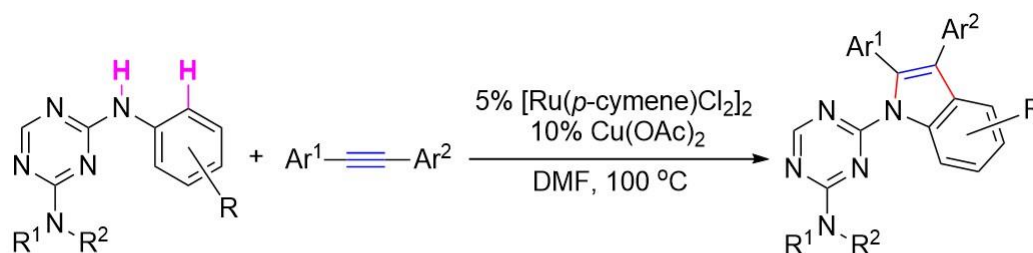


Ruthenium Catalyzed Oxidative Synthesis of *N*-(2-triazine)indoles by C-H Activation

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* Correspondence: zengming@zjut.edu.cn



- 17 examples yields up to 76%
- Triazine ring as directing group
- Lower loading of oxidant

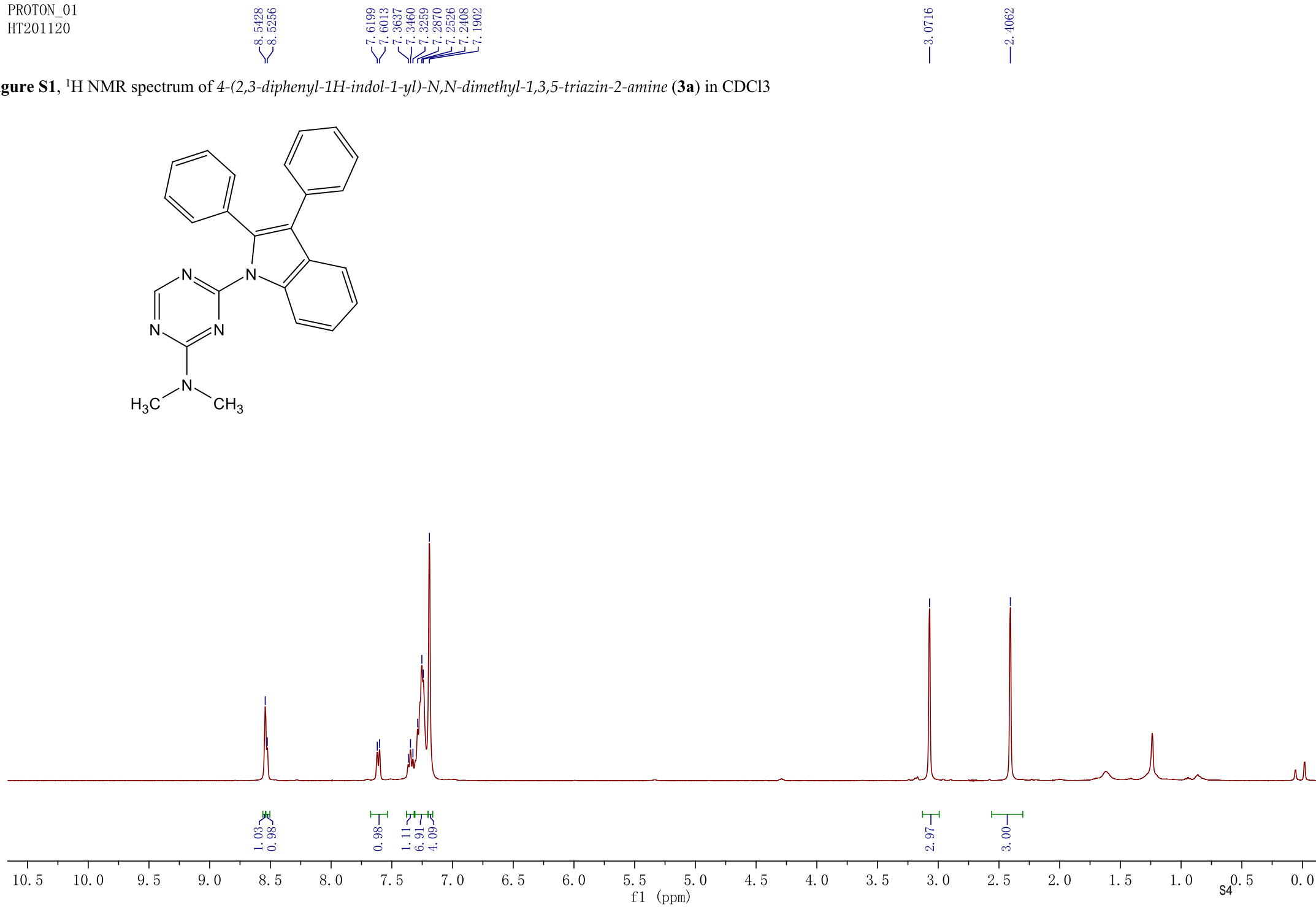
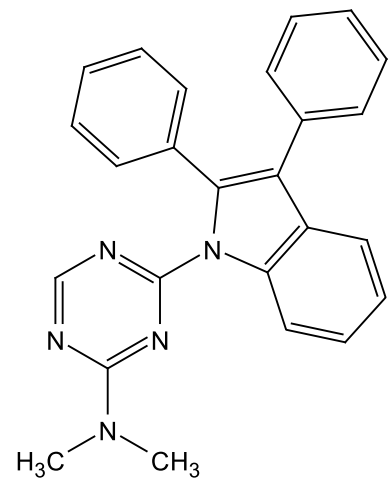
1,3,5 triazines, especially indole functionalized triazine derivatives, exhibit excellent activities, such as anti-tumor, antibacterial, and anti-inflammatory activities. Traditional methods for the synthesis of *N*-(2-triazine) indoles suffer from unstable materials and tedious operations. Transition-metal-catalyzed C-C/C-N coupling provides a powerful protocol for the synthesis of indoles by the C-H activation strategy. Here, we report the efficient ruthenium-catalyzed oxidative synthesis of *N*-(2-triazine) indoles by C-H activation from alkynes and various substituted triazine derivatives in a moderate to good yield, and all of the *N*-(2-triazine) indoles were characterized by ^1H NMR, ^{13}C NMR, and HRMS. This protocol can apply to the gram-scale synthesis of the *N*-(2-triazine) indole in a moderate yield. Moreover, the reaction is proposed to be performed via a six-membered ruthenacycle (II) intermediate, which suggests that the triazine ring could offer chelation assistance for the formation of *N*-(2-triazine) indoles.

The ^1H and ^{13}C spectra of compounds

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Figure S4	^{13}C spectra of 3b	S7
Figure S5	^1H spectra of 3c	S8
Figure S6	^{13}C spectra of 3c	S9
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Figure S8	^{13}C spectra of 3d	S11
Figure S9	^1H spectra of 3e	S12
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Figure S11	^1H spectra of 3f	S14
Figure S12	^{13}C spectra of 3f	S15
Figure S13	^1H spectra of 3g	S16
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Figure S15	^1H spectra of 3h	S18
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Figure S20	^{13}C spectra of 3j	S23
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Figure S22	^{13}C spectra of 3k	S25
Figure S23	^1H spectra of 3m	S26
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Figure S33	^1H spectra of 3r and 3r'	S36
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Figure S35	^1H spectra of 1a	S38
Figure S36	^{13}C spectra of 1a	S39
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Figure S43	The analysis of relative yield of the isomers 3r and 3r' by ^1H NMR.	S46

PROTON_01
HT201120



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20201221-C13-WHF-HT201120
CDC13

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162.9550

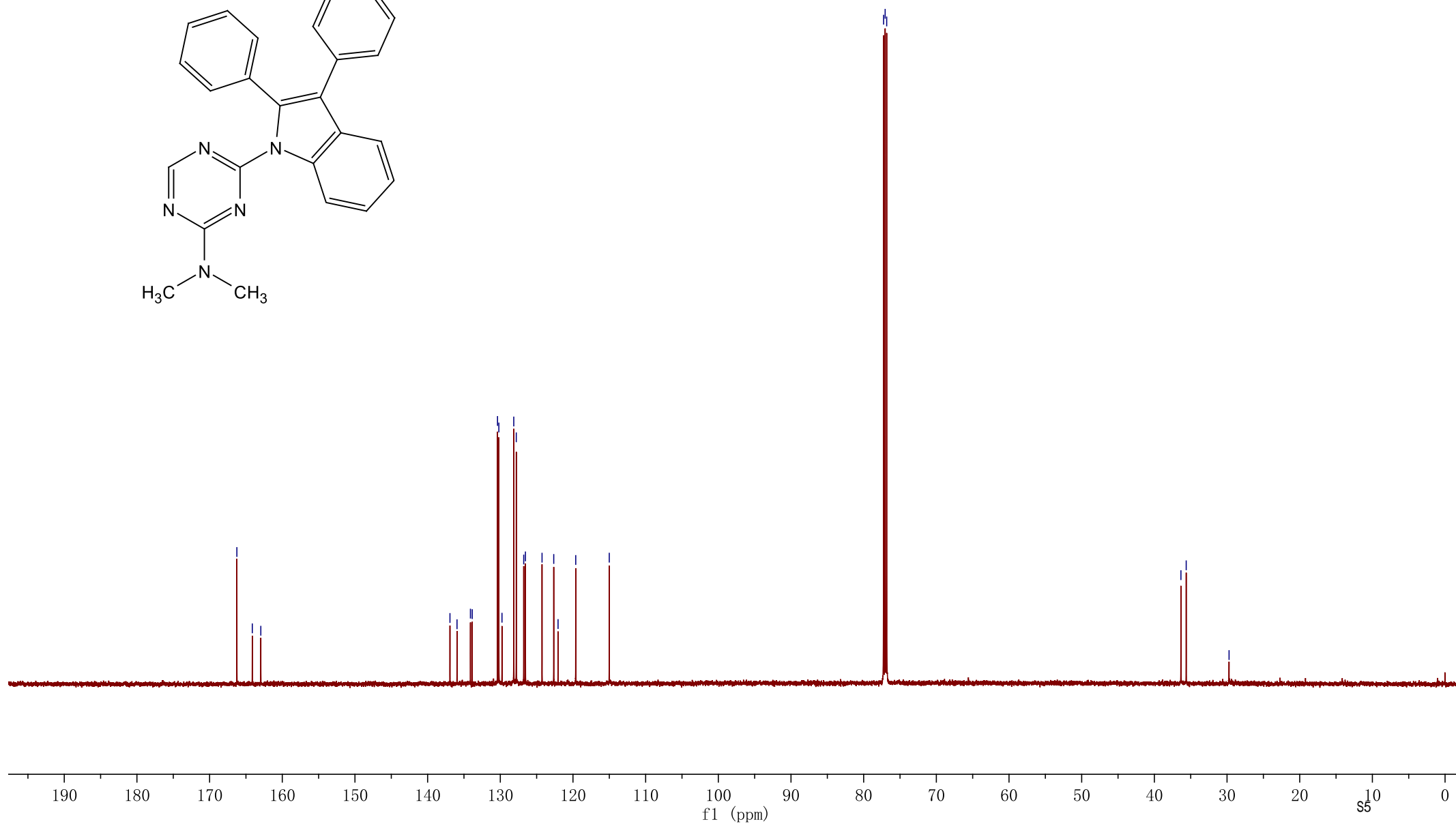
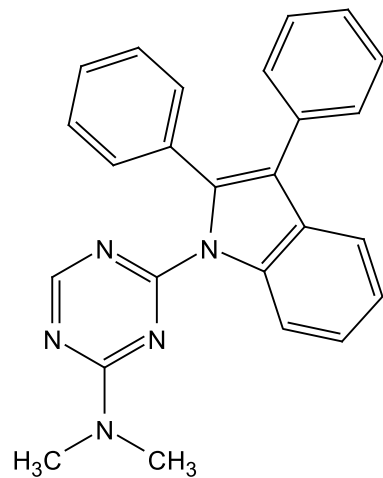
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133.8647
130.3848
130.2008
129.7703
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126.5456
124.2590
122.6470
122.0544
119.6210
115.0074

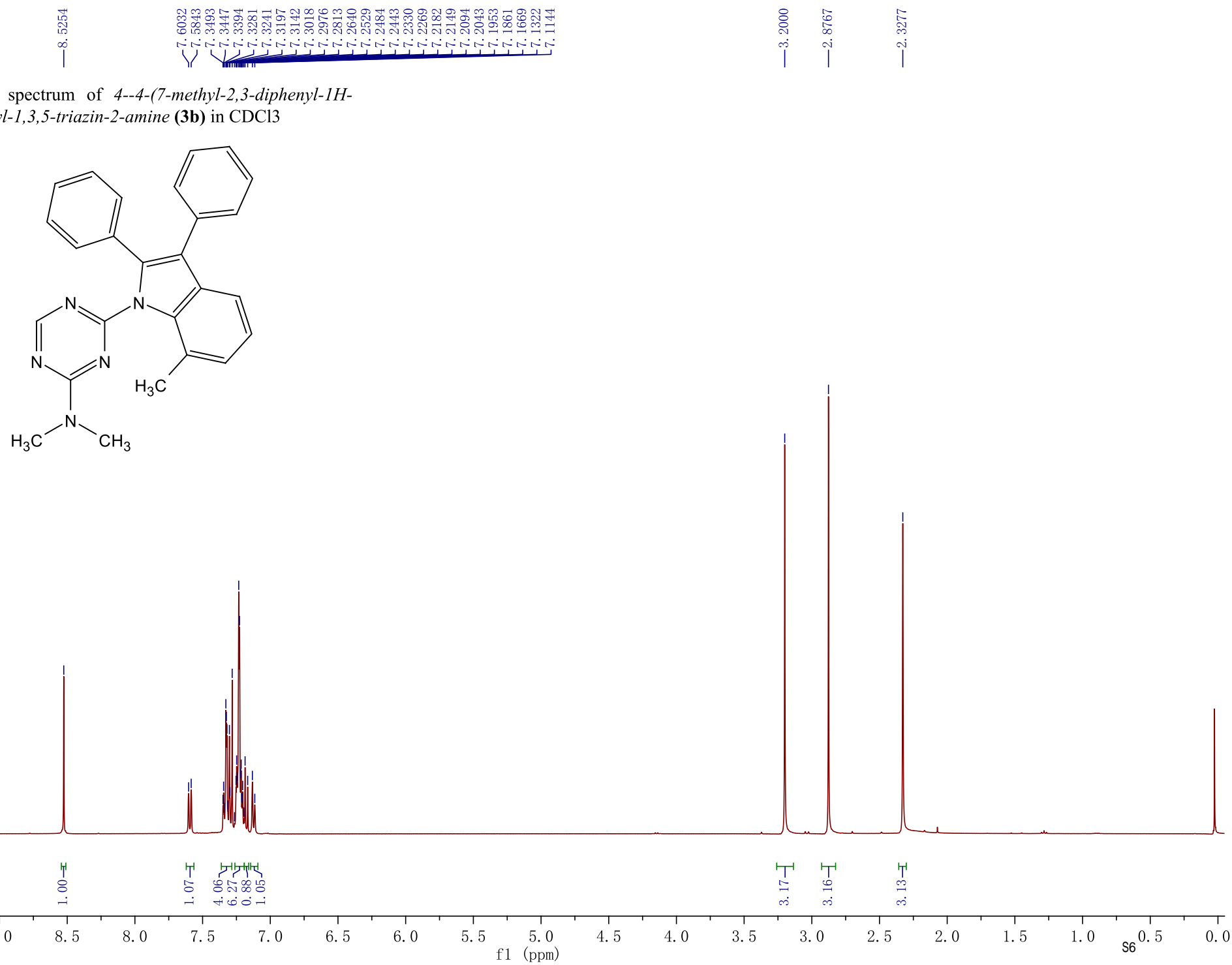
77.2571
77.0455
76.8338

36.3460
35.6192

29.7229

Figure S2, ^{13}C NMR spectrum of 4-(2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3a**) in CDCl_3





165.8925
164.5306
164.4068

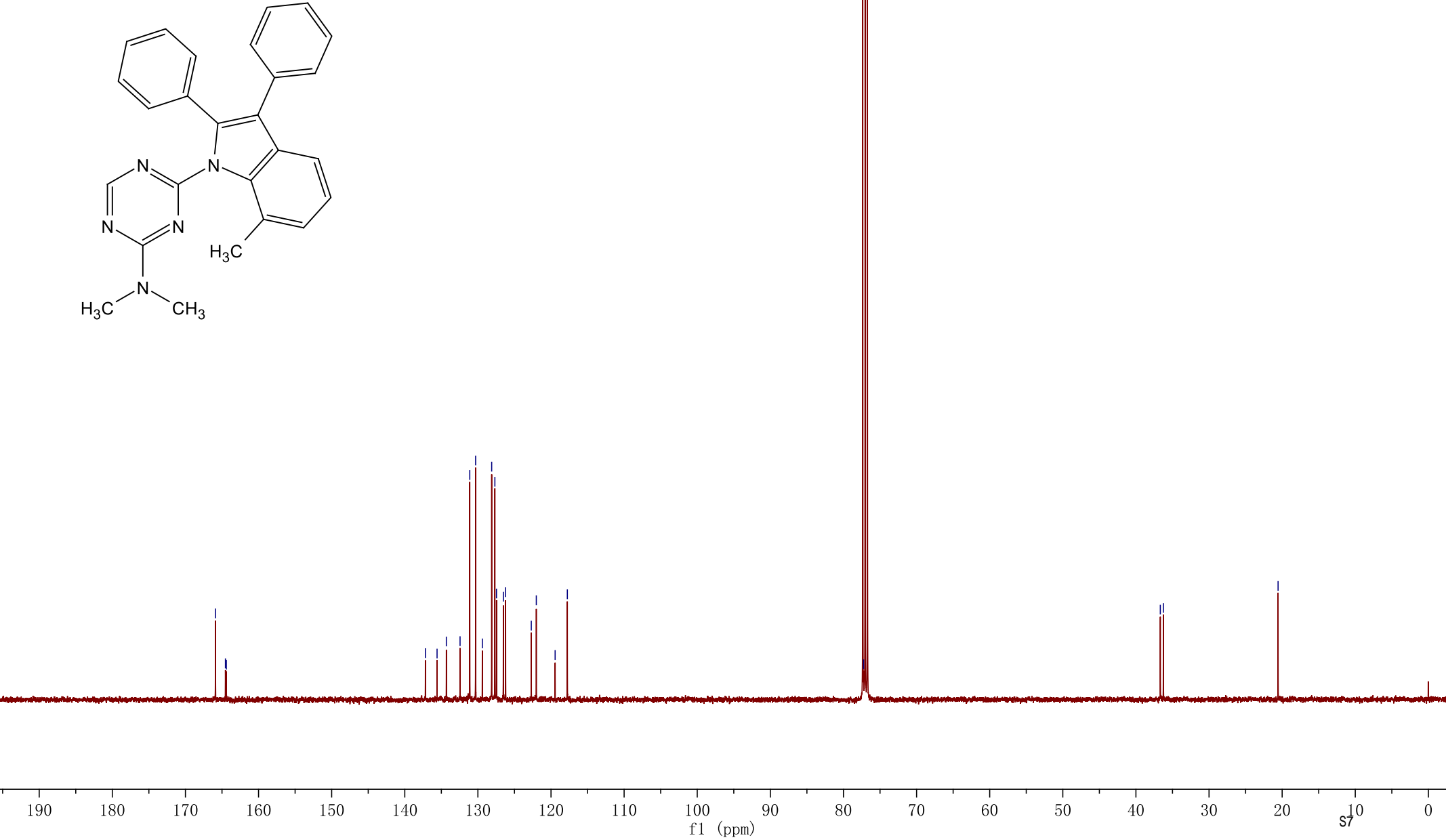
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130.3094
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128.1146
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127.4557
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126.2096
122.6984
122.0107
119.4366
117.7681

77.3593
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77.0417
76.7241

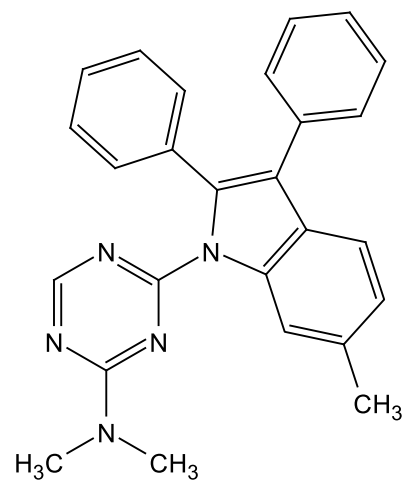
36.6652
36.2457

20.5575

Figure S4, ^{13}C NMR spectrum of 4--4-(7-methyl-2,3-diphenyl-1*H*-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3b**) in CDCl_3



PROTON_01
zm-55

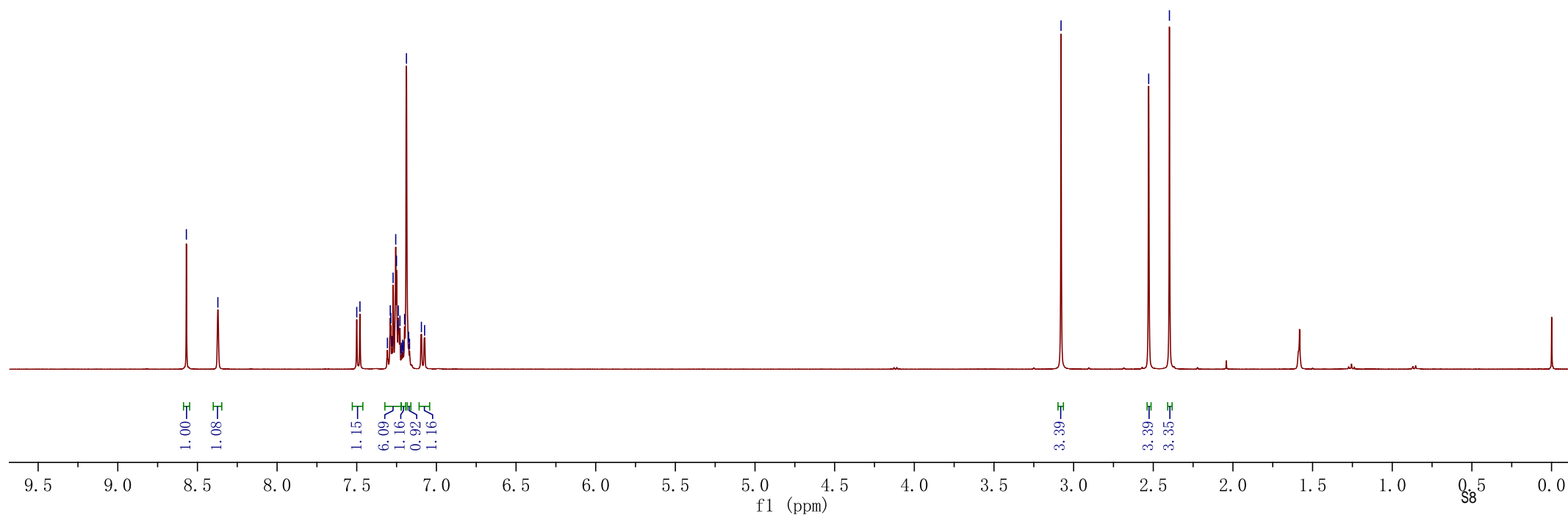


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8.3717
8.3006
7.4799
7.3075
7.2896
7.2861
7.2789
7.2718
7.2553
7.2505
7.2423
7.2385
7.2288
7.2204
7.2167
7.2121
7.2076
7.1997
7.1881
7.1741
7.1687
7.0941
7.0740

3.0790

2.5288
2.3987

Figure S5, ^1H NMR spectrum of *N,N*-dimethyl-4-(6-methyl-2,3-diphenyl-1*H*-indol-1-yl)-1,3,5-triazin-2-amine (**3c**) in CDCl_3



20210924-C13-WHF-55
20210924-C13-WHF-55
CDC13

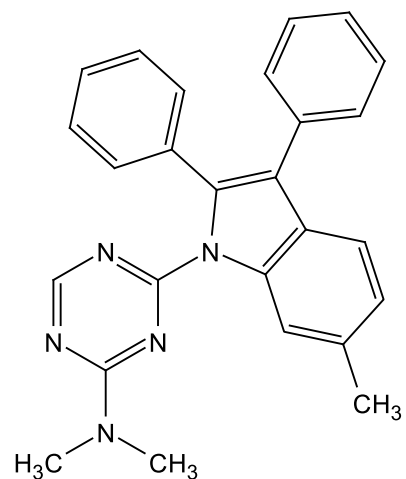
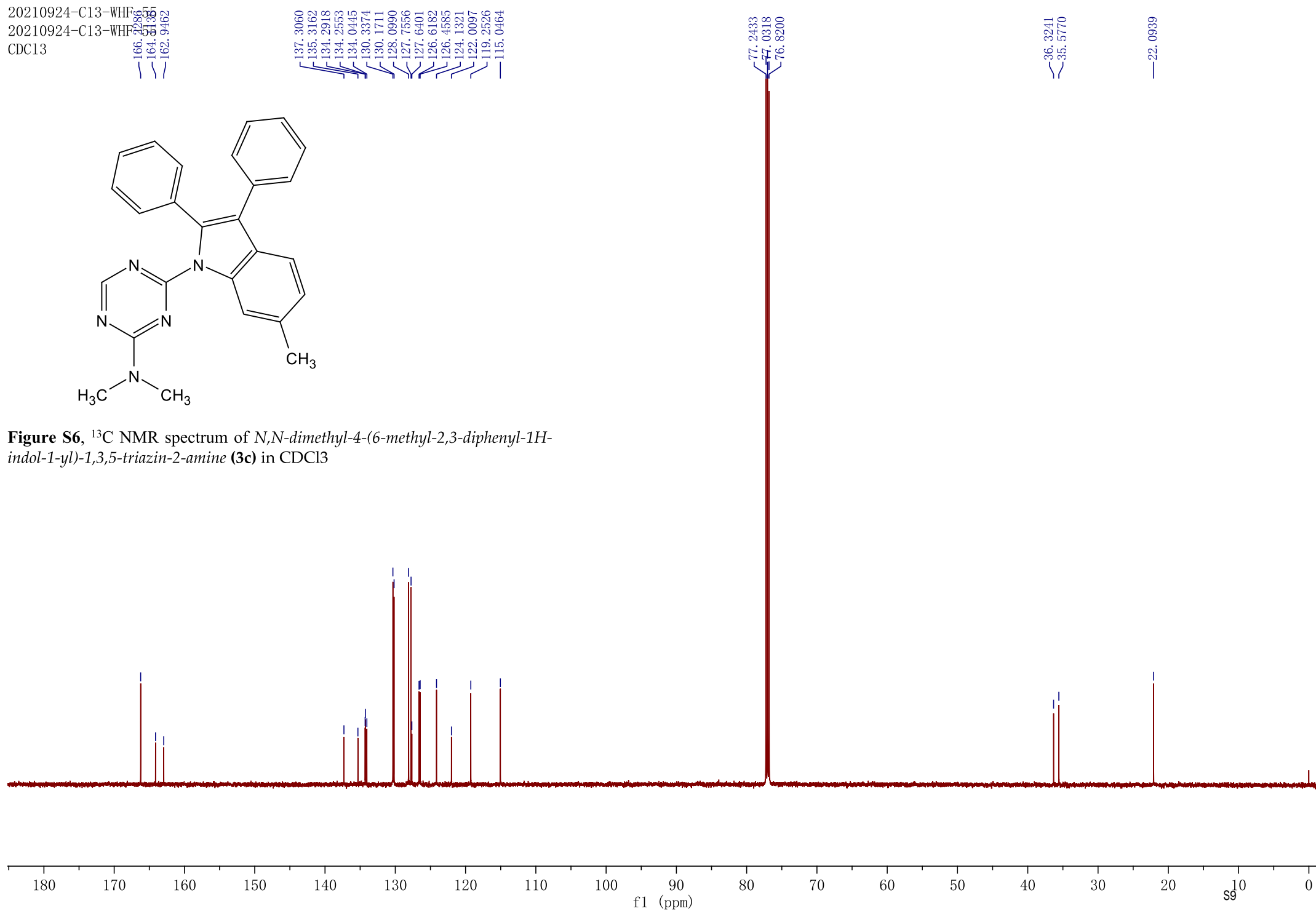


Figure S6, ^{13}C NMR spectrum of *N,N*-dimethyl-4-(6-methyl-2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-amine (**3c**) in CDCl_3



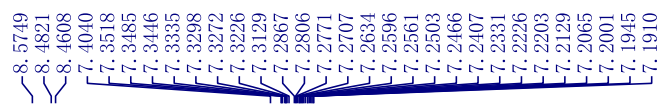
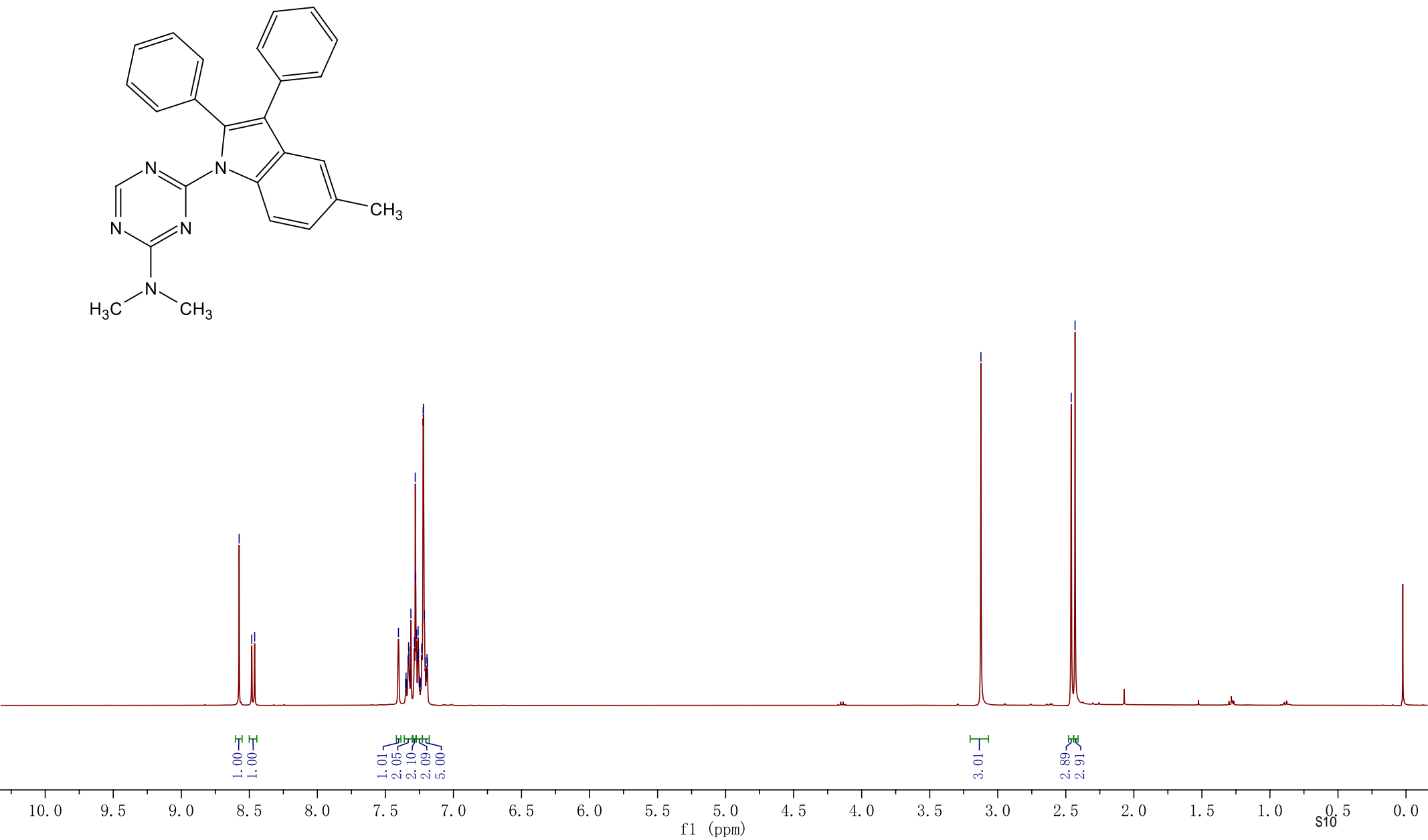


Figure S7, ¹H NMR spectrum of *N,N*-dimethyl-4-(5-methyl-2,3-diphenyl-1*H*-indol-1-yl)-1,3,5-triazin-2-amine (**3d**) in CDCl₃



20220117zm
F210607

165.8063
163.5539
162.7801

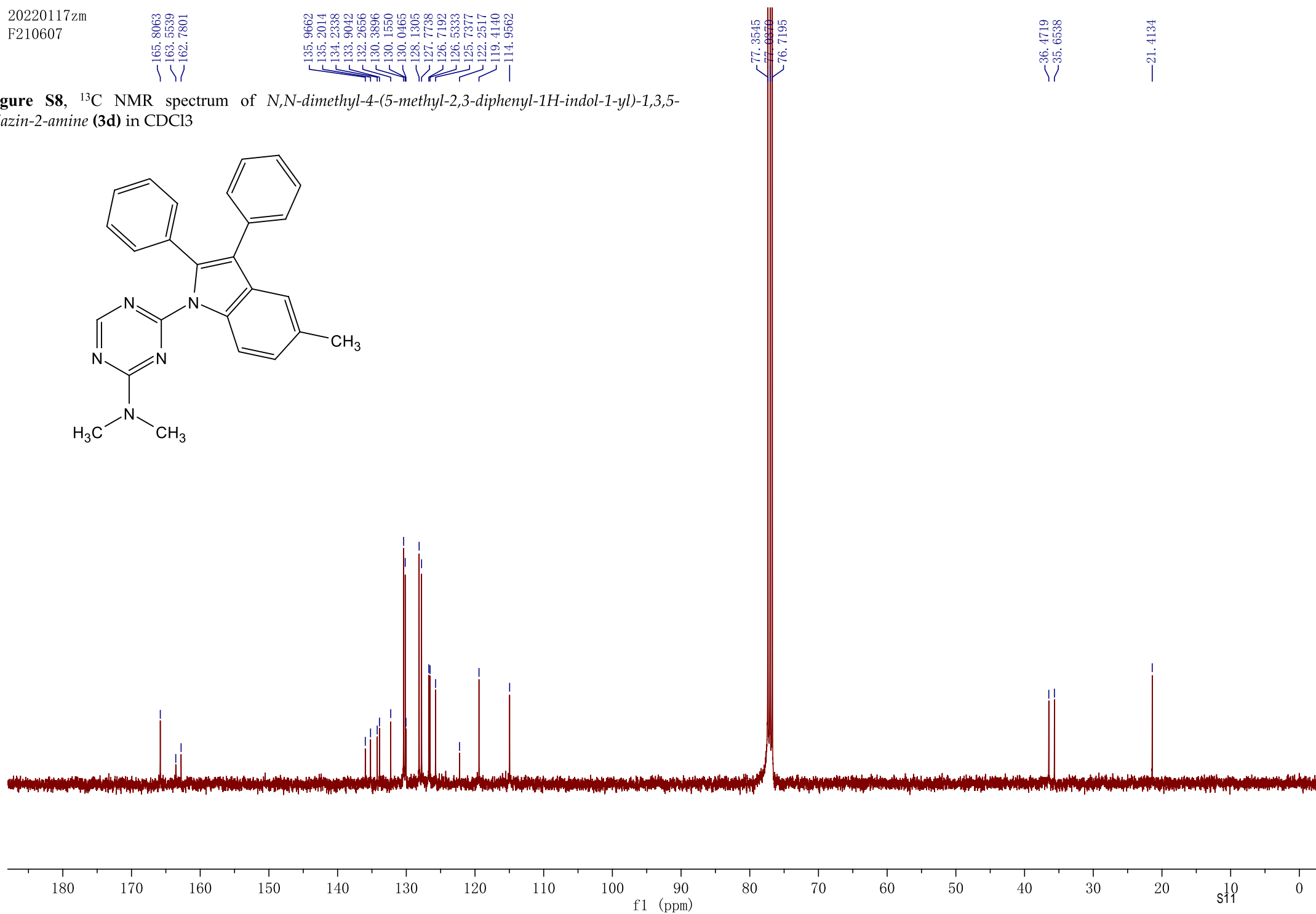
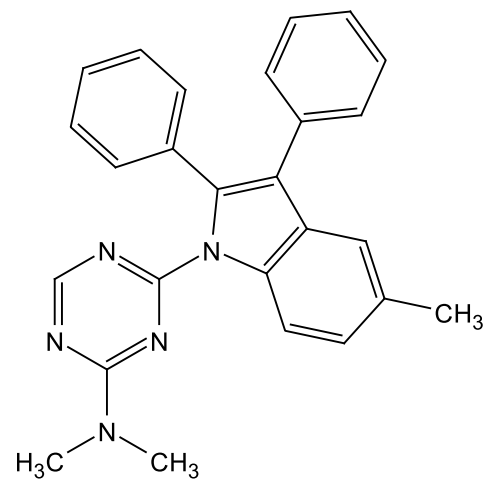
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135.2014
134.2338
133.9042
132.2656
130.3896
130.1550
130.0465
128.1305
127.7738
126.7192
126.5333
125.7377
122.2517
119.4140
114.9562

77.3545
77.0856
76.7195

36.4719
35.6538

21.4134

Figure S8, ^{13}C NMR spectrum of *N,N*-dimethyl-4-(5-methyl-2,3-diphenyl-1*H*-indol-1-yl)-1,3,5-triazin-2-amine (**3d**) in CDCl_3



F-20220222
F20220222

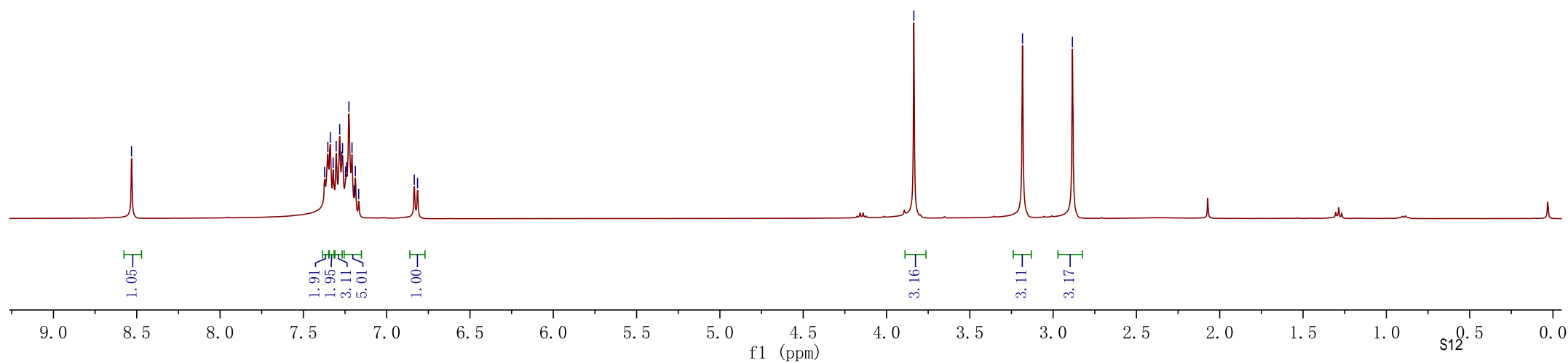
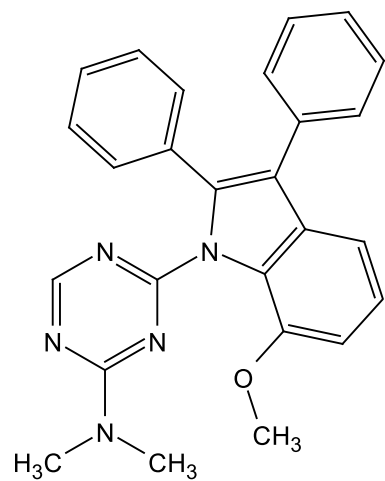
8.5315
7.3723
7.3531
7.3383
7.3210
7.3030
7.2818
7.2700
7.2649
7.2468
7.2400
7.2266
7.2081
7.1949
7.1878
7.1680
6.8343
6.8148

3.8361

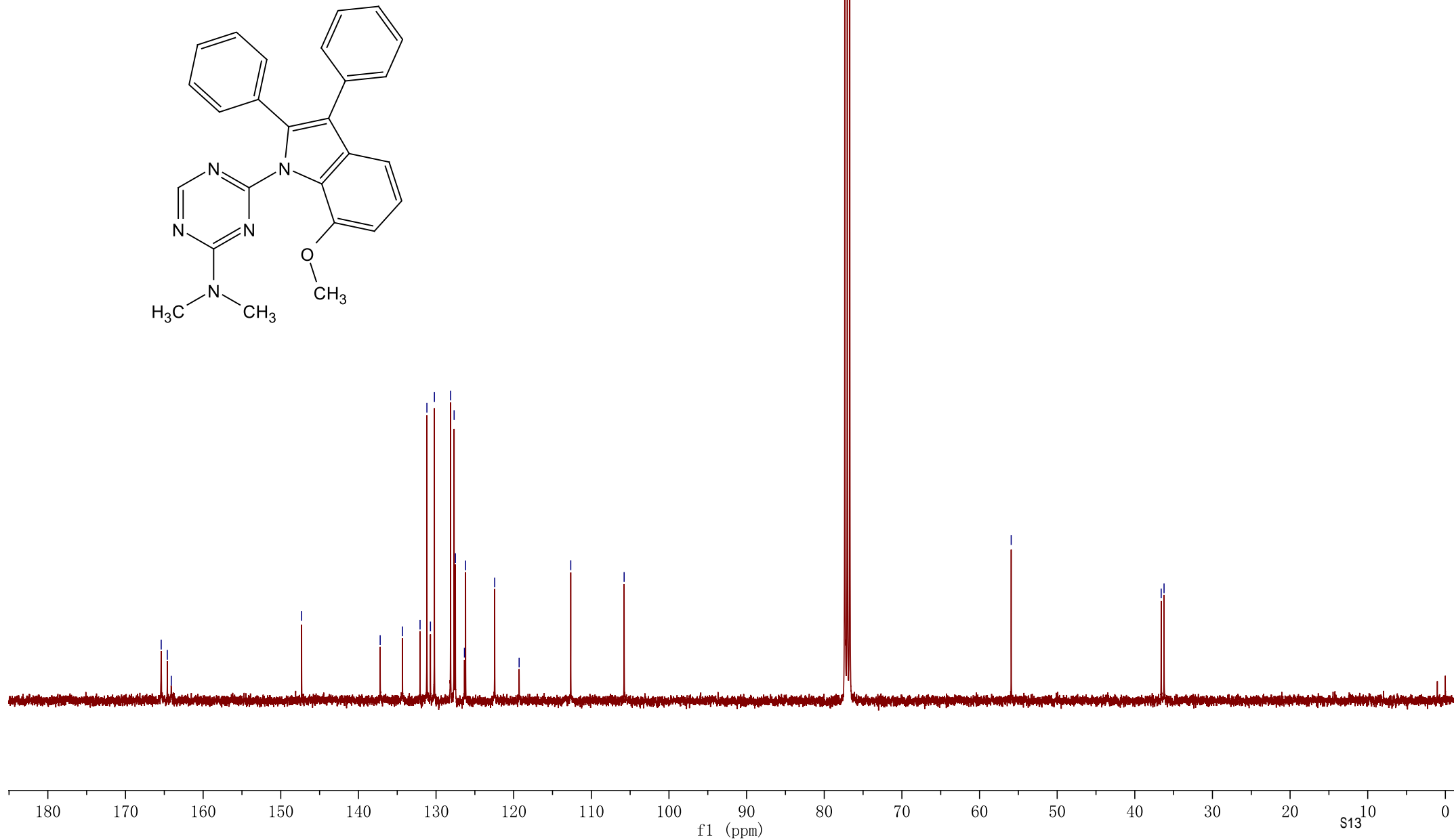
3.1839

2.8843

Figure S9, ^1H NMR spectrum of 4-(7-methoxy-2,3-diphenyl-1H-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3e**) in CDCl_3

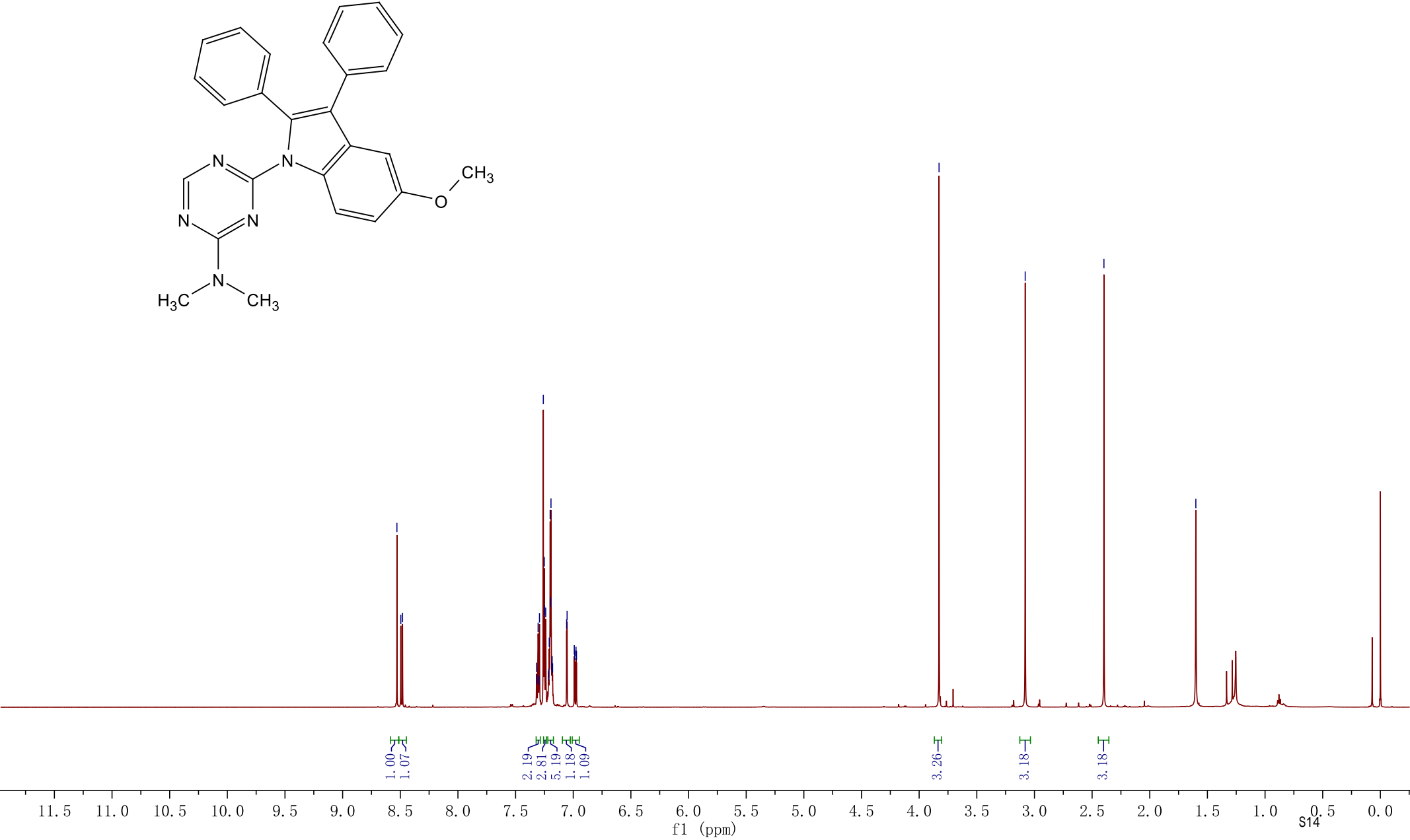


The chemical structure shows a 1H-imidazole ring substituted with a methyl group (H₃C-N-CH₃) at the 1-position and a 2-methoxy-5-phenyl-1H-indol-3-yl group at the 4-position. The indole ring has a methoxy group (O-CH₃) at the 2-position and a phenyl ring at the 5-position.



20190419-H1-WHF-327
20190419-H1-WHF-327
CDC13

Figure S11, ¹H NMR spectrum of 4-(5-methoxy-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3f**) in CDCl₃



¹³C
F-1016

166.0213
163.8460
162.7520

156.1021

136.6085
134.2326
133.8760
131.7571
130.5632
130.2985
130.1596
128.1988
127.7636
126.7526
126.5496
122.2180

116.2150
113.2545

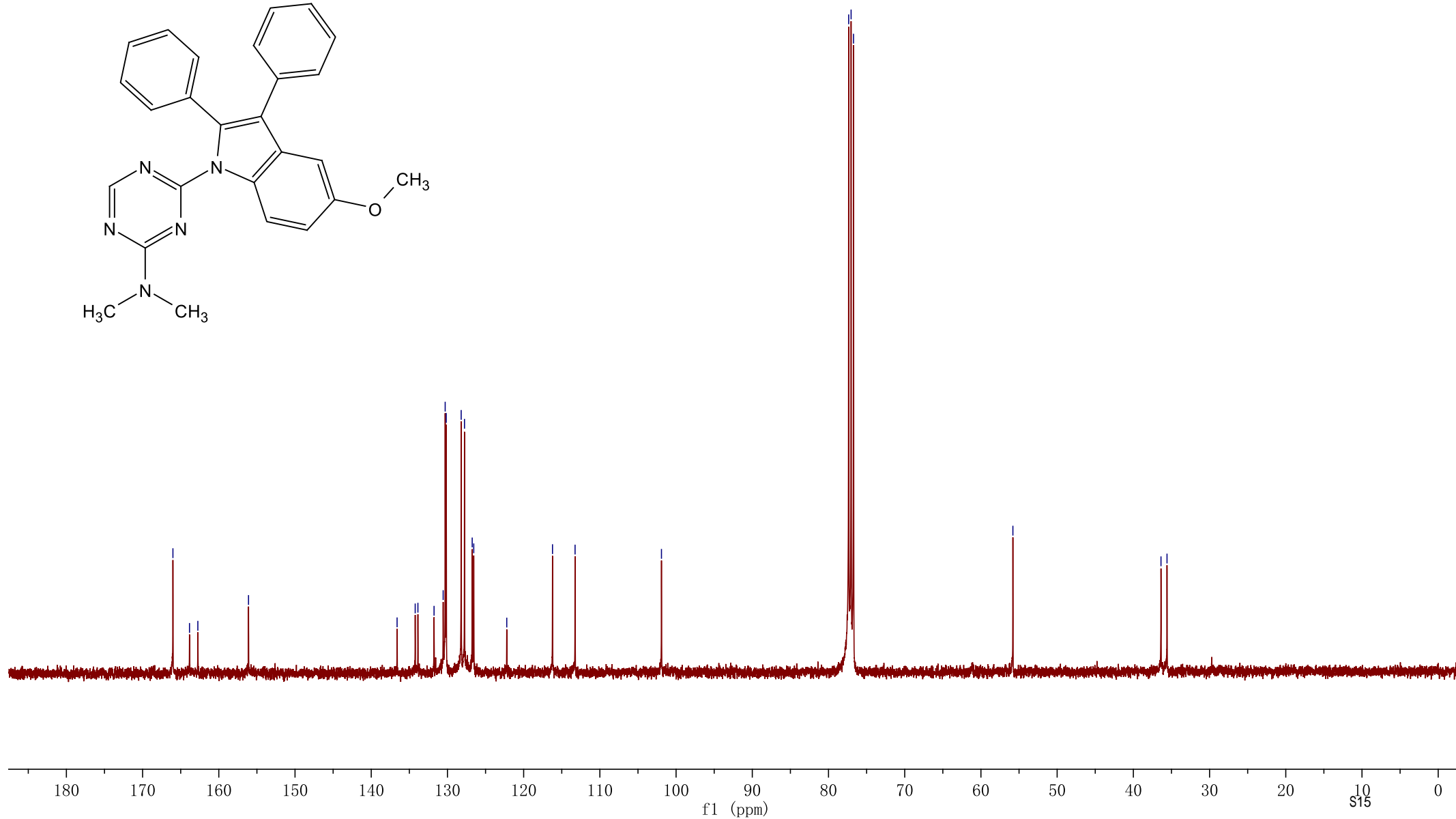
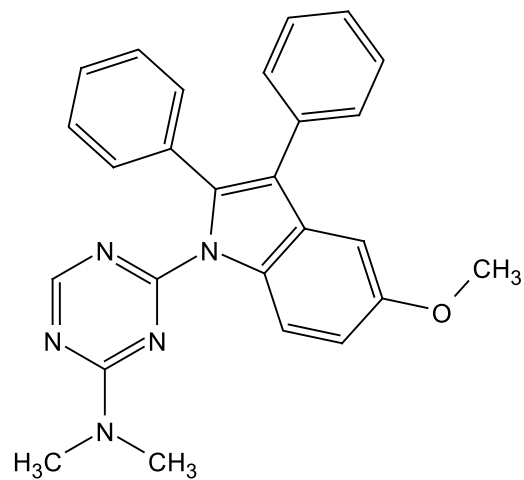
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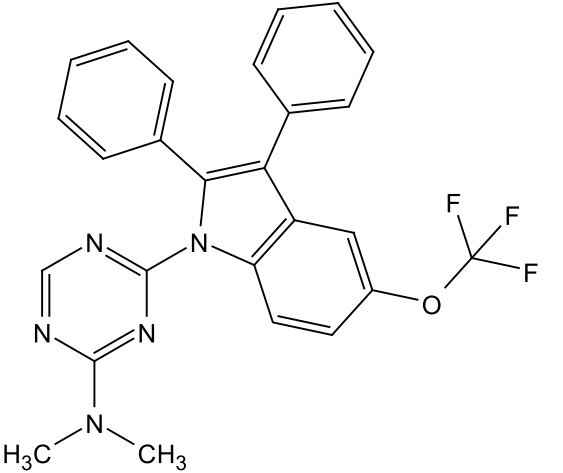
77.3542
77.0366
76.7189

55.8064

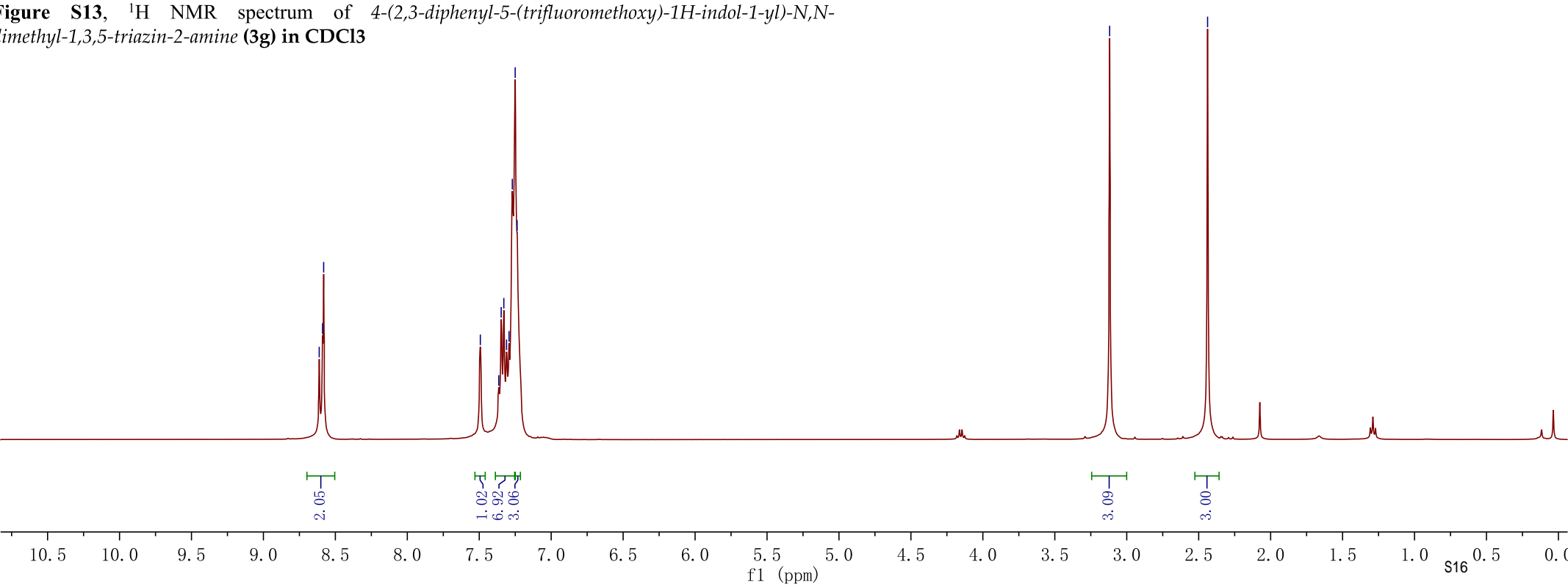
36.3747
35.5843

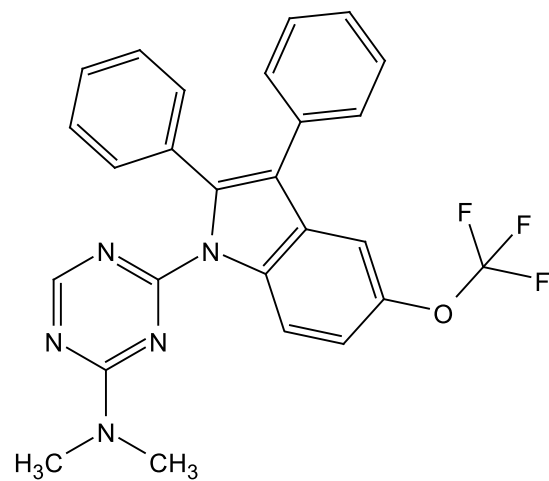
Figure S12, ¹H NMR spectrum of 4-(5-methoxy-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3f**) in CDCl₃





8.6122
8.5892
8.5815
7.4926
7.3645
7.3476
7.3293
7.3104
7.2930
7.2704
7.2503
7.2370
3.1190
2.4383





166.3119
164.0982
162.7838

145.0577

135.0902

133.6454

133.1274

130.3330

130.1780

130.1431

128.3600

127.9090

127.1335

126.8763

121.7418

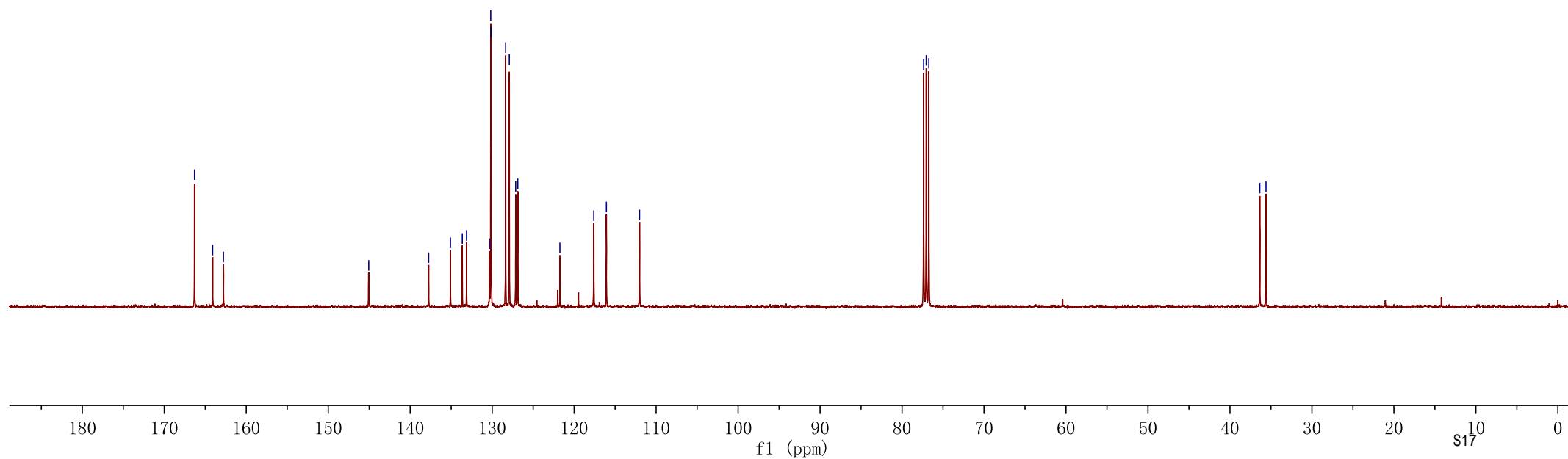
117.6072

116.0669

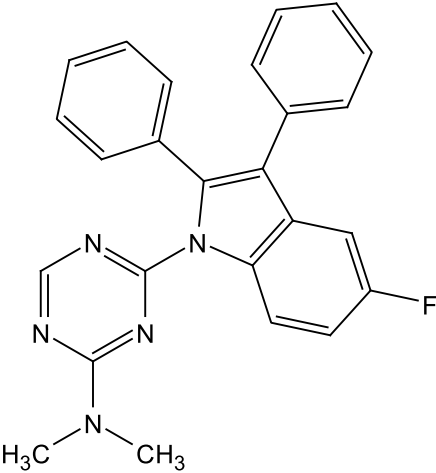
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77.3659
77.0483
76.7307

36.3607
35.6037



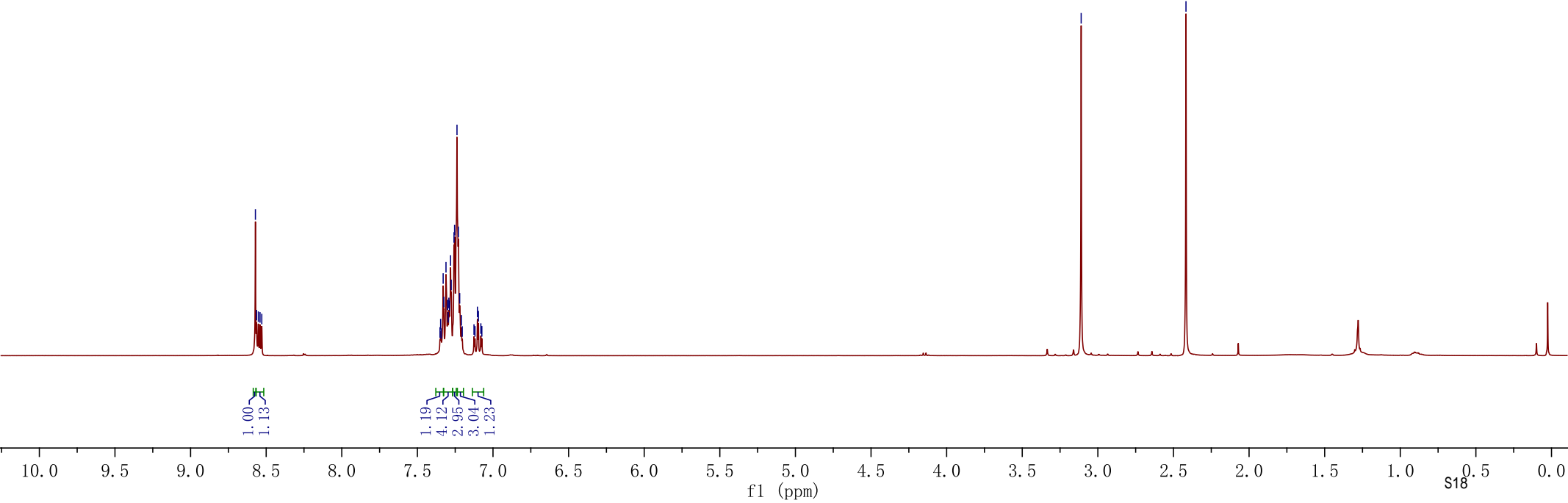
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F-1015



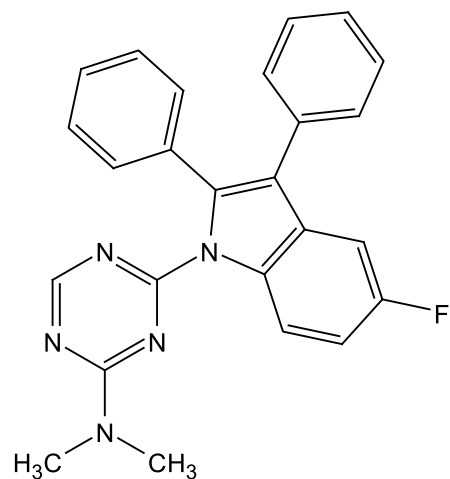
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8.5638
8.5519
8.5408
8.5292
7.3505
7.3464
7.3426
7.3297
7.3258
7.3110
7.3003
7.2965
7.2921
7.2882
7.2807
7.2767
7.2579
7.2541
7.2382
7.2290
7.2204
7.2090
7.2036
7.1258
7.1192
7.1031
7.0966
7.0805
7.0739

3.1104
2.4173

Figure S15, ¹H NMR spectrum of 4-(5-fluoro-2,3-diphenyl-1H-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3h**) in CDCl₃



¹³C
F-1015



166.2402
164.0398
162.7905
160.6960
158.3260

137.4745
133.8616
133.3819
133.2548
130.6736
130.5785
130.1705
130.1243
128.2763

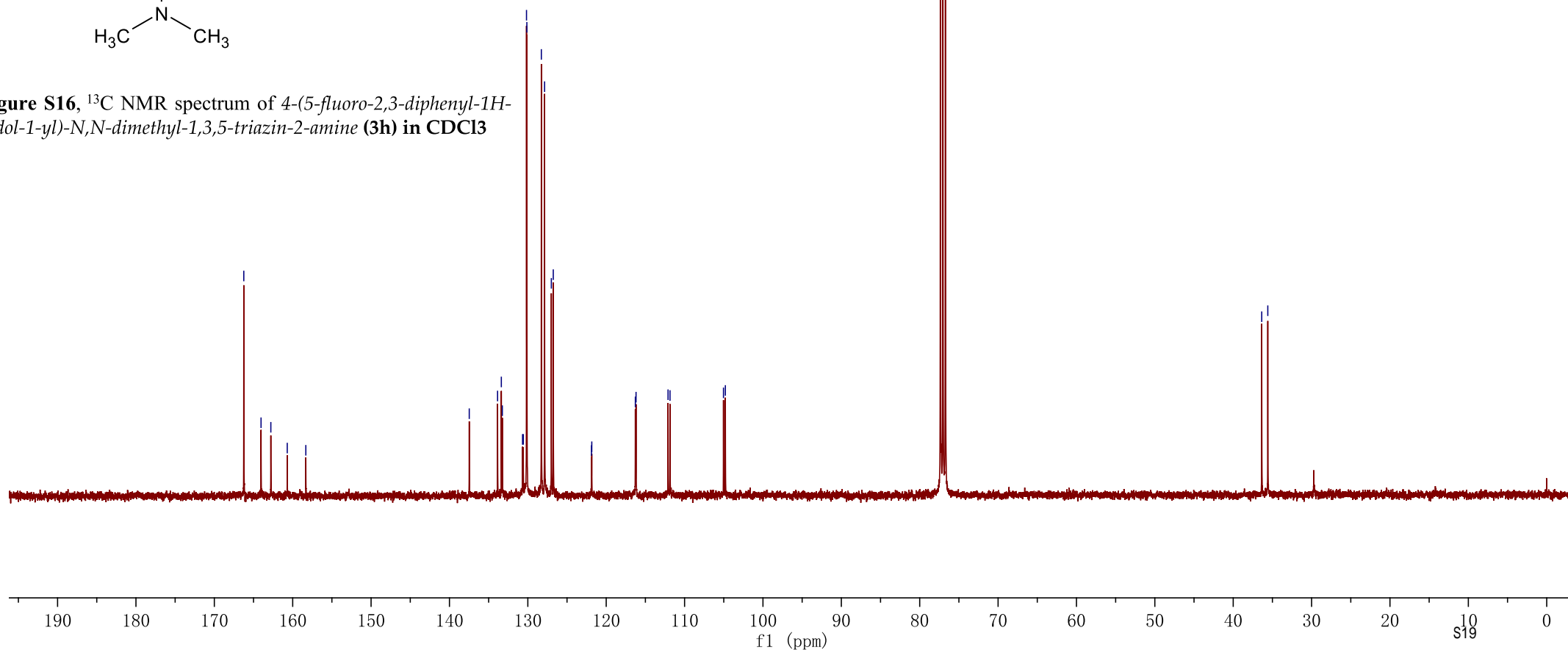
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127.0009
126.7548
121.8803
121.8405

116.2823
116.1943
112.1094
111.8614

105.0377
104.7973

77.3619
77.0444
76.7267

36.3619
35.5868



¹H
F-1017

7.3535
7.3371
7.3335
7.3171
7.3115
7.3010
7.2976
7.2818
7.2559
7.2396
7.2241
7.2158
7.2074

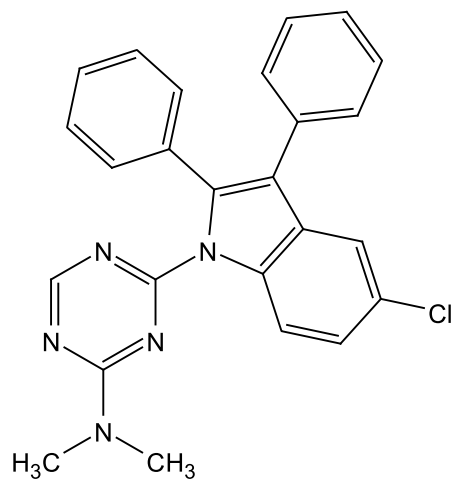
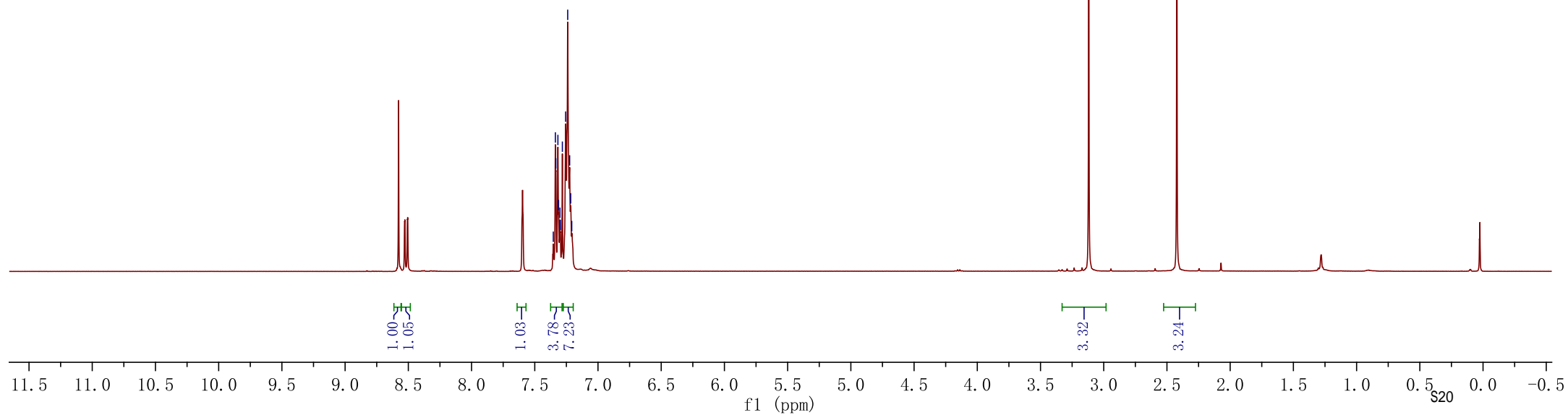


Figure S17, ¹H NMR spectrum of 4-(5-chloro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3i**) in CDCl₃



¹³C
F-1017

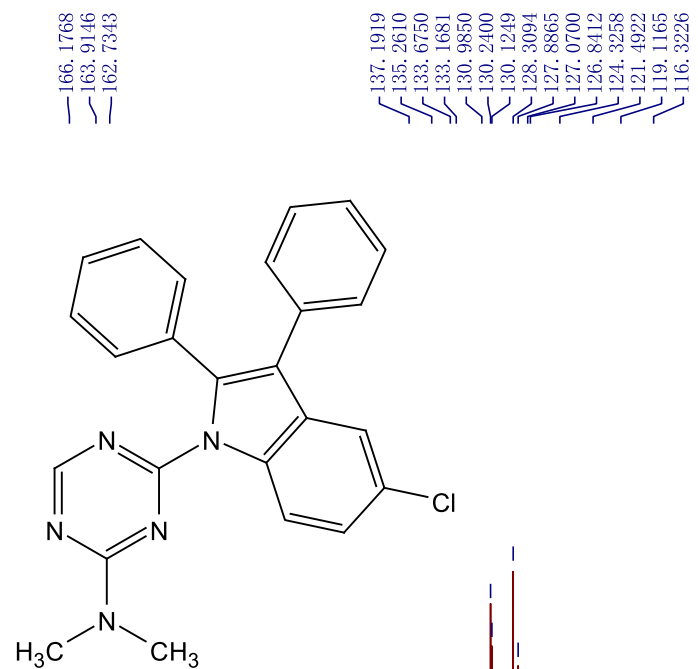
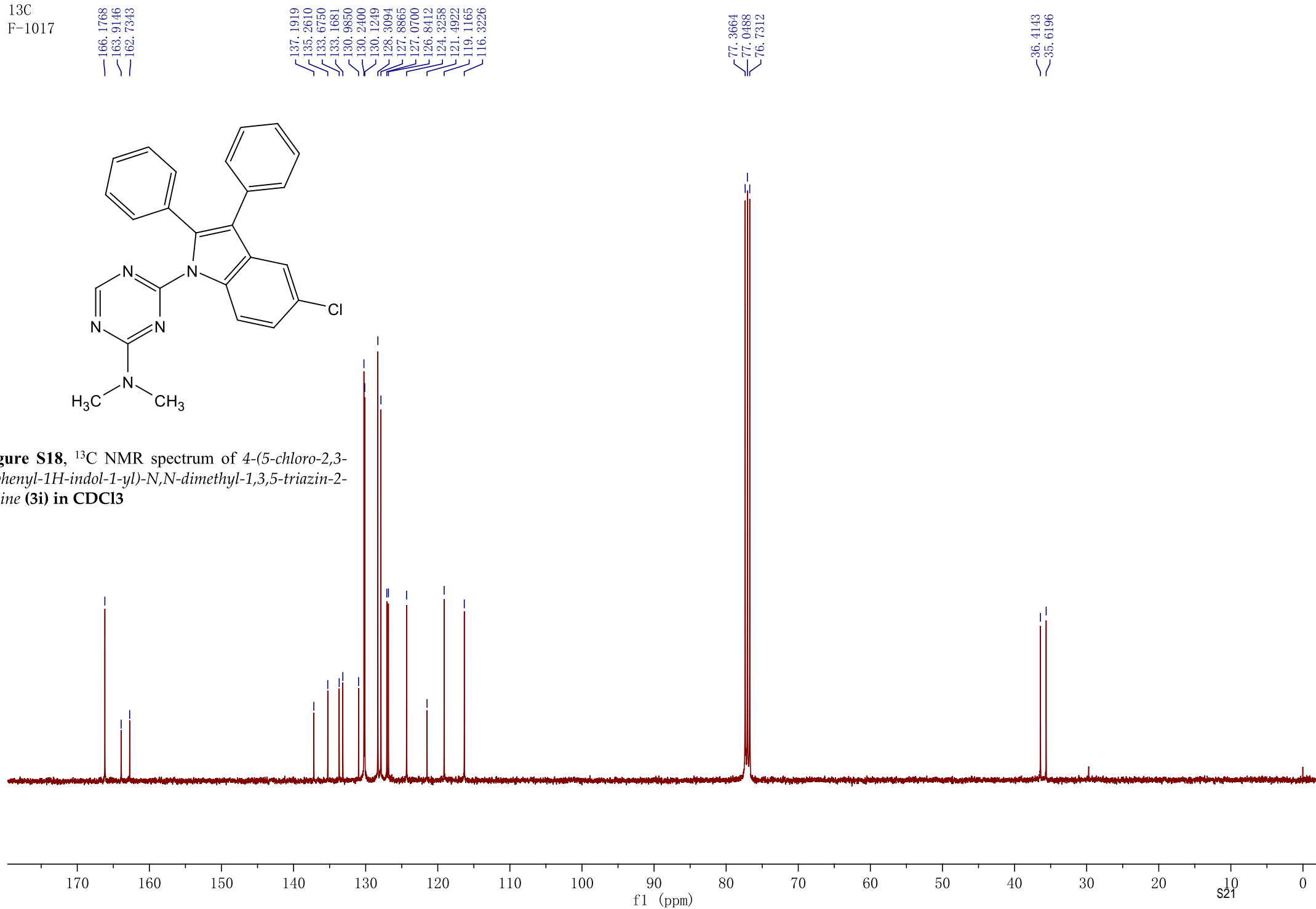


Figure S18, ¹³C NMR spectrum of 4-(5-chloro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3i**) in CDCl₃



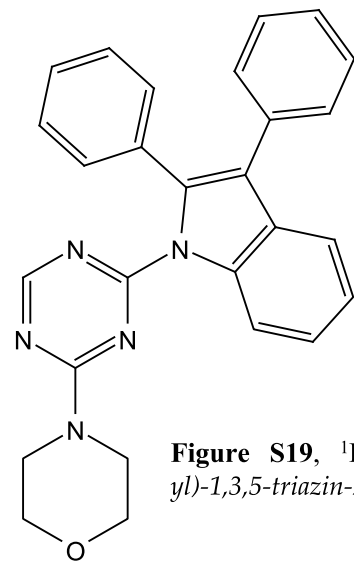
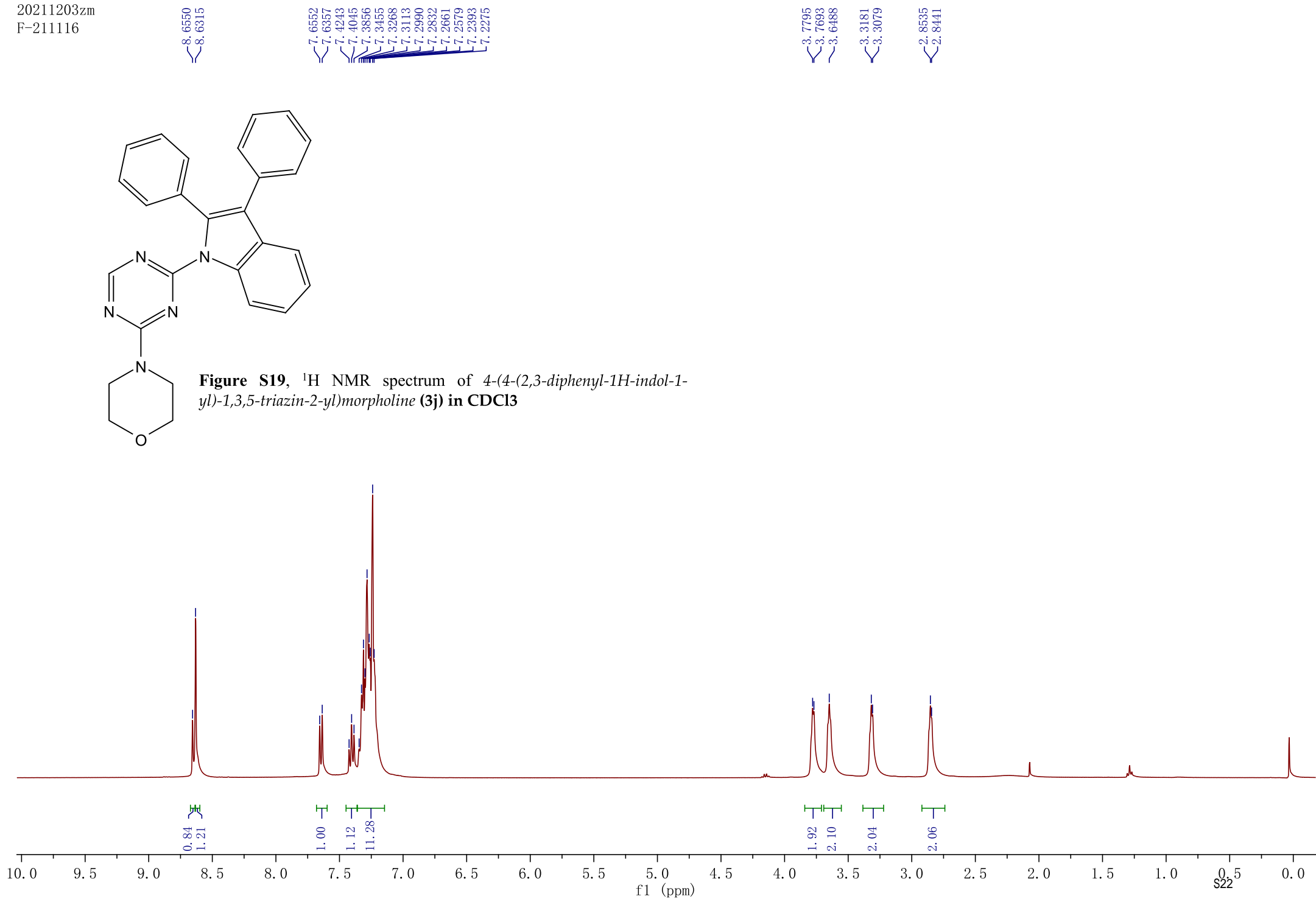


Figure S19, ¹H NMR spectrum of 4-(4-(2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-yl)morpholine (**3j**) in CDCl₃



20211208zm
f2111116

166.3939
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162.9570
136.9068
135.7344
134.3674
133.5844
130.3428
130.1969
129.8748
128.1776
127.8280
126.7536
126.6792
124.5148
122.9354
122.7516
119.7056
115.4352

77.3593
77.2450
77.0417
76.7241
66.5612
66.4730
43.7372
42.8995

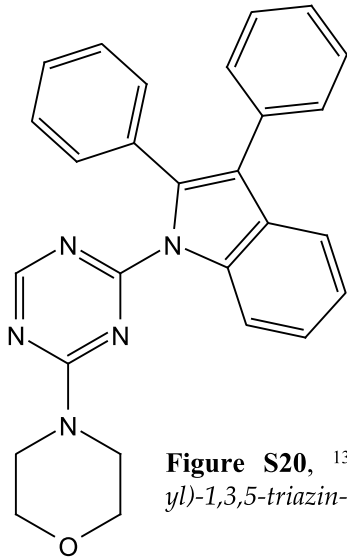
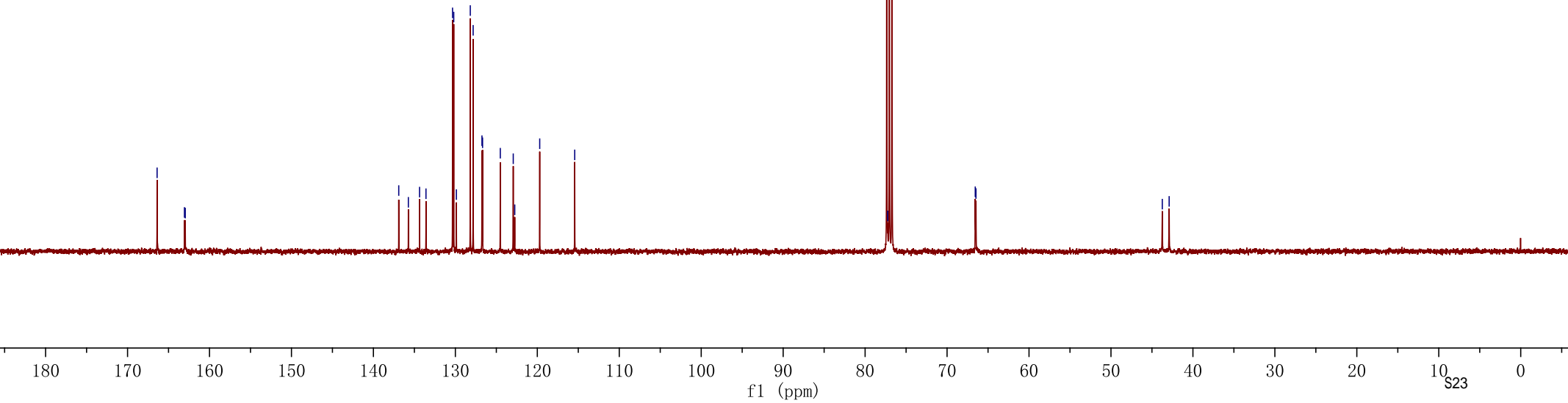


Figure S20, ¹³C NMR spectrum of 4-(4-(2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-yl)morpholine (**3j**) in CDCl₃



20211203zm
1118

8.6400
8.6191
8.6011

7.6529
7.6338
7.4151
7.4120
7.3971
7.3942
7.3913
7.3763
7.3732
7.3459
7.3427
7.3383
7.3359
7.3247
7.3212
7.3145
7.3071
7.2881
7.2807
7.2740
7.2701
7.2574
7.2537
7.2451
7.2402
7.2318
7.2301
7.2246
7.2224

3.8142
3.8029
3.7908

2.9192
2.9072
2.8946

2.3899
2.3777
2.3655
2.2857
2.0698
2.0564
2.0442

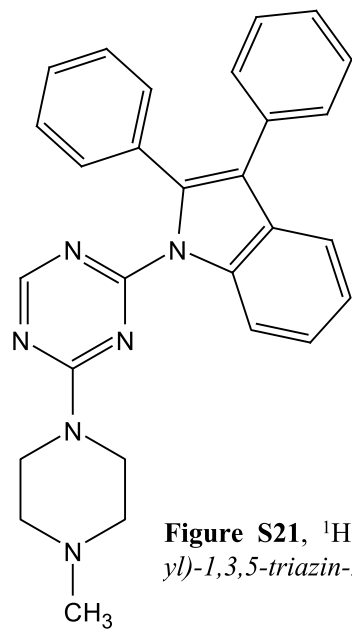
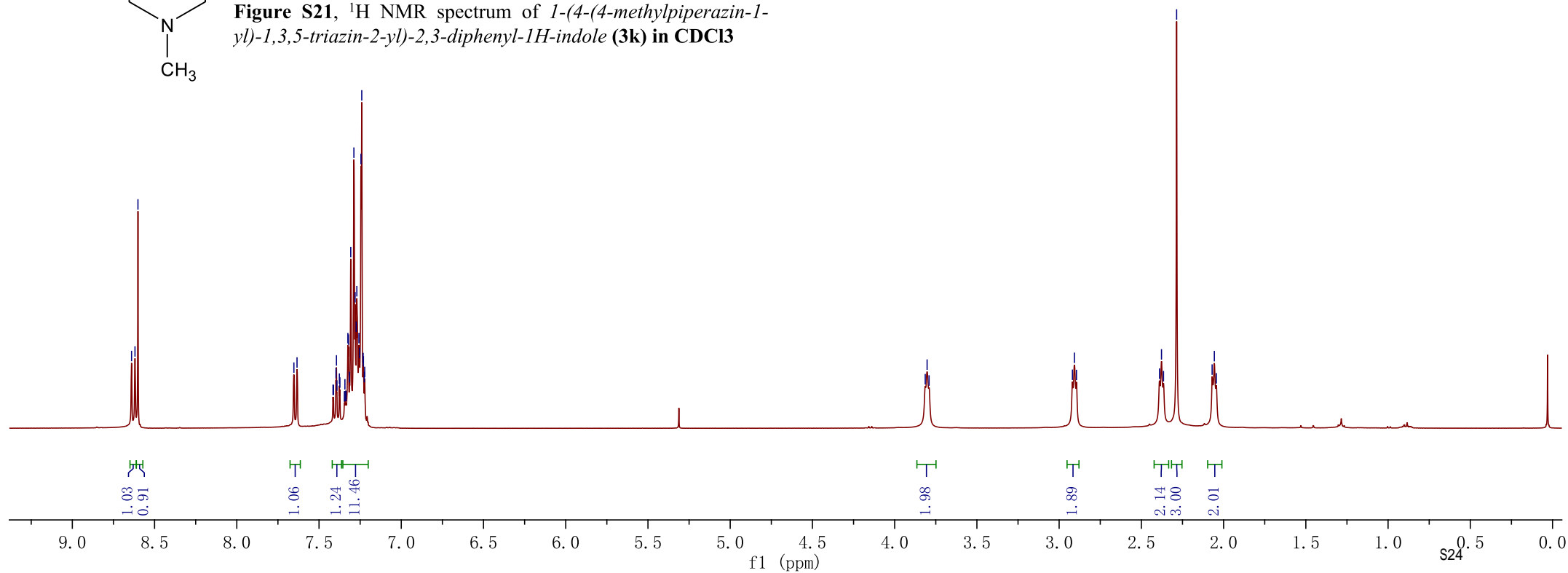


Figure S21, ¹H NMR spectrum of 1-(4-(4-methylpiperazin-1-yl)-1,3,5-triazin-2-yl)-2,3-diphenyl-1H-indole (**3k**) in CDCl₃



166.5801
163.1975
163.1454
136.9187
135.8370
134.2987
133.7254
130.3664
130.1923
129.8109
128.1522
127.8107
126.7819
126.5986
124.3845
122.7779
122.4091
119.6369
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77.2546
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76.7338
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54.5432
46.0174
43.0515
42.3092

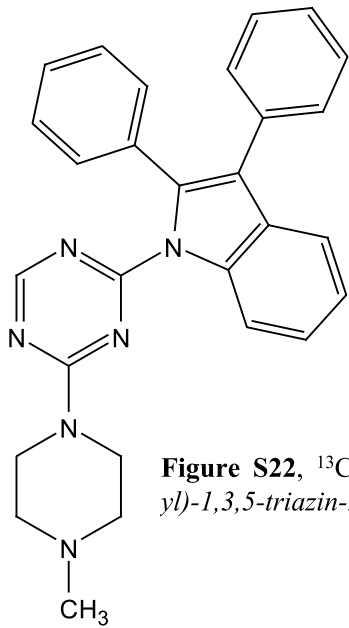
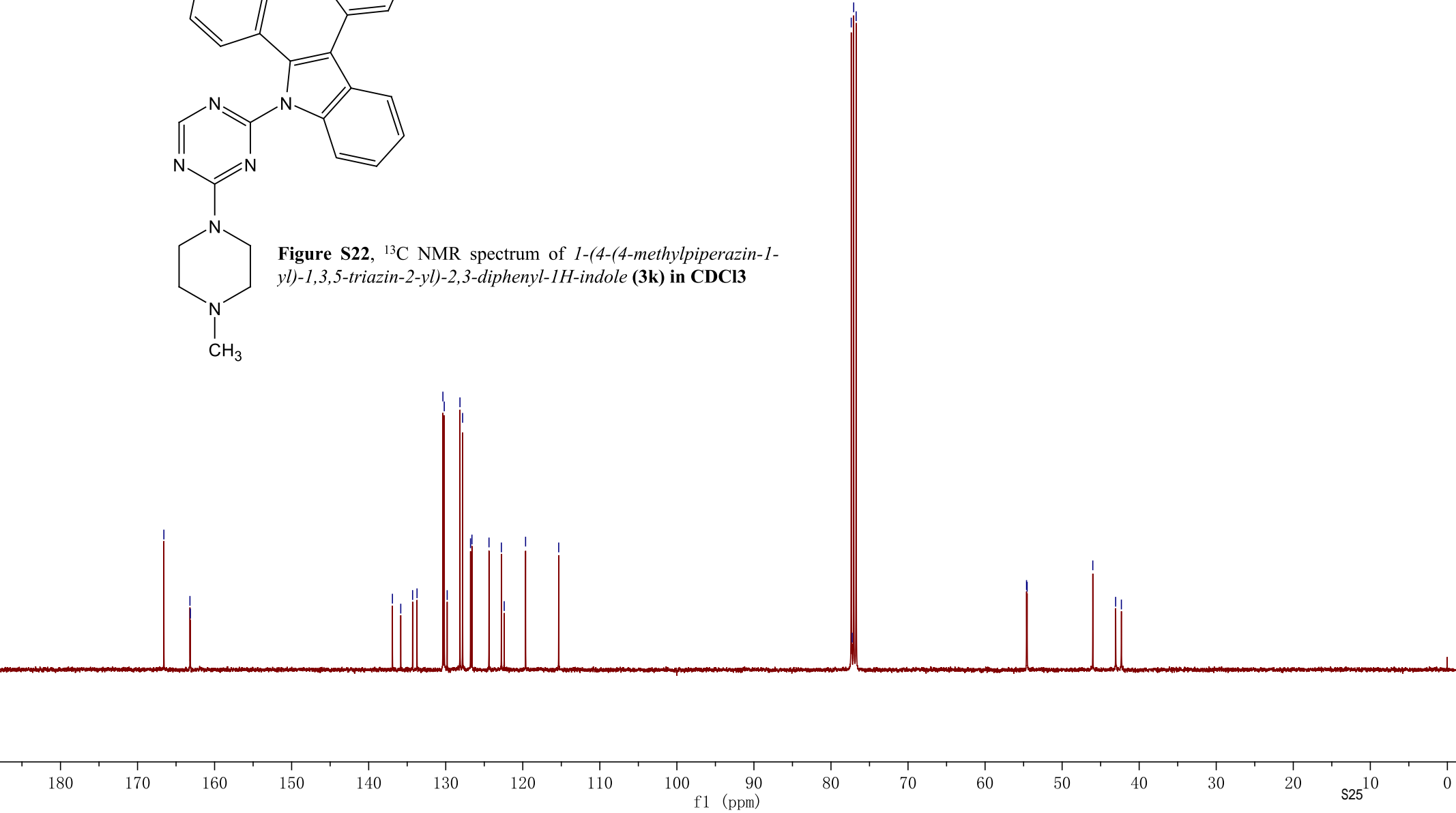


Figure S22, ¹³C NMR spectrum of *1-(4-(4-methylpiperazin-1-yl)-1,3,5-triazin-2-yl)-2,3-diphenyl-1H-indole (3k)* in CDCl₃



20211223zm
f211204

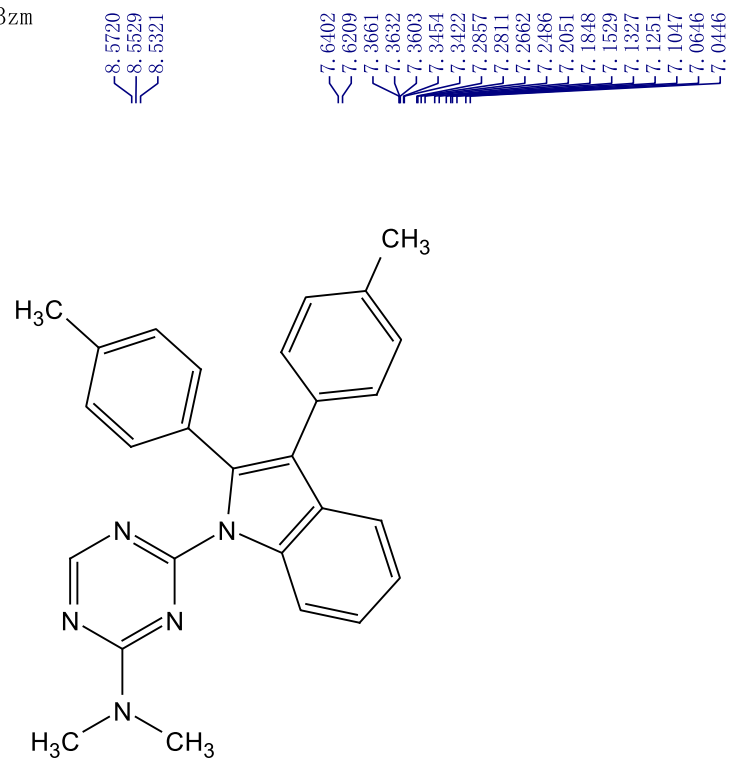
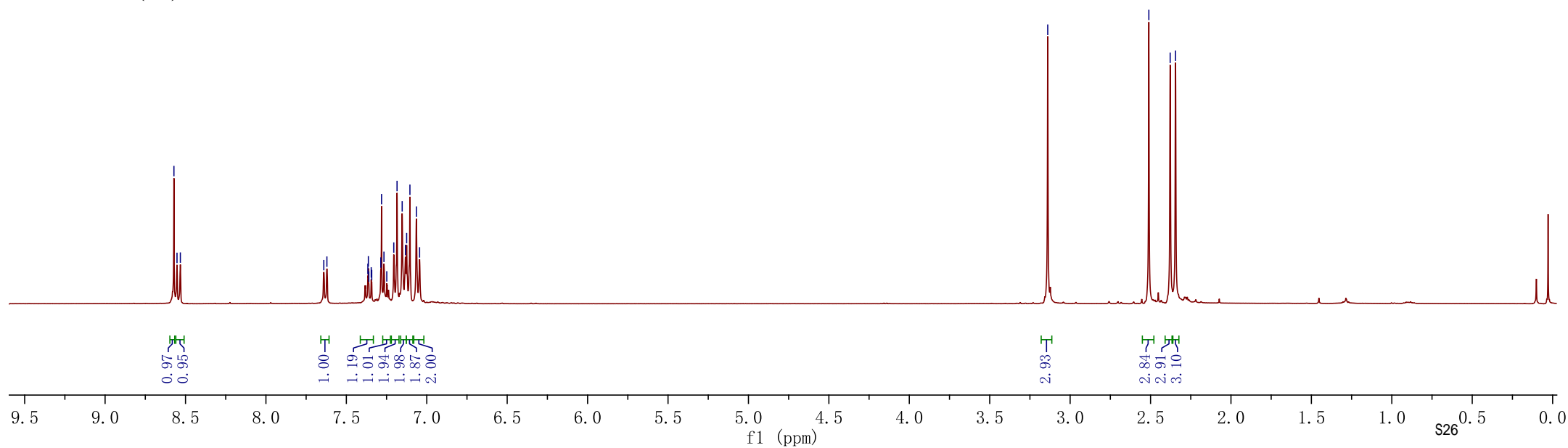


Figure S23, ^1H NMR spectrum of 4-(2,3-di-p-tolyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3m**) in CDCl_3



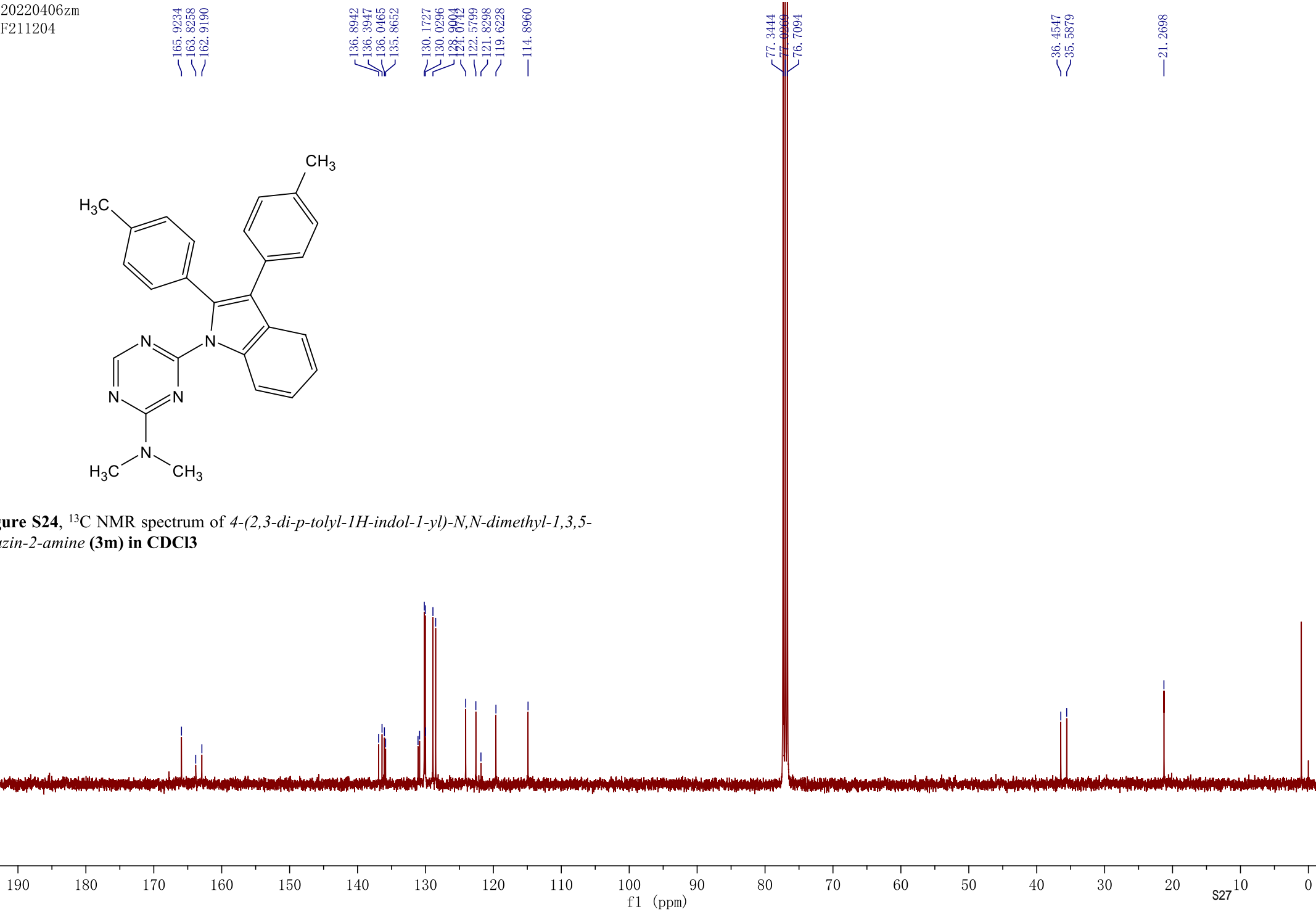
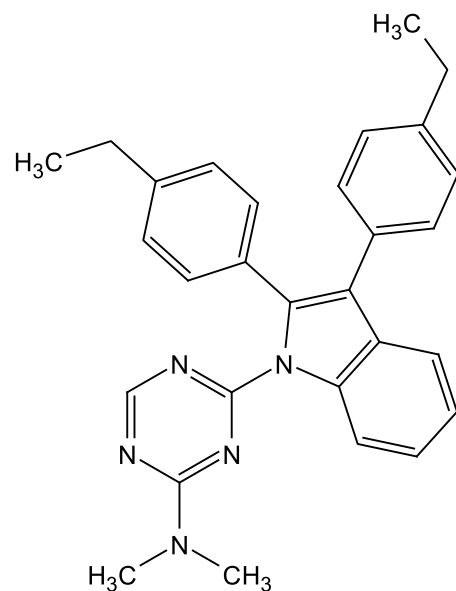


Figure S24, ¹³C NMR spectrum of 4-(2,3-di-*p*-tolyl-1*H*-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3m**) in CDCl₃

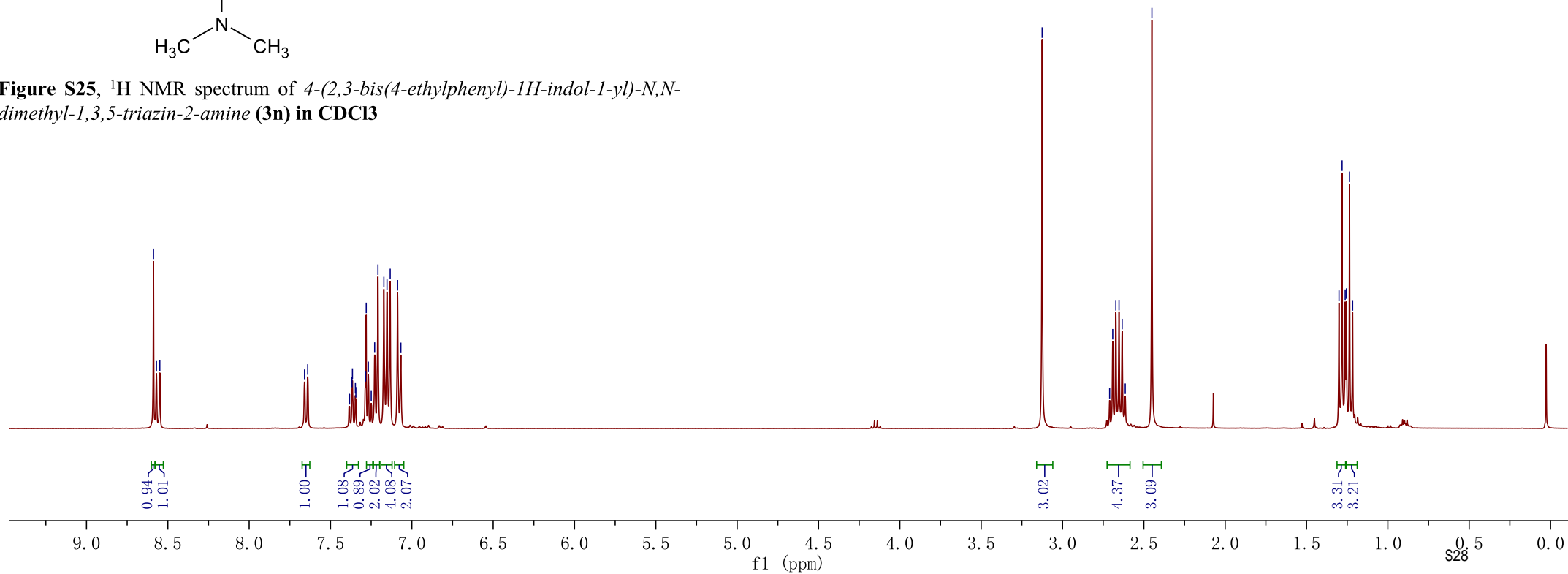


8.5881
8.5700
8.5492
7.6594
7.6399
7.3856
7.3828
7.3674
7.3649
7.3469
7.3441
7.2846
7.2802
7.2674
7.2496
7.2285
7.2082
7.1718
7.1527
7.1329
7.0875
7.0674

3.1250
2.7103
2.6913
2.6720
2.6525
2.6333
2.6143
2.4504

1.3001
1.2811
1.2621
1.2544
1.2354
1.2164

Figure S25, ^1H NMR spectrum of 4-(2,3-bis(4-ethylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3n**) in CDCl_3

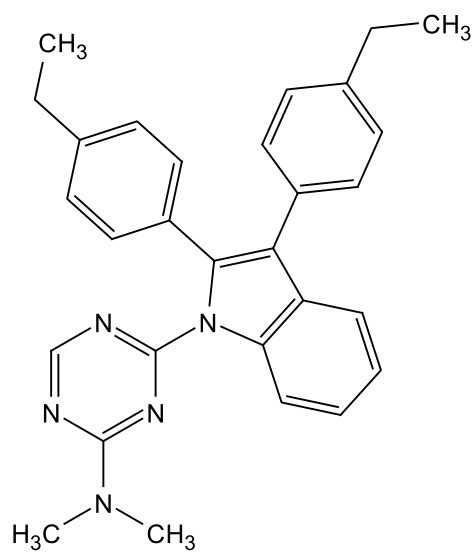


165.9791
163.8273
162.9218

142.8310
142.2831

136.9093
135.8797

131.0688
130.2161
130.1092
130.0094
127.6159
127.3232
124.0782
122.5692
119.8905
119.8865

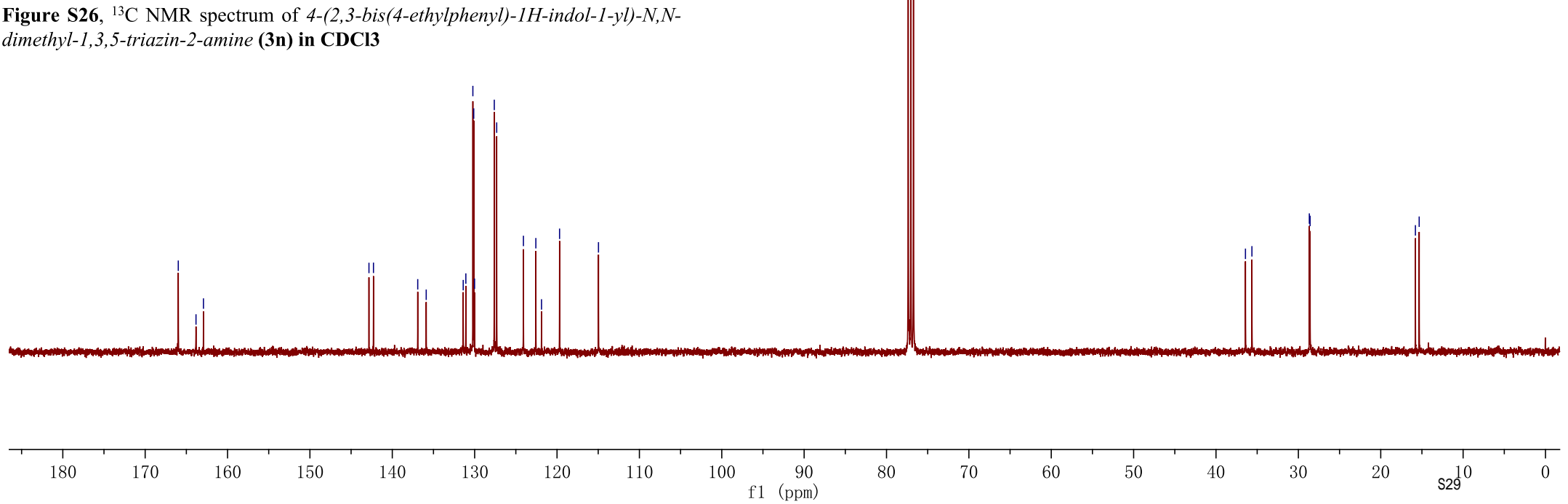


77.3635
77.0460
76.7285

36.4228
35.6374

28.6689
28.5767

15.7903
15.3317



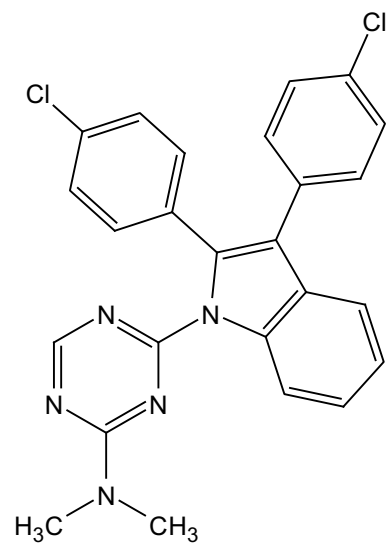
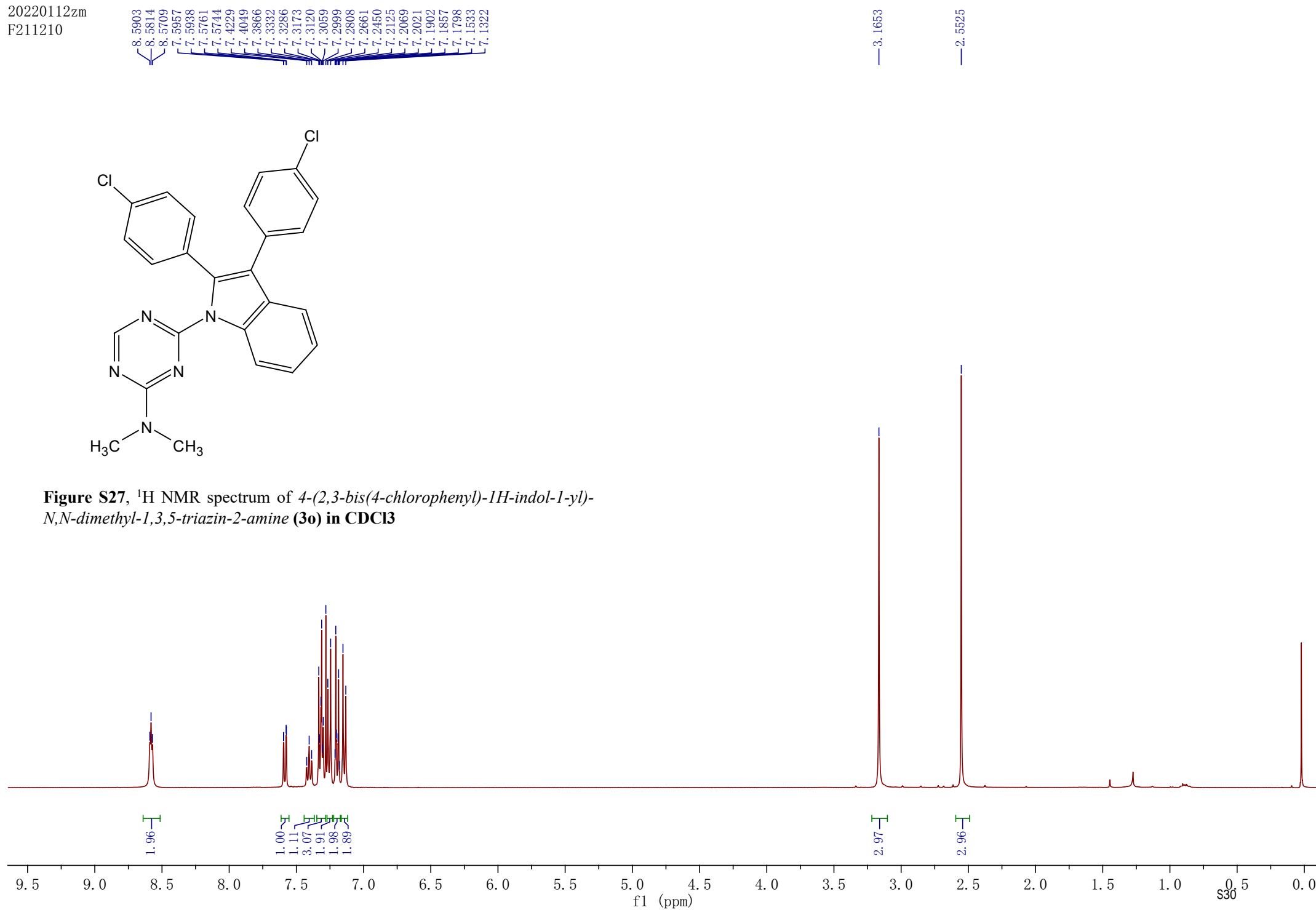


Figure S27, ^1H NMR spectrum of 4-(2,3-bis(4-chlorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3o**) in CDCl_3



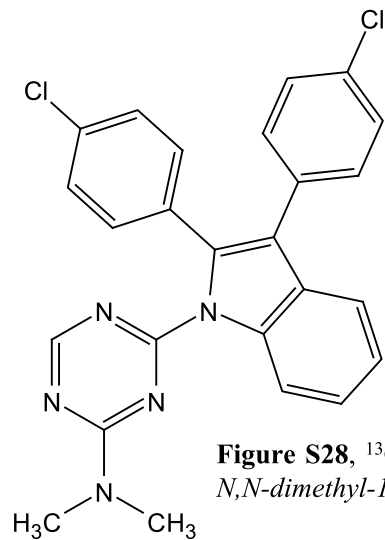
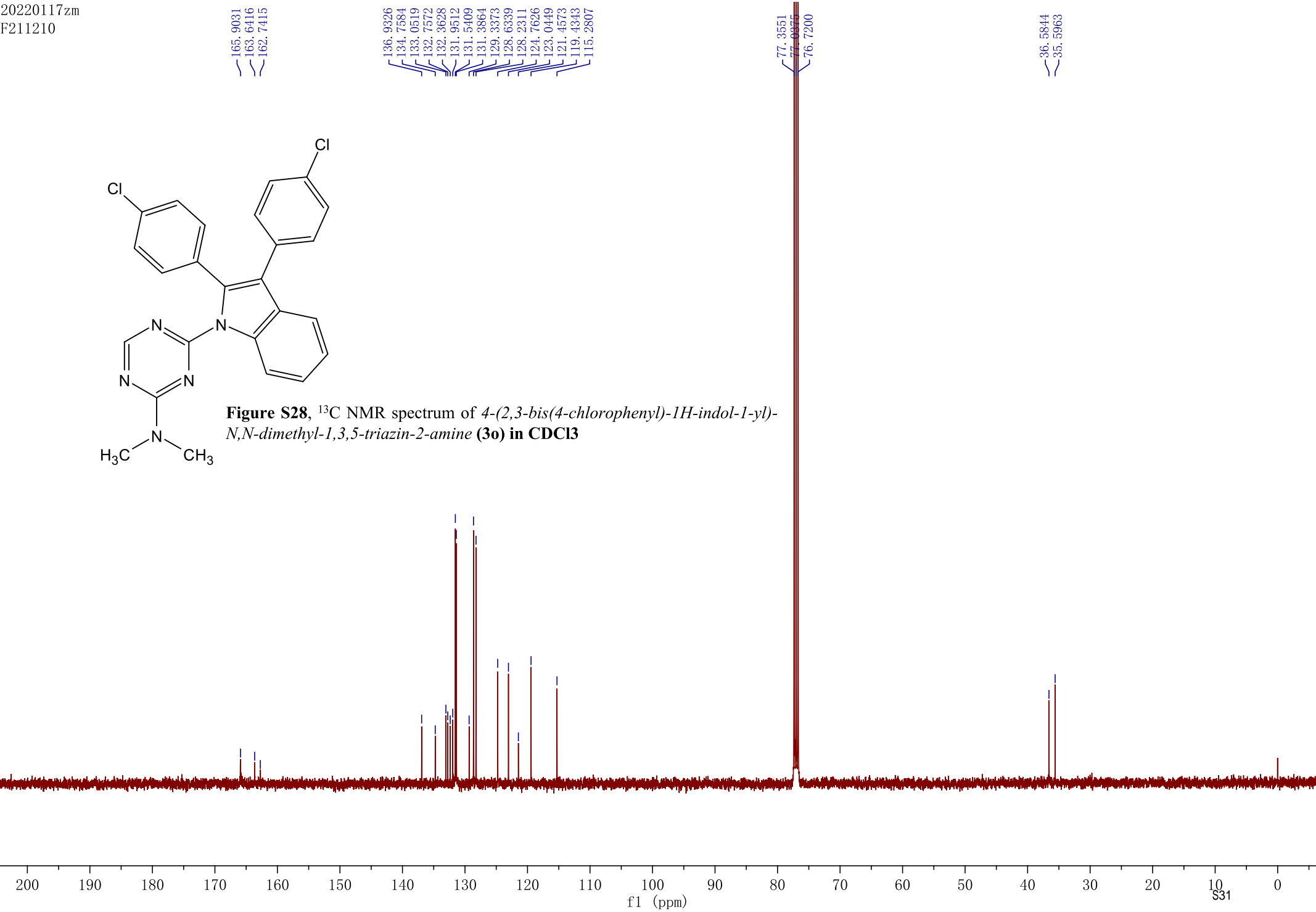


Figure S28, ¹³C NMR spectrum of 4-(2,3-bis(4-chlorophenyl)-1*H*-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3o**) in CDCl₃



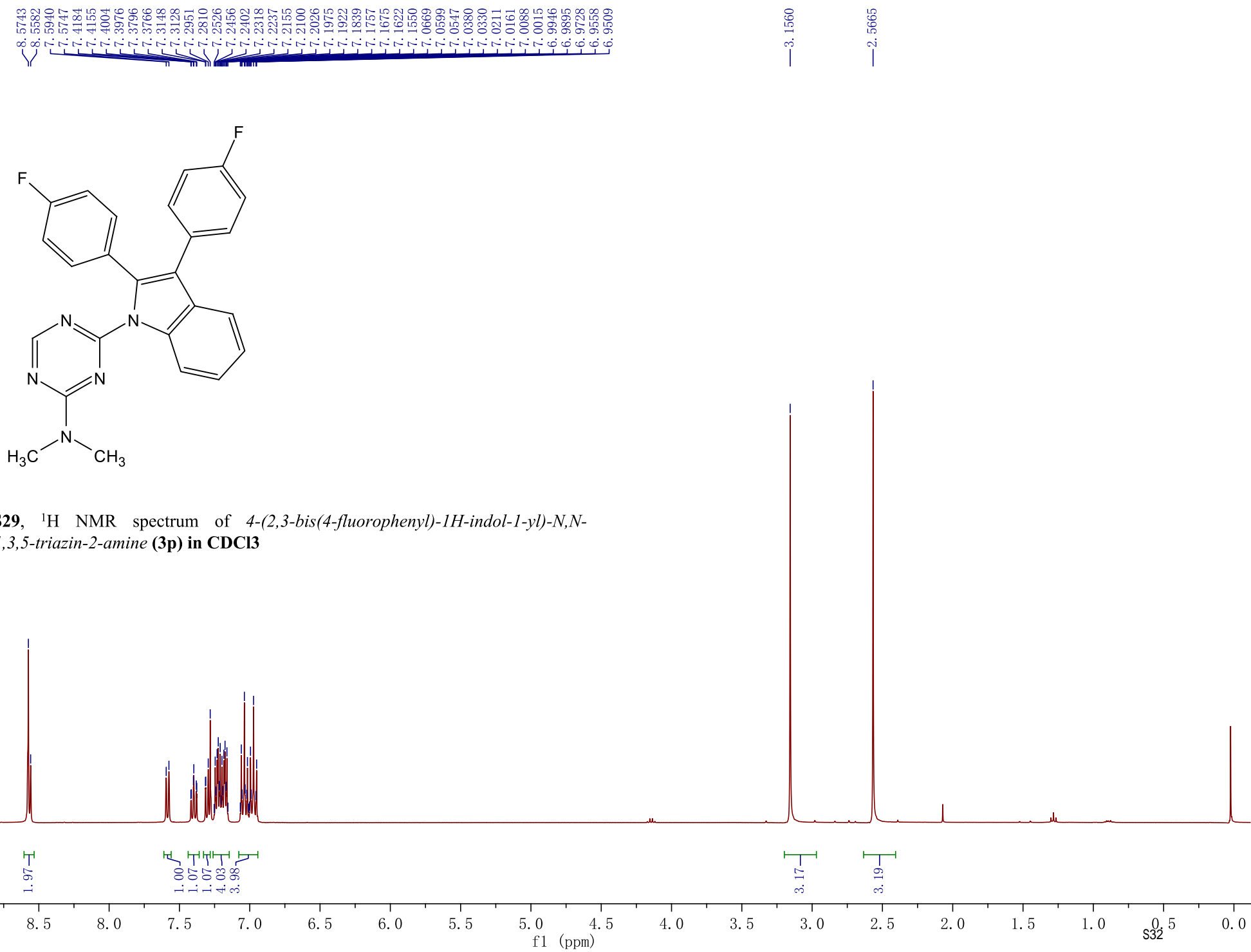


Figure S29, ¹H NMR spectrum of 4-(2,3-bis(4-fluorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3p**) in CDCl₃

20220117zm
F220101

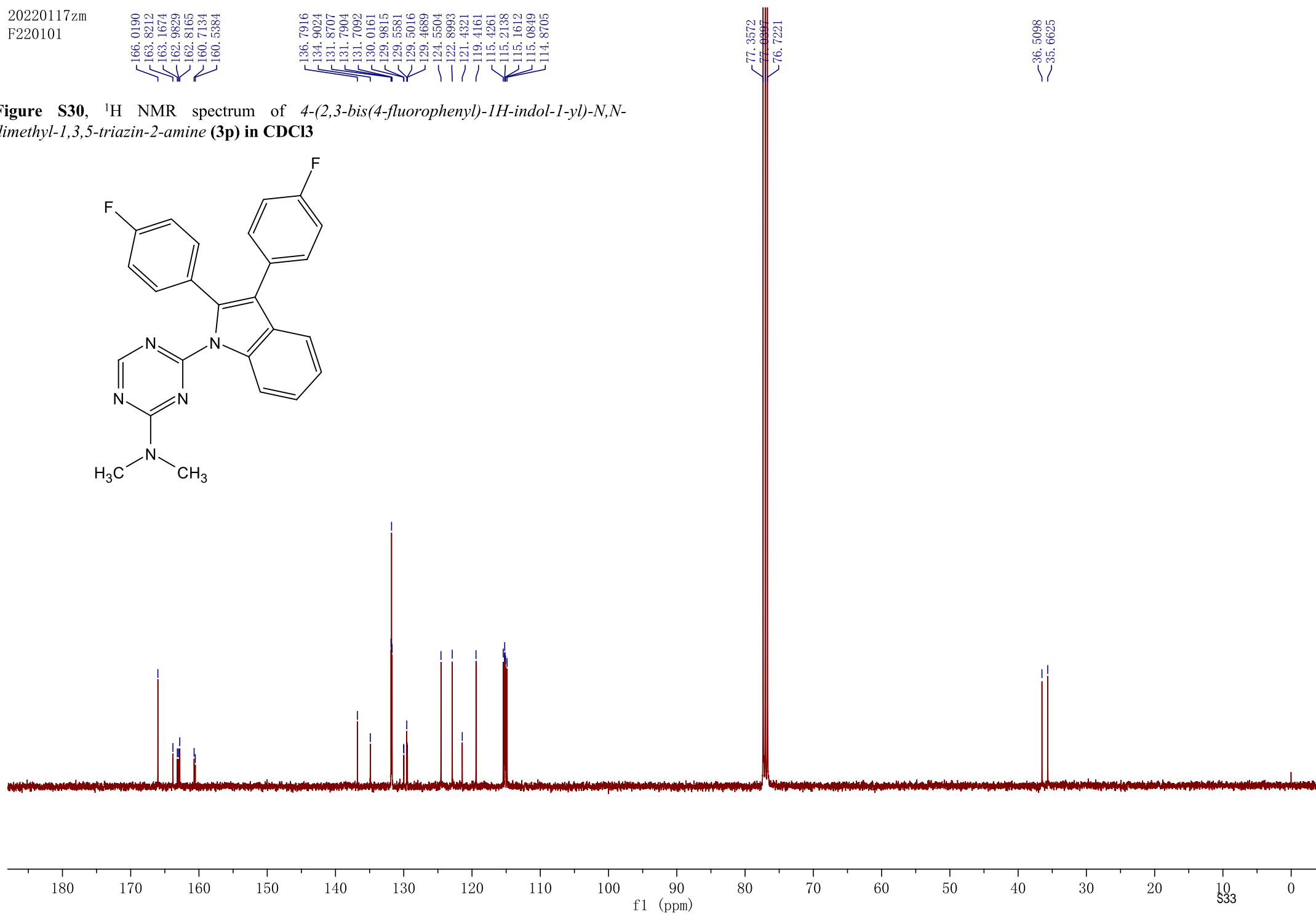
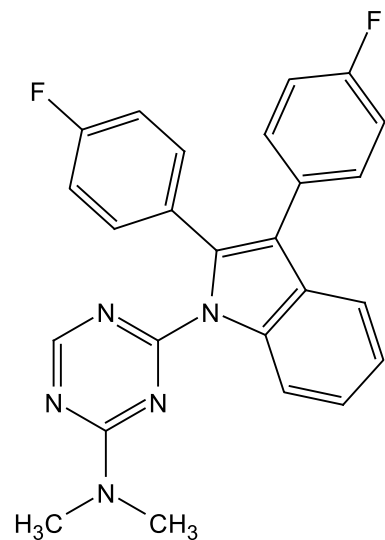
166.0190
163.8212
163.1674
162.9829
162.8165
160.7134
160.5384

136.7916
134.9024
131.8707
131.7904
131.7092
130.0161
129.9815
129.5581
129.5016
129.4689
124.5504
122.8993
121.4321
119.4161
115.4261
115.2138
115.1612
115.0849
114.8705

77.3572
77.0857
76.7221

36.5098
35.6625

Figure S30, ^1H NMR spectrum of 4-(2,3-bis(4-fluorophenyl)-1*H*-indol-1-yl)-*N,N*-dimethyl-1,3,5-triazin-2-amine (**3p**) in CDCl_3



20220112zm
F220105

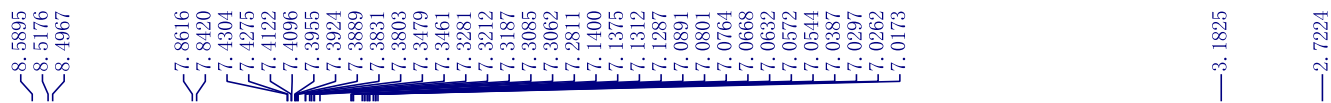
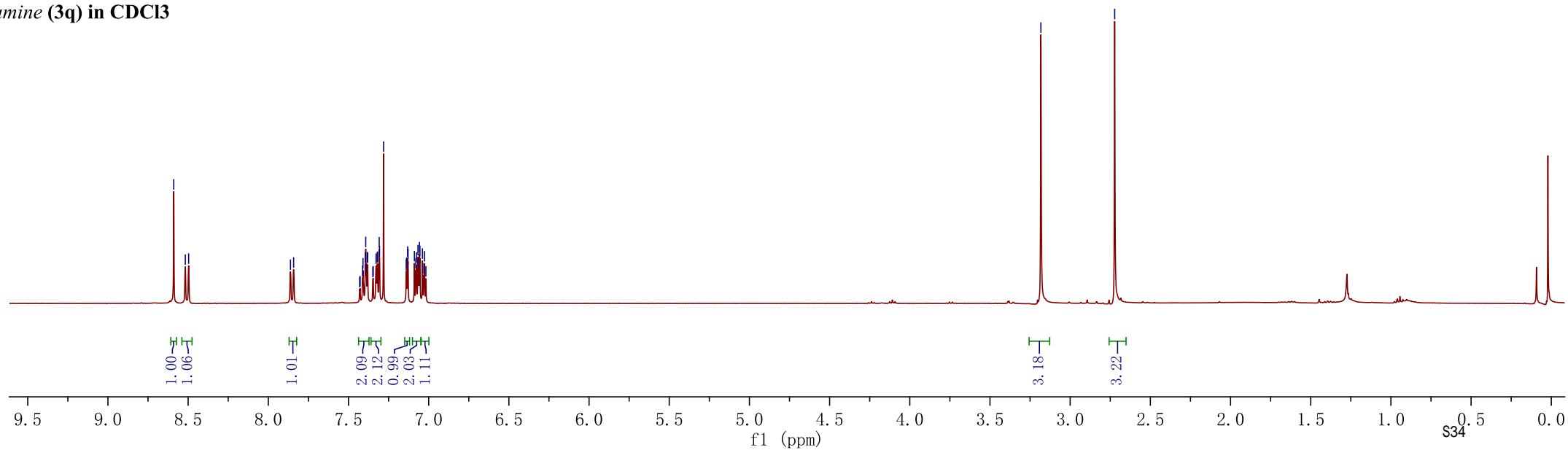
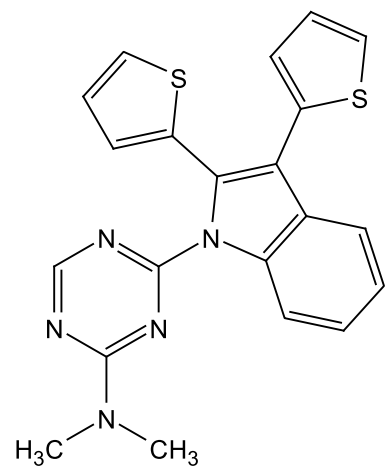


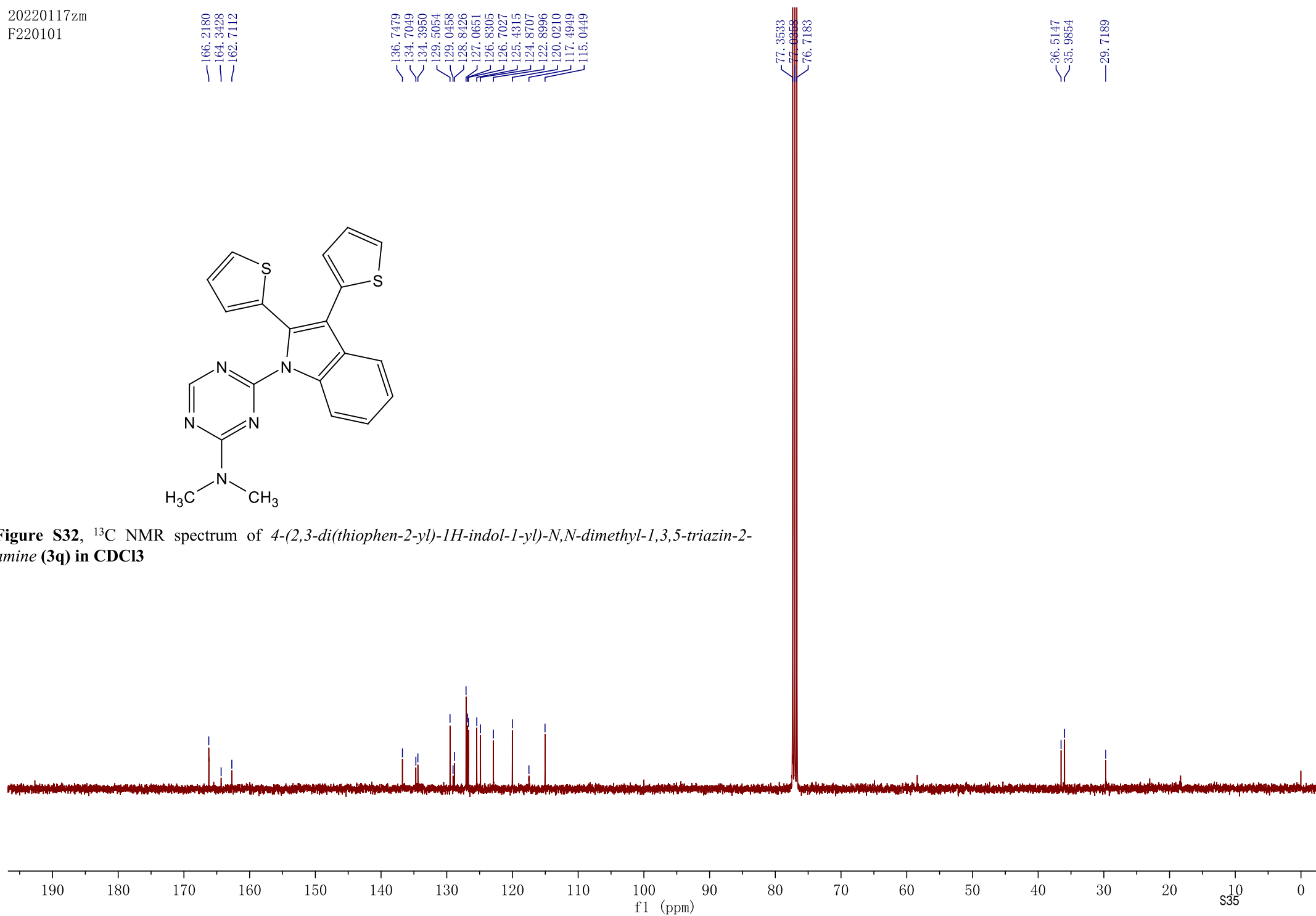
Figure S31, ¹H NMR spectrum of 4-(2,3-di(thiophen-2-yl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (3q) in CDCl₃





166.2180
164.3428
162.7112
136.7479
134.7049
134.3950
129.5054
129.0458
128.8426
127.0651
126.8305
126.7027
125.4315
124.8707
122.8996
120.0210
117.4949
115.0449
77.3533
77.0858
76.7183
36.5147
35.9854
29.7189

Figure S32, ¹³C NMR spectrum of 4-(2,3-di(thiophen-2-yl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3q**) in CDCl₃



20211112zm
f211104

8.5926
8.5770
8.5561

7.6283
7.6088
7.3888
7.3687
7.3504
7.2927
7.2811
7.2739
7.2555
7.2193
7.2146
7.1978
7.1317
7.1141
7.0669
7.0469
6.8817
6.8606

3.8351

3.1455
3.1337

2.5945
2.5757
2.5566
2.4545

1.6614
1.6428
1.6243
1.6060

0.9807
0.9625
0.9442

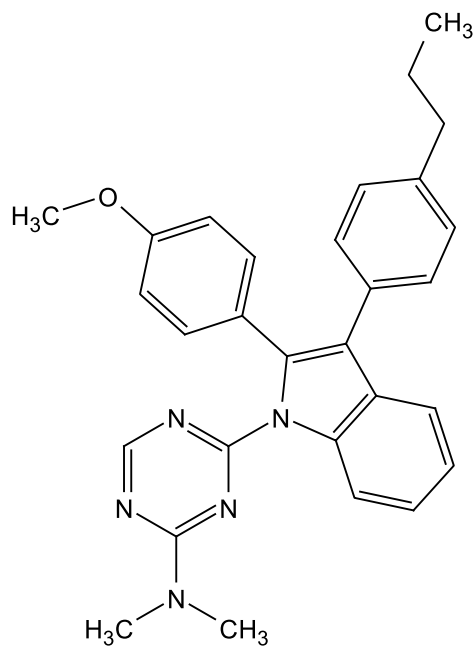
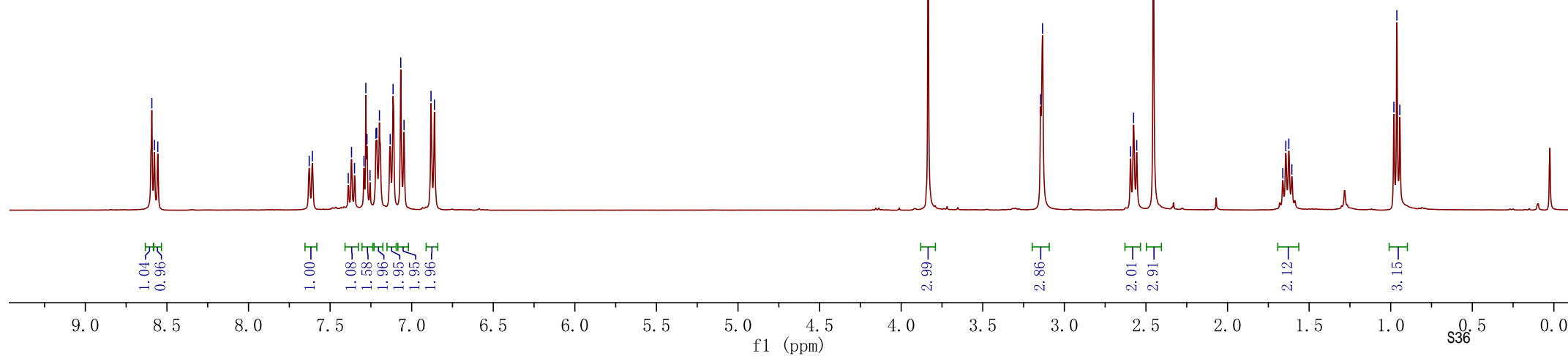


Figure S33, ^1H NMR spectrum of 4-(2-(4-methoxyphenyl)-3-(4-propylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3r** and **3r'**) in CDCl_3



20211116zm
1104

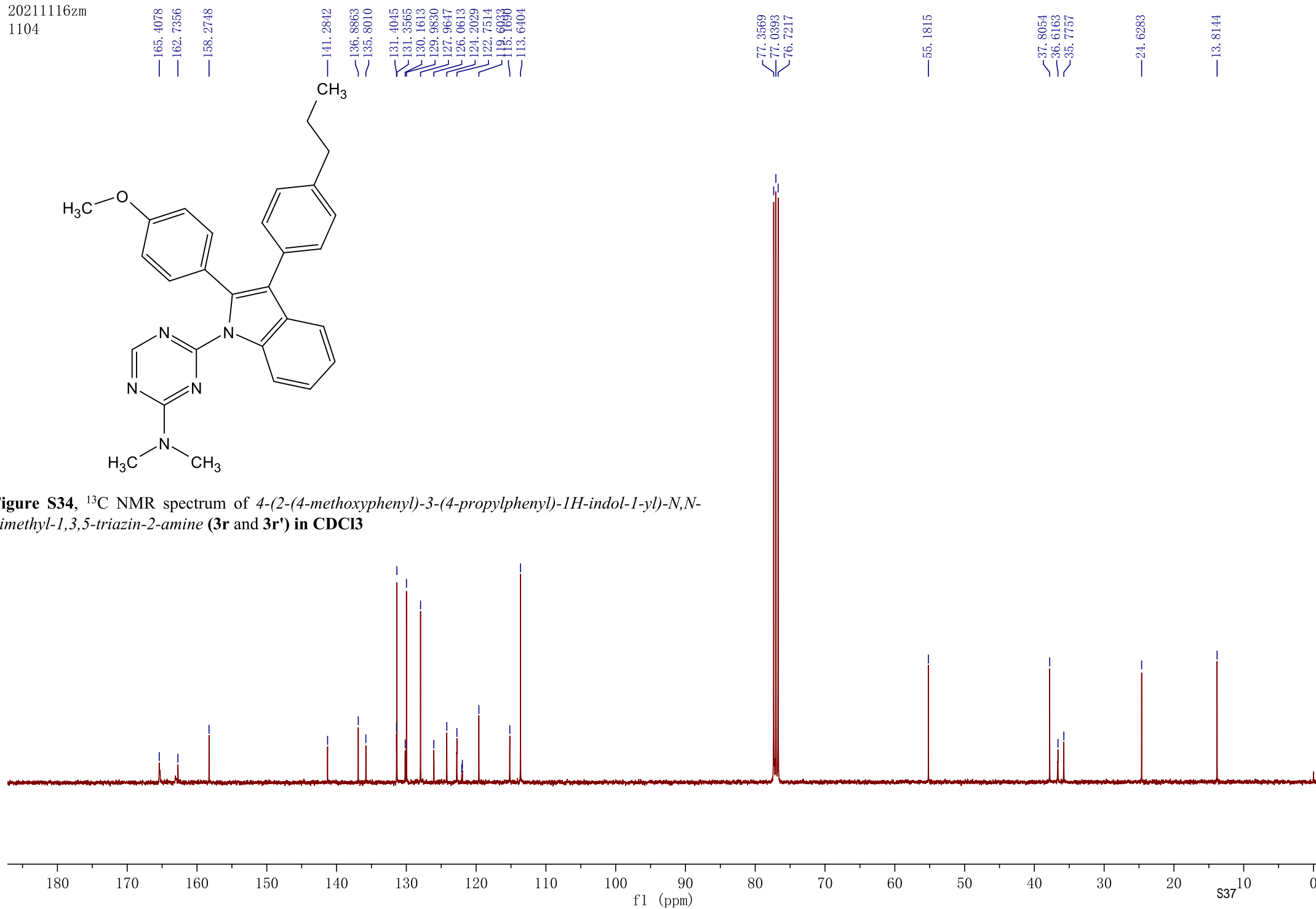
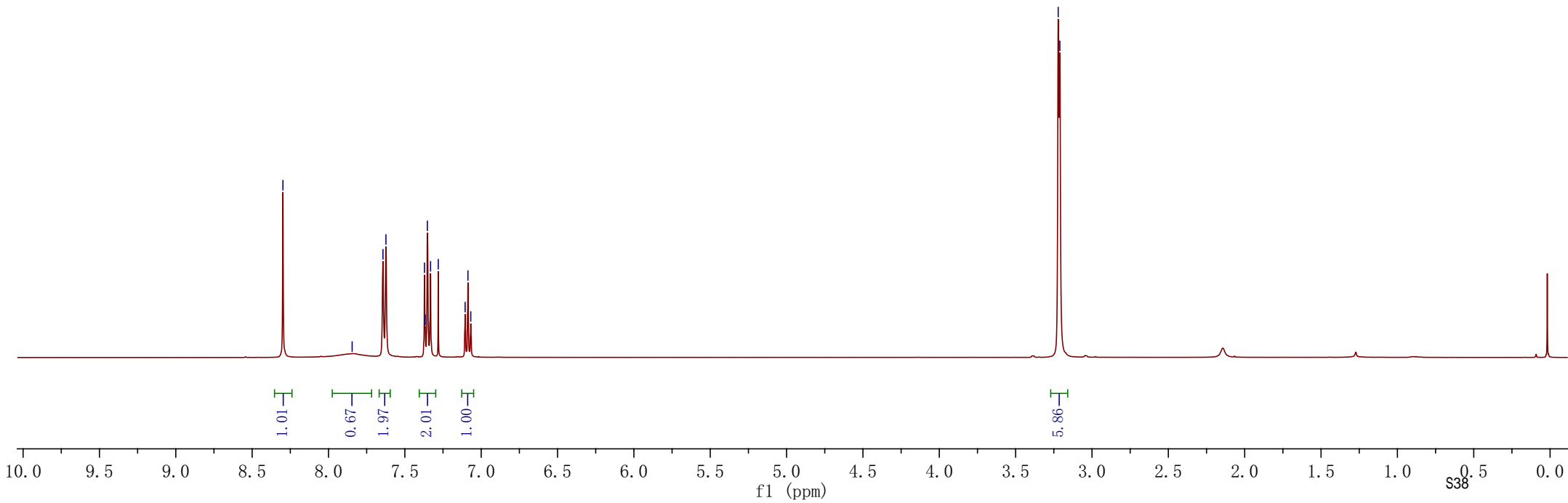


Figure S34, ¹³C NMR spectrum of 4-(2-(4-methoxyphenyl)-3-(4-propylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine (**3r** and **3r'**) in CDCl₃



Figure S35, ¹H NMR spectrum of *N*²,*N*²-dimethyl-*N*⁴-phenyl-1,3,5-triazine-2,4-diamine (**1a**) in CDCl₃



20220117zm
20211128

165.3911
164.5384
163.1780

138.7478

128.8372

123.1583

120.2078

77.3639
77.0463
76.7287

36.4359

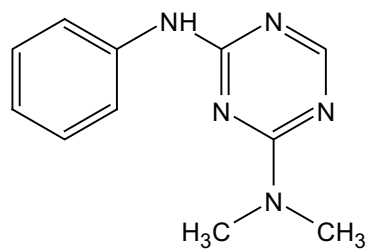
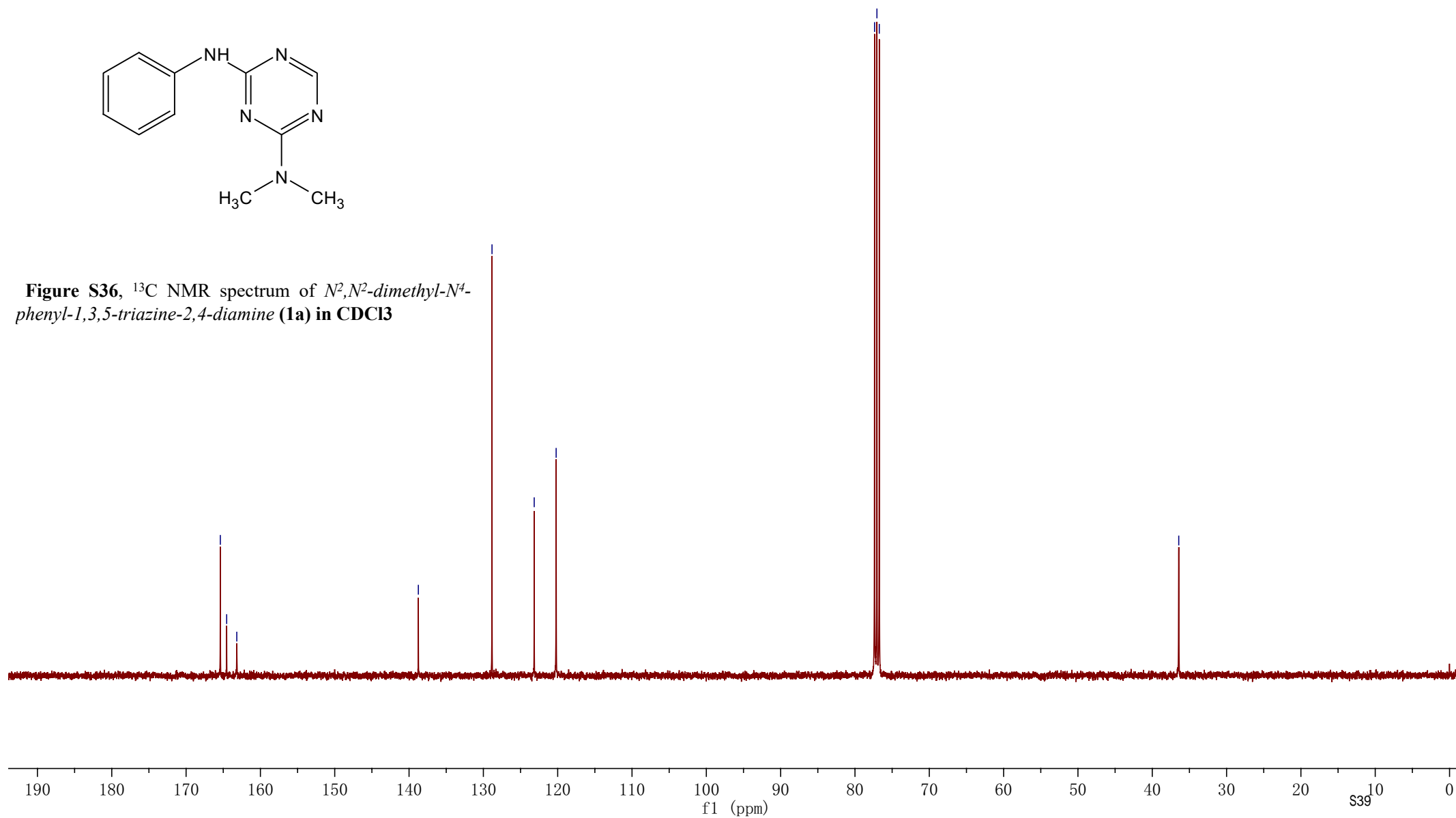
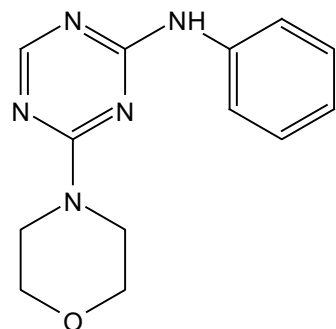


Figure S36, ^{13}C NMR spectrum of N^2,N^2 -dimethyl- N^4 -phenyl-1,3,5-triazine-2,4-diamine (**1a**) in CDCl_3



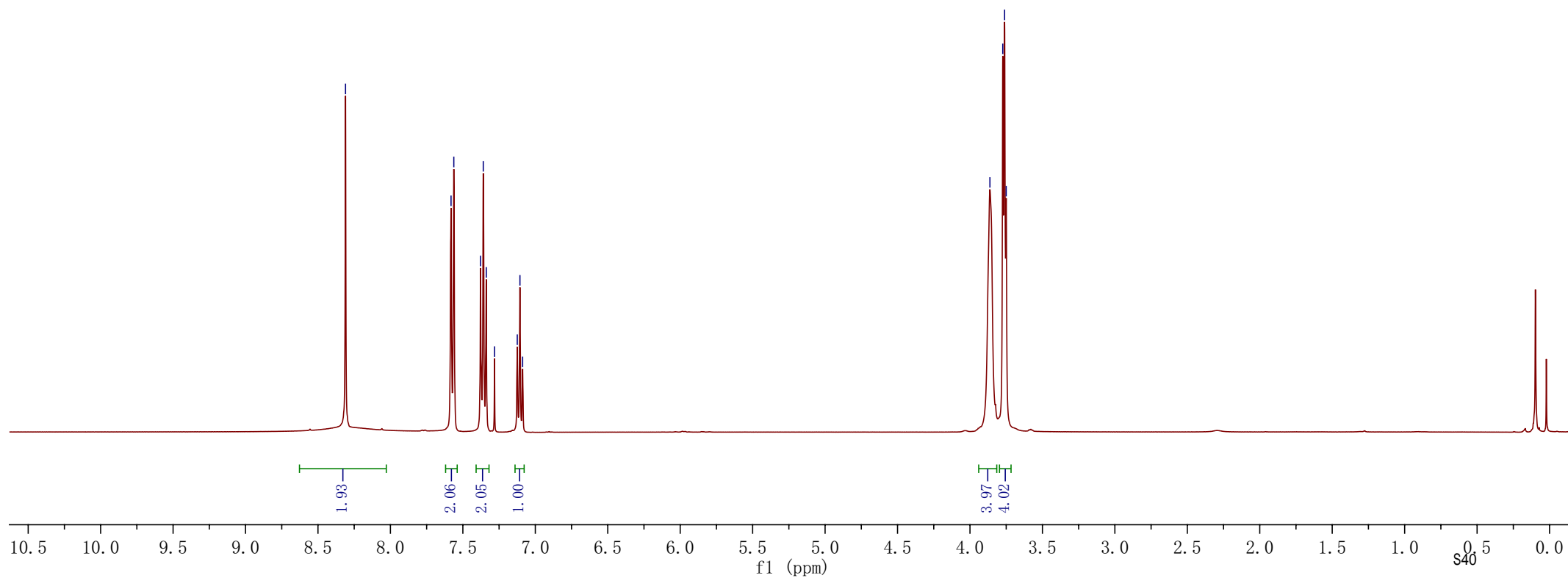
20230412zm
1j CDCl₃



8.3099
7.5816
7.5625
7.3781
7.3592
7.3385
7.2815
7.1245
7.1060
7.0875

3.8624
3.7737
3.7611
3.7500

Figure S37, ¹H NMR spectrum of *4-morpholino-N-phenyl-1,3,5-triazin-2-amine (1j)* in CDCl₃



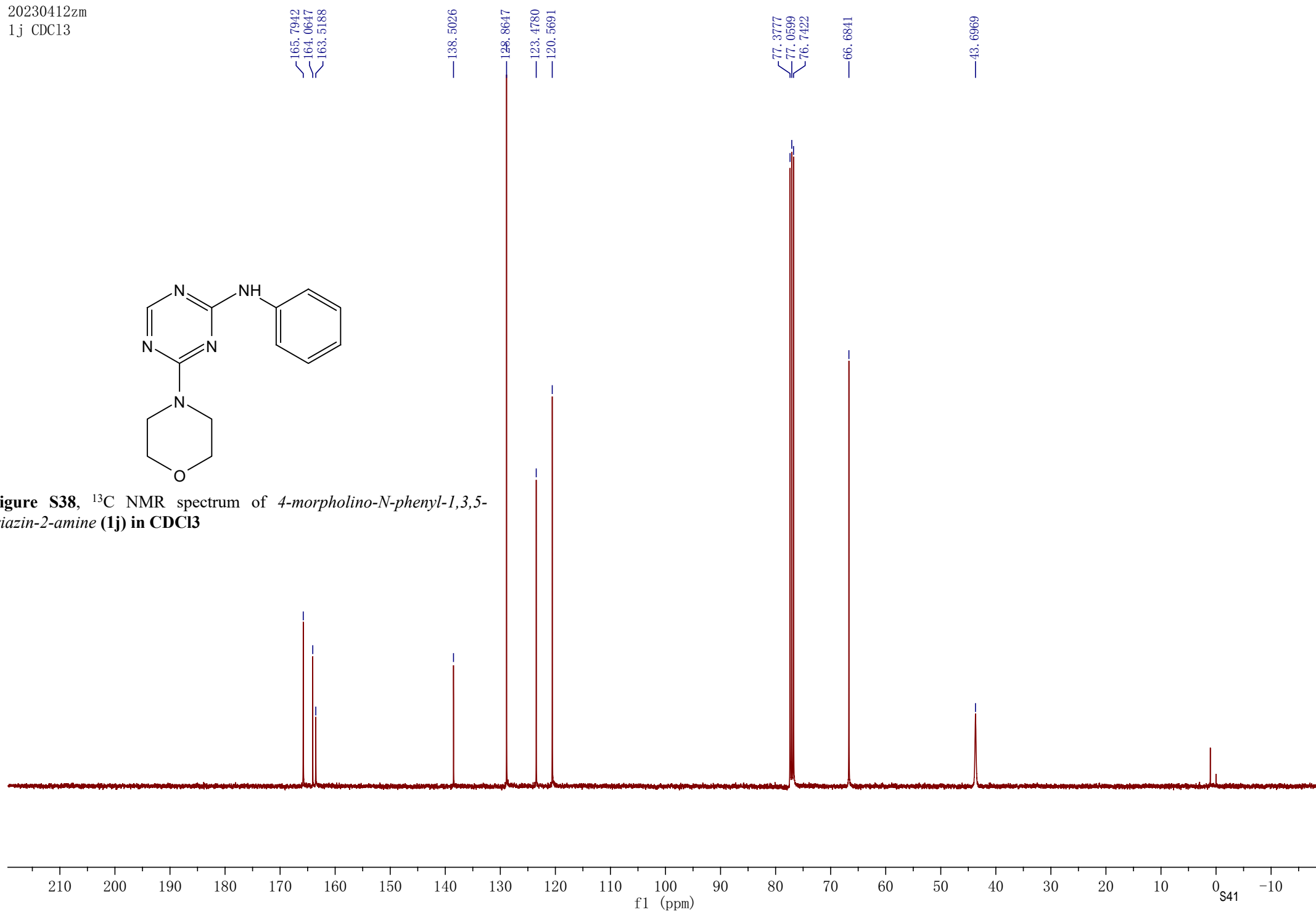
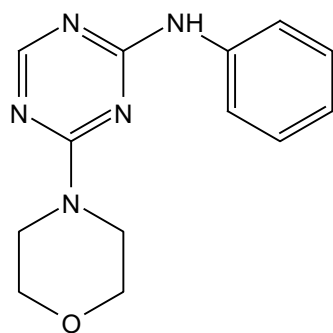


Figure S38, ¹³C NMR spectrum of 4-morpholino-N-phenyl-1,3,5-triazin-2-amine (**1j**) in CDCl₃

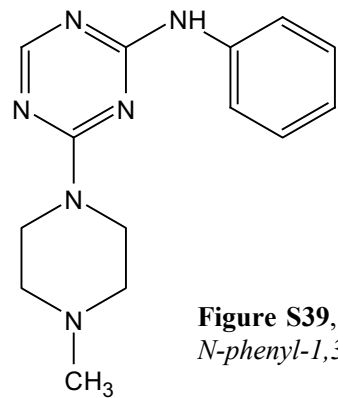
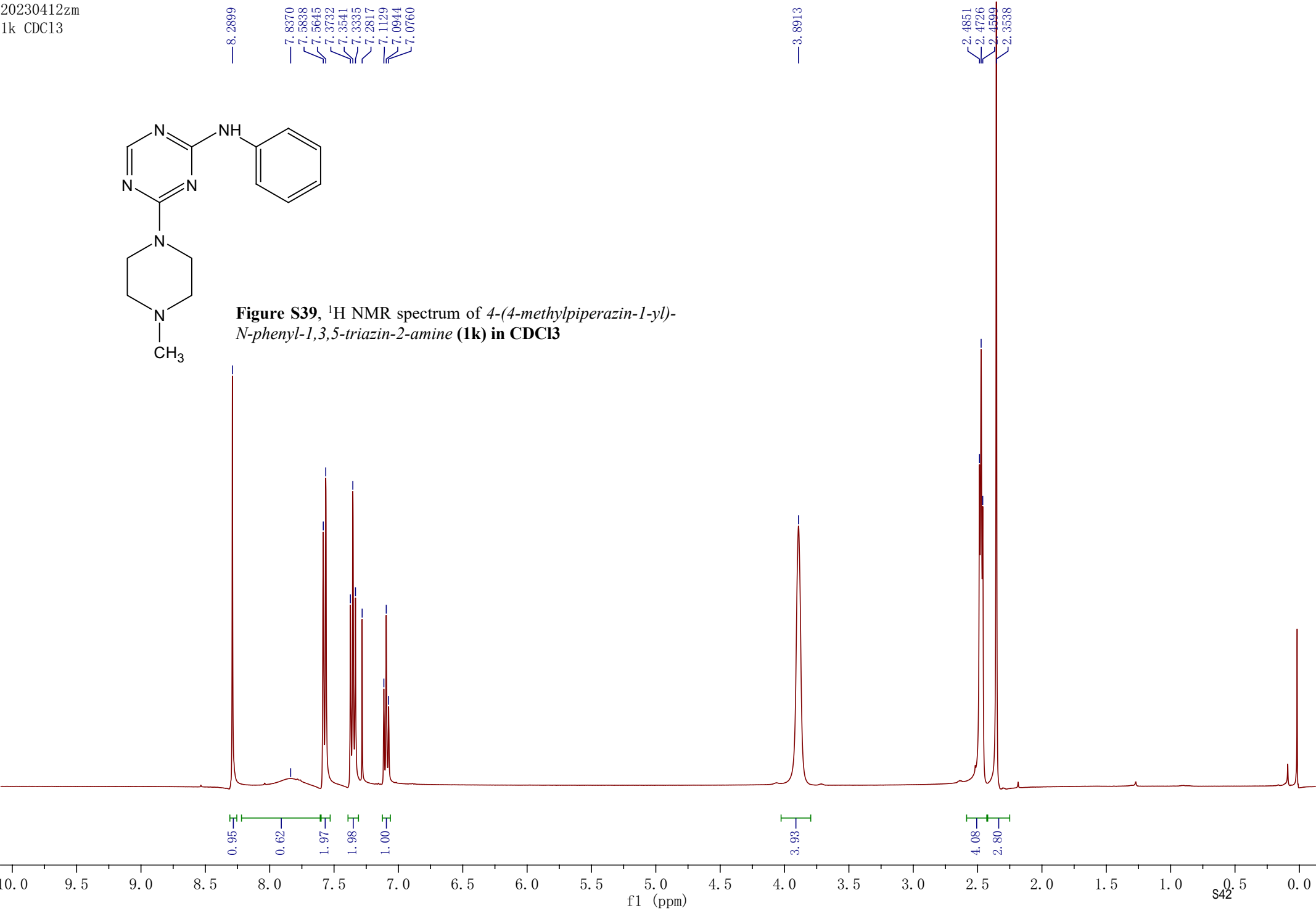
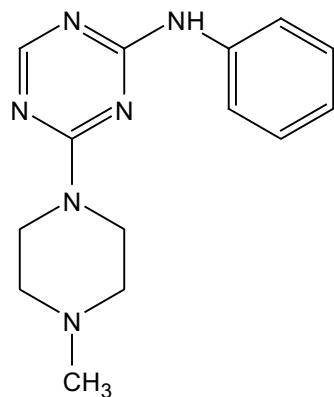


Figure S39, ¹H NMR spectrum of 4-(4-methylpiperazin-1-yl)-*N*-phenyl-1,3,5-triazin-2-amine (**1k**) in CDCl₃



20230412zm
1k CDCl₃



165.8184
163.8658
163.5359

138.5601

128.8527

123.3341

120.4190

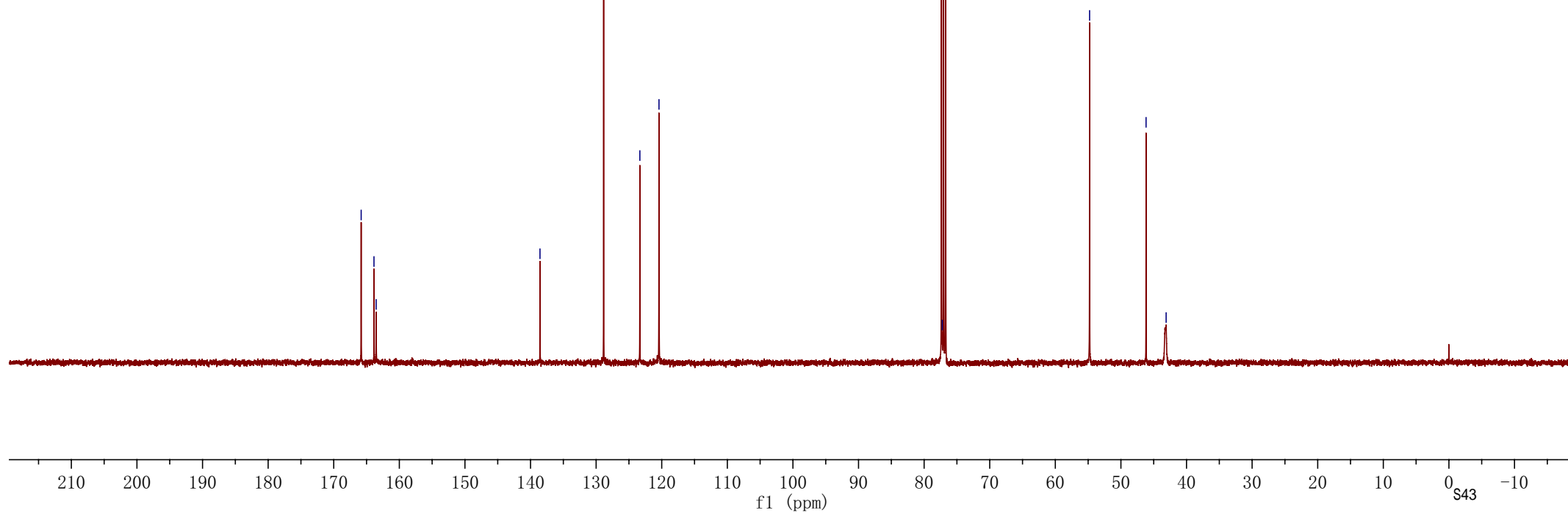
77.3552
77.2389
77.0376
76.7201

54.7750

46.1673

43.1069

Figure S40, ¹³C NMR spectrum of 4-(4-methylpiperazin-1-yl)-*N*-phenyl-1,3,5-triazin-2-amine (**1k**) in CDCl₃



20230412zm
1L CDC13

7.6469
7.6445
7.6254
7.5804
7.3482
7.3294
7.3085
7.0714
7.0530
7.0345

3.2162
3.2075

2.3471

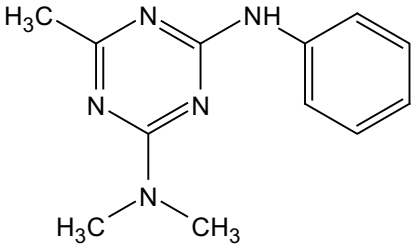
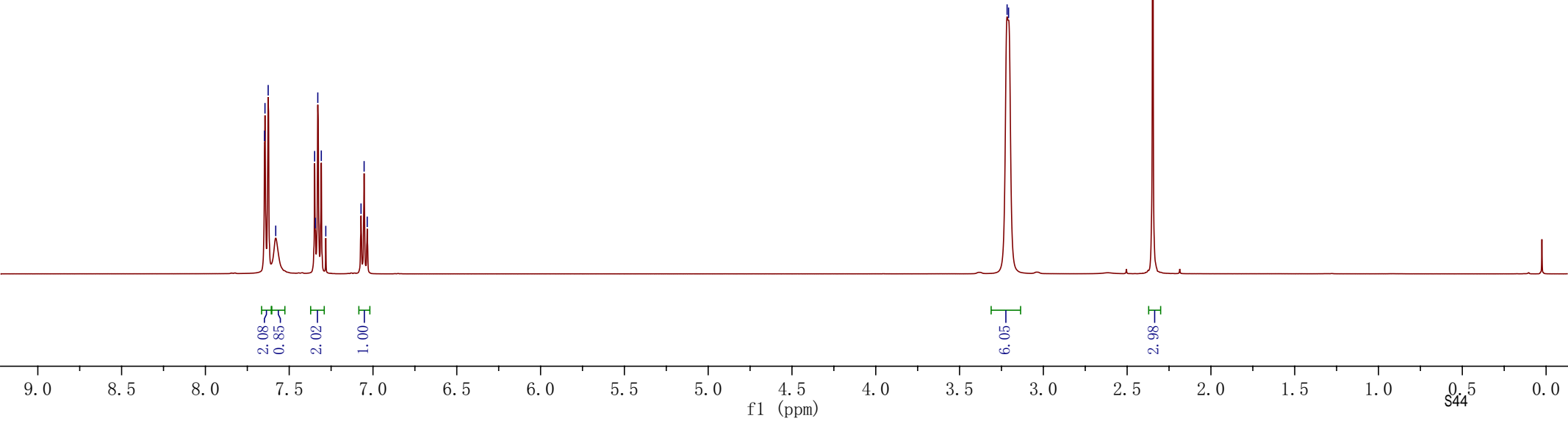


Figure S41, ¹H NMR spectrum of *N*²,*N*²,6-trimethyl-*N*⁴-phenyl-1,3,5-triazine-2,4-diamine (**1l**) in CDCl₃



20230412zm
1L CDCl3

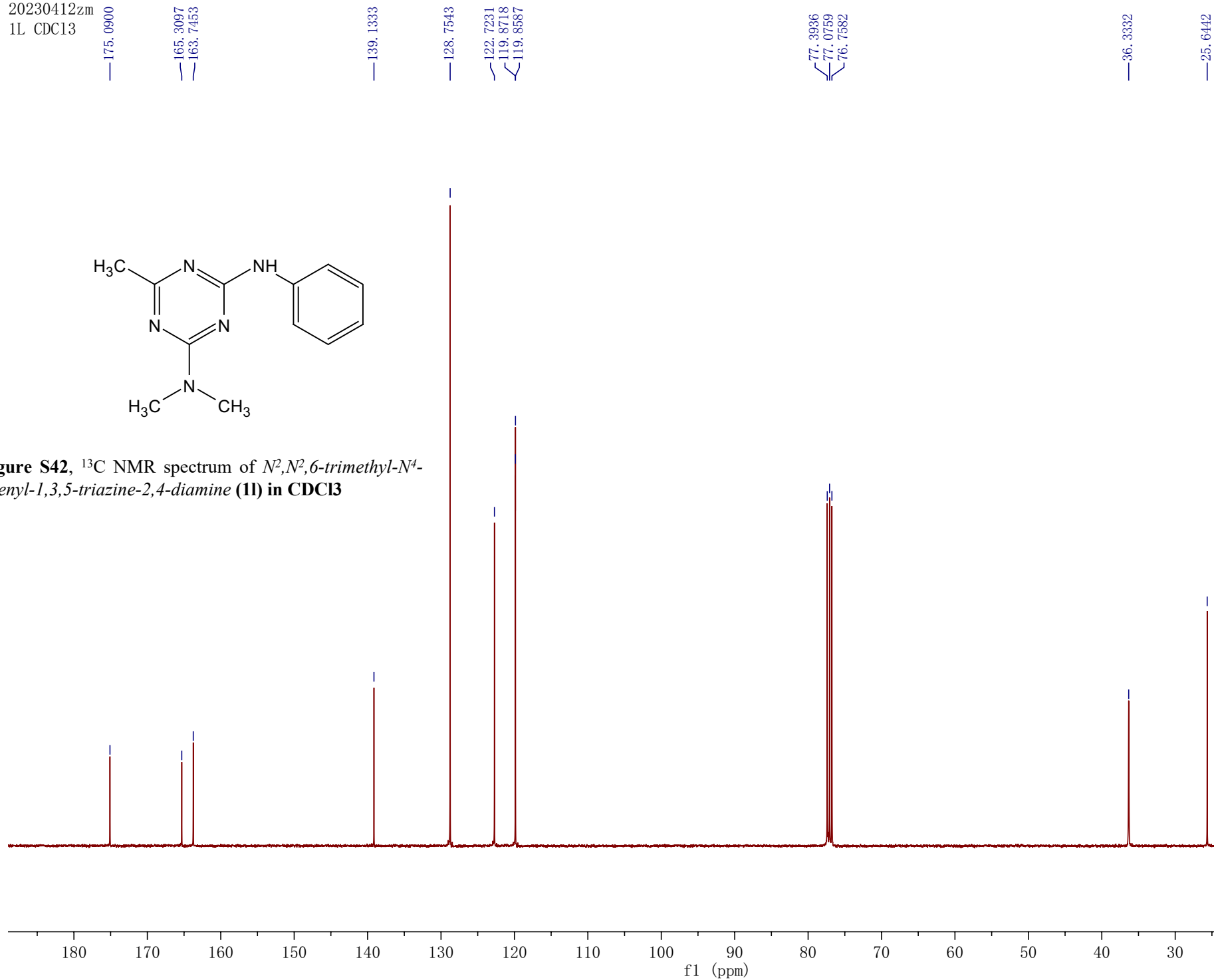
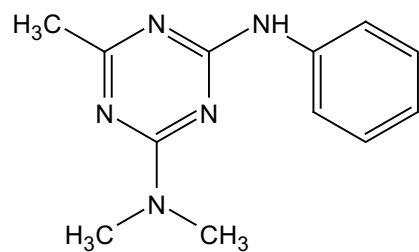


Figure S42, ¹³C NMR spectrum of *N*²,*N*²,6-trimethyl-*N*⁴-phenyl-1,3,5-triazine-2,4-diamine (**1I**) in CDCl₃

20211112zm
f211104

8.5926
8.5770
8.5561

7.6283
7.6088
7.3888
7.3687
7.3504
7.2927
7.2811
7.2739
7.2555
7.2193
7.2146
7.1978
7.1317
7.1141
7.0669
7.0469
6.8817
6.8606

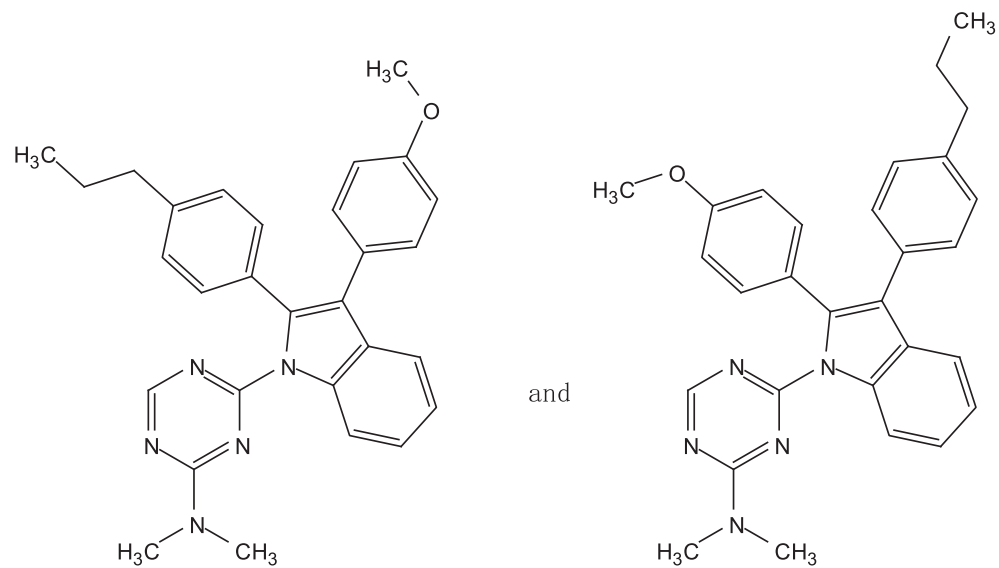
3.8351

3.1455
3.1337

2.5945
2.5757
2.5566
2.4545

1.6793
1.6614
1.6428
1.6243
1.6060
1.5880

0.9807
0.9625
0.9442



and

20211112zm
f211104

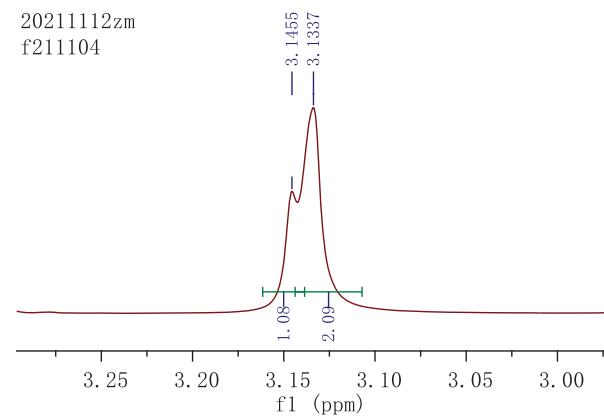


Figure S43. The isomers **3r** and **3r'**.

