Alkynyl Acylammoniums as Electrophilic 3C Synthons in a Formal [3+3] Annulation: Access to Functionalized 4*H*-Pyran-4-ones

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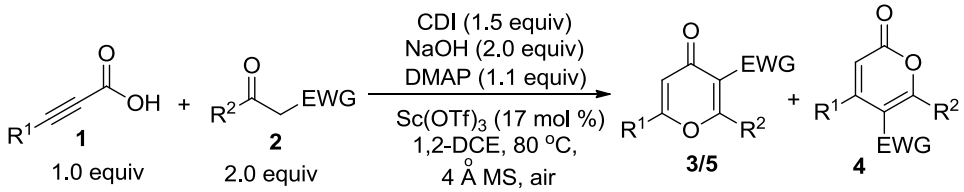
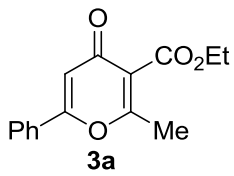
General Methods and Materials. All reactions were carried out in dry glassware, and were monitored by analytical thin-layer chromatography (TLC), which was visualized by ultraviolet light (254 nm). All solvents were obtained from commercial sources and were purified according to standard procedures. Alkynyl carboxylic acids **1**[1] and substrates **2**[2] are commercially available or prepared according to known procedures. Compound **12** was prepared from acyl chloride and imidazole according to the known procedure. [3] Purification of the products was accomplished by flash chromatography using silica gel (200-300 mesh). All NMR spectra were recorded on Bruker spectrometers, running at 300 MHz or 500 MHz for ^{1}H and 75 MHz or 125 MHz for ^{13}C respectively. Chemical shifts (δ) and coupling constants (J) are reported in ppm and Hz respectively. The solvent signals were used as references (residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm, δ_c = 77.0 ppm). The following abbreviations are used to indicate the multiplicity in NMR spectra: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet). High resolution mass spectrometry (HRMS) was recorded on TOF perimer for ESI^+.

General procedure for the synthesis of γ-pyrones 3/5 or α-pyrones 4:



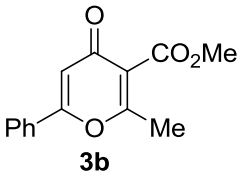
To an oven-dried 25 mL round-bottom flask was charged with acid **1** (0.35 mmol), substrate **2** (0.7 mmol), CDI (97 mg, 0.6 mmol), DMAP (51 mg, 0.385 mmol), $Sc(OTf)_3$ (30 mg, 0.06 mmol), 200 mg of 4 Å MS and NaOH (28 mg, 0.7 mmol). Then anhydrous 1,2-DCE (4 mL) was added to the flask and the resulting mixture was heated at 80 ^{o}C in air for a period time until the completion of the reaction as monitored by TLC. The mixture was cooled to room temperature. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (10:1) as the eluent to afford products **3/5** or **4**.



Ethyl 2-methyl-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (3a). 59 mg, 65% yield, white solid, mp: 105-106 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (d, J = 6.3 Hz, 2H), 7.44-7.54 (m, 3H), 6.77

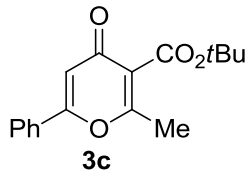
(s, 1H), 4.40 (q, J = 6.9 Hz, 2H), 2.49 (s, 3H), 1.38 (t, J = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.7, 165.4, 164.5, 162.8, 131.4, 130.5, 128.9, 125.6, 121.6, 111.0, 61.6, 18.5, 14.0. HRMS (ESI) calcd for $C_{15}H_{15}O_4$ $(M+H)^+$: 259.0965, found 259.0964.

Methyl 2-methyl-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (**3b**). 48 mg, 56% yield, white solid, mp: 130-131 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 6.7 Hz, 2H), 7.47-7.54 (m, 3H), 6.81 (s, 1H), 3.93 (s, 3H), 2.51 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.8, 166.2, 165.1, 162.9, 131.6, 130.6, 129.1, 125.7, 121.3, 111.2, 52.6, 18.8. HRMS (ESI) calcd for $C_{14}H_{13}O_4$ $(M+H)^+$: 245.0808, found 245.0805.



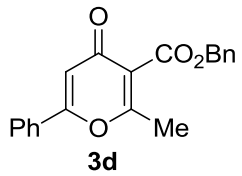
3b

***tert*-Butyl 2-methyl-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (3c**). 41 mg, 41% yield, white solid, mp: 145-146 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71-7.74 (m, 2H), 7.42-7.51 (m, 3H), 6.72 (s, 1H), 2.45 (s, 3H), 1.59 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.9, 164.1, 163.8, 162.8, 131.4, 130.8, 129.0, 123.0, 111.3, 82.8, 28.1, 18.4. HRMS (ESI) calcd for $C_{17}H_{19}O_4$ $(M+H)^+$: 287.1278, found 287.1281.



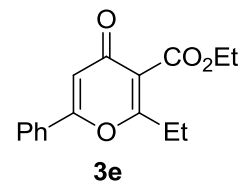
3c

Benzyl 2-methyl-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (3d). 65 mg, 58% yield, white solid, mp: 123-124 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.73-7.75 (m, 2H), 7.46-7.54 (m, 5H), 7.37-7.40 (m, 2H), 7.33 (m, 1H), 6.81 (s, 1H), 5.38 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.8, 165.9, 164.5, 162.9, 135.4, 131.6, 130.6, 129.1, 128.6, 128.3, 125.8, 121.4, 111.2, 67.4, 18.7. HRMS (ESI) calcd for $C_{20}H_{17}O_4$ $(M+H)^+$: 321.1121, found 321.1118.



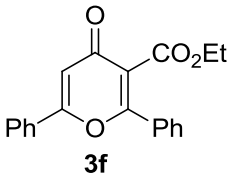
3d

Ethyl 2-ethyl-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (3e). 48 mg, 50% yield, colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.79-7.78 (m, 2H), 7.58-7.52 (m, 3H), 6.81 (s, 1H), 4.43 (q, J = 7.1 Hz, 2H), 2.81 (q, J = 7.6 Hz, 2H), 1.41 (t, J = 7.3 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.79, 168.79, 164.26, 162.71, 131.31, 130.46, 128.82, 125.41, 120.81, 110.68, 61.41, 25.73, 13.84, 11.38. HRMS (ESI) calcd for $C_{16}H_{17}O_4$ $(M+H)^+$: 273.1121, found 273.1125.



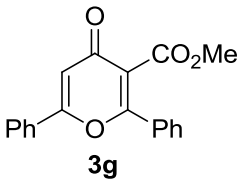
3e

Ethyl 4-oxo-2,6-diphenyl-4*H*-pyran-3-carboxylate (**3f**). 78 mg, 70% yield, colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 6.5 Hz, 2H), 7.73 (d, J = 7.5 Hz, 2H), 7.50-7.58 (m, 6H), 6.93 (s, 1H), 4.28 (q, J = 7.0 Hz, 2H), 1.17 (t, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.0, 164.3, 163.0, 161.9, 131.4, 131.2, 131.0, 130.3, 128.8, 128.5, 127.5, 125.5, 121.4, 110.5, 61.5, 13.4. HRMS (ESI) calcd for $C_{20}H_{17}O_4$ $(M+H)^+$: 321.1121, found 321.1117.



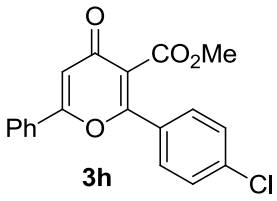
3f

Methyl 4-oxo-2,6-diphenyl-4*H*-pyran-3-carboxylate (**3g**). 84 mg, 78% yield, white solid, mp: 153-154 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, J = 6.6 Hz, 2H), 7.71 (d, J = 6.9 Hz, 2H), 7.52-7.57 (m, 6H), 6.90 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.3, 165.2, 163.4, 162.4, 131.7, 131.6, 131.4, 130.7, 129.1, 128.9, 127.7, 125.9, 121.5, 110.9, 52.7. HRMS (ESI) calcd for $C_{19}H_{15}O_4$ $(M+H)^+$: 307.0965, found 307.0962.



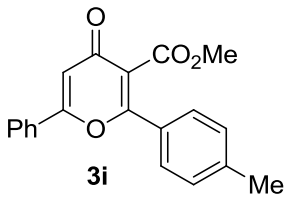
3g

Methyl 2-(4-chlorophenyl)-4-oxo-6-phenyl-4*H*-pyran-3-carboxylate (**3h**). 73 mg, 61% yield, white solid, mp: 128-129 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.79 (d, J = 6.6 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.49-7.54 (m, 5H), 6.89 (s, 1H), 3.82 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.1, 165.1, 163.5, 161.2, 138.0, 131.8, 130.6, 129.8, 129.3, 129.2, 129.1, 125.9, 121.7, 111.0, 52.9. HRMS (ESI) calcd for $C_{19}H_{14}ClO_4$ $(M+H)^+$: 341.0575, found 341.0578.



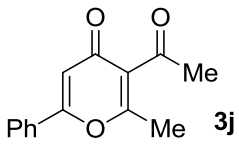
3h

Methyl 4-oxo-6-phenyl-2-(*p*-tolyl)-4*H*-pyran-3-carboxylate (**3i**). 93 mg, 83% yield, white solid, mp: 137-138 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.81 (d, J = 6.9 Hz, 2H), 7.61 (d, J = 8.1 Hz, 2H), 7.50-7.53 (m, 3H), 7.32 (d, J = 7.8 Hz, 2H), 6.89 (s, 1H), 3.81 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.4, 165.5, 163.3, 162.6, 142.2, 131.7, 130.8, 129.7, 129.1, 128.5, 127.7, 125.9, 121.0, 110.8, 52.8, 21.5. HRMS (ESI) calcd for $C_{20}H_{17}O_4$ $(M+H)^+$: 321.1121, found 321.1121.



3i

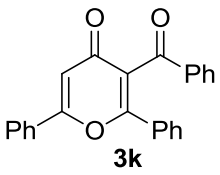
3-Acetyl-2-methyl-6-phenyl-4*H*-pyran-4-one (**3j**). 29 mg, 36% yield, white solid, mp: 140-141 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, J = 7.3 Hz, 2H), 7.56-7.46



3j

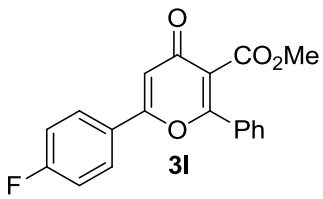
(m, 3H), 6.78 (s, 1H), 2.61 (s, 3H), 2.50 (s, 3H). ^{13}C NMR (125MHz, $CDCl_3$): δ 200.25, 177.49, 167.22, 162.71, 131.60, 130.57, 129.08, 126.93, 125.77, 111.80, 31.93, 18.87. HRMS (ESI) calcd for $C_{14}H_{13}O_3$ $(M+H)^+$: 229.0859, found 229.0864.

3-Benzoyl-2,6-diphenyl-4*H*-pyran-4-one (**3k**). 38 mg, 31% yield, white solid, mp: 183-184 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.93 (d, J = 7.7 Hz, 2H), 7.87 (d, J = 6.8 Hz, 2H), 7.63 (d, J = 7.5 Hz, 2H), 7.57-7.52 (m, 4H), 7.44-7.40 (m, 3H), 7.37 (t, J = 7.5 Hz, 2H), 6.93 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.13, 177.89, 163.59, 161.60, 136.58, 133.80, 131.69, 131.27, 131.18, 130.84, 129.30, 129.16, 128.80, 128.69, 128.19, 126.14, 125.91, 110.98. HRMS (ESI) calcd for $C_{24}H_{17}O_3$ $(M+H)^+$: 353.1172, found 353.1178.



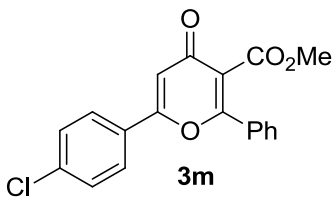
3k

Methyl 6-(4-fluorophenyl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3l**). 52 mg, 46% yield, white solid, mp: 166-167 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80-7.82 (m, 2H), 7.69-7.71 (m, 2H), 7.57 (m, 1H), 7.50-7.53 (m, 2H), 7.20 (t, J = 8.5 Hz, 2H), 6.84 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.14, 165.12, 164.76 (d, J = 252.3 Hz), 162.42, 131.62, 131.26, 128.95, 128.16 (d, J = 8.6 Hz), 127.72, 126.93 (d, J = 2.1 Hz), 121.48, 116.44 (d, J = 22.2 Hz), 110.67, 52.74. HRMS (ESI) calcd for $C_{19}H_{14}FO_4$ $(M+H)^+$: 325.0871, found 325.0869.



3l

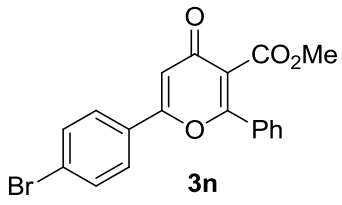
Methyl 6-(4-chlorophenyl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3m**). 73 mg, 61% yield, white solid, mp: 170-171 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 7.5 Hz, 2H), 7.57 (t, J = 7.0 Hz, 1H), 7.48-7.54 (m, 4H), 6.86 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.06, 165.05, 162.42, 162.24, 138.03, 131.65, 131.18, 129.48, 129.15, 128.95, 127.70, 127.16, 121.56, 111.00, 52.74. HRMS (ESI) calcd for $C_{19}H_{14}ClO_4$ $(M+H)^+$: 341.0575, found 341.0570.



3m

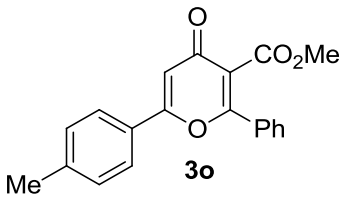
Methyl 6-(4-bromophenyl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3n**). 58 mg, 43% yield, white solid, mp: 191-192 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70-7.68 (m,

2H), 7.66-7.64 (m, 4H), 7.58 (t, J = 6.8 Hz, 1H), 7.53-7.51 (m, 2H), 6.88 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.10, 165.06, 162.49, 162.36, 132.50, 131.68, 131.22, 129.66, 128.99, 127.75, 127.34, 126.48, 121.64, 111.08, 52.79. HRMS (ESI) calcd for $C_{19}H_{14}BrO_4$ $(M+H)^+$: 385.0070, found 385.0076.



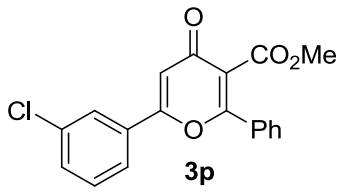
3n

Methyl 4-oxo-2-phenyl-6-(*p*-tolyl)-4*H*-pyran-3-carboxylate (**3o**). 74 mg, 66% yield, white solid, mp: 149-150 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.89-7.72 (m, 4H), 7.50-7.57 (m, 3H), 7.30 (d, J = 7.5 Hz, 2H), 6.85 (s, 1H), 3.79 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.35, 165.31, 163.57, 162.24, 142.41, 131.50, 131.43, 129.85, 128.89, 127.87, 127.72, 125.83, 121.39, 110.20, 52.69, 21.43. HRMS (ESI) calcd for $C_{20}H_{17}O_4$ $(M+H)^+$: 321.1121, found 321.1118.



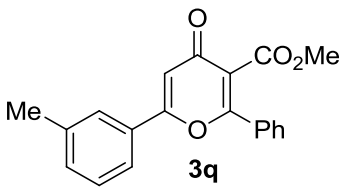
3o

Methyl 6-(3-chlorophenyl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3p**). 68 mg, 57% yield, white solid, mp: 96-97 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.71-7.67 (m, 3H), 7.58 (t, J = 7.3 Hz, 1H), 7.55-7.50 (m, 3H), 7.45 (t, J = 7.9 Hz, 1H), 6.88 (s, 1H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.02, 165.01, 162.58, 161.87, 135.41, 132.51, 131.70, 131.14, 130.47, 129.00, 127.75, 125.96, 124.05, 121.71, 111.59, 52.78. HRMS (ESI) calcd for $C_{19}H_{14}ClO_4$ $(M+H)^+$: 341.0575, found 341.0579.



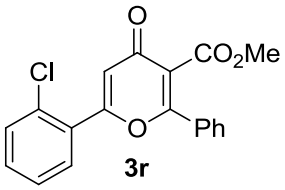
3p

Methyl 4-oxo-2-phenyl-6-(m-tolyl)-4*H*-pyran-3-carboxylate (**3q**). 49 mg, 44%, yield, white solid, mp: 132-133 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 7.2 Hz, 2H), 7.62-7.58 (m, 2H), 7.58-7.49 (m, 3H), 7.39 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 6.88 (s, 1H), 3.80 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.31, 165.26, 163.61, 162.37, 138.98, 132.52, 131.51, 131.39, 130.65, 129.02, 128.90, 127.73, 126.41, 123.12, 121.48, 110.83, 52.69, 21.40. HRMS (ESI) calcd for $C_{20}H_{17}O_4$ $(M+H)^+$: 321.1121, found 321.1124.



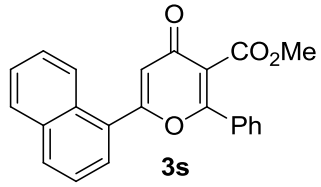
3q

Methyl 6-(2-chlorophenyl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3r**). 50 mg, 42% yield, white solid, mp: 153-154 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70 (d, J = 7.5 Hz, 2H), 7.56-7.51 (m, 3H), 7.50-7.44 (m, 3H), 7.40 (t, J = 7.5 Hz, 1H), 6.74 (s, 1H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.96, 165.19, 163.00, 162.58, 132.74, 132.05, 131.60, 131.09, 130.81, 130.58, 128.82, 127.76, 127.22, 121.43, 116.48, 52.76. HRMS (ESI) calcd for $C_{19}H_{14}ClO_4$ $(M+H)^+$: 341.0575, found 341.0575.



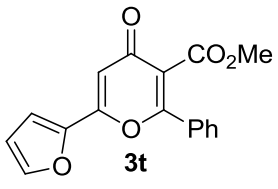
3r

Methyl 6-(naphthalen-1-yl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3s**). 34 mg, 27% yield, white solid, mp: 153-154 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10-8.09 (m, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.96-7.94 (m, 1H), 7.72-7.68 (m, 3H), 7.60-7.56 (m, 3H), 7.52 (t, J = 7.3 Hz, 1H), 7.46 (t, J = 7.4 Hz, 2H), 6.79 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.12, 165.34, 164.96, 162.89, 133.64, 131.66, 131.56, 131.09, 130.14, 129.37, 128.81, 128.73, 127.85, 127.67, 127.55, 126.60, 124.95, 124.32, 121.48, 116.46, 52.77. HRMS (ESI) calcd for $C_{23}H_{17}O_4$ $(M+H)^+$: 357.1121, found 357.1120.



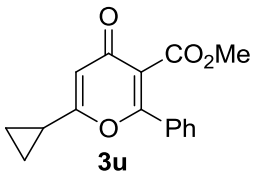
3s

Methyl 6-(furan-2-yl)-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (**3t**). 19 mg, 18% yield, colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69-7.65 (m, 2H), 7.61 (d, J = 1.0 Hz, 1H), 7.57-7.53 (m, 1H), 7.50 (t, J = 7.4 Hz, 2H), 7.01 (d, J = 3.5 Hz, 1H), 6.77 (s, 1H), 6.58 (dd, J = 3.5, 1.7 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.78, 165.16, 161.79, 155.31, 145.91, 145.42, 131.62, 131.20, 128.92, 127.74, 121.63, 112.87, 112.45, 108.64, 52.80. HRMS (ESI) calcd for $C_{17}H_{13}O_5$ $(M+H)^+$: 297.0757, found 297.0761.



3t

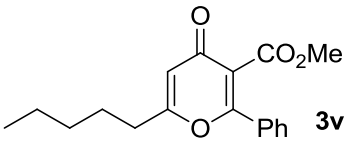
Methyl 4-cyclopropyl-2-oxo-6-phenyl-2*H*-pyran-5-carboxylate (**3u**). 41 mg, 43% yield, colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.53 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 7.1 Hz, 1H), 7.44 (t, J = 7.5 Hz, 2H), 6.27 (s, 1H), 3.74 (s, 3H), 1.90-1.82 (m, 1H), 1.11-1.04 (m, 4H).



3u

^{13}C NMR (125 MHz, $CDCl_3$): δ 175.73, 169.61, 165.32, 161.72, 131.34, 131.22, 128.77, 127.41, 121.19, 111.09, 52.59, 13.83, 8.33. HRMS (ESI) calcd for $C_{16}H_{15}O_4$ $(M+H)^+$: 271.0965, found 271.0965.

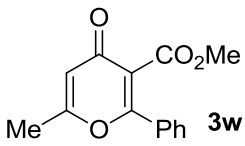
Methyl 4-oxo-6-pentyl-2-phenyl-4*H*-pyran-3-carboxylate (3v). 19 mg, 18% yield,



3v

colorless liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (d, J = 7.5 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.47 (t, J = 7.5 Hz, 2H), 6.26 (s, 1H), 3.77 (s, 3H), 2.59 (t, J = 7.5 Hz, 2H), 1.74-1.68 (m, 2H), 1.39-1.36 (m, 4H), 0.92 (t, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.34, 169.26, 165.41, 162.57, 131.42, 131.38, 128.80, 127.63, 121.14, 113.37, 52.72, 33.52, 30.96, 26.28, 22.22, 13.79. HRMS (ESI) calcd for $C_{18}H_{21}O_4$ $(M+H)^+$: 301.1434, found 301.1438.

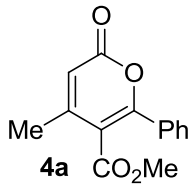
Methyl 6-methyl-4-oxo-2-phenyl-4*H*-pyran-3-carboxylate (3w). 34 mg, 40% yield,



3w

colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.62-7.59 (m, 2H), 7.75-7.43 (m, 3H), 6.26 (s, 1H), 3.76 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.21, 165.62, 165.35, 162.71, 131.44, 131.28, 128.78, 127.66, 121.11, 114.13, 52.69, 19.82. HRMS (ESI) calcd for $C_{14}H_{13}O_4$ $(M+H)^+$: 245.0808, found 245.0815.

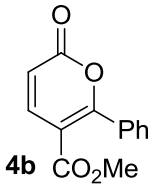
Methyl 4-methyl-2-oxo-6-phenyl-2*H*-pyran-5-carboxylate (**4a**). 20 mg, 23% yield,



4a

white solid, mp: 99-100 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57 (d, J = 7.4 Hz, 2H), 7.52-7.41 (m, 3H), 6.16 (s, 1H), 3.66 (s, 3H), 2.25 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.60, 161.04, 160.32, 153.69, 131.88, 128.52, 127.80, 113.26, 112.44, 52.46, 20.16. HRMS (ESI) calcd for $C_{14}H_{13}O_4$ $(M+H)^+$: 245.0808, found 245.0811.

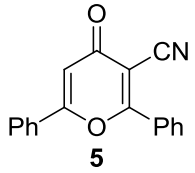
Methyl 2-oxo-6-phenyl-2H-pyran-5-carboxylate (4b). 39 mg, 48% yield, colorless



4b

liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.86 (d, J = 9.7 Hz, 1H), 7.58-7.43 (m, 5H), 6.34 (d, J = 9.7 Hz, 1H), 3.71 (s, 3H). ^{13}C NMR (75MHz, $CDCl_3$): δ 167.2, 164.9, 160.1, 144.1, 132.1, 131.2, 129.1, 128.0, 113.2, 109.4, 52.2. HRMS (ESI) calcd for $C_{13}H_{11}O_4$ $(M+H)^+$: 231.0652, found 231.0656.

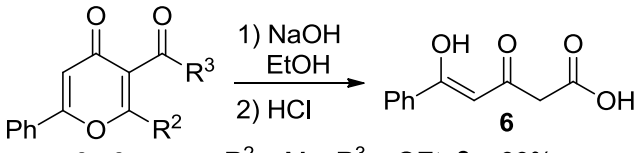
4-Oxo-2,6-diphenyl-4*H*-pyran-3-carbonitrile (**5**). 49 mg, 51% yield, white solid,



5

mp: 177-178 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09 (d, J = 7.5 Hz, 2H), 7.82 (d, J = 7.0 Hz, 2H), 7.68 (t, J = 7.5 Hz, 1H), 7.54-7.64 (m, 5H), 6.91 (s, 1H). ^{13}C NMR (75MHz, $CDCl_3$): δ 175.1, 170.3, 163.7, 133.3, 132.4, 129.8, 129.6, 129.4, 129.2, 128.4, 126.0, 113.4, 109.9, 102.0. HRMS (ESI) calcd for $C_{18}H_{12}NO_2$ $(M+H)^+$: 274.0863, found 274.0859.

Procedure for the synthesis of compound 6 from 3a or 3g.



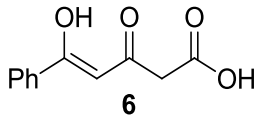
3a/**3g** **6**

R^2 = Me, R^3 = OEt, **3a**, 99%

R^2 = Ph, R^3 = OMe, **3g**, 50%

To a 10 mL round-bottom flask was charged with **3a**/**3g** (0.1 mmol) and 3 mL of EtOH. Then 5 mL of 1M NaOH (aq) was added and the resulting mixture was stirred for a period of time until the completion of the reaction as monitored by TLC. The solution was acidified to pH = 3 with 1M HCl, and was subsequently extracted with DCM. Then, the organic phase was dried over anhydrous $MgSO_4$. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (1:2) as the eluent to afford product **6**.

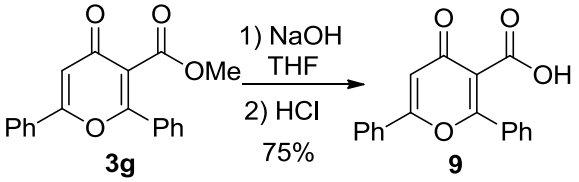
5-Hydroxy-3-oxo-5-phenylpent-4-enoic acid (**6**). 20 mg from **3a** and 10 mg from **3g**.



6

Colorless liquid. Know compound.[3] ^{1}H NMR (500 MHz, $CDCl_3$): δ 15.44 (brs, 1H), 7.89 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.3 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 6.28 (s, 1H), 3.57 (s, 2H).

Procedure for the synthesis of compound 9.

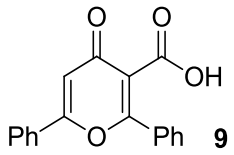


3g **9**

To a 10 mL round-bottom flask was charged with **3g** (31 mg, 0.1 mmol) and 3 mL of THF. Then 5 mL of 1M NaOH (aq) was added and the resulting mixture was stired

for a period of time until the completion of the reaction as monitored by TLC. The solution was acidified to pH = 3 with 1M HCl, and was subsequently extracted with DCM. Then, the organic phase was dried over anhydrous $MgSO_4$. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (1:2) as the eluent to afford 22 mg of compound **9**.

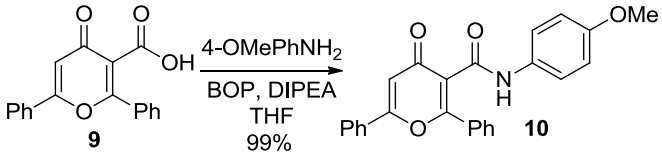
4-Oxo-2,6-diphenyl-4*H*-pyran-3-carboxylic acid (9). White solid, mp: 202-203 ^{o}C.



9

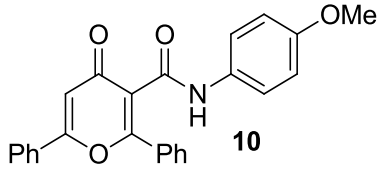
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H), 7.69-7.66 (m, 2H), 7.61-7.51 (m, 6H), 7.11 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 181.97, 173.18, 165.01, 163.06, 132.83, 131.87, 131.75, 129.45, 129.31, 128.21, 126.33, 113.41, 110.17. HRMS (ESI) calcd for $C_{18}H_{13}O_4$ $(M+H)^+$: 293.0808, found 293.0815.

Procedure for the synthesis of compound 10 from 9.



To a 10 mL round-bottom flask was charged with **9** (29 mg, 0.1 mmol), BOP (66 mg, 0.15 mmol), 3 mL of THF and DIPEA (26 mg, 0.2 mmol). After 5 mins, 4-$OMePhNH_2$ (15 mg, 0.12 mmol) was added to the solution, and the resulting mixture was stired for a period of time until the completion of the reaction as monitored by TLC. Then, the reaction mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (3:1) as the eluent to afford 39 mg of compound **10**.

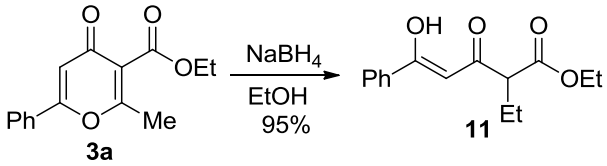
***N*-(4-methoxyphenyl)-4-oxo-2,6-diphenyl-4*H*-pyran-3-carboxamide (10)**. White solid, mp: 177-178 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.94 (brs, 1H), 7.82 (d, J = 7.5 Hz, 2H), 7.68 (d, J = 7.0 Hz, 2H), 7.49-7.57 (m, 8H), 6.99 (s, 1H), 6.84 (d, J = 9.0 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.47, 169.65, 163.09, 160.27, 156.32, 133.18, 131.99, 131.43, 131.05, 130.13, 129.21, 128.77, 128.26, 126.02, 122.03, 118.69, 113.99, 111.24, 55.43. HRMS (ESI) calcd for $C_{25}H_{20}NO_4$



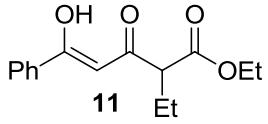
10

$(M+H)^+$: 398.1387, found 398.1395.

Procedure for the synthesis of compound 11.

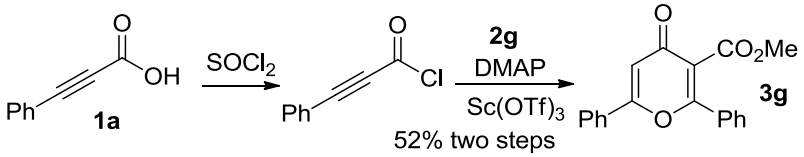


To a 10 mL round-bottom flask was charged with **3a** (26 mg, 0.1 mmol), 10 mg of $NaBH_4$ (0.25 mmol) and 3 mL of EtOH. The mixture was stirred at room temperature for 4h. The mixture was concentrated and the residue was purified by chromatography on silica gel using hexane/EtOAc (1:1) as the eluent to afford 25 mg of compound **11**.



Ethyl 2-ethyl-5-hydroxy-3-oxo-5-phenylpent-4-enoate (11). Colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 15.85 (brs, 1H), 7.88 (d, J = 7.2 Hz, 2H), 7.56-7.42 (m, 3H), 6.28 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.31 (t, J = 7.5 Hz, 1H), 2.09-1.90 (m, 2H), 1.28 (t, J = 7.2 Hz, 3H), 1.00 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 193.41, 182.24, 170.23, 134.26, 132.49, 128.66, 127.05, 95.67, 61.29, 57.84, 22.98, 14.13, 11.94. HRMS (ESI) calcd for $C_{15}H_{19}O_4$ $(M+H)^+$: 263.1278, found 263.1284.

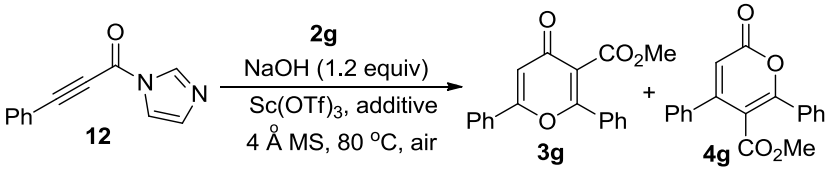
Procedure for the synthesis of product 3g from acid chloride.



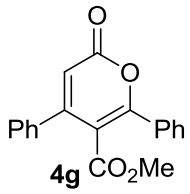
To an oven-dried 25 mL round-bottom flask was charged with acid **1a** (51 mg, 0.35 mmol) and 5 mL of $SOCl_2$. The resulting mixture was refluxed for 2h, and then $SOCl_2$ was removed under reduced pressure. Then, substrate **2g** (125 mg, 0.7 mmol), DMAP (85 mg, 0.7 mmol), and $Sc(OTf)_3$ (30 mg, 0.06 mmol) was added to the residue followed by addition of anhydrous 1,2-DCE (4 mL). The resulting mixture was heated at 80^{o}C in air for a period time until the completion of the reaction as monitored by TLC. The mixture was cooled to room temperature. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (10:1) as the eluent to afford 56

mg of product **3g** (52%).

Procedure for the reaction of alkynyl acyl imidazole 12 with 2g.



To an oven-dried 10 mL round-bottom flask was charged with **12** (39 mg, 0.2 mmol) **2g** (71 mg, 0.4 mmol), additive (none or certain amount of DMAP), $Sc(OTf)_3$ (17 mg, 0.034 mmol), 200 mg of 4 Å MS and NaOH (10 mg, 0.24 mmol). Then anhydrous 1,2-DCE (3 mL) was added to the flask and the resulting mixture was heated at 80 ^{o}C in air for a period time until the completion of the reaction as monitored by TLC. The mixture was cooled to room temperature. The mixture was concentrated under reduced pressure. The residue was purified by chromatography on silica gel using hexane/EtOAc (10:1) as the eluent to afford products **3g** and/or **4g**. 6 mg of **3g** and 31 mg of **4g** were obtained when none of additive was added. 32 mg of **3g** and 5 mg of **4g** were obtained when 20 mol % of DMAP was added. 40 mg of **3g** was obtained when 1.1 equiv of DMAP was added.



Methyl 2-oxo-4,6-diphenyl-2*H*-pyran-5-carboxylate (**4g**). Colorless liquid. Known compound. [5] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64 (d, J = 6.6 Hz, 2H), 7.50-7.43 (m, 6H), 7.37-7.35 (m, 2H), 6.29 (s, 1H), 3.46 (s, 3H).

References:

[1] a) J. Lim, J. Choi, H.-S. Kim, I. S. Kim, K. C. Nam, J. Kim, S. Lee, *J. Org. Chem.* **2016**, *81*, 303; b) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 18326.

[2] R. Balamurugan, S. Manojveer, *Chem. Commun.* **2011**, *47*, 11143.

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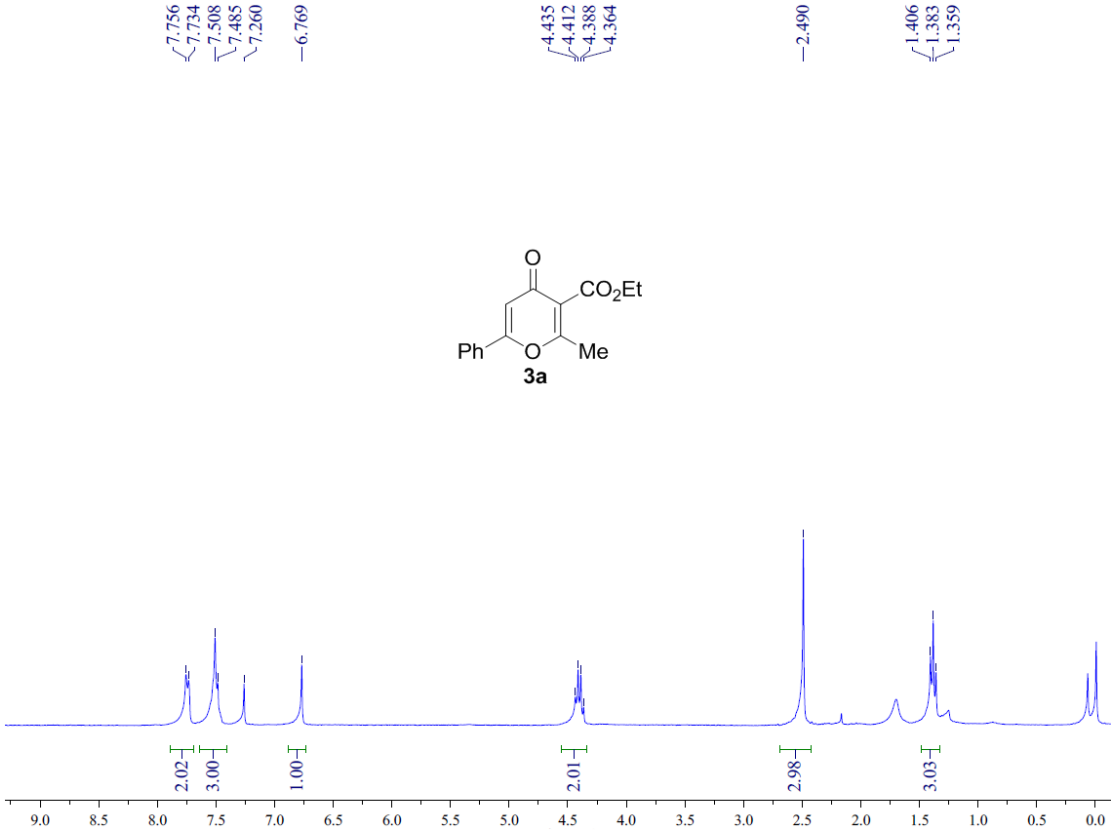
[4] D. Schmidt, J. Conrad, I. Klaiber, U. Beifuss, *Chem. Commun.* **2006**, 4732.

[5] R. Manikandan, M. Jeganmohan *Org. Lett.* **2014**, *16*, 652.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6.769
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4.412
4.388
4.364
2.490
1.406
1.383
1.359
O
CO2Et
Ph
O
Me
3a
2.02
3.00
1.00
2.01
2.98
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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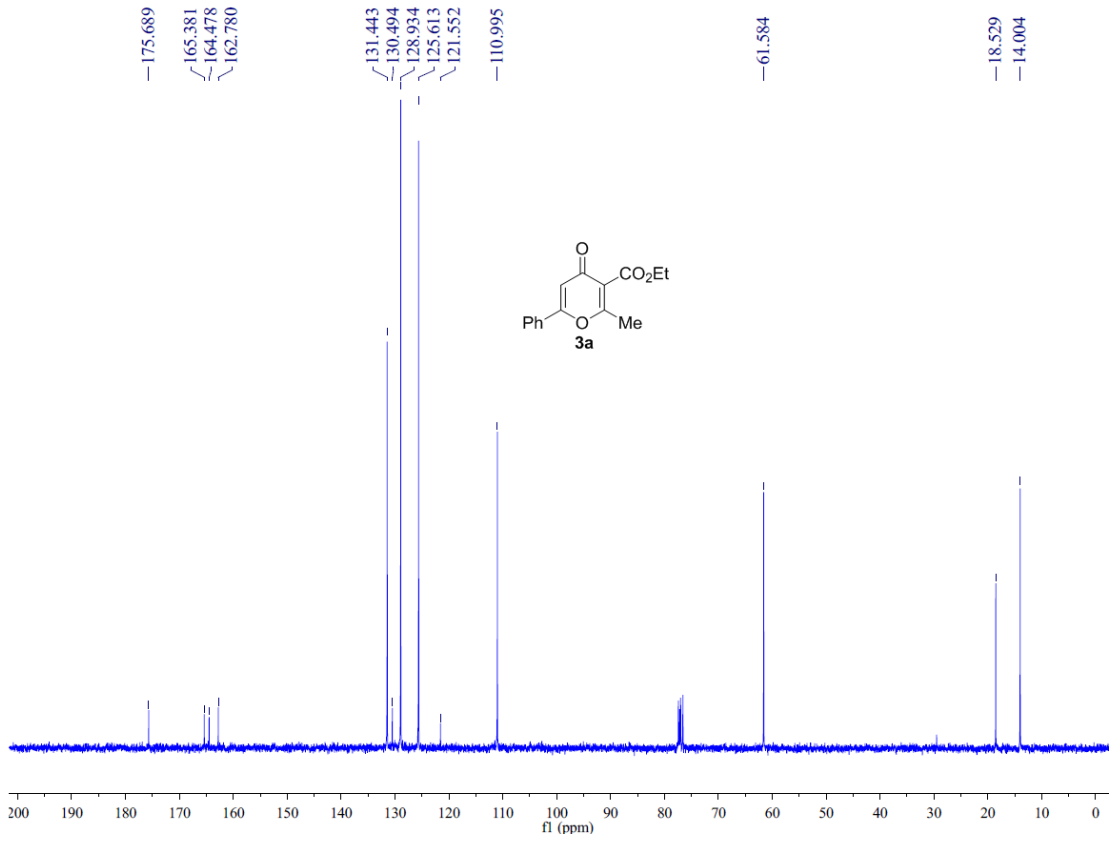
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128.934
125.613
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110.995
61.584
18.529
14.004
O
CO2Et
Ph
O
Me
3a
200
190
180
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110
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90
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50
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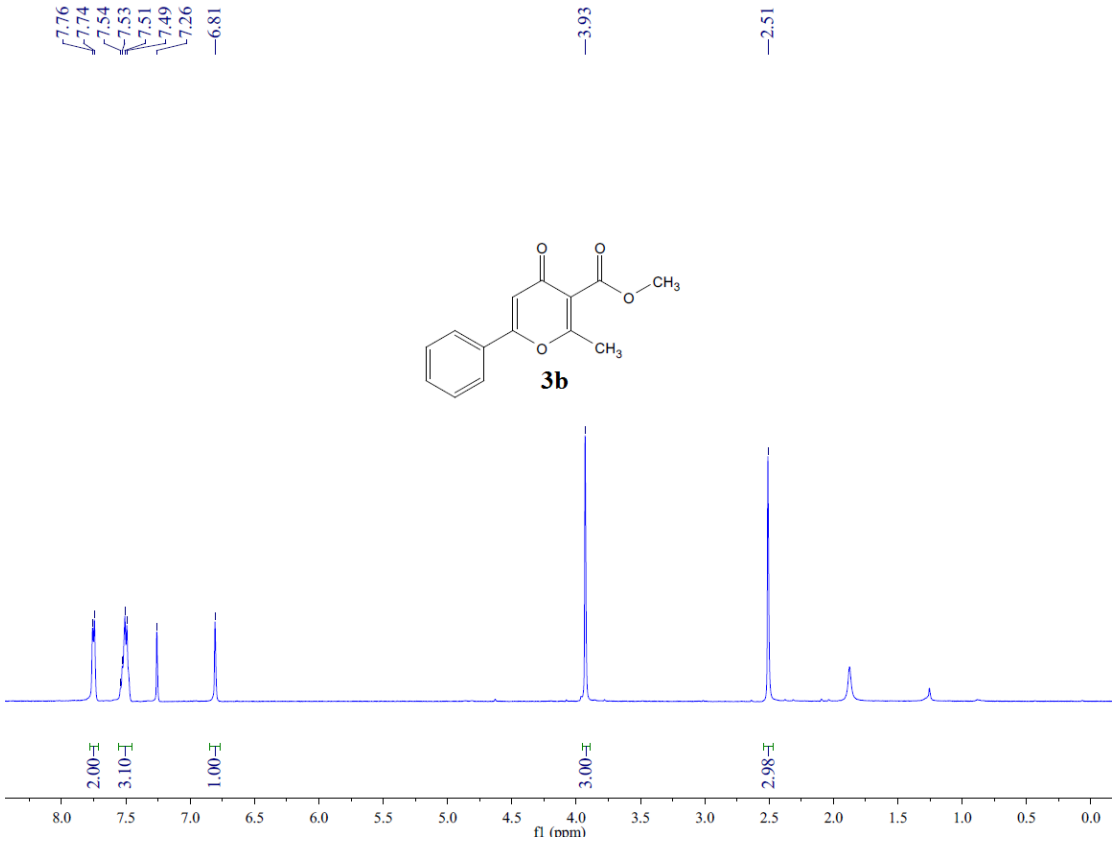
30
20
10
0
f1 (ppm)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3.00
2.98
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6.5
6.0
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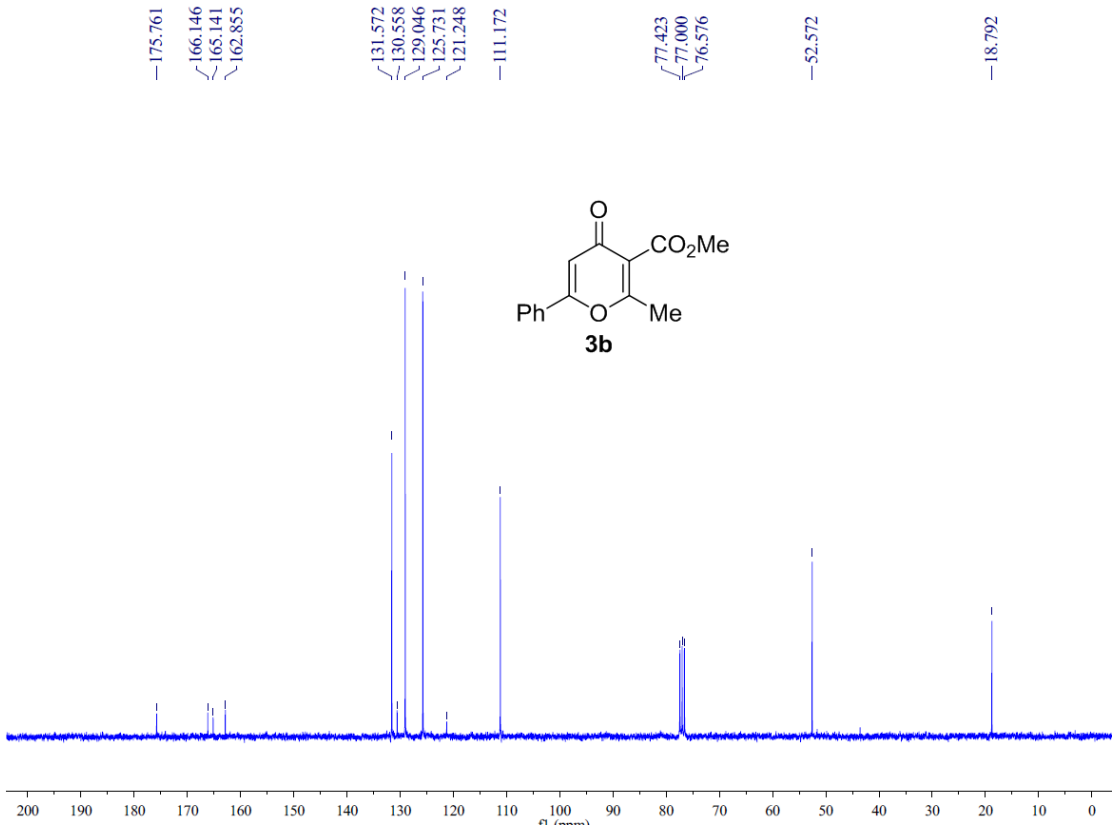
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3b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162.855
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130.558
129.046
125.731
121.248
111.172
77.423
77.000
76.576
52.572
18.792
O
CO2Me
Ph
O
Me
200
190
180
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150
140
130
120
110
100
90
80
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60
50
40
30
20
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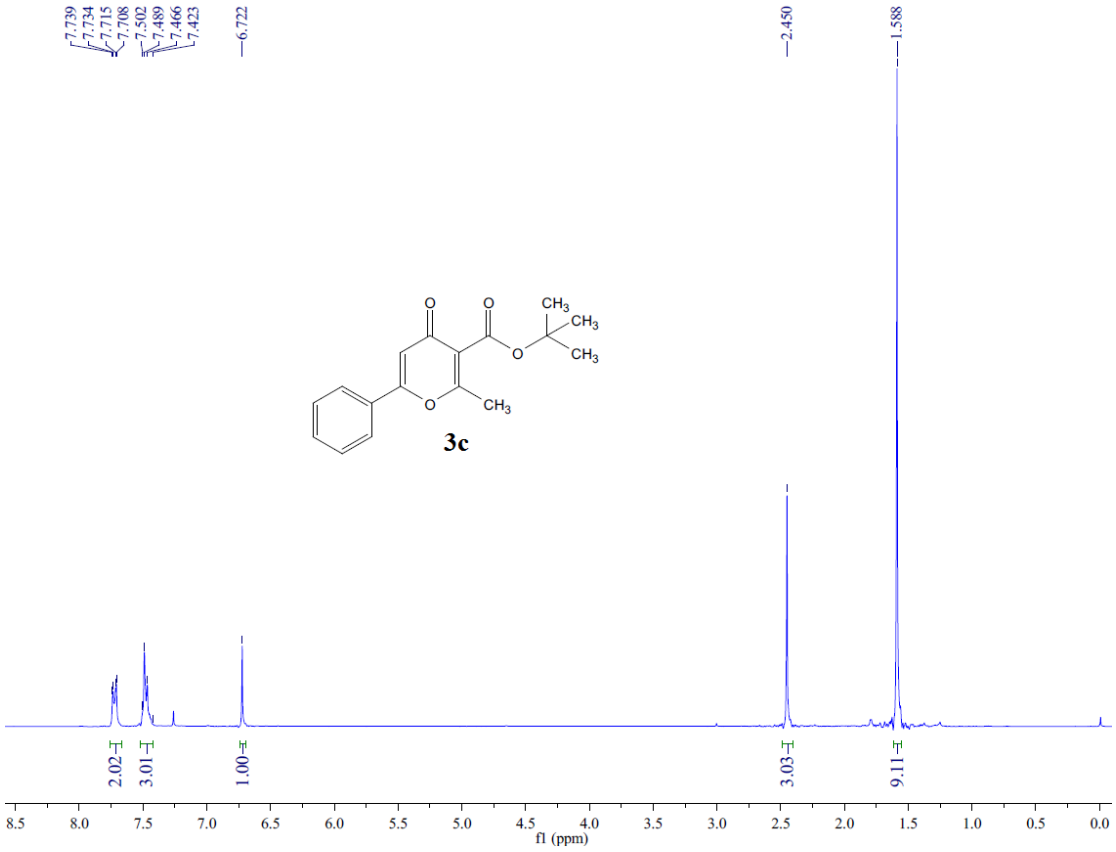
0

3b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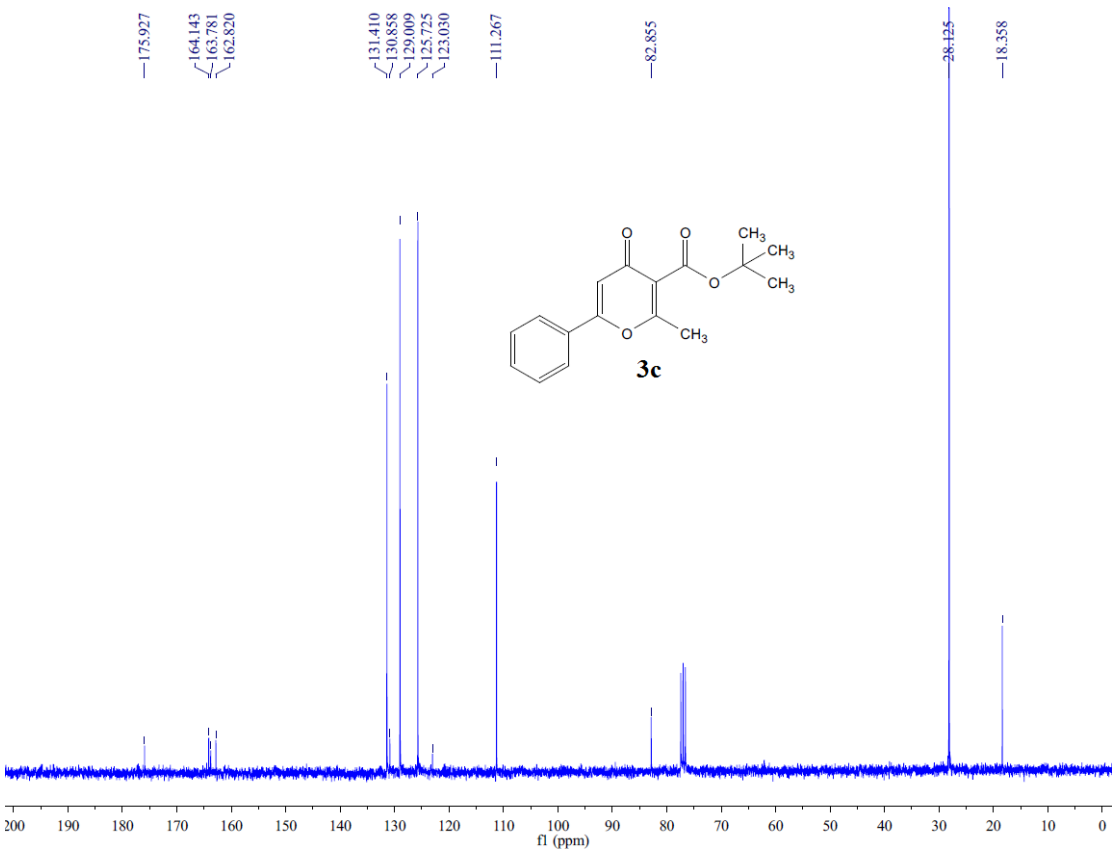
7.423
6.722
2.450
1.588
2.02
3.01
1.00
3.03
9.11
fl (ppm)

3c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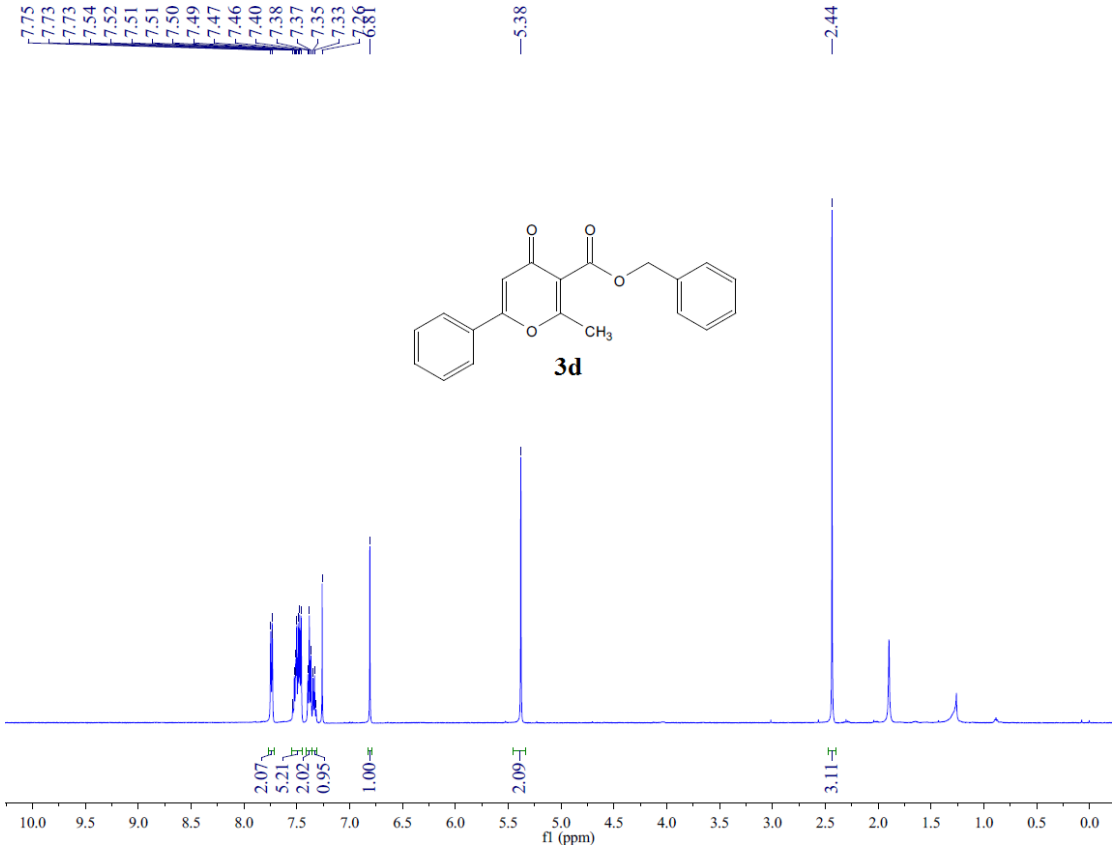
18.358
fl (ppm)

3c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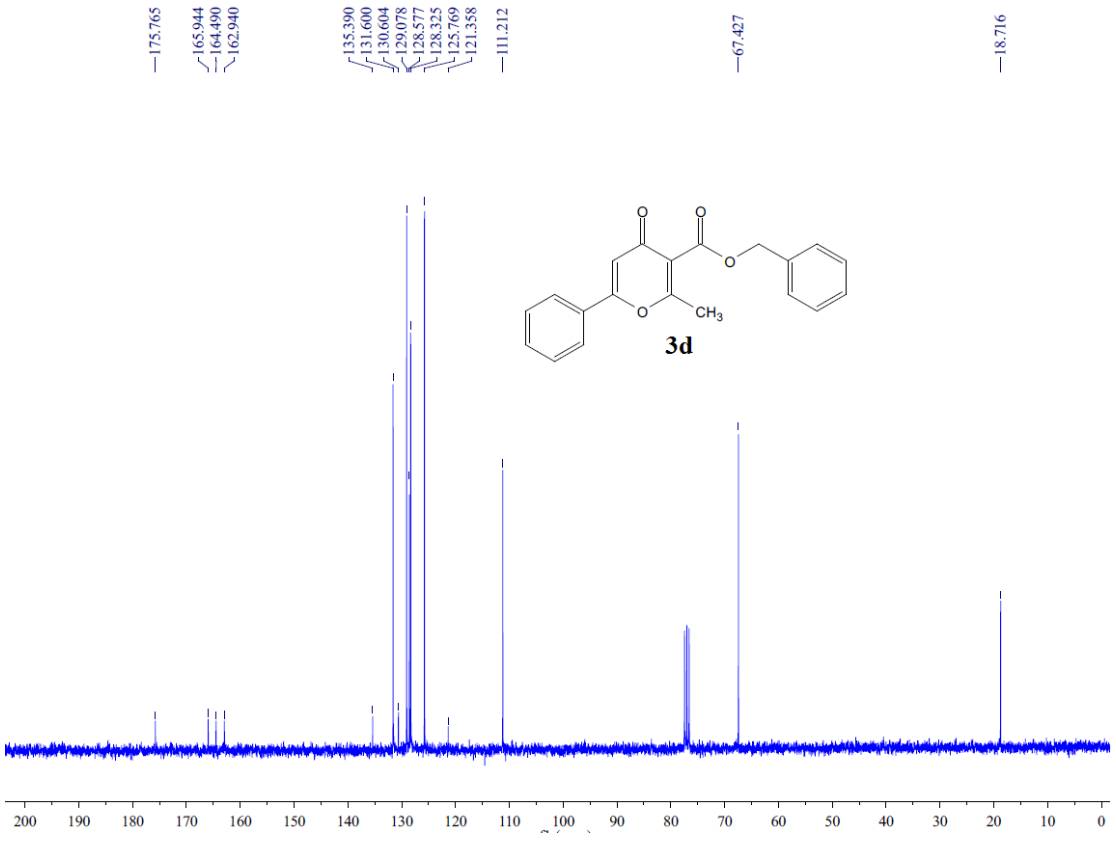
7.50
7.49
7.47
7.46
7.40
7.38
7.37
7.35
7.33
7.26
6.81
5.38
2.44
O
O
O
O
CH3
3d
2.07
5.21
2.02
0.95
1.00
2.09
3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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129.078
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125.769
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O
O
O
CH3
3d
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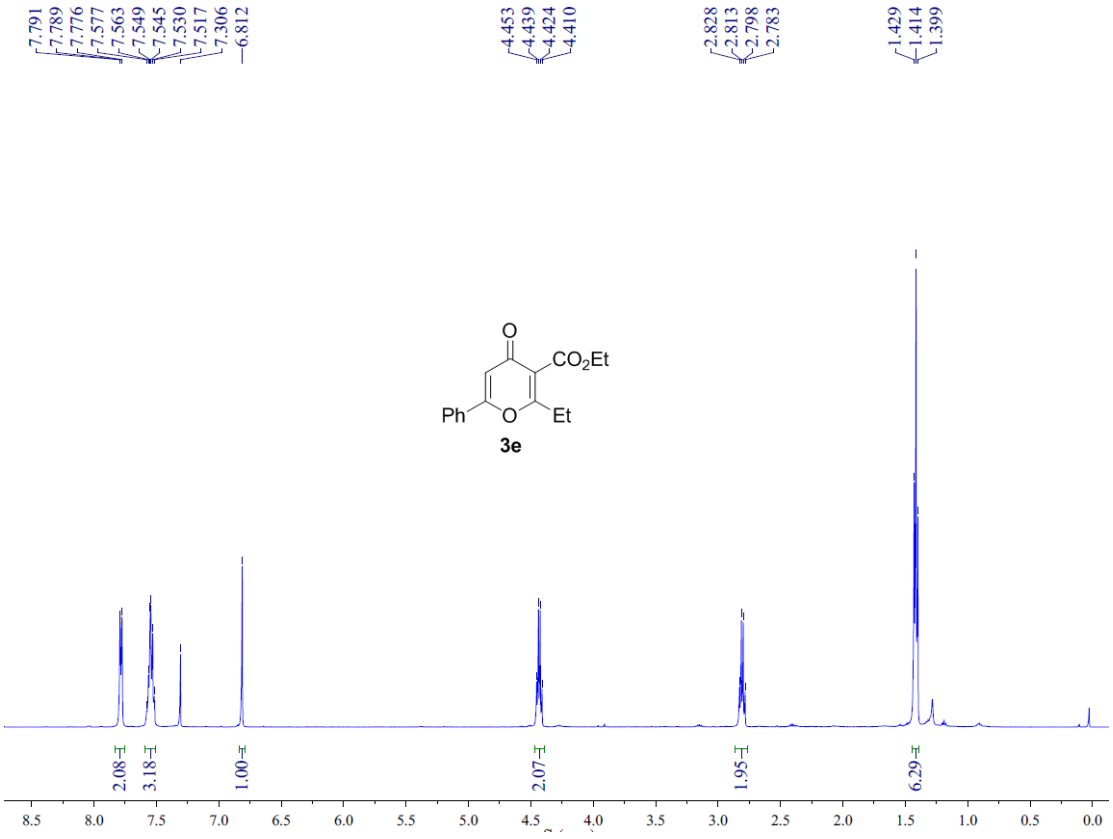
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7.776
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7.563
7.549
7.545
7.530
7.517
7.306
6.812
4.453
4.439
4.424
4.410
2.828
2.813
2.798
2.783
1.429
1.414
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CO2Et
Ph
O
Et
3e
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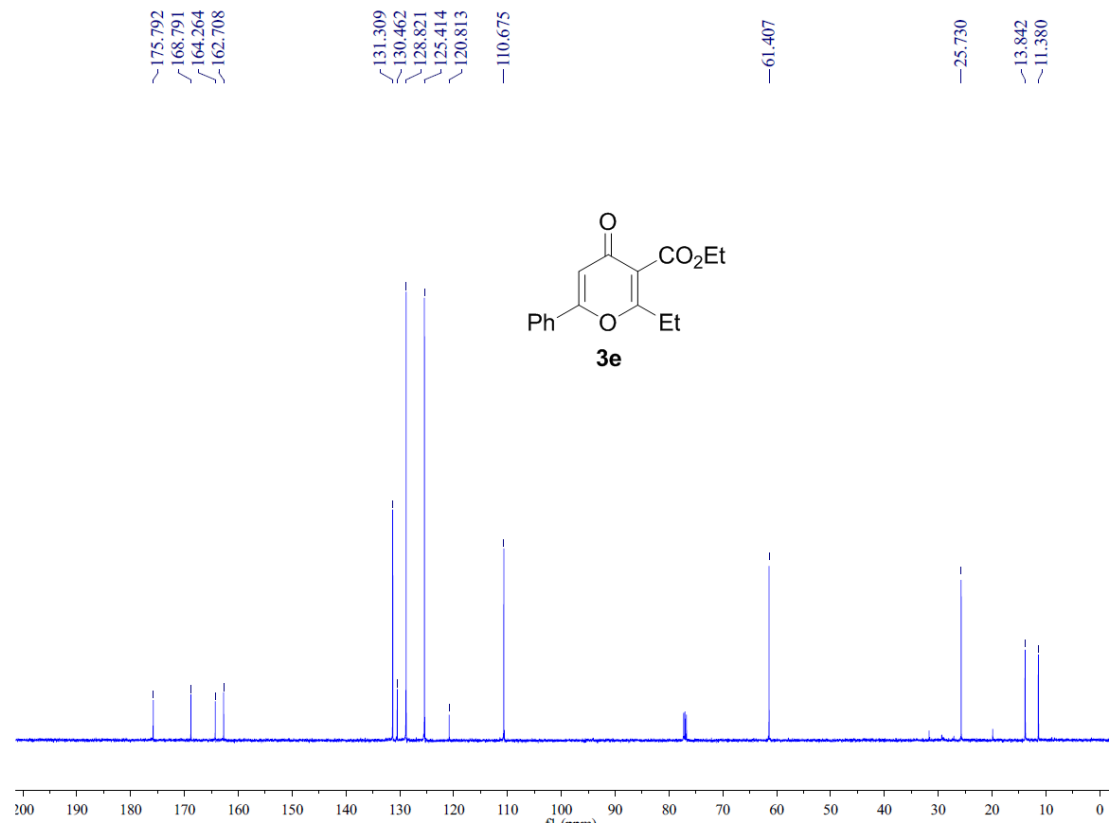
3.18
1.00
2.07
1.95
6.29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130.462
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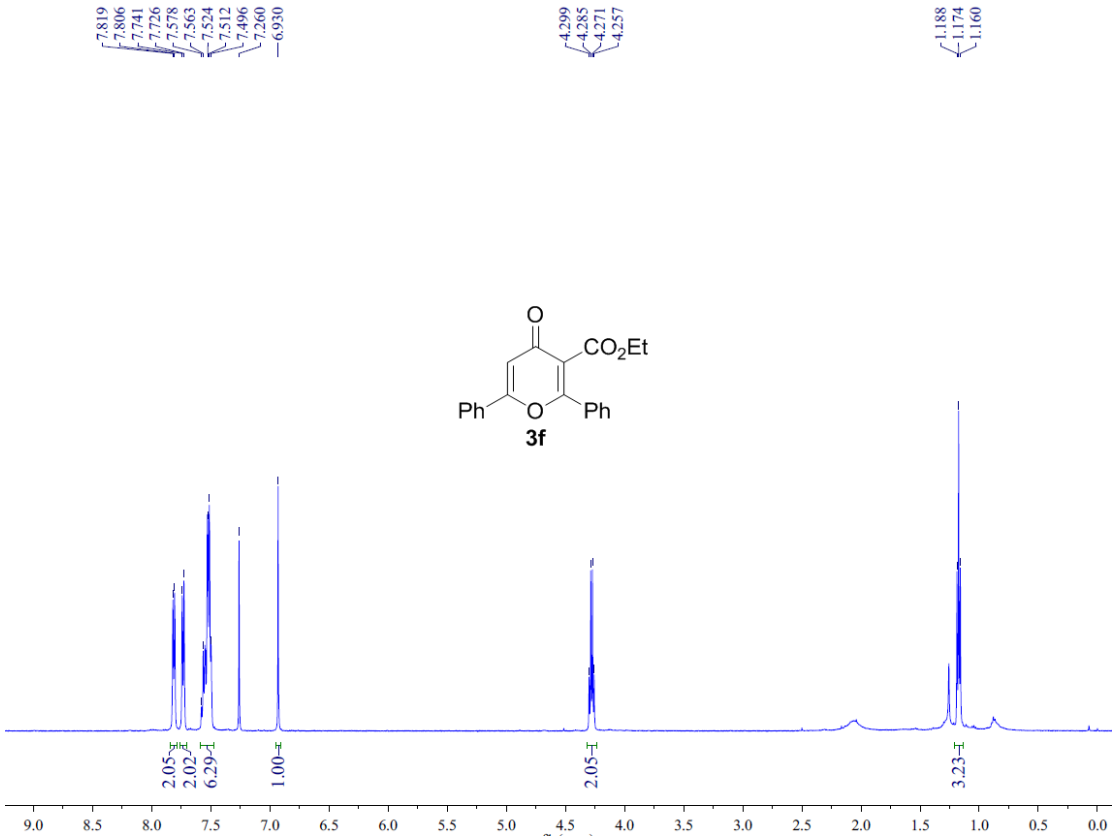
25.730
13.842
11.380
O
CO2Et
Ph
O
Et
3e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7.726
7.578
7.563
7.524
7.512
7.496
7.260
6.930
4.299
4.285
4.271
4.257
1.188
1.174
1.160
O
CO2Et
Ph
O
Ph
3f
2.05
2.02
6.29
1.00
2.05
3.23
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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1.0
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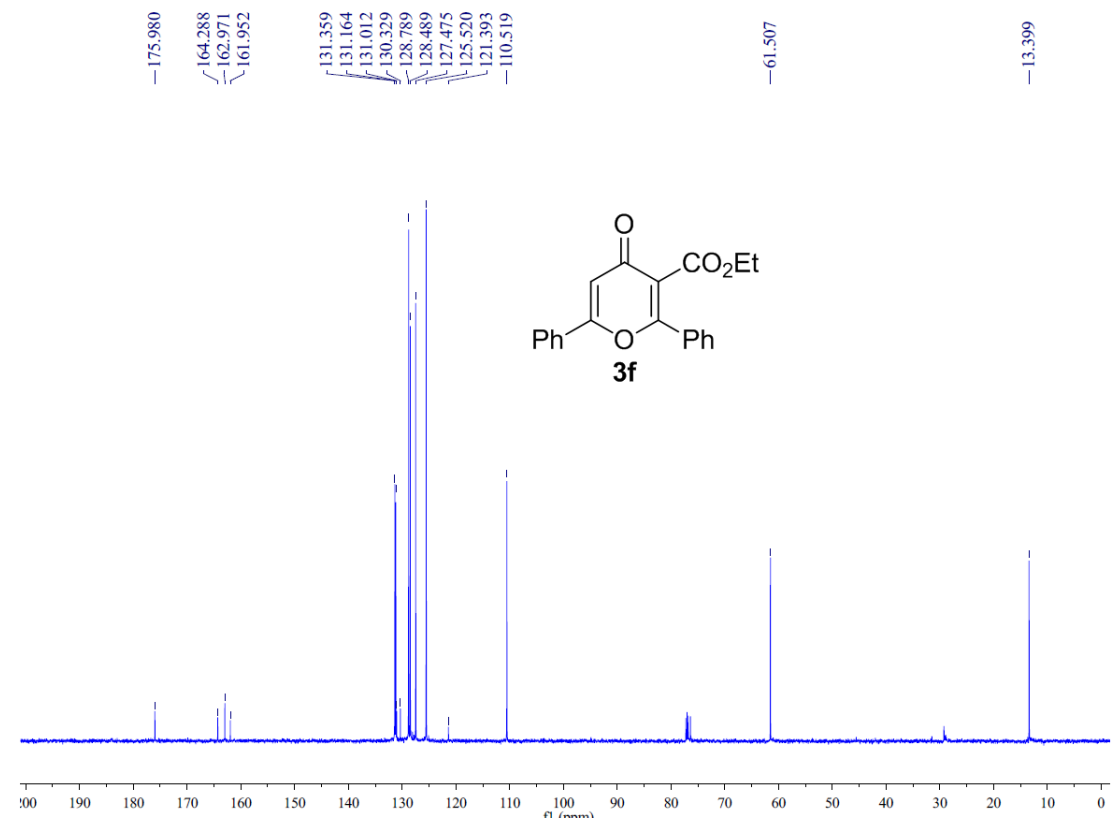
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162.971
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131.012
130.329
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128.489
127.475
125.520
121.393
110.519
61.507
13.399
O
CO2Et
Ph
O
Ph
3f
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150
140
130
120
110
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70
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30
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10
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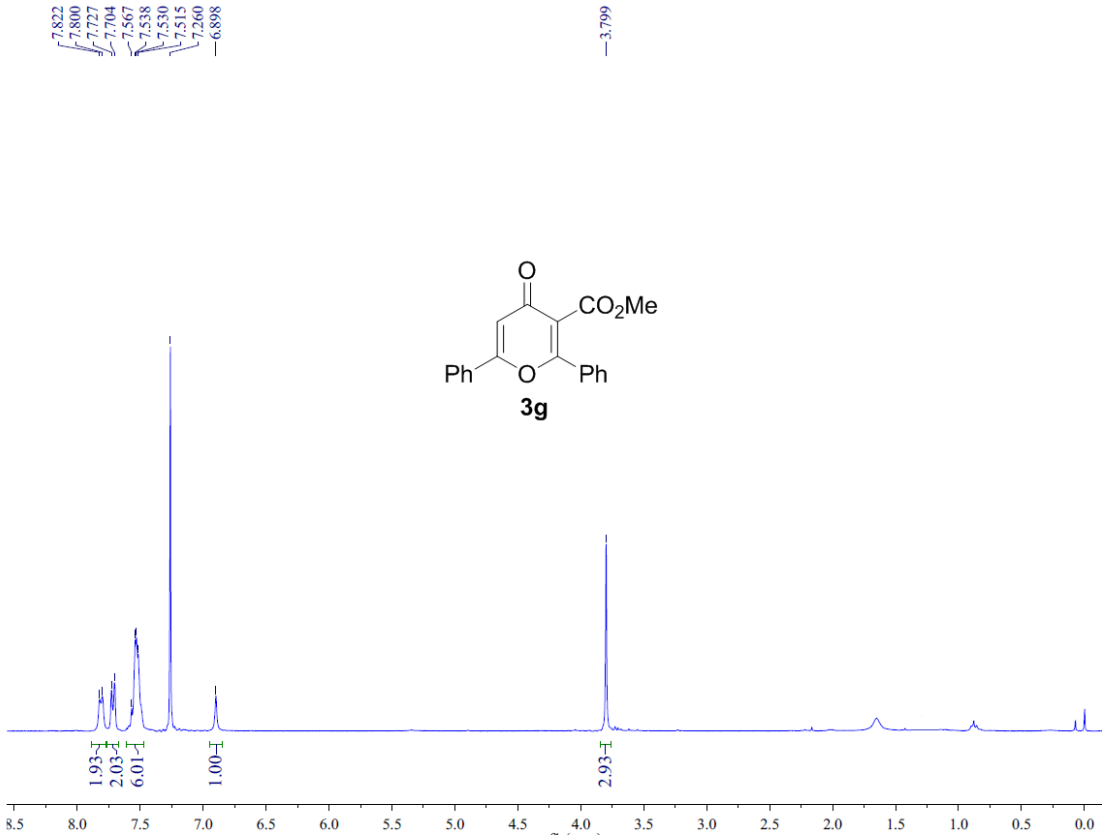
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7.800
7.727
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7.567
7.538
7.530
7.515
7.260
6.898
3.799
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CO2Me
Ph
O
Ph
3g
1.93
2.03
6.01
1.00
2.93
8.5
8.0
7.5
7.0
6.5
6.0
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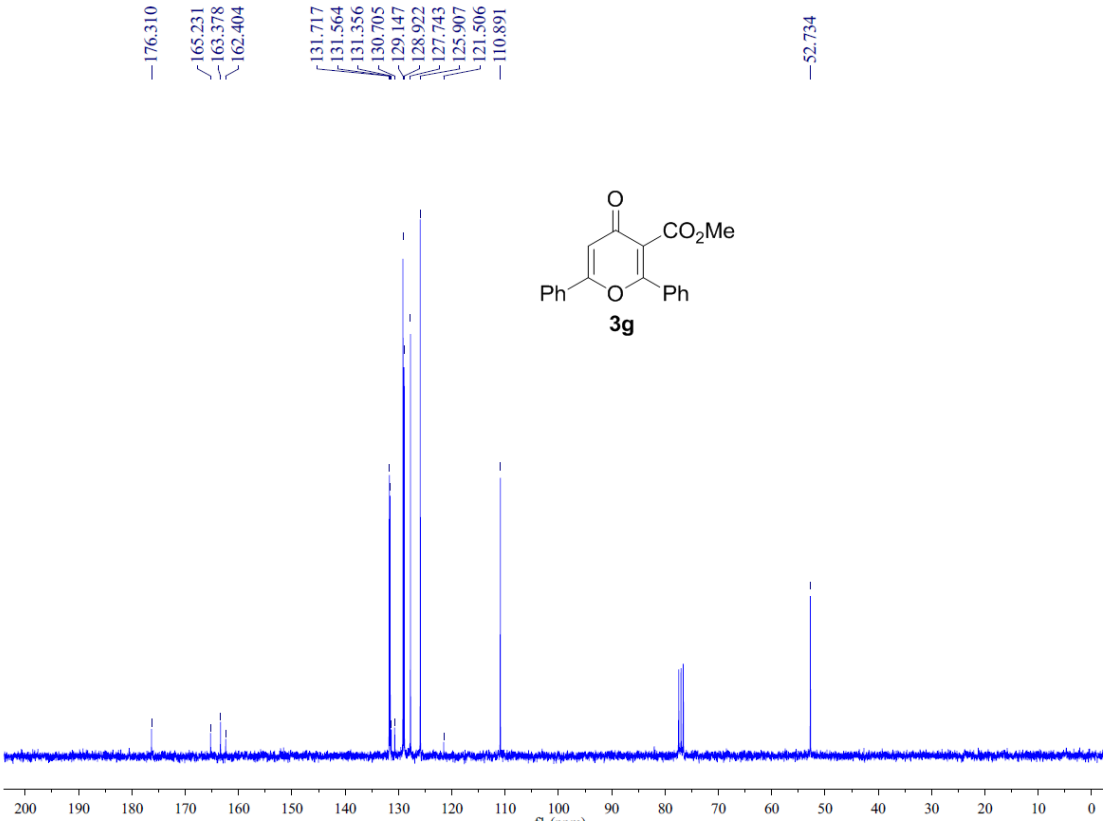
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131.564
131.356
130.705
129.147
128.922
127.743
125.907
121.506
110.891
52.734
O
CO2Me
Ph
O
Ph
3g
200
190
180
170
160
150
140
130
120
110
100
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70
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20
10
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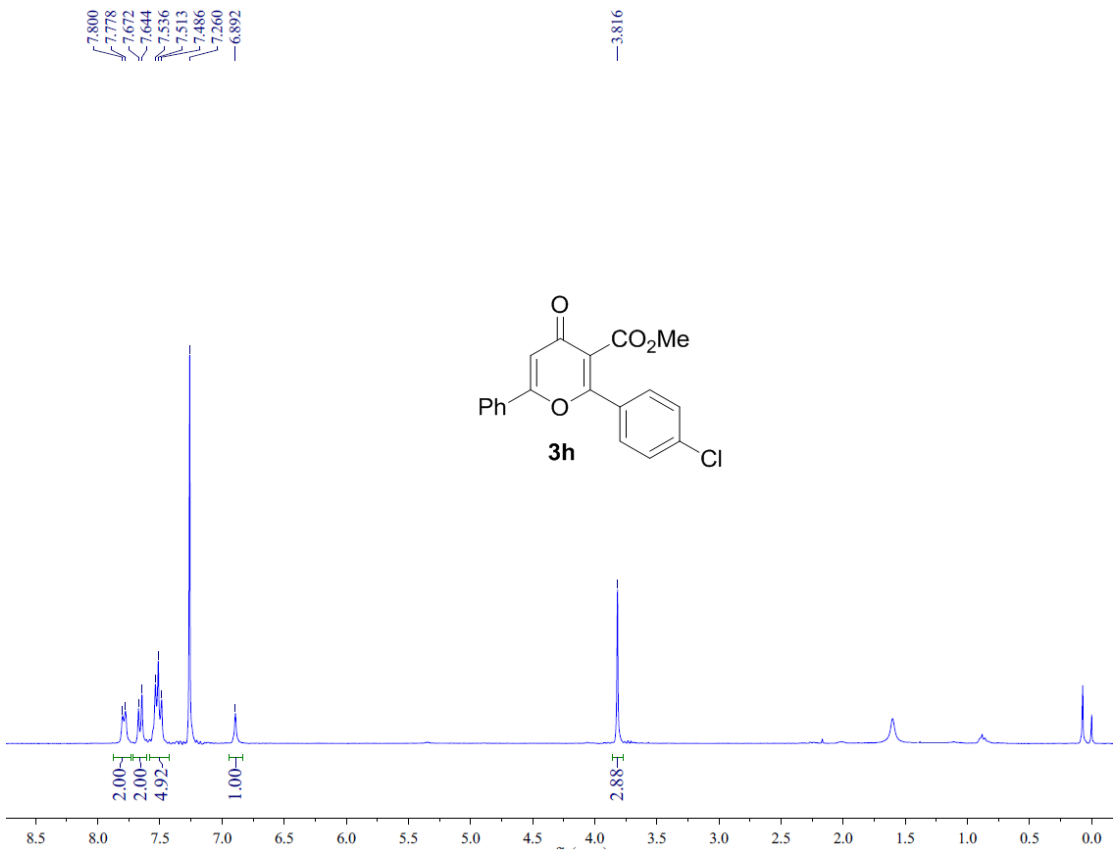
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7.778
7.672
7.644
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7.513
7.486
7.260
6.892
3.816
O
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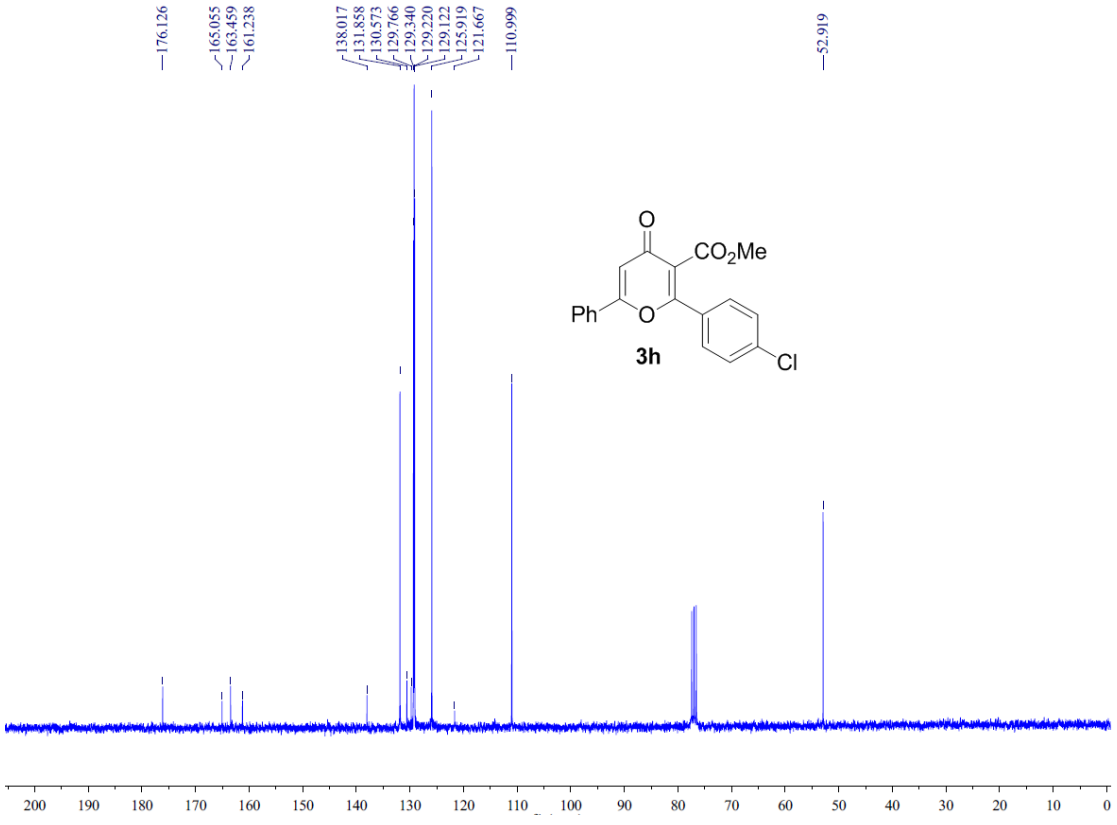
Ph
O
Cl
3h
2.00
2.00
4.92
1.00
2.88
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0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130.573
129.766
129.340
129.220
129.122
125.919
121.667
110.999
52.919
O
CO2Me
Ph
O
Cl
3h
200
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180
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150
140
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110
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70
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10
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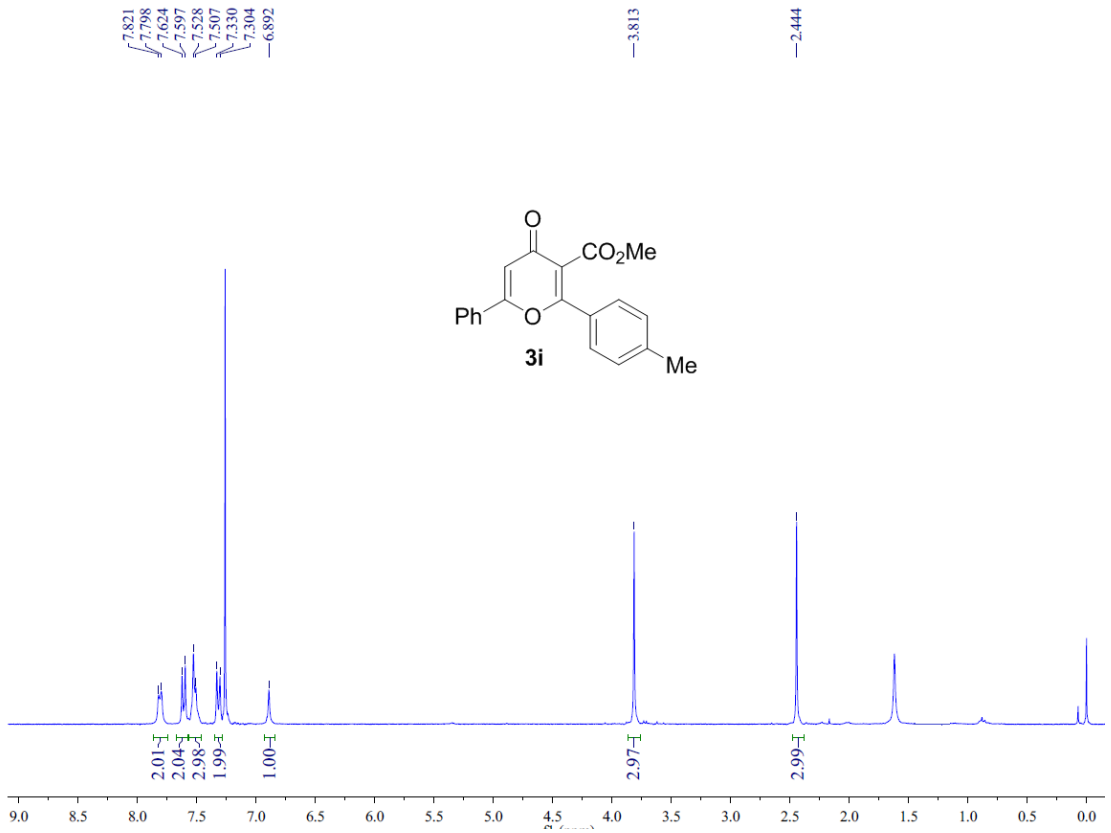
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7.624
7.597
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7.507
7.330
7.304
6.892
3.813
2.444
O
CO2Me
Ph
O
Me
3i
2.01
2.04
2.98
1.99
1.00
2.97
2.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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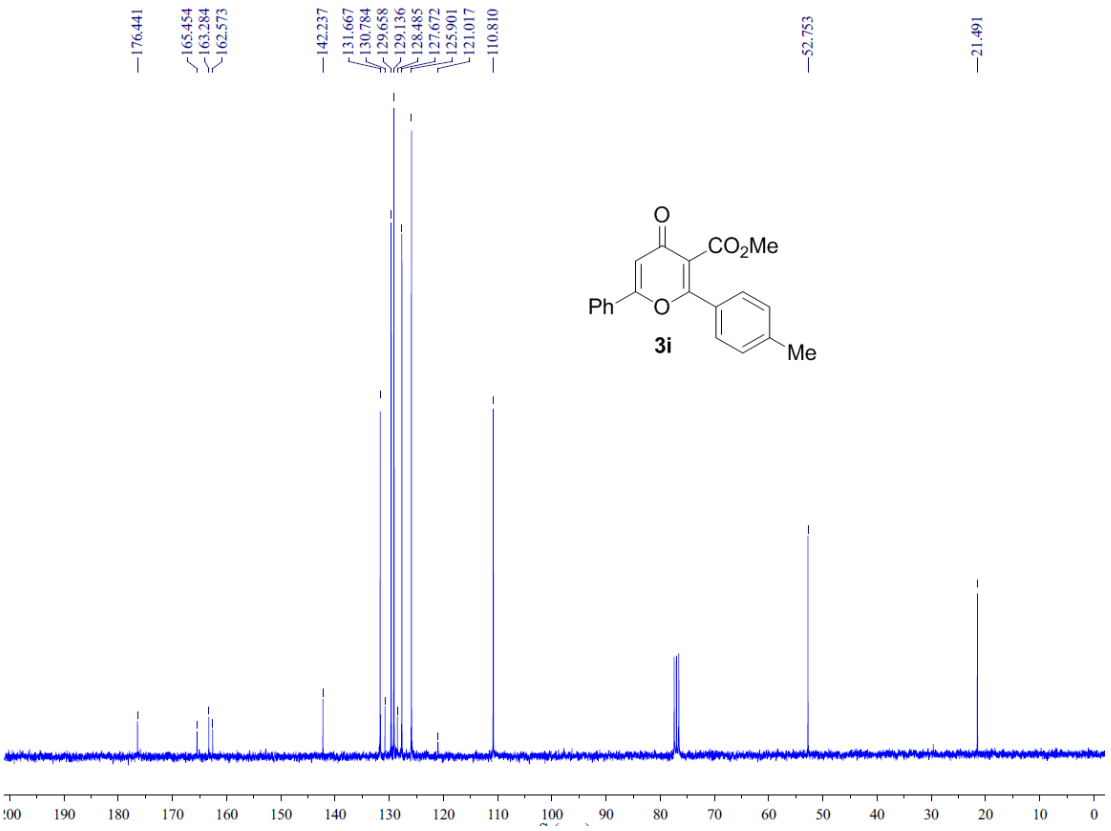
0.0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129.658
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128.485
127.672
125.901
121.017
110.810
52.753
21.491
O
CO2Me
Ph
O
Me
3i
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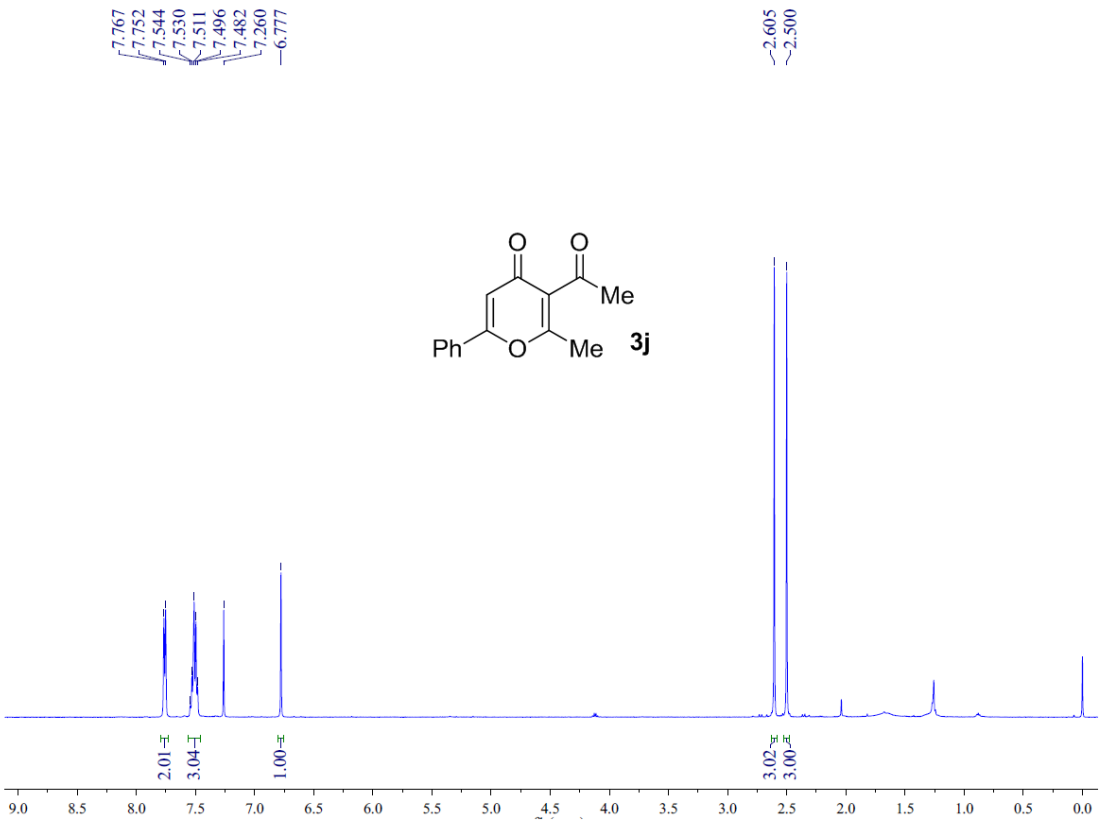
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7.544
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7.260
6.777
2.605
2.500
O
O
Me
Ph
O
Me
3j
2.01
3.04
1.00
3.02
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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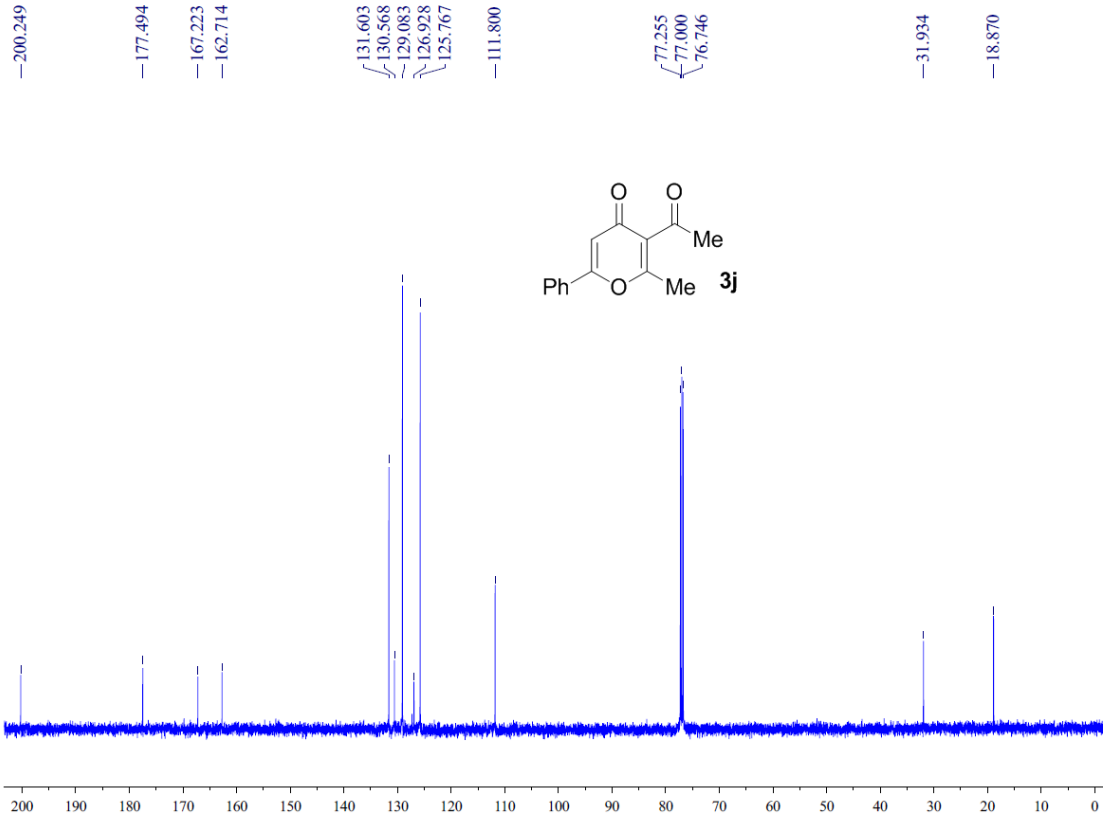
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77.000
76.746
31.934
18.870
O
O
Me
Ph
O
Me
3j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.941
7.926
7.877
7.864
7.637
7.622
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7.523
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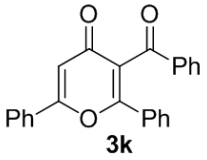
6.934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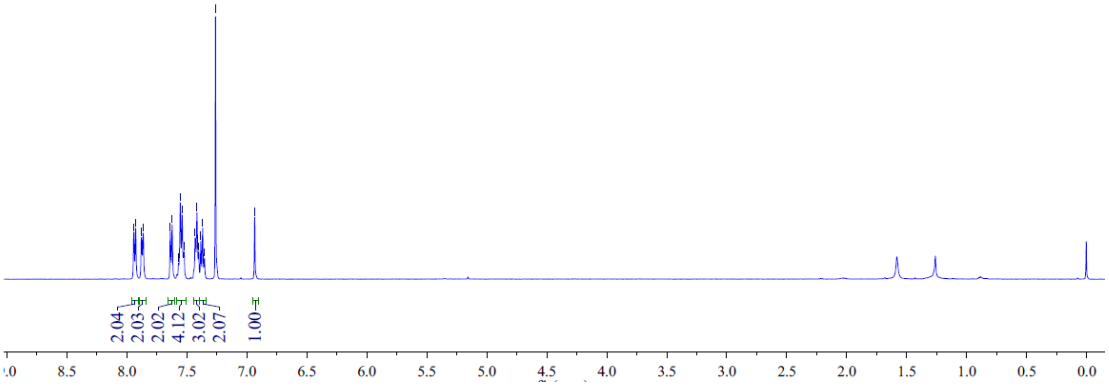
O
Ph
Ph
O
Ph

3k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8.5
8.0
7.5
7.0
6.5
6.0
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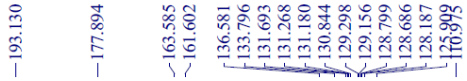
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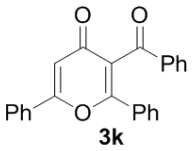
77.000
76.745


O
O
Ph
Ph
O
Ph

3k

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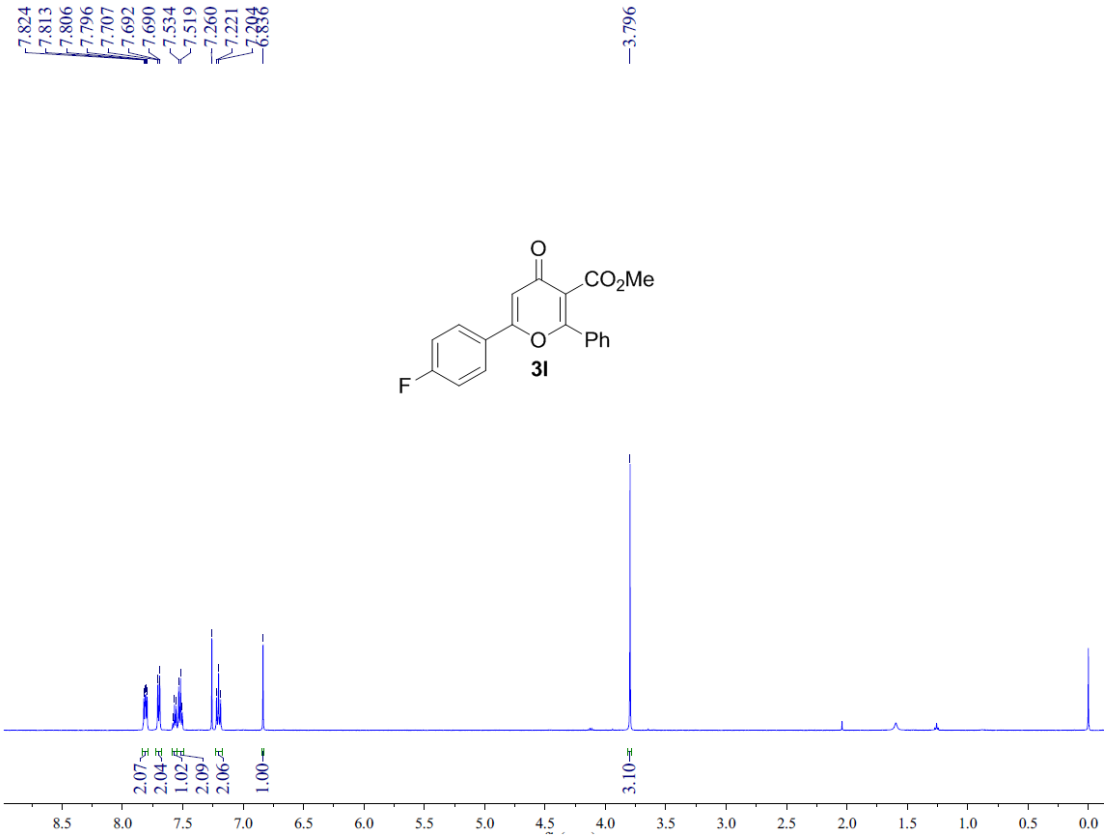
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7.260
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7.204
6.836
3.796
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CO2Me
O
Ph
F
3l
2.07
2.04
1.02
2.09
2.06
1.00
3.10
8.5
8.0
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7.0
6.5
6.0
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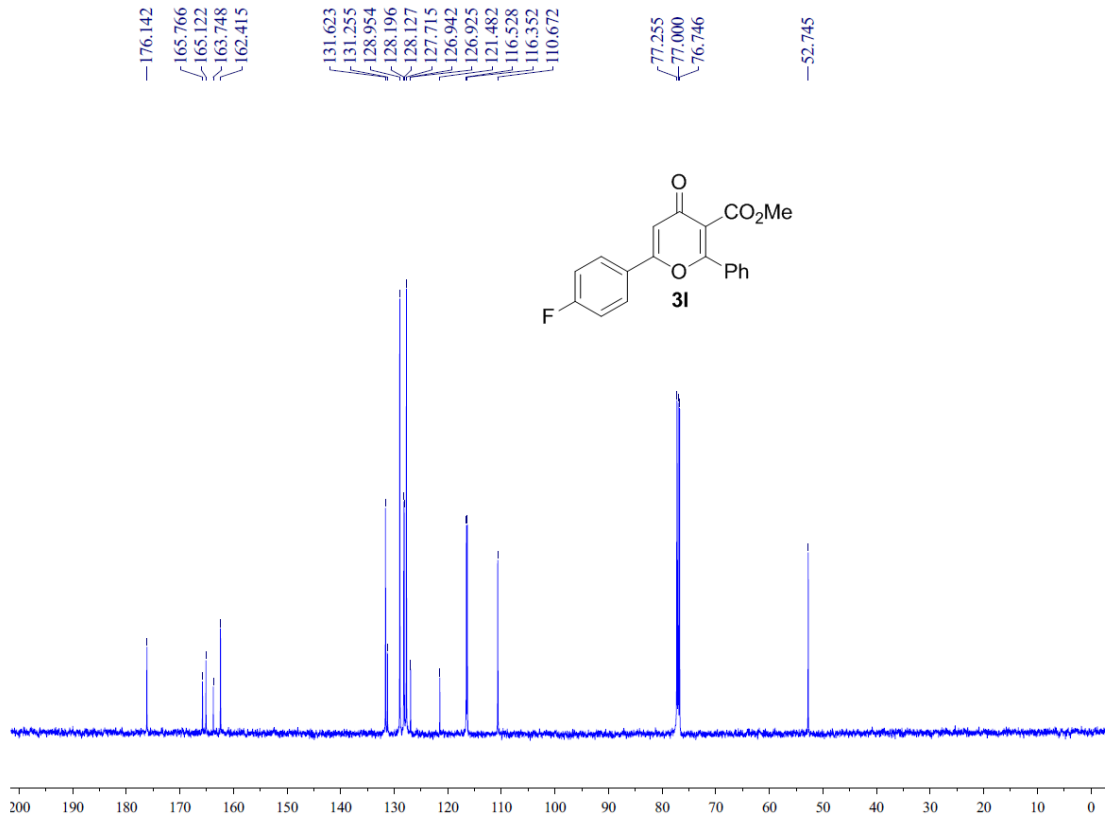
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116.528
116.352
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77.255
77.000
76.746
52.745
O
CO2Me
O
Ph
F
3l
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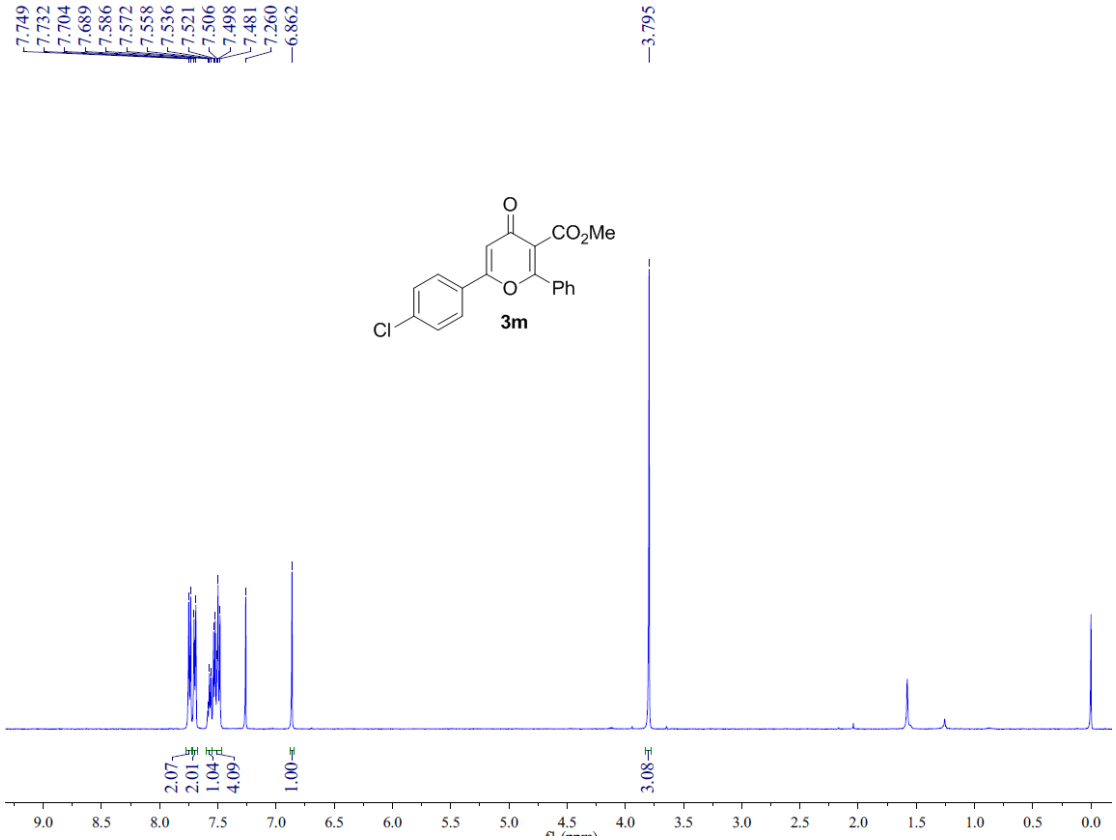
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7.481
7.260
6.862
3.795
O
CO2Me
O
Ph
Cl
3m
2.07
2.01
1.04
4.09
1.00
3.08
9.0
8.5
8.0
7.5
7.0
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6.0
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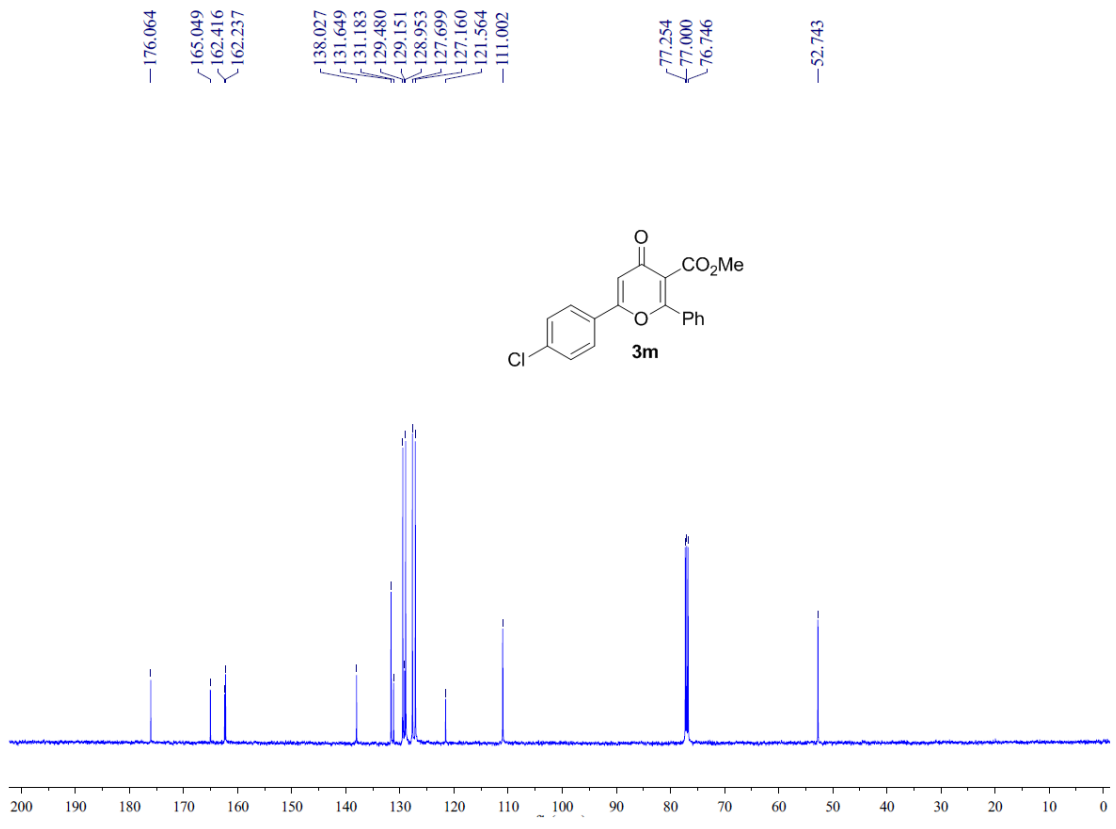
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121.564
111.002
77.254
77.000
76.746
52.743
O
CO2Me
O
Ph
Cl
3m
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150
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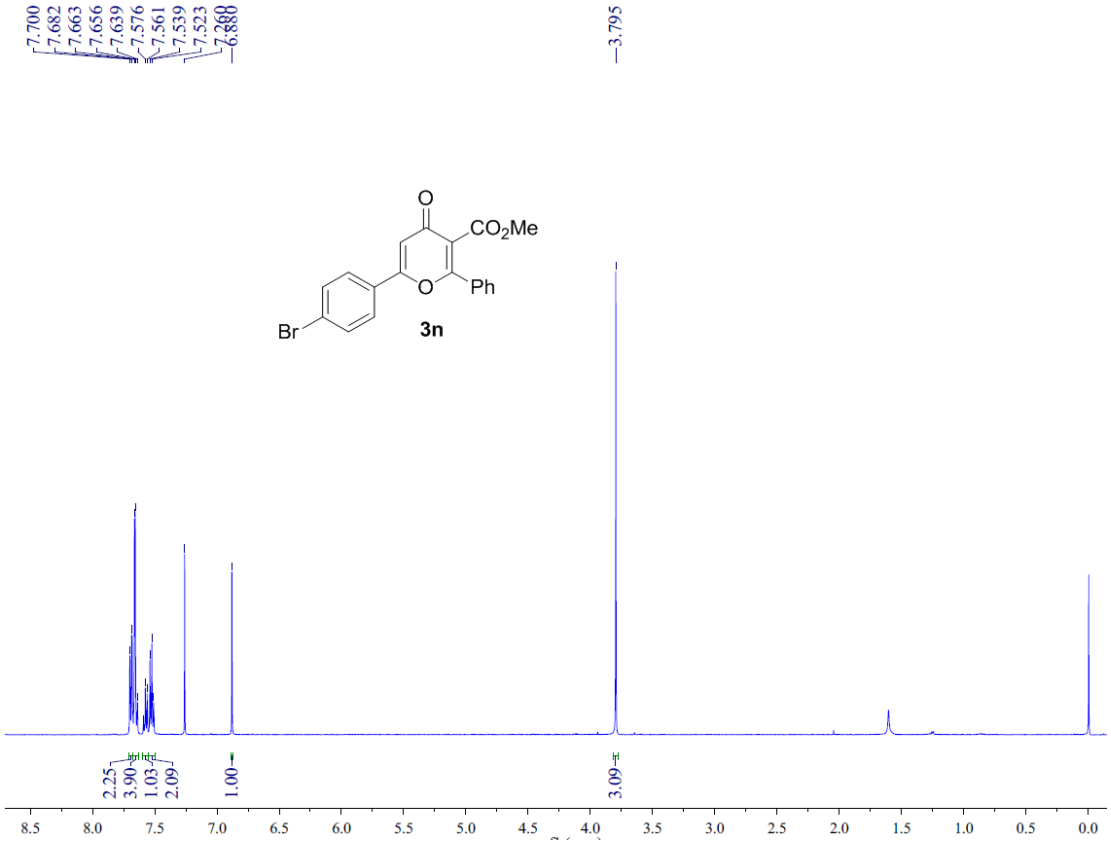
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7.539
7.523
3.795
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CO2Me
Ph
O
Br
3n
2.25
3.90
1.03
2.09
1.00
3.09
8.5
8.0
7.5
7.0
6.5
6.0
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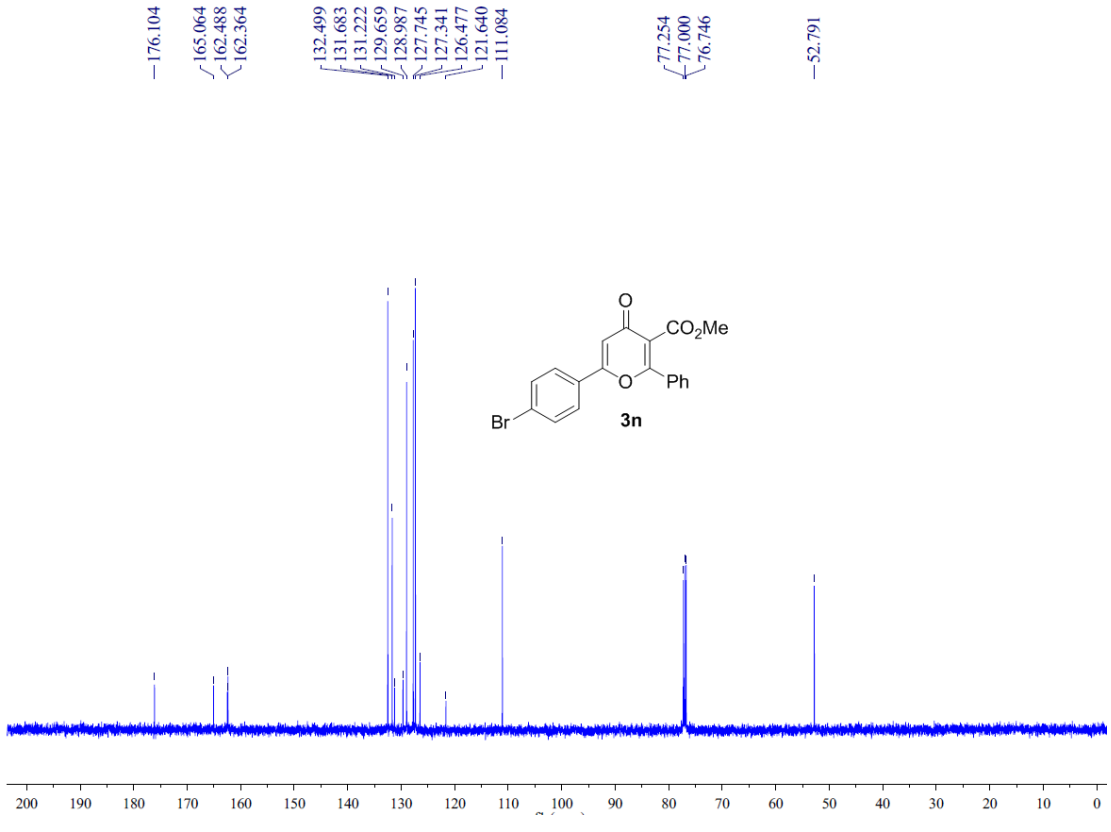
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77.000
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52.791
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Ph
O
Br
3n
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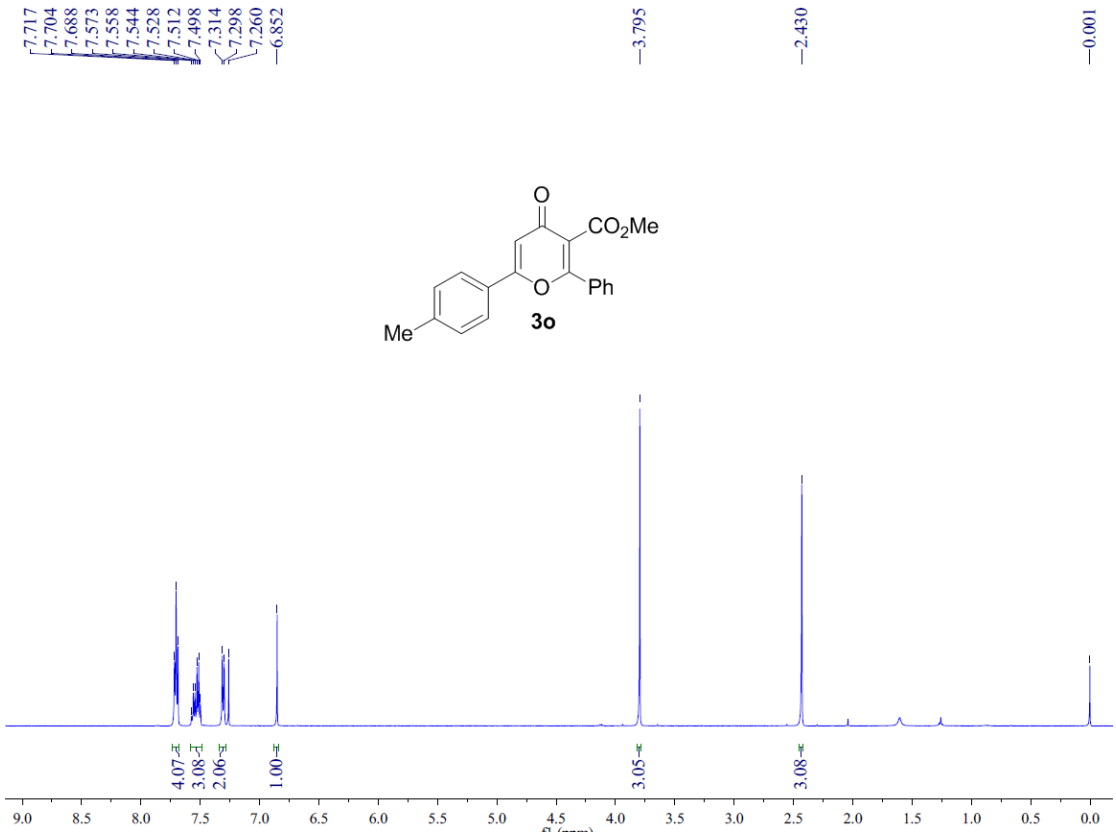
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7.544
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7.512
7.498
7.314
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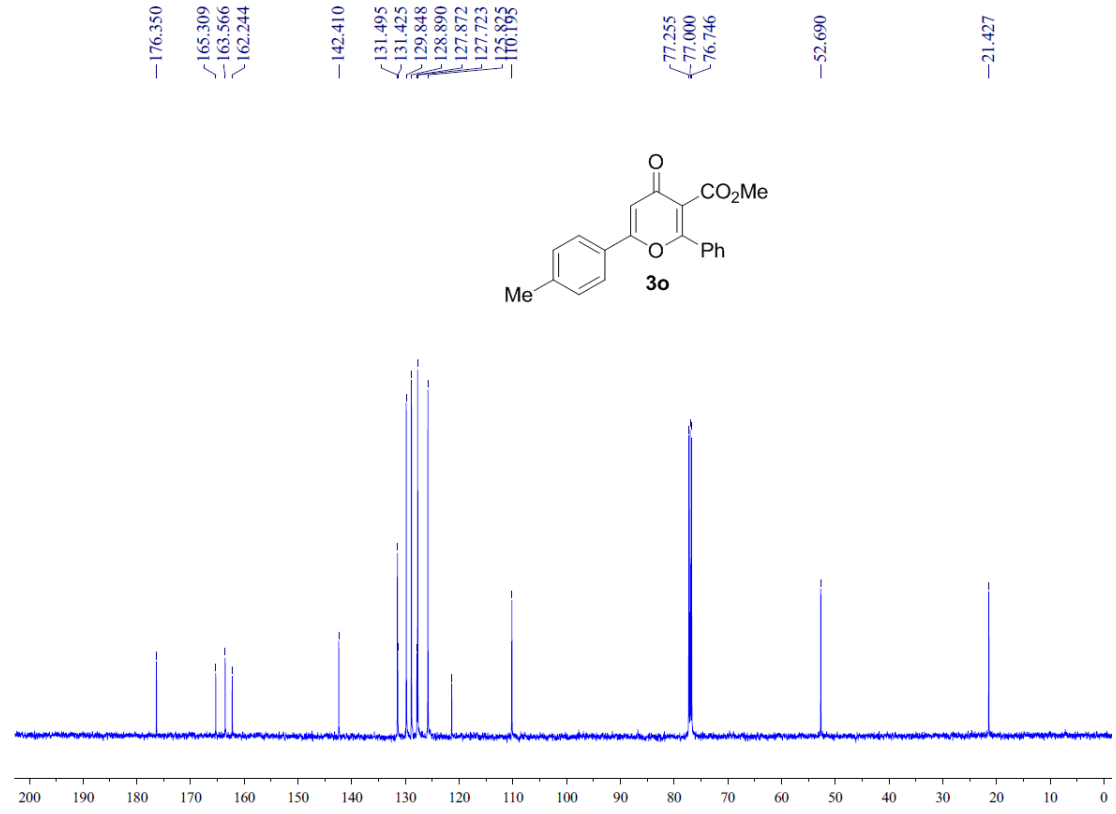
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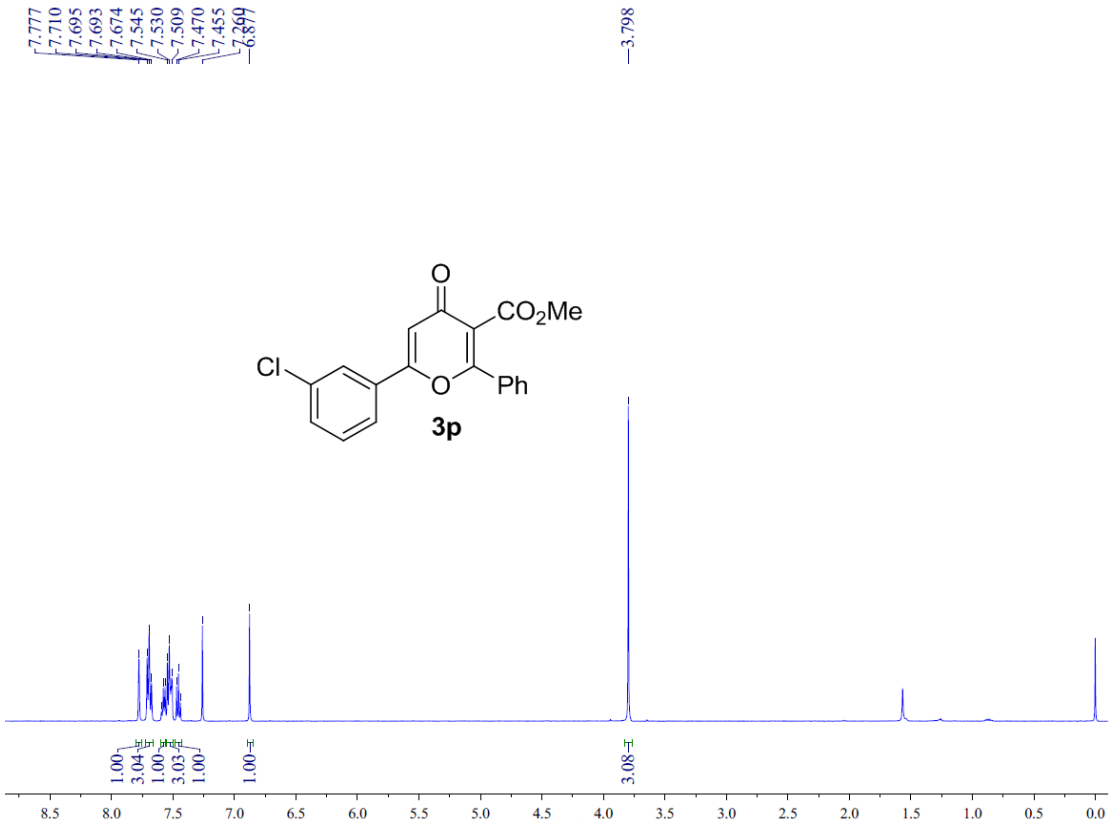
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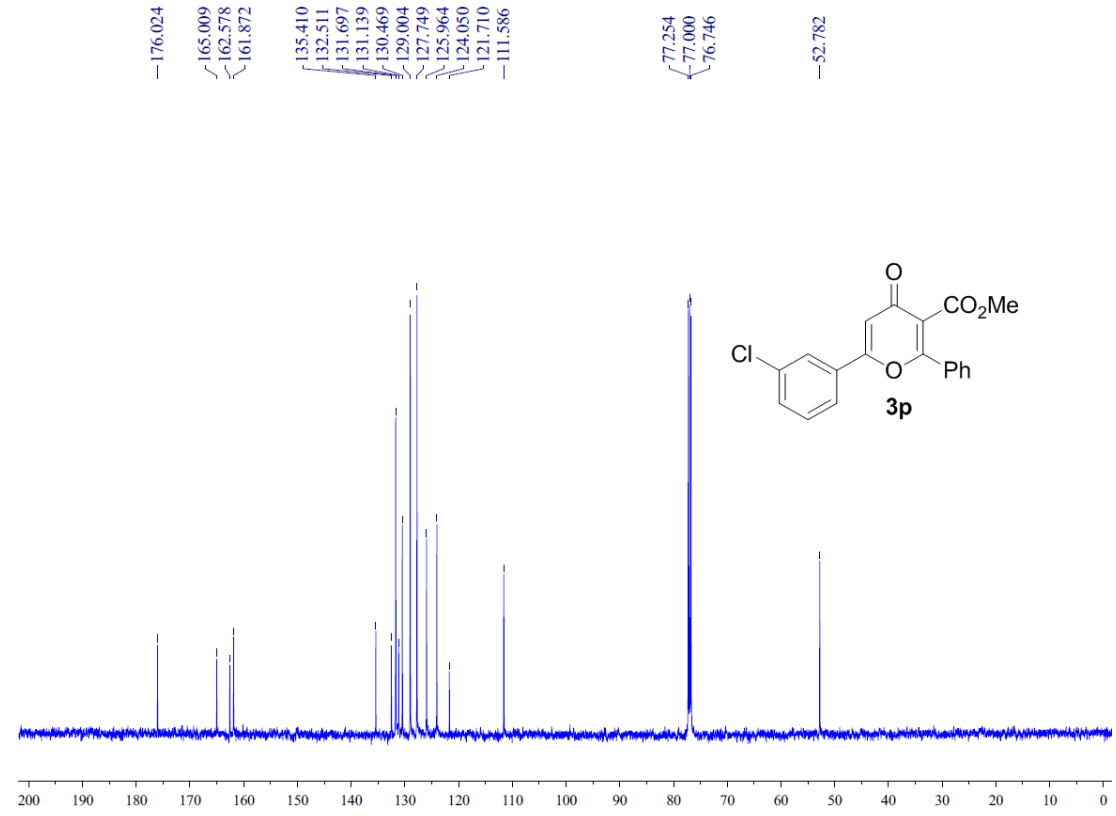
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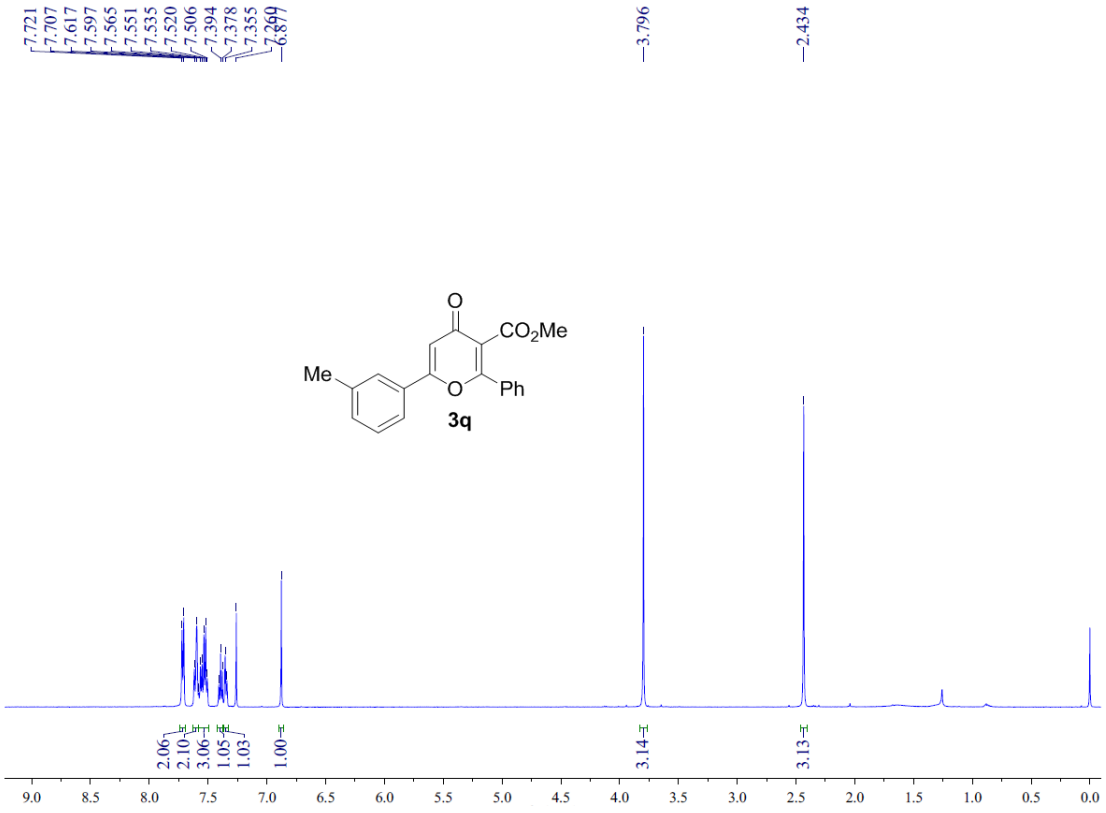
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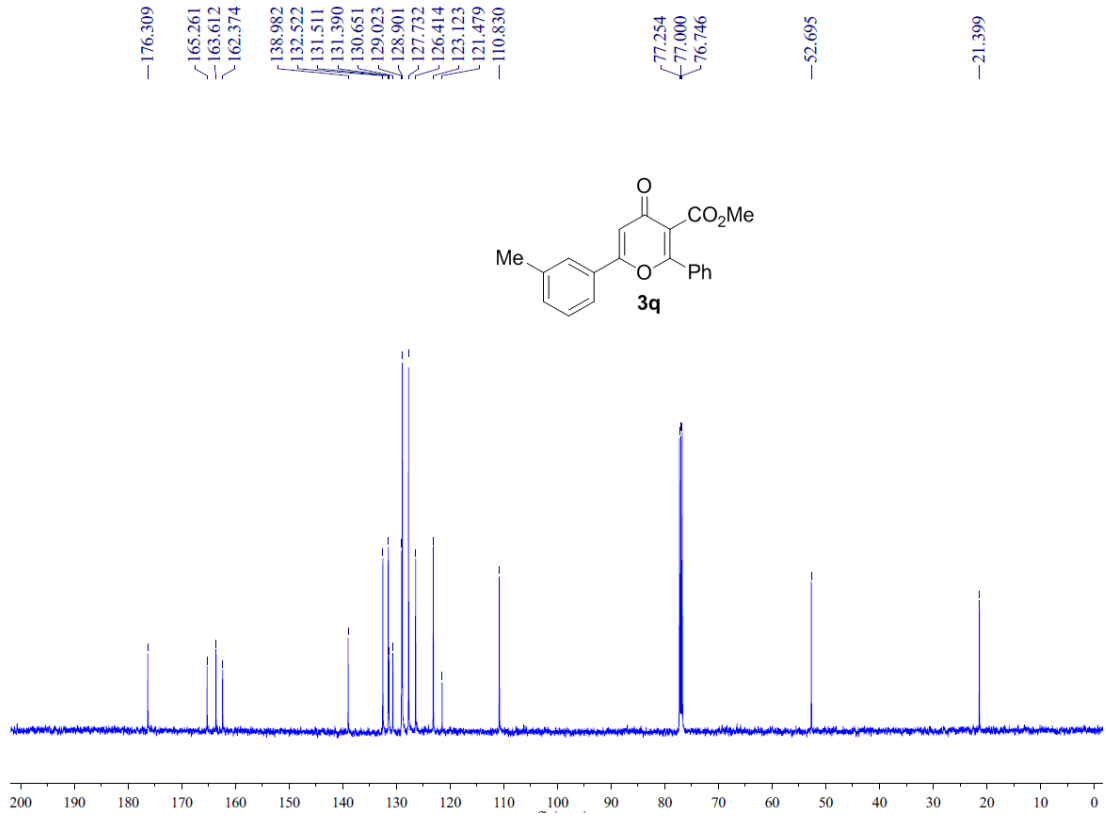
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Me
O
Ph
3q
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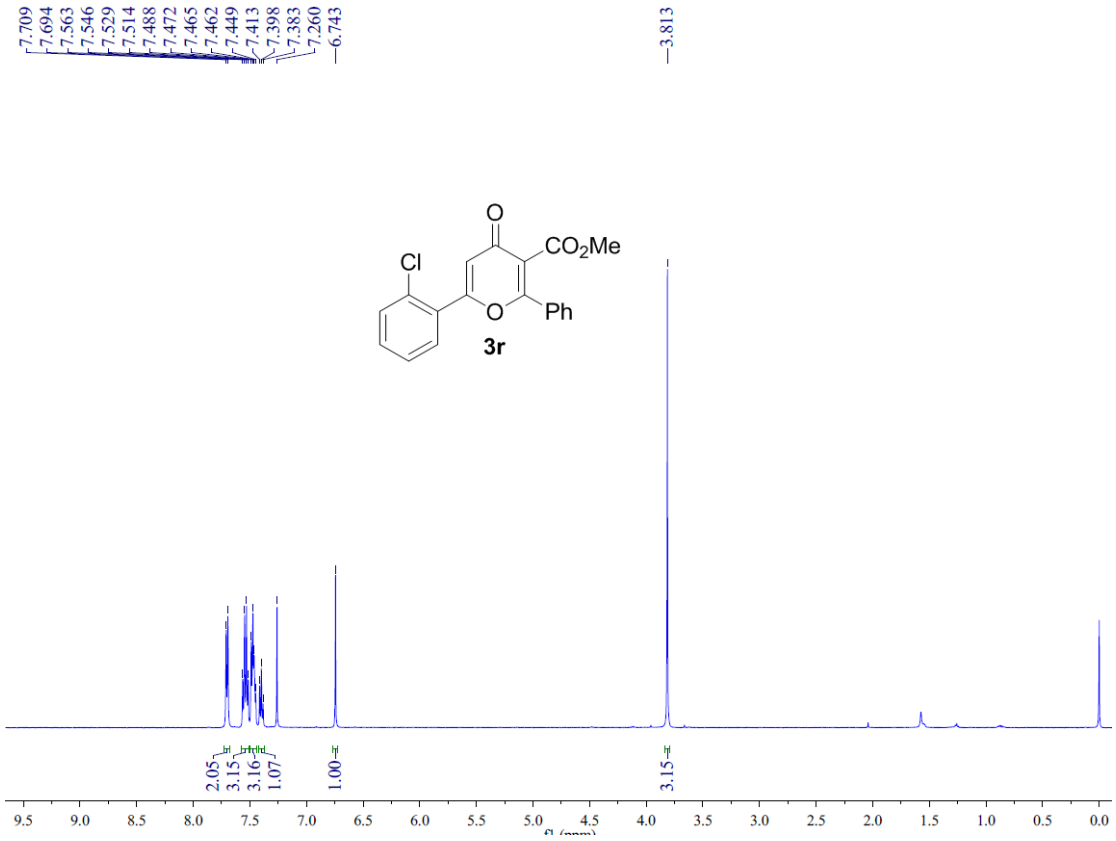
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Ph
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1.00
3.15
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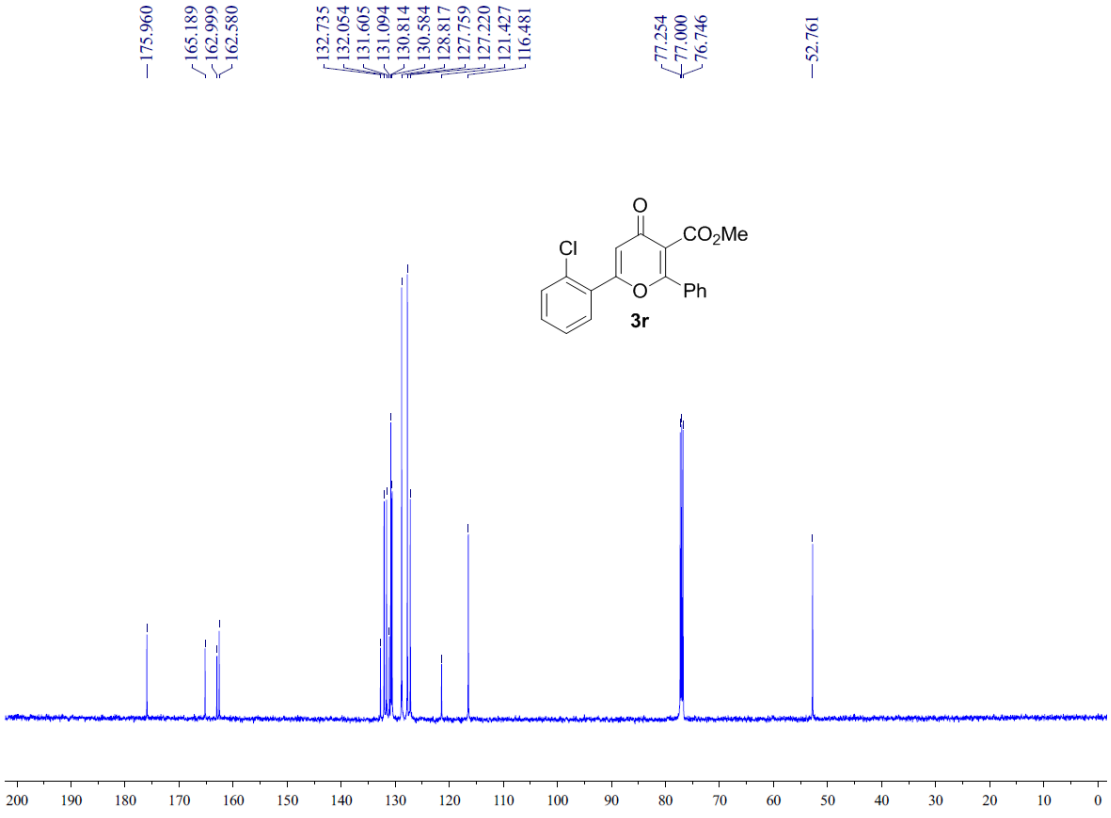
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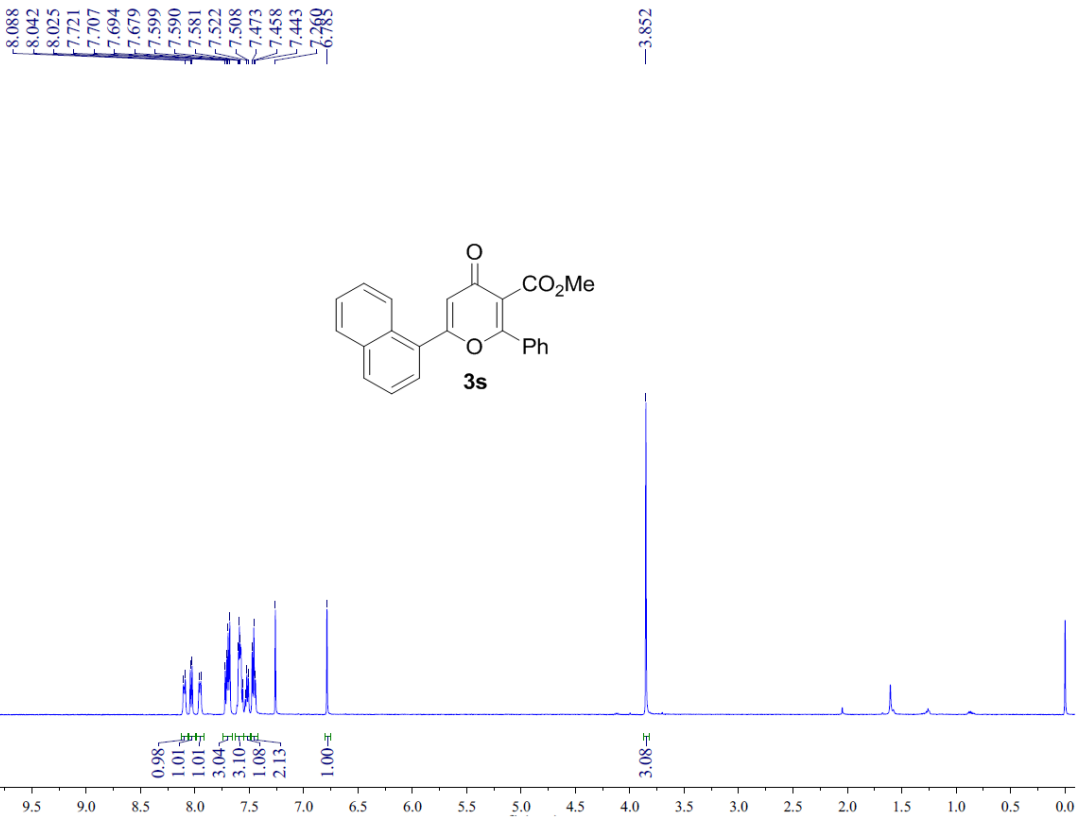
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O
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1.01
3.04
3.10
1.08
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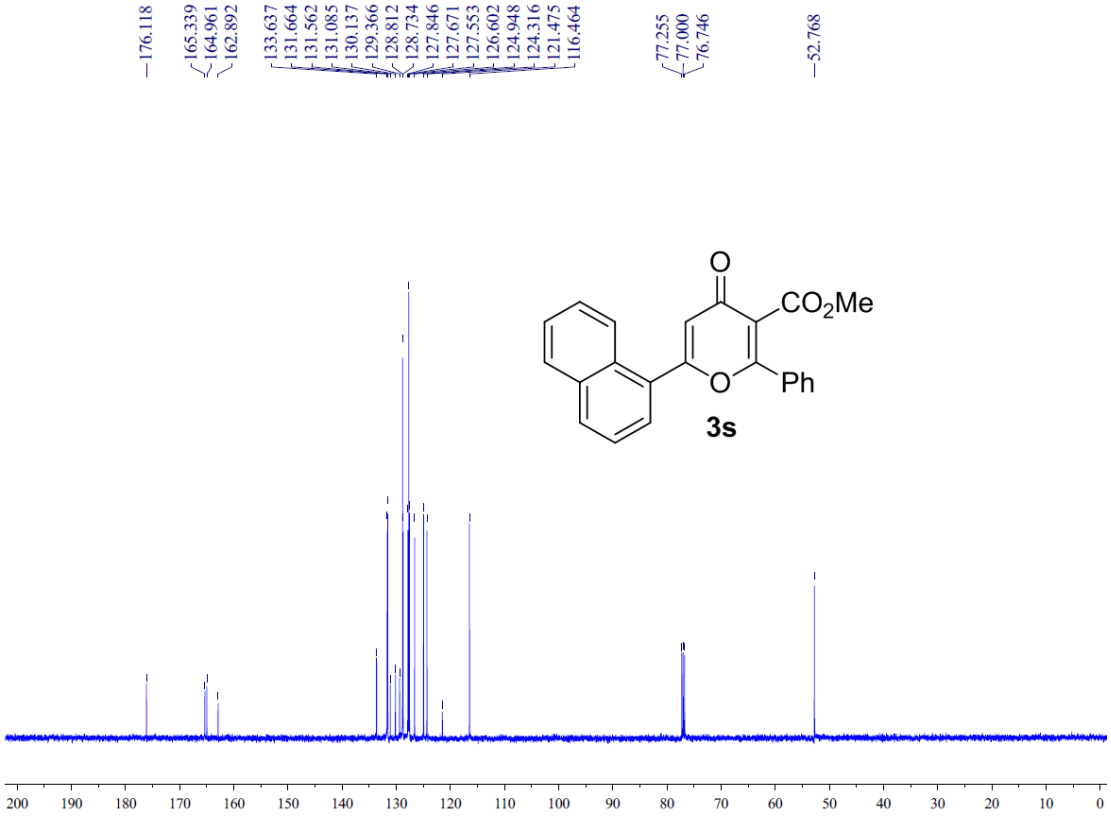
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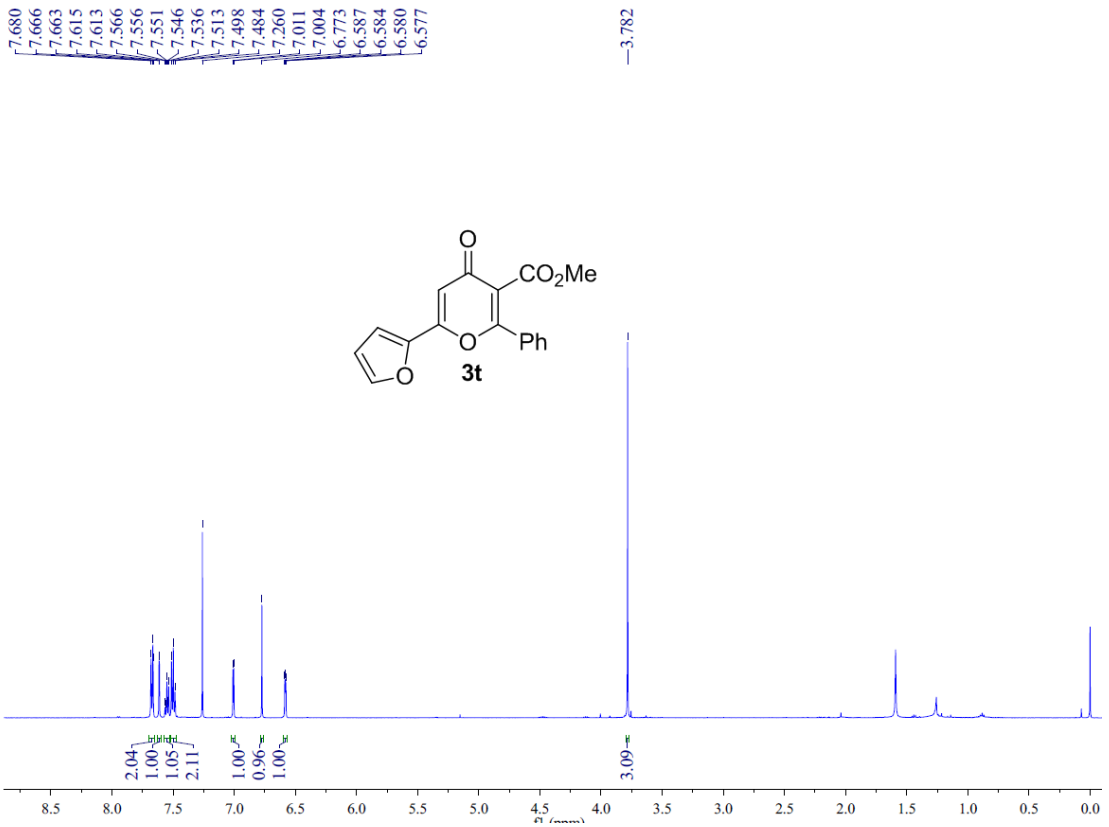
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6.577
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Ph
O
O
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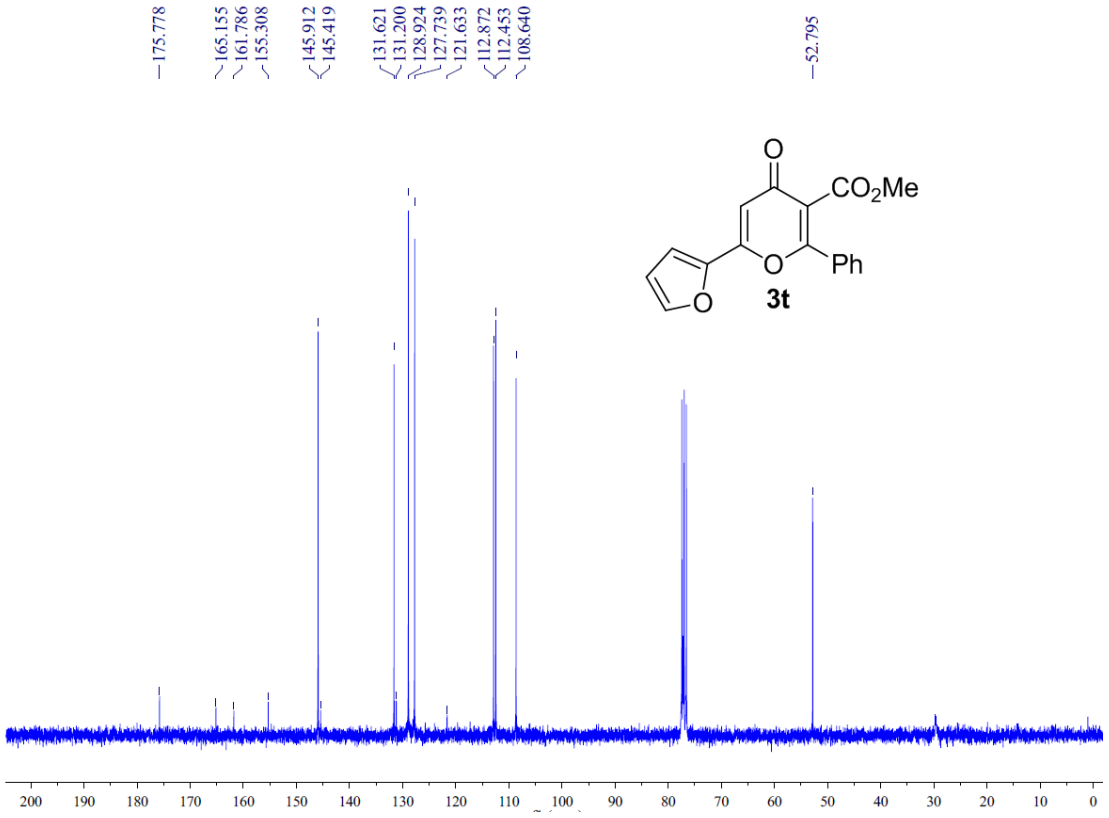
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Ph
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O
3t
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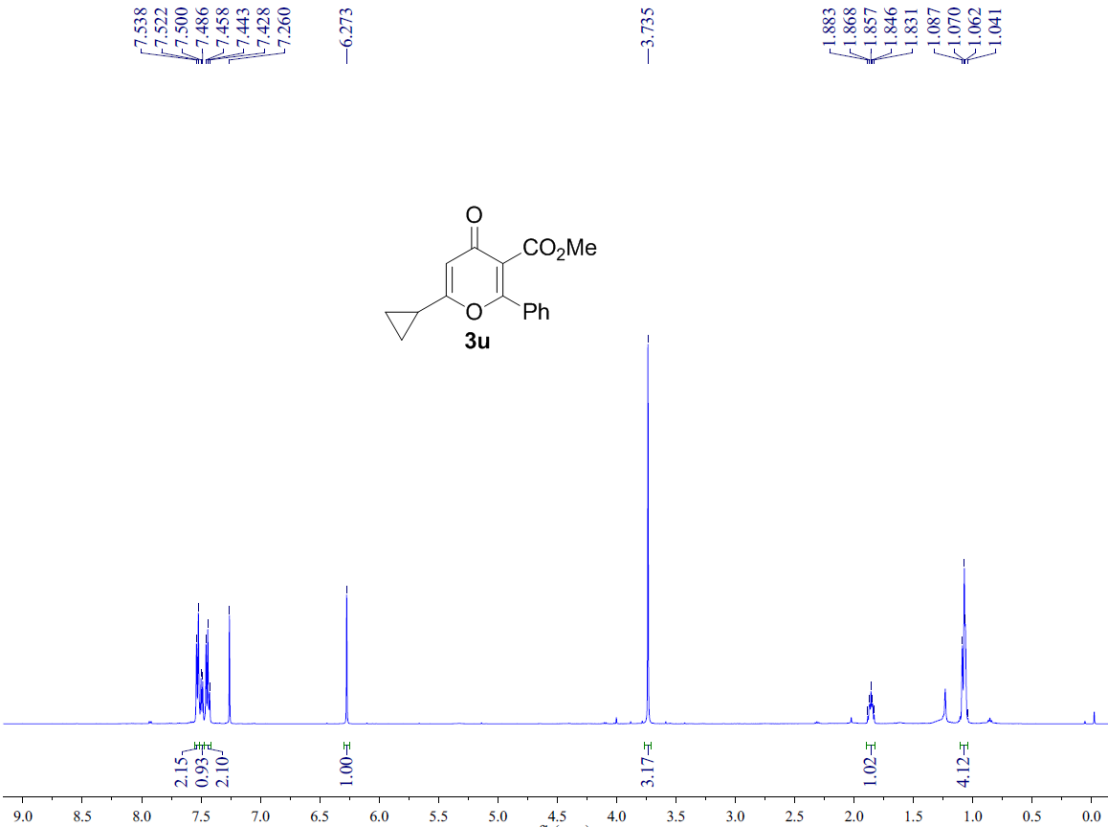
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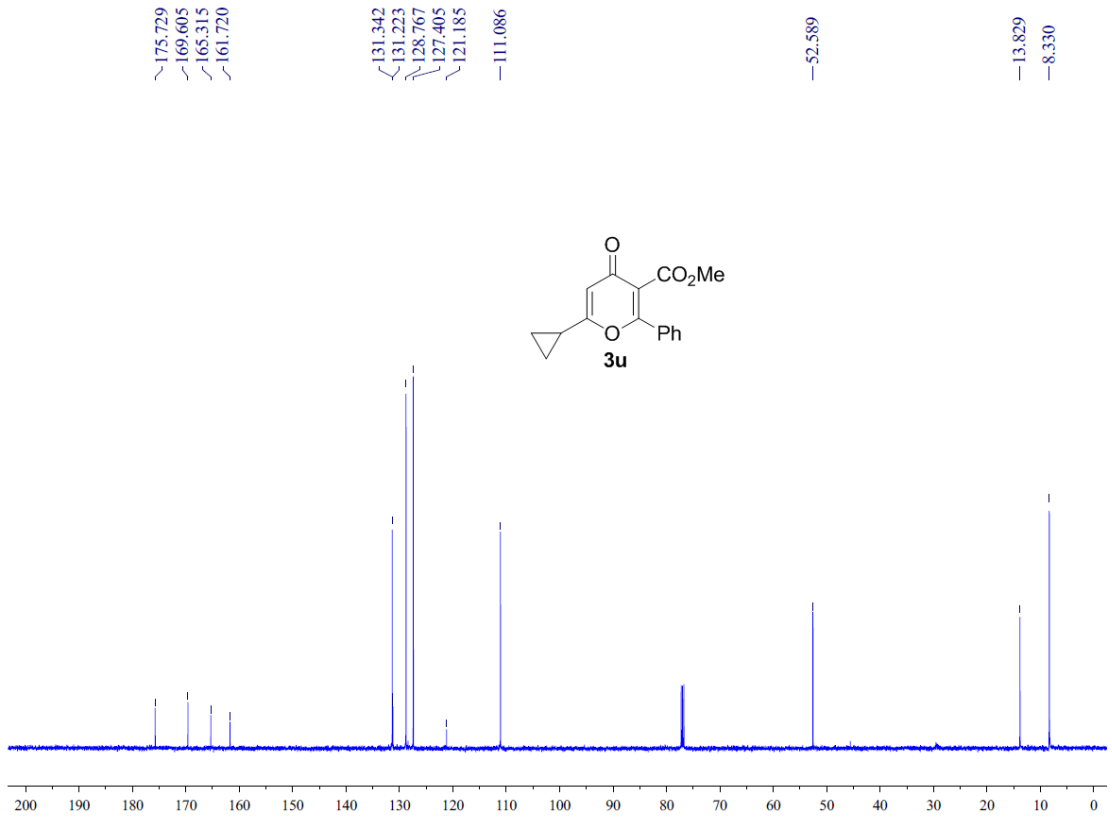
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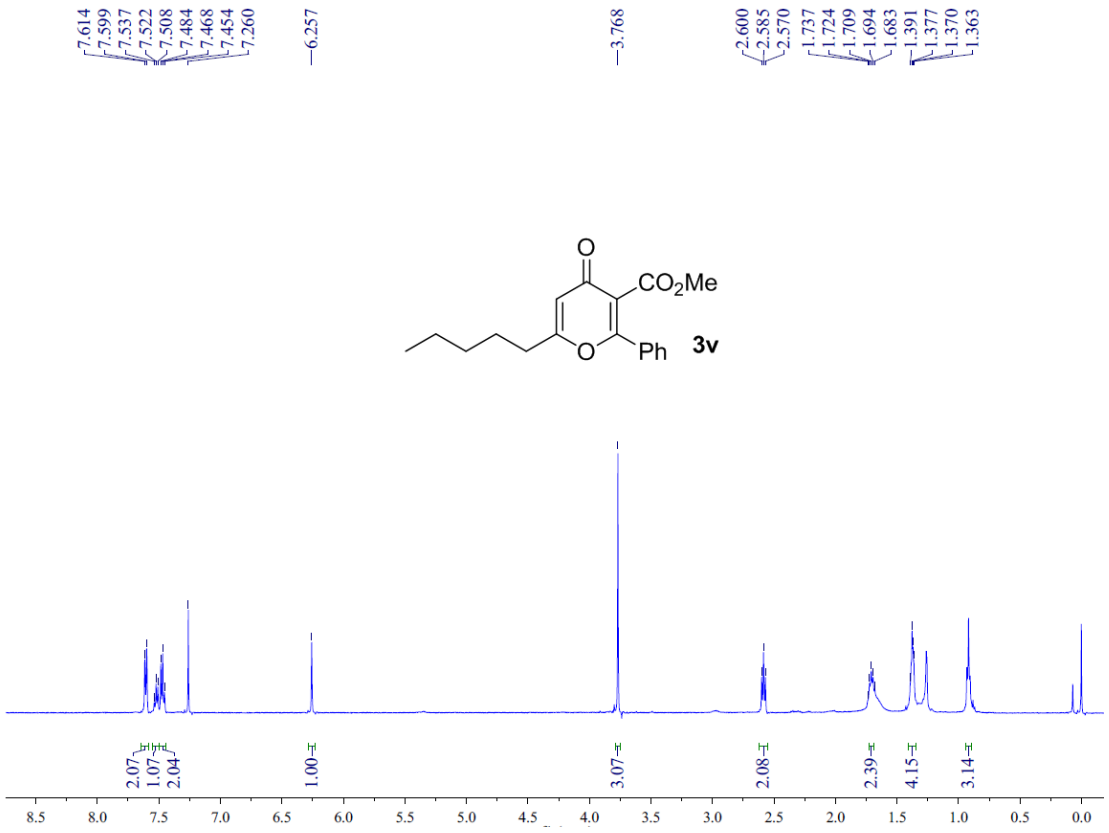
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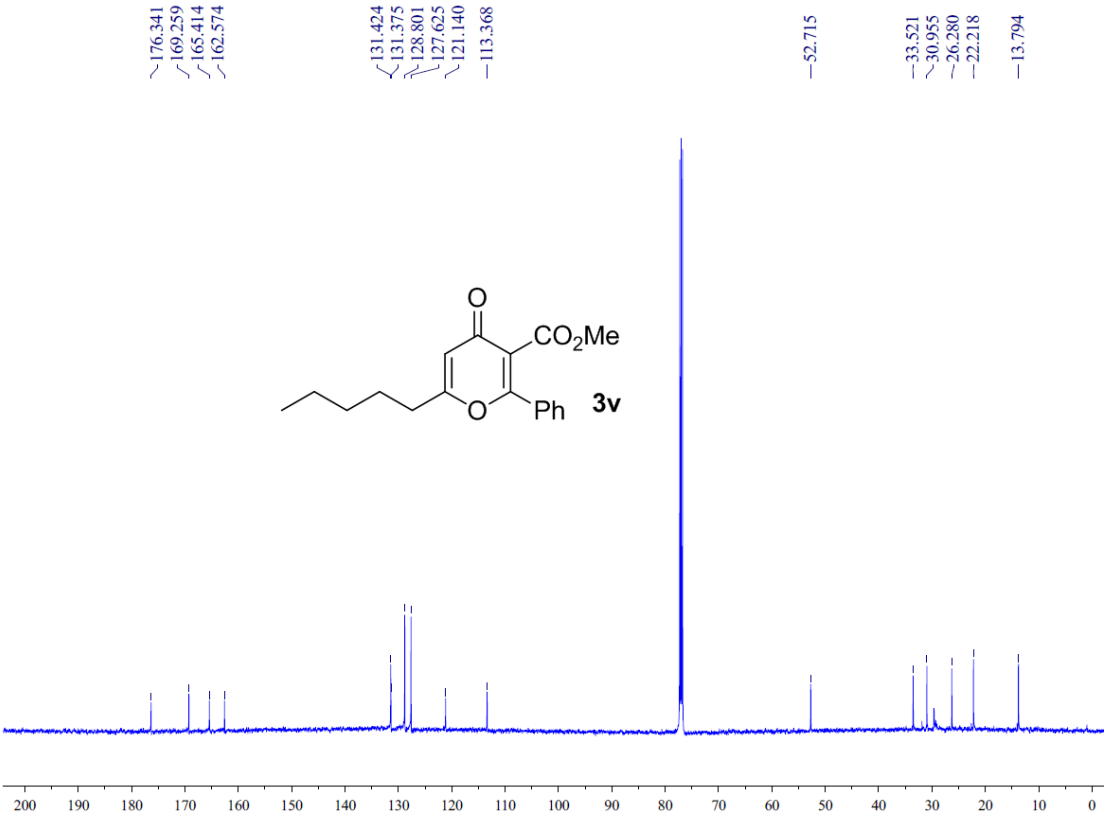
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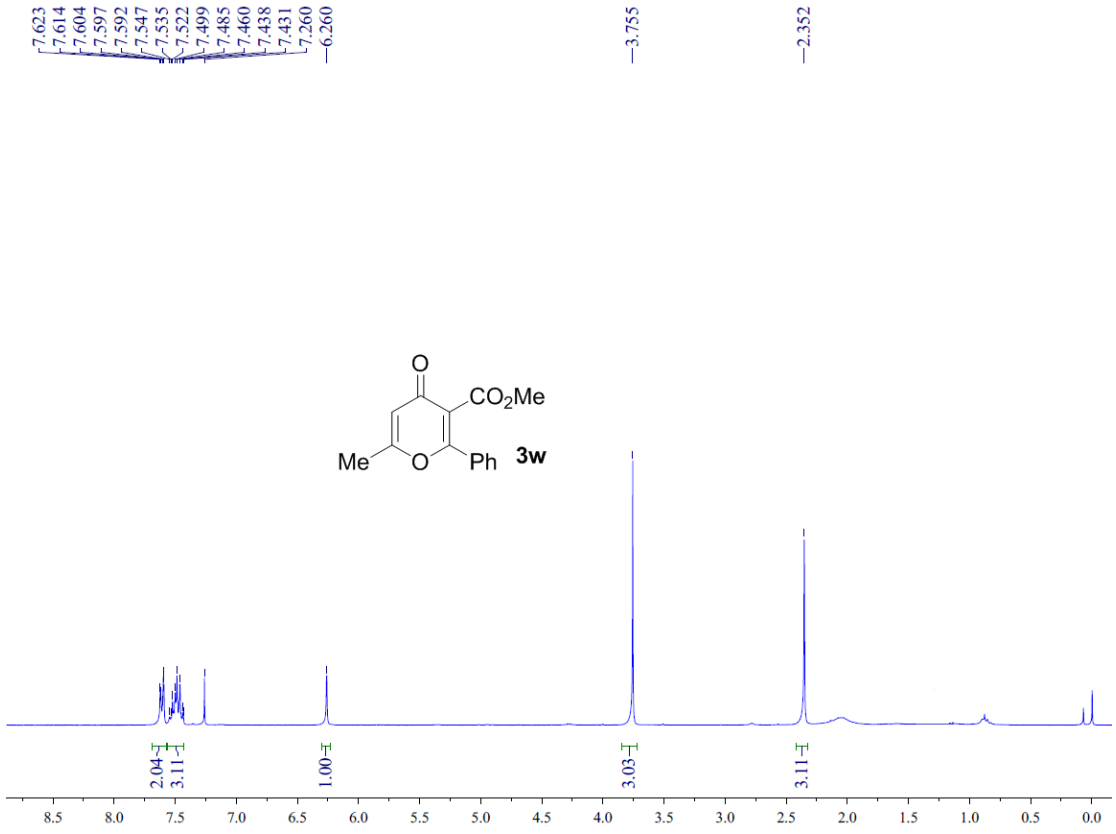
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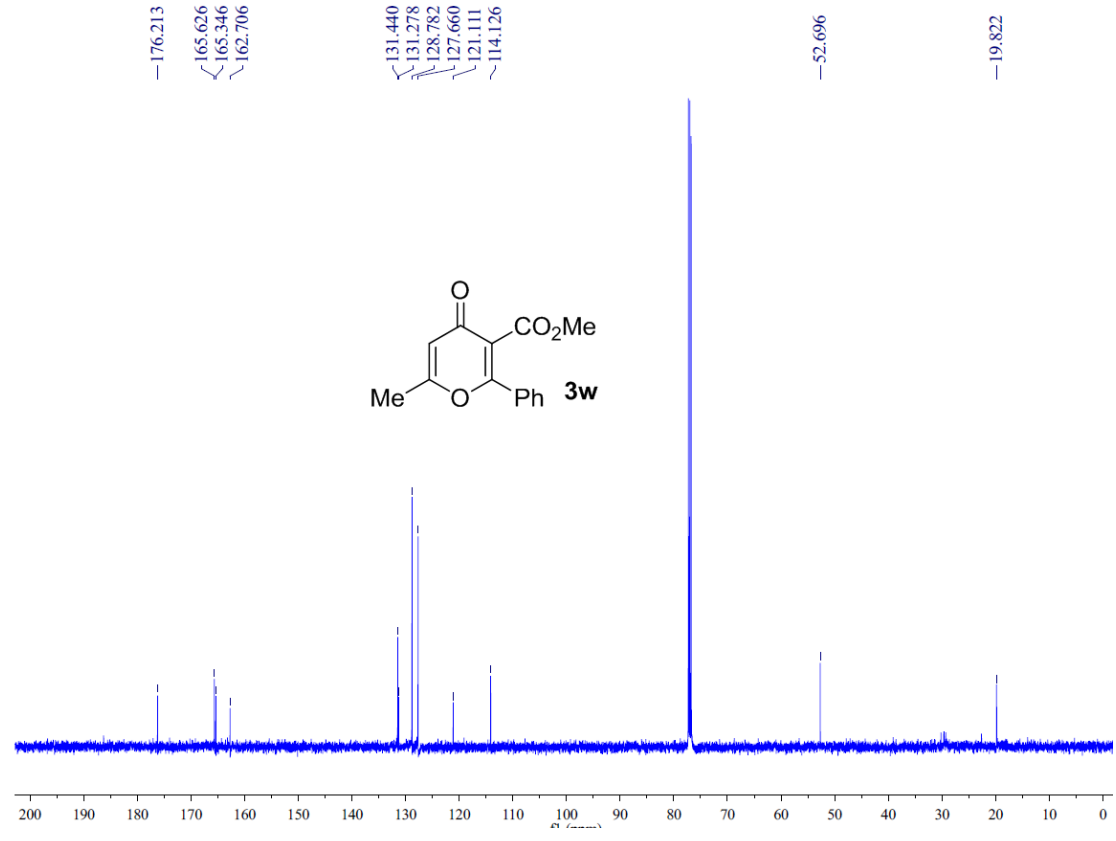
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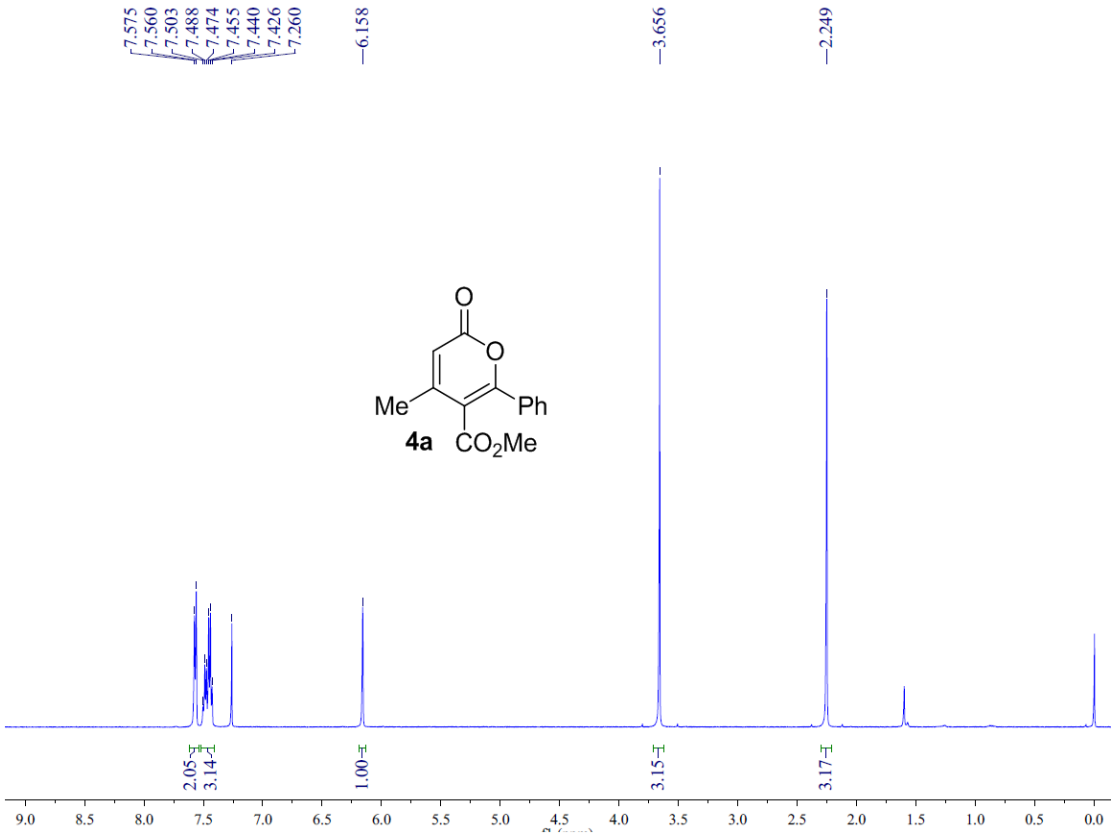
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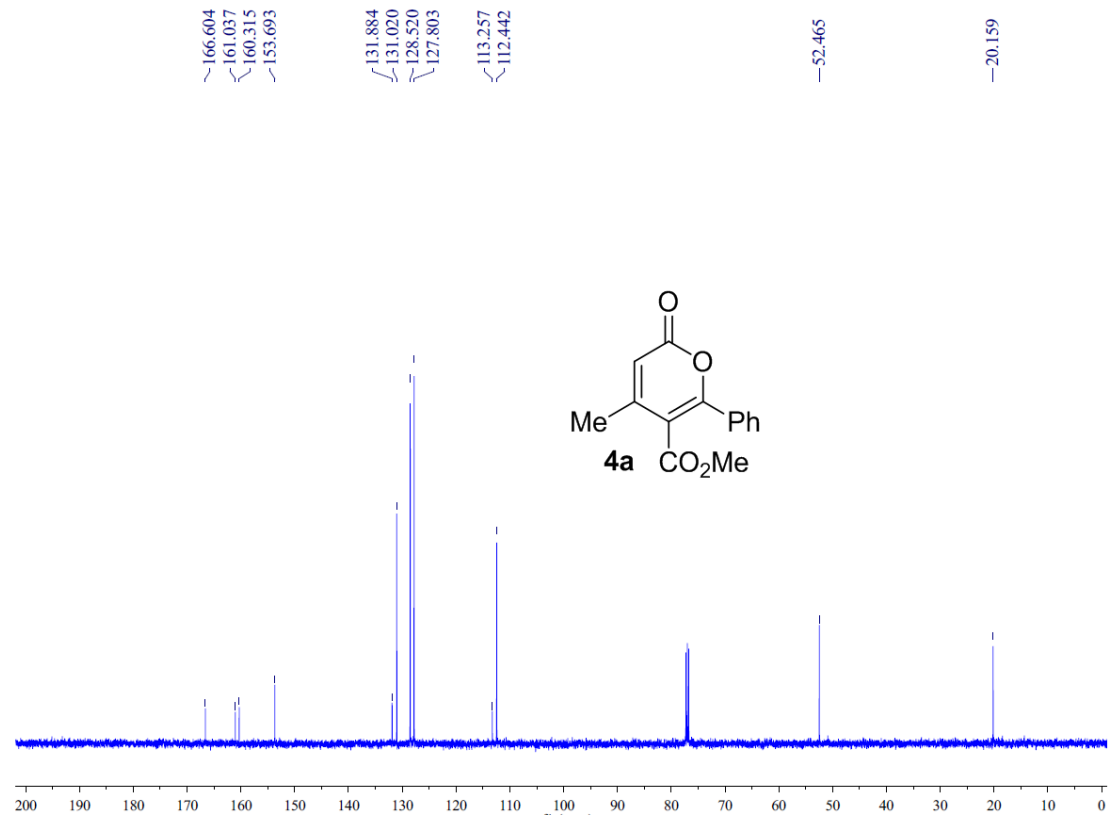
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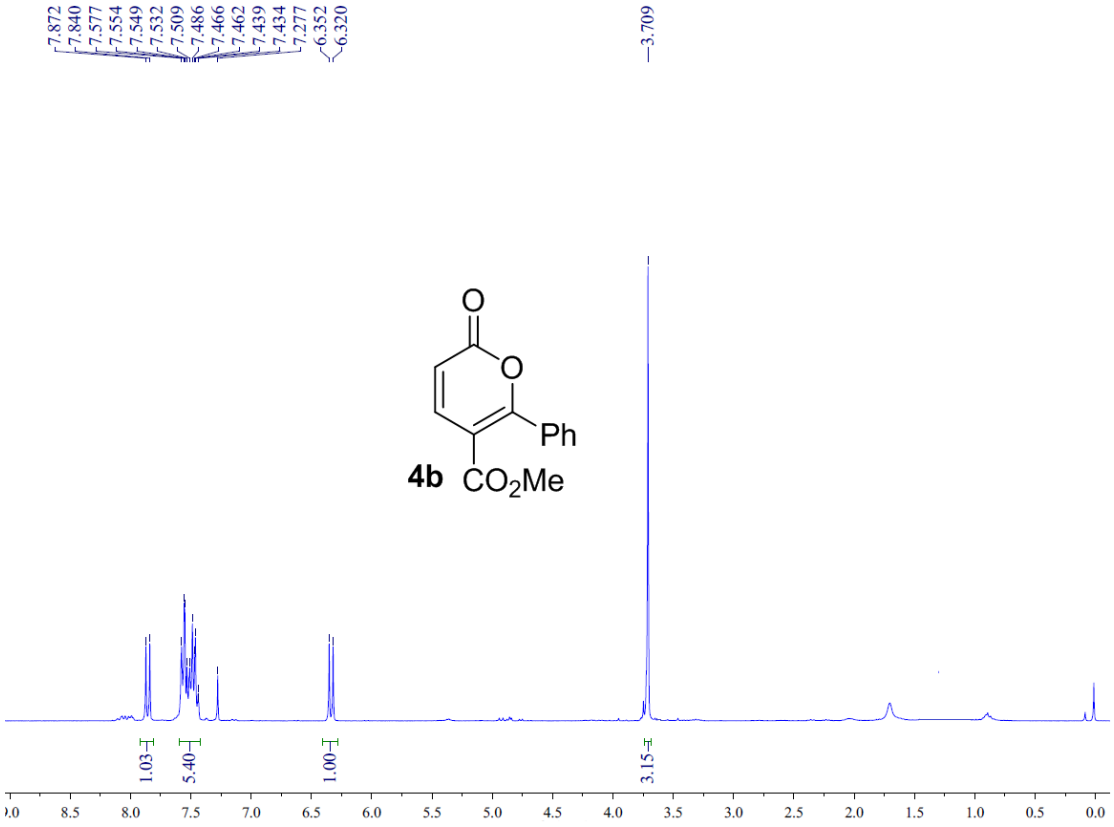
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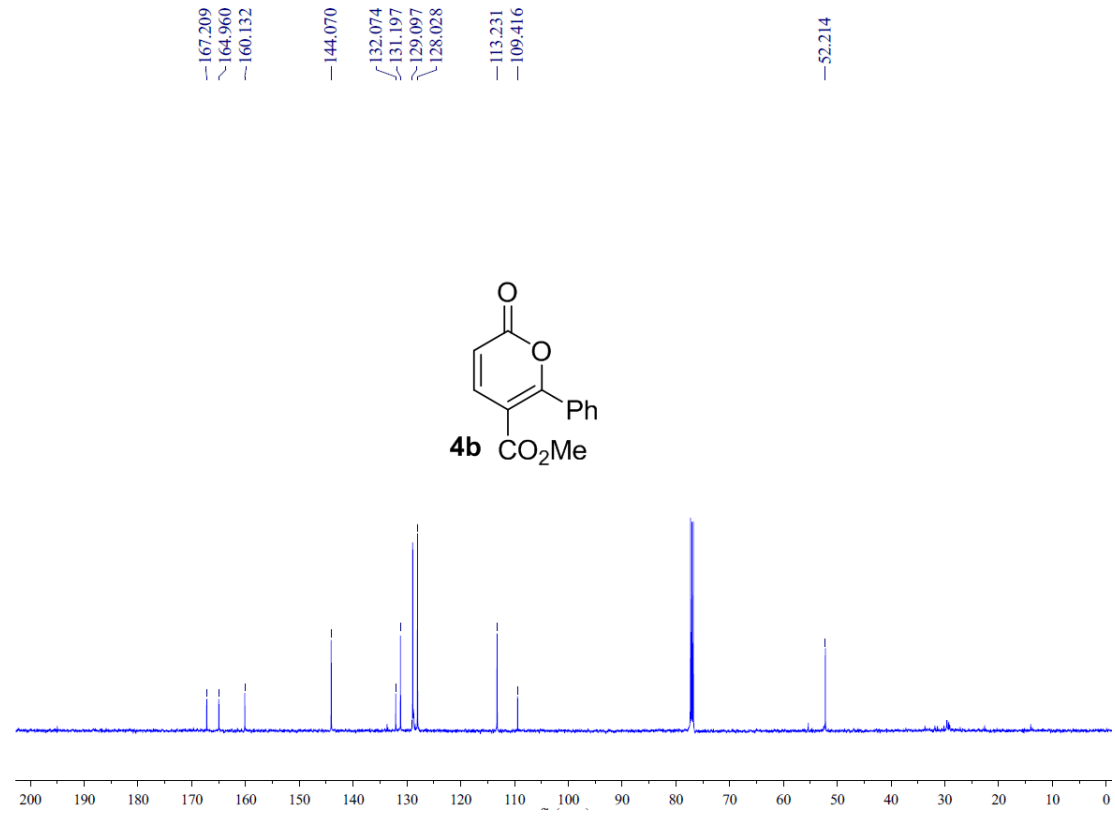
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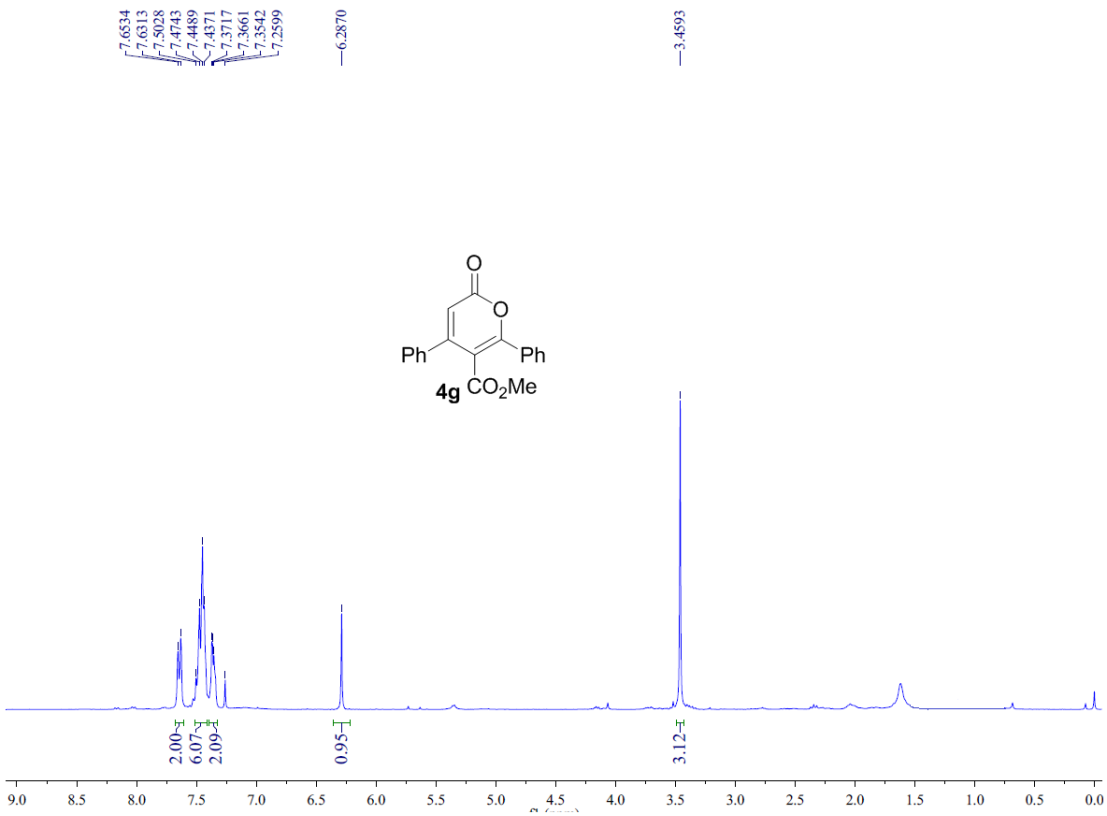
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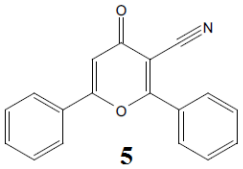
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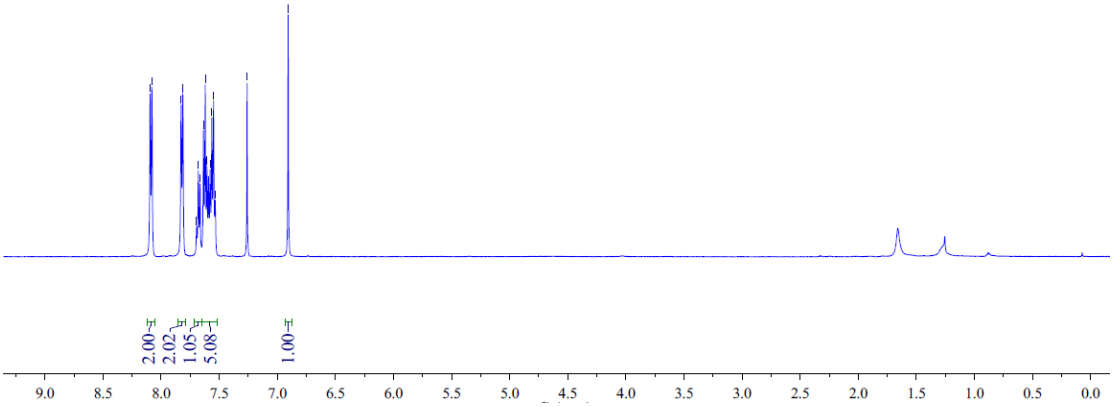
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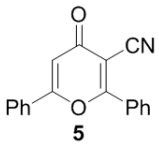
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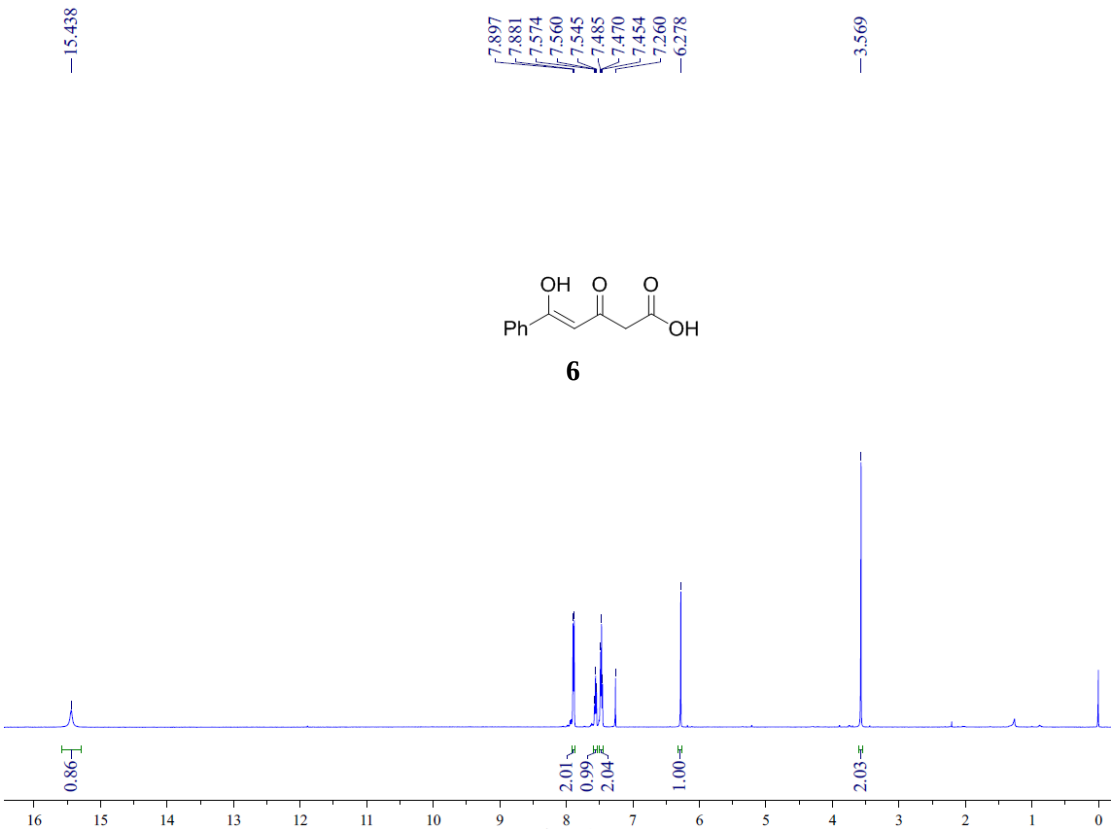
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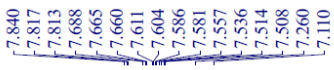
6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7.813
7.688
7.665
7.660
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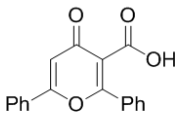
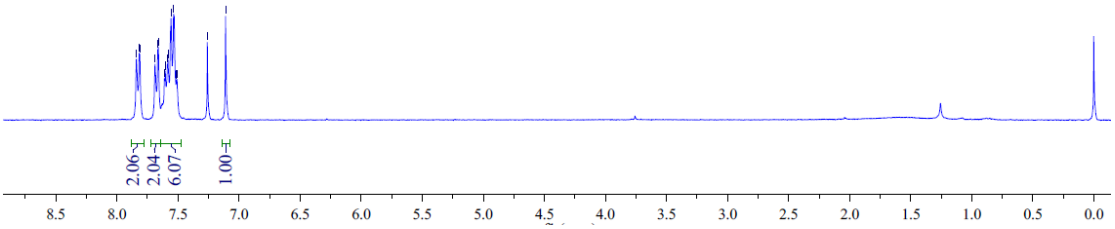
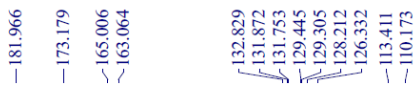
7.604
7.586
7.581
7.557
7.536
7.514
7.508
7.260
7.110


O
O
OH
Ph
O
Ph

9


2.06
2.04
6.07
1.00
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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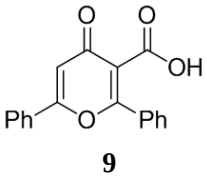
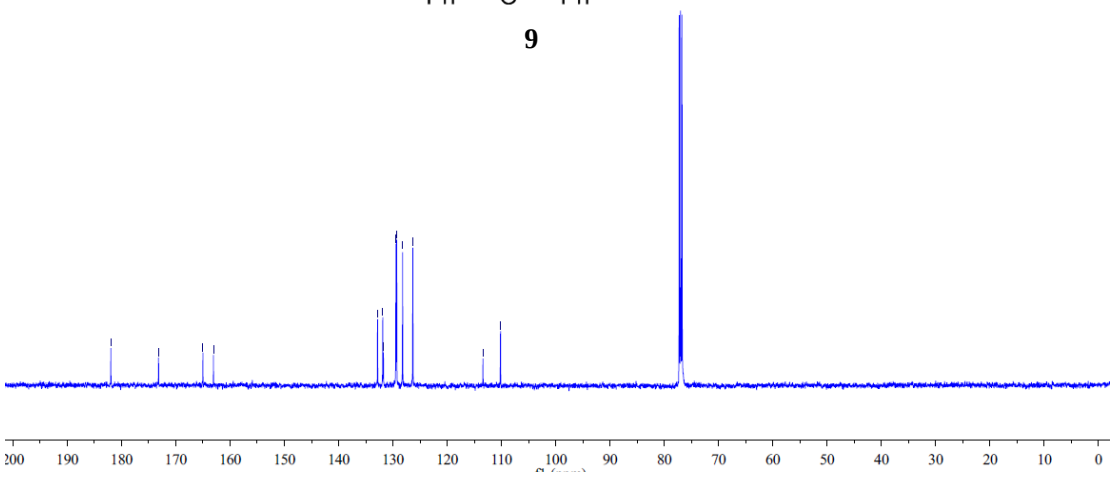
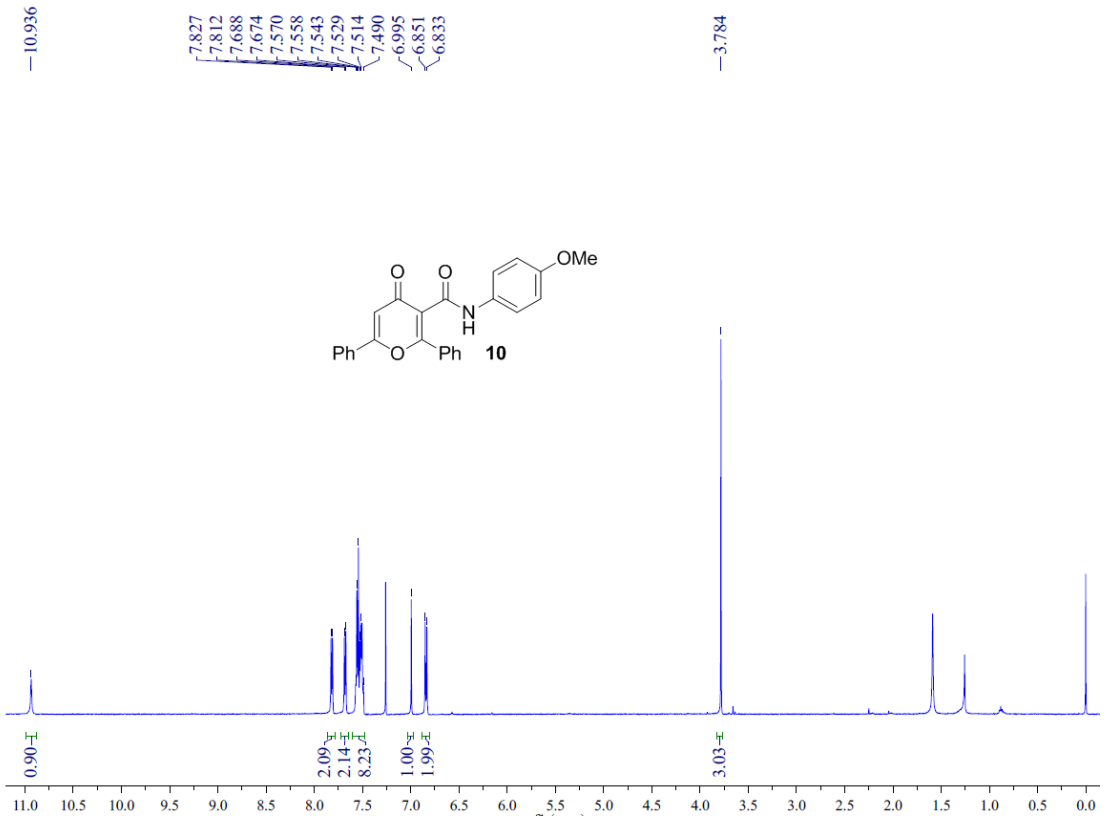
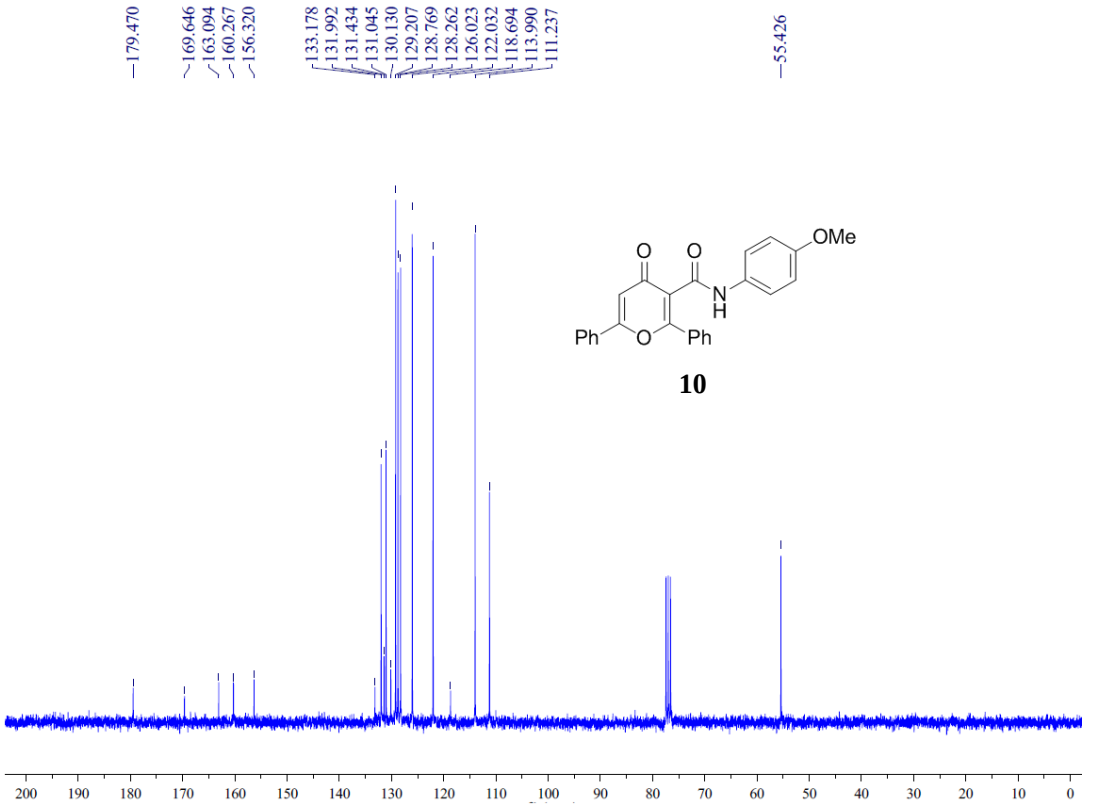
173.179
165.006
163.064
132.829
131.872
131.753
129.445
129.305
128.212
126.332
113.411
110.173


O
O
OH
Ph
O
Ph

9


200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


10.936
7.827
7.812
7.688
7.674
7.570
7.558
7.543
7.529
7.514
7.490
6.995
6.851
6.833
3.784
OMe
O
O
N
H
Ph
O
Ph
10
0.90
2.09
2.14
8.23
1.00
1.99
3.03
11.0 10.5 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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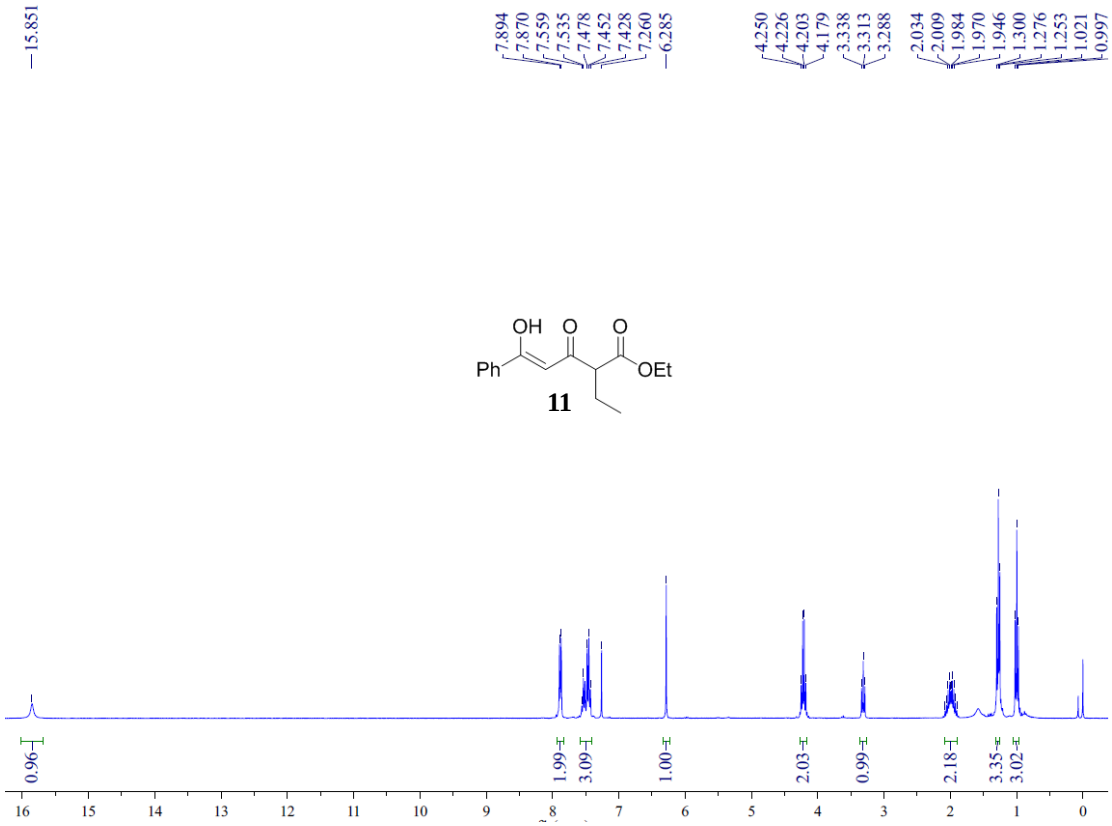
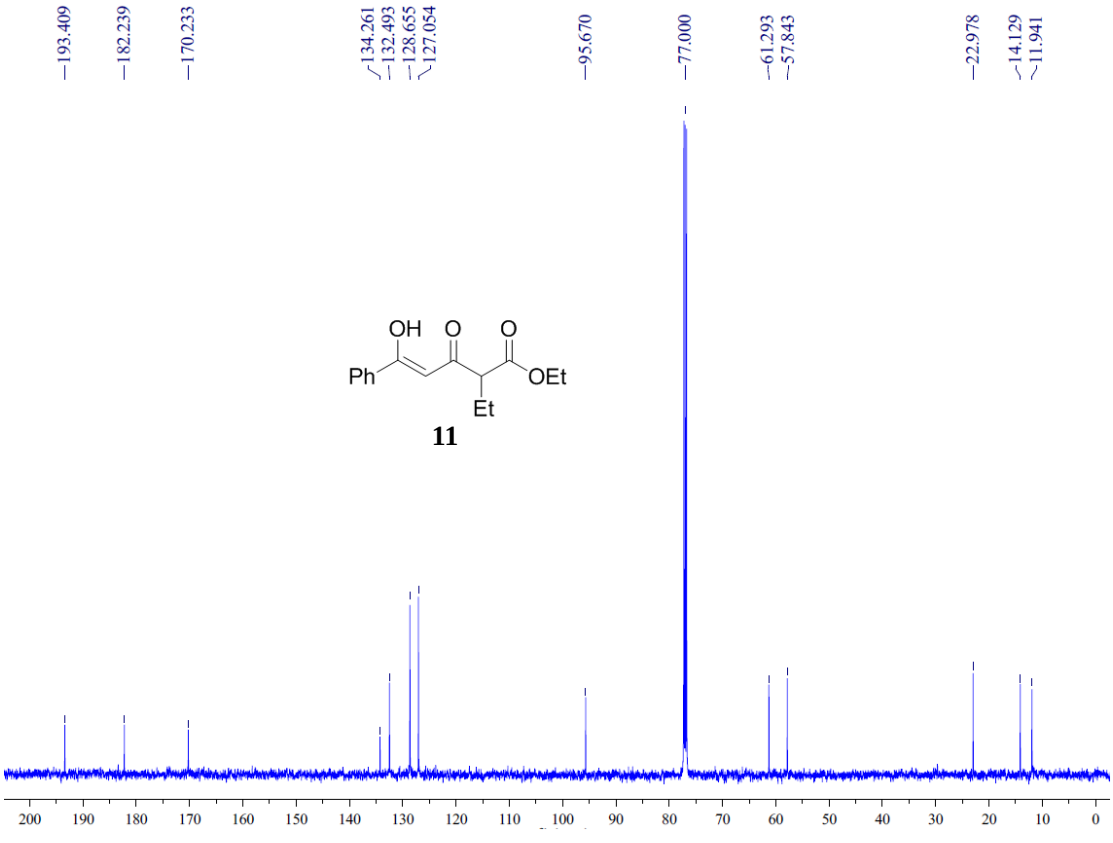
163.094
160.267
156.320
133.178
131.992
131.434
131.045
130.130
129.207
128.769
128.262
126.023
122.032
118.694
113.990
111.237
55.426
OMe
O
O
N
H
Ph
O
Ph
10
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


15.851
7.894
7.870
7.559
7.535
7.478
7.452
7.428
7.260
6.285
4.250
4.226
4.203
4.179
3.338
3.313
3.288
2.034
2.009
1.984
1.970
1.946
1.300
1.276
1.253
1.021
0.997
OH
O
O
Ph
OEt
11
0.96
1.99
3.09
1.00
2.03
0.99
2.18
3.35
3.02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182.239
170.233
134.261
132.493
128.655
127.054
95.670
77.000
61.293
57.843
22.978
14.129
11.941
OH
O
O
Ph
OEt
Et
11