Electronic Supplementary Information

Improved, gram-scale synthesis of sildenafil in water using arylacetic acid as the acyl source in the pyrazolo[4,3-*d*]pyrimidin-7-one ring formation

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Contents

General considerations

Unless noted otherwise, all reagents and solvents were purchased from commercial sources and used as received. All reactions were performed in a screw capped sealed tube. The ^{1}H and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 as solvent using a 400 MHz and 100 MHz spectrometer respectively with Me_4Si as an internal standard. Coupling constants (*J* values) are reported in hertz (Hz). Column chromatography was performed on silica gel (60-120 mesh, 100-200 mesh or 230-400 mesh).

I. Experimental Procedures

1. Preparation of 2-ethoxyphenylacetic acid (10)

In an oven-dried screw cap sealed tube equipped with a magnetic stir bar was charged with 2-hydroxyphenylacetic acid (0.5 mmol), ethyl iodide (1 equiv) and K_2CO_3 (1 equiv). CH_3CN (2 mL) was then added in the sealed tube. The tube was sealed and the mixture was allowed to stir at 80 ˚C for 4 h. The reaction mixture was cooled to room temperature and then extracted with EtOAc. The organic layer was dried over sodium sulphate, concentrated under reduced pressure and purified by using column chromatography (100-200 # silica, EtOAc – Hexane = 3:7) to give the desired product as off-white solid.

2. Typical procedure for the synthesis of 1-methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7)

In an oven-dried screw cap sealed tube equipped with a magnetic stir bar was charged with 4-amino-1-methyl-3-propyl-1H-pyrazole-5-carboxamide (0.5 mmol), phenylacetic acid (1 equiv) and $K_2S_2O_8$ (3 equiv). Water (2 mL) was then added in the sealed tube. The tube was sealed and the mixture was allowed to stir at 80 ˚C for 12 h. The reaction mixture was cooled to room temperature and then extracted with EtOAc. The organic layer was dried over sodium sulphate, concentrated under reduced pressure and purified by using column chromatography (100-200 # silica, EtOAc – Hexane = 3:7) to give the desired cyclized product.

3. Typical procedure for the synthesis of 5-(2-ethoxyphenyl)-1-methyl-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (5)

In an oven-dried screw cap sealed tube equipped with a magnetic stir bar was charged with 4-amino-1-methyl-3-propyl-1H-pyrazole-5-carboxamide (0.5 mmol), 2-ethoxyphenylacetic acid (1 equiv) and $K_2S_2O_8$ (3 equiv). Water (2 mL) was then added in the sealed tube. The tube was sealed and the mixture was allowed to stir at 80 ˚C for 12 h. The reaction mixture was cooled to room temperature and then extracted with EtOAc. The organic layer was dried over sodium sulphate, concentrated under reduced pressure and purified by using column chromatography (100-200 # silica, EtOAc – Hexane = 3:7) to give the desired cyclized product.

4. Typical procedure for the synthesis of 4-ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfonyl chloride (5a)

Following a literature procedure,[1] 5-(2-ethoxyphenyl)-1-methyl-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (0.3 mmol) was added portion wise to chlorosulphonic acid (0.25 mL) and thionyl chloride (0.1 mL) at 0 ˚C. The reaction mixture was allowed to stir at room temperature overnight. Then the reaction mixture was poured to crushed ice. White precipitates were formed, which were then filtered, washed with cold water and dried under reduced pressure to give the desired product as white solid (115 mg, 92%).

5. Typical procedure for the synthesis of5-(2-Ethoxy-5-((4-methylpiperazin-1-yl)sulfonyl)phenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (Sildenafil) (4)

To a solution of sulfonyl chloride derivative (0.25 mmol) in acetone (2 mL), excess of *N*-methyl piperazine was added. The resulting mixture was stirred at room temperature for 3 h. After the completion of the reaction, acetone was concentrated under reduced pressure and the residue was washed with cold water. The resulting precipitates were filtered, washed with cold water and dried under reduced pressure to give the desired product as white solid (125 mg, 90%)

6. General procedure for the synthesis of 2-arylquinazolin-4(3H)-ones (9,9a-9j)

In an oven-dried screw cap sealed tube equipped with a magnetic stir bar was charged with 2-aminobenzamide derivatives (0.25 mmol), arylacetic acid (1 equiv) and $K_2S_2O_8$ (3 equiv). Water

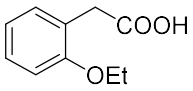
(1 mL) was then added in the sealed tube. The tube was sealed and the mixture was allowed to stir at 80 ˚C for 6 - 12 h. The reaction mixture was cooled to room temperature and then extracted with EtOAc. The organic layer was dried over sodium sulphate, concentrated under reduced pressure and purified by using column chromatography (100-200 # silica, EtOAc – Hexane = 3:7) to give the desired cyclized product.

7. General procedure for the synthesis of 2-arylbenzo[d]thiazoles (12a-12h)

In an oven-dried screw cap sealed tube equipped with a magnetic stir bar was charged with 2-aminothiophenol (0.25 mmol), arylacetic acid (1 equiv) and $K_2S_2O_8$ (3 equiv). Water (1 mL) was then added in the sealed tube. The tube was sealed and the mixture was allowed to stir at 80 ˚C for 6 - 12 h. The reaction mixture was cooled to room temperature and then extracted with EtOAc. The organic layer was dried over sodium sulphate, concentrated under reduced pressure and purified by using column chromatography (100-200 # silica, EtOAc – Hexane = 3:7) to give the desired cyclized product.

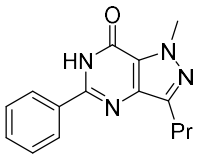
II. Characterization data

2-Ethoxyphenylacetic acid (10)



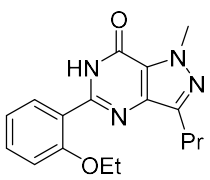
White solid (85%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.11 (s, 1H), 7.22 (dt, J = 8.2, 1.7 Hz, 1H), 7.17 (dd, J = 7.4, 1.5 Hz, 1H), 6.93 (d, J = 8 Hz,1H), 6.86(dt, J = 7.4, 1.0 Hz, 1H), 4.00 (q, J = 6.9 Hz, 2H), 3.49 (s, 2H), 1.29 (t, J = 6.9 Hz, 3H).

1-methyl-5-phenyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (7)[2]



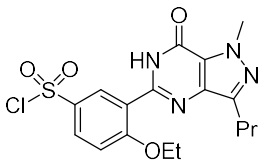
White solid (59%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.41 (s, 1H), 8.07-8.06 (m, 2H), 7.60-7.51 (m, 3H), 4.15 (s, 3H), 2.80 (t, J = 7.3 Hz, 2H), 1.76 (sx, J = 7.0 Hz, 2H),0.96 (t, J = 7.3 Hz, 3H).

5-(2-Ethoxyphenyl)-1-methyl-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one (5)[3]



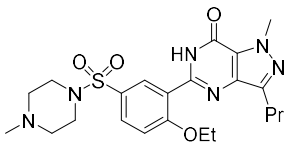
White solid (67%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.13 (s, 1H), 8.49 (dd, J = 7.9, 1.6 Hz, 1H), 7.49 (dt, J = 8.5, 1.7 Hz, 1H), 7.17 (t, J = 7.9 Hz, 1H), 7.06 (d, J = 8.3 Hz, 1H), 4.33-4.28 (m, 5H), 2.90 (t, J = 7.4 Hz, 2H),1.80 (sx, J = 7.6 Hz, 2H),1.62 (t, J = 7.0 Hz, 3H),1.05 (t, J = 7.3 Hz, 3H).

4-Ethoxy-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl)benzenesulfonyl chloride (5a)[3]



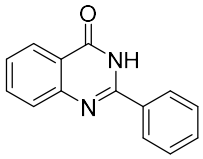
White solid (92%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.80 (s, 1H), 9.09 (d, *J* = 2.6 Hz, 1H), 8.10 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.25 (d, *J* = 9 Hz, 1H), 4.42 (q, *J* = 8.5 Hz, 2H), 4.28 (s, 3H), 2.96 (t, *J* = 7.4 Hz, 2H),1.86 (sx, *J* = 7.4 Hz, 2H),1.66 (t, *J* = 7.0 Hz, 3H),1.05 (t, *J* = 7.3 Hz, 3H).

5-(2-Ethoxy-5-((4-methylpiperazin-1-yl)sulfonyl)phenyl)-1-methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one (Sildenafil) (4)[3]



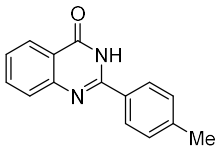
White solid (90%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.83 (s, 1H), 8.82 (d, *J* = 2.2 Hz, 1H), 7.83 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.14 (d, *J* = 8.8 Hz, 1H), 4.36 (q, *J* = 6.9 Hz, 2H), 4.28 (s, 3H), 3.10 (bs, 4H), 2.92 (t, *J* = 7.4 Hz, 2H), 2.50 (bs, 4H), 2.28 (s, 3H),1.86 (sx, *J* = 7.4 Hz, 2H),1.64 (t, *J* = 6.9 Hz, 3H),1.03 (t, *J* = 7.3 Hz, 3H).

2-Phenylquinazolin-4(3H)-one (9)[3]



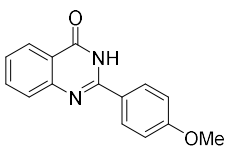
White solid (72%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.09 (s, 1H), 8.36 (d, *J* = 7.7 Hz, 1H), 8.23-8.21 (m, 2H), 7.87-7.81 (m, 2H), 7.26-7.60 (m, 3H), 7.55 (dt, *J* = 6.6, 1.6 Hz, 1H).

2-(*p*-Tolyl)quinazolin-4(3H)-one (9a)[3]



White solid (62%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.31 (s, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 2H), 7.83-7.81 (m, 2H), 7.53 (dt, *J* = 8.1, 2.0 Hz, 1H), 7.40 (d, *J* = 7.9 Hz, 2H), 2.48 (s, 3H).

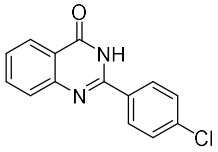
2-(4-Methoxyphenyl)quinazolin-4(3H)-one (9b)[3]



White solid (68%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.99 (s, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 8.19 (d, *J* = 8.8 Hz, 2H), 7.82-7.80 (m, 2H), 7.52-7.48 (m, 1H),

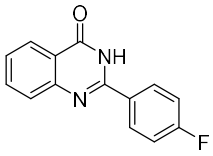
7.10 (d, *J* = 8.8 Hz, 2H), 3.93 (s, 3H).

2-(4-Chlorophenyl)quinazolin-4(3H)-one (9c)[3]



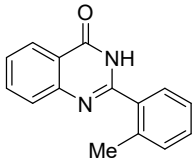
White solid (65%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.60 (s, 1H), 8.22-8.15 (m, 3H), 7.87(dt, *J* = 8.3, 1.4 Hz, 1H), 7.76 (d, *J* = 8 Hz, 1H), 7.64(d, *J* = 8.6 Hz, 2H), 7.56 (dt, *J* = 8.0, 1.0 Hz, 1H).

2-(4-Fluorophenyl)quinazolin-4(3H)-one (9d)[3]



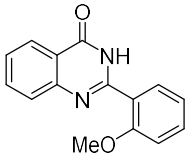
White solid (62%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.5 (s, 1H), 8.28-8.24 (m, 2H), 8.17 (d, *J* = 7.9 Hz,1H), 7.86 (dt,*J* = 8.2, 1.4 Hz, 1H), 7.75 (d,*J* = 8.0 Hz,1H), 7.55 (t, *J* = 7.8 Hz, 1H) 7.42-7.38 (m, 2H).

2-(*o*-Tolyl)quinazolin-4(3H)-one (9e)[3]



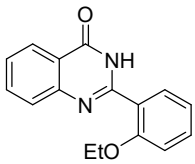
White solid (76%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.60 (s, 1H), 8.33 (d, *J* = 7.8 Hz, 1H), 7.85-7.80 (m, 2H), 7.57- 7.52 (m, 2H), 7.47-7.43 (m, 1H), 7.38-7.34 (m, 2H), 2.55 (s, 3H).

2-(2-Methoxyphenyl)quinazolin-4(3H)-one (9f)[4]



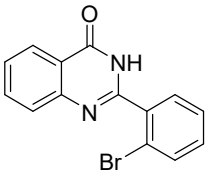
White solid (78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.95 (s, 1H), 8.58 (d, *J* = 7.8 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.82-7.77 (m, 2H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.51 (t, *J* =7.0 Hz, 1H), 7.22 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J* = 8.3 Hz, 1H), 4.09 (s, 3H).

2-(2-Ethoxyphenyl)quinazolin-4(3H)-one (9g)[4]



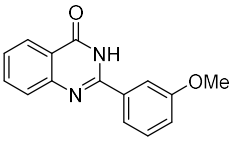
White solid (69%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.05 (s, 1H), 8.16 (d, *J* = 7.9 Hz, 1H), 7.85 (dt, *J* = 8.3, 1.4 Hz, 1H), 7.78 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.72 (d, *J* = 8 Hz, 1H), 7.55-7.50 (m, 2H), 7.19 (d, *J* = 8.3 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 4.18 (q, *J* = 6.9 Hz, 2H), 1.36 (t, *J* = 6.9 Hz, 3H).

2-(2-Bromophenyl)quinazolin-4(3H)-one (9h)[3]



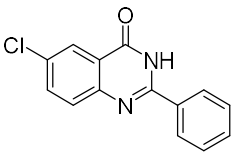
White solid (45%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.31 (bs, 1H), 8.32-8.29 (m, 1H), 7.84-7.83 (m, 2H), 7.77 (t, *J* = 8.6 Hz, 2H), 7.58-7.53 (m, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.44 (dt, *J* = 7.7, 1.6 Hz, 1H).

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (9i)[3]



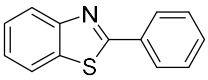
White solid (65%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.53 (s, 1H), 8.17 (d, *J* = 7.8 Hz, 1H), 7.87 (dt, *J* = 8.3, 1.4 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.76-7.75 (m, 2H), 7.55 (t, *J* = 7.1 Hz, 1H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 8.2, 2.4 Hz, 1H), 3.87 (s, 3H).

6-Chloro-2-phenylquinazolin-4(3H)-one (9j)[3]



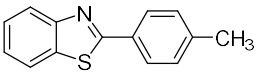
White solid (69%); ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.71 (s, 1H), 8.19-8.16 (m, 2H), 8.10 (d, *J* = 2.4 Hz, 1H), 7.88 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.61-7.54 (m, 3H).

2-Phenylbenzo[d]thiazole (12a)[3]



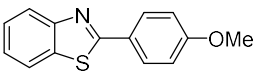
White solid (78%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14-8.09 (m, 3H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.56-7.50 (m, 4H), 7.43 (dt, *J* = 8.1, 1.1 Hz, 1H).

2-(*p*-Tolyl)benzo[d]thiazole (12b)[3]



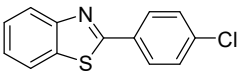
White solid (69%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.53 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.41 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.33 (d, *J* = 7.9 Hz, 2H), 2.45 (s, 3H).

2-(4-Methoxyphenyl)benzo[d]thiazole (12c)[5]



White solid (72%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08-8.04 (m, 3H), 7.9 (d, *J* = 7.9 Hz, 1H), 7.51 (dt, *J* = 7.3, 1.1 Hz, 1H), 7.39 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.04-7.00 (m, 2H), 3.90 (s, 3H).

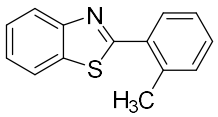
2-(4-Chlorophenyl)benzo[d]thiazole (12d)[3]



White solid (60%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.2 Hz, 1H),

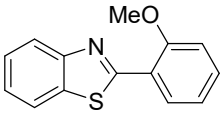
8.02-8.00 (m, 2H), 7.89 (d, *J* = 7.9 Hz, 1H), 7.51-7.44 (m, 3H), 7.40 (dt, *J* = 8.0, 1.0 Hz, 1H).

2-(*o*-Tolyl)benzo[d]thiazole (12e)[3]



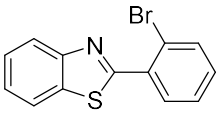
White solid (68%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.1 Hz, 1H), 7.97 (d, *J* = 7.9 Hz, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.56 (dt, *J* = 8.3, 1.2 Hz, 1H), 7.45-7.32 (m, 4H), 2.69 (s, 3H).

2-(2-Methoxyphenyl)benzo[d]thiazole (12f)[6]



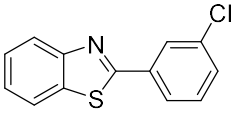
White solid (70%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.58 (dd, *J* = 7.8, 1.4 Hz, 1H), 8.14 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.53-7.38 (m. 3H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 4.06 (s, 3H).

2-(2-Bromophenyl)benzo[d]thiazole (12g)[7]



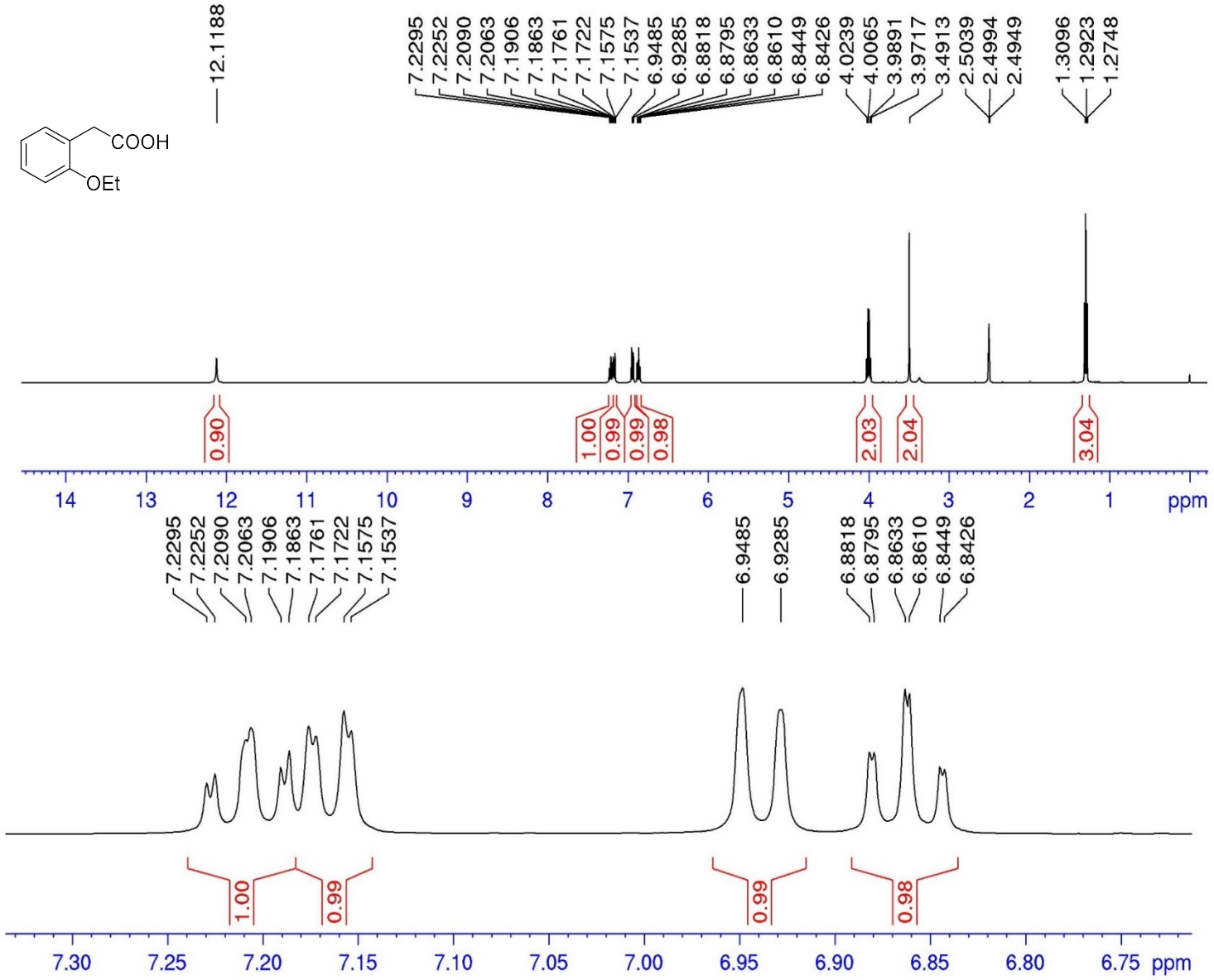
White solid (58%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, *J* = 8.0 Hz, 1H), 8.03 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.70 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.58 (dt, *J* = 7.3, 1.1 Hz, 1H), 7.49-7.44 (m, 2H), 7.37 (dt, *J* = 7.8, 1.7 Hz, 1H).

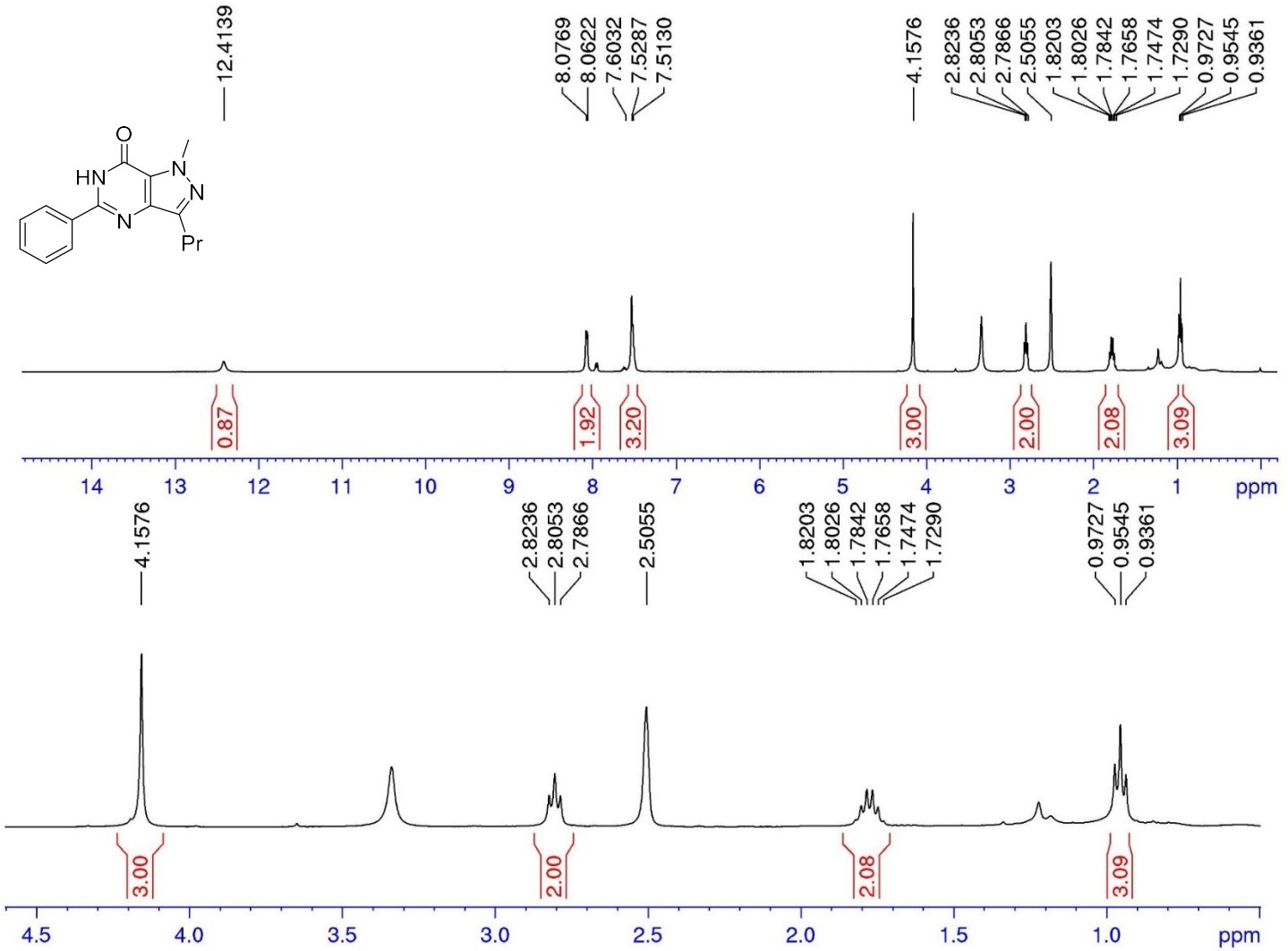
2-(3-Chlorophenyl)benzo[d]thiazole (12h)[7]



White solid (65%); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14-8.09 (m, 2H), 7.97-7.92 (m, 2H), 7.55 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.49-7.41 (m, 3H).

III. NMR Spectras

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7.6032
7.5287
7.5130
4.1576
2.8236
2.8053
2.7866
2.5055
1.8203
1.8026
1.7842
1.7658
1.7474
1.7290
0.9727
0.9545
0.9361
HN
O
N
N
N
Pr
0.87
1.92
3.20
3.00
2.00
2.08
3.09
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
4.1576
2.8236
2.8053
2.7866
2.5055
1.8203
1.8026
1.7842
1.7658
1.7474
1.7290
0.9727
0.9545
0.9361
3.00
2.00
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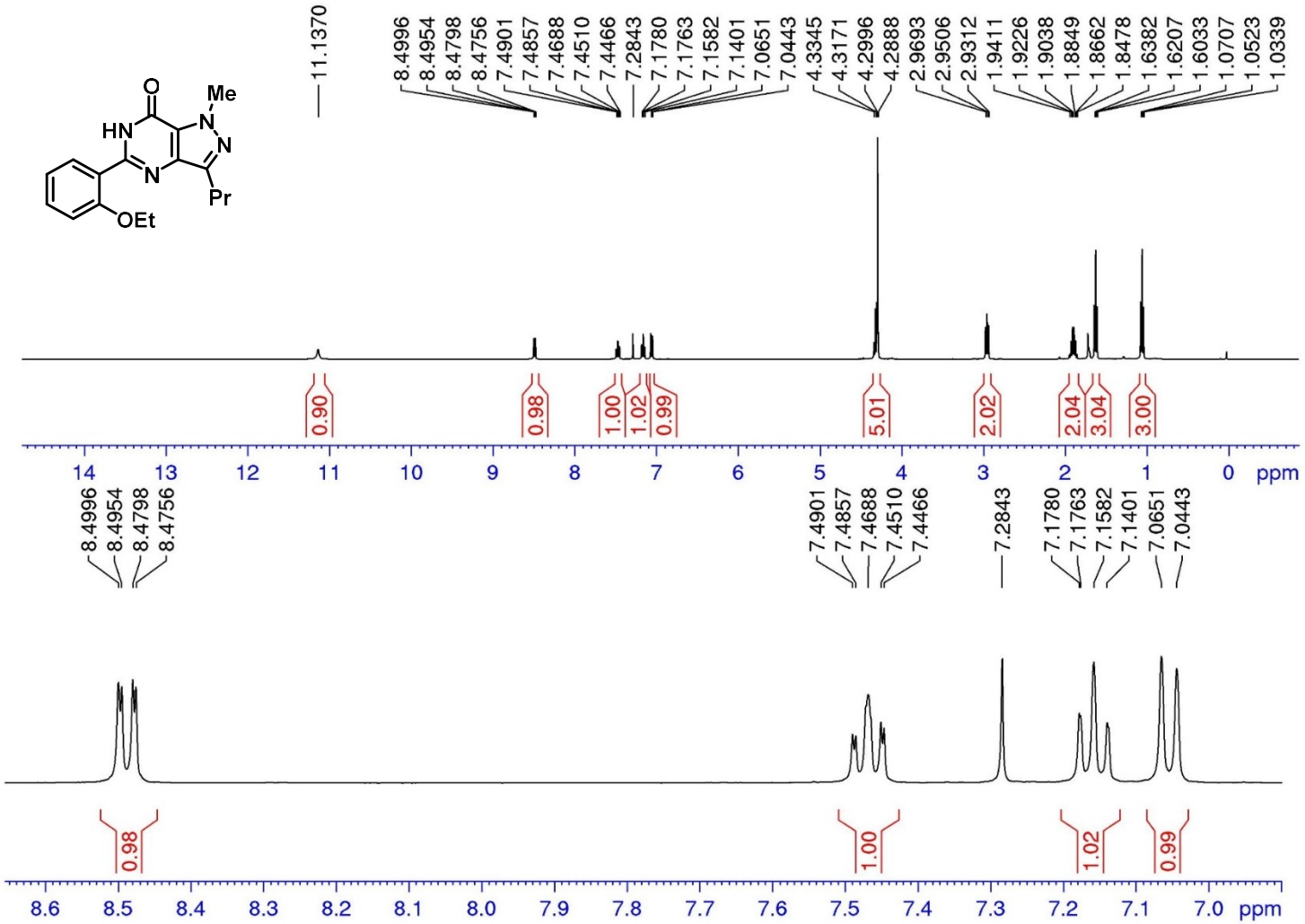
3.09
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm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7.4857
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7.4466
7.2843
7.1780
7.1763
7.1582
7.1401
7.0651
7.0443
4.3345
4.3171
4.2996
4.2888
2.9693
2.9506
2.9312
1.9411
1.9226
1.9038
1.8849
1.8662
1.8478
1.6382
1.6207
1.6033
1.0707
1.0523
1.0339
0.90
0.98
1.00
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2.02
2.04
3.04
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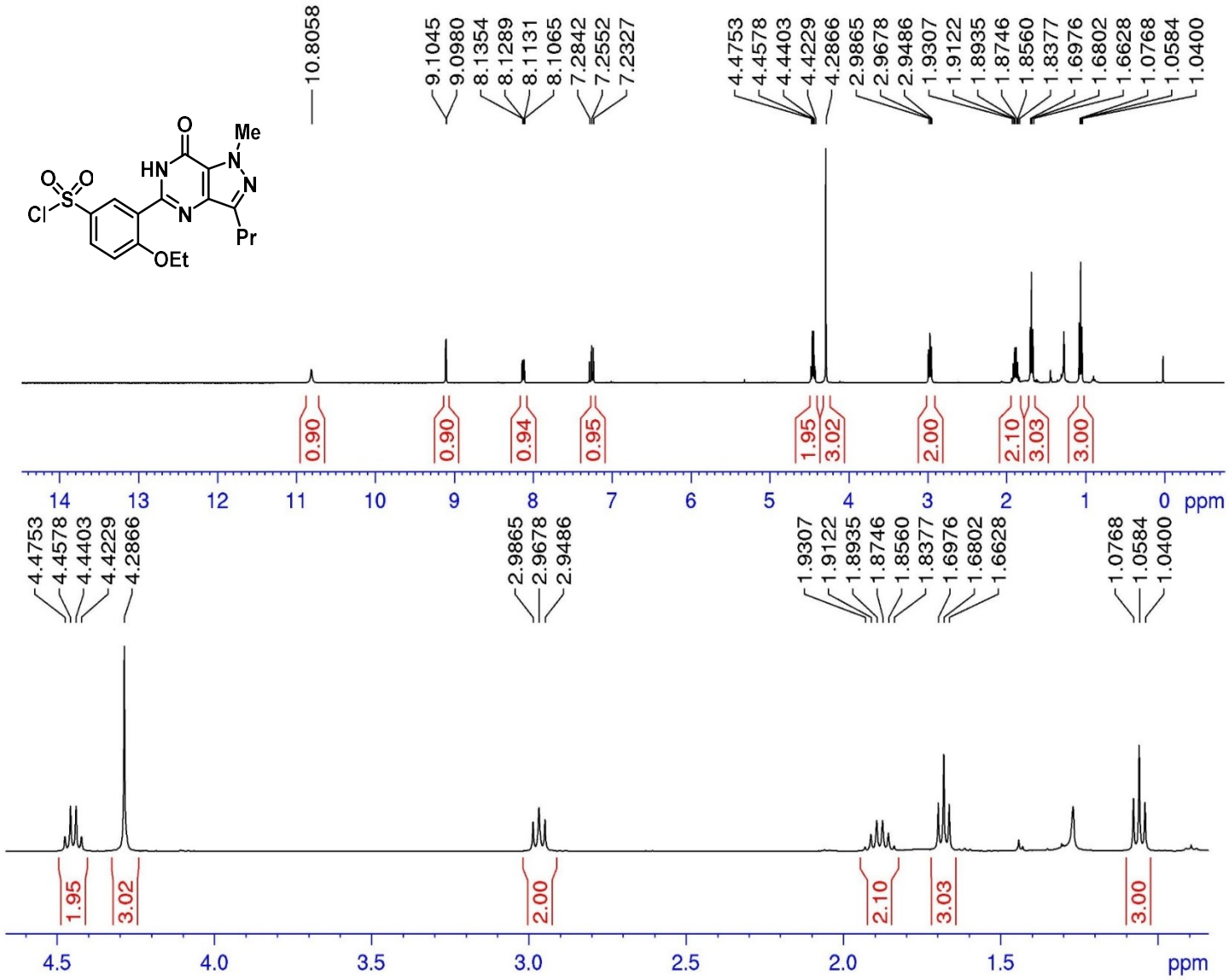
ppm
0.98
1.00
1.02
0.99
ppm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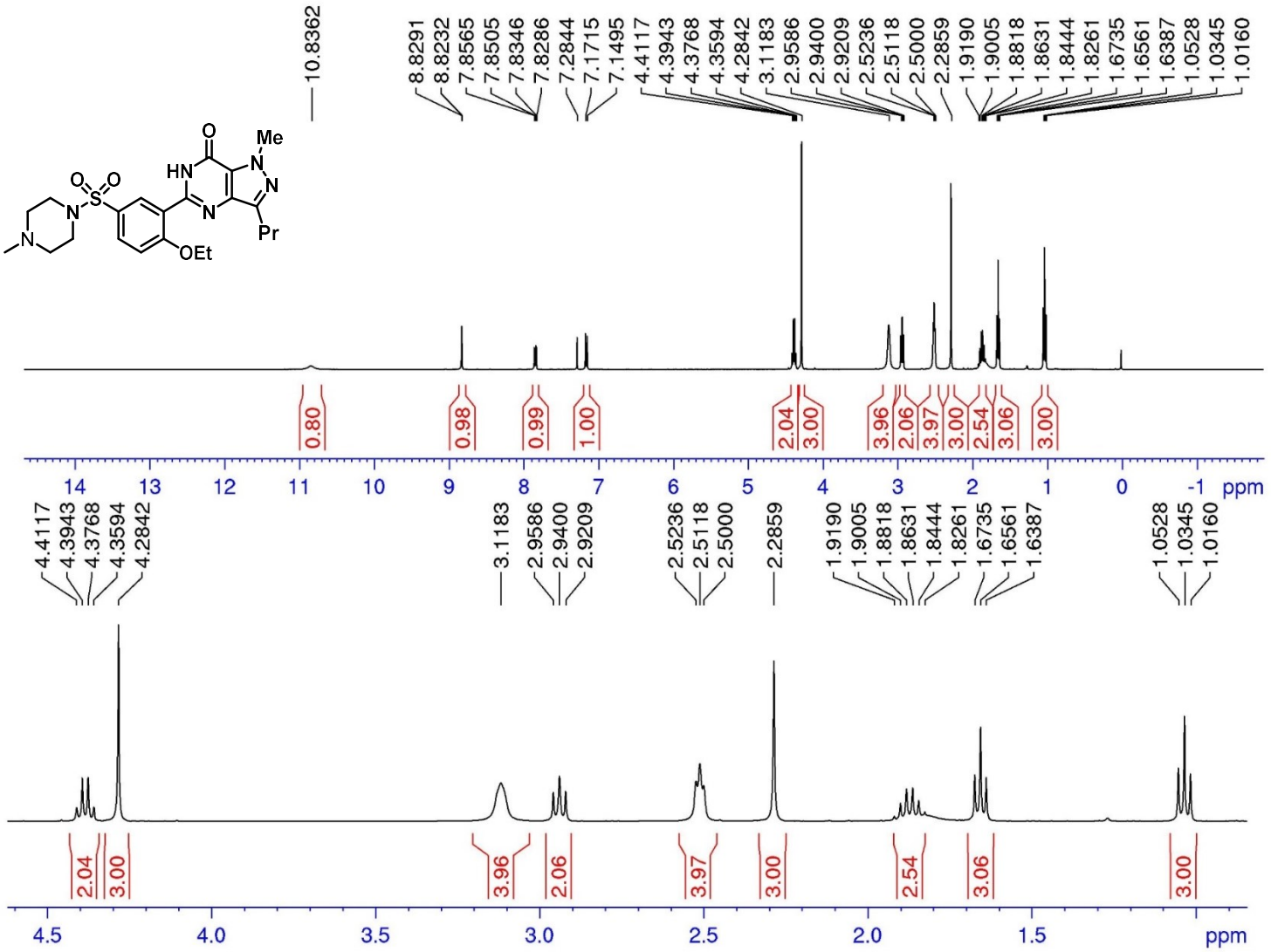
9.0980
8.1354
8.1289
8.1131
8.1065
7.2842
7.2552
7.2327
4.4753
4.4578
4.4403
4.4229
4.2866
2.9865
2.9678
2.9486
1.9307
1.9122
1.8935
1.8746
1.8560
1.8377
1.6976
1.6802
1.6628
1.0768
1.0584
1.0400
0.90
0.90
0.94
0.95
1.95
3.02
2.00
2.10
3.03
3.00
ppm
1.95
3.02
2.00
2.10
3.03
3.00
ppm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7.8505
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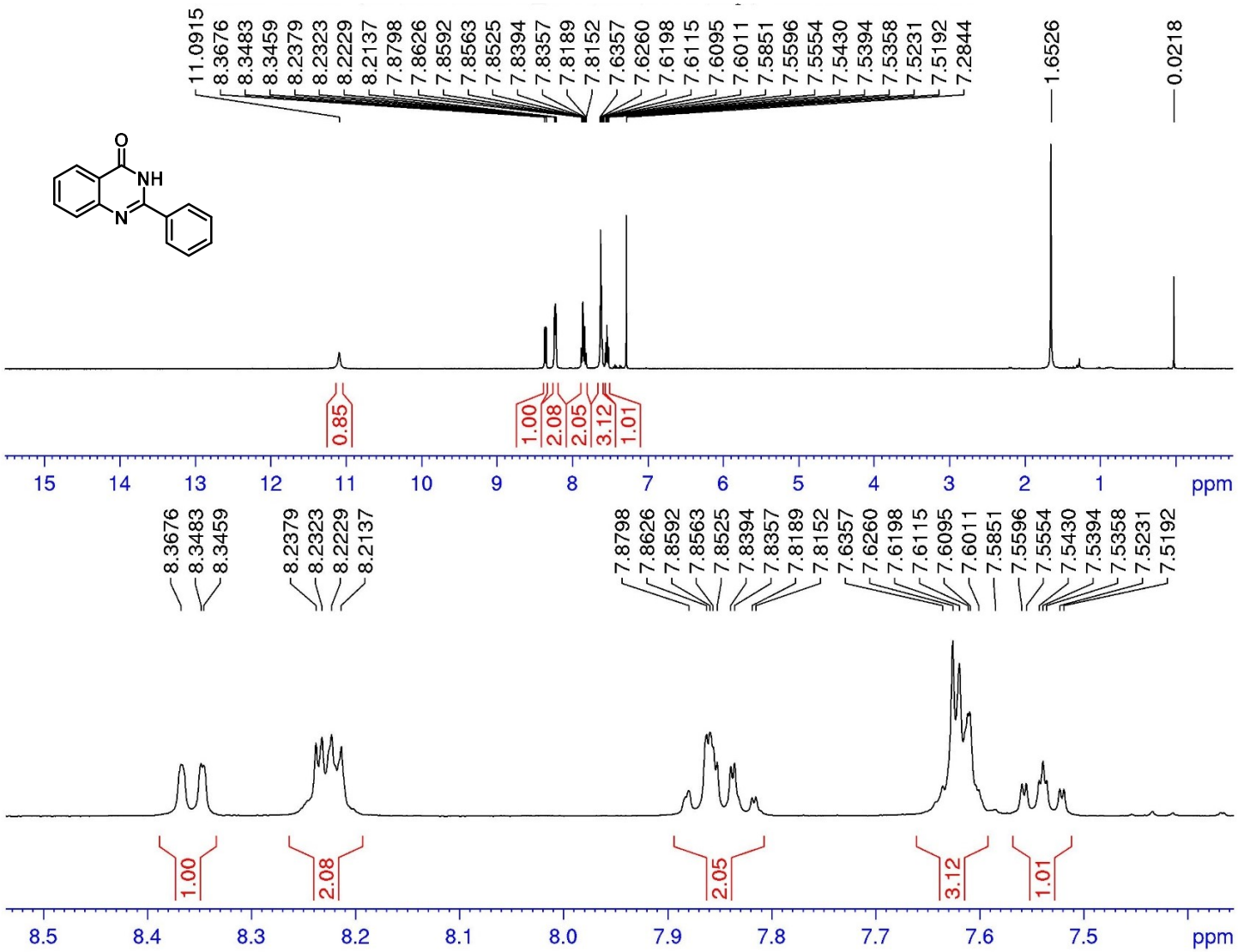
4.4117
4.3943
4.3768
4.3594
4.2842
3.1183
2.9586
2.9400
2.9209
2.5236
2.5118
2.5000
2.2859
1.9190
1.9005
1.8818
1.8631
1.8444
1.8261
1.6735
1.6561
1.6387
1.0528
1.0345
1.0160
0.80
0.98
0.99
1.00
2.04
3.00
3.96
2.06
3.97
3.00
2.54
3.06
3.00
ppm
Me
HN
N
N
O
O
S
O
N
N
Pr
OEt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8.2229
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7.8798
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7.8592
7.8563
7.8525
7.8394
7.8357
7.8189
7.8152
7.6357
7.6260
7.6198
7.6115
7.6095
7.6011
7.5851
7.5596
7.5554
7.5430
7.5394
7.5358
7.5231
7.5192
7.2844
1.6526
0.0218
O
NH
N
0.85
1.00
2.08
2.05
3.12
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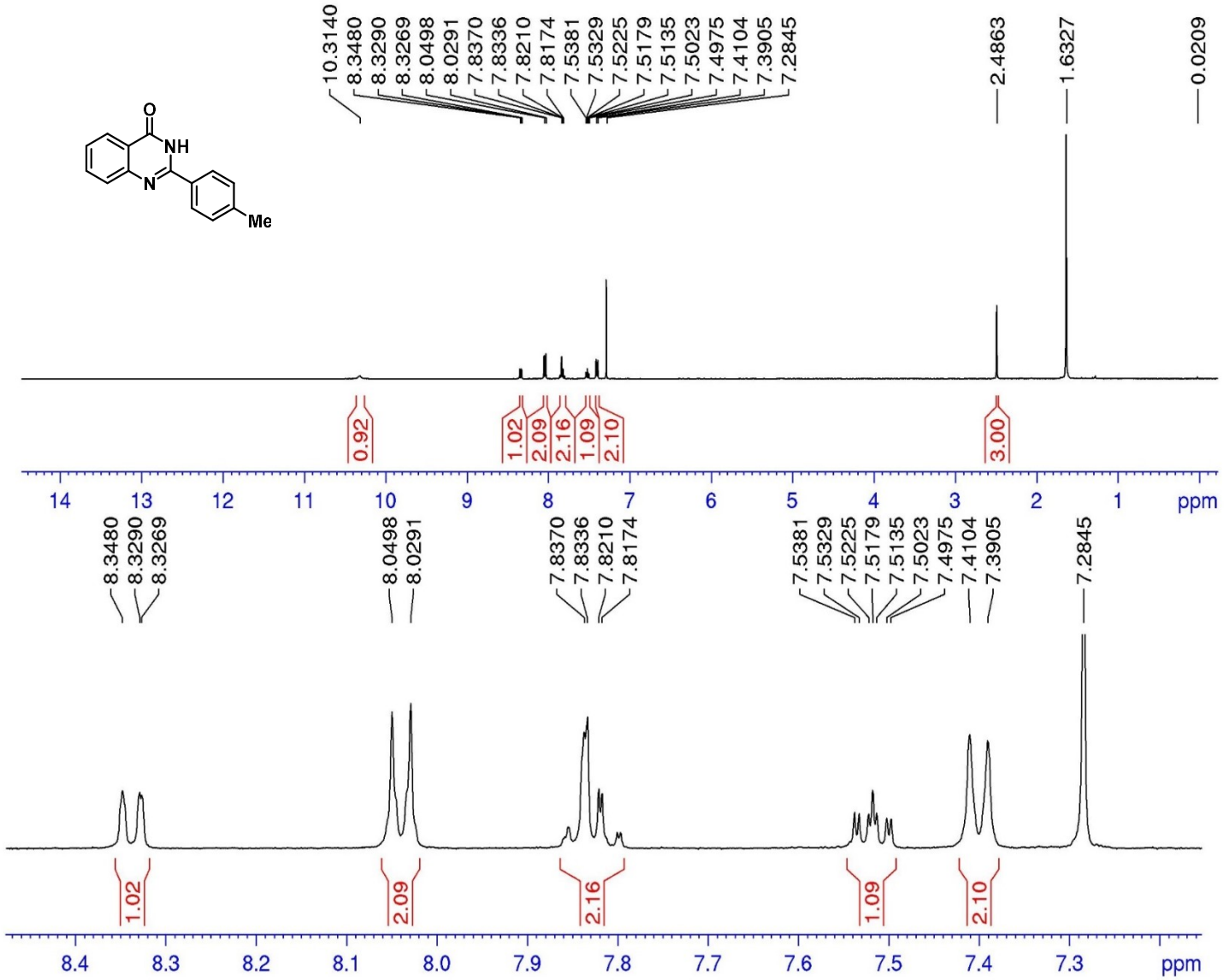
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 ppm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7.5381
7.5329
7.5225
7.5179
7.5135
7.5023
7.4975
7.4104
7.3905
7.2845
2.4863
1.6327
0.0209
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NH
N
Me
0.92
1.02
2.09
2.16
1.09
2.10
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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8.3
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8.1
8.0
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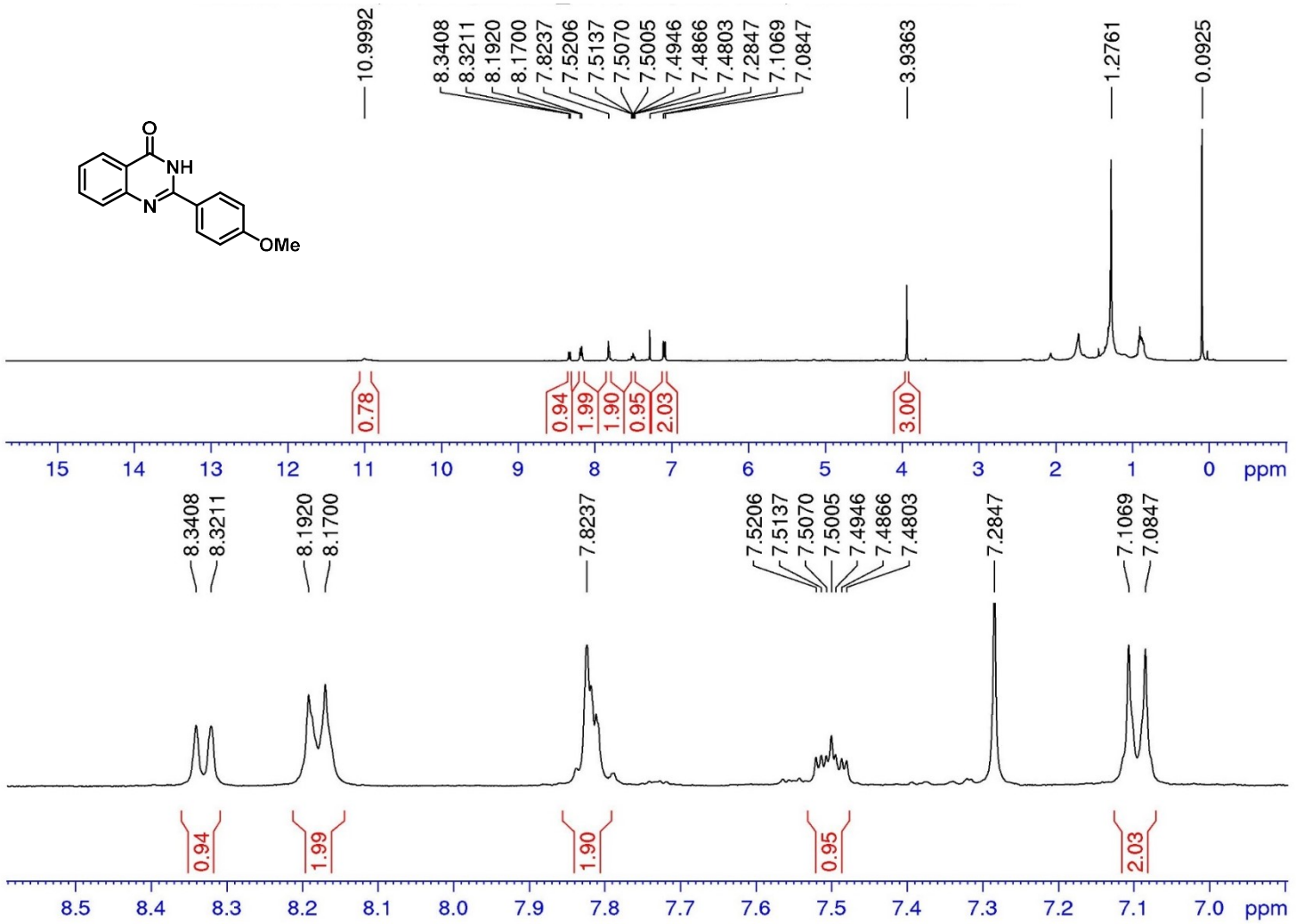
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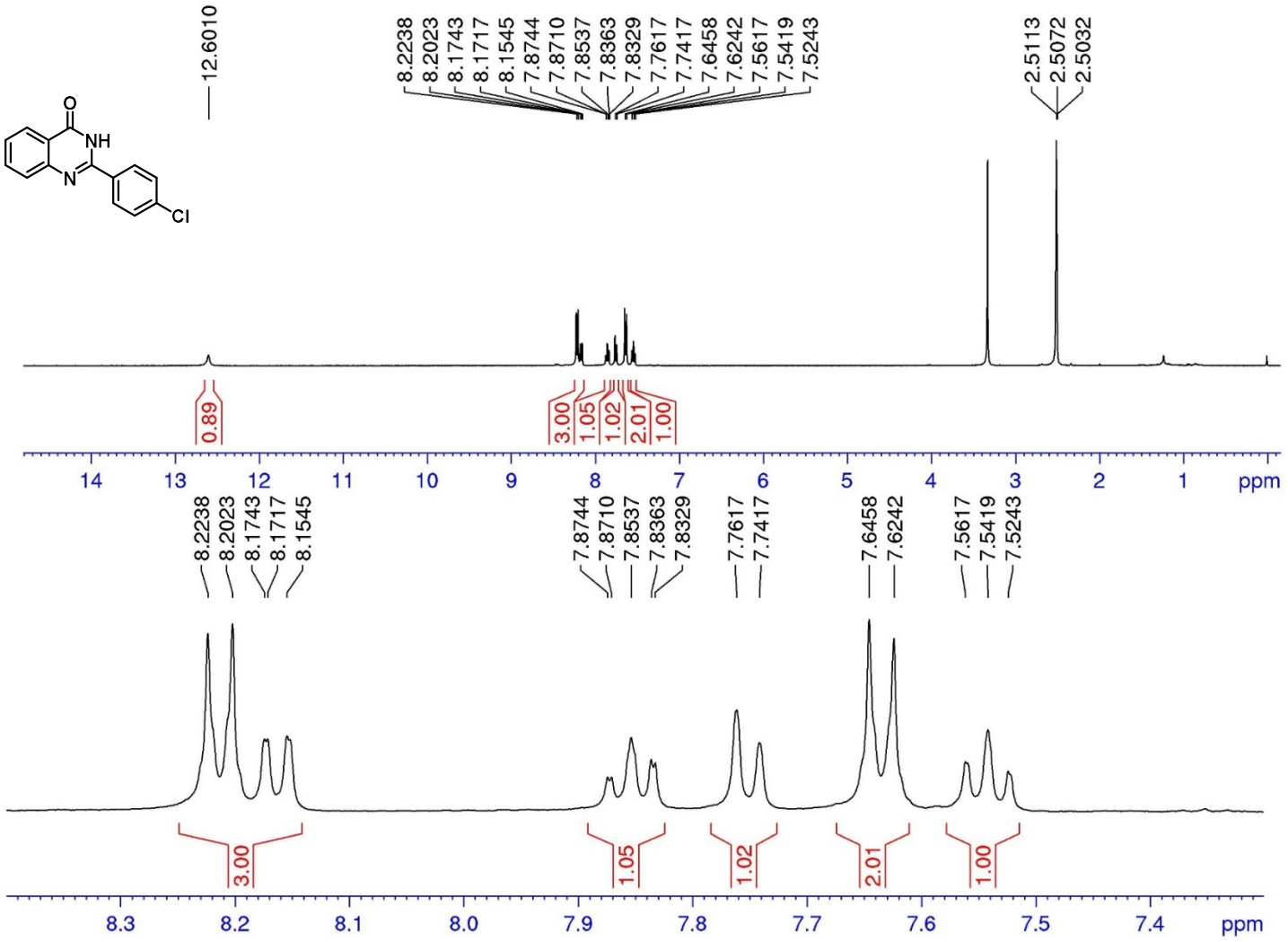
7.4803
7.2847
7.1069
7.0847
3.9363
1.2761
0.0925
O
NH
N
OMe
0.78
0.94
1.99
1.90
0.95
2.03
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
8.3408
8.3211
8.1920
8.1700
7.8237
7.5206
7.5137
7.5070
7.5005
7.4946
7.4866
7.4803
7.2847
7.1069
7.0847
0.94
1.99
1.90
0.95
2.03
8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm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7.8329
7.7617
7.7417
7.6458
7.6242
7.5617
7.5419
7.5243
2.5113
2.5072
2.5032
O
NH
N
Cl
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1.05
1.02
2.01
1.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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8.2
8.1
8.0
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7.7
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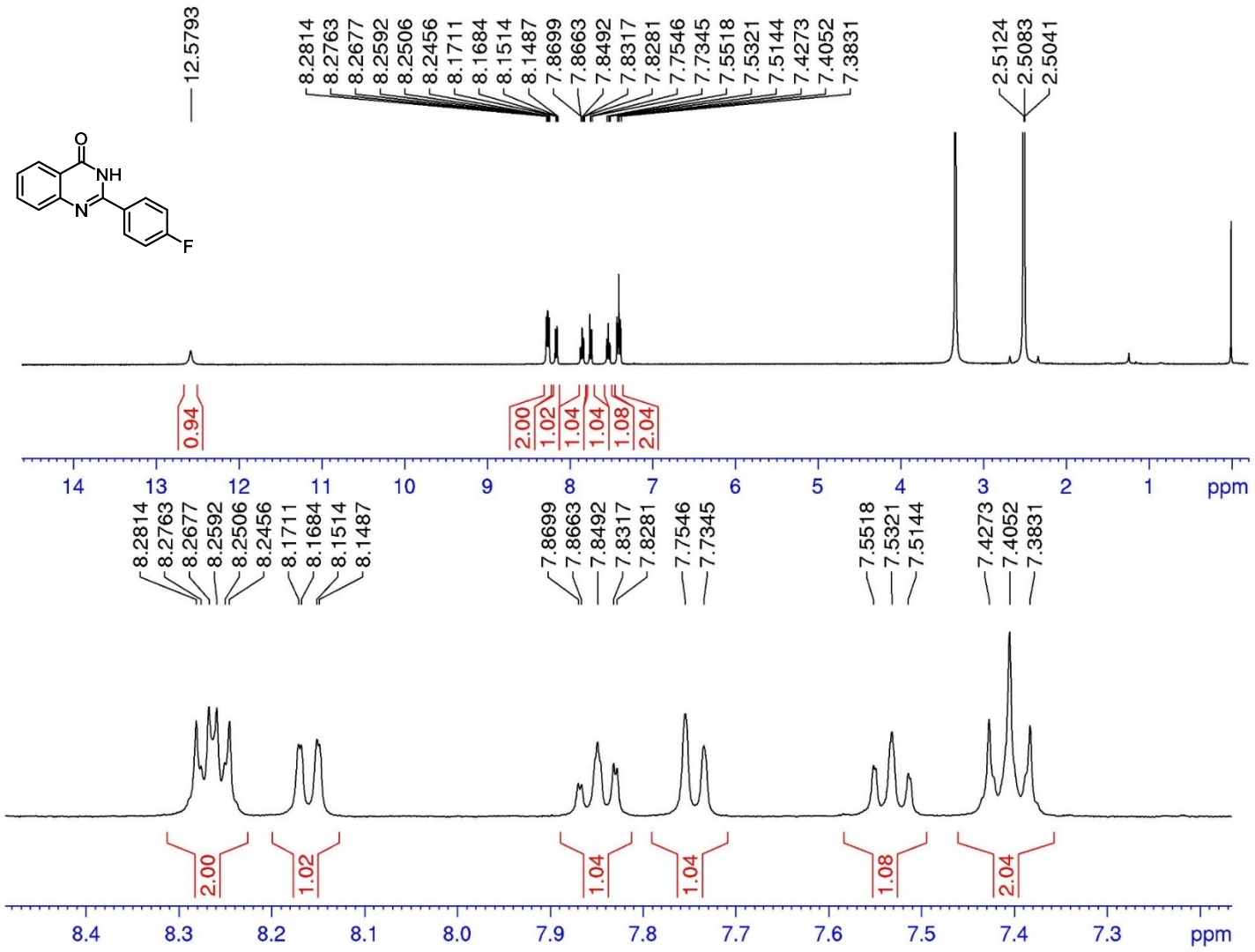
7.5
7.4
ppm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7.8317
7.8281
7.7546
7.7345
7.5518
7.5321
7.5144
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7.3831
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2.5083
2.5041
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1.08
2.04
ppm
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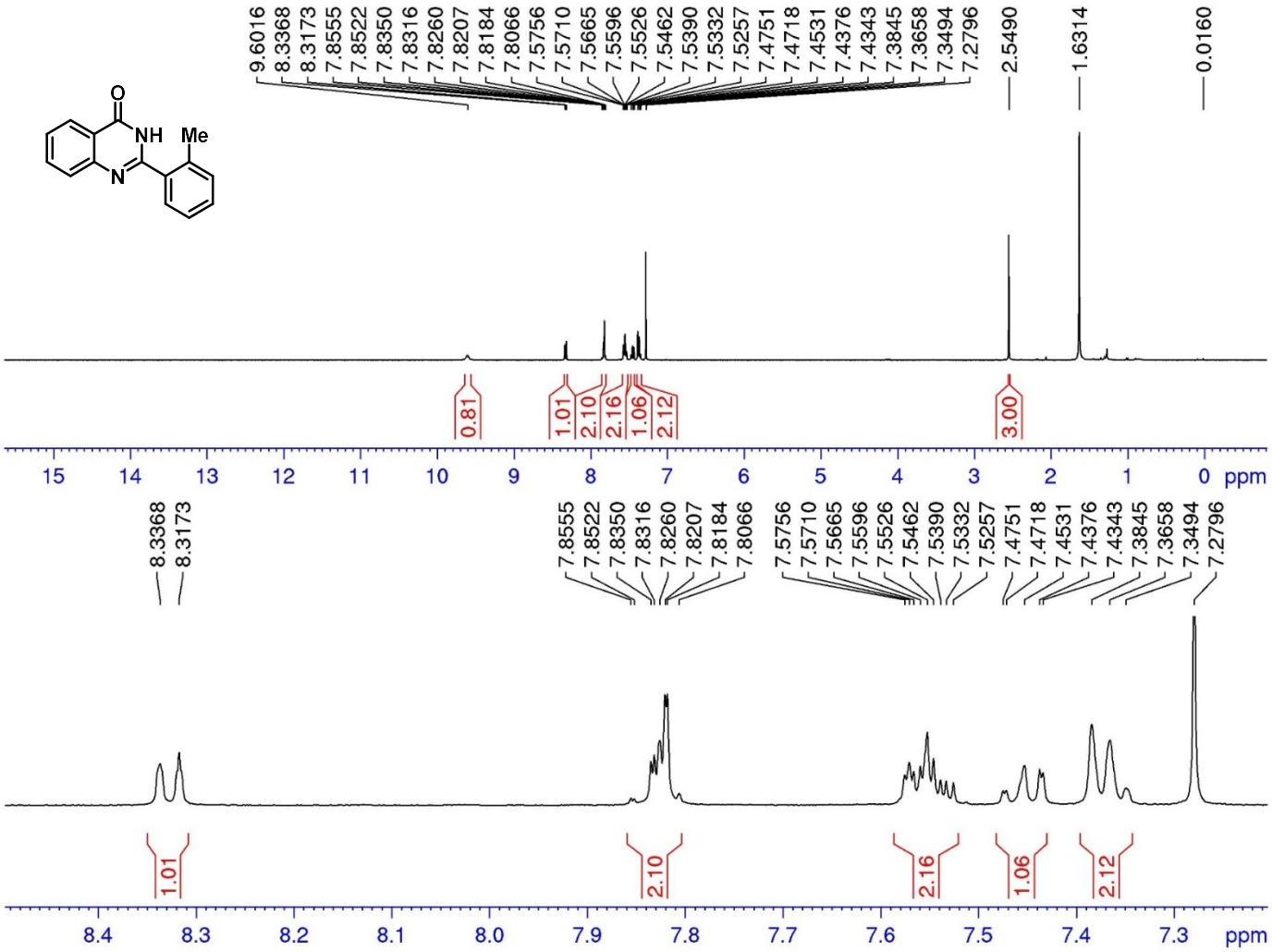
1.04
1.04
1.08
2.04
ppm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7.8522
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7.5756
7.5710
7.5665
7.5596
7.5526
7.5462
7.5390
7.5332
7.5257
7.4751
7.4718
7.4531
7.4376
7.4343
7.3845
7.3658
7.3494
7.2796
2.5490
1.6314
0.0160
O
NH
Me
N
0.81
1.01
2.10
2.16
1.06
2.12
3.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
8.3368
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7.8555
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7.5665
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7.5526
7.5462
7.5390
7.5332
7.5257
7.4751
7.4718
7.4531
7.4376
7.4343
7.3845
7.3658
7.3494
7.2796
1.01
2.10
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1.06
2.12
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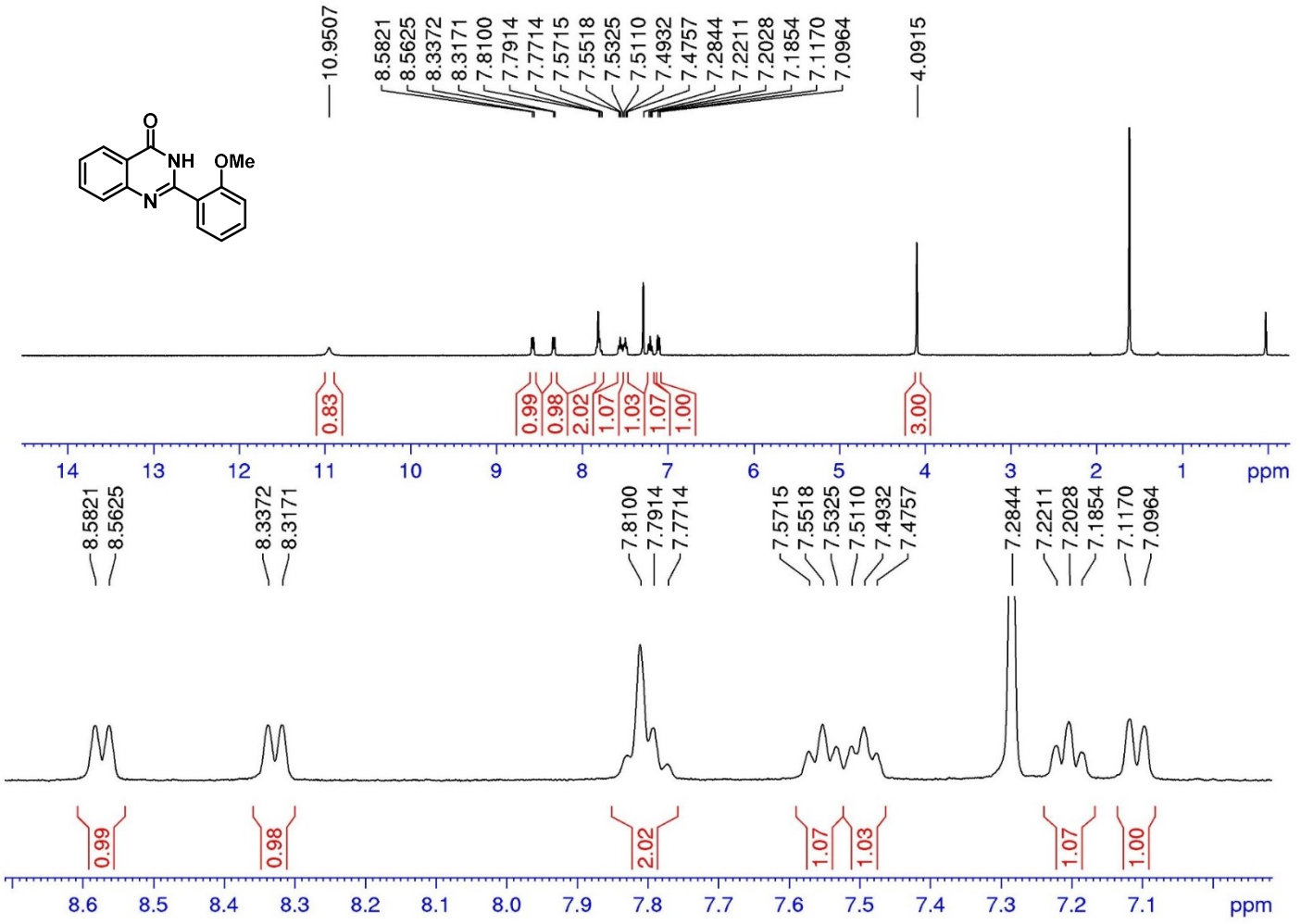
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7.5110
7.4932
7.4757
7.2844
7.2211
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7.1854
7.1170
7.0964
4.0915
O
NH
OMe
N
0.83
0.99
0.98
2.02
1.07
1.03
1.07
1.00
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
8.6
8.5
8.4
8.3
8.2
8.1
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7.8
7.7
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7.5
7.4
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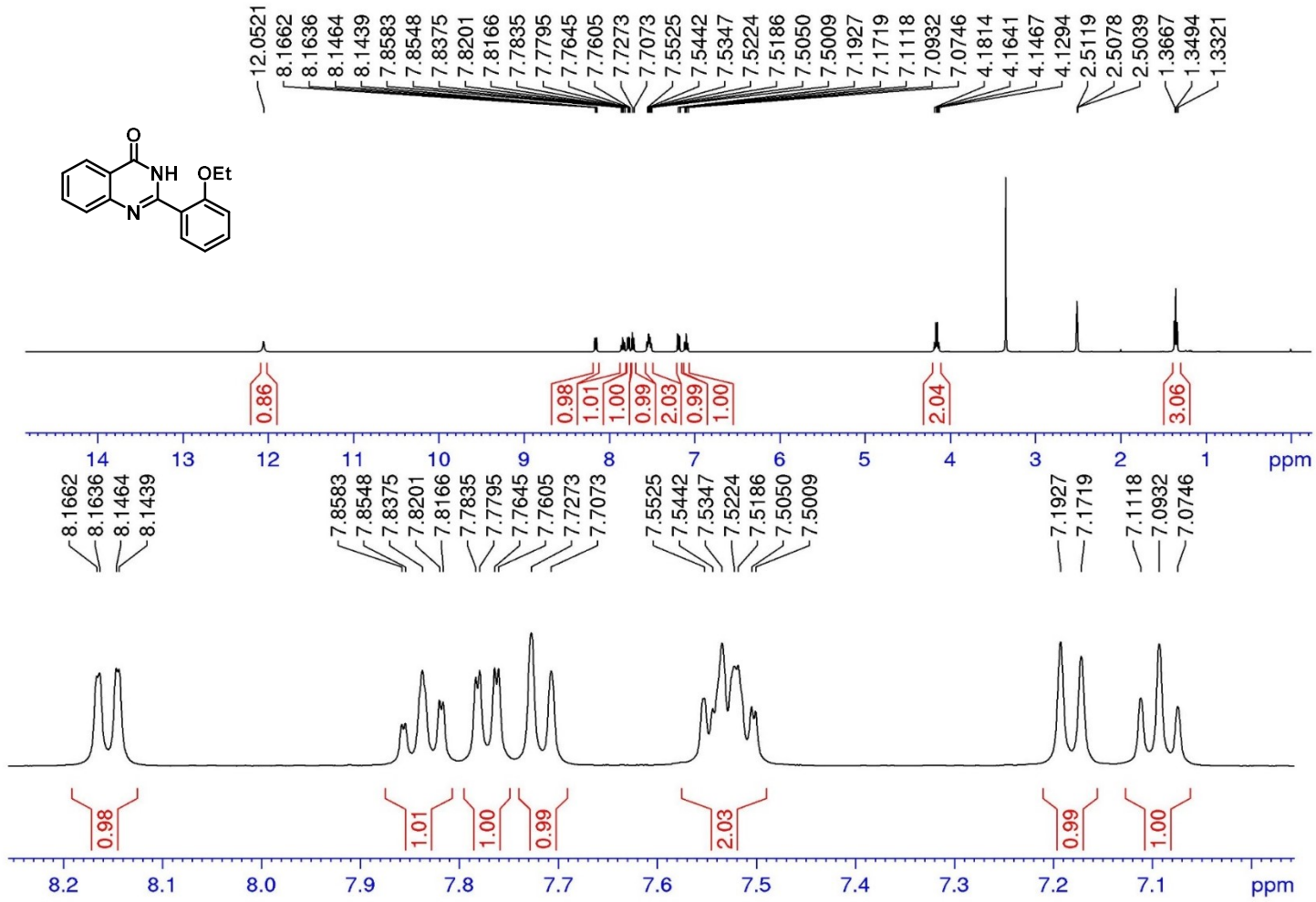
ppm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7.7795
7.7645
7.7605
7.7273
7.7073
7.5525
7.5442
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7.5009
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7.1118
7.0932
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1.3494
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O
NH
OEt
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0.99
2.03
0.99
1.00
2.04
3.06
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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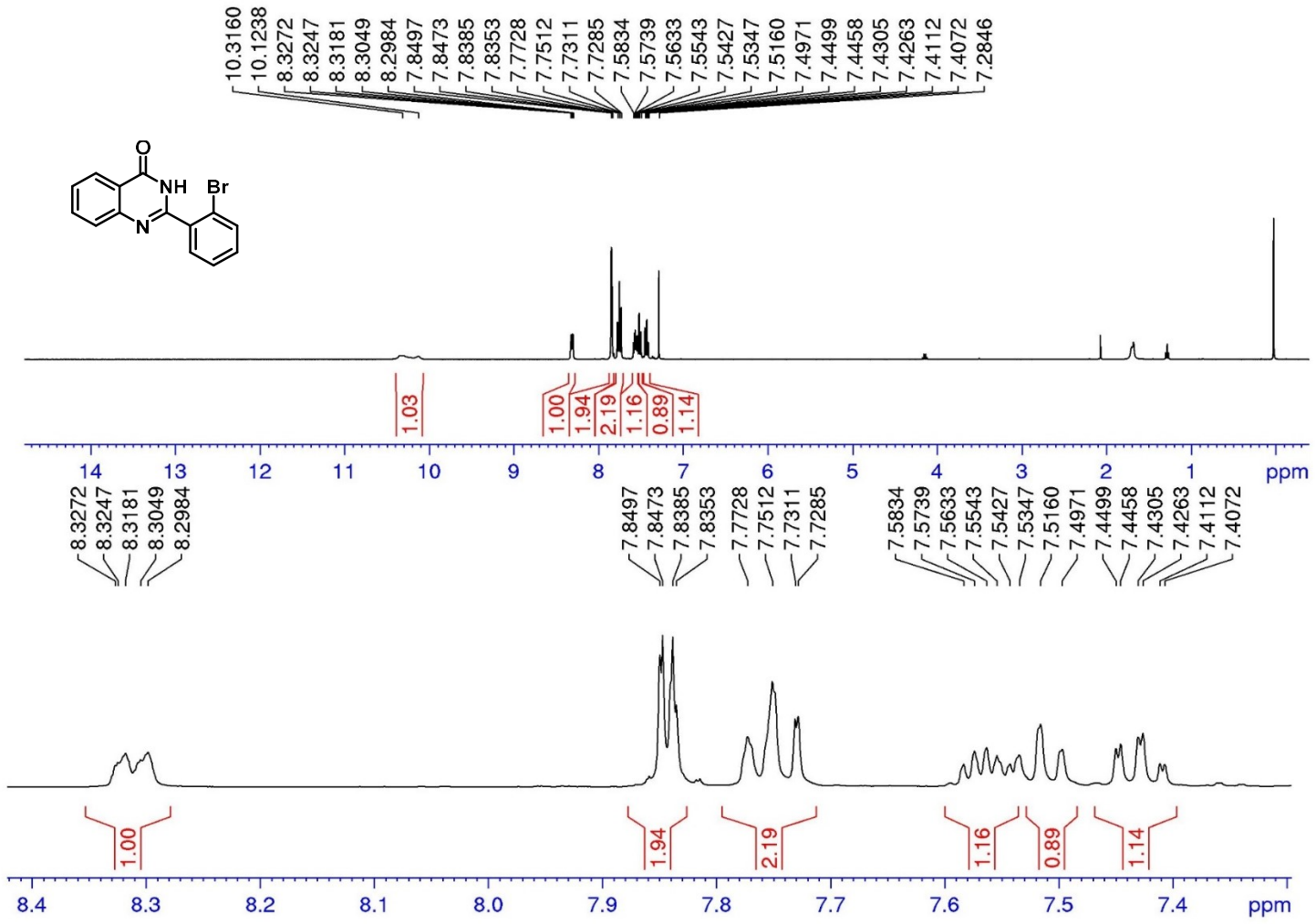
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7.7512
7.7311
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7.5739
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7.5543
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NH
Br
N
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ppm
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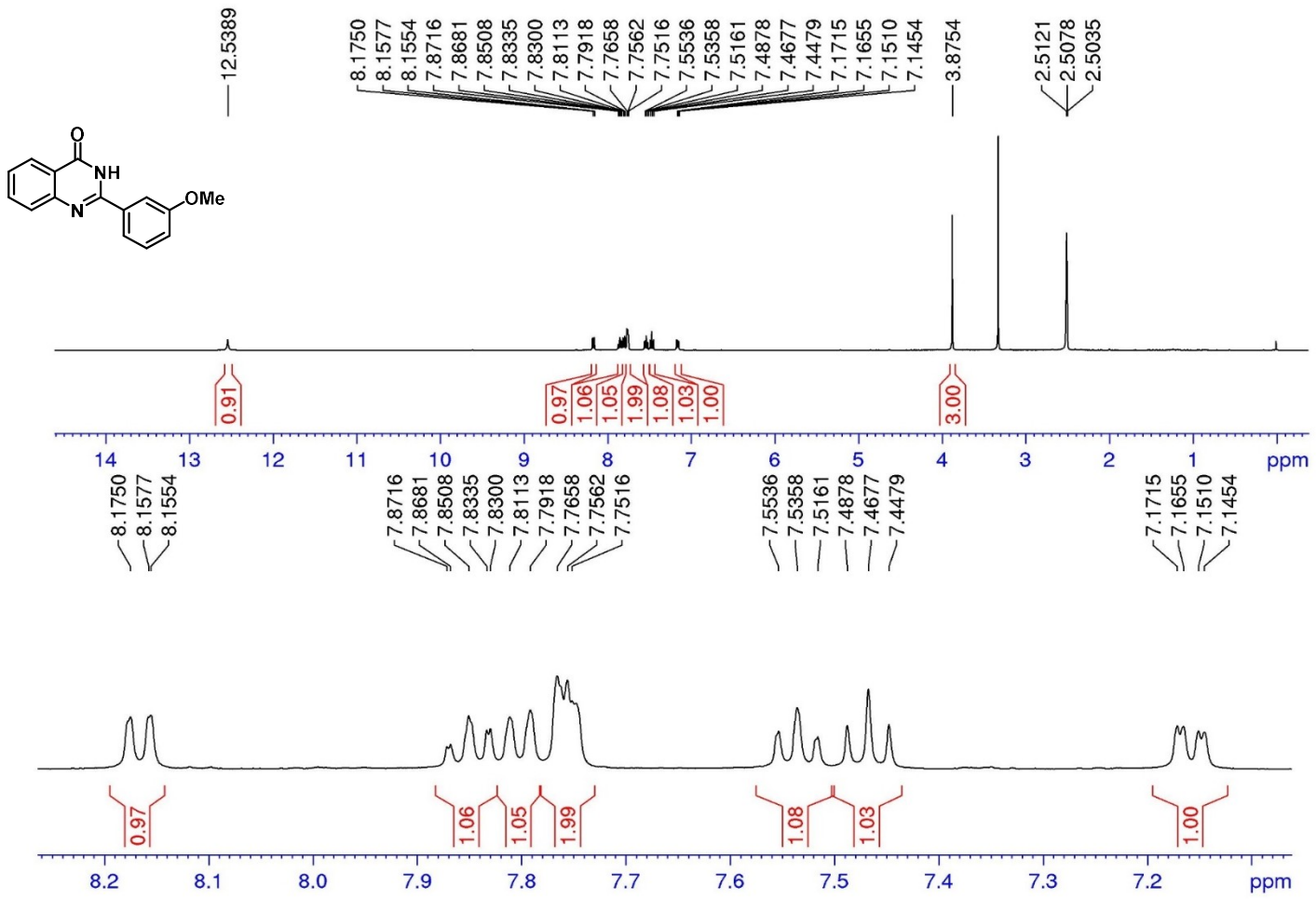
1.14
ppm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7.7562
7.7516
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7.5161
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7.1655
7.1510
7.1454
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2.5035
O
NH
N
OMe
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0.97
1.06
1.05
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1.08
1.03
1.00
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
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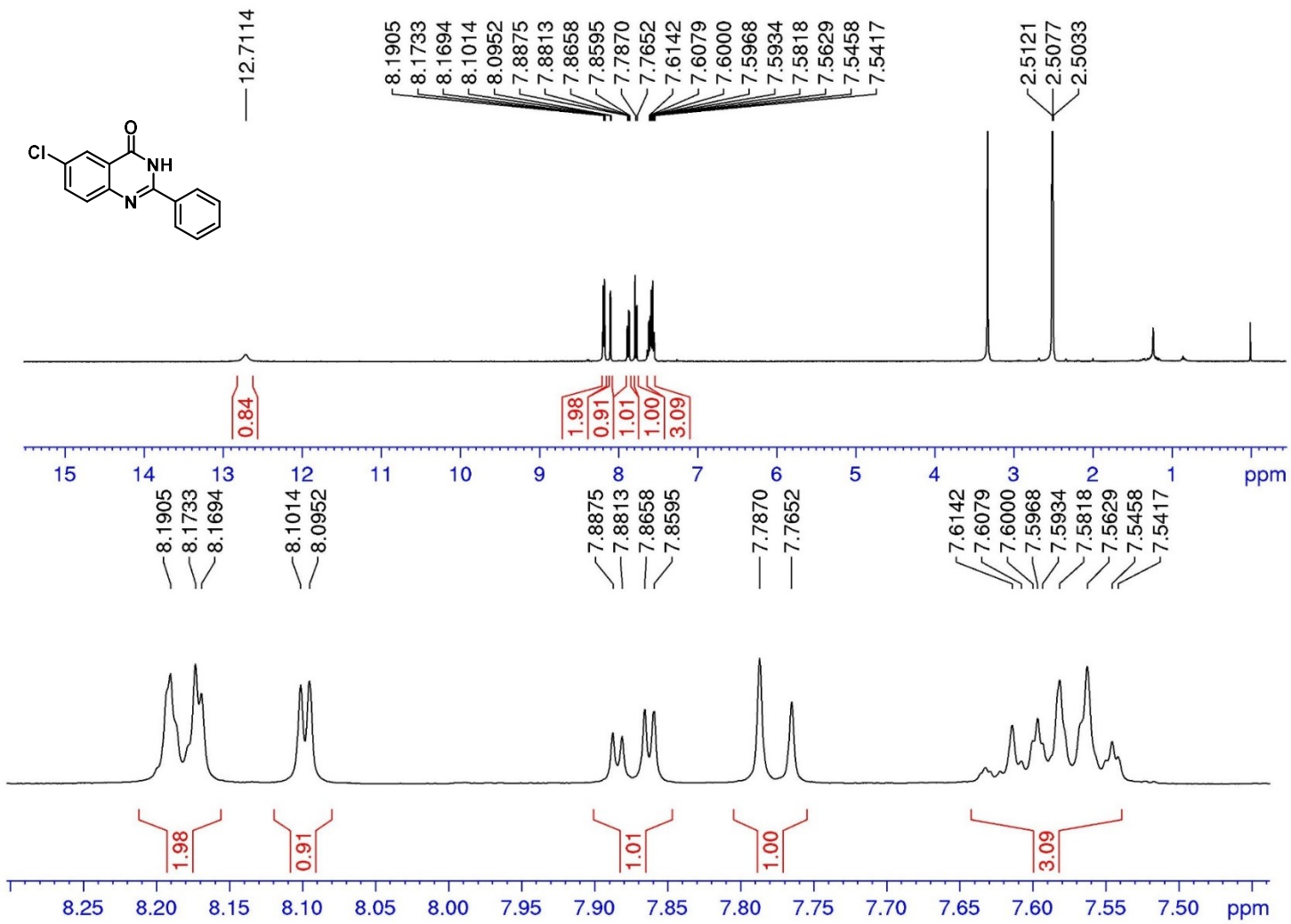
7.2
ppm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7.6079
7.6000
7.5968
7.5934
7.5818
7.5629
7.5458
7.5417
2.5121
2.5077
2.5033
Cl
O
NH
N
0.84
1.98
0.91
1.01
1.00
3.09
ppm
8.25
8.20
8.15
8.10
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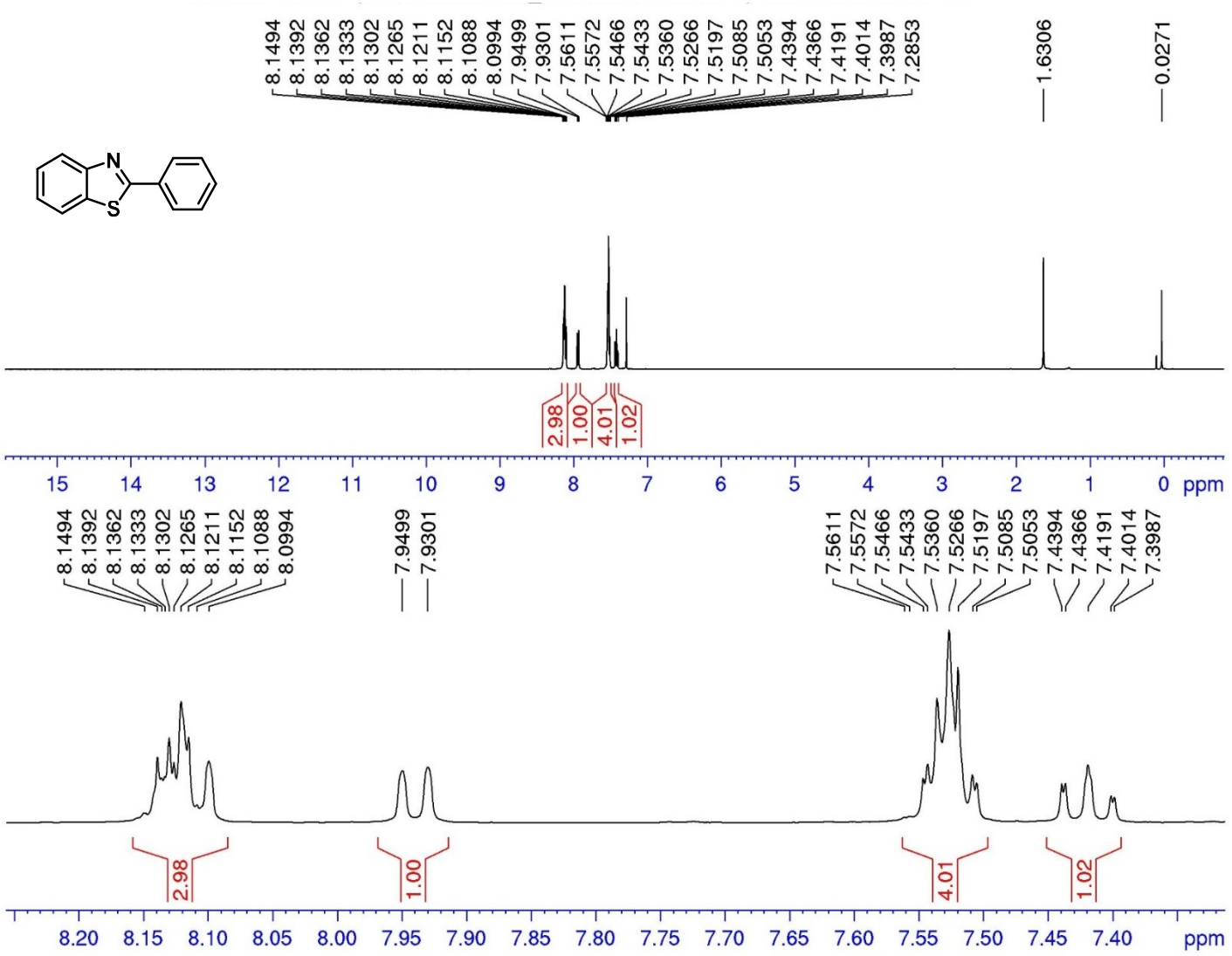
7.75
7.70
7.65
7.60
7.55
7.50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7.9499
7.9301
7.5611
7.5572
7.5466
7.5433
7.5360
7.5266
7.5197
7.5085
7.5053
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7.4366
7.4191
7.4014
7.3987
7.2853
1.6306
0.0271
N
S
2.98
1.00
4.01
1.02
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
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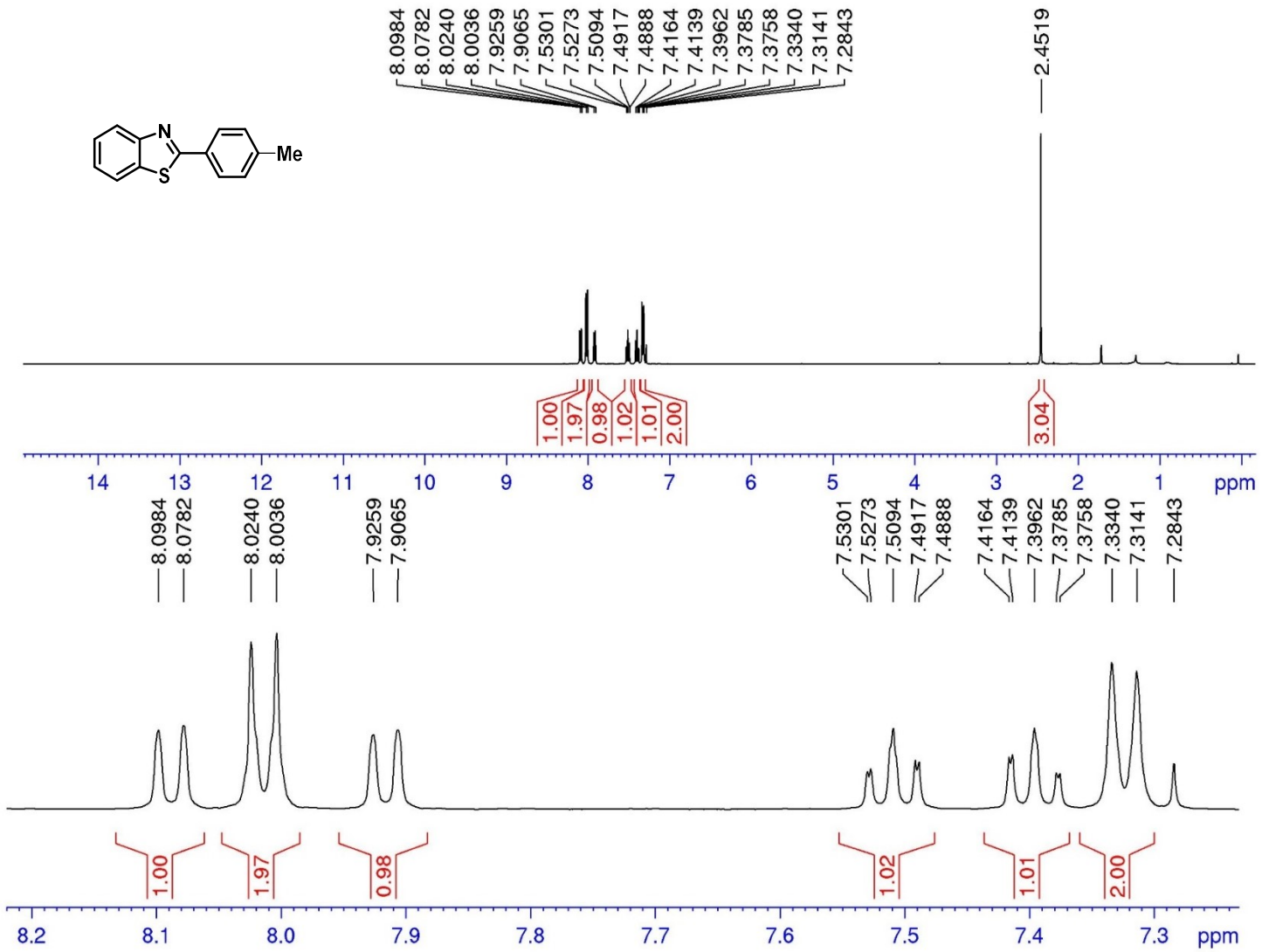
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7.5094
7.4917
7.4888
7.4164
7.4139
7.3962
7.3785
7.3758
7.3340
7.3141
7.2843
2.4519
N
S
Me
1.00
1.97
0.98
1.02
1.01
2.00
3.04
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
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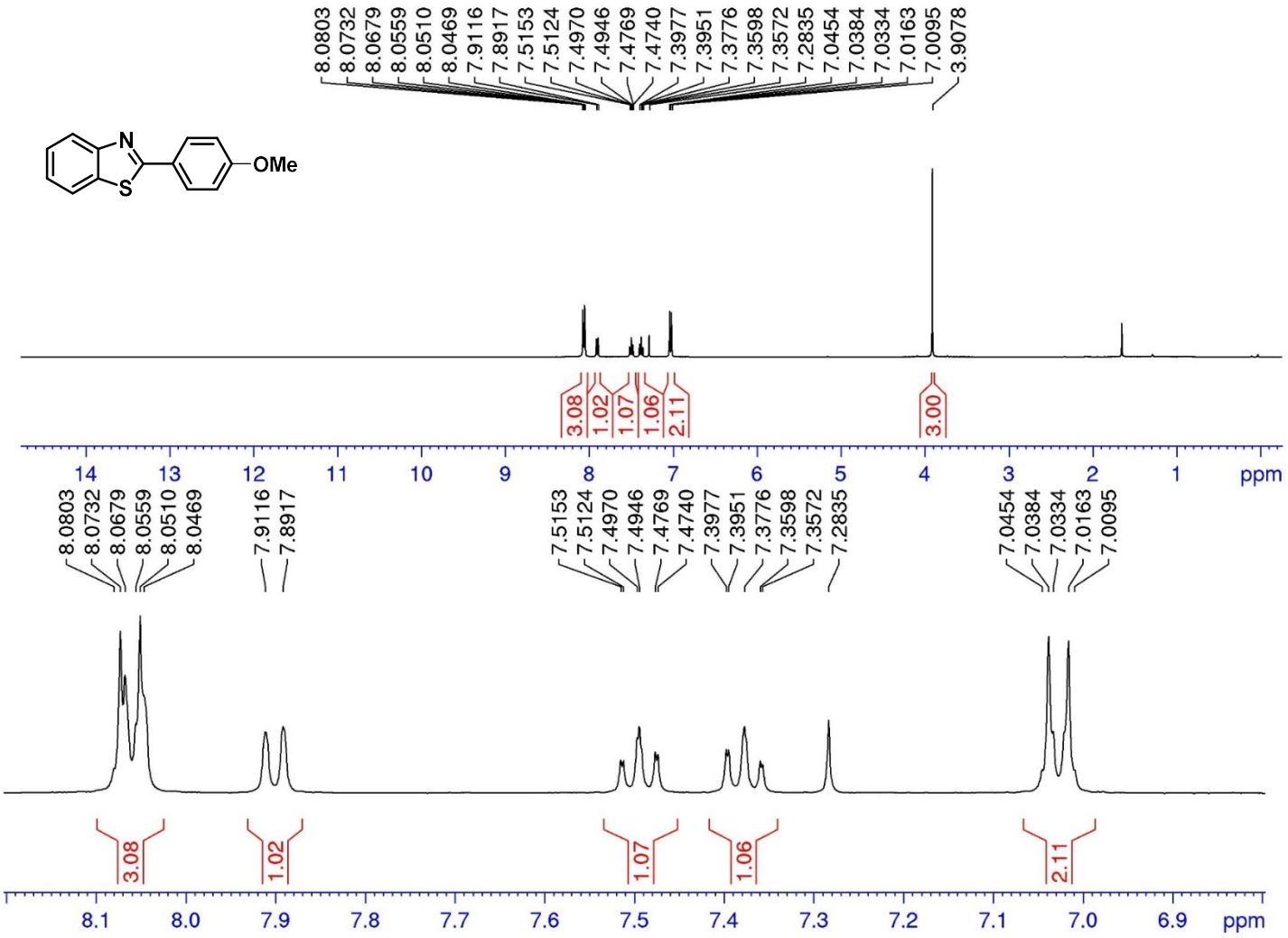
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm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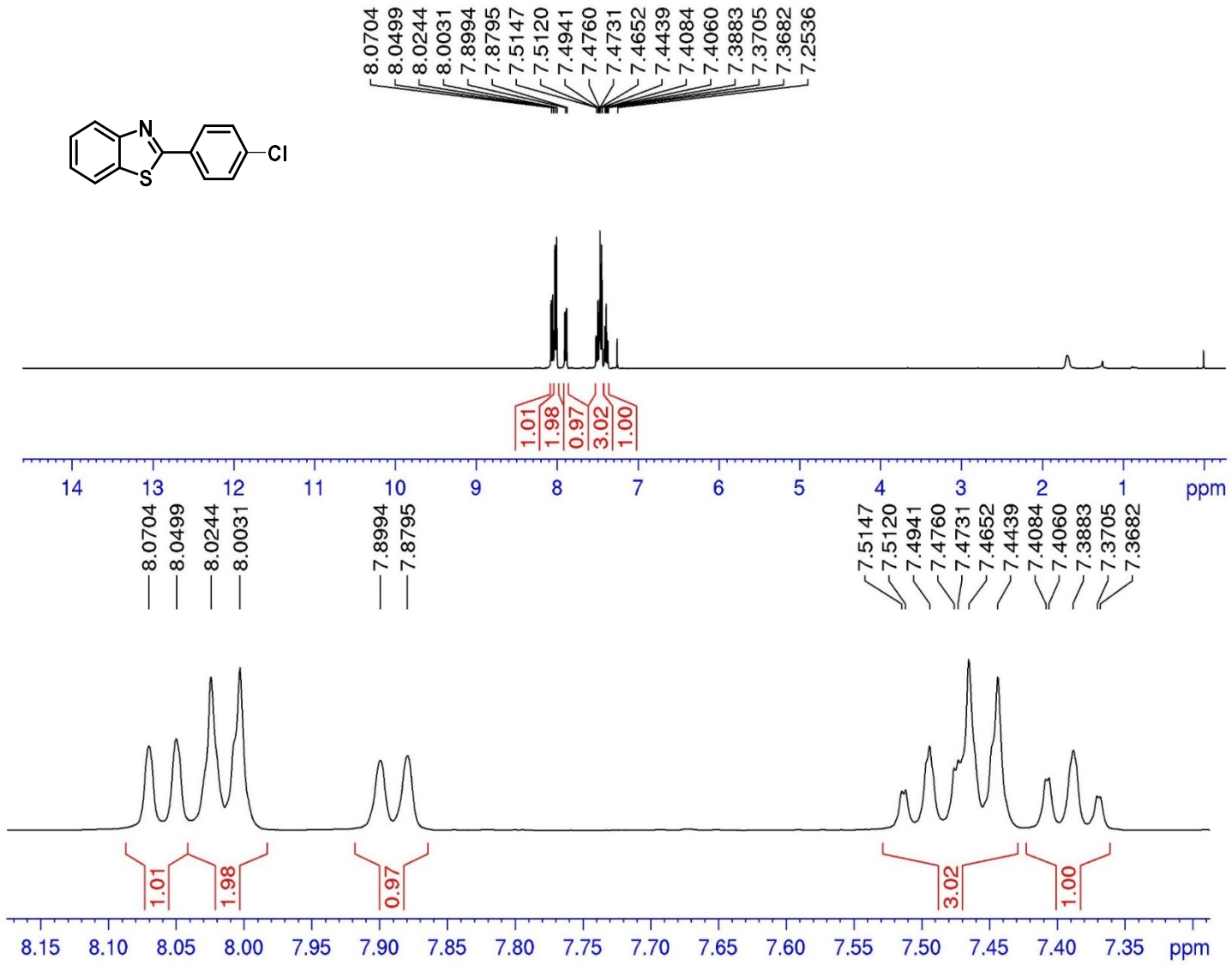
7.4946
7.4769
7.4740
7.3977
7.3951
7.3776
7.3598
7.3572
7.2835
7.0454
7.0384
7.0334
7.0163
7.0095
3.9078
N
S
OMe
3.08
1.02
1.07
1.06
2.11
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
6.9
ppm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7.5147
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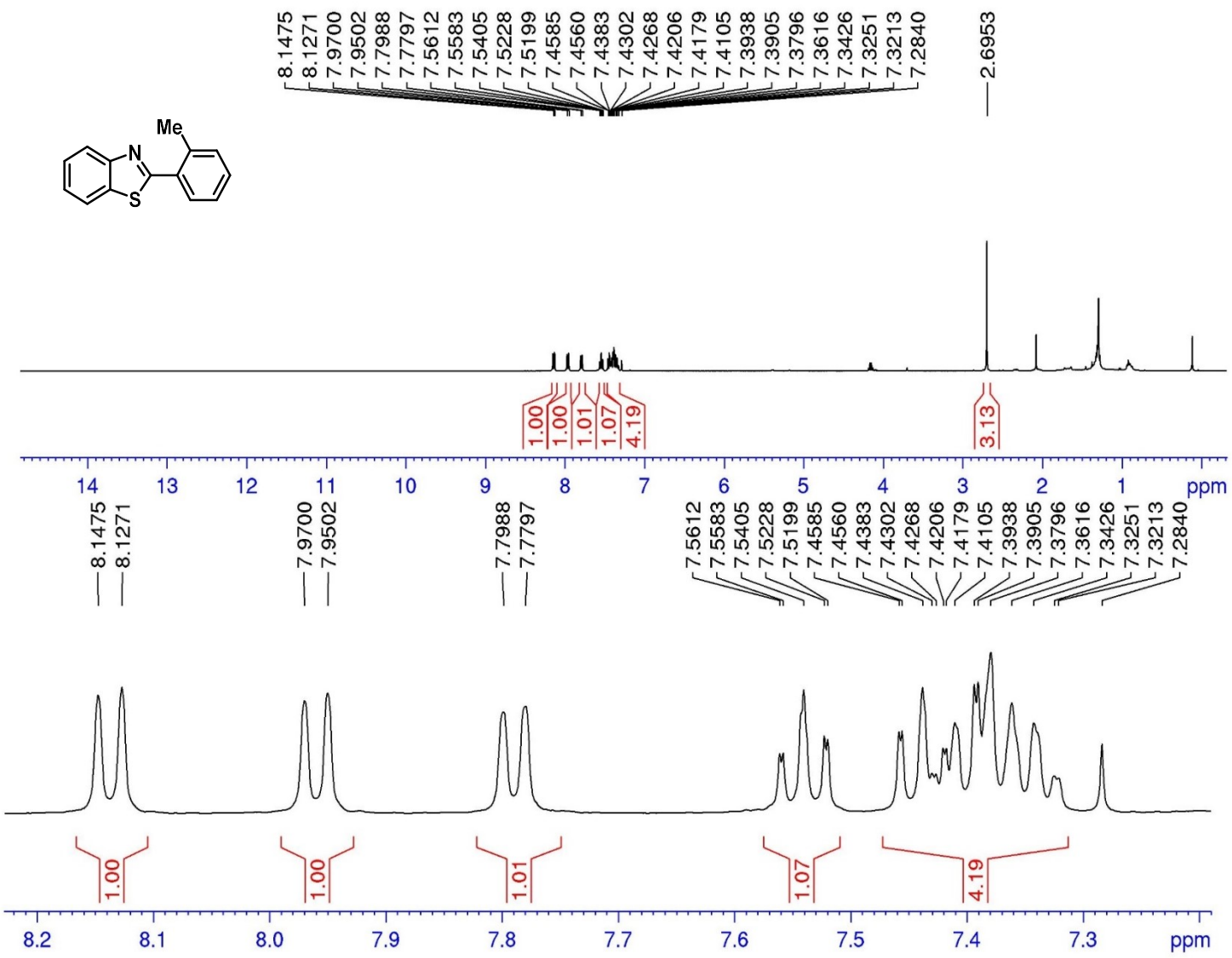
7.4760
7.4731
7.4652
7.4439
7.4084
7.4060
7.3883
7.3705
7.3682
7.2536
N
S
Cl
1.01
1.98
0.97
3.02
1.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
8.15 8.10 8.05 8.00 7.95 7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 ppm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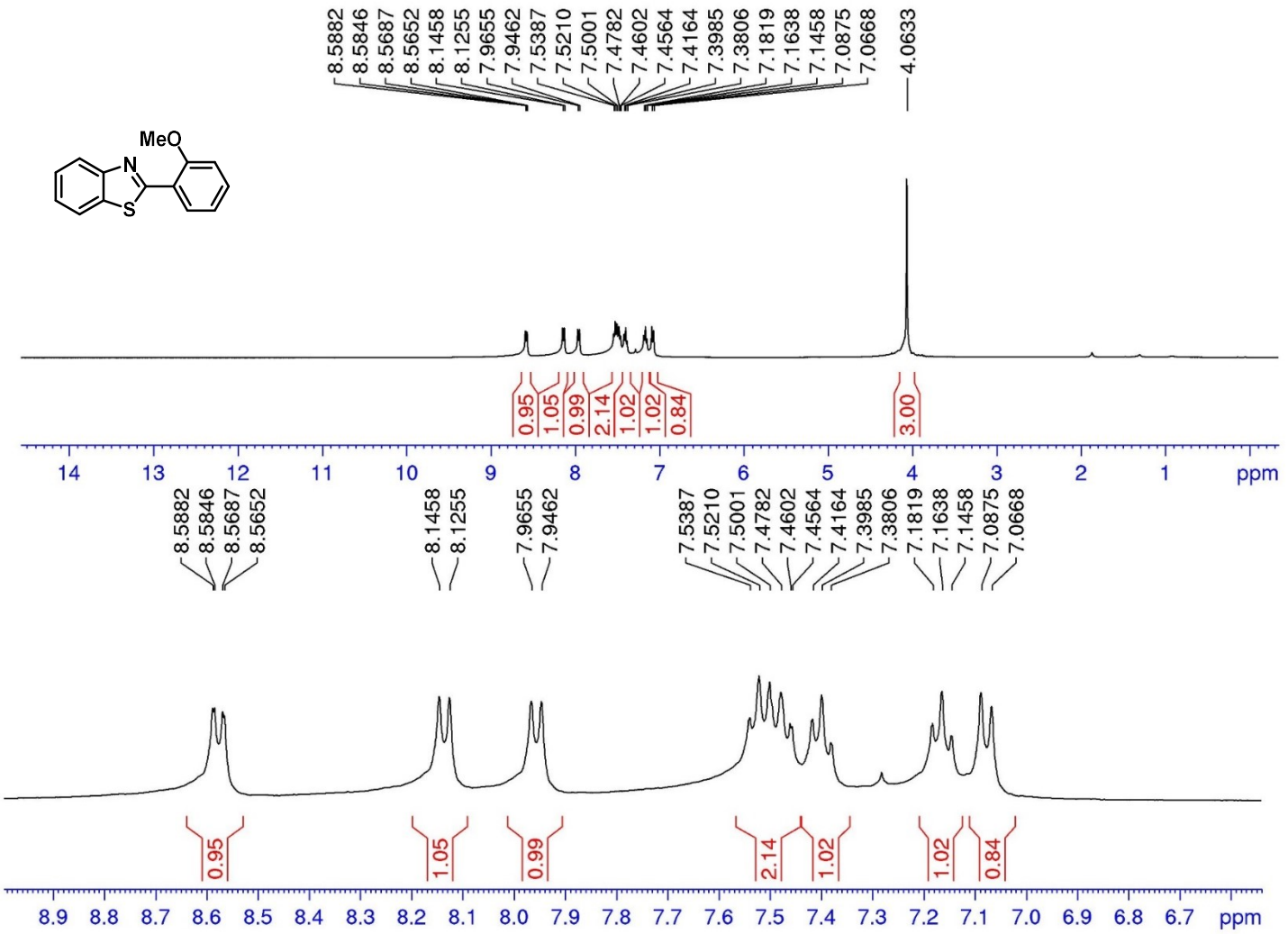
7.5199
7.4585
7.4560
7.4383
7.4302
7.4268
7.4206
7.4179
7.4105
7.3938
7.3905
7.3796
7.3616
7.3426
7.3251
7.3213
7.2840
2.6953
Me
N
S
1.00
1.00
1.01
1.07
4.19
3.13
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm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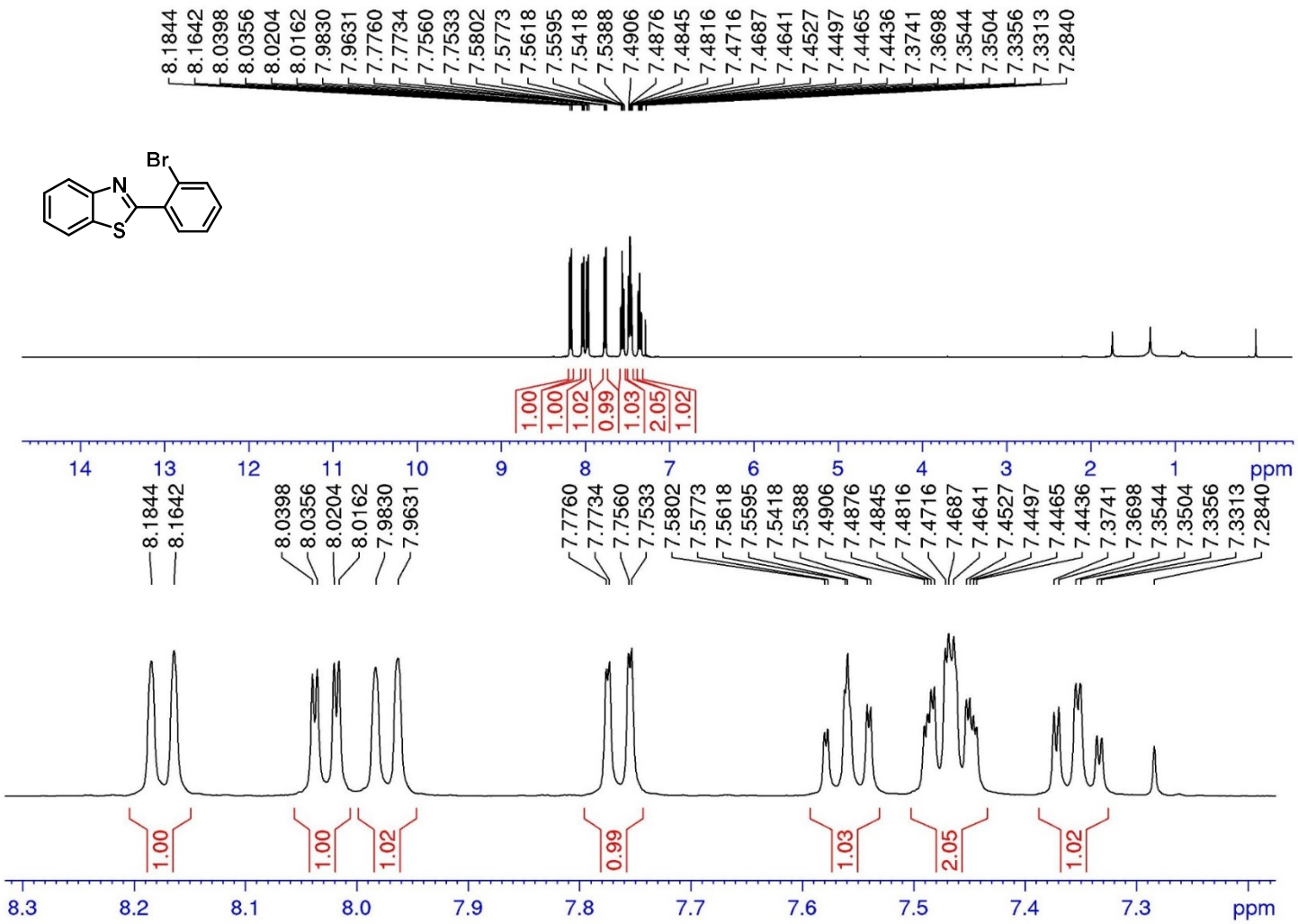
8.5687
8.5652
8.1458
8.1255
7.9655
7.9462
7.5387
7.5210
7.5001
7.4782
7.4602
7.4564
7.4164
7.3985
7.3806
7.1819
7.1638
7.1458
7.0875
7.0668
4.0633
MeO
N
S
0.95
1.05
0.99
2.14
1.02
1.02
0.84
3.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 ppm
8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 ppm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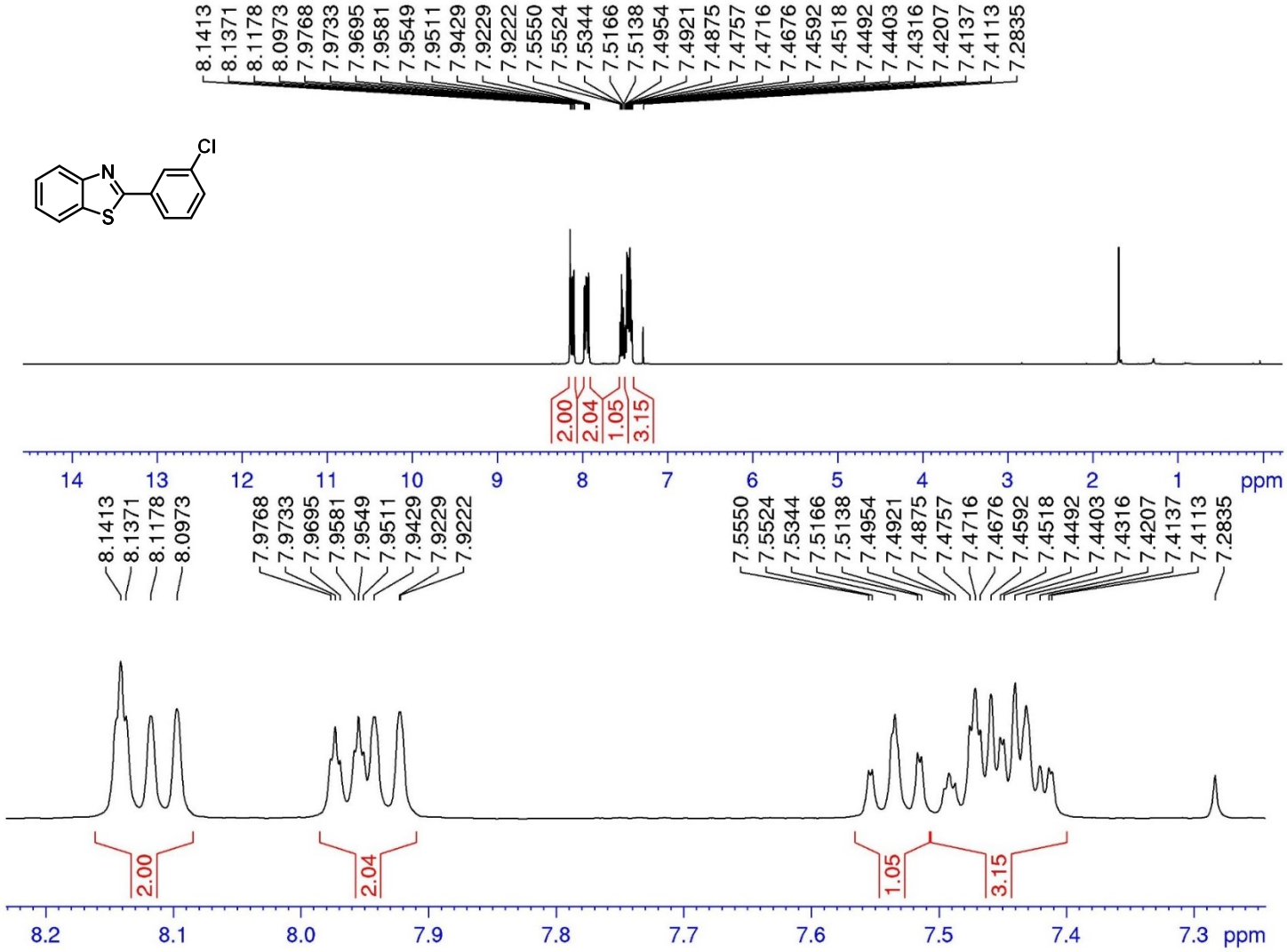
8.0204
8.0162
7.9830
7.9631
7.7760
7.7734
7.7560
7.7533
7.5802
7.5773
7.5618
7.5595
7.5418
7.5388
7.4906
7.4876
7.4845
7.4816
7.4716
7.4687
7.4641
7.4527
7.4497
7.4465
7.4436
7.3741
7.3698
7.3544
7.3504
7.3356
7.3313
7.2840
Br
N
S
1.00
1.00
1.02
0.99
1.03
2.05
1.02
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm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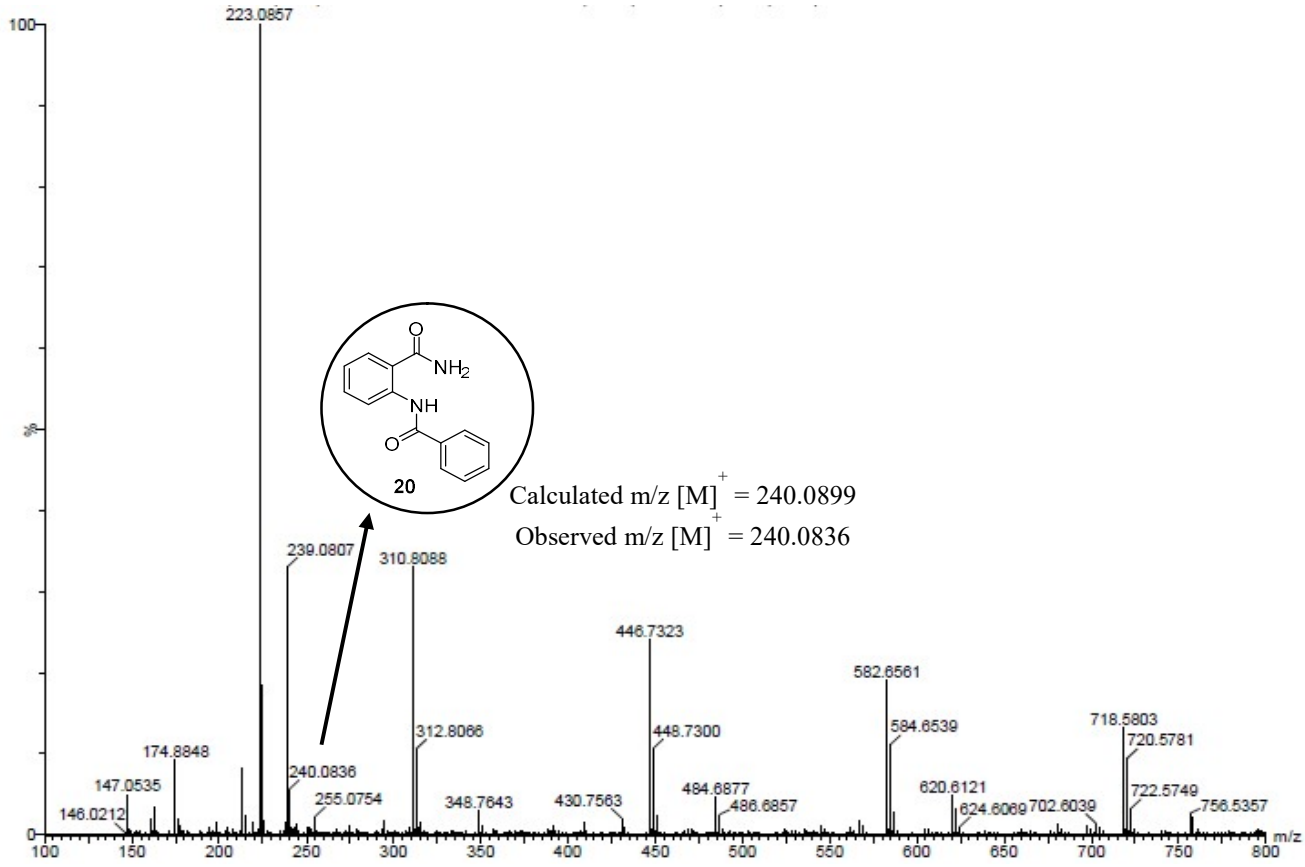
7.9429
7.9229
7.9222
7.5550
7.5524
7.5344
7.5166
7.5138
7.4954
7.4921
7.4875
7.4757
7.4716
7.4676
7.4592
7.4518
7.4492
7.4403
7.4316
7.4207
7.4137
7.4113
7.2835
Cl
N
S
2.00
2.04
1.05
3.15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
ppm


223.0857
100
%
0
NH2
NH
O
O
20
Calculated m/z [M]+ = 240.0899
Observed m/z [M]+ = 240.0836
239.0807
310.8088
446.7323
582.6561
312.8066
448.7300
584.6539
718.5803
720.5781
174.8848
240.0836
147.0535
255.0754
348.7643
430.7563
484.6877
486.6857
620.6121
624.6069
702.6039
722.5749
146.0212
756.5357
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
m/z

IV. References

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