Copper-catalyzed synthesis of pyrido-fused quinazolinones from 2-aminoarylmethanols and isoquinolines or tetrahydroisoquinolines

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Suporting information

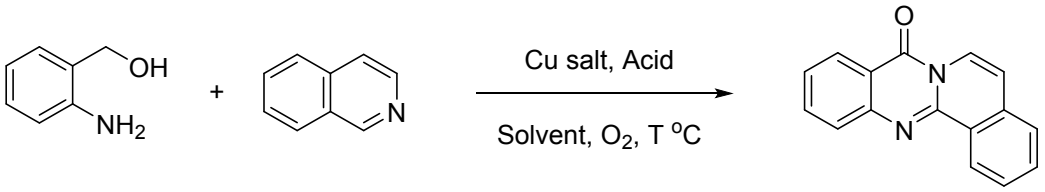
1. Materials and instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich, Acros, Energy Chemicals, and Aladdin, and were used as received without any further purification unless otherwise noted. Gas chromatographic (GC) analyses were performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis held samples at 100 ^{o}C for 1 min; heated them from 100 to 280 ^{o}C at 40 ^{o}C/min; held them at 280 ^{o}C for 8 min. Inlet and detector

temperatures were set constant at 280 ^{o}C. The GC yield was calculated using diphenyl ether as the internal standard. GC-MS analyses were analyzed on a Shimadzu GCMS-QP2010Ultra with a ZB-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC-MS analysis held samples at 50 ^{o}C for 2 min; heated samples from 50 to 280 ^{o}C at 10 ^{o}C/min and held them at 280 ^{o}C for 10 min. Inlet temperature was set constant at 280 ^{o}C. MS spectra were compared with the spectra gathered in the NIST library. The ^{1}H NMR and ^{13}C NMR were recorded on Bruker AV 500 spectrometers using residual solvent peak as a reference. HR-MS spectra were recorded by an Agilent HPLC 1200 Series coupled to Bruker micrOTOF-QII.

2. Optimization studies

Table S1. Screening of conditions for the condensation of 2-aminobenzyl alcohol with isoquinoline (detailed data)



1a **2a** **3aa**

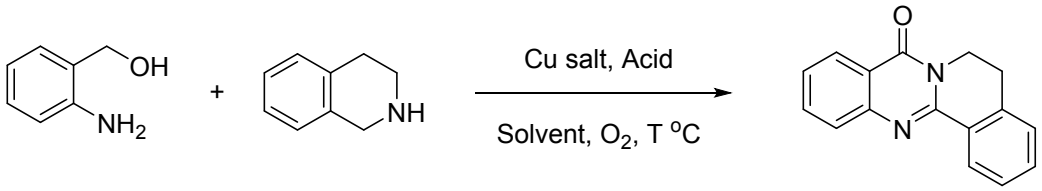
Entry	**1a**:**2a** molar ratio (mol:mol)	Additive	Solvent	Catalyst	Ligand	Temp (°C)	Time (h)	GC yield(%)
1	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	80	12	27
2	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	100	12	52
3	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	120	12	51
4	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	140	12	46
5	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	100	12	37 (under air)
6	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2$ (20%)	-	100	12	0 (under Ar)
7	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(OAc)_2.H_2O$ (20%)	-	100	12	53
8	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuSO_4$ (20%)	-	100	12	42
9	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(NO_3)_2.3H_2O$ (20%)	-	100	12	35
10	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	64
11	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2.2H_2O$ (20%)	-	100	12	55
12	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuBr_2$ (20%)	-	100	12	62
13	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	CuBr (20%)	-	100	12	61
14	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	CuCl (20%)	-	100	12	63
15	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	CuI (20%)	-	100	12	62
16	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Cu(acac)_2$ (20%)	-	100	12	23
17	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	CuO (20%)	-	100	12	33
18	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	Cu_2O (20%)	-	100	12	12
19	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuFe_2O_4$ (20%)	-	100	12	15

20	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$FeCl_3$ (20%)	-	100	12	27
21	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$FeCl_3.6H_2O$ (20%)	-	100	12	26
22	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Fe(NO_3)_3.9H_2O$ (20%)	-	100	12	17
23	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$FeSO_4$ (20%)	-	100	12	12
24	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Fe(OAc)_2$ (20%)	-	100	12	22
25	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Fe_2(SO_4)_3$ (20%)	-	100	12	25
26	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$Fe(acac)_3$ (20%)	-	100	12	34
27	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	-	-	100	12	0
28	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (5%)	-	100	12	19
29	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (10%)	-	100	12	27
30	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (15%)	-	100	12	48
31	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	64
32	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (25%)	-	100	12	64
33	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (30%)	-	100	12	58
34	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	2,2'-bipyridine	100	12	51
35	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	1,10-phenanthroline	100	12	67
36	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	pyridine	100	12	62
37	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	DABCO	100	12	64
38	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	triphenylphosphine	100	12	65
39	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	nicotinic acid	100	12	37
40	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	acetyl acetone	100	12	59
41	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	TMEDA	100	12	61
42	1:1	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	32
43	1:1.5	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	38
44	1:2	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	46
45	1:2.5	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	58
46	1:3	$TsOH.H_2O$ (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	64
47	1:3	benzoic acid (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	52
48	1:3	4-NO_2 benzoic acid (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	58
49	1:3	formic acid (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	37

50	1:3	acetic acid (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	46
51	1:3	CH_3SO_3H (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	65
52	1:3	H_3PO_4 (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	16
53	1:3	TFA (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	63
54	1:3	PivOH (1.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	37
55	1:3	-	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	6
56	1:3	$TsOH.H_2O$ (0.1)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	44
57	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	68
58	1:3	$TsOH.H_2O$ (0.3)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	65
59	1:3	$TsOH.H_2O$ (0.5)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	63
60	1:3	$TsOH.H_2O$ (1.0)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	66
61	1:3	$TsOH.H_2O$ (0.2)	p-xylene (0.5 mL)	$CuCl_2$ (20%)	-	100	12	28
62	1:3	$TsOH.H_2O$ (0.2)	toluene (0.5 mL)	$CuCl_2$ (20%)	-	100	12	31
63	1:3	$TsOH.H_2O$ (0.2)	chlorobenzene (0.5 mL)	$CuCl_2$ (20%)	-	100	12	33
64	1:3	$TsOH.H_2O$ (0.2)	diethyl carbonate (0.5 mL)	$CuCl_2$ (20%)	-	100	12	0
65	1:3	$TsOH.H_2O$ (0.2)	1,4-dioxane (0.5 mL)	$CuCl_2$ (20%)	-	100	12	16
66	1:3	$TsOH.H_2O$ (0.2)	H_2O (0.5 mL)	$CuCl_2$ (20%)	-	100	12	0
67	1:3	$TsOH.H_2O$ (0.2)	n-butanol (0.5 mL)	$CuCl_2$ (20%)	-	100	12	0
68	1:3	$TsOH.H_2O$ (0.2)	ethylene glycol (0.5 mL)	$CuCl_2$ (20%)	-	100	12	0
69	1:3	$TsOH.H_2O$ (0.2)	acetic acid (0.5 mL)	$CuCl_2$ (20%)	-	100	12	22
70	1:3	$TsOH.H_2O$ (0.2)	DMAc (0.5 mL)	$CuCl_2$ (20%)	-	100	12	67
71	1:3	$TsOH.H_2O$ (0.2)	NMP (0.5 mL)	$CuCl_2$ (20%)	-	100	12	64
72	1:3	$TsOH.H_2O$ (0.2)	DMSO (0.5 mL)	$CuCl_2$ (20%)	-	100	12	58
73	1:3	$TsOH.H_2O$ (0.2)	DMSO:chlorobenzene (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	62
74	1:3	$TsOH.H_2O$ (0.2)	DMSO:pyridine (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	61
75	1:3	$TsOH.H_2O$ (0.2)	DMSO:p-xylene (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	65
76	1:3	$TsOH.H_2O$ (0.2)	DMSO:H_2O (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	22
77	1:3	$TsOH.H_2O$ (0.2)	DMF:chlorobenzene (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	64
78	1:3	$TsOH.H_2O$ (0.2)	DMF:pyridine (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	66
79	1:3	$TsOH.H_2O$ (0.2)	DMF:p-xylene (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	62
80	1:3	$TsOH.H_2O$ (0.2)	DMF:H_2O (1:1) (0.5 mL)	$CuCl_2$ (20%)	-	100	12	28
81	1:3	$TsOH.H_2O$	DMF (0.2 mL)	$CuCl_2$ (20%)	-	100	12	38

		(0.2)						
82	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	$CuCl_2$ (20%)	-	100	12	68
83	1:3	$TsOH.H_2O$ (0.2)	DMF (1.0 mL)	$CuCl_2$ (20%)	-	100	12	73
84	1:3	$TsOH.H_2O$ (0.2)	DMF (1.2 mL)	$CuCl_2$ (20%)	-	100	12	78
85	1:3	$TsOH.H_2O$ (0.2)	DMF (1.5 mL)	$CuCl_2$ (20%)	-	100	12	81
86	1:3	$TsOH.H_2O$ (0.2)	DMF (2 mL)	$CuCl_2$ (20%)	-	100	12	71
87	1:3	$TsOH.H_2O$ (0.2)	DMF (2.5 mL)	$CuCl_2$ (20%)	-	100	12	66
88	1:3	$TsOH.H_2O$ (0.2)	DMF (3 mL)	$CuCl_2$ (20%)	-	100	12	60
89	1:3	Triflic acid (0.2)	DMF (1.5 mL)	$CuCl_2$ (20%)	-	100	12	73

Table S2. Screening of conditions for the condensation of 2-aminobenzyl alcohol with tetrahydroisoquinoline (detailed data)



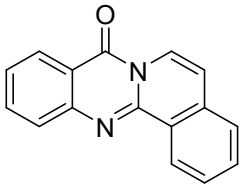
1a **4a** **5aa**

Entry	**1a**:**4a** molar ratio (mol/mol)	Additive	Solvent	Catalyst	Temp (°C)	Time (h)	GC yield
1	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(OAc)_2$ (20%)	80	12	45
2	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(OAc)_2$ (20%)	100	12	68
3	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(OAc)_2$ (20%)	120	12	69
4	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(OAc)_2$ (20%)	140	12	53
5	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(OAc)_2.H_2O$ (20%)	100	12	67
6	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$CuSO_4$ (20%)	100	12	63
7	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(NO_3)_2.3H_2O$ (20%)	100	12	48
8	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$CuCl_2$ (20%)	100	12	71

9	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$CuCl_2.2H_2O$ (20%)	100	12	65
10	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$CuBr_2$ (20%)	100	12	69
11	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	76
12	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuCl (20%)	100	12	72
13	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuI (20%)	100	12	74
14	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	$Cu(acac)_2$ (20%)	100	12	37
15	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuO (20%)	100	12	18
16	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	Cu_2O (20%)	100	12	22
17	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	-	100	12	6
18	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (5%)	100	12	47
19	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (10%)	100	12	66
20	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (15%)	100	12	71
21	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	77
22	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (25%)	100	12	74
23	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (30%)	100	12	76
24	1:1	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	43
25	1:1.5	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	50
26	1:2	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	58
27	1:2.5	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	68
28	1:3	$TsOH.H_2O$ (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	76
29	1:3	benzoic acid (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	52
30	1:3	4-NO_2 benzoic acid (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	60
31	1:3	formic acid (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	38
32	1:3	acetic acid (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	44
33	1:3	H_3PO_4 (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	60
34	1:3	PivOH (1.5)	DMF (1.0 mL)	CuBr (20%)	100	12	49
35	1:3	-	DMF (1.0 mL)	CuBr (20%)	100	12	5
36	1:3	$TsOH.H_2O$ (0.1)	DMF (1.0 mL)	CuBr (20%)	100	12	64
37	1:3	$TsOH.H_2O$ (0.3)	DMF (1.0 mL)	CuBr (20%)	100	12	84
38	1:3	$TsOH.H_2O$ (0.2)	DMAc (1.0 mL)	CuBr (20%)	100	12	78
39	1:3	$TsOH.H_2O$ (0.2)	NMP (1.0 mL)	CuBr (20%)	100	12	67

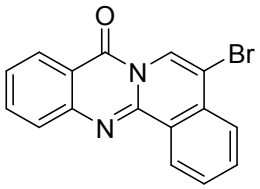
40	1:3	$TsOH.H_2O$ (0.2)	DMSO (1.0 mL)	CuBr (20%)	100	12	63
41	1:3	$TsOH.H_2O$ (0.2)	DMF (0.2 mL)	CuBr (20%)	100	12	77
42	1:3	$TsOH.H_2O$ (0.2)	DMF (0.5 mL)	CuBr (20%)	100	12	86

3. Characterization data for all products



8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3aa)

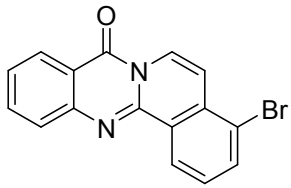
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a light yellow solid, 78% yield (37.7 mg). 1H NMR (500 MHz, $CDCl_3$, ppm) δ 9.01 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 8.57 (dd, J = 7.5 Hz, 2.0 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.81 (t, J = 7.0 Hz, 1H), 7.65 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.59–7.54 (m, 2H), 7.43 (t, J = 7.5 Hz, 1H), 6.95 (dd, J = 7.5 Hz, 1.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.4, 147.4, 146.2, 134.8, 132.9, 132.2, 128.5, 127.4, 127.3, 127.3, 126.4, 125.8, 121.9, 117.7, 113.2. One carbon signal could not be located. This compound is known.[1]



5-bromo-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ab)

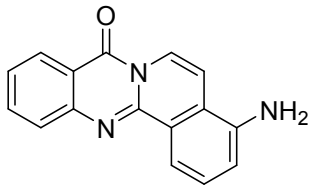
[1] *Chem. Commun.*, 2016, **52**, 12869-12872

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a light yellow solid, 81% yield (53.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.01 (d, J = 8.0 Hz, 1H), 8.85 (s, 1H), 8.40 (d, J = 7.5 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.83 (d, J = 3.0 Hz, 2H), 7.77 (t, J = 7.0 Hz, 1H), 7.66 (t, J = 7.5 Hz, 1H), 7.50–7.47 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 158.3, 147.1, 145.0, 134.9, 132.6, 131.8, 129.3, 127.68, 127.67, 127.36, 127.35, 126.3, 126.1, 122.7, 117.6, 109.8. HRMS (ESI) *m/z* calcd. for $C_{16}H_{10}BrN_2O^+$ $(M+H)^+$ 324.9971, found 324.9977.



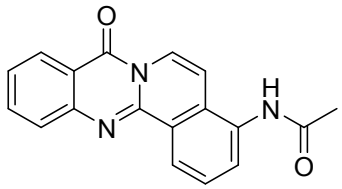
4-bromo-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ac)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a light yellow solid, 83% yield (54.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.98 (d, J = 8.5 Hz, 1H), 8.63 (d, J = 8.0 Hz, 1H), 8.41 (d, J = 8.0 Hz, 1H), 7.90 (d, J = 7.0 Hz, 1H), 7.83–7.82 (m, 2H), 7.51–7.48 (m, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.34 (d, J = 8.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.1, 147.2, 145.2, 135.8, 134.9, 132.1, 129.2, 128.9, 127.6, 127.2, 126.6, 126.1, 123.1, 121.4, 117.7, 111.3. HRMS (ESI) *m/z* calcd. for $C_{16}H_{10}BrN_2O^+$ $(M+H)^+$ 324.9971, found 324.9979.



4-amino-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ad)

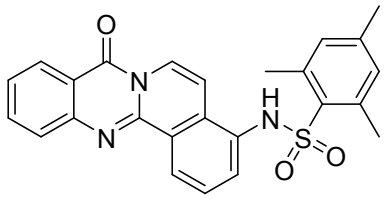
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a light yellow solid, 52% yield (27.2 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 8.44 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 7.5 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.94 (t, J = 7.0 Hz, 1H), 7.85 (d, J= 8.0 Hz, 1H), 7.56 (t, J = 7.5 Hz, 1H), 7.50 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 8.0 Hz, 1H), 7.04 (d, J = 7.5 Hz, 1H), 5.99 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, ppm) δ 159.1, 147.6, 146.8, 145.4, 135.3, 129.6, 128.0, 127.7, 127.1, 126.0, 119.2, 119.1, 117.5, 116.5, 114.4, 109.1. HRMS (ESI) *m/z* calcd. for $C_{16}H_{12}N_3O^+$ $(M+H)^+$ 262.0975, found 262.0979.



***N*-(8-oxo-8*H*-isoquinolino[1,2-*b*]quinazolin-4-yl)acetamide (3ae)**

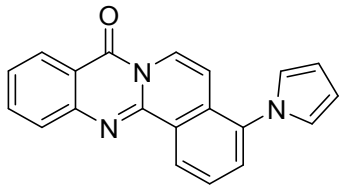
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as an off-white solid, 68% yield (41.3 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 10.08 (s, 1H), 8.84 (d, J = 8.0 Hz, 1H), 8.58 (d, J = 8.0 Hz, 1H), 8.35 (d, J = 7.5 Hz, 1H), 7.99–7.95 (m, 2H), 7.89 (d, J = 8.5 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 2.20 (s, 3H). ^{13}C

NMR (125 MHz, DMSO-d_6, ppm) δ 169.6, 159.0, 147.4, 146.1, 135.6, 134.2, 128.9, 128.8, 128.0, 127.7, 127.5, 127.2, 126.4, 123.9, 121.8, 117.8, 109.0, 23.8. HRMS (ESI) *m/z* calcd. for $C_{18}H_{14}N_3O_2^+$ $(M+H)^+$ 304.1081, found 304.1086.



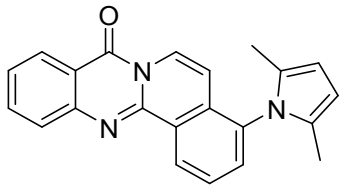
2,4,6-trimethyl-*N*-(8-oxo-8*H*-isoquinolino[1,2-*b*]quinazolin-4-yl)benzenesulfonamide (3af)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 1:1) as a white solid, 42% yield (37.5 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 10.15 (s, 1H), 8.85 (d, J = 7.0 Hz, 1H), 8.49 (d, J = 6.5 Hz, 1H), 8.32 (dd, J = 6.5 Hz, 1.0 Hz, 1H), 7.96–7.93 (m, 1H), 7.86 (d, J = 7.0 Hz, 1H), 7.61–7.57 (m, 2H), 7.35 (d, J = 7.0 Hz, 1H), 7.27 (dd, J = 6.5 Hz, 0.5 Hz, 1H), 6.99 (s, 2H), 2.38 (s, 6H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6, ppm) δ 158.4, 146.8, 145.3, 142.0, 138.6, 135.1, 133.9, 131.769, 131.762, 131.6, 130.0, 129.9, 128.4, 127.9, 127.2, 127.1, 126.7, 126.0, 124.9, 121.7, 117.3, 108.3, 22.5, 20.3. One carbon signal could not be located. HRMS (ESI) *m/z* calcd. for $C_{25}H_{22}N_3O_3S^+$ $(M+H)^+$ 444.1376, found 444.1381.



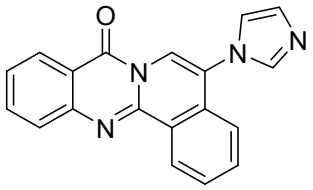
4-(1*H*-pyrrol-1-yl)-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ag)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a light yellow solid, 50% yield (31.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.12–9.10 (m, 1H), 8.57 (d, J = 7.0 Hz, 1H), 8.44 (dd, J = 6.5 Hz, 1.0 Hz, 1H), 7.90 (d, J = 6.5 Hz, 1H), 7.86 (td, J = 6.5 Hz, 1.0 Hz, 1H), 7.68–7.66 (m, 2H), 7.53–7.51 (m, 1H), 6.94 (t, J = 2.0 Hz, 2H), 6.90 (d, J = 7.5 Hz, 1H), 6.43 (t, J = 2.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.1, 147.4, 145.5, 137.5, 134.9, 129.5, 129.2, 128.6, 128.2, 127.6, 127.3, 126.6, 126.1, 123.0, 122.8, 117.8, 110.0, 108.0. HRMS (ESI) *m/z* calcd. for $C_{20}H_{14}N_3O^+$ $(M+H)^+$ 312.1131, found 312.1133.



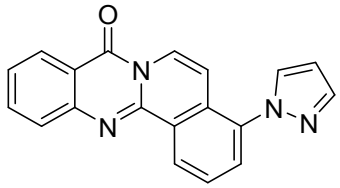
4-(2,5-dimethyl-1*H*-pyrrol-1-yl)-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ah)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white crystal, 38% yield (25.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.10 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.84 (d, J = 8.5 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 7.67 (t, J = 7.5 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 6.27 (d, J = 7.5 Hz, 1H), 5.93 (s, 2H), 1.86 (d, J = 0.5 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.2, 147.4, 145.6, 135.2, 135.0, 132.2, 131.9, 129.6, 128.7, 128.3, 127.6, 127.4, 127.3, 126.1, 123.3, 117.8, 107.9, 106.2, 12.7. HRMS (ESI) *m/z* calcd. for $C_{22}H_{18}N_3O^+$ $(M+H)^+$ 340.1444, found 340.1450.



5-(1*H*-imidazol-1-yl)-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ai)

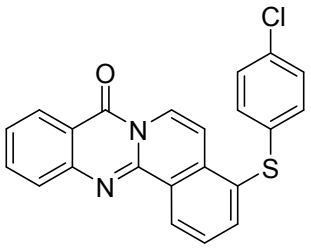
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 76% yield (47.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.18–9.17 (m, 1H), 8.79 (s, 1H), 8.46 (d, J = 7.0 Hz, 1H), 7.95–7.89 (m, 2H), 7.84 (s, 1H), 7.77–7.73 (m, 2H) 7.57 (t, J = 6.5 Hz, 1H), 7.36 (s, 1H), 7.33–7.32 (m, 1H), 7.28 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.0, 147.3, 145.0, 135.4, 132.9, 130.7, 130.2, 129.7, 127.88, 127.84, 127.7, 127.4, 126.5, 123.1, 121.9, 121.5, 120.0, 117.7. One carbon signal could not be located. HRMS (ESI) *m/z* calcd. for $C_{19}H_{13}N_4O^+$ $(M+H)^+$ 313.1084, found 313.1091.



4-(1*H*-pyrazol-1-yl)-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3aj)

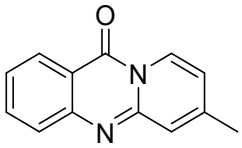
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 78% yield (48.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.16 (d, J = 6.5 Hz, 1H), 8.60 (d, J = 6.5 Hz, 1H), 8.44 (dd, J = 6.5 Hz, 1.0 Hz, 1H), 7.90 (d, J = 6.5 Hz, 1H), 7.86 (td, J = 6.5 Hz, 1.0 Hz, 2H), 7.79 (d, J = 2.0 Hz, 1H), 7.74 (dd, J = 6.5 Hz, 1.0 Hz, 1H), 7.69 (t, J = 6.5 Hz, 1H), 7.53–

7.51 (m, 1H), 7.08 (d, J = 7.0 Hz, 1H), 6.57 (t, J = 2.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.1, 147.3, 145.4, 141.6, 136.6, 135.0, 131.4, 128.9, 128.7, 128.1, 127.6, 127.5, 127.3, 126.1, 123.0, 117.9, 108.1, 107.3. One carbon signal could not be located. HRMS (ESI) *m/z* calcd. for $C_{19}H_{13}N_4O^+$ $(M+H)^+$ 313.1084, found 313.1092.



4-((4-chlorophenyl)thio)-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ak)

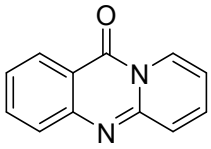
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 75% yield (58.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.03 (d, J = 8.0 Hz, 1H), 8.55 (d, J = 8.0 Hz, 1H), 8.37 (td, J = 8.0 Hz, 0.5 Hz, 1H), 7.81–7.76 (m, 2H), 7.72 (dd, J = 7.5 Hz, 0.5 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.46–7.41 (m, 2H), 7.17–7.15 (m, 2H), 7.06–7.04 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.2, 147.4 ,145.8, 137.9, 134.9, 134.5, 134.2, 132.9, 130.8, 130.5, 129.5, 128.9, 128.6, 127.9, 127.6, 127.3, 126.0, 122.9, 117.7, 110.0. HRMS (ESI) *m/z* calcd. for $C_{22}H_{14}ClN_2OS^+$ $(M+H)^+$ 389.0510, found 389.0515.



7-methyl-11*H*-pyrido[2,1-*b*]quinazolin-11-one (3an)

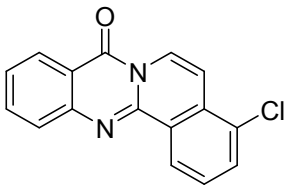
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh

or 37−63 μm, hexanes/ethyl acetate = 3:1) as a yellow solid, 39% yield (16.4 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.77 (d, J = 6.5 Hz, 1H), 8.41 (dd, J = 6.5 Hz, 2.0 Hz, 1H), 7.82–7.79 (m 1H), 7.74 (d, J = 7.0 Hz, 1H), 7.44–7.41 (m, 1H), 7.27–7.26 (d, m, 1H), 6.69 (dd, J = 6.0 Hz, 1.5 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.0, 148.9, 1478., 145.8, 134.9, 127.2, 126.7, 125.9, 124.7, 123.7, 116.0, 115.5, 21.4. This compound is known.[2]



11*H*-pyrido[2,1-*b*]quinazolin-11-one (3ao)

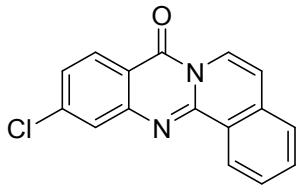
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a yellow solid, 30% yield (11.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.86 (td, J = 6.5 Hz, 0.5 Hz, 1H), 8.44 (dd, 6.5 Hz, 1.0 Hz, 1H), 7.85–7.82 (m, 1H), 7.77 (d, J = 7.0 Hz, 1H), 7.50–7.45 (m, 3H), 6.86–6.84 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 158.9, 148.5, 147.7, 135.0, 134.0, 127.3, 126.9, 126.7, 126.3, 125.2, 116.3, 112.4. This compound is known.[3]



4-chloro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ap)

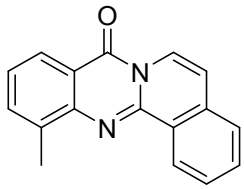
[2] *Adv. Synth. Catal*. 2018, **360**, 659.
[3] *Adv. Synth. Catal*. 2018, **360**, 659.

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 46% yield (26.1 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.07 (d, J = 7.0 Hz, 1H), 8.75 (s, 1H), 8.42 (dd, J = 6.5 Hz, 1H), 8.00 (d, J = 6.5 Hz, 1H), 7.86–7.84 (m, 2H), 7.81 (t, J = 6.5 Hz, 1H), 7.70 (t, J = 7.0 Hz, 1H), 7.52–7.49 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 158.4, 147.2, 145.0, 134.9, 132.5, 131.2, 129.3, 127.7, 127.6, 127.4, 127.3, 126.1, 123.8, 120.4, 120.1, 117.6. HRMS (ESI) *m/z* calcd. for $C_{16}H_{10}ClN_2O^+$ $(M+H)^+$ 281.0476, found 281.0486.



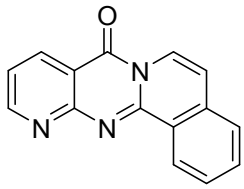
11-chloro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ba)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 86% yield (48.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.98 (d, J = 6.0 Hz, 1H), 8.55 (d, J = 6.0 Hz, 1H), 8.29 (d, J = 7.5 Hz, 1H), 7.81 (s, 1H), 7.68–7.58 (m, 3H), 7.36 (d, J = 7.0 Hz, 1H), 6.99 (d, J = 6.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 158.8, 148.1, 147.1, 141.2, 133.1, 132.6, 128.78, 128.76, 127.5, 126.9, 126.7, 126.57, 126.50, 121.7, 116.0, 113.6. HRMS (ESI) *m/z* calcd. for $C_{16}H_{10}ClN_2O^+$ $(M+H)^+$ 281.0476, found 281.0492.



12-methyl-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (3ca)

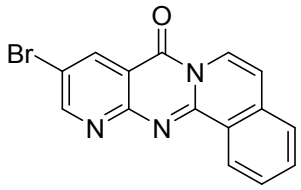
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 88% yield (45.8 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.96 (d, J = 8.0 Hz, 1H), 8.50 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.0 Hz, 1H), 7.61–7.58 (m, 2H), 7.54–7.48 (m, 2H), 7.28 (t, J = 7.5 Hz, 1H), 6.89 (d, J = 7.5 Hz, 1H), 2.69 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.7, 146.0, 144.8, 135.9, 135.0, 132.7, 131.9, 128.3, 127.8, 127.1, 126.3, 125.3, 124.9, 121.9, 117.6, 113.0, 17.5. HRMS (ESI) *m/z* calcd. for $C_{17}H_{13}N_2O^+$ $(M+H)^+$ 261.1022, found 261.1030.



8*H*-pyrido[2',3':4,5]pyrimido[2,1-*a*]isoquinolin-8-one (3da)

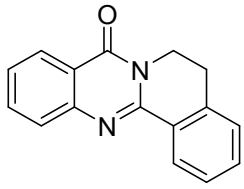
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 2:1) as a yellow solid, 63% yield (31.3 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.21 (d, J = 6.5 Hz, 1H), 9.09 (d, J = 1.5 Hz, 1H), 8.74 (dd, J = 6.5 Hz, 1.5 Hz, 1H), 8.57 (d, J = 6.5 Hz, 1H), 7.74 (td, J = 6.5 Hz, 0.5 Hz, 1H), 7.66 (t, J = 6.5 Hz, 1H), 7.62 (d, J = 6.5 Hz, 1H), 7.45–7.43 (m, 1H), 7.09 (d, J = 6.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.8, 157.1, 156.7, 148.9, 136.9, 133.3, 133.0, 128.8, 128.1, 126.9, 126.4, 121.4, 121.1, 114.1, 112.7. This compound is known.[4]

[4] *Org. Lett.* 2015, **17**, 6, 1569–1572



10-bromo-8*H*-pyrido[2',3':4,5]pyrimido[2,1-*a*]isoquinolin-8-one (3ea)

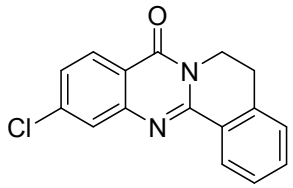
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 2:1) as a white solid, 59% yield (38.5 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.19 (d, J = 8.5 Hz, 1H), 9.04 (d, J = 2.5 Hz, 1H), 8.83 (d, J = 2.5 Hz, 1H), 8.57 (d, J = 8.0 Hz, 1H), 7.76 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.68–7.64 (m, 2H), 7.12 (d, J = 8.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 159.0, 158.2, 155.1, 149.2, 138.6, 133.4, 133.3, 129.1, 128.2, 126.8, 126.6, 121.4, 116.4, 114.6, 113.6. HRMS (ESI) *m/z* calcd. for $C_{15}H_9BrN_3O^+$ $(M+H)^+$ 325.9924, found 325.9928.



5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5aa)

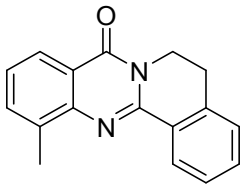
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white crystal, 80% yield (39.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.38 (d, J = 7.5 Hz, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.67–7.62 (m, 2H), 7.38–7.31 (m, 3H), 7.17 (d, J = 6.0 Hz, 1H), 4.31 (t, J = 6.5 Hz, 2H), 2.99 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.6, 149.3, 147.8, 137.0,

134.1, 131.6, 129.5, 128.0, 127.608, 127.606, 127.4, 126.8, 126.5, 120.7, 39.5, 27.4. This compound is known.[5]



11-chloro-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ba)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 69% yield (39.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.39 (d, J = 8.0 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.70 (d, J = 2.0 Hz, 1H), 7.42 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.32 (dd, J = 8.5 Hz, 2.0 Hz, 1H), 7.22 (d, J = 7.5 Hz, 1H), 4.32 (t, J = 6.5 Hz, 2H), 3.03 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.1, 150.5, 148.7, 140.3, 137.1, 132.0, 129.2, 128.3, 128.1, 127.7, 127.5, 127.078, 127.071, 119.1, 39.6, 27.3. This compound is known.[5]

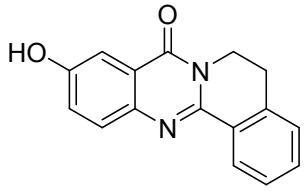


12-methyl-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ca)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a light yellow solid, 57% yield (29.7 mg).

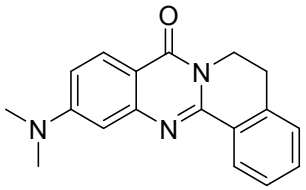
[5] *Adv. Synth. Catal*. 2018, **360**, 659.

^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.53 (dd, J = 6.0 Hz, 1.0 Hz, 1H), 8.15 (d, J = 6.5 Hz, 1.0 Hz, 1H), 7.59 (ddd, J = 6.0 Hz, 1.0 Hz, 1.0 Hz, 1H), 7.46 (td, J = 6.5 Hz, 1.0 Hz, 1H), 7.42 (td, J = 6.5 Hz, 1.0 Hz, 1H), 7.33 (t, J = 6.5 Hz, 1H), 7.27 (dd, J = 6.0 Hz, 0.5 Hz, 1H), 4.40 (t, J = 5.5 Hz, 2H), 3.09 (t, J = 5.5 Hz, 2H), 2.70 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.0, 148.0, 146.2, 136.9, 136.1, 134.7, 131.5, 129.9, 128.0, 127.5, 127.4, 126.1, 124.5, 120.7, 39.5, 27.4, 17.2. This compound is known.[6]



10-hydroxy-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ea)

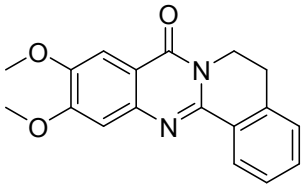
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a yellow solid, 67% yield (35.4 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 10.16 (br s, 1H), 8.31 (d, J = 7.0 Hz, 1H), 7.62 (d, J = 8.5 Hz, 1H), 7.50 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.46 (d, J = 3.0 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.38 (d, J = 7.5 Hz, 1H), 7.30 (dd, J = 8.5 Hz, 3.0 Hz, 1H), 4.28 (t, J = 6.0 Hz, 2H), 3.09 (t, J = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, ppm) δ 160.7, 156.6, 146.8, 141.0, 137.68, 137.67 131.6, 129.7, 129.5, 128.2, 127.6, 127.3, 124.4, 121.8, 109.6, 27.0. This compound is known.[7]



[6] *Adv. Synth. Catal*. 2018, **360**, 659.
[7] *Tetrahedron Lett.* 2014, **26**, 3607.

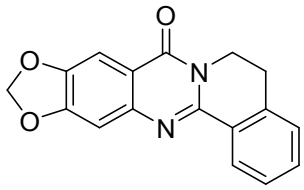
11-(dimethylamino)-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5fa)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a light yellow solid, 74% yield (43.1 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 8.35 (d, J = 8.0 Hz, 1H), 7.94 (d, J = 9.0 Hz, 1H), 7.53 (td, J = 7.5 Hz, 1.0 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.40 (d, J = 7.5 Hz, 1H), 6.97 (dd, J = 9.0 Hz, 2.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 4.24 (t, J = 6.5 Hz, 2H), 3.09–3.07 (m, 8H). ^{13}C NMR (125 MHz, DMSO-d_6, ppm) δ 160.5, 154.7, 149.7, 149.4, 138.1, 131.9, 129.8, 128.2, 127.8, 127.7, 127.5, 113.1, 109.7, 106.2, 39.1, 27.1. One carbon signal could not be located. HRMS (ESI) *m/z* calcd. for $C_{18}H_{17}N_3O^+$ $(M+H)^+$ 292.1444, found 292.1454.



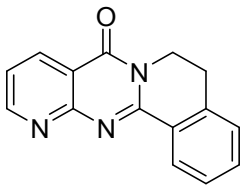
10,11-dimethoxy-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ga)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a white solid, 79% yield (48.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.43 (d, J = 7.5 Hz, 1H), 7.64 (s, 1H), 7.48–7.41 (m, 2H), 7.29 (d, J = 7.5 Hz, 1H), 7.18 (s, 1H), 4.42 (t, J = 6.5 Hz, 2H), 4.03 (s, 3H), 4.02 (s, 3H), 3.10 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 160.9, 155.0, 149.0, 148.3, 144.1, 136.8, 131.4, 129.7, 127.61, 127.60, 127.5, 114.2, 107.9, 105.8, 56.35, 56.31, 39.5, 27.5. This compound is known. [8]



5,6-dihydro-8*H*-[1,3]dioxolo[4,5-*g*]isoquinolino[1,2-*b*]quinazolin-8-one (5ha)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a white solid, 82% yield (47.9 mg). ^{1}H NMR (500 MHz, DMSO-d_6, ppm) δ 8.32 (d, J = 8.0 Hz, 1H), 7.53 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.47–7.43 (m, 2H), 7.40 (d, J = 7.5 Hz, 1H), 7.19 (s, 1H), 6.23 (s, 2H), 4.28 (t, J = 6.5 Hz, 2H), 3.10 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, ppm) δ 160.9, 154.0, 148.9, 147.9, 146.0, 138.3, 132.4, 129.9, 128.6, 128.0, 127.9, 116.0, 106.2, 103.6, 103.3, 27.3. One carbon signal could not be located. HRMS (ESI) *m/z* calcd. for $C_{17}H_{13}N_2O_3^+$ $(M+H)^+$ 293.0921, found 293.0928.

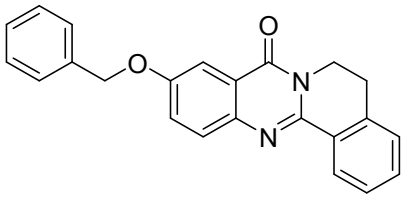


5,6-dihydro-8*H*-pyrido[2',3':4,5]pyrimido[2,1-*a*]isoquinolin-8-one (5da)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a light yellow solid, 42% yield (20.9 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.99 (s, 1H), 8.67 (d, J = 8.0 Hz, 1H), 8.64 (d, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.46 (t, J = 7.5 Hz, 1H), 7.42–7.40 (m, 1H), 7.31 (d,

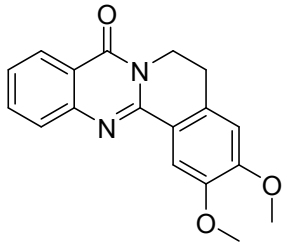
[8] *Chem. Commun.*, 2016, **52**, 12869-12872

J = 7.5 Hz, 1H), 4.42 (t, *J* = 6.0 Hz, 2H), 3.14 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 162.1, 157.8, 156.2, 152.7, 137.2, 136.4, 132.6, 129.1, 128.8, 127.8, 127.4, 121.9, 115.9, 39.8, 27.2. This compound is known. [9]



10-(benzyloxy)-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ia)

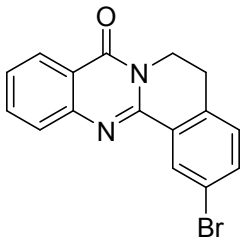
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 75% yield (53.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.37 (d, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 3.0 Hz, 1H), 7.64 (d, *J* = 9.0 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.37–7.31 (m, 5H), 7.27 (d, *J* = 7.0 Hz, 1H), 7.19 (d, *J* = 7.0 Hz, 1H), 5.10 (s, 2H), 4.33 (t, *J* = 6.0 Hz, 2H), 3.01 (t, *J* = 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.4, 157.4, 147.5, 142.5, 136.7, 136.4, 131.3, 129.6, 129.3, 128.6, 128.1, 127.7, 127.68, 127.62, 127.4, 125.1, 121.4, 107.4, 70.5, 39.7, 27.5. This compound is known. [10]



2,3-dimethoxy-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ab)

[9] *Chem. Commun.*, 2016, **52**, 12869-12872
[10] *Tetrahedron Lett.* 2014, **26**, 3607.

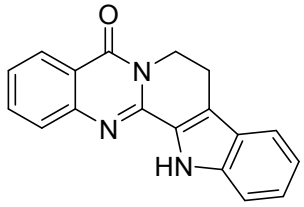
0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 3:1) as a white solid, 70% yield (43.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.29 (d, J = 7.5 Hz, 1H), 7.98 (s, 1H), 7.76–7.72 (m, 2H), 7.43 (td, J = 7.0 Hz, 2.0 Hz, 1H), 6.73 (s, 1H), 4.40 (t, J = 6.5 Hz, 2H), 4.03 (s, 3H), 3.96 (s, 3H), 3.03 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.8, 152.2, 149.3, 148.6, 147.9, 134.1, 130.9, 127.3, 126.9, 126.1, 121.8, 120.5, 110.0, 109.7, 56.2, 56.1, 39.7, 27.0. This compound is known.



2-bromo-5,6-dihydro-8*H*-isoquinolino[1,2-*b*]quinazolin-8-one (5ac)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, hexanes/ethyl acetate = 5:1) as a white solid, 76% yield (49.7 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 8.56 (d, J = 2.0 Hz, 1H), 8.23 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 7.71–7.67 (m, 2H), 7.51 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 7.42–7.39 (m, 1H), 7.10 (d, J = 8.0 Hz, 1H), 4.33 (t, J = 6.5 Hz, 2H), 2.99 (t, J = 6.5 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.5, 148.0, 147.5, 135.7, 134.5, 134.4, 131.4, 130.8, 129.1, 127.7, 126.94, 126.92, 121.4, 120.8, 39.4, 27.0. This compound is known.[11]

[11] *Chem. Commun.*, 2016, **52**, 12869-12872



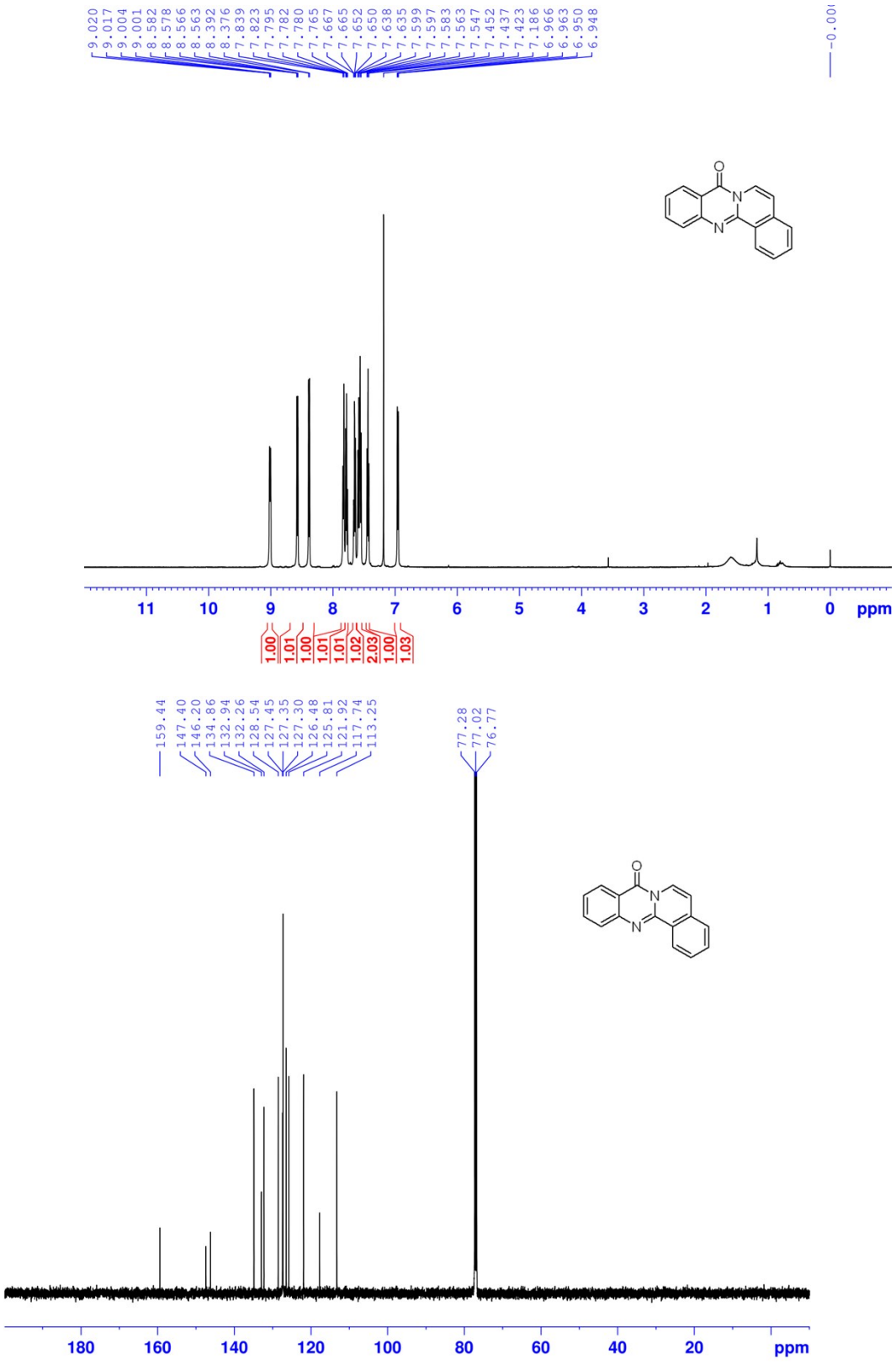
8,13-dihydroindolo[2',3':3,4]pyrido[2,1-*b*]quinazolin-5(7*H*)-one (5ad)

0.1 mmol scale for each reaction tube, product isolation based on the combination of 2 parallel reaction tubes. Purified by column chromatography on silica gel (230−400 mesh or 37−63 μm, ethyl acetate/ethanol = 50:1) as a light yellow solid, 63% yield (36.2 mg). ^{1}H NMR (500 MHz, $CDCl_3$, ppm) δ 9.37 (s, 1H), 8.24 (dd, J = 8.0 Hz, 1.5 Hz, 1H), 7.63 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.58–7.55 (m, 2H), 7.35 (td, J = 7.5 Hz, 1.5 Hz, 1H), 7.32 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.10 (t, J = 8.0 Hz, 1H), 4.51 (t, J = 7.0 Hz, 2H), 3.16 (t, J =7.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, ppm) δ 161.6, 147.5, 145.0, 138.3, 134.3, 127.2, 127.1, 126.5, 126.2, 125.64, 125.61, 121.1, 120.6, 120.1, 118.4, 112.1, 41.1, 19.6. This compound is known.[12]

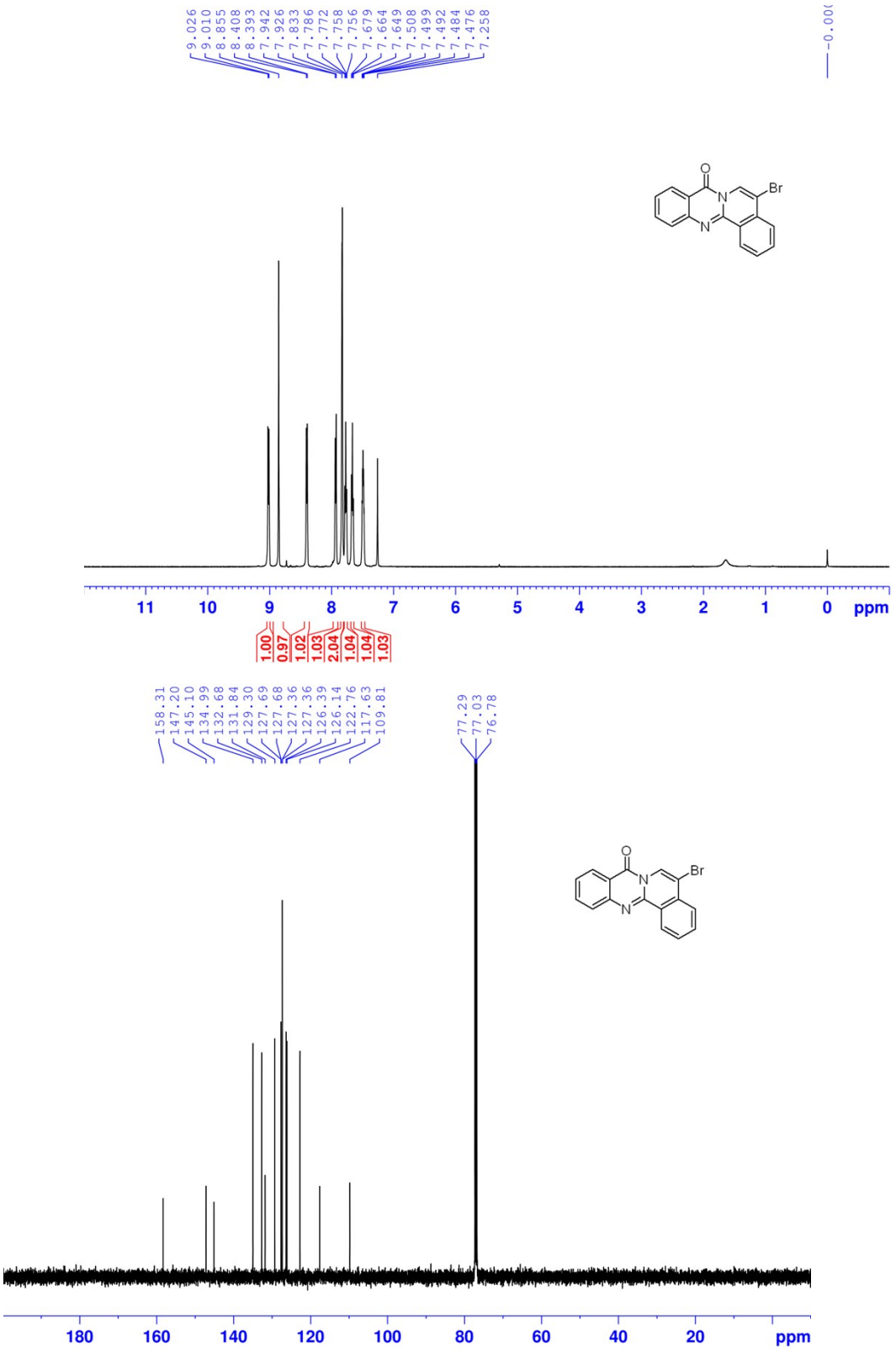
4. Copies of ^{1}H and ^{13}C NMR Spectra

[12] *Chem. Commun.*, 2016, **52**, 12869-12872

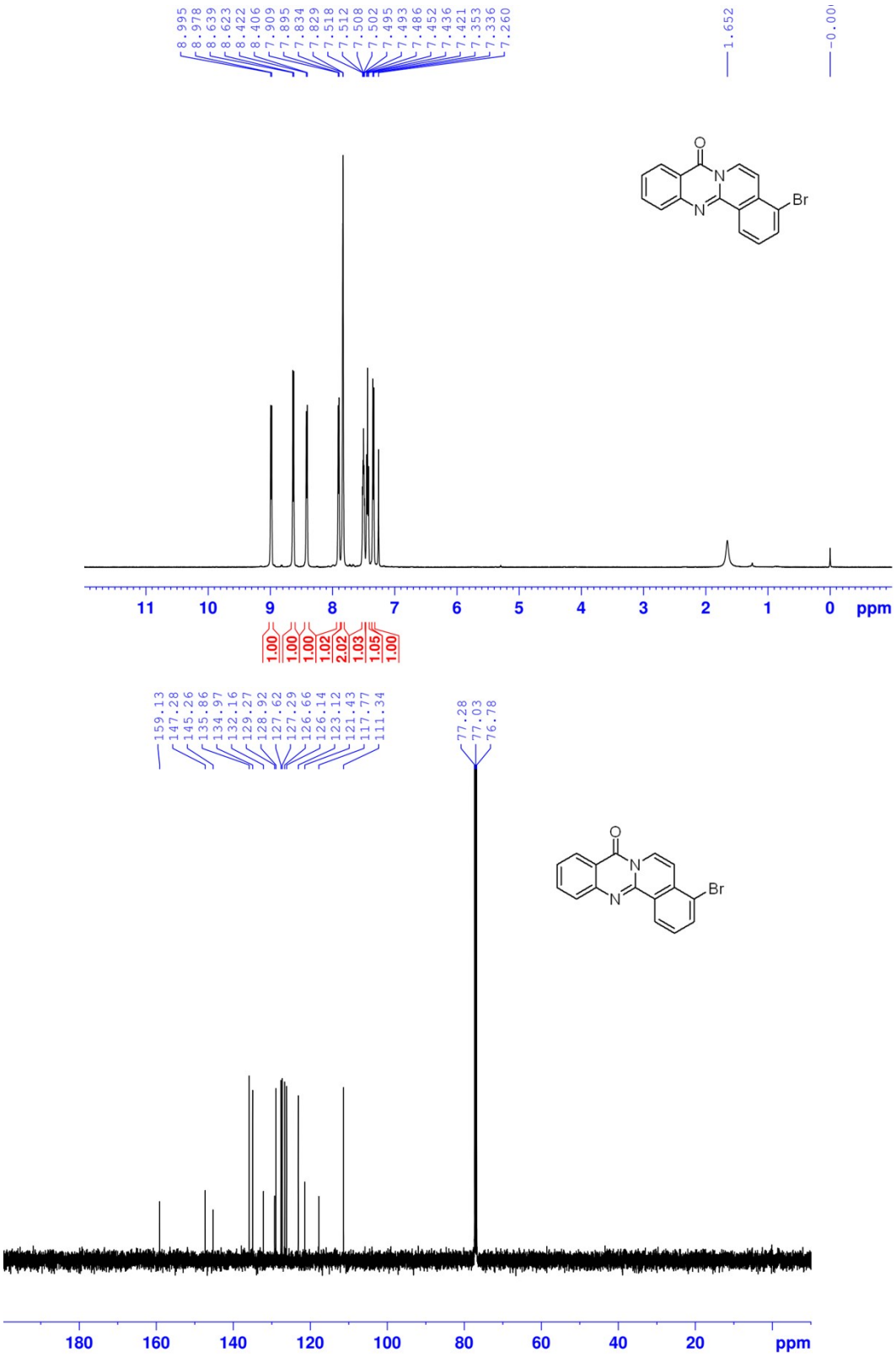
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3aa**



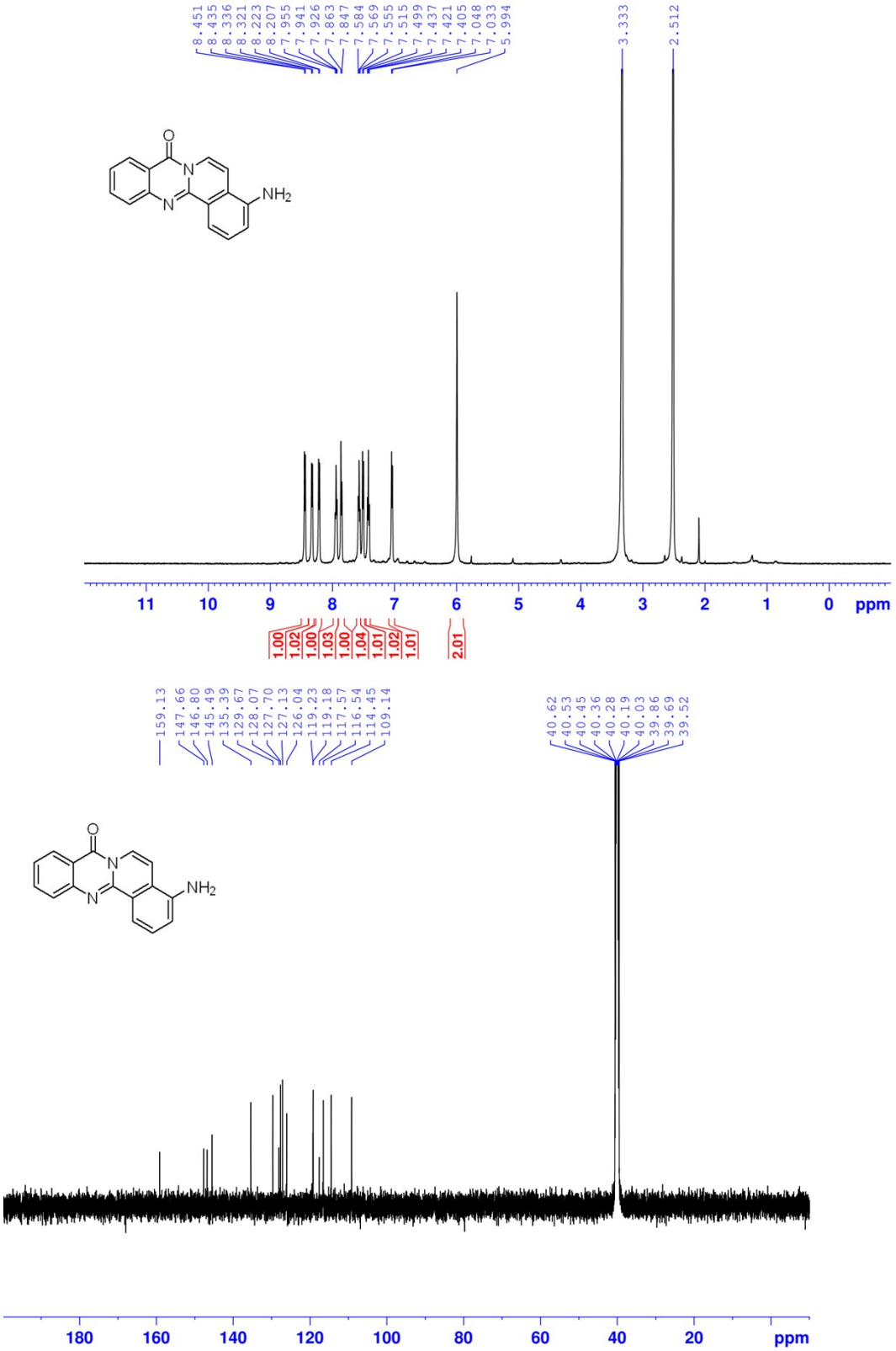
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ab**



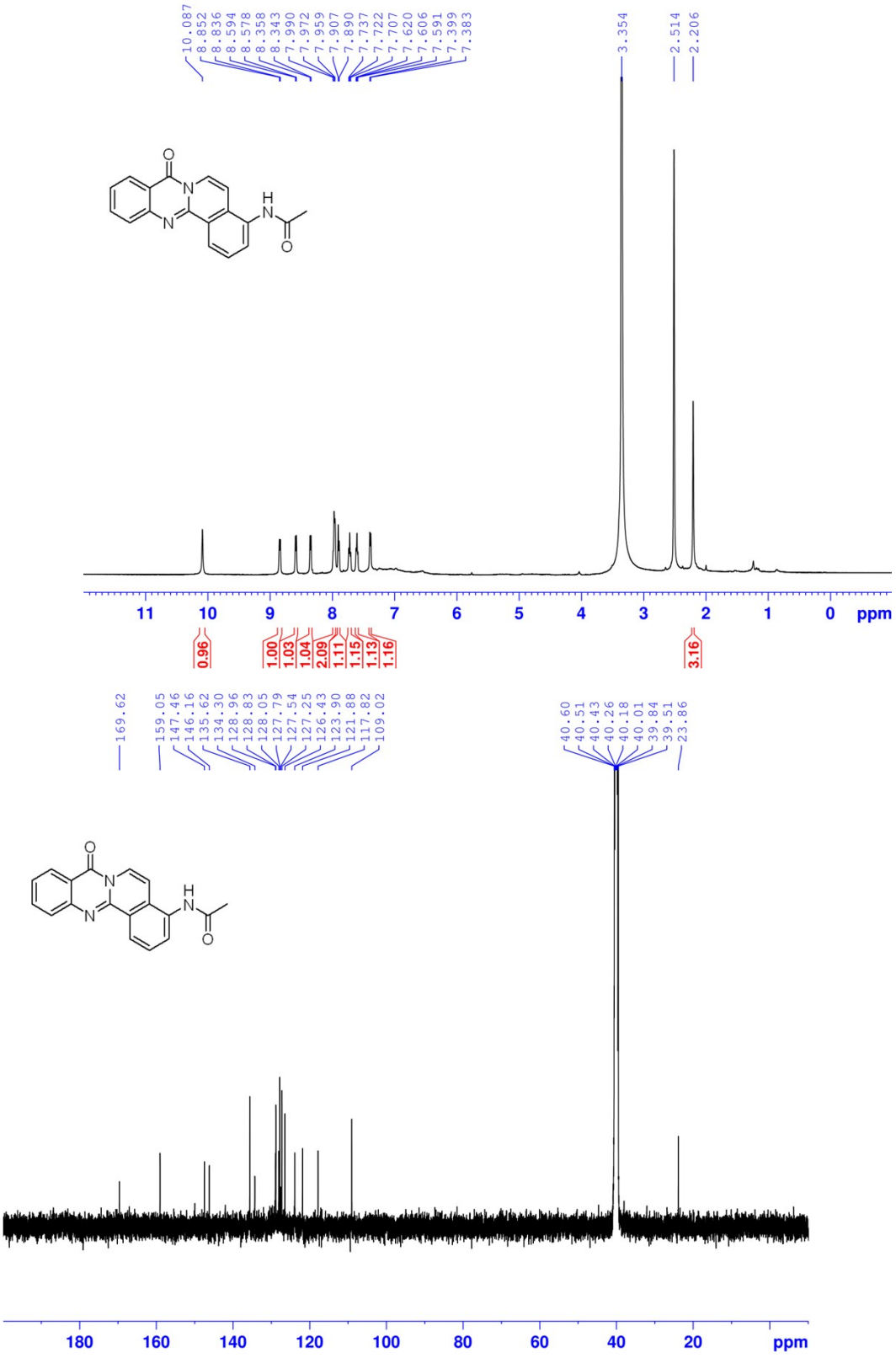
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ac**



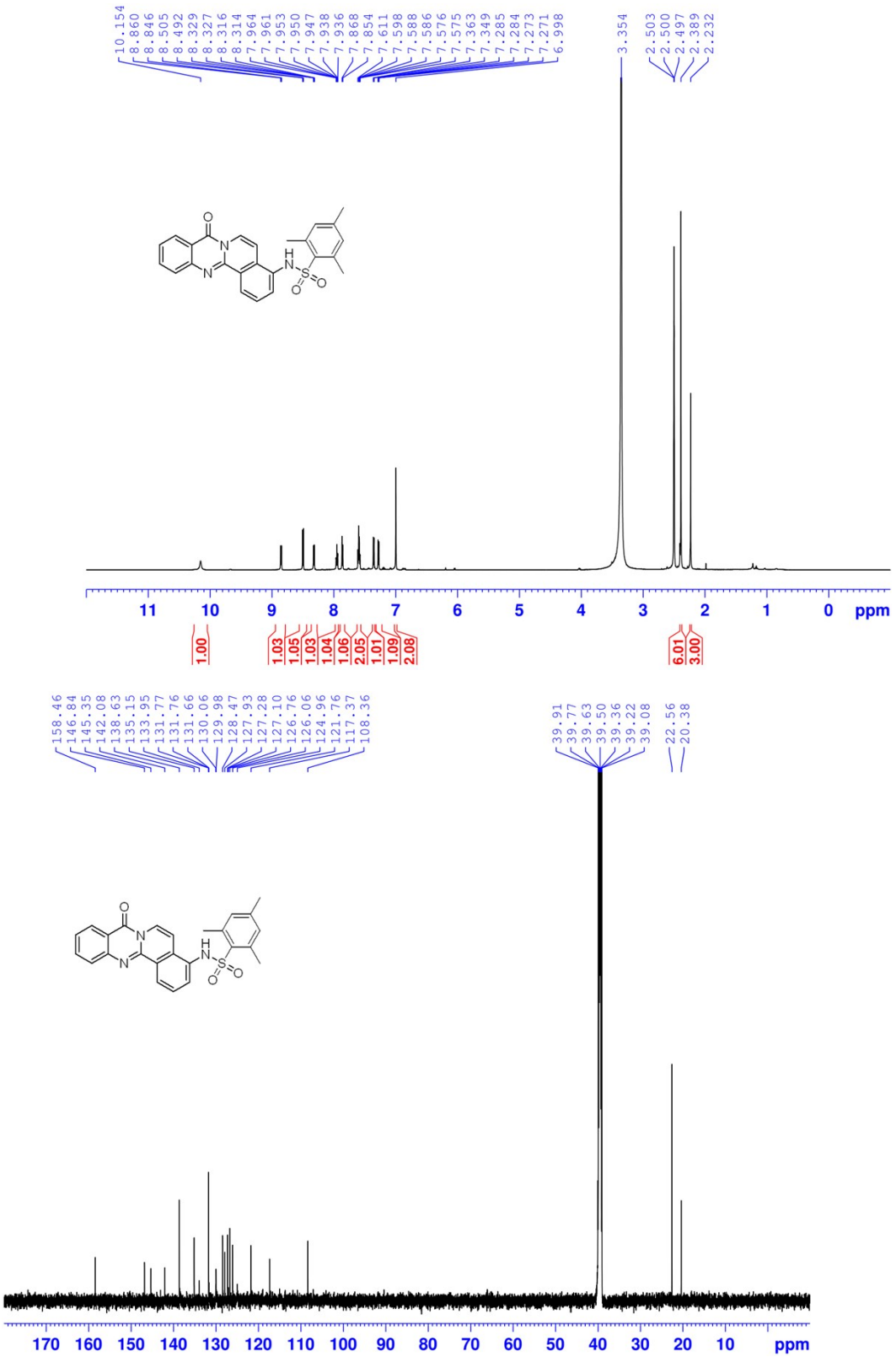
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3ad**



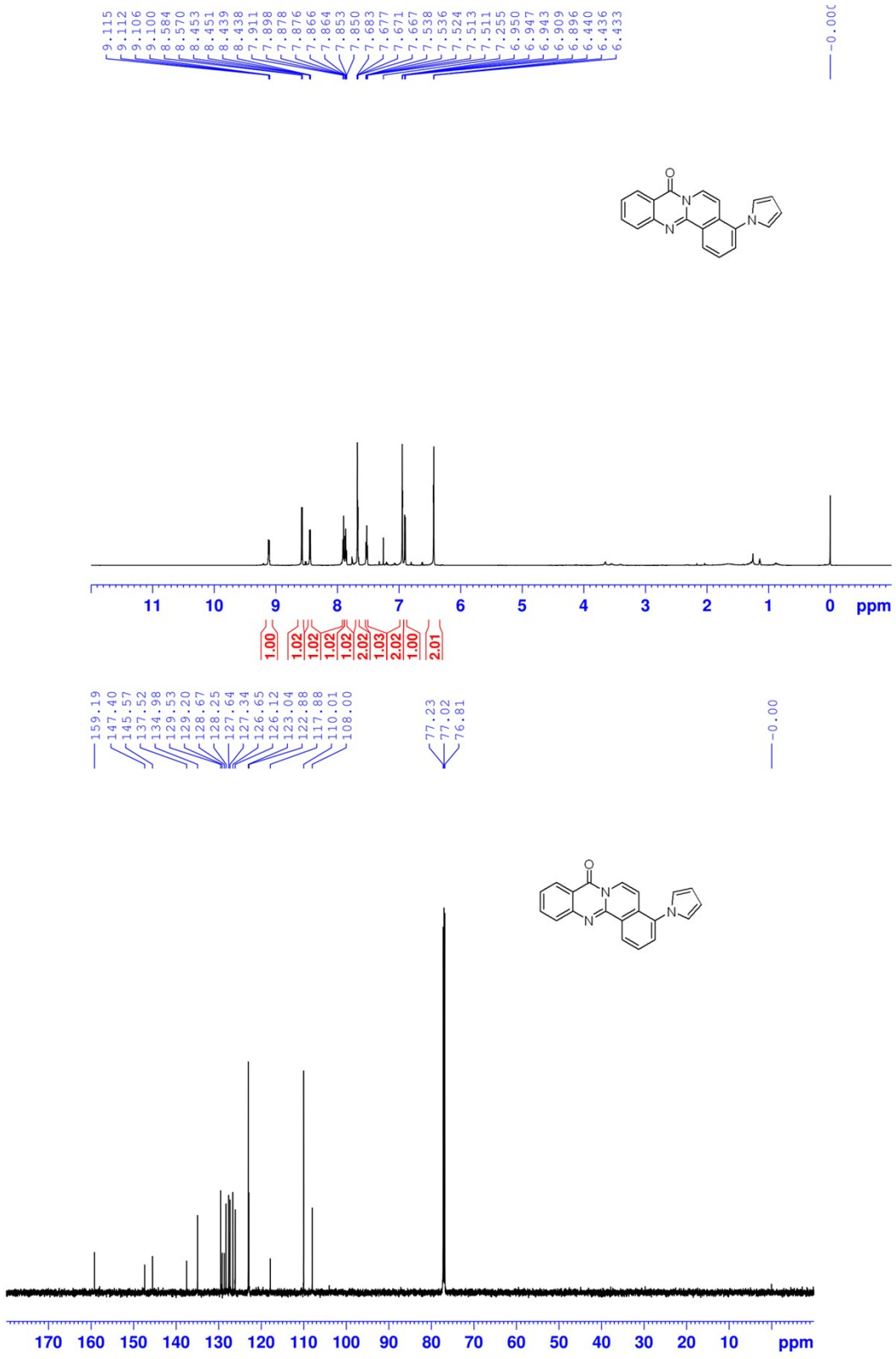
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3ae**



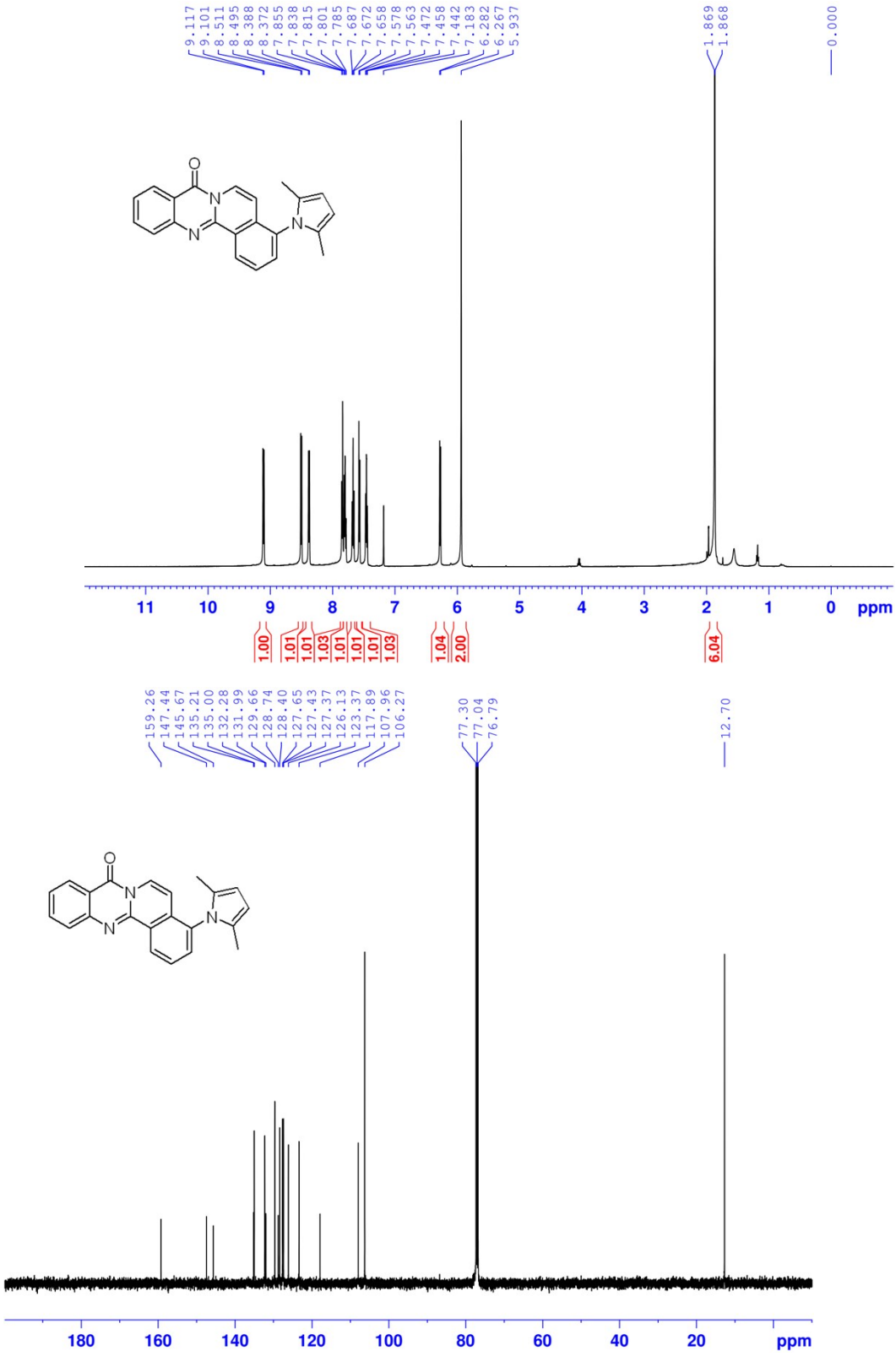
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3af**



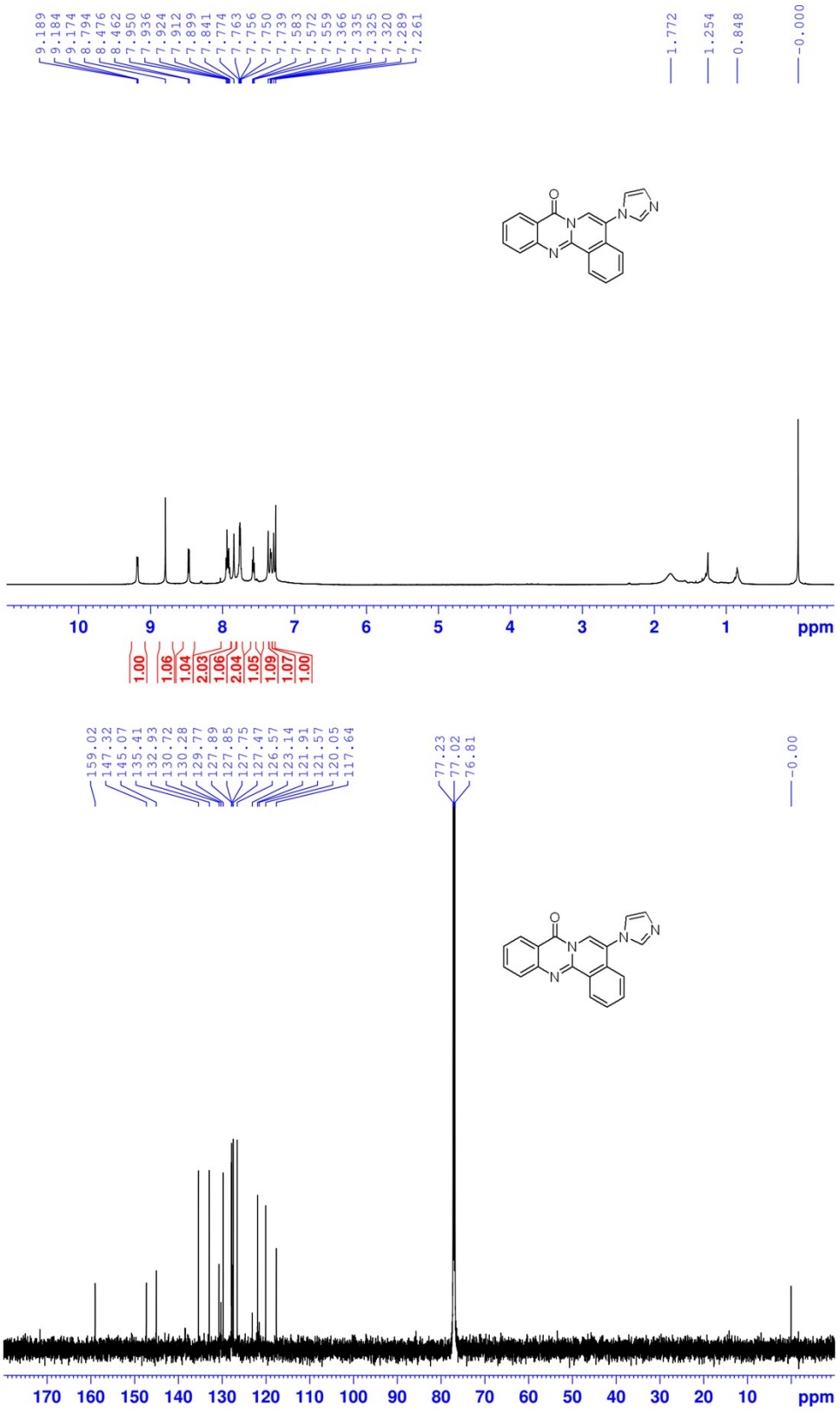
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ag**



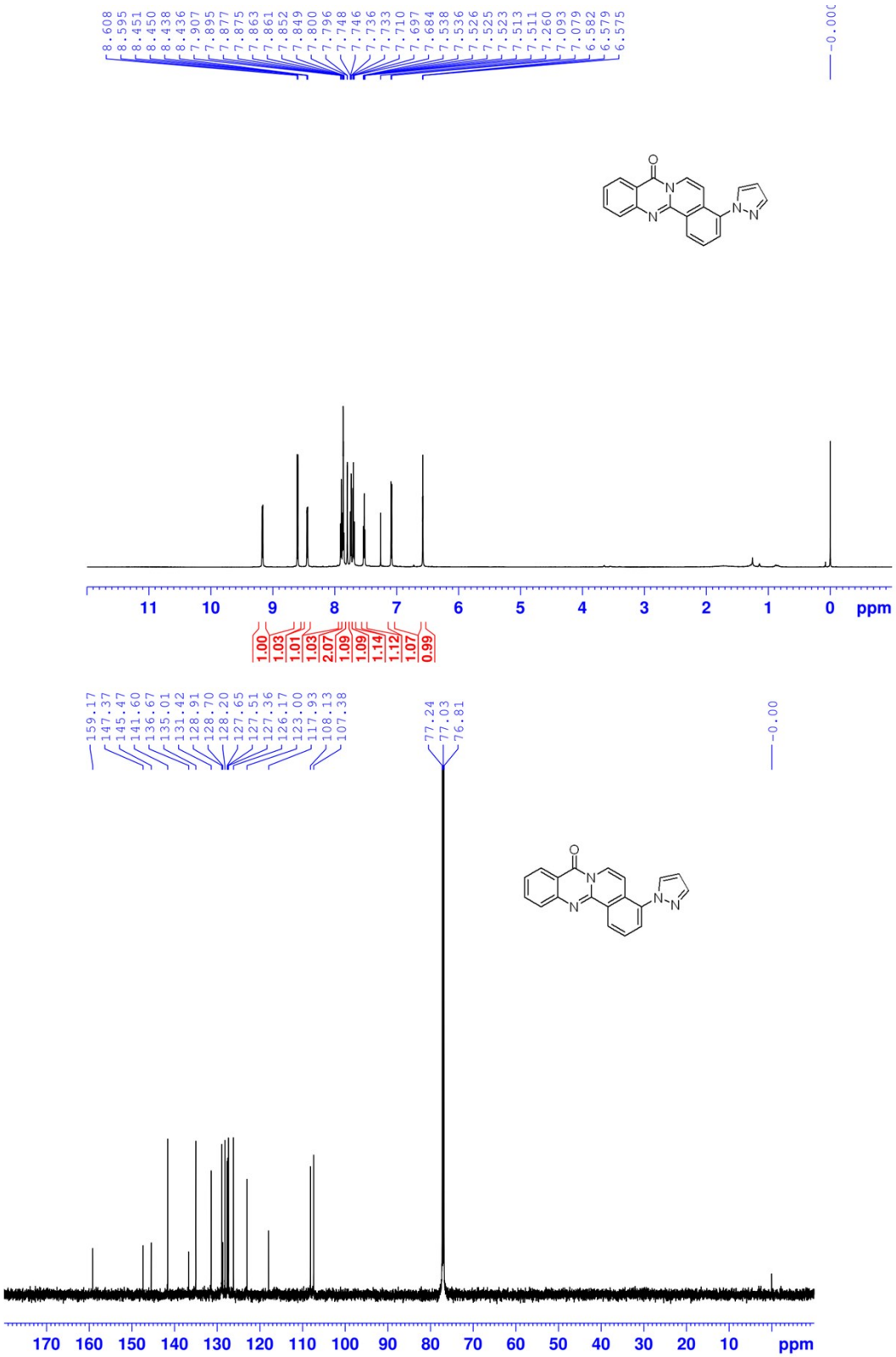
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ah**



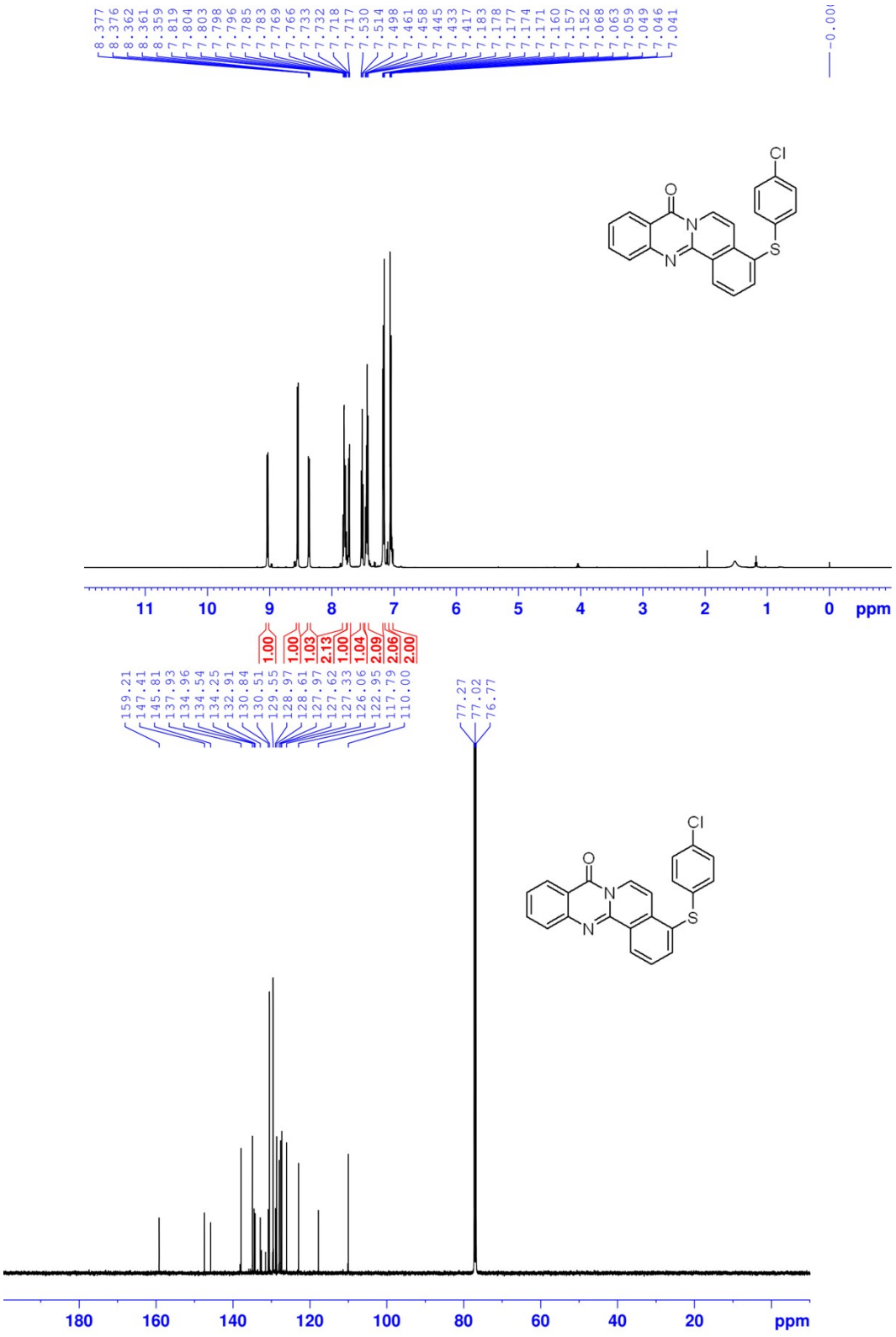
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3ai**



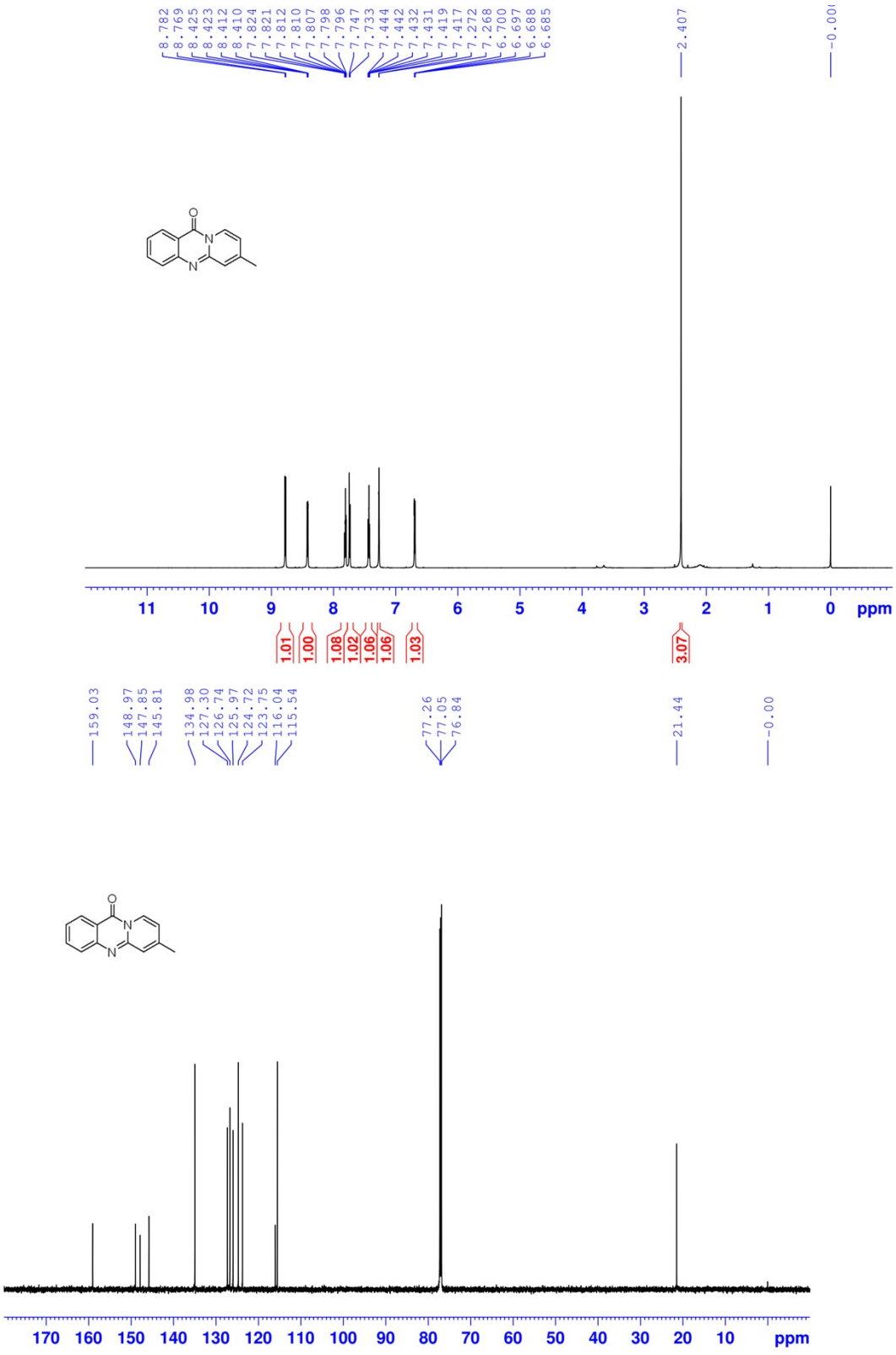
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3aj**



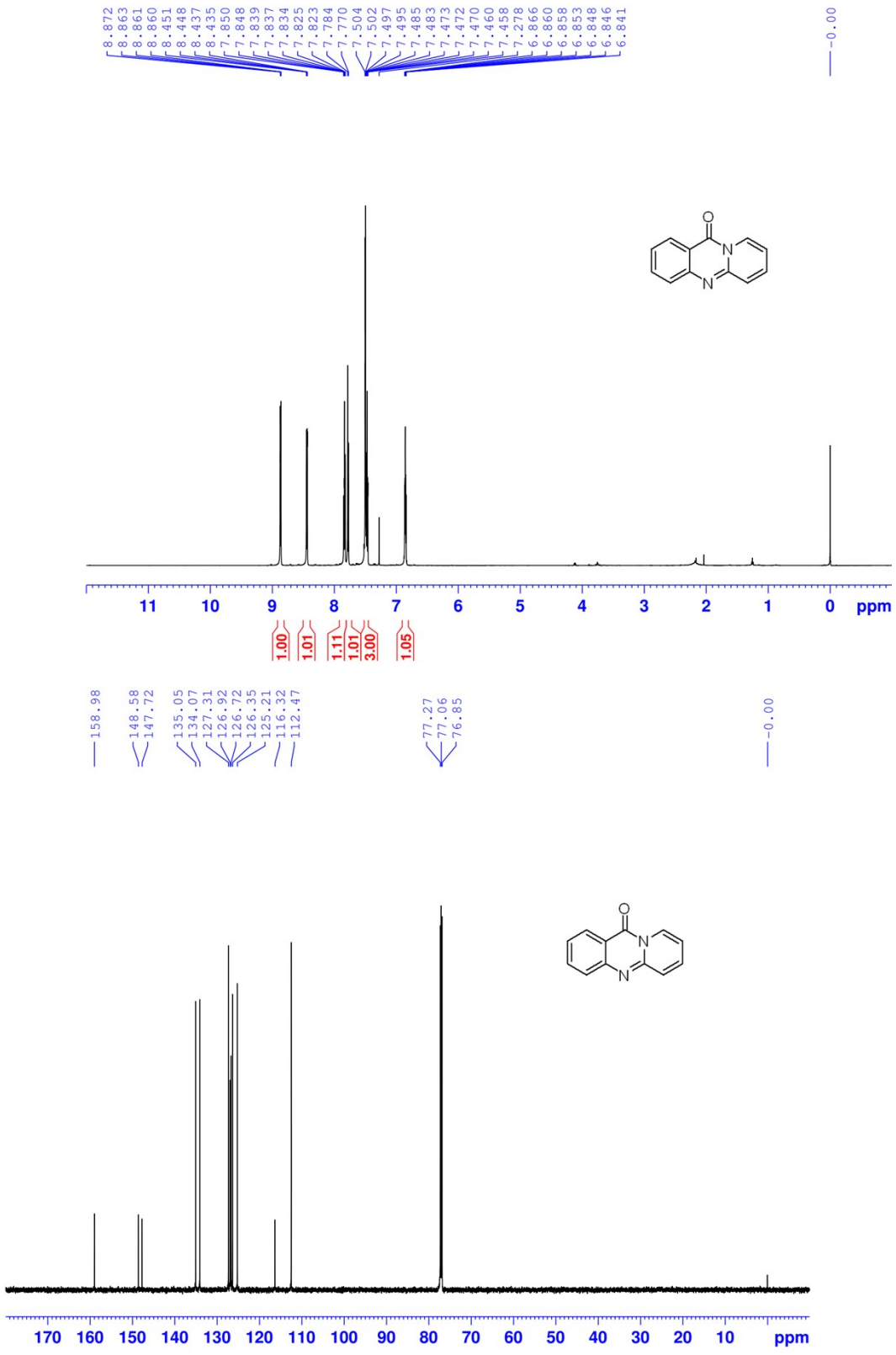
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ak**



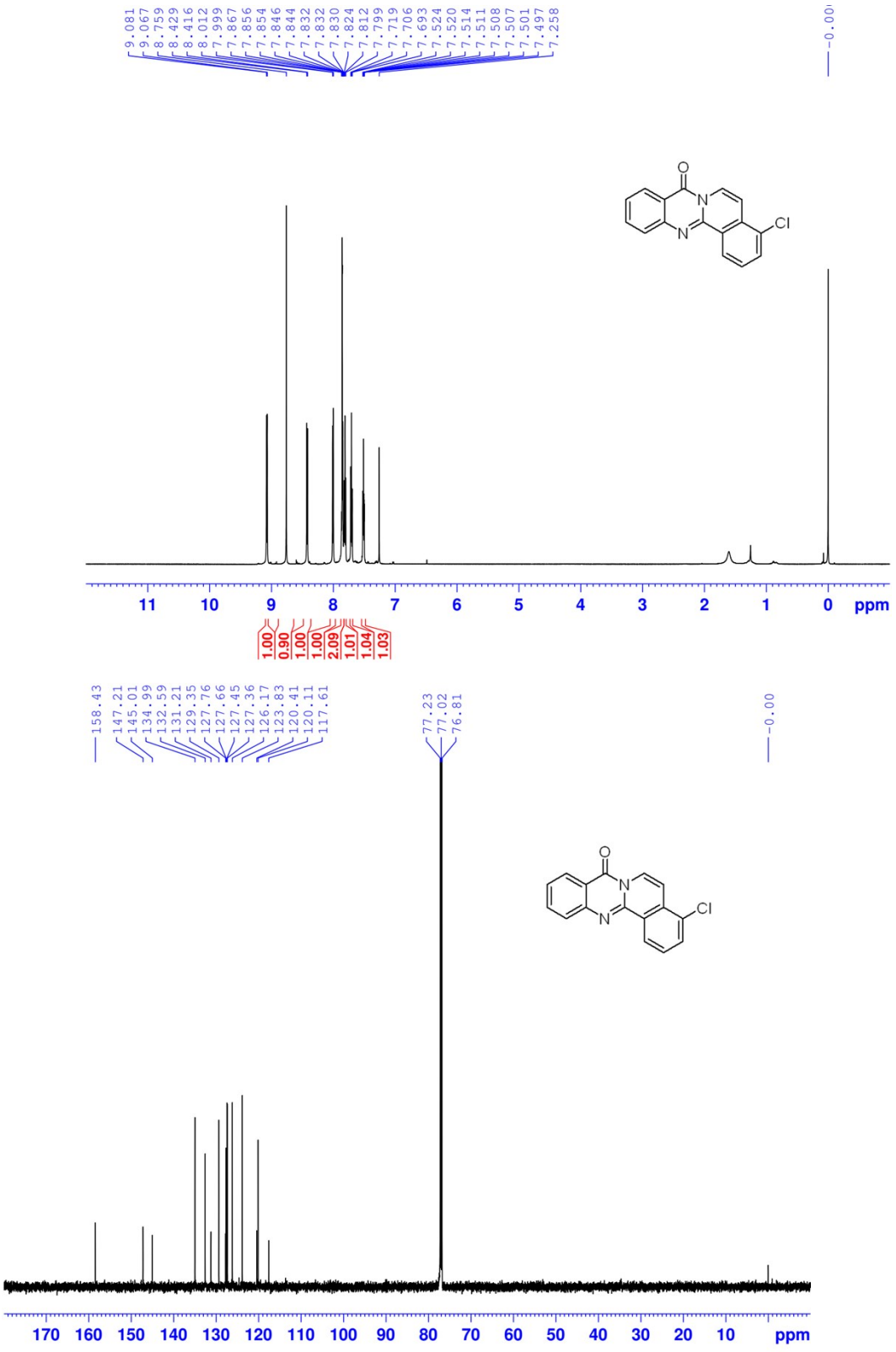
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3an**



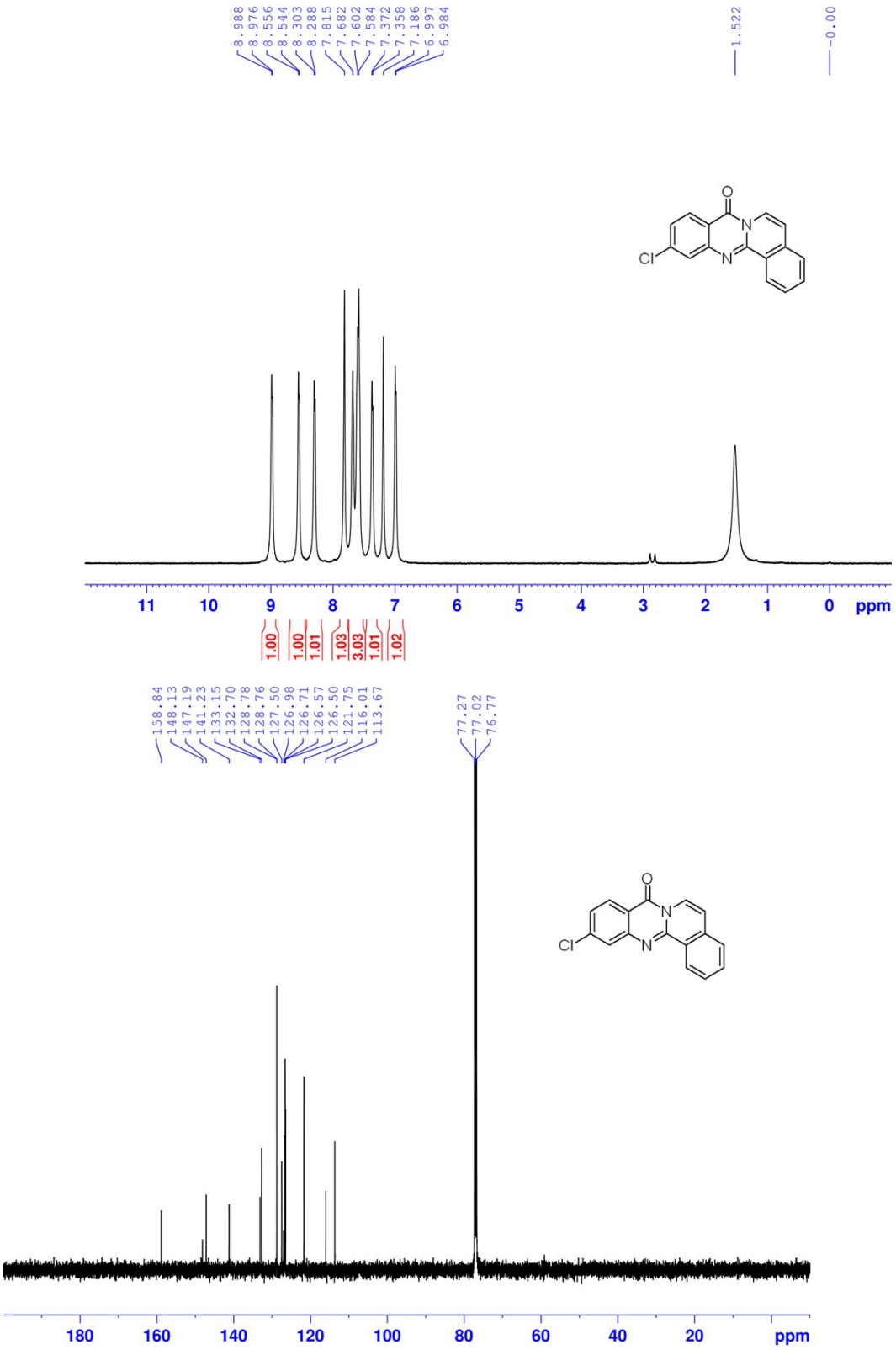
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ao**



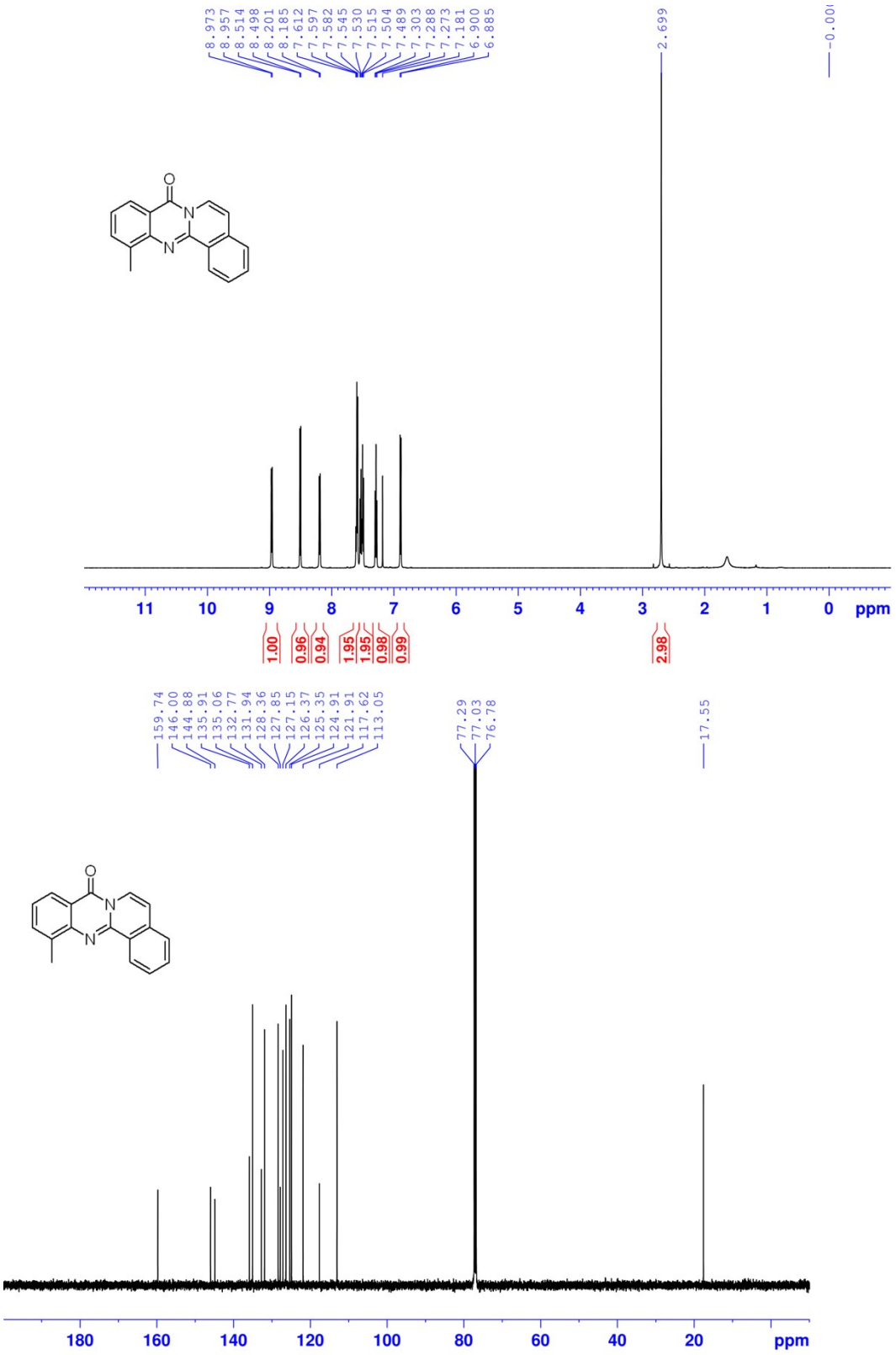
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ap**



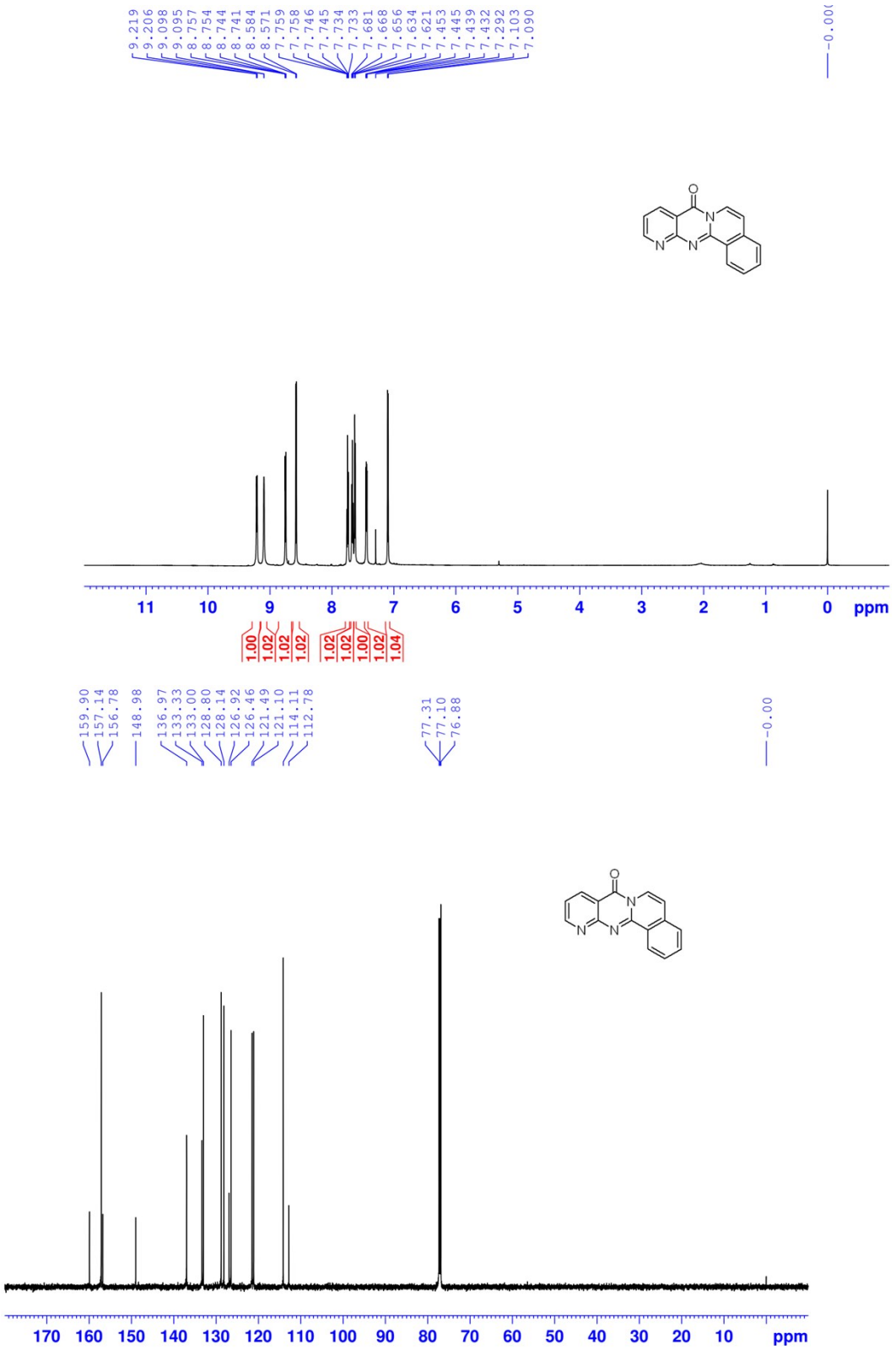
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ba**



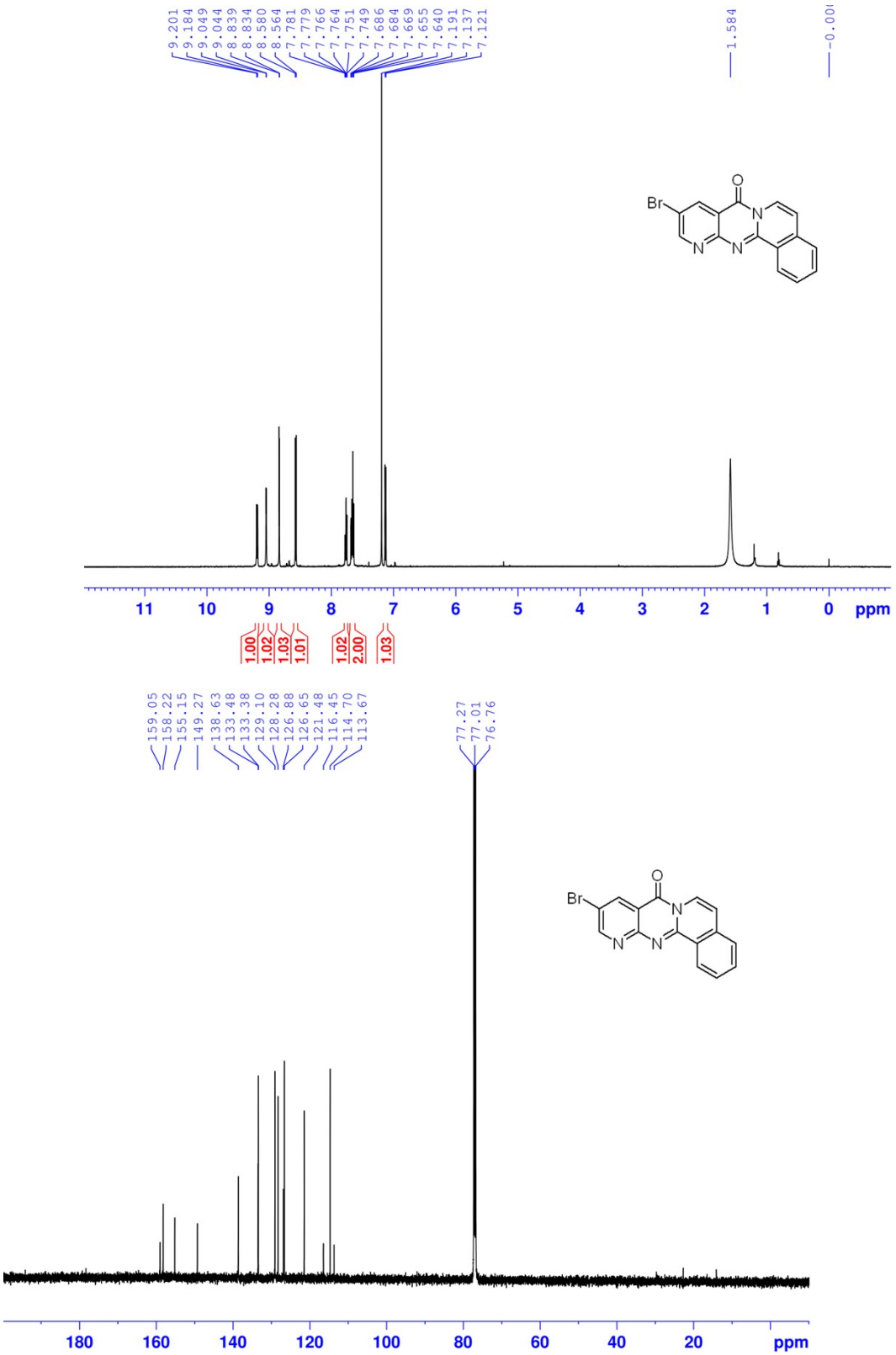
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ca**



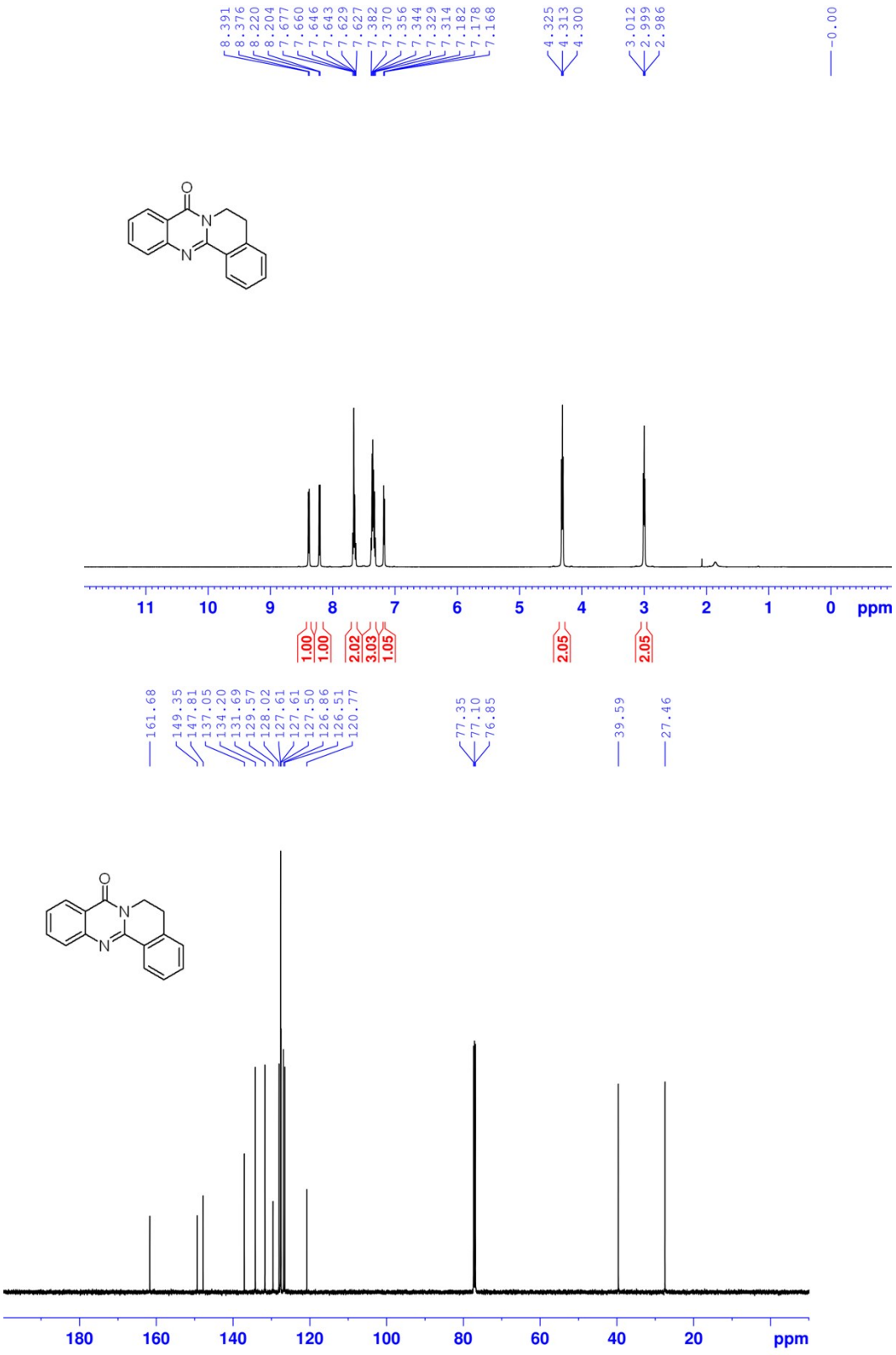
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **3da**



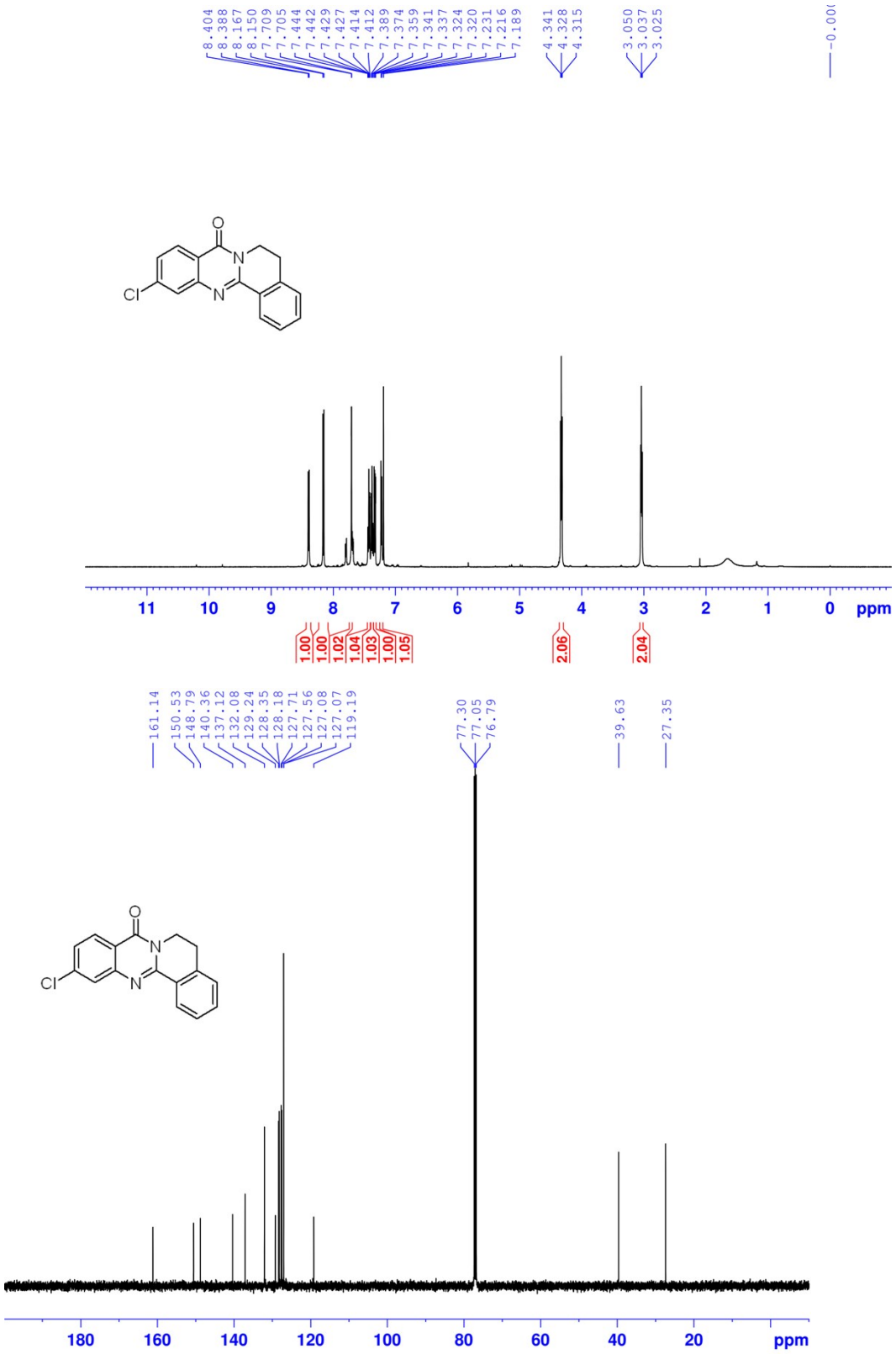
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **3ea**



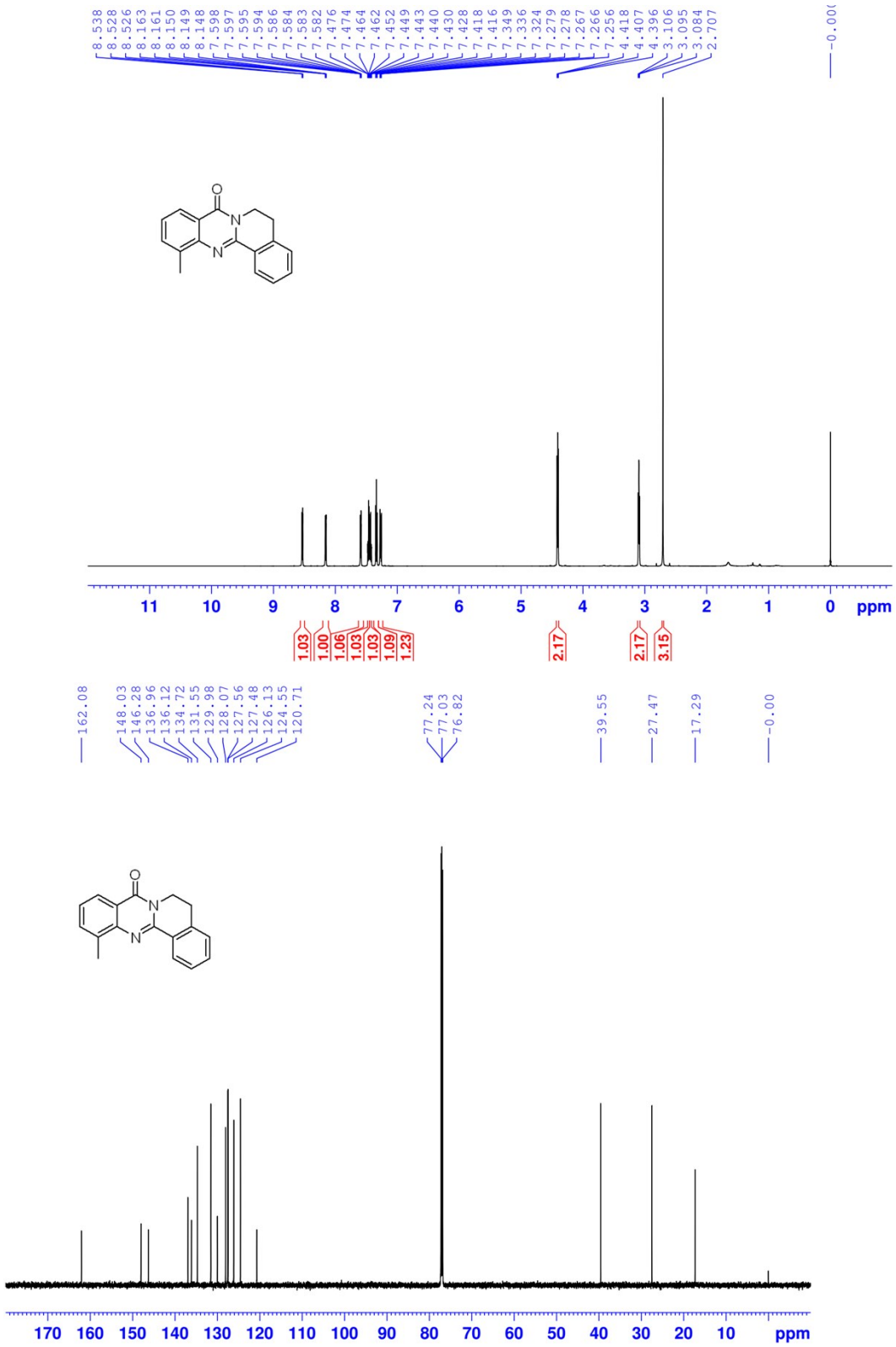
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5aa**



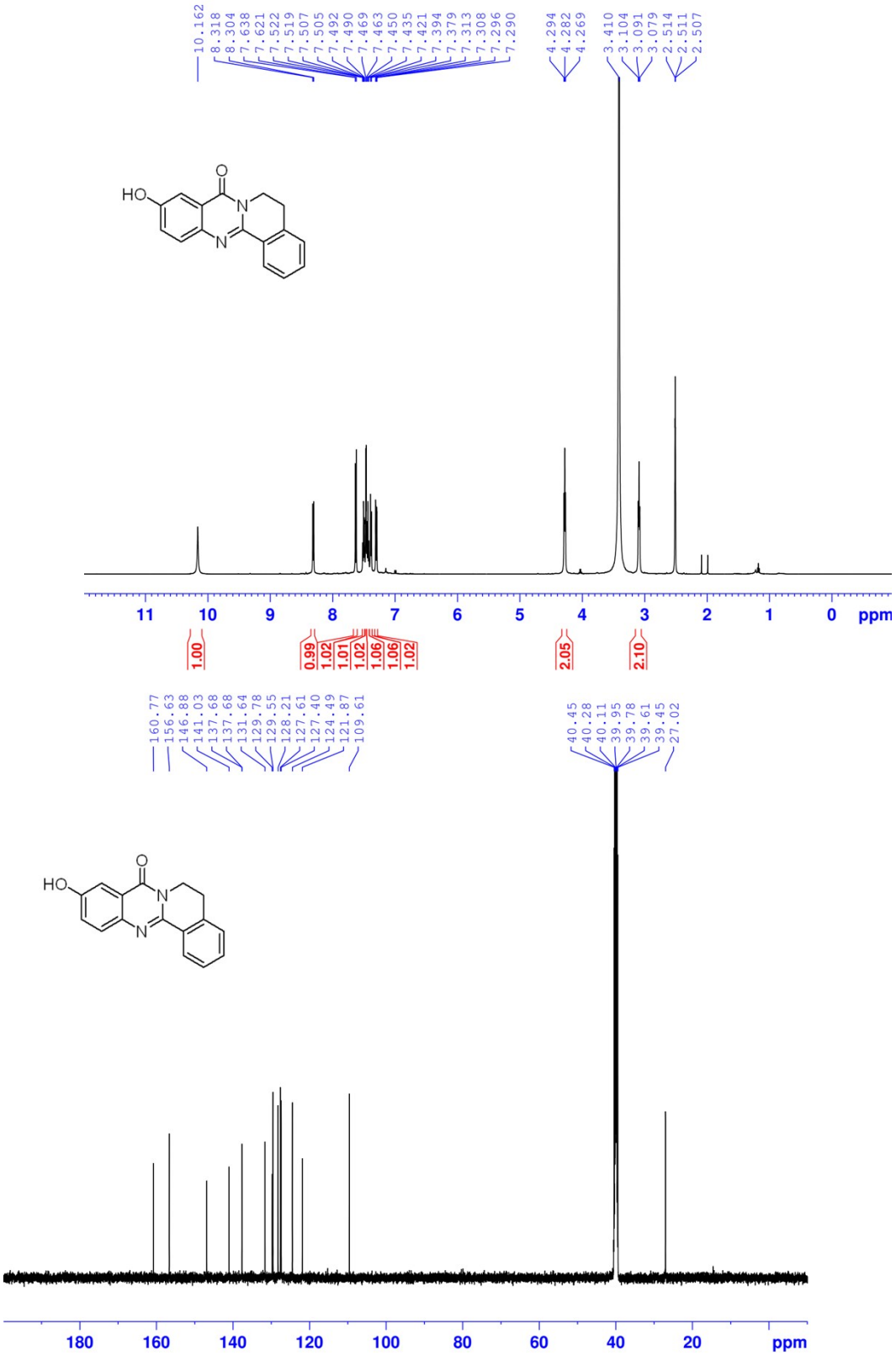
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ba**



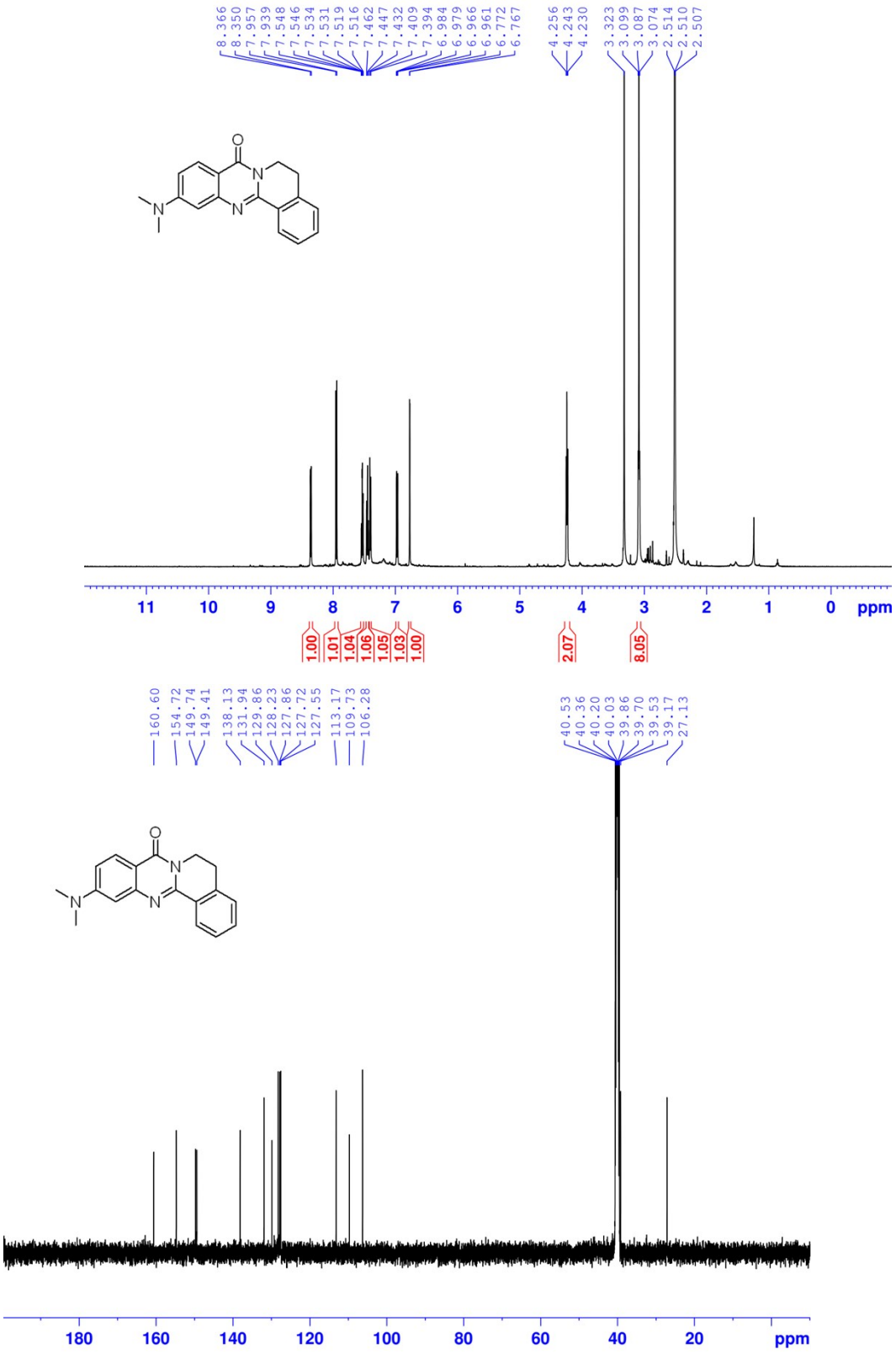
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ca**



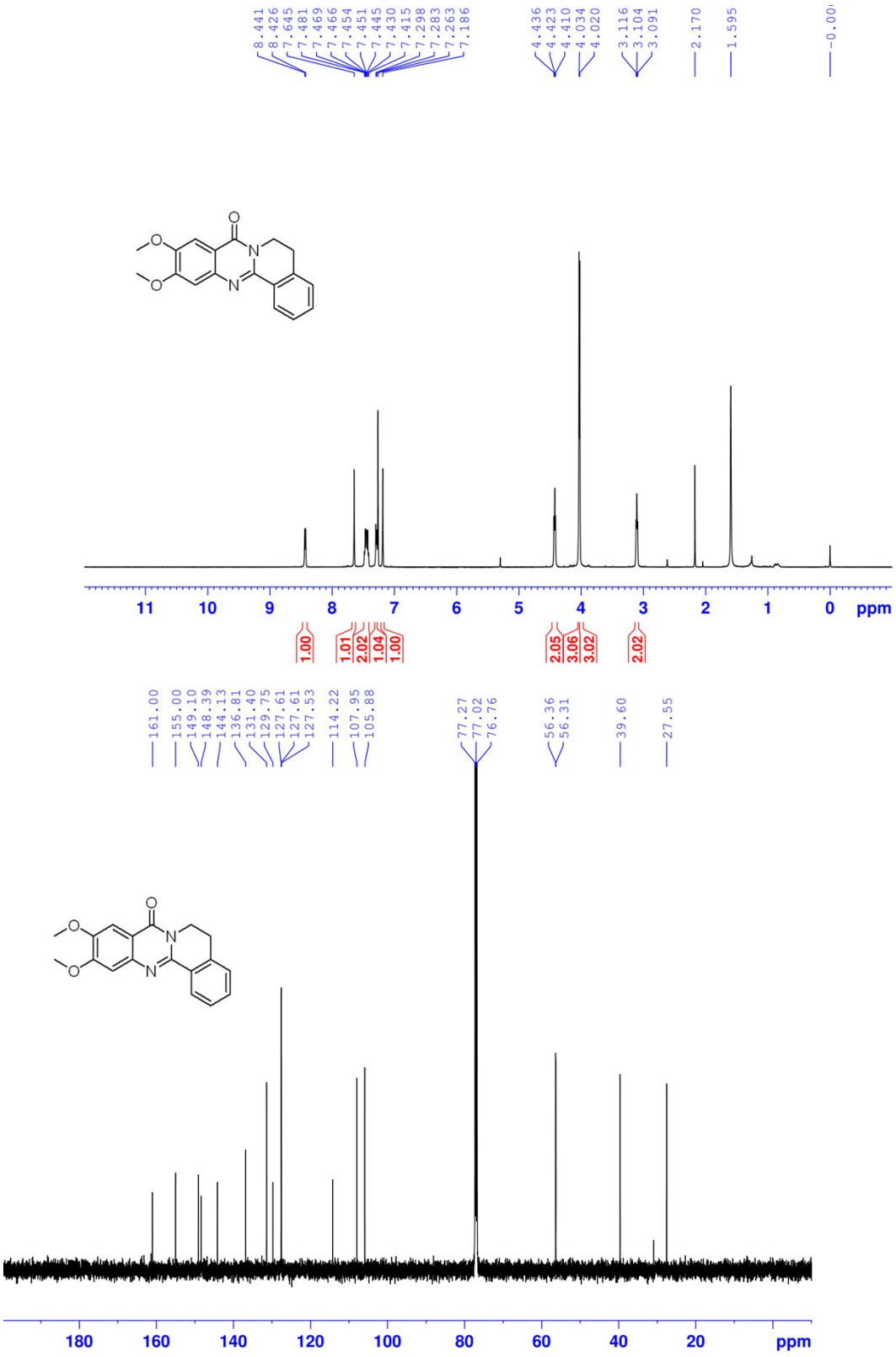
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **5ea**



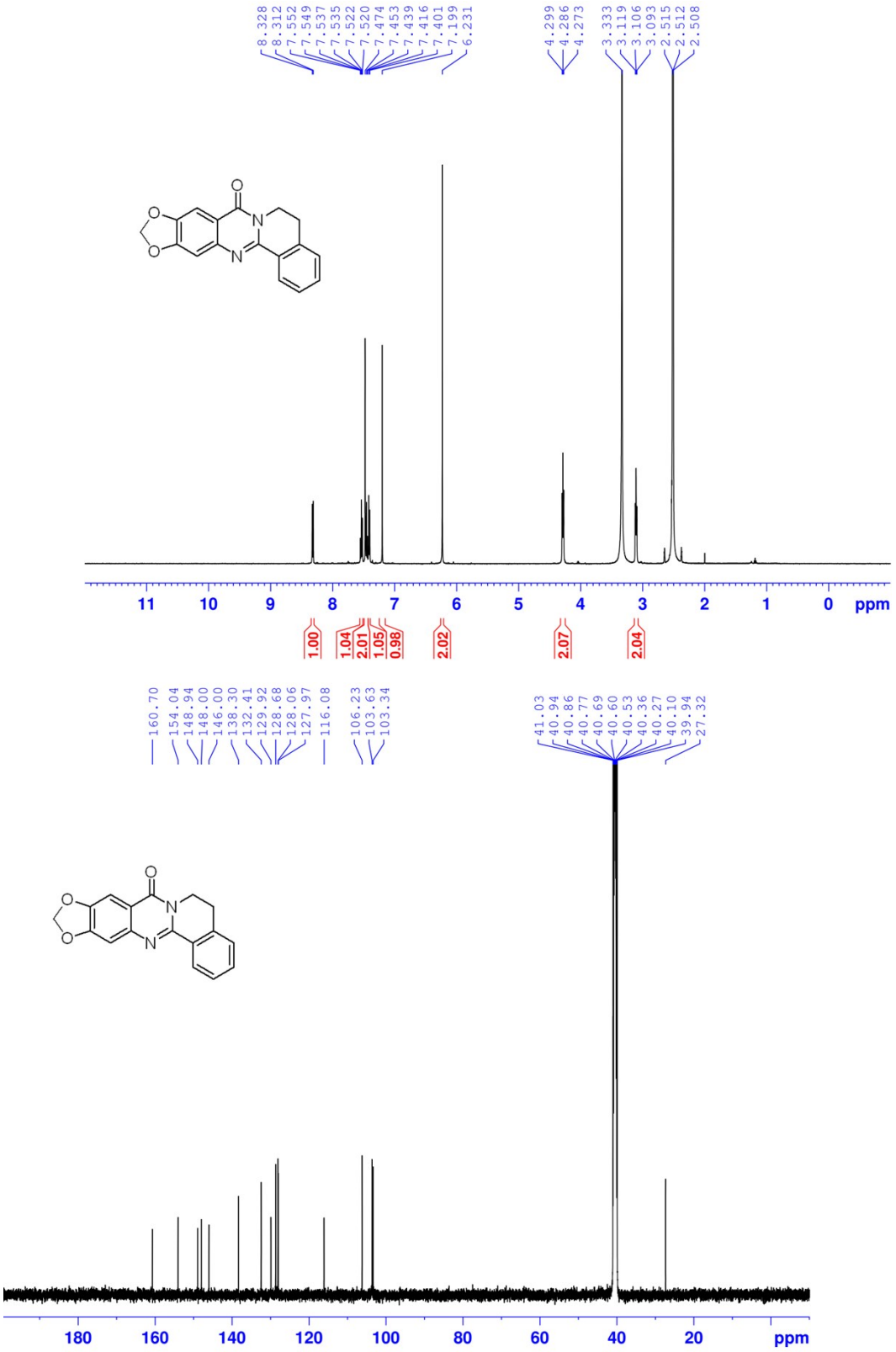
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **5fa**



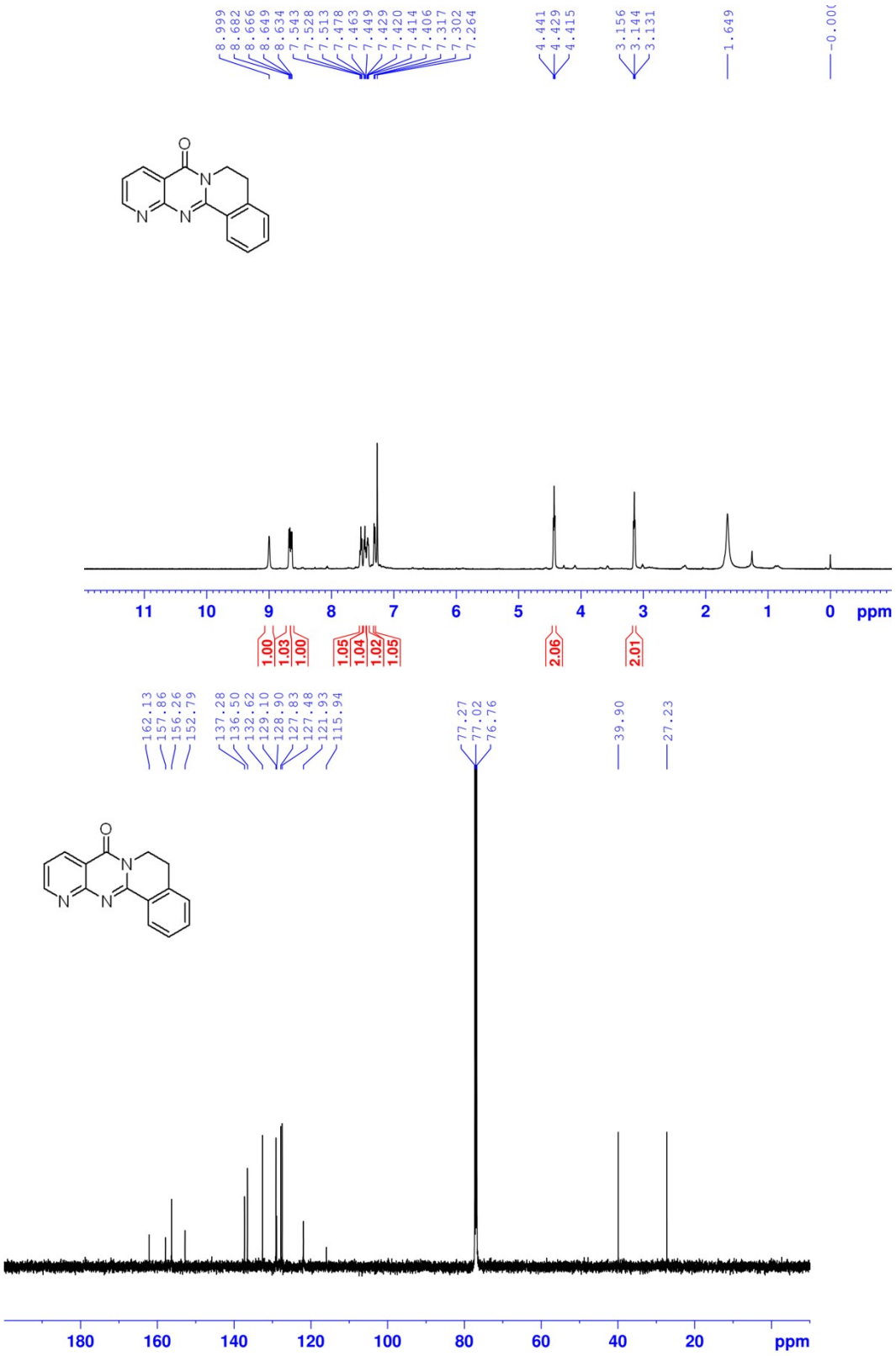
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ga**



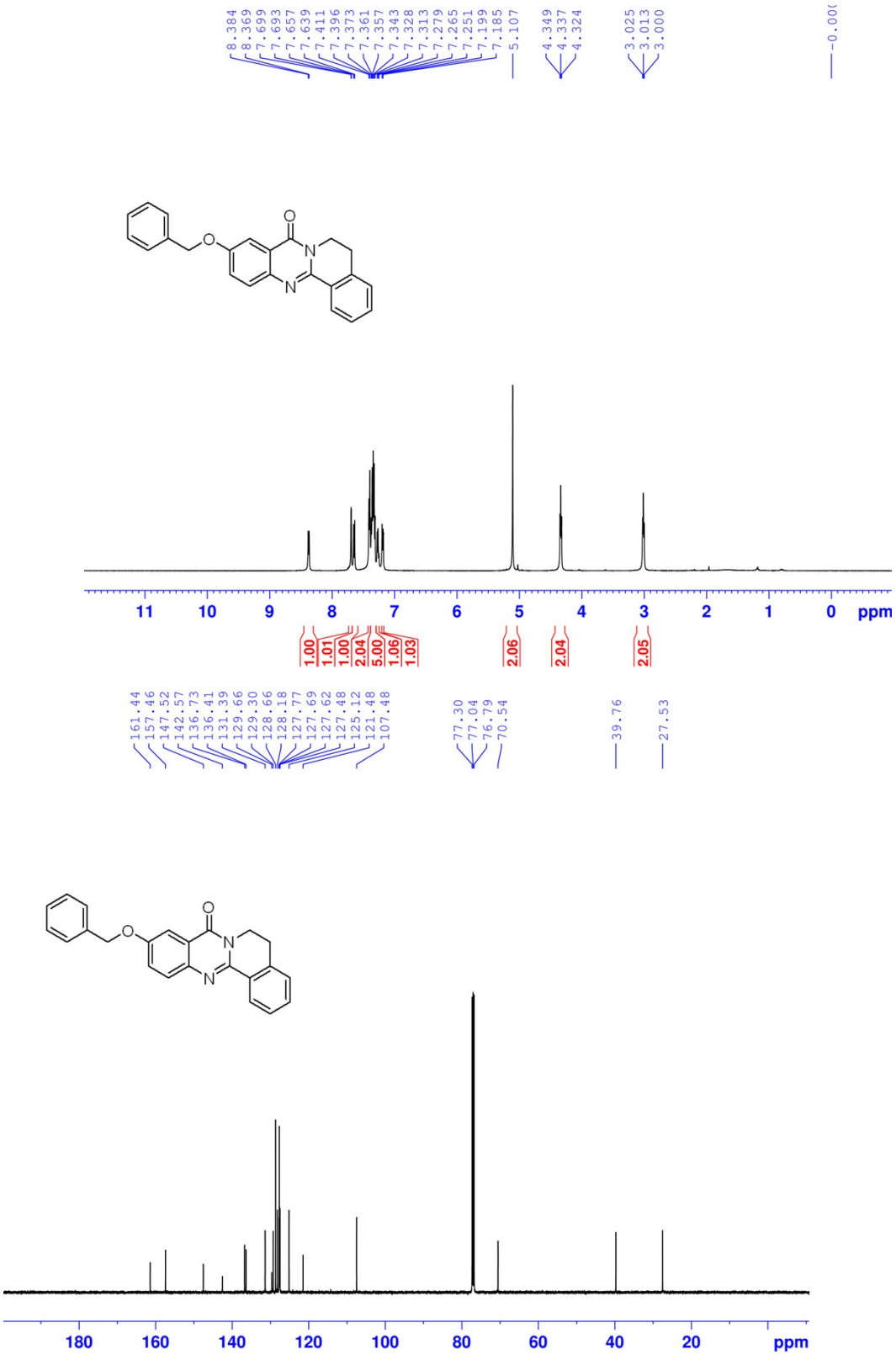
^{1}H NMR (DMSO-d_6, 500 MHz) and ^{13}C NMR (DMSO-d_6, 125 MHz) spectra of **5ha**



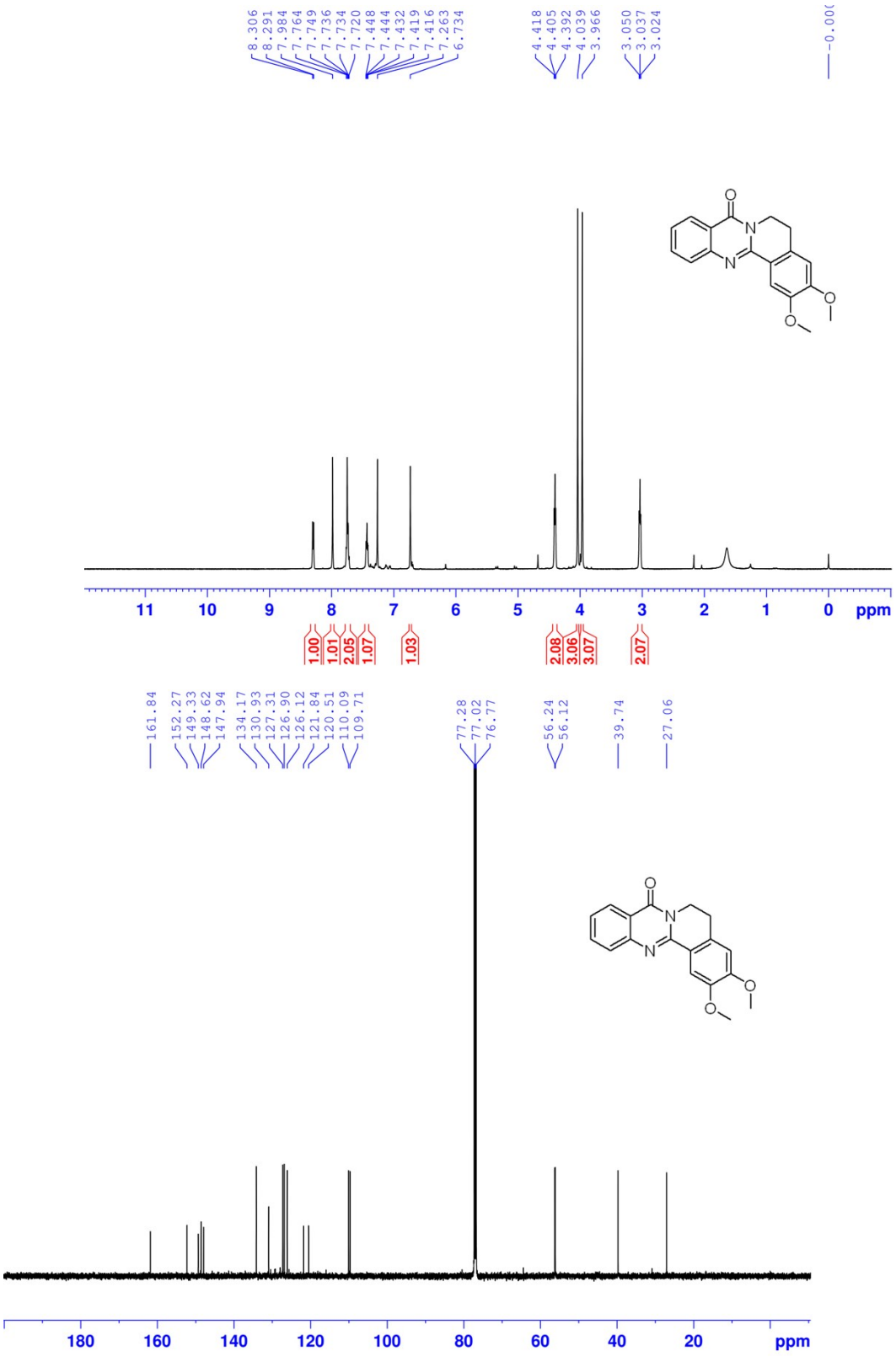
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5da**



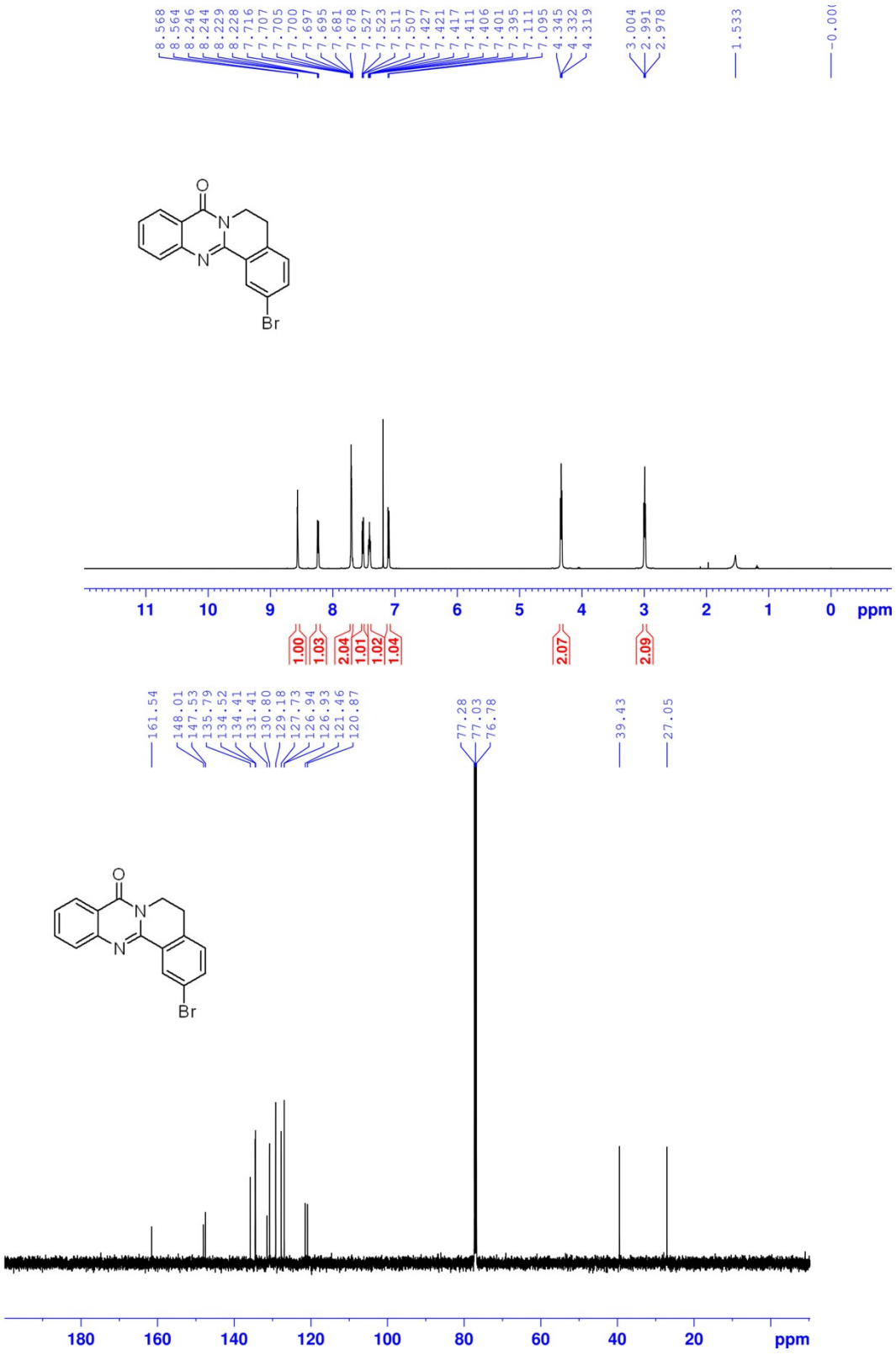
^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ia**



^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ab**



^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ac**



^{1}H NMR ($CDCl_3$, 500 MHz) and ^{13}C NMR ($CDCl_3$, 125 MHz) spectra of **5ad**