Supporting Information

Investigating *N*-Methoxy-*N*'-Aryl Ureas in Oxidative C-H Olefination Reactions: An Unexpected Oxidation Behaviour

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List of content

1. General Information

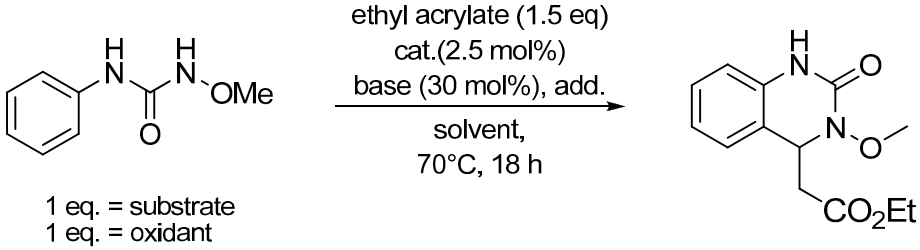
Unless otherwise noted, all reactions were carried out under an atmosphere of argon in flame-dried glassware. Reaction temperatures are reported as the temperature of the bath surrounding the vessel unless otherwise stated. The dry solvents used were purified by distillation over the drying agents indicated in parentheses and were transferred under argon: THF (Na/benzophenone), CH_2Cl_2 (CaH_2), toluene (CaH_2). Anhydrous 1,2-DCE, NEt_3, DMF, DME, dioxane, acetone, MeOH, EtOH, *t*-AmOH and MeCN were purchased from Acros Organics and stored over molecular sieves under argon. Anhydrous *t*-BuOH was purchased from Alfa Aesar and stored over molecular sieves under argon.
Commercially available chemicals were obtained from Acros Organics, Aldrich Chemical Co., Strem Chemicals, Alfa Aesar, ABCR and TCI Europe and used as received unless otherwise stated.
NMR-spectra were recorded on a Bruker ARX-300, AV-300, AV-400 MHz or on a Varian Associated, Varian 600 unity plus. Chemical shifts (δ) are quoted in ppm downfield of tetramethylsilane and were referenced to the solvent peak ($CDCl_3$ ^{1}H NMR: 7.26 ppm, ^{13}C NMR: 77.16 ppm, DMSO-d^6 ^{1}H NMR: 2.50 ppm, ^{13}C NMR: 39.52 ppm). Coupling constants (*J*) are quoted in Hz. ^{1}H- and ^{13}C-peak attributions were determined by DEPT, ^{1}H-^{1}H gCOSY, ^{1}H-^{13}C gHSQC, ^{1}H-^{13}C gHMBC or by analogy. To describe the multiplicities of the signals, the following abbreviations were used: s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet, br s: broad singlet, app: apparent.
Infrared spectra were recorded on a Varian Associated FT-IR 3100 Excalibur with ATR unit. Characteristic absorption maxima are quoted in cm^{-1}. ESI mass spectra were recorded on a Bruker Daltonics MicroTof.
Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished with short wave UV light and/or $KMnO_4$ staining solution followed by gentle heating.

Flash column chromatography was performed on Merck silica gel (40-63 mesh) by using standard laboratory techniques**.** Solvents used for flash column chromatography were destilled to remove higher boiling impurities.

2. Optimization of Reaction Conditions

i) Use of a second equivalent of substrate 2a as oxidant.

General Procedure A1:



1 eq. = substrate
1 eq. = oxidant

2a **4aa**

A flame-dried 10 mL screw-capped schlenck tube was transferred to a glove-box and charged with urea **2a** (33.2 mg, 0.2 mmol, 2.0 eq.), $[Cp^*RhCl_2]_2$ (1.6 mg, 2.5 µmol, 0.025 eq.) and NaOAc (2.5 mg, 0.03 mmol, 0.3 eq.). Ethyl acrylate (32.0 µL, 0.3 mmol, 3.0 eq.) and dry solvent (1 mL) was added under an argon atmosphere via syringe. The reaction mixture was placed in a pre-heated oilbath (70 °C) and stirred for 18 h. After cooling to room-temperature, the solvent was removed under reduced pressure and the crude reaction mixture dried. CH_2Br_2 was added and the yield determined by ^{1}H NMR integration of the signal at 5.22 ppm.

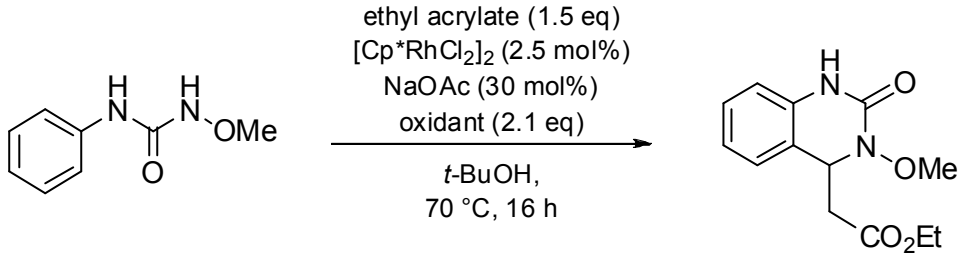
Table 1: Optimization of reaction conditions.

entry	cat.	base	add.	solvent	yield[a]
1	$[Cp^*RhCl_2]_2$	CsOAc	-	*t*-AmylOH	63 (60)
2	$[Cp^*RhCl_2]_2$	CsOAc	-	MeOH	36
3	$[Cp^*RhCl_2]_2$	CsOAc	-	Dioxane	59
4	$[Cp^*RhCl_2]_2$	CsOAc	-	THF	57
5	$[Cp^*RhCl_2]_2$	CsOAc	-	1,2-DCE	58
6	$[Cp^*RhCl_2]_2$	CsOAc	-	DME	55
7	$[Cp^*RhCl_2]_2$	CsOAc	-	*t*-BuOH	67
8	$[Cp^*RhCl_2]_2$	KOAc	-	*t*-BuOH	74
9	**$[Cp^*RhCl_2]_2$**	**NaOAc**	**-**	***t*-BuOH**	**78**
10	$[Cp^*RhCl_2]_2$	NaOAc	-	EtOH	43
11	$[Cp^*RhCl_2]_2$	NaOAc	-	Acetone	48
12	$[Cp^*RhCl_2]_2$	Ag_2CO_3	-	t-AmylOH	traces
13	$[Cp^*RhCl_2]_2$	CsOPiv	-	*t*-BuOH	65
14	$[Cp^*RhCl_2]_2$	NaOAc	$AgSbF_6$ (10mol%)	*t*-BuOH	64
15	$[Cp^*RhCl_2]_2$	NaOAc	-	t-BuOH	65[b]
16	$[Cp^*RhCl_2]_2$	NaOAc	-	t-BuOH	62[c]
17	$[Cp^*RhCl_2]_2$	NaOAc	-	t-BuOH	75[d]
18	**$[Cp^*RhCl_2]_2$**	**NaOAc**	**-**	**t-BuOH**	**77(75)[d,e]**
19	$[Cp^*RhCl_2]_2$	-	-	*t*-AmylOH	0
20	$RhCl_3$	CsOAc	-	*t*-AmylOH	0
21	$Pd(OAc)_2$	--	Ac_2O, $TsOH*H_2O$	THF	0
22	$Pd(OAc)_2$	NaOAc	-	*t*-BuOH	0
23	$[Rh(cod)Cl]_2$	NaOAc	-	*t*-BuOH	0
24	$Rh(PPh_3)_3Cl$	NaOAc	-	*t*-BuOH	0
25	$Rh_2(OAc)_4$	NaO*t*-Bu	IMes·HCl	*t*-BuOH	0

a) Yields were determined by ^{1}H NMR with CH_2Br_2 as an internal standard; isolated yields are given in parentheses. b) 1 mol% of $[Cp^*RhCl_2]_2$ was used. c) Reaction mixture was heated to 60 °C. d) Reaction vessel was not flame-dried and kept under air during the reaction. e) 1 eq. of ethyl acrylate was used.

ii) Use of an external oxidant.

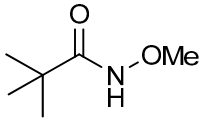
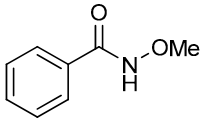
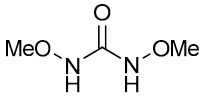
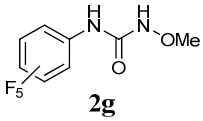
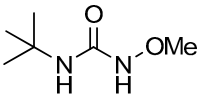
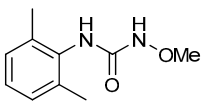
General Procedure A2:



2a **4aa**

A flame-dried 10 mL screw-capped schlenck tube was transferred to a glove-box and charged with urea **2a** (24.9 mg, 0.15 mmol, 1.0 eq.), $[Cp^*RhCl_2]_2$ (2.3 mg, 2.5 µmol, 0.025 eq.), NaOAc (3.7 mg, 0.03 mmol, 0.3 eq.) and the oxidant (see table 2). Ethyl acrylate (23.9 µL, 0.225 mmol, 1.5 eq.) and dry solvent (1.5 mL) was added via syringe. The reaction mixture was placed in a pre-heated oilbath (70 °C) and stirred at this temperature. After 18 h, the reaction mixture was filtered through a short pad of celite and the solvent was removed under reduced pressure. The crude reaction mixture was dried, CH_2Br_2 was added and the yield of **4aa** was determined by ^{1}H NMR integration of the signal at 5.22 ppm.

Table 2 Screening of external oxidants.

entry	oxidant	eq. (ox)	yield[a]	entry	oxidant	eq. (ox)	yield[a]
1	none	1.0	78	2	$Cu(OAc)_2$	2.1	18
3	$Cu(OAc)_2$, O_2	0.2, 1 atm	0	4	CAN	2.1	0[b]
5	Ag_2CO_3	2.1	27	6	AgOAc	2.1	11
7	$KHSO_5$	2.1	0	8	$K_2S_2O_8$	2.1	28
9	*m*-CPBA	2.1	0[b]	10	t-BuOOH	2.1	28
11	benzoquinone	2.0	0[b]	12	quinoline *N*-oxide	2.1	28[d]
13	anthraquinone	2.0	34	14	TEMPO	2.1	32
15	NMO	2.0	43	16	**2b**	1.2	0
17	**2c**	1.2	0	18	**2e**	1.2	35
19		2.0	42	20		1.0	13
21	 **2f**	2.1	25	22	 **2g**	2.1	39[c]
23	 **2h**	2.1	53[d]	24	 **2i**	2.1	37[c]

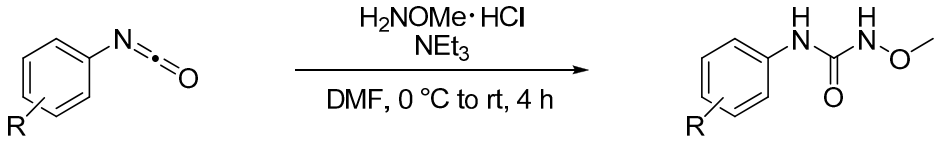
If not otherwise stated, an approximately equal amount of N-phenyl urea, resulting from reduction of the substrate was observed along with the formation of the quinazolinone.

[a]Yield of **4aa** was determined by ^{1}H NMR using CH_2Br_2 as an internal standard. [b]With 2 equivalents of **2a**. Isolated yield in parentheses. [c]Mainly decomposition was observed. [c]Only a trace amount of the reduced oxidant was detected by HRMS. [d]The amount of *N*-phenyl urea was determined to be 42%.

3. General Procedures for the Synthesis of Substrates 2

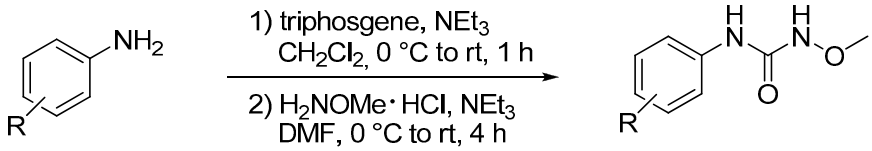
i) Synthesis of *N*-methoxy-*N*'-aryl ureas:

General Procedure B:



Following a modified procedure from Mellay-Hamon,[1] triethylamine (1.15 eq.) was added to a solution of methoxyamine hydrochloride (1.10 eq.) in DMF (10 mL) at room-temperature in a flame-dried round-bottom flask. The resulting white suspension was cooled to 0 °C when aryl isocyanate (1.00 eq.) was added dropwise. The ice bath was removed and the reaction mixture stirred for 4 hours. The solvent was removed under vacuum and the residue suspended in EtOAc and filtered to remove the non-soluble triethylammoniumchloride salt. Pure *N*-methoxy-*N*'aryl ureas **2** were obtained by recrystallization or flash column chromatography (see below).

General Procedure C:



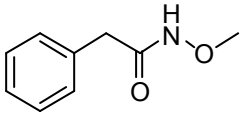
Following a modified procedure from Randad,[2] a solution of triphosgene (0.95 g, 3.2 mmol, 0.40 eq.) in dry CH_2Cl_2 (20 mL) was prepared under an argon atmosphere in a flame-dried round-bottom flask and cooled to 0 °C. A solution of aryl amine (8.0 mmol, 1.0 eq.) and triethylamine (2.44 mL, 17.6 mmol, 2.20 eq.) in CH_2Cl_2 (15 mL), which was prepared in a flame-dried round-bottom flask, was added slowly via canula. After 15 minutes, the icebath was removed and the reaction mixture was allowed to stir at room-temperature. TLC analysis (pentane/EtOAc) indicated conversion of the amine. In a separate flame-dried flask, dry triethylamine (2.44 mL, 17.6 mmol, 2.20 eq.) was added under an argon atmosphere to a solution of methoxyamine hydrochloride (735 mg, 8.80 mmol, 1.10 eq.) in dry DMF (10 mL, 1 M) at room-temperature. The resulting white suspension was cooled to 0 °C and the solution containing the isocyanate was added via canula. The ice bath was removed and the reaction mixture stirred for 4 hours. The solvent was removed under vacuum and the residue suspended in EtOAc and filtered to remove the non-soluble triethylammoniumchloride salt. Pure *N*-methoxy-*N*'-aryl ureas **2** were obtained by flash column chromatography.

General Procedure D:

Following a modified procedure from Mellay-Hamon,[1] triethylamine (1.59 mL, 11.5 mmol, 1.15 eq.) was added to a solution of oxyamine hydrochloride (11.0 mmol, 1.10 eq.) in dry DMF (10 mL) at room-temperature under an argon atmosphere in a flame-dried round-bottom flask. The resulting white suspension was cooled to 0 °C when aryl (thio)isocyanate (10.0 mmol, 1.00 eq.) was added dropwise. The ice bath was removed and the reaction mixture stirred for 4 hours. The solvent was removed under vacuum and the residue suspended in EtOAc and filtered to remove the non-soluble triethylammoniumchloride salt. Pure urea compounds (**2**) were obtained by recrystallization or flash column chromatography (see below).

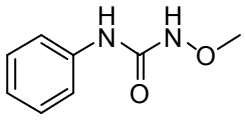
4. Preparation and characterization of Substrates 1-2

***N*-Methoxy-2-phenylacetamide (1)**



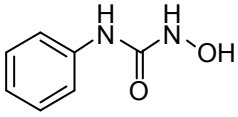
Following a modified procedure by Fagnou et al., [3] *O*-methylhydroxylamine hydrochloride (301.0 mg, 3.6 mmol, 1.2 eq.) and K_2CO_3 (829.0 mg, 6.0 mmol, 2.0 eq.) were combined in a 2:1 mixture of EtOAc (24 mL) and H_2O (12 mL) in a flame-dried 50 mL round-bottom flask. The flask was capped and the mixture was cooled in an ice bath. No special precautions were taken to exclude moisture or oxygen. Phenylacetylchloride (0.39 mL, 3.0 mmol, 1.0 eq.) was added dropwise and the mixture was stirred and allowed to warm to rt. After 16 h, the reaction mixture was diluted with EtOAc and washed twice with water and brine. The organic layers were dried over $MgSO_4$, filtered and concentrated. The pure product **1** (410 mg, 82% yield) was obtained without any further purification. **R_F** (pentane/EtOAc 25:75) = 0.25; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 8.71 (br s, 1H, NH), 7.37 – 7.21 (m, 5H, CH_{ar}), 3.69 (s, 3H, OCH_3), 3.48 (s, 2H, CH_2); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 168.8 (C_q), 134.0 (C_q), 129.3 (CH), 129.0 (CH), 127.5 (CH), 64.4 (OCH_3), 40.8 (CH_2); **ESI-MS:** calculated $[C_9H_{11}NO_2Na]^+$: 188.0682, found: 188.0687; **ATR-FTIR (cm^{-1}):** 3157, 2959, 1644, 1351, 1494, 1454, 1351, 1147, 1077, 1060, 973, 946, 775, 694, 616, 545, 541.

***N*-Methoxy-*N*'-phenylurea (2a).**



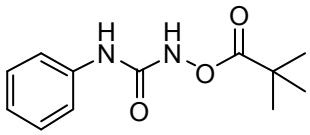
Following general procedure B on a 15 mmol scale, the title compound **2a** was obtained as a white solid (2.36 g, 95% yield) after flash column chromatography (pentane/EtOAc 50:50). $\mathbf{R_F}$ (pentane/EtOAc 60:40) = 0.26; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 7.58 (br s, 1H, NH), 7.48 (m, 2H, CH_{ortho}), 7.33 (m, 2H, CH_{meta}), 7.10 (tt, *J* = 7.4 Hz, *J* = 1.3 Hz, 1H, CH_{para}), 6.70 (br s, 1H, NH), 3.79 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 157.4 (C_q), 137.3 (C_q), 129.1 (CH), 124.0 (CH), 119.9 (CH), 64.7 (CH_3); **ESI-MS:** calculated $[C_8H_{10}N_2O_2Na]^+$: 189.0634, found: 189.0640; **ATR-FTIR (cm^{-1}):** 3303, 3208, 3059, 2873, 1650, 1594, 1526, 1498, 1440, 1335, 1324, 1236, 1098, 1078, 1029, 944, 867, 748, 691, 666, 616, 588.

***N*-Hydroxy,*N*'-phenylurea (2b).**



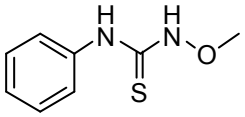
Following general procedure D on a 30 mmol scale, the reaction mixture was separated into two parts (20 and 10 mL of size, the smaller portion was used for the synthesis of *N*-(Pivaloyloxy)-*N*'-Phenylurea **2c**). The title compound **2b** was obtained from the bigger portion as white hairy crystals (2.13 g, 70% yield) after flash column chromatography (pentane/EtOAc 50:50, 1% AcOH). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.30; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 8.95 (s, 1H, OH), 8.81 (s, 1H, NH), 8.74 (s, 1H, NH), 7.61 (d, *J* = 8.2 Hz, 2H, CH_{ortho}), 7.24 (dd, *J* = 8.3 Hz, *J* = 7.3 Hz, 2H, CH_{meta}), 6.95 (t, *J* = 7.3 Hz, 1H, CH_{para}); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 158.6 (C_q), 139.4 (C_q), 128.4 (CH), 122.1 (CH), 119.2 (CH); **ESI-MS:** calculated $[C_7H_8N_2O_2Na]^+$: 175.0478, found: 175.0488; **ATR-FTIR (cm^{-1}):** 3390, 3225, 3056, 1712, 1630, 1595, 1532, 1500, 1446, 1312, 1229, 1073, 752, 689, 616.

***N*-(Pivaloyloxy),*N*'-phenylurea (2c).**



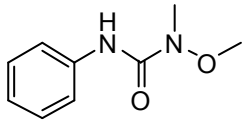
To an unpurified solution of *N*-hydroxy,*N*'-phenylurea (**2b**, approx. 10 mmol) in DMF was added THF (20 mL), triethylamine (1.80 mL, 13.0 mmol, 1.30 eq.) and pivaloylchloride (1.35 mL, 11.0 mmol, 1.10 eq.) at 0 °C. The reaction mixture was quenched with water (80 mL) and subsequently extracted with Et_2O (3 x 30 mL), dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (pentane/EtOAc 7:1 to 4:1) afforded the title compound **2c** as a white solid (901 mg, 39% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.68; **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.45 (s, 1H, NH), 7.50 (s, 1H, NH), 7.27 (m, 2H, CH_{ortho}), 7.16 (m, 2H, CH_{meta}), 6.97 (tt, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, CH_{para}), 1.22 (s, 9H, $C(CH_3)_3$); **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 177.1 (C_q), 156.3 (C_q), 137.0 (C_q), 129.1 (CH), 124.3 (CH), 120.2 (CH), 38.4 (C_q) 27.0 (CH_3); **ESI-MS:** calculated $[C_{12}H_{16}N_2O_3Na]^+$: 259.1053, found: 259.1049; **ATR-FTIR (cm^{-1}):** 3305, 2975, 1771, 1674, 1600, 1551, 1500, 1480, 1445, 1314, 1248, 1217, 1092, 1080, 1023, 872, 797, 749, 692, 627.

***N*-Methoxy-*N*'-phenylthiourea (2d).**



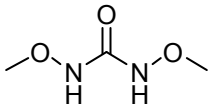
Following general procedure D on a 20 mmol scale, the title compound **2d** was obtained as a pale-yellow solid (1.51 g, 41% yield) after flash column chromatography (pentane/EtOAc 3:1 to 1:1). $\mathbf{R_F}$ (pentane/EtOAc 75:25) = 0.18; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 10.11 (br s, 1H, NH), 7.34 (m, 2H, CH_{meta}), 7.02 (tt, *J* = 7.4 Hz, *J* = 1.0 Hz, 1H, CH_{para}), 6.96 (m, 2H, CH_{ortho}), 4.13 (br s, 1H, NH), 3.17 (s, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 138.6 (C_q), 129.8 (CH), 122.6 (C_q), 114.9 (CH), 112.1 (C_q), 48.6 (CH_3); **ESI-MS:** calculated $[C_8H_{10}N_2OSNa]^+$: 205.0406, found: 205.0411. Compound decomposed at 0°C, before an IR spectrum was recorded.

***N*-Methoxy-*N*-methyl,*N*'-phenylurea (2e).**



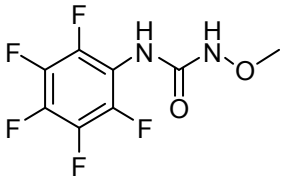
Following general procedure D on a 20 mmol scale, the title compound **2e** was obtained as a white solid (3.01 g, 83% yield) after flash column chromatography (pentane/EtOAc 4:1 to 5:2). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.52; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 7.74 (br s, 1H, NH), 7.47 (app d, *J* = 8.1 Hz, 2H, CH_{ortho}), 7.30 (m, 2H, CH_{meta}), 7.05 (tt, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, CH_{para}), 3.74 (s, 3H, OCH_3), 3.17 (s, 3H, NCH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 157.3 (C_q), 138.1 (C_q), 129.0 (CH), 123.5 (CH), 119.5 (CH), 61.7 (CH_3), 35.0 (CH_3); **ESI-MS:** calculated $[C_9H_{12}N_2O_2Na]^+$: 203.0791, found: 203.0783; **ATR-FTIR (cm^{-1}):** 3305, 1662, 1591, 1525, 1500, 1443, 1432, 1336, 1240, 1185, 1173, 1117, 1026, 972, 908, 749, 686, 638, 591.

***N*,*N*'-dimethoxyurea (2f).**



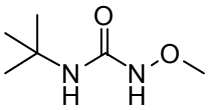
Following a procedure from Boyland and Nery, [4] methoxyamine hydrochloride (1.67 g, 20 mmol, 2.0 eq.) and $KHCO_3$ (15.1 g, 150 mmol, 7.5 eq.) were dissolved in a mixture of dioxane (15 mL) and H_2O (5 mL). The solution was cooled to 0 °C, when a solution of phosgene in toluene (20%, 4.9 mL, 10 mmol, 1.0 eq.) was added slowly via a pressure-equalizing dropping-funnel, which was then washed with dioxane (20 mL). The icebath was removed and the reaction mixture was allowed to warm to room-temperature and stirred for 18 hours. The reaction mixture was filtered, the residue washed with EtOH (5 mL), and the combined filtrate and washings were concentrated. The residue was extracted with EtOH and the extract dried over $MgSO_4$ and diluted with ether at 0 °C until the precipitation of inorganic salts stopped. The suspension was filtered and the filtrate was concentrated and dried to give the title compound **2f** (0.68 g, 57% yield) as a colorless oil. $\mathbf{R_F}$ (pentane/EtOAc 25:75) = 0.23; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 8.54 (s, 2H, NH), 3.65 (s, 6H, OCH_3); **^{13}C NMR (75 MHz, $CDCl_3$-d^6)** δ = 160.6 (C_q), 64.5 (OCH_3); **ESI-MS:** calculated $[C_3H_8N_2O_3Na]^+$: 143.0427, found: 143.0399; **ATR-FTIR (cm^{-1}):** 3221, 1658, 1599, 1492, 1439, 1388, 1315, 1193, 1082, 959, 927, 758, 693, 662.

***N*-Methoxy-*N*'-(pentafluorophenyl)urea (2g).**



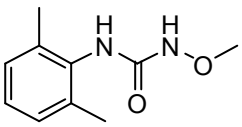
Following general procedure C on a 10 mmol scale, the title compound **2g** was obtained after purification by flash column chromatography (pentane/EtOAc 75:25) as a white solid (0.49 g, 21% yield). $\mathbf{R_F}$ (pentane/EtOAc 5:1) = 0.15; **^{1}H NMR (400 MHz, DMSO-d^6)** δ = 9.98 (s, 1H, NH), 9.05 (s, 1H, NH), 3.65 (s, 3H, OCH_3); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 156.7 (C_q), 143.5 (app d, *J* = 242 Hz, CF), 139.0 (app d, *J* = 250 Hz, CF), 137.2 (dt, *J* = 245 Hz, *J* = 16 Hz, CF), 113.7 (dt, *J* = 15 Hz, *J* = 4 Hz, C_q), 64.1 (CH_3); **^{19}F NMR (300 MHz, DMSO-d^6)** δ = -146.14 (m, 2F, CF_{ar}), -158.3 (t, J = 23.1 Hz, 1F, CF_{ar}), -164.02 (m, 2H, CF_{ar}); **ESI-MS:** calculated $[C_8H_5F_5N_2O_2Na]^+$: 279.0163, found: 279.0154; **ATR-FTIR (cm^{-1}):** 3272, 3219, 1677, 1653, 1529, 1496, 1459, 1333, 1298, 1099, 1005, 971, 814, 776, 752, 672, 613, 575, 526.

***N*-Methoxy-*N*'-(*tert*-butyl)urea (2h).**



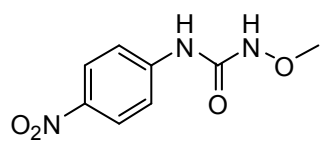
Following general procedure B on a 10 mmol scale, the title compound **2h** was obtained after flash column chromatography (pentane/EtOAc 50:50) as a white crystalline solid (1.26 g, 86% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.41; **^{1}H NMR (300 MHz, CDCl$_3$)** δ = 7.38 (br s, 1H, NH), 5.53 (br s, 1H, NH), 3.61 (s, 3H, OCH_3), 1.32 (s, 9H, $C(CH_3)_3$); **^{13}C NMR (75 MHz, CDCl$_3$)** δ = 159.1 (C_q), 63.9 (OCH_3), 50.4 (C_q), 29.2 (CH_3); **ESI-MS:** calculated $[C_8H_{13}N_2O_2Na]^+$: 169.0972, found: 169.0959; **ATR-FTIR (cm^{-1}):** 3310, 2973, 2938, 1659, 1553, 1476, 1457, 1394, 1363, 1274, 1217, 1115, 1057, 1023, 963, 804, 767, 650.

***N*-Methoxy-*N*'-(2,6-dimethylphenyl)urea (2i).**



Following general procedure B on a 12 mmol scale, the title compound **2i** was obtained after recrystallization from EtOAc (45 °C to -20 °C) as a white crystalline solid (2.26 g, 97% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.33; **^{1}H NMR (400 MHz, CDCl$_3$)** δ = 8.08 (br s, 1H, NH), 7.15 – 7.06 (m, 3H, CH_{ar}), 7.05 (br s, 1H, NH), 3.78 (s, 3H, OCH_3), 2.28 (s, 6H, CH_3); **^{13}C NMR (100 MHz, CDCl$_3$)** δ = 158.2 (C_q), 136.0 (C_q), 133.0 (C_q), 128.3 (CH), 127.4 (CH), 64.6 (OCH_3), 18.4 (CH_3); **ESI-MS:** calculated $[C_{10}H_{14}N_2O_2Na]^+$: 217.0947, found: 217.0955; **ATR-FTIR (cm^{-1}):** 3392, 3191, 3077, 2969, 1670, 1591, 1508, 1468, 1376, 1295, 1215, 1080, 953, 790, 750, 721, 699, 612, 562.

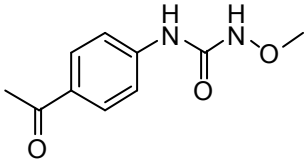
***N*-Methoxy-*N*'-(*p*-nitrophenyl)urea (2j).**



Following general procedure C on a 8 mmol scale, the title compound **2j** was obtained after purification by flash column chromatography as a yellow solid (1.06 g, 63% yield). $\mathbf{R_F}$

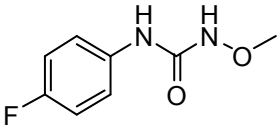
(pentane/EtOAc 33:67) = 0.31; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.93 (br s, 1H, NH), 9.54 (br s, 1H, NH), 8.17 (app d, *J* = 9.3 Hz, 2H, CH_{ar}), 7.88 (app d, *J* = 9.3 Hz, 2H, CH_{ar}), 3.64 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 156.3 (C_q), 146.0 (C_q), 141.5 (C_q), 124.7 (CH), 118.6 (CH), 64.1 (CH_3); **ESI-MS:** calculated $[C_8H_9N_3O_4Na]^+$: 234.0485, found: 234.0486; **ATR-FTIR (cm^{-1}):** 3312, 3199, 3084, 2947, 2831, 1662, 1613, 1593, 1538, 1499, 1414, 1334, 1322, 1238, 1179, 1092, 940, 858, 848, 832, 751, 727, 682, 591.

***N*-Methoxy-*N*'-(*p*-acetylphenyl)urea (2k).**



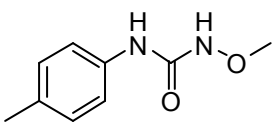
Following general procedure B on a 3.2 mmol scale, the title compound **2k** was obtained after purification by flash column chromatography (pentane/EtOAc 33:67) as a white solid (312 mg, 47% yield). **R_F** (pentane/EtOAc 25:75) = 0.39; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.74 (s, 1H, NH), 9.23 (s, 1H, NH), 7.88 (app d, *J* = 8.9 Hz, 2H, CH_{ar}), 7.75 (app d, *J* = 8.9 Hz, 2H, CH_{ar}), 3.63 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 196.5 (C_q), 156.6 (C_q), 143.9 (C_q), 130.9 (C_q), 129.3 (CH), 118.4 (CH), 64.0 (CH_3), 26.4 (CH_3); **ESI-MS:** calculated $[C_{10}H_{12}N_2O_3Na]^+$: 231.0740, found: 231.0741; **ATR-FTIR (cm^{-1}):** 3339, 3206, 1677, 1663, 1586, 1524, 1509, 1409, 1360, 1320, 1306, 1270, 1241, 1180, 1090, 1051, 1025, 1006, 951, 829, 801, 748, 660, 590.

***N*-Methoxy-*N*'-(*p*-fluorophenyl)urea (2l).**



Following general procedure B on a 10 mmol scale, the title compound **2l** was obtained after recrystallization from EtOAc (40 °C to -20 °C) as a white crystalline solid (1.27 g, 69 %). **R_F** (pentane/EtOAc 50:50) = 0.29; **^{1}H NMR (400 MHz, DMSO-d^6)** δ = 9.53 (s, 1H, NH), 8.96 (s, 1H, NH), 7.6 (m, 2H, CH_{ar}), 7.06 (m, 2H, CH_{ar}), 3.61 (s, 3H, OCH_3); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 157.7 (d, *J* = 239.2 Hz, C_{para}), 153.4 (d, *J* = 2.3 Hz, C_{ipso}), 121.3 (d, *J* = 7.8 Hz, C_{ortho}), 114.9 (d, *J* = 22.1 Hz, C_{meta}), 63.8 (CH_3); **^{19}F{^{1}H} NMR (282 MHz, DMSO-d^6)** δ = -120.87 (s); **ESI-MS:** calculated $[C_8H_9FN_2O_2Na]^+$: 207.0540, found: 207.0557; **ATR-FTIR (cm^{-1}):** 3333, 3243, 1663, 1610, 1527, 1508, 1411, 1313, 1212, 1158, 949, 830, 805, 673, 609, 564, 516.

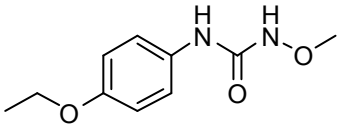
***N*-Methoxy-*N*'-(*p*-tolyl)urea (2m).**



Following general procedure B on a 15 mmol scale, the title compound **2m** was obtained after flash column chromatography (pentane/EtOAc 50:50) as a white solid (2.51 g, 93% yield). **R_F** (pentane/EtOAc 50:50) = 0.36; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.42 (s, 1H, NH), 8.76 (s, 1H, NH), 7.45 (dt, *J* = 8.4 Hz, *J* = 1.8 Hz, 2H, CH_{ar}), 7.06 (app d, *J* = 8.3 Hz, 2H, CH_{ar}),

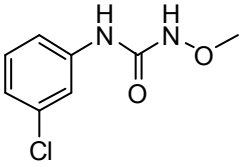
3.61 (s, 3H, OCH_3), 2.23 (s, 3H, $C_{ar}CH_3$); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 157.1 (C_q), 136.5 (C_q), 131.3 (C_q), 128.9 (CH), 119.7 (CH), 63.8 (CH_3), 20.4 (CH_3); **ESI-MS:** calculated $[C_9H_{12}N_2O_2Na]^+$: 203.0791, found: 203.0799; **ATR-FTIR (cm^{-1}):** 3310, 3206, 1651, 1593, 1513, 1440, 1407, 1325, 1236, 1094, 945, 817, 790, 751, 668.

_N_-Methoxy-_N_'-(_p_-ethoxyphenyl)urea (2n).



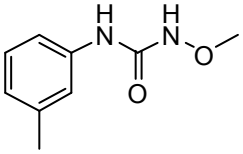
Following general procedure B on a 10 mmol scale, the title compound **2n** was obtained after recrystallization from EtOAc (50 °C to -20 °C) as a white crystalline solid (928 mg, 44 %). **R_F** (pentane/EtOAc 50:50) = 0.33; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.38 (s, 1H, NH), 8.73 (s, 1H, NH), 7.45 (app d, J = 8.9 Hz, 2H, CH_{ar}), 6.83 (app d, J = 8.9 Hz, 2H, CH_{ar}), 3.96 (q, J = 7.0 Hz, 2H, OCH_2), 3.60 (s, 3H, OCH_3) 1.30 (t, J = 7.0 Hz, 3H, CH_2CH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 157.3 (C_q), 154.1 (C_q), 131.9 (C_q), 121.4 (CH), 114.2 (CH), 63.8 (CH_3), 63.1 (CH_2), 14.7 (CH_3); **ESI-MS:** calculated $[C_{10}H_{14}N_2O_3Na]^+$: 233.0897, found: 233.0899; **ATR-FTIR (cm^{-1}):** 3334, 3190, 2971, 1653, 1597, 1518, 1473, 1421, 1391, 1321, 1301, 1267, 1228, 1175, 1117, 1091, 1050, 958, 923, 833, 804, 792, 715, 649, 626.

_N_-Methoxy-_N_'-(_m_-chlorophenyl)urea (2o).



Following general procedure B on a 7.5 mmol scale, the title compound **2o** was obtained by recrystallization from pentane/EtOAc 2:1 (40 °C to -20 °C) as a white solid (1.01 g, 67% yield). **R_F** (pentane/EtOAc 75:25) = 0.16; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.48 (s, 1H, NH), 9.08 (s, 1H, NH), 7.80 (tr, J = 2 Hz, 1H, CH_{ortho}), 7.55 (dd, J = 8.3 Hz, J = 1.1 Hz, 1H, CH_{ar}), 7.27 (app t, J = 8.1 Hz, 1H, CH_{ar}), 7.02 (dd, J = 8.0 Hz, J = 1.0 Hz, 1H, CH_{ar}), 3.62 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 156.9 (C_q), 140.8 (C_q), 132.9 (C_q), 130.1 (CH), 122.1 (C_q), 118.9 (CH), 117.8 (CH), 64.0 (CH_3); **ESI-MS:** calculated $[C_8H_9ClN_2O_2Na]^+$: 223.0245, found: 223.0245; **ATR-FTIR (cm^{-1}):** 3327, 3203, 3078, 1655, 1589, 1526, 1483, 1427, 1414, 1305, 1227, 1099, 1079, 1014, 999, 951, 874, 783, 745, 674, 632, 587.

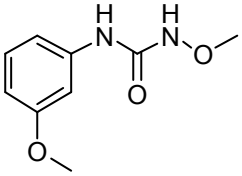
_N_-Methoxy-_N_'-(_m_-tolyl)urea (2p).



Following general procedure B on a 15 mmol scale, the title compound **2p** was obtained by recrystallization from Et_2O (40 °C to -20 °C) as a white solid (1.84 g, 68% yield). **R_F** (pentane/EtOAc 67:33) = 0.34; **^{1}H NMR (400 MHz, DMSO-d^6)** δ = 9.48 (s, 1H, NH), 8.77 (s, 1H, NH), 7.43 (s, 1H, CH_{ortho}), 7.38 (app d, J = 8.2 Hz, 1H, CH_{ar}), 7.13 (app t, J = 7.8 Hz, 1H, CH_{ar}), 6.81 (d, J = 7.6 Hz, 1H, CH_{ar}), 3.62 (s, 3H, OCH_3), 2.26 (s, 3H, CH_3); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 157.1 (C_q), 139.0 (C_q), 137.6 (C_q), 128.3 (CH), 123.2 (C_q), 120.1 (CH), 116.8

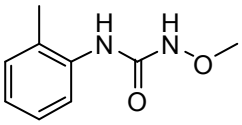
(CH), 63.9 (CH_3), 21.2 (CH_3); **ESI-MS:** calculated $[C_9H_{12}N_2O_2Na]^+$: 203.0791, found: 203.0784; **ATR-FTIR (cm^{-1}):** 3301, 3205, 1651, 1592, 1533, 1439, 1322, 1284, 1250, 1170, 1093, 1018, 956, 929, 897, 803, 768, 752, 690, 626, 591.

***N*-Methoxy-*N*'-(*m*-methoxyphenyl)urea (2q).**



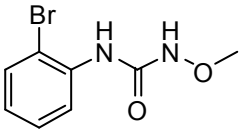
Following general procedure B on a 10 mmol scale, purification by careful flash column chromatography (pentane/EtOAc 60:40) afforded the title compound **2q** as a white solid (1.51 g, 76% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.35; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 7.73 (br s, 1H, NH), 7.58 (br s, 1H, NH), 7.21 (dd, *J* = 10.3 Hz, *J* = 5.6 Hz, 1H, CH_{meta}), 7.21 (s, 1H, CH_{ortho}), 6.98 (ddd, *J* = 8.1 Hz, *J* = 2.0 Hz, *J* = 0.8 Hz, 1H, CH_{ar}), 6.65 (ddd, *J* = 8.3 Hz, *J* = 2.5 Hz, *J* = 0.8 Hz, 1H, CH_{ar}), 3.80 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 160.3 (C_q), 157.2 (C_q), 138.6 (C_q), 129.8 (CH), 112.0 (C_q), 109.8 (CH), 105.6 (CH), 64.7 (CH_3), 55.4; **ESI-MS:** calculated $[C_9H_{12}N_2O_3Na]^+$: 219.0740, found: 219.0735; **ATR-FTIR (cm^{-1}):** 3299, 3224, 1653, 1606, 1594, 1528, 1450, 1430, 1335, 1286, 1199, 1159, 1097, 1035, 965, 932, 853, 773, 751, 685.

***N*-Methoxy-*N*'-(*o*-tolyl)urea (2r).**



Following general procedure B on a 15 mmol scale, the title compound **2r** was obtained after recrystallization from EtOAc (50 °C to -20 °C) as white hairy crystals (1.52 g = 56% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.48; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.50 (s, 1H, NH), 8.24 (s, 1H, NH), 7.46 (d, *J* = 7.7 Hz, 1H, CH_{ar}), 7.17 (m, 2H, CH_{ar}), 7.06 (td, *J* = 7.4 Hz, *J* = 0.7 Hz, 1H, CH_{ar}), , 3.66 (s, 3H, OCH_3), 2.22 (s, 3H, CH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 157.3 (C_q), 136.4 (C_q), 131.4 (C_q), 130.1 (CH), 126.0 (CH), 124.5 (CH), 124.5 (CH), 63.9 (CH_3), 17.6 (CH_3); **ESI-MS:** calculated $[C_9H_{12}N_2O_2Na]^+$: 203.0791, found: 203.0792; **ATR-FTIR (cm^{-1}):** 3411, 3157, 3082, 1678, 1585, 1527, 1457, 1312, 1284, 1252, 1183, 1082, 1045, 961, 809, 762, 721, 655, 594, 583.

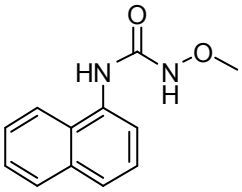
***N*-Methoxy-*N*'-(*o*-bromophenyl)urea (2s).**



Following general procedure C on a 10 mmol scale, the title compound **2s** was obtained after purification by careful flash column chromatography (pentane/EtOAc 90:10 to 75:25) as a white solid (802 mg, 33% yield). $\mathbf{R_F}$ (pentane/EtOAc 75:25) = 0.36; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 8.27 (dd, *J* = 8.0 Hz, *J* = 1.5 Hz, 1H, CH_{ar}), 8.23 (s, 1H, NH), 8.00 (br s, 1H, NH), 7.53 (dd, *J* = 8.3 Hz, *J* = 1.6 Hz, 1H, CH_{ar}), 7.31 (m, 1H, CH_{ar}), 6.95 (dt, *J* = 7.8 Hz, *J* = 1.6 Hz, 1H, CH_{ar}), 3.84 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 157.0 (C_q), 136.5 (C_q), 132.3 (CH), 128.5 (CH), 124.7 (CH), 121.1 (CH), 113.5 (CH), 64.9 (CH_3);

ESI-MS: calculated $[C_8H_9BrN_2O_2Na]^+$: 266.9740, 268.9719, found: 266.9735, 268.9714; **ATR-FTIR (cm^{-1}):** 3377, 3170, 3087, 1680, 1590, 1578, 1535, 1439, 1306, 1232, 1082, 1049, 1023, 960, 774, 745, 644, 602.

***N*-Methoxy-*N*'-(1-naphthyl)urea (2t).**

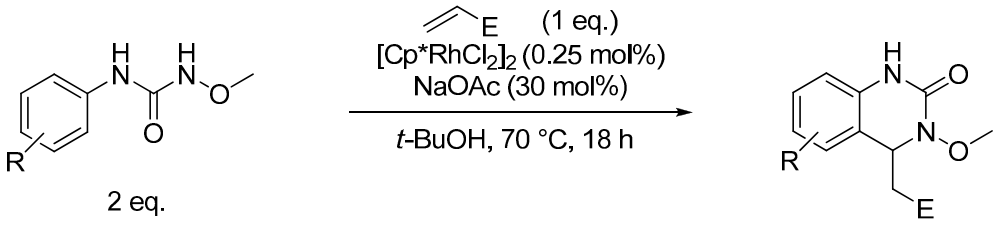


Following general procedure C on a 10 mmol scale, the title compound **2t** was obtained after purification by flash column chromatography (pentane/EtOAc 67:33 to 50:50) as a violet solid (0.96 g, 55% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.39; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 8.13 (s, 1H, NH), 8.02 (s, 1H, NH), 7.93 (d, *J* = 7.4 Hz, 1H, CH_{ar}), 7.88 (m, 2H, CH_{ar}), 7.70 (d, *J* = 8.1 Hz, 1H, CH_{ar}), 7.57 – 7.46 (m, 3H, CH_{ar}), 3.86 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 158.1 (C_q), 134.2 (C_q), 131.8 (C_q), 128.8 (CH), 127.3 (C_q), 126.4 (CH), 126.1 (CH), 125.9 (CH), 125.5 (CH), 120.6 (CH), 120.3 (CH), 64.8 (CH_3); **ESI-MS:** calculated $[C_{12}H_{12}N_2O_2Na]^+$: 239.0791, found: 239.0796; **ATR-FTIR (cm^{-1}):** 3391, 3143, 3051, 2893, 1667, 1520, 1502, 1348, 1263, 1105, 1082, 984, 945, 815, 796, 772, 745.

5. General Procedures for the Synthesis of 4

i) Synthesis of 3-methoxy-3,4-dihydroquinazolin-2(*1H*)-ones:

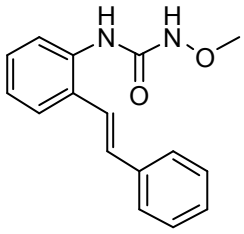
General Procedure E:



An oven-dried 50 mL screw-capped tube was charged with *N*-Methoxy,*N*'-aryl urea **2** (2.0 mmol, 2.0 eq.), pentamethylcyclopentadienylrhodium(III) chloride dimer $[Cp^*RhCl_2]_2$ (15.5 mg, 0.025 mmol, 0.025 eq.) and sodium acetate (24.6 mg, 0.30 mmol, 0.30 eq.). Dry *t*-BuOH (10 mL) and the desired olefin (1.0 mmol, 1.0 equiv) were added via syringe. The reaction vessel was sealed and placed in an pre-heated oil bath and stirred overnight at 70 °C. After 18 hours, TLC analysis indicated full conversion of the starting material and the reaction mixture was cooled to room-temperature. Filtration through a short pad of silica gel and washing with EtOAc was followed by removal of the solvents under reduced pressure. The orange to brown residue was purified by flash column chromatography to yield pure 3-methoxy-3,4-dihydroquinazolin-2(*1H*)-ones **4**.

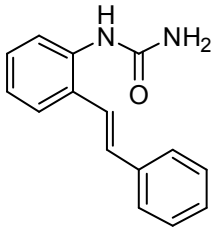
6. Preparation and Characterization of 3-5

(*E*)-1-Methoxy-3-(2-styrylphenyl)urea (3).



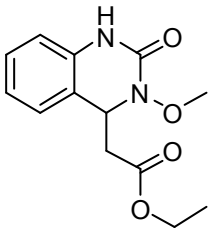
Following a modified protocol of general procedure D (Ag_2CO_3 was used instead of NaOAc; *t*-AmylOH was used instead of *t*-BuOH), the title compound **3** was obtained after flash column chromatography (pentane/EtOAc 75:25 to 50:50) as an off-white solid (125 mg, 47% yield) along with the reduced Heck-product (**3**^{red}, see below for characterization). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.54; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.54 (s, 1H, NH), 8.67 (s, 1H, NH), 7.74 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H, CH_{ar}), 7.59 – 7.53 (m, 2H, CH_{ar}), 7.46 – 7.34 (m, 3H, CH_{ar}), 7.32 (d, *J* = 16.6 Hz, 1H, CH_{olefin}), 7.32 – 7.18 (m, 3H, CH_{ar}), 7.18 (d, *J* = 16.5 Hz, 1H, CH_{olefin}), 3.68 (s, 1H, OCH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 157.7 (C_q), 137.2 (C_q), 135.5 (C_q), 131.8 (C_q), 129.5 (CH), 128.8 (2×CH), 127.8 (2×CH), 126.4 (2×CH), 126.4 (CH), 125.6 (CH), 125.2 (CH), 124.2 (CH), 63.9 (OCH_3); **ESI-MS:** calculated $[C_{16}H_{16}N_2O_2Na]^+$: 291.1104, found: 286.1099; **ATR-FTIR (cm^{-1}):** 3324, 3201, 1682, 1658, 1601, 1513, 1497, 1485, 1449, 1305, 1268, 1235, 1156, 1091, 1025, 1001, 959, 821, 758, 714, 687, 639, 627, 581, 523.

(*E*)-1-(2-styrylphenyl)urea (3^{red}).



Obtained as a beige solid (37 mg, 15% yield). **R_F** (pentane/EtOAc 50:50) = 0.16; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 8.12 (s, 1H, NH), 7.78 (dd, *J* = 8.2 Hz, *J* = 1.1 Hz, 1H, CH_{ar}), 7.66 – 7.58 (m, 3H, CH_{ar}), 7.44 – 7.37 (m, 2H, CH_{ar}), 7.34 (d, J = 16.2 Hz, 1H, CH_{olefin}), 7.30 – 7.26 (m, 1H, CH_{ar}), 7.24 – 7.17 (m, 1H, CH_{ar}), 7.13 (d, *J* = 16.1 Hz, 1H, CH_{olefin}), 7.03 (ddd, *J* = 7.6 Hz, *J* = 7.3 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 6.05 (s, 2H, NH_2); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 156.1 (C_q), 137.3 (C_q), 137.1 (C_q), 129.8 (C_q), 128.6 (2×CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 126.6 (2×CH), 125.6 (CH), 123.8 (CH), 122.7 (CH), 122.6 (CH); **ESI-MS:** calculated $[C_{15}H_{14}N_2ONa]^+$: 261.0998, found: 261.0996; **ATR-FTIR (cm^{-1}):** 3418, 3332, 3296, 3216, 3057, 3026, 1655, 1610, 1581, 1535, 1496, 1483, 1450, 1357, 1293, 1253, 1049, 1024, 1004, 964, 823, 755, 686, 597. 555.

Ethyl 2-(3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4aa).

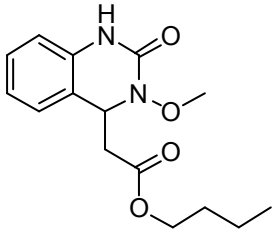


Following general procedure D, the title compound **4aa** was obtained after careful flash column chromatography (pentane/EtOAc 40:60) as an off-white solid (198 mg, 75% yield). **R_F** (pentane/EtOAc 50:50) = 0.24; **^{1}H NMR (300 MHz, CDCl$_3$)** δ = 8.94 (s, 1H, NH), 7.20 (m, 2H, CH_{ar}), 6.95 (dt, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, CH_{ar}), 6.88 (d, *J* = 7.6 Hz, 1H, CH_{ar}), 5.22 (dd, *J* = 8.1 Hz, *J* = 4.8 Hz, 1H, NCH), 4.09 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 3.04 (dd, *J* = 15.2 Hz, *J* = 4.8 Hz, 1H, CH_2), 2.63 (dd, *J* = 15.2 Hz, *J* = 8.1 Hz, 1H, CH_2), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, CDCl$_3$)** δ = 170.7 (C_q), 155.4 (C_q), 135.1 (C_q), 129.1 (CH), 126.4 (CH), 122.6 (CH), 121.4 (C_q), 114.9 (CH), 62.8 (OCH_3), 60.9 (OCH_2), 57.9 (NCH), 37.9 (CH_2), 14.2 (CH_3); **ESI-MS:** calculated $[C_{13}H_{16}N_2O_4Na]^+$: 287.1002, found: 287.1006; **ATR-FTIR (cm^{-1}):** 3071, 2974, 2937, 1729, 1694, 1601, 1499, 1400, 1287, 1216, 1192, 1166, 1122, 1089, 994, 962, 863, 754, 687, 616, 555.

Big scale procedure for the synthesis of 4aa.

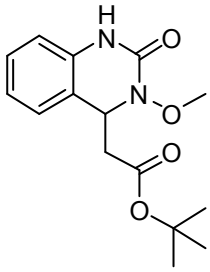
An oven-dried 250 mL round-bottom flask, equipped with a magnetic stir bar, was charged with urea **2a** (2.5 g, 15.0 mmol, 2.0 eq.), NaOAc (184.5 mg, 2.25 mmol, 0.3 eq.) and $[Cp^*RhCl_2]_2$ (46.4 mg, 0.075 mmol, 0.01 eq.). Freshly distilled ethyl acrylate (798 µL, 7.5 mmol, 1.0 eq.) and dry *t*-AmylOH was added via glass-tight syringe. The flask was sealed with a glass-stopper and the reaction mixture was placed in a preheated-oilbath (70°C) and stirred for 24 hours. After cooling to room-temperature, the volatiles were evaporated under reduced pressure and the crude product purified by flash column chromatography (6 × 17 cm SiO_2, pentane/EtOAc 40:60) to afford the desired product **4aa** as an off-white solid (1.37 g, 69% yield). For analytic data, see above.

***n*-Butyl 2-(3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ab).**



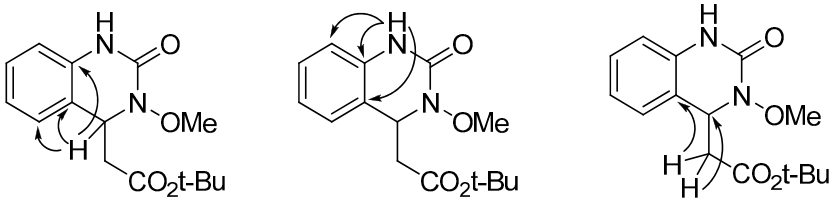
Following general procedure D, the title compound **4ab** was obtained after flash column chromatography (pentane/EtOAc 67:33) as an pale orange oil (221 mg, 75% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.38; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.72 (s, 1H, NH), 7.16 (m, 2H, CH_{ar}), 6.90 (td, *J* = 7.5 Hz, *J* = 0.6 Hz, 1H, CH_{ar}), 6.83 (d, *J* = 7.8 Hz, 1H, CH_{ar}), 5.13 (dd, *J* = 6.9 Hz, *J* = 5.5 Hz, 1H, NCH), 3.95 (t, *J* = 6.6 Hz, 2H, OCH_2), 3.65 (s, 3H, OCH_3), 2.82 (dd, *J* = 14.6 Hz, *J* = 5.3 Hz, 1H, $(O)CCH_2$), 2.55 (dd, *J* = 14.6 Hz, *J* = 7.0 Hz, 1H, $(O)CCH_2$), 1.46 (m, 2H, CH_2), 1.22 (m, 2H, CH_2), 0.83 (t, *J* = 7.3 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 169.9 (C_q), 153.3 (C_q), 135.9 (C_q), 128.7 (CH), 126.2 (CH), 121.5 (CH), 121.1 (C_q), 114.0 (CH), 63.9 (OCH_3), 62.0 (OCH_2), 57.6 (NCH), 37.5 ($(O)CCH_2$), 30.0 (CH_2), 18.5 (CH_2), 13.5 (CH_3); **ESI-MS:** calculated $[C_{15}H_{20}N_2O_4Na]^+$: 315.1315, found: 315.1312; **ATR-FTIR (cm^{-1}):** 3239, 3091, 2961, 2934, 1700, 1601, 1501, 1438, 1394, 1289, 1257, 1146, 1026, 998, 964, 753, 689, 624, 569.

***t*-Butyl 2-(3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ac).**

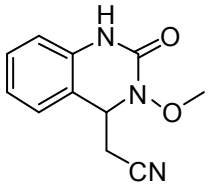


Following general procedure D, the title compound **4ac** was obtained after careful flash column chromatography (pentane/EtOAc 60:40) as a white solid (212 mg, 72% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.42; **^{1}H NMR (400 MHz, DMSO-d^6)** δ = 9.68 (s, 1H, NH), 7.17 (m, 2H, CH_{ar}), 6.91 (td, *J* = 7.5 Hz, *J* = 1.1 Hz, 1H, CH_{ar}), 6.81 (dd, *J* = 7.9 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 5.09 (dd, *J* = 6.7 Hz, *J* = 5.5 Hz, 1H, NCH), 3.65 (s, 3H, OCH_3), 2.70 (dd, *J* = 14.5 Hz, *J* = 5.4 Hz, 1H, $(O)CCH_2$), 2.46 (dd, *J* = 14.6 Hz, *J* = 6.9 Hz, 1H, $(O)CCH_2$), 1.32 (s, 9H, $C(CH_3)_3$); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 169.1 (C_q), 153.2 (C_q), 135.9 (C_q), 128.6 (CH), 126.3 (CH), 121.4 (CH), 121.1 (C_q), 114.0 (CH), 80.3 (OC_q), 61.9 (OCH_3), 57.6 (NCH), 38.7 ($(O)CCH_2$), 30.0 (CH_2), 27.5 (CH_2); **ESI-MS:** calculated $[C_{15}H_{20}N_2O_4Na]^+$: 315.1315, found: 315.1313; **ATR-FTIR (cm^{-1}):** 3087, 1968, 1931, 1702, 1600, 1493, 1368, 1350, 1286, 1265, 1226, 1138, 1120, 1087, 996, 963, 916, 847, 751, 695, 625, 592.

The structure of compounds **4** was unambiguously confirmed by 2D-NMR analysis. Key ^{1}H-^{13}C gHMBC correlations are the following:

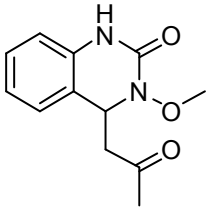


2-(3-Methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetonitrile (4ad).



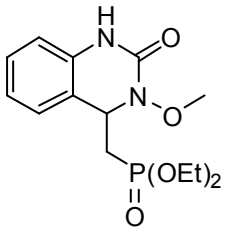
Following a modified protocol (24 hours additional heating at 90 °C) of general procedure D, the title compound **4ad** was obtained after flash column chromatography (pentane/EtOAc 1:1 to 2:3) as a beige solid (97 mg, 44% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.14; **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.91 (s, 1H, NH), 7.29 (m, 2H, CH_{ar}), 7.06 (td, *J* = 7.6 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 6.92 (dd, *J* = 8.3 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 4.98 (dd, *J* = 8.5 Hz, *J* = 3.4 Hz, 1H, NCH), 3.87 (s, 3H, OCH_3), 3.07 (dd, *J* = 16.4 Hz, *J* = 3.5 Hz, 1H, $NCCH_2$), 2.76 (dd, *J* = 16.5 Hz, *J* = 8.5 Hz, 1H, $NCCH_2$); **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 154.5 (C_q), 135.0 (C_q), 130.1 (CH), 126.7 (CH), 123.1 (CH), 118.9 (C_q), 116.6 (C_q), 115.2 (CH), 63.4 (OCH_3), 58.1 (NCH), 21.6 ($NCCH_2$); **ESI-MS:** calculated $[C_{11}H_{11}N_3O_2Na]^+$: 240.0743, found: 240.0734; **ATR-FTIR (cm^{-1}):** 3213, 3080, 1963, 2928, 1691, 1603, 1504, 1448, 1319, 1308, 1261, 1191, 1098, 1021, 989, 795, 741, 696, 595.

3-Methoxy-4-(2-oxopropyl)-3,4-dihydroquinazolin-2(1H)-one (4ae).



Following general procedure D, the title compound was obtained after flash column chromatography (pentane/EtOAc 25:75) as a pale-yellow solid (96 mg, 41% yield). $\mathbf{R_F}$ (pentane/EtOAc 25:75) = 0.22; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.71 (s, 1H, NH), 7.17 (m, 2H, CH_{ar}), 6.90 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 6.81 (d, *J* = 7.8 Hz, 1H, CH_{ar}), 5.18 (dd, *J* = 7.1 Hz, *J* = 5.5 Hz, 1H, NCH), 3.62 (s, 3H, OCH_3), 2.97 (dd, *J* = 16.1 Hz, *J* = 5.2 Hz, 1H, $(O)CCH_2$), 2.69 (dd, *J* = 16.1 Hz, *J* = 7.1 Hz, 1H, $(O)CCH_2$), 2.06 (s, 3H, $(O)CCH_3$); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 205.8 (C_q), 153.8 (C_q), 135.8 (C_q), 128.5 (CH), 126.3 (CH), 122.2 (C_q), 121.5 (CH), 114.0 (CH), 61.9 (OCH_3), 56.7 (NCH), 50.0 ($(O)CCH_2$), 30.3 (CH_3); **ESI-MS:** calculated $[C_{12}H_{14}N_2O_3Na]^+$: 257.0897, found: 257.0897; **ATR-FTIR (cm^{-1}):** 3209, 3080, 2980, 2935, 2906, 1714, 1682, 1600, 1493, 1441, 1404, 1360, 1322, 1281, 1161, 1149, 1095, 1050, 1026, 986, 941, 748, 696, 636, 600, 585, 560.

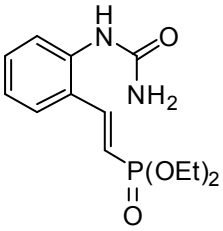
Diethyl (3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)methylphosphonate (4af).



Following general procedure D, the title compound **4af** was obtained after flash column chromatography (pentane/EtOAc 1:2) as an off-white solid (78 mg, 26% yield) along with the reduced Heck product (see below for characterization). $\mathbf{R_F}$ (EtOAc/EtOH 9:1) = 0.35; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.06 (s, 1H, NH), 7.33 (d, *J* = 6.9 Hz, 1H, CH_{ar}), 7.15 (td, *J* = 7.8 Hz, *J* = 1.3 Hz, 1H, CH_{ar}), 6.91 (td, *J* = 7.6 Hz, *J* = 1.0 Hz, 1H, CH_{ar}), 6.84 (d, *J* = 7.9 Hz, 1H, CH_{ar}), 5.02 (m, 1H, NCH), 3.95 (m, 2H, $POCH_2$), 3.80 (m, 2H, $POCH_2$), 3.75 (s, 3H, OCH_3), 2.56 (ddd, *J* = 20.4 Hz, *J* = 15.0 Hz, *J* = 2.8 Hz, 1H, PCH_2); 2.10 (ddd, *J* = 17.7 Hz, *J* = 15.0 Hz, *J* = 10.1 Hz, 1H, PCH_2), 1.19 (t, *J* = 7.1 Hz, 3H, CH_3),

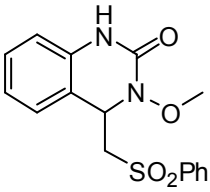
1.04 (t, J = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 155.8 (C_q), 135.1 (C_q), 129.0 (CH), 127.5 (CH), 122.2 (CH), 121.5 (d, J = 1.6 Hz, CH), 114.7 (CH), 62.8 (OCH_3), 61.9 (d, J = 6.3 Hz, OCH_2), 61.7 (d, J = 6.5 Hz, OCH_2), 56.7 (NCH), 27.7 (d, J = 138.1 Hz, PCH_2), 16.3 (d, J = 6.2 Hz, CH_3), 16.1 (d, J = 6.6 Hz, CH_3); **^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$)** δ = 26.17 (s); **ESI-MS:** calculated $[C_{14}H_{21}N_2O_5PNa]^+$: 351.1080, found: 351.1076; **ATR-FTIR (cm^{-1}):** 3228, 2980, 2909, 1706, 1601, 1501, 1440, 1391, 1290, 1247, 1223, 1161, 1501, 1022, 993, 962, 888, 831, 755, 729, 687, 594, 566.

(*E*)-Diethyl 2-ureidostyrylphosphonate.



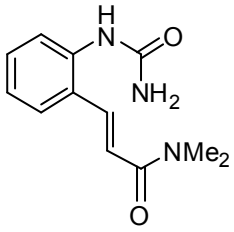
Obtained as a white solid (75 mg, 25% yield). **R_F** (EtOAc/EtOH 9:1) = 0.29; **^{1}H NMR (400 MHz, DMSO-d^6)** δ = 8.28 (br s, 1H, NH), 7.73 (d, J = 7.6 Hz, 1H, CH_{ar}), 7.64 – 7.49 (m, 2H, CH_{ar}, CH_{olefin}), 7.32 (t, J = 7.4 Hz, 1H, CH_{ar}), 7.09 (t, J = 7.5 Hz, 1H, CH_{ar}), 6.48 (t, J = 17.9 Hz, 1H, CH_{olefin}), 6.04 (br s, 2H, NH_2), 4.11 – 3.97 (m, 4H, $P(OCH_2)_2$), 1.26 (t, J = 7.0 Hz, 6H, 2×CH_3); **^{13}C NMR (100 MHz, DMSO, d^6)** δ = 156.2 (C_q), 143.1 (d, J = 7.9 Hz, C_q), 138.2 (CH_{ar}), 127.1 (d, J = 22.7, CH_{olefin}), 126.5 (CH_{ar}), 124.4 (CH_{ar}), 123.5 (CH_{ar}), 115.0 (d, J = 186.0 Hz, PCH_{olefin}), 61.2 (d, J = 5.4 Hz, 2×OCH_2), 16.3 (d, J = 6.2 Hz, 2×CH_3); **^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$)** δ = 19.33 (s) (s); **ESI-MS:** calculated $[C_{13}H_{19}N_2O_4PNa]^+$: 321.0975, found: 321.0972; **ATR-FTIR (cm^{-1}):** 4413, 3335, 3224, 2983, 1689, 1668, 1633, 1605, 1574, 1531, 1456, 1362, 1303, 1249, 1216, 1163, 1049, 1025, 965, 855, 832, 765, 748, 687, 644, 588, 545.

3-Methoxy-4-(phenylsulfonylmethyl)-3,4-dihydroquinazolin-2(1H)-one (4ag).



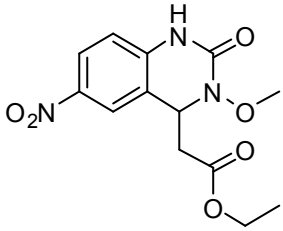
Following general procedure D, the title compound **4ag** was obtained after flash column chromatography (pentane/EtOAc 1:2) as an off-white solid (231 mg, 69% yield). **R_F** (pentane/EtOAc 1:2) = 0.21; **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.77 (s, 1H, NH), 7.81 (m, 2H, CH_{ar}), 7.56 (m, 1H, CH_{ar}), 7.46 (m, 2H, CH_{ar}), 7.39 (dd, J = 7.6 Hz, J = 1.0 Hz, 1H, CH_{ar}), 7.14 (td, J = 7.5 Hz, J = 1.4 Hz, 1H, CH_{ar}), 6.94 (td, J = 7.6 Hz, J = 1.0 Hz, 1H, CH_{ar}), 6.76 (dd, J = 7.9 Hz, J = 1.0 Hz, 1H, CH_{ar}), 5.25 (dd, J = 8.4 Hz, J = 2.1 Hz, 1H, NCH), 3.77 (dd, J = 14.0 Hz, J = 2.2 Hz, 1H, $NCCH_2$), 3.60 (s, 3H, OCH_3), 3.35 (dd, J = 14.0 Hz, J = 8.4 Hz, 1H, $NCCH_2$); **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 155.2 (C_q), 139.8 (C_q), 134.7 (C_q), 134.0 (CH), 129.6 (CH), 129.4 (CH), 127.9 (CH), 127.7 (CH), 123.0 (CH), 120.3 (C_q), 114.8 (CH), 62.7 (OCH_3), 57.4 (O_2SCH_2), 55.6 (NCH); **ESI-MS:** calculated $[C_{16}H_{16}N_2O_4SNa]^+$: 355.0723, found: 355.0725; **ATR-FTIR (cm^{-1}):** 3228, 3088, 2981, 2934, 1692, 1601, 1498, 1443, 1421, 1387, 1343, 1286, 1272, 1161, 1130, 1085, 987, 905, 823, 746, 690, 631, 605.

(*E*)-*N*,*N*-dimethyl-3-(2-ureidophenyl)acrylamide (5).



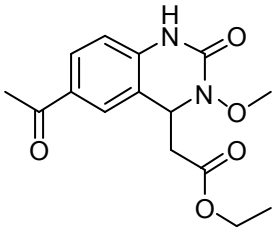
Following general procedure D, the title compound **5** was obtained after flash column chromatography (EtOAc/EtOH 1:9) as an off-white solid (126 mg, 55% yield). $\mathbf{R_F}$ (EtOAc/EtOH 9:1) = 0.23; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 8.22 (s, 1H, NH), 7.75 – 7.63 (m, 3H, 2×CH_{ar}, CH_{olefin}), 7.33 – 7.24 (m, 1H, CH_{ar}), 7.07 (d, *J* = 15.4 Hz, 1H, CH_{olefin}), 7.04 (t, *J* = 7.3 Hz, 1H, CH_{ar}), 6.06 (s, 2H, NH_2), 3.15 (s, 3H, CH_3), 2.94 (s, 3H, CH_3); **^{13}C NMR (100 MHz, DMSO-d^6)** δ = 165.7 (C_q), 156.1 (C_q), 138.2 (C_q), 136.4 (CH), 126.9 (CH), 126.6 (C_q), 123.3 (CH), 122.9 (CH), 119.7 (CH), 36.9 (CH_3), 35.4 (CH_3); **ESI-MS:** calculated $[C_{12}H_{15}N_3O_2Na]^+$: 286.1056, found: 286.1052; **ATR-FTIR (cm^{-1}):** 3409, 3277, 3201, 1664, 1640, 1621, 1589, 1576, 1538, 1500, 1454, 1414, 1394, 1356, 1300, 1356, 1300, 1265, 1149, 1012, 970, 889, 801, 754, 745 ,636, 603, 573.

Ethyl 2-(3-methoxy-6-nitro-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ja).



Following general procedure D, the title compound **4ja** was obtained after flash column chromatography (pentane/EtOAc 33:67 to 25:75) as a pale-yellow solid (221 mg, 71% yield). $\mathbf{R_F}$ (pentane/EtOAc 33:67) = 0.35; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.40 (s, 1H, NH), 8.14 (m, 2H, CH_{ar}), 6.99 (d, *J* = 8.4 Hz, 1H, CH_{ar}), 5.33 (dd, *J* = 7.8 Hz, *J* = 4.2 Hz, 1H, NCH), 4.15 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.86 (s, 3H, OCH_3), 3.09 (dd, *J* = 15.7 Hz, *J* = 4.2 Hz, 1H, (O)CCH_2), 2.73 (dd, *J* = 15.7 Hz, *J* = 8.1 Hz, 1H, (O)CCH_2), 1.22 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 169.9 (C_q), 154.4 (C_q), 142.8 (C_q), 140.9 (C_q), 125.4 (CH), 123.1 (CH), 121.7 (C_q), 115.2 (CH), 63.1 (OCH_3), 61.4 (OCH_2), 57.4 (NCH), 37.8 ((O)CCH_2), 14.2 (CH_3); **ESI-MS:** calculated $[C_{13}H_{15}N_3O_6Na]^+$: 332.0853, found: 332.0870; **ATR-FTIR (cm^{-1}):** 3094, 2936, 1705, 1622, 1597, 1529, 1485, 1434, 1420, 1394, 1372, 1331, 1304, 1285, 1257, 1223, 1155, 1088, 1048, 1014, 1011, 975, 899, 884, 834, 798, 751, 729, 712, 660, 625, 594.

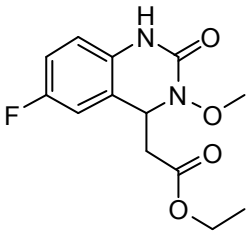
Ethyl 2-(6-acetyl-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ka).



Following a modified protocol of general procedure D (reaction was carried out on a 0.3 mmol scale), the title compound **4ka** was obtained after flash column chromatography (pentane/EtOAc 25:75) as an off-white solid (68 mg, 74% yield). $\mathbf{R_F}$ (pentane/EtOAc 25:75) = 0.24; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.56 (s, 1H, NH), 7.77 (m, 2H, CH_{ar}), 6.92 (d, *J* = 8.9 Hz, 1H, CH_{ar}), 5.24 (dd, *J* = 7.6 Hz, *J* = 4.9 Hz, 1H, NCH), 4.05 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.77 (s, 3H, OCH_3), 2.99 (dd, *J* = 15.4 Hz, *J* = 4.8 Hz, 1H, (O)CCH_2), 2.63 (dd, *J* = 15.4 Hz, *J* = 7.8 Hz, 1H, (O)CCH_2), 2.48 (s, 3H, CH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 196.4 (C_q), 170.3 (C_q), 154.8 (C_q), 139.5 (C_q), 131.7 (C_q), 129.9 (CH), 127.3 (C_q), 121.1 (CH), 114.8 (CH), 62.8 (OCH_3),

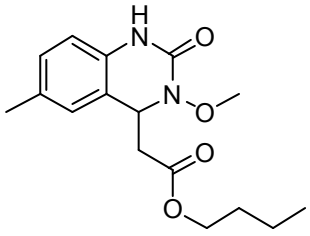
61.1 (OCH_2), 57.6 (NCH), 38.1 ((O)CCH_2), 26.4 ((O)CCH_3), 14.1 (CH_3); **ESI-MS:** calculated $[C_{15}H_{18}N_2O_5Na]^+$: 329.1108, found: 329.1109; **ATR-FTIR (cm^{-1}):** 3192, 3063, 2894, 2939, 1715, 1695, 1678, 1599, 1511, 1428, 1383, 1369, 1357, 1336, 1293, 1277, 1259, 1224, 1187, 1150, 1128, 1094, 1012, 997, 972, 920, 897, 838, 796, 755, 717.

Ethyl 2-(6-fluoro-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4la).



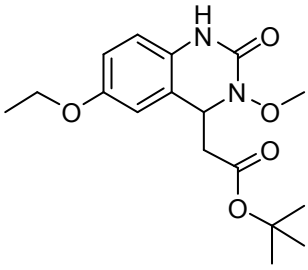
Following general procedure D, the title compound **4la** was obtained after flash column chromatography (pentane/EtOAc 40:60) as a white solid (186 mg, 66% yield). $\mathbf{R_F}$ (pentane/EtOAc 40:60) = 0.28; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.54 (s, 1H, NH), 6.94 – 6.83 (m, 3H, CH_{ar}), 6.95 (dt, *J* = 7.4 Hz, *J* = 1.1 Hz, 1H, CH_{ar}), 6.88 (d, *J* = 7.6 Hz, 1H, CH_{ar}), 5.14 (dd, *J* = 8.3 Hz, *J* = 4.5 Hz, 1H, NCH), 4.08 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.78 (s, 3H, OCH_3), 3.02 (dd, *J* = 15.4 Hz, *J* = 4.6 Hz, 1H, CH_2), 2.61 (dd, *J* = 15.4 Hz, *J* = 8.4 Hz, 1H, CH_2), 1.17 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.4 (C_q), 158.1 (d, *J* = 239.5 Hz, C_q), 155.5 (C_q), 131.4 (d, *J* = 2.5 Hz, C_q), 122.8 (d, *J* = 7.9 Hz, C_q), 116.3 (d, *J* = 8.0 Hz, CH), 115.8 (d, *J* = 23.0 Hz, CH), 113.2 (d, *J* = 24.2 Hz, CH), 62.8 (OCH_3), 61.0 (OCH_2), 57.6 (d, *J* = 1.4 Hz, NCH), 37.4 (CH_2), 14.1 (CH_3); **^{19}F{^{1}H} NMR (282 MHz, $CDCl_3$)** δ = - 120.2 (s); **ESI-MS:** calculated $[C_{13}H_{15}FN_2O_4Na]^+$: 305.0908, found: 305.0911; **ATR-FTIR (cm^{-1}):** 3200, 3091, 2978, 2931, 1730, 1693, 1503, 1433, 1392, 1370, 1346, 1311, 1294, 1256, 1232, 1216, 1159, 1147, 1111, 1092, 1017, 999, 974, 924, 879, 861, 822, 789, 715, 688, 622, 581.

***n*-Butyl 2-(3-methoxy-6-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4mb).**



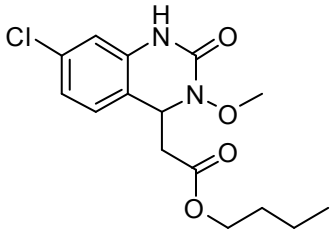
Following general procedure D, the title compound **4mb** was obtained after flash column chromatography (pentane/EtOAc 67:33) as an off-white solid (235 mg, 77% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.28; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.62 (s, 1H, NH), 6.99 (dd, *J* = 8.1 Hz, *J* = 1.4 Hz, 1H, CH_{ar}), 6.93 (s, 1H, CH_{ar}), 6.71 (d, *J* = 8.0 Hz, 1H, CH_{ar}), 5.06 (dd, *J* = 7.1 Hz, *J* = 5.4 Hz, 1H, NCH), 3.96 (m, 2H, OCH_2), 3.64 (s, 3H, OCH_3), 2.80 (dd, *J* = 14.5 Hz, *J* = 5.4 Hz, 1H, (O)CCH_2), 2.52 (dd, *J* = 14.5 Hz, *J* = 7.3 Hz, 1H, (O)CCH_2), 2.19 (s, 3H, CH_3), 1.46 (m, 2H, CH_2), 1.22 (m, 2H, CH_2), 0.83 (t, *J* = 7.3 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 170.0 (C_q), 153.4 (C_q), 133.4 (C_q), 130.4 (C_q), 129.1 (CH), 126.5 (CH), 121.1 (C_q), 114.0 (CH), 63.8 (OCH_3), 62.0 (OCH_2), 57.7 (NCH), 37.5 ((O)CCH_2), 30.1 (CH_2), 20.3 (CH_2), 18.5 (CH_3) 13.5 (CH_3); **ESI-MS:** calculated $[C_{16}H_{22}N_2O_4Na]^+$: 329.1472, found: 329.1465; **ATR-FTIR (cm^{-1}):** 3220, 2960, 2934, 1699, 1514, 1428, 1292, 1260, 1229, 1174, 1158, 1052, 1026, 1004, 821, 757, 711, 681, 619, 573.

***t*-Butyl 2-(6-ethoxy-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4nc).**



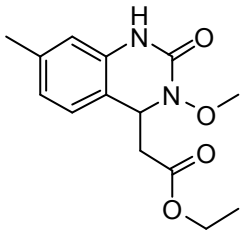
Following a modified protocol (24 hours additional heating at 90 °C) of general procedure D, the title compound **4nc** was obtained after flash column chromatography (pentane/EtOAc 33:67) as an off-white solid (141 mg, 42% yield). $\mathbf{R_F}$ (pentane/EtOAc 27:75) = 0.39; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.06 (s, 1H, NH), 6.78 – 6.61 (m, 3H, CH_{ar}), 5.06 (dd, *J* = 7.8 Hz, *J* = 4.9 Hz, 1H, NCH), 3.89 (m, 2H, OCH_2), 3.73 (s, 3H, OCH_3), 2.90 (dd, *J* = 15.2 Hz, *J* = 4.8 Hz, 1H, (O)CCH_2), 2.46 (dd, *J* = 15.2 Hz, *J* = 8.0 Hz, 1H, (O)CCH_2), 1.33 (s, 9H, $C(CH_3)_3$), 1.29 (t, *J* = 7.0 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.1 (C_q), 155.5 (C_q), 154.4 (C_q), 128.5 (CH), 122.6 (CH), 115.9 (C_q), 115.5 (CH), 112.2 (C_q), 81.2 (OC_q), 64.0 (OCH_2), 62.6 (OCH_3), 58.1 (NCH), 38.9 ((O)CCH_2), 28.0 ($C(CH_3)_3$), 14.9 (CH_3); **ESI-MS:** calculated $[C_{17}H_{24}N_2O_5Na]^+$: 359.1577, found: 359.1576; **ATR-FTIR (cm^{-1}):** 3192, 3082, 2975, 2933, 1715, 1688, 1511, 1433, 1392, 1366, 1338, 1298, 1264, 1241, 1140, 1116, 1046, 980, 937, 845, 813, 757, 716, 692, 611, 589.

***n*-Butyl 2-(7-chloro-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ob).**



Following general procedure D, the title compound **4ob** was obtained after flash column chromatography (pentane/EtOAc 67:33, 1% Et_3N) as a white solid (single regioisomer, 196 mg, 61% yield). $\mathbf{R_F}$ (CH_2Cl_2/EtOH 97:3) = 0.36; **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 9.60 (s, 1H, NH), 7.08 (d, *J* = 8.2 Hz, 1H, CH_{ar}), 6.96 (d, *J* = 2.0 Hz, 1H, CH_{ar}), 6.87 (dd, *J* = 8.2 Hz, *J* = 2.0 Hz, 1H, CH_{ar}), 5.15 (dd, *J* = 8.4 Hz, *J* = 4.5 Hz, 1H, NCH), 4.0 (t, *J* = 6.7 Hz, 2H, OCH_2), 3.80 (s, 3H, OCH_3), 3.02 (dd, *J* = 15.4 Hz, *J* = 4.6 Hz, 1H, (O)CCH_2), 2.60 (dd, *J* = 15.4 Hz, *J* = 8.4 Hz, 1H, (O)CCH_2), 1.50 (m, 2H, CH_2), 1.23 (m, 2H, CH_2), 0.84 (t, *J* = 7.4 Hz, 3H, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 170.6 (C_q), 155.2 (C_q), 136.4 (C_q), 134.7 (C_q), 127.6 (CH), 122.4 (CH), 119.8 (C_q), 115.0 (CH), 64.8 (OCH_2), 62.8 (OCH_3), 57.4 (NCH), 37.6 ((O)CCH_2), 30.4 (CH_2) 19.01 (CH_2), 13.6 (CH_3); **ESI-MS:** calculated $[C_{15}H_{19}ClN_2O_4Na]^+$: 349.0926, found: 349.0920; **ATR-FTIR (cm^{-1}):** 3212, 3102, 2960, 2877, 1728, 1694, 1600, 1497, 1449, 1433, 1387, 1366, 1293, 1261, 1197, 1162, 1115, 1086, 992, 963, 945, 854, 793, 783, 732, 663, 589, 581.

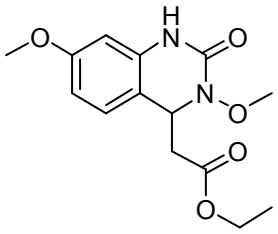
Ethyl 2-(3-methoxy-7-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4pa).



Following general procedure D, the title compound **4pa** was obtained after flash column chromatography (pentane/EtOAc 33:67 to 25:75) as a white solid (184 mg, 67% yield, ~13:1 mixture of regioisomers). Analytical data is given only for the major regioisomer. $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.22; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.26 (s,

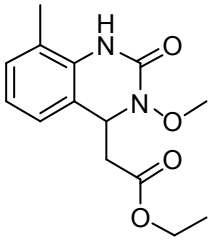
1H, NH), 7.02 (d, J = 7.7 Hz, 1H, CH_{ar}), 6.72 (m, 2H, CH_{ar}), 5.16 (dd, J = 8.0 Hz, J = 4.8 Hz, 1H, NCH), 4.07 (q, J = 7.1 Hz, 2H, OCH_2), 3.79 (s, 3H, OCH_3), 3.00 (dd, J = 15.2 Hz, J = 4.8 Hz, 1H, (O)CCH_2), 2.59 (dd, J = 15.2 Hz, J = 8.0 Hz, 1H, (O)CCH_2), 2.23 (s, 3H, CH_3) 1.17 (t, J = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.7 (C_q), 155.6 (C_q), 139.1 (C_q), 135.0 (C_q), 126.1 (CH), 123.2 (CH), 118.5 (C_q), 115.4 (CH), 62.6 (OCH_3), 60.8 (OCH_2), 57.6 (NCH), 38.0 ((O)CCH_2), 21.1 (CH_3), 14.1 (CH_3); **ESI-MS:** calculated $[C_{14}H_{18}N_2O_4Na]^+$: 301.1159, found: 301.1165; **ATR-FTIR (cm^{-1}):** 3223, 3110, 2976, 2934, 1726, 1694, 1629, 1596, 1491, 1418, 1372, 1309, 1292, 1167, 1150, 1095, 1037, 1012, 946, 864, 804, 749, 675, 587.

Ethyl 2-(3,7-dimethoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4qa).



Following general procedure D, the title compound **4qa** was obtained after flash column chromatography (pentane/EtOAc 33:67) as a white solid (215 mg, 73% yield, > 24:1 mixture of regioisomers). Analytical data is given only for the major regioisomer. **R_F** (pentane/EtOAc 33:67) = 0.26; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.18 (s, 1H, NH), 7.00 (d, J = 8.4 Hz, 1H, CH_{ar}), 6.42 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H, CH_{ar}), 6.38 (d, J = 2.4 Hz, 1H, CH_{ar}), 5.09 (dd, J = 8.1 Hz, J = 4.7 Hz, 1H, NCH), 4.00 (q, J = 7.3 Hz, 2H, OCH_2), 3.73 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3), 2.94 (dd, J = 15.2 Hz, J = 4.7 Hz, 1H, (O)CCH_2), 2.54 (dd, J = 15.4 Hz, J = 8.2 Hz, 1H, (O)CCH_2), 1.13 (t, J = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.7 (C_q), 160.3 (C_q), 155.4 (C_q), 136.3 (C_q), 127.3 (CH), 113.7 (C_q), 108.2 (CH), 100.4 (CH), 62.6 (OCH_3), 60.8 (OCH_2), 57.4 (NCH), 55.4 (OCH_3), 38.0 ((O)CCH_2), 13.1 (CH_3); **ESI-MS:** calculated $[C_{14}H_{18}N_2O_5Na]^+$: 317.1108, found: 317.1107; **ATR-FTIR (cm^{-1}):** 3221, 3144, 2973, 2931, 1719, 1685, 1627, 1597, 1521, 1422, 1390, 1372, 1353, 1283, 1230, 1205, 1162, 1138, 1101, 1036, 1015, 996, 975, 957, 857, 772, 761, 688, 625.

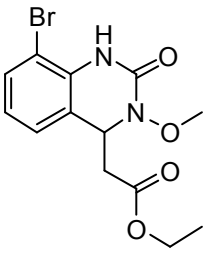
Ethyl 2-(3-methoxy-8-methyl-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4ra).



Following general procedure D, the title compound was obtained after flash column chromatography (pentane/EtOAc 60:40) as a white solid (166 mg, 60% yield). **R_F** (pentane/EtOAc 50:50) = 0.29; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 8.12 (s, 1H, NH), 7.07 – 6.94 (m, 2H, CH_{ar}), 6.84 (d, J = 7.6 Hz, 1H, CH_{ar}), 5.14 (dd, J = 8.3 Hz, J = 4.7 Hz, 1H, NCH), 4.06 (q, J = 7.1 Hz, 2H, OCH_2), 3.76 (s, 3H, OCH_3), 3.01 (dd, J = 15.1 Hz, J = 4.7 Hz, 1H, (O)CCH_2), 2.57 (dd, J = 15.1 Hz, J = 8.3 Hz, 1H, (O)CCH_2), 2.24 (s, 3H, CH_3), 1.16 (t, J = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.6 (C_q), 155.1 (C_q), 133.3 (C_q), 130.4 (CH), 124.2 (CH), 122.8 (C_q), 122.3 (CH), 121.5 (C_q), 62.6 (OCH_3), 60.7 (OCH_2), 58.1 (NCH), 55.4 (OCH_3), 37.6 ((O)CCH_2), 16.9 (CH_3), 14.0 (CH_3); **ESI-MS:** calculated $[C_{14}H_{18}N_2O_4Na]^+$: 301.1159, found: 301.1157; **ATR-FTIR (cm^{-1}):** 3229, 3176, 3094, 2977,

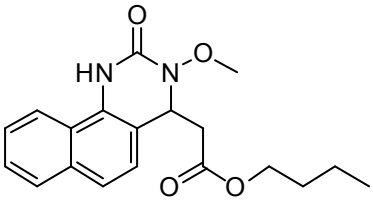
2930, 1726, 1685, 1603, 1490, 1481, 1401, 1370, 1345, 1303, 1291, 1261, 1218, 1169, 1146, 1095, 1035, 1008, 977, 938, 850, 815, 767, 740, 720, 696, 678, 643, 549.

Ethyl 2-(8-bromo-3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (4sa).



Following a modified protocol (24 hours additional heating at 90°C) of general procedure D, the title compound **4sa** was obtained after flash column chromatography (pentane/EtOAc 75:25 to 67:33) as a yellow oil (221 mg, 64% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.42; **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 7.34 (dd, *J* = 8.1 Hz, *J* = 1.2 Hz, 1H, CH_{ar}), 7.21 (s, 1H, NH), 7.10 (d, *J* = 7.6 Hz, 1H, CH_{ar}), 6.77 (t, *J* = 7.9 Hz, 1H, CH_{ar}), 5.12 (dd, *J* = 8.4 Hz, *J* = 4.5 Hz, 1H, NCH), 4.01 (qd, *J* = 7.1 Hz, *J* = 1.3 Hz, 2H, OCH_2), 3.72 (s, 3H, OCH_3), 2.97 (dd, *J* = 15.4 Hz, *J* = 4.5 Hz, 1H, (O)CCH_2), 2.54 (dd, *J* = 15.4 Hz, *J* = 8.5 Hz, 1H, (O)CCH_2), 1.11 (t, *J* = 7.2 Hz, 3H, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 170.1 (C_q), 153.3 (C_q), 133.0 (C_q), 132.1 (CH), 125.8 (CH), 123.3 (CH), 122.8 (C_q), 108.2 (C_q), 62.7 (OCH_3), 60.8 (OCH_2), 57.8 (NCH), 37.3 ((O)CCH_2), 14.0 (CH_3); **ESI-MS:** calculated $[C_{13}H_{15}BrN_2O_4Na]^+$: 365.0107, found: 365.0098; **ATR-FTIR (cm^{-1}):** 3243, 3089, 2980, 2936, 1692, 1605, 1484, 1388, 1372, 1282, 1252, 1178, 1153, 1094, 1039, 1003, 967, 911, 857, 776, 755, 736, 695, 651, 621.

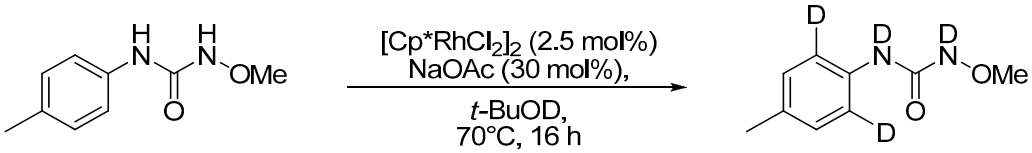
***n*-Butyl 2-(3-methoxy-2-oxo-1,2,3,4-tetrahydrobenzo[h]quinazolin-4-yl)acetate (4tb).**



Following a modified protocol (24 hours additional heating at 90°C on a 0.5 mmol scale) of general procedure D, the title compound **4tb** was obtained after flash column chromatography (pentane/EtOAc 60:40) as a brownish oil (86 mg, 50% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.47; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 9.23 (s, 1H, NH), 8.18 (d, *J* = 8.3 Hz, 1H, CH_{ar}), 7.83 – 7.78 (m, 1H, CH_{ar}), 7.58 – 7.47 (m, 3H, CH_{ar}), 7.29 (d, *J* = 8.3 Hz, 1H, CH_{ar}), 5.38 (dd, *J* = 7.9 Hz, *J* = 4.8 Hz, 1H, NCH), 4.04 (td, *J* = 6.7 Hz, *J* = 1.2 Hz, 2H, OCH_2), 3.92 (s, 3H, OCH_3), 3.15 (dd, *J* = 15.2 Hz, *J* = 4.8 Hz, 1H, (O)CCH_2), 2.73 (dd, *J* = 15.2 Hz, *J* = 7.9 Hz, 1H, (O)CCH_2), 1.52 (m, 2H, CH_2), 1.25 (m, 2H, CH_2), 0.84 (t, *J* = 7.3 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 170.9 (C_q), 155.4 (C_q), 133.6 (C_q), 130.5 (C_q), 128.5 (CH), 126.7 (CH), 126.7 (CH), 123.9 (CH), 122.9 (CH), 121.7 (C_q), 120.8 (CH), 116.6 (C_q), 64.9 (OCH_2), 62.8 (OCH_3), 58.5 (NCH), 38.0 ((O)CCH_2), 30.5 (CH_2), 19.1 (CH_2), 13.7 (CH_3); **ESI-MS:** calculated $[C_{19}H_{22}N_2O_4Na]^+$: 365.1472, found: 365.1464; **ATR-FTIR (cm^{-1}):** 3244, 3205, 2959, 2934, 1727, 1681, 1584, 1528, 1435, 1406, 1287, 1275, 1146, 1033, 1017, 968, 809, 745, 683, 664, 626, 566.

7. Mechanistic Studies

1. Reversibility of the C–H activation step.

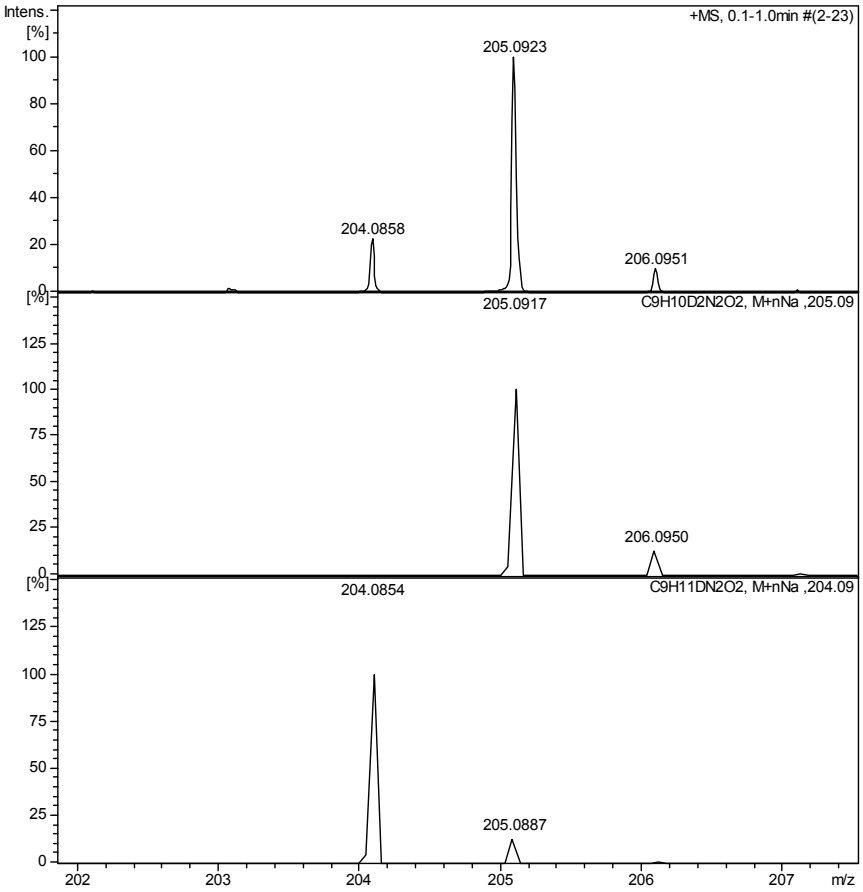


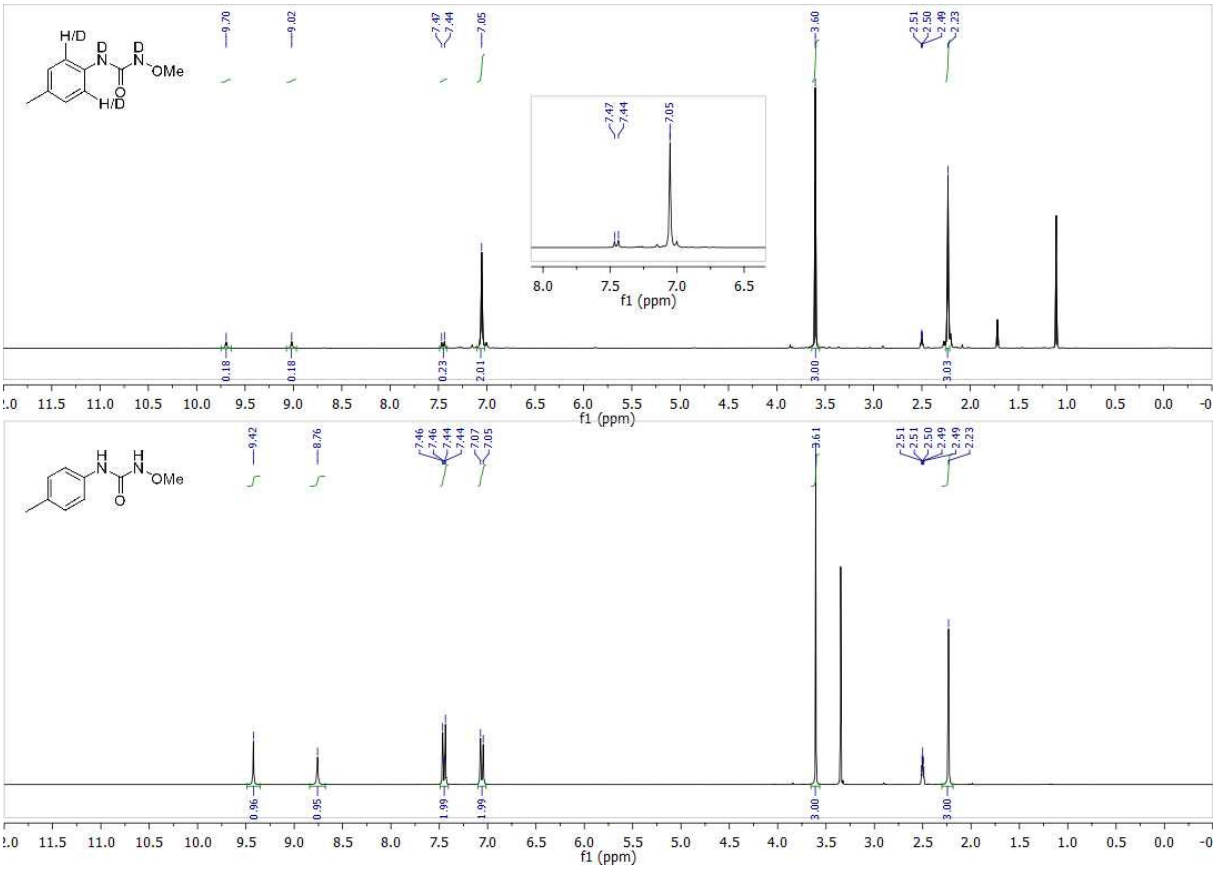
A flame-dried 10 mL screw-capped schlenck tube was flame-dried and backfilled with argon. The reaction vessel was transferred to a glovebox and charged with *N*-methoxy-*N*'-(*p*-tolyl)urea (**2m**) (36.0 mg, 0.200 mmol, 2.00 eq.), $[Cp^*RhCl_2]_2$ (1.5 mg, 0.0025 mmol, 0.025 eq.) and sodium acetate (2.5 mg, 0.030 mmol, 0.30 eq.). Dry, monodeuterated *t*-BuOD (1 mL) was added via syringe and the reaction mixture was placed in a pre-heated oilbath and stirred for 16 hours at 70 °C. After this time, the reaction mixture was cooled to room-temperature and filtered through a short pad of silica gel. After removing the solvent, the sample was subjected to ^{1}H NMR analysis. A small sample was taken for HRMS-analysis. This sample was further dissolved in MeOH and dried (five cylces) to remove deuterium incorporation on the urea nitrogens.

^{1}H NMR analysis indicates, that 11% of the ortho-positions show no deuterium incorporation by comparison of the integrals of the ortho and meta protons, although no distinction between mono and non-deuteration could be made due to the symmetric nature of the substrate.

This result was confirmed by HRMS. The collected data clearly shows, that the non-deuterated compound constitutes to around 1%, wheras 18% are mono-deuterated **2m**.

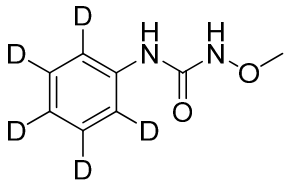
Entry	m/z		S/N	Intensity	FWHM	%
1	203.0828	5203	196.3	11886	0.0390	1.4
2	204.0858	6364	2565.8	154621	0.0321	18.3
3	205.0923	6318	11339.5	684599	0.0325	79.9
4	206.0951	6605	1182.8	71656	0.0312	0.3
5	207.0972	6293	103.0	6335	0.0329	0


Intens.
[%]
+MS, 0.1-1.0min #(2-23)
205.0923
204.0858
206.0951
205.0917
C9H10D2N2O2, M+nNa ,205.09
206.0950
204.0854
C9H11DN2O2, M+nNa ,204.09
205.0887
m/z


H/D
OMe
f1 (ppm)

2. Determination of the intermolecular kinetic isotope effect.

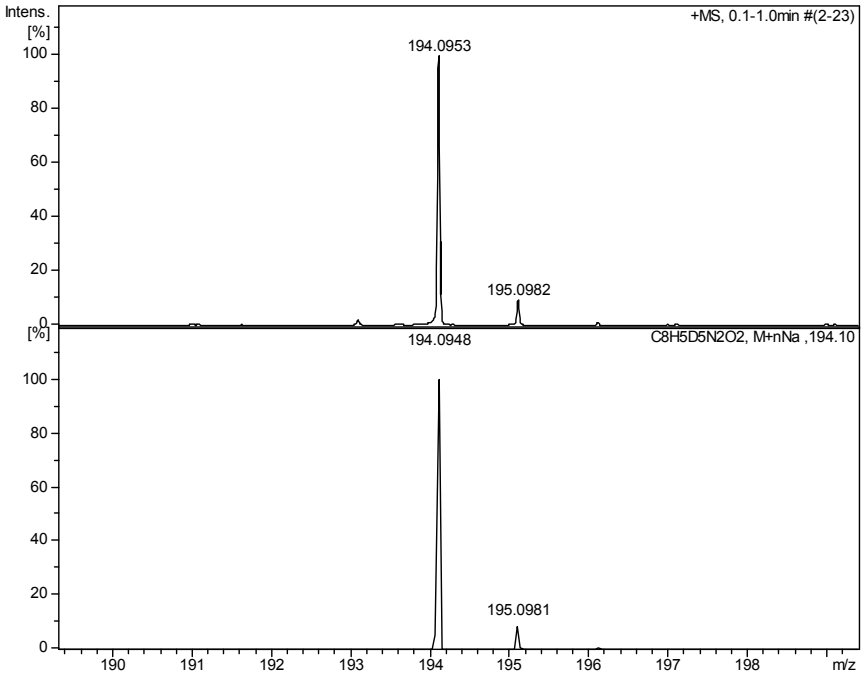
N-Methoxy,*N*'-(pentadeuterophenyl)urea (d^5-2a).



Following general procedure C on a 9 mmol scale, the title compound d^5-**2a** was obtained after purification by flash column chromatography (pentane/EtOAc 67:33) as a white solid (680 mg, 46% yield). $\mathbf{R_F}$ (pentane/EtOAc 50:50) = 0.47; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 7.69 (br s, 1H, NH), 7.59 (br s, 1H, NH), 3.78 (s, 3H, OCH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 157.4 (C_q), 137.2 (C_q), 128.6 (t, *J* = 24.6 Hz, CD), 123.5 (t, *J* = 24.5 Hz, CD), 119.4 (t, *J* = 24.7 Hz, CD), 64.7 (CH_3); **^{2}D NMR (77 MHz, $CHCl_3$)** δ = 7.55 (br s, 2D, CD_{ar}), 7.40 (br s, 2D, CD_{ar}), 7.16 (br s, 2D, CD_{ar}) **ESI-MS:** calculated $[C_8H_5D_5N_2ONa]^+$: 194.0948, found: 194.0943; **ATR-FTIR (cm^{-1}):** 3305, 3206, 1652, 1569, 1511, 1467, 1441, 1392, 1345, 1307, 1266, 1193, 1096, 941, 821, 806, 758, 746, 688, 630, 599, 582, 552.

The grade of deuteration was determined by HRMS (~98.2 %)

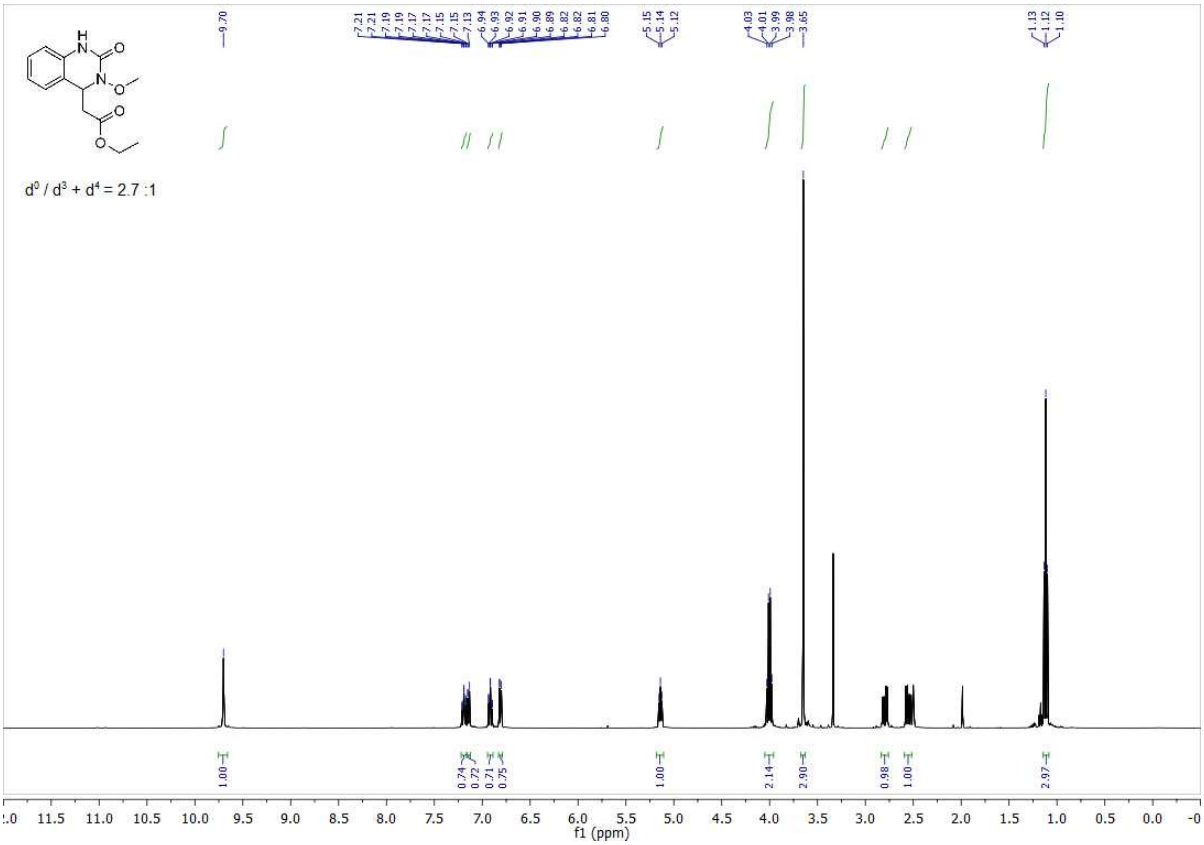
Entry	d^x	m/z	Res.	S/N	Intensity	FWHM	%
1	d^4	193.1307	6324	6324	7547	0.0305	1.8
2	d^5	194.1374	6069	6069	404959	0.0320	97.3
3	d^6	195.1405	6098	6098	37527	0.0320	0.9
4	d^7	196.1423	6329	632	3696	0.0310	0



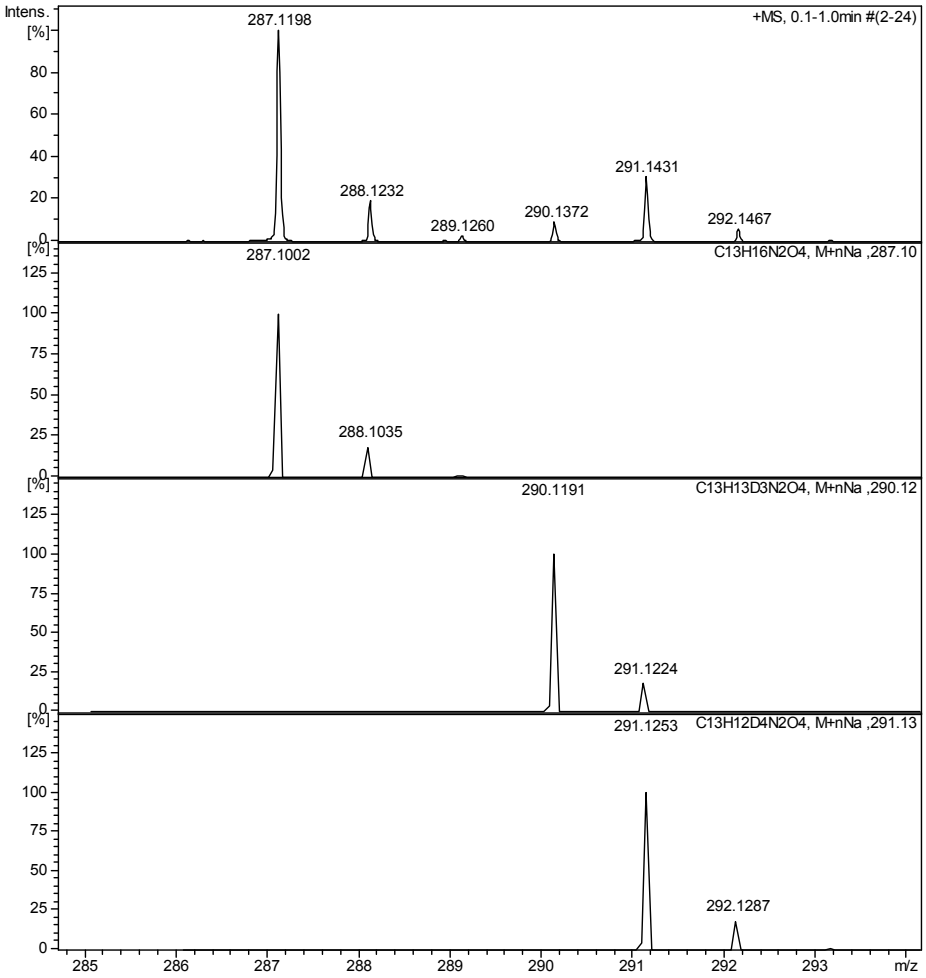
i) One-pot competition experiment between 2a and d^5-2a

A flame-dried screw-capped sealed tube, equipped with a magnetic stir bar was charged with urea **2a** (166.2 mg, 1.00 mmol, 1.00 eq.), d^5-**2a** (171.2 mg, 1.00 mmol, 1.00 eq.), $[Cp^*RhCl_2]_2$ (15.5 mg, 0.025 mmol, 0.025 eq.) and NaOAc (24.6 mg, 0.30 mmol, 0.30 eq.) in a glove-box. Dry THF (10 mL) and ethyl acrylate (106.4 µL, 1.00 mmol, 1.00 eq.) were added via syringe. The reaction mixture was placed in a pre-heated oilbath (70 °C) and stirred for 2 hours. The reaction was stopped by cooling to 0 °C and subsequent filtration through a short pad of silica gel with EtOAc. The solvents were removed in vacuo and the residue subjected to flash column chromatography (pentane/EtOAc 40:60) to afford d^x-**4aa** as an off-white solid (55.4 mg, 20% yield).

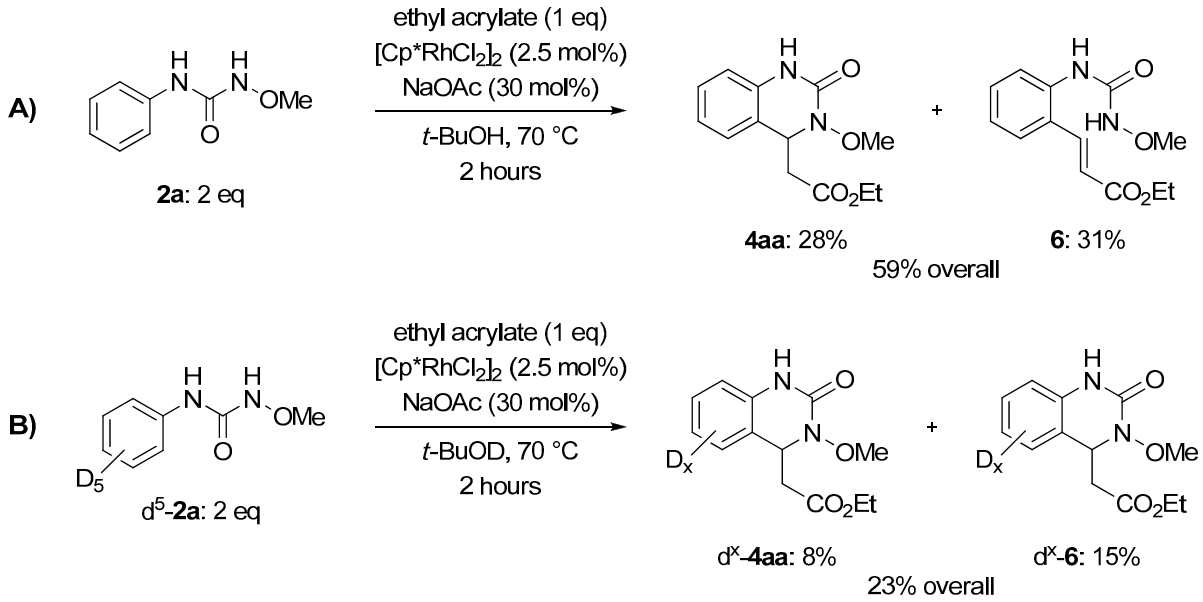
The grade of deuteration was determined by ^{1}H NMR and HRMS analysis and revealed a k_H/k_D value of 2.7.



Entry	d^x	m/z	Res.	S/N	Intensity	FWHM	%
1	d^0	287.1577	7395	12394.3	776182	0.0388	73
2	d^1	288.1616	7555	2419.4	152304	0.0381	0
3	d^2	289.1650	7303	326.0	20745	0.0396	0
4	d^3	290.1767	7627	1158.7	73665	0.0380	7
5	d^4	291.1831	7421	3730.3	237861	0.0392	20
6	d^5	292.1873	7734	691.3	44394	0.0378	0
7	d^6	293.1897	7749	90.4	5963	0.0378	0



ii) Comparison of the reaction of 2a and d^5-2a in *t*-BuOH/D

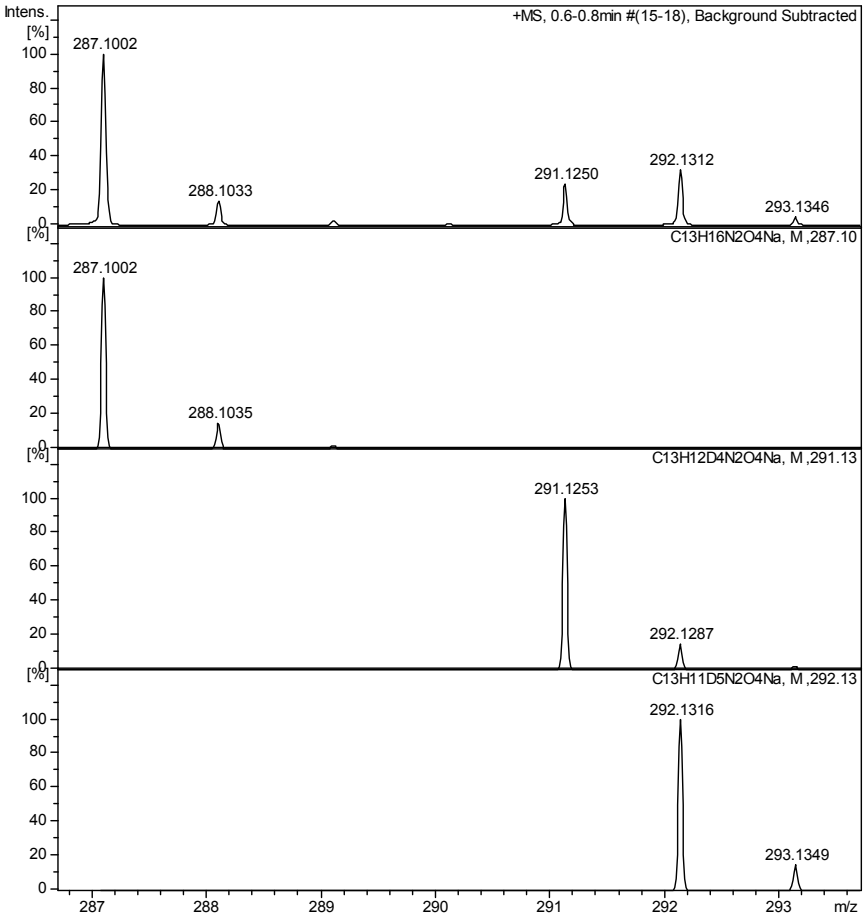


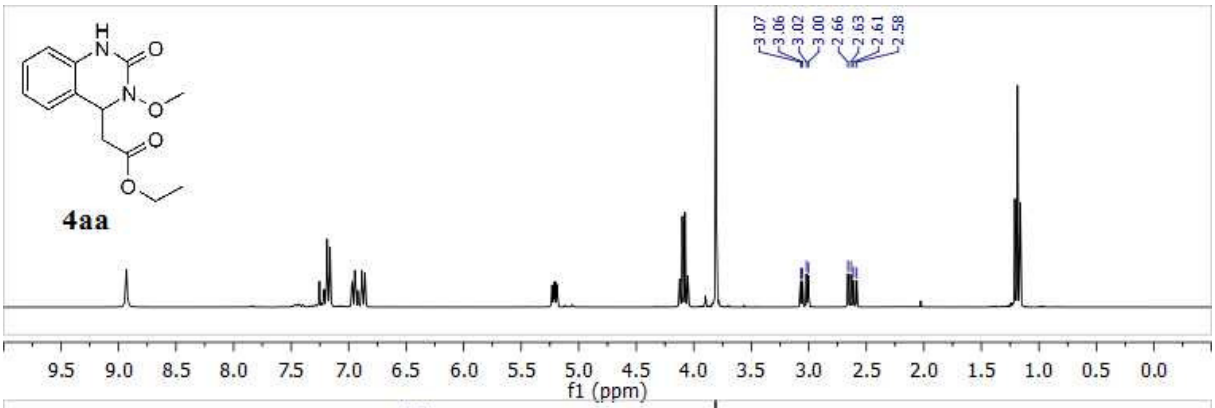
A flame-dried 10 mL screw-capped schlenck tube was charged with **2a** (33.2 mg, 0.20 mmol, 2.00 eq.), $[Cp^*RhCl_2]_2$ (1.5 mg, 0.0025 mmol, 0.025 eq.) and NaOAc (2.5 mg, 0.03 mmol, 0.3 eq.) in a glove-box. Another flame-dried 10 mL screw-capped schlenck tube was charged with d^5-**2a** (34.2 mg, 0.20 mmol, 2.00 eq.), and same amounts of $[Cp^*RhCl_2]_2$ and NaOAc. Ethyl acrylate (10.6 µL, 0.1 mmol, 1.0 eq.) and *t*-BuOH (1 mL, in the case of **2a**) or *t*-BuOD (1 mL, in the case of d^5-**2a**) was added via syringe. The reaction mixtures were placed in a pre-heated oilbath (70 °C) and stirred for 2 hours. After cooling to 30 °C, the reaction mixture was filtered through a short pad of silica gel with EtOAc. Solvents were removed under reduced pressure and the residue dried. CH_2Br_2 was added as an internal standard and the yields of d^x-**4aa** determined by ^{1}H NMR analysis. Both samples were combined, dried and submitted for HRMS analysis.

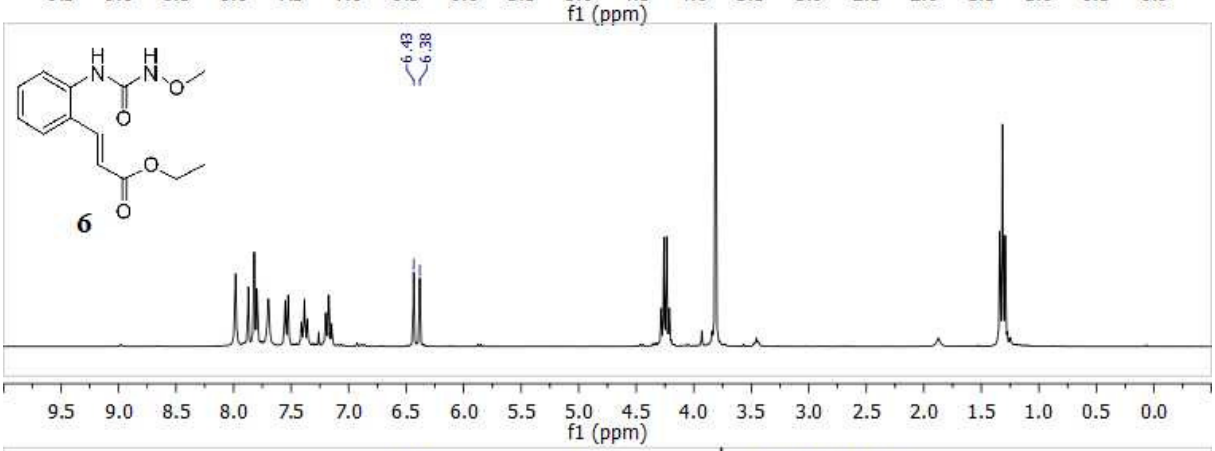
^{1}H NMR analysis revealed in both cases mixtures of Heck (**6**) and cyclised products (**4aa**). The values for both products were added and a k_H/k_D value of 2.6 was obtained.

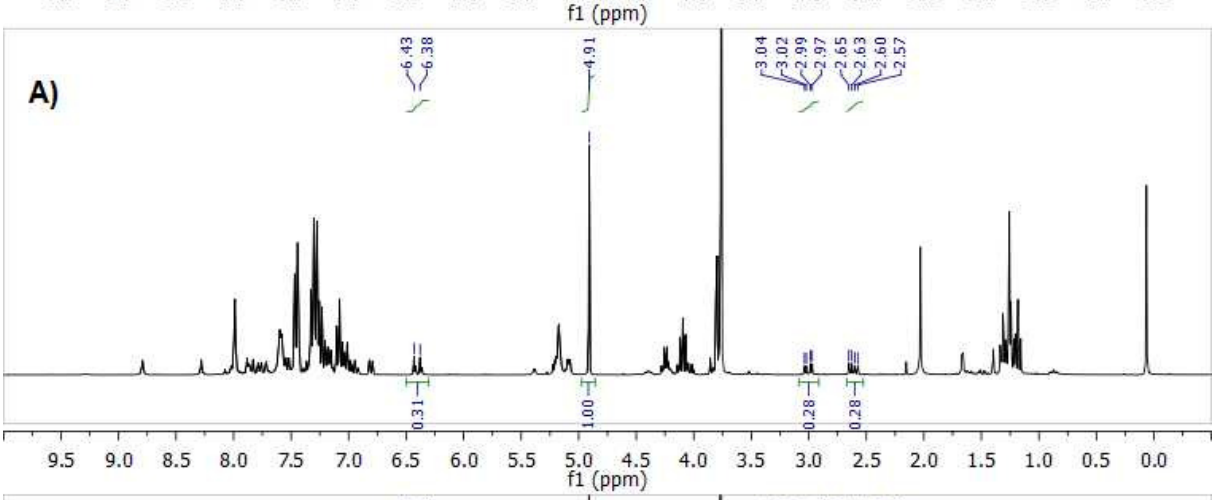
HRMS analysis revealed a k_H/k_D value of 2.3 after addition of the values for d^4-**4aa** and d^5-**4aa**.

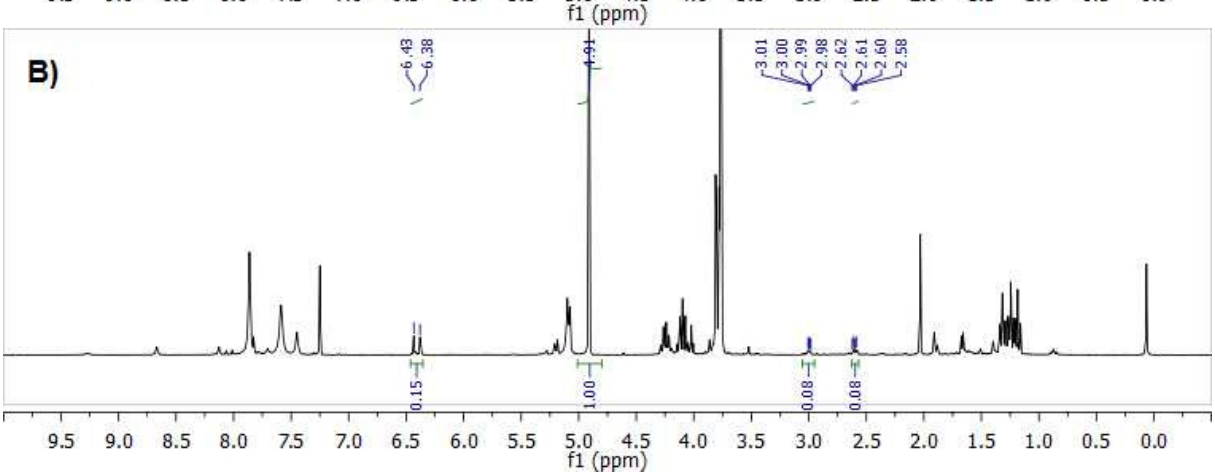
Entry	d^x	m/z	Res.	S/N	Intensity	FWHM	%
1	d^0	287.1002	7280	5600.2	491455	0.0394	69.9
2	d^1	288.1034	7484	807.7	71250	0.0385	0
3	d^2	289.1087	7121	65.9	5935	0.0406	0
4	d^3	290.1170	7024	129.9	11601	0.0412	0
5	d^4	291.1251	7376	1224.4	101970	0.0395	14.6
6	d^5	292.1312	7476	1564.8	140072	0.0391	15.5
7	d^6	293.1347	7440	251.3	22675	0.0394	0
8	d^7	294.1351	6979	38.2	3379	0.0393	0


Intens.
[%]
+MS, 0.6-0.8min #(15-18), Background Subtracted
287.1002
288.1033
291.1250
292.1312
293.1346
C13H16N2O4Na, M ,287.10
287.1002
288.1035
C13H12D4N2O4Na, M ,291.13
291.1253
292.1287
C13H11D5N2O4Na, M ,292.13
292.1316
293.1349
m/z


4aa
3.07
3.06
3.02
3.00
2.66
2.63
2.61
2.58
f1 (ppm)

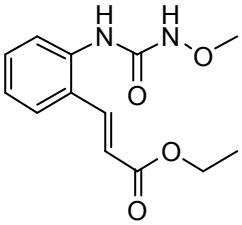

6
6.43
6.38
f1 (ppm)


A)
6.43
6.38
4.91
3.04
3.02
2.99
2.97
2.65
2.63
2.60
2.57
0.31
1.00
0.28
0.28
f1 (ppm)


B)
6.43
6.38
4.91
3.01
3.00
2.99
2.98
2.62
2.61
2.60
2.58
0.15
1.00
0.08
0.08
f1 (ppm)

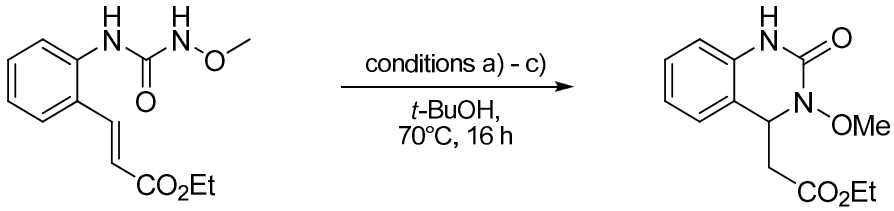
3. Mechanistic investigation of the intramolecular Michael addition

(*E*)-Ethyl 3-(2-(3-methoxyureido)phenyl)acrylate (6).



Following a modified protocol of general procedure D, wherein the reaction was stopped after two hours, the title compound **6** was obtained after careful flash column chromatography (pentane/EtOAc 50:50) as a white solid (31 mg, 12% yield, *E*/*Z* = 97:3 as determined by ^{1}H NMR). **R_F** (pentane/EtOAc 50:50) = 0.25; **^{1}H NMR (300 MHz, $CDCl_3$)** δ = 7.98 (s, 1H, NH), 7.89 – 7.78 (m, 2H, CH_{ar}, CH_{olefin}), 7.70 (s, 1H, NH), 7.54 (d, *J* = 7.5 Hz, 1H, CH_{ar}), 7.38 (t, *J* = 7.9 Hz, 1H, CH_{ar}), 7.17 (t, *J* = 7.5 Hz, 1H, CH_{ar}), 6.41 (d, *J* = 15.9 Hz, 1H, CH_{olefin}), 4.25 (q, *J* = 7.1 Hz, 2H, OCH_2), 3.81 (s, 3H, OCH_3), 1.32 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, $CDCl_3$)** δ = 166.8 (C_q), 157.5 (C_q), 139.3 (CH), 135.6 (C_q), 131.0 (CH), 127.5 (CH), 127.2 (C_q), 125.4 (CH), 124.3 (CH), 120.8 (CH), 64.8 (OCH_3), 60.8 (OCH_2), 14.4 (CH_3); **ESI-MS:** calculated $[C_{13}H_{16}D_5N_2O_4Na]^+$: 287.1002, found: 287.1020; **ATR-FTIR (cm^{-1}):** 3297, 3209, 2982, 2942, 1710, 1655, 1638, 1516, 1486, 1364, 1312, 1290, 1181, 1092, 1033, 982, 865, 805, 762, 739, 715, 670, 638, 592.

i) Intramolecular Michael-addition as a single step

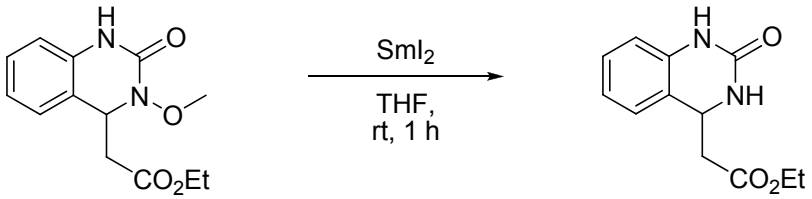


Entry	Conditions	^{1}H NMR yield
a)	$[Cp^*RhCl_2]_2$ (0.025 mol%), NaOAc (0.3 eq.)	95
b)	NaOAc (0.3 eq.)	98
c)	---	0, only decomp. observed

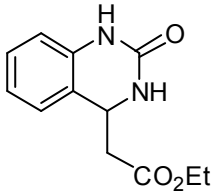
A flame-dried screw-capped 10 mL schlenck tube was charged with olefinated substrate **6** (7.0 mg, 0.027 mmol, 1.00 eq.), $[Cp^*RhCl_2]_2$ (0.40 mg, 0.66 µmol, 0.025 eq., only for a)) and NaOAc (0.7 mg, 0.008 mmol, 0.3 eq., only for a) and b)). Dry *tert*-butyl alcohol (0.3 mL) was added and the reaction mixture was placed in a pre-heated oil bath and stirred for 16 hours at 70 °C. After cooling to room-temperature, the solvent was removed and the crude product dried. CH_2Br_2 was added as an internal standard and the yield of **4aa** determined by ^{1}H NMR analysis.

These experiments show, that the intramolecular Michael-addition is most likely base catalyzed. Spontaneous addition does not occur under base-free conditions, and neither the starting material nor the cyclized compound was observed.

8. N–O bond cleavage of product 4aa.

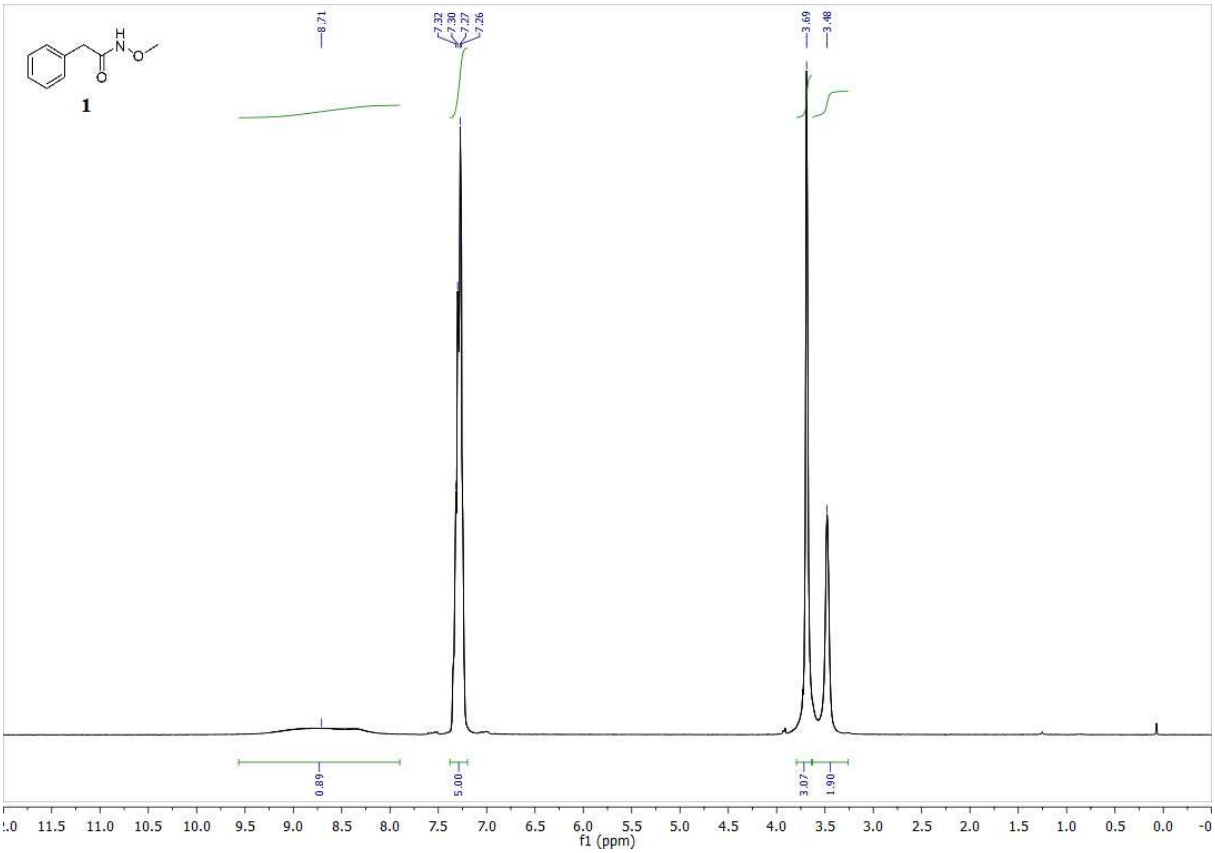


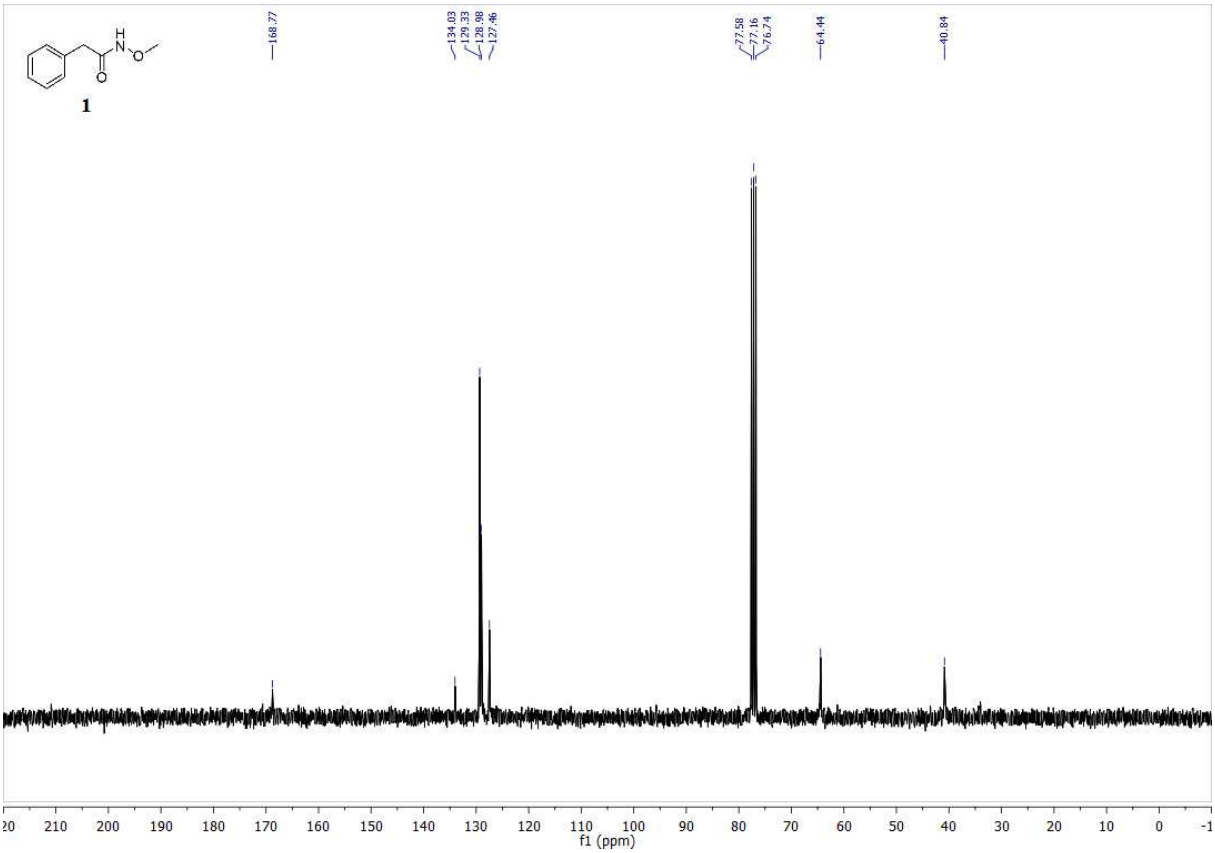
Ethyl 2-(2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (7).

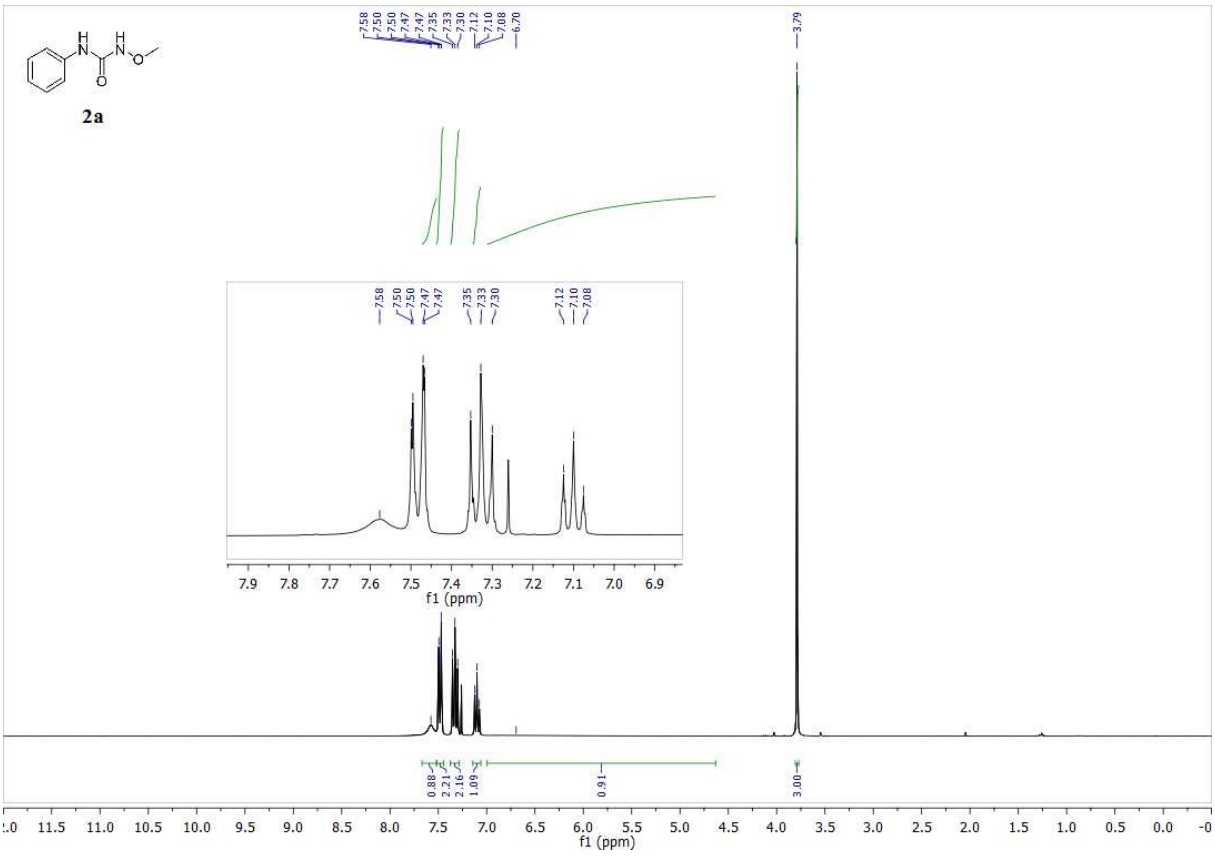


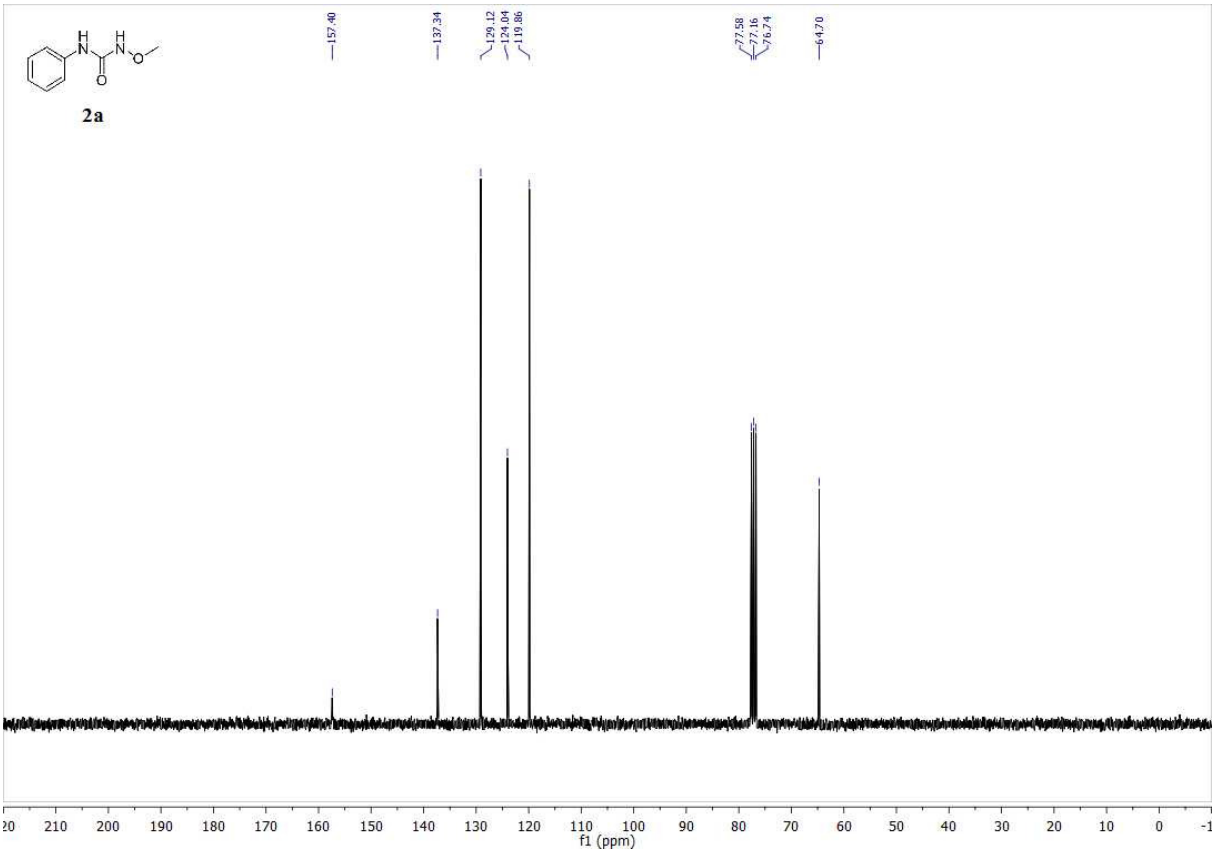
In a flame-dried round-bottom flask, Ethyl 2-(3-methoxy-2-oxo-1,2,3,4-tetrahydroquinazolin-4-yl)acetate (**4aa**) (79.3 mg, 0.300 mmol, 1.00 eq.) was dissolved in dry THF (5 mL). SmI_2-solution (0.1 M in THF, 7.2 mL, 0.72 mmol, 2.40 eq.) was added slowly via syringe at room-temperature. Once the reaction mixture keeps its dark-green solution for over 5 min, the reaction is complete, as can be monitored by TLC analysis. The solvent was removed under reduced pressure and the residue purified by flash column chromatography (pentane/EtOAc 10:90) to afford the title compound **7** as a pale-yellow solid (63 mg, 89% yield). $\mathbf{R_F}$ (pentane/EtOAc 25:75) = 0.21; **^{1}H NMR (300 MHz, DMSO-d^6)** δ = 9.18 (s, 1H, NH), 7.17 – 7.08 (m, 1H, CH_{ar}), 7.07 (d, J = 7.6 Hz, 1H, CH_{ar}), 6.94 (br s, 1H, NH), 6.89 – 6.80 (m, 1H, CH_{ar}), 6.79 (d, J = 7.7 Hz, 1H, CH_{ar}), 4.75 (td, J = 6.2 Hz, J = 2.8 Hz, 1H, NCH), 4.02 (q, J = 7.1 Hz, 2H, OCH_2), 2.72 – 2.52 (m, 1H, CH_2), 1.13 (t, J = 7.1 Hz, 3H, CH_3); **^{13}C NMR (75 MHz, DMSO-d^6)** δ = 169.9 (C_q), 153.5 (C_q), 137.4 (C_q), 128.1 (CH), 125.7 (CH), 121.0 (CH), 120.4 (C_q), 113.8 (CH), 60.1 (OCH_2), 50.4 (NCH), 43.1 (CH_2), 13.9 (CH_3); **ESI-MS:** calculated $[C_{12}H_{14}N_2O_3Na]^+$: 257.0897, found: 257.0905; **ATR-FTIR (cm^{-1}):** 3220, 3069, 2982, 2911, 1729, 1688, 1604, 1459, 1422, 1369, 1323, 1297, 1289, 1250, 1201, 1151, 1111, 1088, 1046, 1012, 952, 802, 765, 751, 616, 573.

9. ^{1}H NMR and ^{13}C NMR spectras






2a
7.58
7.50
7.50
7.47
7.47
7.35
7.33
7.30
7.12
7.10
7.08
6.70
3.79
f1 (ppm)
0.88
2.21
2.16
1.09
0.91
3.00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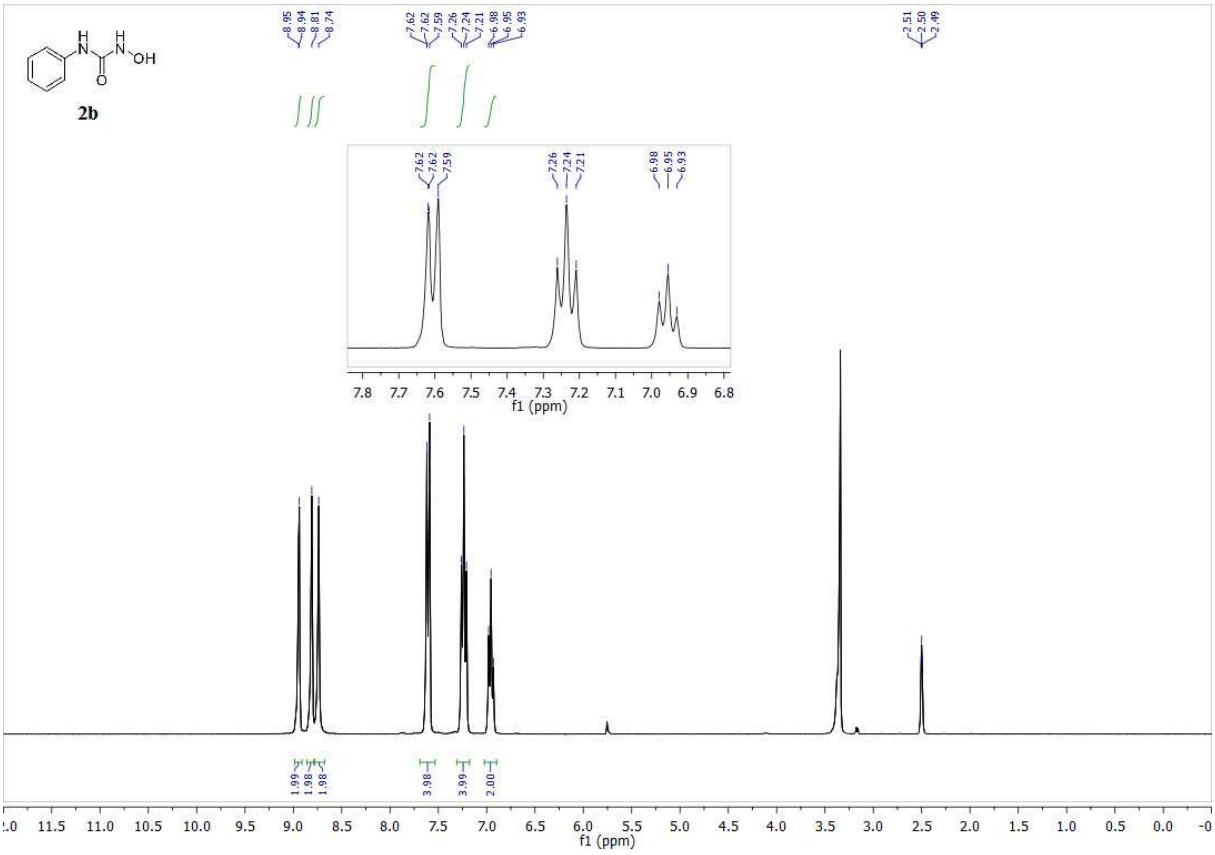
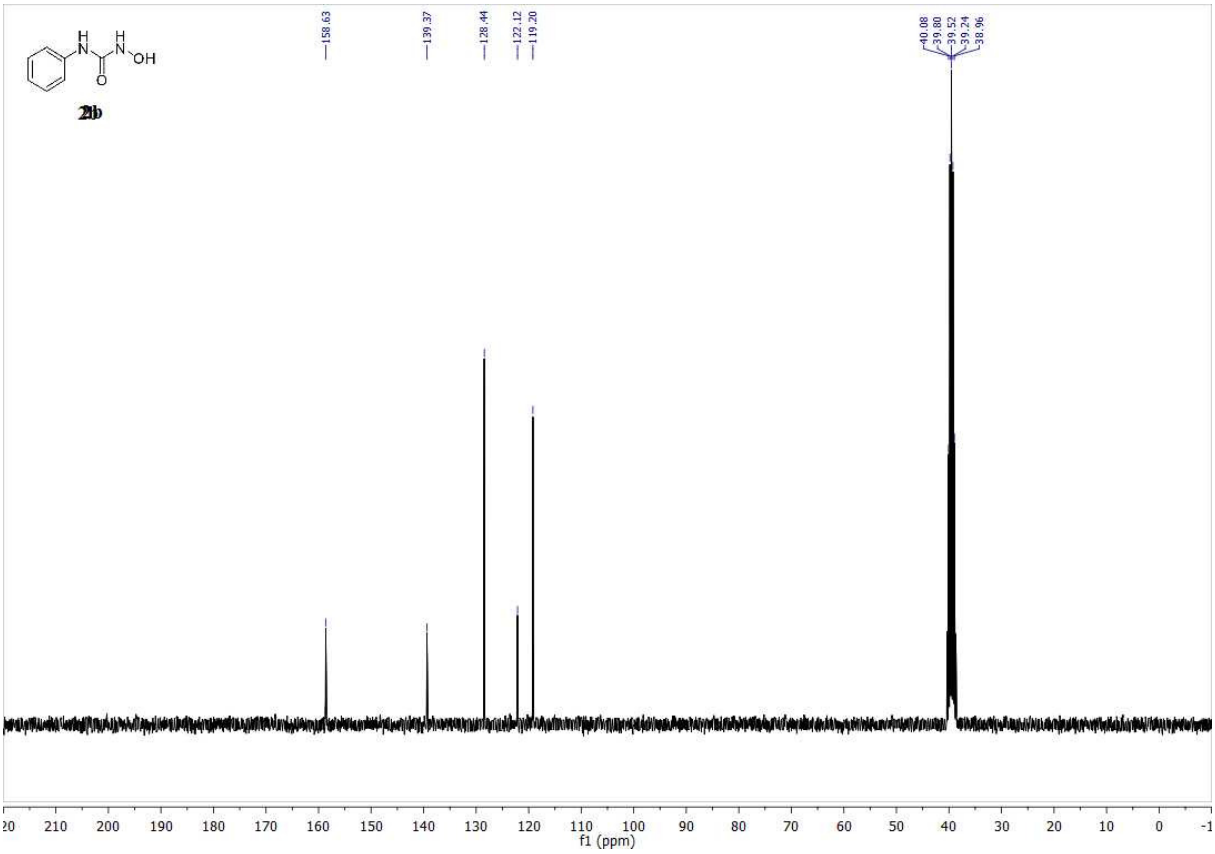
137.34
129.12
124.04
119.86
77.58
77.16
76.74
64.70
f1 (ppm)


2b
8.95
8.94
8.81
8.74
7.62
7.62
7.59
7.26
7.24
7.21
6.98
6.95
6.93
2.51
2.50
2.49
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
1.99
1.98
1.98
3.98
3.99
2.00
f1 (ppm)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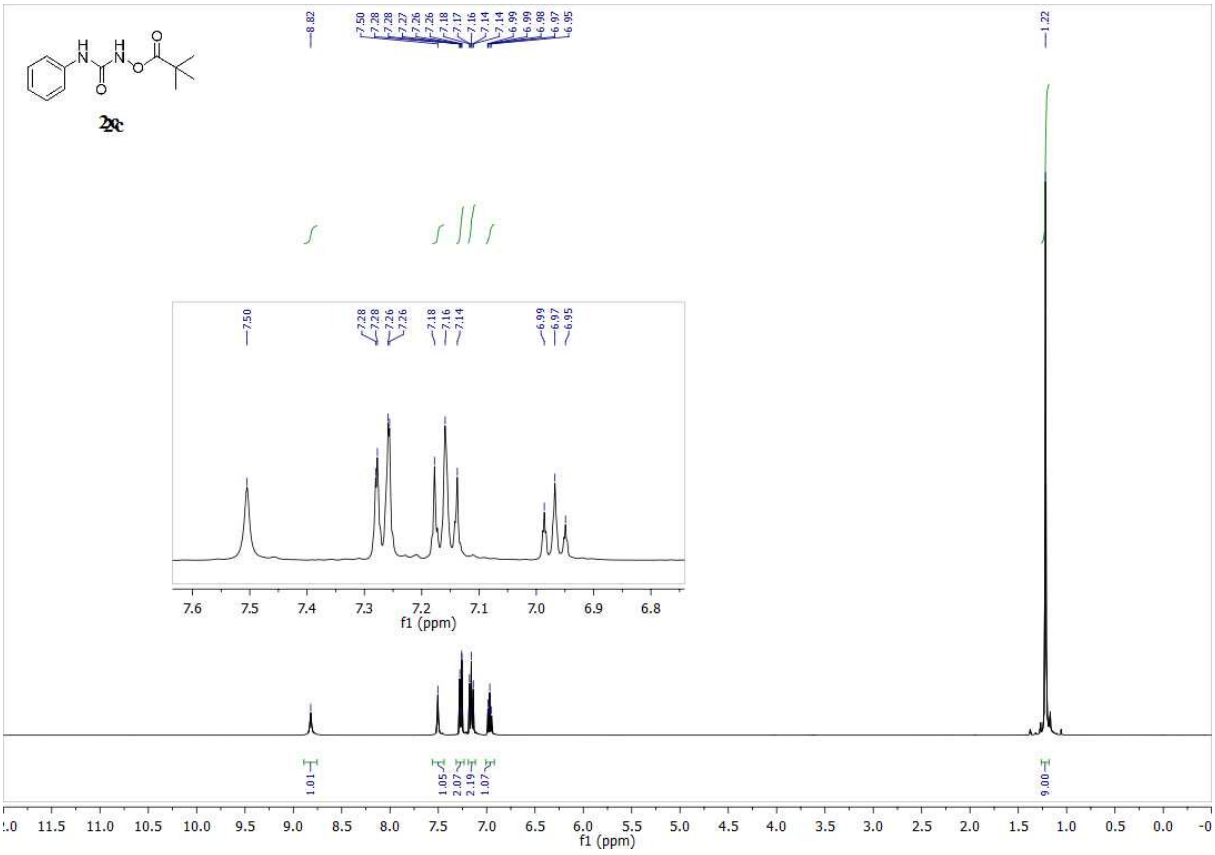
128.44
122.12
119.20
40.08
39.80
39.52
39.24
38.96
f1 (ppm)


2c
8.82
7.50
7.28
7.27
7.26
7.18
7.17
7.16
7.14
6.99
6.98
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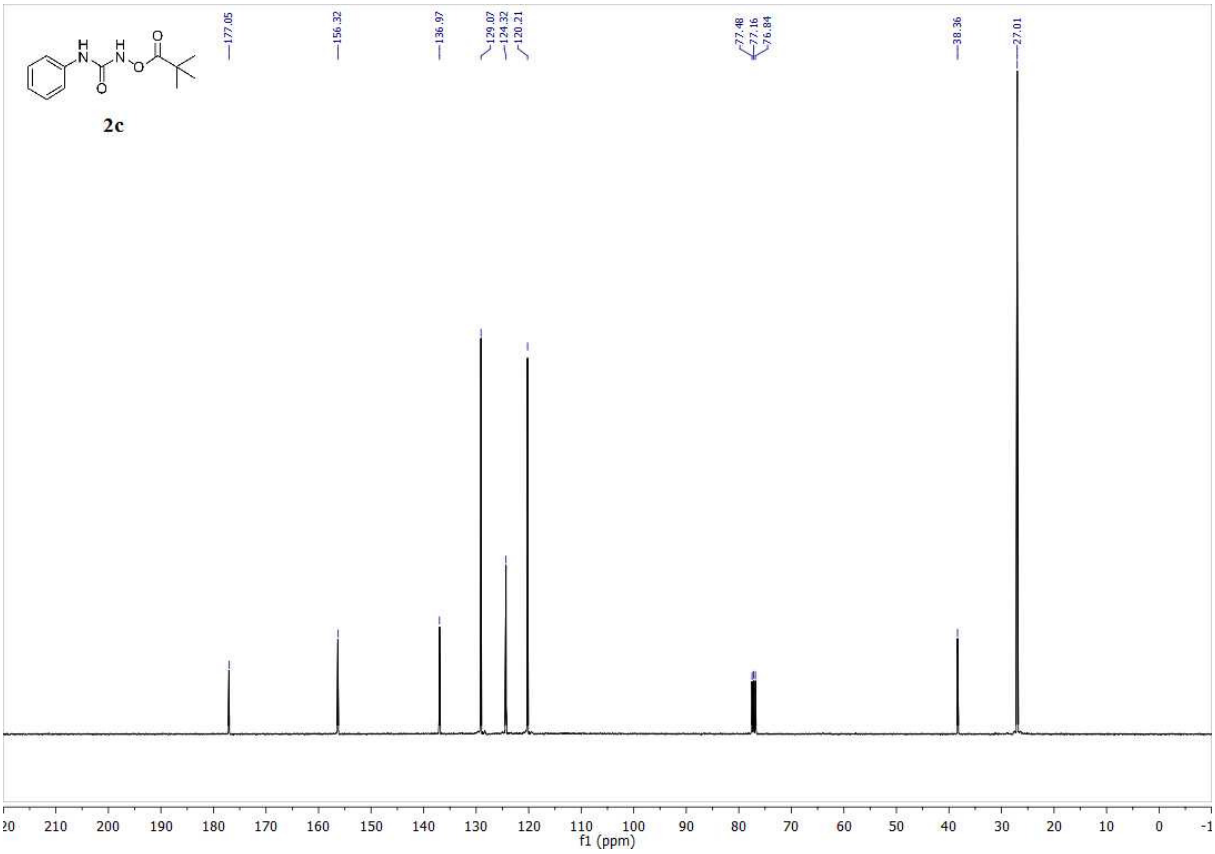
6.95
1.22
1.01
1.05
2.07
2.19
1.07
9.00
f1 (ppm)


2c
177.05
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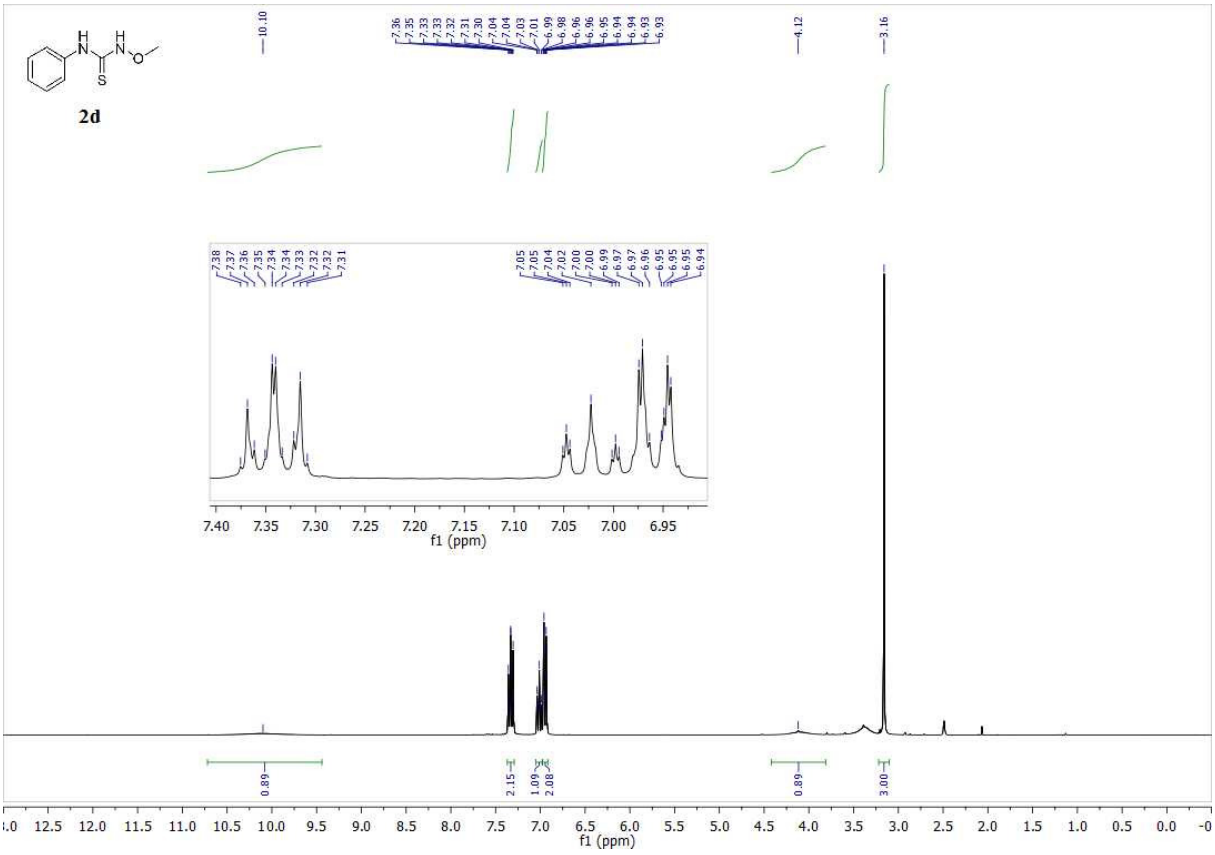
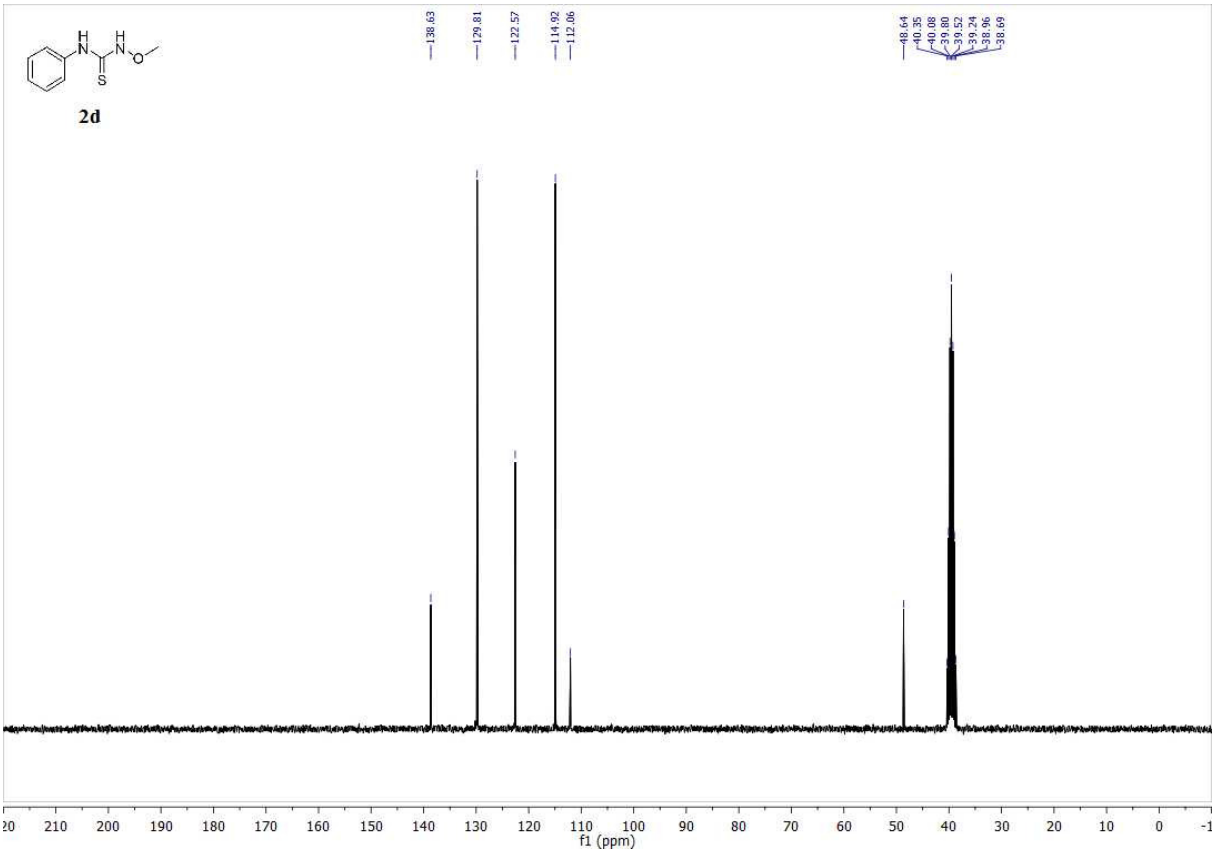
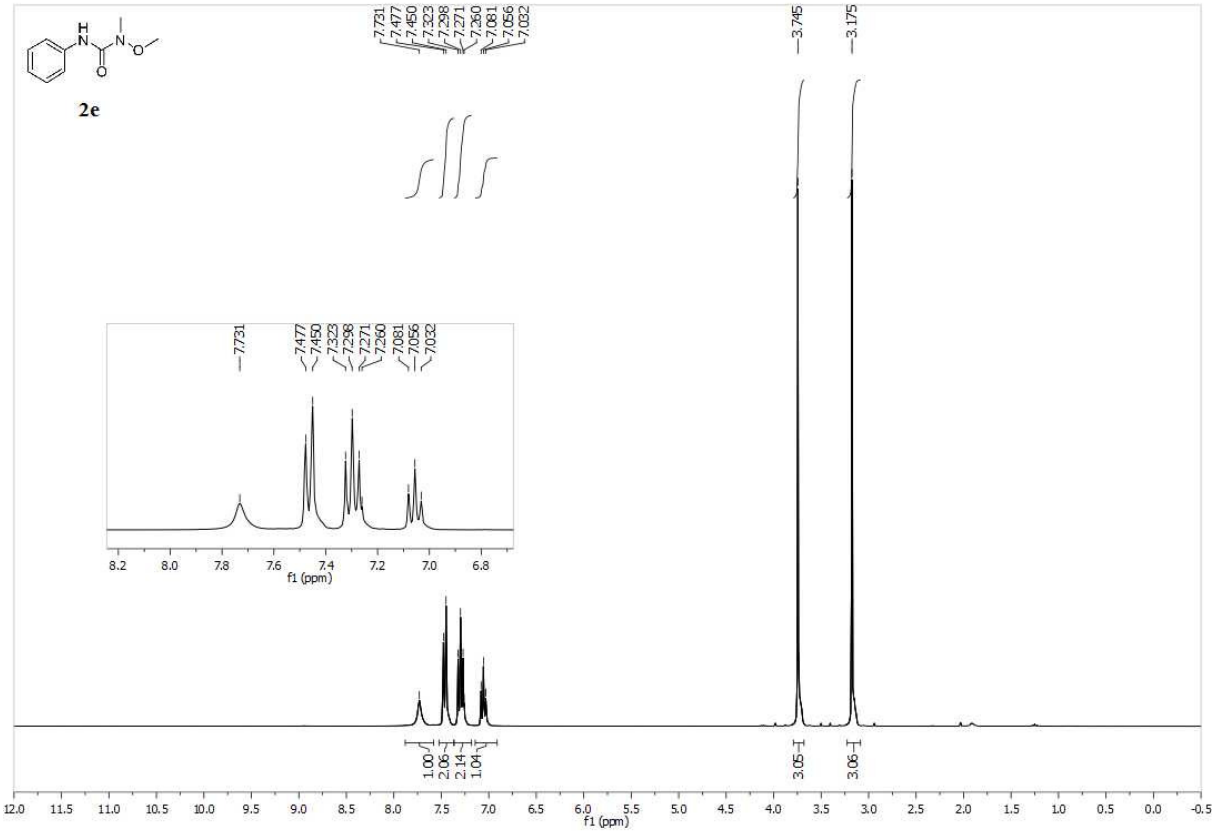
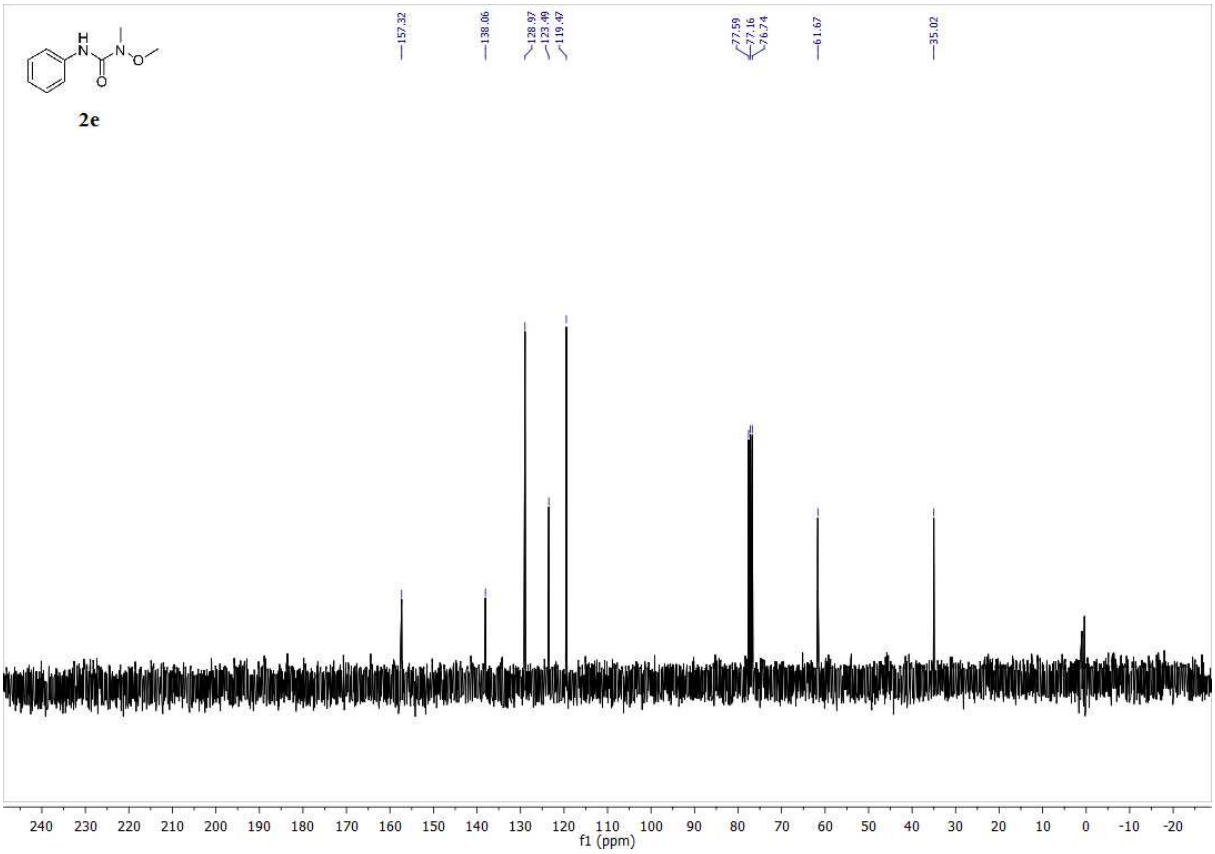
136.97
129.07
124.32
120.21
77.48
77.16
76.84
38.36
27.01
f1 (ppm)


2d
10.10
7.36
7.35
7.33
7.32
7.31
7.30
7.04
7.04
7.03
7.01
6.99
6.98
6.96
6.96
6.95
6.94
6.94
6.93
6.93
4.12
3.16
7.38
7.37
7.36
7.35
7.34
7.34
7.33
7.32
7.32
7.31
7.05
7.05
7.04
7.02
7.00
7.00
6.99
6.97
6.97
6.96
6.95
6.95
6.95
6.94
7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95
f1 (ppm)
0.89
2.15
1.09
2.08
0.89
3.00
f1 (ppm)


2d
138.63
129.81
122.57
114.92
112.06
48.64
40.35
40.08
39.80
39.52
39.24
38.96
38.69
f1 (ppm)


2e
7.731
7.477
7.450
7.323
7.298
7.271
7.260
7.081
7.056
7.032
3.745
3.175
f1 (ppm)
1.00
2.06
2.14
1.04
3.05
3.06


2e
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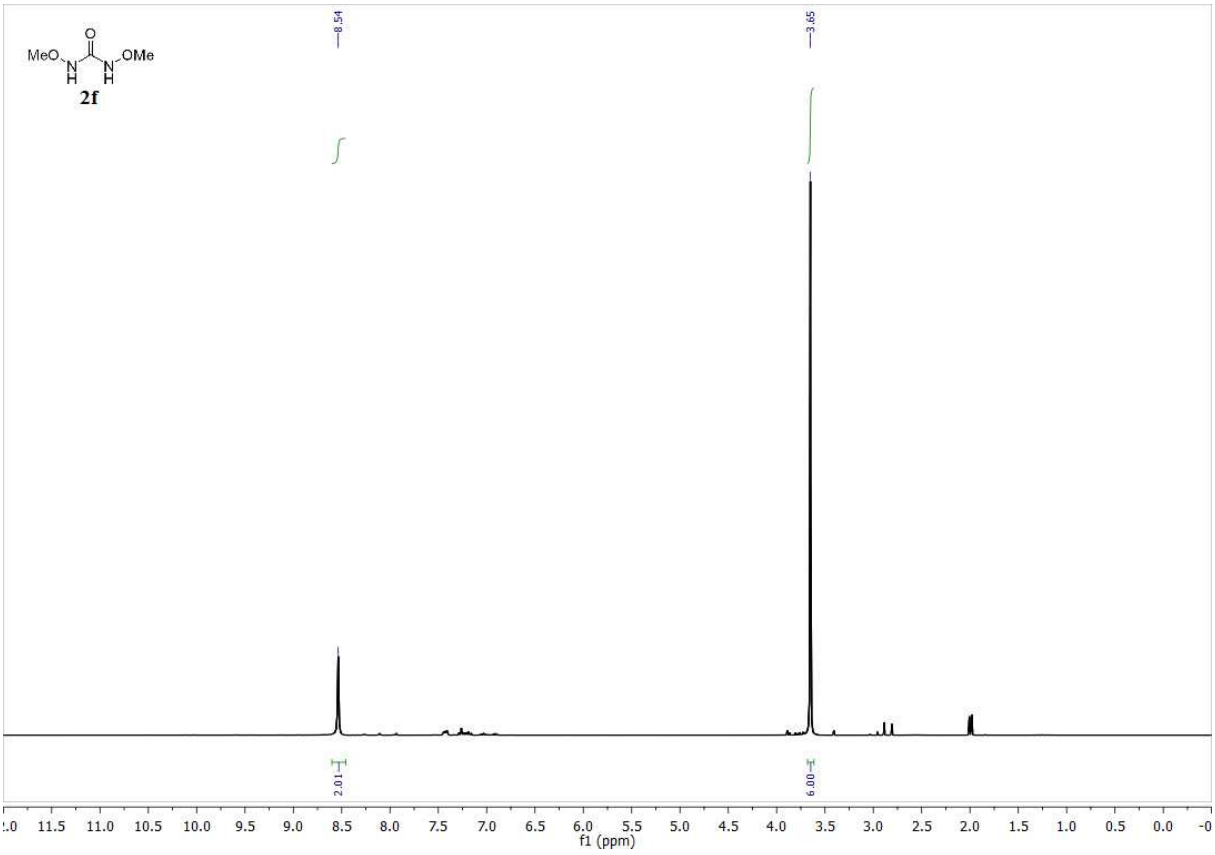
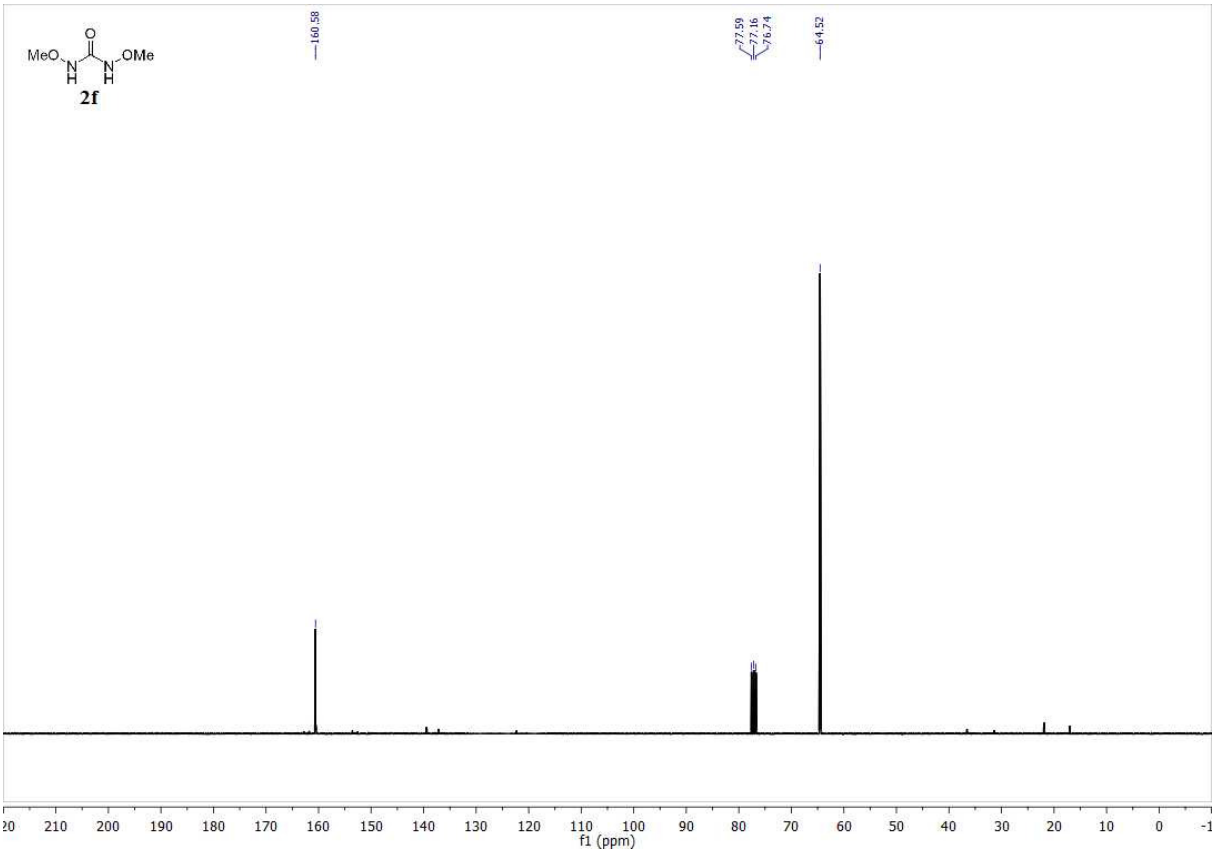
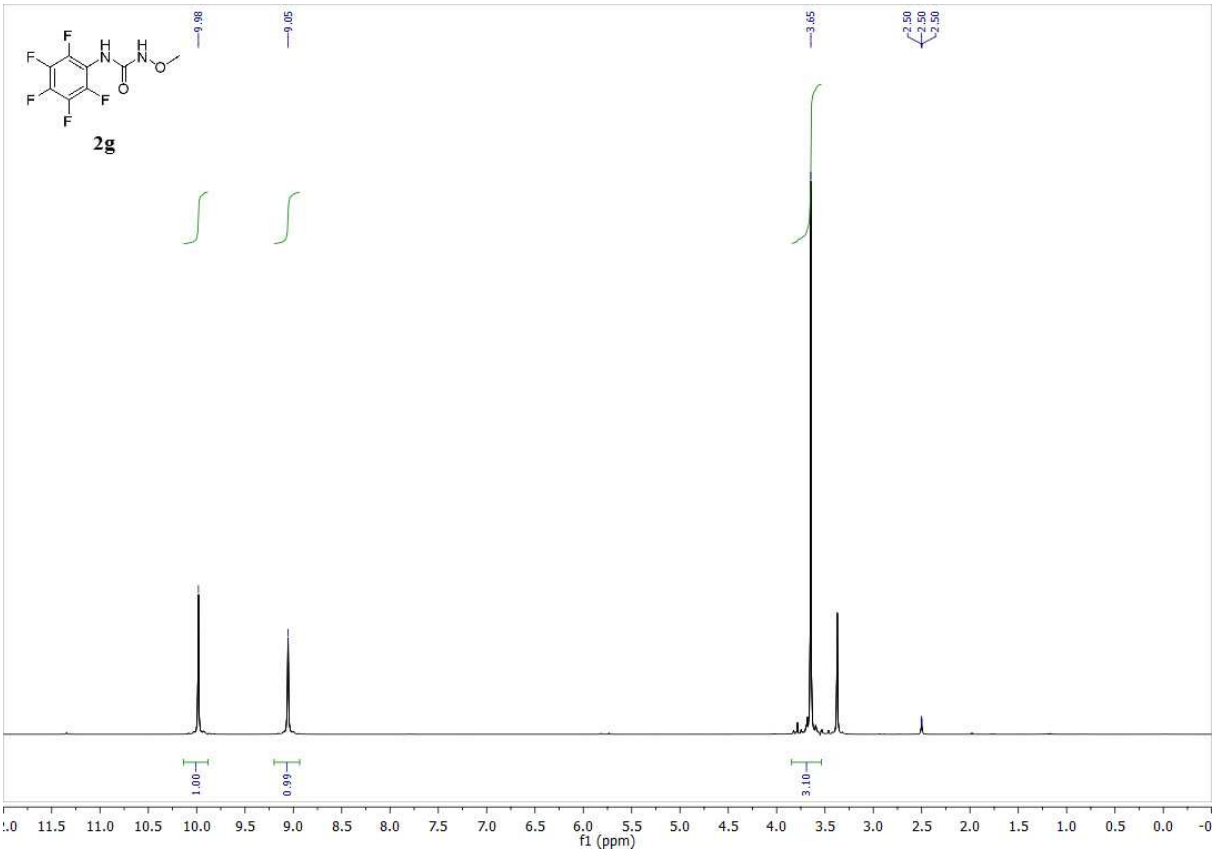
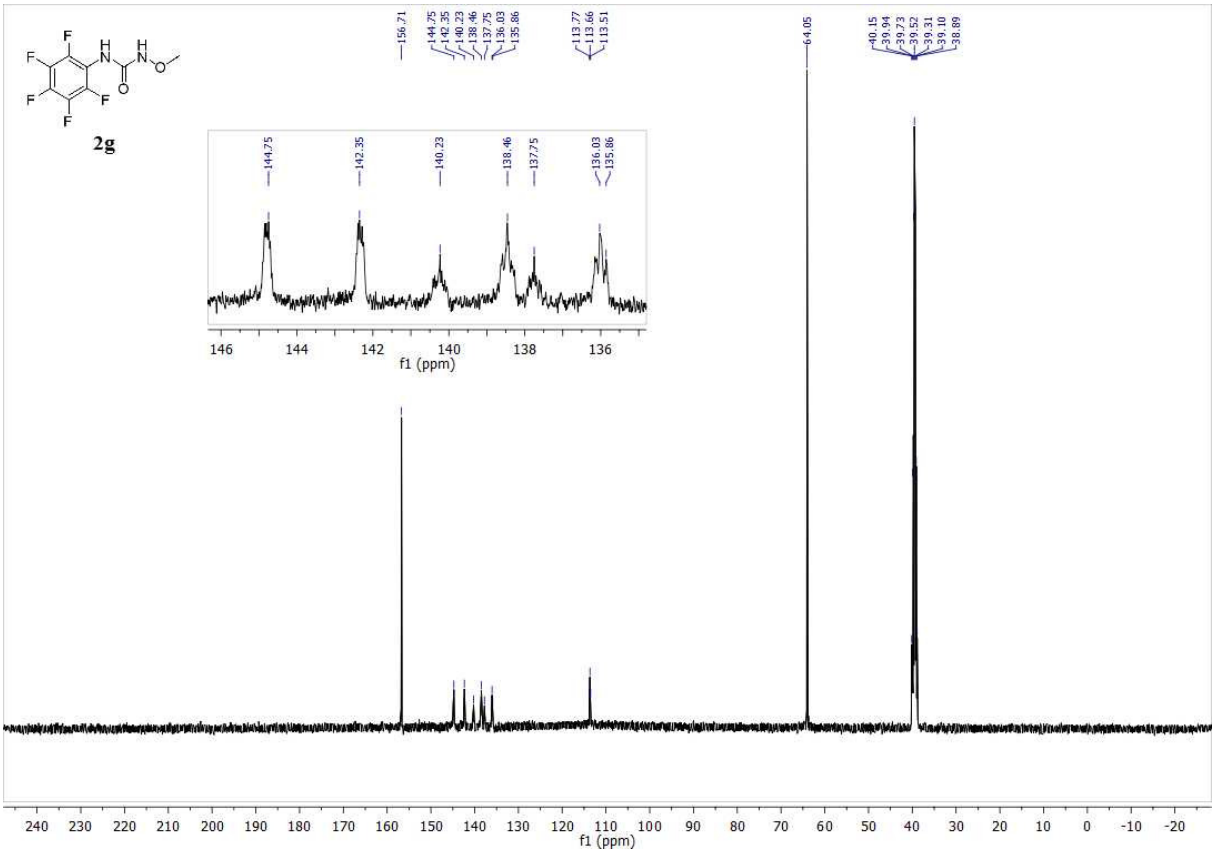
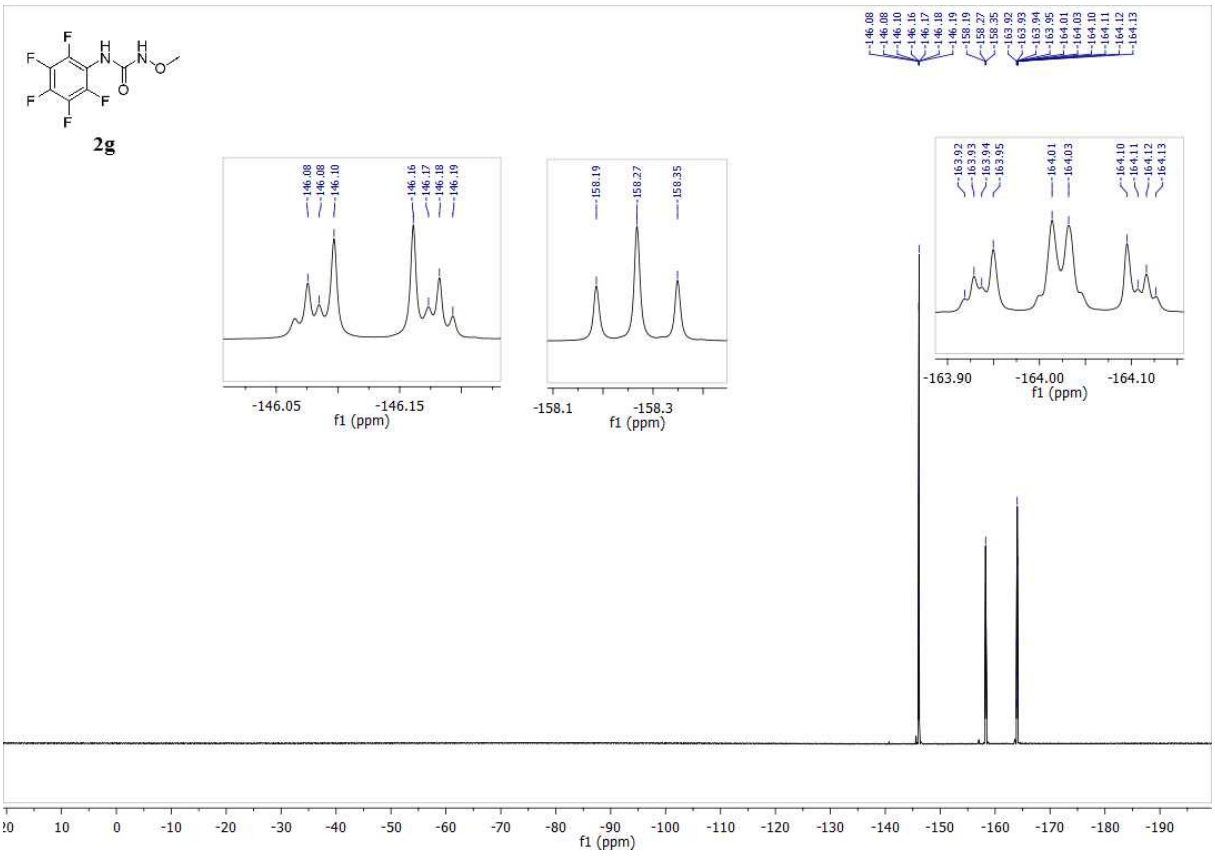
138.06
128.97
123.49
119.47
77.59
77.16
76.74
61.67
35.02
f1 (ppm)










2g
-146.08
-146.08
-146.10
-146.16
-146.17
-146.18
-146.19
-146.05
-146.15
f1 (ppm)
-158.19
-158.27
-158.35
-158.1
-158.3
f1 (ppm)
-163.92
-163.93
-163.94
-163.95
-164.01
-164.03
-164.10
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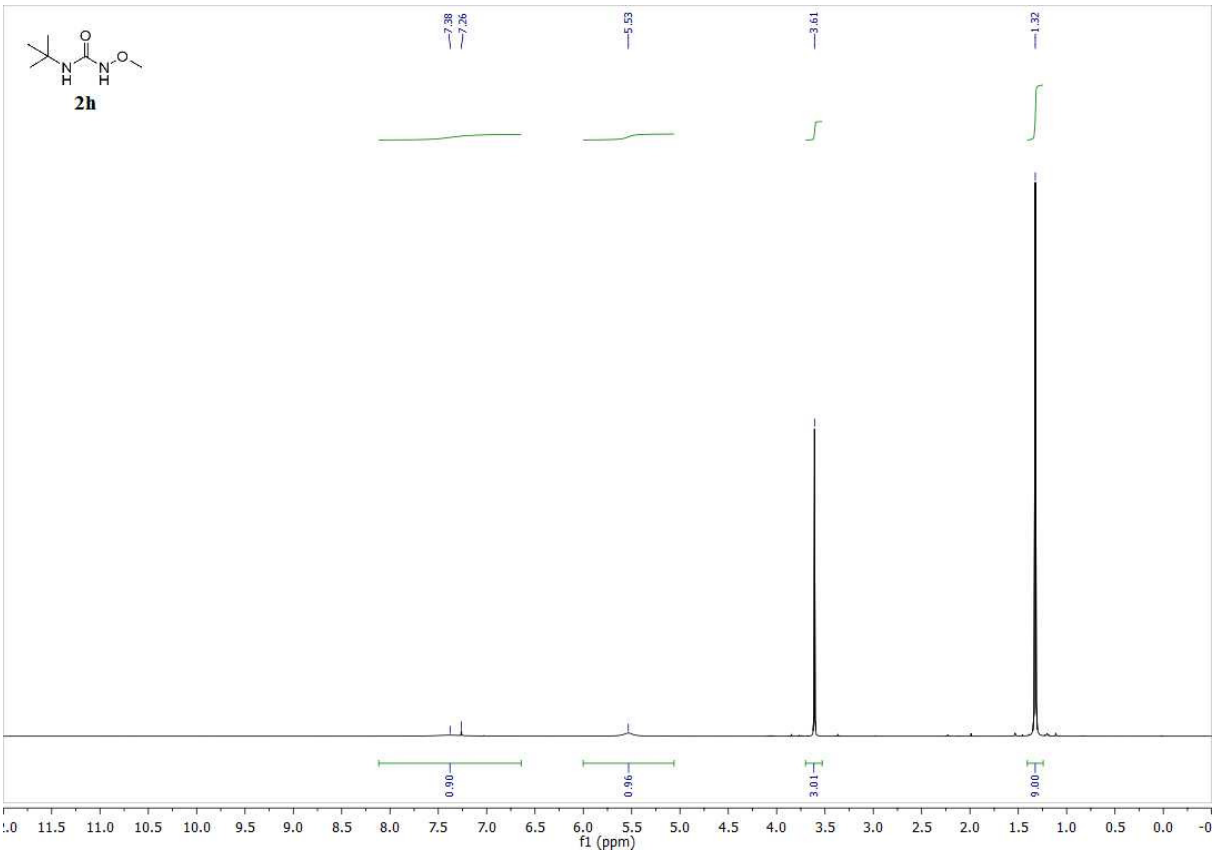
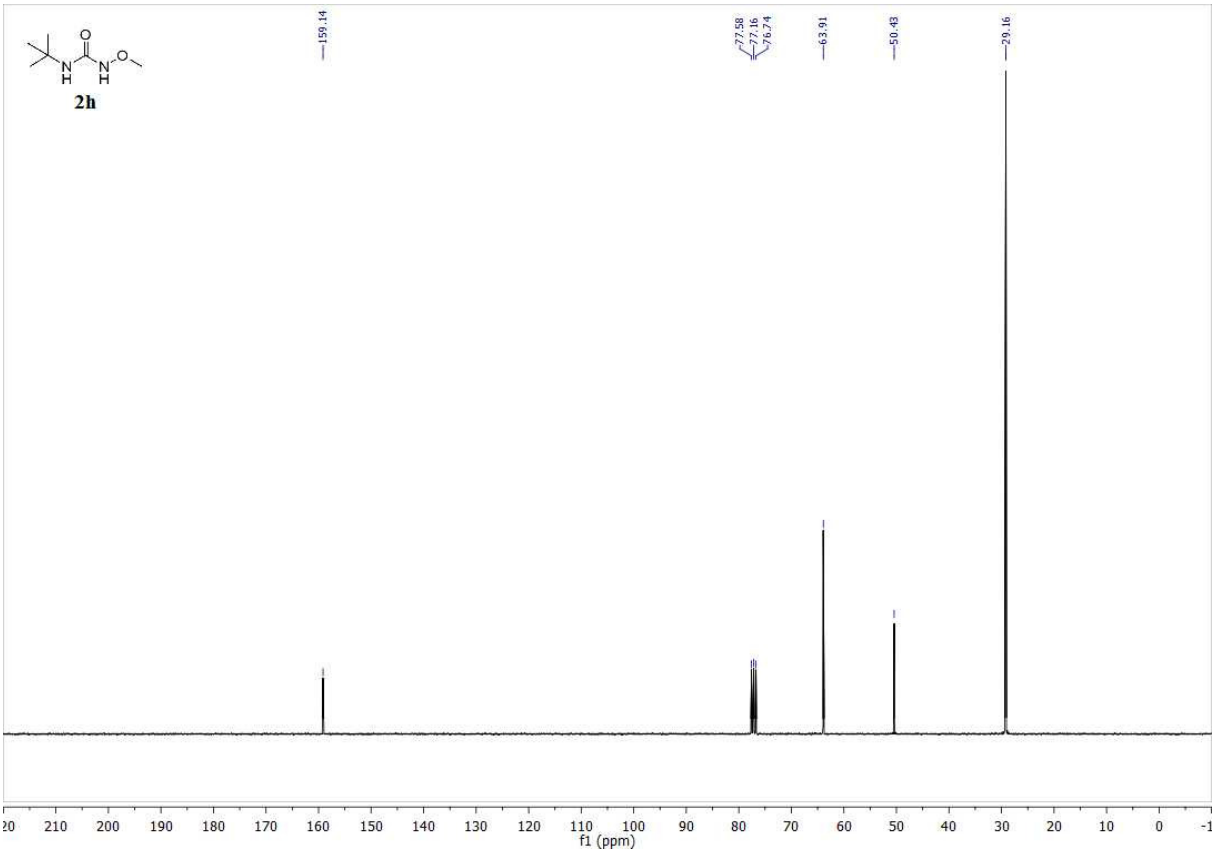
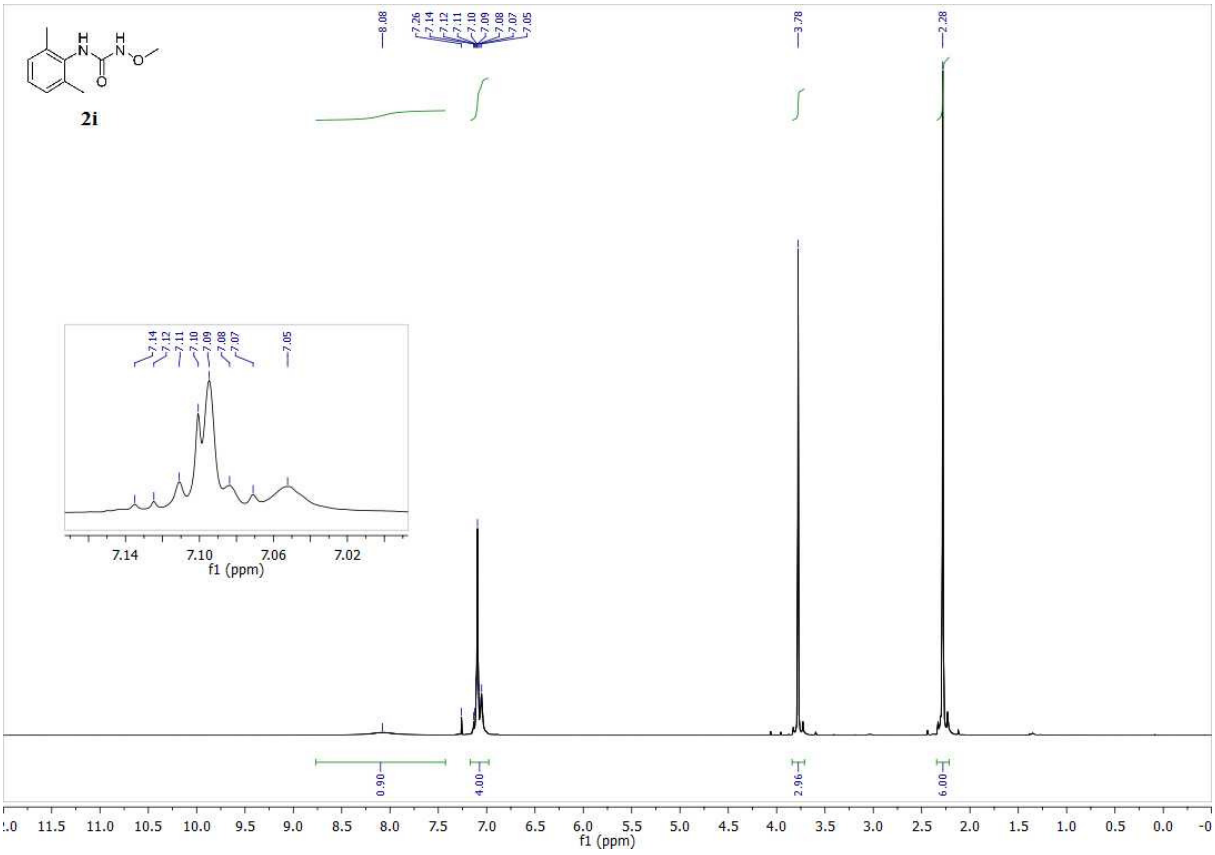
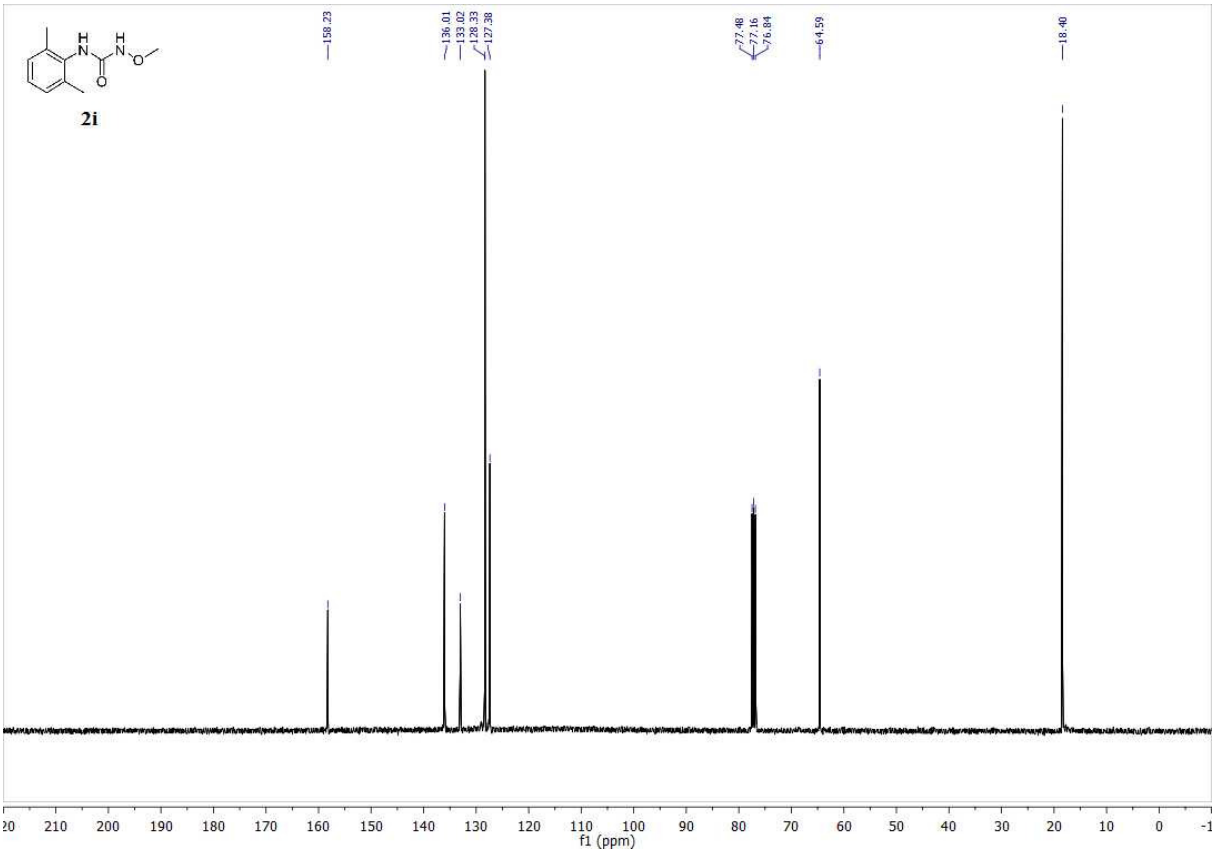
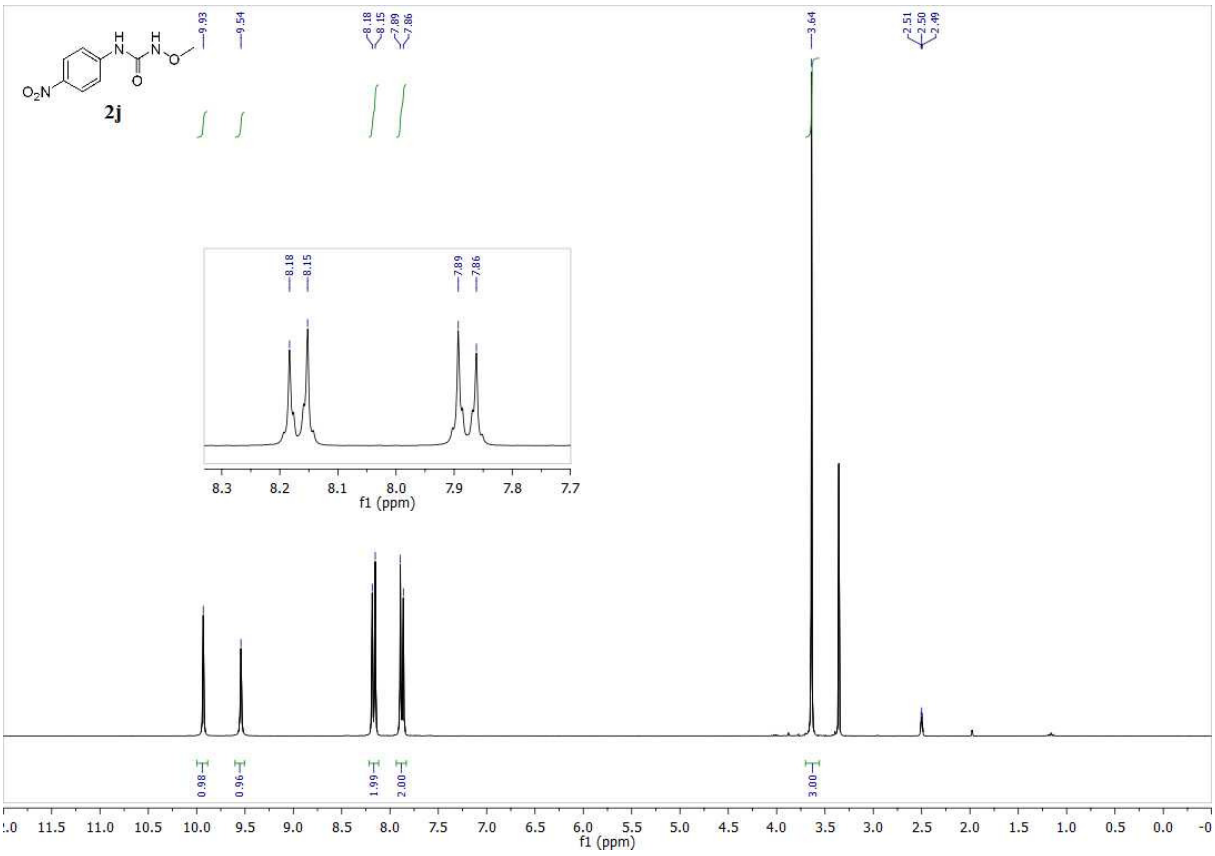
-164.00
-164.10
f1 (ppm)
f1 (ppm)

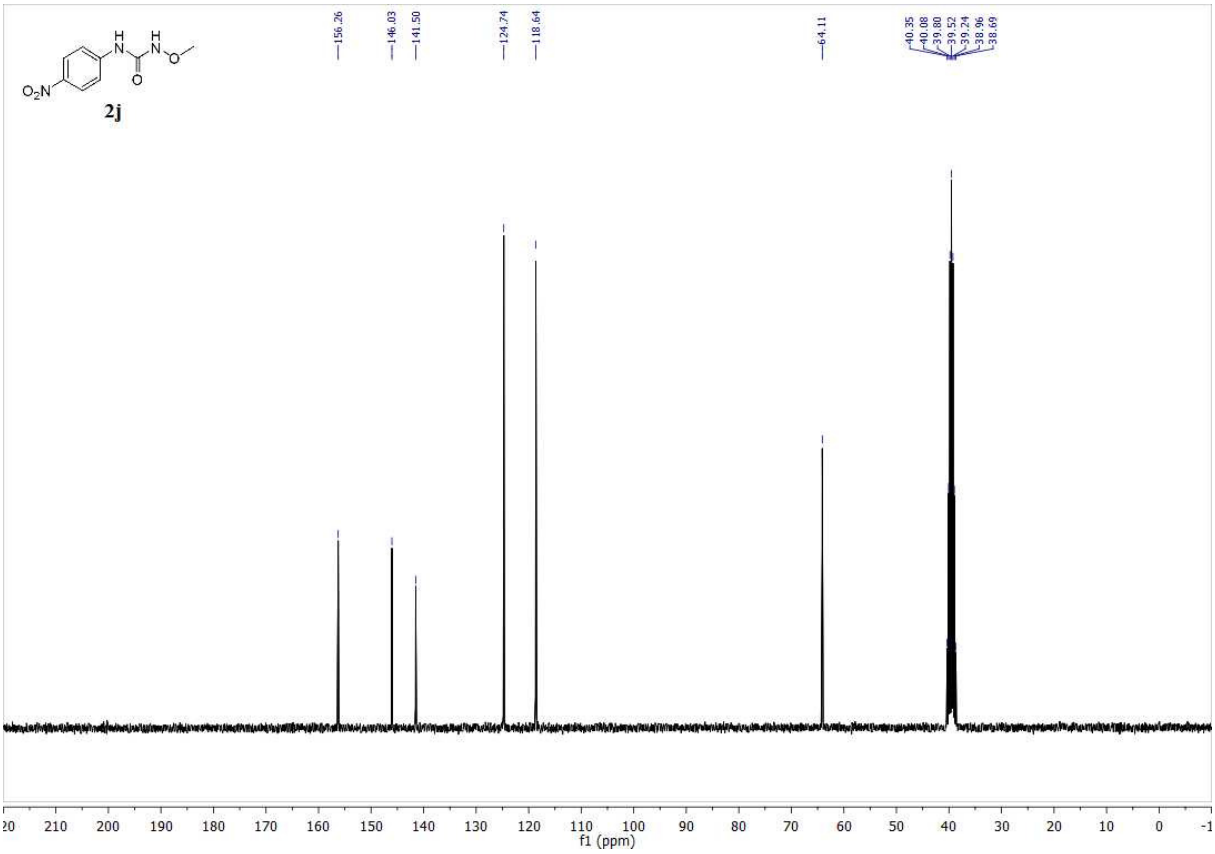

2h
7.38
7.26
5.53
3.61
1.32
0.90
0.96
3.01
9.00
f1 (ppm)

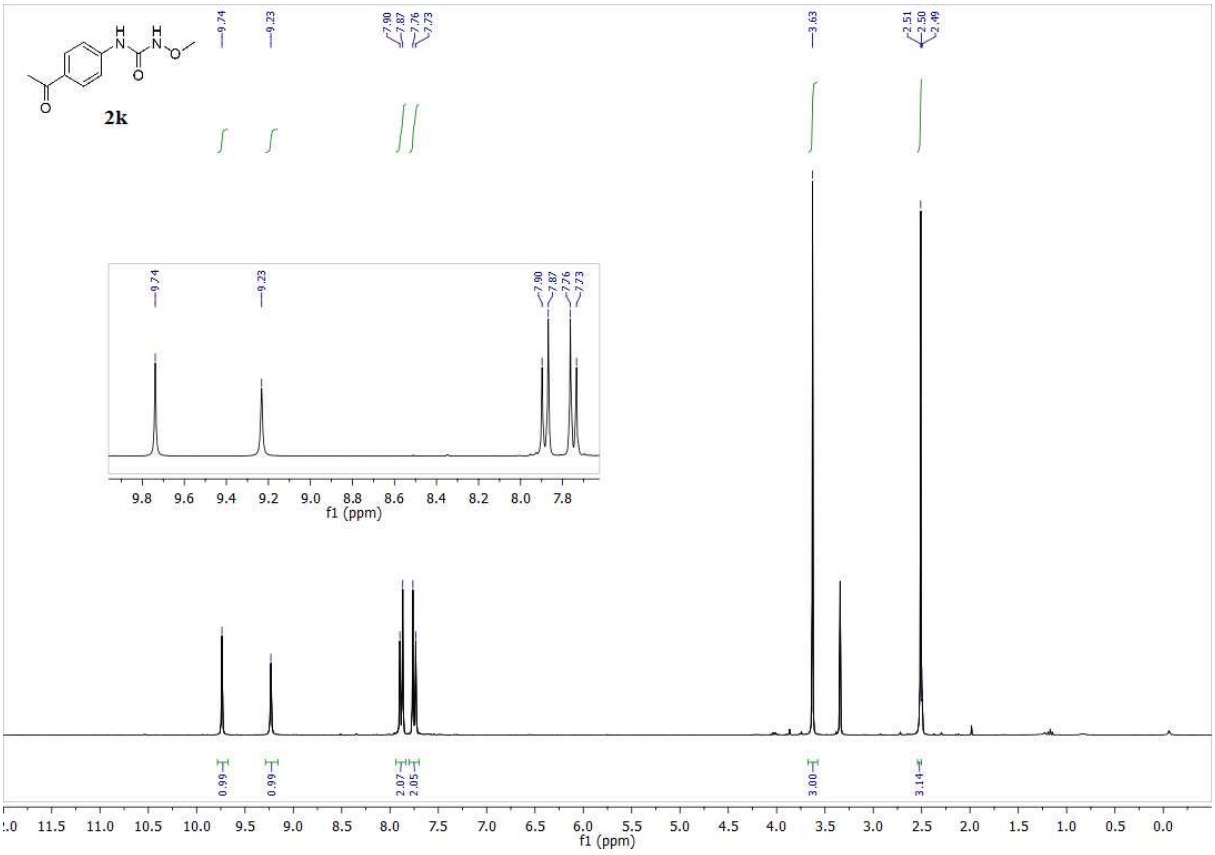

2h
159.14
77.58
77.16
76.74
63.91
50.43
29.16
f1 (ppm)

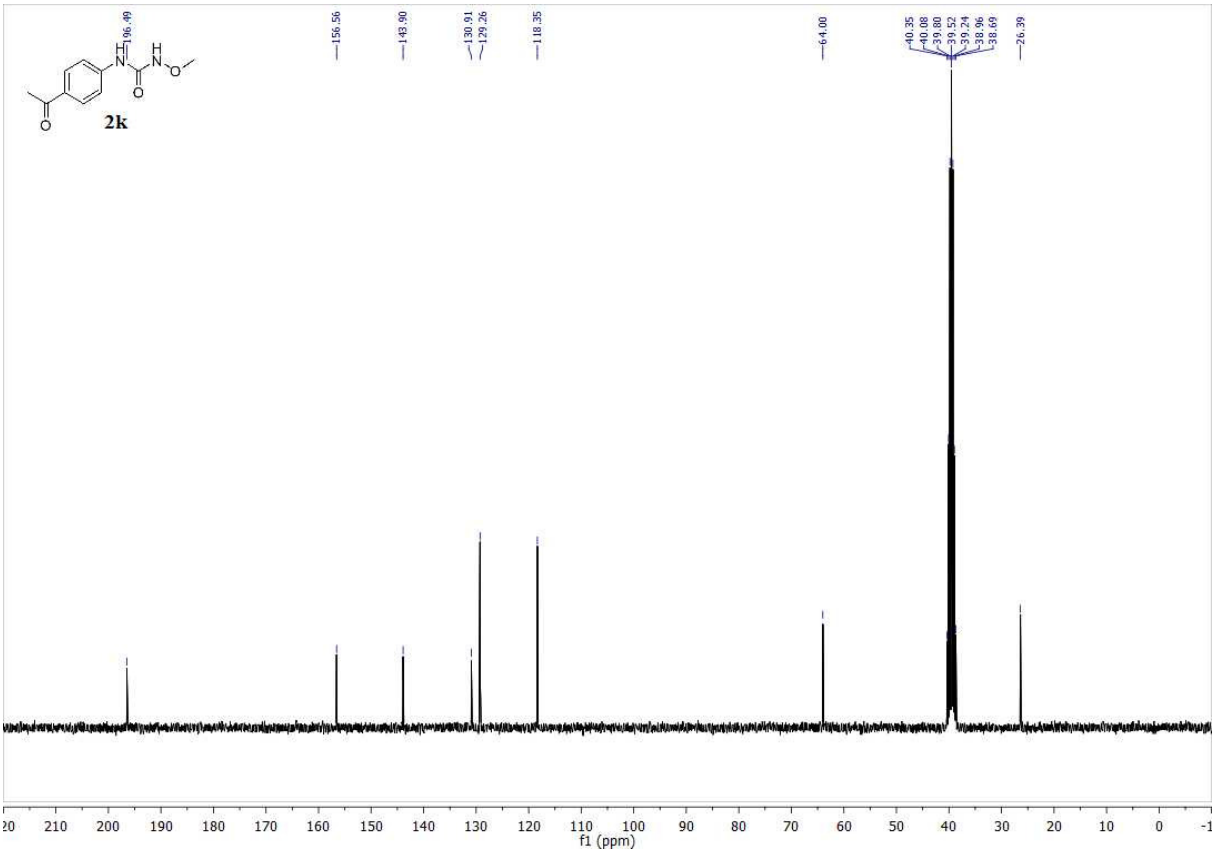

2i
8.08
7.26
7.14
7.12
7.11
7.10
7.09
7.08
7.07
7.05
3.78
2.28
7.14
7.12
7.11
7.10
7.09
7.08
7.07
7.05
7.14
7.10
7.06
7.02
f1 (ppm)
0.90
4.00
2.96
6.00
f1 (ppm)

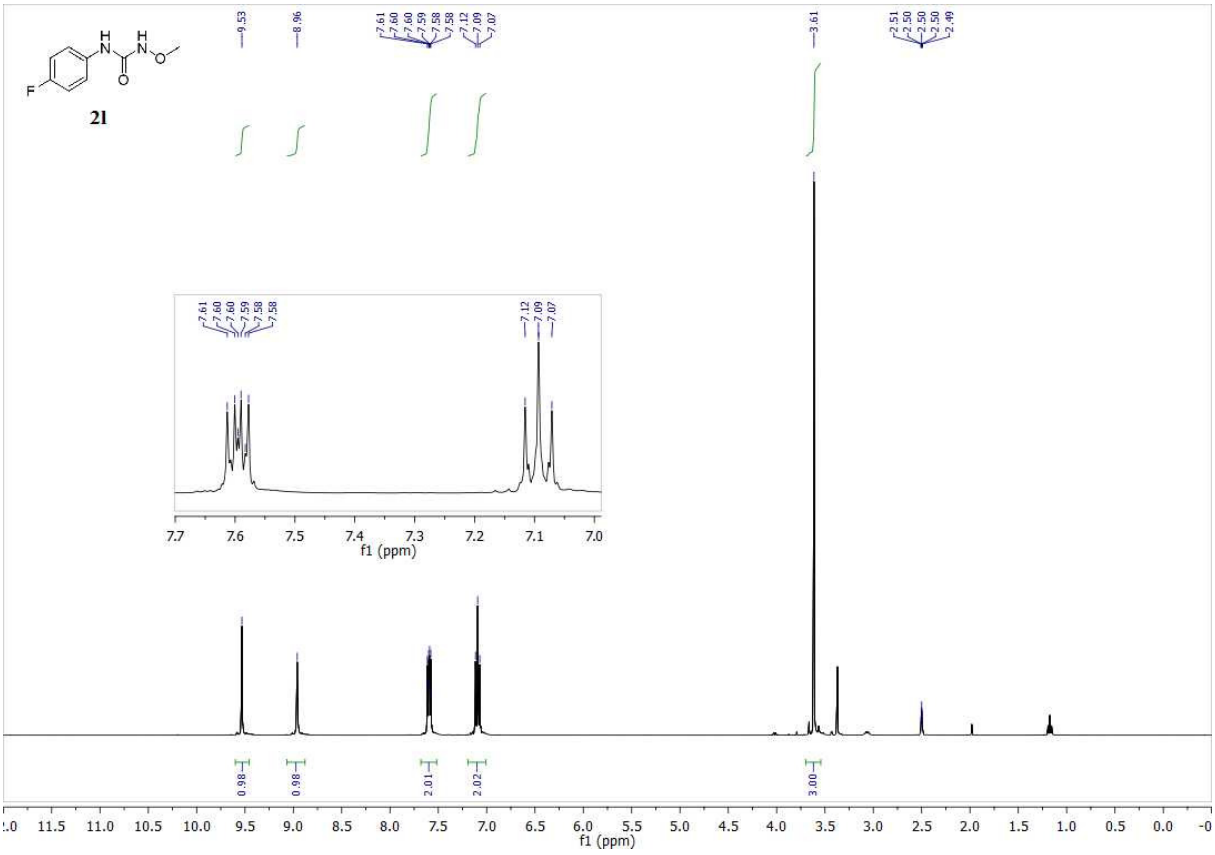

2i
158.23
136.01
133.02
128.33
127.38
77.48
77.16
76.84
64.59
18.40
f1 (ppm)

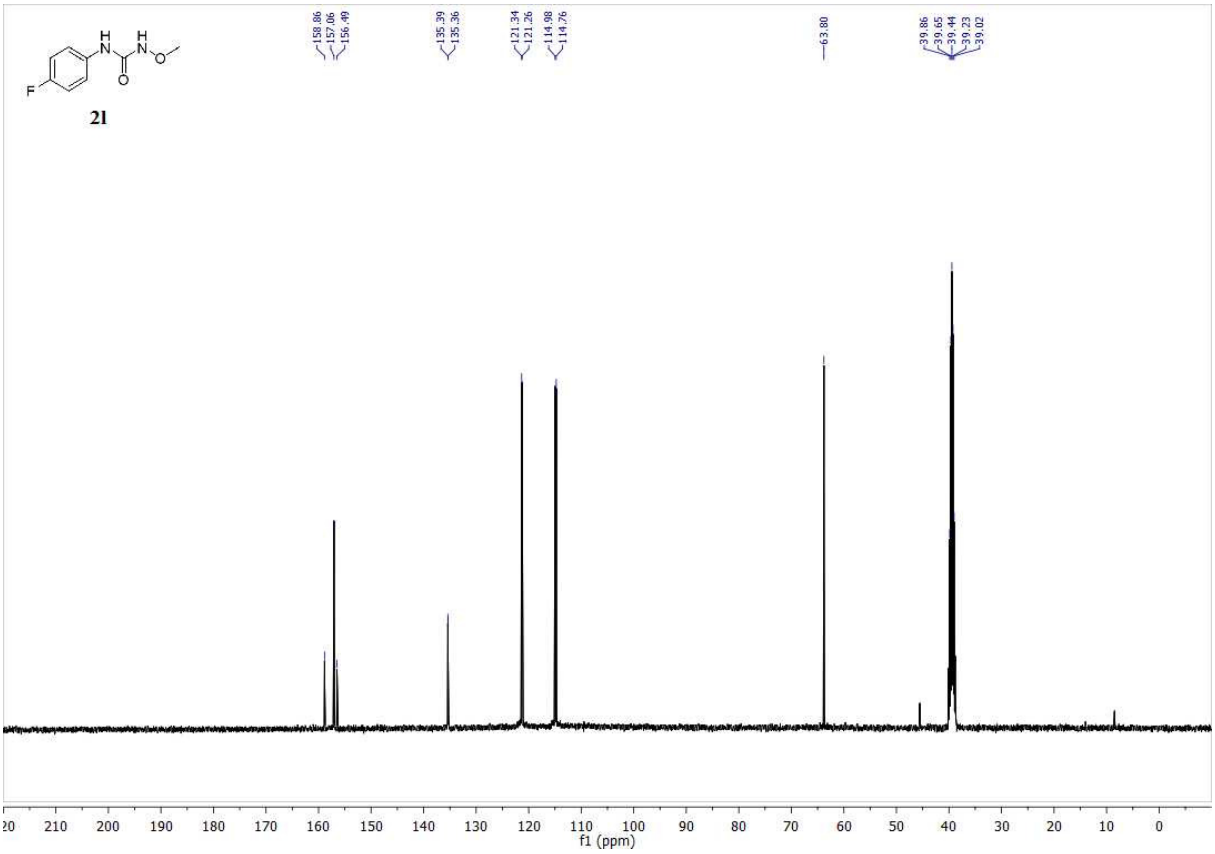


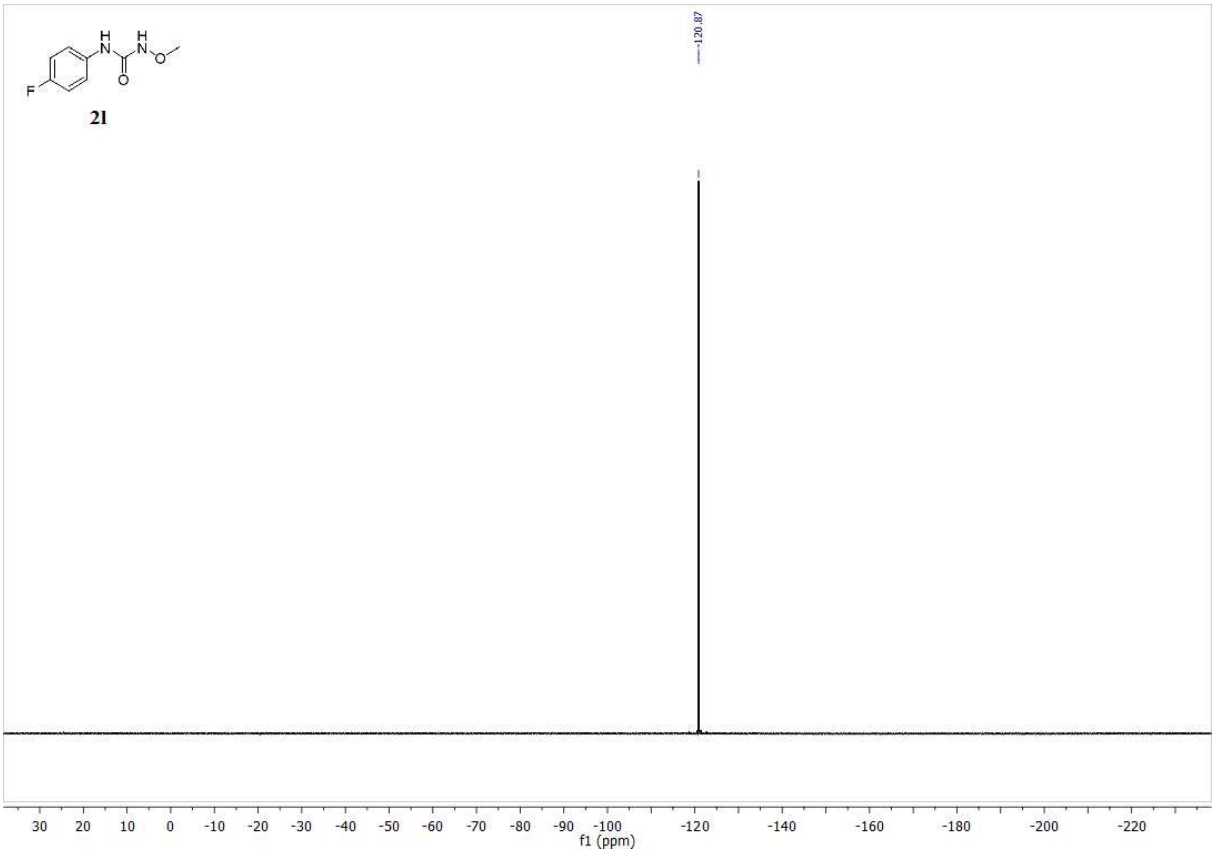


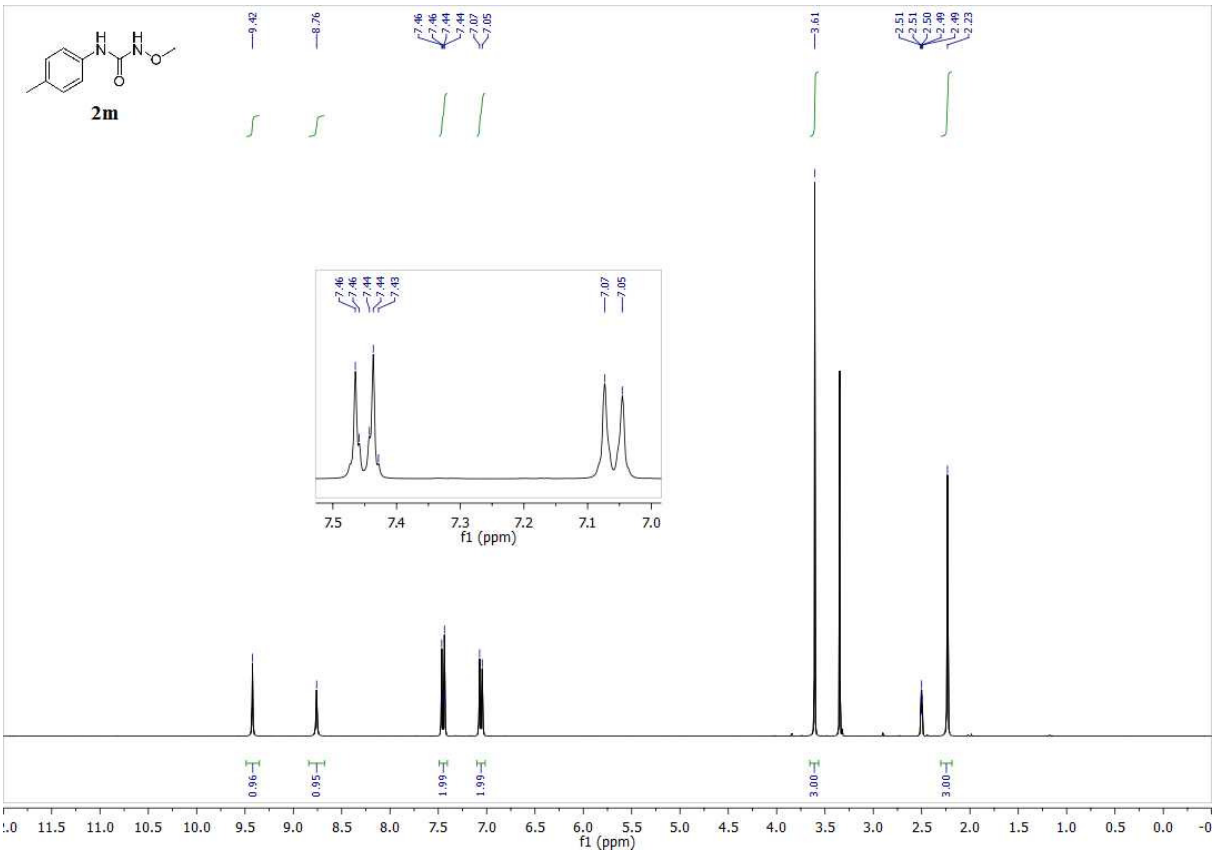

2k
9.74
9.23
7.90
7.87
7.76
7.73
3.63
2.51
2.50
2.49
0.99
0.99
2.07
2.05
3.00
3.14
f1 (ppm)

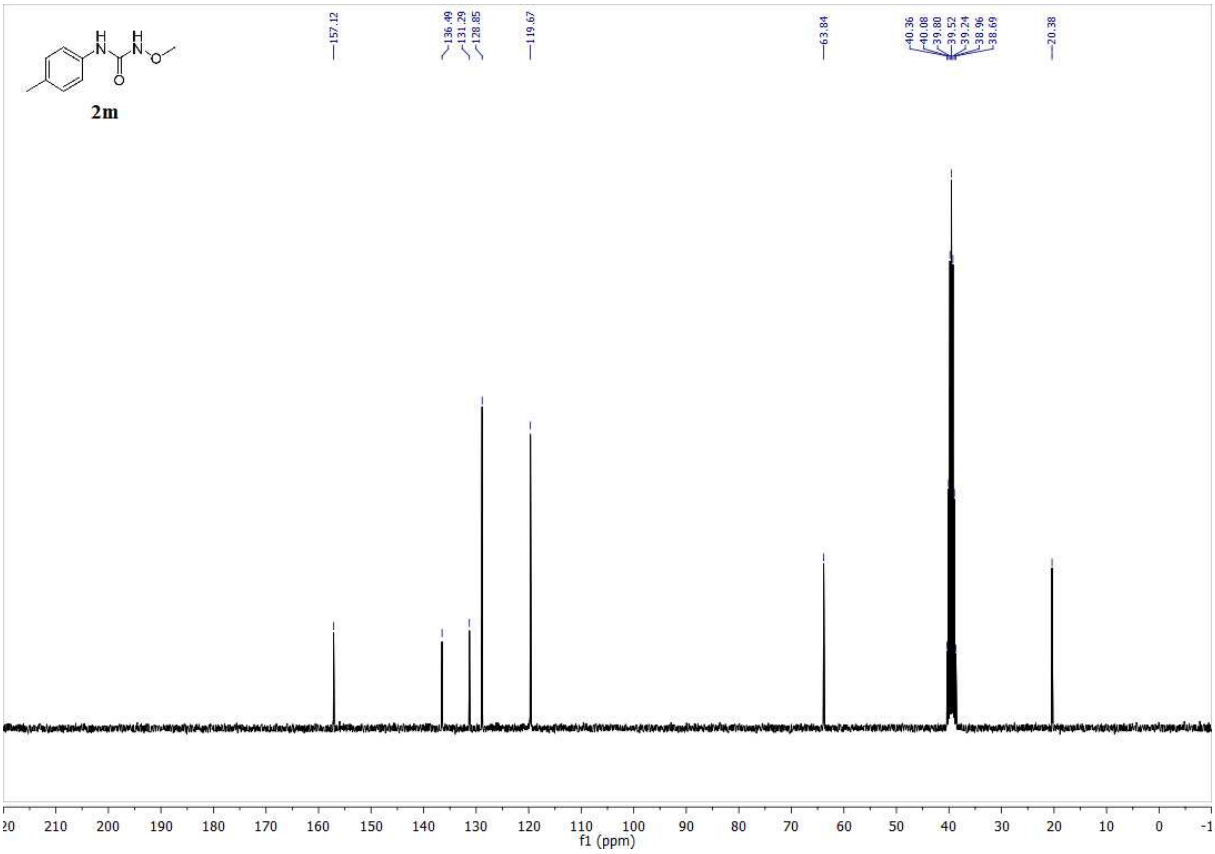

2k
196.49
156.56
143.90
130.91
129.26
118.35
64.00
40.35
40.08
39.80
39.52
39.24
38.96
38.69
26.39
f1 (ppm)

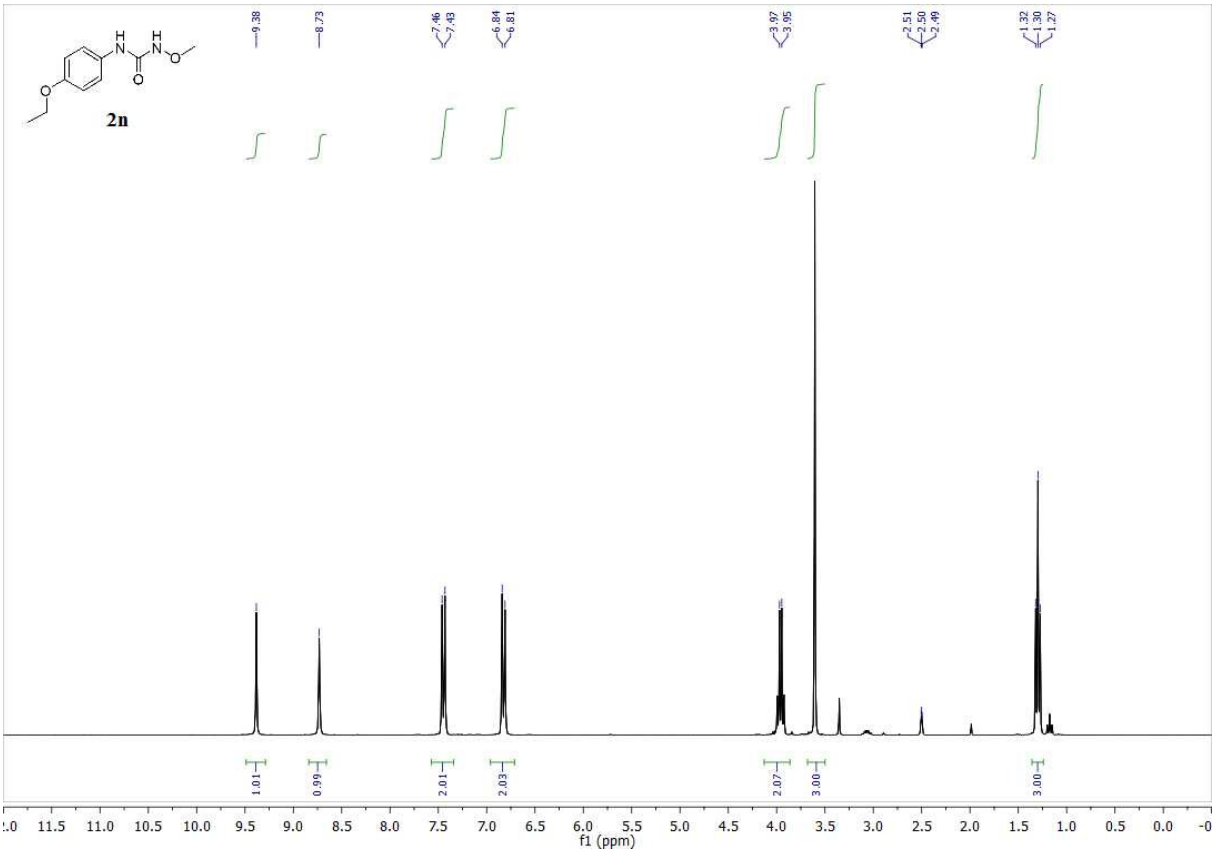

21
9.53
8.96
7.61
7.60
7.60
7.59
7.58
7.58
7.12
7.09
7.07
3.61
2.51
2.50
2.50
2.50
2.49
0.98
0.98
2.01
2.02
3.00
f1 (ppm)

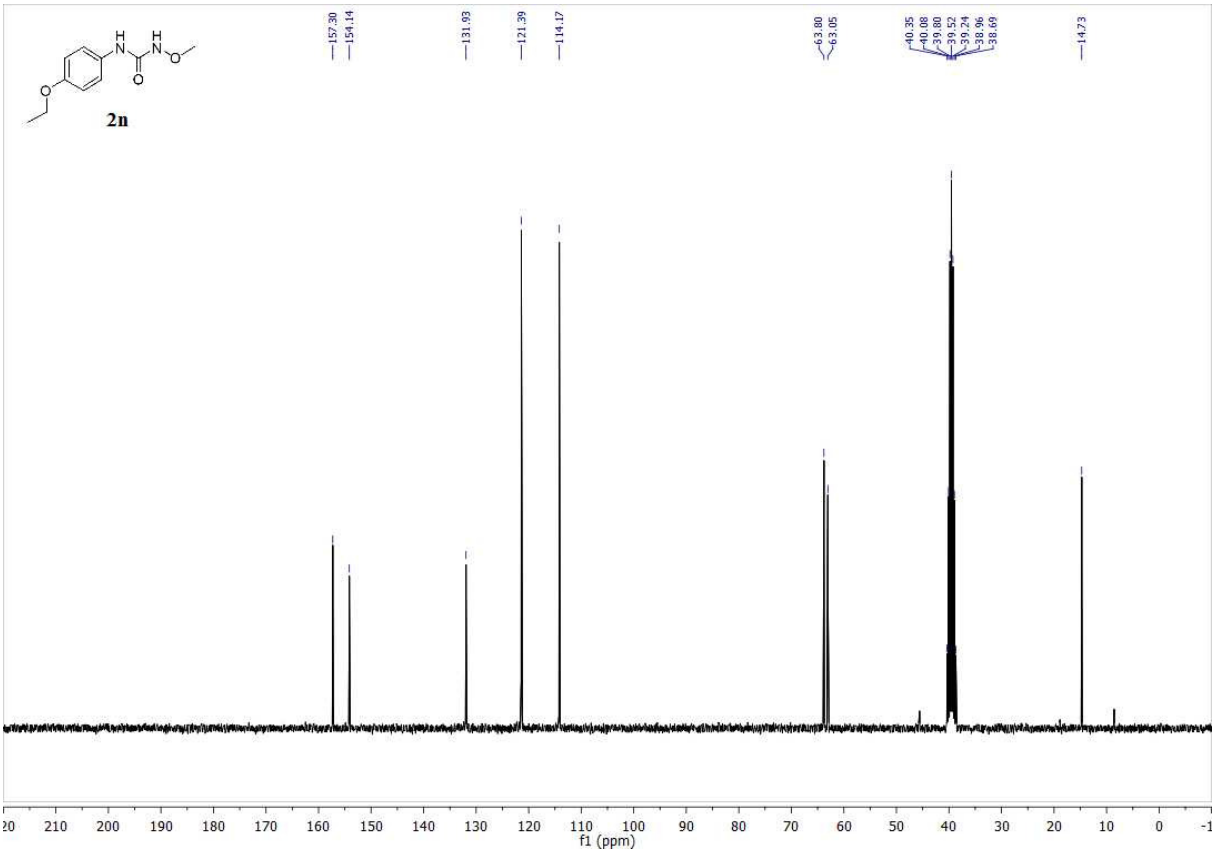

21
158.86
157.06
156.49
135.39
135.36
121.34
121.26
114.98
114.76
63.80
39.86
39.65
39.44
39.23
39.02
f1 (ppm)

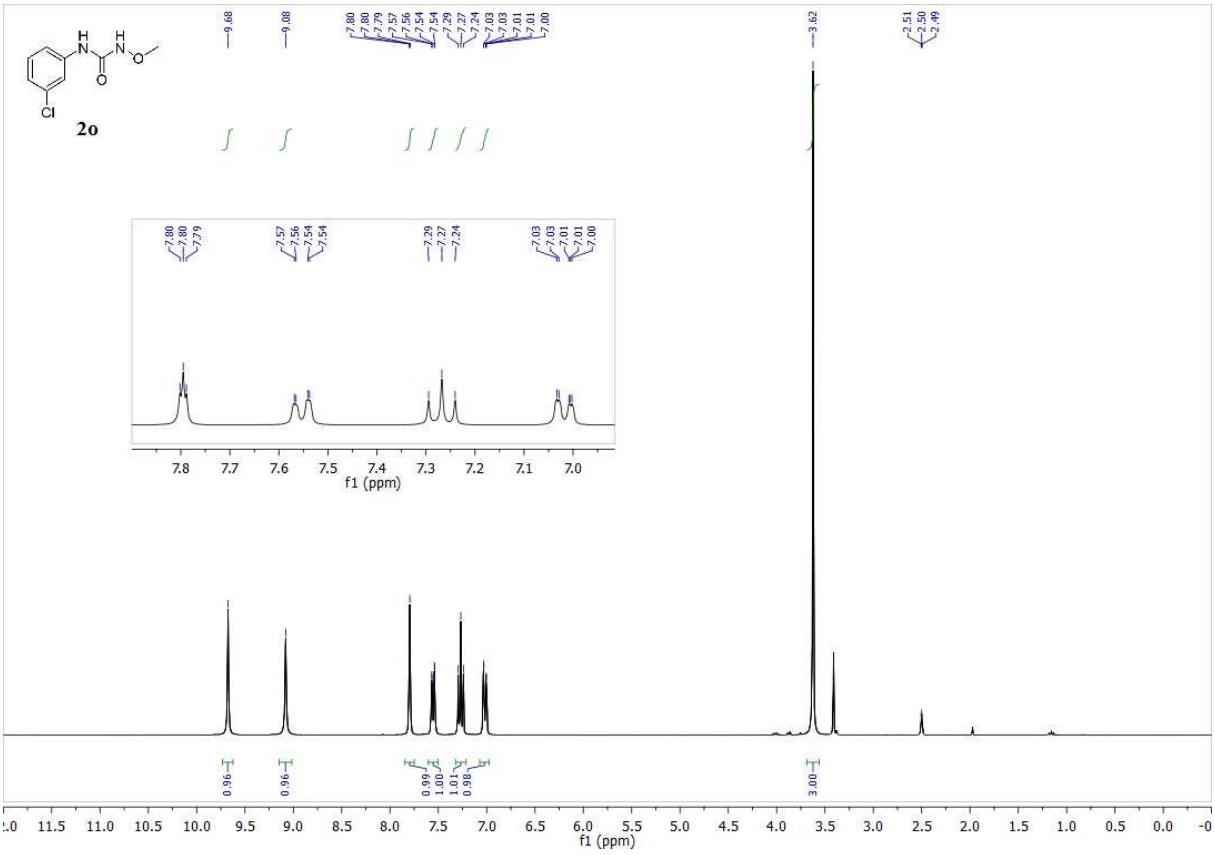


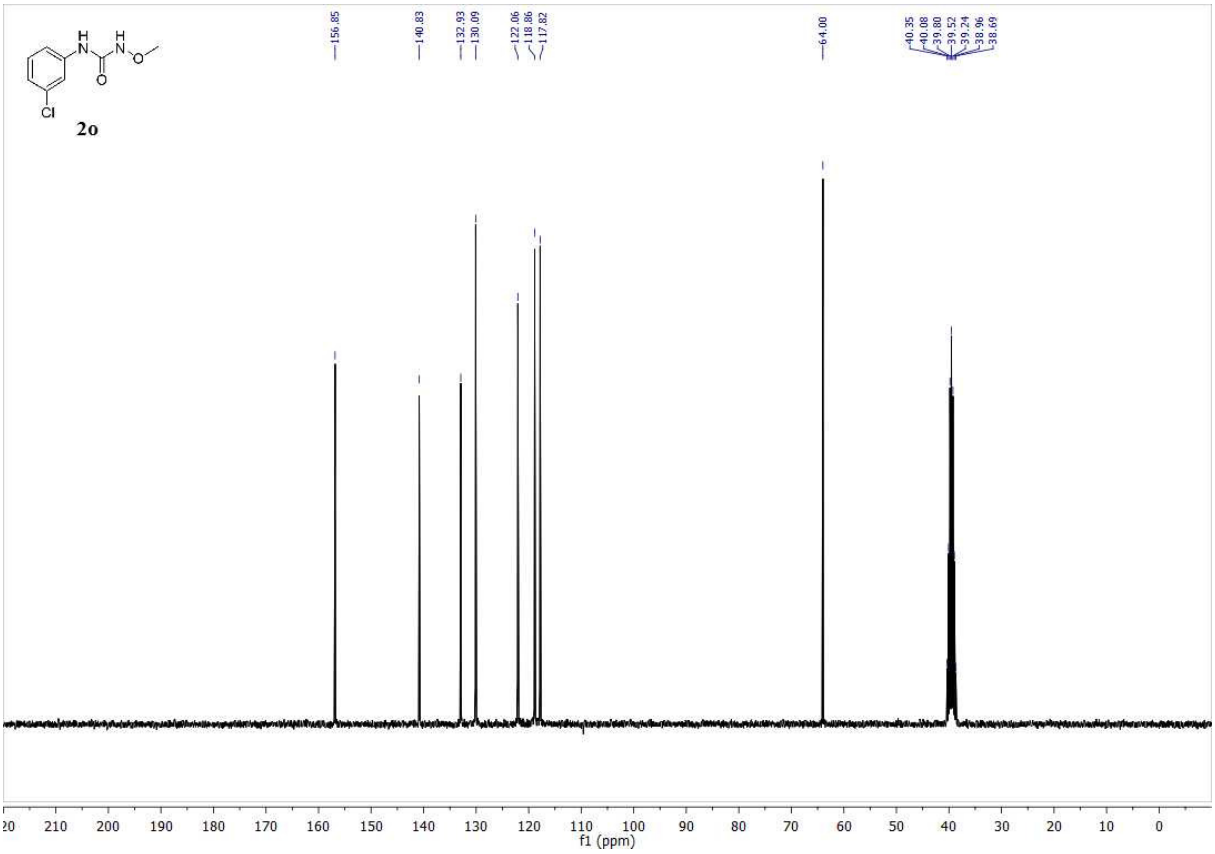

2m
9.42
8.76
7.46
7.46
7.44
7.44
7.07
7.05
3.61
2.51
2.51
2.50
2.49
2.49
2.23
7.46
7.46
7.44
7.44
7.43
7.07
7.05
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
0.96
0.95
1.99
1.99
3.00
3.00
f1 (ppm)

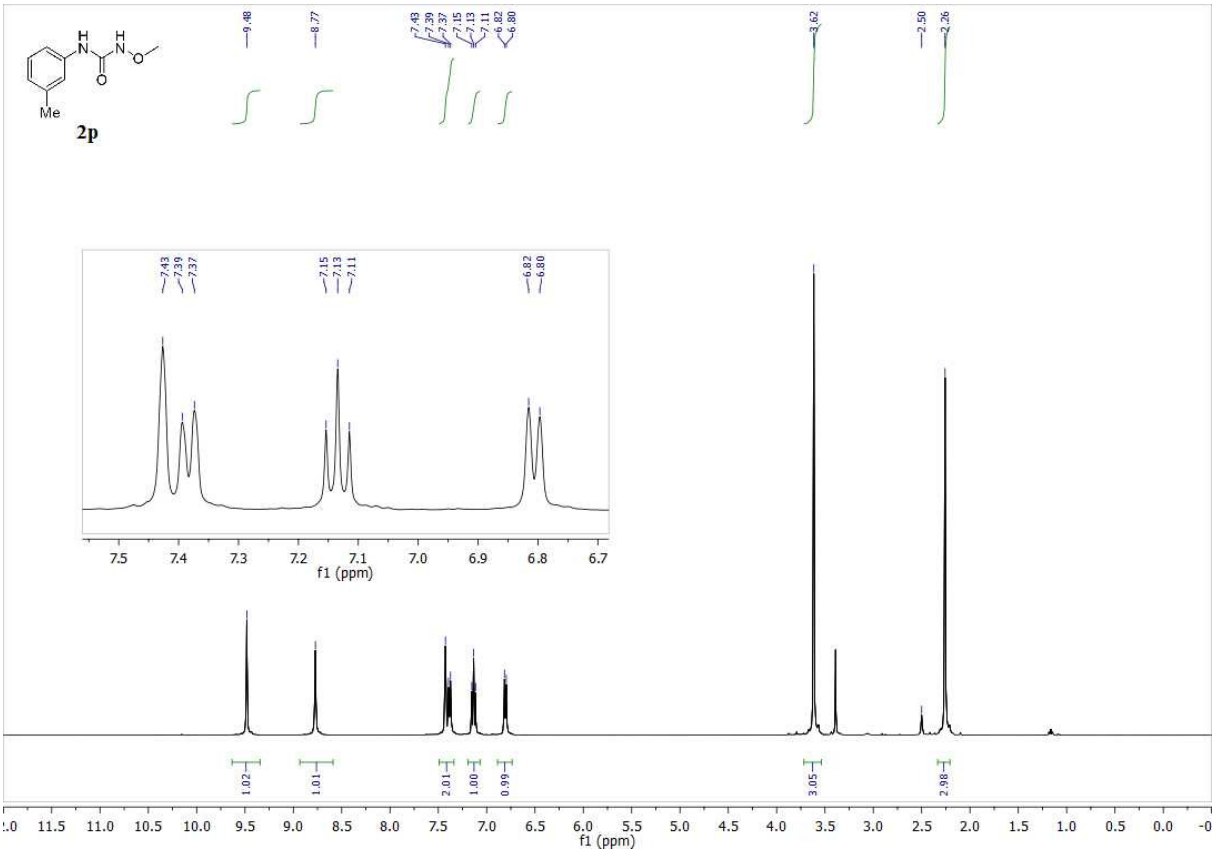

2m
157.12
136.49
131.29
128.85
119.67
63.84
40.36
40.08
39.80
39.52
39.24
38.96
38.69
20.38
f1 (ppm)

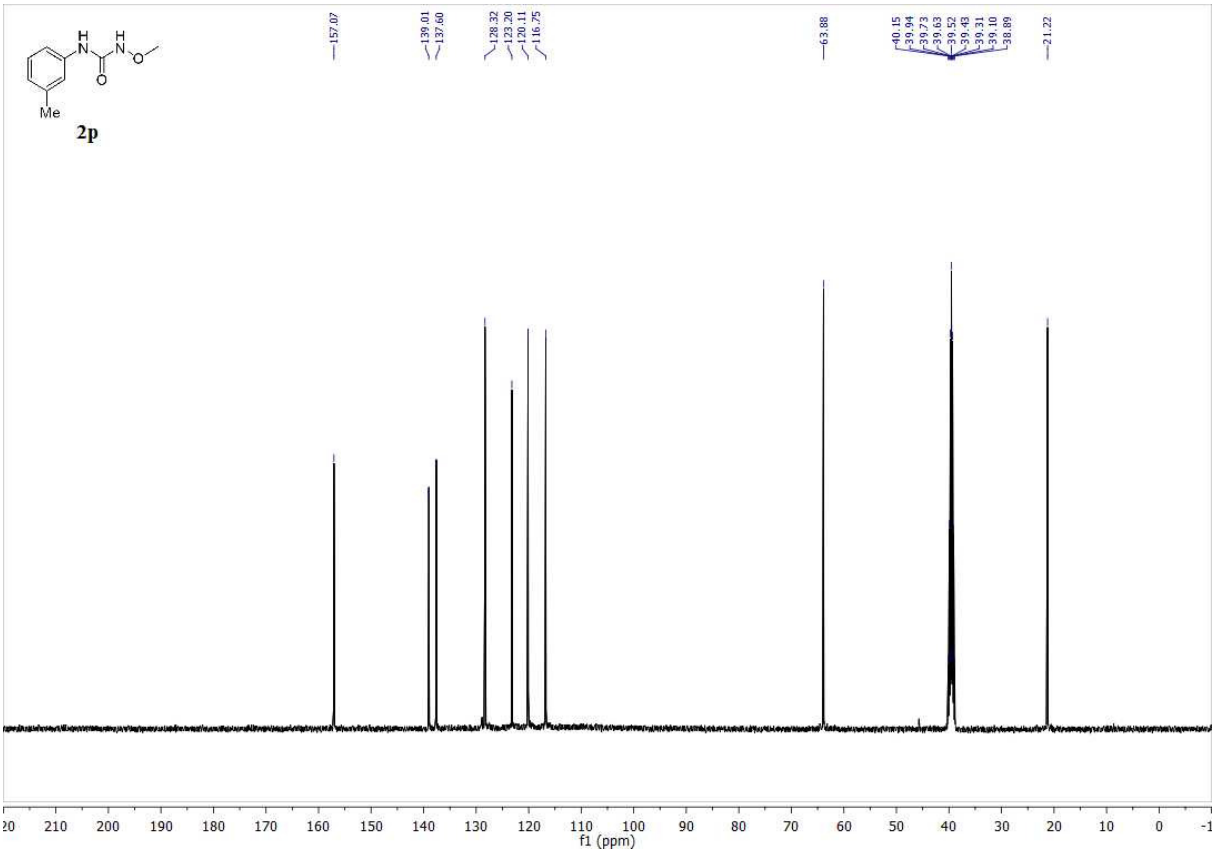

2n
9.38
8.73
7.46
7.43
6.84
6.81
3.97
3.95
2.51
2.50
2.49
1.32
1.30
1.27
1.01
0.99
2.01
2.03
2.07
3.00
3.00
f1 (ppm)

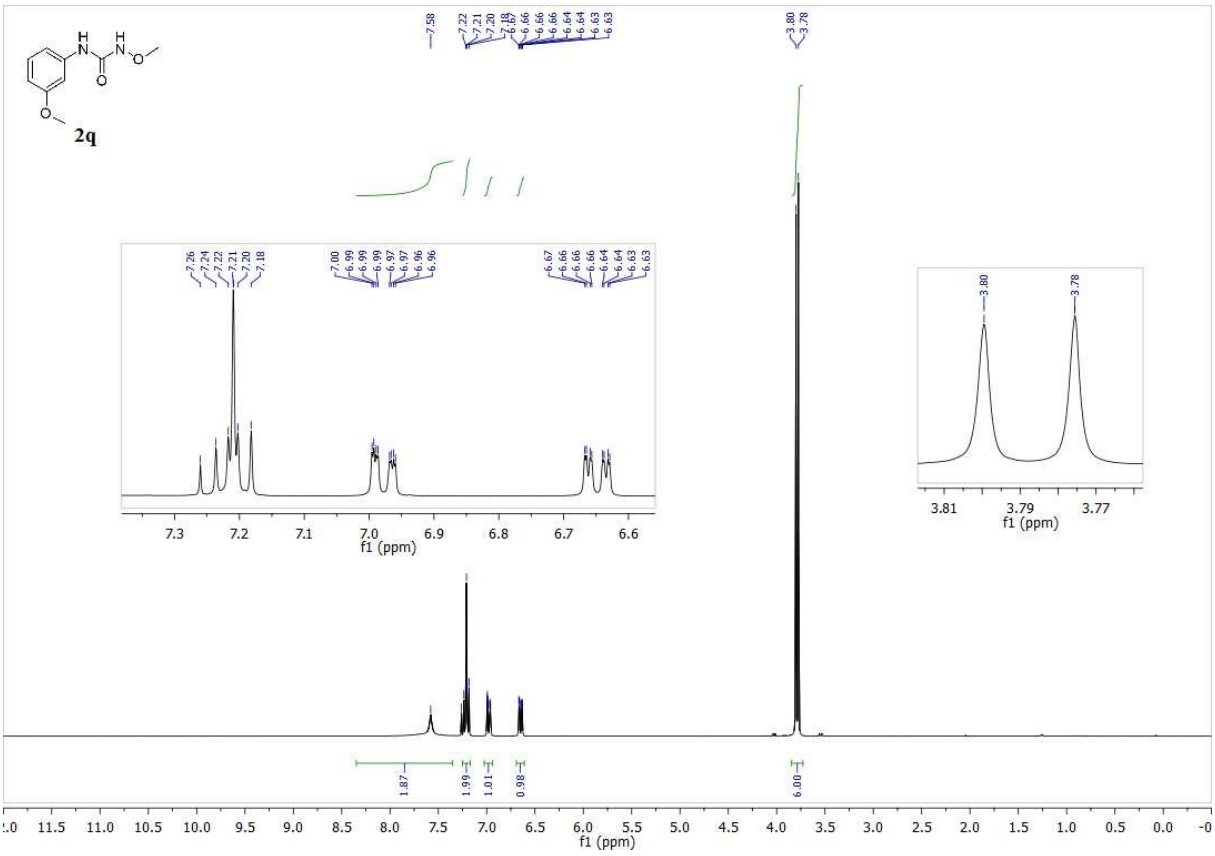

2n
157.30
154.14
131.93
121.39
114.17
63.80
63.05
40.35
40.08
39.80
39.52
39.24
38.96
38.69
14.73
f1 (ppm)

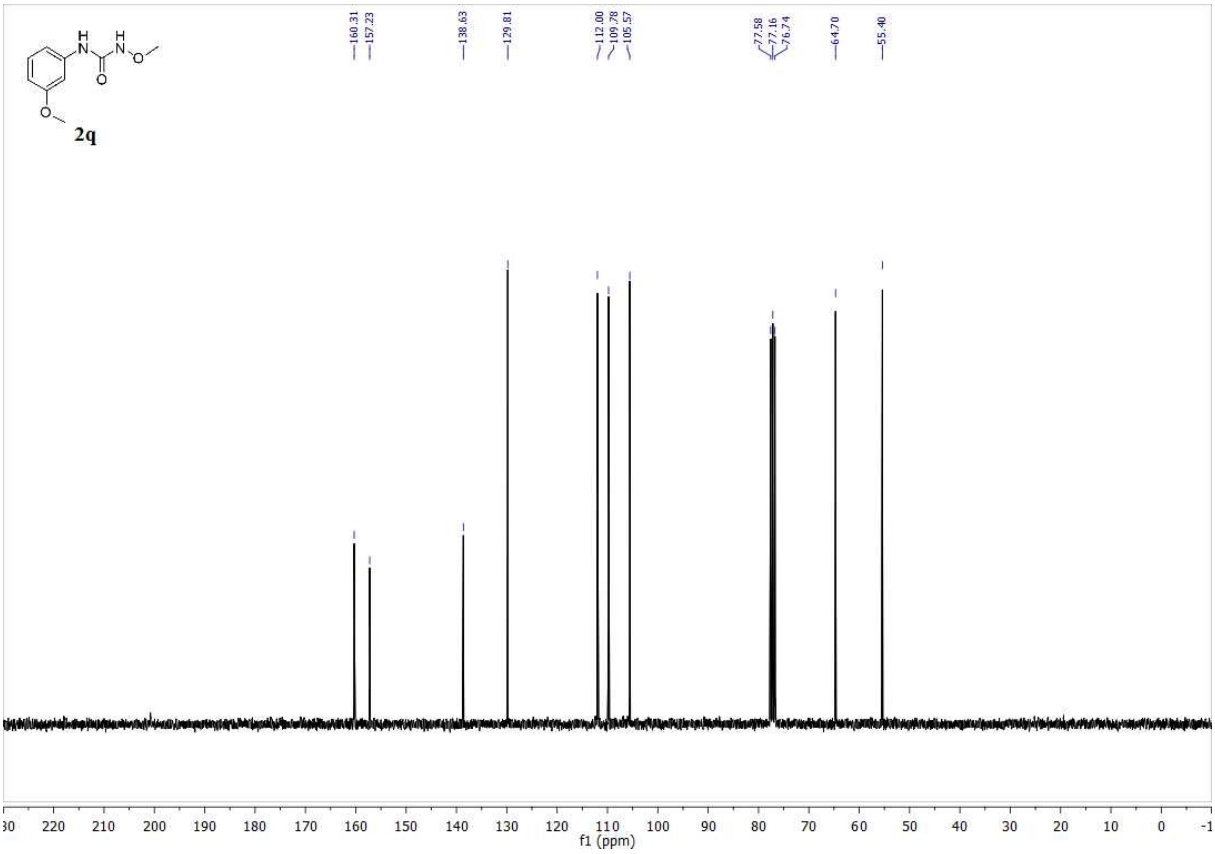

2o
f1 (ppm)

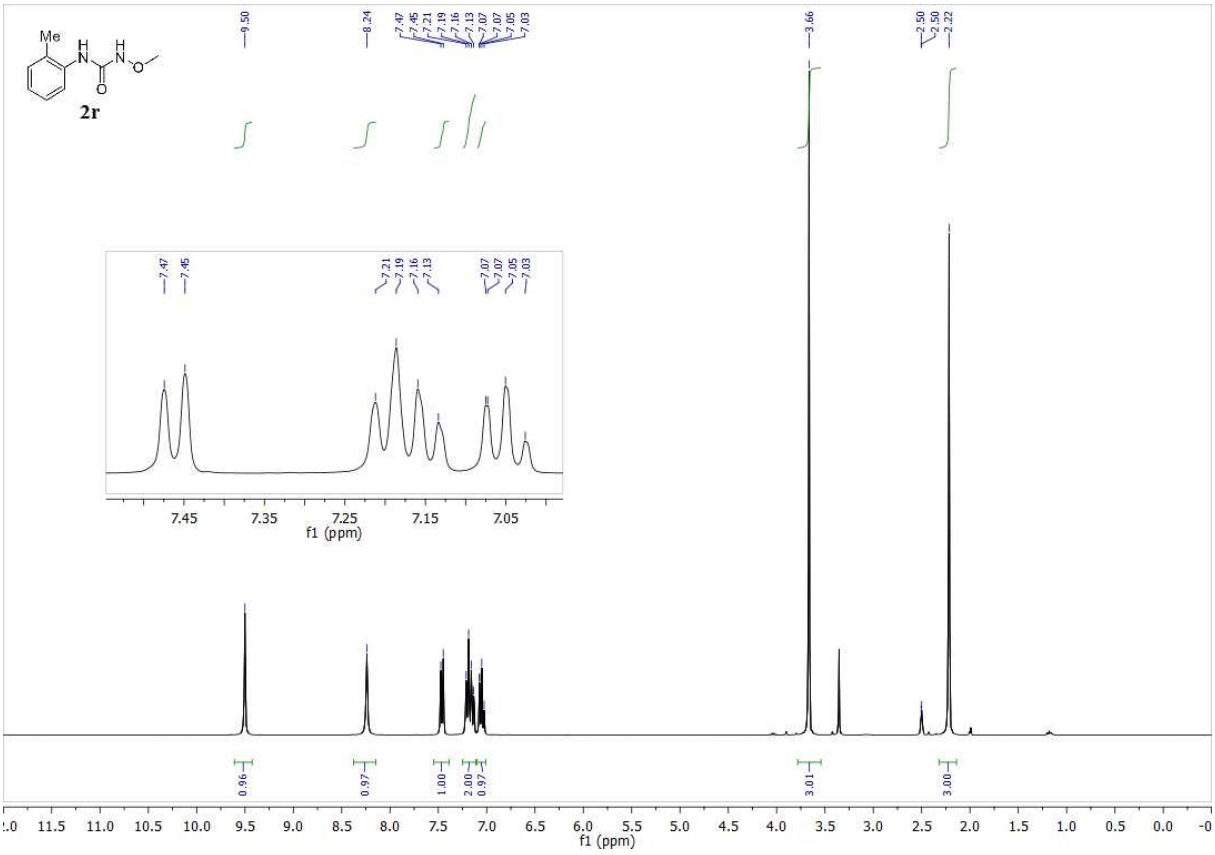

2o
f1 (ppm)

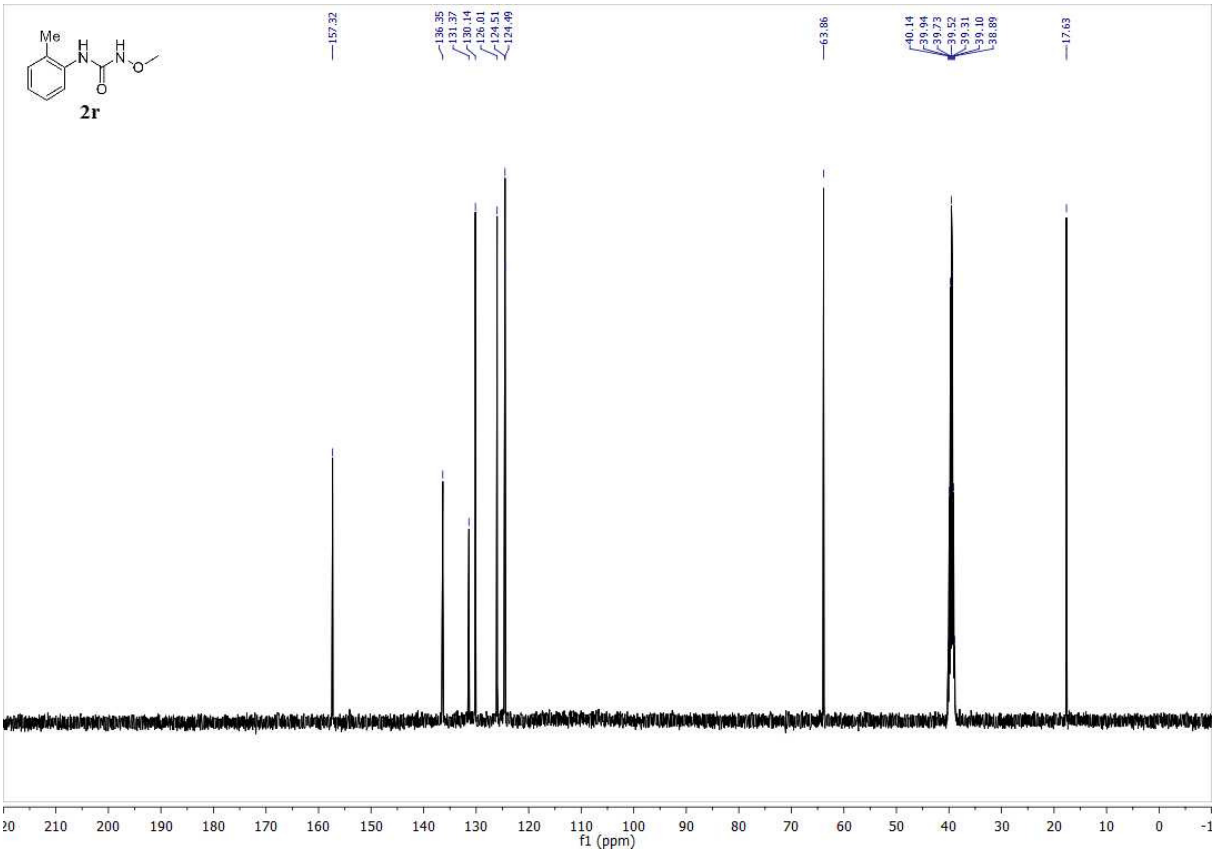

Me
2p
9.48
8.77
7.43
7.39
7.37
7.15
7.13
7.11
6.82
6.80
3.62
2.50
2.26
1.02
1.01
2.01
1.00
0.99
3.05
2.98
f1 (ppm)

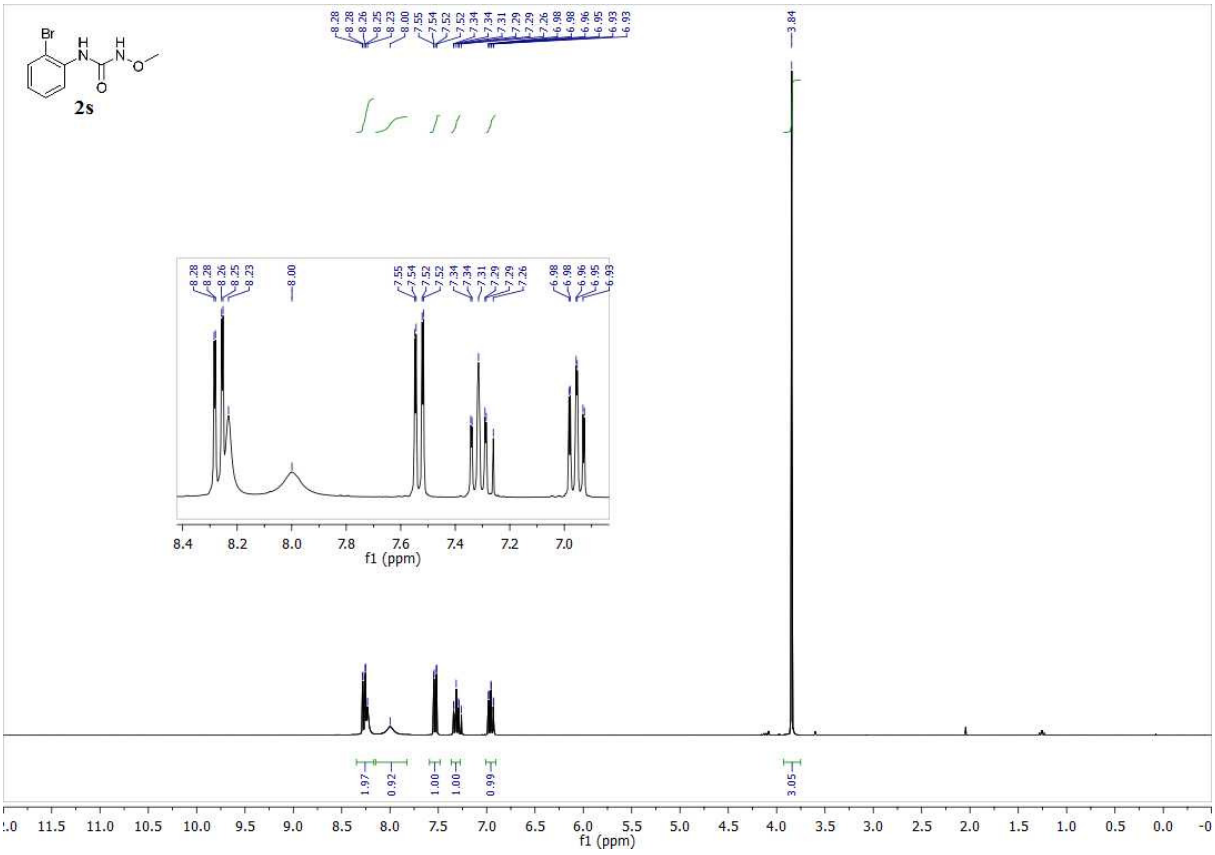

Me
2p
157.07
139.01
137.60
128.32
123.20
120.11
116.75
63.88
40.15
39.94
39.73
39.63
39.52
39.43
39.31
39.10
38.89
21.22
f1 (ppm)

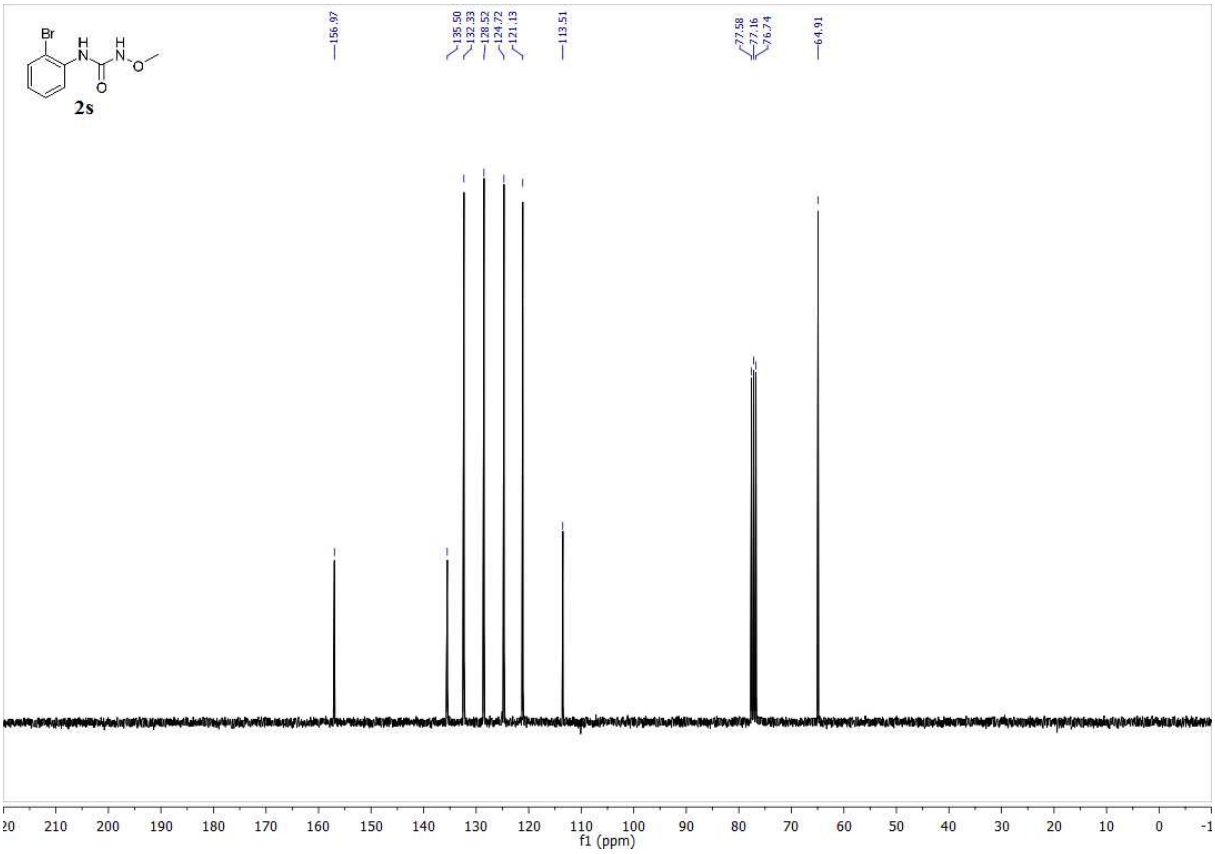

2q
f1 (ppm)

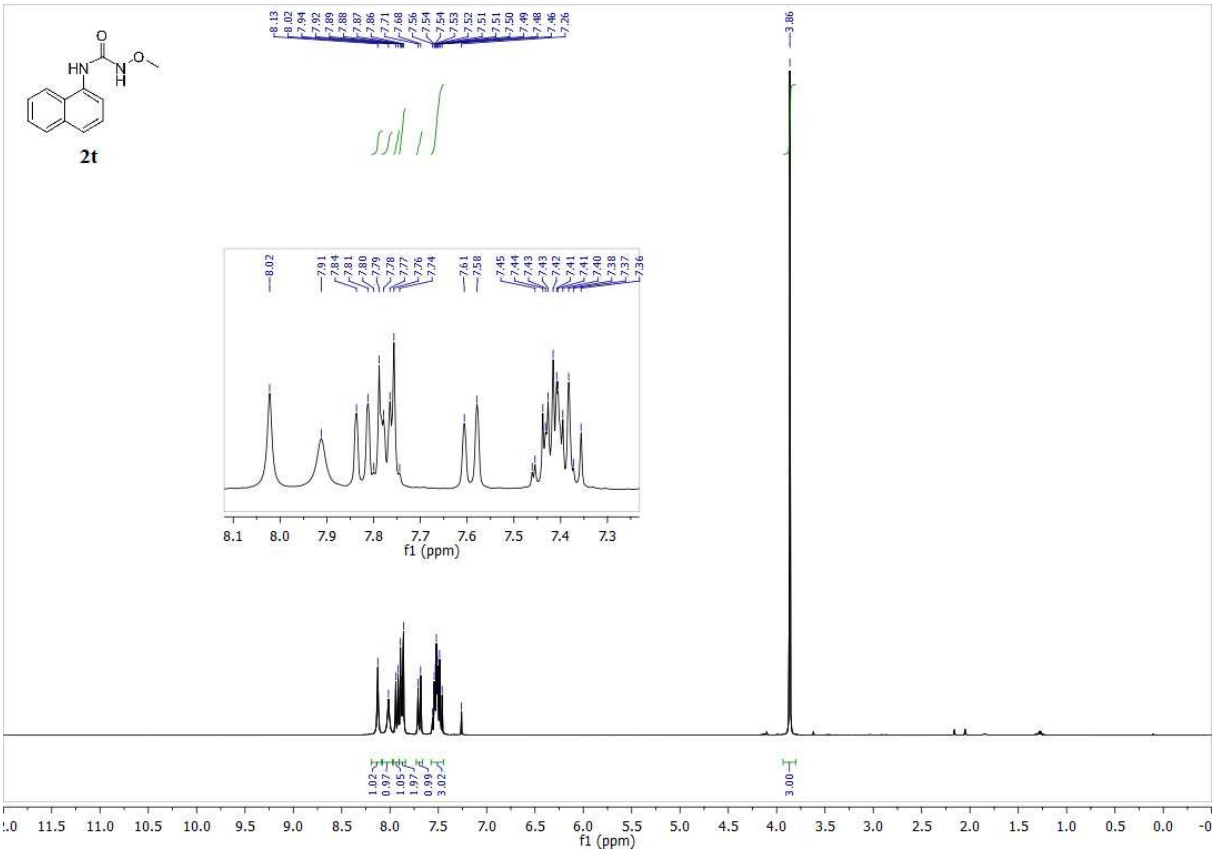

2q
f1 (ppm)

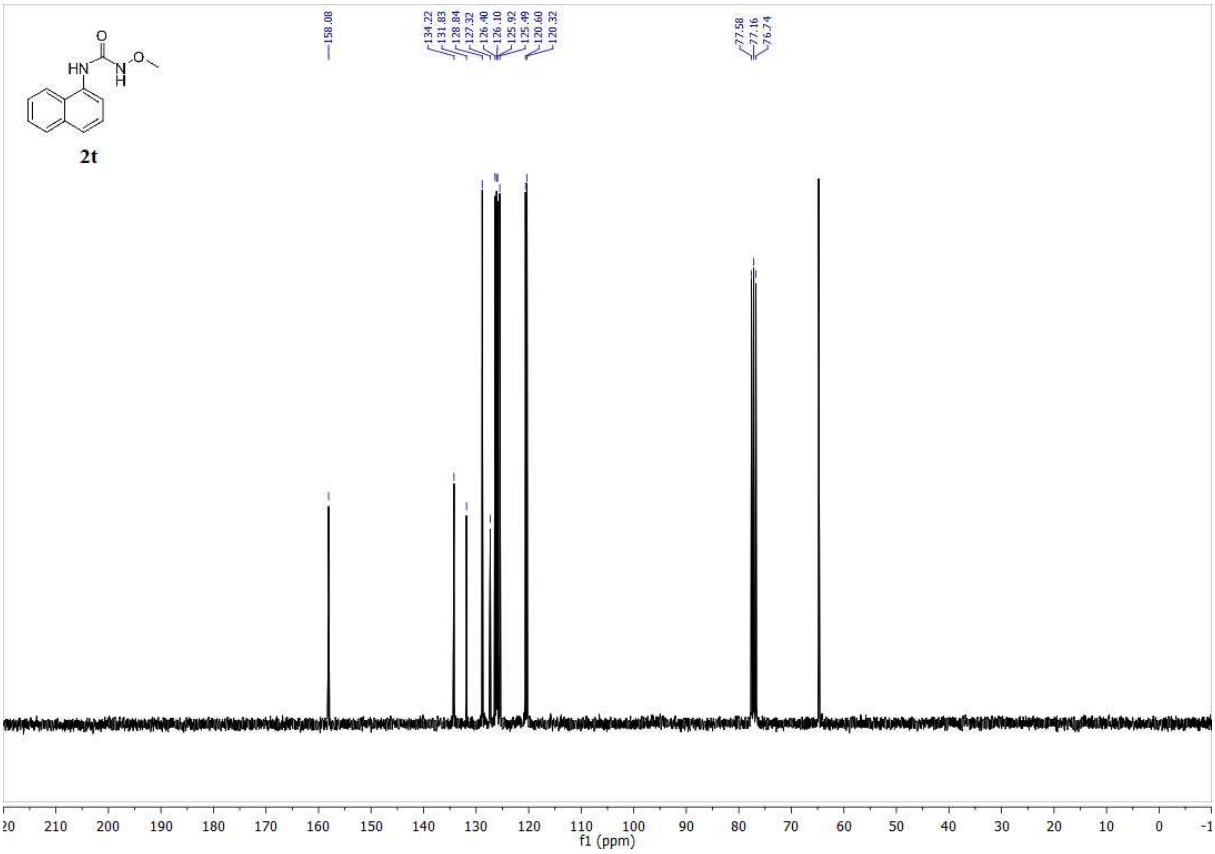

Me
H
N
H
N
O
O
2r
9.50
8.24
7.47
7.45
7.21
7.19
7.16
7.13
7.07
7.07
7.05
7.03
3.66
2.50
2.50
2.22
7.45
7.35
7.25
7.15
7.05
f1 (ppm)
0.96
0.97
1.00
2.00
0.97
3.01
3.00
f1 (ppm)

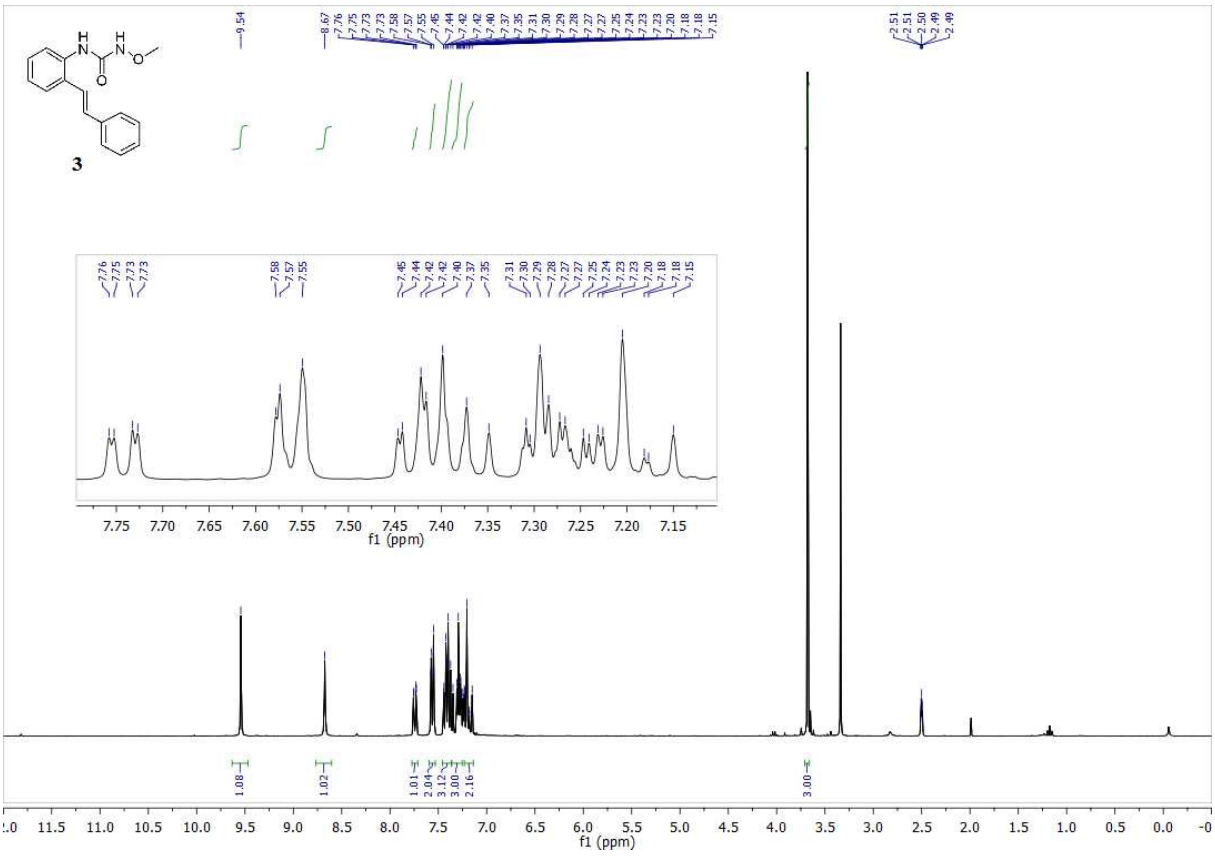

Me
H
N
H
N
O
O
2r
157.32
136.35
131.37
130.14
126.01
124.51
124.49
63.86
40.14
39.94
39.73
39.52
39.31
39.10
38.89
17.63
f1 (ppm)

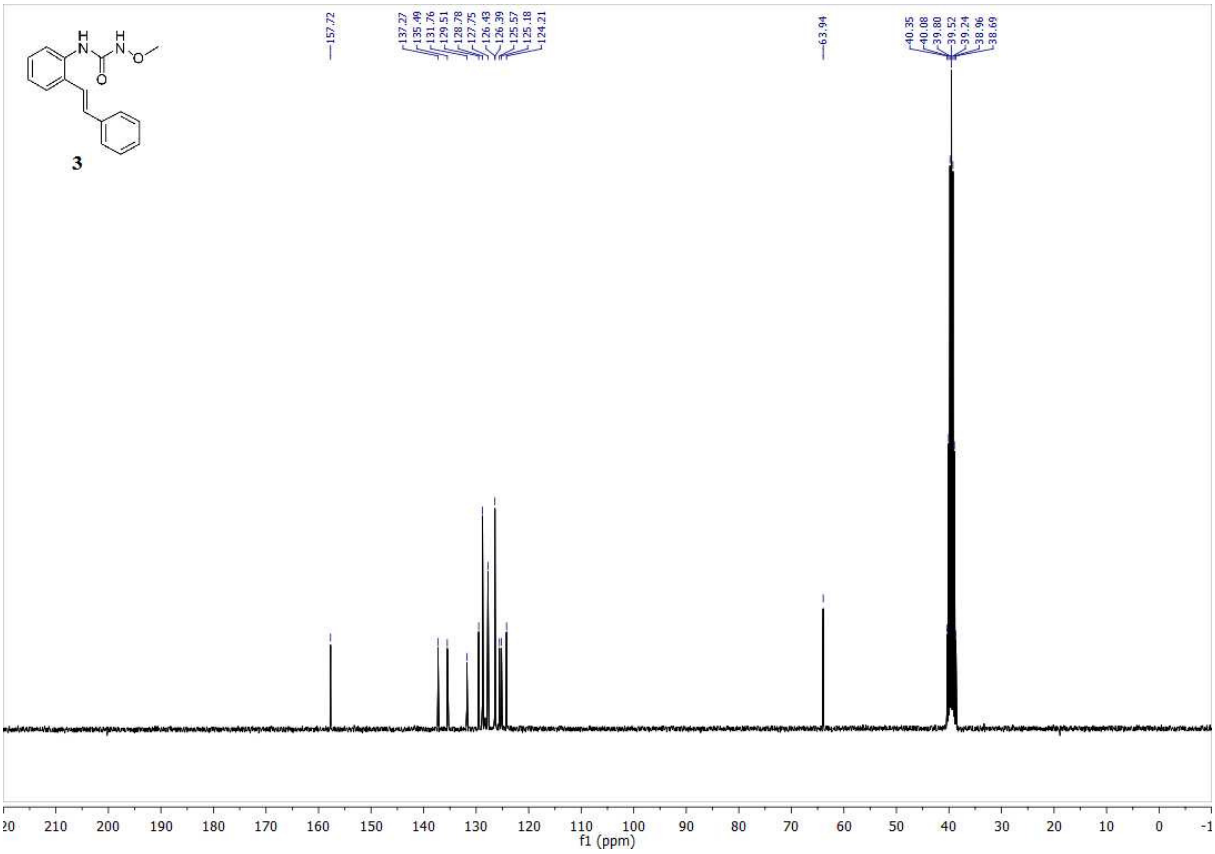

Br
H
N
H
N
O
O
2s
8.28
8.28
8.26
8.26
8.25
8.23
8.23
8.00
7.55
7.54
7.54
7.52
7.52
7.34
7.34
7.31
7.29
7.29
7.26
6.98
6.98
6.96
6.95
6.93
6.93
3.84
1.97
0.92
1.00
1.00
0.99
3.05
f1 (ppm)

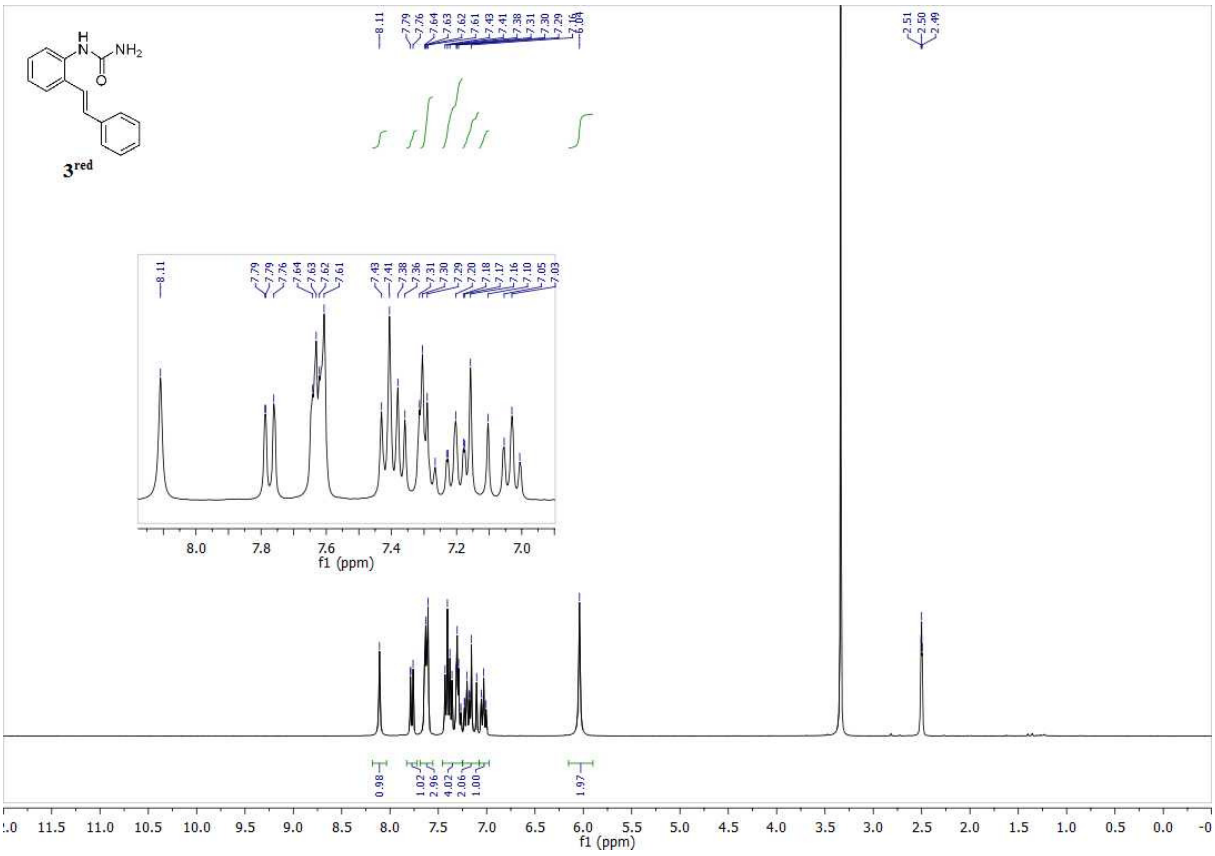

Br
H
N
H
N
O
O
2s
156.97
138.50
132.33
128.52
124.72
121.13
113.51
77.58
77.16
76.74
64.91
f1 (ppm)

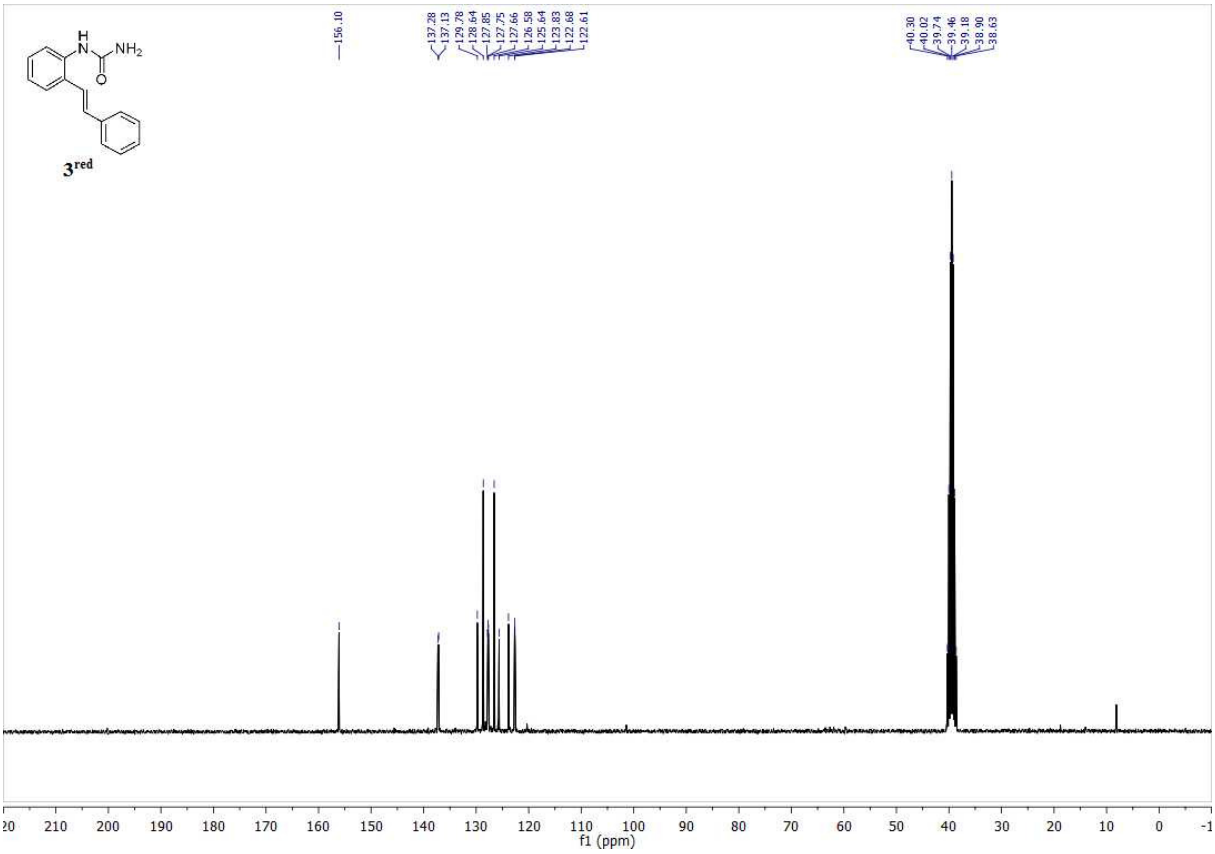

2t
f1 (ppm)

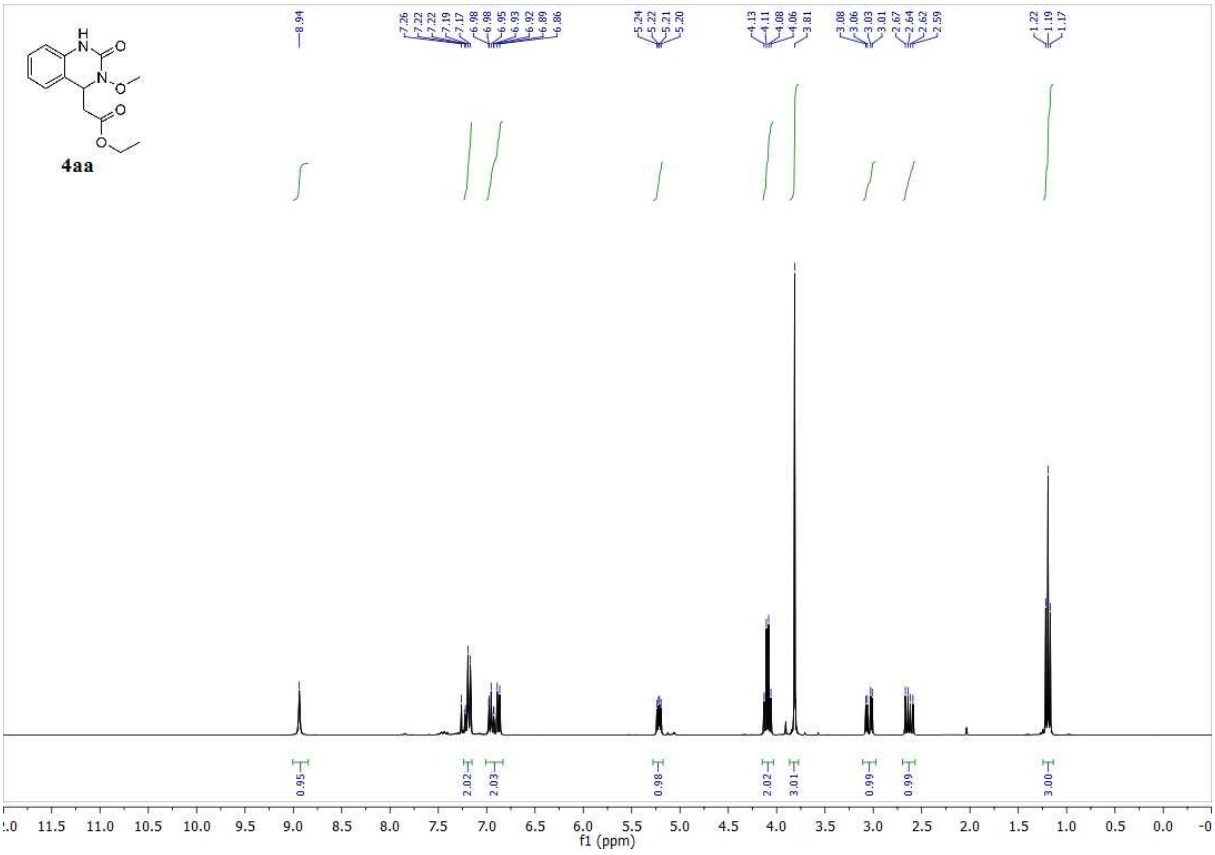

2t
f1 (ppm)

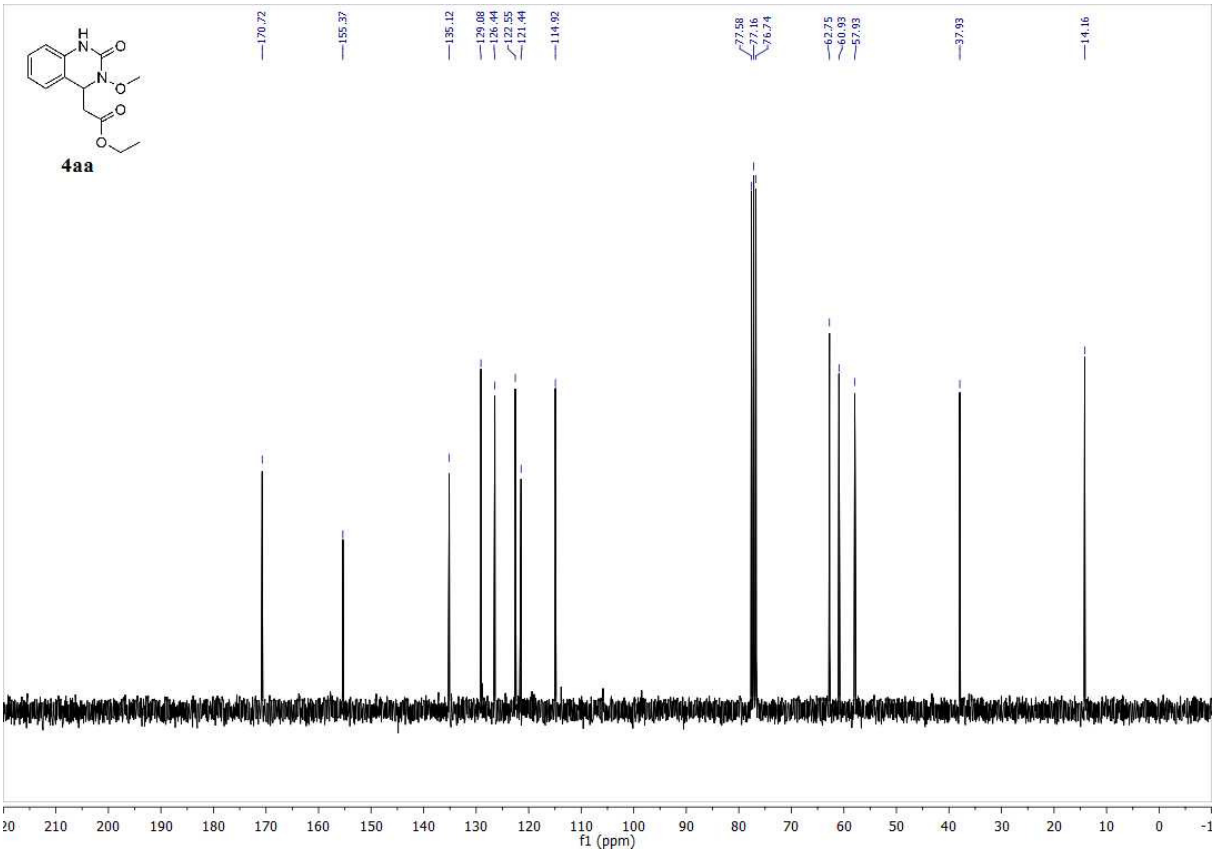

3
f1 (ppm)

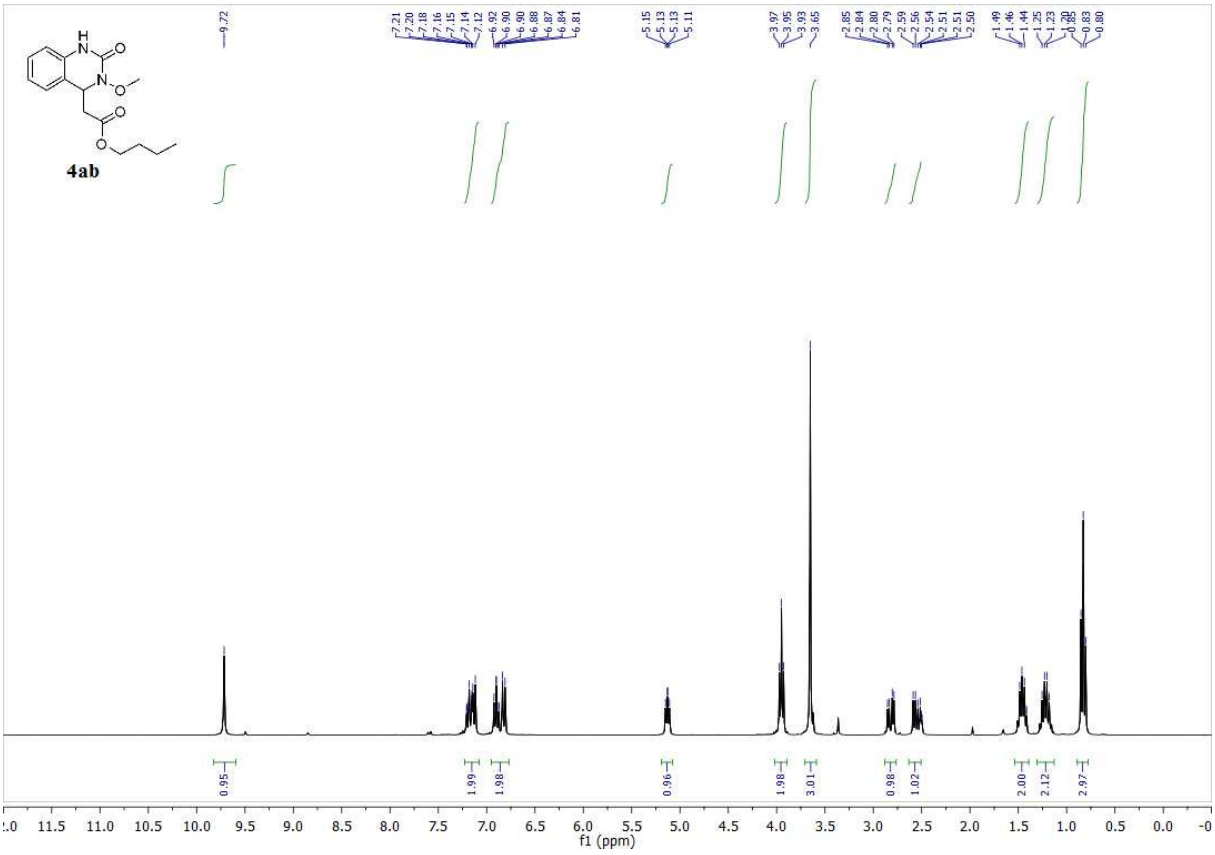

3
f1 (ppm)

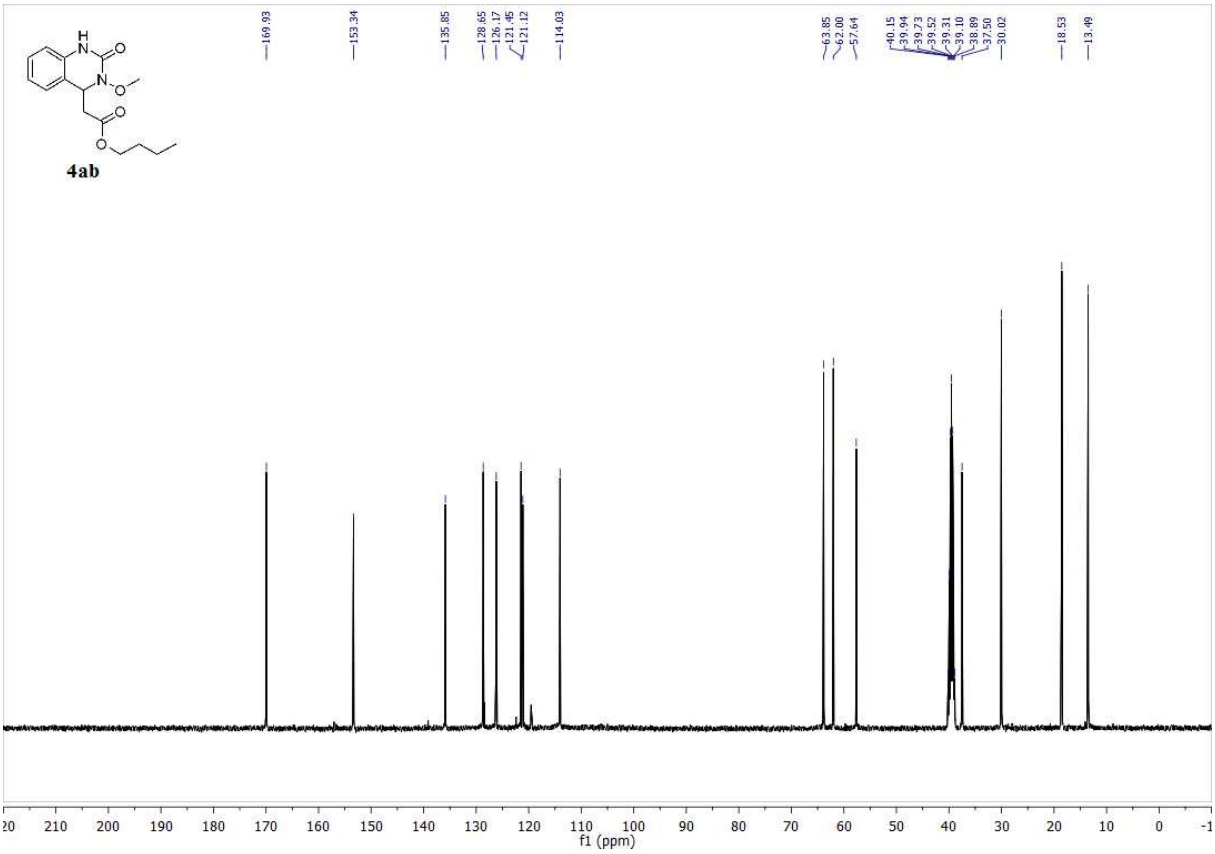

3red
f1 (ppm)

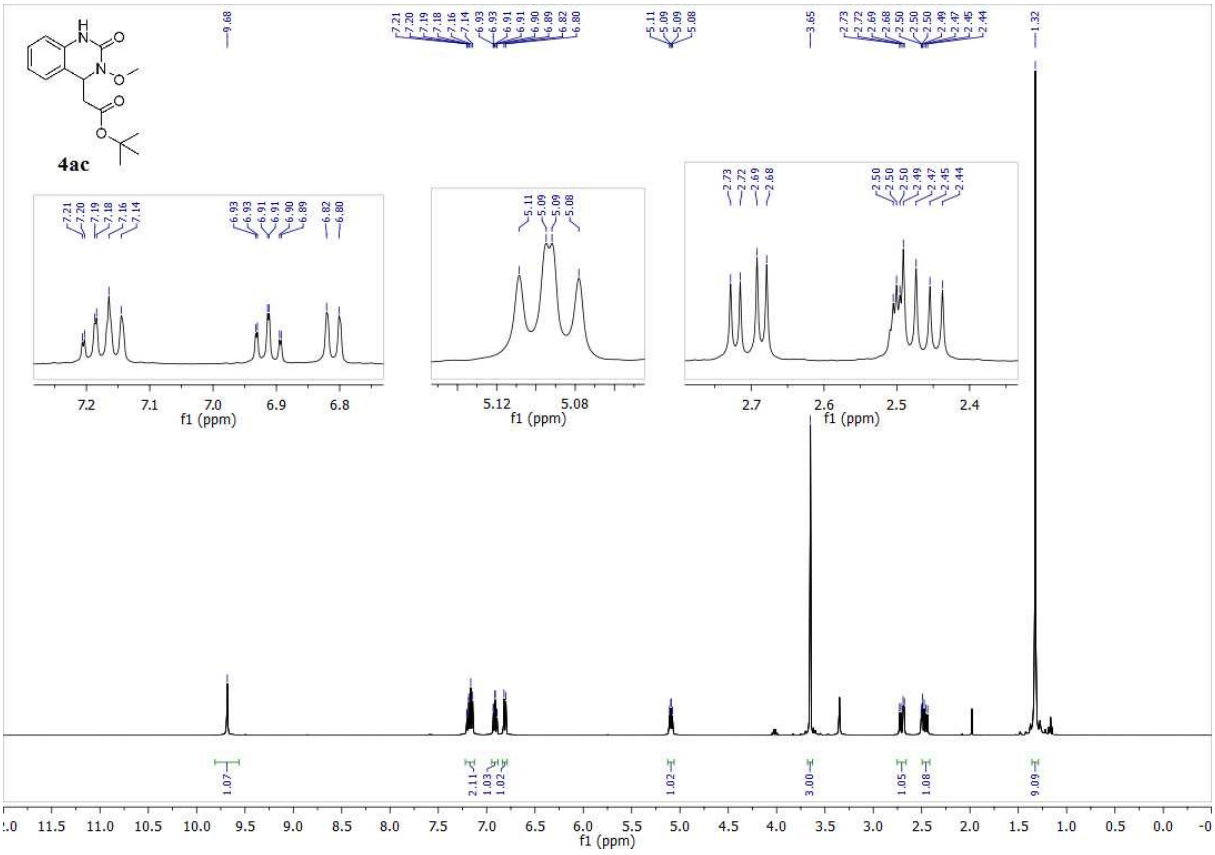

3red
f1 (ppm)

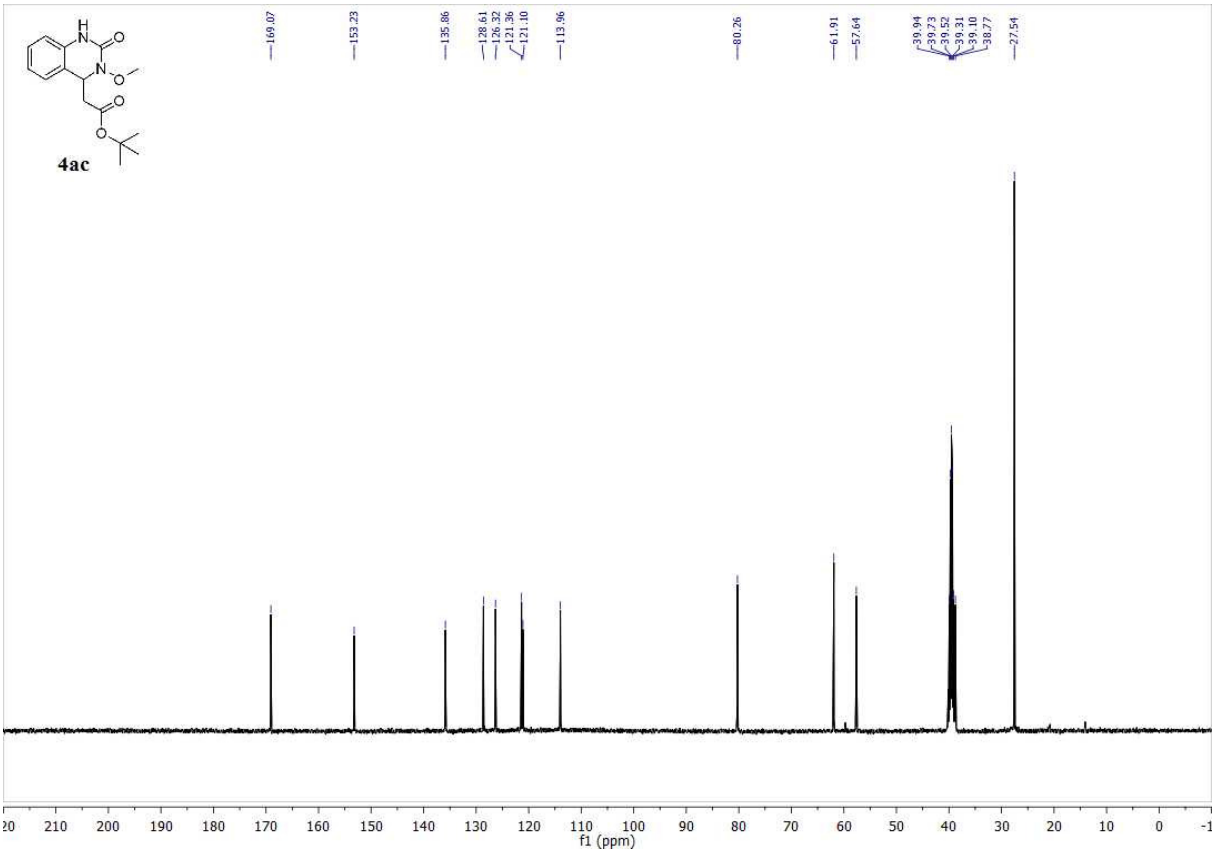

4aa
f1 (ppm)

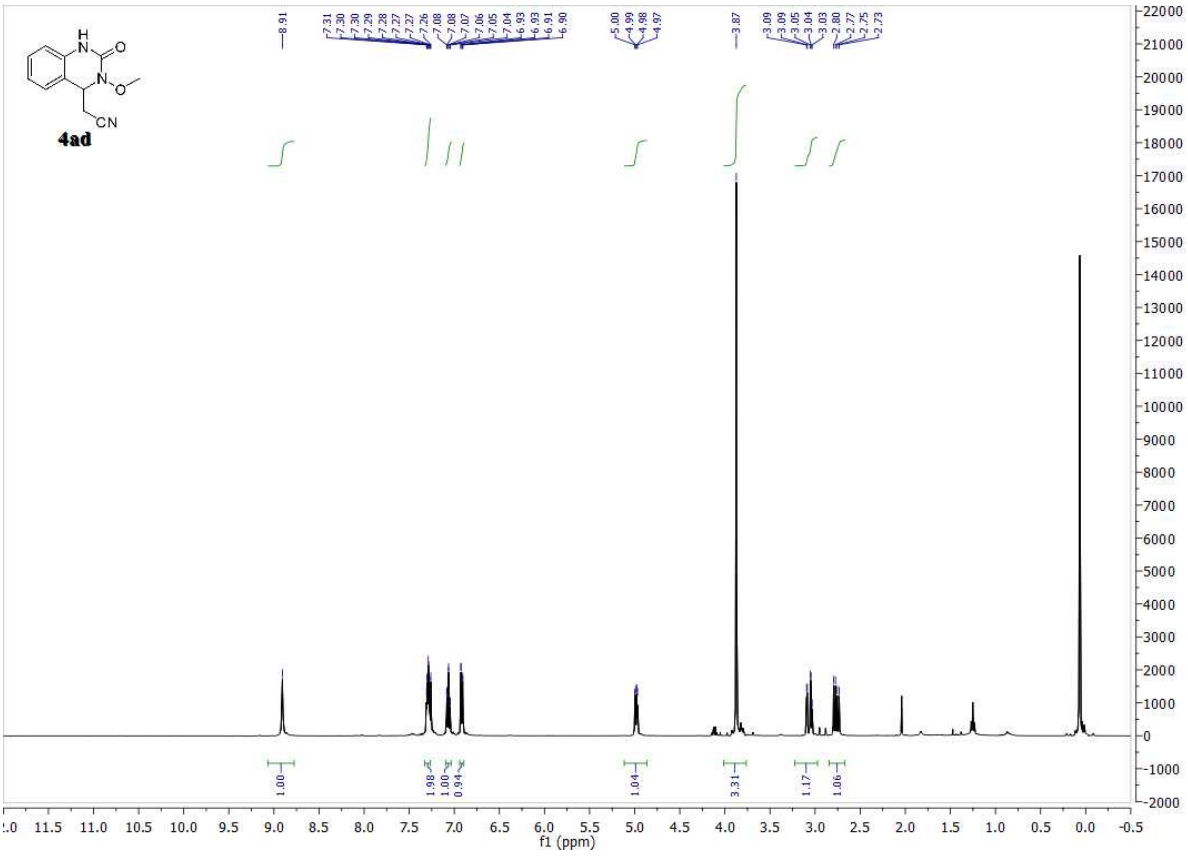

4aa
f1 (ppm)

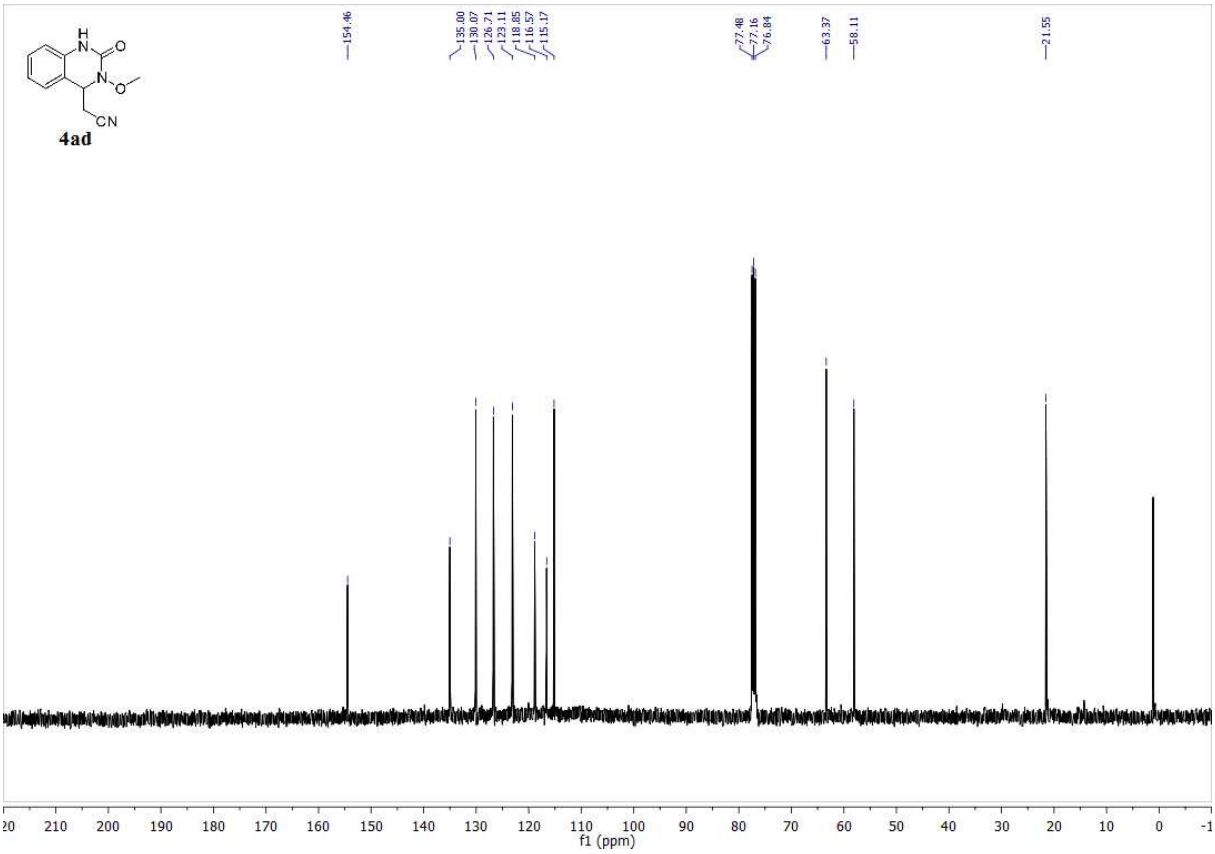

4ab
f1 (ppm)

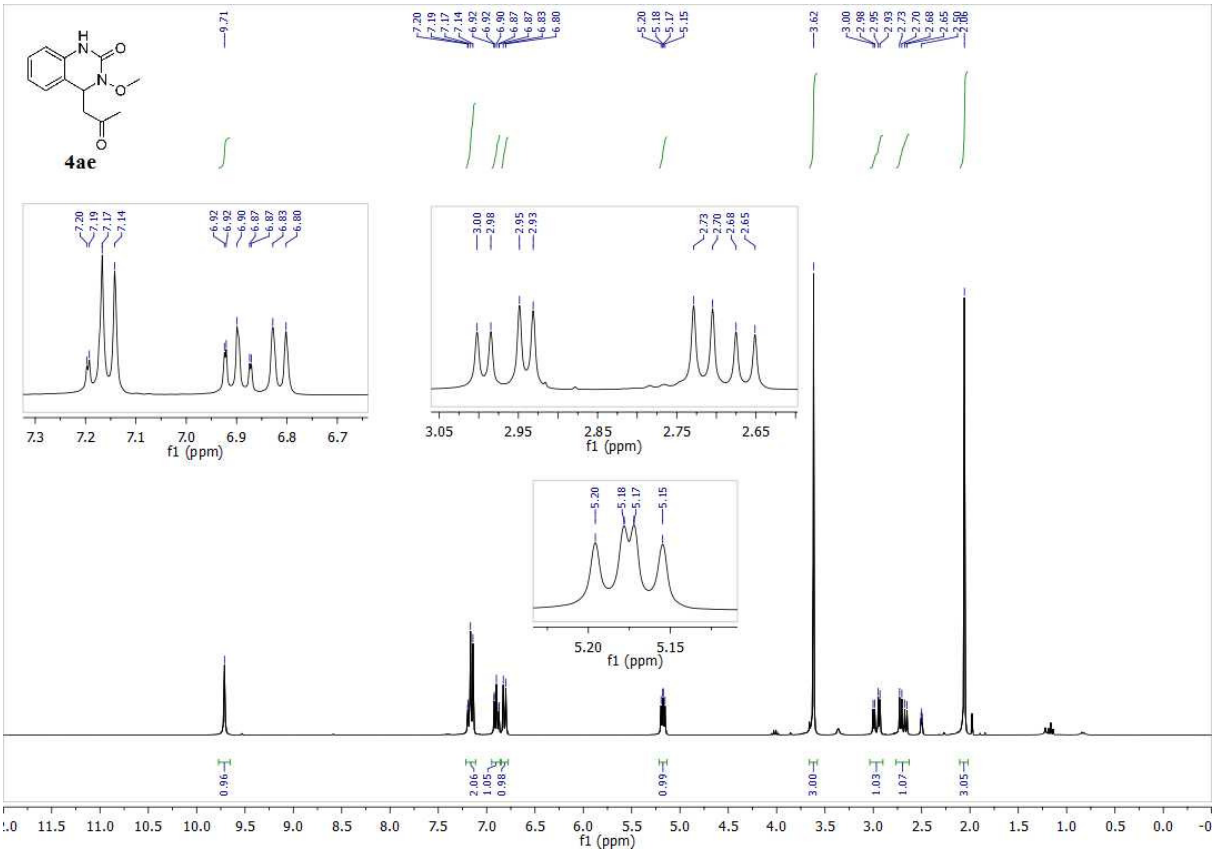

4ab
f1 (ppm)

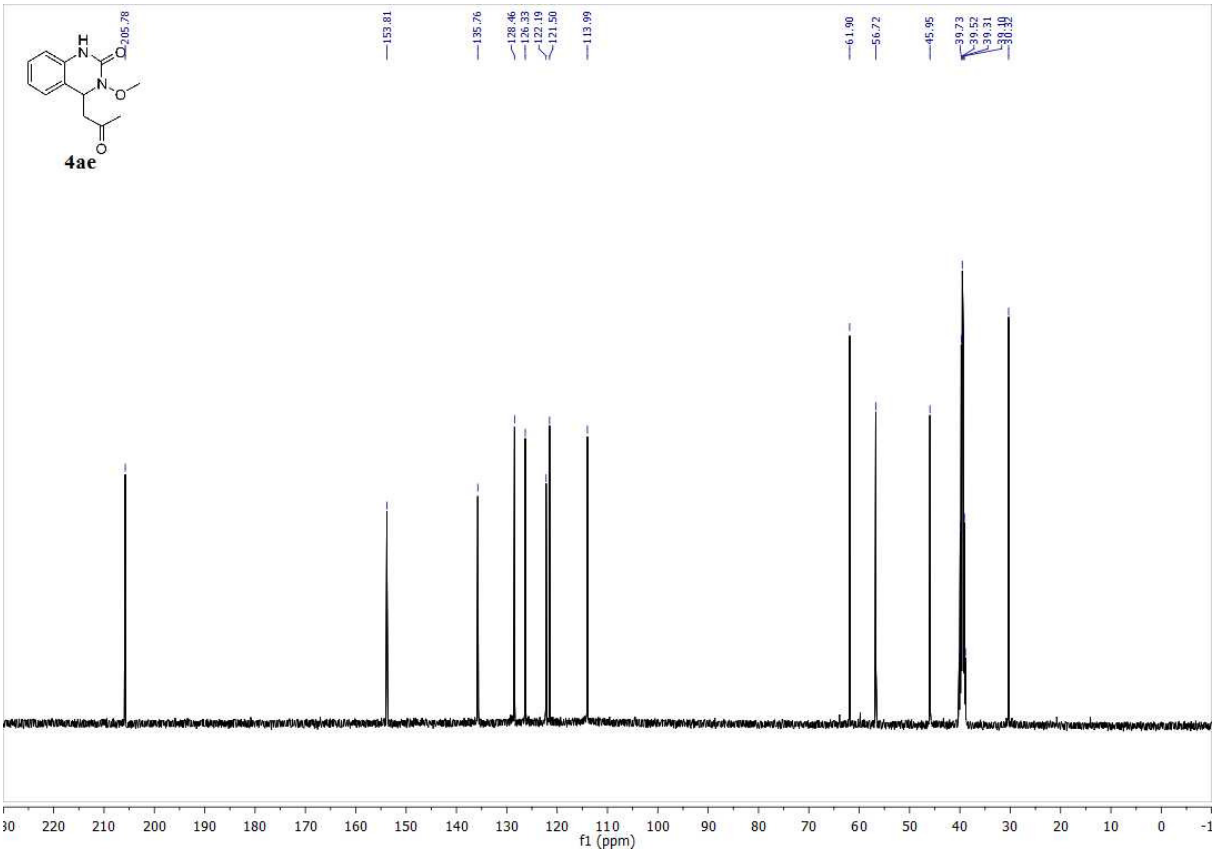

4ac
f1 (ppm)

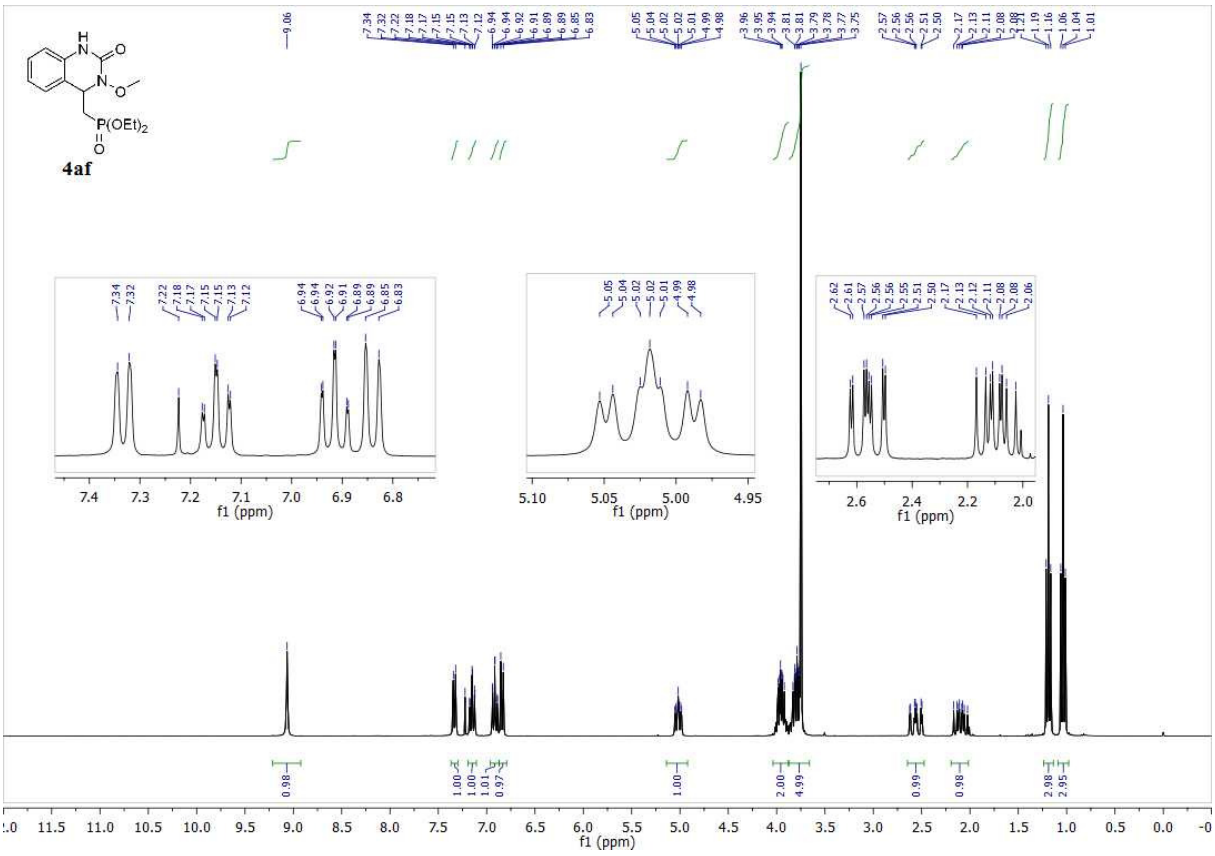

4ac
f1 (ppm)

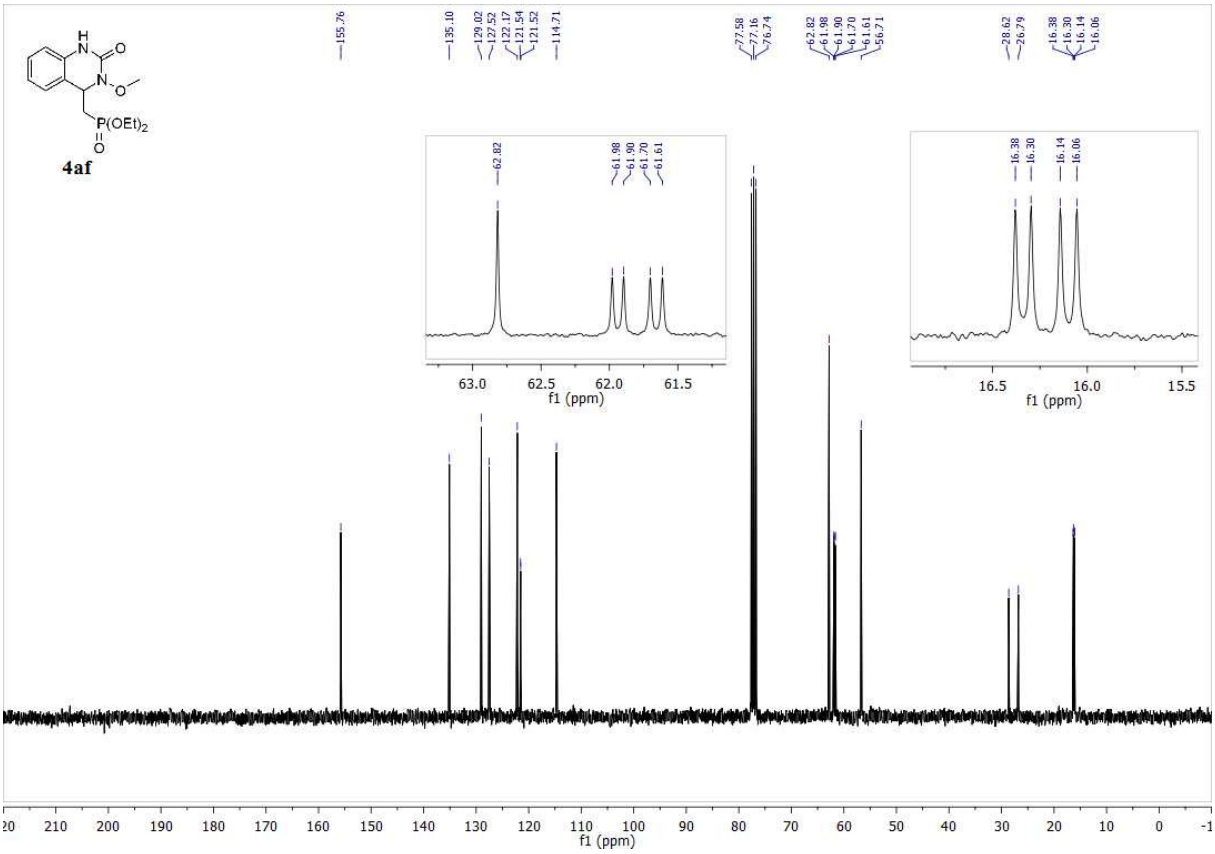

4ad
f1 (ppm)

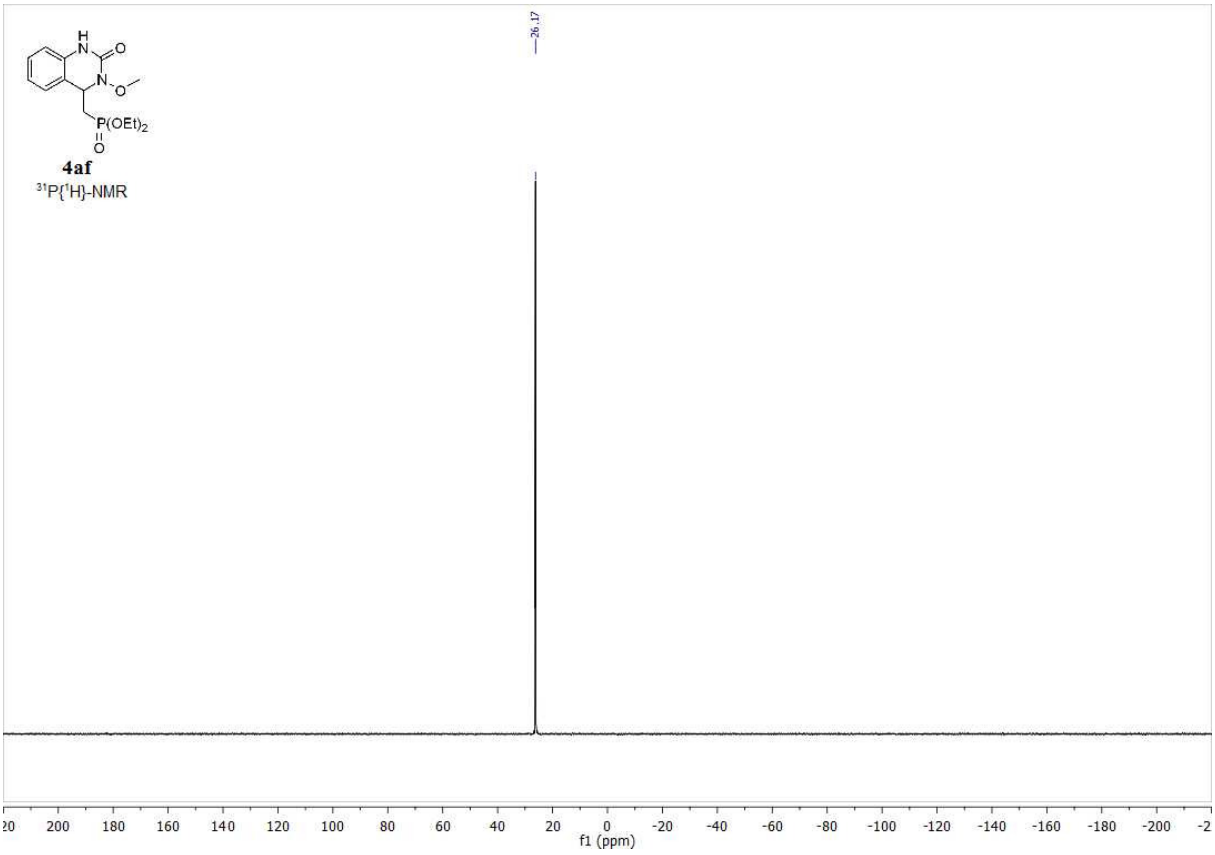

4ad
f1 (ppm)

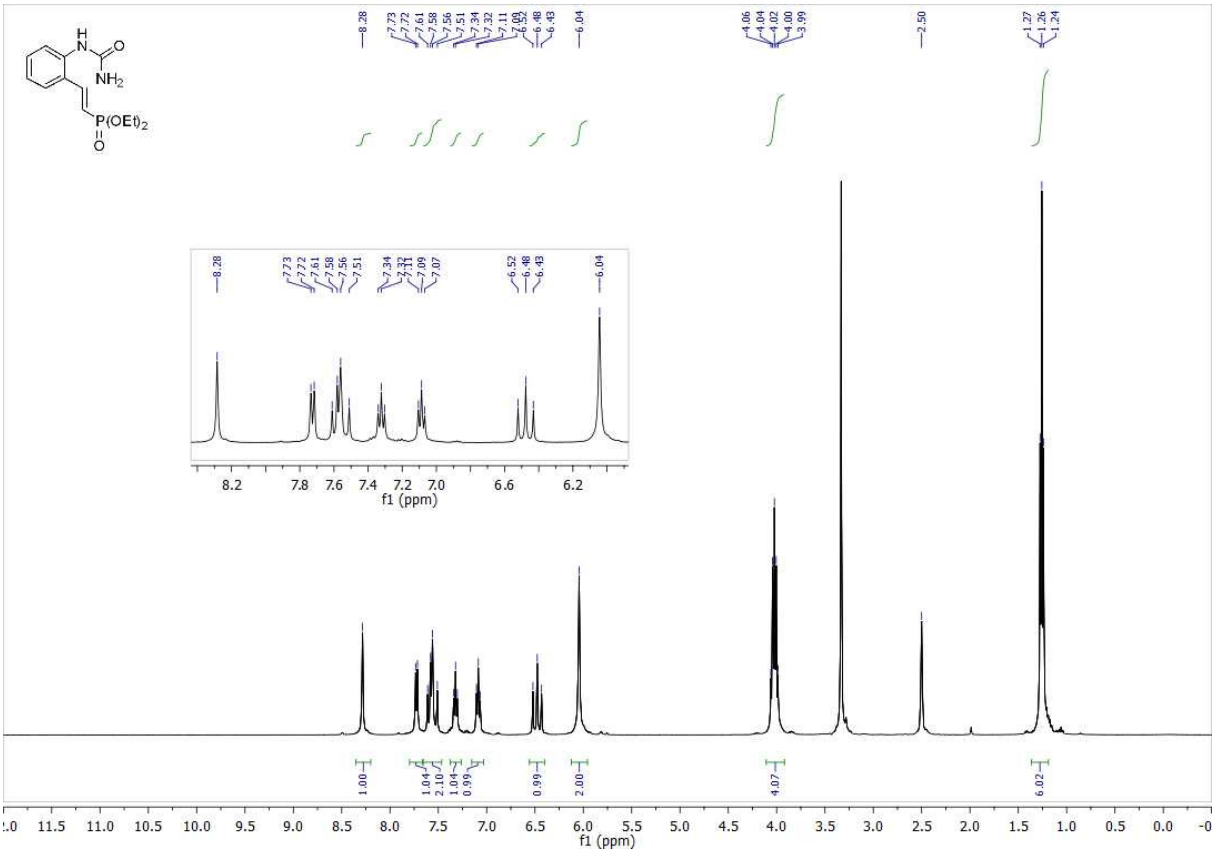

4ae
f1 (ppm)

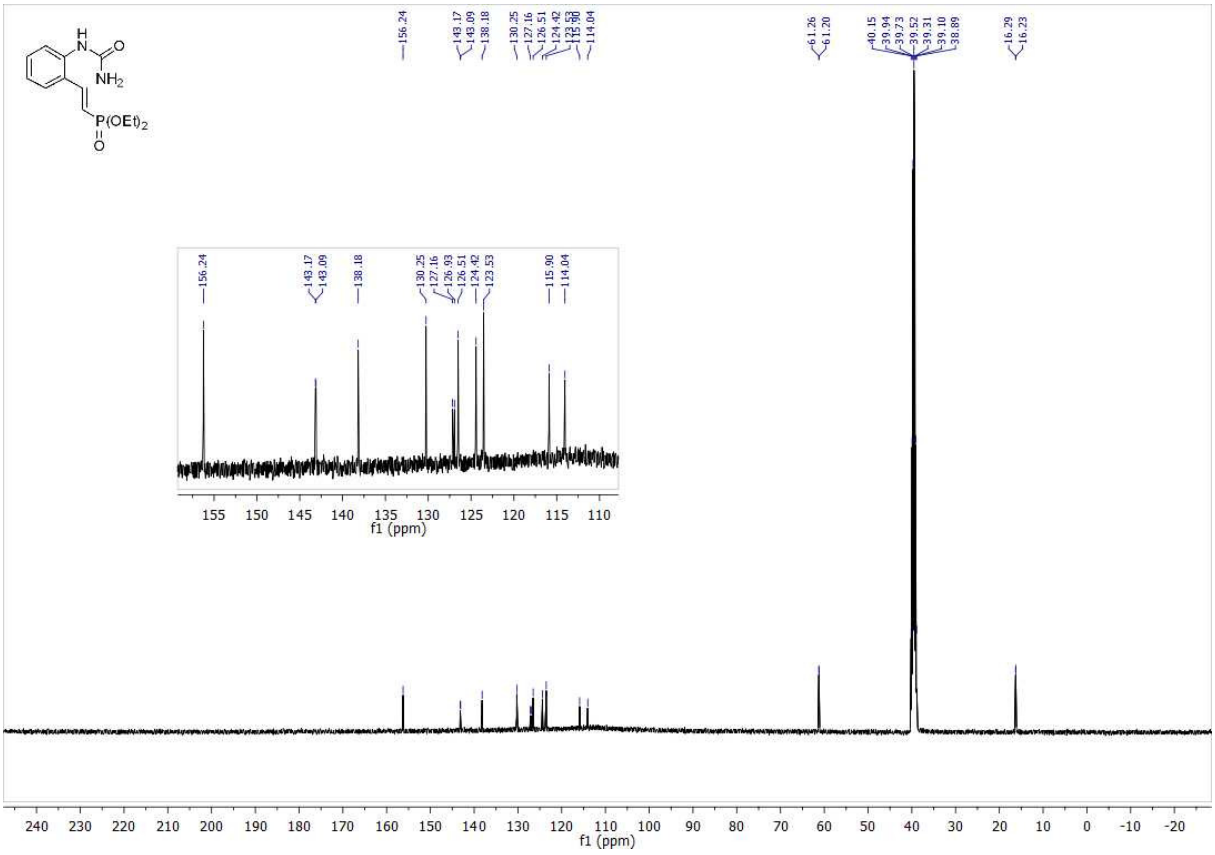

4ae
f1 (ppm)

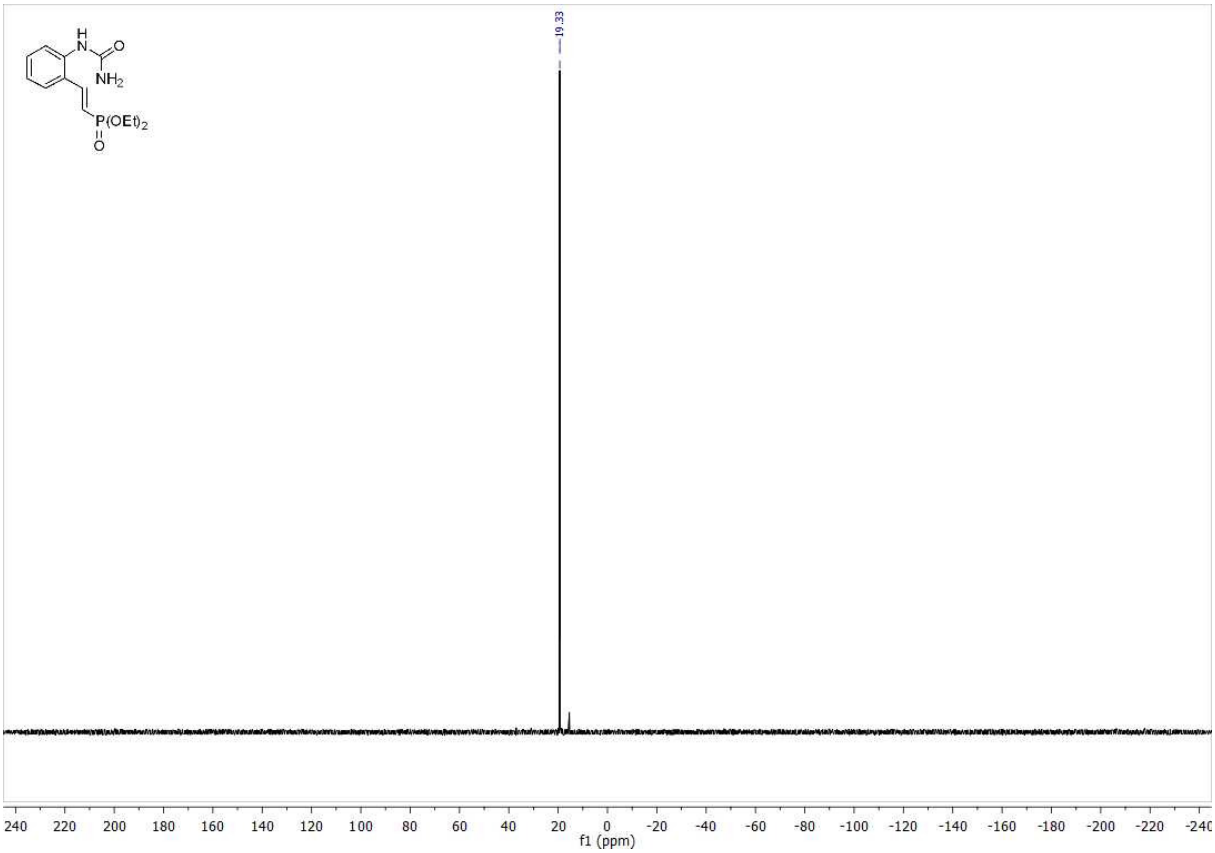

4af
f1 (ppm)

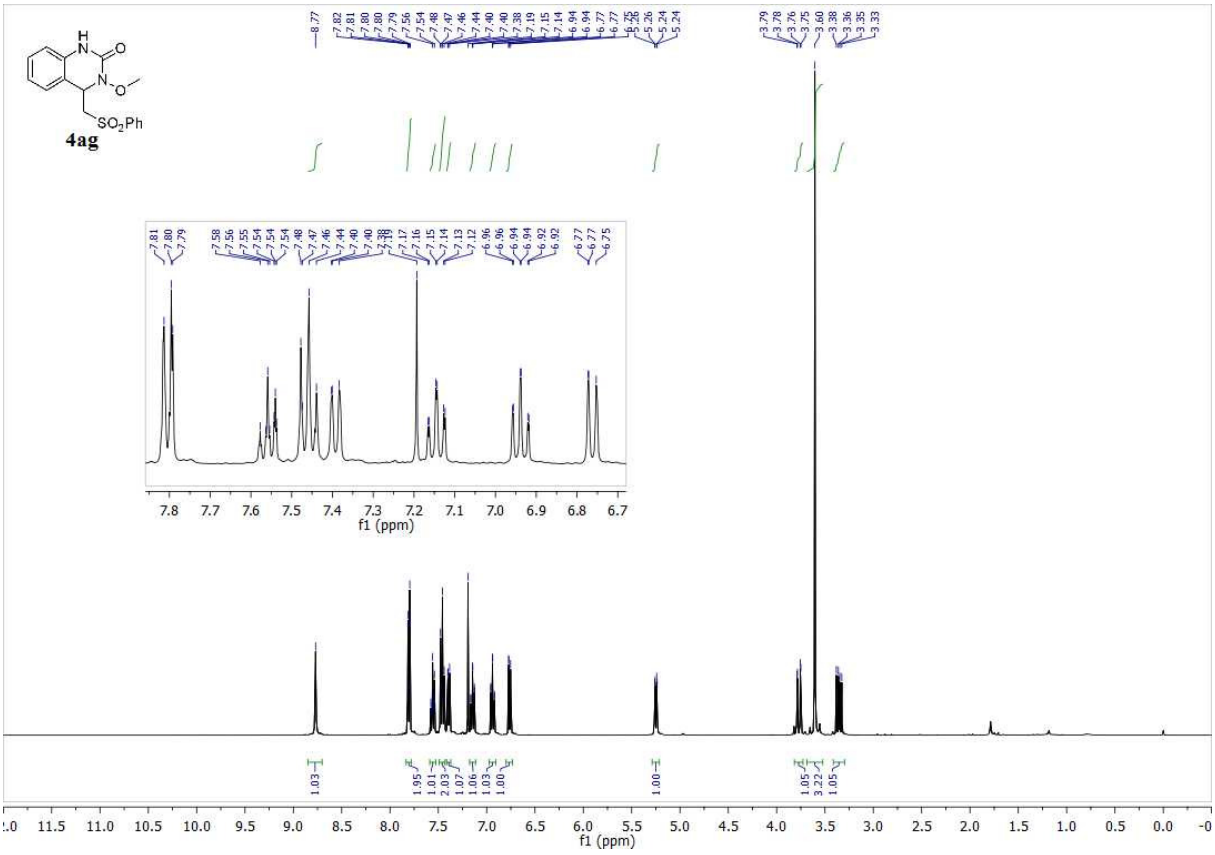

4af
f1 (ppm)

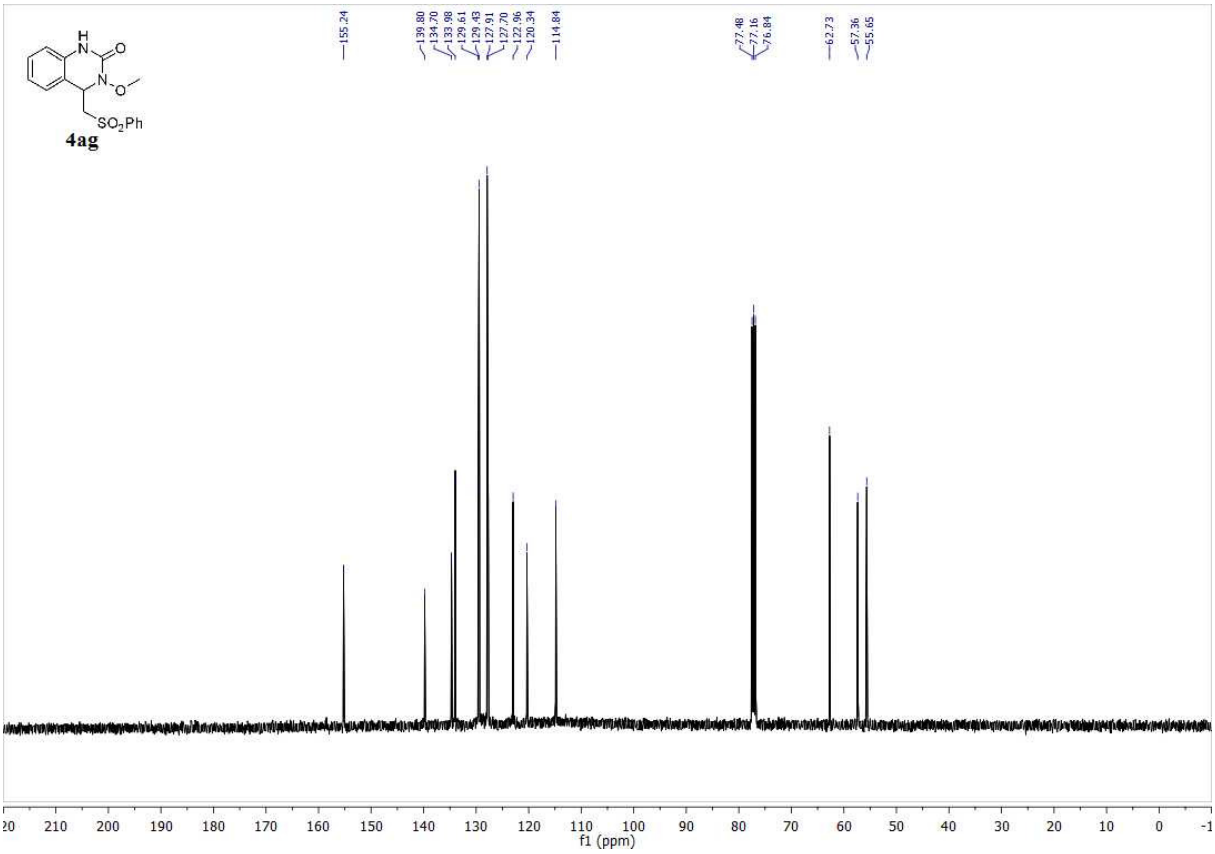

4af
$^{31}P\{^{1}H\}$-NMR
26.17
f1 (ppm)

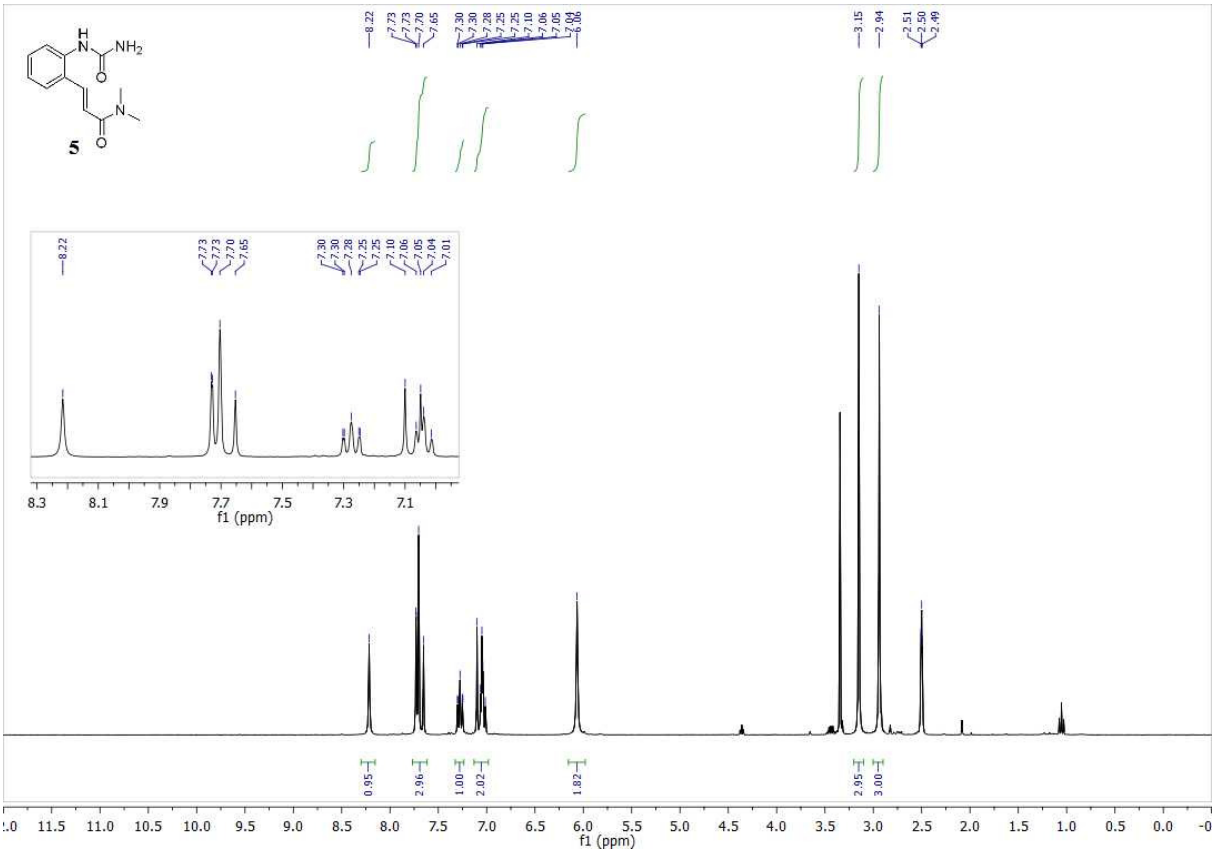

8.28
7.73
7.72
7.61
7.58
7.56
7.51
7.34
7.32
7.11
7.09
7.07
6.52
6.48
6.43
6.04
4.06
4.04
4.02
4.00
3.99
2.50
1.27
1.26
1.24
1.00
1.04
2.10
1.04
0.99
0.99
2.00
4.07
6.02
f1 (ppm)

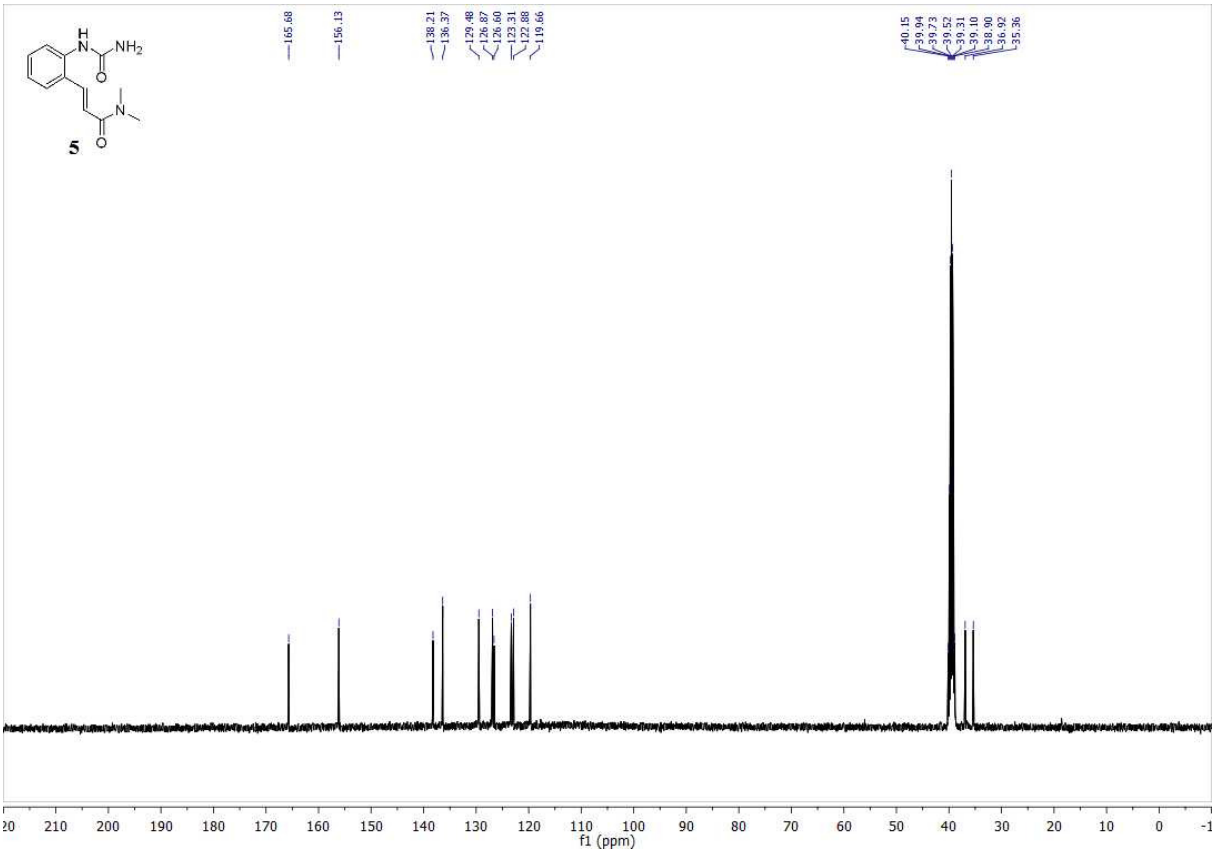

H
N
O
NH2
P(OEt)2
O
156.24
143.17
143.09
138.18
130.25
127.16
126.51
124.42
123.53
115.90
114.04
61.26
61.20
40.15
39.94
39.73
39.52
39.31
39.10
38.89
16.29
16.23
155 150 145 140 135 130 125 120 115 110
f1 (ppm)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

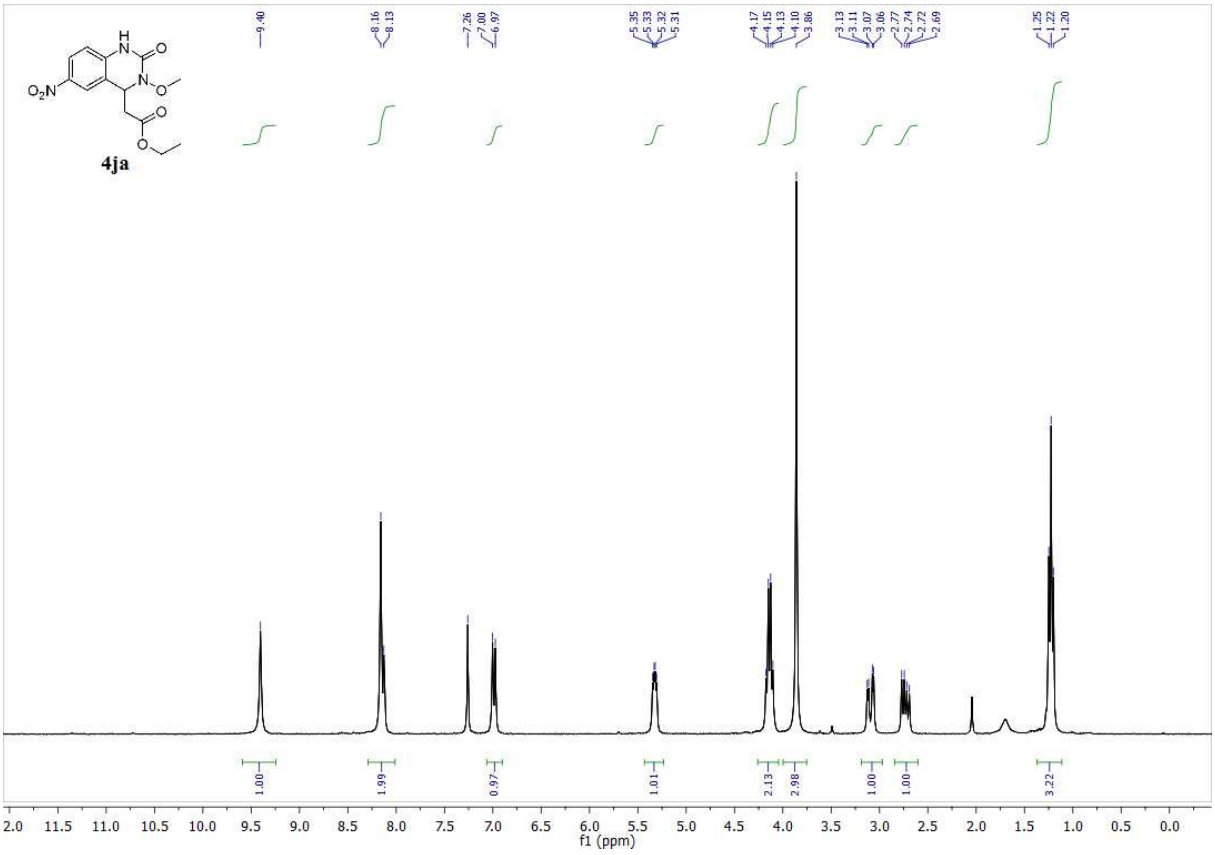

H
N
O
NH2
P(OEt)2
O
19.33
240 220 200 180 160 140 120 100 80 60 40 20 0 -20 -40 -60 -80 -100 -120 -140 -160 -180 -200 -220 -240
f1 (ppm)

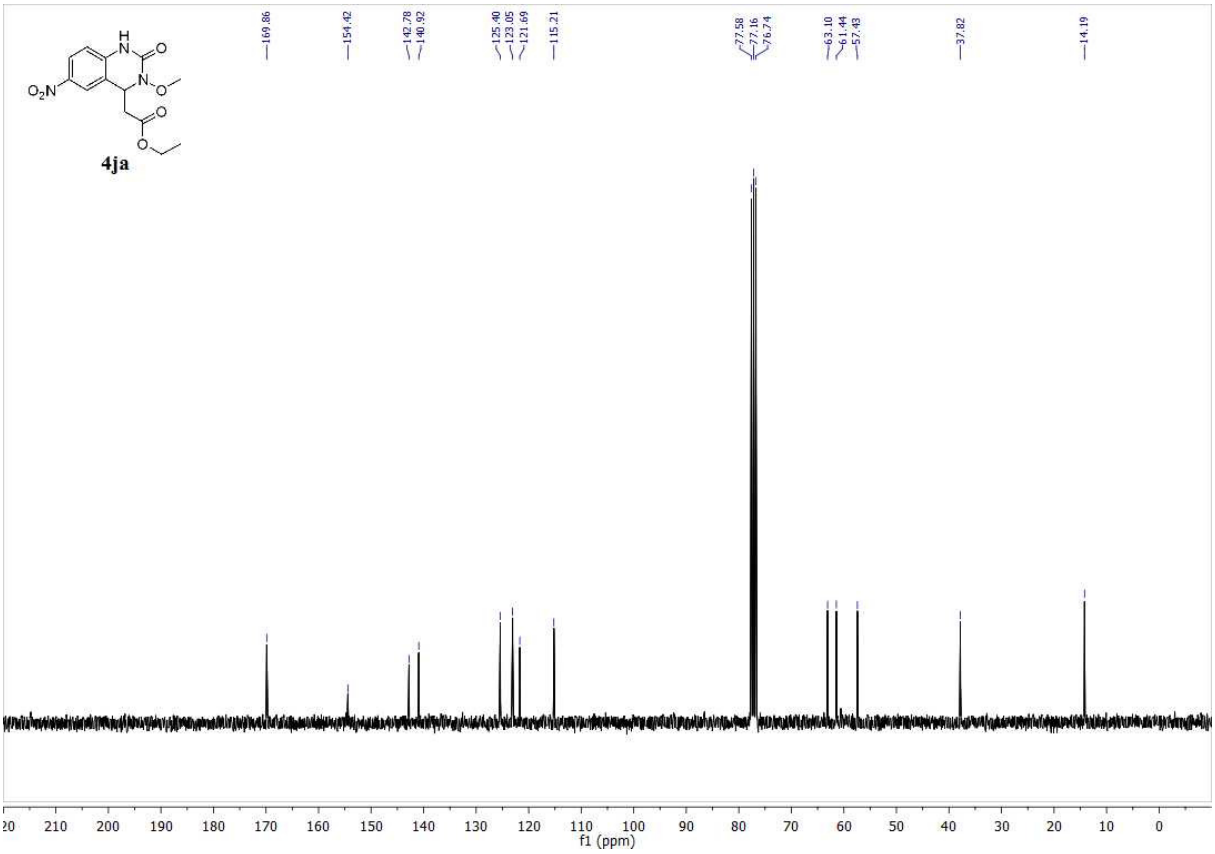

4ag
f1 (ppm)

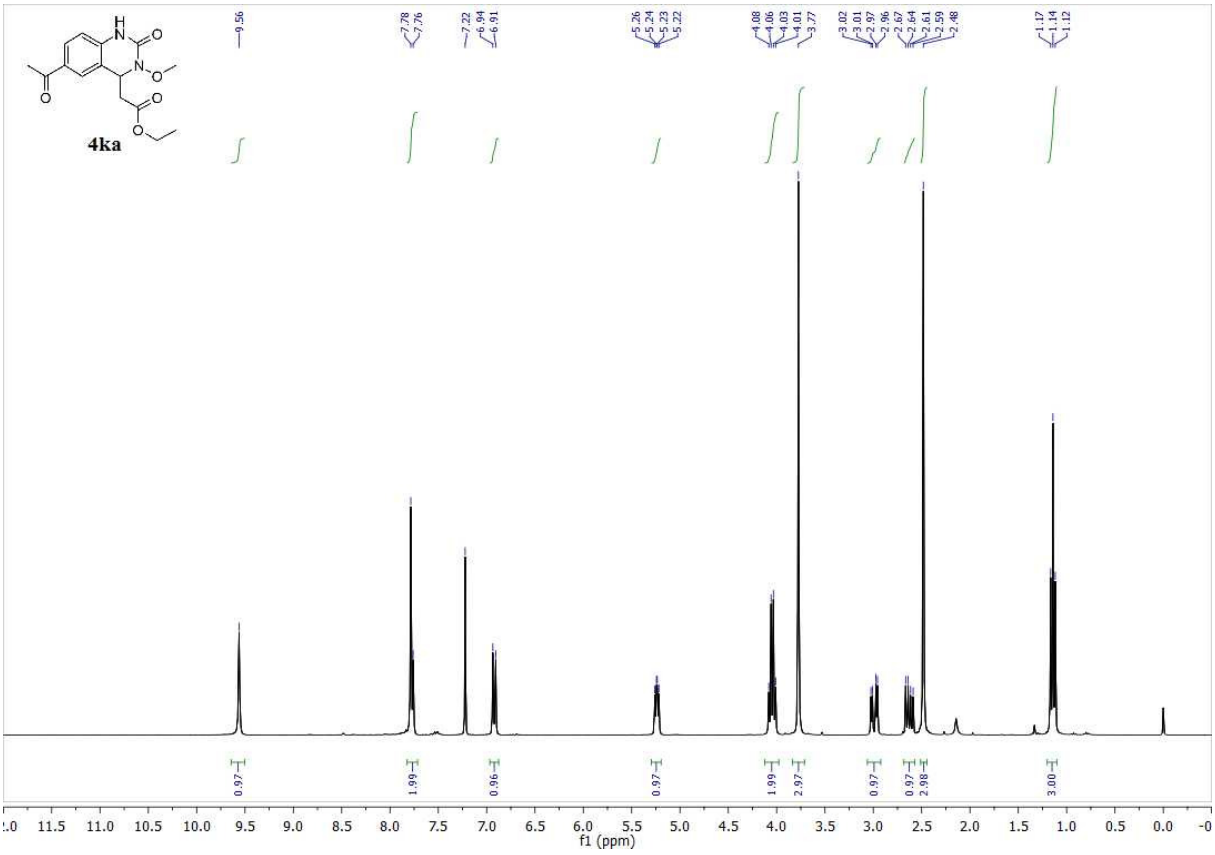

4ag
f1 (ppm)

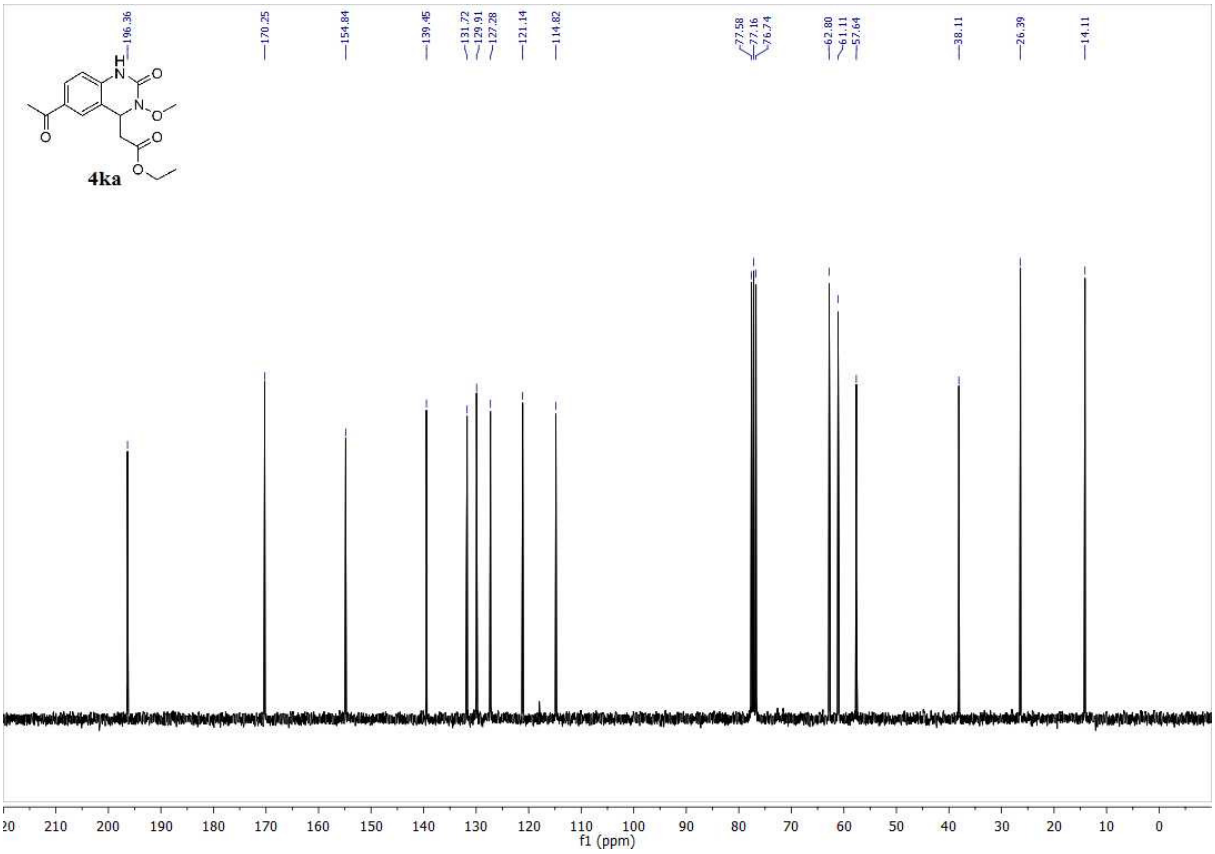

5
f1 (ppm)

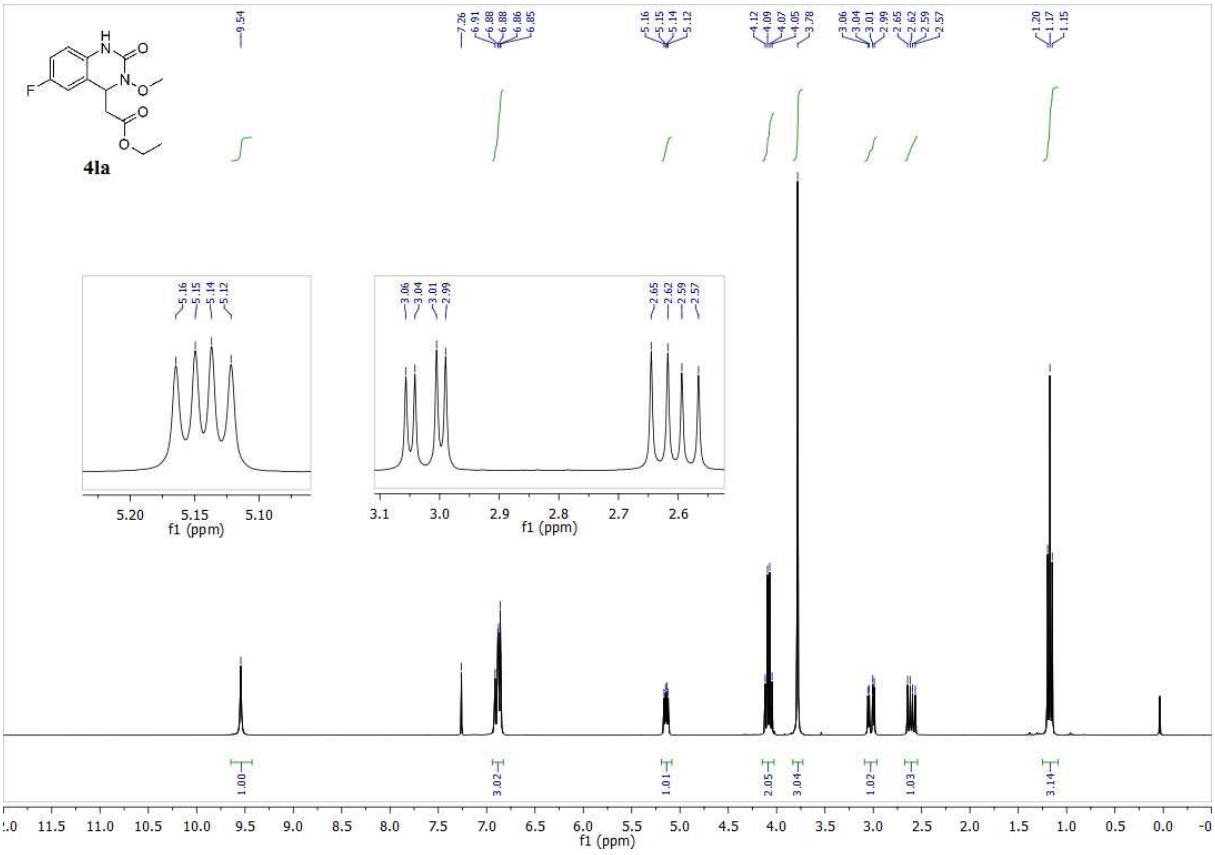

5
f1 (ppm)

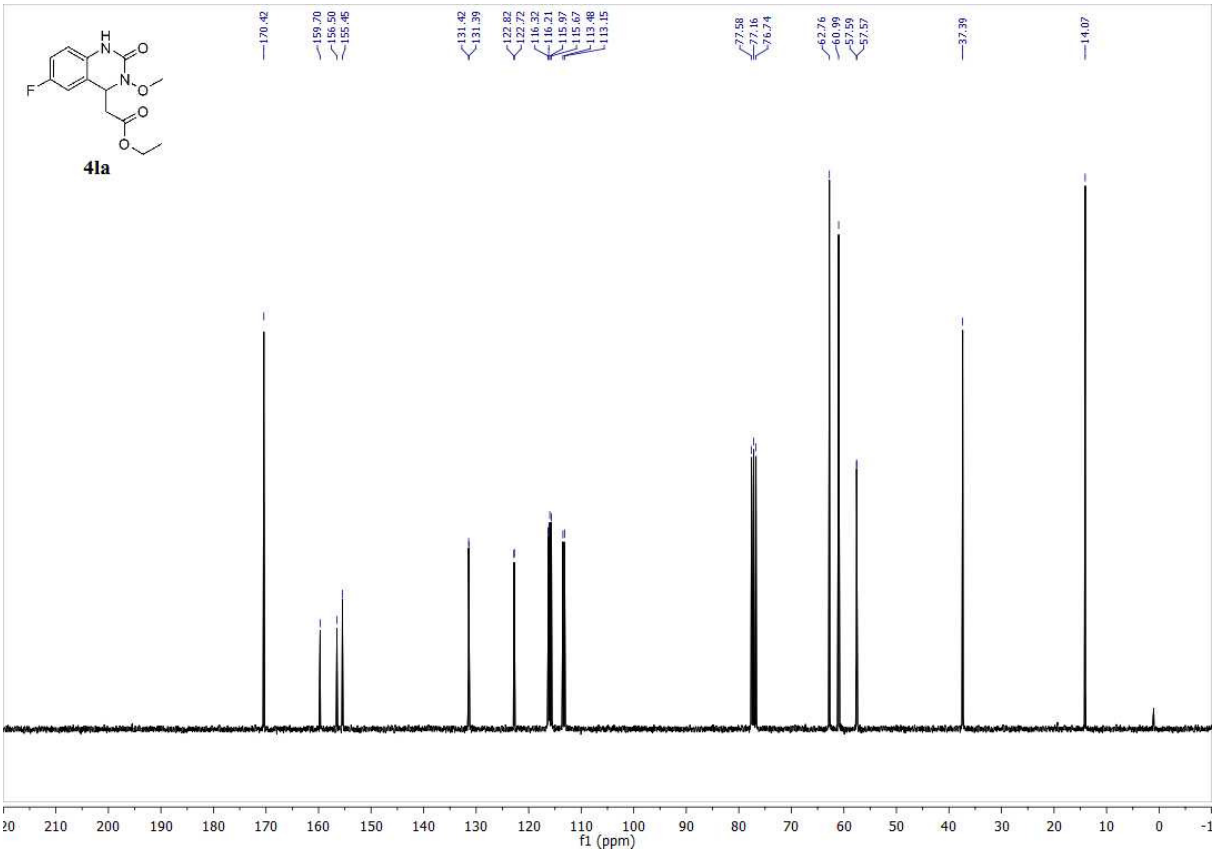

4ja
9.40
8.16
8.13
7.26
7.00
6.97
5.35
5.33
5.32
5.31
4.17
4.15
4.13
4.10
3.86
3.13
3.11
3.07
3.06
2.77
2.74
2.72
2.69
1.25
1.22
1.20
1.00
1.99
0.97
1.01
2.13
2.98
1.00
1.00
3.22
f1 (ppm)

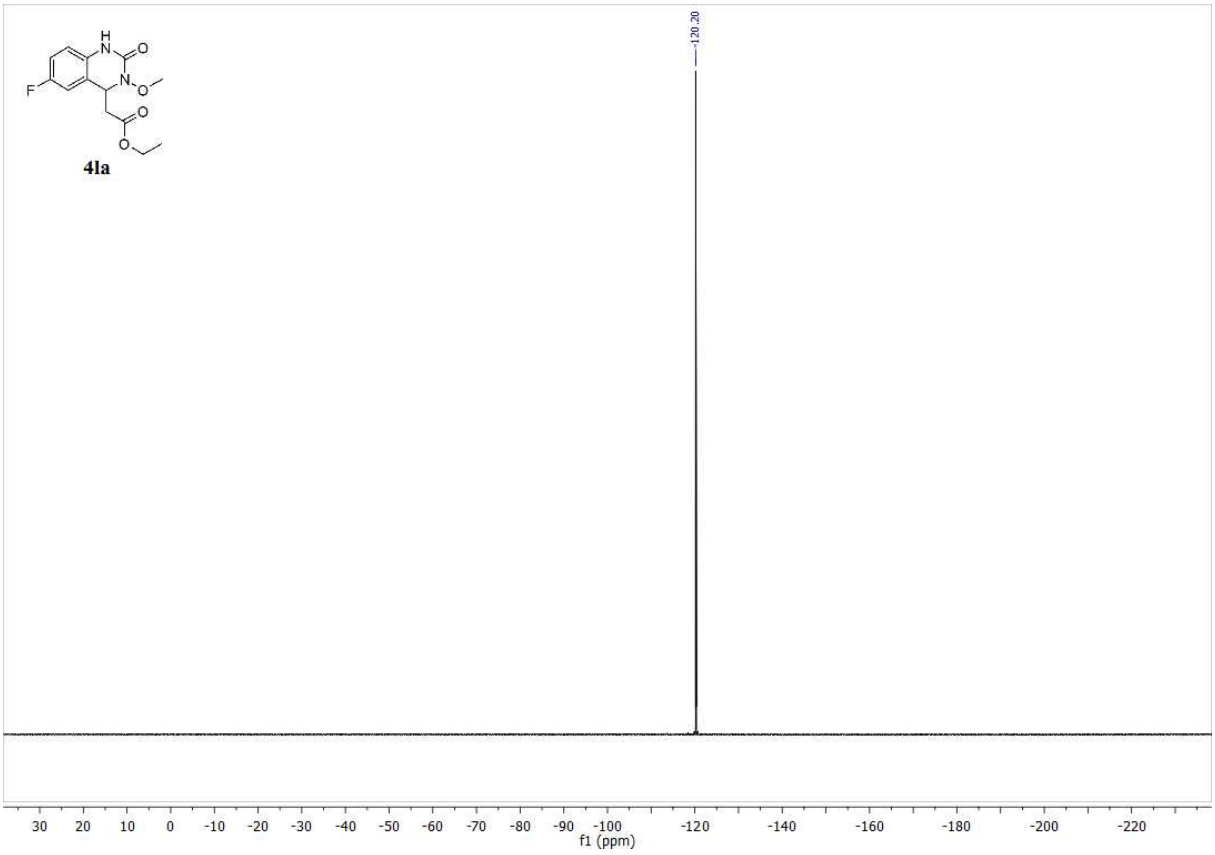

4ja
169.86
154.42
142.78
140.92
125.40
123.05
121.69
115.21
77.58
77.16
76.74
63.10
61.44
57.43
37.82
14.19
f1 (ppm)


4ka
9.56
7.78
7.76
7.22
6.94
6.91
5.26
5.24
5.23
5.22
4.08
4.06
4.03
4.01
3.77
3.02
3.01
2.97
2.96
2.67
2.64
2.61
2.59
2.48
1.17
1.14
1.12
0.97
1.99
0.96
0.97
1.99
2.97
0.97
0.97
2.98
3.00
f1 (ppm)

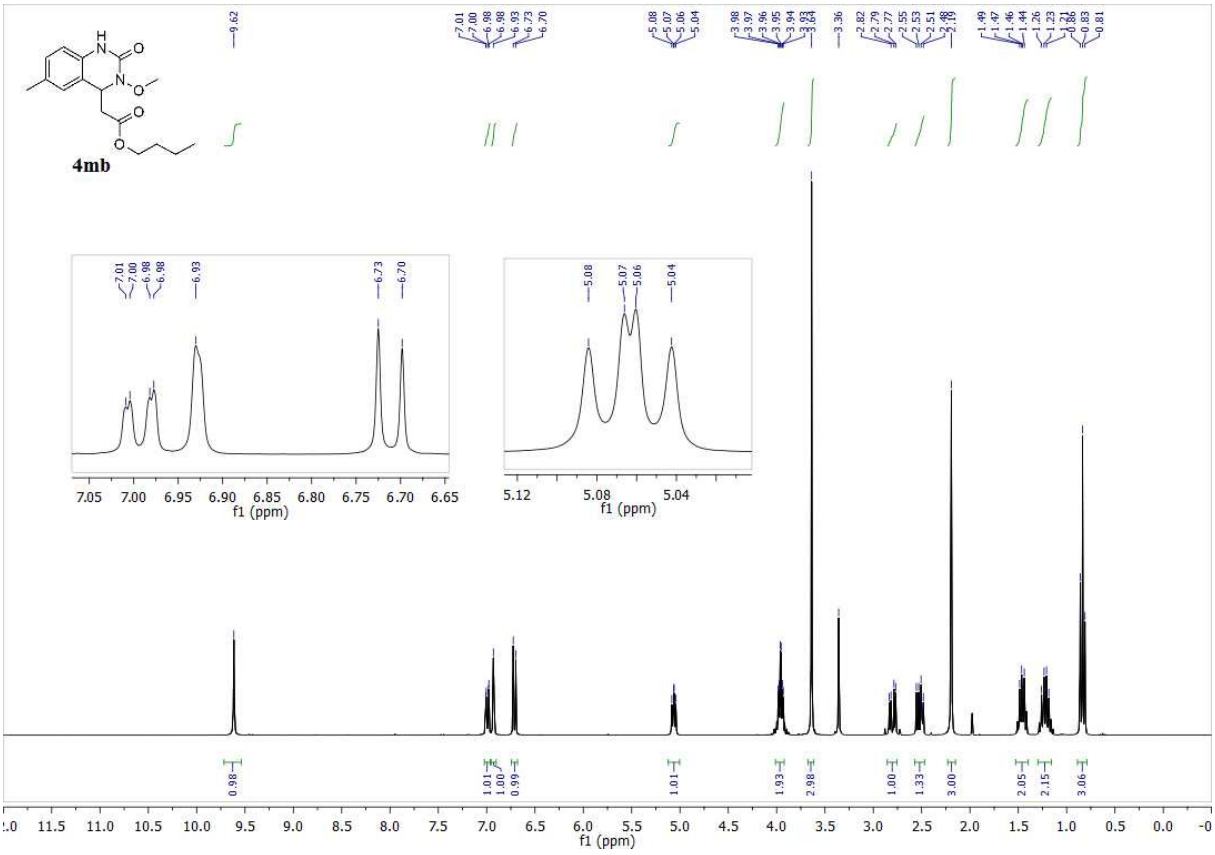

4ka
196.36
170.25
154.84
139.45
131.72
129.91
127.28
121.14
114.82
77.58
77.16
76.74
62.80
61.11
57.64
38.11
26.39
14.11
f1 (ppm)

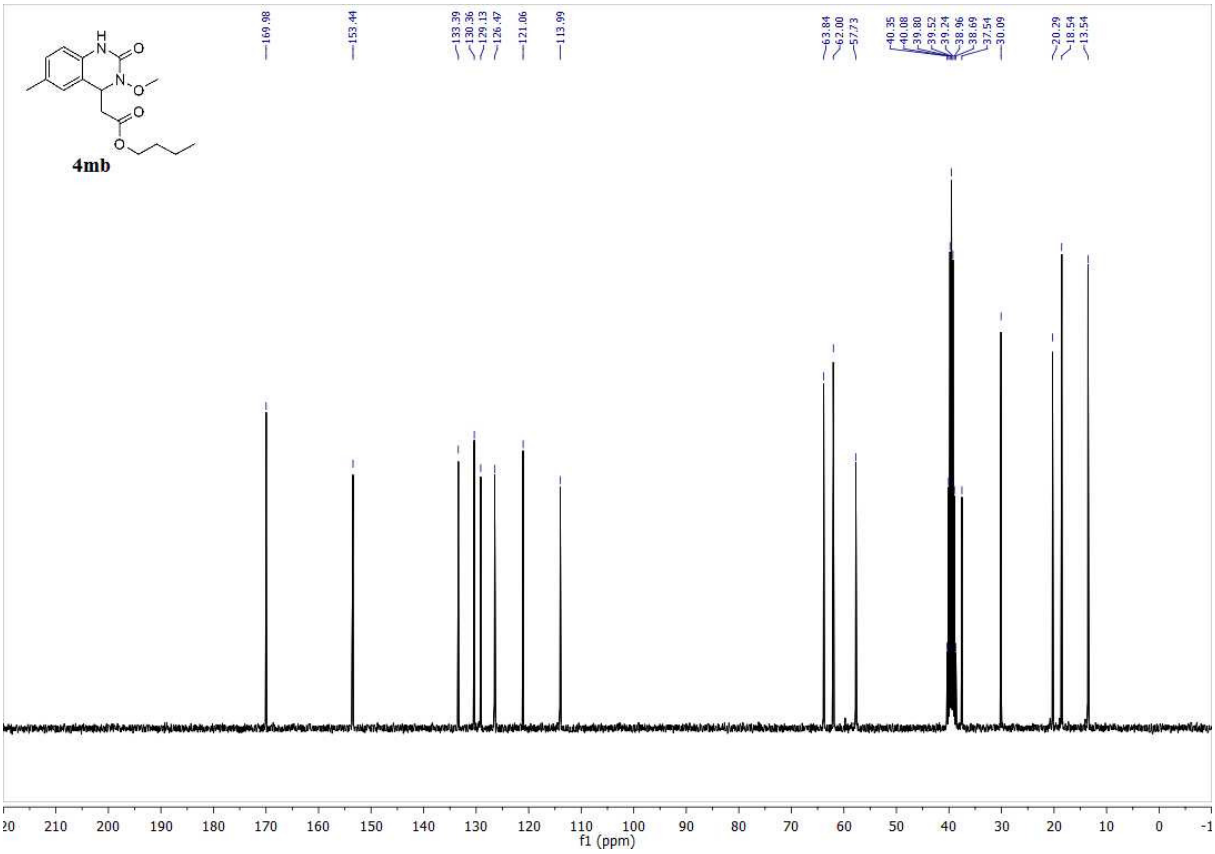

4la
f1 (ppm)

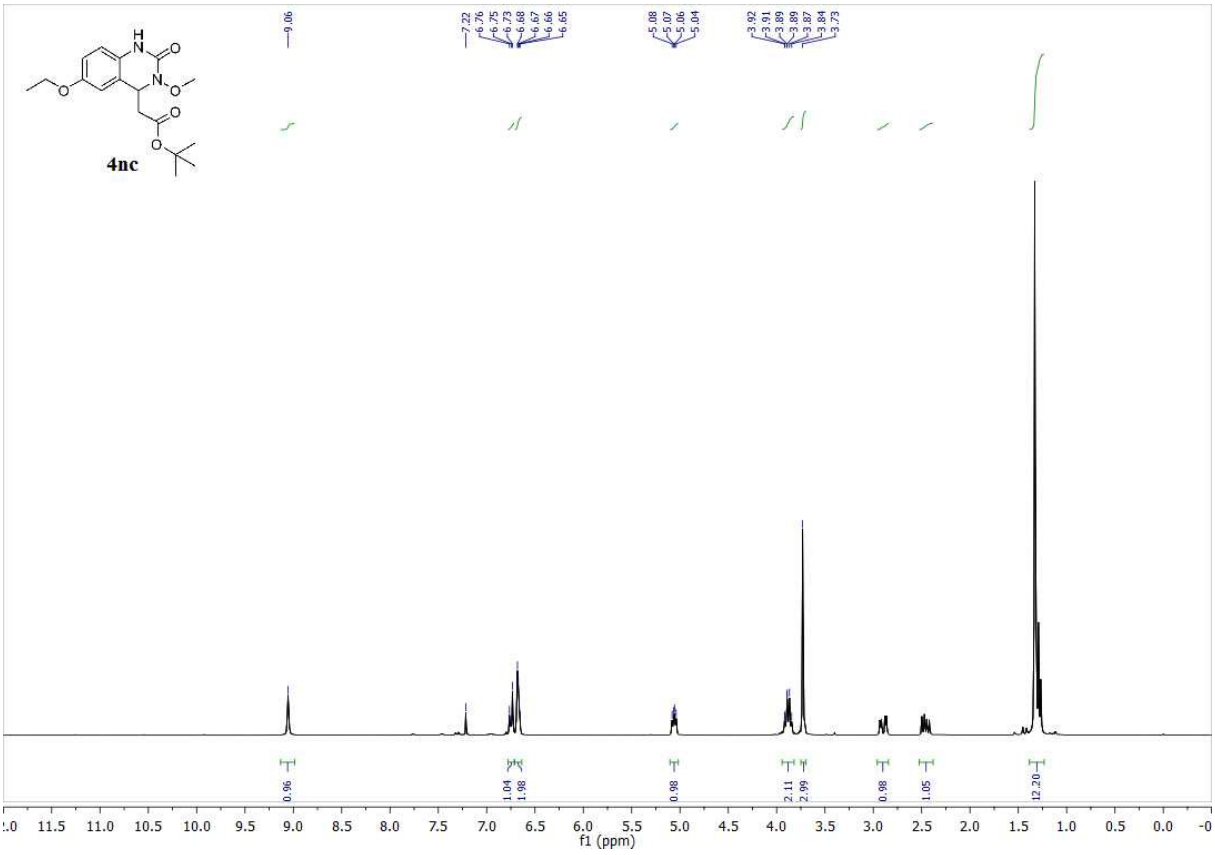

4la
f1 (ppm)

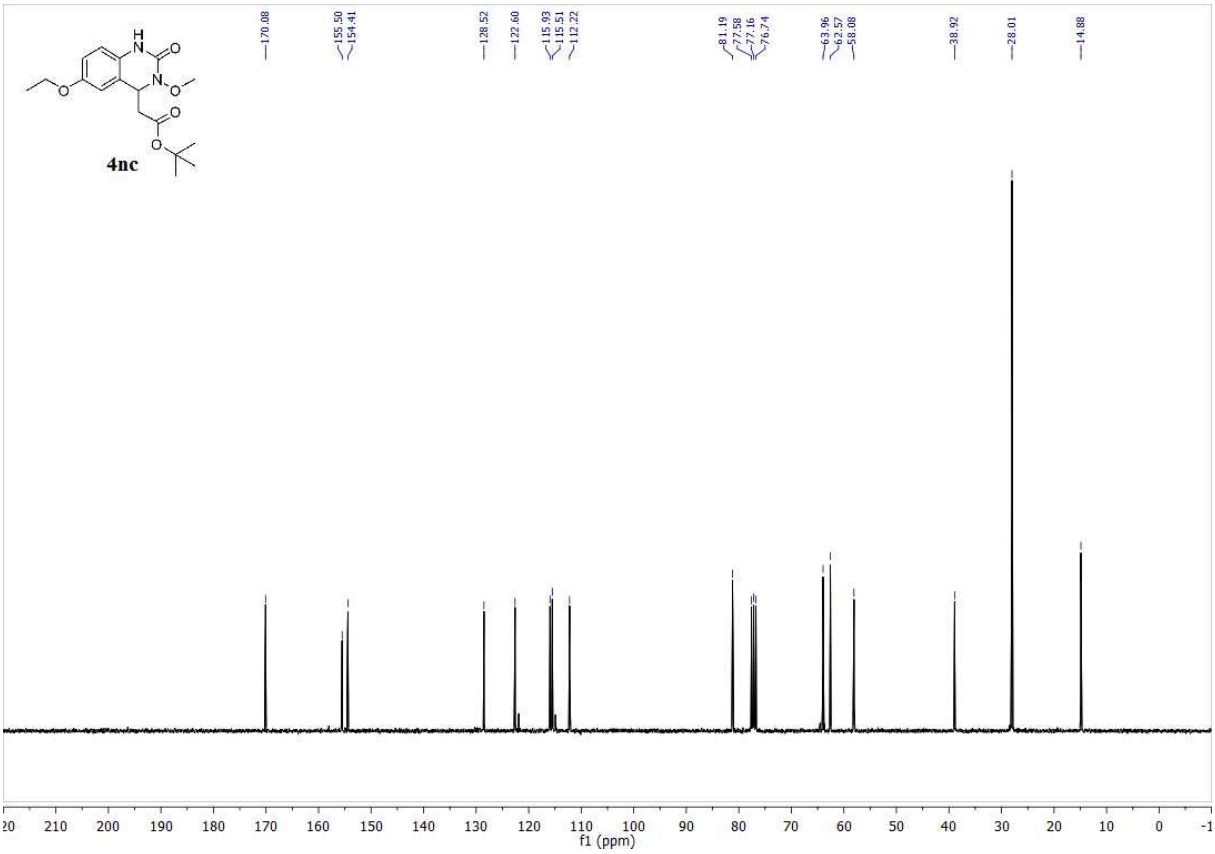

-120.20
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-120
-140
-160
-180
-200
-220
f1 (ppm)

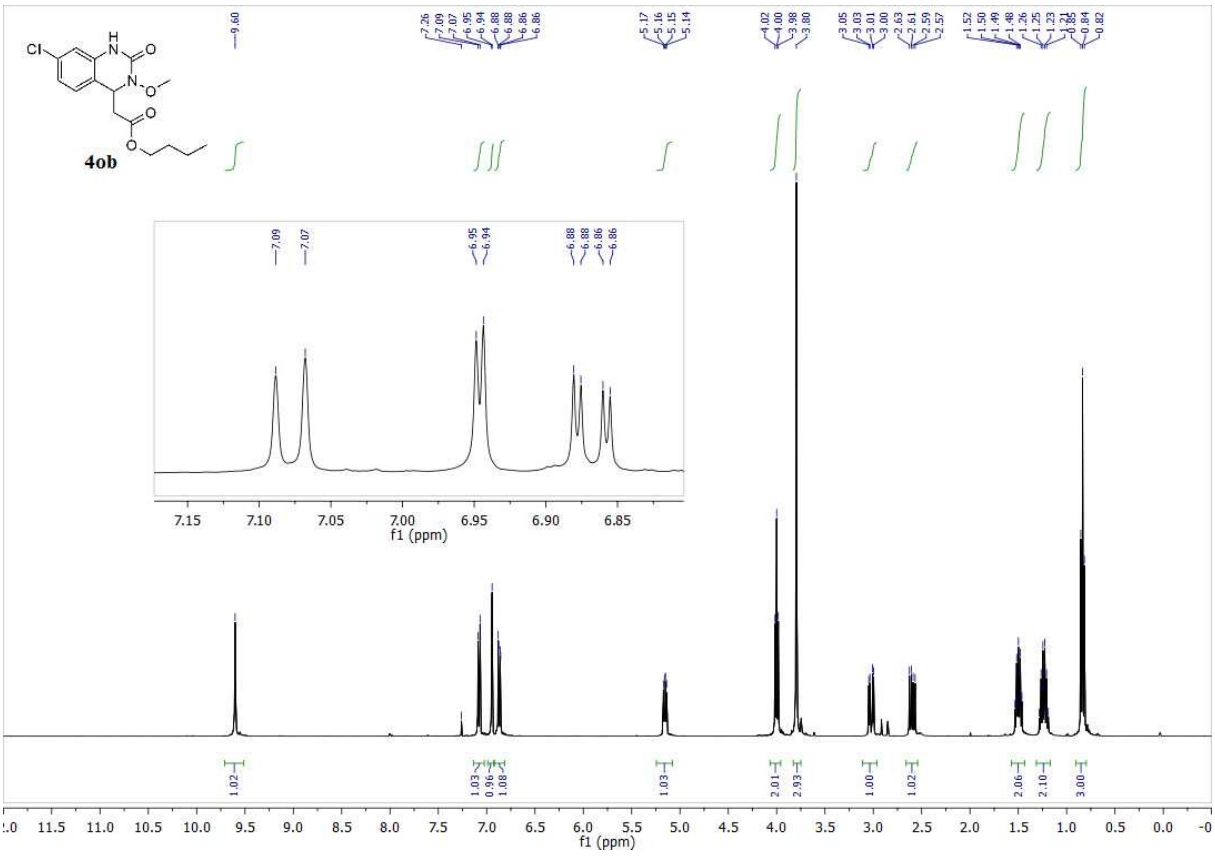
4la

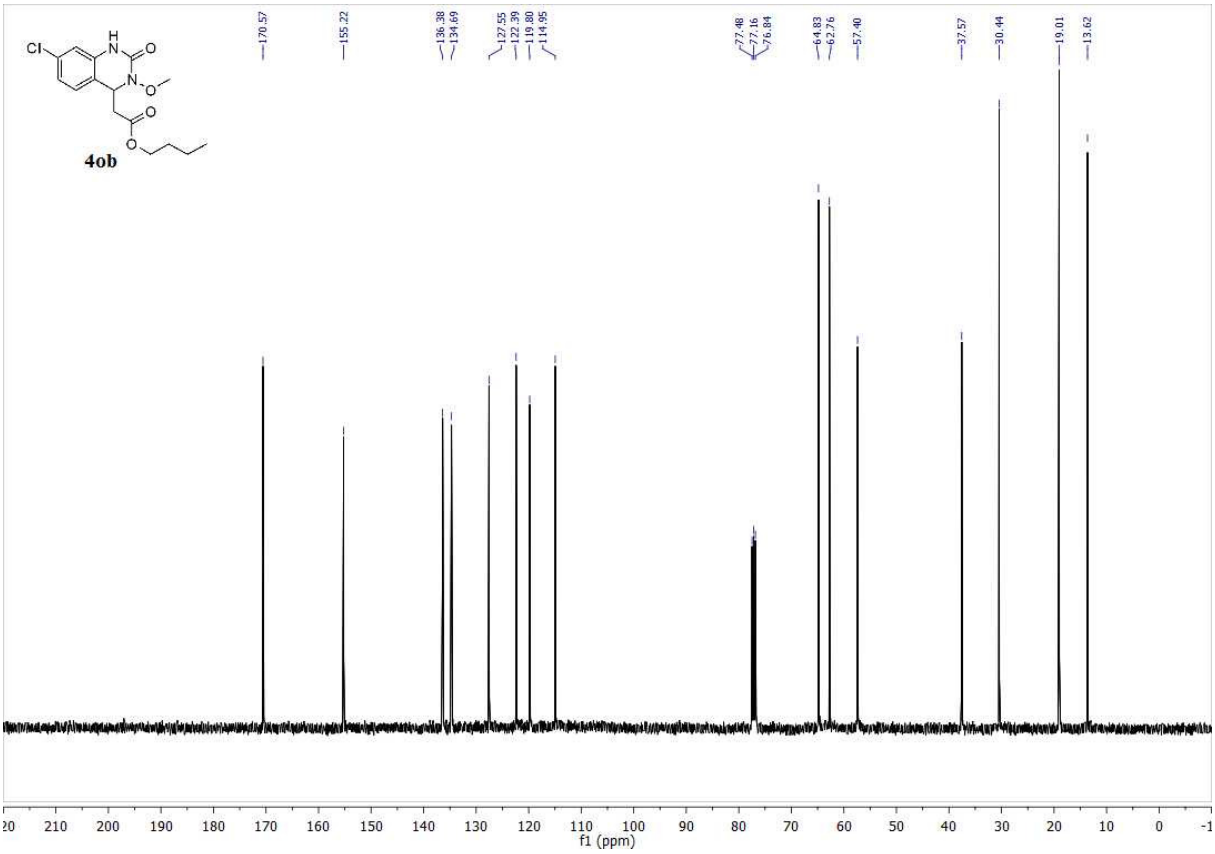

4mb
f1 (ppm)


4mb
f1 (ppm)


4nc
9.06
7.22
6.76
6.75
6.73
6.68
6.67
6.66
6.65
5.08
5.07
5.06
5.04
3.92
3.91
3.89
3.89
3.87
3.84
3.73
0.96
1.04
1.98
0.98
2.11
2.99
0.98
1.05
12.20
f1 (ppm)


4nc
170.08
155.50
154.41
128.52
122.60
115.93
115.51
112.22
81.19
77.58
77.16
76.74
63.96
62.57
58.08
38.92
28.01
14.88
f1 (ppm)


4ob
f1 (ppm)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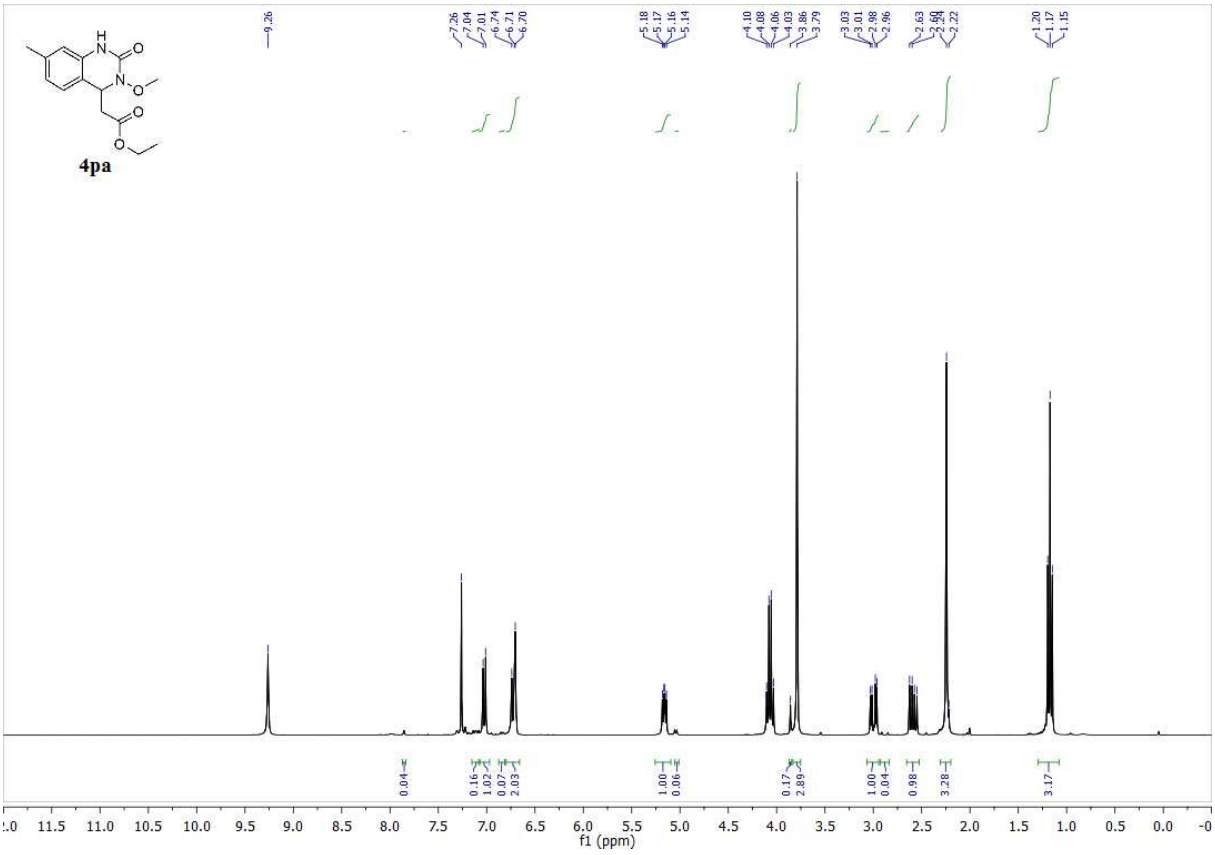
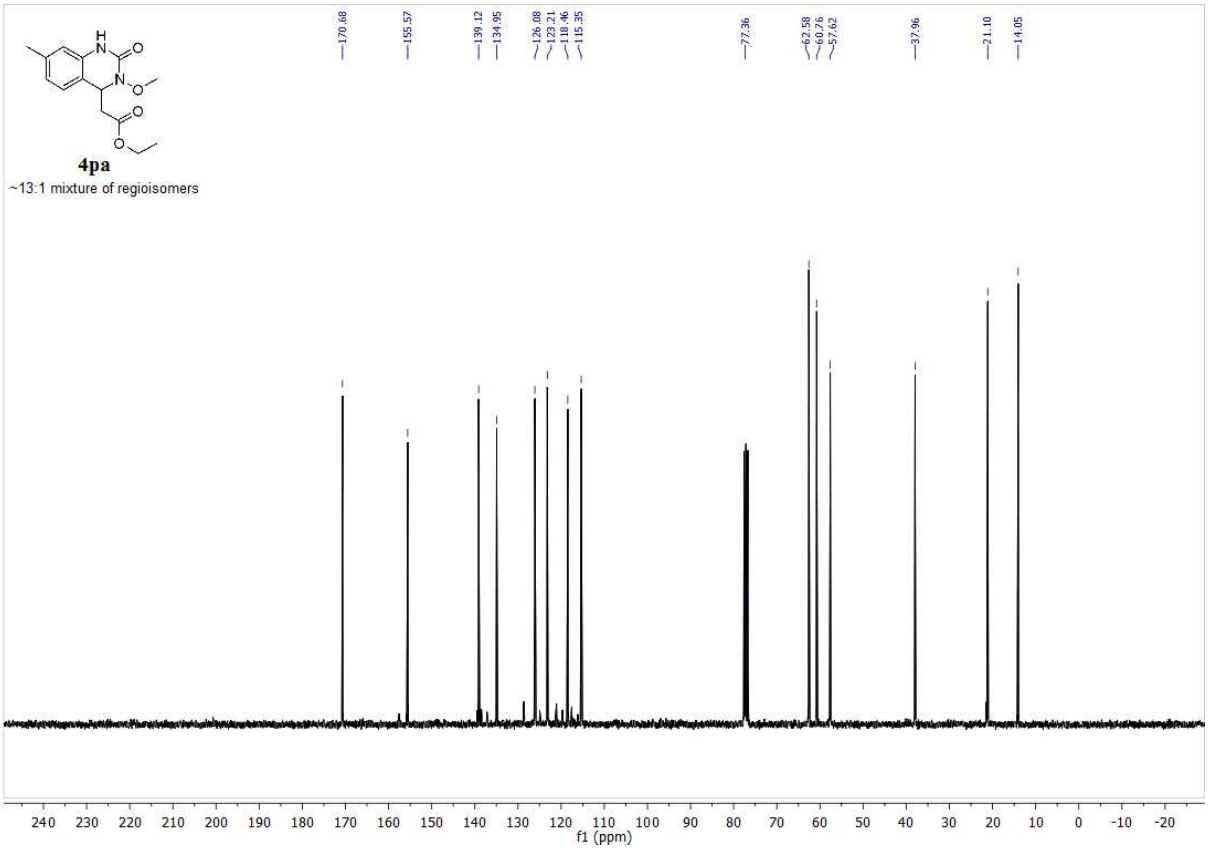
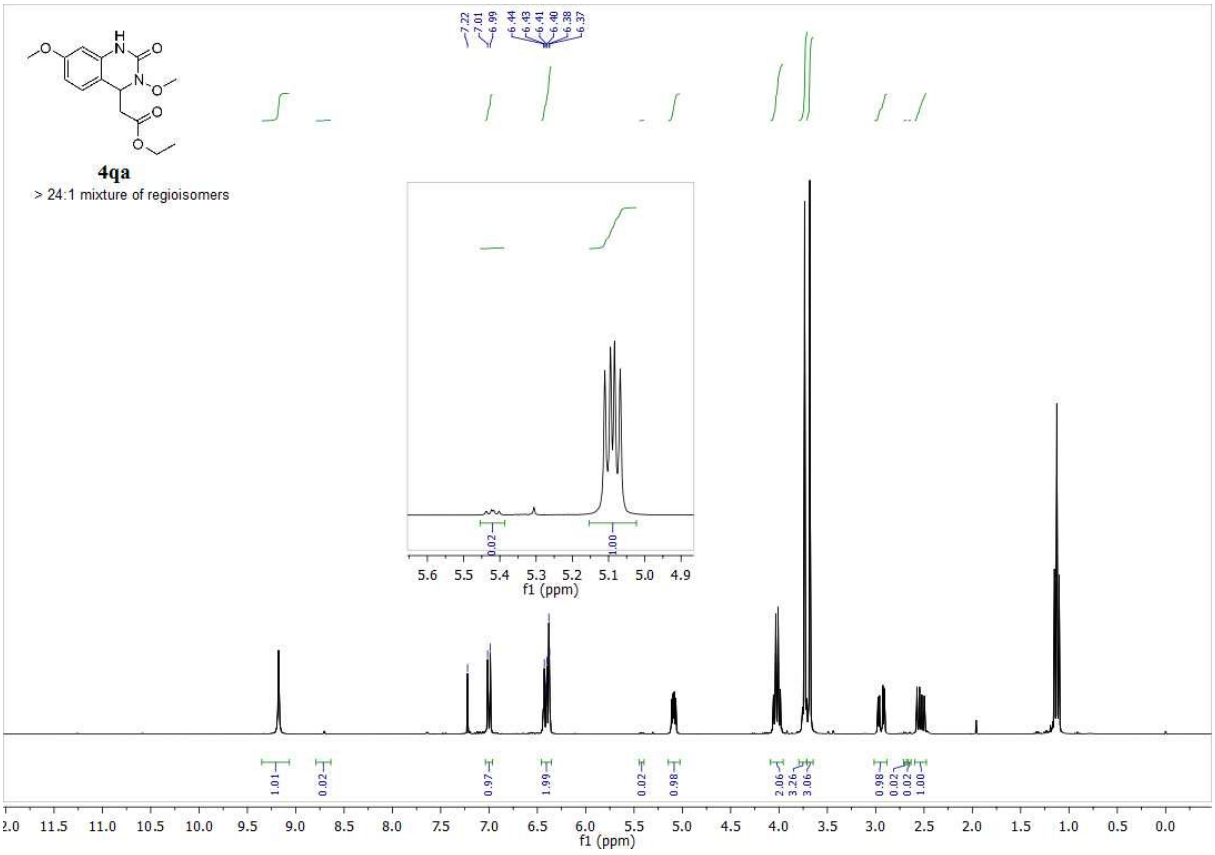
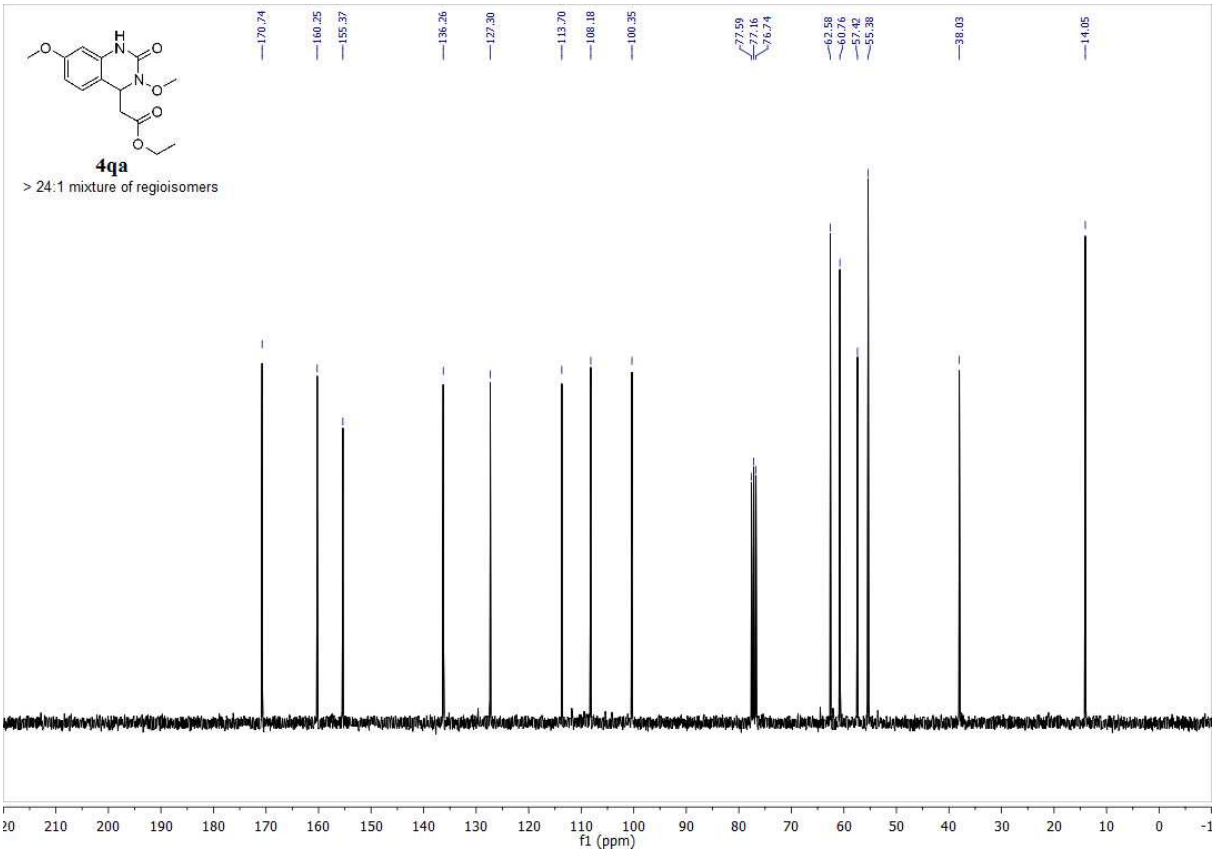
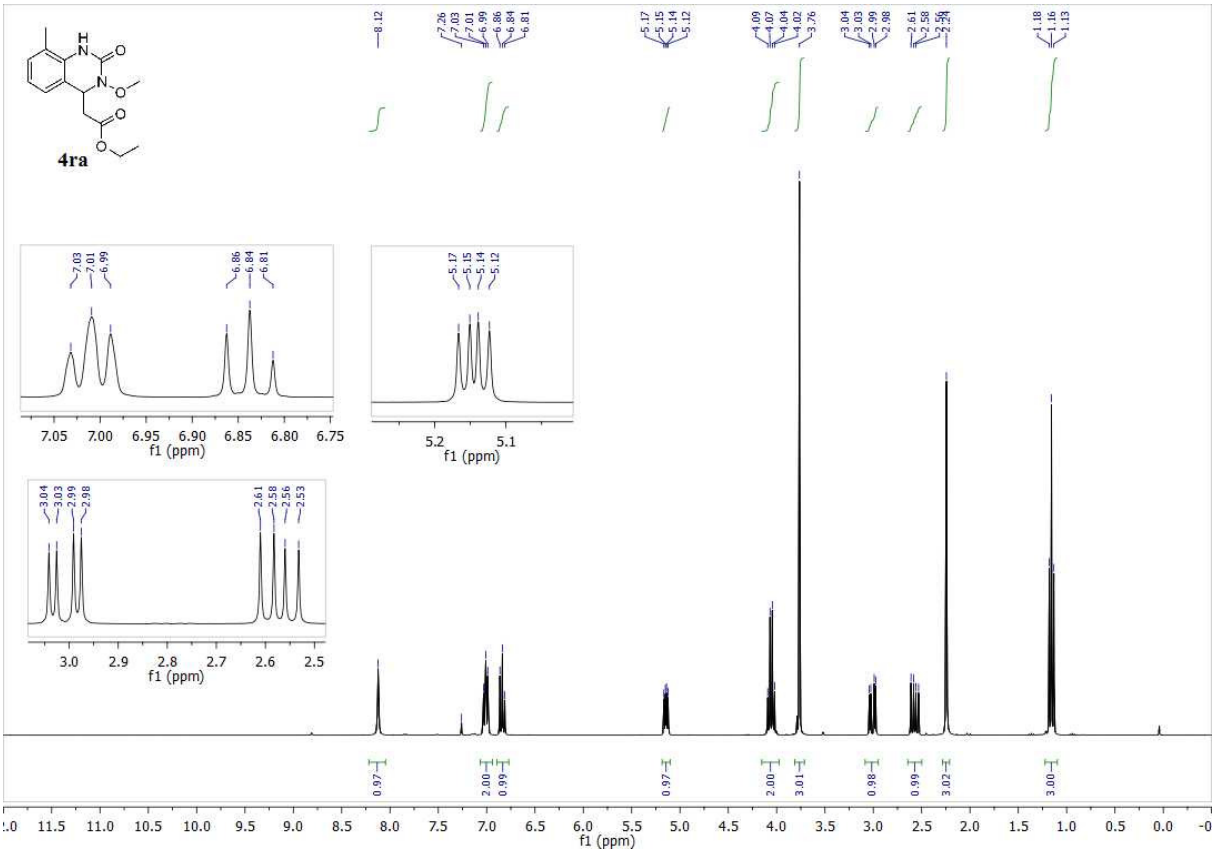
f1 (ppm)

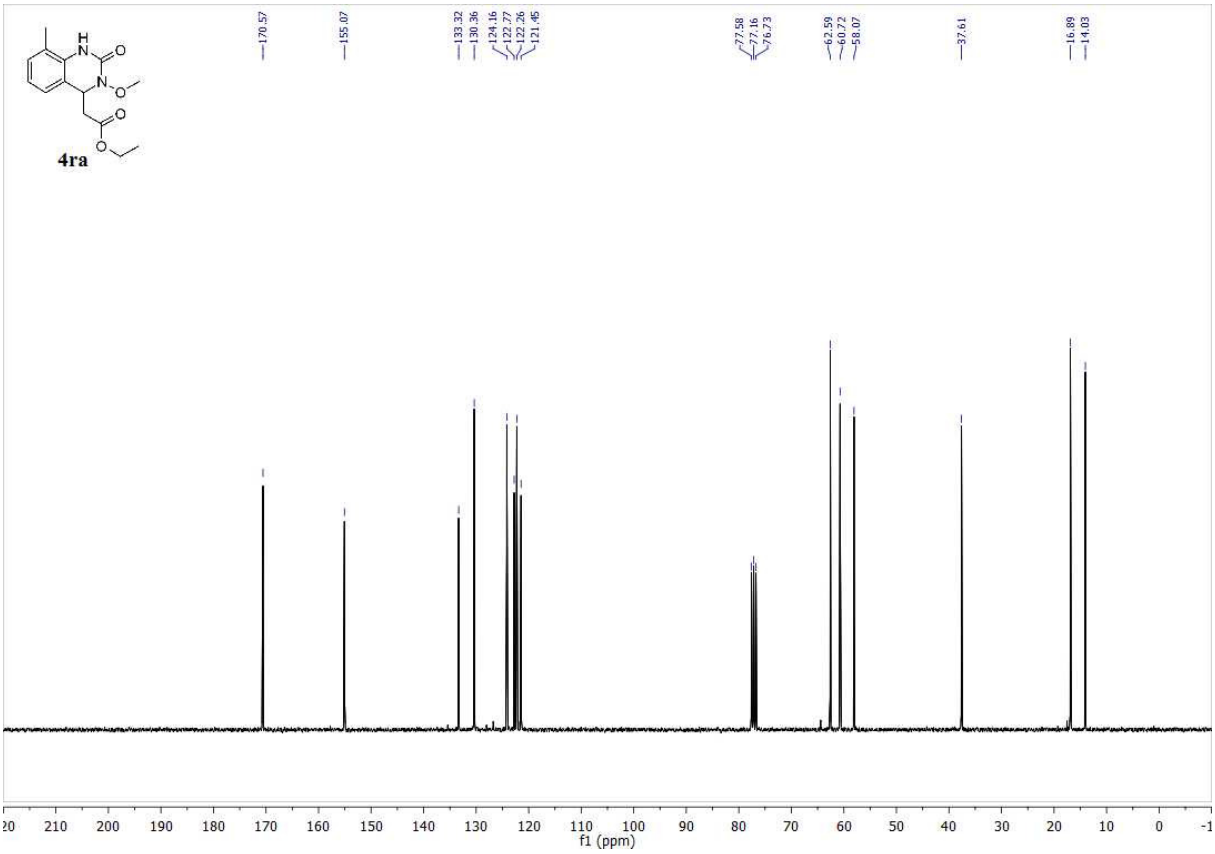

4pa
f1 (ppm)

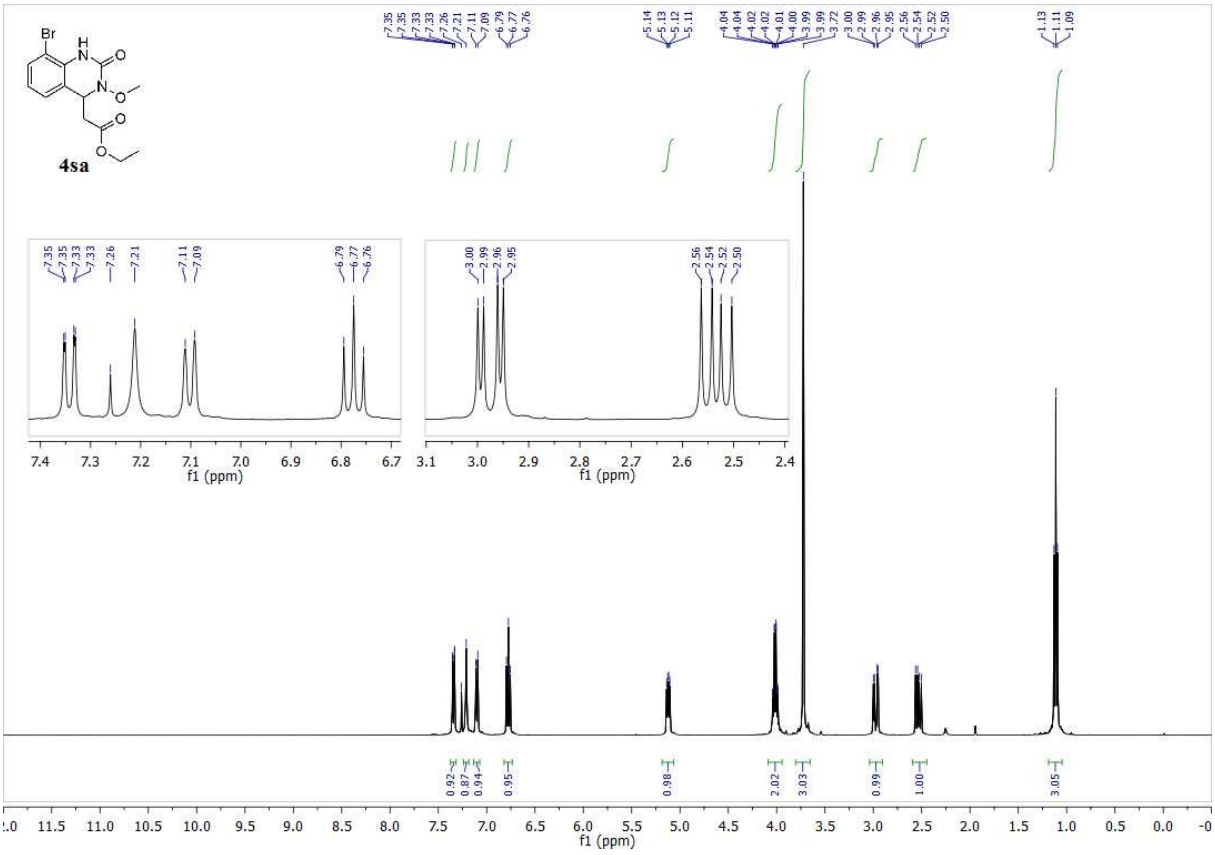

4pa
~13:1 mixture of regioisomers
f1 (ppm)

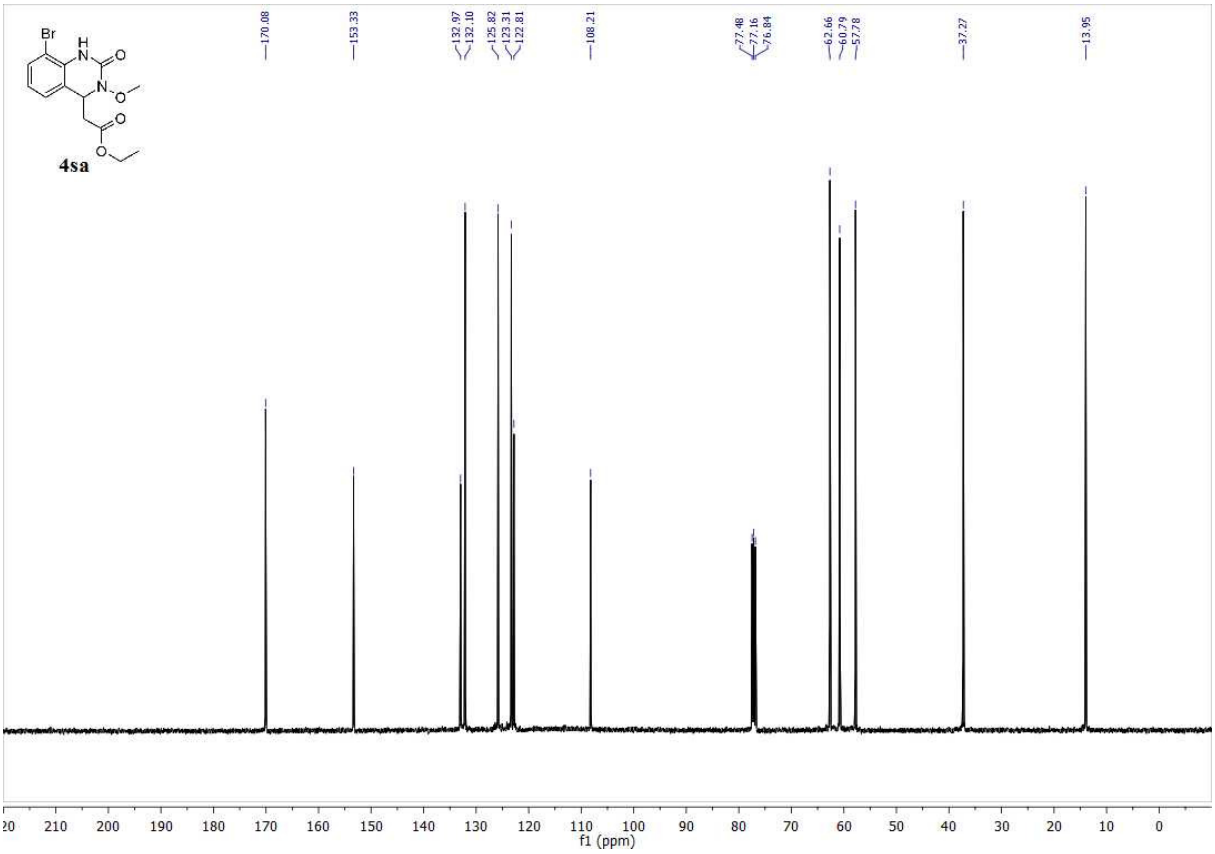

4qa
> 24:1 mixture of regioisomers
f1 (ppm)

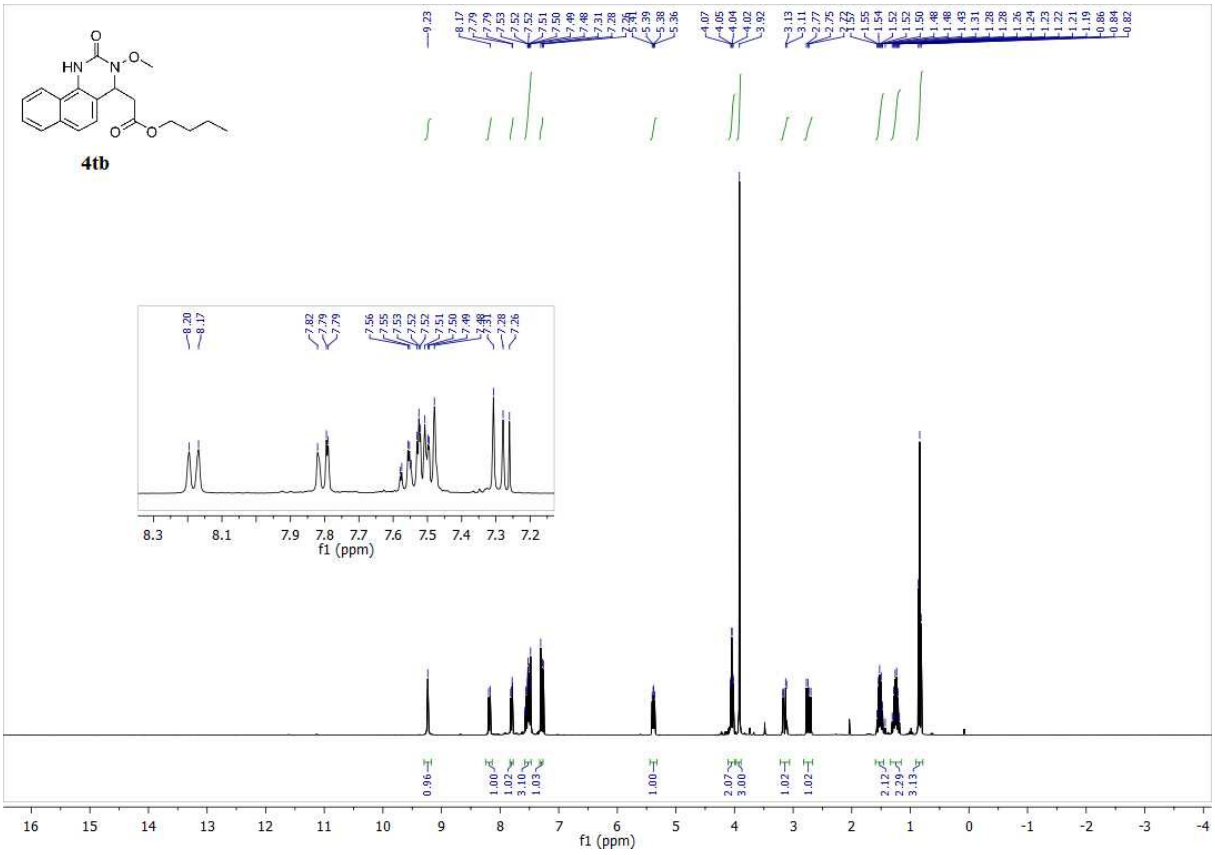

4qa
> 24:1 mixture of regioisomers
f1 (ppm)

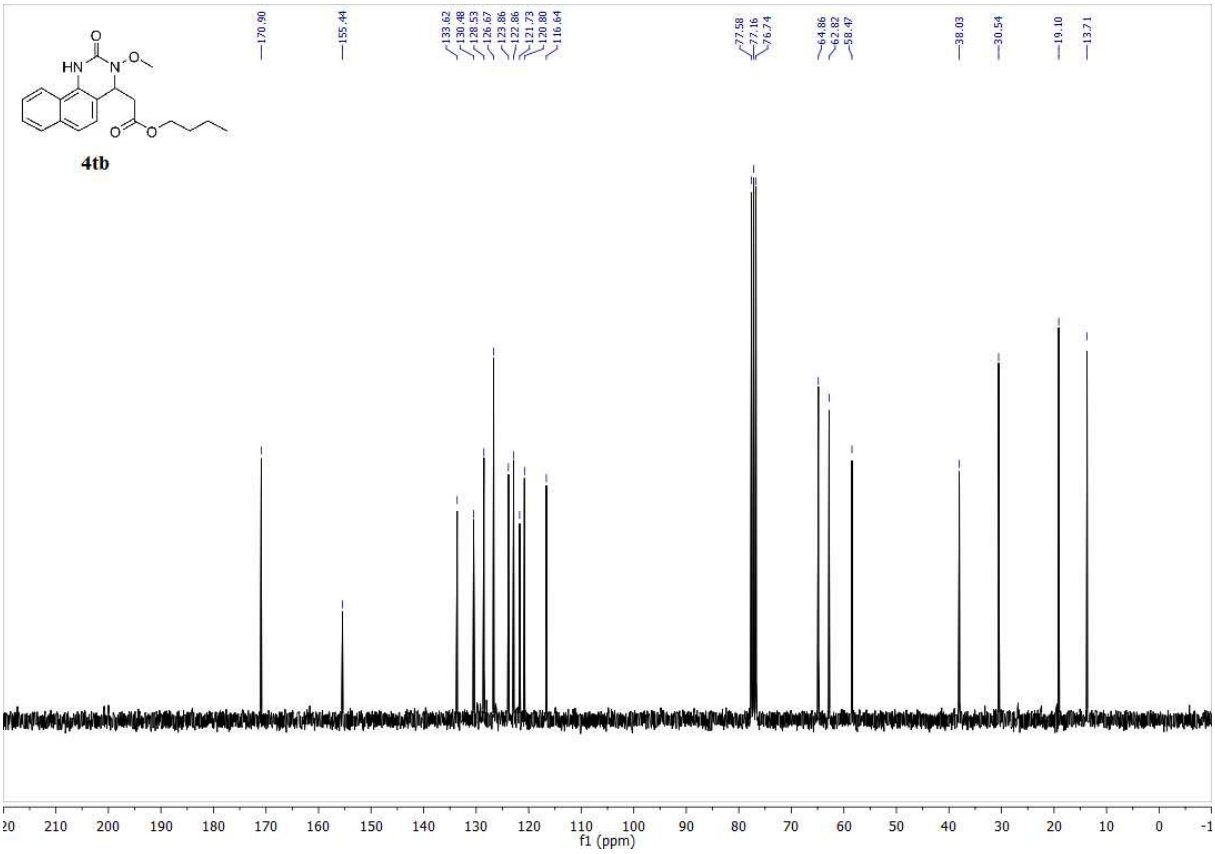

4ra
f1 (ppm)

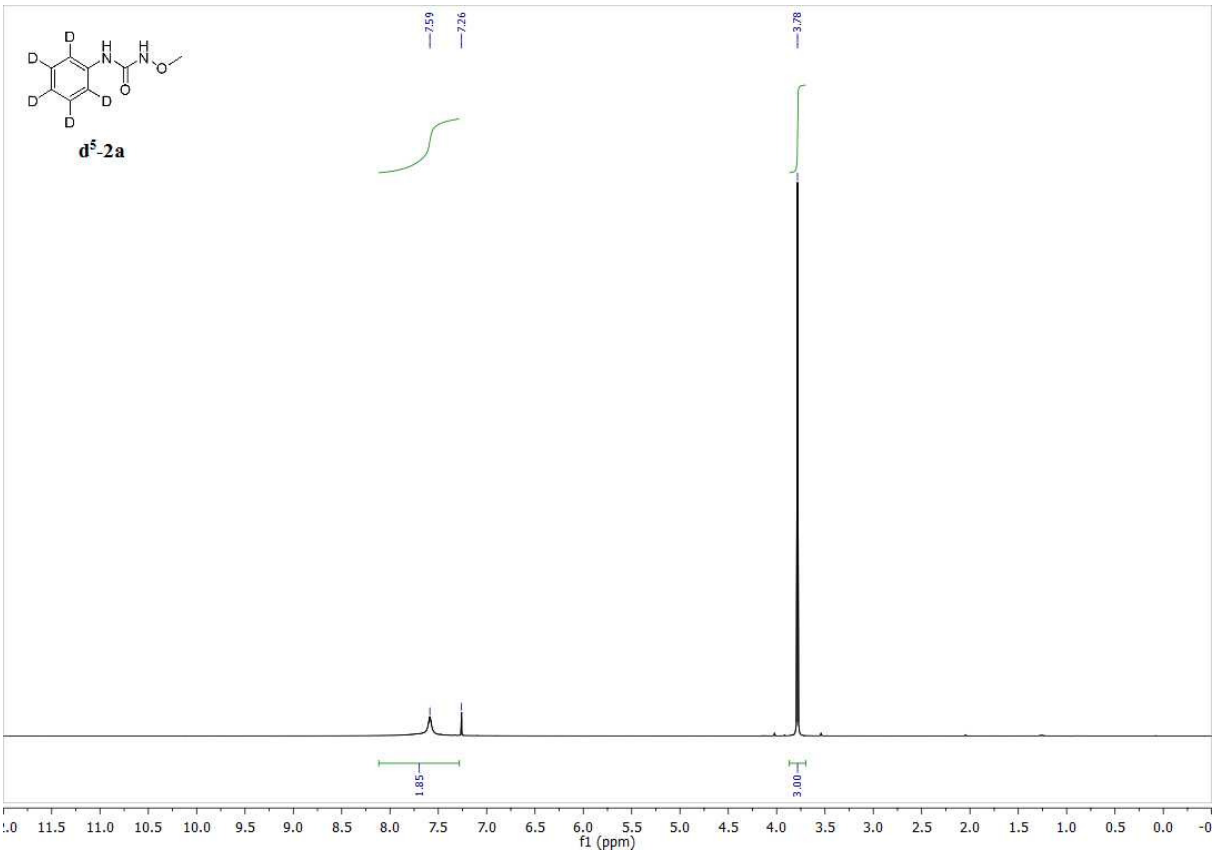

4ra
f1 (ppm)

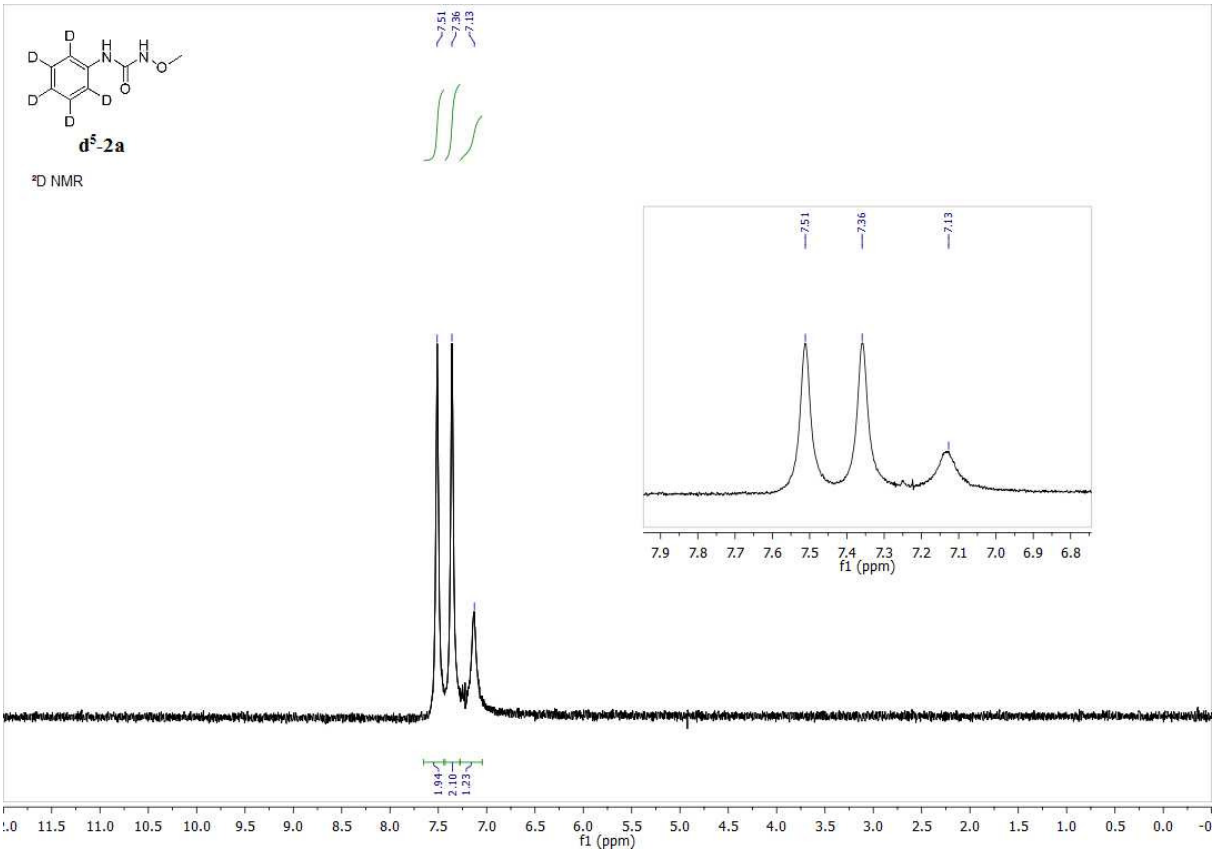

4sa
f1 (ppm)

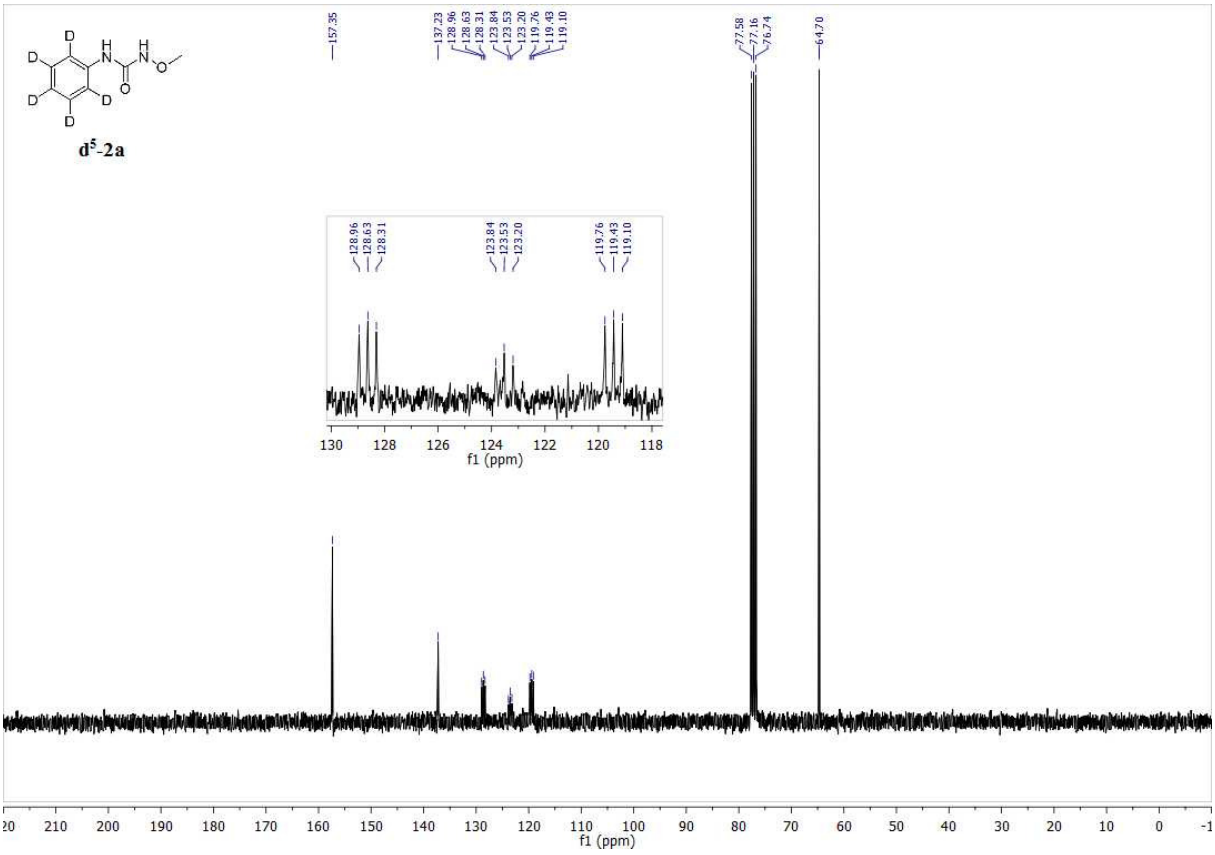

4sa
f1 (ppm)

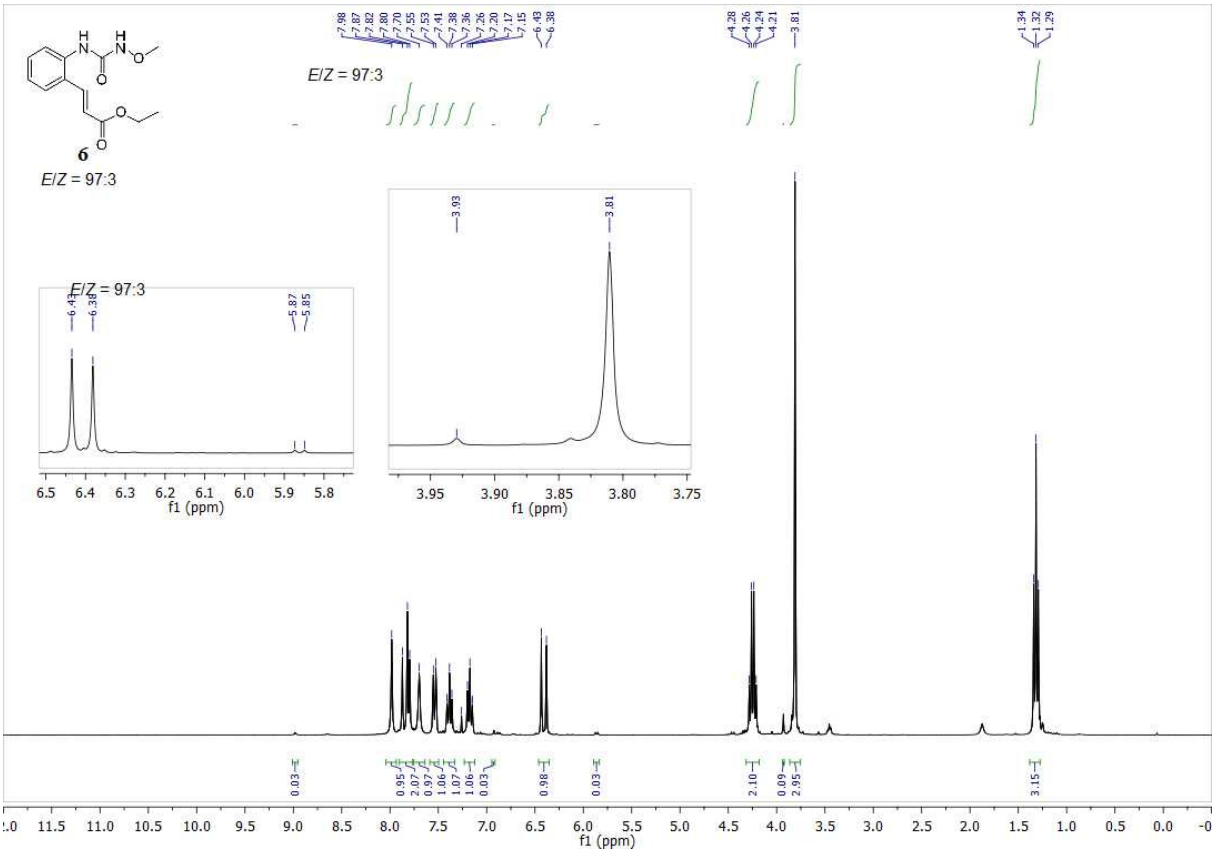

4tb
f1 (ppm)

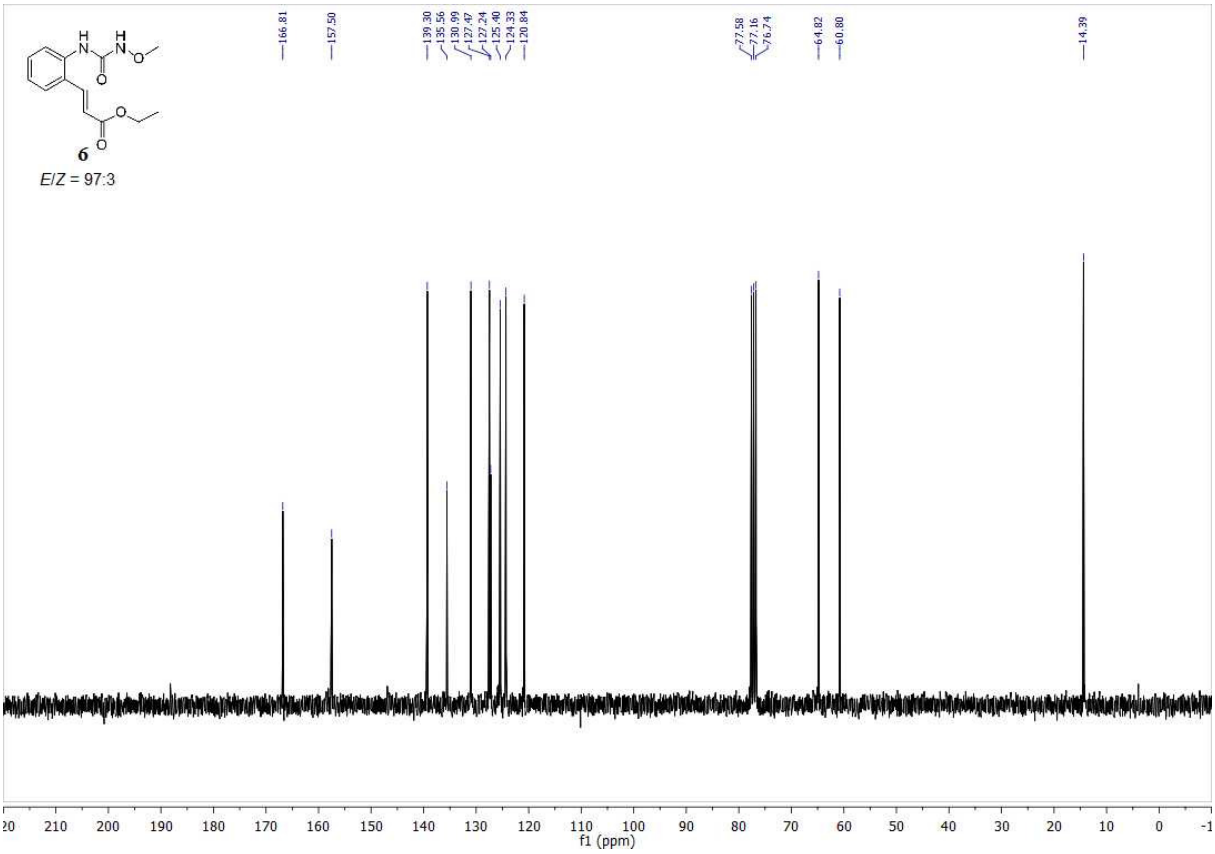

4tb
f1 (ppm)

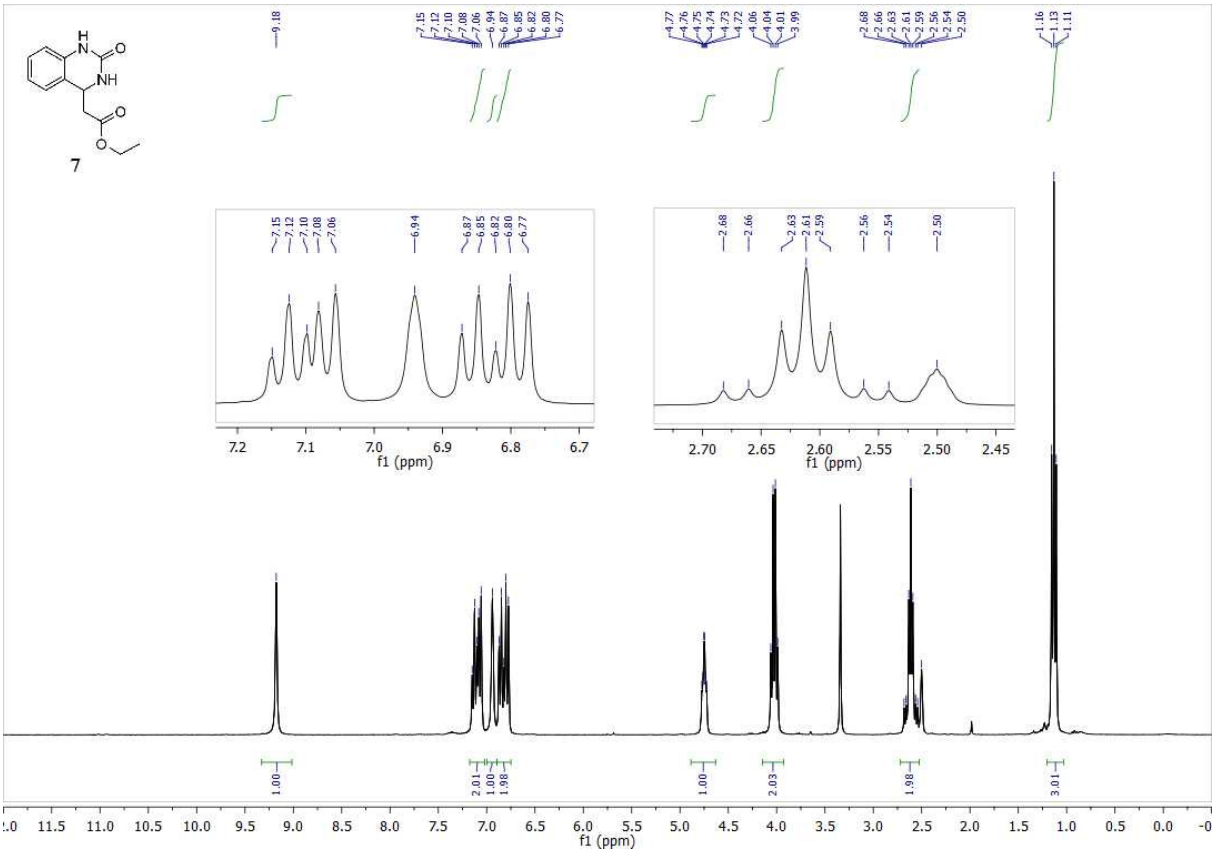

d5-2a
7.59
7.26
3.78
1.85
3.00
f1 (ppm)

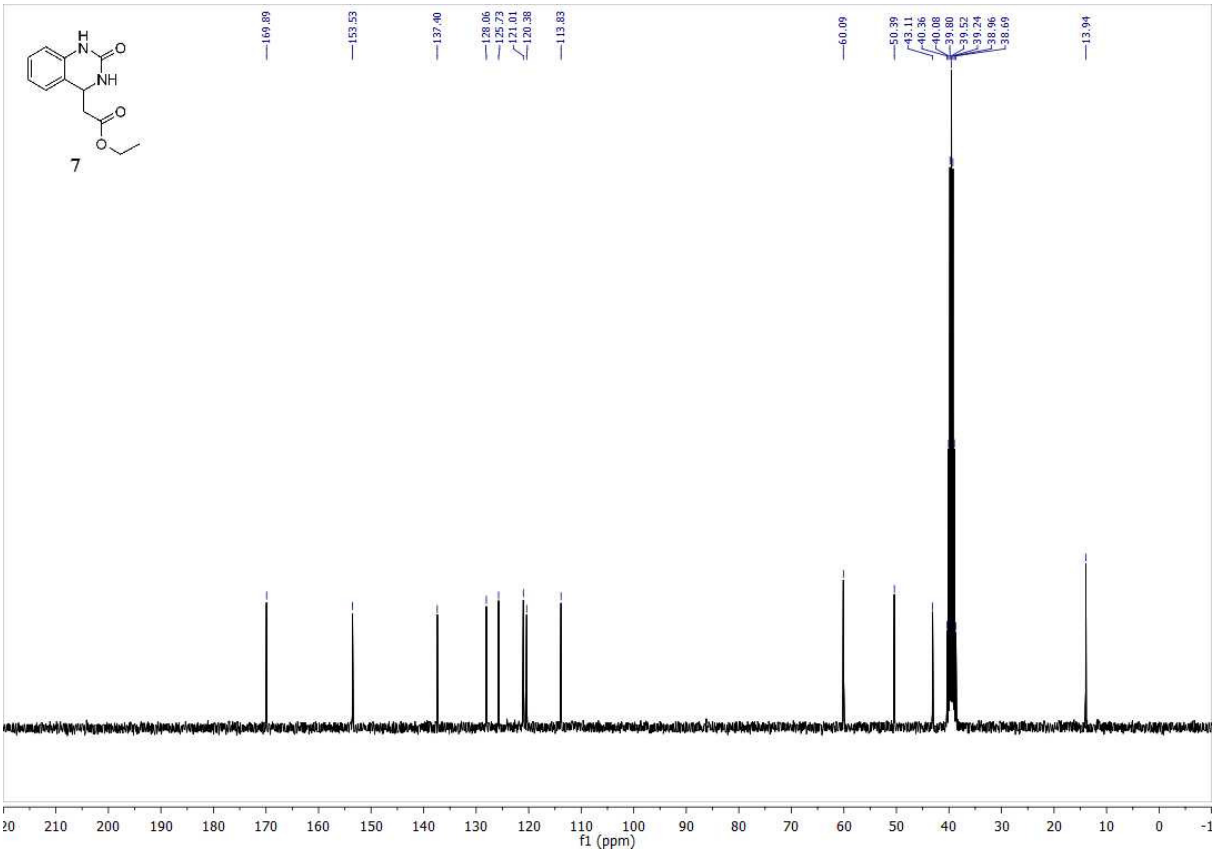

d5-2a
2D NMR
7.51
7.36
7.13
1.94
2.10
1.23
f1 (ppm)




6
E/Z = 97:3
E/Z = 97:3
E/Z = 97:3
f1 (ppm)
f1 (ppm)
f1 (ppm)


6
E/Z = 97:3
f1 (ppm)


7
f1 (ppm)


7
f1 (ppm)

10. References:

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