

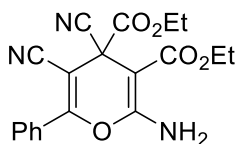
Reactions of diethyl dicyanofumarate with β -keto nitriles and β -keto esters: synthesis of polyfunctional 4*H*-pyrans

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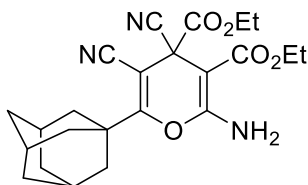
Experimental

Solvents were purified and dried by standard procedures before use. ^1H and ^{13}C NMR spectra (400 and 100 MHz, respectively), as well as DEPT-135 spectra were acquired on a JEOL JNM-ECX400 spectrometer in CDCl_3 using residual solvent signal (7.26 ppm for ^1H nuclei, 77.2 ppm for ^{13}C nuclei) as internal standard. Chemical shifts are reported in δ unit-parts per million (ppm). Splitting patterns are designated as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Elemental analysis was performed on a Euro Vector EA-3000 CHNS-analyzer. Melting points were determined by the capillary method on an SRS OptiMelt MPA100 apparatus. Reaction progress and purity of the obtained compounds were monitored by thin-layer chromatography (TLC) on Merck Silica gel 60 F₂₅₄ plates, eluted with CHCl_3 , and visualized under UV light and iodine vapor.

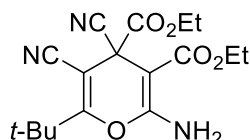
Synthesis of diethyl 2-amino-4-cyano-4*H*-pyran-3,4-dicarboxylates 3a–c (general procedure). A mixture of diethyl dicyanofumarate **1** (220 mg, 1 mmol) and β -keto nitrile **2a–c** (1 mmol) in *o*-xylene (6 ml) was refluxed under argon until TLC showed complete conversion (4–9 h). The solvent was distilled off under reduced pressure. The residue was purified by column chromatography (eluent CHCl_3 – CCl_4 , 3:1) and recrystallized from EtOH. In the case of compound **3b**, the product precipitated upon cooling and was collected by filtration.



Diethyl 2-amino-4,5-dicyano-6-phenyl-4*H*-pyran-3,4-dicarboxylate (3a). Reaction time 6 h. Yield 260 mg (71%), light yellow crystals, mp 164–165 °C. IR spectrum, ν , cm^{-1} : 3267 (NH_2), 2970, 2214 (CN), 1736 (C=O), 1678 (C=O), 1589, 1369, 1254, 1215, 1096, 1026, 779, 694. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.37 (3H, t, J = 7.2, CH_3), 1.39 (3H, t, J = 7.2, CH_3), 4.27–4.36 (2H, m, CH_2), 4.43 (2H, q, J = 7.2, CH_2), 4.74 (1H, br. s, NH_2), 7.44–7.47 (3H, m, Ph), 7.50–7.53 (2H, m, Ph), 9.50 (1H, s, NH_2). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 13.8 (CH_3), 14.2 (CH_3), 62.3 (CH_2), 64.3 (CH_2), 74.9 (C), 95.4 (C), 110.4 (CN), 115.5 (CN), 125.6 (2CH Ph), 129.5 (2CH Ph), 130.6 (CH Ph), 132.4 (C), 133.9 (C), 139.0 (C), 159.1 (C), 159.4 (C), 166.5 (C). Found, %: C 62.05; H 4.61; N 11.35. $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_5$. Calculated, %: C 62.12; H 4.66; N 11.44.

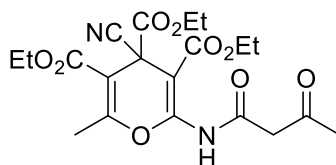


Diethyl 6-(adamantan-1-yl)-2-amino-4,5-dicyano-4H-pyran-3,4-dicarboxylate (3b). Reaction time 4 h. Yield 235 mg (55%), light yellow crystals, mp 189–190 °C. IR spectrum, ν , cm^{-1} : 3323, 3296 (NH_2), 2903, 2853 (CH Ad), 2214 (CN), 1740 (C=O), 1678 (C=O), 1584, 1307, 1281, 1024, 777. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.35 (3H, t, $J = 7.2$, CH_3), 1.39 (3H, t, $J = 7.2$, CH_3), 1.64–1.87 (12H, m, $\text{CH}_2 \text{ Ad}$), 2.06 (3H, br. s, CH Ad), 4.03 (1H, br. s, NH_2), 4.29 (2H, q, $J = 7.2$, CH_2), 4.40–4.45 (2H, m, CH_2), 9.33 (1H, s, NH_2). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 13.8 (CH_3), 14.2 (CH_3), 28.2 (3CH Ad), 36.36 (3 CH_2 Ad), 36.44 (3 CH_2 Ad), 41.8 (C Ad), 62.1 (CH_2O), 64.2 (CH_2O), 73.3 (C), 100.2 (C), 111.9 (CN), 115.5 (CN), 130.2 (C), 142.7 (C), 158.6 (C), 159.6 (C), 167.1 (C). Found, %: C 64.99; H 6.36; N 9.77. $\text{C}_{23}\text{H}_{27}\text{N}_3\text{O}_5$. Calculated, %: C 64.93; H 6.40; N 9.88.

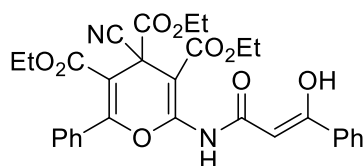


Diethyl 2-amino-6-(tert-butyl)-4,5-dicyano-4H-pyran-3,4-dicarboxylate (3c). Reaction time 9 h. Yield 160 mg (46%), light yellow crystals, mp 119–120 °C. IR spectrum, ν , cm^{-1} : 3302 (NH_2), 2965 ($\text{CH } t\text{-Bu}$), 2214 (CN), 1740 (C=O), 1694 (C=O), 1620, 1589, 1304, 1263, 1221, 1202, 1099, 1020, 941, 775. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.13 (9H, s, $t\text{-Bu}$), 1.35 (3H, t, $J = 7.2$, CH_3), 1.39 (3H, t, $J = 7.2$, CH_3), 3.90 (1H, br. s, NH_2), 4.29 (2H, q, $J = 7.2$, CH_2), 4.39–4.47 (2H, m, CH_2), 9.30 (1H, s, NH_2). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 13.8 (CH_3), 14.2 (CH_3), 24.9 (Me_3C), 39.8 (Me_3C), 62.1 (CH_2), 64.2 (CH_2), 73.6 (C), 100.3 (C), 111.7 (CN), 115.4 (CN), 130.1 (C), 142.7 (C), 158.5 (C), 159.5 (C), 167.0 (C). Found, %: C 58.71; H 6.04; N 12.01. $\text{C}_{17}\text{H}_{21}\text{N}_3\text{O}_5$. Calculated, %: C 58.78; H 6.09; N 12.10.

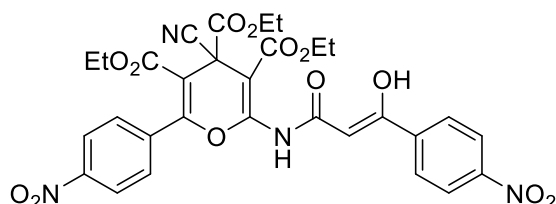
Synthesis of triethyl 4-cyano-2-(1,3-dioxoalkylamino)-4H-pyran-3,4,5-tricarboxylates (6a–c) (general procedure). A mixture of diethyl dicyanofumarate **1** (220 mg, 1 mmol) and β -keto ester **4a–c** (2 mmol) in *o*-xylene (6 ml) was refluxed under argon until TLC showed complete conversion (6–17 h). The solvent was distilled off under reduced pressure. The residue was purified by column chromatography on silica gel (eluent $\text{CHCl}_3\text{--CCl}_4$, 1:1) followed by recrystallization from EtOH.



Triethyl 4-cyano-6-(1,3-dioxobutylamino)-2-methyl-4H-pyran-3,4,5-tricarboxylate (6a). Reaction time 17 h. Yield 150 mg (38%), colorless crystals, mp 124–125 °C. IR spectrum, ν , cm^{-1} : 3248 (NH), 2997, 2970, 2210 (CN), 1748 (C=O), 1647, 1570, 1366, 1258, 1215, 1092, 1026, 775. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.25 (3H, t, $J = 7.2$, CH_3CH_2), 1.26 (3H, t, $J = 7.2$, CH_3CH_2), 1.31 (3H, t, $J = 7.2$, CH_3CH_2), 2.11 (3H, s, CH_3CO), 2.42 (3H, s, CH_3), 3.93 (1H, d, $J = 19.2$, CH_2), 4.05 (1H, d, $J = 19.2$, CH_2), 4.14–4.26 (6H, m, 3 CH_2O), 10.47 (1H, br. s, NH). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 13.9 (CH_3), 14.1 (CH_3), 14.27 (CH_3), 14.32 (CH_3), 30.1 (CH_3CO), 45.1 (CH_2), 60.4 (CH_2), 61.7 (CH_2), 61.9 (CH_2), 63.0 (CH_2), 73.4 (C-4), 111.4 (C), 115.4 (CN), 153.5 (C), 163.0 (C), 166.0 (C), 166.8 (2C), 171.5 (C), 204.4 (C). Found, %: C 54.97; H 5.48; N 6.33. $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_9$. Calculated, %: C 55.04; H 5.54; N 6.42.

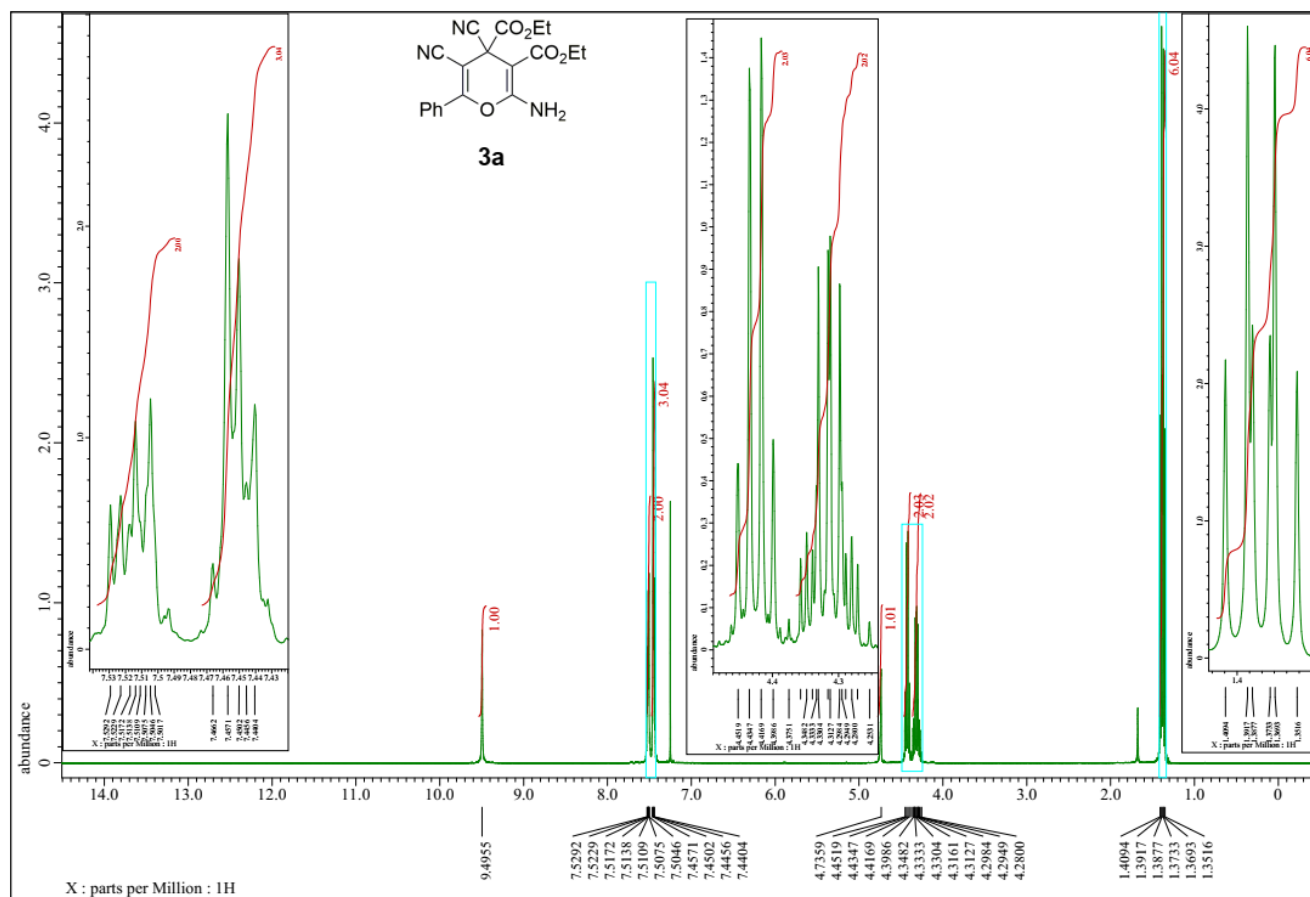


Triethyl (Z)-4-cyano-2-(3-hydroxy-1-oxo-3-phenylprop-2-enylamino)-6-phenyl-4H-pyran-3,4,5-tricarboxylate (6b). Reaction time 12 h. Yield 240 mg (47%), yellow crystals, mp 161–162 °C. IR spectrum, ν , cm^{-1} : 3422, 3294 (NH, OH), 2978, 2365 (CN), 1740 (C=O), 1694 (C=O), 1651, 1620, 1520, 1288, 1265, 1157, 1123, 1096, 1022, 922, 775, 687. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.18 (3H, t, $J = 7.2$, CH_3), 1.25 (3H, t, $J = 7.2$, CH_3), 1.27 (3H, t, $J = 7.2$, CH_3), 4.07–4.37 (6H, m, $3\text{CH}_2\text{O}$), 6.10 (1H, s, CH enol), 7.31–7.62 (10H, m, H Ar, NH, OH), 7.76 (2H, d, $J = 7.3$, H Ar). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 14.0 (CH_3), 14.3 (CH_3), 14.7 (CH_3), 59.4 (CH_2), 60.6 (CH_2), 62.2 (CH_2), 67.6 (C), 82.1 (C), 97.0 (CH enol), 109.1 (C), 116.9 (C), 126.8 (2CH Ph), 127.8 (2CH Ph), 128.5 (C), 129.1 (2CH Ph), 129.2 (2CH Ph), 130.3 (C), 130.8 (CH Ph), 132.6 (CH Ph), 154.8 (C), 160.5 (C), 162.1 (C), 162.3 (C), 163.3 (C), 166.7 (2C). Found, %: C 64.19; H 4.97; N 4.90. $\text{C}_{30}\text{H}_{28}\text{N}_2\text{O}_9$. Calculated, %: C 64.28; H 5.03; N 5.00.

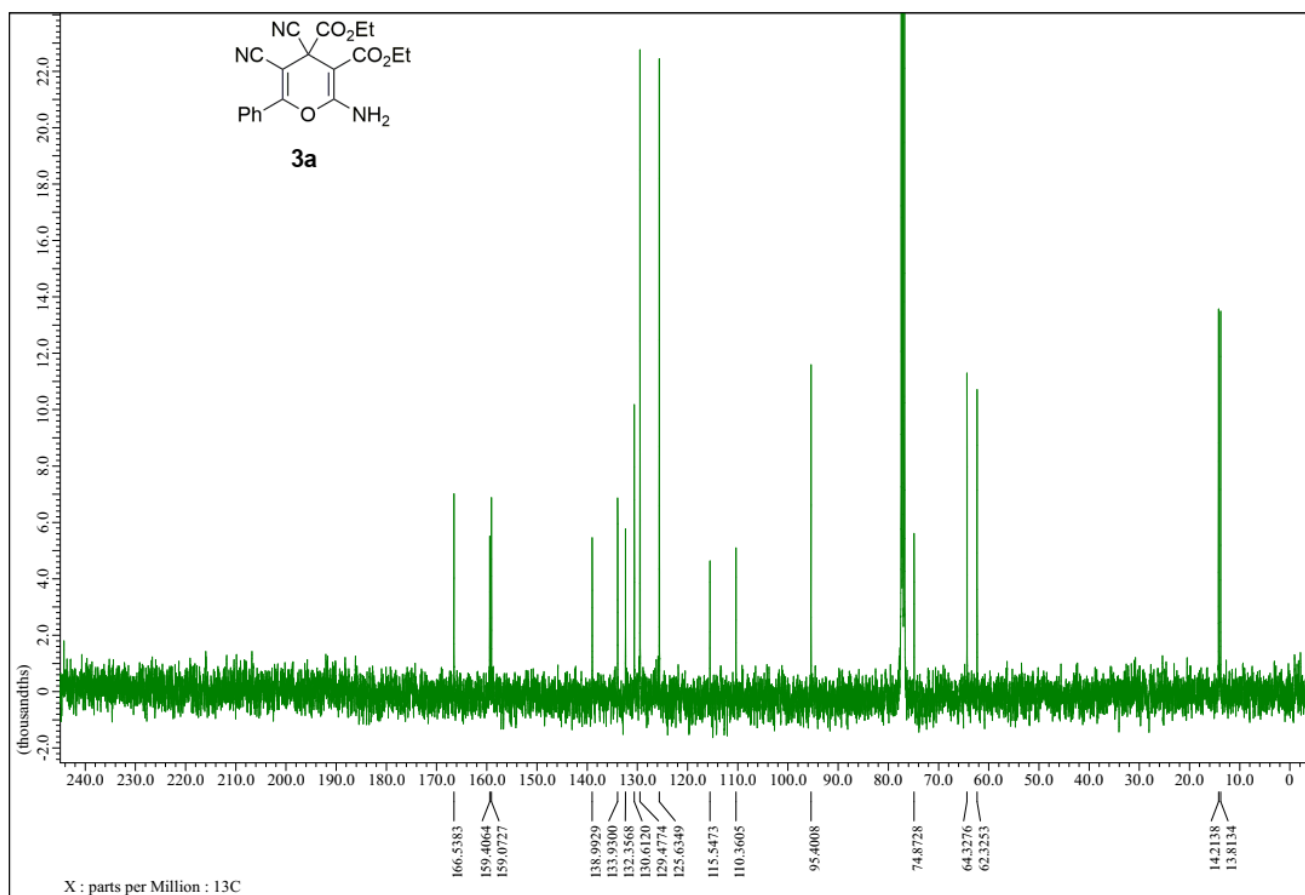


Triethyl (Z)-4-cyano-2-[3-hydroxy-3-(4-nitrophenyl)-1-oxoprop-2-enylamino]-6-(4-nitrophenyl)-4H-pyran-3,4,5-tricarboxylate (6c). Reaction time 6 h. Yield 260 mg (44%), yellow crystals, mp 208–209 °C. IR spectrum, ν , cm^{-1} : 3441, 3321, 1744, 1709, 1659, 1628, 1597, 1520, 1346, 1319, 1285, 1207, 961, 941, 860, 818. ^1H NMR spectrum (CDCl_3), δ , ppm (J , Hz): 1.22 (3H, t, $J = 7.2$, CH_3), 1.25 (3H, t, $J = 7.2$, CH_3), 1.30 (3H, t, $J = 7.2$, CH_3), 4.10–4.41 (6H, m, 3CH_2), 6.27 (1H, s, CH enol), 7.51 (2H, br. s, NH, OH), 7.79 (2H, d, $J = 8.9$, H Ar), 7.92 (2H, d, $J = 8.9$, H Ar), 8.19 (2H, d, $J = 8.9$, H Ar), 8.31 (2H, d, $J = 8.9$, H Ar). ^{13}C NMR spectrum (CDCl_3), δ , ppm: 14.0 (CH_3), 14.3 (CH_3), 14.7 (CH_3), 59.7 (CH_2), 61.2 (CH_2), 62.6 (CH_2), 67.8 (C), 81.9 (C), 99.9 (CH enol), 111.9 (C), 117.1 (C), 123.1 (2CH), 124.4 (2CH), 127.6 (2CH), 130.2 (2CH), 134.2 (C), 135.7 (C), 148.9 (C), 150.0 (C), 154.3 (C), 159.2 (C), 159.3 (C), 159.4 (C), 162.6 (C), 165.9 (C), 166.3 (C). Found, %: C 55.43; H 3.98; N 8.55. $\text{C}_{30}\text{H}_{26}\text{N}_4\text{O}_{13}$. Calculated, %: C 55.39; H 4.03; N 8.61.

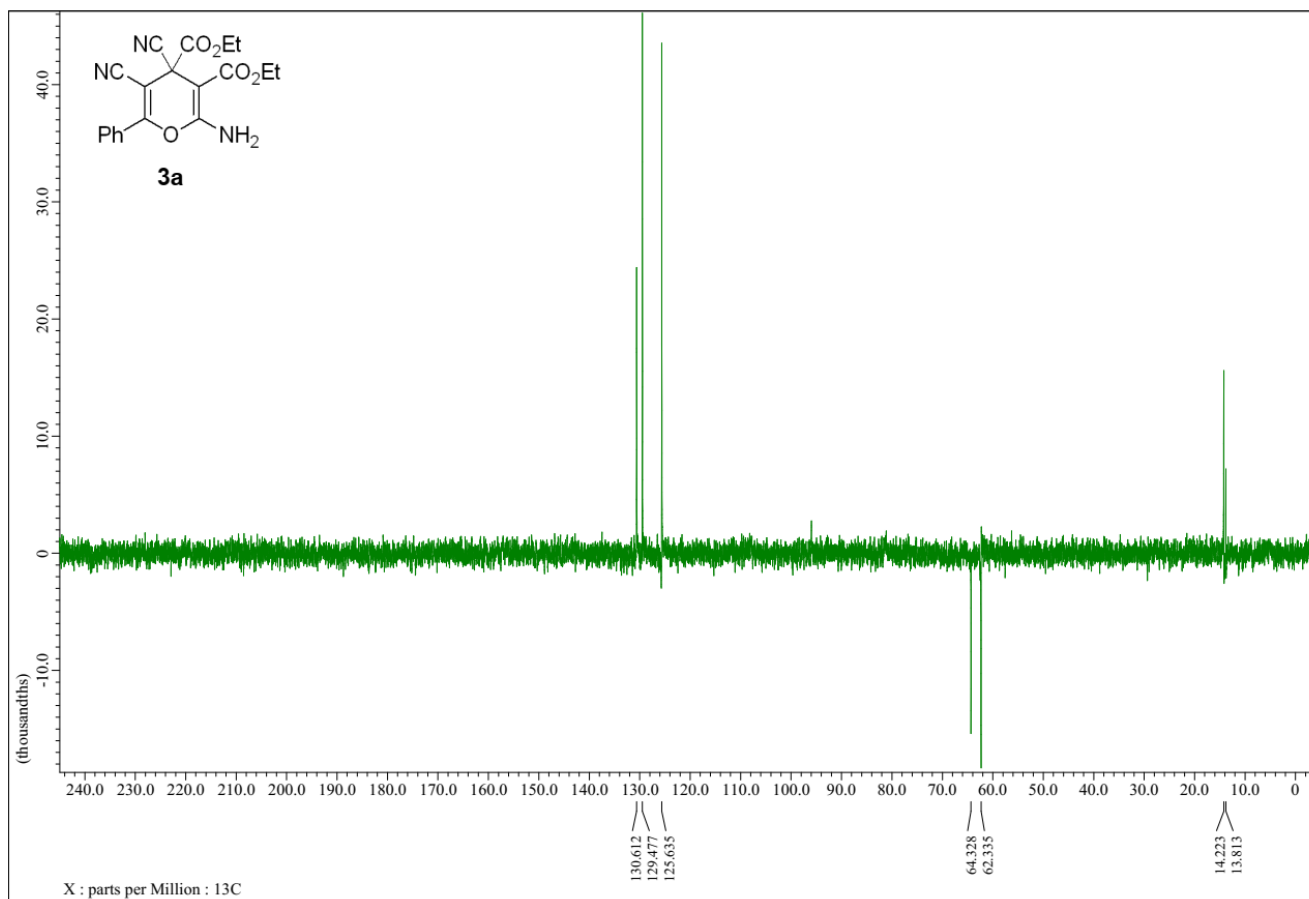
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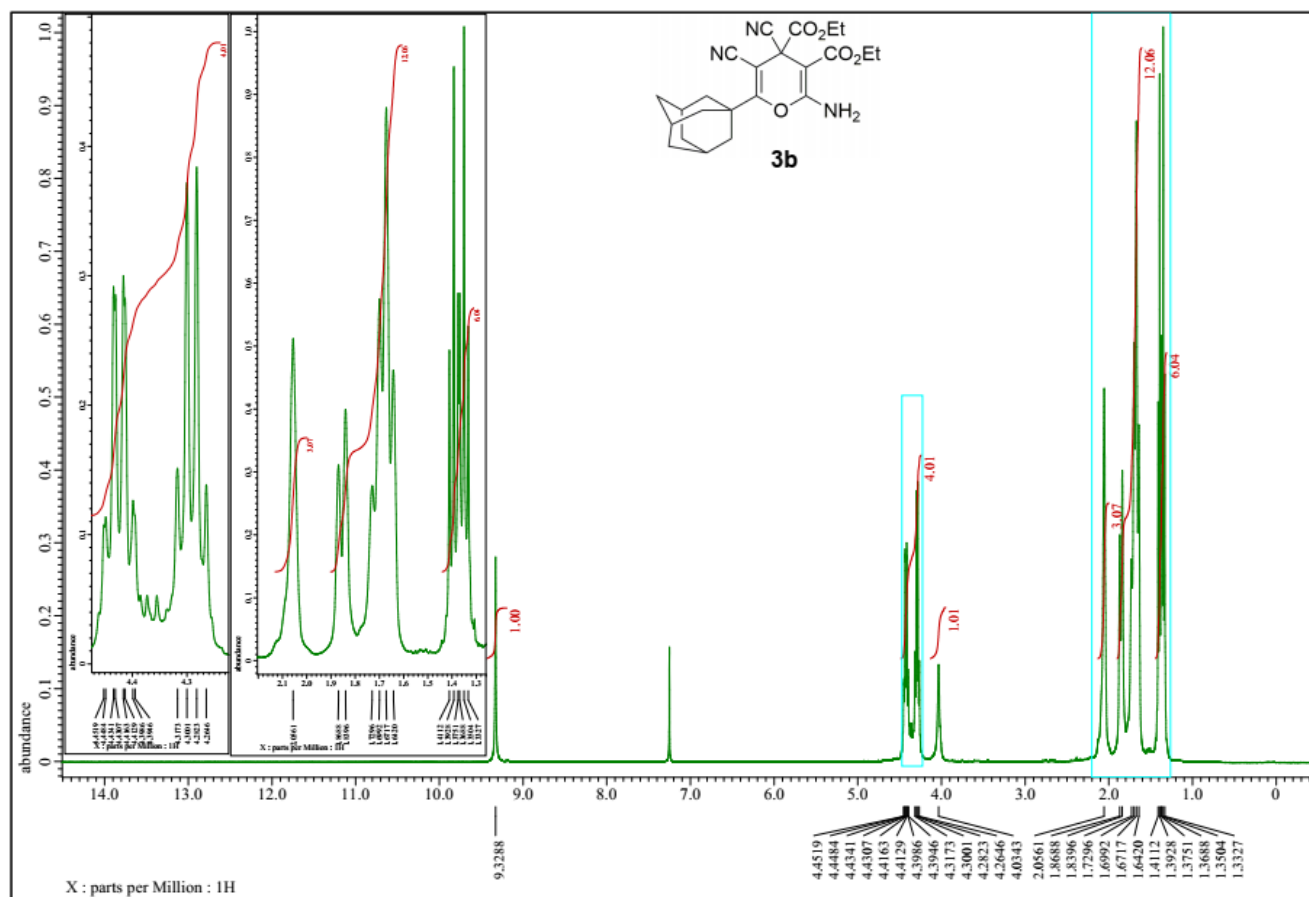
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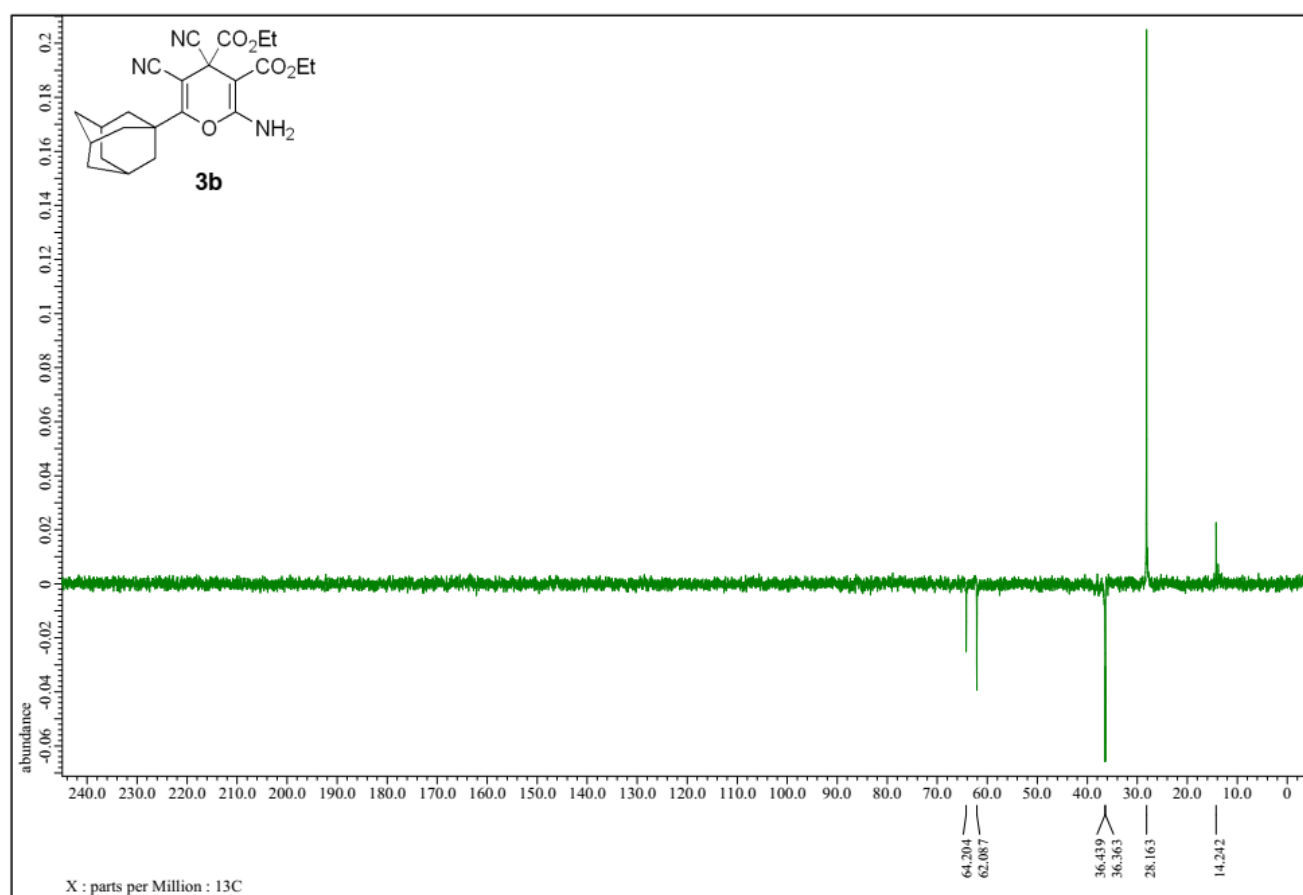
DEPT-135



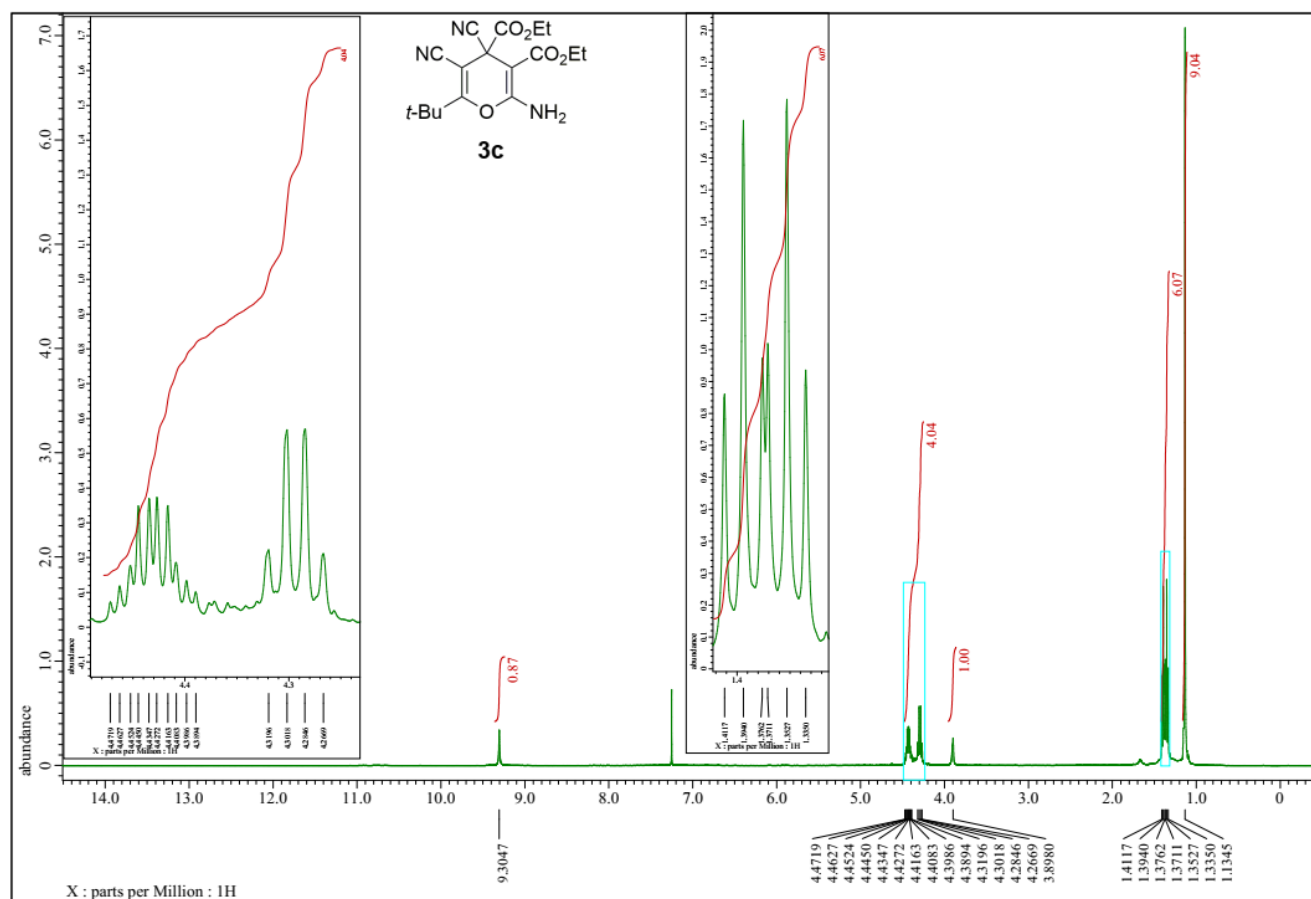
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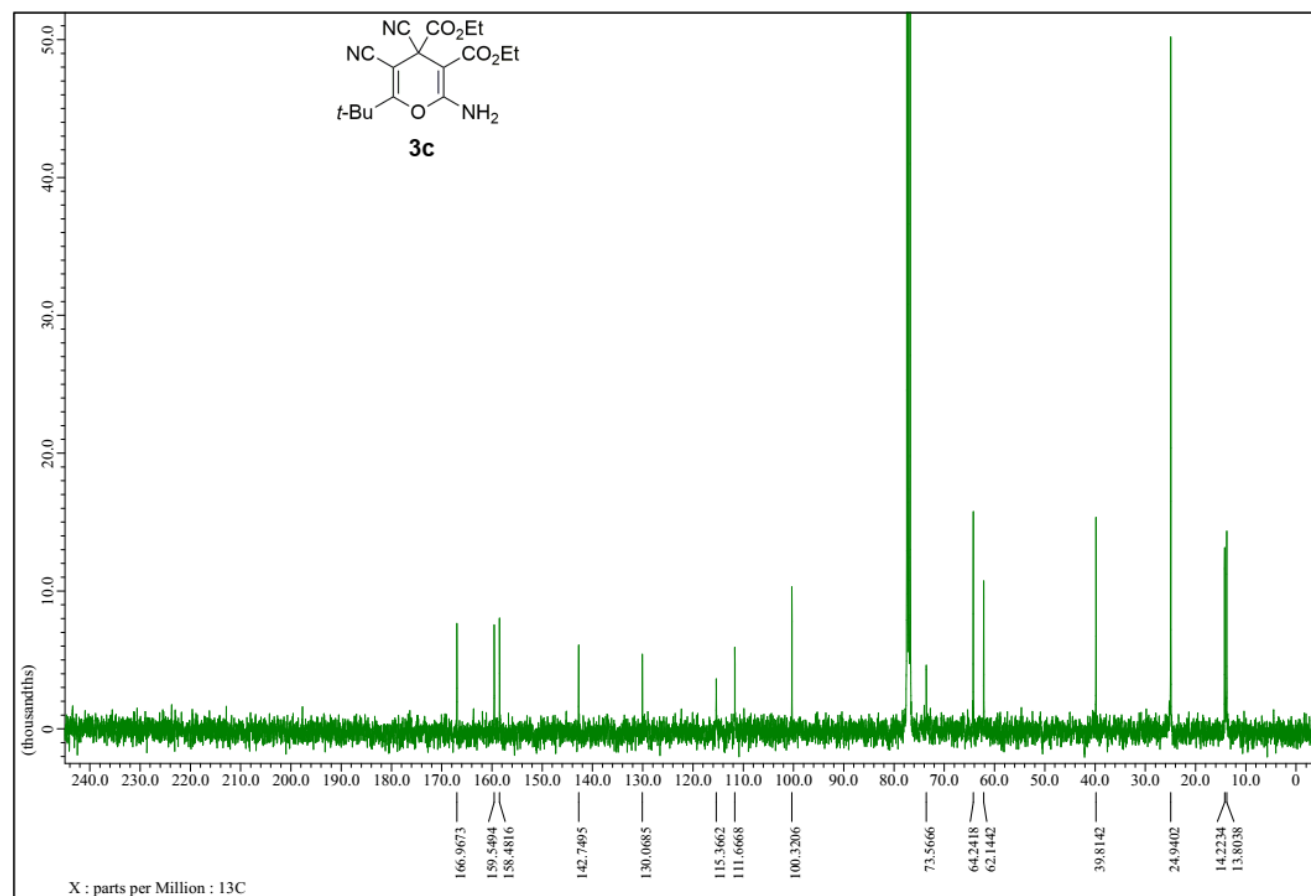
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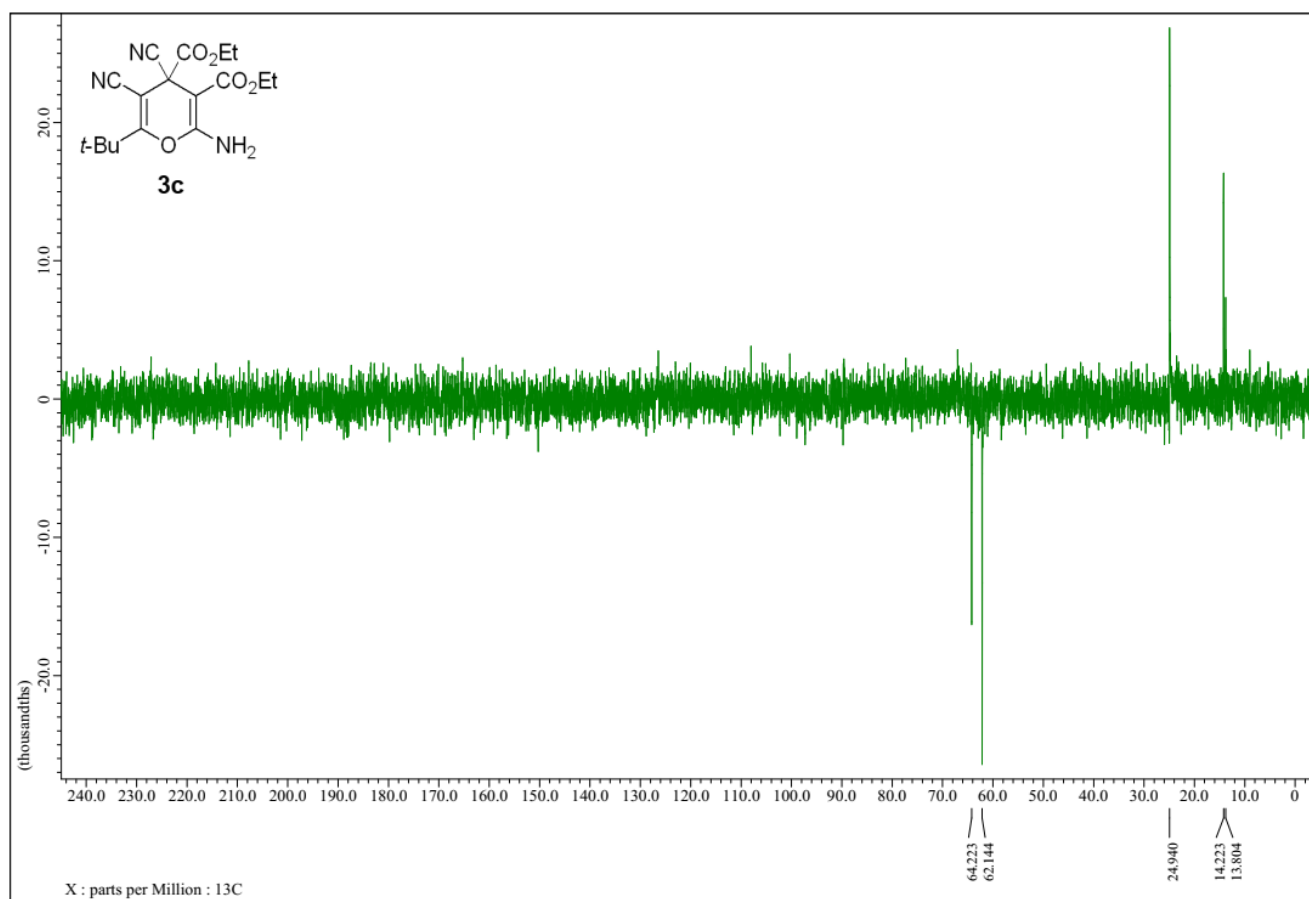
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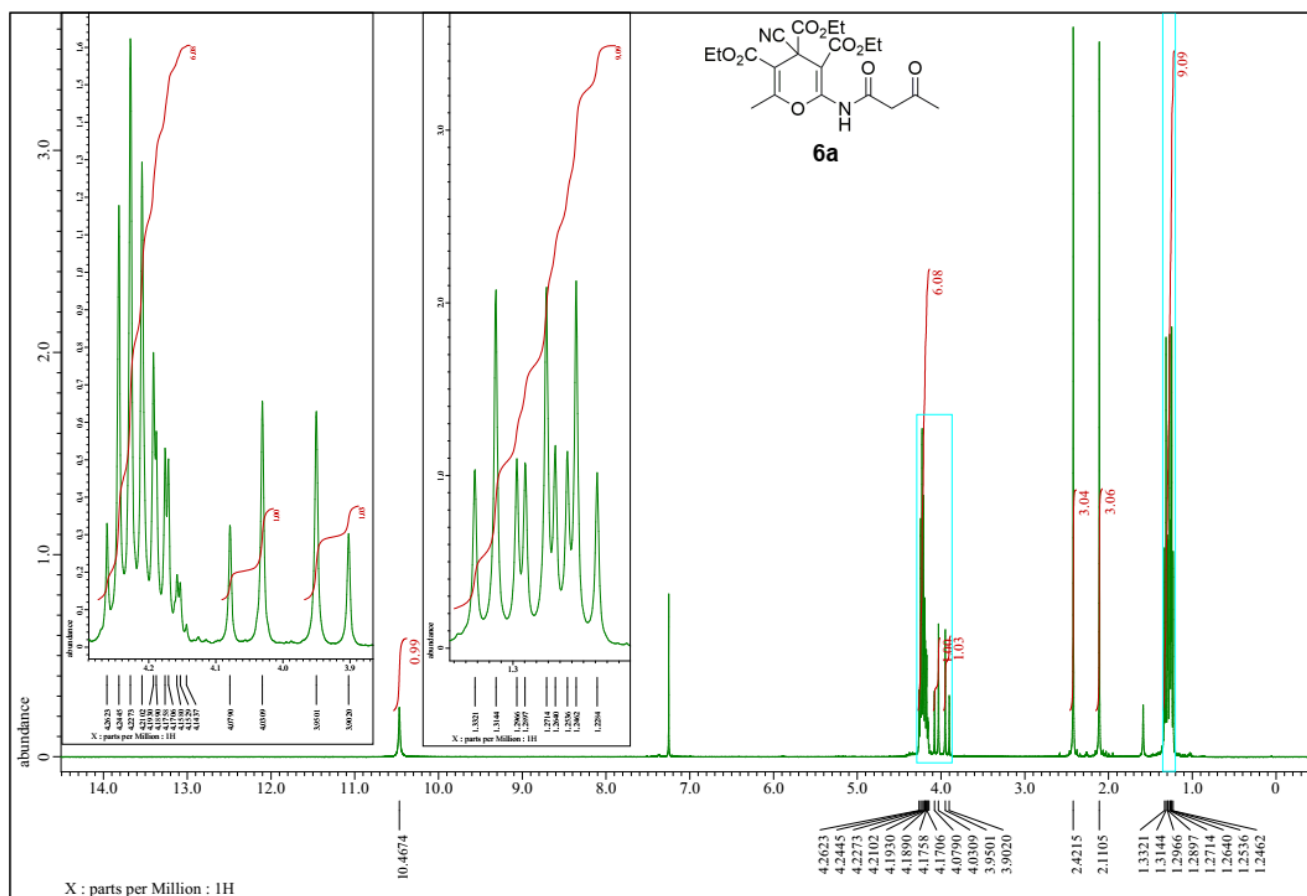
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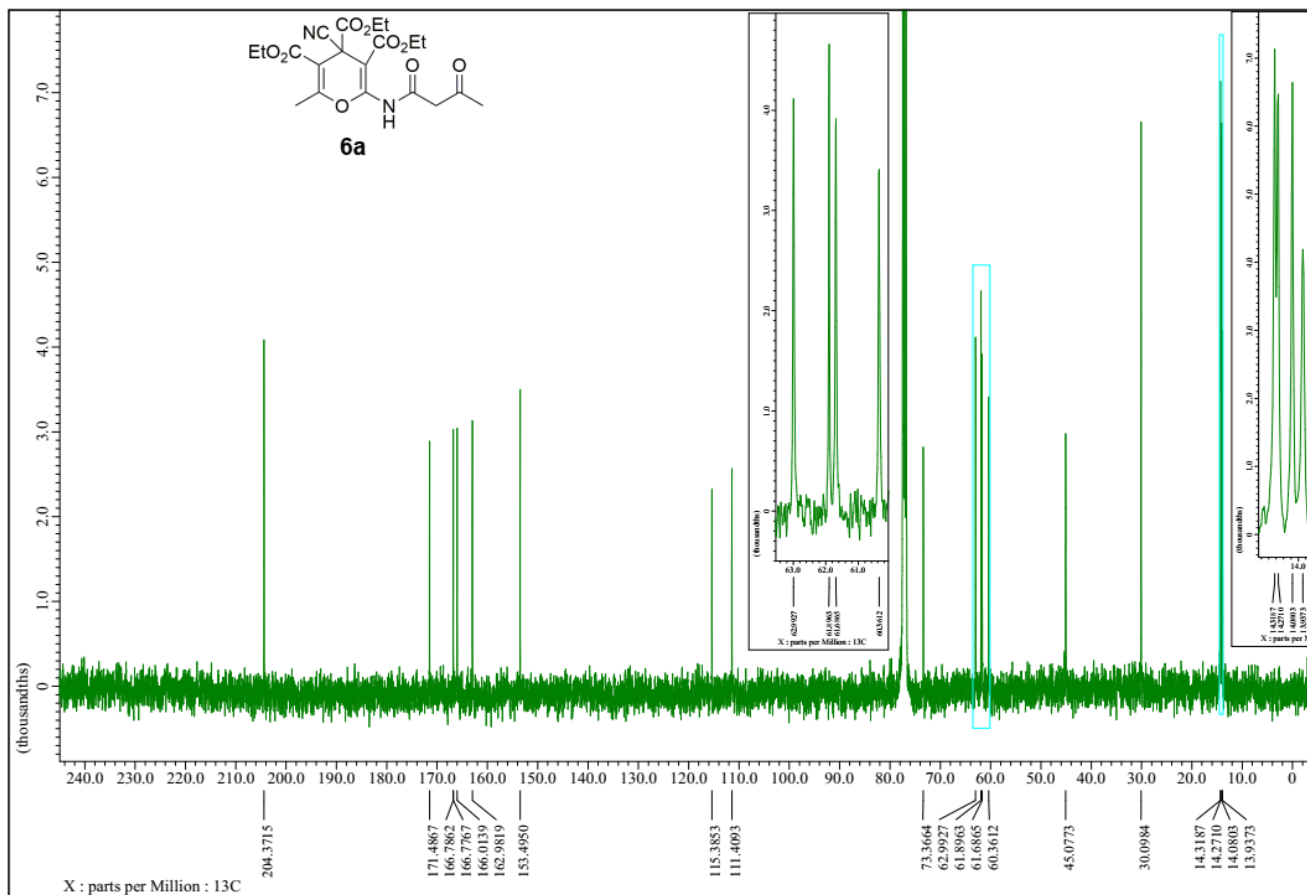
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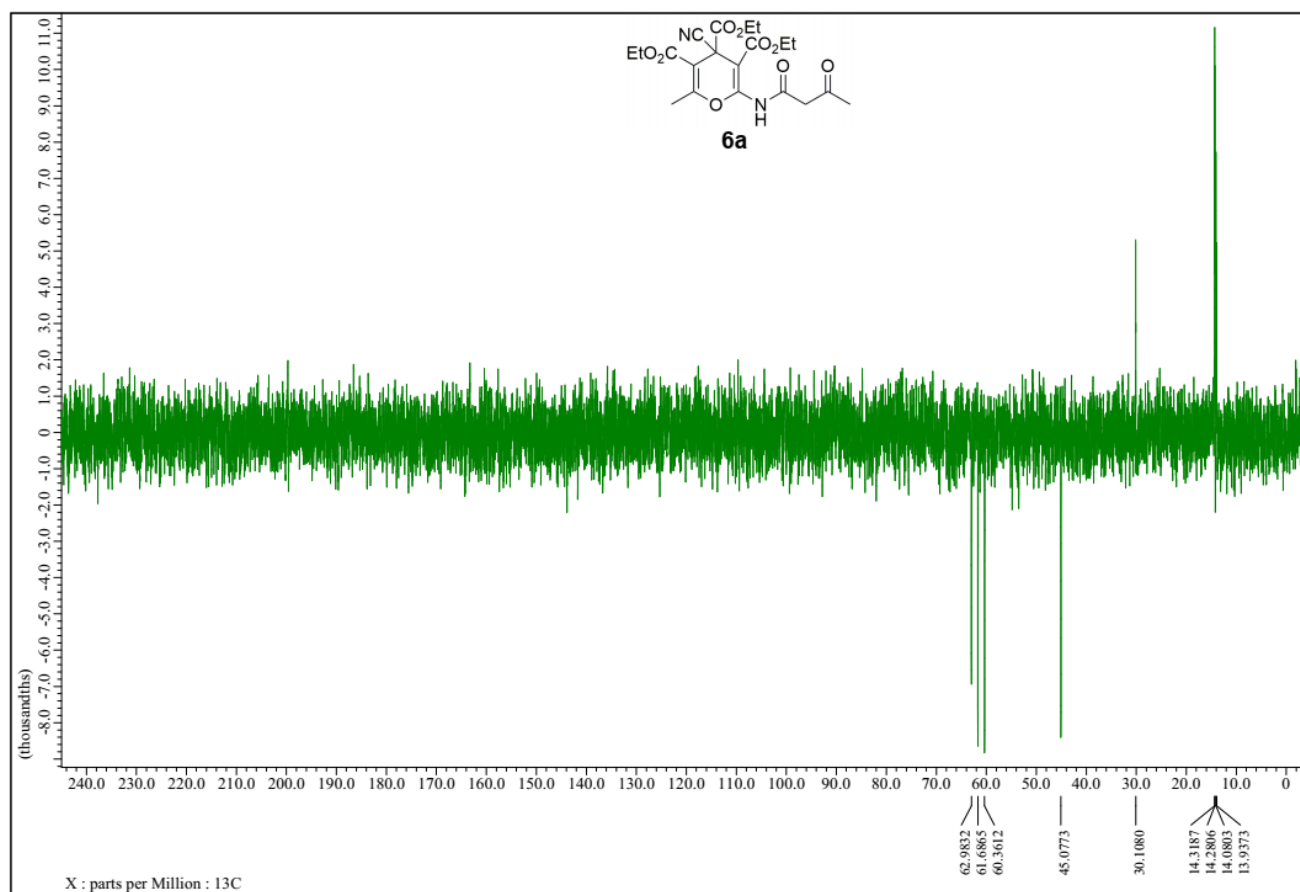
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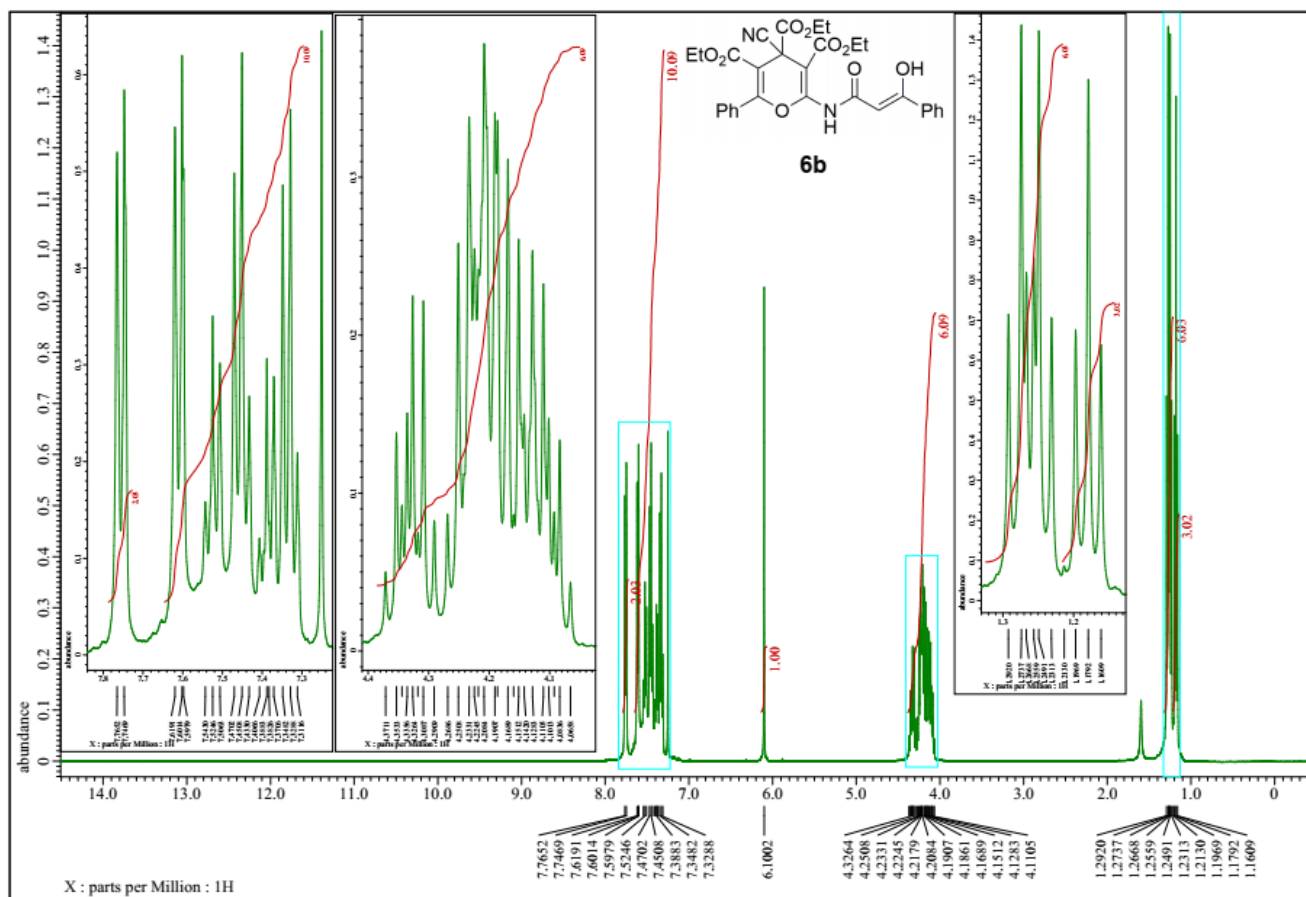
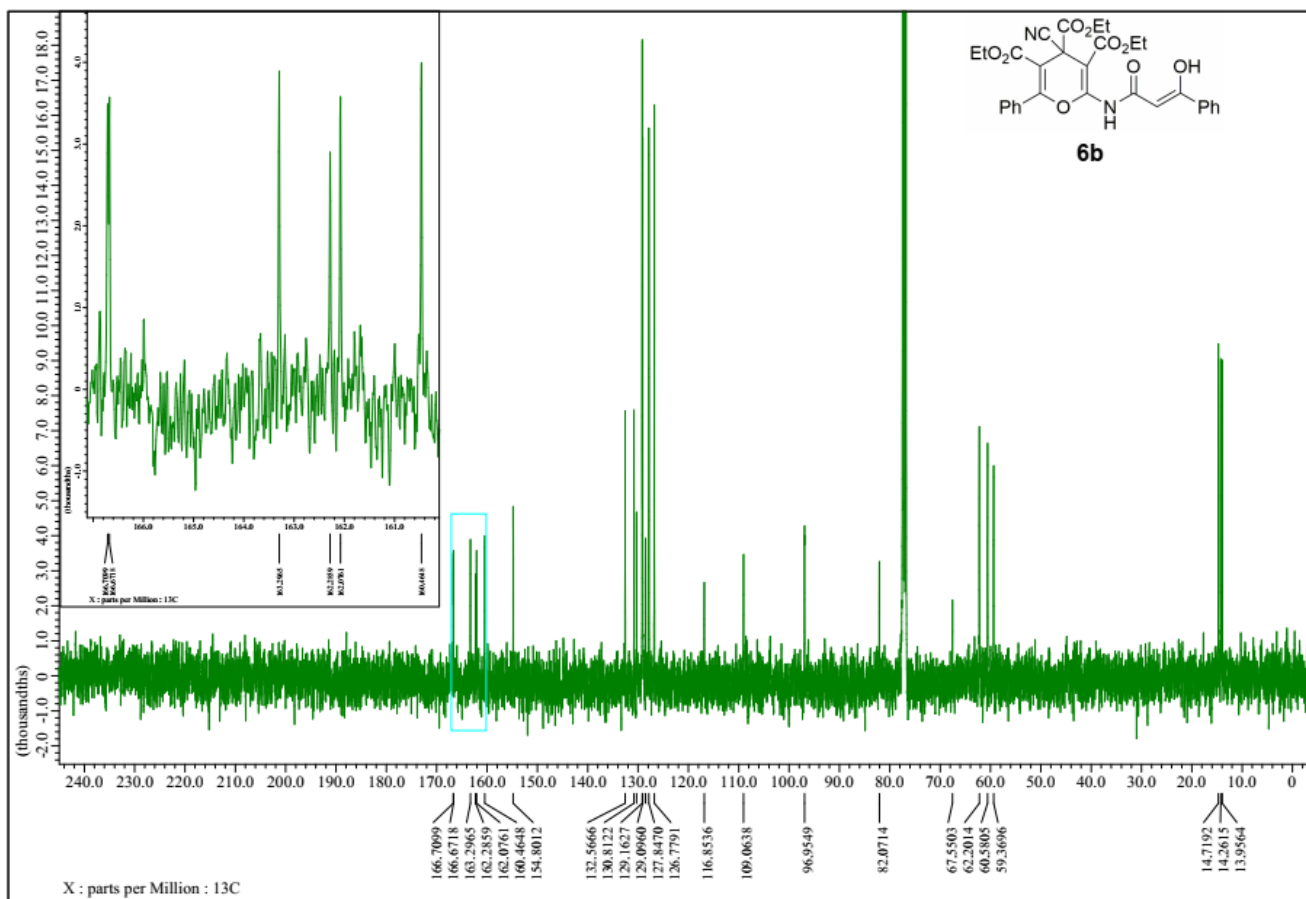


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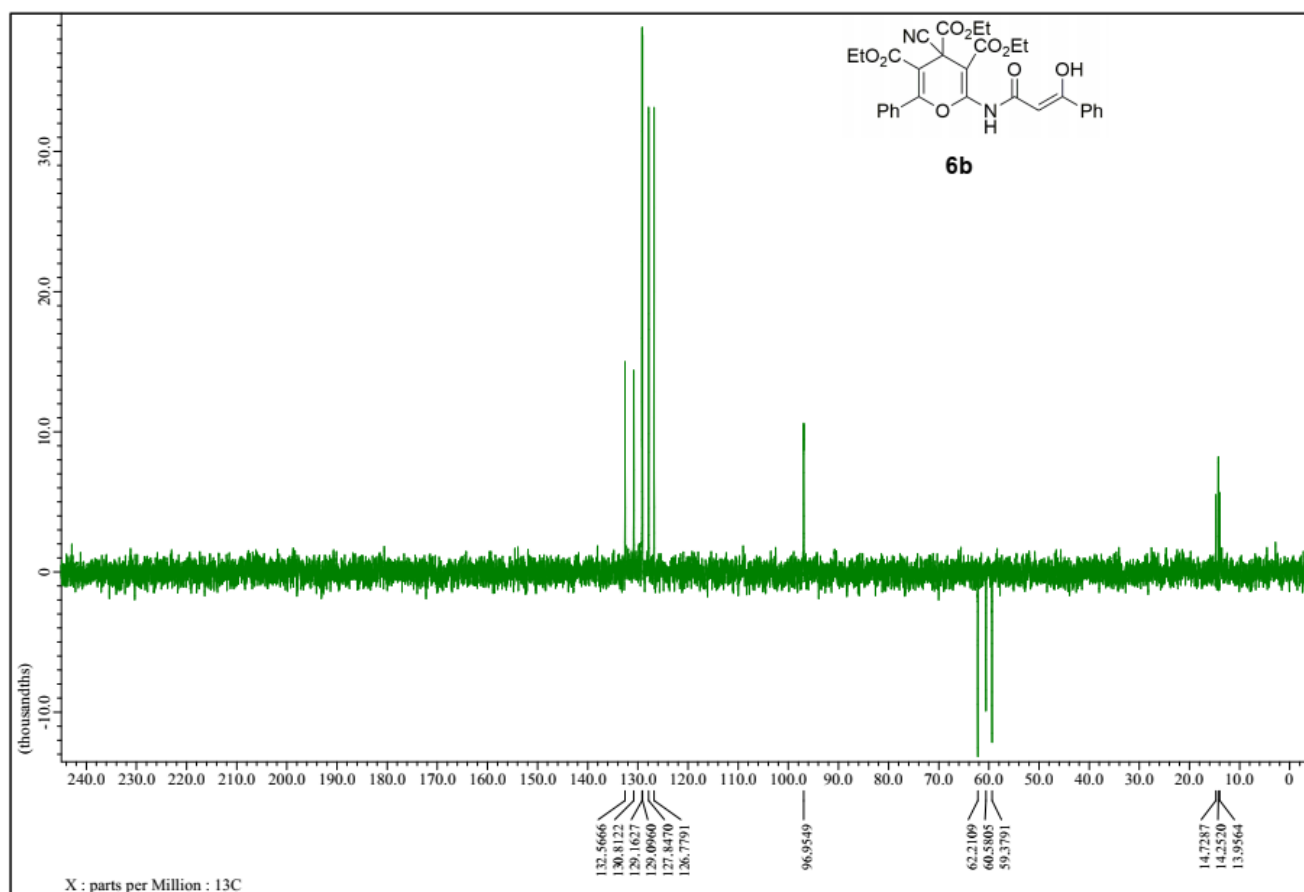


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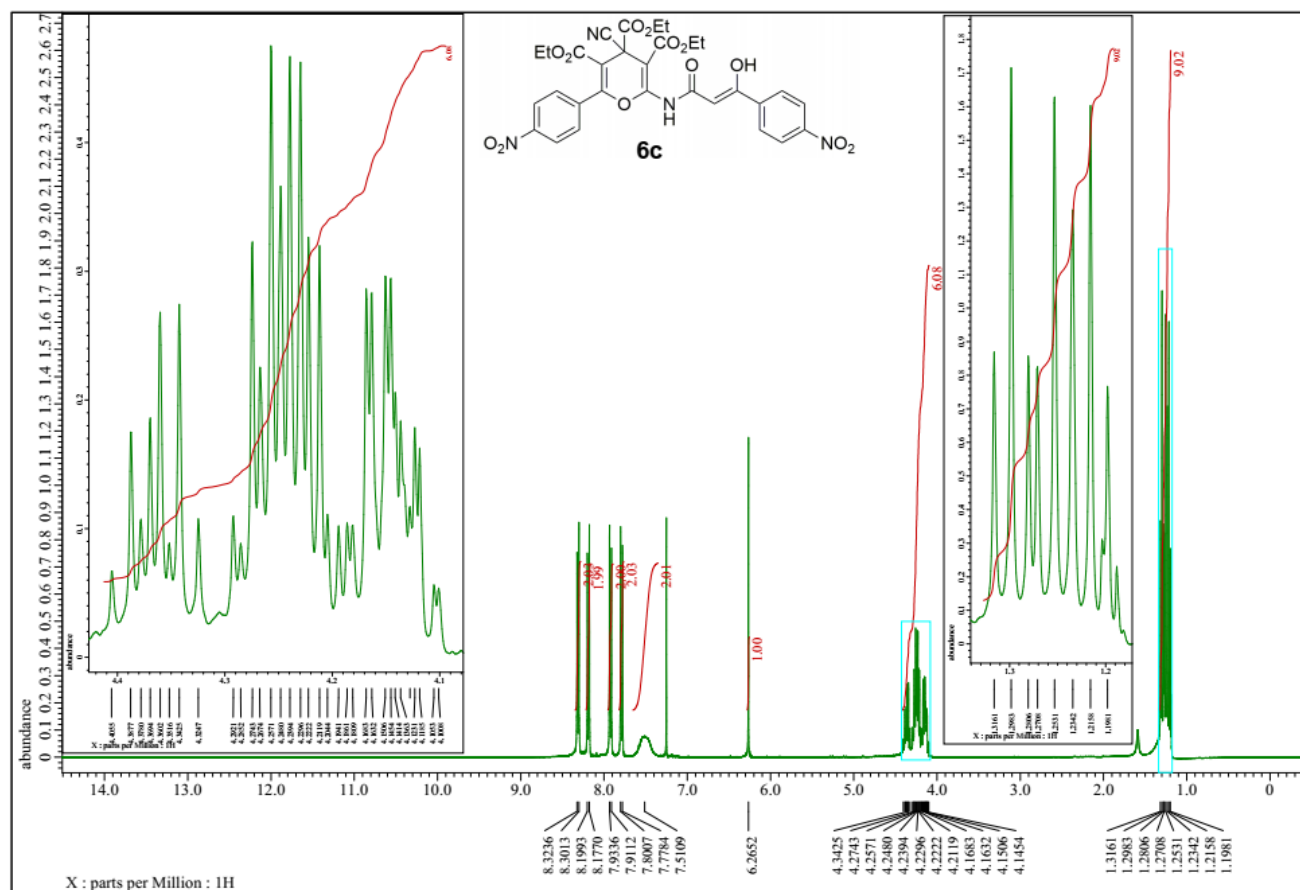


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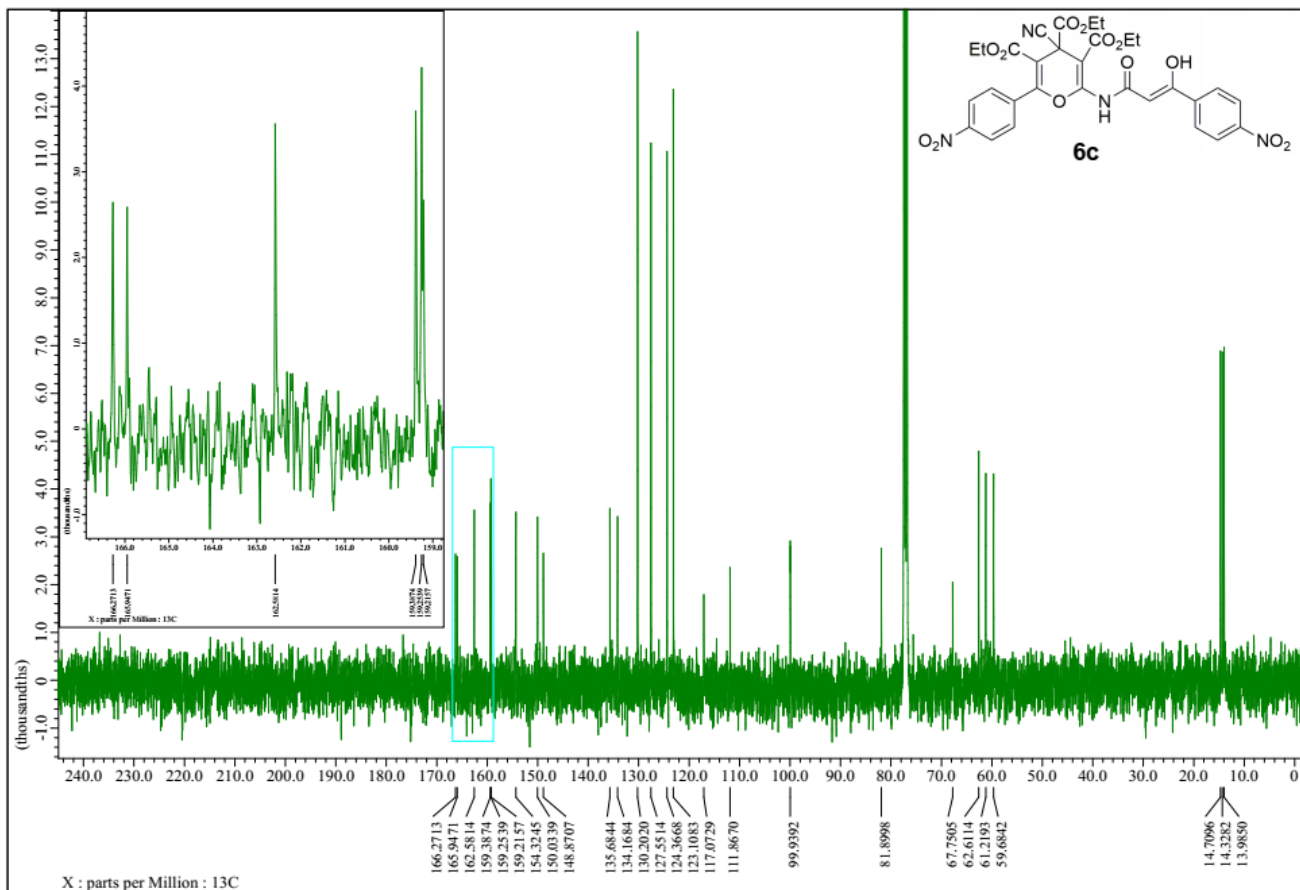
DEPT-135



¹H NMR



¹³C NMR



DEPT-135

