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Supporting Information

Direct and Versatile Synthesis of Red-Shifted Azobenzenes

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Materials and methods

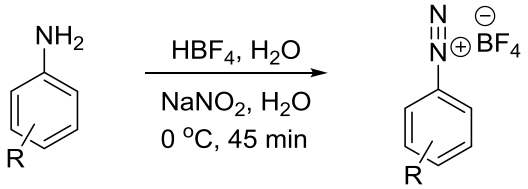
All chemicals for synthesis were obtained from commercial sources and used as received unless stated otherwise.

Thin Layer Chromatography (TLC) was performed using commercial Kieselgel 60, F254 silica gel plates with fluorescence-indicator UV_{254} (*Merck*, TLC silica gel *60 F_{254}*). For detection of components, UV light at λ = 254 nm or λ = 365 nm was used. Alternatively, oxidative staining using aqueous basic potassium permanganate solution ($KMnO_4$) or aqueous acidic cerium phosphomolybdic acid solution (Seebach's stain) was used. Flash chromatography was performed on silica gel (Silicycle Siliaflash P60, 40-63 mm, 230-400 mesh). Drying of solutions was performed with $MgSO_4$ and volatiles were removed with a rotary evaporator.

Nuclear Magnetic Resonance spectra were measured with an Agilent Technologies 400-MR (400/54 Premium Shielded) spectrometer (400 MHz). All spectra were measured at room temperature (22–24 °C). Chemical shifts for ^{1}H- and ^{13}C-NMR measurements were determined relative to the residual solvent peaks in ppm (δ_H 7.26 for $CHCl_3$, 2.50 for DMSO and 2.05 ppm for Acetone, δ_C 77.16 for $CHCl_3$ and 39.52 for DMSO). The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; brs, broad signal. All ^{13}C-NMR spectra are ^{1}H-broadband decoupled. High-resolution mass spectrometric measurements were performed on a Thermo scientific LTQ Orbitrap XL with ESI ionization. Melting points were recorded using a Stuart analogue capillary melting point SMP11 apparatus. For spectroscopic measurements, solutions in Uvasol® grade solvents were measured in a 10 mm quartz cuvette. UV-Vis absorption spectra were recorded on an Agilent 8453 UV-Visible absorption Spectrophotometer.

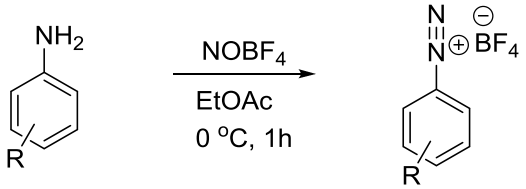
Synthesis

Aryldiazonium salt preparation, method A:[1]



To a solution of aniline (1.00 mmol) in H_2O (0.4 mL) was added 50 wt. % aq. HBF_4 (0.34 mL) and the mixture was stirred while cooling on ice. Subsequently, a solution of $NaNO_2$ (1.00 mmol, 69.0 mg) in H_2O (0.2 mL) was added dropwise. After addition, the reaction mixture was stirred for 45 min on ice and subsequently filtered over a glass filter. The obtained crystals were washed with Et_2O (4 x 20 mL) and dried under vacuum. The products were stored at room temperature in the dark under N_2 atmosphere to prevent degradation.

Aryldiazonium salt preparation, method B:[2]



To a stirred solution of aniline (1.00 mmol) in EtOAc (2.2 mL) at 0 °C was added $NOBF_4$ (1.00 mmol, 117 mg) in small portions. After addition, the mixture was stirred at 0 °C for 1 h and subsequently filtered over a glass filter. The obtained crystals were washed with Et_2O (2 x 20 mL) and pentane (2 x 20 mL) and dried under vacuum. The products were stored at room temperature in the dark under N_2 atmosphere to prevent degradation.

Table S1. Aryldiazonium structures with ^{1}H-NMR and IR analysis.

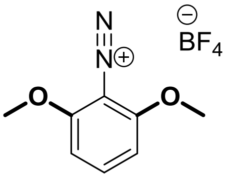
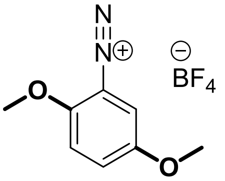
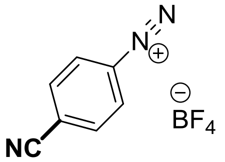
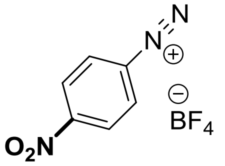
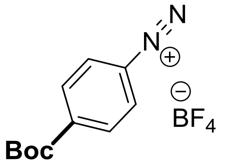
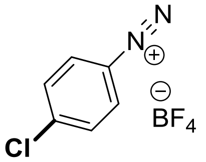
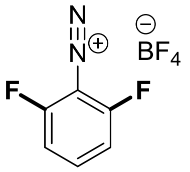
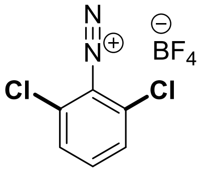
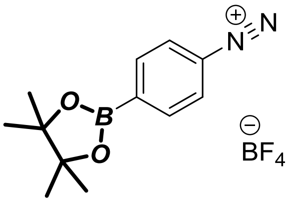
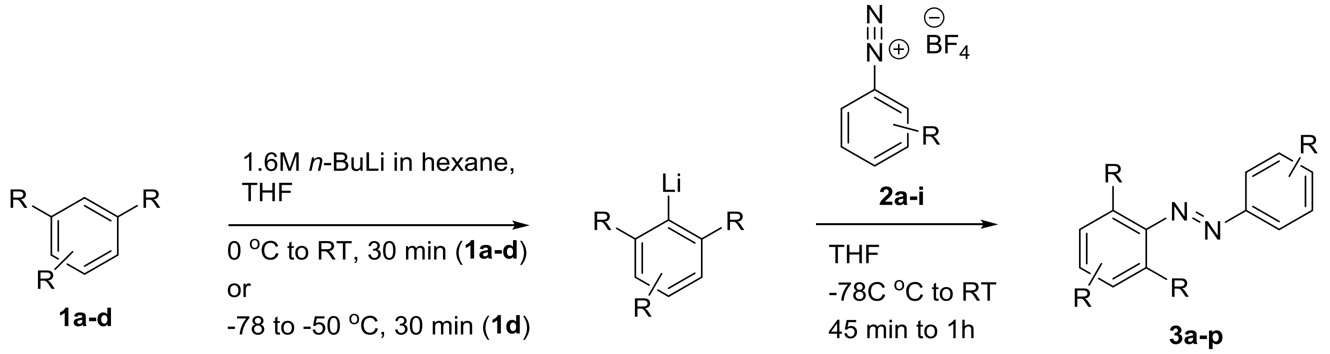
Compound (Yield)	**Structure**	**^{1}H-NMR**	**IR**
2a (>98%) **Method A**		**^{1}H NMR (400 MHz, DMSO-d_6): *δ*** 8.18 (t, *J* = 8.7 Hz, 1H), 7.14 (d, *J* = 8.7 Hz, 2H), 4.15 (s, 6H).	IR (neat, cm^{-1}): 2238 (N≡N)
2b (85%) **Method A**		**^{1}H NMR (400 MHz, Acetone-d_6): *δ*** 8.08 (d, *J* = 3.1 Hz, 1H), 7.92 (dd, *J* = 9.6, 3.1 Hz, 1H), 7.73 (d, *J* = 9.6 Hz, 1H), 4.30 (s, 3H), 3.92 (s, 3H).	IR (neat, cm^{-1}): 2252 (N≡N)
2d (86%) **Method A**		**^{1}H NMR (400 MHz, Acetone-d_6): *δ*** 9.04 (d, *J* = 9.0 Hz, 2H), 8.50 (d, *J* = 9.1 Hz, 2H).	IR (neat, cm^{-1}): 2290 (N≡N)
2e (66%) **Method A**		**^{1}H NMR (400 MHz, Acetone-d_6): *δ*** 9.16 (d, *J* = 9.0 Hz, 2H), 8.85 (d, *J* = 9.1 Hz, 2H).	IR (neat, cm^{-1}): 2307 (N≡N)
2f (59%) **Method A**		**^{1}H NMR (400 MHz, Acetone-d_6): *δ*** 8.95 (d, *J* = 8.5 Hz, 2H), 8.52 (d, *J* = 8.6 Hz, 2H), 1.63 (s, 12H).	IR (neat, cm^{-1}): 2299 (N≡N)
2g (89%) **Method B**		**^{1}H NMR (400 MHz, DMSO-d_6): *δ*** 8.67 (d, *J* = 8.6 Hz, 2H), 8.10 (d, *J* = 8.6 Hz, 2H).	IR (neat, cm^{-1}): 2289 (N≡N)
2h (31%) **Method A**		**^{1}H NMR (400 MHz, DMSO-d_6): *δ*** 8.58 – 8.45 (m, 1H), 7.99 – 7.86 (m, 2H).	IR (neat, cm^{-1}): 2289 (N≡N)
2i (46%) **Method A**		**^{1}H NMR (400 MHz, DMSO-d_6): *δ*** 8.31 (t, *J* = 8.3 Hz, 1H), 8.19 (d, *J* = 8.4 Hz, 2H).	IR (neat, cm^{-1}): 2285 (N≡N)
2j (84%) **Method B**		**^{1}H NMR (400 MHz, DMSO-d_6): *δ*** 8.61 (d, *J* = 8.7 Hz, 2H), 8.14 (d, *J* = 8.6 Hz, 2H), 1.31 (s, 12H).	IR (neat, cm^{-1}): 2294 (N≡N)

Table S2. Optimization of ***n*-butyllithium** and **2a** concentrations in the novel synthetic methodology leading to the conditions as defined in entry 5.

Entry	*n*-BuLi (equiv)[a]	2a (equiv)	Isolated Yield 3a (%)
1	1.0	1.2	71
2	1.0	1.4	64
3	1.2	1.0	48
4	1.4	1.0	23
5	1.0	1.0	86

[a] 1.6 M in hexanes

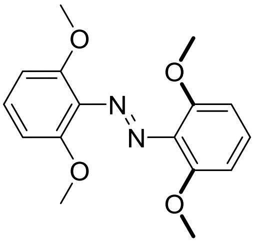
Synthetic methodology



To a stirred solution of **1** (1.00 mmol) in THF (1.0 mL) in an oven-dried Schlenk flask under N_2 atmosphere at 0 °C*+ was slowly added 1.6M *n*-BuLi in hexane (625 µL, 1.00 mmol). Subsequently the reaction mixture was allowed to warm up to room temperature over 30 min. This mixture was added to a solution of **2** (1.00 mmol) in THF (1.0 mL) in an oven-dried Schlenk flask under N_2 atmosphere at -78 °C. The reaction mixture was slowly heated to room temperature over 1h and subsequently 2.0 mL saturated aqueous $NaHCO_3$ solution was added. The resulting solution was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). Evaporation of all the volatiles yielded the crude product. The product, dissolved in EtOAc, was either precipitated in pentane or subjected to short flash chromatography (Pentane:EtOAc, 95:5 to 3:1) yielding pure azobenzenes.

*Note 1: For compound **1d**, a slightly modified lithiation procedure was utilized starting at -78 °C instead of 0 °C, and warming to -50 °C instead of room temperature in 30 min before addition to a solution of **2** in THF.

+Note 2: For the synthesis of **3p-r**, **1e** was kept at -78 °C after lithiation and reverse addition of a suspension of **2a,j,h** was applied to prevent the formation of side products due to benzyne formation.



2,2’,6,6’-tetra-methoxyazobenzene **(3a)**

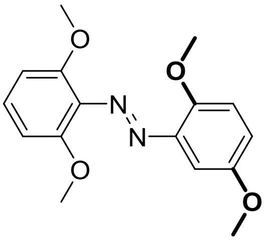
Yield: 86% (261 mg), brown/yellow crystals

Melting point: 138-140 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.28 (t, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 4H), 3.71 (s, 12H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 152.0, 133.9, 129.9, 105.8, 56.6.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{16}H_{19}N_2O_4$: 303.1339; Found: 303.1344



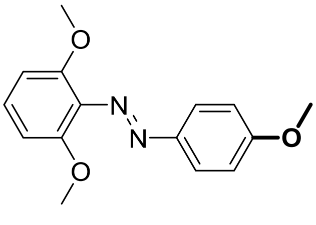
2,2’,5’,6-tetra-methoxyazobenzene (**3b**)

Yield: 59% (180 mg), red oil

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.27 (t, J = 8.4 Hz, 1H), 7.18 (d, J = 9.1 Hz, 1H), 7.11 (dd, J = 9.1, 3.1 Hz, 1H), 6.89 (d, J = 3.1 Hz, 1H), 6.78 (d, J = 8.5 Hz, 2H), 3.85 (s, 3H), 3.72 (s, 3H), 3.71 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 151.7, 147.2, 133.6, 129.0, 124.5, 114.7, 105.6, 56.5, 56.07.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{16}H_{19}N_2O_4$: 303.1339; Found: 303.1344



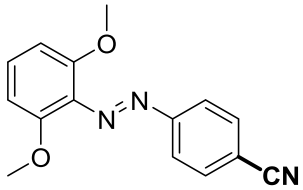
2,6,4’-trimethoxyazobenzene (**3c**)

Yield: 91% (248 mg), red oil

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.88 – 7.64 (m, 2H), 7.25 (t, J = 8.4 Hz, 1H), 7.14 – 7.01 (m, 2H), 6.86 – 6.59 (m, 2H), 3.84 (s, 3H), 3.71 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 162.2, 151.7, 147.2, 133.6, 129.0, 124.5, 114.7, 105.6, 56.5, 56.1.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{15}H_{17}N_2O_4$: 273.1233; Found: 273.1238



2,6-dimethoxy-4’-cyano-azobenzene (**3d**)

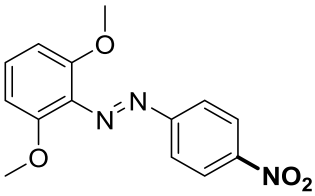
Yield: 81% (217 mg), dark red solid

Melting point: 92-93 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.03 (d, J = 8.5 Hz, 2H), 7.86 (d, J = 8.5 Hz, 2H), 7.37 (t, J = 8.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 3.76 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 155.0, 152.5, 134.2, 133.0, 131.6, 123.1, 118.9, 113.4, 105.6, 56.6.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{15}H_{14}N_3O_2$: 268.1080; Found: 268.1085



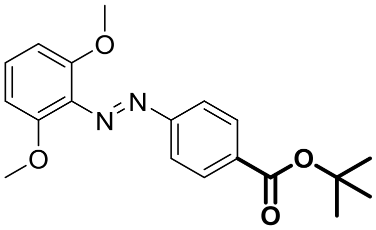
2,6-dimethoxy-4’-nitro-azobenzene (**3e**)

Yield: 67% (193 mg), red oil

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.38 (d, J = 9.0 Hz, 2H), 7.92 (d, J = 9.0 Hz, 2H), 7.38 (t, J = 8.5 Hz, 1H), 6.82 (d, J = 8.5 Hz, 2H), 3.78 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 156.3, 152.7, 148.6, 133.0, 132.0, 125.4, 123.3, 105.6, 56.7.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{14}H_{14}N_3O_4$: 288.0978; Found: 288.0984



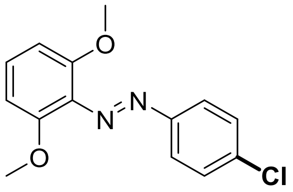
2,6-dimethoxy-4’-Boc-azobenzene (**3f**)

Yield: 45% (154 mg), red oil

^{1}H NMR (400 MHz, DMSO-d_6): δ 8.09 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.34 (t, J = 8.4 Hz, 1H), 6.81 (d, J = 8.5 Hz, 2H), 3.77 (s, 6H), 1.57 (s, 9H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 164.3, 154.9, 151.8, 132.9, 130.2, 122.03, 105.13, 81.13, 56.14, 27.71.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{19}H_{23}N_2O_4$: 343.1652; Found: 343.1658



2,6-dimethoxy-4’-chloro-azobenzene (**3g**)

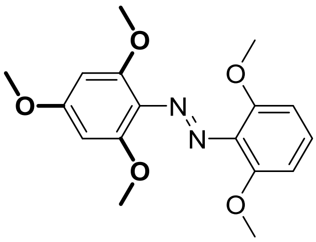
Yield: 77% (213 mg), orange solid

Melting point: 77-78 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-*d$_6$*): *δ* 7.77 (d, *J* = 8.7 Hz, 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.31 (t, *J* = 8.4 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 2H), 3.74 (s, 6H).

^{13}C NMR (100 MHz, DMSO-*d$_6$*): *δ* 152.1, 151.5, 136.2, 133.2, 130.4, 129.8, 124.2, 105.6, 56.6.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{14}H_{14}ClN_2O_2$: 277.0738; Found: 277.0743



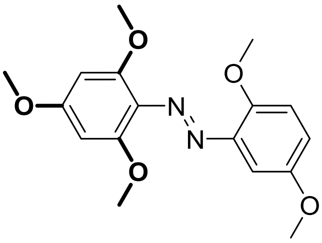
2,2’,6,6’,4-pentamethoxyazobenzene (**3h**)

Yield: 81% (269 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d$_6$*): *δ* 7.21 (t, *J* = 8.4 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 2H), 6.33 (s, 2H), 3.84 (s, 3H), 3.73 (s, 6H), 3.68 (s, 6H).

^{13}C NMR (100 MHz, DMSO-*d$_6$*): *δ* 162.0, 154.5, 151.5, 134.8, 128.6, 127.7, 105.8, 92.0, 56.5, 56.5, 56.0.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{17}H_{21}N_2O_5$: 333.1445; Found: 333.1450



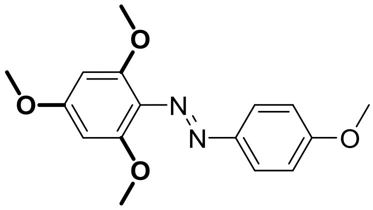
2,2’,4,5’,6-pentamethoxyazobenzene (**3i**)

Yield: 41% (137 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d$_6$*): *δ* 7.11 (d, *J* = 9.0 Hz, 1H), 7.02 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.86 (d, *J* = 3.2 Hz, 1H), 6.35 (s, 2H), 3.85 (d, *J* = 4.5 Hz, 6H), 3.76 (s, 6H), 3.72 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 161.8, 154.2, 153.8, 151.0, 143.7, 128.1, 117.6, 115.7, 101.1, 92.1, 57.5, 56.6, 55.9, 55.9.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{17}H_{21}N_2O_5$: 333.1445; Found: 333.1450



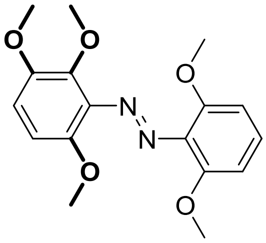
2,4,4’,6-tetramethoxyazobenzene (**3j**)

Yield: 86% (260 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 7.73 (d, *J* = 9.0 Hz, 2H), 7.05 (d, *J* = 9.0 Hz, 2H), 6.36 (s, 2H), 3.84 (s, 3H), 3.82 (s, 3H), 3.77 (s, 6H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 161.5, 161.3, 154.1, 147.8, 127.5, 124.1, 114.6, 92.1, 56.5, 55.8.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{16}H_{19}N_2O_4$: 303.1339; Found: 303.1343



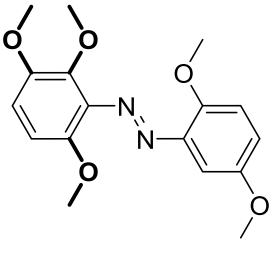
2,2’,3,6,6’-pentamethoxyazobenzene (**3k**)

Yield: 76% (253 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 7.31 (td, *J* = 8.4, 1.9 Hz, 1H), 6.98 (dd, *J* = 9.1, 1.9 Hz, 1H), 6.88 – 6.73 (m, 3H), 3.78 (d, *J* = 1.9 Hz, 3H), 3.74 (d, *J* = 1.9 Hz, 6H), 3.70 (d, *J* = 1.9 Hz, 3H), 3.58 (d, *J* = 1.9 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 152.2, 147.7, 146.6, 139.8, 133.6, 130.4, 112.6, 107.9, 105.7, 61.6, 56.9, 56.8, 56.6.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{17}H_{21}N_2O_5$: 333.1445; Found: 333.1449



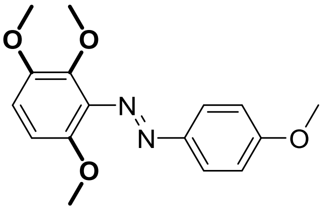
2,2’,3,5’,6-pentamethoxyazobenzene (**3l**)

Yield: 58% (193 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 7.21 (d, *J* = 9.1 Hz, 1H), 7.14 (dd, *J* = 9.1, 3.1 Hz, 1H), 6.99 (d, *J* = 9.1 Hz, 1H), 6.94 (d, *J* = 3.1 Hz, 1H), 6.83 (d, *J* = 9.2 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.73 (s, 6H), 3.70 (s, 3H), 3.63 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 153.7, 151.9, 147.6, 146.6, 142.3, 140.1, 139.6, 119.7, 115.6, 112.6, 107.7, 100.4, 62.1, 57.1, 56.8, 56.7, 56.0.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{17}H_{21}N_2O_5$: 333.1445; Found: 333.1450



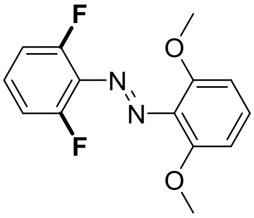
2,3,4’,6-tetramethoxyazobenzene (**3m**)

Yield: 64% (193 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 7.80 (d, *J* = 9.0 Hz, 2H), 7.11 (d, *J* = 9.0 Hz, 2H), 6.97 (d, *J* = 9.2 Hz, 1H), 6.82 (d, *J* = 9.2 Hz, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.69 (s, 3H), 3.63 (s, 3H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 162.5, 147.6, 147.1, 146.4, 140.2, 139.3, 124.7, 114.9, 112.2, 107.7, 61.8, 56.8, 56.7, 56.1.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{16}H_{19}N_2O_4$: 303.1339; Found: 303.1344



2,6-difluor-2’,6’-dimethoxyazobenzene (**3n**)

Yield: 82% (228 mg), red solid

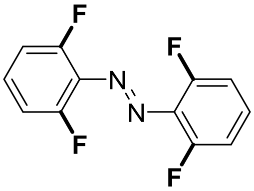
Melting point: 128-129 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-*d*$_6$): *δ* 7.57 – 7.44 (m, 1H), 7.37 (t, *J* = 8.5 Hz, 1H), 7.28 (td, *J* = 9.0, 2.1 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 3.76 (s, 6H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): *δ* 155.9 (d, *J* = 4.7 Hz), 153.3 (d, *J* = 4.6 Hz), 152.3 , 133.5 , 131.7 , 131.5 (t, *J* = 10.3 Hz), 113.9 – 112.8 (m), 105.6, 56.7 .

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -123.88 (m).

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{14}H_{13}F_2N_2O_2$: 279.0939; Found: 279.0944



2,2’,6,6’-tetrafluoroazobenzene (**3o**)

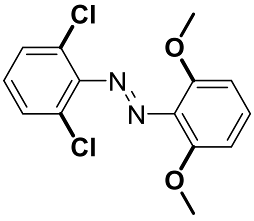
Yield: 77 % (196 mg), red oil

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 7.68 – 7.52 (m, 2H), 7.34 (t, J = 9.2 Hz, 4H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 156.3 (d, J = 4.0 Hz), 153.7 (d, J = 4.3 Hz), 133.6 (t, J = 10.7 Hz), 113.6 (dd, J = 19.9, 3.6 Hz).

^{19}F NMR (376 MHz, DMSO-*d*$_6$): δ -122.01 (dd, J = 10.1, 5.9 Hz).

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{12}H_7F_4N_2$: 255.0539; Found: 255.0544



2,6-dichloro-2’,6’-dimethoxyazobenzene (**3p**)

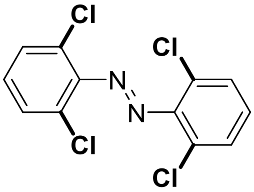
Yield: 91 % (284 mg), red solid (Ethyl acetate)

Melting point: 79-82 °C

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 7.59 (d, J = 8.1 Hz, 2H), 7.49 – 7.26 (m, 2H), 6.84 (d, J = 8.5 Hz, 2H), 3.79 (s, 6H).

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 153.1, 148.9, 132.6, 132.3, 129.77, 129.6, 125.7, 105.6, 56.7.

HR-MS (ESI, [M+H]$^+$): Calcd. for $C_{14}H_{12}Cl_2N_2O_2$: 311.03486; Found: 311.03447



2,6,2’,6’-tetrachloroazobenzene (**3q**)

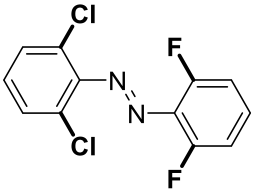
Yield: 92 % (296 mg), bright orange solid

Melting point: 120- 121 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 7.71 (d, 4H), 7.51 (t, J = 7.7, 2H)

^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 146.9, 131.7, 130.4, 126.5.

HR-MS (ESI, $[M+H]^+$): Calcd. for $C_{12}H_6Cl_4N_2$: 320.9328; Found: 320.9324



2,6-dichloro-2',6'-difluoroazobenzene (**3r**)

Yield: 89 % (256 mg), dark red solid

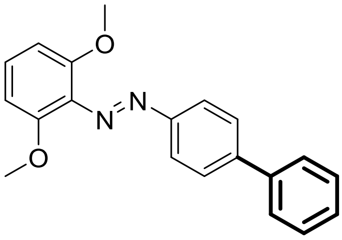
Melting point: 66-69 °C (Ethyl acetate)

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.74 – 7.67 (m, 1H), 7.66 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 8.1 Hz, 1H), 7.39 (t, J = 9.0 Hz, 2H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 156.5 (d, J = 4.1 Hz), 153.9 (d, J = 4.1 Hz), 148.1 , 134.4 (t, J = 10.6 Hz), 130.9 , 130.1 , 125.7 , 113.8 (dd, J = 19.7, 3.6 Hz).

^{19}F NMR (376 MHz, DMSO-d_6): δ -121.29 (dd, J = 10.1, 6.2 Hz).

HR-MS (ESI, $[M+H]^+$): Calcd. for $C_{12}H_6Cl_4N_2$: 286.9948; Found: 286.9949



2,6-dimethoxy-4'-phenylazobenzene (**3s**)

After reaction of 1,3 dimethoxybenzene with para-boronic ester aryldiazonium salt as described in the general methodology, direct addition of a solution of bromobenzene (172 mg, 1.10 mmol), $Pd(PPh_3)_4$ (57.0 mg, 0.05 mmol), 1M aqueous K_2CO_3 (2.0 mL) and dioxane (2.0 mL) to the reaction mixture, led to a biphasic mixture which was heated to reflux under N_2 atmosphere for 16h. After cooling to room temperature H_2O was added and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried ($MgSO_4$) and the pure product was obtained after purification by flash chromatography (Pentane:EtOAc 9:1 to 3:1).

Yield: 41% (130 mg), light orange oil

^{1}H NMR (400 MHz, DMSO-d_6): δ 7.86 (s, 4H), 7.75 (d, J = 7.1 Hz, 2H), 7.50 (t, J = 7.5 Hz, 2H), 7.41 (t, J = 7.3 Hz, 1H), 7.30 (t, J = 8.5 Hz, 1H), 6.80 (d, J = 8.5 Hz, 2H), 3.74 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 152.1, 151.9, 143.2, 139.5, 133.5, 129.9, 129.5, 128.6, 127.9, 127.3, 123.2, 105.6, 56.6.

HR-MS (ESI, $[M+Na]^+$): Calcd. for $C_{20}H_{18}N_2O_2$: 341.1260 ; Found: 341.1265

UV-Vis Spectroscopy

Solutions were prepared in DMSO or as a mixture of four buffer salts (Bis-TRIS, TRIS, MES, sodium acetate, 25 mM each) to ensure the pH could be easily adjusted between 2 and 10 by addition of small quantities of concentrated hydrochloric acid and sodium hydroxide. All the compounds were dissolved in DMSO and thermally adapted by heating at 150 °C for 2 min. The measurements were taken with final concentrations of 20 μM in DMSO or 1 vol% DMSO in buffer.

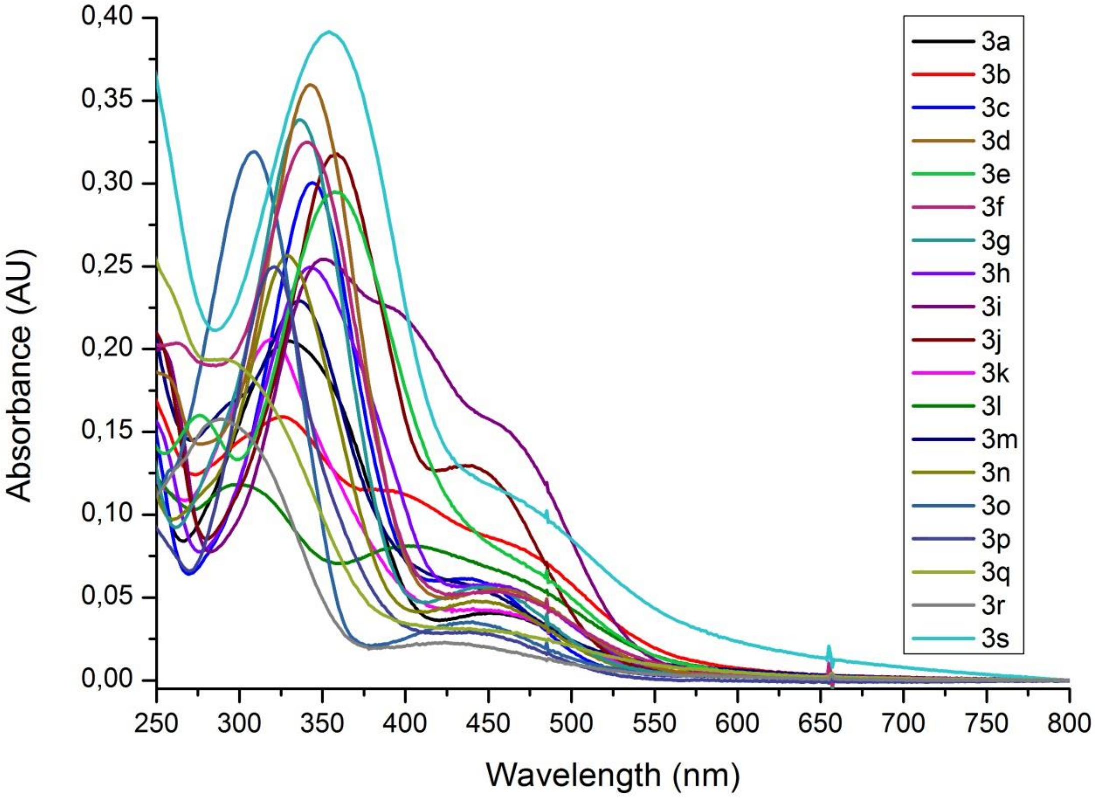


Figure S1. Absorption spectra of the newly synthesized azobenzene derivatives **3a** – **3p** (20 μM in buffer with 1 vol% DMSO at pH=7)

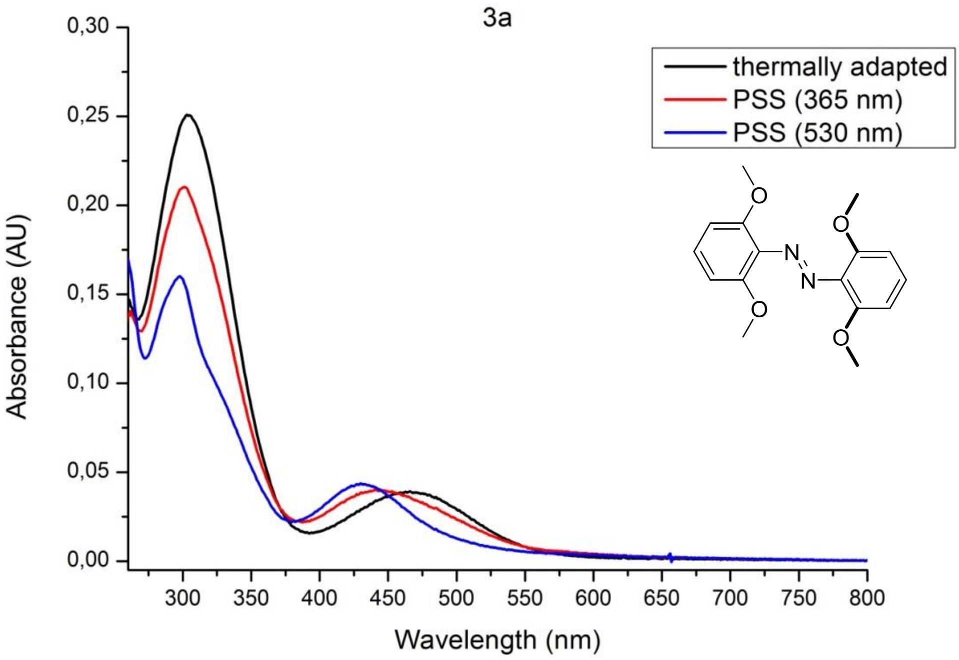


Figure S2. Absorption spectra for the photoisomerization of compound **3a** (DMSO, 37 °C, 20 μM). Photostationary states after thermal adaptation, 365 nm irradiation and 530 nm irradiation were obtained.

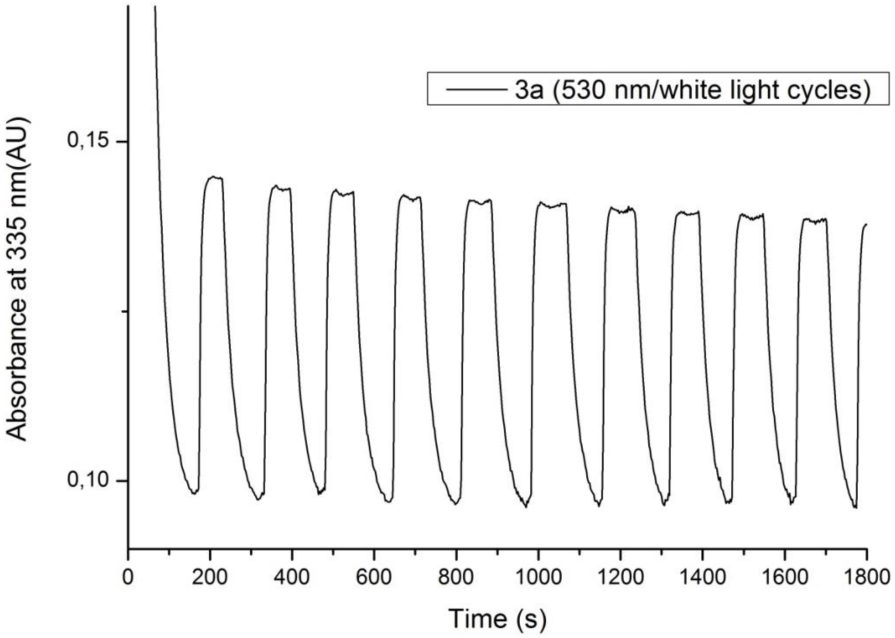


Figure S3. Reversible photosisomerization of **3a** (37 °C, Buffer with 1 vol% DMSO at pH=7, 20 μM) in the presence of 10 mM glutathione (GSH). Ten cycles of 530 nm/white light irradiation could be performed without the observation of significant fatigue or reduction.

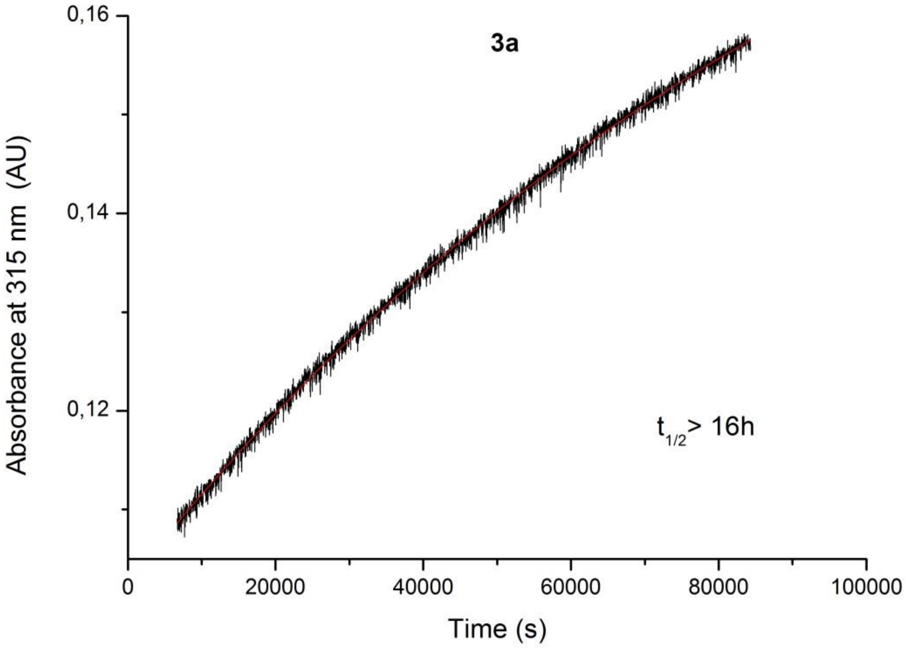


Figure S4. Determination of half-life for **3a** at 37 °C in DMSO. First, PSS was reached upon 530 nm irradiation, after which the absorption was measured at λ_{max} = 315 nm. Line presents the fitting with single exponential process.

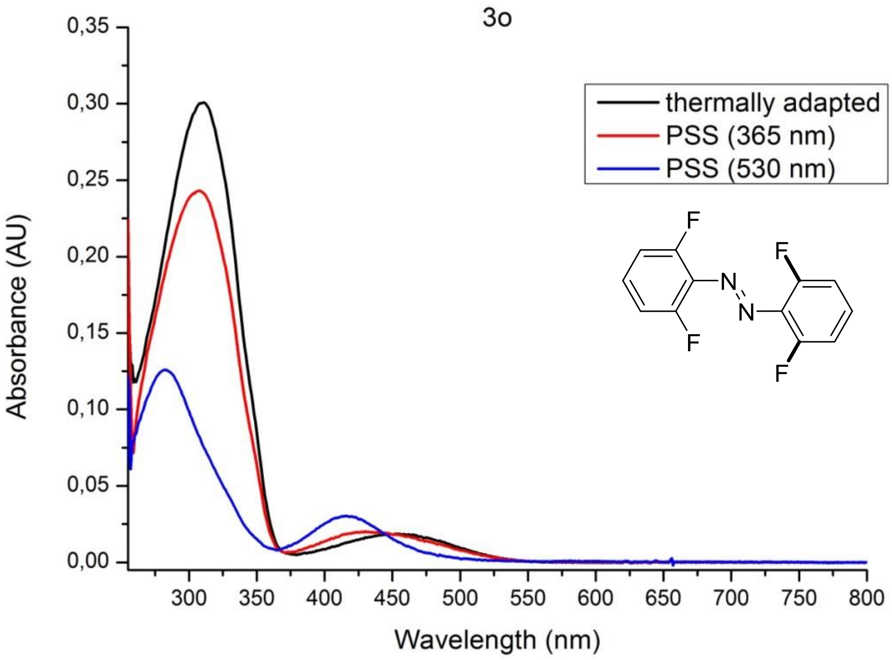


Figure S5. Absorption spectra for the photoisomerization of compound **3o** (DMSO, 37 °C, 20 μM). Photostationary states after thermal adaptation, 365 nm irradiation and 530 nm irradiation were obtained.

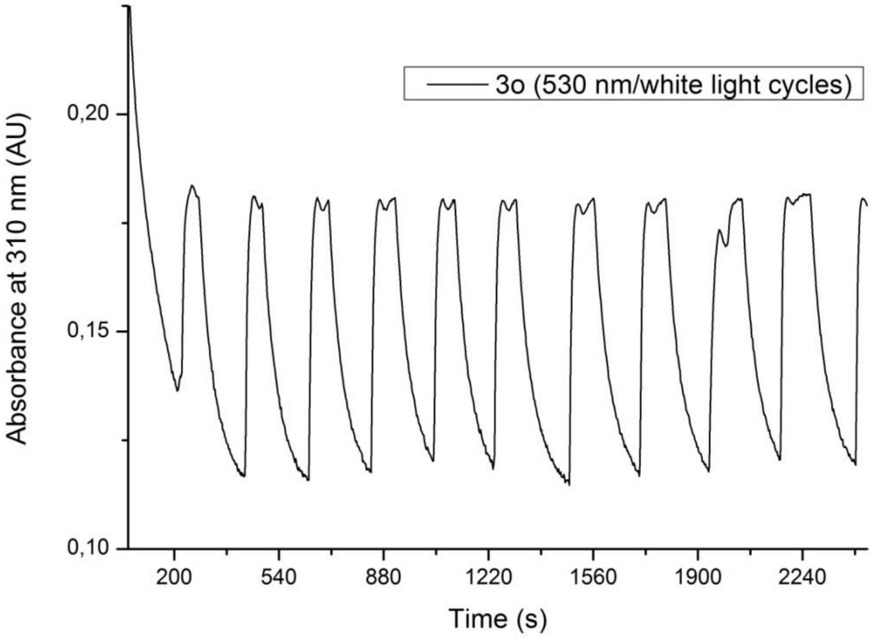


Figure S6. Reversible photosisomerization of **3o** (37 °C, Buffer with 1 vol% DMSO at pH=7, 20 μM) in the presence of 10 mM glutathione (GSH). Ten cycles of 530 nm/white light irradiation could be performed without the observation of significant fatigue or reduction.

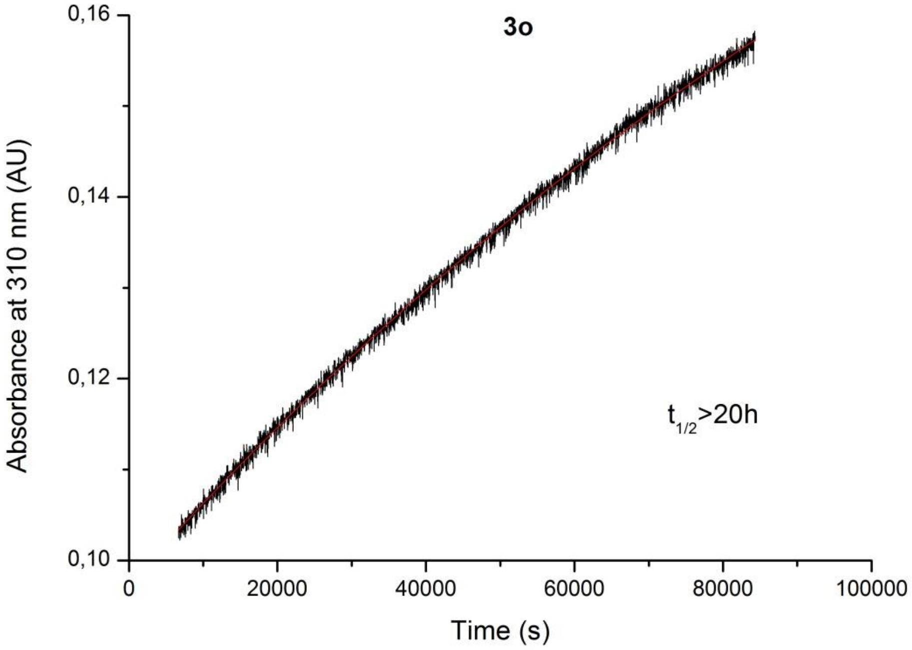


Figure S7. Determination of half-life for **3o** at 37 °C in DMSO. First, PSS was reached upon 530 nm irradiation, after which the absorption was measured at λ_{max} = 310 nm. Line presents the fitting with single exponential process.

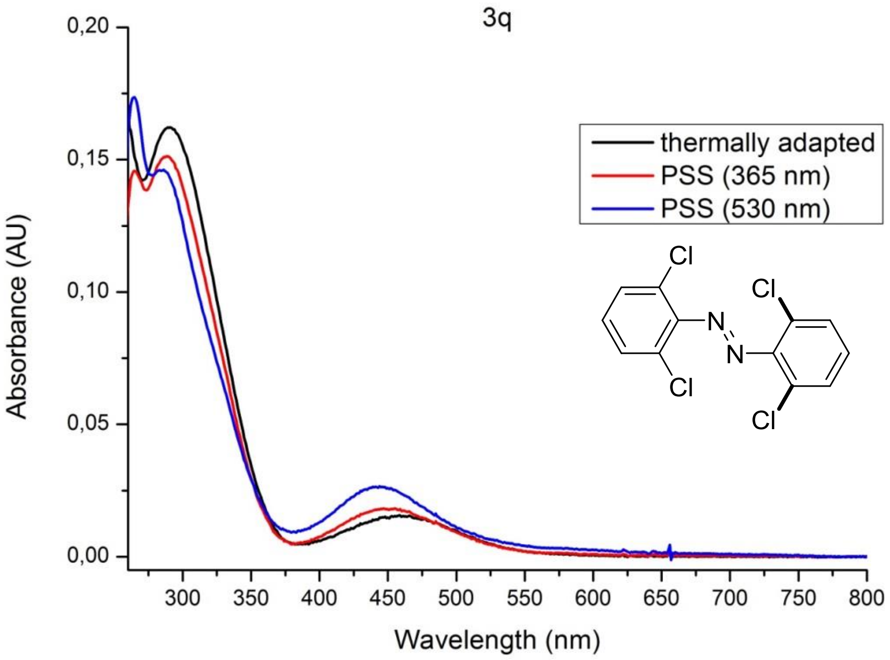


Figure S8. Absorption spectra for the photoisomerization of compound **3q** (DMSO, 37 °C, 20 µM). Photostationary states after thermal adaptation, 365 nm irradiation and 530 nm irradiation were obtained.

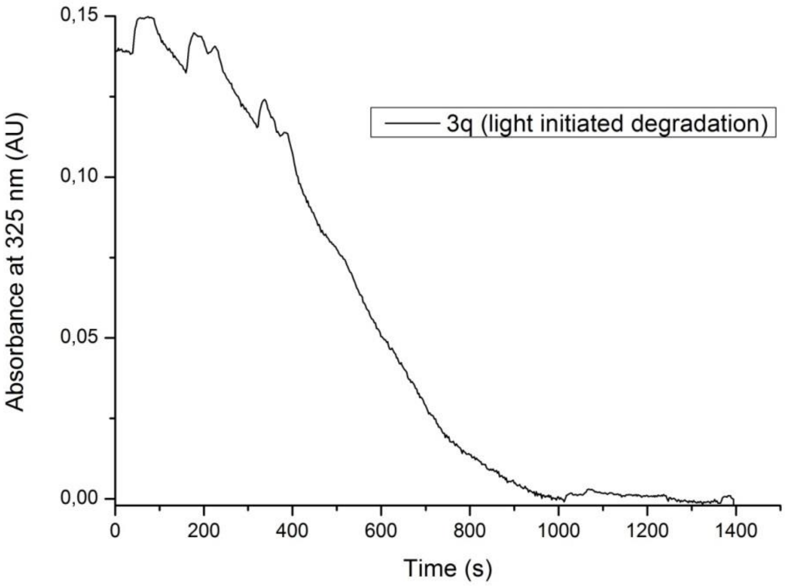


Figure S9. Reversible photosisomerization of **3q** (37 °C, Buffer with 1 vol% DMSO at pH=7, 20 µM) in the presence of 10 mM glutathione (GSH). After two cycles of 530 nm/white light irradiation, degradation was initiated which led to a full reduction of the absorbance within 20 minutes. This was irreversible and could not be prevented by white light irradiation, 530 nm irradiation or no light exposure.

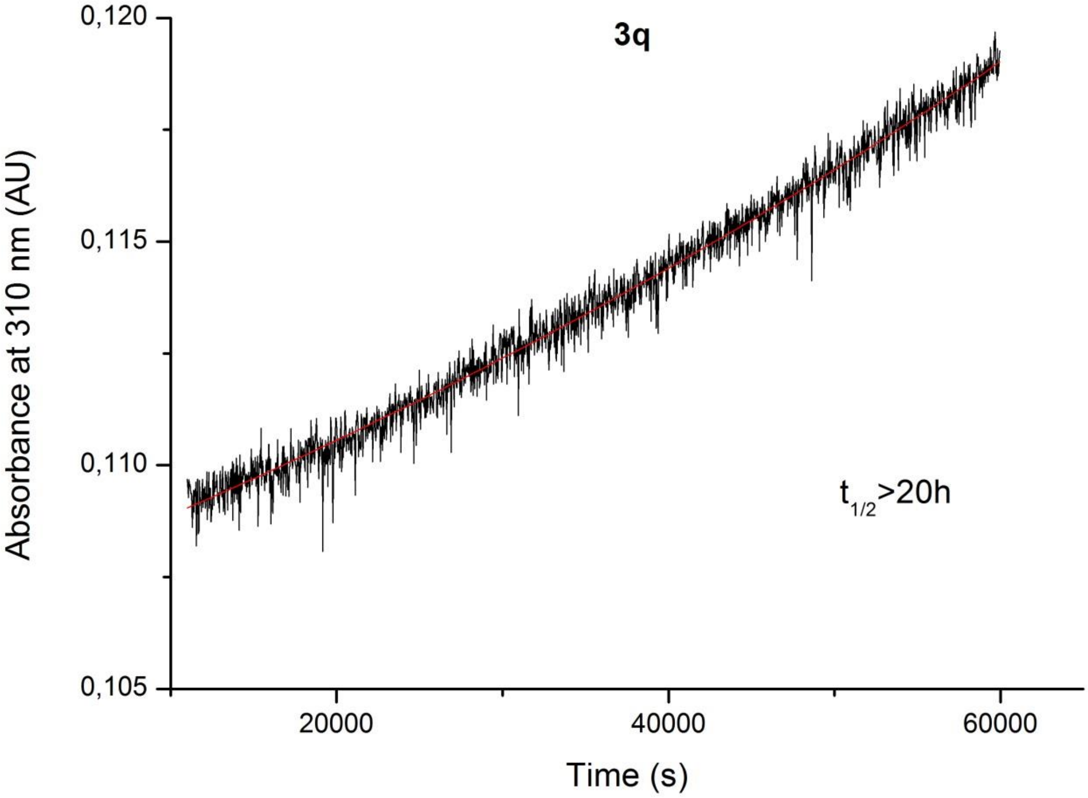


Figure S10. Determination of half-life for **3q** at 37 °C in DMSO. First, PSS was reached upon 530 nm irradiation, after which the absorption was measured at λ_{max} = 310 nm. Line presents the fitting with single exponential process.

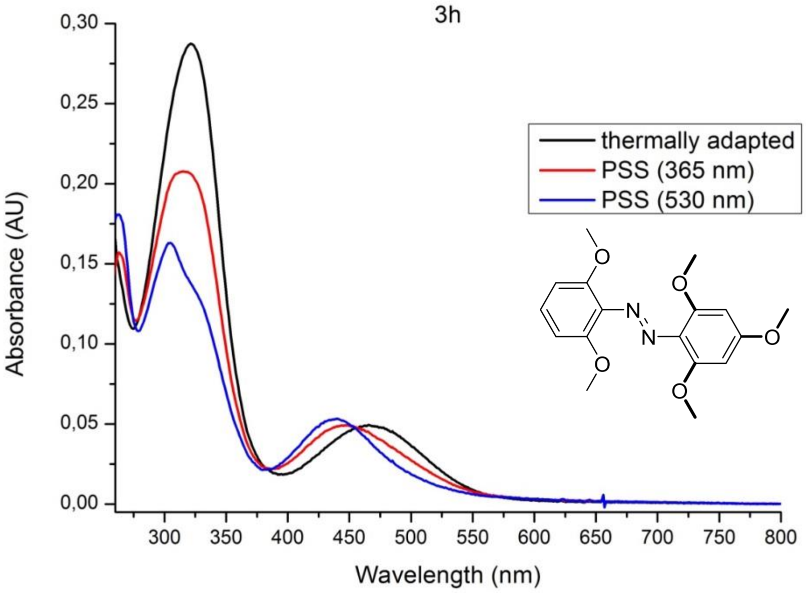


Figure S11. Absorption spectra for the photoisomerization of compound **3h** (DMSO, 37 °C, 20 μM). Photostationary states after thermal adaptation, 365 nm irradiation and 530 nm irradiation were obtained.

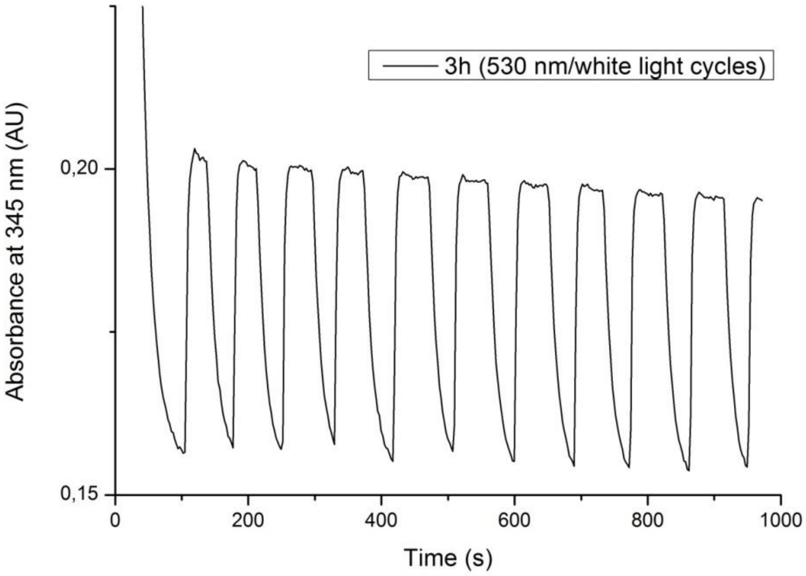


Figure S12. Reversible photosisomerization of **3h** (37 °C, Buffer with 1 vol% DMSO at pH=7, 20 μM) in the presence of 10 mM glutathione (GSH). Ten cycles of 530 nm/white light irradiation could be performed without the observation of significant fatigue or reduction.

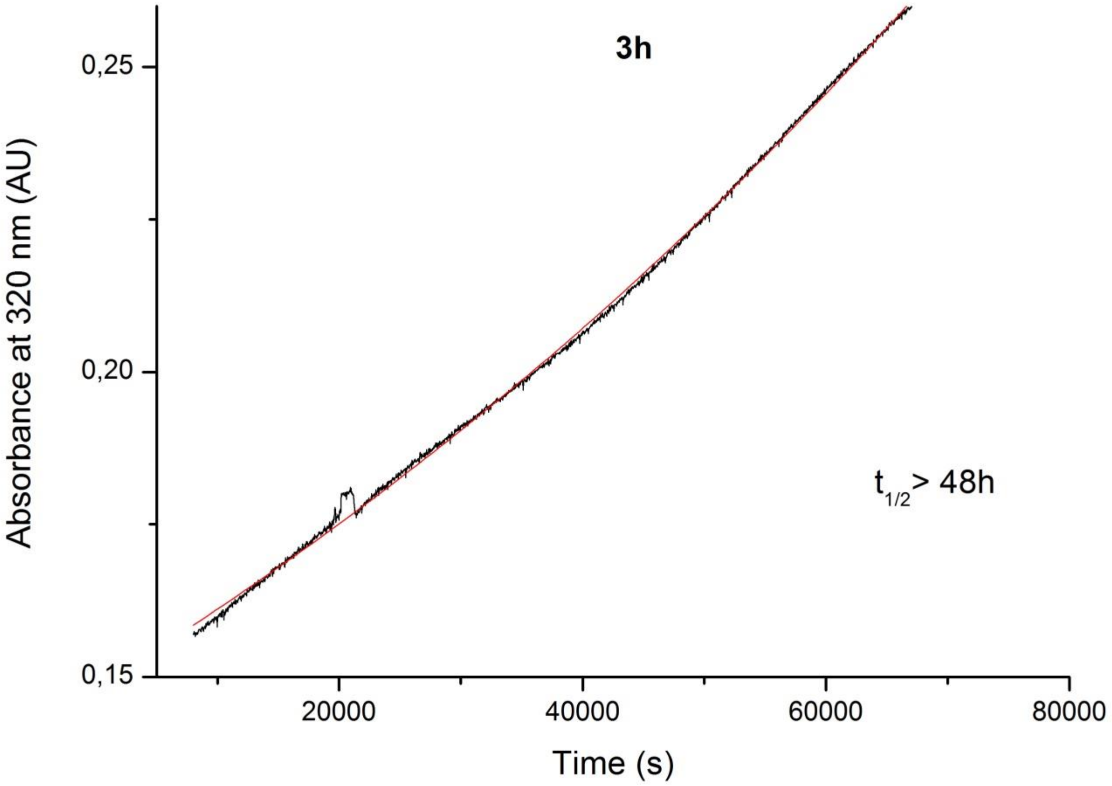


Figure S13. Determination of half-life for **3h** at 37 °C in DMSO. First, PSS was reached upon 530 nm irradiation, after which the absorption was measured at λ_{max} = 310 nm. Line presents the fitting with single exponential process.

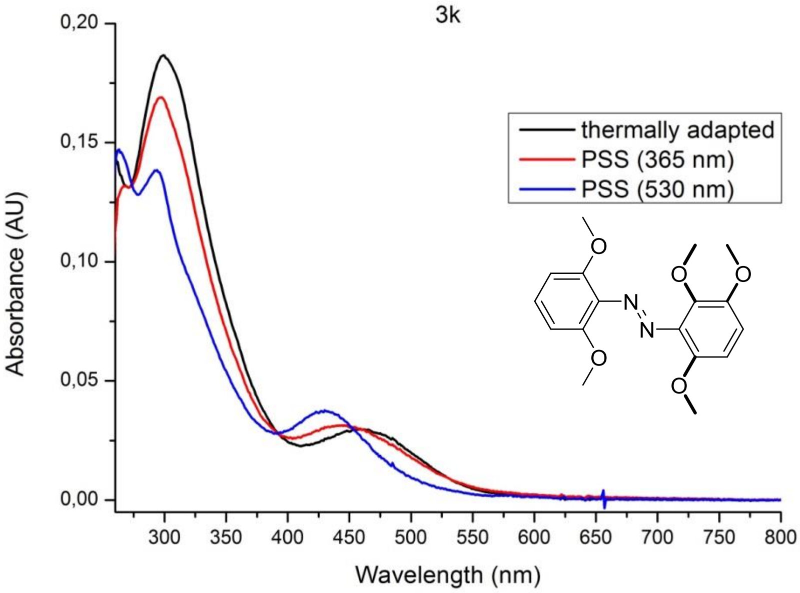


Figure S14. Absorption spectra for the photoisomerization of compound **3k** (DMSO, 37 °C, 20 μM). Photostationary states after thermal adaptation, 365 nm irradiation and 530 nm irradiation were obtained.

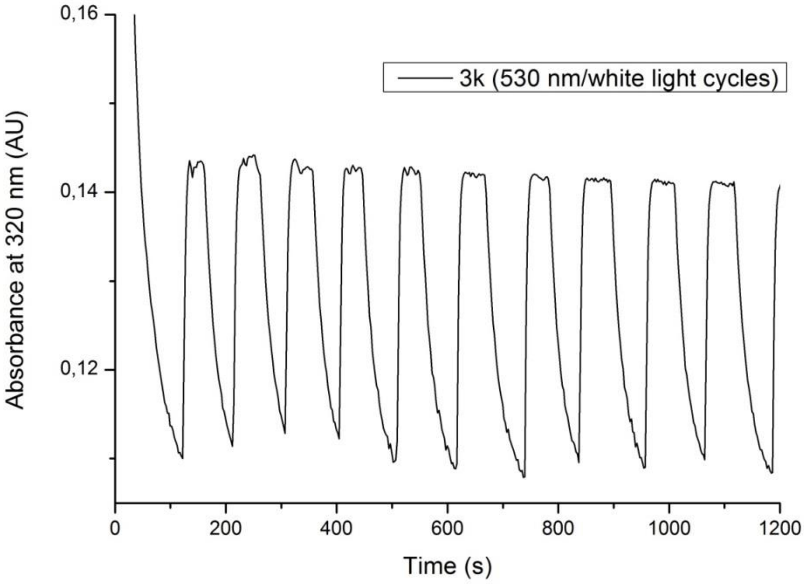


Figure S15. Reversible photosisomerization of **3k** (37 °C, Buffer with 1 vol% DMSO at pH=7, 20 μM) in the presence of 10 mM glutathione (GSH). Ten cycles of 530 nm/white light irradiation could be performed without the observation of significant fatigue or reduction.

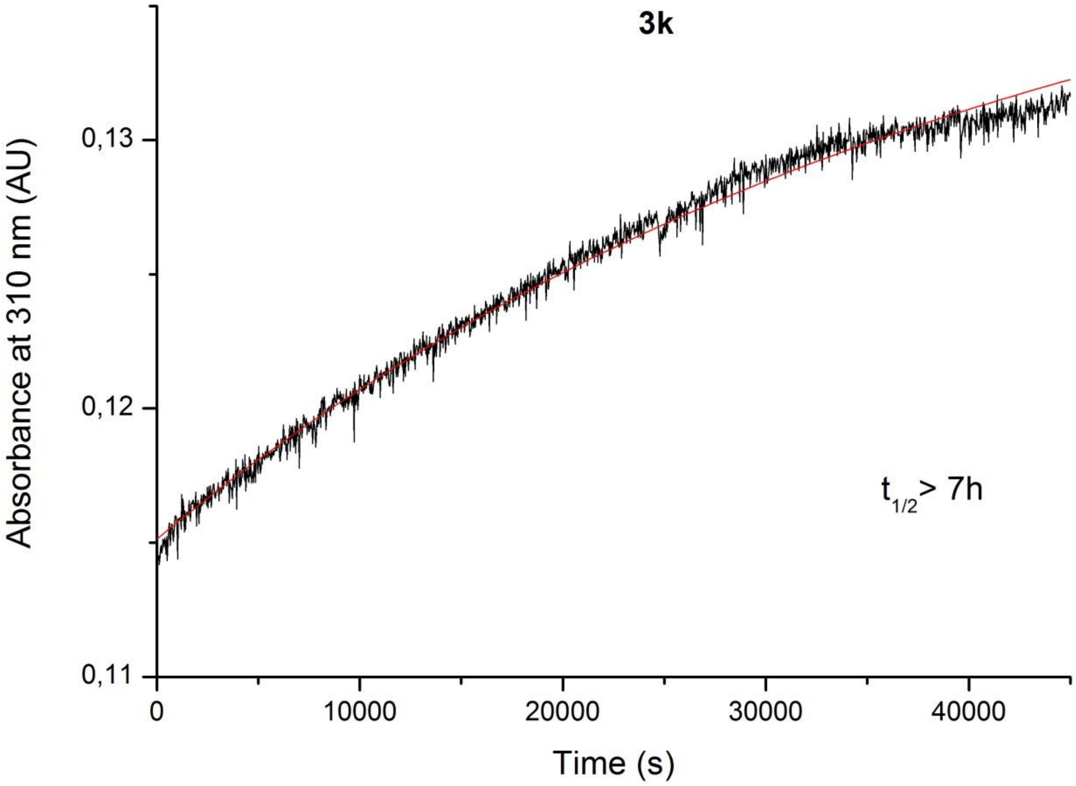


Figure S16. Determination of half-life for **3k** at 37 °C in DMSO. First, PSS was reached upon 530 nm irradiation, after which the absorption was measured at λ_{max} = 310 nm. Line presents the fitting with single exponential process.

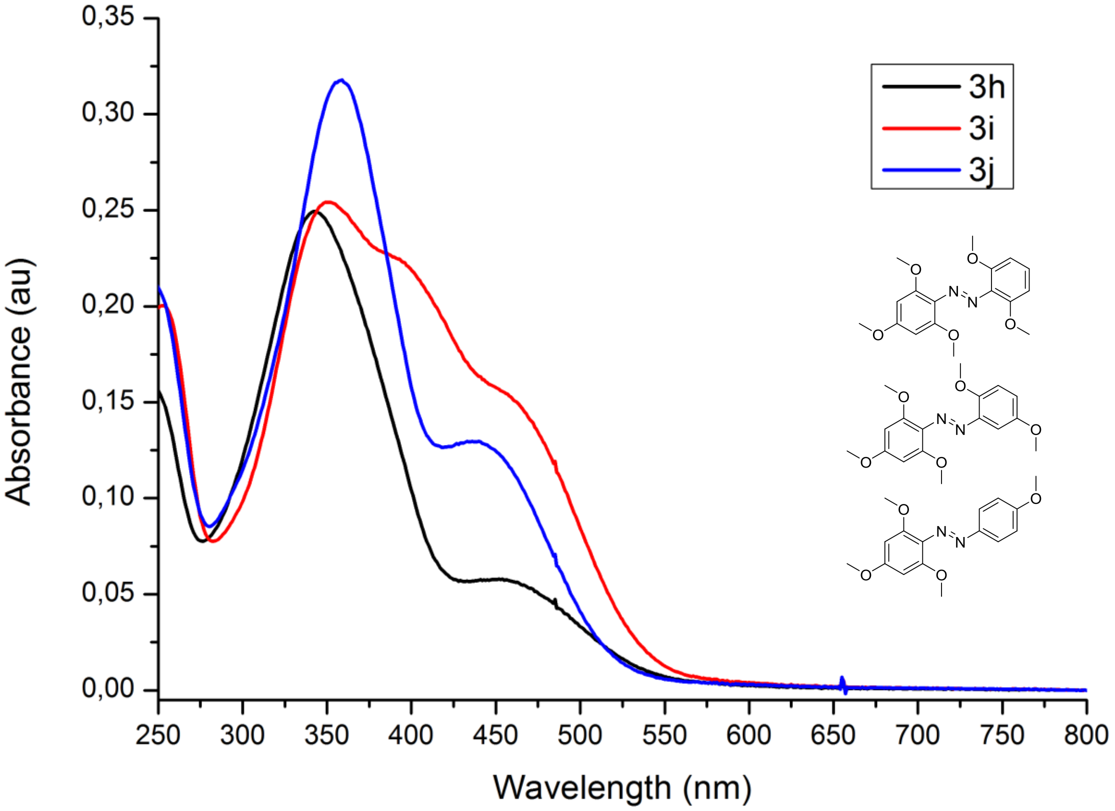


Figure S17. Absorption spectra of compound **3h-j** (20 μM in buffer with 1 vol% DMSO at pH=7) showing the distinct differences in absorption spectrum caused by a changing substitution pattern (2,6-dimethoxy to 2,5-dimethoxy to 4-methoxy substituents).

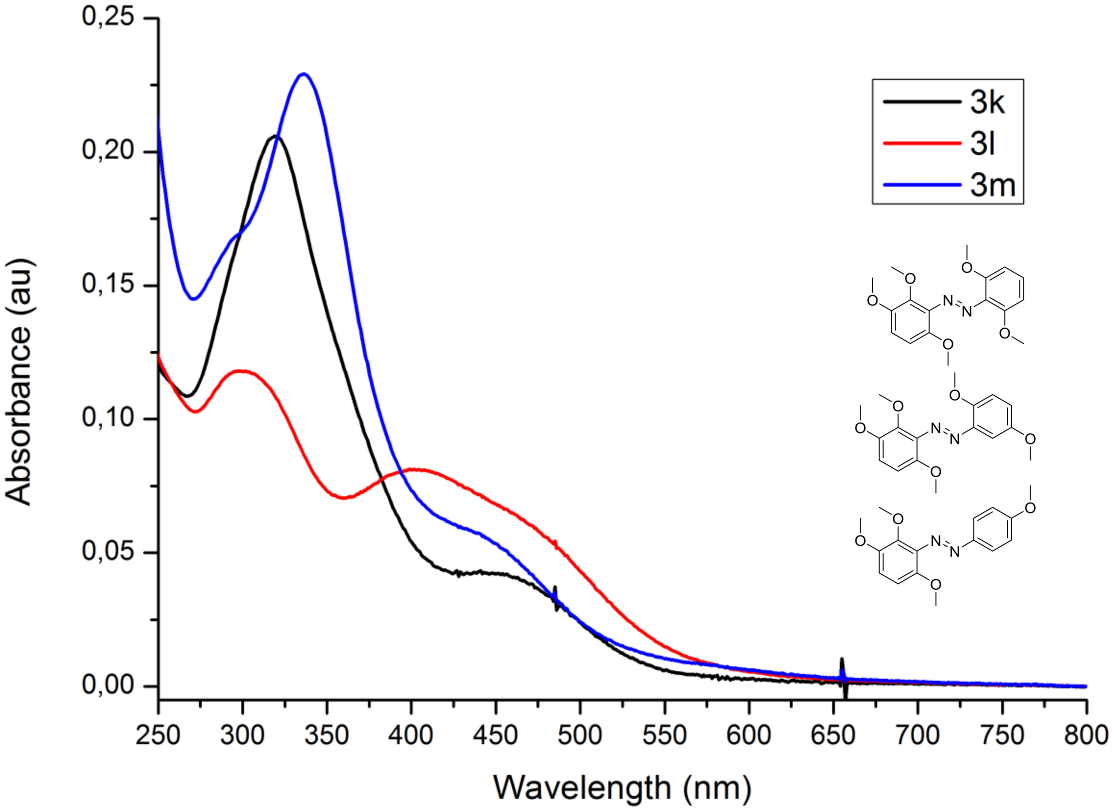


Figure S18. Absorption spectra of compound **3k-m** (20 µM in buffer with 1 vol% DMSO at pH=7) showing the distinct differences in absorption spectrum caused by a changing substitution pattern (2,6-dimethoxy to 2,5-dimethoxy to 4-methoxy substituents).

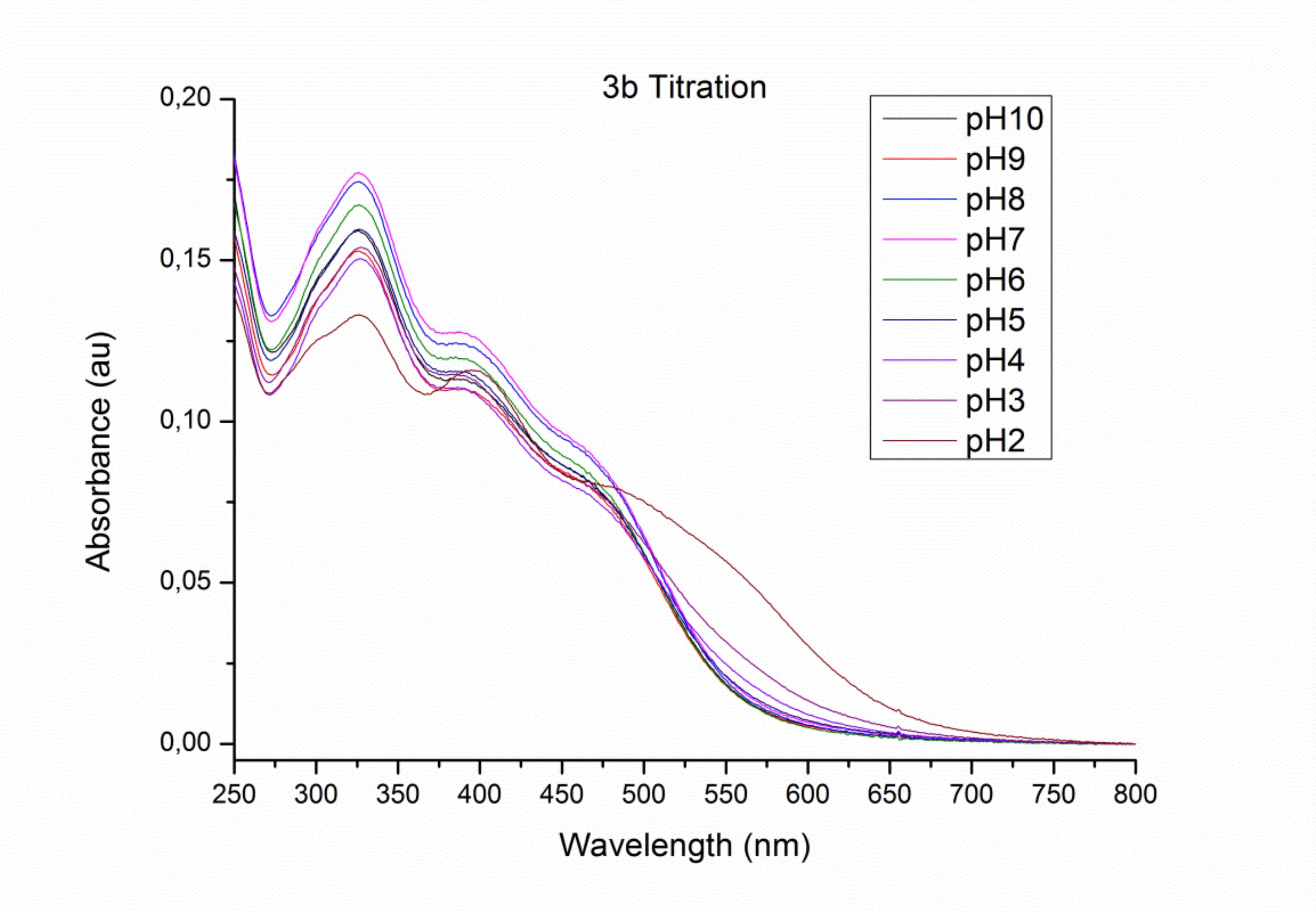


Figure S19. Titration curve of compound **3b** (20 μM in buffer with 1 vol% DMSO) showing the different absorption spectra at different pH.

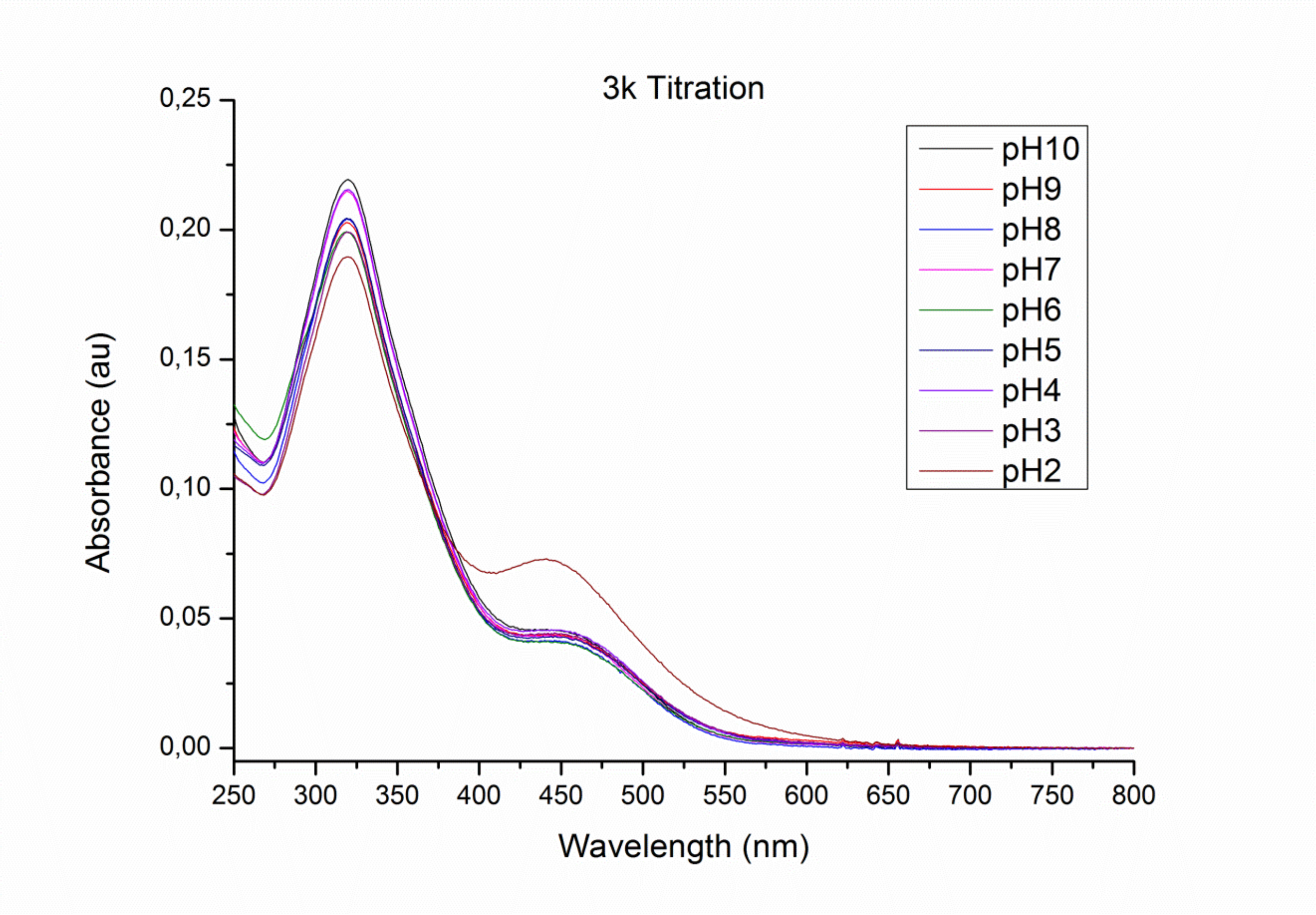
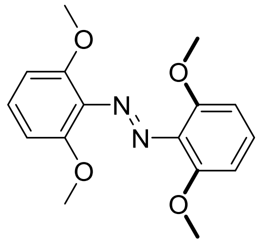
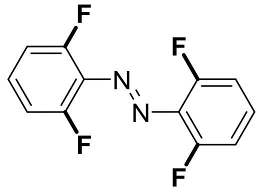
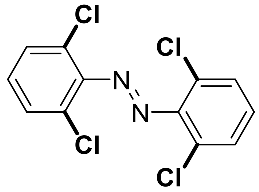
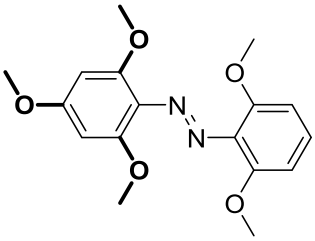
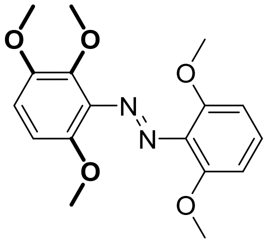
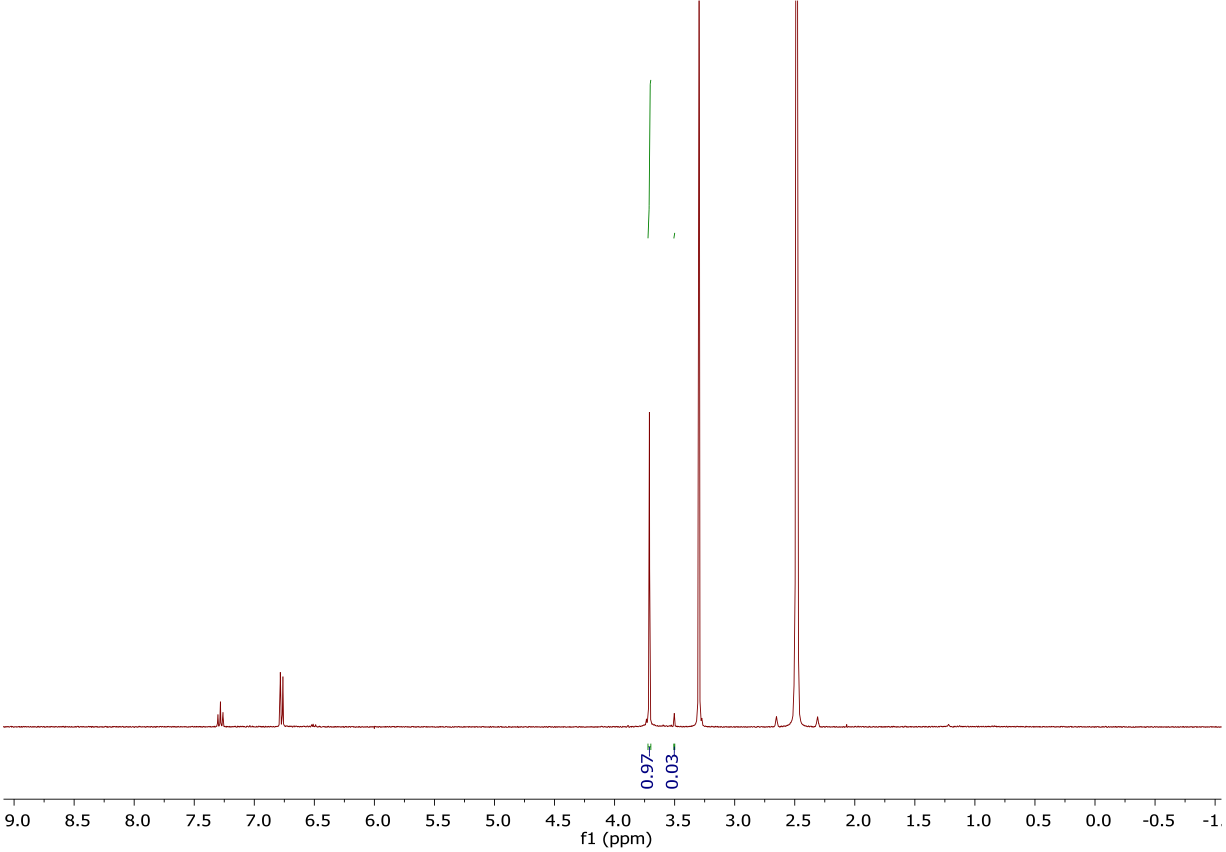


Figure S20. Titration curve of compound **3k** (20 µM in buffer with 1 vol% DMSO) showing the different absorption spectra at different pH.

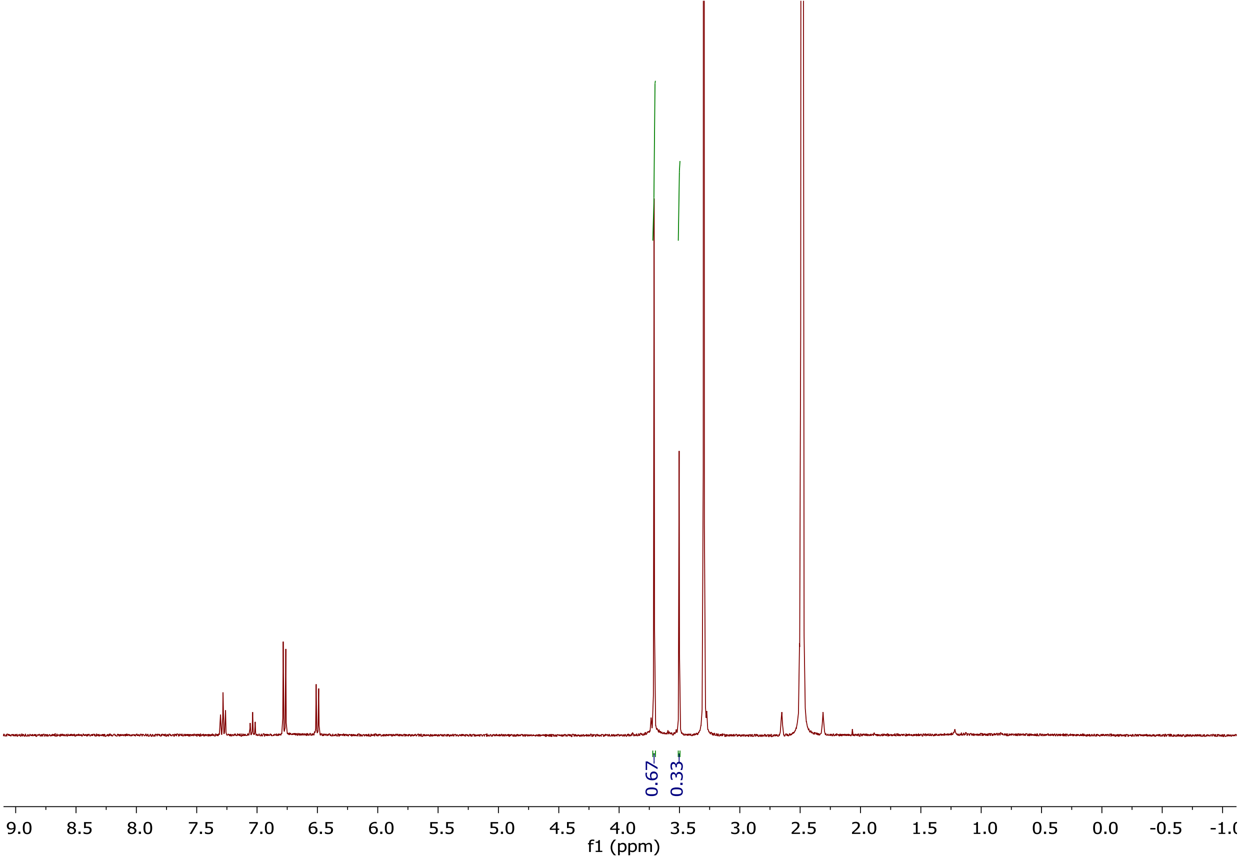
Table S3. Photostationary states (PSS, DMSO-d_6, ^{1}H-NMR) at different wavelengths of irradiation.

Compound	***Trans:cis* (thermally adapted)**	***Trans:cis* (365 nm irradiated)**	***Trans:cis* (530 nm irradiated)**
 **3a**	97:3	67:33	17:83
 **3o**	98:2	75:25	8:92
 **3q**	>97:3	65:35	38:62
 **3h**	>97:3	54:46	23:77
 **3k**	89:11	61:39	20:80

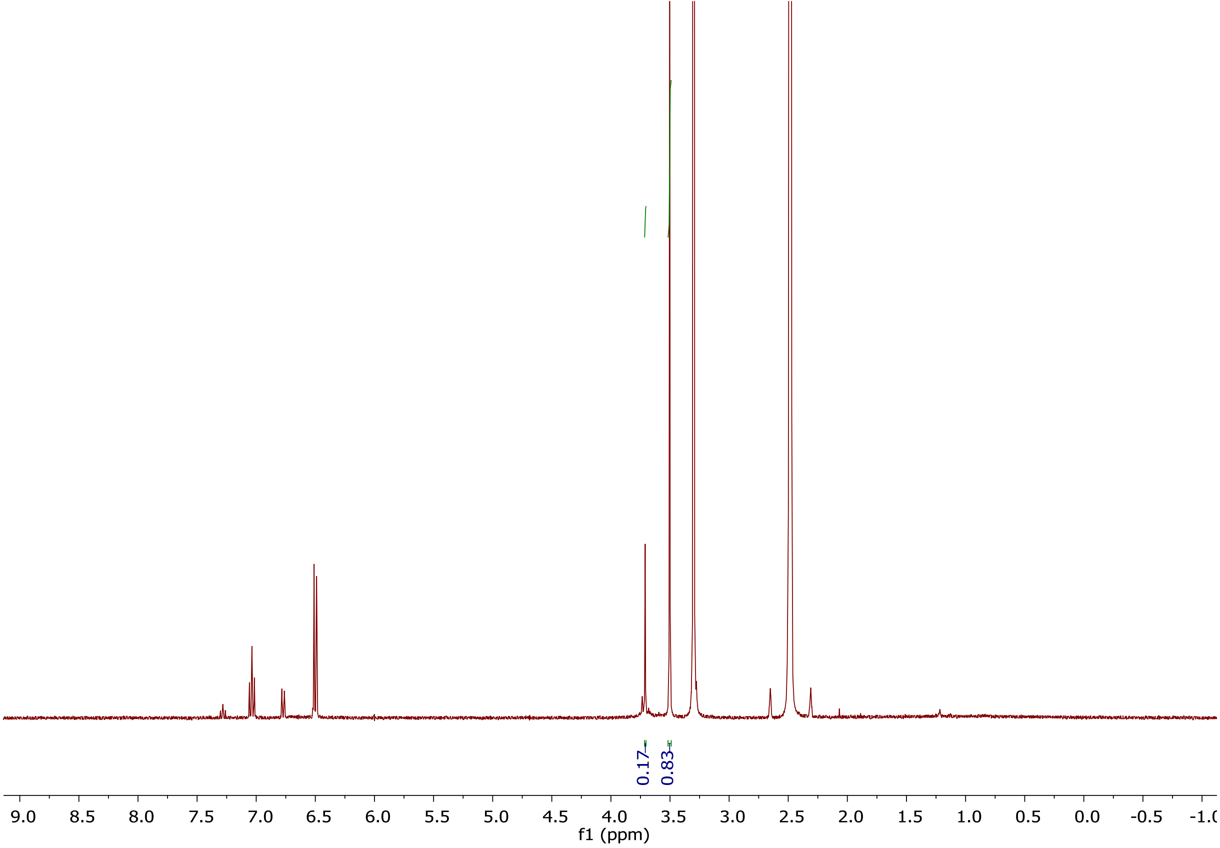
3a (thermally adapted):



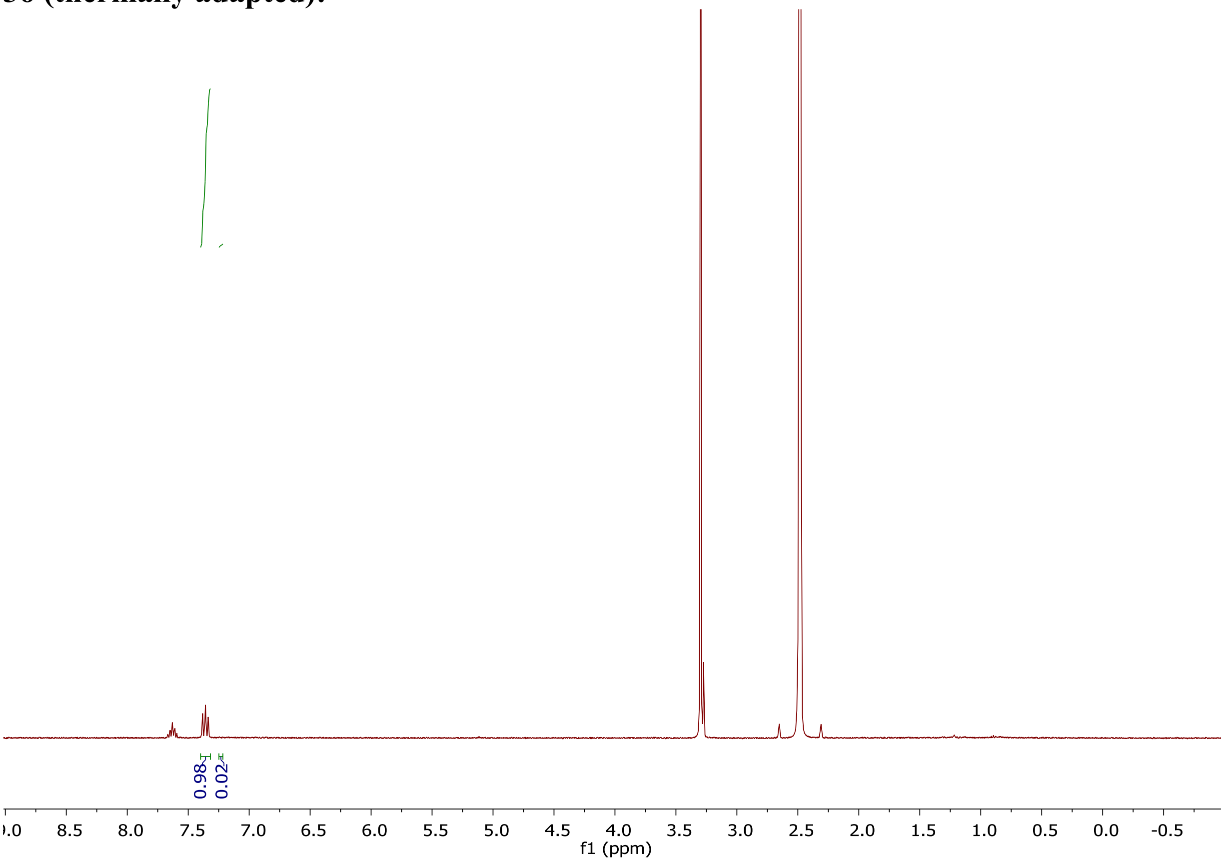
3a (PSS 365 nm irradiation):



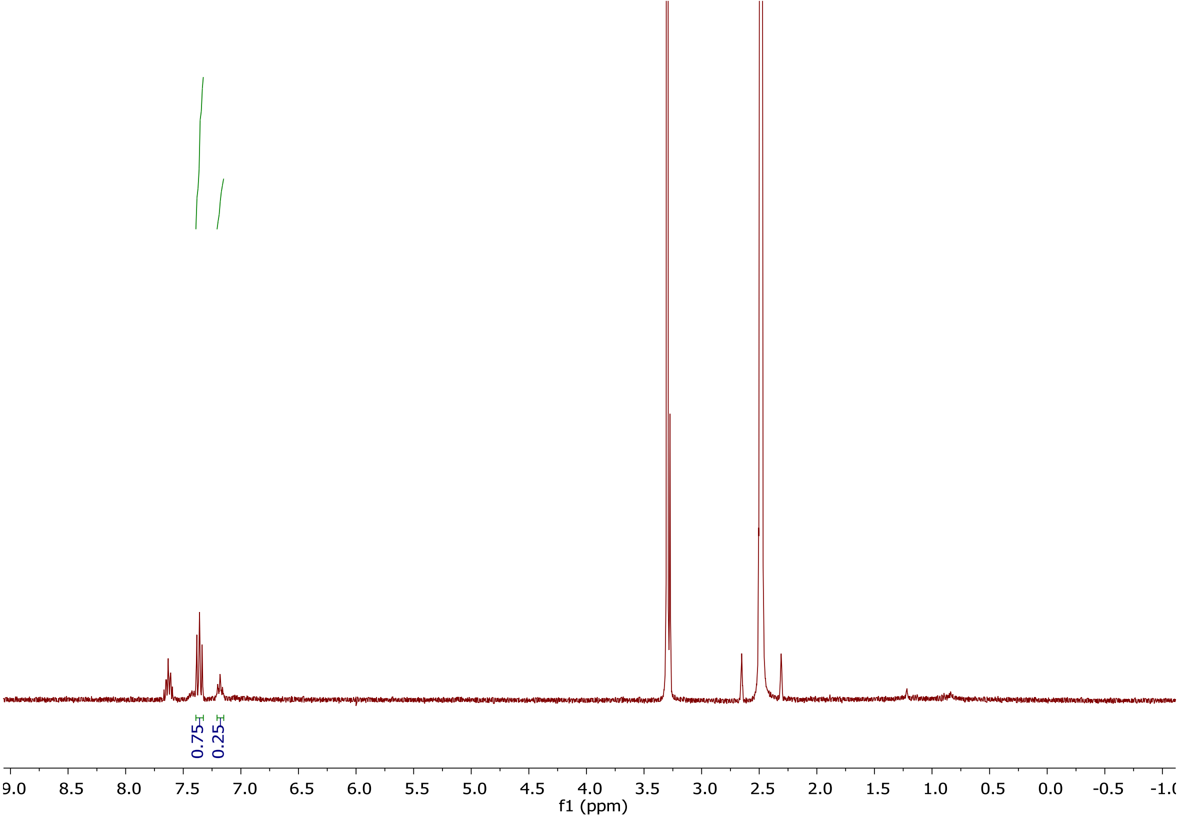
3a (PSS 530 nm irradiation):



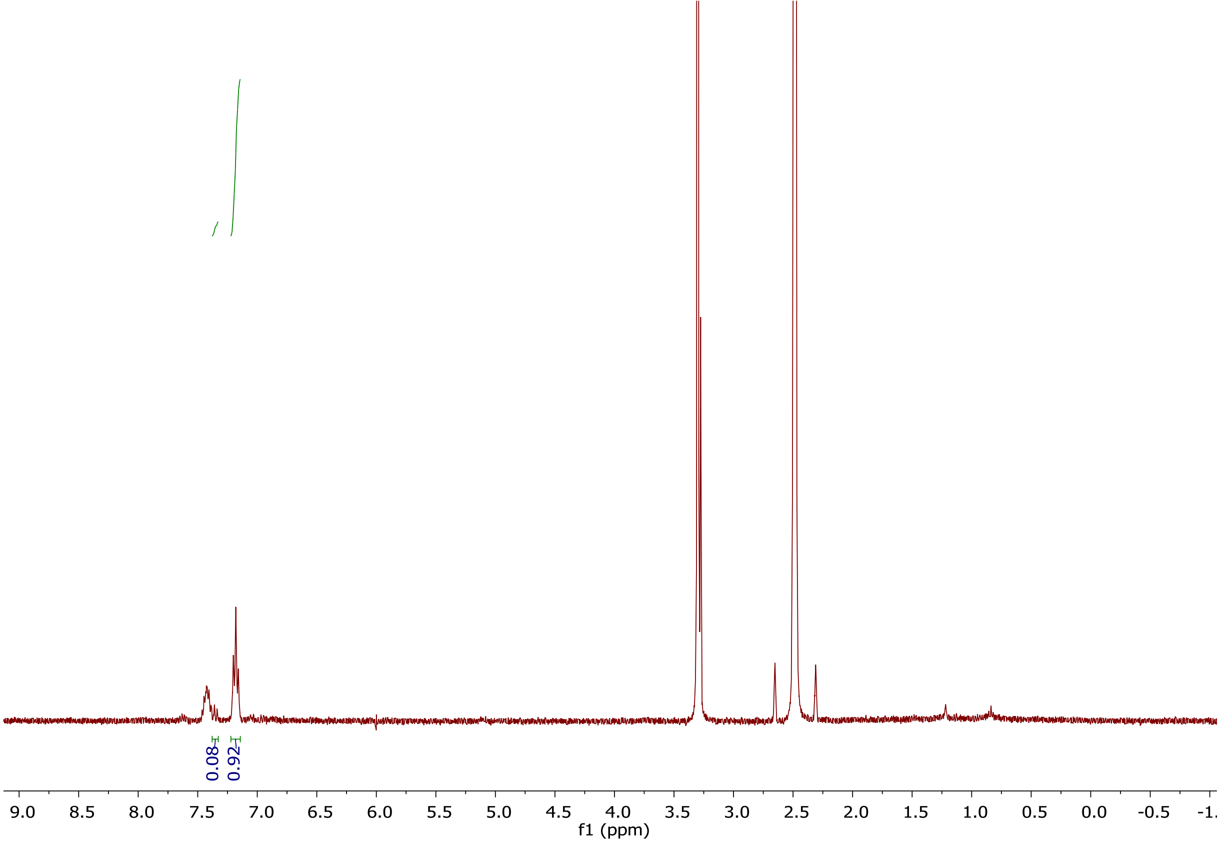
3o (thermally adapted):



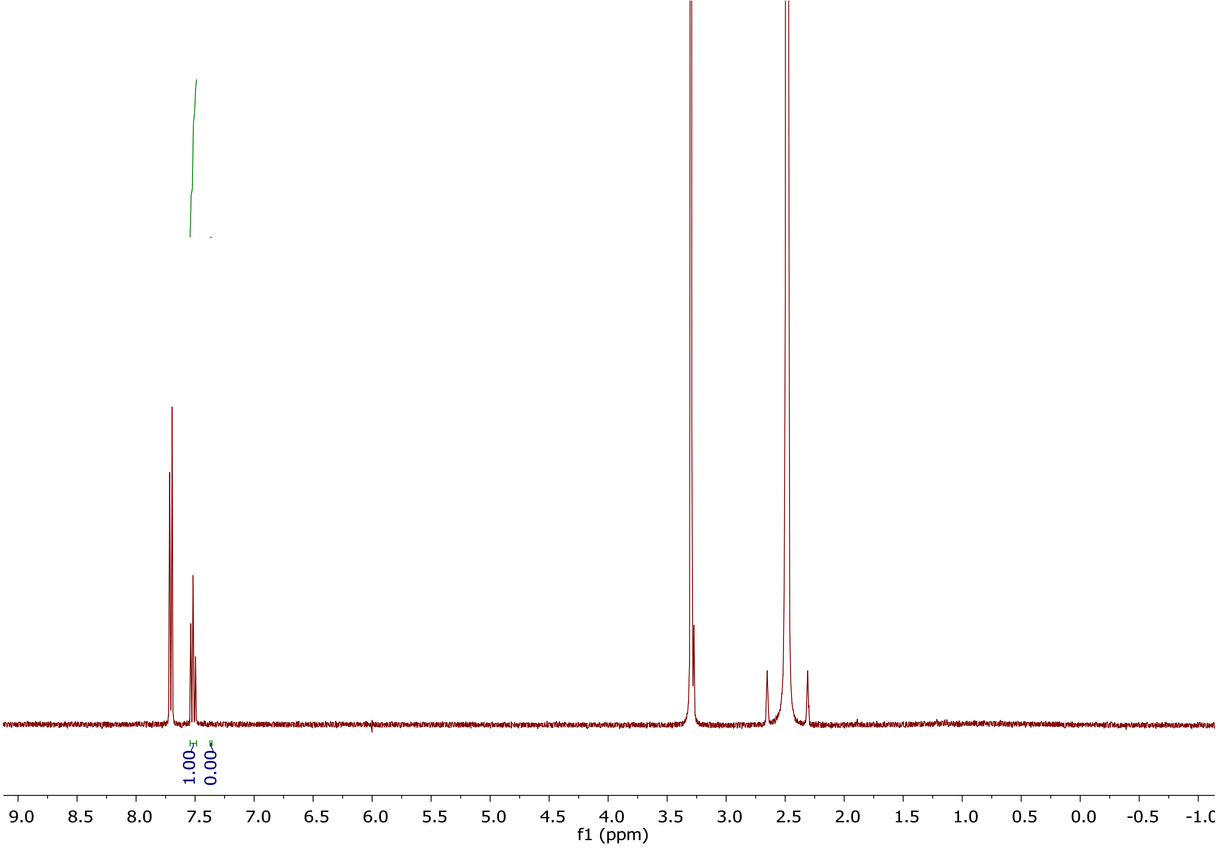
3o (PSS 365 nm irradiated):



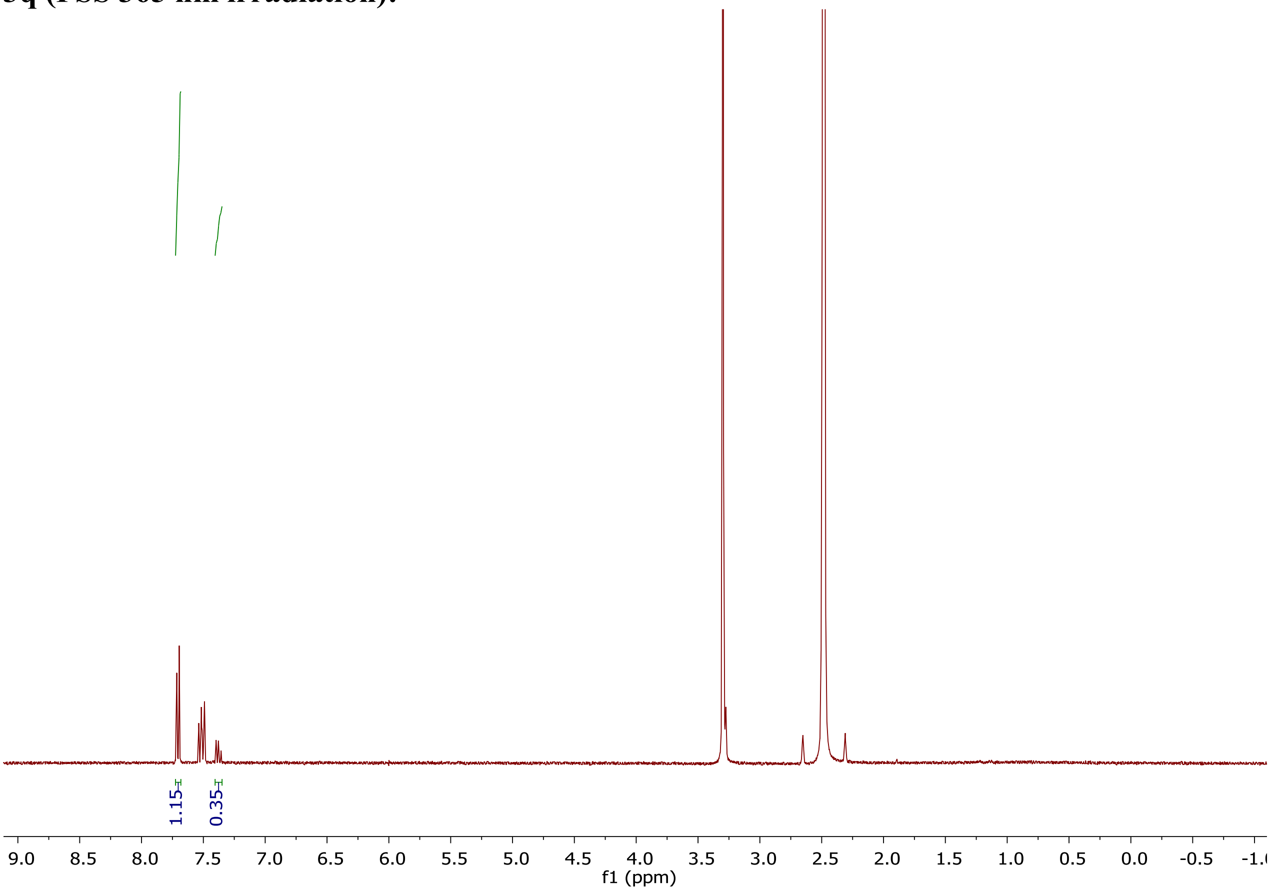
3o (PSS 530 nm irradiated):



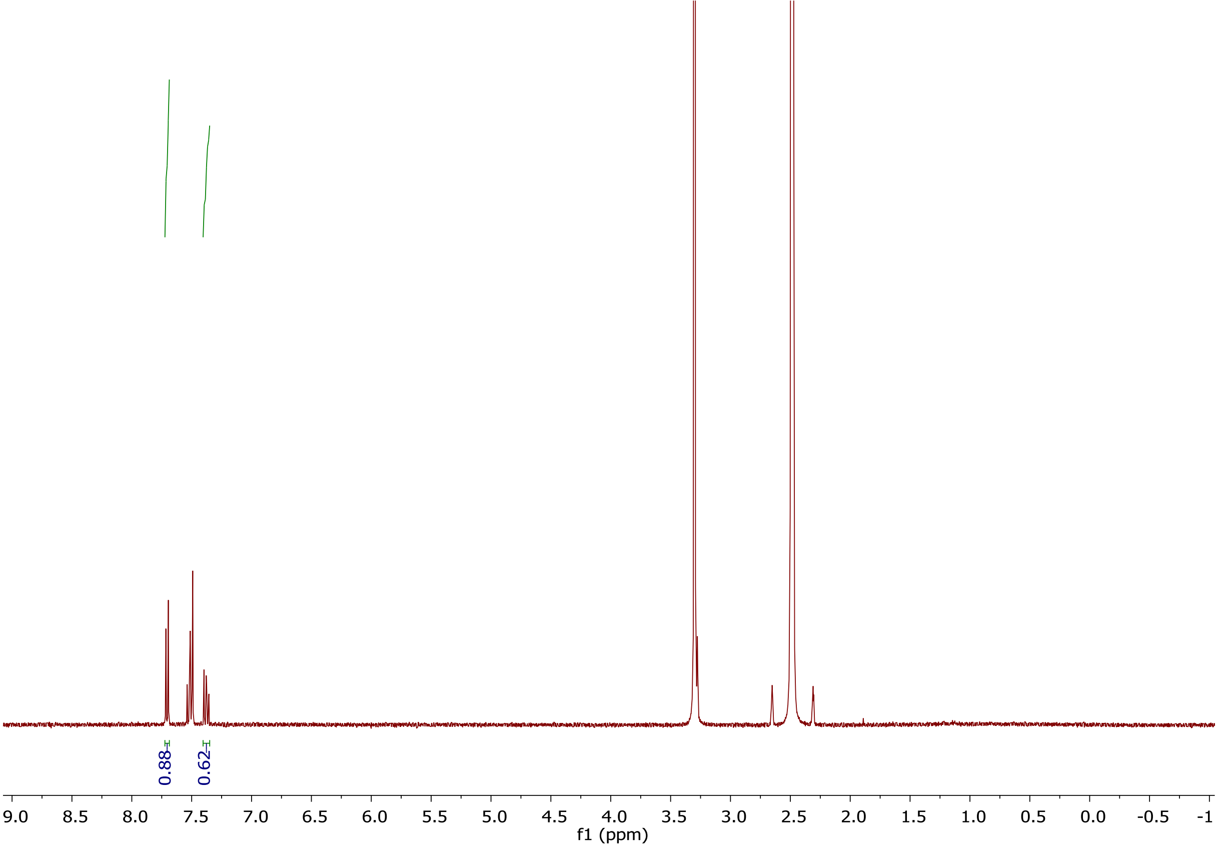
3q (thermally adapted):



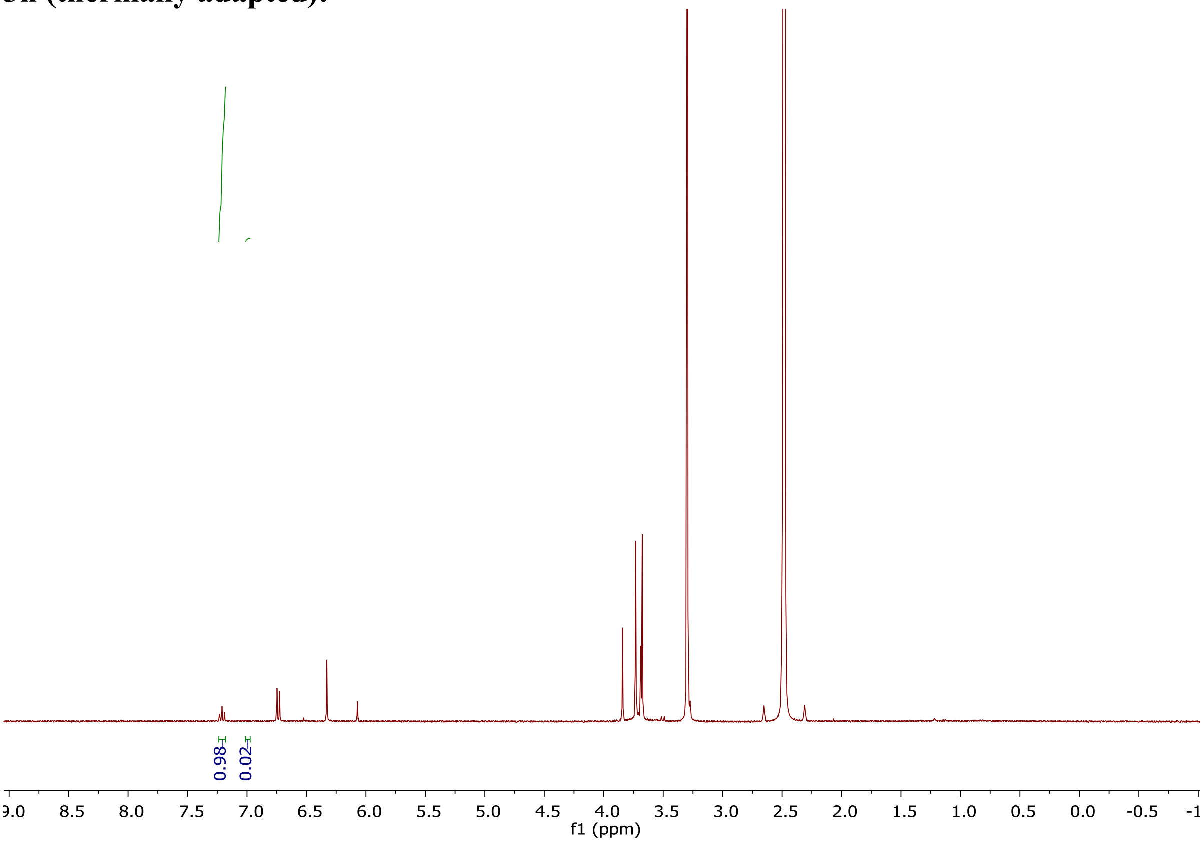
3q (PSS 365 nm irradiation):



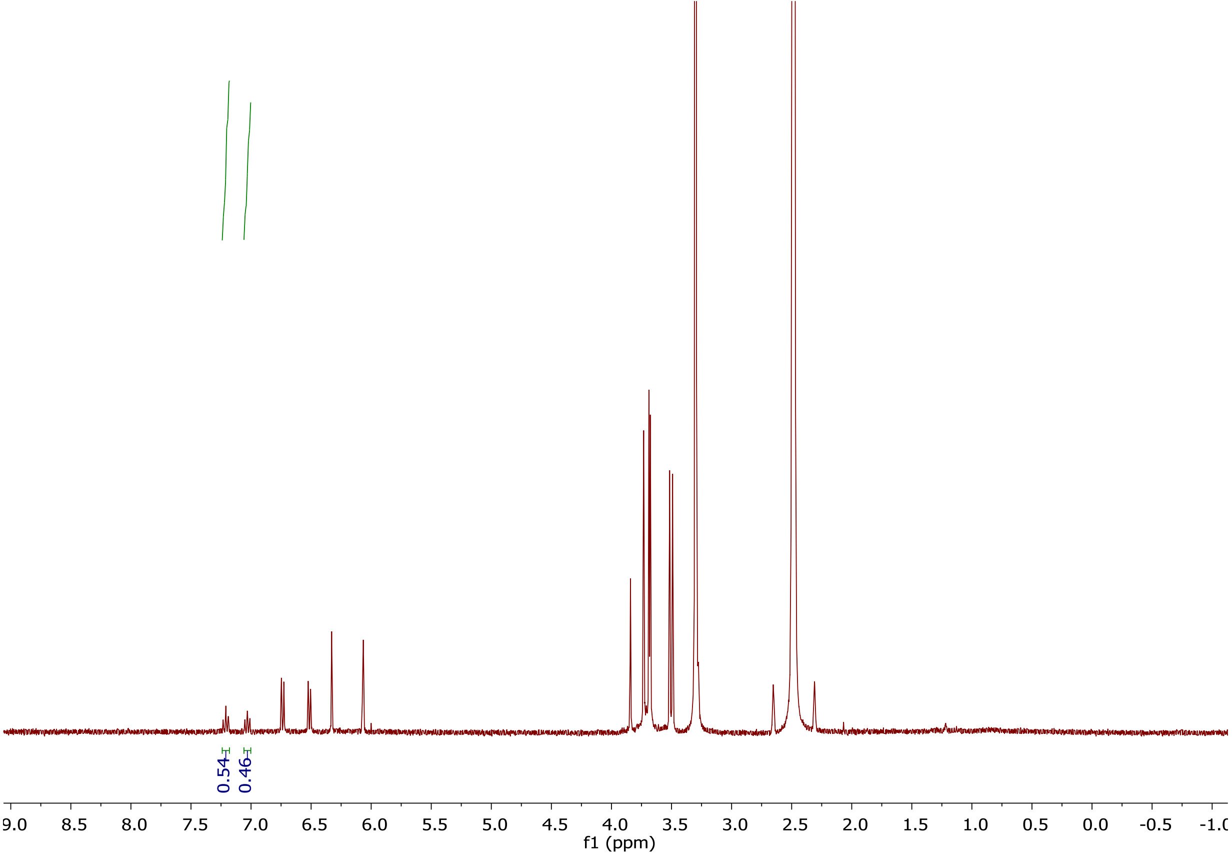
3q (530 nm irradiation):



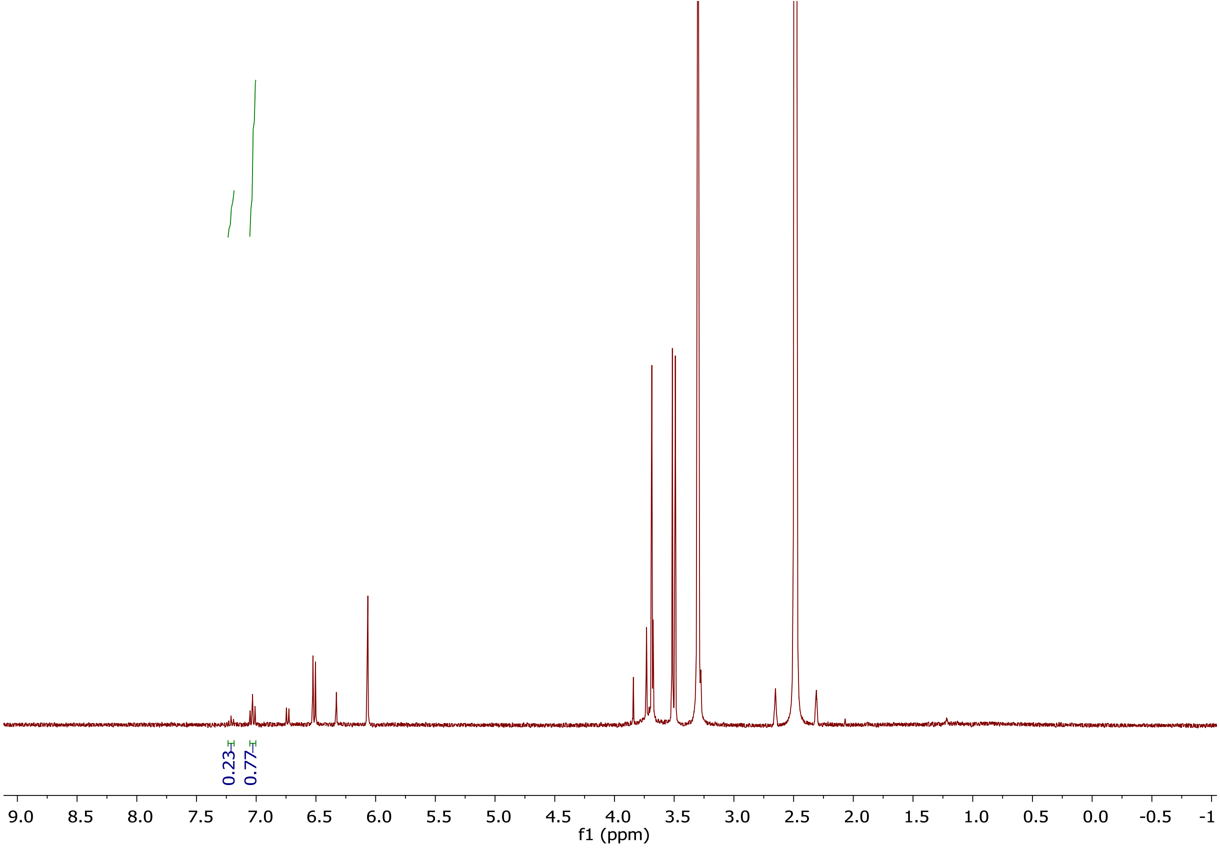
3h (thermally adapted):



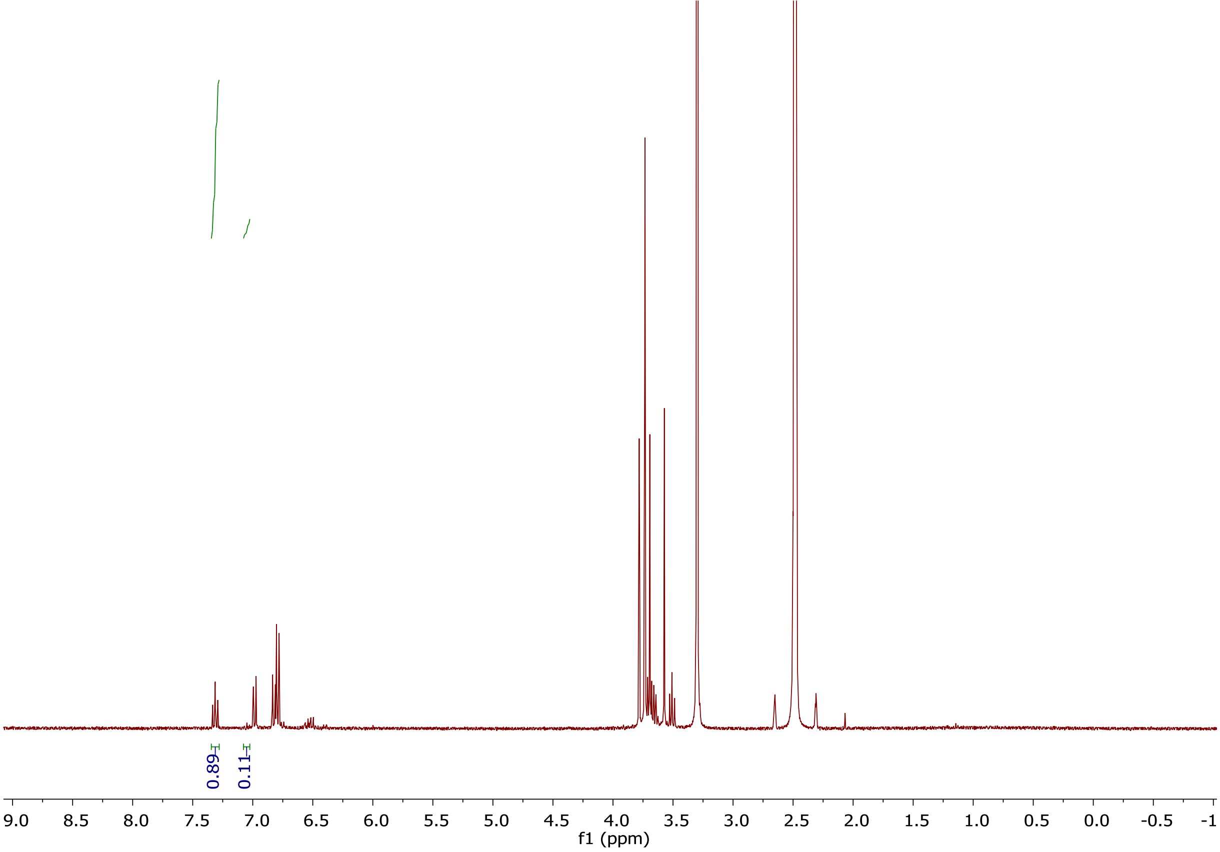
3h (PSS 365 nm irradiation):



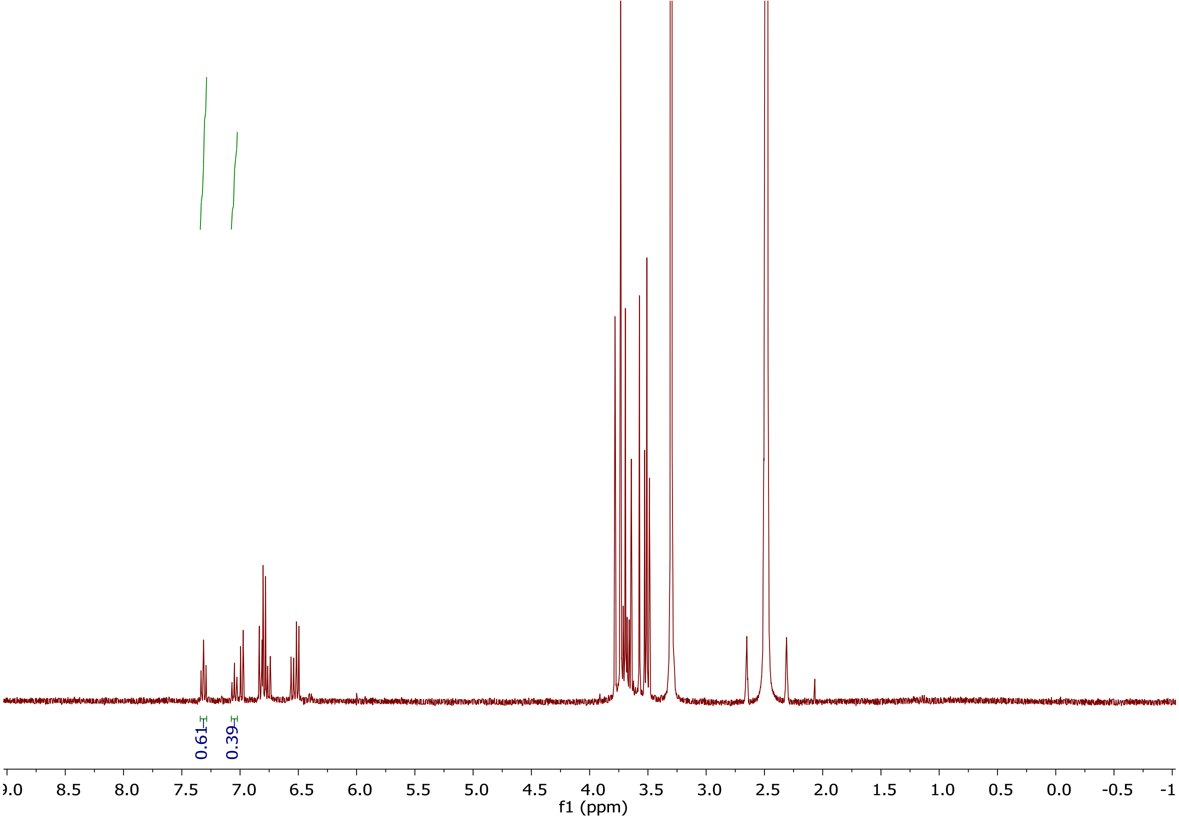
3h (PSS 530 nm irradiation):



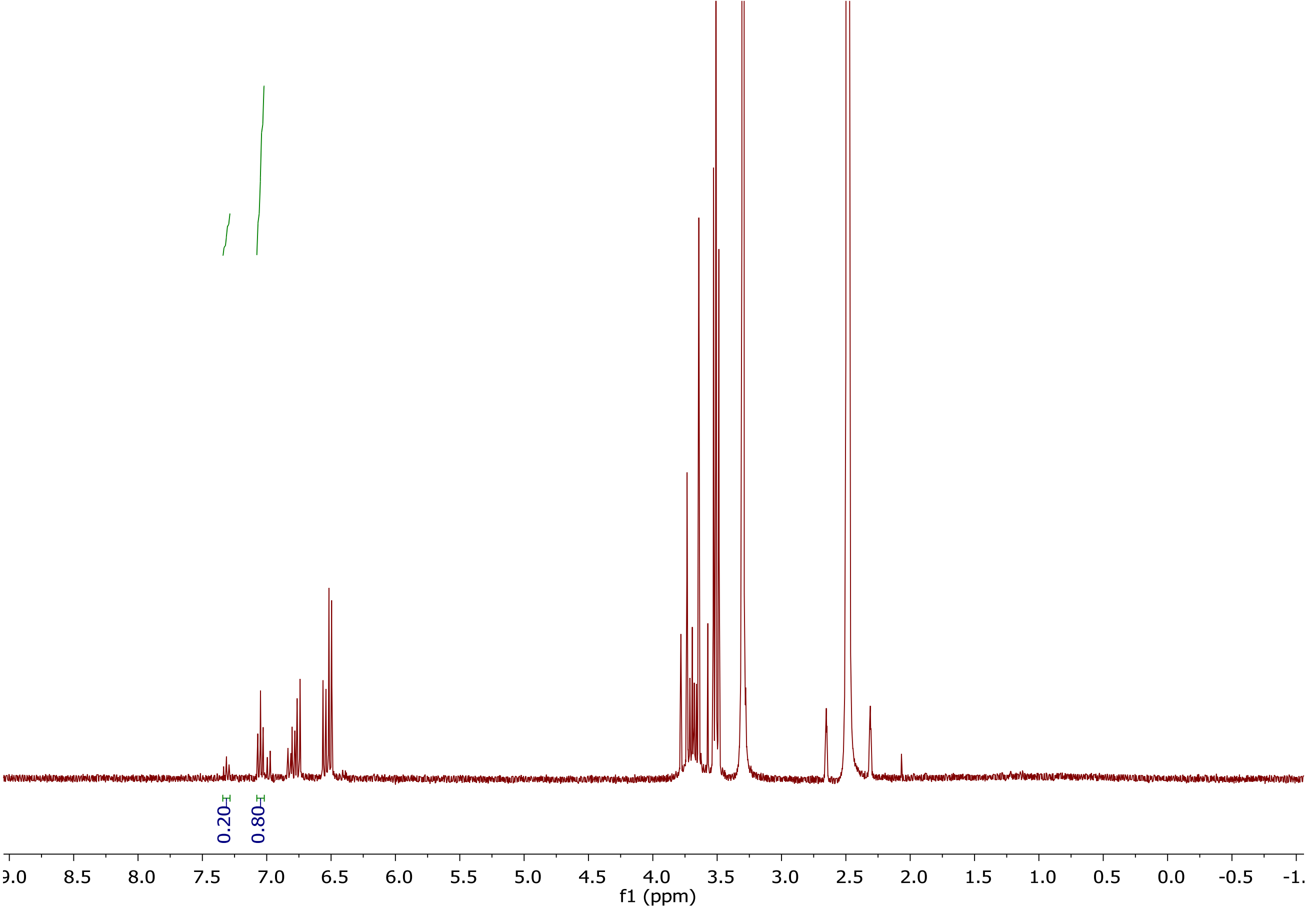
3k (thermally adapted):



3k (PSS 365 nm irradiation):

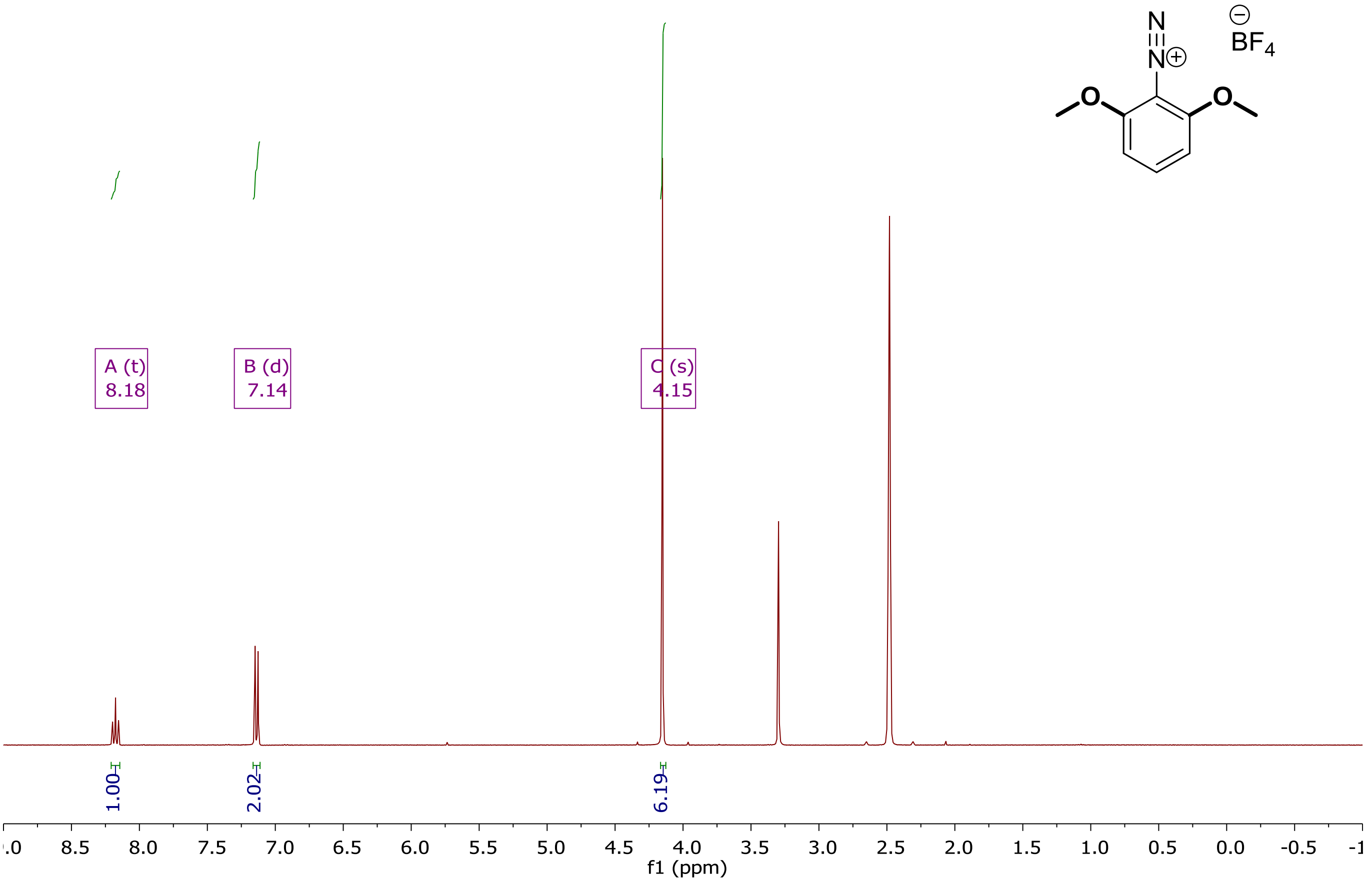


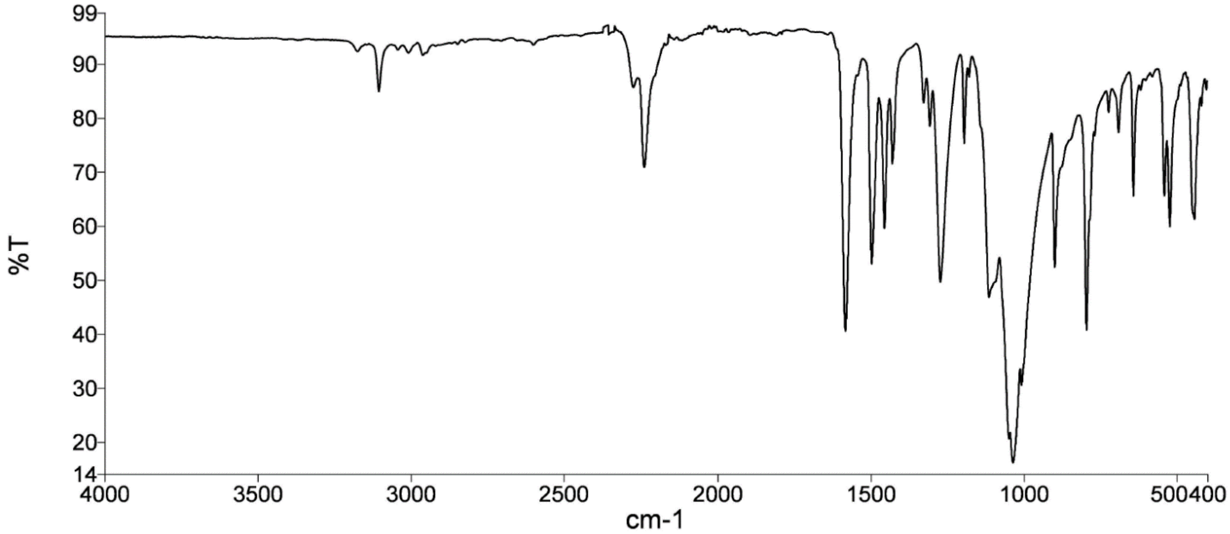
3k (PSS 530 nm irradiation):



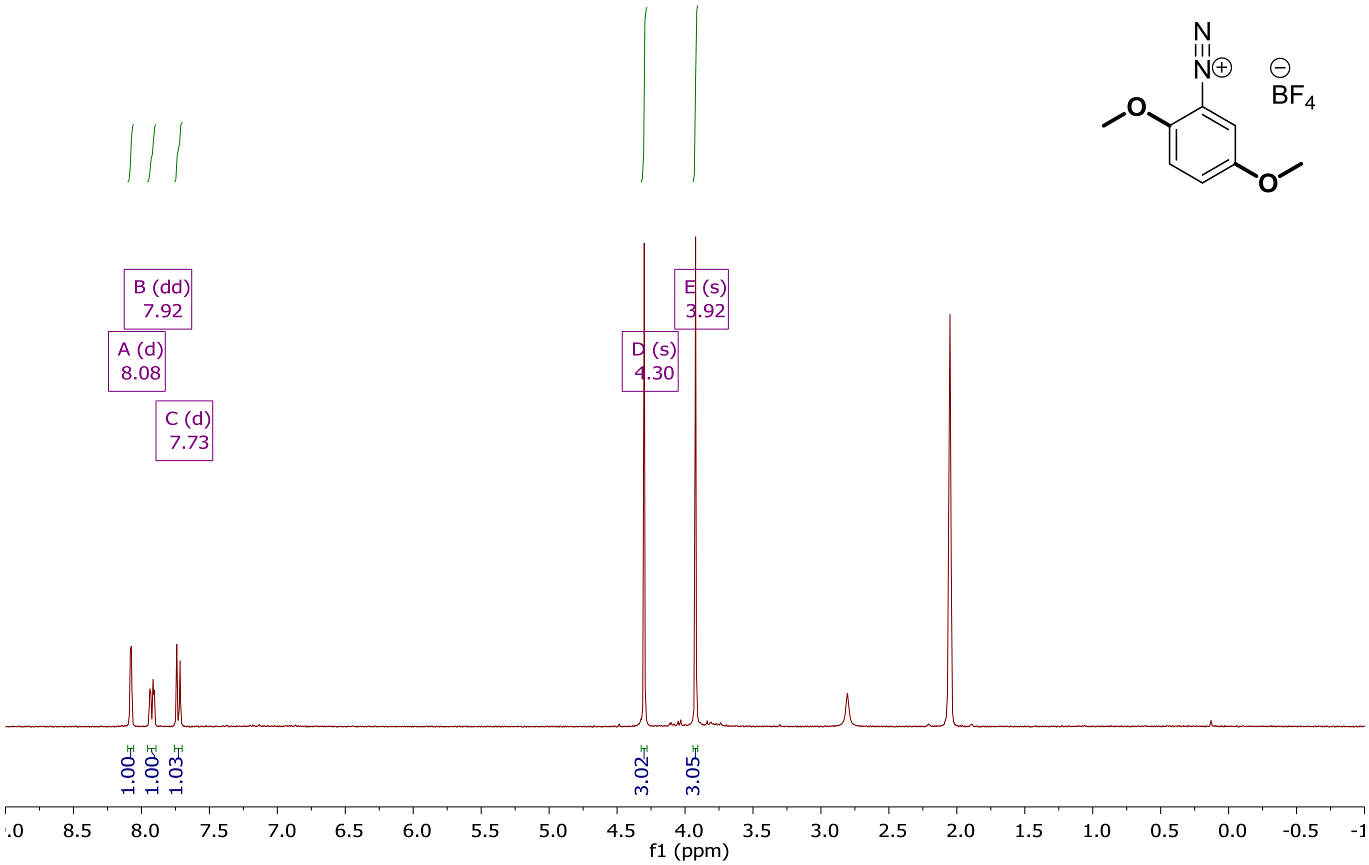
^{1}H, ^{13}C-NMR (DMSO-d$_6$), HR-MS (ESI+) and IR (neat) spectra

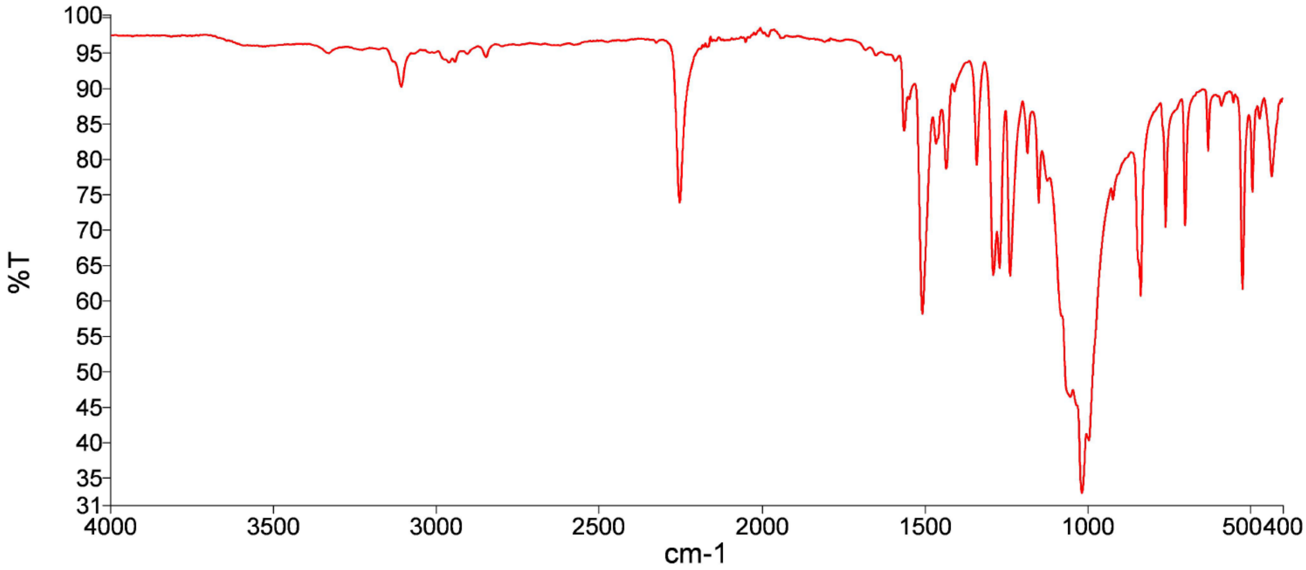
2a:



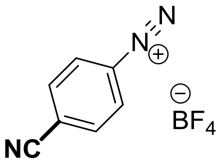


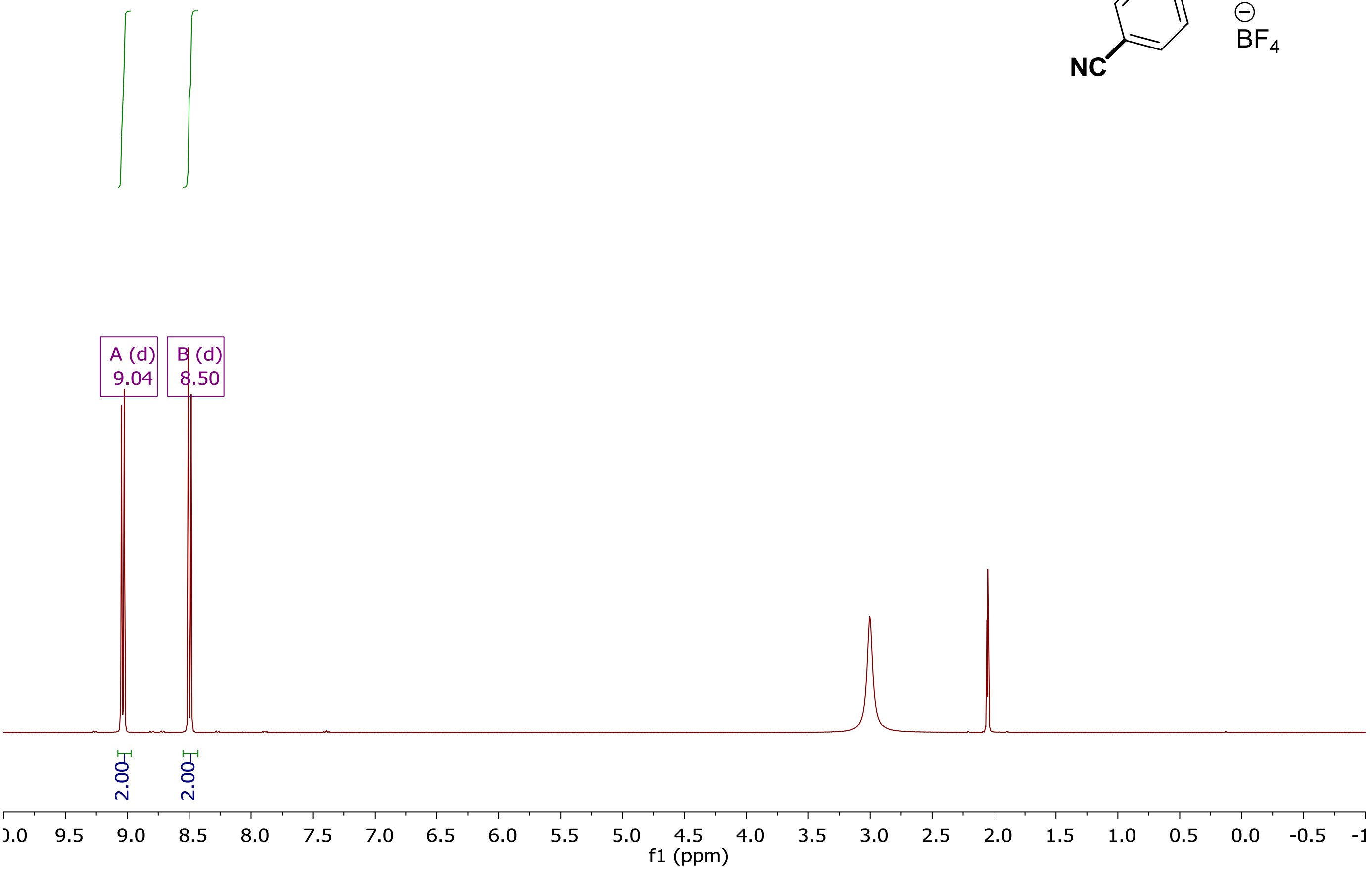
2b:

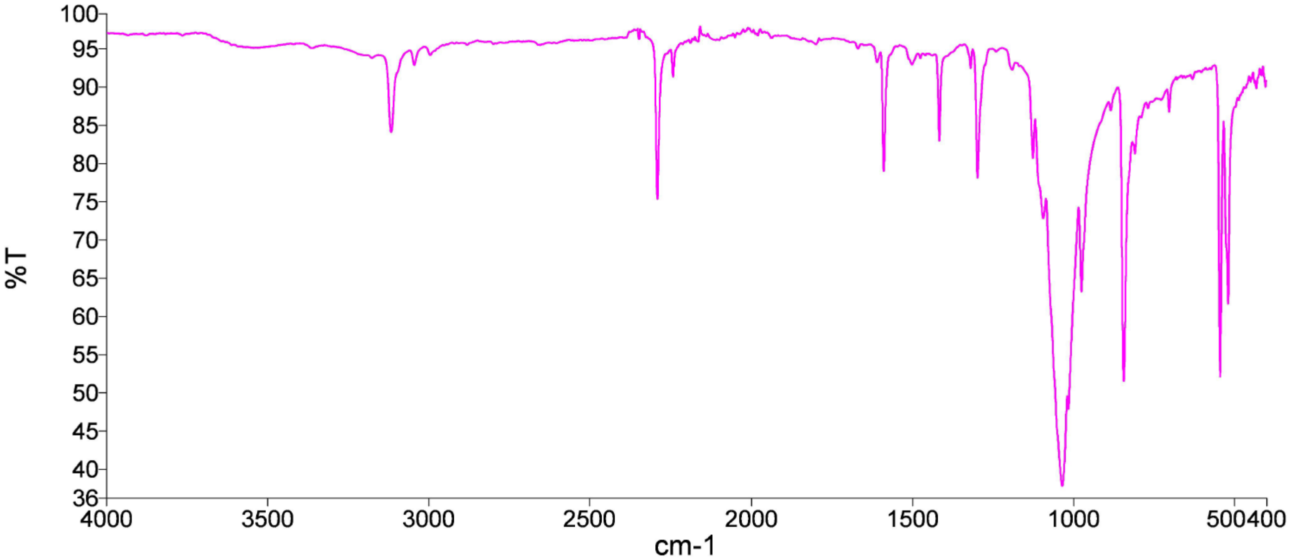

N
N⊕
⊖
BF4
O
O
B (dd)
7.92
A (d)
8.08
C (d)
7.73
D (s)
4.30
E (s)
3.92
1.00
1.00
1.03
3.02
3.05
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


100
95
90
85
80
75
70
65
60
55
50
45
40
35
31
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

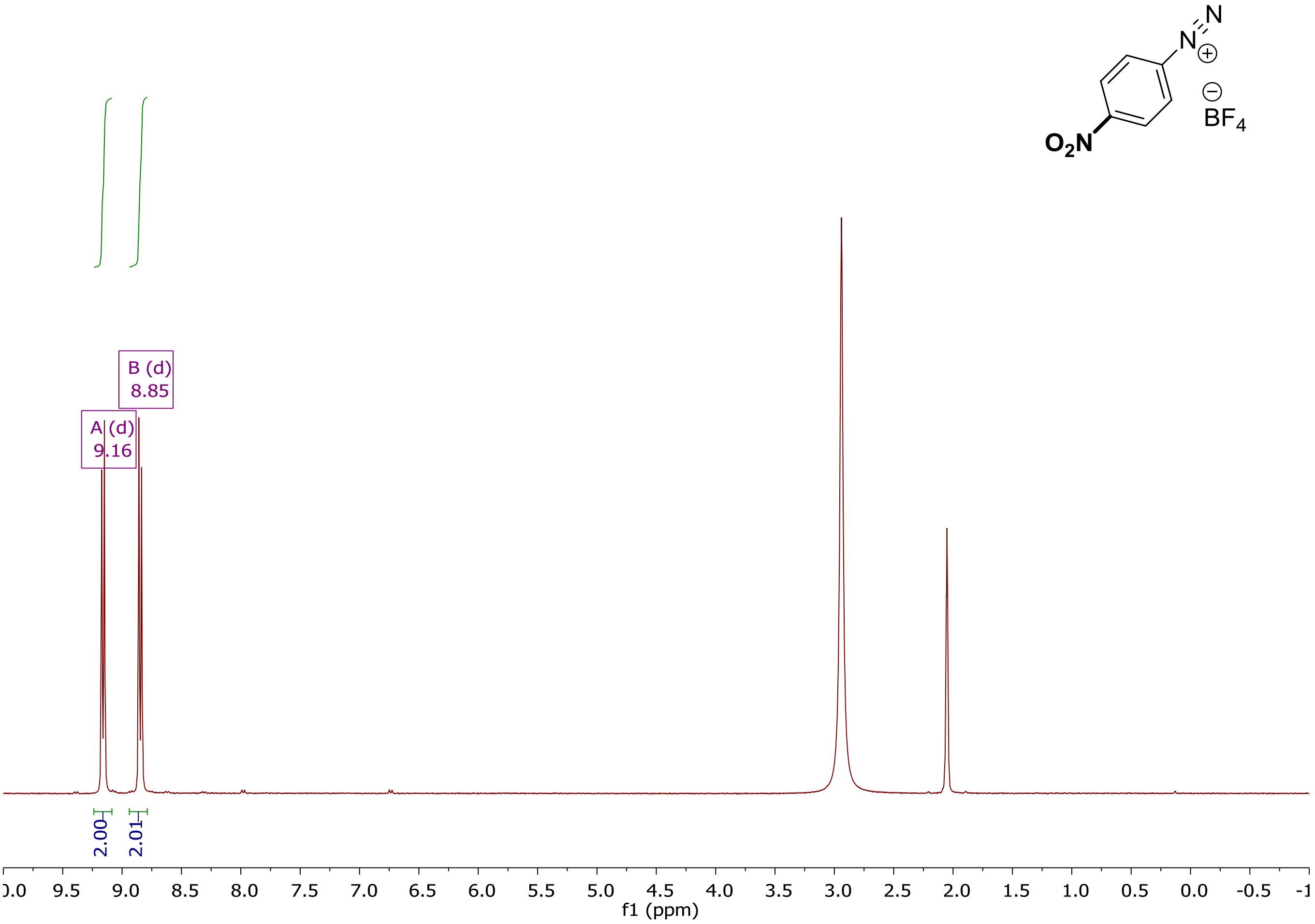
2d:

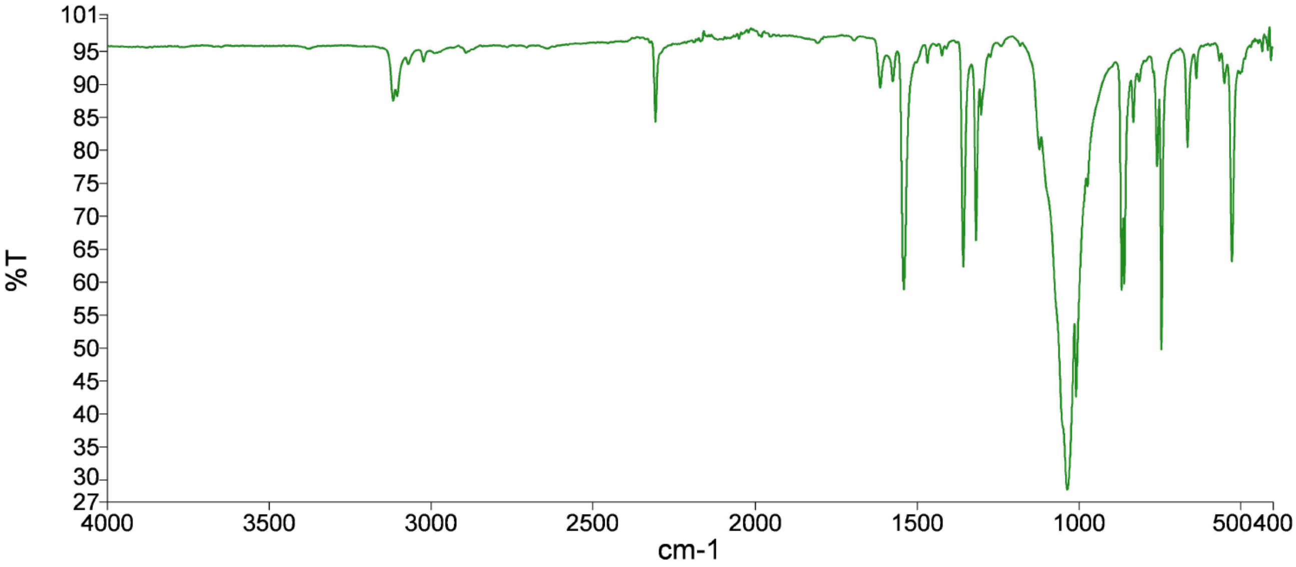

N
N
⊕
⊖
BF4
NC


A (d)
9.04
B (d)
8.50
2.00
2.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

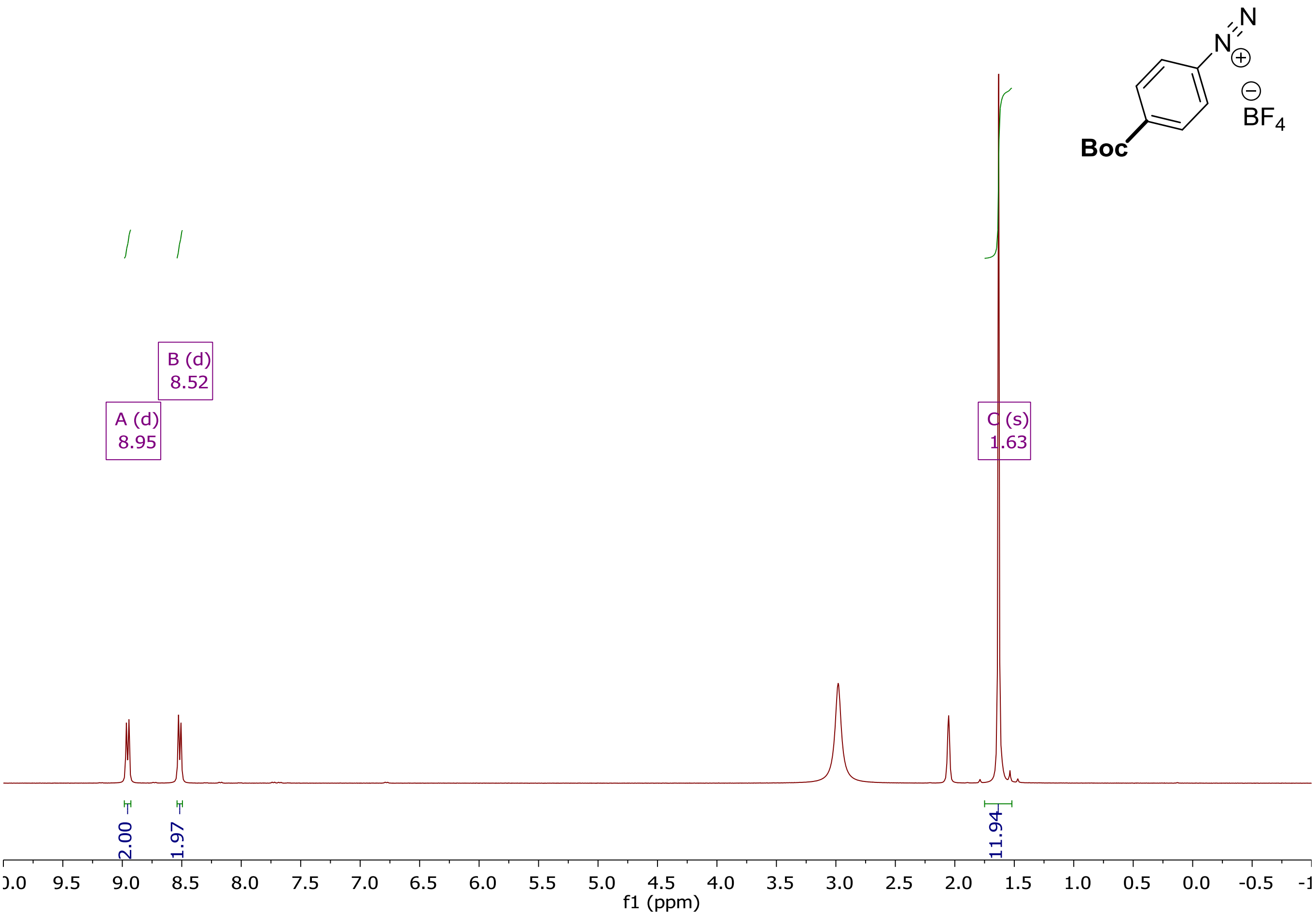

100
95
90
85
80
75
70
65
60
55
50
45
40
36
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

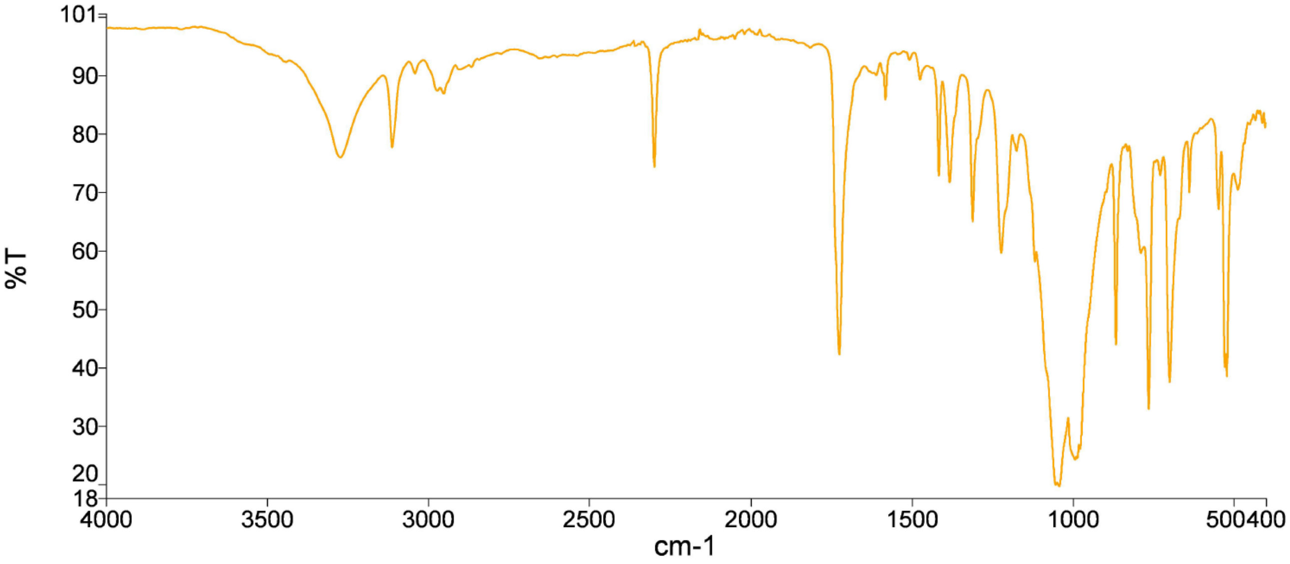
2e:


N
N
⊕
⊖
BF4
O2N
B (d)
8.85
A (d)
9.16
2.00
2.01
).0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

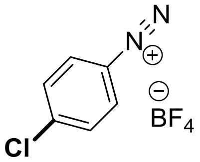

101
95
90
85
80
75
70
65
60
55
50
45
40
35
30
27
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

2f:

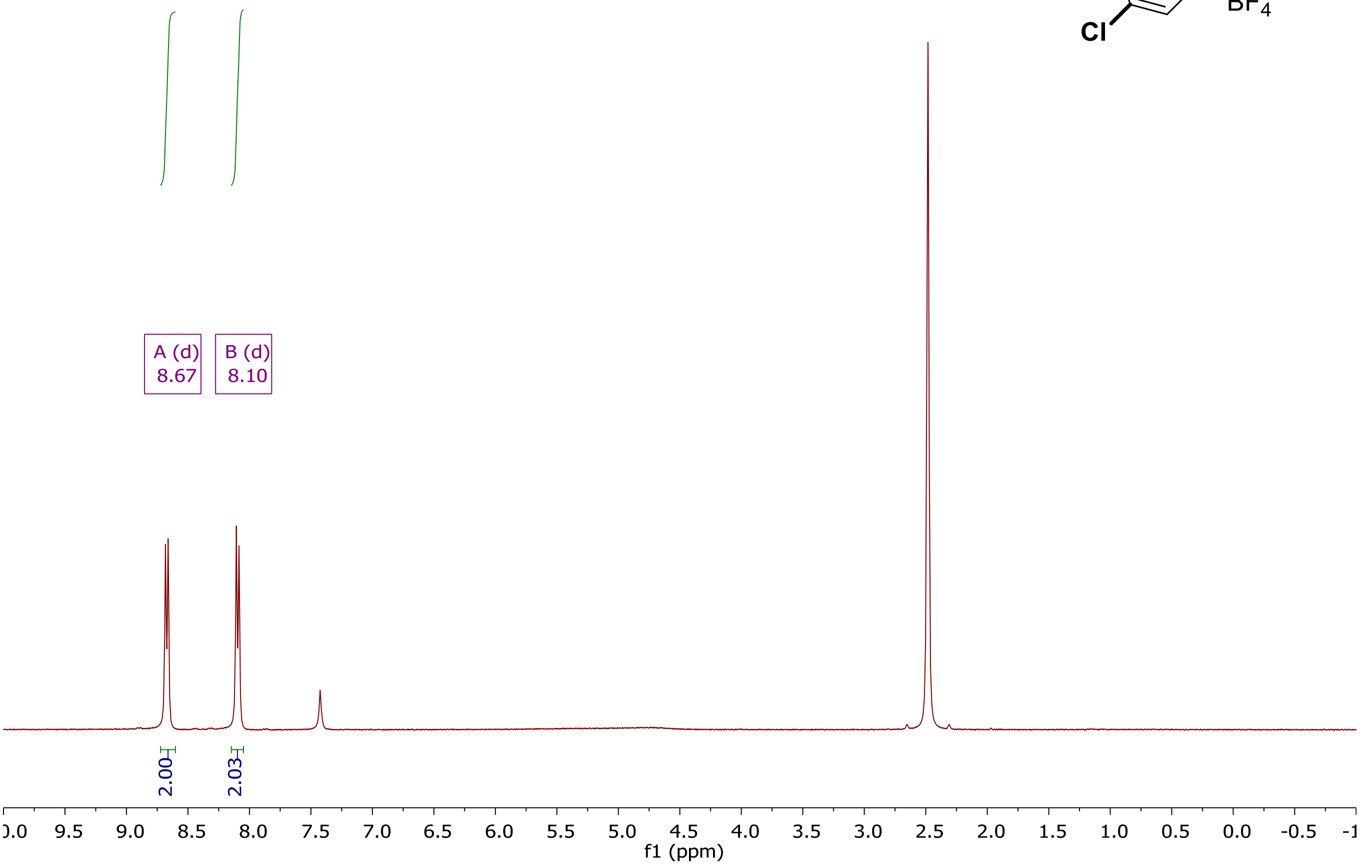

N
N
⊕
⊖
BF4
Boc
A (d)
8.95
B (d)
8.52
C (s)
1.63
2.00
1.97
11.94
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


101
90
80
70
60
50
40
30
20
18
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

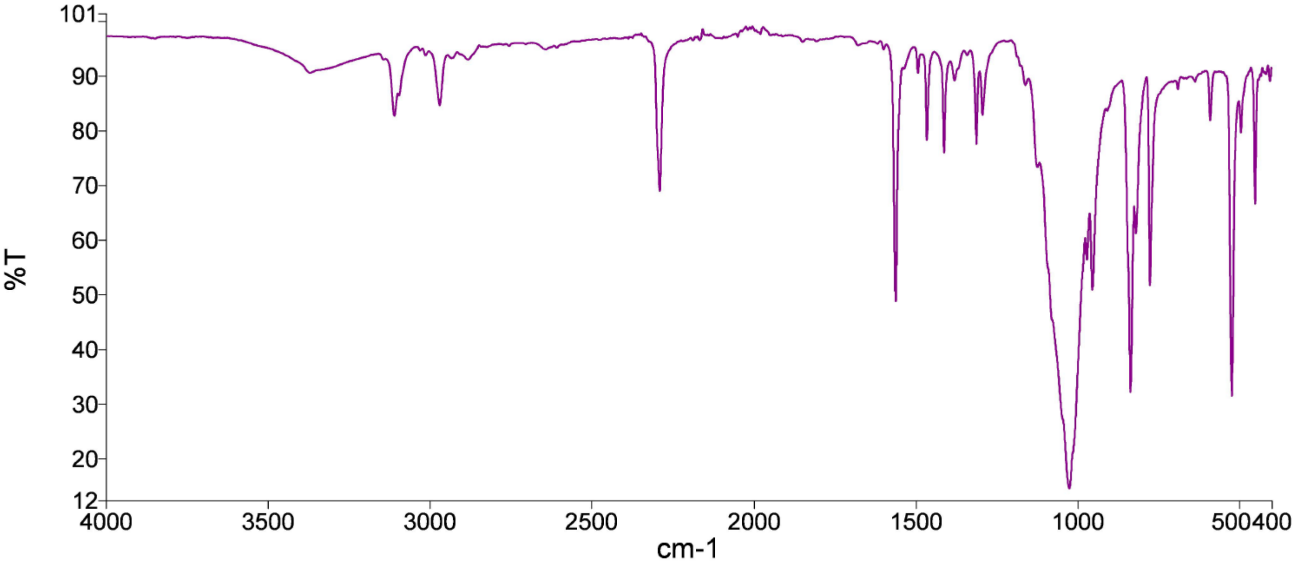
2g:



N
N
⊕
⊖
BF4
Cl

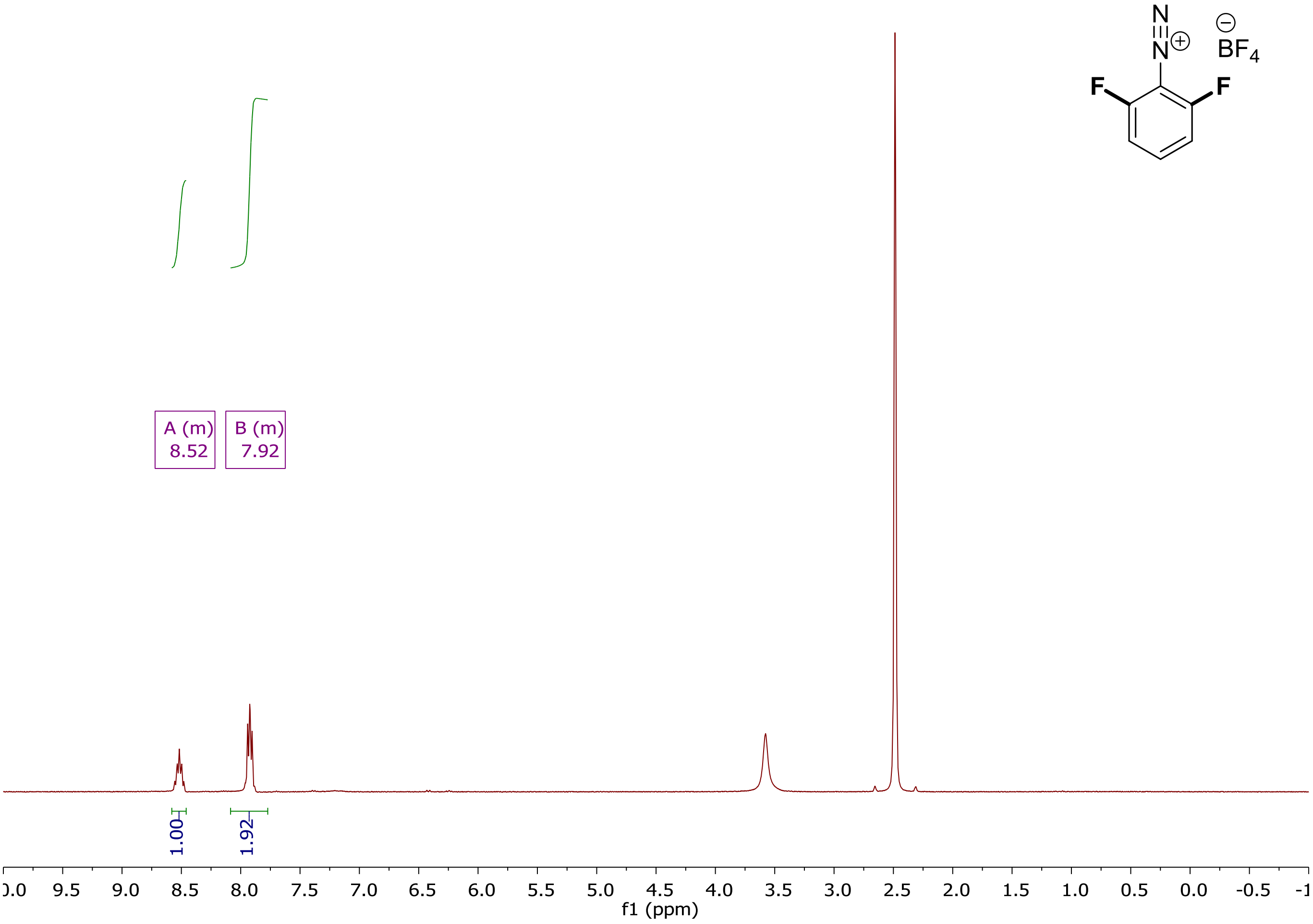


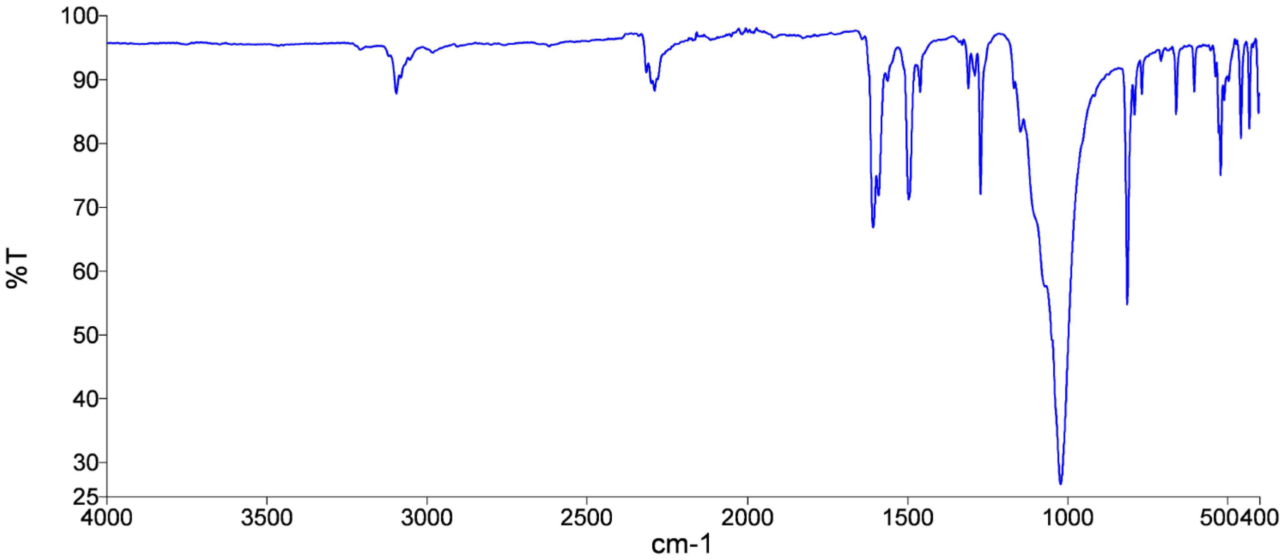
A (d)
8.67
B (d)
8.10
2.00
2.03
).0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



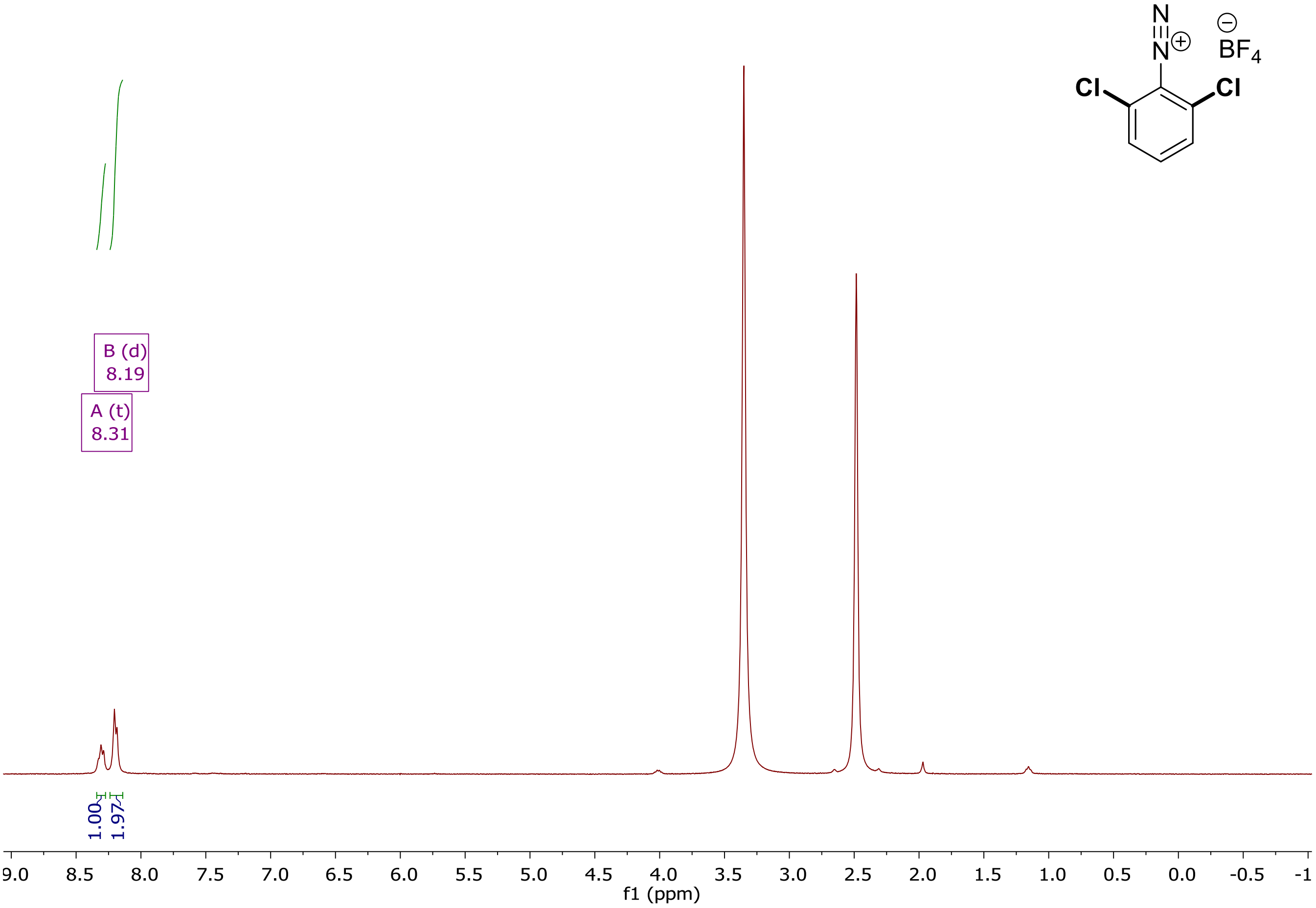
101
90
80
70
60
50
40
30
20
12
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

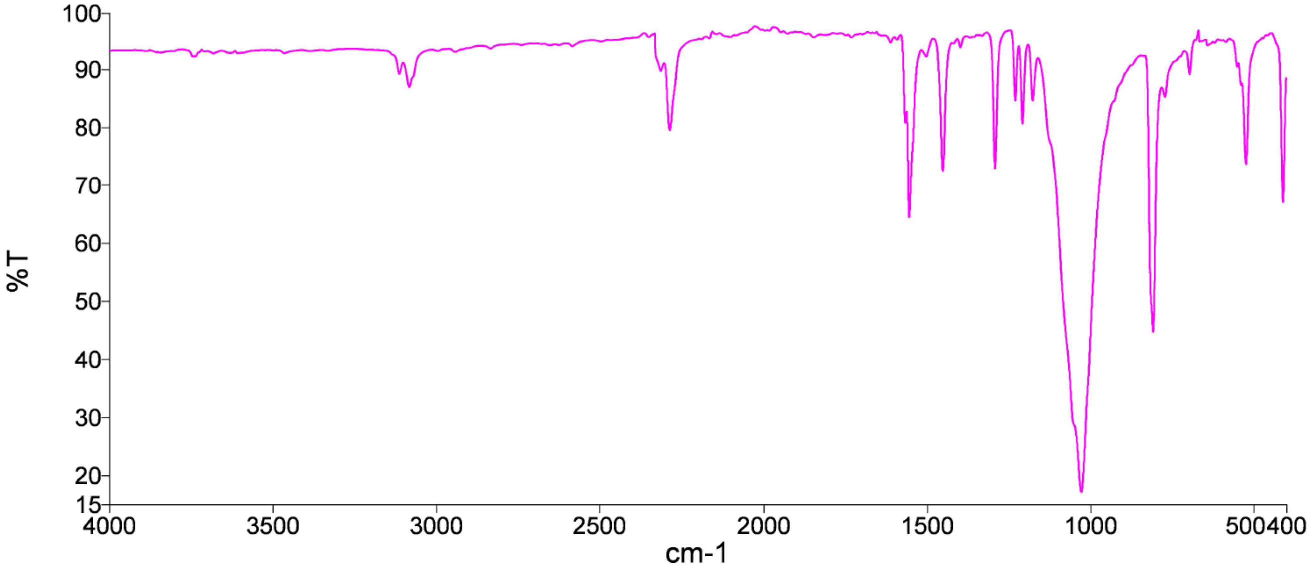
2h:


N
N
BF4
F
F
A (m)
8.52
B (m)
7.92
1.00
1.92
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

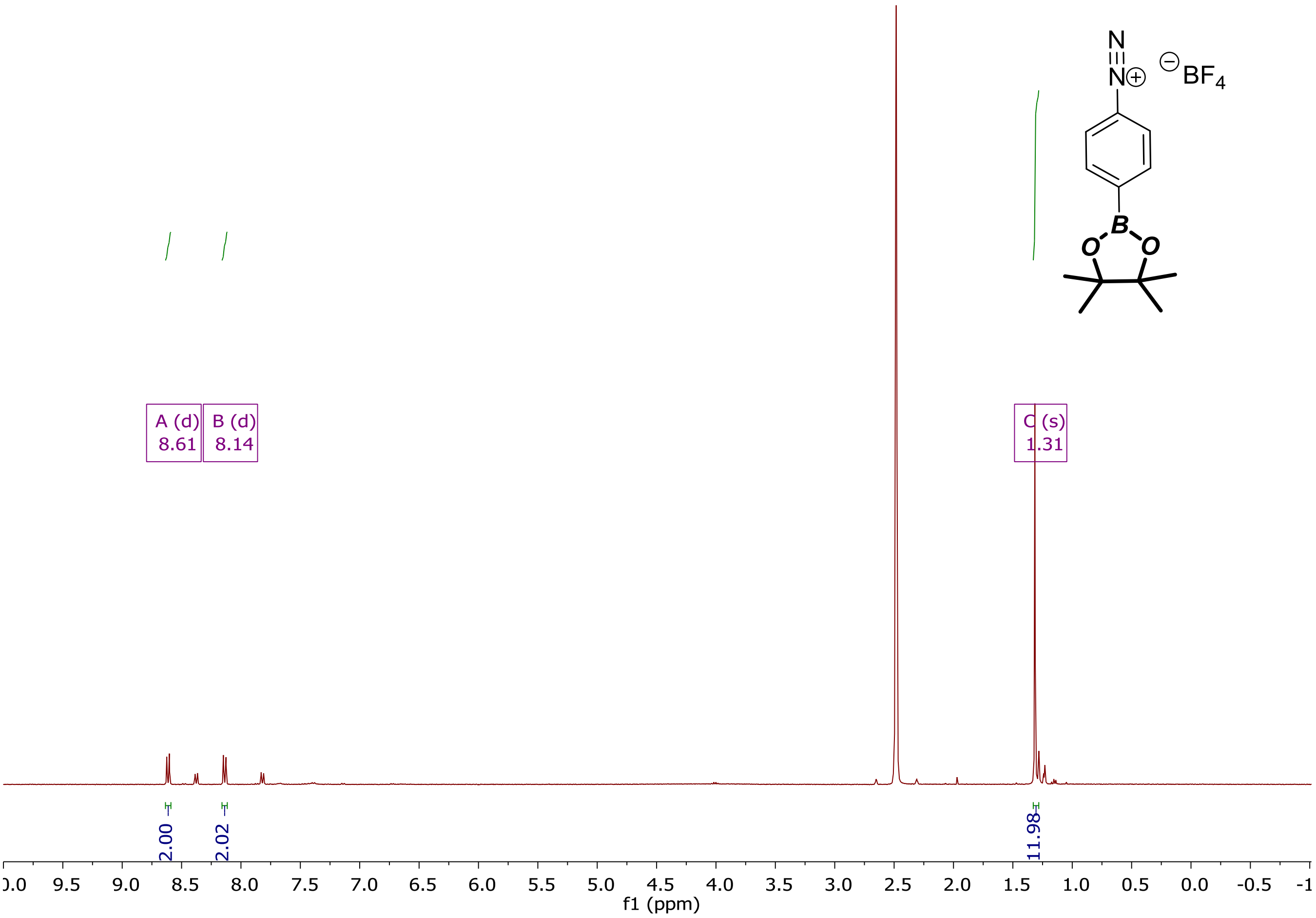

100
90
80
70
60
50
40
30
25
%T
4000
3500
3000
2500
2000
1500
1000
500
400
cm-1

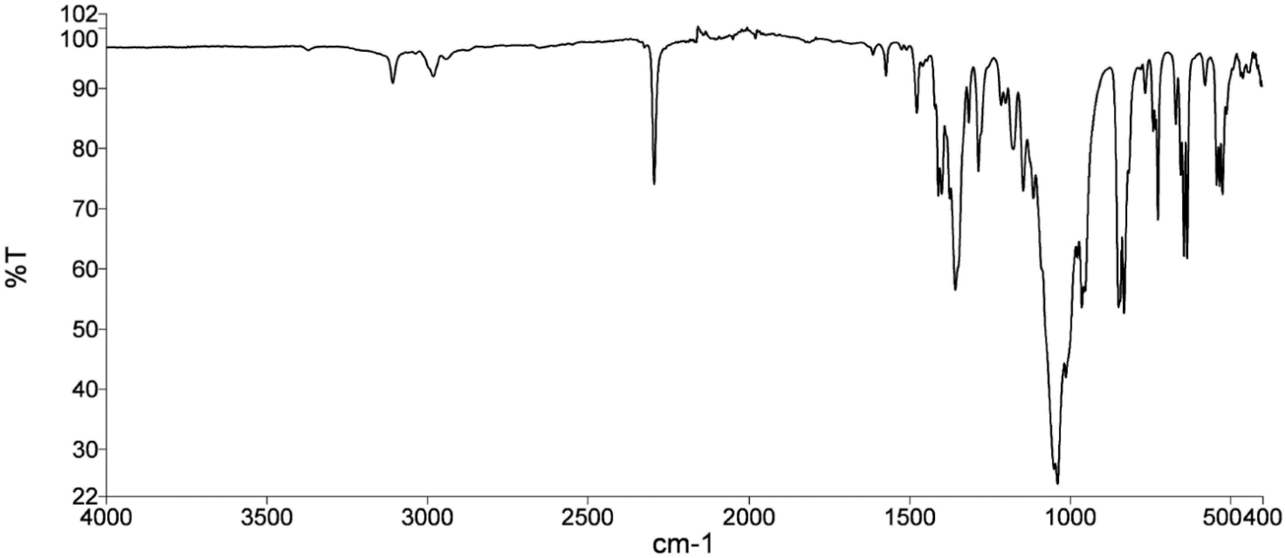
2i:


N
N⊕
⊖
BF4
Cl
Cl
B (d)
8.19
A (t)
8.31
1.00
1.97
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


100
90
80
70
60
50
40
30
20
15
%T
4000
3500
3000
2500
2000
1500
1000
500400
cm-1

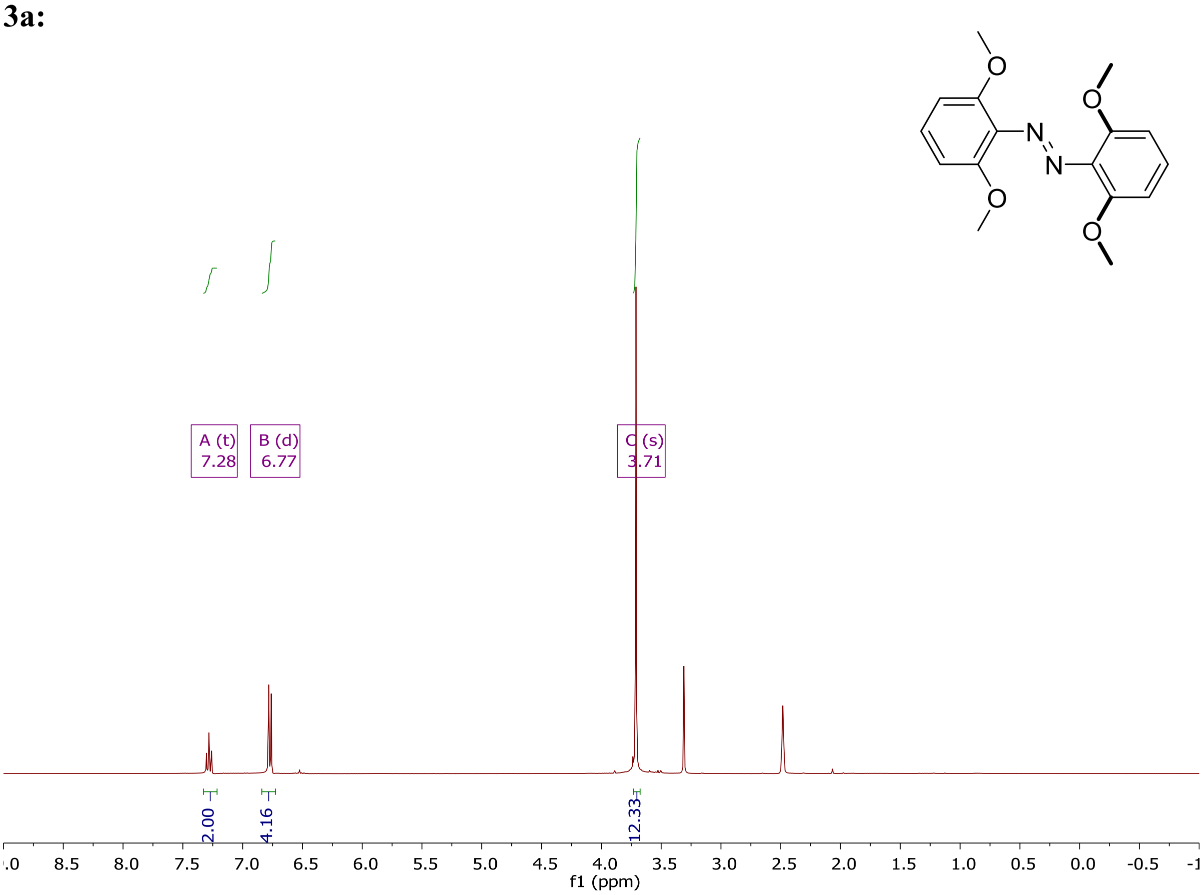
2j: Upon preparation of the NMR sample, some hydrolysis of the pinacol boronic ester was observed, which becomes apparent in the ^{1}H-NMR spectrum at 8.4 and 7.8 ppm.

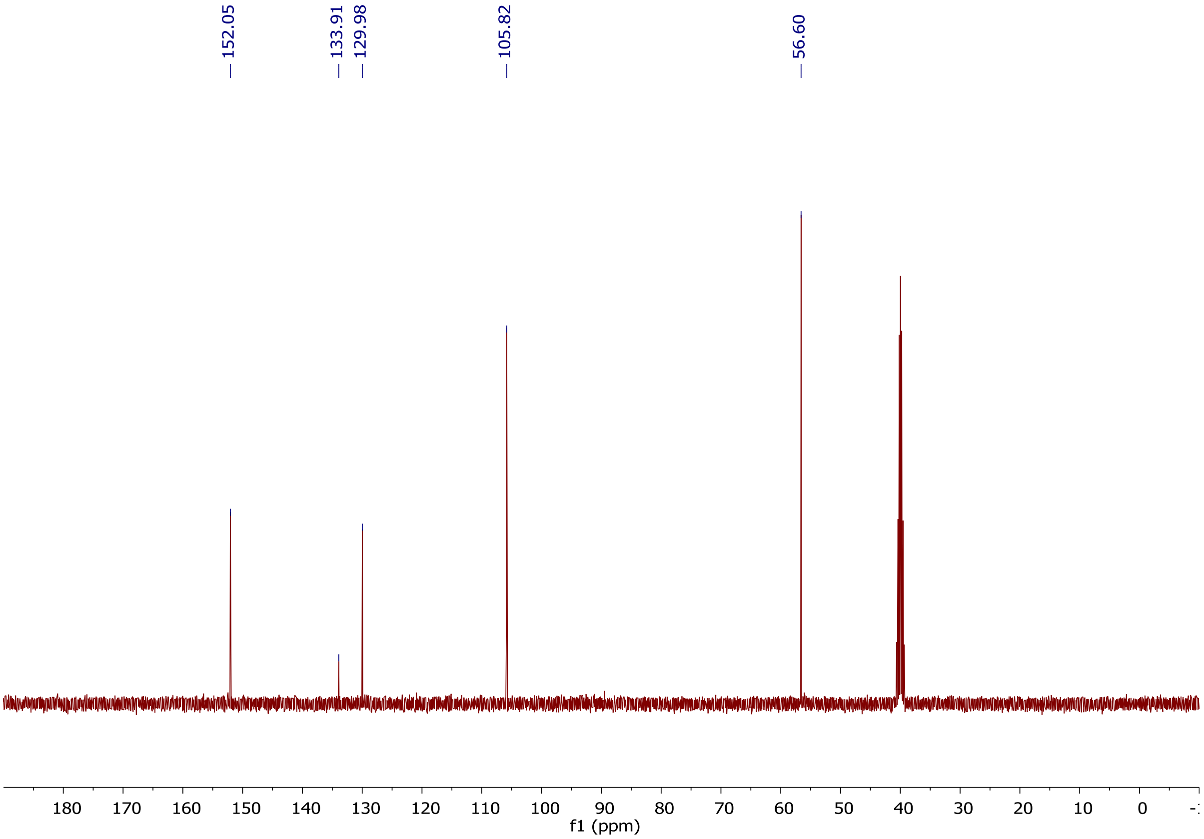


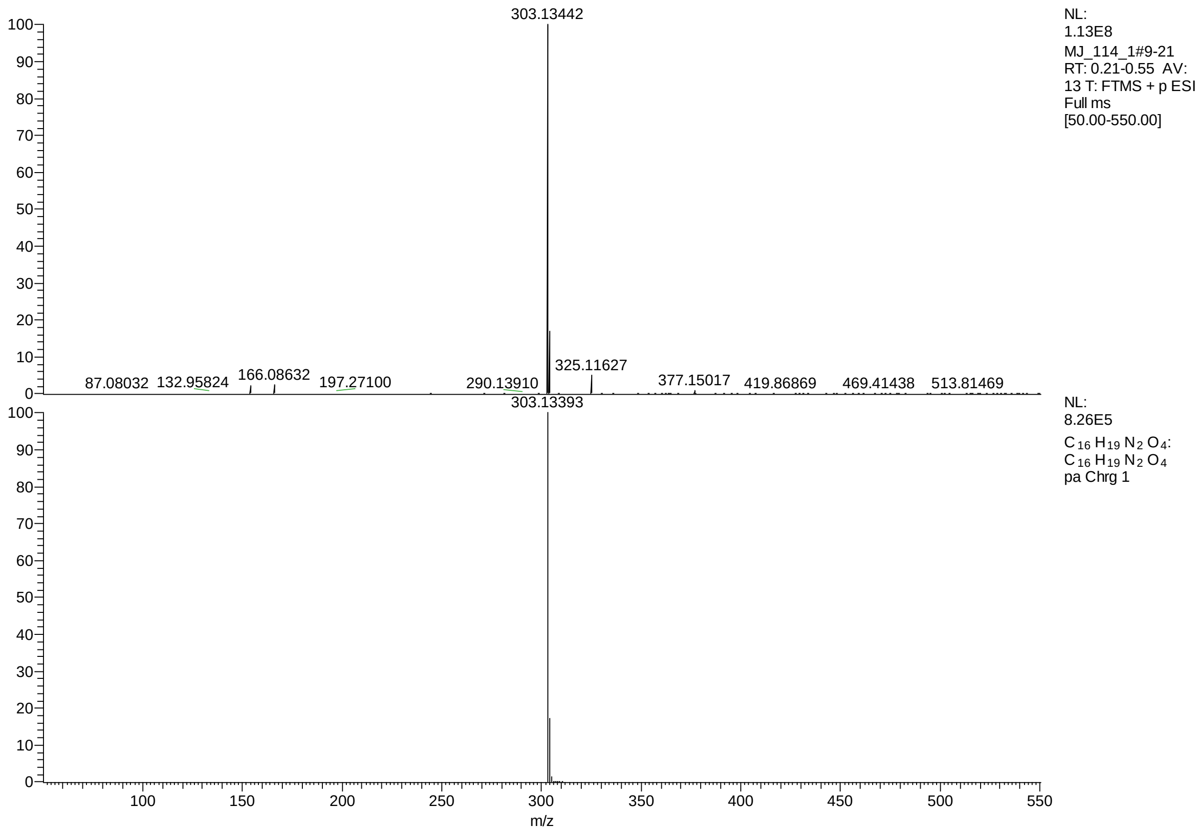


3a:

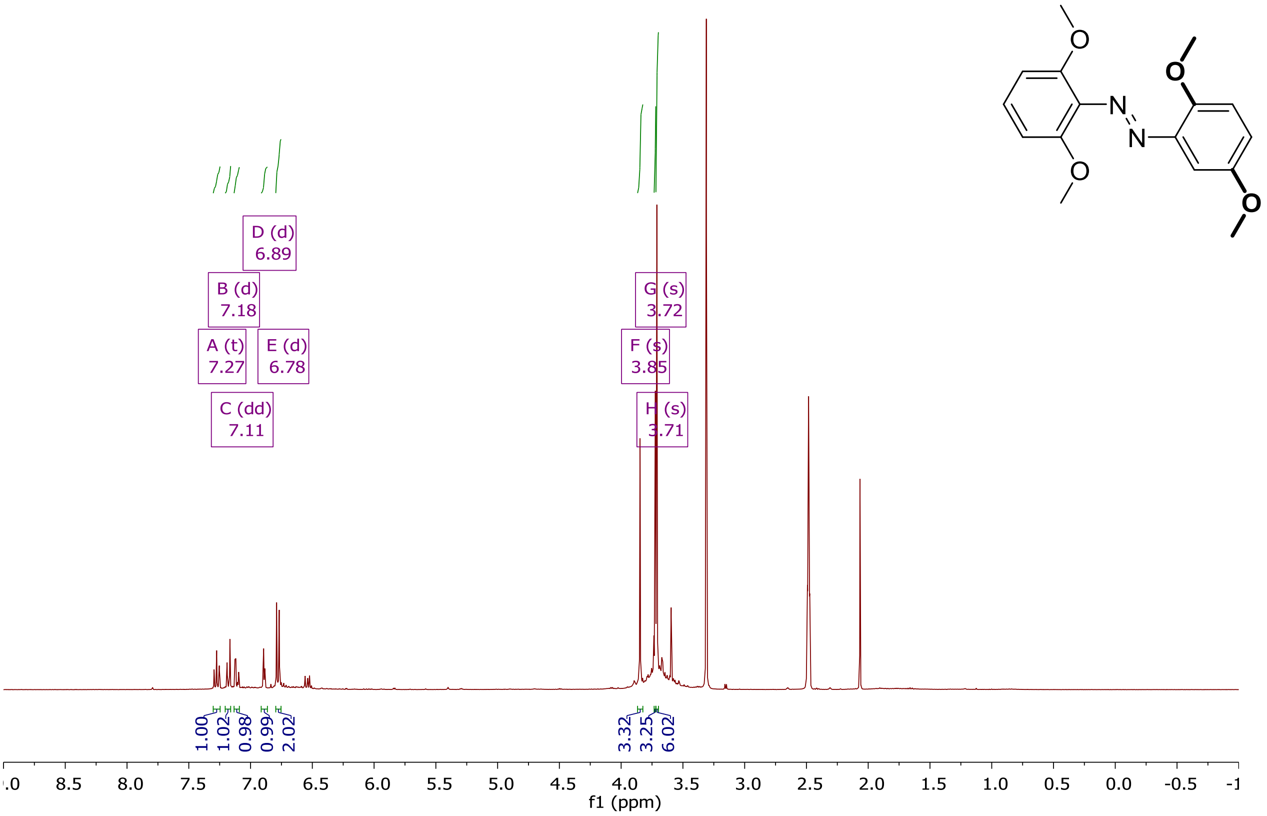
O
N
N
O
O
O

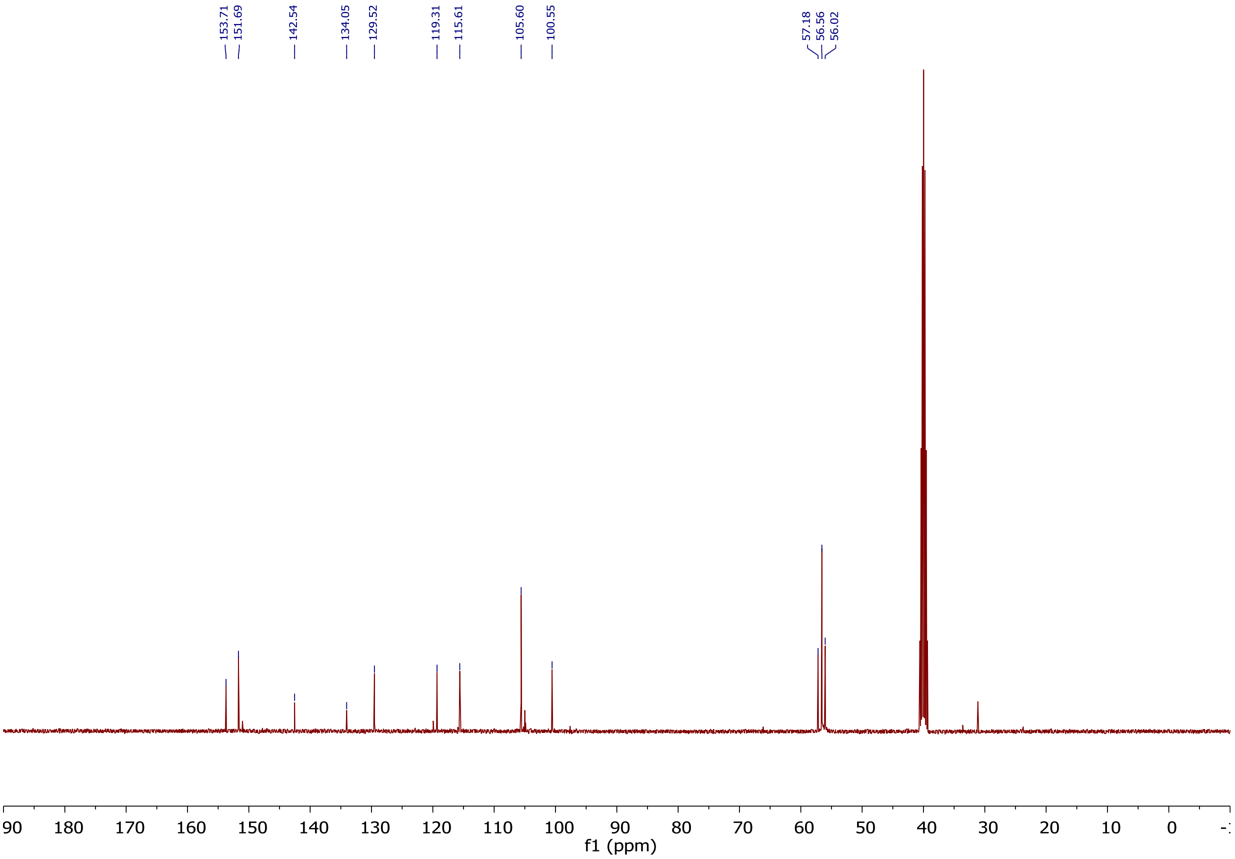

A (t)
7.28
B (d)
6.77
C (s)
3.71
2.00
4.16
12.33
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

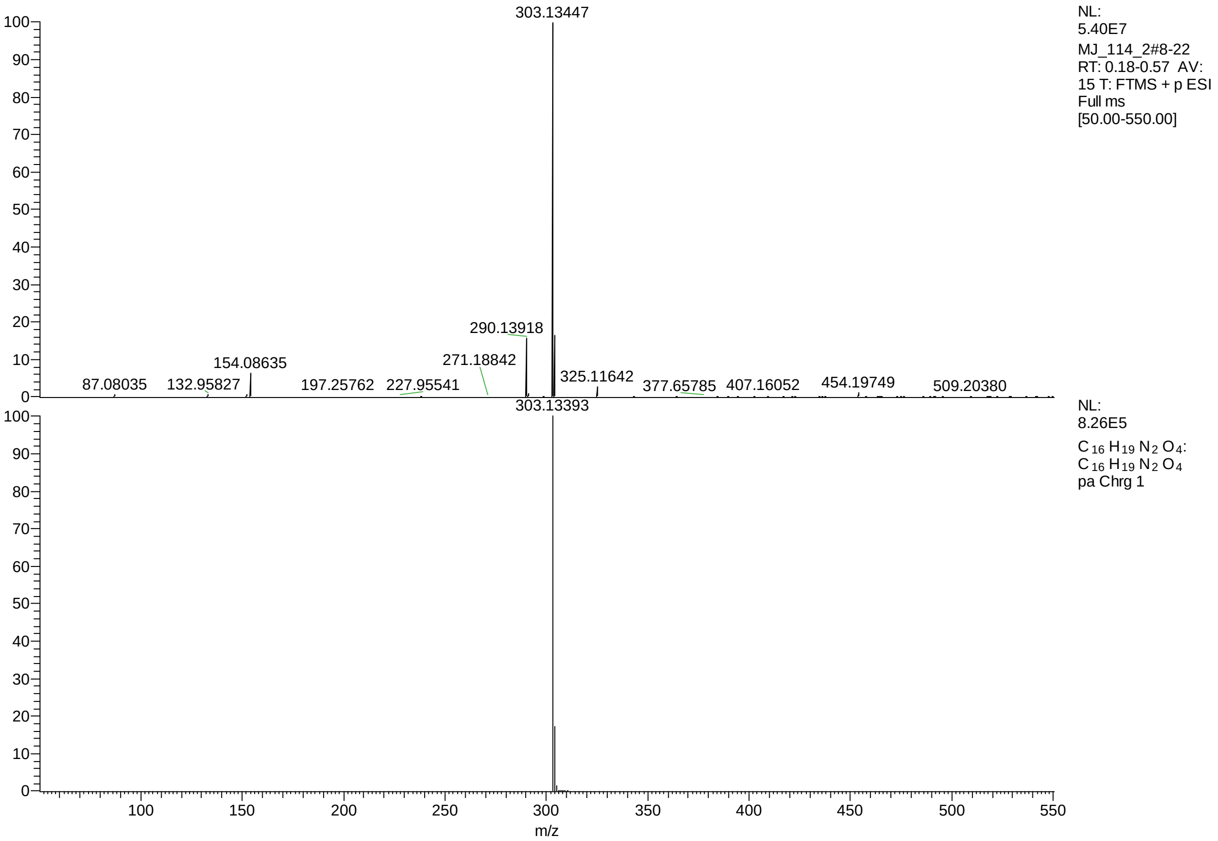

152.05
133.91
129.98
105.82
56.60
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-
f1 (ppm)



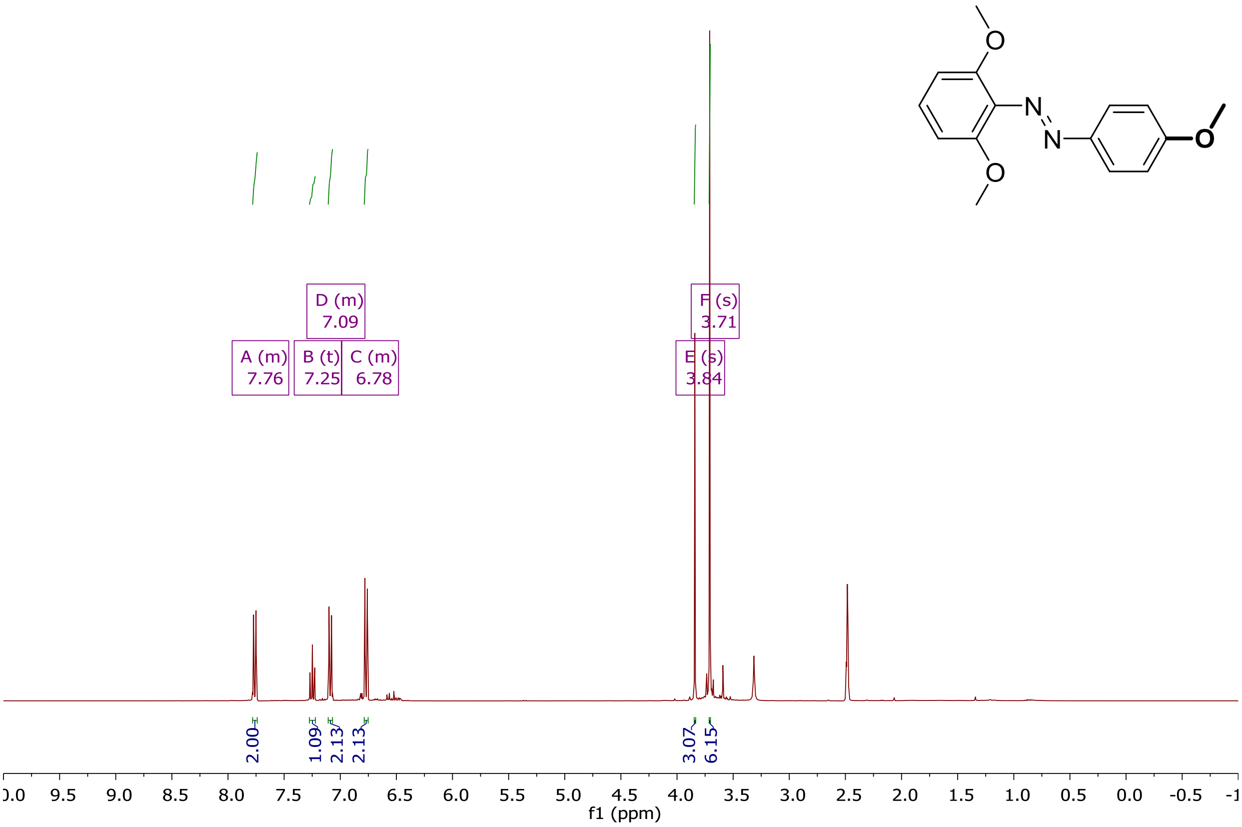
3b: After thermal adaption, no full conversion to the *trans* isomer was observed which became apparent in the ^{1}H-NMR and ^{13}C-NMR spectrum showing small quantities of the *cis* isomer.

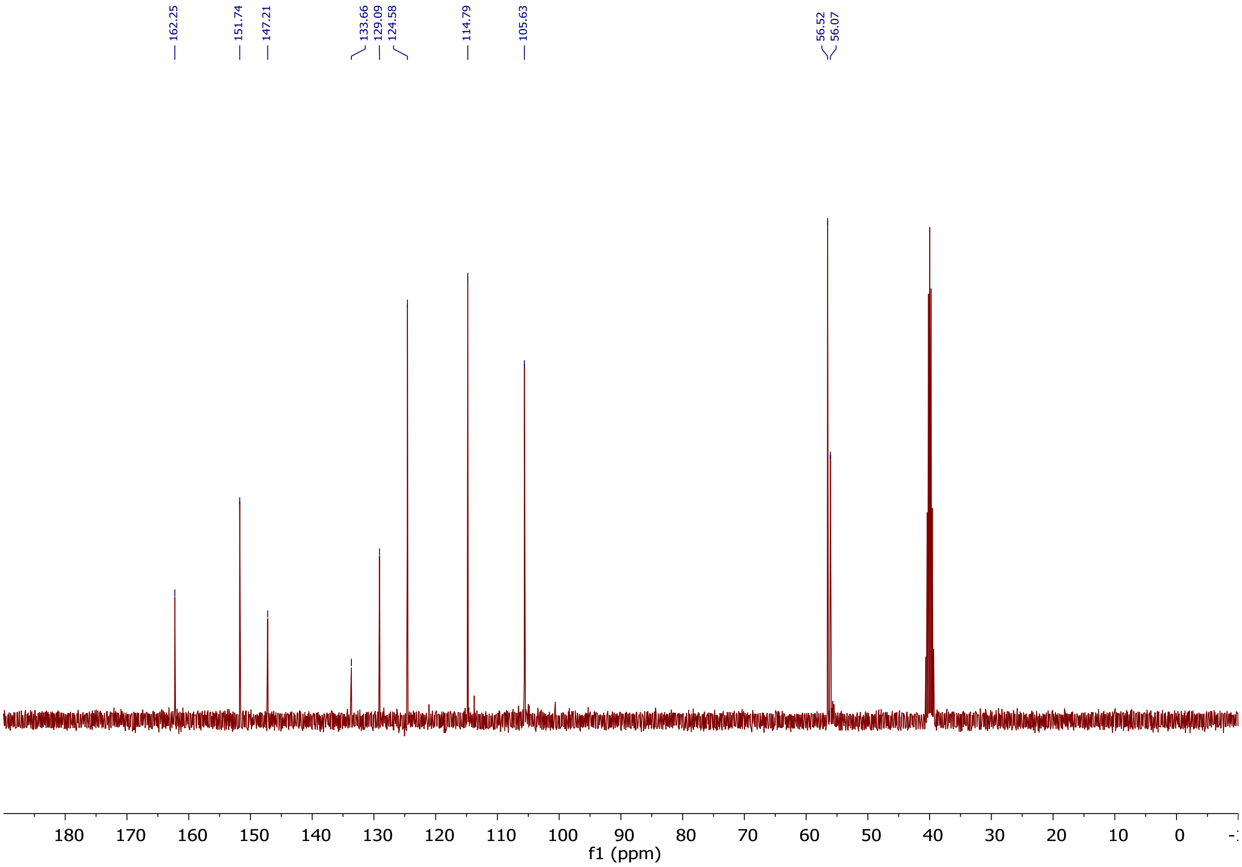


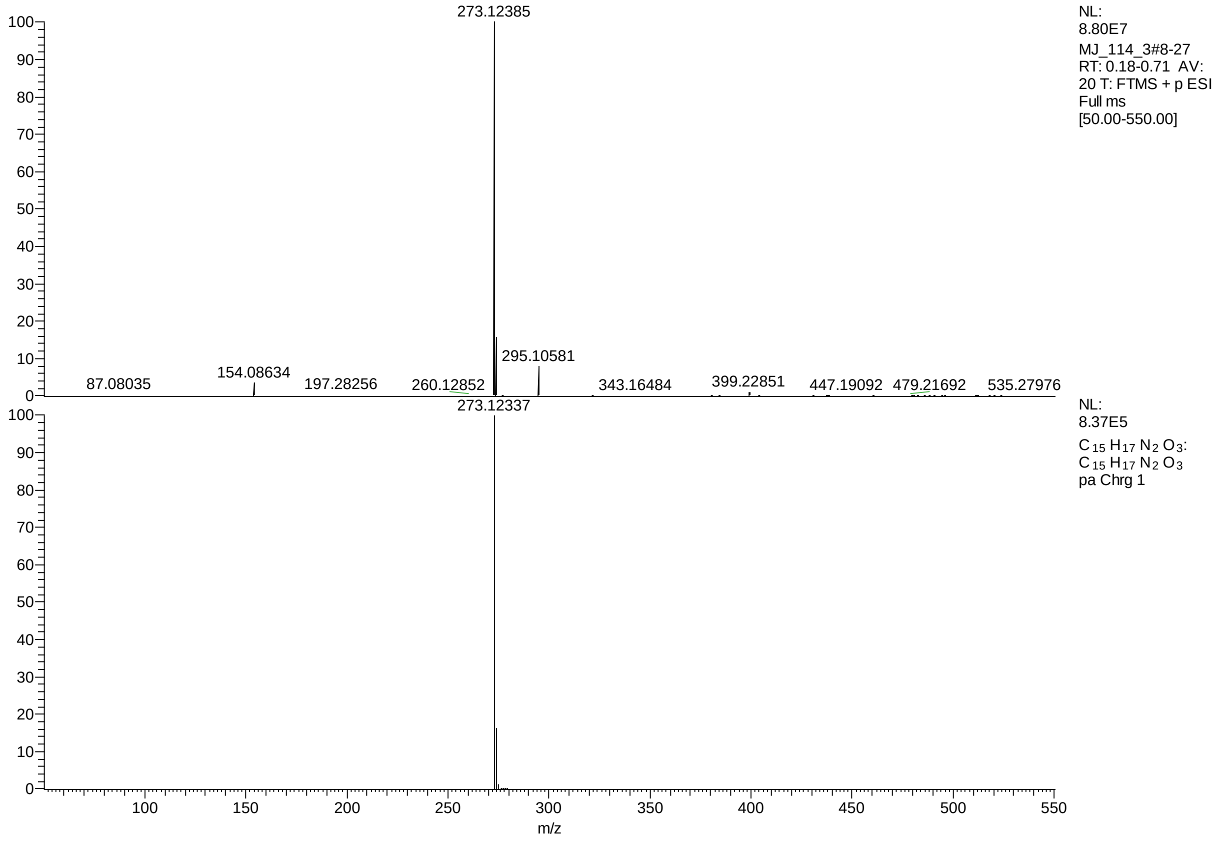

153.71
151.69
142.54
134.05
129.52
119.31
115.61
105.60
100.55
57.18
56.56
56.02
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


303.13447
NL:
5.40E7
MJ_114_2#8-22
RT: 0.18-0.57 AV:
15 T: FTMS + p ESI
Full ms
[50.00-550.00]
290.13918
271.18842
154.08635
87.08035
132.95827
197.25762
227.95541
325.11642
377.65785
407.16052
454.19749
509.20380
303.13393
NL:
8.26E5
C 16 H19 N2 O4:
C 16 H19 N2 O4
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

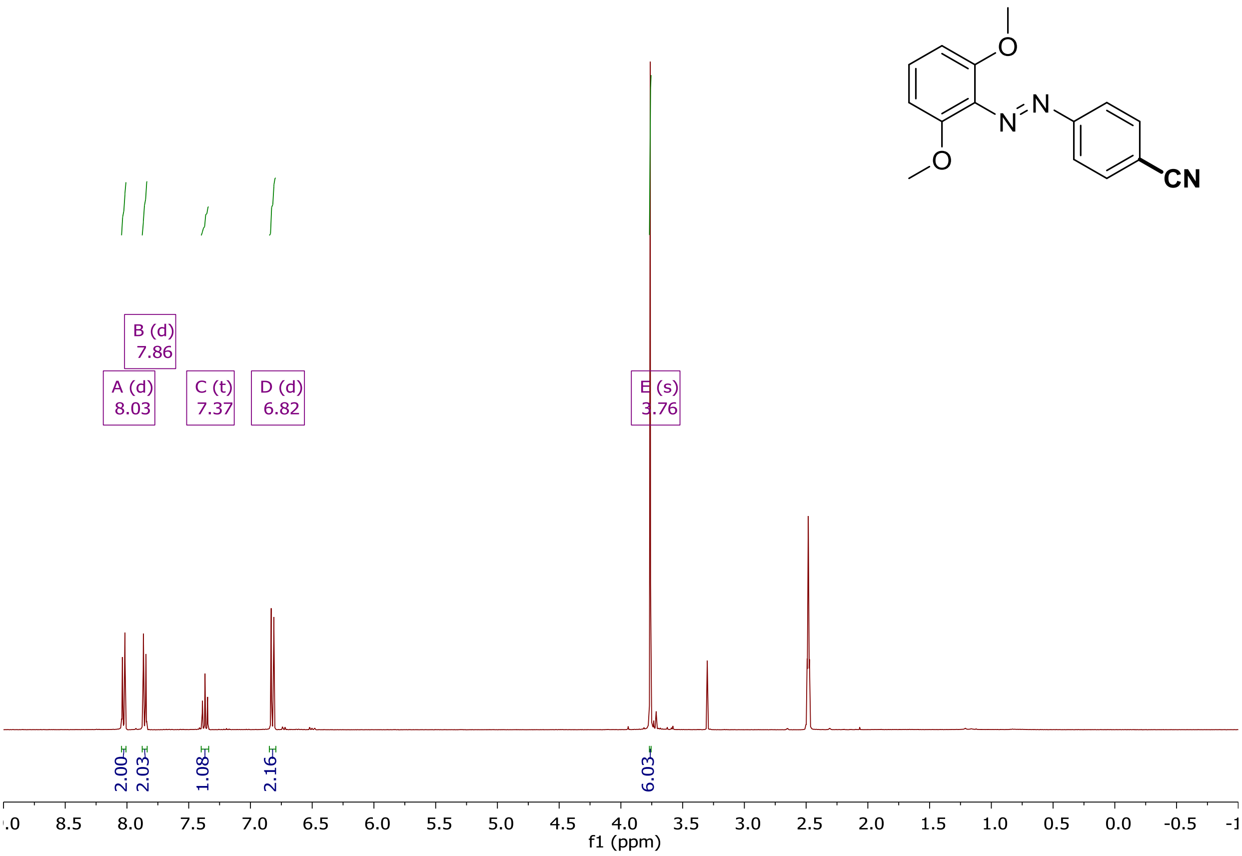
3c: After thermal adaption, no full conversion to the *trans* isomer was observed which became apparent in the ^{1}H-NMR and ^{13}C-NMR spectrum showing small quantities of the *cis* isomer.

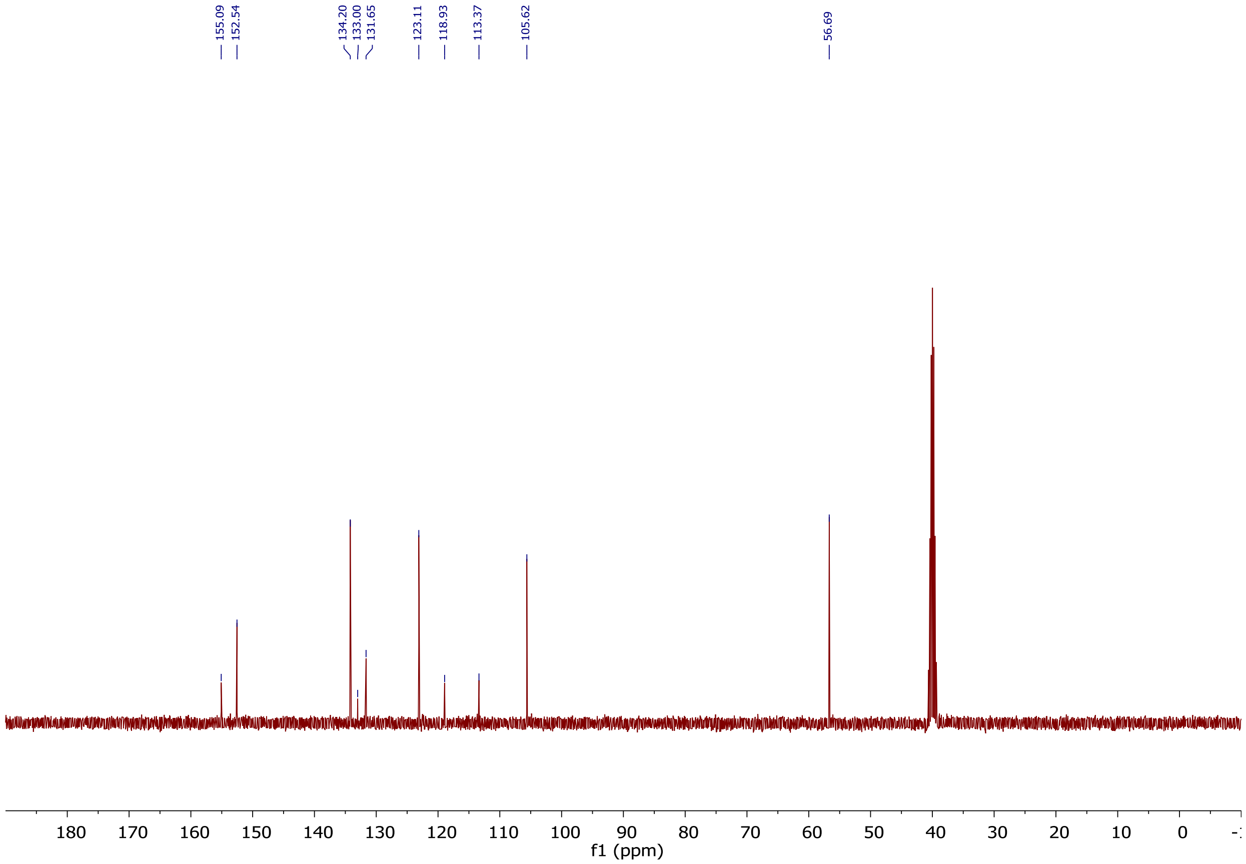


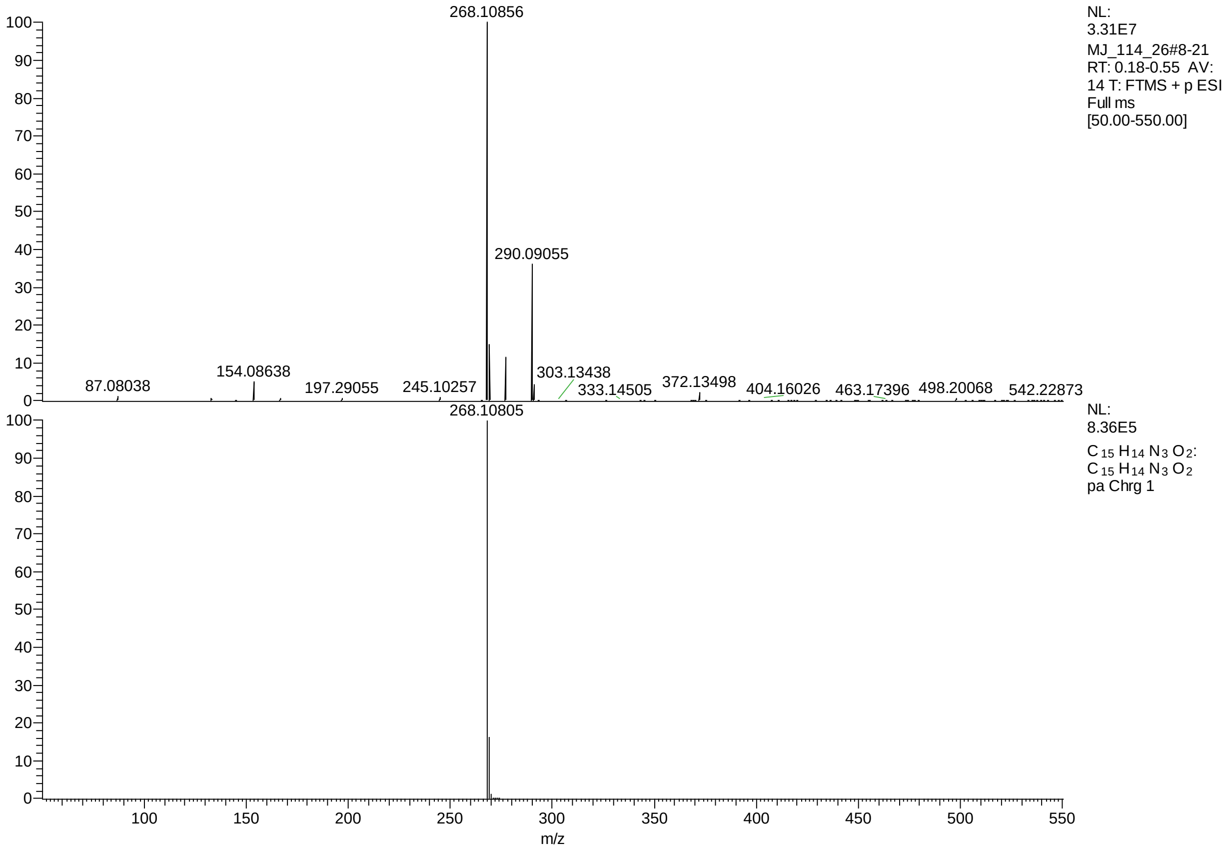



273.12385
NL:
8.80E7
MJ_114_3#8-27
RT: 0.18-0.71 AV:
20 T: FTMS + p ESI
Full ms
[50.00-550.00]
87.08035
154.08634
197.28256
260.12852
295.10581
343.16484
399.22851
447.19092
479.21692
535.27976
273.12337
NL:
8.37E5
C 15 H 17 N 2 O 3:
C 15 H 17 N 2 O 3
pa Chrg 1
0
10
20
30
40
50
60
70
80
90
100
100
150
200
250
300
350
400
450
500
550
m/z

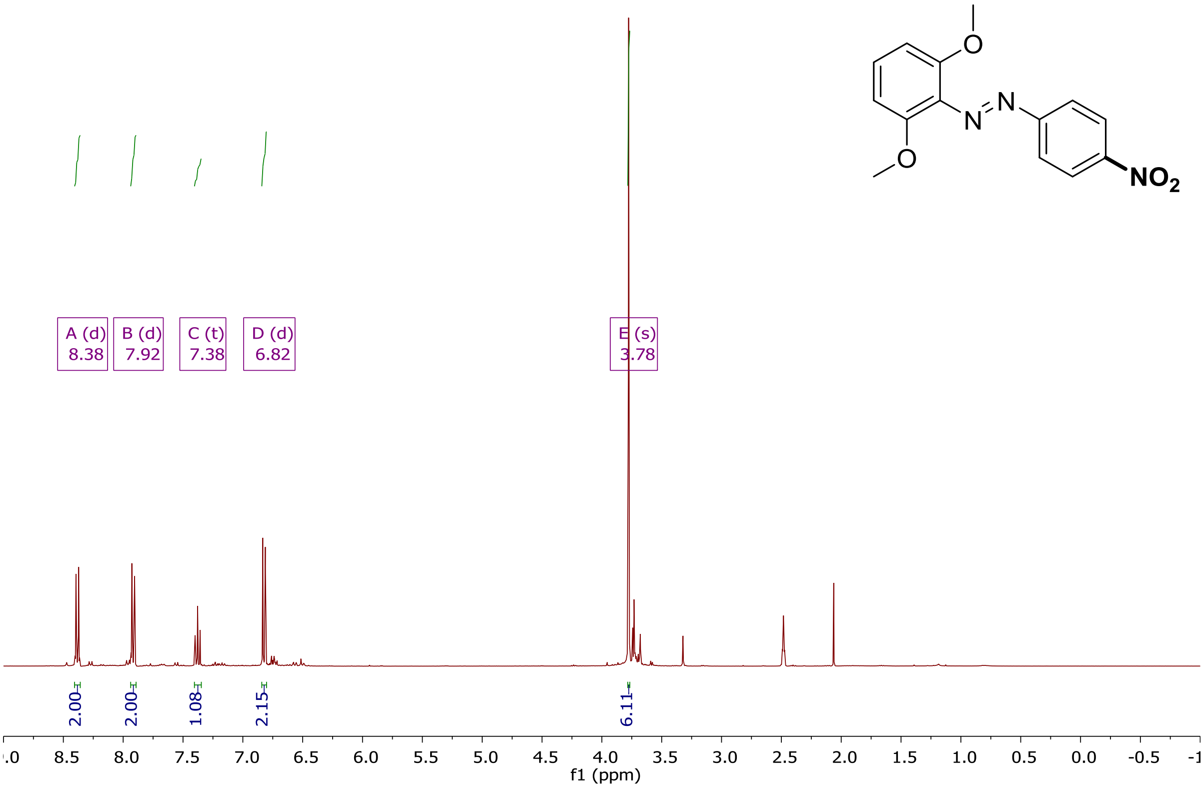
3d:

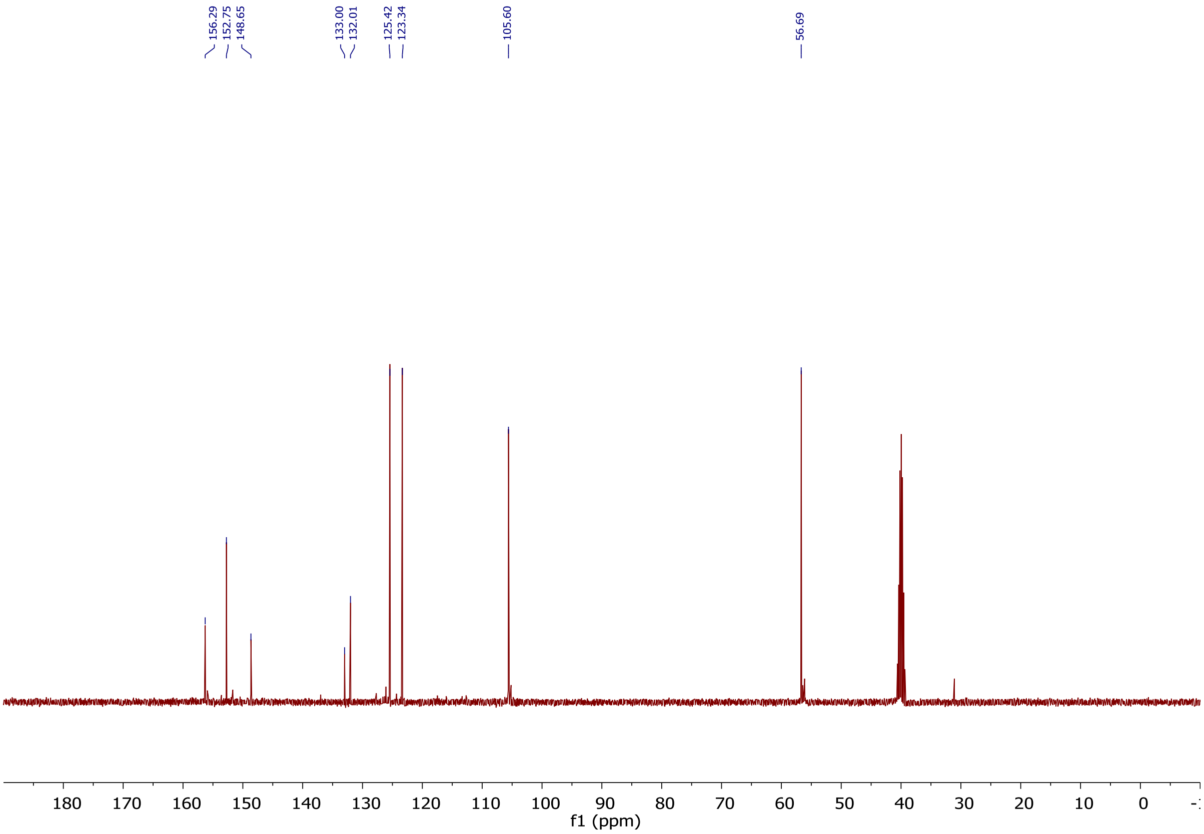

O
N
N
O
CN
B (d)
7.86
A (d)
8.03
C (t)
7.37
D (d)
6.82
E (s)
3.76
2.00
2.03
1.08
2.16
6.03
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

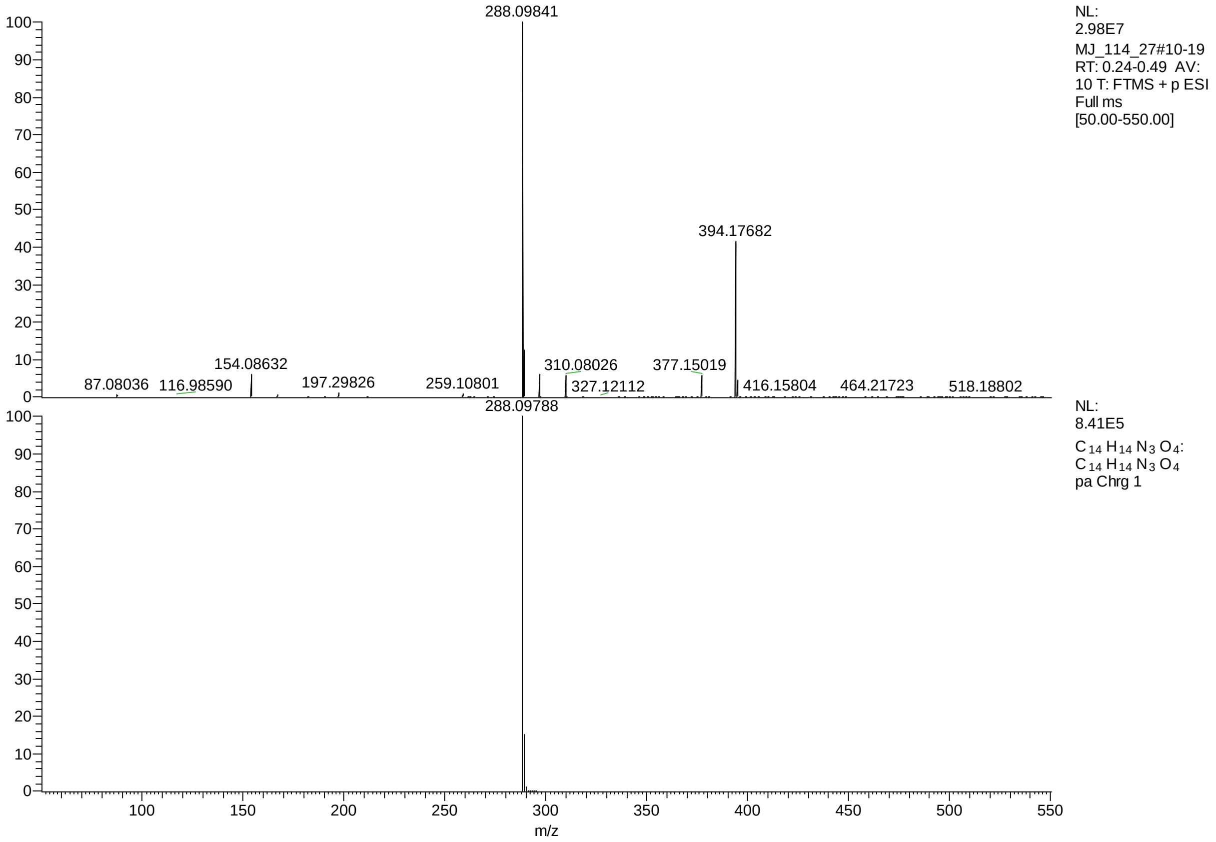

155.09
152.54
134.20
133.00
131.65
123.11
118.93
113.37
105.62
56.69
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


268.10856
290.09055
87.08038
154.08638
197.29055
245.10257
303.13438
333.14505
372.13498
404.16026
463.17396
498.20068
542.22873
NL:
3.31E7
MJ_114_26#8-21
RT: 0.18-0.55 AV:
14 T: FTMS + p ESI
Full ms
[50.00-550.00]
268.10805
NL:
8.36E5
C 15 H 14 N 3 O 2:
C 15 H 14 N 3 O 2
pa Chrg 1
0 10 20 30 40 50 60 70 80 90 100
100 150 200 250 300 350 400 450 500 550
m/z

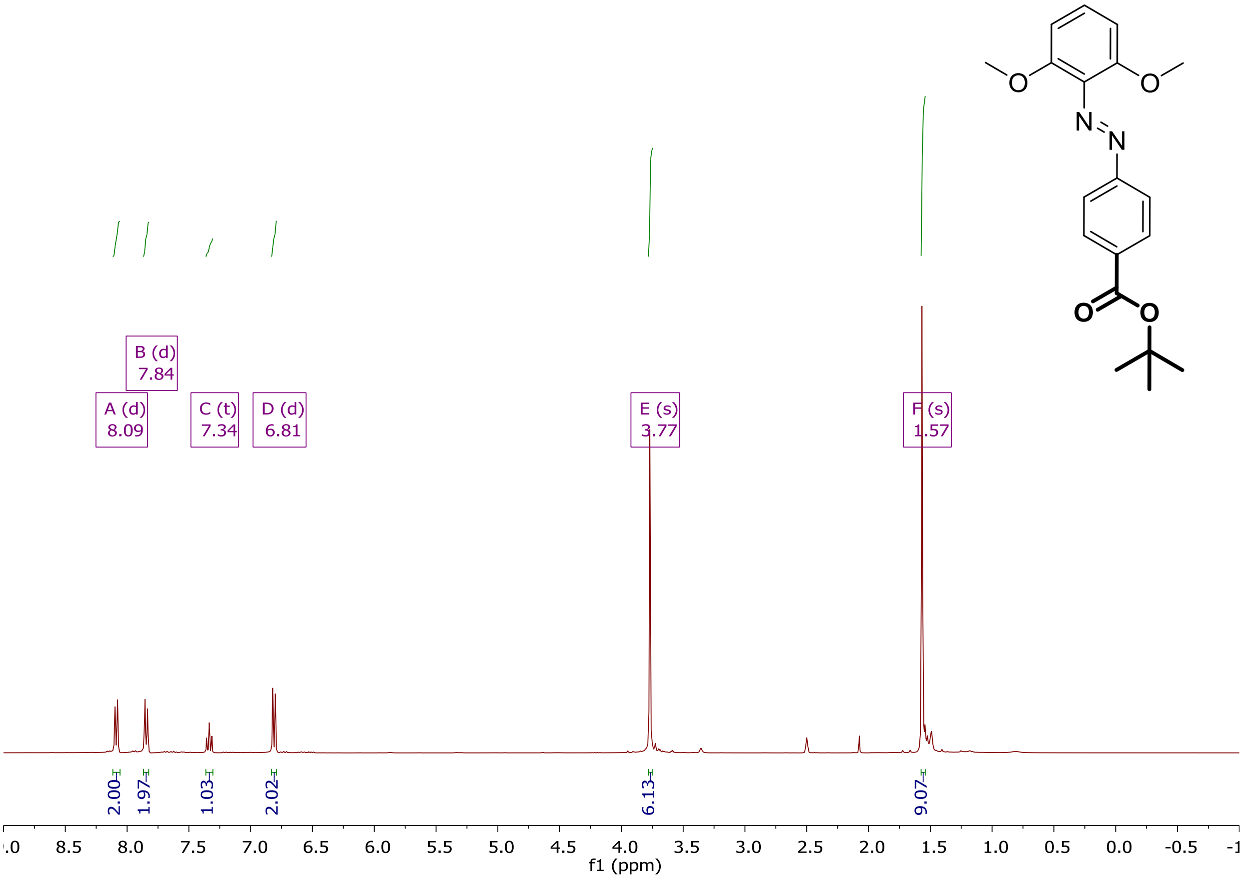
3e: After thermal adaption, no full conversion to the *trans* isomer was observed which became apparent in the ^{1}H-NMR and ^{13}C-NMR spectrum showing small quantities of the *cis* isomer.

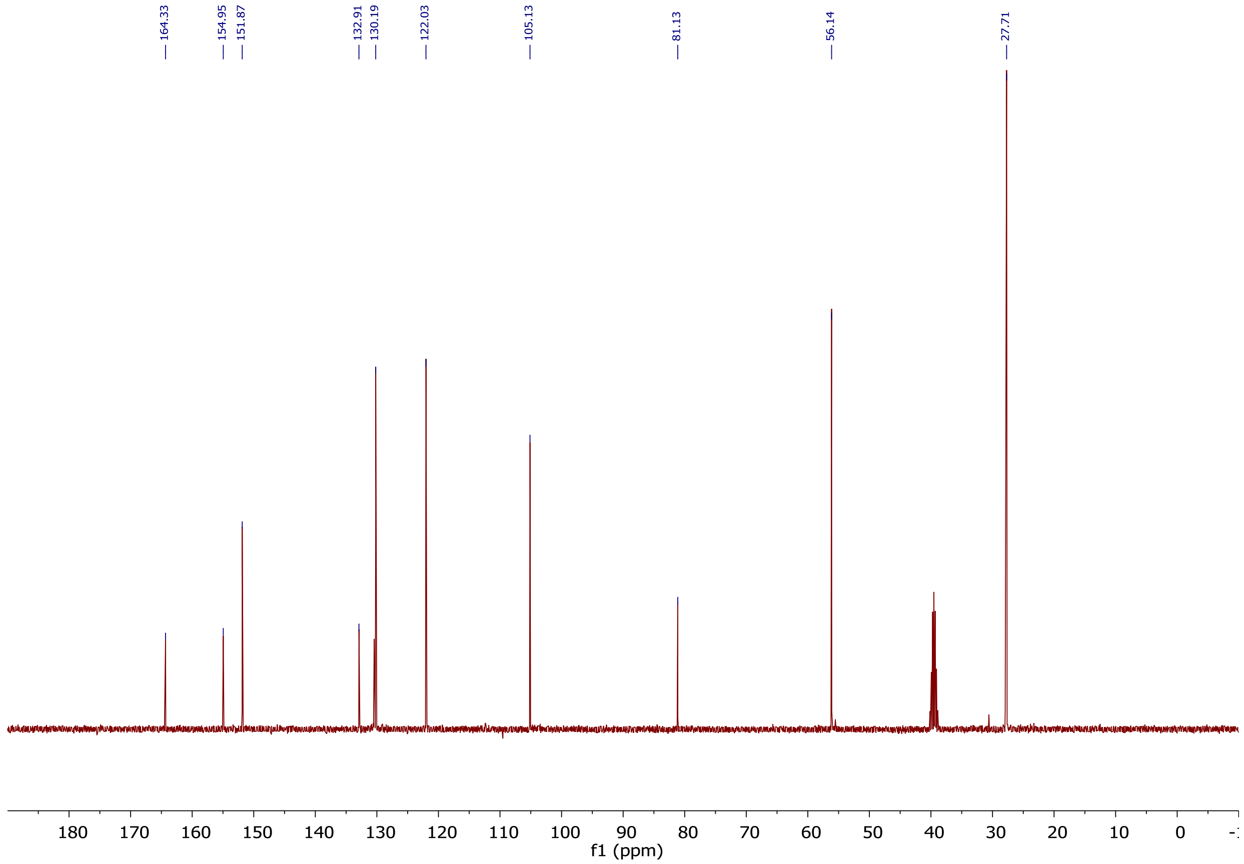


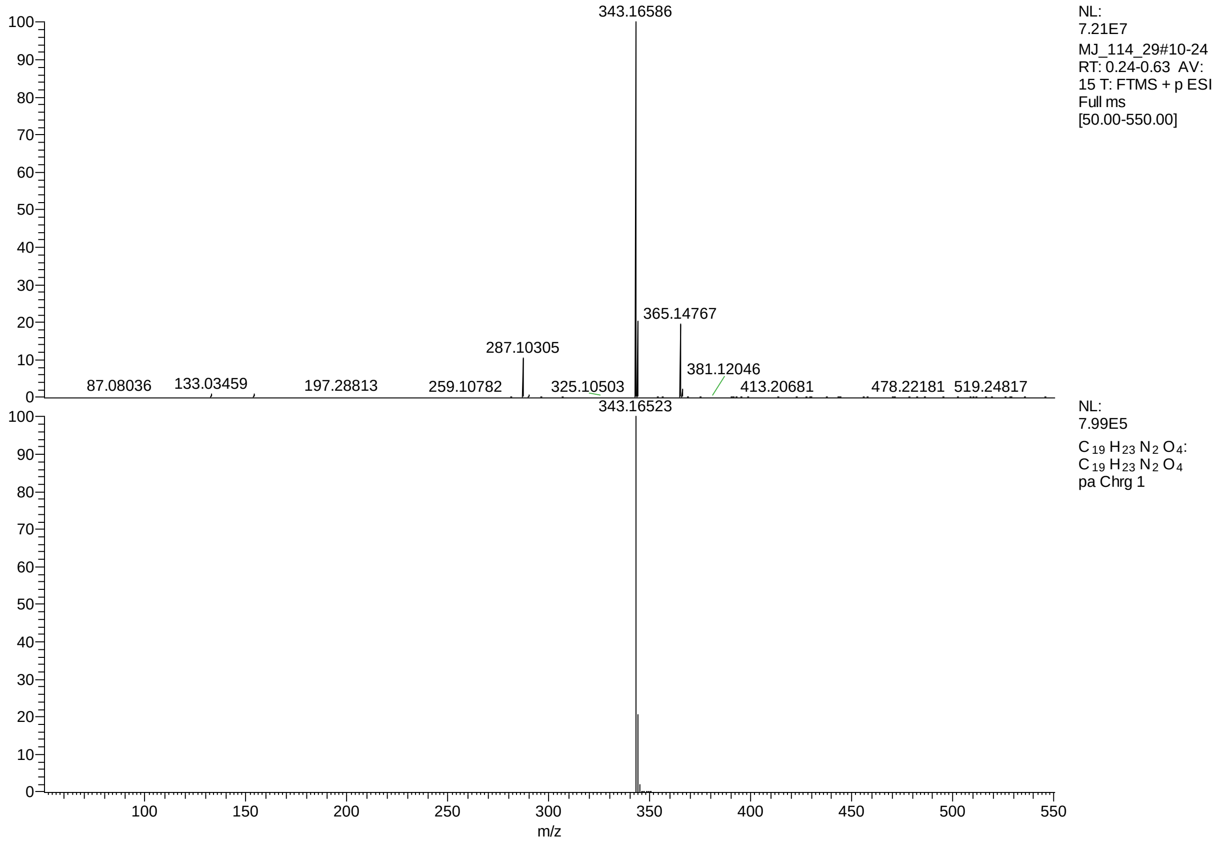



288.09841
394.17682
154.08632
310.08026
377.15019
87.08036
116.98590
197.29826
259.10801
327.12112
416.15804
464.21723
518.18802
NL: 2.98E7
MJ_114_27#10-19
RT: 0.24-0.49 AV: 10 T: FTMS + p ESI Full ms [50.00-550.00]
288.09788
NL: 8.41E5
C 14 H 14 N 3 O 4: C 14 H 14 N 3 O 4
pa Chrg 1
m/z

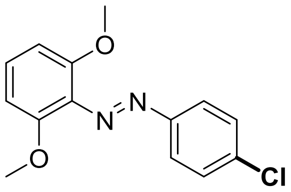
3f:


A (d) 8.09
B (d) 7.84
C (t) 7.34
D (d) 6.81
E (s) 3.77
F (s) 1.57
2.00
1.97
1.03
2.02
6.13
9.07
f1 (ppm)
O
N
N
O
O

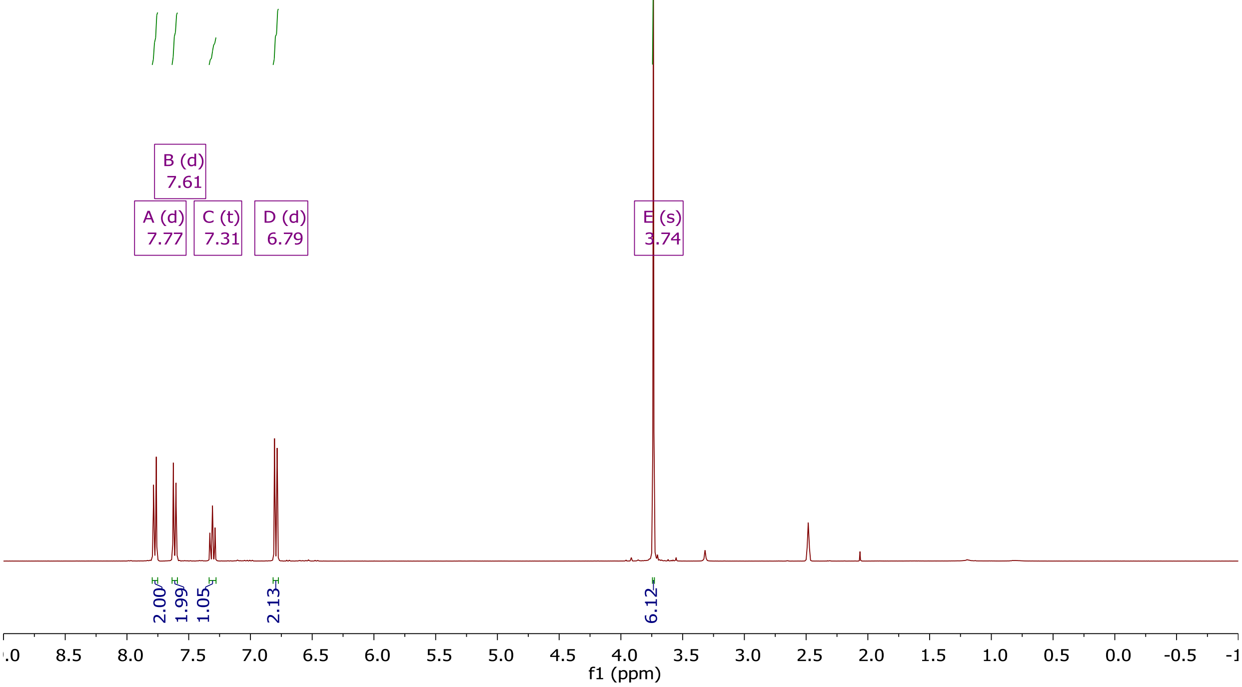

164.33
154.95
151.87
132.91
130.19
122.03
105.13
81.13
56.14
27.71
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


343.16586
NL:
7.21E7
MJ_114_29#10-24
RT: 0.24-0.63 AV:
15 T: FTMS + p ESI
Full ms
[50.00-550.00]
365.14767
287.10305
381.12046
87.08036
133.03459
197.28813
259.10782
325.10503
413.20681
478.22181
519.24817
343.16523
NL:
7.99E5
$C_{19}H_{23}N_2O_4$:
$C_{19}H_{23}N_2O_4$
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

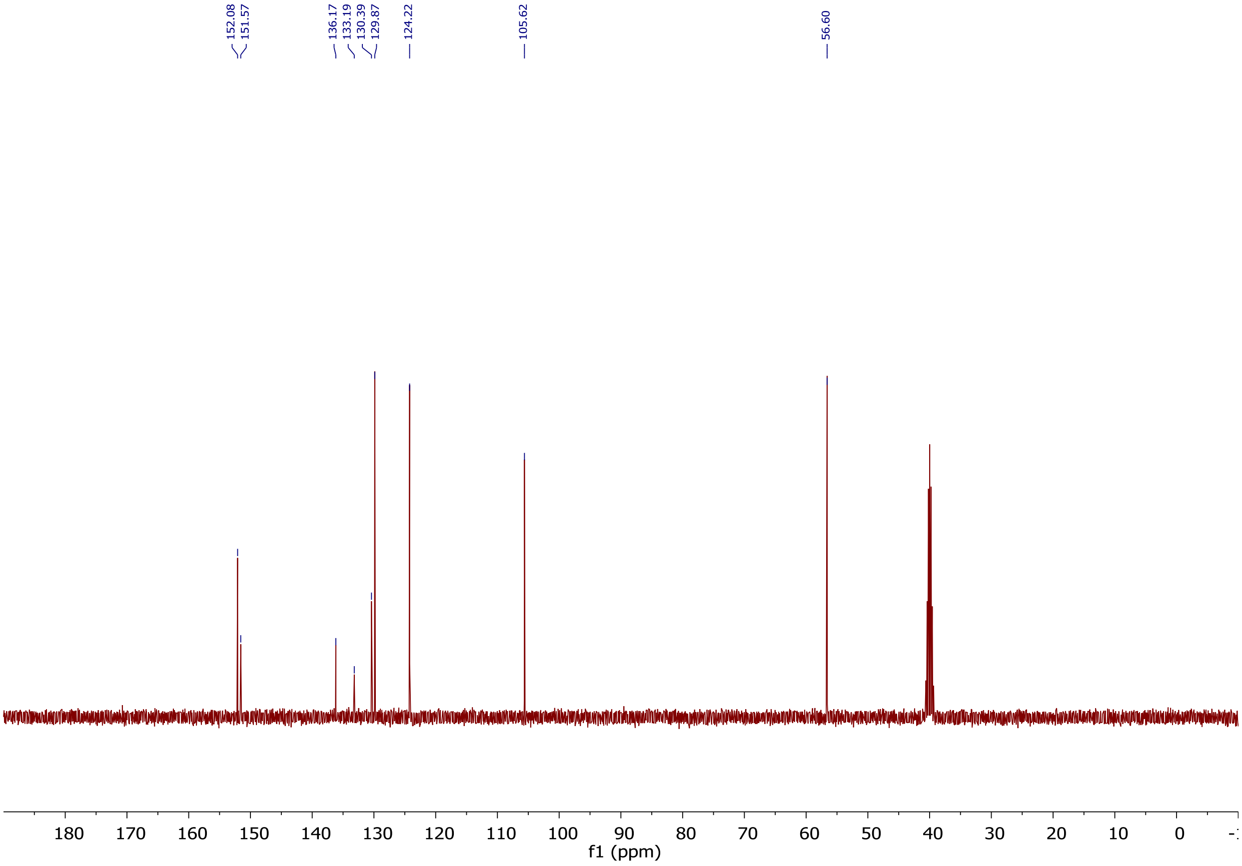
3g:



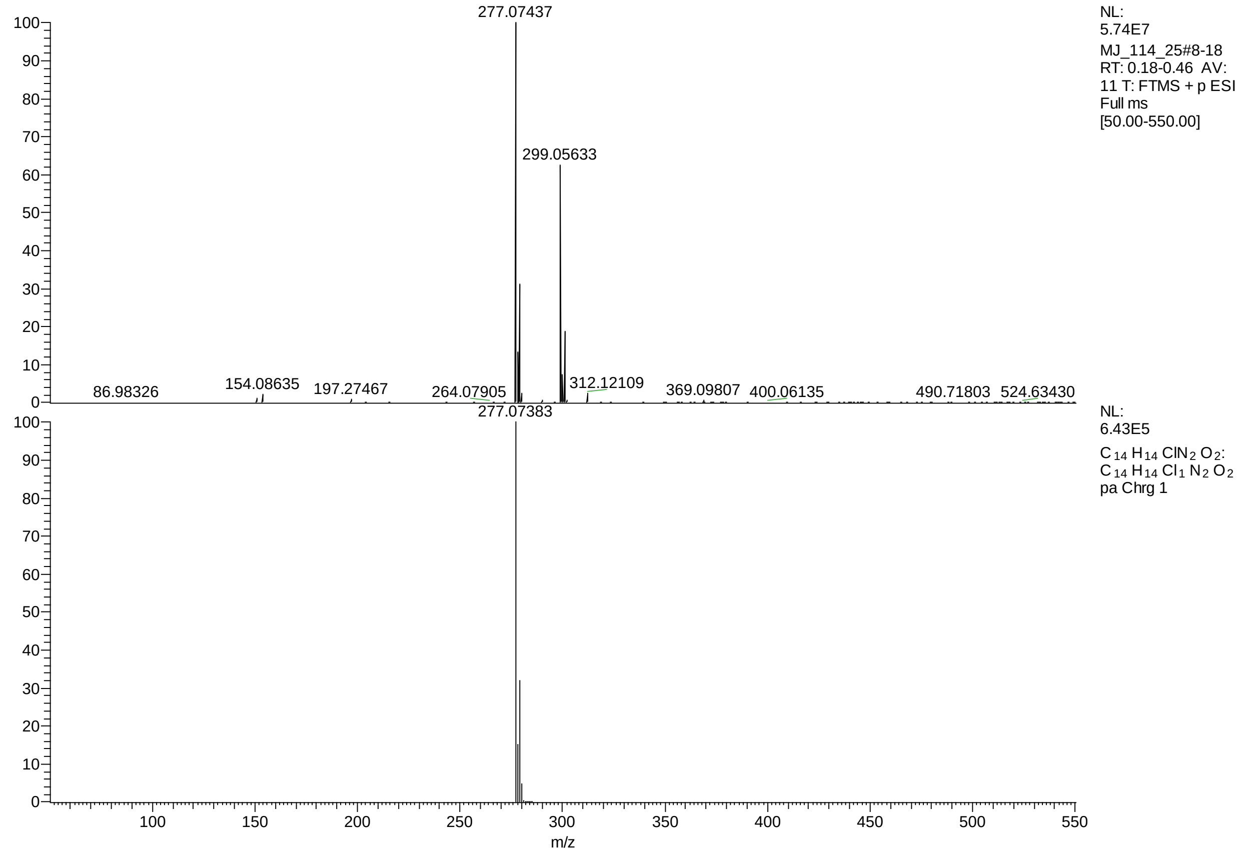
O
N
N
O
Cl



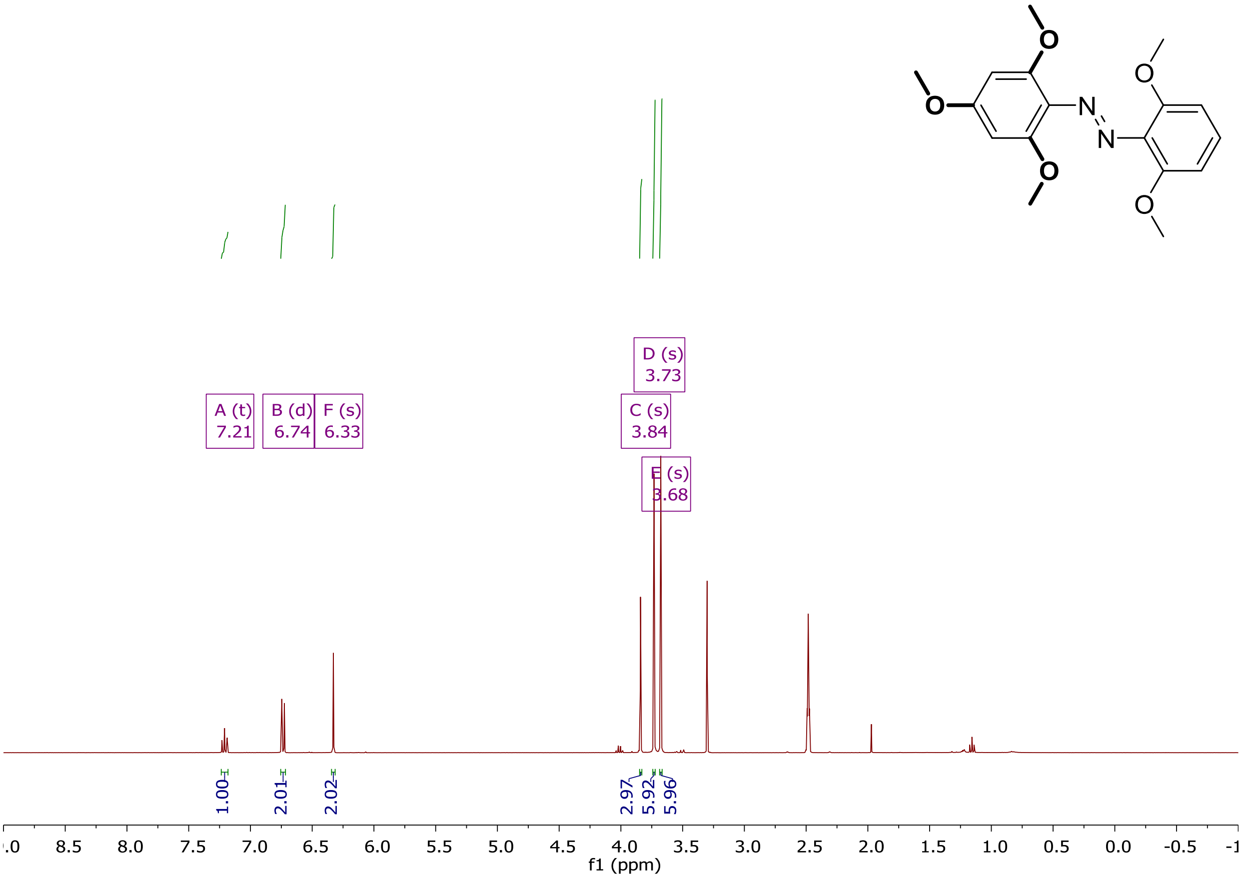
B (d)
7.61
A (d)
7.77
C (t)
7.31
D (d)
6.79
E (s)
3.74
2.00
1.99
1.05
2.13
6.12
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

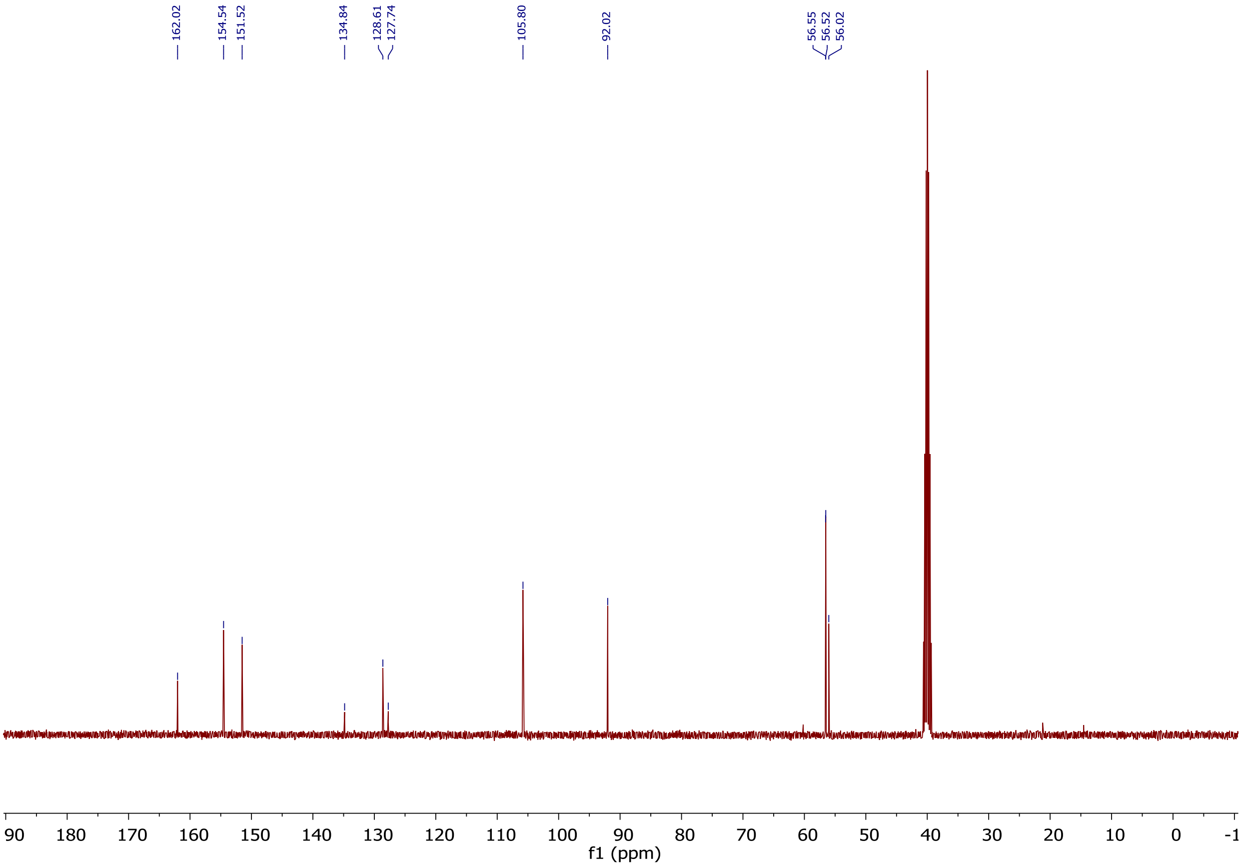


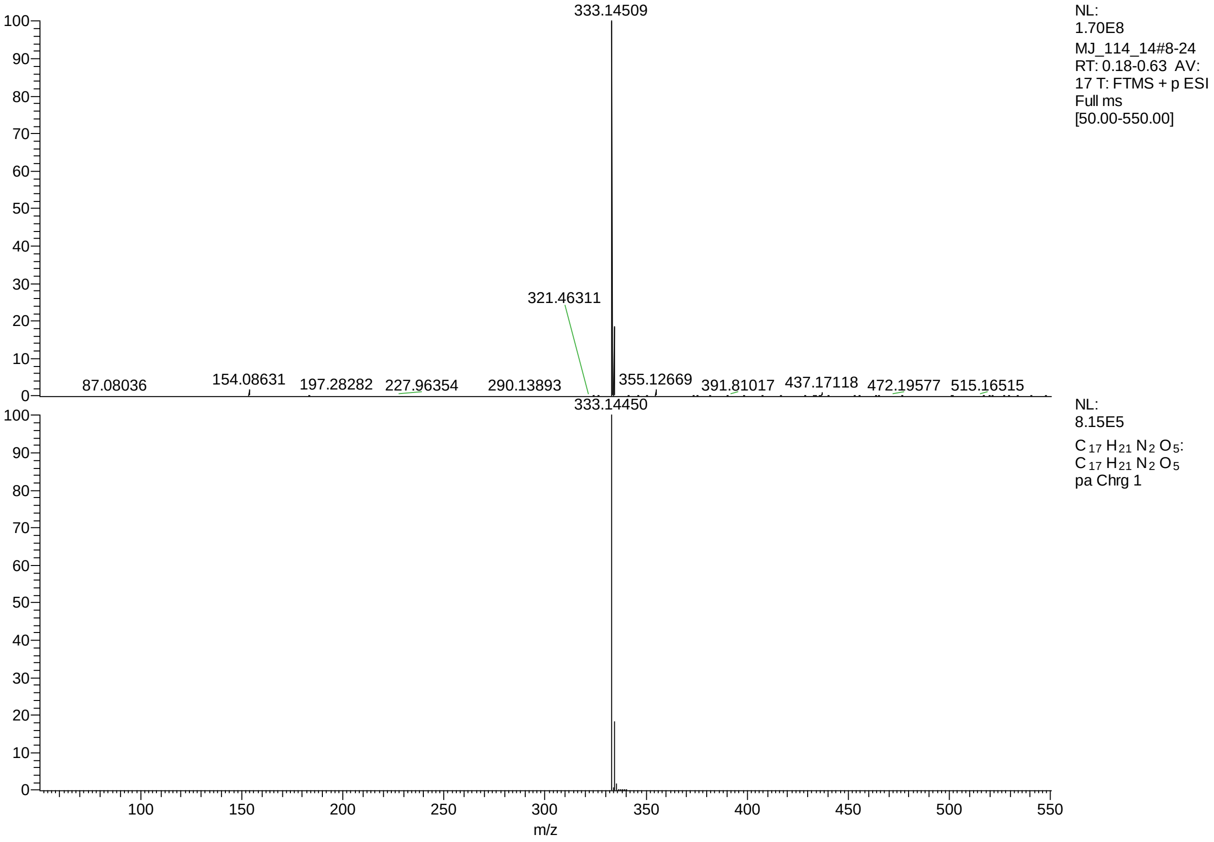
152.08
151.57
136.17
133.19
130.39
129.87
124.22
105.62
56.60
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-:
f1 (ppm)


277.07437
299.05633
86.98326
154.08635
197.27467
264.07905
312.12109
369.09807
400.06135
490.71803
524.63430
NL:
5.74E7
MJ_114_25#8-18
RT: 0.18-0.46 AV:
11 T: FTMS + p ESI
Full ms
[50.00-550.00]
277.07383
NL:
6.43E5
C 14 H 14 ClN 2 O 2:
C 14 H 14 Cl 1 N 2 O 2
pa Chrg 1
0
10
20
30
40
50
60
70
80
90
100
100
150
200
250
300
350
400
450
500
550
m/z

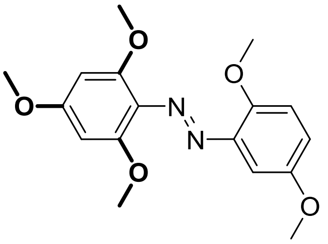
3h:

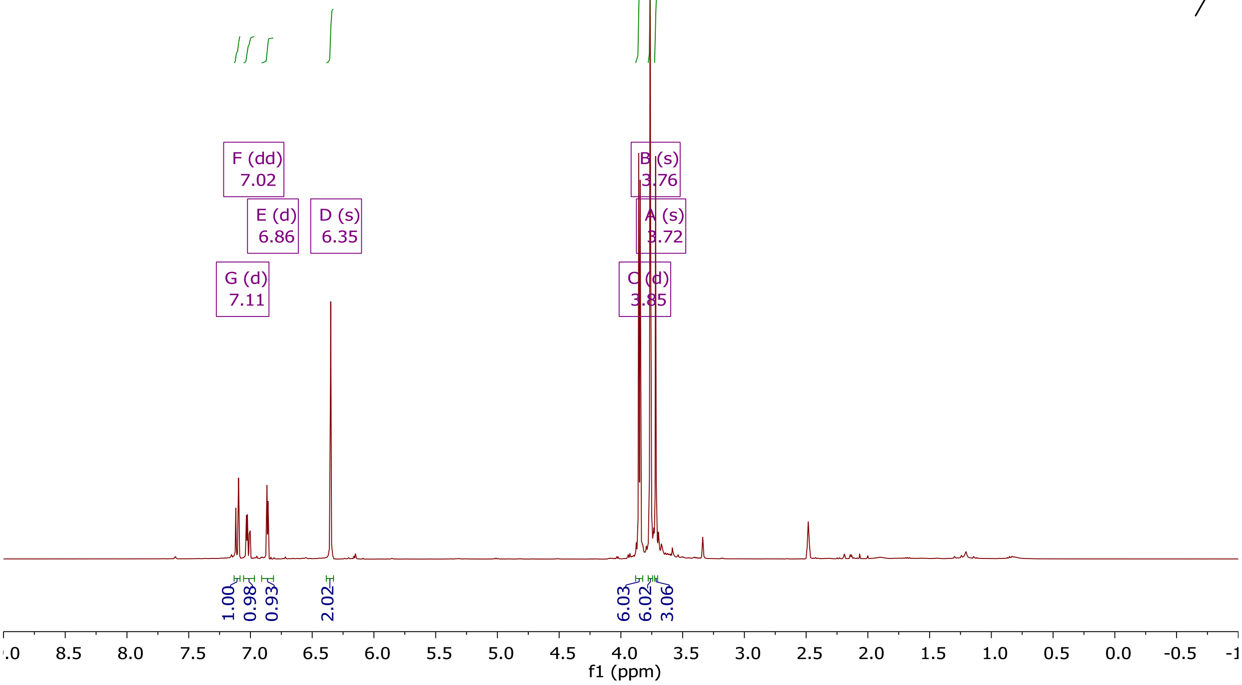

O
O
O
N
N
O
O
A (t)
7.21
B (d)
6.74
F (s)
6.33
D (s)
3.73
C (s)
3.84
E (s)
3.68
1.00
2.01
2.02
2.97
5.92
5.96
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

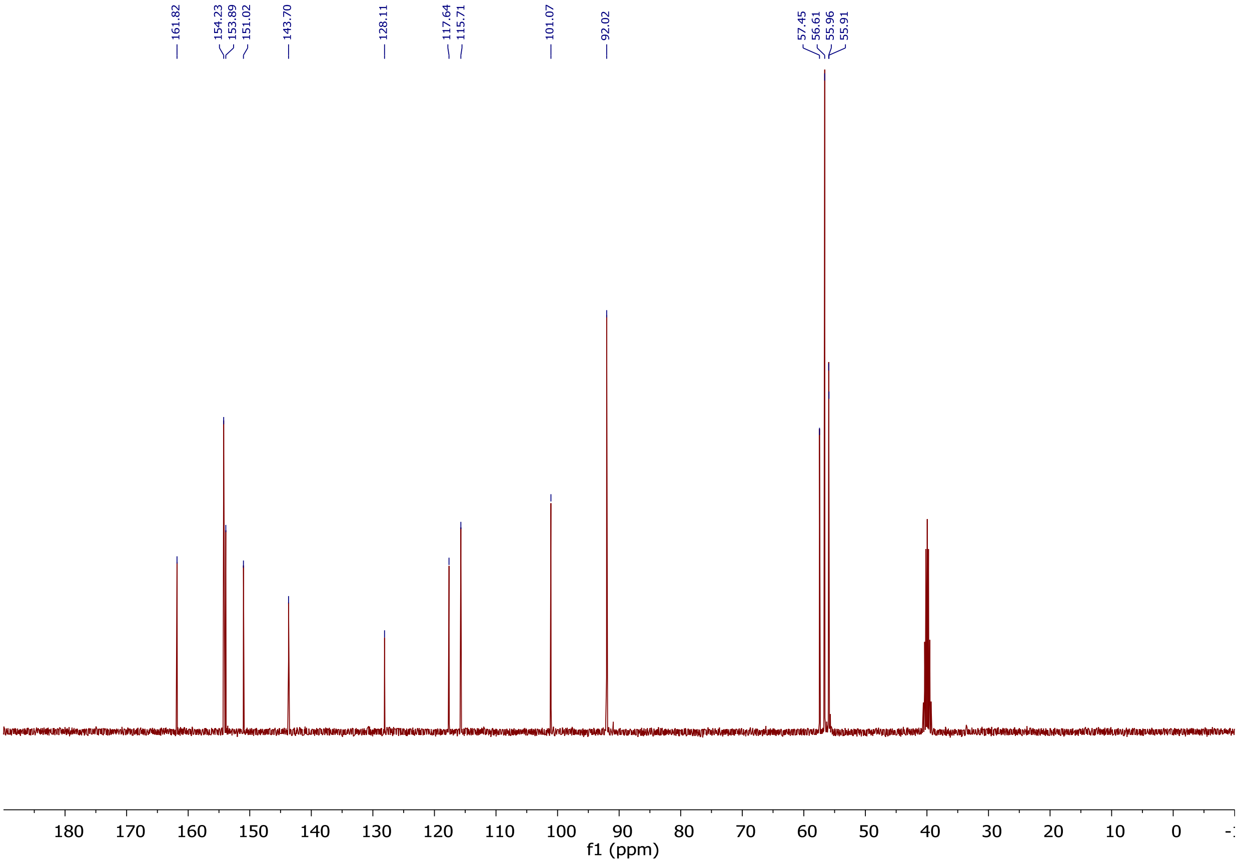

162.02
154.54
151.52
134.84
128.61
127.74
105.80
92.02
56.55
56.52
56.02
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

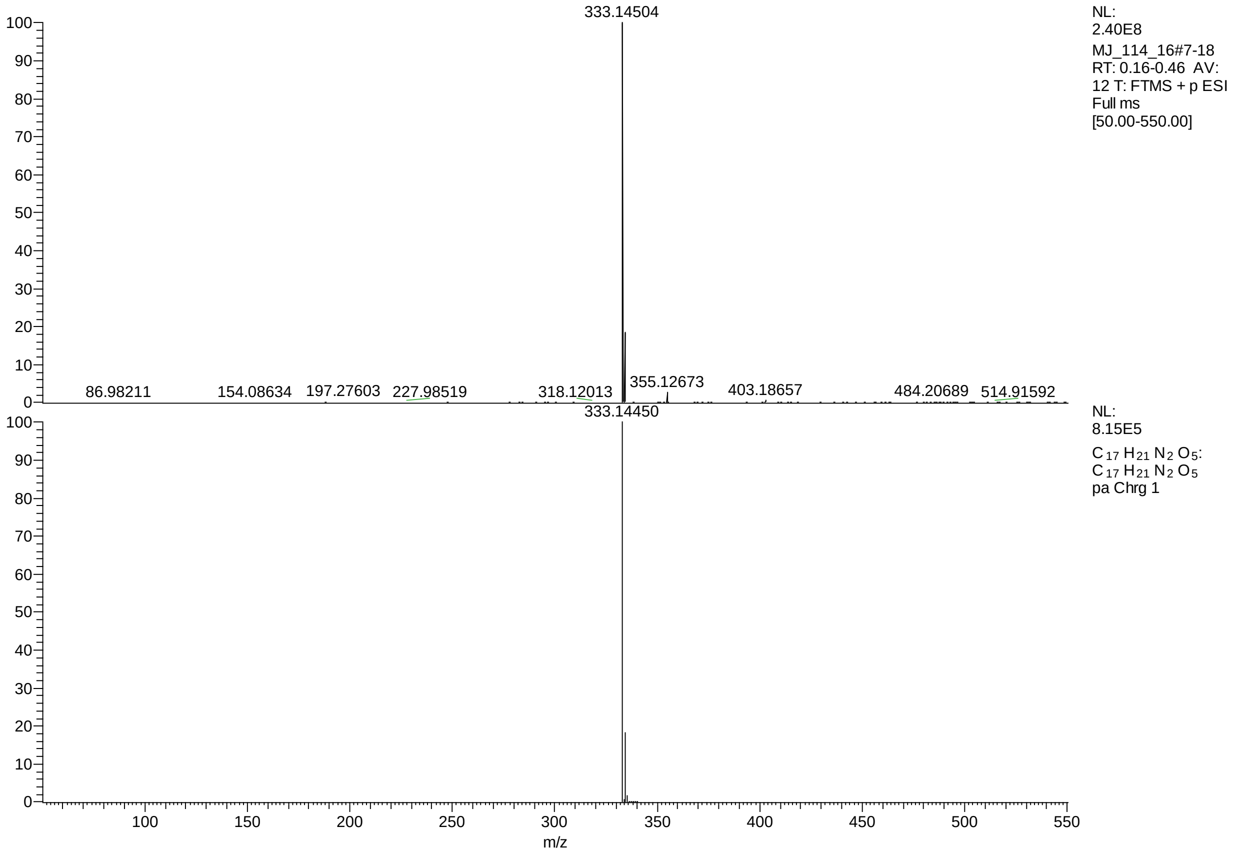

333.14509
NL:
1.70E8
MJ_114_14#8-24
RT: 0.18-0.63 AV:
17 T: FTMS + p ESI
Full ms
[50.00-550.00]
321.46311
87.08036
154.08631
197.28282
227.96354
290.13893
355.12669
391.81017
437.17118
472.19577
515.16515
333.14450
NL:
8.15E5
C 17 H 21 N 2 O 5:
C 17 H 21 N 2 O 5
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

3i:

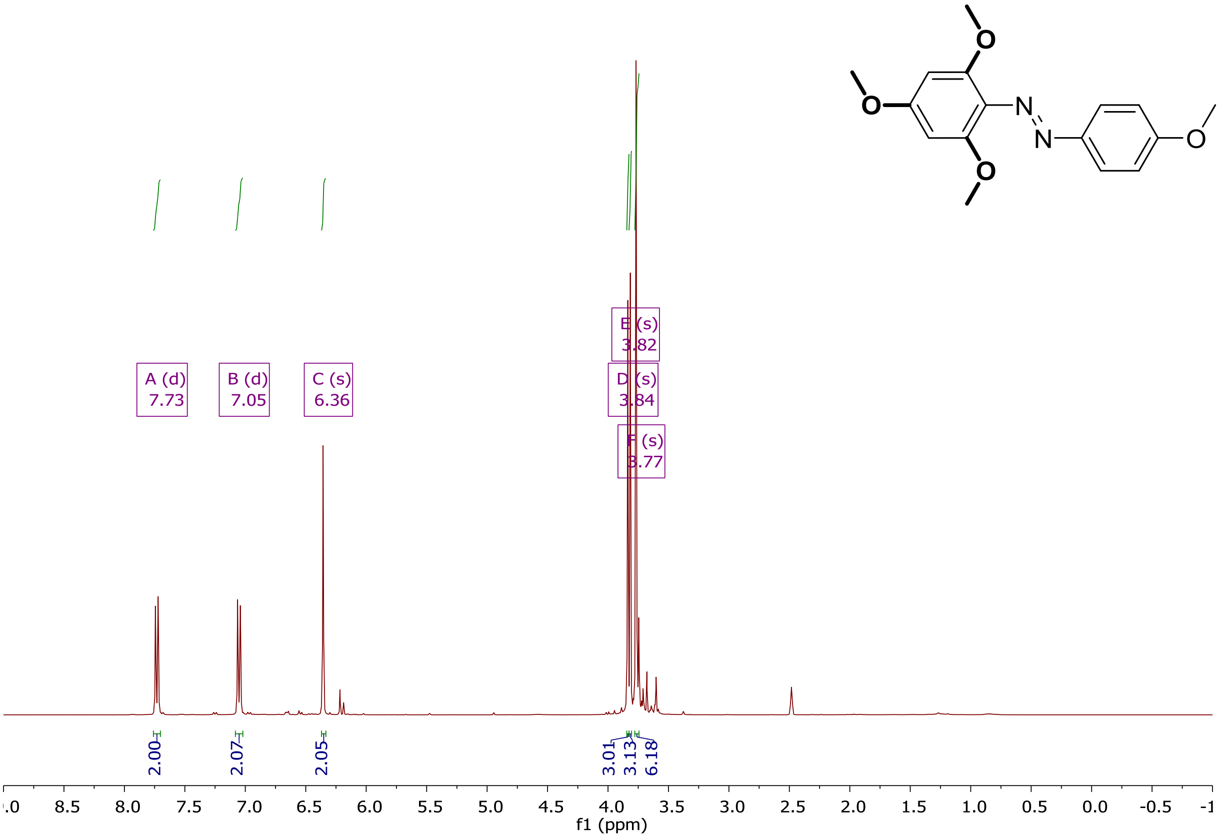

O
O
O
N
N
O
O

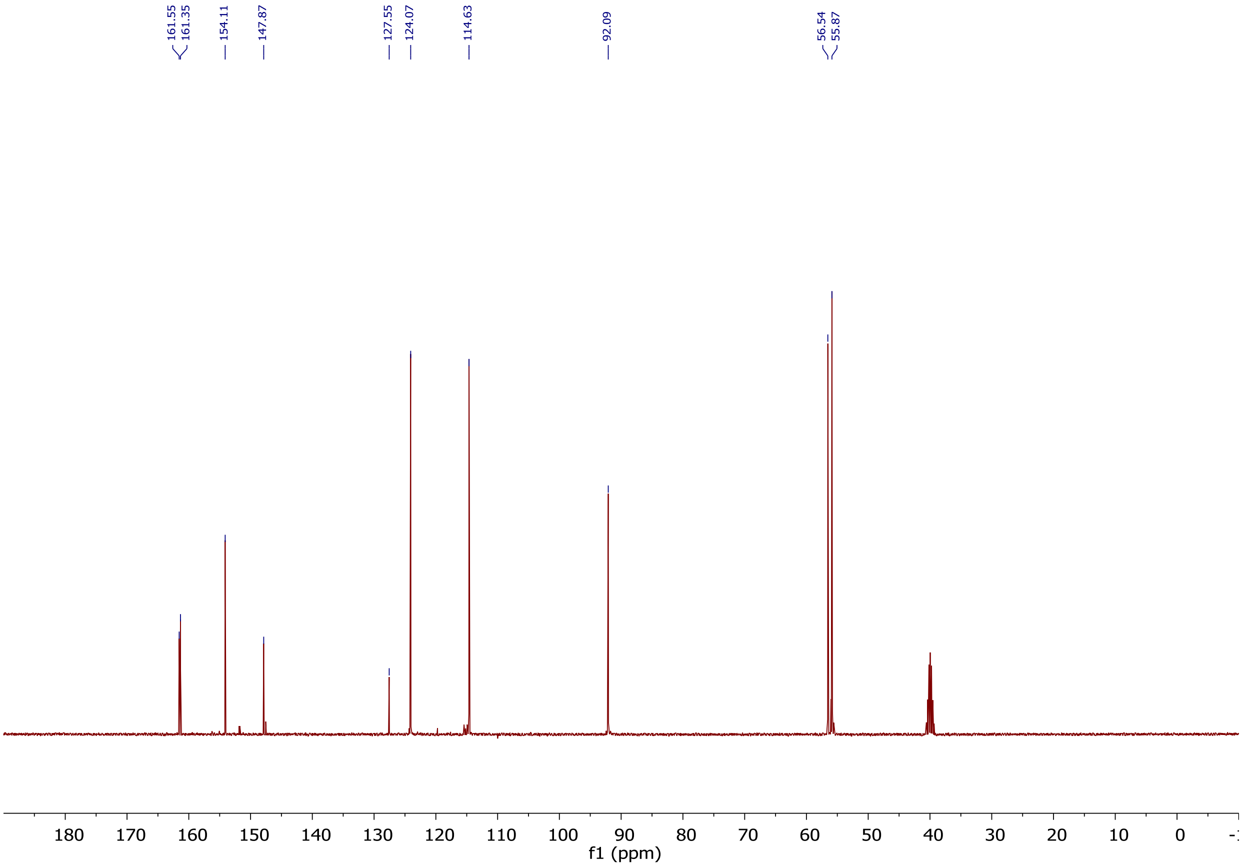

F (dd)
7.02
E (d)
6.86
D (s)
6.35
G (d)
7.11
B (s)
3.76
A (s)
3.72
C (d)
3.85
1.00
0.98
0.93
2.02
6.03
6.02
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

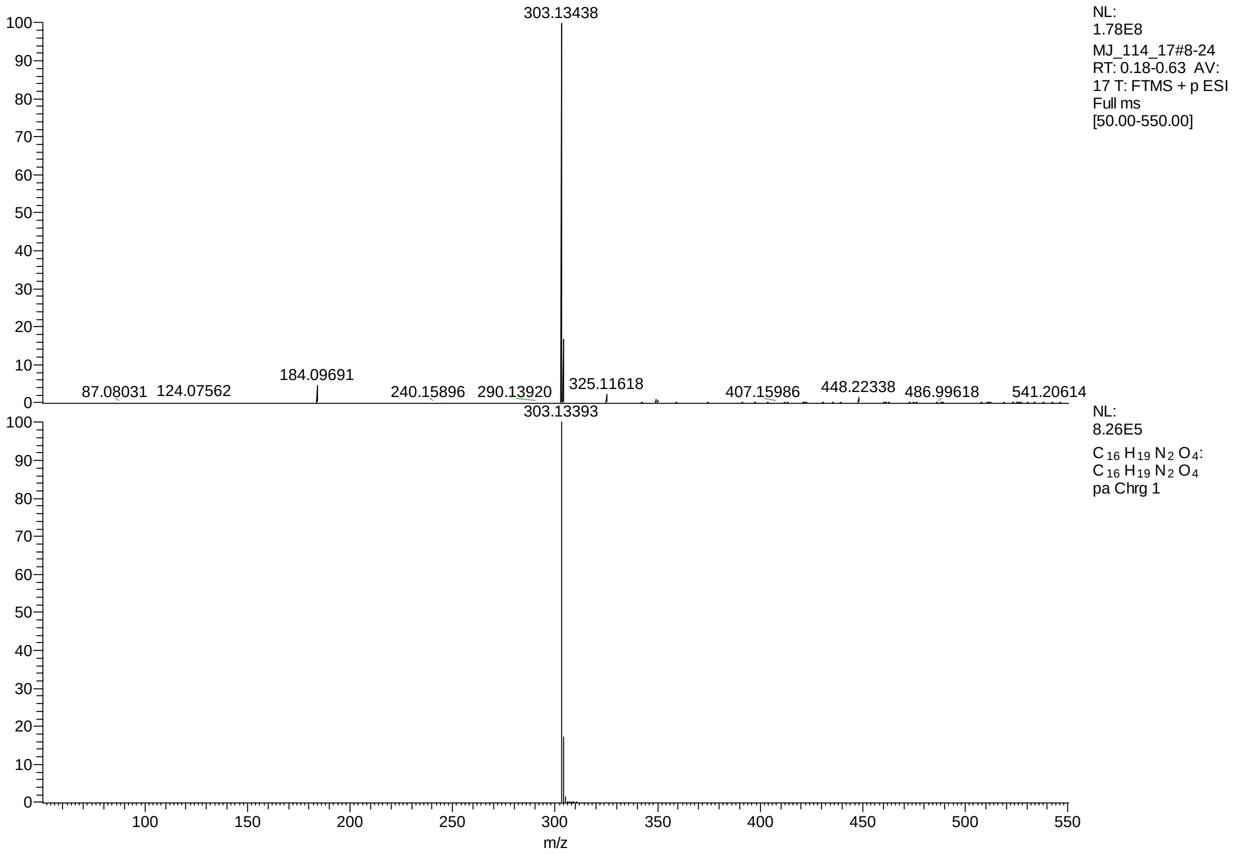

161.82
154.23
153.89
151.02
143.70
128.11
117.64
115.71
101.07
92.02
57.45
56.61
55.96
55.91
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



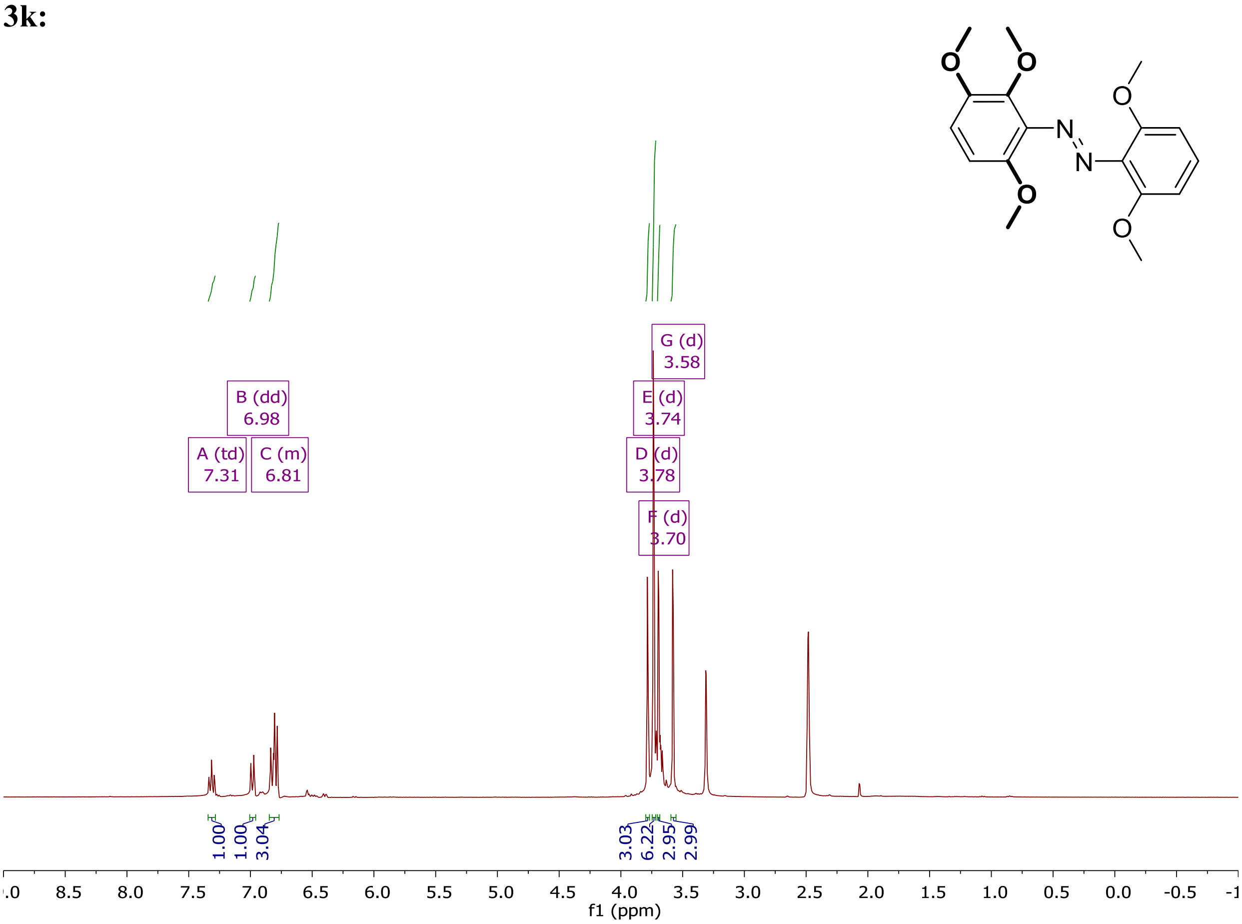
3j: After thermal adaption, no full conversion to the *trans* isomer was observed which became apparent in the ^{1}H-NMR and ^{13}C-NMR spectrum showing small quantities of the *cis* isomer.



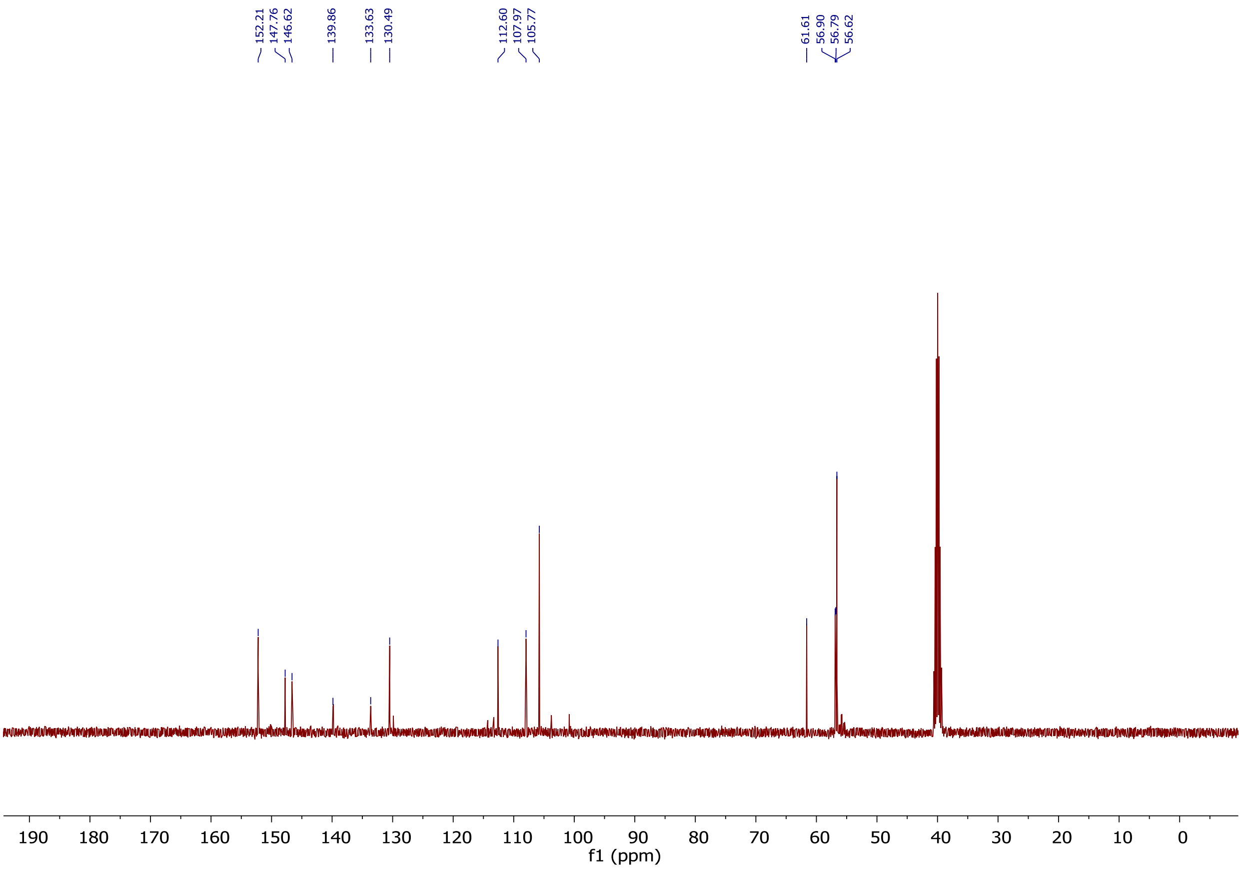

161.55
161.35
154.11
147.87
127.55
124.07
114.63
92.09
56.54
55.87
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


303.13438
NL:
1.78E8
MJ_114_17#8-24
RT: 0.18-0.63 AV:
17 T: FTMS + p ESI
Full ms
[50.00-550.00]
87.08031
124.07562
184.09691
240.15896
290.13920
325.11618
407.15986
448.22338
486.99618
541.20614
303.13393
NL:
8.26E5
C 16 H19 N2 O4:
C 16 H19 N2 O4
pa Chrg 1
0 10 20 30 40 50 60 70 80 90 100
100 150 200 250 300 350 400 450 500 550
m/z

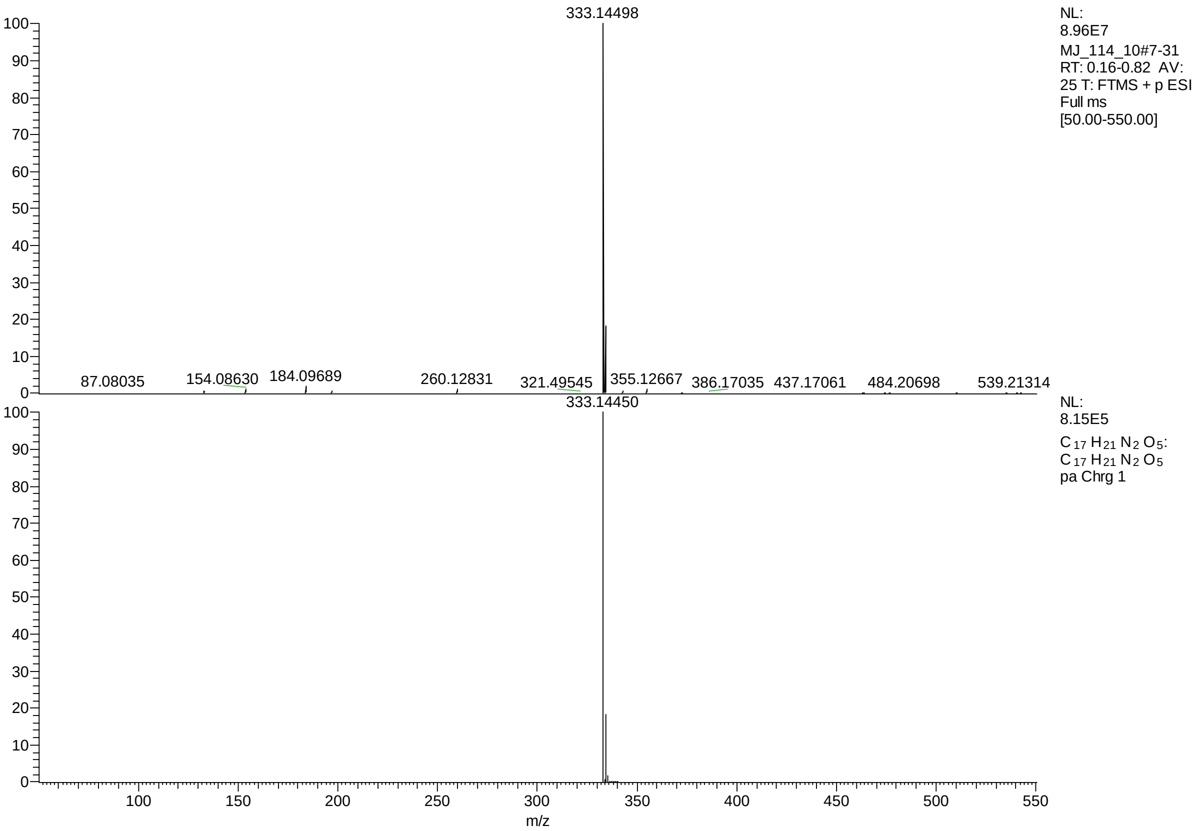
3k:



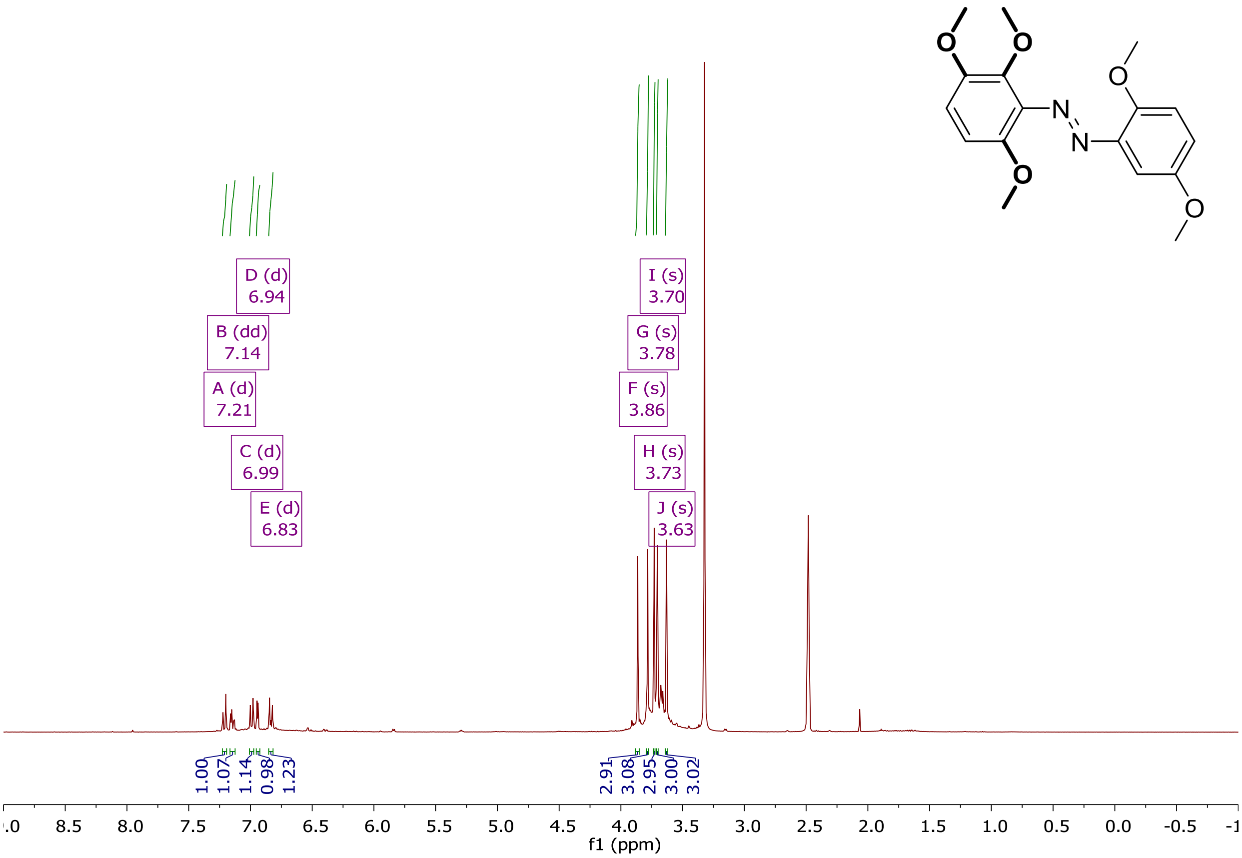
O
O
O
N
N
O
O
B (dd)
6.98
A (td)
7.31
C (m)
6.81
G (d)
3.58
E (d)
3.74
D (d)
3.78
F (d)
3.70
1.00
1.00
3.04
3.03
6.22
2.95
2.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

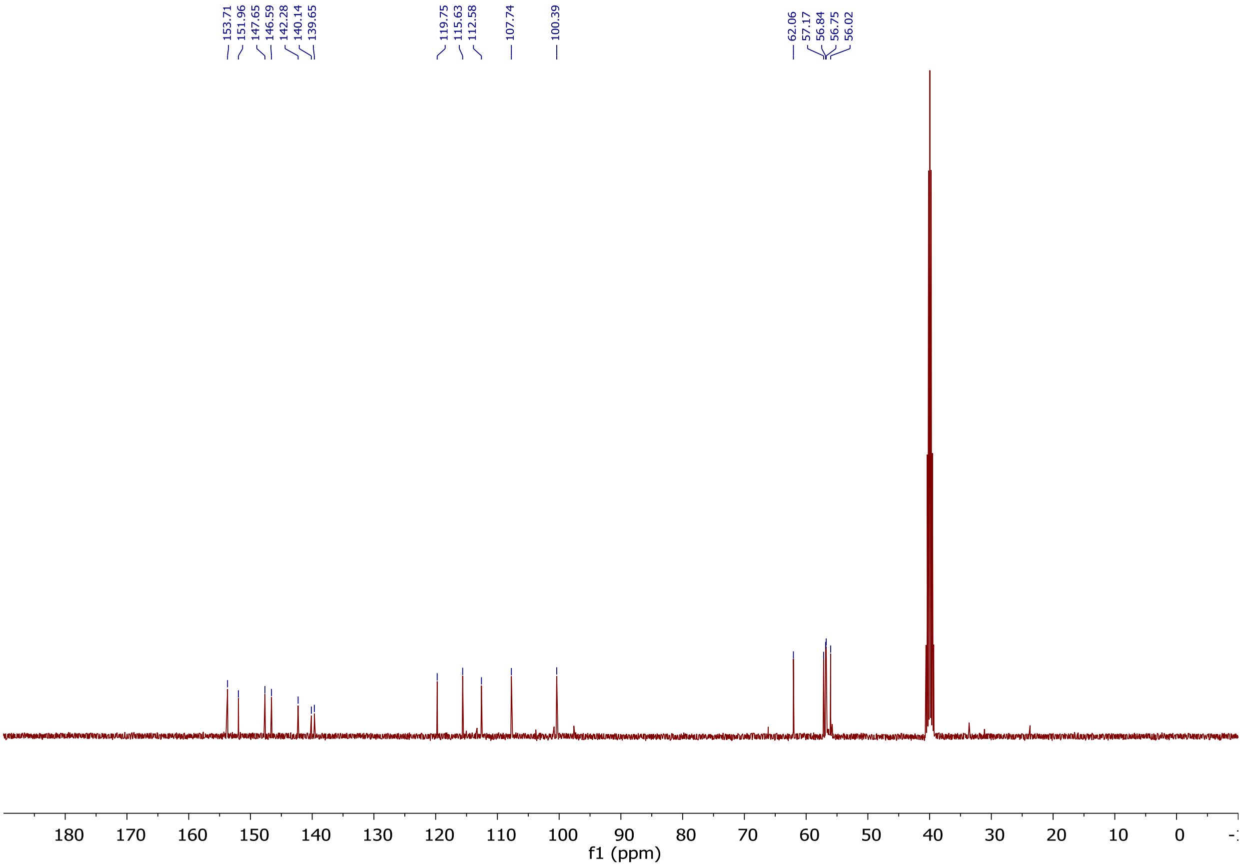


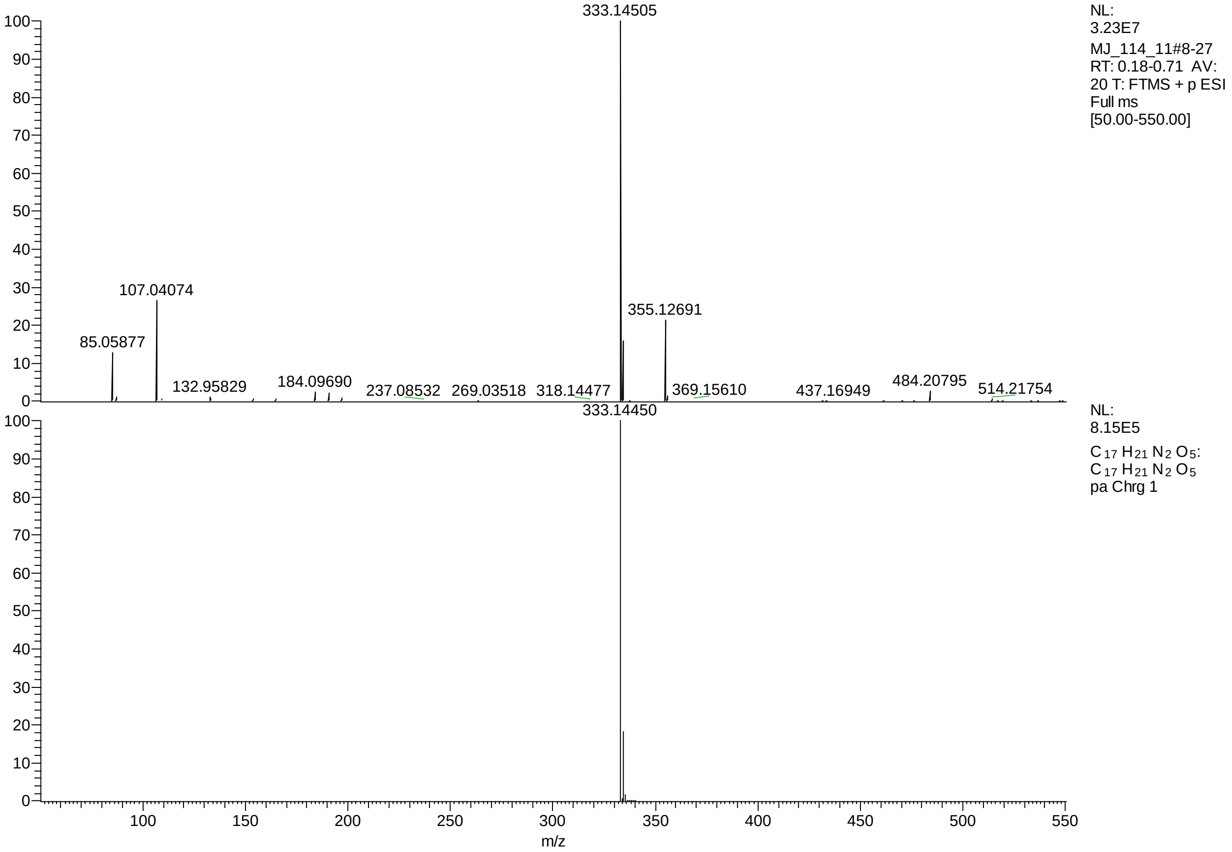
152.21
147.76
146.62
139.86
133.63
130.49
112.60
107.97
105.77
61.61
56.90
56.79
56.62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


333.14498
NL:
8.96E7
MJ_114_10#7-31
RT: 0.16-0.82 AV:
25 T: FTMS + p ESI
Full ms
[50.00-550.00]
87.08035
154.08630
184.09689
260.12831
321.49545
355.12667
386.17035
437.17061
484.20698
539.21314
333.14450
NL:
8.15E5
$C_{17}H_{21}N_2O_5$:
$C_{17}H_{21}N_2O_5$
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

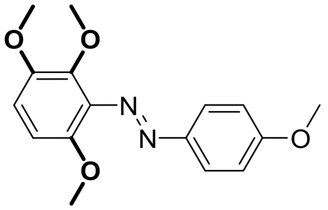
3l:

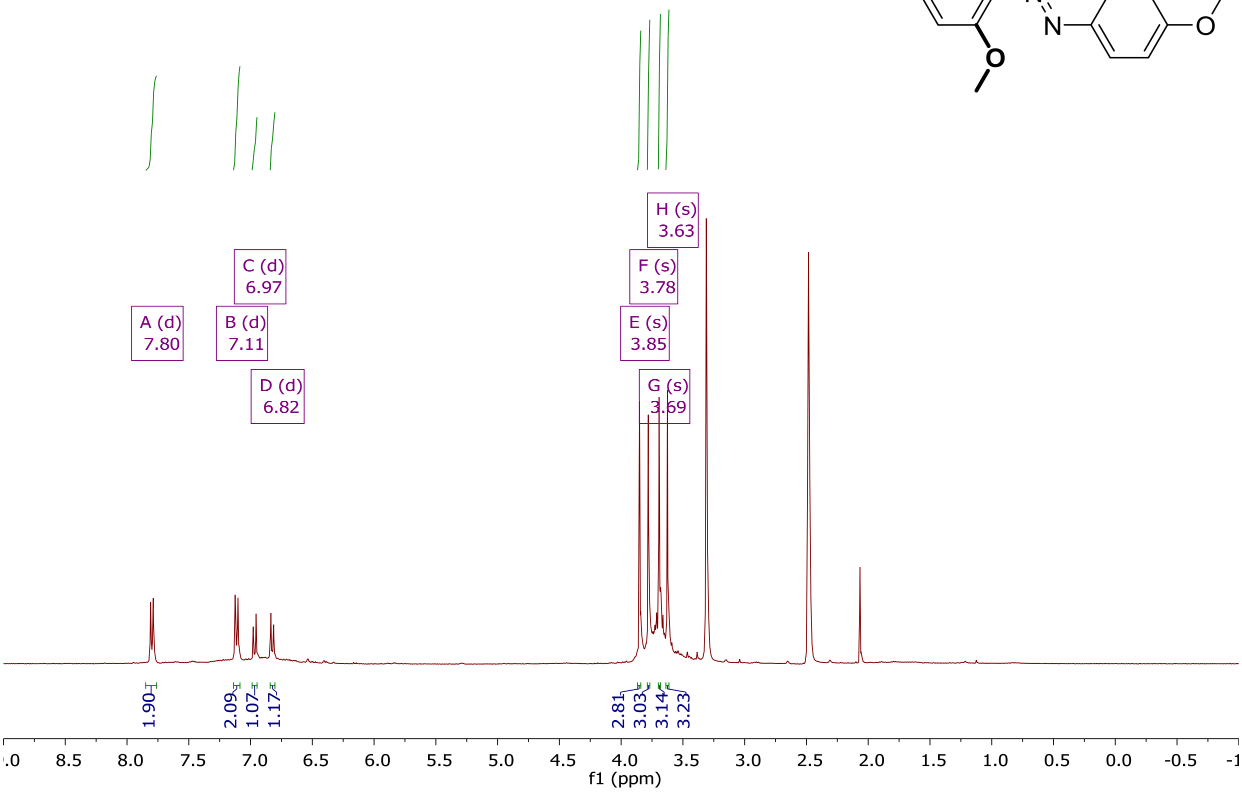

O
O
O
N
N
O
O
D (d)
6.94
B (dd)
7.14
A (d)
7.21
C (d)
6.99
E (d)
6.83
I (s)
3.70
G (s)
3.78
F (s)
3.86
H (s)
3.73
J (s)
3.63
1.00
1.07
1.14
0.98
1.23
2.91
3.08
2.95
3.00
3.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


153.71
151.96
147.65
146.59
142.28
140.14
139.65
119.75
115.63
112.58
107.74
100.39
62.06
57.17
56.84
56.75
56.02
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

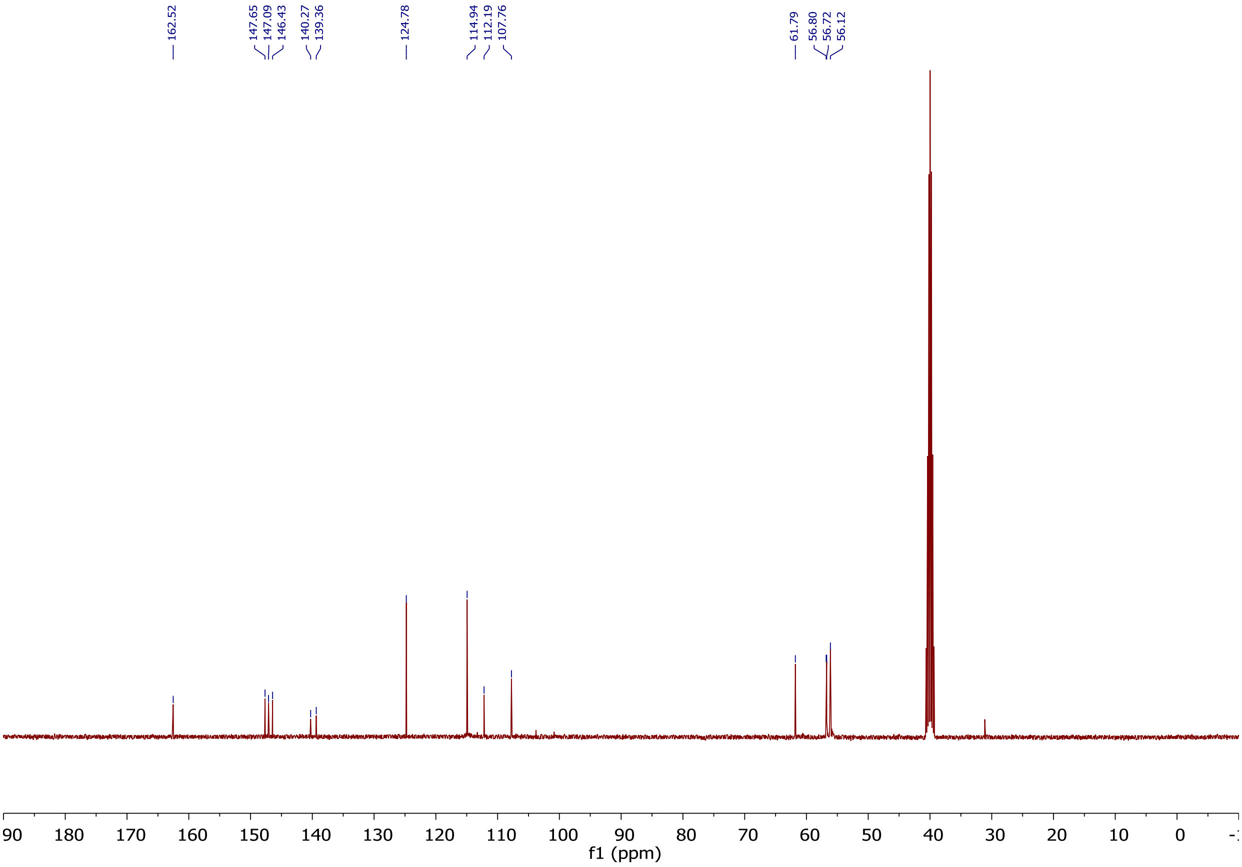

333.14505
NL:
3.23E7
MJ_114_11#8-27
RT: 0.18-0.71 AV:
20 T: FTMS + p ESI
Full ms
[50.00-550.00]
107.04074
85.05877
355.12691
132.95829
184.09690
237.08532
269.03518
318.14477
369.15610
437.16949
484.20795
514.21754
333.14450
NL:
8.15E5
C 17 H 21 N 2 O 5:
C 17 H 21 N 2 O 5
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

3m:

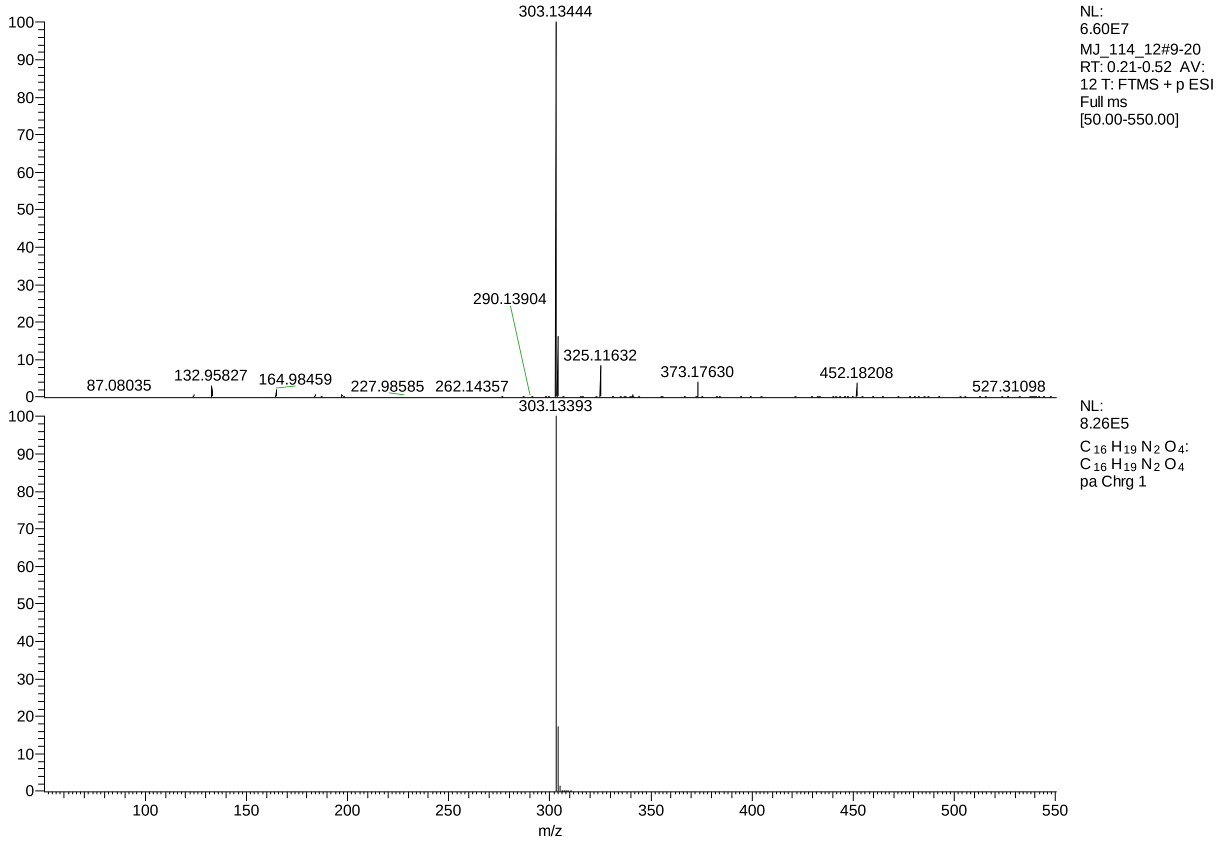




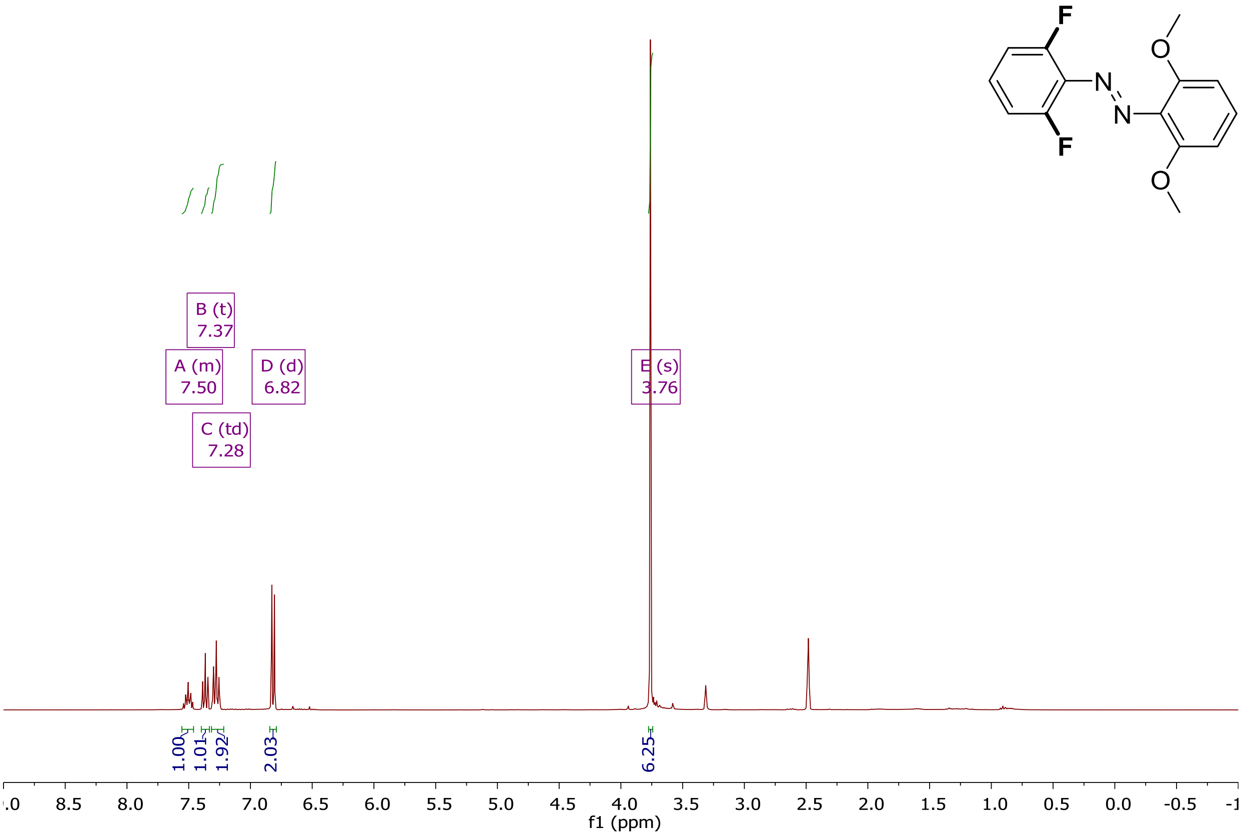
H (s)
3.63
C (d)
6.97
F (s)
3.78
A (d)
7.80
B (d)
7.11
E (s)
3.85
D (d)
6.82
G (s)
3.69
1.90
2.09
1.07
1.17
2.81
3.03
3.14
3.23
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

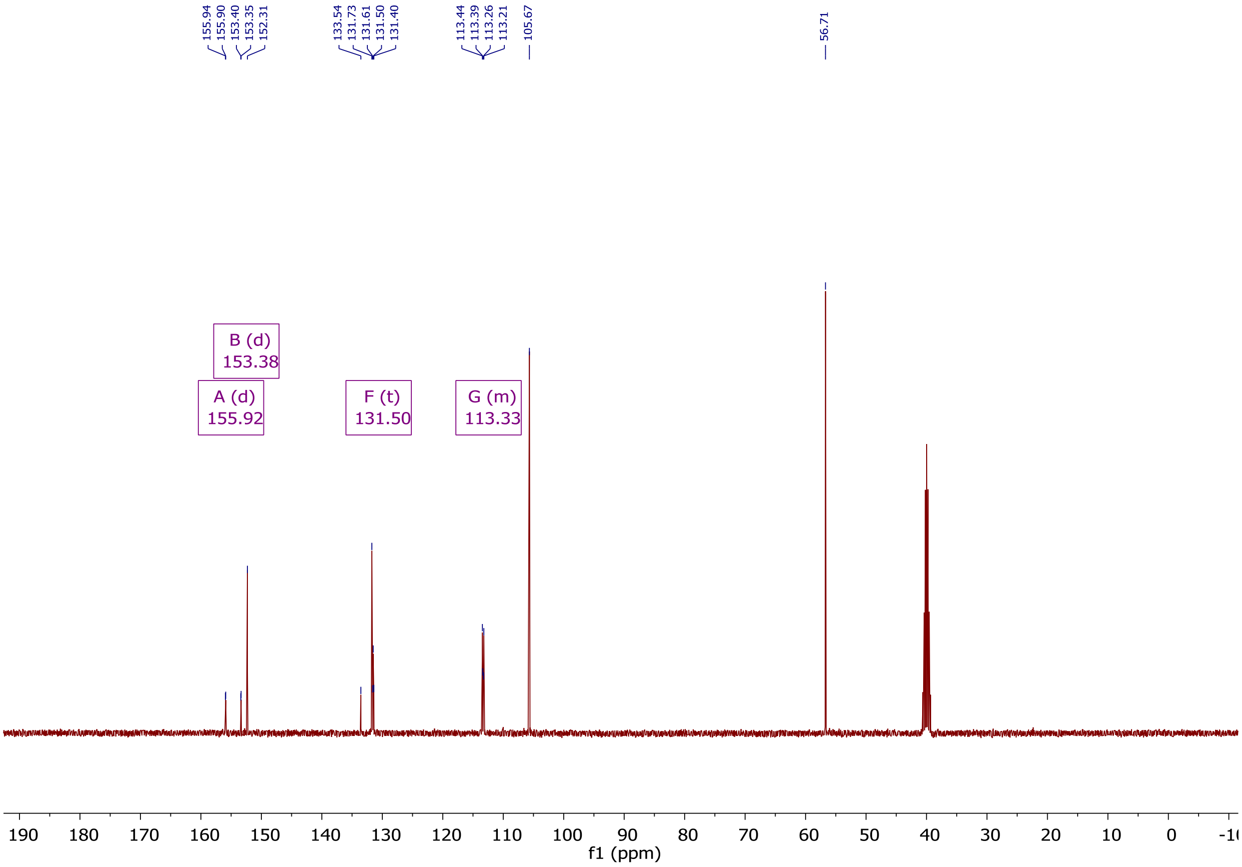


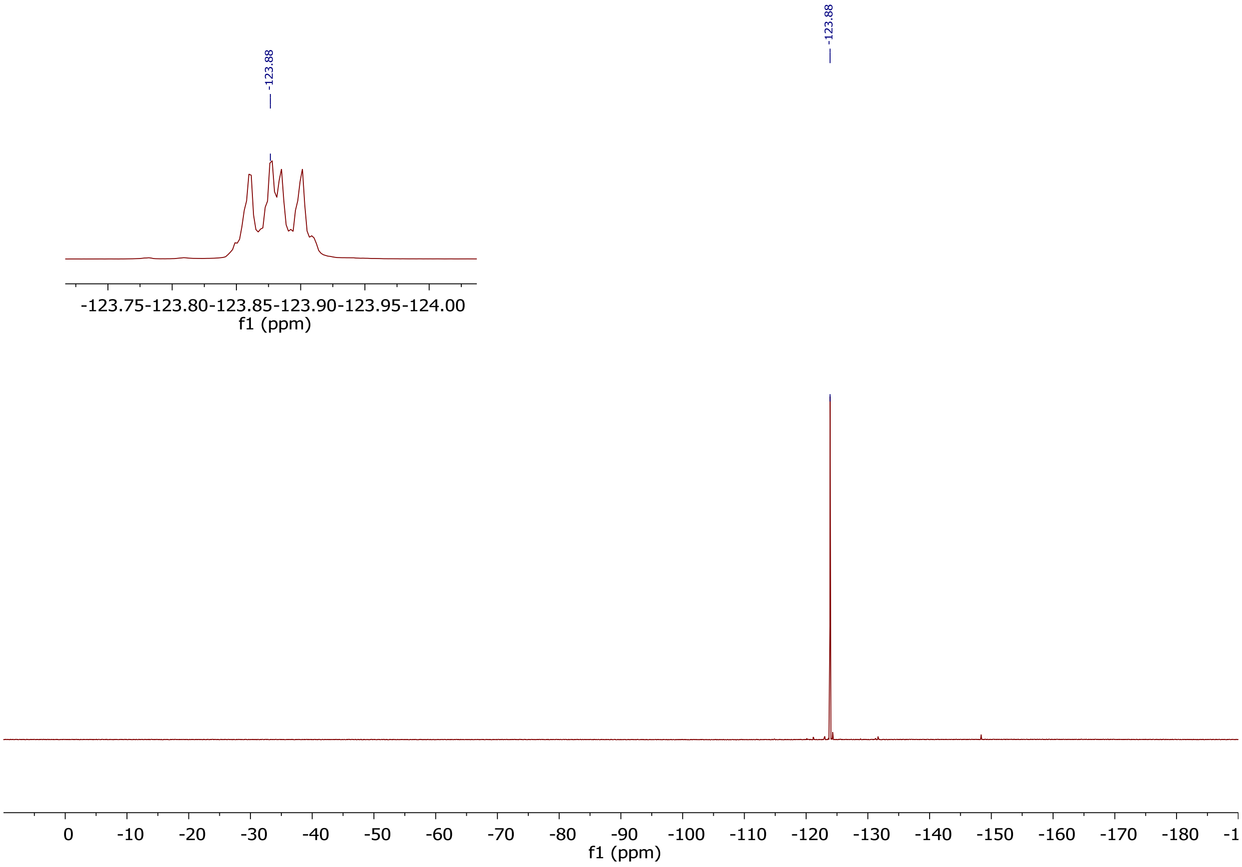
162.52
147.65
147.09
146.43
140.27
139.36
124.78
114.94
112.19
107.76
61.79
56.80
56.72
56.12
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

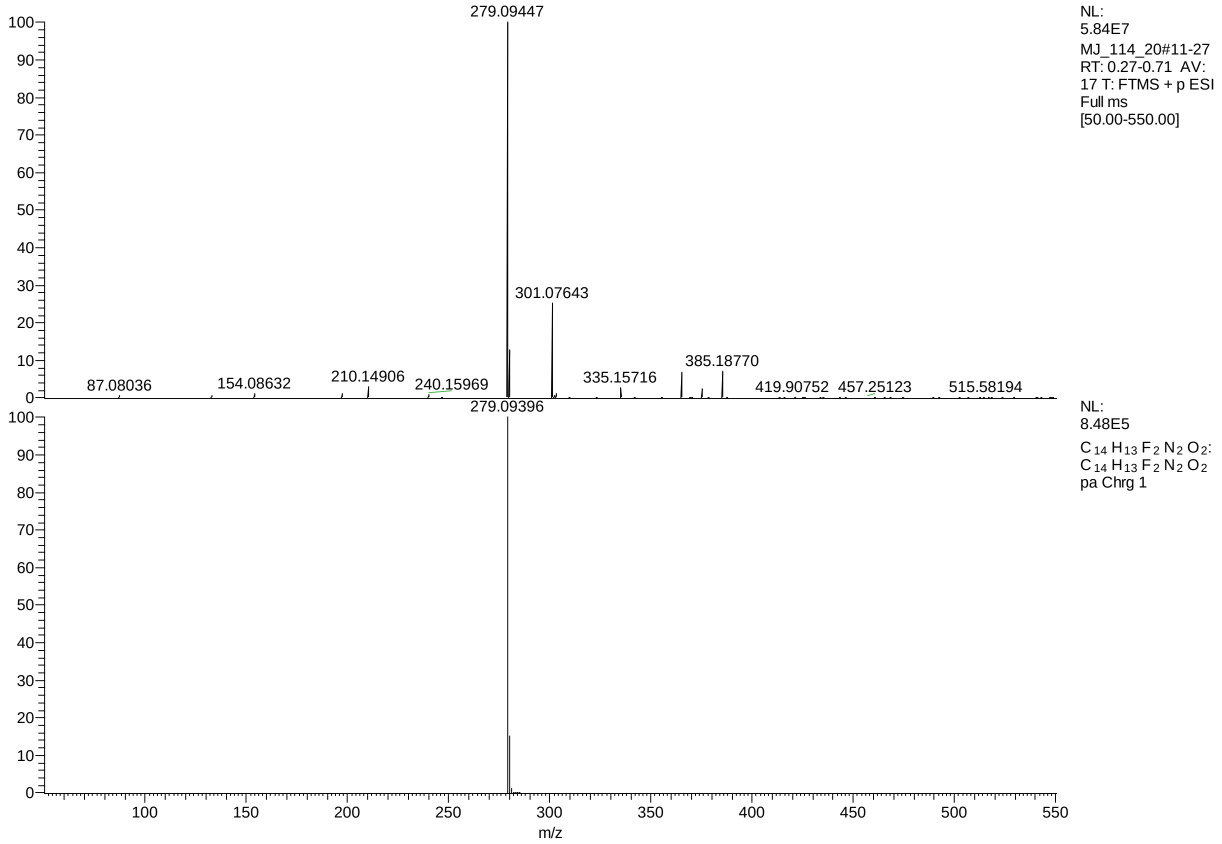

303.13444
NL:
6.60E7
MJ_114_12#9-20
RT: 0.21-0.52 AV:
12 T: FTMS + p ESI
Full ms
[50.00-550.00]
290.13904
325.11632
373.17630
452.18208
527.31098
87.08035
132.95827
164.98459
227.98585
262.14357
303.13393
NL:
8.26E5
$C_{16}H_{19}N_2O_4$:
$C_{16}H_{19}N_2O_4$
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
100
150
200
250
300
350
400
450
500
550
m/z

3n:

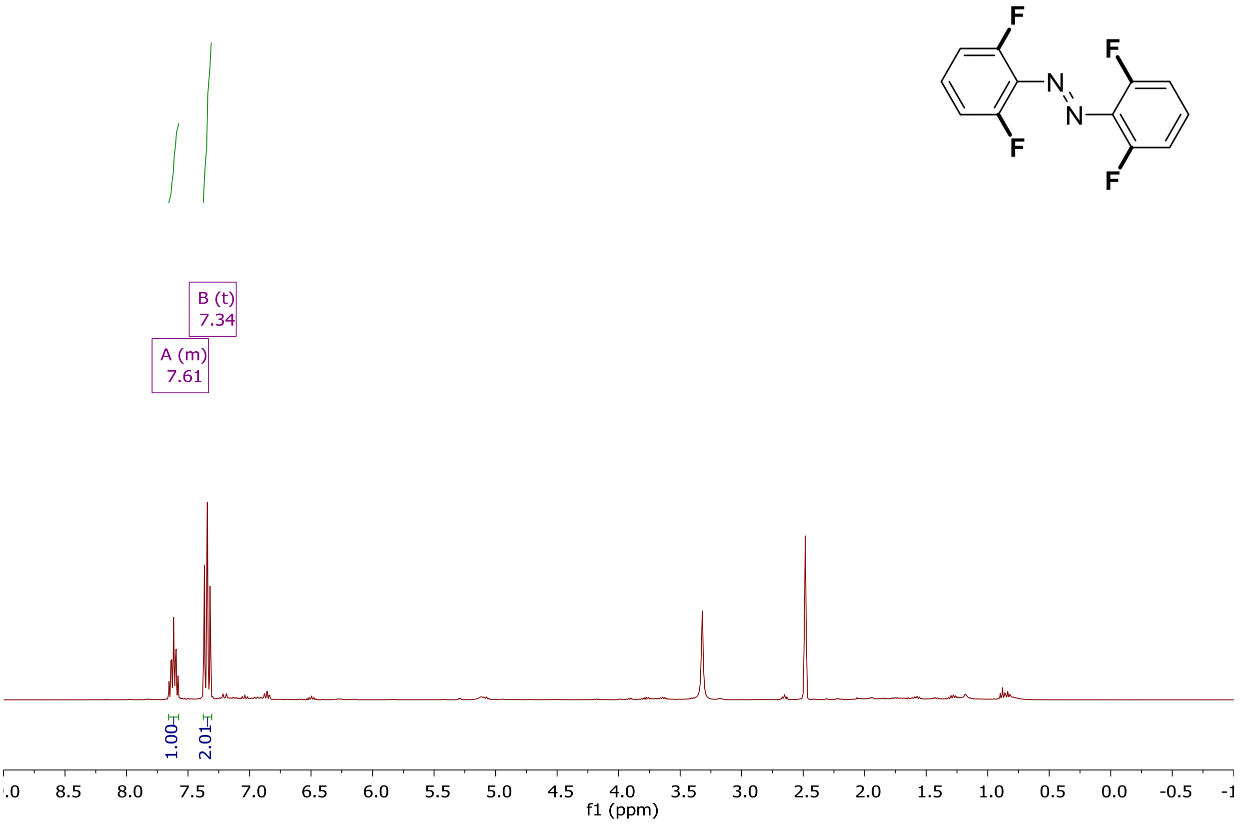

F
F
N
N
O
O
B (t)
7.37
A (m)
7.50
D (d)
6.82
C (td)
7.28
E (s)
3.76
1.00
1.01
1.92
2.03
6.25
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

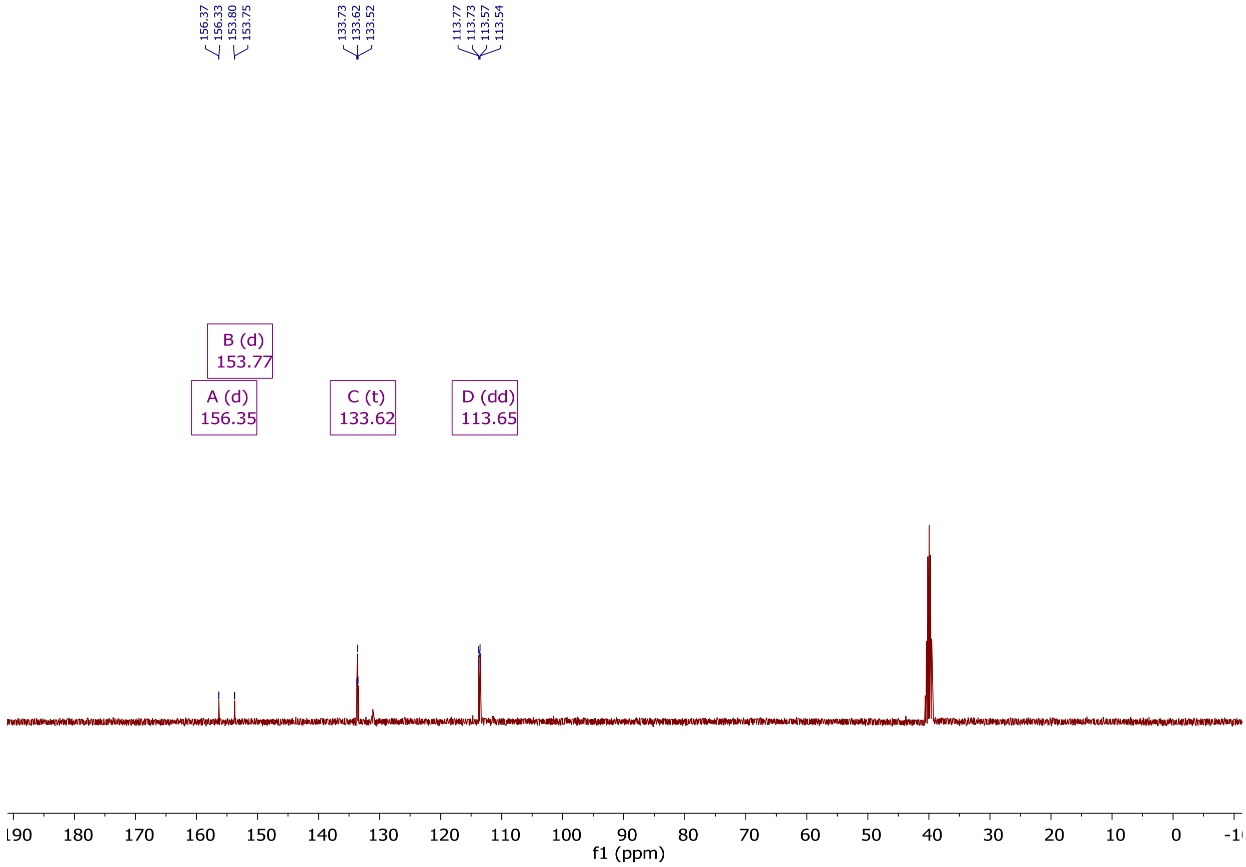

155.94
155.90
153.40
153.35
152.31
133.54
131.73
131.61
131.50
131.40
113.44
113.39
113.26
113.21
105.67
56.71
B (d)
153.38
A (d)
155.92
F (t)
131.50
G (m)
113.33
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)

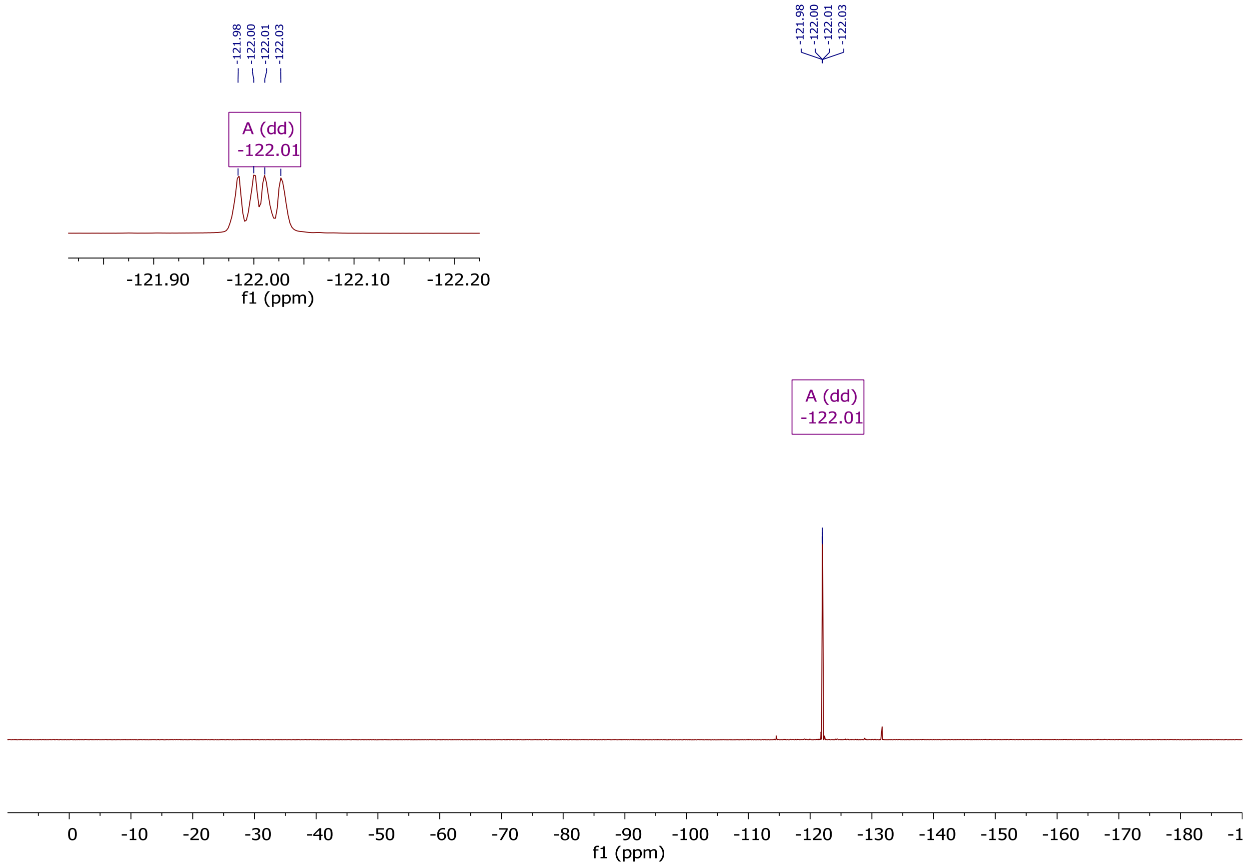

-123.88
-123.88
-123.75-123.80-123.85-123.90-123.95-124.00
f1 (ppm)
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -1
f1 (ppm)

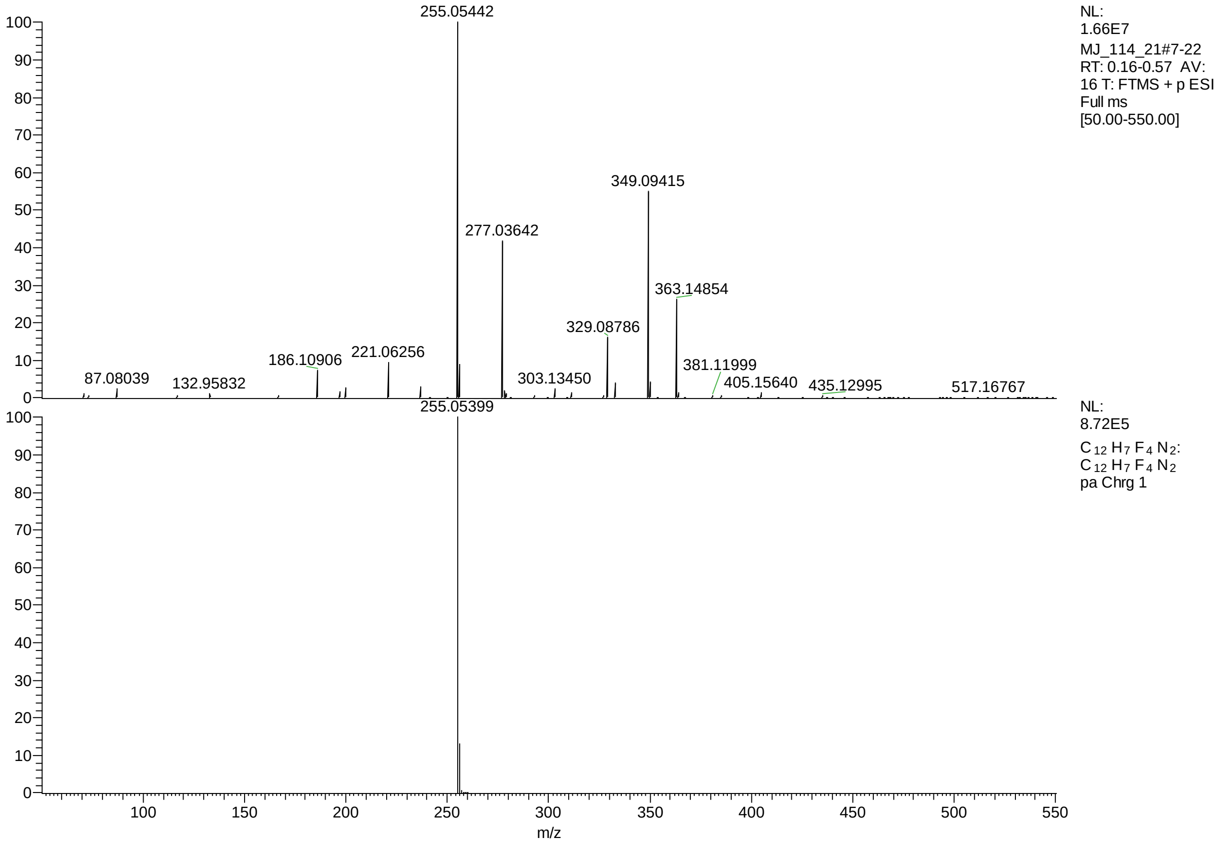


3o: After thermal adaption, no full conversion to the *trans* isomer was observed which became apparent in the ^{1}H-NMR and ^{13}C-NMR spectrum showing small quantities of the *cis* isomer.

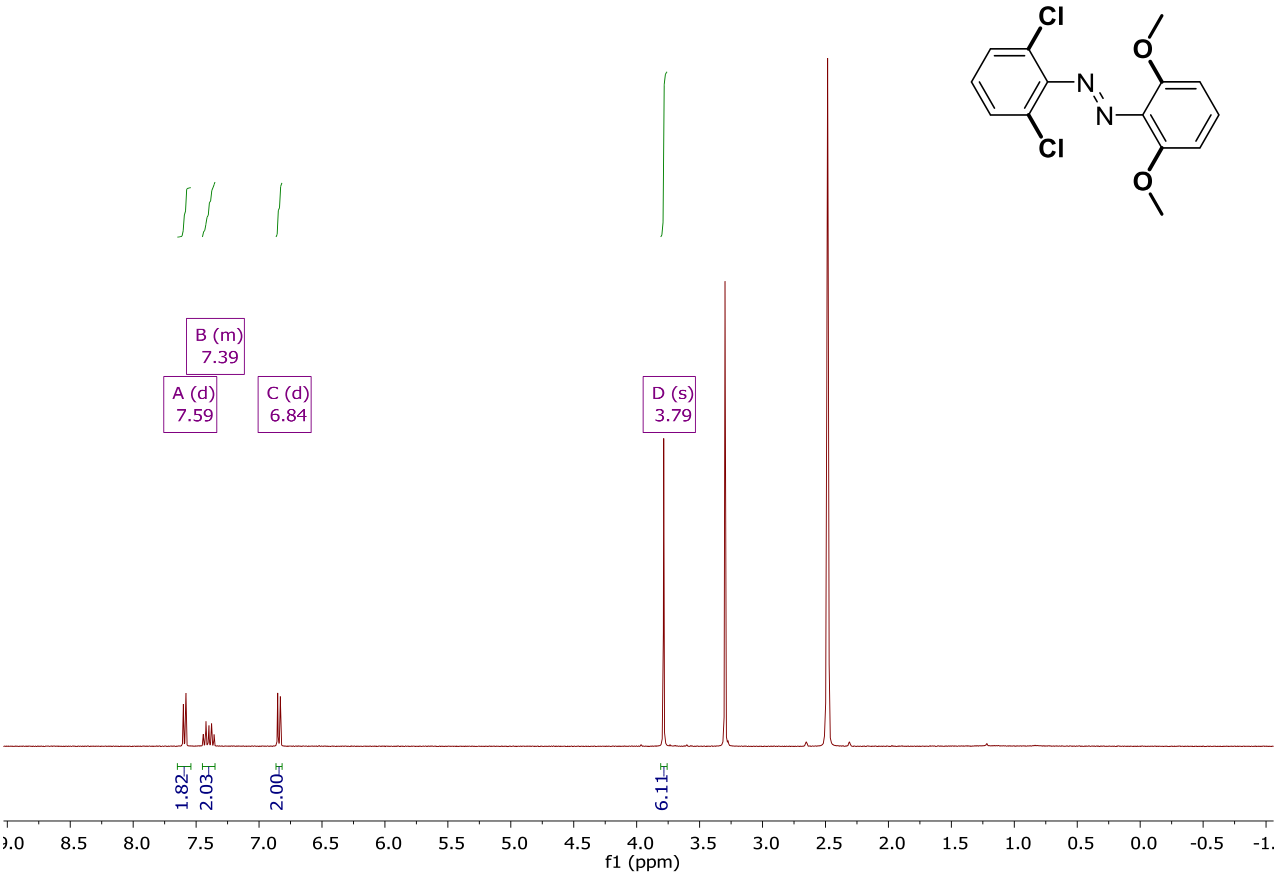


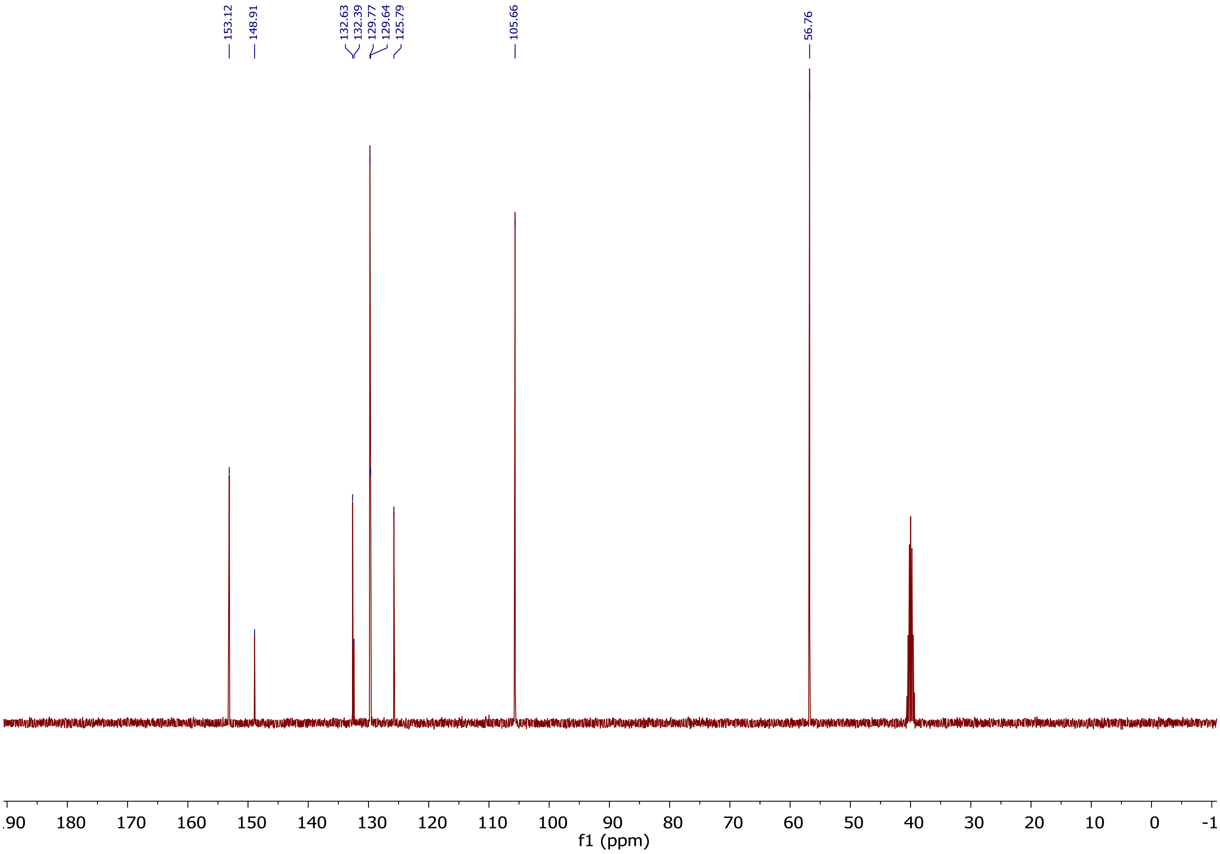

156.37
156.33
153.80
153.75
133.73
133.62
133.52
113.77
113.73
113.57
113.54
B (d)
153.77
A (d)
156.35
C (t)
133.62
D (dd)
113.65
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

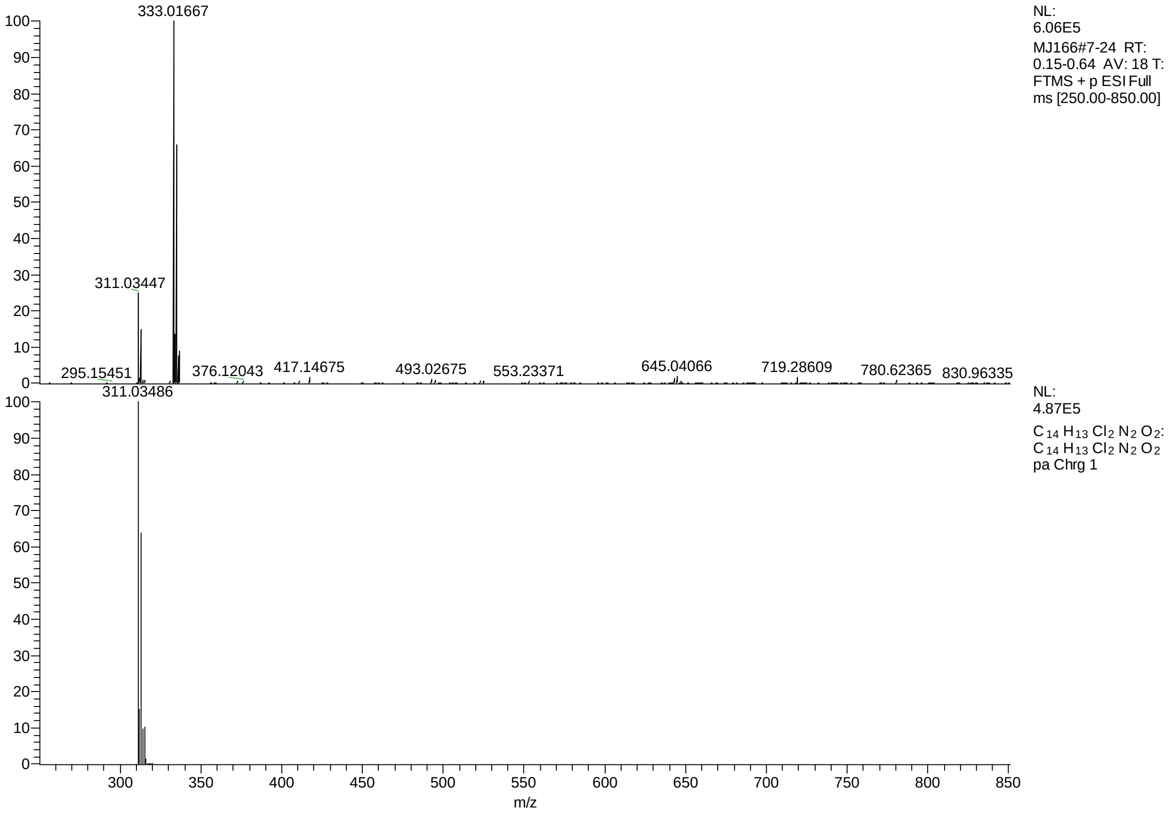

-121.98
-122.00
-122.01
-122.03
A (dd)
-122.01
-121.90
-122.00
-122.10
-122.20
f1 (ppm)
-121.98
-122.00
-122.01
-122.03
A (dd)
-122.01
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


255.05442
277.03642
349.09415
363.14854
329.08786
186.10906
221.06256
87.08039
132.95832
303.13450
381.11999
405.15640
435.12995
517.16767
NL:
1.66E7
MJ_114_21#7-22
RT: 0.16-0.57 AV:
16 T: FTMS + p ESI
Full ms
[50.00-550.00]
255.05399
NL:
8.72E5
C 12 H7 F4 N2:
C 12 H7 F4 N2
pa Chrg 1
m/z

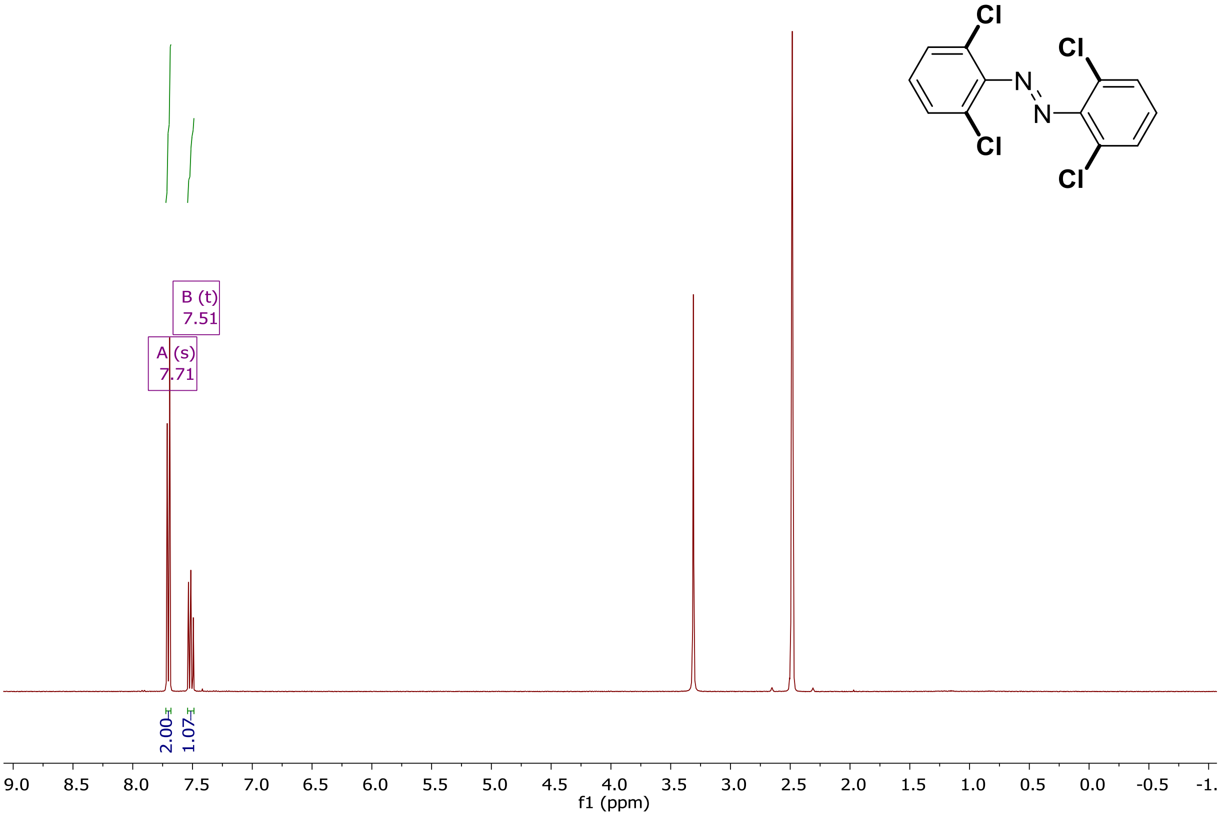
3p:

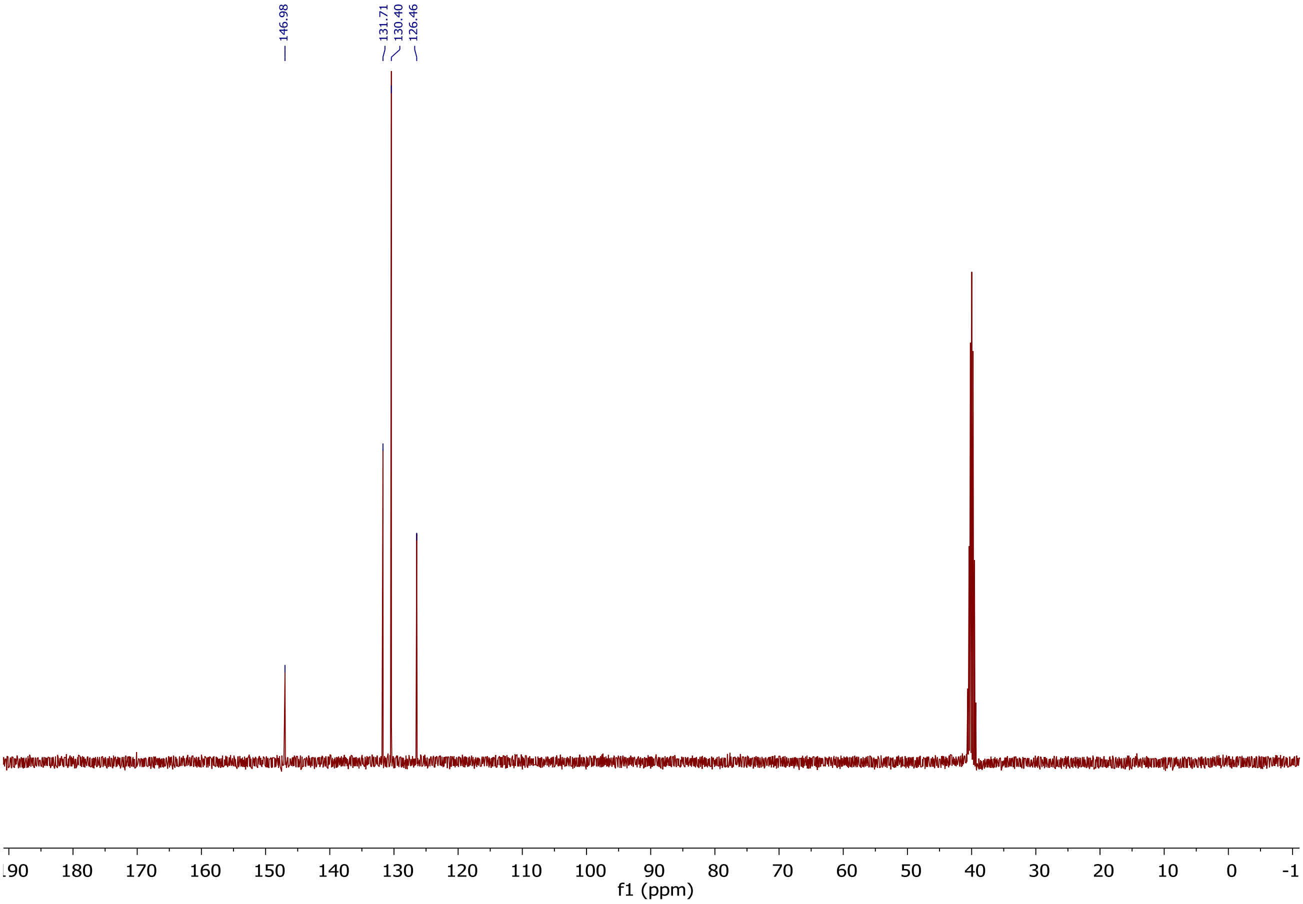

Cl
Cl
N
N
O
O
B (m)
7.39
A (d)
7.59
C (d)
6.84
D (s)
3.79
1.82
2.03
2.00
6.11
f1 (ppm)

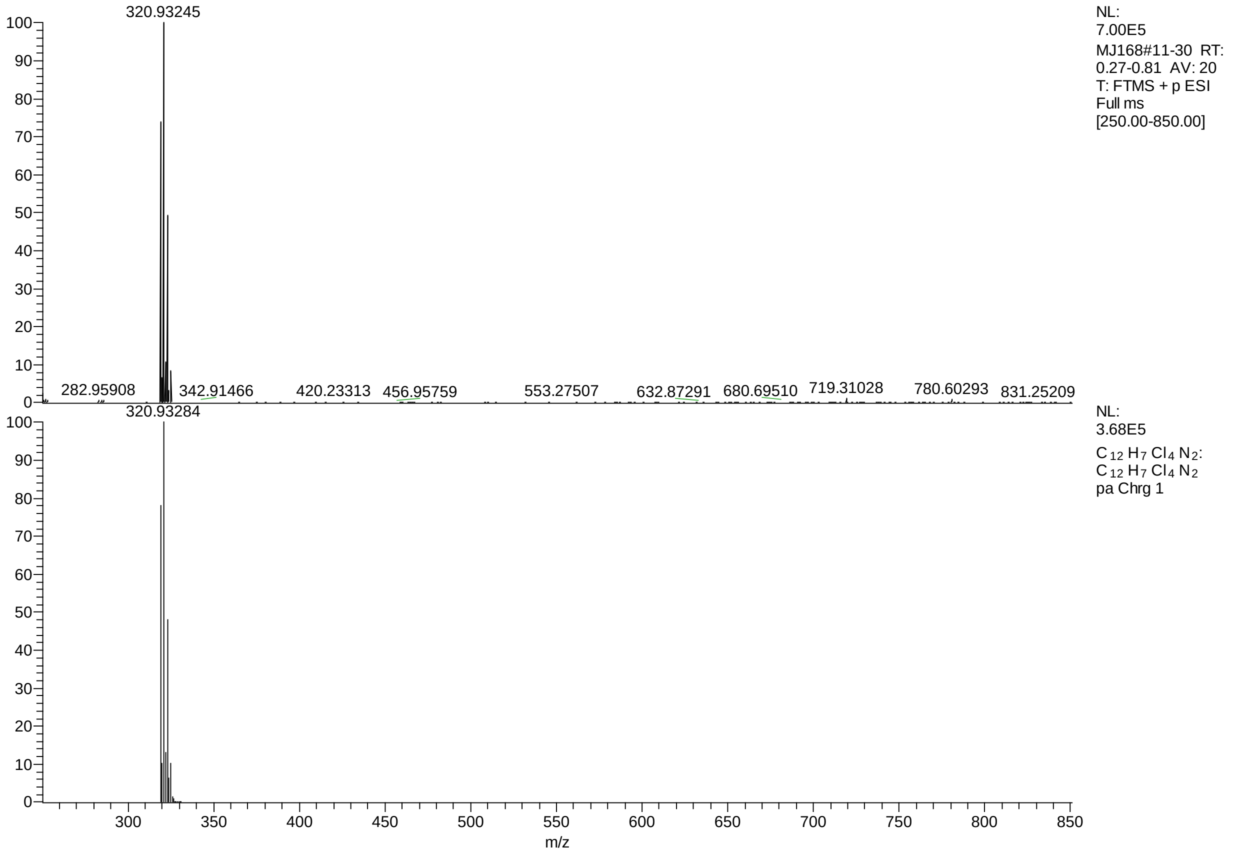

153.12
148.91
132.63
132.39
129.77
129.64
125.79
105.66
56.76
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


333.01667
311.03447
295.15451
376.12043
417.14675
493.02675
553.23371
645.04066
719.28609
780.62365
830.96335
NL:
6.06E5
MJ166#7-24 RT:
0.15-0.64 AV: 18 T:
FTMS + p ESI Full
ms [250.00-850.00]
311.03486
NL:
4.87E5
C 14 H 13 Cl 2 N 2 O 2:
C 14 H 13 Cl 2 N 2 O 2
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
300
350
400
450
500
550
600
650
700
750
800
850
m/z

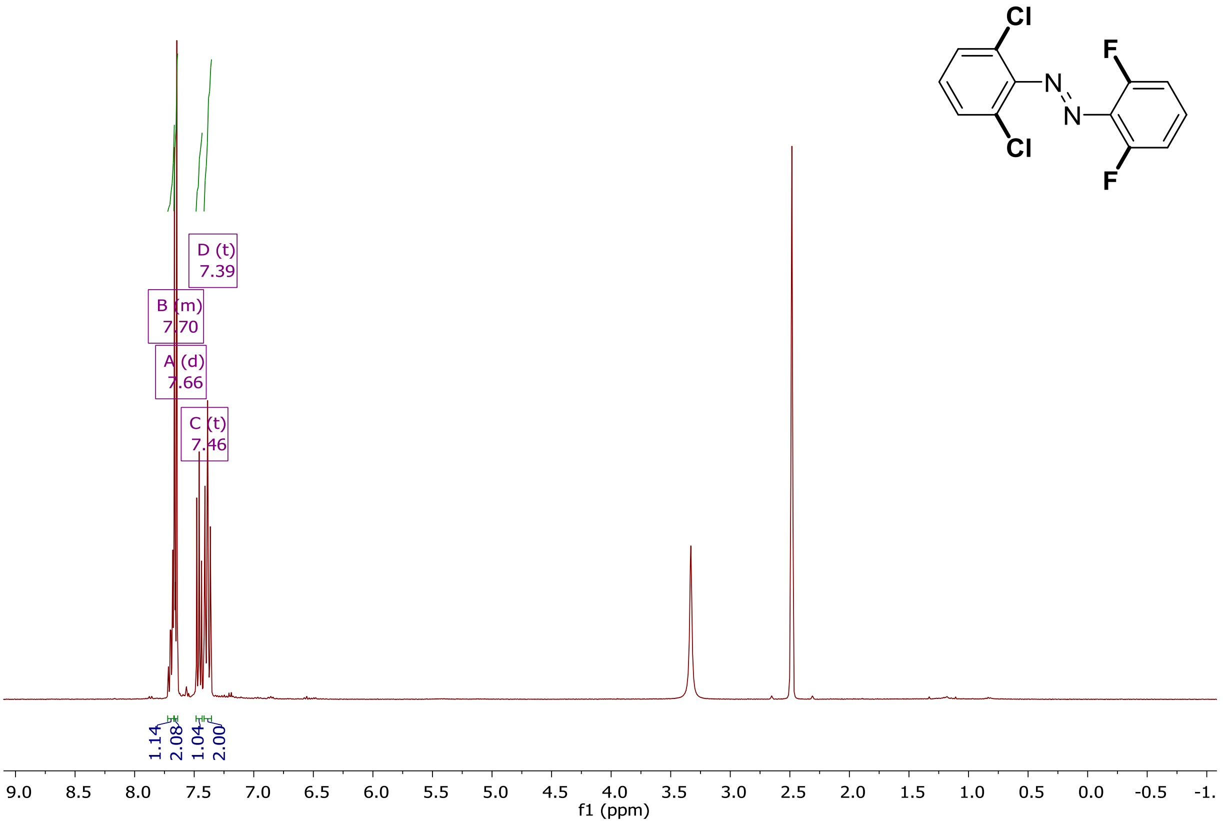
3q:

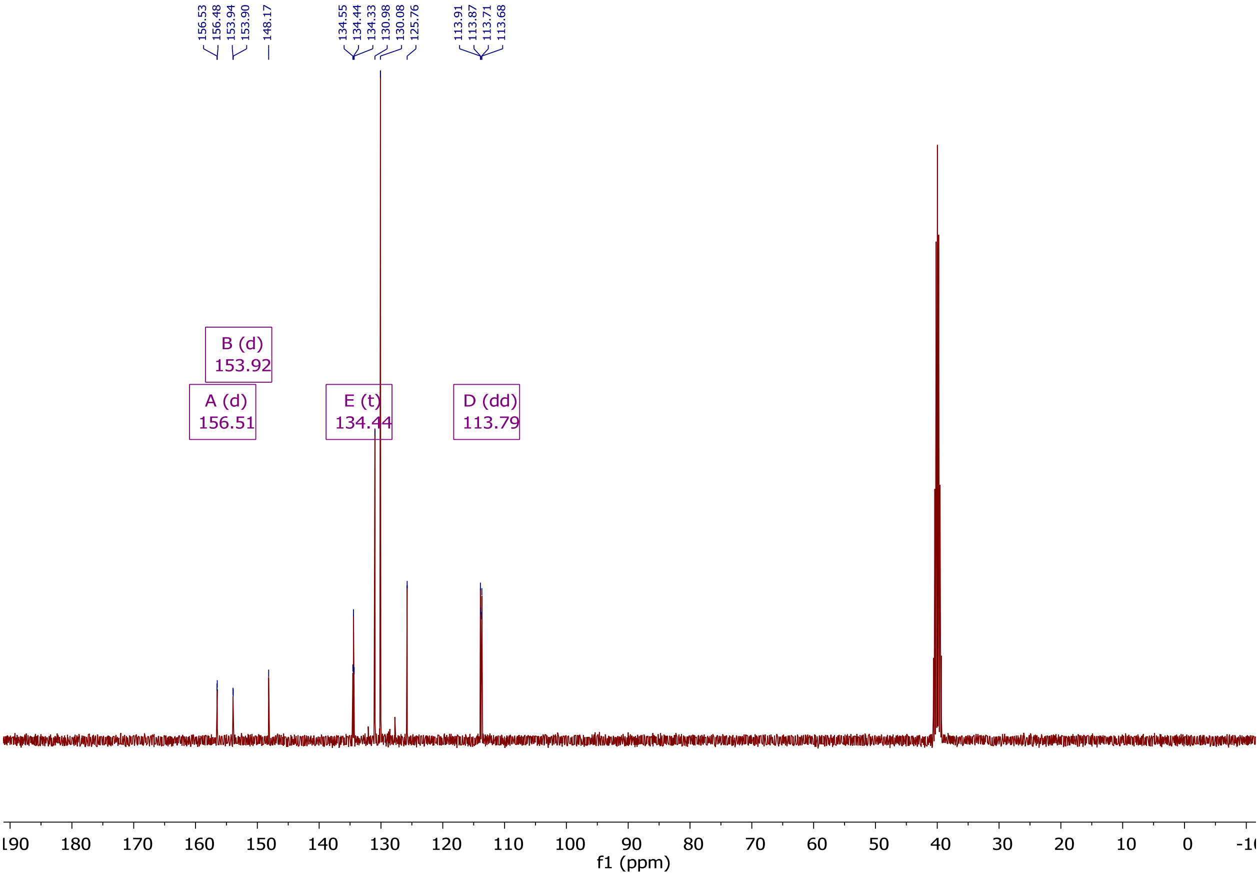

Cl
N
N
Cl
Cl
Cl
B (t)
7.51
A (s)
7.71
2.00
1.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

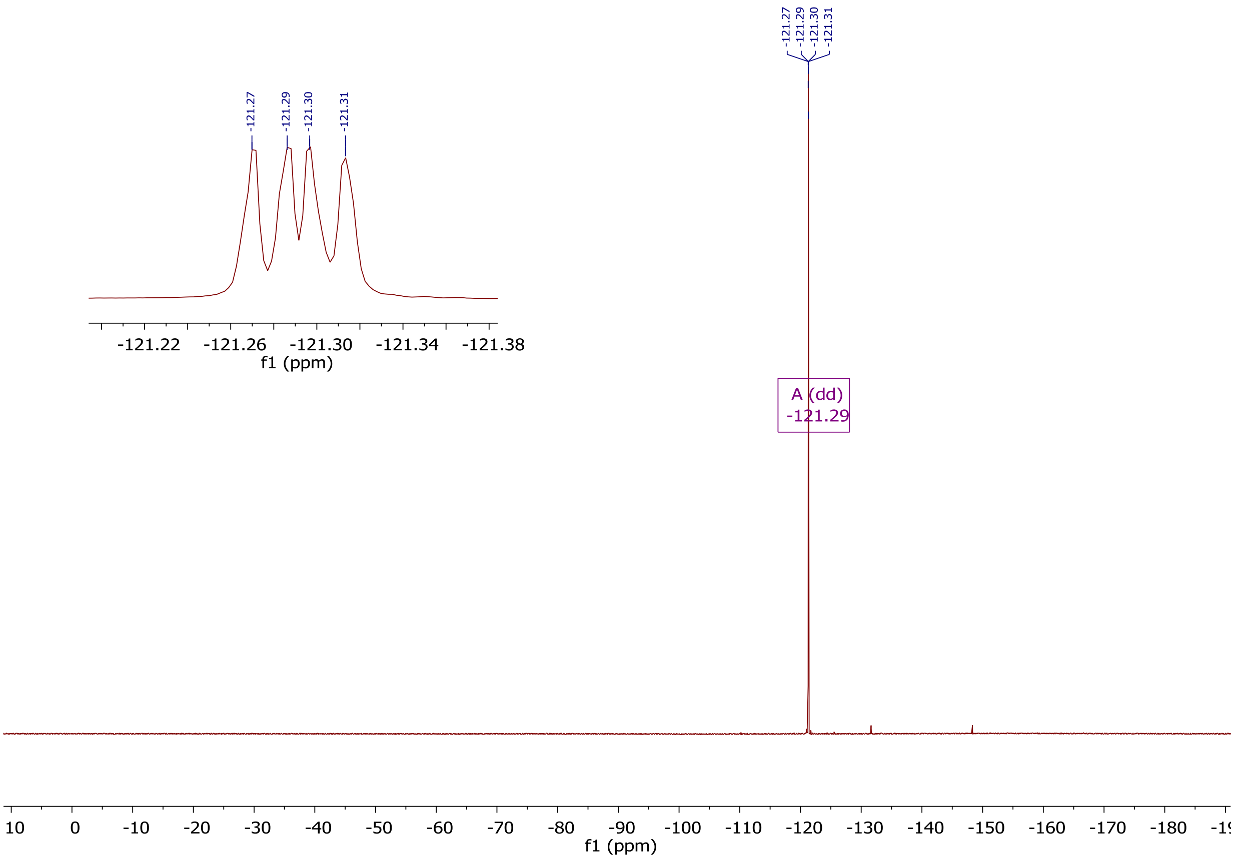

146.98
131.71
130.40
126.46
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)

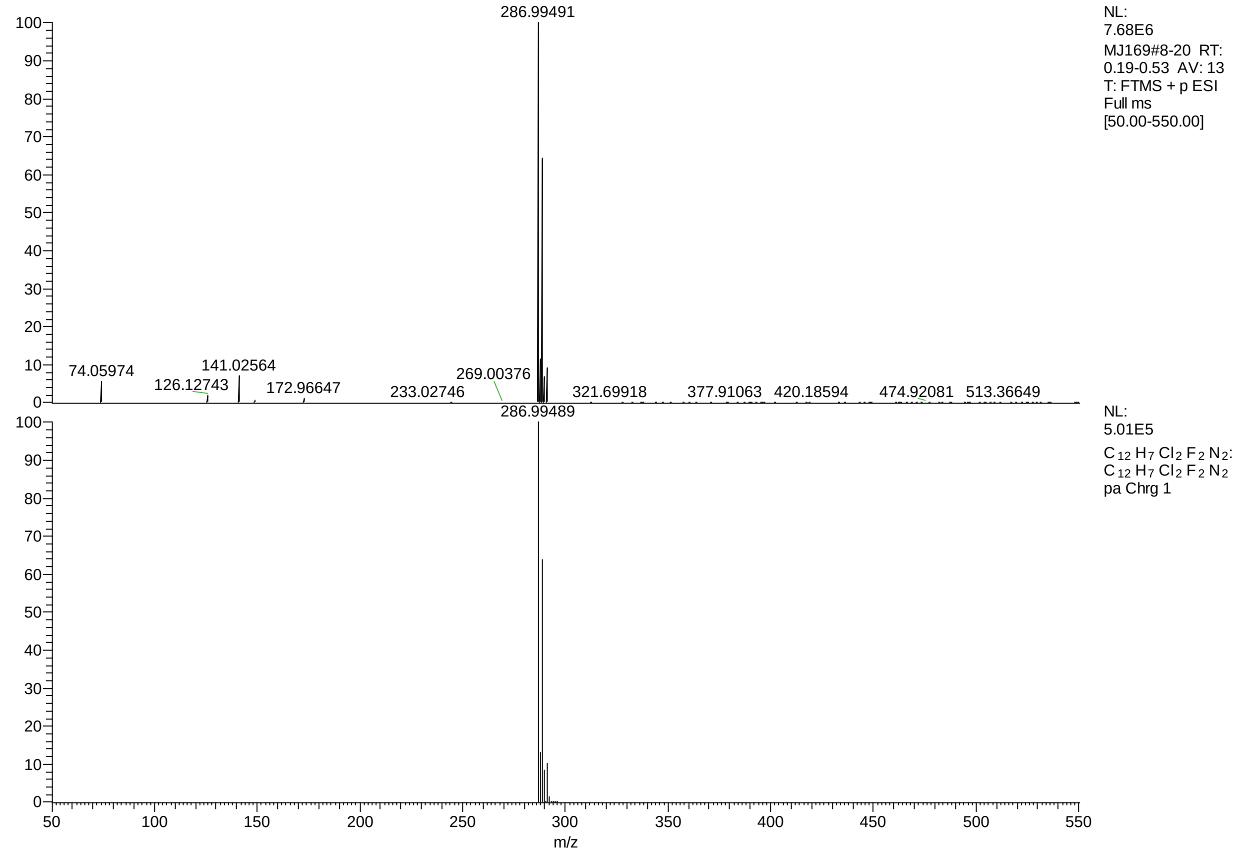

320.93245
NL:
7.00E5
MJ168#11-30 RT:
0.27-0.81 AV: 20
T: FTMS + p ESI
Full ms
[250.00-850.00]
282.95908
342.91466
420.23313
456.95759
553.27507
632.87291
680.69510
719.31028
780.60293
831.25209
320.93284
NL:
3.68E5
C 12 H7 Cl4 N2:
C 12 H7 Cl4 N2
pa Chrg 1
0
10
20
30
40
50
60
70
80
90
100
300
350
400
450
500
550
600
650
700
750
800
850
m/z

3r:

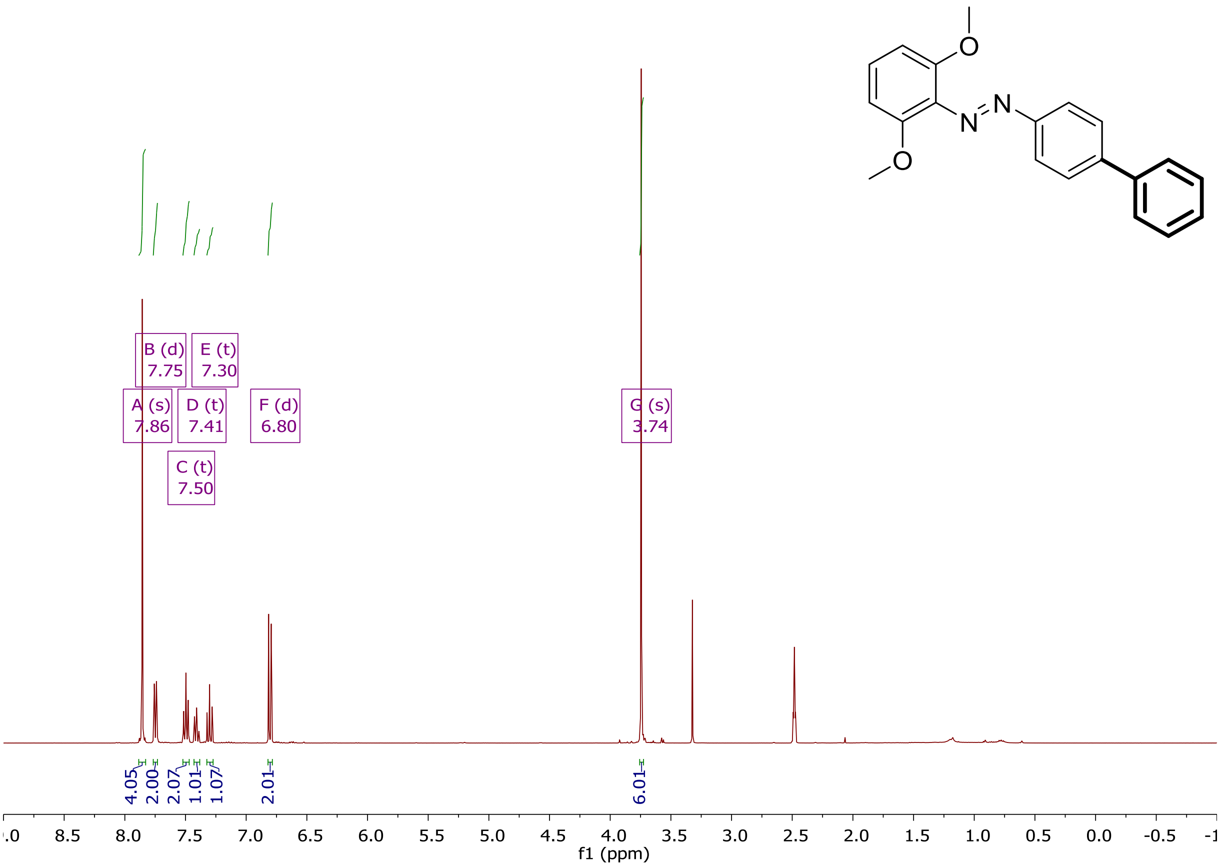

Cl
F
N
N
Cl
F
D (t)
7.39
B (m)
7.70
A (d)
7.66
C (t)
7.46
1.14
2.08
1.04
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

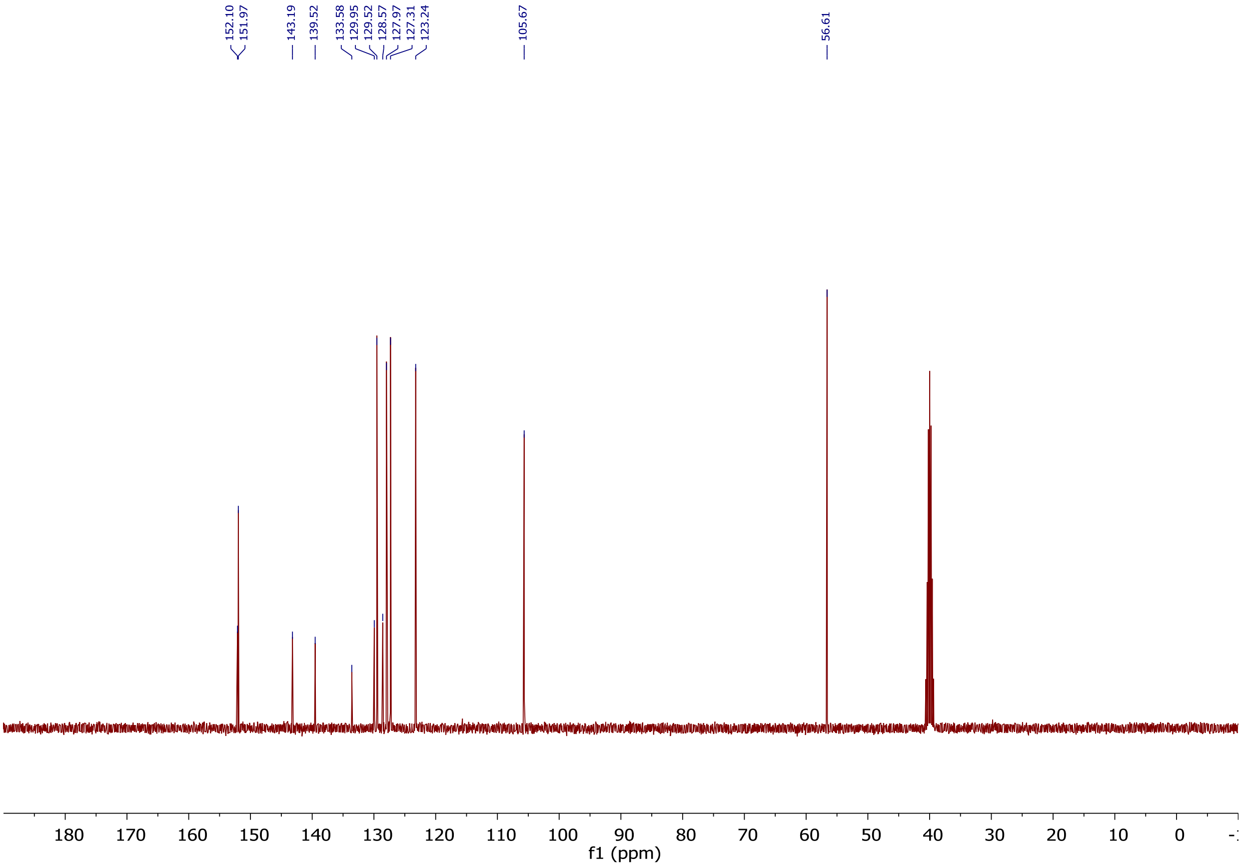

156.53
156.48
153.94
153.90
148.17
134.55
134.44
134.33
130.98
130.08
125.76
113.91
113.87
113.71
113.68
B (d)
153.92
A (d)
156.51
E (t)
134.44
D (dd)
113.79
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

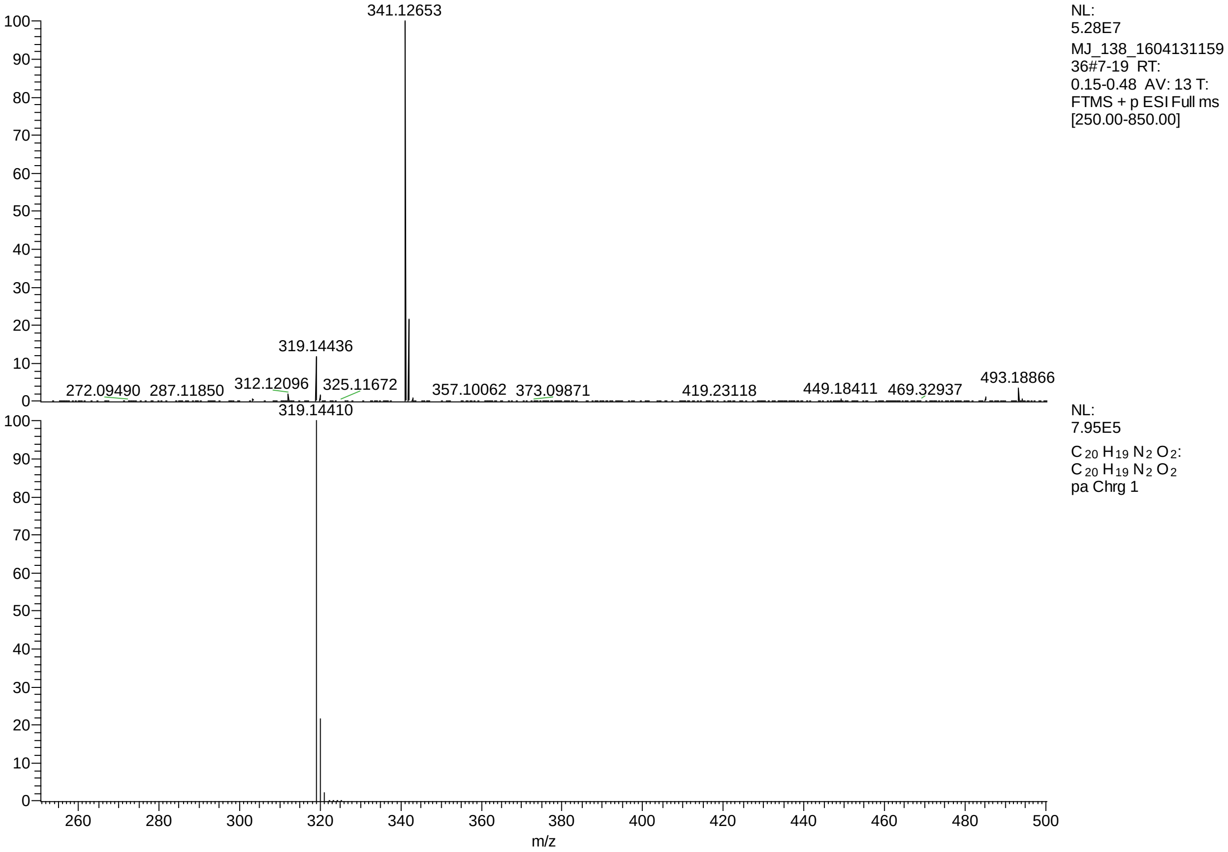

-121.27
-121.29
-121.30
-121.31
-121.27
-121.29
-121.30
-121.31
-121.22
-121.26
-121.30
-121.34
-121.38
f1 (ppm)
A (dd)
-121.29
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


286.99491
NL:
7.68E6
MJ169#8-20 RT:
0.19-0.53 AV: 13
T: FTMS + p ESI
Full ms
[50.00-550.00]
74.05974
126.12743
141.02564
172.96647
233.02746
269.00376
321.69918
377.91063
420.18594
474.92081
513.36649
286.99489
NL:
5.01E5
C 12 H 7 Cl 2 F 2 N 2:
C 12 H 7 Cl 2 F 2 N 2
pa Chrg 1
m/z
0
10
20
30
40
50
60
70
80
90
100
50
100
150
200
250
300
350
400
450
500
550

3s:


O
N
N
O
A (s)
7.86
B (d)
7.75
C (t)
7.50
D (t)
7.41
E (t)
7.30
F (d)
6.80
G (s)
3.74
4.05
2.00
2.07
1.01
1.07
2.01
6.01
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


152.10
151.97
143.19
139.52
133.58
129.95
129.52
128.57
127.97
127.31
123.24
105.67
56.61
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


341.12653
NL:
5.28E7
MJ_138_1604131159
36#7-19 RT:
0.15-0.48 AV: 13 T:
FTMS + p ESI Full ms
[250.00-850.00]
319.14436
272.09490
287.11850
312.12096
325.11672
357.10062
373.09871
419.23118
449.18411
469.32937
493.18866
319.14410
NL:
7.95E5
C 20 H 19 N 2 O 2:
C 20 H 19 N 2 O 2
pa Chrg 1
100
90
80
70
60
50
40
30
20
10
0
260
280
300
320
340
360
380
400
420
440
460
480
500
m/z

References

[1] P. S. J. Canning, K. McCrudden, H. Maskill, B. Sexton, *J. Chem. Soc. Perkin Trans. 2* **1999**, 2735–2740.

[2] U. Wannagat, G. Hohlstein, *Chem. Ber.* **1955**, *88*, 1839–1846.