Supplementary Material (ESI) for Chemical Communications
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Supporting information

Direct functionalization of BODIPY dyes by oxidative nucleophilic hydrogen substitution at the 3- or 3,5-positions

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Experimental procedures and characterization data

Chemicals where purchased from Acros Organics, and used as received. All reactions were carried out in flame dried glassware, but no special precautions were to taken for the exclusion of moisture. Solvents were not dried prior to use. Oxygen gas was 99.5% pure.
^{1}H and ^{13}C NMR spectra were recorded at room temperature on a Bruker Avance 300 instrument operating at a frequency of 300 MHz for ^{1}H and 75 MHz for ^{13}C. In the case of ambiguous assignments, spectra were run on a Bruker 400 or Bruker 600. ^{1}H NMR spectra in $CDCl_3$ were referenced to tetramethylsilane (0.00 ppm) as an internal standard. ^{13}C NMR spectra in $CDCl_3$ were referenced to the $CDCl_3$ (77.67 ppm) signal. ^{1}H NMR spectra in CD_3CN were referenced to CH_3CN (1.94 ppm) as an internal standard. ^{13}C NMR spectra in CD_3CN were referenced to the CD_3CN (118.2 ppm) signal. Mass spectra were recorded on a Hewlett-Packard 5989A mass spectrometer (EI mode and CI mode). High-resolution mass data were obtained with a Kratos MS50TC instrument. Melting points were taken on a Reichert Thermovar and are uncorrected. ^{19}F-NMR were recorded on a Bruker 600 MHz, and referenced to $CFCl_3$.
Absorption spectra where recorded on a Perkin Elmer Lambda 40. For the corrected steady-state emission spectra, a SPEX Fluorolog was used. Freshly prepared samples in 1-cm quartz cells were utilized to perform all UV–vis absorption and emission measurements. For the determination of the relative fluorescence quantum yields (Φ_f) in solution, only dilute solutions with an absorbance below 0.1 at the excitation wavelength of 500 nm were used. Rhodamine 6G ($\Phi_f = 0.95$)in spectrograde ethanol (Fluka) was used as standard to determine the fluorescence quantum yields. All spectroscopic measurements were done at 20 °C.
8-arylated BODIPY dyes were prepared according to standard literature procedures, through a water based dipyrromethane synthesis[i] and oxidation and condensation.[ii]

Oxidative substitution:

Optimization of reaction protocol:

Table 1: Optimization of oxidative nucleophlic hydrogen substitution with butylamine.

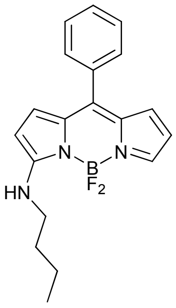
Solvent	Oxidizer	Reaction Time	Yield (%)
-[a]	Air	16 h	11
CH_3CN	O_2	5 days	33
THF	O_2	14 days	16[b]
DMSO	O_2	24 h	41
DMF	O_2	16 h	65
NMP	O_2	16 h	55
DMF	Air	24 h	48
DMF	DDQ	48 h	26
DMF	PCA	48 h	31
DMF	$AgPyMnO_4$	48 h	16

a) Butylamine was used as the solvent; b) Reaction not complete at this stage

Oxidative subsitution: General procedure for amine substitution

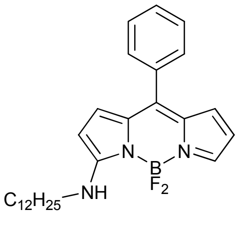
To a solution of BODIPY **1** (0.5 mmol, 134 mg) in DMF (5ml) is added the corresponding amine (0.55 mmol, 2.1 equiv.). The mixture is flushed with oxygen and stirred at room temperature for the indicated time under an oxygen atmosphere. Subsequently, the solution is poured in diethyl ether (100 ml), washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product is purified by filtration over a silica pad with dichloromethane as solvent.

3-(*N*-Butylamino)-8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4a



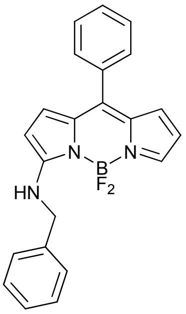
Red crystals; Mp 120°C; ^{1}H-NMR ($CDCl_3$, 600 MHz): δ 7.47 (m, 6H), 6.93 (d, 1H, J = 5.49 Hz), 6.42 (d, 1H, J = 2.73 Hz), 6.33 (d, 1H, J = 1.83 Hz), 6.32 (s, br, 1H, NH), 6.18 (d, 1H, J = 4.56 Hz), 3.41 (q, 2H, J = 6.39 Hz, J = 13.68 Hz), 1.73 (m, 2H), 1.46 (m, 2H), 0.97 (t, 3H, J = 9.72 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 161.9, 136.2, 134.7, 133.5, 132.8, 132.6, 130.9, 130.4, 129.1, 128.2, 119.8, 113.4, 110.4, 44.5, 32.2, 19.8, 13.7; ^{19}F-NMR ($CDCl_3$, 564 MHz): δ -149.50 (q, J = 35 Hz); MS (EI): 339; HRMS: Calculated for $C_{19}H_{20}N_3BF_2$: 339.17183, found 339.17353.

3-(*N*-Dodecylamino)-8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4b



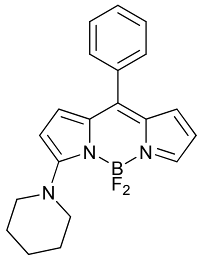
Red oil; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.46 (s, 6H), 6.93 (d, 1H, J = 4.56 Hz), 6.41 (s, 1H), 6.33 (s, 1H), 6.28 (s, br, 1H, NH), 6.18 (d, 1H, J = 5.49 Hz), 3.39 (q, 2H, J = 6.39 Hz, J = 12.78 Hz)), 1.69 (m, 2H), 1.26 (m, 18 H), 0.87 (t, 3H, J = 7.32 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 161.9, 136.2, 134.8, 133.5, 132.8, 131.0, 130.4, 129.2, 128.3, 119.9, 113.5, 110.4, 44.9, 32.0, 30.2, 29.7, 29.6, 29.5, 29.4, 29.3, 26.7, 22.8, 14.2; MS (EI): 451; HRMS: Calculated for $C_{27}H_{36}N_3BF_2$: 451.2970, found 451.29731.

3-(*N*-Benzylamino)-8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4c



Red solid; Mp 156°C; ^{1}H-NMR (CDCl$_3$, 300 MHz): δ 7.88 (d, 1H, J = 8.22 Hz), 7.43 (m, 10H), 6.9 (d, 1H, J = 4.56 Hz), 6.66 (s, br, 1H, NH), 6.34 (s, 1H), 6.13 (d, 1H, J = 4.6 Hz), 4.61 (d, 1H, J = 6.39 Hz); ^{13}C-NMR (CDCl$_3$, 75 MHz): δ 161.9, 136.7, 136.2, 134.6, 133.9, 133.4, 132.7, 131.7, 130.4, 129.8, 129.3, 129.1, 128.2, 126.9, 120.6, 113.8, 110.3, 48.3; MS (EI): 373; HRMS: Calculated for $C_{22}H_{18}N_3BF_2$: 373.1561, found 373.15777.

3-(*N*-Piperidinyl)-8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene 4d

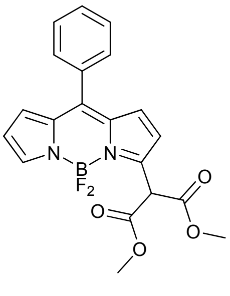


Red crystals; Mp 55°C; ^{1}H-NMR (CDCl$_3$, 300 MHz): δ 7.44 (m, 6H), 6.86 (d, 1H, J = 5.46 Hz), 6.32 (s, 2H), 6.26 (d, 1H, J = 5.49 Hz), 3.90 (d, 4H, J = 4.56 Hz), 1.78 (m, 6H); ^{13}C-NMR (CDCl$_3$, 150 MHz): δ 162.1, 135.7, 135.6, 135.4, 131.9, 131.5, 130.7, 130.5, 128.9, 128.1, 117.9, 113.9, 51.9, 26.5, 24.8; IR (thin film): 2937, 2857; MS (EI): 351; HRMS: Calculated for $C_{20}H_{20}N_3BF_2$: 351.17183, found 351.17179.

Oxidative subsitution: General procedure for malonate substitution

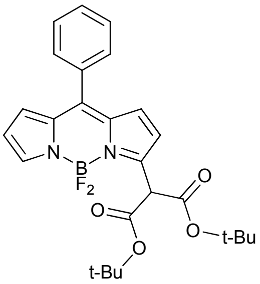
To a solution of BODIPY **1** (0.5 mmol, 134 mg) in DMF (5ml) is added the corresponding malonate (0.55 mmol, 1.1 equiv.), followed by Na_2CO_3 (1 mmol, 106 mg, 2 equiv.). The mixture is flushed with oxygen and stirred at room temperature for the indicated time under an oxygen atmosphere. Subsequently, the solution is poured in diethyl ether (100 ml), washed with diluted aqueous HCl and brine, dried over MgSO4, filtered, and evaporated to dryness. The crude product is purified by column chromatography (silica, CH_2Cl_2).

Dimethyl 2-(8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacen-3-yl) malonate



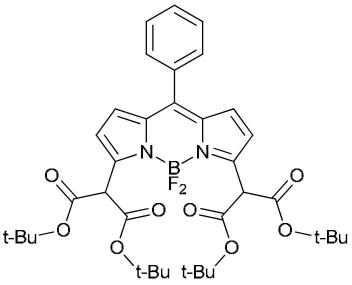
Orange solid; Mp 138°C; ^{1}H-NMR (CDCl$_3$, 400 MHz): δ 7.88 (s, 1H), 7.58-7.48 (m, 5H), 6.92 (d, 1H, J = 4.28 Hz), 6.88 (d, 1H, J = 4 Hz), 6.68 (d, 1H, J = 4.28 Hz), 6.52 (m, 1H), 5.52 (s, 1H), 3.81 (s, 6H); ^{13}C-NMR (CDCl$_3$, 150 MHz): δ 166.7, 150.5, 147.1, 144.1, 134.9, 133.5, 131.8, 131.5, 130.7, 130.4, 128.4, 119.5, 118.8, 53.3, 51.8; MS (EI): 398; HRMS: Calculated for $C_{20}H_{17}N_2O_4BF_2$: 398.1249, found 398.12325.

Di-*t*-butyl 2-(8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacen-3-yl) malonate



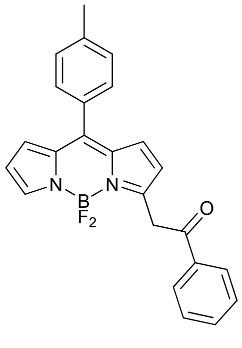
Orange solid; ^{1}H-NMR (CDCl$_3$, 400 MHz): δ 7.86 (s, 1H), 7.58-7.48 (m, 5H), 6.92 (d, 1H, J = 4.28 Hz), 6.85 (d, 1H, J = 3.76 Hz), 6.70 (d, 1H, J = 4.52 Hz), 6.50 (d, 1H, J = 2.52 Hz), 5.30 (s, 1H), 1.50 (s, 18H); ^{13}C-NMR (CDCl$_3$, 100 MHz): δ 165.5, 153.0, 146.6, 143.2, 135.2, 134.7, 133.9, 132.1, 130.8, 130.7, 130.5, 128.5, 119.9, 118.3, 82.9, 54.6, 27.9; MS (EI): 482; HRMS: Calculated for $C_{26}H_{29}BF_2N_2O_4$: 482.2188, found 482.2194.

3,5-*Bis*-(di-*t*-butylmalon-2-yl)-8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene



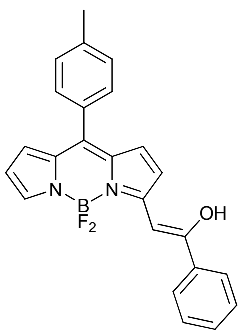
Orange solid; Mp 178°C; ^{1}H-NMR (CDCl$_3$, 300 MHz): δ 7.53 (m, 5H), 6.84 (d, 2H, J = 4.14 Hz), 6.67 (d, 2H, J = 4.14 Hz), 1.49 (s, 36H); ^{13}C-NMR (CDCl$_3$, 100 MHz): δ 165.5, 151.9, 145.8, 134.7, 133.8, 131.2, 130.5, 128.4, 119.6, 82.8, 54.4, 27.9; MS (EI): 696; HRMS: Calculated for $C_{37}H_{47}BF_2N_2O_8$: 696.3394, found 696.3394.

3-(Phenacyl)-8-(*p*-tolyl)-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene



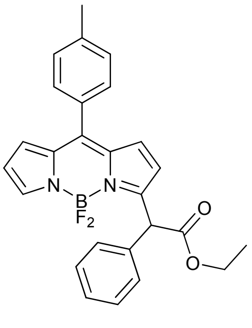
To a solution of 8-tolyl-BODIPY (0.5 mmol, 141 mg) in DMF (5ml) is added acetophenone (3g, 1.1 equiv.) followed by potassium bis(trimethylsilyl)amide (KHMDS, 1 mmol, 200 mg, 2 equiv.). The mixture is flushed with oxygen and stirred at room temperature for 6h under an oxygen atmosphere. Subsequently, the dark solution is poured in diethyl ether (100 ml), washed with diluted aqueous HCl and brine, dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product is purified by column chromatography (silica, CH_2Cl_2).

Orange solid; Mp 113-115°C; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.09 (d, 2H, J = 7.32 Hz), 7.99 (s, 1H), 7.61-7.44 (m, 5H), 7.31 (d, 2H, J = 7.74 Hz), 6.94 (d, 1H, J = 3.9 Hz), 6.86 (d, 1H, J = 3.39 Hz), 6.51 (m, 2H), 4.70 (s, 2H), 2.46 (s, 3H); ^{1}H-NMR (CD_3CN, 600 MHz): 8.05 (d, 2H, J = 7.14 Hz), 7.83 (s, 1H), 7.66 (t, 1H, J = 7.56 Hz), 7.55 (t, 2H, J = 7.5 Hz), 7.51 (d, 2H, J = 8.28 Hz), 7.38 (d, 2H, J = 7.56 Hz), 7.01 (d, 1H, J = 3.78 Hz), 6.90 (d, 1H, J = 3.36 Hz), 6.56 (m, 2H), 4.75 (s, 2H), 2.45 (s, 3H); ^{13}C-NMR (CD_3CN, 100 MHz): δ 195.7, 157.2, 147.2, 142.6, 142.4, 137.4, 136.0, 134.9, 134.4, 133.4, 133.2 ,131.6, 131.5, 131.0, 130.0, 129.7, 129.1, 122.5, 118.8, 39.7, 21.3; ^{19}F-NMR ($CDCl_3$, 565 MHz): δ -144.6 (q, J = 31 Hz) ppm; MS (EI): 400; HRMS: Calculated for $C_{24}H_{19}BF_2N_2O$: 400.1559, found 400.15672.



^{1}H-NMR (CD_3CN, 600 MHz): 7.89 (m, 2H), 7.81 (d, 1H, J = 5.16 Hz), 7.43 (m, 3H), 7.40 (d, 2H, J = 7.32 Hz), 7.27 (d, 2H, J = 7.38 Hz), 7.11 (s, 1H), 6.74 (d, 1H, J = 5.16 Hz), 6.66 (s, 1H), 6.16 (d, 1H, J = 2.22 Hz), 6.04 (d, 1H, J = 2.16 Hz), 2.40 (s, 3H, Tolyl-CH_3) ; ^{13}C-NMR (CD_3CN, 150 MHz): δ 185.6, 166.9, 144.0, 138.9, 1138.5, 135.0 134.2, 133.2, 132.0, 131.2, 130.7, 129.6, 129.0, 127.7, 126.7, 126.0, 121.0, 112.2, 111.7, 92.9, 21.2.

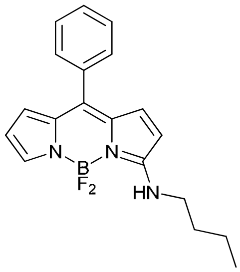
Ethyl (8-phenyl-4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacen-3-yl) phenylacetate



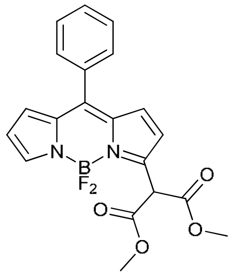
To a solution of 8-tolyl-BODIPY (0.5 mmol, 134 mg) in DMF (5ml) is added ethyl phenylacetate (90 mg, 1.1 equiv.) followed by NaO*t*Bu (1 mmol, 112 mg, 2 equiv.). The mixture is flushed with oxygen and stirred at room temperature for 6h under an oxygen atmosphere. Subsequently, the dark solution is poured in diethyl ether (100 ml), washed with diluted aqueous HCl and brine, dried over $MgSO_4$, filtered, and evaporated to dryness. The crude product is purified by column chromatography (silica, CH_2Cl_2).

Orange solid; No crystals obtained; ^{1}H-NMR ($CDCl_3$, 300 MHz): δ 7.84 (s, 1H), 7.47-7.28 (m, 9H), 6.88-6.84 (m, 2H), 6.54 (d, 1H, J = 4.5 Hz), 6.50 (m, 1H), 5.76 (s, 1H), 4.33-4.15 (m, 2H), 2.44 (s, 3H), 1.27 (t, 3H, J = 7.14 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz): δ 170.6, 158.2, 146.9, 142.4, 141.1, 136.5, 135.2, 134.5, 132.1, 131.1, 130.9, 130.6, 130.3, 129.2, 129.0, 128.7, 127.9, 120.0, 117.9, 61.8, 51.1, 23.5, 14.1; MS (EI): 444; HRMS: Calculated for $C_{26}H_{23}BF_2N_2O_2$: 444.1821, found 444.1837.

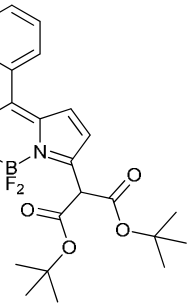
Spectroscopic data



4a



4e



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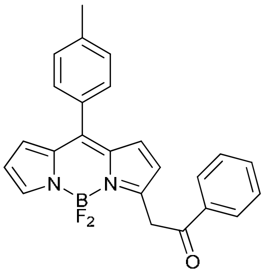
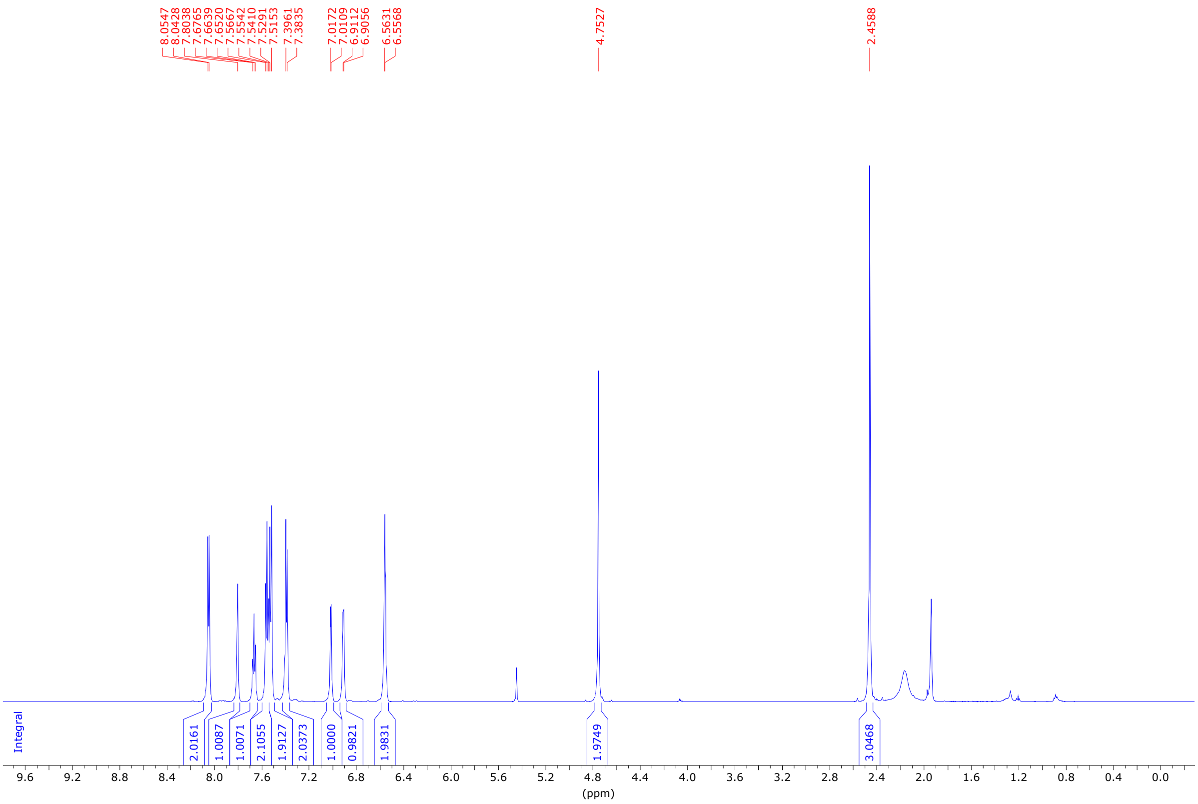


4h

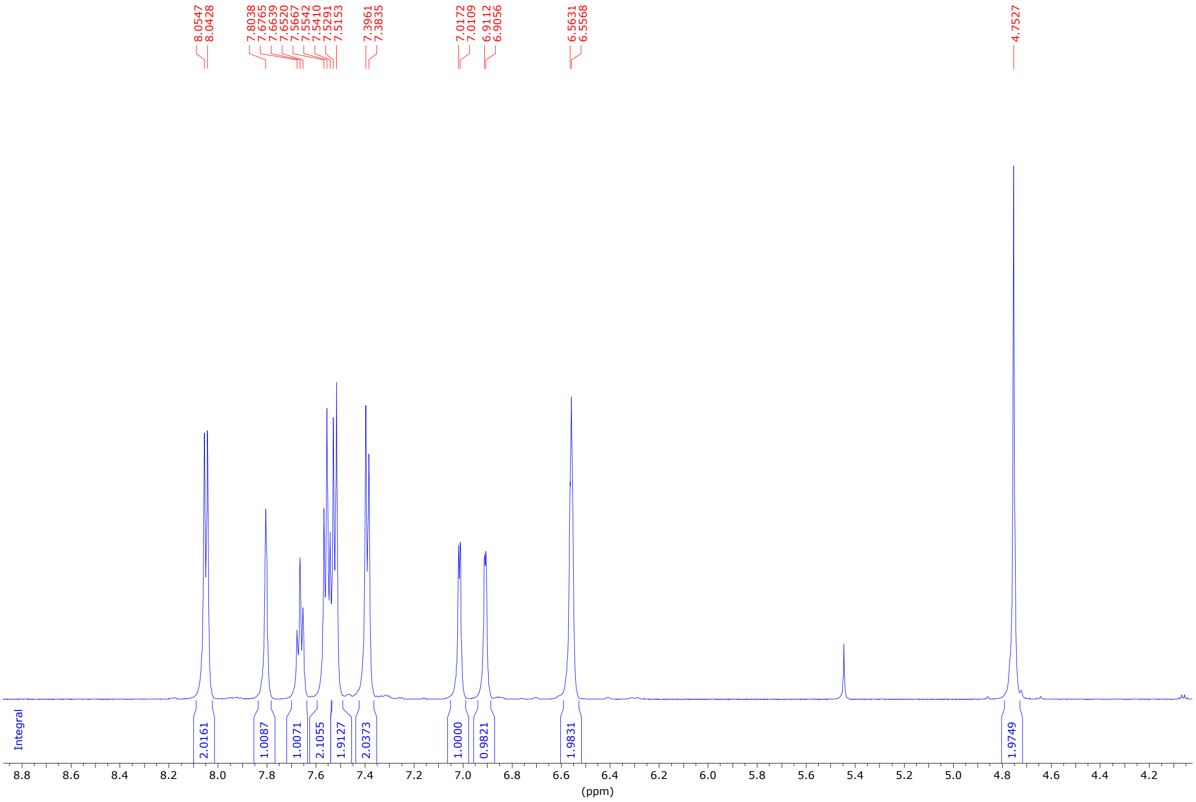
BODIPY	Solvent	λ_{abs} / nm	λ_{em} /nm	$\Delta\bar{\nu}$ /cm^{-1}	Φ_f
4a	MeCN	466	530	2591	0.013
	MeOH	468	529	2464	0.012
	THF	493	533	1522	0.019
	Toluene	505	533	1040	0.033
4e	MeCN	502	520	690	0.017
	MeOH	503	520	650	0.041
	THF	506	523	642	0.064
	Toluene	509	526	635	0.14
4f	MeCN	503	521	687	0.03
	MeOH	504	520	611	0.040
	THF	507	523	603	0.06
	Toluene	509	527	671	0.14
4h	MeCN	551	592	1257	0.002
	MeOH	569	625	1575	0.022
	THF	506	523	642	0.08
	Toluene	508	526	674	0.087

NMR-analysis of base induced tautomerization

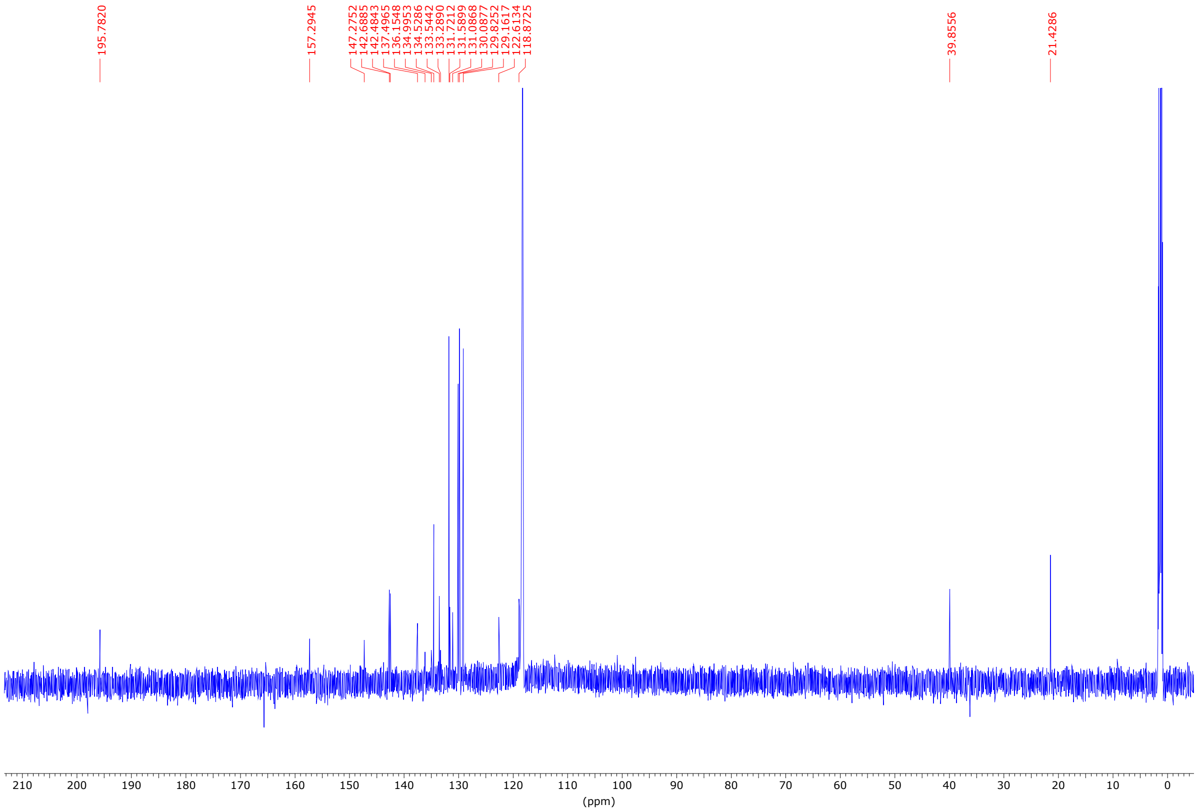
4h, ^{1}H, 600 MHz, CD$_3$CN, Full spectrum ↓



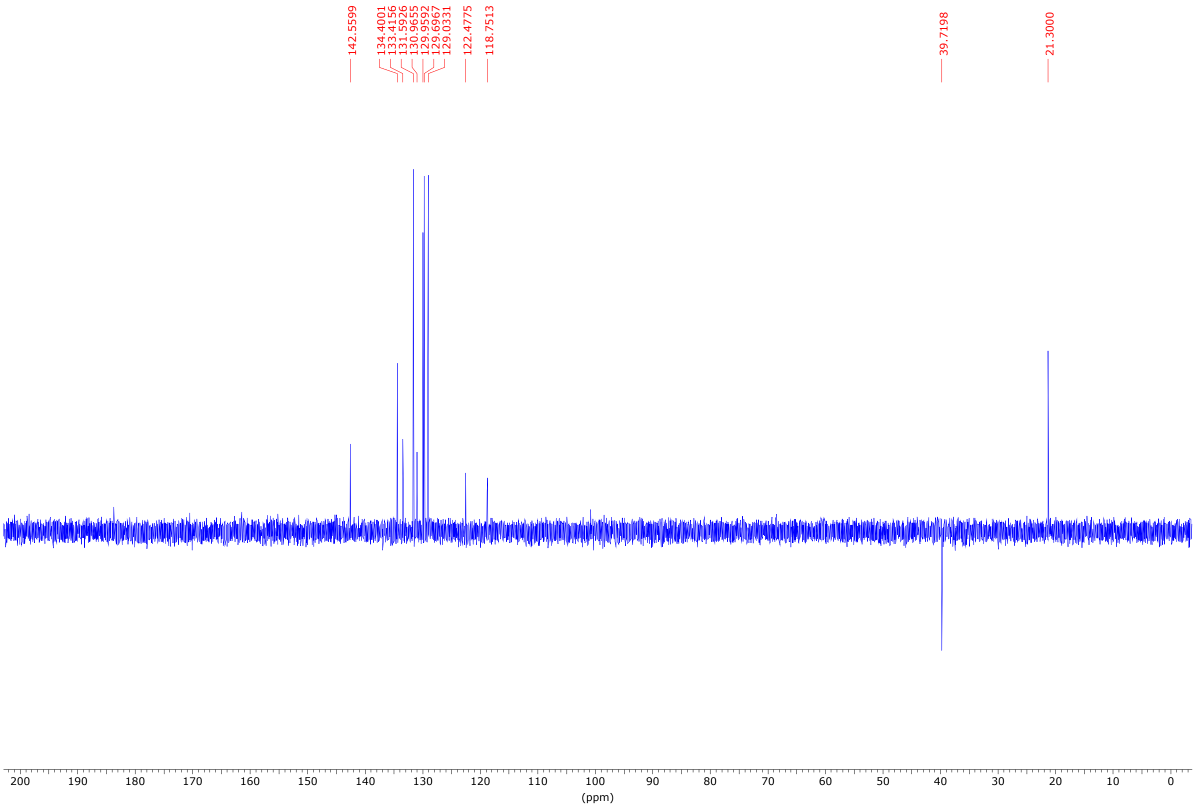
4h, ^{1}H, 600 MHz, CD$_3$CN, Zoom ↓



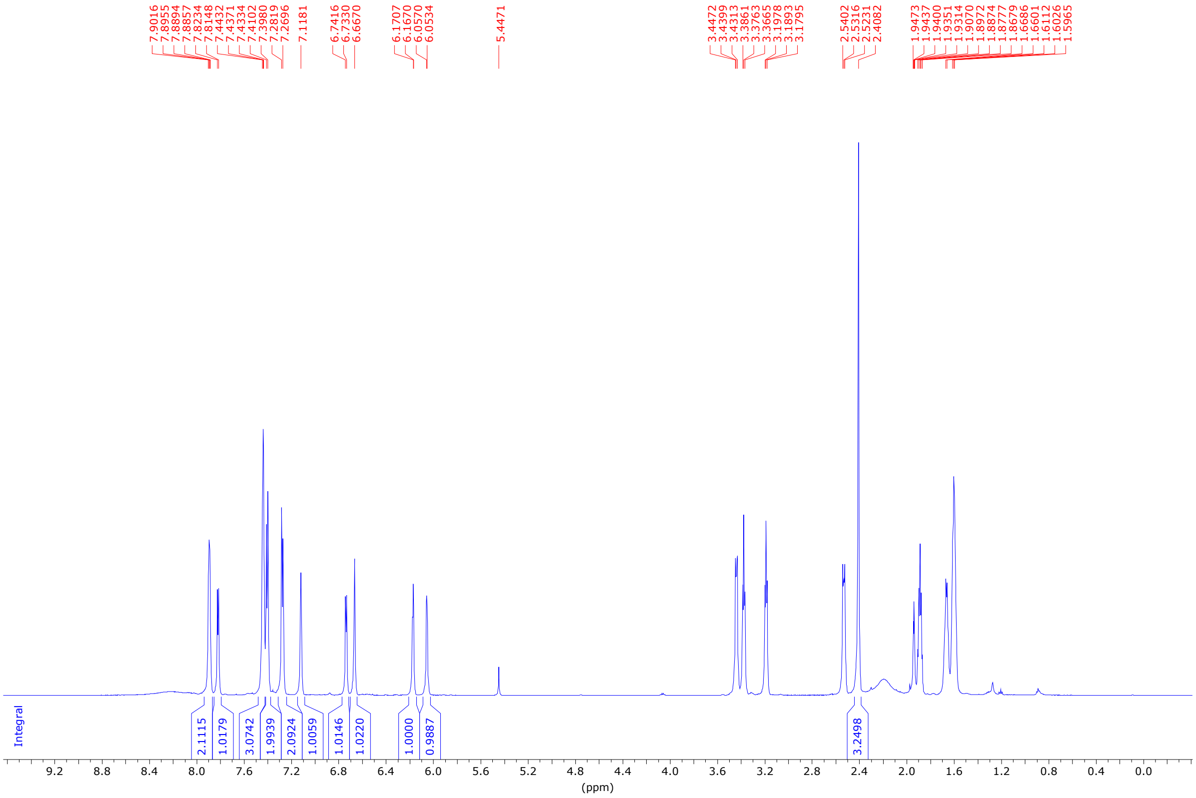
4h, ^{13}C , 600 MHz, CD_3CN ↓



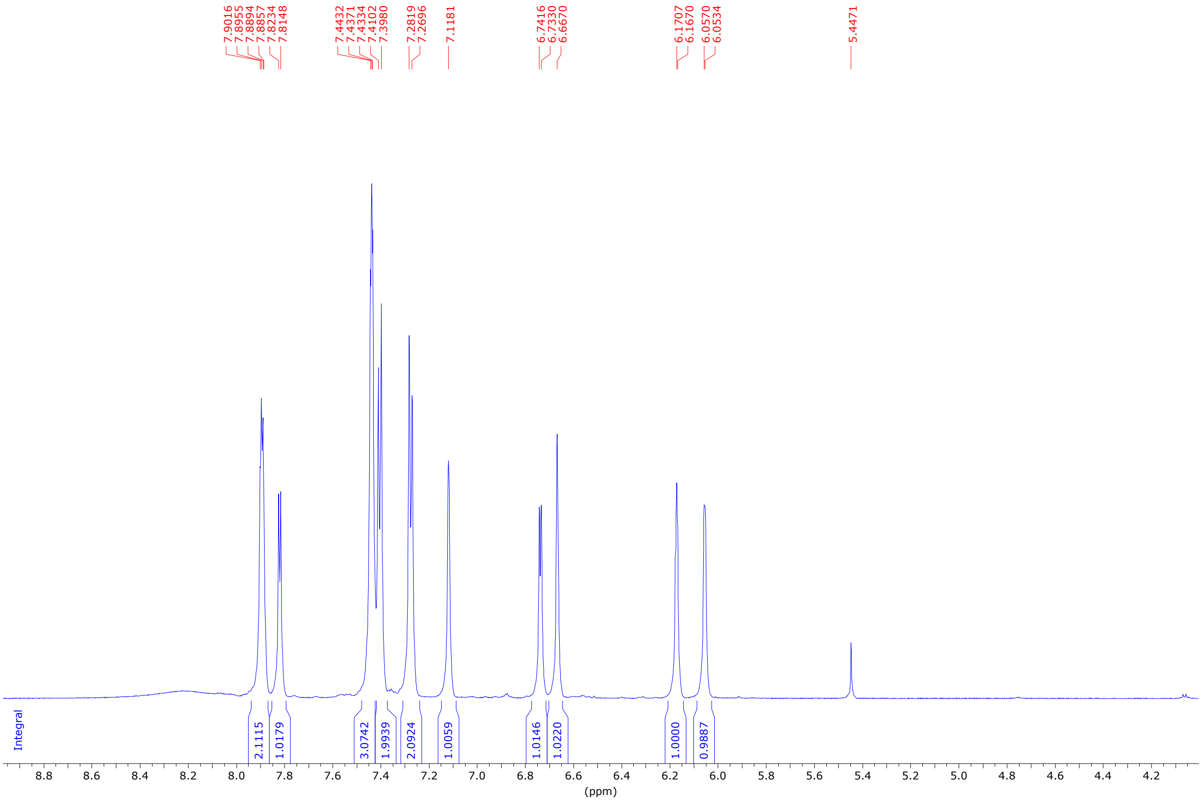
4h, DEPT, 600 MHz, CD_3CN ↓



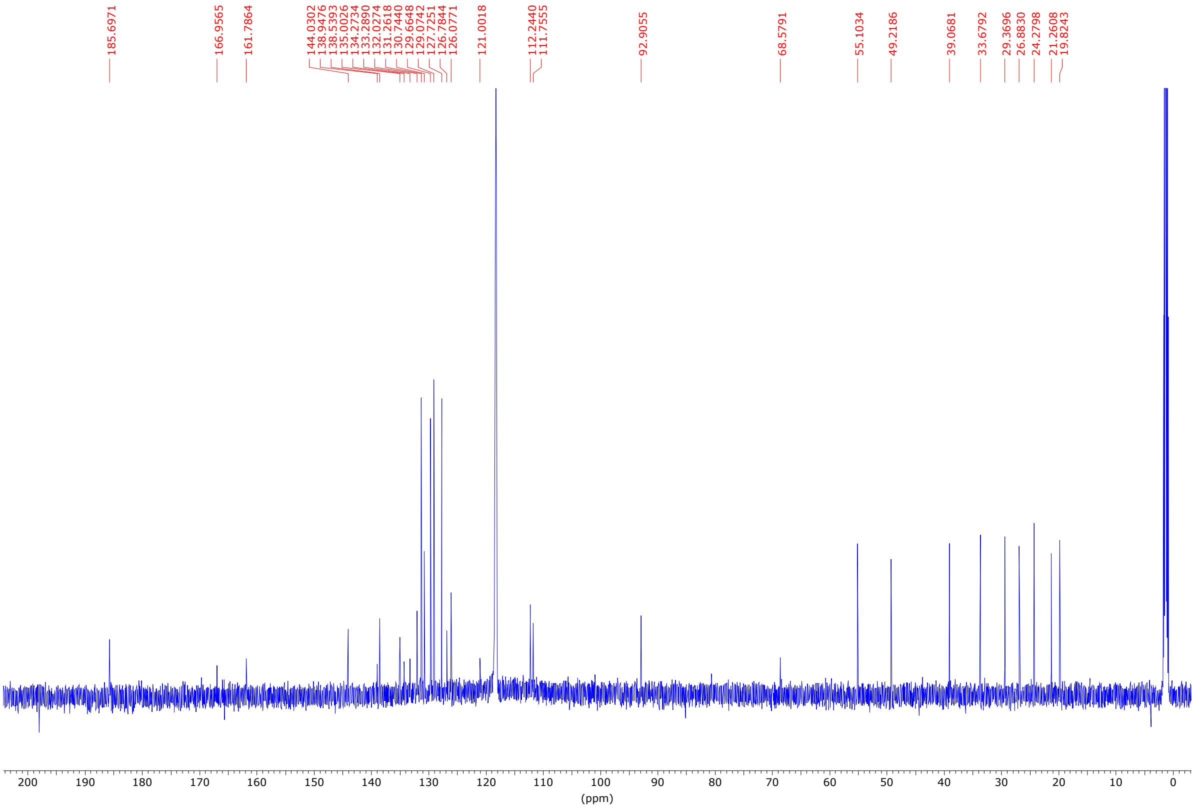
4h, ^{1}H, 600 MHz, CD_3CN + DBU, Full spectrum ↓



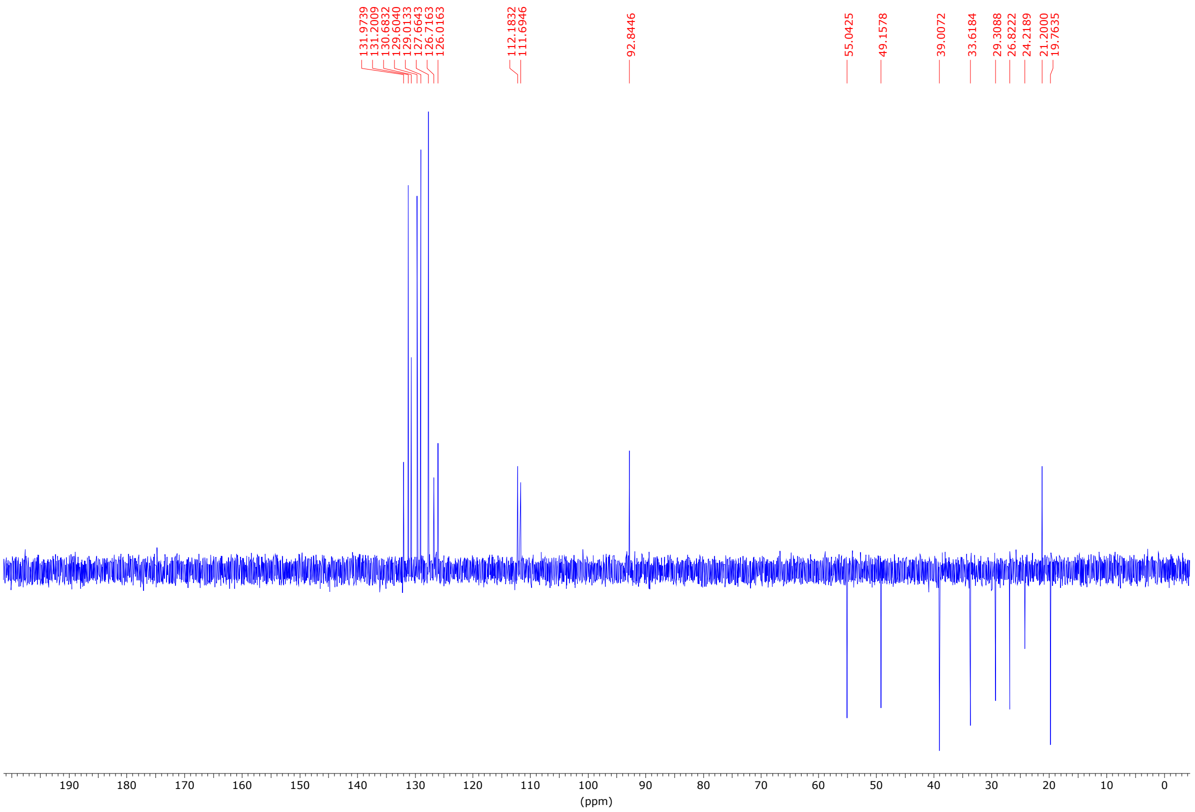
4h, ^{1}H , 600 MHz, CD_3CN + DBU, Zoom ↓



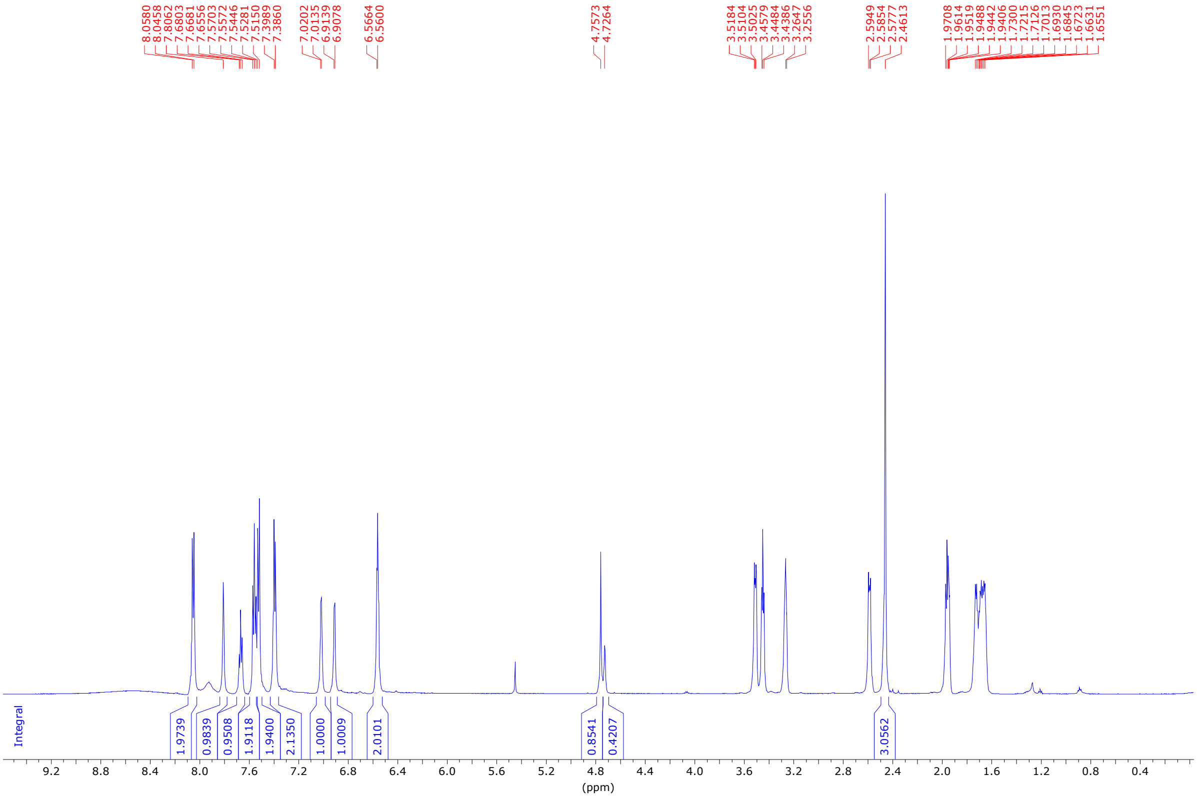
4h, ^{13}C, 600 MHz, CD_3CN + DBU ↓



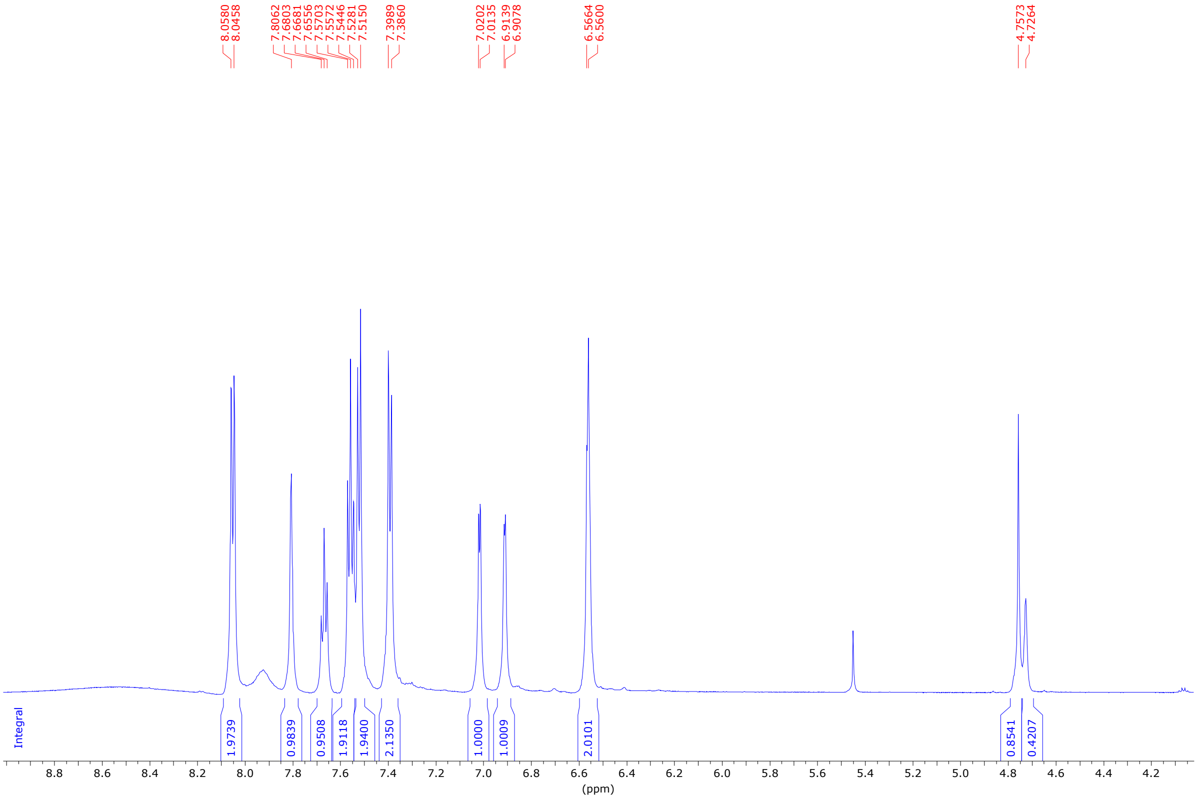
4h, DEPT , 600 MHz, CD_3CN + DBU ↓



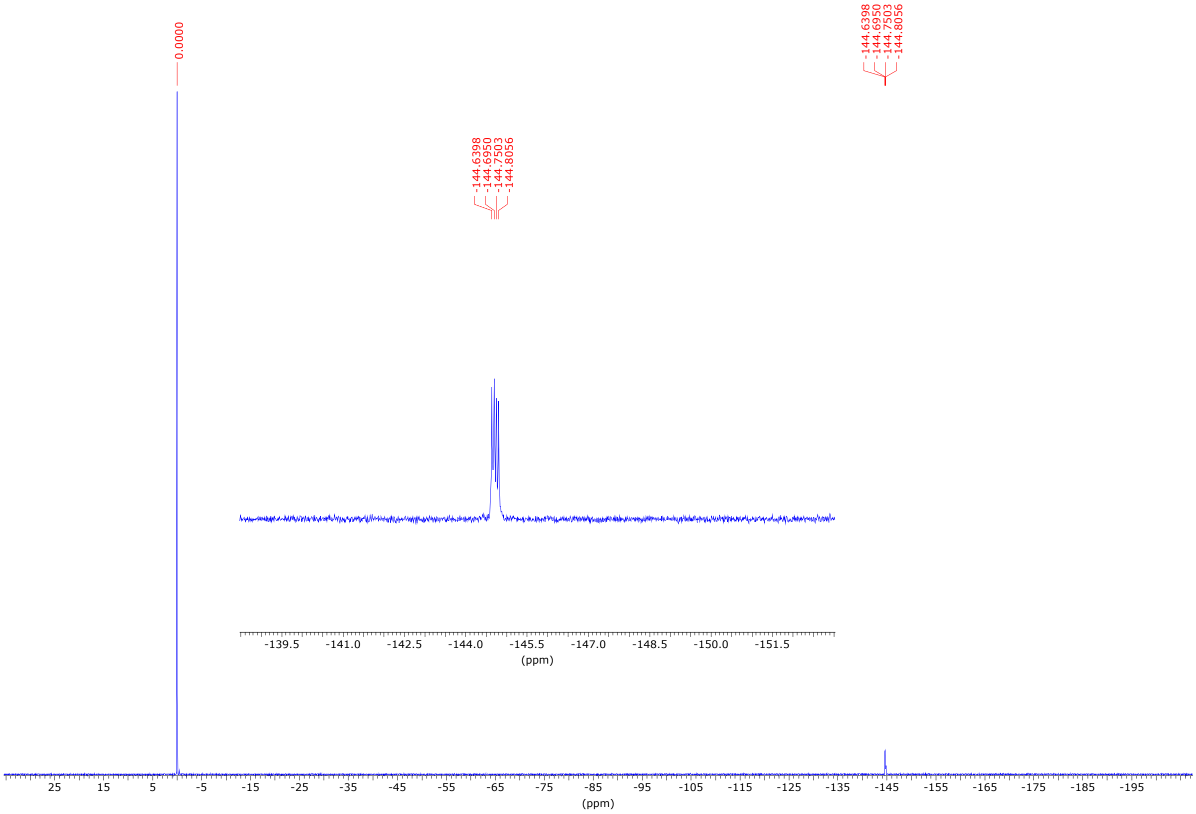
4h, ^{1}H, 600 MHz, CD$_3$CN + DBU + CF$_3$COOD, Full spectrum ↓



4h, ^{1}H, 600 MHz, CD$_3$CN + DBU + CF$_3$COOD, Zoom ↓

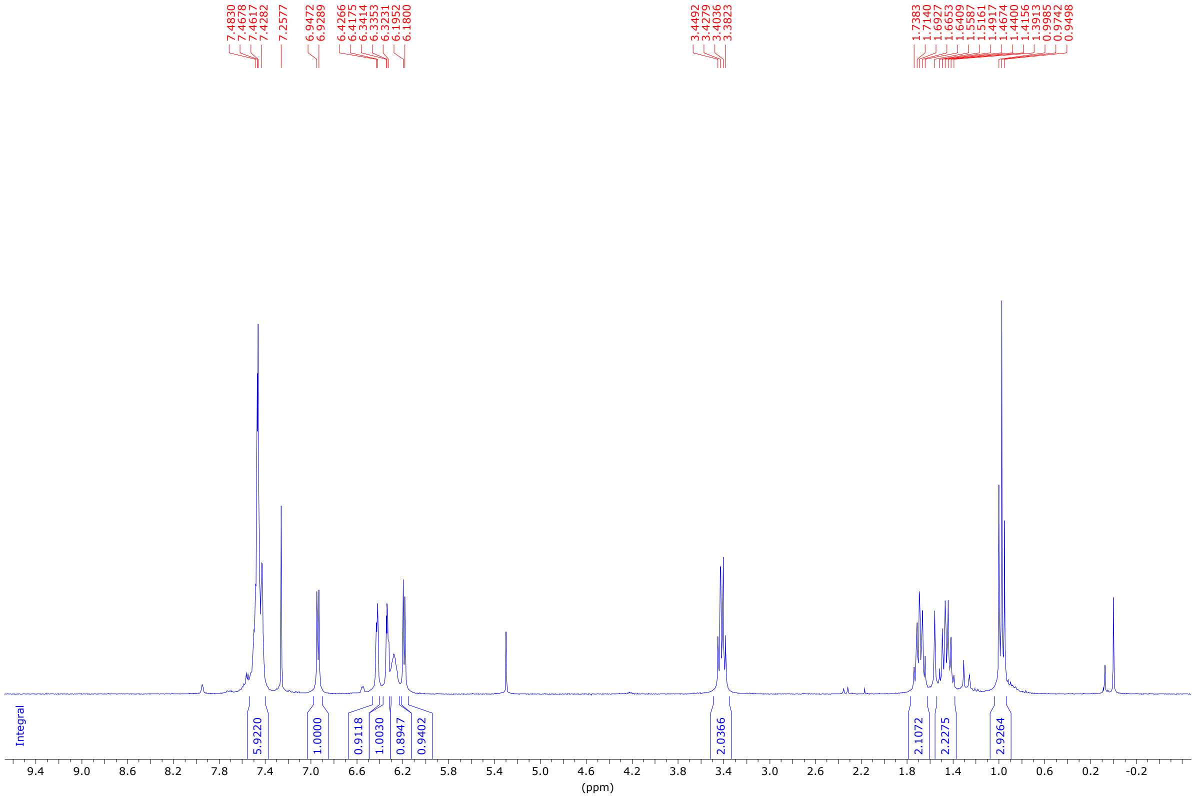


4h, ^{19}F, 600 MHz, $CDCl_3$ ↓

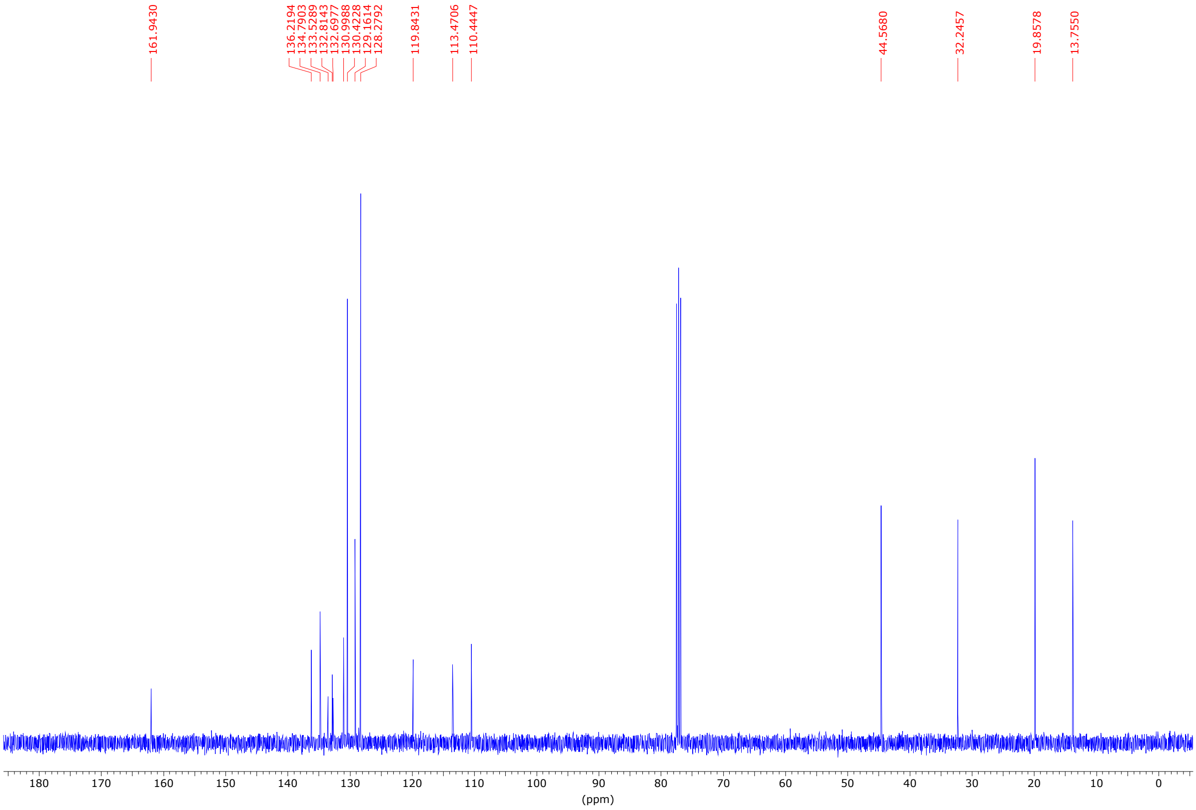


NMR-spectra of new compounds

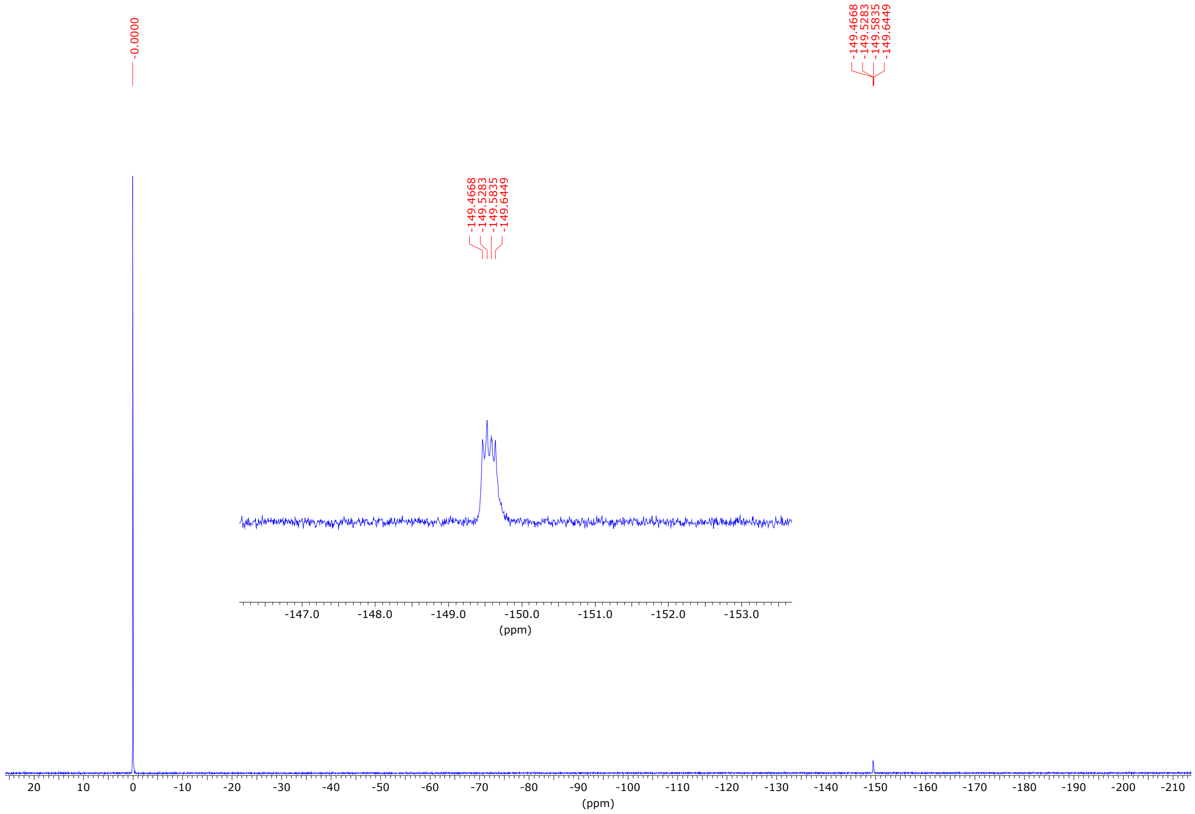
4a, ^{1}H, 300 MHz, $CDCl_3$ ↓



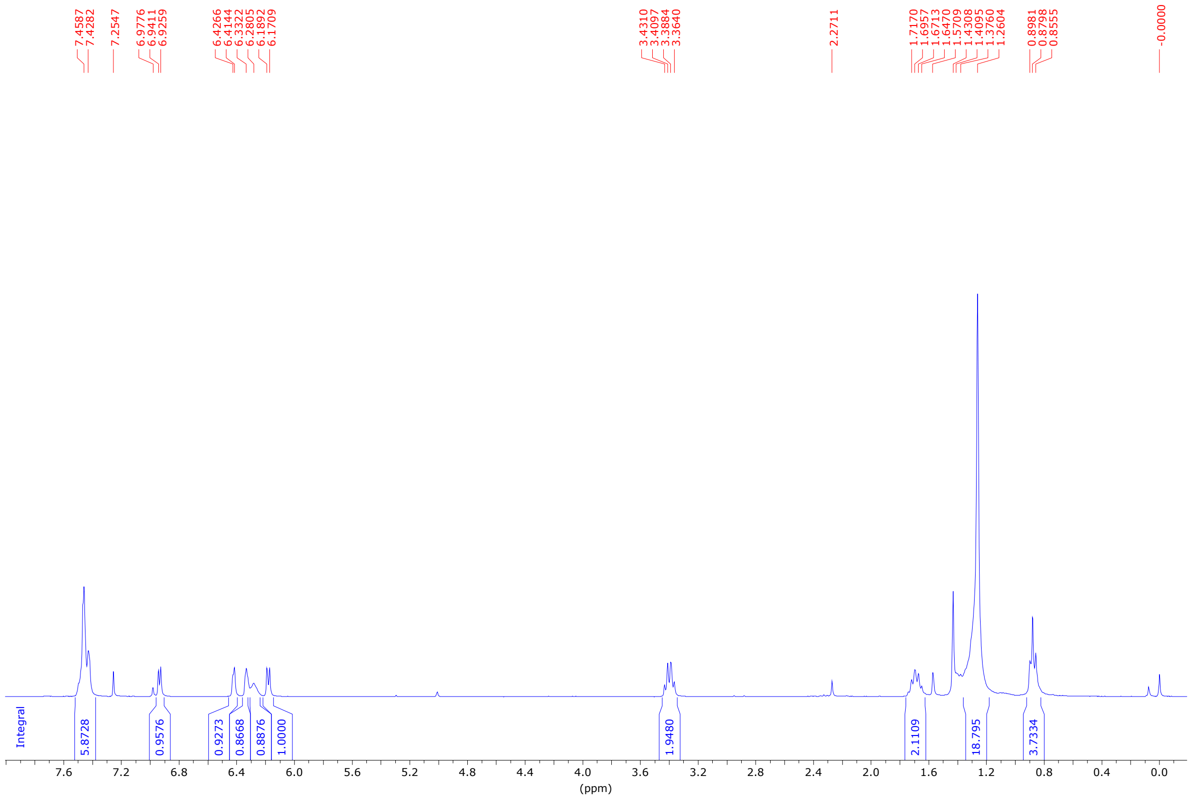
4a, ^{13}C, 400 MHz, CDCl$_3$ ↓



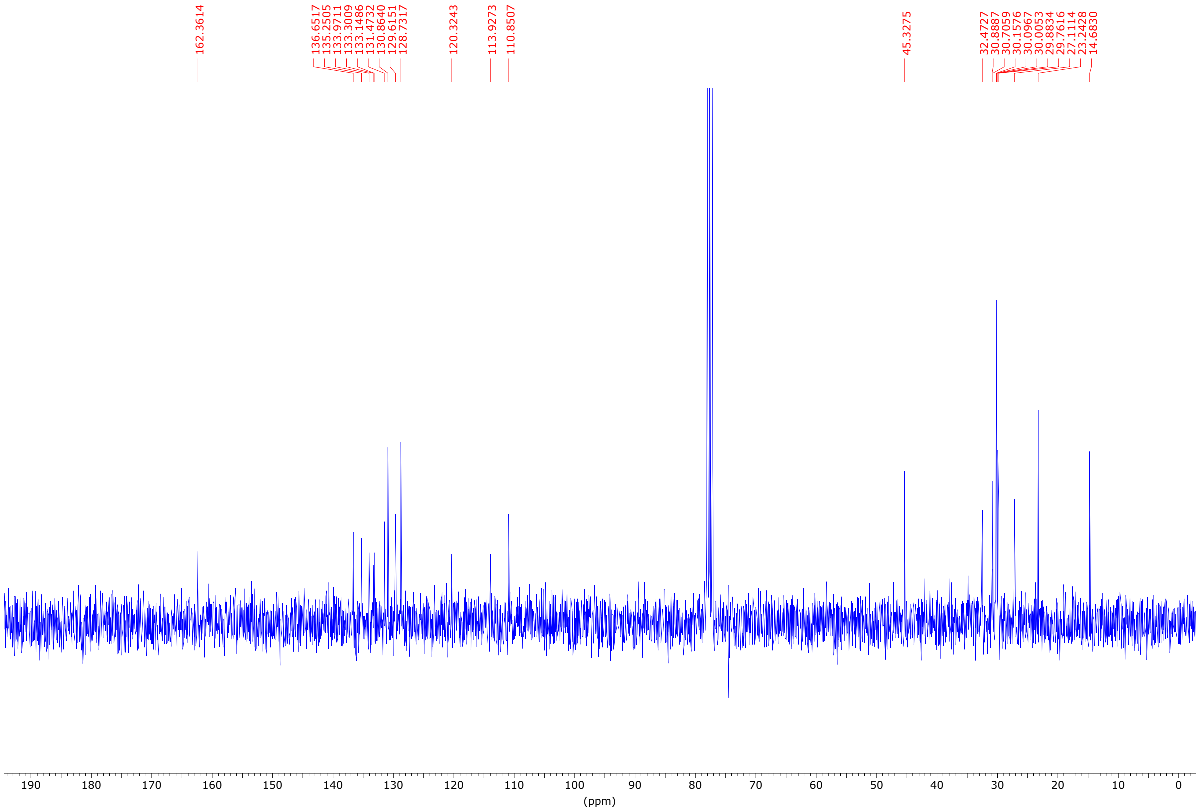
4a, ^{19}F, 600 MHz, CDCl$_3$ ↓



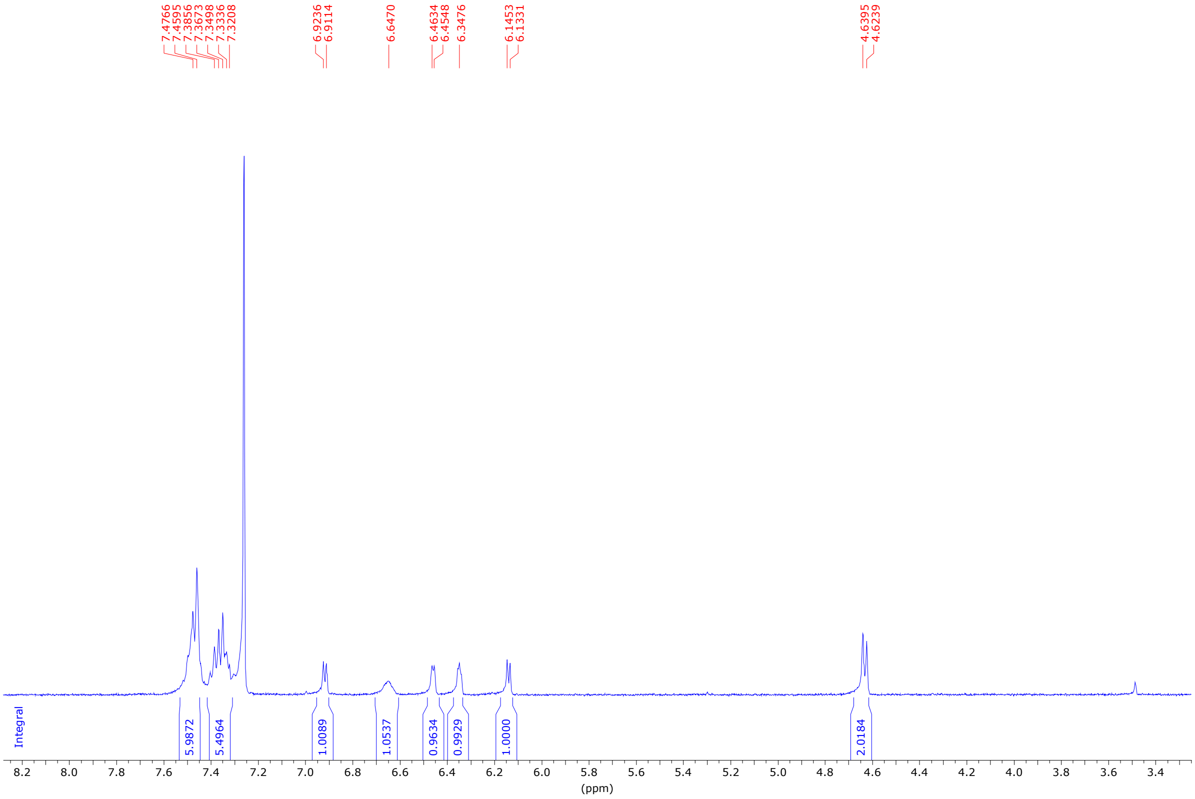
4b, ^{1}H, 300 MHz, $CDCl_3$ ↓



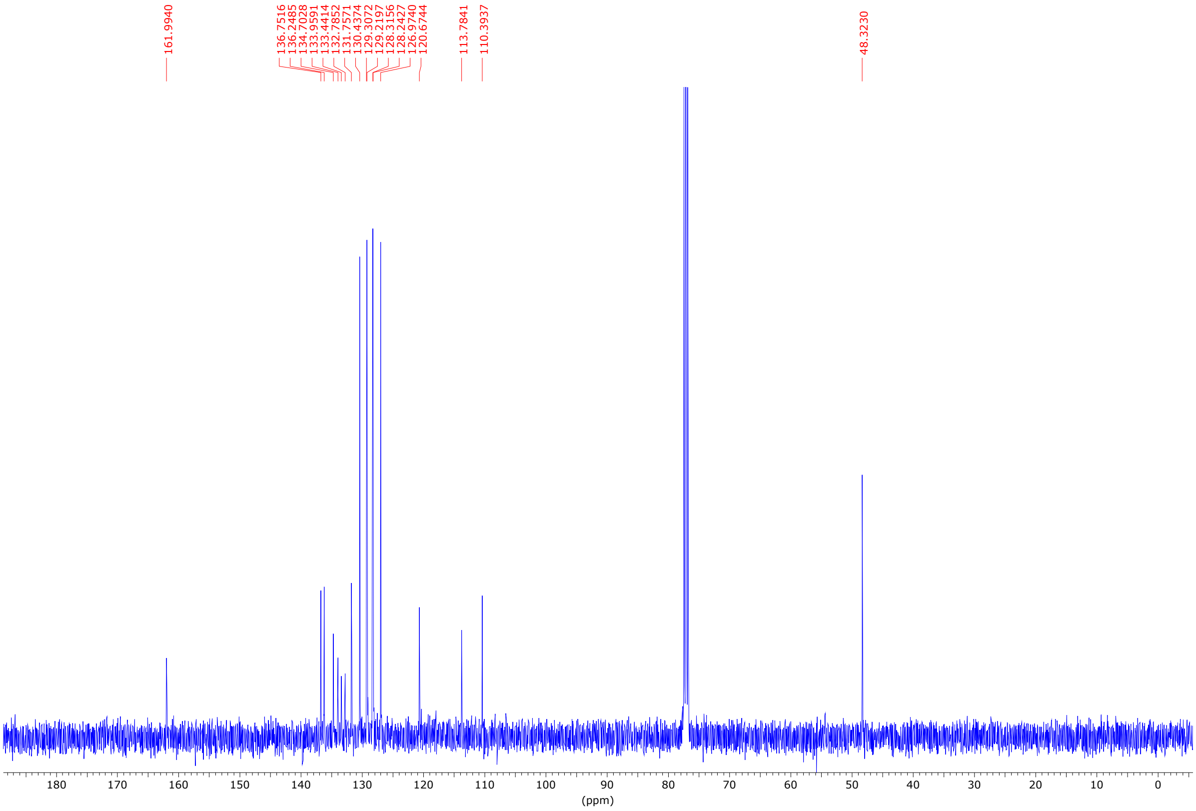
4b, ^{13}C, 300 MHz, $CDCl_3$ ↓



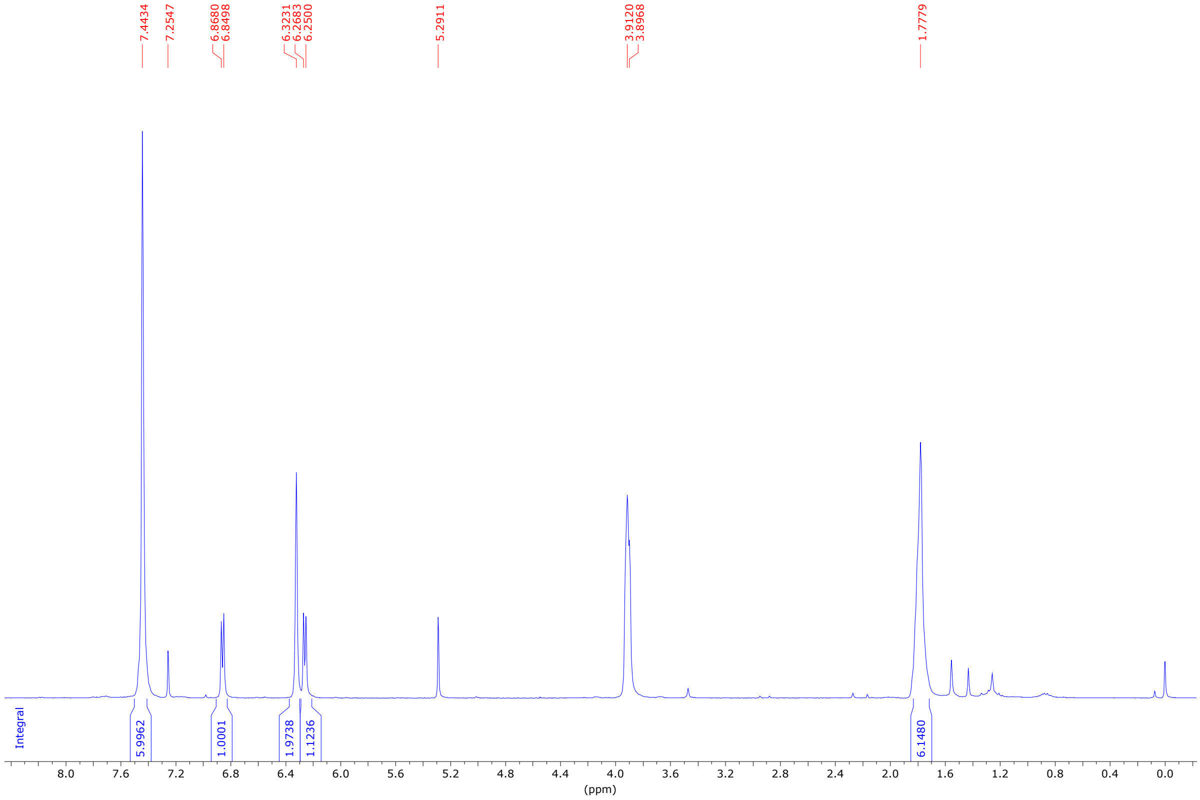
4c, ^{1}H, 400 MHz, $CDCl_3$ ↓



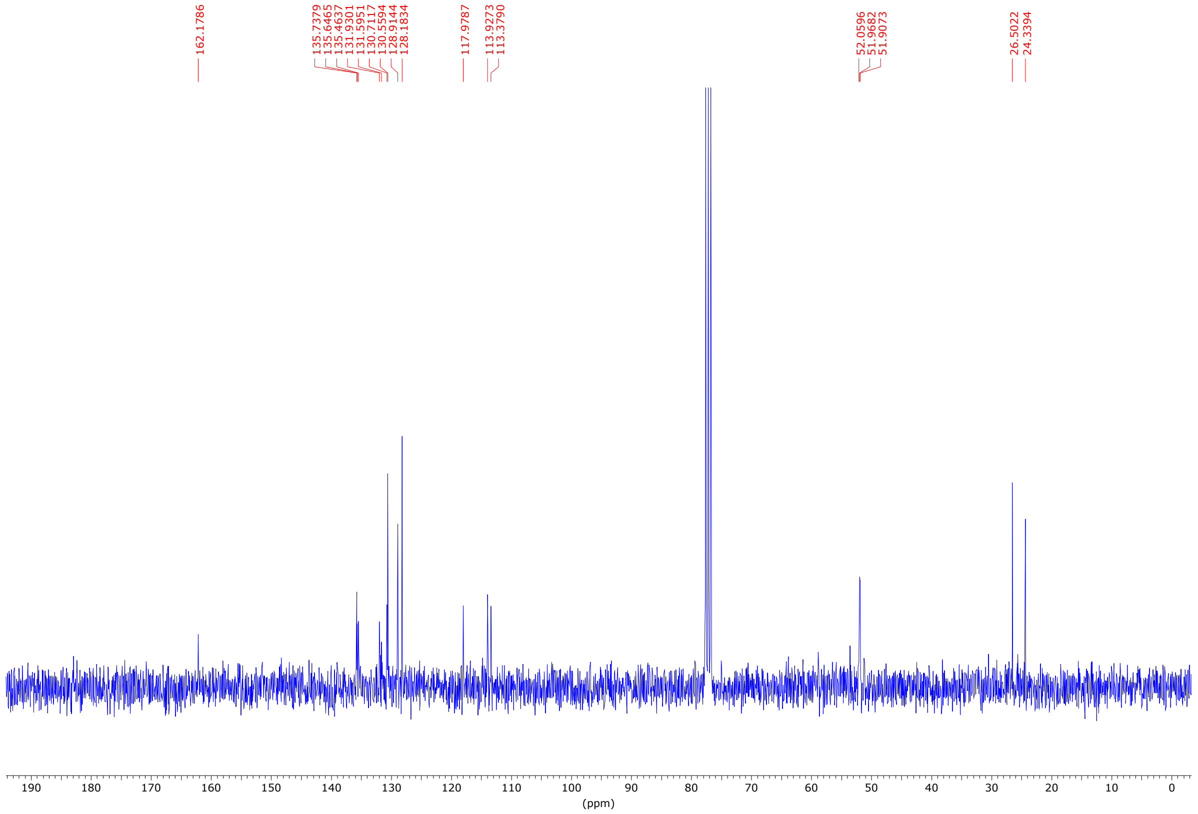
4c, ^{13}C, 400 MHz, $CDCl_3$ ↓



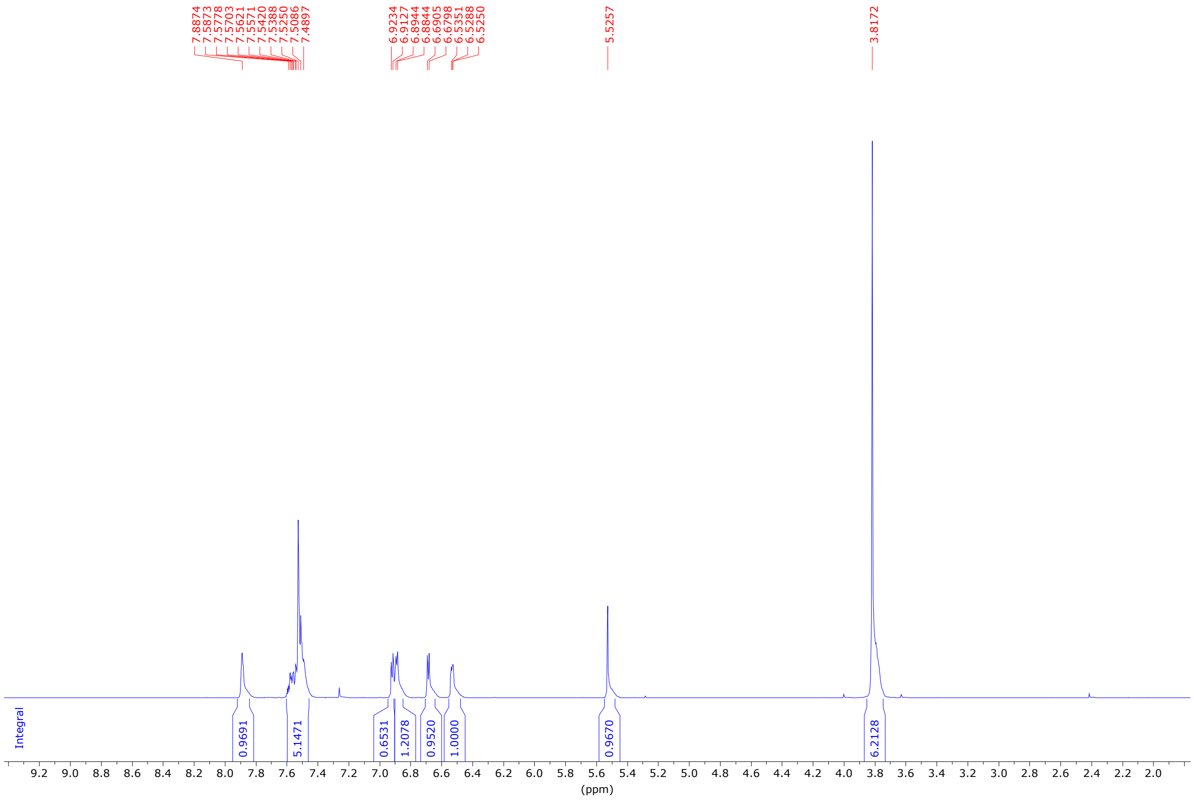
4d, ^{1}H, 300 MHz, $CDCl_3$ ↓



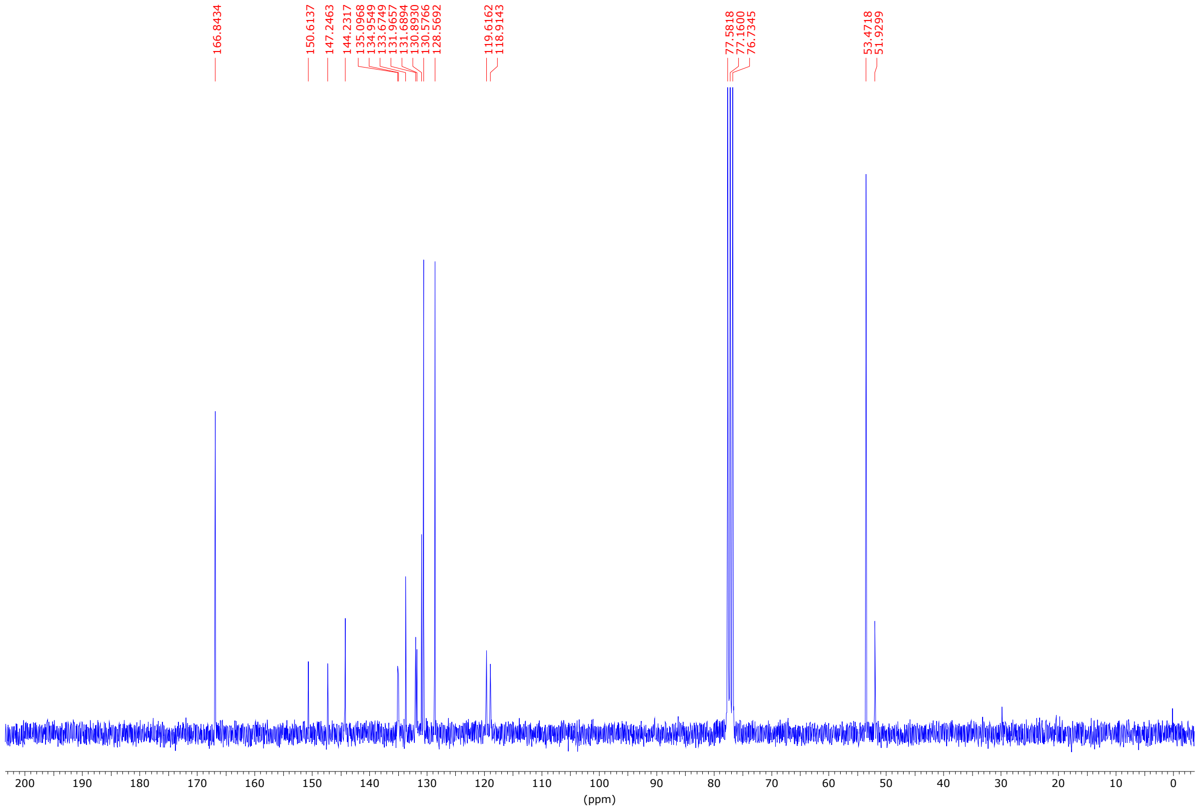
4d, ^{13}C, 300 MHz, $CDCl_3$ ↓



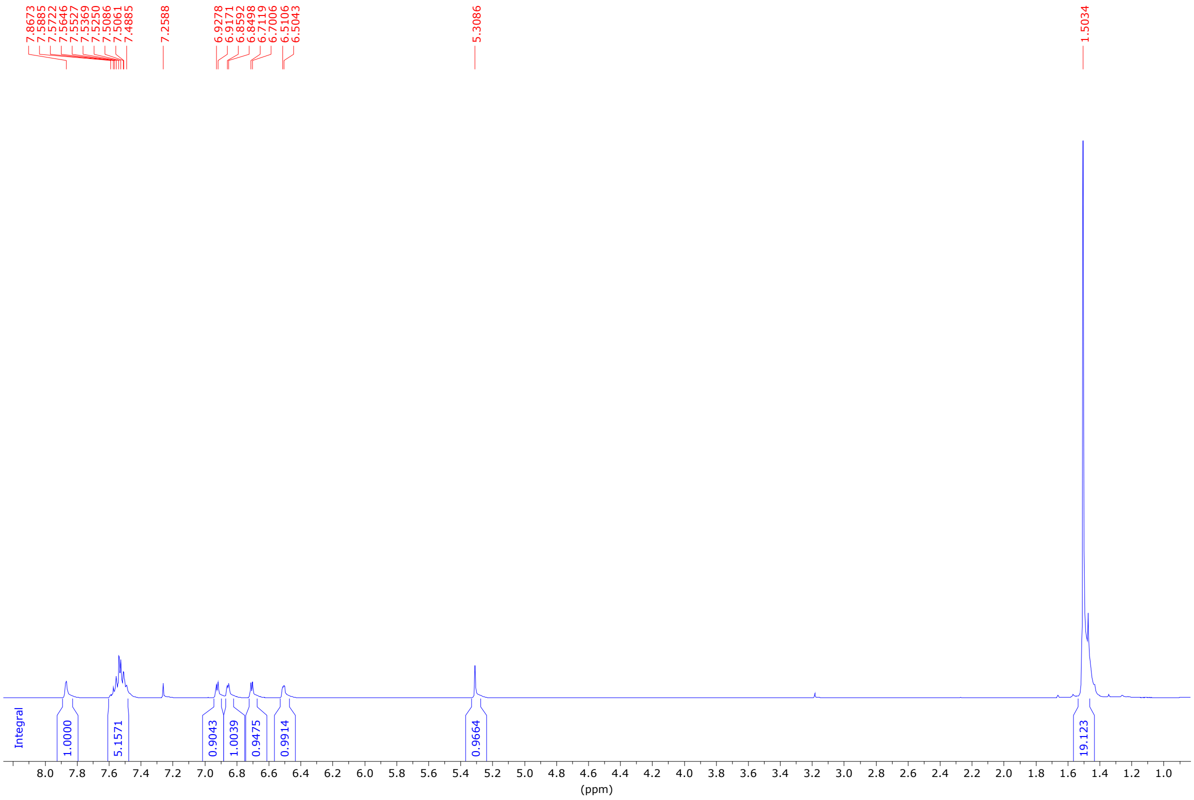
4e, ^{1}H, 400 MHz, $CDCl_3$ ↓



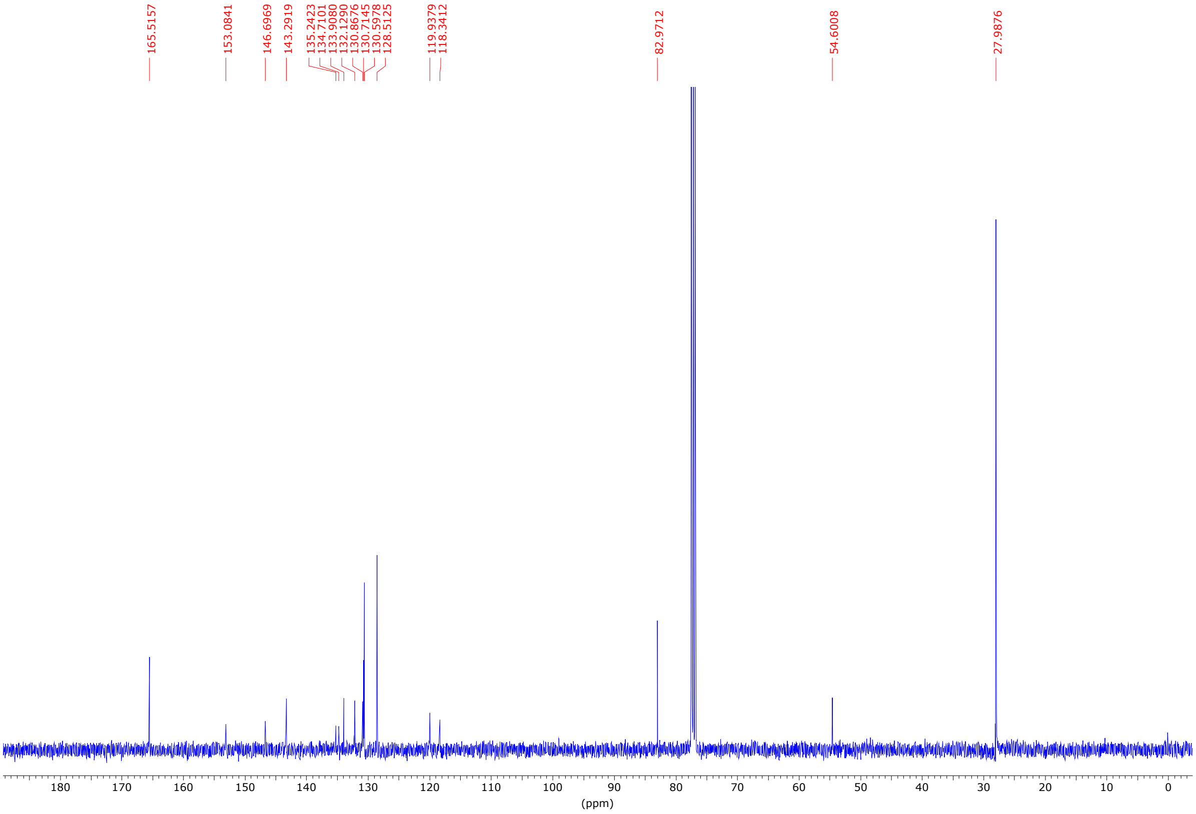
4e, ^{13}C, 400 MHz, $CDCl_3$ ↓



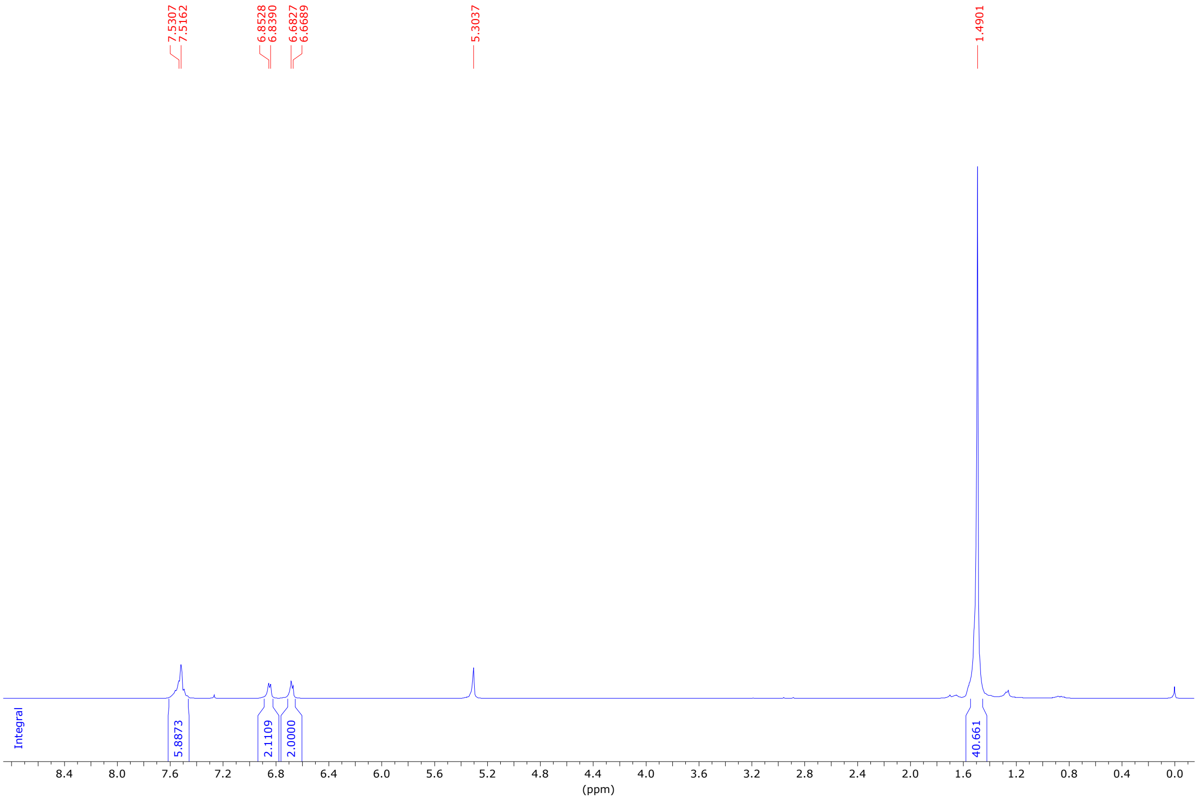
4f, ^{1}H, 400 MHz, CDCl$_3$ ↓



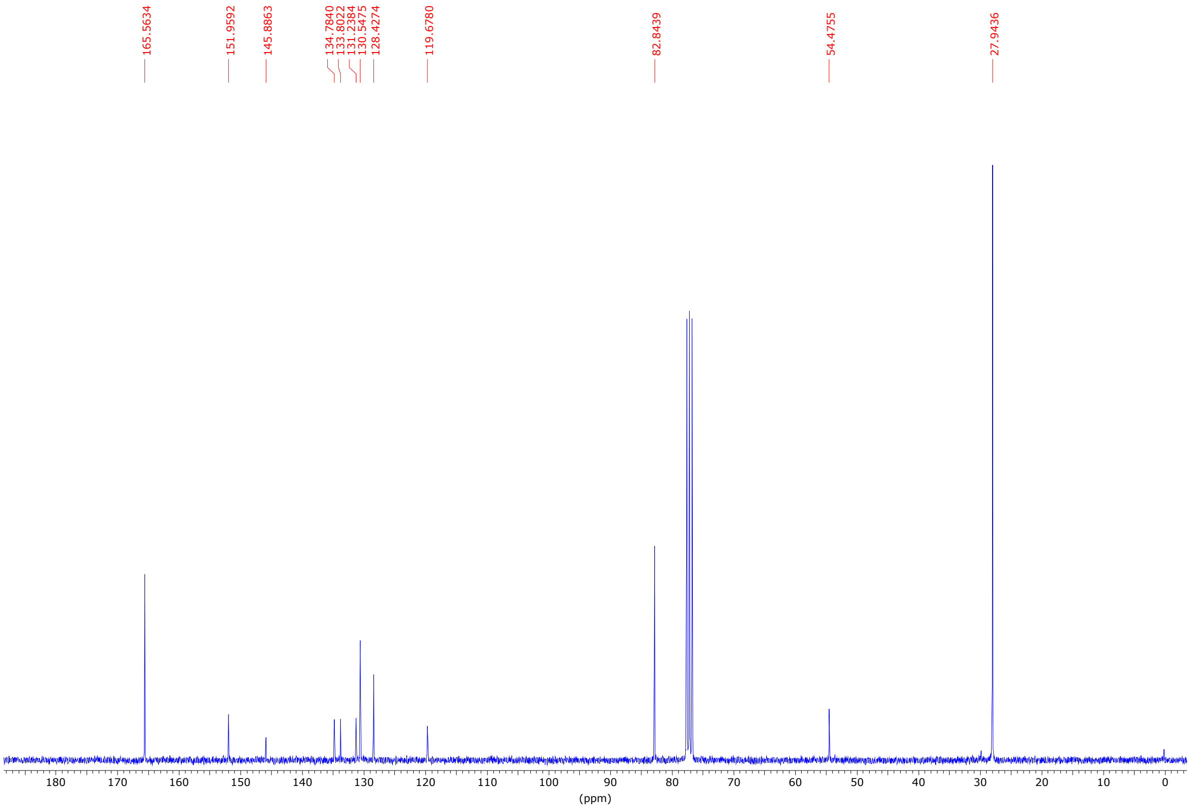
4f, ^{13}C, 400 MHz, CDCl$_3$ ↓



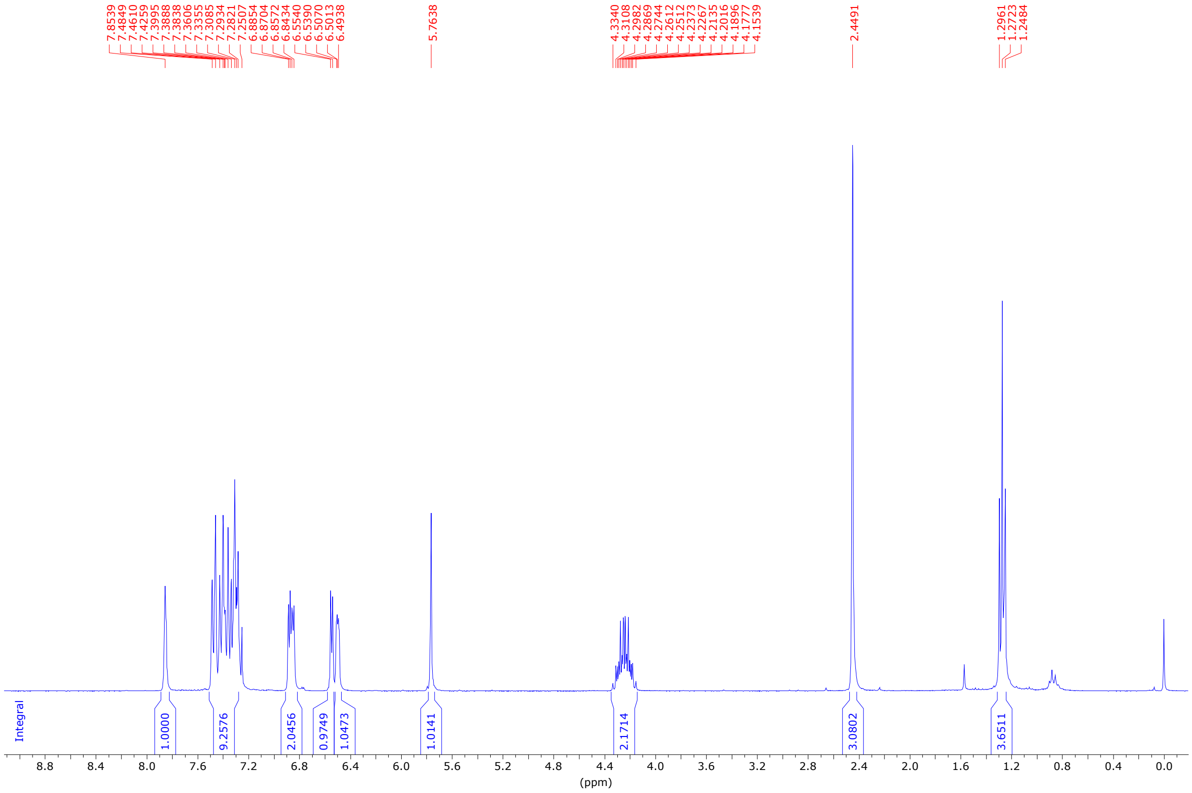
4g, ^{1}H, 300 MHz, $CDCl_3$ ↓



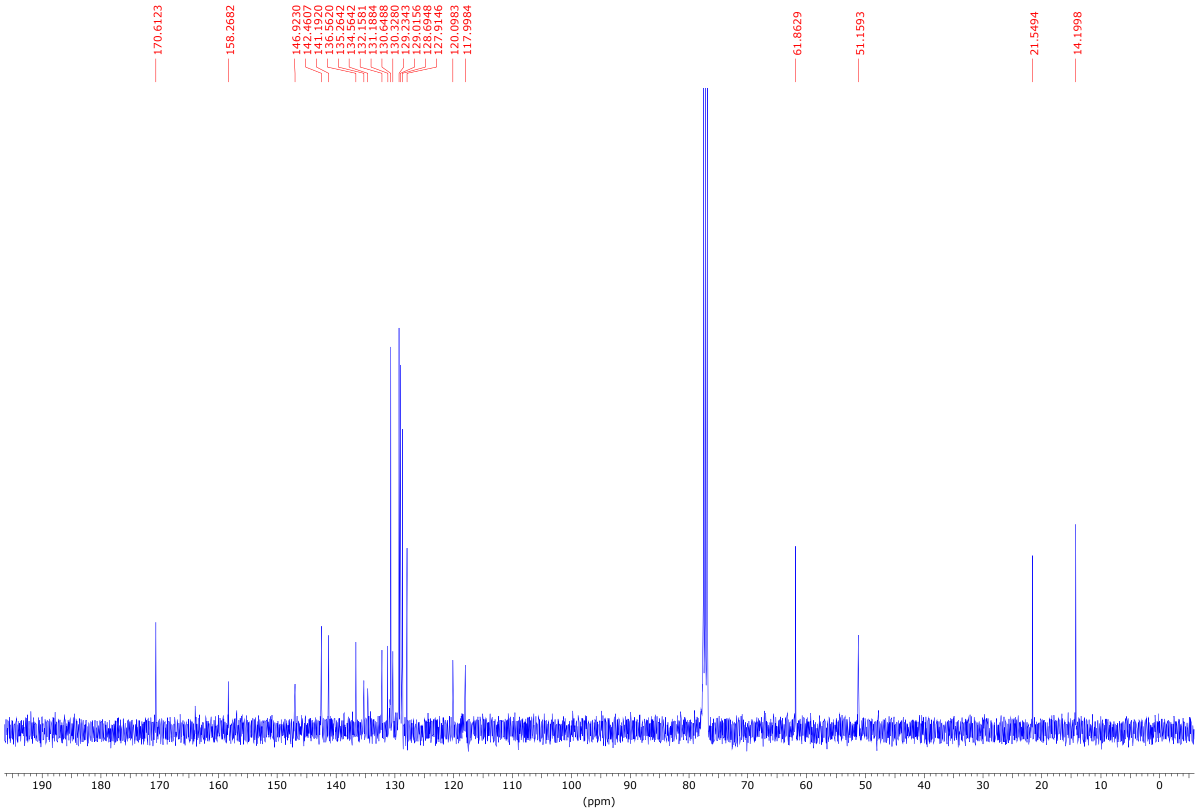
4g, ^{13}C, 300 MHz, $CDCl_3$ ↓



4i, ^{1}H, 300 MHz, CDCl$_3$ ↓



4i, ^{13}C, 400 MHz, CDCl$_3$ ↓



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[i] T. Rohand, E. Dolusic, T. Ngo, W. Maes, W. Dehaen, *ARKIVOC*, 2007, **10**, 307.

[ii] H. Kee, C. Kirmaier, L. Yu, P. Thamyongkit, W. Youngblood, M. Calder, L. Ramos, B. Noll, D. Bocian, W. Scheidt, R. Birge, J. Lindsey, D. Holten, *J. Phys. Chem. B*, 2005, **109**, 20433-20443.