SUPPORTING INFORMATION

for

Direct Catalytic Synthesis of *β*-acylamino Cyclobutanones *via* Three-Component Mannich Reactions

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Table of contents

1. General information

All reagents obtained from commercial sources were used without further purification. Anhydrous solvents were obtained from commercial sources and used without further drying. Nitrogen gas dried on a column of Drierite® was used as inert atmosphere. The reactions were monitored using LC-MS and GC-MS instruments.

Analytical LC-MS: Agilent HP1200 LC with Agilent 6140 quadrupole MS, operating in positive or negative ion electrospray ionization mode. Molecular weight scan range was 100 to 1350 m/z. Parallel UV detection was done at 210 nm and 254 nm. Samples were supplied as a 1 mM solution in MeCN or in THF/water (1:1) with 5 µL loop injection. LC-MS analyses were performed on two instruments, one of which was operated with basic, and the other with acidic eluents.

Basic LC-MS: Gemini-NX, 3 µm, C18, 50 mm × 3.00 mm i.d. column at 23 °C, at a flow rate of 1 mL min^{-1} using 5 mM aq NH_4HCO_3 solution and MeCN as eluents.

Acidic LC-MS: ZORBAX Eclipse XDB-C18, 1.8 µm, 50 mm × 4.6 mm i.d. column at 40 °C, at a flow rate of 1 mL min^{-1} using water and MeCN as eluents, both containing 0.02 V/V% formic acid.

Combination gas chromatography and low-resolution mass spectrometry were performed on Agilent 6850 gas chromatograph and Agilent 5975C mass spectrometer using 15 m × 0.25 mm column with 0.25 µm HP-5MS coating and helium as carrier gas. Ion source: EI^+, 70 eV, 230 °C, quadrupole: 150 °C, interface: 300 °C.

Flash chromatography was performed on ISCO CombiFlash Rf 200i or ISCO CombiFlash Torrent® with pre-packed silica-gel cartridges (Redi*Sep*® R_f Gold High Performance).

Preparative HPLC purifications were performed on an ISCO CombiFlash EZ Prep system with a Gemini-NX® 10 µm C18, 250 mm × 50 mm column running at a flow rate of 118 mL min^{-1} with UV diode array detection.

^1H NMR, ^{19}F NMR and proton-decoupled ^{13}C NMR measurements were performed on Bruker Avance III 500 MHz spectrometer and Bruker Avance III 400 MHz spectrometer, using DMSO-d_6 or $CDCl_3$ as solvent. ^1H and ^{13}C NMR data are in the form of delta values, given in part per million (ppm), using the residual peak of the solvent as internal standard (DMSO-d_6: 2.50 ppm (^1H) / 39.5 ppm (^{13}C); $CDCl_3$: 7.26 ppm (^1H) / 77.0 ppm (^{13}C)). Splitting patterns are designated as: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sp (septet), m (multiplet), br s (broad singlet), dd (doublet of doublets), td (triplet of doublets), qd (quartet of doublets), dt (doublet of triplets). In some cases due to tautomers or amide rotamers two sets of signals appear in the spectra.

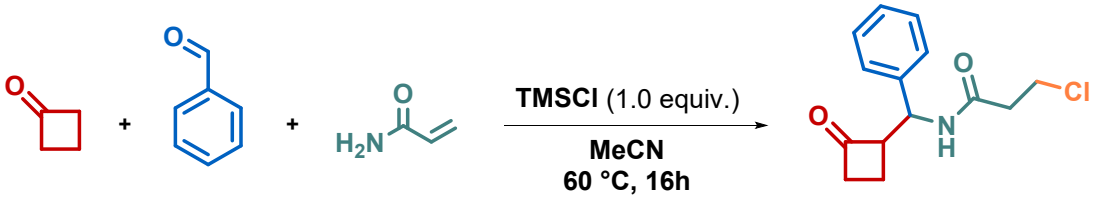
HRMS were determined on a Shimadzu IT-TOF-MS, ion source temperature 200 °C, ESI +/-, ionization voltage: (±)4.5 kV. Mass resolution: min. 10000.

2. Experimental procedures

2.1. General procedure for the three-component Mannich reactions

To a suspension of the corresponding aldehyde (3 mmol, 1.0 equiv.), amide (4.5 mmol, 1.5 equiv.), and cycloalkanone (1.5 mL, 20.1 mmol, 6.7 equiv.), $Cu(OTf)_2$ (219 mg, 0.6 mmol, 0.2 equiv.) and TIPSCl (964 µL, 4.5 mmol, 1.5 equiv.) were added. The mixture was stirred vigorously at 60 °C until the complete consumption of the starting materials, followed by TLC, HPLC, and HPLC-MS. Upon completion of the reaction, the mixture was diluted with ACN and purified by reverse-phased preparative HPLC (eluent: MeCN / 5 mM $(NH_4)HCO_3$ solution). Fractions containing product were concentrated *in vacuo* and the remaining solvent was lyophilized to give the corresponding products.

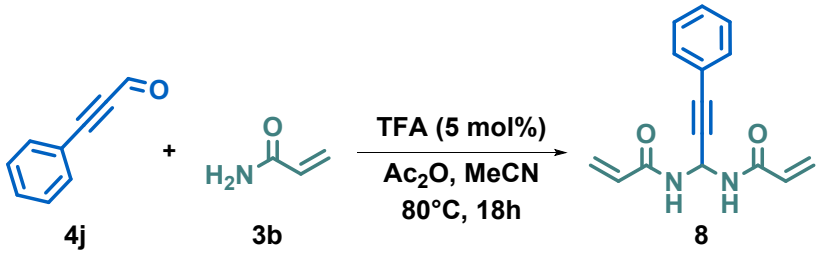
2.2 Synthesis of 3-chloro-*N*-[(2-oxocyclobutyl)-phenyl-methyl]propanamide (5)



1a **2a** **3b** **5**

To a mixture containing benzaldehyde (**2a**) (3 mmol, 1.0 equiv.) acrylamide (**3b**) (4.5 mmol, 1.5 equiv.) in cyclobutanone (**1a**) (0.7 mL, 9 mmol, 3 equiv.) in 5 mL acetonitrile, TMSCl (381 µL, 3 mmol, 1 equiv.) was added. The mixture was stirred vigorously at 60 °C for 16 h. Upon completion of the reaction, the volatiles were evaporated, and the crude product was purified by flash chromatography (eluent: n-Heptane / EtOAc). Compound **5** was isolated in 74% yield.

2.3 Synthesis of *N*-[3-phenyl-1-(prop-2-enoylamino)prop-2-ynyl]prop-2-enamide (8)

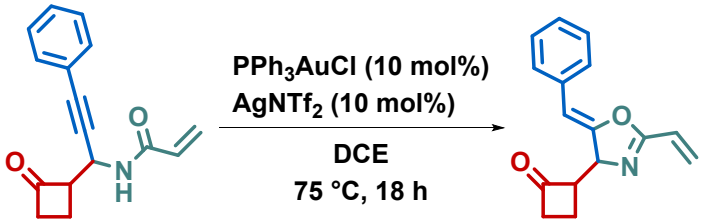


4j **3b** **8**

Compound **8** was prepared according to the procedure reported in the literature.[S1]

In a 100 ml round bottom flask, equipped with a reflux condenser and magnetic stirring bar, aldehyde **4j** (1.0 g, 7.68 mmol) and acrylamide (**3b**) (2 equiv.) were dissolved in acetonitrile (2 mL/mmol), To the mixture, acetic anhydride (2.5 equiv.) and 2,2,2-trifluoroacetic acid (0.05 equiv.) were added. The reaction mixture was heated to 80 °C and stirred overnight. Upon completion, white precipitation occurred. After cooling, 5 mL diethyl ether was added to the mixture and stirred for an additional 30 min. The precipitate was filtered, washed with MeCN (5 mL) and diethyl ether (2x5 mL) to obtain bisaminal **8** as a white solid in 93% yield.

2.4 Synthesis of (*Z*)-2-(5-benzylidene-2-vinyl-4,5-dihydrooxazol-4-yl)cyclobutan-1-one (9)

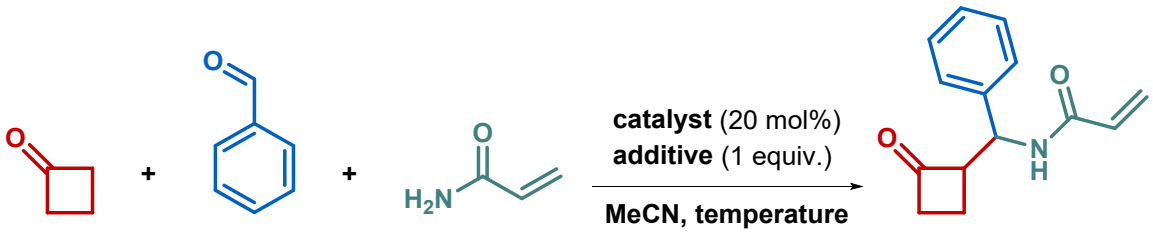


4jb **9**

To a 10 mL round bottom flask, equipped with a reflux condenser and magnetic stirring bar, *β*-acylamino cyclobutanone **4jb** (1.0 mmol), PPh_3AuCl (0.1 equiv.) and $AgNTf_2$ (0.1 equiv.) were added. The reaction vessel was evacuated and purged with nitrogen three times. DCE (4 mL/mmol) was added *via* syringe to the flask. The reaction mixture was stirred at 75 °C for 18h under inert atmosphere. Upon completion, the mixture was cooled to RT and the solvent was evaporated. The crude product was purified by flash chromatography to give corresponding oxazoline **9** product in 22% yield.

3. Optimization of reaction conditions for the 3-component Mannich reaction

3.1. Catalyst screen

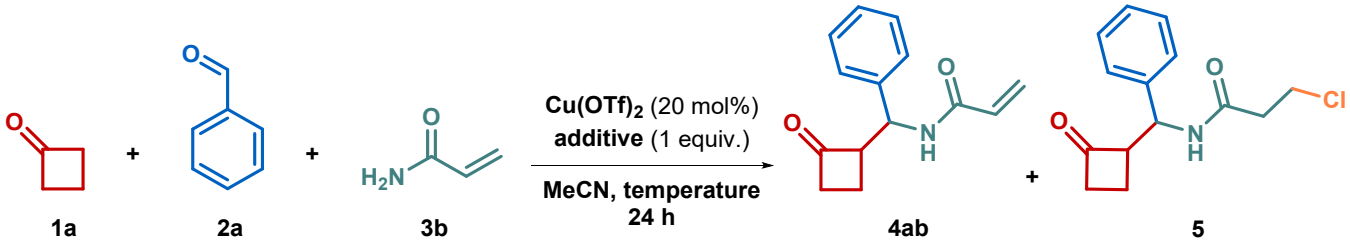


1a + **2a** + **3b** → **4ab**

Entry[a]	Catalyst / additive	Temperature (°C)	Conversion[b] (%)
1	- / -	25	-
2	$InCl_3$ / -	25	<5
3	$AuCl_3$ (10mol%) / -	25	<5
3	$AuCl_3$ (10mol%) / -	60	42
4	$RuCl_3$ / -	60	<5
5	$Sc(OTf)_3$ / -	60	<5
6	$Ga(OTf)_3$ / -	60	33
7	$Cu(OTf)_2$ / -	60	51
8	- / TMSCl	60	n.d[d]
9	$AuCl_3$ / TMSCl	60	50
10	$Cu(OTf)_2$ / TMSCl	60	73 (47%)[c]
11	$Fe(OTf)_3$ / TMSCl	60	53
12	$Cu(OAc)_2$ / TMSCl	60	62
13	$Cu(TFA)_2$ / TMSCl	60	59
15	$Cu(OTf)_2$ / TIPSCl	60	87 (65%)[c]

[a]General conditions: aldehyde **2a** (1 mmol), amide **3b** (1.5 equiv), ketone **1a** (3 equiv.), **catalyst** (0.2 equiv.) and **additive** (1 equiv.) was stirred in MeCN (0.5 mL, 2.0 M) for 24 h. [b]Conversion calculated by the relative area% of **4ab** in the mixture by HPLC-MS at 210 nm. [c]Isolated yield for **4ab**. [d]Only HCl adduct **5** derived from **4ab** could be isolated in 74% yield.

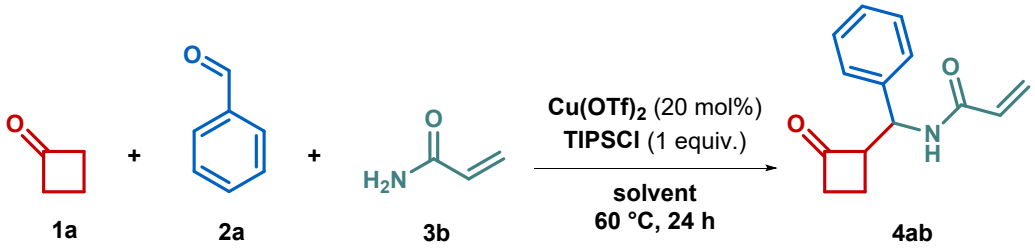
3.2. Silyl chloride screen



Entry[a]	Additive	Temperature (°C)	Conversion[b] (%)	Chemoselectivity (%)	
				4ab	5
1	TESCl	25	44	85	15
2	TESCl	60	77	82	18
3	DMPSCl	25	37	88	12
4	DMPSCl	60	79	84	16
5	TBDMSCl	25	<5	n.d.	n.d.
6	TBDMSCl	60	67	80	20
7	TBDPSCl	25	<5	n.d.	n.d.
8	TBDPSCl	60	69	82	18
9	TIPSCl	25	<5	n.d.	n.d.
10	TIPSCl	60	87 (65%)[c]	95	5

[a]General conditions: aldehyde **2a** (1 mmol), amide **3b** (1.5 equiv), ketone **1a** (3 equiv.), **Cu(OTf)$_2$** (0.2 equiv.) and **additive** (1 equiv.) was stirred in MeCN (0.5 mL, 2.0 M) at different temperature for 24 h. [b]Conversion calculated by the relative area% of **4ab** in the mixture by HPLC-MS at 210 nm. [c]Isolated yield for **4ab**.

3.3. Solvent screen



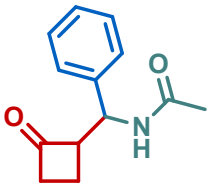
1a 2a 3b 4ab

Entry[a]	Solvent	Conversion[b] (%)
1	MeCN	87 (65%)[c]
2	DCE	77
3	Toluene	80
4	THF	72
5	TFT	79
6	MeCN (1 mL, 1.0 M)	85
7	MeCN (1.5 mL, 0.67 M)	82
8	MeCN (2 mL, 0.5 M)	81
9	none	>99 (77%)[c,d]

[a]General coniditions: aldehyde **2a** (1 mmol), amide **3b** (1.5 equiv), ketone **1a** (3 equiv.), **Cu(OTf)$_2$** (0.2 equiv.) and **TIPSCl** (1 equiv.) was stirred in **solvent** at 60 °C for 24 h. [b]Conversion calculated by the relative area% of **4ab** in the mixture by HPLC-MS at 210 nm. [c]Isolated yield for **4ab**. [d]Reaction time: 3 hours.

4. Characterization data

N-[(2-oxocyclobutyl)-phenyl-methyl]acetamide (4aa)



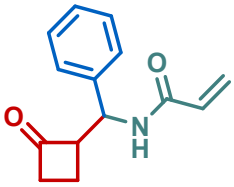
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and acetamide (**3a**) as substrates, 334 mg (51%) of **4aa** was isolated as a colorless oil. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{13}H_{15}NO_2H$ [M+H$^+$]: 218.1176, found: 218.1177.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.42/8.35 (d, *J* = 8.7 Hz, 1H); 7.33-7.20 (m, 5H); 5.16/5.08 (t, *J* = 9.0 Hz, 1H); 3.81-3.75/3.71-3.64 (m, 1H); 3.01-2.91 (m, 1H); 2.88-2.79 (m, 1H); 2.05-1.98/1.96-1.87 (m, 1H); 1.96-1.87/1.68-1.61 (m, 1H) 1.85/1.83 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/208.0; 168.6/168.3; 141.6/141.2; 128.3/128.2 and 127.1/126.8; 127.0/126.9; 63.5/64.2; 51.7/50.8; 44.1/44.0; 22.7/22.6; 14.3/13.7.

N-[(2-oxocyclobutyl)-phenyl-methyl]prop-2-enamide (4ab)



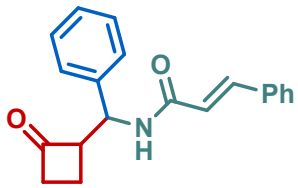
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and acrylamide (**3b**) as substrates, 530 mg (77%) of **4ab** was isolated as white crystals (m.p.: 83 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{15}NO_2Na$ [M+Na$^+$]: 252.0995, found: 252.1000.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.66/8.57 (d, *J* = 8.8 Hz, 1H); 7.34-7.22 (m, 5H) 6.32/6.29 (dd, *J* = 10.2, 15.2 Hz, 1H); 6.10/6.06 (d, *J* = 12.8 Hz, 1H); 5.62/5.60 (d, *J* = 10.0 Hz, 1H); 5.25/5.17 (t, *J* = 8.5 Hz, 1H); 3.88-3.81 (m, 1H); 3.02-2.93 (m, 1H); 2.88-2.81 (m, 1H); 2.08-2.00/1.96-1.87 (m, 1H); 1.96-1.87/1.70-1.63 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/207.8; 164.0/163.7; 141.2/141.0; 131.6/131.4; 128.3/128.2 and 127.1/126.8; 127.1/126.8; 125.8/125.5; 64.0/63.3; 51.8/50.9; 44.1/44.0; 14.3/13.8.

(*E*)-*N*-[(2-oxocyclobutyl)-phenyl-methyl]-3-phenyl-prop-2-enamide (4ac)



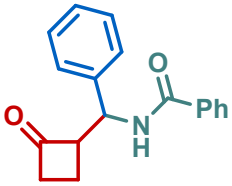
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and 3-phenyl-2-propenamid (**3c**) as substrates, 531 mg (58%) of **4ac** was isolated as white crystals (m.p.: 155-157 °C). Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{20}H_{19}NO_2H$ [M+H$^+$]: 306.1488, found: 306.1491.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.69/8.62 (d, *J* = 8.8 Hz, 1H); 7.57-7.55 (m, 2H) 7.45-7.24 (m, 8H) 7.43/7.41 (d, *J* = 15.8 Hz, 1H); 6.74/6.71 (d, *J* = 15.8 Hz, 1H); 5.32/5.24 (t, *J* = 8.3 Hz, 1H); 3.91-3.85/3.81-3.75 (m, 1H); 3.04-2.94 (m, 1H); 2.90-2.83 (m, 1H); 2.10-2.03/2.00-1.90 (m, 1H); 2.00-1.90/1.73-1.67 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/207.9; 164.3/164.1; 141.3/141.1; 139.2/139.0; 134.8/134.8; 129.5/129.5; 128.9 (2C); 128.3/128.2; 127.5/127.5; 127.1/127.1; 127.0/126.8; 122.1/121.9; 64.2/63.4; 51.9/51.0; 44.2/44.1; 14.3/13.7.

N-[(2-oxocyclobutyl)-phenyl-methyl]benzamide (4ad)



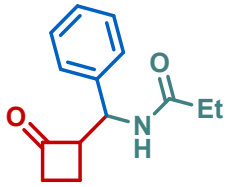
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and benzamide (**3d**) as substrates, 365 mg (44%) of **4ad** was isolated as white crystals (m.p.: 127 °C, decomposed). Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{18}H_{17}NO_2H$ [M+H$^+$]: 280.1332, found: 280.1336.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.93/8.86 (d, *J* = 8.4 Hz, 1H); 7.85-7.82 (m, 2H) 7.55-7.24 (m, 8H) 5.37 (t, *J* = 9.0 Hz) 5.30/5.28 (dd, *J* = 8.3, 10.7 Hz, 1H); 4.00-3.94/3.92-3.85 (m, 1H); 3.06-2.90 (m, 2H); 2.16-2.08/2.01-1.88 (m, 1H); 2.01-1.88/1.73-1.66 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.4/207.8; 166.1/165.6; 141.6/141.4; 134.7/134.4; 128.3/128.3; 128.2/128.1 and 127.4/127.4; 127.2/127.1; 131.3/131.2 and 127.2/127.0; 64.0/63.0; 53.9/52.8; 44.0/44.0; 14.8/14.4.

N-[(2-oxocyclobutyl)-phenyl-methyl]propanamide (4ae)



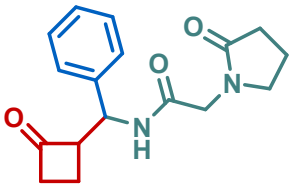
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and propanamide (**3e**) as substrates, 437 mg (63%) of **4ae** was isolated as light brown crystals (m.p.: 90-92 °C). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{17}NO_2H$ [M+H$^+$]: 232.1332, found: 232.1333.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.32/8.27 (d, *J* = 9.3 Hz, 1H); 7.32-7.21 (m, 5H) 5.17/5.09 (t, *J* = 9.0 Hz, 1H); 3.82-3.75/3.71-3.64 (m, 1H); 3.00-2.80 (m, 2H); 2.17-2.05 (m, 2H) 2.17-2.05/1.95-1.85 (m, 1H); 1.95-1.85/1.68-1.61 (m, 1H); 0.98/0.98 (t, *J* = 7.8 Hz, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/208.0; 172.4/172.0; 141.6/141.3; 128.3/128.2 and 127.0/126.8; 127.0/126.8; 64.2/63.5; 51.6/50.6; 44.1/44.0; 28.5/28.4; 14.3/13.6; 10.0/9.9.

N-[(2-oxocyclobutyl)-phenyl-methyl]-2-(2-oxopyrrolidin-1-yl)acetamide (4af)



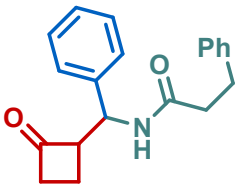
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and (2-oxopyrrolidin-1-yl)acetamide (**3f**) as substrates, 432 mg (48%) of **4af** was isolated as a yellow oil. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{17}H_{20}N_2O_3H$ [M+H$^+$]: 301.1547, found: 301.1549.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.54/8.51 (d, *J* = 8.7 Hz, 1H); 7.33-7.22 (m, 5H) 5.09/5.16 (t, *J* = 8.4 Hz, 1H); 3.86/3.83 (s/d, *J* = 1.7 Hz, 2H); 3.86-3.79/3.77-3.71 (m, 1H); 3.36-3.29 (m, 2H); 3.02-2.81 (m, 2H); 2.22 (t, *J* = 8 Hz, 2H); 2.07-2.00/1.95-1.88 (m, 1H); 1.95-1.88/1.69-1.62 (m, 1H); 1.95-1.88 (m, 2H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/207.9; 174.3/174.3; 167.2/166.8; 141.2/140.8; 128.3/128.2 and 127.1/126.8; 127.2/127.0; 64.0/63.2; 51.9/50.9; 47.1/47.0; 44.8/44.9; 44.2/44.0; 30.0/30.0; 17.4/17.4; 14.4/13.7.

N-[(2-oxocyclobutyl)-phenyl-methyl]-3-phenyl-propanamide (4ag)



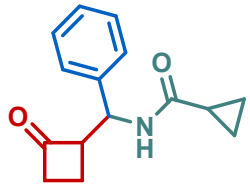
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and 3-phenyl-propanamide (**3g**) as substrates, 406 mg (44%) of **4ag** was isolated as brown crystals (m.p.: 96-98 °C). Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{20}H_{21}NO_2H$ [M+H$^+$]: 308.1645, found: 308.1644.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.41/8.33 (d, *J* = 8.8 Hz, 1H); 7.35-7.13 (m, 10H) 5.18/5.12 (t, *J* = 8.5 Hz, 1H); 3.80-3.74/3.72-3.66 (m, 1H); 2.99-2.74 (m, 2H); 2.81 (t, *J* = 7.0 Hz, 2H); 2.48-2.37 (m, 2H); 1.99-1.92/1.92-1.79 (m, 1H); 1.92-1.79/1.66-1.59 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/207.9; 170.8/170.7; 141.4/141.2 and 141.2/141.0; 128.2 (2C) / 128.2 (2C), 128.2/128.1 and 127.1/126.8; 127.0/126.8 and 125.8/125.9; 64.1/63.5; 51.6/50.7; 44.2/44.0; 36.9/36.8; 31.1/31.1; 14.3/13.7.

N-[(2-oxocyclobutyl)-phenyl-methyl]cyclopropanecarboxamide (4ah)



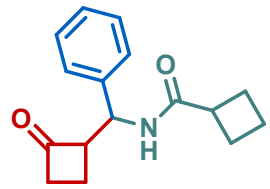
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and cyclopropanecarboxamide (**3h**) as substrates, 270 mg (37%) of **4ah** was isolated as white amorphous solid (m.p.: 107-109 °C). Reaction time: 2 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{17}NO_2H$ [M+H$^+$]: 244.1332, found: 244.1340.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.62/8.56 (d, *J* = 8.7 Hz, 1H); 7.36-7.18 (m, 10H) 5.18/5.10 (t, *J* = 8.4 Hz, 1H); 3.84-3.76/3.76-3.66 (m, 1H); 3.04-2.76 (m, 2H); 2.10-1.97/1.97-1.84 (m, 1H); 1.97-1.84/1.70-1.57 (m, 1H); 1.97-1.84/1.70-1.57 (m, 1H); 0.73-0.53 (m, 4H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/208.0; 172.1/171.8; 141.6/141.3; 128.3/128.2 and 127.1/126.8; 127.0/126.9; 64.3/63.6; 51.8/50.9; 44.1/44.0; 14.3/13.7; 13.5/13.4; 6.5/6.4 and 6.3/6.3.

N-[(2-oxocyclobutyl)-phenyl-methyl]cyclobutanecarboxamide (4ai)



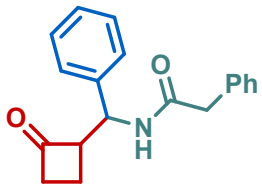
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and cyclobutanecarboxamide (**3i**) as substrates, 363 mg (47%) of **4ai** was isolated as white crystals (m.p.: 82-84 °C). Reaction time: 2 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{19}NO_2H$ [M+H$^+$]: 258.1488, found: 258.1488.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.18/8.12 (d, *J* = 8.7 Hz, 1H); 7.34-7.19 (m, 5H) 5.16/5.08 (t, *J* = 8.5 Hz, 1H); 3.82-3.75/3.71-3.65 (m, 1H); 3.11-2.99 (m, 1H); 2.99-2.78 (m, 2H); 2.20-1.58 (m, 8H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/208.0; 173.4/173.0; 141.6/141.3; 128.2/128.1 and 127.0/126.8; 127.0/126.8; 64.2/63.5; 51.7/50.6; 44.1/44.0; 38.5/38.5; 24.8/24.6; 24.4/24.3; 17.8/17.8 and 14.4/13.7.

N-[(2-oxocyclobutyl)-phenyl-methyl]-2-phenyl-acetamide (4aj)



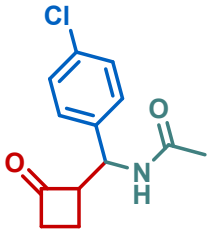
Prepared according to the general procedure described in **S2.1** using benzaldehyde (**2a**) and 2-phenylacetamide (**3j**) as substrates, 466 mg (53%) of **4aj** was isolated as a yellow oil. Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{19}H_{19}NO_2H$ [M+H$^+$]: 294.1488, found: 258.1496.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.67/8.59 (d, *J* = 8.7 Hz, 1H); 7.40-7.15 (m, 10H) 5.15/5.09 (t, *J* = 8.8 Hz, 1H); 3.85-3.77/3.77-3.69 (m, 1H); 3.51-3.41 (m, 2H); 3.00-2.90 (m, 1H); 2.86-2.76 (m, 2H); 2.06-1.96/1.94-1.82 (m, 1H); 1.94-1.82/1.66-1.59 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/207.8; 169.5/169.3; 141.3/141.1 and 136.4/136.4; 129.0/128.9, 128.2/128.1, 128.2/128.1 and 127.0/126.8; 127.0/126.9 and 126.3/126.2; 64.2/63.5; 51.8/50.9; 44.1/44.0; 42.2/42.2; 14.3/13.7.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]acetamide (4ba)



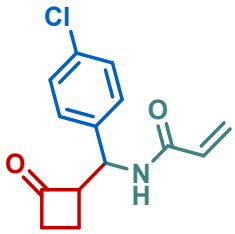
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and acetamide (**3a**) as substrates, 399 mg (53%) of **4ba** was isolated as a colorless oil. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{13}H_{14}ClNO_2H$ [M+H$^+$]: 252.0786, found: 252.0782.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.44/8.38 (d, *J* = 8.8 Hz, 1H); 7.41-7.28 (m, 4H); 5.13/5.07 (t, *J* = 9.0 Hz, 1H); 3.80-3.71/3.71-3.63 (m, 1H); 3.02-2.91 (m, 1H); 2.91-2.79 (m, 1H); 2.09-1.95/1.93-1.85 (m, 1H); 1.93-1.85/1.69-1.59 (m, 1H) 1.85/1.83 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/207.7; 168.7/168.4; 140.7/140.3; 131.6/131.5; 128.9/128.7 and 128.2/128.1; 63.9/63.2; 51.1/50.5; 44.1/44.0; 22.6/22.6; 14.2/13.8.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]prop-2-enamide (4bb)



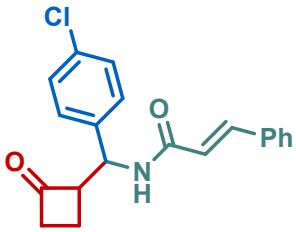
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and acrylamide (**3b**) as substrates, 410 mg (52%) of **4bb** was isolated as white crystals (m.p.: 110 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{14}ClNO_2H$ [M+H$^+$]: 264.0786, found: 264.0782.

^{1}H-NMR (500 MHz, DMSO), (both diastereomers): δ 8.69/8.60 (d, *J* = 8.5 Hz, 1H); 7.42-7.29 (m, 4H); 6.30/6.28 (dd, *J* = 10.2, 17.0 Hz, 1H); 6.09/6.06 (dd, *J* = 2.1, 17.1 Hz, 1H); 5.62/5.60 (dd, *J* = 2.1, 8.7 Hz, 1H); 5.23/5.17 (t, *J* = 8.9 Hz, 1H); 3.87-3.78/3.78-3.69 (m, 1H); 3.06-2.94/3.06-2.92 (m, 1H); 2.93-2.83/2.92-2.80 (m, 1H); 2.10-2.00/1.96-1.86 (m, 1H); 1.96-1.84/1.71-1.61 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 207.9/207.6; 164.0/163.8; 140.3/140.1; 131.7/131.6; 131.5/131.3; 129.0/128.9 and 128.3/128.2; 126.0/125.7; 63.7/63.0; 51.2/50.6; 44.1/44.1; 14.2/14.0.

(*E*)-*N*-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]-3-phenyl-prop-2-enamide (4bc)



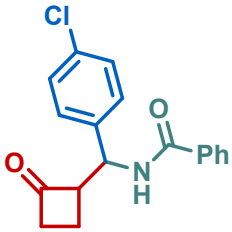
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and cynnamamide (**3c**) as substrates, 661 mg (65%) of **4bc** was isolated as white crystals (m.p.: 135-137 °C). Reaction time: 6 h.

HRMS(TOF+, m/Z): calcd. for $C_{20}H_{18}ClNO_2H$ [M+H$^+$]: 340.1099, found: 340.1114.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.72/8.65 (d, *J* = 8.9 Hz, 1H); 7.57 (d, *J* = 7.1 Hz, 1H) 7.45-7.33 (m, 8H) 7.42 (d, *J* = 13.2 Hz, 1H); 6.71/6.70 (d, *J* = 15.8 Hz, 1H); 5.29/5.23 (t, *J* = 8.8 Hz, 1H); 3.90-3.82/3.81-3.73 (m, 1H); 3.06-2.95 (m, 1H); 2.94-2.82 (m, 1H); 2.12-2.02/1.99-1.89 (m, 1H); 1.99-1.89/1.72-1.65 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 207.7/207.7; 164.4/164.2; 140.4/140.2; 139.4/139.2; 134.8/134.8; 131.7/131.6; 129.6/129.5; 129.0/129.0; 129.0/128.8; 128.3/128.2; 127.6/127.5; 121.9/121.7; 63.9/63.1; 51.3/51.7; 44.2/44.1; 14.2/13.9.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]benzamide (4bd)



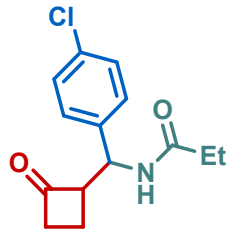
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and benzamide (**3d**) as substrates, 310 mg (33%) of **4bd** was isolated as white crystals (m.p.: 140 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{18}H_{16}ClNO_2H$ [M+H$^+$]: 314.0950, found: 314.0950.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.95/8.88 (d, *J* = 8.6 Hz, 1H); 7.85-7.80 (m, 2H); 7.57-7.51 (m, 1H)*;* 7.50-7.36 (m, 6H) 5.34/5.29 (t/dd, *J* = 9.2 Hz / 8.3, 10.6 Hz, 1H); 3.98-3.91/3.91-3.83 (m, 1H); 3.08-2.89 (m, 2H); 2.17-2.08/1.99-1.86 (m, 1H); 1.99-1.86/1.74-1.64 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/207.6; 166.1/165.7; 140.7/140.5; 134.5/134.2; 131.7/131.6; 131.3/131.2; 129.1/129.0; 128.3/128.3 and 128.2/128.1; 127.4/127.4; 63.7/62.7; 52.1/51.6; 44.1/44.0; 14.6/14.6.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]propanamide (4be)



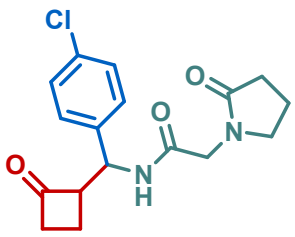
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and propanamide (**3e**) as substrates, 374 mg (47%) of **4be** was isolated as yellow crystals (m.p.: 103-105 °C). Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{16}ClNO_2H$ [M+H$^+$]: 266.0942, found: 266.0939.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.36/8.30 (d, *J* = 8.8 Hz, 1H); 7.40-7.28 (m, 4H) 5.14/5.08 (t, *J* = 9.0 Hz, 1H); 3.82-3.72/3.71-3.63 (m, 1H); 3.02-2.79 (m, 2H); 2.19-2.05 (m, 2H) 2.05-1.98/1.94-1.83 (m, 1H); 1.94-1.83/1.69-1.60 (m, 1H); 0.97 (t, *J* = 7.6 Hz, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.0/207.7; 172.5/172.2; 140.7/140.4; 131.6/131.4; 128.9/128.7 and 128.2/128.1; 64.0/63.2; 51.1/50.3; 44.1/44.0; 28.4/28.4; 14.2/13.8; 10.0/9.9.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]-2-(2-oxopyrrolidin-1-yl)acetamide (4bf)



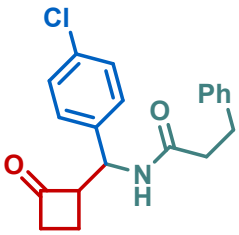
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and (2-oxopyrrolidin-1-yl)acetamide (**3f**) as substrates, 481 mg (48%) of **4bf** was isolated as brown crystals (m.p.: 115 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{17}H_{19}ClN_2O_3H$ [M+H$^+$]: 335.1157, found: 335.1155.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.56/8.52 (d, *J* = 8.7 Hz, 1H); 7.42-7.29 (m, 4H); 5.13/5.08 (t, *J* = 8.9 Hz, 1H); 3.85/3.83 (d, *J* = 4.9 Hz, 2H); 3.90-3.79/3.77-3.69 (m, 1H); 3.36-3.28 (m, 2H); 3.04-2.81 (m, 2H); 2.21 (t, *J* = 8.2 Hz, 2H); 2.07-2.00/1.96-1.82 (m, 1H); 1.96-1.82/1.70-1.60 (m, 1H); 1.96-1.82 (m, 2H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.0/207.6; 174.4/174.3; 167.2/166.8; 140.3/140.0; 131.8/131.6; 128.9/128.8 and 128.3/128.2; 63.7/62.9; 51.3/50.6; 47.1/47.0; 44.9/44.8; 44.2/44.0; 30.0/29.9; 17.4/17.4; 14.3/13.9.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]-3-phenyl-propanamide (4bg)



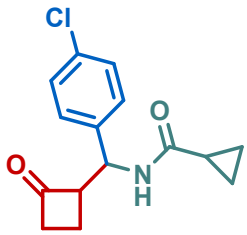
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and 3-phenyl-propanamide (**3g**) as substrates, 358 mg (35%) of **4bg** was isolated as brown crystals (m.p.: 96 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{20}H_{20}ClNO_2H$ [M+H$^+$]: 342.1255, found: 342.1248.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.43/8.35 (d, *J* = 8.8 Hz, 1H); 7.39-7.13 (m, 9H) 5.13/5.10 (t, *J* = 8.6 Hz, 1H); 3.78-3.64 (m, 1H); 3.00-2.73 (m, 2H); 2.80 (t, *J* = 7.5 Hz, 2H); 2.48-2.36 (m, 2H); 2.01-1.92/1.92-1.84 (m, 1H); 1.84-1.73/1.67-1.55 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/207.7; 170.9/170.8; 141.2/141.1 and 140.6/140.2; 131.5/131.4; 128.9/128.7, 128.2 (3C) / 128.2, 128.2/128.0; 125.9/125.8; 63.8/63.1; 51.0/50.4; 44.2/44.0; 36.8/36.8; 31.0/31.0; 14.1/13.9.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]cyclopropanecarboxamide (4bh)



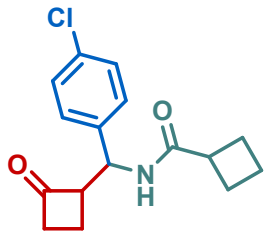
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and cyclopropanecarboxamide (**3h**) as substrates, 457 mg (55%) of **4bh** was isolated as brown crystals (m.p.: 128-130 °C). Reaction time: 2 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{16}ClNO_2H$ [M+H$^+$]: 278.0942, found: 278.0939.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.65/8.58 (d, *J* = 8.8 Hz, 1H); 7.42-7.28 (m, 4H) 5.15/5.09 (t, *J* = 8.9 Hz, 1H); 3.81-3.74/3.74-3.67 (m, 1H); 3.04-2.92/2.92-2.78 (m, 2H); 2.10-2.00/1.96-1.84 (m, 1H); 1.96-1.84/1.68-1.56 (m, 1H); 1.96-1.84/1.68-1.56 (m, 1H); 0.73-0.54 (m, 4H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.0/207.7; 172.2/171.9; 140.7/140.4; 131.6/131.5; 128.9/128.7 and 128.2/128.1; 63.9/63.2; 51.2/50.6; 44.1/44.1; 14.2/13.9; 13.5/13.5; 6.5/6.5 and 6.4/6.4.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]cyclobutanecarboxamide (4bi)



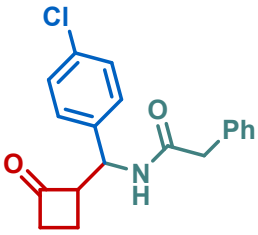
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and cyclobutanecarboxamide (**3i**) as substrates, 332 mg (38%) of **4bi** was isolated as yellow crystals (m.p.: 118 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{18}ClNO_2H$ [M+H$^+$]: 292.1099, found: 292.1103.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.20/8.15 (d, *J* = 8.8 Hz, 1H); 7.41-7.27 (m, 4H) 5.13/5.07 (t, *J* = 9.0 Hz, 1H); 3.80-3.72/3.71-3.63 (m, 1H); 3.09-3.00 (m, 1H); 3.00-2.91/2.90-2.80 (m, 2H); 2.18-1.58 (m, 8H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.0/207.7; 173.4/173.1; 140.7/140.5; 131.6/131.4; 128.9/128.7 and 128.2/128.1; 63.9/63.1; 51.1/50.3; 44.1/44.0; 38.5/38.5; 24.7/24.6; 24.4/24.3; 17.8/17.8 and 14.3/13.9.

N-[(4-chlorophenyl)-(2-oxocyclobutyl)methyl]-2-phenyl-acetamide (4bj)



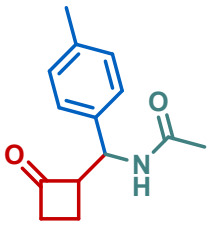
Prepared according to the general procedure described in **S2.1** using 4-Chlorobenzaldehyde (**2b**) and 2-phenyl-acetamide (**3j**) as substrates, 491 mg (50%) of **4bj** was isolated as yellow crystals (m.p.: 144 °C, decomposed). Reaction time: 4 h.

HRMS(TOF+, m/Z): calcd. for $C_{19}H_{18}ClNO_2H$ [M+H$^+$]: 328.1098, found: 328.1103.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.71/8.62 (d, *J* = 8.8 Hz, 1H); 7.43-7.16 (m, 9H); 5.13/5.08 (t, *J* = 8.7 Hz, 1H); 3.83-3.68 (m, 1H); 3.52-3.40 (m, 2H); 3.02-2.91/2.89-2.75 (m, 2H); 2.09-1.97/1.95-1.82 (m, 1H); 1.95-1.82/1.69-1.59 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.1/207.6; 169.6/169.5; 140.5/140.2 and 136.3/136.3; 131.6/131.5; 129.0/128.9, 128.9/128.8, 128.2/128.2 and 128.1 (2C); 126.3/126.3; 63.9/63.2; 51.2/50.6; 44.2/44.1; 42.2/42.2; 14.1/13.9.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]acetamide (4ca)



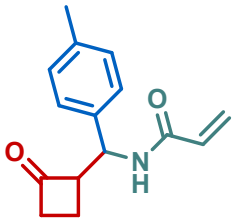
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and acetamide (**3a**) as substrates, 208 mg (30%) of **4ca** was isolated as yellow oil. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{17}NO_2H$ [M+H$^+$]: 232.1332, found: 232.1330.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.36/8.30 (d, *J* = 9.1 Hz, 1H); 7.25-7.08 (m, 4H); 5.11/5.03 (t, *J* = 9.0 Hz, 1H); 3.79-3.70/3.68-3.60 (m, 1H); 3.00-2.89/2.87-2.79 (m, 2H); 2.26 (s, 3H); 2.05-1.96/1.95-1.87 (m, 1H); 1.95-1.87/1.67-1.57 (m, 1H); 1.84/1.81 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/208.1; 168.5/168.2; 138.5/138.2; 136.1/135.9; 128.8/128.7 and 127.0/126.7; 64.3/63.6; 51.4/50.5; 44.1/44.0; 22.6/22.6; 20.6/20.6; 14.3/13.6.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]prop-2-enamide (4cb)



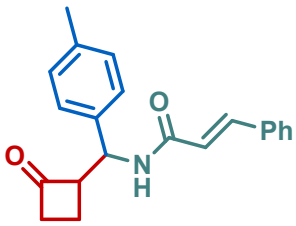
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and acrylamide (**3b**) as substrates, 328 mg (45%) of **4cb** was isolated as yellow oil. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{17}NO_2H$ [M+H$^+$]: 244.1332, found: 244.1332.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.60/8.52 (d, *J* = 9.0 Hz, 1H); 7.25-7.08 (m, 5H) 6.30/6.28 (t, *J* = 17.0 Hz, 1H); 6.09/6.06 (dd, *J* = 2.2, 13.5 Hz, 1H); 5.60/5.59 (t, *J* = 10.1 Hz, 1H); 5.21/5.12 (t, *J* = 9.1 Hz, 1H); 3.86-3.76/3.76-3.66 (m, 1H); 3.03-2.91/2.88-2.78 (m, 2H); 2.27 (s, 3H); 2.08-1.98/1.95-1.84 (m, 1H); 1.95-1.84/1.69-1.59 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/207.9; 163.9/163.6; 138.2/138.0; 136.3/136.1; 131.7/131.5; 128.9/128.8 and 127.0/126.8; 125.8/125.5; 64.1/63.4; 51.6/50.7; 44.1/44.1; 20.6/20.6; 14.4/13.8.

(*E*)-*N*-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]-3-phenyl-prop-2-enamide (4cc)



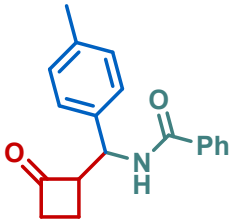
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and cynnamamide (**3c**) as substrates, 565 mg (59%) of **4cc** was isolated as white crystals (m.p.: 51 °C, decomposed). Reaction time: 1 h.

HRMS(TOF+, m/Z): calcd. for $C_{21}H_{21}NO_2H$ [M+H$^+$]: 320.1645, found: 320.1647.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.64/8.57 (d, *J* = 9.0 Hz, 1H); 7.57-7.55 (m, 2H) 7.45-7.34 (m, 4H); 7.24/7.23 (d, *J* = 18.9 Hz, 2H); 7.14/7.13 (d, *J* = 7.8 Hz, 2H); 6.74/6.70 (d, *J* = 16.0 Hz, 1H); 5.28/5.20 (t, *J* = 9.0 Hz, 1H); 3.90-3.81/3.80-3.71 (m, 1H); 3.04-2.92 (m, 1H); 2.90-2.81 (m, 1H); 2.27 (s, 3H); 2.10-2.01/1.99-1.88 (m, 1H); 1.99-1.88/1.73-1.62 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/208.0; 164.3/164.0; 141.3/141.1; 139.2/138.9; 138.3/138.1 and 134.9/134.8; 136.2/136.1; 129.5/129.4; 128.9 (2C); 128.9/128.8; 127.5/127.5; 127.0/126.8; 122.1/122.0; 64.3/63.5; 51.6/50.8; 44.1/44.1; 20.7/20.6; 14.3/13.7.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]benzamide (4cd)



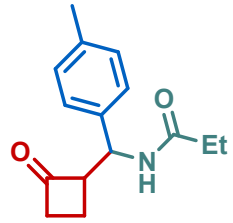
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and benzamide (**3d**) as substrates, 326 mg (37%) of **4cd** was isolated as white crystals (m.p.: 42 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{19}H_{19}NO_2H$ [M+H$^+$]: 294.1488, found: 294.1482.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.88/8.80 (d, *J* = 8.8 Hz, 1H); 7.85-7.79 (m, 2H) 7.56-7.50 (m, 1H); 7.49-7.43 (m, 2H); 7.30/7.29 (d, *J* = 19.1 Hz, 1H); 7.13 (t, *J* = 8.1 Hz, 2H); 5.33 (t, *J* = 8.6 Hz, 1H); 5.24 (dd, *J* = 8.4 Hz, 10.6 Hz, 1H); 3.98-3.91/3.90-3.83 (m, 1H); 3.07-2.87 (m, 2H); 2.27 (s, 3H); 2.16-2.05/2.00-1.86 (m, 1H); 2.00-1.86/1.72-1.62 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.5/207.9; 166.0/165.5; 138.7/138.4; 136.2/136.0; 134.7/134.5; 131.3/131.1; 128.9/128.7; 128.2/128.2 and 127.4/127.4; 127.2/127.0; 64.1/63.1; 52.5/51.7; 44.0/44.0; 20.7/20.7; 14.8/14.4.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]propanamide (4ce)



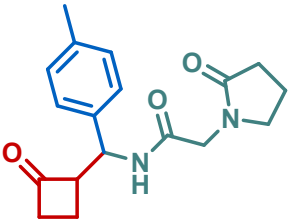
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and propanamide (**3e**) as substrates, 272 mg (37%) of **4ce** was isolated as white crystals (m.p.: 117-119 °C). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{19}NO_2H$ [M+H$^+$]: 246.1488, found: 246.1495.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.27/8.22 (d, *J* = 9.1 Hz, 1H); 7.22-7.08 (m, 4H) 5.12/5.04 (t, *J* = 9.0 Hz, 1H); 3.80-3.71/3.70-3.61 (m, 1H); 3.00-2.89/2.88-2.78 (m, 2H); 2.26 (s, 3H); 2.17-1.95 (m, 2H); 2.17-1.95/1.95-1.84 (m, 1H); 1.95-1.84/1.67-1.57 (m, 1H); 0.97 (t, *J* = 7.6 Hz, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/208.1; 172.3/172.0; 138.6/138.3; 136.1/135.9; 128.8/128.7 and 127.0/126.7; 64.3/63.7; 51.4/50.4; 44.1/44.0; 28.5/28.4; 20.6/20.6; 14.3/13.6; 10.1/9.9.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]-2-(2-oxopyrrolidin-1-yl)acetamide (4cf)



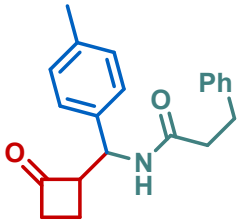
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and (2-oxopyrrolidin-1-yl)acetamide (**3f**) as substrates, 415 mg (44%) of **4cf** was isolated as colorless oil. Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{18}H_{22}N_2O_3H$ [M+H$^+$]: 315.1703, found: 315.1698.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.48/8.43 (d, *J* = 8.8 Hz, 1H); 7.23-7.08 (m, 4H); 5.11/5.04 (t, *J* = 9.0 Hz, 1H); 3.86/3.83 (s/d, *J* = 1.7 Hz, 2H); 3.87-3.76/3.76-3.66 (m, 1H); 3.36-3.29 (m, 2H); 3.04-2.78 (m, 2H); 2.27 (s, 3H); 2.21 (t, *J* = 8.3 Hz, 2H); 2.09-1.97/1.97-1.84 (m, 1H); 1.97-1.84/1.69-1.57 (m, 1H); 1.97-1.84 (m, 2H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/208.0; 174.3/174.3; 167.0/166.7; 138.1/137.8; 136.3/136.1; 128.9/128.8 and 127.0/126.8; 64.1/63.3; 51.6/50.7; 47.1/47.0; 44.9/44.8; 44.1/44.0; 30.0/30.0; 20.7/20.6; 17.4/17.3; 14.4/13.7.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]-3-phenyl-propanamide (4cg)



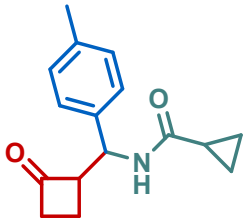
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and 3-phenyl-propanamide (**3g**) as substrates, 578 mg (60%) of **4cg** was isolated as yellow crystals (m.p.: 90 °C, decomposed). Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{21}H_{23}NO_2H$ [M+H$^+$]: 322.1801, found: 322.1789.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.35/8.28 (d, *J* = 9.0 Hz, 1H); 7.28-7.05 (m, 9H) 5.12/5.07 (t, *J* = 8.7 Hz, 1H); 3.77-3.70/3.70-3.62 (m, 1H); 2.98-2.72 (m, 2H); 2.80 (t, *J* = 7.8 Hz, 2H); 2.48-2.33 (m, 2H); 2.27 (s, 3H); 1.99-1.76 (m, 1H); 1.99-1.76/1.65-1.57 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/208.0; 170.7/170.6; 141.3/141.2 and 138.4/138.0; 136.0/135.9; 128.7/128.7, 128.2 (3C) / 128.2 and 127.0/126.7; 125.8/125.8; 64.2/63.6; 51.3/50.4; 44.1/44.0; 36.9/36.8; 31.1/31.1; 20.6/20.6; 14.2/13.7.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]cyclopropanecarboxamide (4ch)



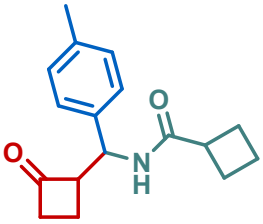
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and cyclopropanecarboxamide (**3h**) as substrates, 486 mg (63%) of **4ch** was isolated as white crystals (m.p.: 133-135 °C). Reaction time: 2 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{19}NO_2H$ [M+H$^+$]: 258.1488, found: 258.1479.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.57/8.50 (d, *J* = 9.0 Hz, 1H); 7.19/7.18 (d, *J* = 16.5 Hz, 2H); 7.12/7.11 (d, *J* = 8.0 Hz, 2H) 5.13/5.05 (t, *J* = 9.0 Hz, 1H); 3.81-3.73/3.72-3.63 (m, 1H); 3.01-2.76 (m, 2H); 2.27 (s, 3H); 2.08-1.99/1.96-1.83 (m, 1H); 1.96-1.83/1.67-1.57 (m, 1H); 1.96-1.83/1.67-1.57 (m, 1H); 0.70-0.54 (m, 4H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/208.0; 172.0/171.7; 138.6/138.3; 136.1/135.9; 128.8/128.7 and 127.0/126.7; 64.4/63.7; 51.6/50.7; 44.1/44.0; 20.6/20.6; 14.3/13.7; 13.6/13.4; 6.4/6.4 and 6.3/6.3.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]cyclobutanecarboxamide (4ci)



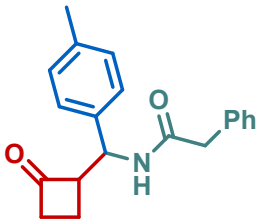
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and cyclobutanecarboxamide (**3i**) as substrates, 407 mg (50%) of **4ci** was isolated as a yellow oil. Reaction time: 4 h.

HRMS(TOF+, m/Z): calcd. for $C_{17}H_{21}NO_2H$ [M+H$^+$]: 272.1645, found 272.1636.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.11/8.07 (d, *J* = 9.1 Hz, 1H); 7.20-7.08 (m, 5H) 5.11/5.03 (t, *J* = 9.1 Hz, 1H); 3.79-3.71/3.68-3.60 (m, 1H); 3.11-2.98 (m, 1H); 2.99-2.78 (m, 2H); 2.26 (s, 3H); 2.18-1.54 (m, 8H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/208.0; 173.3/172.9; 138.6/138.3; 136.1/135.9; 128.8/128.7 and 126.9/126.7; 64.3/63.6; 51.4/50.4; 44.0/44.0; 38.5/38.5; 24.7/24.6; 24.4/24.3; 17.8/17.6 and 14.4/13.7; 20.6/20.6.

N-[(2-oxocyclobutyl)-(*p*-tolyl)methyl]-2-phenyl-acetamide (4cj)



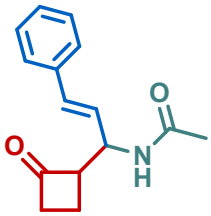
Prepared according to the general procedure described in **S2.1** using 4-Methylbenzaldehyde (**2c**) and 2-phenyl-acetamide (**3j**) as substrates, 516 mg (56%) of **4cj** was isolated as white crystals (m.p.: 132 °C, decomposed). Reaction time: 4 h.

HRMS(TOF+, m/Z): calcd. for $C_{20}H_{21}NO_2H$ [M+H$^+$]: 308.1645, found 308.1638.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.62/8.54 (d, *J* = 9.0 Hz, 1H); 7.32-7.06 (m, 9H); 5.11/5.04 (t, *J* = 8.8 Hz, 1H); 3.81-3.74/3.74-3.66 (m, 1H); 3.51-3.39 (m, 2H); 3.02-2.90/2.85-2.73 (m, 2H); 2.26 (s, 3H); 2.05-1.95/1.94-1.82 (m, 1H); 1.94-1.82/1.65-1.57 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.3/207.9; 169.5/169.2; 138.3/138.1 and 136.4/136.4; 136.1/136.0; 129.0/128.9, 128.8/128.7, 128.1/128.1 and 126.9/126.8; 126.3/126.2; 64.3/63.6; 51.5/50.7; 44.1/44.0; 42.2/42.2; 20.6/20.6; 14.2/13.7.

(*E*)-*N*-(1-(2-oxocyclobutyl)-3-phenylallyl)acetamide (4da)



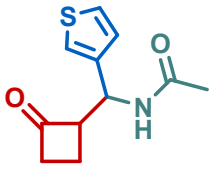
Prepared according to the general procedure described in **S2.1**, 168 mg (23%) of **4da** was isolated as brown crystals. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{17}NO_2H$ [M+H$^+$]: 244.1332, found: 244.1334.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.11/8.09 (d, *J* = 9.2 Hz, 1H); 7.44-7.20 (m, 5H); 6.50/6.46 (d, *J* = 16.7 Hz, 1H); 6.22/6.19 (dd, *J* = 5.6, 16.0 Hz, 1H); 4.69/4.75 (dd, *J* = 7.5, 14.0 Hz, 1H); 3.65-3.46 (m, 1H); 3.09-2.78 (m, 2H); 2.11-1.72 (m, 2H); 1.88/1.86 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 209.2/209.1; 169.2/169.1; 136.9/136.8; 130.6/129.7; 129.1/128.2; 128.1/128.0; 129.1 (2C) and 126.7 (2C); 63.8/63.5; 50.4/49.8; 45.1/44.7; 23.2/23.1, 14.1/14.1.

N-((2-oxocyclobutyl)(thiophen-3-yl)methyl)acetamide (4ea)



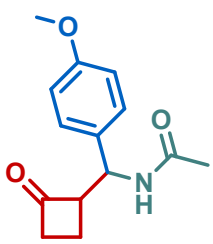
Prepared according to the general procedure described in **S2.1**, 298 mg (44%) of **4ea** was isolated as colorless crystals. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{11}H_{13}NO_2SNa$ [M+Na$^+$]: 246.0559, found: 246.0553.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.31/8.29 (d, *J* = 9.2 Hz, 1H); 7.51-7.02 (m, 3H); 5.26/5.22 (dd, *J* = 7.8, 8.8 Hz, 1H); 3.85-3.58 (m, 1H); 3.07-2.76 (m, 2H); 2.08-1.64 (m, 2H); 1.85/1.83 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.7/208.6; 169.0/168.9; 142.8/142.3; 127.5/127.5, 126.7/126.6 and 122.2/121.9; 64.4/64.0; 48.1/47.1; 44.8/44.5; 23.1/23.0, 14.8/13.9.

N-((4-methoxyphenyl)(2-oxocyclobutyl)methyl)acetamide (4fa)



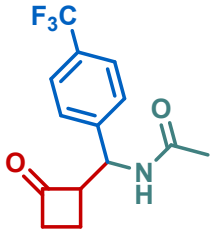
Prepared according to the general procedure described in **S2.1**, 274 mg (37%) of **4fa** was isolated as brown crystals. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{17}NO_3H$ [M+H$^+$]: 248.1281, found: 248.1283.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.34/8.29 (d, *J* = 8.8 Hz, 1H); 7.27-7.18 and 6.91-6.84 (m, 4H); 5.11/5.03 (t, *J* = 9.0 Hz, 1H); 3.73/3.73 (s, 3H), 3.70-3.60 (m, 1H); 3.04-2.78 (m, 2H); 2.11-1.56 (m, 2H); 1.82/1.84 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.9/208.9; 168.7/168.7; 158.7/158.7; 133.7/133.7; 128.7/128.4 and 114.1/114.0; 64.9/64.2; 55.5/55.5; 51.6/50.8; 44.5/44.5; 23.1/23.1; 14.8/14.2.

N-((2-oxocyclobutyl)(thiazol-5-yl)methyl)acetamide (4ga)



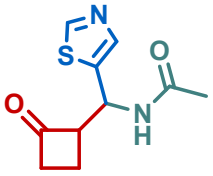
Prepared according to the general procedure described in **S2.1** under inert atmosphere, 522 mg (61%) of **4ga** was isolated as brown crystals. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{14}F_3NO_2H$ [M+H$^+$]: 286.0977, found: 286.0981.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.48/8.42 (d, *J* = 8.4 Hz, 1H); 7.69 (t, *J* = 7.4 Hz, 2H); 7.55/7.51 (d, *J* = 8.0 Hz, 2H); 5.21/5.16 (t, *J* = 8.5 Hz, 1H), 3.84-3.77/3.76-3.70 (m, 1H); 3.05-2.94 (m, 1H); 2.94-2.78 (m, 1H), 2.05 + 1.67 (qd, *J* = 10.4, 5.4 Hz + tt, *J* = 10.5, 7.3 Hz, 1H); 1.93 (td, *J* = 11.6, 10.5, 6.2 Hz, 1H); 1.86/1.85 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 207.7/207.4; 168.8/168.6; 146.4/146.0; 127.8/127.6; 125.1/125.1 and 125.0/125.0; 63.6/62.9; 51.4/50.9; 44.2/44.0; 22.5/22.5; 14.1/13.8.

N-((2-oxocyclobutyl)(thiazol-5-yl)methyl)acetamide (4ha)



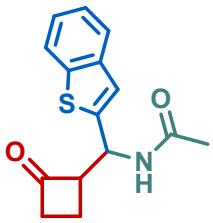
Prepared according to the general procedure described in **S2.1**, 229 mg (34%) of **4ha** was isolated as colorless solid. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{10}H_{12}N_2O_2SH$ [M+H$^+$]: 225.0692, found: 225.0694.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.99/8.98 (d, *J* = 4.0 Hz, 1H); 8.54/8.50 (d, *J* = 8.8 Hz, 1H); 7.78/7.76 (s, 1H); 5.47/5.44 (t, *J* = 7.4 Hz, 1H); 3.94-3.74 (m, 1H); 3.12-2.82 (m, 2H); 2.21-1.68 (m, 2H); 1.85/1.84 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 207.8/207.6; 169.2/169.1; 154.2/154.0; 141.1/140.9; 140.2/139.8; 64.0/63.4; 45.8/44.9; 44.9/44.6; 23.0/22.9; 15.1/14.3.

N-(benzo[b]thiophen-2-yl(2-oxocyclobutyl)methyl)acetamide (4ia)



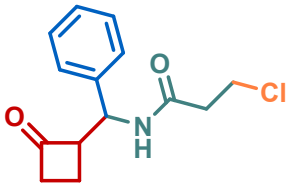
Prepared according to the general procedure described in **S2.1**, 475 mg (58%) of **4ia** was isolated as beige powder. Reaction time: 3 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{15}NO_2S$ H $[M+H^+]$: 274.0896, found: 274.0901.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.54/8.50 (d, *J* = 8.5 Hz, 1H); 7.89 (d, *J* = 7.8 Hz, 1H); 7.78 (dd, *J* = 7.9 Hz, 3.2 Hz, 1H); 7.41-7.26 (m, 3H); 5.50/5.43 (t, *J* = 8.2 Hz, 1H); 4.04-3.95/3.90-3.75 (m, 1H); 3.12-2.99/2.98-2.85 (m, 2H); 2.14 (dtd, *J* = 25.5, 10.5, 5.5 Hz, 1H); 2,01/1.82 (ddd, *J* = 18.0, 10.5, 7.6 Hz, 1H); 1.89/1.88 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) 207.3/207.1; 168.8/168.6; 146,1/145.7; 139.2/139.2; 138.5/138.5; 124.3/124.3, 124.1/124.1, 123.3/123.3 and 122.3/122.3; 121.0/120.9; 63.4/62.9; 48.1/46.9; 44.5/44.2; 22.4/22.4; 14.7/13.6.

3-chloro-*N*-[(2-oxocyclobutyl)-phenyl-methyl]propanamide (5)



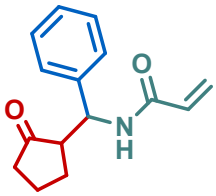
Prepared according to the general procedure described in **S2.2**, 588.5 mg (74%) of **5** was isolated as brown crystals. Reaction time: 16 h.

HRMS(TOF+, m/Z): calcd. for $C_{14}H_{16}ClNO_2H$ $[M+H^+]$: 266.0942, found: 266.0947.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.57/8.52 (d, *J* = 9.0 Hz, 1H); 7.37-7.21 (m, 5H); 5.21/5.14 (t, *J* = 8.7 Hz, 1H); 3.85-3.68 (m, 1H); 3.77 (m, 2H); 3.02-2.77 (m, 2H); 2.68-2.56 (m, 2H); 2.09-1.98/1.98-1.87 (m, 1H); 1.98-1.87/1.76-1.67 (m, 1H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.2/207.8; 168.4/168.2; 141.9/141.2; 131.6/131.4; 128.2/128.2 and 127.1/126.8; 127.1/126.9; 64.1/63.5; 51.7/50.9; 44.2/44.0; 41.1/41.0; 38.2/38.2; 14.2/13.7.

N-((2-oxocyclopentyl)(phenyl)methyl)acrylamide (6a)



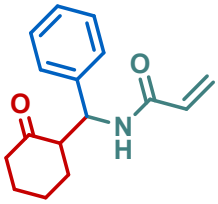
Prepared according to the general procedure described in **S2.1**, 168 mg (46%) of **6a** was isolated as white crystals. Reaction time: 4 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{17}NO_2H$ [M+H$^+$]: 244.1332, found: 244.1332.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.62/8.30 (d, *J* = 8.6 Hz, 1H); 7.36-7.18 (m, 5H); 6.37/6.34 (dd, *J* = 10.2, 17.1 Hz, 1H); 6.06/6.06 (dd, *J* = 2.1, 17.0 Hz, 1H); 5.59/5.59 (dd, *J* = 2.2, 10.2 Hz, 1H); 5.34/5.25 (dd, *J* = 5.0, 8.8 Hz, 1H); 2.74-2.57 (m, 1H); 2.28-1.34 (m, 6H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 217.5/217.2; 164.5/164.2; 142.5/141.3; 132.1/131.9; 127.4/127.2; 128.7/128.6 (2C) and 127.6/127.0 (2C); 126.1/126.0; 53.8/53.4; 52.2/51.5; 38.6/38.5; 26.3/25.0, 20.2/20.2.

N-((2-oxocyclohexyl)(phenyl)methyl)acrylamide (6b)



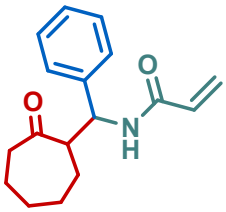
Prepared according to the general procedure described in **S2.1**, 378 mg (49%) of **6b** was isolated as white crystals. Reaction time: 4 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{19}NO_2$ H [M+H$^+$]: 258.1489, found: 258.1491.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.46/8.30 (d, *J* = 8.5 Hz, 1H); 7.34-7.20/7.32-7.16 (m, 5H); 6.24/6.28 (dd, *J* = 10.2, 17.0 Hz, 1H); 6.02/6.06 (dd, *J* = 2.1, 17.0 Hz, 1H); 5.56/5.58 (dd, *J* = 2.2, 10.2 Hz, 1H); 5.23/5.32 (t, *J* = 8.8 Hz, 1H); 2.87-2.80/2.97-2.90 (m, 1H); 2.39-2.27/2.37-2.23 (m, 2H); 1.90-1.17/2.01-1.48 (m, 6H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 211.0/210.6; 164.0/164.3; 141.7/142.8; 132.1/132.1; 127.4/127.1; 128.6/128.5 (2C) and 127.8/127.7 (2C); 125.8/126.0; 55.3/55.1; 52.4/51.4; 41.5/42.0; 31.0/30.0, 29.1/29.1, 23.4/24.0 (3C).

N-((2-oxocycloheptyl)(phenyl)methyl)acrylamide (6c)



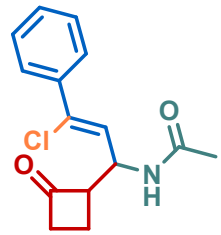
Prepared according to the general procedure described in **S2.1**, 431 mg (53%) of **6c** was isolated as white crystals. Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{17}H_{21}NO_2H$ [M+H$^+$]: 272.1645, found: 272.1647.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.46/8.44 (d, *J* = 8.7 Hz, 1H); 7.41-7.20/7.31-7.16 (m, 5H); 6.19/6.28 (dd, *J* = 10.2, 17.0 Hz, 1H); 6.00/6.07 (dd, *J* = 2.1, 17.0 Hz, 1H); 5.54/5.60 (dd, *J* = 2.1, 10.2 Hz, 1H); 5.09/5.22 (t, *J* = 9.2 Hz, 1H); 3.05-2.95/3.16-3.04 (m, 1H); 2.52-2.33/2.38-2.15 (m, 2H); 1.88-1.01/1.92-1.06 (m, 6H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 213.3/213.1; 163.9/164.4; 141.6/142.3; 132.1/132.0; 127.6/127.3; 128.7/128.7 (2C) and 128.0/127.5 (2C); 125.8/126.2; 56.7/56.4; 54.4/53.8; 42.6/43.6; 28.8/28.7, 28.5/28.6, 27.9/27.9, 24.3/23.9 (4C).

N-[(*Z*)-3-chloro-1-(2-oxocyclobutyl)-3-phenyl-allyl]acetamide (7)



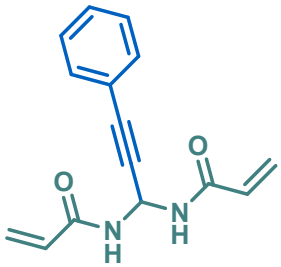
Prepared according to the general procedure described in **S2.1** using phenylpropargyl aldehyde (**4j**) and acetamide (**3a**) as substrates, 424 mg (51%) of **7** was isolated as brown crystals. Reaction time: 5 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{16}ClNO_2H$ [M+H$^+$]: 278.0942, found: 278.0943.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.18/8.17 (d, *J* = 8.0 Hz, 1H); 7.60-7.38 (m, 5H); 6.35/6.21 (d, *J* = 8.9 Hz, 1H); 5.07 (m, 1H); 3.69-3.59 (m, 1H); 3.06-2.95/2.95-2.83 (m, 1H); 2.12-1.76 (m, 1H); 1.84/1.83 (s, 3H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 208.6/208.0; 168.8/168.5; 136.6/136.6; 132.7/132.3; 129.3/129.2; 128.7/128.7 and 126.2/126.2; 126.0/126.0; 62.9/62.7; 47.7/47.7; 44.8/44.6; 22.6/22.6; 13.4/13.1.

N-[3-phenyl-1-(prop-2-enoylamino)prop-2-ynyl]prop-2-enamide (8)



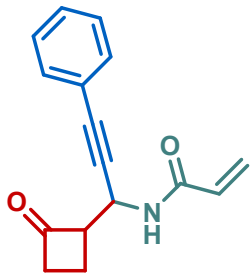
Prepared according to the general procedure described in **S2.3**, 1820 mg (93%) of **8** was isolated as a white solid (m.p.: 231-233 °C). Reaction time: 18 h.

HRMS(TOF+, m/Z): calcd. for $C_{15}H_{14}N_2O_2Na$ [M+Na$^+$]: 277.0947, found: 277.0948.

^{1}H-NMR (500 MHz, DMSO) δ 9.15 (d, *J* = 7.7 Hz, 2H); 7.48-7.37 (m, 5H); 6.55 (t, *J* = 7.6 Hz, 1H); 6.30 (dd, *J* = 10.1, 17.1 Hz, 2H); 6.18 (dd, *J* = 2.2, 17.1 Hz, 2H); 5.68 (dd, *J* = 2.2, 10.1 Hz, 2H).

^{13}C-NMR (126 MHz, DMSO) δ 163.4 (2C); 131.5 (2C); 130.8 (2C); 129.0; 128.8 (2C); 126.8 (2C); 121.4; 86.7; 81.7; 46.6.

N-[1-(2-oxocyclobutyl)-3-phenyl-prop-2-ynyl]prop-2-enamide (4jb)



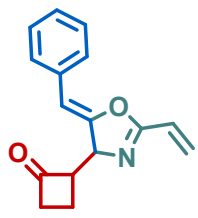
Prepared according to the general procedure described in **S2.1** using bisaminal (**8**) and cyclobutanone (**1a**) as substrates, 334.5 mg (44%) of **4jb** was isolated as a white solid (m.p.: 126-128 °C). Reaction time: 7 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{15}NO_2H$ [M+H$^+$]: 254.1178, found: 254.1166.

^{1}H-NMR (500 MHz, DMSO) (both diastereomers) δ 8.79 (d, *J* = 8.3 Hz, 1H); 7.47-7.35/7.46-7.35 (m, 5H); 6.32 (dd, *J* = 10.0, 17.1 Hz, 1H); 6.15 (dd, *J* = 3.2, 17.1 Hz, 1H); 5.66 (dd, *J* = 2.6, 10.2 Hz, 1H); 5.15/5.14 (dd, *J* = 6.9, 8.2 Hz, 1H); 3.81-3.70 (m, 1H); 3.17-2.88/3.14-2.85 (m, 2H); 2.22-1.98/2.22-1.89 (m, 2H).

^{13}C-NMR (126 MHz, DMSO) (both diastereomers) δ 207.8/207.6; 164.2/164.2; 131.4/131.4; 129.4/129.3; 132.0/131.9 (2C) and 129.2/129.2 (2C); 126.9/126.9; 122.3/122.1; 87.6/87.0; 83.5/83.0; 63.3/63.0; 45.5/45.1; 40.4/40.4; 14.3/14.0.

(*Z*)-2-(5-benzylidene-2-vinyl-4,5-dihydrooxazol-4-yl)cyclobutan-1-one (9)



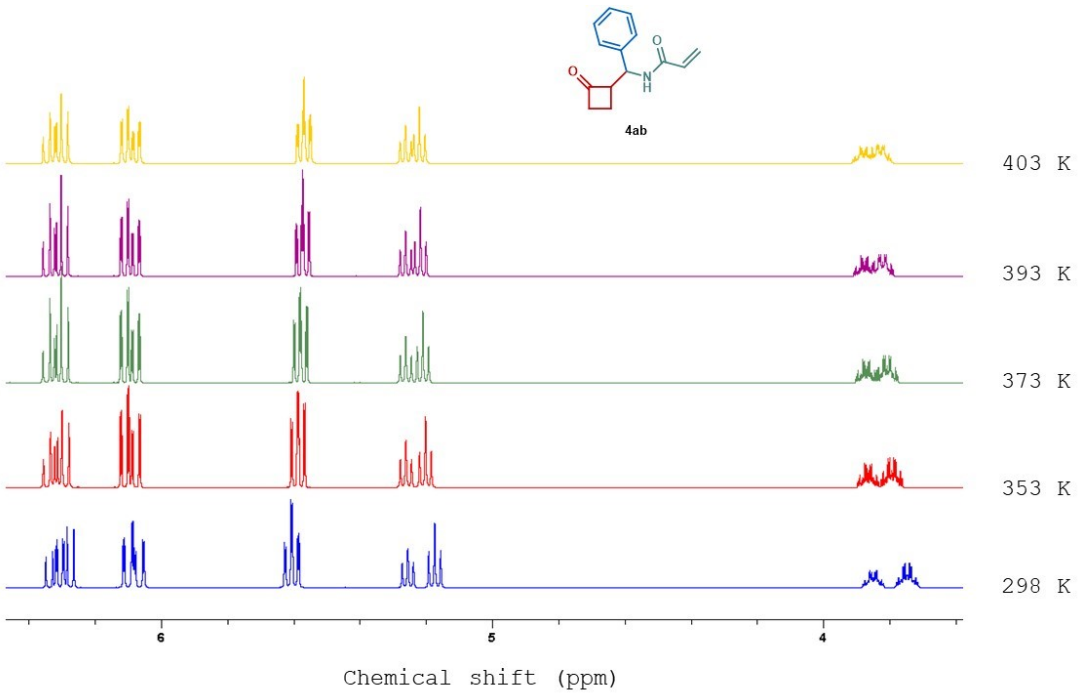
Prepared according to the general procedure described in **S2.4**, 56 mg (22%) of **9** was isolated as a yellow oil. Reaction time: 18 h.

HRMS(TOF+, m/Z): calcd. for $C_{16}H_{15}NO_2H$ [M+H$^+$]: 254.1176, found: 254.1177.

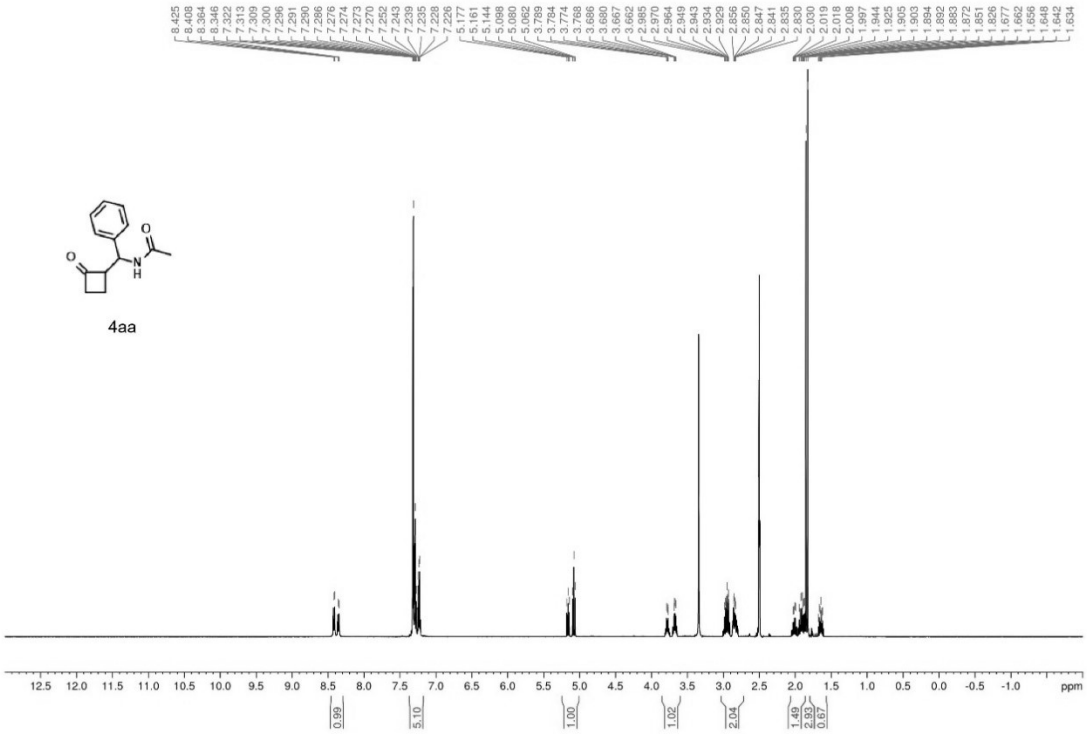
^{1}H-NMR (500 MHz, DMSO) (both diastereomers) 7.57-7.16 (m, 5H); 6.51/6.45 (dd, *J* = 10.9, 17.7 Hz, 1H); 6.31-6.02/6.27-5.99 (d, *J* = 11.1 Hz, 2H); 5.86/5.69 (d, *J* = 2.4 Hz, 1H); 5.19/5.08 (dd, *J* = 2.3, 4.9 Hz, 1H); 3.93-3.89 (m, 1H); 3.16-2.62 (m, 2H); 2.26-1.91 (m, 2H).

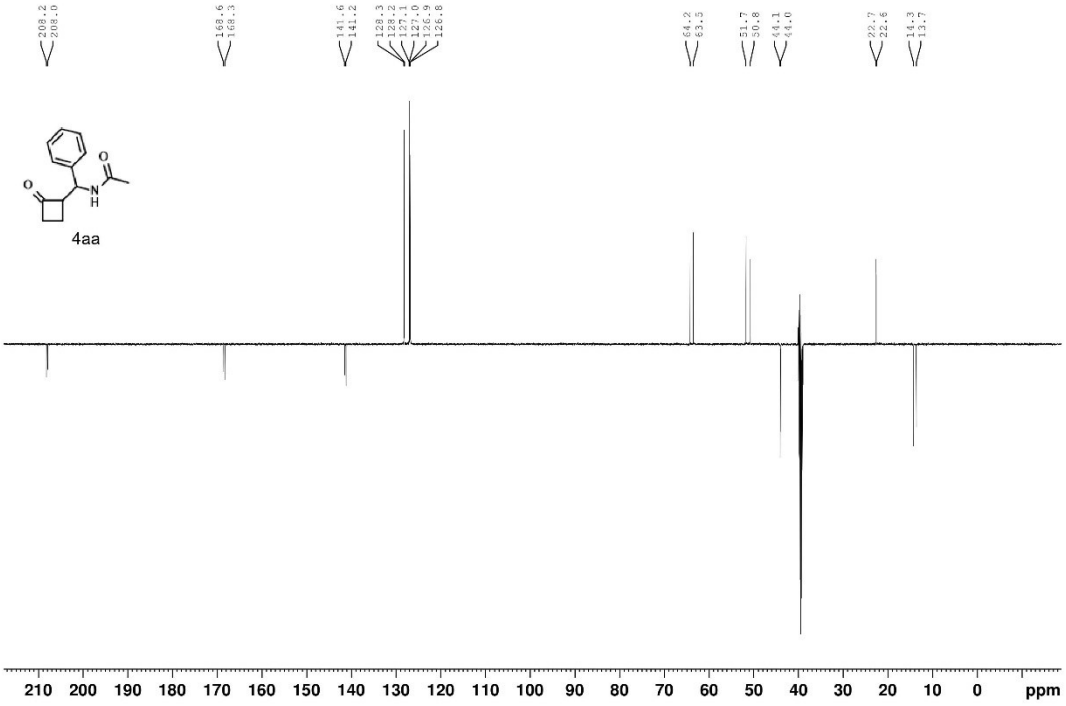
^{13}C-NMR (126 MHz, DMSO) (both diastereomers) 208.7/208.7; 161.8/161.6; 153.4/153.2; 134.9/134.8; 129.2/129.0; 129.1/129.1 and 128.2/128.2, 126.8/126.7, 124.1/124.0; 101.1/101.0; 68.8/68.2; 64.0/63.1; 45.3/45.2; 14.0/12.1.

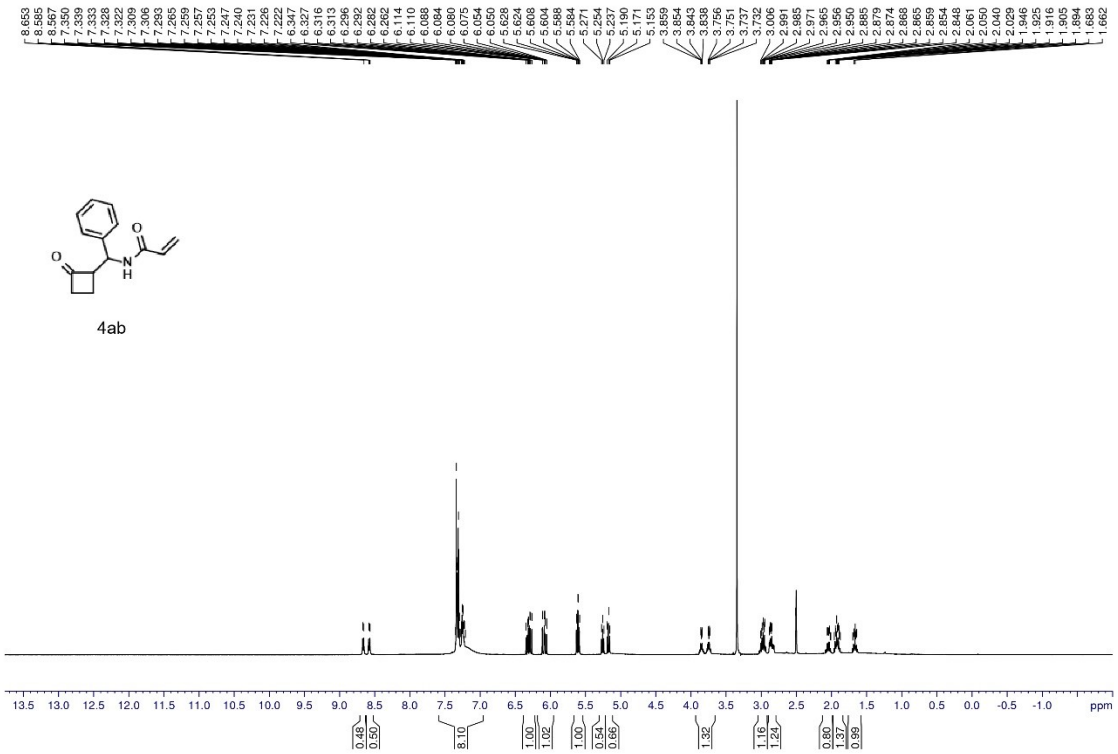
4.1 Temperature Dependence of Proton NMR Chemical Shifts for compound 4ab



5. Collection of NMR spectra



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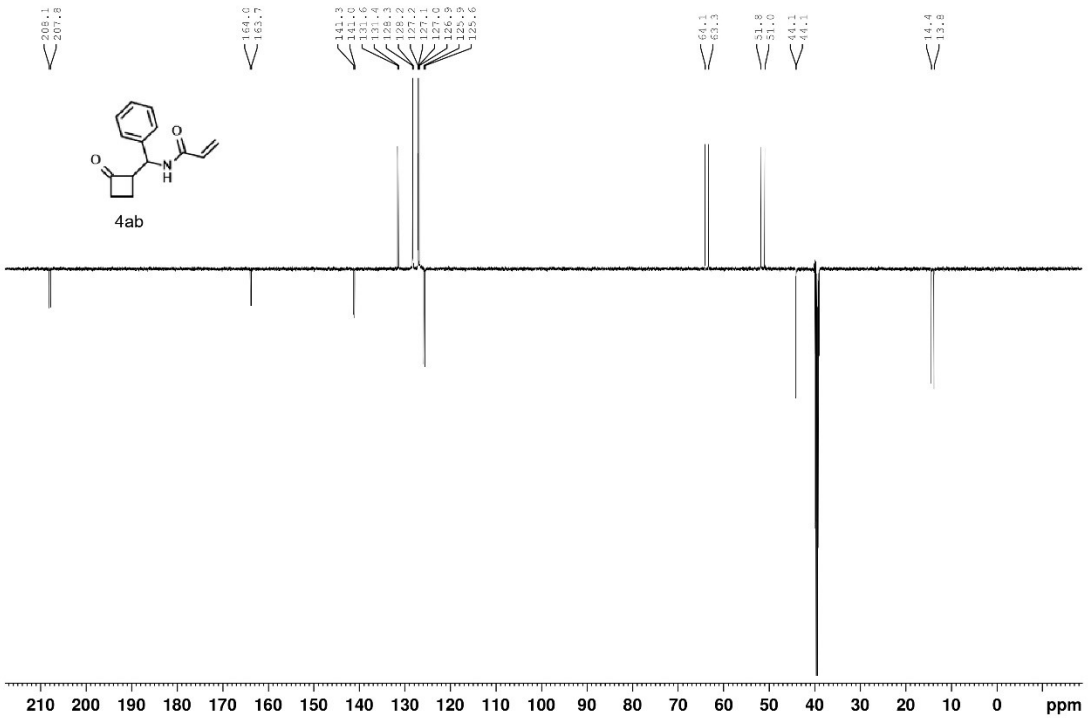
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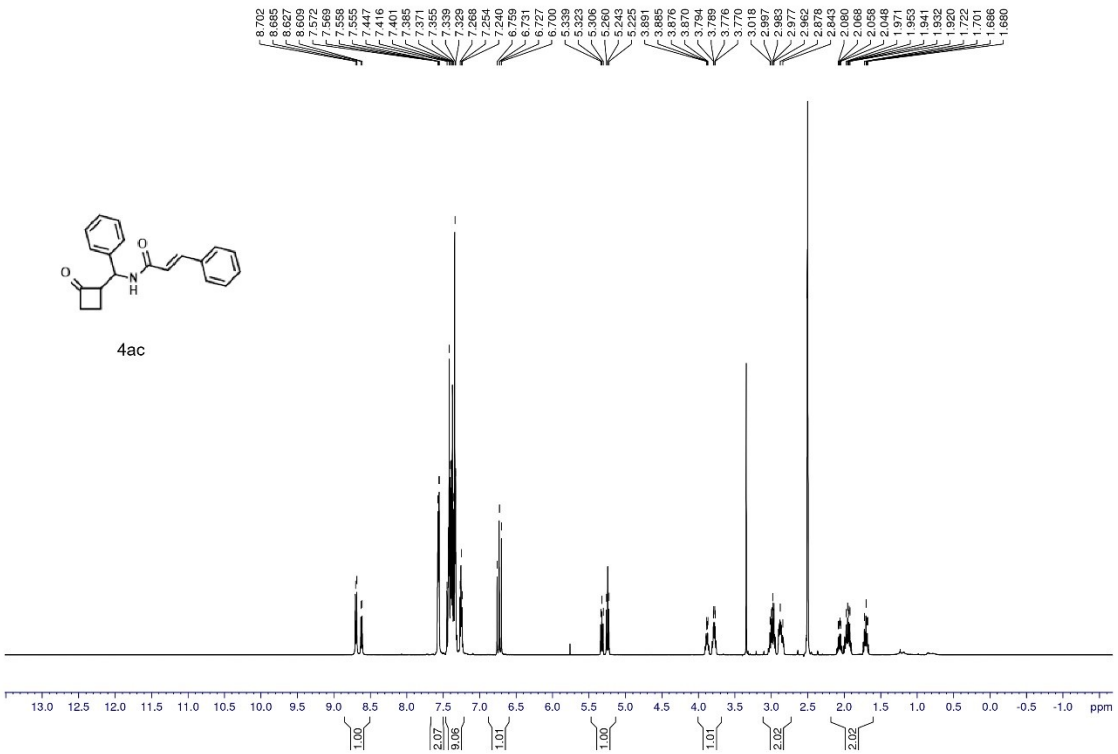
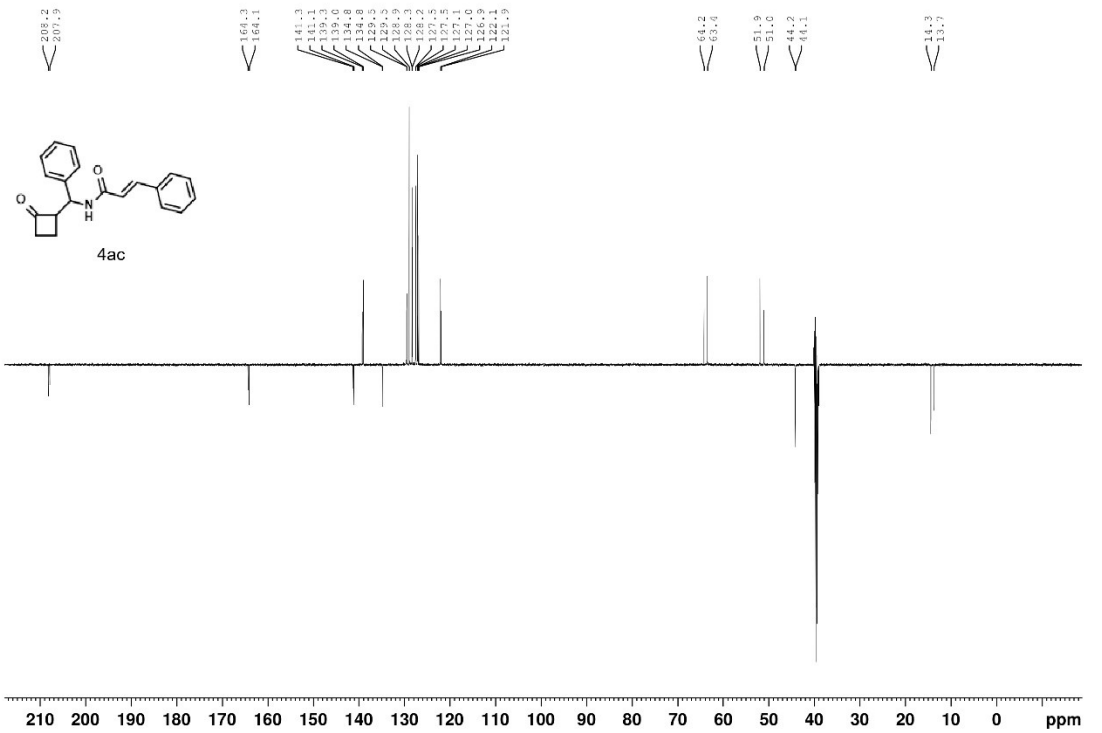

4ac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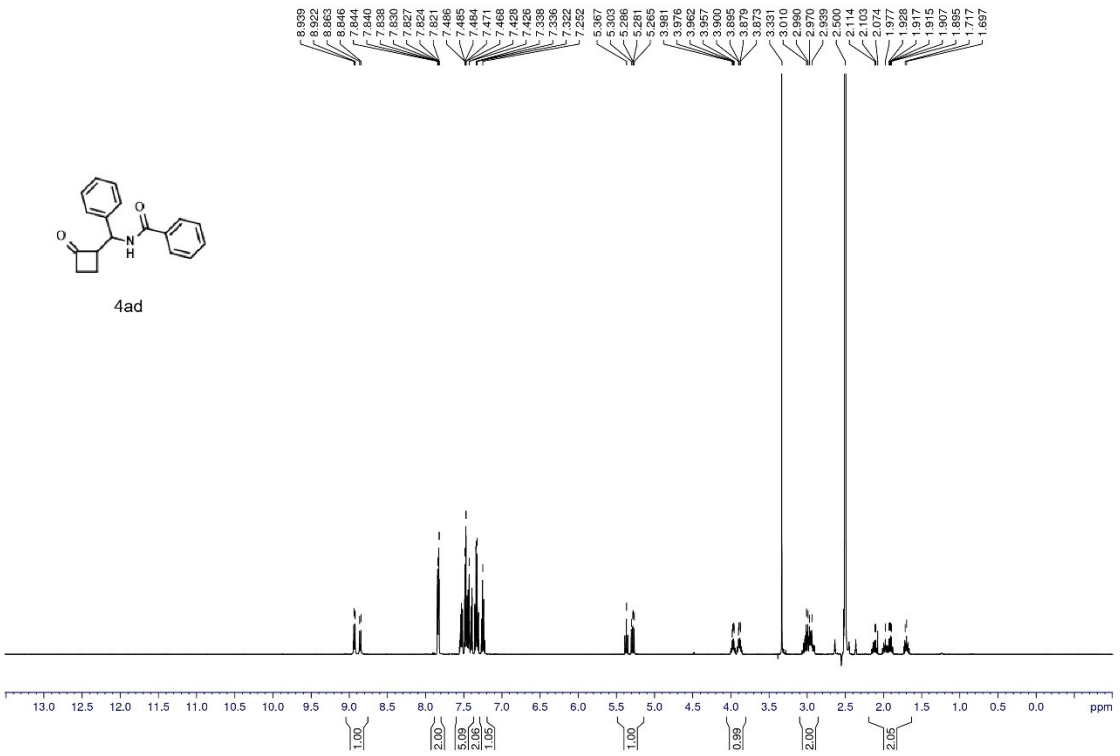
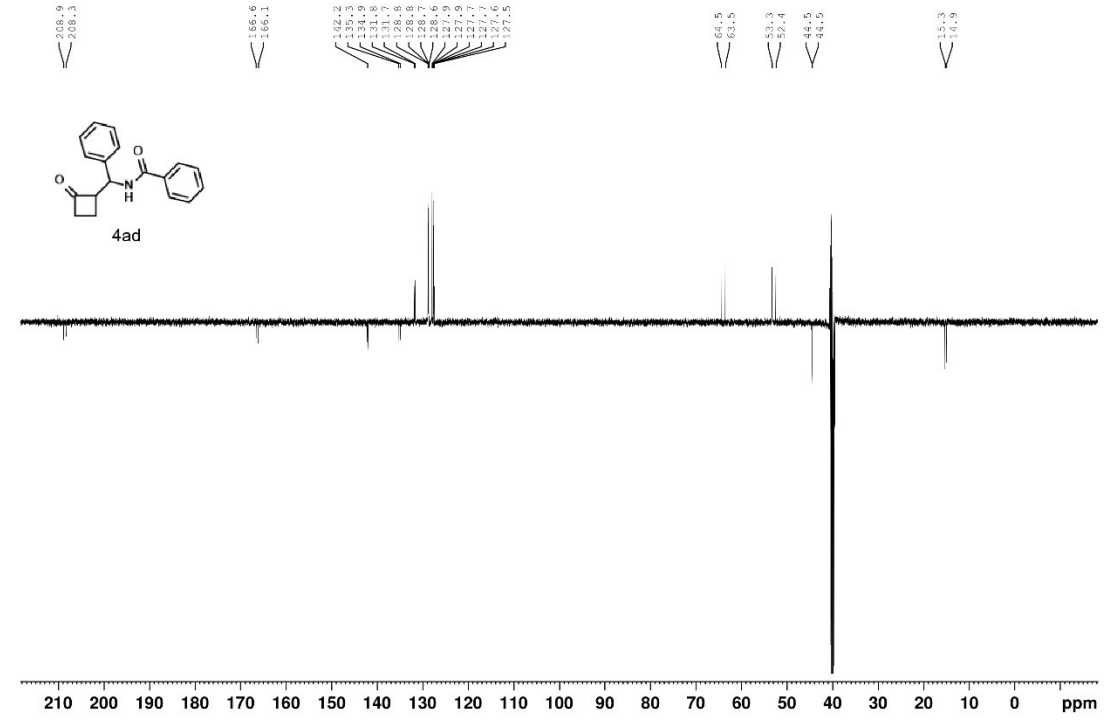
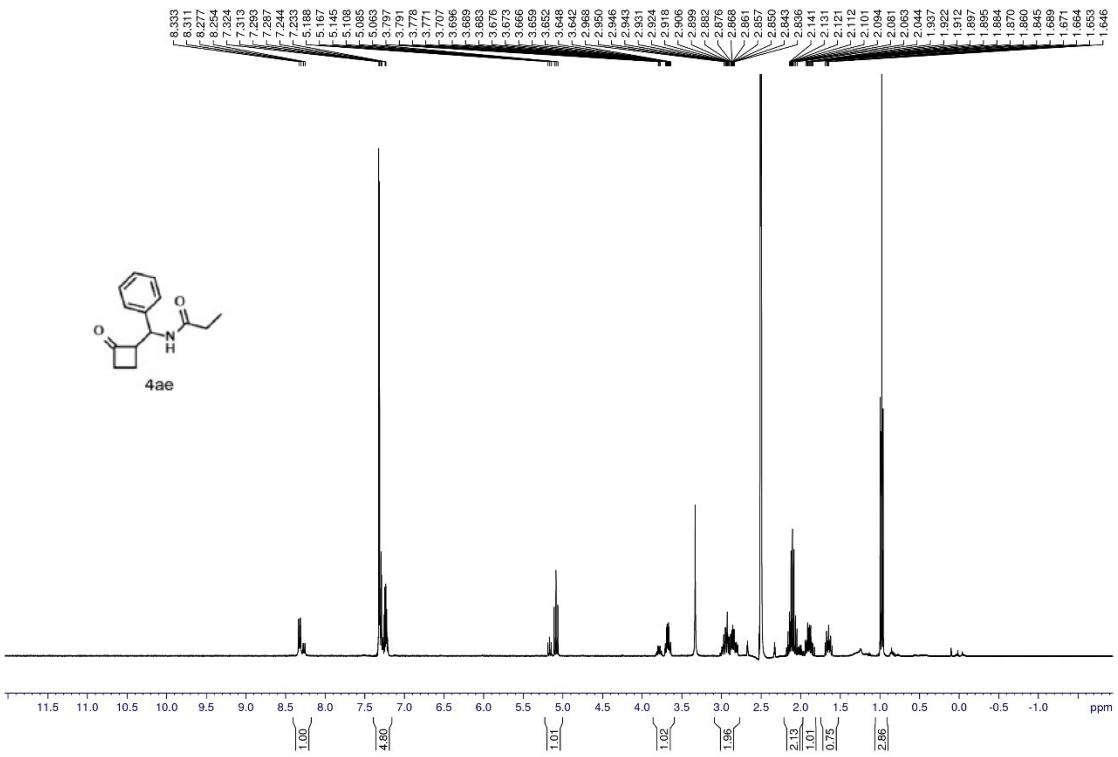
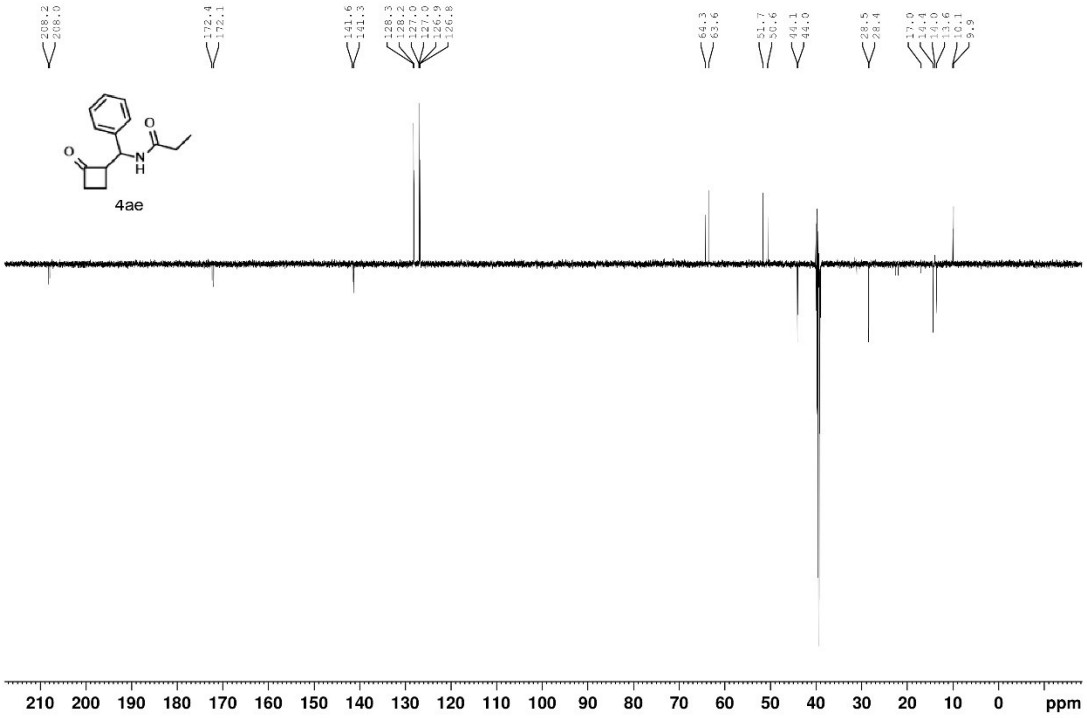
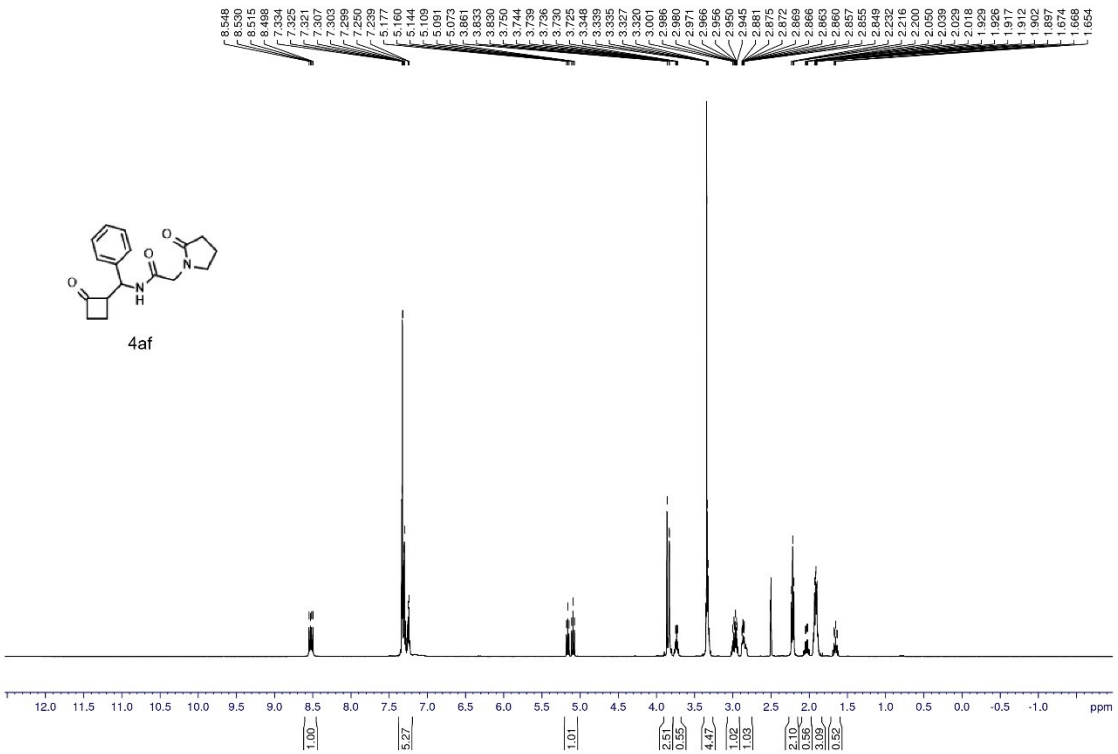
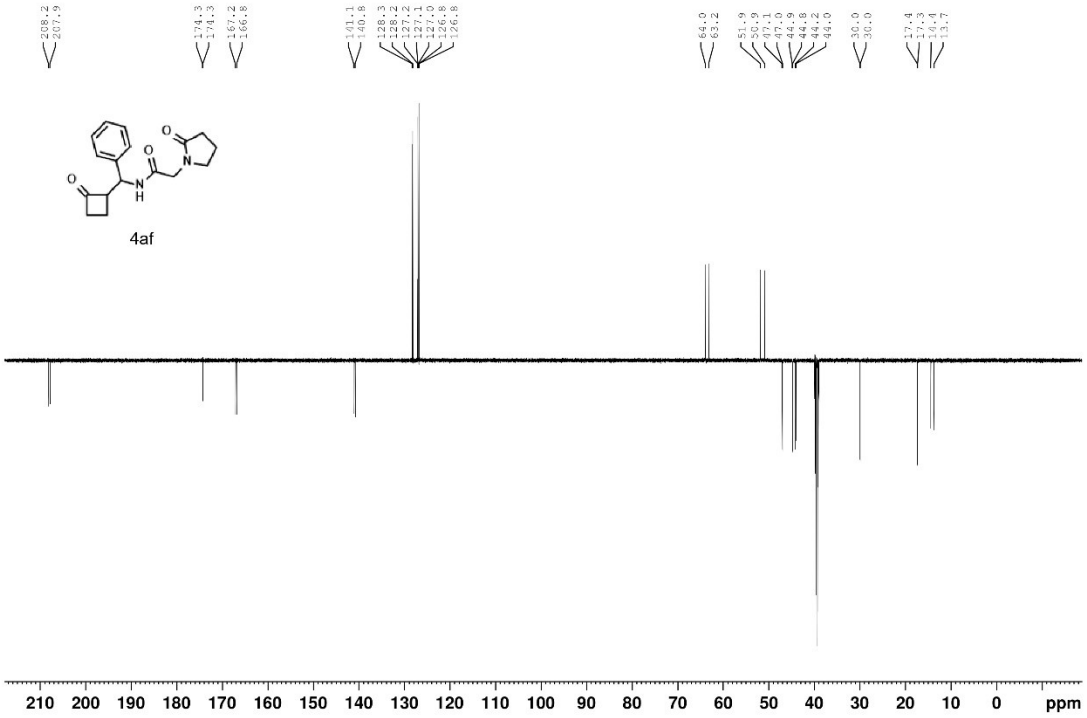

8.939
8.922
8.863
8.846
7.844
7.840
7.838
7.830
7.827
7.824
7.821
7.486
7.485
7.484
7.471
7.468
7.428
7.426
7.338
7.336
7.322
7.252
5.367
5.303
5.286
5.281
5.265
3.981
3.976
3.962
3.957
3.900
3.895
3.879
3.873
3.331
3.010
2.990
2.970
2.939
2.500
2.114
2.103
2.074
1.977
1.928
1.917
1.915
1.907
1.895
1.717
1.697
O
O
N
H
4ad
13.0 12.5 12.0 11.5 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 ppm
1.00
2.00
5.09
2.06
1.05
1.00
0.99
2.00
2.05

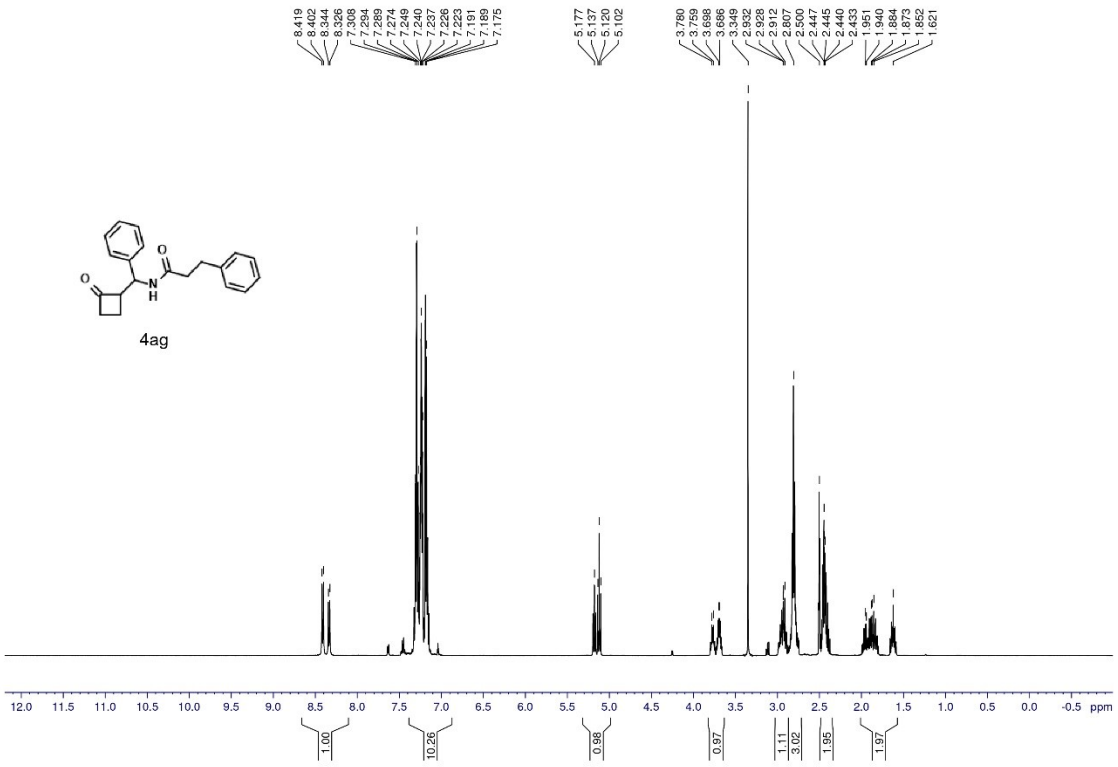

208.9
208.3
166.6
166.1
142.2
135.3
134.9
131.8
131.7
128.8
128.8
128.7
128.6
127.9
127.9
127.7
127.7
127.6
127.5
64.5
63.5
53.3
52.4
44.5
44.5
15.3
14.9
O
O
N
H
4ad
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4ae
ppm


4ae
ppm


4af
ppm


4af
ppm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8.402
8.344
8.326
7.308
7.294
7.289
7.274
7.249
7.240
7.237
7.226
7.223
7.191
7.189
7.175
5.177
5.137
5.120
5.102
3.780
3.759
3.698
3.686
3.349
2.932
2.928
2.912
2.807
2.500
2.447
2.445
2.440
2.433
1.951
1.940
1.884
1.873
1.852
1.621
4ag
12.0 11.5 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 ppm
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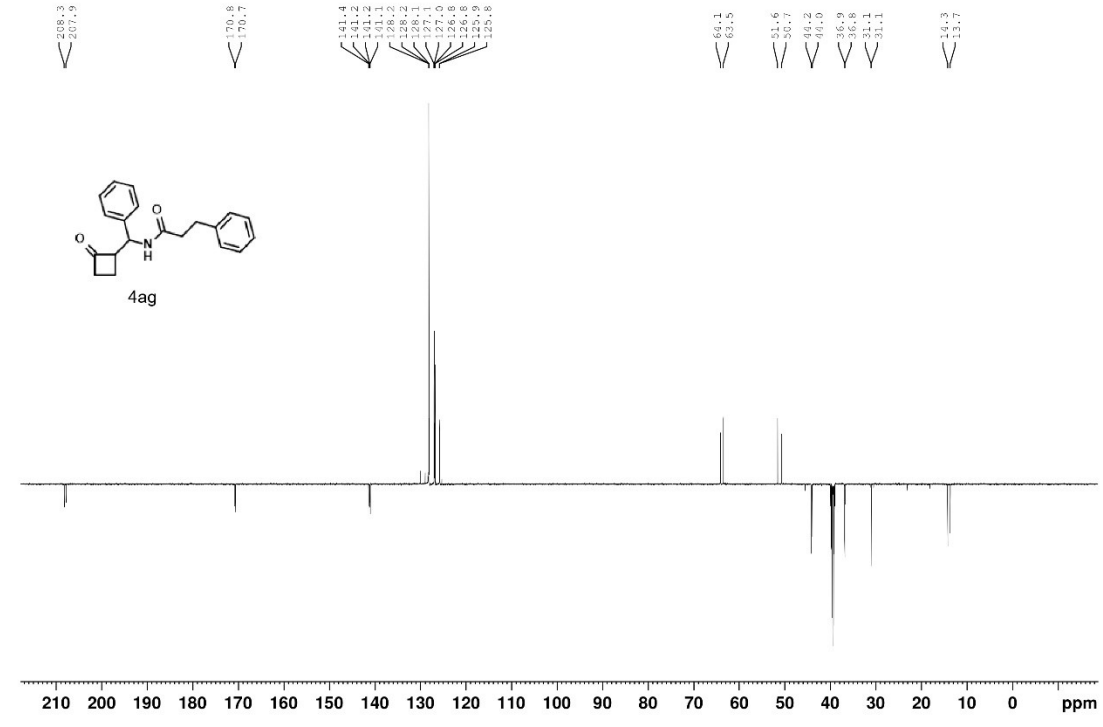
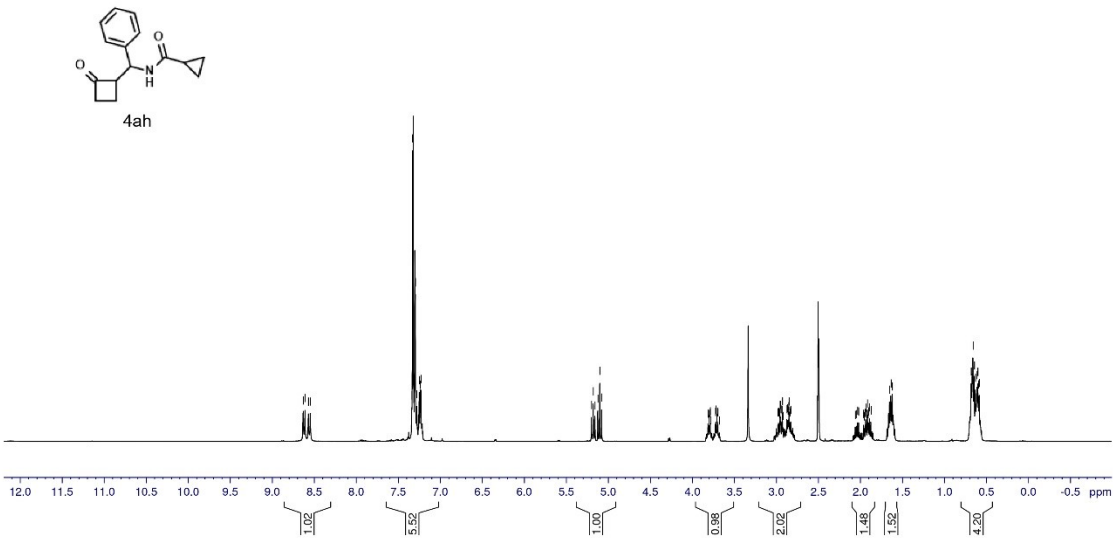
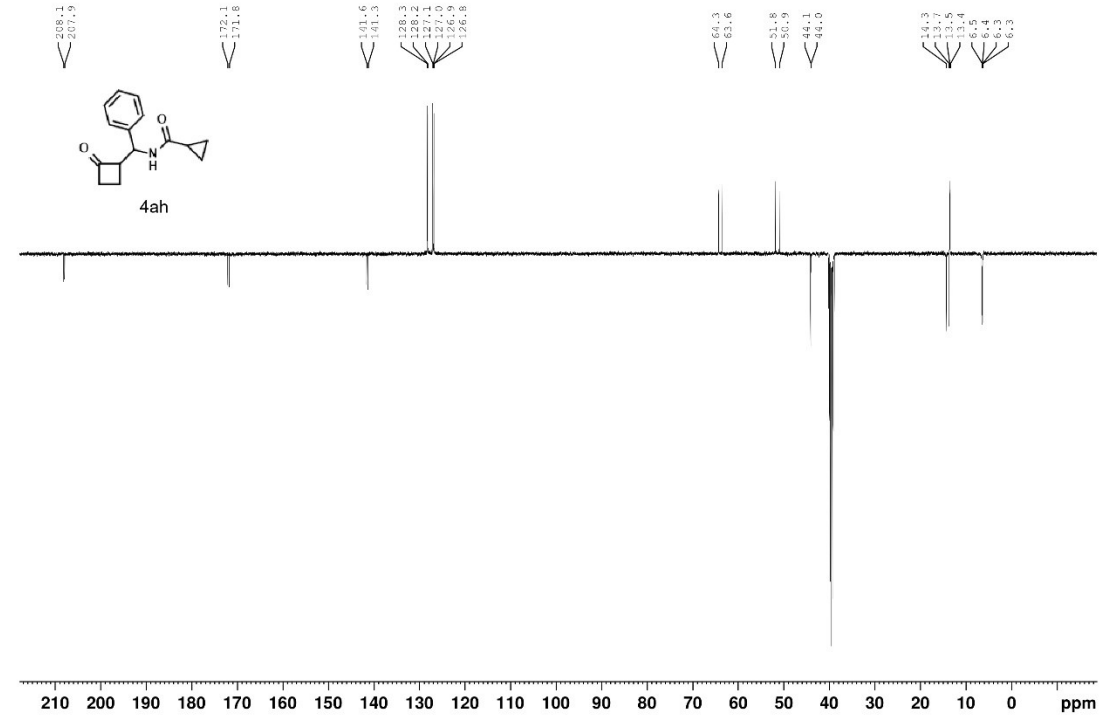
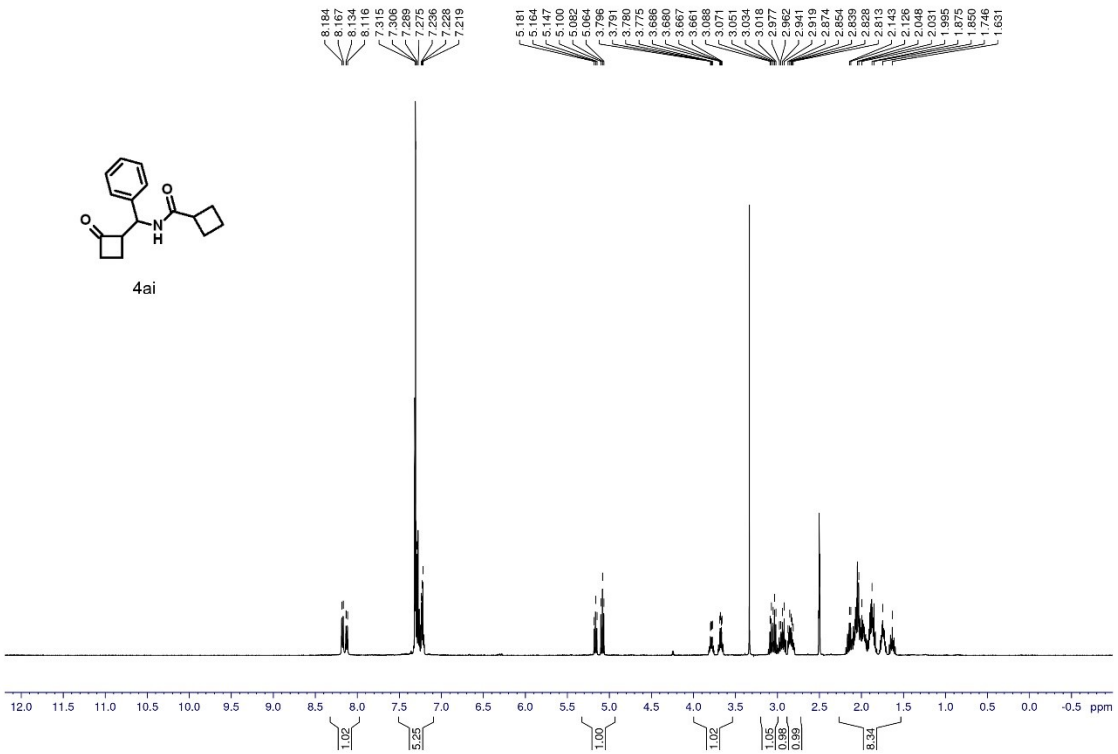
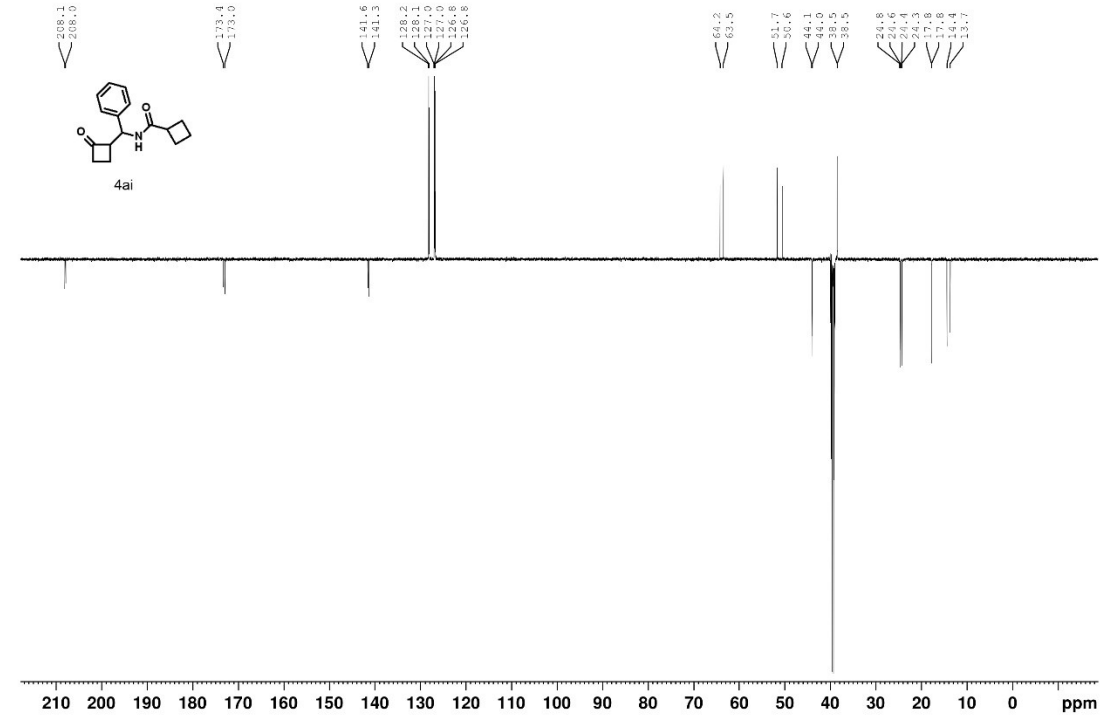
10.26
0.98
0.97
1.11
3.02
1.95
1.97

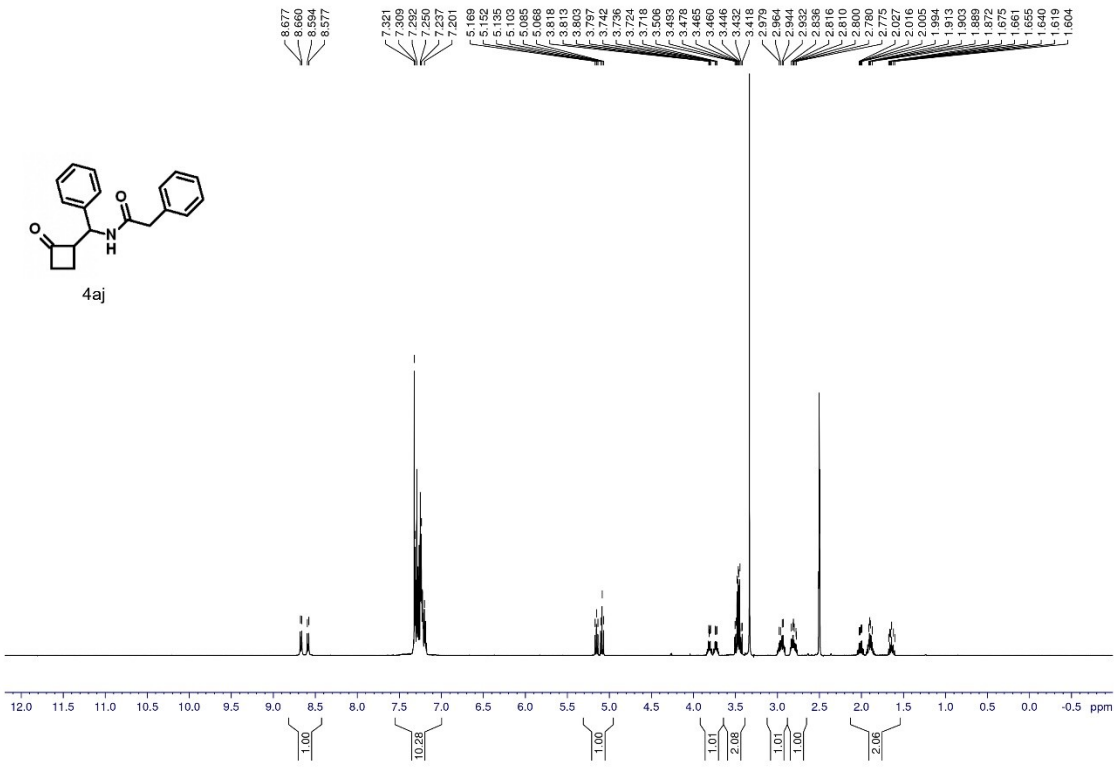

208.3
207.9
170.8
170.7
141.4
141.2
141.2
141.1
128.2
128.2
128.1
127.1
127.0
126.8
126.8
125.9
125.8
64.1
63.5
51.6
50.7
44.2
44.0
36.9
36.8
31.1
31.1
14.3
13.7
4ag
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

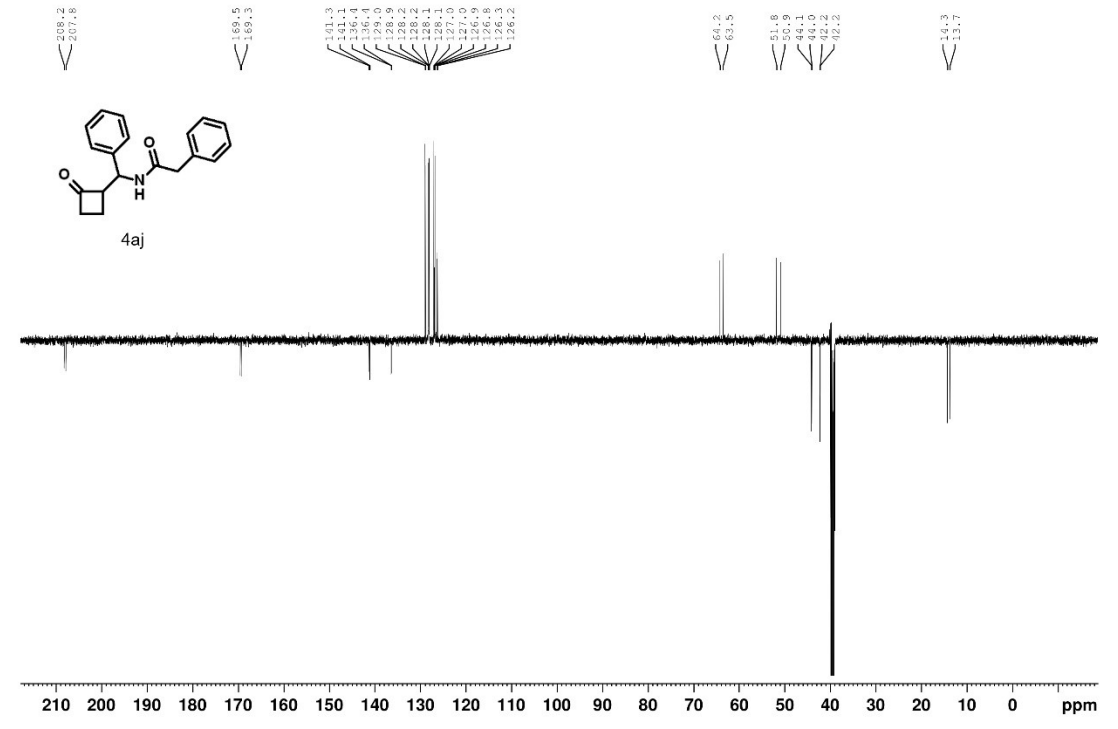

4ah
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 ppm
1.02
5.52
1.00
0.98
2.02
1.48
1.52
4.20

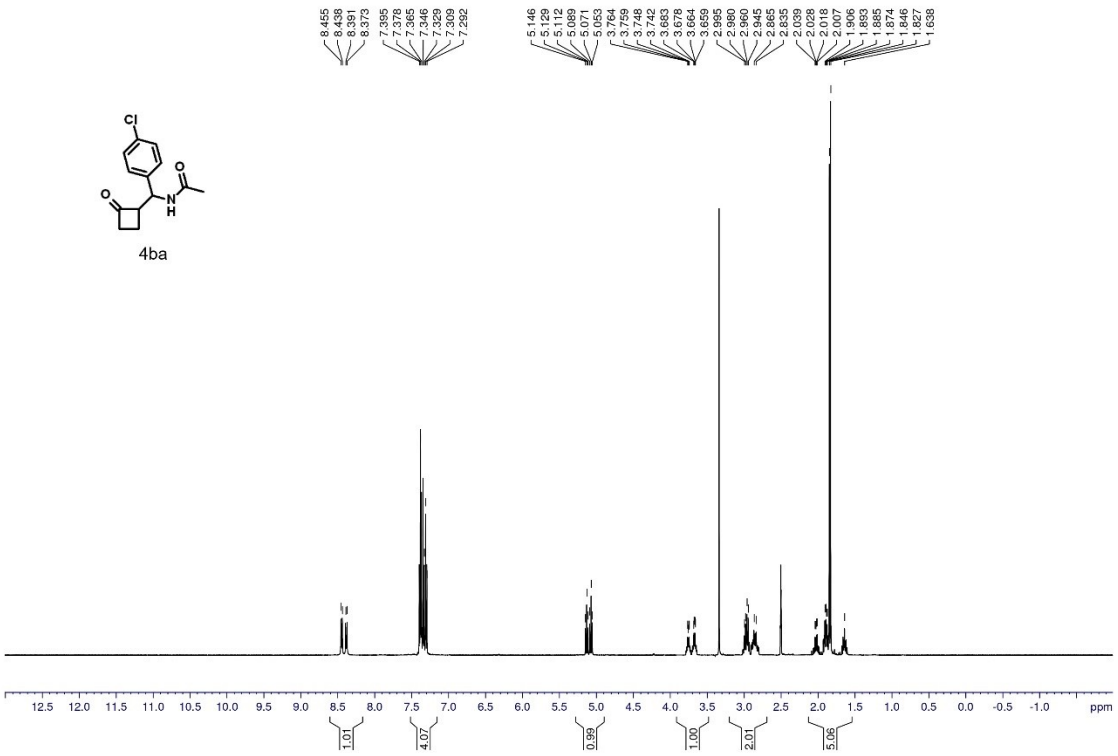

208.1
207.9
172.1
171.8
141.6
141.3
128.3
128.2
127.1
127.0
126.9
126.8
64.3
63.6
31.8
30.9
44.1
44.0
14.3
13.7
13.5
13.4
8.5
6.4
6.3
6.3
4ah
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

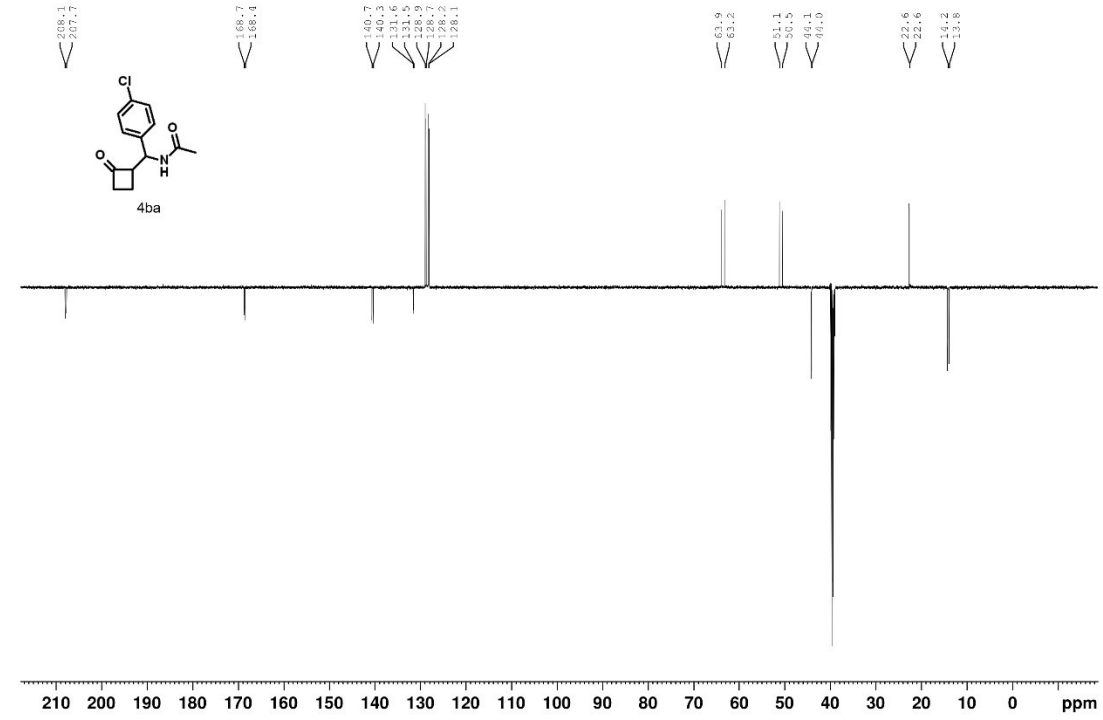

8.184
8.167
8.134
8.116
7.315
7.306
7.289
7.275
7.236
7.228
7.219
5.181
5.164
5.147
5.100
5.082
5.064
3.796
3.791
3.780
3.775
3.686
3.680
3.667
3.661
3.088
3.071
3.051
3.034
3.018
2.977
2.962
2.941
2.919
2.874
2.854
2.839
2.828
2.813
2.143
2.126
2.048
2.031
1.995
1.875
1.850
1.746
1.631
4ai
12.0 11.5 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 ppm
1.02
5.25
1.00
1.02
1.05
0.98
0.99
8.34

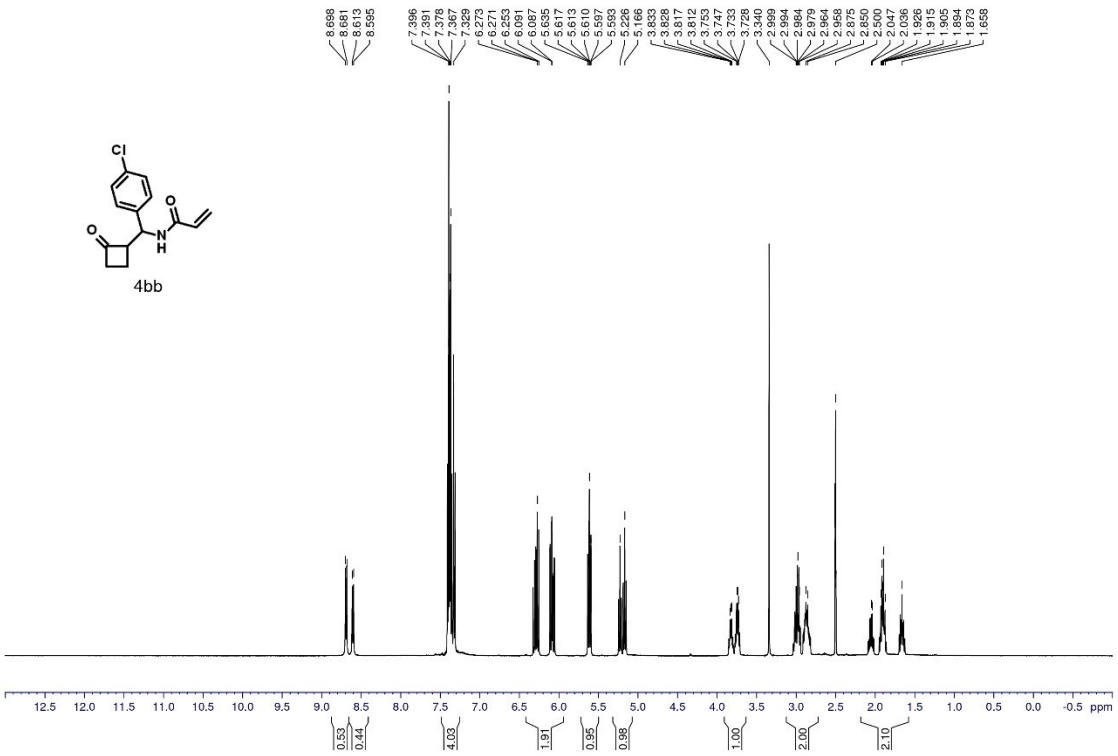

208.1
208.0
173.4
173.0
141.6
141.3
128.2
128.1
127.1
127.0
126.8
126.8
64.2
63.5
51.7
50.6
44.1
44.0
38.5
38.5
24.8
24.6
24.4
24.3
17.8
17.8
14.4
13.7
4ai
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

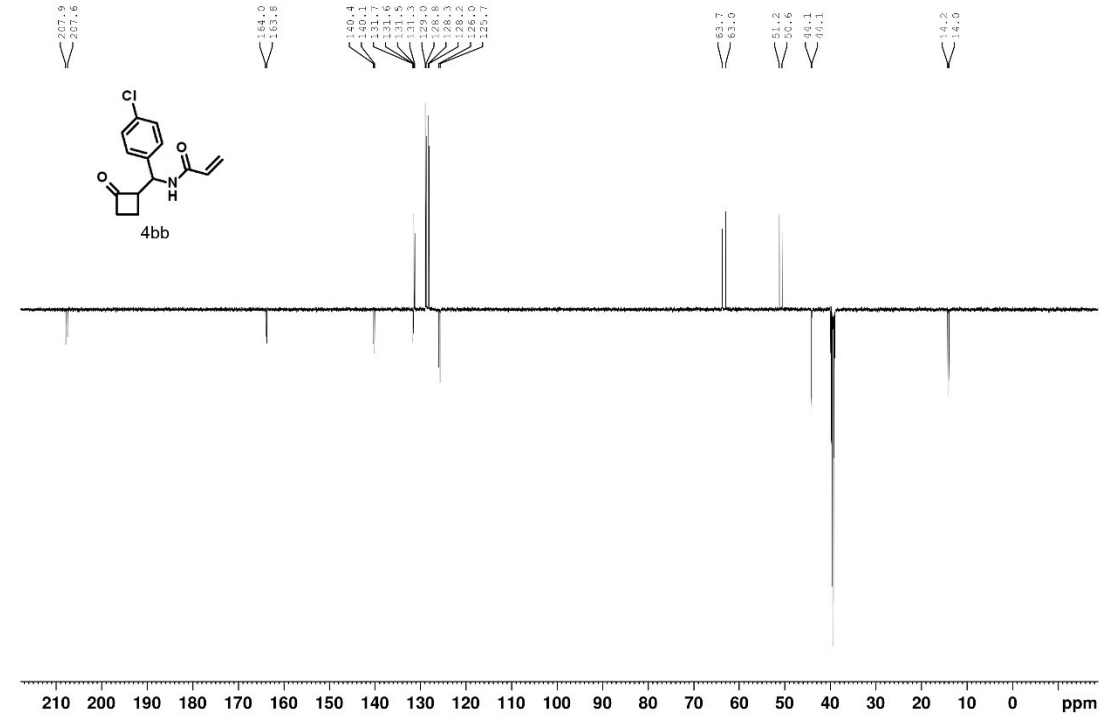

8.677
8.660
8.594
8.577
7.321
7.309
7.292
7.250
7.237
7.201
5.169
5.152
5.135
5.103
5.085
5.068
3.818
3.813
3.803
3.797
3.742
3.736
3.724
3.718
3.506
3.493
3.478
3.465
3.460
3.446
3.432
3.418
2.979
2.964
2.944
2.932
2.836
2.816
2.810
2.800
2.780
2.775
2.027
2.016
2.005
1.994
1.913
1.903
1.889
1.872
1.675
1.661
1.655
1.640
1.619
1.604
O
N
H
O
4aj
12.0 11.5 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 ppm
1.00
10.28
1.00
1.01
2.08
1.01
1.00
2.06

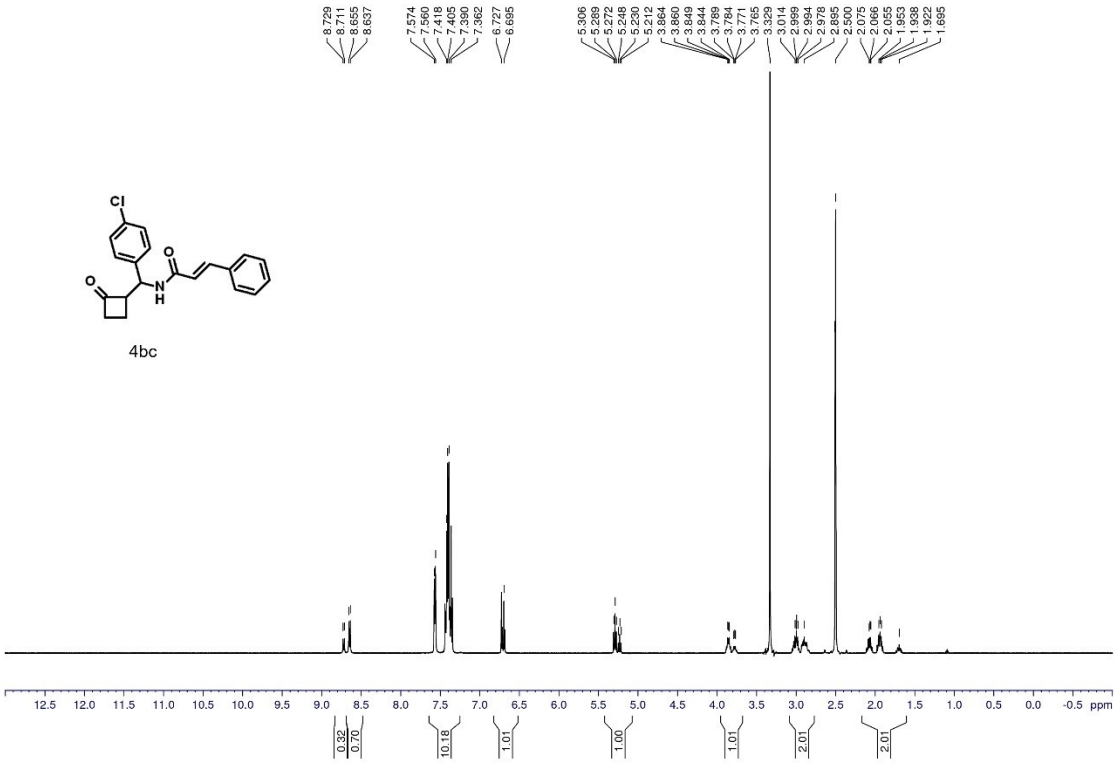

208.2
207.8
169.5
169.3
141.3
141.1
136.4
129.0
128.9
128.2
128.1
128.1
127.0
127.0
126.9
126.8
126.3
126.2
64.2
63.5
51.8
50.9
44.1
44.0
42.2
42.2
14.3
13.7
O
N
H
O
4aj
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.455
8.438
8.391
8.373
7.395
7.378
7.365
7.346
7.329
7.309
7.292
5.146
5.129
5.112
5.089
5.071
5.053
3.764
3.759
3.748
3.742
3.683
3.678
3.664
3.659
2.995
2.980
2.960
2.945
2.865
2.835
2.039
2.028
2.018
2.007
1.906
1.893
1.885
1.874
1.846
1.827
1.638
Cl
O
O
N
H
4ba
12.5 12.0 11.5 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 ppm
1.01
4.07
0.99
1.00
2.01
5.06


208.1
207.7
168.7
168.4
140.7
140.3
131.6
131.5
128.9
128.7
128.2
128.1
63.9
63.2
51.1
50.5
44.1
44.0
22.6
22.6
14.2
13.8
Cl
O
O
N
H
4ba
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.698
8.681
8.613
8.595
7.396
7.391
7.378
7.367
7.329
6.273
6.271
6.253
6.091
6.087
5.635
5.617
5.613
5.610
5.597
5.593
5.226
5.166
3.833
3.828
3.817
3.812
3.753
3.747
3.733
3.728
3.340
2.999
2.994
2.984
2.979
2.964
2.958
2.875
2.850
2.500
2.047
2.036
1.926
1.915
1.905
1.894
1.873
1.658
Cl
O
O
N
H
4bb
12.5 12.0 11.5 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 ppm
0.53
0.44
4.03
1.91
0.95
0.98
1.00
2.00
2.10


207.9
207.6
164.0
163.8
140.4
140.1
131.7
131.6
131.5
131.3
129.0
128.8
128.3
128.2
126.0
125.7
63.7
63.0
51.2
50.6
44.1
44.1
14.2
14.0
Cl
O
O
N
H
4bb
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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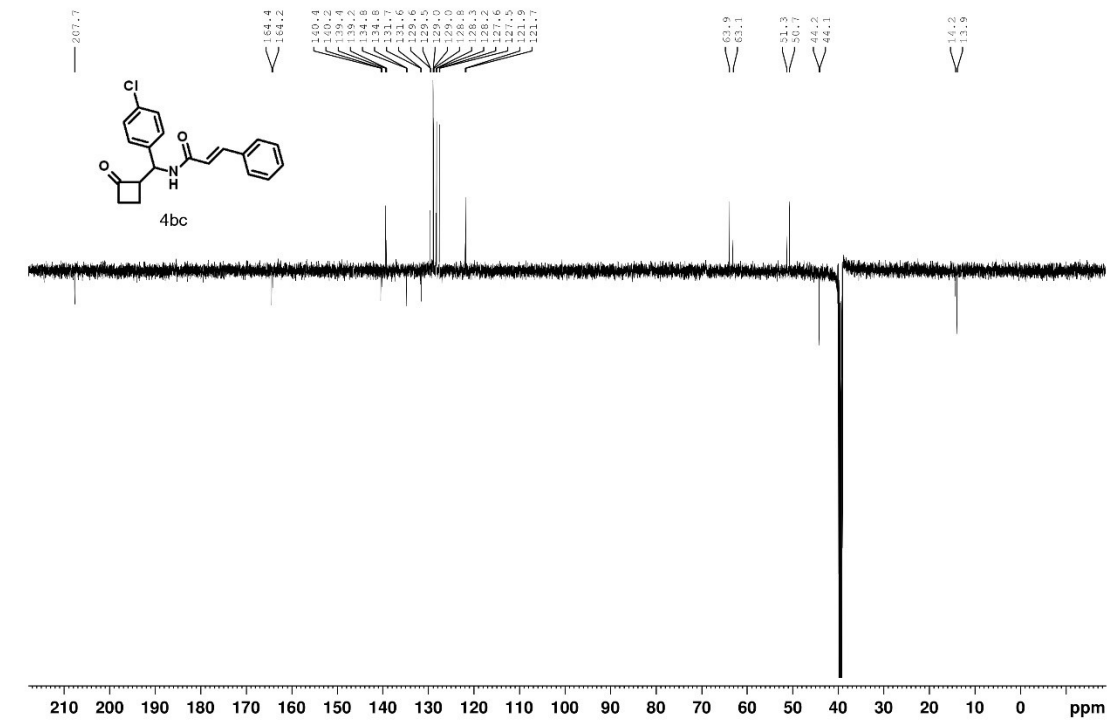
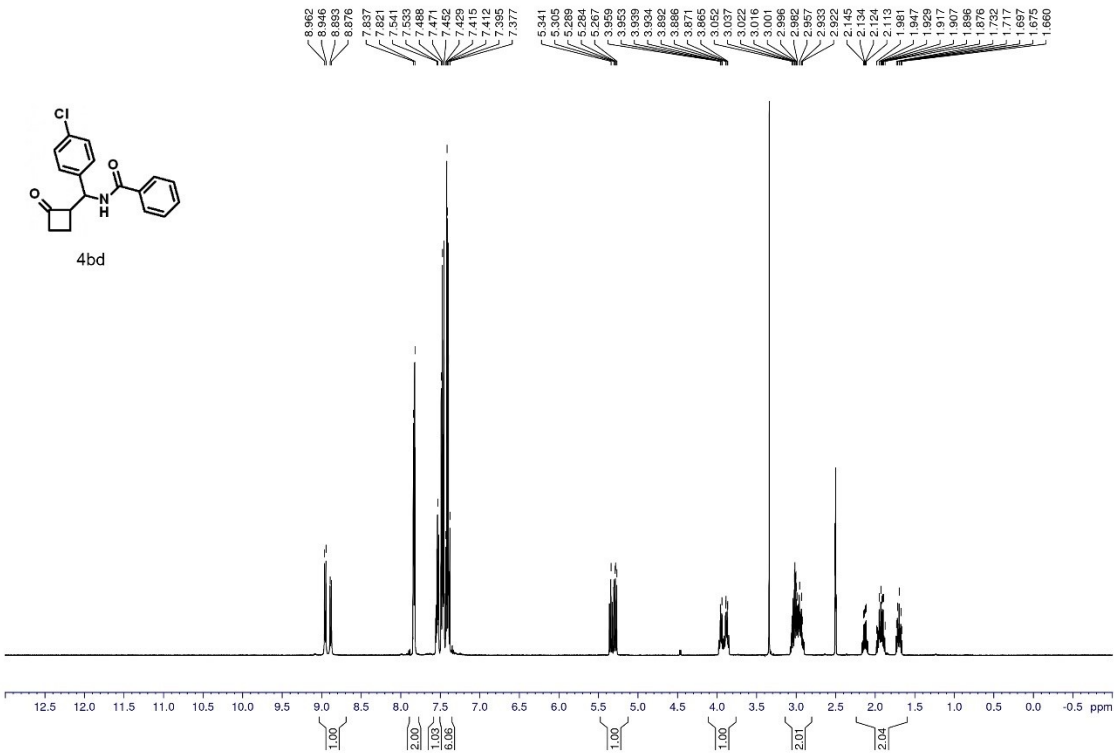
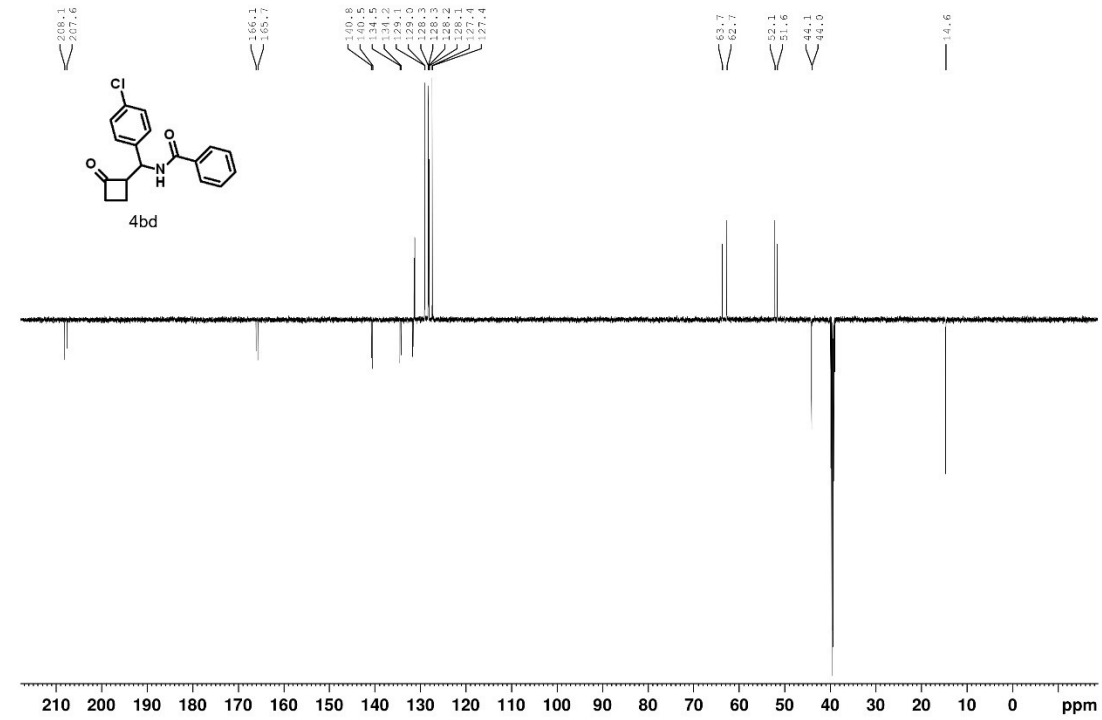
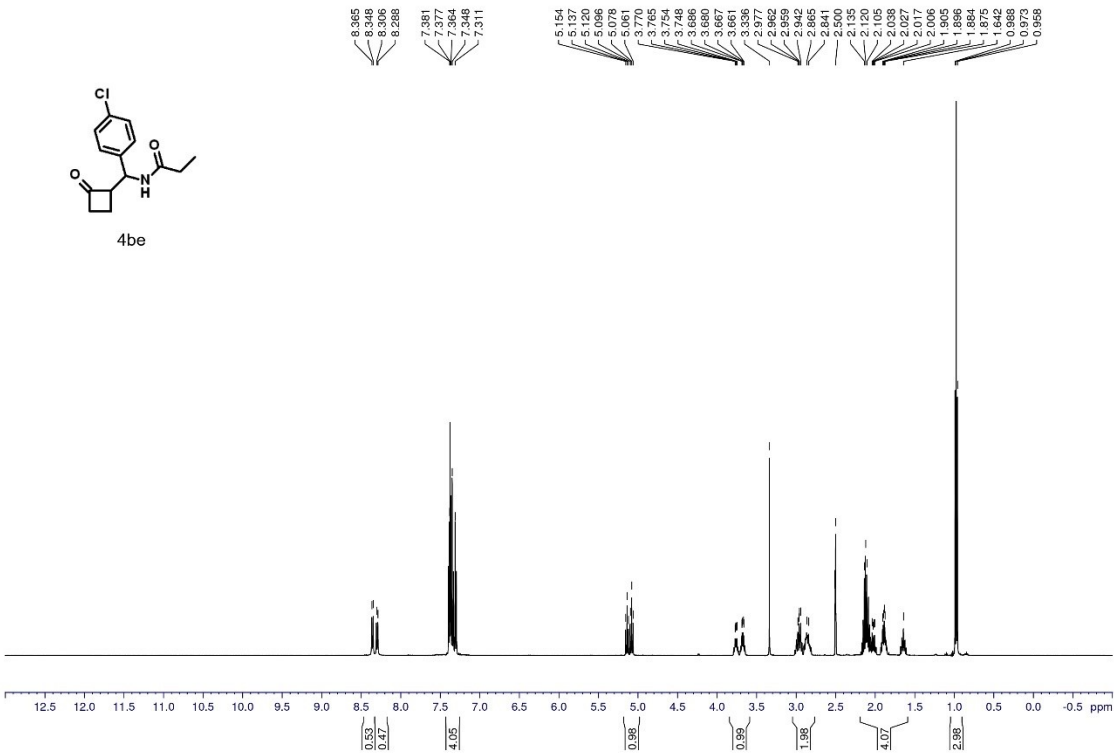
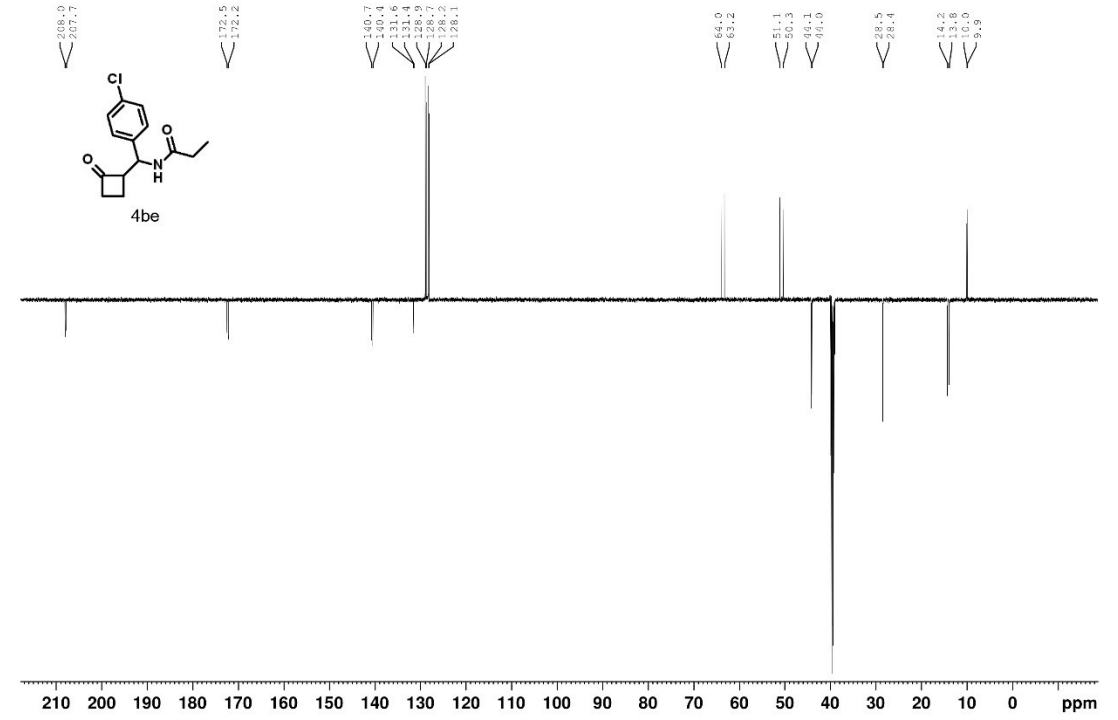
8.711
8.655
8.637
7.574
7.560
7.418
7.405
7.390
7.362
6.727
6.695
5.306
5.289
5.272
5.248
5.230
5.212
3.864
3.860
3.849
3.844
3.789
3.784
3.771
3.765
3.329
3.014
2.999
2.994
2.978
2.895
2.500
2.075
2.066
2.055
1.953
1.938
1.922
1.695
Cl
O
N
H
O
4bc
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 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 ppm
0.32
0.70
10.18
1.01
1.00
1.01
2.01
2.01

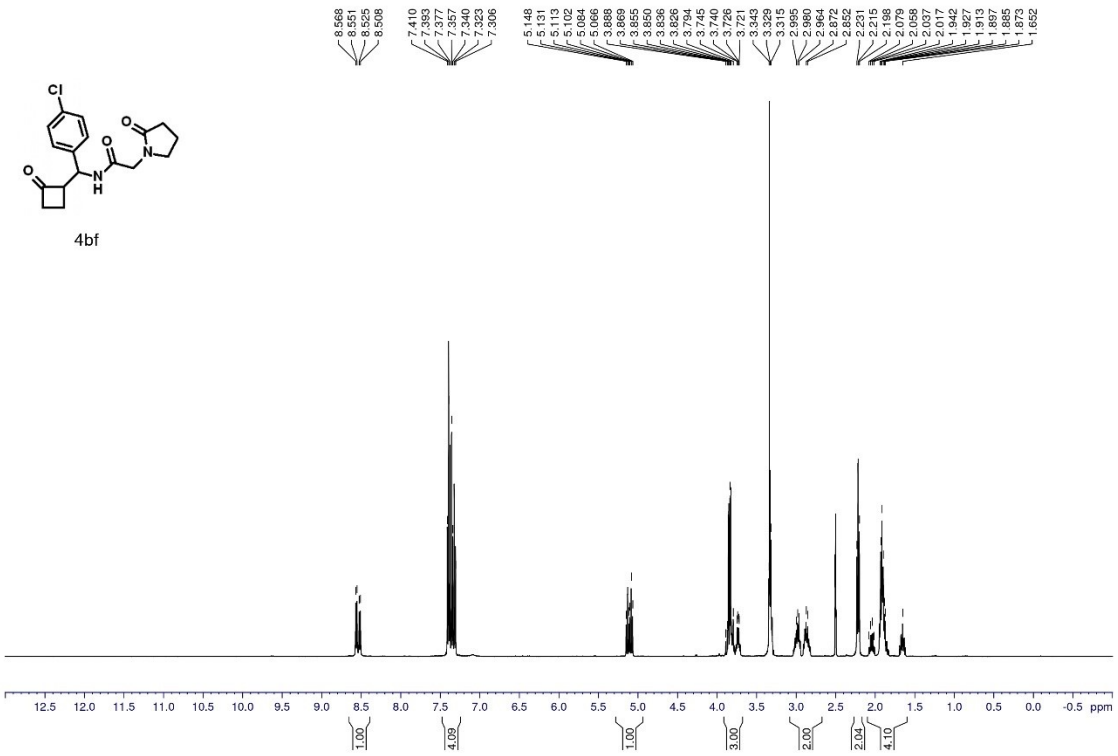

207.7
164.4
164.2
140.4
140.2
139.4
139.2
134.8
134.6
131.7
131.6
129.6
129.5
129.0
129.0
128.8
128.3
128.2
127.6
127.5
121.9
121.7
63.9
63.1
51.3
50.7
44.2
44.1
14.2
13.9
Cl
O
N
H
O
4bc
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

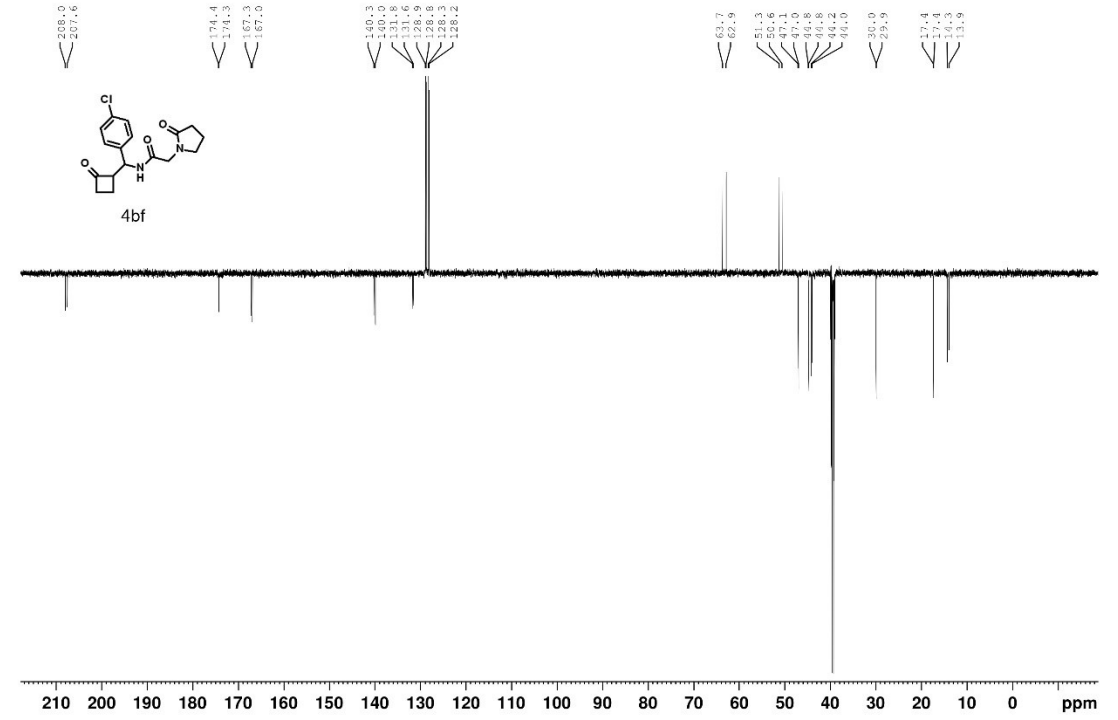

4bd


4bd


8.365
8.348
8.306
8.288
7.381
7.377
7.364
7.348
7.311
5.154
5.137
5.120
5.096
5.078
5.061
3.770
3.765
3.754
3.748
3.686
3.680
3.667
3.661
3.336
2.977
2.962
2.959
2.942
2.865
2.841
2.500
2.135
2.120
2.105
2.038
2.027
2.017
2.006
1.905
1.896
1.884
1.875
1.642
0.988
0.973
0.958
Cl
O
N
H
O
4be
12.5 12.0 11.5 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 ppm
0.53
0.47
4.05
0.98
0.99
1.98
4.07
2.98


208.0
207.7
172.5
172.2
140.7
140.4
131.6
131.4
128.9
128.7
128.2
128.1
64.0
63.2
51.1
50.3
44.1
40.0
28.5
28.4
14.2
13.8
10.0
9.9
Cl
O
N
H
O
4be
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4bf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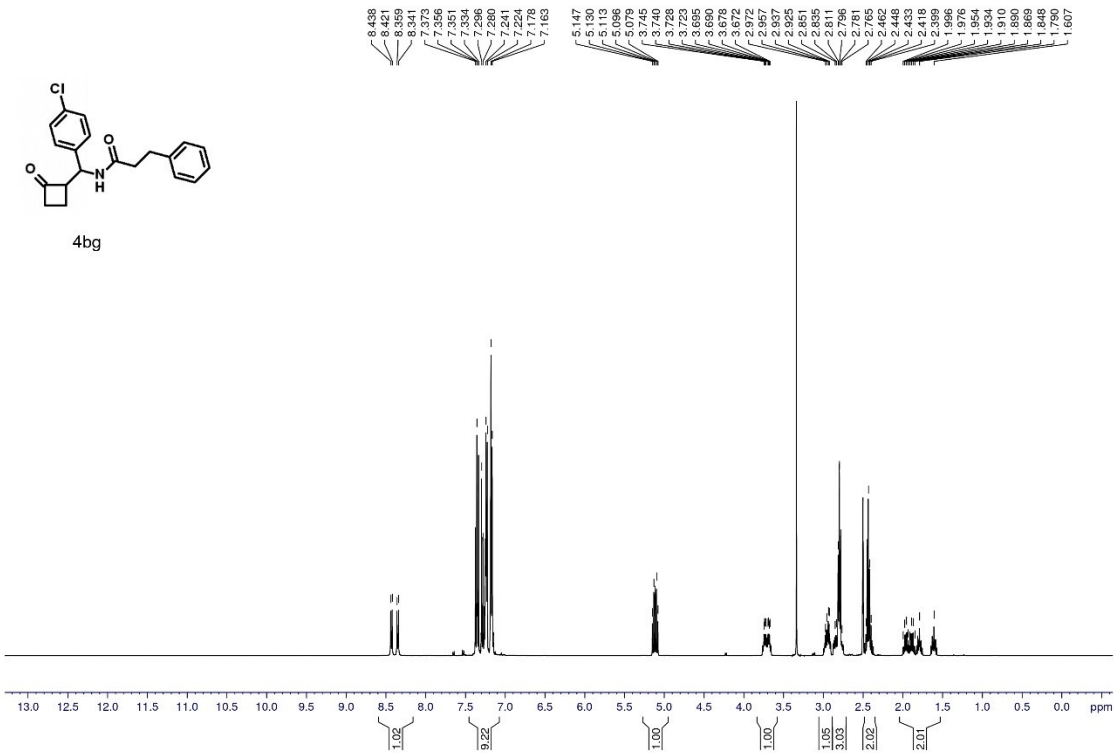
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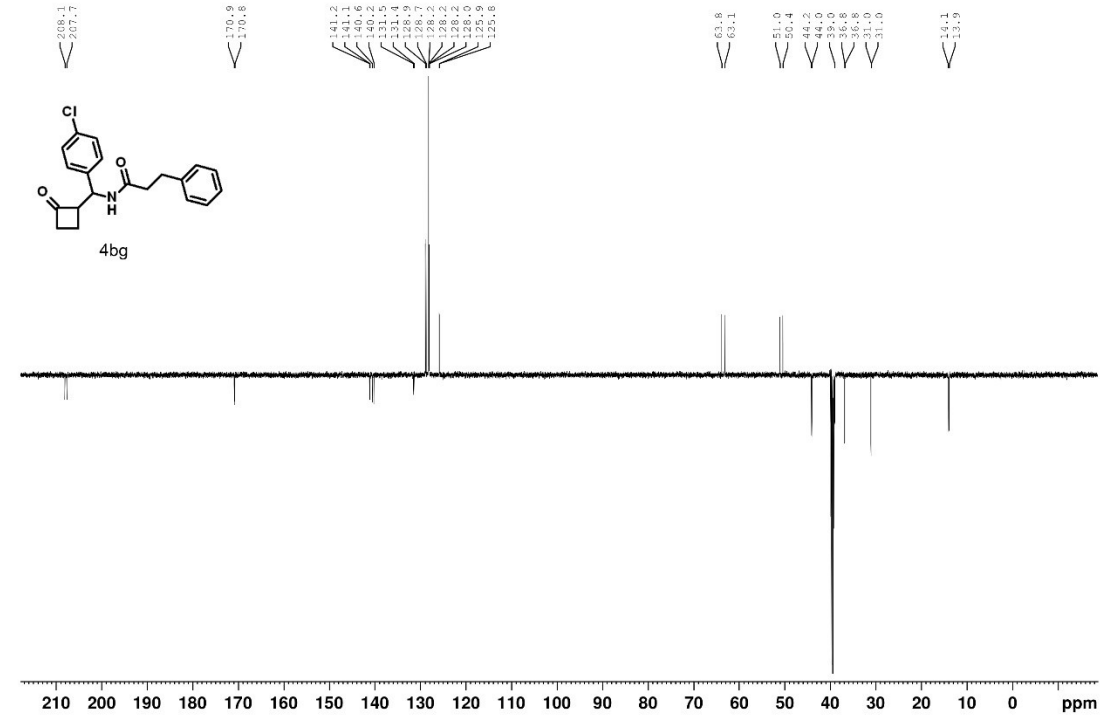
8.421
8.359
8.341
7.373
7.356
7.351
7.334
7.296
7.280
7.241
7.224
7.178
7.163
5.147
5.130
5.113
5.096
5.079
3.745
3.740
3.728
3.723
3.695
3.690
3.678
3.672
2.972
2.957
2.937
2.925
2.851
2.835
2.811
2.796
2.781
2.765
2.462
2.448
2.433
2.418
2.399
1.996
1.976
1.954
1.934
1.910
1.890
1.869
1.848
1.790
1.607
Cl
O
N
H
O
4bg
13.0 12.5 12.0 11.5 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 ppm
1.02
9.22
1.00
1.00
1.05
3.03
2.02
2.01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207.7
170.9
170.8
141.2
141.1
140.6
140.2
131.5
131.4
128.9
128.7
128.2
128.2
128.2
128.0
125.9
125.8
63.8
63.1
51.0
50.4
44.2
44.0
39.0
36.8
36.8
31.0
31.0
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13.9
Cl
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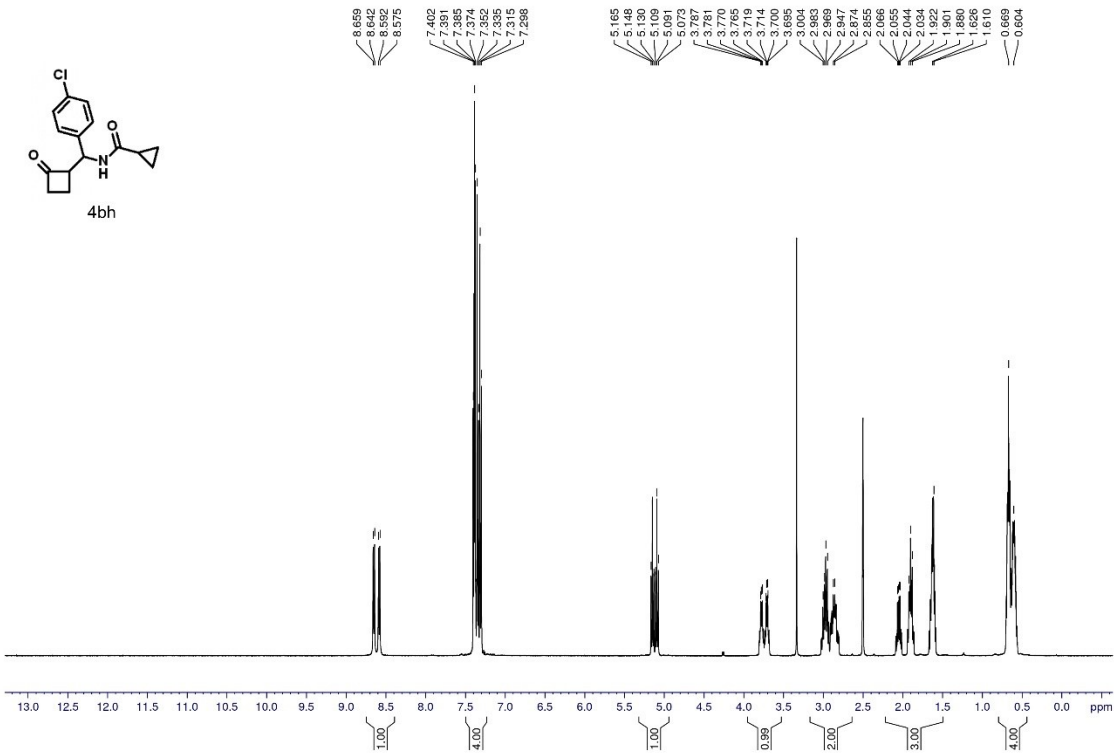
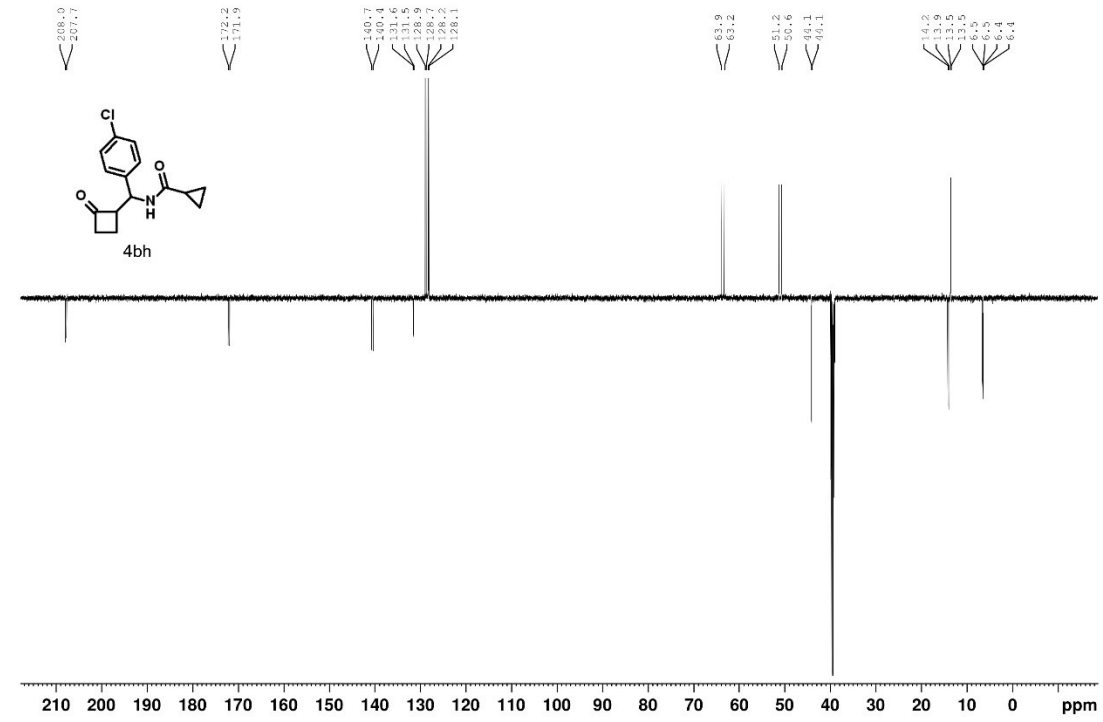
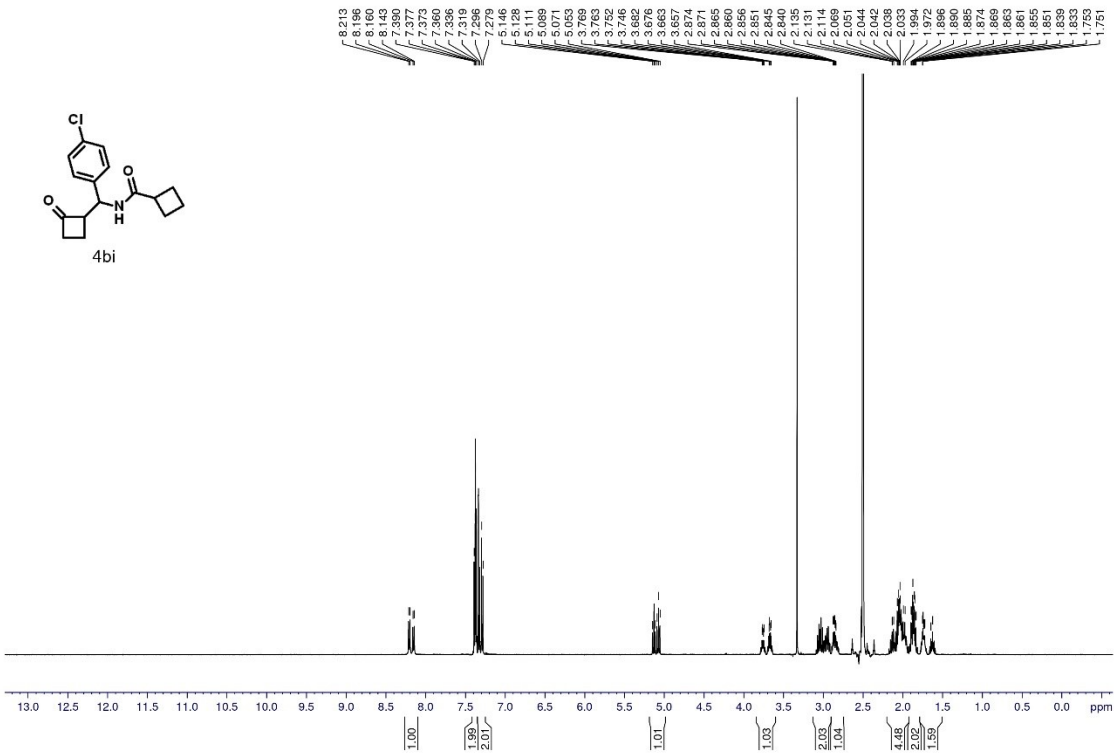
H
O
4bg
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4bh
8.659
8.642
8.592
8.575
7.402
7.391
7.385
7.374
7.352
7.335
7.315
7.298
5.165
5.148
5.130
5.109
5.091
5.073
3.787
3.781
3.770
3.765
3.719
3.714
3.700
3.695
3.004
2.983
2.969
2.947
2.874
2.855
2.066
2.055
2.044
2.034
2.022
1.901
1.880
1.626
1.610
0.669
0.604
13.0 12.5 12.0 11.5 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 ppm
1.00
4.00
1.00
0.99
2.00
3.00
4.00


4bh
208.0
207.7
172.2
171.9
140.7
140.4
131.6
131.5
128.9
128.7
128.2
128.1
63.9
63.2
51.2
50.6
44.1
40.1
14.2
13.9
13.5
13.5
6.5
6.5
6.4
6.4
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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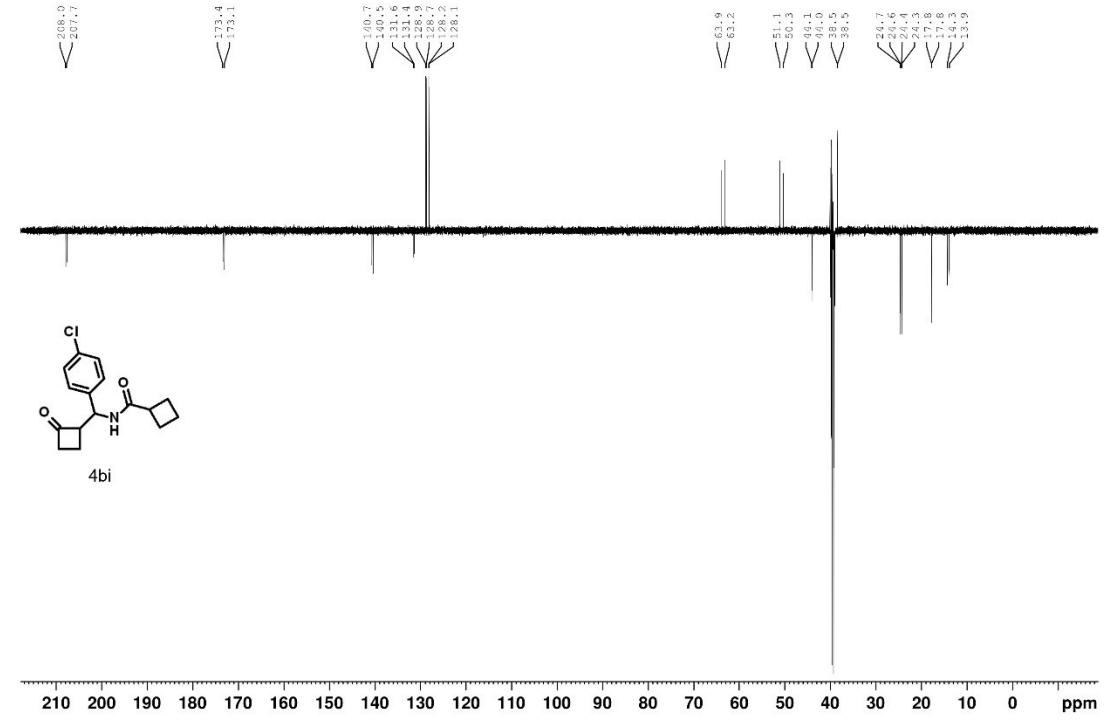
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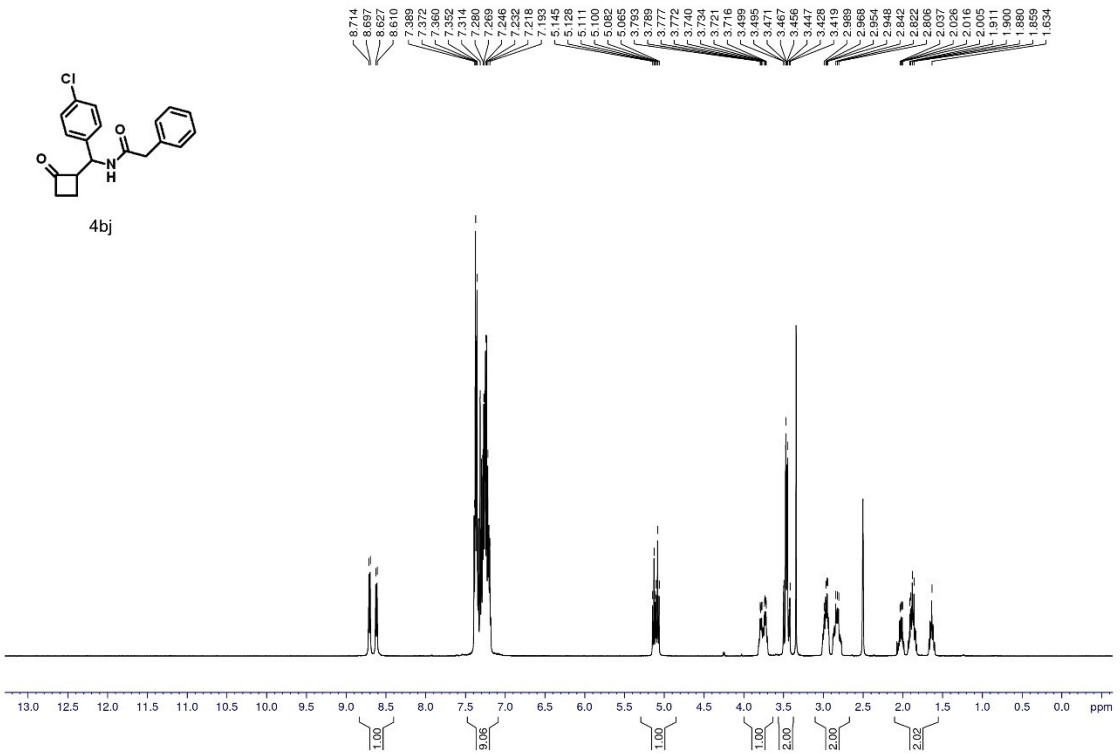
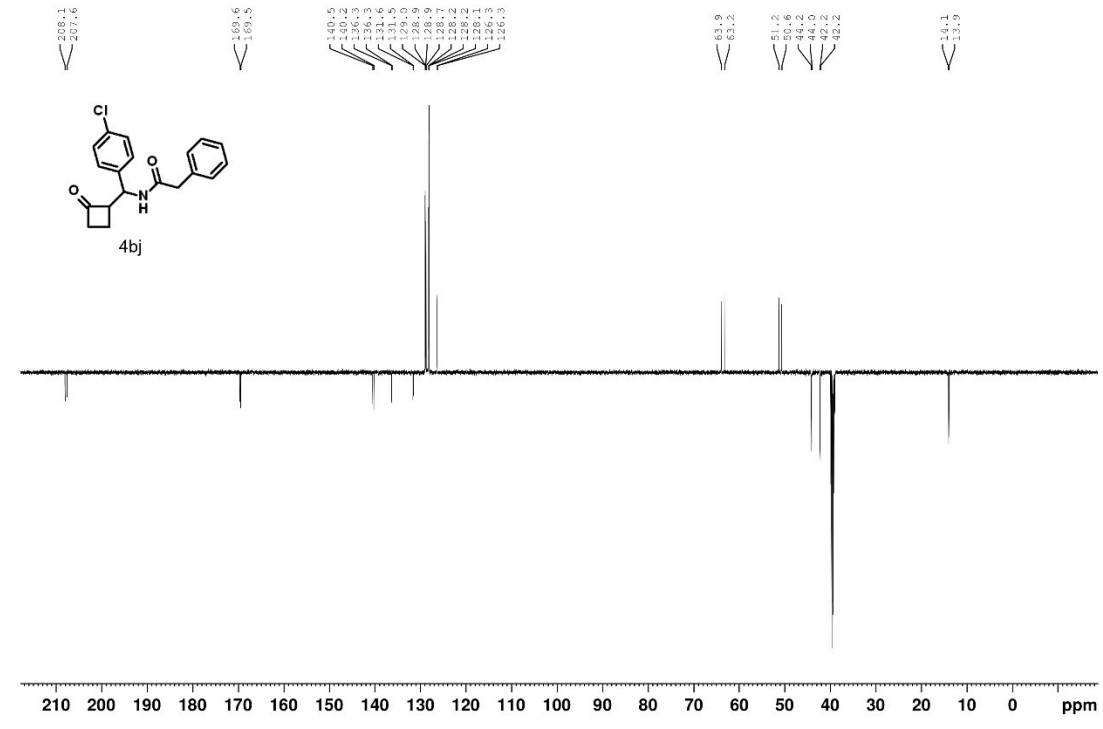
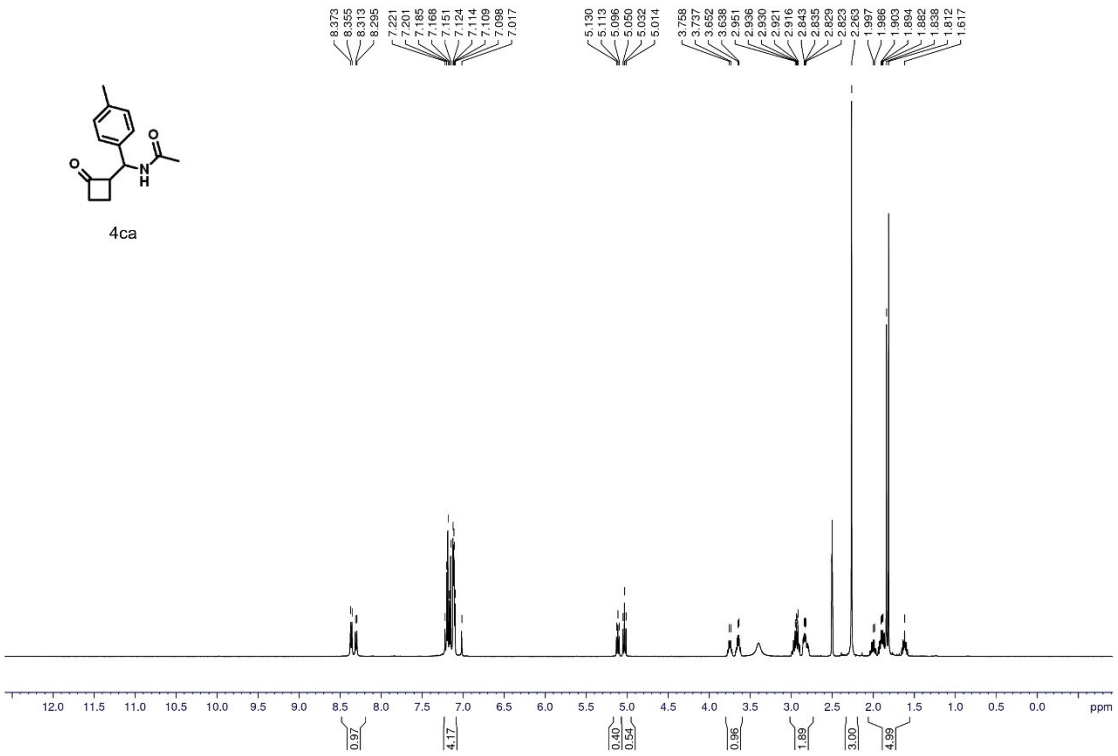
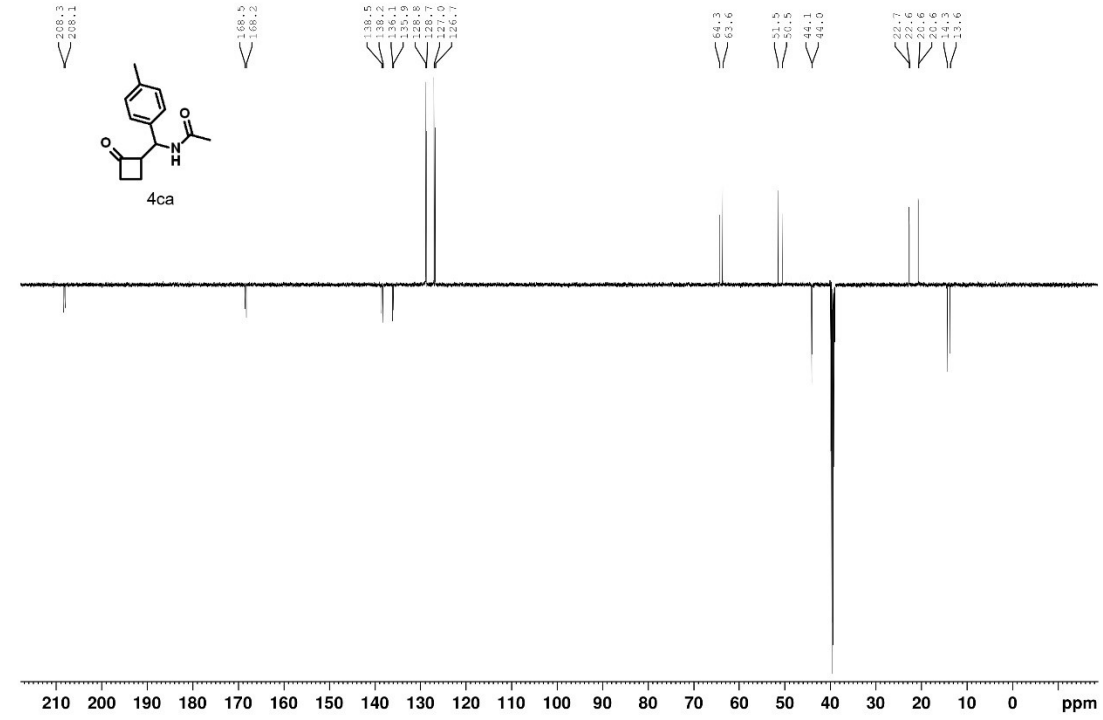
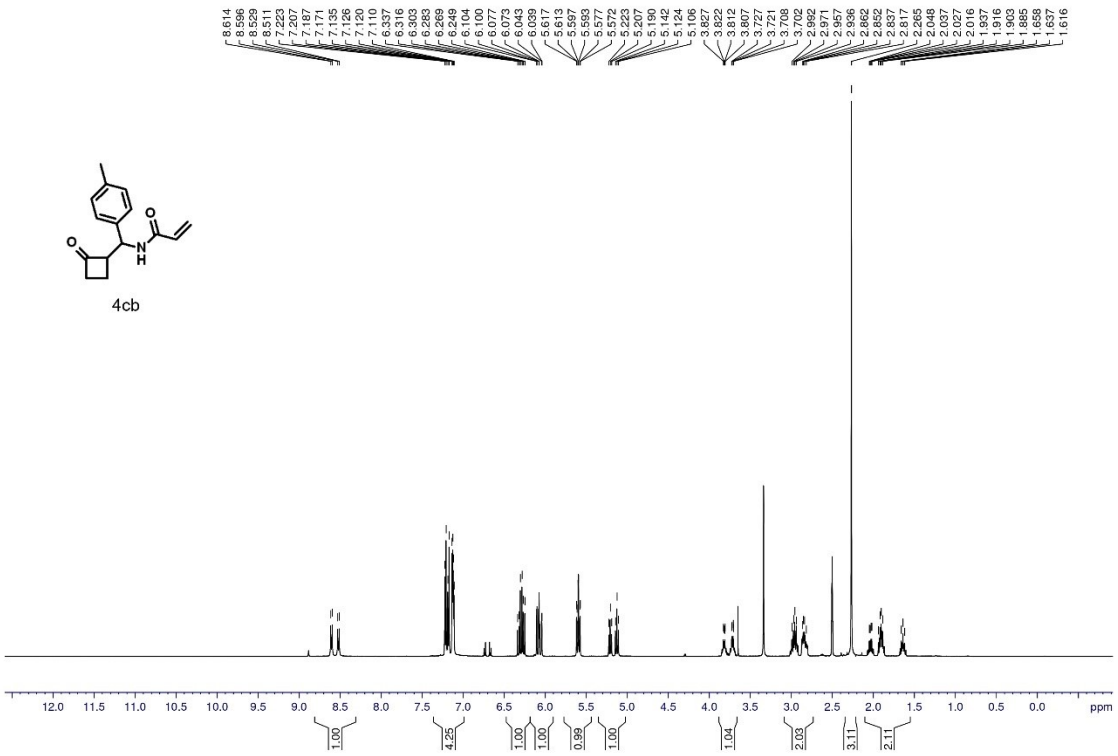

4bj
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.00 9.06 1.00 1.00 2.00 2.00 2.02


4bj
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.373
8.355
8.313
8.295
7.221
7.201
7.185
7.168
7.151
7.124
7.114
7.109
7.098
7.017
5.130
5.113
5.096
5.050
5.032
5.014
3.758
3.737
3.657
3.638
2.951
2.936
2.930
2.921
2.916
2.843
2.835
2.829
2.823
2.263
1.997
1.986
1.903
1.894
1.882
1.838
1.812
1.617
4ca
12.0 11.5 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 ppm
0.97
4.17
0.40
0.54
0.96
1.89
3.00
4.99


208.3
208.1
168.5
168.2
138.5
138.2
136.1
135.9
128.8
128.7
127.0
126.7
64.3
63.6
51.5
50.5
44.1
44.0
22.7
22.6
20.6
20.6
14.3
13.6
4ca
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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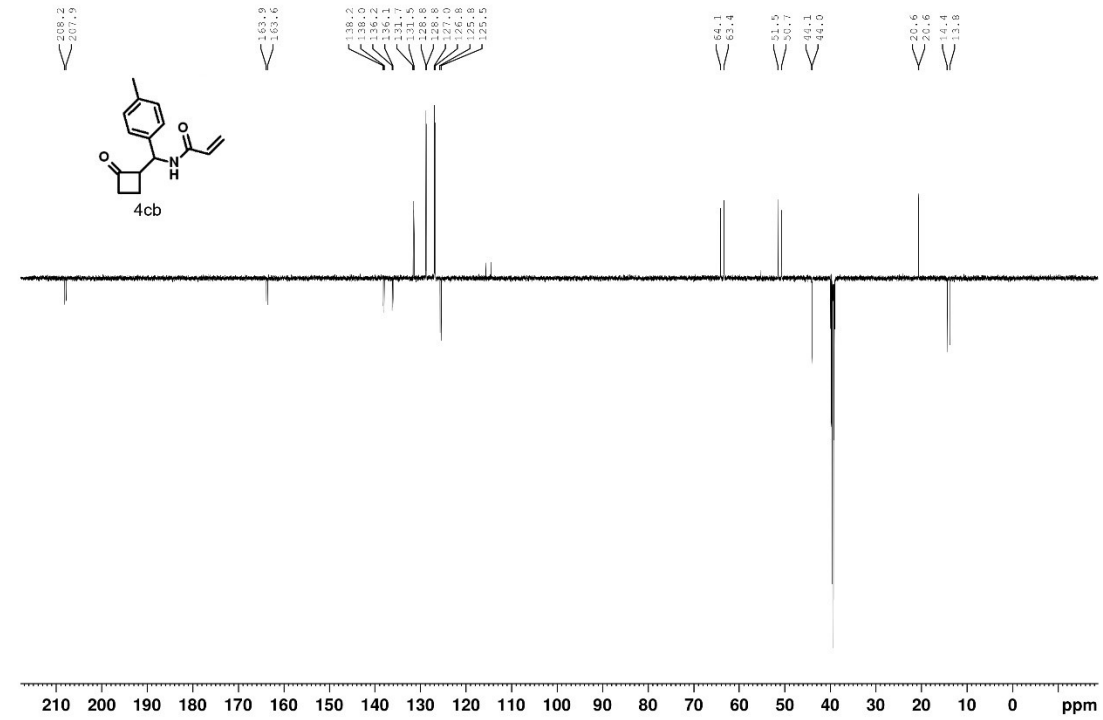
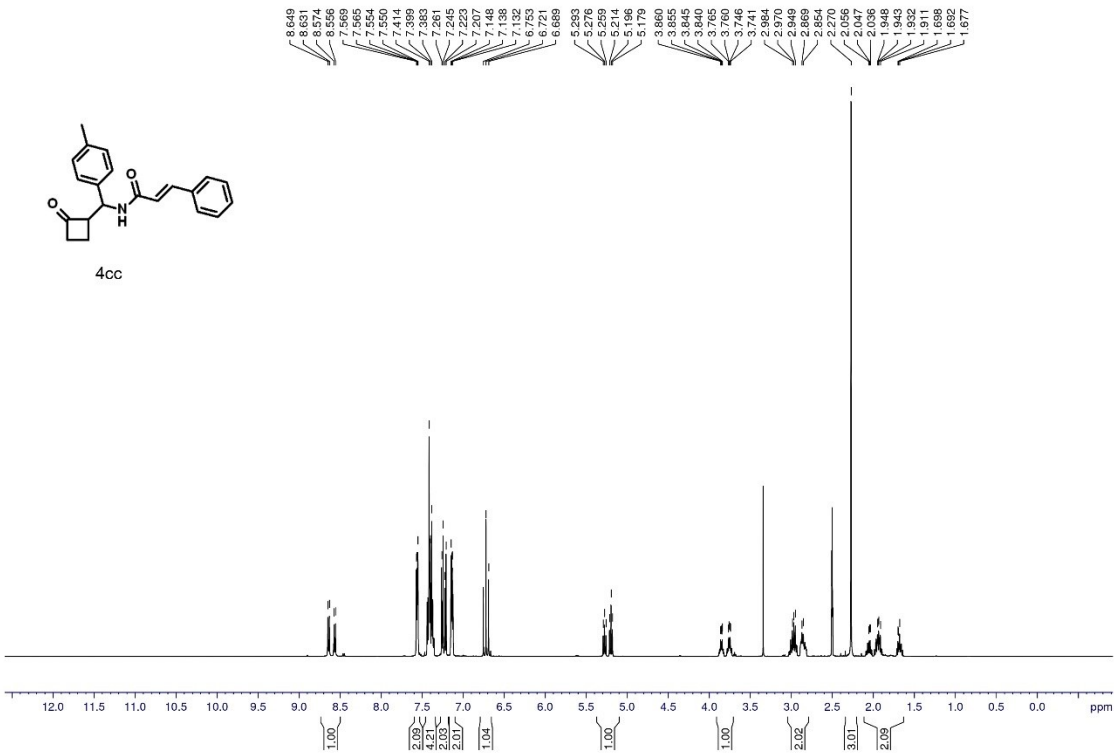
8.596
8.529
8.511
7.223
7.207
7.187
7.171
7.135
7.126
7.120
7.110
6.337
6.316
6.303
6.283
6.269
6.249
6.104
6.100
6.077
6.073
6.043
6.039
5.617
5.613
5.597
5.593
5.577
5.572
5.223
5.207
5.190
5.142
5.124
5.106
3.827
3.822
3.812
3.807
3.727
3.721
3.708
3.702
2.992
2.971
2.957
2.936
2.862
2.852
2.837
2.817
2.265
2.048
2.037
2.027
2.016
1.937
1.916
1.903
1.885
1.658
1.637
1.616
4cb
12.0 11.5 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 ppm
1.00
4.25
1.00
1.00
0.99
1.00
1.04
2.03
3.11
2.11


208.2
207.9
163.9
163.6
138.2
138.0
136.2
136.1
131.7
131.5
128.8
128.8
127.0
126.8
125.8
125.5
64.1
63.4
51.5
50.7
44.1
44.0
20.6
20.6
14.4
13.8
4cb
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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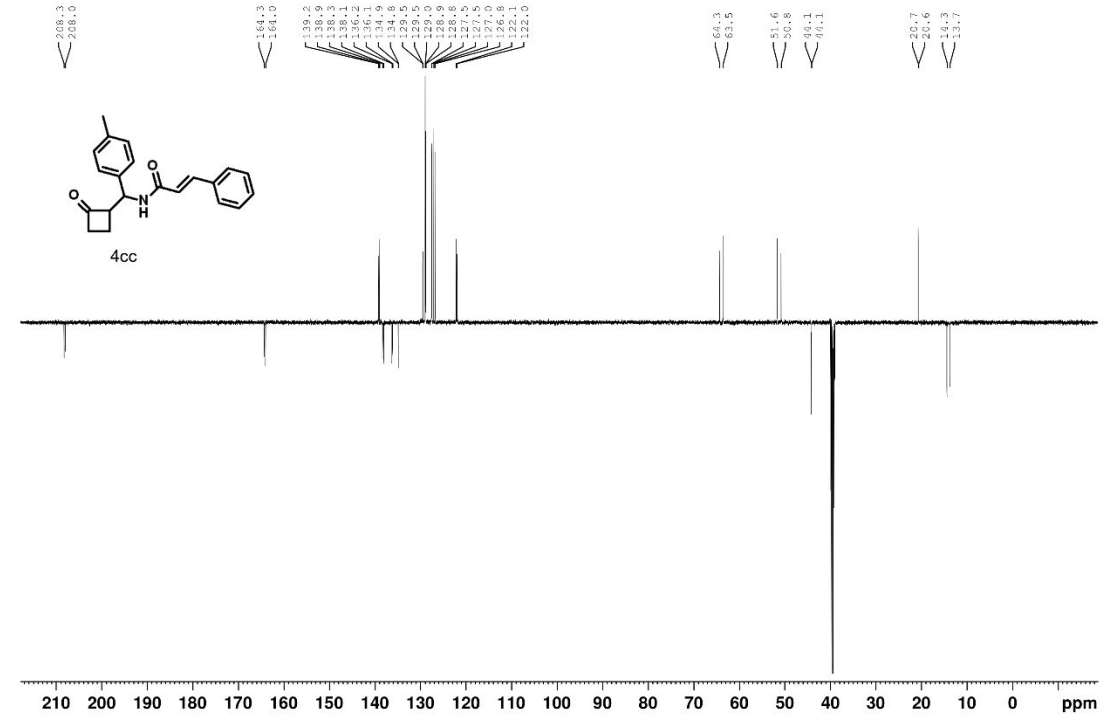
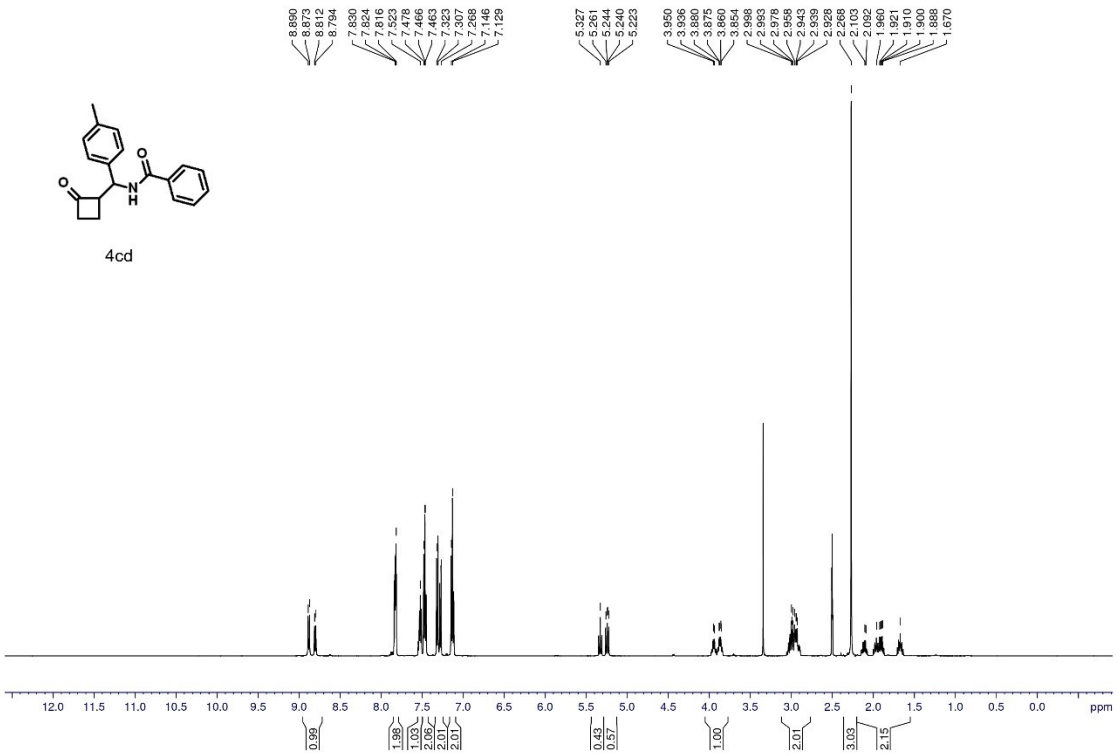

4cc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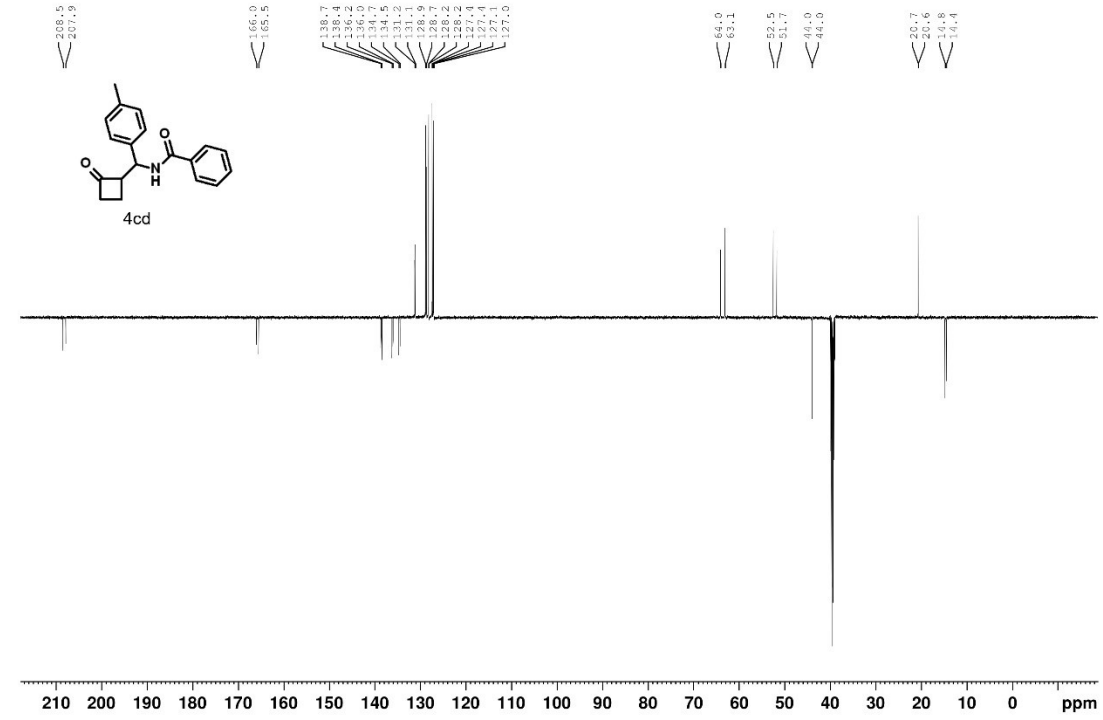
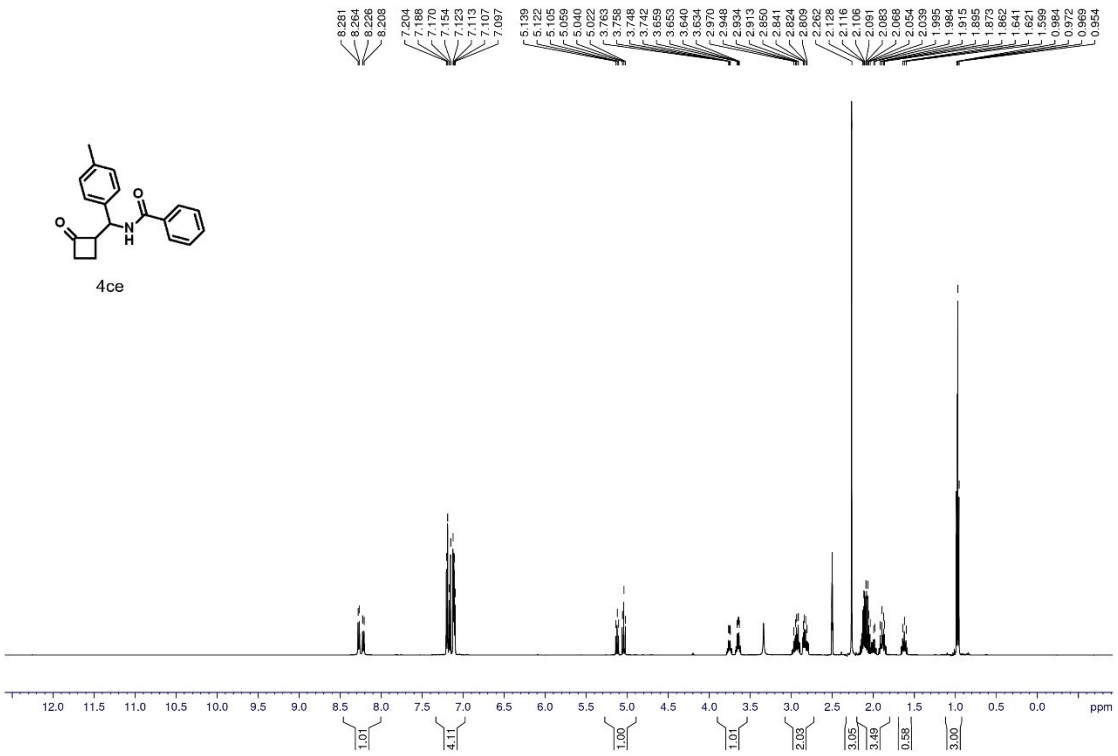
8.873
8.812
8.794
7.830
7.824
7.816
7.523
7.478
7.466
7.463
7.323
7.307
7.288
7.146
7.129
5.327
5.261
5.244
5.240
5.223
3.950
3.936
3.880
3.875
3.860
3.854
2.998
2.993
2.978
2.958
2.943
2.939
2.928
2.268
2.103
2.092
1.960
1.921
1.910
1.900
1.898
1.670
4cd
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 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 ppm
0.99
1.98
1.03
2.06
2.01
2.01
0.43
0.57
1.00
2.01
3.03
2.15


208.5
207.9
166.0
165.5
138.7
138.4
136.2
136.0
134.7
134.5
131.2
131.1
128.9
128.7
128.2
128.2
127.4
127.4
127.1
127.0
64.0
63.1
52.5
51.7
44.0
44.0
20.7
20.6
14.8
14.4
4cd
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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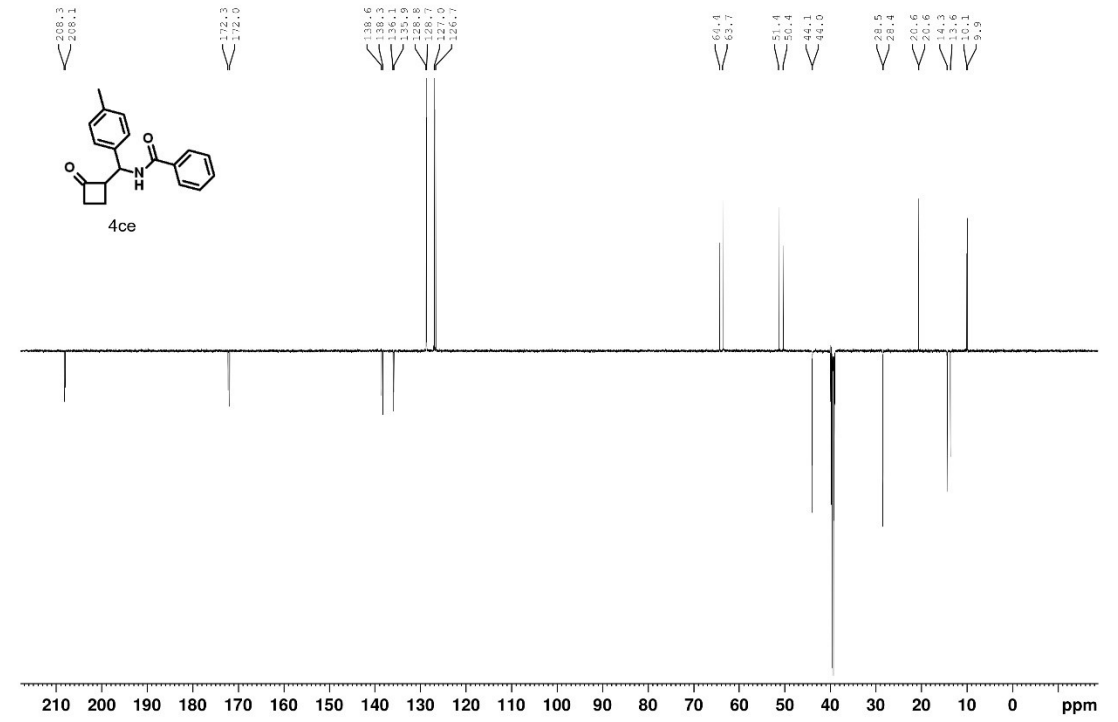
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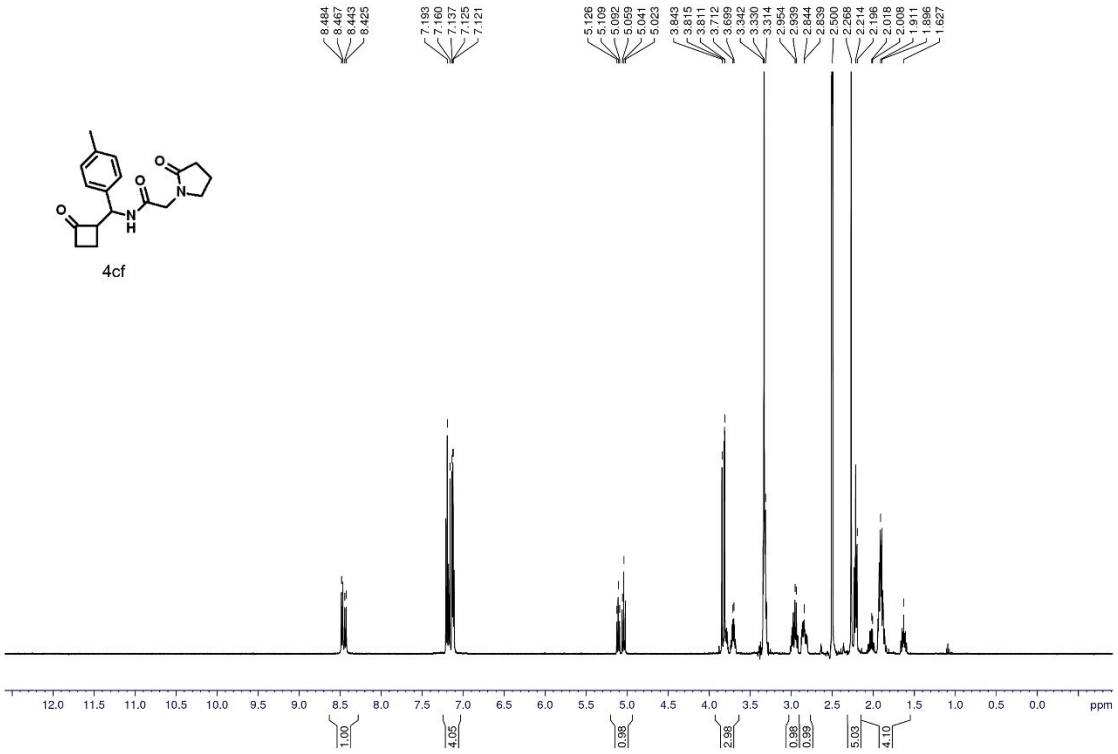
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8.443
8.425
7.193
7.160
7.137
7.125
7.121
5.126
5.109
5.092
5.059
5.041
5.023
3.843
3.815
3.811
3.712
3.699
3.342
3.330
3.314
2.954
2.939
2.844
2.839
2.500
2.268
2.214
2.196
2.018
2.008
1.911
1.896
1.627
4cf
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 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 ppm
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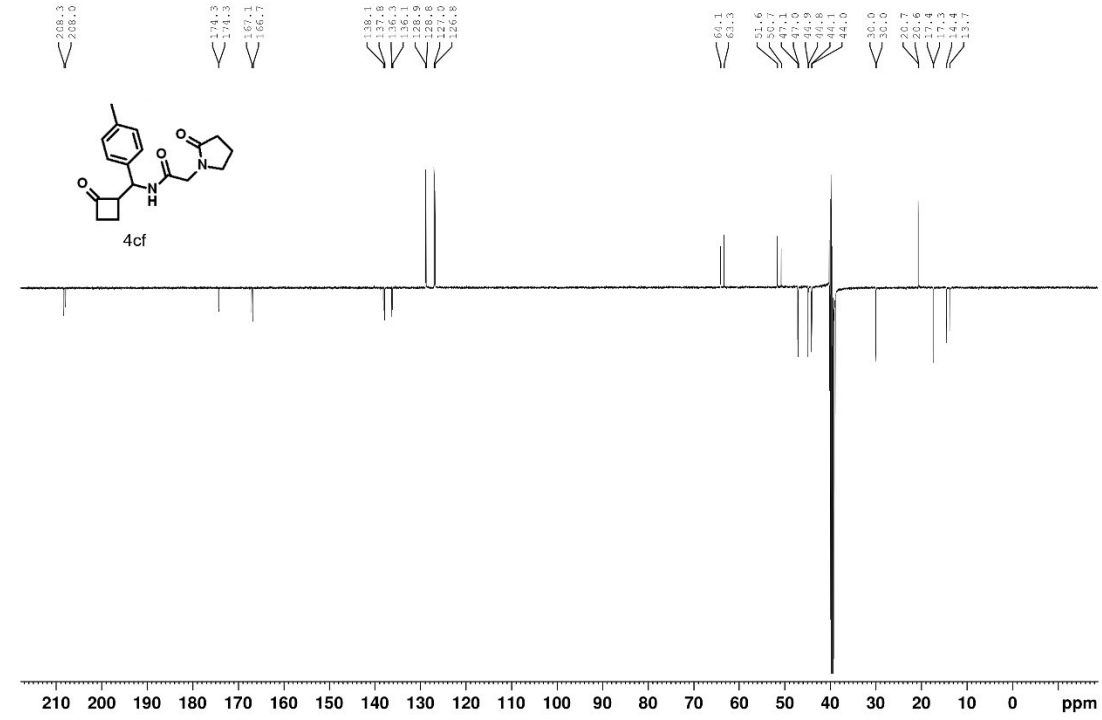
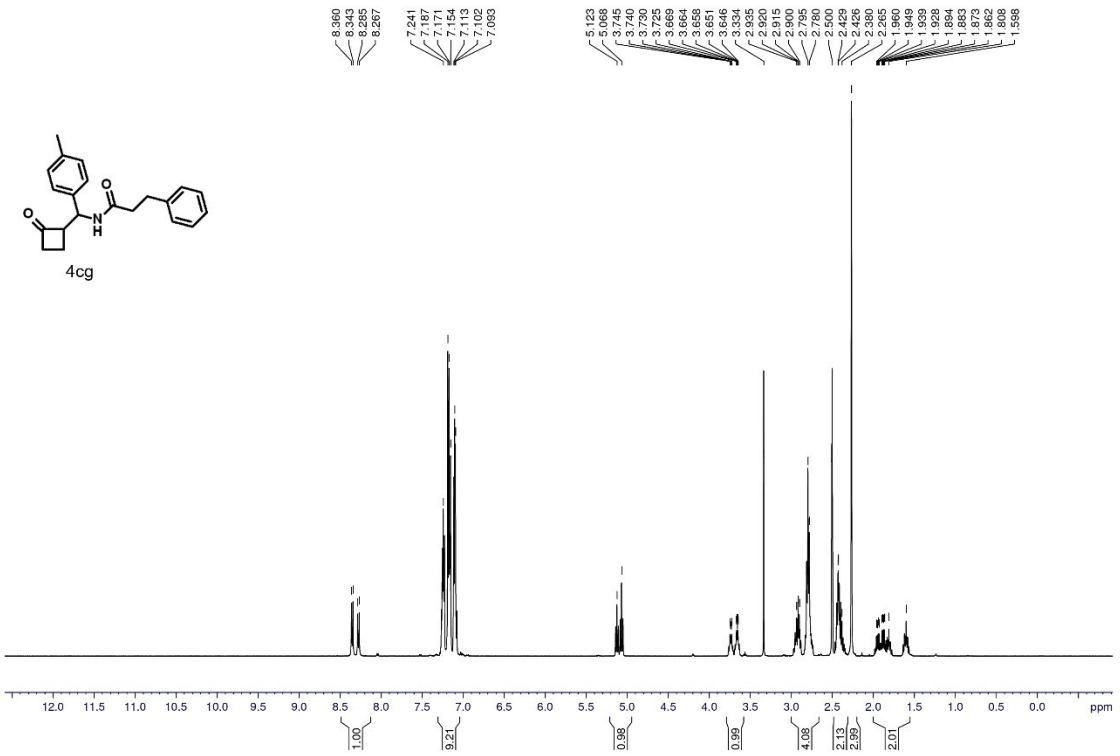
4.05
0.98
2.98
0.98
0.98
5.03
4.10


208.3
208.0
174.3
174.3
167.1
166.7
138.1
137.8
136.3
136.1
128.9
128.8
127.0
126.8
60.1
63.3
51.6
50.7
47.1
47.0
46.9
46.8
44.1
44.0
30.0
30.0
20.7
20.6
17.4
17.3
14.4
13.7
4cf
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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8.343
8.285
8.267
7.241
7.187
7.171
7.154
7.113
7.102
7.093
5.123
5.068
3.745
3.740
3.730
3.725
3.669
3.664
3.658
3.651
3.646
3.334
2.935
2.920
2.915
2.900
2.795
2.780
2.500
2.429
2.426
2.380
2.265
1.960
1.949
1.939
1.928
1.884
1.853
1.873
1.862
1.808
1.598
4cg
12.0 11.5 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 ppm
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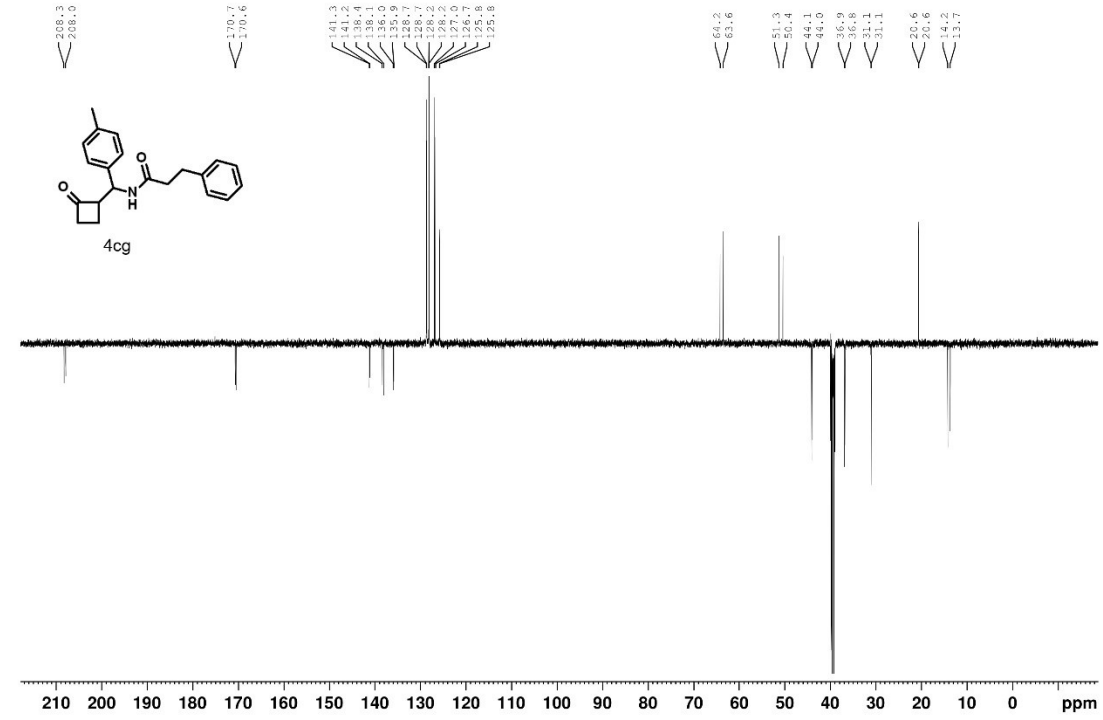
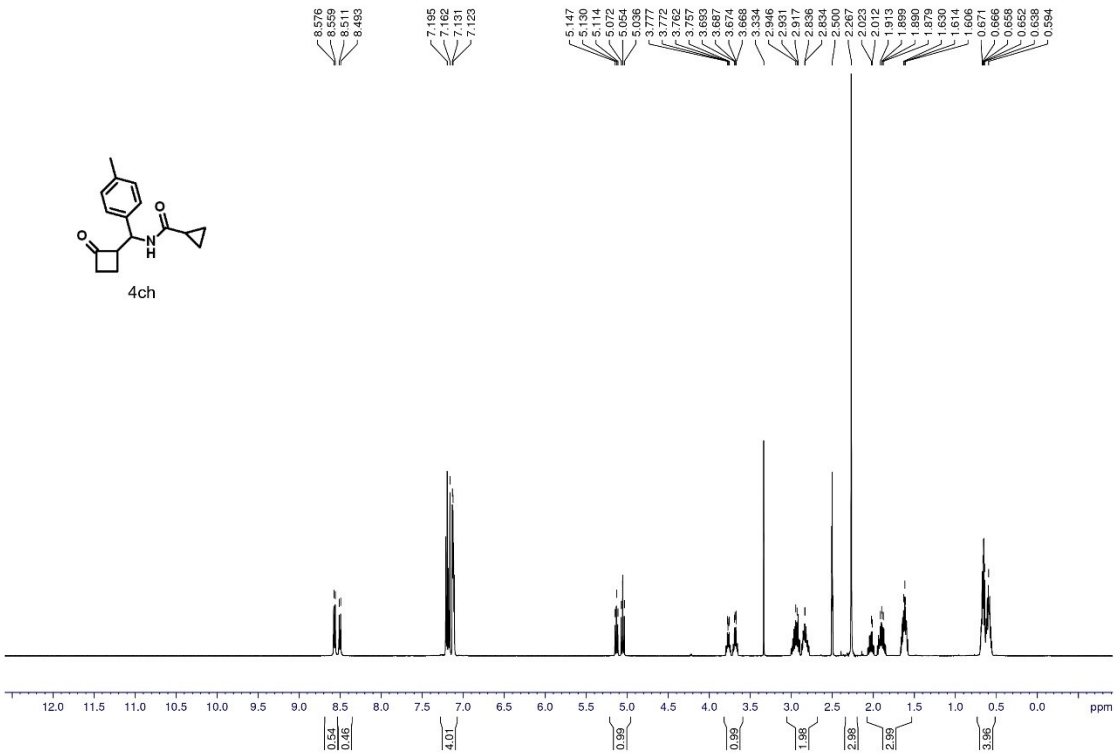
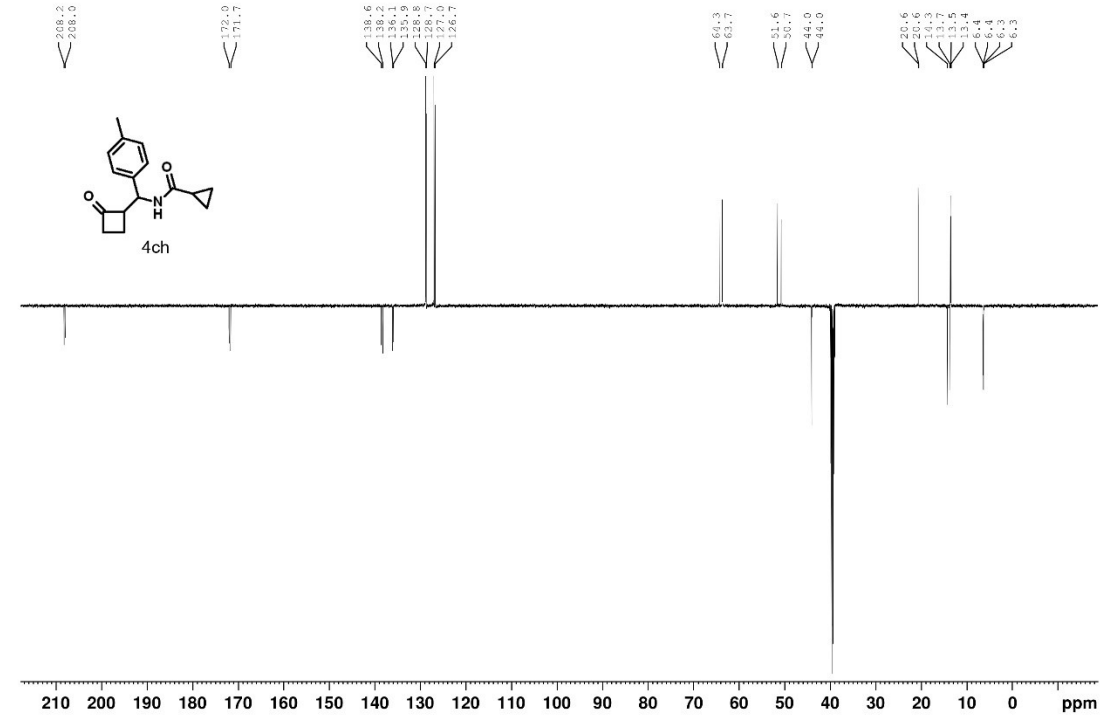
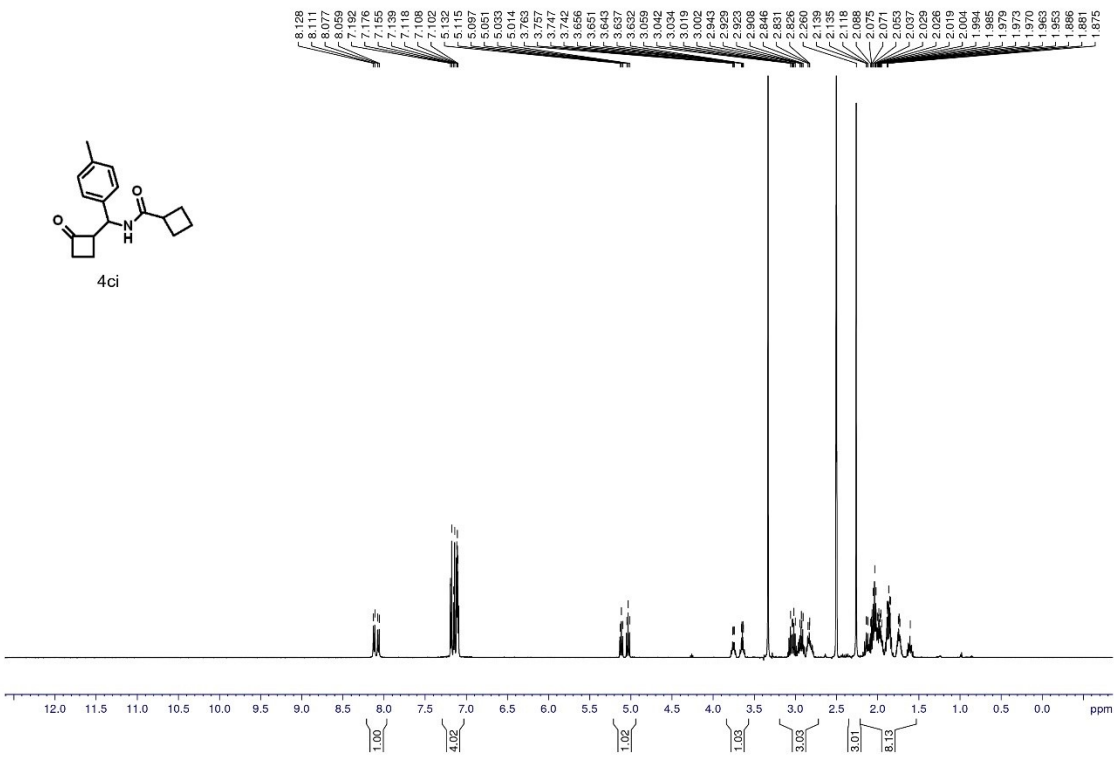
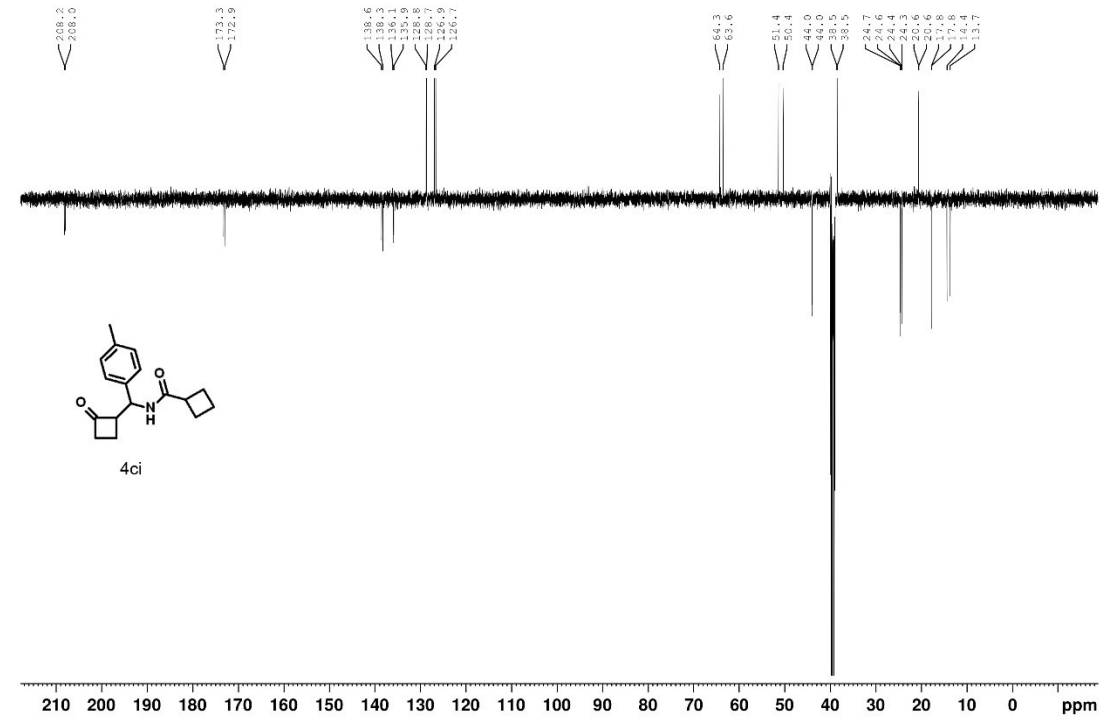
9.21
0.98
0.99
4.06
2.13
2.99
2.01

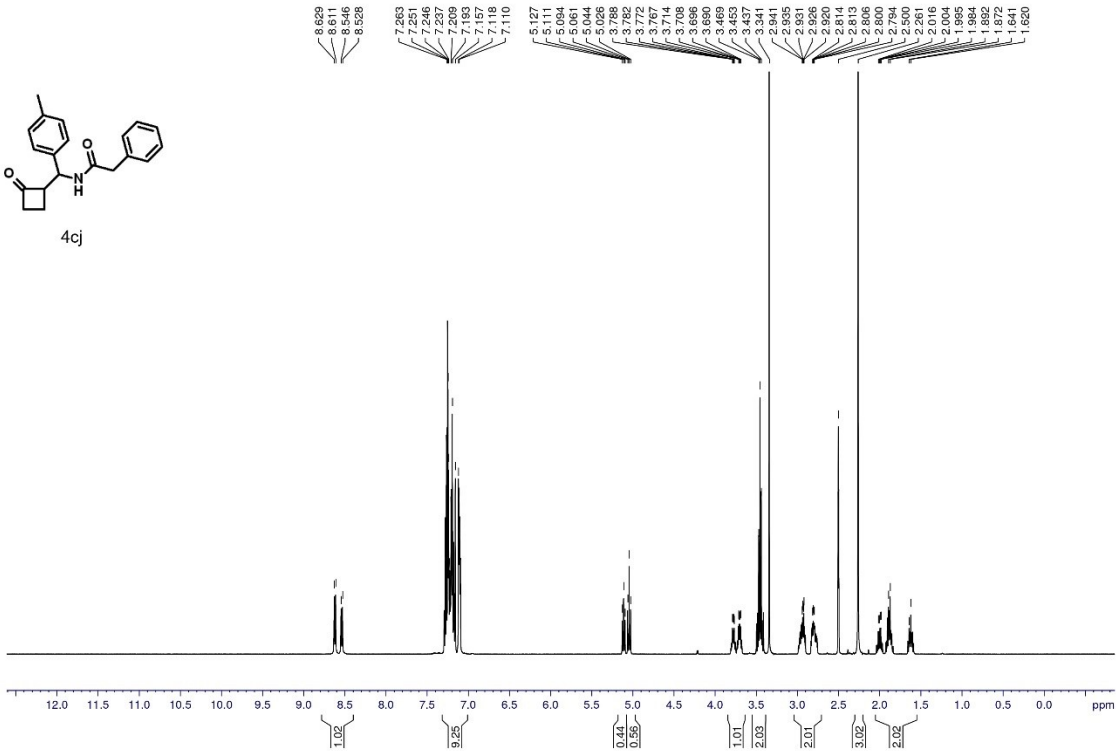

208.3
208.0
170.7
170.6
141.3
141.2
138.4
138.1
136.0
135.9
128.7
128.7
128.2
128.2
127.0
126.7
125.8
125.8
64.2
63.6
51.3
50.4
44.1
44.0
36.9
36.8
31.1
31.1
20.6
20.6
14.2
13.7
4cg
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.576
8.559
8.511
8.493
7.195
7.162
7.131
7.123
5.147
5.130
5.114
5.072
5.054
5.036
3.777
3.772
3.762
3.757
3.693
3.687
3.674
3.668
3.334
2.946
2.931
2.917
2.836
2.834
2.560
2.267
2.023
2.012
1.913
1.899
1.890
1.879
1.630
1.614
1.606
0.671
0.666
0.658
0.652
0.638
0.594
4ch
12.0 11.5 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 ppm
0.54
0.46
4.01
0.99
0.99
1.98
2.98
2.99
3.96


208.2
208.0
172.0
171.7
138.6
138.2
136.1
135.9
128.8
128.7
127.0
126.7
64.3
63.7
51.6
50.7
44.0
44.0
20.6
20.6
14.3
13.7
13.5
13.4
6.4
6.4
6.3
6.3
4ch
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


4ci
ppm


4ci
ppm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8.528
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7.237
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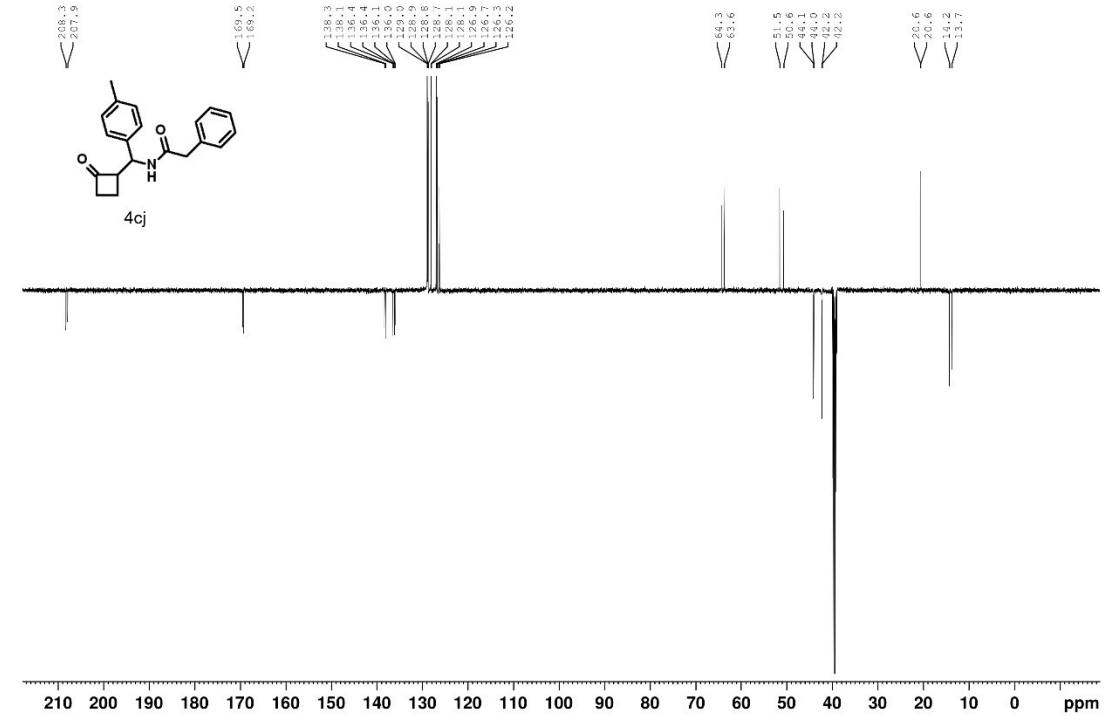
7.193
7.157
7.118
7.110
5.127
5.111
5.094
5.061
5.044
5.026
4.788
3.782
3.772
3.767
3.714
3.708
3.696
3.690
3.469
3.453
3.437
3.341
2.941
2.935
2.931
2.926
2.920
2.814
2.813
2.806
2.800
2.794
2.500
2.261
2.016
2.004
1.995
1.984
1.892
1.872
1.641
1.620
4cj
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 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 ppm
1.02
9.25
0.44
0.56
1.01
2.03
2.01
3.02
2.02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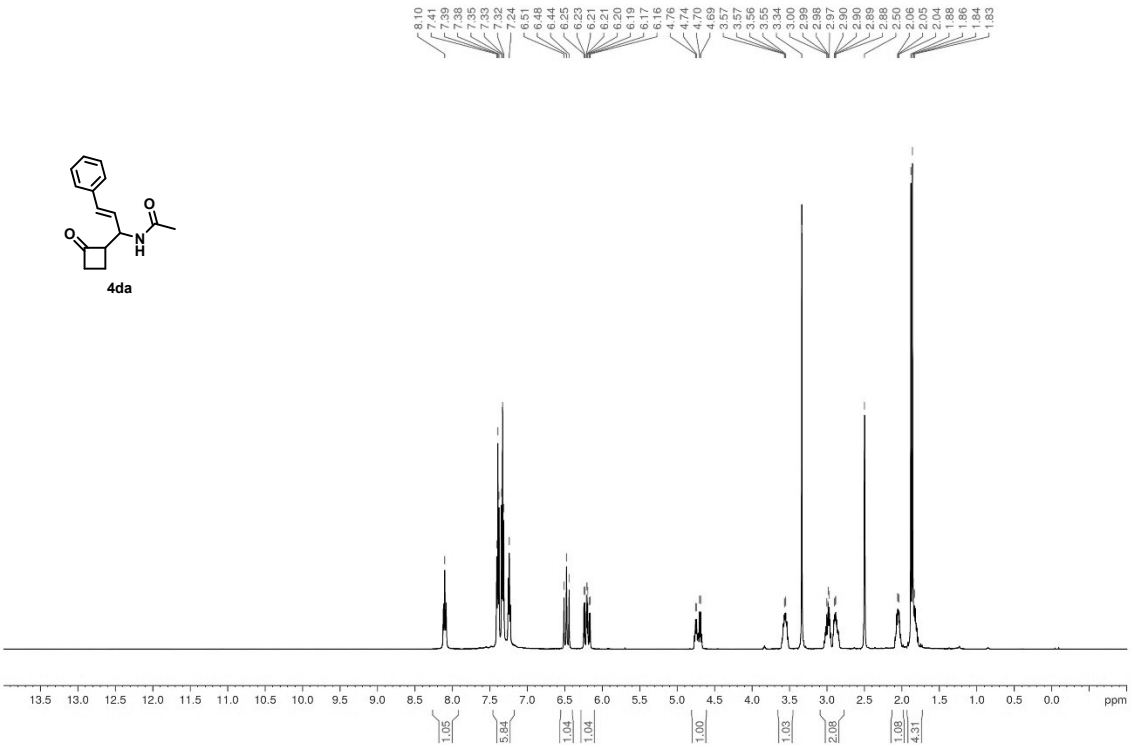
207.9
169.5
169.2
138.3
138.1
136.4
136.4
136.1
136.1
129.0
128.9
128.8
128.7
128.1
128.1
126.9
126.7
126.3
126.2
64.3
63.6
51.5
50.6
44.1
44.0
42.2
42.2
20.6
20.6
14.2
13.7
4cj
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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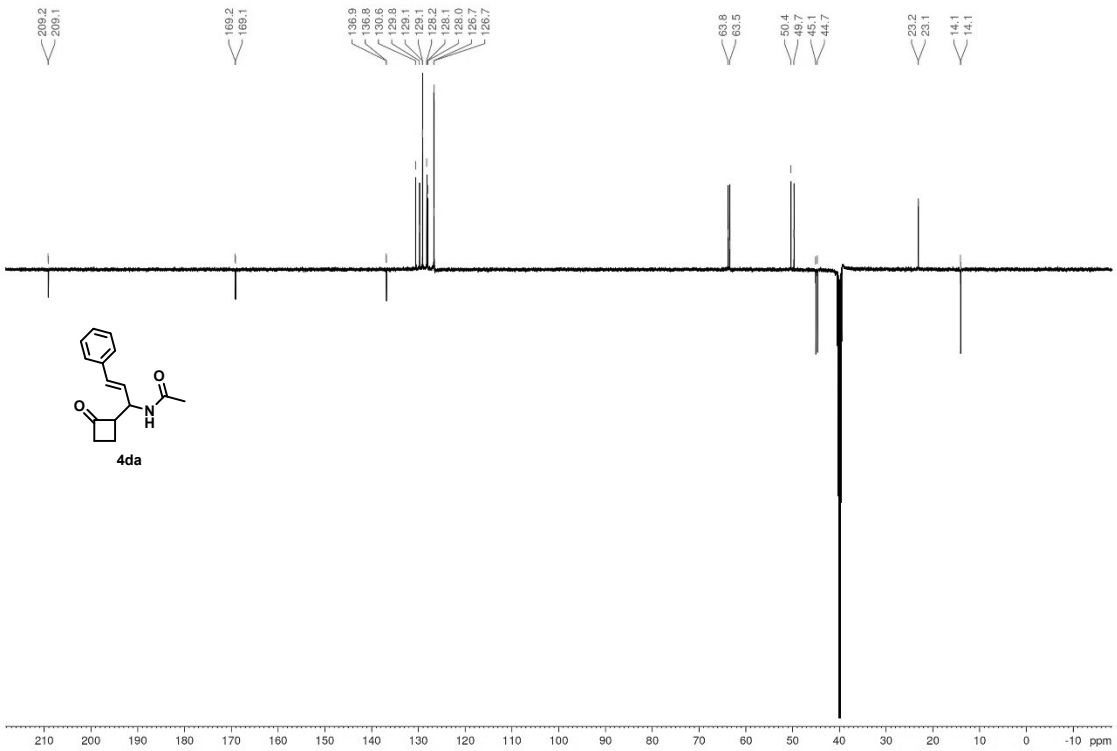
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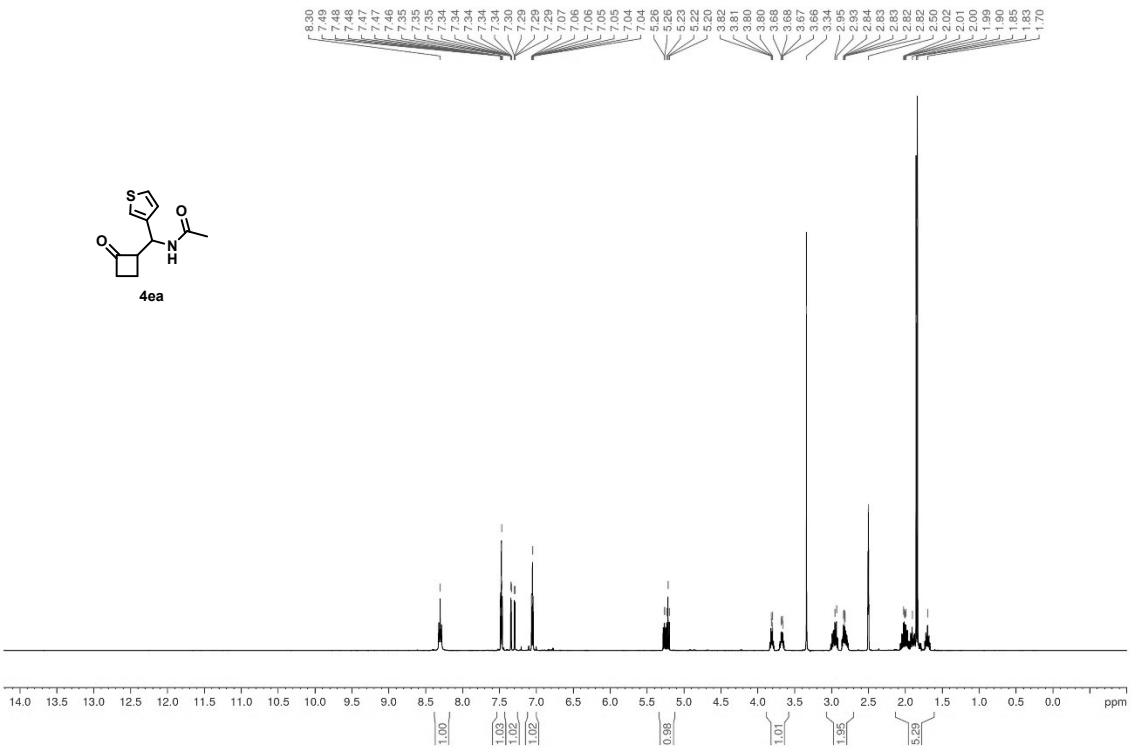
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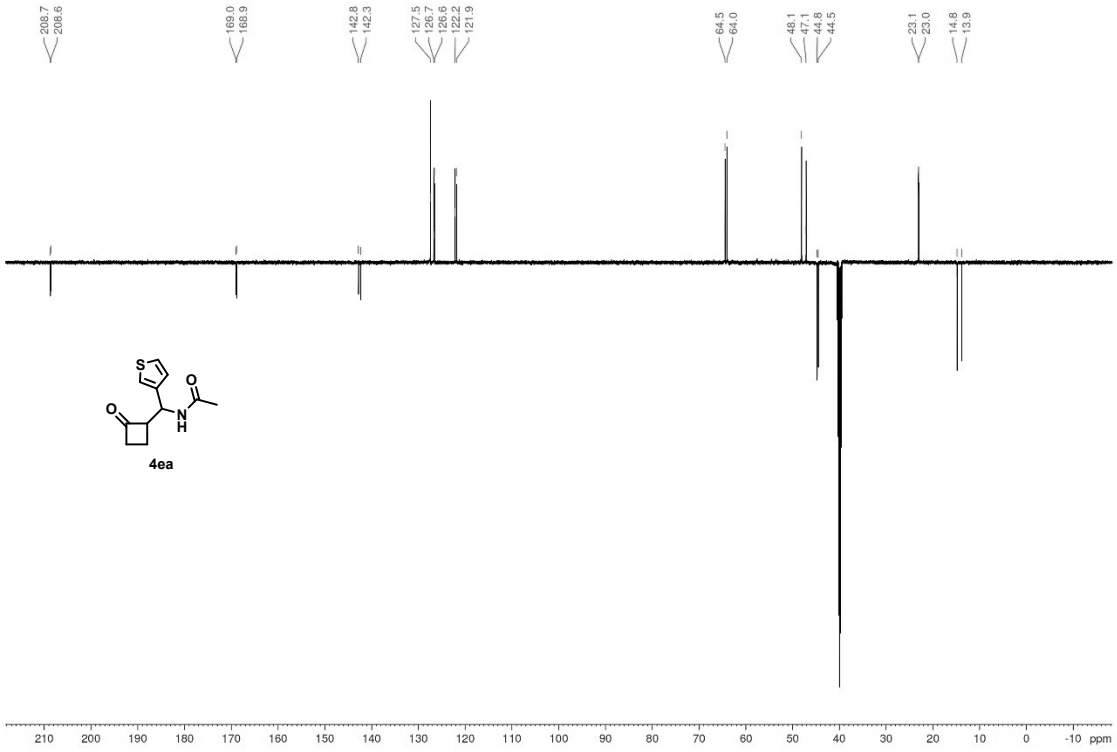
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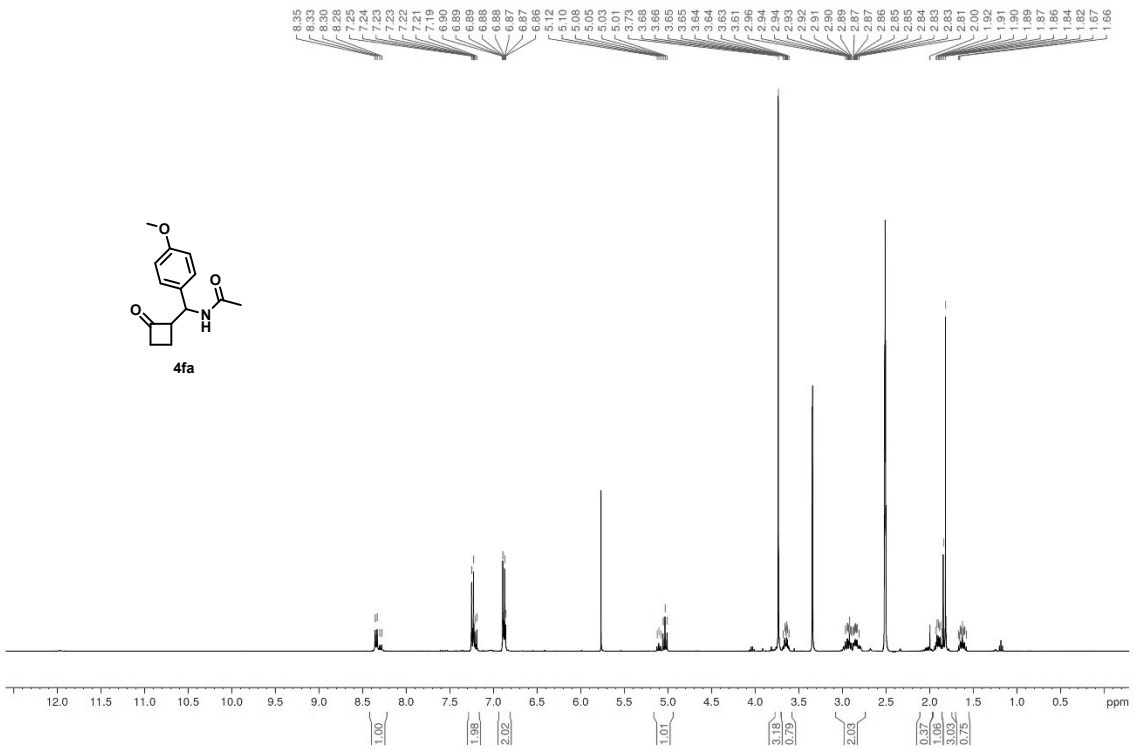
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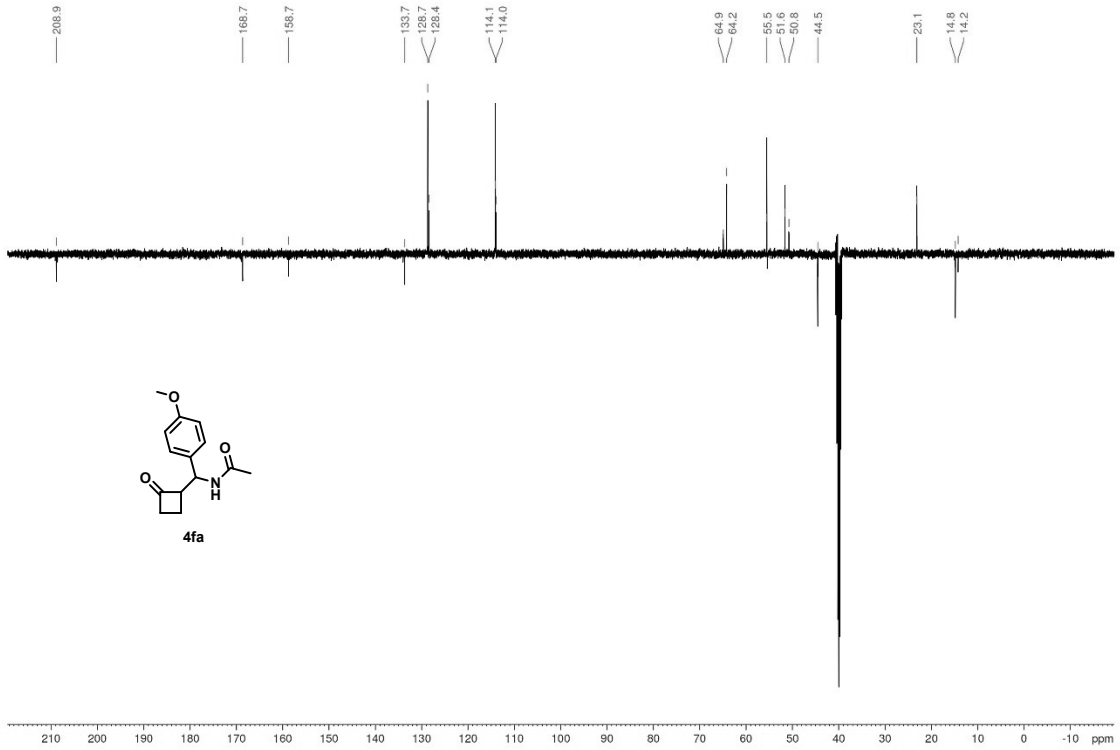
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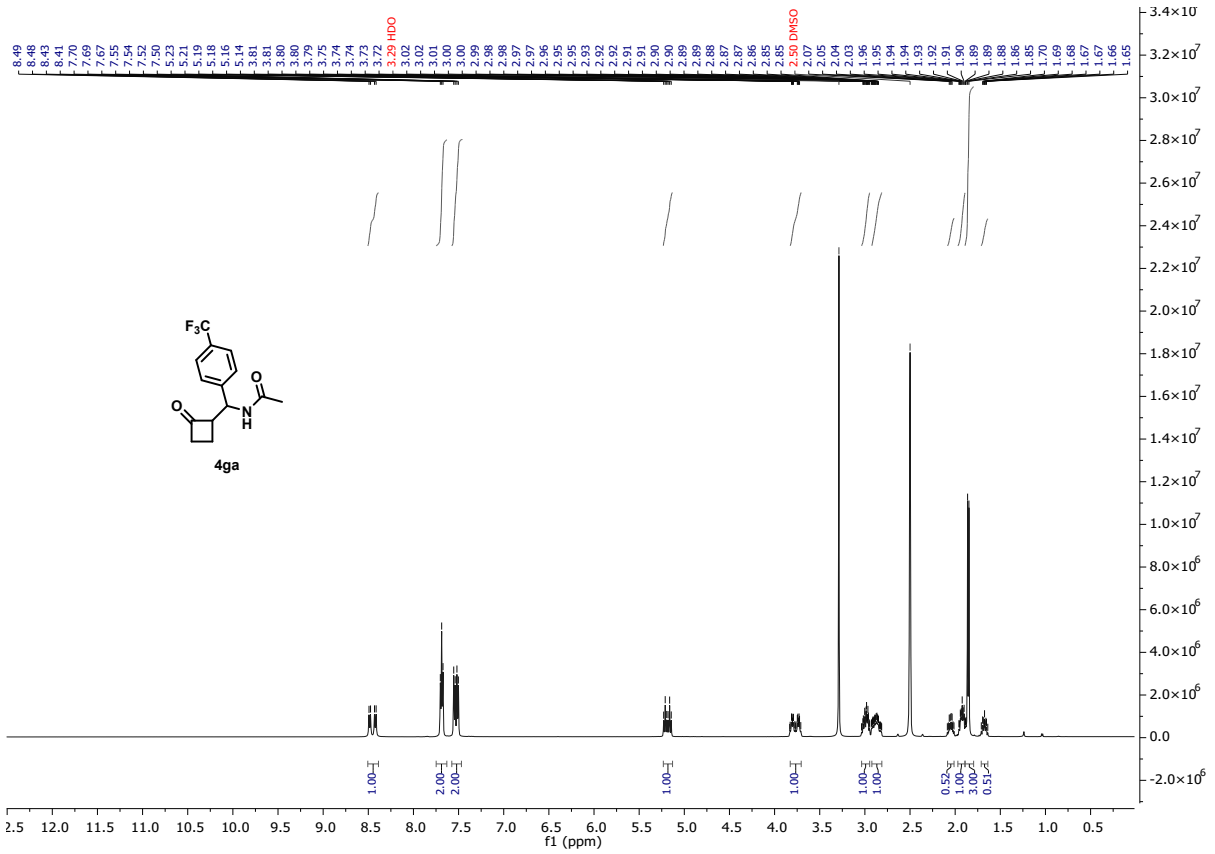
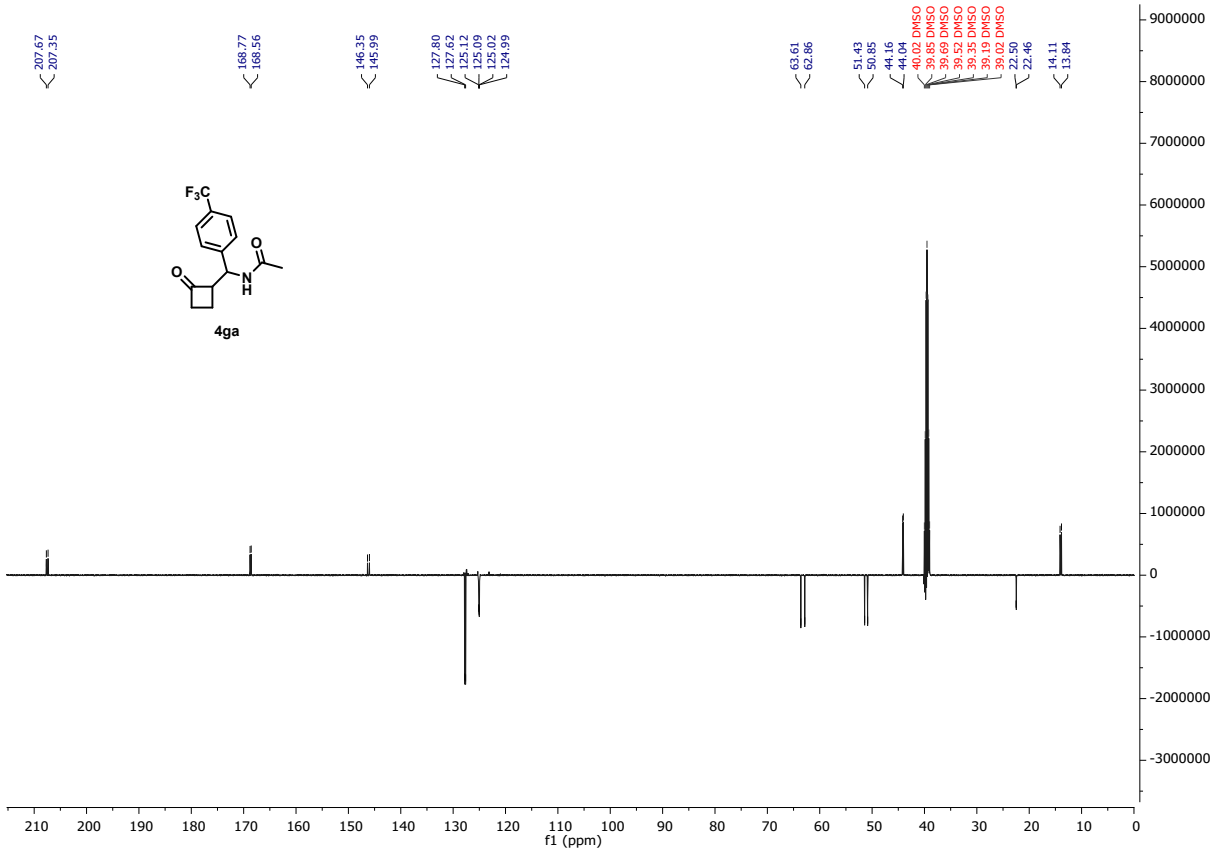
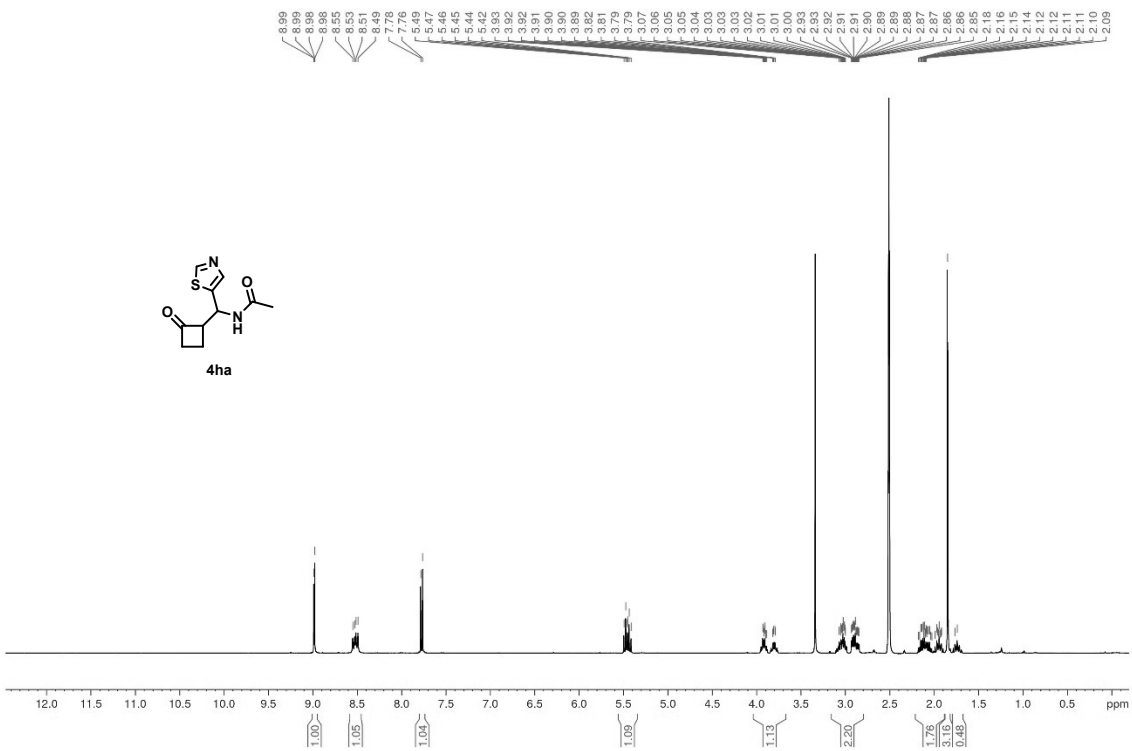
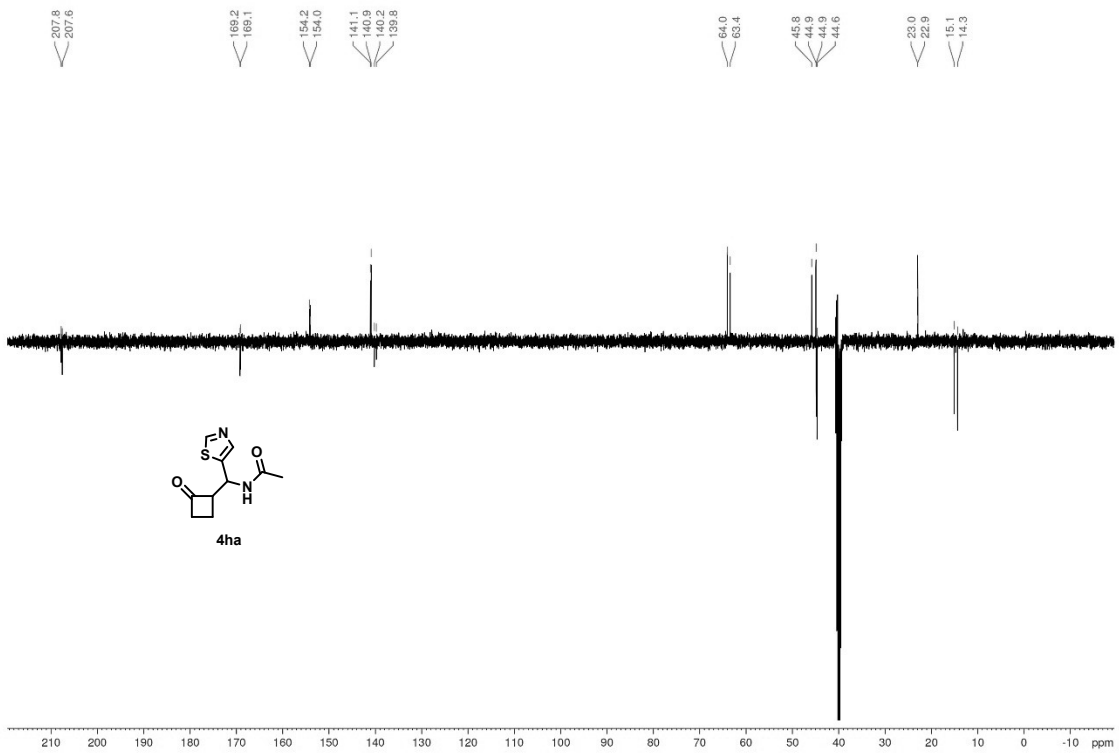
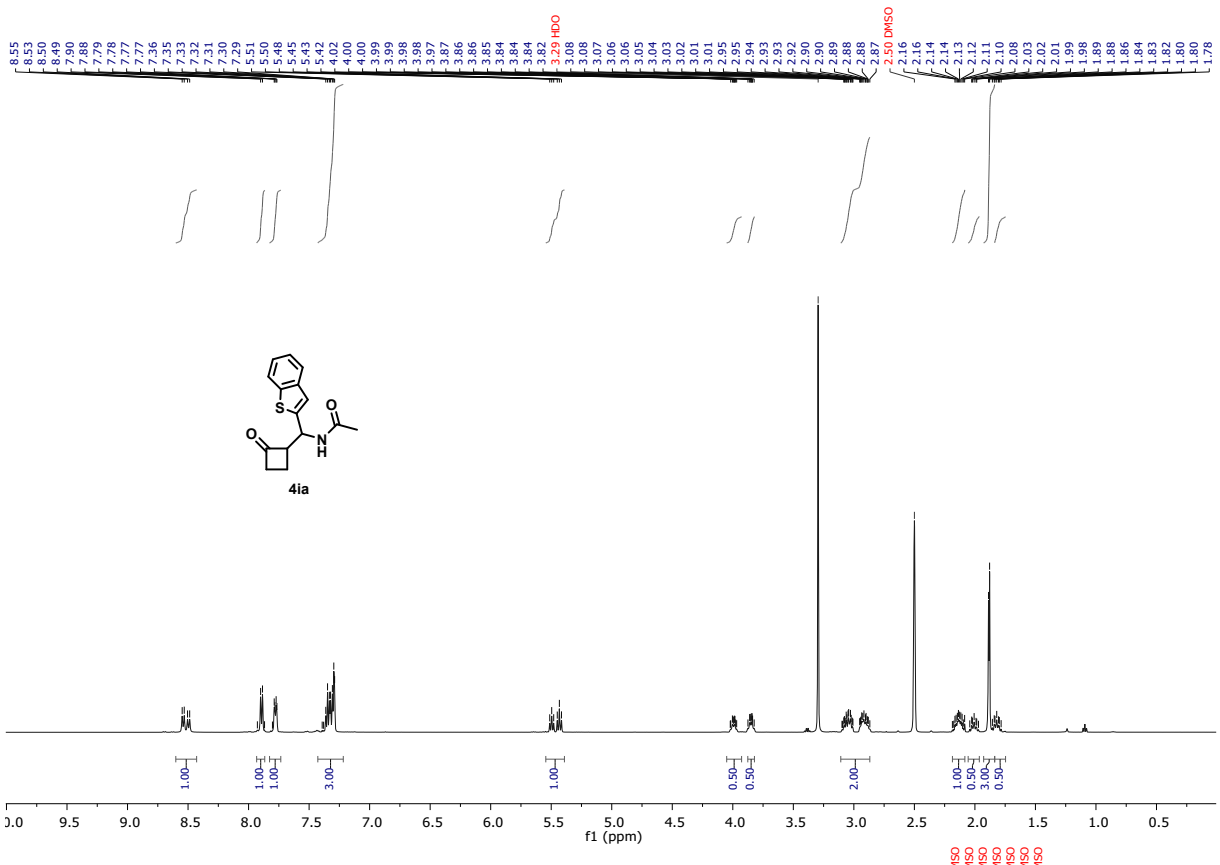
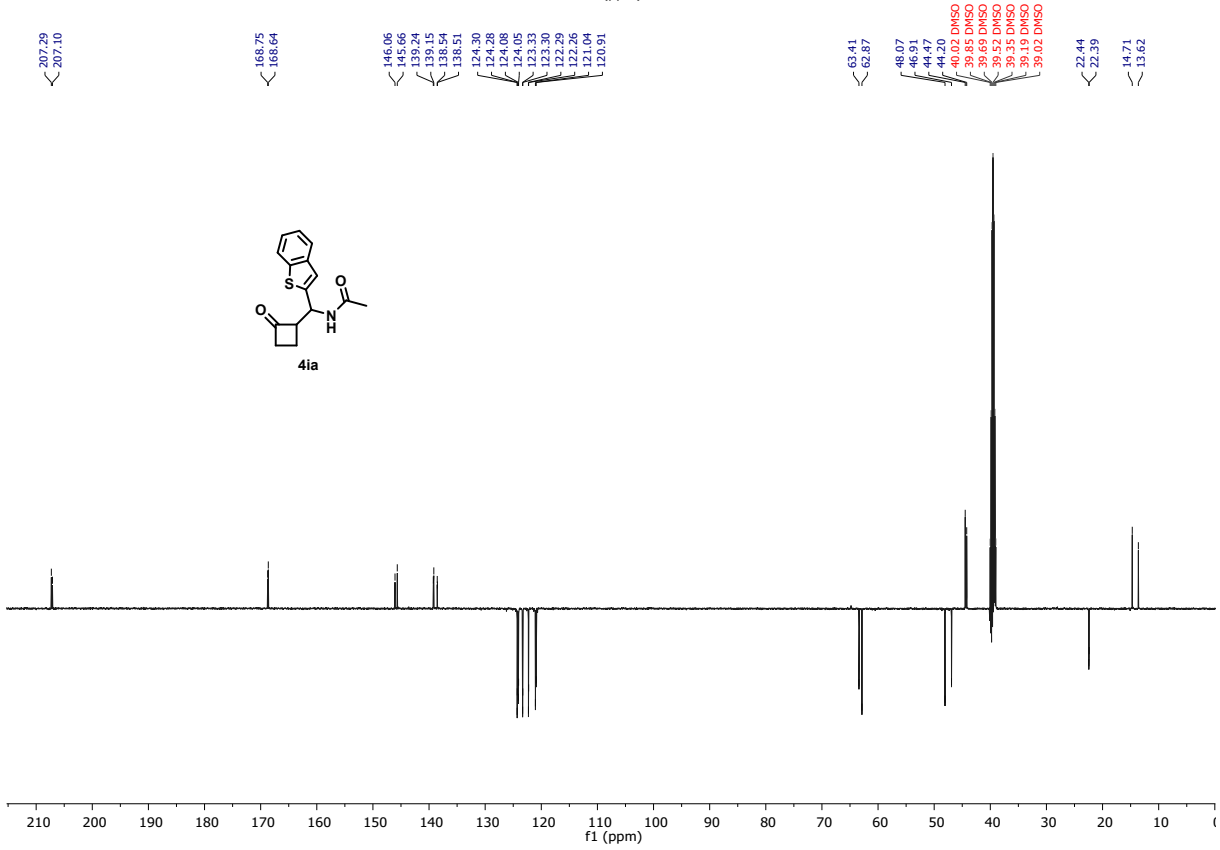

4ga
f1 (ppm)

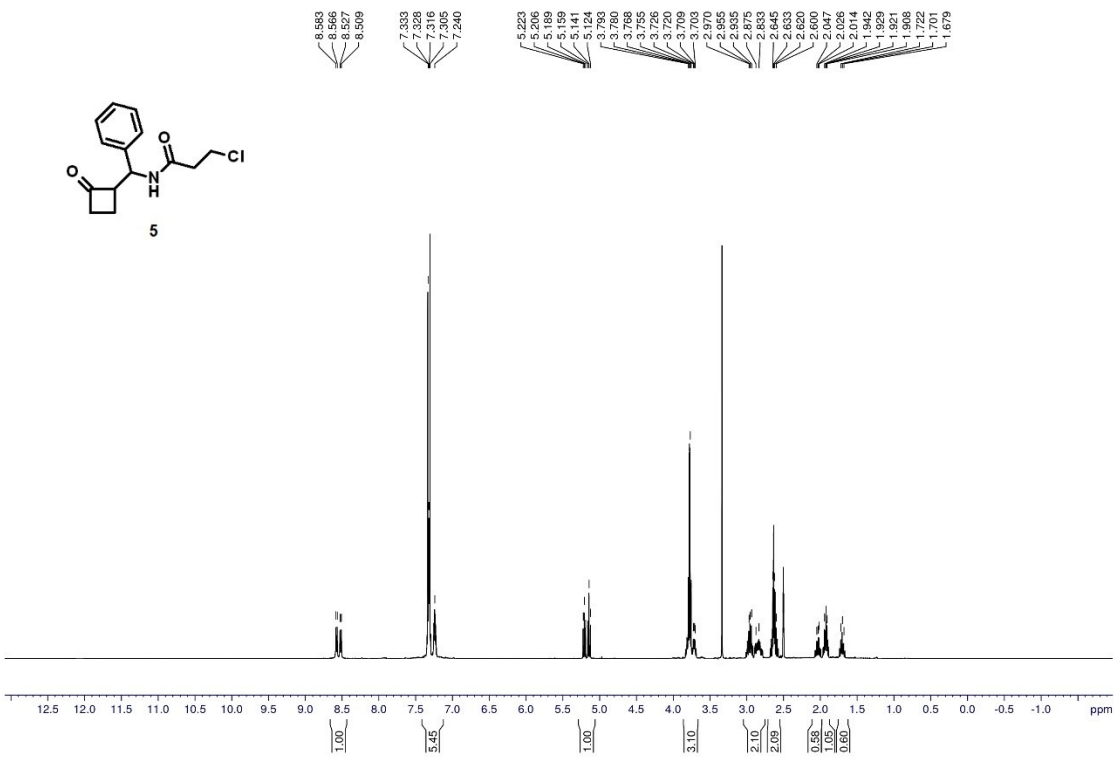

4ga
f1 (ppm)


4ha


4ha


4ia
f1 (ppm)


4ia
f1 (ppm)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8.527
8.509
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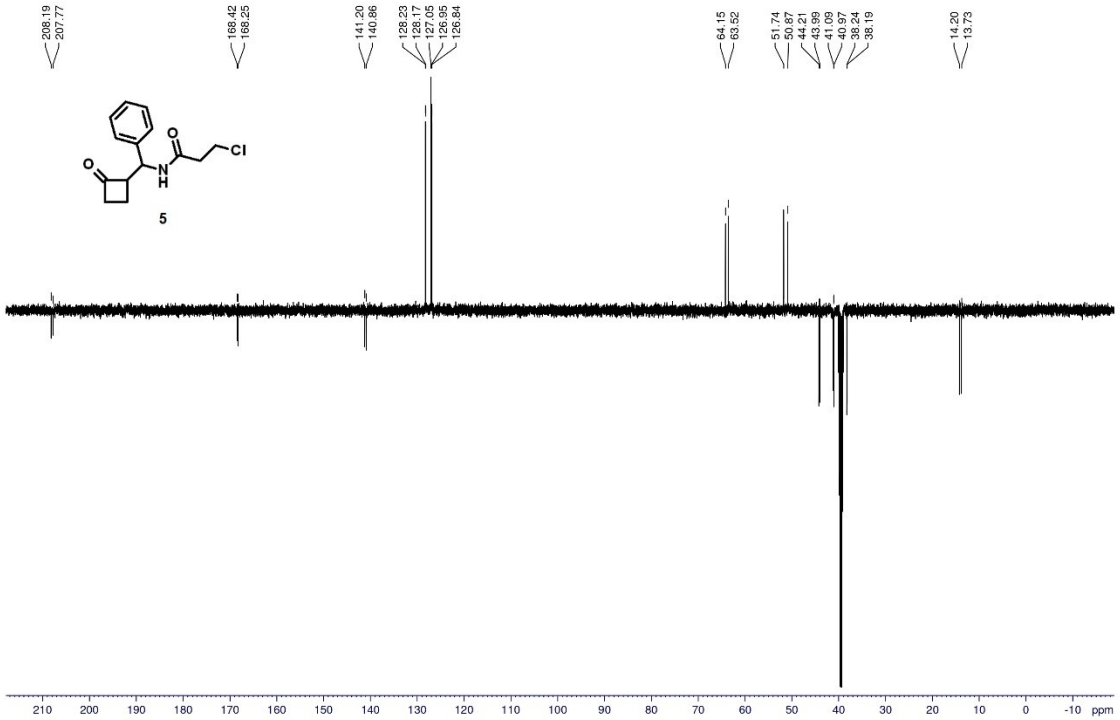
7.328
7.316
7.305
7.240
5.223
5.206
5.189
5.159
5.141
5.124
3.783
3.780
3.768
3.735
3.726
3.720
3.709
3.703
2.970
2.955
2.935
2.875
2.833
2.645
2.633
2.620
2.600
2.047
2.026
2.014
1.942
1.929
1.921
1.908
1.722
1.701
1.679
O
O
N
H
Cl
5
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 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 ppm
1.00
5.45
1.00
3.10
2.10
2.09
0.58
1.05
0.60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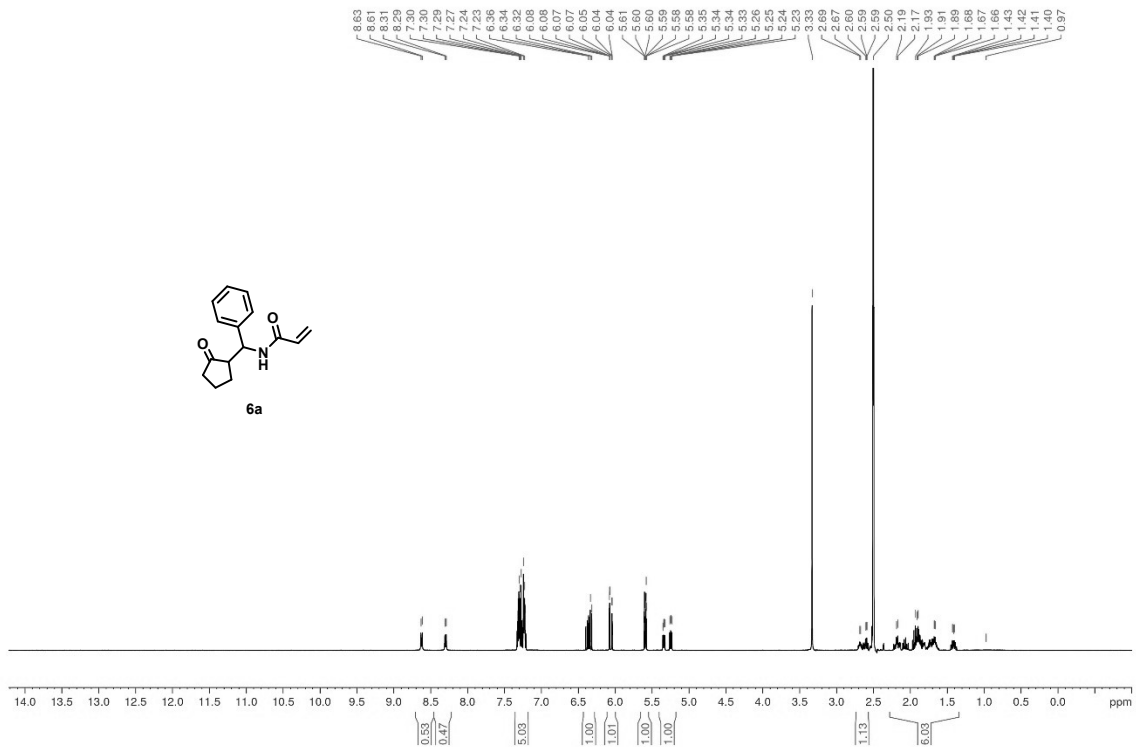
207.77
168.42
168.25
141.20
140.86
128.23
128.17
127.05
126.95
126.84
64.15
63.52
51.74
50.87
44.21
43.99
41.09
40.97
38.24
38.19
14.20
13.73
O
O
N
H
Cl
5
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm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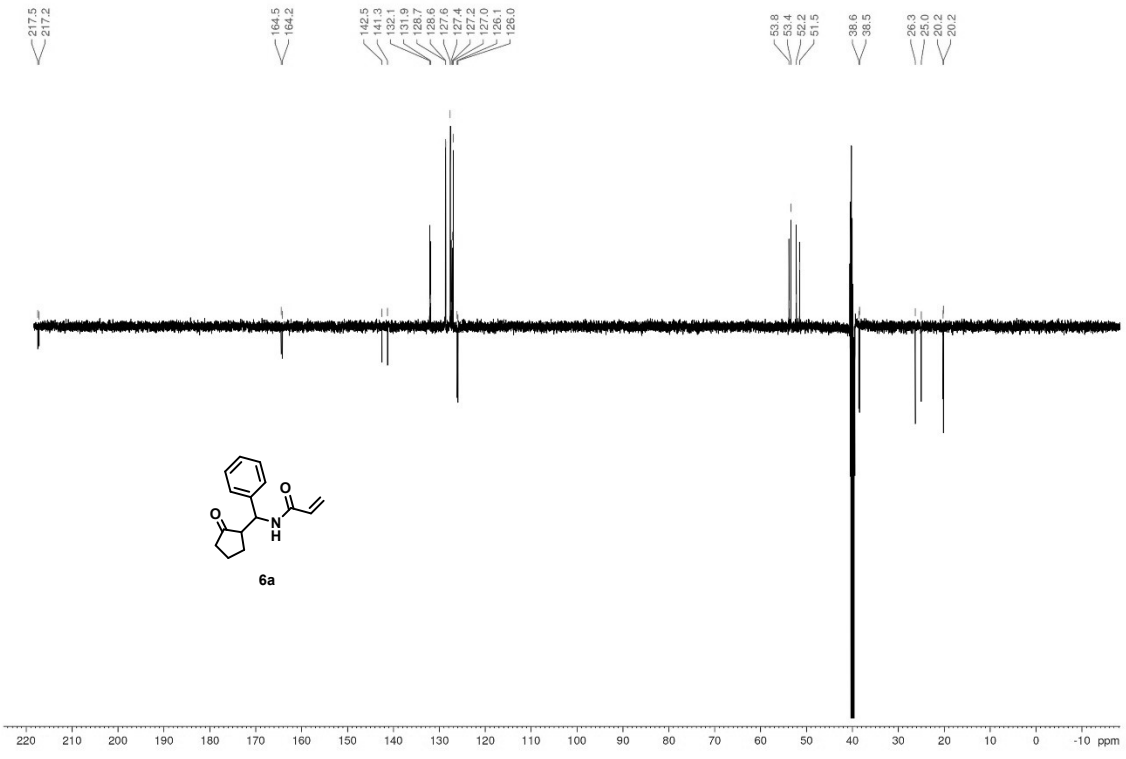
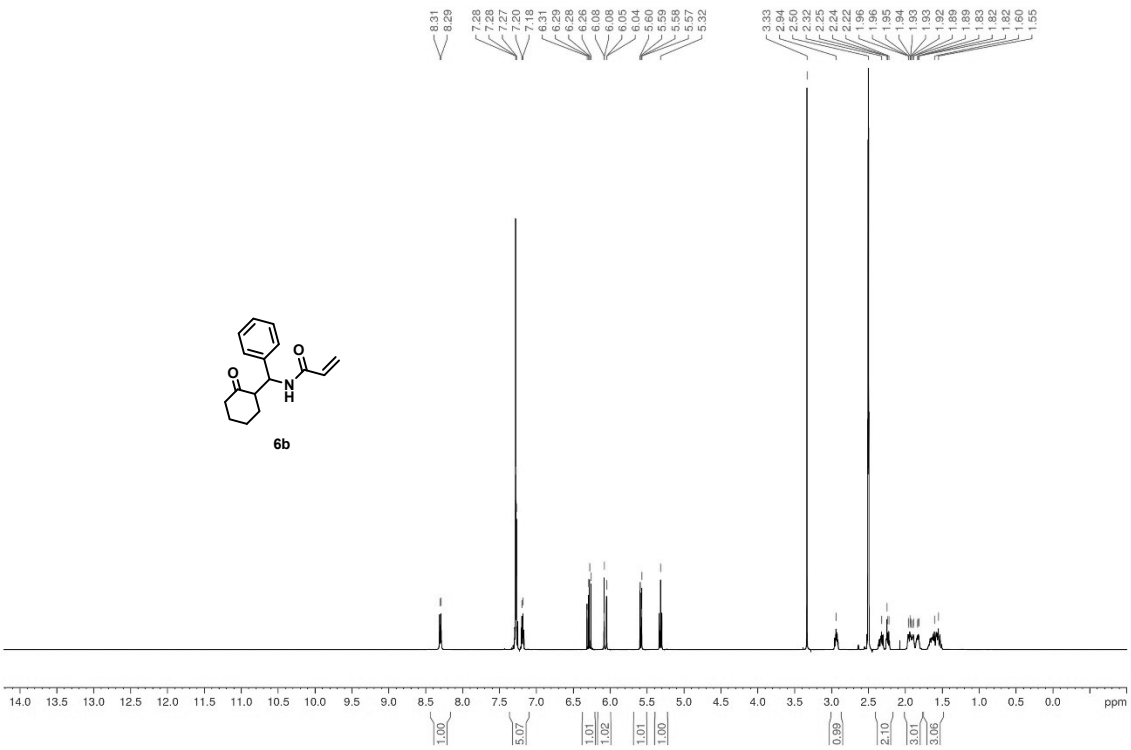
8.61
8.31
8.29
7.30
7.30
7.29
7.27
7.24
7.23
6.36
6.34
6.32
6.08
6.08
6.07
6.07
6.05
6.04
6.04
5.61
5.60
5.60
5.59
5.58
5.58
5.35
5.34
5.34
5.33
5.26
5.25
5.24
5.23
5.23
2.89
2.67
2.60
2.59
2.59
2.50
2.19
2.17
1.93
1.91
1.89
1.68
1.67
1.66
1.43
1.42
1.41
1.40
0.97
O
O
N
H
6a
14.0 13.5 13.0 12.5 12.0 11.5 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 ppm
0.53
0.47
5.03
1.00
1.01
1.00
1.00
1.13
6.03


217.5
217.2
164.5
164.2
142.5
141.3
132.1
131.9
128.7
128.6
127.6
127.4
127.2
127.0
126.1
126.0
53.8
53.4
52.2
51.5
38.6
38.5
26.3
25.0
20.2
20.2
O
O
N
H
6a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm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8.29
7.28
7.28
7.27
7.20
7.18
6.31
6.29
6.28
6.26
6.08
6.06
6.05
6.04
5.60
5.59
5.58
5.57
5.32
3.33
2.94
2.50
2.32
2.25
2.24
2.22
1.96
1.95
1.94
1.93
1.92
1.89
1.89
1.83
1.82
1.82
1.60
1.55
O
O
N
H
6b
14.0 13.5 13.0 12.5 12.0 11.5 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 ppm
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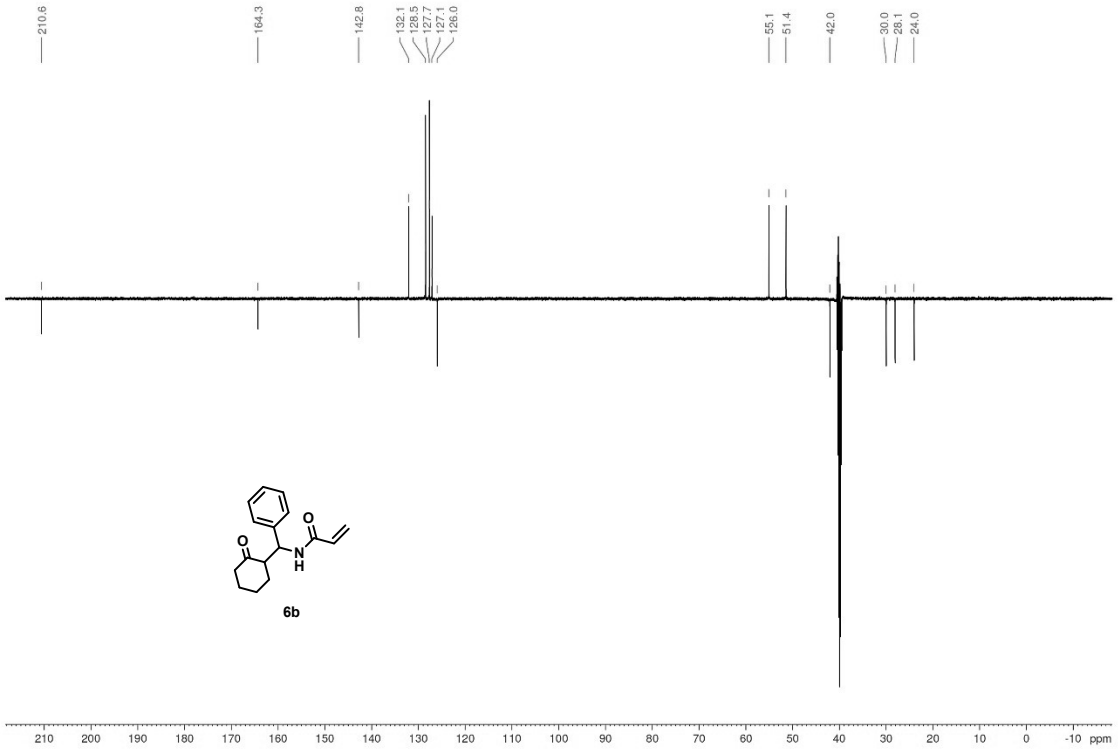
5.07
1.01
1.02
1.01
1.00
0.99
2.10
3.01
3.06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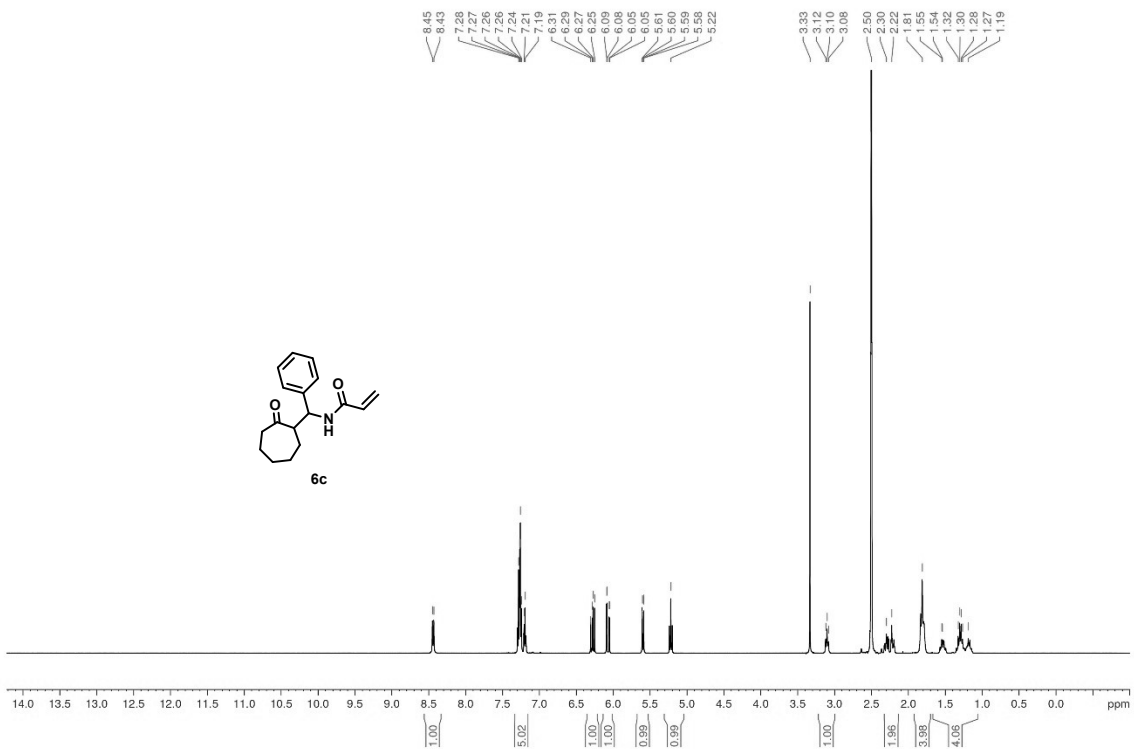
164.3
142.8
132.1
128.5
127.7
127.1
126.0
55.1
51.4
42.0
30.0
28.1
24.0
O
O
N
H
6b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm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7.28
7.27
7.26
7.24
7.21
7.19
6.31
6.29
6.27
6.25
6.09
6.08
6.05
6.05
5.61
5.60
5.59
5.58
5.22
3.33
3.12
3.10
3.08
2.50
2.30
2.22
1.81
1.55
1.54
1.32
1.30
1.28
1.27
1.19
O
O
N
H
6c
14.0 13.5 13.0 12.5 12.0 11.5 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 ppm
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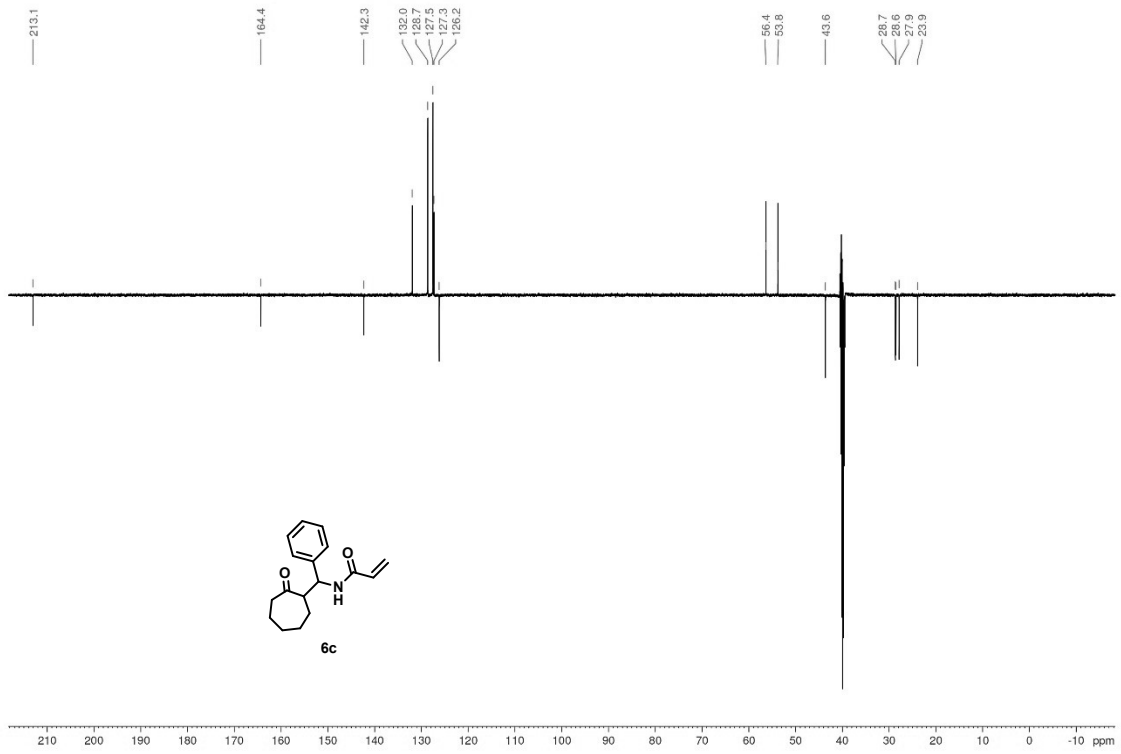
5.02
1.00
1.00
0.99
0.99
1.00
1.98
3.99
4.06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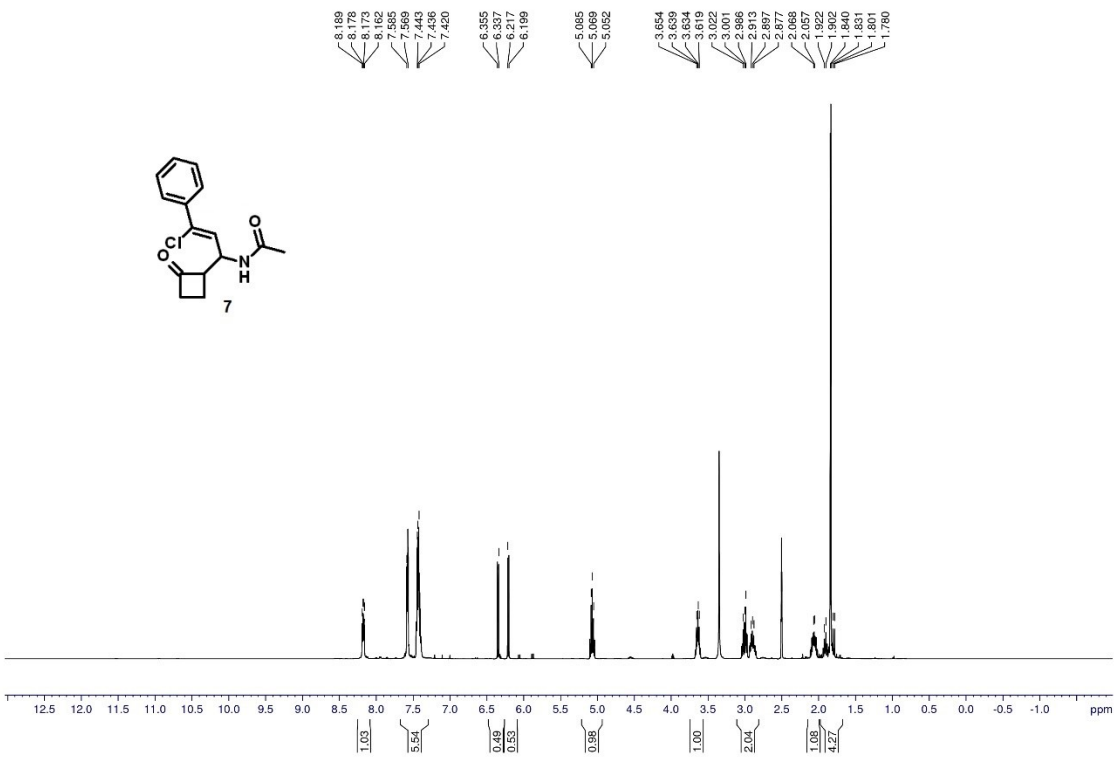
164.4
142.3
132.0
128.7
127.5
127.3
126.2
56.4
53.8
43.6
28.7
28.6
27.9
23.9
O
O
N
H
6c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm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8.173
8.162
7.585
7.569
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7.436
7.420
6.355
6.337
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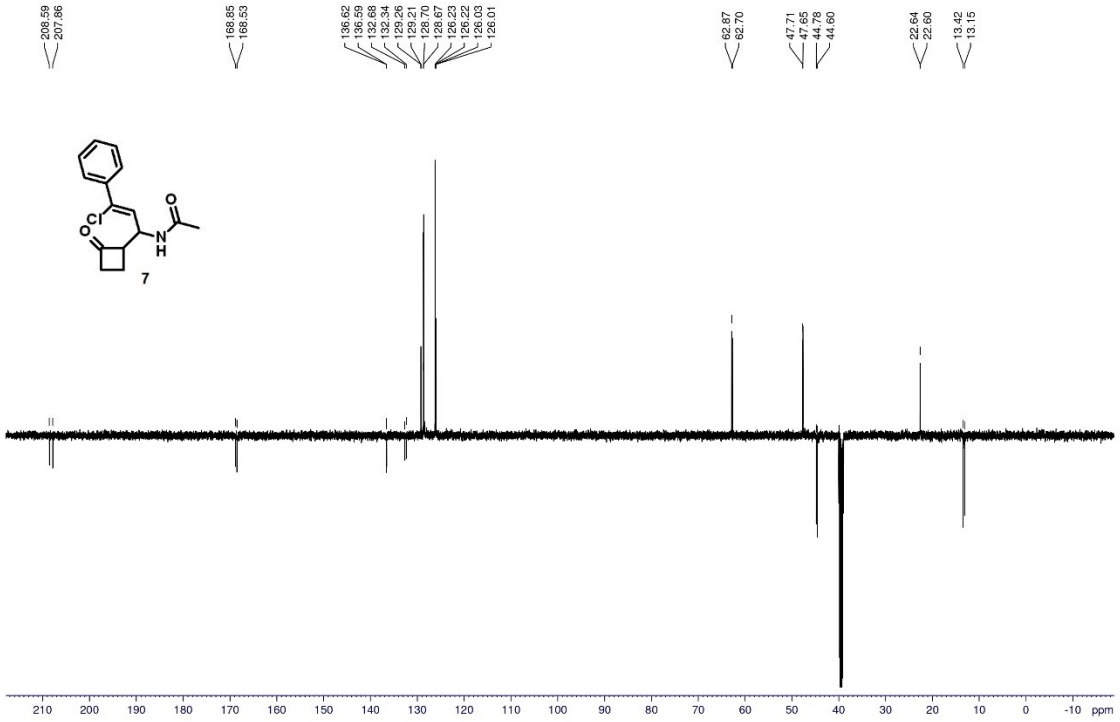
6.199
5.085
5.069
5.052
3.654
3.639
3.634
3.619
3.022
3.001
2.986
2.813
2.677
2.577
2.068
2.057
1.922
1.902
1.840
1.831
1.801
1.780
Cl
O
N
H
O
7
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 ppm
1.03
5.54
0.49
0.53
0.98
1.00
2.04
1.08
4.27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207.86
168.85
168.53
136.62
136.59
132.68
132.34
129.26
129.21
128.70
128.67
126.23
126.22
126.03
126.01
62.87
62.70
47.71
47.65
44.78
44.60
22.64
22.60
13.42
13.15
Cl
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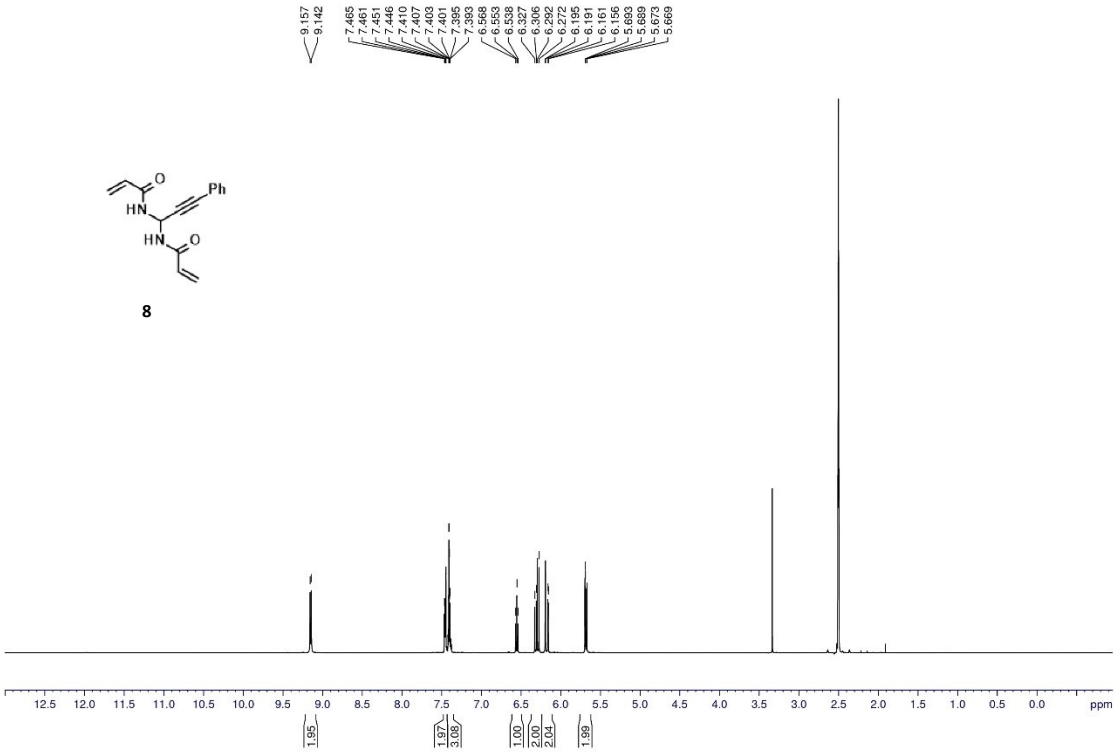
7
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm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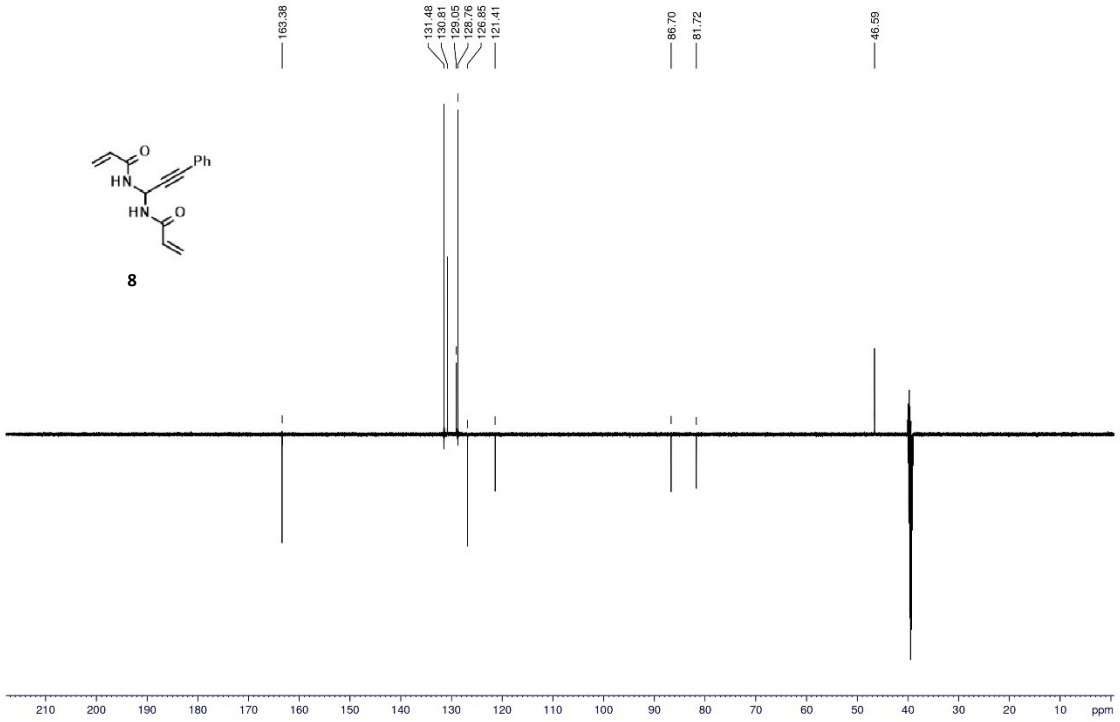
9.142
7.465
7.461
7.451
7.446
7.410
7.407
7.403
7.401
7.395
7.393
6.568
6.553
6.538
6.327
6.306
6.292
6.272
6.195
6.191
6.161
6.156
5.693
5.689
5.673
5.669
Ph
HN
HN
O
O
8
ppm
1.95
1.97
3.08
1.00
2.00
2.04
1.99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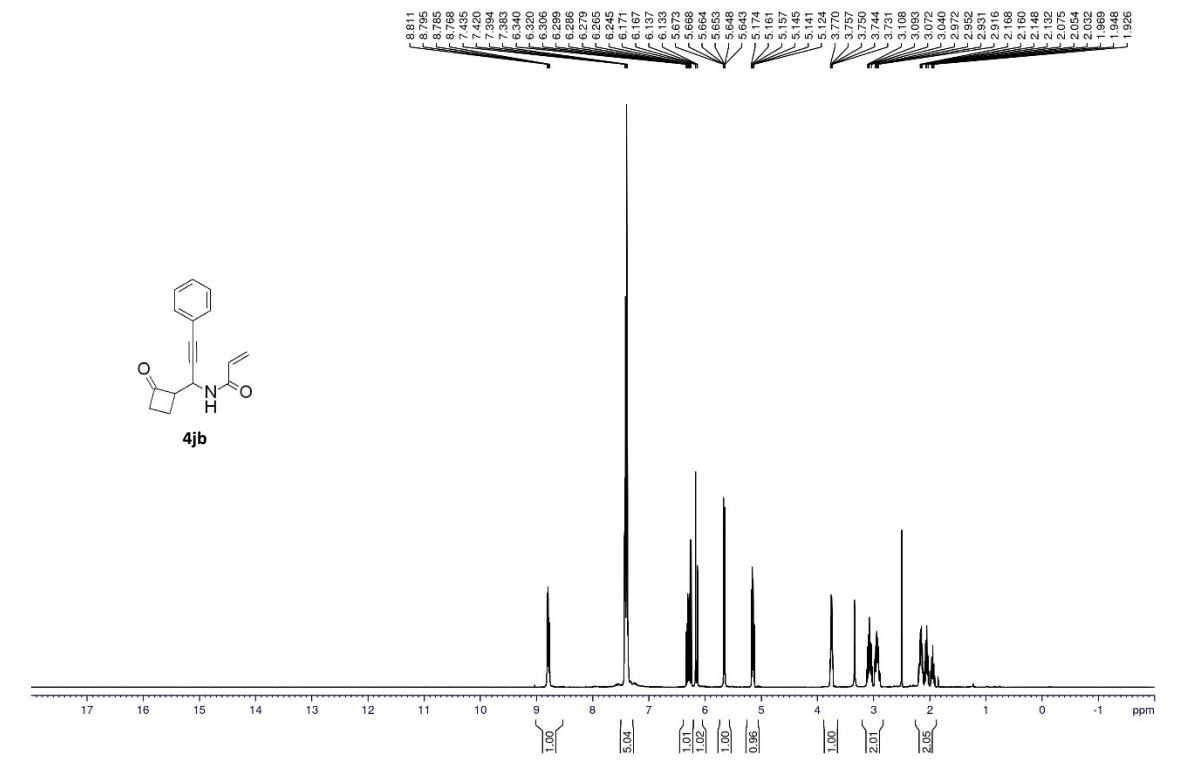
128.76
126.85
121.41
86.70
81.72
46.59
Ph
HN
HN
O
O
8
ppm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8.795
8.785
8.768
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7.420
7.394
7.383
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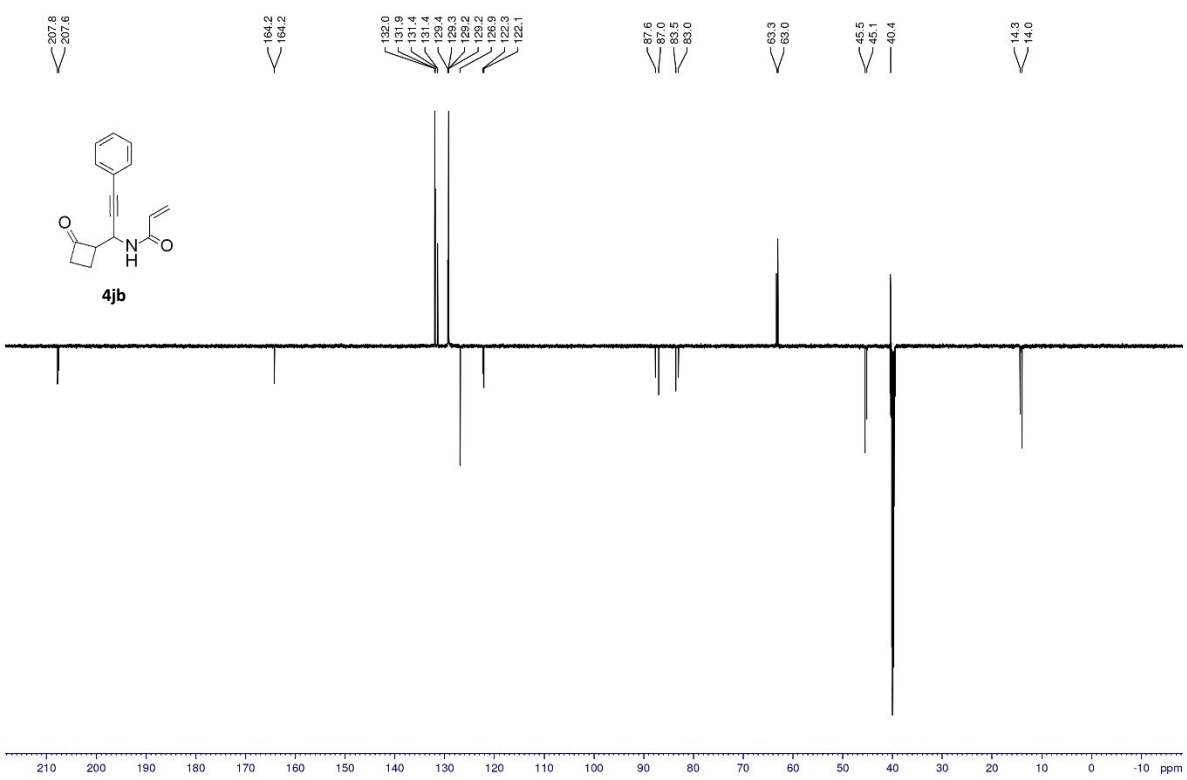
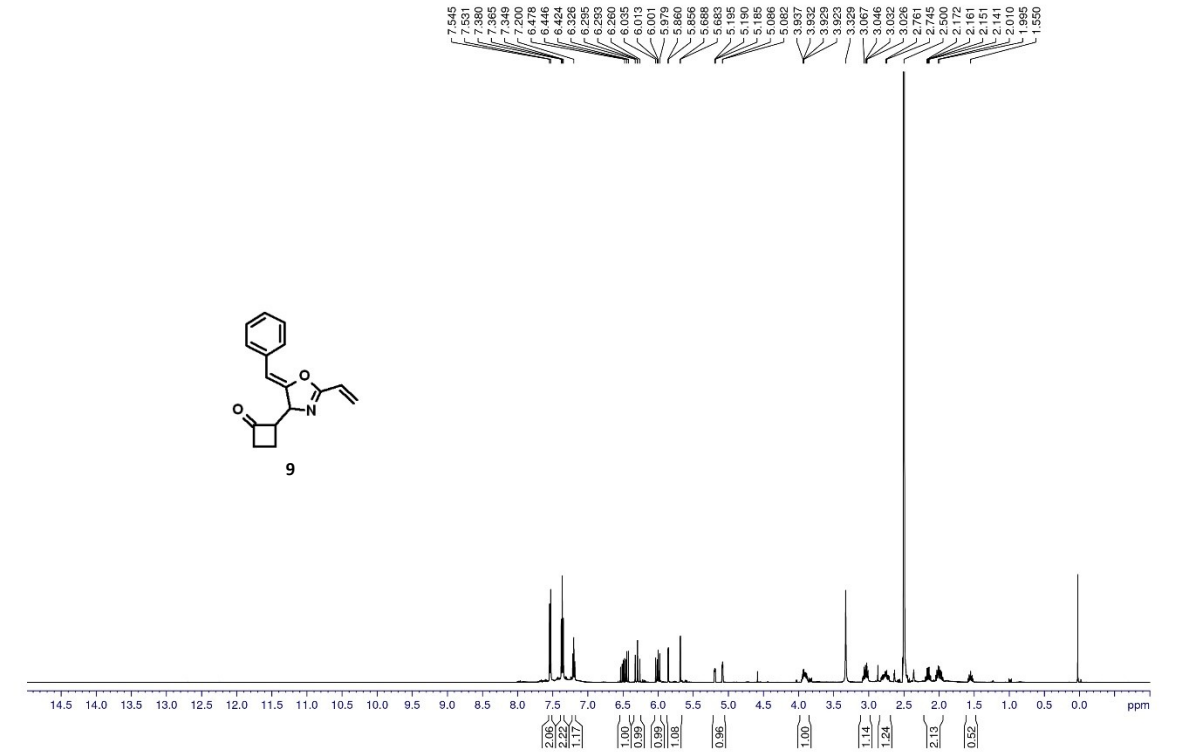
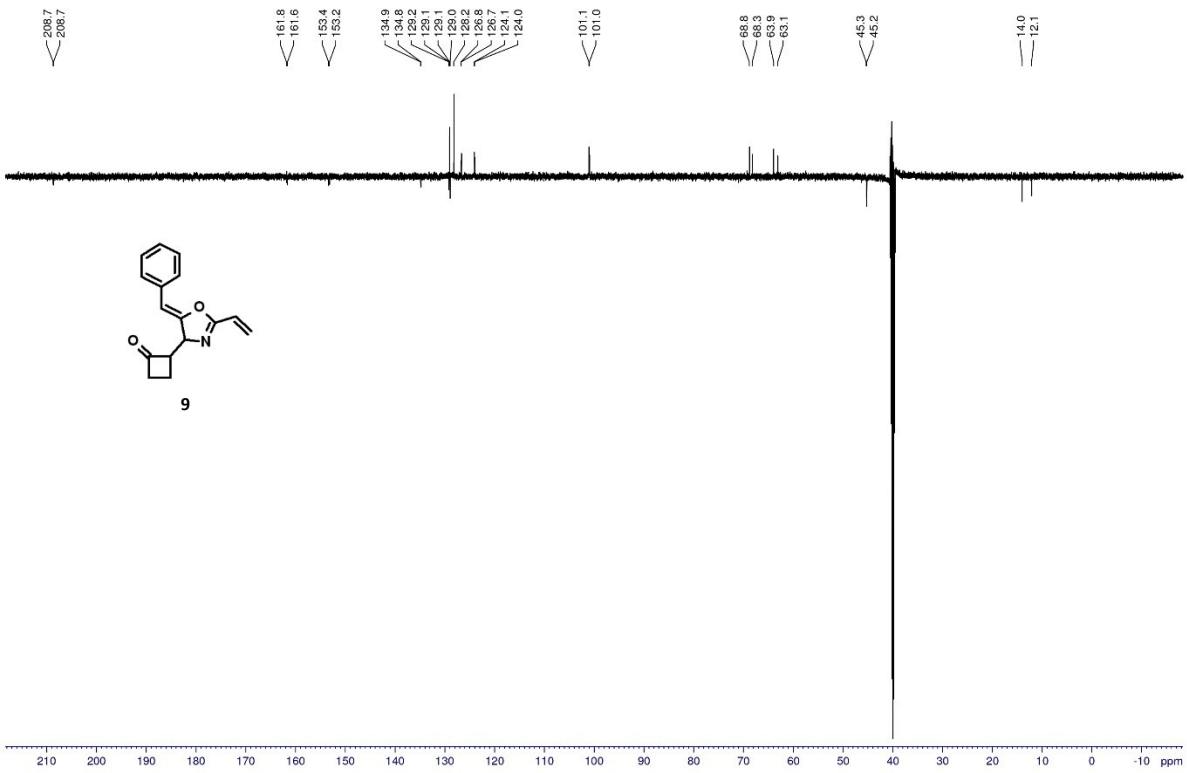
6.320
6.306
6.299
6.286
6.279
6.265
6.245
6.171
6.167
6.137
6.133
6.123
5.668
5.664
5.653
5.648
5.643
5.174
5.161
5.157
5.145
5.141
5.124
3.770
3.757
3.750
3.744
3.731
3.108
3.093
3.072
3.040
2.972
2.952
2.931
2.916
2.168
2.160
2.148
2.132
2.075
2.054
2.032
1.969
1.948
1.926
4jb
17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
1.00
5.04
1.01
1.02
1.00
0.96
1.00
2.01
2.05


207.8
207.6
164.2
164.2
132.0
131.9
131.4
131.4
129.4
129.3
129.2
129.2
126.9
122.3
122.1
87.6
87.0
83.5
83.0
63.3
63.0
45.5
45.1
40.4
14.3
14.0
4jb
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm


7.545
7.531
7.380
7.365
7.349
7.200
6.478
6.446
6.424
6.326
6.295
6.293
6.260
6.035
6.013
6.001
5.979
5.860
5.856
5.688
5.683
5.195
5.190
5.185
5.086
5.082
3.937
3.932
3.928
3.923
3.329
3.067
3.046
3.032
3.026
2.761
2.745
2.500
2.172
2.161
2.151
2.141
2.010
1.995
1.550
O
N
O
9
ppm
2.06
2.22
1.17
1.00
0.99
0.99
1.08
0.96
1.00
1.14
1.24
2.13
0.52


208.7
208.7
161.8
161.6
153.4
153.2
134.9
134.8
129.2
129.1
129.1
129.0
128.2
126.8
126.7
124.1
124.0
101.1
101.0
68.8
68.3
63.9
63.1
45.3
45.2
14.0
12.1
O
N
O
9
ppm

6. References

(S1) T. Yurino, Y. Aota, D. Asakawa, T. Kano and K. Maruoka, *Tetrahedron*, 2016, **72**, 3687-3700.