

Supporting Information

Fragment-Based Discovery of 8-Hydroxyquinoline Inhibitors of the HIV-1 Integrase-LEDGF/p75 Interaction

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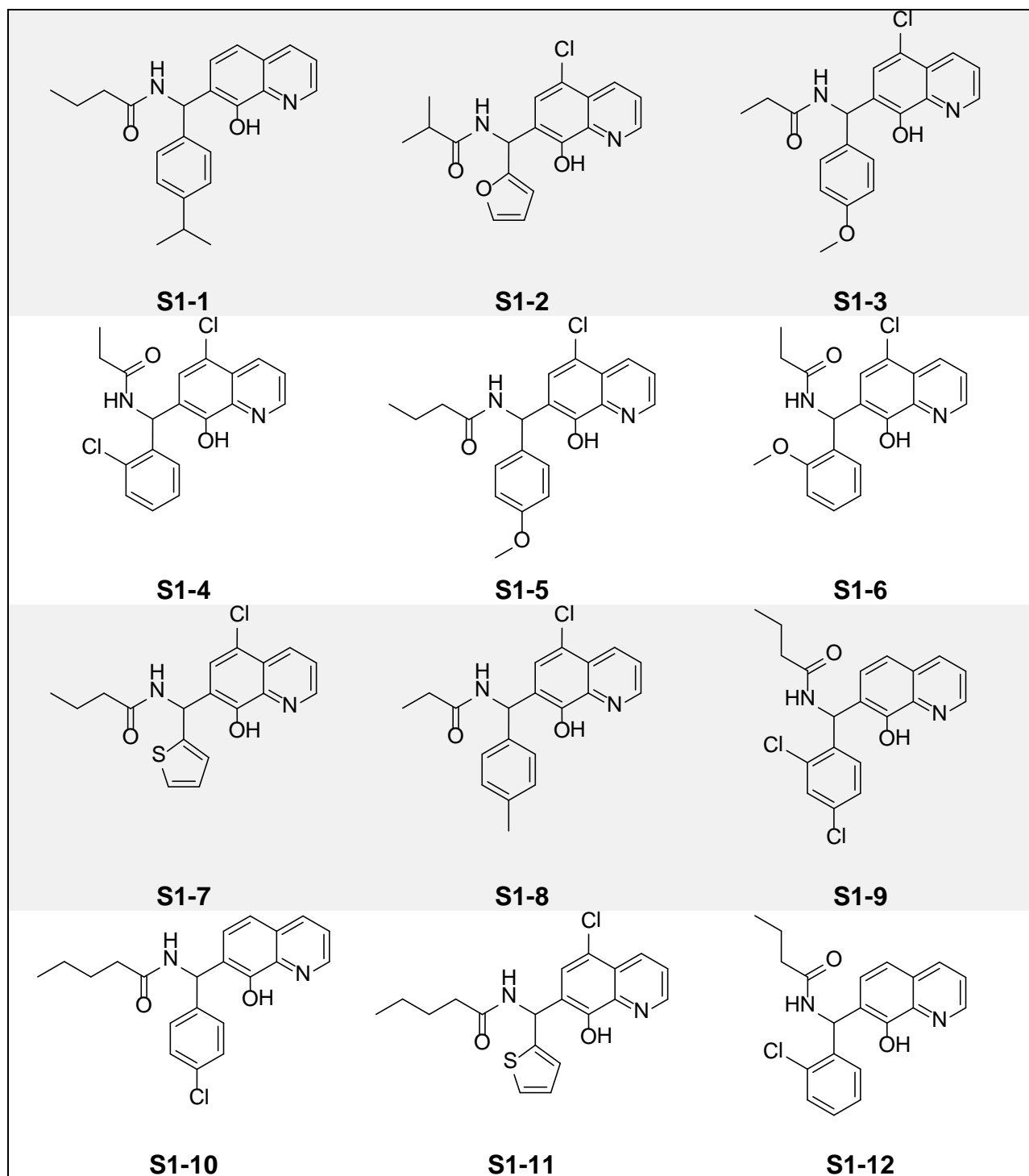
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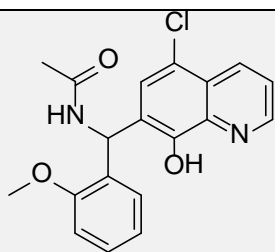
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Supplementary Figure 1. Structures of Inactive 8-Hydroxyquinoline Analogues Containing C2 and C6 Substitutions.

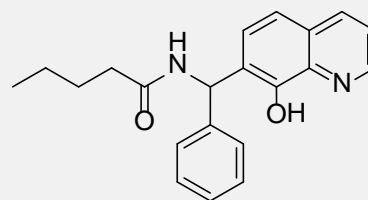




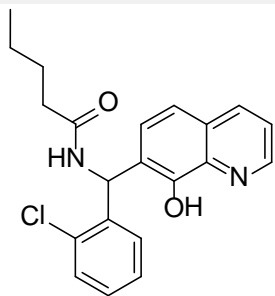
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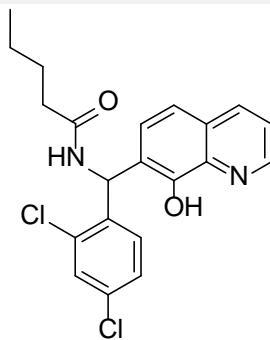
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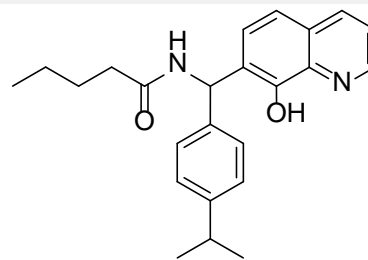
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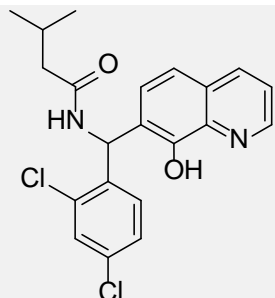
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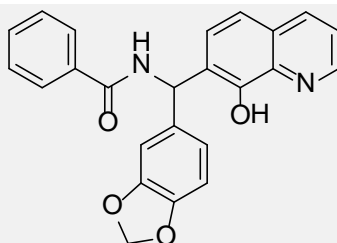
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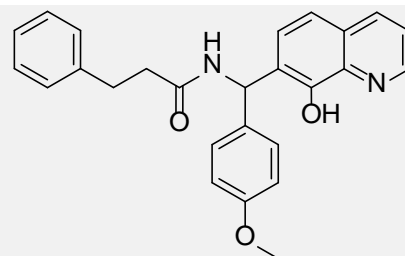
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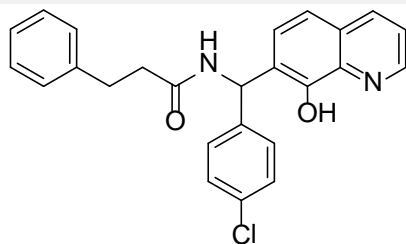
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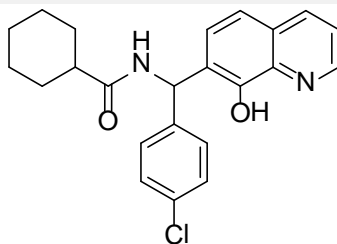
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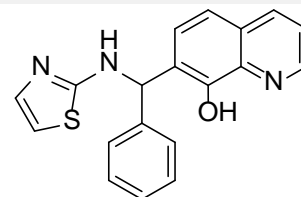
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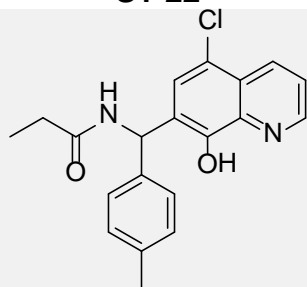
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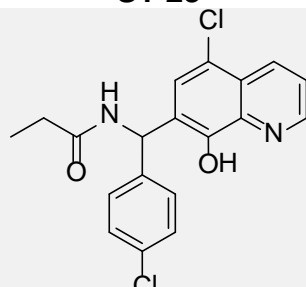
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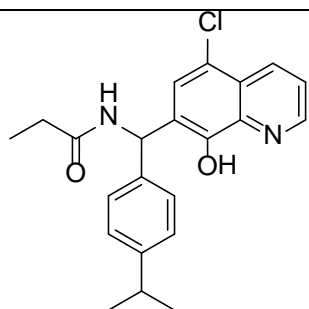
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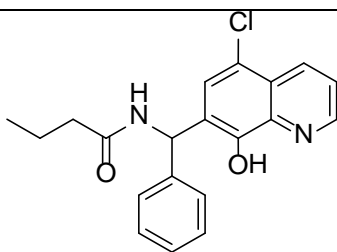
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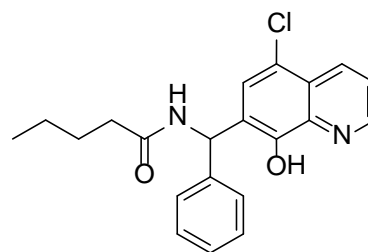
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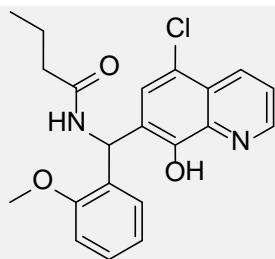
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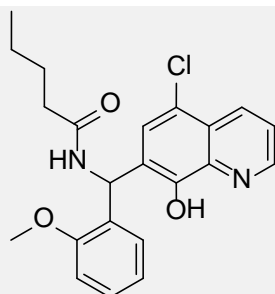
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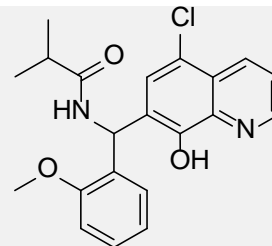
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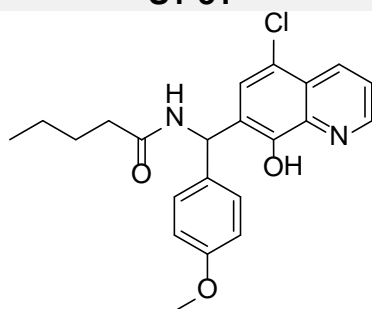
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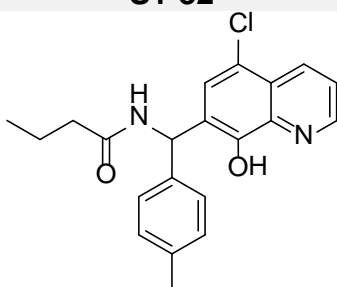
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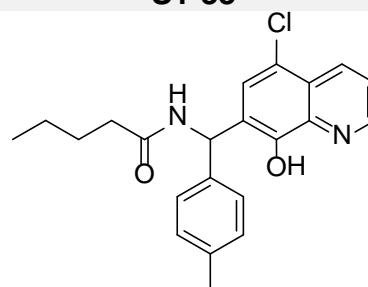
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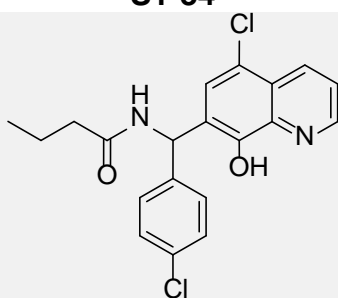
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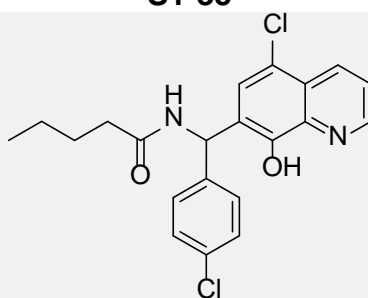
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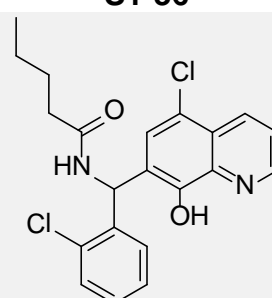
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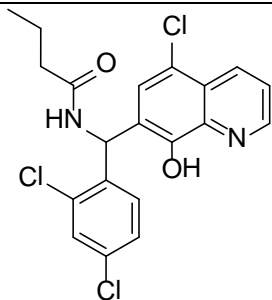
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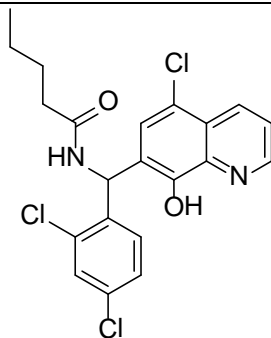
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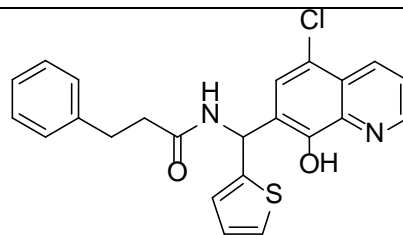
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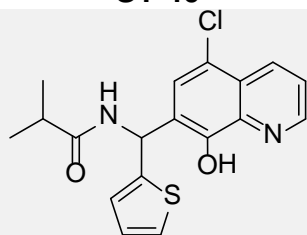
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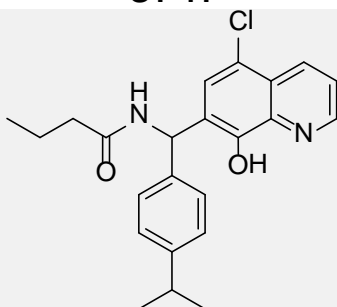
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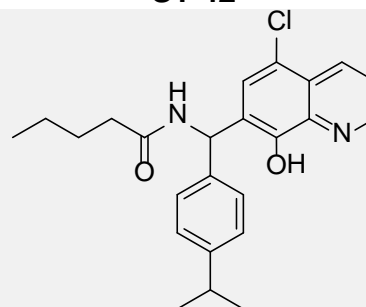
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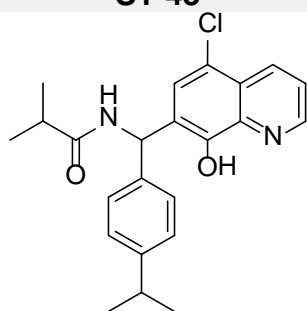
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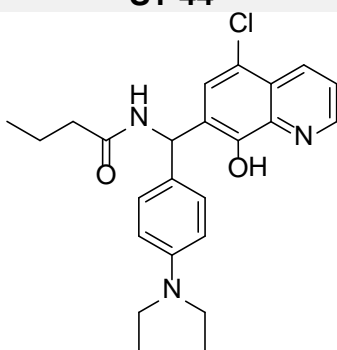
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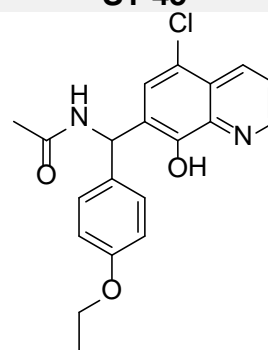
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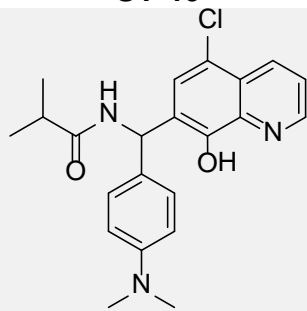
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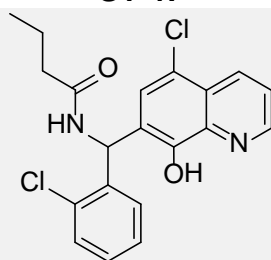
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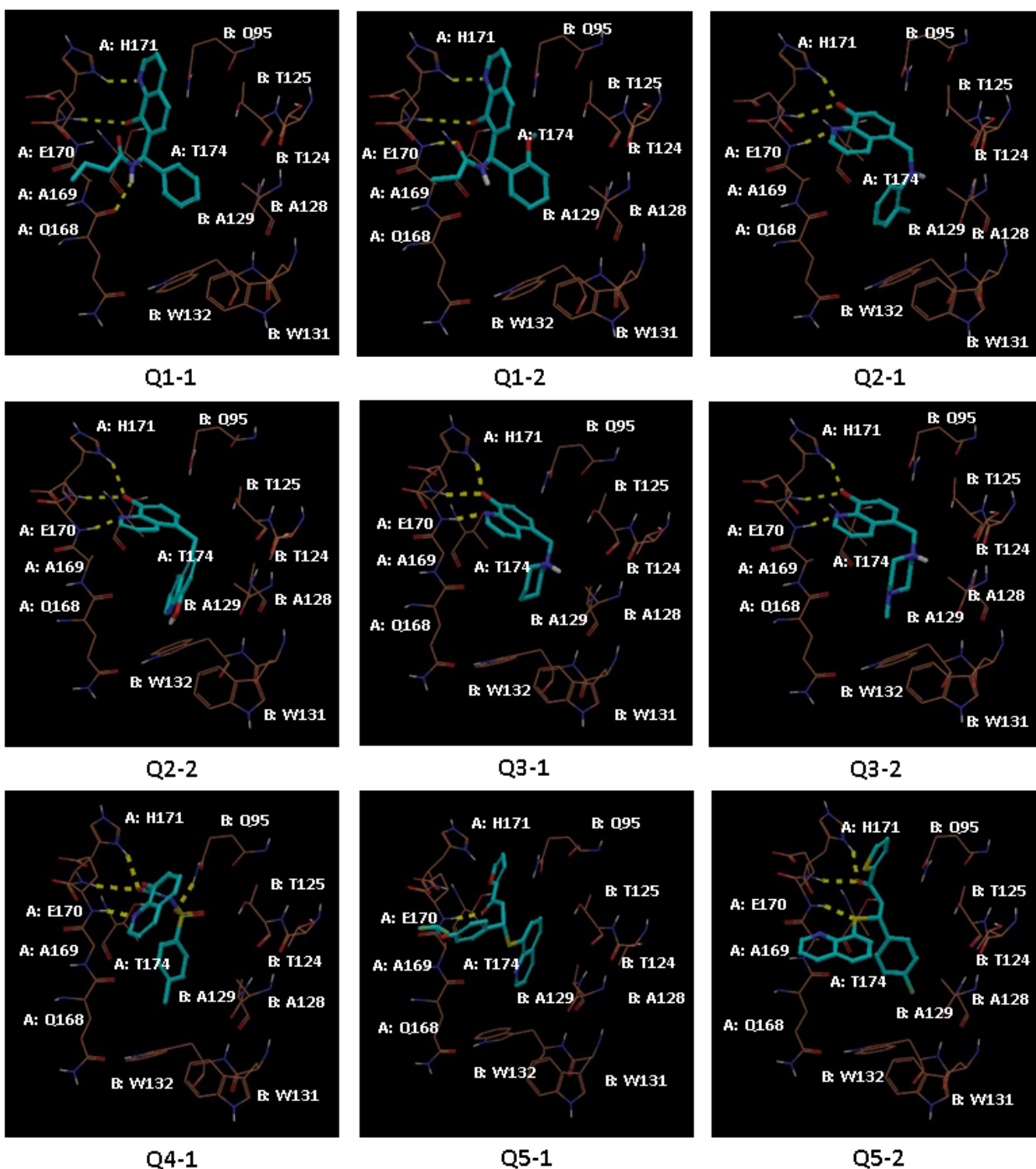


S1-49



S1-50

Supplementary Figure 2. Molecular Docking Poses of Selected 8-Hydroxyquinolines. Top compounds exhibited highly similar binding modes, forming H-bonds with IN residues E170 or H171, in addition to packing variable hydrophobic moieties into the hydrophobic pocket formed by IN residues Ala 128, Ala 129, Gln 168, Trp 131, and Trp 132.



Supplementary Table 1. AlphaScreen Data for 8-Hydroxyquinoline Compounds with IC₅₀

Values above 5 μ M.

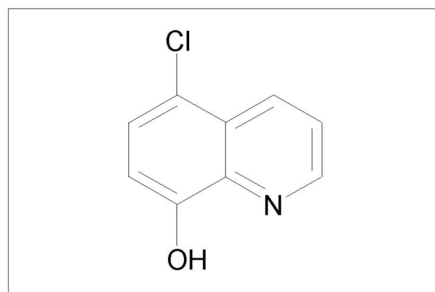
Compound	IN-LEDGF (IC₅₀, μM)
Q1-13	5.0 \pm 1
Q1-14	5.0 \pm 5
Q1-15	5.7 \pm 1.7
Q1-16	7.0 \pm 5
Q1-17	7.0 \pm 5
Q1-18	7.0 \pm 4
Q1-19	7.4 \pm 2.9
Q1-20	8.0 \pm 6
Q1-21	8.0 \pm 6
Q1-22	9.0 \pm 9
Q1-23	9.9 \pm 1.6
Q1-24	10 \pm 5
Q1-25	11 \pm 7
Q1-26	12 \pm 5
Q1-27	13 \pm 5
Q1-28	13 \pm 9
Q1-29	14 \pm 10
Q1-30	14 \pm 7
Q1-31	14 \pm 8
Q1-32	15 \pm 0
Q1-33	16 \pm 3
Q1-34	17 \pm 3
Q1-35	19 \pm 7
Q2-15	5.2 \pm 3.3
Q2-16	10.9 \pm 3.8
Q3-10	12.5 \pm 4.9
Q4-2	5.0 \pm 1
Q4-3	6.0 \pm 1
Q4-4	10.7 \pm 1.8
Q4-5	>20
Q4-6	>20
Q4-7	>20
Q5-3	5.0 \pm 2

Supplementary Table 2. Hydrogen bond distances between ligand and protein atoms.

Ligand	Protein atom	Ligand atom	Distance (Å)
Q	B:Q95-side chain NH	Quinolino N	2.095
8-OH-Q	A:H171-side chain NH	8-O ⁻	1.703
	A:H171-backbone NH	8-O ⁻	2.626
	A:E170-backbone NH	Quinolino N	1.957
QA	A:H171-side chain NH	8-O ⁻	1.711
	A:H171-backbone NH	8-O ⁻	2.592
	A:E170-backbone NH	Quinolino N	2.008
QB	A:H171-backbone NH	8-O ⁻	2.956
	A:E170-backbone NH	Quinolino N	1.868
QC	A:H171-side chain NH	8-O ⁻	1.707
	A:H171-backbone NH	8-O ⁻	2.608
	A:E170-backbone NH	Quinolino N	1.986
Q1-1	A:H171-side chain NH	Quinolino N	2.154
	A:H171-backbone NH	8-O ⁻	2.847
	A:Q168-backbone NH	CONH	2.214
Q1-2	A:H171-side chain NH	Quinolino N	2.145
	A:H171-backbone NH	8-O ⁻	2.872
	A:E170-backbone NH	C=O	2.336
Q2-1	A:H171-side chain NH	8-O ⁻	1.882
	A:H171-backbone NH	8-O ⁻	2.635
	A:E170-backbone NH	Quinolino N	2.014
Q2-2	A:H171-side chain NH	8-O ⁻	2.389
	A:H171-backbone NH	8-O ⁻	2.497
	A:E170-backbone NH	Quinolino N	2.059
Q3-1	A:H171-side chain NH	8-O ⁻	1.983
	A:H171-backbone NH	8-O ⁻	2.460
	A:E170-backbone NH	Quinolino N	2.000
Q3-2	A:H171-side chain NH	8-O ⁻	1.980
	A:H171-backbone NH	8-O ⁻	2.440
	A:E170-backbone NH	Quinolino N	1.926
Q4-1	A:H171-side chain NH	C=O	2.394
	A:H171-backbone NH	C=O	2.862

	A:E170-backbone NH	Quinolino N	2.264
	B:Q95-side chain NH	S=O	2.256
Q5-1	A:E170-backbone NH	C=O	2.005
Q5-2	A:H171-side chain NH	C=O	2.041
	A:H171-backbone NH	C=O	2.427
	A:E170-backbone NH	8-S	2.512

NKTA B0659434



BSI 0006815

0659434

C₉H₆ClNO

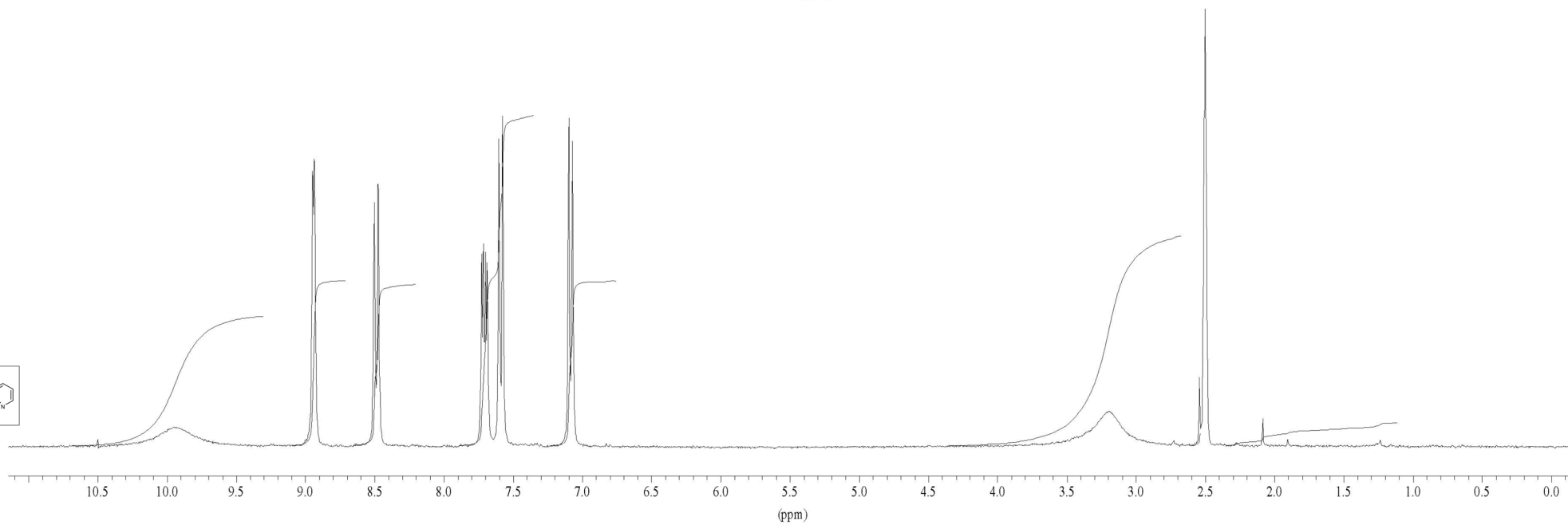
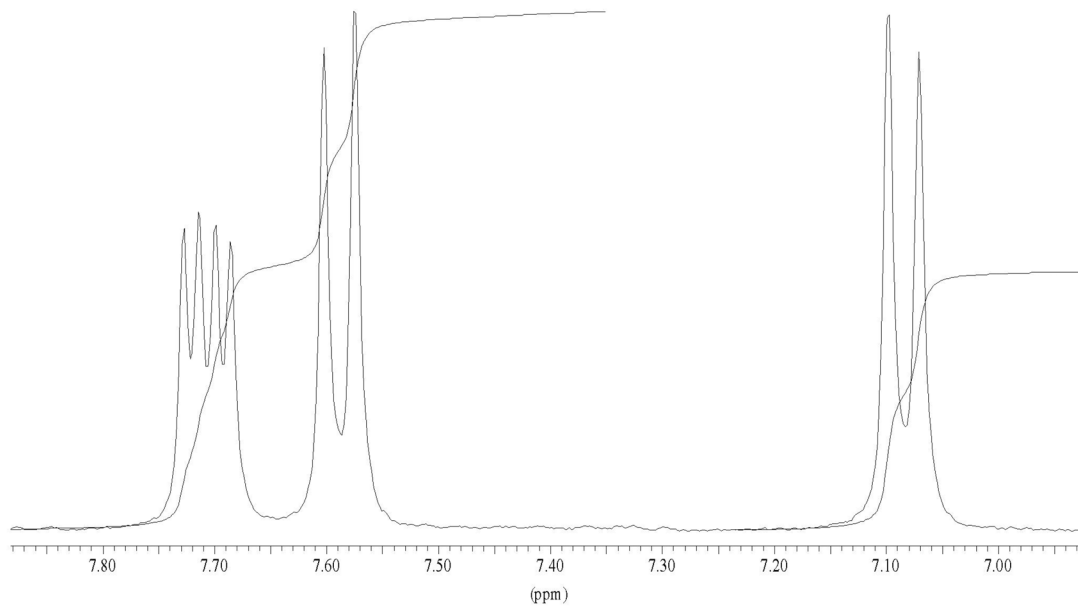
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BAS 0659434

18.11.99

Solv. DMSO

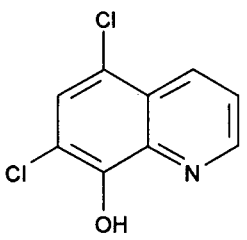

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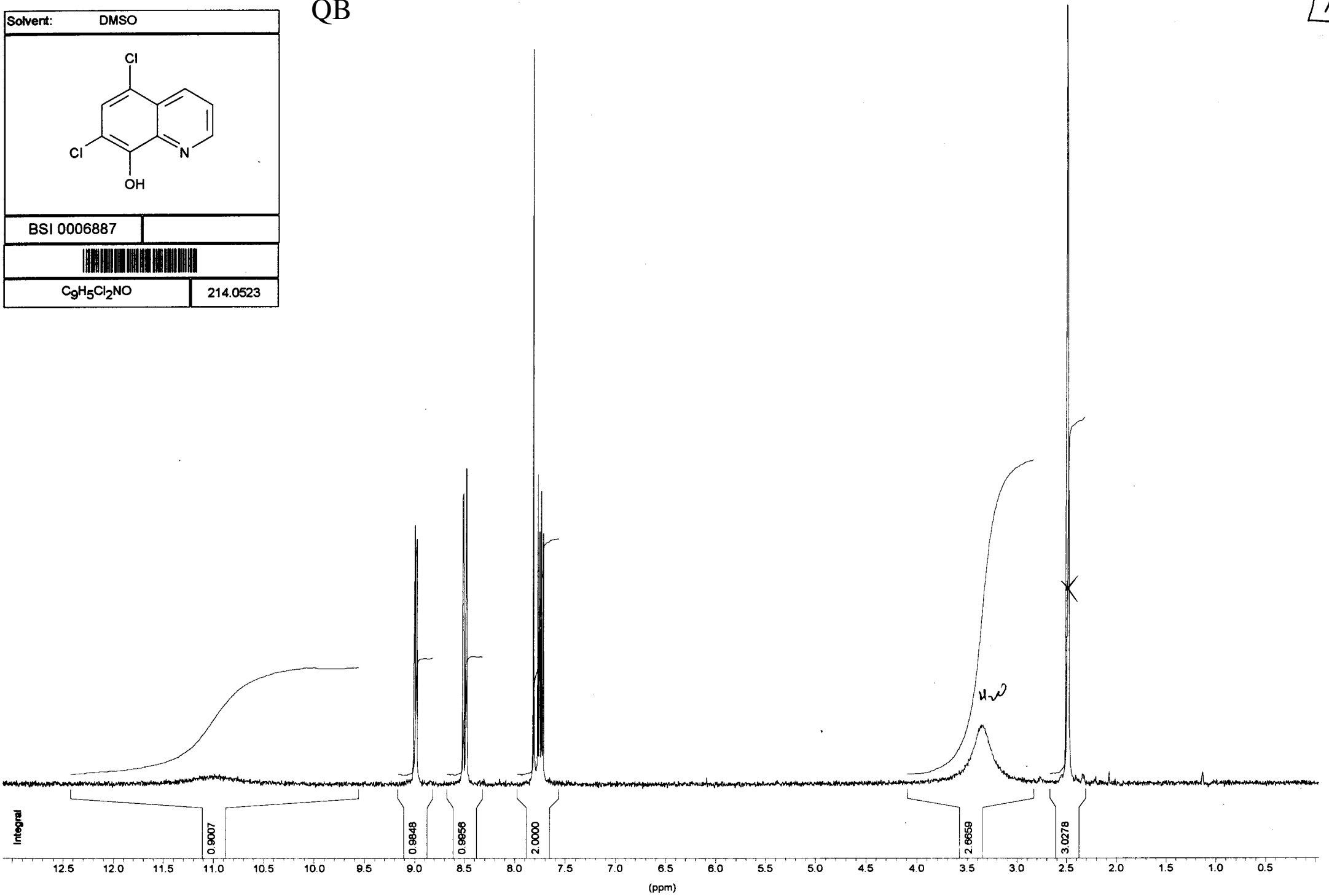


196237

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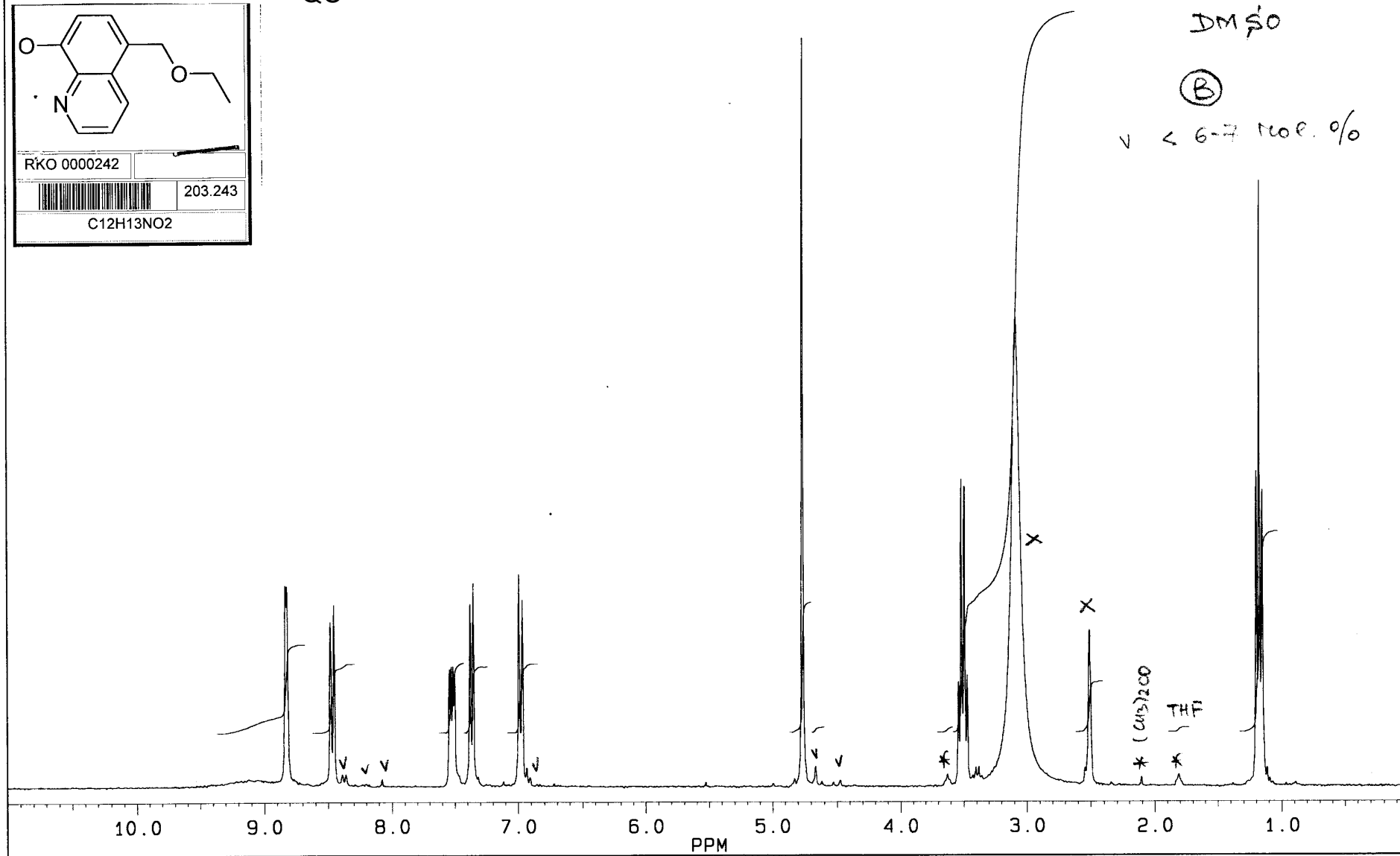
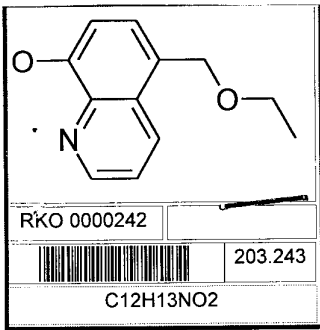
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BSI 0006887	
	
C ₉ H ₅ Cl ₂ NO	214.0523

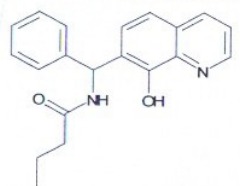


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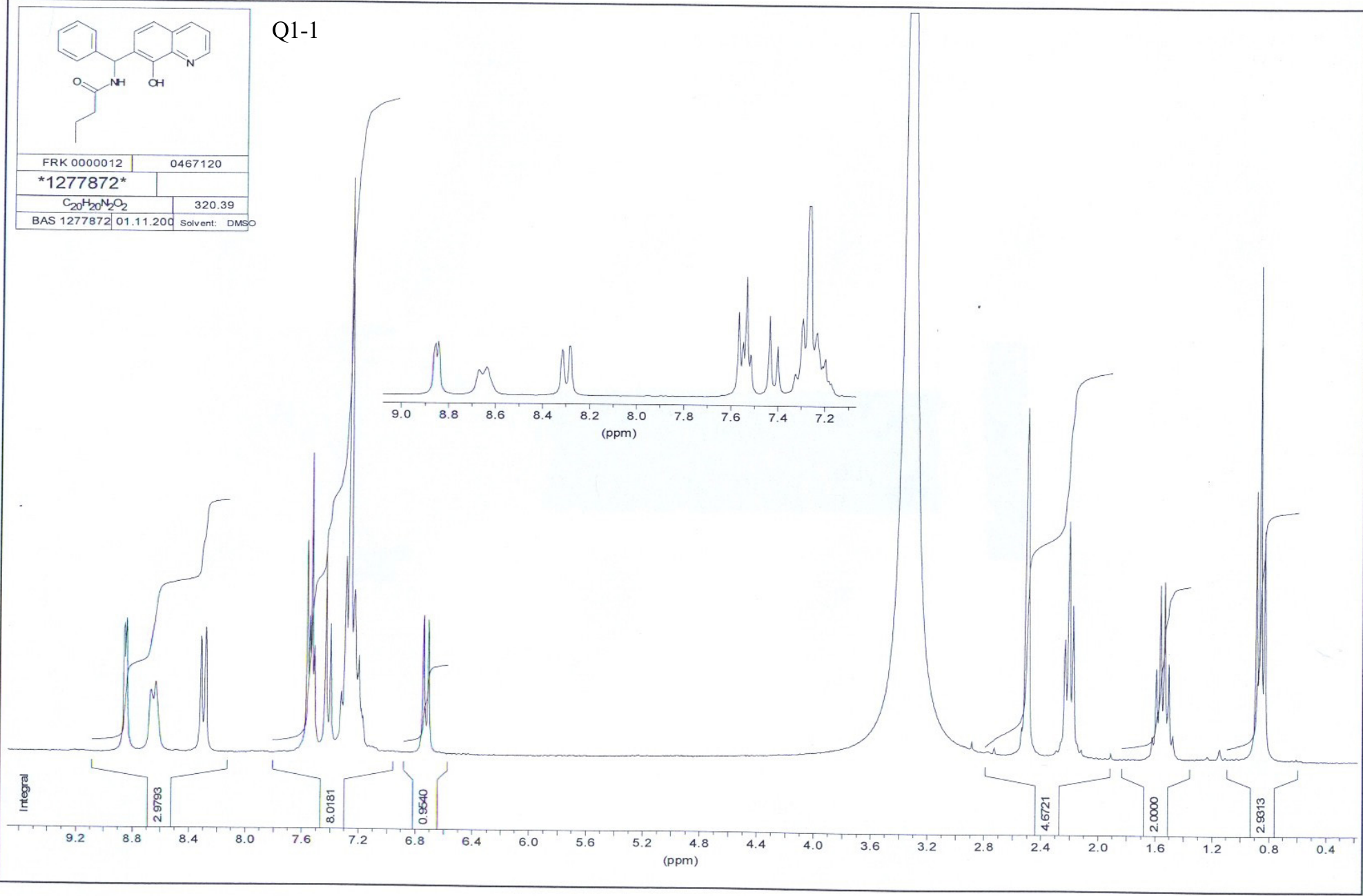
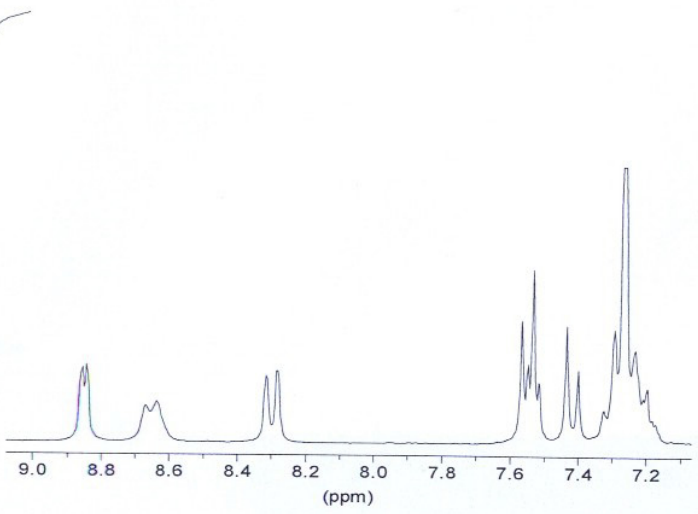


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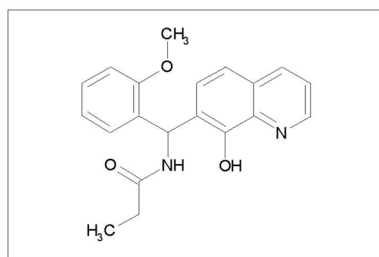


Q1-1

FRK 0000012	0467120
1277872	
C ₂₀ H ₂₀ N ₂ O ₂	320.39
BAS 1277872	01.11.200 Solvent: DMSO



BAS 1277866



FRK 0000006

1277866

C₂₀H₂₀N₂O₃

336.3940

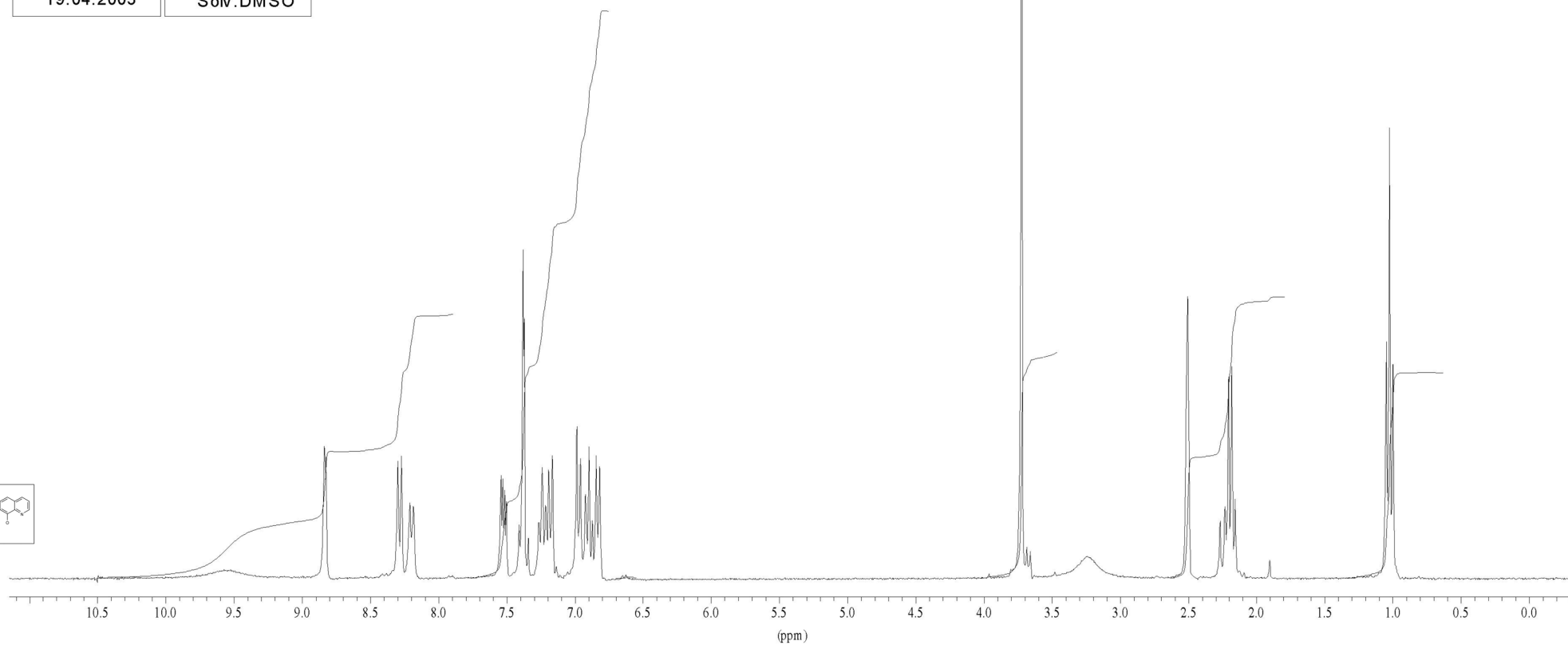
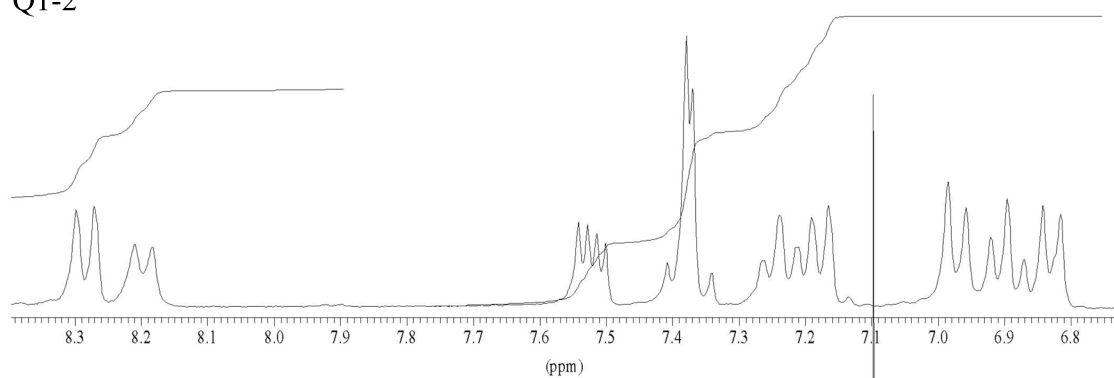
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0493844

19.04.2003

Solv. DMSO

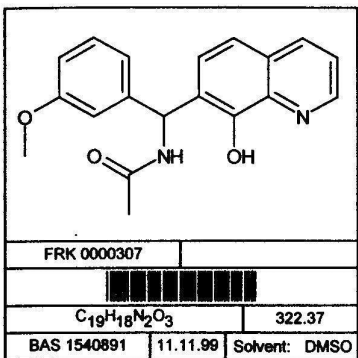
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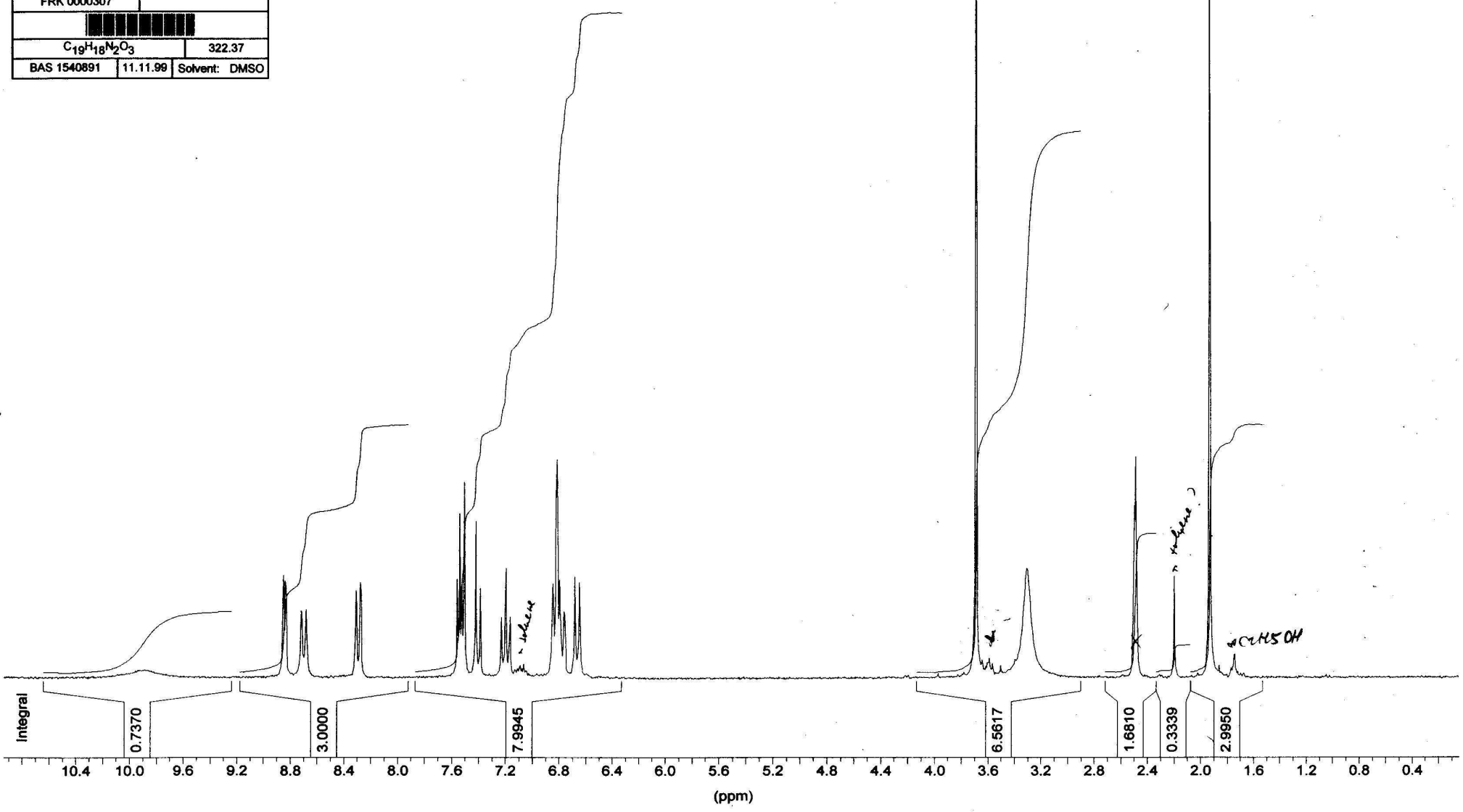
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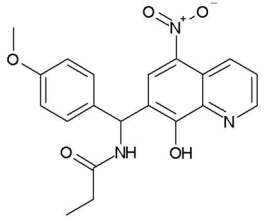
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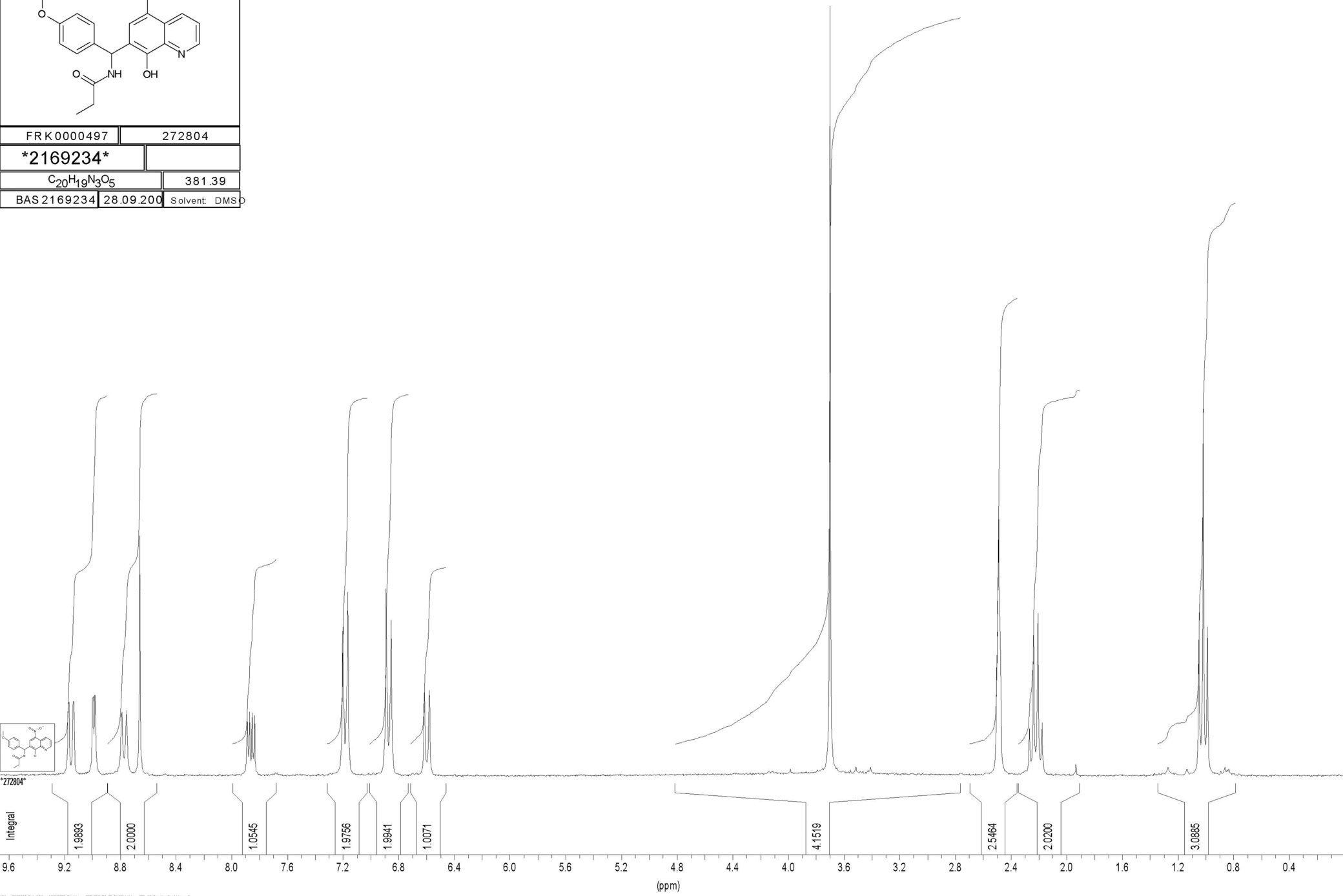
Σ = 100%



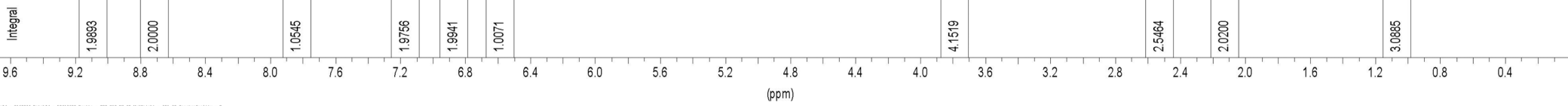
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2169234	
C ₂₀ H ₁₉ N ₃ O ₅	381.39
BAS 2169234	28.09.200 Solvent: DMSO

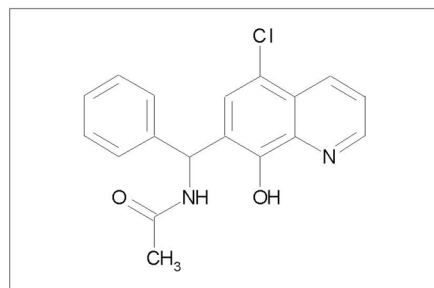


272804



NKTA B1923170

Q1-5



FRK 0000365

1923170

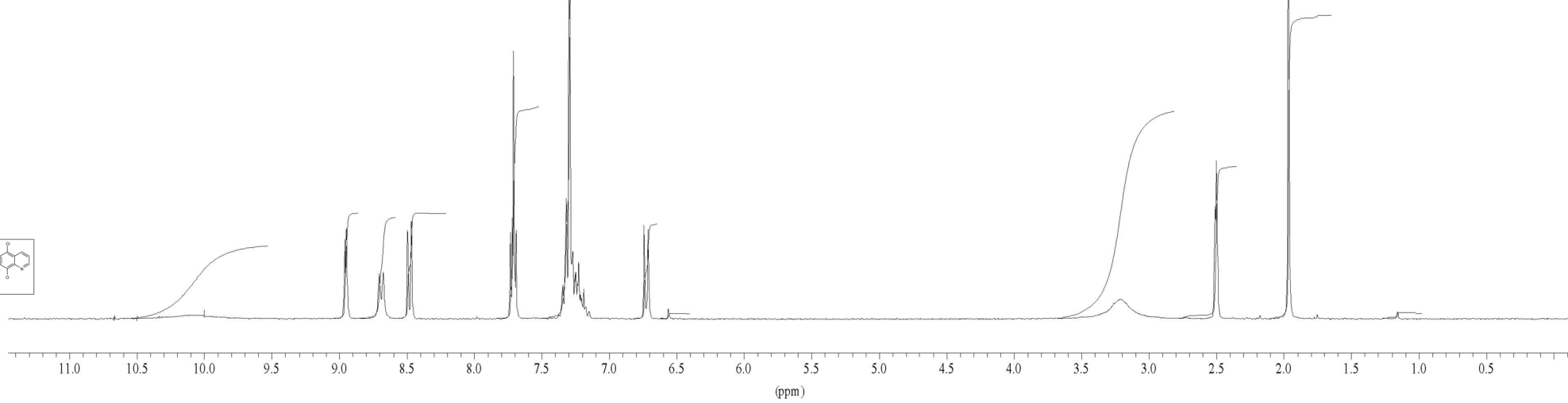
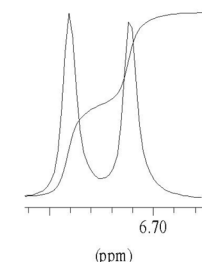
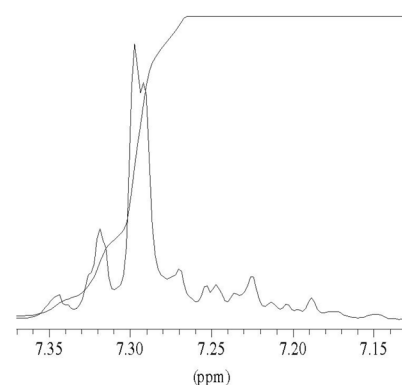
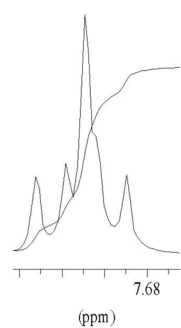
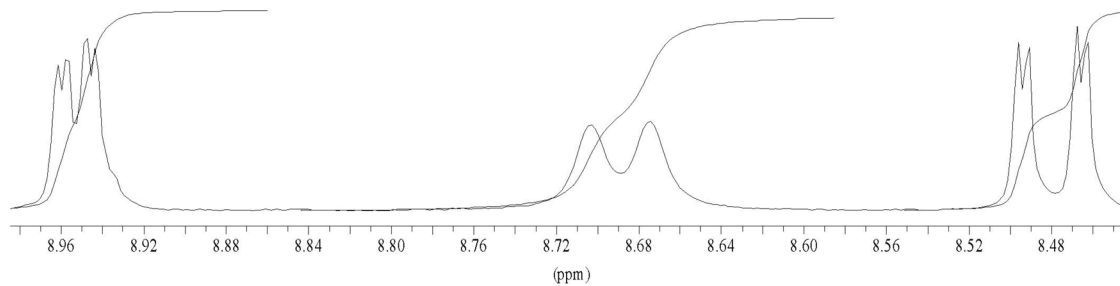
C₁₈H₁₅ClN₂O₂

326.7855

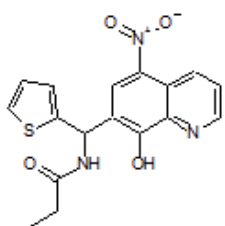
BAS 1923170

27.01.2000

Solv. DMSO

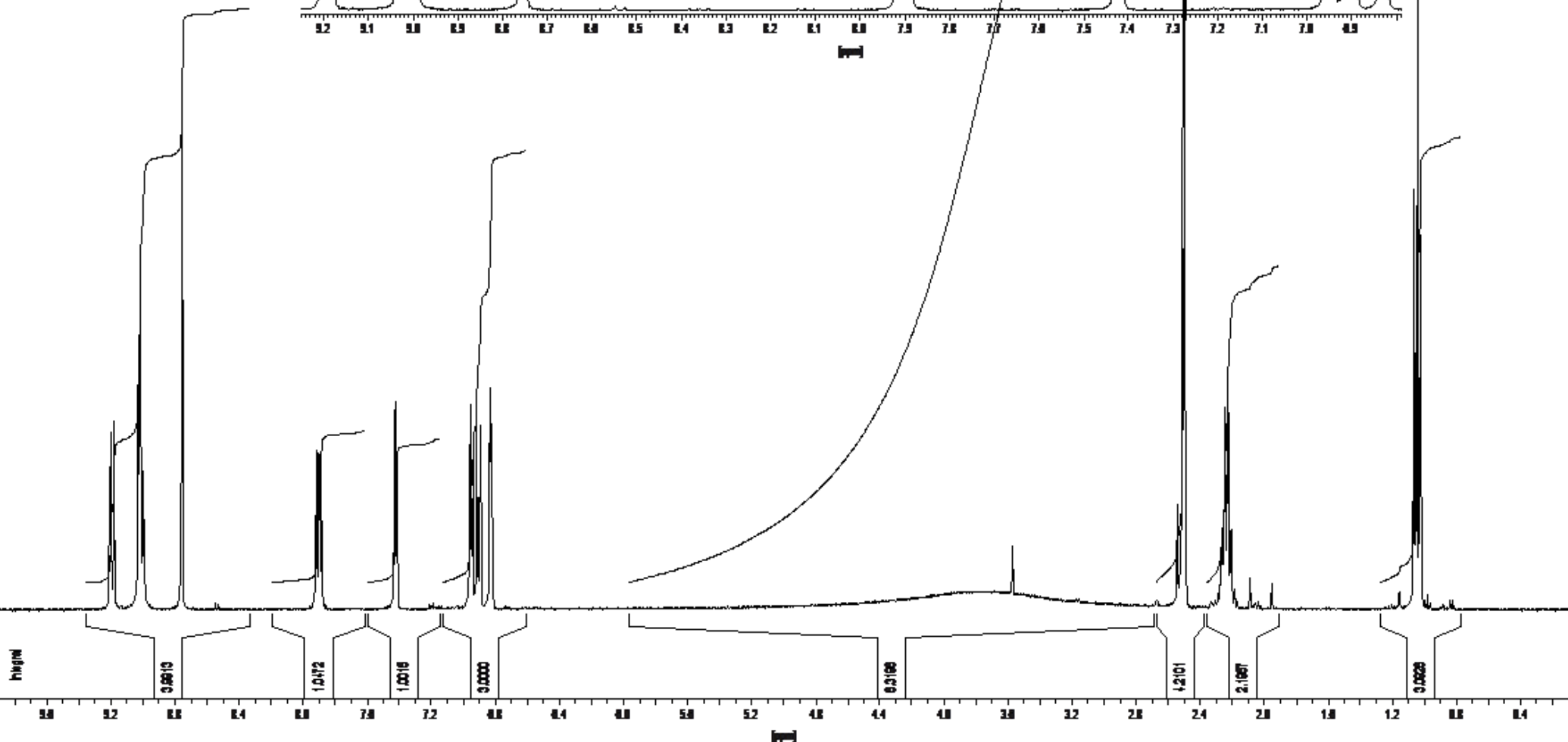
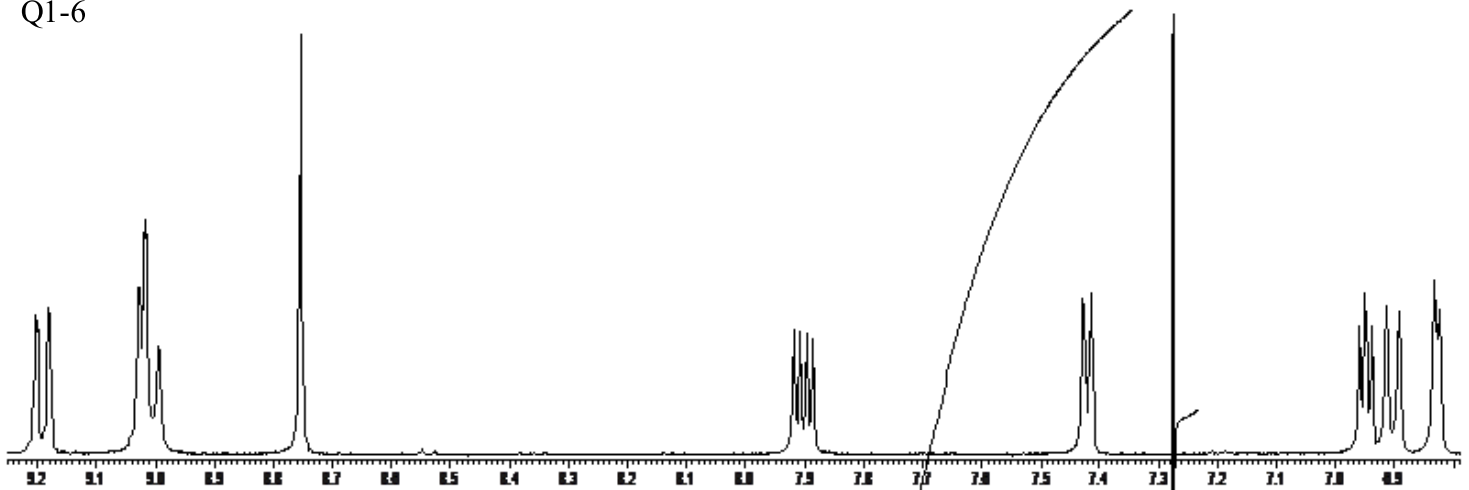


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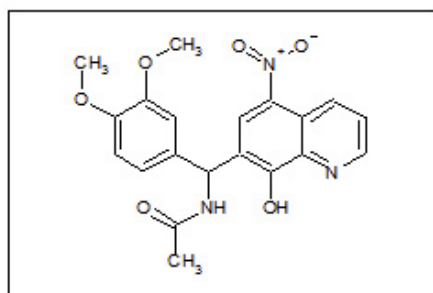


Q1-6

FRK 0000503	247432
2169240	
C ₁₇ H ₁₅ N ₃ O ₄ S	357.39
BAS 2169240	12.05.2000 Solvent: DMSO



Integration values: 0.0019, 1.0172, 1.0016, 0.0000, 0.0160, 4.2101, 2.1607, 0.0020



FRK 0000400

1923205

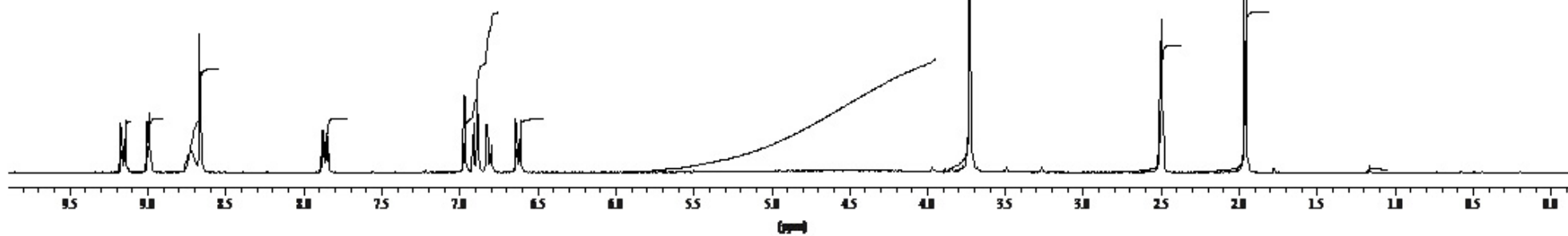
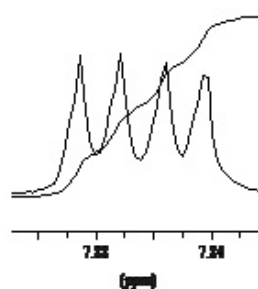
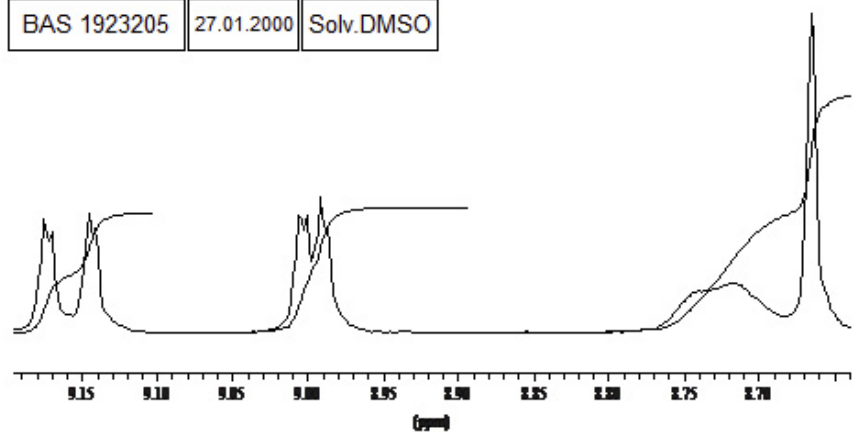
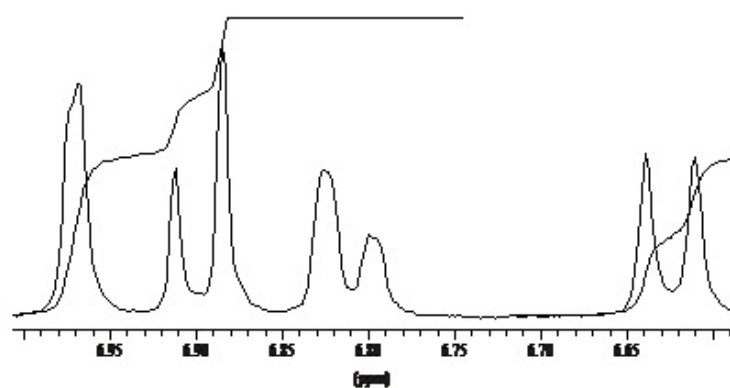
 $C_{20}H_{19}N_3O_6$

397.3909

BAS 1923205

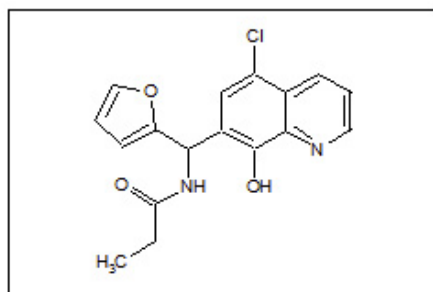
27.01.2000

Solv.DMSO

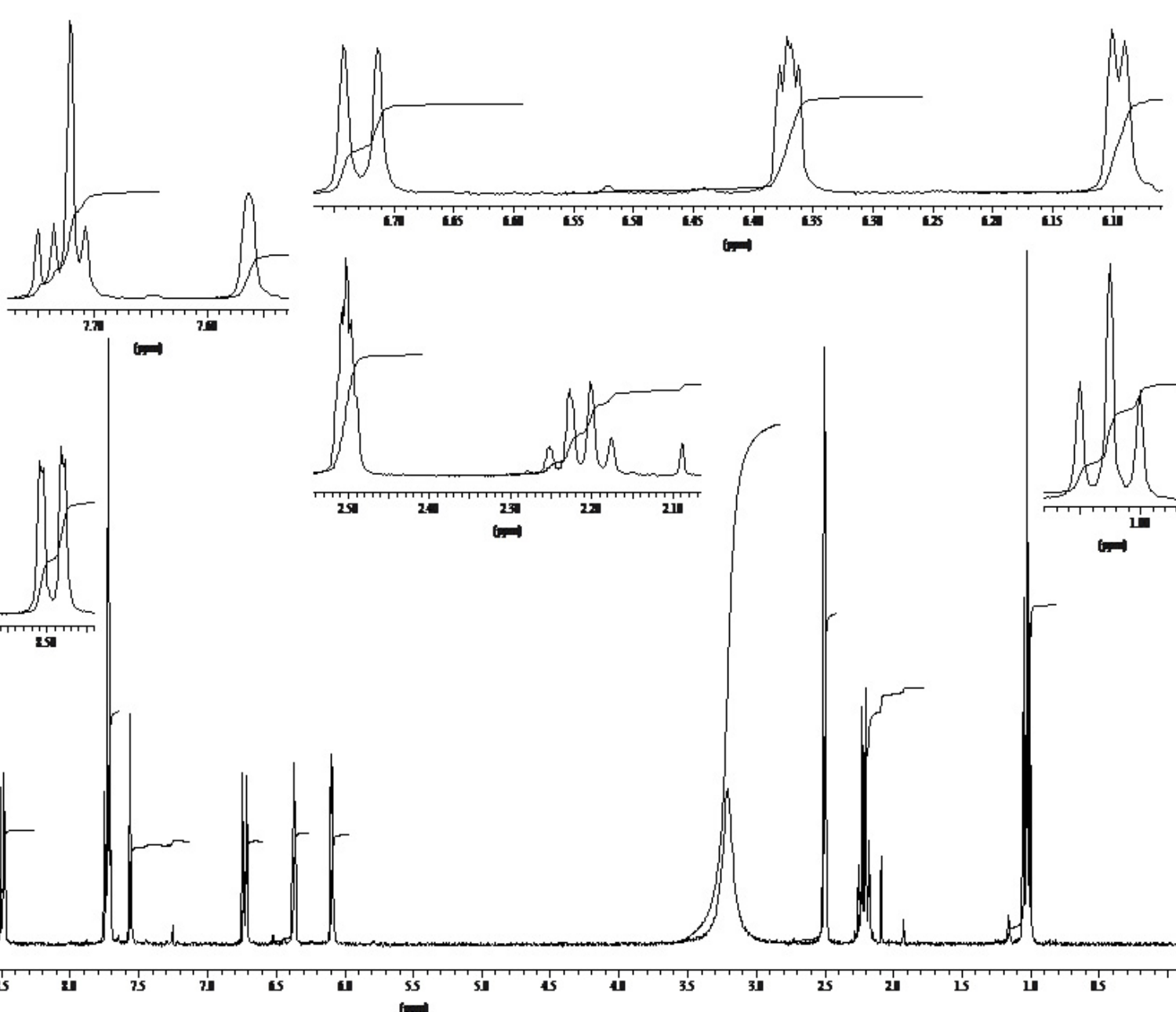


NKTA B1923185

Q1-8

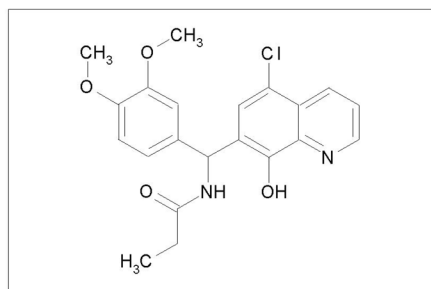


FRK 0000380	
1923185	
C ₁₇ H ₁₅ ClN ₂ O ₃	330.7737
BAS 1923185	27.01.2000 Solv.DMSO



NKTA B1923191

Q1-9



FRK 0000386

1923191

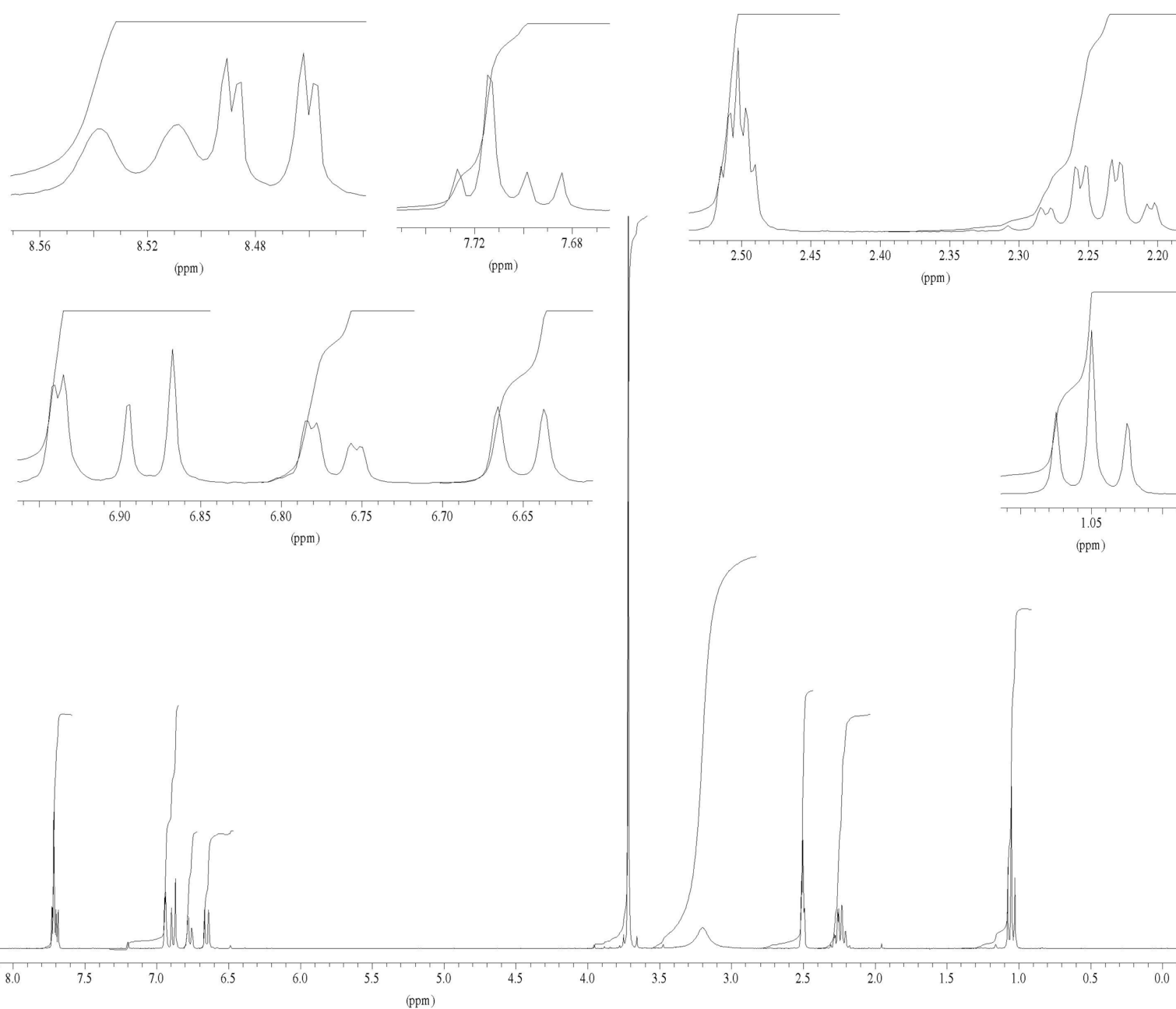
C₂₁H₂₁ClN₂O₄

400.8655

BAS 1923191

27.01.2000

Solv. DMSO

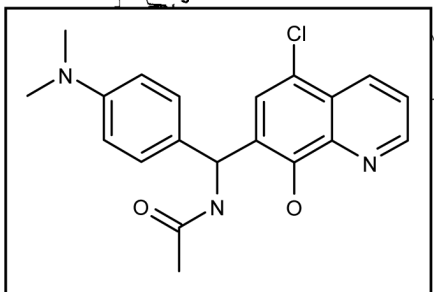
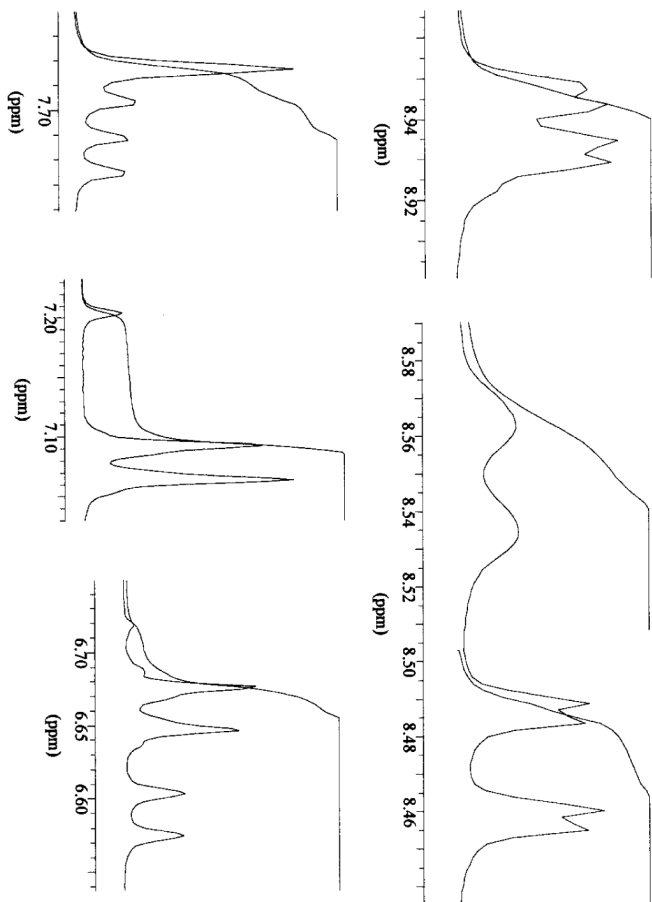


229064

NKTA B1923172

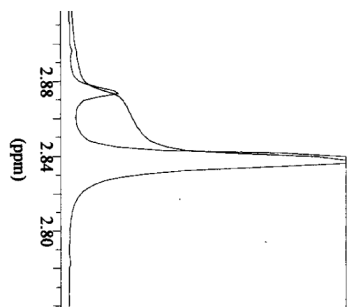
FRK 0000367		
C ₂₀ H ₂₀ ClN ₃ O ₂	369.8543	
BAS 1923172	27.01.2000	Solv. DMSO

Q1-10



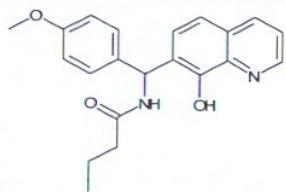
(ppm)

229048

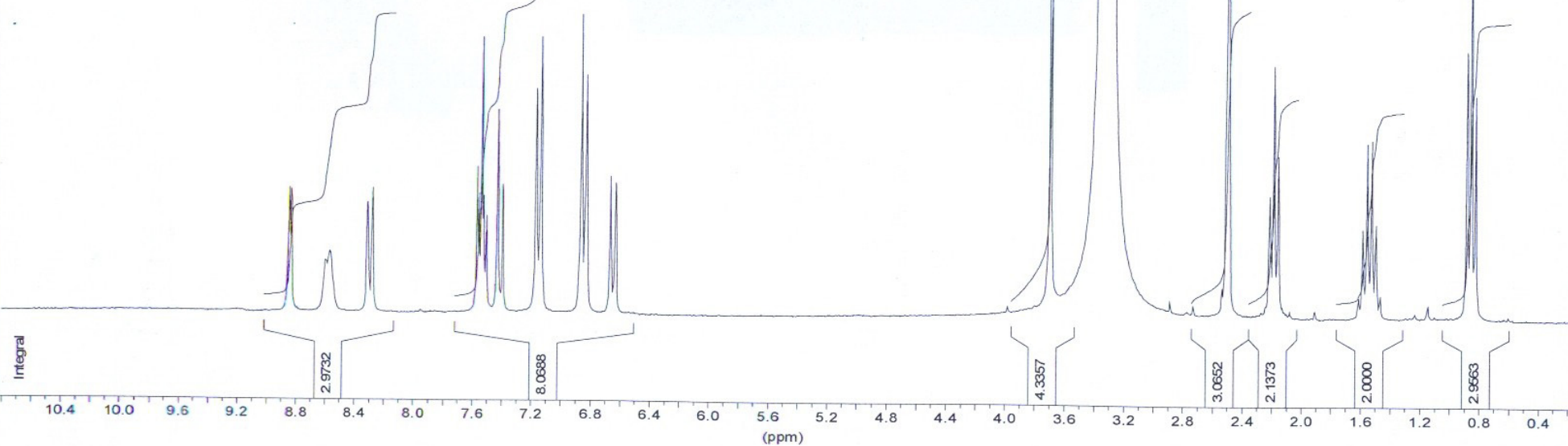
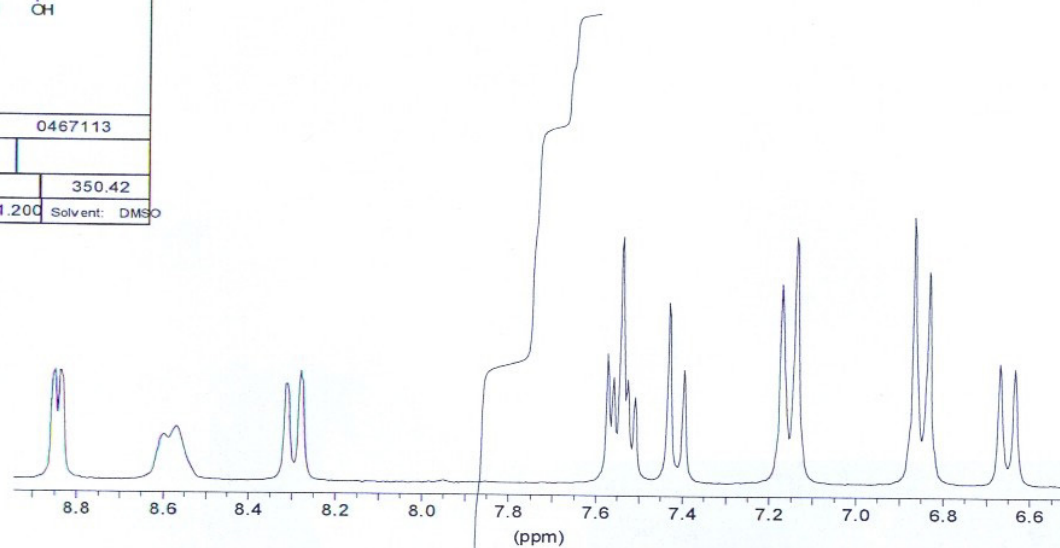


B
7/10/09/06

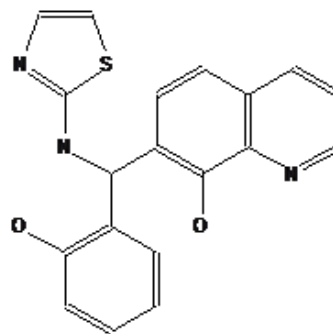
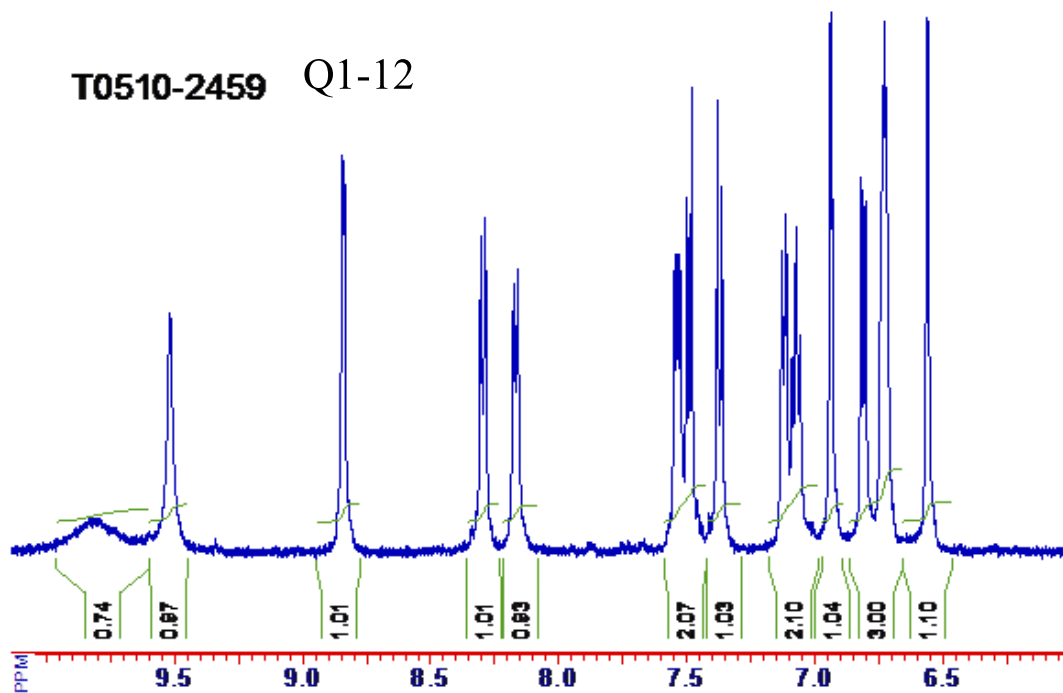
Q1-11



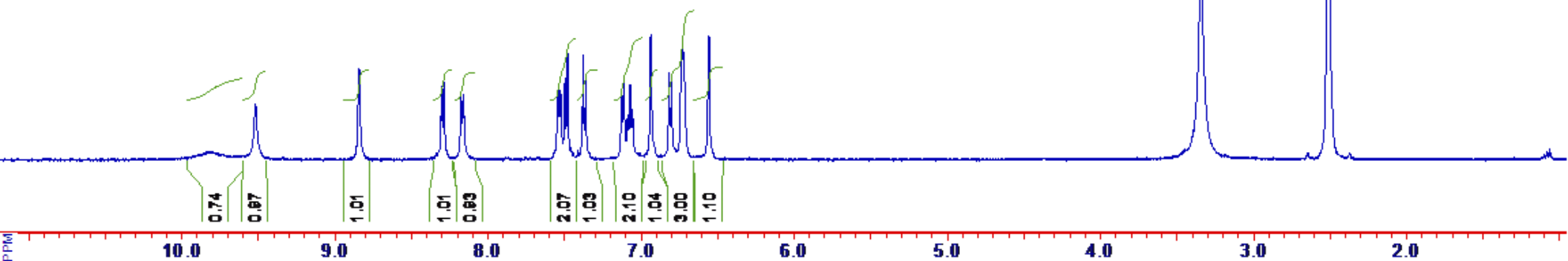
FRK 0000018	0467113
1277878	
C ₂₁ H ₂₂ N ₂ O ₃	350.42
BAS 1277878	01.11.200 Solvent: DMSO



T0510-2459 Q1-12



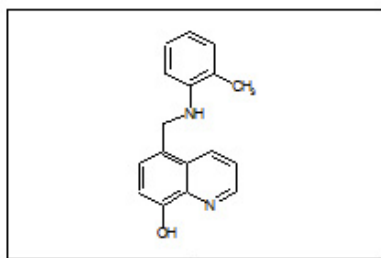
T0510-2459 Kovina-K-2 C19H15N3O2S
349.41



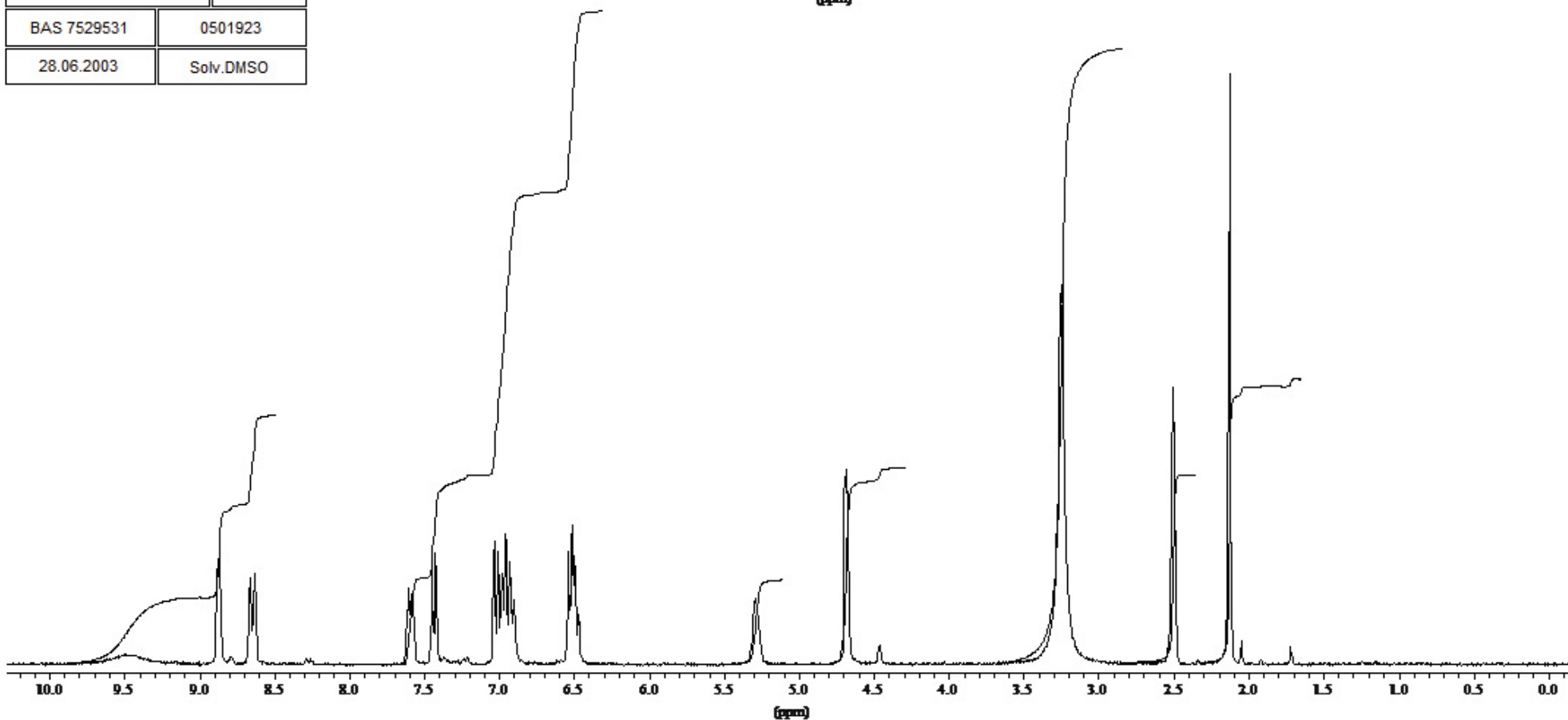
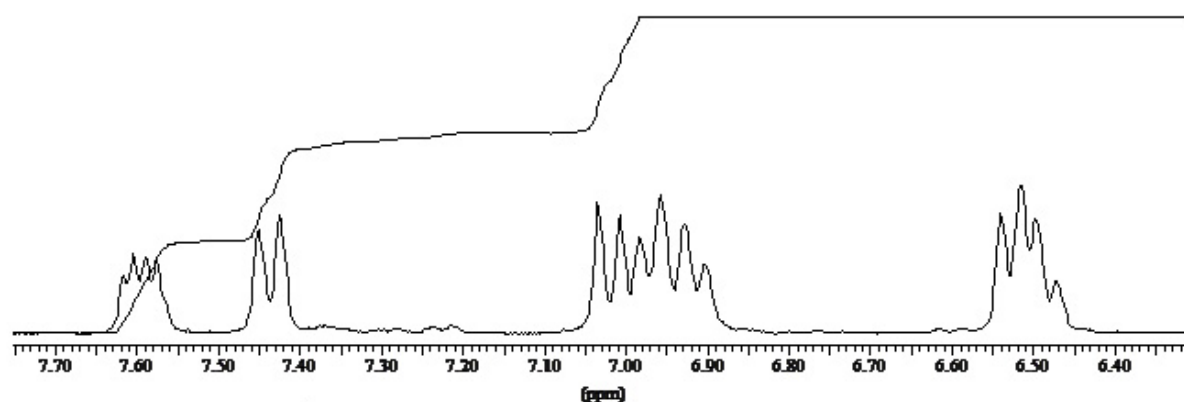
File name: T0510-2459	Vaskivska Lyudmila	SF: 500.0680 MHz	MSC: 1	PW: 0.00 usec, RG: 200	St 65536
Date: 18-Jan-2013	Solvent: DMSO	SW: 8503 Hz	TE: 0 K	AQ: 1.93 sec, RD: 0.00 sec	*T0510-2459*

BAS 7529531

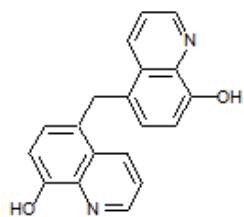
Q2-1



YAP 0000072	
7529531	
C ₁₇ H ₁₆ N ₂ O	264.3299
BAS 7529531	0501923
28.06.2003	Solv.DMSO



Q2-2

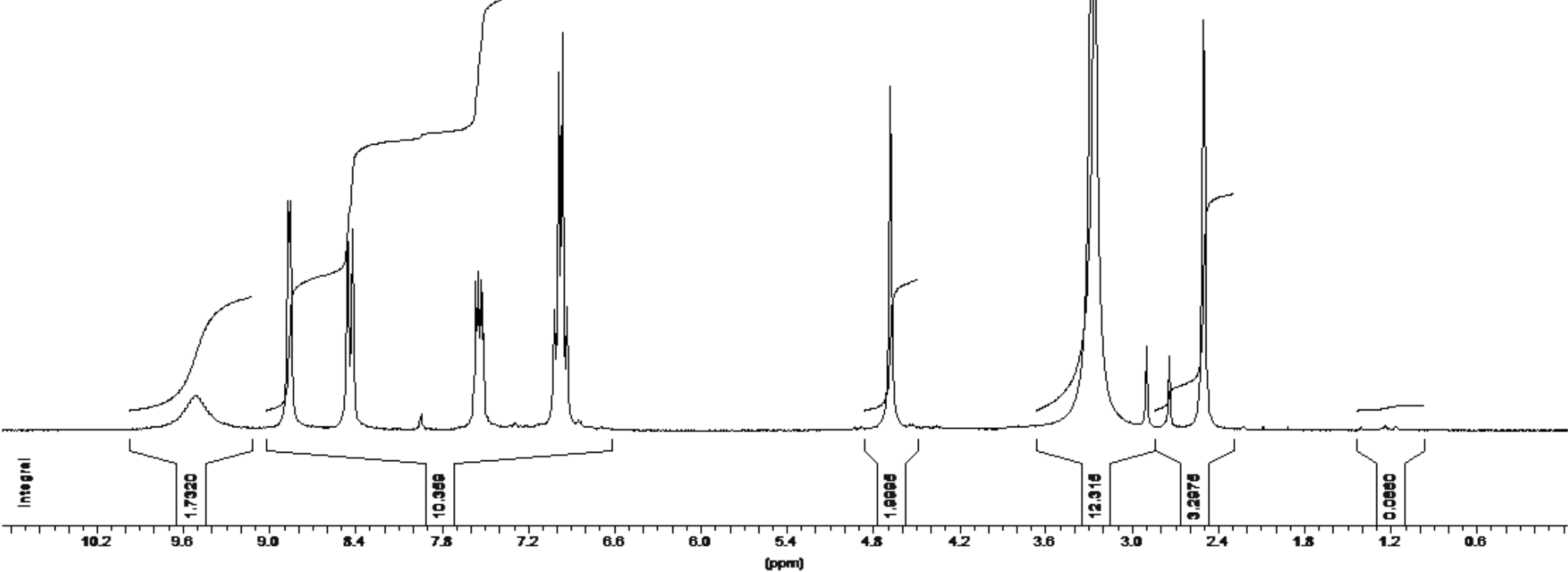
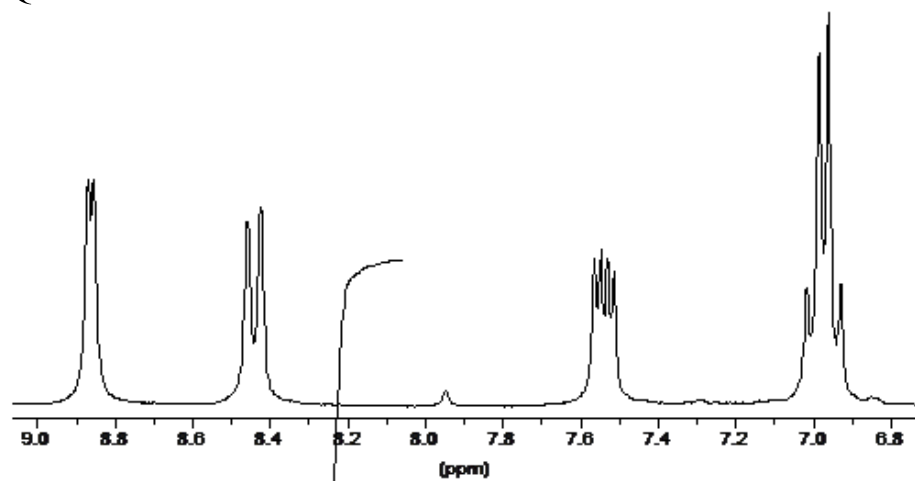


RRP 0002070 0528953

6575110

C₁₉H₁₄N₂O₂ 302.34

BAS 6575110 16.10.2003 Solvent: DMSO



1.7920

10.966

1.0000

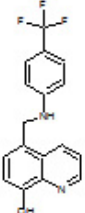
12.916

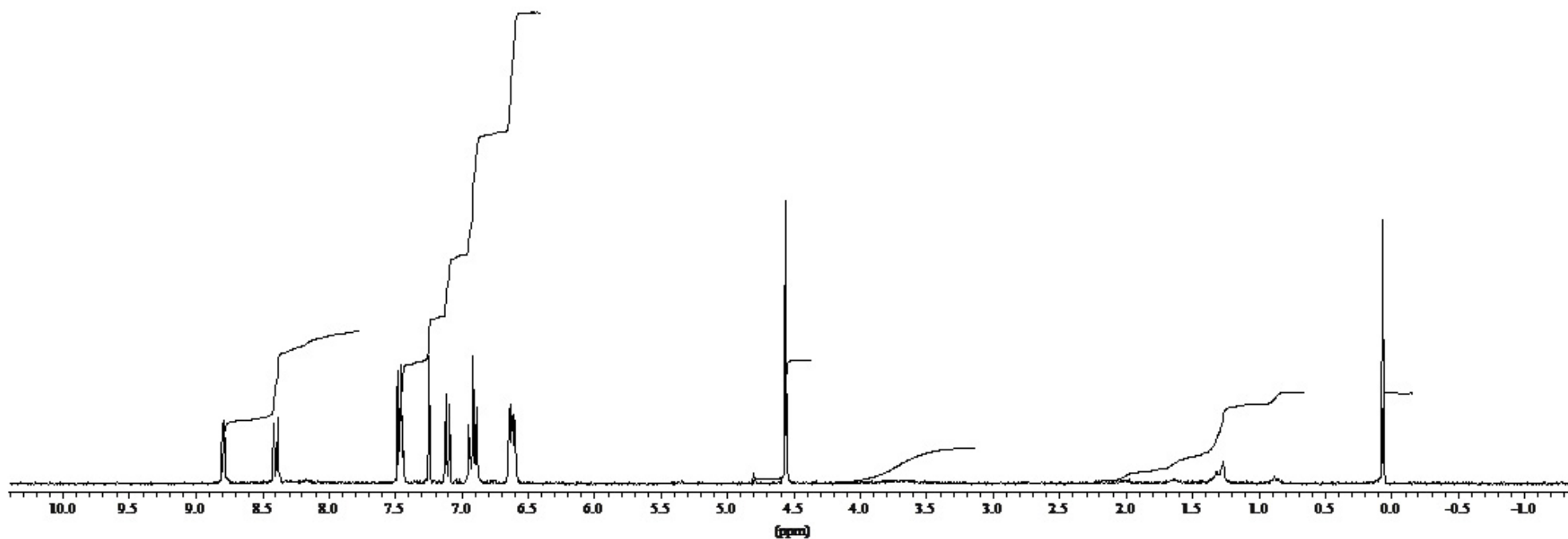
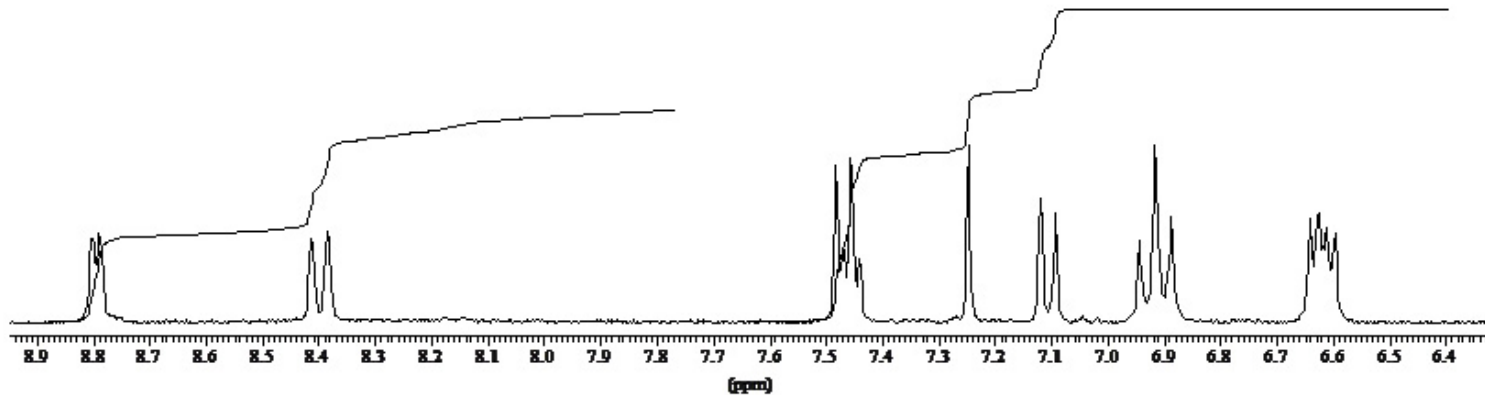
0.2676

0.0000

B 7529529 CDCL3

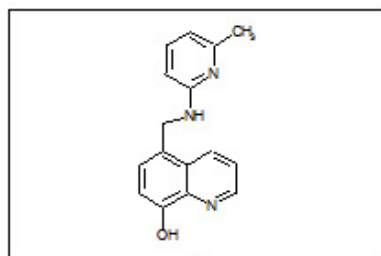
Q2-3

	
YAP 0000070	
7529529	
$C_{17}H_{13}F_3N_2O$	318.3012
BAS 7529529	0531460
01.11.2003	Solv.CDCl3



B 7529564 CDCl3

Q2-4



YAP 0000105

7529564

C₁₆H₁₅N₃O

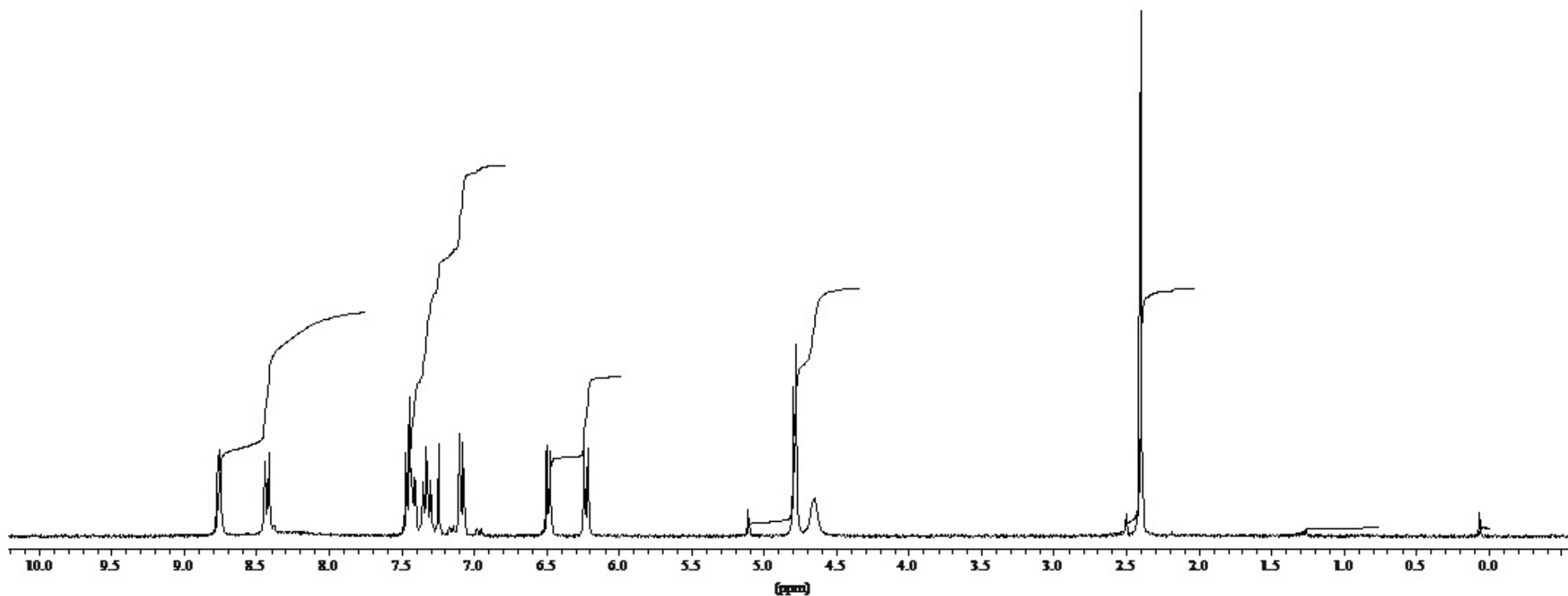
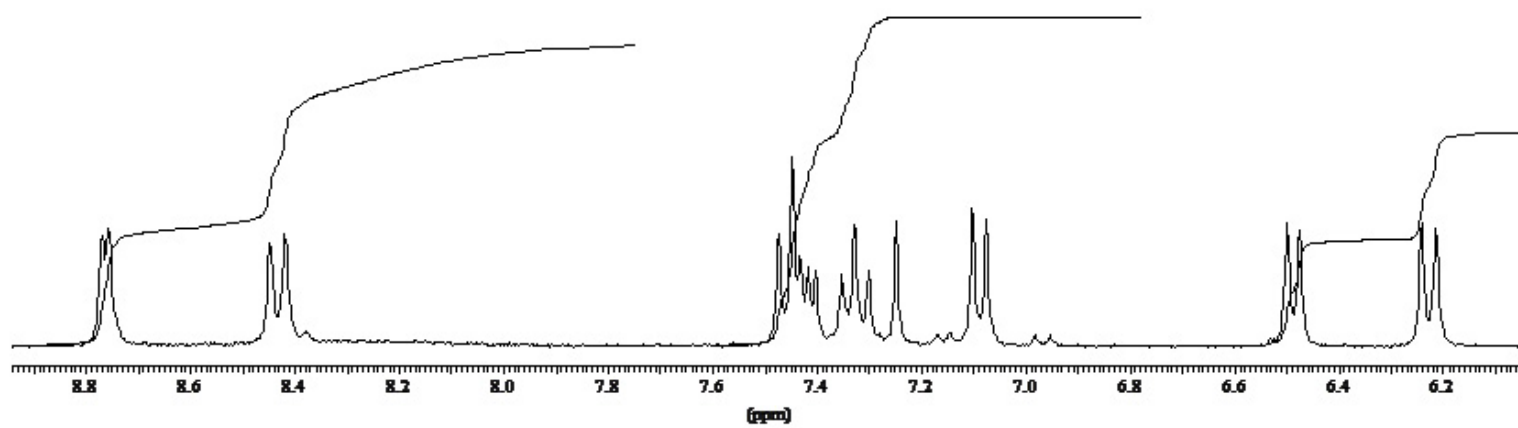
265.3175

BAS 7529564

0531463

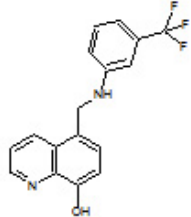
01.11.2003

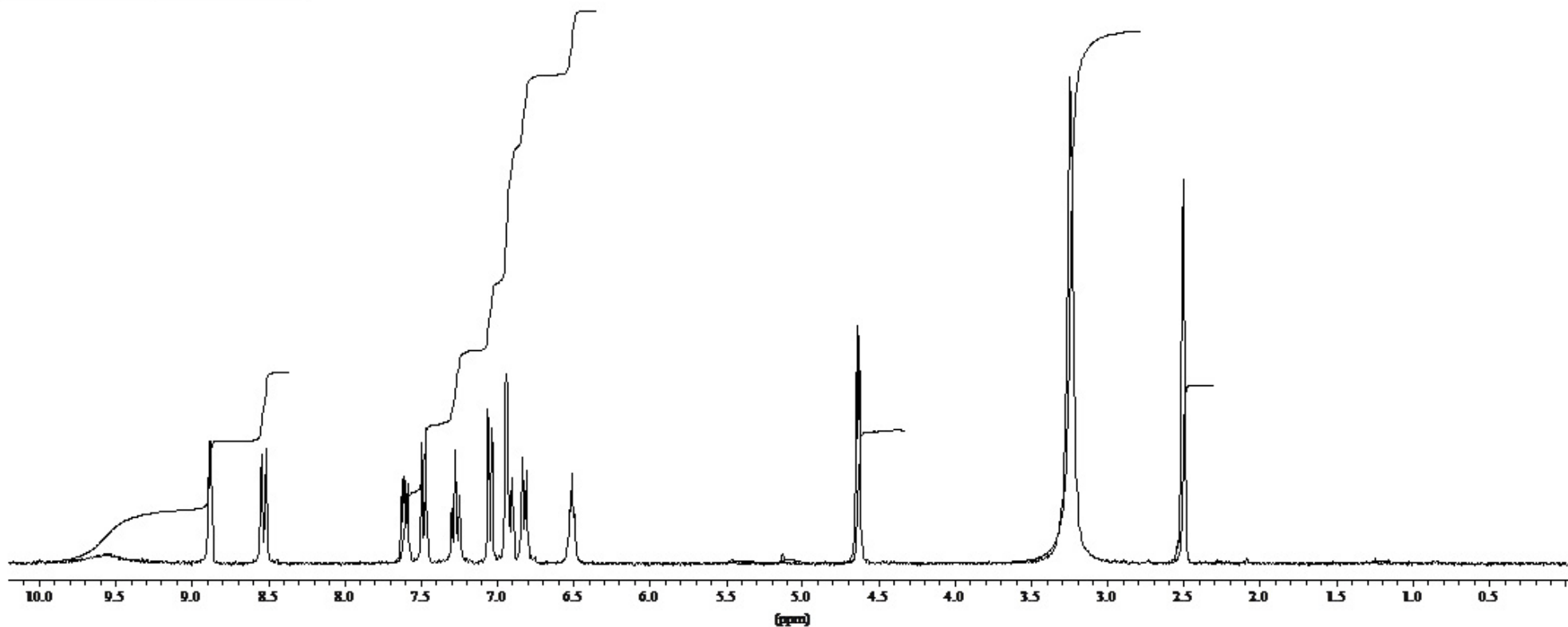
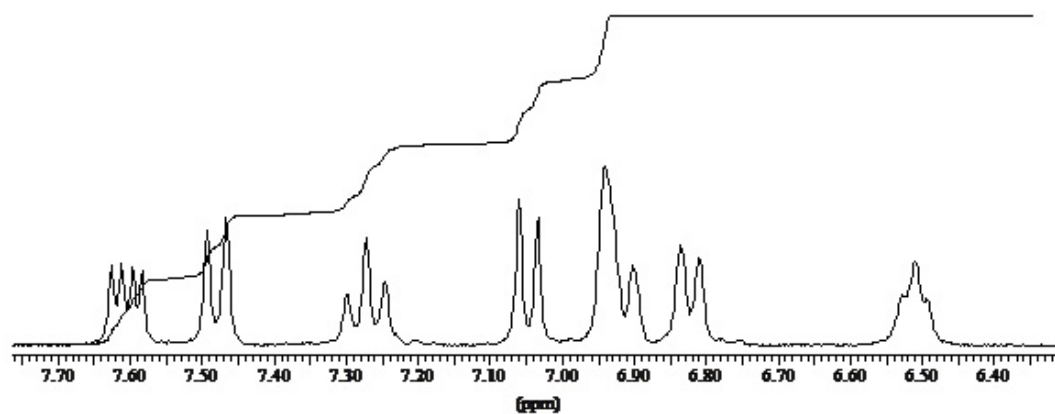
Solv.CDCl3



BAS 7529526

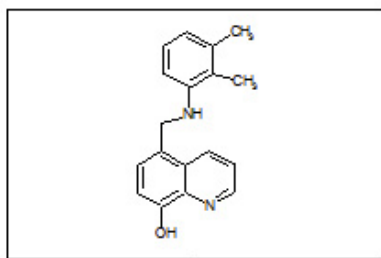
Q2-5

	
YAP 0000067	
7529526	
C ₁₇ H ₁₃ F ₃ N ₂ O	318.3012
BAS 7529526	0501919
28.06.2003	Solv.DMSO

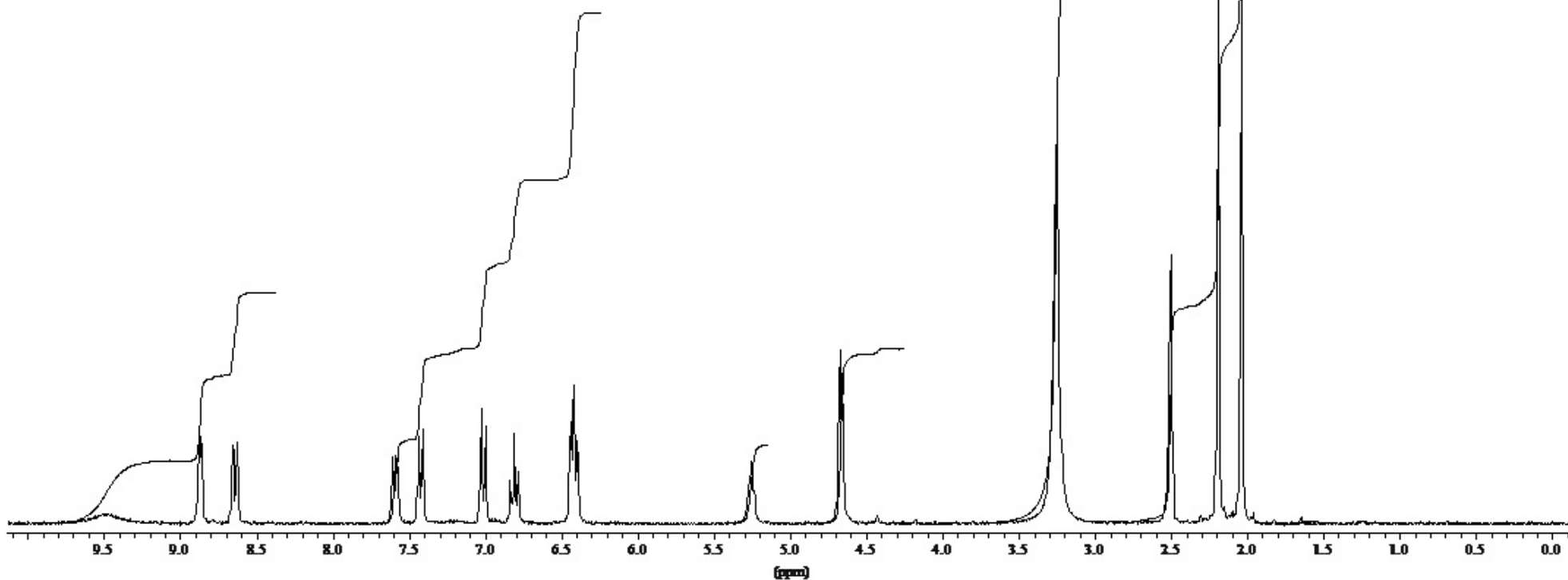
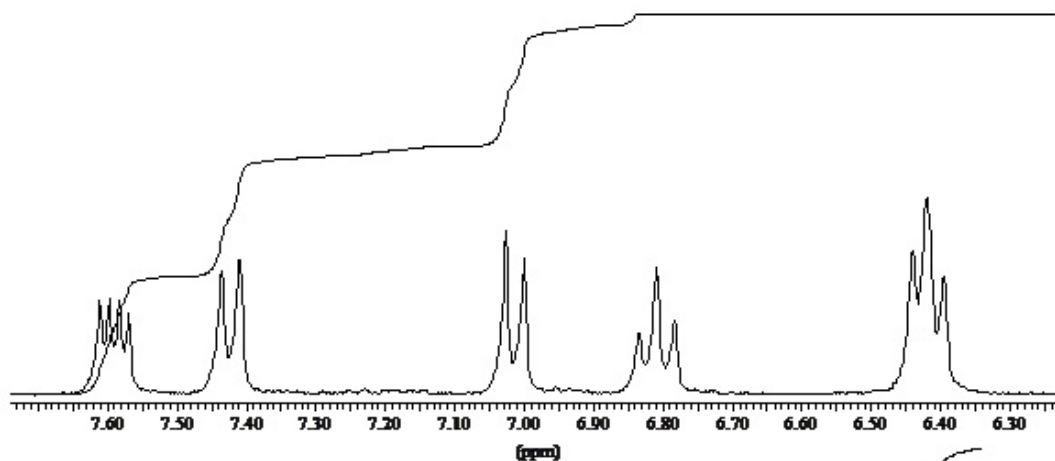


BAS 7529537

Q2-6

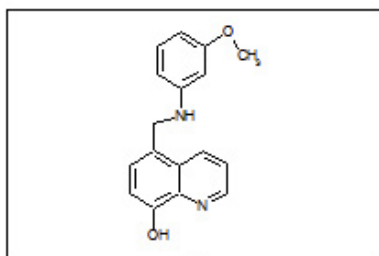


YAP 0000078	
7529537	
C ₁₈ H ₁₈ N ₂ O	278.3570
BAS 7529537	0501926
28.06.2003	Solv.DMSO



B 7529530 CDCL3

Q2-7



YAP 0000071

7529530

C₁₇H₁₆N₂O₂

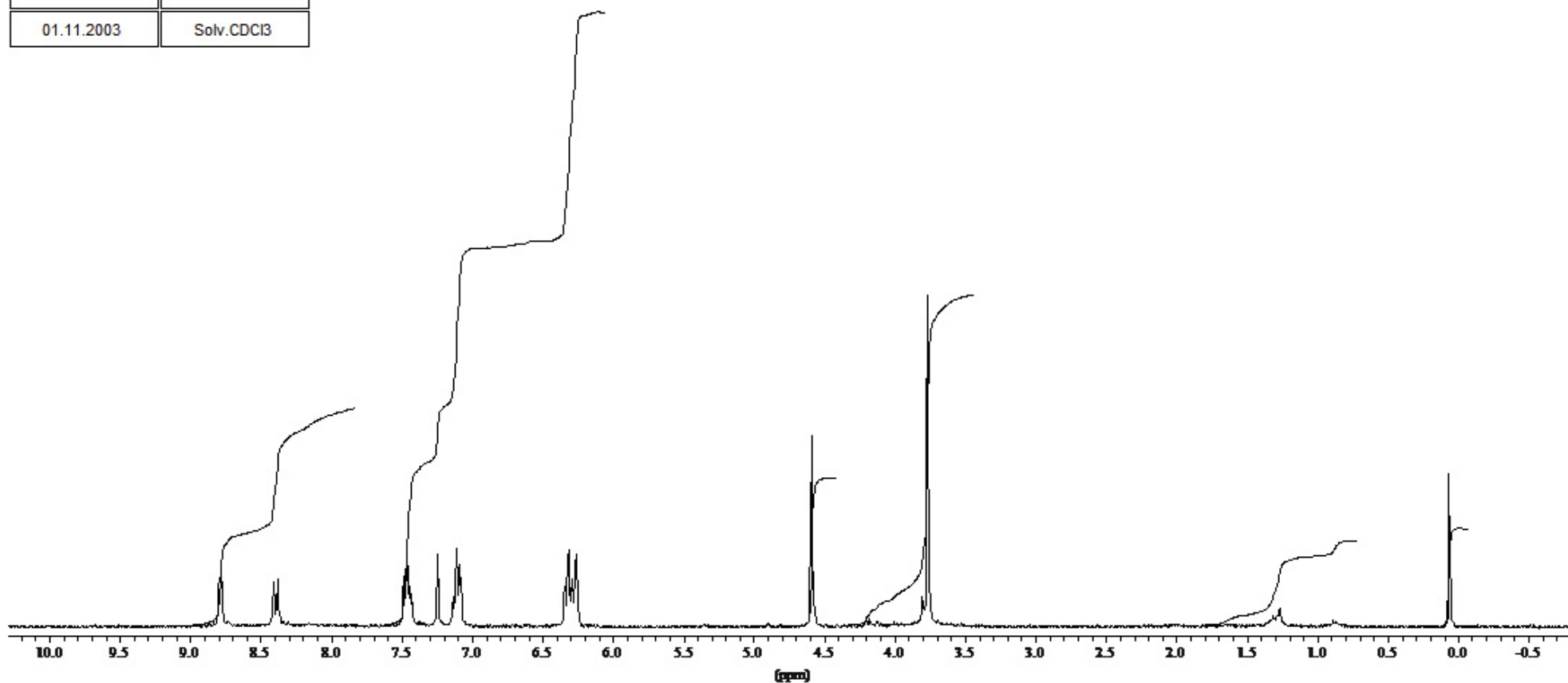
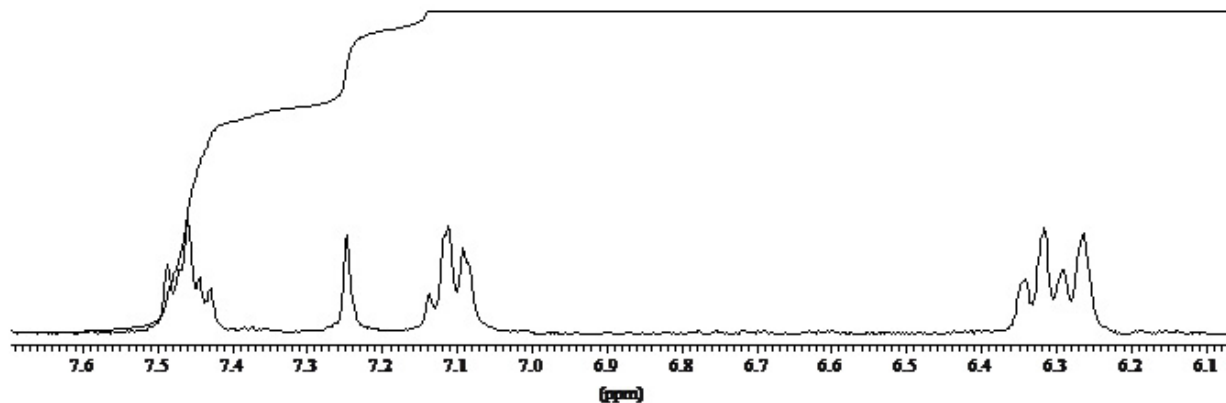
280.3293

BAS 7529530

0531461

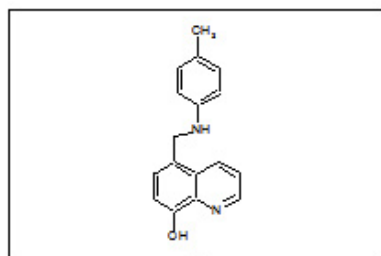
01.11.2003

Solv.CDCl3



B 7529528 CDCL3

Q2-8



YAP 0000069

7529528

C₁₇H₁₆N₂O

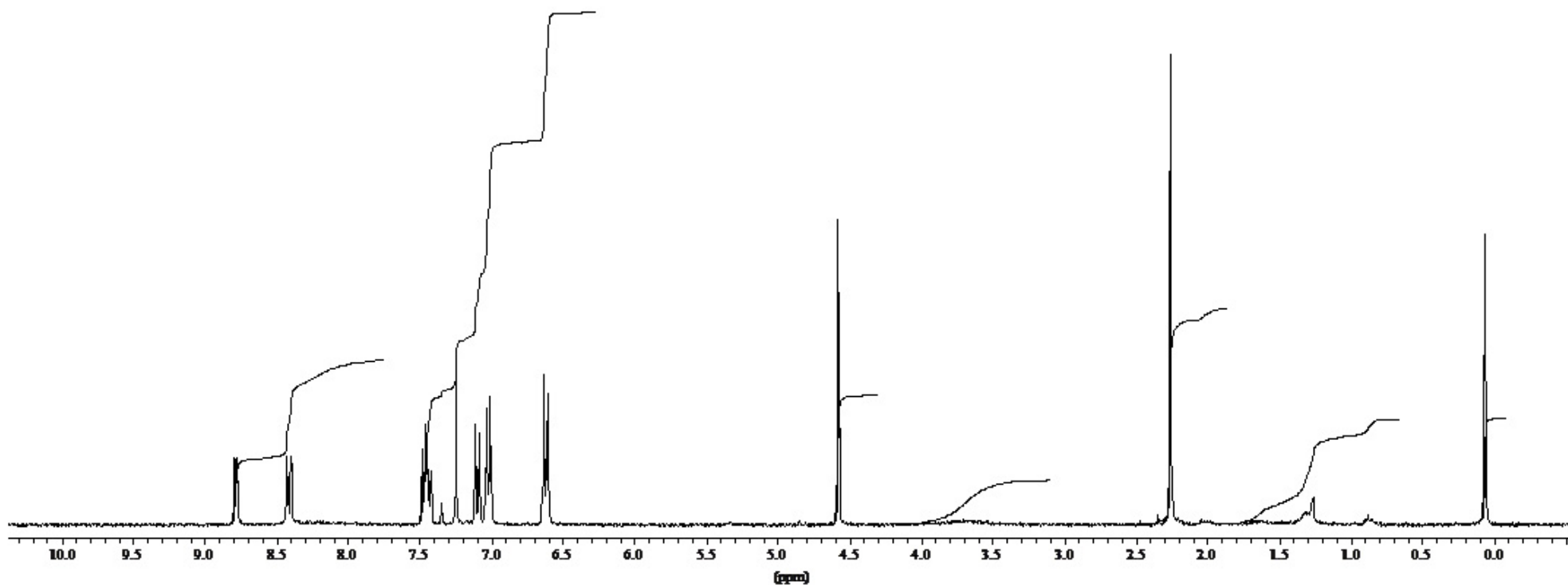
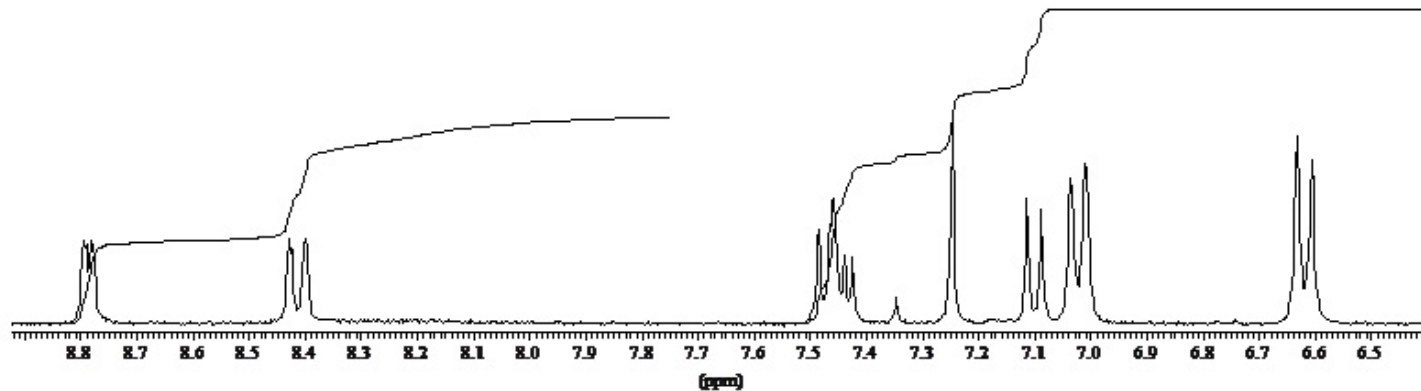
264.3299

BAS 7529528

0531459

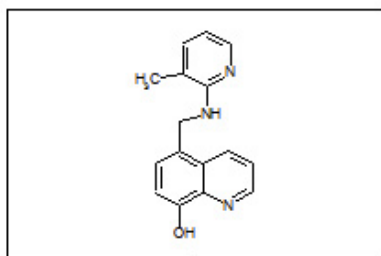
01.11.2003

Solv.CDCl3

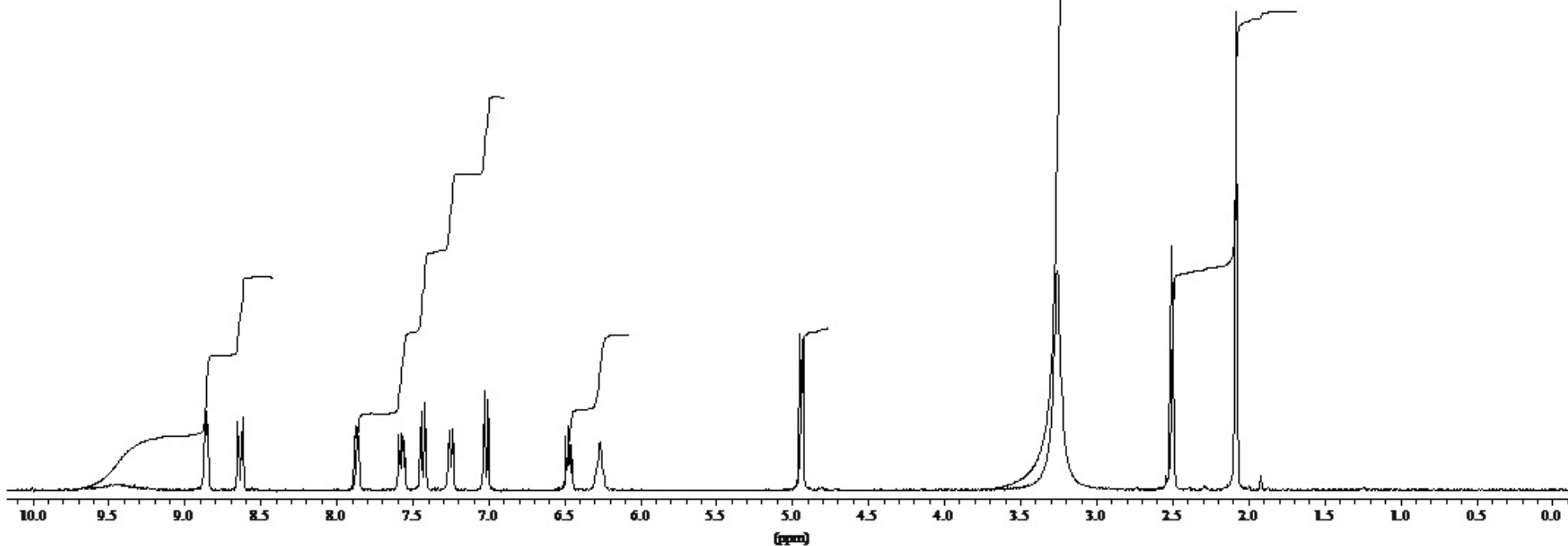
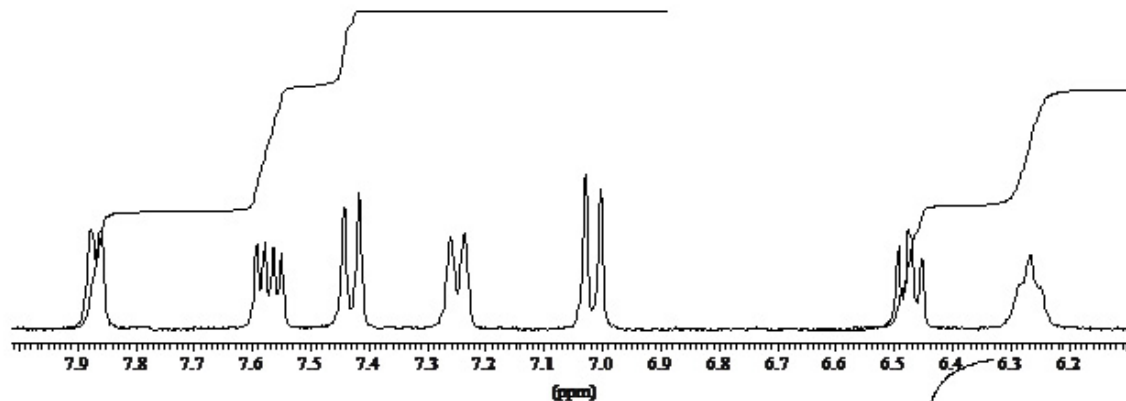


BAS 7529563

Q2-9

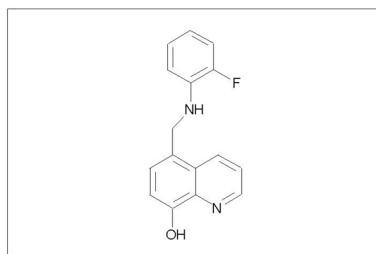


YAP 0000104	
7529563	
C ₁₆ H ₁₅ N ₃ O	265.3175
BAS 7529563	0501930
28.06.2003	Solv.DMSO



BAS 7529505

Q2-10



YAP 0000046

7529505

$C_{16}H_{13}FN_2O$

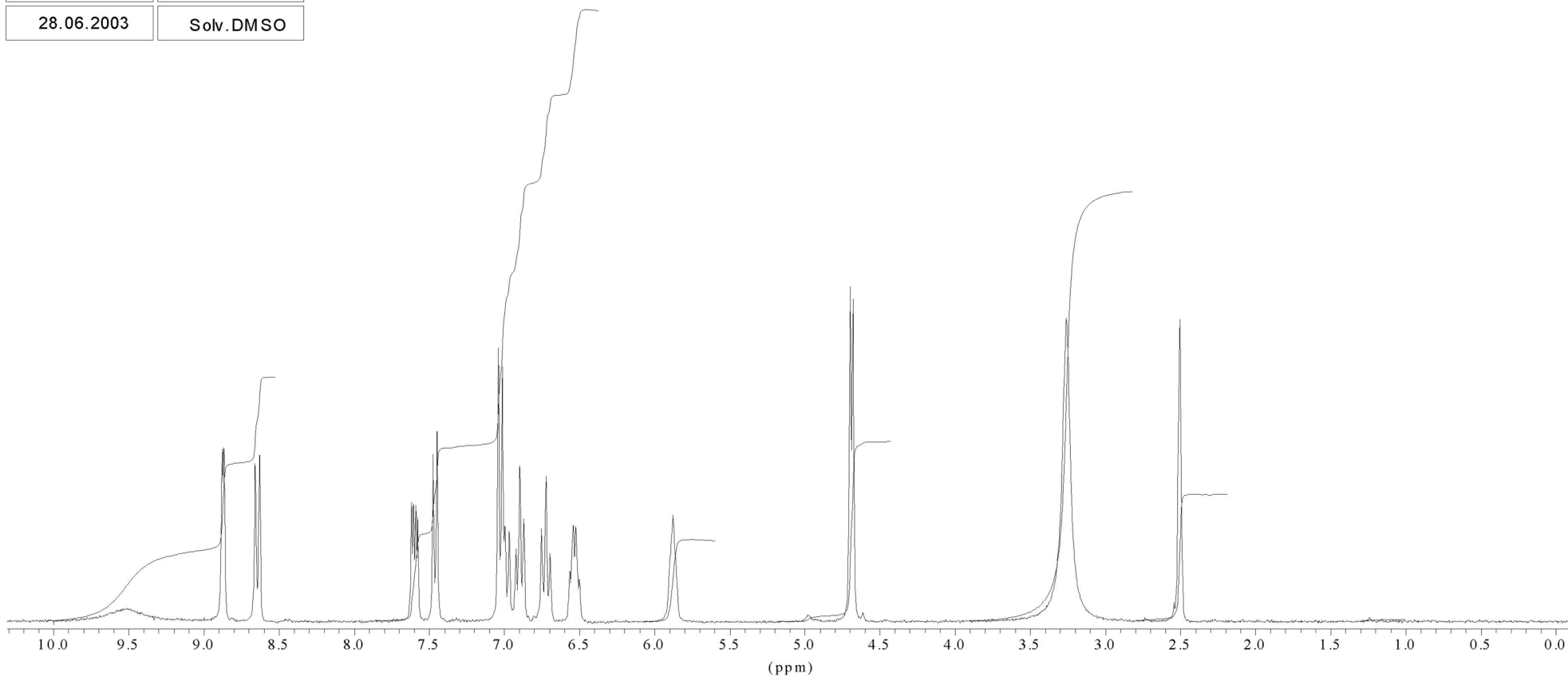
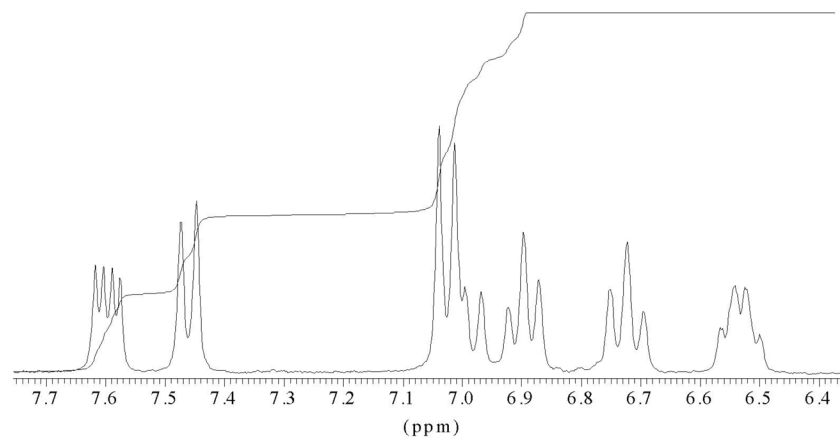
268.2932


BAS 7529505

0501904

28.06.2003

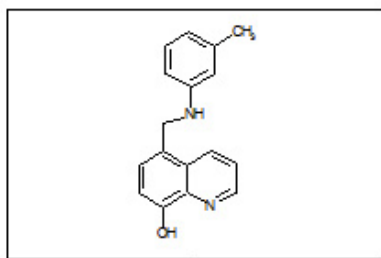
Solv. DMSO



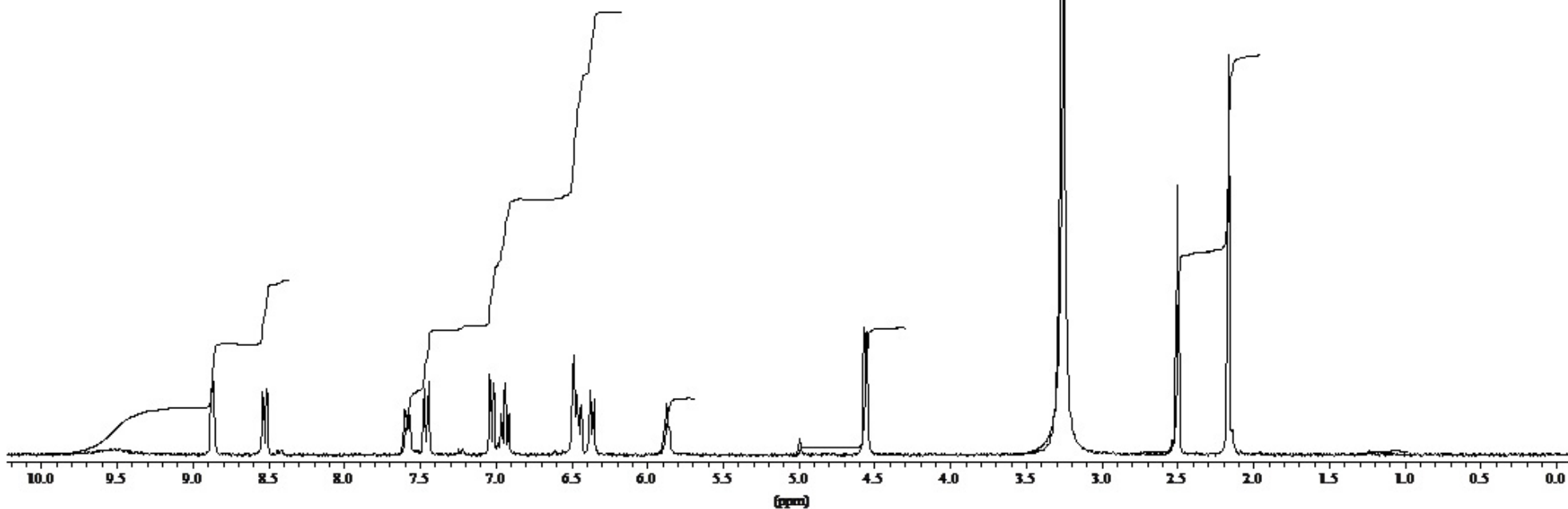
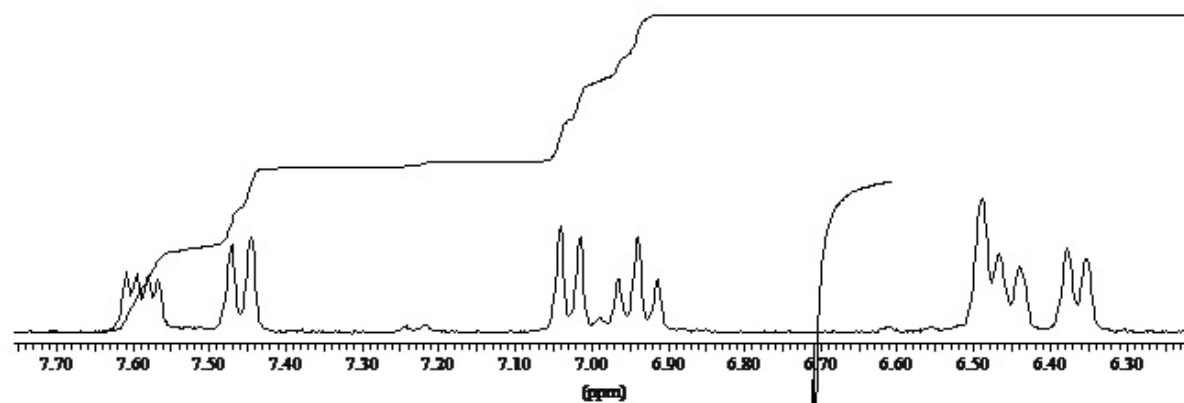

501904

BAS 7529535

Q2-11

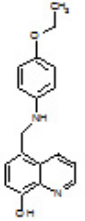


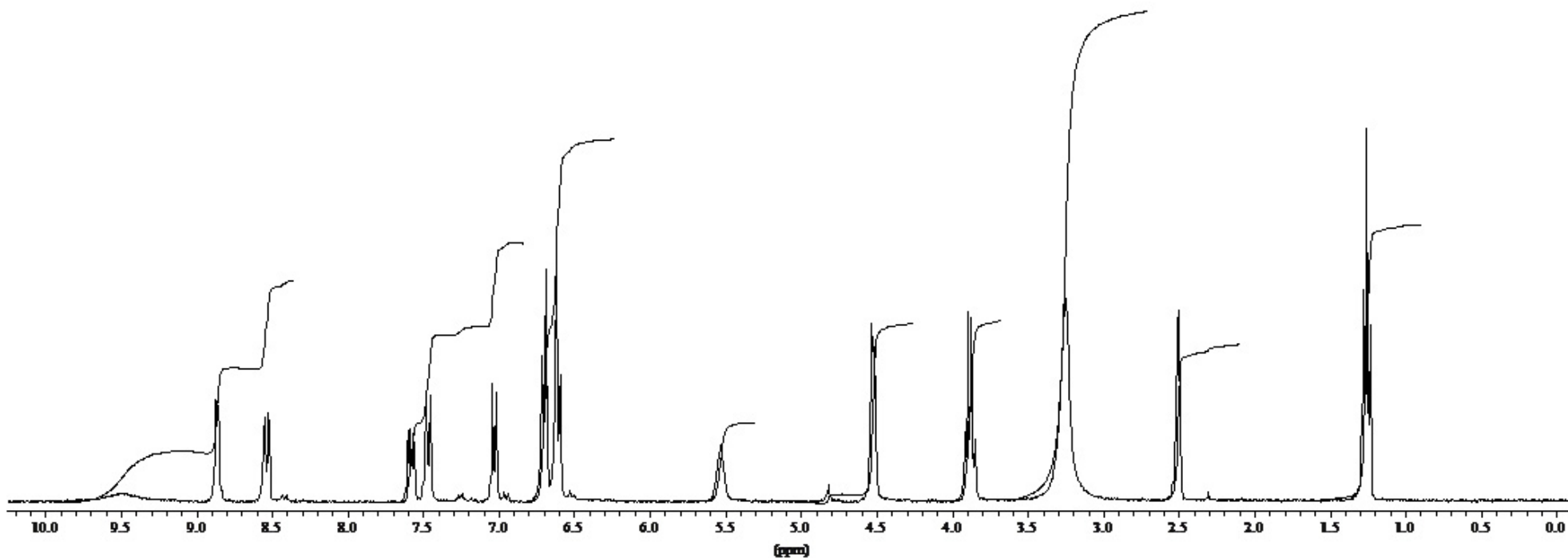
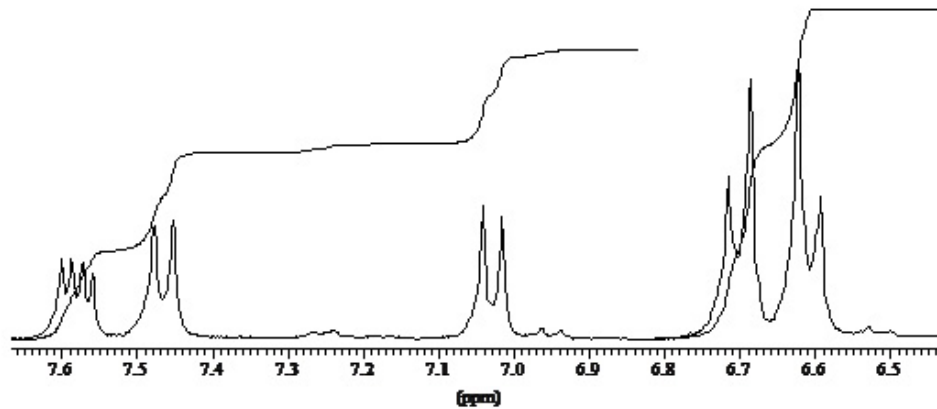
YAP 0000076	
7529535	
C ₁₇ H ₁₆ N ₂ O	264.3299
BAS 7529535	0501924
28.06.2003	Solv.DMSO



BAS 7529509

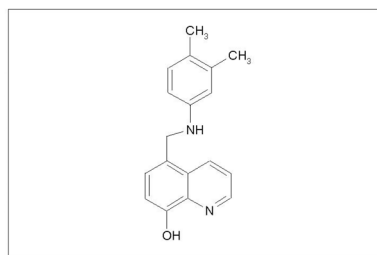
Q2-12

	
YAP 0000050	
7529509	
C ₁₈ H ₁₈ N ₂ O ₂	294.3564
BAS 7529509	0501908
28.06.2003	Solv.DMSO



B 7529536 CDCL3

Q2-13



YAP 0000077

7529536

C₁₈H₁₈N₂O

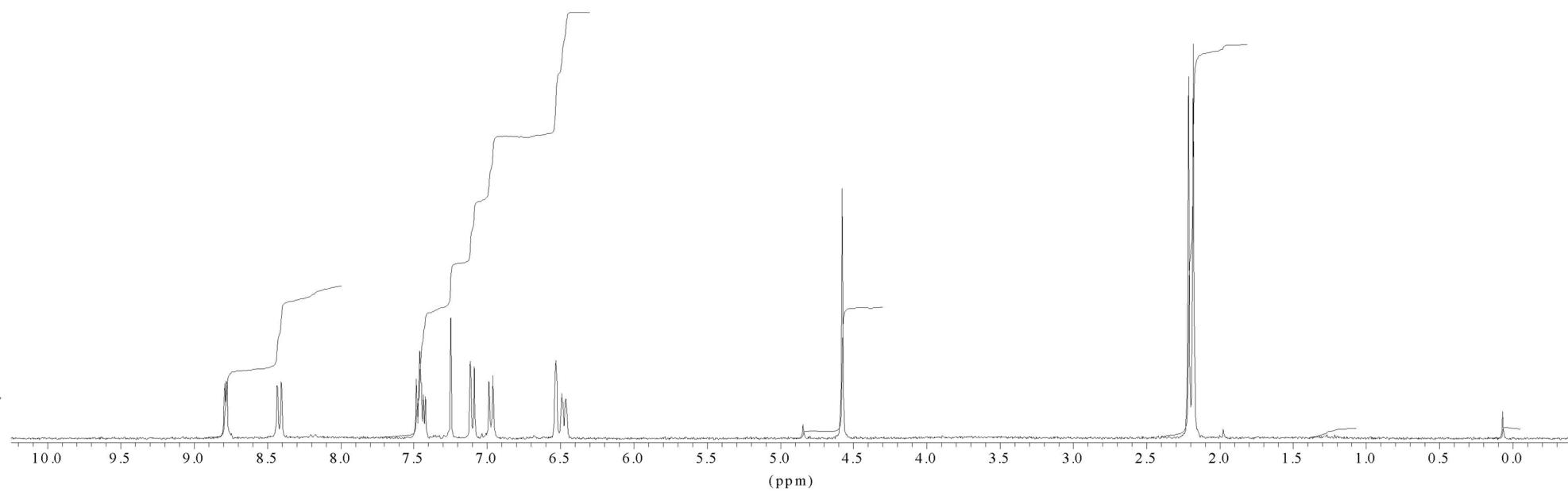
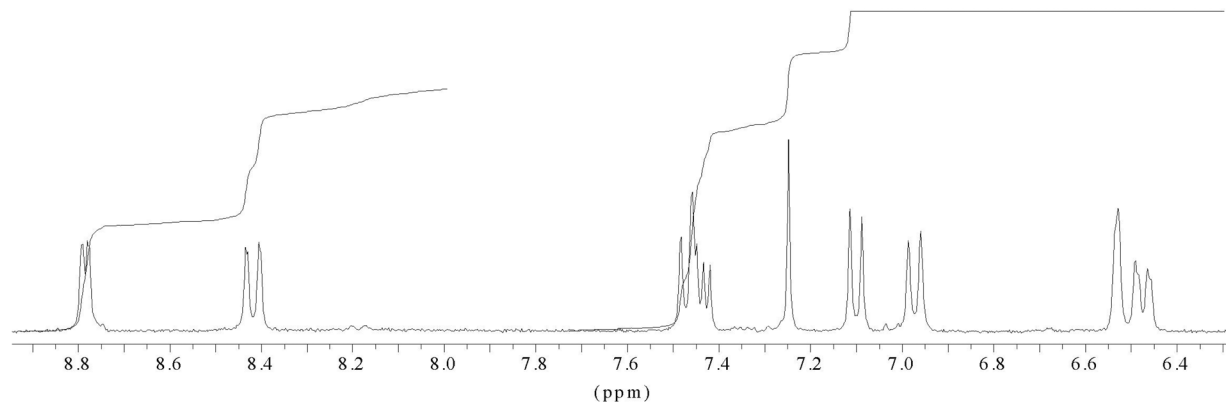
278.3570

BAS 7529536

0531462

01.11.2003

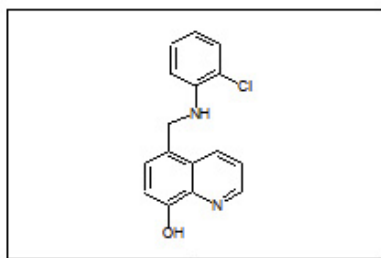
Solv.CDCl3



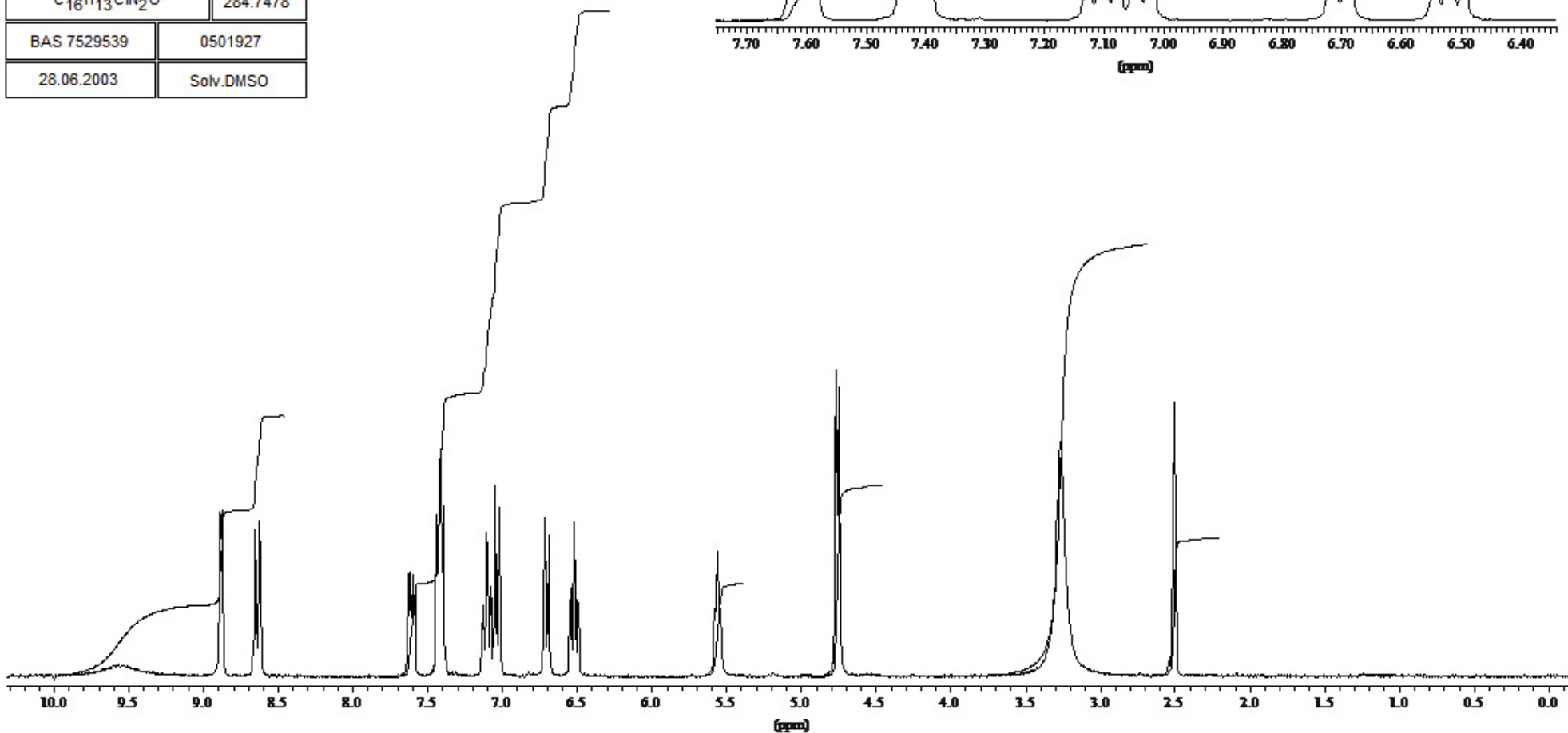
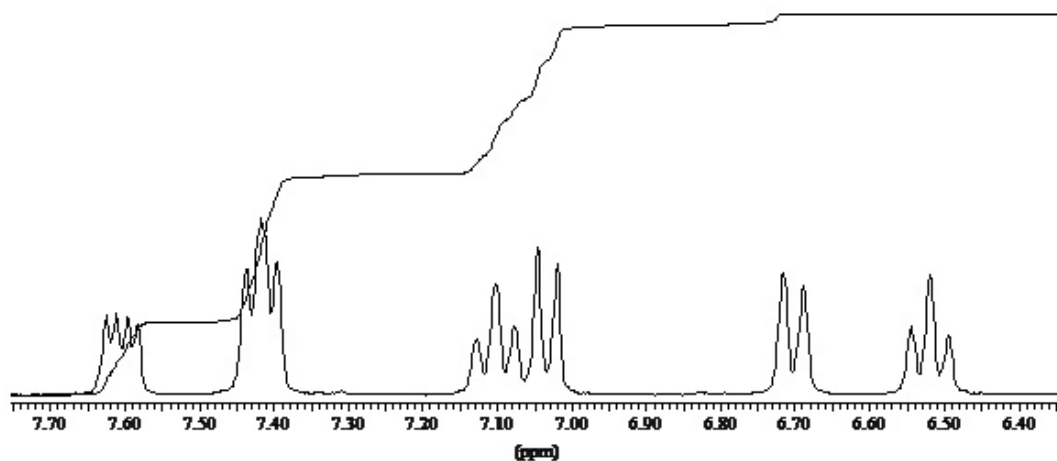
531462

BAS 7529539

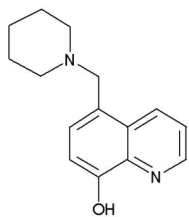
Q2-14



YAP 0000080	
7529539	
$C_{16}H_{13}ClN_2O$	284.7478
BAS 7529539	0501927
28.06.2003	Solv.DMSO



Q3-1



YAP 0000075

0521184

7529534

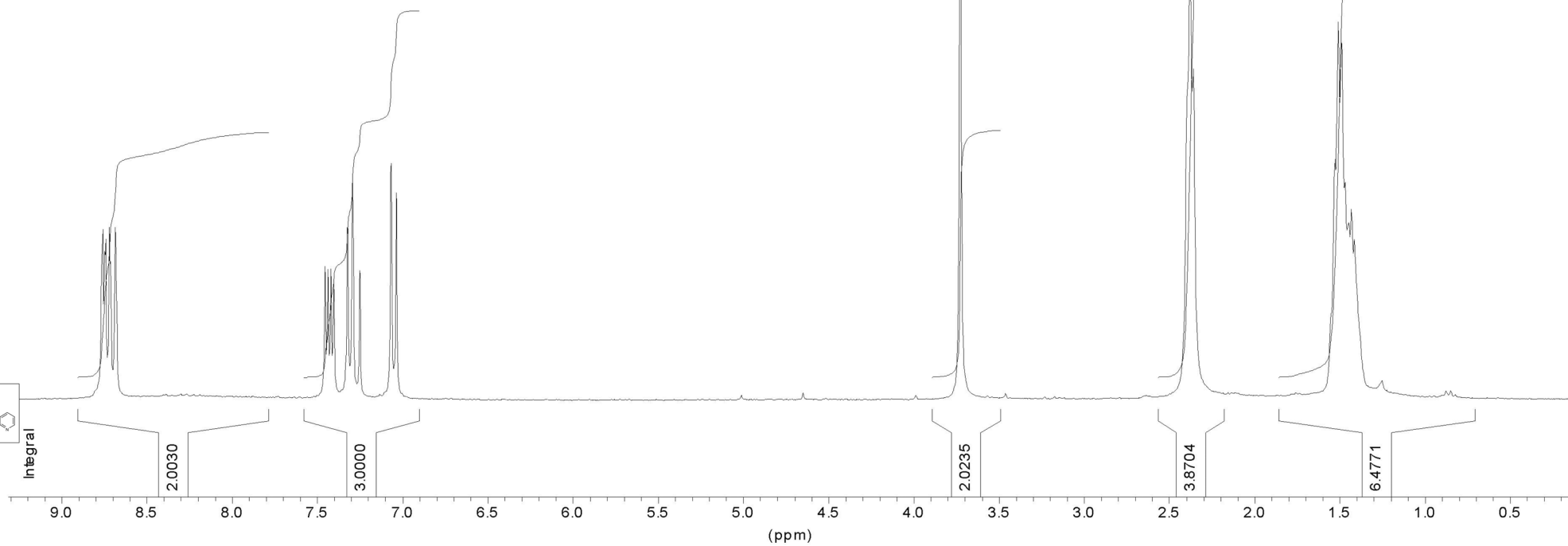
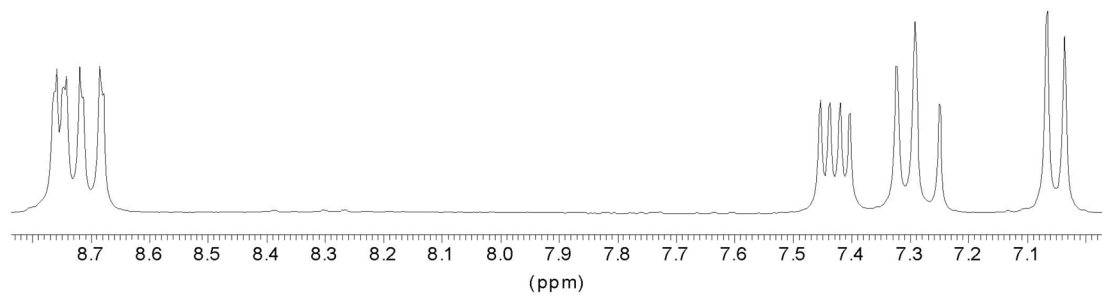
C₁₅H₁₈N₂O

242.32

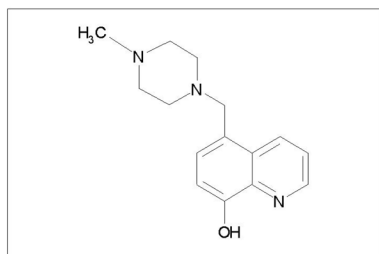
BAS 7529534

16.09.2003

Solvent:CDCl₃



BAS 7529515



YAP 000056

7529515

C₁₅H₁₉N₃O

257.3382

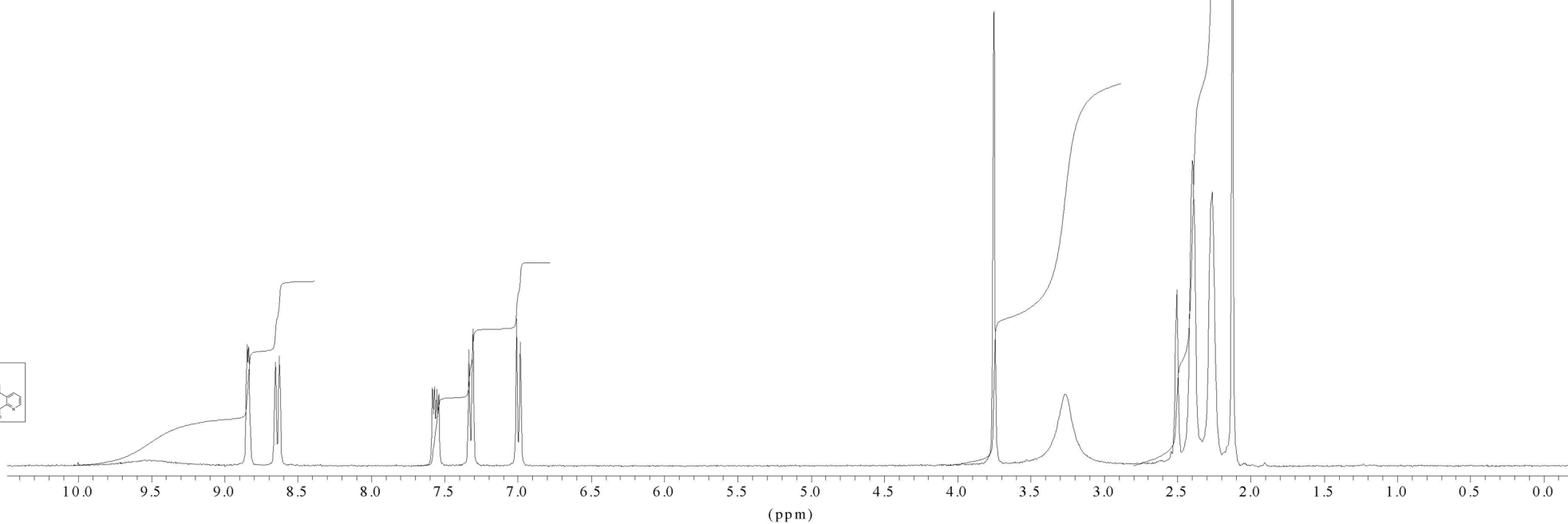
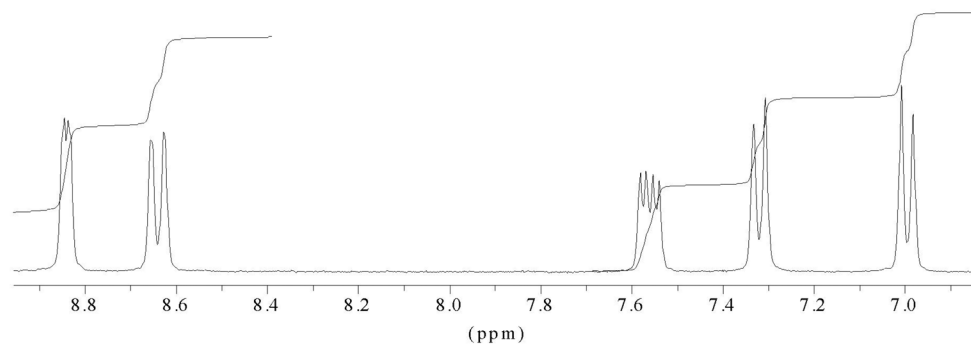
BAS 7529515

0501911

28.06.2003

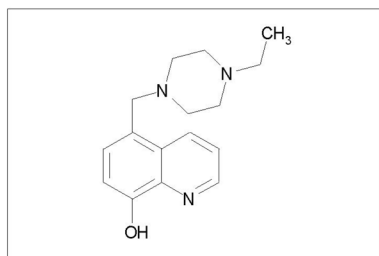
Solv. DMSO

Q3-2



501911

BAS 7529516



YAP 000057

7529516

C₁₆H₂₁N₃O

271.3653

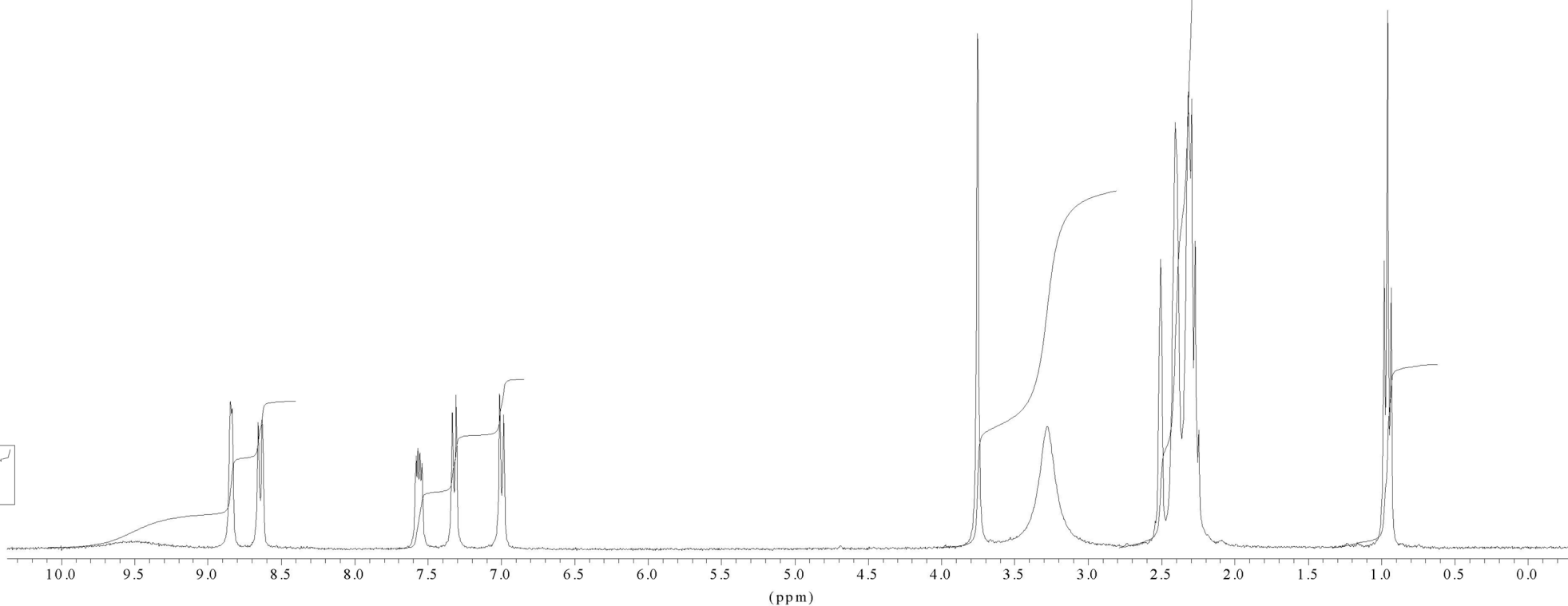
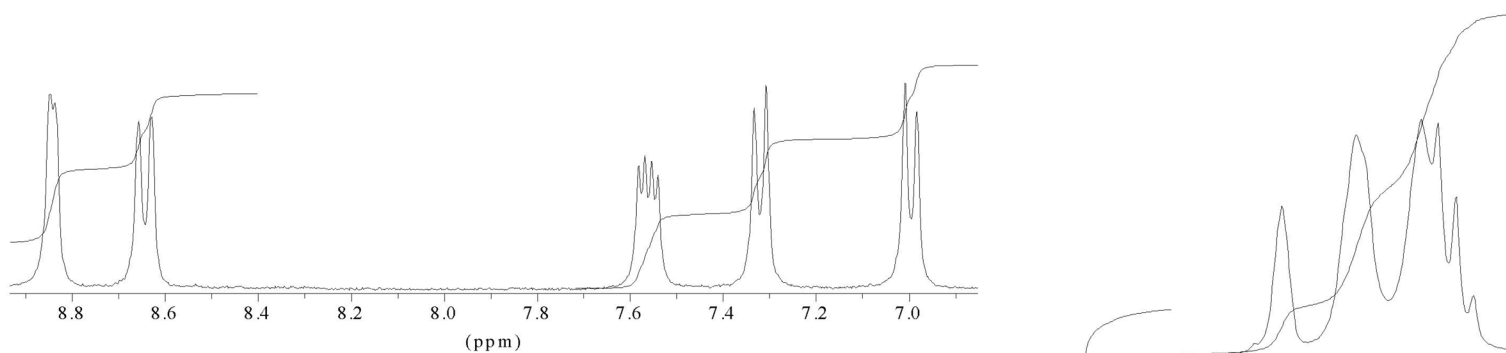
BAS 7529516

0501912

28.06.2003

Solv. DMSO

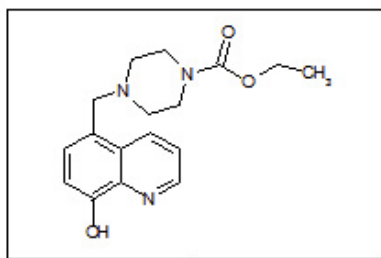
Q3-3



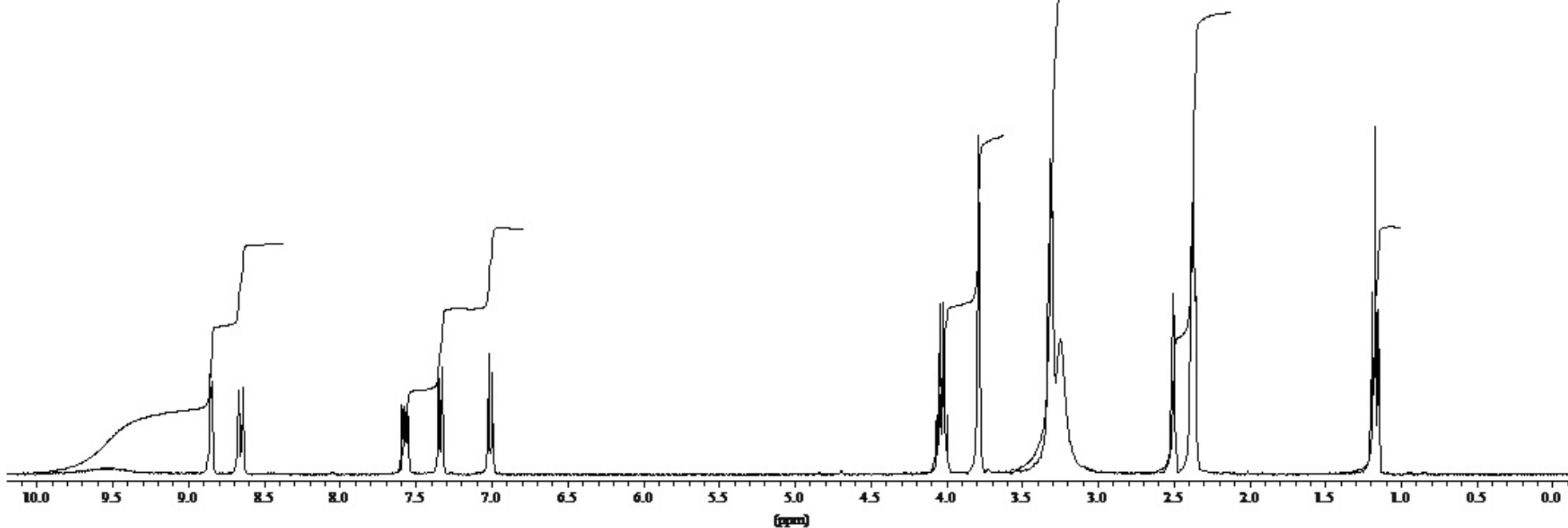
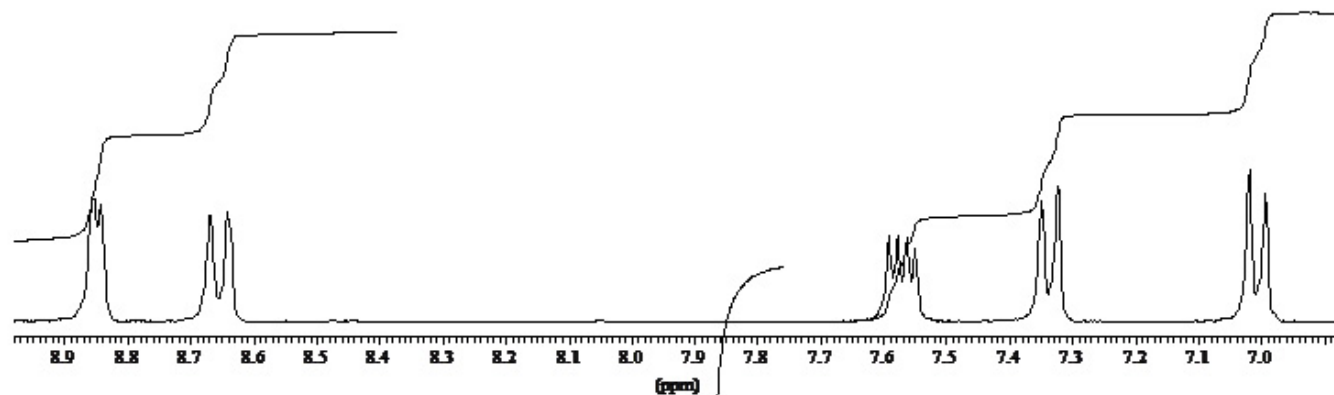
501912

BAS 7529517

Q3-4

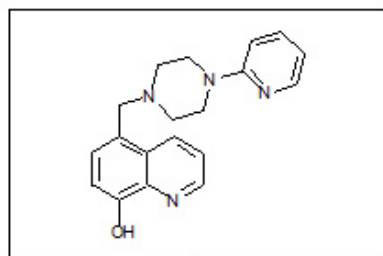


YAP 0000058	
7529517	
C ₁₇ H ₂₁ N ₃ O ₃	315.3752
BAS 7529517	0501913
28.06.2003	Solv.DMSO

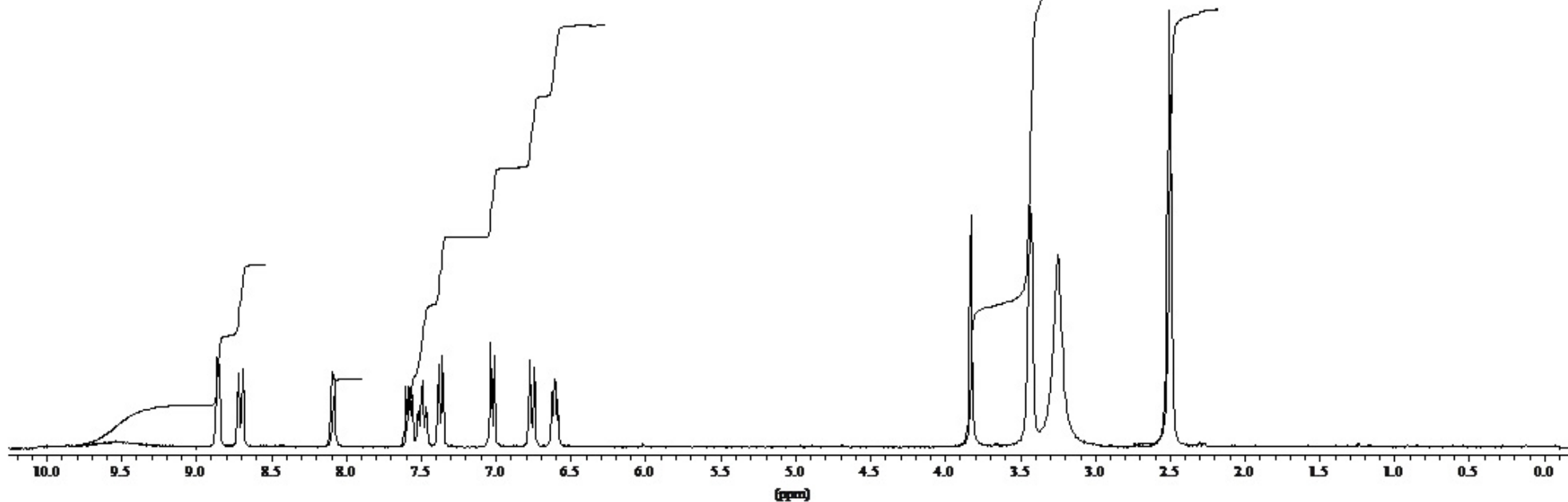
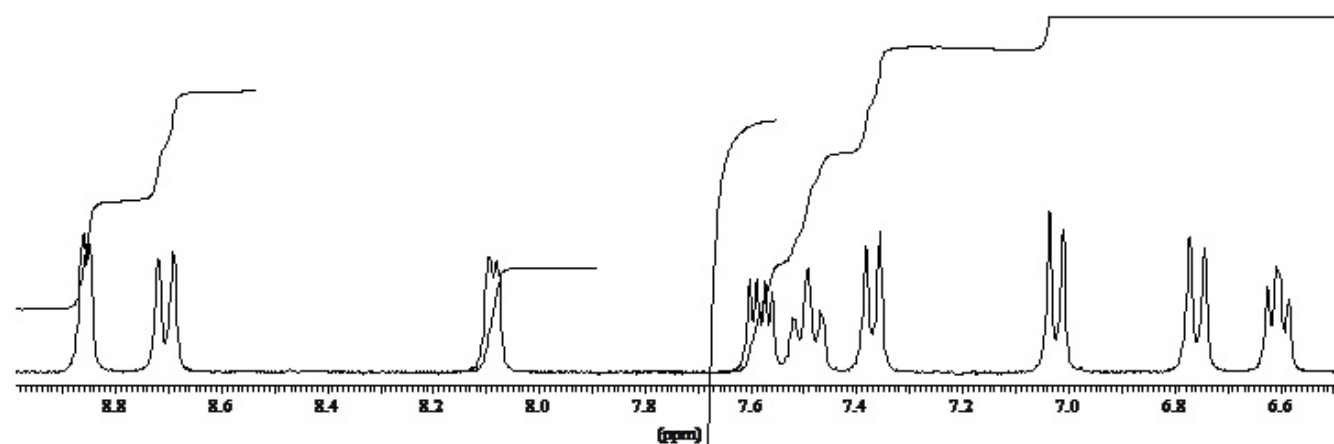


BAS 7529519

Q3-5

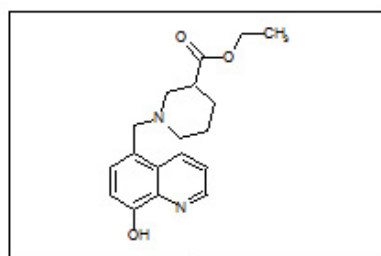


YAP 0000060	
7529519	
C ₁₉ H ₂₀ N ₄ O	320.3974
BAS 7529519	0501914
28.06.2003	Solv.DMSO

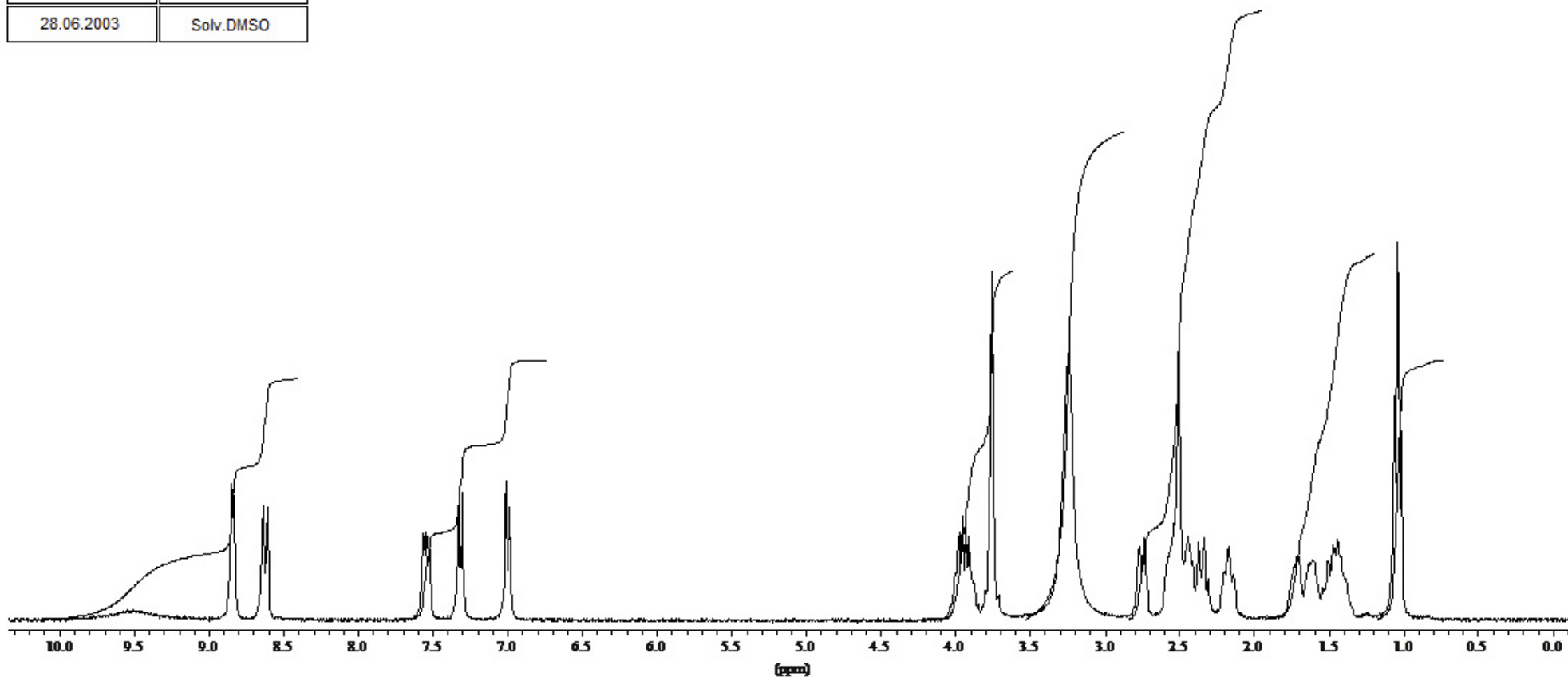
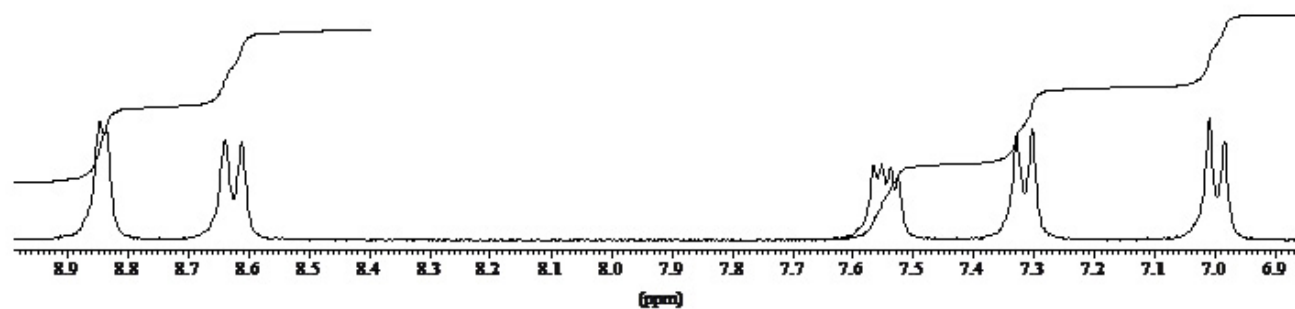


BAS 7529512

Q3-6

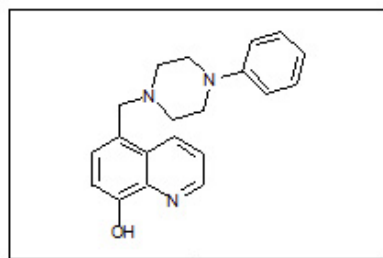


YAP 0000053	
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C ₁₈ H ₂₂ N ₂ O ₃	314.3876
BAS 7529512	0501910
28.06.2003	Solv.DMSO

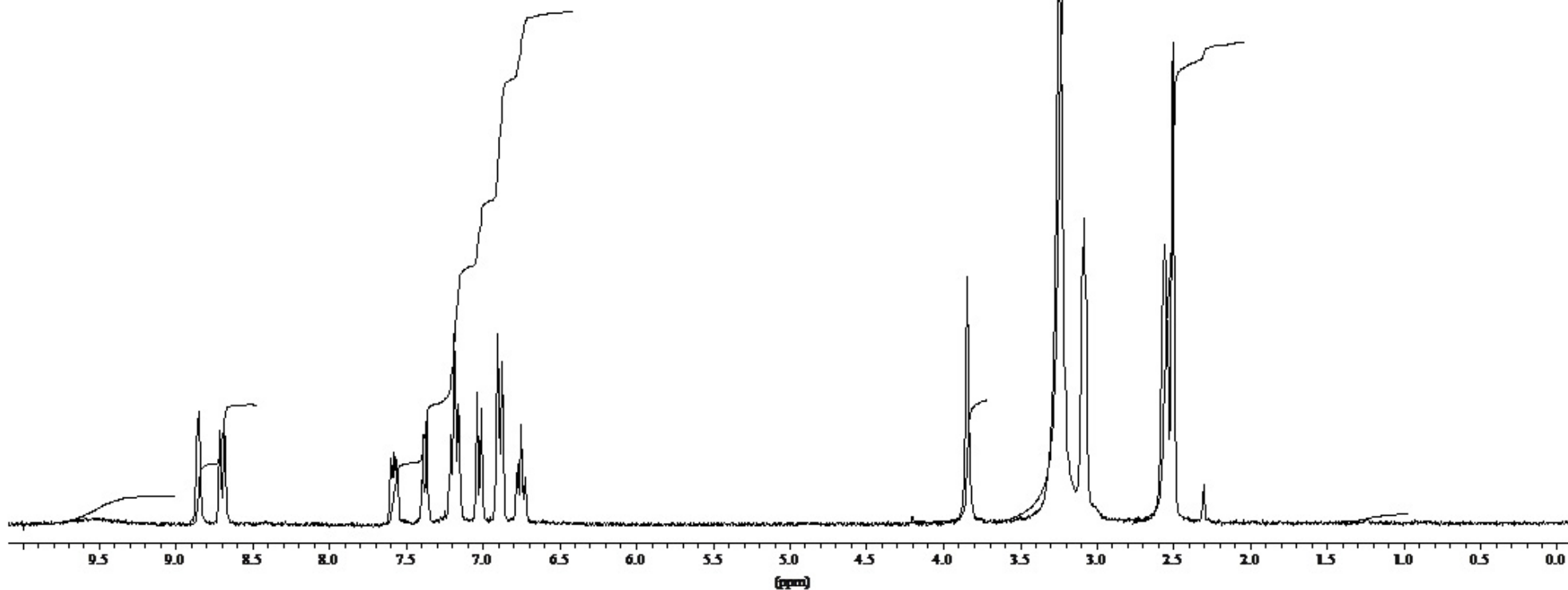
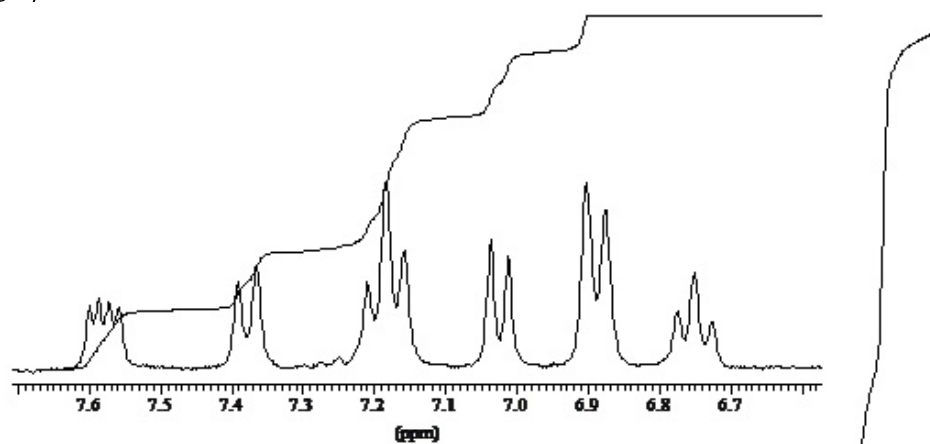


BAS 7529522

Q3-7

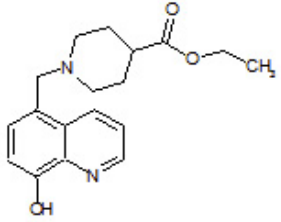


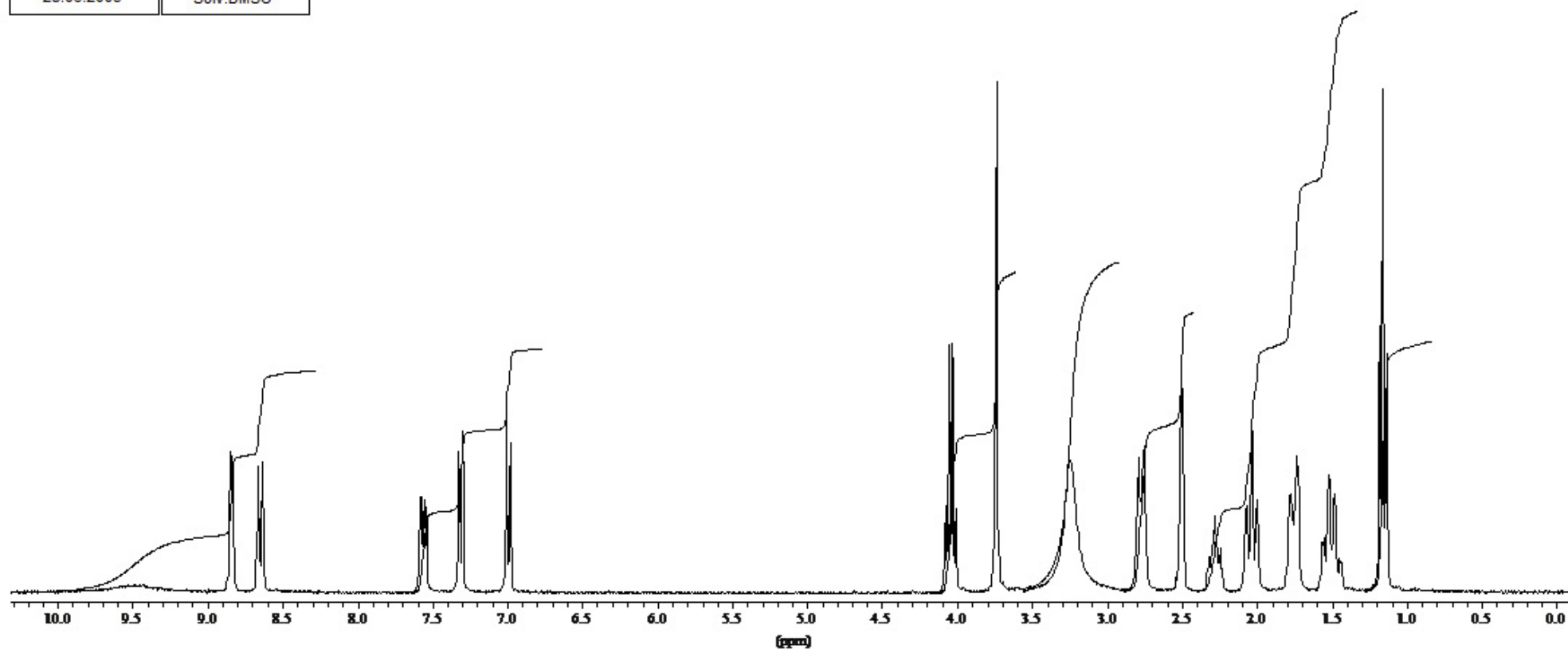
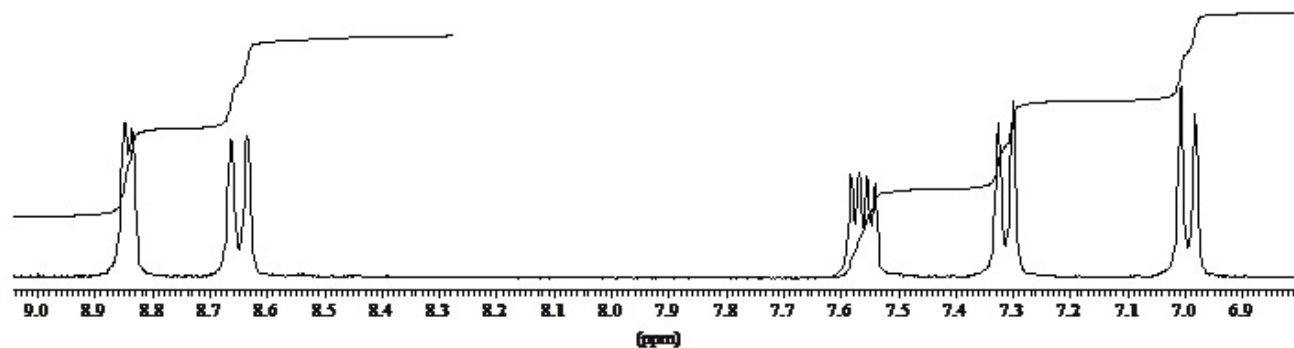
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7529522	
C ₂₀ H ₂₁ N ₃ O	319.4099
BAS 7529522	0501917
28.06.2003	Solv.DMSO



BAS 7529511

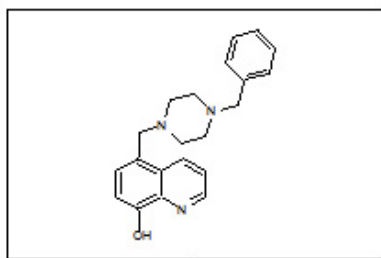
Q3-8

	
YAP 0000052	
7529511	
C ₁₈ H ₂₂ N ₂ O ₃	314.3876
BAS 7529511	0501909
28.06.2003	Solv.DMSO

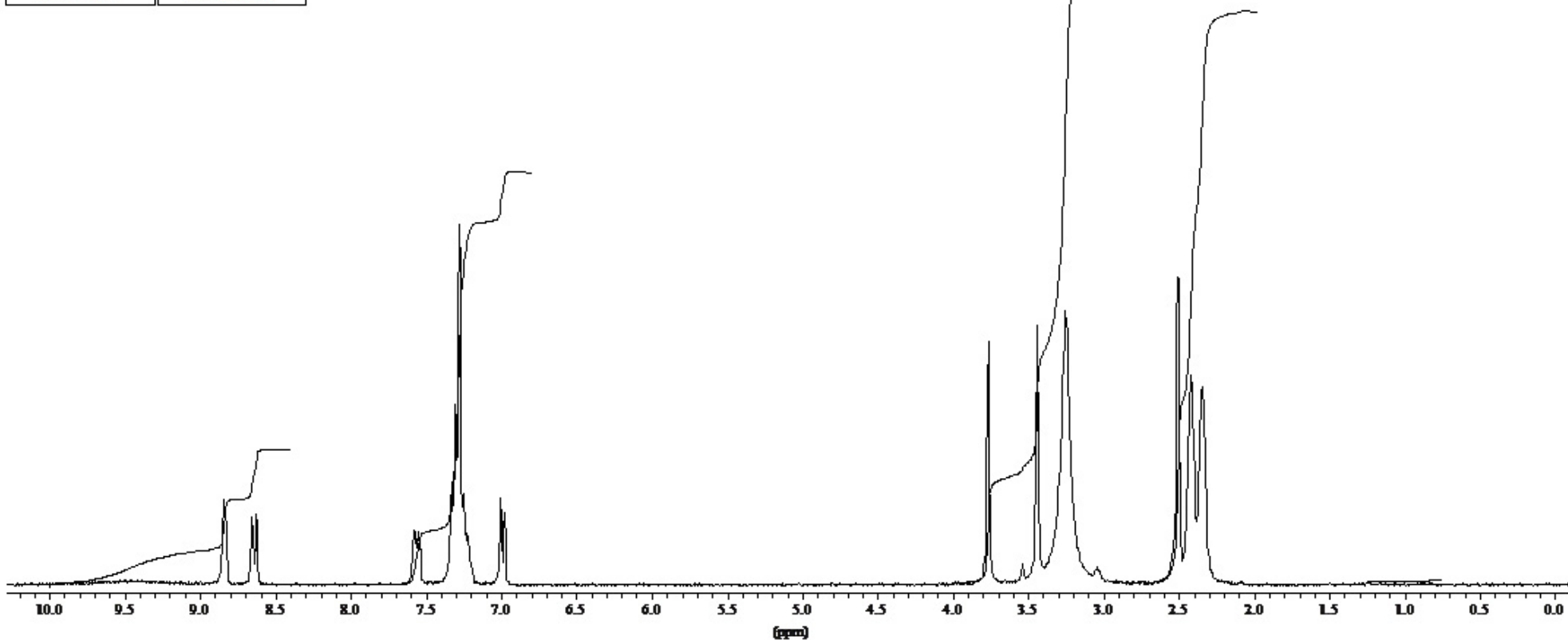
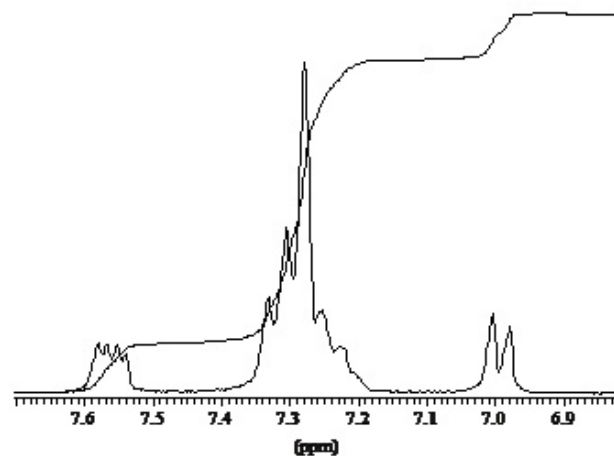


BAS 7529521

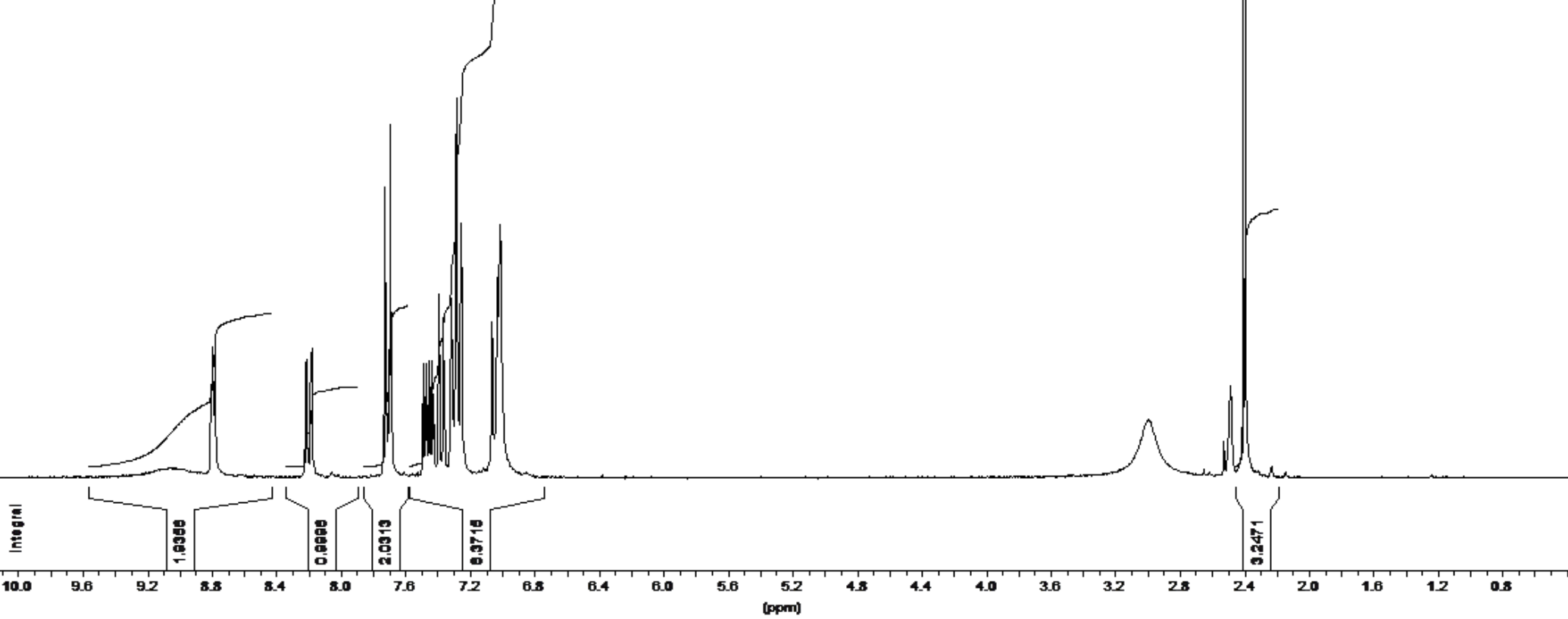
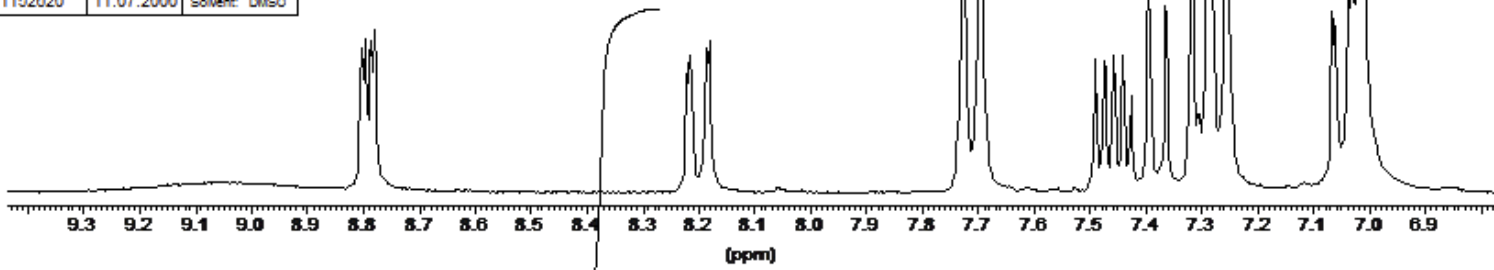
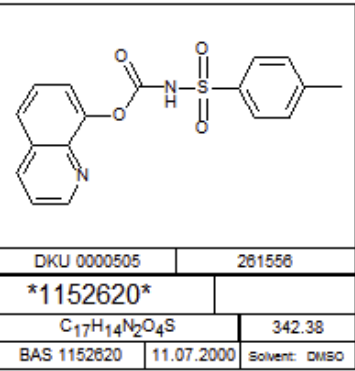
Q3-9



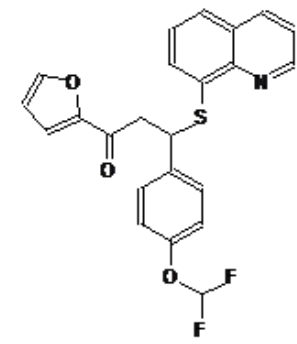
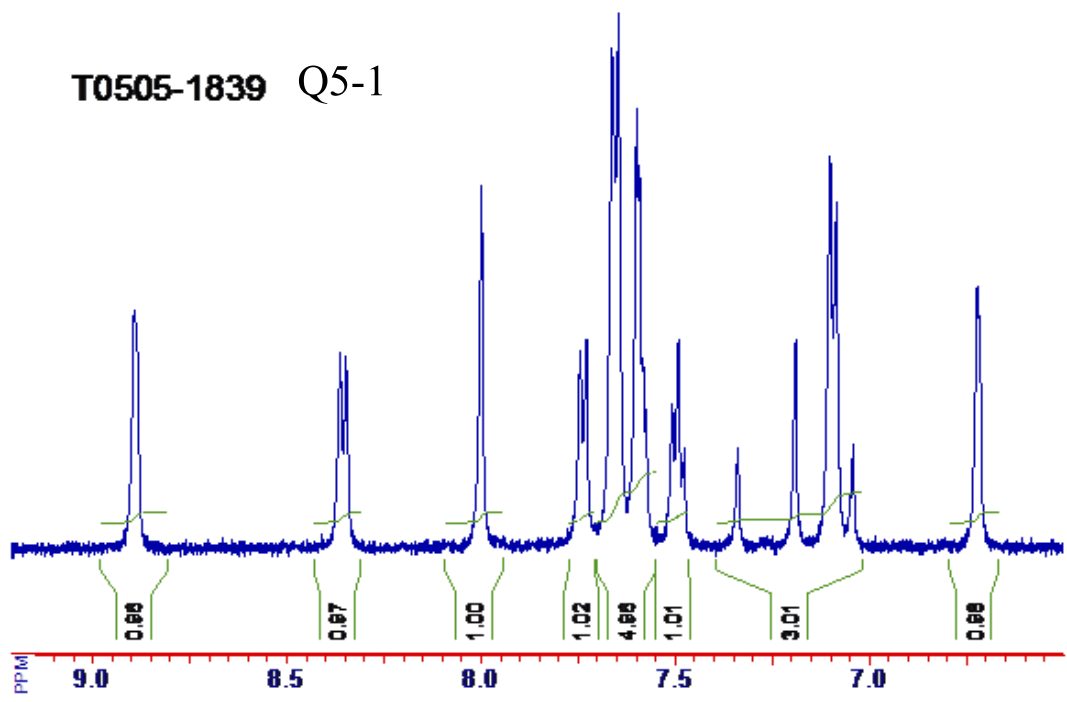
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BAS 7529521	0501916
28.06.2003	Solv.DMSO



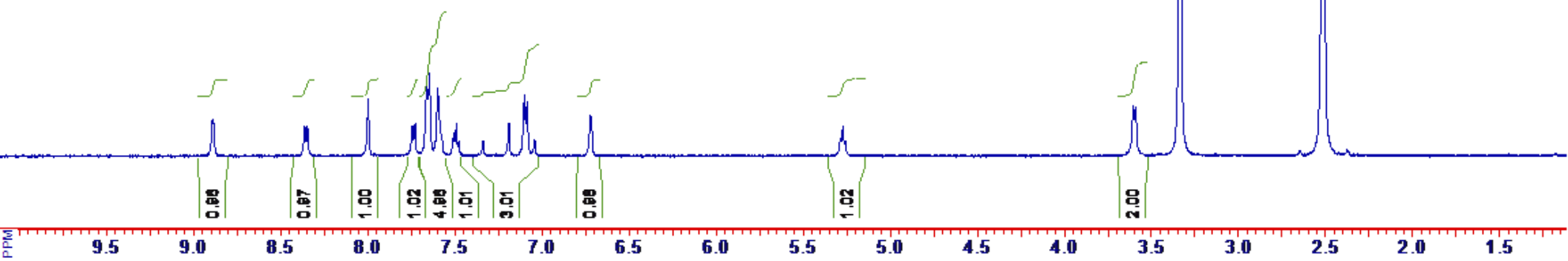
Q4-1



T0505-1839 Q5-1

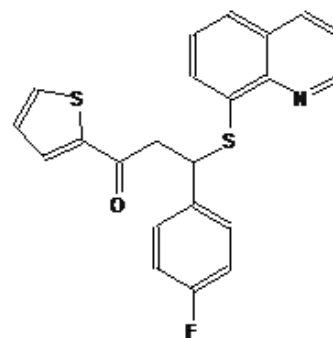


T0505-1839 C₂₃H₁₇F₂N₁O₃S
425.45

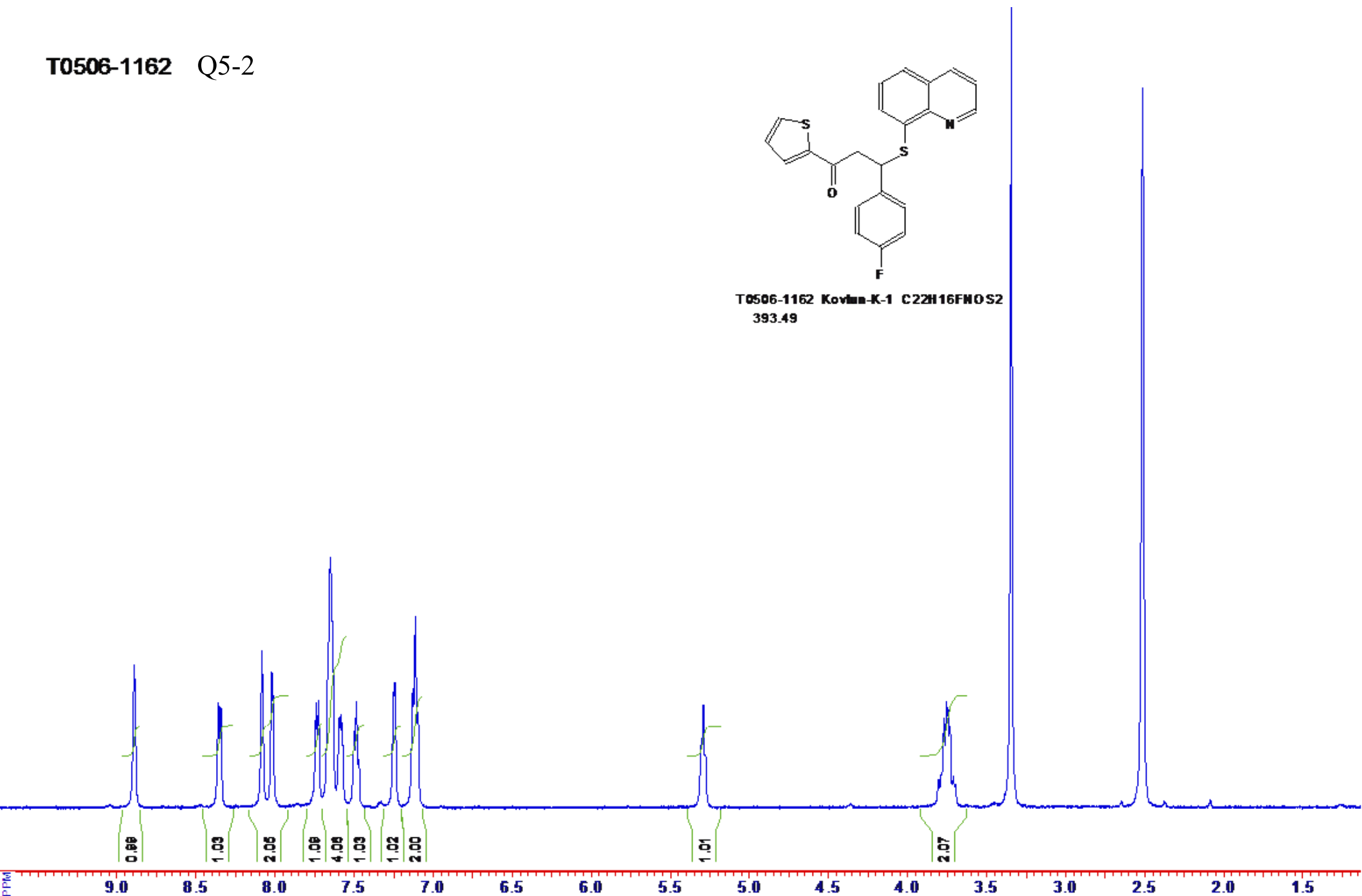


File name: T0505-1839	Vaskivska Lyudmila	SF: 500.0680 MHz	MSC: 1	PW: 0.00 usec, RG: 200	SI 65536
Date: 18-Jan-2013	Solvent: DMSO	SW: 8503 Hz	TE: 0 K	AQ: 1.93 sec, RD: 0.00 sec	*T0505-1839*

T0506-1162 Q5-2



T0506-1162 Kovina-K-1 C₂₂H₁₆FNOS₂
393.49



File name: T0506-1162	Vaskivska Lydmila	SF: 500.0680 MHz	MSC: 1	PW: 0.00 usec, RG: 200	SI 65536
Date: 18-Jan-2013	Solvent: DMSO	SW: 8503 Hz	TE: 0 K	AQ: 1.93 sec, RD: 0.00 sec	*T0506-1162*