# The Direct Access to 4-Carboxy-1,8-naphthyridines and Related Compounds through Pfitzinger-type Chemistry

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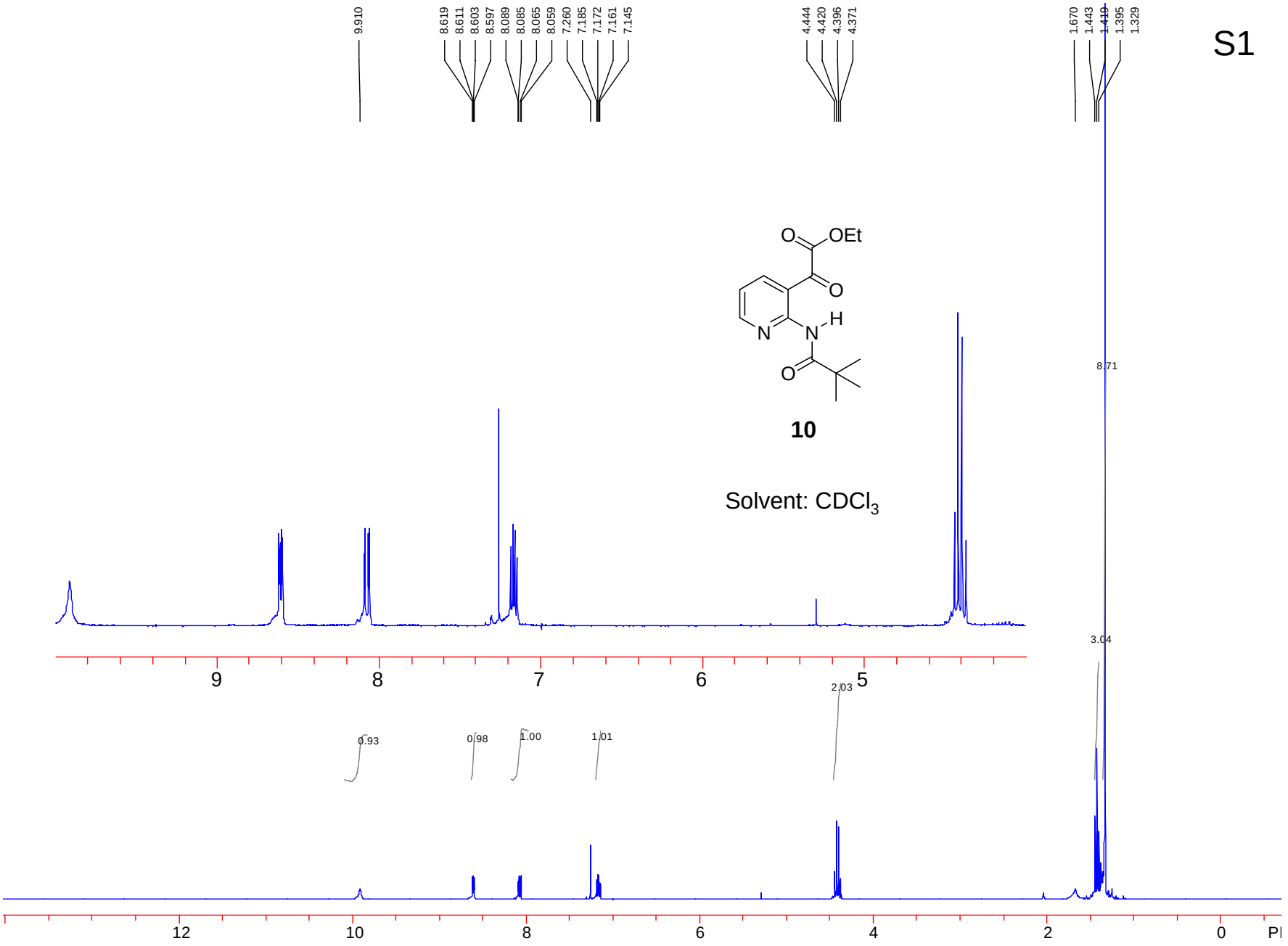
## Supporting Information

| $^{1}$H and $^{13}$C NMR spectra of compounds | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Compound | **10** | **4** | **17** | **18** | **19** | **20** | **22** | **23** | **25** | **28** | **29** | **30** | **31** |
| $^{1}$H NMR | S1 | S3 | S5 | S7 | S9 | S11 | S13 | S15 | S17 | S19 | S21 | S23 | S25 |
| $^{13}$C NMR | S2 | S4 | S6 | S8 | S10 | S12 | S14 | S16 | S18 | S20 | S22 | S24 | S26 |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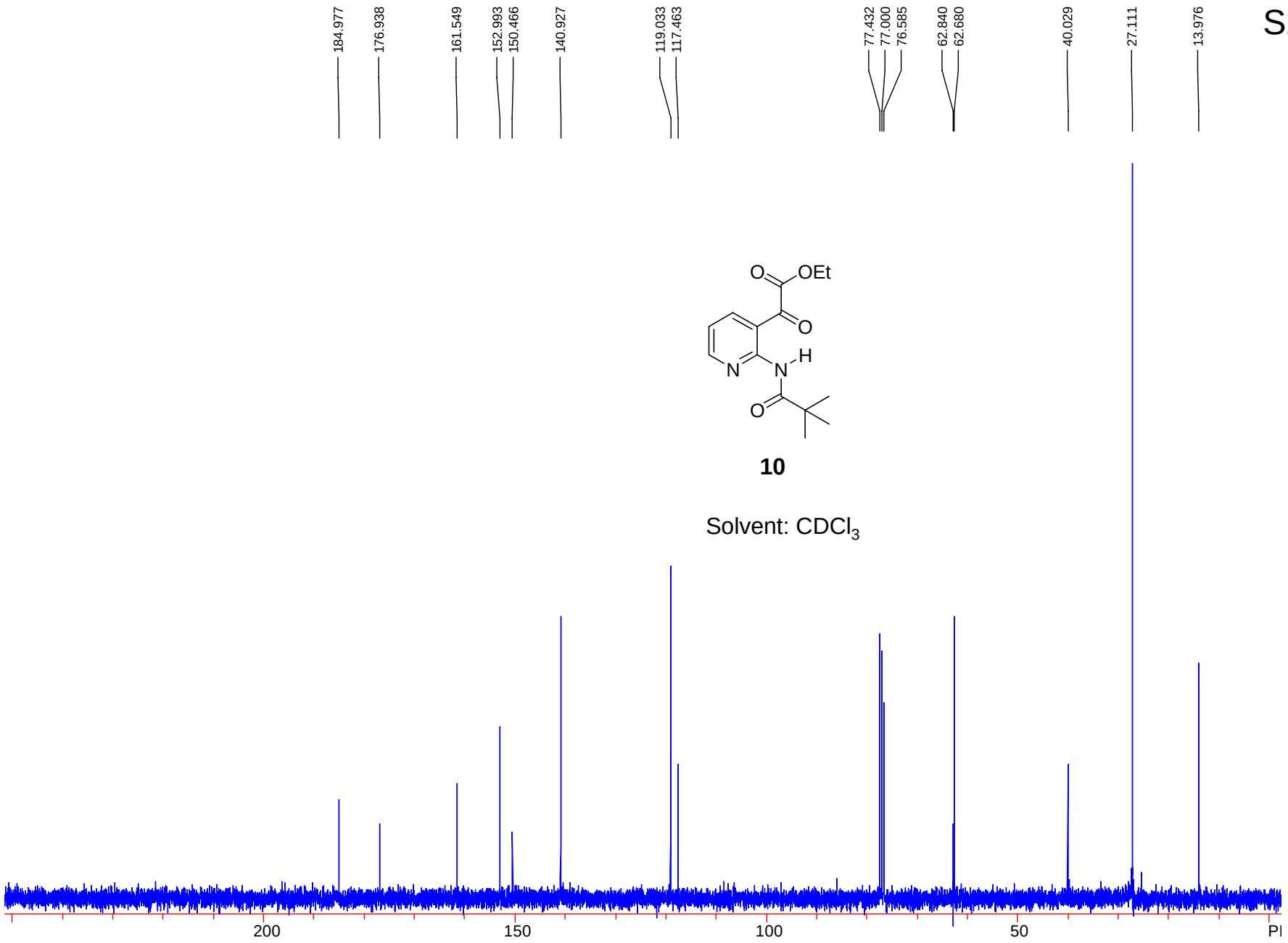
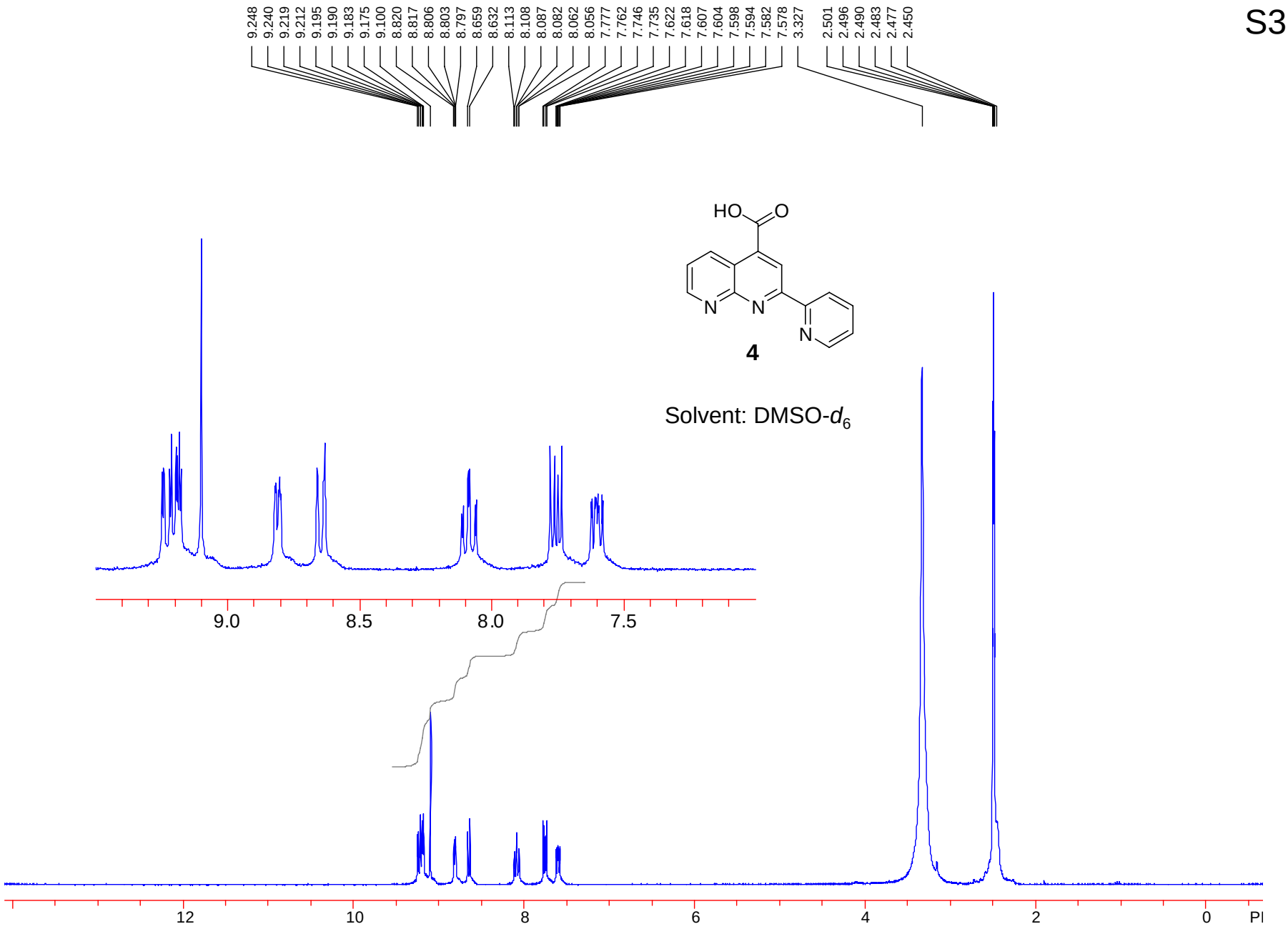
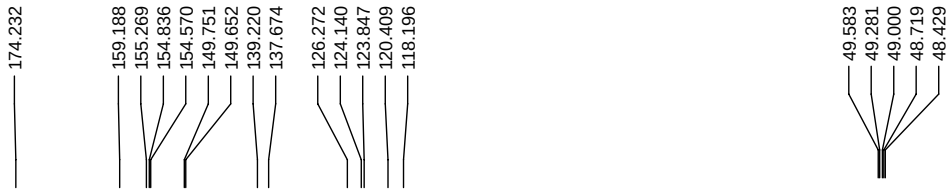
8.619
8.611
8.603
8.597
8.089
8.085
8.065
8.059
7.260
7.185
7.172
7.161
7.145
4.444
4.420
4.396
4.371
1.670
1.443
1.419
1.395
1.329
O
OEt
O
H
N
N
O
10
Solvent: CDCl3
8.71
3.04
2.03
0.93
0.98
1.00
1.01
9
8
7
6
5
12
10
8
6
4
2
0
PI

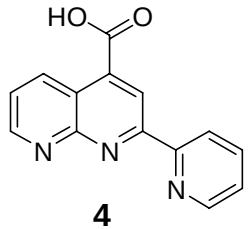



**10**

Solvent: $CDCl_3$

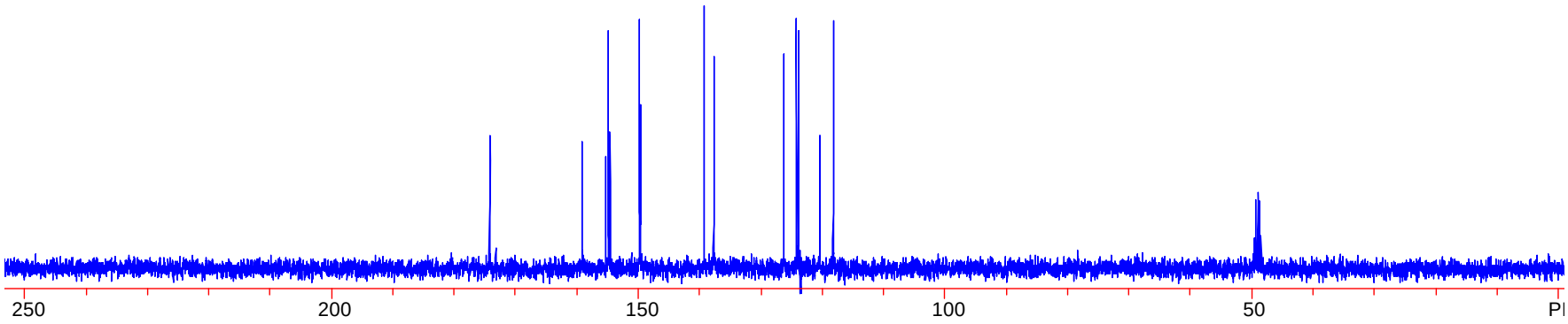

9.248
9.240
9.219
9.212
9.195
9.190
9.183
9.175
9.100
8.820
8.817
8.806
8.803
8.797
8.659
8.632
8.113
8.108
8.087
8.082
8.062
8.056
7.777
7.762
7.746
7.735
7.622
7.618
7.607
7.604
7.598
7.594
7.582
7.578
3.327
2.501
2.496
2.490
2.483
2.477
2.450
HO
O
N
N
N
4
Solvent: DMSO-$d_6$
9.0
8.5
8.0
7.5
12
10
8
6
4
2
0
PI

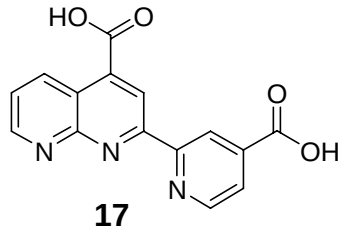



**4**

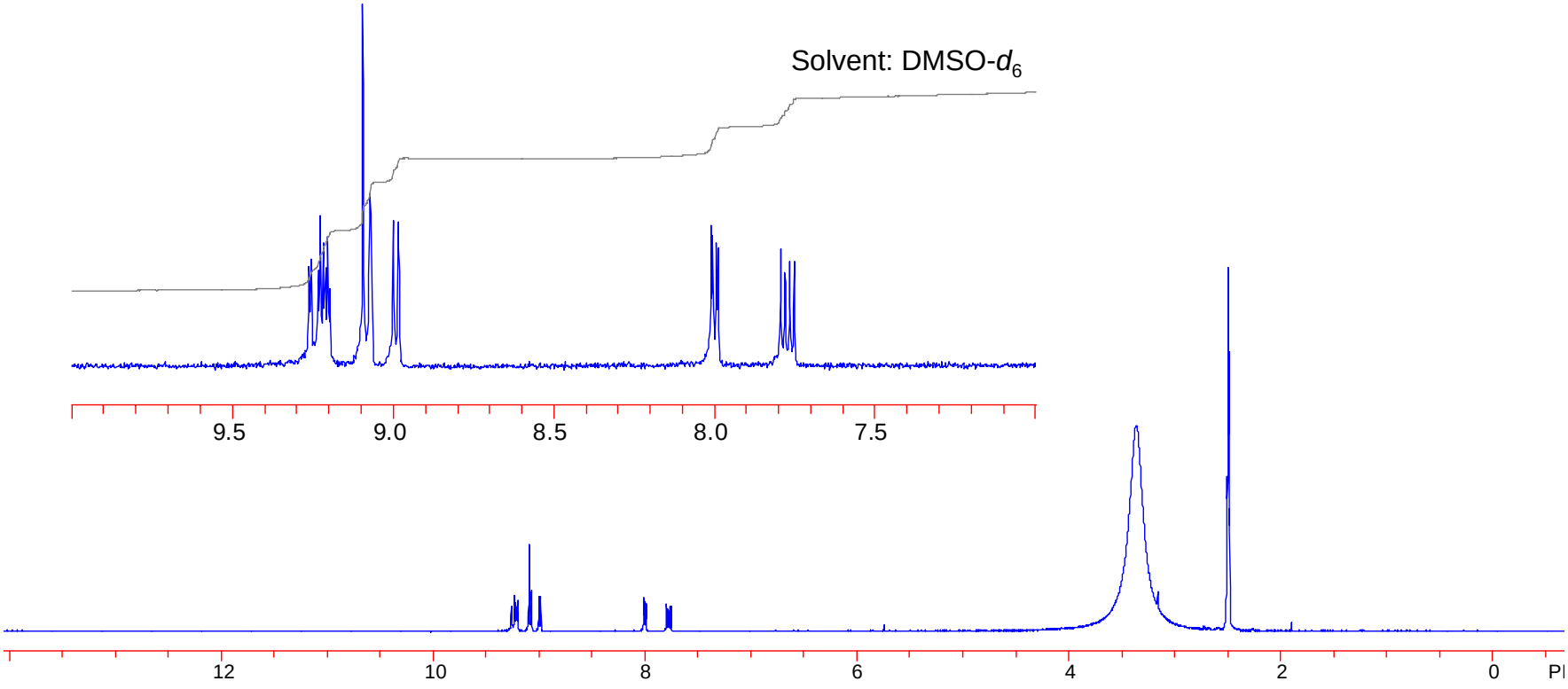
Solvent: $D_2O/CD_3OD$
with added KOH

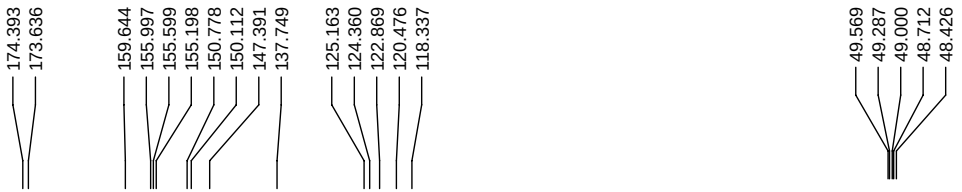


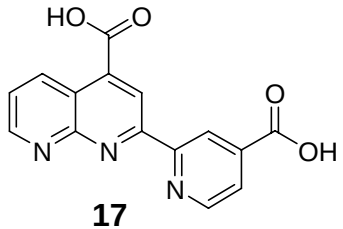




**17**

Solvent: DMSO-$d_6$

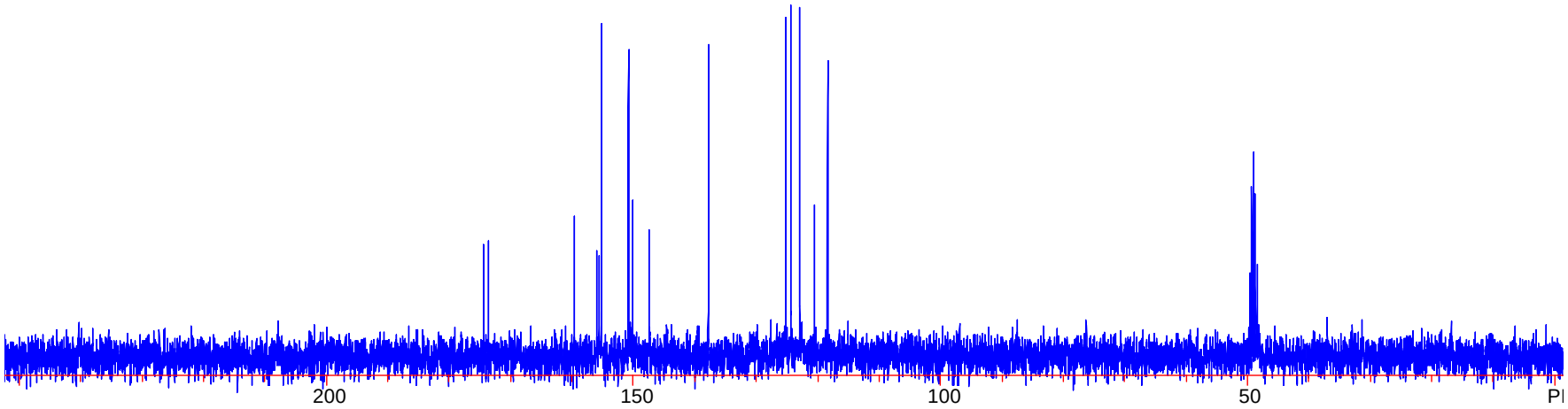


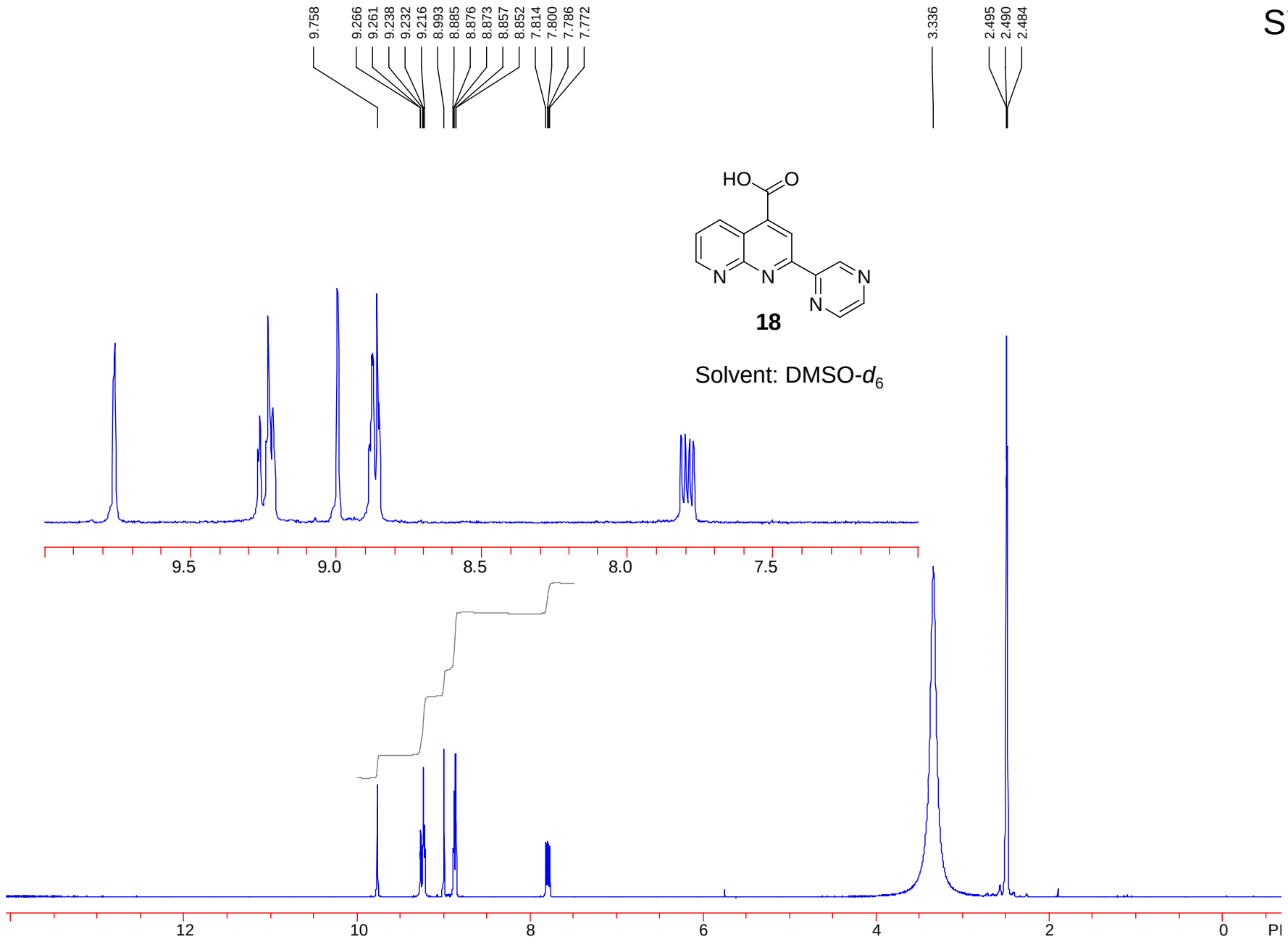


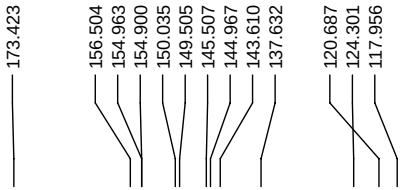



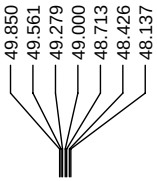

**17**

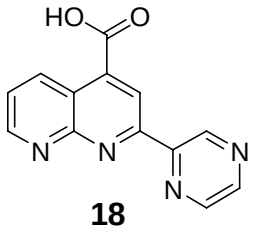
Solvent: $D_2O/CD_3OD$
with added KOH




9.758
9.266
9.261
9.238
9.232
9.216
8.993
8.885
8.876
8.873
8.857
8.852
7.814
7.800
7.786
7.772
3.336
2.495
2.490
2.484
HO
O
N
N
N
N
18
Solvent: DMSO-$d_6$
9.5
9.0
8.5
8.0
7.5
12
10
8
6
4
2
0
PI

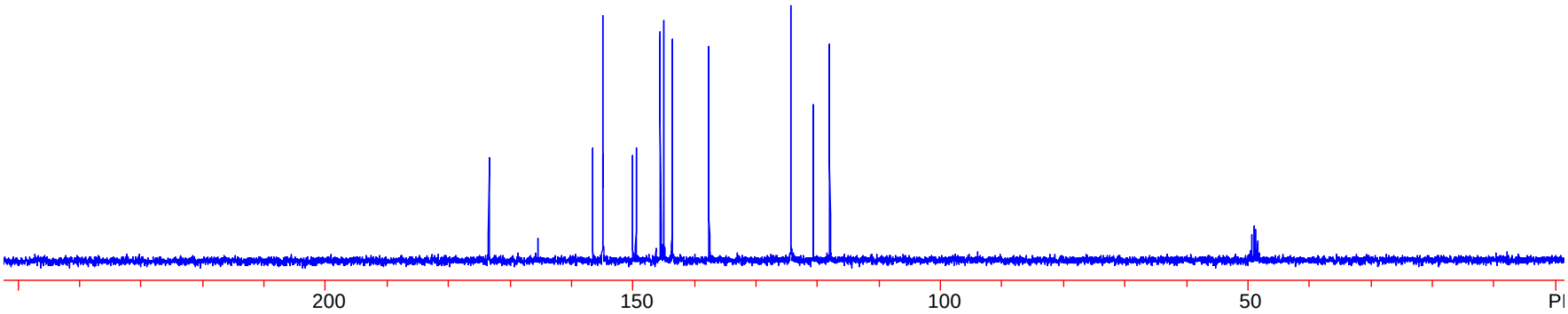


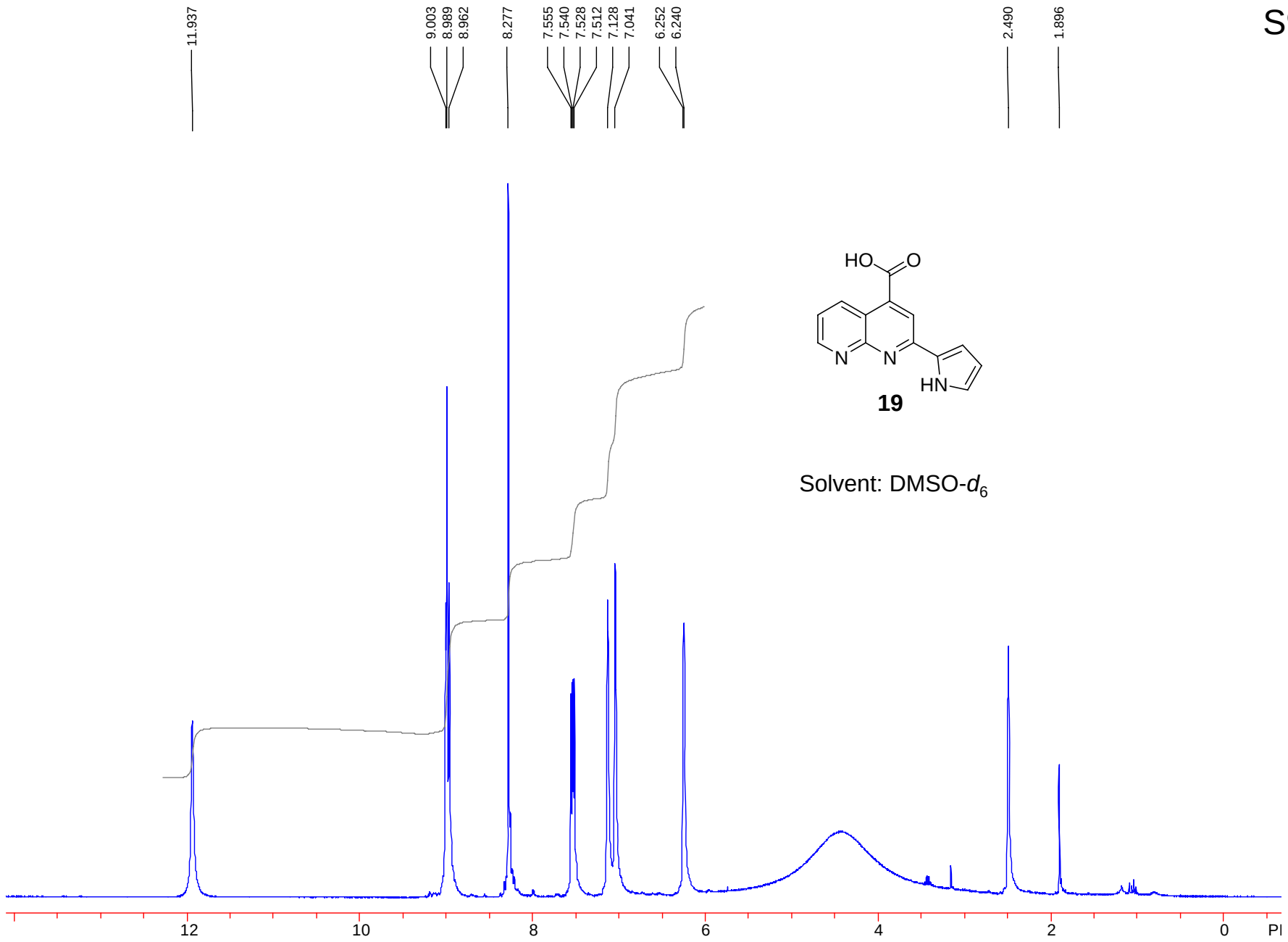




**18**

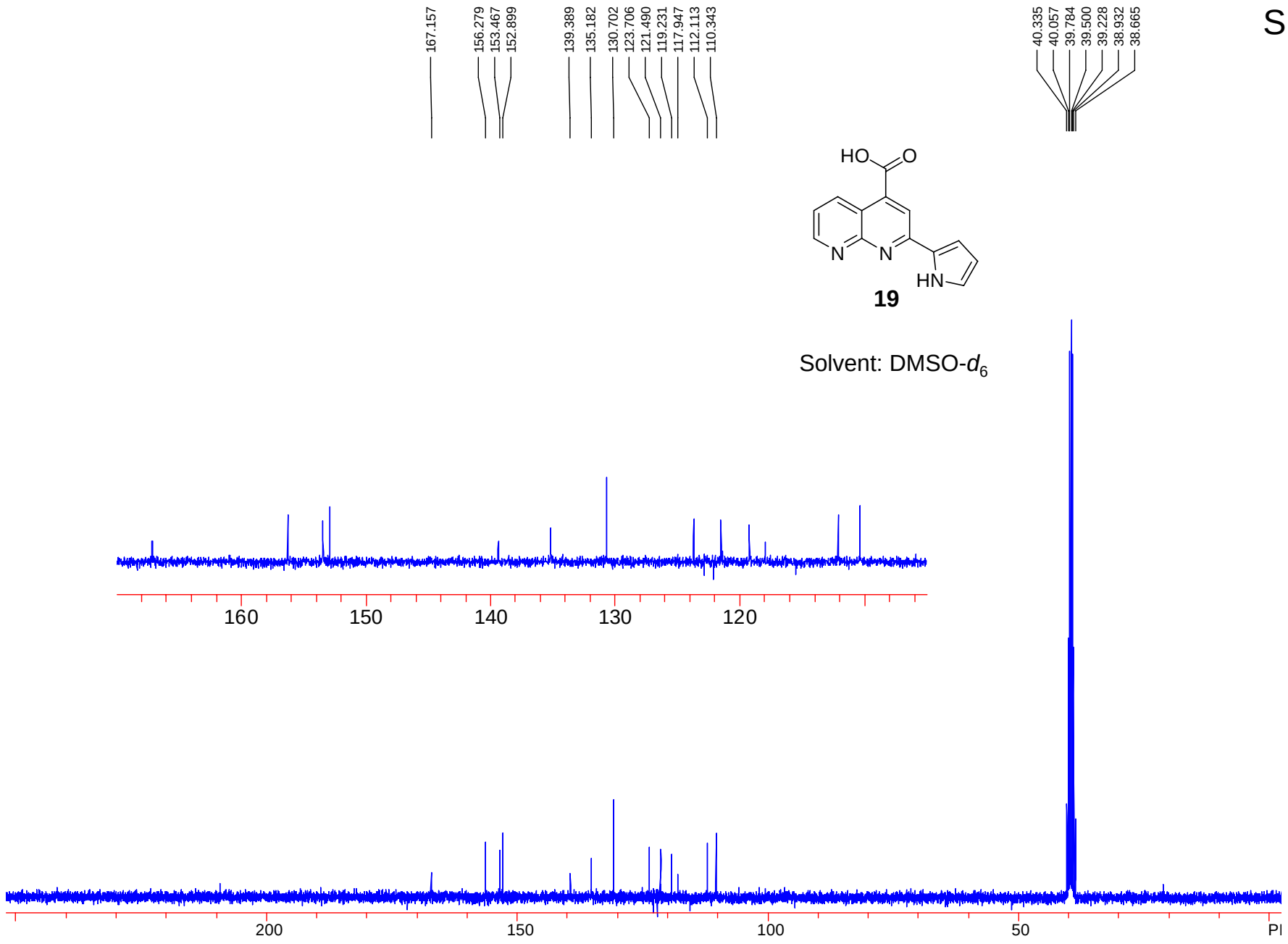
Solvent: $D_2O/CD_3OD$
with added KOH





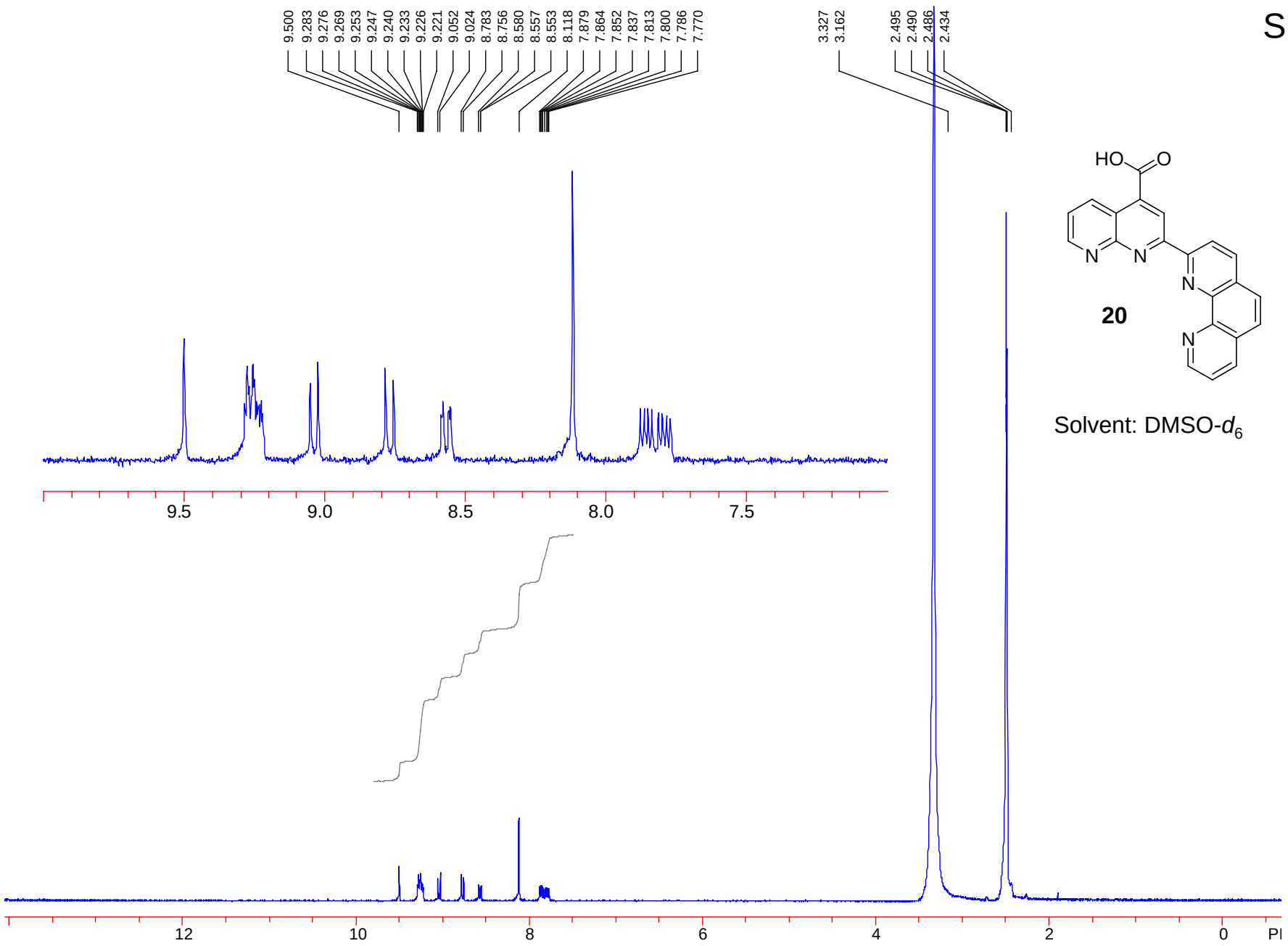

**19**

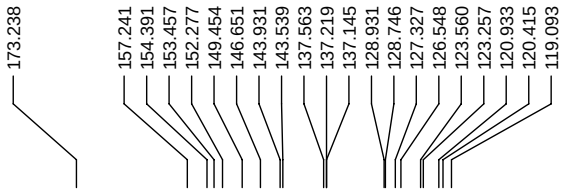
Solvent: DMSO-$d_6$

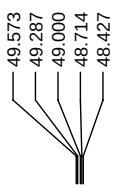


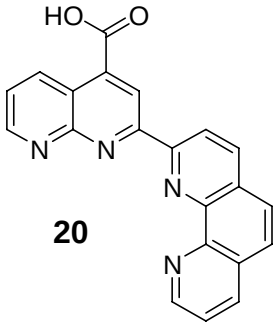

**19**

Solvent: DMSO-$d_6$


9.500
9.283
9.276
9.269
9.253
9.247
9.240
9.233
9.226
9.221
9.052
9.024
8.783
8.756
8.580
8.557
8.553
8.118
7.879
7.864
7.852
7.837
7.813
7.800
7.786
7.770
3.327
3.162
2.495
2.490
2.486
2.434
HO
O
N
N
N
N
20
Solvent: DMSO-$d_6$
9.5
9.0
8.5
8.0
7.5
12
10
8
6
4
2
0
PI

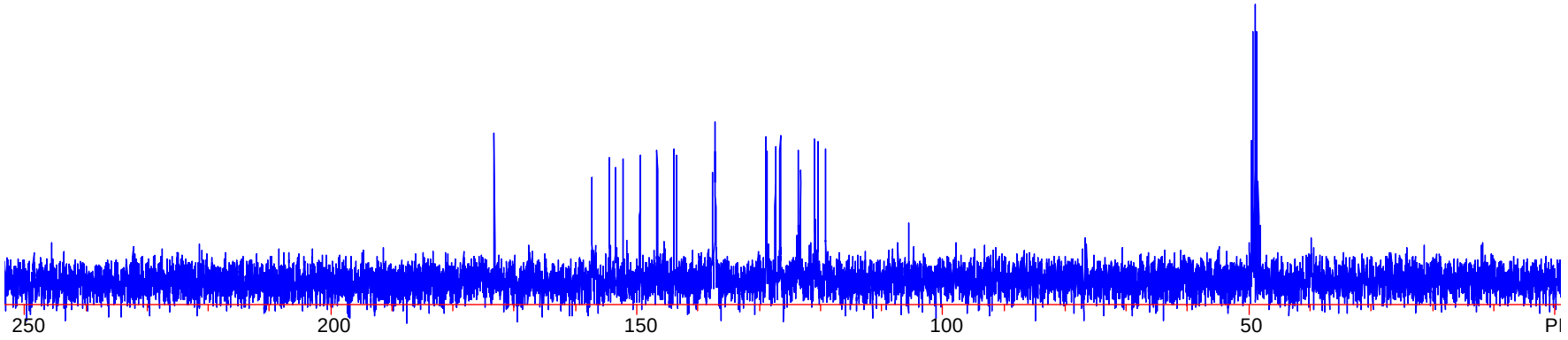


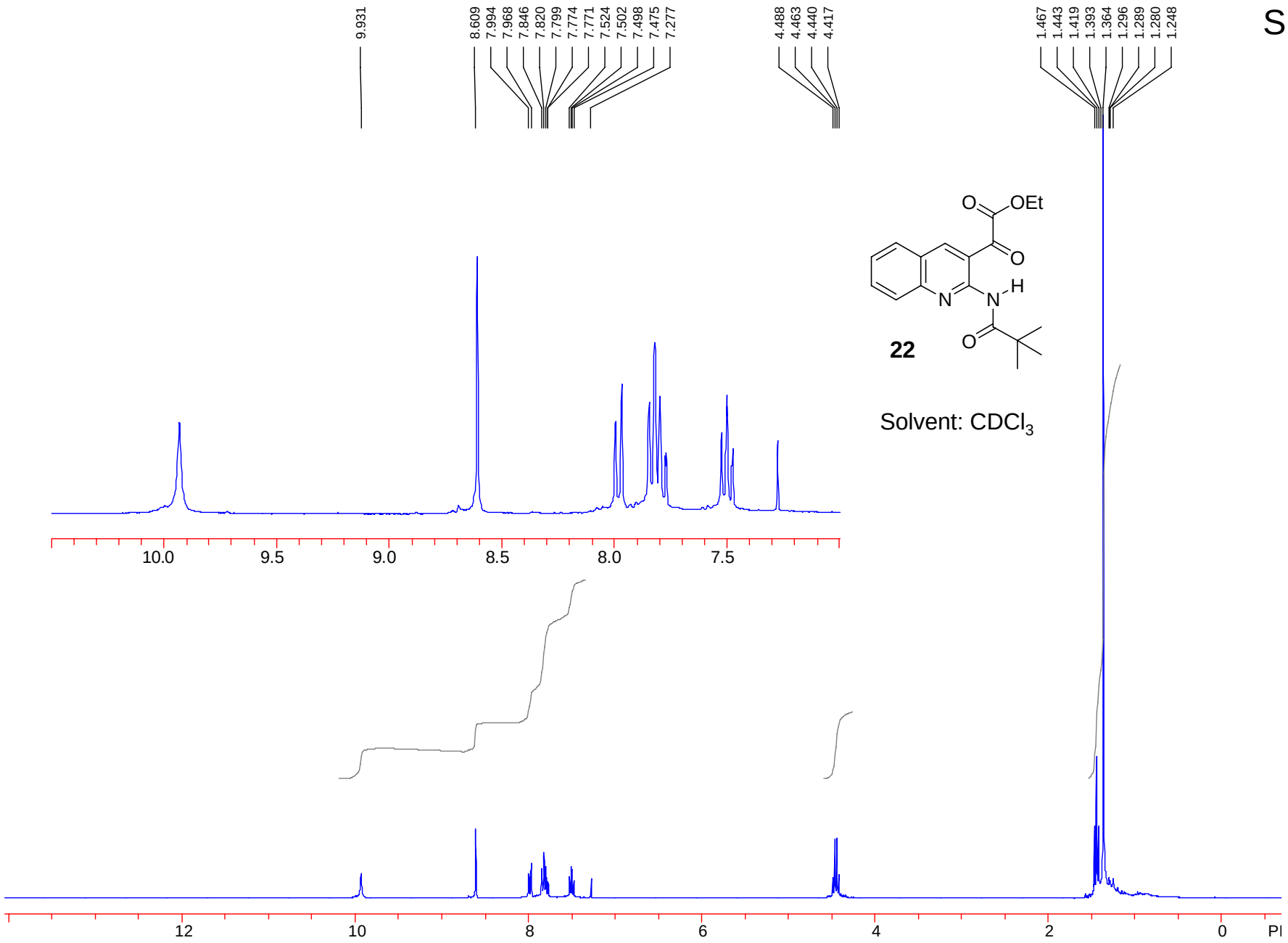



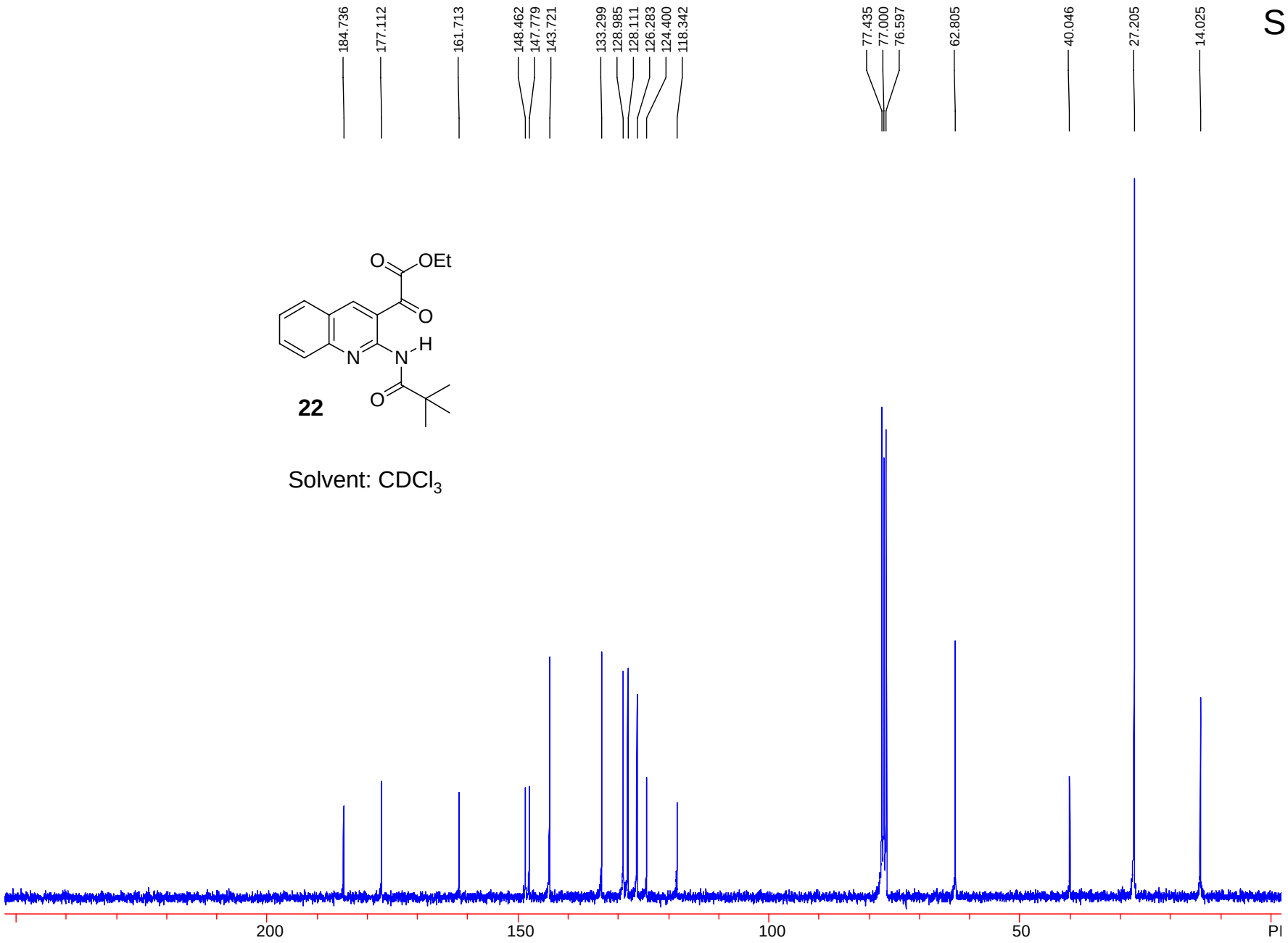



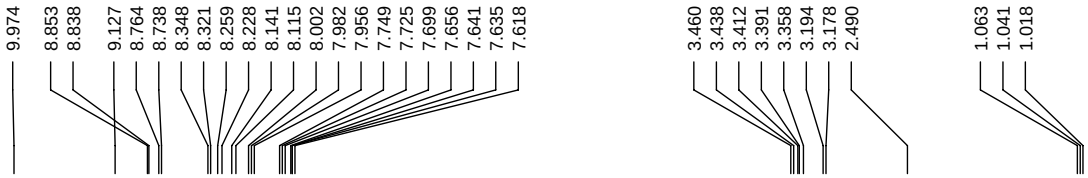

**20**

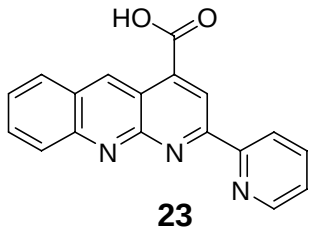
Solvent: $D_2O/CD_3OD$ with added KOH




9.931
8.609
7.994
7.968
7.846
7.820
7.799
7.774
7.771
7.524
7.502
7.498
7.475
7.277
4.488
4.463
4.440
4.417
1.467
1.443
1.419
1.393
1.364
1.296
1.289
1.280
1.248
O
OEt
O
N
N
H
O
22
Solvent: CDCl3
10.0
9.5
9.0
8.5
8.0
7.5
12
10
8
6
4
2
0
PI

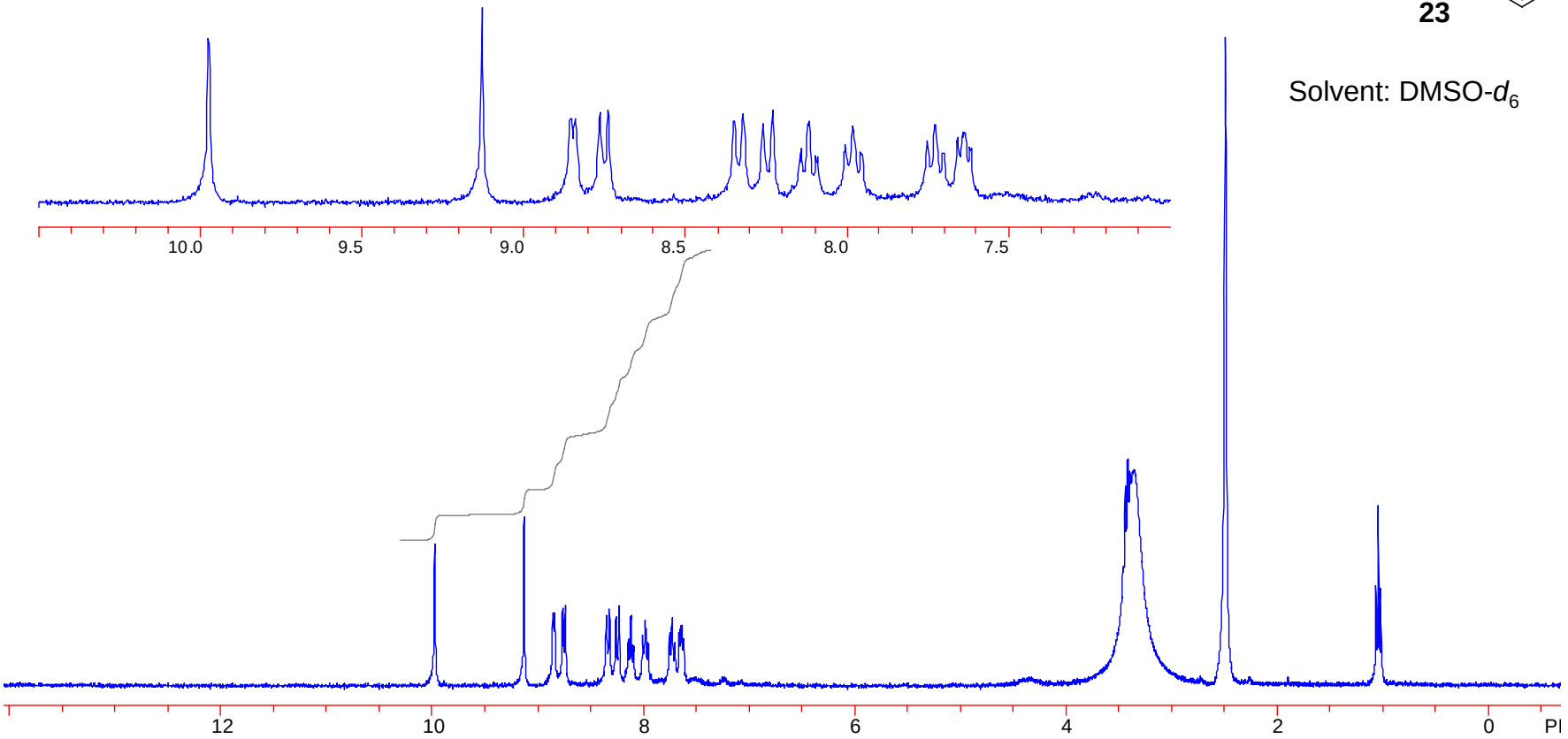

184.736
177.112
161.713
148.462
147.779
143.721
133.299
128.985
128.111
126.283
124.400
118.342
77.435
77.000
76.597
62.805
40.046
27.205
14.025
O
OEt
O
N
N
H
O
22
Solvent: CDCl3
200
150
100
50
Pl

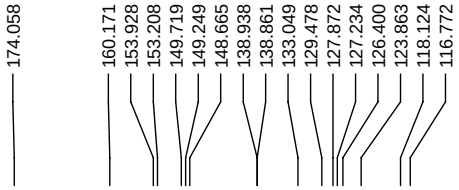


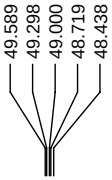



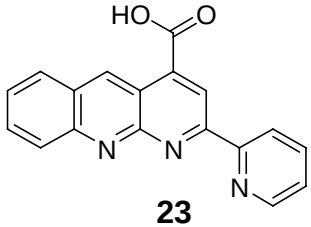

**23**

Solvent: DMSO-$d_6$



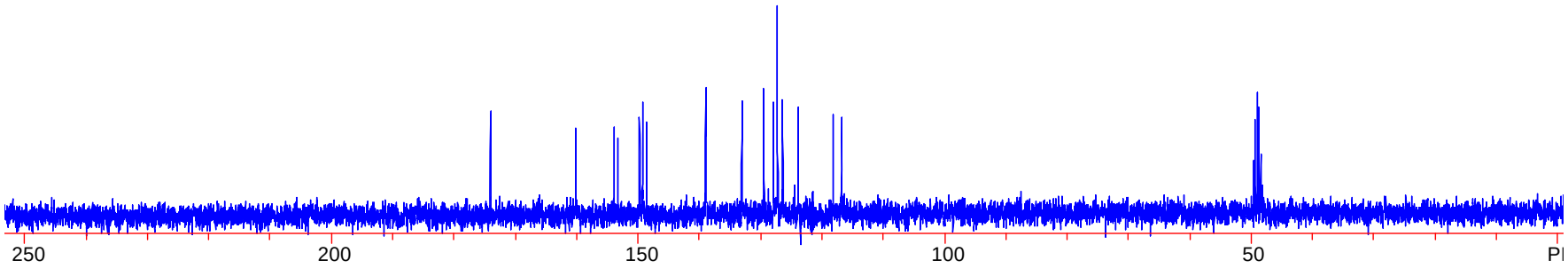


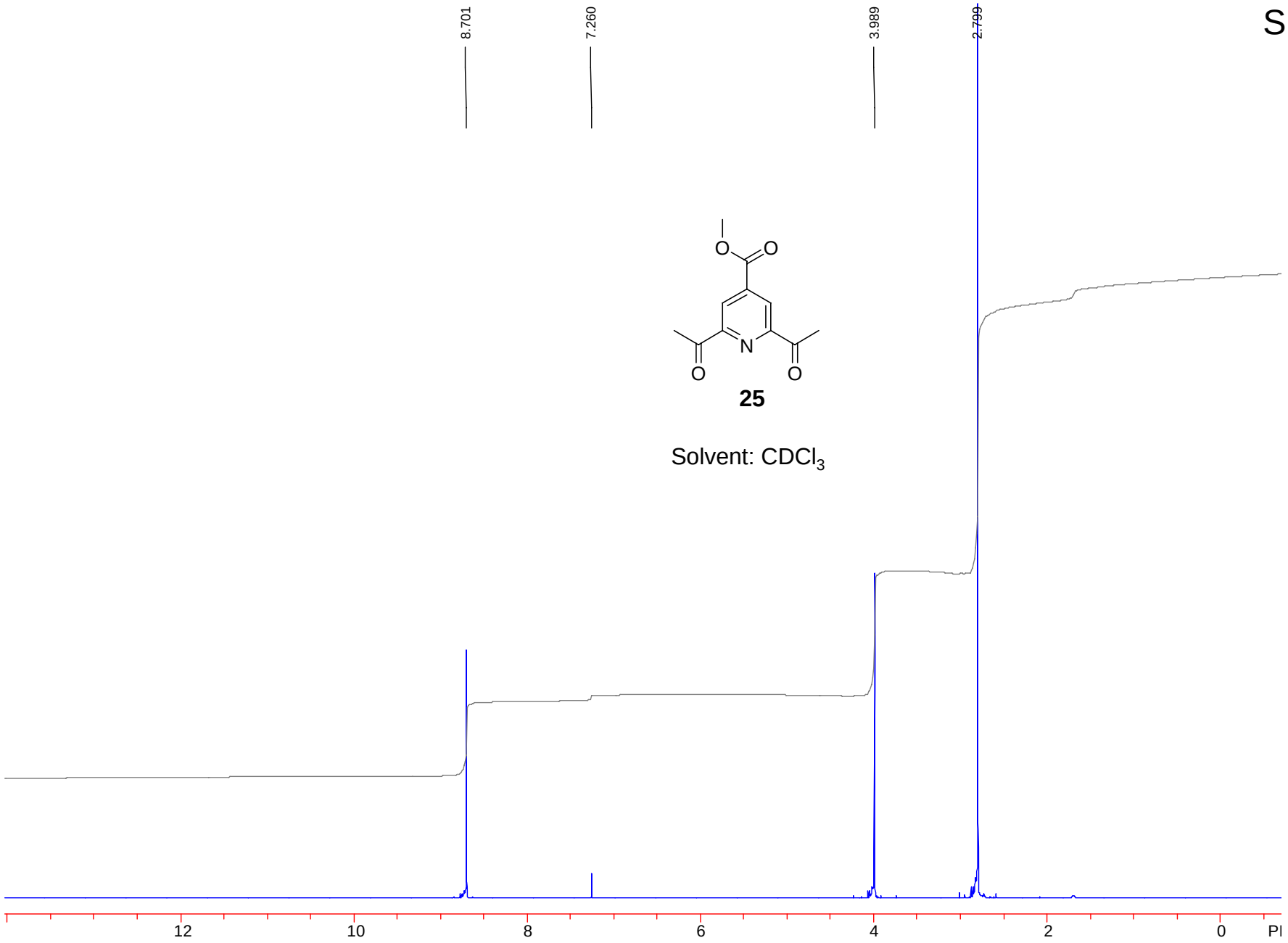




**23**

Solvent: $D_2O/CD_3OD$
with added KOH

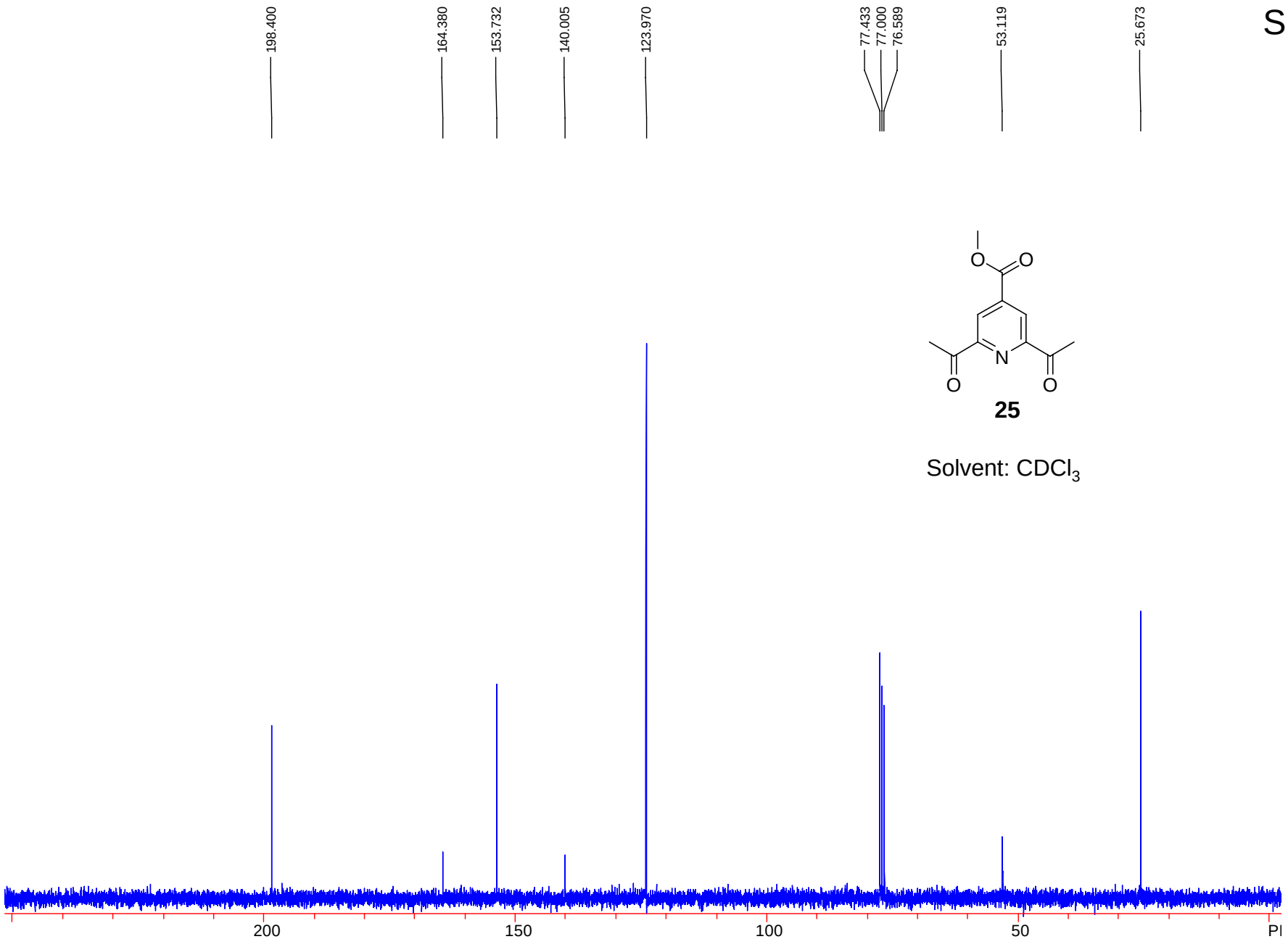


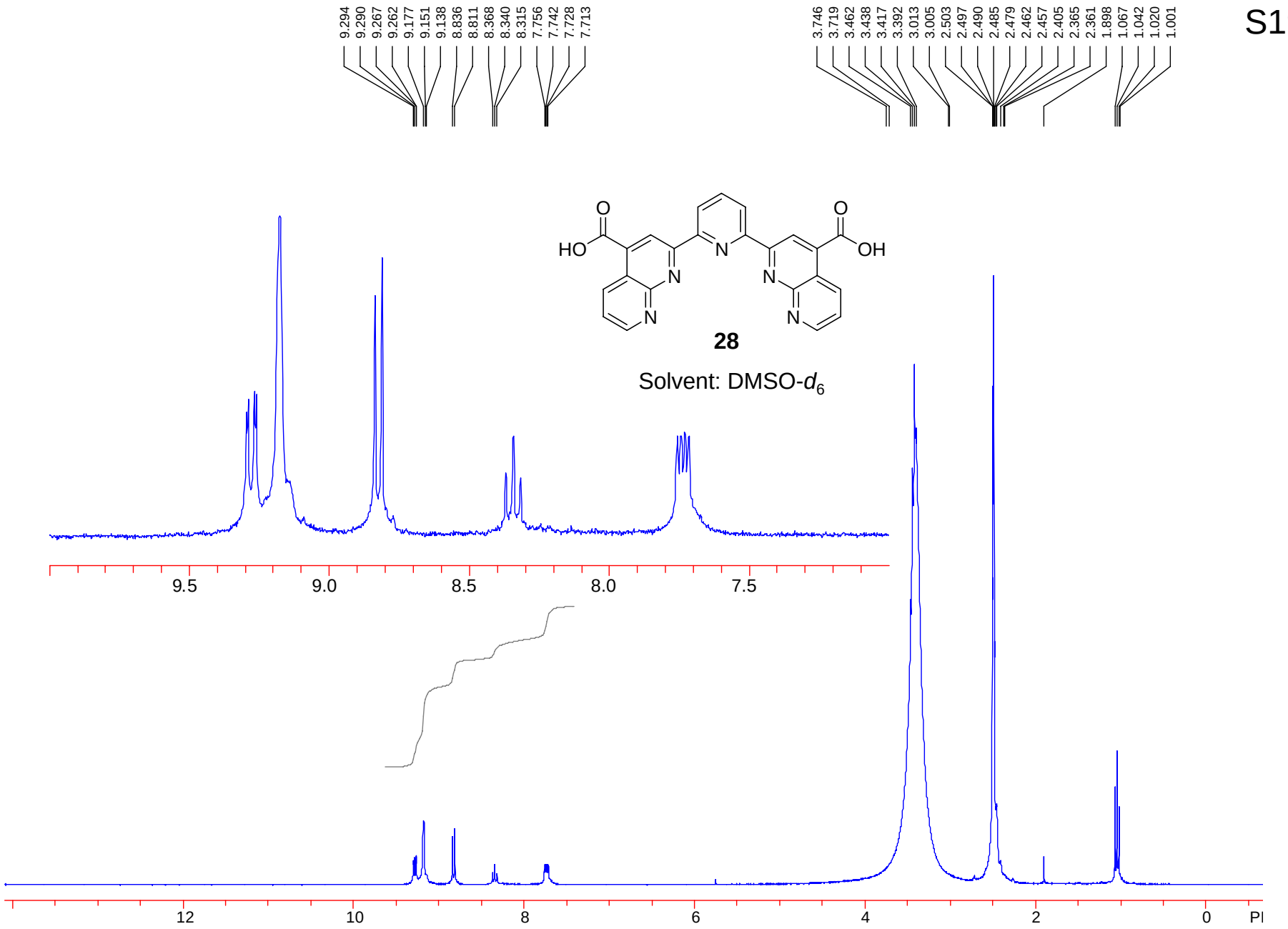


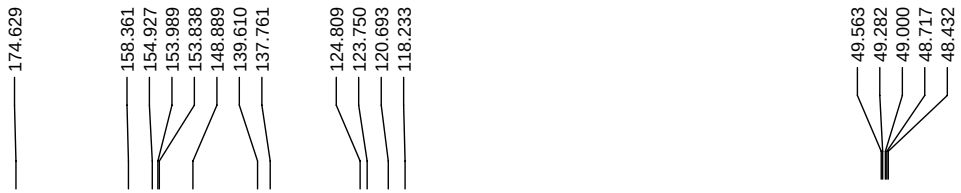


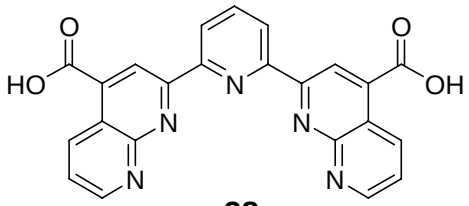

**25**

Solvent: $CDCl_3$


198.400
164.380
153.732
140.005
123.970
77.433
77.000
76.589
53.119
25.673
O
O
N
O
O
25
Solvent: CDCl3
200
150
100
50

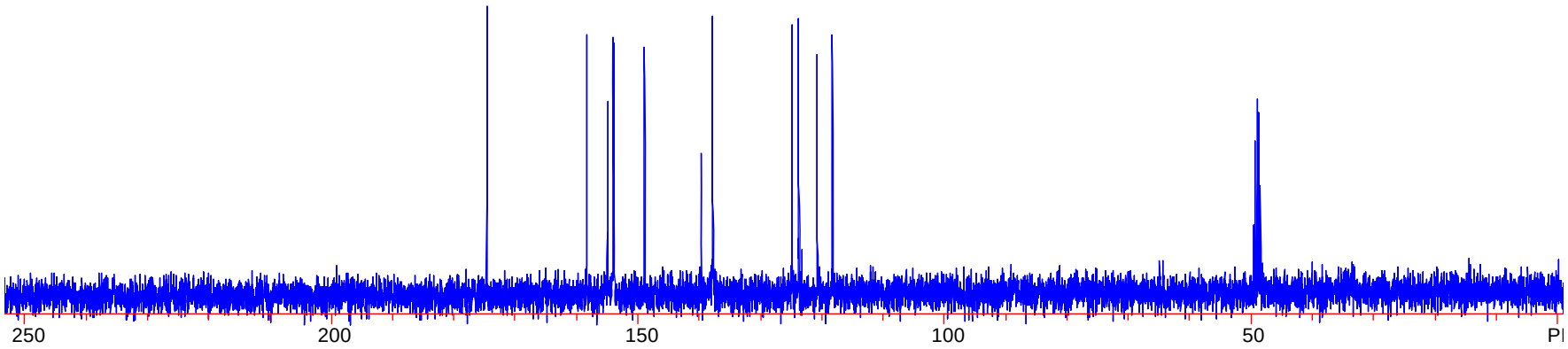

9.294
9.290
9.267
9.262
9.177
9.151
9.138
8.836
8.811
8.368
8.340
8.315
7.756
7.742
7.728
7.713
3.746
3.719
3.462
3.438
3.417
3.392
3.013
3.005
2.503
2.497
2.490
2.485
2.479
2.462
2.457
2.405
2.365
2.361
1.898
1.067
1.042
1.020
1.001
HO
O
N
N
N
N
O
OH
28
Solvent: DMSO-$d_6$
9.5
9.0
8.5
8.0
7.5
12
10
8
6
4
2
0
PI

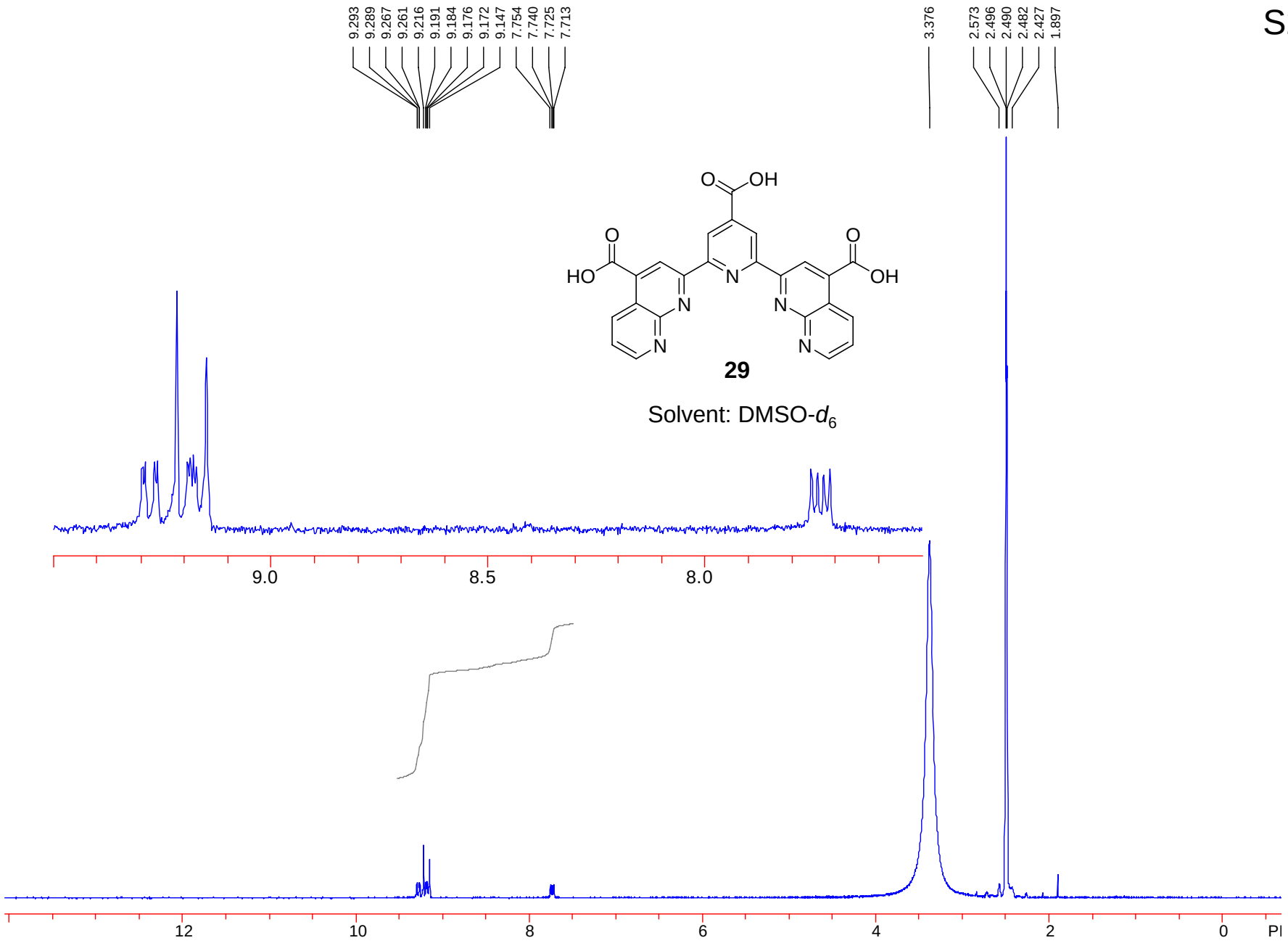


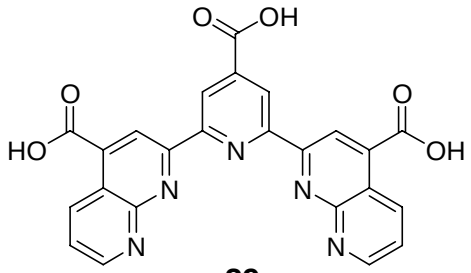




**28**

Solvent: $D_2O/CD_3OD$
with added KOH

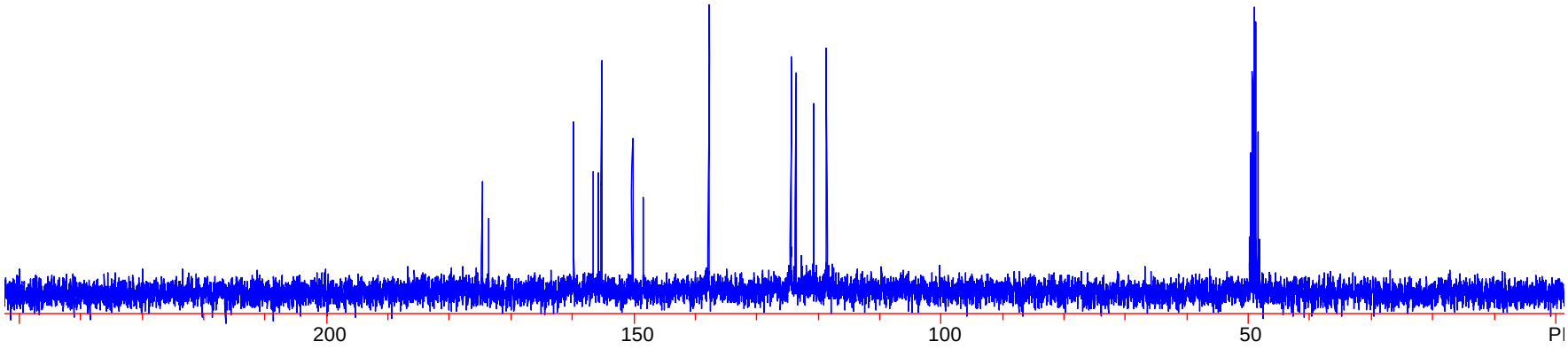


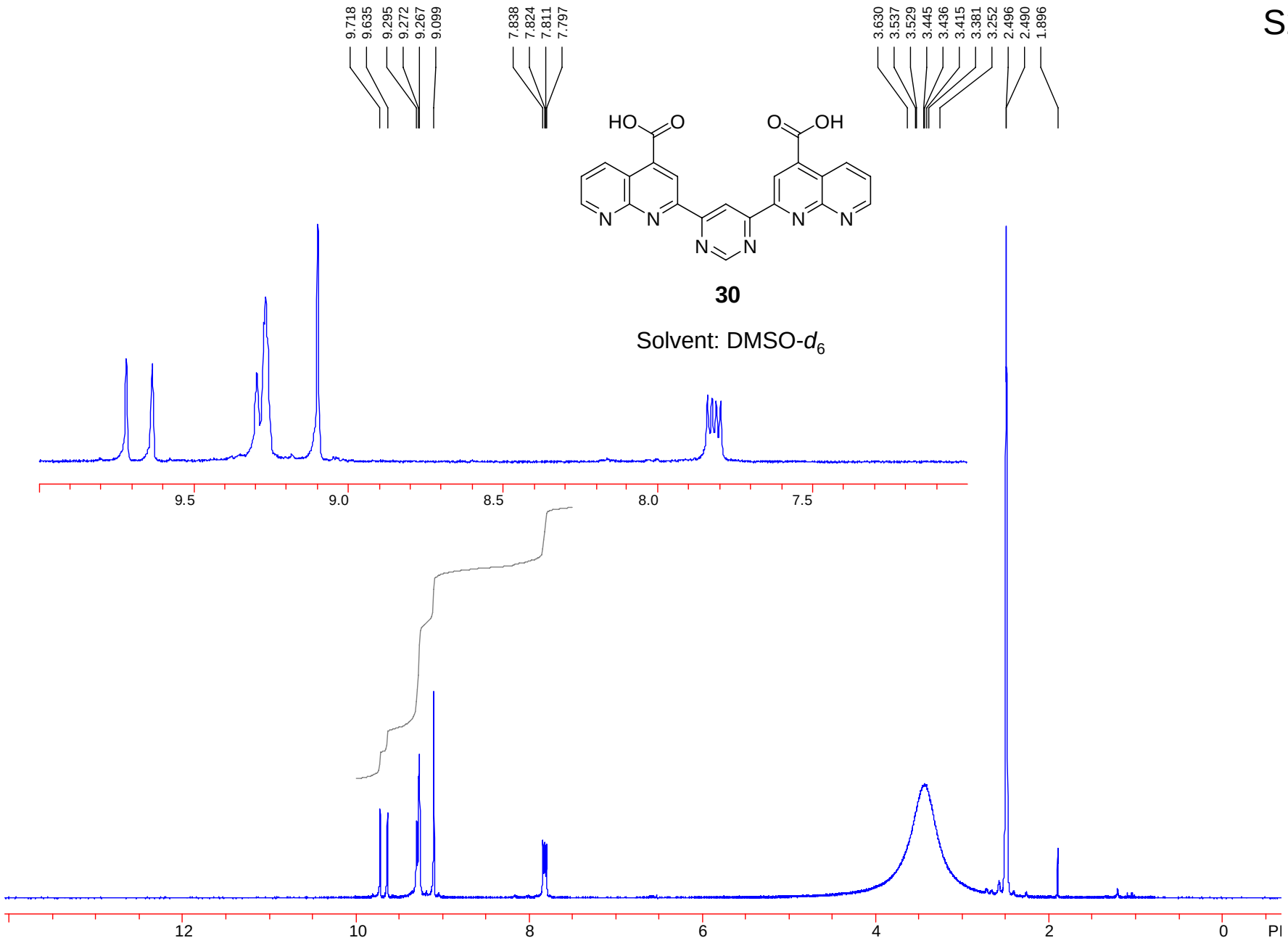

9.293
9.289
9.267
9.261
9.216
9.191
9.184
9.176
9.172
9.147
7.754
7.740
7.725
7.713
3.376
2.573
2.496
2.490
2.482
2.427
1.897
O
OH
HO
O
N
N
N
N
O
OH
29
Solvent: DMSO-$d_6$
9.0
8.5
8.0
12
10
8
6
4
2
0
PI


**29**

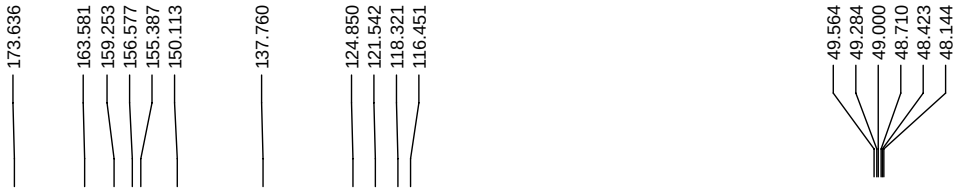
Solvent: $D_2O/CD_3OD$
with added KOH

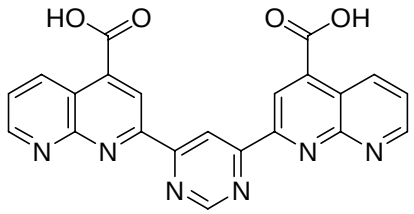





**30**

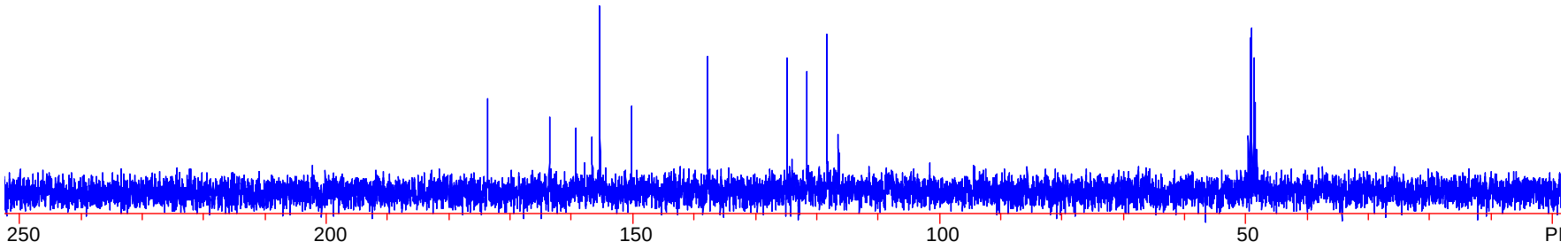
Solvent: DMSO-$d_6$

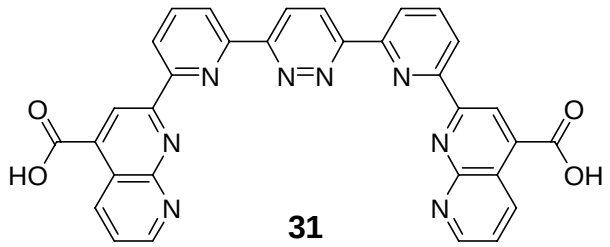



**30**

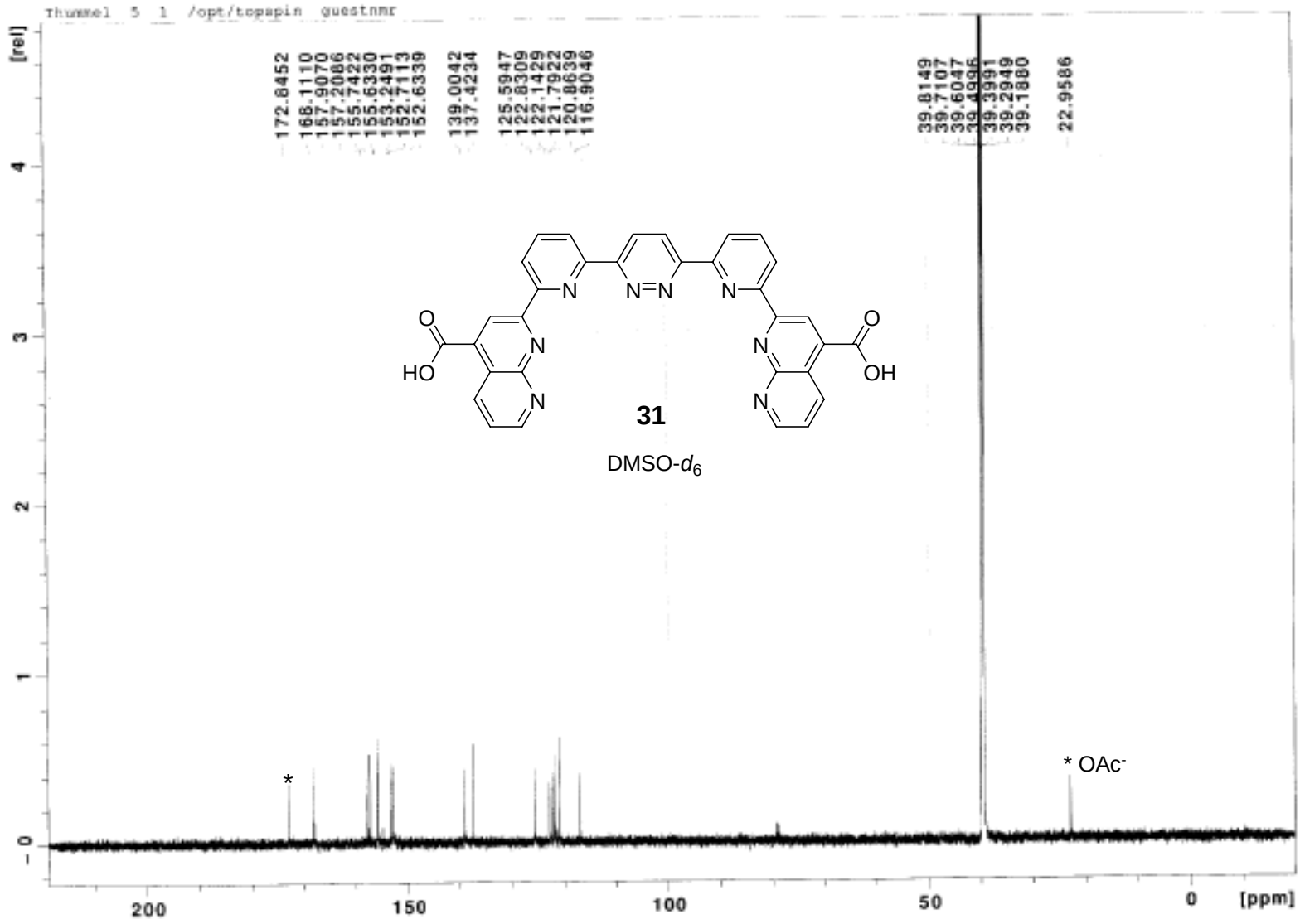
Solvent: $D_2O/CD_3OD$
with added KOH






**31**

Solvent: DMSO-$d_6$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39.2949
39.1880
22.9586
HO
O
N
N=N
N
OH
31
DMSO-$d_6$
*
* OAc-
200
150
100
50
0
[ppm]

**2-(Pyrazin-2′-yl)-1,8-naphthyridine-4-carboxylic acid (18).** The synthetic procedure as described for **4** was followed. The mixture of 2-acetylpyrazine (**14**, 82 mg, 0.67 mmol), **10** (222 mg, 0.80 mmol), KOH (220 mg, 3.93 mmol), and EtOH (15 mL) was refluxed for 20 h. Treatment of the crude product with water, $CH_2Cl_2$, and HOAc gave **18** as a colorless solid (133 mg, 79%), mp > 280 °C: $^1$H NMR (DMSO-$d_6$) δ 9.76 (s, 1H), 9.27-9.22 (m, 2H), 8.99 (s, 1H), 8.89-8.85 (m, 2H), 7.80 (dd, $J$ = 4.2, 8.4 Hz, 1H); $^{13}$C NMR ($D_2O$/$CD_3OD$/KOH) δ 173.4, 156.5, 155.0, 154.9, 150.0, 149.5, 145.5, 145.0, 143.6, 137.6, 124.3, 120.7, 118.0; IR (ATR, cm$^{-1}$) ν 1716, 1586. Anal. Calcd for $C_{13}H_8N_4O_2 \cdot 0.5\ H_2O$ (261.24) C, 59.77; H, 3.47; N, 21.45. Found: C, 59.83; H, 3.49; N, 21.38.

**2-(1′*H*-pyrrol-2′-yl)-1,8-naphthyridine-4-carboxylic acid (19).** The synthetic procedure as described for **4** was followed. The reaction of **10** (138 mg, 0.50 mmol), 2-acetylpyrrole (**15**, 55 mg, 0.50 mmol), and KOH (108 mg, 1.92 mmol) in EtOH (10 mL) for 40 h gave **19** as a yellow precipitate. Treatment of the crude product with water, $CH_2Cl_2$, and HOAc gave a yellow solid (70 mg, 59%), mp 249-251 ºC: $^1$H NMR (DMSO-$d_6$) δ 11.95 (s, 1H), 9.01 (dd, $J$ = 1.8, 4.5 Hz, 1H), 8.98 (dd, $J$ = 1.8, 8.1 Hz, 1H), 8.29 (s, 1H), 7.55 (dd, $J$ = 4.5, 8.1 Hz, 1H), 7.13 (m, 1H), 7.03 (m, 1H), 6.25 (m, 1H); $^{13}$C NMR (DMSO-$d_6$) δ 167.2, 156.3, 153.4, 152.9, 139.4, 135.2, 130.7, 123.7, 121.5, 119.2, 118.0, 112.1, 110.3; IR (ATR, cm$^{-1}$) ν 1617, 1571. Anal. Calcd for $C_{13}H_9N_3O_2 \cdot 1.2H_2O$ (260.85): C, 59.86; H, 4.40; N, 16.11. Found: C, 60.12; H, 4.20; N, 15.95.

**2-(1′,10′-Phenanthrolin-2′-yl)-1,8-naphthyridine-4-carboxylic acid (20).** The synthetic procedure as described for **4** was followed. The overnight reaction of **10** (138 mg, 0.50 mmol), 2-acetyl-1,10-phenanthroline (80 mg, 0.36 mmol), and KOH (110 mg, 1.96 mmol) in refluxing EtOH (10 mL) produced a yellow precipitate. Treatment of the crude product with water, $CH_2Cl_2$, and HOAc gave **20** as a colorless solid (105 mg, 83%), mp > 300 ºC: $^1$H NMR (DMSO-$d_6$) δ 9.50 (s, 1H), 9.28-9.22 (m, 3H), 9.04 (d, $J$ = 8.4 Hz, 1H), 8.77 (d, $J$ = 8.1 Hz, 1H), 8.57 (dd, $J$ = 1.2, 8.1 Hz, 1H), 8.12 (s, 2H), 7.86 (dd, $J$ = 4.5, 8.1 Hz, 1H), 7.79 (dd, $J$ = 4.2, 8.4 Hz, 1H); $^{13}$C NMR ($D_2O$/$CD_3OD$/KOH) δ 173.2, 157.2, 154.4, 153.4, 152.3, 149.4, 146.7, 143.9, 143.5, 137.6, 137.2, 137.1, 128.9, 128.7, 127.3, 126.5, 123.6, 123.2, 120.9, 120.4, 119.1; IR (ATR, cm$^{-1}$) ν 1658, 1631, 1596, 1572, 1533. Anal. Calcd for $C_{21}H_{12}N_4O_2 \cdot 0.8H_2O$ (366.76): C, 68.77; H, 3.74; N, 15.28. Found: C, 68.52; H, 3.48; N, 15.21.