Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Direct conjugate alkylation of α,β-unsaturated carbonyls by Ti^{III}-catalysed reductive umpolung of simple activated alkenes

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SUPPORTING INFORMATION

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Materials and methods

All reactions have been carried out in flame-dried Schlenk–tubes under argon atmosphere (argon 5.0) using dry solvents unless noticed otherwise. Absolute THF was dried over potassium under argon atmosphere and freshly distilled prior to use. Ethyl acetate and cyclohexane for column chromatography was purchased in technical quality and purified by destillation with a rotary evaporator. Hexanes was purchased from VWR. Dichloromethane and diethyl ether were purchased in p.a. quality from Aldrich. Zinc powder was purchased from Merck and used without further activation. Manganese powder (325 mesh) was purchased from Alfa Aesar and used as received. Chlorotrimethylsilane was purchased from Acros and used as received. Titanocene dichloride was purchased from Alfa Aesar and used as received. Triethylamine hydrochloride was purchased from Aldrich and purified by crystallisation from chloroform. All other chemicals were purchased from Aldrich and used without further purification. An IKAmag temperature modulator in combination with an oil bath or stainless steel heating block was used to control the reaction temperatures. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualised by UV fluorescence quenching, $KMnO_4$-staining, or *p*-anisaldehyde-staining. In general, Macherey-Nagel Silica gel 60 (particle size 0.04–0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 (500 MHz and 125 MHz), a Bruker Avance II 400 (400 MHz and 100 MHz), or a Varian Mercury 300 HFCP (300 MHz, ^{1}H only) spectrometer and reported to $CDCl_3$ (δ = 7.26 ppm and δ = 77.16 ppm, respectively) or benzene-d_6 (δ = 7.16 ppm and δ = 128.00 ppm, respectively). The following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, br = broad signal, ps = pseudo. IR spectra were recorded on a Perkin Elmer Spectrum 65 FT-IR-spectrometer and are reported in frequency of absorption. Low and high resolution mass analyses were performed by the service department at the Institute for Organic Chemistry and Biochemistry, Freiburg University using a Thermo Finnigan TSQ 700 for electron impact ionisation (EI) at 70 eV, 200 ºC. High resolution mass analyses (HRMS) were carried out on a Thermo Exactive with Orbitrap-Analyzer using atmospheric pressure chemical ionisation (APCI or ESI).

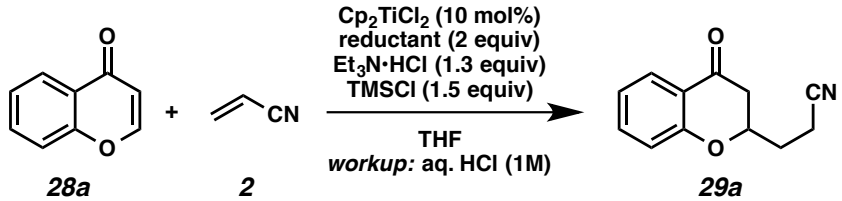
Compounds **3**, **4**, **7–14**, **16**, **20** and **21**, were reported in a preceding communication to this full paper.[1]

Compounds **22a–d**,**g–i**, **23a–d**,**g–i**, **24a–d**, **25a–d**, **28a**,**f**, **29a**,**f**,**30a–c**, **31a–c**, **32a–c**,**33a**,**c**,**34a**,**c**, **35–39**, **41**, **46**,**48–51**, were reported in a preceding communication to this full paper.[2]

Full characterisation data was included for compounds that were previously described in the literature, but for which no complete characterisation could be found.

Additional screening tables

Table S1. Reaction screening of the reductive coupling between **28a** and acrylonitrile.

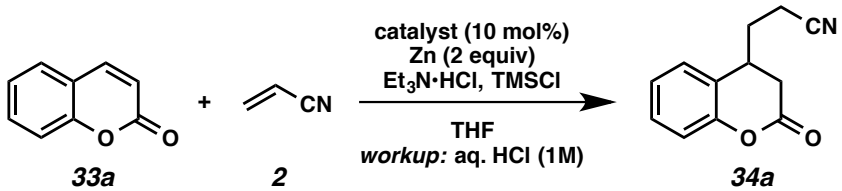


28a *2* *29a*

Entry	Reductant	equiv 2	*c* / M	*t* / h	*T* / ºC	Yield[a] / %
1	Zn	1	0.4	24	35	20
2	Zn	2	0.4	24	35	21
3	Zn	3	0.4	24	35	16
4	Zn	4	0.4	24	35	27
5	Zn	5	0.4	24	35	36[b]
6	Zn	5	0.4	4	35	30
7	Zn	5	0.2	4	35	31
8	Zn	5	0.1	4	35	27
9	Zn	5	1.0	4	35	38
10	Zn	10	0.4	4	35	33
11	Zn	5	0.4	24	35	27[c]
12	Zn	5	0.4	24	23	20
13	Zn	5	0.4	24	50	27
14	Zn	5	0.4	24	35	50[b,d]
15	Zn	5	0.4	2	35	44[b,d]
16	Zn	5	0.4	3	35	45[b,d]
17	Mn	5	0.4	24	35	50[b,d]

[a] Yield of isolated material. [b] 0.5 mmol reaction. [c] 5 mol% Cp_2TiCl_2. [d] Slow addition of **28a** via syringe-pump.

Table S2. Reaction screening of the reductive coupling between **33a** and acrylonitrile.



33a *2* *34a*

Entry	Catalyst (mol%)	equiv 2	equiv Et_3N•HCl	equiv TMSCl	*t* / h	*T* / ºC	*c* / M	Ratio[a] 34a:33a	Yield[b] / %
1	Cp_2TiCl_2 (10)	5	1.3	1.5	24	35	0.4	1:1	42
2	Cp_2TiCl_2 (10)	10	1.3	1.5	24	35	0.4	0.6:1	-[c]
3	Cp_2TiCl_2 (10)	5	1.3	0	24	35	0.4	-	-[d]
4	Cp_2TiCl_2 (10)	5	2.6	1.5	24	35	0.4	0.7:1	-[c]
5	Cp_2TiCl_2 (10)	5	2.6	3.0	24	35	0.4	-	-[d]
6	Cp_2TiCl_2 (10)	5	2.6	3.0	24	35	0.2	1:1	-[c]
7	Cp_2TiCl_2 (10)	10	2.6	3.0	24	35	0.2	-	-[d]
8	Cp_2TiCl_2 (10)	5	1.3	1.5	24	23	0.4	2.2:1	15
9	Cp_2TiCl_2 (10)	5	1.3	1.5	72	35	0.4	1:1	28
10	Cp_2TiCl_2 (20)	5	1.3	1.5	24	35	0.4	1:1	-[c]
11	$Cp_2Ti(OPh)_2$ (10)	5	1.3	1.5	24	35	0.4	1:1	-[c]
12	*rac*-(ebthi)$TiCl_2$ (10)	5	1.3	1.5	24	35	0.4	1:0	40[e]

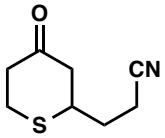
[a] Product:substrate ratio determined by ^{1}H-NMR. [b] Yield of isolated material. [c] Product was not isolated. [d] Product was not formed. [e] Full conversion of substrate **33a**.

Standard procedure for the Ti^{III}-catalysed reductive umpolung.

A flame-dried 50 ml-Schlenk tube containing a magnetic stirbar was charged under argon atmosphere with Cp_2TiCl_2 (12.4 mg, 0.05 mmol, 10 mol%), Zn (65.0 mg, 1.00 mmol, 2.0 equiv) und $Et_3N{\cdot}HCl$ (89.5 mg, 0.650 mmmol, 1.3 equiv). Stirring was started. The vessel was evacuated and backfilled with argon after a few minutes. Absolute THF (1.25 ml) was added and after 1 min the mixture had turned from red to lime-green. The substrate (e.g. **1**, 0.5 mmol, 1.0 equiv) was added followed by the cross-coupling partner (e.g. **2**, 2.5 mmol, 5 equiv) and TMSCl (95.2 µl, 1.5 equiv). The reaction vessel was sealed with a greased glass-stopper and the reaction stirred for the given time at 35 ºC in an oil bath or at the given temperature after which the reaction was brought back to room temperature. Unless noted otherwise, workup was carried out by addition of 1N aqueous HCl (4 ml) and CH_2Cl_2 and stirring was continued for 30 minutes at room temperature (23 ºC). The mixture was transferred into a separation funnel containing H_2O (20 ml) and CH_2Cl_2 (20 ml). The biphasic mixture was shaken, the organic layer separated and the aqueous layer extracted with additional CH_2Cl_2 (3 × 10 ml). The combined organic extracts were dried (Na_2SO_4), concentrated and purified by flash chromatography as described.

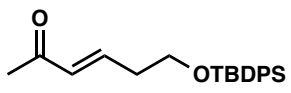
Workup with TBAF under kinetically controlled conditions (see Tables 5 and 6).
The reaction was setup as described in the standard procedure. After the given reaction time, all volatile components were removed under reduced pressure and heating was discontinued. The residue was treated with CH_2Cl_2 (5 ml) and cooled to –78 ºC. At that temperature, TBAF (1M in THF, 2.50 ml, 2.5 equiv) was added dropwise. The mixture was stirred for another 3 h at –78 ºC and then allowed to warm to room temperature (23 ºC). The mixture was transferred into a separation funnel containing H_2O (20 ml) and CH_2Cl_2 (20 ml). The biphasic mixture was shaken, the organic layer separated and the aqueous layer extracted with additional CH_2Cl_2 (3 × 10 ml). The combined organic extracts were dried (Na_2SO_4), concentrated and purified by flash chromatography as described.

Synthesis and characterisation data of new compounds



15

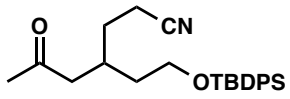
3-(4-Oxotetrahydrothiopyran-2-yl)propanenitrile (15). Prepared from 2,3-dihydrothiopyran-4-one [3] following the standard procedure with the following modification for syringe pump addition: The reaction was setup using only 0.45 ml of THF for the generation of titanium(III). Then, acrylonitrile (**2**) and TMSCl *were added first* to the reaction mixture followed by a slow addition of a solution of 2,3-dihydrothiopyran-4-one in 0.8 ml abs. THF (total THF volume = 1.25 ml) with a syringe pump to the reaction mixture at 35 ºC. Then, the vessel was sealed and stirred at 35 ºC for 24 h followed by the standard workup procedure. The product was obtained after column chromatography (cyclohexane/EtOAc, 1:1, R_f = 0.33) as a yellow oil in 46% yield (39.3 mg, 0.23 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.82-1.91 (m, 1H), 1.93-2.03 (m, 1H), 2.47 (ddd, *J* = 0.9, 9.4, 13.8 Hz, 1H), 2.51-2.56 (m, 2H), 2.57-2.65 (m, 1H), 2.68-2.75 (m, 1H), 2.81 (ddd, *J* = 1.1, 3.7, 10.1 Hz, 1H), 2.86-2.94 (m, 1H), 2.99 (ddd, *J* = 5.2, 6.2, 13.9 Hz, 1H), 3.18-3.25 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.19, 27.49, 30.66, 42.95, 43.19, 49.88, 118.68, 207.08. MS (EI, 70 eV): m/z (%) = 169.1 $[M]^+$ (100), 115.0 (60), 88.1 (47), 81.2 (56), 60.3 (27). HRMS (CI, MeOH) calcd for $C_8H_{12}ONS^+$ [M+H]+: 170.06396, found: 170.06410. IR (NaCl): ν [cm^{-1}] = 2927, 2414, 2245, 1709, 1416, 1318, 1273, 1243, 1158, 750.



S1

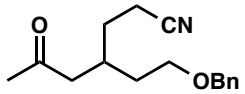
(*E*)-6-((*tert*-butyldiphenylsilyl)oxy)hex-3-en-2-one (S1). [4] *O*-TBDPS-3-oxypropanal [5] (2.17 g, 6.95 mmol) was added to a mixture of triphenylphosphoranylideneacetone[6] (2.3 g, 7.2 mmol) in benzene (70 ml). The mixture was stirred and heated to reflux at 80 ºC for 88 h. The reaction was allowed to cool to room temperature and the solvent was removed under reduced pressure. The product was

isolated after column chromatography (hexanes/EtOAc, 2:1, R_f = 0.9) in 94% yield (2.30 g, 6.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (s, 9H), 2.23 (s, 3H), 2.45 (ddt, *J* = 1.5, 3.5, 5.9 Hz, 2H), 3.80 (t, *J* = 6.32 Hz, 2H), 6.10 (dt, *J* = 1.5 , 15.9 Hz, 1H), 6.82 (tt, *J* = 7.0, 16.0 Hz, 1H), 7.35–7.47 (m, 6H), 7.63–7.68 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.3, 26.7, 26.9, 35.8, 62.4, 127.8, 129.8, 133.0, 133.6, 135.6, 145.2, 198.6. MS (EI, 70 eV): m/z (%) = 295.2 $[M\text{-}C_4H_9]^+$ (99), 265.2 (40), 251.1 (14), 217.1 (17), 199.1 (100), 187.1 (21). HRMS (CI, NH_3): calcd for $C_{22}H_{32}O_2NSi^+$ $[M+NH_4]^+$: 370.22023, found: 370.22070. IR (NaCl): ν [cm^{-1}] = 3071, 3049, 3015, 2999, 2958, 2931, 2893, 2858, 1962, 1891, 1827, 1776, 1699, 1677, 1926, 1589, 1473, 1428, 1390, 1361, 1254, 1112, 979, 938, 823, 799, 739.



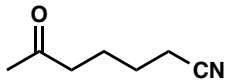
17

4-(2-((*tert*-Butyldiphenylsilyl)oxy)ethyl)-6-oxoheptanenitrile (17). Prepared according to the standard procedure from **S1**. The reaction was run at 0 ºC for 50 h followed by standard workup with 1N HCl and extraction with dichloromethane. Purified by column chromatography (Hexanes/EtOAc, 5:1, R_f = 0.4) and isolated as a colourless oil in 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (s, 9H), 1.46–1.62 (m, 2H), 1.65 (dt, *J* = 6.5, 7.4 Hz, 2H), 2.09 (s, 3H), 2.20 (hept, *J* = 6.3 Hz, 1H), 2.26 (dt, *J* = 1.7, 7.7 Hz, 2H), 2.35 (dd, *J* = 7.2, 17.0 Hz, 1H), 2.46 (dd, *J* = 5.6, 17.1 Hz, 1H), 3.67 (dt, *J* = 1.9, 6.2 Hz, 2H), 7.36–7.46 (m, 6H), 7.63–7.67 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.97, 19.27, 27.02, 29.91, 30.44, 30.46, 35.77, 47.60, 61.54, 119.78, 127.89, 129.91, 133.64, 135.70, 207.62. MS (EI, 70 eV): m/z (%) = 350.2 $[M\text{-}C_4H_9]^+$ (73), 272.2 (38), 199.1 (100). HRMS (CI, NH_3): calcd for $C_{25}H_{37}N_2O_2Si^+$ $[M+NH_4]^+$: 425. 26243, found: 425.26270. IR (NaCl): ν [cm^{-1}] = 3071, 2957, 2931, 2893, 2858, 2246, 1715, 1472, 1428, 1360, 1390, 1261, 1160, 1111, 998, 938, 823, 738, 703, 614, 505.



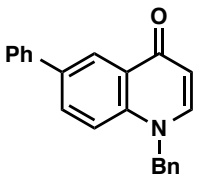
18

4-(2-(Benzyloxy)ethyl)-6-oxoheptanenitrile (18). Prepared according to the standard procedure from (*E*)-6-(benzyloxy)hex-3-en-2-one.[7] The reaction was run at 0 ºC for 50 h followed by standard workup with 1N HCl and extraction with dichloromethane. Purified by column chromatography (Hexanes/EtOAc, 3:1, R_f = 0.67. Isolated as a colourless oil in 48% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55–1.73 (m, 4H), 2.10 (s, 3H), 2.21 (hept, *J* = 6.5 Hz, 1H), 2.34 (dd, *J* = 7.2, 8.0 Hz, 2H), 2.39 (dd, *J* = 6.7, 17.4 Hz, 1H), 2.52 (dd, *J* = 6.1, 17.2 Hz, 1H), 3.48 (t, *J* = 6.1 Hz, 2H), 4.46 (s, 2H), 7.28–7.37 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 15.01, 30.11, 30.49, 31.03, 33.28, 47.66, 67.95, 73.22, 119.84, 127.84, 127.84, 128.56, 138.32, 207.64. MS (EI, 70 eV): m/z (%) = 259.3 $[M]^+$ (1), 216.1 (14), 168.1 (7), 152.1 (80), 124.1 (20), 110.1 (22), 107.0 (35), 91.1 (100), 82.2 (7), 65.1 (6), 59.2 (5), 43.5 (32). HRMS (CI, NH_3): calcd for $C_{16}H_{29}N_3O_2^+$ $[M+NH_4]^+$: 277.1960, found: 277.19170. IR (NaCl): ν [cm^{-1}] = 3030, 2924, 2855, 2244, 1712, 1453, 1422, 1359, 1161, 1096, 737, 699.



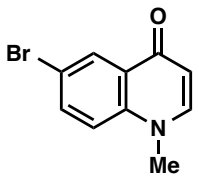
19

6-Oxoheptanenitrile (19).[8] Prepared from methyl vinyl ketone and acrylonitrile according to the standard procedure with a reaction time of 14 h. Isolated after column chromatography (CH_2Cl_2/EtOAc, 15:1, R_f = 0.7) in 17% yield. The analytical data matched the previously reported values. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62–1.77 (m, 4H), 2.15 (s, 3H), 2.35 (t, *J* = 6.92 Hz, 2H), 2.50 (t, *J* = 6.74, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.29, 22.79, 25.00, 30.08, 42.57, 119.55, 207.77.



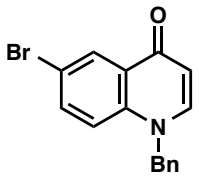
22f

***N*-Benzyl-6-phenyl-4-quinolone (22f)**. To a solution of 6-phenyl-4-quinolone[9] (2.71 mmol, 1 equiv) and KOH (1.5 equiv) in dry MeOH (c = 1.0M) was added BnBr (10 equiv) and the reaction mixture was stirred at room temperature (23 ºC) for 23 h. The mixture was transferred to a separation funnel followed by addition of CH_2Cl_2 (50 ml) and H_2O (50 ml). The mixture was shaken the organic layer separated and the aqueous layer extracted with additional CH_2Cl_2 (3 × 50 ml). The combined organic layers were washed with brine (50 ml), dried (Na_2SO_4), and concentrated. Purification via column chromatography (CH_2Cl_2/EtOAc, 1:6, R_f = 0.15) afforded **22f** as a white foam in 72% yield (605 mg, 1.94 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 5.24 (s, 2H), 6.36 (d, J = 7.7 Hz, 1H), 7.16-7.19 (m, 2H), 7.29-7.39 (m, 5H), 7.41-7.46 (m, 2H), 7.63 (d, J = 7.7 Hz, 1H), 7.65 (m, 2H), 7.79 (dd, J = 2.4, 8.9 Hz, 1H), 8.72 (dd, J = 0.4, 2.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 55.63, 110.64, 116.76, 124.96, 126.19, 127.18, 127.65, 127.75, 128.45, 128.96, 129.38, 131.09, 135.24, 136.66, 139.51, 139.61, 143.49, 178.42. MS (EI, 70 eV): m/z (%) = 311.1 $[M]^+$ (83), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{22}H_{18}NO^+$ $[M+H]^+$: 312.13884, found: 312.13884. IR (ATR): ν [cm^{-1}] = 3055, 2935, 1606, 1501, 1474, 1305, 1223, 1116, 1055, 942.



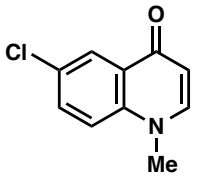
22j

N-Methyl-6-bromo-4-quinolone (22j).[10] Synthesised from 6-Bromo-4-quinolone[10] (1.94 mmol) and methyl iodide in analogy to **22f** with a reaction time of 21 h. Product **22j** was received after workup in analytically pure form as a yellow solid in 83% yield (384 mg, 1.61 mmol). The analytical data matched the literature values. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.75 (s, 3H), 6.19 (d, J = 7.7 Hz, 1H), 7.23 (d, J = 9.0 Hz, 1H), 7.46 (d, J = 7.7 Hz, 1H), 7.68 (dd, J = 2.4, 9.0 Hz, 1H), 8.49 (d, J = 2.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 40.70, 110.43, 117.35, 117.61, 128.30, 129.43, 135.12, 139.42, 143.89, 176.87. MS (EI, 70 eV): m/z (%) = 239.0 [M, ^{81}Br]$^+$ (99), 237.0 [M, ^{79}Br]$^+$ (100), 211.0 [M, ^{81}Br]$^+$ (485), 209.0 [M, ^{79}Br]$^+$ (50), 130.1 HRMS (APCI, MeOH) calcd for $C_{10}H_9NO^{79}Br^+$ $[M+H]^+$: 237.98675, found: 237.98680. IR (ATR): ν [cm^{-1}] = 3063, 2934, 1619, 1571, 1541, 1452, 1367, 1256, 1181, 1119, 1085, 1006, 823.



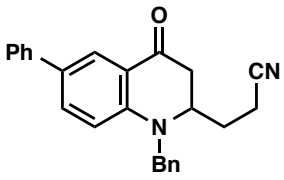
22k

N-Benzyl-6-bromo-4-quinolone (22k). Synthesised from 6-Bromo-4-quinolone[10] (3.58 mmol) and benzyl bromide in analogy to **22f** with a reaction time of 21 h. Product **22k** was isolated after column chromatography (CH_2Cl_2/EtOAc, 1:1, R_f = 0.14) as a yellow solid in 56% yield (636 mg, 2.03 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 5.29 (s, 2H), 6.30 (d, J = 7.7 Hz, 1H), 7.09-7.13 (m, 2H), 7.16 (dd, J = 0.2, 9.1 Hz, 1H), 7.28-7.37 (m, 3H), 7.56 (dd, J = 2.4, 9.1 Hz, 1H), 7.61 (d, J = 7.7 Hz, 1H), 8.55 (dd, J = 0.2, 2.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 56.69, 110.76, 117.62, 118.15, 126.08, 128.54, 128.72, 129.38, 129.63, 134.74, 135.13, 138.95, 143.85, 176.95. MS (EI, 70 eV): m/z (%) = 315.0 [M, ^{81}Br]$^+$ (57), 313.0 [M, ^{79}Br]$^+$ (56), 195.9 [M, ^{81}Br]$^+$ (7), 193.9 [M, ^{79}Br]$^+$ (7), 115.0 (16), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{16}H_{13}NO^{79}Br^+$ $[M+H]^+$: 314.01805, found: 314.01810. IR (ATR): ν [cm^{-1}] = 3055, 2983, 1695, 1606, 1581, 1474, 1264, 1177, 1100, 1044, 1026, 895.



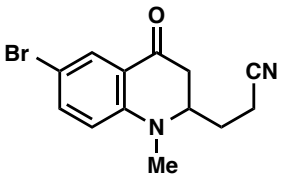
22l

N-Methyl-6-chloro-4-quinolone (22l).[10] Synthesised from 6-chloro-4-quinolone[10] (1.94 mmol) and methyl iodide in analogy to **22f** with a reaction time of 21 h. Product **22j** was received after workup in analytically pure form as a yellow solid in 83% yield (384 mg, 1.61 mmol). The analytical data matched the literature values. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.78 (s, 3H), 6.23 (d, *J* = 7.8 Hz, 1H), 7.33 (d, *J* = 9.1 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.59 (dd, *J* = 2.7, 9.1 Hz, 1H), 8.39 (dd, *J* = 0.5, 2.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 40.79, 110.42, 117.14, 126.39, 128.11, 130.11, 132.52, 139.15, 143.85, 177.10. MS (EI, 70 eV): m/z (%) = 195.0 [M, $^{37}Cl]^+$ (32), 193.0 [M, $^{35}Cl]^+$ (100), 165.0 (18), 150.0 (6). HRMS (APCI, MeOH) calcd for $C_{10}H_8{}^{35}ClNONa^+$ $[M+Na]^+$: 216.01921, found: 216.01930. IR (ATR): ν [cm^{-1}] = 3043, 2995, 1616, 1552, 1488, 1451, 1338, 1598, 1232, 1158, 1124, 1101, 1008, 907, 857, 837, 817, 778, 716.



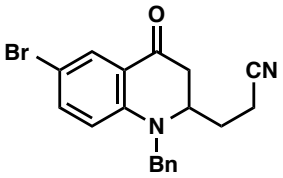
23f

3-(1-Benzyl-4-oxo-6-phenyl-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (23f). Prepared according to the standard procedure from **22f** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.53) afforded **23f** as a yellow oil in 21% yield (38.3 mg, 0.105 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.93-2.04 (m, 1H), 2.04-2.13 (m, 1H), 2.34 (ddd, *J* = 6.8, 7.9, 17.2 Hz, 1H), 2.44 (ddd, *J* = 6.8, 6.8, 17.2 Hz, 1H), 2.64 (dd, *J* = 2.3, 16.4 Hz, 1H), 3.14 (ddd, *J* = 0.6, 5.9, 16.4 Hz, 1H), 3.85-3.91 (m, 1H), 4.79 (d, *J* = 16.3 Hz, 1H), 4.88 (d, *J* = 16.3 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 7.27-7.42 (m, 8H), 7.53-7.54 (m, 1H), 7.55-7.56 (m, 1H), 7.62 (dd, *J* = 2.4, 8.8 Hz, 1H), 8.16 (d, *J* = 2.2 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.30, 25.76, 41.09, 54.79, 57.59, 114.73, 118.59, 119.67, 125.88, 126.32, 126.84, 126.90, 127.96, 128.87, 129.16, 130.25, 134.72, 137.09, 139.79, 148.15, 192.13. MS (EI, 70 eV): m/z (%) = 366.2 $[M]^+$ (55), 312.1 (34), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{25}H_{23}N_2O^+$ $[M+H]^+$: 367.18104, found: 367.18040. IR (ATR): ν [cm^{-1}] = 3059, 3030, 2929, 2245, 1671, 1613, 1549, 1514, 1485, 1452, 1418, 1341, 1224, 1189, 1134, 1056, 1027, 905.



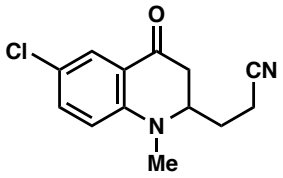
23j

3-(6-Bromo-1-methyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (23j). Prepared according to the standard procedure from **22j** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.46) afforded **23j** as a yellow oil in 31% yield (45.5 mg, 0.155 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.85 (dddd, *J* = 6.8, 6.8, 8.2, 14.1 Hz, 1H), 1.95-2.04 (m, 1H), 2.32 (ddd, *J* = 6.7, 8.0, 17.2 Hz, 1H), 2.41 (ddd, *J* = 6.8, 6.8, 17.2 Hz, 1H), 2.58 (dd, *J* = 1.9, 16.5 Hz, 1H), 3.06 (ddd, *J* = 0.8, 6.1, 16.5 Hz, 1H), 3.11 (s, 3H), 3.77 (dddd, *J* = 2.2, 6.2, 6.2, 8.4 Hz, 1H), 6.54 (d, *J* = 8.9 Hz, 1H), 7.47 (dd, *J* = 2.6, 8.9 Hz, 1H), 7.93 (dd, *J* = 0.2, 2.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.29, 24.82, 38.72, 40.82, 59.54, 109.58, 115.27, 118.41, 120.25, 130.06, 138.65, 148.28, 191.01. MS (EI, 70 eV): m/z (%) = 294.0 [M, $^{81}Br]^+$ (31), 292.0 [M, $^{79}Br]^+$ (31), 240.0 [M, $^{81}Br]^+$ (99), 238.0 [M, $^{79}Br]^+$ (100), 159.0 (33), 131.0 (28). HRMS (APCI, MeOH) calcd for $C_{13}H_{13}N_2ONa^{79}Br^+$ $[M+Na]^+$: 315.01089, found: 315.01090. IR (ATR): ν [cm^{-1}] = 3055, 2934, 2249, 1673, 1599, 1551, 1420, 1385, 1188, 1100, 983.



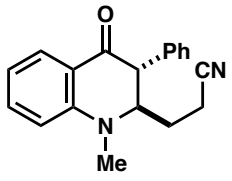
23k

3-(1-Benzyl-6-bromo-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (23k). Prepared according to the standard procedure from **22k** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.61) afforded **23k** as a yellow oil in 32% yield (58.8 mg, 0.159 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.19 (dddd, *J* = 6.8, 6.8, 8.1, 14.1 Hz, 1H), 1.99-2.08 (m, 1H), 2.31 (ddd, *J* = 6.6, 7.9, 17.2 Hz, 1H), 2.40 (ddd, *J* = 6.8, 6.8, 17.2 Hz, 1H), 2.59 (dd, *J* = 2.3, 16.5 Hz, 1H), 3.07 (ddd, *J* = 0.6, 5.9, 16.5 Hz, 1H), 3.84 (dddd, *J* = 2.3, 6.2, 6.2, 8.3 Hz, 1H), 4.49 (d, *J* = 16.3 Hz, 1H), 4.97 (d, *J* = 16.3 Hz, 1H), 6.57 (d, *J* = 9.1 Hz, 1H), 7.28-7.33 (m, 3H), 7.34-7.39 (m, 3H), 7.97 (d, *J* = 2.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.23, 25.59, 40.76, 54.86, 57.59, 109.92, 116.21, 118.44, 120.70, 126.71, 128.04, 129.18, 130.18, 136.59, 138.56, 147.63, 190.90. MS (EI, 70 eV): m/z (%) = 370.1 [M, ^{81}Br]$^+$ (46), 368.1 [M, ^{79}Br]$^+$ (50), 316.0 [M, ^{81}Br]$^+$ (41), 314.0 [M, ^{79}Br]$^+$ (41), 236.1 (9), 179.1 (5), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{19}H_{17}N_2ONa^{79}Br^+$ [M+Na]$^+$: 391.04219, found: 391.04210. IR (ATR): ν [cm^{-1}] = 3055, 2930, 2248, 1675, 1597, 1487, 1421, 1298, 1264, 1099, 908.



23l

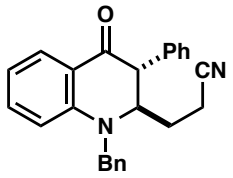
3-(6-Chloro-1-methyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (23l). Prepared according to the standard procedure from **22l** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.45) afforded **23l** as a yellow oil in 29% yield (36.0 mg, 0.144 mmol). A reaction with Mn as reductant resulted in 28% yield. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.80-1.90 (m, 1H), 1.95-2.05 (m, 1H), 2.32 (ddd, *J* = 6.7, 8.0, 17.2 Hz, 1H), 2.40 (ddd, *J* = 6.9, 6.9, 17.2 Hz, 1H), 2.59 (dd, *J* = 2.2, 16.5 Hz, 1H), 3.07 (ddd, *J* = 0.9, 6.6, 16.5 Hz, 1H), 3.12 (s, 3H), 3.75 (dddd, *J* = 2.2, 6.1, 6.1, 8.3 Hz, 1H), 6.60 (d, *J* = 8.9 Hz, 1H), 7.35 (dd, *J* = 2.6, 9.0 Hz, 1H), 7.79 (d, *J* = 2.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.30, 24.83, 38.77, 40.91, 59.58, 114.93, 118.46, 119.75, 122.65, 126.99, 135.94, 147.97, 191.16. MS (EI, 70 eV): m/z (%) = 250.1 [M, ^{37}Cl]$^+$ (7), 248.1 [M, ^{35}Cl]$^+$ (21), 196.0 [M, ^{37}Cl]$^+$ (34), 194.0 [M, ^{35}Cl]$^+$ (100), 131 (5). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}{}^{35}ClN_2O^+$ [M+H]$^+$: 249.07947, found: 249.07960. IR (ATR): ν [cm^{-1}] = 2959, 2244, 1664, 1602, 1551, 1496, 1446, 1407, 1343, 1315, 1247, 1202, 1185, 1101, 1048, 1009, 988, 932, 908, 892, 846.



26c

***anti*-3-(1-Methyl-4-oxo-3-phenyl-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (26c)**. Prepared according to the standard procedure from **24c**[2] and acrylonitrile (**2**) with a reaction time of 24 h. Workup was carried out using TBAF at –78 ºC as described in the standard procedure for quenching under kinetic control. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.54) afforded **26c** as a yellow oil in 26% yield (38.1 mg, 0.131 mmol). A second fraction contained **25c**,[2] which was isolated in 63% yield (91.5 mg, 0.315 mmol). Combined yield: 89%. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.01 (ddt, *J* = 7.2, 7.2, 14.2 Hz, 1H), 2.18 (ddt, *J* = 7.2, 7.2, 14.2 Hz, 1H), 2.46 (td, *J* = 2.5, 7.2 Hz, 2H), 3.12 (s, 3H), 3.59 (d, *J* = 1.7 Hz, 1H), 3.86 (td, *J* = 1.7, 7.2 Hz, 1H), 6.66 (dd, *J* = 0.3, 8.5 Hz, 1H), 6.76 (ddd, *J* = 0.9, 7.1, 7.9 Hz, 1H), 7.19-7.25 (m, 4H), 7.26-7.29 (m, 1H), 7.45 (ddd, *J* = 1.8, 7.1, 8.6 Hz, 1H), 7.89 (ddd, *J* = 0.3, 1.8, 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.58, 26.47, 39.30, 54.74, 65.03, 113.25, 117.27, 118.37, 118.61, 127.44, 127.69, 128.61, 128.99, 136.58, 137.16, 148.83, 192.53. MS (EI, 70 eV): m/z (%) = 290.1 [M]$^+$ (82),

236.1 (84), 208.1 (100), 193.0 (77), 147.0 (92), 104.0 (43), 77.0 (52). HRMS (APCI, MeOH) calcd for $C_{19}H_{19}N_2O^+$ $[M+H]^+$: 291.14974, found: 291.14960. IR (ATR): ν [cm^{-1}] = 2031, 2161, 1707, 1667, 1604, 1563, 1496, 1246, 1163, 1034.



26d

***anti*-3-(1-Benzyl-4-oxo-3-phenyl-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (26d)**. Prepared according to the standard procedure from **24d**[2] and acrylonitrile (**2**) with a reaction time of 24 h. Workup was carried out using TBAF at –78 ºC as described in the standard procedure for quenching under kinetic control. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.55) afforded **26d** as a yellow oil in 22% yield (40.6 mg, 0.111 mmol). Single crystals suitible for X-ray analysis were received by crystallisation from *i*-PrOH at room temperature. A second fraction contained **25d**,[2] which was isolated in 47% yield (86.4 mg, 0.236 mmol). Combined yield: 69%. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.09-2.16 (m, 2H), 2.42 (ddt, *J* = 7.4, 7.4, 17.2 Hz, 1H), 2.50 (ddt, *J* = 6.8, 6.8, 17.2 Hz, 1H), 3.73 (d, *J* = 1.9 Hz, 1H), 3.94 (ddd, *J* = 1.9, 6.4, 8.2 Hz, 1H), 4.36 (d, *J* = 16.0 Hz, 1H), 4.58 (d, *J* = 16.0 Hz, 1H), 6.62 (d, *J* = 8.6 Hz, 1H), 6.77-6.81 (m, 3H), 7.09-7.19 (m, 4H), 7.22-7.29 (m, 4H), 7.35 (ddd, *J* = 1.8, 7.1, 8.6 Hz, 1H), 8.02 (ddd, *J* = 0.3, 1.8, 7.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.41, 25.97, 54.24, 55.17, 65.17, 114.07, 117.62, 118.48, 119.68, 127.00, 127.56, 127.63, 127.81, 128.34, 128.74, 128.97, 136.43, 136.58, 137.32, 148.841, 193.00. MS (EI, 70 eV): m/z (%) = 366.1 $[M]^+$ (65), 312.1 (62), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{25}H_{23}N_2O^+$ $[M+H]^+$: 367.18104, found: 367.18130. IR (ATR): ν [cm^{-1}] = 3060, 2930, 2246, 1666, 1602, 1491, 1316, 1266, 1171, 1113, 1041, 1002, 978.

X-ray analysis of compound 26d (CCDC 1440299)

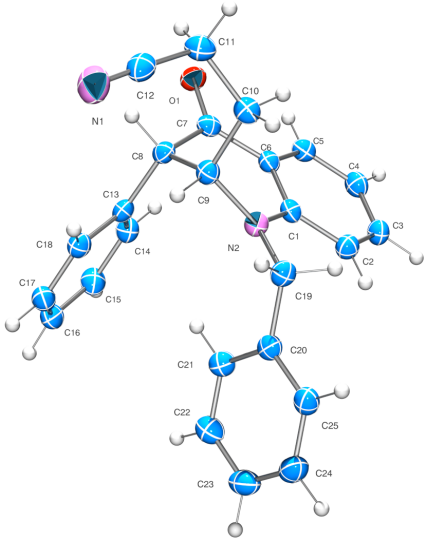
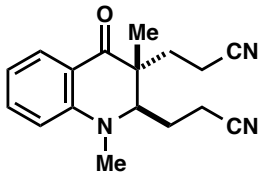


Table S3. Crystal data and structure refinement for mk569al.

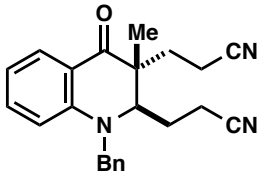
Identification code	mk569al
Empirical formula	C25 H22 N2 O
Formula weight	366.44
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21/n
Unit cell dimensions	a = 9.4307(6) A alpha = 90 deg. b = 17.1837(5) A beta = 91.937(2) deg. c = 11.8533(6) A gamma = 90 deg.
Volume	1919.78(17) A^3
Z, Calculated density	4, 1.268 Mg/m^3
Absorption coefficient	0.078 mm^-1
F(000)	776
Crystal size	0.180 x 0.100 x 0.080 mm
Theta range for data collection	2.088 to 27.490 deg.
Limiting indices	-12<=h<=12, -22<=k<=22, -15<=l<=15
Reflections collected / unique	19028 / 4396 [R(int) = 0.0993]
Completeness to theta = 25.242	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.996 and 0.809
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4396 / 0 / 342
Goodness-of-fit on F^2	0.963

Final R indices [I>2sigma(I)]	R1 = 0.0454, wR2 = 0.0929
R indices (all data)	R1 = 0.1028, wR2 = 0.1160
Extinction coefficient	0.0082(16)
Largest diff. peak and hole	0.222 and -0.334 e.A^-3



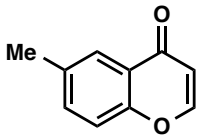
27a

***anti*-3,3'-1,3-Dimethyl-4-oxo-1,2,3,4-tetrahydroquinoline-2,3-diyl)dipropanenitrile (27a)**. Prepared from **24a** and acrylotnitrile (**2**) according to the standard procedure with a reaction time of 24 h. Workup was carried out by addition of TBAF (1M in THF, 1.5 ml, 3.0 equiv) at 0 ºC followed by stirring of the mixture at 0 ºC for additional 60 min. The mixture was transferred into a separation funnel containing H_2O (20 ml) and CH_2Cl_2 (20 ml) and from then on workup was continued as described in the standard procedure. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.68) afforded **27a** as a yellow oil in 42% yield (58.5 mg, 0.208 mmol). A second fraction contained **25a** (30% yield). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.16 (s, 3H), 1.85-1.91 (m, 1H), 1.94-2.00 (m, 2H), 2.06-2.13 (m, 1H), 2.13-2.19 (m, 1H), 2.23-2.33 (m, 2H), 2.34-2.41 (m, 1H), 3.26 (s, 3H), 3.37 (dd, *J* = 5.3, 8.5 Hz, 1H), 6.66 (dd, *J* = 0.3, 8.4 Hz, 1H), 6.76 (ddd, *J* = 0.9, 7.1, 7.9 Hz, 1H), 7.45 (ddd, *J* = 1.7, 7.1, 8.6 Hz, 1H), 7.82 (ddd, *J* = 0.2, 1.7, 7.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.49, 15.31, 16.35, 24.00, 31.98, 40.62, 47.97, 68.39, 113.28, 117.37, 117.62, 118.78, 119.42, 128.57, 136.57, 147.88. 195.82. MS (EI, 70 eV): m/z (%) = 281.1 $[M]^+$ (93), 227.1 (100), 174.0 (77), 144.1 (52), 77.0 (32). HRMS (APCI, MeOH) calcd for $C_{17}H_{20}N_3O^+$ $[M+H]^+$: 282.16064, found: 282.16090. IR (ATR): ν [cm^{-1}] = 3056, 2936, 2248, 1668, 1605, 1565, 1496, 1461, 1345, 1265, 1208, 1042, 908.



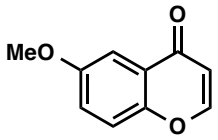
27b

***anti*-3,3'-(-1-Benzyl-3-methyl-4-oxo-1,2,3,4-tetrahydroquinoline-2,3-diyl)dipropanenitrile (27b)**.
Prepared from **24b** and acrylotnitrile (**2**) according to the standard procedure with a reaction time of 24 h. Workup was carried out by addition of TBAF (1M in THF, 1.5 ml, 3.0 equiv) at 0 ºC followed by stirring of the mixture at 0 ºC for additional 60 min. The mixture was transferred into a separation funnel containing H_2O (20 ml) and CH_2Cl_2 (20 ml) and from then on workup was continued as described in the standard procedure. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.73) afforded **27b** as a yellow oil in 39% yield (70.4 mg, 0.197 mmol). A second fraction contained **25b** (42% yield). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.22 (s, 3H), 1.61-1.71 (m, 1H), 1.92-2.08 (m, 5H), 2.28-2.30 (m, 1H), 2.30-2.32 (m, 1H), 3.37 (dd, *J* = 4.6, 7.6 Hz, 1H), 4.35 (d, *J* = 15.7 Hz, 1H), 4.97 (d, *J* = 15.7 Hz, 1H), 6.78 (ddd, *J* = 0.9, 7.1, 7.9 Hz, 1H), 6.92 (d, *J* = 8.5 Hz, 1H), 7.33-7.46 (m, 6H), 7.88 (ddd, *J* = 0.3, 1.8, 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.15, 15.44, 16.43, 24.71, 32.07, 47.68, 54.61, 65.05, 113.59, 117.64, 118.98, 119.11, 127.91, 128.51, 128.96, 129.31, 136.49, 136.68, 147.99, 195.74. MS (EI, 70 eV): m/z (%) = 357.1 $[M]^+$ (21), 205.1 (20), 250.1 (10), 158.0 (9), 121.0 (8), 91.0 (100). HRMS (APCI, MeOH) calcd for $C_{23}H_{24}N_3O^+$ $[M+H]^+$: 358.19194, found: 358.19210. IR (ATR): ν [cm^{-1}] = 2932, 2251, 1688, 1602, 1563, 1488, 1453, 1383, 1347, 1315, 1216, 1168, 1095, 1047, 1028, 905, 724.



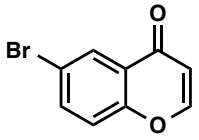
28b

6-Methylchromone (28b).[11] Prepared according to the literature. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.43 (s, 3H), 6.30 (d, *J* = 6.0 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.46 (ddd, *J* = 0.6, 2.3, 8.6 Hz, 1H), 7.81 (d, *J* = 6.0 Hz, 1H), 7.97-7.99 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 20.97, 112.86, 117.98, 124.63, 125.18, 135.03, 135.29, 154.87, 154.23, 177.78. MS (EI, 70 eV): m/z (%) = 160.1 $[M]^+$ (100), 131.1 (20), 106.1 (7), 78.2 (6). HRMS (APCI, MeOH) calcd for $C_{10}H_9O_2^+$ $[M+H]^+$: 161.06025, found: 161.06030. IR (ATR): ν [cm^{-1}] = 3096, 3064, 2992, 2912, 1648, 1570, 1481, 1440, 1322, 1203, 1135, 1034, 957, 821.



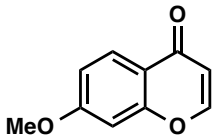
28c

6-Methoxychromone (28c).[11] Prepared according to the literature. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.89 (s, 3H), 6.32 (d, *J* = 6.0 Hz, 1H), 7.25 (dd, *J* = 3.1, 9.2 Hz, 1H), 7.25 (dd, *J* = 0.4, 9.2 Hz, 1H), 7.56 (d, *J* = 3.1 Hz, 1H), 7.83 (d, *J* = 6.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 55.97, 104.90, 112.18, 119.65, 123.91, 125.55, 151.44, 155.07, 157.02, 177.52. MS (EI, 70 eV): m/z (%) = 176.3 $[M]^+$ (59), 146.3 (10), 79.1 (92), 63.3 (100). HRMS (APCI, MeOH) calcd for $C_{10}H_9O_3^+$ $[M+H]^+$: 177.05517, found: 177.05520. IR (NaCl): ν [cm^{-1}] = 3494, 3432, 3062, 2970, 2939, 2838, 1628, 1586, 1483, 1327, 1311, 1228, 1020, 828.



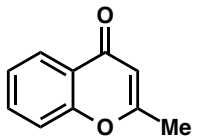
28d

6-Bromochromone (28d).[11] Prepared according to the literature. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 6.36 (d, *J* = 6.0 Hz, 1H), 7.36 (d, *J* = 0.3 Hz, 1H), 7.75 (dd, *J* = 2.5, 8.9 Hz, 1H), 7.85 (d, *J* = 6.0 Hz, 1H), 8.33 (d, *J* = 0.3, 2.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 113.16, 118.82, 120.25, 126.28, 128.59, 136.85, 155.36, 155.49, 176.26. MS (EI, 70 eV): m/z (%) = 226.0 [M, ^{81}Br]$^+$ (100), 224.0 [M, ^{79}Br]$^+$ (98), 198.0 [M, ^{81}Br]$^+$ (32), 196.0 [M, ^{79}Br]$^+$ (20), 171.9 [M, ^{81}Br]$^+$ (10), 169.9 [M, ^{79}Br]$^+$ (12), 89.1 (9), 63.3 (11). HRMS (APCI, MeOH) calcd for $C_9H_6O_2{}^{79}Br^+$ $[M+H]^+$: 224.95512, found: 224.95500. IR (NaCl): ν [cm^{-1}] = 3111, 3072, 3049, 1638, 1608, 1559, 1464, 1308, 1231, 1137, 1056, 1022, 899, 818.



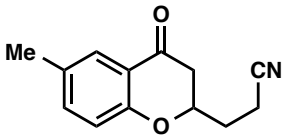
28e

7-Methoxychromone (28e).[11] Prepared according to the literature. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.89 (s, 3H), 6.32 (d, *J* = 6.0 Hz, 1H), 7.25 (dd, *J* = 3.1, 9.2 Hz, 1H), 7.25 (dd, *J* = 0.4, 9.2 Hz, 1H), 7.56 (d, *J* = 3.1 Hz, 1H), 7.83 (d, *J* = 6.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 55.97, 104.90, 112.18, 119.65, 123.91, 125.55, 151.44, 155.07, 157.02, 177.52. MS (EI, 70 eV): m/z (%) = 176.3 $[M]^+$ (59), 146.3 (10), 79.1 (92), 63.3 (100). HRMS (APCI, MeOH) calcd for $C_{10}H_9O_3^+$ $[M+H]^+$: 177.05517, found: 177.05520. IR (NaCl): ν [cm^{-1}] = 3494, 3432, 3062, 2970, 2939, 2838, 1628, 1586, 1483, 1327, 1311, 1228, 1020, 828.



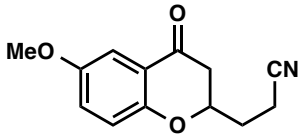
28f

2-Methylchromone (28f).[12] Prepared according to the literature. The analytical data matched the literature values.



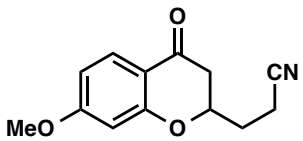
29b

3-(6-Methyl-4-oxochroman-2-yl)propanenitrile (29b). Prepared according to the standard procedure from **28b** and acrylonitril (**2**) with Mn (2.0 equiv) as reductant and a reaction time of 24 h. Column chromatography (cyclohexane/EtOAc, 1:1, R_f = 0.40) afforded **29b** as a yellow oil in 42% yield (45.2 mg, 0.209 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.03-2.09 (m, 1H), 2.15-2.23 (m, 1H), 2.31 (s, 3H), 2.65 (dd, *J* = 1.7, 5.6 Hz, 1H), 2.66-2.68 (m, 1H), 2.70 (s, 1H), 2.71 (d, *J* = 1.9 Hz, 1H), 4.51-4.57 (m, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 7.31 (dd, *J* = 4.1, 8.4 Hz, 1H), 7.69 (d, *J* = 4.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 13.49, 20.49, 30.72, 42.73, 75.48, 117.68, 118.56, 120.60, 126.76, 131.52, 137.39, 158.87, 191.30. MS (EI, 70 eV): m/z (%) = 215.1 $[M]^+$ (80), 161.1 (16), 134.1 (100), 106.1 (11), 78.2 (9). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_2^+$ $[M+H]^+$: 216.10245, found: 216.10230. IR (NaCl): ν [cm^{-1}] = 3003, 2930, 2872, 2247, 1689, 1617, 1577, 1489, 1420, 1292, 1227, 1134, 824.



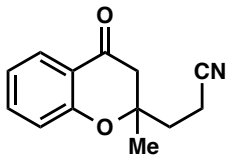
29c

3-(6-Methoxy-4-oxochroman-2-yl)propanenitrile (29c). Prepared according to the standard procedure from **28c** and acrylonitril (**2**) with Mn (2.0 equiv) as reductant and a reaction time of 24 h. Column chromatography (cyclohexane/EtOAc, 1:1, R_f = 0.40) afforded **29c** as a yellow-brown solid in 37% yield (42.5 mg, 0.184 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.05 (dddd, *J* = 3.3, 7.7, 8.3, 14.3 Hz, 1H), 2.18 (dddd, *J* = 5.9, 6.8, 9.4, 14.3 Hz, 1H), 2.63-2.67 (m, 2H), 2.69 (s, 1H), 2.71 (d, *J* = 1.5 Hz, 1H), 3.79 (s, 3H), 4.48-4.55 (m, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 7.09 (dd, *J* = 3.2, 9.0 Hz, 1H), 7.30 (d, *J* = 3.2 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 13.47, 30.67, 42.59, 55.87, 75.61, 107.56, 118.86, 119.18, 120.85, 125.41, 154.49, 155.47, 191.12. MS (EI, 70 eV): m/z (%) = 231.0 $[M]^+$ (54), 177.0 (19), 150.0 (100), 107.0 (11), 79.0 (7). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_3^+$ $[M+H]^+$: 232.09737, found: 232.09750. IR (NaCl): ν [cm^{-1}] = 3155, 2903, 2839, 2253, 1688, 1488, 1432, 1383, 1286, 1214, 1094, 908, 734.



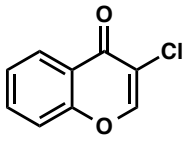
29e

3-(7-Methoxy-4-oxochroman-2-yl)propanenitrile (29e). Prepared according to the standard procedure from **28c** and acrylonitril (**2**) with Mn (2.0 equiv) as reductant and a reaction time of 24 h. Column chromatography (cyclohexane/EtOAc, 1:1, R_f = 0.40) afforded **29e** as a yellow-brown solid in 32% yield (37.0 mg, 0.158 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.06 (dddd, *J* = 3.4, 7.6, 8.3, 14.4 Hz, 1H), 2.19 (dddd, *J* = 5.9, 6.9, 9.4, 14.4 Hz, 1H), 2.64-2.66 (m, 3H), 2.68 (d, *J* = 2.7 Hz, 1H), 3.84 (s, 3H), 4.56 (dddd, *J* = 3.4, 6.5, 6.5, 9.5 Hz, 1H), 6.43 (d, *J* = 2.4 Hz, 1H), 6.61 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 13.53, 30.72, 42.33, 55.78, 75.93, 100.91, 110.45, 114.87, 118.83, 128.93, 163.75, 166.32, 189.64. MS (EI, 70 eV): m/z (%) = 231.1 $[M]^+$ (25), 150.0 (100), 122.0 (17). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_3^+$ $[M+H]^+$: 232.09737, found: 232.09740. IR (NaCl): ν [cm^{-1}] = 2939, 2253, 1678, 1608, 1576, 1497, 1444, 1352, 1297, 1264, 1199, 1160, 1120, 1022, 910.



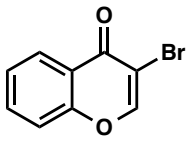
29f

3-(2-Methyl-4-oxochroman-2-yl)propanenitrile (29f). Prepared according to the standard procedure from **28c** and acrylonitril (**2**) with a reaction time of 24 h. Column chromatography (cyclohexane/EtOAc, 1:1, R_f = 0.40) afforded **29f** as a yellow oil in 17% yield (18.8 mg, 0.087 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.45 (s, 3H), 2.03 (ddd, *J* = 6.9, 8.4, 14.4 Hz, 1H), 2.18-2.19 (m, 1H), 2.53 (ddd, *J* = 6.8, 8.7, 17.0 Hz, 1H), 2.58 (ddd, *J* = 6.5, 8.4, 17.0 Hz, 1H), 2.68 (d, *J* = 16.4 Hz, 1H), 2.80 (dd, *J* = 0.6, 16.4 Hz, 1H), 6.94 (ddd, *J* = 0.4, 1.0, 8.4 Hz, 1H), 7.02 (ddd, *J* = 1.0, 7.2, 7.8 Hz, 1H), 7.49 (ddd, *J* = 1.8, 7.2, 8.4 Hz, 1H), 7.86 (ddd, *J* = 0.4, 1.8, 7.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 11.87, 23.35, 35.07, 47.29, 79.29, 118.35, 119.22, 120.27, 121.57, 126.75, 136.61, 158.97, 191.13. MS (EI, 70 eV): m/z (%) = 215.0 $[M]^+$ (100), 161.0 (97), 120.0 (87), 92.1 (28). HRMS (APCI, MeOH) calcd for $C_{13}H_{13}NO_2Na^+$ $[M+Na]^+$: 238.08440, found: 238.08430. IR (ATR): ν [cm^{-1}] = 3055, 2983, 2253, 1689, 1473, 1384, 1307, 1224, 1117, 1086, 906.



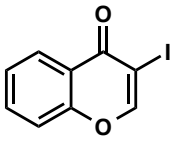
30d

3-Chlorochromone (30d).[13,14] Prepared according to a literature procedure.[13] The analytical data matched the literature values.[14] ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 7.44-7.50 (m, 2H), 7.71 (ddd, *J* = 1.7, 7.1, 8.6 Hz, 1H), 8.15 (s, 1H), 8.27 (ddd, *J* = 0.5, 1.7, 8.0 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 118.28, 121.02, 123.61, 125.91, 126.46, 134.22, 152.16, 156.16, 172.36. MS (EI, 70 eV): m/z (%) = 181.9 [M, ^{37}Cl]$^+$ (33), 179.9 [M, ^{35}Cl]$^+$ (100), 152.0 (22), 120.0 (31), 92.0 (24). HRMS (APCI, MeOH) calcd for $C_9H_5O_2{}^{35}ClNa^+$ $[M+Na]^+$: 202.98758, found: 202.98770. IR (ATR): ν [cm^{-1}] = 3052, 1662, 1567, 1370, 1347, 1313, 1220, 1173, 1115, 927.



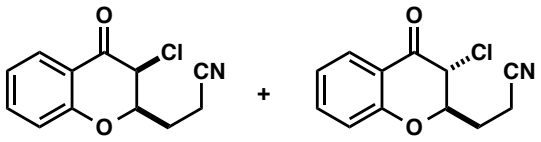
30e

3-Bromochromone (30e).[15] Prepared according to the literature procedure. The analytical data matched the literature values.



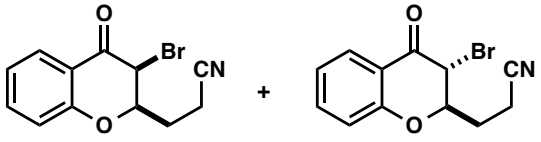
30f

3-Iodochromone (30f).[16] Prepared according to a modified literature procedure: To a solution of (*E*)-3-(dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-one[17] (2.73 g, 14.3 mmol, 1.0 equiv) in CHCl (100 ml) was added I_2 (3.62 g, 28.6 mmol, 2 equiv) and the dark, brown-violet mixture was stirred for 70 h at room temperature (23 ºC). The mixture was then washed with saturated aqueous $Na_2S_2O_3$-solution (3 × 100 ml). The combined aqueous layers were extracted with $CHCl_3$ (2 × 100 ml). The organic layers were combined, dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.59) to afford **30e** as a yellow solid in 52% yield (2.02 g, 7.53 mmol). The analytical data matched the literature values.



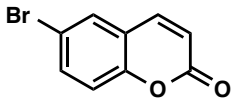
31d ***32d***

***syn*- and *anti*-3-(3-Chloro-4-oxochroman-2-yl)propanenitrile (31d, 32d)**. Prepared according to the standard procedure from **30d** and acrylonitrile (**2**) with a reaction time of 24 h and a modified workup procedure. All volatiles were removed under reduced pressure. The residue was treated with CH_2Cl_2 (5 ml), stirred, and cooled to 0 ºC. Aqueous HCl (6M, 4 ml) was added and stirring was continued at 0 ºC for another 3 h. The mixture was allowed to warm to room temperature (23 ºC) and workup was continued as in the standard procedure by addition of H_2O and CH_2Cl_2, followed by separation, extraction and drying of the organic layer as described. Column chromatography (cyclohexane/Et_2O, 1:1, R_f = 0.15–0.21) afforded the products as a 1.6:1 diastereomeric mixture in form of a yellow oil in 49% yield (58.3 mg, 0.247 mmol). Workup of the reaction under kinetically controlled conditions (see standard procedure for quench with TBAF at –78 ºC) followed by column chromatography afforded a 1:1.8 diastereomeric mixture of the products in 54% yield (63.4 mg, 0.269 mmol). D1 = diastereomer 1, D2 = diastereomer 2. The relative configuration of each diastereomer could not be determined from the mixture. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.07 (dddd, *J* = 3.3, 7.0, 8.8, 14.3 Hz, 1H, D2), 2.19-2.29 (m, 1H, D1), 2.46-2.55 (m, 2H, D1 + D2), 2.67-2.77 (m, 4H, D1 + D2), 4.32 (d, *J* = 1.9 Hz, 1H, D2), 4.47-4.56 (m, 2H, D1), 4.64 (ddd, *J* = 1.9, 3.4, 9.9 Hz, 1H, D2), 7.02-7.07 (m, 2H, D1 + D2), 7.10-7.15 (m, 2H, D1 + D2), 7.55 (ddd, *J* = 1.8, 7.2, 8.9 Hz, 1H, D1), 7.57 (ddd, *J* = 1.8, 7.2, 8.4 Hz, 1H, D2), 7.93 (ddd, *J* = 0.4, 1.8, 7.9 Hz, 1H, D1), 7.94 (ddd, *J* = 0.4, 1.8, 7.9 Hz, 1H, D2). ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D1): δ = 13.25, 28.68, 60.28, 79.83, 118.83, 118.25, 118.77, 122.96, 128.19, 137.05, 159.69, 185.13. ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D2): δ = 13.43, 27.36, 57.96, 76.74, 117.88, 118.25, 118.47, 122.87, 128.48, 137.05, 159.83, 184.85. MS (EI, 70 eV): m/z (%) = 237.0 [M, ^{37}Cl]$^+$ (8), 235.0 [M, ^{35}Cl]$^+$ (24), 200.0 (7), 120.0 (100), 92.0 (17). HRMS (APCI, MeOH) calcd for $C_{12}H_{10}ON_2{}^{35}ClNa^+$ [M+Na]$^+$: 258.02978, found: 258.02990. IR (ATR): ν [cm^{-1}] = 3055, 2248, 1699, 1616, 1580, 1501, 1474, 1362, 1262, 1224, 1150, 1116, 895.



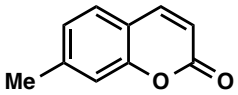
31e ***32e***

***syn*- and *anti*-3-(3-Bromo-4-oxochroman-2-yl)propanenitrile (31e, 32e)**. Prepared according to the standard procedure from **30e** and acrylonitrile (**2**) with a reaction time of 24 h and a modified workup procedure. All volatiles were removed under reduced pressure. The residue was treated with CH_2Cl_2 (5 ml), stirred, and cooled to 0 ºC. Aqueous HCl (6M, 4 ml) was added and stirring was continued at 0 ºC for another 3 h. The mixture was allowed to warm to room temperature (23 ºC) and workup was continued as in the standard procedure by addition of H_2O and CH_2Cl_2, followed by separation, extraction and drying of the organic layer as described. Column chromatography (cyclohexane/Et_2O, 1:1, R_f = 0.16–0.19) afforded the products as a 3.5:1 diastereomeric mixture in form of a yellow oil in 42% yield (59.3 mg, 0.212 mmol). Workup of the reaction under kinetically controlled conditions (see standard procedure for quench with TBAF at –78 ºC) followed by column chromatography afforded a 1:4.9 diastereomeric mixture of the products in 42% yield (58.9 mg, 0.209 mmol). D1 = diastereomer 1, D2 = diastereomer 2. The relative configuration of each diastereomer could not be determined from the mixture. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.04 (dddd, *J* = 3.3, 6.9, 8.9, 14.3 Hz, 1H, D2), 2.17-2.27 (m, 1H, D1), 2.39-2.48 (m, 1H, D1), 2.48-2.55 (m, 1H, D2), 2.64-2.79 (m, 4H, D1 + D2), 4.37 (ddd, *J* = 1.8, 3.3, 9.7 Hz, 1H, D2), 4.04 (d, *J* = 1.8 Hz, 1H, D2), 4.58-4.66 (m, 2H, D1), 7.04 (ddd, *J* = 0.4, 1.1, 8.4 Hz, 1H, D1), 7.04-7.07 (m, 1H, D2), 7.12 (ddd, *J* = 1.0, 7.2, 8.2 Hz, 1H, D1), 7.13 (ddd, *J* = 1.4, 7.2, 8.1 Hz, 1H, D2), 7.55-7.59 (m, 1H, D2), 7.57 (ddd, *J* = 1.8, 7.2, 8.4 Hz, 1H, D1), 7.93 (ddd, *J* = 0.4, 1.8, 7.9 Hz, 1H, D1), 7.96 (ddd, *J* = 0.3, 1.7, 7.9 Hz, 1H, D2). ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D1): δ = 13.57, 28.98, 50.64, 79.89, 117.98, 118.37, 118.93, 122.93, 128.26, 137.13, 159.12, 184.67. ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D2): δ = 13.31, 29.24, 49.85, 76.25, 117.83, 118.19, 118.49, 122.91, 128.54, 136.94, 159.83, 185.03. MS (EI, 70 eV): m/z (%) = 280.9 [M, ^{81}Br]$^+$ (23), 279.0 [M, ^{79}Br]$^+$ (22), 200.0 (37), 160.0 (13), 131.0 (17), 120.0 (100), 92.0 (18). HRMS (APCI, MeOH) calcd for $C_{12}H_{10}ON_2{}^{79}BrNa^+$ [M+Na]$^+$: 301.97926, found: 301.97920. IR (ATR): ν [cm^{-1}] = 3055, 2985, 2249, 1695, 1606, 1581, 1474, 1367, 1178, 1099, 1042, 895.



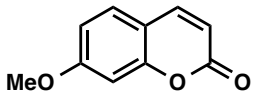
33b

6-Bromocoumarin (33b).[18] Prepared according to a literature procedure.[19] The analytical data matched the literature values.[18]



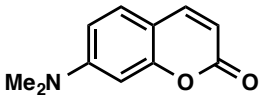
33d

7-Methylcoumarin (33d). This compound was purchased from Sigma-Aldrich (CAS 2445-83-2) and used as received.



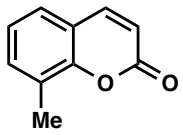
33e

7-Methoxycoumarin (33e).[20] Prepared from commercially available umbelliferone (CAS 93-35-6, Sigma-Aldrich) according to the literature procedure. The analytical data matched the literature values.



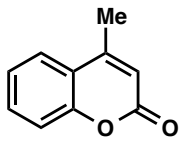
33f

7-(Dimethylamino)-coumarin (33f).[21] Prepared according to the literature procedure. The analytical data matched the literature values. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.04 (s, 3H), 6.05 (d, *J* = 9.4 Hz, 1H), 6.49 (d, *J* = 2.5 Hz, 1H), 6.58 (dd, *J* = 2.5, 8.7 Hz, 1H), 7.25 (d, *J* = 8.7 Hz, 1H), 7.53 (dd, *J* = 0.6, 9.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 40.21, 98.19, 108.85, 109.08, 109.92, 128.58, 143.73, 153.02, 156.44, 162.14. MS (EI, 70 eV): m/z (%) = 189.0 $[M]^+$ (100), 160.1 (35), 44.6 (7). HRMS (APCI, MeOH) calcd for $C_{11}H_{12}NO_2^+$ $[M+H]^+$: 190.08680, found: 190.08700. IR (ATR): ν [cm^{-1}] = 2935, 1697, 1605, 1579, 1501, 1473, 1463, 1433, 1363, 1304, 1223, 1199, 1116, 1055, 941, 763.



33g

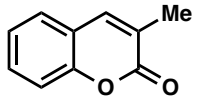
8-Methylcoumarin (33g).[22] Prepared according to a literature procedure.[21] ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.45 (s, 3H), 6.41 (d, *J* = 9.5 Hz, 1H), 7.17 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.29-7.33 (m, 1H), 7.36-7.39 (m, 1H), 7.68 (d, *J* = 9.5 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.47, 116.44, 118.68, 124.06, 125.65, 126.46, 133.25, 143.84, 152.53, 161.06. MS (EI, 70 eV): m/z (%) = 160.0 $[M]^+$ (100), 132.1 (41), 104.0 (9). HRMS (APCI, MeOH) calcd for $C_{10}H_9O_2^+$ $[M+H]^+$: 161.05971, found: 161.05971. IR (ATR): ν [cm^{-1}] = 3054, 1755, 1604, 1401, 1264, 1239, 1119, 1081, 922, 732.



33h

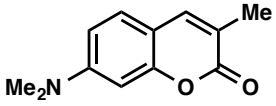
4-Methylcoumarin (33h).[23] Prepared according to a literature procedure.[24] ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.44 (d, *J* = 1.3 Hz, 3H), 6.29 (q, *J* = 1.3 Hz, 1H), 7.29 (ddd, *J* = 1.2, 7.3, 7.0 Hz, 1H), 7.33 (ddd, *J* = 0.4, 1.2, 8.3 Hz, 1H), 7.52 (ddd, *J* = 1.6, 7.3, 8.3 Hz, 1H), 7.60 (dd, *J* = 1.6, 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 18.67, 115.25, 117.19, 120.08. 124.26, 124.62, 131.82, 152.34, 153.66, 160.79. MS (EI, 70 eV): m/z (%) = 160.0 $[M]^+$ (100), 131.0 (94), 103.1 (9). HRMS

(APCI, MeOH) calcd for $C_{10}H_8O_2Na^+$ $[M+Na]^+$: 183.04220, found: 183.04220. IR (ATR): ν [cm^{-1}] = 3055, 1732, 1625, 1608, 1568, 1468, 1385, 1367, 1264, 1185, 1036, 960.



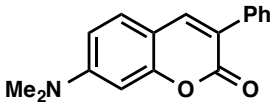
33i

3-Methylcoumarin (33i).[25] Prepared according to a literature procedure.[21] ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.22 (d, *J* = 1.4 Hz, 3H), 7.24 (ddd, *J* = 1.2, 7.2, 7.7 Hz, 1H), 7.29-7.32 (m, 1H), 7.41 (dd, *J* = 1.6, 7.7 Hz, 1H), 7.43-7.48 (m, 1H), 7.50-7.52 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 17.23, 116.56, 119.69, 124.32, 125.97, 127.00, 130.52, 139.24, 153.38, 162.25. MS (EI, 70 eV): m/z (%) = 160.0 $[M]^+$ (100), 131.1 (56), 77.1 (8). HRMS (APCI, MeOH) calcd for $C_{10}H_9O_2^+$ $[M+H]^+$: 161.06025, found: 161.06030. IR (ATR): ν [cm^{-1}] = 3041, 2988, 2950, 2922, 1703, 1625, 1610, 1489, 1463, 1449, 1371, 1295, 1194, 1154, 1076, 946, 752.



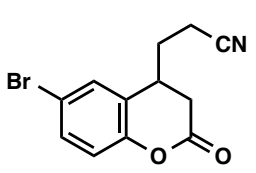
33j

7-(Dimethylamino)-3-methylcoumarin (33j). Prepared following a literature procedure[21] from 4-(Dimethylamino)-2-hydroxybenzaldehyde and Ethyl 2-(triphenylphosphoranylidene)propanoate on a 6.05 mmol scale. The reaction mixture was heated to 180 ºC for 2 h. Column chromatography (*n*-hexane/EtOAc, 2:1, R_f = 0.34) afforded the title compound as a red-orange solid in 72% yield (890 mg, 4.38 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.13 (d, *J* = 1.2 Hz, 3H), 3.02 (s, 6H), 6.50 (d, *J* = 2.5 Hz, 1H), 6.58 (dd, *J* = 2.5, 8.7 Hz, 1H), 7.20 (d, *J* = 8.7 Hz, 1H), 7.36-7.37 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 16.86, 40.25, 98.15, 109.09, 109.55, 119.06, 127.61, 138.93, 152.18, 155.47, 163.31. MS (EI, 70 eV): m/z (%) = 203.0 $[M]^+$ (100), 174.1 (29), 86.6 (6). HRMS (APCI, MeOH) calcd for $C_{12}H_{14}NO_2^+$ $[M+H]^+$: 204.10245, found: 204.10240. IR (ATR): ν [cm^{-1}] = 2892, 1697, 1635, 1529, 1450, 1394, 1285, 1234, 1066, 919.



33k

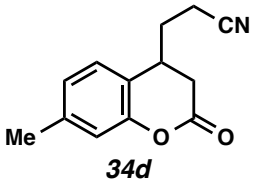
7-(Dimethylamino)-3-phenylcoumarin (33k).[26] Prepared following a literature procedure[21] from 4-(Dimethylamino)-2-hydroxybenzaldehyde and Ethyl 2-phenyl-2-(triphenylphosphoranylidene)acetate on a 6.05 mmol scale. The reaction mixture was heated to 180 ºC for 2 h. Column chromatography (*n*-hexane/EtOAc, 2:1, R_f = 0.27) afforded the title compound as a red-orange solid in 29% yield (458 mg, 1.73 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 3.06 (s, 6H), 6.54 (d, *J* = 2.5 Hz, 1H), 6.62 (dd, *J* = 2.5, 8.7 Hz, 1H), 7.31-7.36 (m, 2H), 7.39-7.44 (m, 2H), 7.68-7.71 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 40.24, 97.78, 109.35, 109.68, 121.63, 127.87, 128.34, 128.75, 135.83, 140.58, 152.84, 155.93, 161.59. MS (EI, 70 eV): m/z (%) = 265.1 $[M]^+$ (100), 237.1 (16), 165.0 (48), 118.4 (68), 82.4 (14). HRMS (APCI, MeOH) calcd for $C_{17}H_{16}NO_2^+$ $[M+H]^+$: 266.11810, found: 266.11830. IR (ATR): ν [cm^{-1}] = 2905, 1709, 1672, 1447, 1348, 1235, 821.



34b

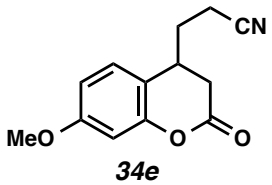
3-(6-Bromo-2-oxochroman-4-yl)propanenitrile (34b). Prepared according to the standard procedure from **33b** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/Et_2O, 1:1, R_f = 0.15) afforded **34b** as a yellow solid in 36% yield (50.0 mg, 0.178 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.83-1.91 (m, 1H), 1.91-1.99 (m, 1H), 2.36 (ddd, *J* = 6.8, 8.1, 17.2 Hz, 1H), 2.45 (ddd, *J* = 6.6, 6.6, 17.2 Hz, 1H), 2.80 (dd, *J* = 3.1, 16.2 Hz, 1H), 2.91 (dd, *J* = 5.8, 16.2 Hz, 1H), 3.19 (dddd, *J* = 3.0, 6.2, 6.2, 9.1 Hz, 1H), 6.98 (d, *J* = 8.6 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 7.44 (dd, *J* = 2.4, 8.6 Hz, 1H). ^{13}C-NMR ($CDCl_3$,

100.6 MHz): δ = 14.99, 29.79, 33.86, 34.14, 17.46, 118.35, 119.46, 126.33, 130.68, 132.39, 150.38, 166.42. MS (EI, 70 eV): m/z (%) = 281.0 [M, $^{81}Br]^+$ (51), 279.0 [M, $^{79}Br]^+$ (50), 227.0 [M, $^{81}Br]^+$ (100), 225.0 [M, $^{79}Br]^+$ (99), 182.9 [M, $^{81}Br]^+$ (8), 180.9 [M, $^{79}Br]^+$ (7), 118.0 (45), 89.0 (14). HRMS (CI, MeOH) calcd for $C_{12}H_{10}NO_2{}^{35}Cl^{79}Br^-$ [M+Cl]$^-$: 313.95834, found: 313.95880. IR (NaCl): ν [cm^{-1}] = 3054, 2987, 2305, 1775,1479, 1421, 1265, 1170, 1149, 1067, 896, 738.



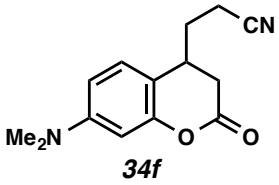
34d

3-(7-Methyl-2-oxochroman-4-yl)propanenitrile (34d). Prepared according to the standard procedure from **33d** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/Et_2O, 1:1, R_f = 0.15) afforded **34d** as a yellow oil in 46% yield (49.0 mg, 0.228 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.81 (dddd, *J* = 6.2, 6.6, 9.6, 13.8 Hz, 1H), 1.94 (dddd, *J* = 6.2, 6.6, 8.6, 13.8 Hz, 1H), 2.31 (ddd, *J* = 6.7, 8.6, 17.1 Hz, 1H), 2.35 (s, 3H), 2.41 (ddd, *J* = 6.4, 6.4, 17.1 Hz, 1H), 2.76 (dd, *J* = 2.9, 16.0 Hz, 1H), 2.91 (dd, *J* = 5.9, 16.0 Hz, 1H), 3.17 (dddd, *J* = 2.9, 6.0, 6.0, 9.0 Hz, 1H), 6.89-6.91 (m, 1H), 6.95-6.98 (m, 1H), 7.11 (d, *J* = 7.7 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 14.99, 21.16, 30.04, 33.62, 34.84, 118.10, 118.72, 120.88, 125.54, 127.74, 139.77, 151.16, 167.51. MS (EI, 70 eV): m/z (%) = 215.0 $[M]^+$ (37), 161.0 (100), 117.0 (14). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_2^+$ $[M+H]^+$: 216.10245, found: 216.10230. IR (NaCl): ν [cm^{-1}] = 3031, 2925, 2857, 2245, 1768, 1625, 1581, 1507, 1420, 1260, 1231, 1145, 1124, 1070, 867, 821.



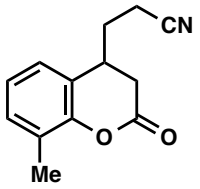
34e

3-(7-Methoxy-2-oxochroman-4-yl)propanenitrile (34e). Prepared according to the standard procedure from **33e** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/Et_2O, 1:1, R_f = 0.10) afforded **34e** as a yellow solid in 45% yield (52.5 mg, 0.227 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.79 (dddd, *J* = 6.1, 6.6, 9.6, 13.8 Hz, 1H), 1.93 (dddd, *J* = 6.1, 6.4, 8.6, 13.8 Hz, 1H), 2.30 (ddd, *J* = 6.6, 8.6, 17.1 Hz, 1H), 2.41 (ddd, *J* = 6.3, 6.3, 17.1 Hz, 1H), 2.77 (dd, *J* = 2.8, 16.0 Hz, 1H), 2.92 (dd, *J* = 5.9, 16.0 Hz, 1H), 3.16 (dddd, *J* = 2.8, 5.9, 5.9, 9.0 Hz, 1H), 3.79 (s, 3H), 6.64 (d, *J* = 2.6 Hz, 1H), 6.70 (dd, *J* = 2.6, 8.4 Hz, 1H), 7.13 (d, *J* = 8.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.00, 30.21, 33.33, 34.94, 55.67, 103.30, 110.77, 115.77, 118.74, 128.58, 152.13, 160.46, 167.30. MS (EI, 70 eV): m/z (%) = 231.1 $[M]^+$ (17), 177.1 (100), 121.1 (8). HRMS (CI, MeOH) calcd for $C_{13}H_{17}N_2O_3^+$ $[M+NH_4]^+$: 249.12392, found: 249.12400. IR (NaCl): ν [cm^{-1}] = 2923, 2840, 2245, 1769, 1624, 1585, 1508, 1357, 1272, 1189, 1148, 1123, 1107, 1070, 1032, 971.



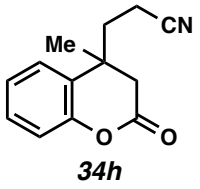
34f

3-(7-(Dimethylamino)-2-oxochroman-4-yl)propanenitrile (34f). Prepared according to the standard procedure from **33f** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.69) afforded a 1.4:1 mixture of **33f** and **34f** (62.7 mg) as a yellow solid. From this mixture, the yield in **34f** was calculated to be 26% (31.4 mg, 0.128 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.78 (dddd, *J* = 6.0, 6.7, 9.7, 13.7 Hz, 1H), 1.92 (dddd, *J* = 5.8, 6.8, 8.6, 13.7 Hz, 1H), 2.31 (ddd, *J* = 6.7, 8.6, 17.0 Hz, 1H), 2.39 (ddd, *J* = 6.0, 6.7, 17.0 Hz, 1H), 2.74 (dd, *J* = 2.8, 15.9 Hz, 1H), 2.88-2.93 (m, 1H), 2.95 (s, 3H), 3.08-3.14 (m, 1H), 6.41 (d, *J* = 2.6 Hz, 1H), 6.48 (dd, *J* = 2.6, 8.4 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.04, 30.54, 33.25, 35.39, 40.44, 101.05, 108.58, 110.76, 118.93, 128.36, 130.10, 151.47, 152.17, 167.95. MS (EI, 70 eV): m/z (%) = 244.1 $[M]^+$ (2), 190.0 (100), 134.0 (4). HRMS (ESI, MeOH) calcd for $C_{14}H_{16}N_2O_2Na^+$ $[M+Na]^+$: 267.11095, found: 267.11140. IR (ATR): ν [cm^{-1}] = 2928, 2247, 1764, 1628, 1566, 1521, 1445, 1359, 1264, 1145, 994, 921, 702.



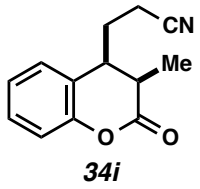
34g

3-(8-Methyl-2-oxochroman-4-yl)propanenitrile (34g). Prepared according to the standard procedure from **33g** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/CH_2Cl_2/Et_2O, 3:3:1, R_f = 0.42) afforded **34g** as a yellow solid in 36% yield (50.0 mg, 0.178 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.79-1.88 (m, 1H), 1.90-1.99 (m, 1H), 2.31 (s, 3H), 2.32 (ddd, *J* = 6.7, 8.6, 17.1 Hz, 1H), 2.41 (ddd, *J* = 6.4, 6.4, 17.1 Hz, 1H), 2.78 (dd, *J* = 2.8, 16.0 Hz, 1H), 2.91 (dd, *J* = 5.8, 16.0 Hz, 1H), 3.19 (dddd, *J* = 2.8, 5.9, 5.9, 8.8 Hz, 1H), 7.03-7.08 (m, 2H), 7.14-7.19 (m, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.07, 15.71, 29.92, 34.16, 34.74, 118.69, 123.84, 124.36, 125.55, 127.16, 130.88, 149.54, 167.43. MS (EI, 70 eV): m/z (%) = 215.1 $[M]^+$ (55), 161.1 (100), 117.0 (16), 77.0 (6). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_2^+$ $[M+H]^+$: 216.10191, found: 216.10204. IR (ATR): ν [cm^{-1}] = 2928, 2254, 1766, 1469, 1269, 1079, 903, 723.



34h

3-(4-Methyl-2-oxochroman-4-yl)propanenitrile (34h). Prepared according to the standard procedure from **33h** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/Et_2O, 1:1, R_f = 0.17) afforded **34h** as a colourless oil in 33% yield (35.9 mg, 0.167 mmol). ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.47 (s, 3H), 1.98-2.08 (m, 2H), 2.21 (ddd, *J* = 6.8, 8.7, 16.8 Hz, 1H), 2.31 (ddd, *J* = 6.8, 9.2, 16.8 Hz, 1H), 2.68 (d, *J* = 15.8 Hz, 1H), 2.74 (d, *J* = 15.8 Hz, 1H), 7.13 (ddd, *J* = 0.4, 1.3, 8.1 Hz, 1H), 7.22 (ddd, *J* = 1.2, 7.1, 7.7 Hz, 1H), 7.27 (ddd, *J* = 0.3, 1.9, 7.7 Hz, 1H), 7.35 (ddd, *J* = 1.9, 7.2, 8.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.82, 24.56, 35.35, 36.23, 41.84, 117.89, 118.95, 125.12, 125.18, 127.76, 129.43, 151.01, 167.00 MS (EI, 70 eV): m/z (%) = 215.1 $[M]^+$ (33), 200.0 (7), 161.1 (100), 115.0 (9). HRMS (APCI, MeOH) calcd for $C_{13}H_{14}NO_2^+$ $[M+H]^+$: 216.10245, found: 216.10260. IR (ATR): ν [cm^{-1}] = 2924, 2248, 1766, 1610, 1487, 1449, 1276, 1192, 1131, 1071, 944.



34i

***syn*-3-(3-Methyl-2-oxochroman-4-yl)propanenitrile (34i)**. Prepared according to the standard procedure from **33i** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (*n*-pentane/Et_2O, 1:1, R_f = 0.24) afforded **34i** as a colourless oil in 44% yield (49.1 mg, 0.228 mmol). A single crystal suitible for X-ray analysis was obtained by crystallisation from CH_2Cl_2/Et_2O by slow evaporation at room temperature. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.40 (d, *J* = 6.7 Hz, 3H), 1.43-1.52 (m, 1H), 2.05-2.16 (m, 1H), 2.16-2.24 (m, 1H), 2.36-2.43 (m, 1H), 3.01-3.09 (m, 2H), 7.09 (dd, *J* = 1.2, 8.1 Hz, 1H), 7.15 (ddd, *J* = 1.2, 7.4, 7.4 Hz, 1H), 7.24 (dd, *J* = 1.7, 7.4 Hz, 1H), 7.33 (ddd, *J* = 1.7, 7.4, 8.1 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.35, 15.03, 24.94, 38.46, 39.69, 117.68, 118.872, 124.55, 125.66, 128.09, 129.41, 151.11, 170.70. MS (EI, 70 eV): m/z (%) = 215.0 $[M]^+$ (21), 161.0 (100), 105.1 (9). HRMS (APCI, MeOH) calcd for $C_{13}H_{17}N_2O_2^+$ $[M+NH_4]^+$: 233.12900, found: 233.12920. IR (ATR): ν [cm^{-1}] = 2983, 2939, 2246, 1761, 1611, 1588, 1456, 1425, 1383, 1364, 1194, 1141, 1117, 1081, 1050, 973, 759.

X-ray analysis of 34i (CCDC 1440298)

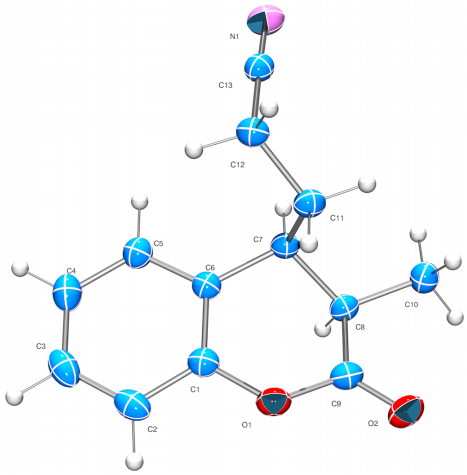
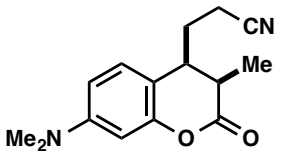


Table S4. Crystal data and structure refinement for mk568al.

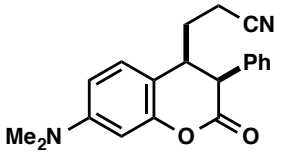
Identification code	mk568al
Empirical formula	C13 H13 N O2
Formula weight	215.24
Temperature	100(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21/c
Unit cell dimensions	a = 5.6624(4) A alpha = 90 deg. b = 13.0517(9) A beta = 100.888(4) deg. c = 15.2377(8) A gamma = 90 deg.
Volume	1105.86(12) A^3
Z, Calculated density	4, 1.293 Mg/m^3
Absorption coefficient	0.088 mm^-1
F(000)	456
Crystal size	0.100 x 0.100 x 0.100 mm
Theta range for data collection	2.071 to 27.415 deg.
Limiting indices	-7<=h<=7, -16<=k<=14, -19<=l<=19
Reflections collected / unique	10410 / 2522 [R(int) = 0.0458]
Completeness to theta = 25.242	99.8 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2522 / 0 / 198
Goodness-of-fit on F^2	1.051
Final R indices [I>2sigma(I)]	R1 = 0.0402, wR2 = 0.0892
R indices (all data)	R1 = 0.0572, wR2 = 0.0952
Extinction coefficient	0.036(4)
Largest diff. peak and hole	0.215 and -0.209 e.A^-3



+ *33j* (1.4:1 mixture)

34j

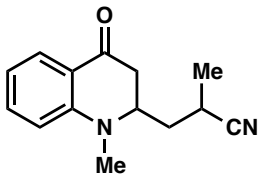
***syn*-3-(7-(Dimethylamino)-3-methyl-2-oxochroman-4-yl)propanenitrile (34j)**. Prepared according to the standard procedure from **33j** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.78) afforded a 1.4:1 mixture of **34j** and **33j** (83.9 mg) as a yellow solid. From this the yield in **34j** was calculated to be 38% (49.4 mg, 0.189 mmol). The relative configuration of **34j** was assigned in analogy to **34i**. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.36 (d, *J* = 6.9 Hz, 3H), 1.37-1.45 (m, 1H), 2.02-2.10 (m, 1H), 2.16-2.25 (m, 1H), 2.36 (ddd, *J* = 4.6, 6.7, 16.8 Hz, 1H), 2.89-2.93 (m, 1H), 2.94 (s, 6H), 2.96-3.02 (m, 1H), 6.39 (d, *J* = 2.6 Hz, 1H), 6.46 (dd, *J* = 2.6, 8.4 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 12.57, 14.98, 25.52, 38.89, 39.03, 40.43, 100.98, 108.20, 112.52, 119.14, 128.41, 151.42, 151.99, 171.38. MS (EI, 70 eV): m/z (%) = 258.2 $[M]^+$ (59), 204.1 (100), 160.1 (7). HRMS (ESI, MeOH) calcd for $C_{15}H_{18}N_2O_2Na^+$ $[M+Na]^+$: 281.12660, found: 281.12680. IR (ATR): ν [cm^{-1}] = 2923, 2807, 2246, 1761, 1708, 1609, 1519, 1486, 1445, 1381, 1283, 1266, 1183, 1137, 1083, 981.



+ *33k* (1:1.4 mixture)

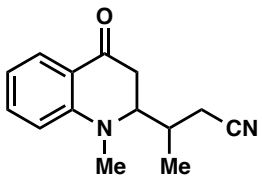
34k

***syn*-3-(7-(Dimethylamino)-2-oxo-3-phenylchroman-4-yl)propanenitrile (34k)**. Prepared according to the standard procedure from **33k** and acrylonitrile (**2**) with a reaction time of 24 h. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.81) afforded a 1:1.4 mixture of **34k** and **33k** (93.1 mg) as a yellow solid. From this the yield in **34k** was calculated to be 24% (39.3 mg, 0.122 mmol). The relative configuration of **34k** was assigned in analogy to **34i**. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.62 (dddd, *J* = 4.8, 7.2, 11.8, 13.2 Hz, 1H), 1.94-2.03 (m, 1H), 2.13 (ddd, *J* = 7.4, 9.2, 16.8 Hz, 1H), 2.29 (ddd, *J* = 4.8, 7.4, 16.8 Hz, 1H), 2.97 (s, 3H), 3.07-3.15 (m, 1H), 4.24 (d, *J* = 5.2 Hz, 1H), 6.49 (ddd, *J* = 2.6, 8.3, 8.3 Hz, 1H), 7.07 (d, *J* = 8.3 Hz, 1H), 7.37-7.39 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 15.09, 25.85, 40.41, 40.79, 50.67, 100.97, 108.39, 112.04, 128.93, 127.98, 128.29, 128.71, 129.86, 134.29, 151.54, 151.83, 168.39. MS (EI, 70 eV): m/z (%) = 320.2 $[M]^+$ (65), 266.2 (48), 202.1 (100), 146.1 (6). HRMS (ESI, MeOH) calcd for $C_{20}H_{20}N_2O_2Na^+$ $[M+Na]^+$: 343.14225, found: 343.14230. IR (ATR): ν [cm^{-1}] = 2930, 2242, 1761, 1708, 1570, 1522, 1496, 1382, 1245, 1235, 1137, 1115, 1063, 1001, 907.



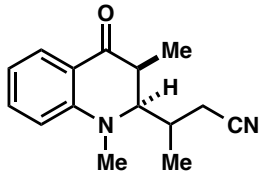
***40* (1.3:1 d.r.)**

2-Methyl-3-(1-methyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanenitrile (40). Prepared according to the standard procedure from **22a** and methacrylonitrile with a reaction time of 24 h on a 1 mmol scale. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.61) afforded **40** as a 1.3:1 diastereomeric mixture in 36% yield (81.0 mg, 0.355 mmol). The relative configuration of the major diastereomer could not be assigned. NMR data for the diastereomeric mixture: ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.29 (d, *J* = 7.0 Hz, 3H), 1.32 (d, *J* = 7.0 Hz, 3H), 1.69 (ddd, *J* = 4.8, 10.4, 14.9 Hz, 1H), 1.77-1.82 (m, 2H), 2.04 (ddd, *J* = 5.5, 9.4, 14.9 Hz, 1H), 2.51 (dd, *J* = 2.1, 16.2 Hz, 1H), 2.57-2.66 (m, 3H), 3.07 (s, 3H), 3.07-3.14 (m, 2H), 3.20 (s, 3H), 3.79-3.85 (m, 1H), 3.88 (dddd, *J* = 2.1, 4.0, 6.0, 9.4 Hz, 1H), 6.61-6.63 (m, 1H), 6.64-6.65 (m, 1H), 6.69-6.75 (m, 2H), 7.39-7.44 (m, 2H), 7.82-7.87 (m, 2H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 18.34, 18.65, 22.54, 23.53, 32.21, 35.48, 37.87, 39.61, 40.73, 42.35, 58.84, 59.46, 113.22, 113.38, 116.84, 116.14, 121.75, 122.18, 127.67, 127.80, 136.15, 149.09, 149.87, 192.36, 192.49. MS (EI, 70 eV): m/z (%) = 228.2 $[M]^+$ (18), 160.1 (100). HRMS (APCI, MeOH) calcd for $C_{14}H_{16}N_2ONa^+$ $[M+Na]^+$: 251.11603, found: 251.11610. IR (ATR): ν [cm^{-1}] = 3055, 2939, 2239, 1670, 1603, 1563, 1460, 1435, 1295, 1265, 1206, 1134, 998, 908.



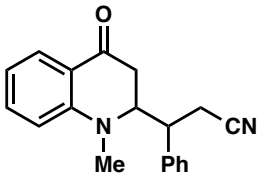
42 (1.6:1 d.r.)

3-(1-Methyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)butanenitrile (42). Prepared according to the standard procedure from **22a** and crotononitrile (1.5 equiv, *E*:*Z* = ~2:1) with a reaction time of 24 h on a 1 mmol scale. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.70) afforded **42** as a 1.6:1 diastereomeric mixture in 29% yield (65.1 mg, 0.285 mmol). The relative configuration of the major diastereomer could not be assigned. D1 = diastereomer 1; D2 = diastereomer 2. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.08 (d, *J* = 6.7 Hz, 3H, D1), 1.11 (d, *J* = 6.8 Hz, 3H, D2), 2.29-2.41 (m, 6H, D1 + D2), 2.63 (dd, *J* = 1.7, 16.4 Hz, 1H, D2), 2.68 (dd, *J* = 2.2, 16.4 Hz, 1H, D1), 3.01-3.11 (m, 2H, D1 + D2), 3.17 (s, 3H, D2), 3.22 (s, 3H, D1), 3.46-3.53 (m, 2H, D1 + D2), 6.61-6.65 (m, 2H, D1 + D2), 6.68-6.74 (m, 2H, D1 + D2), 7.38-7.43 (m, 2H, D1 + D2), 7.81 (ddd, *J* = 0.4, 1.8, 7.8 Hz, 1H, D2), 7.82 (ddd, *J* = 0.5, 1.8, 7.8 Hz, 1H, D1). ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D1): δ = 16.36, 22.50, 31.74, 39.19, 40.23, 64.12, 113.11, 116.56, 116.77, 117.99, 119.45, 127.63, 136.19, 149.45, 192.51. ^{13}C-NMR ($CDCl_3$, 100.6 MHz, D2): δ = 17.42, 21.48, 32.33, 39.55, 40.19, 64.21, 112.77, 113.36, 116.56, 117.73, 119.02, 127.61, 136.33, 149.76, 192.48. MS (EI, 70 eV): m/z (%) = 228.2 $[M]^+$ (9), 160.1 (100). HRMS (APCI, MeOH) calcd for $C_{14}H_{17}N_2O^+$ $[M+H]^+$: 229.13409, found: 229.13420. IR (ATR): ν [cm^{-1}] = 2919, 2161, 1667, 1590, 1495, 1434, 1344, 1207, 1159, 1035.



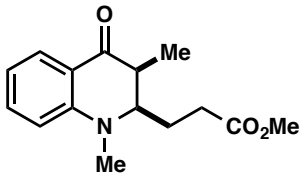
43 (1.4:1 d.r. at C3)

3-(*syn*-1,3-Dimethyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)butanenitrile (43). Prepared according to the standard procedure from **24a** and crotononitrile (*E*:*Z* = ~2:1) with a reaction time of 24 h. Workup was carried out by evaporation of the volatiles under reduced pressure. The residue was dissolved in CH_2Cl_2 and the mixture was cooled to 0 ºC. Aqueous HCl (6M, 4 ml) was added and the mixture stirred at 0 ºC for 3 h. The mixture was allowed to warm to room temperature followed by extraction/drying/concentration as in the standard procedure. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.56) afforded **43** as a 1.2:1 diastereomeric mixture in 28% yield (34.0 mg, 0.140 mmol). The relative configuration of the major diastereomer could not be assigned. NMR data for the diastereomeric mixture: ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 0.85 (d, *J* = 6.9 Hz, 3H), 1.24 (d, *J* = 6.9 Hz, 3H), 1.28 (d, *J* = 7.0 Hz, 3H), 1.29 (d, *J* = 7.0 Hz, 3H), 2.06 (dd, *J* = 8.8, 16.6 Hz, 1H), 2.23 (dd, *J* = 4.7, 16.6 Hz, 1H), 2.29-2.54 (m, 4H), 3.13 (s, 3H), 3.24 (s, 3H), 3.26-3.35 (m, 2H), 3.51 (dd, *J* = 4.0, 6.2 Hz, 1H), 3.65 (dd, *J* = 3.4, 6.4 Hz, 1H), 6.61 (ddd, *J* = 0.4, 0.4, 8.4 Hz, 1H), 6.62 (ddd, *J* = 0.4, 0.4, 8.4 Hz, 1H), 6.65-6.71 (m, 2H), 7.26-7.42 (m, 2H), 7.78 (dd, *J* = 0.4, 1.8 Hz, 1H), 7.79 (dd, *J* = 0.4, 1.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 11.30, 11.48, 16.49, 19.72, 21.75, 24.49, 32.17, 33.16, 41.13, 41.26, 44.06, 44.31, 67.98, 69.43, 112.42, 112.59, 116.47, 116.62, 118.34, 118.58, 119.15, 119.59, 127.29, 127.43, 135.77, 136.05, 150.09, 150.71, 195.62, 195.69. MS (EI, 70 eV): m/z (%) = 242.2 $[M]^+$ (31), 174.2 (100), 146.3 (13). HRMS (APCI, MeOH) calcd for $C_{15}H_{19}N_2O_+$ $[M+H]^+$: 243.1497, found: 243.1494. IR (ATR): ν [cm^{-1}] = 3464, 2936, 2252, 1709, 1673, 1605, 1500, 1313, 1288. 1264, 1252, 1228, 1048, 1037, 936, 859.



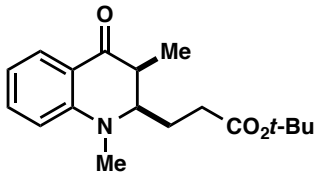
44 (1.6:1 d.r.)

3-(1-Methyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)-3-phenylpropanenitrile (44). Prepared according to the standard procedure from **22a** and cinnamonitrile (1.5 equiv, *E*:*Z* = ~1.2:1) with a reaction time of 24 h on a 1 mmol scale. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.70) afforded **44** as a 1.6:1 diastereomeric mixture in 18% yield (51.4 mg, 0.176 mmol). The relative configuration of the major diastereomer could not be assigned. NMR data for the diastereomeric mixture: ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 2.46 (s, 3H), 2.66 (dd, *J* = 4.1, 17.1 Hz, 1H), 2.73-2.79 (m, 2H), 3.14 (dd, *J* = 5.9, 16.4 Hz, 1H), 3.42 (ddd, *J* = 4.1, 9.0, 9.0 Hz, 1H), 3.93 (ddd, *J* = 2.2, 5.9, 9.5 Hz, 1H), 6.39 (dd, *J* = 0.4, 8.5 Hz, 1H), 6.72 (ddd, *J* = 0.9, 7.1, 7.9 Hz, 1H), 7.13-7.16 (m, 2H), 7.29-7.33 (m, 3H), 7.39 (ddd, *J* = 1.8, 7.1, 8.7 Hz, 1H), 7.86 (ddd, *J* = 0.4, 1.8, 7.8 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 20.44, 39.67, 40.53, 41.29, 65.38, 113.00, 116.60, 117.78, 119.14, 127.63, 127.86, 128.29, 129.19, 136.36, 139.44, 149.43, 192.21. MS (EI, 70 eV): m/z (%) = 290.1 $[M]^+$ (1), 160.0 (100), 131.0 (19). HRMS (APCI, MeOH) calcd for $C_{19}H_{19}N_2O^+$ $[M+H]^+$: 291.14974, found: 291.14980. IR (ATR): ν [cm^{-1}] = 2928, 2252, 1669, 1607, 1563, 1493, 1264, 1206, 1095, 1033, 905.



45

Methyl 3-(*syn*-1,3-dimethyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanoate (45). Prepared according to the standard procedure from **24a** and methyl acrylate with a reaction time of 24 h. Workup was carried out following the procedure for the kinetic quench with TBAF at –78 ºC. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.51) afforded **45** in 35% yield (45.7 mg, 0.175 mmol) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.21 (d, *J* = 7.0 Hz, 3H), 1.85-1.91 (m, 2H), 2.27-2.32 (m, 2H), 3.12 (s, 3H), 3.14 (qd, *J* = 5.4, 7.0 Hz, 1H), 3.52 (ddd, *J* = 5.4, 7.2, 7.2 Hz, 1H), 3.61 (s, 3H), 6.57-6.59 (m, 1H), 6.67 (ddd, *J* = 0.9, 7.1, 7.9 Hz, 1H), 7.37 (ddd, *J* = 1.8, 7.1, 8.5 Hz, 1H), 7.83 (ddd, *J* = 0.4, 1.8, 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 10.95, 21.98, 31.47, 34.49, 45.12, 51.69, 65.59, 112.73, 116.20, 119.25, 127.62, 135.55, 149.53, 173.19, 196.06. MS (EI, 70 eV): m/z (%) = 261.1 $[M]^+$ (53), 174.2 (100), 146.3 (22). HRMS (APCI, MeOH) calcd for $C_{15}H_{20}NO_3^+$ $[M+H]^+$: 262.1443, found: 262.1440. IR (ATR): ν [cm^{-1}] = 2952, 1733, 1673, 1605, 1495, 1564, 1356, 1264, 1201, 1166, 907, 728.



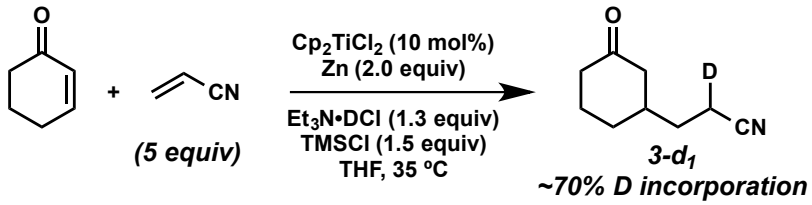
47

***tert*-Butyl 3-(*syn*-1,3-dimethyl-4-oxo-1,2,3,4-tetrahydroquinolin-2-yl)propanoate (47)**. Prepared according to the standard procedure from **24a** and *tert*-butyl acrylate with a reaction time of 24 h. Workup was carried out following the procedure for the kinetic quench with TBAF at –78 ºC. Column chromatography (CH_2Cl_2/EtOAc, 10:1, R_f = 0.62) afforded **47** in 37% yield (56.4 mg, 0.186 mmol) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 400.1 MHz): δ = 1.21 (d, *J* = 7.0 Hz, 3H), 1.42 (s, 9H), 1.79-1.89 (m, 2H), 2.13-2.27 (m, 2H), 3.13 (s, 3H), 3.14 (qd, *J* = 5.3, 7.0 Hz, 1H), 3.50-3.55 (m, 1H), 6.58-6.61 (m, 1H), 6.67 (ddd, *J* = 1.0, 7.1, 7.9 Hz, 1H), 7.38 (ddd, *J* = 1.8, 7.1, 8.6 Hz, 1H), 7.83 (ddd, *J* = 0.4, 1.8, 7.9 Hz, 1H). ^{13}C-NMR ($CDCl_3$, 100.6 MHz): δ = 10.99, 21.89, 28.19, 32.83, 39.57,45.22, 65.58, 80.72, 112.73, 116.09, 119.26, 127.65, 135.53, 149.54, 172.19, 196.19. MS (EI, 70 eV): m/z (%) = 303.0 $[M]^+$ (16), 275.0 (17), 173.9 (100), 146.0 (16). HRMS (ESI, MeOH) calcd for $C_{18}H_{25}NO_3Na^+$ $[M+Na]^+$: 326.1732, found:

326.1730. IR (ATR): ν [cm^{-1}] = 3054, 2984, 1728, 1674, 1564, 1495, 1461, 1355, 1264, 1201, 1166, 1038, 977, 731.

Deuteration experiment with $Et_3N{\cdot}DCl$

The coupling of cyclohexenone (**1**) with acrylonitrile (**2**) was carried out following the standard procedure with $Et_3N{\cdot}DCl$ instead of $Et_3N{\cdot}HCl$. An approximated 70% deuterium incorporation at C2 was observed by ^{1}H NMR. Fragmentation mass analysis (EI, 70 eV) confirmed the deuteration at this position.



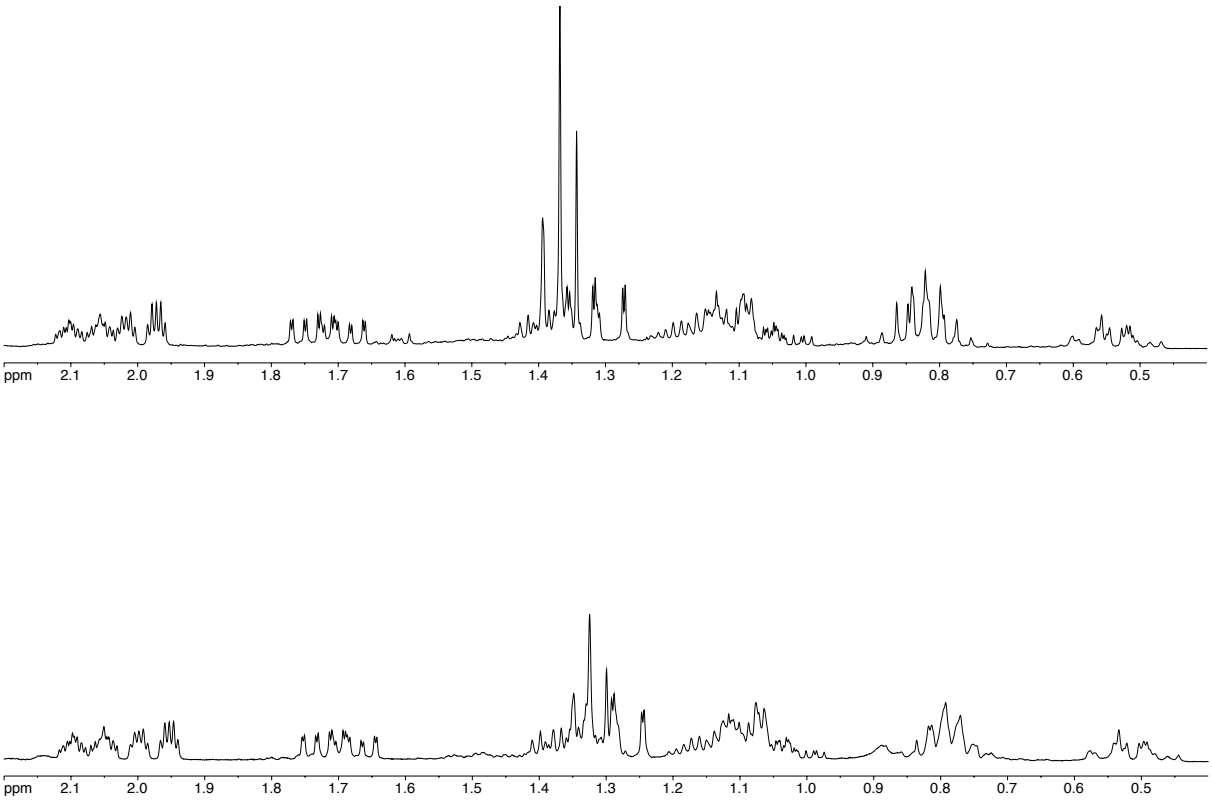


Figure S1. ^{1}H NMR spectra (in benzene-d_6) of the undeuterated **3** (top) and partially deuterated **3–d$_1$** (bottom). The triplet at 1.37 (top) and 1.32 (bottom) is the NMR signal CH_2-group alpha to the nitrile and it is reduced by ~70% in the bottom spectrum.

Computational details

The structure optimisations and single-point calculations were performed on the DFT level with the TURBOMOLE 6.5 package.[27] For these DFT calculations, the resolution-of-identity (RI) approximation[28] for the Coulomb integrals was applied together with matching default auxiliary basis sets.[29] Furthermore, the *m4*-grid was applied. For all structure optimisations and single point calculations, the D3 dispersion correction scheme[30] with applied Becke-Johnson (BJ) damping[31] was used. Structure optimisations were carried out in solution using the TPSS density functional,[32] the triple-zeta basis set def2-TZVP,[33] and the cosmo continuum solvation model (COSMO)[34] as implemented in TURBOMOLE. The dielectric constant was set to 7.4 (THF). The final optimisation level was TPSS-D3-COSMO/def2-TZVP. Stationary points were confirmed by absence of imaginary frequencies in the output of the TURBOMOLE module *NumForce*. Single point energies were calculated in the gas phase on the PW6B95[35]-D3/def2-QZVP level.[33]

Single point energies and spin density populations

[$Cp_2Ti^{III}Cl$]-acrylonitrile:

```
total energy      =  -1868.23074299262 (PW6B95-D3/def2-QZVP)

atomic populations from spin  density:
atom          sum       n(s)      n(p)      n(d)      n(f)      n(g)
  1 c        -0.00387  -0.00016  -0.00378   0.00006   0.00000  -0.00000
  2 c        -0.00259  -0.00037  -0.00258   0.00038  -0.00002   0.00000
  3 c        -0.00301  -0.00059  -0.00225  -0.00018   0.00001  -0.00000
  4 c        -0.00086  -0.00024  -0.00055  -0.00003  -0.00005  -0.00000
  5 h         0.00044  -0.00000   0.00044   0.00000   0.00000   0.00000
  6 c         0.00012   0.00004   0.00019  -0.00006  -0.00005   0.00000
  7 h        -0.00006   0.00004  -0.00011   0.00000  -0.00000   0.00000
  8 h        -0.00005  -0.00006   0.00001   0.00000   0.00000   0.00000
  9 ti        0.69783   0.00833   0.02657   0.66283   0.00013  -0.00003
 10 c         0.00536   0.00013   0.00552  -0.00020  -0.00008   0.00000
 11 c        -0.00001   0.00015  -0.00020   0.00002   0.00001   0.00000
 12 c        -0.01118  -0.00038  -0.01084   0.00002   0.00001  -0.00000
 13 c        -0.00464  -0.00004  -0.00474   0.00018  -0.00004   0.00000
 14 c        -0.00638  -0.00009  -0.00627   0.00000  -0.00002   0.00000
 15 h         0.00023   0.00024  -0.00001   0.00001  -0.00000   0.00000
 16 h         0.00007   0.00006   0.00001   0.00000   0.00000   0.00000
 17 h        -0.00008  -0.00013   0.00005   0.00000   0.00000   0.00000
 18 h        -0.00019  -0.00012  -0.00007  -0.00000   0.00000   0.00000
 19 h         0.00038   0.00031   0.00006   0.00001   0.00000   0.00000
 20 cl        0.05333   0.00010   0.05270   0.00052   0.00001   0.00000
 21 n        -0.01887  -0.00084  -0.01794  -0.00009  -0.00000   0.00000
 22 h        -0.00018  -0.00019   0.00001   0.00000   0.00000   0.00000
 23 h         0.00126   0.00107   0.00018   0.00002   0.00000   0.00000
 24 c         0.11952   0.00225   0.11765   0.00024  -0.00061  -0.00001
 25 c        -0.03191  -0.00118  -0.03110   0.00031   0.00005  -0.00000
 26 c         0.21317   0.00654   0.20805  -0.00144  -0.00003   0.00005
 27 h         0.00023   0.00077  -0.00062   0.00008  -0.00000   0.00000
 28 h        -0.00398  -0.00403   0.00005   0.00001   0.00000   0.00000
 29 h        -0.00407  -0.00445   0.00036   0.00001   0.00000   0.00000
```

[$Cp_2Ti^{III}Cl$]-cyclohexenone:

```
total energy      =  -2007.71887617989 (PW6B95-D3/def2-QZVP)

atomic populations from spin  density:
atom          sum       n(s)      n(p)      n(d)      n(f)      n(g)
  1 c         0.00313  -0.00026   0.00339   0.00007  -0.00006   0.00000
  2 c        -0.00712  -0.00095  -0.00621   0.00003   0.00002  -0.00000
  3 c        -0.00841  -0.00073  -0.00763  -0.00001  -0.00004  -0.00000
  4 c        -0.00400  -0.00018  -0.00363  -0.00013  -0.00006  -0.00000
  5 h        -0.00035  -0.00035  -0.00000   0.00000   0.00000   0.00000
  6 c        -0.00885   0.00013  -0.00899   0.00002  -0.00000  -0.00000
  7 h         0.00021   0.00018   0.00003  -0.00000   0.00000   0.00000
  8 h         0.00022   0.00009   0.00013  -0.00000  -0.00000   0.00000
  9 ti        0.79144   0.00800   0.02076   0.76286  -0.00017  -0.00001
 10 c        -0.00520  -0.00061  -0.00455  -0.00002  -0.00003  -0.00000
 11 c        -0.00429  -0.00021  -0.00414   0.00004   0.00002  -0.00000
 12 c        -0.00406  -0.00064  -0.00313  -0.00022  -0.00007   0.00000
 13 c        -0.01193  -0.00044  -0.01154   0.00005   0.00000  -0.00000
```

14	c	0.00824	-0.00002	0.00843	-0.00004	-0.00013	0.00000
15	h	0.00065	0.00063	0.00001	0.00001	0.00000	0.00000
16	h	0.00028	0.00025	0.00003	0.00000	0.00000	0.00000
17	h	-0.00028	-0.00030	0.00002	-0.00000	0.00000	0.00000
18	h	0.00020	0.00016	0.00003	0.00001	0.00000	0.00000
19	h	-0.00011	-0.00013	0.00002	0.00000	0.00000	0.00000
20	o	-0.04948	0.00010	-0.04956	-0.00002	0.00000	0.00000
21	cl	0.01654	-0.00196	0.01800	0.00051	-0.00001	0.00000
22	h	-0.00008	-0.00012	0.00003	0.00001	0.00000	0.00000
23	h	-0.00013	-0.00012	-0.00002	-0.00000	0.00000	0.00000
24	c	0.15504	0.00421	0.15461	-0.00354	-0.00030	0.00006
25	c	-0.00301	-0.00037	-0.00276	0.00012	0.00000	-0.00000
26	c	-0.05126	-0.00119	-0.05013	0.00009	-0.00003	-0.00000
27	c	0.15656	0.00399	0.15333	-0.00072	-0.00007	0.00003
28	c	-0.00197	-0.00044	-0.00159	0.00004	0.00001	0.00000
29	c	0.00427	0.00025	0.00412	-0.00010	0.00000	0.00000
30	h	0.01119	0.01102	0.00016	0.00000	0.00000	0.00000
31	h	0.00307	0.00301	0.00005	0.00001	0.00000	0.00000
32	h	-0.00020	-0.00020	-0.00000	0.00000	0.00000	0.00000
33	h	-0.00035	-0.00032	-0.00003	0.00000	0.00000	0.00000
34	h	0.00216	0.00204	0.00011	0.00001	0.00000	0.00000
35	h	0.00972	0.00946	0.00026	-0.00000	0.00000	0.00000
36	h	0.00029	0.00096	-0.00072	0.00004	0.00000	0.00000
37	h	-0.00212	-0.00227	0.00014	0.00000	0.00000	0.00000

Coordinates

[$Cp_2Ti^{III}Cl$]-cyclohexenone:

Energy = -2006.099278697

C	1.9330301	-2.1139811	-0.6597398
C	3.0690138	-1.3247282	-0.9468576
C	3.6923367	-0.9809529	0.2880476
C	2.9424755	-1.5691760	1.3311572
H	3.3973010	-1.0208035	-1.9309686
C	1.8449615	-2.2560668	0.7522441
H	1.2215688	-2.4894127	-1.3819365
H	1.0546037	-2.7567258	1.2934428
Ti	1.5257641	0.0507888	0.2595248
C	0.5684220	1.8913562	-0.9880318
C	1.0631786	2.4183309	0.2221549
C	1.6608719	1.3603870	-1.7217833
C	2.8434972	1.6066250	-0.9705271
C	2.4756999	2.2316048	0.2443602
H	1.6040980	0.8711117	-2.6849821
H	-0.4713166	1.8462380	-1.2816024
H	0.4761067	2.8501800	1.0188036
H	3.8473971	1.3371525	-1.2652137
H	3.1422646	2.5149076	1.0474924
O	-0.3304426	-0.6357137	-0.0025959
Cl	1.0010222	0.4544972	2.6022839
H	4.5735195	-0.3655001	0.4090986
H	3.1364138	-1.4620523	2.3881001
C	-1.5702794	-0.3282814	0.0789093
C	-2.5597084	-1.2378540	-0.6055539
C	-2.0433383	0.8383856	0.7557540
C	-3.3698346	1.1513673	0.7961765
C	-4.4231241	0.2872476	0.1694221
C	-3.9477989	-1.1672010	0.0446855
H	-4.6735259	0.6868963	-0.8273670
H	-5.3476631	0.3434135	0.7557231
H	-4.6649970	-1.7568470	-0.5353466
H	-3.8939509	-1.6079257	1.0478941
H	-2.1602004	-2.2572351	-0.6008177
H	-2.6258181	-0.9275330	-1.6607643
H	-1.3051750	1.4583652	1.2533416
H	-3.6863733	2.0591352	1.3054720

[$Cp_2Ti^{III}Cl$]-acrylonitrile:

Energy = -1868.182311675

C	1.1633983	2.2755663	0.9800111

C	2.1555398	1.8709299	0.0580452
C	1.5118369	1.5993245	-1.1853870
C	0.1231065	1.8044116	-1.0175927
H	3.2150700	1.7870756	0.2596725
C	-0.0927166	2.2189373	0.3320405
H	1.3270739	2.5140189	2.0201036
H	-1.0497398	2.4268730	0.7895533
Ti	0.7178213	-0.0120574	0.3577037
C	2.2796596	-1.7467887	0.7398811
C	0.9951802	-2.3471179	0.6103790
C	2.6125773	-1.1636127	-0.5042967
C	1.5358804	-1.4000508	-1.4077639
C	0.5509445	-2.1466648	-0.7223354
H	3.5178879	-0.6159992	-0.7275199
H	2.8724723	-1.7061200	1.6425536
H	0.4417432	-2.8354788	1.3994033
H	1.4787814	-1.0683547	-2.4352435
H	-0.3964214	-2.4677579	-1.1321143
Cl	0.5505567	-0.1039732	2.8078042
N	-1.3158107	-0.3465833	0.2981539
H	2.0017409	1.2784925	-2.0934690
H	-0.6390292	1.6605932	-1.7715841
C	-2.4717901	-0.5166323	0.2342003
C	-3.8542498	-0.7417806	0.1541469
C	-4.7690067	0.2532210	0.0710864
H	-4.1579088	-1.7864658	0.1666313
H	-4.4788240	1.2985699	0.0598299
H	-5.8257738	0.0174246	0.0161066

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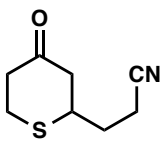
^{1}H and ^{13}C NMR Spectra of new compounds


O
CN
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ppm
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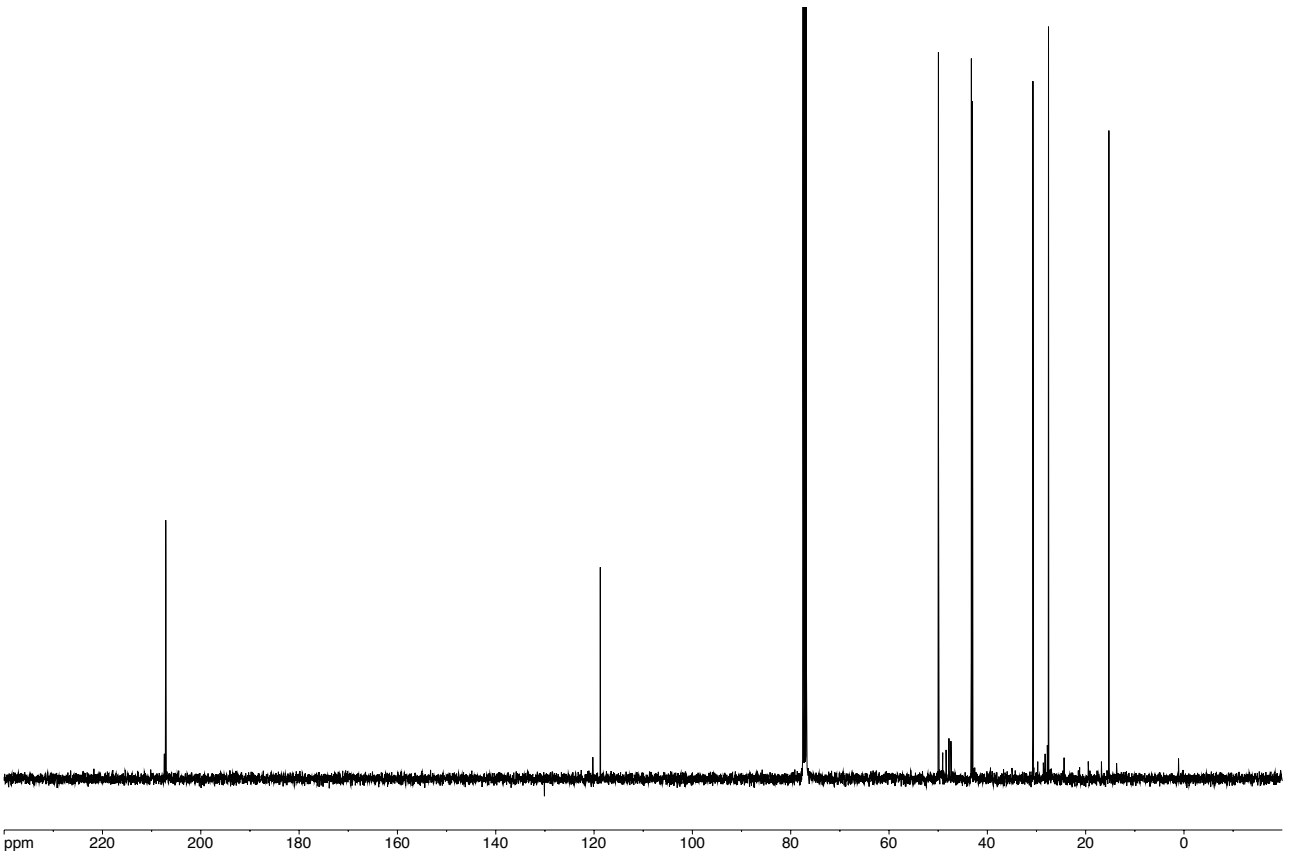
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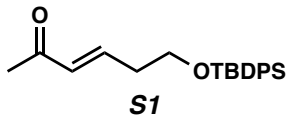
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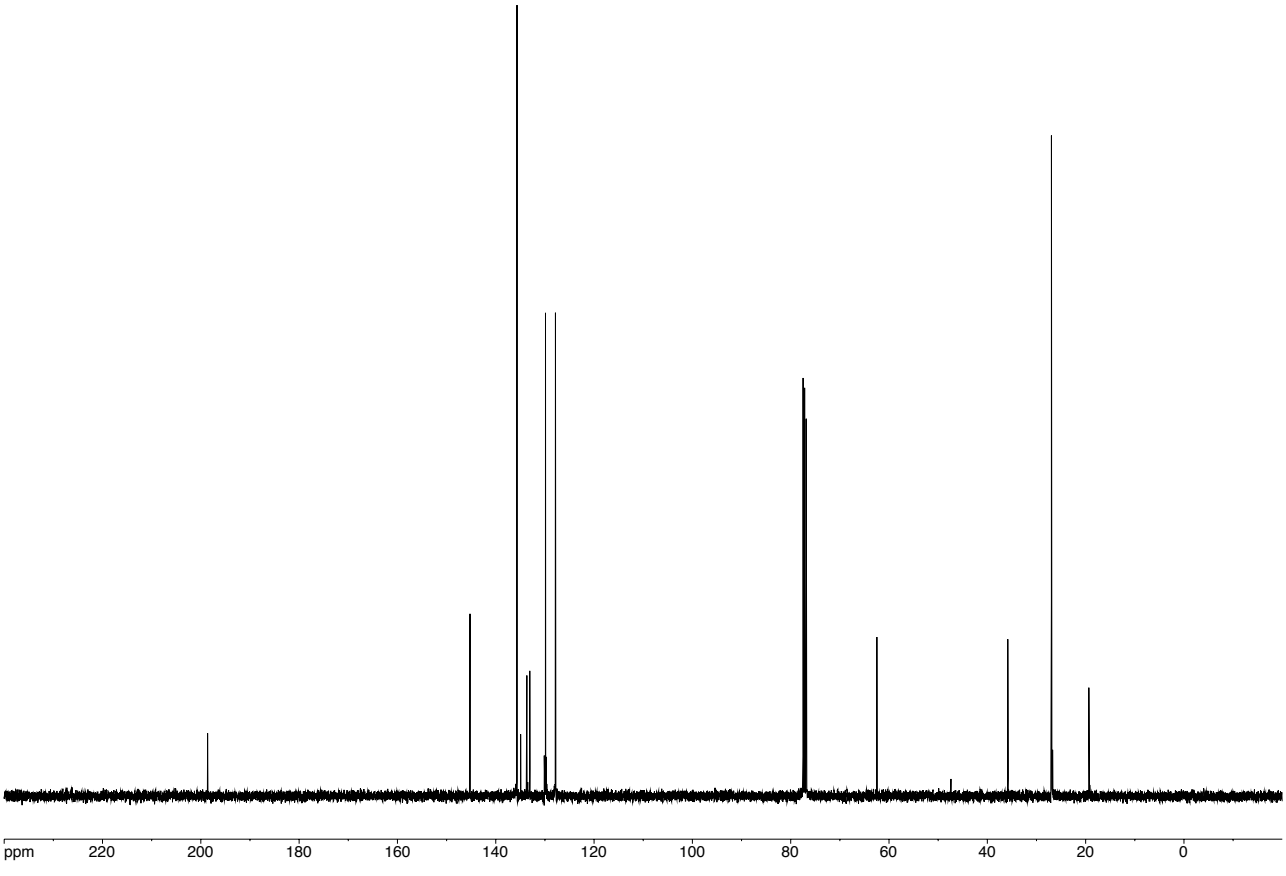
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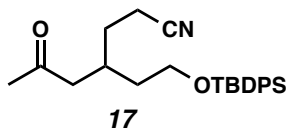
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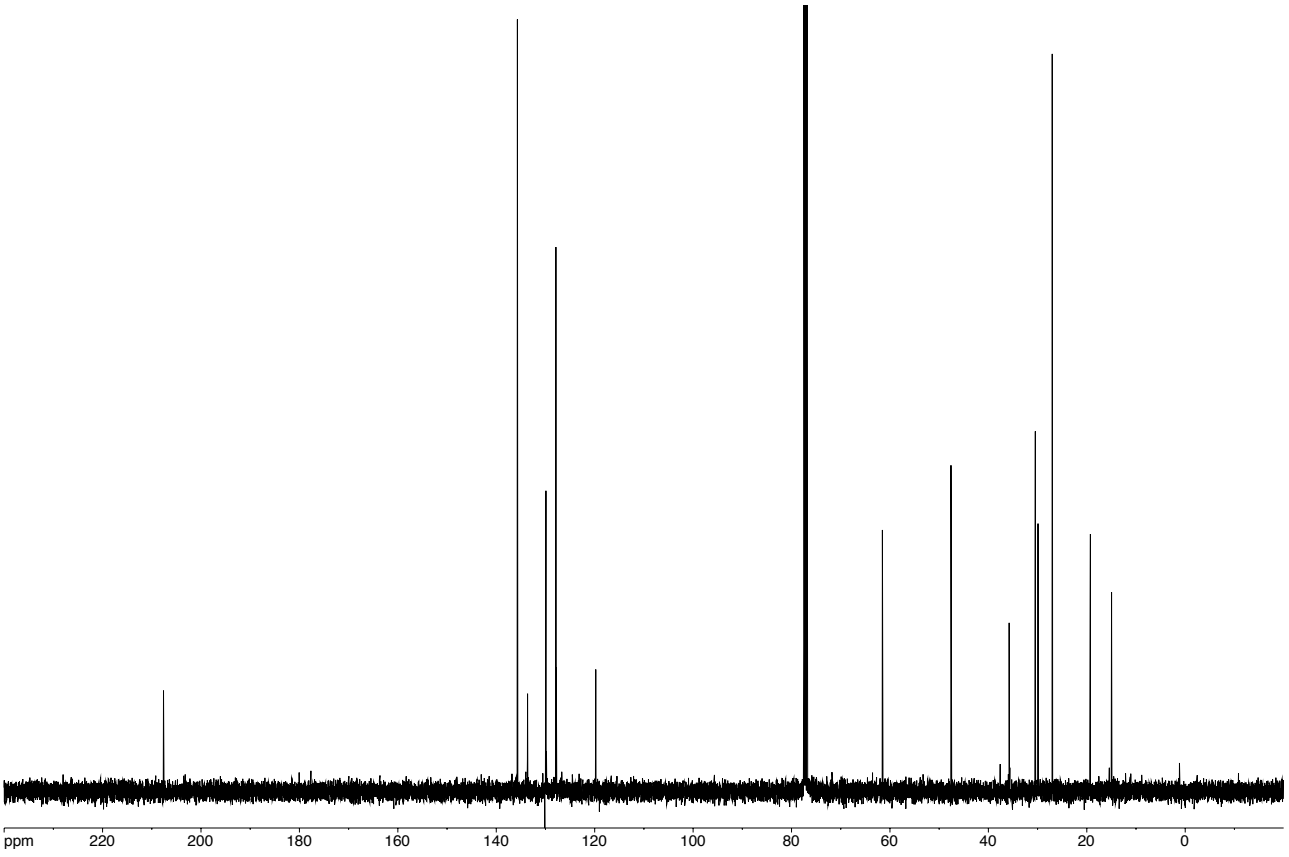
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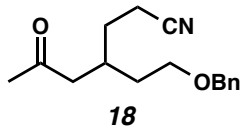
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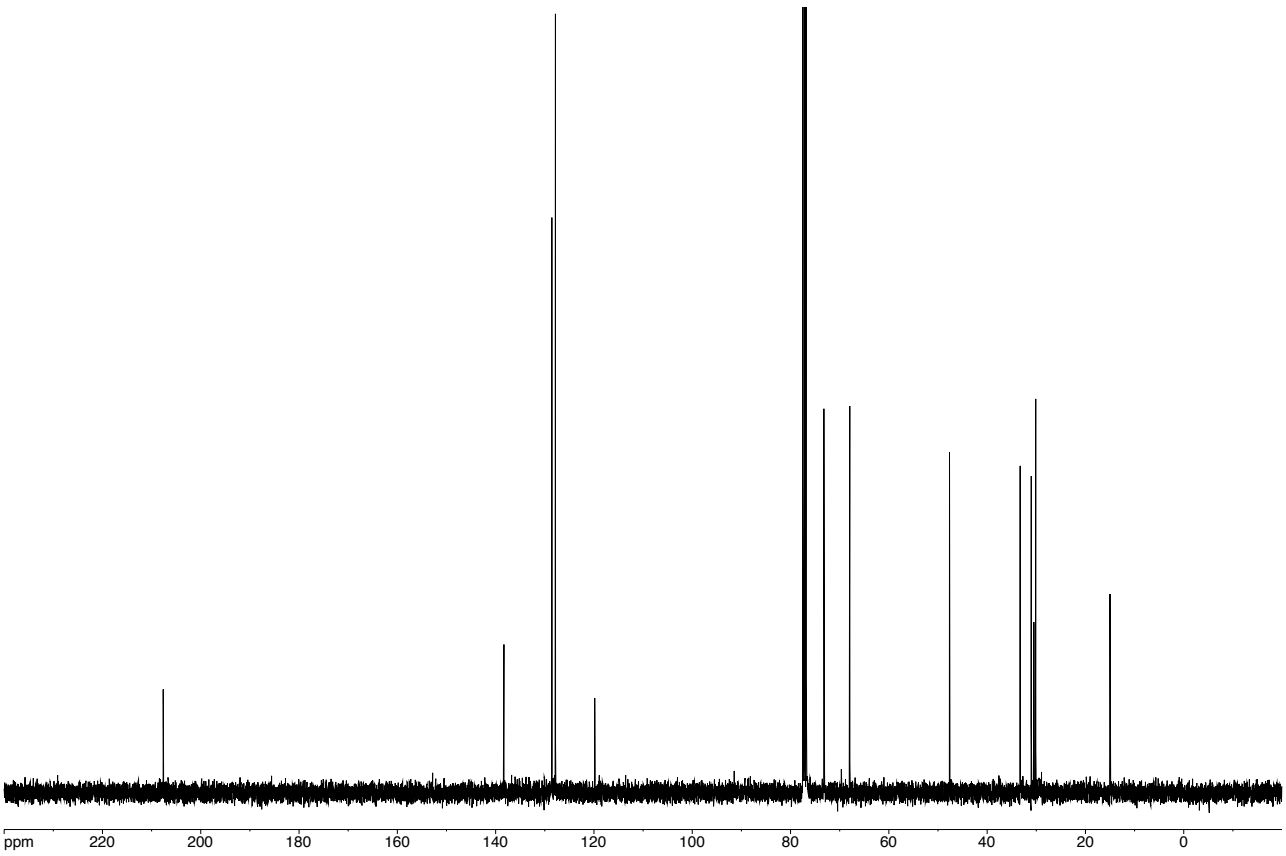
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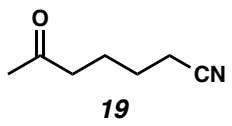
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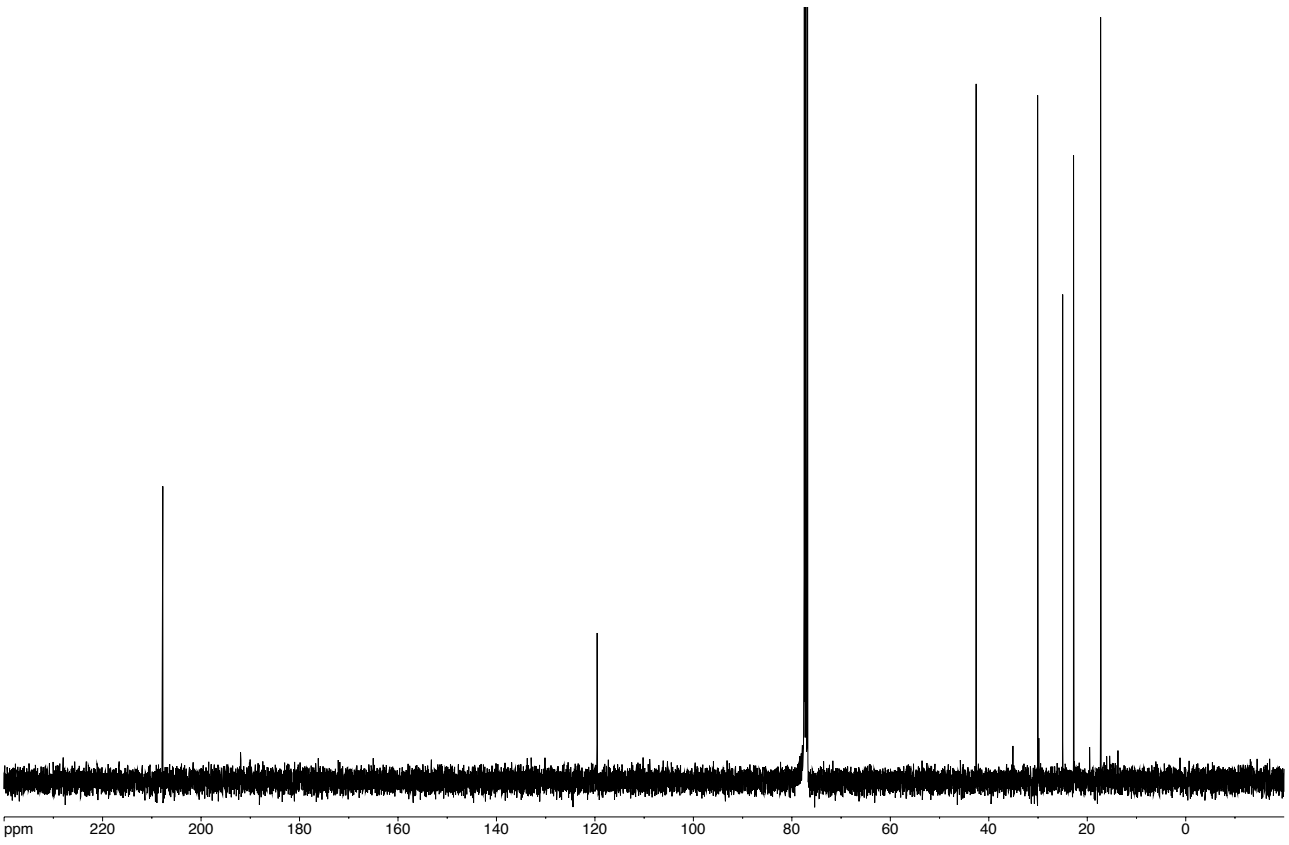
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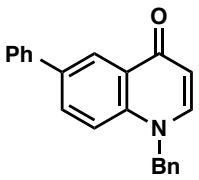
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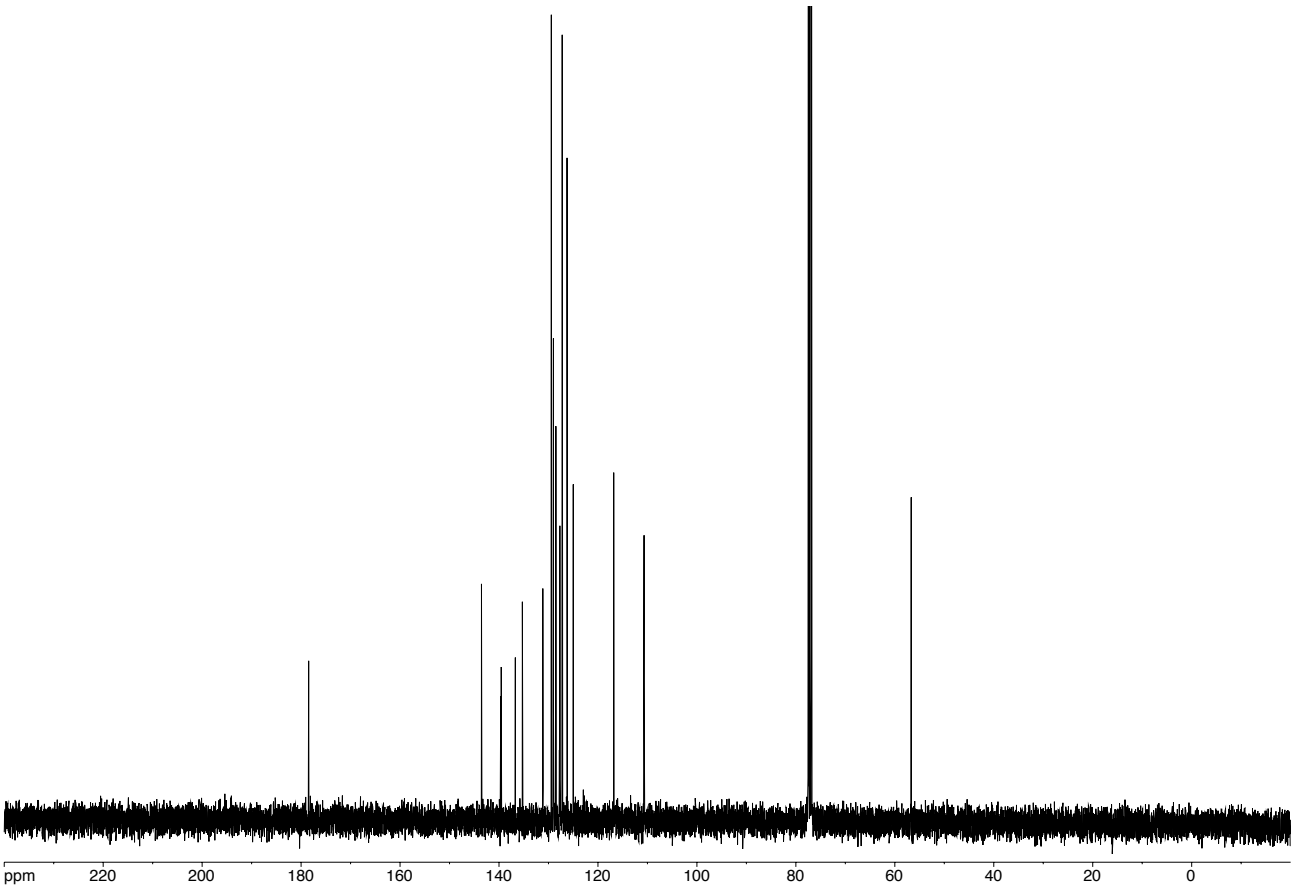
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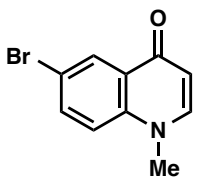
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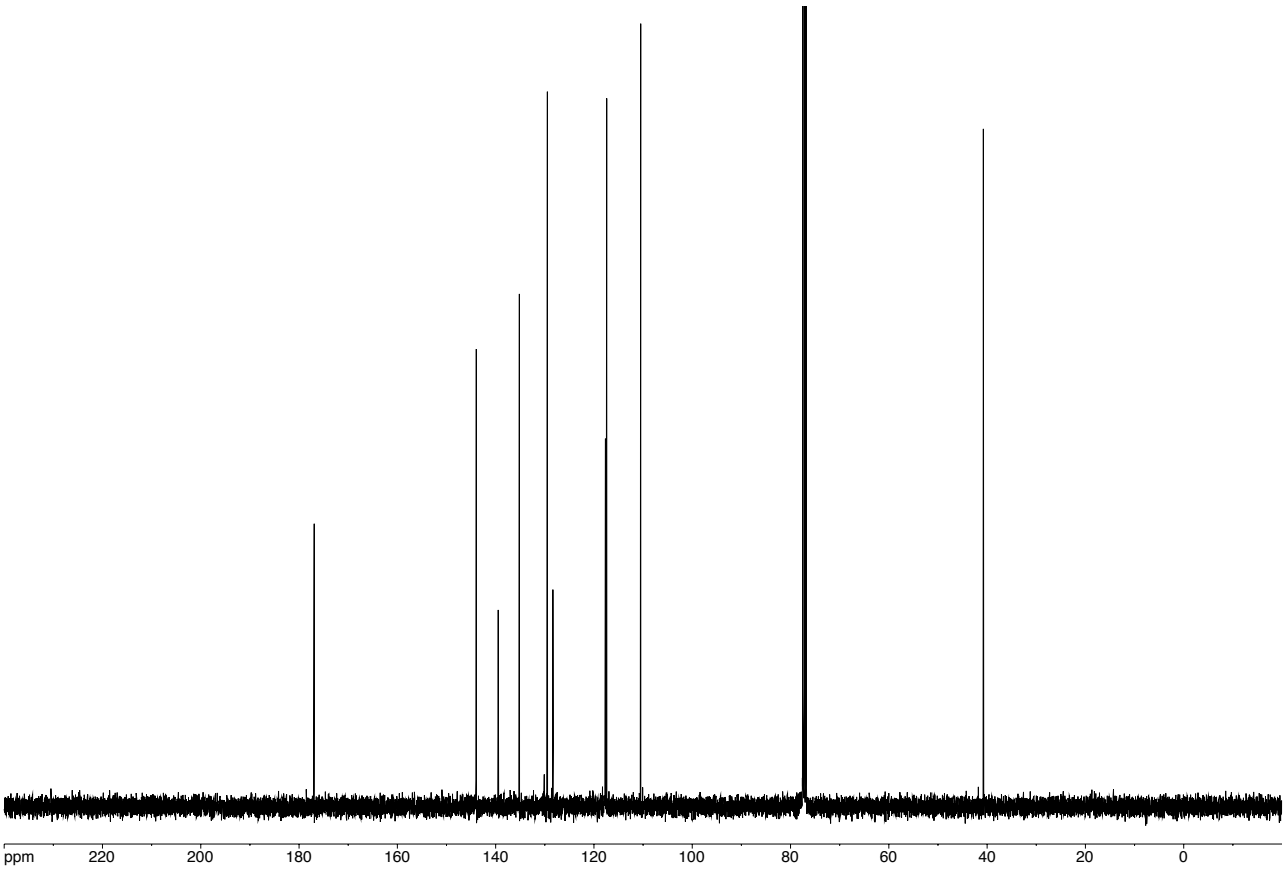
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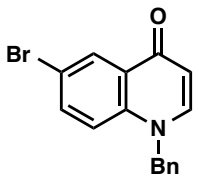
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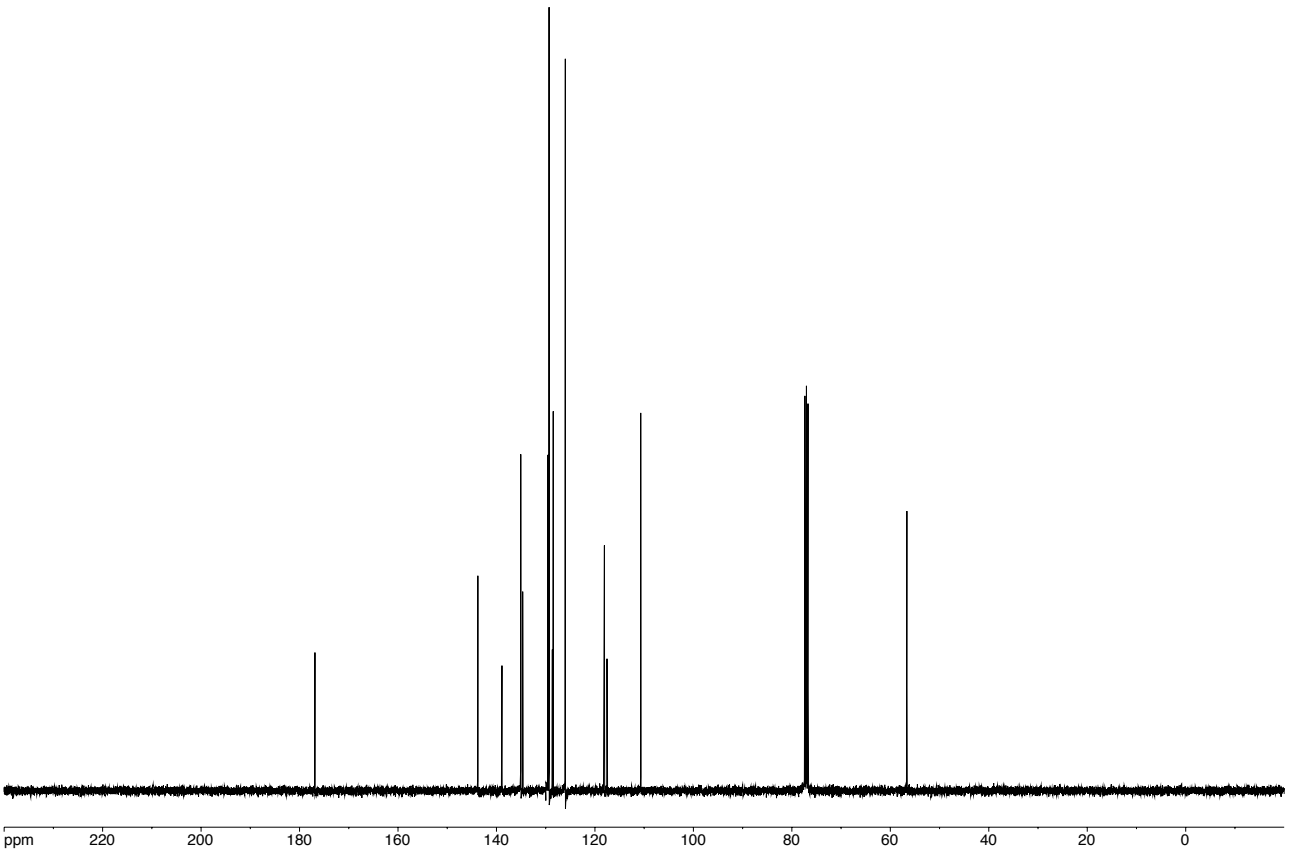
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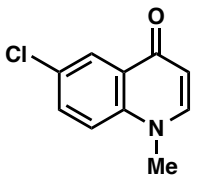
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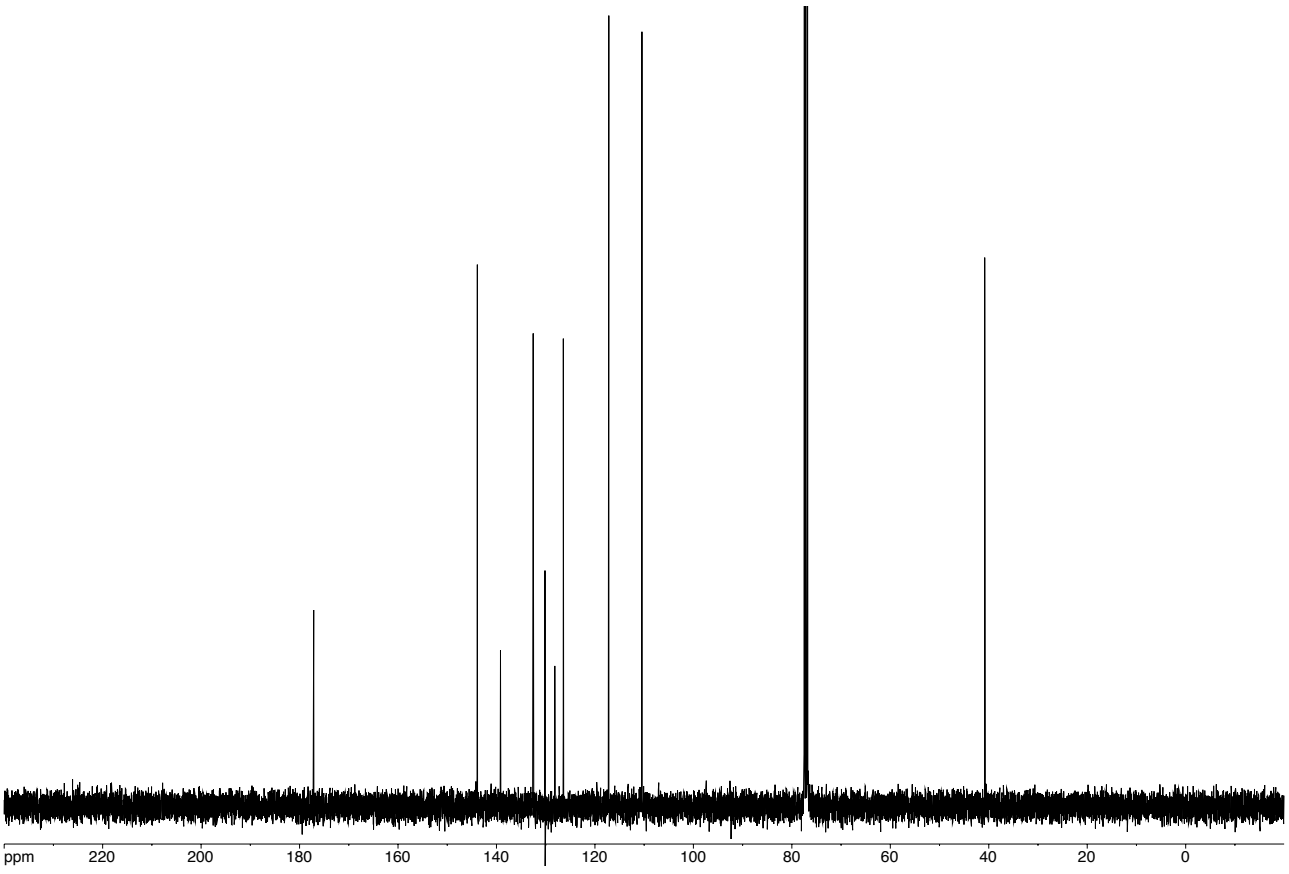
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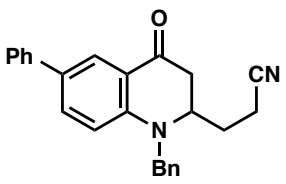
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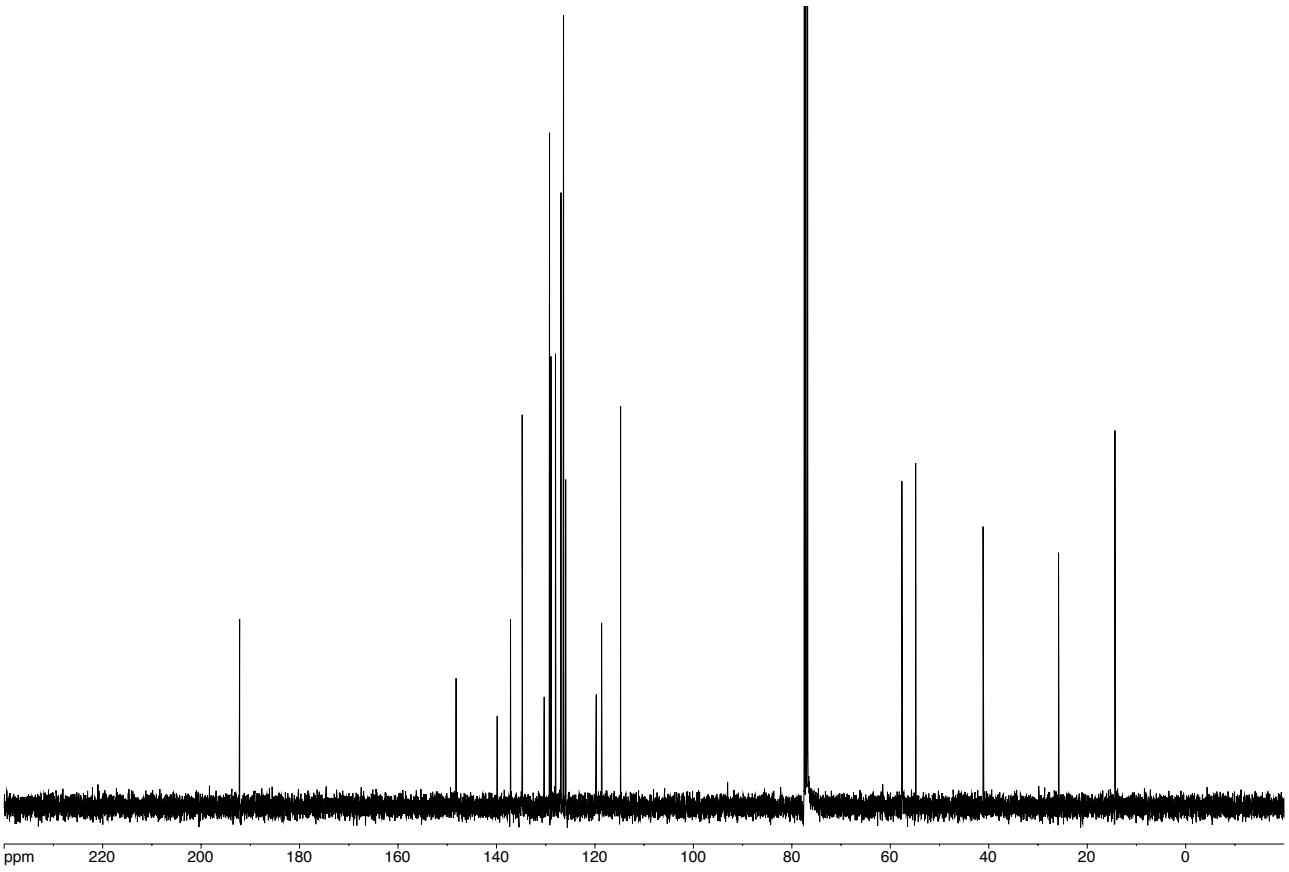
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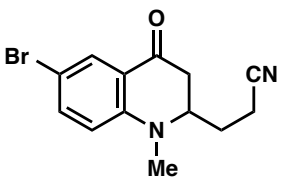
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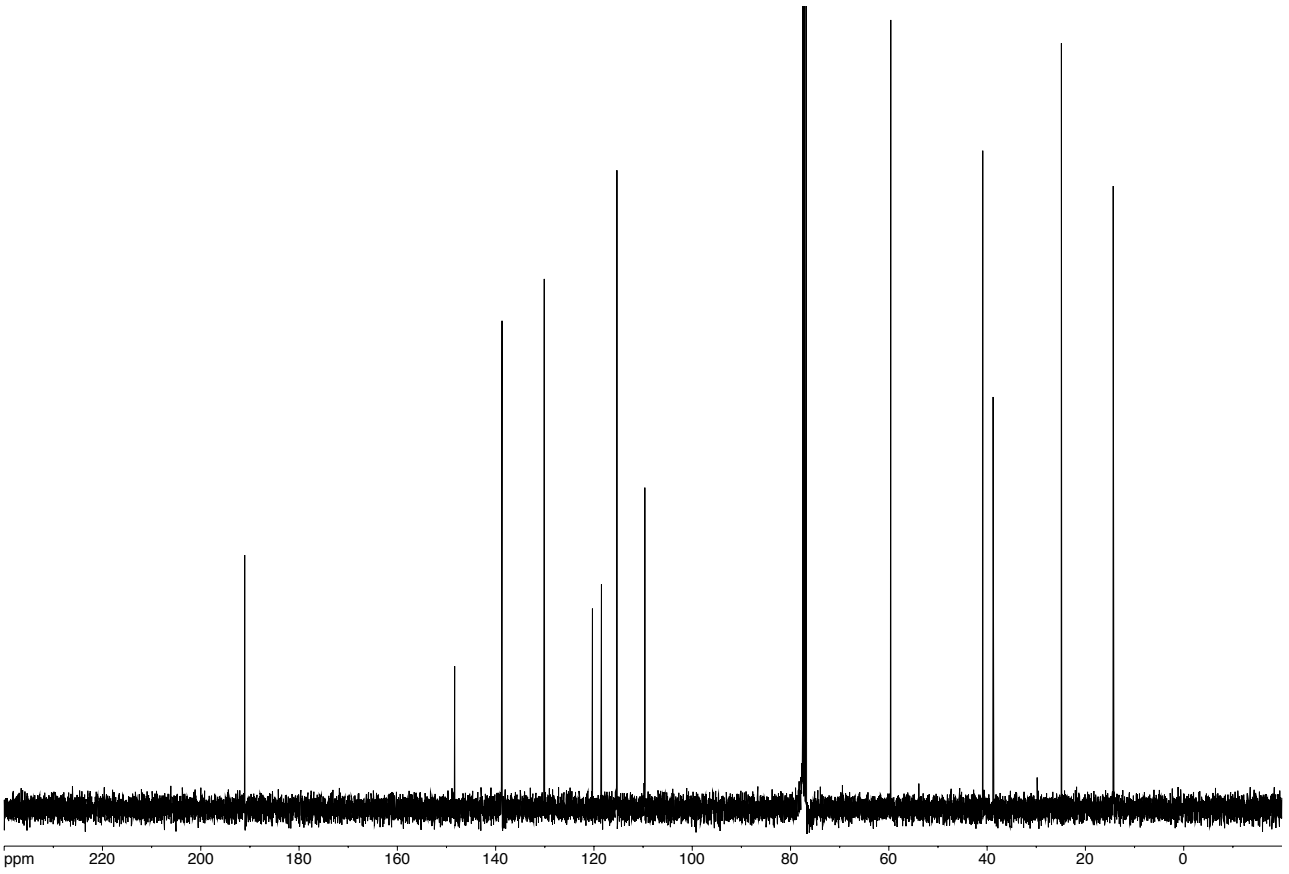
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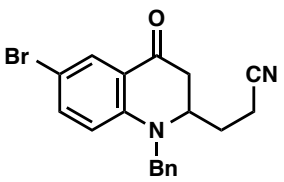
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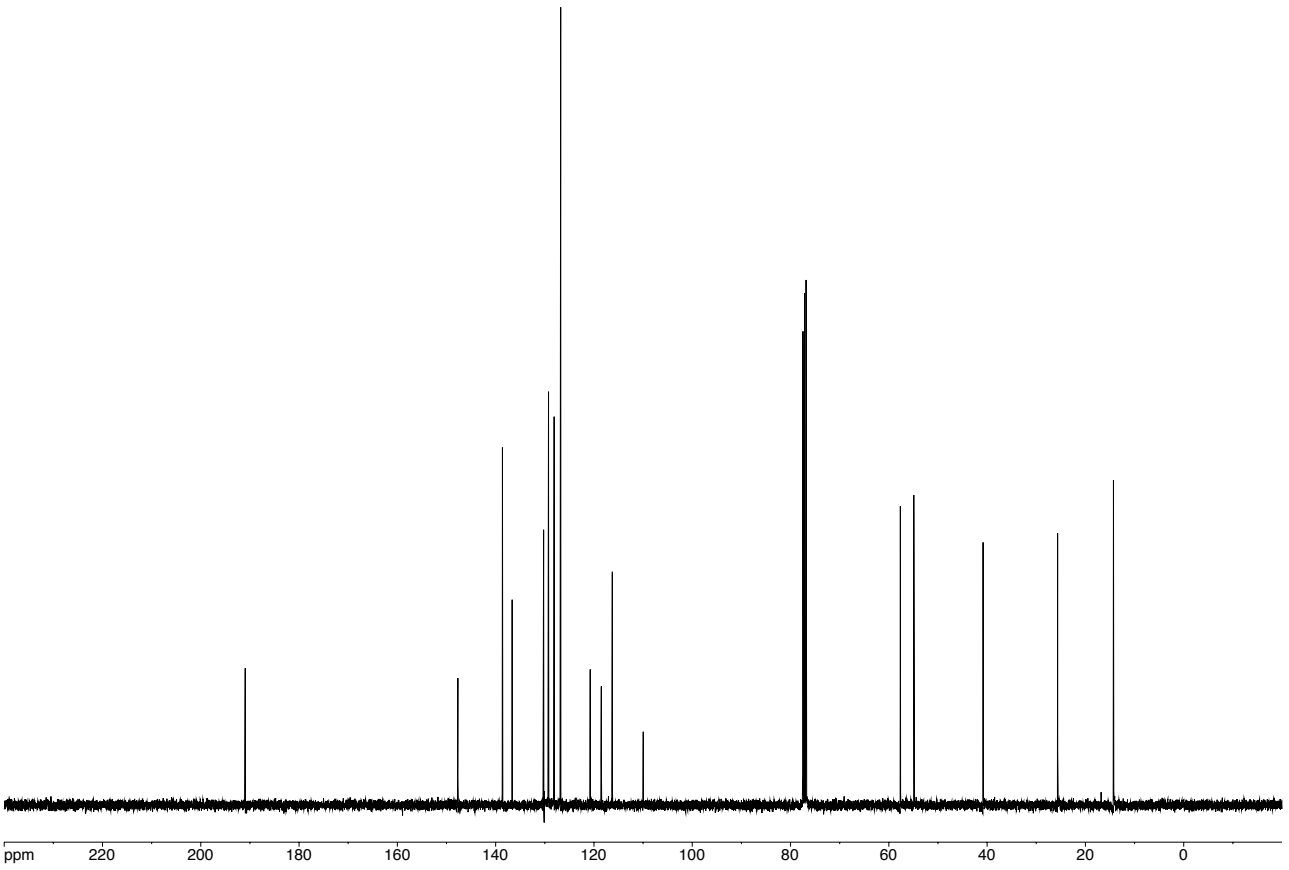
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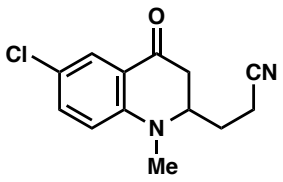
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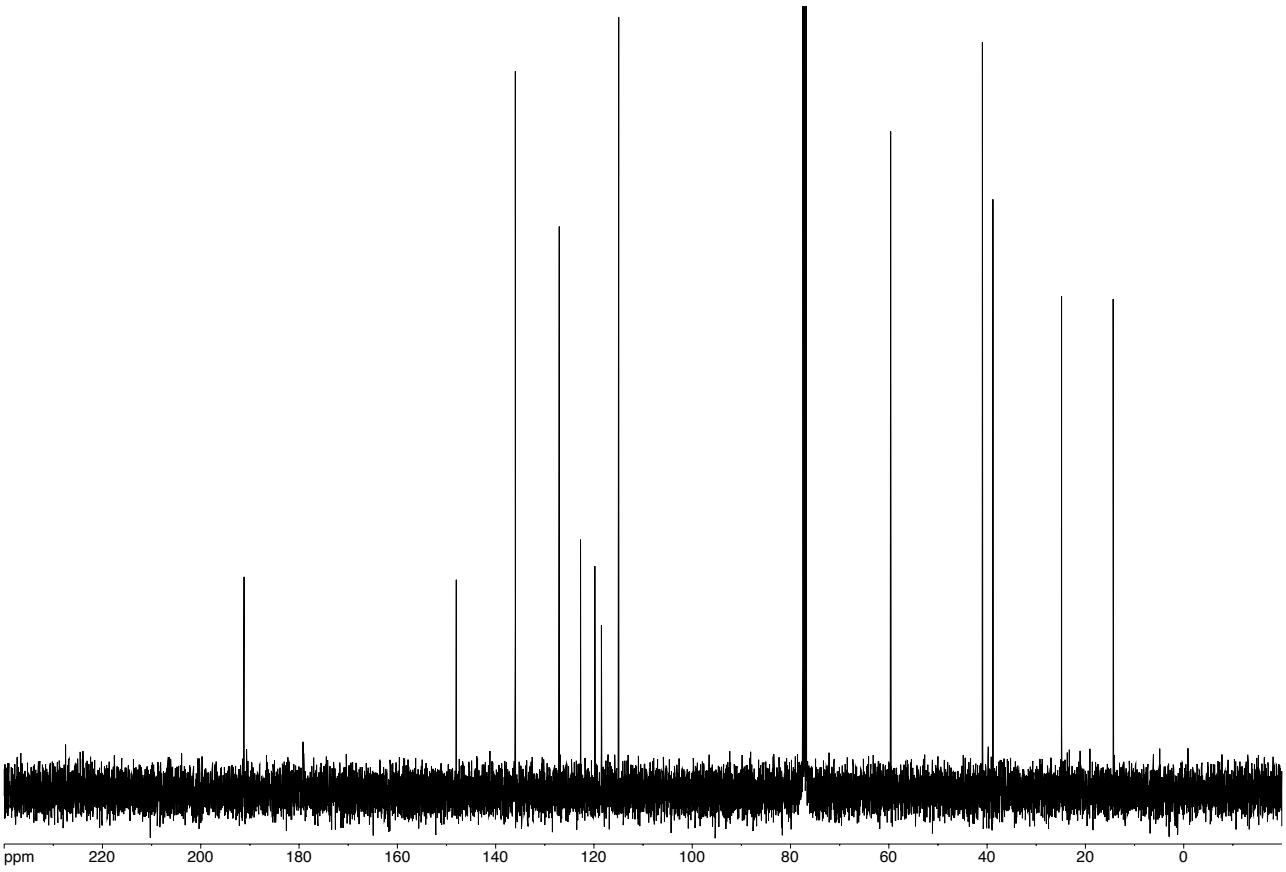
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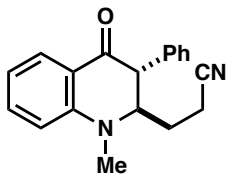
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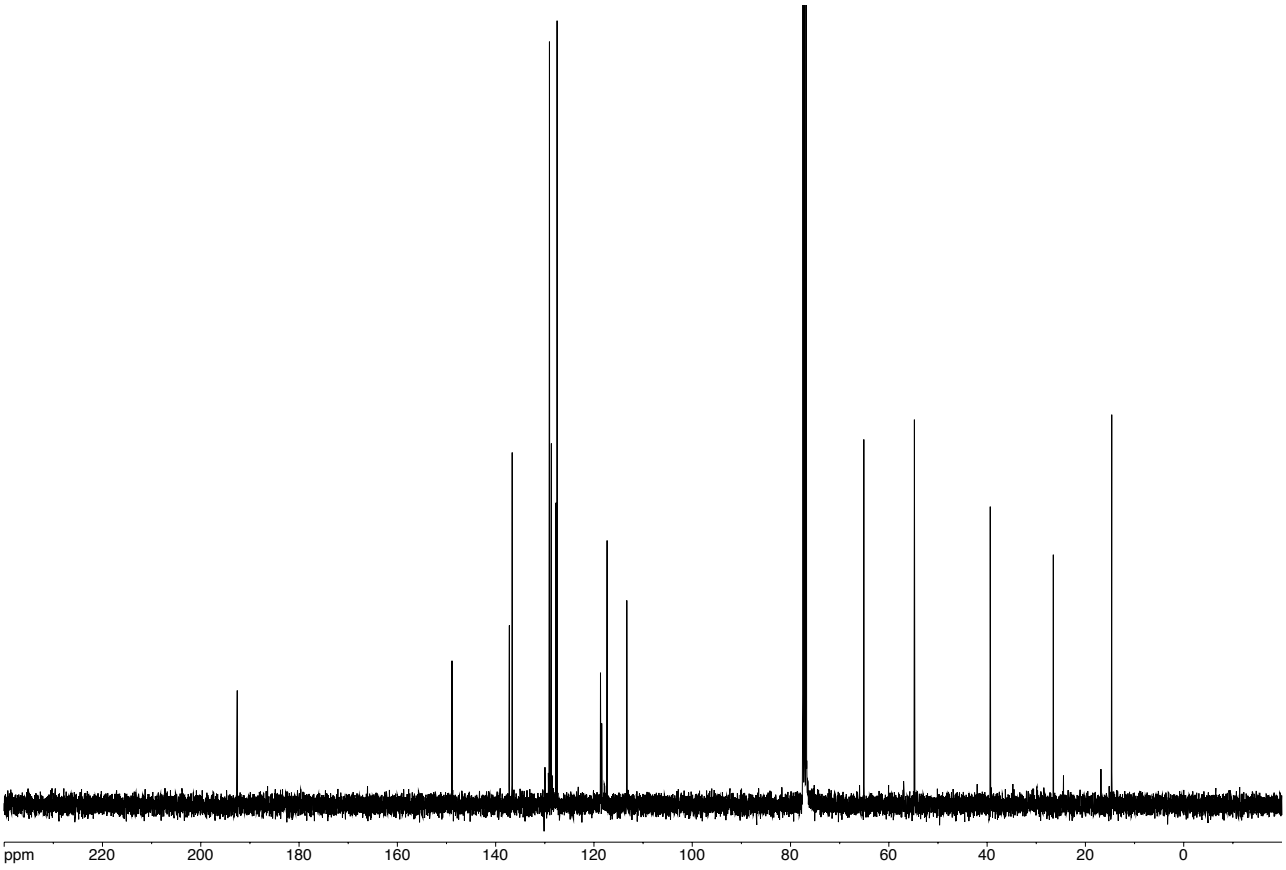
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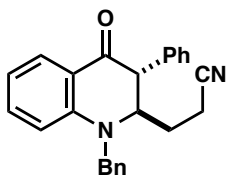
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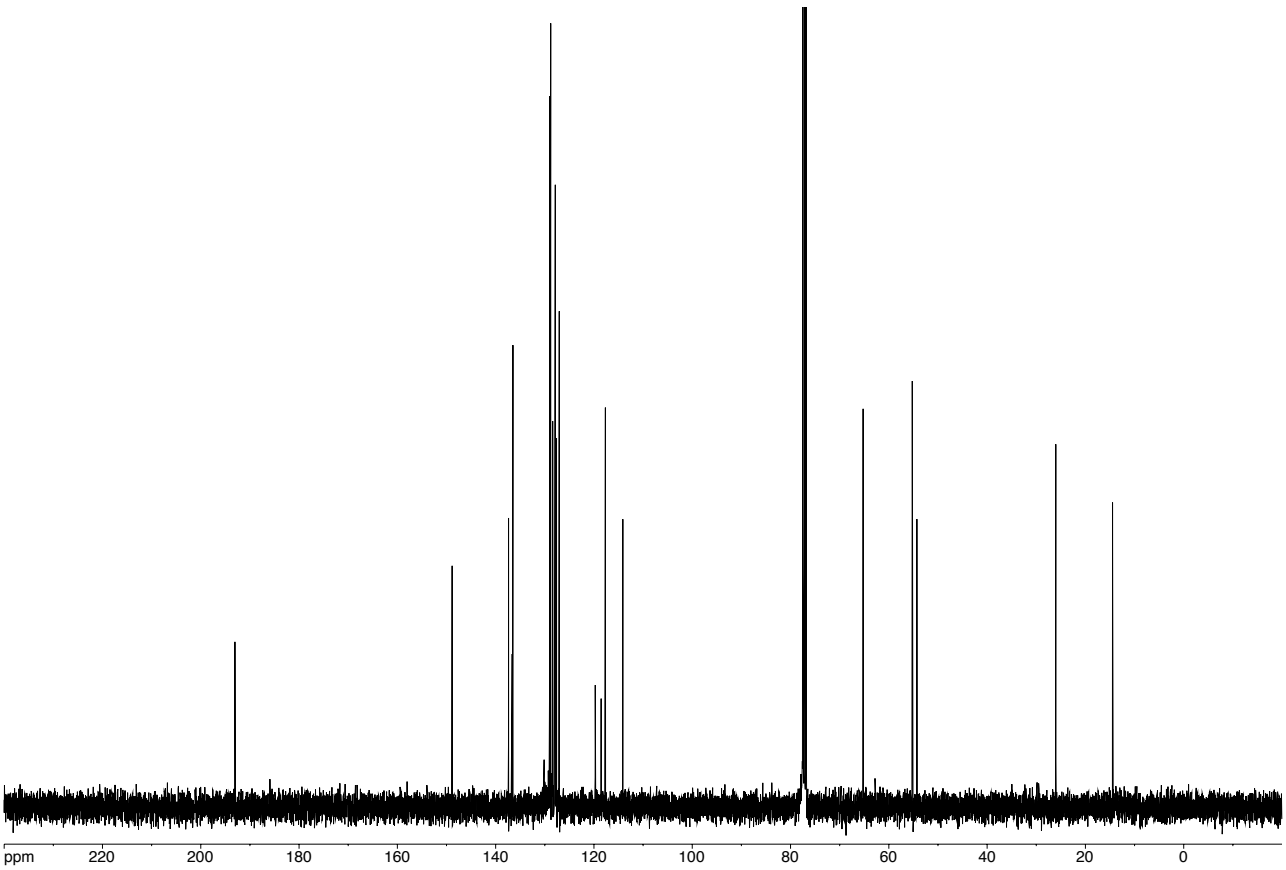
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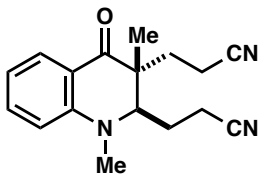
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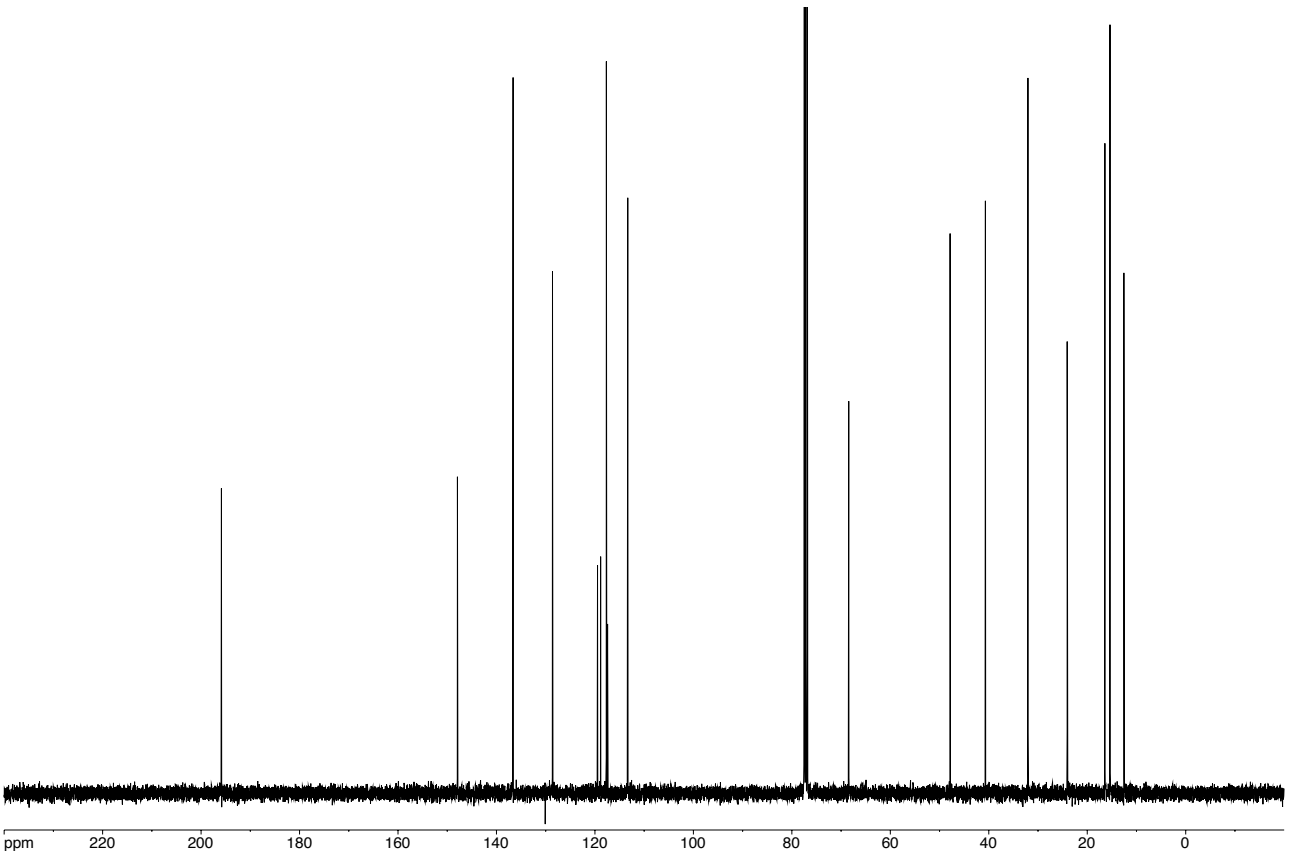
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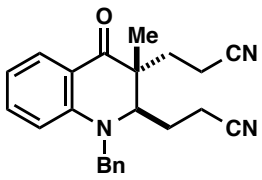
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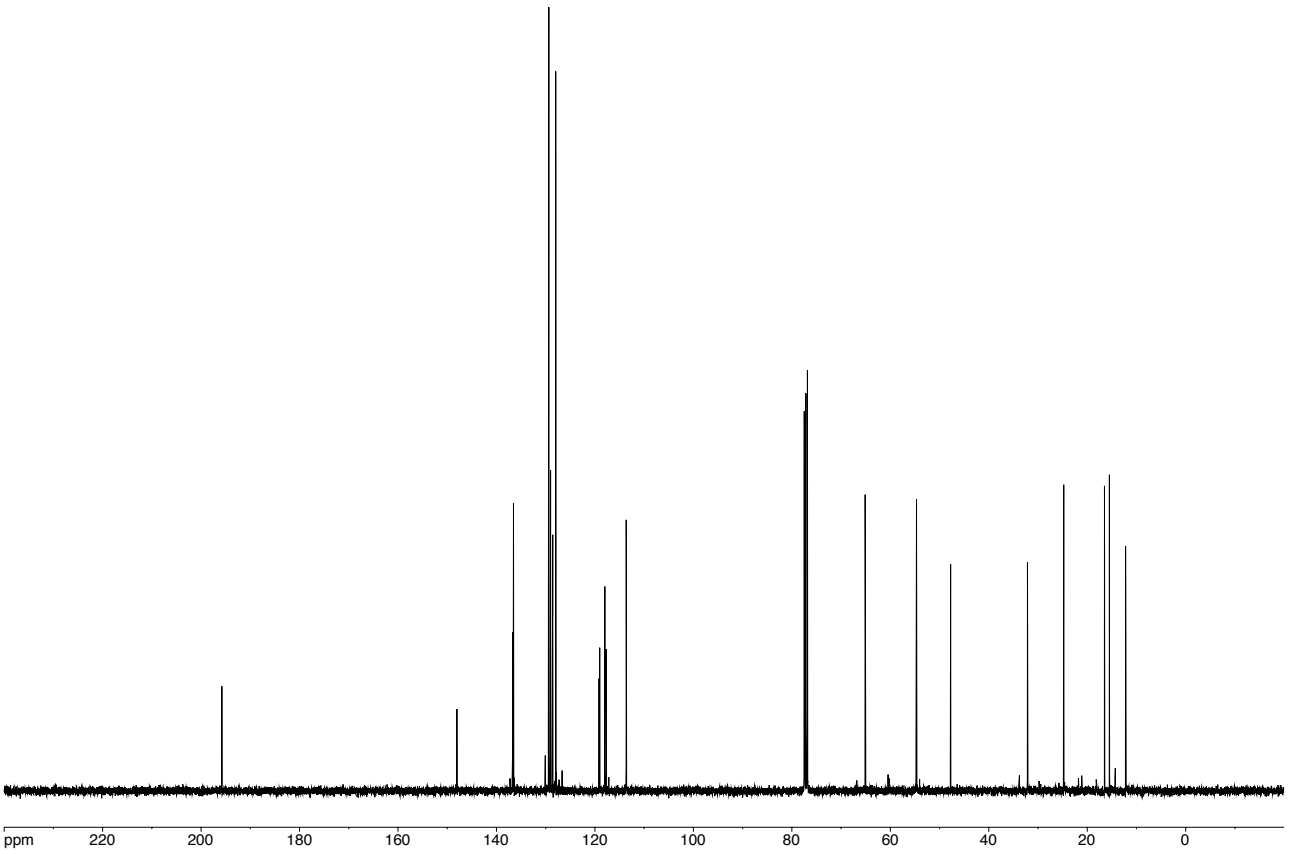
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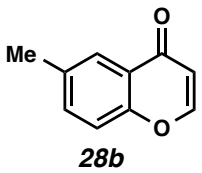
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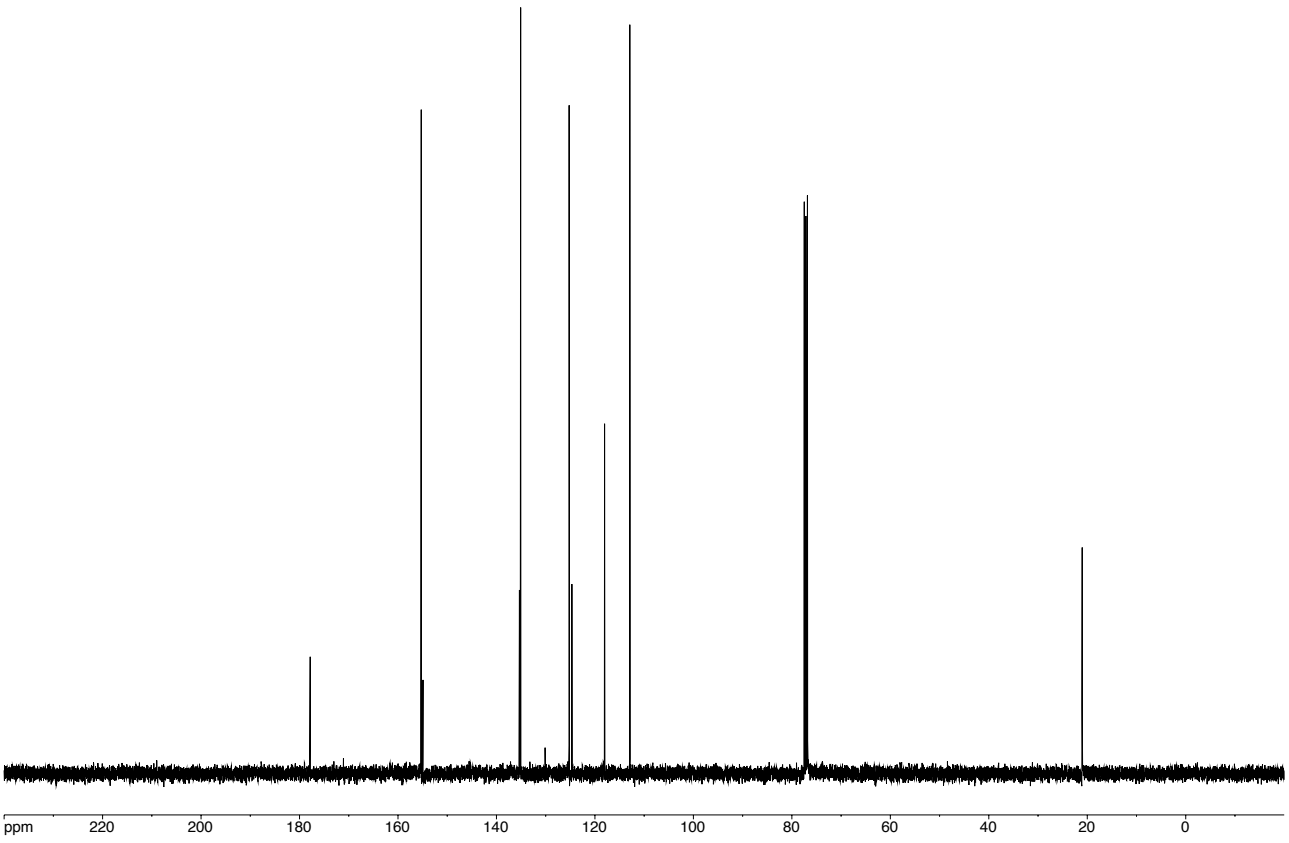
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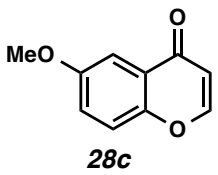
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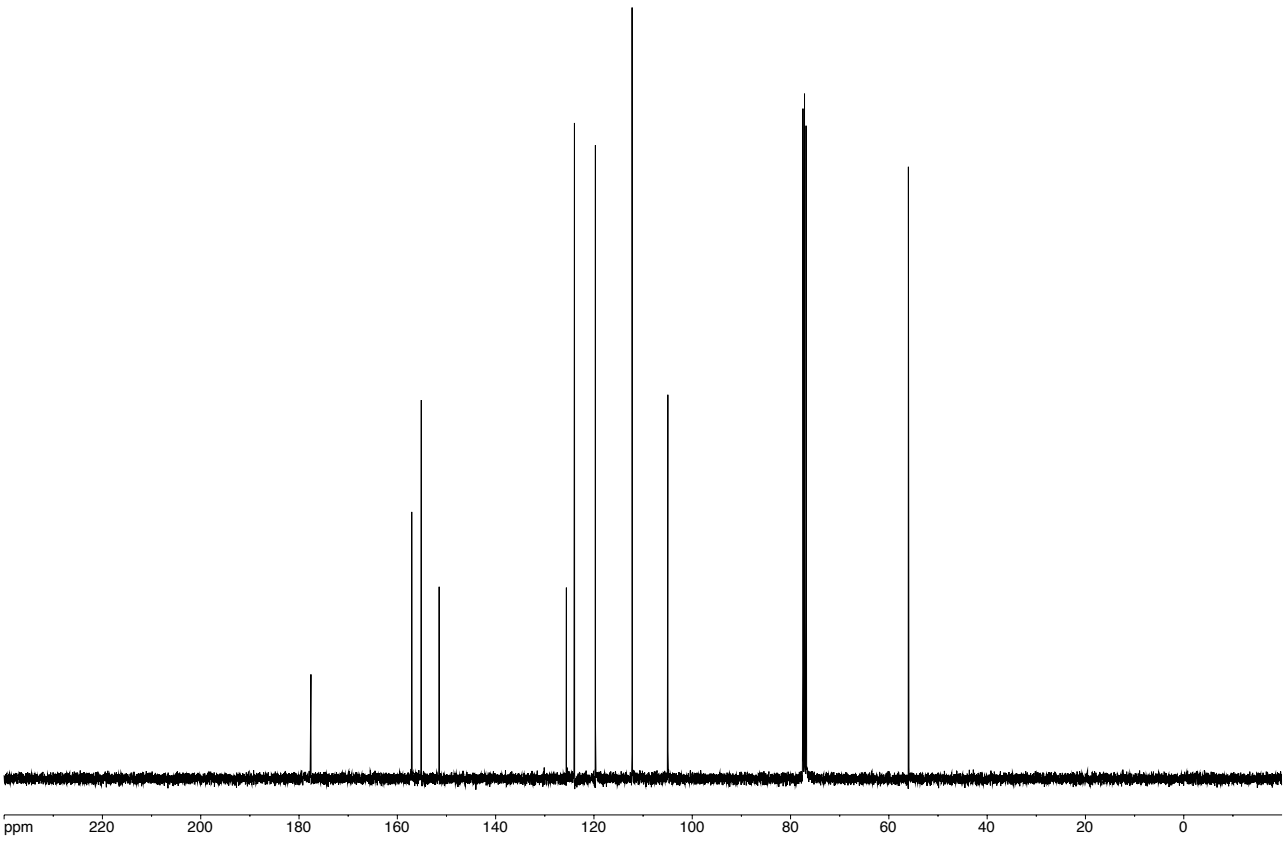
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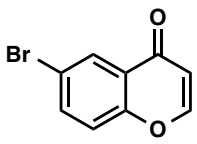
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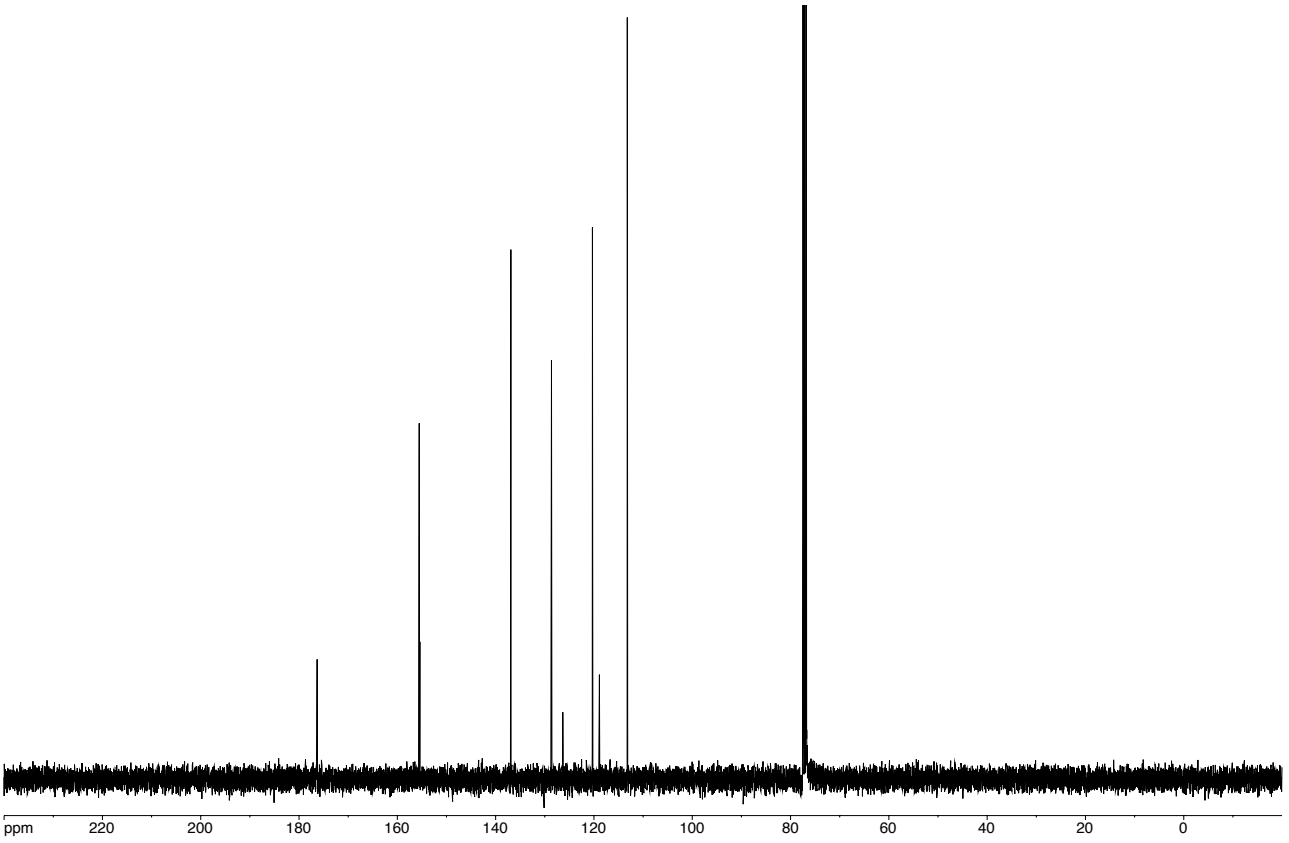
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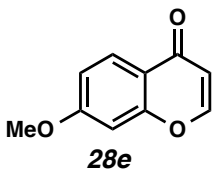
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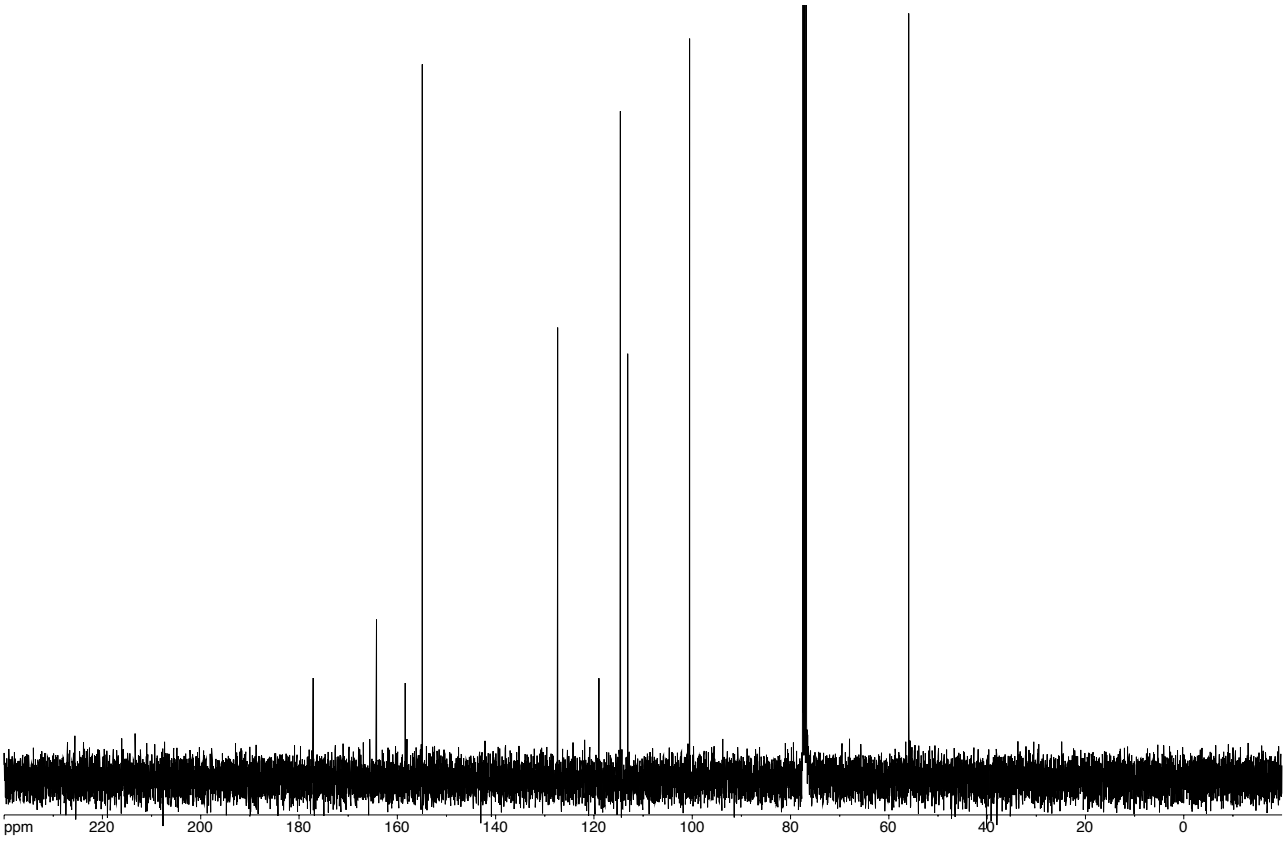
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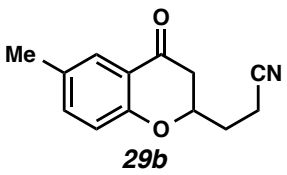
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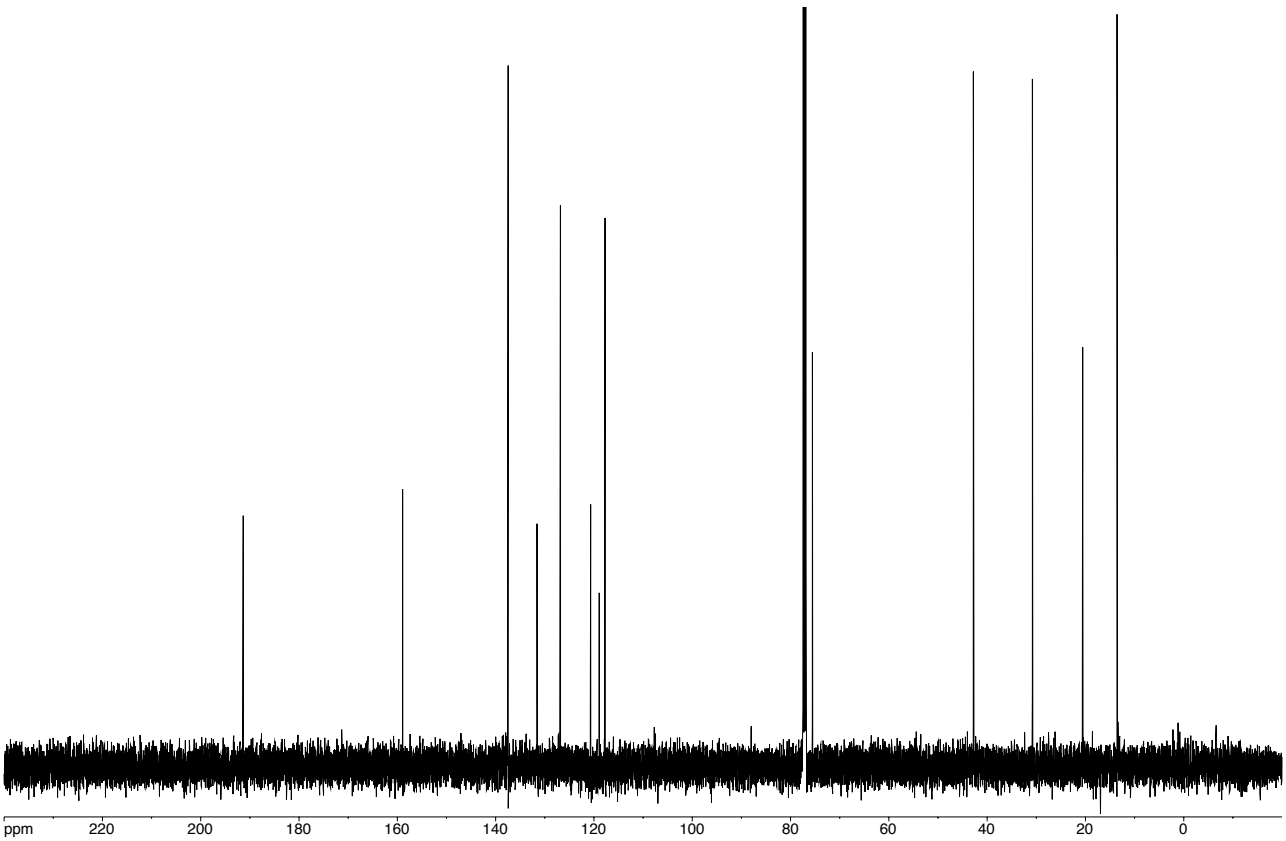
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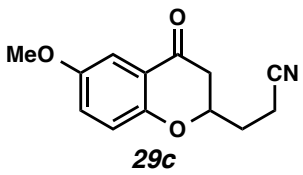
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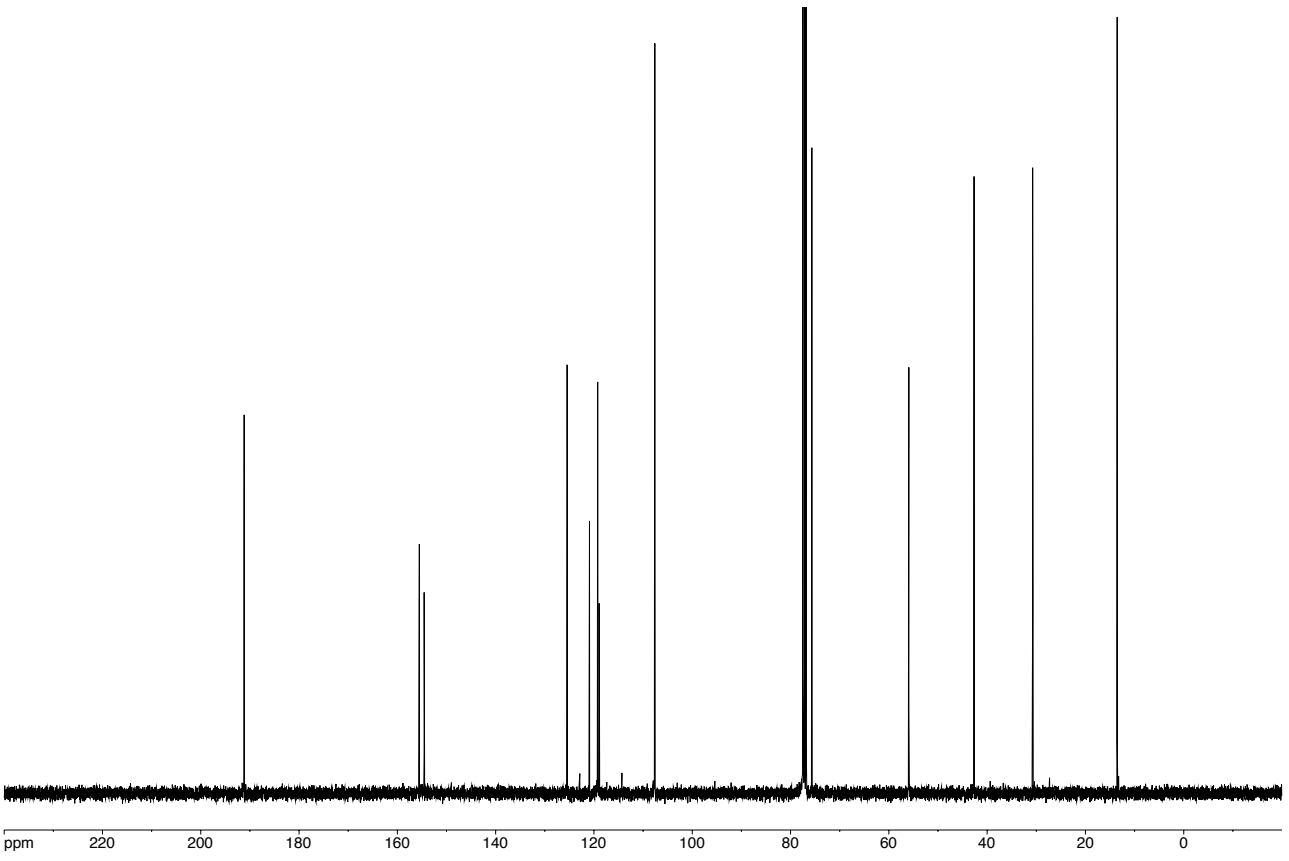
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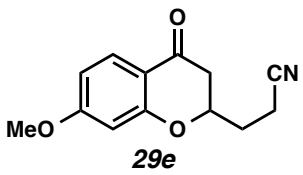
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29e

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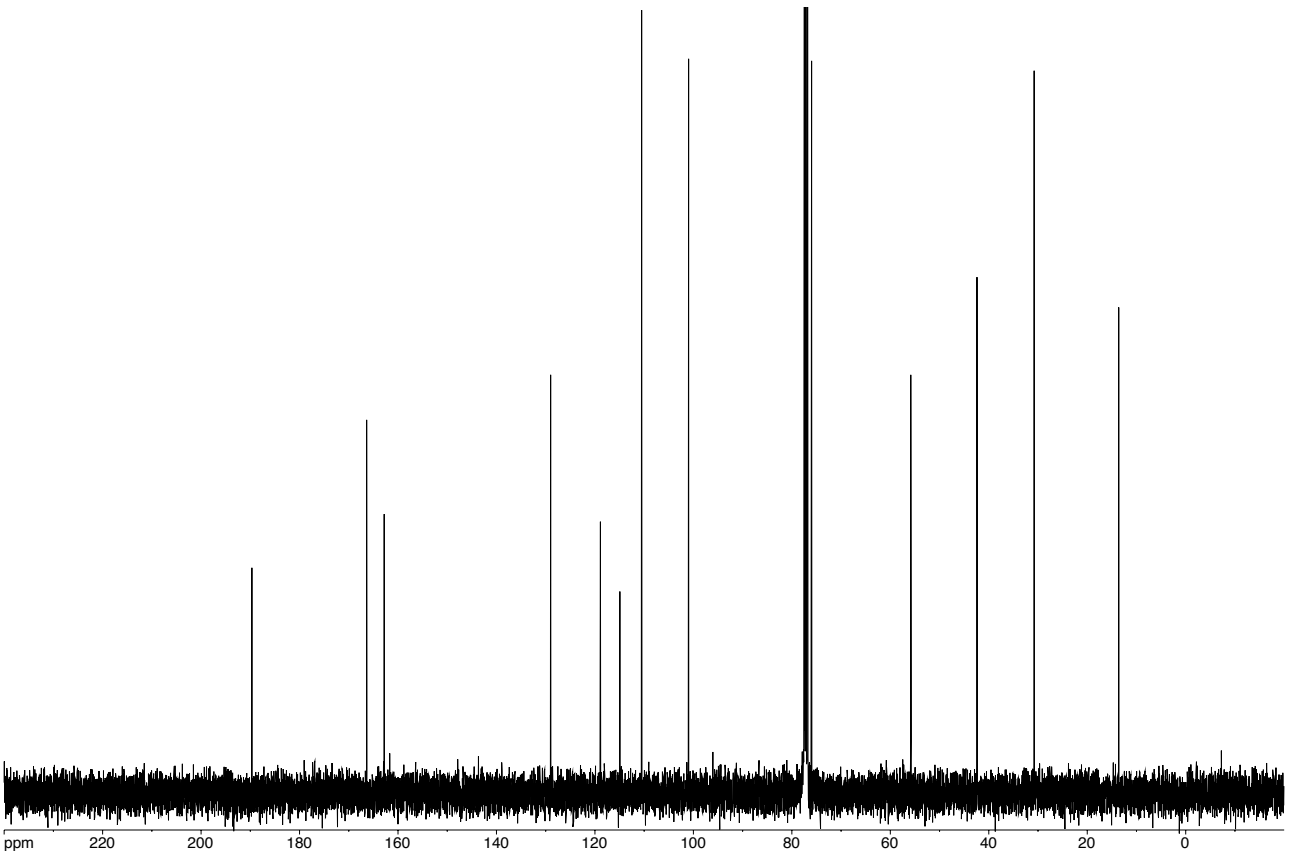
ppm
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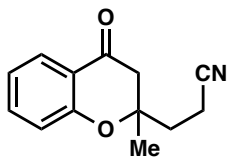
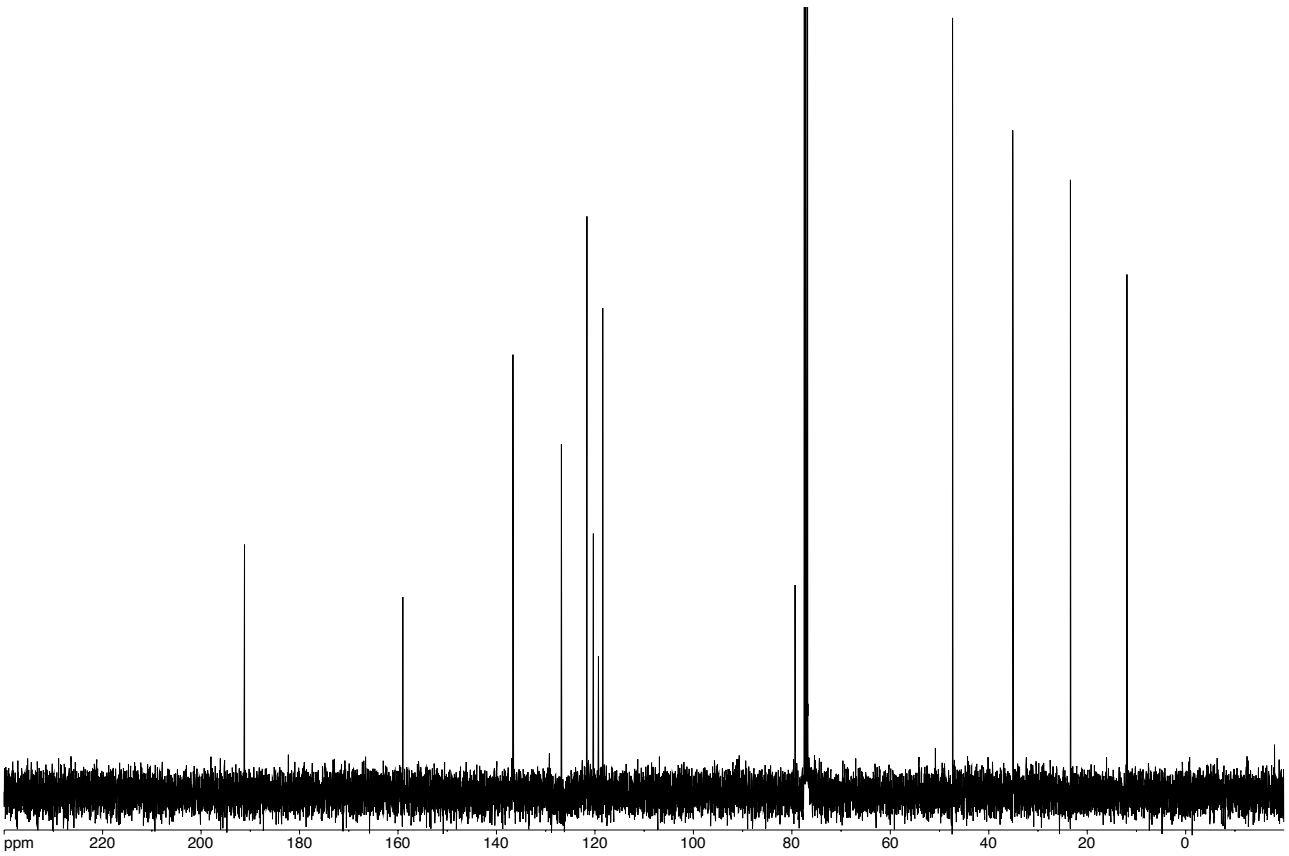

O
CN
O
Me

29f

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
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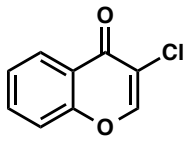
O
Cl
O

30d

ppm
10
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7
6
5
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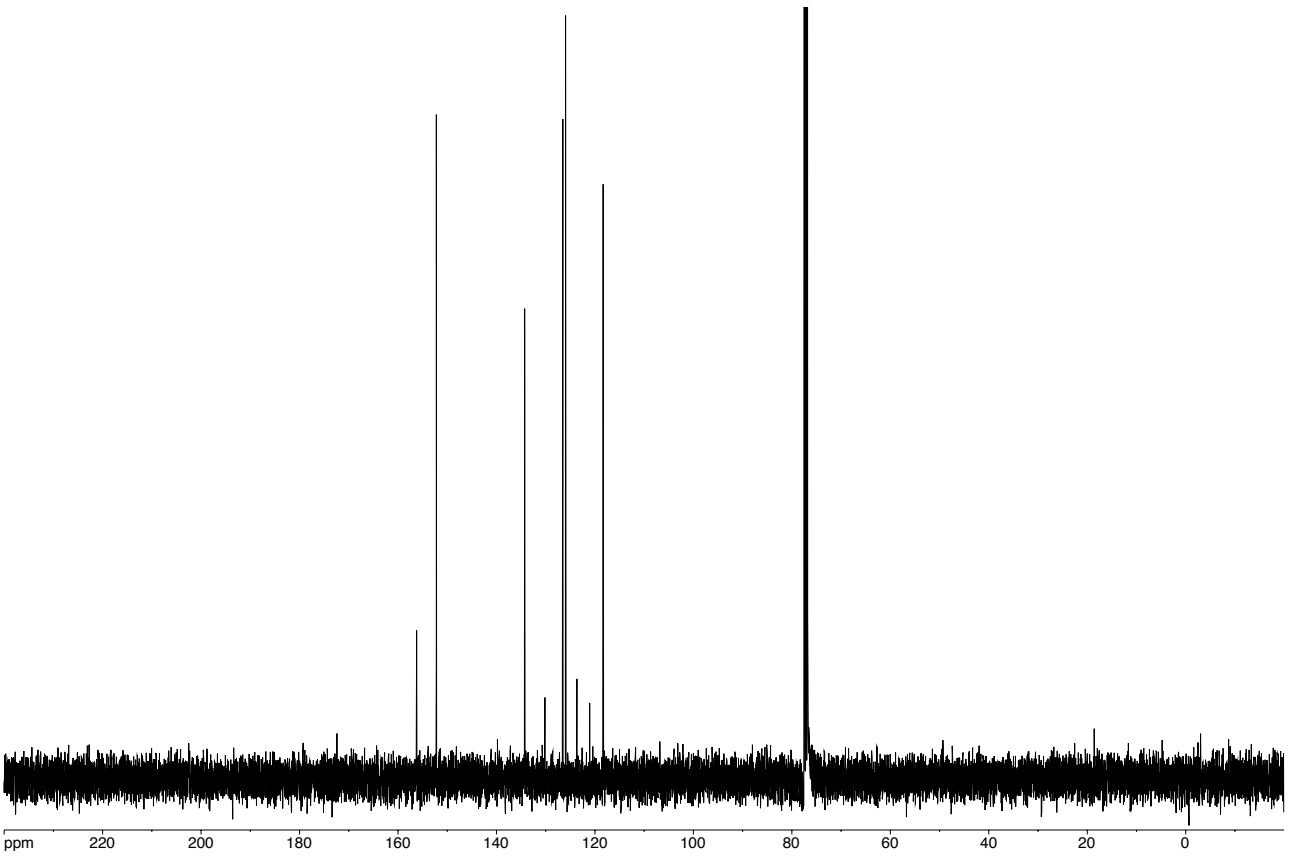
3
2
1
0


ppm
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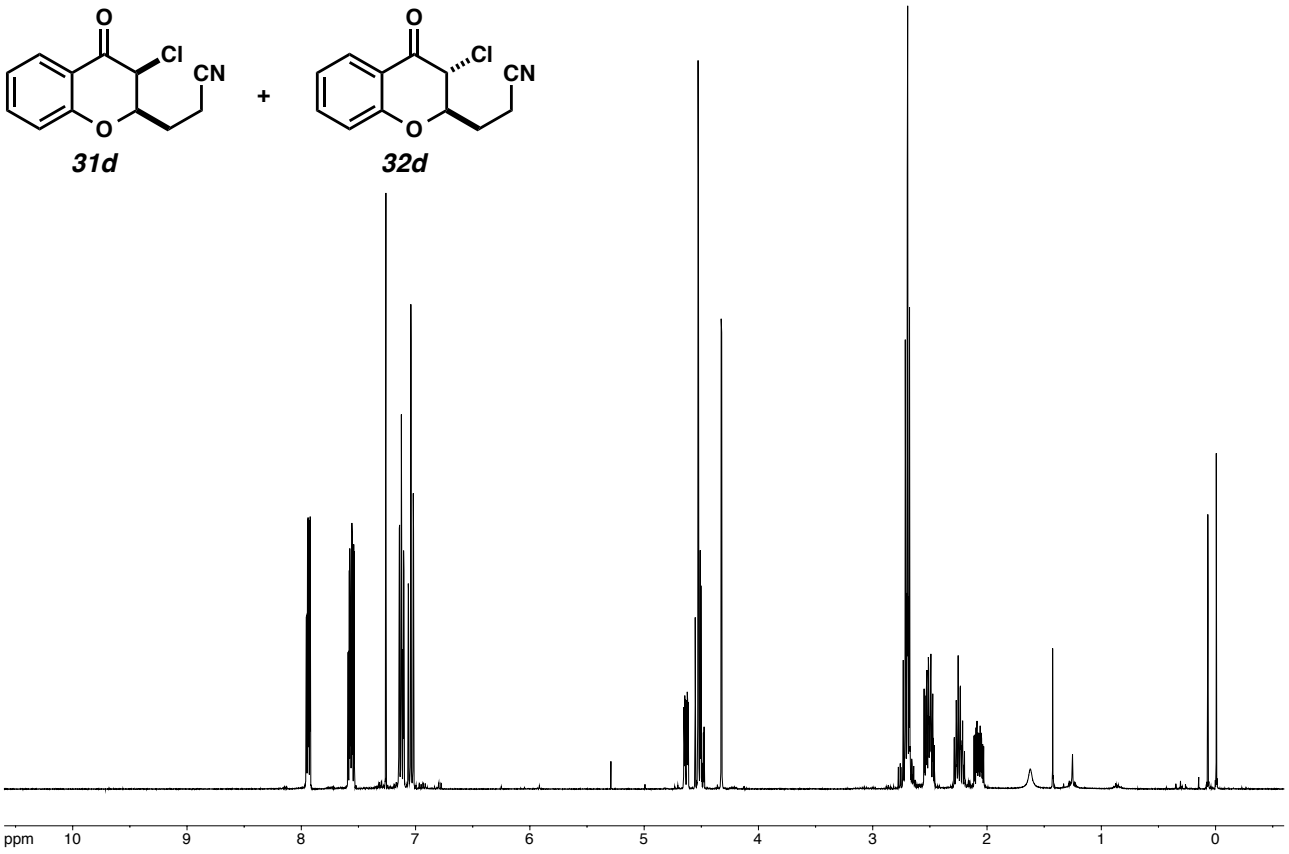
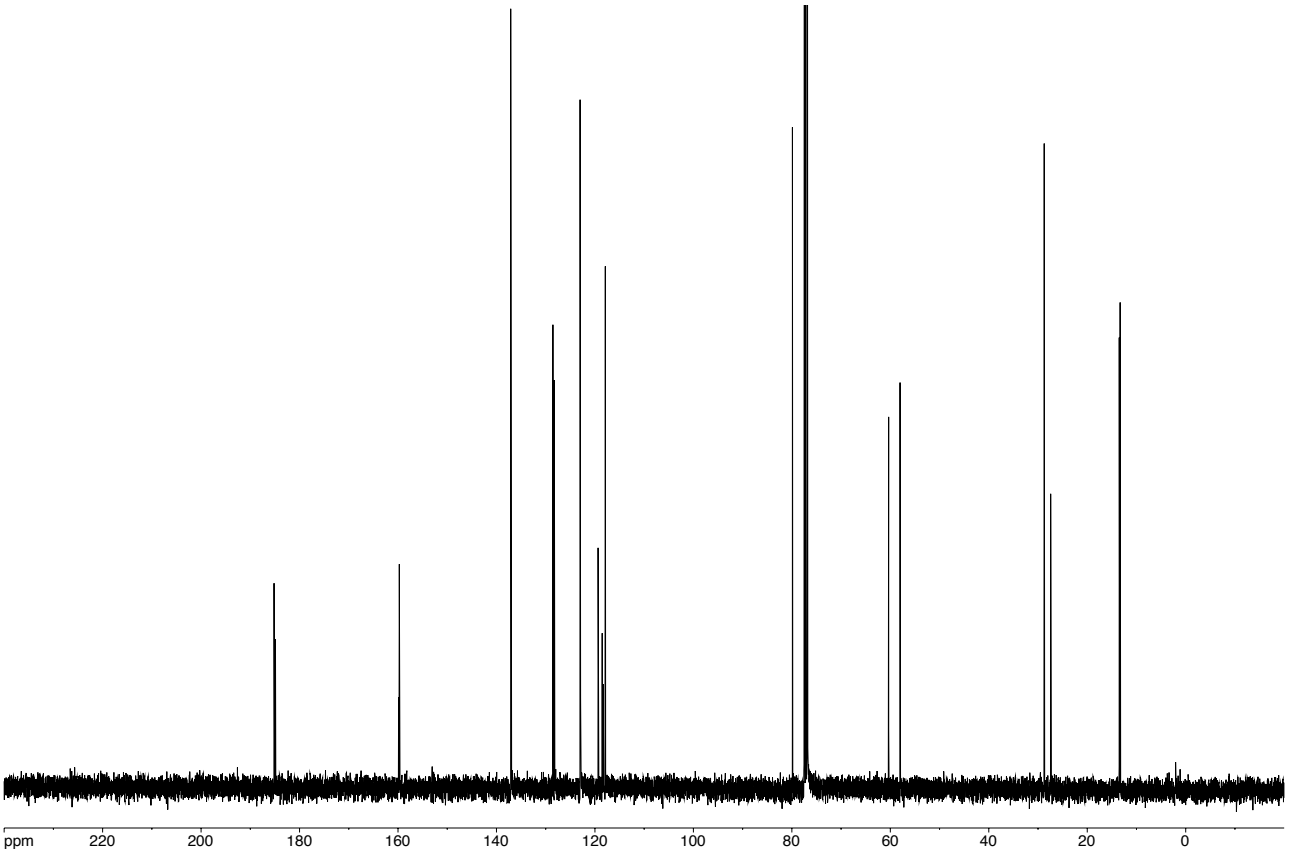

O
Cl
CN
O
+
O
Cl
CN
O
ppm
10
9
8
7
6
5
4
3
2
1
0

31d *32d*


ppm
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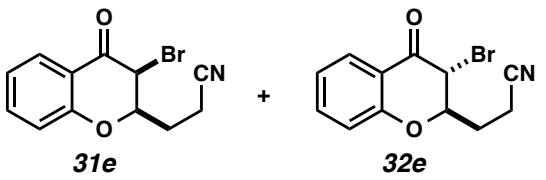
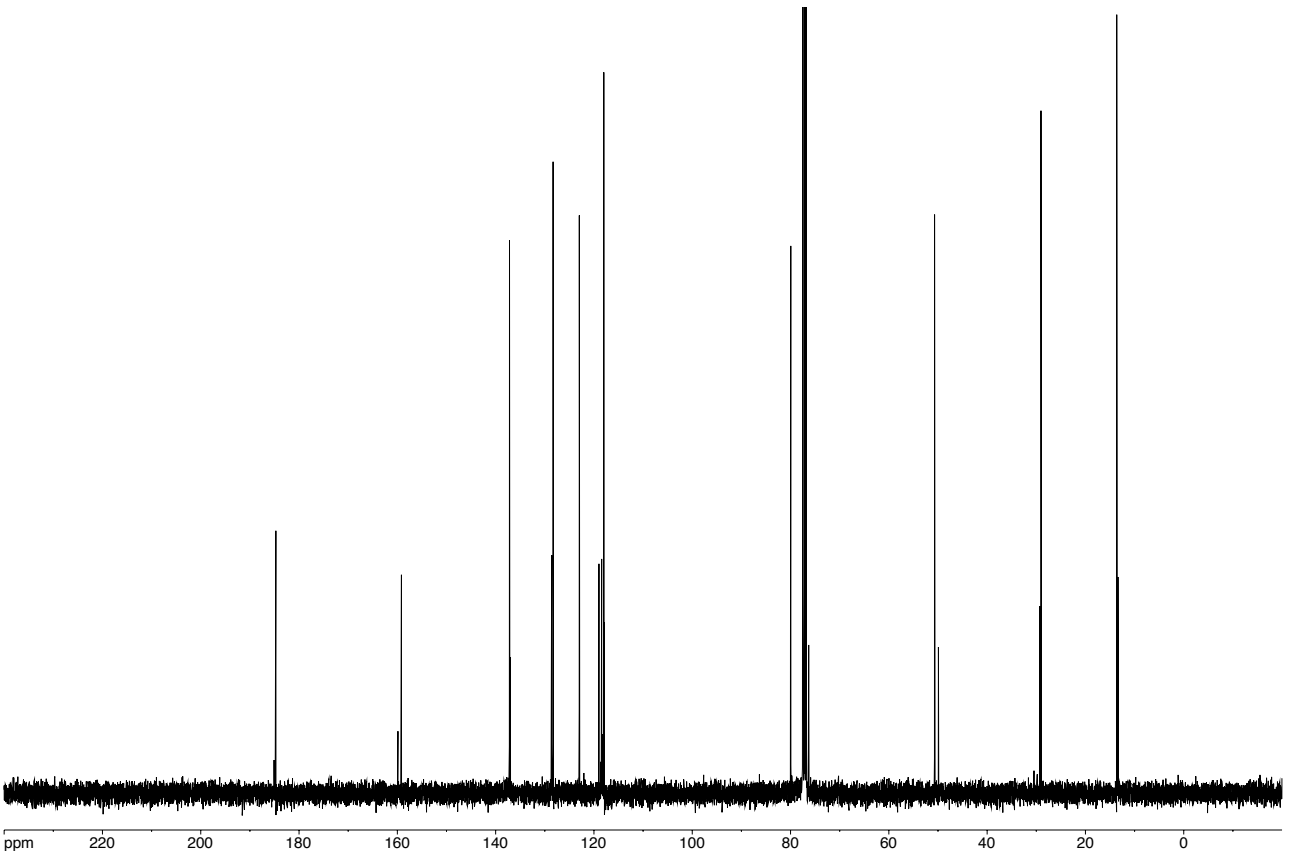

O
Br
CN
O

31e + ***32e***

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
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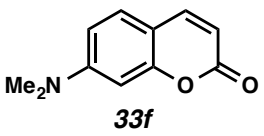
Me2N
O
O

33f

ppm
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7
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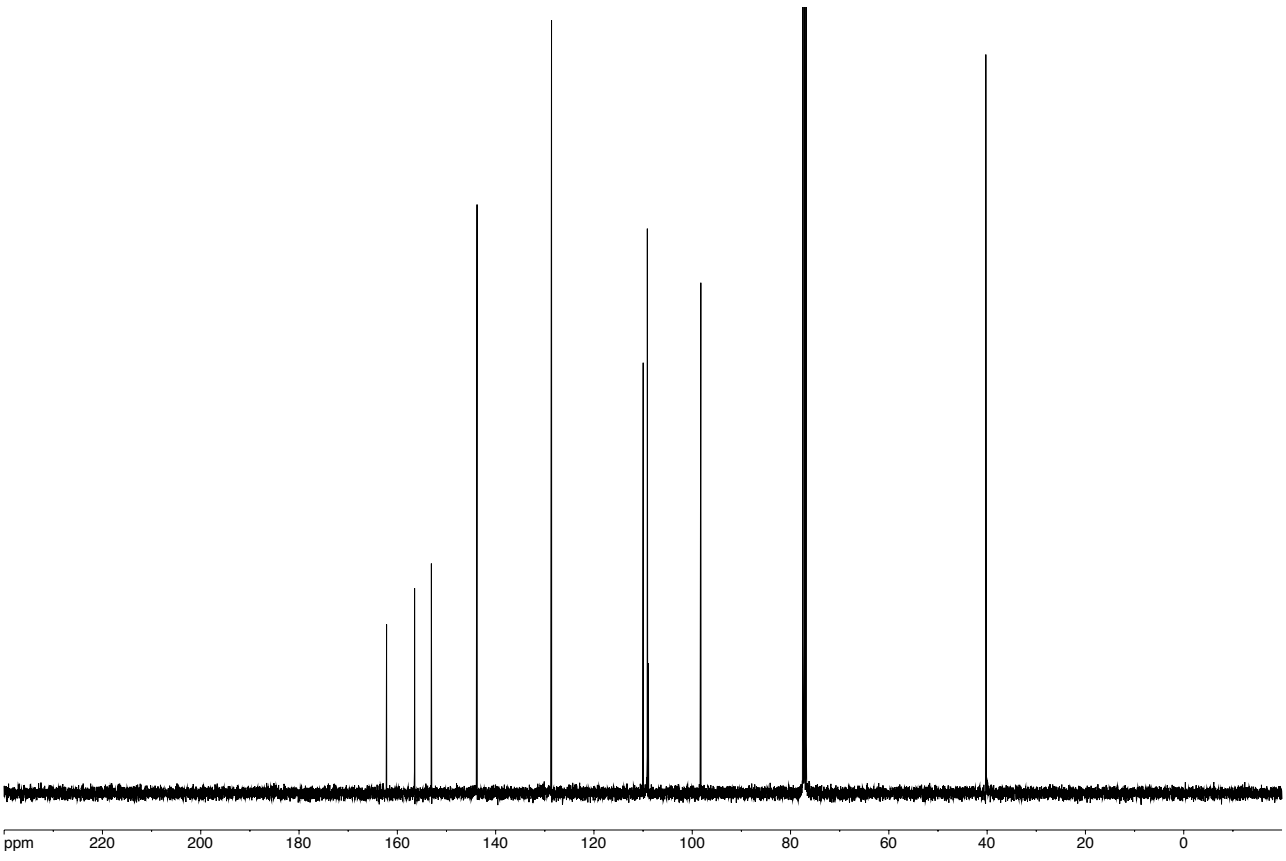
3
2
1
0


ppm
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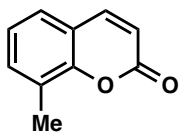
O
O
Me

33g

ppm
10
9
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7
6
5
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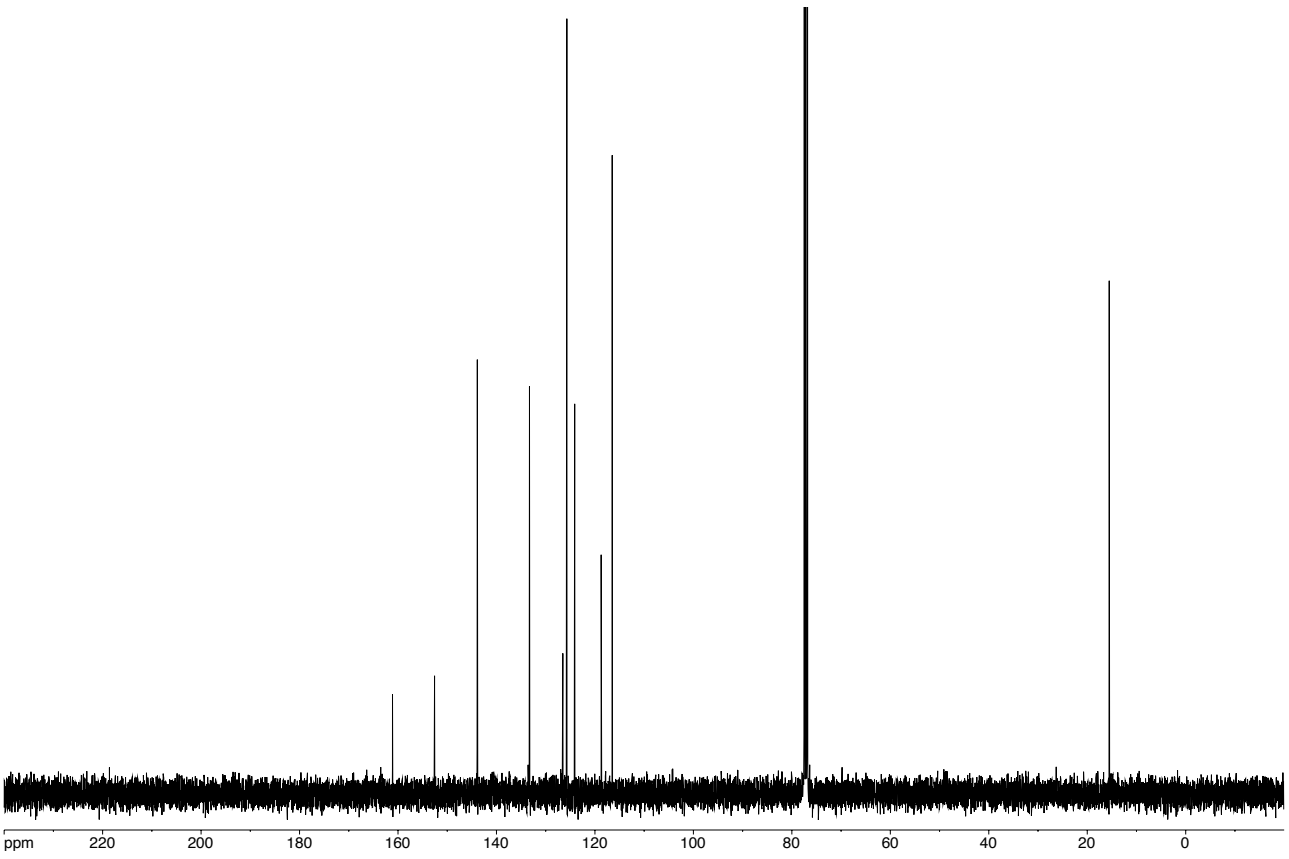
3
2
1
0


ppm
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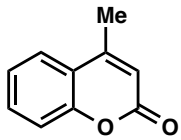
Me
O
O

33h

ppm
10
9
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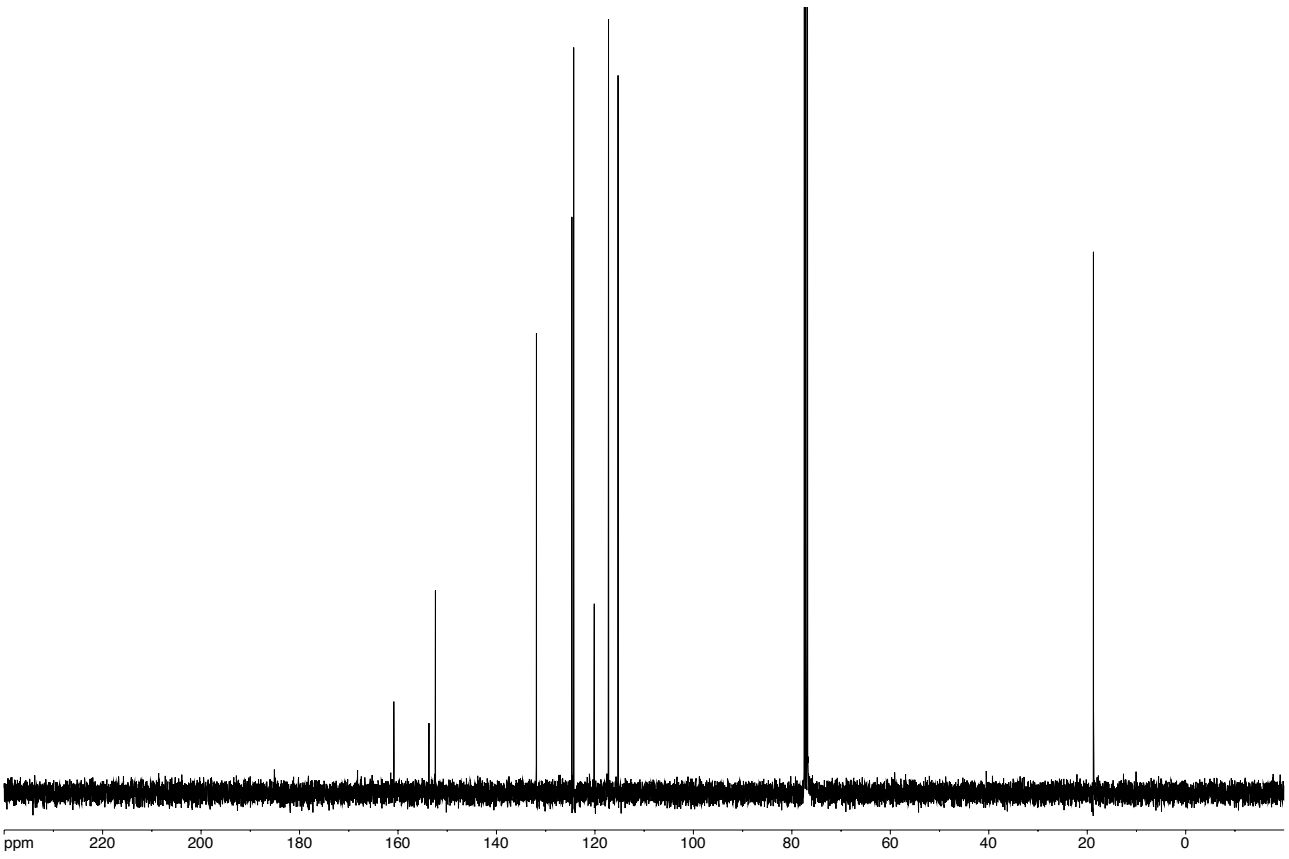
7
6
5
4
3
2
1
0


ppm
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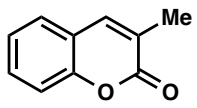
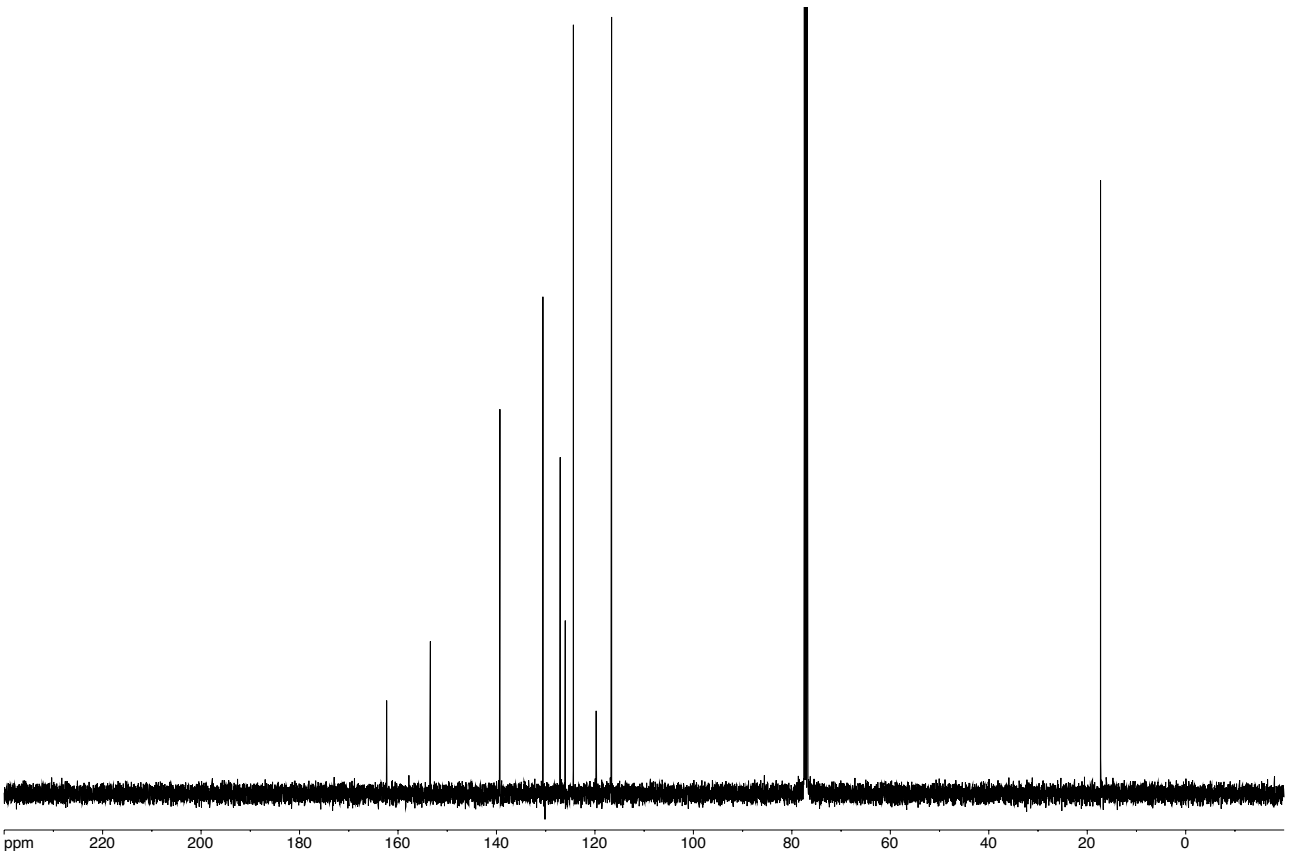

Me
O
O

33i

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
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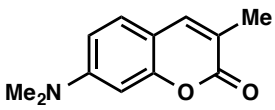
Me
Me2N
O
O

33j

ppm
10
9
8
7
6
5
4
3
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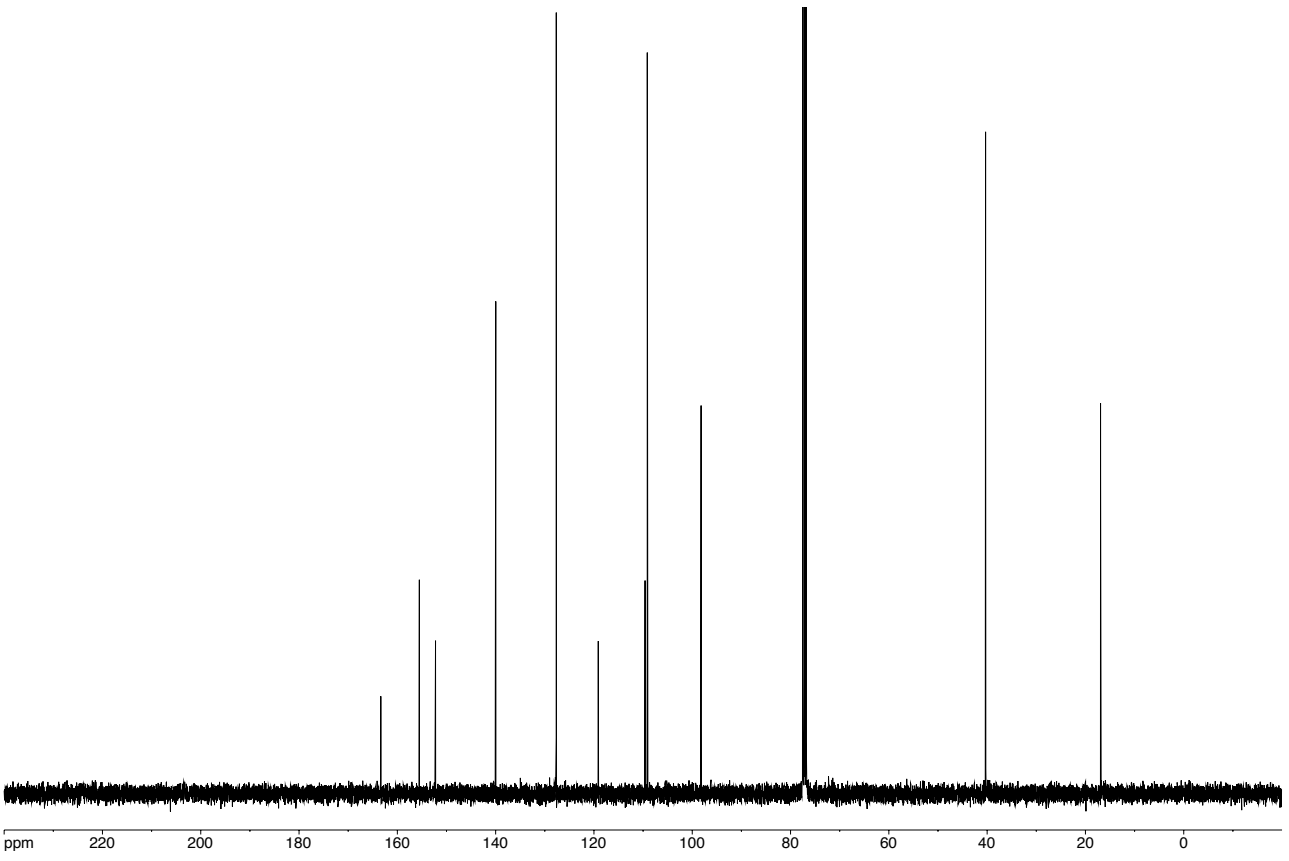
1
0


ppm
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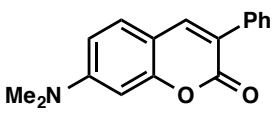
Ph
Me2N
O
O

33k

ppm
10
9
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7
6
5
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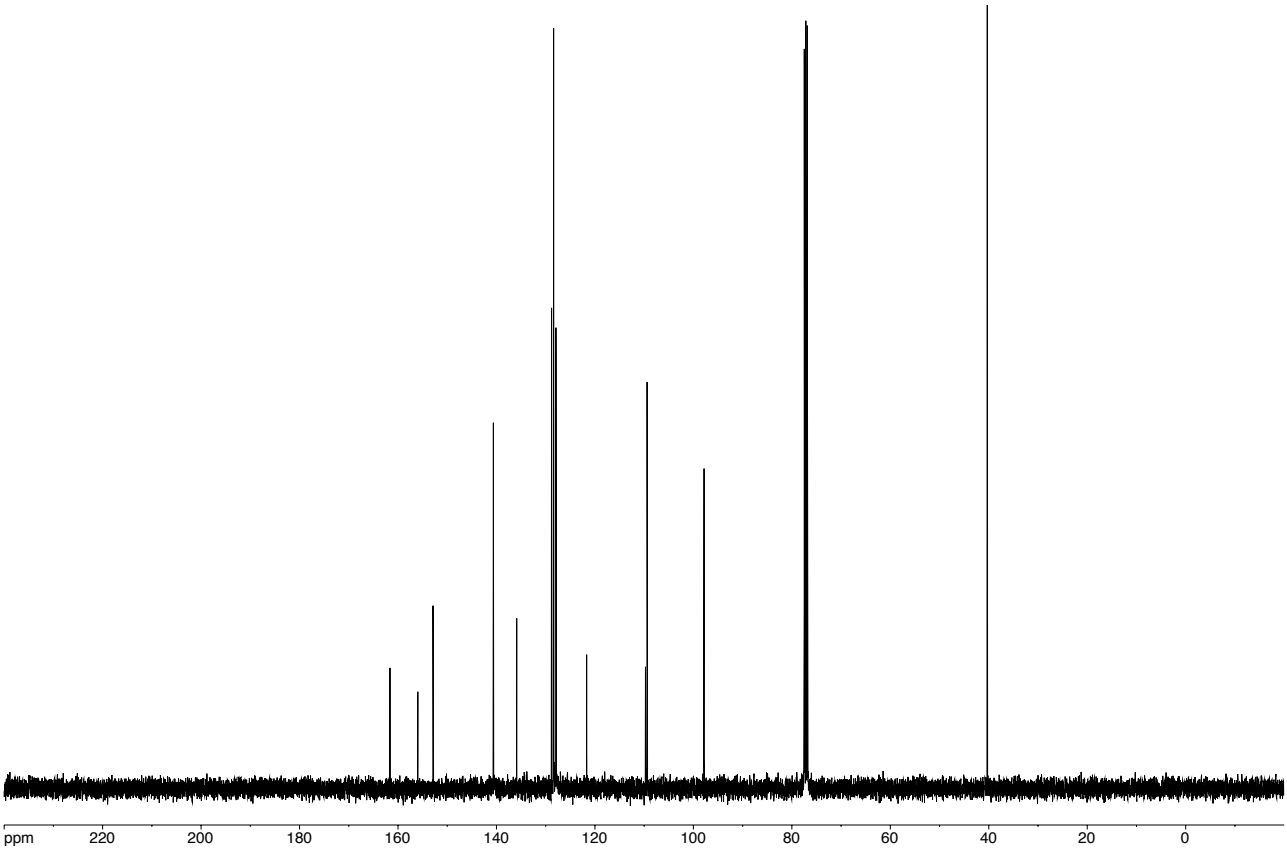
ppm
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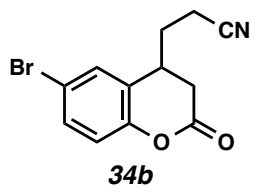
CN
Br
O
O

34b

ppm
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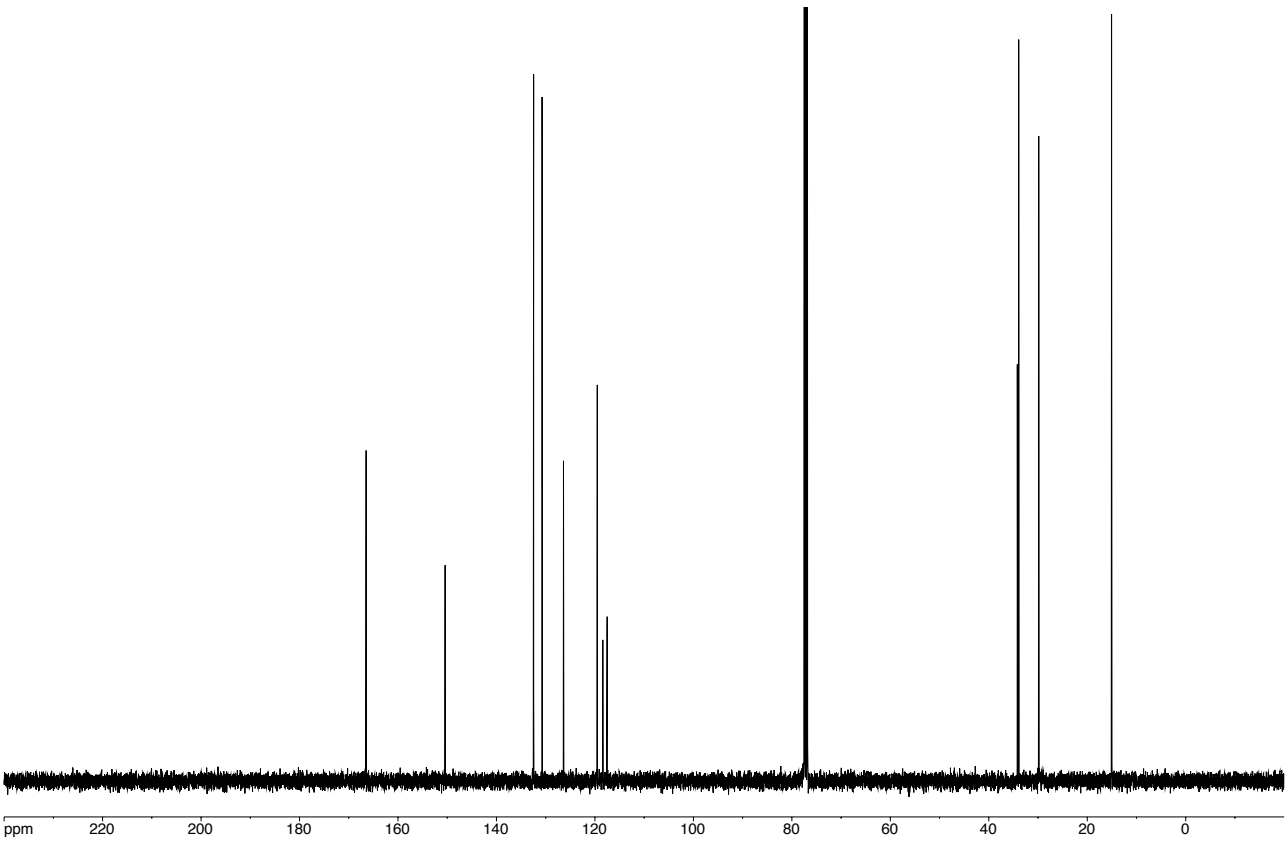
ppm
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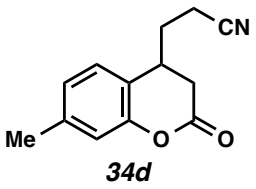
CN
Me
O
O

34d

ppm
10
9
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7
6
5
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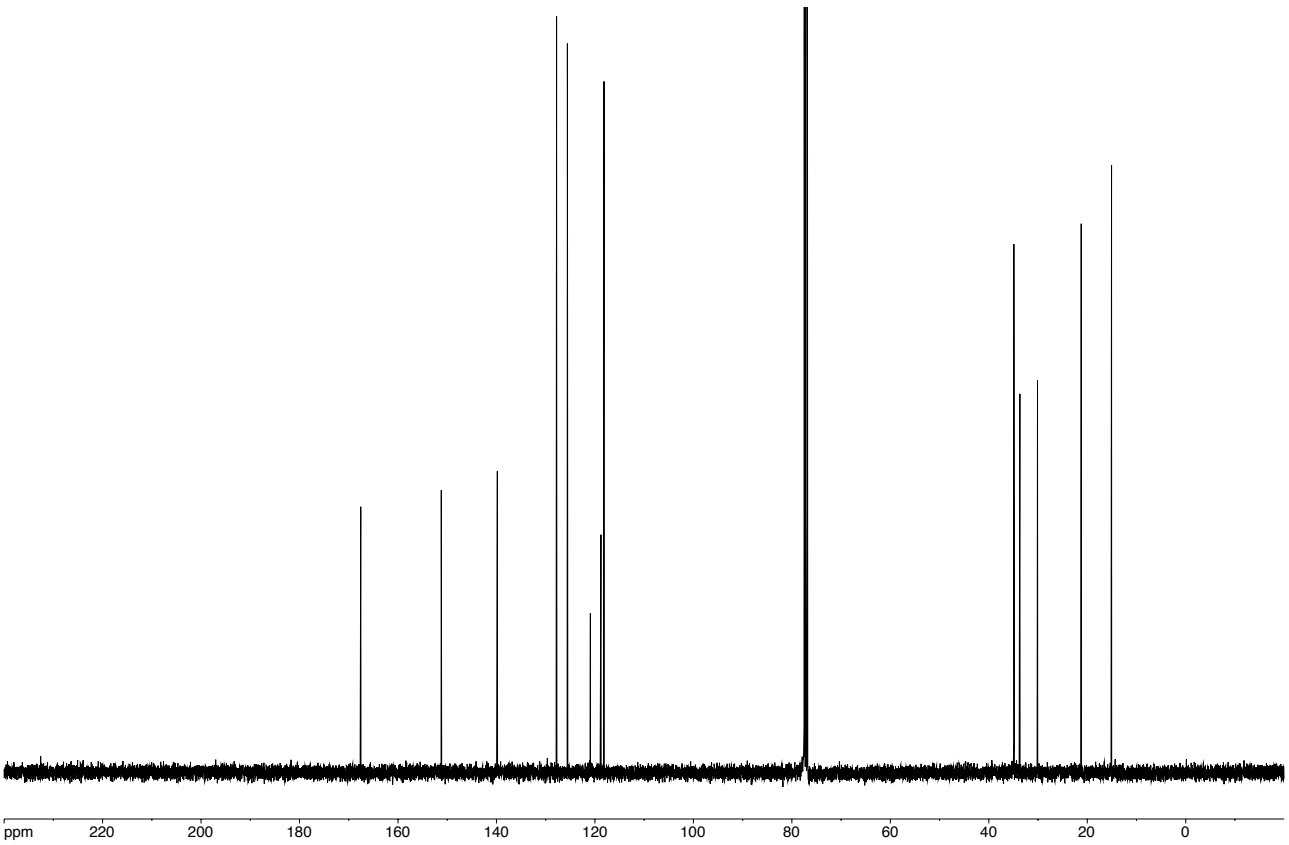
3
2
1
0


ppm
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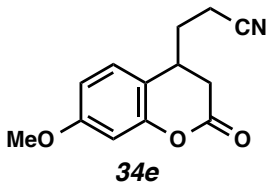
CN
MeO
O
O

34e

ppm
10
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7
6
5
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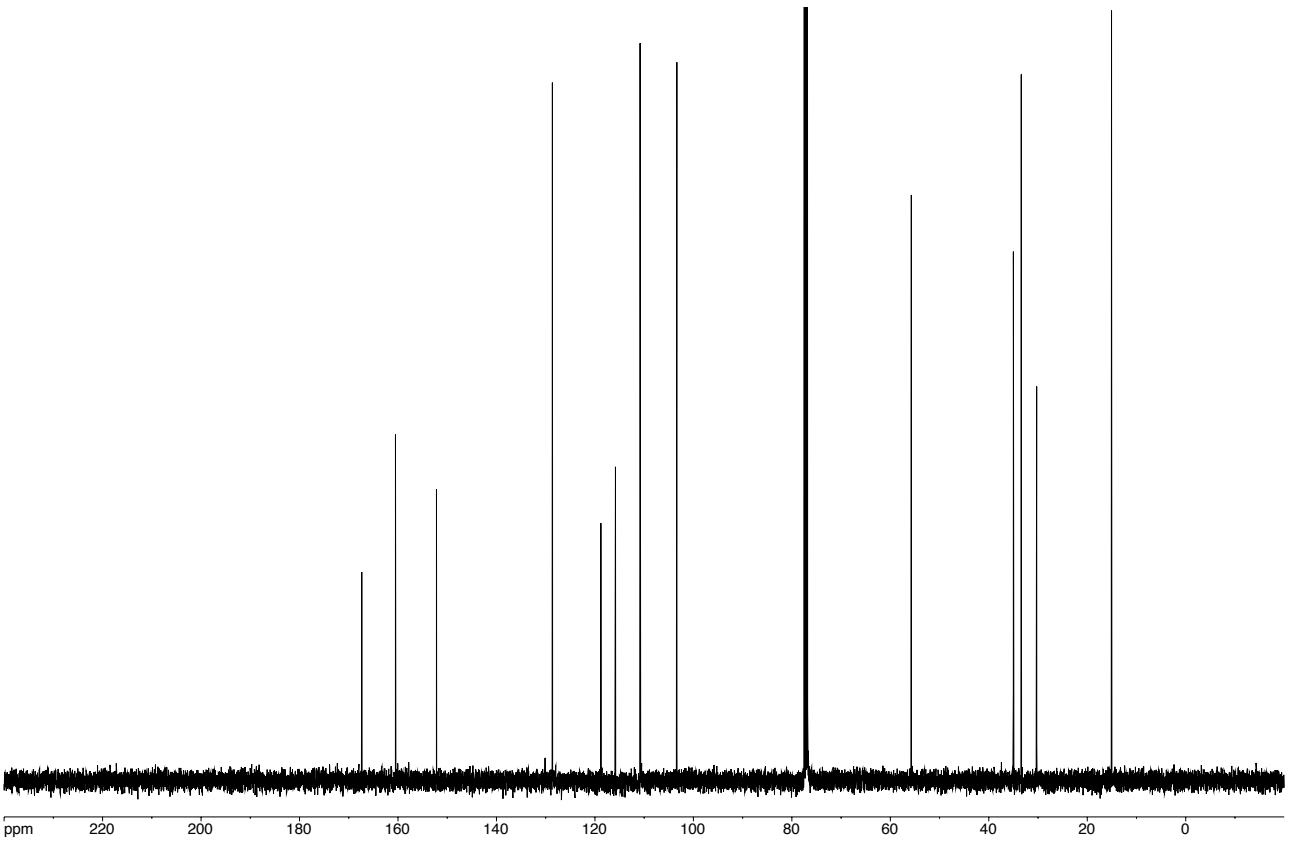
0


ppm
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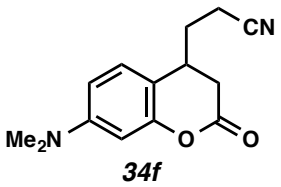
CN
Me2N
O
O

34f

ppm
10
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6
5
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1
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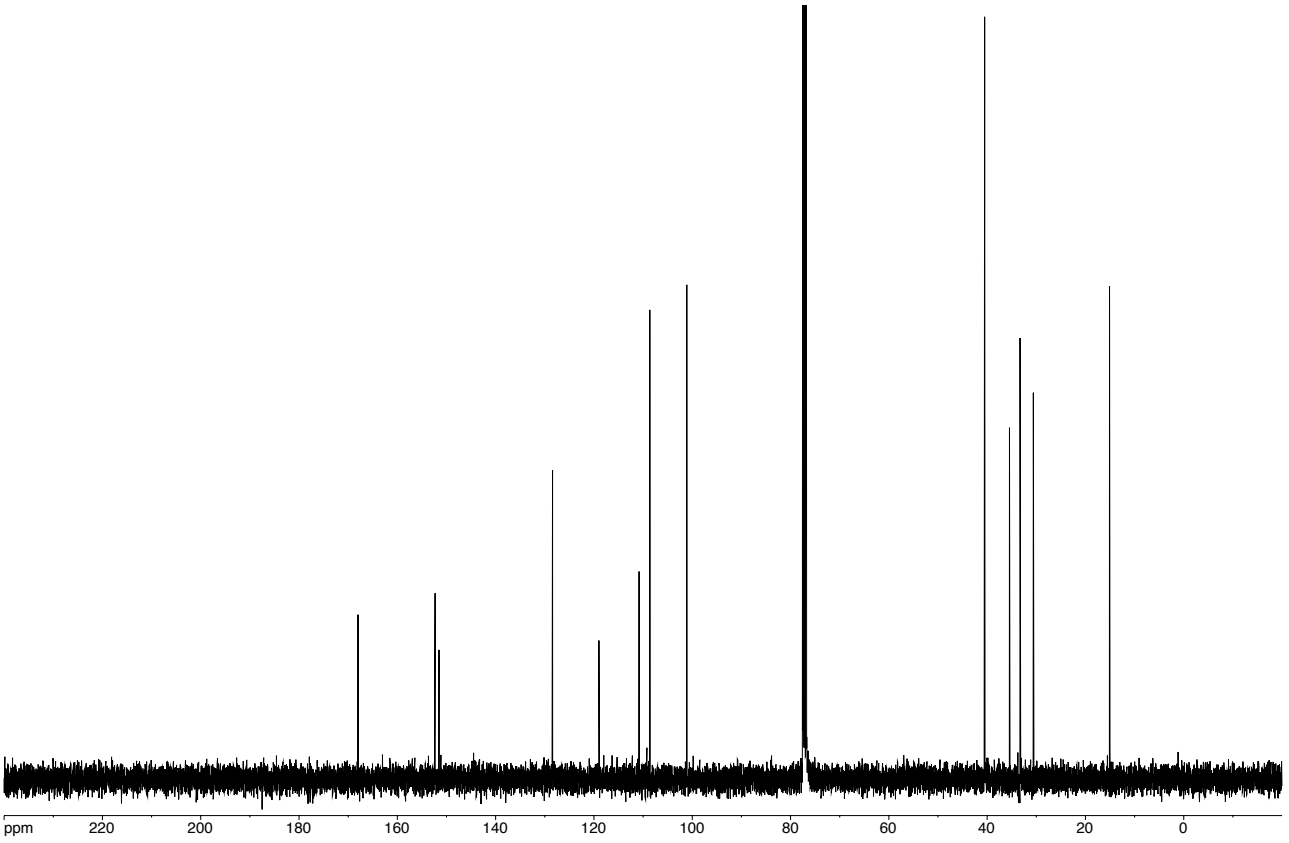
ppm
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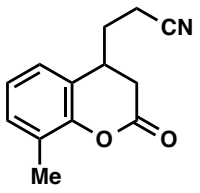
CN
O
O
Me

34g

ppm
10
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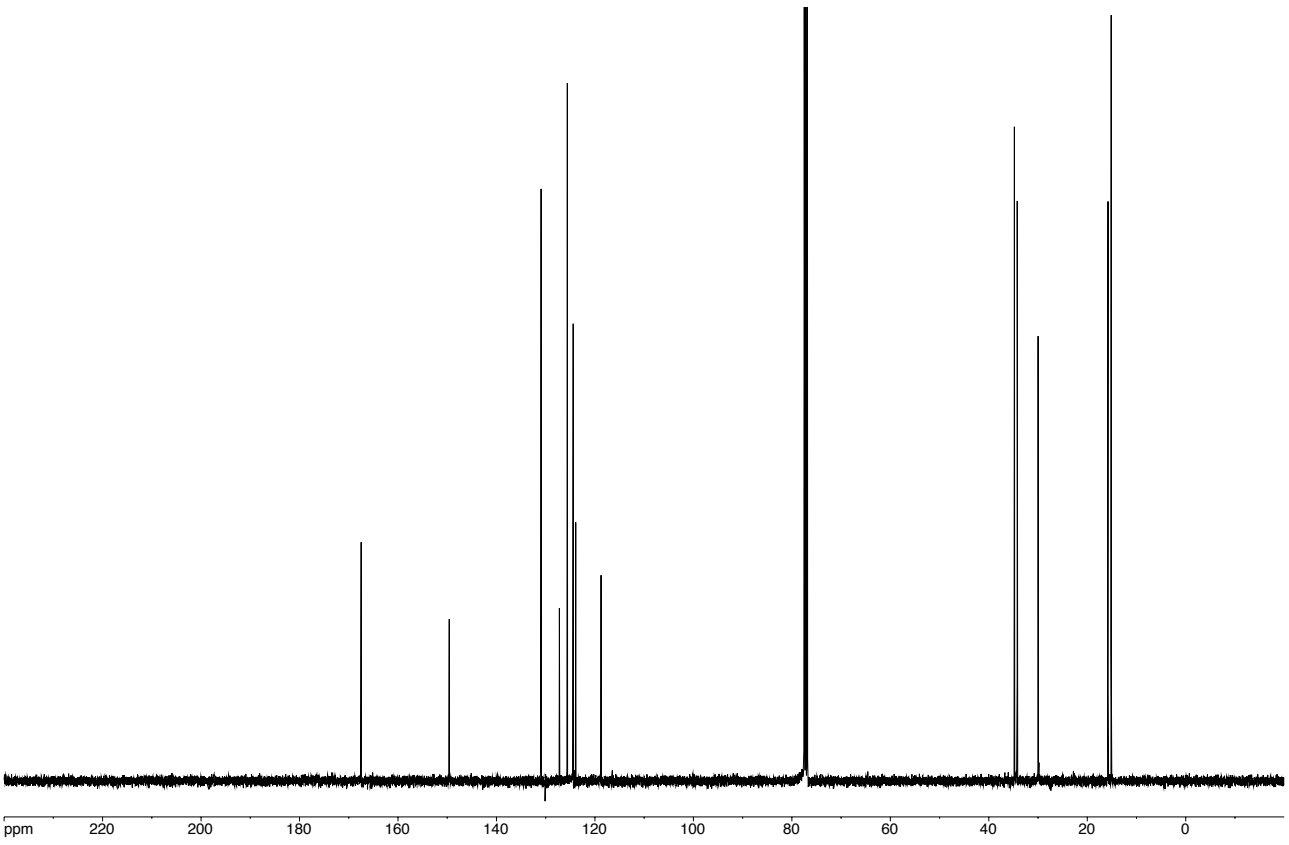
7
6
5
4
3
2
1
0


ppm
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100
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60
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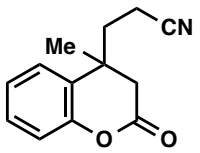
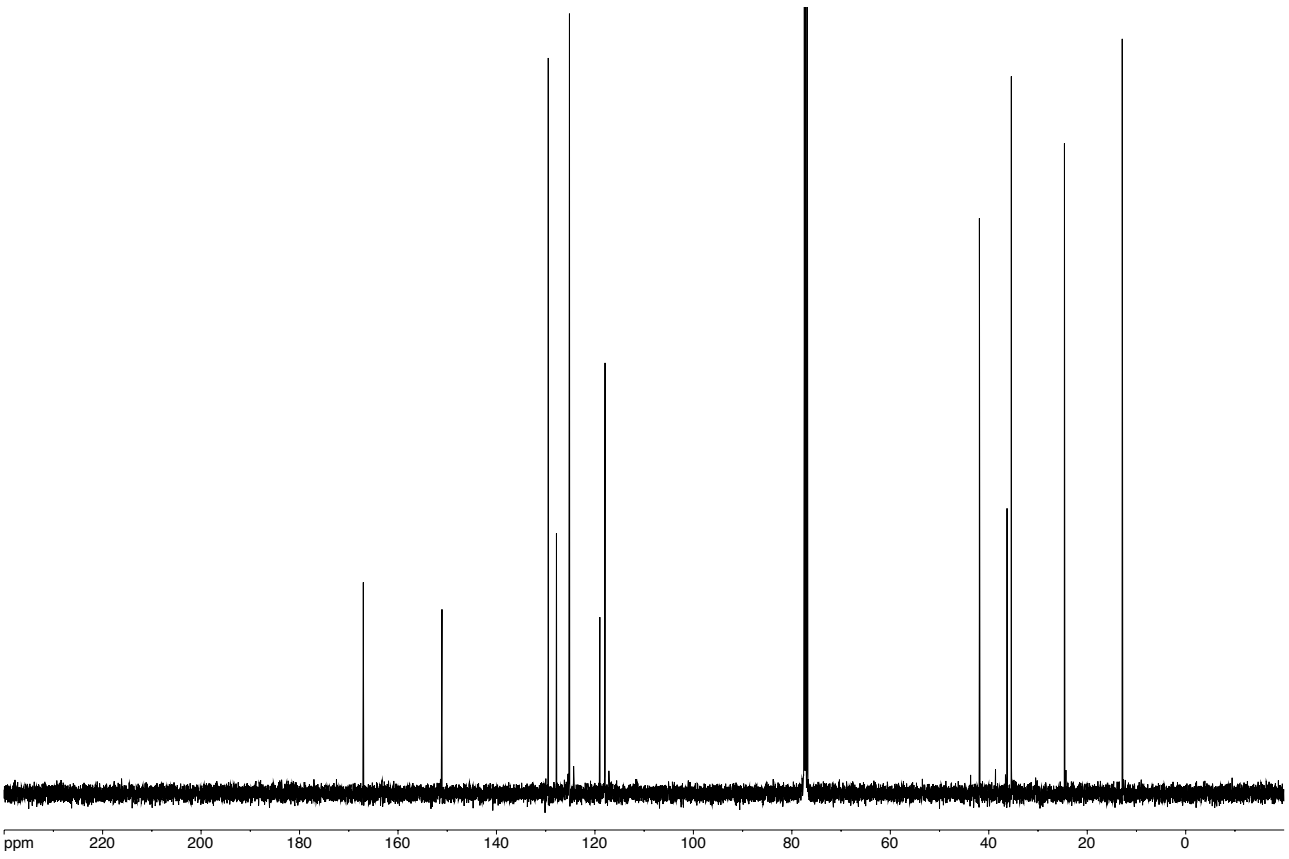

Me
CN
O
O

34h

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
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200
180
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100
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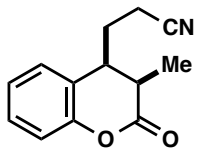
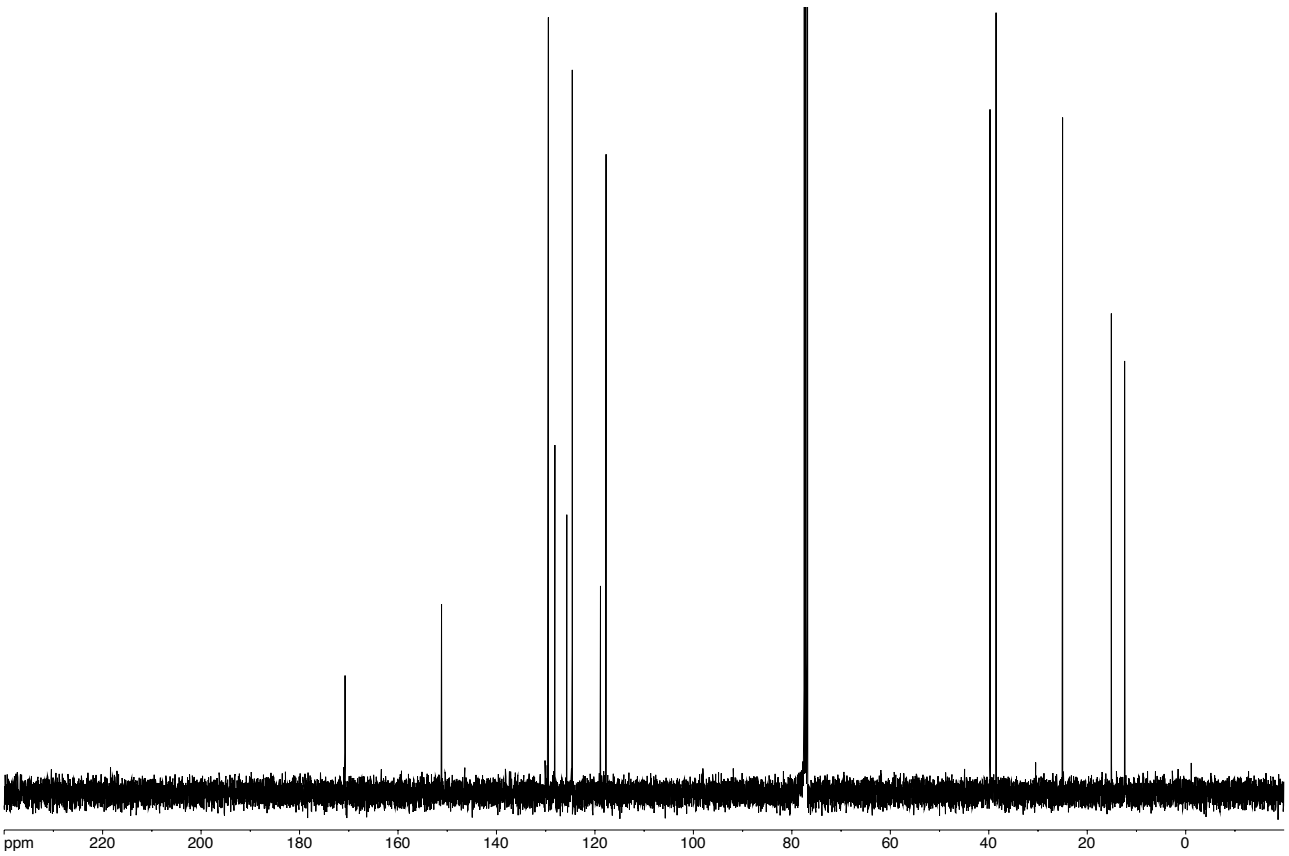
20
0


CN
Me
O
O

34i

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
220
200
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140
120
100
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60
40
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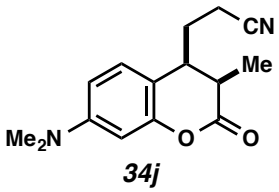
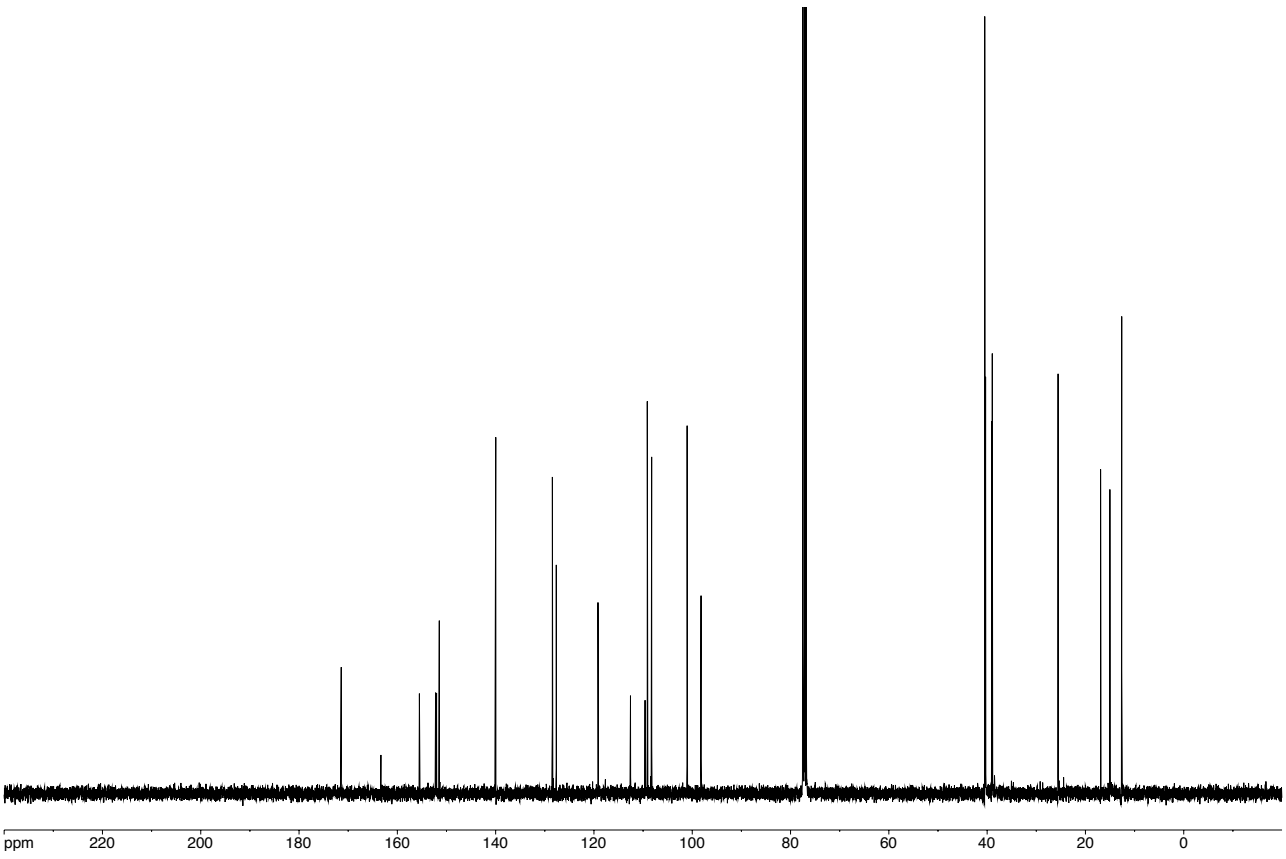
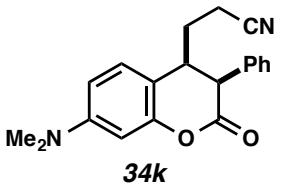


34j

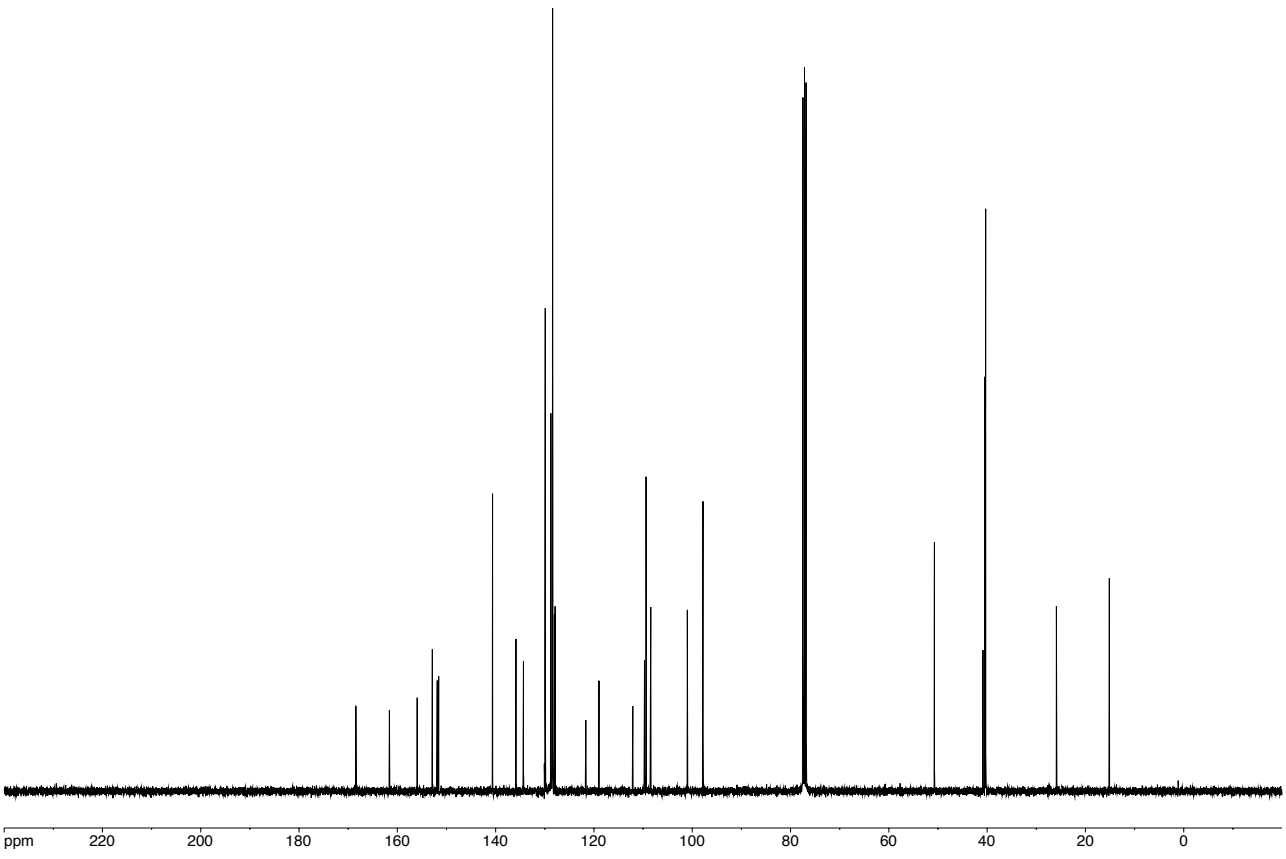
+ *33j* (1.4:1 mixture)

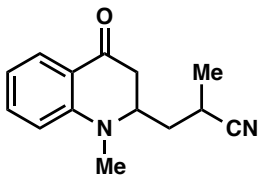




34k

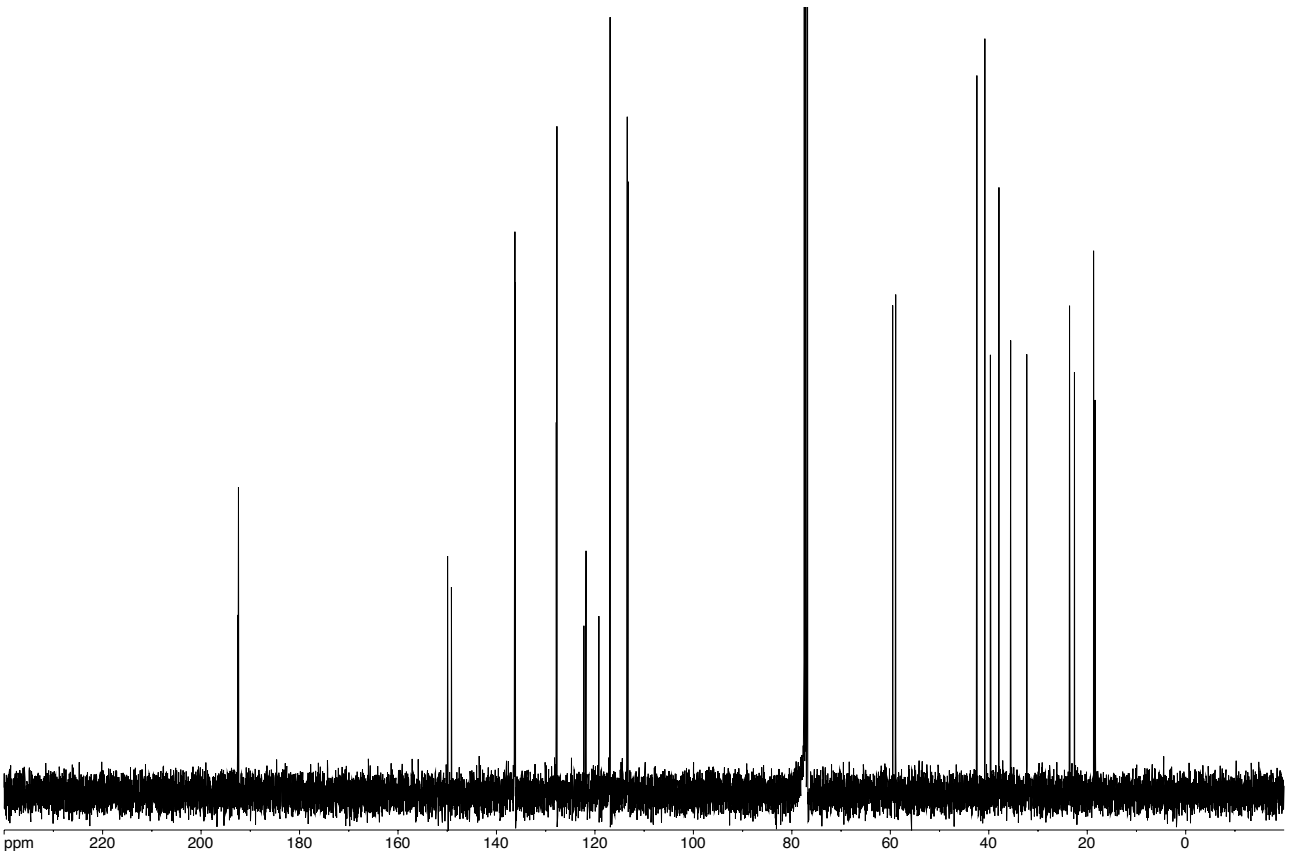
+ *33k* (1:1.4 mixture)

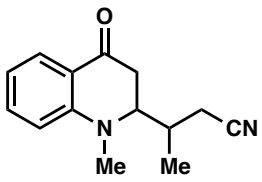



O
Me
N
CN
Me

40 (1.3:1 d.r.)

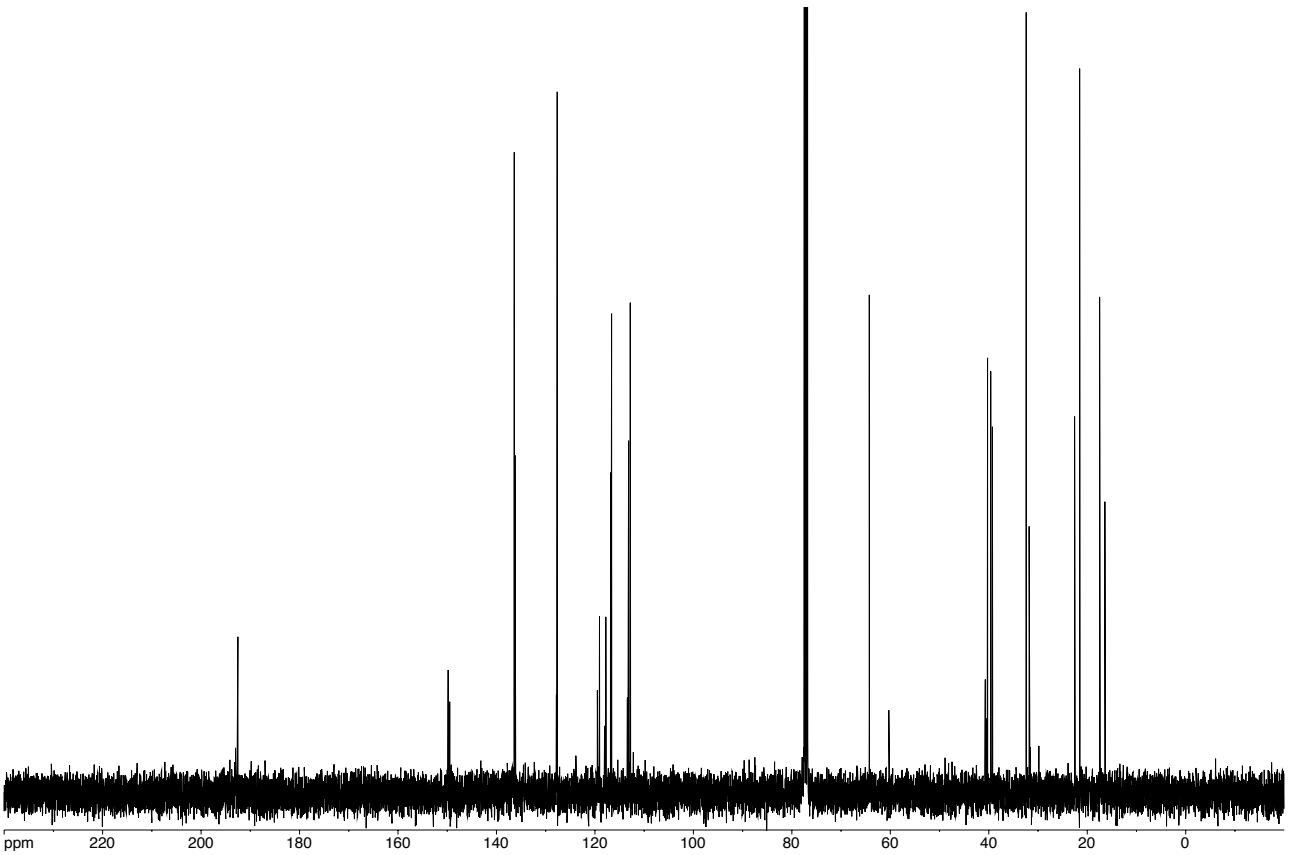
ppm
10
9
8
7
6
5
4
3
2
1
0

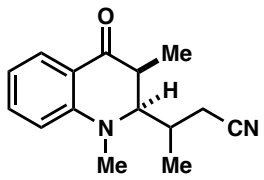

ppm
220
200
180
160
140
120
100
80
60
40
20
0


O
N
Me
Me
CN

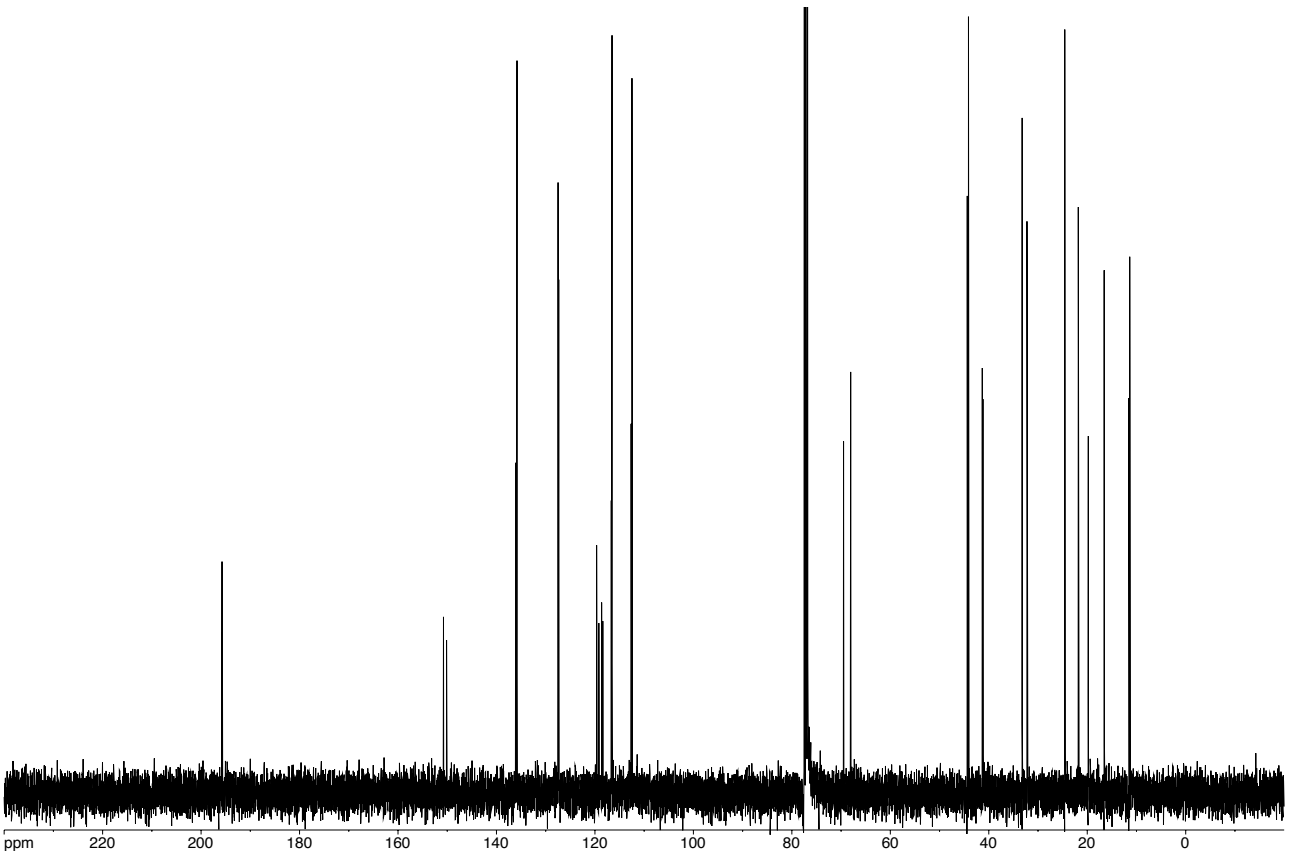
42 (1.6:1 d.r.)

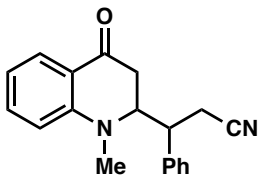
ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
220
200
180
160
140
120
100
80
60
40
20
0



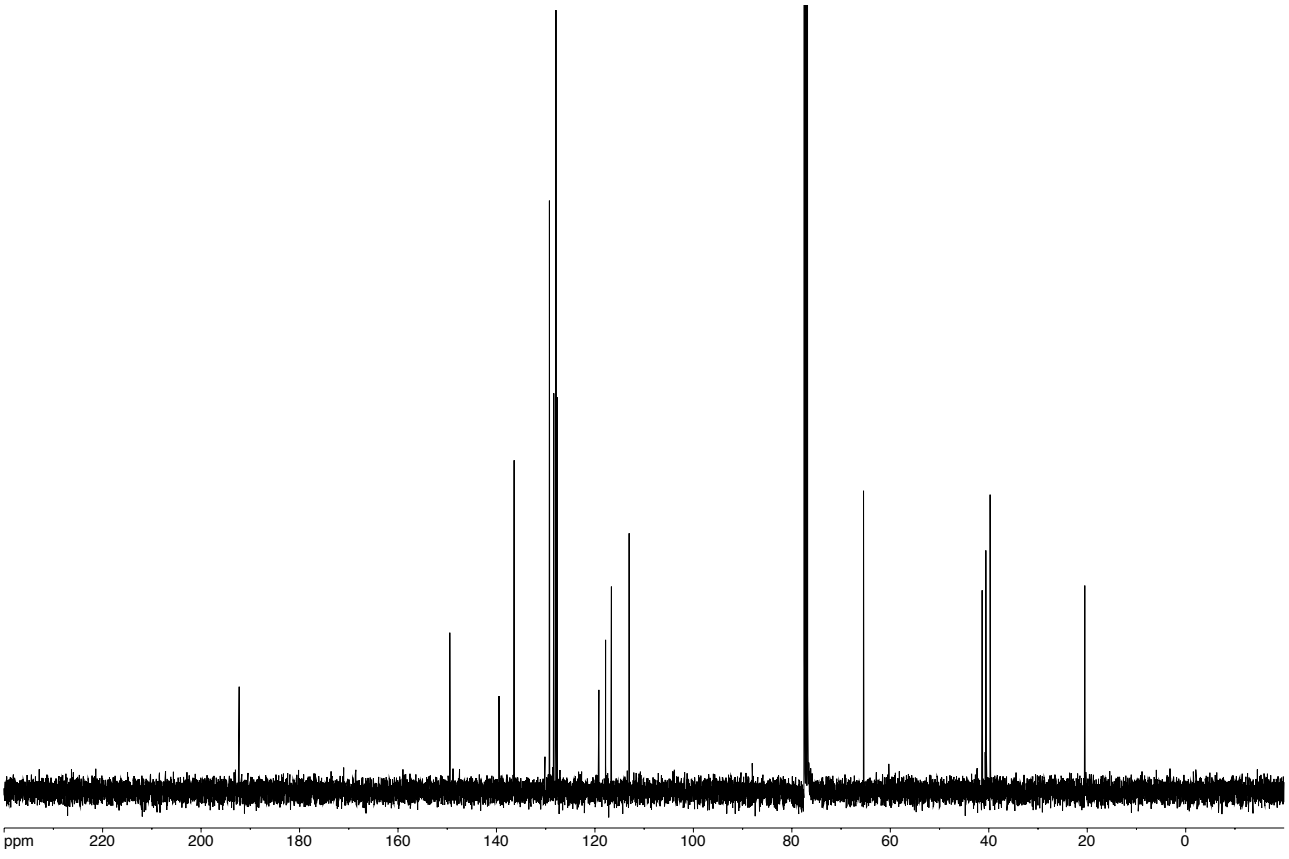
43 (1.4:1 d.r. at C3)

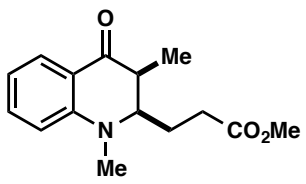



O
N
Me
Ph
CN

44 (1.6:1 d.r.)

ppm
10
9
8
7
6
5
4
3
2
1
0


ppm
220
200
180
160
140
120
100
80
60
40
20
0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N
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CO2Me

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7
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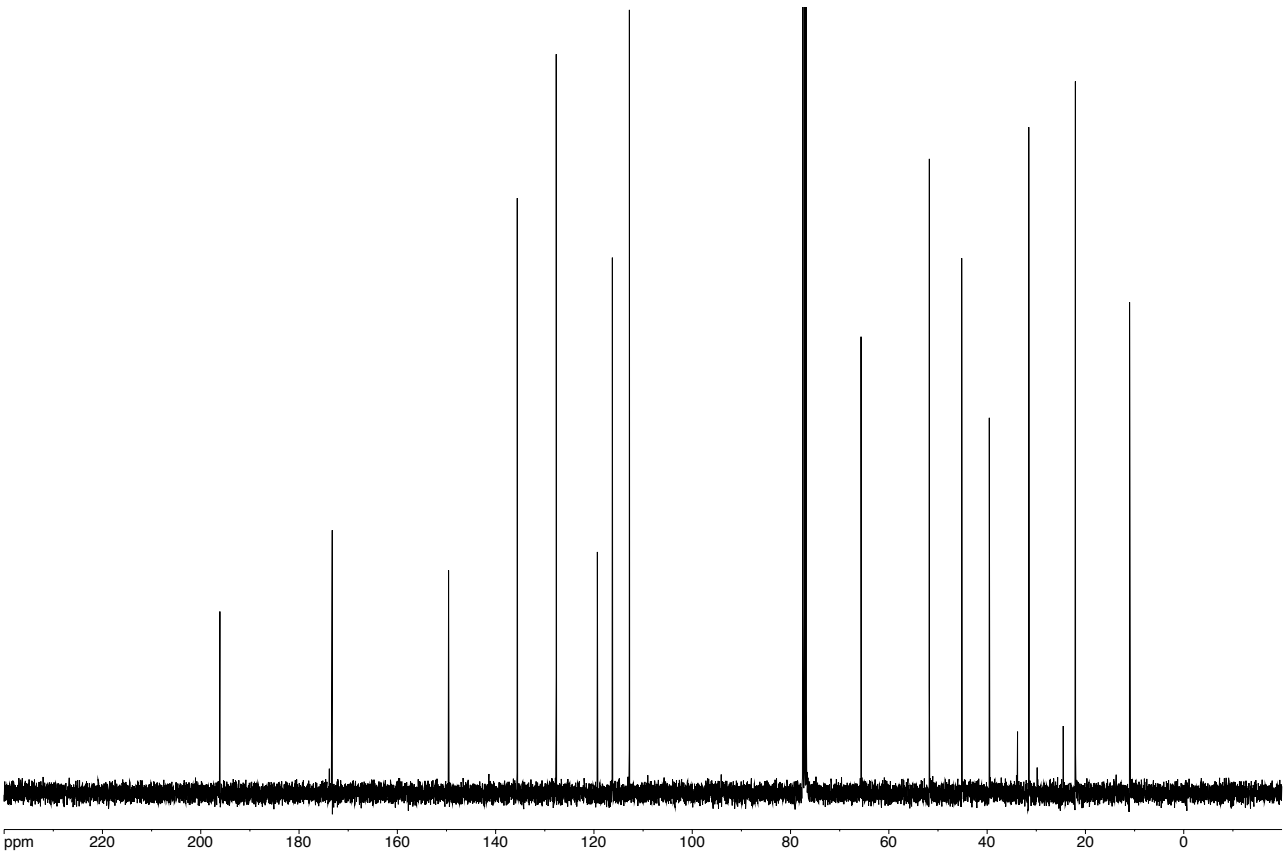
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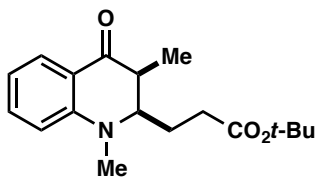
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N
Me
CO2t-Bu

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ppm
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7
6
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2
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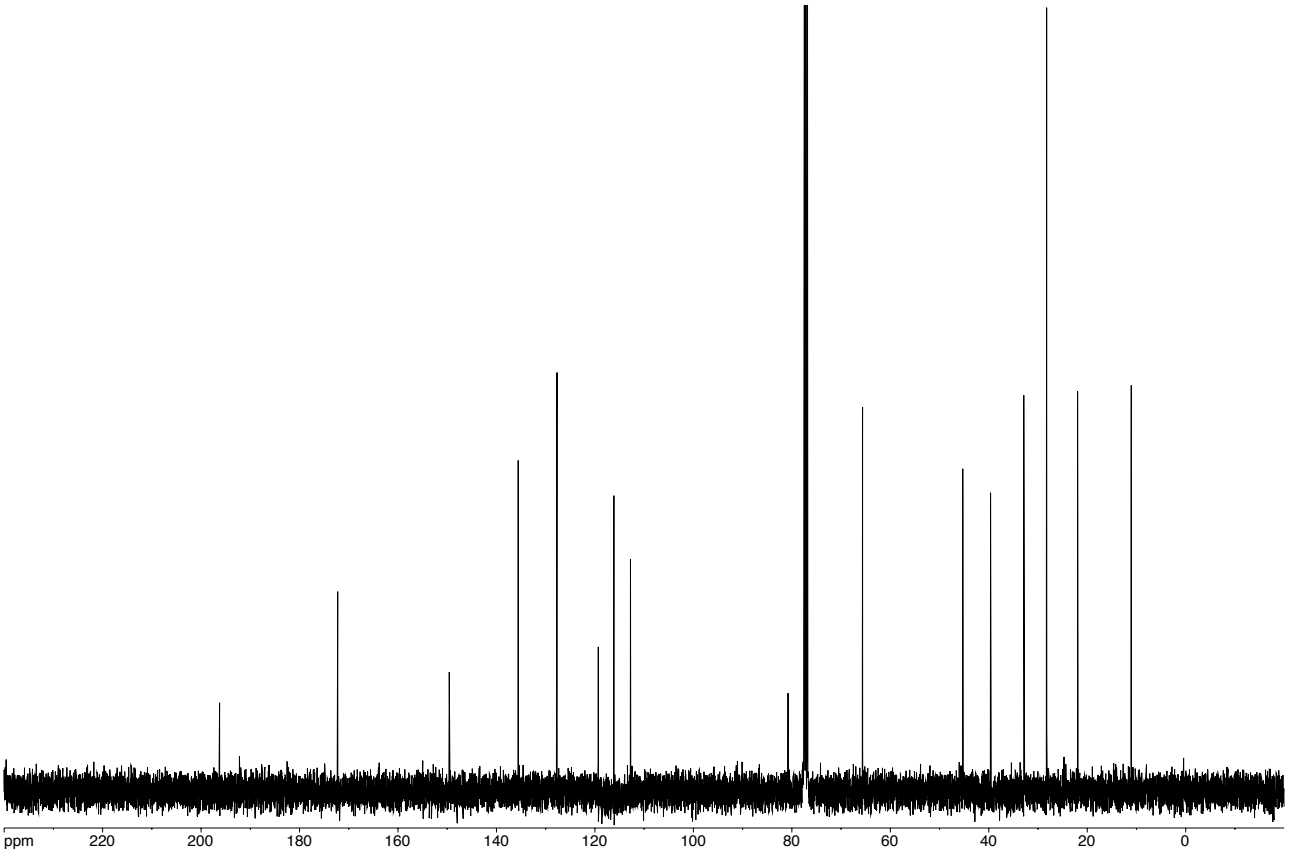
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