Supporting Information available

An integration of condensation/ Ullmann-type coupling/ bicyclization sequences: copper-catalyzed three-component direct synthesis of [1,2,4]triazolo[1,5-*b*]isoquinolin-5(1*H*)-ones

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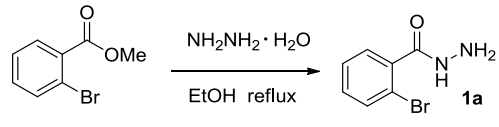
1. General

All *o*-halogenated benzohydrazides (**1a-1c**, **1e-1h**), aldehydes (**2a-2o**), nitriles (**3a-3c**) and other reagents were obtained from commercial suppliers and used without further purification. o-halogenated benzohydrazides (**1a-1h**) could also be prepared from methyl 2-bromobenzoates according to the classical hydrazinolysis. Dimethyl Sulphoxide (DMSO) was distilled from calcium hydride. TLC analysis was performed using pre-coated glass plates. Column chromatography was performed using silica gel (200-300 mesh). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. ^1H NMR spectra were recorded on a Varian Mercury 400 or 600 MHz spectrometer Chemical shifts are reported in ppm, relative to the internal standard of tetramethylsilane (TMS). HRMS were obtained on an Apex-Ultra MS equipped with an electrospray source. Melting points were determined using XT-4 apparatus and not corrected.

2. Experimental procedures and characterizations of substrates

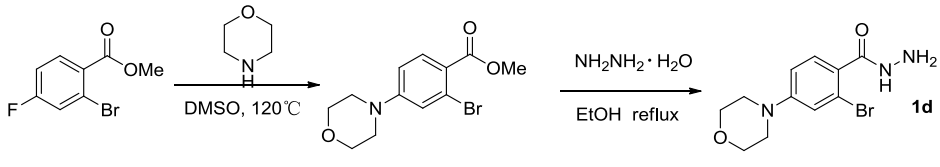
2.1 Synthesis of substrates **1** according to the related article[1].(**1a** as an example)



A solution of methyl 2-bromobenzoate (10mmol, 2.15g) and (85%) hydrazine hydrate (200mmol, 11.76g) was refluxed at 80 ℃ for 3 hours. The solvent (EtOH) was removed under reduced pressure and the residue was extracted with EtOAc three times. The combined organic solvent was dried (Na_2SO_4) and concentrated. The crude product was then recrystallized from EtOH. Compound **1a** was obtained as a white solid (1.85g, 86% yield).

The other substrates **1b-1c**, **1e-1h** were prepared according to the above procedure.

2.2 Synthesis of substrates **1d**.



Methyl 2-bromo-4- fluorobenzoate (1.16 g, 5 mmol, 1 equiv) and morpholine(2.18 mL, 25 mmol, 5 equiv) were dissolved in DMSO (5 mL), and the solution was stirred at 120 ℃ for 1 hour. Subsequently, the reaction mixture was partitioned between EtOAc and H_2O. The aqueous layer was extracted with EtOAc (3 times). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification by flash chromatography using EtOAc/Petroleum ether (1:20) afforded 1.39 g of an off-white solid (93%)[2]. Then substrates **1d** were prepared according to the above procedure.

2. Synthesis of 4aa-4ap, 4ba-4ja

2.1. General procedure for preparation of 4 (4aa as an example)

General procedure: A sealed tube was charged with 2-bromobenzohydrazide **1a** (107 mg, 0.5 mmol) , benzaldehyde **2a** (53 mg, 0.5 mmol), methyl 2-cyanoacetate **3a** (49.5 mg, 0.5 mmol) Cu_2O (7.6 mg, 0.05mmol) and K_2CO_3 (103.5 mg, 0.75mmol) at room temperature, and then dried solvent DMSO (3 mL) was added. The resulting mixture was stirred at 100 ℃ in a sealed vessel under air, after disappearance of the reactant (monitored by TLC), then added 50mL water to the mixture, extracted with EtOAc 3 times (3 × 50 mL). The extract was washed with

30% NaCl solution (V/V), dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (chloroform / methyl alcohol = 30:1) to yield the desired product **4aa** as a yellow solid (92% yield).

3. Optimization of the Reaction Conditions

4. Molecular Structure and Crystallographic Data

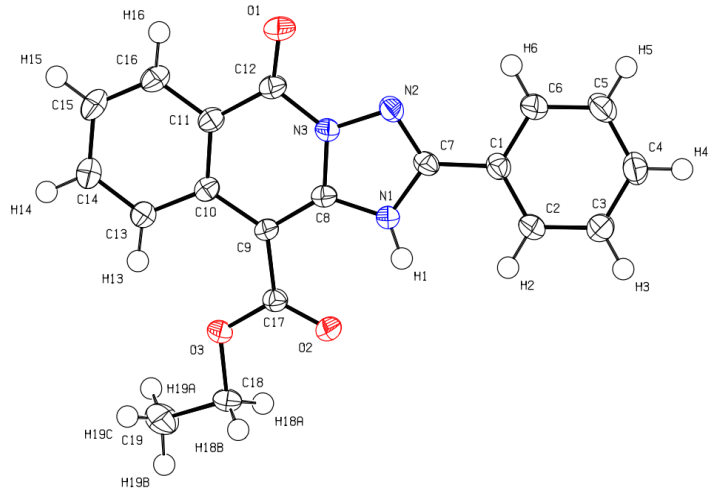


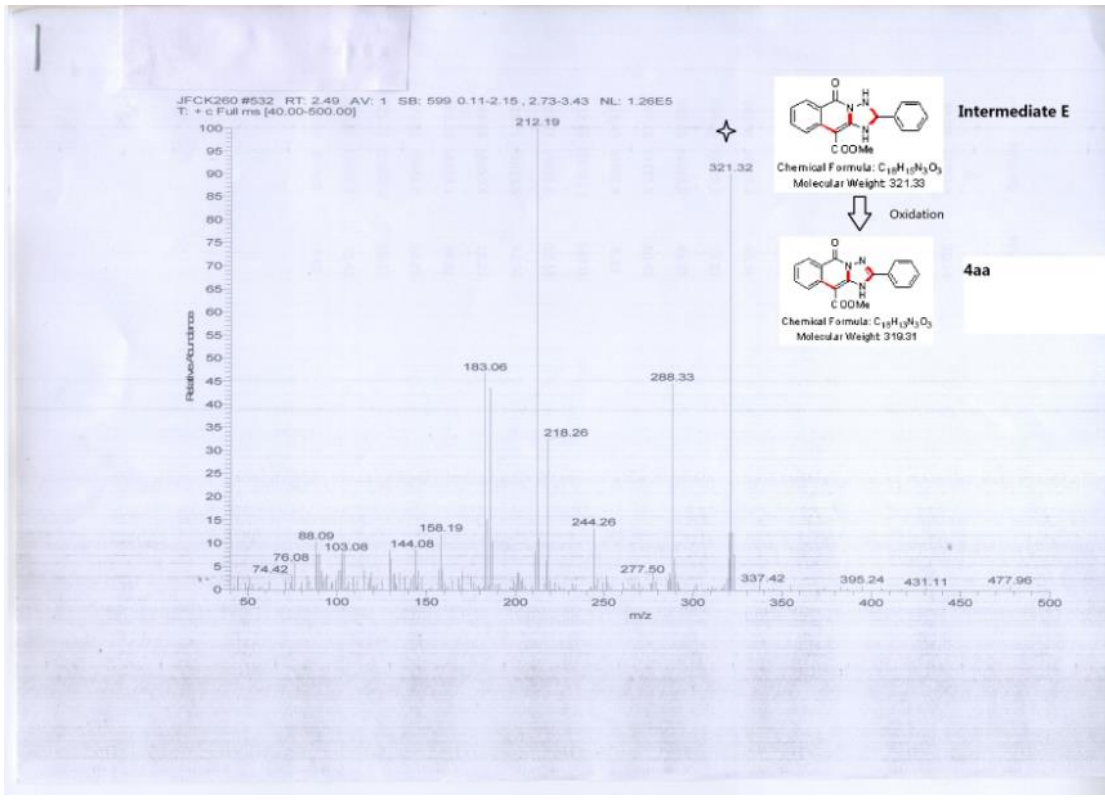
Figure S1 X-ray crystal structure of **4ga.**

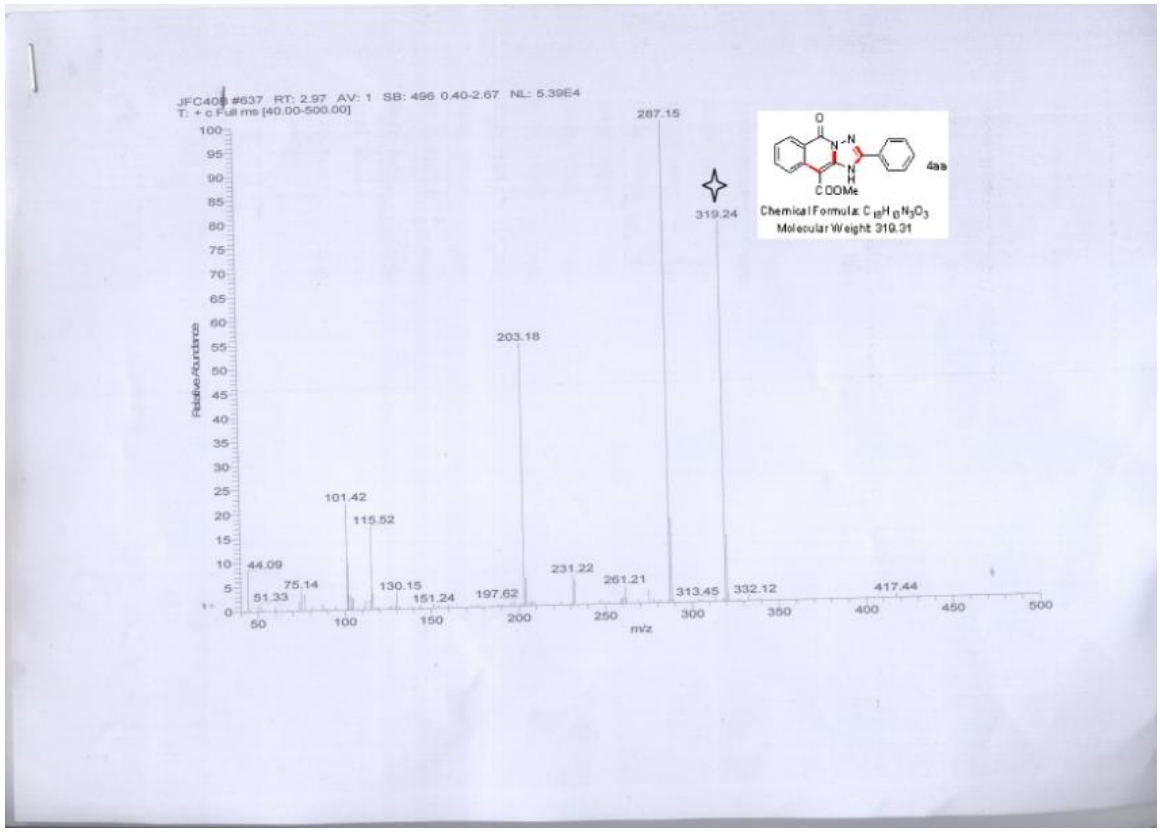
Table S1. Crystal data and structure refinement for compound **4ga** (CCDC: 972885)

Empirical formula	$C_{19}H_{15}N_3O_3$		Absorption coefficient	0.100 mm^{-1}
Formula weight	333.34		F(000)	1392
Temperature	100(2) K		Crystal size	0.23 x 0.20 x 0.20 mm^3
Wavelength	0.71073 Å		Reflections collected	13809
Crystal system	Monoclinic		Independent reflections	4495 [R(int) = 0.0776]
Space group	C2/c		Max. and min. transmission	0.9803 and 0.9774
Unit cell dimensions	a = 18.370Å	α= 90°	Refinement method	Full-matrix least-squares on F^2
	b = 6.849 Å	β= 91.718°	Goodness-of-fit on F^2	1.049
	c = 24.489Å	γ = 90°	Final R indices [I>2sigma(I)]	R1 = 0.0433, wR2 = 0.1159
Volume	3080.0 $Å^3$		R indices (all data)	R1 = 0.0528, wR2 = 0.1216
Z	8		Largest diff. peak and hole	0.412 and -0.338 $e.^{-3}$
Density (calculated)	1.438 Mg/m^3			

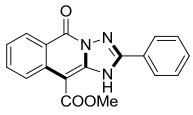
5. The MS Spectra of possible intermediate E and 4aa

2-bromobenzohydrazid **1a**, benzaldehyde **2a** and methyl 2-cyanoacetate **3a** were heating in DMSO at 60 ℃ under Ar atmosphere for 6 h. The mixture was extracted with EtOAc. Then the extract was detected by MS and corresponding spectra is illustrated in the following figure.Notably, intermediate E is not suitable to purification by column chromatography and easily transformed into **4aa** under air. The MS Spectra of **4aa** was also detected as shown in the fugure below.



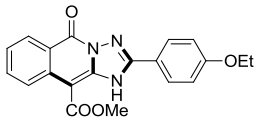

JFC409 #637 RT: 2.97 AV: 1 SB: 496 0.40-2.67 NL: 5.39E4
T: + c Full ms [40.00-500.00]
Relative Abundance
m/z
287.15
319.24
203.18
101.42
115.52
44.09
75.14
51.33
130.15
151.24
197.62
231.22
261.21
313.45
332.12
417.44
4aa
COOMe
Chemical Formula: C18H17N3O3
Molecular Weight: 319.31

6. Spectral data of compound 4aa-4ap, 4ba-4ha.

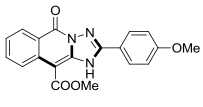


methyl 5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate

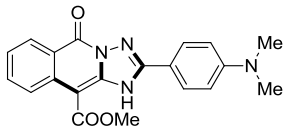
(4aa): yellow solid, mp 137-139 ℃; IR (KBr):3449, 1701, 1659, 1611, 1590, 1552, 1480, 1456, 1434, 1296, 1196, 1155, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 11.46 (s, 1H), 8.60 (d, *J* = 8.0 Hz, 1H), 8.54 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 6.4 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.56-7.51 (m, 3H), 7.33 (t, *J* = 7.2 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.6, 156.3, 150.7, 146.3, 134.6, 133.1, 132.3, 129.2, 128.4, 126.9, 124.1, 123.8, 123.6, 119.6, 82.5, 51.8; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{14}N_3O_3$: 320.1030; found: 320.1031.



methyl 2-(4-ethoxyphenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ab): yellow solid, mp 97-99 ℃; IR (KBr): 3503, 1691, 1653, 1611, 1508, 1482, 1443, 1297, 1258, 1177, 1155, 1030 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 12.54 (s, 1H), 8.91 (d, *J* = 8.4 Hz, 1H), 8.33 (d, *J* = 7.2 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.71 (t, *J* =7.2 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 8.4 Hz, 2H), 4.10-4.07 (m, 2H), 3.92 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 161.4, 155.6, 151.9, 145.9, 135.6, 132.8, 129.9, 127.3, 123.8, 123.2, 118.6, 116.4, 114.6, 81.8, 63.6, 51.4, 14.6; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{18}N_3O_4$: 364.1292; found: 364.1296.

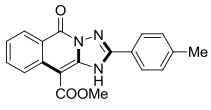


methyl 2-(4-methoxyphenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ac): yellow solid; mp 199-201 ℃; IR (KBr): 3438, 1705, 1655, 1607, 1508, 1484, 1452, 1299, 1254, 1181, 1156, 1031 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.33 (s, 1H), 8.59 (d, *J* = 8.4 Hz, 1H), 8.52 (d, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.61 (t, *J* =7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 3.98 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.8, 162.0, 155.50, 151.8，145.9，135.5，132.7, 129.9, 127.2, 123.7, 123.0, 118.6, 116.6, 114.2, 81.7, 55.5, 51.3; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{16}N_3O_4$: 350.1135; found: 350.1130.

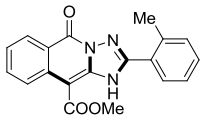


methyl 2-(4-(dimethylamino)phenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ad): yellow solid; >300 ℃; IR (KBr): 3436, 1656, 1608, 1516, 1485, 1441, 1300, 1197, 1153, 1036 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.26 (s,

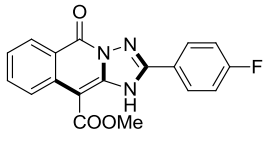
1H), 8.70 (d, *J* = 7.8 Hz, 1H), 8.60 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 2H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 2H), 4.06 (s, 3H), 2.97 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 156.5, 152.4, 151.3, 146.4, 134.7, 132.9, 128.4, 128.1, 124.2, 123.4, 119.7, 111.3, 109.9, 82.4, 51.8, 39.8 ; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{19}N_4O_3$: 363.1452; found: 363.1458.



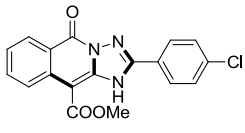
methyl 5-oxo-2-(p-tolyl)-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ae): yellow solid; mp 155-157 ℃; IR (KBr): 3447, 1706, 1655, 1611, 1483, 1440, 1295, 1192, 1155, 1031cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.49 (s, 1H), 8.69 (d, *J* = 8.4 Hz, 1H), 8.60 (d, *J* = 8.4 Hz, 1H), 7.94 (d, *J* = 7.8 Hz, 2H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 2H), 4.05 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ =167.4, 156.2, 150.7, 146.1, 143.0, 134.5, 132.9, 129.7, 128.2, 126.7, 124.0, 123.4, 120.8, 119.5, 82.4, 51.7, 21.4; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{16}N_3O_3$: 334.1186; found: 334.1189.



methyl 5-oxo-2-(o-tolyl)-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4af) : yellow solid; mp 187-189 ℃; IR (KBr): 3457, 1699, 1651, 1610, 1550, 1482, 1434, 1296, 1198, 1159,1025 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.51 (s, 1H), 8.73-8.71 (m, 1H), 8.58 (t, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 7.71 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.32 (t, *J* = 8.4 Hz, 2H), 4.02 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.5, 156.4, 151.2, 145.9, 137.9, 134.8, 133.2, 131.7, 131.6, 129.2, 128.4, 126.3, 124.2, 123.54, 123.51, 119.6, 82.4, 51.8, 21.1; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{16}N_3O_3$: 334.1186; found: 334.1192.

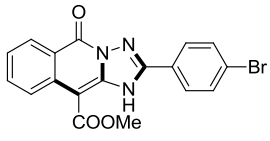


methyl 2-(4-fluorophenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ag): brown solid; mp 215-217 ℃; IR (KBr): 3423, 1705, 1643, 1612, 1508, 1483, 1441, 1295, 1227, 1195, 1157,1029 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.81 (s, 1H), 8.94-8.92 (m, 1H), 8.34-8.32 (m, 1H), 8.23-8.20 (m, 2H), 7.74-7.71 (m, 1H), 7.50-7.47 (m, 2H), 7.39-7.36 (m, 1H), 3.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4, 166.2, 163.7, 156.3, 150.1, 146.2, 134.6, 133.1, 129.5, 129.4, 128.2, 124.2, 123.6, 120.2, 119.4, 116.6, 116.3, 82.7, 51.7; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{18}H_{13}FN_3O_3$: 338.0936; found: 338.0942.



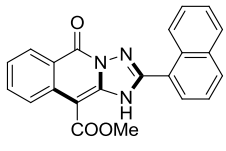
methyl 2-(4-chlorophenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carbox

ylate (4ah): brown solid; mp 115-117 ℃; IR (KBr): 3437, 1708, 1641, 1609, 1546, 1482,1437, 1294, 1198, 1155,1089, 1031,1014 cm-1; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.78 (s, 1H), 8.86 (d, J = 8.8 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.0 Hz, 2H), 7.67 (t, J = 9.2 Hz, 3H), 7.33 (t, J = 7.6 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.7, 155.5, 151.2, 145.9, 136.7, 135.5, 132.7, 130.0, 128.9, 127.2, 123.7, 123.5, 123.1, 118.5, 81.9, 51.3; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{13}ClN_3O_3$: 354.0640; found: 354.0642.



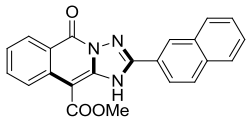
methyl

2-(4-bromophenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carbox ylate (4ai): brown solid; mp 159-161 ℃; IR (KBr): 3444, 1701, 1667, 1610, 1487, 1431, 1310, 1191, 1021 cm-1; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.76 (s, 1H), 8.87 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.81 (d, J = 8.0 Hz, 2H), 7.69 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.2 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.8, 155.5, 151.4, 146.0, 135.5, 132.8, 131.9, 130.2, 127.3, 125.7, 123.8, 123.1, 118.6, 109.3, 81.9, 51.3; HRMS (ESI): m/z [M +Na]$^+$ calcd for $C_{18}H_{12}BrN_3O_3Na$: 419.9954; found: 419.9959.



methyl

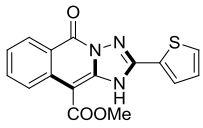
2-(naphthalen-1-yl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carbo xylate (4aj): brown solid; mp 136-138 ℃; IR (KBr): 3518, 1704, 1656, 1610, 1556, 1454, 1329, 1298, 1261, 1225, 1188, 1155, 1127, 1032 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 13.19 (s, 1H), 9.05 (d, J = 9.0 Hz, 1H), 8.39 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 5.4 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 5.4 Hz, 1H), 8.02 (d, J = 7.2 Hz, 1H), 7.75 (d, J = 6.6 Hz, 2H), 7.68-7.67 (m, 2H), 7.40 (t, J = 7.8 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.9, 156.2, 150.8, 145.3, 134.9, 133.3, 133.0, 132.3, 129.9, 128.4, 128.3, 128.1, 127.9, 126.6, 124.7, 124.3, 124.1, 123.4, 121.0, 119.3, 82.5, 51.6; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{16}N_3O_3$: 370.1186; found: 370.1189.



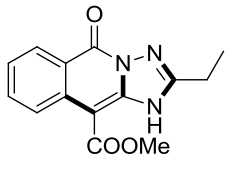
methyl

2-(naphthalen-2-yl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carbo xylate (4ak):brown solid; mp >300 ℃;IR (KBr): 3299, 1694, 1650, 1601, 1553, 1485, 1439, 1353, 1310, 1207, 1180, 1162, 1030 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.93 (s, 1H), 8.97 (d, J = 8.4 Hz, 1H), 8.87 (s, 1H), 8.38 (d, J = 7.8 Hz, 1H), 8.21 (d, J = 7.2 Hz, 1H), 8.15 (d, J = 6.0 Hz, 2H), 8.05 (d, J = 6.6 Hz, 1H), 7.77 (t, J = 7.2 Hz, 1H), 7.68-7.67 (m, 2H), 7.41 (t, J = 7.2 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 155.6, 152.1, 146.1, 135.6, 134.1, 132.8, 132.1, 128.9, 128.8,

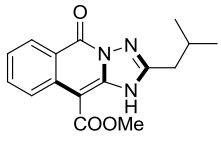
128.5, 128.1, 127.8, 127.3, 127.2, 124.2, 123.8, 123.1, 121.8, 118.6, 81.9, 51.4; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{16}N_3O_3$: 370.1186; found: 370.1193.



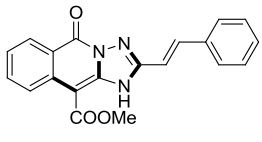
methyl 5-oxo-2-(thiophen-2-yl)-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4al): yellow solid; mp 97-99 ℃; IR (KBr): 3472, 1679, 1640, 1609, 1483, 1447, 1314, 1195, 1174, 1028 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 12.95 (s, 1H), 8.90 (d, J = 8.4 Hz, 1H), 8.34-8.32 (m, 2H), 7.99-7.97 (m, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.38 (t, J = 7.2 Hz, 1H), 7.34-7.33 (m, 1H), 3.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 155.4, 147.8, 145.8, 135.4, 132.8, 132.4, 131.7, 128.3, 127.2, 126.0, 123.8, 123.1, 118.6, 81.9, 51.3; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{12}N_3O_3S$: 326.0594; found: 326.0598.



methyl 2-ethyl-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4am): brown solid; mp 207-209 ℃; IR (KBr): 3507, 1686, 1638, 1611, 1487, 1448, 1312, 1185, 1134, 1034 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 11.16 (s, 1H), 8.72 (d, J = 9.0 Hz, 1H), 8.59 (d, J = 7.8 Hz, 1H), 7.71 (t, J = 8.4 Hz, 1H), 7.39 (t, J = 7.8 Hz, 1H), 4.01 (s, 3H), 2.98-2.94 (m, 2H), 1.48 (t, J = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.4, 156.4, 155.4, 145.5, 135.1, 132.8, 127.7, 124.0, 123.2, 118.9, 82.6, 51.3, 19.5, 10.8 ; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{14}N_3O_3$: 272.1030; found: 272.1028.

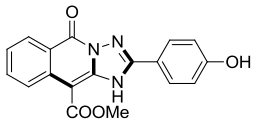


methyl 2-isobutyl-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4an): brown solid; mp >300 ℃; IR (KBr): 3508, 1695, 1664, 1611, 1543, 1483, 1450, 1297, 1184, 1134, 1031cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ = 12.52 (s, 1H), 8.79 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 7.61 (t, J = 7.2 Hz, 1H), 7.27 (t, J = 7.6 Hz, 1H), 3.85 (s, 3H), 2.72 (d, J = 7.2 Hz, 2H), 2.22-2.12 (m, 1H), 0.97 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 155.5, 154.2, 145.3, 135.4, 132.5, 127.2, 123.7, 122.8, 118.4, 81.3, 51.1, 33.8, 26.8, 22.1; HRMS (ESI): m/z $[M - H]^+$ calcd for $C_{16}H_{16}N_3O_3$: 298.1192; found: 298.1197.



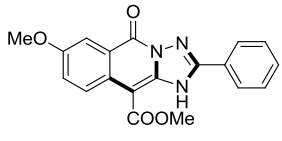
(E)-methyl 5-oxo-2-styryl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ao): yellow solid; mp 78-80 ℃; IR (KBr): 3459, 1702, 1653, 1606, 1485, 1455, 1297, 1147,

1030 ;cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.75 (s, 1H), 8.91 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 7.8 Hz, 1H), 7.94 (d, J = 16.8 Hz, 1H), 7.72 (d, J = 7.2 Hz, 3H), 7.48-7.47 (m, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 16.8 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.9, 155.5, 151.1, 145.5, 139.2, 135.4, 134.8, 132.7, 129.9, 129.0, 127.5, 127.3, 123.8, 122.9, 118.5, 111.6, 81.4, 51.2 ; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{20}H_{16}N_3O_3$: 346.1186; found: 346.1183.



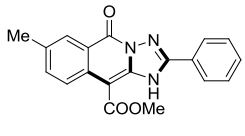
methyl

2-(4-hydroxyphenyl)-5-oxo-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ap): yellow solid, mp >300 ℃; IR (KBr): 3242, 1676, 1653, 1611, 1515, 1484, 1443, 1312, 1279, 1207, 1177, 1025 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.31 (s, 1H), 10.34 (s, 1H), 8.74 (d, J = 7.8 Hz, 1H), 8.19 (d, J = 7.2 Hz, 1H), 7.91 (d, J = 7.8 , 2H), 7.60-7.48 (m, 1H), 7.22 (t, J = 6.0 Hz, 1H), 6.92 (d, J = 7.8 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.8, 160.8, 155.5, 152.1, 145.8, 135.4, 132.5, 130.0, 127.1, 123.7, 122.9, 118.6, 115.7. 115.1, 81.7, 51.3 ; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{14}N_3O_4$: 336.0979; found: 336.0983.



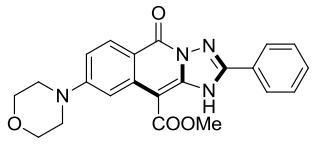
methyl

7-methoxy-5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ba): brown solid; mp 149-151 ℃; IR (KBr): 3448, 1726, 1697, 1644, 1605, 1555, 1497, 1447, 1312, 1154, 1024 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.73 (s, 1H), 8.91 (d, J = 9.0 Hz, 1H), 8.16 (d, J = 7.2 Hz, 2H), 7.71 (s, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.65 (d, J = 7.2 Hz, 2H), 7.40 (d, J = 9.0 Hz, 1H), 3.92 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 164.7, 155.2, 155.0, 152.0, 144.5, 131.9, 129.6, 128.8, 128.3, 125.6, 124.7, 123.1, 119.6, 106.4, 81.7, 55.1, 51.3; HRMS (ESI): m/z [M + Na]$^+$ calcd for $C_{19}H_{15}N_3O_4Na$: 372.0955; found: 372.0956.

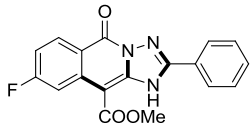


methyl

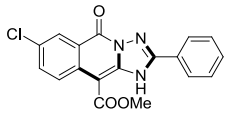
7-methyl-5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ca): yellow solid; mp 133-135 ℃; IR (KBr): 3435, 1705, 1655, 1617, 1594, 1500, 1456, 1300, 1213, 1148, 1028 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.57 (s, 1H), 8.72 (d, J = 8.4 Hz, 1H), 8.10 (d, J = 7.8 Hz, 2H), 8.02 (s, 1H), 7.65 (t, J = 7.2 Hz, 1H), 7.61 (t, J = 7.2 Hz, 2H), 7.44 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 167.8, 155.4, 151.9, 145.3, 134.3, 133.2, 132.4, 131.9, 128.8, 128.2, 126.4, 124.6, 123.7, 118.6, 81.7, 51.3, 20.5; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{19}H_{16}N_3O_3$: 334.1186; found: 334.1192.



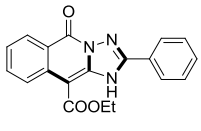
methyl 8-morpholino-5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4da): brown solid; mp 235-237 ℃; IR (KBr): 3435, 1688, 1645, 1607, 1496, 1457, 1298, 1236, 1154, 1121, 1031cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.36 (s, 1H), 8.43 (d, J = 9.6 Hz, 1H), 8.07 (s, 1H), 8.03 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.2 Hz, 1H), 7.55 (t, J = 7.8 Hz, 2H), 6.97 (d, J = 9.0 Hz, 1H), 4.03 (s, 3H), 3.89-3.85 (m, 4H), 3.39-3.35 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 165.0, 155.1, 154.1, 151.6, 146.4, 137.5, 131.8, 128.9, 128.7, 128.2, 124.8, 112.5, 110.8, 105.2, 81.1, 66.0, 51.3, 47.2; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{22}H_{21}N_4O_4$: 405.1557; found: 405.1562.



methyl 8-fluoro-5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ea): yellow solid; >300 ℃; IR (KBr): 3485, 1683, 1643, 1616, 1552, 1500, 1476, 1409, 1320, 1262, 1226, 1181, 1102, 1029 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.60 (s, 1H), 8.63 (t, J = 7.8 Hz, 1H), 8.40-8.35 (m, 1H), 8.08 (d, J = 7.2 Hz, 2H), 7.63 (t, J = 7.2 Hz, 1H), 7.59 (t, J = 7.2 Hz, 2H), 7.12 (t, J = 8.4 Hz, 1H), 4.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.4, 164.8, 155.6, 150.9, 147.1, 137.2, 137.0, 132.5, 131.7, 131.6, 129.3, 127.0, 123.8, 116.5, 112.7, 112.5, 109.8, 109.6, 82.4, 51.9; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{13}FN_3O_3$: 338.0935; found: 338.0935.

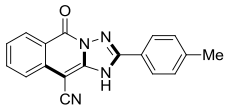


methyl 7-chloro-5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4fa): yellow solid; >300 ℃; IR (KBr): 3417, 1716, 1689, 1625, 1487, 1455, 1316, 1287, 1179, 1025 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 12.87 (s, 1H), 8.89 (d, J = 9.0 Hz, 1H), 8.17 (s, 1H), 8.13 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.65 (t, J = 7.2 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ =164.4, 154.5, 152.5, 145.9, 134.2, 132.6, 132.0, 128.8, 128.4, 127.5, 126.0, 125.7, 124.5, 119.6, 81.8, 51.4; HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{18}H_{13}ClN_3O_3$: 354.0640; found: 354.0643.

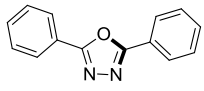


ethyl 5-oxo-2-phenyl-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carboxylate (4ga): yellow solid; mp 236-238 ℃; IR (KBr): 3439, 1691, 1648, 1610, 1552, 1479, 1451, 1369, 1307, 1180, 1157, 1028 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 11.59 (s, 1H), 8.74 (d, J = 8.4 Hz, 1H), 8.61 (d, J = 7.8 Hz, 1H), 8.07 (d, J = 7.2 Hz, 2H), 7.71 (t, J = 7.2 Hz, 1H), 7.61 (d, J = 6.6 Hz, 1H), 7.58 (d, J = 7.2 Hz, 2H), 7.39 (t, J = 7.2 Hz, 1H), 4.53-4.49 (m, 2H), 1.53 (t, J = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6): δ =

164.8, 155.6, 152.2, 146.2, 135.5, 132.9, 132.0, 128.9, 128.2, 127.3, 124.6, 123.9, 123.2, 118.7, 82.2, 60.0, 14.6; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{16}N_3O_3$: 334.1186; found: 334.1187.

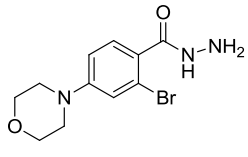


5-oxo-2-(p-tolyl)-1,5-dihydro-[1,2,4]triazolo[1,5-b]isoquinoline-10-carbonitrile (4ha): yellow solid, mp >300 ℃; IR (KBr): 3462, 2206, 1610, 1580, 1536, 1488, 1419, 1369, 1052, 1027 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6): δ = 8.26 (d, J = 7.8 Hz, 1H), 8.15 (d, J = 7.2 Hz, 2H), 7.62 (t, J = 7.2 Hz, 2H), 7.30 (d, J = 7.2 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 162.0, 157.0, 154.4, 139.7, 137.7, 131.9, 129.2, 128.3, 127.7, 127.2, 121.5, 120.2, 119.8, 115.2, 63.3, 21.1; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{18}H_{12}N_4ONa$: 323.0903; found: 323.0908.



2,5-diphenyl-1,3,4-oxadiazole[3]

white solid; mp 139-141 ℃; IR (KBr): 1547, 1480, 1444, 1264,1069, 1024 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.20-8.12 (m, 4H), 7.58-7.51 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.4, 131.6, 128.9, 126.8, 123.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{14}H_{11}N_2O$: 223.0866; found: 223.0867.



2-bromo-4-morpholinobenzohydrazide

colourless solid; mp 207-209 ℃; IR (KBr): 3317, 3275, 2962, 2837, 1601, 1527, 1494, 1453, 1384, 1335, 1307, 1239, 1120, 1026 cm^{-1};
^1H NMR (400 MHz, DMSO-d_6): δ = 9.47-9.27 (m, 1H), 7.23-7.17 (m, 1H), 7.12-7.08 (m, 1H), 6.94 (d, J = 8.4 Hz, 1H), 4.40-4.36 (m, 2H), 3.83-3.52 (m, 4H), 3.24-2.98 (m, 4H);
^{13}C NMR (100 MHz, DMSO-d_6): δ = 166.6, 152.4, 129.8, 126.9, 120.7, 118.0, 113.0, 65.8, 47.4. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{11}H_{15}BrN_3O_2$: 300.0342; found: 300.0342.

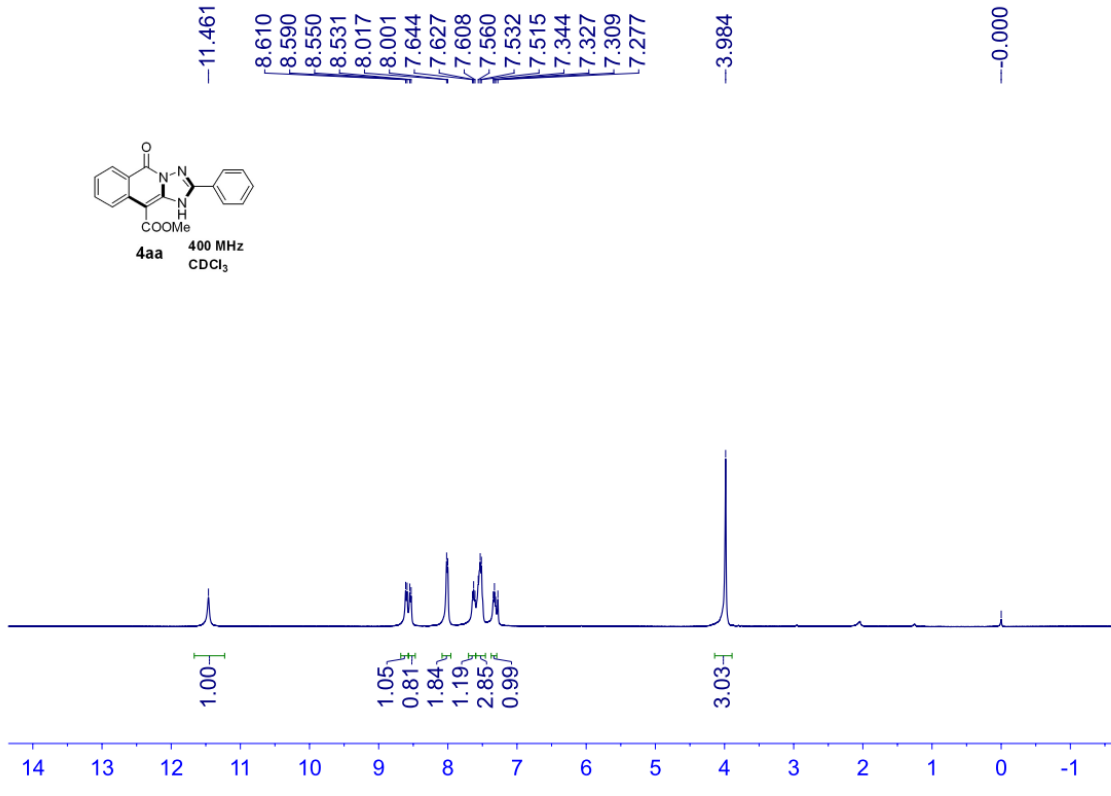
7. Reference

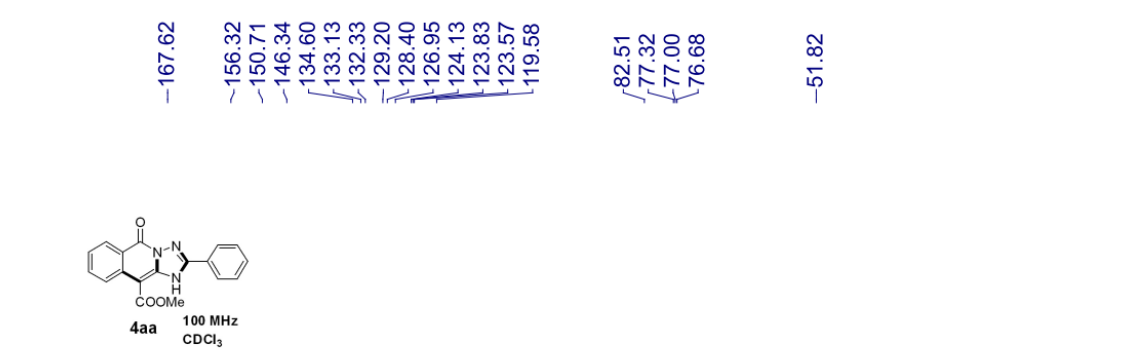
(1) Shailaja M, Anitha M, Manjula A, Vittal Rao B. *Indian Journal of Chemistry*. **2010**, *48B*, 1088.

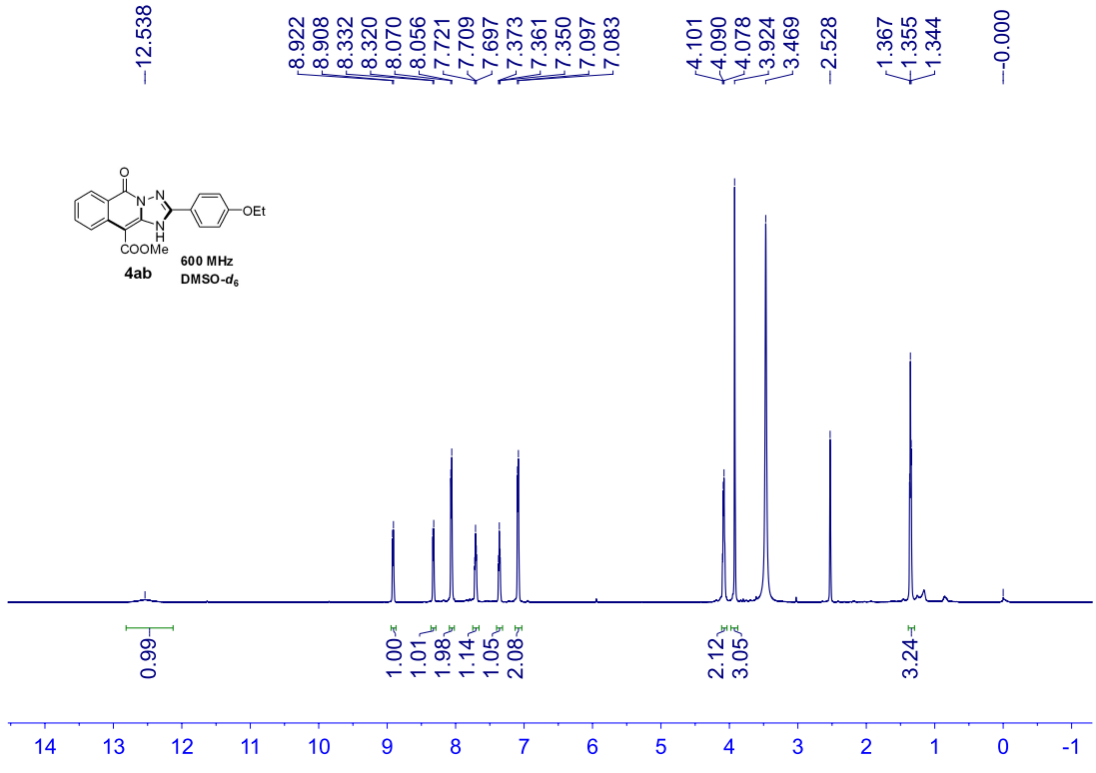
(2) Vlaar, T.; Mampuys, P.; Helliwell, M.; Maes, B. U. W.; Orru, R. V. A.; Ruijter, E. *J. Org. Chem*. **2013**, 78, 6735.

(3) Guin, S.; Ghosh, T.; Rout, S. K.; Banerjee, A.; Patel, B. K. *Org. Lett*. **2011**, 13, 5976.

8. Appendix: spectral copies of ^{1}H NMR, and ^{13}C NMR



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7.697
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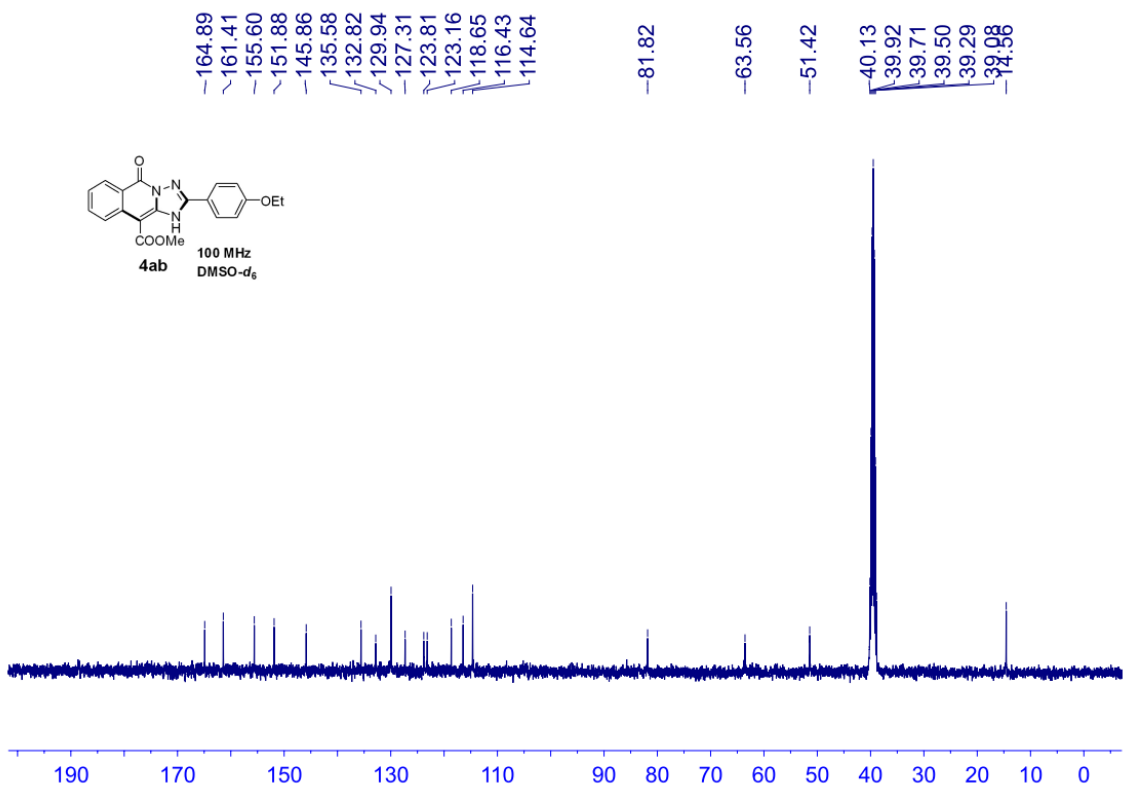
7.350
7.097
7.083
4.101
4.090
4.078
3.924
3.469
2.528
1.367
1.355
1.344
0.000
OEt
COOMe
4ab
600 MHz
DMSO-d6
0.99
1.00
1.01
1.98
1.14
1.05
2.08
2.12
3.05
3.24
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1


164.89
161.41
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132.82
129.94
127.31
123.81
123.16
118.65
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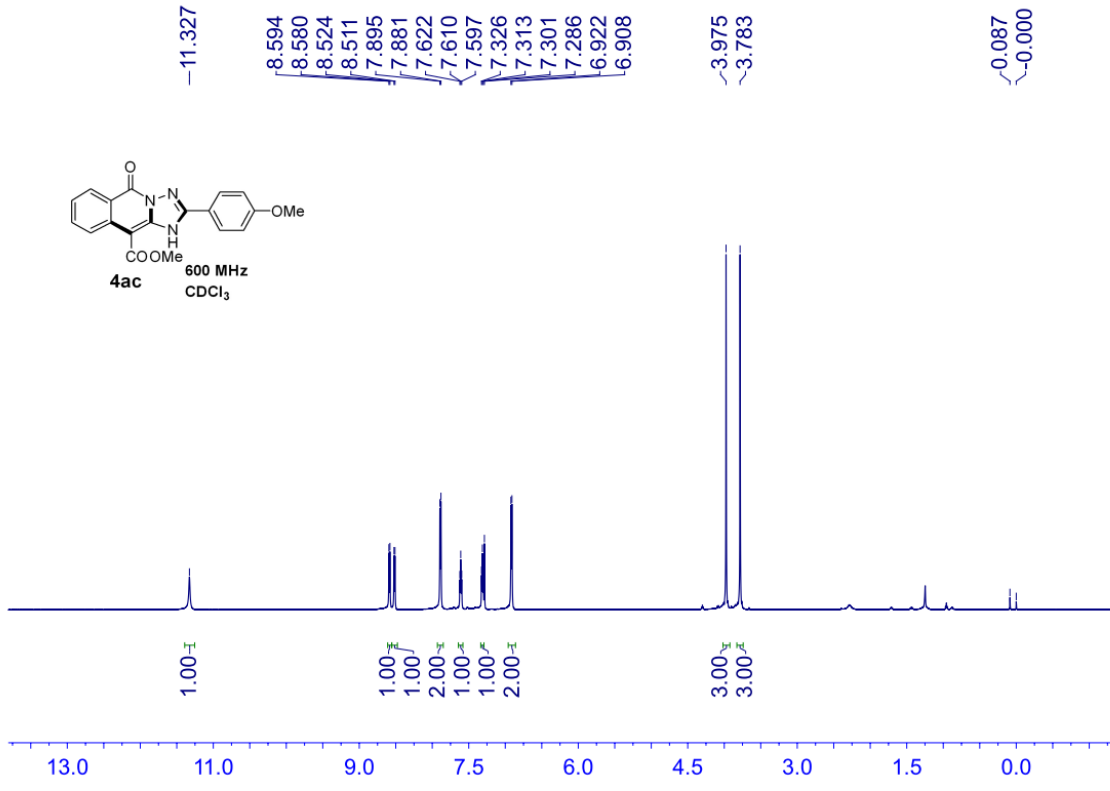
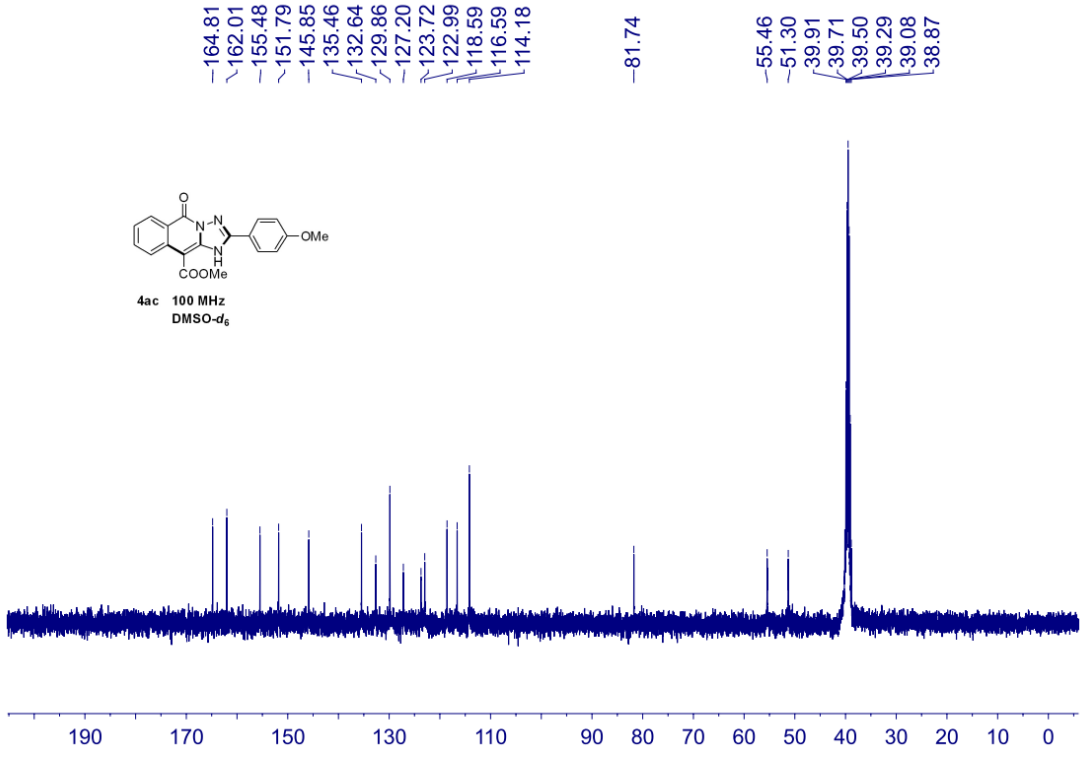
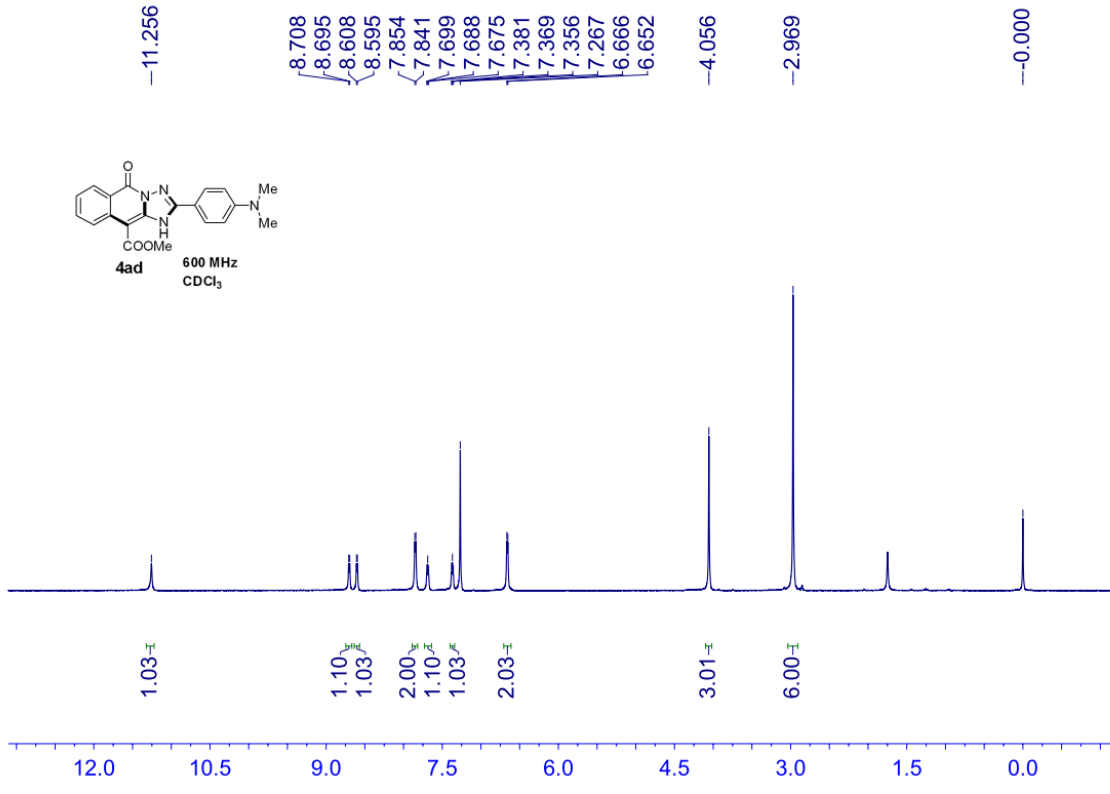
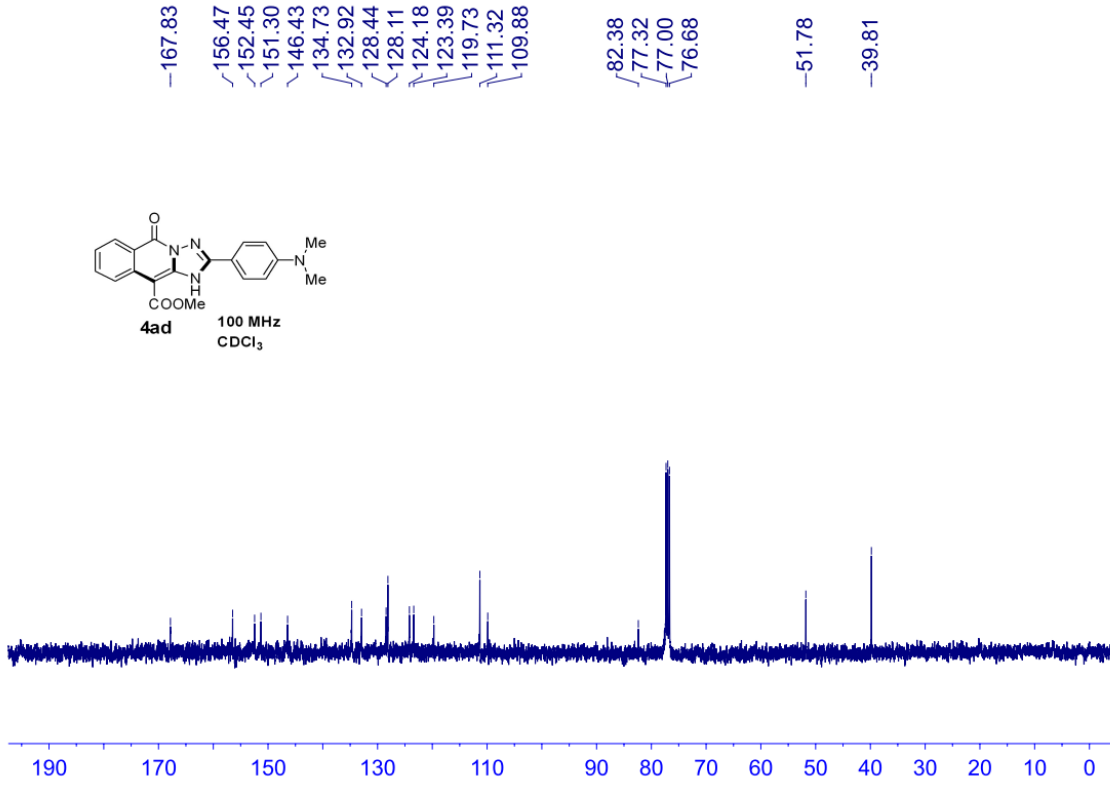
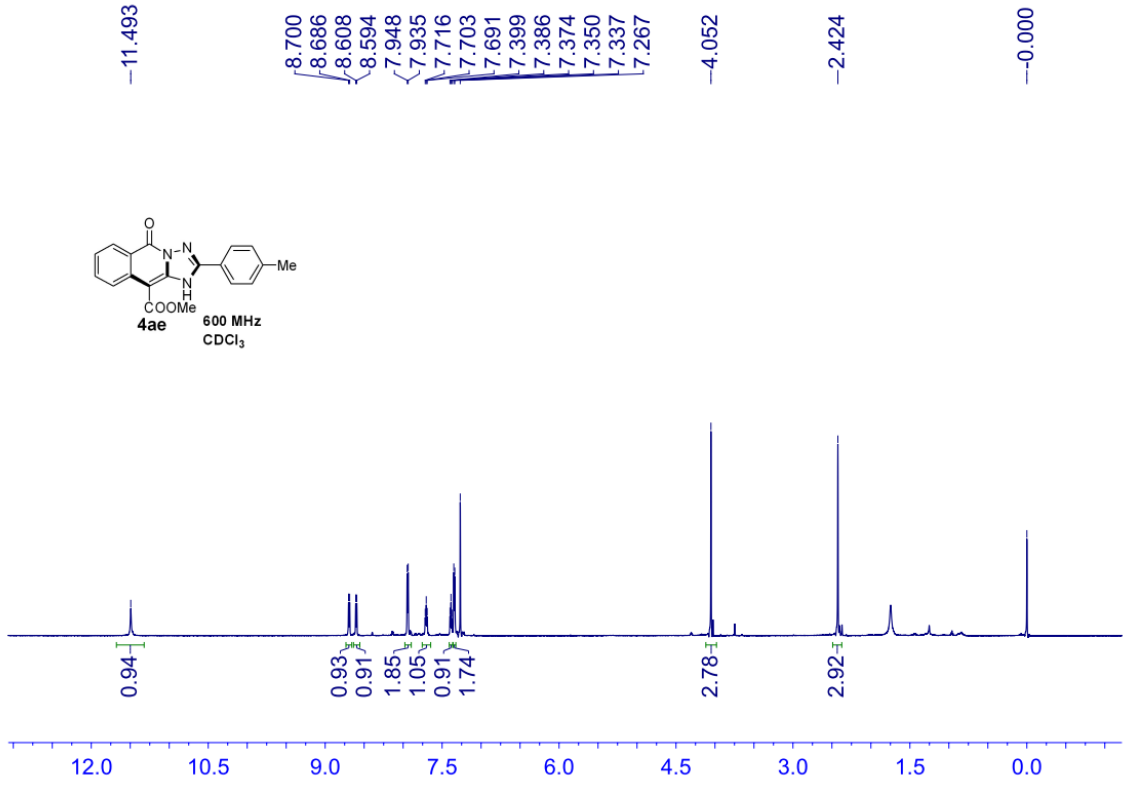
114.64
81.82
63.56
51.42
40.13
39.92
39.71
39.50
39.29
39.08
14.56
OEt
COOMe
4ab
100 MHz
DMSO-d6
190 170 150 130 110 90 80 70 60 50 40 30 20 10 0

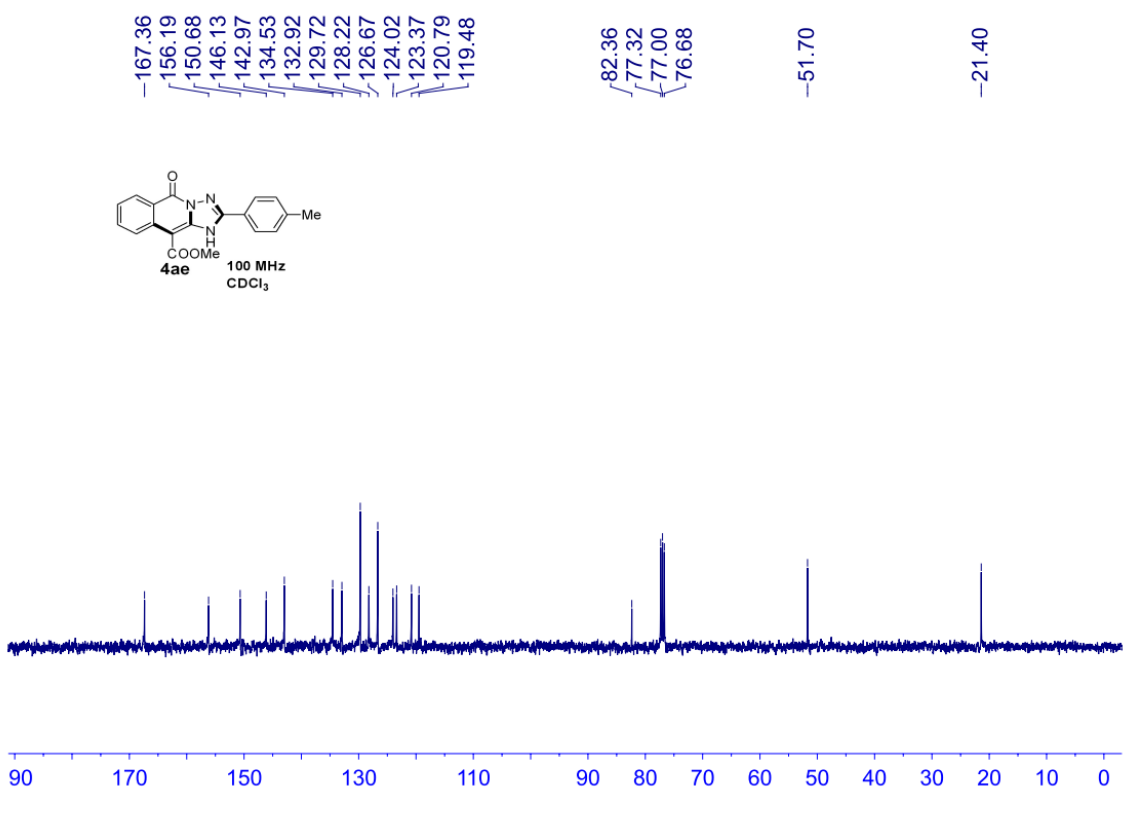

11.327
8.594
8.580
8.524
8.511
7.895
7.881
7.622
7.610
7.597
7.326
7.313
7.301
7.286
6.922
6.908
3.975
3.783
0.087
-0.000
OMe
COOMe
4ac
600 MHz
CDCl3
1.00
1.00
1.00
2.00
1.00
1.00
2.00
3.00
3.00
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0

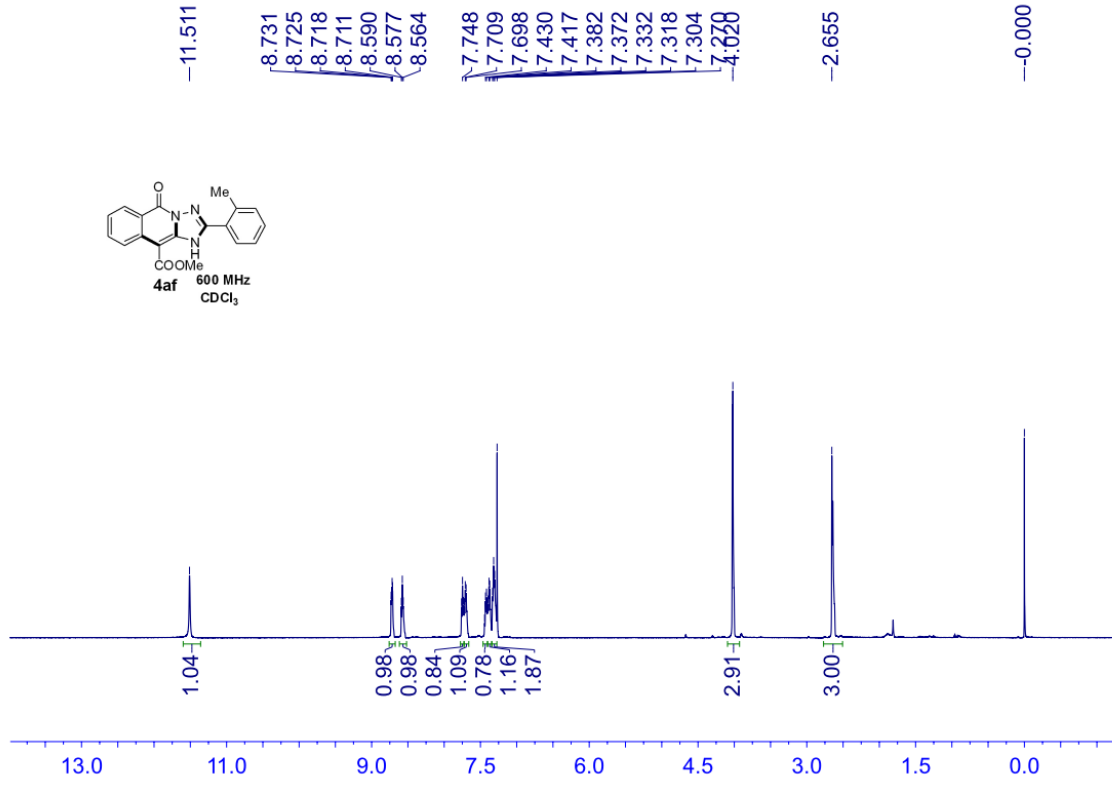

164.81
162.01
155.48
151.79
145.85
135.46
132.64
129.86
127.20
123.72
122.99
118.59
116.59
114.18
81.74
55.46
51.30
39.91
39.71
39.50
39.29
39.08
38.87
OMe
COOMe
4ac 100 MHz
DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

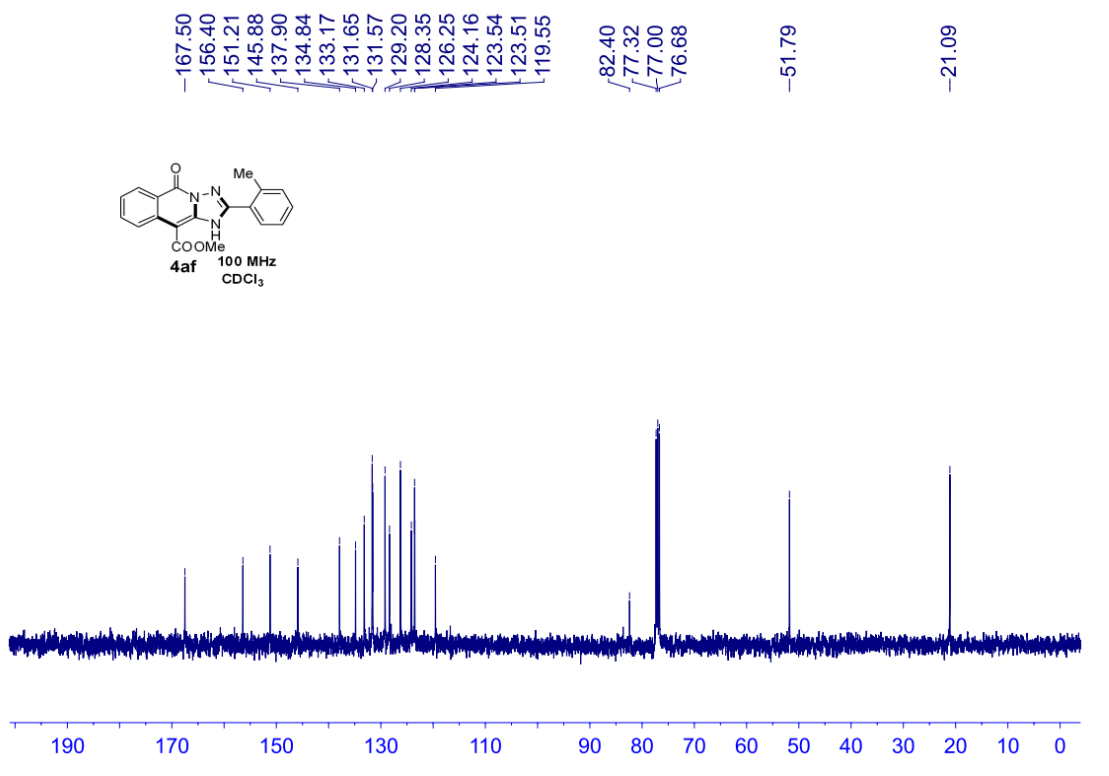

11.256
8.708
8.695
8.608
8.595
7.854
7.841
7.699
7.688
7.675
7.381
7.369
7.356
7.267
6.666
6.652
4.056
2.969
0.000
4ad
600 MHz
CDCl3
1.03
1.10
1.03
2.00
1.10
1.03
2.03
3.01
6.00
12.0
10.5
9.0
7.5
6.0
4.5
3.0
1.5
0.0

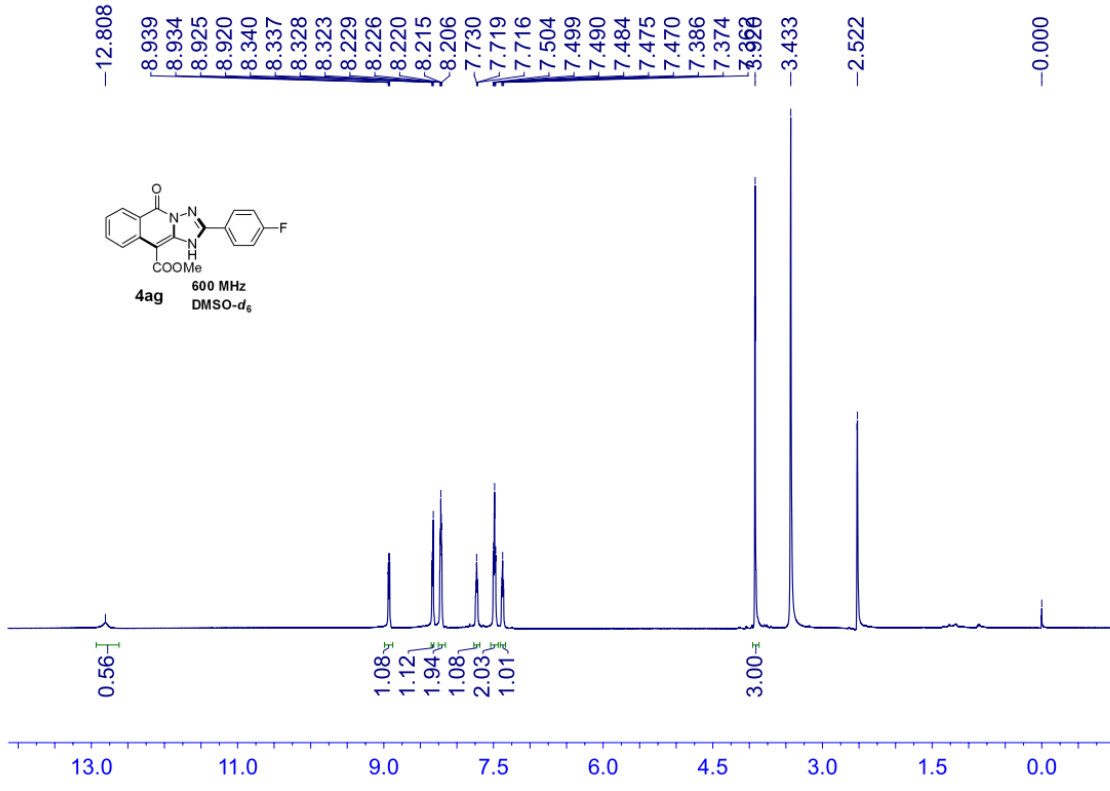

167.83
156.47
152.45
151.30
146.43
134.73
132.92
128.44
128.11
124.18
123.39
119.73
111.32
109.88
82.38
77.32
77.00
76.68
51.78
39.81
4ad
100 MHz
CDCl3
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0


11.493
8.700
8.686
8.608
8.594
7.948
7.935
7.716
7.703
7.691
7.399
7.386
7.374
7.350
7.337
7.267
4.052
2.424
0.000
Me
COOMe
4ae
600 MHz
CDCl3
0.94
0.93
0.91
1.85
1.05
0.91
1.74
2.78
2.92
12.0
10.5
9.0
7.5
6.0
4.5
3.0
1.5
0.0

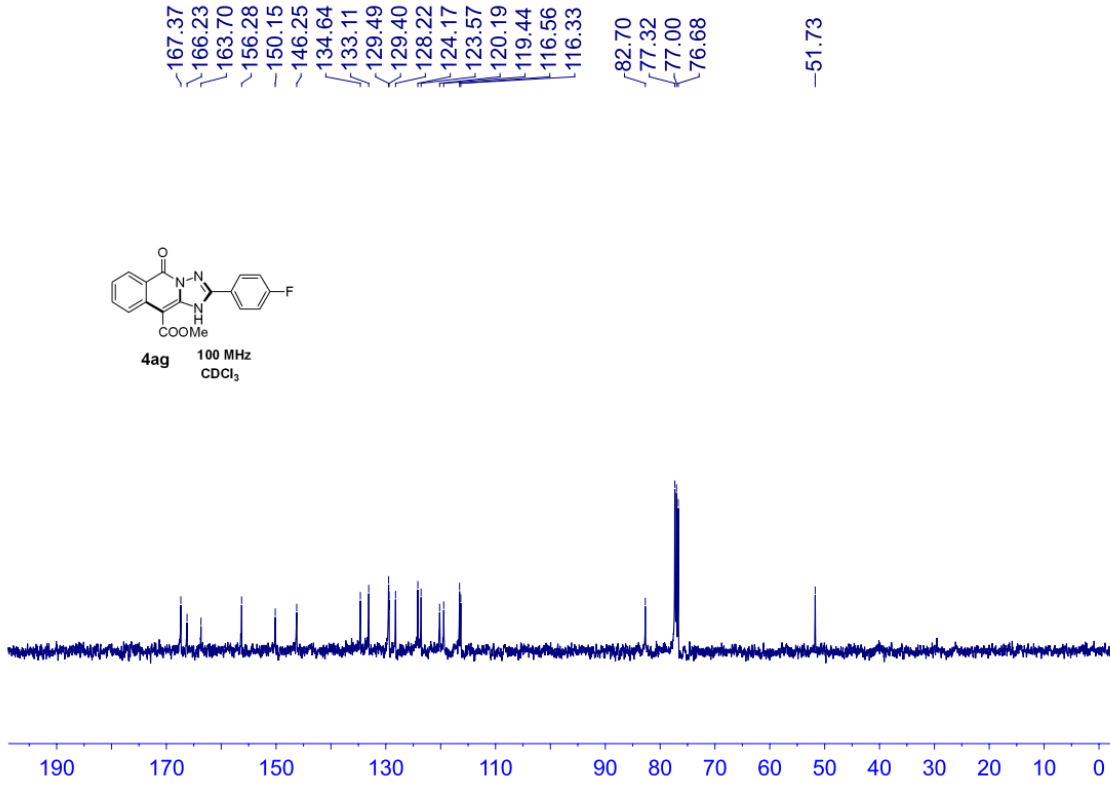

167.36
156.19
150.68
146.13
142.97
134.53
132.92
129.72
128.22
126.67
124.02
123.37
120.79
119.48
82.36
77.32
77.00
76.68
51.70
21.40
Me
COOMe
4ae
100 MHz
CDCl3
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0


11.511
8.731
8.725
8.718
8.711
8.590
8.577
8.564
7.748
7.709
7.698
7.430
7.417
7.382
7.372
7.332
7.318
7.304
4.020
2.655
0.000
Me
COOMe
4af
600 MHz
CDCl3
1.04
0.98
0.98
0.84
1.09
0.78
1.16
1.87
2.91
3.00
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0

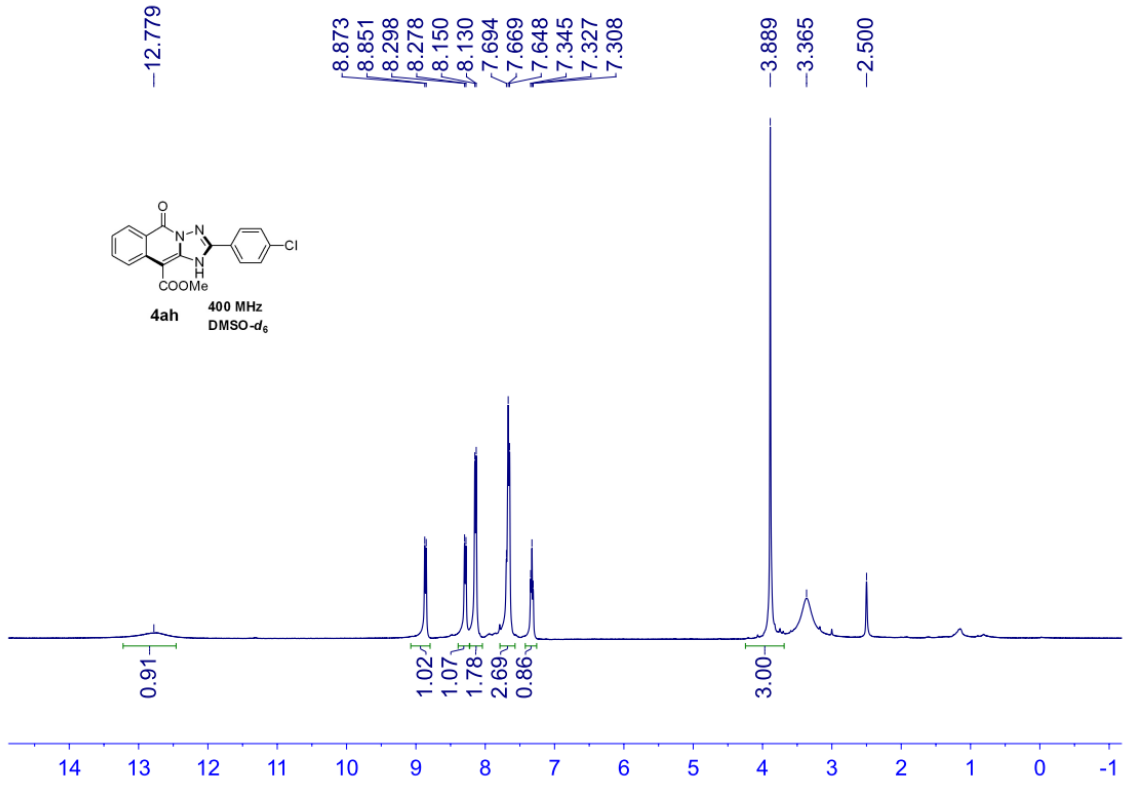

167.50
156.40
151.21
145.88
137.90
134.84
133.17
131.65
131.57
129.20
128.35
126.25
124.16
123.54
123.51
119.55
82.40
77.32
77.00
76.68
51.79
21.09
Me
COOMe
4af
100 MHz
CDCl3
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

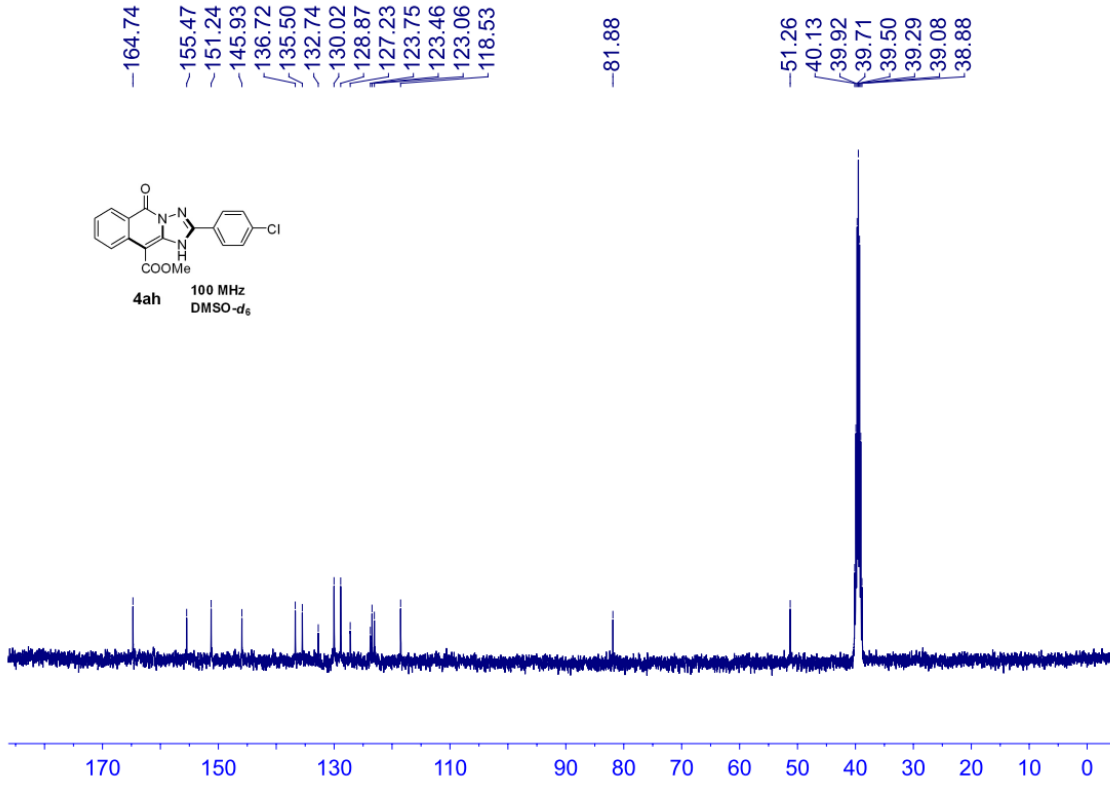


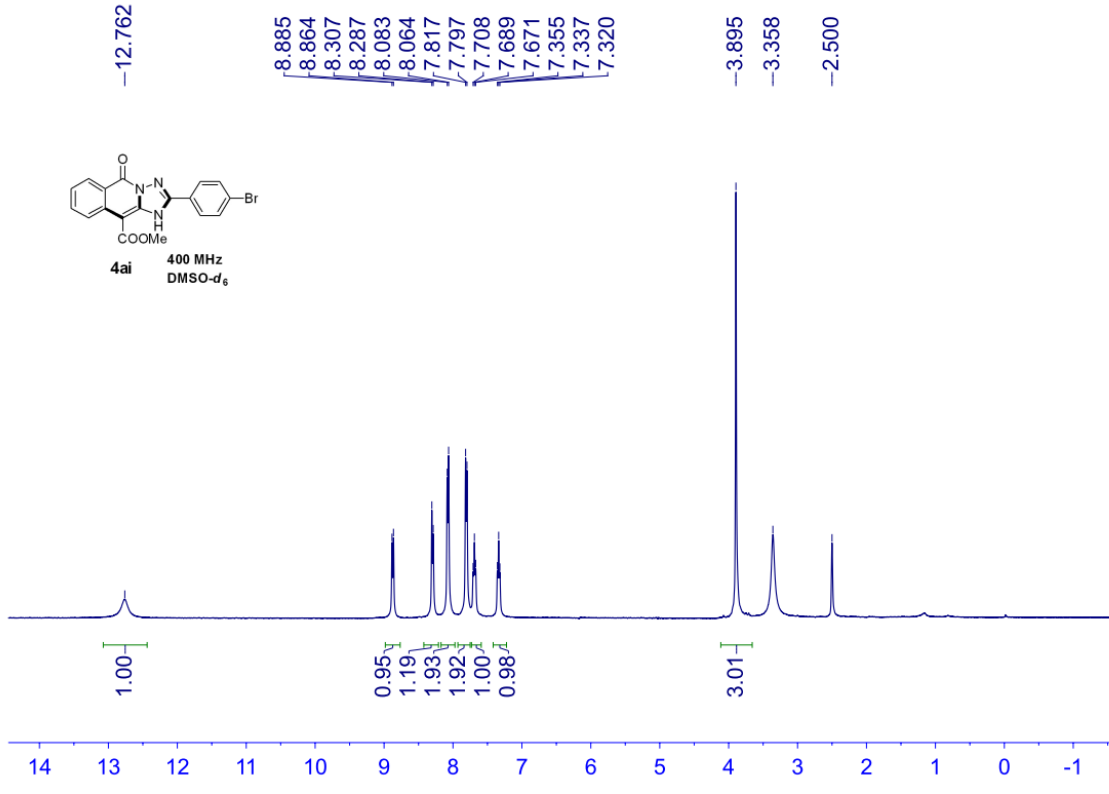
4ag **600 MHz DMSO-d_6**

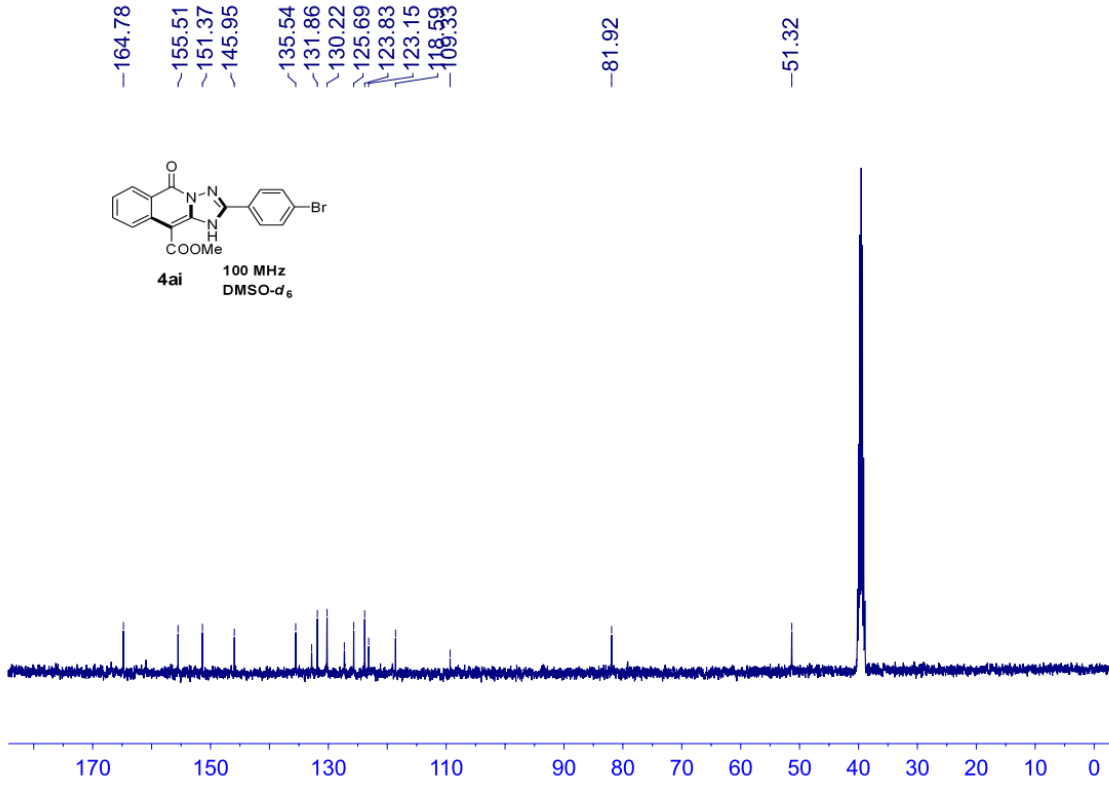


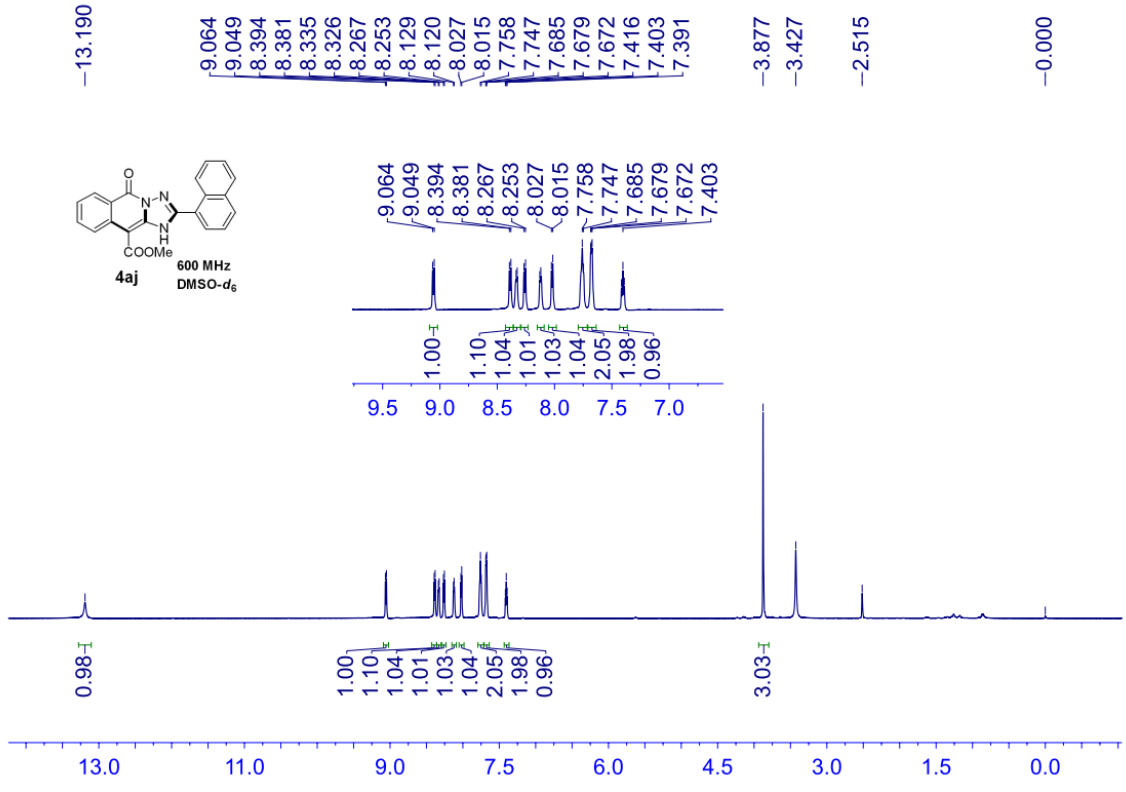
4ag **100 MHz $CDCl_3$**

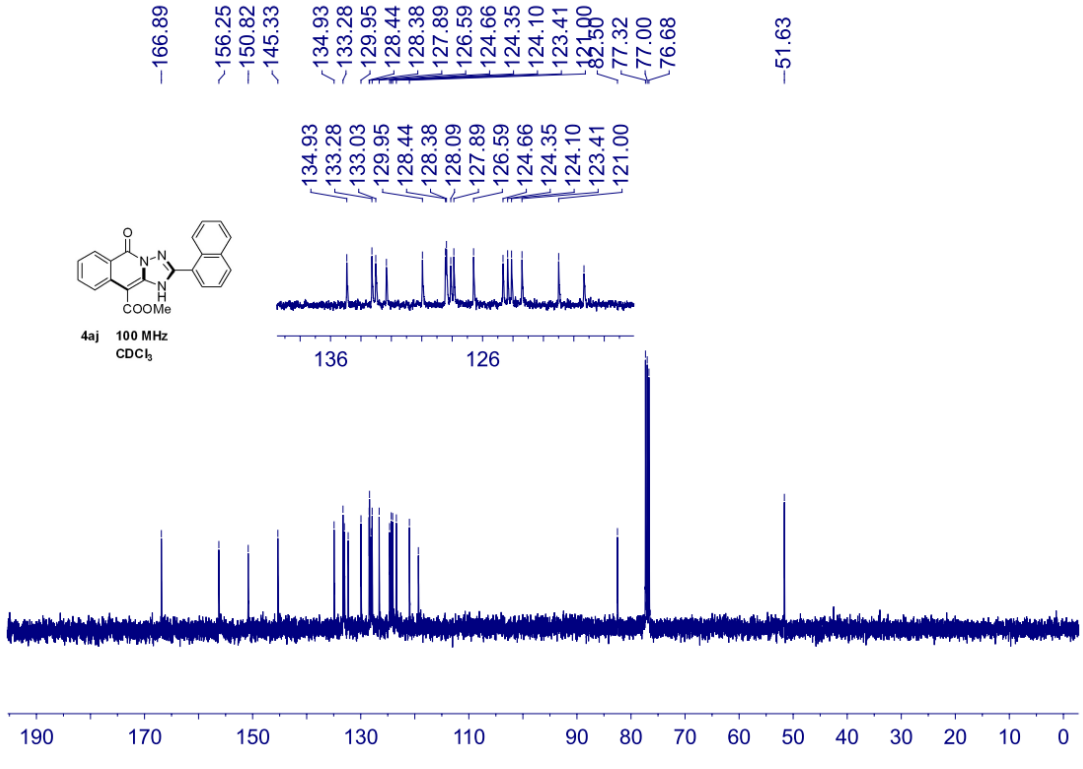

12.779
8.873
8.851
8.298
8.278
8.150
8.130
7.694
7.669
7.648
7.345
7.327
7.308
3.889
3.365
2.500
4ah
400 MHz
DMSO-d_6
0.91
1.02
1.07
1.78
2.69
0.86
3.00

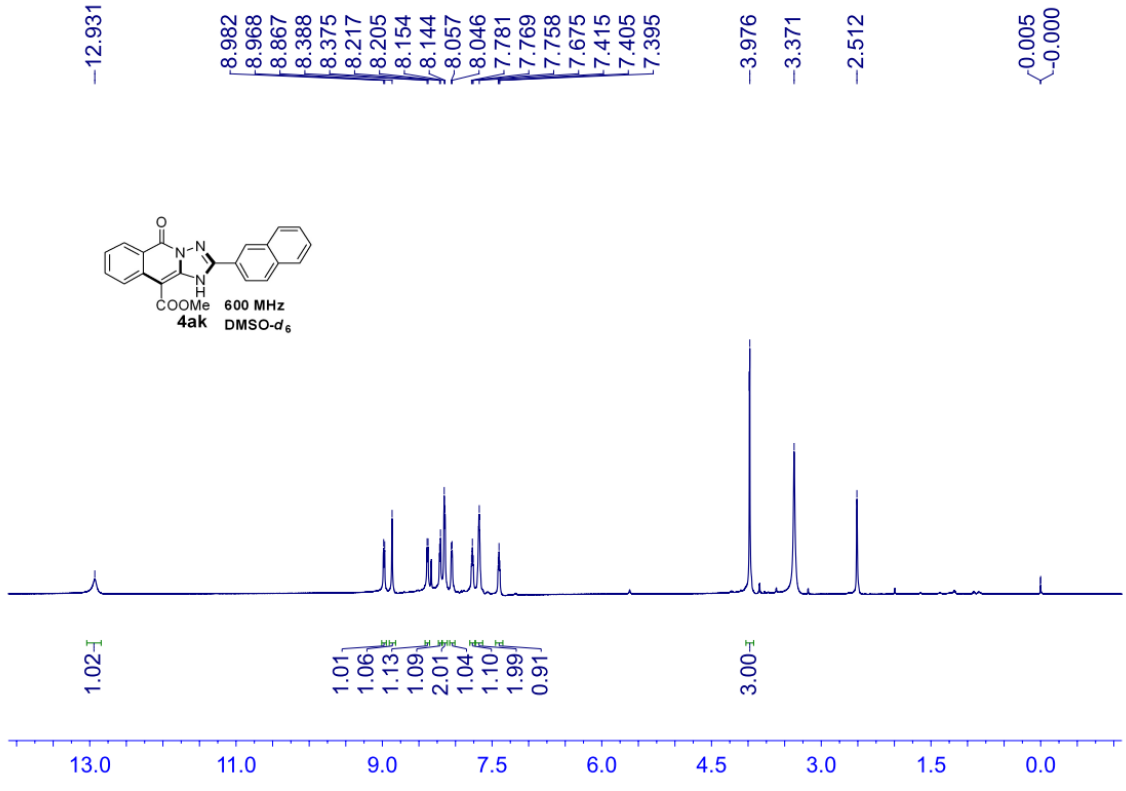

164.74
155.47
151.24
145.93
136.72
135.50
132.74
130.02
128.87
127.23
123.75
123.46
123.06
118.53
81.88
51.26
40.13
39.92
39.71
39.50
39.29
39.08
38.88
4ah
100 MHz
DMSO-d_6

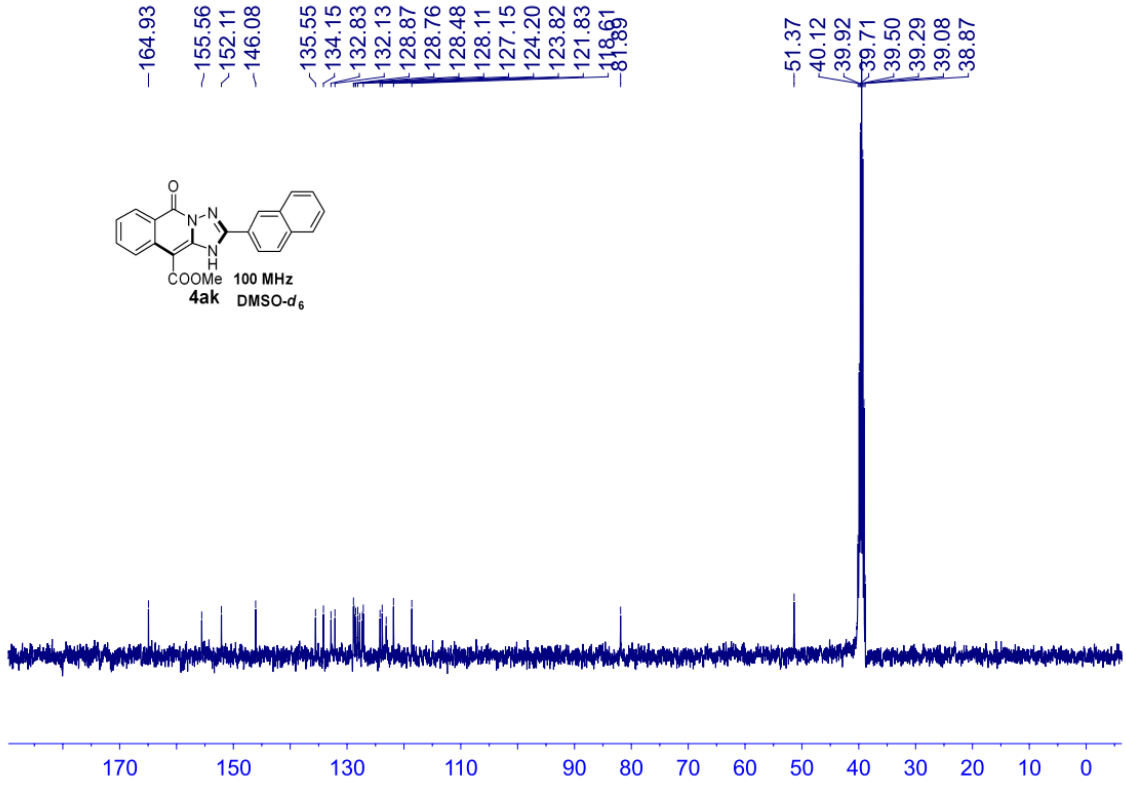

12.762
8.885
8.864
8.307
8.287
8.083
8.064
7.817
7.797
7.708
7.689
7.671
7.355
7.337
7.320
3.895
3.358
2.500
4ai
400 MHz
DMSO-d6
1.00
0.95
1.19
1.93
1.92
1.00
0.98
3.01

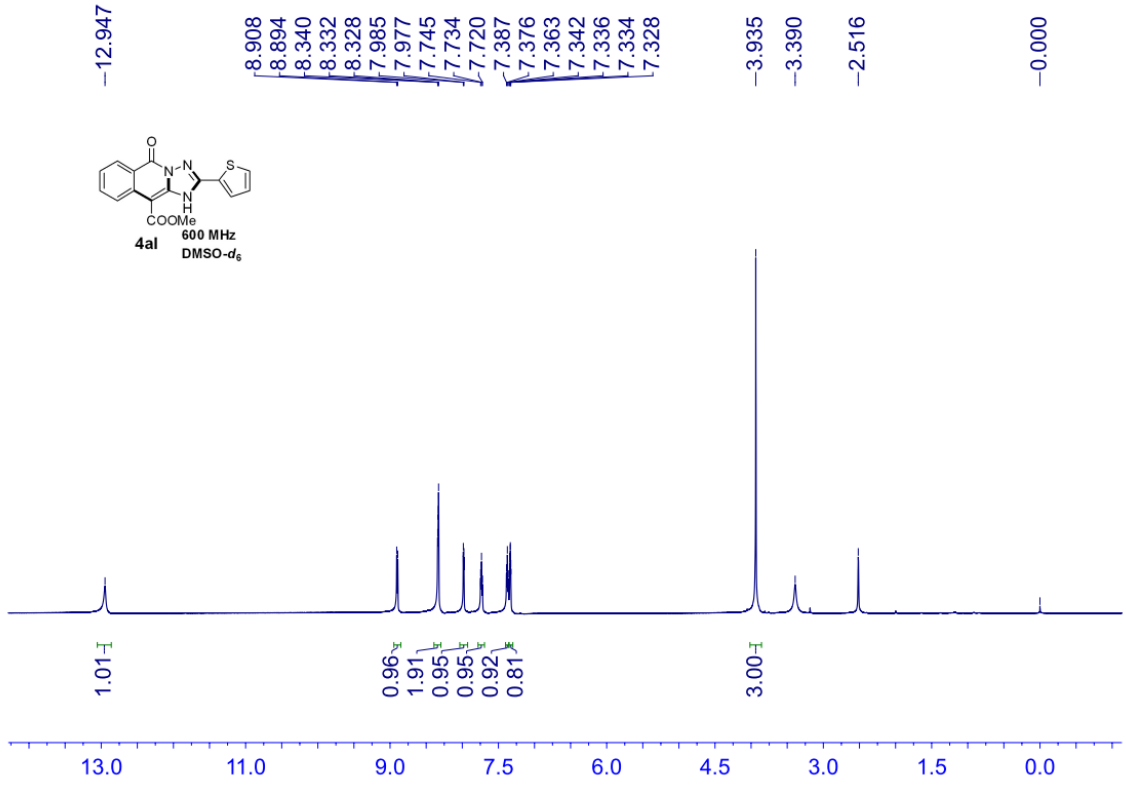

164.78
155.51
151.37
145.95
135.54
131.86
130.22
125.69
123.83
123.15
118.59
109.33
81.92
51.32
4ai
100 MHz
DMSO-d6

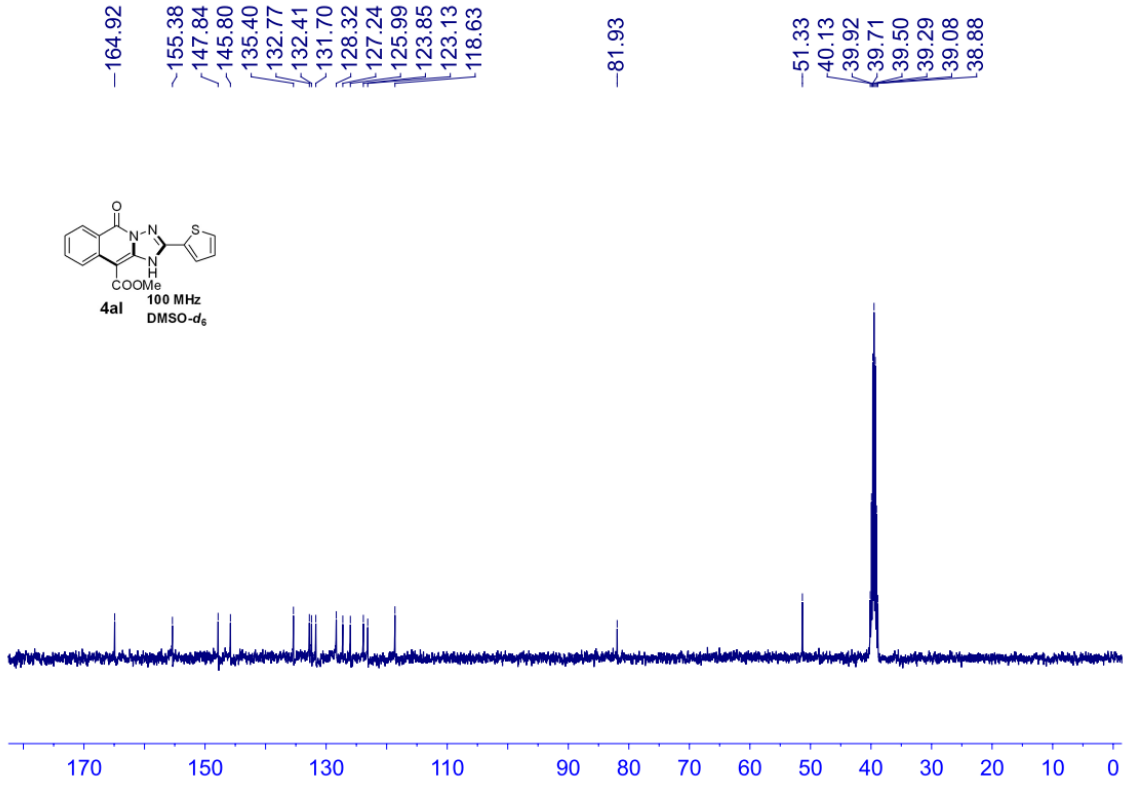

13.190
9.064
9.049
8.394
8.381
8.335
8.326
8.267
8.253
8.129
8.120
8.027
8.015
7.758
7.747
7.685
7.679
7.672
7.416
7.403
7.391
3.877
3.427
2.515
0.000
4aj
600 MHz
DMSO-d6
0.98
1.00
1.10
1.04
1.01
1.03
1.04
2.05
1.98
0.96
3.03
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0


166.89
156.25
150.82
145.33
134.93
133.28
129.95
128.44
128.38
127.89
126.59
124.66
124.35
124.10
123.41
121.00
82.50
77.32
77.00
76.68
51.63
4aj
100 MHz
CDCl3
136
126
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

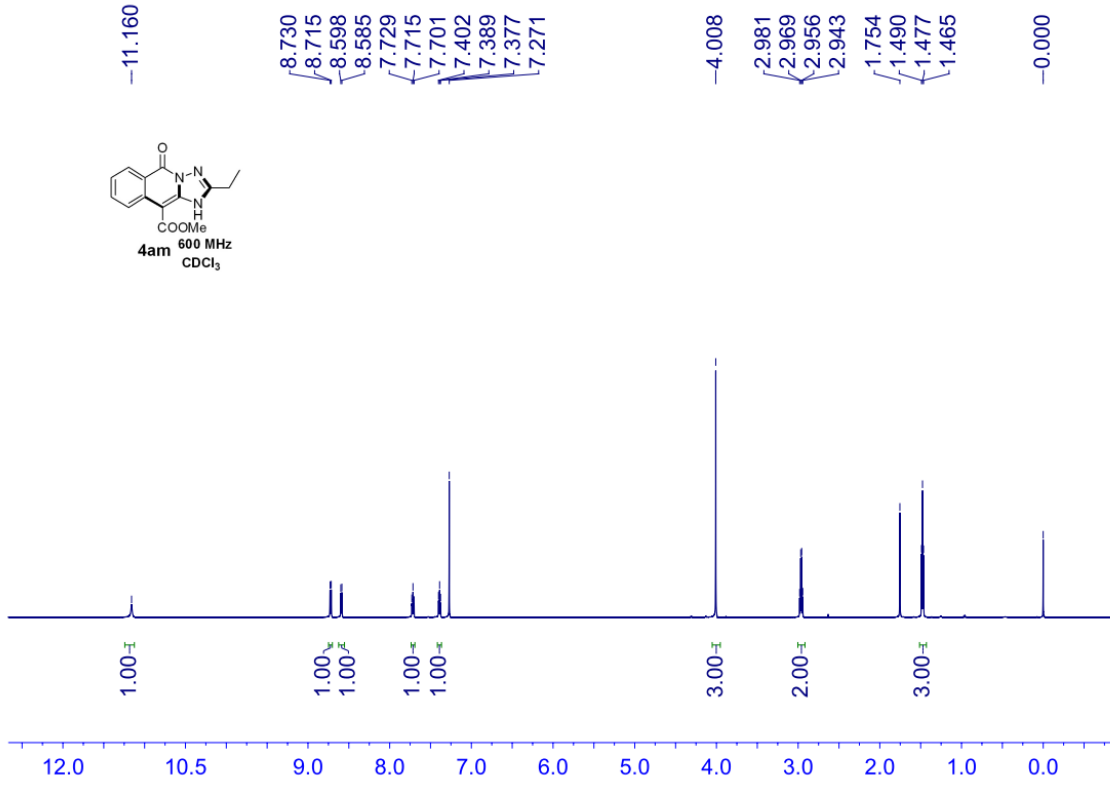

12.931
8.982
8.968
8.867
8.388
8.375
8.217
8.205
8.154
8.144
8.057
8.046
7.781
7.769
7.758
7.675
7.415
7.405
7.395
3.976
3.371
2.512
0.005
0.000
COOMe
4ak
600 MHz
DMSO-d6
1.02
1.01
1.06
1.13
1.09
2.01
1.04
1.10
1.99
0.91
3.00
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0

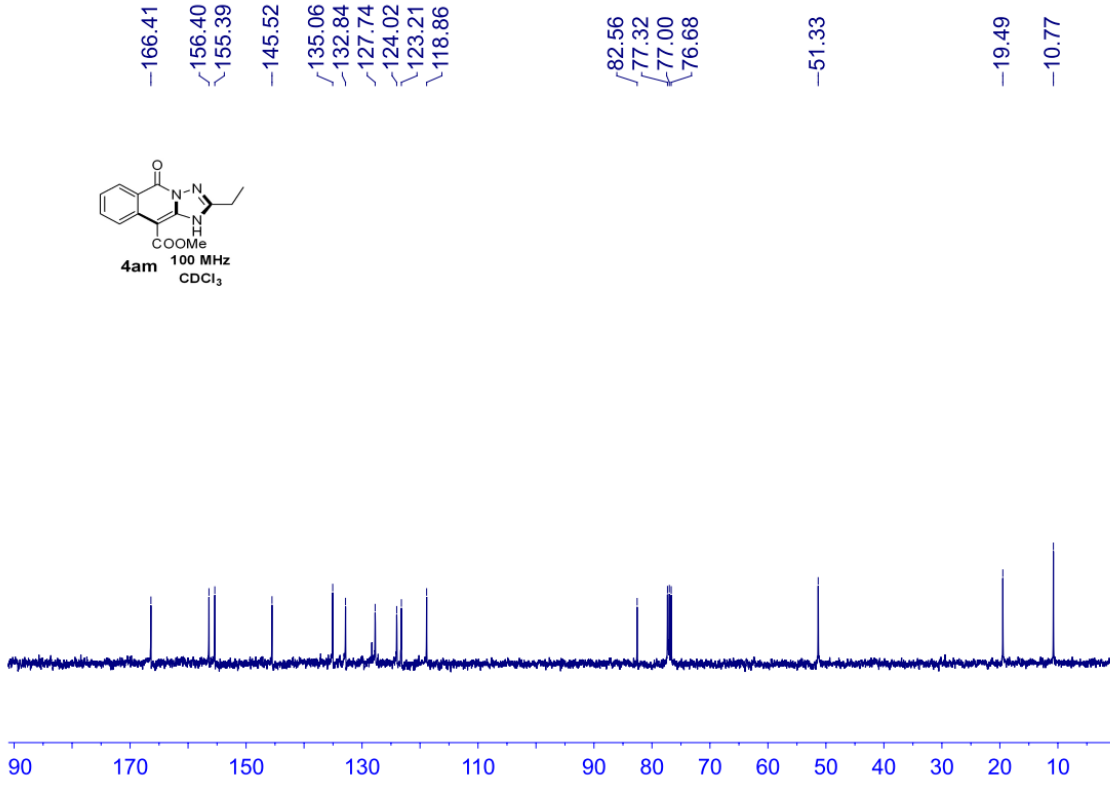

164.93
155.56
152.11
146.08
135.55
134.15
132.83
132.13
128.87
128.76
128.48
128.11
127.15
124.20
123.82
121.83
118.61
81.89
51.37
40.12
39.92
39.71
39.50
39.29
39.08
38.87
COOMe
4ak
100 MHz
DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0

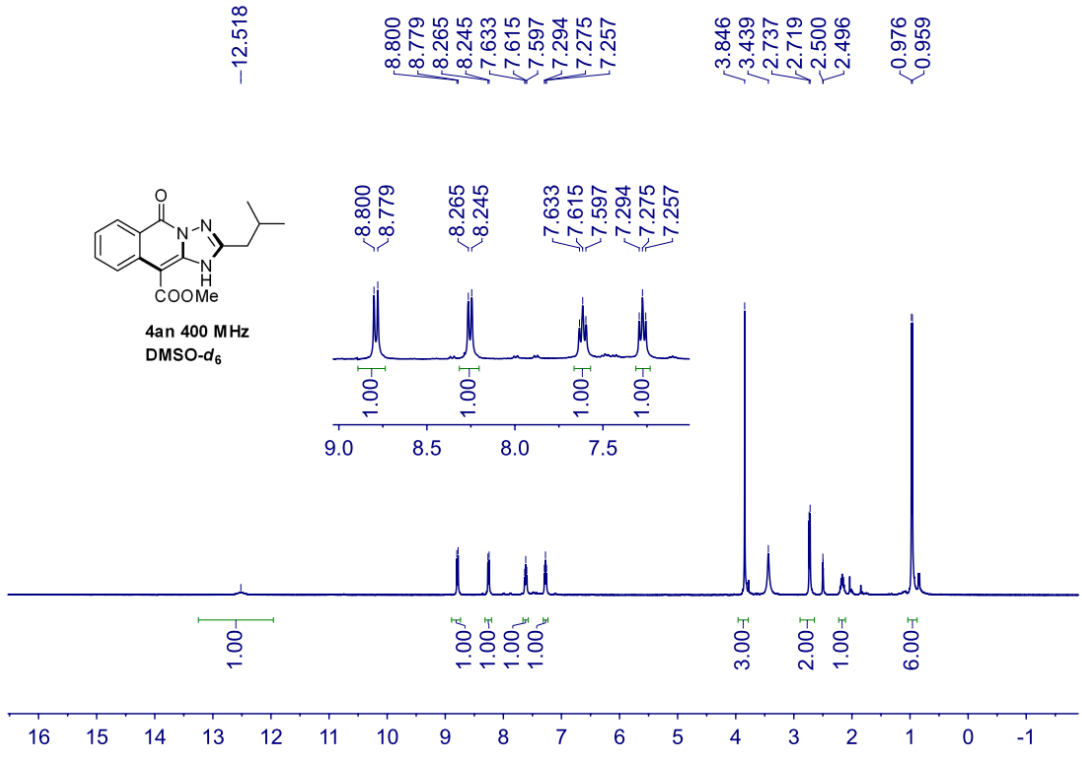

12.947
8.908
8.894
8.340
8.332
8.328
7.985
7.977
7.745
7.734
7.720
7.387
7.376
7.363
7.342
7.336
7.334
7.328
3.935
3.390
2.516
0.000
4al
600 MHz
DMSO-d6
1.01
0.96
1.91
0.95
0.95
0.92
0.81
3.00
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0

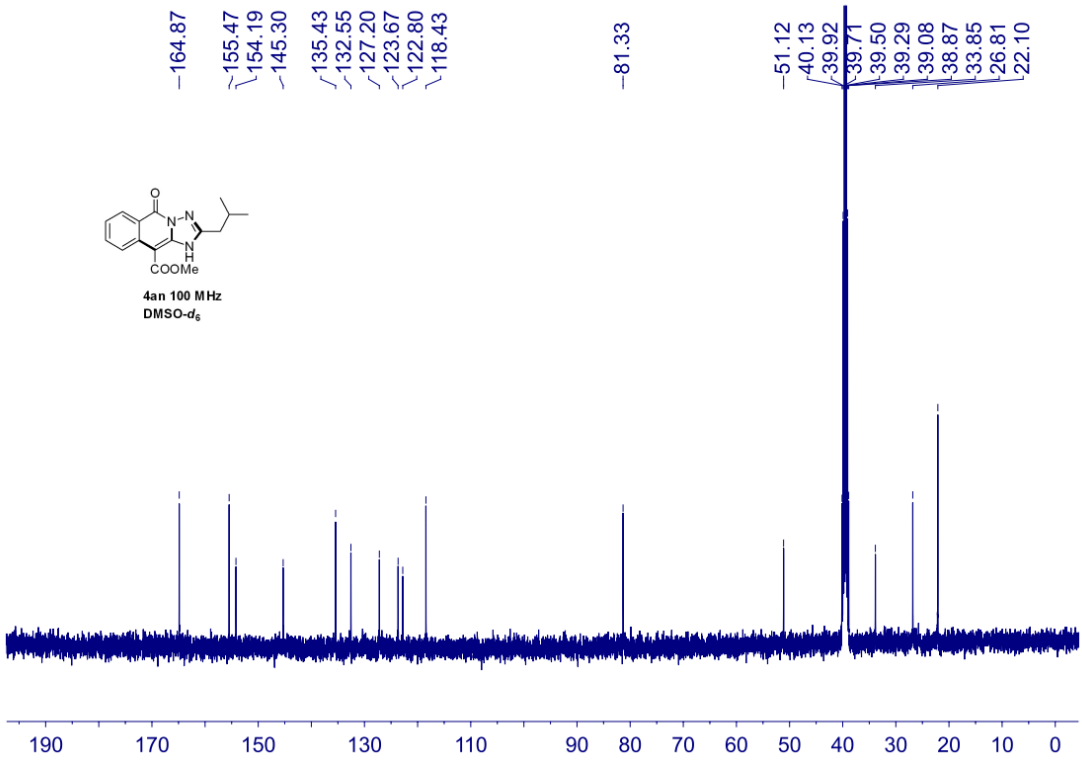

164.92
155.38
147.84
145.80
135.40
132.77
132.41
131.70
128.32
127.24
125.99
123.85
123.13
118.63
81.93
51.33
40.13
39.92
39.71
39.50
39.29
39.08
38.88
4al
100 MHz
DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0

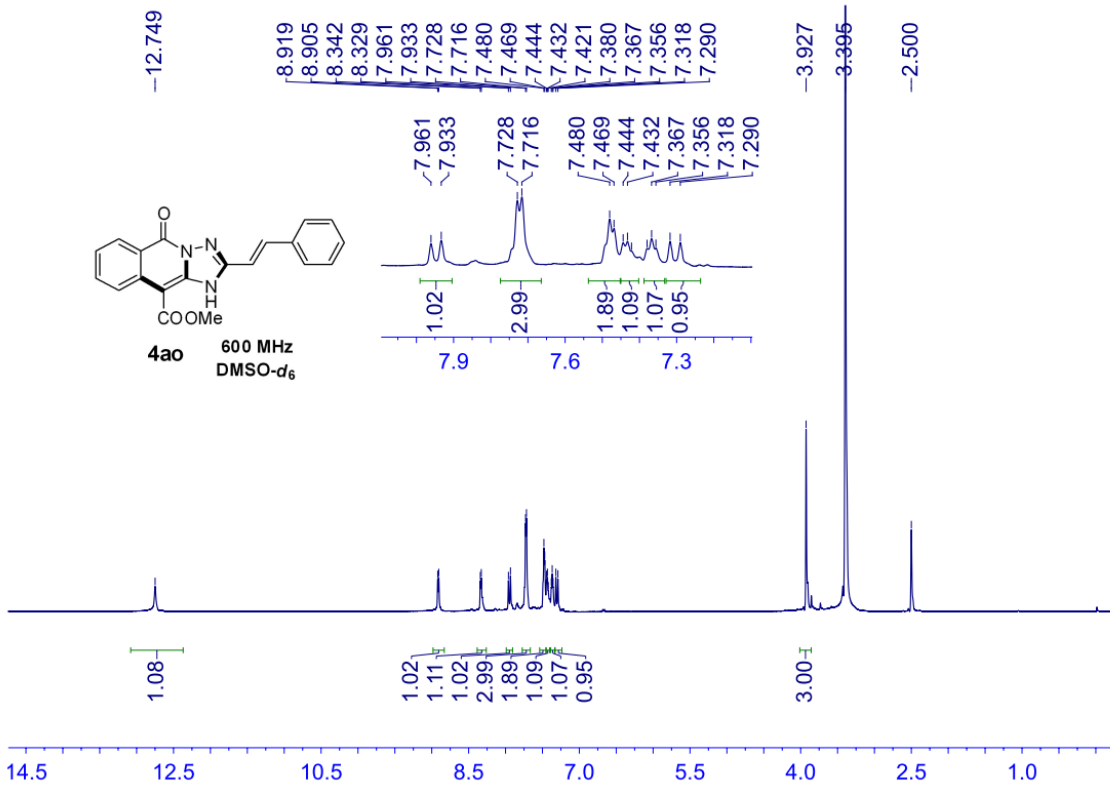
.

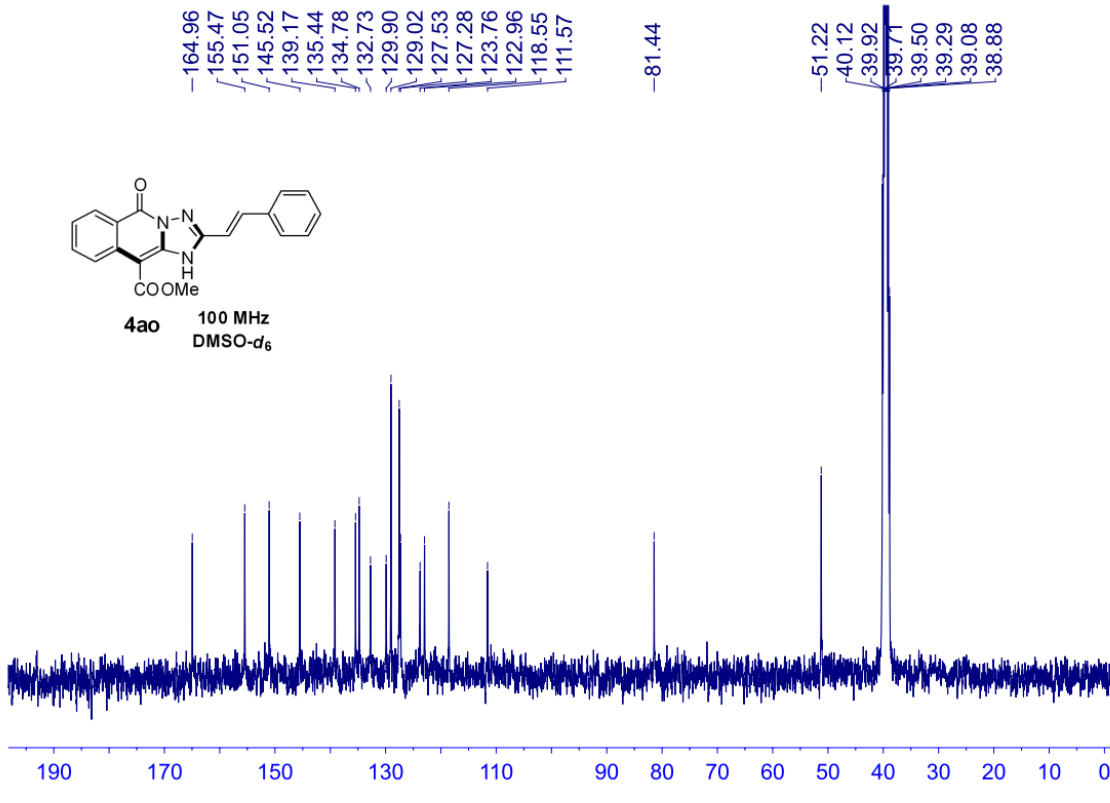

11.160
8.730
8.715
8.598
8.585
7.729
7.715
7.701
7.402
7.389
7.377
7.271
4.008
2.981
2.969
2.956
2.943
1.754
1.490
1.477
1.465
0.000
4am
600 MHz
CDCl3
1.00
1.00
1.00
1.00
1.00
3.00
2.00
3.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

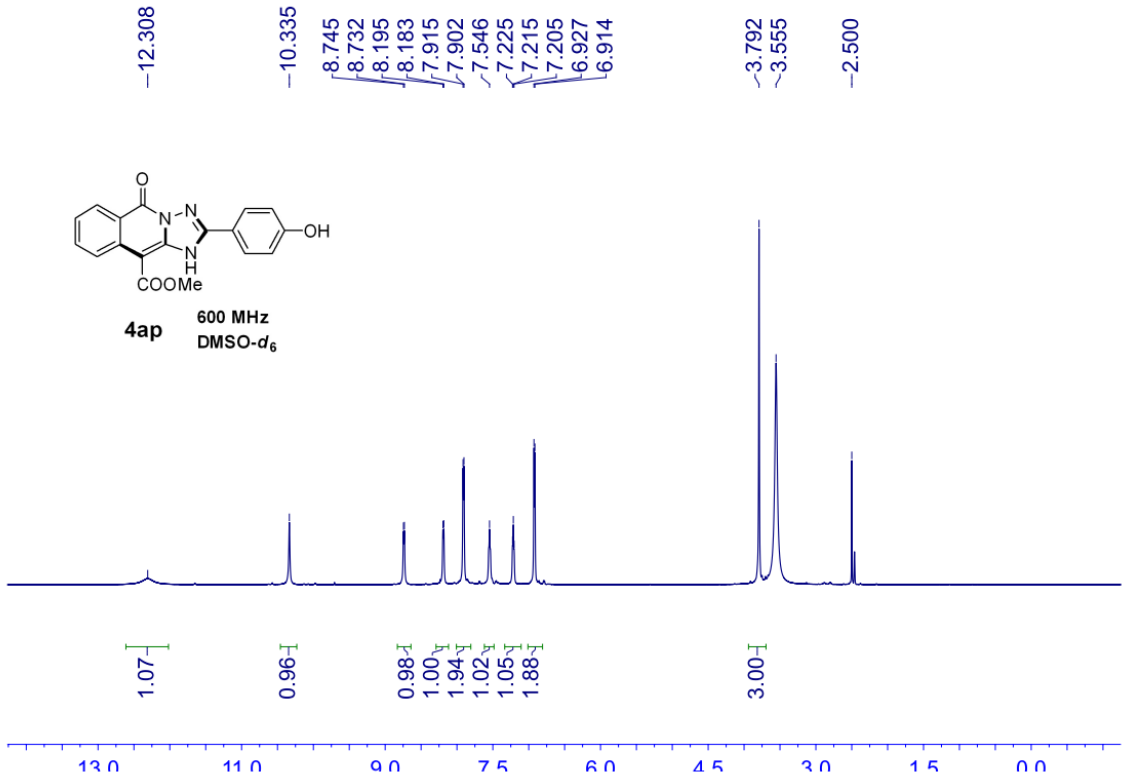

166.41
156.40
155.39
145.52
135.06
132.84
127.74
124.02
123.21
118.86
82.56
77.32
77.00
76.68
51.33
19.49
10.77
4am
100 MHz
CDCl3
90
170
150
130
110
90
80
70
60
50
40
30
20
10
0

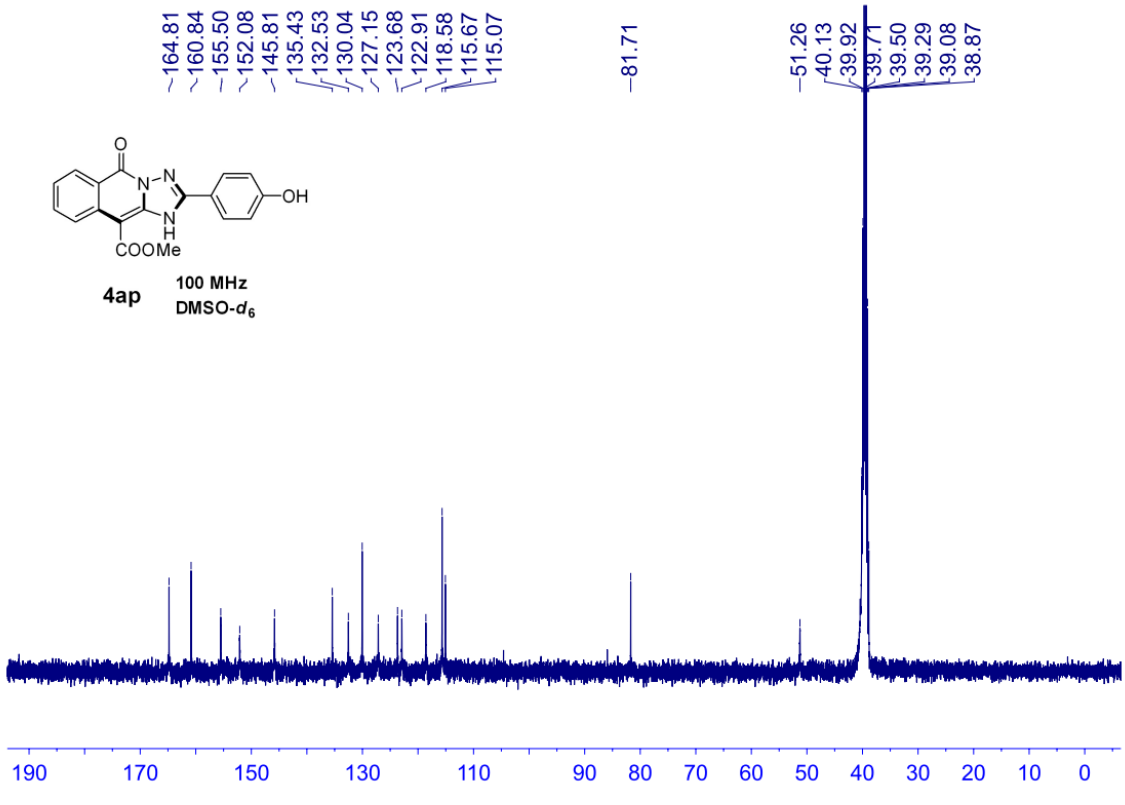

12.518
8.800
8.779
8.265
8.245
7.633
7.615
7.597
7.294
7.275
7.257
3.846
3.439
2.737
2.719
2.500
2.496
0.976
0.959
COOMe
4an 400 MHz
DMSO-d6
1.00
1.00
1.00
1.00
9.0
8.5
8.0
7.5
1.00
1.00
1.00
1.00
1.00
3.00
2.00
1.00
6.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

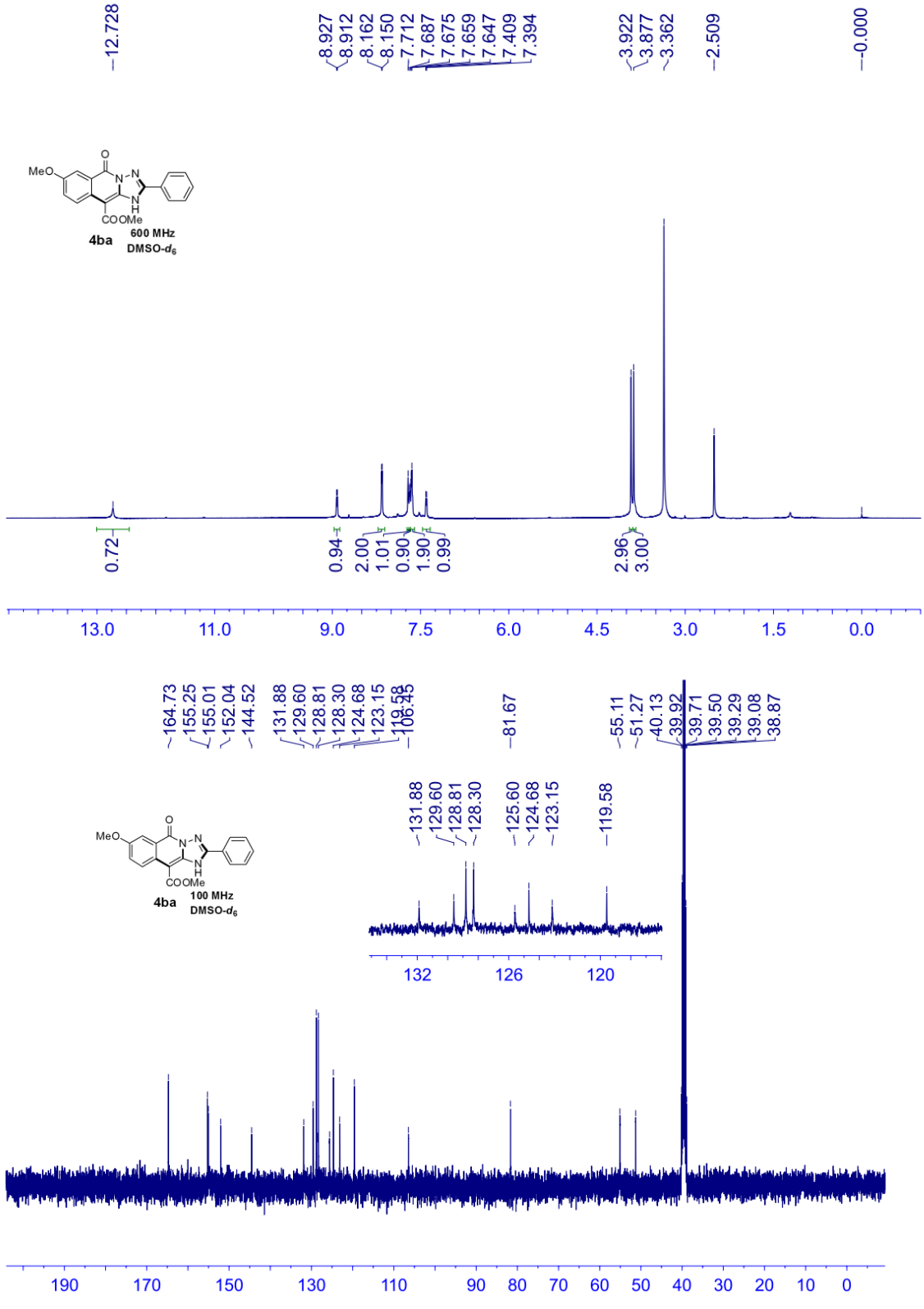

164.87
155.47
154.19
145.30
135.43
132.55
127.20
123.67
122.80
118.43
81.33
51.12
40.13
39.92
39.71
39.50
39.29
39.08
38.87
33.85
26.81
22.10
COOMe
4an 100 MHz
DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

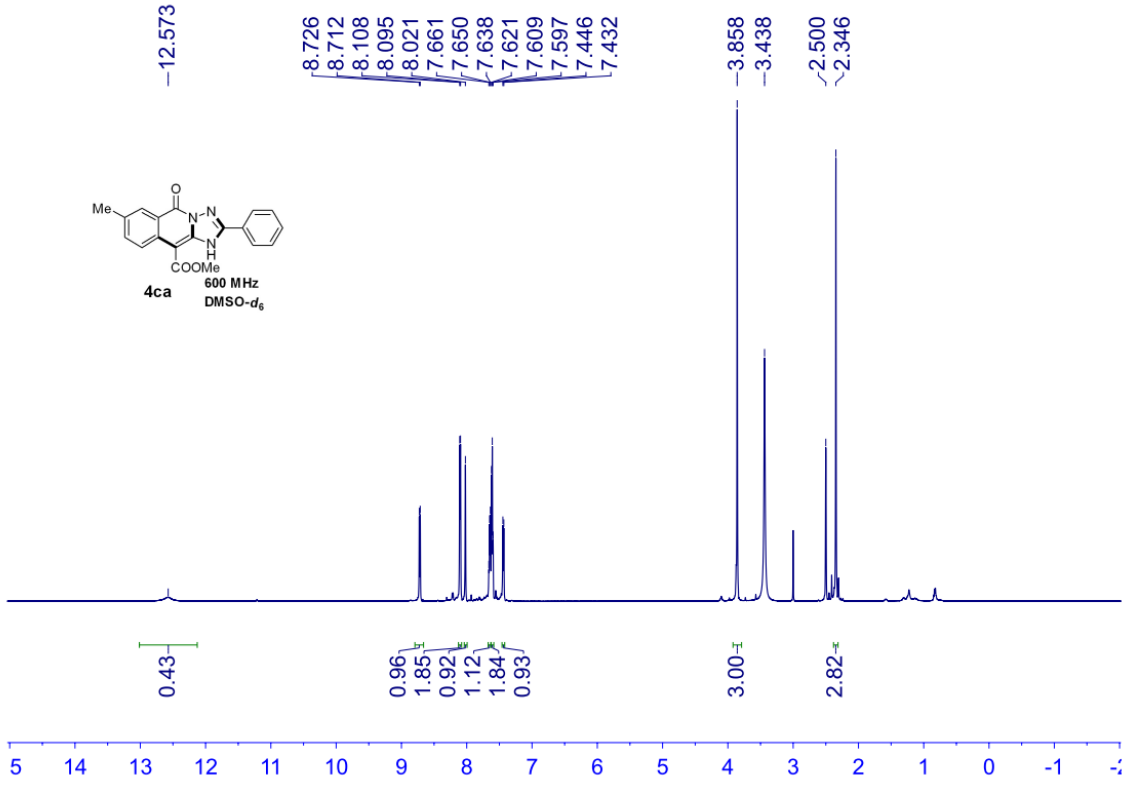

12.749
8.919
8.905
8.342
8.329
7.961
7.933
7.728
7.716
7.480
7.469
7.444
7.432
7.421
7.380
7.367
7.356
7.318
7.290
3.927
3.395
2.500
COOMe
4ao
600 MHz
DMSO-d6
1.08
1.02
1.11
1.02
2.99
1.89
1.09
1.07
0.95
3.00
14.5
12.5
10.5
8.5
7.0
5.5
4.0
2.5
1.0

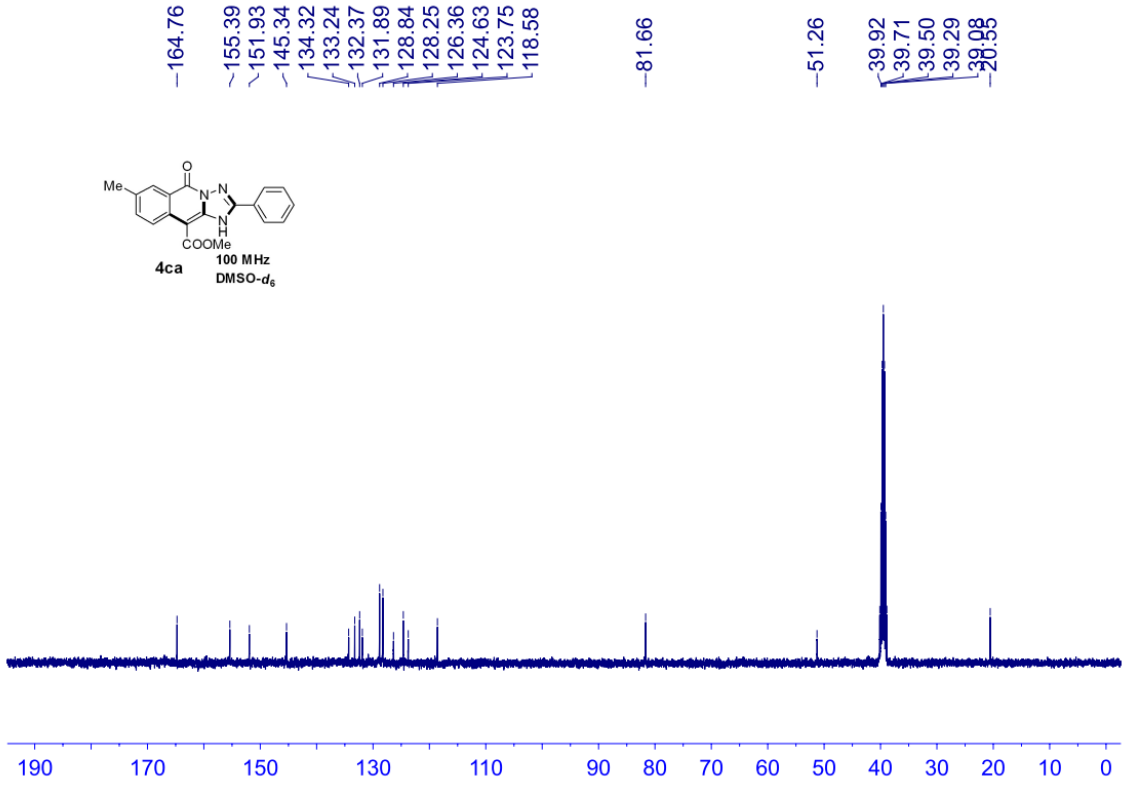

164.96
155.47
151.05
145.52
139.17
135.44
134.78
132.73
129.90
129.02
127.53
127.28
123.76
122.96
118.55
111.57
81.44
51.22
40.12
39.92
39.71
39.50
39.29
39.08
38.88
COOMe
4ao
100 MHz
DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

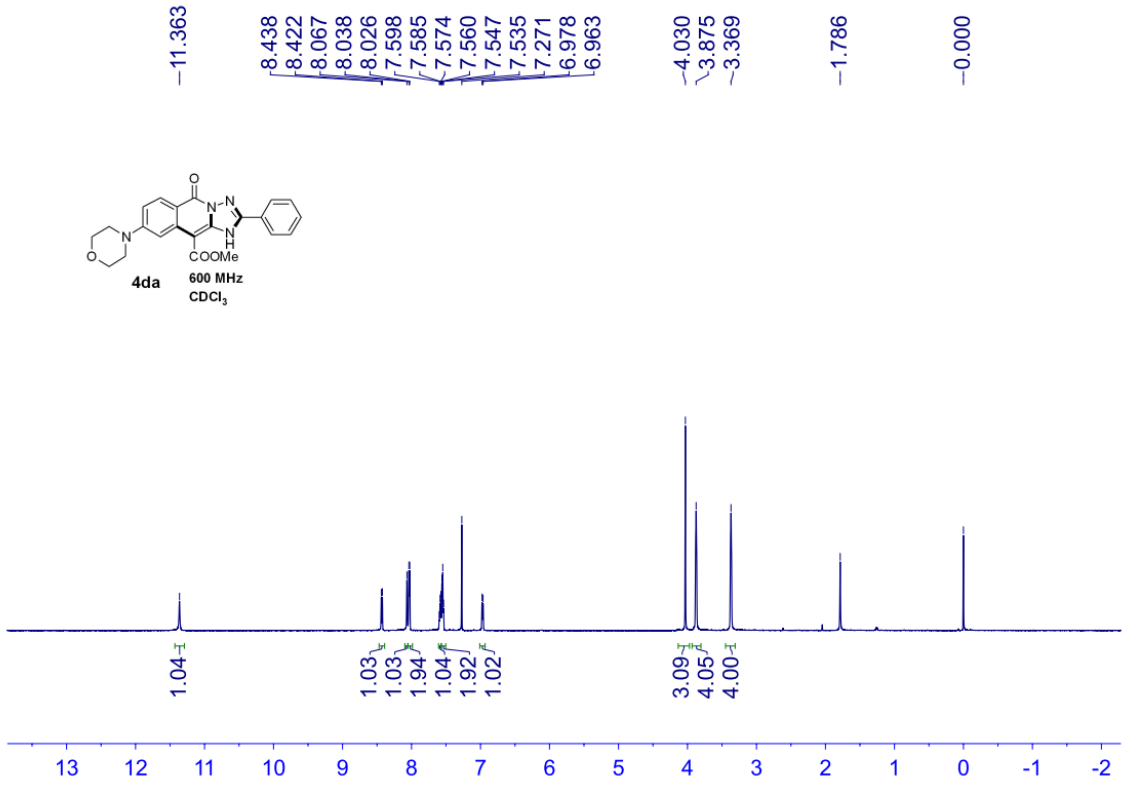

12.308
10.335
8.745
8.732
8.195
8.183
7.915
7.902
7.546
7.225
7.215
7.205
6.927
6.914
3.792
3.555
2.500
OH
COOMe
4ap
600 MHz
DMSO-d6
1.07
0.96
0.98
1.00
1.94
1.02
1.05
1.88
3.00

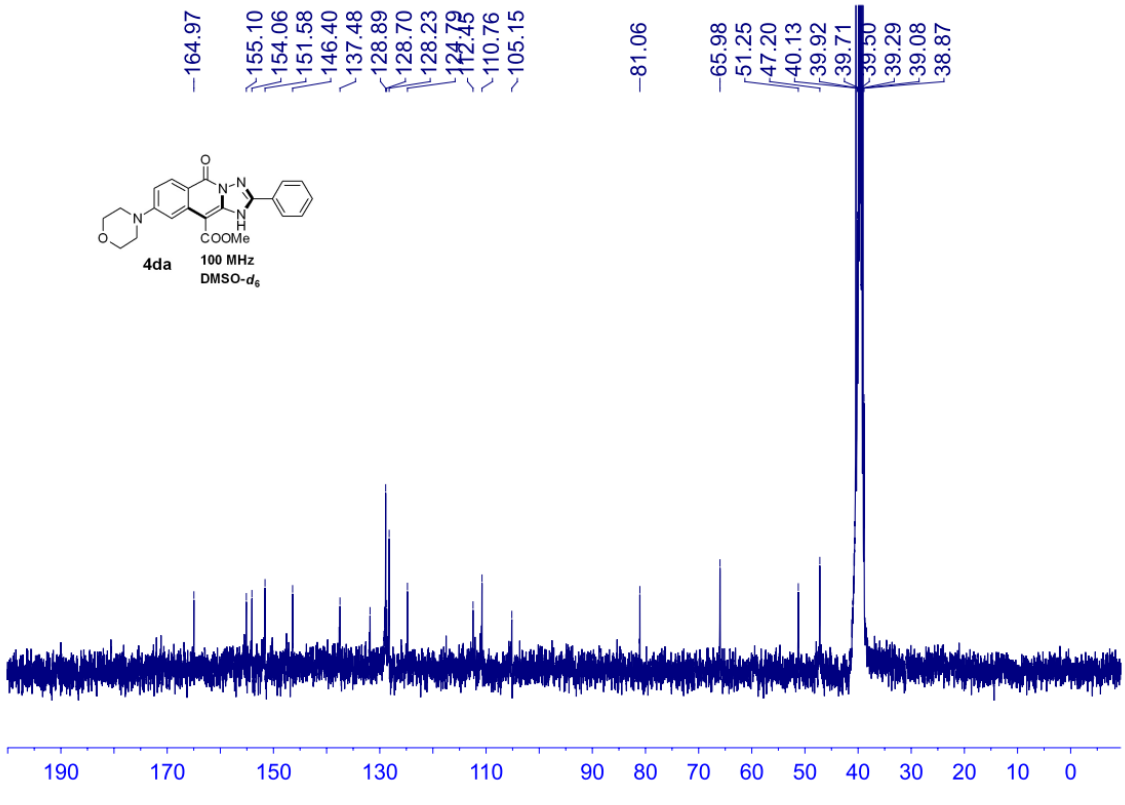

164.81
160.84
155.50
152.08
145.81
135.43
132.53
130.04
127.15
123.68
122.91
118.58
115.67
115.07
81.71
51.26
40.13
39.92
39.71
39.50
39.29
39.08
38.87
OH
COOMe
4ap
100 MHz
DMSO-d6

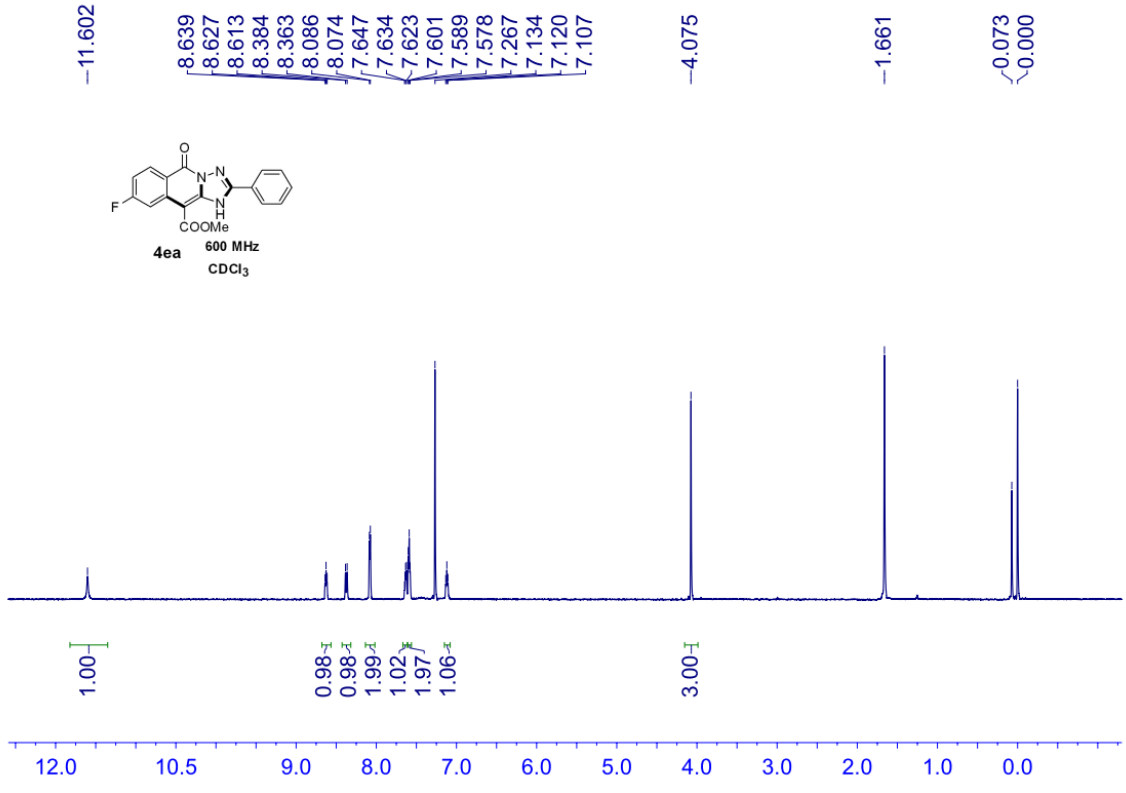

12.728
8.927
8.912
8.162
8.150
7.712
7.687
7.675
7.659
7.647
7.409
7.394
3.922
3.877
3.362
2.509
0.000
MeO
COOMe
4ba
600 MHz
DMSO-d_6
0.72
0.94
2.00
1.01
0.90
1.90
0.99
2.96
3.00
13.0
11.0
9.0
7.5
6.0
4.5
3.0
1.5
0.0
164.73
155.25
155.01
152.04
144.52
131.88
129.60
128.81
128.30
124.68
123.15
119.58
106.45
81.67
55.11
51.27
40.13
39.92
39.71
39.50
39.29
39.08
38.87
MeO
COOMe
4ba
100 MHz
DMSO-d_6
131.88
129.60
128.81
128.30
125.60
124.68
123.15
119.58
132
126
120
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

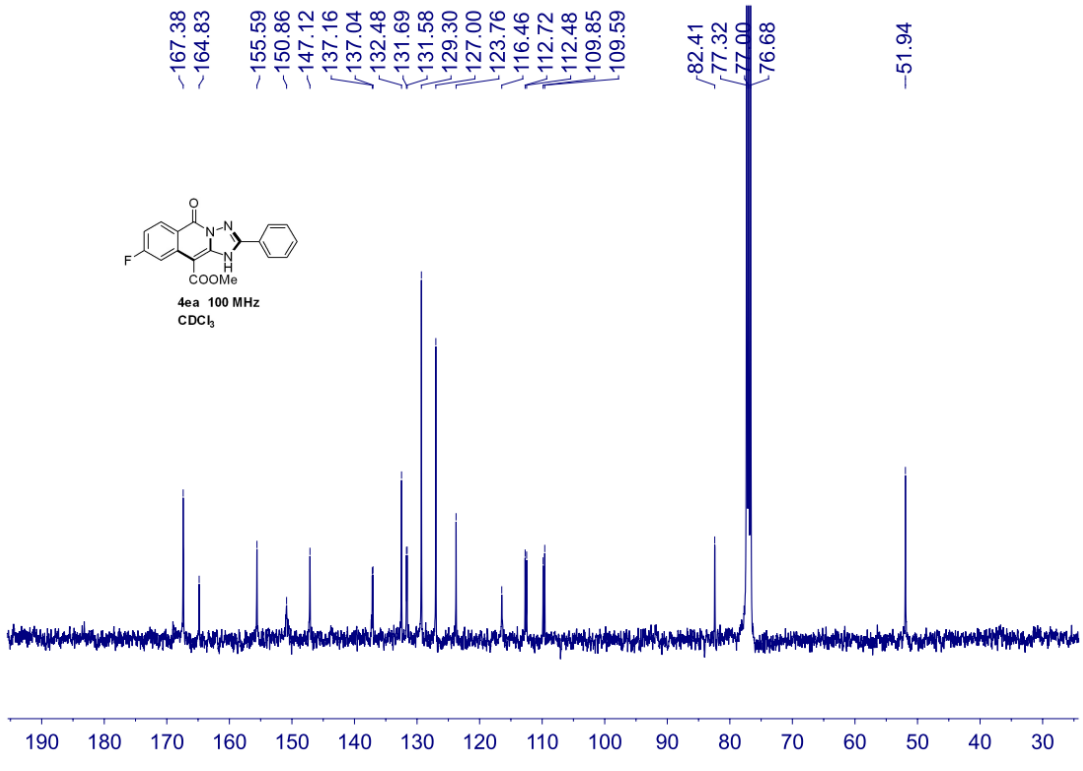

12.573
8.726
8.712
8.108
8.095
8.021
7.661
7.650
7.638
7.621
7.609
7.597
7.446
7.432
3.858
3.438
2.500
2.346
Me
COOMe
4ca
600 MHz
DMSO-d_6
0.43
0.96
1.85
0.92
1.12
1.84
0.93
3.00
2.82
5
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

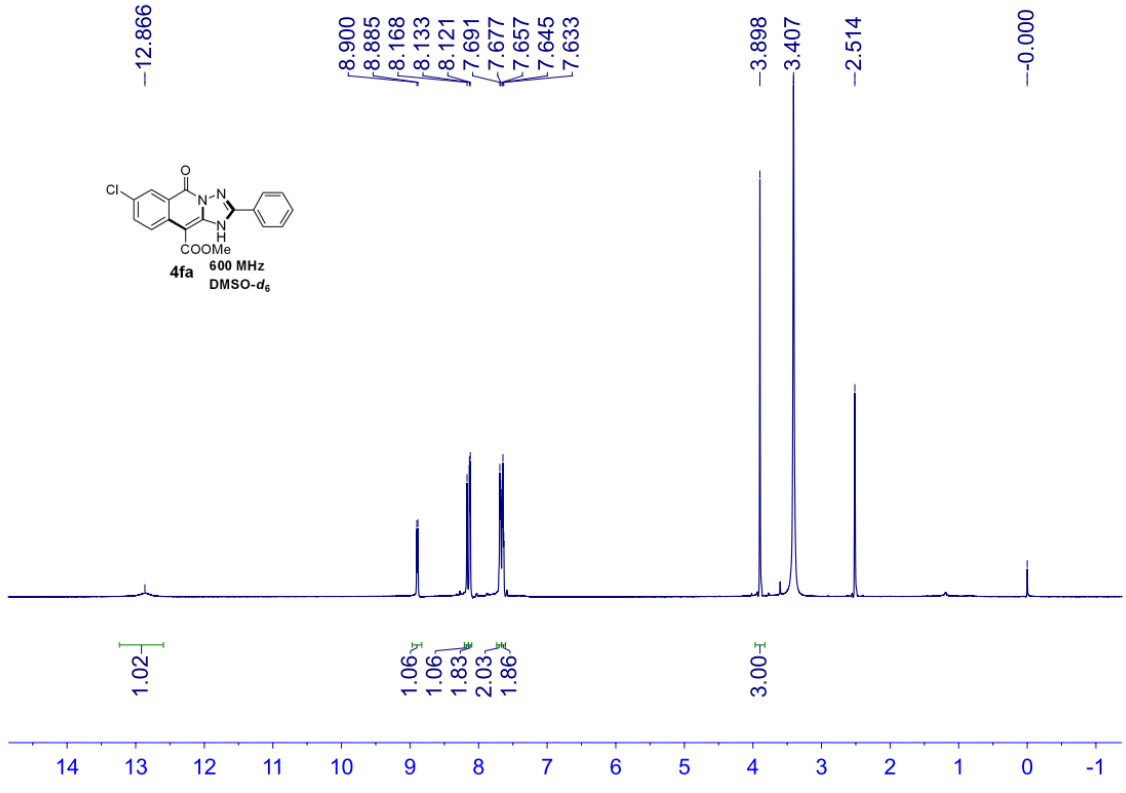

164.76
155.39
151.93
145.34
134.32
133.24
132.37
131.89
128.84
128.25
126.36
124.63
123.75
118.58
81.66
51.26
39.92
39.71
39.50
39.29
20.53
Me
COOMe
4ca
100 MHz
DMSO-d_6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

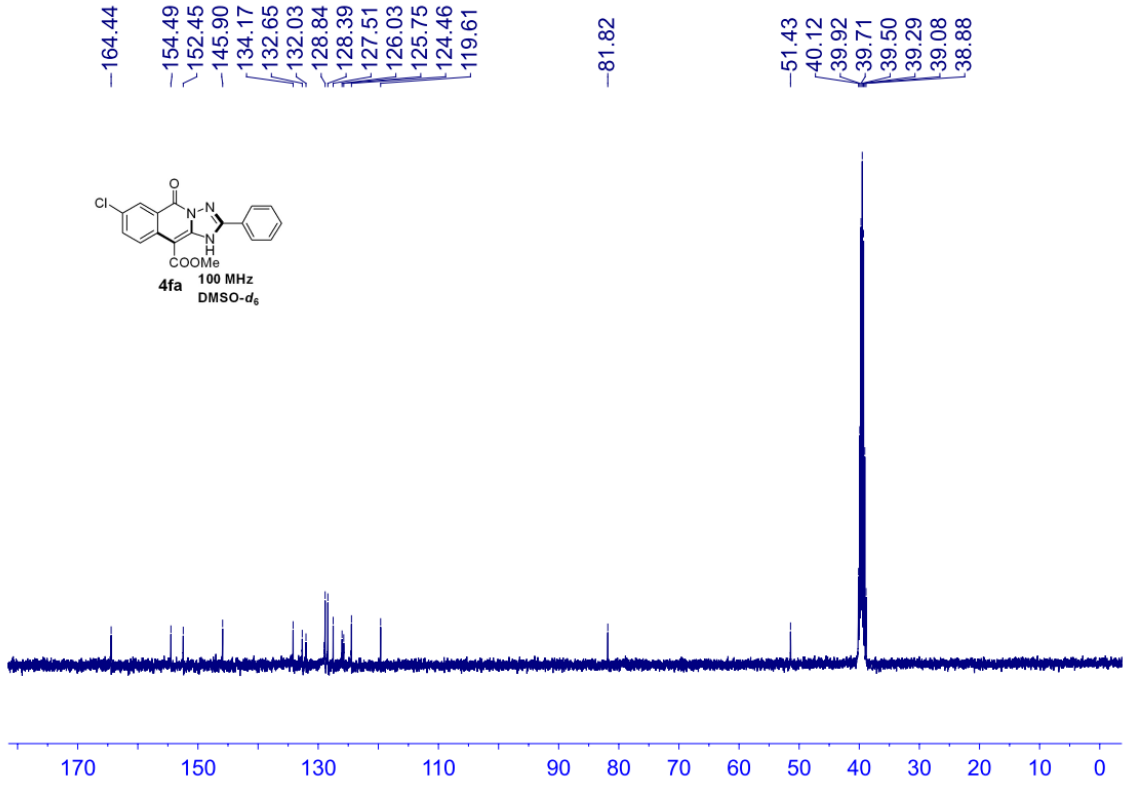

11.363
8.438
8.422
8.067
8.038
8.026
7.598
7.585
7.574
7.560
7.547
7.535
7.271
6.978
6.963
4.030
3.875
3.369
1.786
0.000
4da
600 MHz
CDCl3
1.04
1.03
1.03
1.94
1.04
1.92
1.02
3.09
4.05
4.00
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

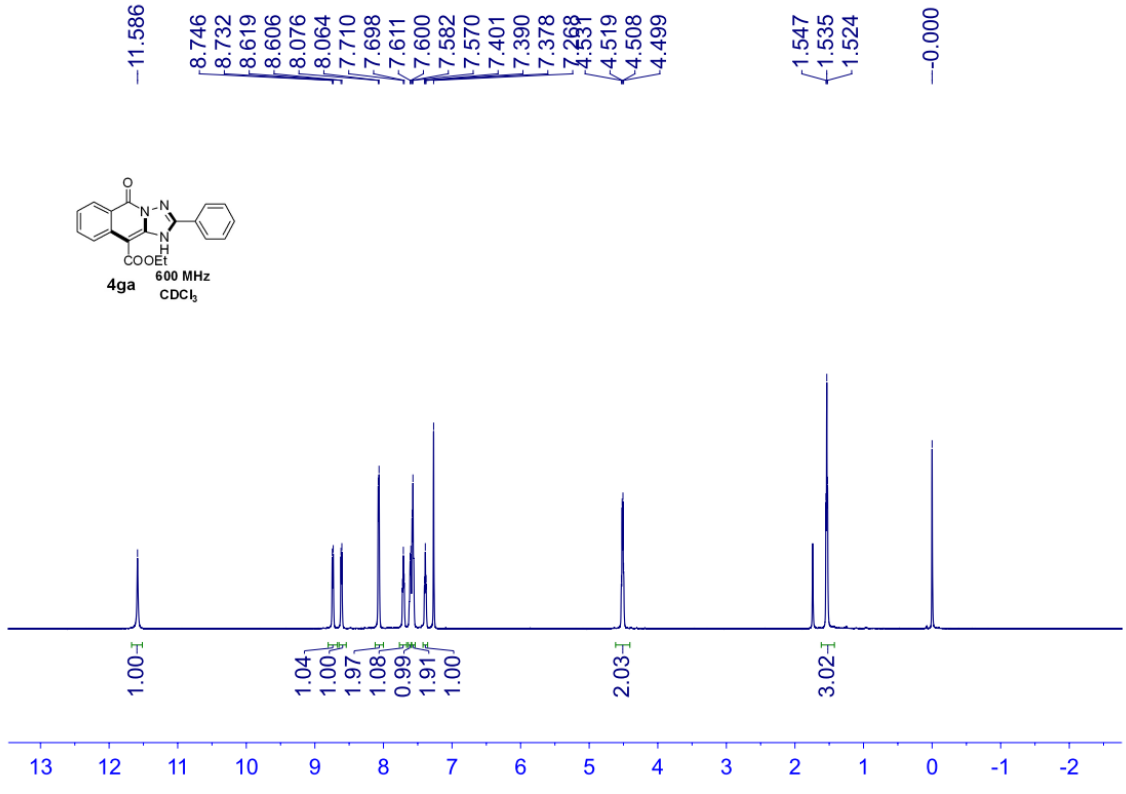

164.97
155.10
154.06
151.58
146.40
137.48
128.89
128.70
128.23
124.79
112.45
110.76
105.15
81.06
65.98
51.25
47.20
40.13
39.92
39.71
39.50
39.29
39.08
38.87
4da
100 MHz
DMSO-d6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0

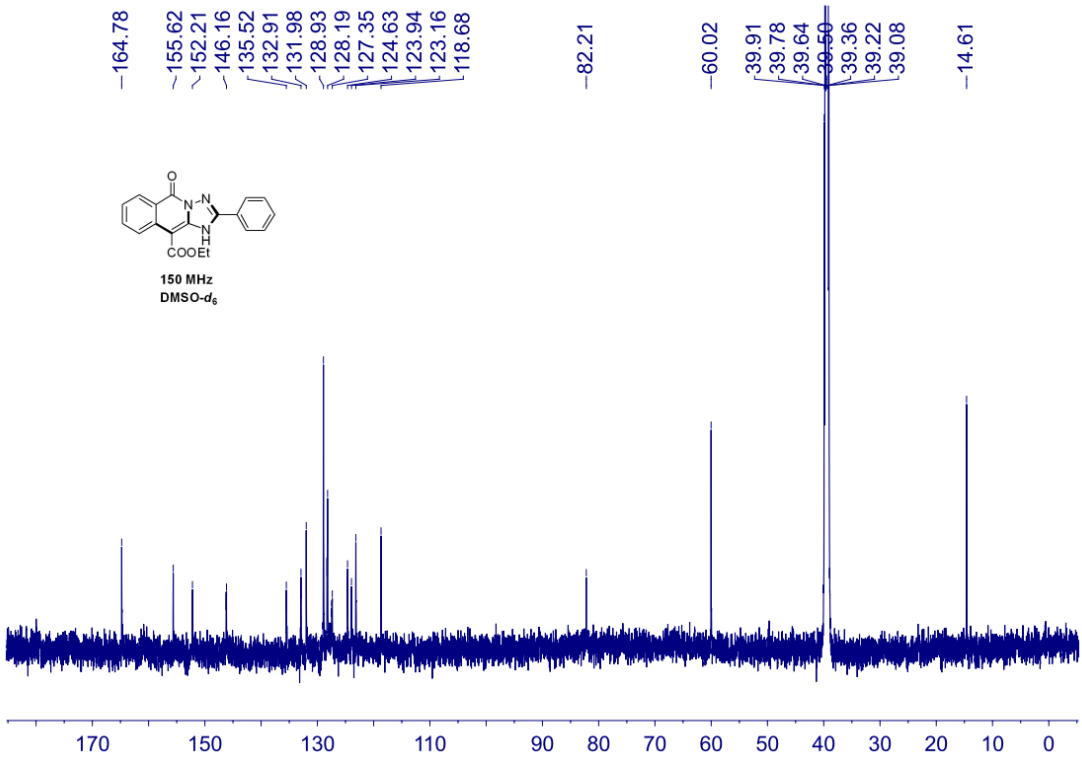

11.602
8.639
8.627
8.613
8.384
8.363
8.086
8.074
7.647
7.634
7.623
7.601
7.589
7.578
7.267
7.134
7.120
7.107
4.075
1.661
0.073
0.000
4ea
600 MHz
CDCl3
1.00
0.98
0.98
1.99
1.02
1.97
1.06
3.00
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

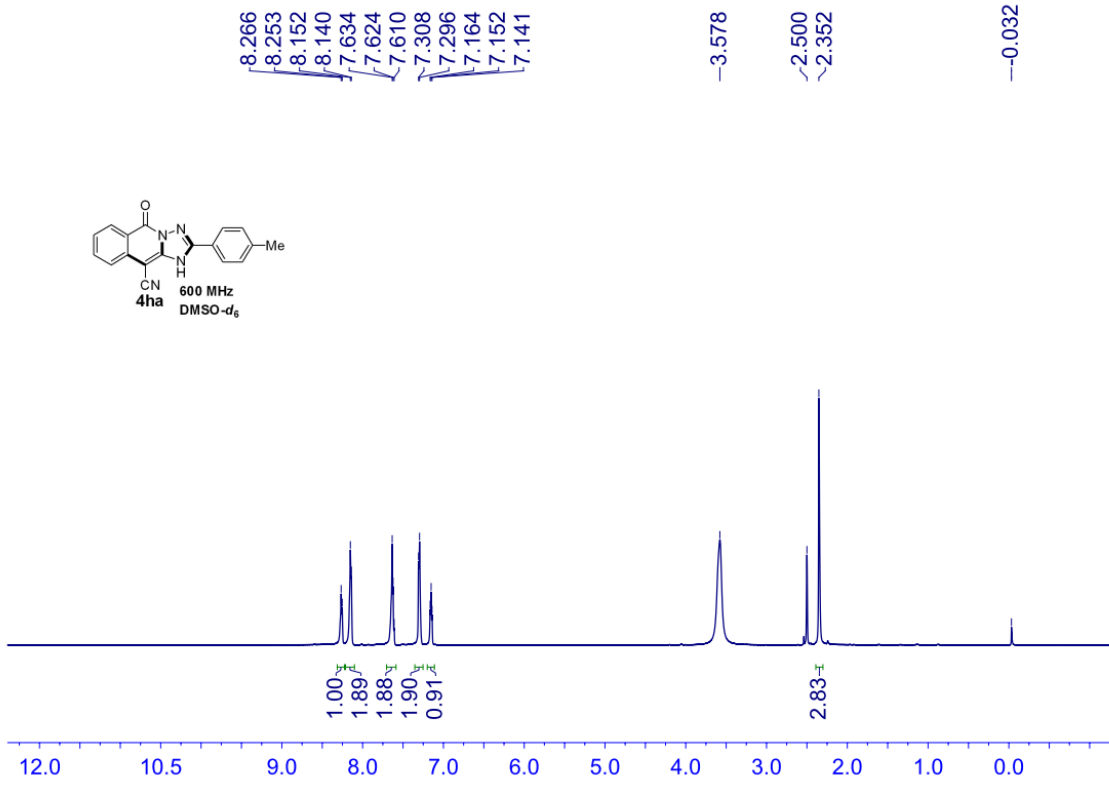

167.38
164.83
155.59
150.86
147.12
137.16
137.04
132.48
131.69
131.58
129.30
127.00
123.76
116.46
112.72
112.48
109.85
109.59
82.41
77.32
77.00
76.68
51.94
4ea 100 MHz
CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30

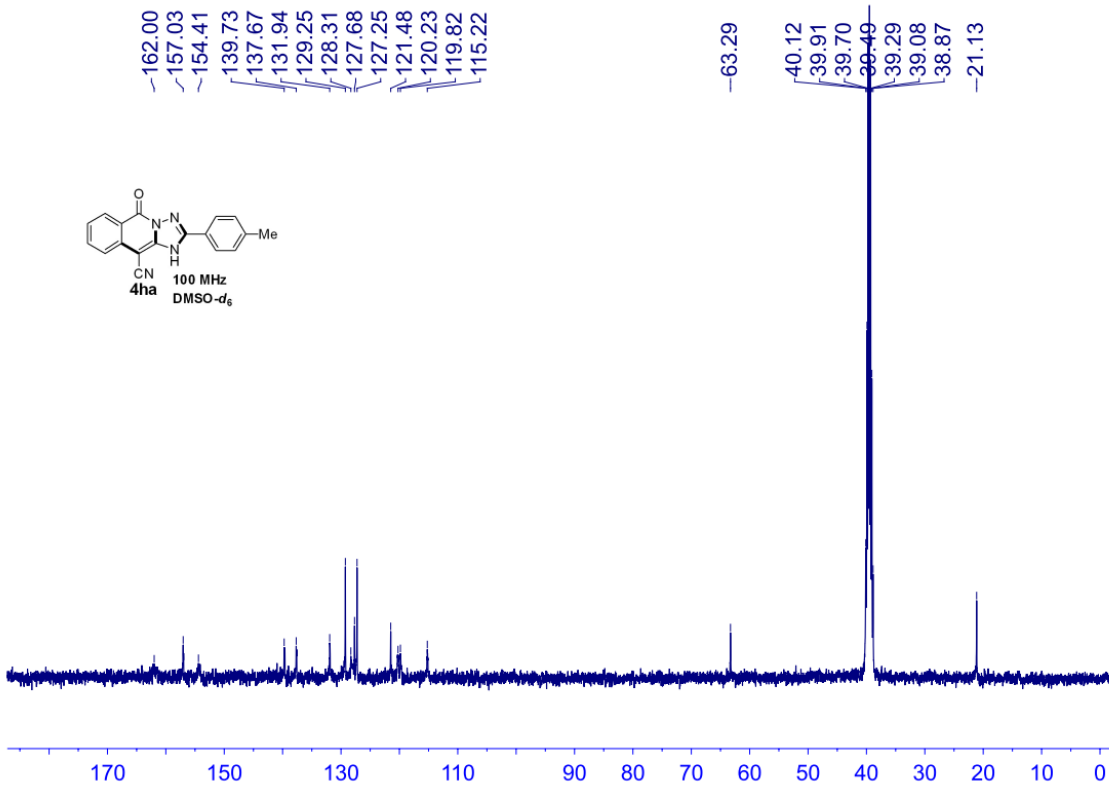

12.866
8.900
8.885
8.168
8.133
8.121
7.691
7.677
7.657
7.645
7.633
3.898
3.407
2.514
0.000
Cl
O
N
N
H
COOMe
4fa
600 MHz
DMSO-d_6
1.02
1.06
1.06
1.83
2.03
1.86
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

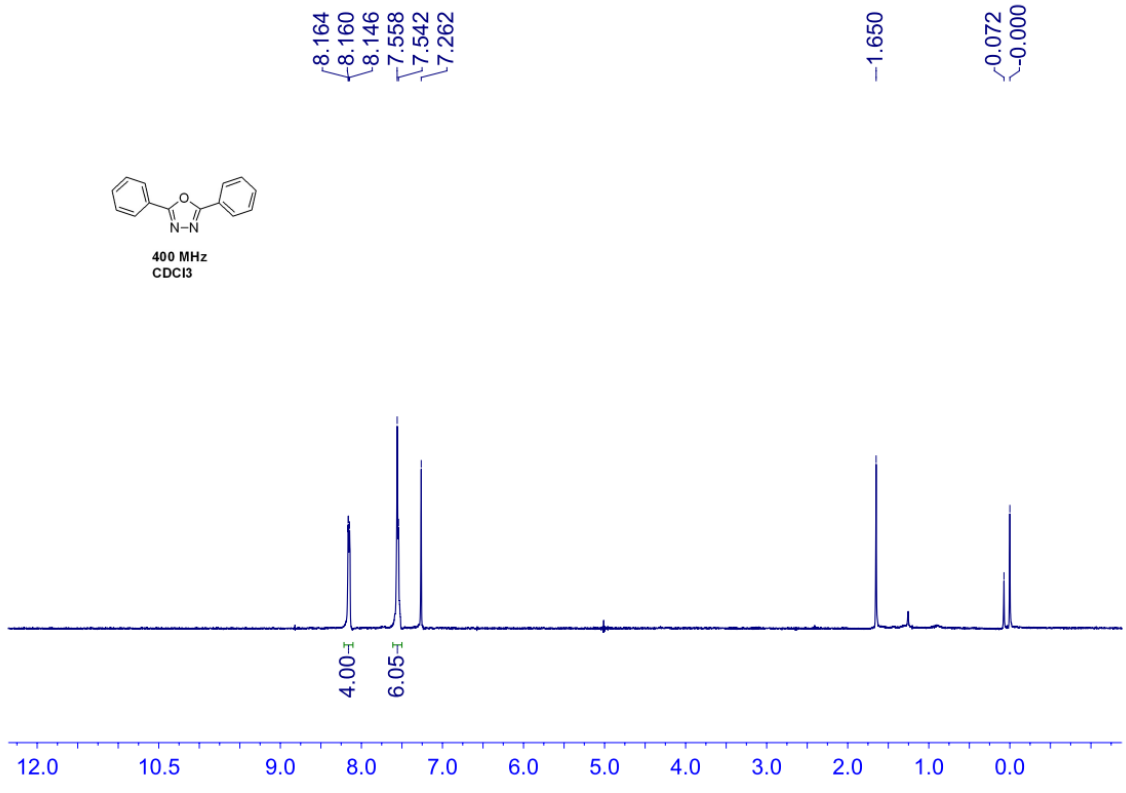

164.44
154.49
152.45
145.90
134.17
132.65
132.03
128.84
128.39
127.51
126.03
125.75
124.46
119.61
81.82
51.43
40.12
39.92
39.71
39.50
39.29
39.08
38.88
Cl
O
N
N
H
COOMe
4fa
100 MHz
DMSO-d_6
170
150
130
110
90
80
70
60
50
40
30
20
10
0

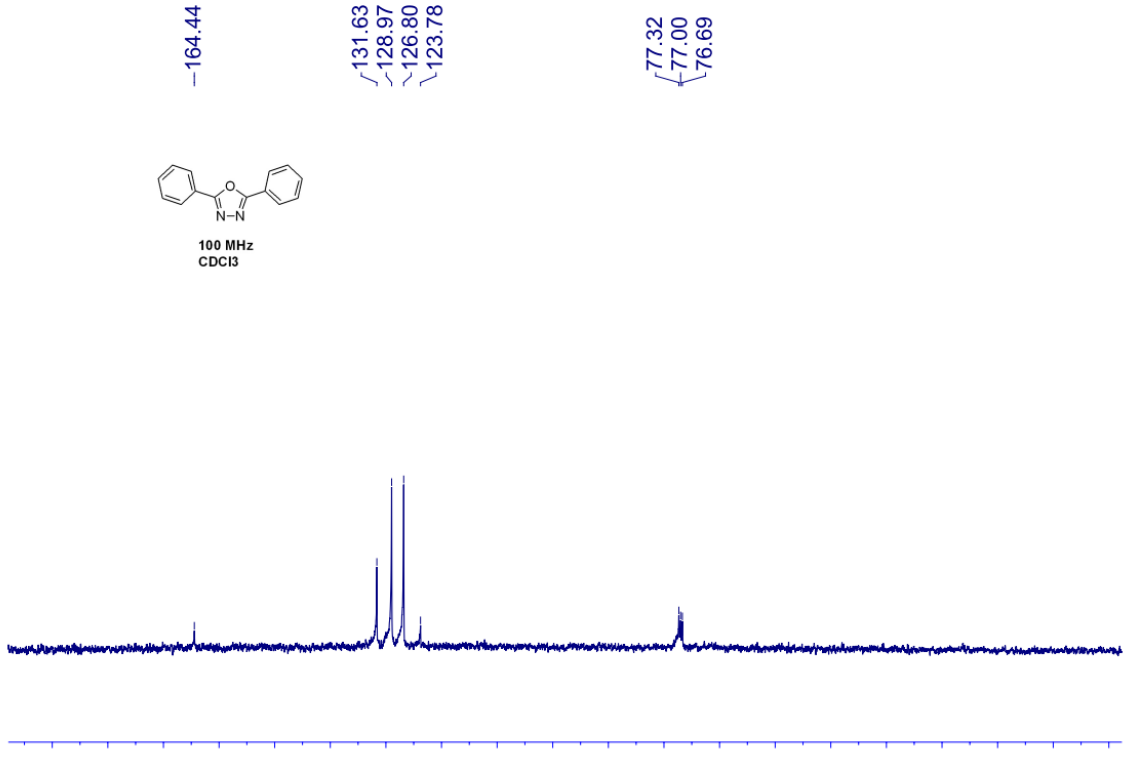

11.586
8.746
8.732
8.619
8.606
8.076
8.064
7.710
7.698
7.611
7.600
7.582
7.570
7.401
7.390
7.378
7.268
4.531
4.519
4.508
4.499
1.547
1.535
1.524
0.000
4ga
600 MHz
CDCl3
1.00
1.04
1.00
1.97
1.08
0.99
1.91
1.00
2.03
3.02
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2

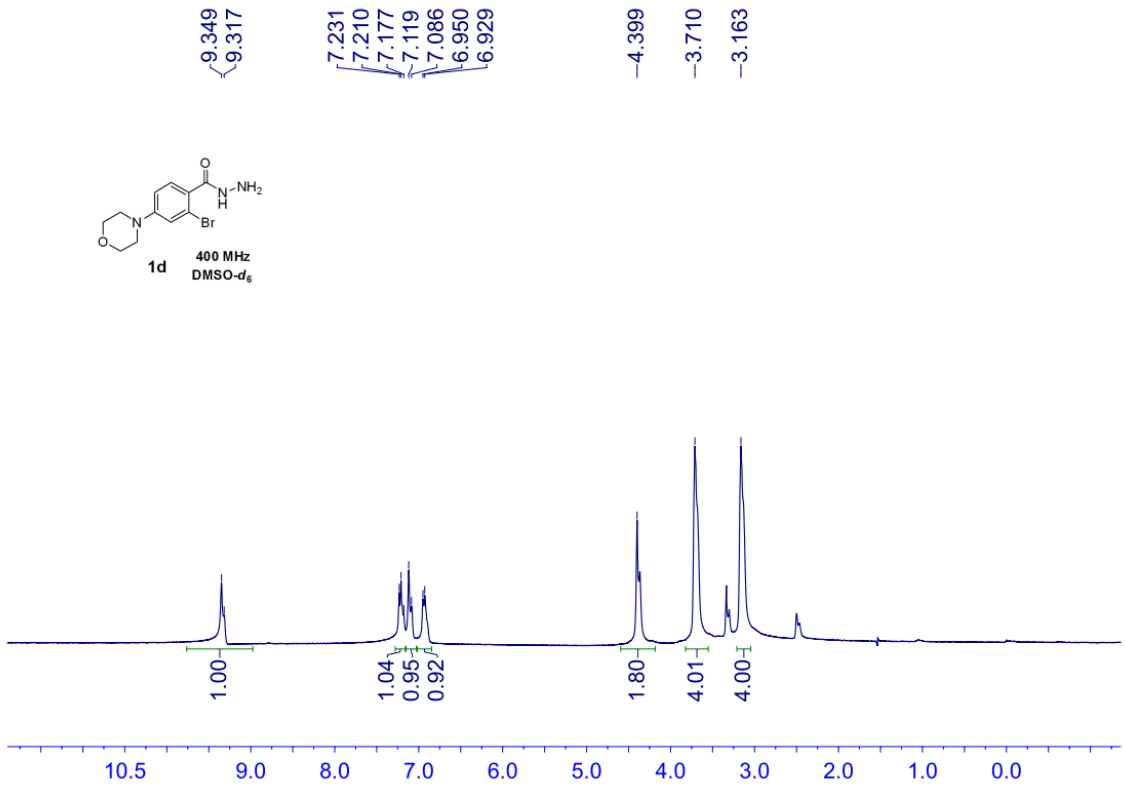

164.78
155.62
152.21
146.16
135.52
132.91
131.98
128.93
128.19
127.35
124.63
123.94
123.16
118.68
82.21
60.02
39.91
39.78
39.64
39.50
39.36
39.22
39.08
14.61
150 MHz
DMSO-d6
170
150
130
110
90
80
70
60
50
40
30
20
10
0

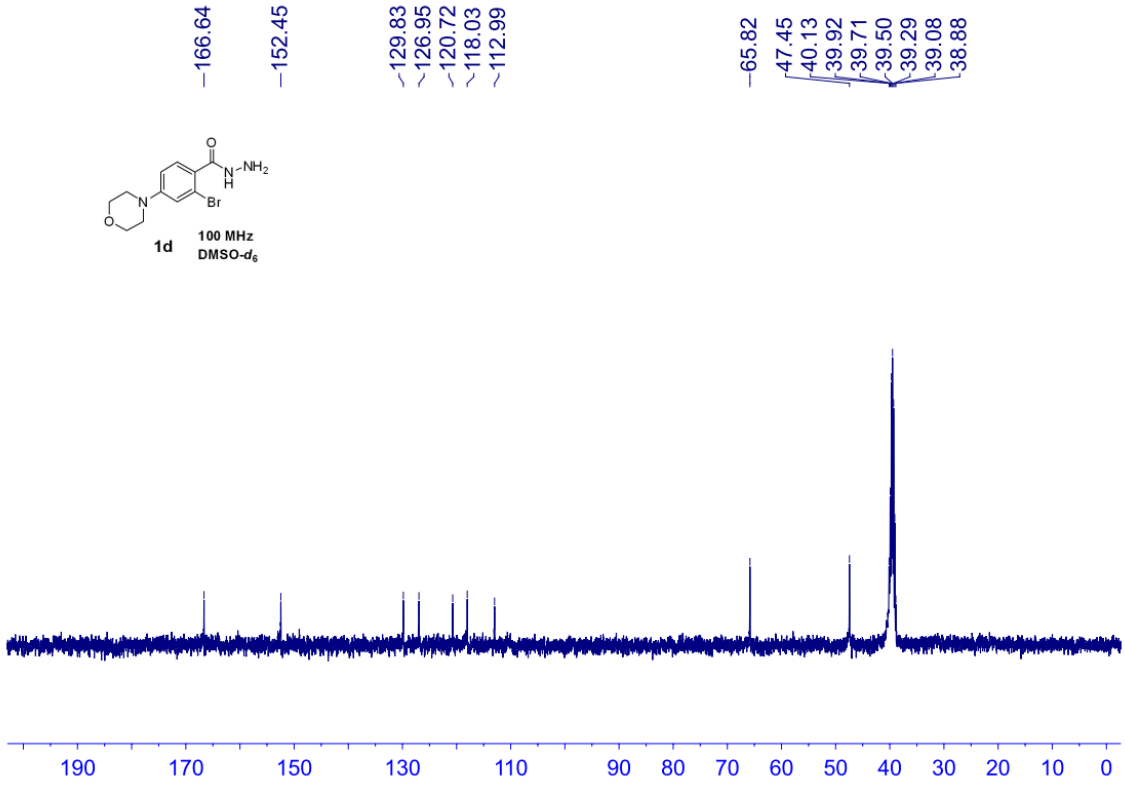

8.266
8.253
8.152
8.140
7.634
7.624
7.610
7.308
7.296
7.164
7.152
7.141
3.578
2.500
2.352
0.032
Me
CN
4ha
600 MHz
DMSO-d_6
1.00
1.89
1.88
1.90
0.91
2.83
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


162.00
157.03
154.41
139.73
137.67
131.94
129.25
128.31
127.68
127.25
121.48
120.23
119.82
115.22
63.29
40.12
39.91
39.70
39.49
39.29
39.08
38.87
21.13
Me
CN
4ha
100 MHz
DMSO-d_6
170
150
130
110
90
80
70
60
50
40
30
20
10
0


8.164
8.160
8.146
7.558
7.542
7.262
1.650
0.072
0.000
400 MHz
CDCl3
4.00
6.05
12.0
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


164.44
131.63
128.97
126.80
123.78
77.32
77.00
76.69
100 MHz
CDCl3


9.349
9.317
7.231
7.210
7.177
7.119
7.086
6.950
6.929
4.399
3.710
3.163
1d
400 MHz
DMSO-d_6
1.00
1.04
0.95
0.92
1.80
4.01
4.00
10.5
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


166.64
152.45
129.83
126.95
120.72
118.03
112.99
65.82
47.45
40.13
39.92
39.71
39.50
39.29
39.08
38.88
1d
100 MHz
DMSO-d_6
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0