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

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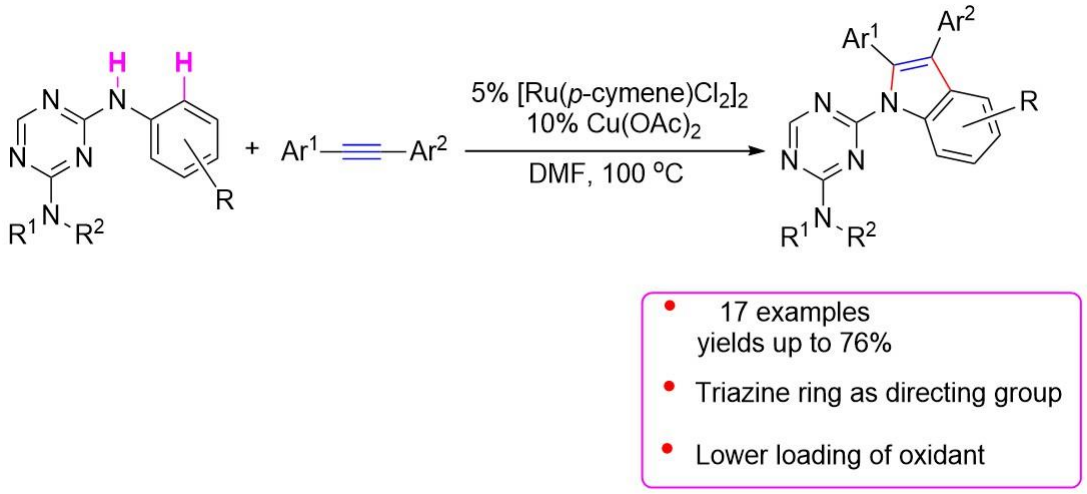

1,3,5 triazines, especially indole functionalized triazine derivatives, exhibit excellent activities, such as anti-tumor, antibacterial, and anti-inflammatory activities. Traditional methods for the synthesis of N-(2-triazine) indoles suffer from unstable materials and tedious operations. Transition-metal-catalyzed 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 ^{1}H 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 ^{1}H and ^{13}C spectra of compounds

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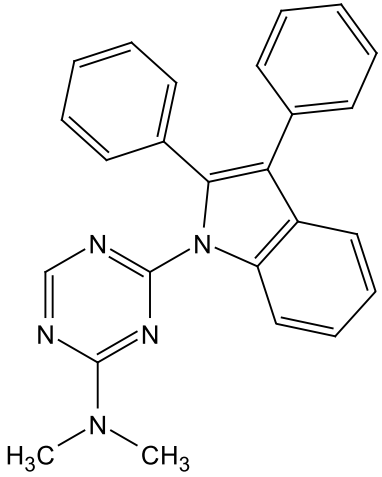
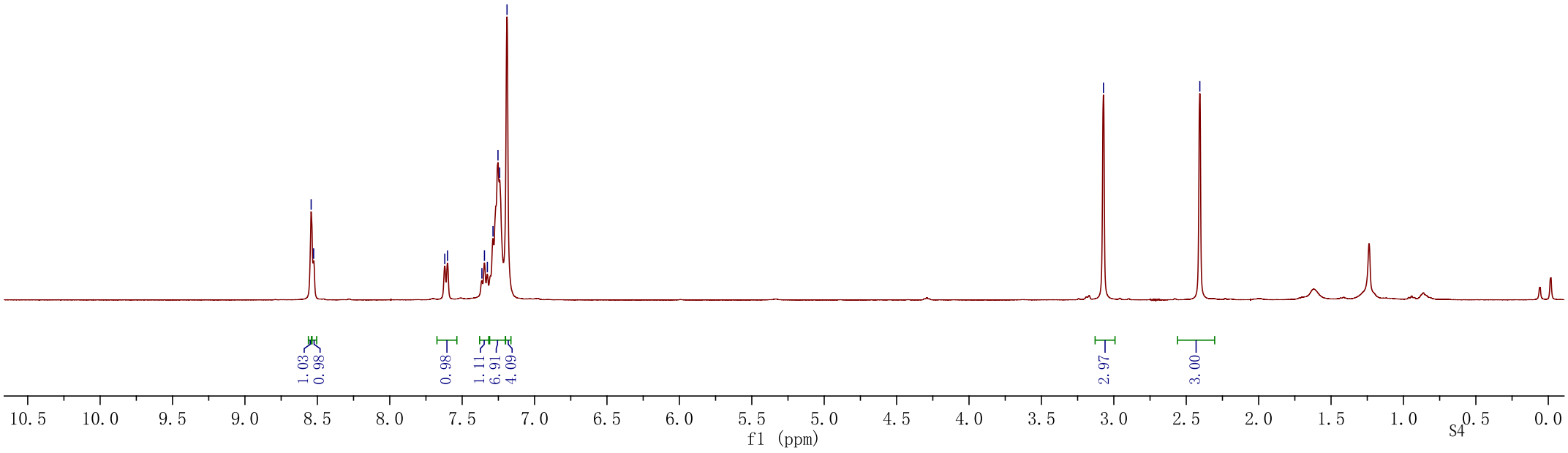
Figure S1, ^{1}H NMR spectrum of *4-(2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* (**3a**) in CDCl3





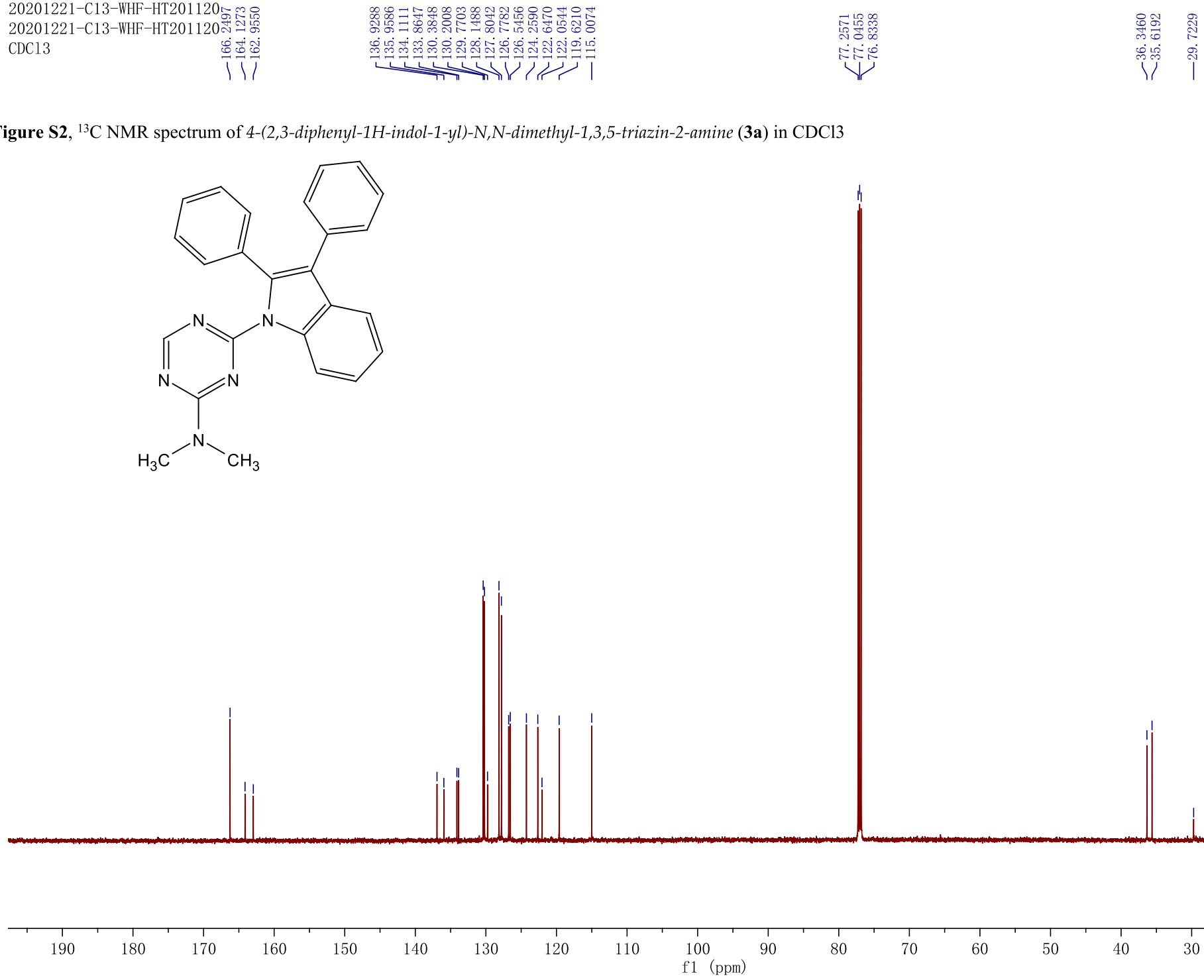


Figure S2, ^{13}C NMR spectrum of *4-(2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* (**3a**) in CDCl3

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Figure S3, ^{1}H NMR spectrum of *4--4-(7-methyl-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3b)** in CDCl3

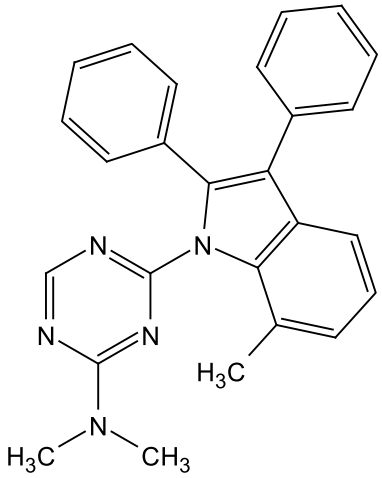

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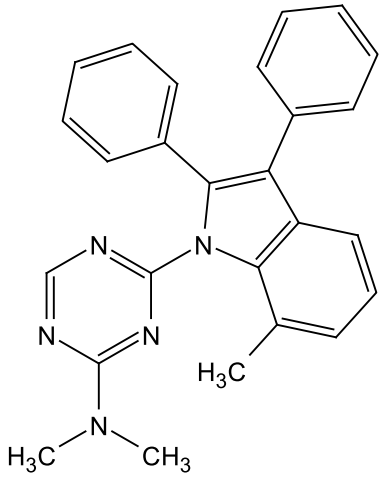
Figure S4, ^{13}C NMR spectrum of *4--4-(7-methyl-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3b)** in CDCl3



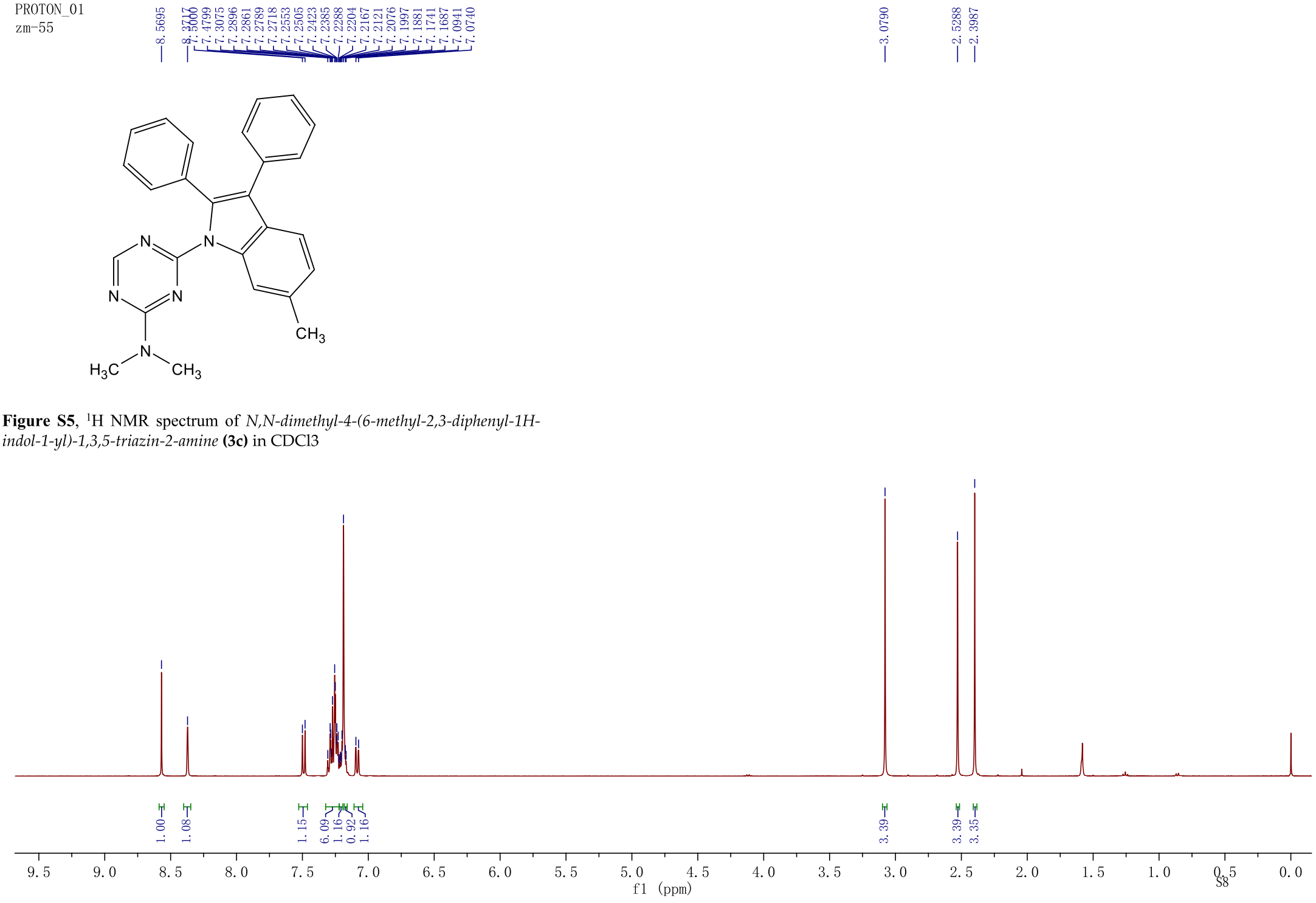


Figure S5, ^{1}H NMR spectrum of *N,N-dimethyl-4-(6-methyl-2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-amine* **(3c)** in CDCl3

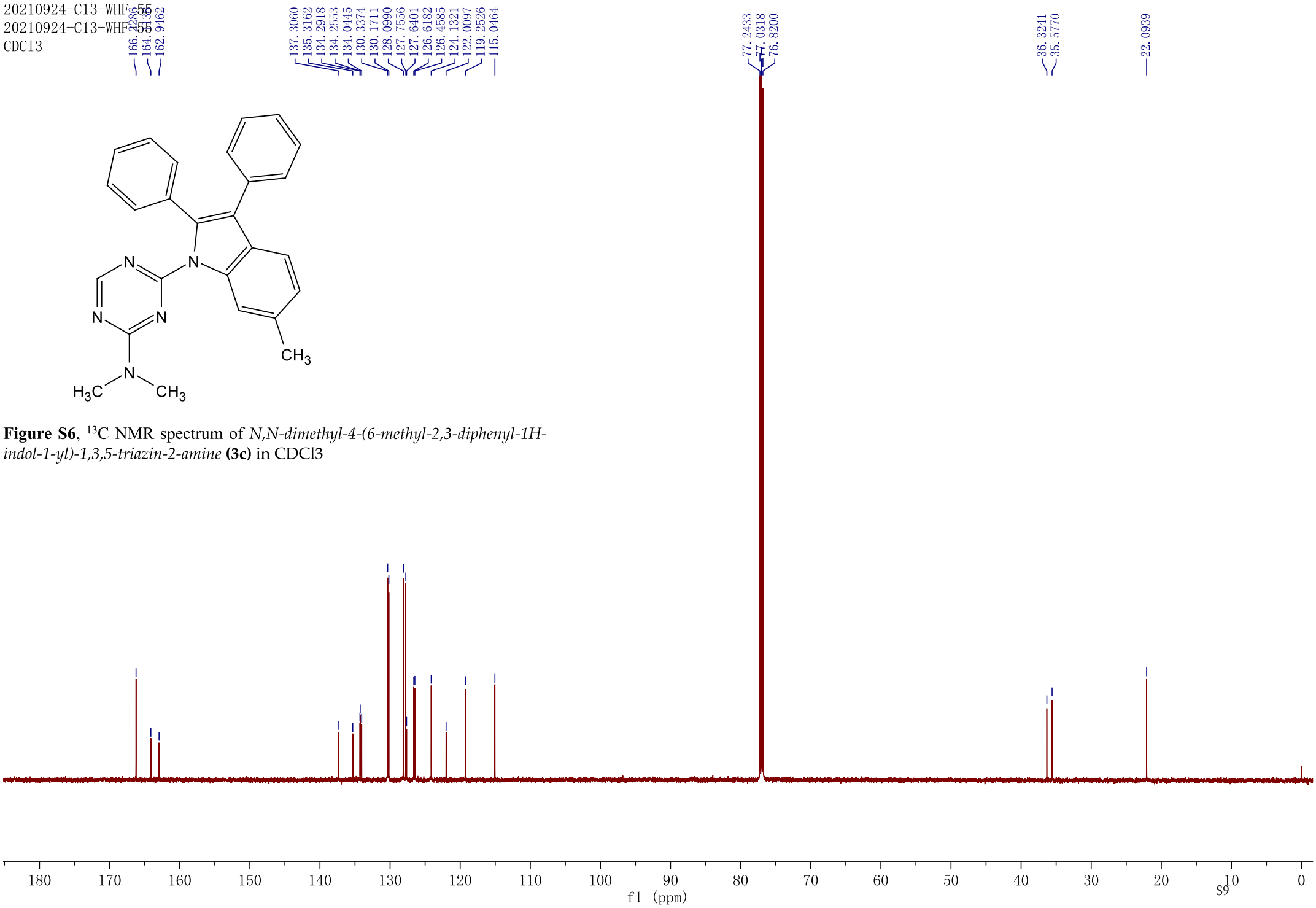


Figure S6, ^{13}C NMR spectrum of *N,N-dimethyl-4-(6-methyl-2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-amine* **(3c)** in CDCl3

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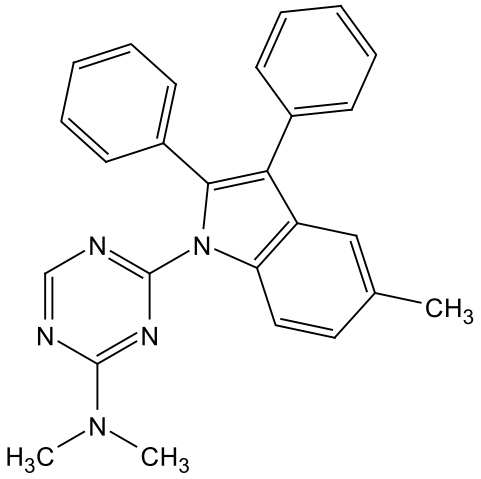
Figure S7, ^{1}H NMR spectrum of *N,N-dimethyl-4-(5-methyl-2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-amine* **(3d)** in CDCl3



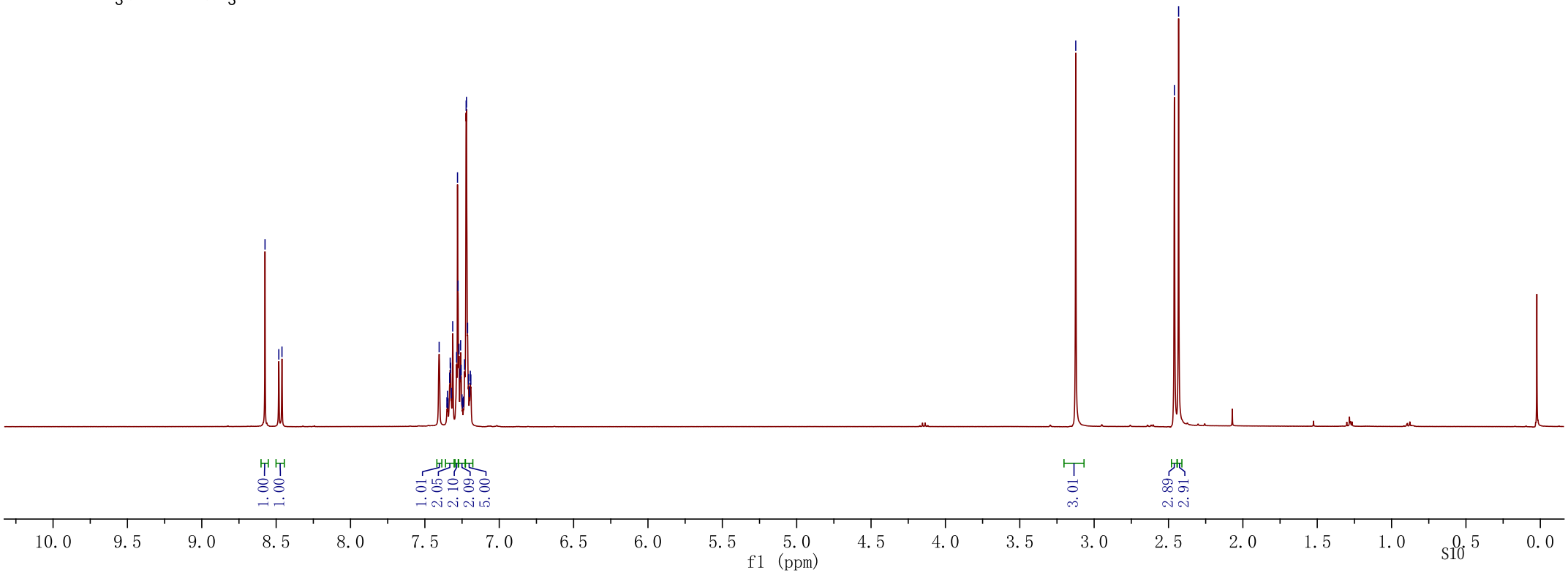


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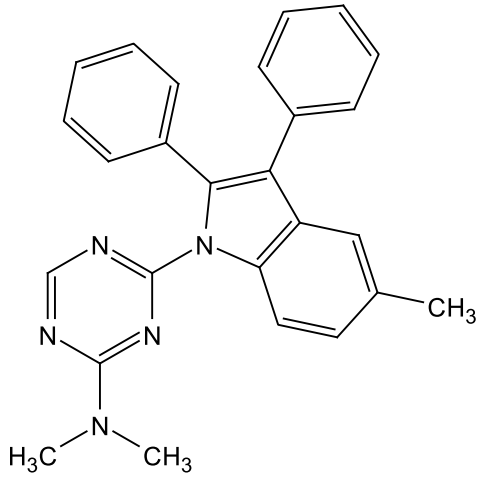
Figure S8, ^{13}C NMR spectrum of *N,N-dimethyl-4-(5-methyl-2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-amine* **(3d)** in CDCl3



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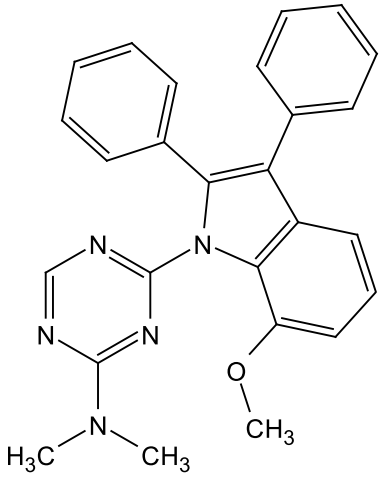
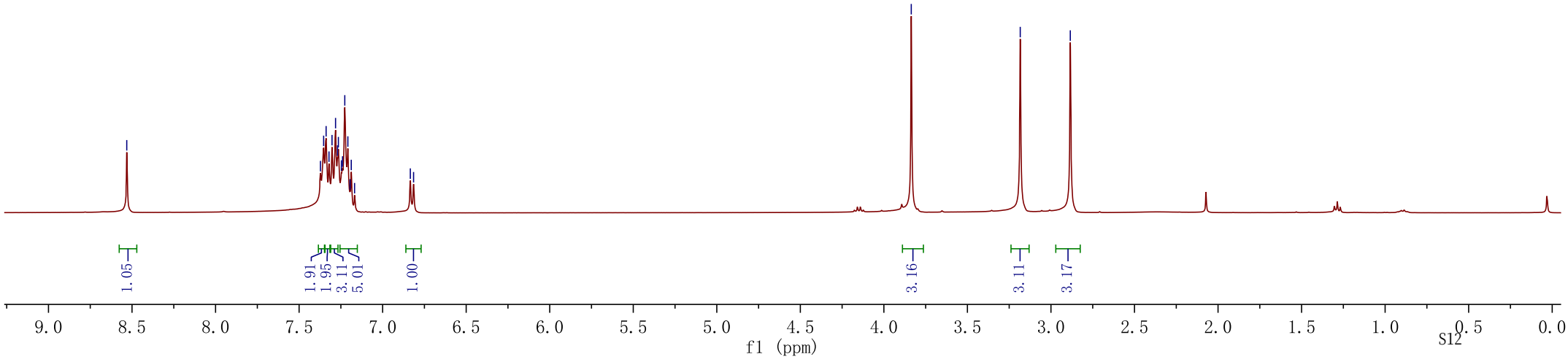
F20220222

Figure S9, ^{1}H NMR spectrum of *4-(7-methoxy-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3e) in CDCl3**





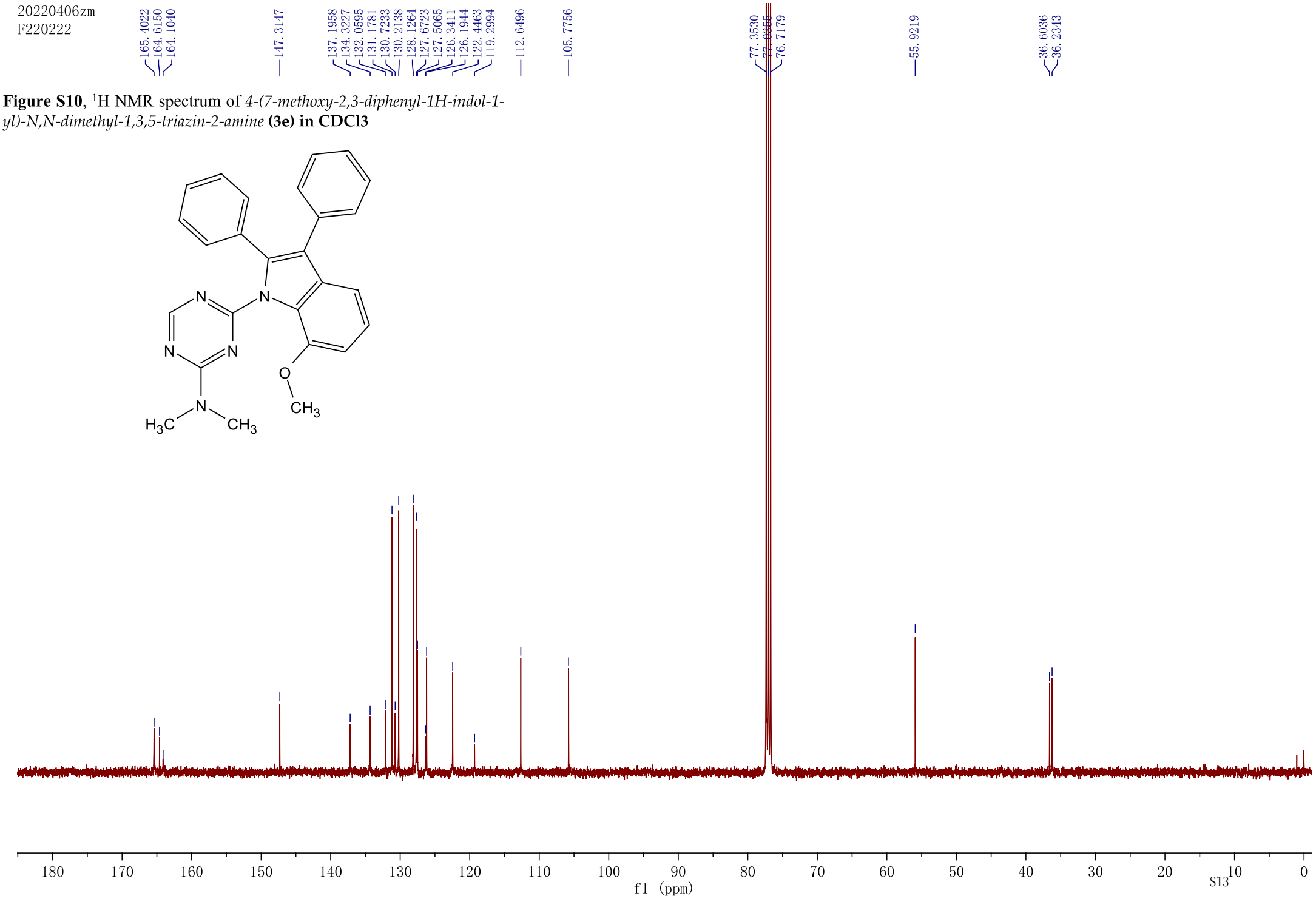
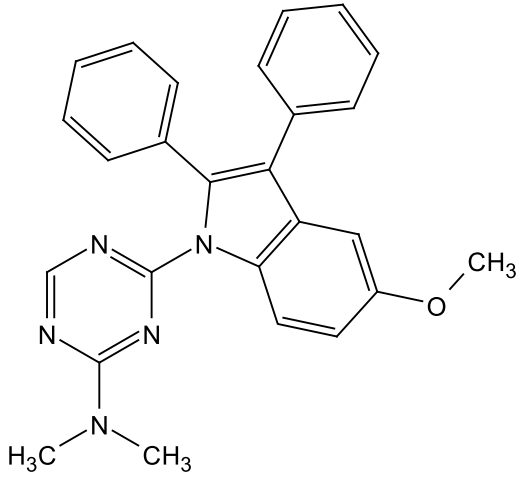


Figure S10, ^{1}H NMR spectrum of *4-(7-methoxy-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3e) in CDCl3**

20190419-H1-WHF-327
20190419-H1-WHF-327
CDCl3

Figure S11, ^{1}H 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**



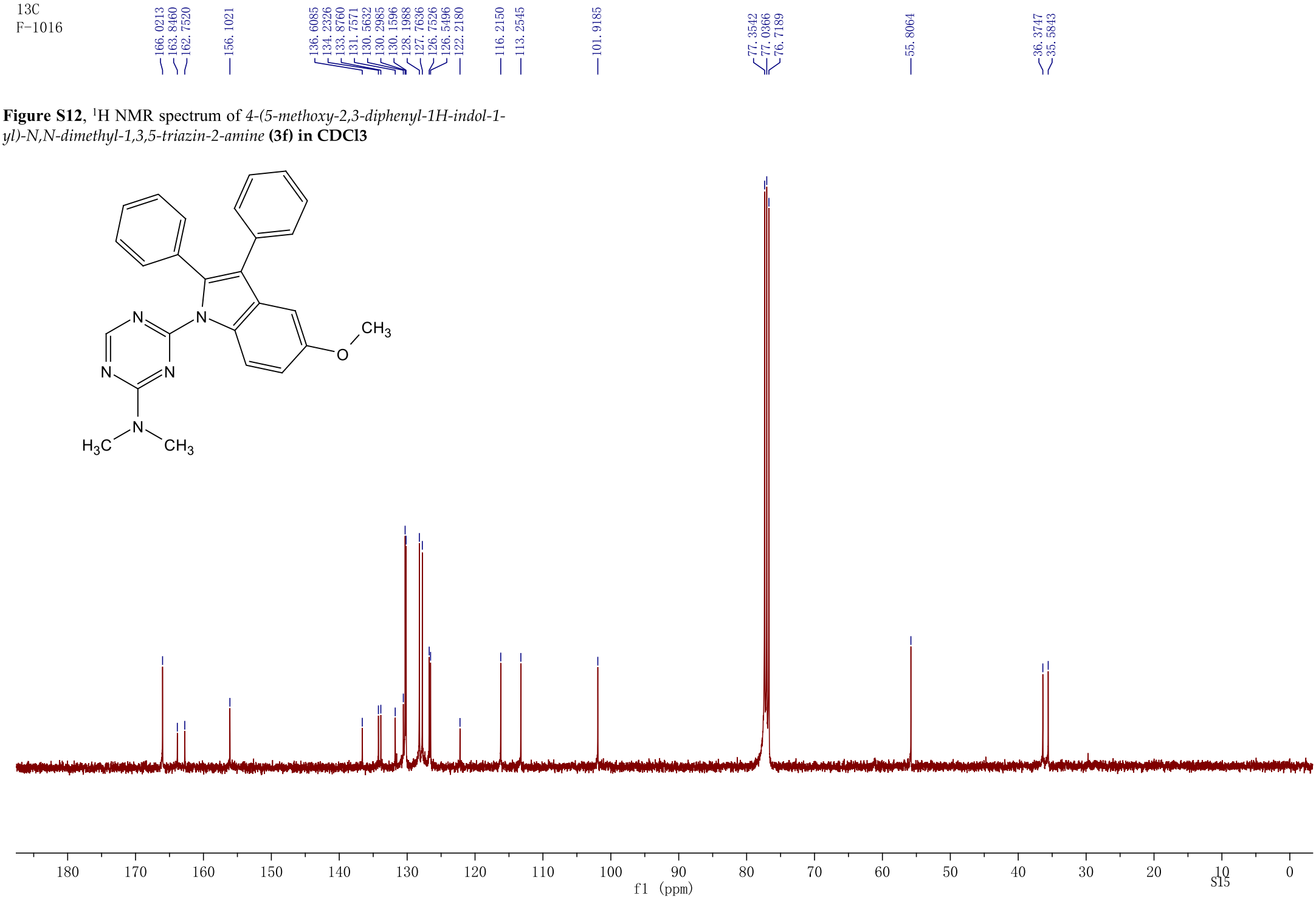


Figure S12, ^{1}H NMR spectrum of *4-(5-methoxy-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3f) in CDCl3**

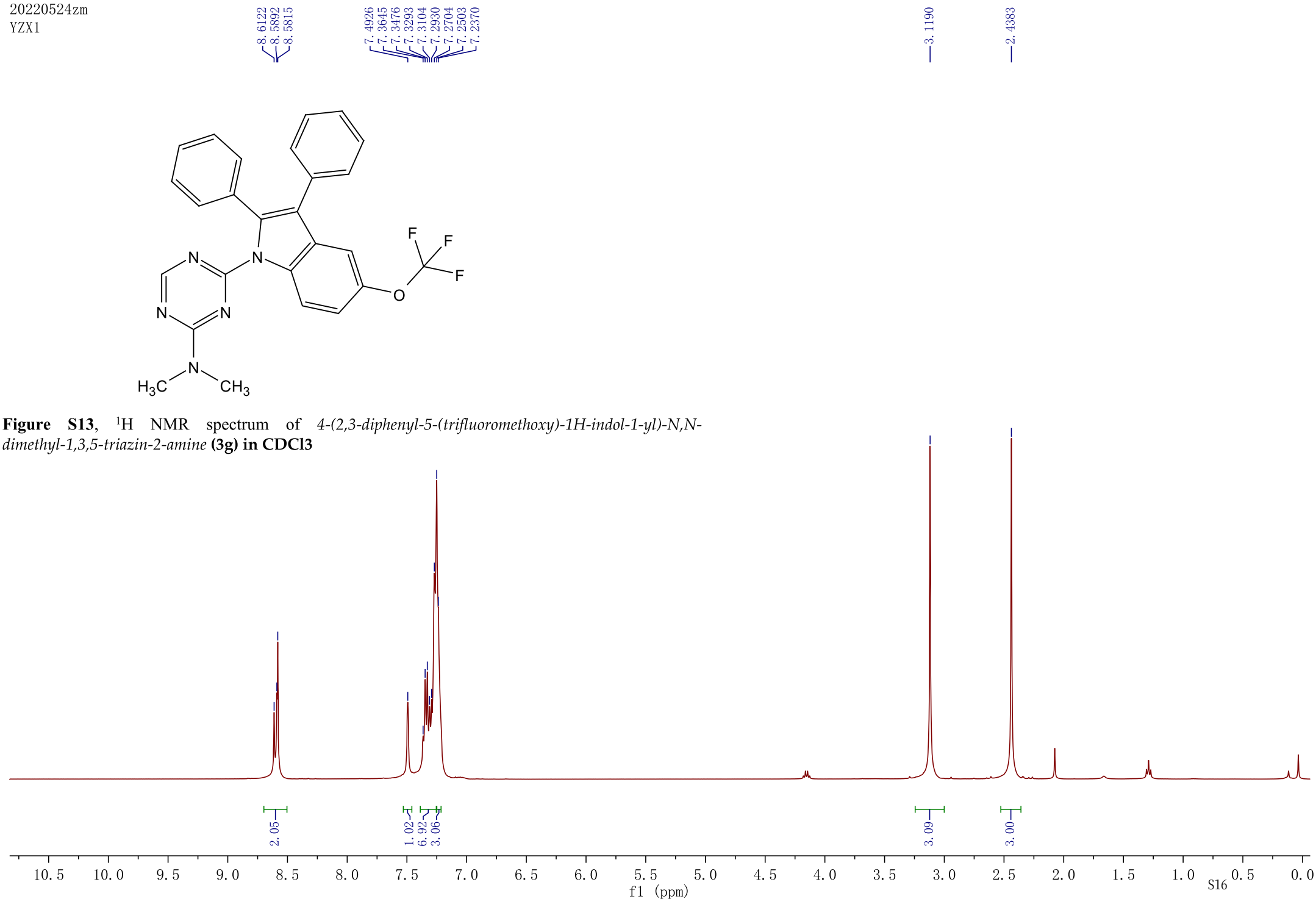


Figure S13, ^{1}H NMR spectrum of *4-(2,3-diphenyl-5-(trifluoromethoxy)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3g) in CDCl3**

20220526zm
YZX1

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
117.6072
116.0669
112.0195
77.3659
77.0483
76.7307
36.3607
35.6037

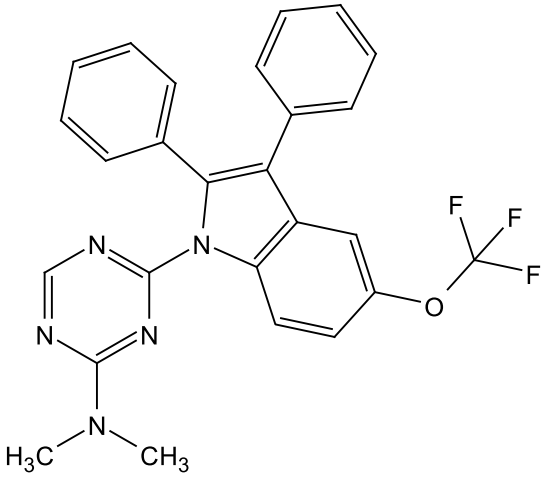
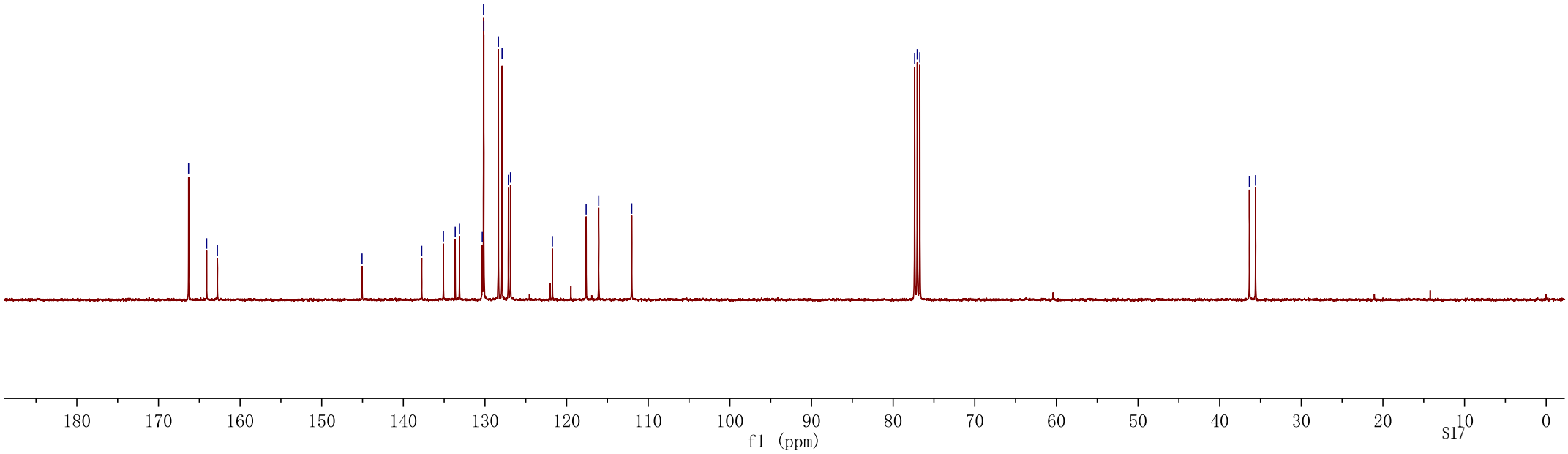


Figure S14, ^{13}C NMR spectrum of *4-(2,3-diphenyl-5-(trifluoromethoxy)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3g) in CDCl3**



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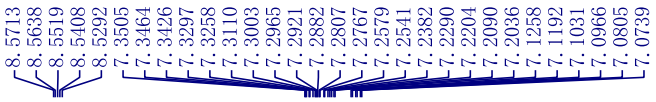


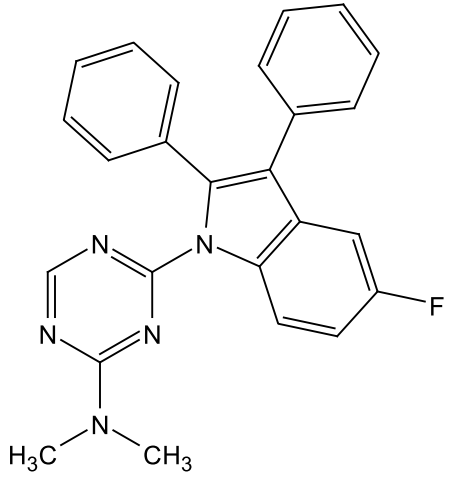
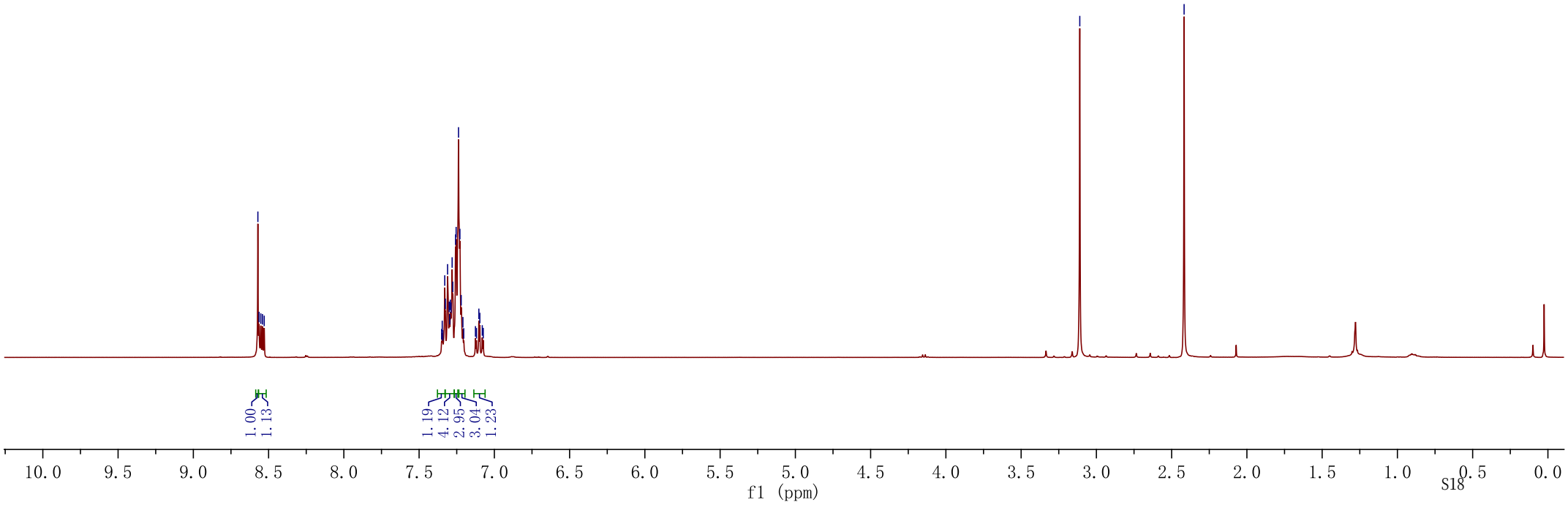


Figure S15, ^{1}H NMR spectrum of *4-(5-fluoro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3h) in CDCl3**



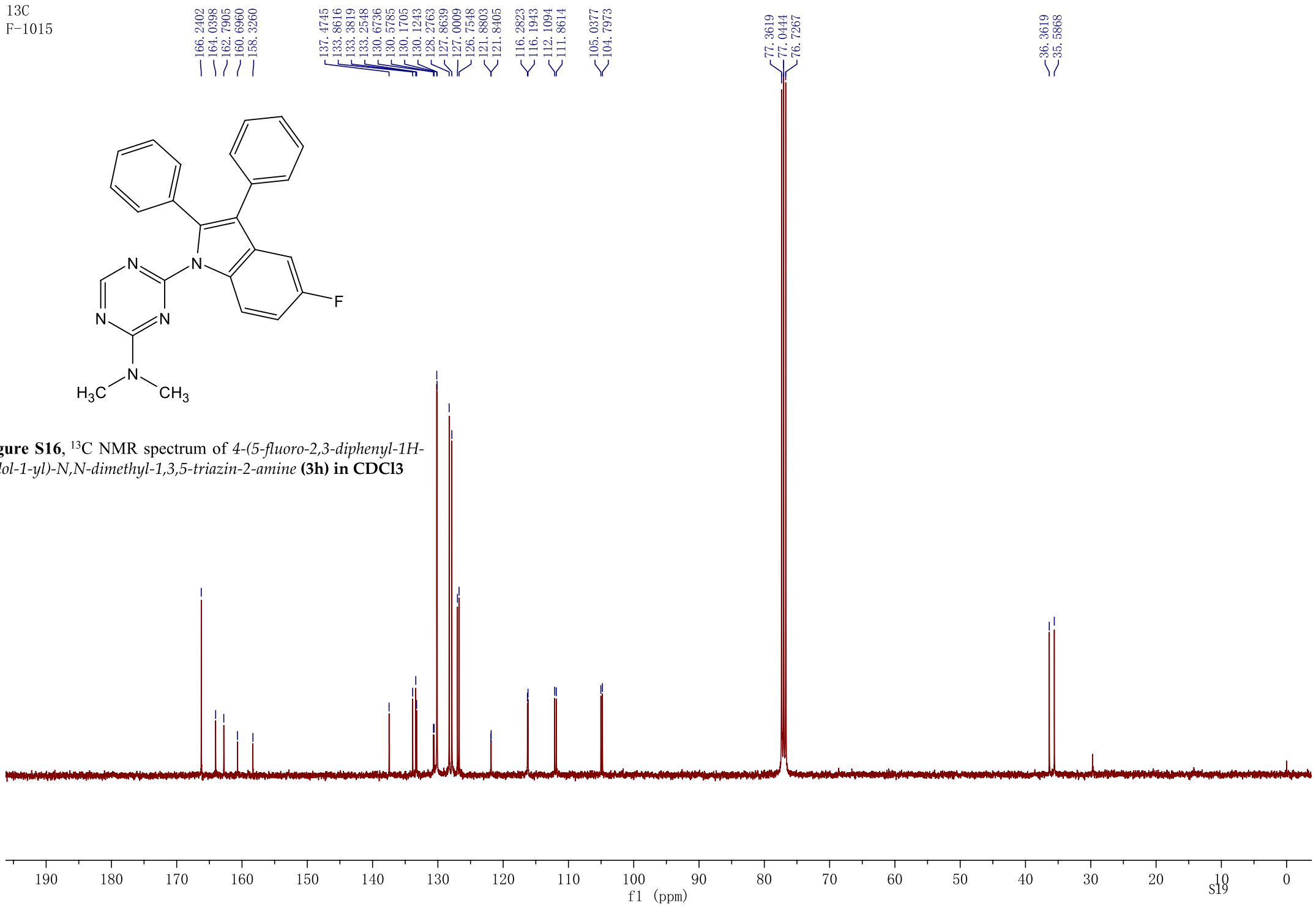


Figure S16, ^{13}C NMR spectrum of *4-(5-fluoro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3h) in CDCl3**

1H
F-1017

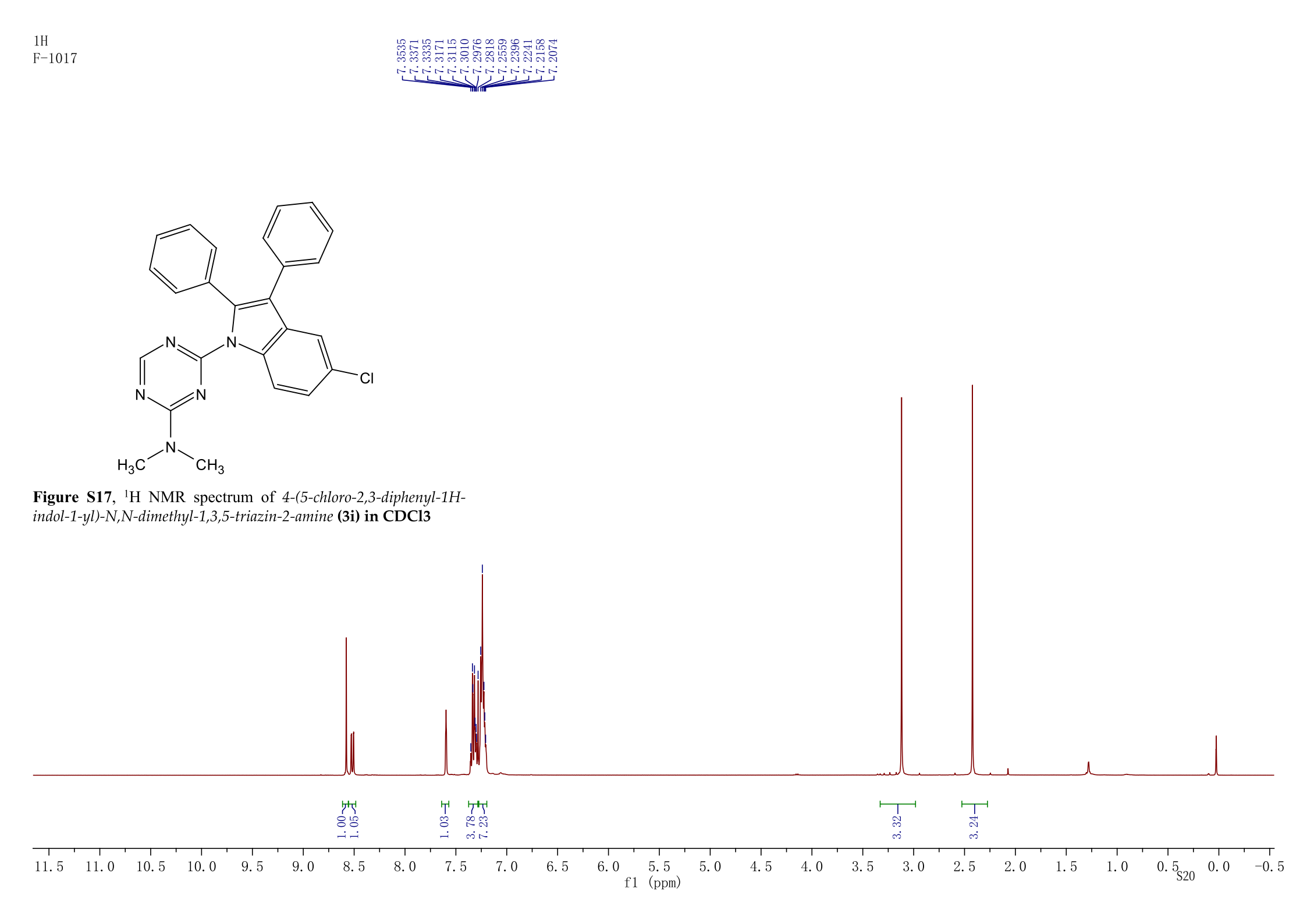


Figure S17, ^{1}H NMR spectrum of *4-(5-chloro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3i) in CDCl3**

13C
F-1017

166.1768
163.9146
162.7343
137.1919
135.2610
133.6750
133.1681
130.9850
130.2400
130.1249
128.3094
127.8865
127.0700
126.8412
124.3258
121.4922
119.1165
116.3226
77.3664
77.0488
76.7312
36.4143
35.6196

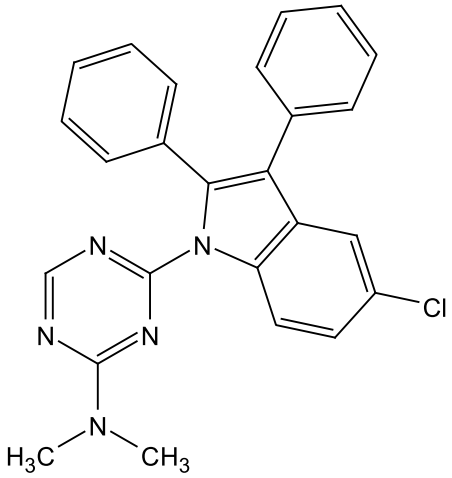


Figure S18, ^{13}C NMR spectrum of *4-(5-chloro-2,3-diphenyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3i) in CDCl3**

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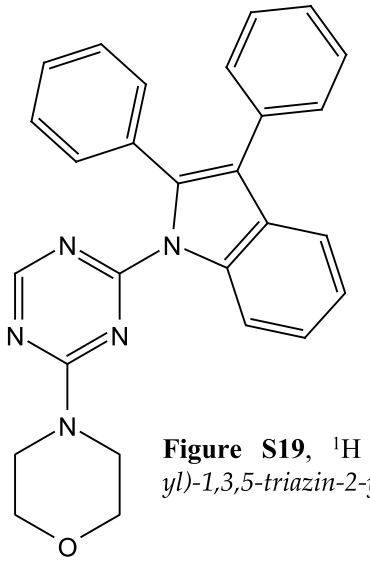

Figure S19, ^{1}H NMR spectrum of *4-(4-(2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-yl)morpholine* **(3j) in CDCl3**

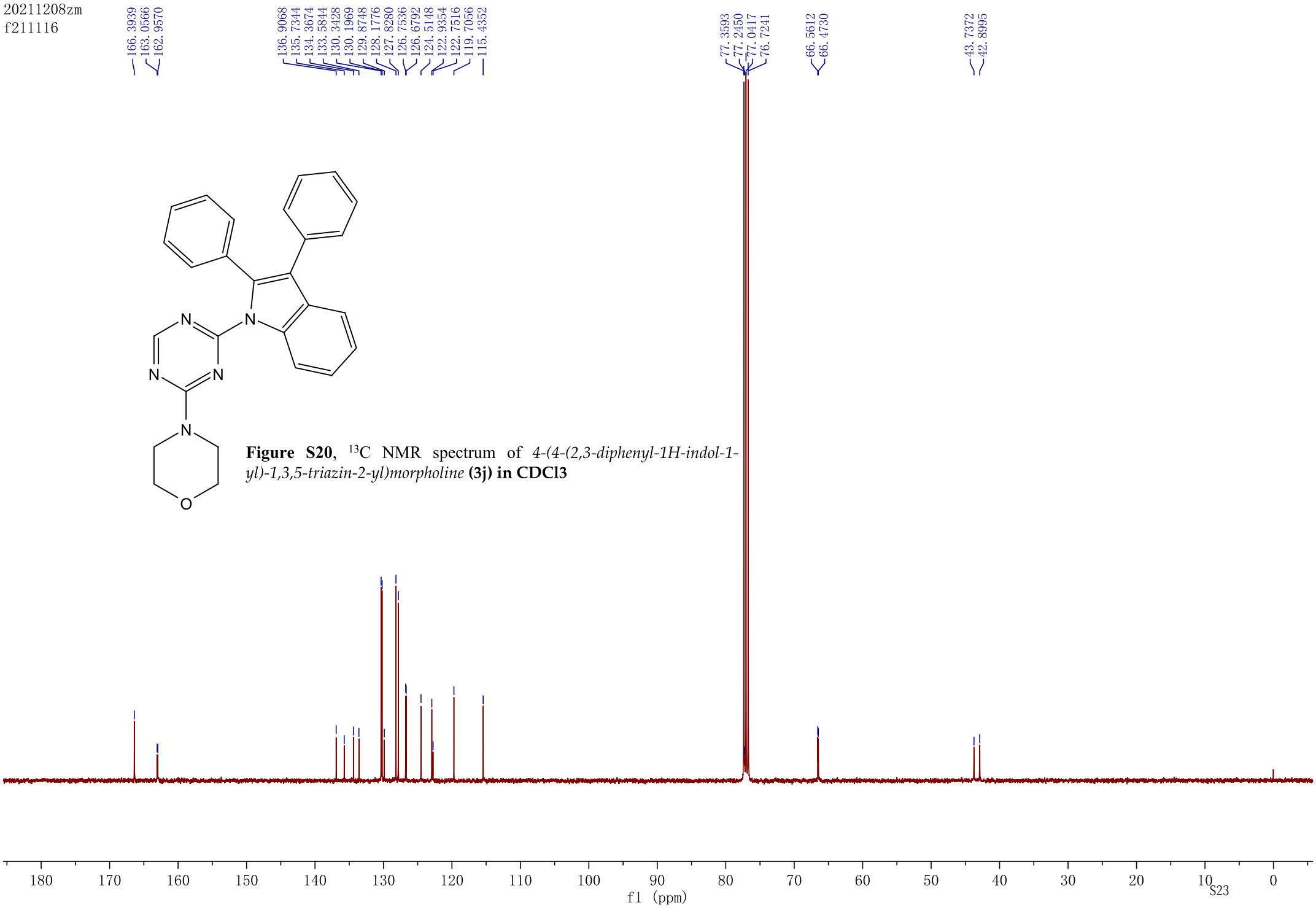

Figure S20, ^{13}C NMR spectrum of *4-(4-(2,3-diphenyl-1H-indol-1-yl)-1,3,5-triazin-2-yl)morpholine* **(3j) in CDCl3**

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1118

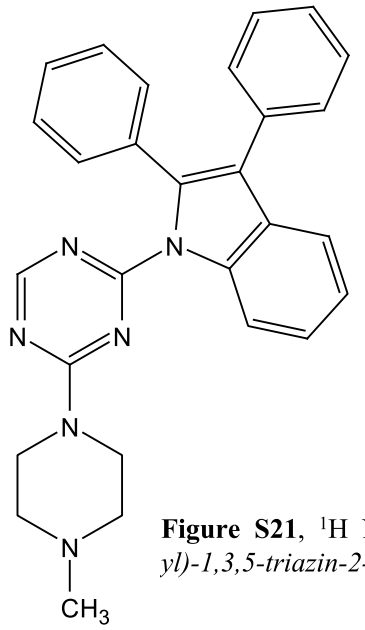
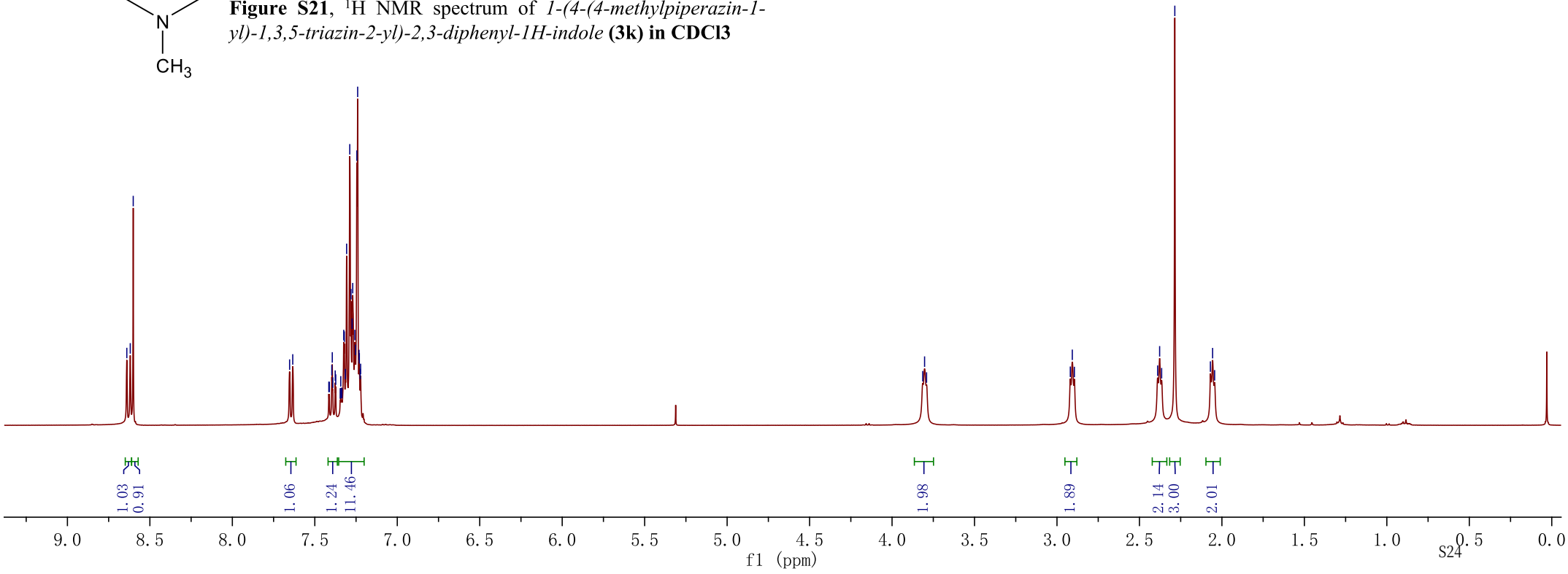


Figure S21, ^{1}H NMR spectrum of *1-(4-(4-methylpiperazin-1-yl)-1,3,5-triazin-2-yl)-2,3-diphenyl-1H-indole* **(3k) in CDCl3**



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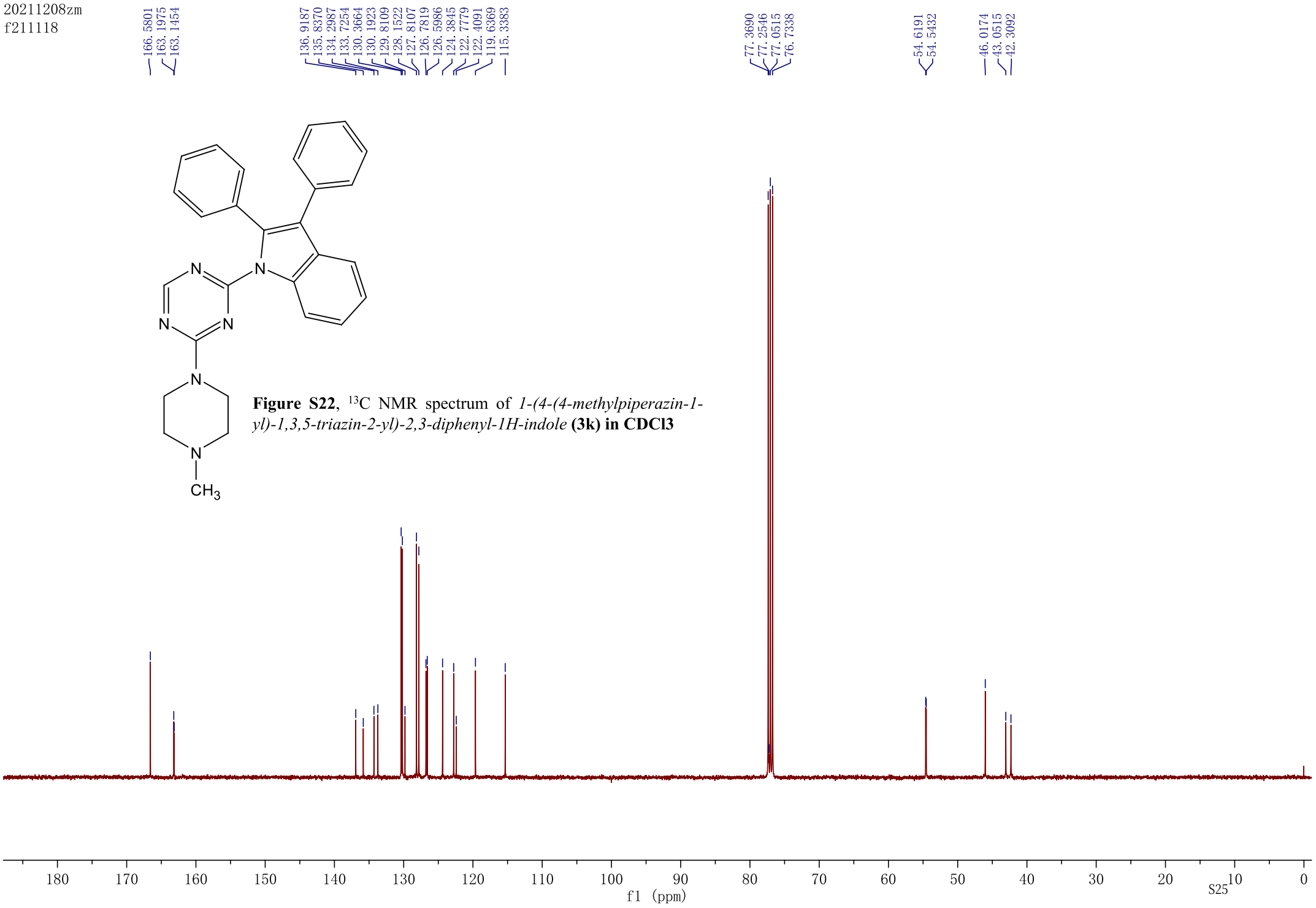

Figure S22, ^{13}C NMR spectrum of *1-(4-(4-methylpiperazin-1-yl)-1,3,5-triazin-2-yl)-2,3-diphenyl-1H-indole* **(3k) in CDCl3**

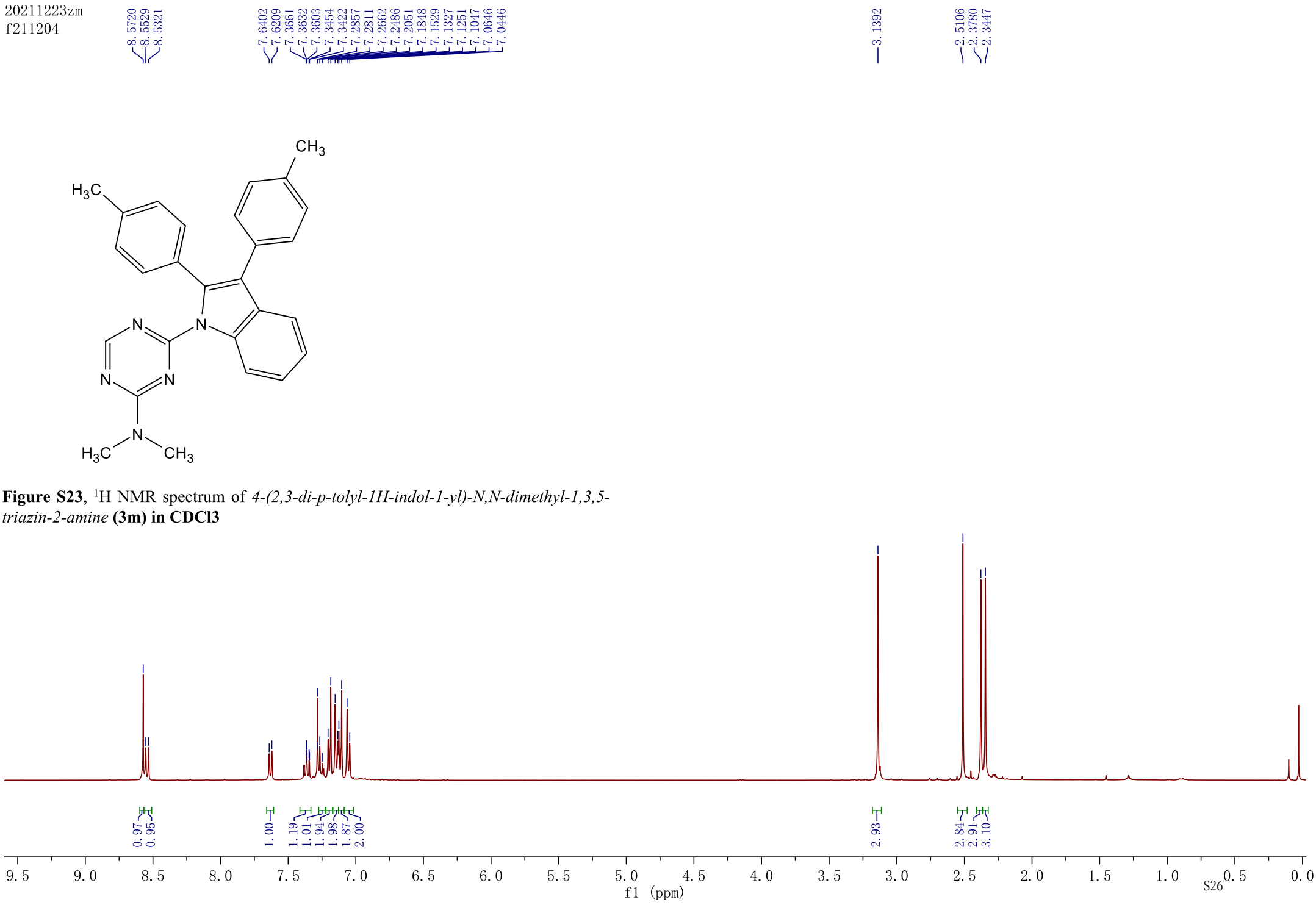

Figure S23, ^{1}H NMR spectrum of *4-(2,3-di-p-tolyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3m) in CDCl3**

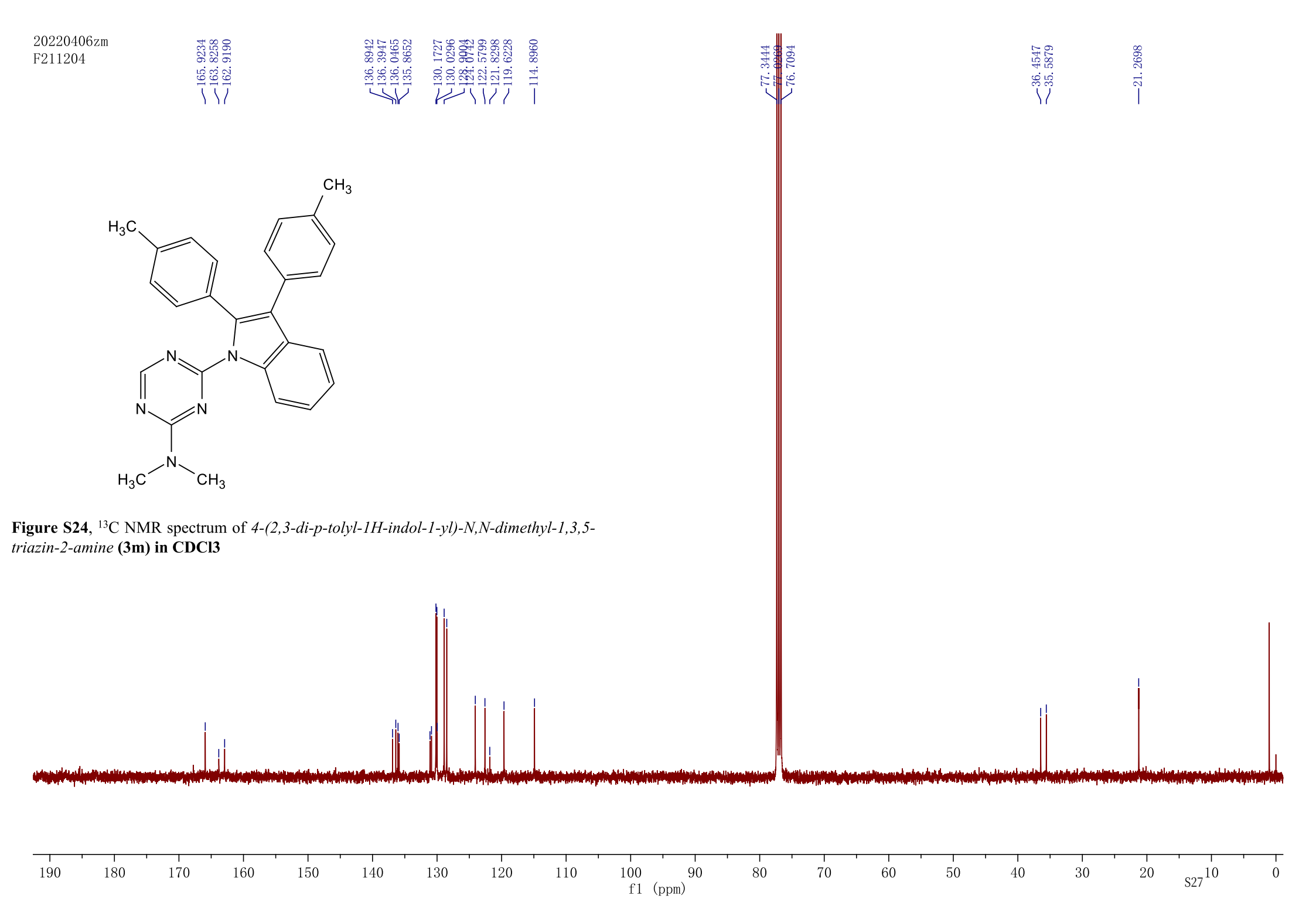

Figure S24, ^{13}C NMR spectrum of *4-(2,3-di-p-tolyl-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3m) in CDCl3**

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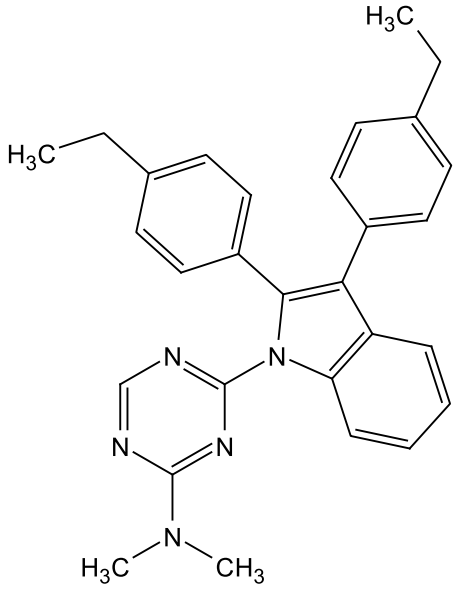
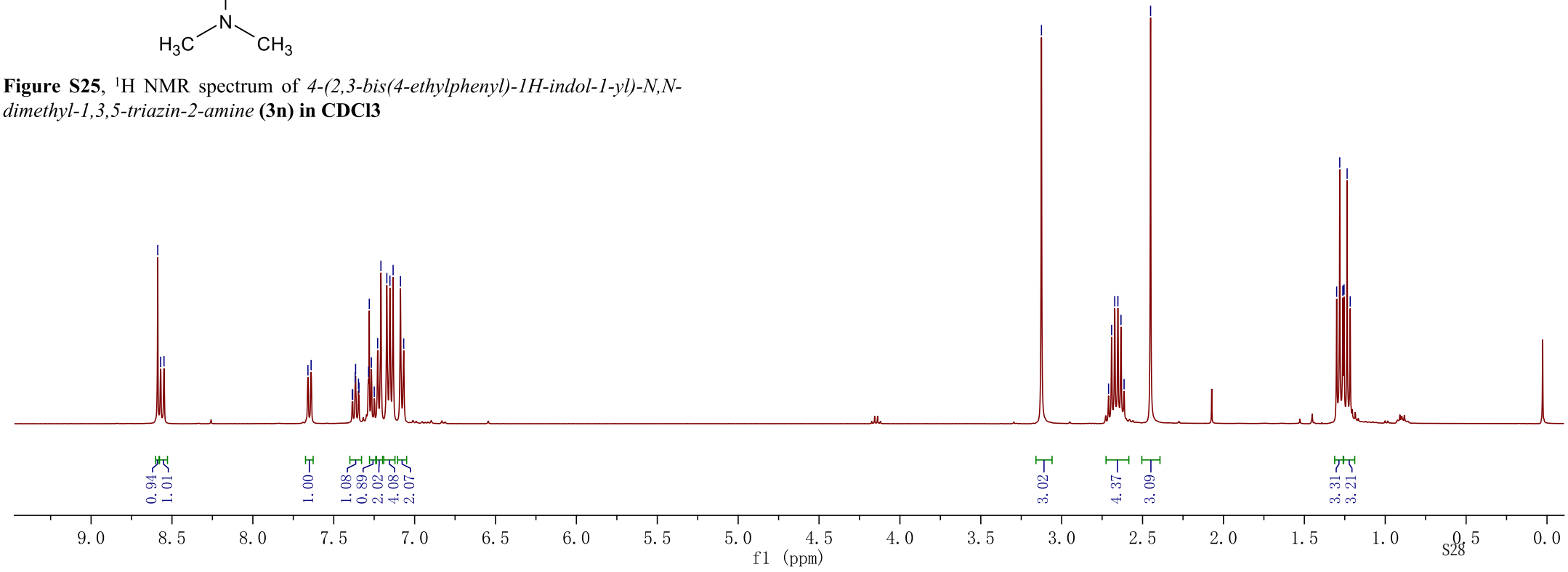


Figure S25, ^{1}H NMR spectrum of *4-(2,3-bis(4-ethylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3n) in CDCl3**



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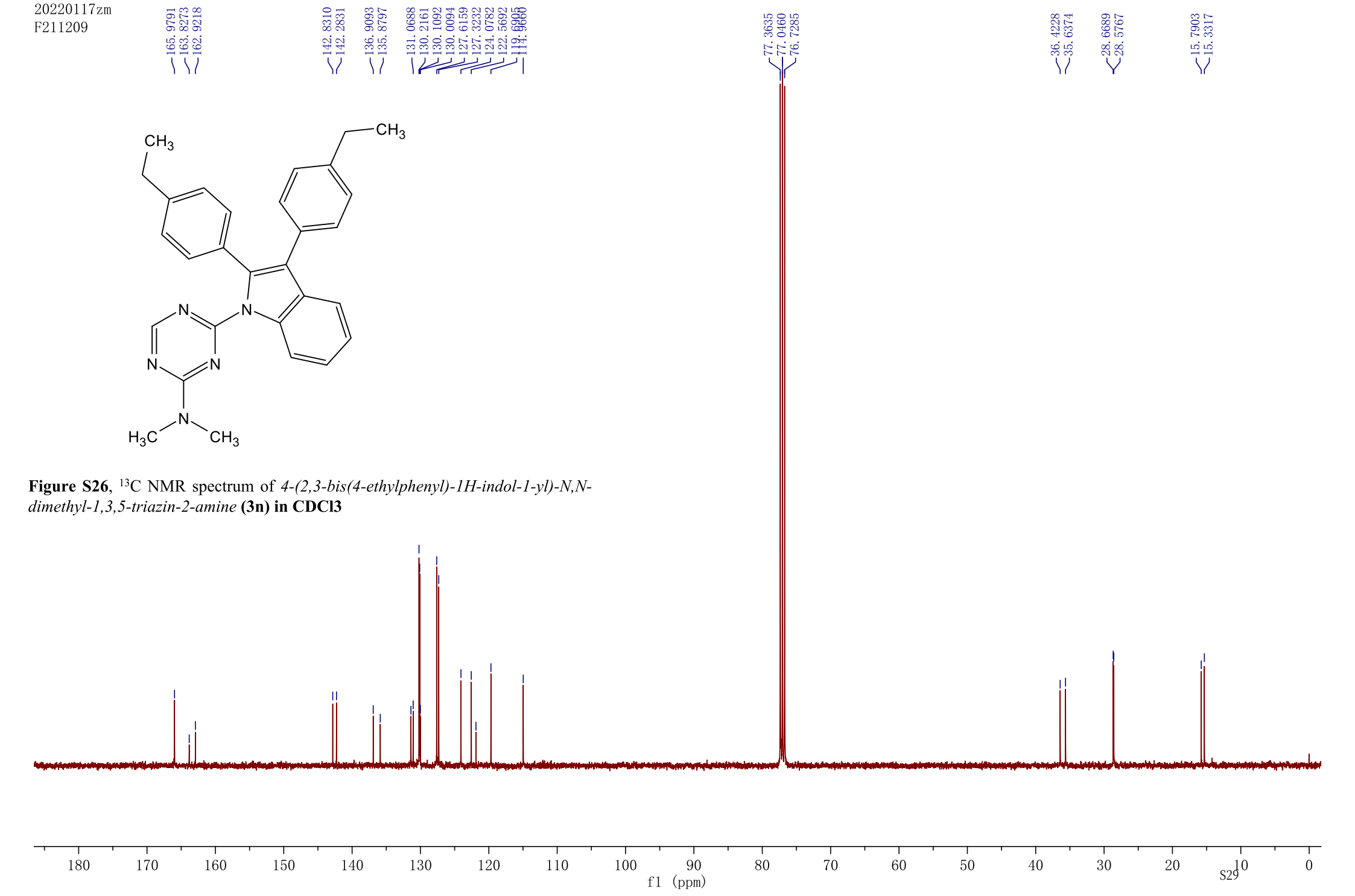
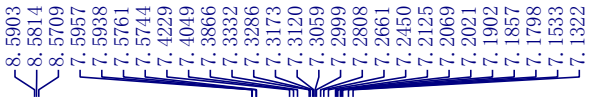


Figure S26, ^{13}C NMR spectrum of *4-(2,3-bis(4-ethylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3n) in CDCl3**



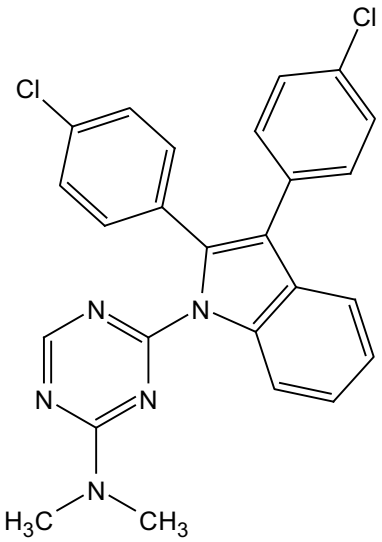
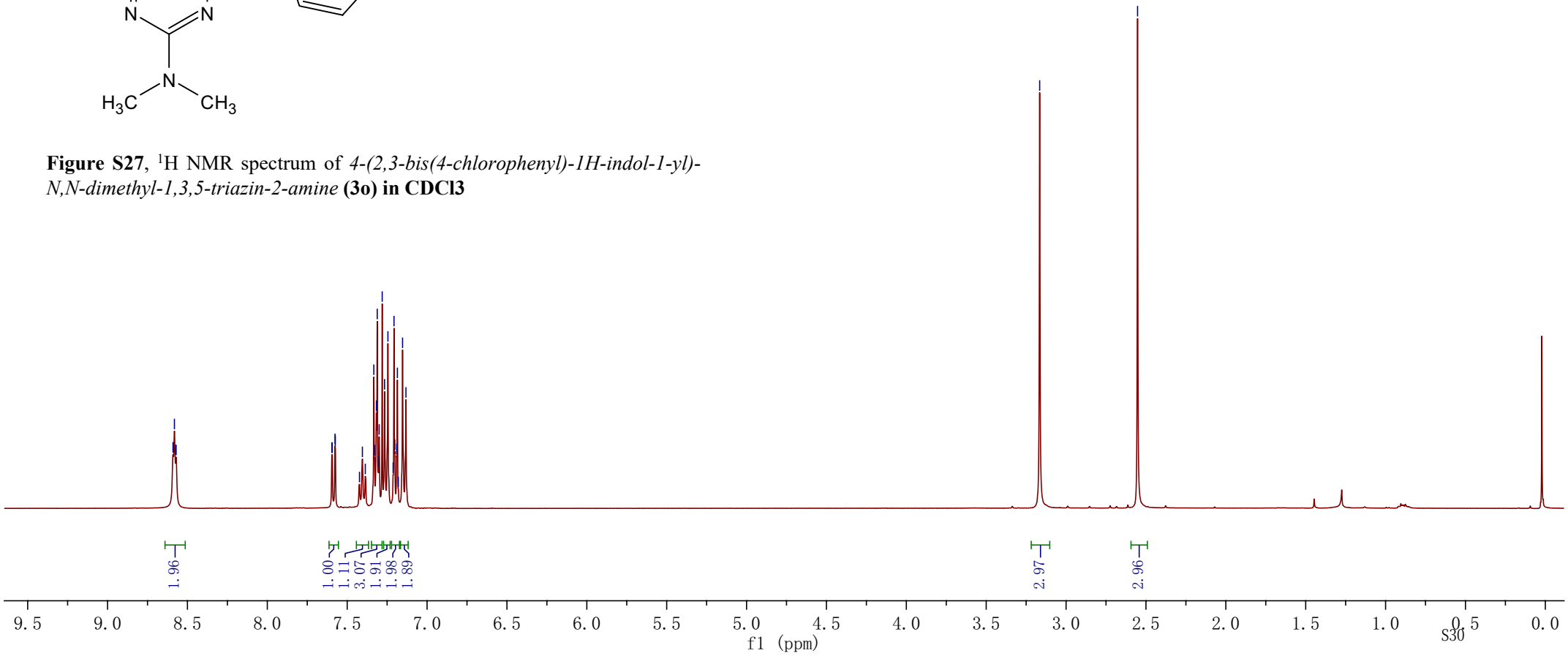


Figure S27, ^{1}H NMR spectrum of *4-(2,3-bis(4-chlorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3o) in CDCl3**



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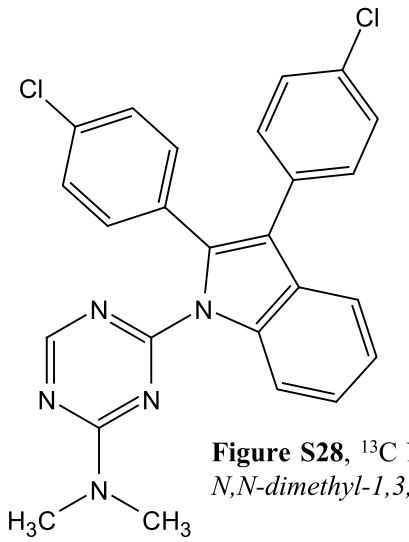

Figure S28, ^{13}C NMR spectrum of *4-(2,3-bis(4-chlorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3o) in CDCl3**

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F220101

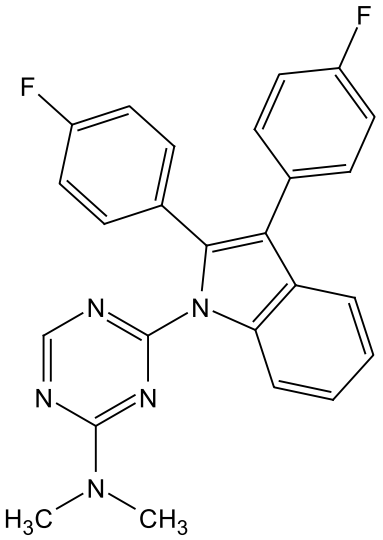
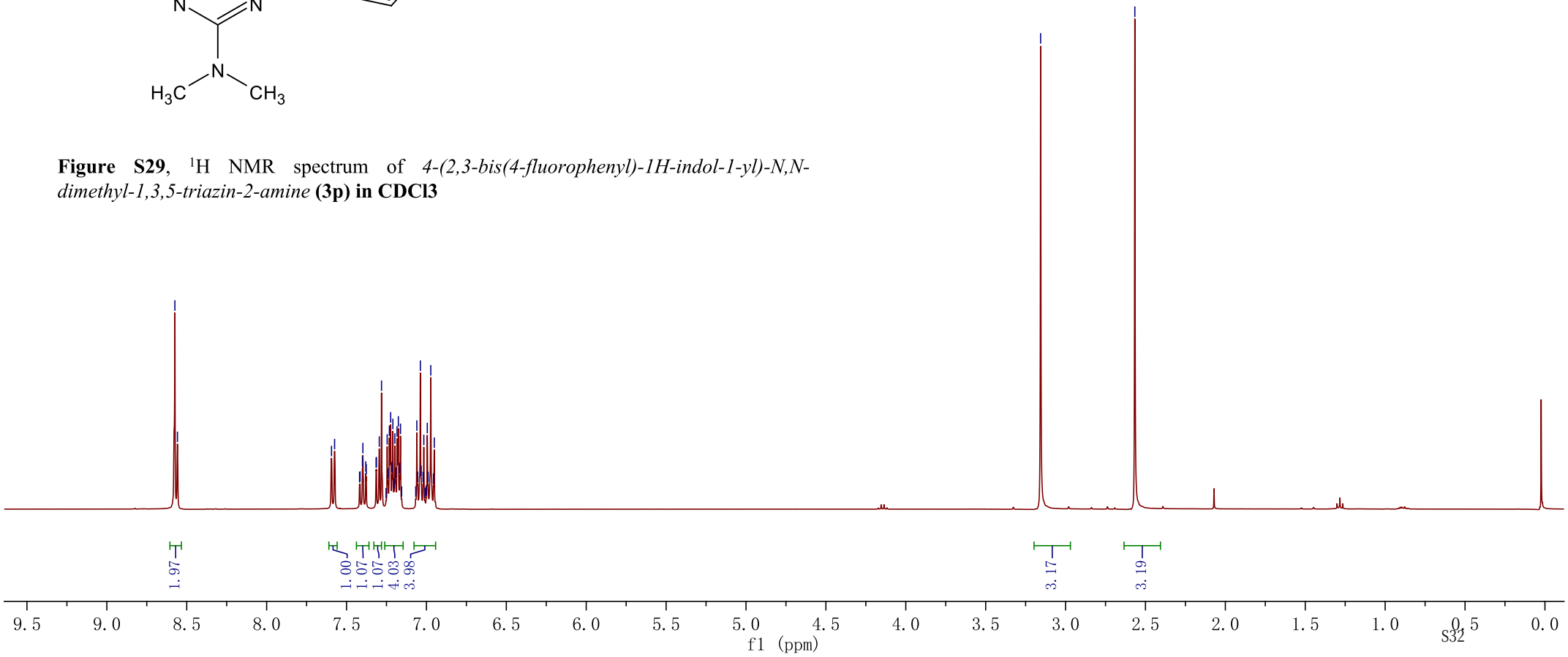


Figure S29, ^{1}H NMR spectrum of *4-(2,3-bis(4-fluorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3p) in CDCl3**



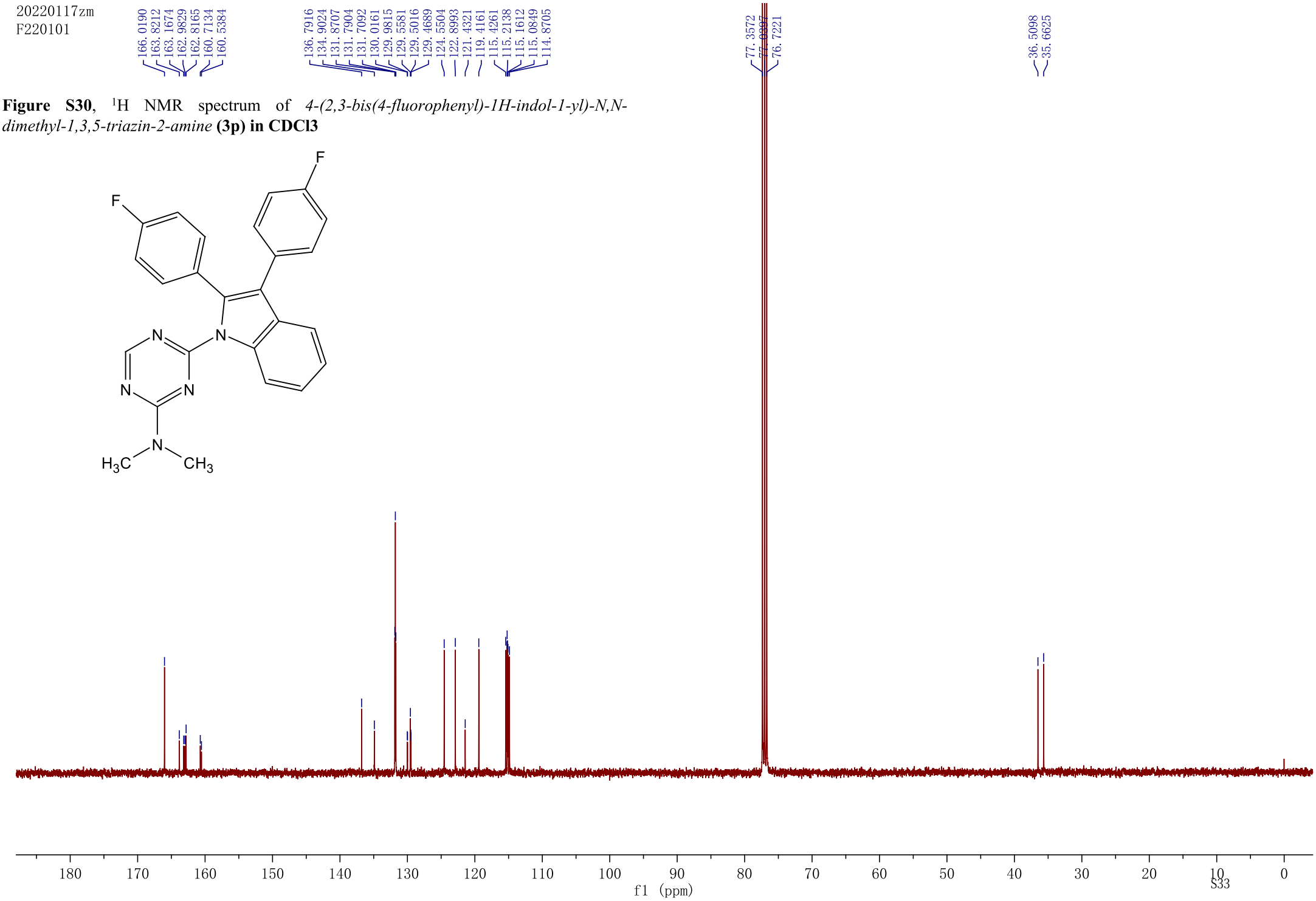
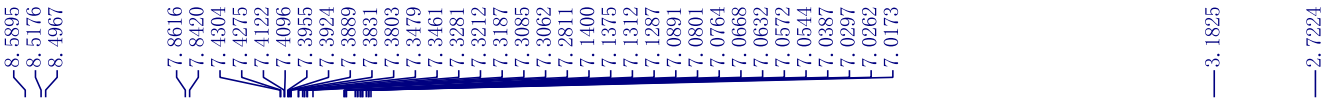


Figure S30, ^{1}H NMR spectrum of *4-(2,3-bis(4-fluorophenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3p) in CDCl3**

20220112zm
F220105



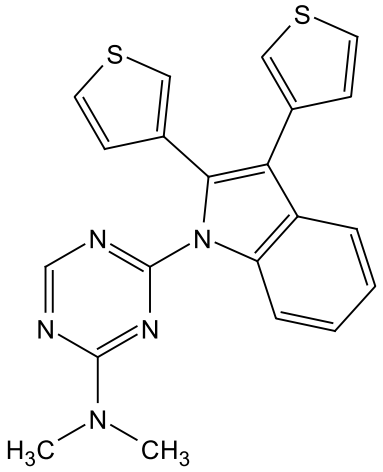
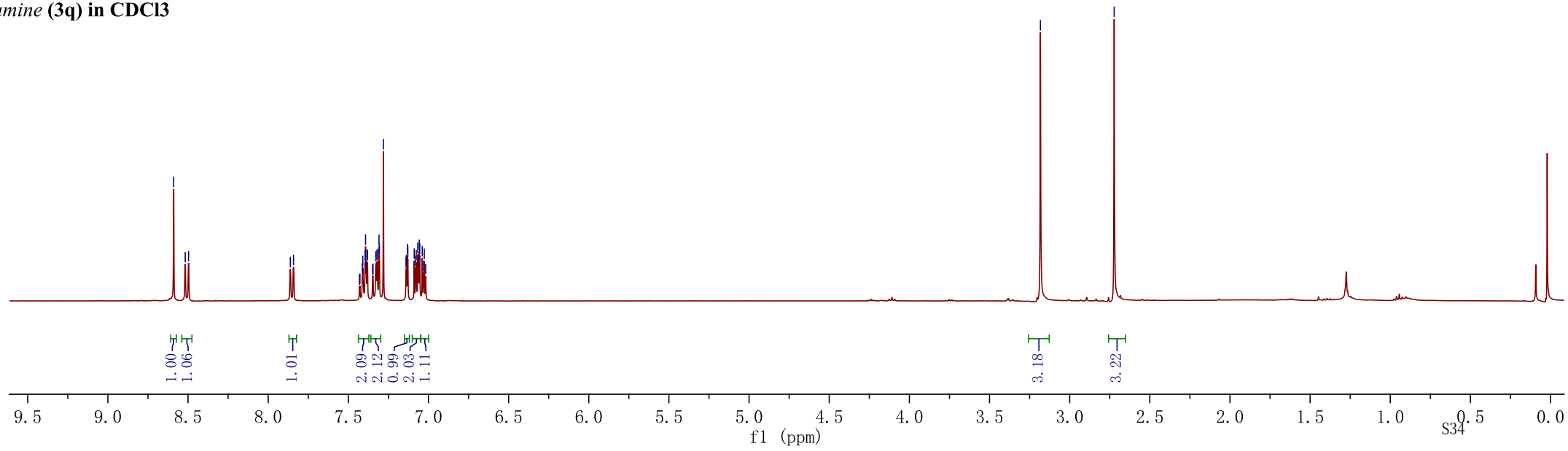


Figure S31, ^{1}H NMR spectrum of *4-(2,3-di(thiophen-2-yl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3q) in CDCl3**



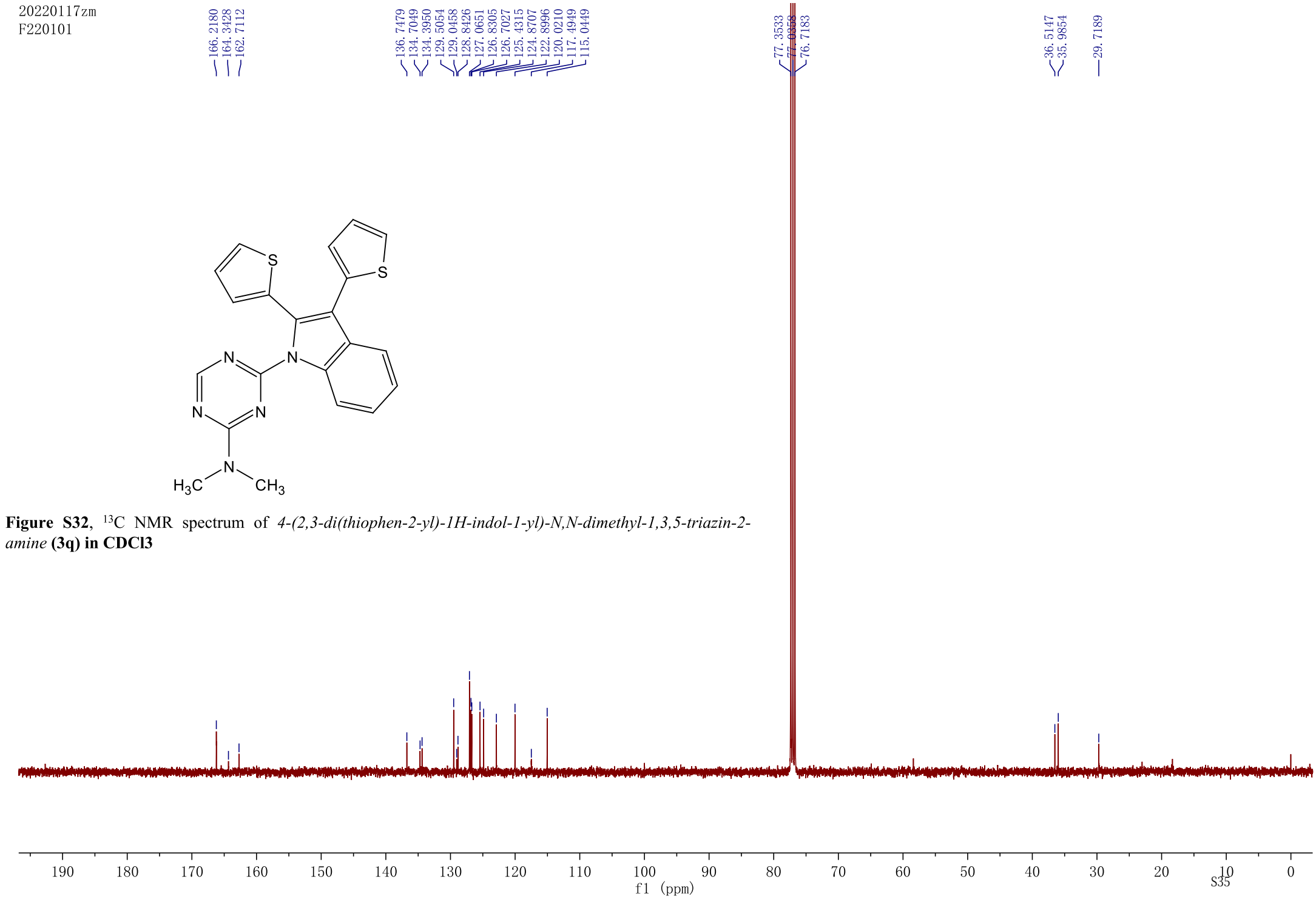


Figure S32, ^{13}C NMR spectrum of *4-(2,3-di(thiophen-2-yl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3q) in CDCl3**

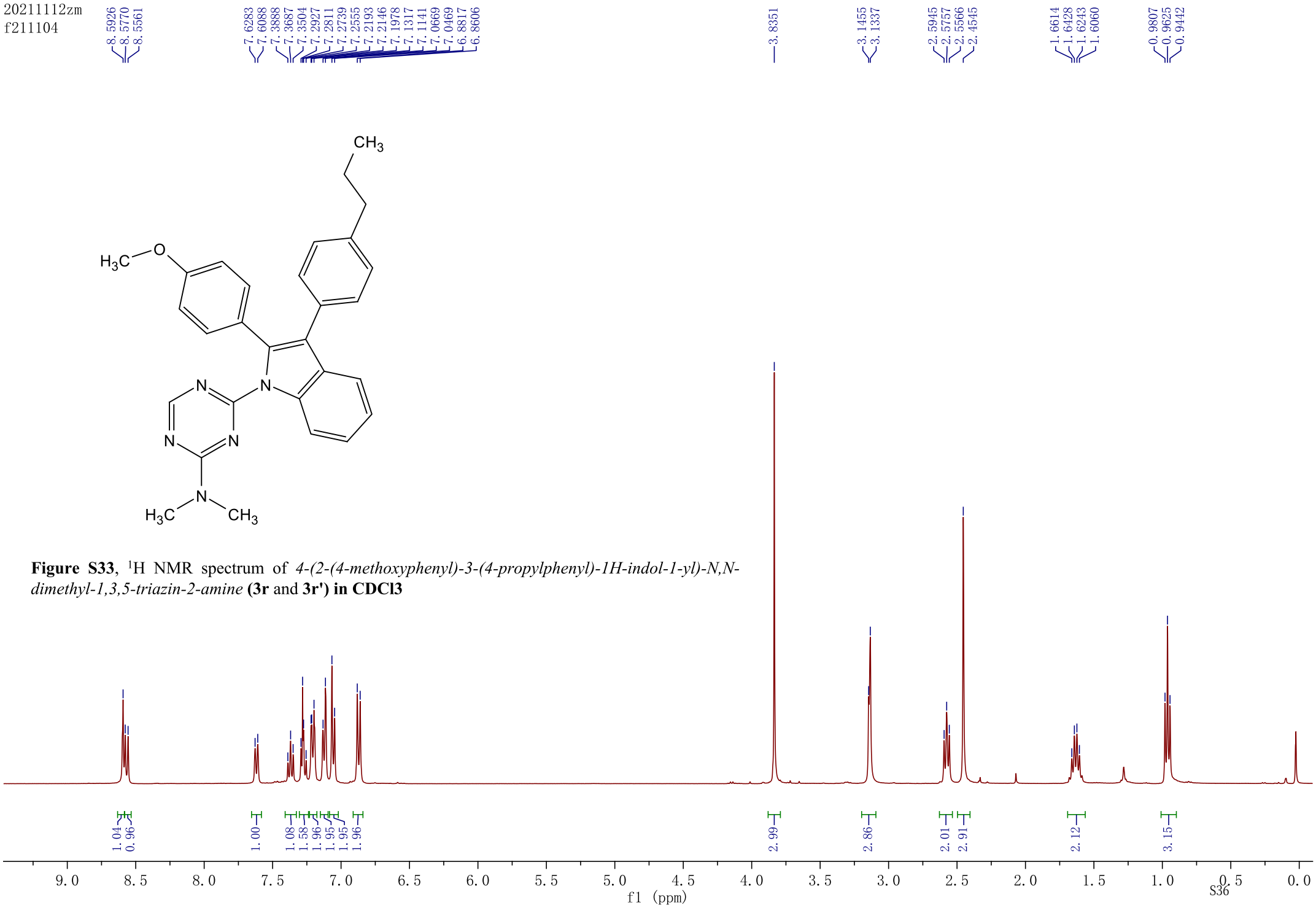


Figure S33, ^{1}H NMR spectrum of *4-(2-(4-methoxyphenyl)-3-(4-propylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3r** and **3r') in CDCl3**

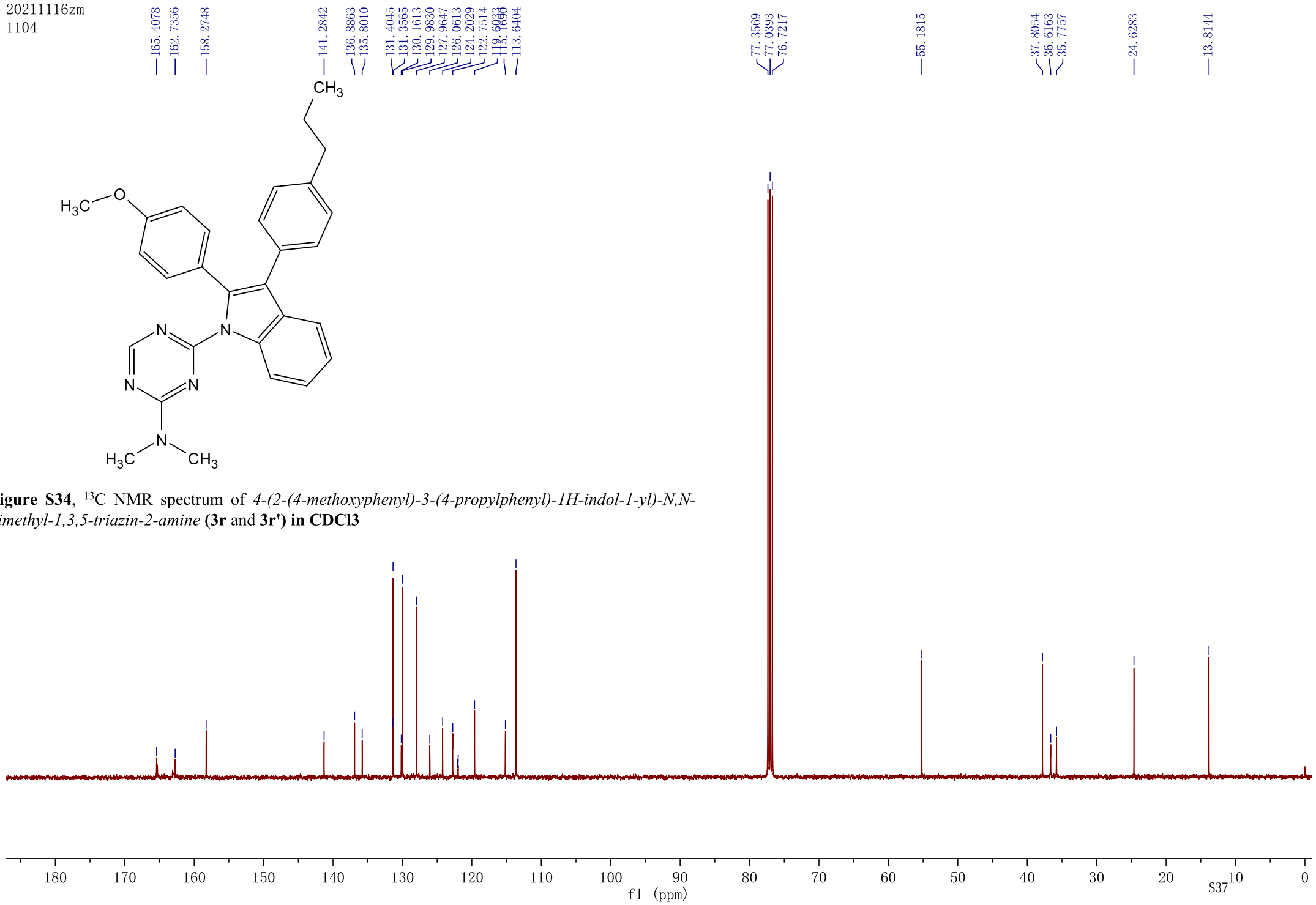


Figure S34, ^{13}C NMR spectrum of *4-(2-(4-methoxyphenyl)-3-(4-propylphenyl)-1H-indol-1-yl)-N,N-dimethyl-1,3,5-triazin-2-amine* **(3r** and **3r') in CDCl3**

20220112zm
ZJH128

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

20220117zm
20211128

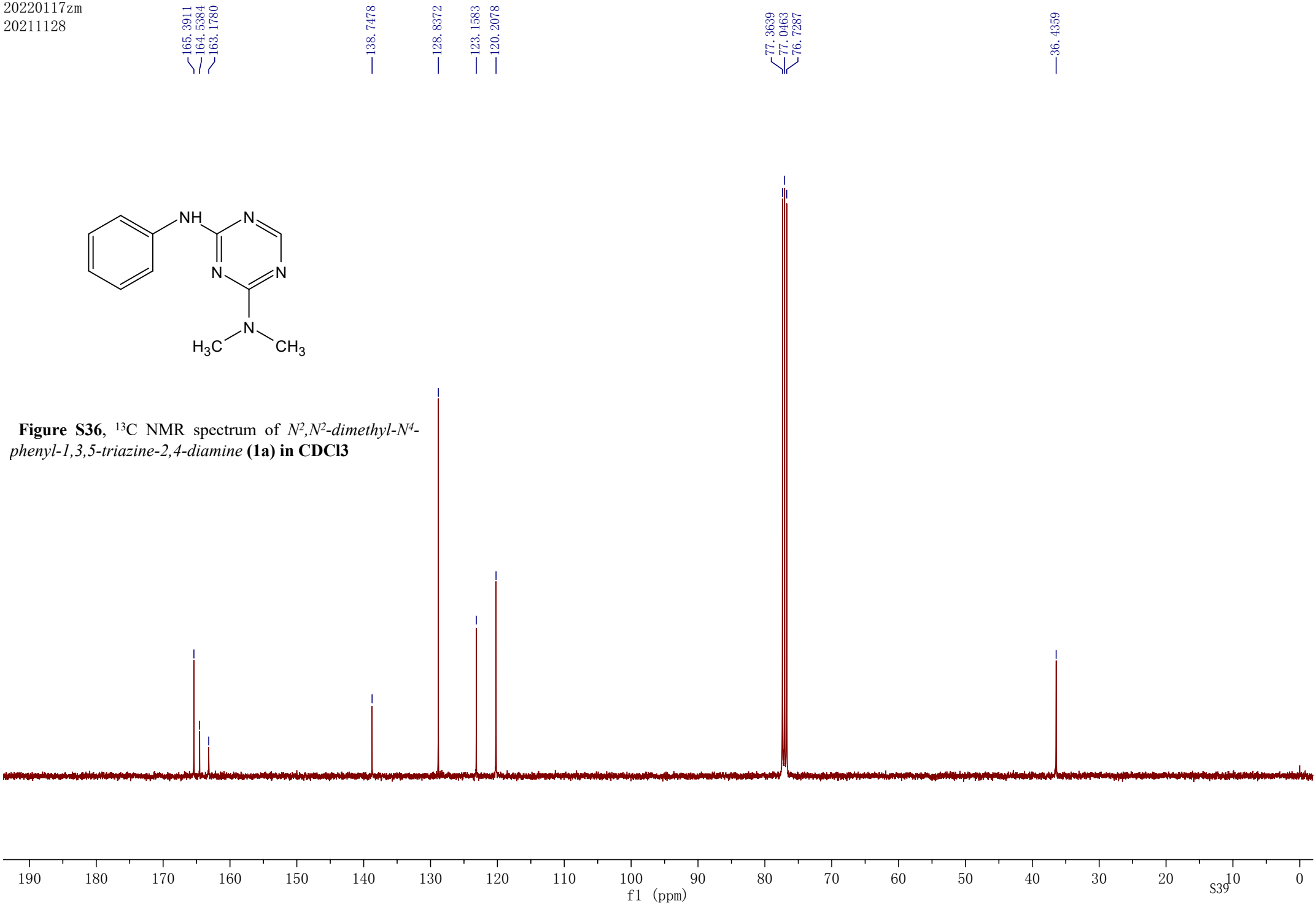


Figure S36, ^{13}C NMR spectrum of *N^2,N^2-dimethyl-N^4-phenyl-1,3,5-triazine-2,4-diamine* **(1a) in CDCl3**

20230412zm
1j CDCl3

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

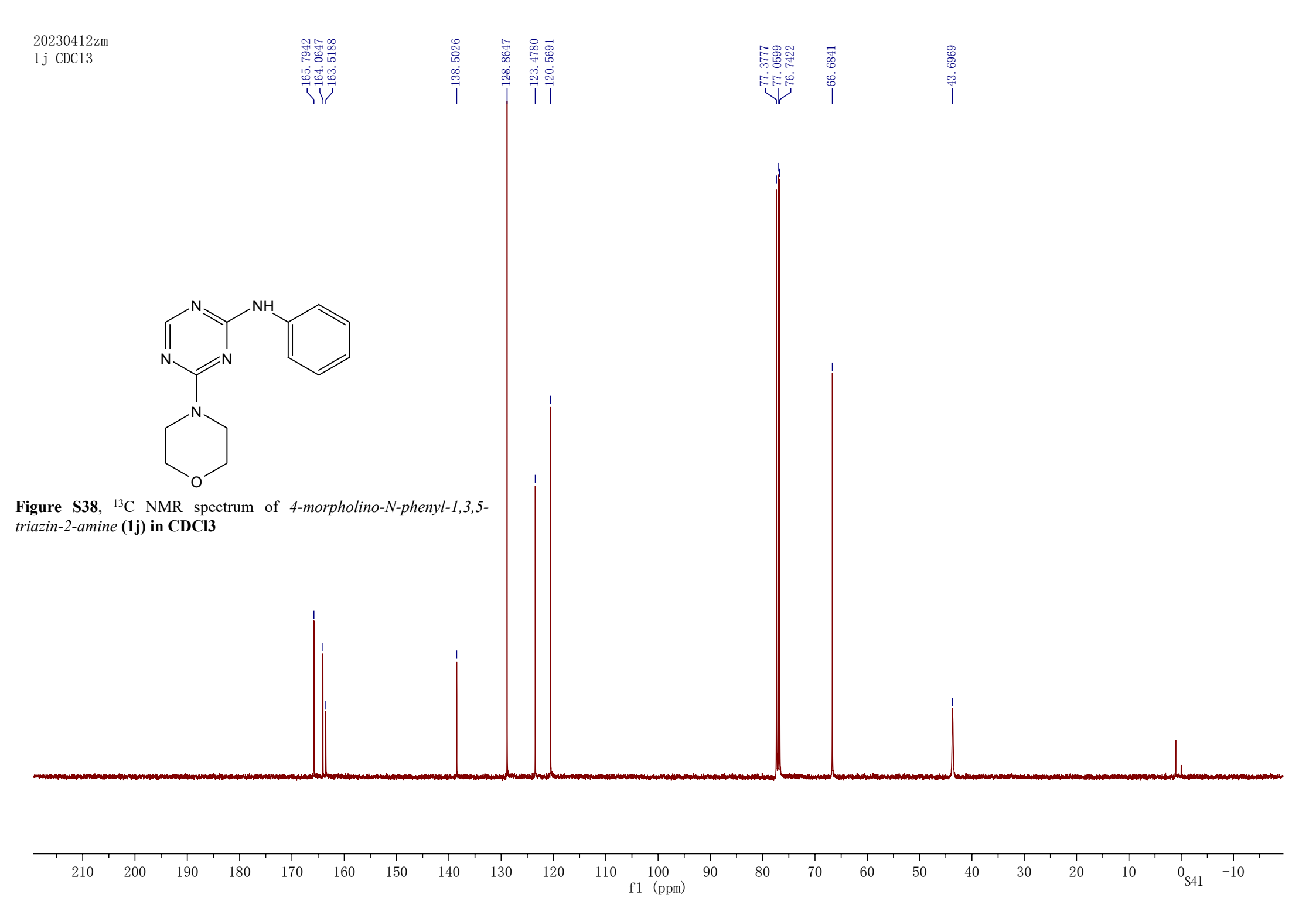


Figure S38, ^{13}C NMR spectrum of *4-morpholino-N-phenyl-1,3,5-triazin-2-amine* **(1j) in CDCl3**

20230412zm
1k CDCl3

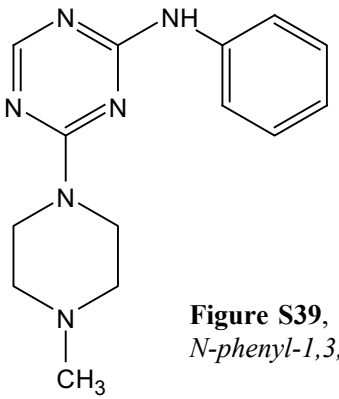


Figure S39, ^{1}H NMR spectrum of *4-(4-methylpiperazin-1-yl)-N-phenyl-1,3,5-triazin-2-amine* **(1k) in CDCl3**

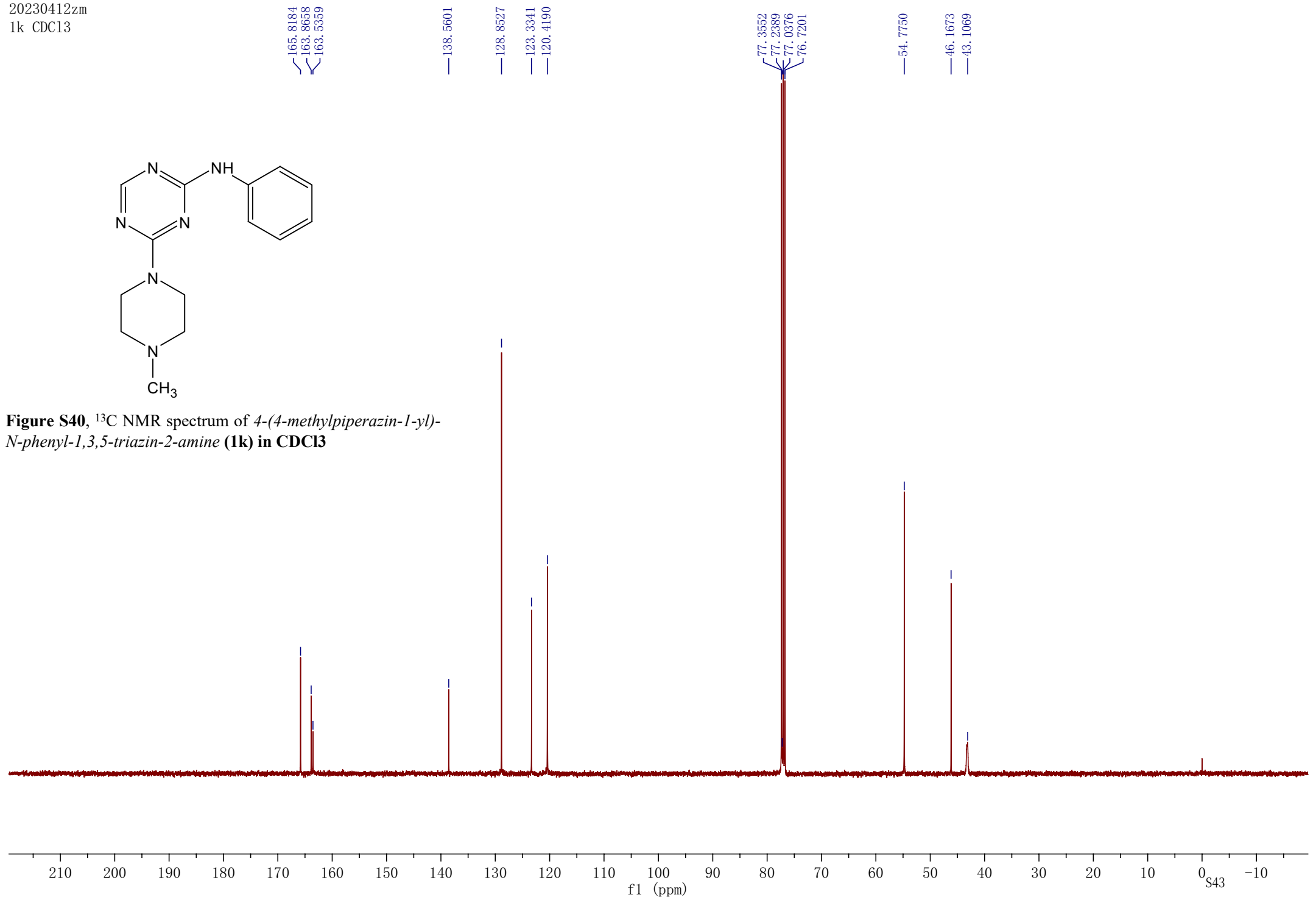


Figure S40, ^{13}C NMR spectrum of *4-(4-methylpiperazin-1-yl)-N-phenyl-1,3,5-triazin-2-amine* **(1k) in CDCl3**

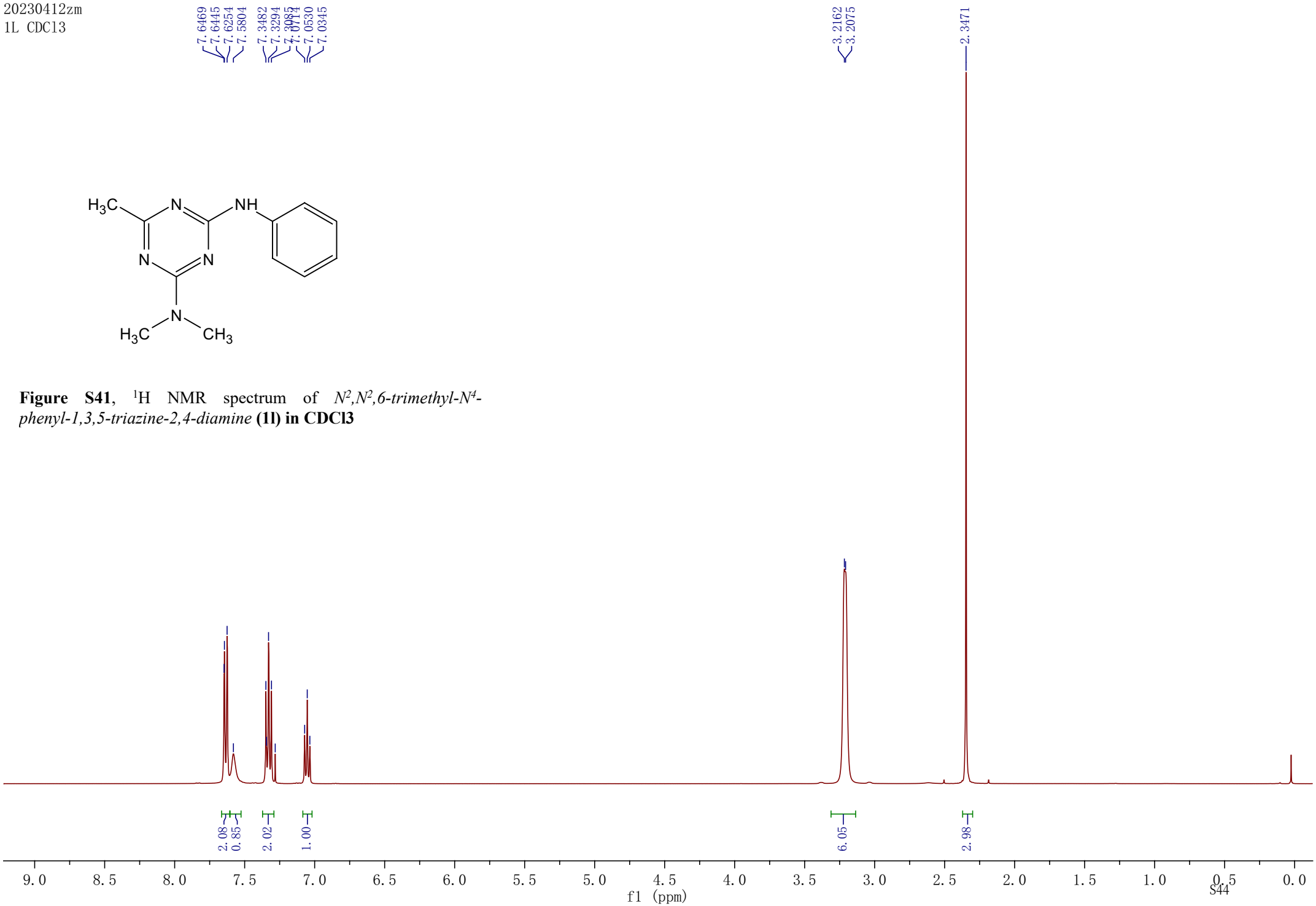


Figure S41, ^{1}H NMR spectrum of *N²,N²,6-trimethyl-N⁴-phenyl-1,3,5-triazine-2,4-diamine* **(1l) in CDCl3**

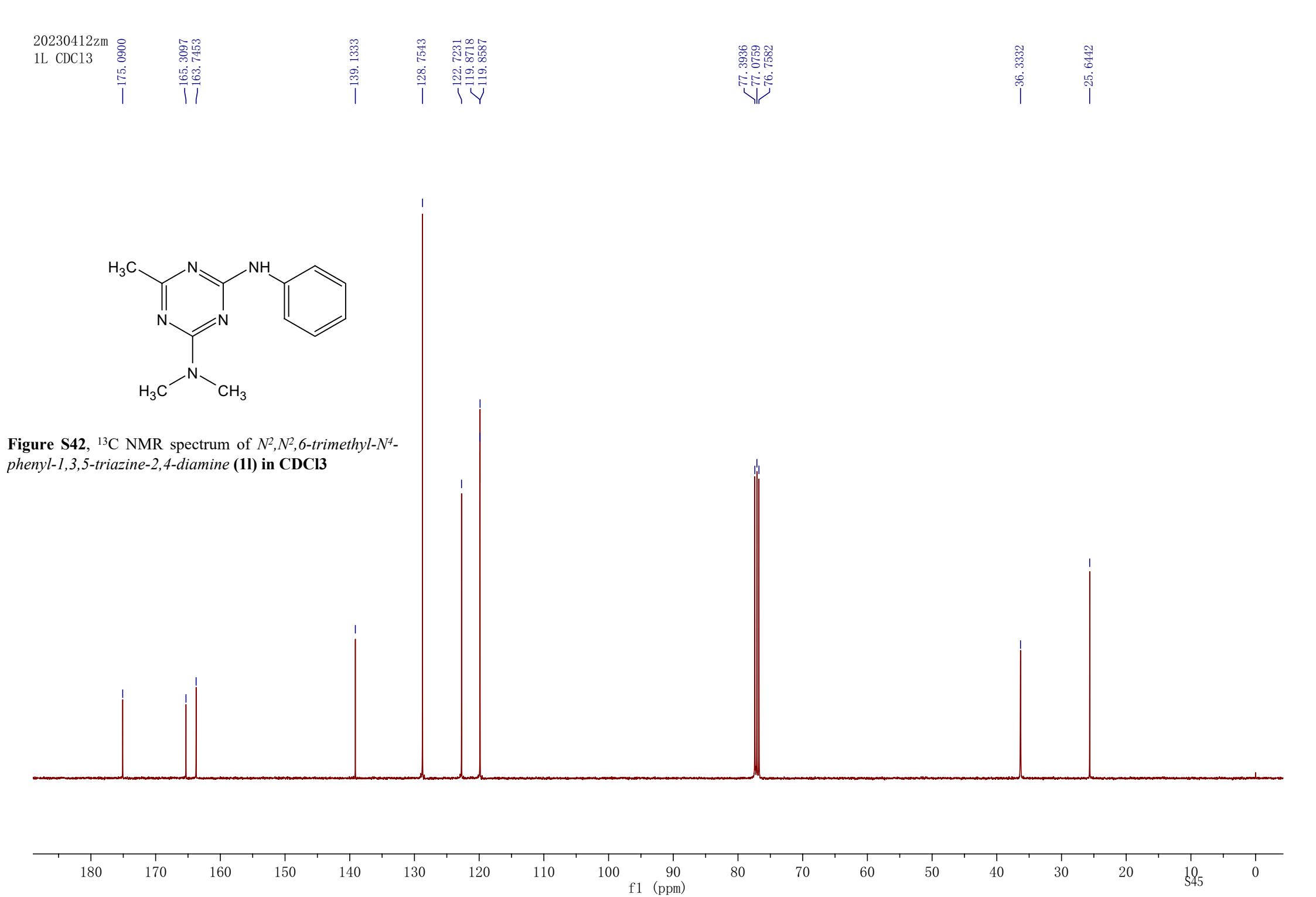


Figure S42, ^{13}C NMR spectrum of *N²,N²,6-trimethyl-N⁴-phenyl-1,3,5-triazine-2,4-diamine* **(1l) in CDCl3**

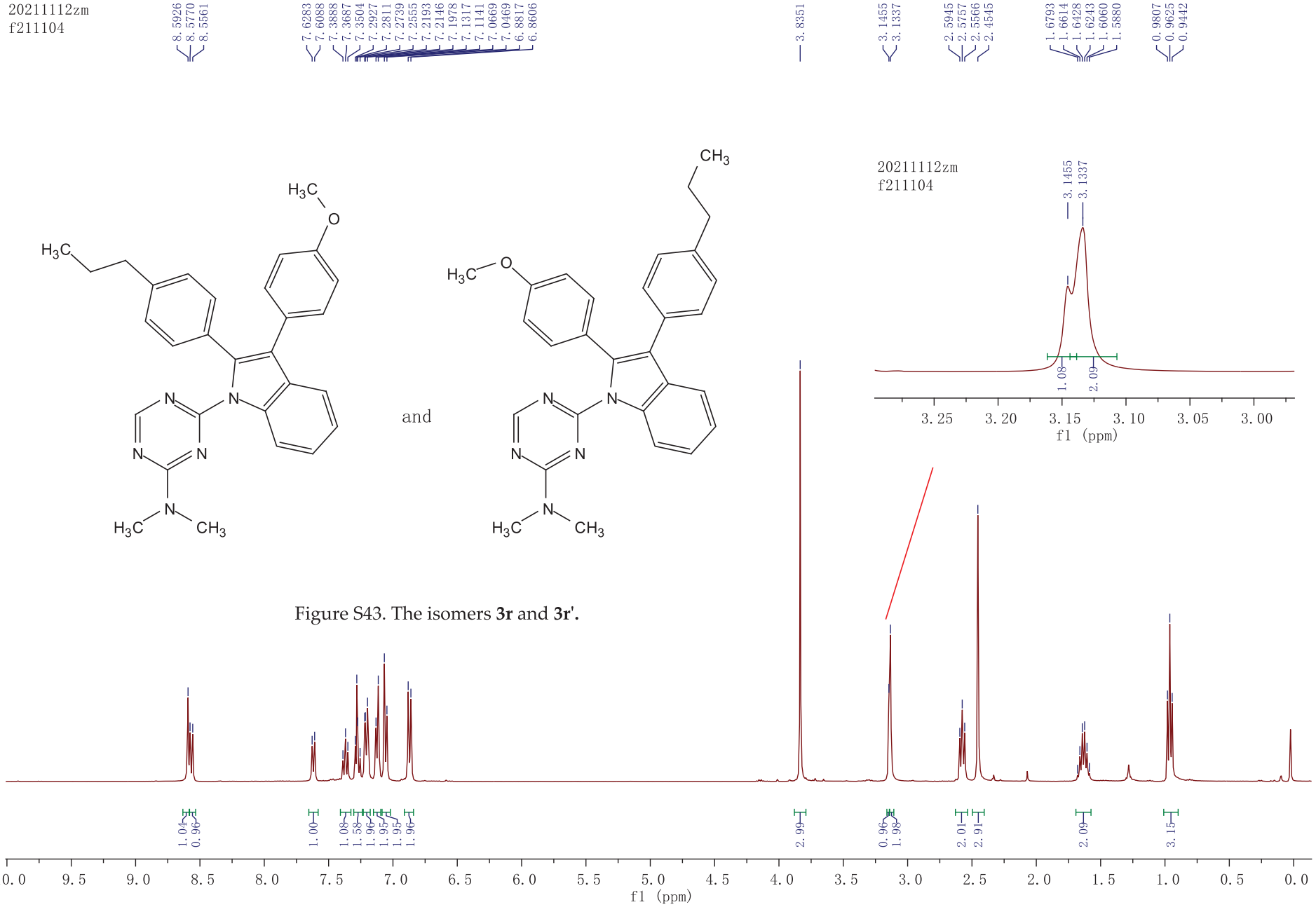


Figure S43. The isomers **3r** and **3r'**.