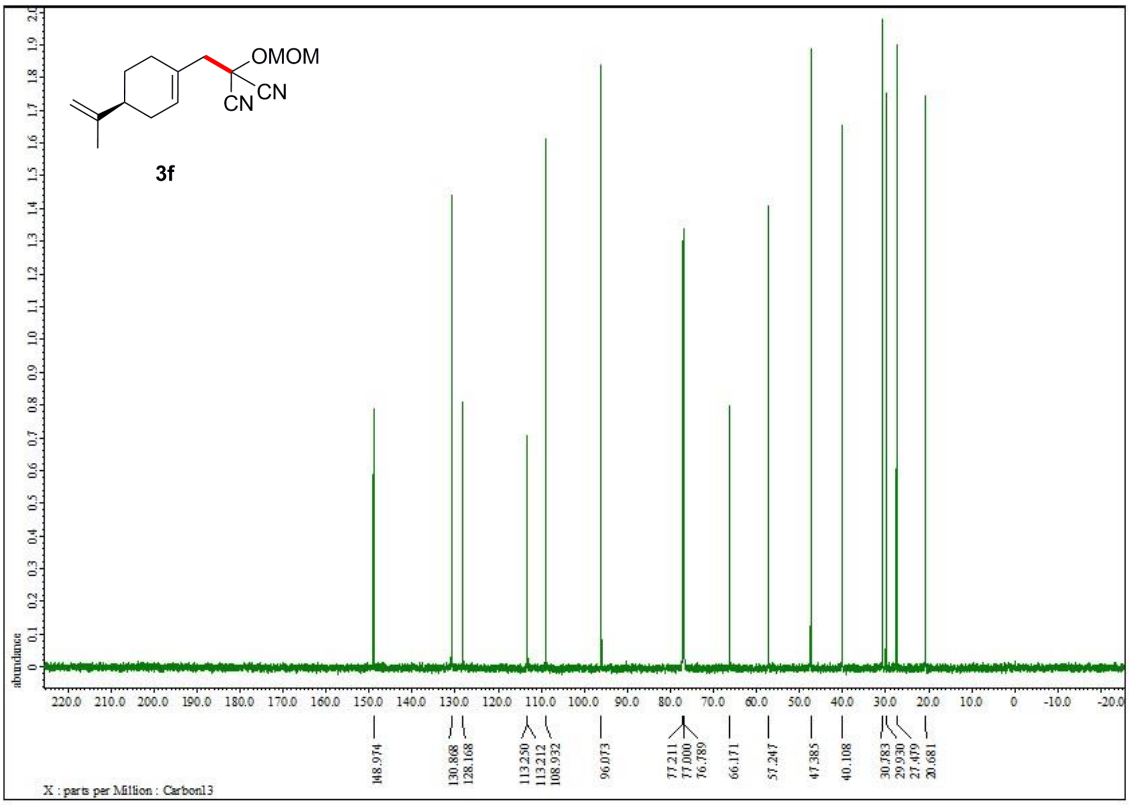
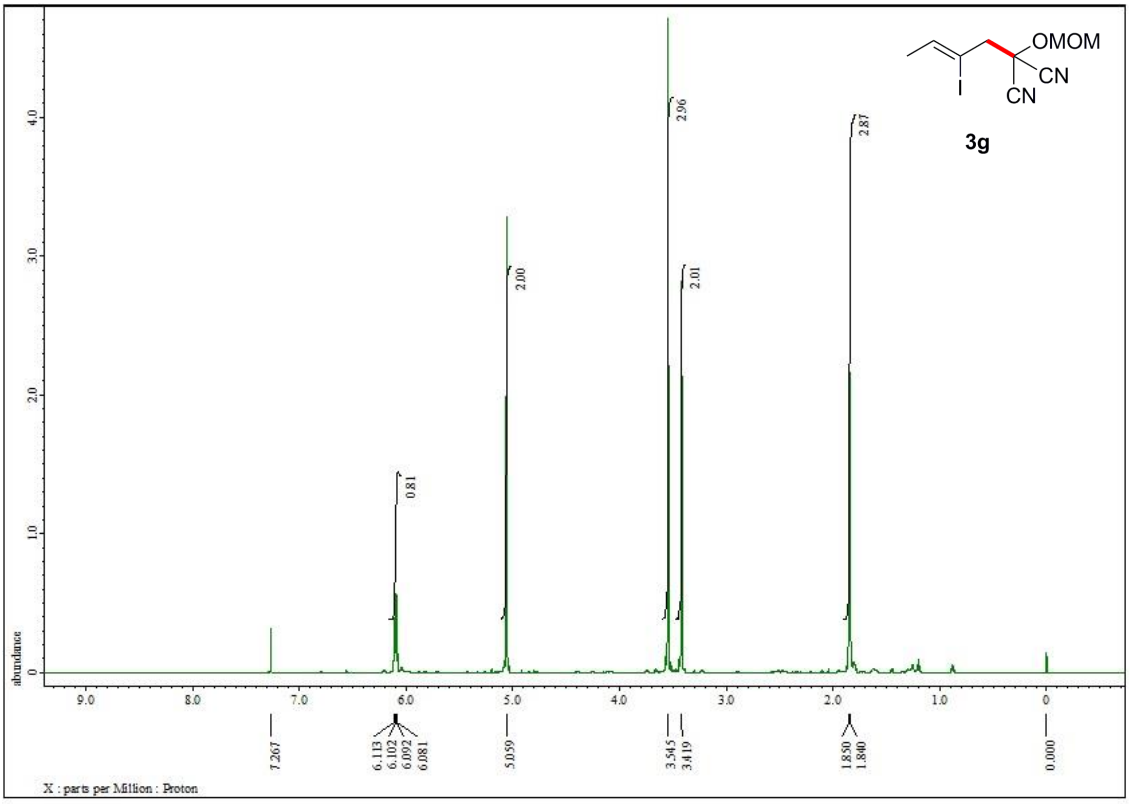
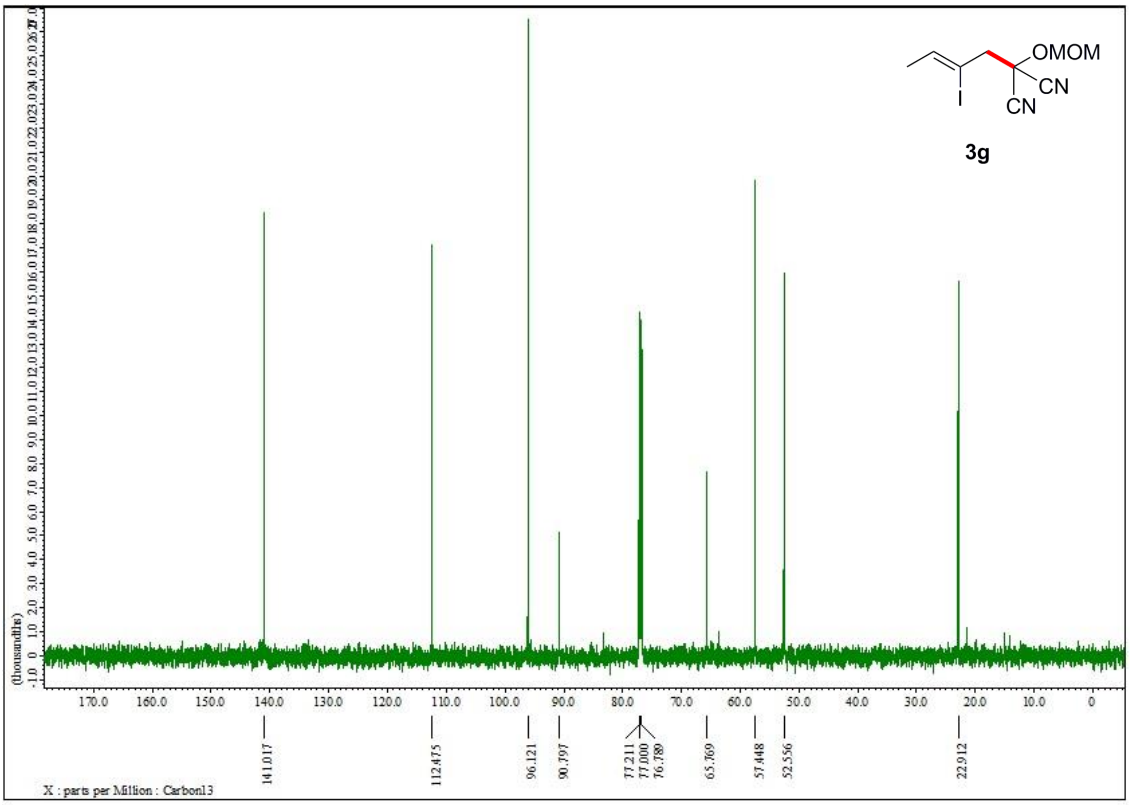
2.00
2.04
1.04
1.01
1.00
abundance
X : parts per Million : Proton

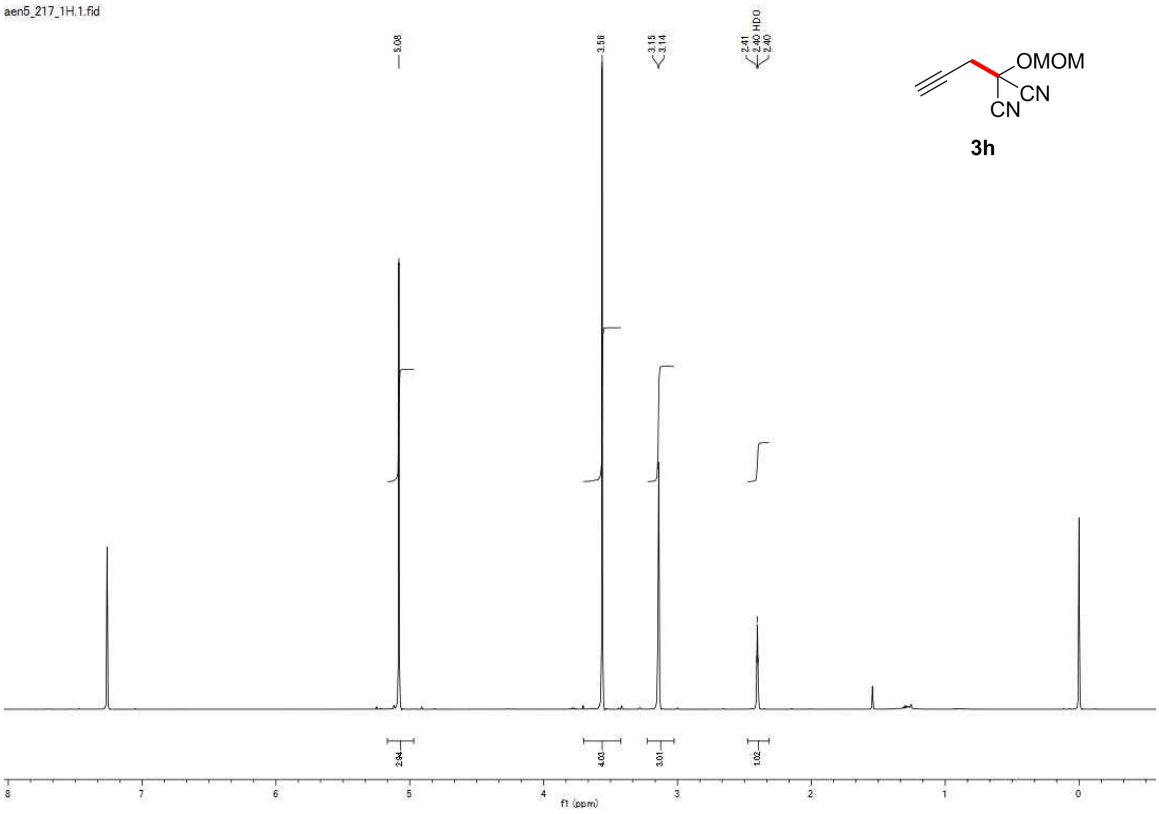

Ph
OMOM
CN
CN
3e
abundance
X : parts per Million : Carbon13

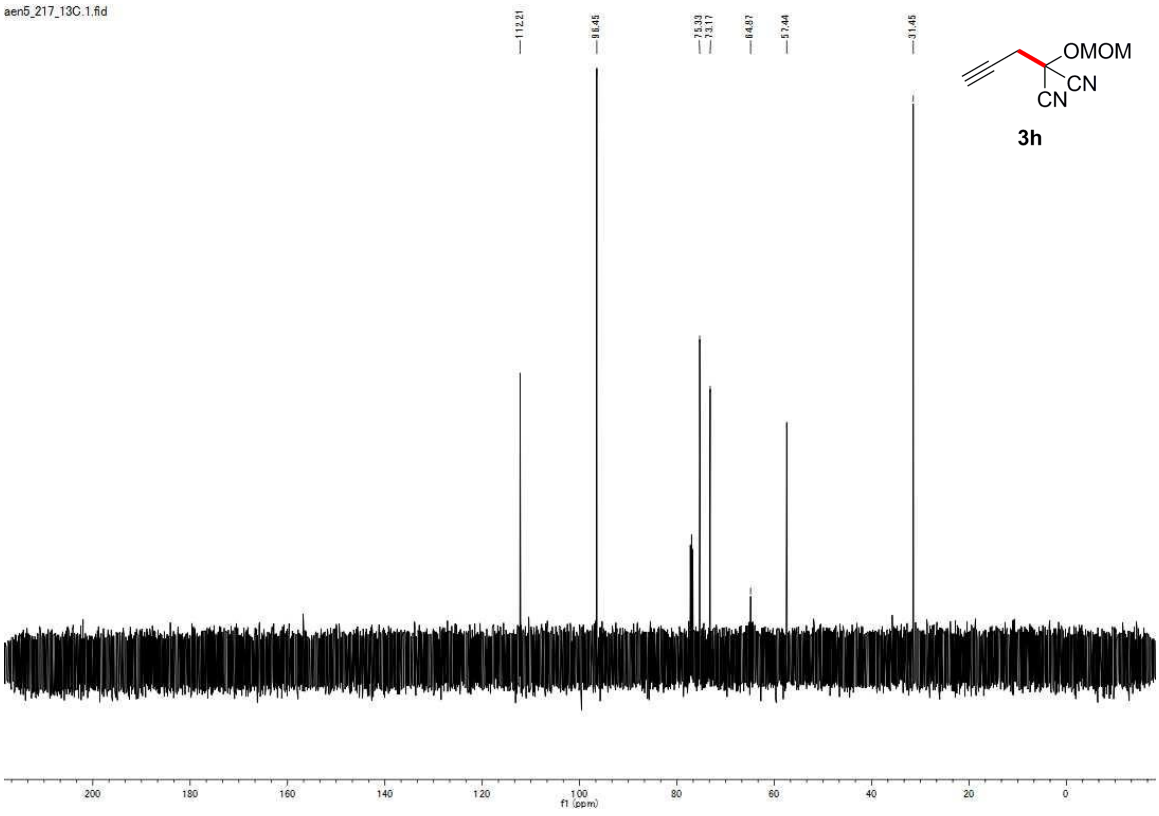

OMOM
CN
CN
3f
abundance
X : parts per Million : Proton

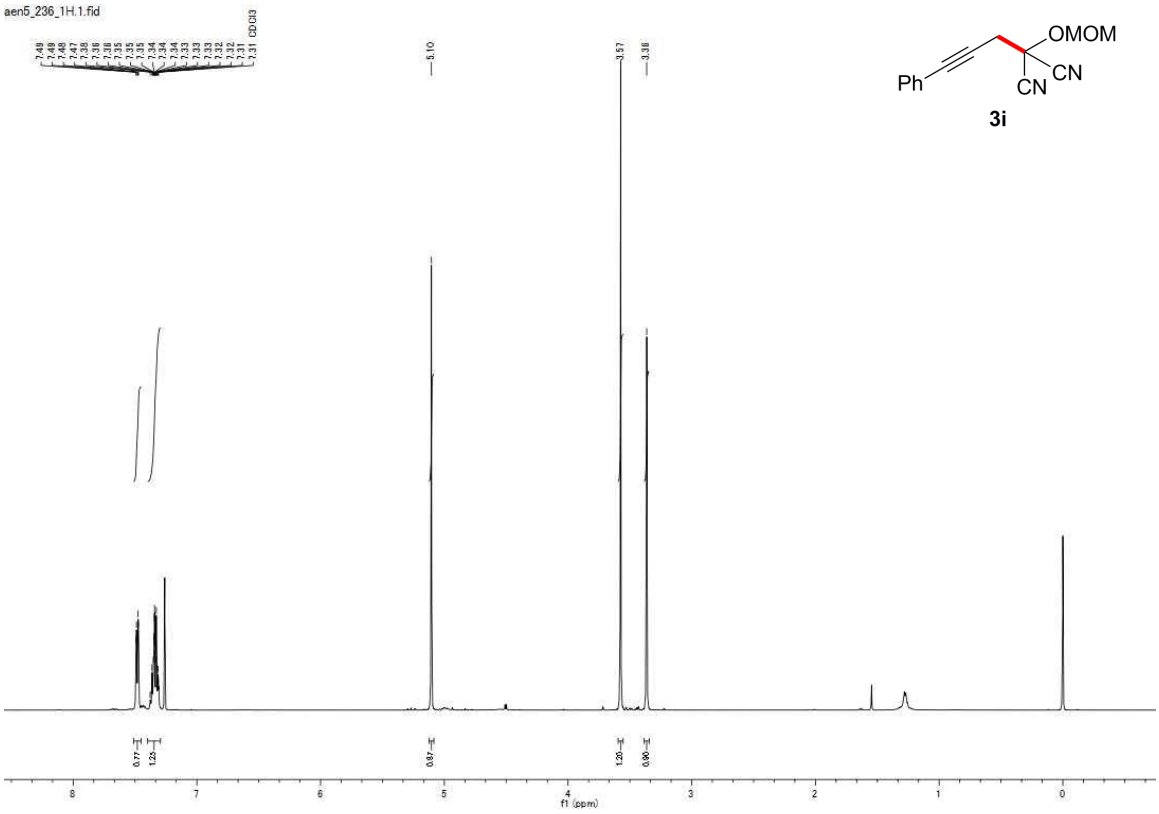

OMOM
CN
CN
3f
abundance
X : parts per Million : Carbon13

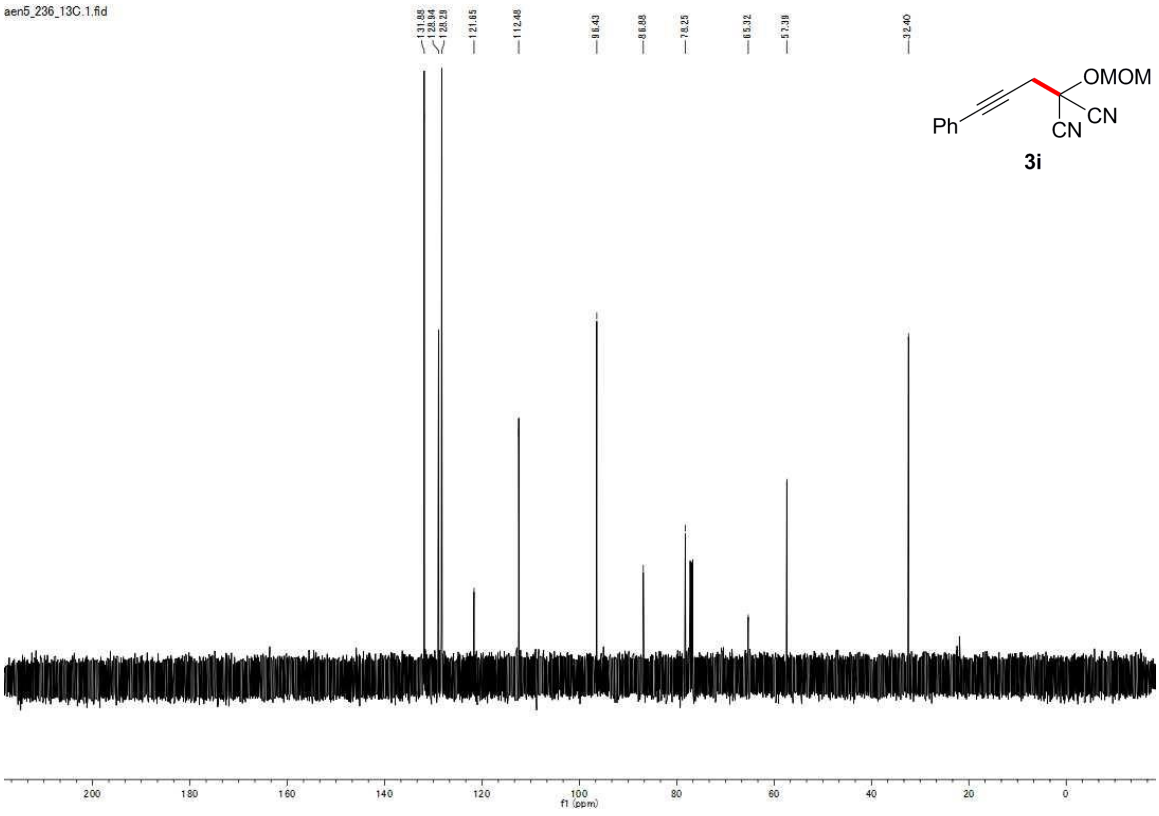

OMOM
CN
CN
I
3g
abundance
0.81
2.00
2.96
2.01
2.87
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.267
6.113
6.102
6.092
6.081
5.059
3.545
3.419
1.850
1.840
0.000
X : parts per Million : Proton

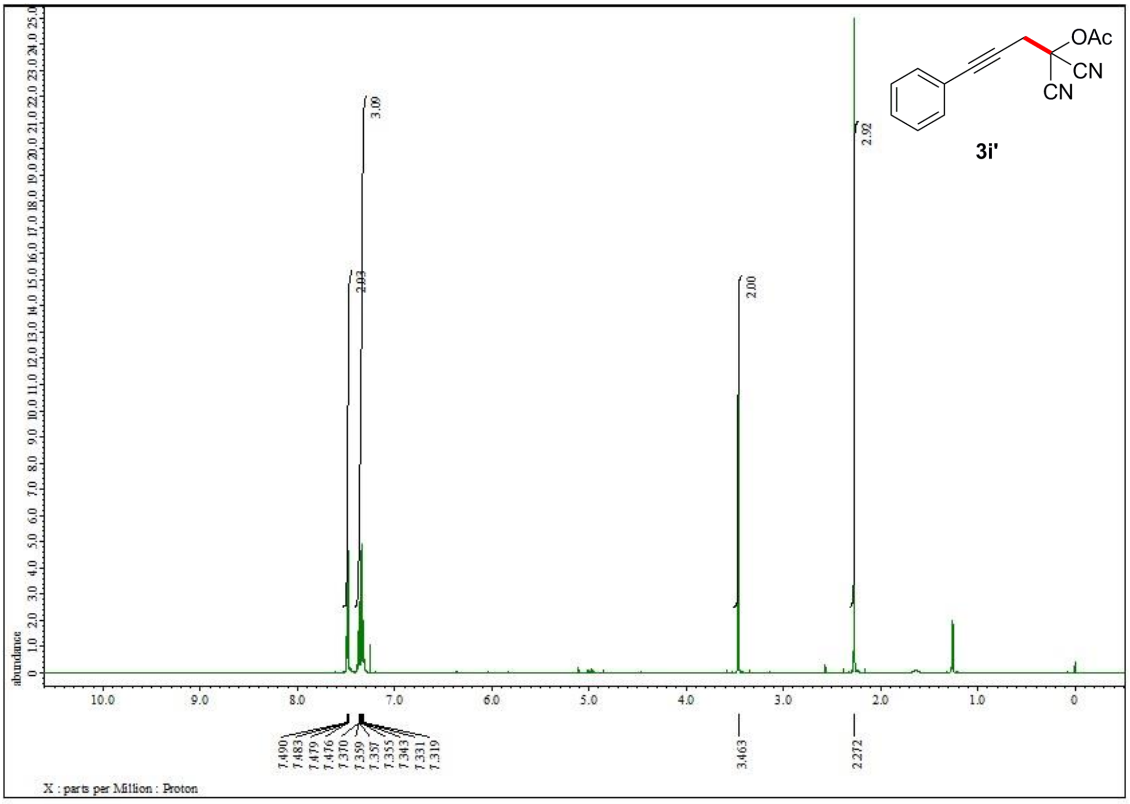

OMOM
CN
CN
I
3g
(thousandths)
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
141.017
112.475
96.121
90.797
77.211
77.000
76.789
65.769
57.448
52.556
22.912
X : parts per Million : Carbon13

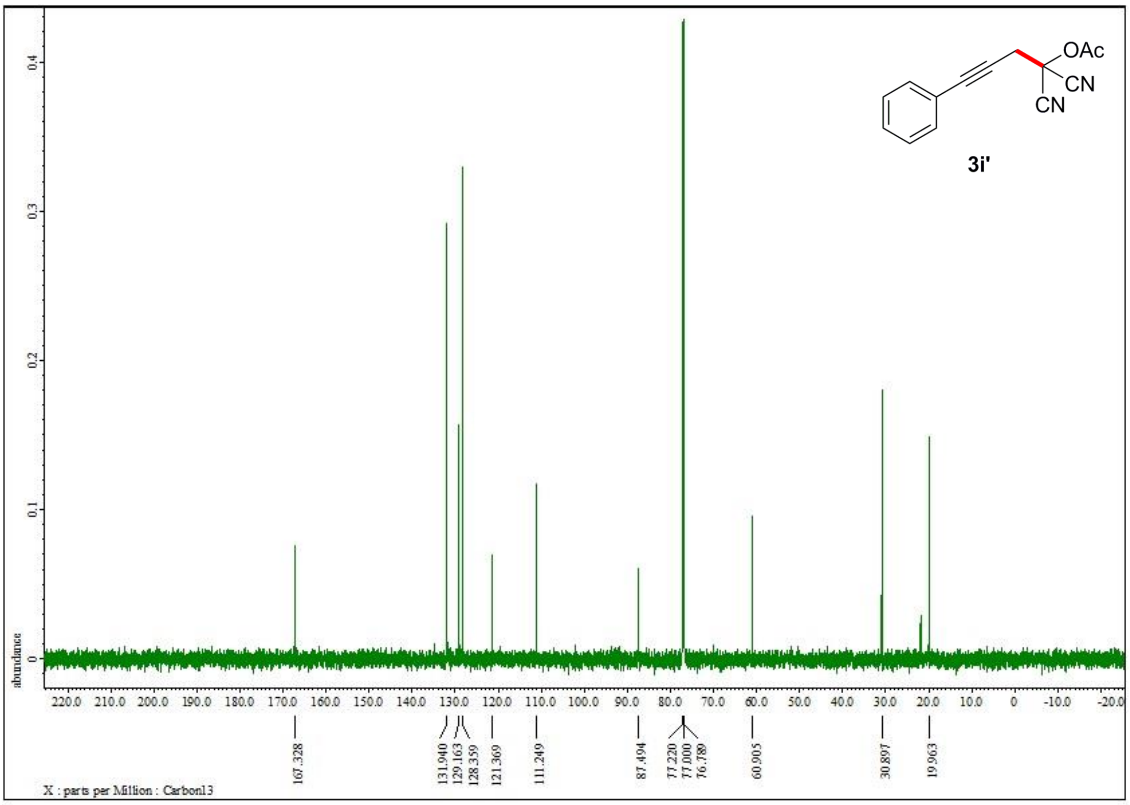

aen5_217_1H.1.fid
5.08
3.56
3.15
2.14
2.41
2.40 HDO
2.40
2.84
4.03
3.01
1.02
f1 (ppm)
OMOM
CN
CN
3h

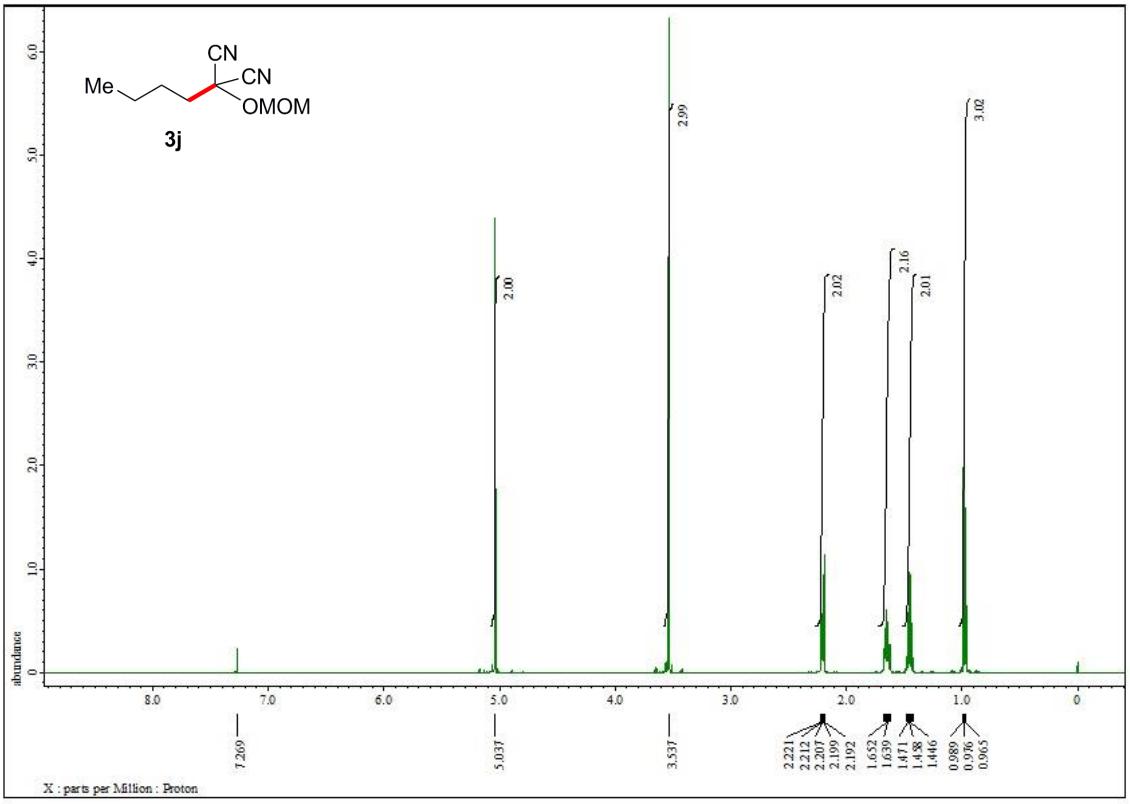

aen5_217_13C.1.fid
112.21
98.45
75.33
73.17
64.07
57.44
31.45
f1 (ppm)
OMOM
CN
CN
3h

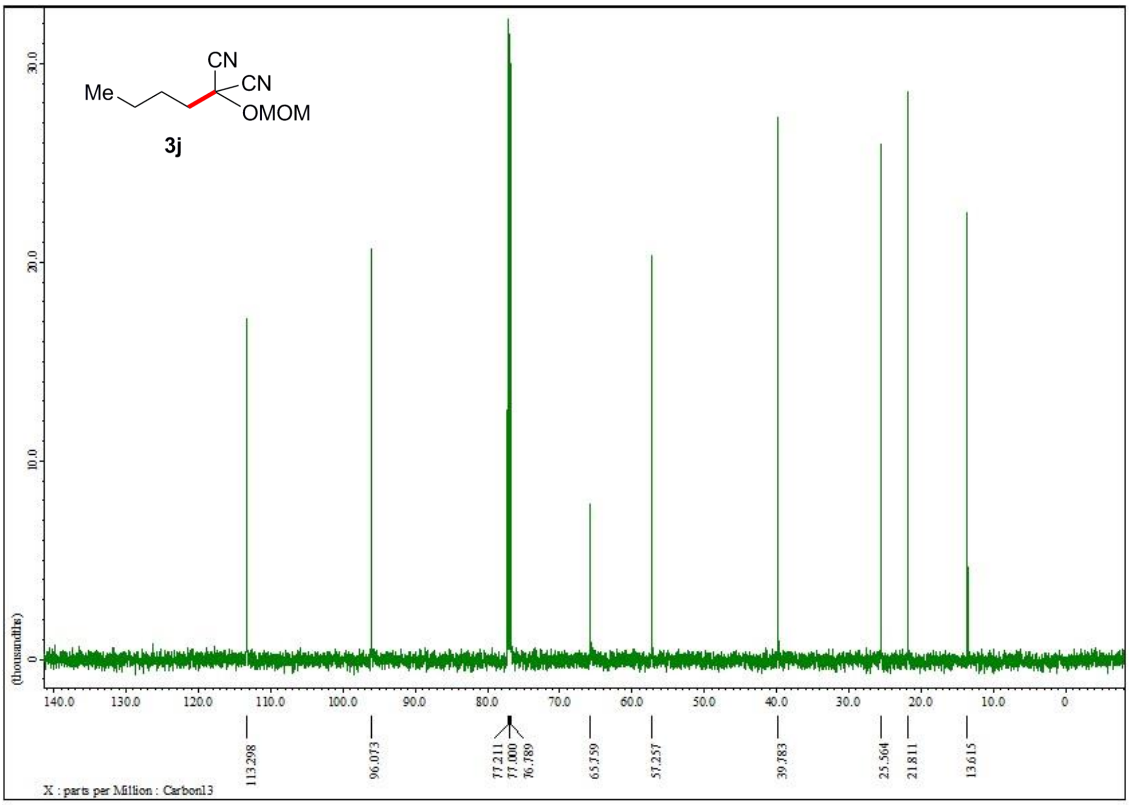

aen5_236_1H.1.fid
OMOM
Ph
CN
CN
3i
f1 (ppm)

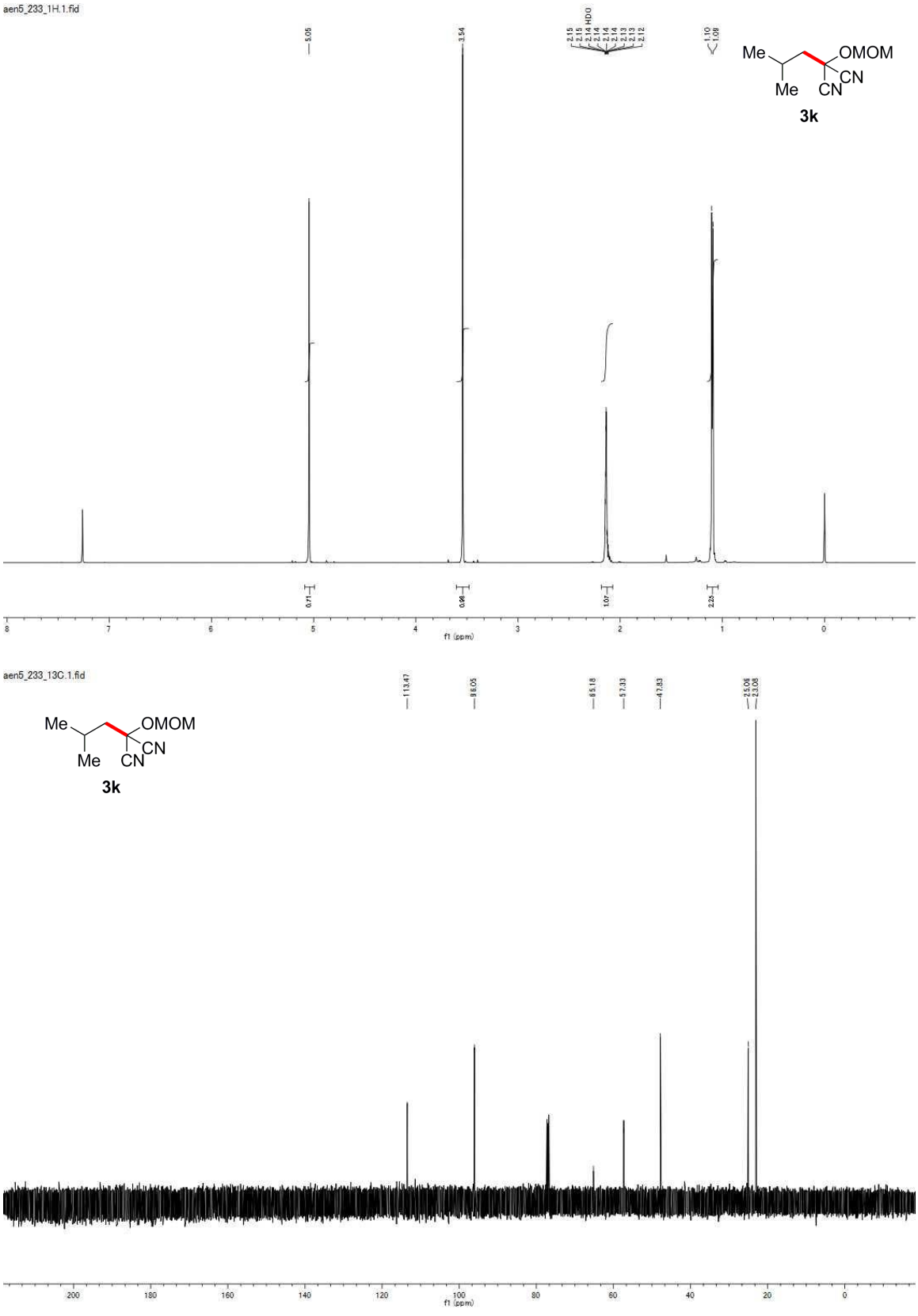

aen5_236_13C.1.fid
OMOM
Ph
CN
CN
3i
f1 (ppm)

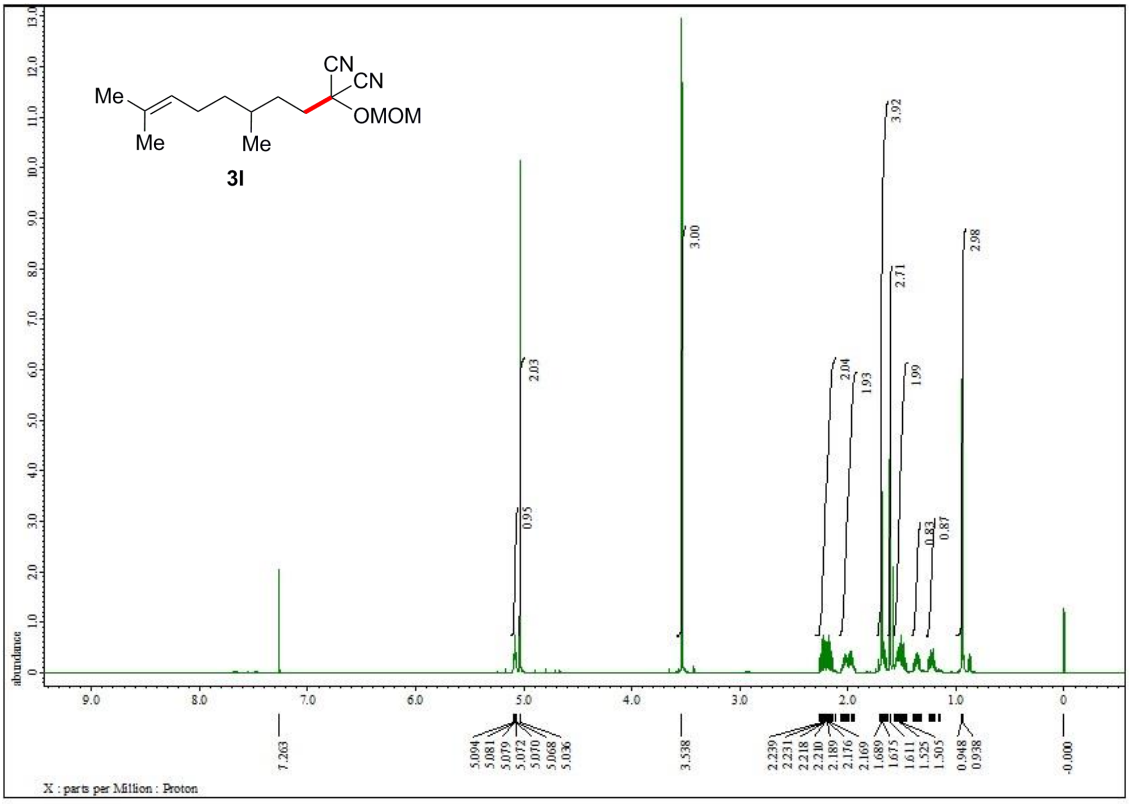

OAc
CN
CN
3i'
3.09
2.93
2.00
2.92
7.490
7.483
7.479
7.476
7.370
7.359
7.357
7.355
7.343
7.331
7.319
3.463
2.272
X : parts per Million : Proton

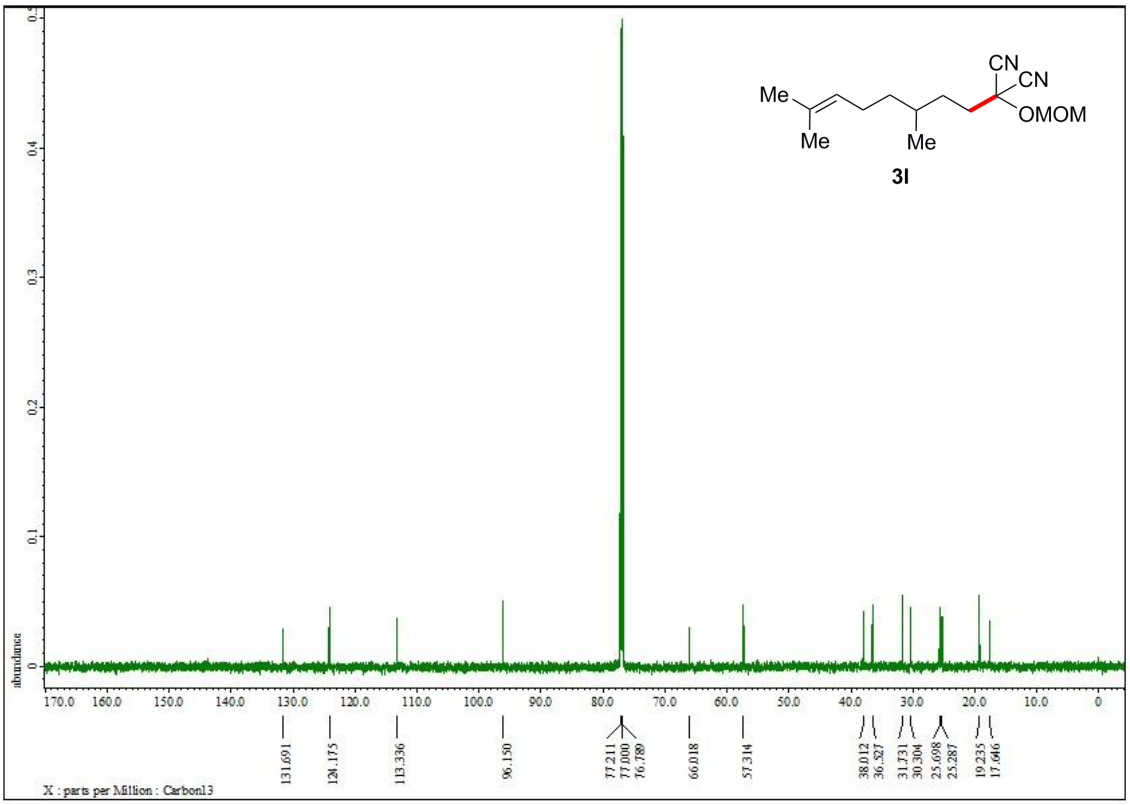

OAc
CN
CN
3i'
167.328
131.940
129.163
128.359
121.369
111.249
87.494
77.220
77.000
76.789
60.905
30.897
19.963
X : parts per Million : Carbon13

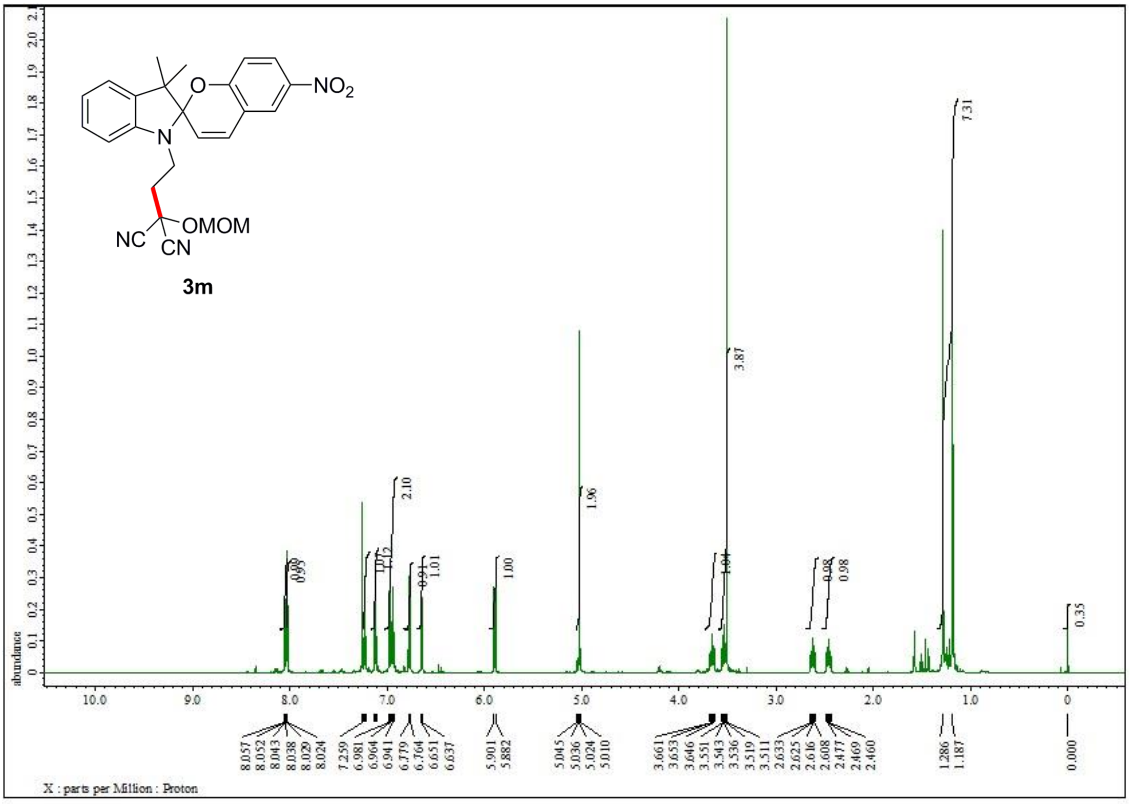

CN
CN
Me
OMOM
3j
2.00
2.99
2.02
2.16
2.01
3.02
abundance
7.269
5.037
3.537
2.221
2.212
2.207
2.199
2.192
1.652
1.639
1.471
1.438
1.446
0.989
0.976
0.965
X : parts per Million : Proton

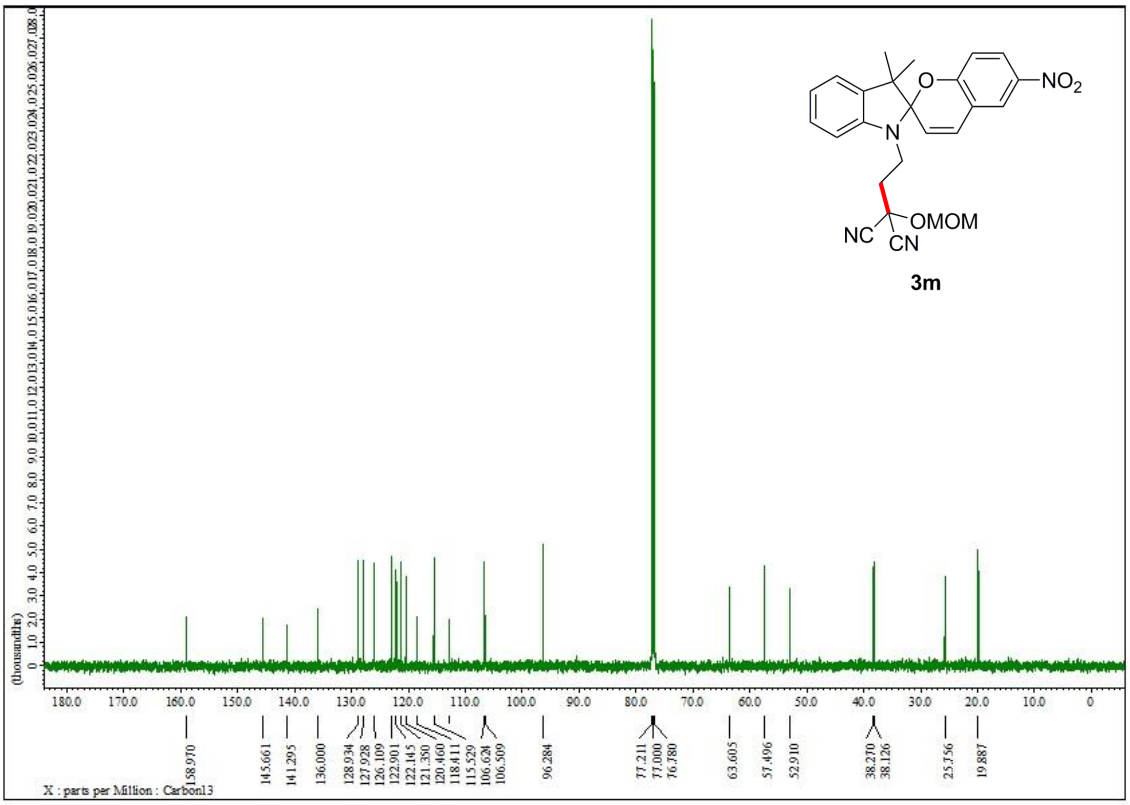

CN
CN
Me
OMOM
3j
(thousandths)
113.298
96.073
77.211
77.000
76.789
65.759
57.257
39.783
25.564
21.811
13.615
X : parts per Million : Carbon13

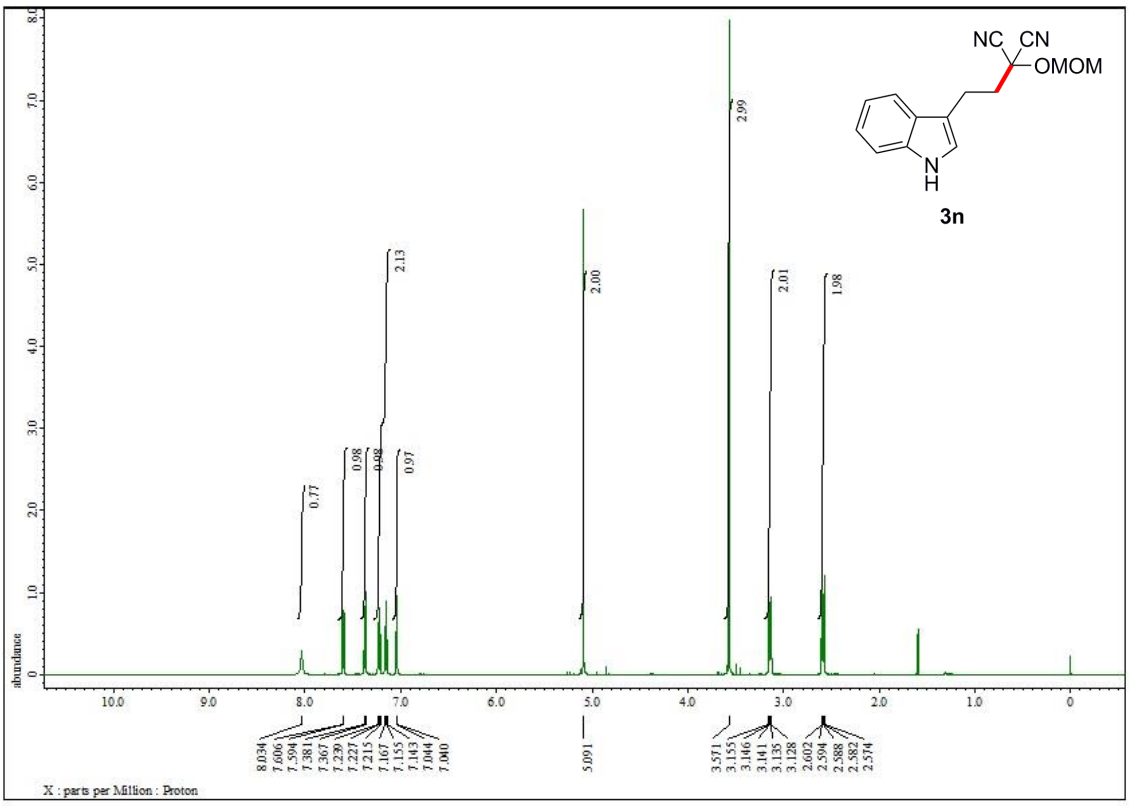

aen5_233_1H.1.fid
5.05
3.54
HDO
1.10
1.08
Me
OMOM
CN
Me
CN
3k
0.71
0.98
1.07
2.25
f1 (ppm)
aen5_233_13C.1.fid
113.47
98.05
65.18
57.33
47.83
25.06
23.08
Me
OMOM
CN
Me
CN
3k
f1 (ppm)

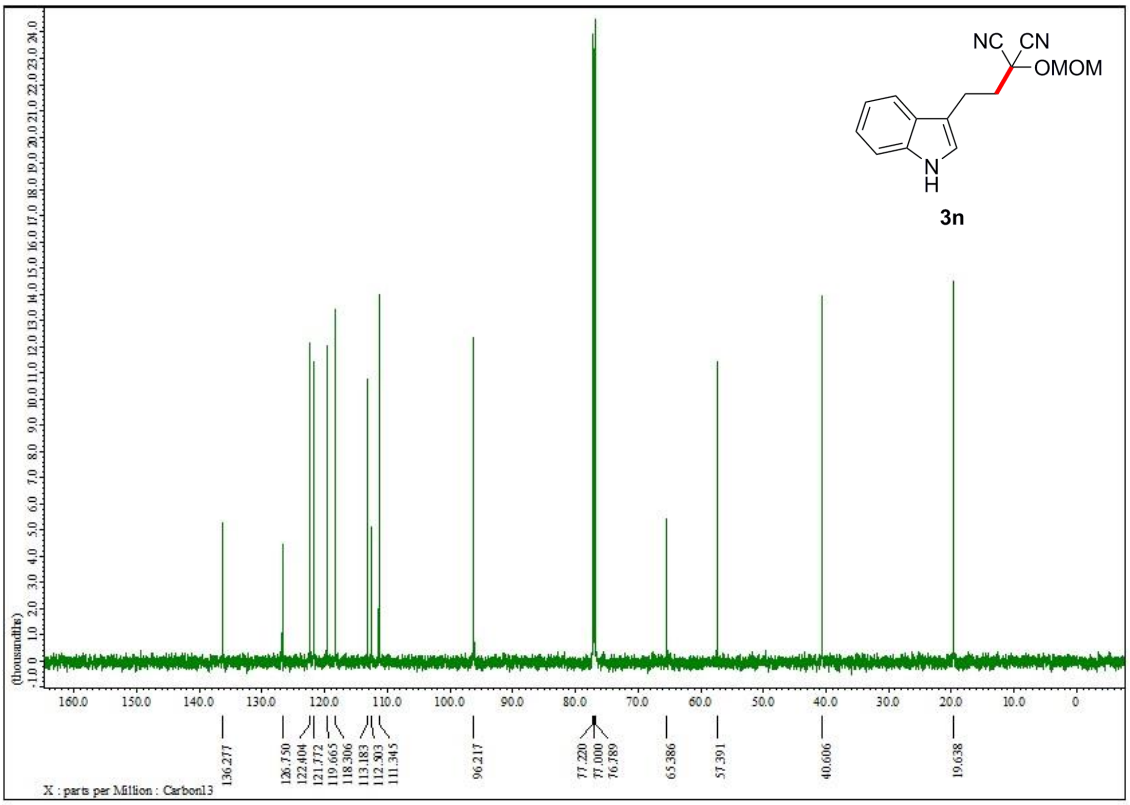

CN
CN
OMOM
Me
Me
Me
3l
abundance
X : parts per Million : Proton

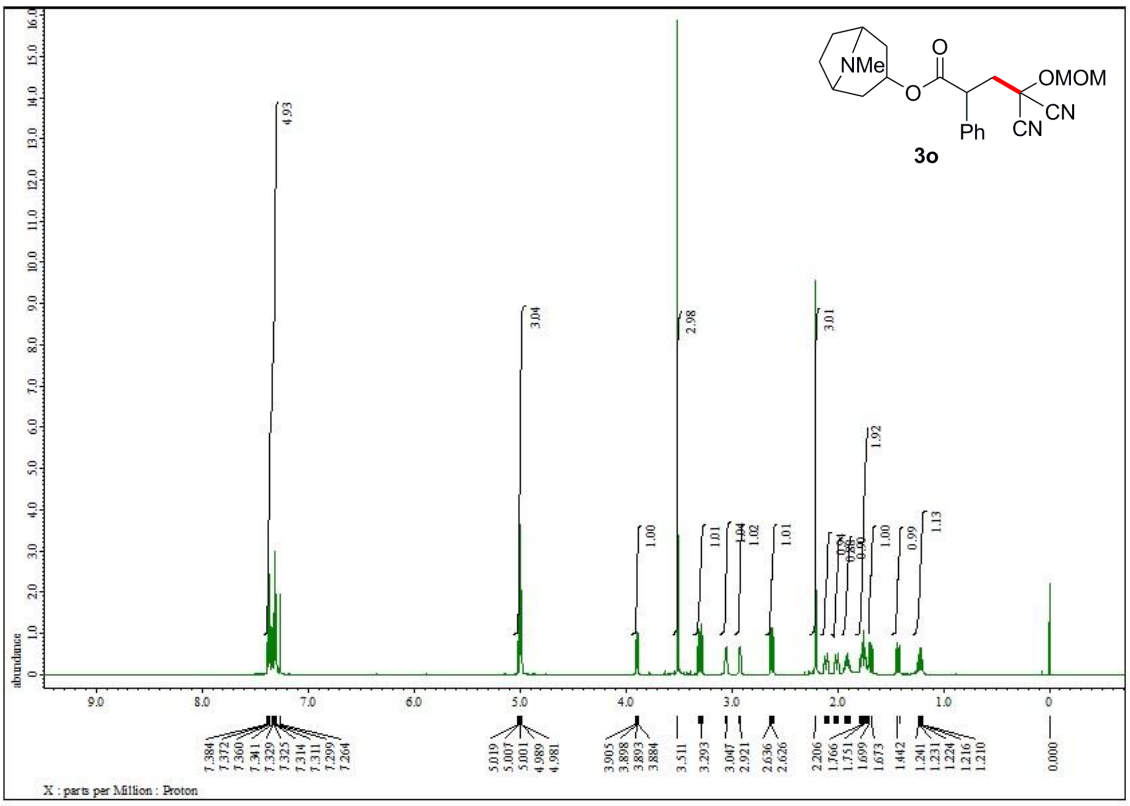

CN
CN
OMOM
Me
Me
Me
3l
abundance
X : parts per Million : Carbon13

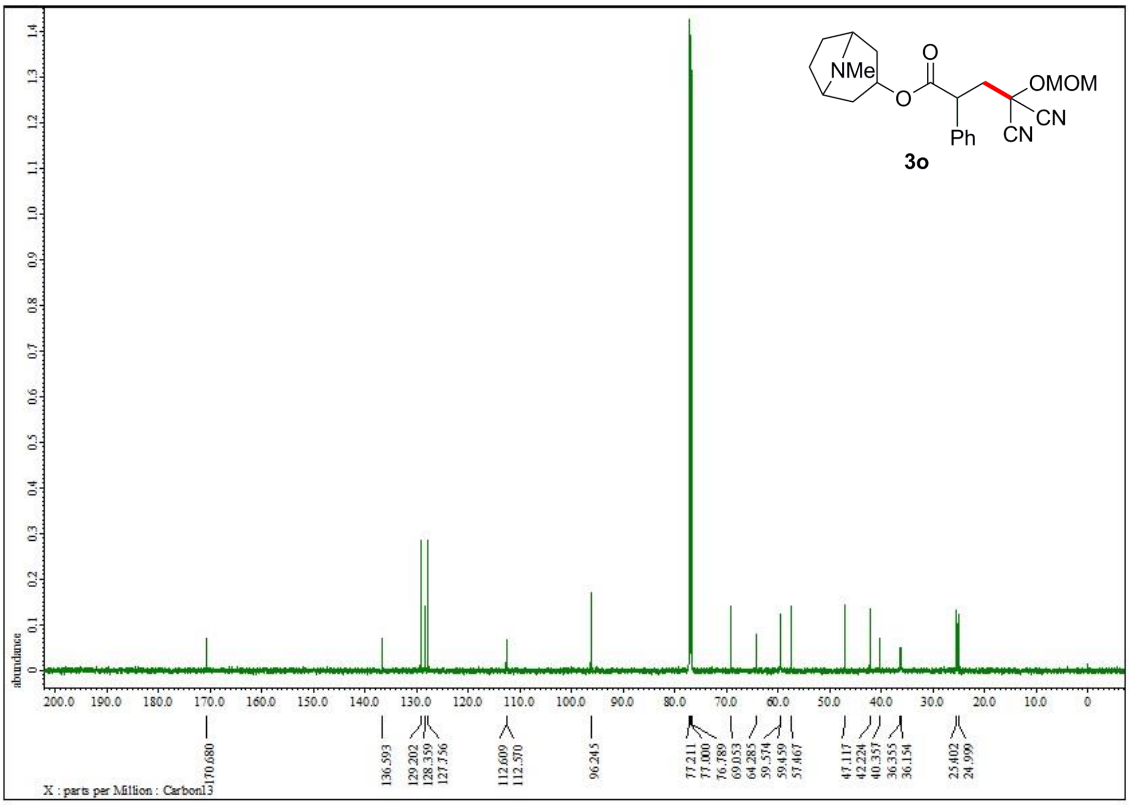

NO2
O
N
NC
CN
OMOM
3m
abundance
X : parts per Million : Proton

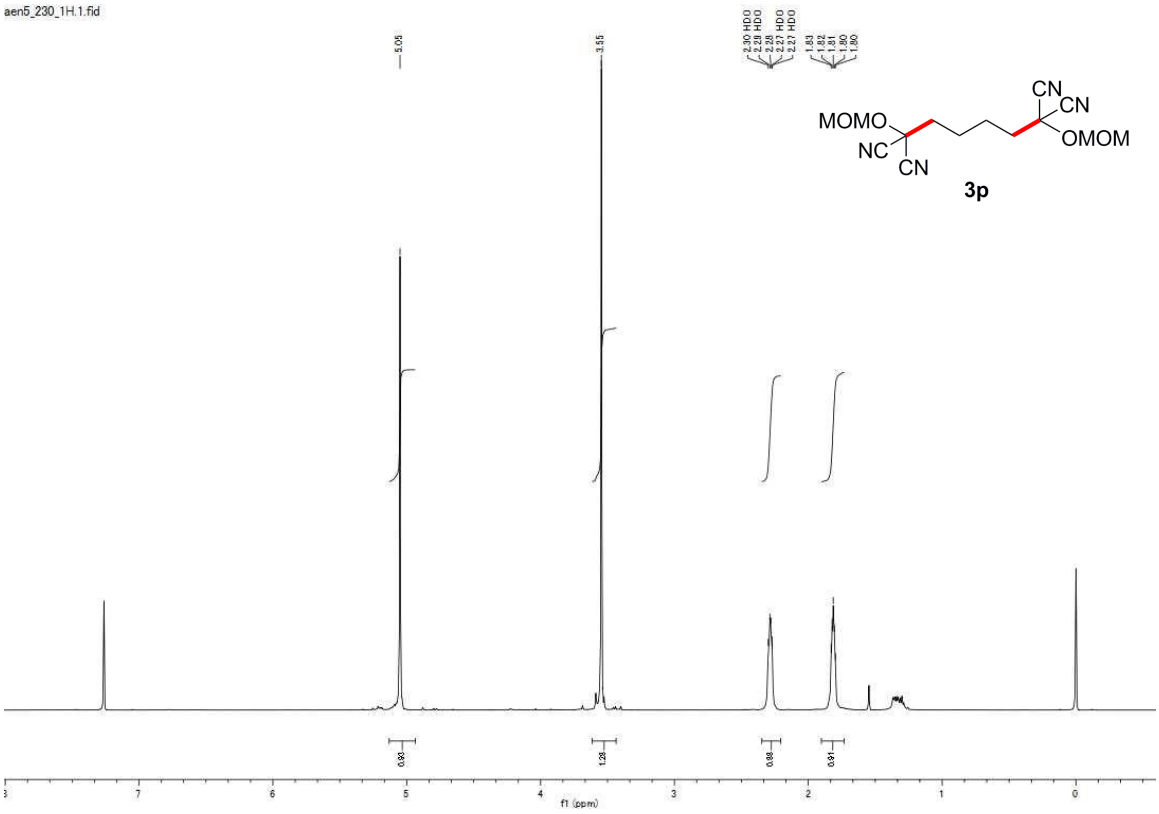

NO2
O
N
NC
CN
OMOM
3m
(thousandths)
X : parts per Million : Carbon13

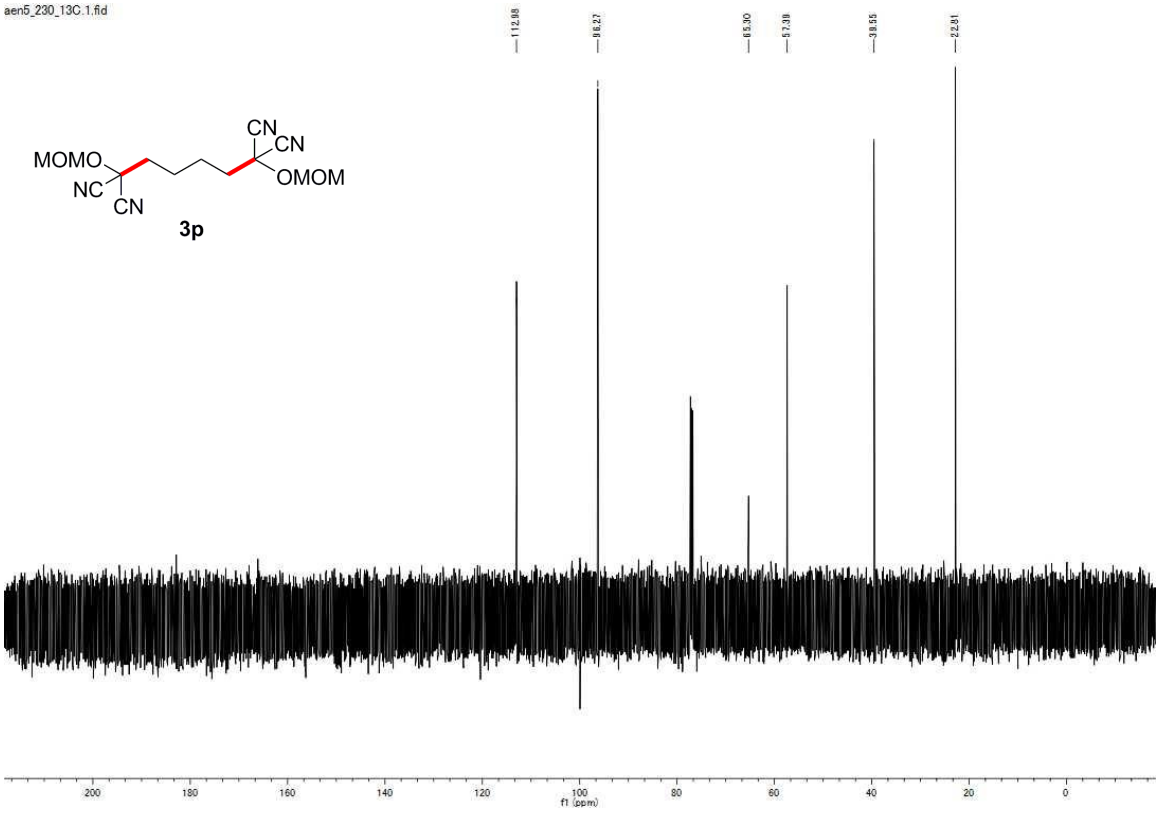

NC CN
OMOM
N
H
3n
abundance
X : parts per Million : Proton

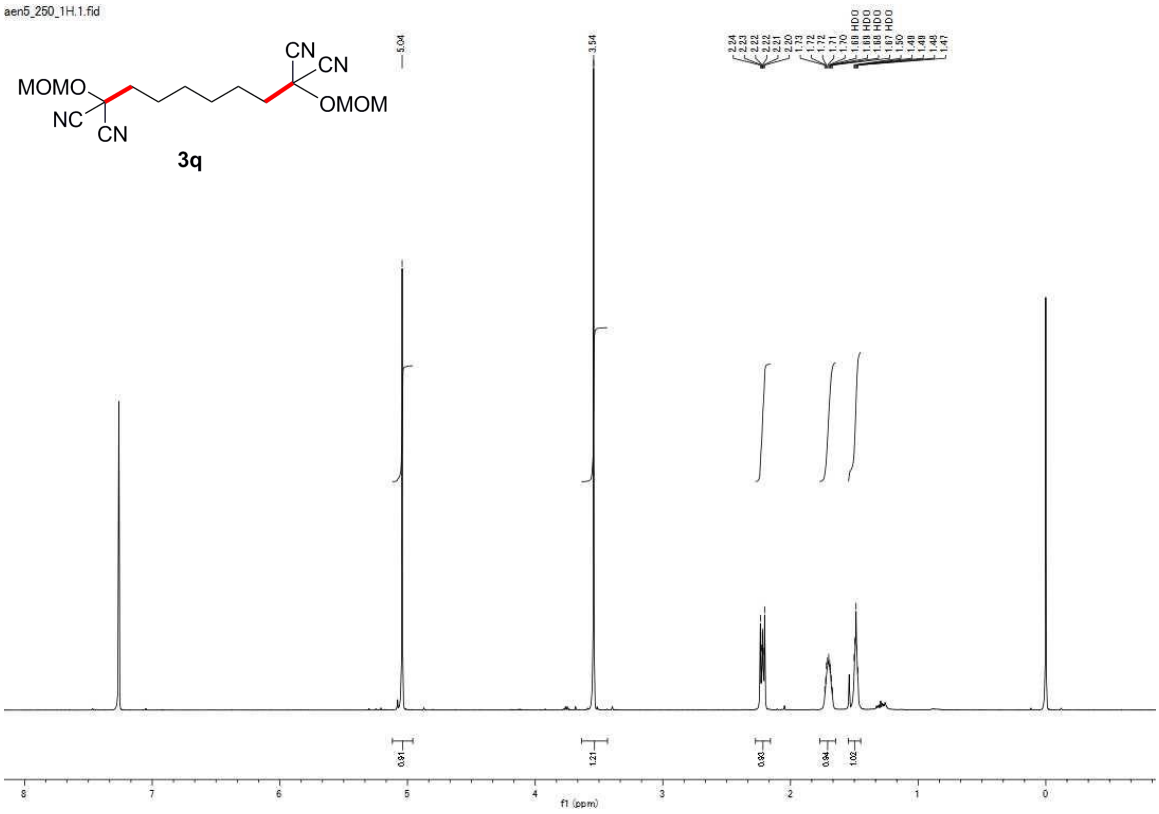

NC CN
OMOM
N
H
3n
(thousandths)
X : parts per Million : Carbon13

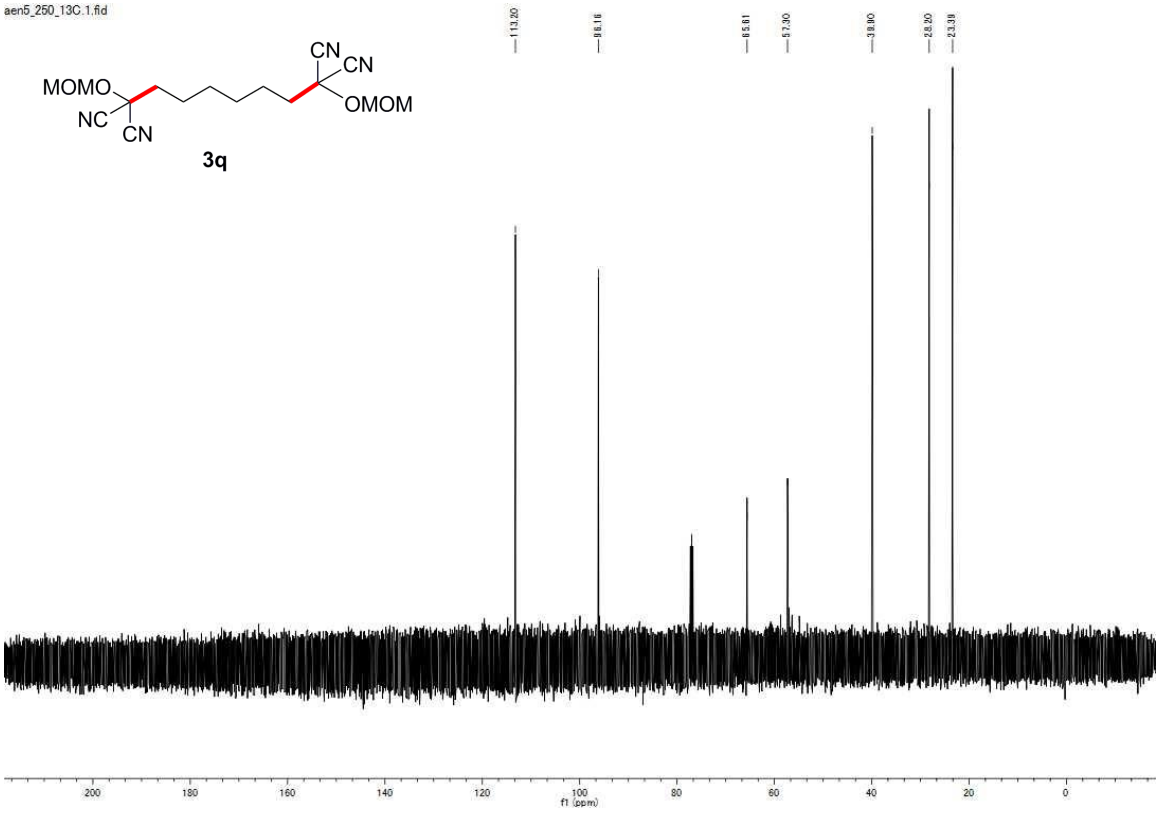

NMe
O
O
OMOM
CN
CN
Ph
3o
4.93
3.04
2.98
3.01
1.92
1.00
1.01
1.04
1.02
1.01
1.00
0.99
1.13
abundance
X : parts per Million : Proton

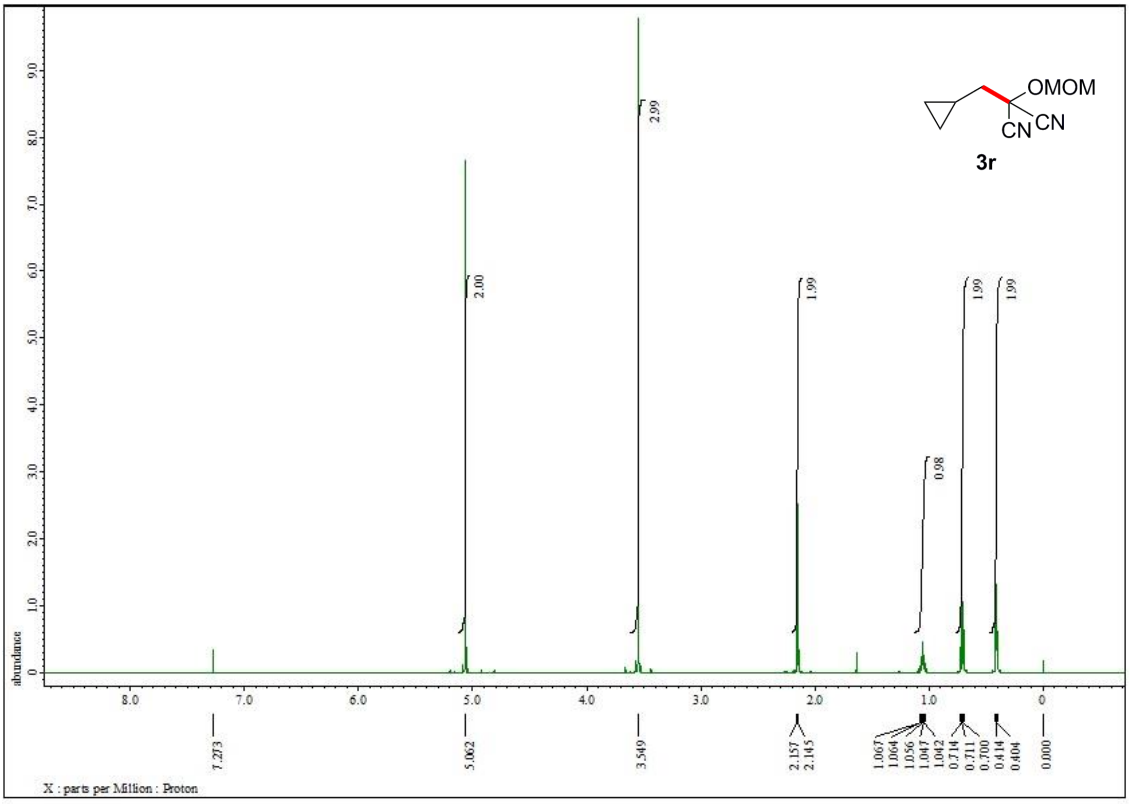

NMe
O
O
OMOM
CN
CN
Ph
3o
abundance
X : parts per Million : Carbon13

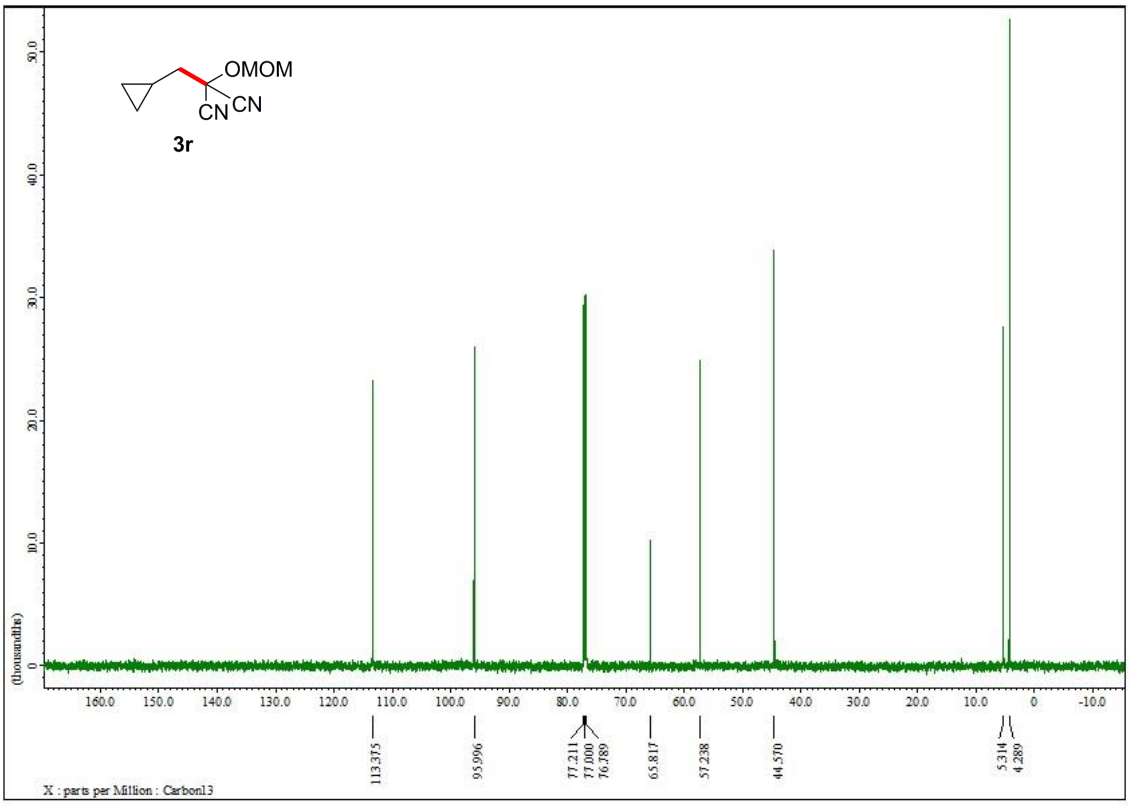

aen5_230_1H.1.fid
5.05
3.55
2.30 HDO
2.28 HDO
2.26
2.27 HDO
2.25 HDO
1.83
1.82
1.81
1.80
1.80
MOMO
NC
CN
CN
CN
OMOM
3p
0.93
1.28
0.98
0.91
f1 (ppm)

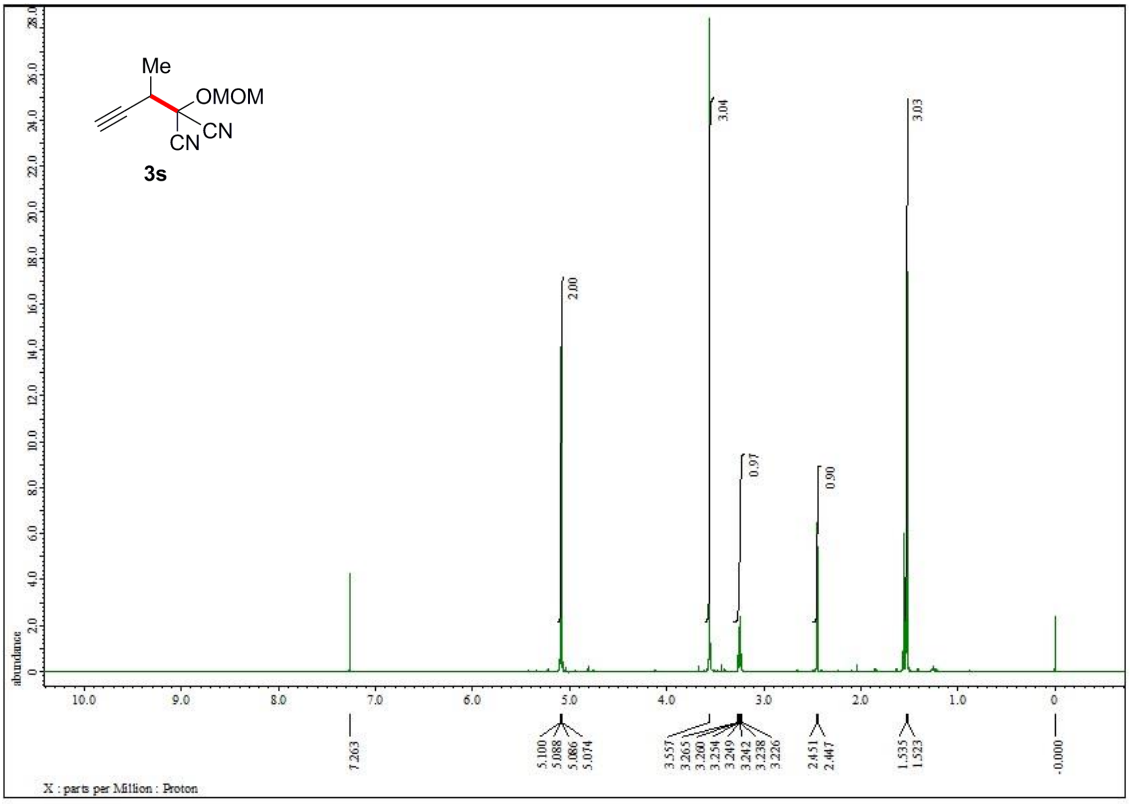

aen5_230_13C.1.fid
112.98
86.27
65.30
57.39
39.55
22.81
MOMO
NC
CN
CN
CN
OMOM
3p
f1 (ppm)

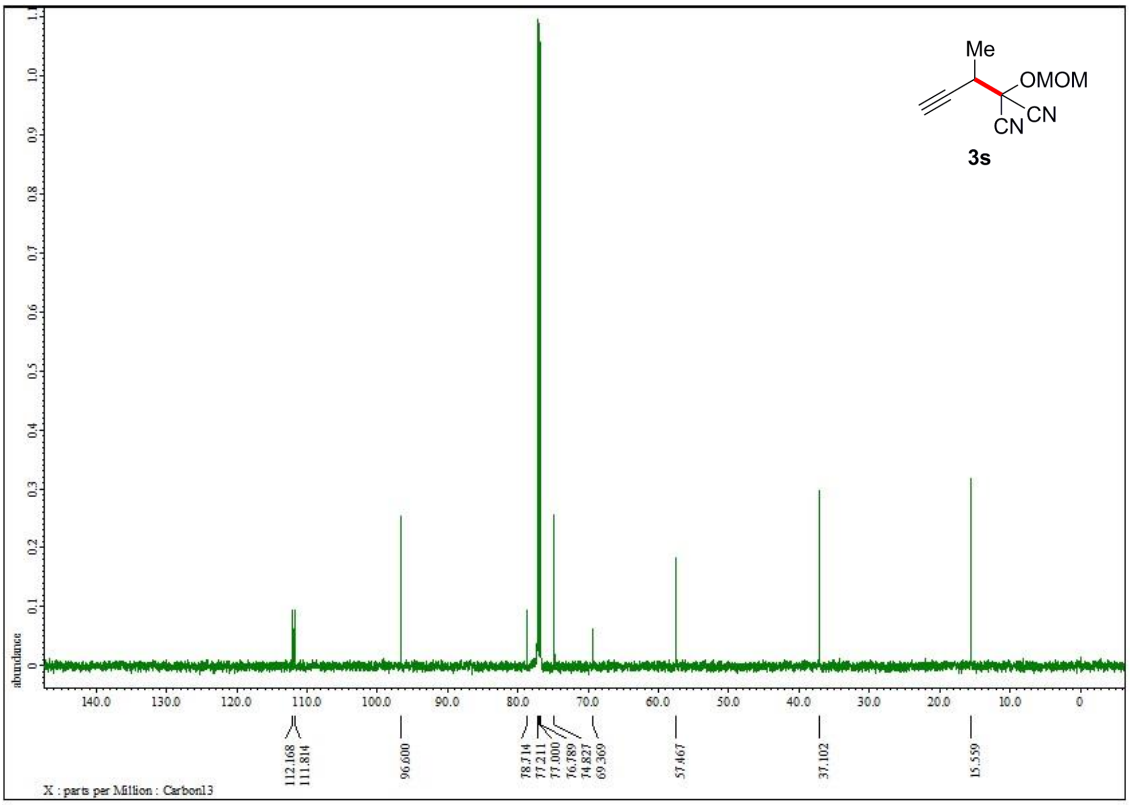

aen5_250_1H.1.fid
MOMO
NC
CN
CN
CN
OMOM
3q
5.04
3.54
0.91
1.21
0.93
0.94
1.02
f1 (ppm)

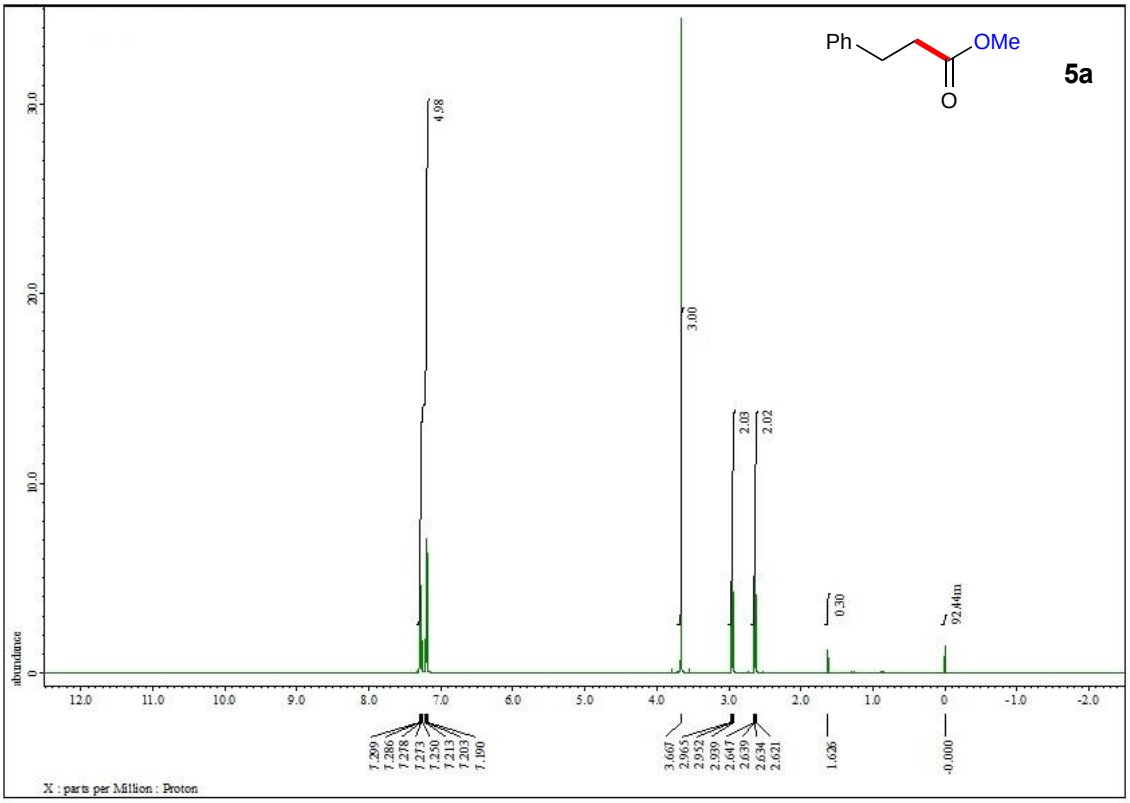

aen5_250_13C.1.fid
MOMO
NC
CN
CN
CN
OMOM
3q
113.20
86.16
65.61
57.30
38.90
28.20
23.38
f1 (ppm)

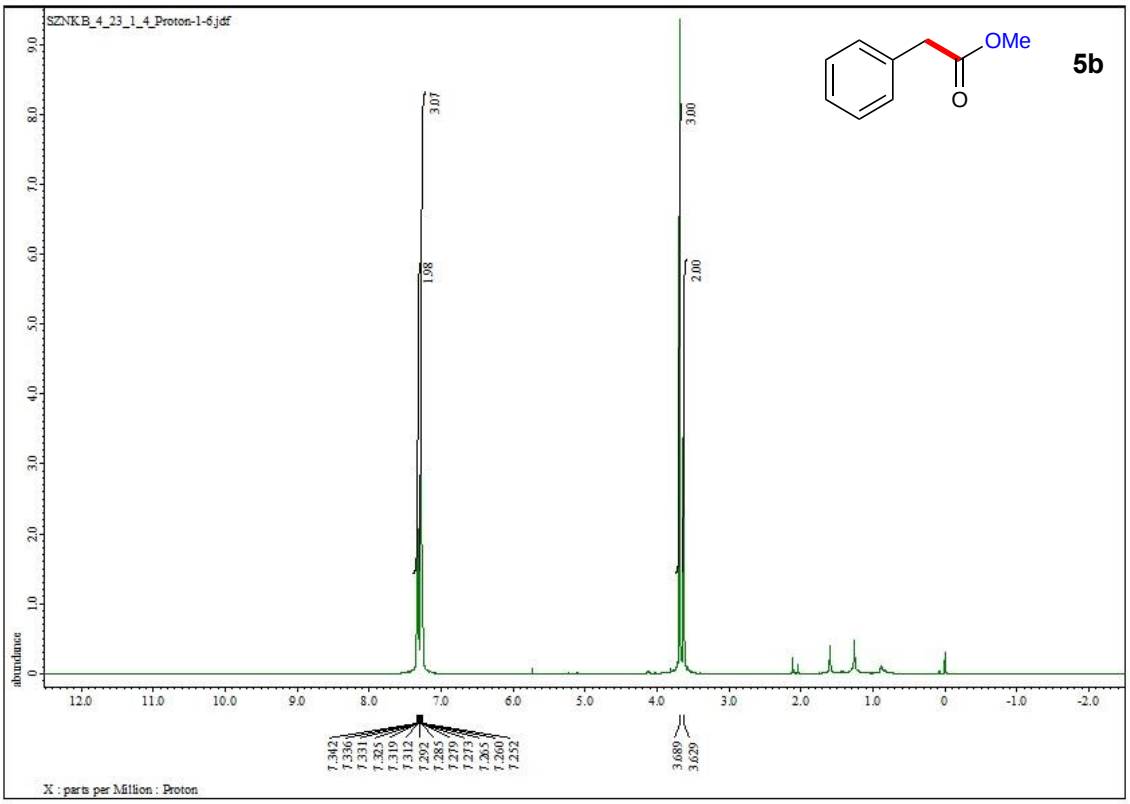

OMOM
CN CN
3r
2.00
2.99
1.99
0.98
1.99
1.99
abundance
7.273
5.062
3.549
2.157
2.145
1.067
1.064
1.056
1.047
1.042
0.714
0.711
0.700
0.414
0.404
0.000
X : parts per Million : Proton

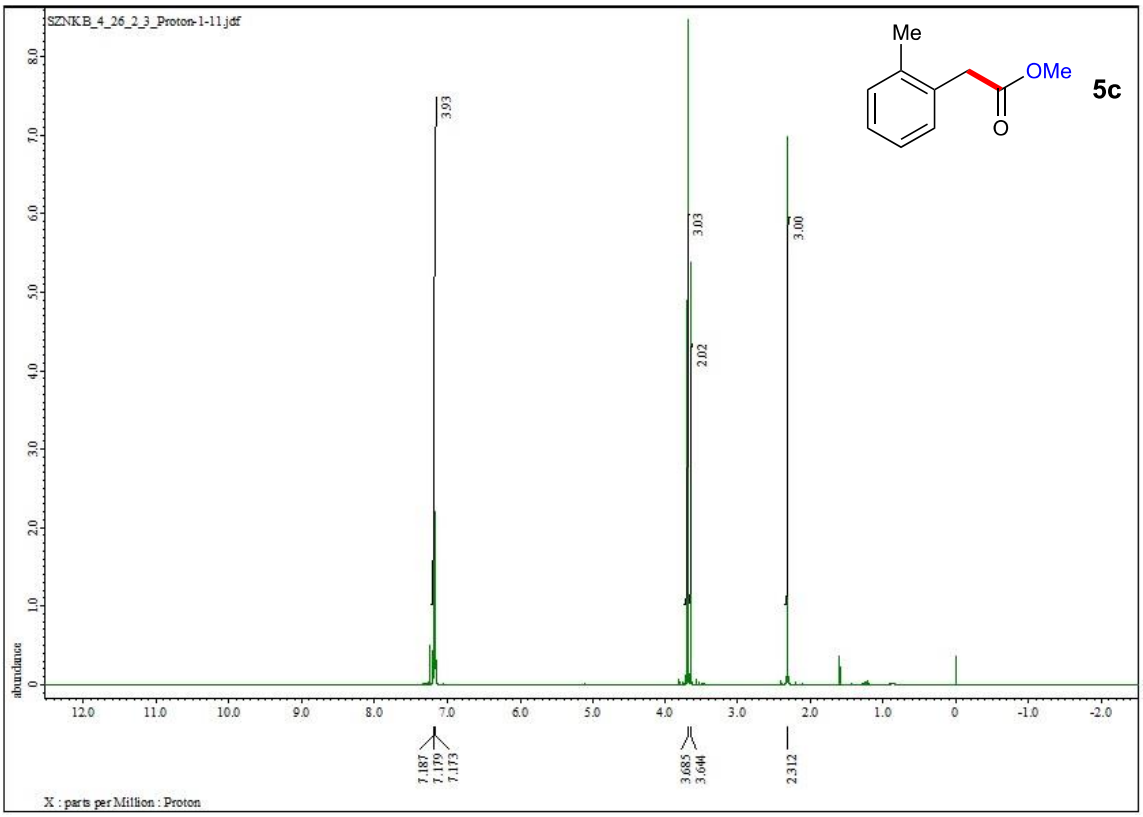

OMOM
CN CN
3r
(thousandths)
113.375
95.996
77.211
77.000
76.789
65.817
57.238
44.570
5.314
4.289
X : parts per Million : Carbon13

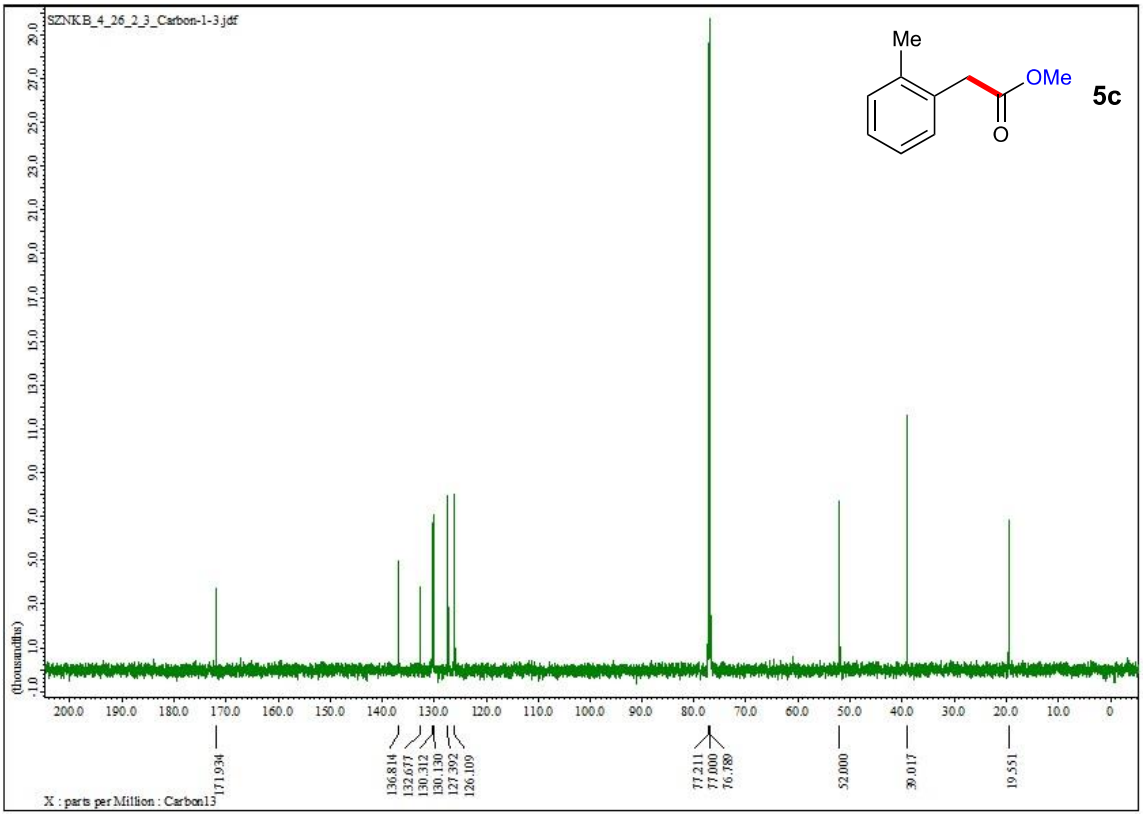

Me
OMOM
CN
CN
3s
3.04
3.03
2.00
0.97
0.90
abundance
7.263
5.100
5.088
5.086
5.074
3.557
3.265
3.260
3.254
3.249
3.242
3.238
3.226
2.451
2.447
1.535
1.523
-0.000
X : parts per Million : Proton

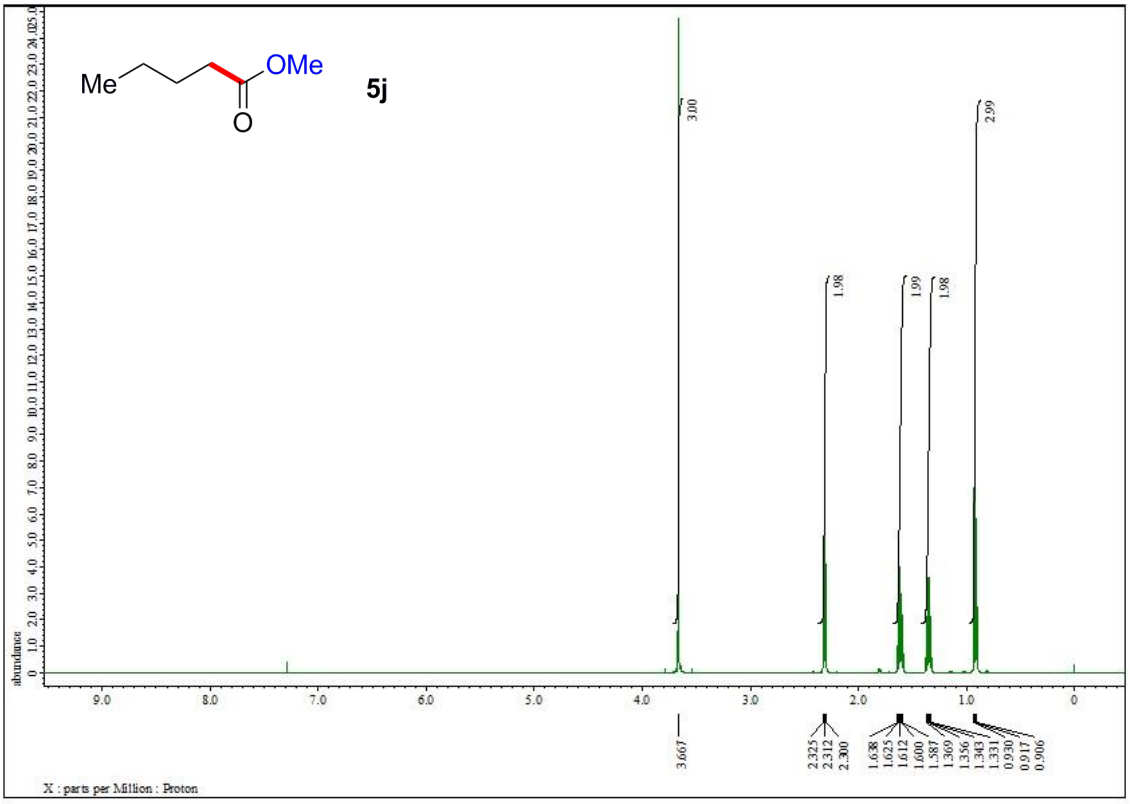

Me
OMOM
CN
CN
3s
abundance
112.168
111.814
96.600
78.714
77.211
77.000
76.789
74.827
69.369
57.467
37.102
15.559
X : parts per Million : Carbon13

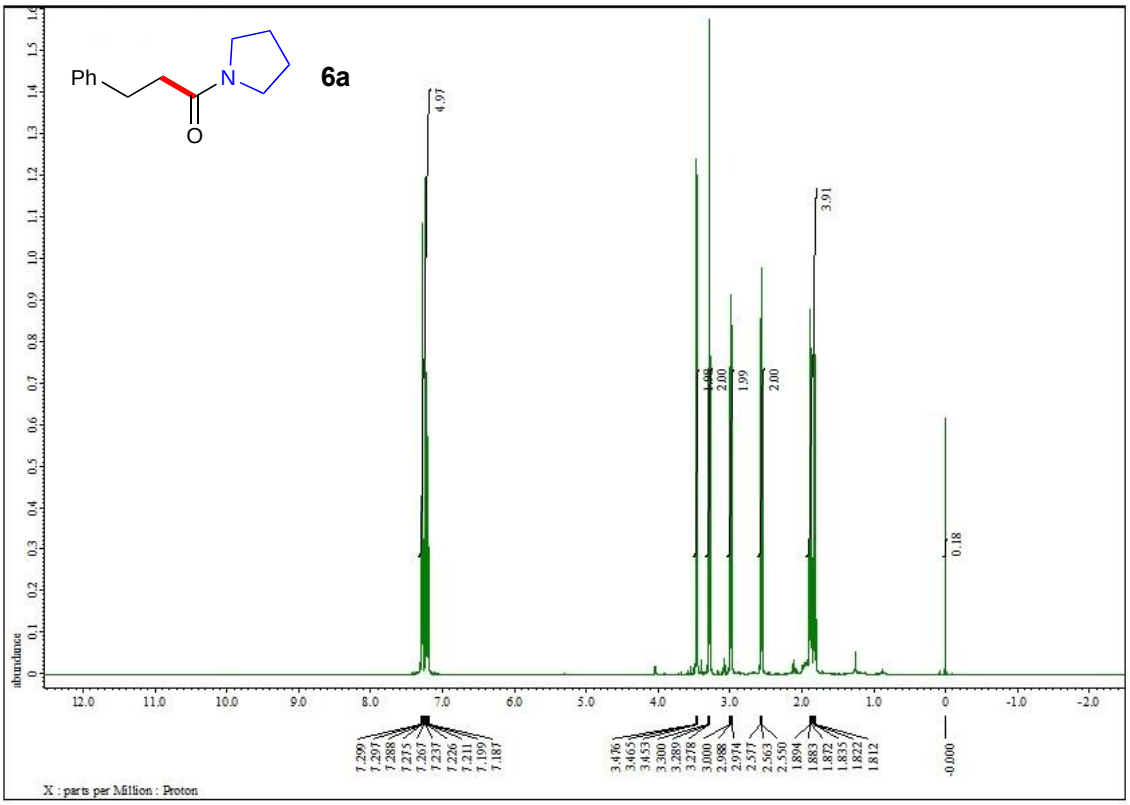

Ph
OMe
O
5a
4.98
3.00
2.03
2.02
0.30
92.44m
abundance
7.299
7.286
7.278
7.273
7.230
7.213
7.203
7.190
3.667
2.965
2.952
2.939
2.647
2.639
2.634
2.621
1.626
-0.000
X : parts per Million : Proton

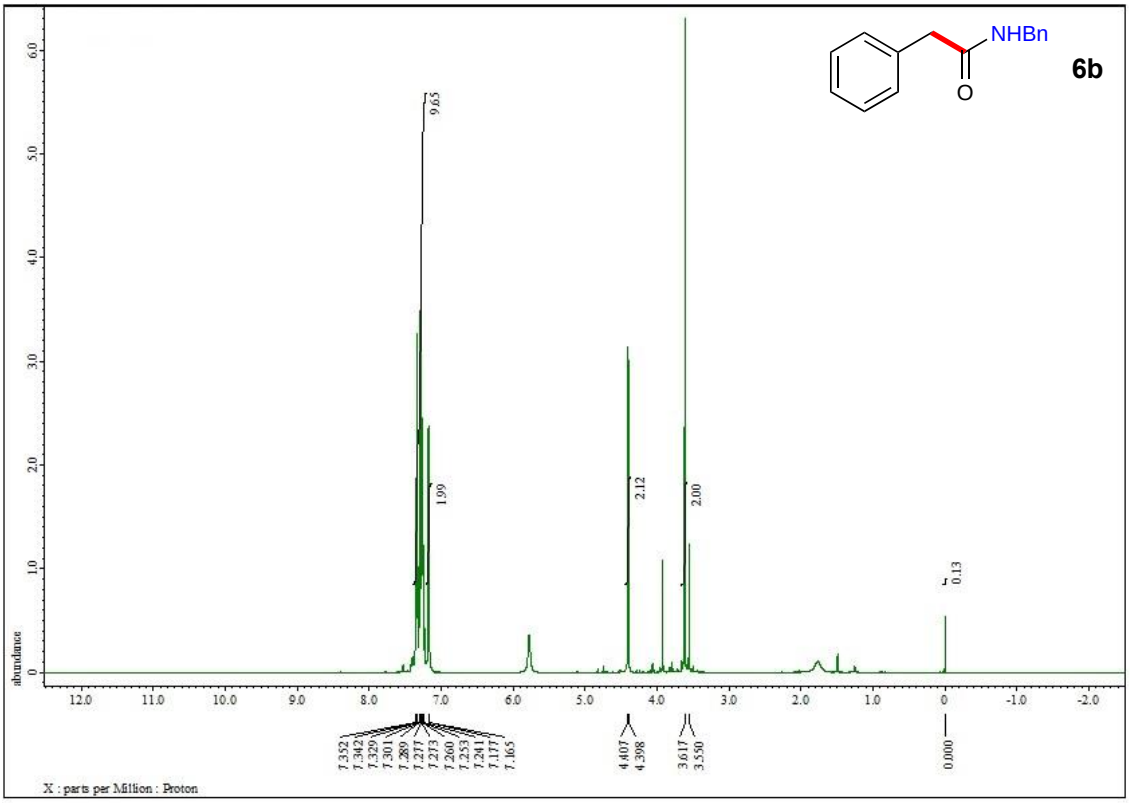

SZNKB_4_23_1_4_Proton-1-6.jdf
OMe
O
5b
3.07
3.00
1.98
2.00
abundance
7.342
7.336
7.331
7.325
7.319
7.312
7.292
7.285
7.279
7.273
7.265
7.260
7.252
3.689
3.629
X : parts per Million : Proton

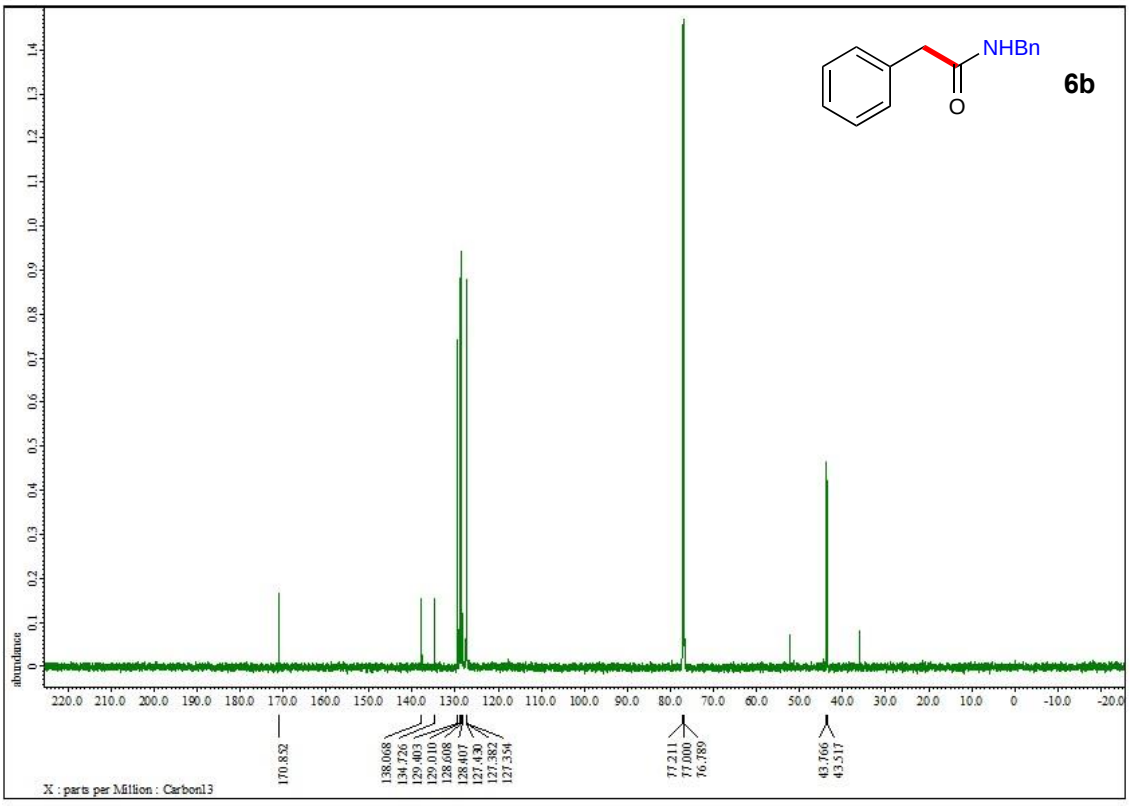

SZNKB_4_26_2_3_Proton-1-11.jdf
Me
OMe
O
5c
3.93
3.03
3.00
2.02
abundance
7.187
7.179
7.173
3.685
3.644
2.312
X : parts per Million : Proton

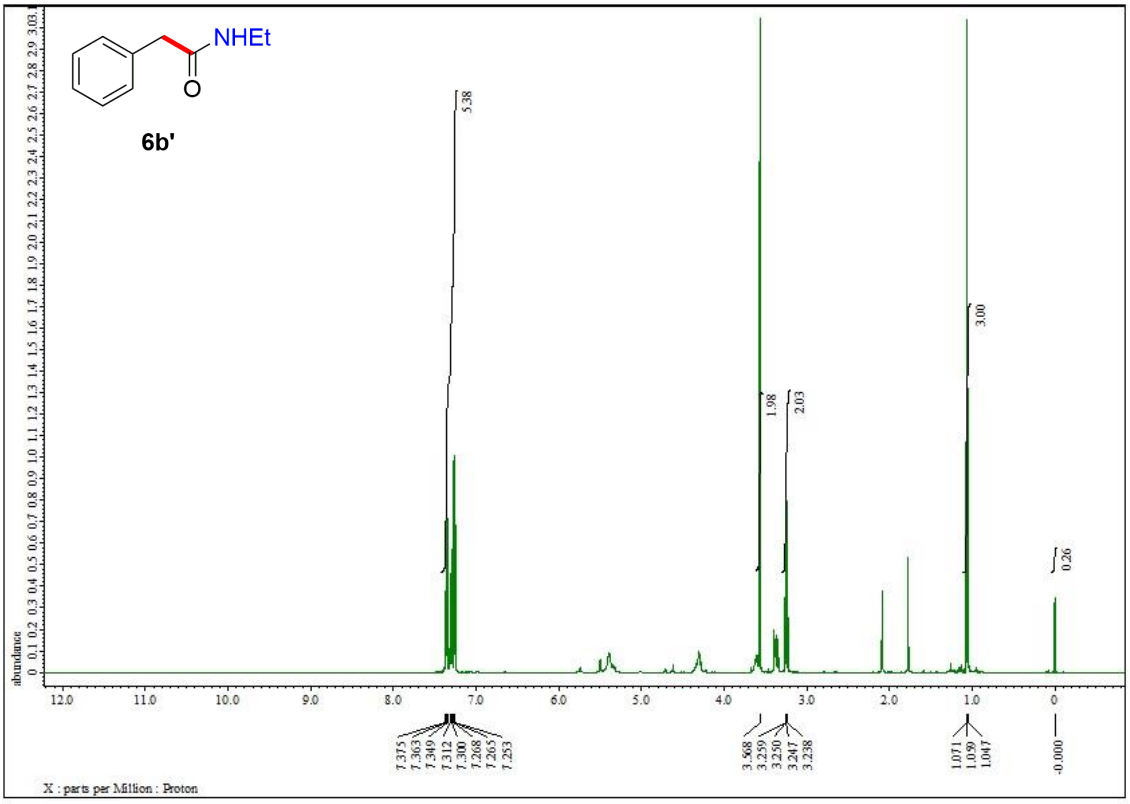

SZNKB_4_26_2_3_Carbon-1-3.jdf
Me
OMe
O
5c
(thousandths)
171.934
136.814
132.677
130.312
130.130
127.392
126.109
77.211
77.000
76.789
52.000
39.017
19.551
X : parts per Million : Carbon13

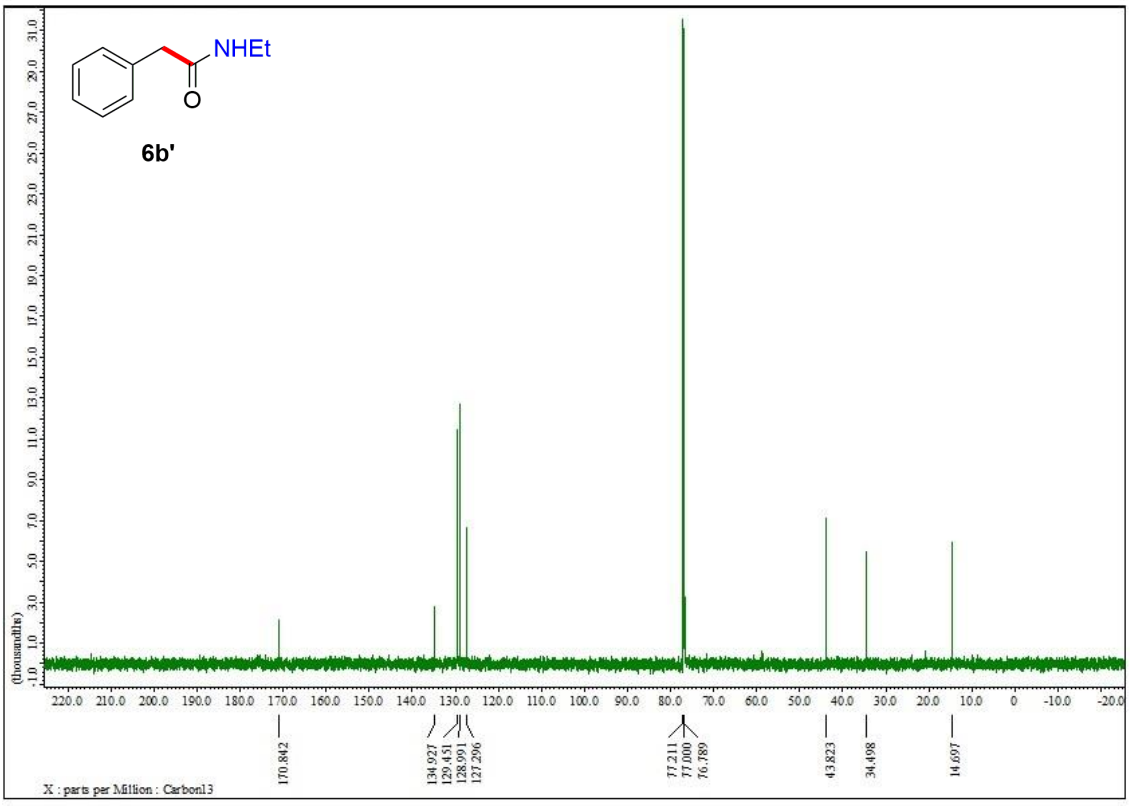

Me
OMe
O
5j
3.00
1.98
1.99
1.98
2.99
abundance
X : parts per Million : Proton

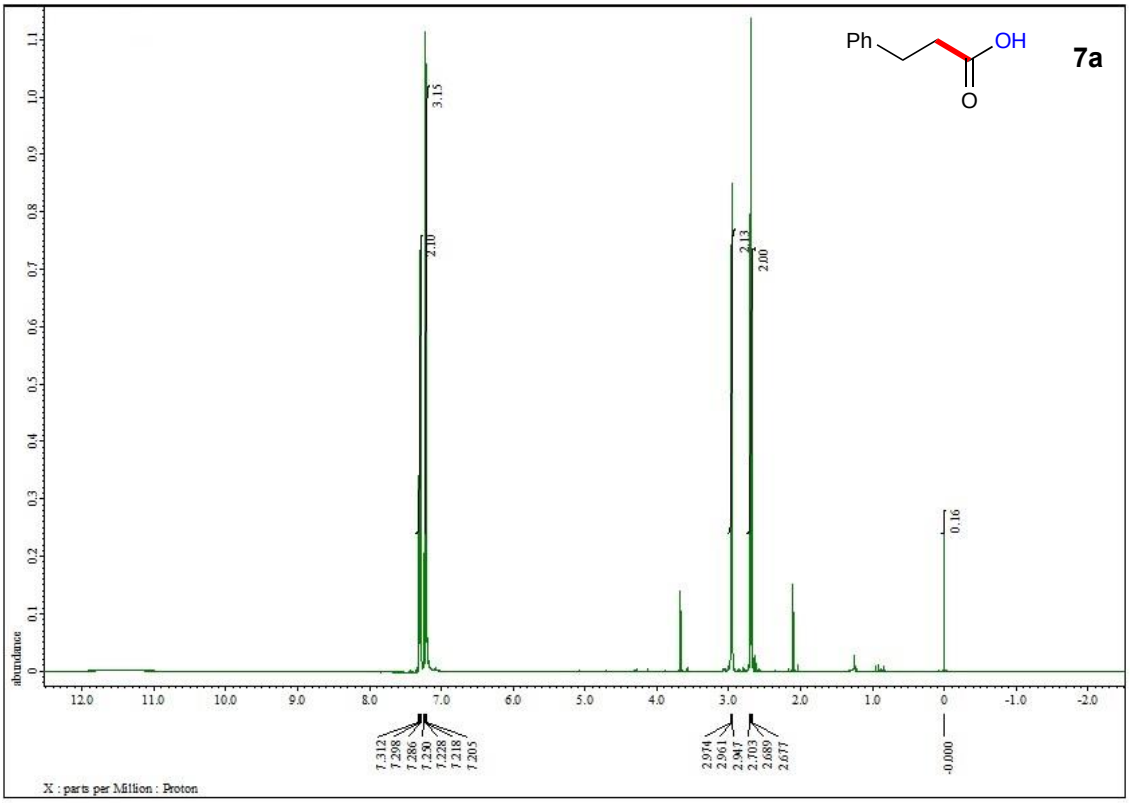

Ph
N
O
6a
4.97
1.98
2.00
1.99
2.00
3.91
0.18
abundance
X : parts per Million : Proton

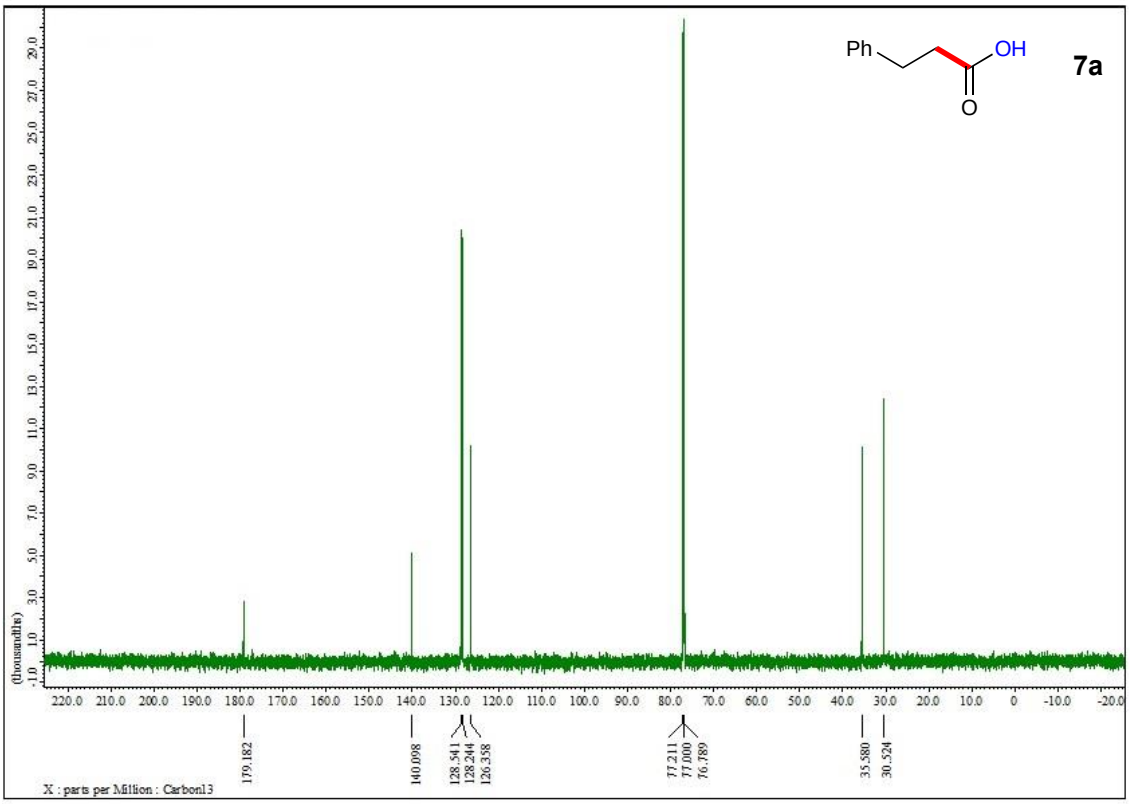

NHBn
O
6b
9.65
1.99
2.12
2.00
0.13
abundance
X : parts per Million : Proton
7.352
7.342
7.329
7.301
7.289
7.277
7.273
7.260
7.253
7.241
7.177
7.165
4.407
4.398
3.617
3.550
0.000

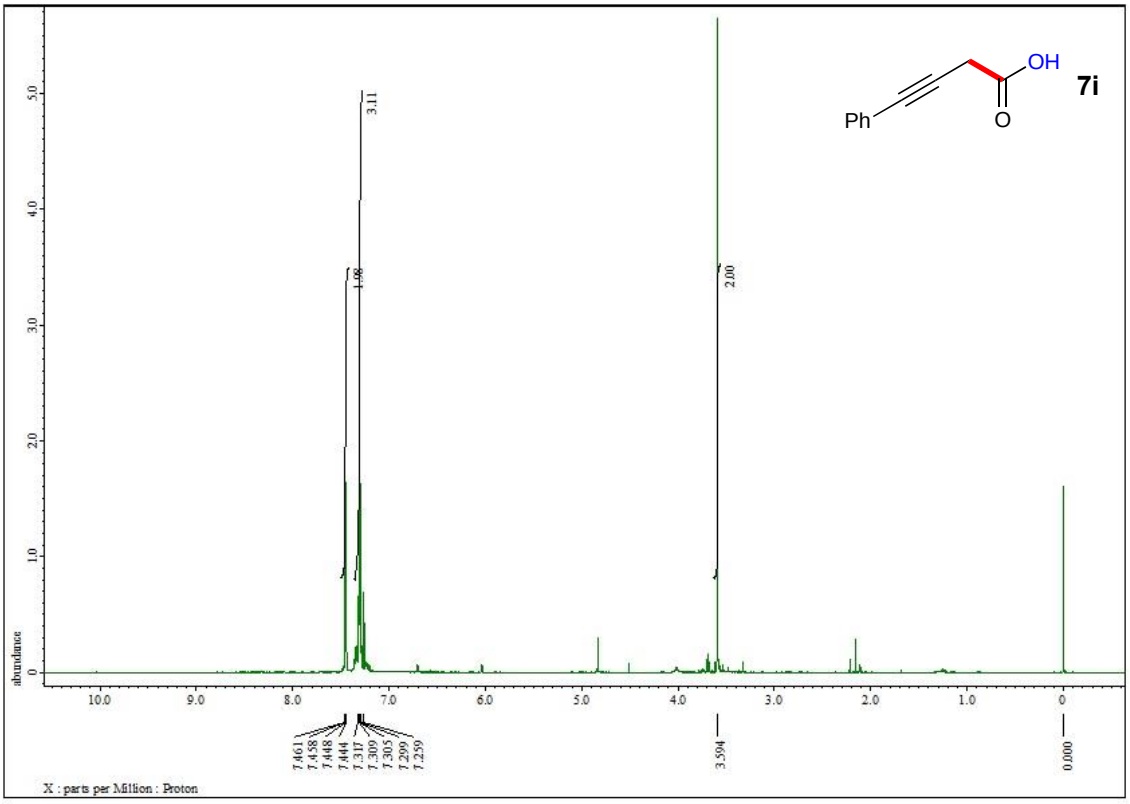

NHBn
O
6b
abundance
X : parts per Million : Carbon13
170.852
138.068
134.726
129.403
129.010
128.608
128.407
127.430
127.382
127.354
77.211
77.000
76.789
43.766
43.517

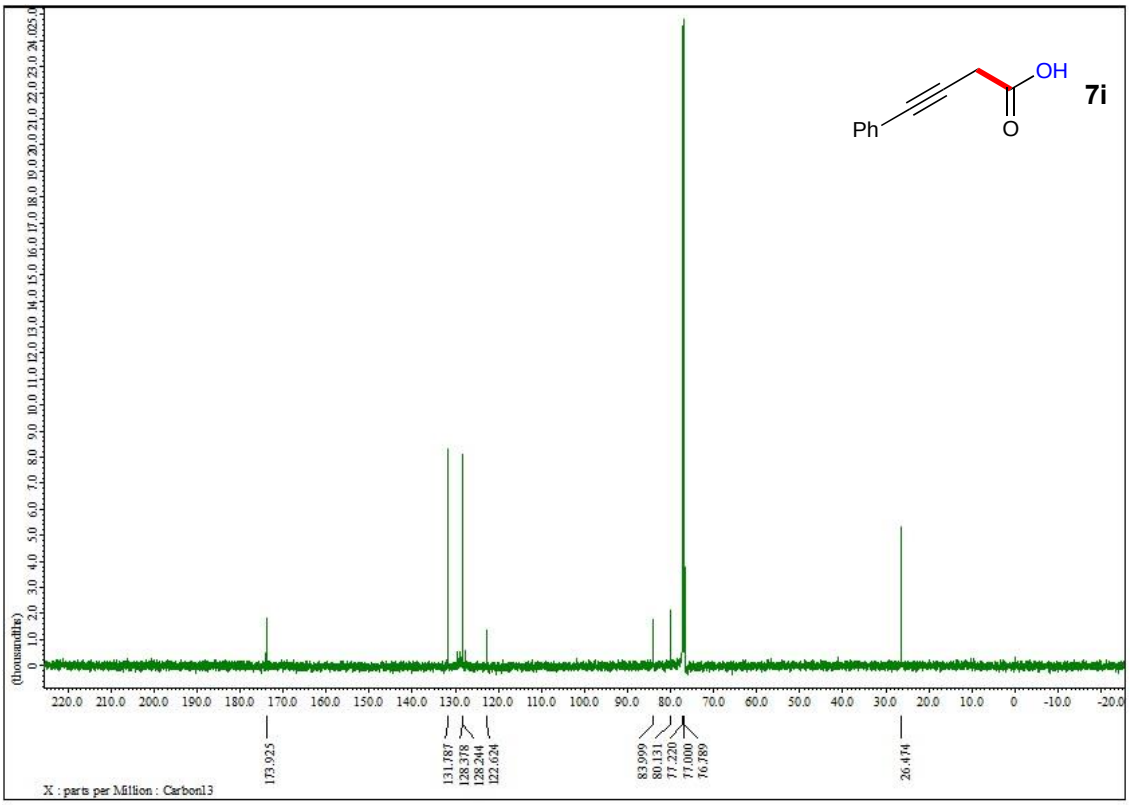

NHEt
O
6b'
5.38
1.98
2.03
3.00
0.26
abundance
7.375
7.363
7.349
7.312
7.300
7.268
7.265
7.253
3.568
3.259
3.250
3.247
3.238
1.071
1.039
1.047
-0.000
X : parts per Million : Proton


NHEt
O
6b'
(thousandths)
170.842
134.927
129.451
128.991
127.296
77.211
77.000
76.789
43.823
34.498
14.697
X : parts per Million : Carbon13


Ph
OH
O
7a
3.15
2.10
2.13
2.00
0.16
abundance
7.312
7.298
7.286
7.230
7.228
7.218
7.205
2.974
2.961
2.947
2.703
2.689
2.677
-0.000
X : parts per Million : Proton


Ph
OH
O
7a
(thousandths)
179.182
140.098
128.541
128.244
126.358
77.211
77.000
76.789
35.580
30.524
X : parts per Million : Carbon13


OH
Ph
O
7i
3.11
1.98
2.00
abundance
7.461
7.458
7.448
7.444
7.317
7.309
7.305
7.299
7.259
3.594
0.000
X : parts per Million : Proton


OH
Ph
O
7i
(thousandths)
173.925
131.787
128.378
128.244
122.624
83.999
80.131
77.220
77.000
76.789
26.474
X : parts per Million : Carbon13