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CuAAC and RuAAC with Alkyne-functionalised Dihydroazulene Photoswitches and Determination of Hammett σ-Constants for Triazoles

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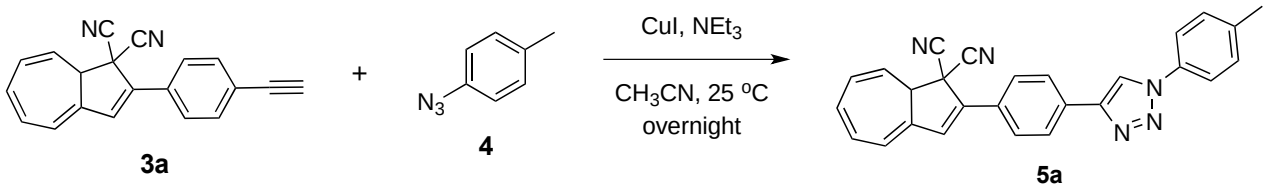
SUPPLEMENTARY MATERIAL

Experimental

General methods. All reactions were performed under an argon atmosphere. All reactions using transition metal catalyst were performed in a solvent flushed with argon, by letting argon flow through the solvent for at least 20 minutes while exposed to ultrasound. All handlings of photochromic compounds were done in the dark. All operations involving DHAs (evaporation of solvents, column chromatography, and reactions) were done in glassware wrapped in tin-foil. Large amounts (> 200 mg) of DHA compounds in solution turn red within minutes, whereas small amounts turn red within seconds in daylight. Compounds **3a** and **3b** were made according to literature procedures (M. Santella, V. Mazzanti, M. Jevric, C. R. Parker, S. L. Broman, A. D. Bond, M. B. Nielsen, *J. Org. Chem.* **2012**, *77*, 8922; S. L. Broman, M. Jevric, M. B. Nielsen, Submitted). The RuAAC reactions were performed in THF (distilled over Na/benzophenone couple). Microwave heating was performed in a Biotage Initiator exp (EU) Microwave synthesizer using suitable vials for the reaction mixtures. Thin layer chromatography (TLC) was carried out on commercially available precoated plates (Silica gel 60 F_{254}); a colour change from yellow to red upon irradiation with UV-light (366 nm, *not* 254 nm) indicated presence of a DHA species. Column chromatography was performed with silica gel 40-63 μm. All melting points are uncorrected, and they were measured on a Stuart automatic melting point apparatus, SMP40. All UV-Vis absorption spectroscopic measurements were performed in a 1-cm path length cuvette. Photolysis experiments were performed using a 150-W Xenon arc lamp equipped with a monochromator; the DHA absorption maximum (lowest energy absorption) for each individual species was chosen as the wavelength of irradiation. The thermal back-reaction was measured at 25 ^{o}C using a Peltier unit in the UV-Vis spectrophotometer. All NMR spectra were acquired on a 500 MHz instrument equipped with a (non-inverse) cryoprobe or a pentaprobe. All chemical shift values in ^{1}H and ^{13}C NMR spectra are referenced to the residual solvent peak ($CDCl_3$ δ_H = 7.26 ppm, δ_C = 77.16 ppm); coupling constants (*J*) are in Hz. In the APT spectra, CH and CH_3 correspond to negative signals and C and CH_2 correspond to positive signals. Both Mass Spectrometry (MS) and High Resolution Mass Spectrometry (HRMS) measurements were acquired using the Electrospray Ionization technique (ESP) on a Bruker MicrOTOF QII instrument. Elemental analyses were performed at the Microanalytical Laboratory at the Department of Chemistry, University of Copenhagen.

Synthesis

2-(4-(1-(p-Tolyl)-1H-1,2,3-triazol-4-yl)phenyl)-1,8a-dihydroazulene-1,1-dicarbonitrile ***5a***

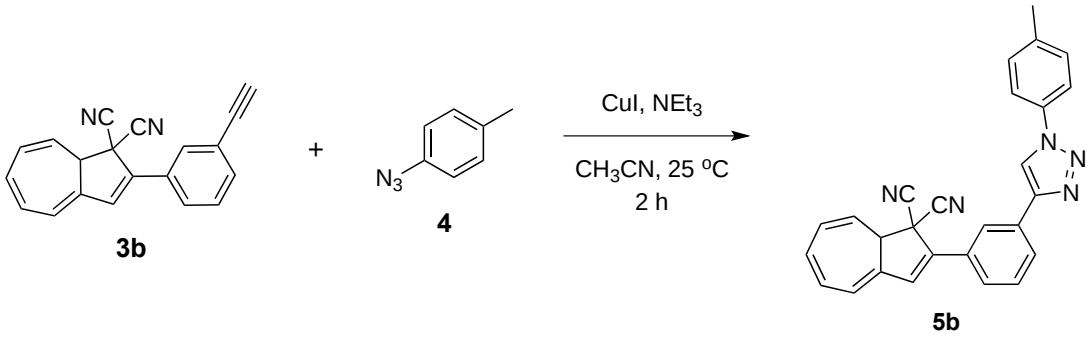


3a **4** **5a**

To a stirring degassed solution of DHA **3a** (100 mg, 0.36 mmol) in CH_3CN (15 mL) was added 4-tolylazide **4** (0.7 mL, 0.36 mmol, 0.5M in *tert*-butyl methyl ether), CuI (68.2 mg, 0.36 mmol) and degassed Et_3N (100 μL, 0.72 mmol) added. The reaction mixture was degassed for a further 10 min, and stirring at room temperature was maintained overnight, after which time the volatiles were removed under reduced pressure. The residue was subjected to flash column chromatography (SiO_2, 1:5 EtOAc / toluene) to afford the product as a yellow powder (122 mg, 83%) containing minor impurities. Recrystallisation from hot EtOAc gave **5a** (101 mg, 68%) as a bright yellow powder. TLC (30% THF / heptane): R_f = 0.27. M.p. 228 °C (decomp.). δ_H (500 MHz, $CDCl_3$) 8.22 (s, 1H, triazole-CH), 8.02 (d, *J* 8.6, 2H), 7.84 (d, *J* 8.6, 2H), 7.68 (d, *J* 8.2, 2H), 7.36 (d, *J* 8.2, 2H), 6.95 (s,

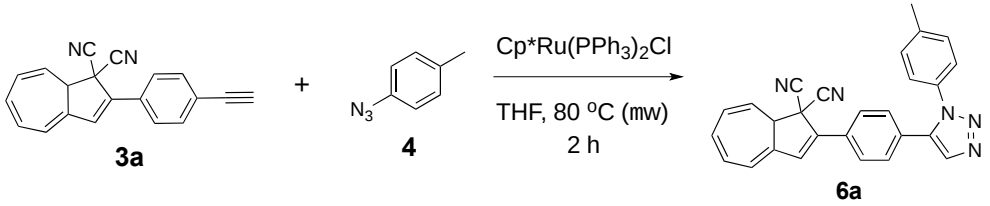
1H, DHA-H3), 6.59 (dd, *J* 11.3, 6.2, 1H), 6.49 (dd, *J* 11.3, 6.1, 1H), 6.37 (d, *J* 6.1, 1H), 6.32 (ddd, *J* 10.2, 6.2, 2.1, 1H), 5.84 (dd, *J* 10.2, 3.8, 1H), 3.82 (dt, *J* 3.8, 2.1, 1H, DHA-H8a), 2.45 (s, 3H, CH_3) ppm. δ_C (125 MHz, $CDCl_3$) 147.3, 139.8, 139.3, 138.8, 134.8, 132.6, 132.0, 131.14, 131.08, 130.5, 130.4, 127.9, 127.0, 126.6, 121.3, 120.7, 119.6, 118.3, 115.3, 112.9, 51.3, 45.3, 21.3 ppm. MS (ESP+) *m/z* = 436 ($[M+Na]^+$). HRMS (ESP+) calcd 436.1533 ($C_{27}H_{19}N_5Na^+$); exp 436.1527 ($[M+Na]^+$). Anal. Calc. for $C_{27}H_{19}N_5$: C 78.43, H 4.63, N 16.94. Found: C 78.07, H 4.31, N 16.76 %.

2-(3-(1-(p-Tolyl)-1H-1,2,3-triazol-4-yl)phenyl)-1,8a-dihydroazulene-1,1-dicarbonitrile ***5b***



To a stirred solution of DHA **3b** (129.4 mg, 0.4616 mmol) and CuI (94.0 mg, 0.494 mmol) in argon-flushed CH_3CN (18 mL), Et_3N (0.13 mL, 0.92 mmol) and a solution of 4-tolylazide **4** (1.85 mL, 0.920 mmol, 0.5 M in *tert*-butyl methyl ether) were added, and the reaction mixture was stirred for 2 h at rt. Upon completion, the cloudy bright yellow reaction mixture was poured into saturated aqueous NH_4Cl (10 mL) and extracted with CH_2Cl_2 (100 mL). The organic extract was washed with brine (25 mL), dried with Na_2SO_4, filtered and concentrated *in vacuo*. The resulting yellow to red residue was purified by flash column chromatography (SiO_2, eluent: neat toluene, then toluene / CH_2Cl_2 (1:1), then CH_2Cl_2 and finally CH_2Cl_2 / EtOAc (8:2)) to afford **5b** (179 mg, 94%) as a yellow to red solid with some impurities. Recrystallisation from boiling EtOAc (30 mL) gave **5b** (93.9 mg, 49%) as a yellow crystalline solid. TLC (3% EtOAc / toluene): R_f = 0.33. M.p. 212 - 213 °C (decomp). δ_H (500 MHz, $CDCl_3$) 8.27 (t, *J* 1.8, 1H), 8.22 (s, 1H, triazole-CH), 7.94 (br dt, *J* 7.9, 1H), 7.77 (ddd, *J* 7.9, 1.8, 0.9, 1H), 7.68 (d, *J* 8.3, 2H), 7.58 (t, *J* 7.9, 1H), 7.35 (br d, *J* 8.3, 2H), 7.03 (s, 1H, DHA-H3), 6.59 (dd, *J* 11.2, 6.3, 1H), 6.49 (dd, *J* 11.2, 6.1, 1H), 6.38 (d, *J* 6.3, 1H), 6.32 (ddd, *J* 10.2, 6.1, 2.0, 1H), 5.84 (dd, *J* 10.2, 3.8, 1H), 3.82 (dt, *J* 3.8, 2.0, 1H, DHA-H8a), 2.45 (s, 3H, CH_3) ppm. δ_C (125 MHz, $CDCl_3$) 147.4, 139.8, 139.3, 138.7, 134.8, 133.4, 131.6, 131.4, 131.2, 131.1, 130.5, 130.1, 127.9, 127.4, 126.0, 123.8, 121.5, 120.7, 119.6, 118.3, 115.3, 112.9, 51.3, 45.4, 21.3 ppm. HRMS (ESP+) calcd 414.1713 ($C_{27}H_{20}N_5^+$); exp 414.1708 ($[M+H]^+$).

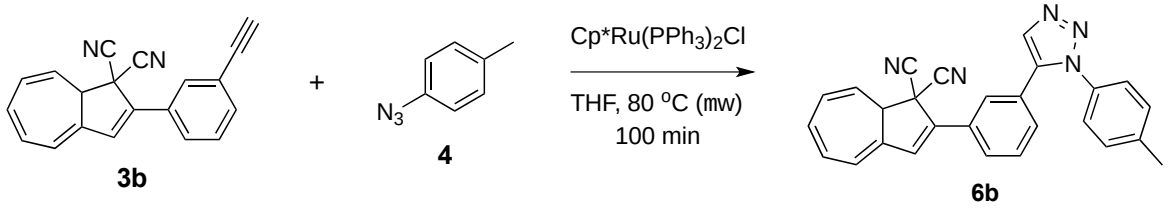
2-(4-(1-(p-Tolyl)-1H-1,2,3-triazol-5-yl)phenyl)-1,8a-dihydroazulene-1,1-dicarbonitrile ***6a***



An argon-flushed solution of DHA **3a** (49.9 mg, 0.18 mmol) and 4-tolylazide **4** (1.0 mL, 0.50 mmol, 0.5 M in *tert*-butyl methyl ether) dissolved in dry THF (5 mL) was added to a dry microwave vial. The catalyst $Ru(PPh_3)_2Cp^*Cl$ (20.0 mg, 25.1 µmol) was added right before sealing the vial; the reaction mixture was then heated at 80 °C for 2 h in a microwave oven. The reaction

mixture was concentrated under reduced pressure and passed through a short plug of silica (gradient: 75% CH_2Cl_2 / heptane, 100% CH_2Cl_2, 2% EtOAc / CH_2Cl_2, 5% EtOAc / CH_2Cl_2, 10% EtOAc / CH_2Cl_2) to afford **6a** as a yellow glassy solid (13.8 mg, 19%). TLC (30% THF / heptane): R_f = 0.27. δ_H (500 MHz, $CDCl_3$) 7.93 (s, 1H, triazole-CH), 7.70 (d, *J* 8.6, 2H), 7.34 (d, *J* 8.6, 2H), 7.27 (br s, 4H), 6.92 (s, 1H, DHA-H3), 6.58 (dd, *J* 11.3, 6.2, 1H), 6.50 (dd, *J* 11.3, 6.1, 1H), 6.37 (d, *J* 6.1, 1H), 6.32 (ddd, *J* 10.2, 6.2, 2.1, 1H), 5.81 (dd, *J* 10.2, 3.8, 1H), 3.79 (dt, *J* 3.8, 2.1, 1H, DHA-H8a), 2.44 (s, 3H, CH_3) ppm. δ_C (125 MHz, $CDCl_3$) 140.0, 138.9, 138.3, 136.7, 134.0, 133.7, 133.5, 131.5, 131.1, 131.0, 130.4, 129.2, 128.2, 127.9, 126.6, 125.2, 121.9, 119.5, 115.0, 112.6, 51.1, 45.0, 21.5 ppm. HRMS (ESP+) calcd 414.1713 ($C_{27}H_{20}N_5^+$); exp 414.1703 ($[M+H]^+$).

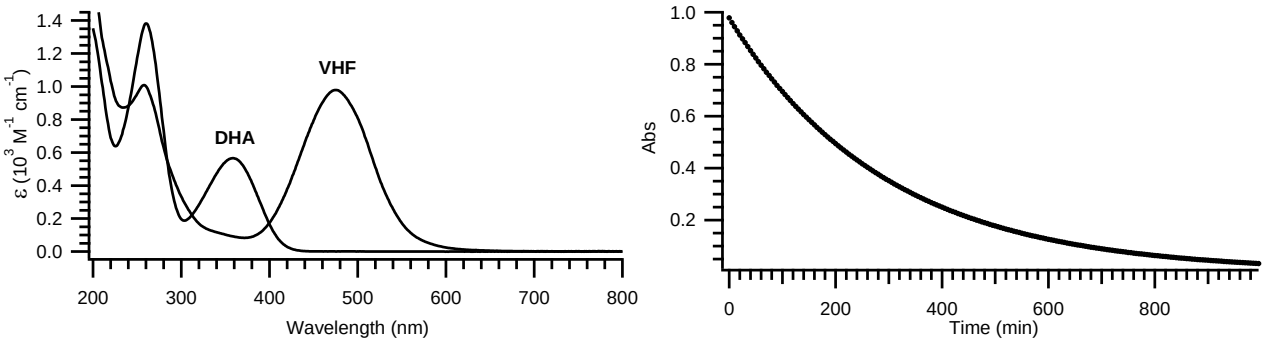
2-(3-(1-(p-Tolyl)-1H-1,2,3-triazol-5-yl)phenyl)-1,8a-dihydroazulene-1,1-dicarbonitrile ***6b***



To a stirred solution of DHA **3b** (147.1 mg, 0.5248 mmol) in argon-flushed THF (10 mL) in a container suitable for microwave irradiation, a solution of 4-tolylazide **4** (2.10 mL, 1.05 mmol, 0.5 M in *tert*-butyl methyl ether) and a solution of $Ru(PPh_3)_2Cp^*Cl$ (83.6 mg, 0.105 mmol) in argon-flushed THF (5 mL) were added. The reaction mixture was heated to 80 °C for 100 min in a microwave oven. The reaction mixture was poured into Et_2O (50 mL) and washed with aqueous NH_4Cl (25 mL), dried with Na_2SO_4, filtered and concentrated *in vacuo*. Purification by flash column chromatography (SiO_2, eluent: neat CH_2Cl_2, then CH_2Cl_2 / EtOAc (50:1), and finally CH_2Cl_2 / EtOAc (20:1)) gave **6b** (52.1 mg, 24%) as a yellow oil, which solidified upon standing. TLC (5% EtOAc / CH_2Cl_2): R_f = 0.30. M.p. 191 - 193 °C (CH_2Cl_2 / heptanes). δ_H (500 MHz, $CDCl_3$) 7.94 (s, 1H, triazole-CH), 7.75 (ddd, *J* 8.0, 1.8, 0.9, 1H), 7.60 (t, *J* 1.8, 1H), 7.46 (t, *J* 8.0, 1H), 7.29 – 7.24 (m, 5H), 6.72 (s, 1H, DHA-H3), 6.57 (dd, *J* 11.2, 6.3, 1H), 6.50 (dd, *J* 11.2, 6.1, 1H), 6.34 (br d, *J* 6.3, 1H), 6.31 (ddd, *J* 10.2, 6.1, 2.0, 1H), 5.79 (dd, *J* 10.2, 3.8, 1H), 3.77 (dt, 3.8, 2.0, 1H, DHA-H8a), 2.42 (s, 3H, CH_3) ppm. δ_C (125 MHz, $CDCl_3$) 140.0, 139.0, 138.3, 136.9, 133.9, 133.8, 133.6, 131.6, 131.5, 130.9, 130.4, 130.0, 129.9, 128.2, 127.9, 126.9, 126.4, 125.3, 121.9, 119.6, 115.0, 112.6, 51.2, 45.3, 21.4 ppm. HRMS (ESP+) calcd 436.1533 ($C_{27}H_{19}N_5Na^+$); exp 436.1519 ($[M+Na]^+$).

UV-Vis Absorption Spectra in CH_3CN / Decay of VHF Absorption (exponential fit)

5b:



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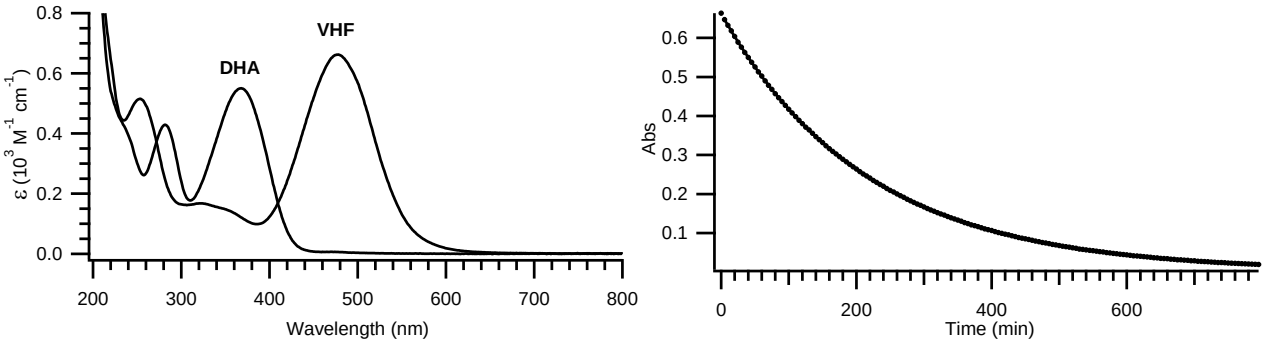

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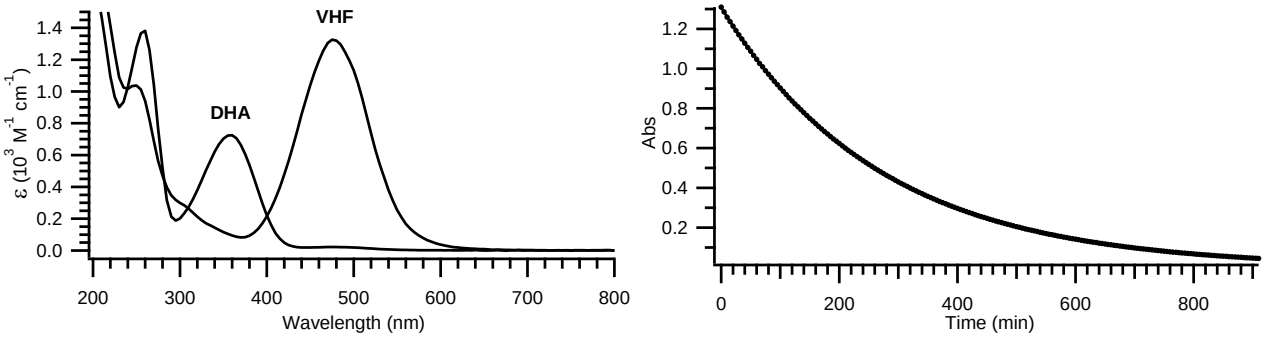
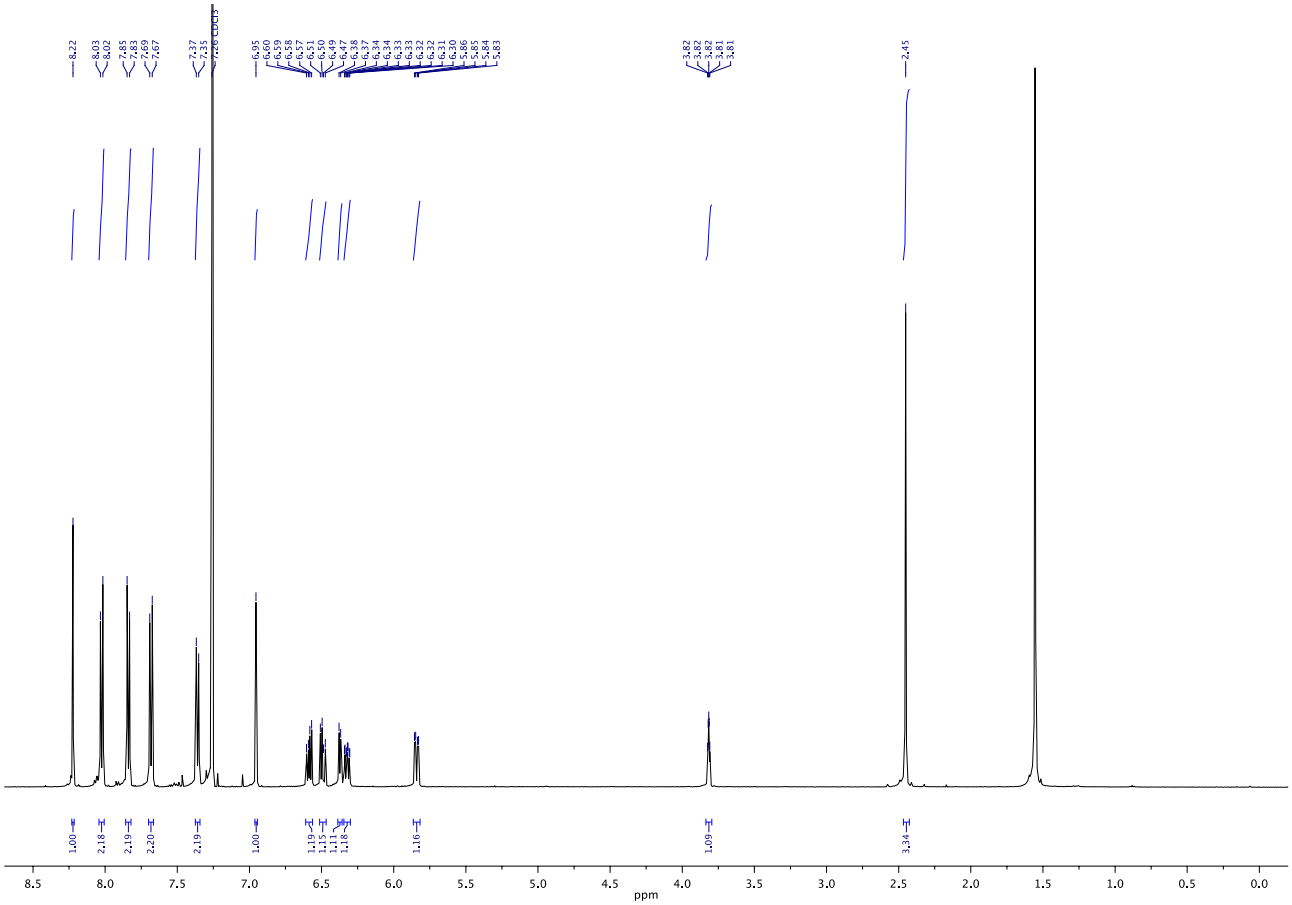
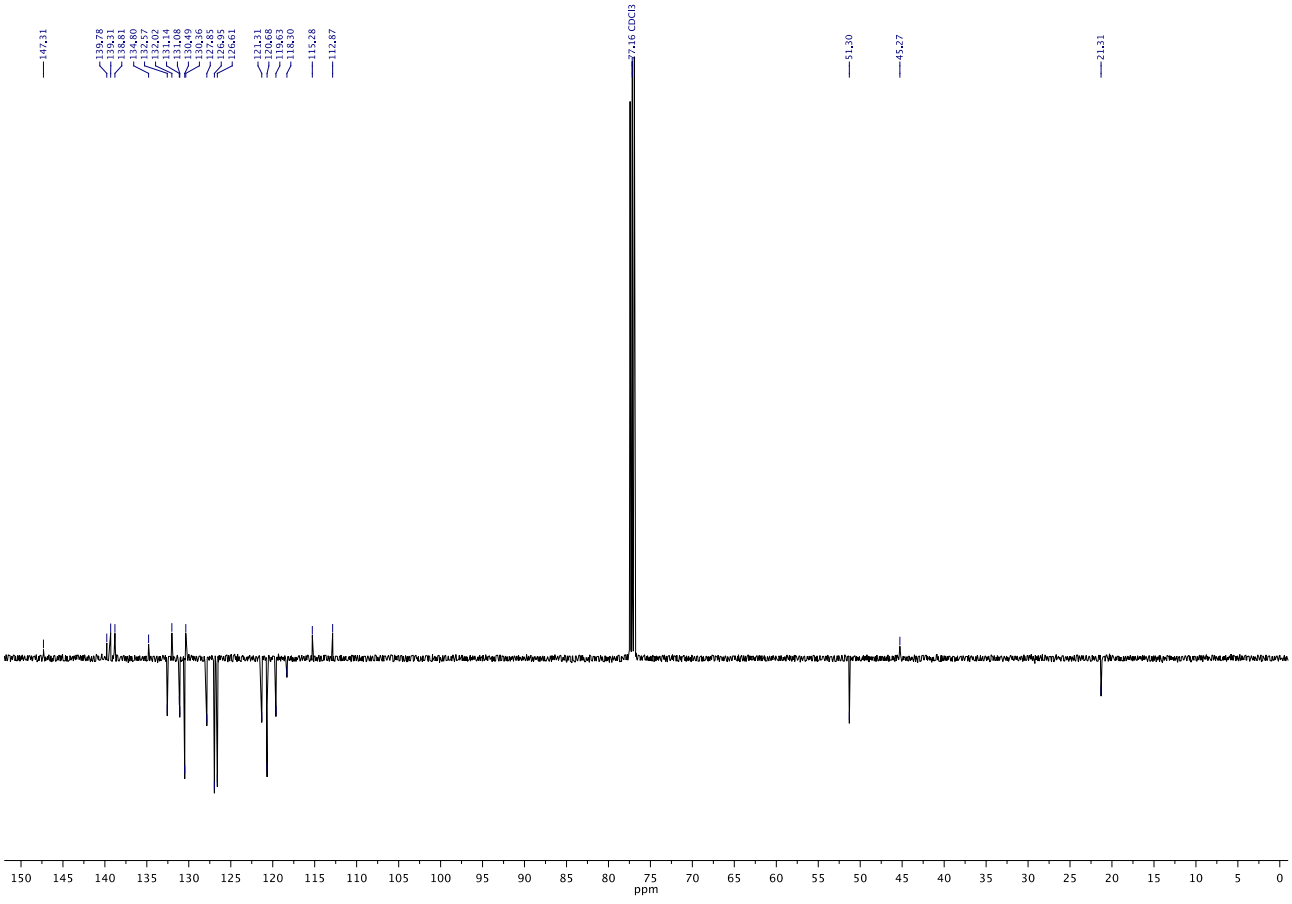


NMR Spectra in $CDCl_3$

5a:





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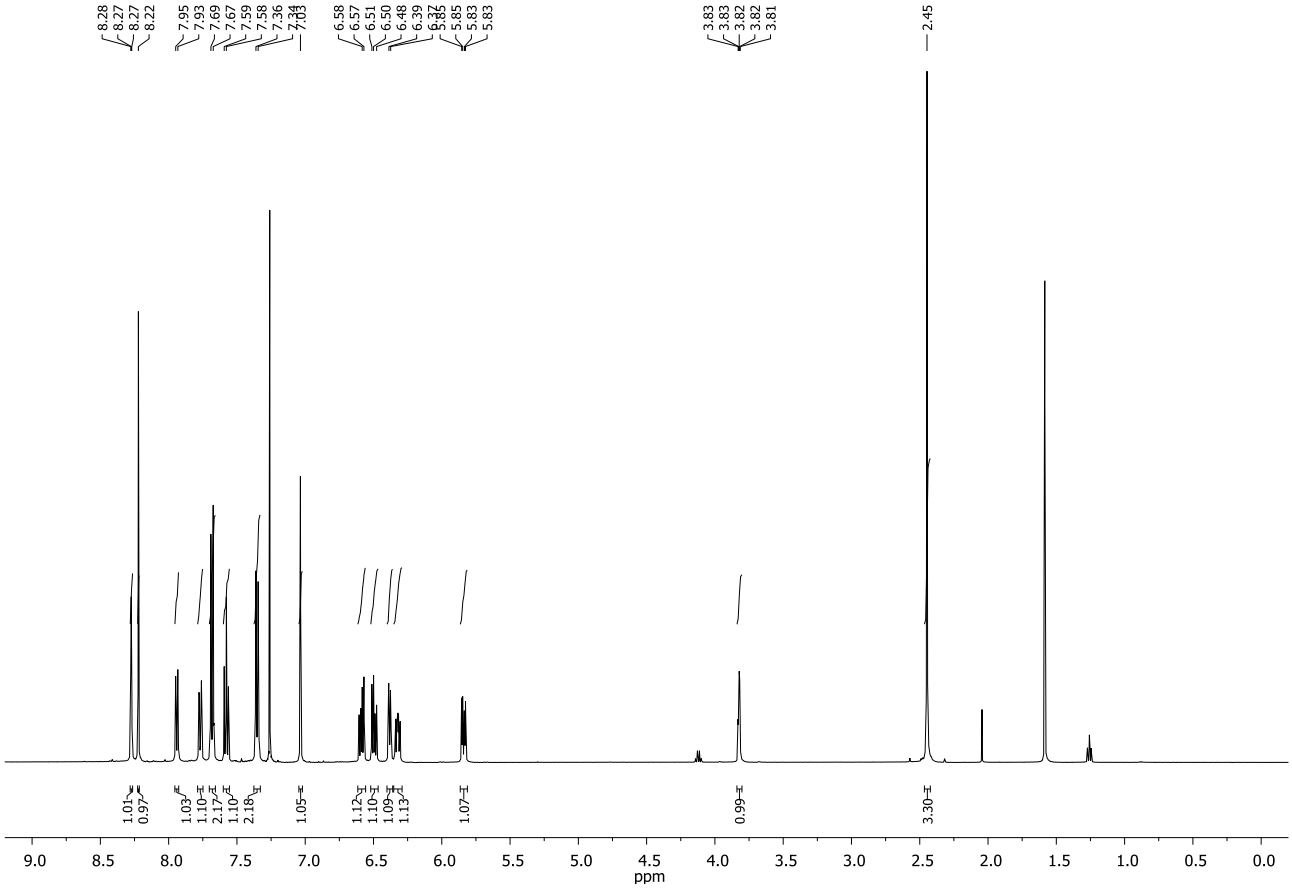
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6.57
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6.39
6.37
5.85
5.83
5.83
3.83
3.83
3.82
3.82
3.81
2.45
1.01
0.97
1.03
1.10
2.17
1.10
2.18
1.05
1.12
1.10
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1.07
0.99
3.30
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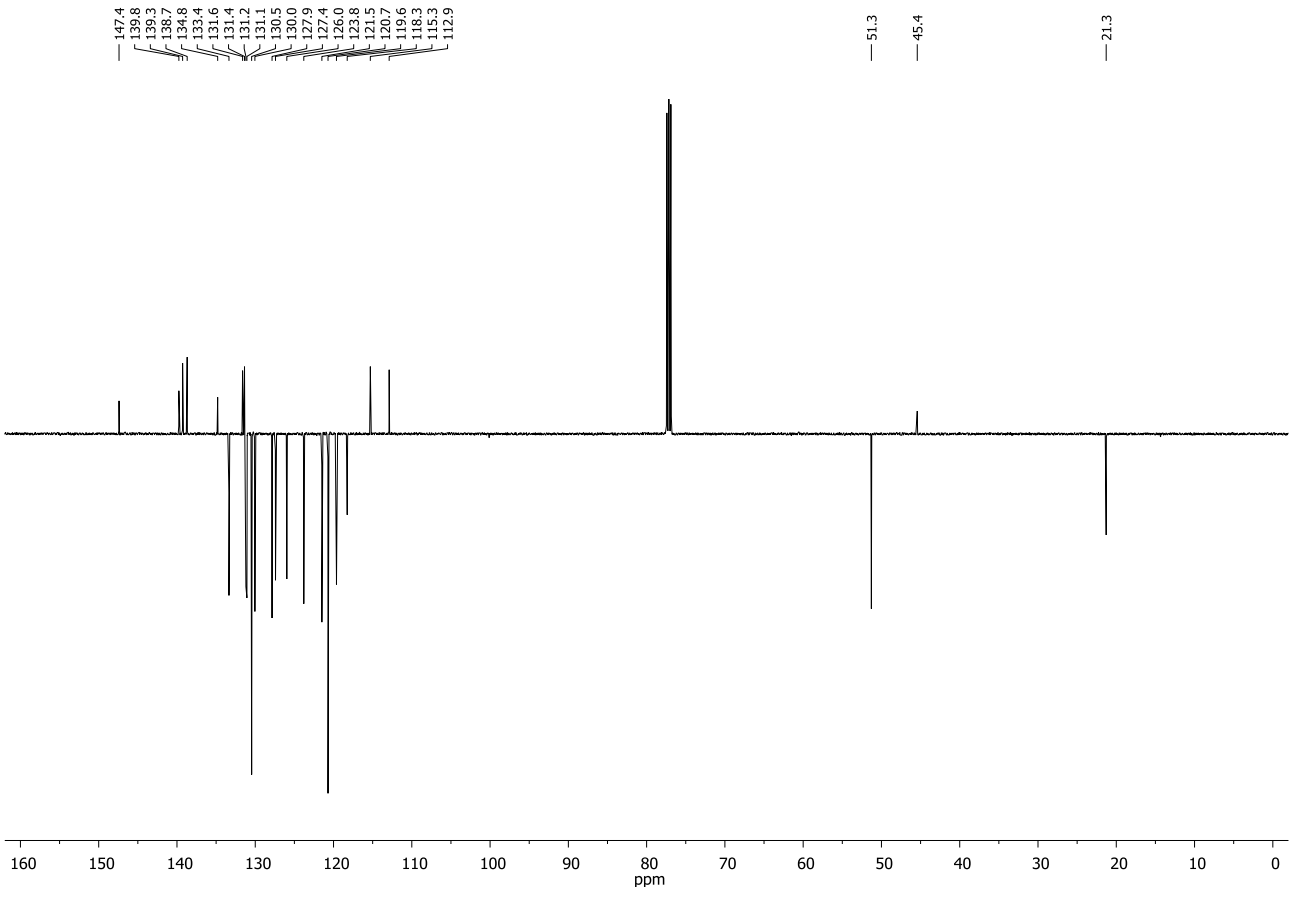
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127.4
126.0
123.8
121.5
120.7
119.6
118.3
115.3
112.9
51.3
45.4
21.3
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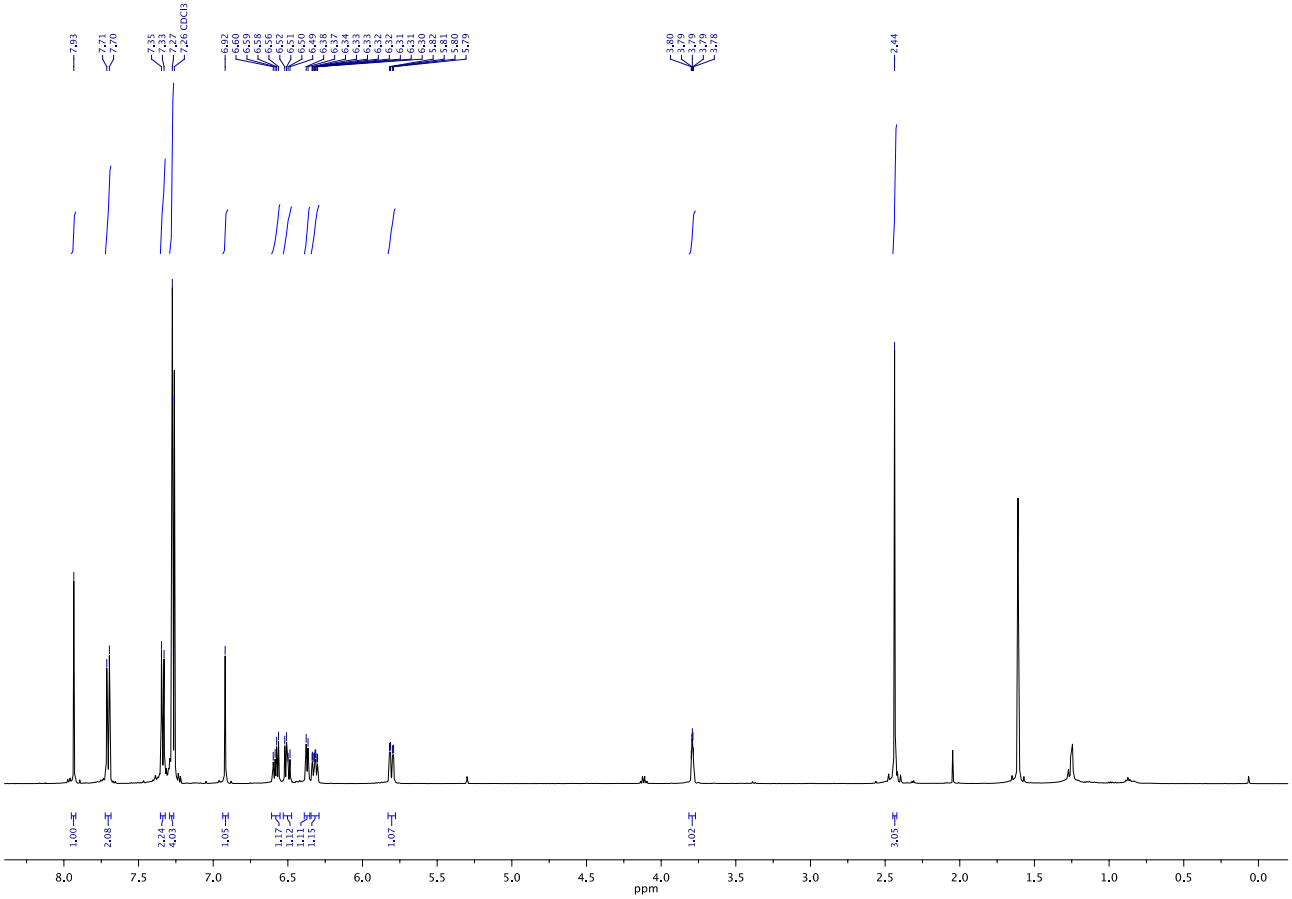
ppm

6a: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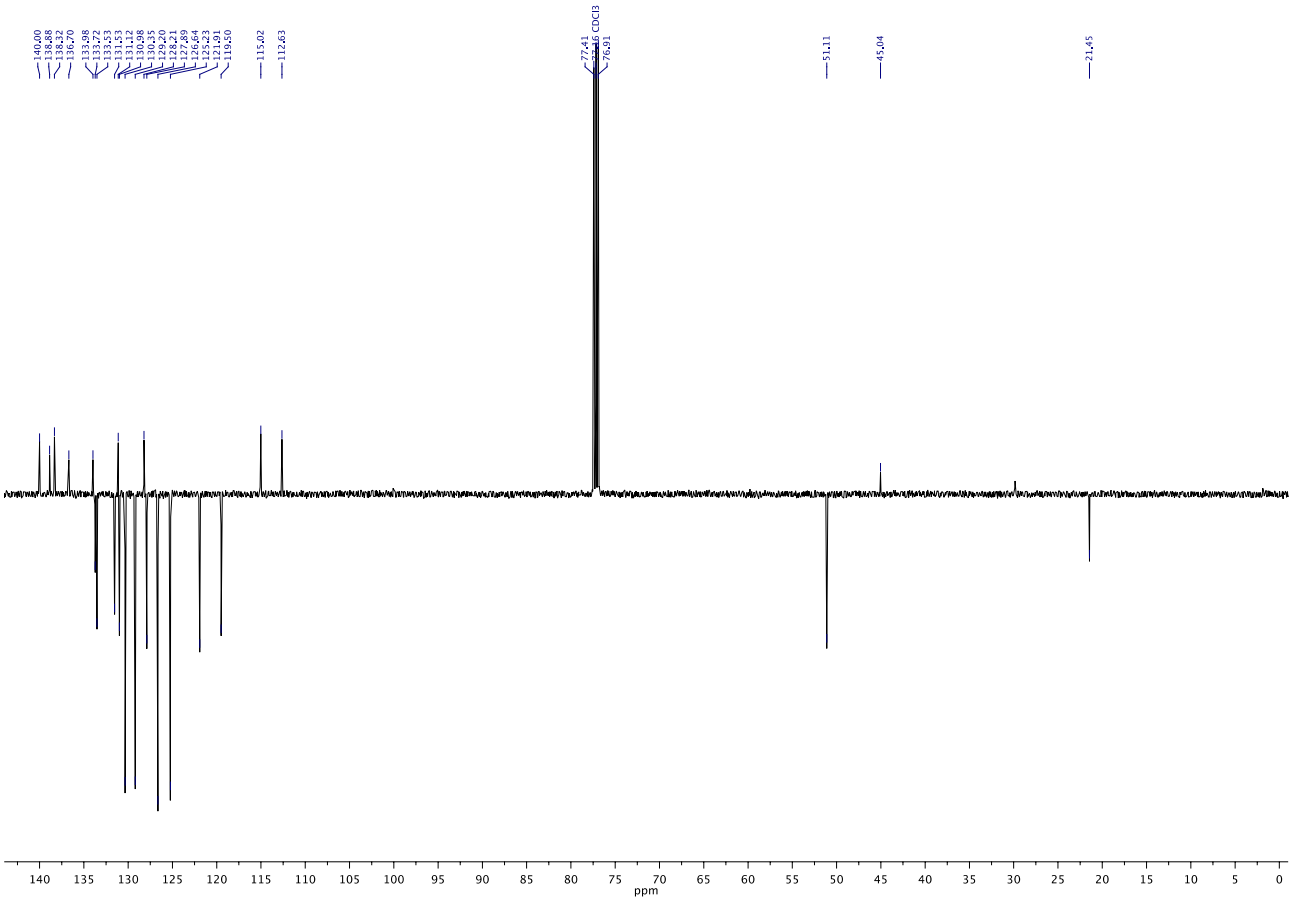
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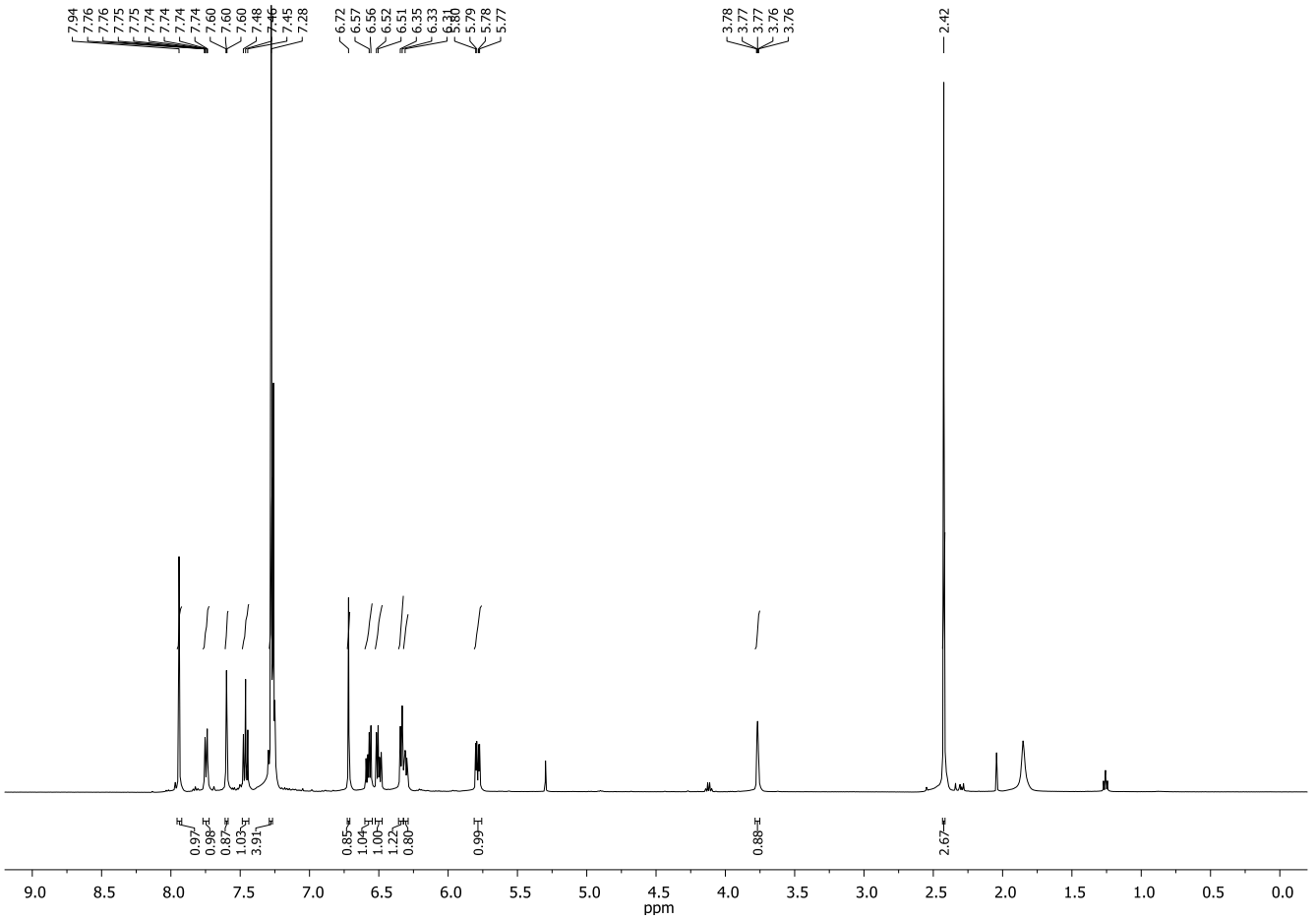
6b: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6.31
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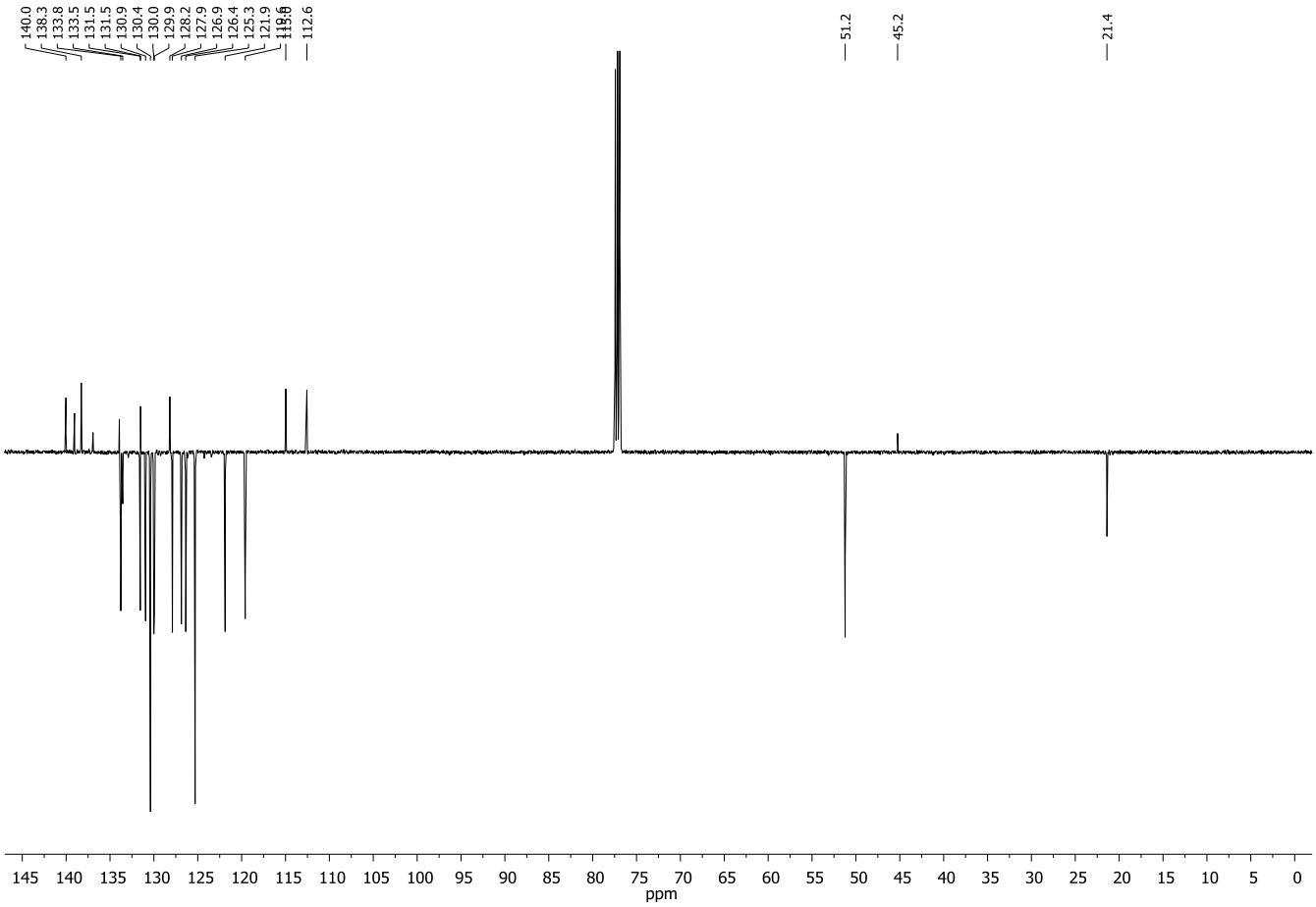
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51.2
45.2
21.4
ppm