Supporting Information

Solvent involved synthesis of pyrrolidin-5-one-2-carboxamides via a sequential Ugi/olefination reaction

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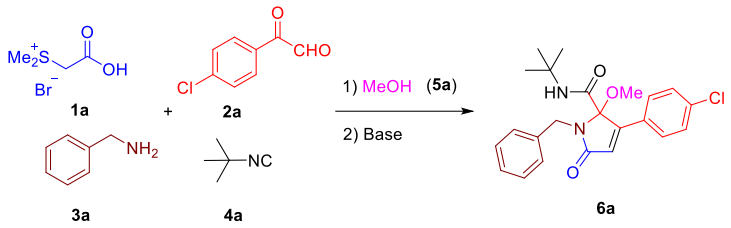
1. General Information.

Unless otherwise noted, materials were purchased from commercial suppliers and used without purification. *N*,*N*-dimethylformamide (DMF) was distilled from K_2CO_3 under high vacuum and fractionated in an all-glass apparatus. Dichloromethane was freshly distilled from calcium hydride. Toluene was distilled from sodium/benzophenone. Other solvents were also purified before using. The material of the reaction vessel is Schlenk tube with common glass. No filters were used in the general procedures. Reactions were monitored by thin layer chromatography (TLC), and column chromatography purifications were performed using 200-300 mesh silica gel. ^{1}H NMR spectra were recorded on 400 MHz spectrophotometers on Bruker AVANCE III. Solvent for NMR are $CDCl_3$ and DMSO-d_6. Chemical shifts are reported in delta (δ) units in parts per million (ppm) relative to the singlet (0 ppm) for tetramethylsilane (TMS), relative to the signal of chloroform (δ = 7.26 ppm, singlet) and dimethyl sulfoxide-d_6 (δ = 2.50 ppm, singlet). Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets), coupling constants (Hz) and integration. ^{13}C NMR spectra were on recorded on 400 (101 MHz) with complete proton decoupling. Chemical shifts are reported in ppm relative to the central line of the heptalet at 77.16 ppm for $CDCl_3$ and 39.52 ppm for DMSO-d_6. Melting point was measured with X-4 melting point instrument. High resolution mass spectra (HRMS) analysis was taken on a Shimadzu LCMS-IT-TOF mass spectrometer.

2. Optimization of Reaction Conditions

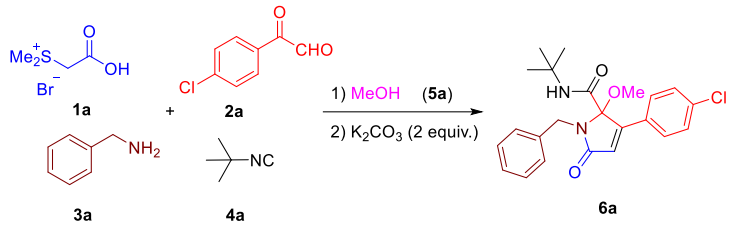
Table *S1*. The Effect of the Base on the Reaction[a]



Entry[a]	Base	Yield[b](%)
1	--	20
2	**DBU**	39
3	**Et_3N**	30
4	**DMAP**	Trace
5	***t*-BuOK**	41
6	**KOH**	40
7	**K_2CO_3**	45

[a]General conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), **3a** (0.24 mmol), **4a** (0.24 mmol), in MeOH (2 mL) at 25 ℃ for 24 h. Then base (0.4 mmol), 25 ℃, 24 h. [b]Yield of isolated product.

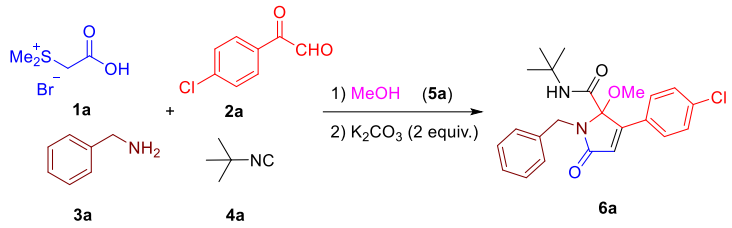
Table *S2*. The Effect of the Temperature on the Reaction[a]



Entry[a]	Temp. [℃]	Yield[b](%)
1	**25**	45
2	**60**	64
3	**80**	18
4	**100**	10

[a]General conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), **3a** (0.24 mmol), **4a** (0.24 mmol), in MeOH (2 mL) for 24 h. Then K_2CO_3 (0.4 mmol), 24 h. [b]Yield of isolated product.

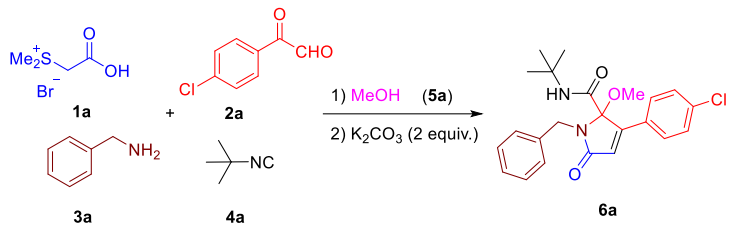
Table *S3*. The Effect of the Equivalent on the Reaction[a]



Entry[a]	1a (Equiv.)	Yield[b](%)
1	**1.2**	64
2	**1.8**	72
3	**2**	82

[a]General conditions: **1a**, **2a** (0.2 mmol), **3a** (0.24 mmol), **4a** (0.24 mmol), in MeOH (2 mL) at 60 ℃ for 24 h. Then K_2CO_3 (0.4 mmol), 60 ℃, 24 h. [b]Yield of isolated product.

Table *S4*. The Effect of the Time on the Reaction[a]



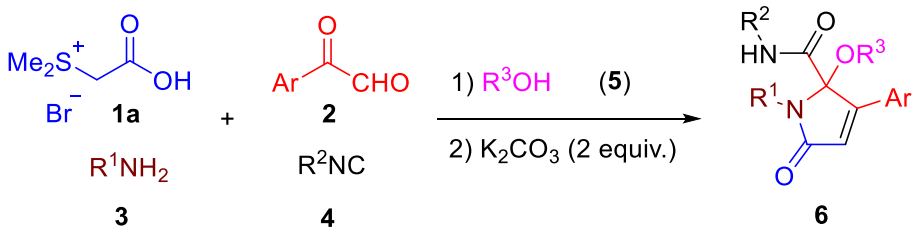
Entry[a]	Time. [h]	Yield[b](%)
1	**24, 24**	82
2	**36, 24**	82
3	**24, 12**	57

[a]General conditions: **1a** (0.36 mmol), **2a** (0.2 mmol), **3a** (0.24 mmol), **4a** (0.24 mmol), in MeOH (2 mL) at 60 ℃. Then K_2CO_3 (0.4 mmol), 60 ℃. [b]Yield of isolated product.

3. Preparation of Substrates

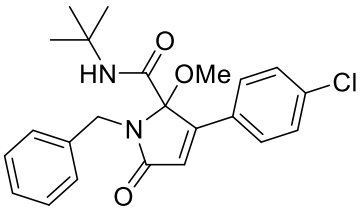
(Carboxymethyl)dimethylsulfonium bromide **1a** was prepared according to procedures.[1] aryl glyoxal **2** were prepared according to procedures.[2]

4. Preparation Characterization Data of Products 6



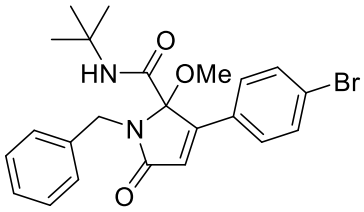
A mixture of (Carboxymethyl)dimethylsulfonium bromide **1a** (80 mg, 0.4 mmol), aryl glyoxal **2** (0.2 mmol), amines **3** (0.24 mmol) and isocyanides **4** (0.24 mmol) was stirred in alcohols (2 mL) at 60 ℃ for 24 h. Then K_2CO_3 (55 mg, 0.4 mmol) was added, the reaction mixture was stirred at 60 ℃ for 24 h. The solvent was removed under reduced pressure and the residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 4:1) to afford pyrrolidin-5-one-2-carboxamides **6**.

1-Benzyl-*N*-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6a):



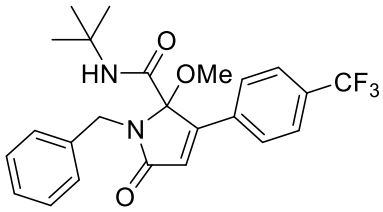
White solid, 67.6 mg, 82% yield; mp 192.2 – 194.1 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.77 (d, J = 8.4 Hz, 2H), 7.54 – 7.51 (m, 3H), 7.30 – 7.29 (m, 4H), 7.24 – 7.22 (m, 1H), 7.06 (s, 1H), 4.47 (d, J = 15.7 Hz, 1H), 4.28 (d, J = 15.7 Hz, 1H), 2.84 (s, 3H), 1.11 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6): δ = 170.0, 164.1, 152.5, 137.3, 135.0, 128.9, 128.8, 128.4, 128.0, 127.8, 126.9, 123.9, 95.3, 51.1, 51.6, 42.0, 27.8. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{25}ClN_2NaO_3$ 435.1446, found: 435.1456.

1-Benzyl-3-(4-bromophenyl)-*N*-(tert-butyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6b):



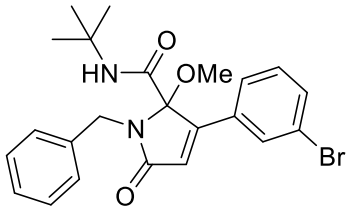
White solid, 54.7 mg, 60% yield; mp 171.4 – 173.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 – 7.50 (m, 2H), 7.47 – 7.45 (m, 2H), 7.36 – 7.34 (m, 2H), 7.31 – 7.27 (m, 3H), 6.88 (br, 1H), 6.66 (s, 1H), 4.69 (d, *J* = 15.4 Hz, 1H), 4.23 (d, *J* = 15.4 Hz, 1H), 2.79 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.2, 152.8, 137.0, 132.2, 129.0, 128.6, 128.4, 128.2, 127.5, 125.0, 124.1, 96.2, 51.9, 51.1, 43.2, 28.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{23}H_{26}BrN_2O_3$ 457.1127, found: 457.1121.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-(4-(trifluoromethyl)phenyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6c):



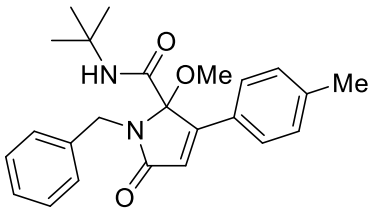
White solid, 50.0 mg, 56% yield; mp 171.4 – 173.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 – 7.70 (m, 2H), 7.65 – 7.63 (m, 2H), 7.37 – 7.35 (m, 2H), 7.32 – 7.29 (m, 2H), 7.27 – 7.23 (m, 1H), 6.90 (br, 1H), 6.75 (s, 1H), 4.71 (d, *J* = 15.4 Hz, 1H), 4.25 (d, *J* = 15.4 Hz, 1H), 2.81 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.0, 164.1, 152.5, 136.9, 133.5, 132.6 (q, *J* = 32.8 Hz), 128.6, 128.5, 127.6, 127.0, 126.0 (m), 125.9 (m), 125.9(0), 96.4, 52.0, 51.2, 43.4, 28.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -63.0 (s, 3F). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{25}F_3N_2NaO_3$ 469.1709, found: 469.1714.

1-Benzyl-3-(3-bromophenyl)-*N*-(tert-butyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6d):



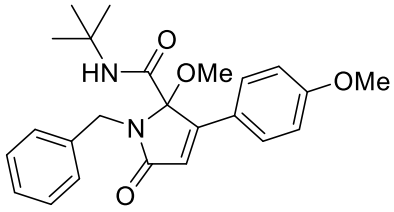
White solid, 52.9 mg, 58% yield; mp 188.1 – 190.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (t, *J* = 1.6 Hz, 1H), 7.52 (t, *J* = 9.3 Hz, 2H), 7.36 – 7.35 (m, 2H), 7.32 – 7.23 (m, 4H), 6.95 (br, 1H), 6.67 (s, 1H), 4.72 (d, *J* = 15.3 Hz, 1H), 4.20 (d, *J* = 15.3 Hz, 1H), 2.79 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2 , 164.1, 152.4, 137.0, 133.3, 132.0, 130.5, 129.5, 128.6, 128.4, 127.5, 125.5, 124.8, 123.1, 96.3, 52.0, 51.1, 43.4, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{25}BrN_2NaO_3$ 479.0941, found: 479.0947.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-(p-tolyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6e):



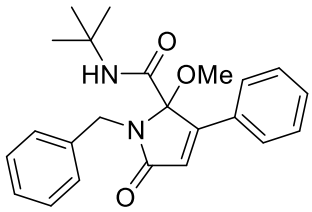
White solid, 47.1 mg, 60% yield; mp 163.4 – 165.2 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 8.2 Hz, 2H), 7.37 – 7.35 (m, 2H), 7.31 – 7.27 (m, 2H), 7.25 – 7.23 (m, 1H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.89 (br, 1H), 6.61 (s, 1H), 4.72 (d, *J* = 15.4 Hz, 1H), 4.21 (d, *J* = 15.4 Hz, 1H), 2.78 (s, 3H), 2.36 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.9, 164.5, 154.0, 141.0, 137.3, 129.7, 128.6, 128.4, 127.4, 127.3, 126.7, 122.6, 96.5, 51.8, 51.0, 43.2, 28.5, 21.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{28}N_2NaO_3$ 415.1992, found: 415.2002.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-3-(4-methoxyphenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6f)：



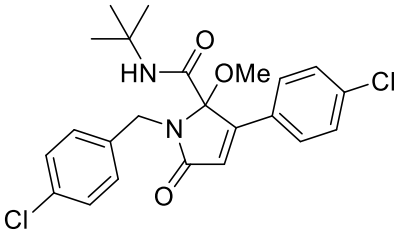
White solid, 50.6 mg, 62% yield; mp 163.4 – 165.2 ºC ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.9 Hz, 2H), 7.30 – 7.27 (m, 2H), 7.23 – 7.19 (m, 2H), 7.17 – 7.13 (m, 1H), 6.82 – 6.79 (m, 3H), 6.45 (s, 1H), 4.63 (d, *J* = 15.4 Hz, 1H), 4.14 (d, *J* = 15.4 Hz, 1H), 3.74 (s, 3H), 2.71 (s, 3H), 1.18 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.0, 164.6, 161.4, 153.7, 137.4, 128.6, 128.4, 128.3(5), 127.3, 122.7, 121.2, 114.3, 96.4, 55.4, 51.8, 51.0, 43.2, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{28}N_2NaO_4$ 431.1941, found: 431.1953.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6g)：



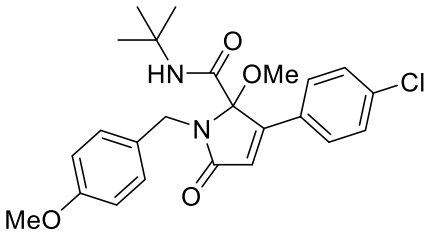
White solid, 57.5 mg, 76% yield; mp 142.6 – 144.7 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60 – 7.58 (m, 2H), 7.39 – 7.36 (m, 5H), 7.32 – 7.28 (m, 2H), 7.24 – 7.22 (m, 1H), 6.90 (br, 1H), 6.66 (s, 1H), 4.73 (d, *J* = 15.4 Hz, 1H), 4.21 (d, *J* = 15.4 Hz, 1H), 2.80 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.7, 164.4, 154.0, 137.2, 130.6, 130.2, 129.0, 128.7, 128.4, 127.5, 126.8, 123.7, 96.5, 51.8, 51.1, 43.3, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{26}N_2NaO_3$ 401.1836, found: 401.1838.

***N*-(tert-butyl)-1-(4-chlorobenzyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6h):**



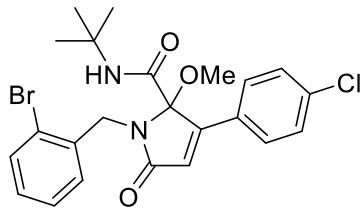
White solid, 51.7 mg, 58% yield; mp 124.5 – 126.5 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.30 – 7.25 (m, 4H), 6.86 (br, 1H), 6.64 (s, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 4.26 (d, *J* = 15.5 Hz, 1H), 2.86 (s, 3H), 1.24 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.1, 152.9, 136.8, 135.5, 133.3, 129.9, 129.3, 128.6, 128.4, 128.0, 123.9, 96.1, 51.9, 51.2, 42.5, 28.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{24}Cl_2N_2NaO_3$ 469.1056, found: 469.1065.

_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-1-(4-methoxybenzyl)-5-oxo-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6i)：



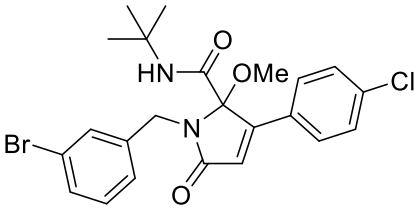
Colorless oil, 49.5 mg, 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 – 7.51 (m, 2H), 7.37 – 7.33 (m, 2H), 7.29 – 7.27 (m, 2H), 6.91 (br, 1H), 6.85 – 6.81 (m, 2H), 6.63 (s, 1H), 4.67 (d, *J* = 15.3 Hz, 1H), 4.14 (d, *J* = 15.3 Hz, 1H), 3.77 (s, 3H), 2.79 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2, 164.2, 159.0, 152.6, 136.5, 129.9, 129.2, 129.1(5), 128.5, 127.9, 124.0, 113.7, 96.3, 55.3, 51.8, 51.0, 42.7, 28.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{27}ClN_2NaO_4$ 465.1552, found: 465.1563.

1-(2-Bromobenzyl)-_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6j)：



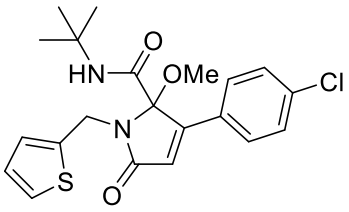
Colorless oil, 54.9 mg, 56% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 – 7.54 (m, 2H), 7.51 – 7.47 (m, 2H), 7.37 – 7.35 (m, 2H), 7.27 – 7.23 (m, 1H), 7.11 – 7.07 (m, 1H), 6.92 (br, 1H), 6.68 (s, 1H), 4.67 (d, *J* = 16.3 Hz, 1H), 4.57 (d, *J* = 16.3 Hz, 1H), 2.93 (s, 3H), 1.17 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.6, 164.0, 153.2, 136.8, 135.9, 132.5, 130.6, 129.3, 129.0, 128.5, 128.0, 127.9, 123.8, 122.6, 95.8, 51.9, 51.2, 42.4, 28.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{24}BrClN_2NaO_3$ 513.0551, found: 513.0555.

1-(3-Bromobenzyl)-_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6k)：



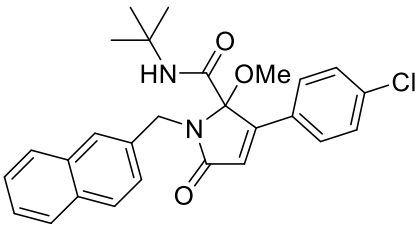
Colorless oil, 52.0 mg, 53% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.6 Hz, 2H), 7.48 (s, 1H), 7.39 – 7.35 (m, 3H), 7.32 – 7.28 (m, 1H), 7.20 – 7.16 (m, 1H), 6.86 (br, 1H), 6.65 (s, 1H), 4.58 (d, *J* = 15.5 Hz, 1H), 4.27 (d, *J* = 15.5 Hz, 1H), 2.87 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.0, 153.0, 139.2, 136.8, 131.5, 130.7, 130.2, 129.3, 128.5, 128.0, 127.3, 123.9, 122.4, 96.1, 52.0, 51.2, 42.6, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{24}BrClN_2NaO_3$ 513.0551, found: 513.0554.

_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-1-(thiophen-2-ylmethyl)-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6l)：



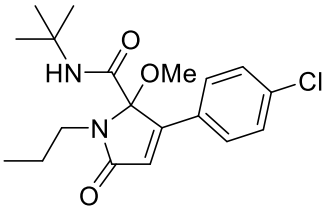
Colorless oil, 55.2 mg, 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.45 (m, 2H), 7.28 (d, *J* = 8.6 Hz, 2H), 7.13 – 7.12 (m, 1H), 6.96 – 6.95 (m, 1H), 6.91 (br, 1H), 6.86 – 6.84 (m, 1H), 6.54 (s, 1H), 4.88 (d, *J* = 15.8 Hz, 1H), 4.22 (d, *J* = 15.8 Hz, 1H), 2.77 (s, 3H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.0, 164.2, 152.9, 139.3, 136.8, 129.3, 128.6, 128.1, 127.4, 126.8, 125.4, 124.0, 96.4, 52.1, 51.2, 37.7, 28.6. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{21}H_{23}ClN_2NaO_3S$ 441.1010, found: 441.1020.

_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-1-(naphthalen-2-ylmethyl)-5-oxo-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6m)：



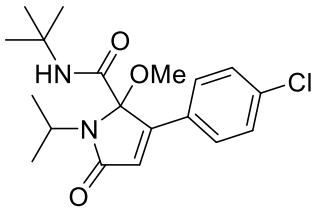
Colorless oil, 56.4 mg, 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.71 (m, 2H), 7.50 – 7.46 (m, 1H), 7.43 – 7.39 (m, 4H), 7.35 – 7.31 (m, 1H), 7.25 – 7.23 (m, 2H), 6.76 (br, 1H), 6.58 (s, 1H), 5.37 (d, *J* = 15.5 Hz, 1H), 4.40 (d, *J* = 15.5 Hz, 1H), 2.34 (s, 3H), 1.19 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2, 164.2, 153.1, 136.7, 133.7, 132.5, 131.8, 129.2, 128.8, 128.6, 128.5, 128.0, 127.8, 126.6, 125.9, 125.1, 124.0, 123.9(7), 96.8, 52.0, 50.9, 41.6, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{27}ClN_2NaO_3$ 485.1602, found: 485.1603.

_N_-(tert-butyl)-3-(4-chlorophenyl)-2-methoxy-5-oxo-1-propyl-2,5-dihydro-1_H_-pyrrole-2-carboxamide (6n)：



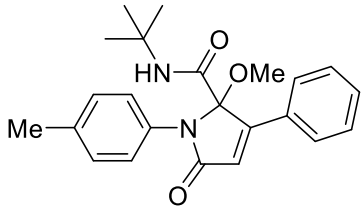
White solid, 47.3 mg, 65% yield; mp 144.2 – 146.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.5 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 6.96 (br, 1H), 6.58 (s, 1H), 3.23 – 3.15 (m, 2H), 3.10 (s, 3H), 1.75 – 1.55 (m, 2H), 1.37 (s, 9H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.6, 152.2, 136.5, 129.2, 128.7, 128.0, 124.4, 95.9, 51.9, 51.0, 41.4, 28.6, 21.7, 11.8. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{19}H_{25}ClN_2NaO_3$ 387.1446, found: 387.1448.

***N*-(tert-butyl)-3-(4-chlorophenyl)-1-isopropyl-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6o):**



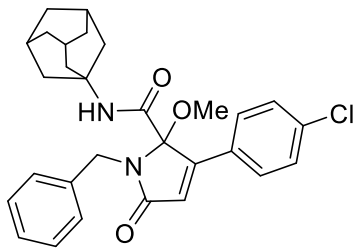
White solid, 45.9 mg, 63% yield; mp 152.2 – 154.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 6.93 (br, 1H), 6.51 (s, 1H), 3.63 – 3.56 (m, 1H), 3.16 (s, 3H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.39 (d, *J* = 6.9 Hz, 3H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 169.9, 164.6,151.6, 136.4, 129.2, 128.7, 127.8, 125.4, 96.2, 51.8, 51.3, 44.9, 28.6, 20.7, 19.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{19}H_{25}ClN_2NaO_3$ 387.1446, found: 387.1447.

***N*-(*tert*-butyl)-2-methoxy-5-oxo-3-phenyl-1-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6p)**



Colorless oil, 49.9 mg, 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 – 7.64 (m, 2H), 7.43 – 7.41 (m, 3H), 7.27 – 7.18 (m, 4H), 6.74 (s, 1H), 6.71 (s, 1H), 3.35 (s, 3H), 2.35 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.3, 164.2, 153.8, 137.3, 132.5, 130.8, 130.0, 129.6, 129.0, 127.0, 126.8, 124.1, 97.3, 51.6, 51.3, 28.2, 21.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{26}N_2NaO_3$ 401.1836 found: 401.1842.

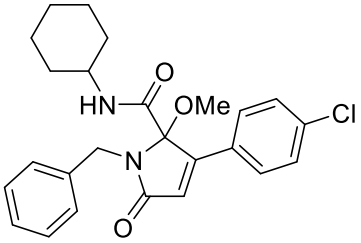
***N*-(adamantan-1-yl)-1-benzyl-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6q):**



White solid, 78.4 mg, 80% yield; mp 172.4 – 174.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.6 Hz, 2H), 7.37 – 7.35 (m, 4H), 7.32 – 7.29 (m, 2H), 7.27 – 7.25 (m, 1H), 6.79 (br, 1H), 6.64 (s, 1H), 4.76 (d, *J* = 15.3 Hz, 1H), 4.17 (d, *J* = 15.3 Hz, 1H), 2.75 (s, 3H), 2.11 – 2.02 (s, 3H), 1.91 (q, *J* = 11.5 Hz, 6H), 1.68 – 1.63 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 163.9, 152.8, 137.2, 136.6, 129.3, 128.7, 128.6, 128.5, 128.0, 127.5, 124.0, 96.4, 52.6, 51.1, 43.4, 41.3, 36.3, 29.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for

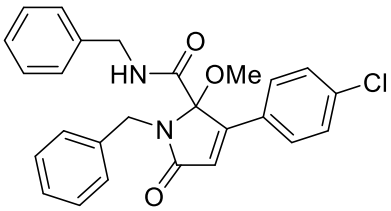
$C_{29}H_{31}ClN_2NaO_3$ 513.1915, found: 513.1926.

1-Benzyl-3-(4-chlorophenyl)-*N*-cyclohexyl-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6r):



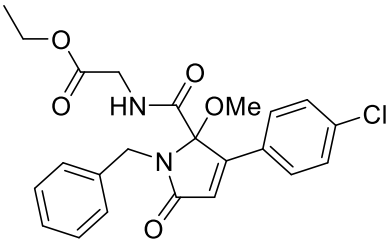
White solid, 54.3 mg, 62% yield; mp 180.0 – 182.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.7 Hz, 2H), 7.36 – 7.33 (m, 4H), 7.32 – 7.25 (m, 3H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.65 (s, 1H), 4.73 (d, *J* = 15.3 Hz, 1H), 4.16 (d, *J* = 15.3 Hz, 1H), 3.70 – 3.61 (m, 1H), 2.78 (s, 3H), 1.81 – 1.77 (m, 2H), 1.72 – 1.61 (m, 4H), 1.37 – 1.28 (m, 2H), 1.20 – 1.17 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.3, 164.3, 152.5, 137.0, 136.7, 129.3, 128.8, 128.6, 128.4, 128.0, 127.6, 124.1, 96.3, 51.0, 48.6, 43.5, 33.0, 32.8, 25.5, 24.9, 24.8. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{27}ClN_2NaO_3$ 461.1602, found: 461.1602.

***N*,1-dibenzyl-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6s):**



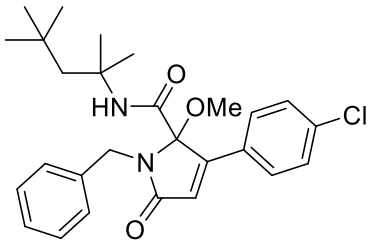
White solid, 44.6 mg, 50% yield; mp 212.7 – 214.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 8.7 Hz, 2H), 7.37 – 7.29 (m, 8H), 7.27 (s, 2H), 7.17– 7.15 (m, 2H), 6.67 (s, 1H), 4.67 (d, *J* = 15.3 Hz, 1H), 4.47– 4.41 (m, 1H), 4.25 (d, *J* = 15.3 Hz, 1H), 4.18 – 4.13 (m, 1H), 2.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.2, 165.4, 152.6, 137.4, 136.8, 136.7(7), 131.6, 129.4, 129.0, 128.8, 128.4, 128.3, 128.1, 127.6, 124.3, 96.3, 51.0, 43.9, 43.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{23}ClN_2NaO_3$ 469.1289, found: 469.1287.

Ethyl(1-benzyl-3-(4-chlorophenyl)-2-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carbonyl)glycinate (6t):



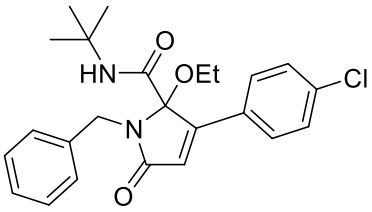
White solid, 56.6 mg, 64% yield; mp 171.2 – 172.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 8.6 Hz, 2H), 7.46 – 7.45 (m, 1H), 7.32 – 7.26 (m, 4H), 7.22 – 7.16 (m, 3H), 6.59 (s, 1H), 4.52 (d, *J* = 15.2 Hz, 1H), 4.35 (d, *J* = 15.2 Hz, 1H), 4.20 – 4.12 (m, 2H), 3.84 – 3.78 (m, 1H), 3.70 – 3.64 (m, 1H), 2.77 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.0, 169.4, 165.9, 152.3, 136.9, 136.8, 129.5, 129.0, 128.3, 128.2, 128.0, 127.6, 124.1, 95.9, 61.9, 51.0, 43.2, 41.3, 14.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{23}ClN_2NaO_5$ 465.1188, found: 465.1194.

1-Benzyl-3-(4-chlorophenyl)-2-methoxy-5-oxo-*N*-(2,4,4-trimethylpentan-2-yl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6u):



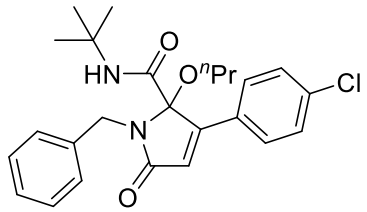
Colorless oil, 49.6 mg, 53% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.6 Hz, 2H), 7.37 – 7.34 (m, 4H), 7.31 – 7.27 (m, 2H), 7.25 – 7.24 (m, 1H), 7.05 (br, 1H), 6.65 (s, 1H), 4.70 (d, *J* = 15.5 Hz, 1H), 4.23 (d, *J* = 15.5 Hz, 1H), 2.82 (s, 3H), 1.58 (d, *J* = 1.4 Hz, 2H), 1.31 (s, 3H), 1.26 (s, 3H), 1.02 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 163.8, 152.7, 137.0, 136.6, 129.2, 128.6, 128.5, 128.4, 128.1, 127.5, 124.2, 96.5, 56.1, 54.2, 51.3, 43.2, 31.7, 27.7. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{27}H_{33}ClN_2NaO_3$ 491.2072, found: 491.2083.

1-Benzyl-*N*-(tert-butyl)-3-(4-chlorophenyl)-2-ethoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6v):



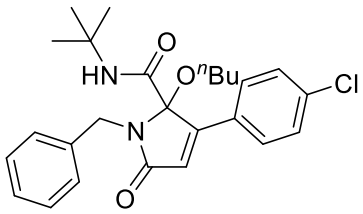
Colorless oil, 52.0 mg, 61% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52 (d, *J* = 8.6 Hz, 2H), 7.36 – 7.34 (m, 4H), 7.31 – 7.27 (m, 3H), 6.95 (br, 1H), 6.61 (s, 1H), 4.78 (d, *J* = 15.4 Hz, 1H), 4.13 (d, *J* = 15.4 Hz, 1H), 2.97 (q, *J* = 7.0 Hz, 2H), 1.29 (s, 9H), 0.73 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.3, 164.4, 153.2, 137.2, 136.6, 129.2, 128.5, 128.4(8), 127.9, 127.5, 123.6, 95.9, 59.6, 51.9, 43.3, 28.5, 14.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{27}ClN_2NaO_3$ 449.1602, found: 449.1607.

1-Benzyl-*N*-(tert-butyl)-3-(4-chlorophenyl)-5-oxo-2-propoxy-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6w):



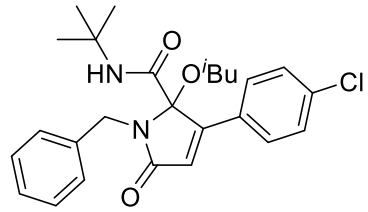
Yellow oil, 47.5 mg, 54% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.6 Hz, 2H), 7.28 (s, 1H), 7.25 – 7.23 (m, 2H), 7.21 – 7.14 (m, 4H), 6.86 (br, 1H), 6.54 (s, 1H), 4.67 (d, *J* = 15.4 Hz, 1H), 4.08 (d, *J* = 15.4 Hz, 1H), 2.85 – 2.72 (m, 2H), 1.24 – 1.22 (s, 2H), 1.20 (s, 9H), 0.55 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.4, 153.1, 137.2, 136.6, 129.2, 128.7, 128.5, 128.4(6), 127.9, 127.5, 123.6, 95.8, 65.4, 51.8, 43.3, 28.5, 22.1, 10.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{25}H_{29}ClN_2NaO_3$ 463.1759, found: 463.1771.

1-Benzyl-2-butoxy-*N*-(tert-butyl)-3-(4-chlorophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6x):



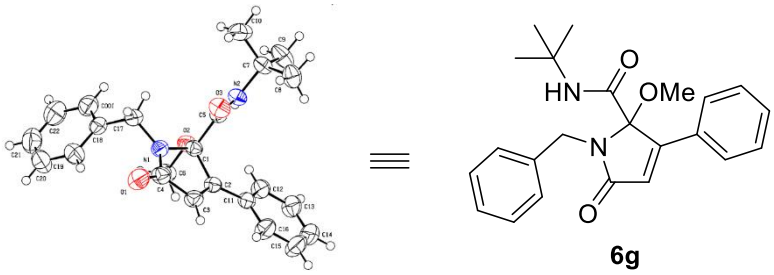
Yellow oil, 47.2 mg, 52% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 – 7.45 (m, 2H), 7.29 – 7.26 (m, 4H), 7.24 – 7.17 (m, 3H), 6.86 (br, 1H), 6.56 (s, 1H), 4.69 (d, *J* = 15.4 Hz, 1H), 4.08 (d, *J* = 15.4 Hz, 1H), 2.88 – 2.78 (m, 2H), 1.21 (s, 9H), 1.08 – 0.83 (m, 4H), 0.65 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.5, 153.2, 137.4, 136.6, 129.2, 128.7, 128.6, 128.5, 128.0, 127.5, 123.6, 95.9, 63.8, 51.8, 43.4, 30.9, 28.5, 19.2, 13.9. HRMS (ESI-TOF) m/z: [M+Na]+ calcd for $C_{26}H_{31}ClN_2NaO_3$ 477.1915, found: 477.1921.

1-Benzyl-*N*-(tert-butyl)-3-(4-chlorophenyl)-2-isobutoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-2-carboxamide (6y):



Yellow oil, 45.4 mg, 50% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.6 Hz, 2H), 7.36 – 7.32 (m, 4H), 7.31 – 7.25 (m, 3H), 6.93 (br, 1H), 6.65 (s, 1H), 4.73 (d, *J* = 15.4 Hz, 1H), 4.19 (d, *J* = 15.5 Hz, 1H), 2.79– 2.75 (m, 1H), 2.63 (t, *J* = 7.7 Hz, 1H), 1.83 – 1.70 (m, 1H), 1.28 (s, 9H), 0.68 (d, *J* = 6.6 Hz, 3H), 0.58 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.4, 164.5, 153.1, 137.3, 136.7, 129.2, 128.7, 128.5, 128.5(1), 128.0, 127.5, 123.6, 95.7, 70.0, 51.8, 43.4, 28.5, 27.8, 19.4, 19.0. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{26}H_{31}ClN_2NaO_3$ 477.1915, found: 477.1917.

5. Crystal Structure of 6g



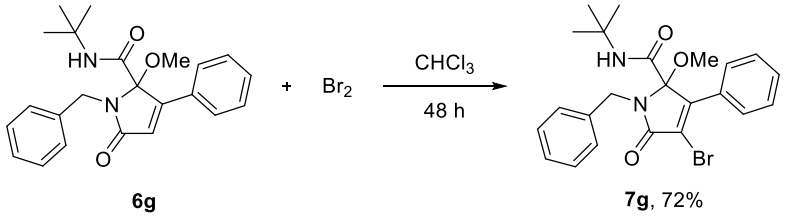
6g

CCDC number	2304061
Identification code	**6g**
Empirical formula	$C_{23}H_{26}N_2O_3$
Formula weight	378.46
Temperature/K	293.79(13)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	11.8456(3)
b/Å	16.4853(4)
c/Å	10.8302(3)
α/°	90
β/°	94.704(2)
γ/°	90
Volume/Å^3	2107.78(9)
Z	4
ρ_{calc}g/cm^3	1.193
μ/mm^{-1}	0.634
F(000)	808.0
Crystal size/mm^3	0.12 × 0.11 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.214 to 148.904
Index ranges	$-13 \le h \le 14$, $-19 \le k \le 20$, $-13 \le l \le 10$
Reflections collected	11225
Independent reflections	4172 [R_{int} = 0.0493, R_{sigma} = 0.0474]
Data/restraints/parameters	4172/0/257
Goodness-of-fit on F^2	1.082
Final R indexes [I>=2σ (I)]	R_1 = 0.0596, wR_2 = 0.1656
Final R indexes [all data]	R_1 = 0.0656, wR_2 = 0.1733
Largest diff. peak/hole / e Å^{-3}	0.23/-0.38

6. Synthetic Application of the Reaction

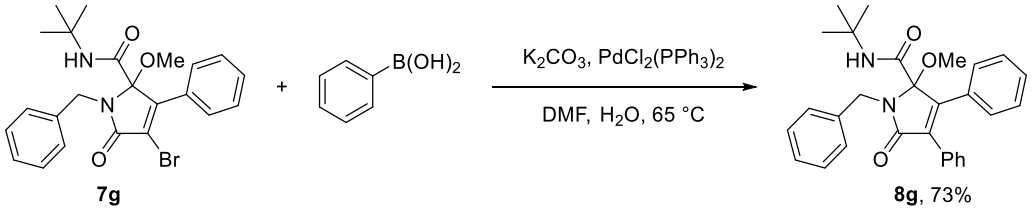
6.1 Derivatization of the 6g, 7g and 16g

1) Synthesis of 1-benzyl-4-bromo-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (7g)



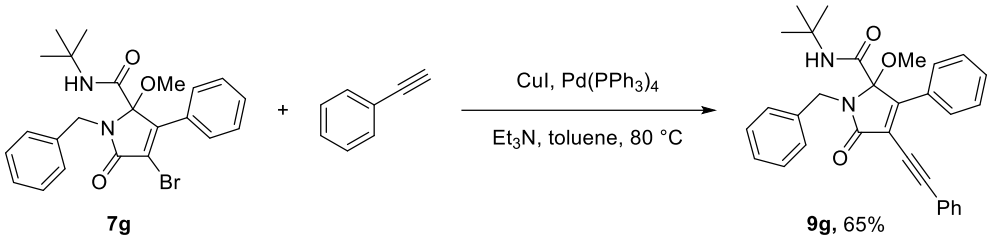
To a mixture of **6g** (0.2 mmol, 75.4 mg) in $CHCl_3$ (2 mL) was added liquid bromine (0.6 mmol, 31 μL). Under the nitrogen atmosphere, the obtained mixture was stirred at room temperature for 48 h. Then the mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **7g** (65.7 mg, 72% yield).

2) Synthesis of 1-benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3,4-diphenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (8g)[3a]



To a mixture of **7g** (0.2 mmol, 91.2 mg) and $PhB(OH)_2$ (0.4 mmol, 48.8 mg) in DMF (4 mL) was added $PdCl_2(PPh_3)_2$ (0.01 mmol, 7.0 mg). Under the nitrogen atmosphere, the obtained mixture was stirred for 30 min at room temperature. Then K_2CO_3 (0.4 mmol, 55.3 mg) in H_2O (1 mL) was added to the mixture, and the obtained mixture was placed in a preheated oil bath at 65 °C, and stirred at 65 °C for 12 h. Water (5 mL) was added to the reaction mixture, and the product was extracted with CH_2Cl_2 (15 mL × 3), and washed with brine (15 mL × 2). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **8g** (66.3 mg, 73% yield).

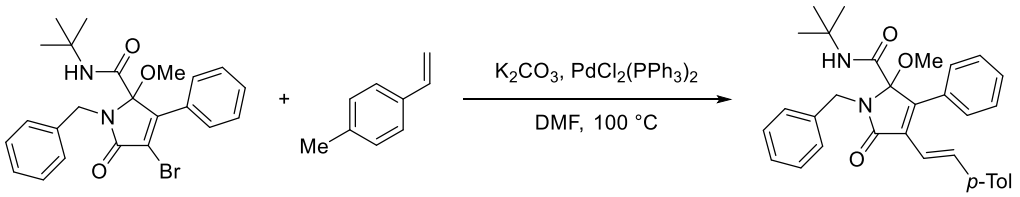
3) Synthesis of 1-benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-4-(phenylethynyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (9g)[3b]



7g **9g**, 65%

To a mixture of **7g** (0.2 mmol, 91.2 mg), CuI (0.004 mmol, 7.6 mg), $Pd(PPh_3)_4$ (0.010 mmol, 11.6 mg) in Et_3N (1 mL) and toluene (1.5 mL) was added ethynylbenzene (0.24 mmol, 24.6 μL). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 80 ℃, and stirred at 80 ℃ for 12 h. Water (2.5 mL) was added to the reaction mixture, and the product was extracted with EtOAc (15 mL × 3), and washed with brine (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **9g** (62.2 mg, 65% yield).

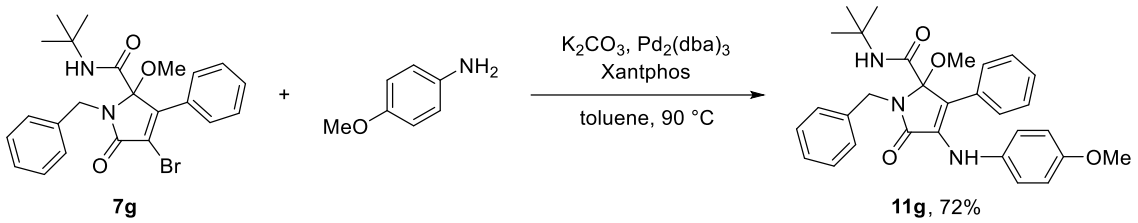
4) Synthesis of (*E*)-1-benzyl-*N*-(tert-butyl)-2-methoxy-4-(4-methylstyryl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (10g)[3b]



7g **10g**, 71%

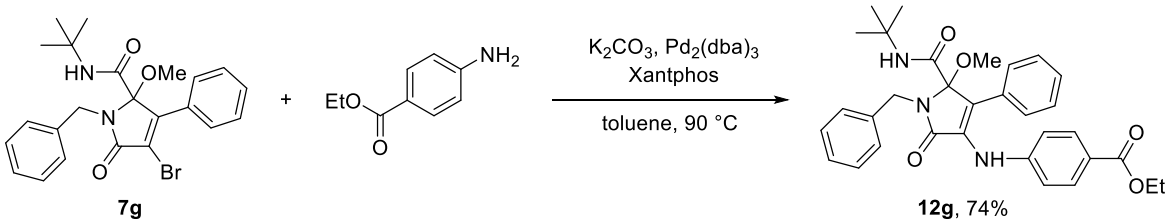
To a mixture of **7g** (0.2 mmol, 91.2 mg), K_2CO_3 (0.4 mmol, 55.3 mg) and $PdCl_2(PPh_3)_2$ (0.010 mmol, 7.0 mg) in DMF (2.0 mL) was added 4-methylstyrene (0.4 mmol, 53 μL). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 100 ℃, and stirred at 100 ℃ for 12 h. Saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to the reaction mixture, and the product was extracted with EtOAc (15 mL × 3), and washed with brine (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **10g** (70.2 mg, 71% yield).

5) Synthesis of 1-benzyl-*N*-(tert-butyl)-2-methoxy-4-((4-methoxyphenyl)amino)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (11g)[3b]



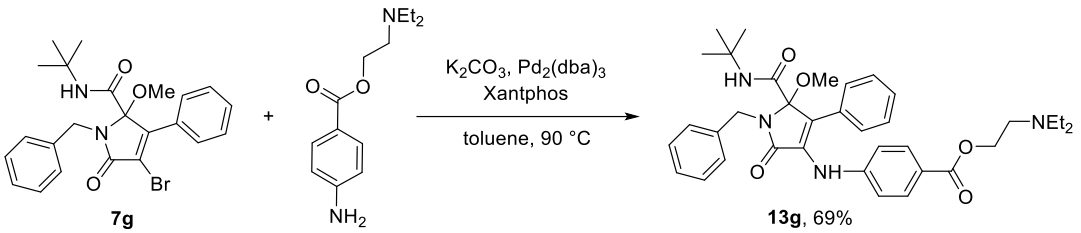
To a mixture of **7g** (0.2 mmol, 91.2 mg), K_2CO_3 (0.4 mmol, 55.3 mg), $Pd_2(dba)_3$ (0.005 mmol, 4.6 mg) and Xantphos (0.010 mmol, 5.8 mg) in toluene (2.0 mL) was added *p*-methoxybenzamide (0.24 mmol, 29.5 mg). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 90 ℃, and stirred at 90 ℃ for 12 h. Saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to the reaction mixture, and the product was extracted with CH_2Cl_2 (15 mL × 3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **11g** (71.9 mg, 72% yield).

6) Synthesis of Ethyl 4-((1-benzyl-5-(tert-butylcarbamoyl)-5-methoxy-2-oxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-3-yl)amino)benzoate (12g)[3b]



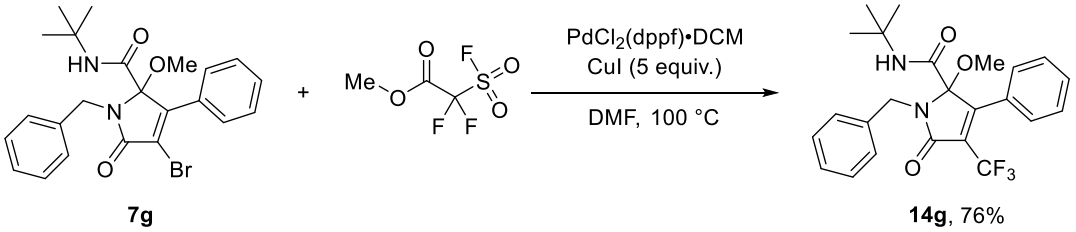
To a mixture of **7g** (0.2 mmol, 91.2 mg), K_2CO_3 (0.4 mmol, 55.3 mg), $Pd_2(dba)_3$ (0.005 mmol, 4.6 mg) and Xantphos (0.010 mmol, 5.8 mg) in toluene (2.0 mL) was added ethyl 4-aminobenzoate (0.24 mmol, 39.6 mg). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 90℃, and stirred at 90 ℃ for 12 h. Saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to the reaction mixture, and the product was extracted with CH_2Cl_2 (15 mL × 3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **12g** (80.1 mg, 74% yield).

7) Synthesis of 2-(diethylamino)ethyl 4-((1-benzyl-5-(tert-butylcarbamoyl)-5-methoxy-2-oxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-3-yl)amino)benzoate (13g)[3b]



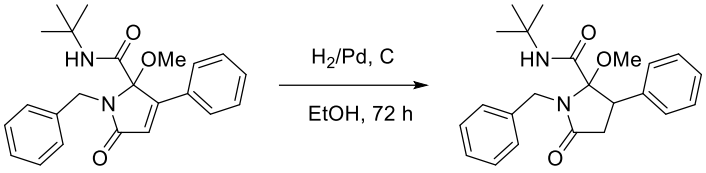
To a mixture of **7g** (0.2 mmol, 91.2 mg), K_2CO_3 (0.4 mmol, 55.3 mg), $Pd_2(dba)_3$ (0.005 mmol, 4.6 mg) and Xantphos (0.010 mmol, 5.8 mg) in toluene (2.0 mL) was added 2-(diethylamino)ethyl 4-aminobenzoate (0.24 mmol, 56.7 mg). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 90 ℃, and stirred at 90 ℃ for 12 h. Saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to the reaction mixture, and the product was extracted with CH_2Cl_2 (15 mL × 3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 40:1) to give **13g** (84.5 mg, 69% yield).

8) Synthesis of 1-benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-4-(trifluoromethyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (14g)[4]



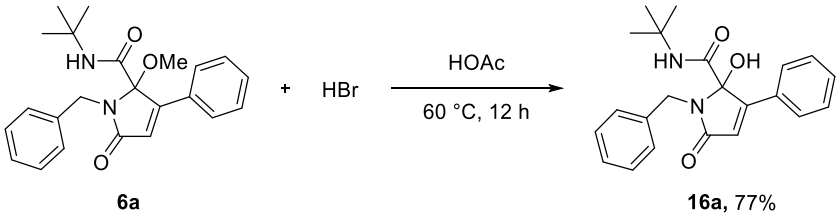
To a mixture of **7g** (0.2 mmol, 91.2 mg), CuI (1.18 mmol, 226 mg) and Pd (dppf)Cl_2·DCM (0.001 mmol, 8 mg) in DMF (2.0 mL) was added methyl 2,2-difluoro-2-(fluorosulfonyl)acetate (1.18 mmol, 227 mg). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 100 ℃, and stirred at 100 ℃ for 24 h. Saturated $NaHCO_3$ aqueous solution (5.0 mL) was added to the reaction mixture, and the product was extracted with EtOAc (15 mL × 3), and washed with brine (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **14g** (67.8 mg, 76% yield).

9) Synthesis of 2-(diethylamino)ethyl 4-((1-benzyl-5-(tert-butylcarbamoyl)-5-methoxy-2-oxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-3-yl)amino)benzoate (15g)[5]



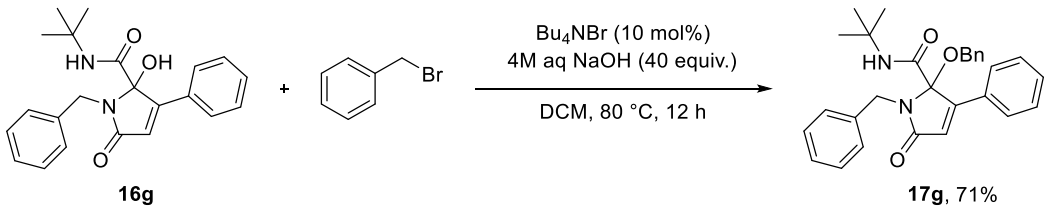
To a mixture of **6g** (0.2 mmol, 75.6 mg) in ethanol (2 mL) was added Pd/C 10% (10 mg). The mixture is placed under hydrogen at a pressure of two bars for 72 h. Then the mixture was concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate =2:1) to give **15g** (49.4 mg, 65% yield).

10) Synthesis of 1-benzyl-*N*-(tert-butyl)-2-hydroxy-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (16g)



To a mixture of **6g** (0.2 mmol, 75.6 mg) in glacial acetic acid (2 mL) was added hydrogen bromide (48% in water, 2 mmol, 0.34 mL). Under the nitrogen atmosphere, the obtained mixture was stirred at 60 ℃ for 12 h. Then the product was extracted with DCM (15 mL × 3), and washed with brine (15 mL). The organic layer was dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **16g** (56.0 mg, 77% yield).

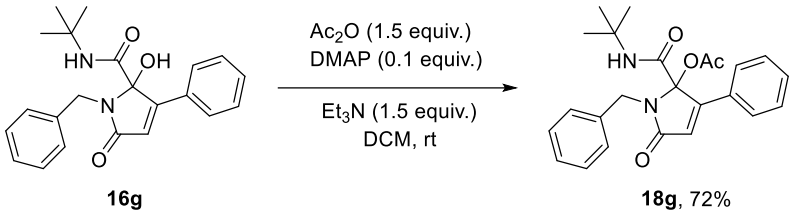
11) Synthesis of 1-benzyl-2-(benzyloxy)-*N*-(tert-butyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (16g)



To a mixture of **16g** (0.2 mmol, 72.8 mg), Bu_4NBr (0.002 mmol, 7 mg) and NaOH (8 mmol, 4M, aq.) in DCM (2.0 mL) was added benzyl bromide (0.6 mmol, 102 mg). Under nitrogen atmosphere, the obtained mixture was placed in a preheated oil bath at 80 ℃, and stirred at 80 ℃ for 12 h. Then the product was extracted with DCM (15 mL × 3), and washed with brine (15 mL). The organic layer

was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **17g** (64.5 mg, 71% yield).

12) Synthesis of 1-benzyl-2-(tert-butylcarbamoyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrol-2-yl acetate (18g)[6]

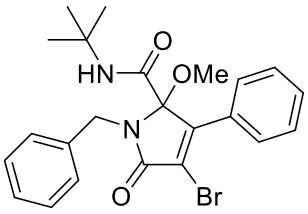


16g **18g**, 72%

To a mixture of **16g** (0.2 mmol, 72.8 mg) in DCM (2 mL) at 0 ℃ was added DMAP (0.02 mmol, 3.2 mg), triethylamine (0.3 mmol, 43 μL) and Ac_2O (0.3 mmol, 28 μL). The reaction mixture was stirred at room temperature for 2 h. After addition of anappropriate volume of aqueous water, the product was extracted with DCM (15 mL × 3), and washed with brine (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) to give **18g** (58.5 mg, 72% yield).

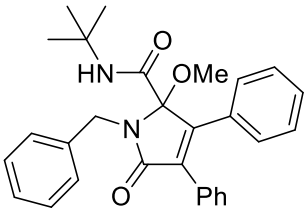
6.2 Characterization Data of Products 7g-18g

1-Benzyl-4-bromo-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (7g):



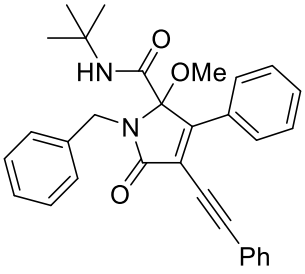
White solid, 65.7 mg, 72% yield; mp 148.1 – 150.1 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 – 7.67 (m, 2H), 7.42 – 7.37 (m, 5H), 7.32 – 7.25 (m, 3H), 6.80 (br, 1H), 4.80 (d, *J* = 15.2 Hz, 1H), 4.20 (d, *J* = 15.2 Hz, 1H), 2.84 (s, 3H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.6, 163.5, 149.1, 136.5, 130.3, 123.0, 129.0, 128.7, 128.5, 128.1, 127.7, 118.9, 96.9, 52.0, 51.2, 44.7, 28.41. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{25}BrN_2NaO_3$ 479.0941, found: 479.0946.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3,4-diphenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (8g):



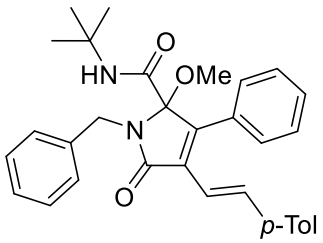
Colorless oil, 66.3 mg, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.34 (m, 4H), 7.24 – 7.17 (m, 11H), 6.77 (br, 1H), 4.73 (d, *J* = 15.1 Hz, 1H), 4.18 (d, *J* = 15.1 Hz, 1H), 2.85 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.6, 164.5, 147.5, 137.1, 135.9, 131.5, 130.6, 130.0, 129.2, 129.0, 128.8, 128.6, 128.4, 128.3, 127.5, 115.5, 95.9, 51.8, 50.8, 44.2, 28.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{29}H_{30}N_2NaO_3$ 477.2149, found: 477.2158.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-4-(phenylethynyl)-2,5-dihydro-1*H*-pyrrole-2-carboxamide (9g):



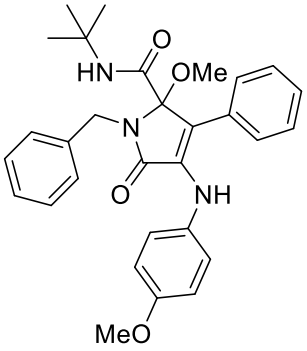
Colorless oil, 62.2 mg, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10 – 8.07 (m, 2H), 7.60 – 7.57 (m, 2H), 7.42 – 7.40 (m, 4H), 7.38 – 7.35 (m, 3H), 7.32 – 7.23 (m, 4H), 6.88 (br, 1H), 4.78 (d, *J* = 15.3 Hz, 1H), 4.26 (d, *J* = 15.3 Hz, 1H), 2.82 (s, 3H), 1.25 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.4, 164.4, 151.3, 136.9, 132.2, 130.8, 130.7, 129.3, 128.8, 128.7, 128.5, 128.4(6), 127.8, 127.6, 122.5, 119.1, 101.2, 95.9, 82.0, 51.9, 51.1, 43.9, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{31}H_{30}N_2NaO_3$ 501.2149, found: 501.2157.

(*E*)-1-benzyl-*N*-(tert-butyl)-2-methoxy-4-(4-methylstyryl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (10g):



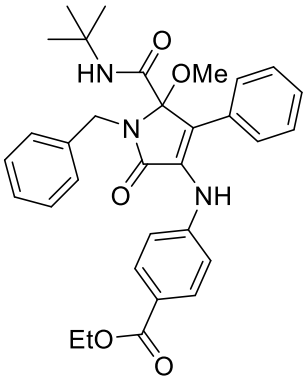
Colorless oil, 70.2 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 16.3 Hz, 1H), 7.36 – 7.33 (m, 6H), 7.27 – 7.17 (m, 6H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.79 (d, *J* = 16.4 Hz, 2H), 4.72 (d, *J* = 15.1 Hz, 1H), 4.11 (d, *J* = 15.1 Hz, 1H), 2.76 (s, 3H), 2.25 (s, 3H), 1.15 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.6, 164.7, 146.1, 138.5, 137.2, 136.7, 134.7, 132.1, 131.7, 129.4, 129.2, 129.0, 129.0(0), 128.7, 128.4, 127.5, 127.1, 116.9, 95.8, 51.8, 50.9, 44.0, 28.4, 21.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{32}H_{34}N_2NaO_3$ 517.2462, found: 517.2462.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-4-((4-methoxyphenyl)amino)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (11g):



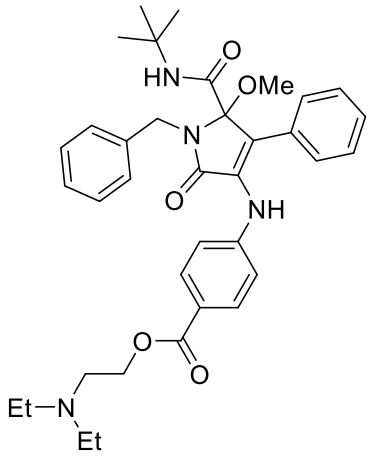
White solid, 71.9 mg, 72% yield; mp 182.1 – 184.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (d, *J* = 7.1 Hz, 2H), 7.26 – 7.16 (m, 3H), 7.99 – 6.95 (m, 3H), 6.92 – 6.90 (m, 2H), 6.80 (s, 1H), 6.59 (s, 1H), 6.50 – 6.43 (m, 4H), 4.72 (d, *J* = 15.2 Hz, 1H), 4.17 (d, *J* = 15.2 Hz, 1H), 3.59 (s, 3H), 2.75 (s, 3H), 1.15 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.8, 165.6, 155.1, 136.9, 132.1, 132.0(9), 131.6, 129.0, 128.4, 128.2, 127.5, 127.5(0), 127.0, 121.5, 113.5, 113.2, 96.3, 55.6, 51.6, 50.5, 44.3, 28.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{30}H_{33}N_3NaO_4$ 522.2363, found: 522.2375.

Ethyl-4-((1-benzyl-5-(tert-butylcarbamoyl)-5-methoxy-2-oxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-3-yl)amino)benzoate (12g):



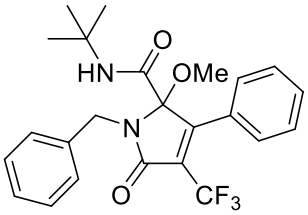
White solid, 80.1 mg, 74% yield; mp 211.6 – 213.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.7 Hz, 2H), 7.34 – 7.32 (m, 2H), 7.26 – 7.16 (m, 3H), 7.07 – 7.01 (m, 6H), 6.81 (s, 1H), 6.51 – 6.47 (m, 2H), 4.72 (d, *J* = 15.2 Hz, 1H), 4.22 – 4.16 (m, 3H), 2.79 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.14 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.4, 166.4, 165.0, 143.1, 136.6, 131.3, 130.6, 130.2, 128.9, 128.4, 128.1, 128.0, 127.9(7), 127.6, 123.1, 119.2, 117.8, 96.2, 60.6, 51.7, 50.8, 44.3, 28.4, 14.4. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{32}H_{35}N_3NaO_5$ 564.2469, found: 564.2477.

2-(Diethylamino)ethyl 4-((1-benzyl-5-(tert-butylcarbamoyl)-5-methoxy-2-oxo-4-phenyl-2,5-dihydro-1*H*-pyrrol-3-yl)amino)benzoate (13g):



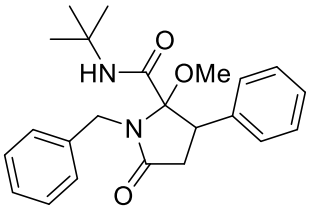
Yellow solid, 84.5 mg, 69% yield; mp 150.3 – 152.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 – 7.57 (m, 2H), 7.59 – 7.57 (m, 2H), 7.34 – 7.32 (m, 2H), 7.25 – 7.18 (m, 5H), 6.82 (s, 1H), 7.55 – 6.47 (m, 2H), 4.72 (d, *J* = 15.2 Hz, 1H), 4.29 – 4.23 (m, 2H), 4.21 (d, *J* = 3.0 Hz, 1H), 2.79 (s, 3H), 2.73 (t, *J* = 6.2 Hz, 2H), 2.57 – 2.51 (m, 3H), 1.14 (s, 9H), 1.02 – 0.95 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 168.4, 166.4, 165.0, 143.1, 136.6, 131.3, 130.6, 130.2, 128.9, 128.4, 128.1, 128.0, 127.9(6), 127.6, 123.1, 119.2, 117.8, 96.2, 60.6, 51.7, 50.8, 44.3, 28.4, 14.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{36}H_{45}N_4O_5$ 613.3384, found: 613.3392.

1-Benzyl-N-(tert-butyl)-2-methoxy-5-oxo-3-phenyl-4-(trifluoromethyl)-2,5-dihydro-1H-pyrrole-2-carboxamide (14g):



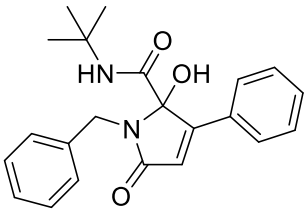
Colorless oil, 67.8 mg, 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.38 – 7.34 (m, 2H), 7.32 – 7.29 (m, 3H), 7.25 – 7.19 (m, 5H), 6.64 (br, 1H), 4.69 (d, *J* = 15.1 Hz, 1H), 4.07 (d, *J* = 15.1 Hz, 1H), 2.80 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 165.6 (m), 162.8, 157.6 (m), 136.2, 130.5, 129.2, 129.0, 128.6, 128.5, 128.4 (d, *J* = 1.7 Hz), 127.9, 126.5 (q, *J* = 33.8 Hz), 120.5 (d, *J* = 272.4 Hz), 96.2, 52.1, 51.4, 44.4, 28.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -59.8 (s, 3F). HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{25}F_3N_2NaO_3$ 469.1709, found: 469.1718.

1-Benzyl-*N*-(tert-butyl)-2-methoxy-5-oxo-3-phenylpyrroiline-2-carboxamide (15g):



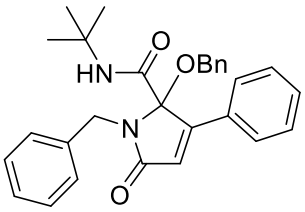
Colorless oil, 49.4 mg, 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 7.1 Hz, 2H), 7.28 – 7.26 (m, 4H), 7.24 – 7.21 (m, 4H), 6.20 (br, 1H), 4.59 (d, *J* = 14.8 Hz, 1H), 4.02 (d, *J* = 14.8 Hz, 1H), 3.76 – 3.71 (m, 1H), 3.35 – 3.28 (m, 1H) , 3.12 (s, 3H), 2.77 – 2.71 (m, 1H), 0.86 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 174.9, 166.1, 137.2, 135.2, 129.4, 128.6, 128.4, 128.3, 127.6, 127.4, 98.9, 50.8, 50.2, 45.0, 41.6, 34.5, 28.2. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{23}H_{28}N_2NaO_3$ 403.1992, found: 403.2001.

1-Benzyl-*N*-(tert-butyl)-2-hydroxy-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (16g):



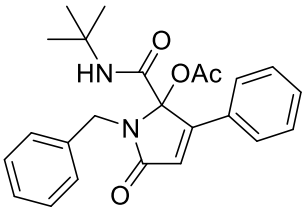
White solid, 56.0 mg, 77% yield; mp 182.0 – 184.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 – 7.48 (m, 2H), 7.31 – 7.30 (m, 3H), 7.27 – 7.19 (m, 6H), 6.41 (s, 1H), 5.01 (d, *J* = 14.9 Hz, 1H), 4.74 (s, 1H), 4.12 (d, *J* = 14.9 Hz, 1H), 1.05 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 171.5, 165.4, 155.9, 136.7, 130.7, 130.6, 129.0, 128.9, 128.7, 128.0, 127.1, 120.7, 68.8, 51.7, 45.2, 28.3. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{22}H_{24}N_2NaO_3$ 387.1679, found: 387.1682.

1-Benzyl-2-(benzyloxy)-*N*-(tert-butyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrole-2-carboxamide (17g):



Colorless oil, 64.5 mg, 71% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 – 7.56 (m, 2H), 7.32– 7.29 (m, 5H), 7.23 – 7.09 (m, 6H), 6.88 (br, 1H), 6.66 (s, 1H), 6.62 (d, *J* = 6.7 Hz, 2H), 4.79 (d, *J* = 15.4 Hz, 1H), 4.10 (d, *J* = 15.4 Hz, 1H), 3.89 (dd, *J* = 25.0, 10.3 Hz, 2H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.8, 164.4, 154.4, 137.4, 135.9, 130.7, 130.1, 129.0, 128.7, 128.6, 128.4, 128.3, 128.2, 127.6, 126.9, 123.5, 96.4, 66.3, 51.9, 43.6, 28.5. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{29}H_{30}N_2NaO_3$ 477.2149, found: 477.2160.

1-benzyl-2-(tert-butylcarbamoyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrrol-2-yl acetate (18g):



White solid, 58.5 mg, 72% yield; mp 182.0 – 183.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.37 (m, 2H), 7.30 – 7.27 (m, 3H), 7.25 – 7.24 (m, 4H), 7.20 – 7.18 (m, 1H), 6.57 (s, 1H), 6.34 (br, 1H), 5.10 (d, *J* = 15.5 Hz, 1H), 3.86 (d, *J* = 15.5 Hz, 1H), 1.31 (s, 9H), 1.28 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 170.5, 166.3, 163.0, 155.3, 137.2, 130.5, 129.9, 129.0, 128.7, 128.6(8), 127.6, 126.9, 122.6, 94.2, 52.4, 43.7, 28.5, 20.8. HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{24}H_{26}N_2NaO_4$ 429.1785, found: 429.1796.

7. Reference

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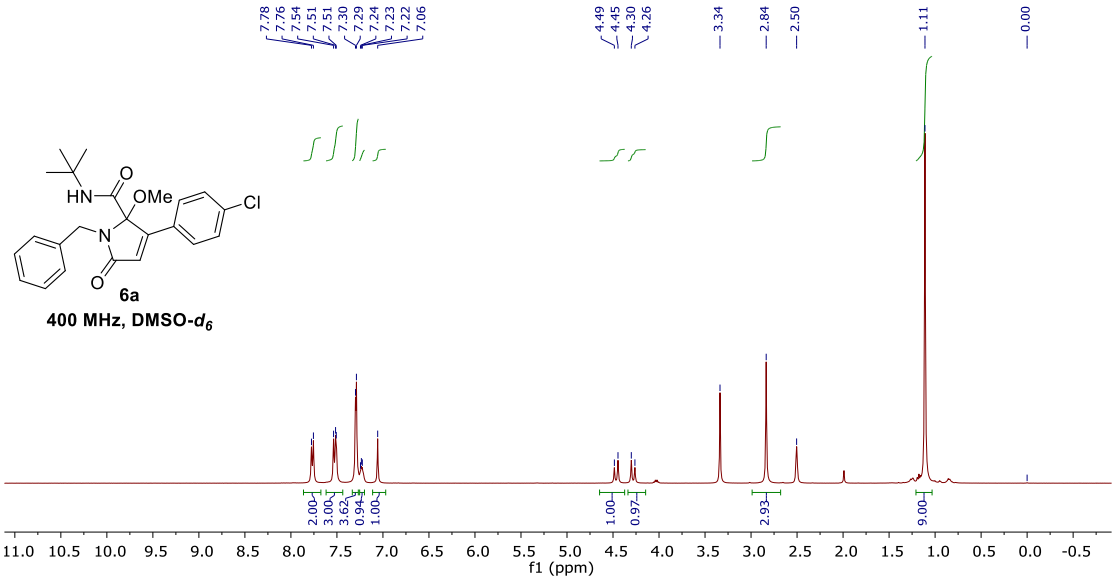
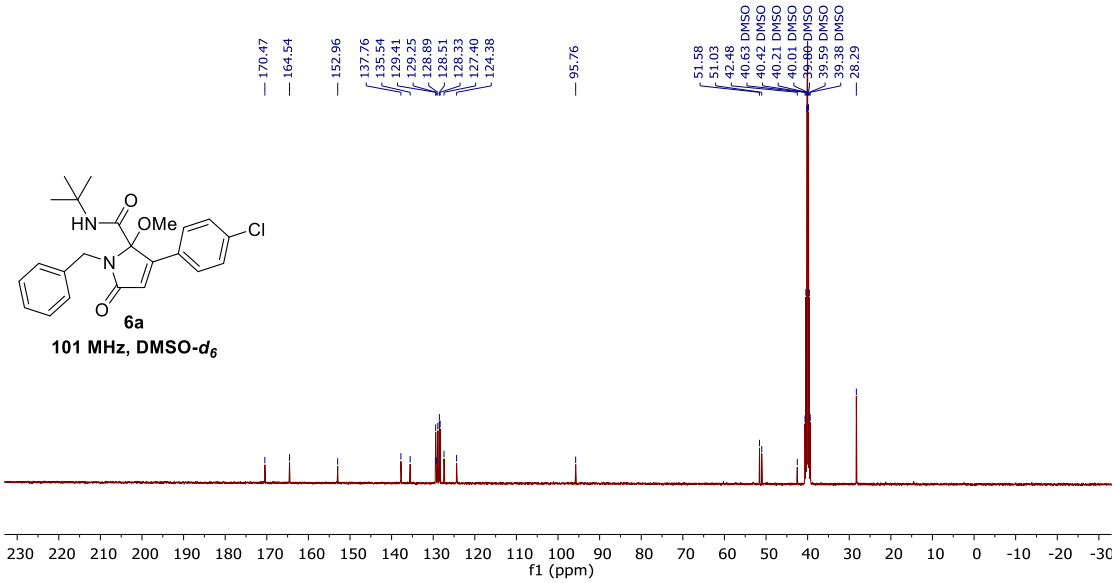
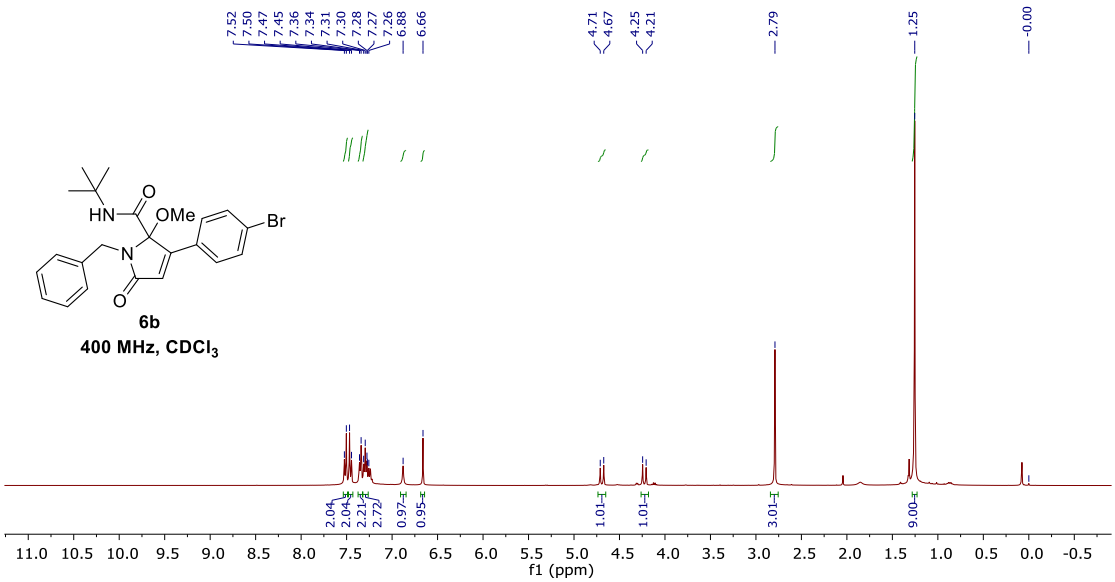
8. Copies of NMR Spectras of Compounds 6a-6x, 7g-18g.



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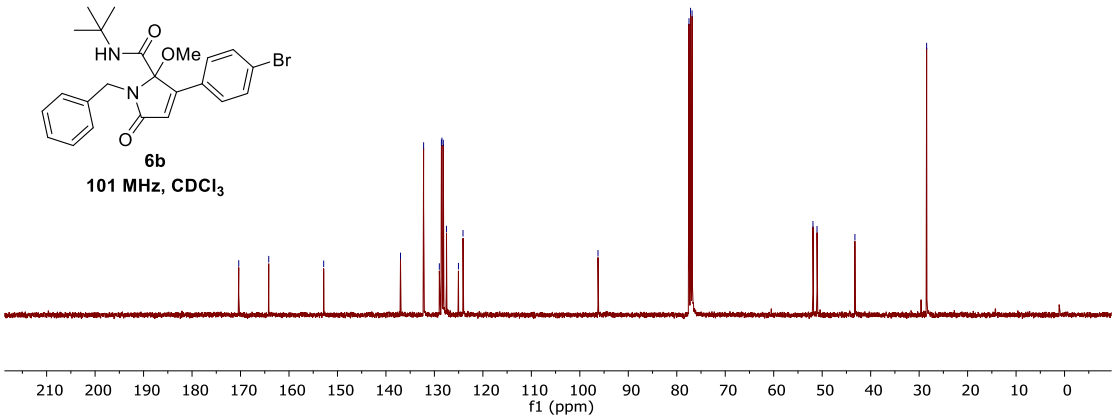
6b
400 MHz, CDCl3
f1 (ppm)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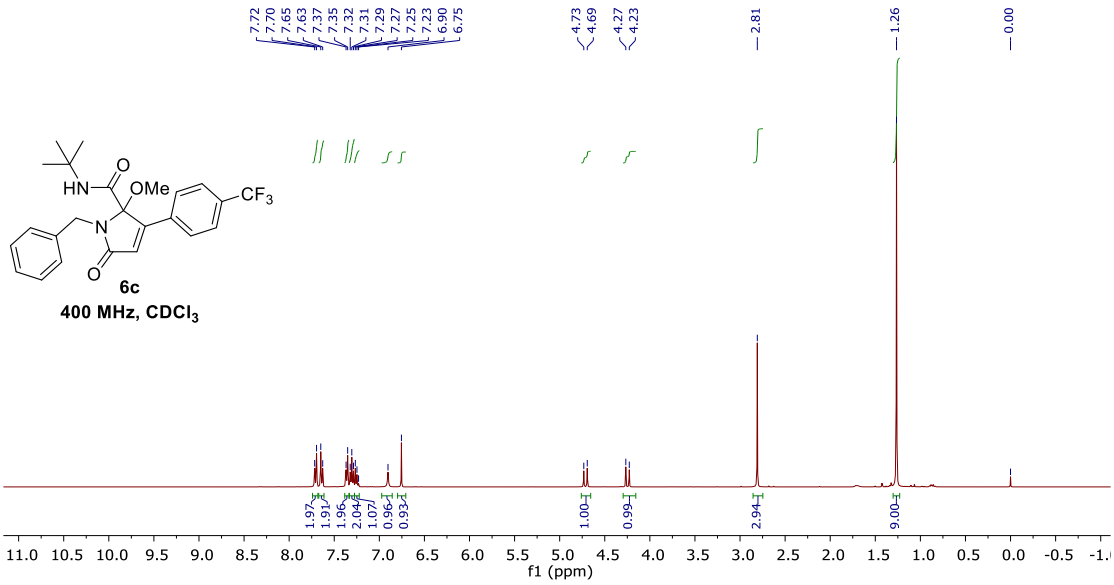
f1 (ppm)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7.35
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7.31
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6.90
6.75
4.73
4.69
4.27
4.23
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CF3
N
O
6c
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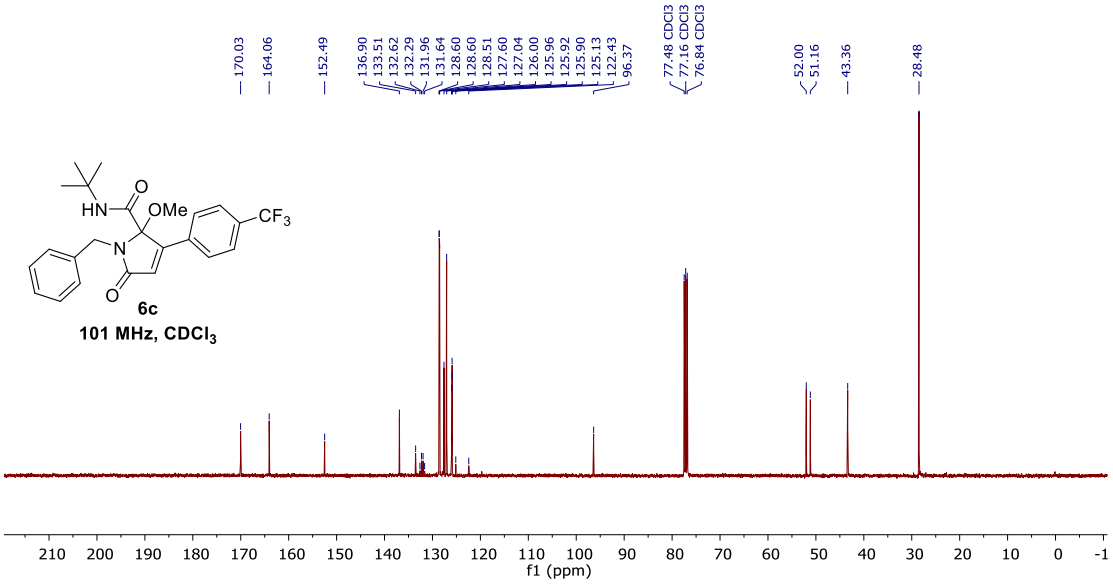
f1 (ppm)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126.00
125.96
125.92
125.90
125.13
122.43
96.37
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
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O
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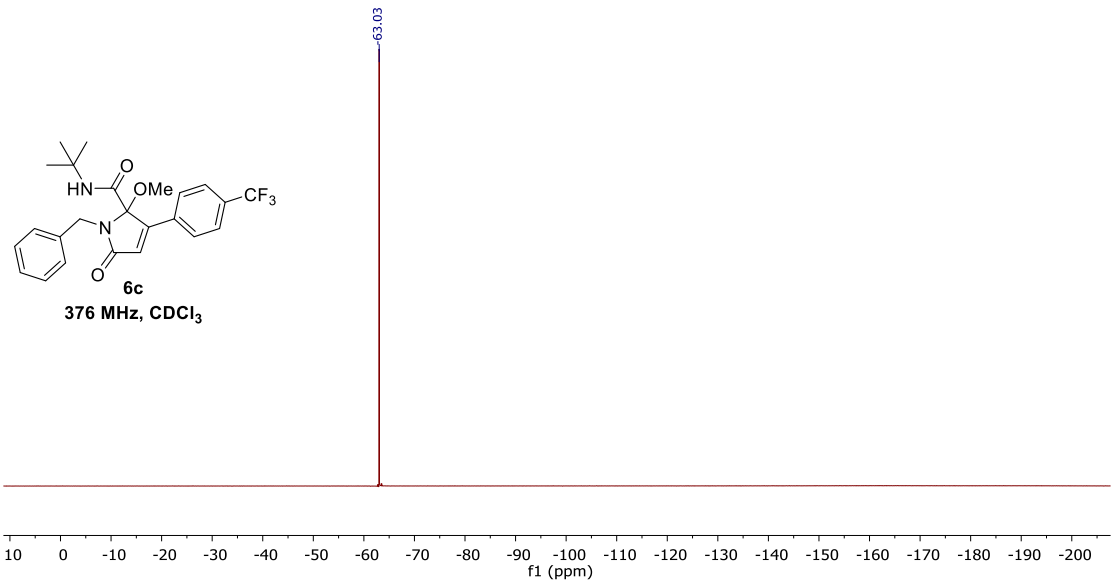
CF3
N
O
6c
101 MHz, CDCl3
f1 (ppm)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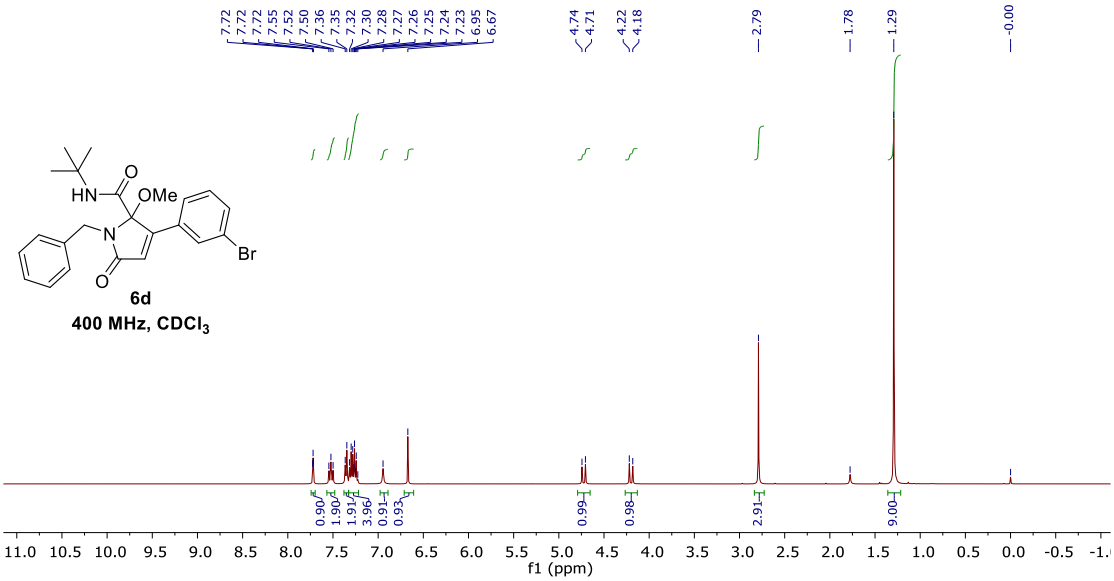
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7.25
7.24
7.23
6.95
6.67
4.74
4.71
4.22
4.18
2.79
1.78
1.29
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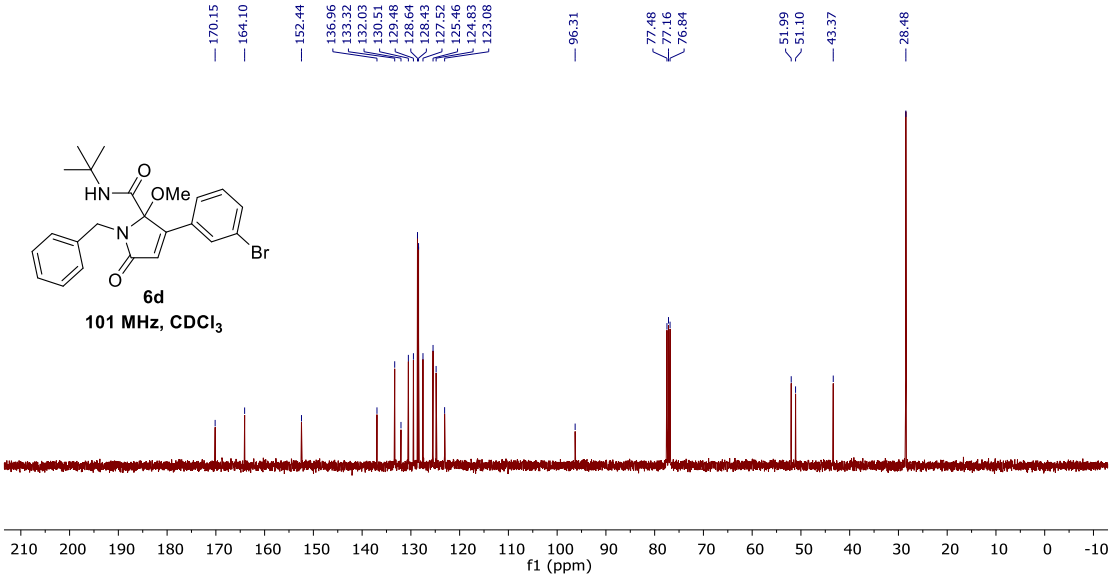
OMe
N
O
Br
6d
400 MHz, CDCl3
0.90
1.90
1.91
3.96
0.91
0.93
0.99
0.98
2.91
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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123.08
96.31
77.48
77.16
76.84
51.99
51.10
43.37
28.48
HN
O
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N
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Br
6d
101 MHz, CDCl3
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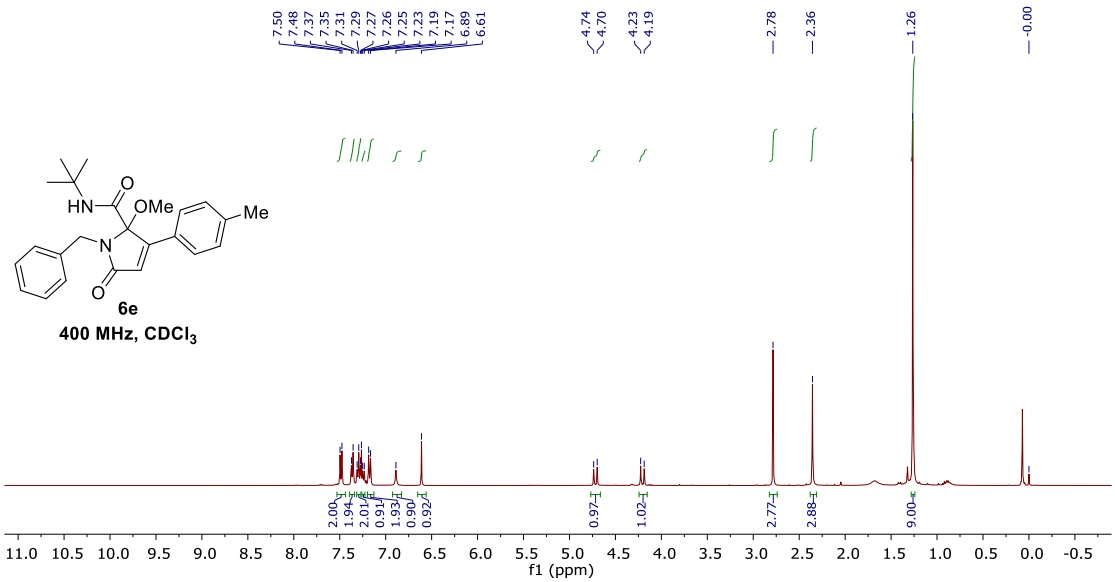
f1 (ppm)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1.26
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Me
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400 MHz, CDCl3
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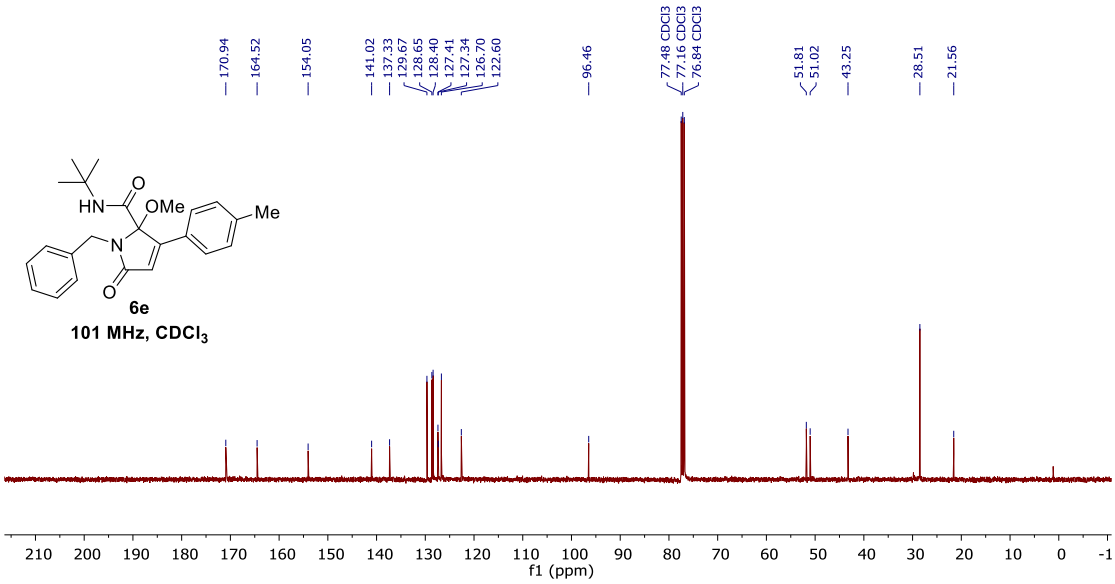
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51.81
51.02
43.25
28.51
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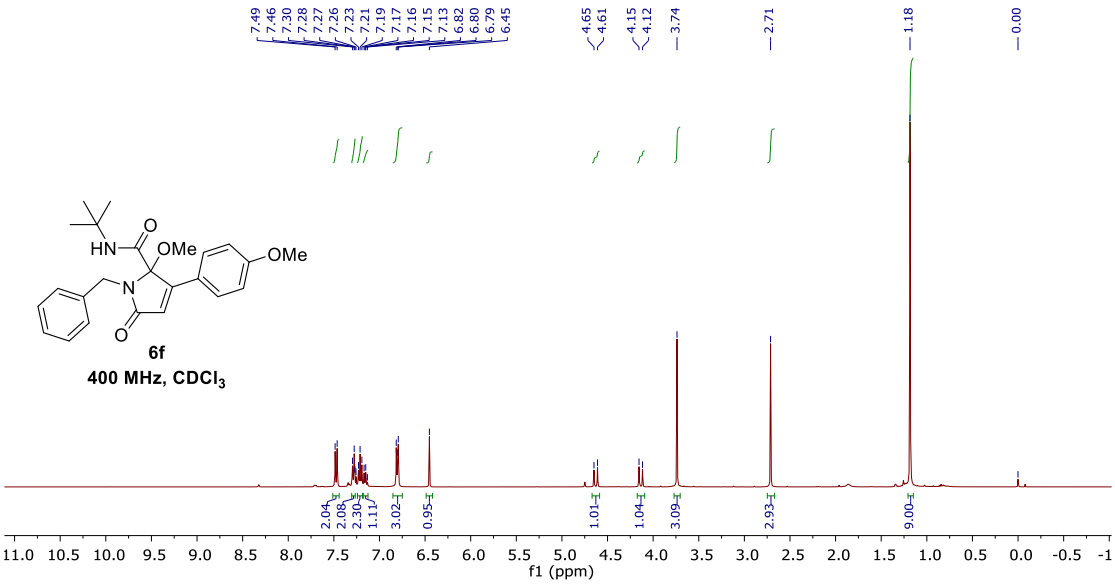
f1 (ppm)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400 MHz, CDCl3
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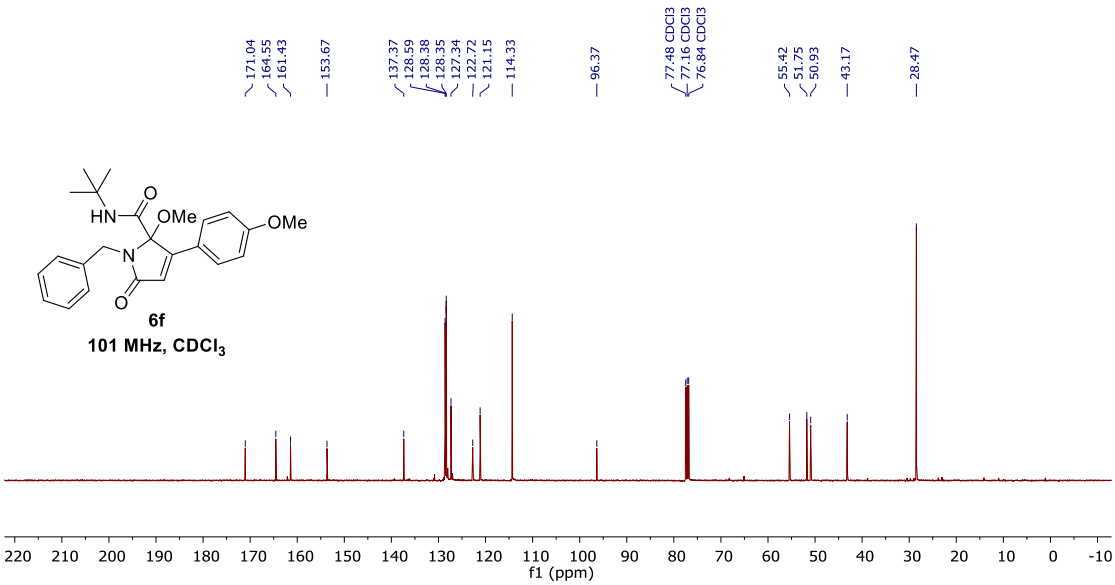
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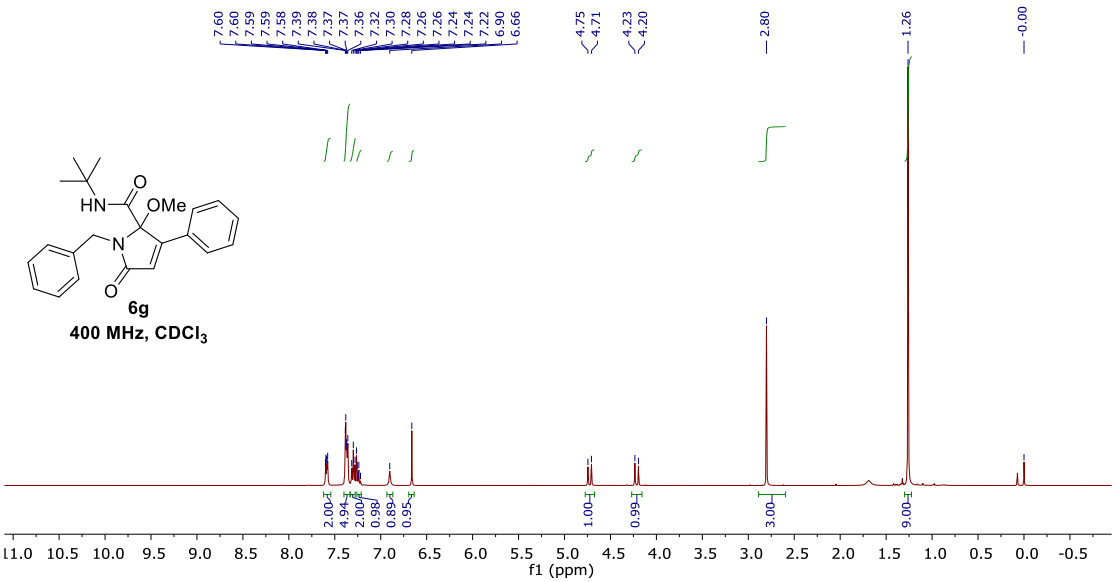
f1 (ppm)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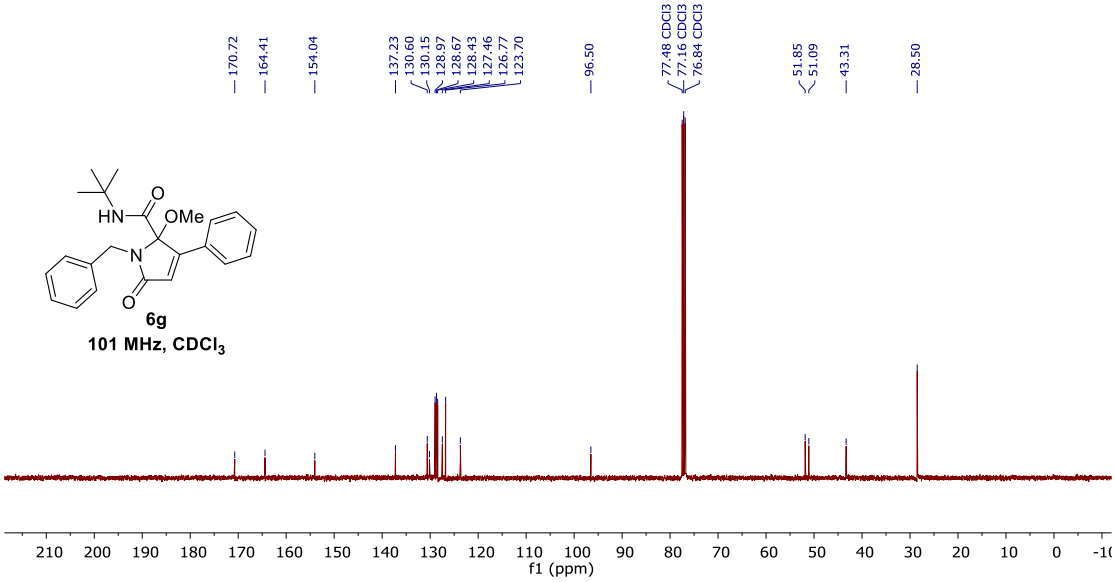
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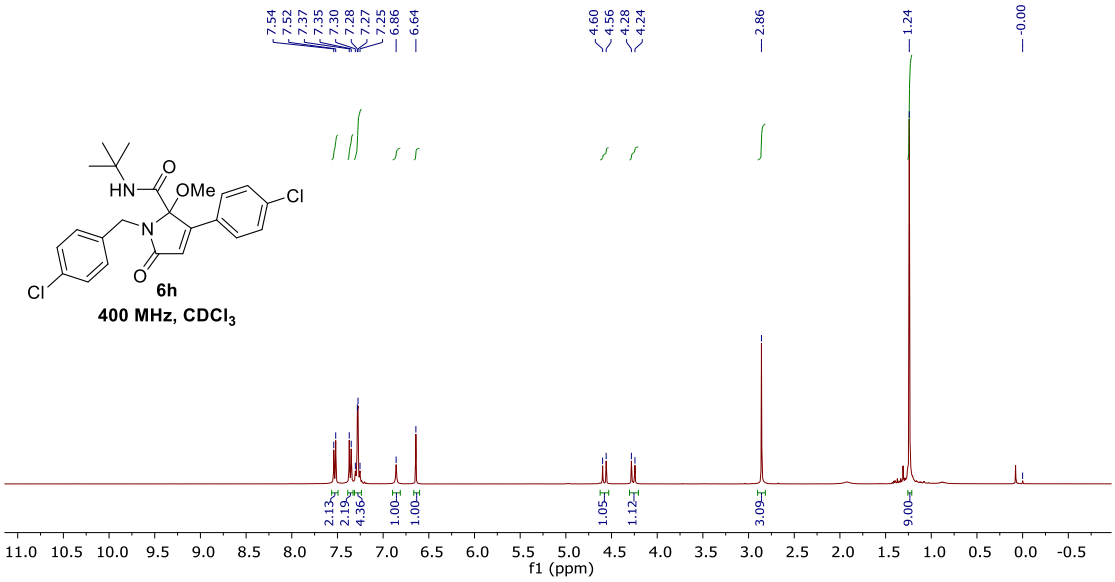
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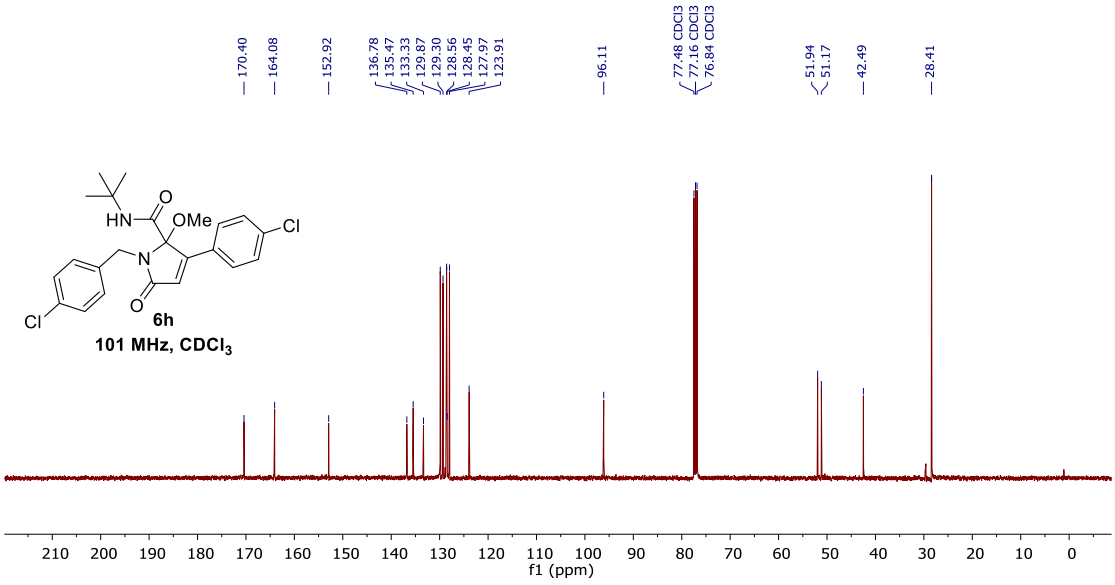
3.09
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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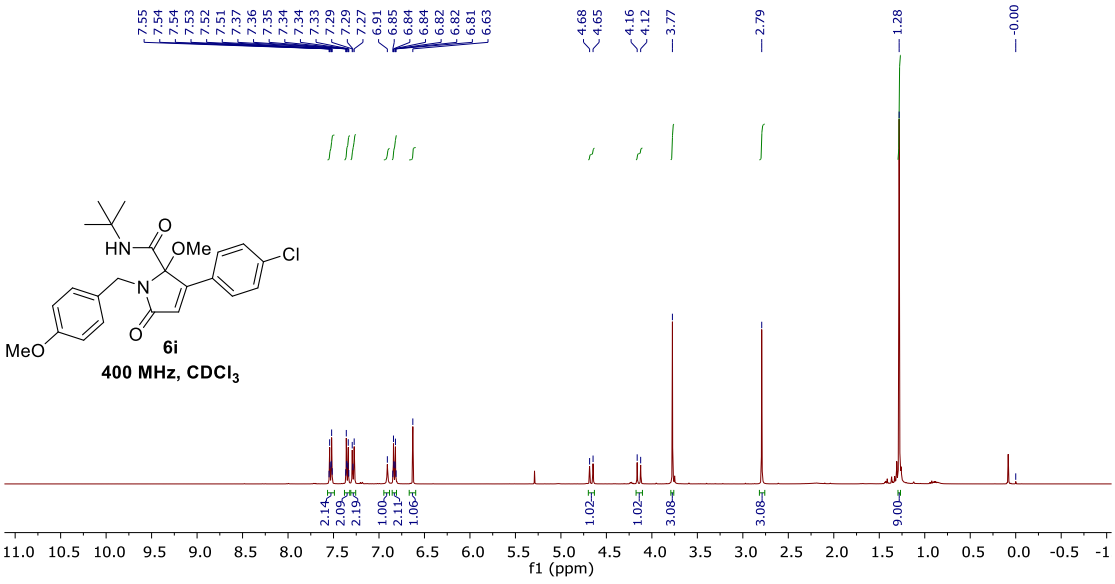
133.33
129.87
129.30
128.56
128.45
127.97
123.91
96.11
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.94
51.17
42.49
28.41
HN
O
OMe
Cl
N
O
Cl
6h
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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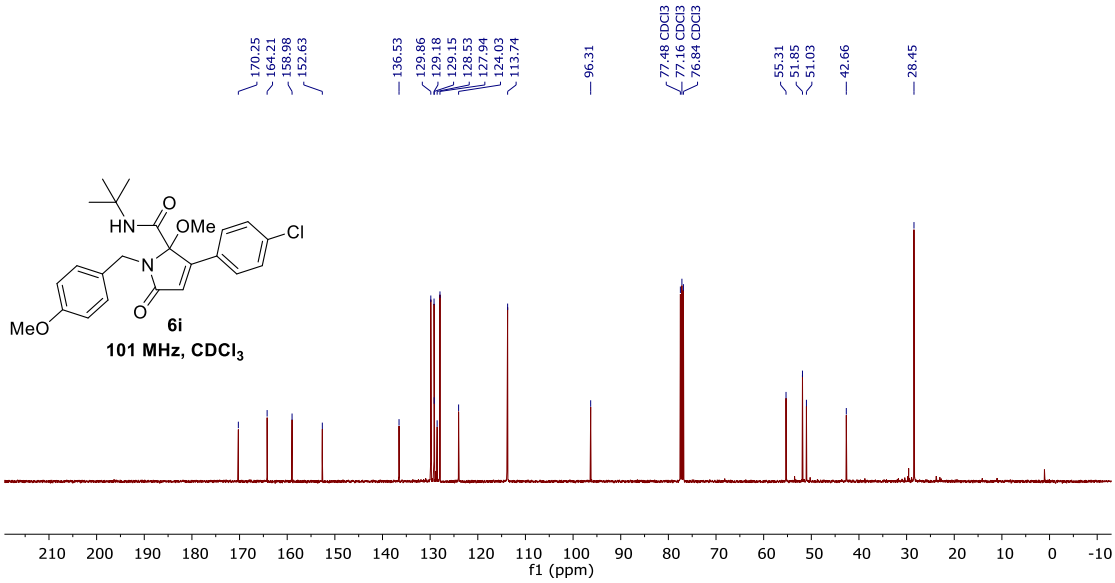
7.29
7.29
7.27
6.91
6.85
6.84
6.84
6.82
6.82
6.81
6.63
4.68
4.65
4.16
4.12
3.77
2.79
1.28
-0.00
HN
O
OMe
Cl
N
O
MeO
6i
400 MHz, CDCl3
2.14
2.05
2.19
1.00
2.11
1.06
1.02
1.02
3.08
3.08
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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127.94
124.03
113.74
96.31
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.31
51.85
51.03
42.66
28.45
HN
O
OMe
Cl
N
O
MeO
6i
101 MHz, CDCl3
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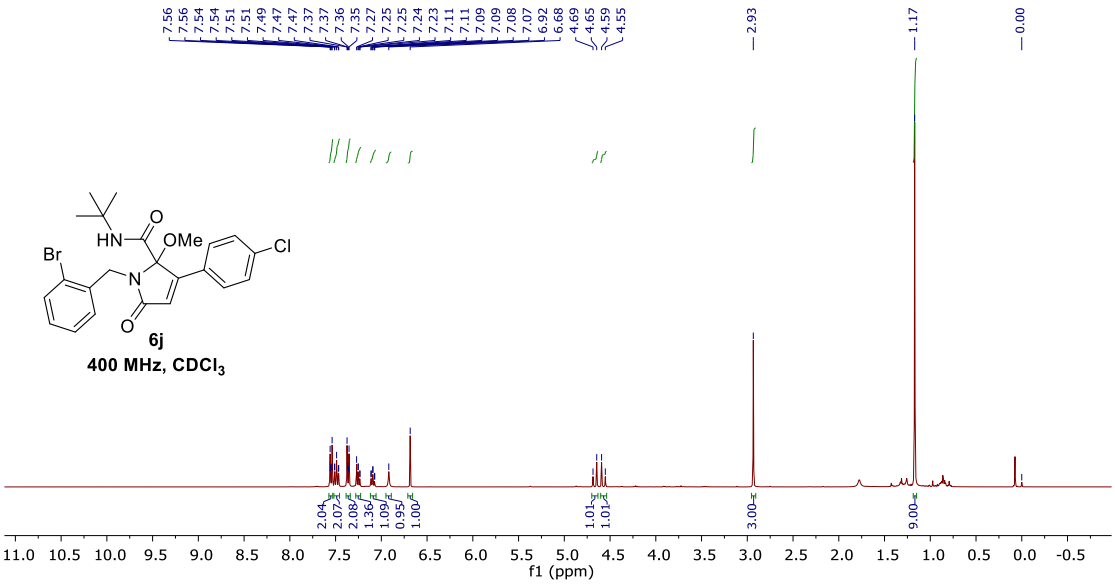
f1 (ppm)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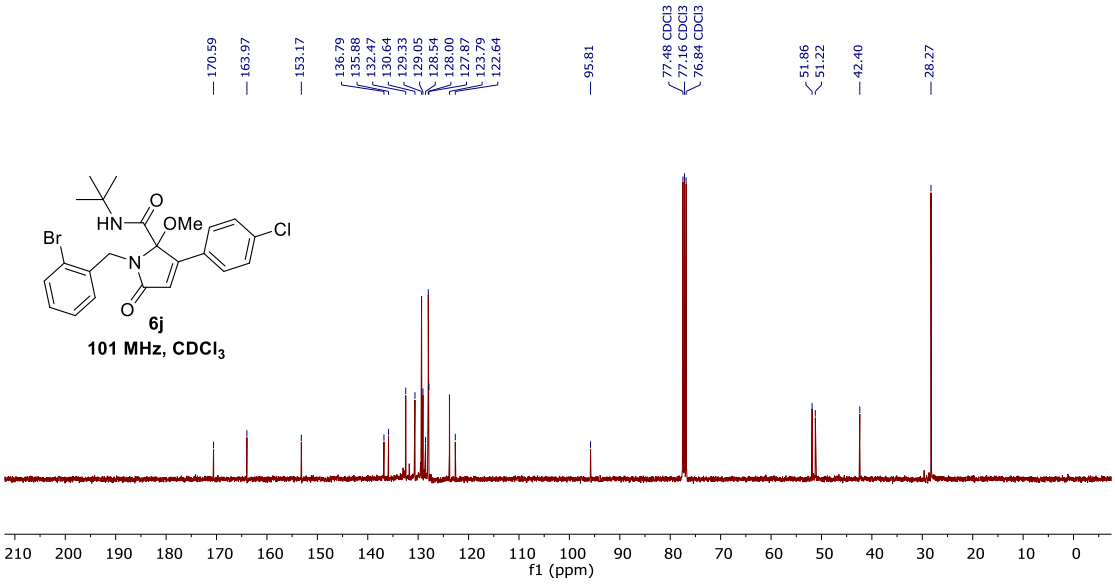
7.27
7.25
7.25
7.24
7.23
7.11
7.11
7.09
7.09
7.08
7.07
6.92
6.68
4.69
4.65
4.59
4.55
2.93
1.17
0.00
HN
O
OMe
Cl
Br
N
O
6j
400 MHz, CDCl3
2.04
2.07
2.08
1.36
1.09
0.95
1.00
1.01
1.01
3.00
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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130.64
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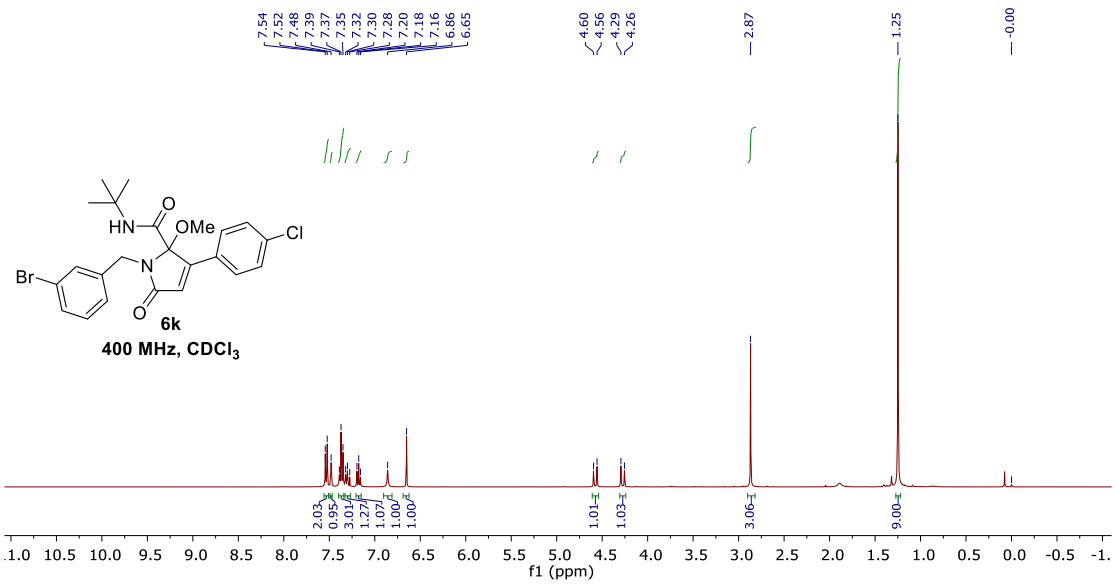
129.05
128.54
128.00
127.87
123.79
122.64
95.81
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.86
51.22
42.40
28.27
HN
O
OMe
Cl
Br
N
O
6j
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.35
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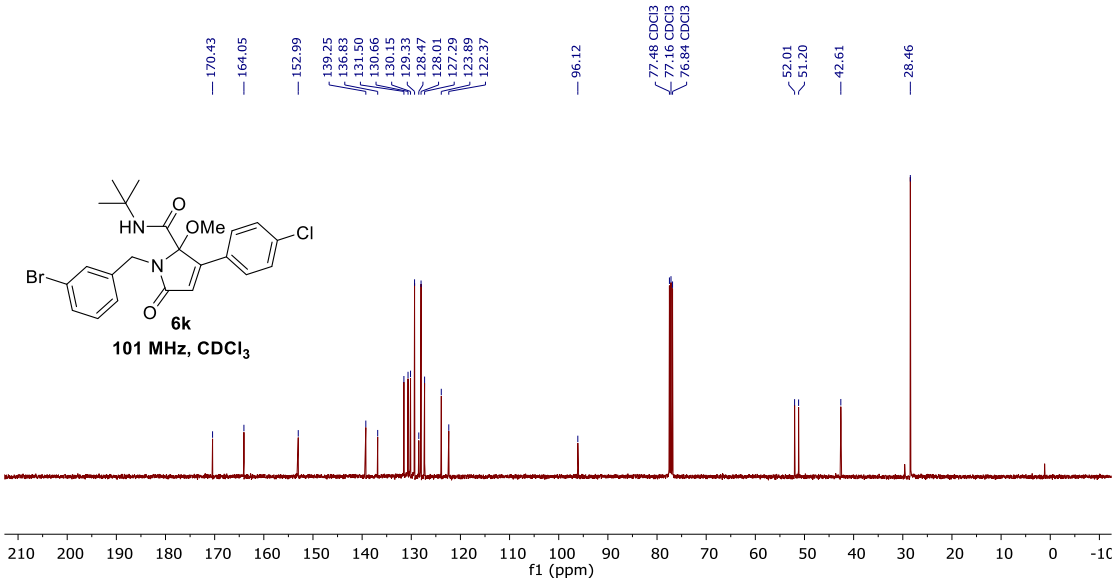
7.30
7.28
7.20
7.18
7.16
6.86
6.65
4.60
4.56
4.29
4.26
2.87
1.25
-0.00
HN
O
OMe
Cl
Br
N
O
6k
400 MHz, CDCl3
2.03
0.95
3.01
1.27
1.07
1.00
1.00
1.01
1.03
3.06
9.00
f1 (ppm)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131.50
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130.15
129.33
128.47
128.01
127.29
123.89
122.37
96.12
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.01
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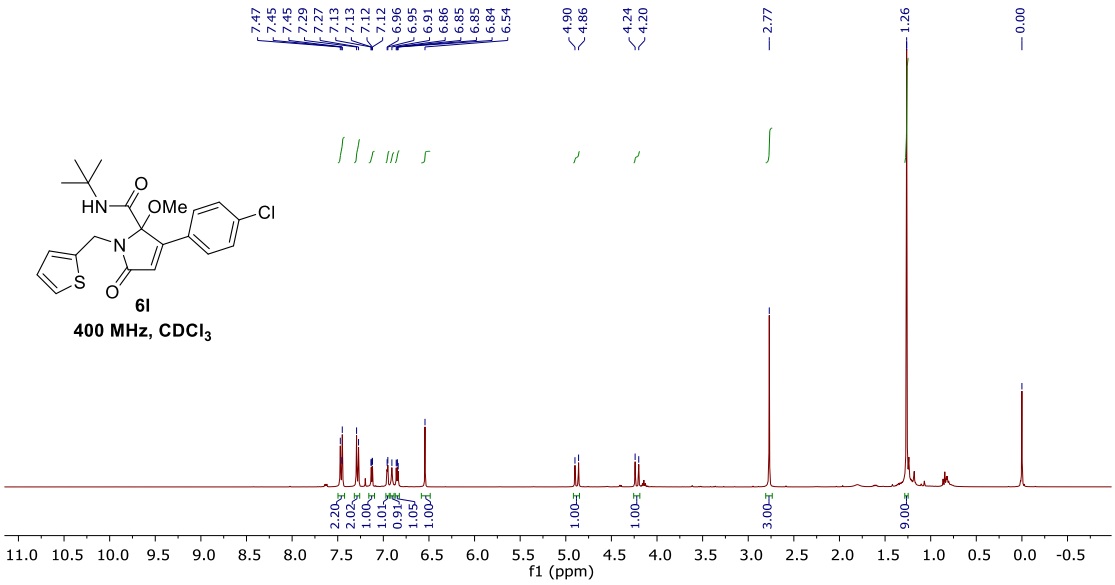
42.61
28.46
HN
O
OMe
Cl
Br
N
O
6k
101 MHz, CDCl3
f1 (ppm)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7.45
7.29
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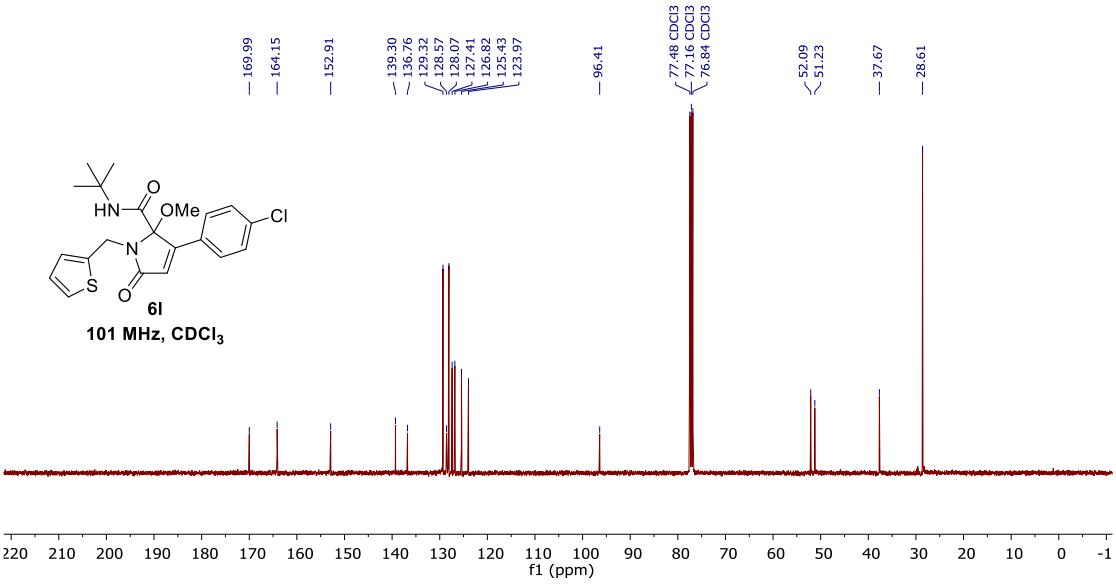
7.13
7.12
7.12
6.96
6.95
6.91
6.86
6.85
6.85
6.84
6.54
4.90
4.86
4.24
4.20
2.77
1.26
0.00
HN
O
OMe
Cl
N
S
O
6l
400 MHz, CDCl3
2.20
2.02
1.00
1.01
0.91
1.05
1.00
1.00
1.00
3.00
9.00
f1 (ppm)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129.32
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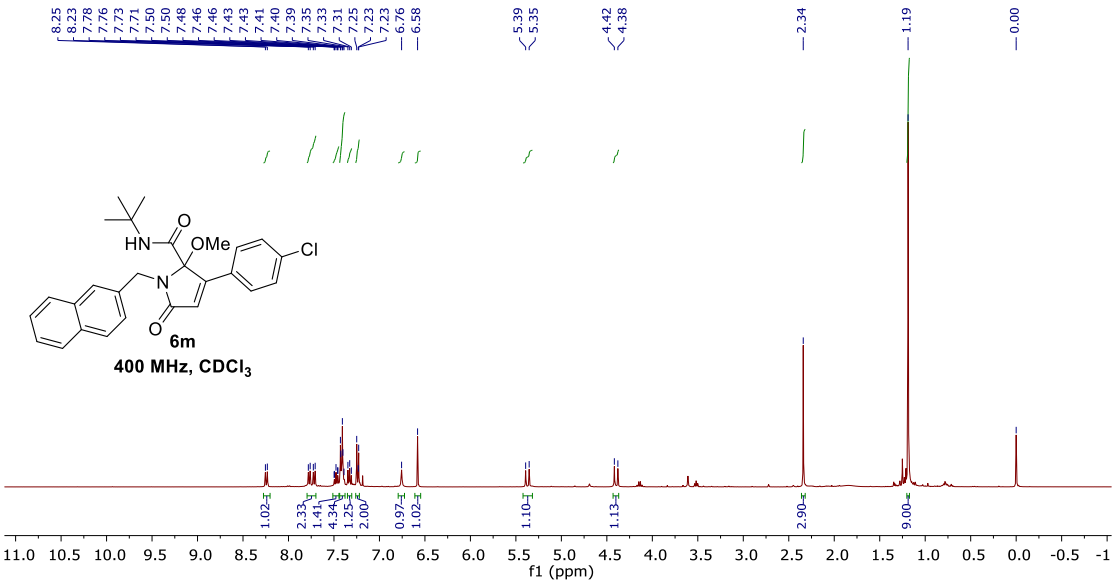
128.07
127.41
126.82
125.43
123.97
96.41
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.09
51.23
37.67
28.61
HN
O
OMe
Cl
N
S
O
6l
101 MHz, CDCl3
f1 (ppm)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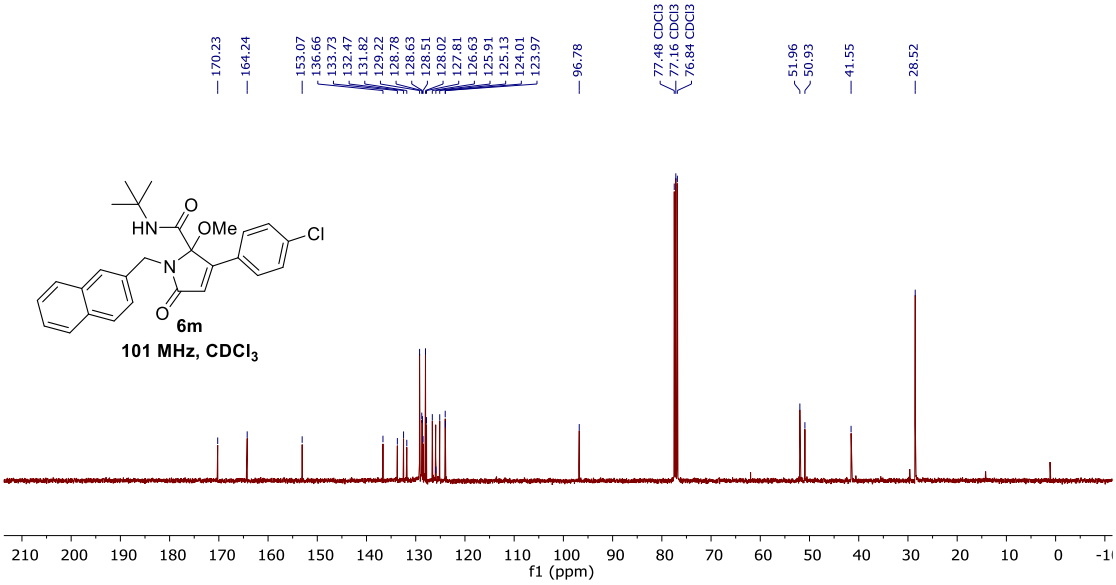
7.71
7.50
7.50
7.48
7.46
7.46
7.43
7.43
7.41
7.40
7.39
7.35
7.33
7.31
7.25
7.23
7.23
6.76
6.58
5.39
5.35
4.42
4.38
2.34
1.19
0.00
HN
O
OMe
Cl
N
O
6m
400 MHz, CDCl3
1.02
2.33
1.41
4.34
1.25
2.00
0.97
1.02
1.10
1.13
2.90
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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136.66
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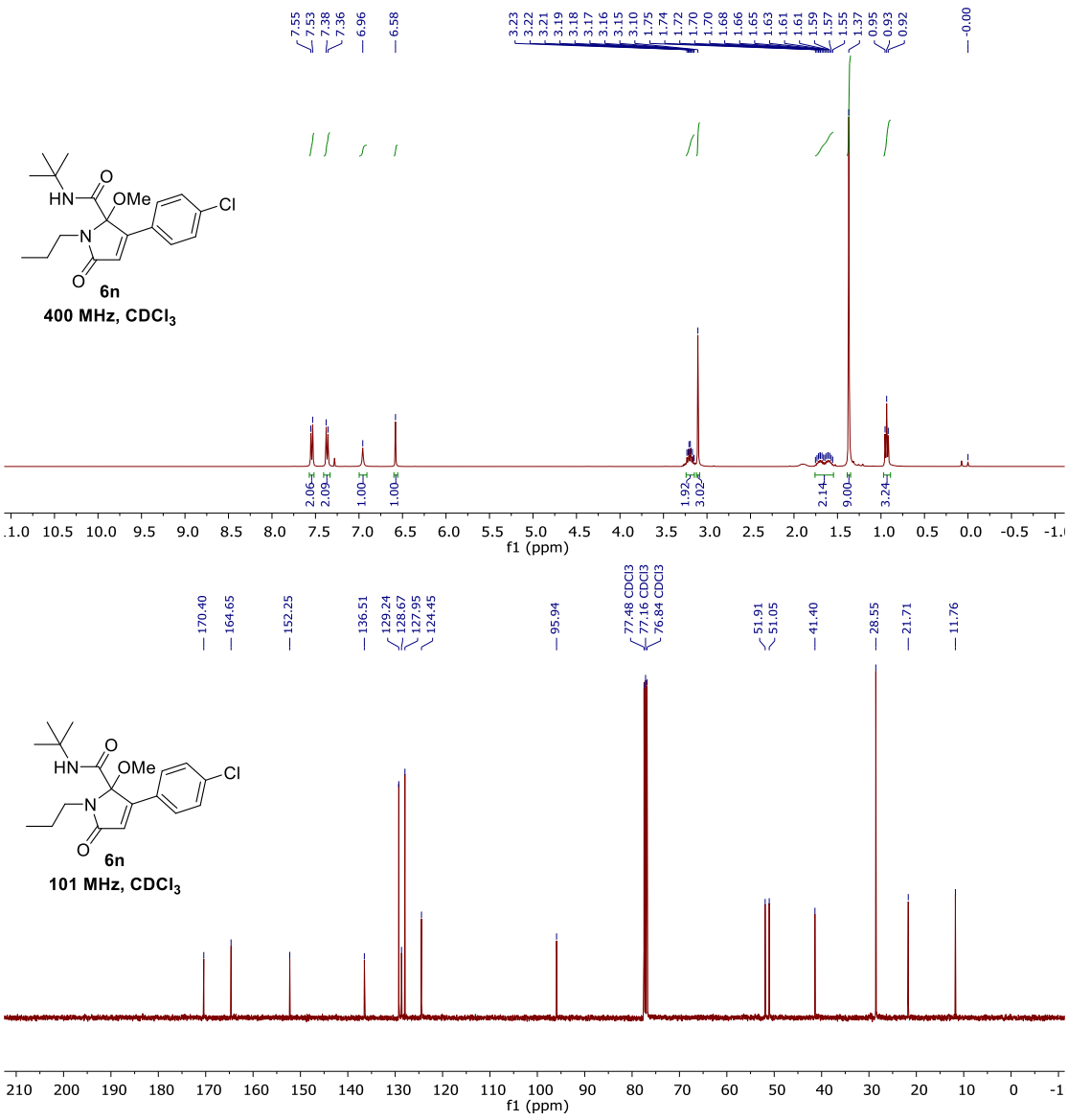
132.47
131.82
129.22
128.78
128.63
128.51
128.02
127.81
126.63
125.91
125.13
124.01
123.97
96.78
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.96
50.93
41.55
28.52
HN
O
OMe
Cl
N
O
6m
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)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6.58
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3.22
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3.19
3.18
3.17
3.16
3.15
3.10
1.75
1.74
1.72
1.70
1.70
1.68
1.66
1.65
1.63
1.61
1.61
1.59
1.57
1.55
1.37
0.95
0.93
0.92
0.00
HN
O
OMe
Cl
N
O
6n
400 MHz, CDCl3
2.06
2.09
1.00
1.00
1.92
3.02
2.14
9.00
3.24
f1 (ppm)
170.40
164.65
152.25
136.51
129.24
128.67
127.95
124.45
95.94
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.91
51.05
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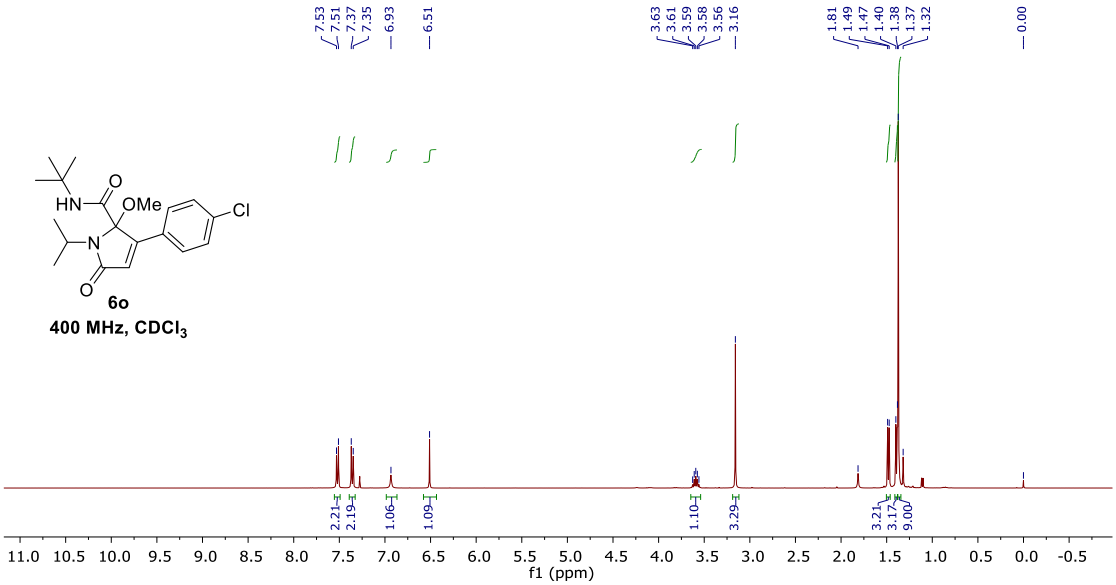
28.55
21.71
11.76
6n
101 MHz, CDCl3
f1 (ppm)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3.58
3.56
3.16
1.81
1.49
1.47
1.40
1.38
1.37
1.32
0.00
HN
O
OMe
Cl
N
O
6o
400 MHz, CDCl3
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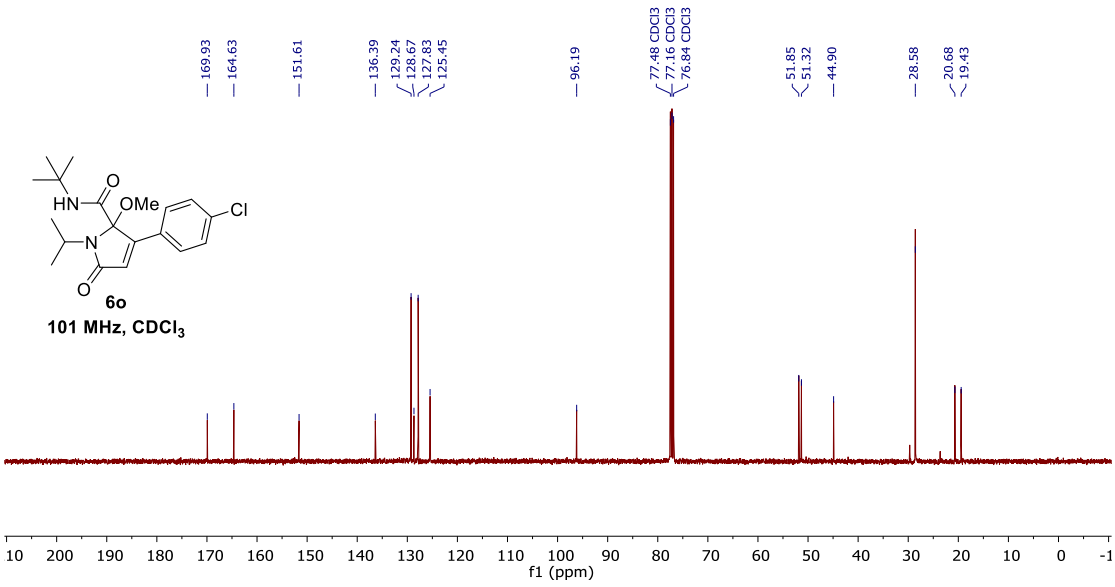
2.19
1.06
1.09
1.10
3.29
3.21
3.17
9.00
f1 (ppm)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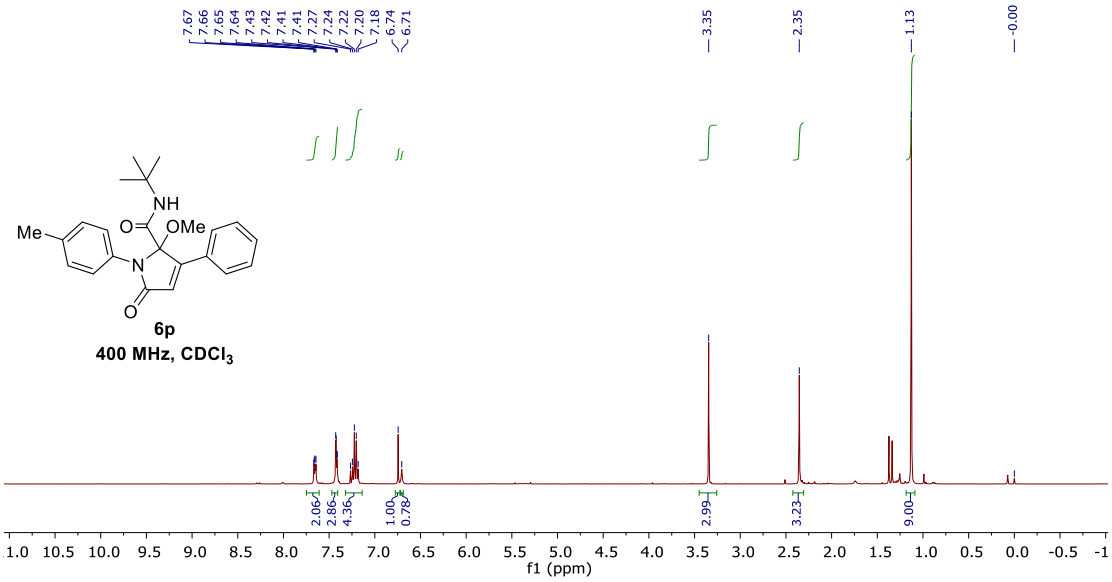
128.67
127.83
125.45
96.19
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.85
51.32
44.90
28.58
20.68
19.43
HN
O
OMe
Cl
N
O
6o
101 MHz, CDCl3
f1 (ppm)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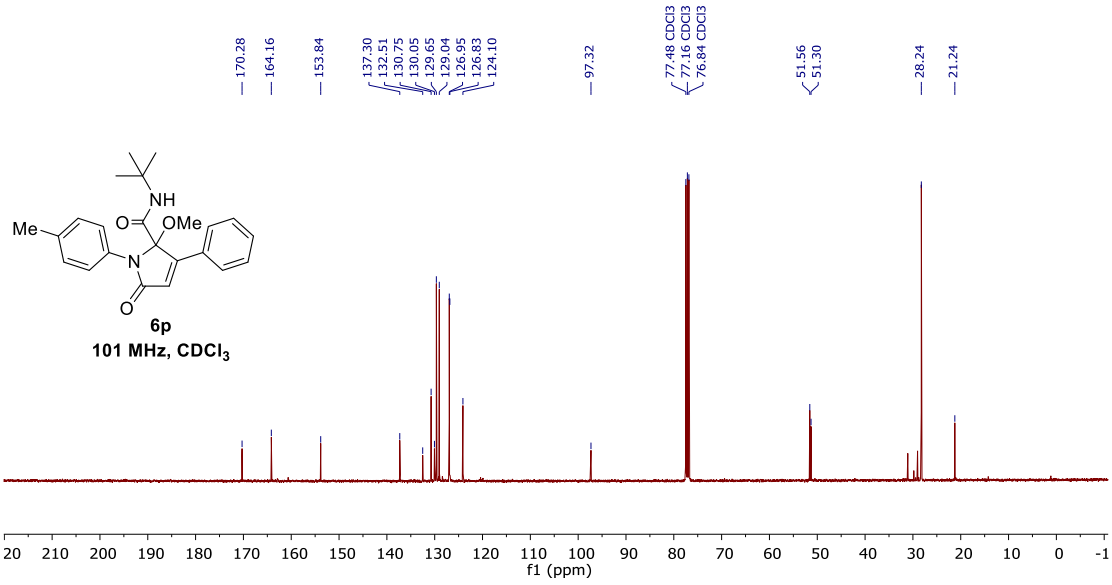
7.41
7.27
7.24
7.22
7.20
7.18
6.74
6.71
3.35
2.35
1.13
-0.00
NH
O
OMe
Me
N
O
6p
400 MHz, CDCl3
2.06
2.86
4.36
1.00
0.78
2.99
3.23
9.00
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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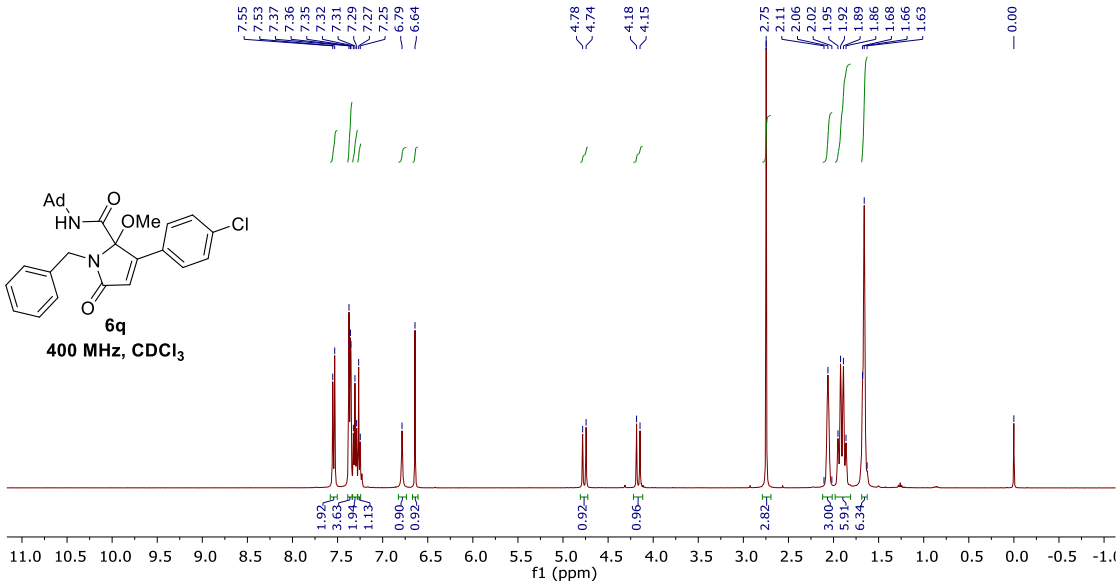
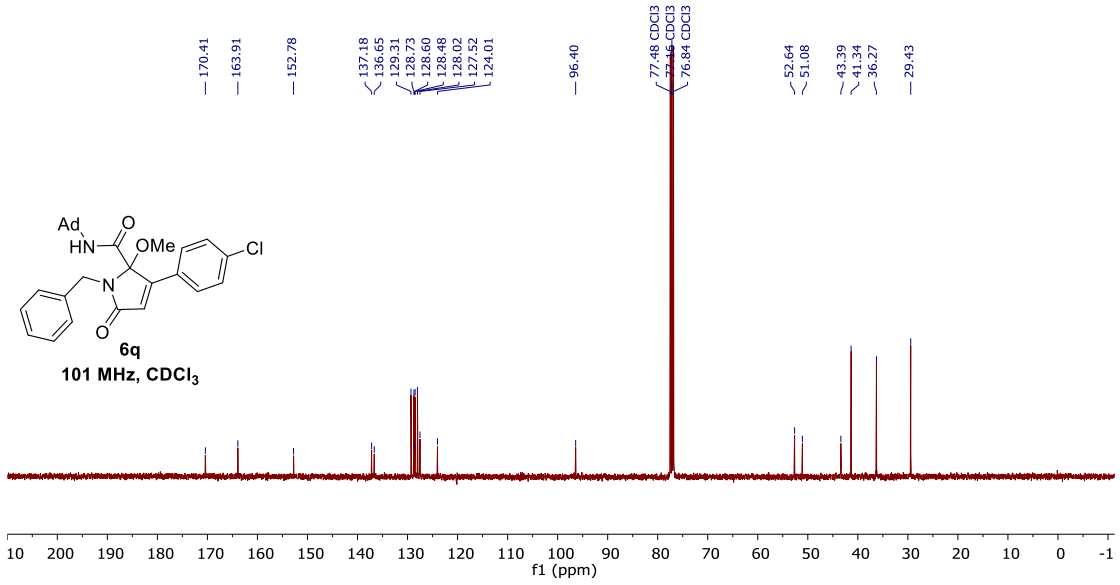
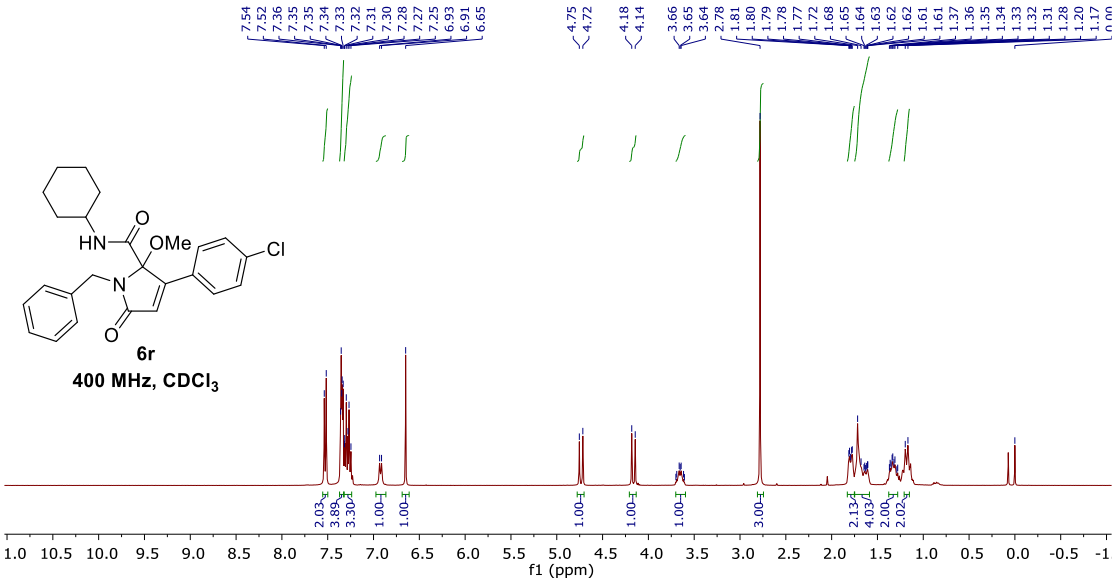
130.75
130.05
129.65
129.04
126.95
126.83
124.10
97.32
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.56
51.30
28.24
21.24
NH
O
OMe
Me
N
O
6p
101 MHz, CDCl3
20 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)





Ad = -adamantyl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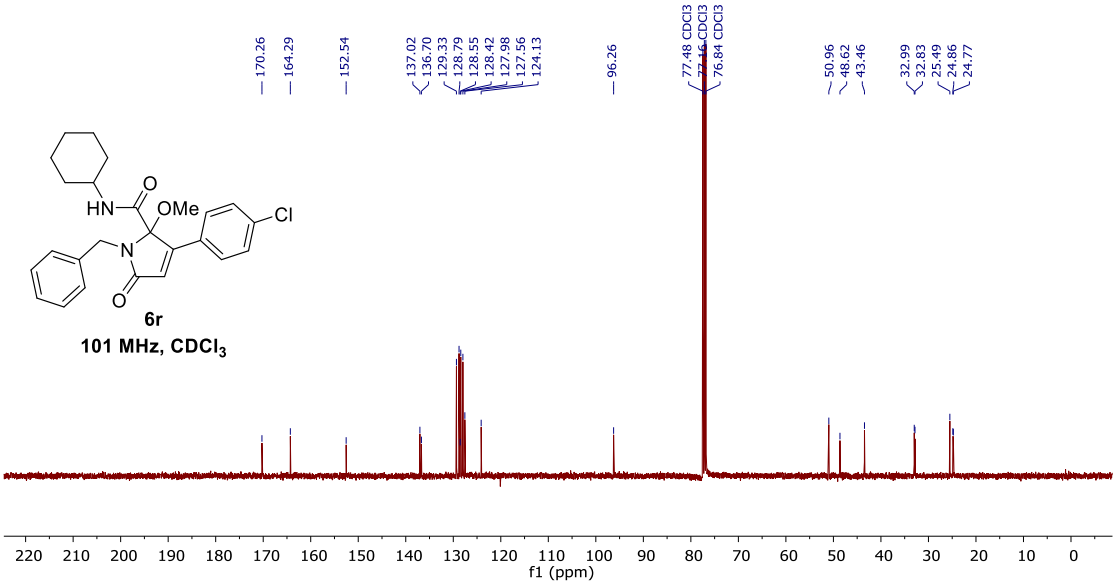
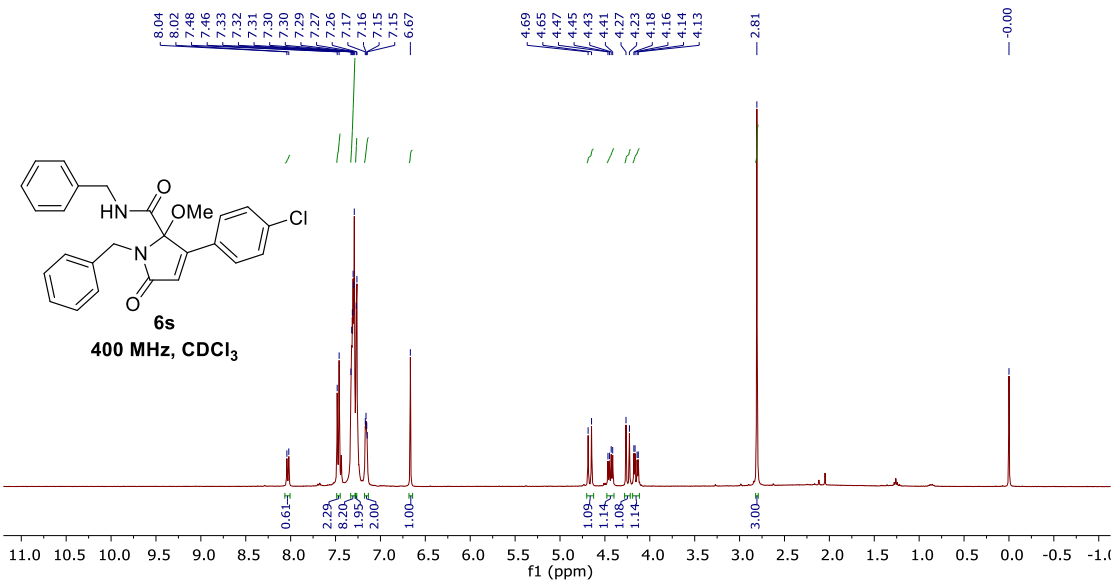
O
OMe
Cl
N
O
6r
400 MHz, CDCl3
f1 (ppm)


HN
O
OMe
Cl
N
O
6r
101 MHz, CDCl3
f1 (ppm)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7.16
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7.15
6.67
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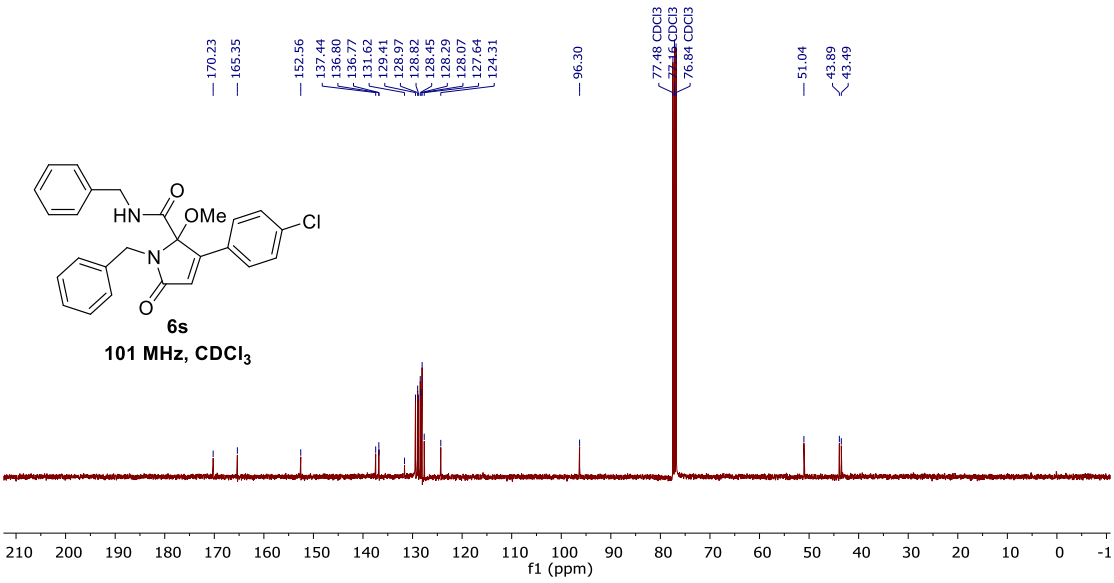
4.41
4.27
4.23
4.18
4.16
4.14
4.13
2.81
-0.00
HN
O
OMe
Cl
N
O
6s
400 MHz, CDCl3
0.61
2.29
8.20
1.95
2.00
1.00
1.09
1.14
1.08
1.14
3.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.82
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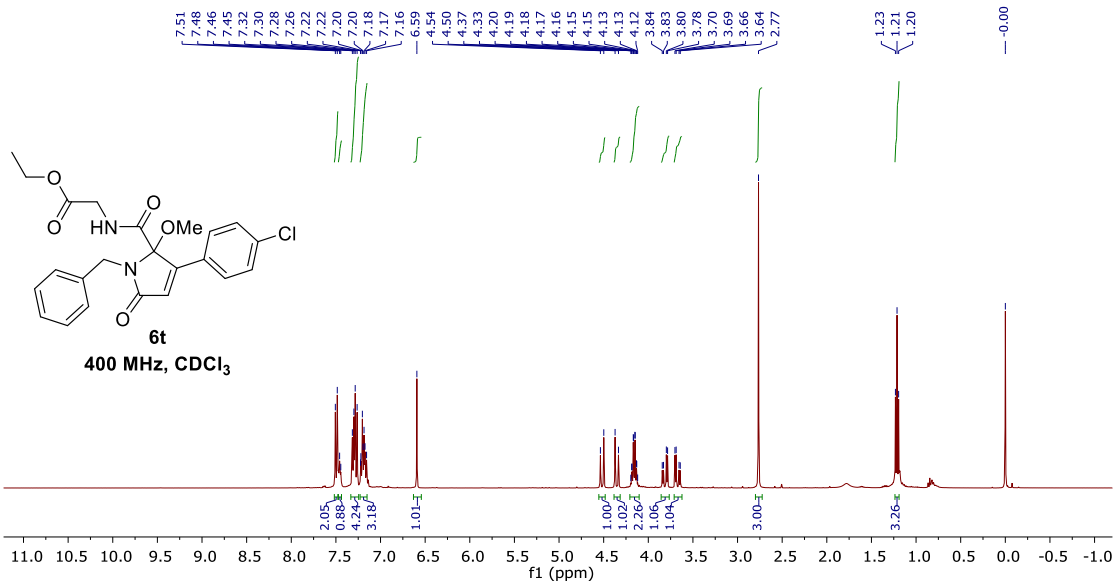
128.29
128.07
127.64
124.31
96.30
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.04
43.89
43.49
HN
O
OMe
Cl
N
O
6s
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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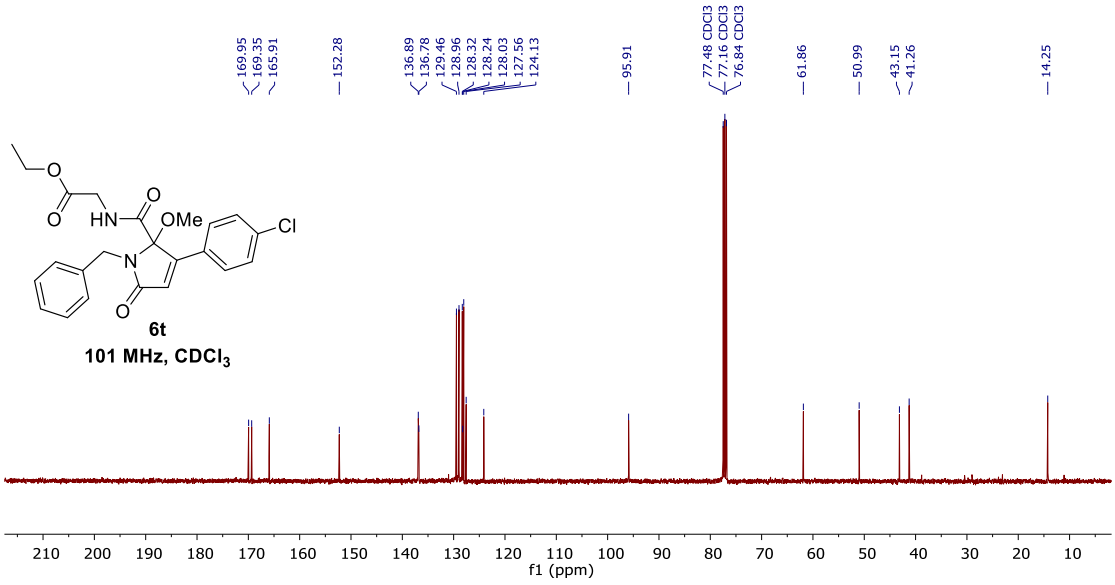
7.17
7.16
6.59
4.54
4.50
4.37
4.33
4.20
4.19
4.18
4.17
4.16
4.15
4.15
4.13
4.13
4.12
3.84
3.83
3.80
3.78
3.70
3.69
3.66
3.64
2.77
1.23
1.21
1.20
-0.00
O
O
HN
O
OMe
Cl
N
O
6t
400 MHz, CDCl3
2.05
0.88
4.24
3.18
1.01
1.00
1.02
2.26
1.06
1.04
3.00
3.26
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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128.32
128.24
128.03
127.56
124.13
95.91
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
61.86
50.99
43.15
41.26
14.25
O
O
HN
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OMe
Cl
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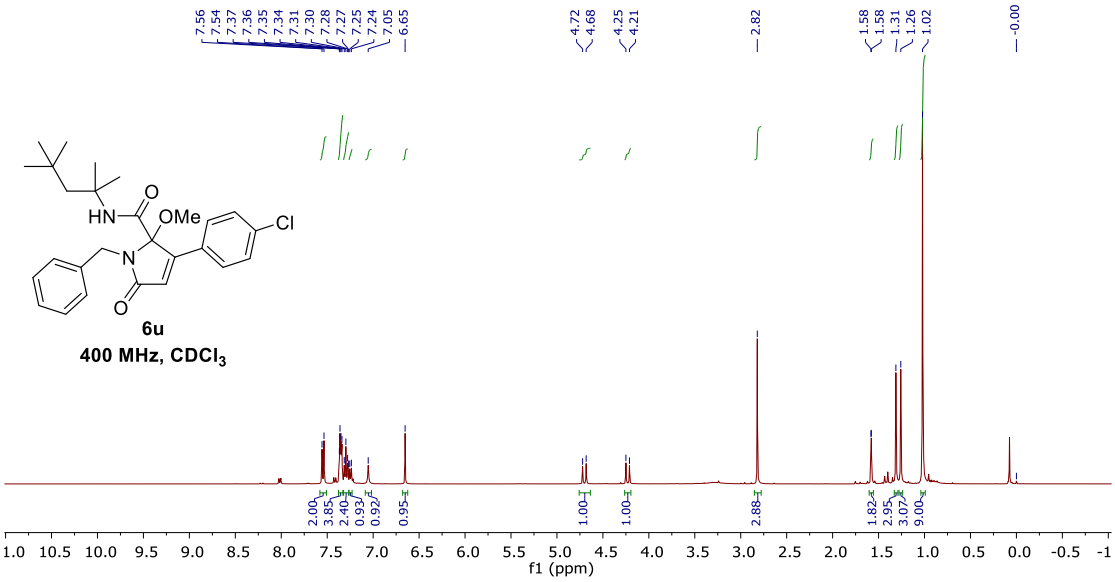
6t
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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7.27
7.25
7.24
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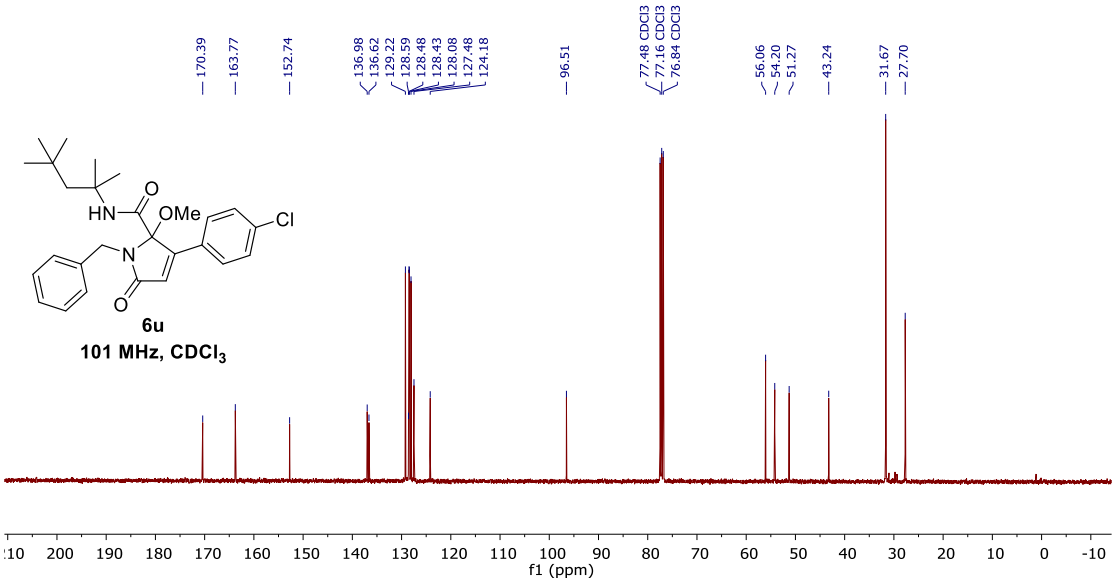
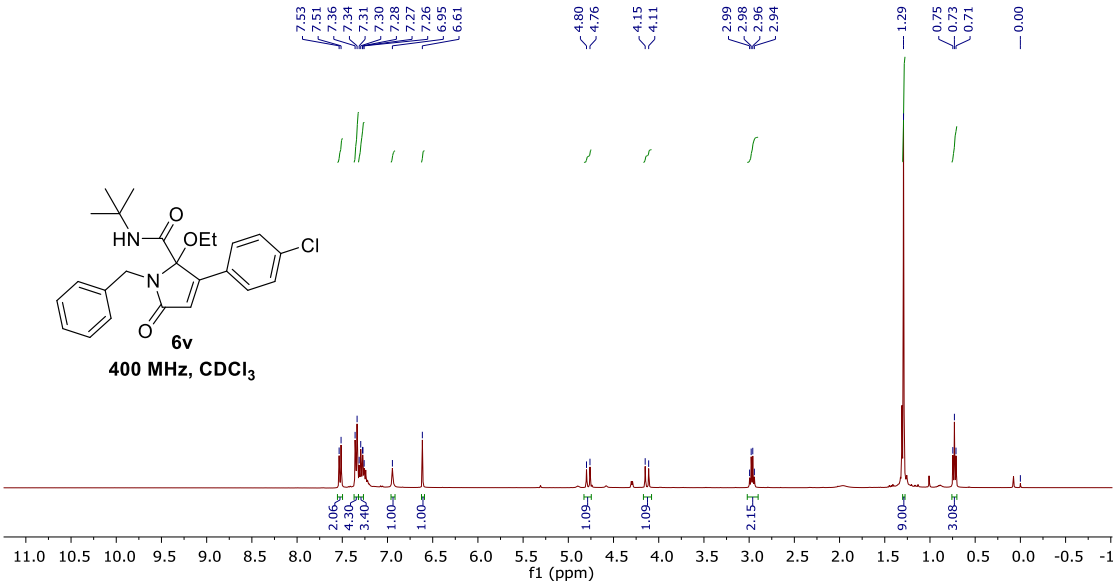
6.65
4.72
4.68
4.25
4.21
2.82
1.58
1.58
1.31
1.26
1.02
-0.00
HN
O
OMe
Cl
N
O
6u
400 MHz, CDCl3
2.00
3.85
2.40
0.93
0.92
0.95
1.00
1.00
2.88
1.82
2.95
3.07
9.00
f1 (ppm)


170.39
163.77
152.74
136.98
136.62
129.22
128.59
128.48
128.43
128.08
127.48
124.18
96.51
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
56.06
54.20
51.27
43.24
31.67
27.70
HN
O
OMe
Cl
N
O
6u
101 MHz, CDCl3
f1 (ppm)


7.53
7.51
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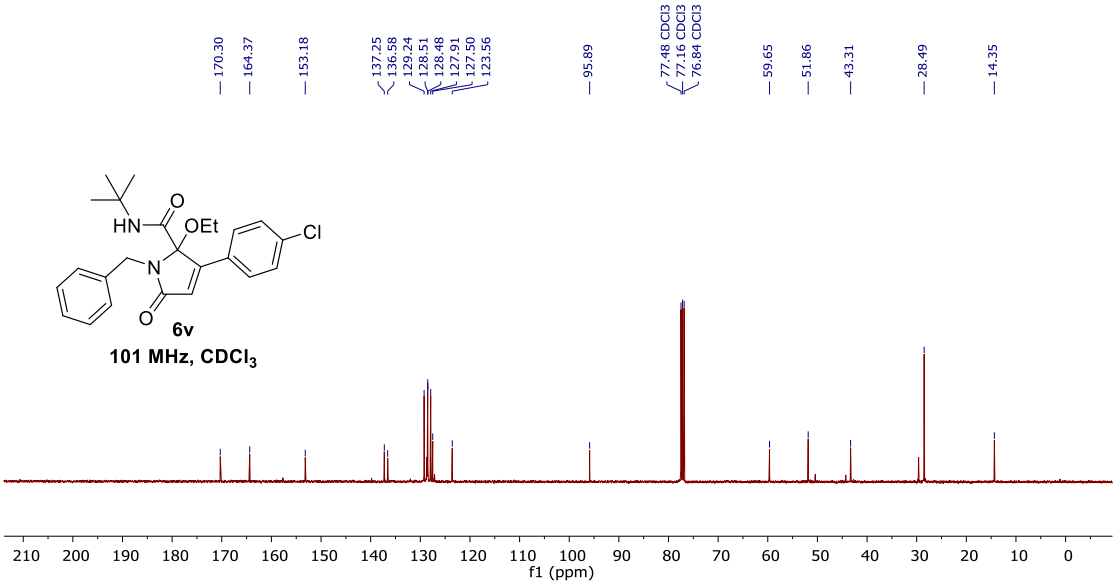
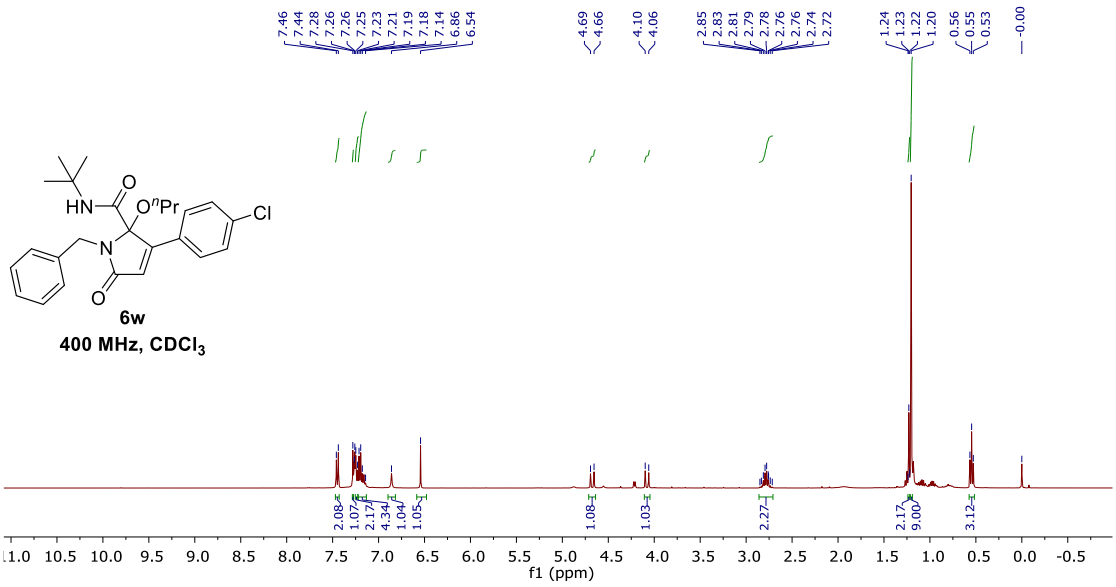
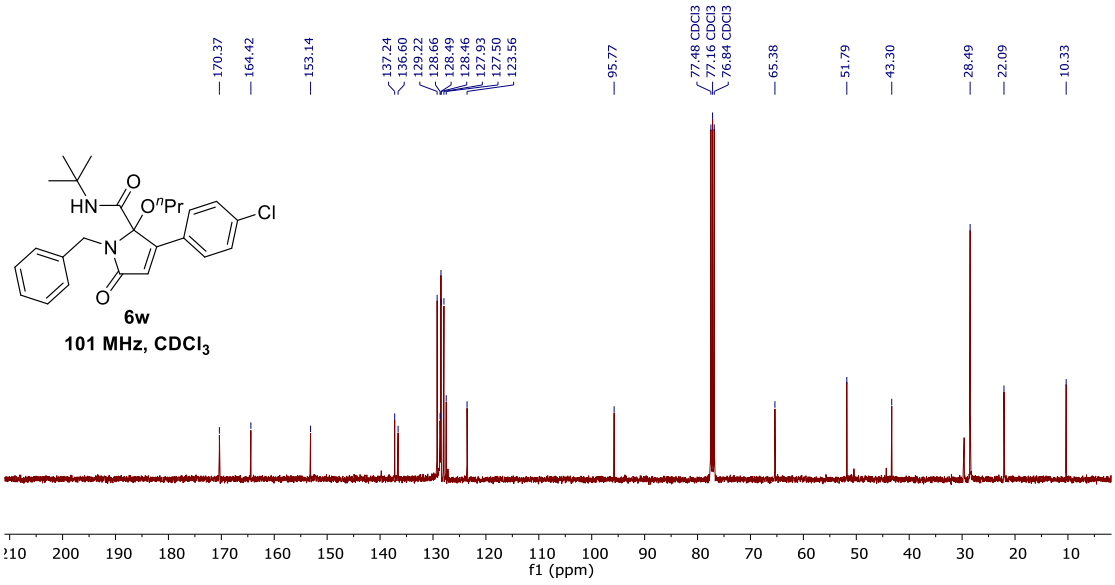
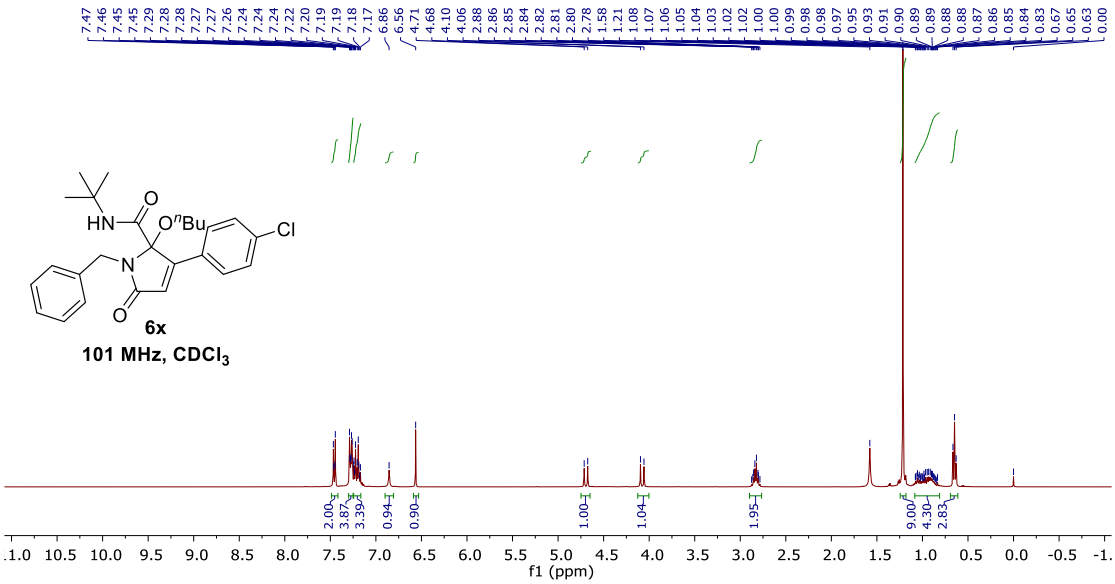
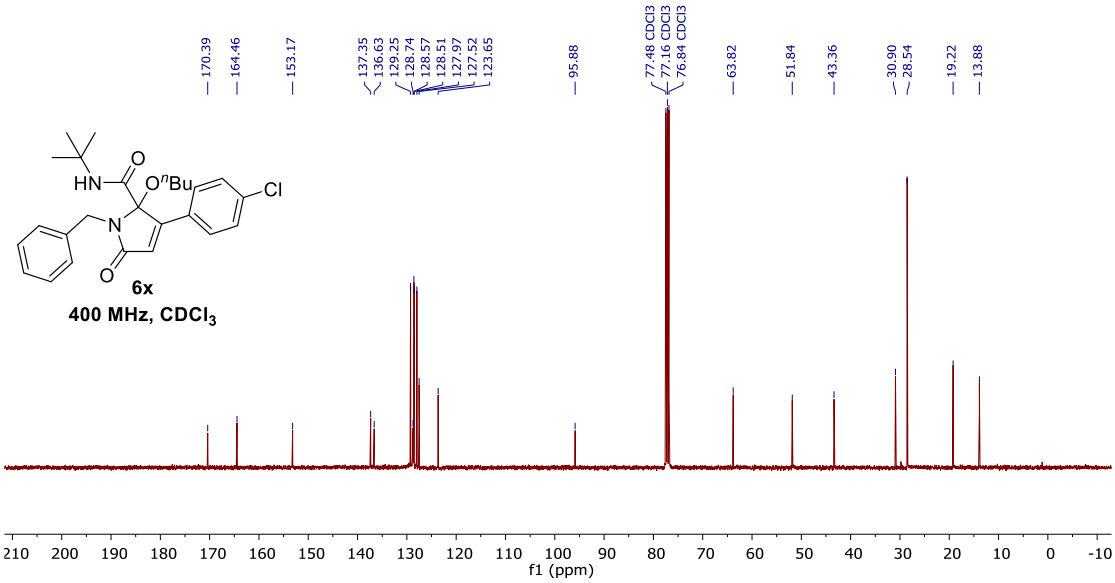
7.34
7.31
7.30
7.28
7.27
7.26
6.95
6.61
4.80
4.76
4.15
4.11
2.99
2.98
2.96
2.94
1.29
0.75
0.73
0.71
0.00
HN
O
OEt
Cl
N
O
6v
400 MHz, CDCl3
2.06
4.30
3.40
1.00
1.00
1.09
1.09
2.15
9.00
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

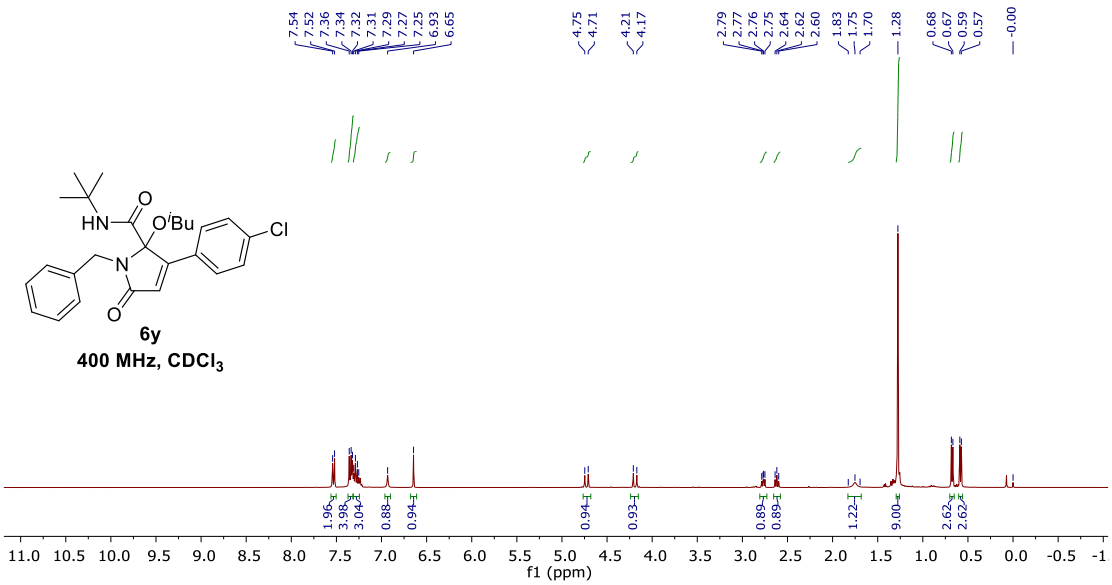

170.30
164.37
153.18
137.25
136.58
129.24
128.51
128.48
127.91
127.50
123.56
95.89
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
59.65
51.86
43.31
28.49
14.35
HN
O
OEt
Cl
N
O
6v
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

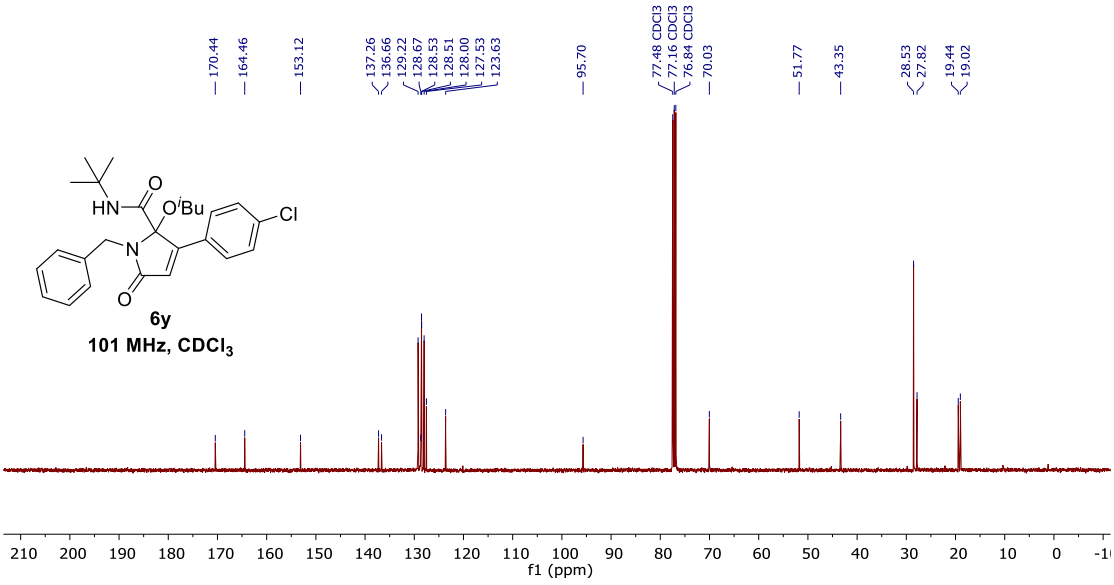

6w
400 MHz, CDCl3
f1 (ppm)

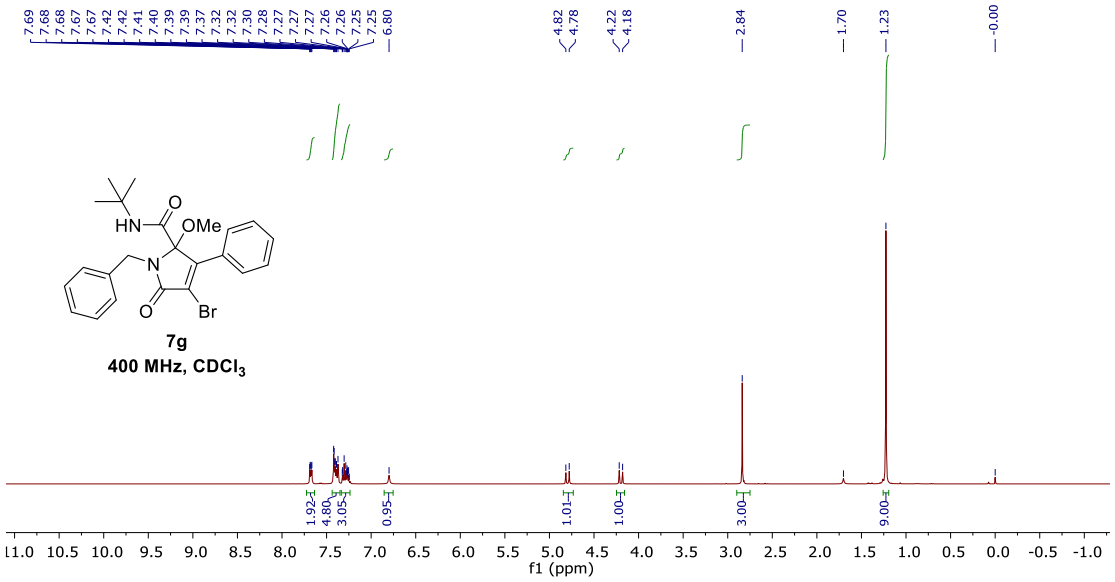

6w
101 MHz, CDCl3
f1 (ppm)


HN
O
O^{n}Bu
Cl
N
O
6x
101 MHz, CDCl$_3$
f1 (ppm)


HN
O
O^{n}Bu
Cl
N
O
6x
400 MHz, CDCl$_3$
f1 (ppm)


HN
O
O^{i}Bu
Cl
N
O
6y
400 MHz, CDCl$_3$
f1 (ppm)


HN
O
O^{i}Bu
Cl
N
O
6y
101 MHz, CDCl$_3$
f1 (ppm)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7.68
7.67
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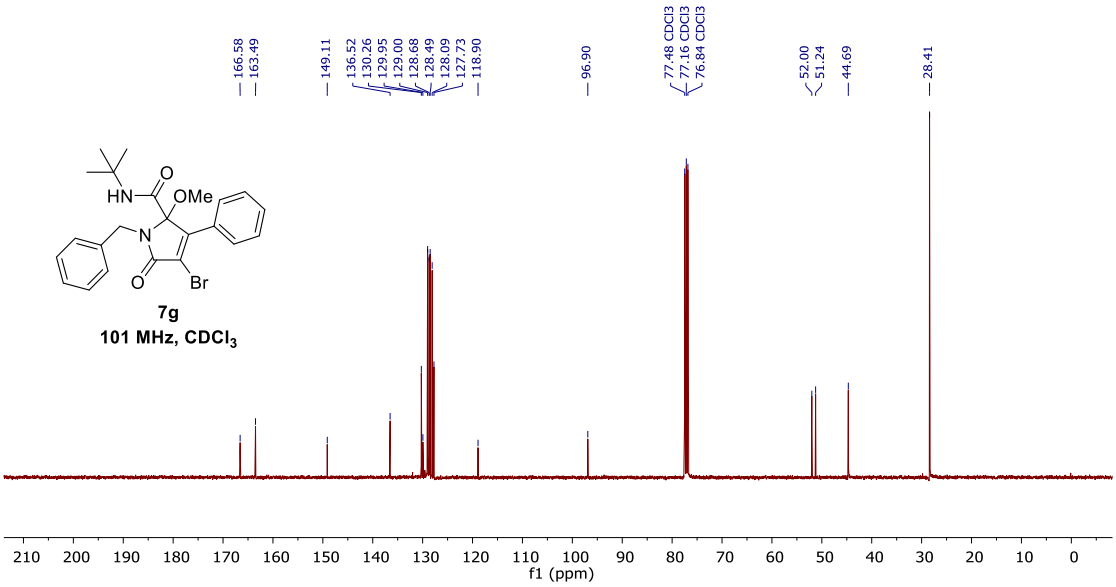
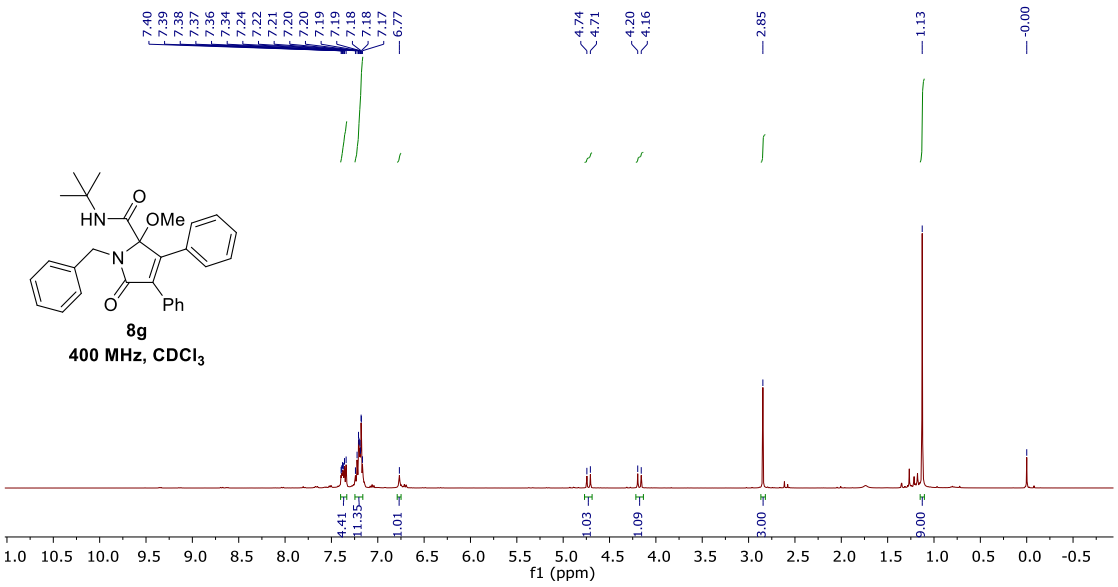
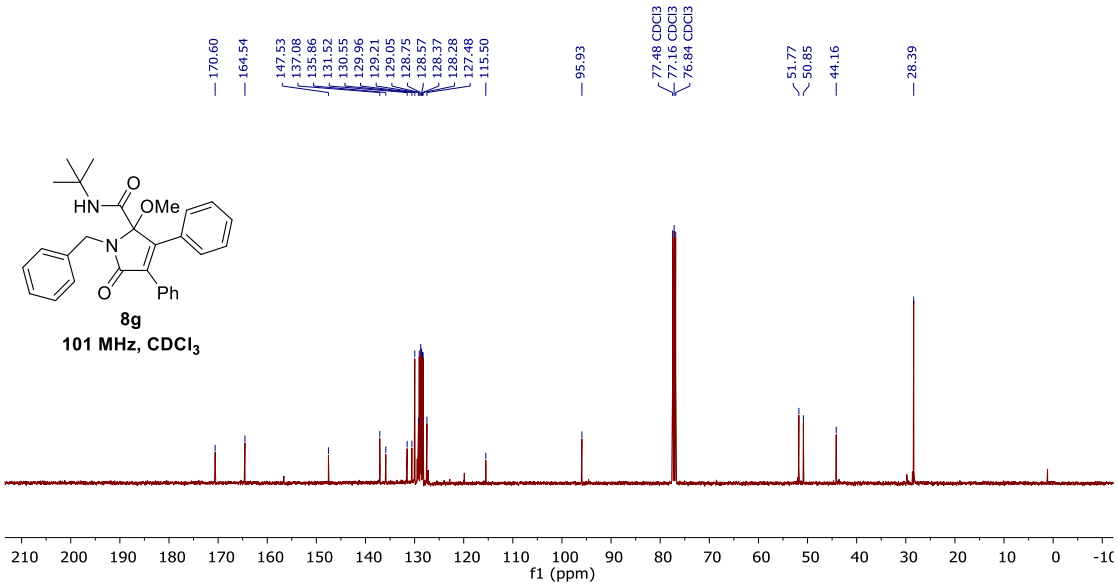
7.42
7.41
7.40
7.39
7.39
7.37
7.32
7.32
7.30
7.28
7.27
7.27
7.27
7.26
7.26
7.25
7.25
6.80
4.82
4.78
4.22
4.18
2.84
1.70
1.23
-0.00
HN
O
OMe
N
O
Br
7g
400 MHz, CDCl3
1.92
4.80
3.05
0.95
1.01
1.00
3.00
9.00
f1 (ppm)


166.58
163.49
149.11
136.52
130.26
129.95
129.00
128.68
128.49
128.09
127.73
118.90
96.90
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.00
51.24
44.69
28.41
HN
O
OMe
N
O
Br
7g
101 MHz, CDCl3
f1 (ppm)


7.40
7.39
7.38
7.37
7.36
7.34
7.24
7.22
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
6.77
4.74
4.71
4.20
4.16
2.85
1.13
-0.00
HN
O
OMe
N
O
Ph
8g
400 MHz, CDCl3
4.41
11.35
1.01
1.03
1.09
3.00
9.00
f1 (ppm)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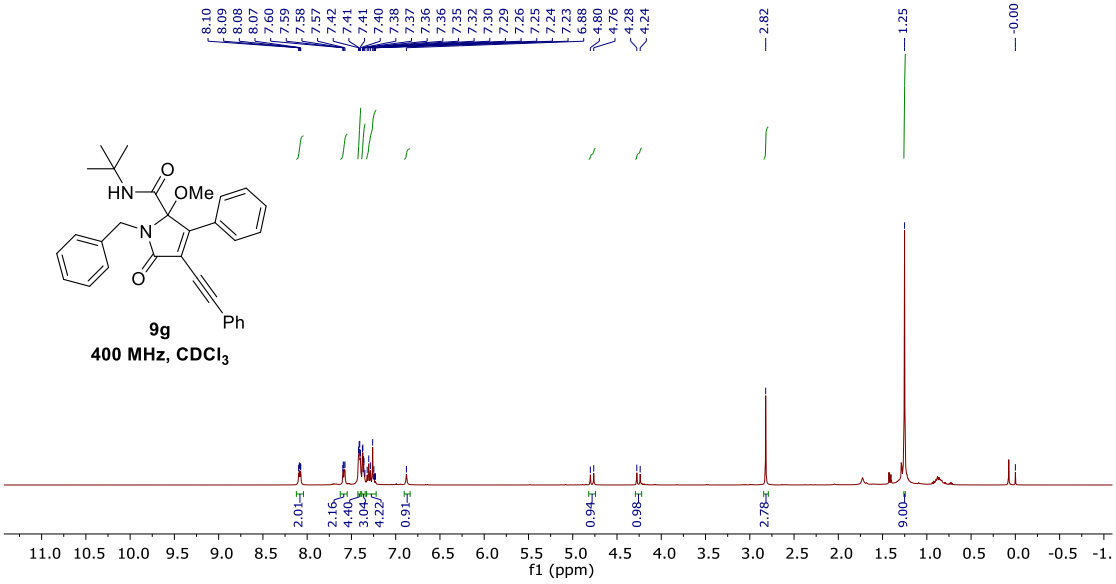
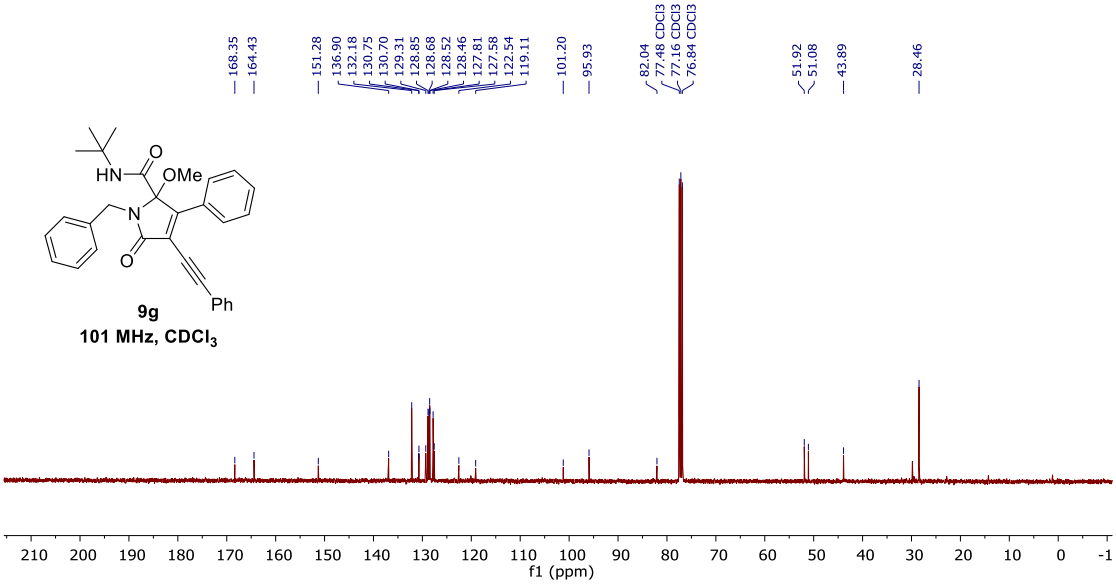
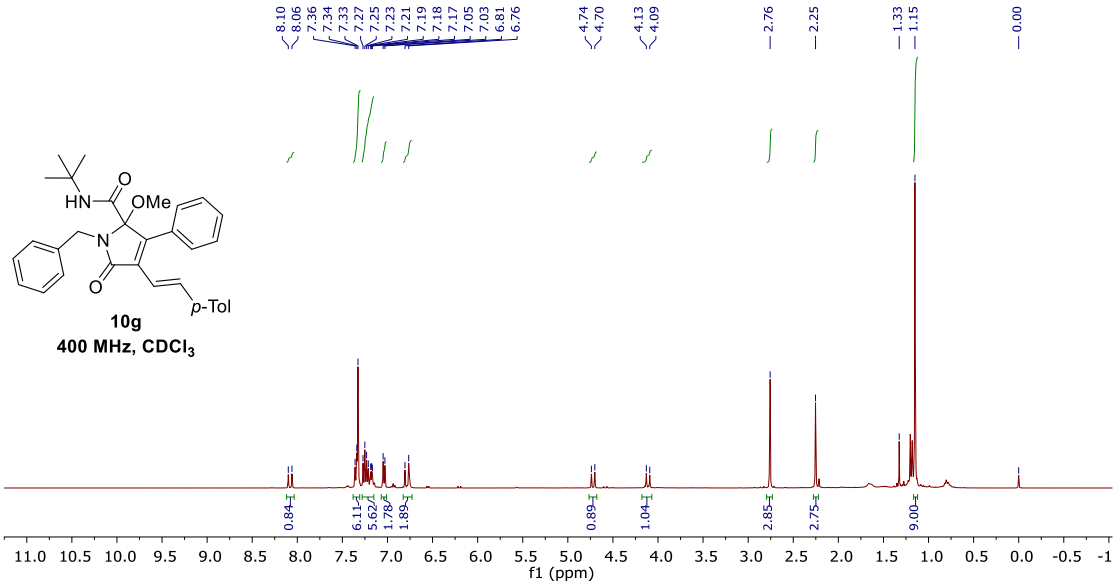
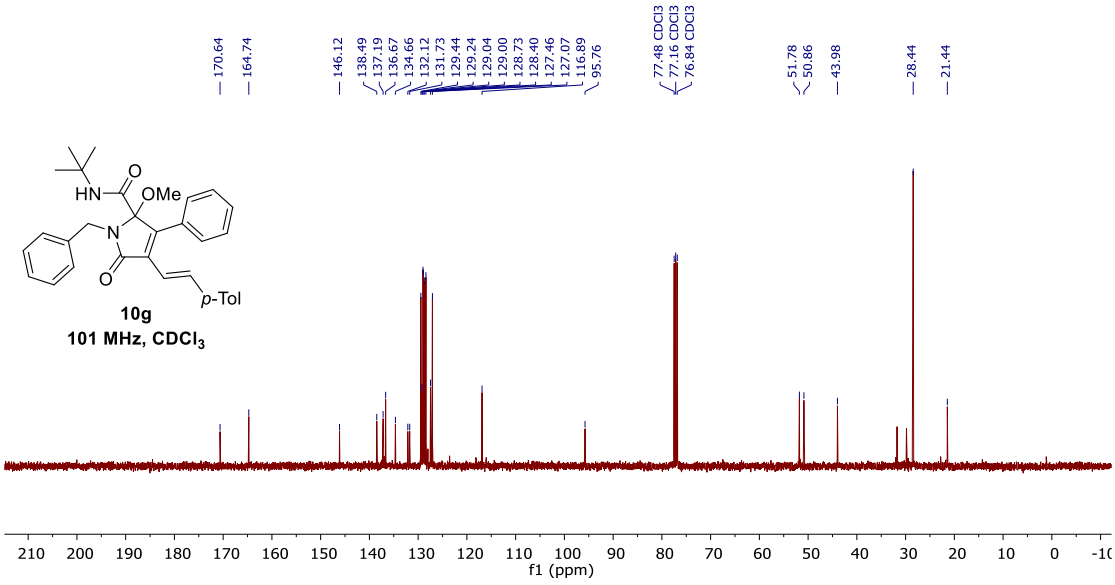
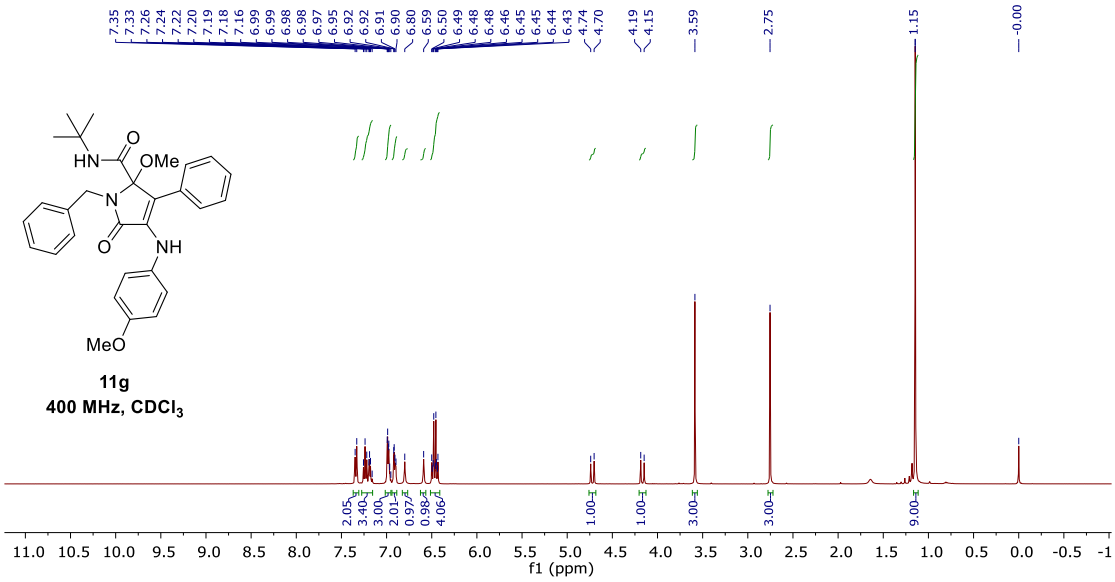
164.54
147.53
137.08
135.86
131.52
130.55
129.96
129.21
129.05
128.75
128.57
128.37
128.28
127.48
115.50
95.93
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
51.77
50.85
44.16
28.39
HN
O
OMe
N
O
Ph
8g
101 MHz, CDCl3
f1 (ppm)

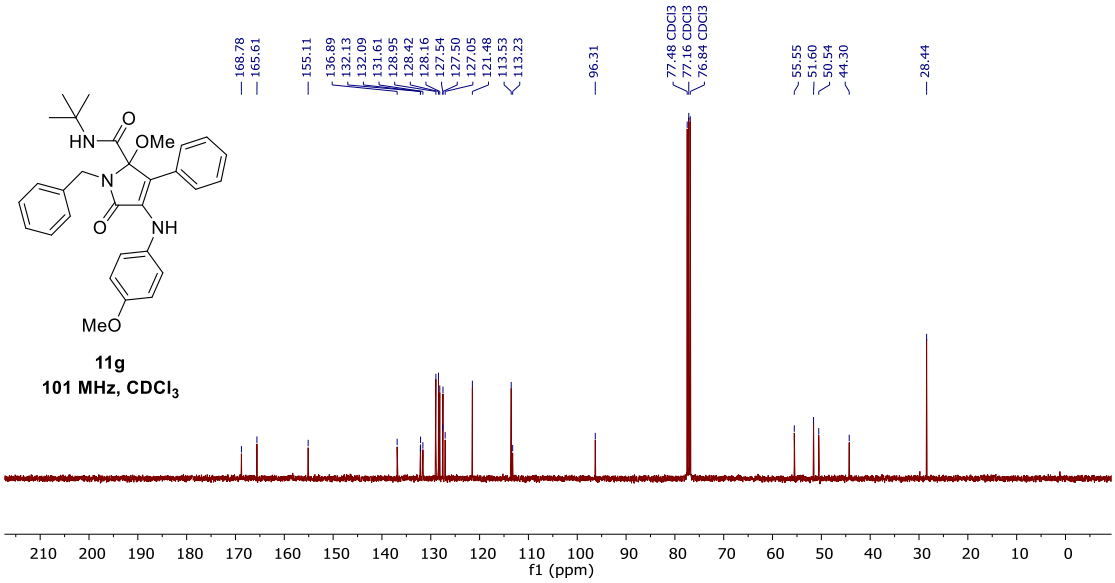

HN
O
OMe
N
O
Ph
9g
400 MHz, CDCl3
f1 (ppm)

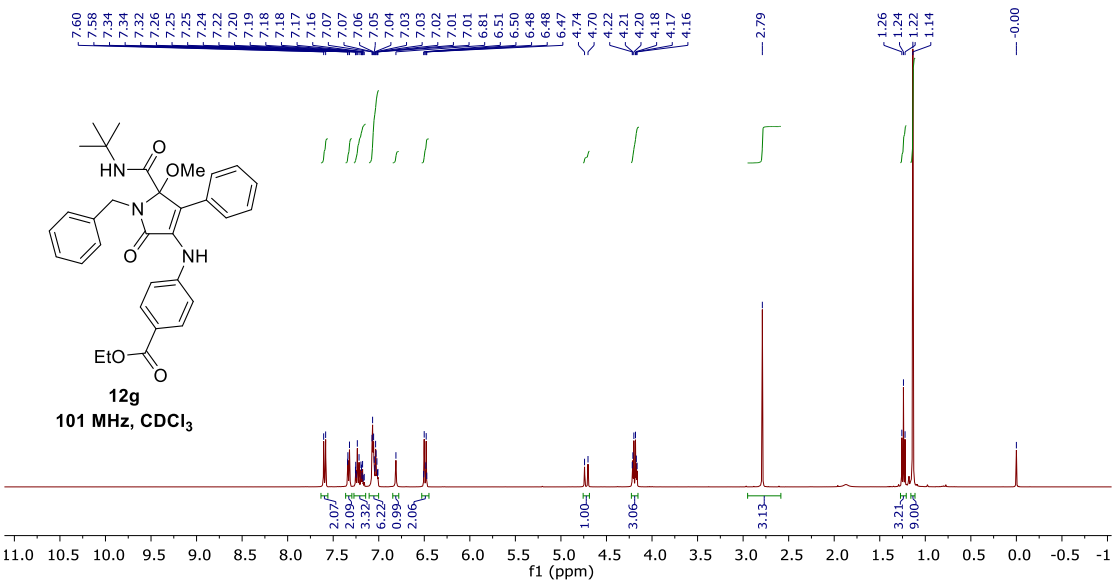

HN
O
OMe
N
O
Ph
9g
101 MHz, CDCl3
f1 (ppm)

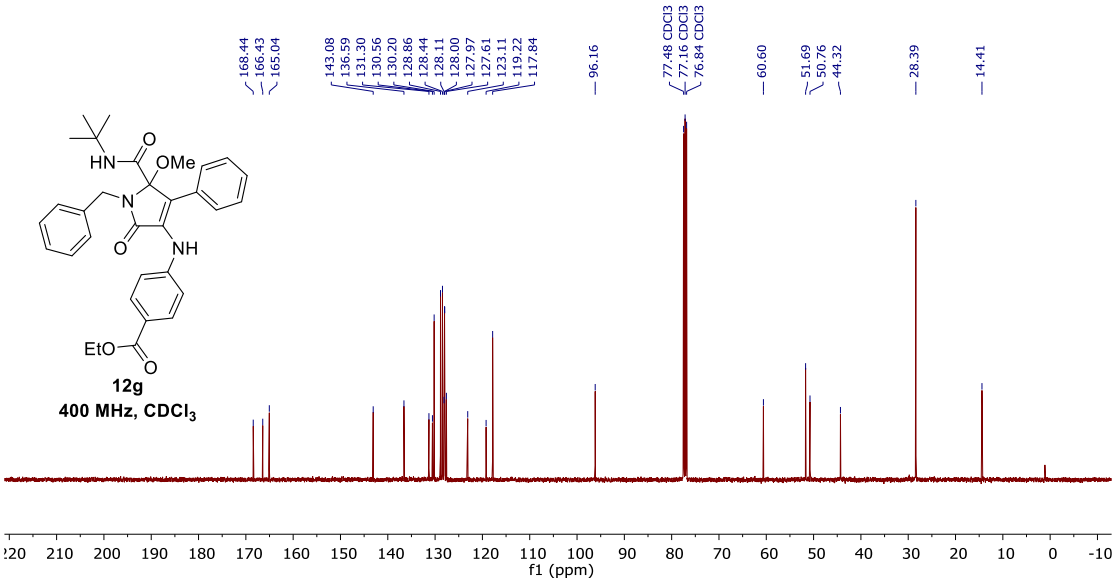

HN
O
OMe
N
O
p-Tol
10g
400 MHz, CDCl3
f1 (ppm)

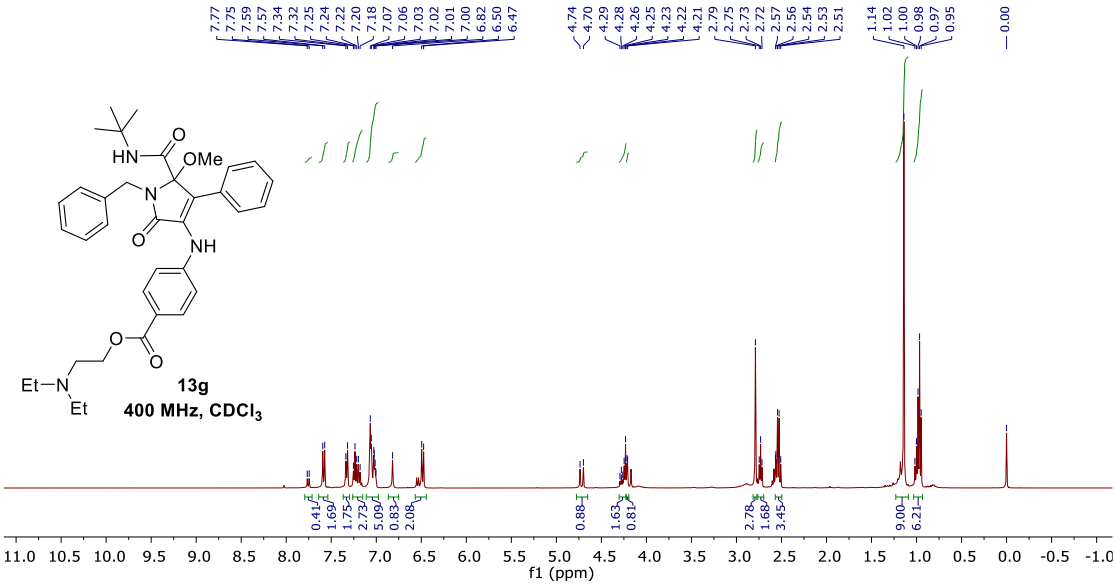

HN
O
OMe
N
O
p-Tol
10g
101 MHz, CDCl3
f1 (ppm)

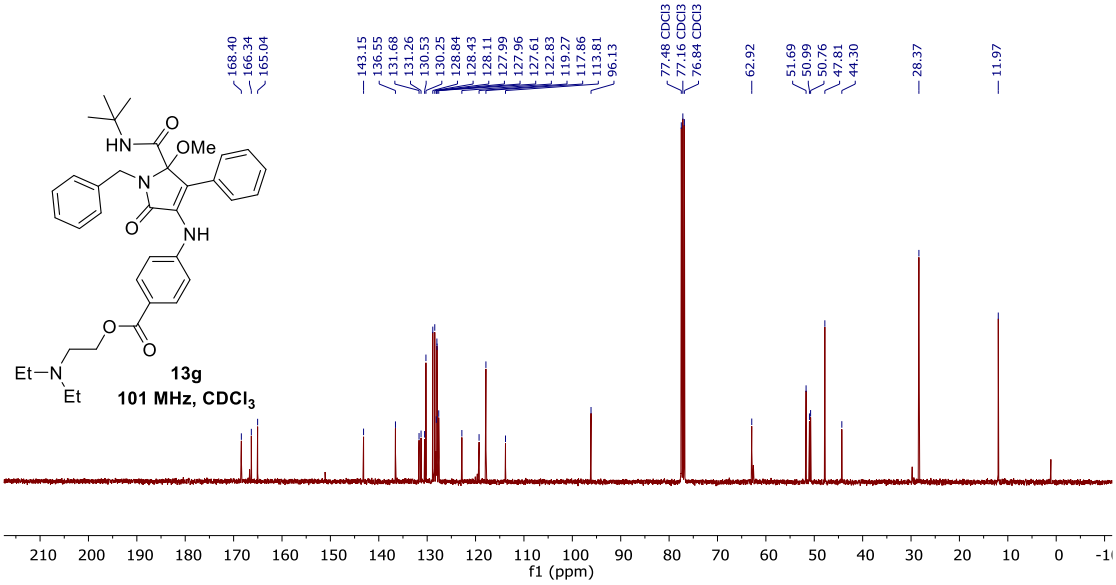

HN
O
OMe
N
O
NH
MeO
11g
400 MHz, CDCl3
f1 (ppm)

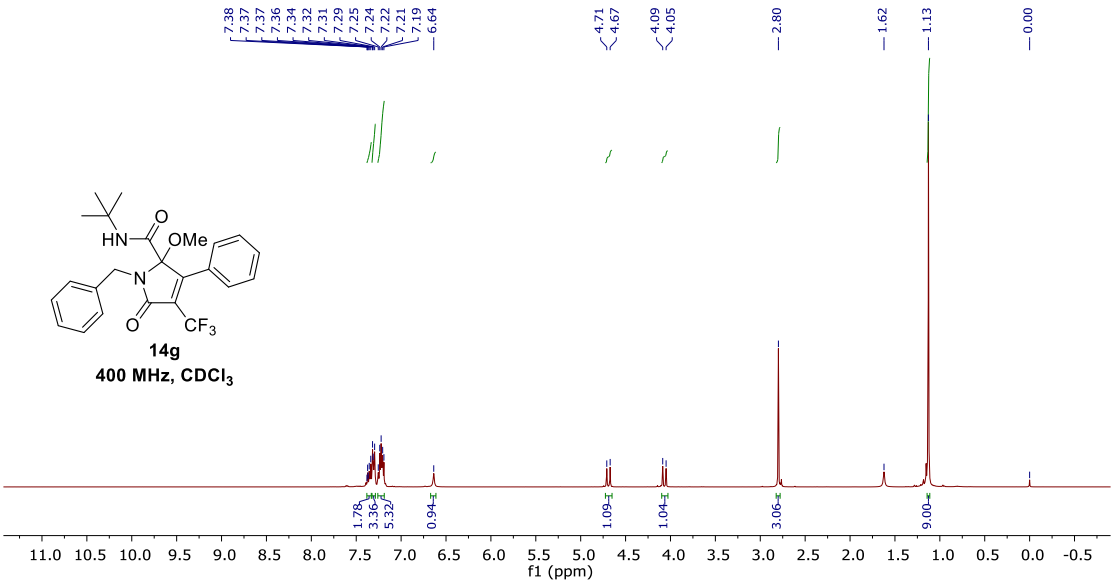

HN
O
OMe
N
O
NH
MeO
11g
101 MHz, CDCl3
f1 (ppm)

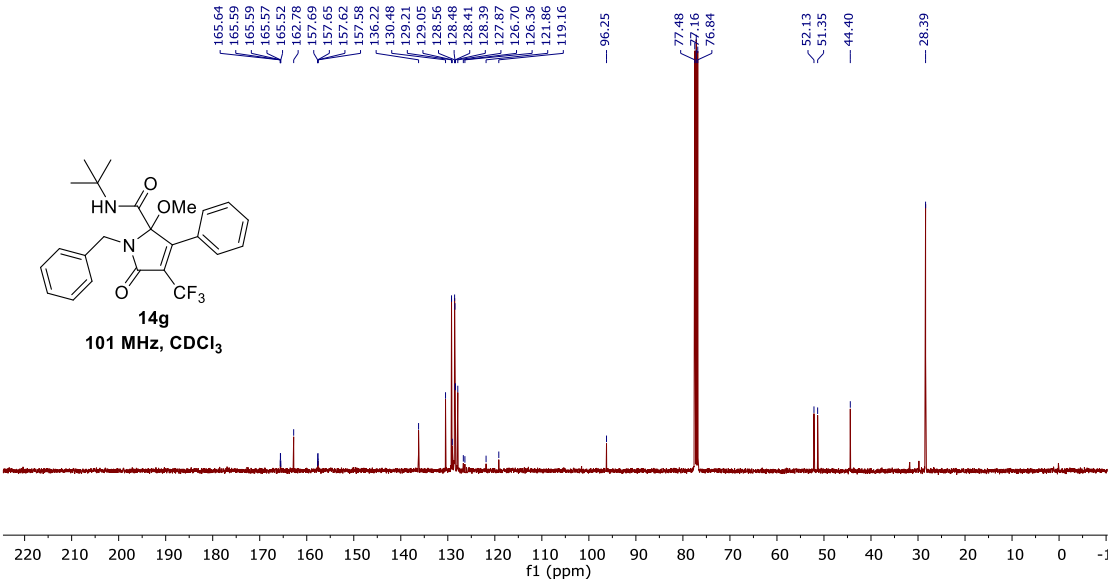

12g
101 MHz, CDCl3
f1 (ppm)

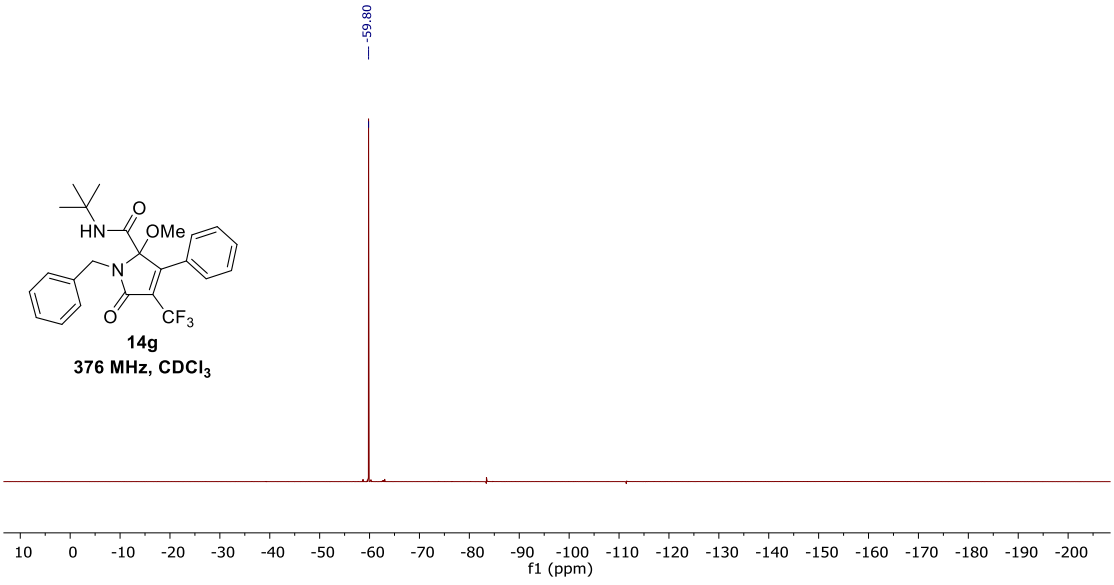

12g
400 MHz, CDCl3
f1 (ppm)

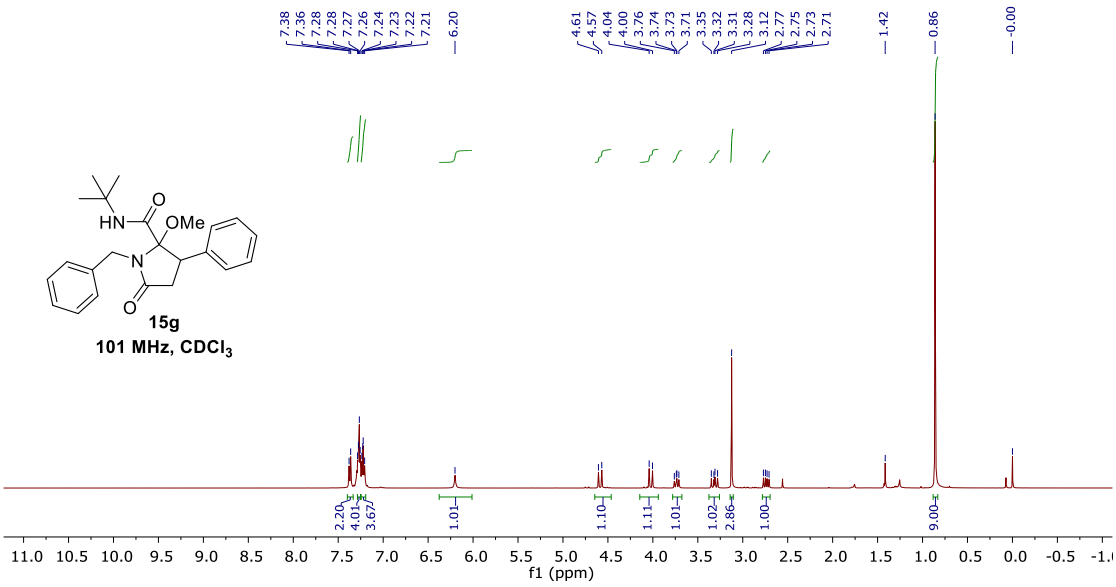

13g
400 MHz, CDCl3
f1 (ppm)

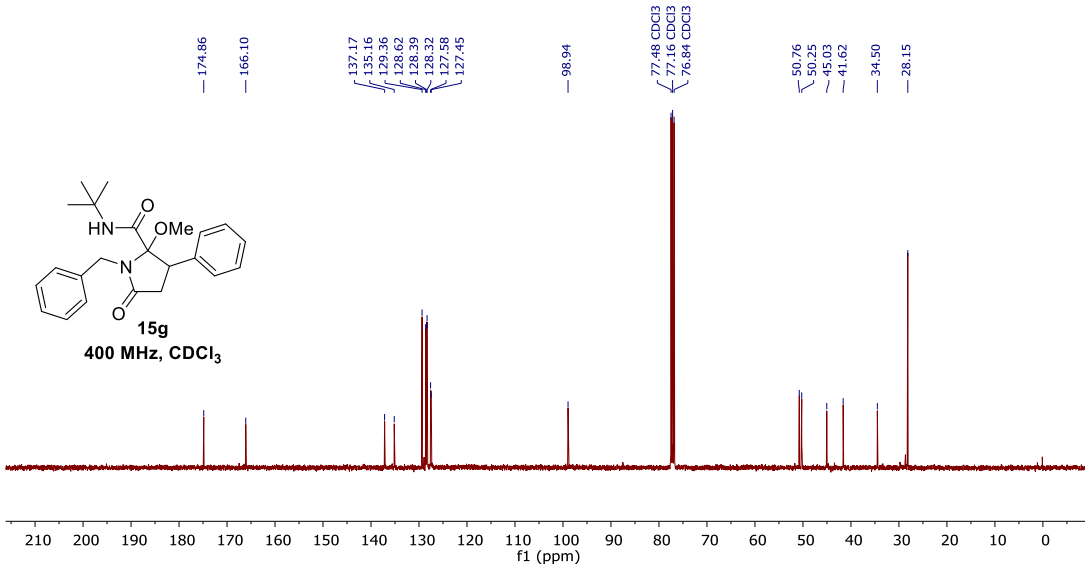

13g
101 MHz, CDCl3
f1 (ppm)

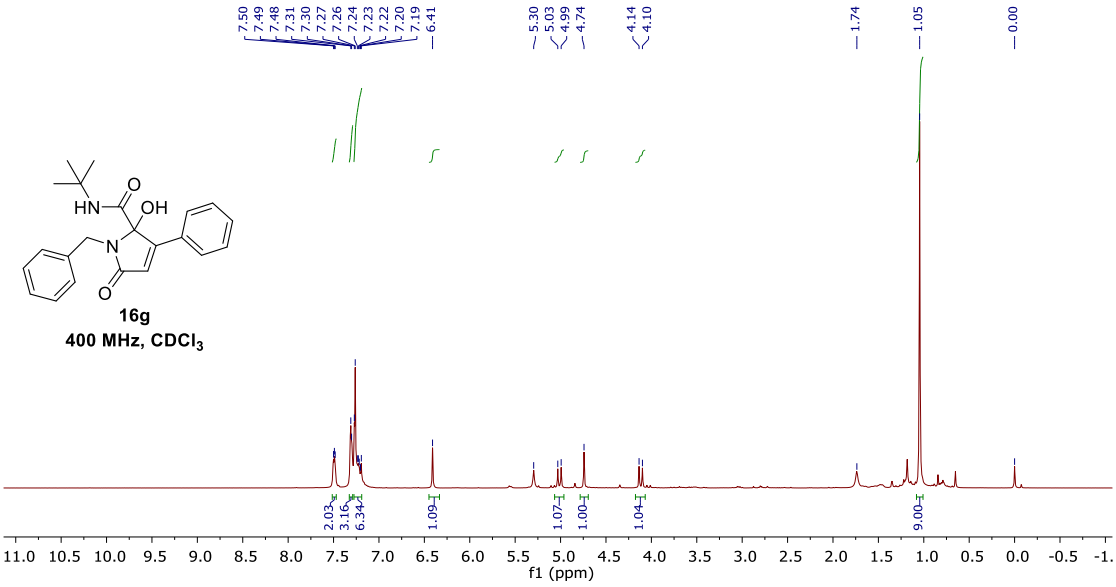

14g
400 MHz, CDCl3


14g
101 MHz, CDCl3


14g
376 MHz, CDCl3


7.38
7.36
7.28
7.28
7.27
7.26
7.24
7.23
7.22
7.21
6.20
4.61
4.57
4.04
4.00
3.76
3.74
3.73
3.71
3.35
3.32
3.31
3.28
3.12
2.77
2.75
2.73
2.71
1.42
0.86
-0.00
HN
O
OMe
N
O
15g
101 MHz, CDCl3
2.20
4.01
3.67
1.01
1.10
1.11
1.01
1.02
2.86
1.00
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


174.86
166.10
137.17
135.16
129.36
128.62
128.39
128.32
127.58
127.45
98.94
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
50.76
50.25
45.03
41.62
34.50
28.15
HN
O
OMe
N
O
15g
400 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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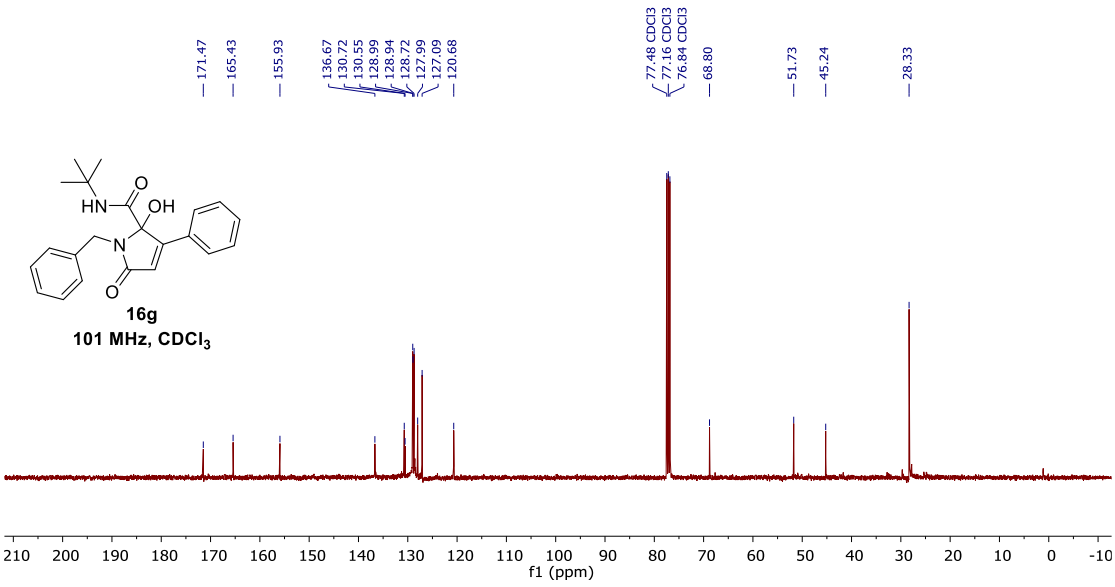
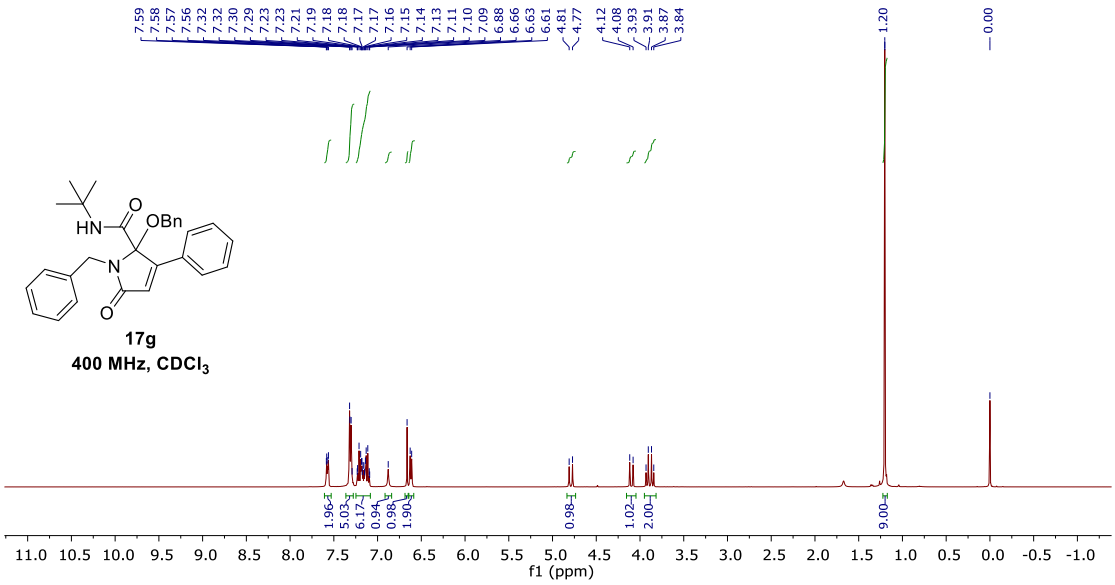
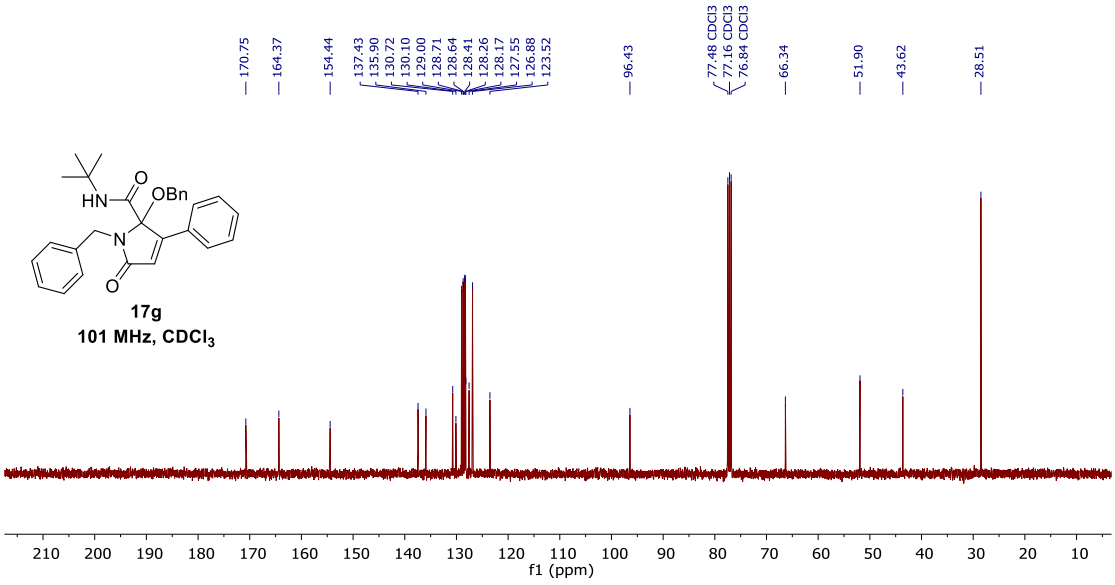
7.30
7.27
7.26
7.24
7.23
7.22
7.20
7.19
6.41
5.30
5.03
4.99
4.74
4.14
4.10
1.74
1.05
0.00
HN
O
OH
N
O
16g
400 MHz, CDCl3
2.03
3.16
6.34
1.09
1.07
1.00
1.04
9.00
f1 (ppm)


171.47
165.43
155.93
136.67
130.72
130.55
128.99
128.94
128.72
127.99
127.09
120.68
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
68.80
51.73
45.24
28.33
HN
O
OH
N
O
16g
101 MHz, CDCl3
f1 (ppm)


7.59
7.58
7.57
7.56
7.32
7.32
7.30
7.29
7.23
7.23
7.21
7.19
7.18
7.18
7.17
7.17
7.16
7.15
7.14
7.13
7.11
7.10
7.09
6.88
6.66
6.63
6.61
4.81
4.77
4.12
4.08
3.93
3.91
3.87
3.84
1.20
0.00
HN
O
OBn
N
O
17g
400 MHz, CDCl3
1.96
5.03
6.17
0.94
0.98
1.90
0.98
1.02
2.00
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


170.75
164.37
154.44
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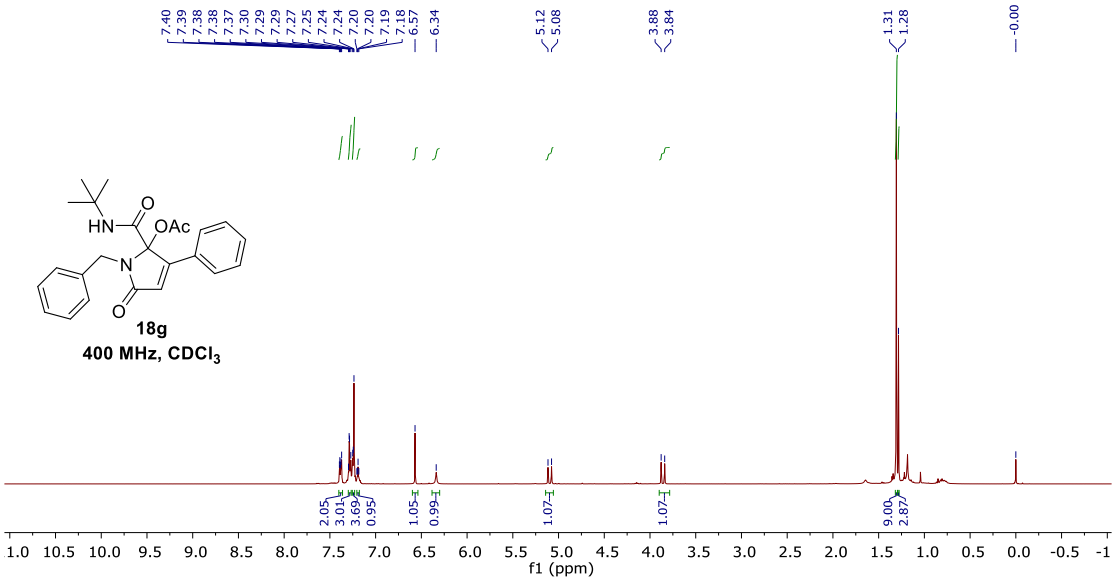
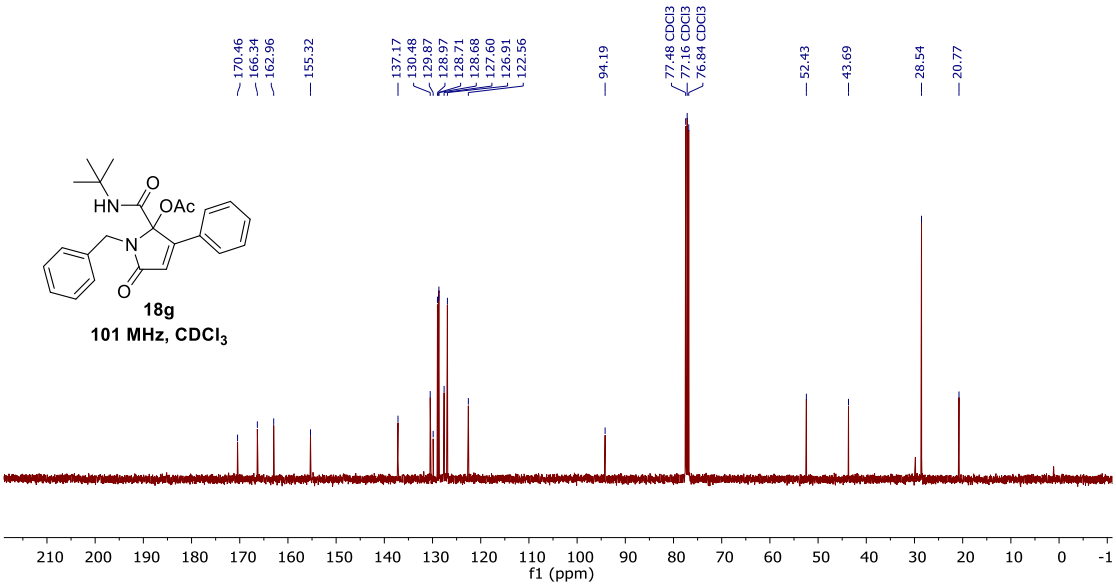
130.72
130.10
129.00
128.71
128.64
128.41
128.26
128.17
127.55
126.88
123.52
96.43
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
66.34
51.90
43.62
28.51
HN
O
OBn
N
O
17g
101 MHz, CDCl3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.40
7.39
7.38
7.38
7.37
7.30
7.29
7.29
7.27
7.25
7.24
7.24
7.20
7.20
7.19
7.18
6.57
6.34
5.12
5.08
3.88
3.84
1.31
1.28
-0.00
HN
O
OAc
N
O
18g
400 MHz, CDCl3
2.05
3.01
3.69
0.95
1.05
0.99
1.07
1.07
9.00
2.87
f1 (ppm)


170.46
166.34
162.96
155.32
137.17
130.48
129.87
128.97
128.71
128.68
127.60
126.91
122.56
94.19
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.43
43.69
28.54
20.77
HN
O
OAc
N
O
18g
101 MHz, CDCl3
f1 (ppm)

9. Copies of HRMS Analysis

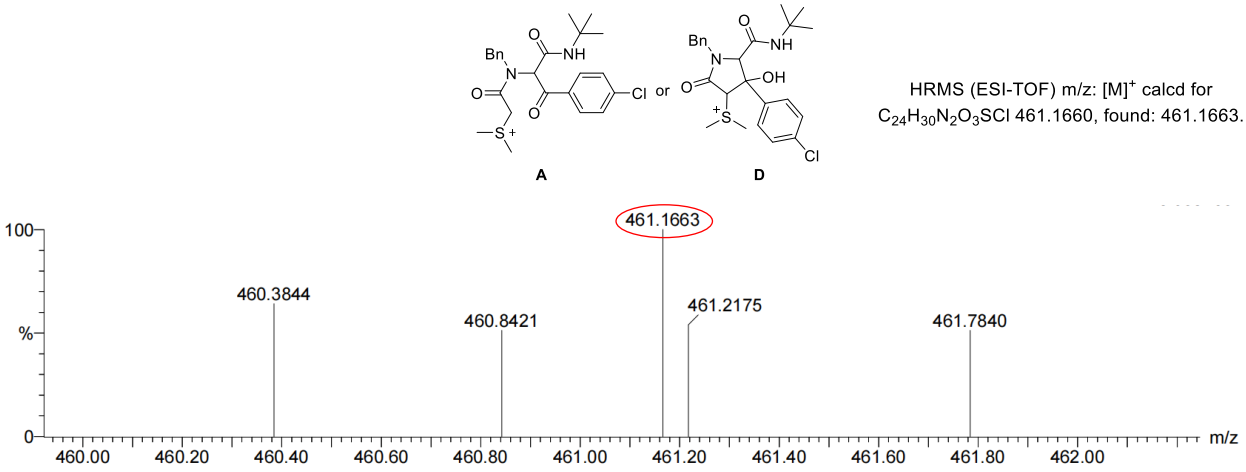


Figure *S1*. HRMS of A or D