

## Supporting Information

# Synthesis and Biological Evaluation of Indolyl-Pyridinyl-Propenones Having Either Methuosis or Microtubule Disruption Activity

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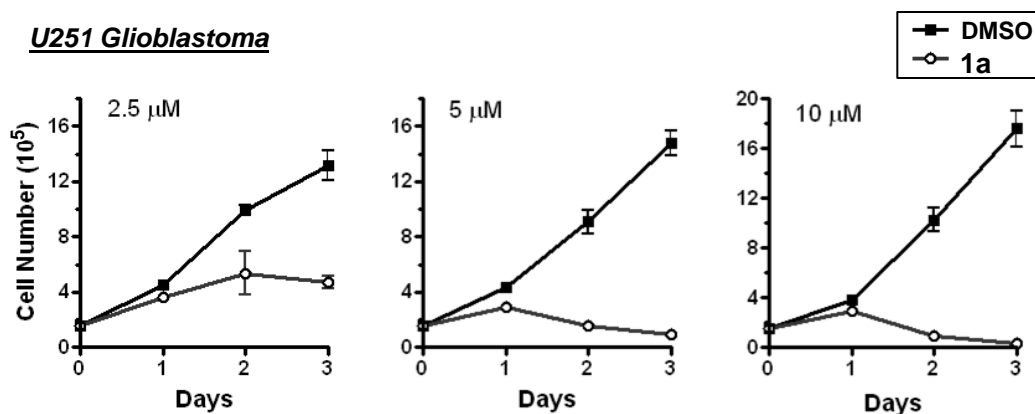
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### U251 Glioblastoma



### Normal Skin Fibroblasts

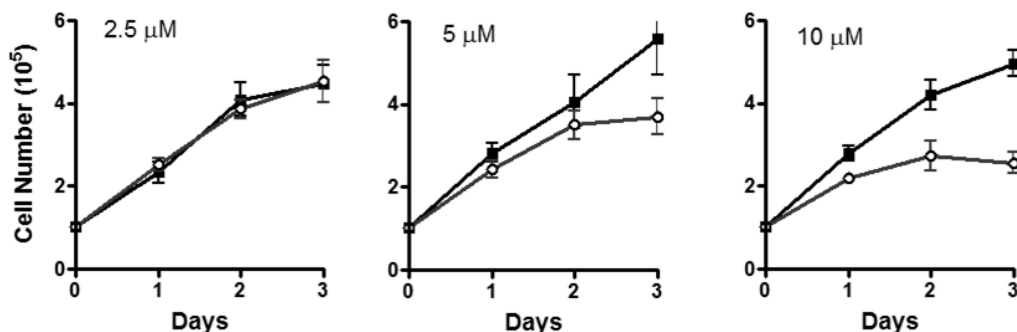


Figure S1. Comparison of the effects of compound **1a** on the growth of U251 GBM cells *versus* normal human skin fibroblasts. Cells were seeded in 35 mm tissue culture dishes. Commencing at 24 h after plating (day-0), compound 1a was added at the indicated concentrations. Control cultures received the equivalent volume of DMSO. On successive days cultures were harvested and the total number of cells per dish was determined. The results for each point are the mean  $\pm$  SD derived from three parallel cultures. The glioblastoma data were reported by us in Figure 2 of Robinson, M.W. et al., *J. Med. Chem.* **2012**, 55, 1940-1956. The fibroblast data were collected at the same time, but were not reported previously.

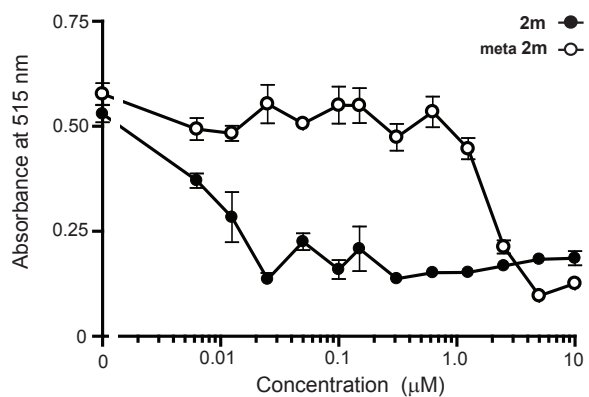
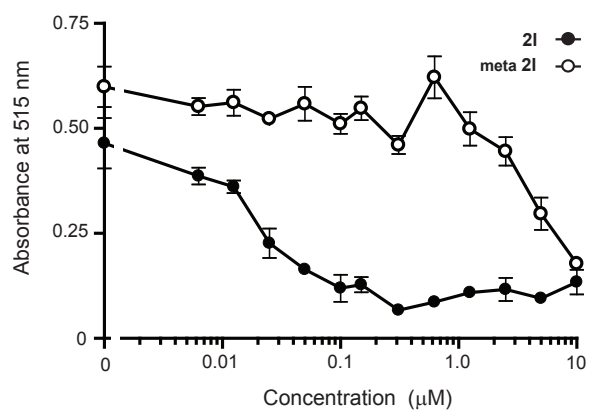
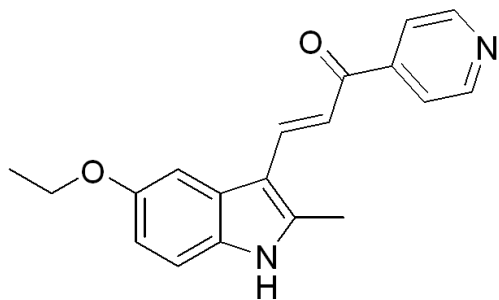
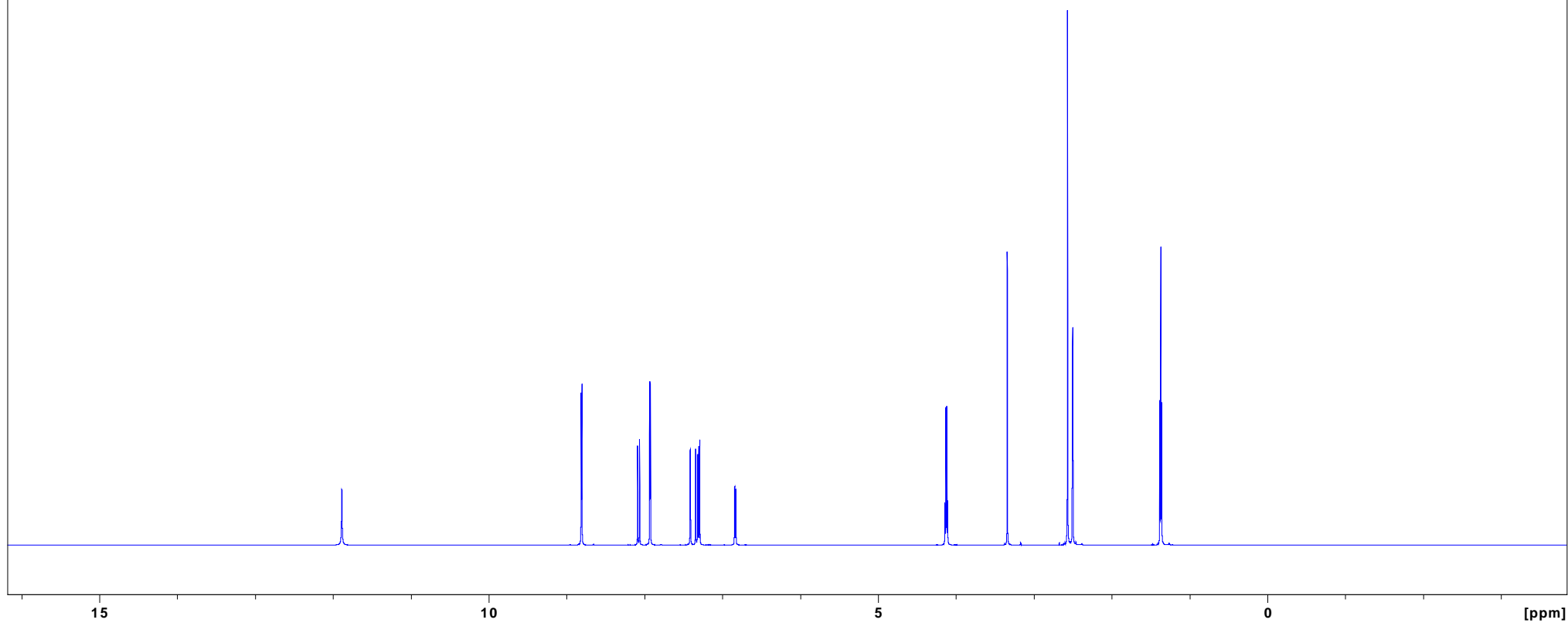


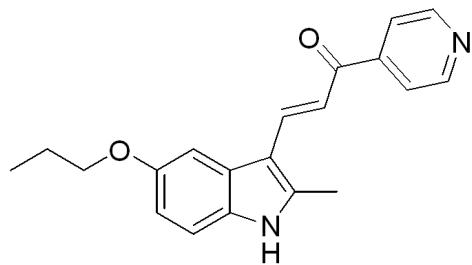
Figure S2. Growth inhibitory activities of the 2-indole carboxylate compounds, **2l** and **2m**, are substantially reduced by changing the pyridinyl nitrogen from the 4 position to the 3 (meta) position. U251 cells were seeded in 96-well plates. After 24 h, compounds were added at the indicated concentrations. SRB assays were performed after an additional 48 h. Each point represents the mean  $\pm$  SEM of values from four wells.



**2a**

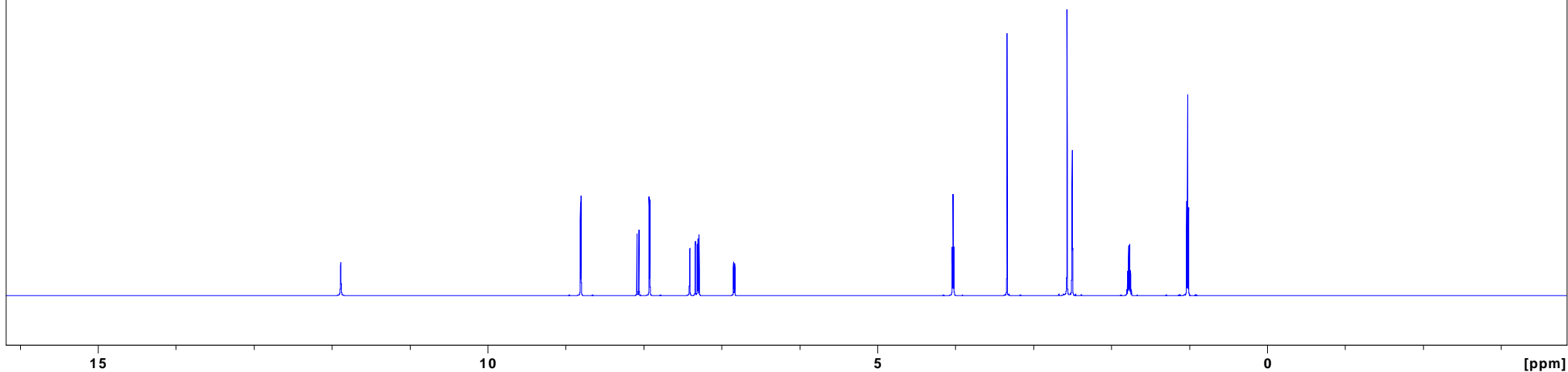
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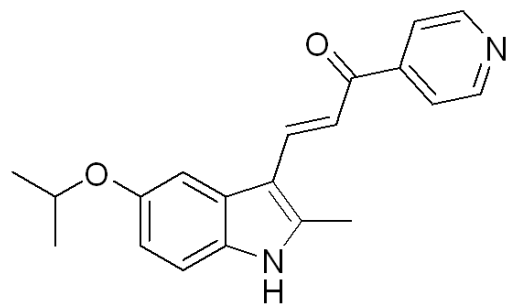




**2b**

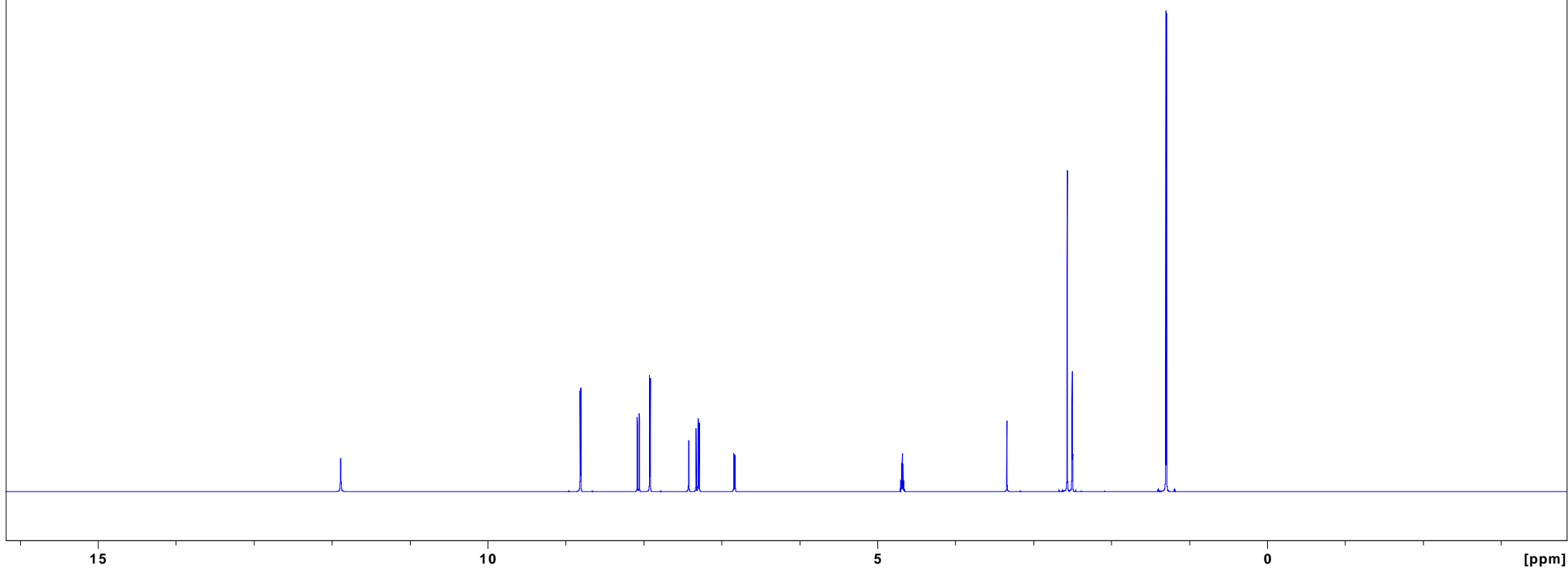
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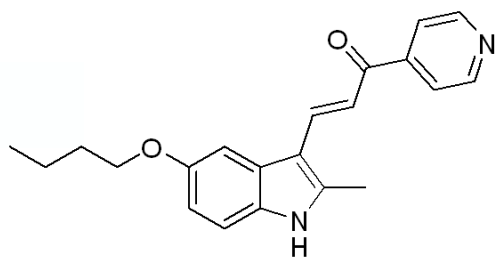


**2c**

$^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)

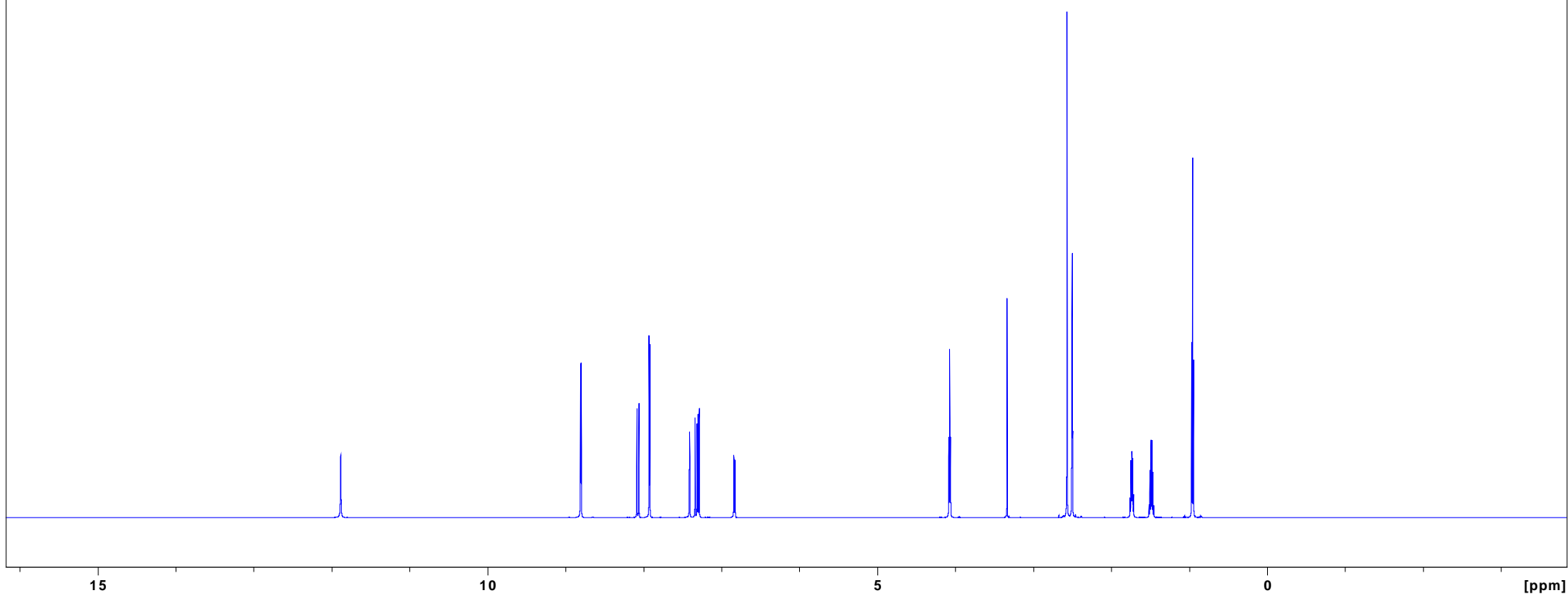


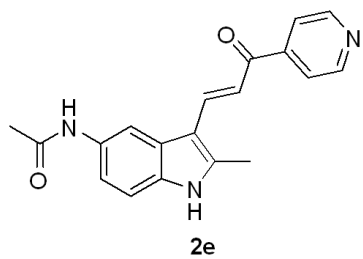




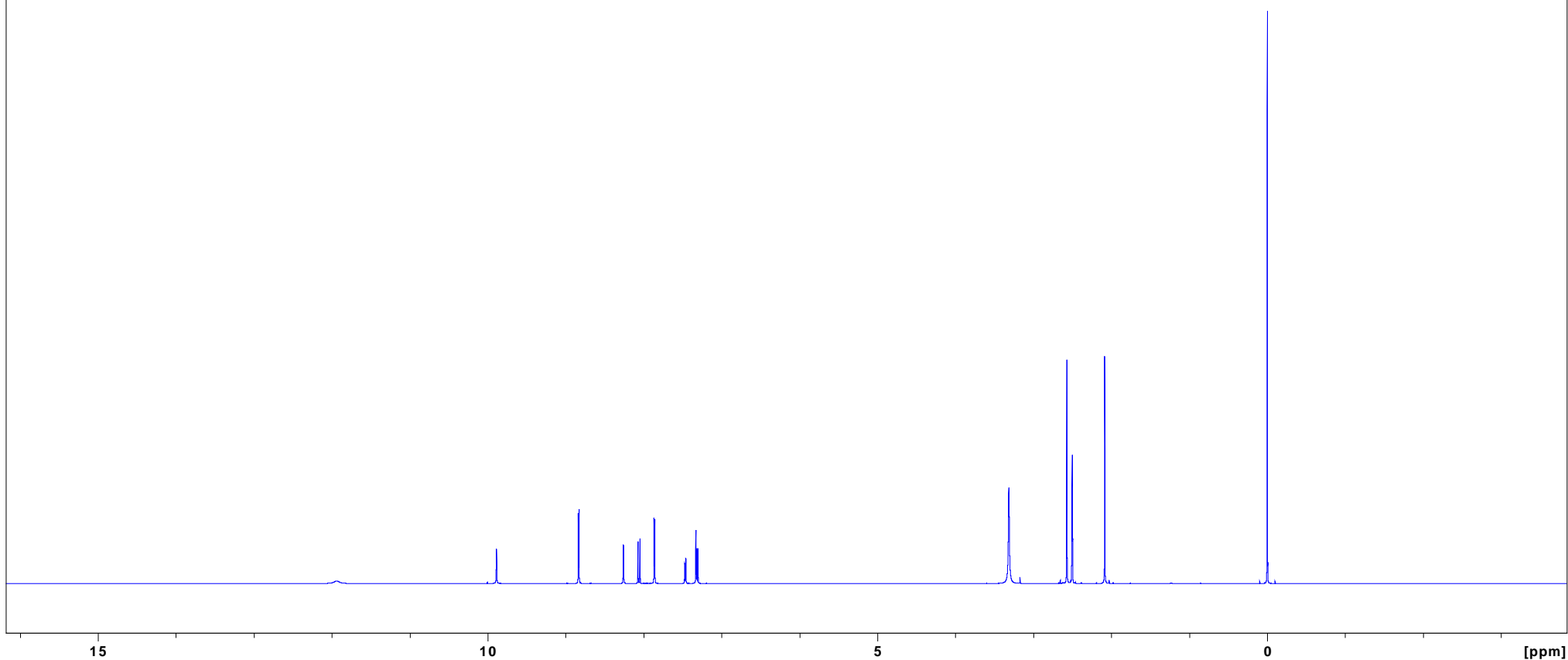
**2d**

$^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)





$^1\text{H}$  NMR (600 MHz,  $d_6$ -DMSO)



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Solvent: DMSO

Ambient temperature

file: MS-1-19

NOVA-600 "inova-wkst"

Relax delay 1 000 sec

Pulse 31 3 degrees

Acq time 3 000 sec

Width 10000 0 Hz

16 repetitions

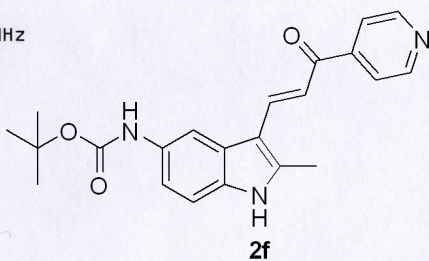
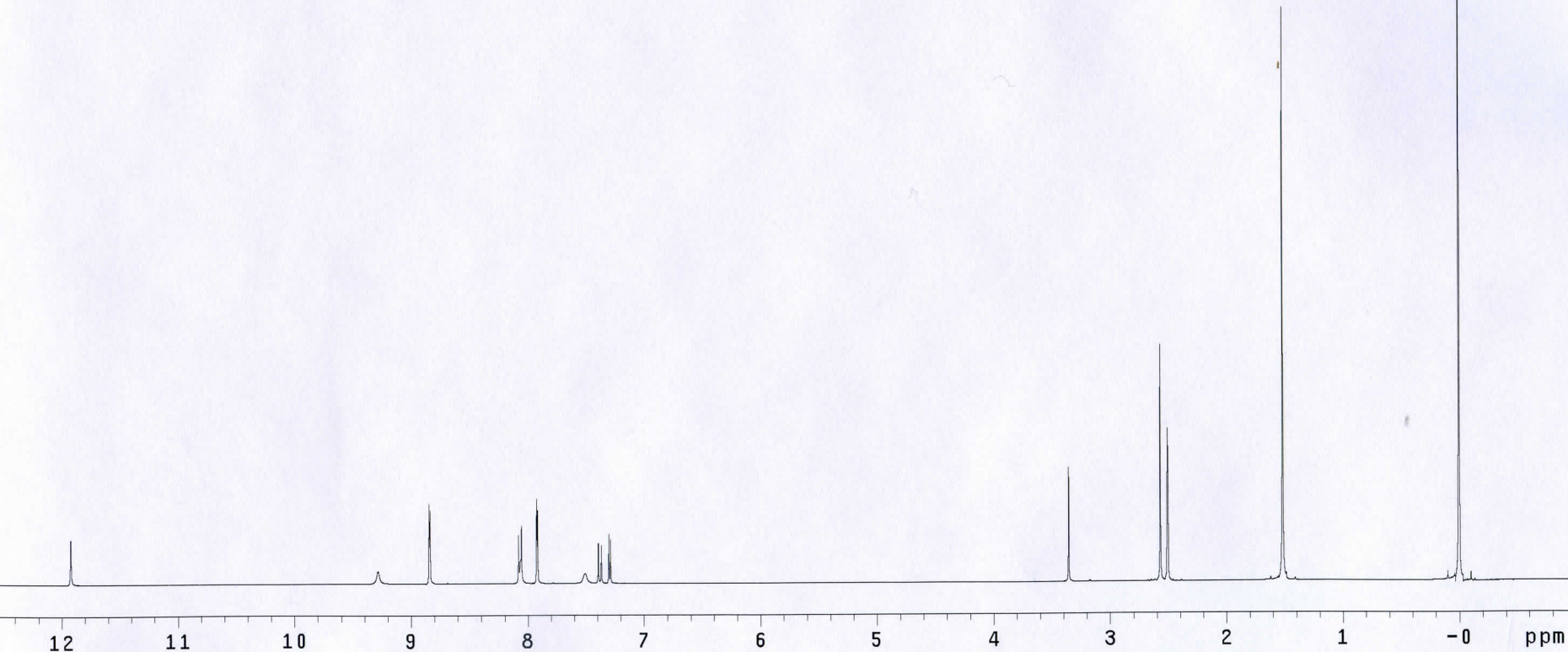
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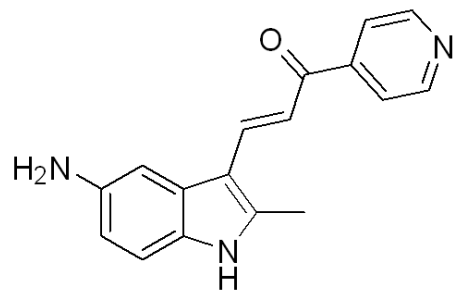
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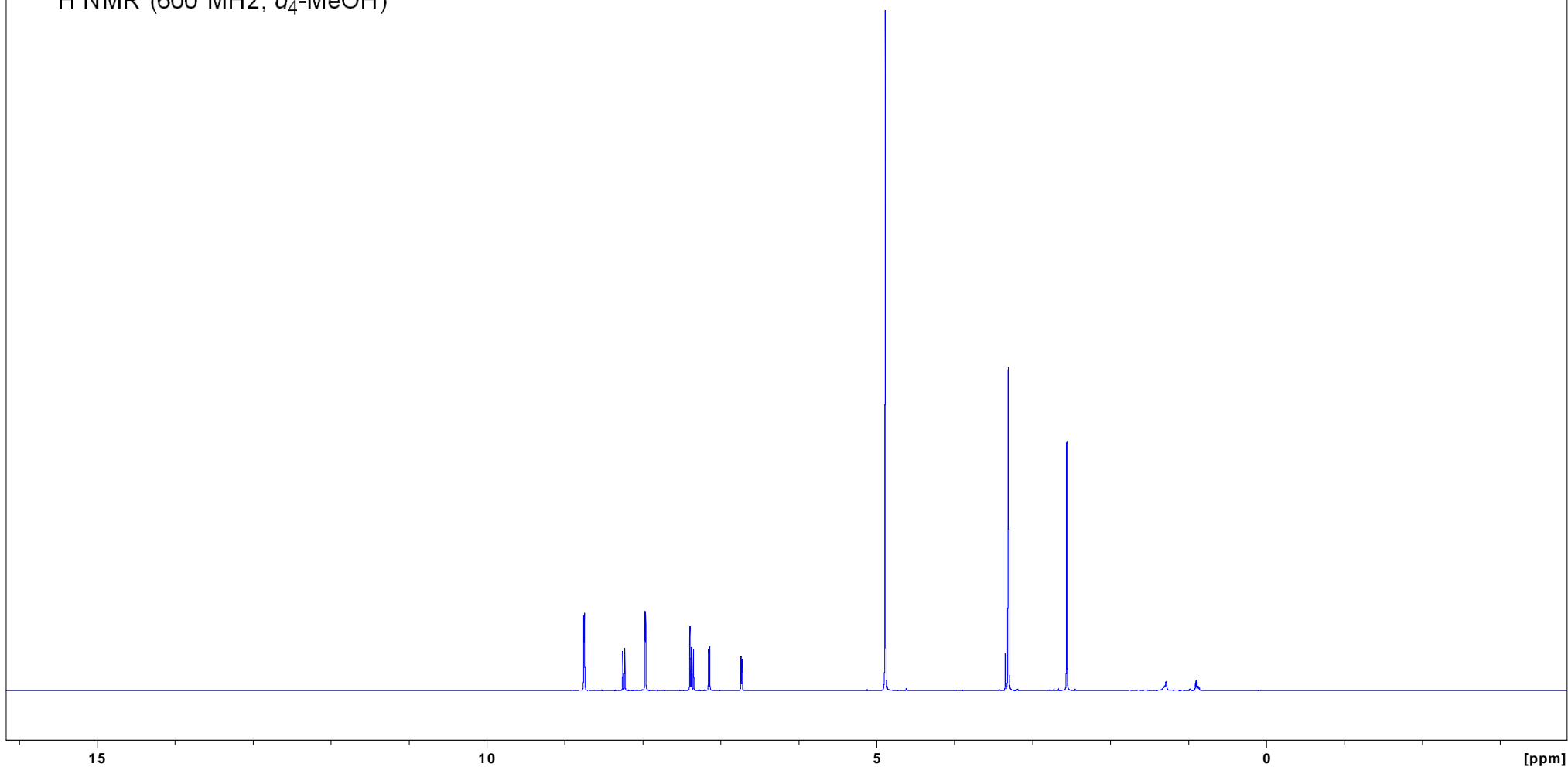
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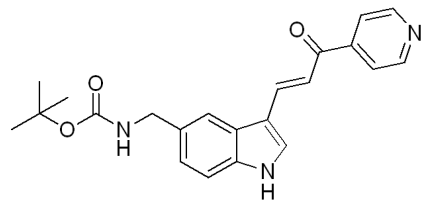
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**2g**

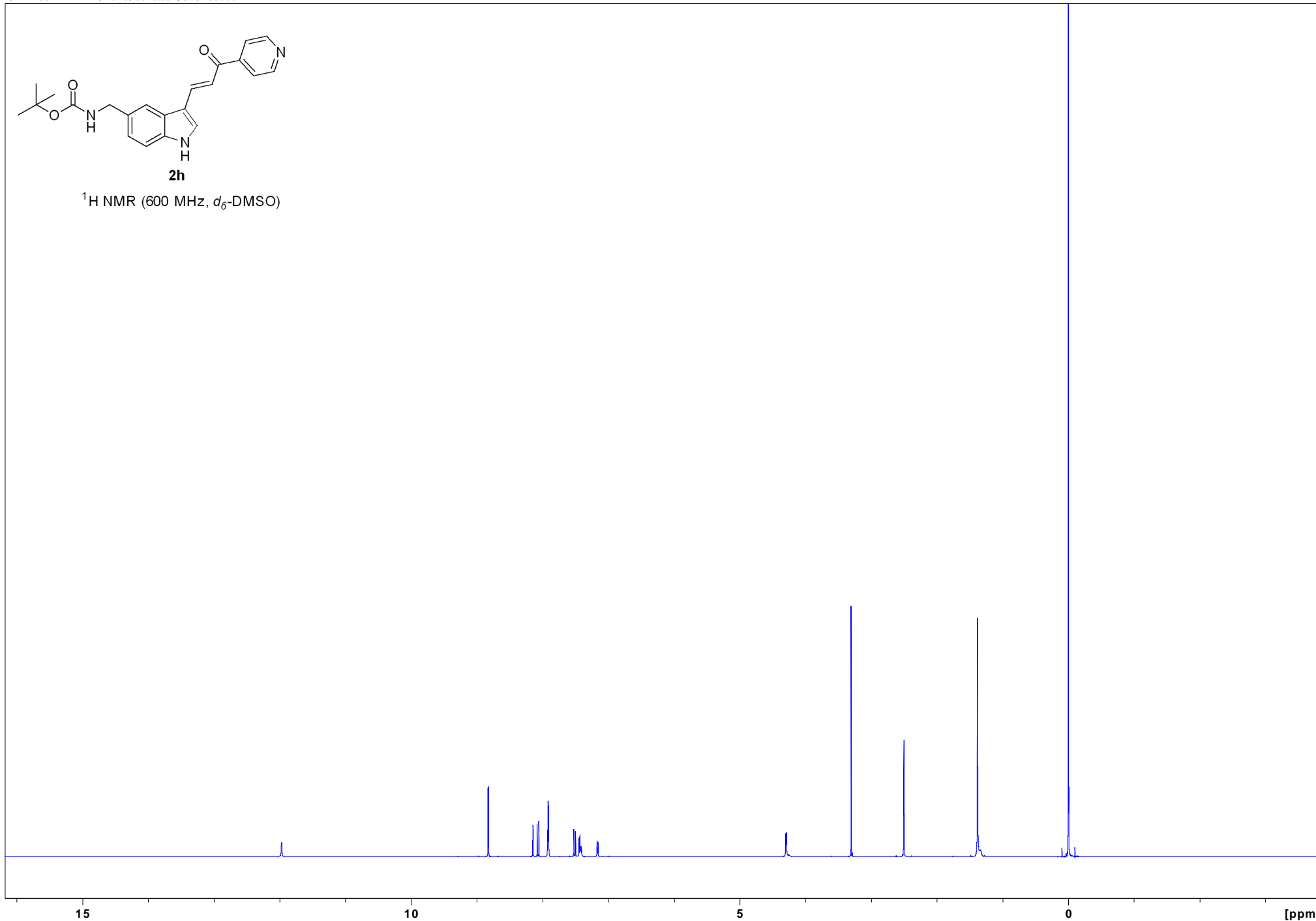
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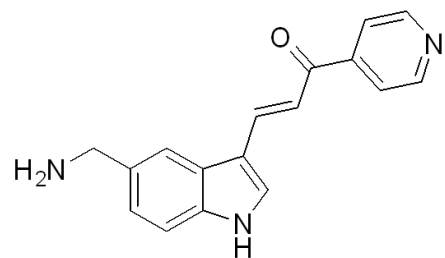




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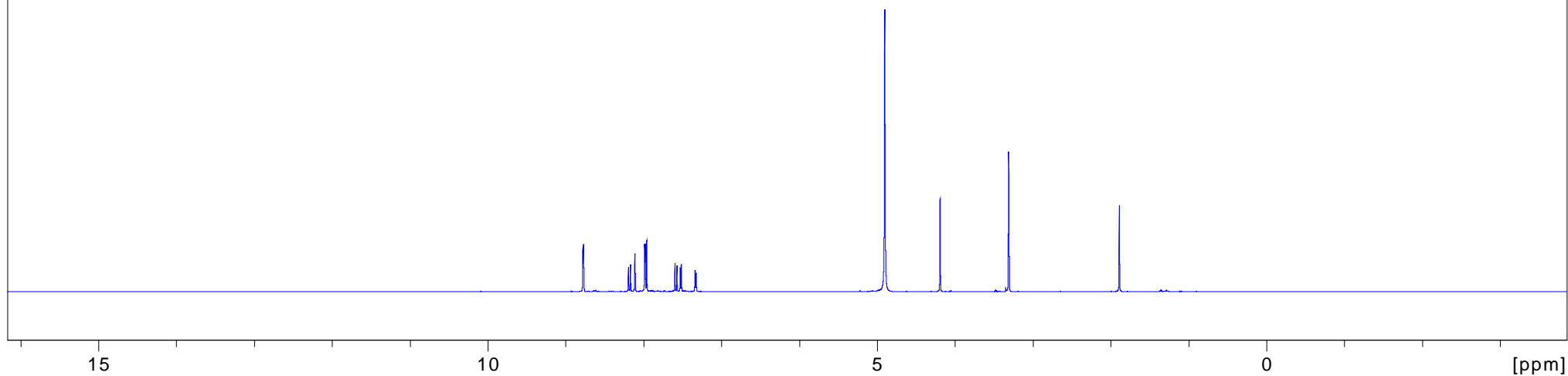
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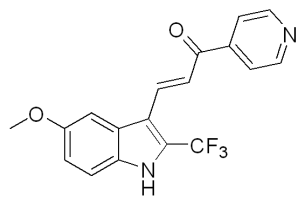




**2i**

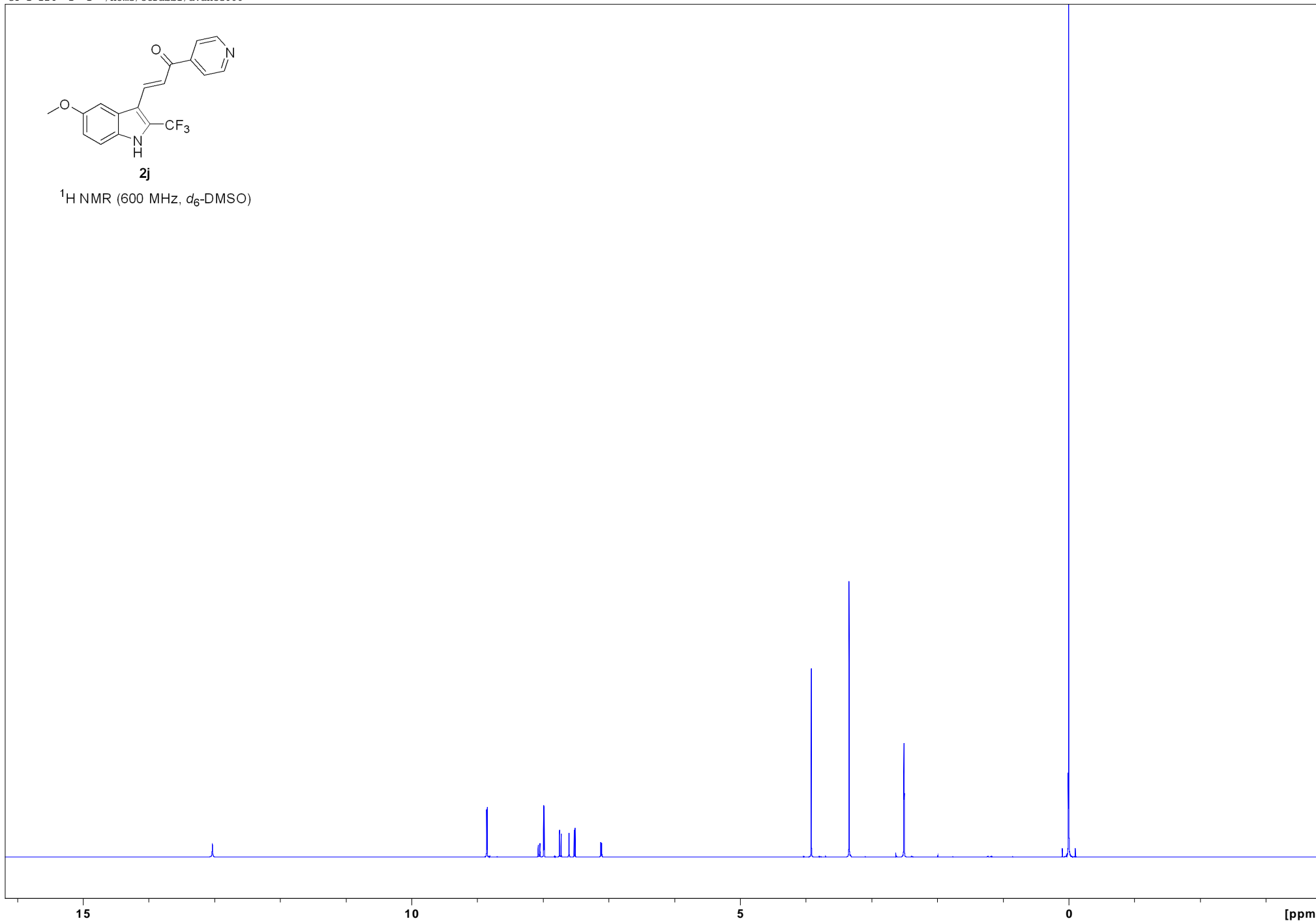
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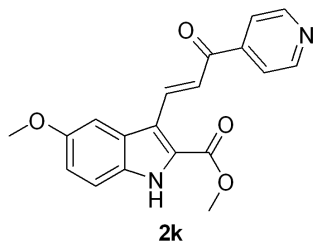




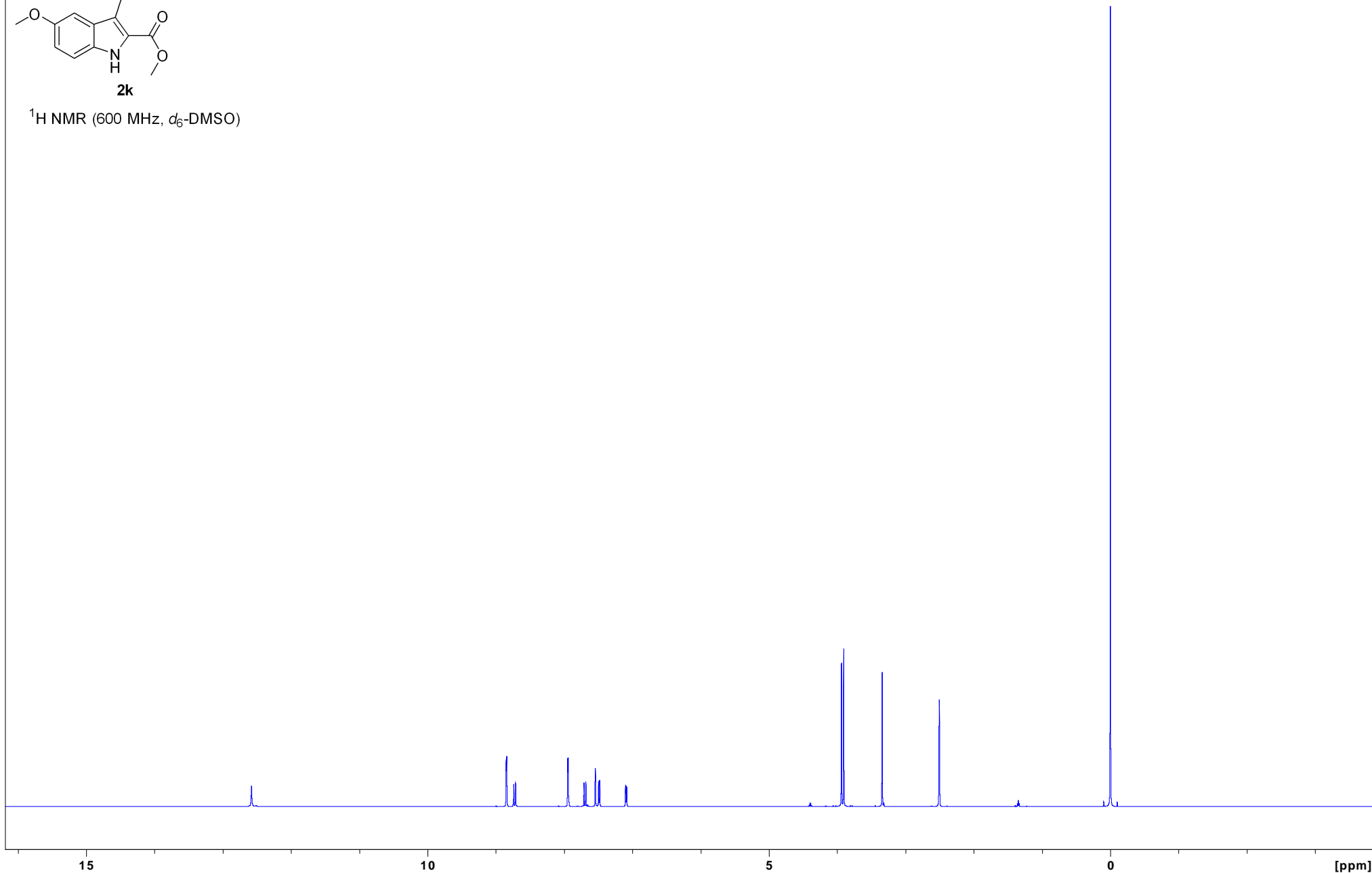
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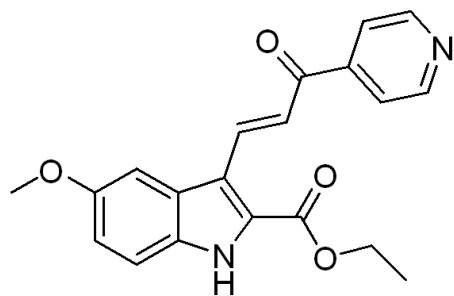




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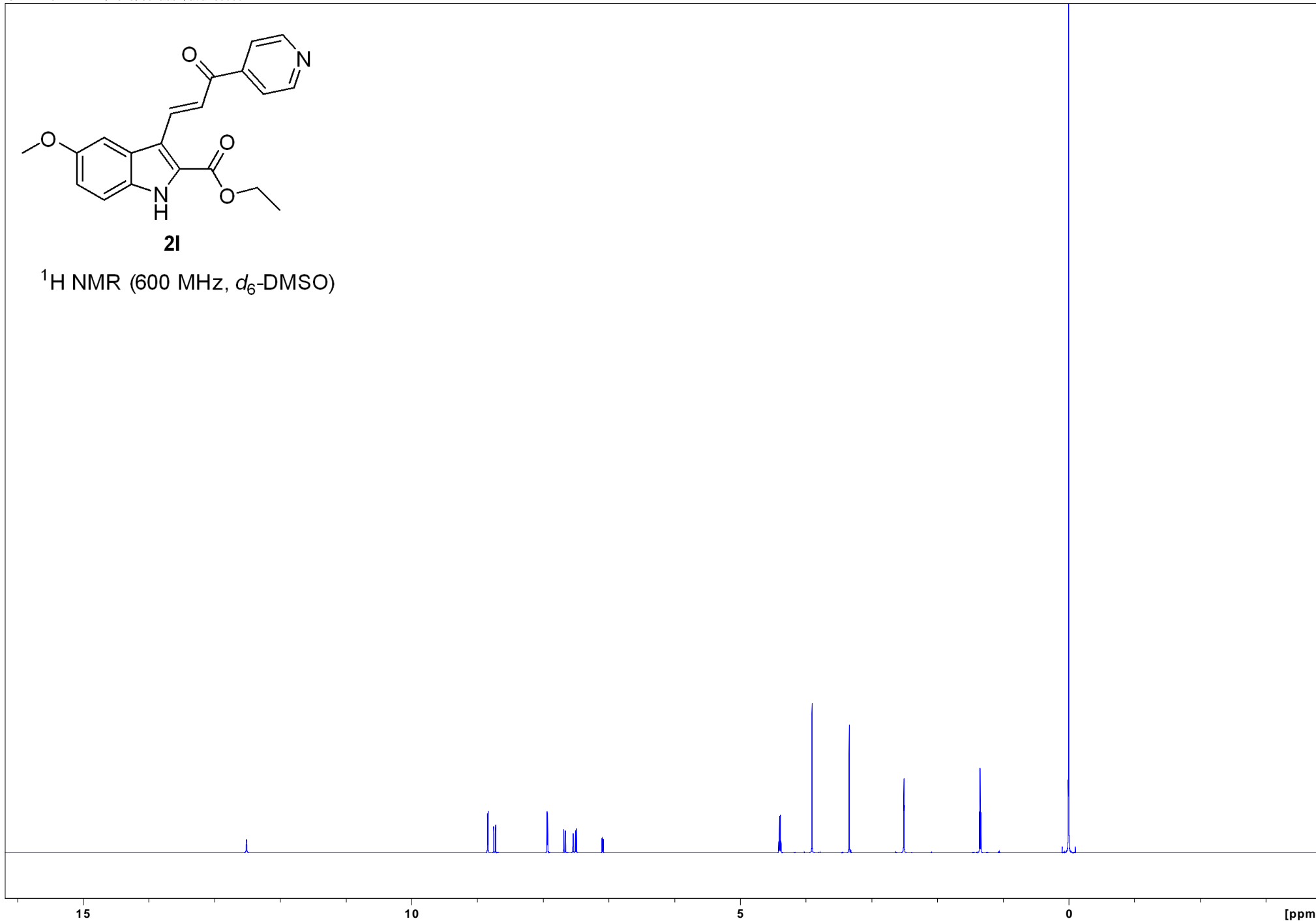


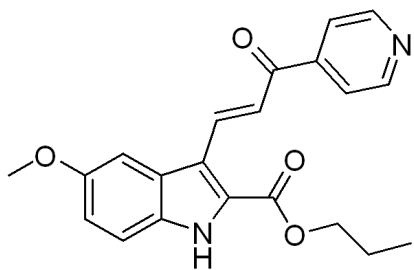




**2I**

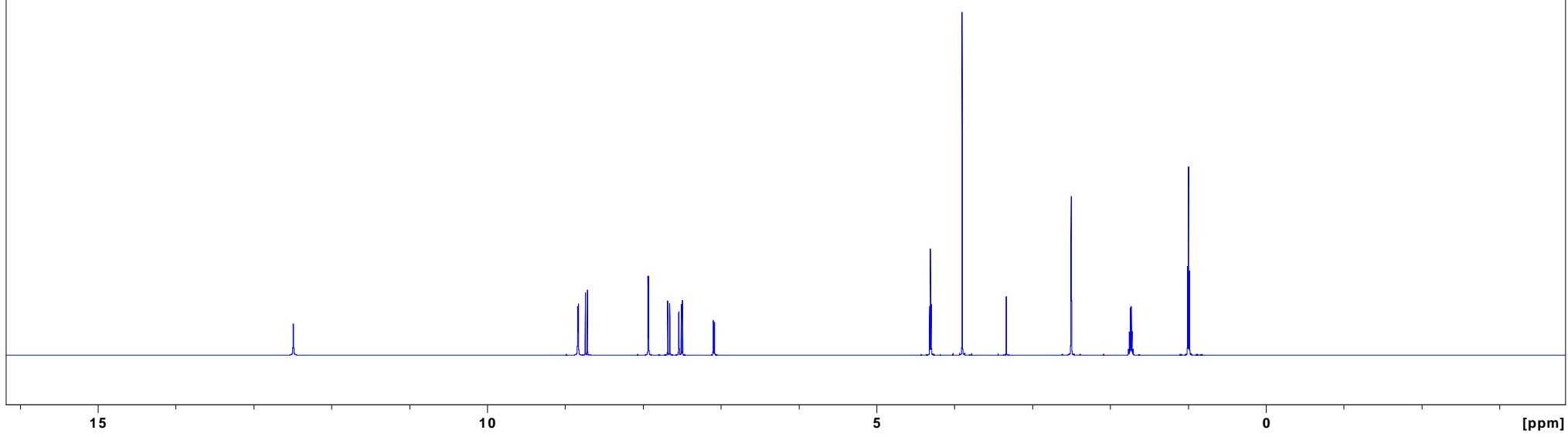
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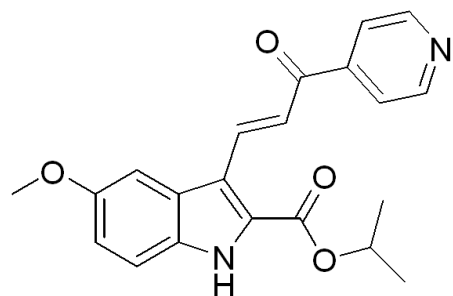




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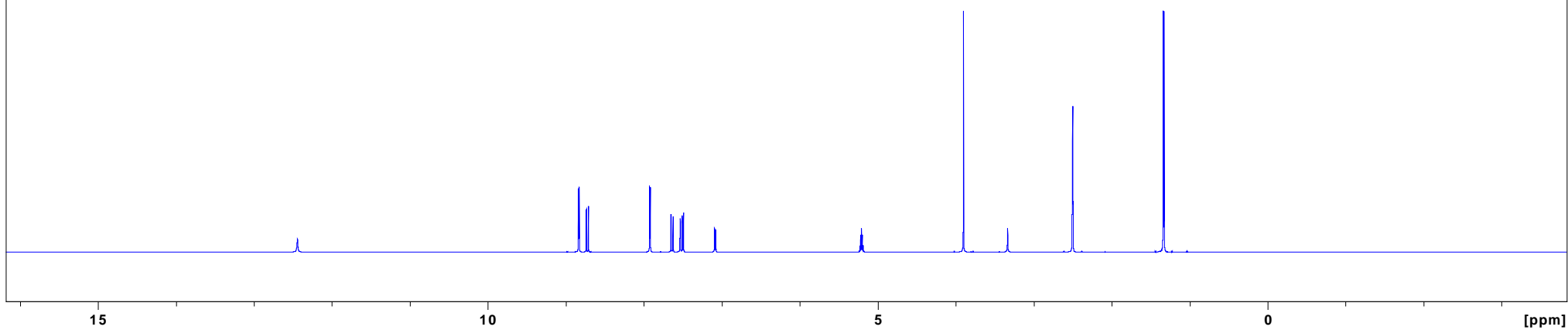
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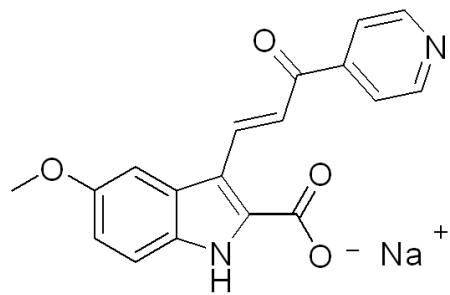




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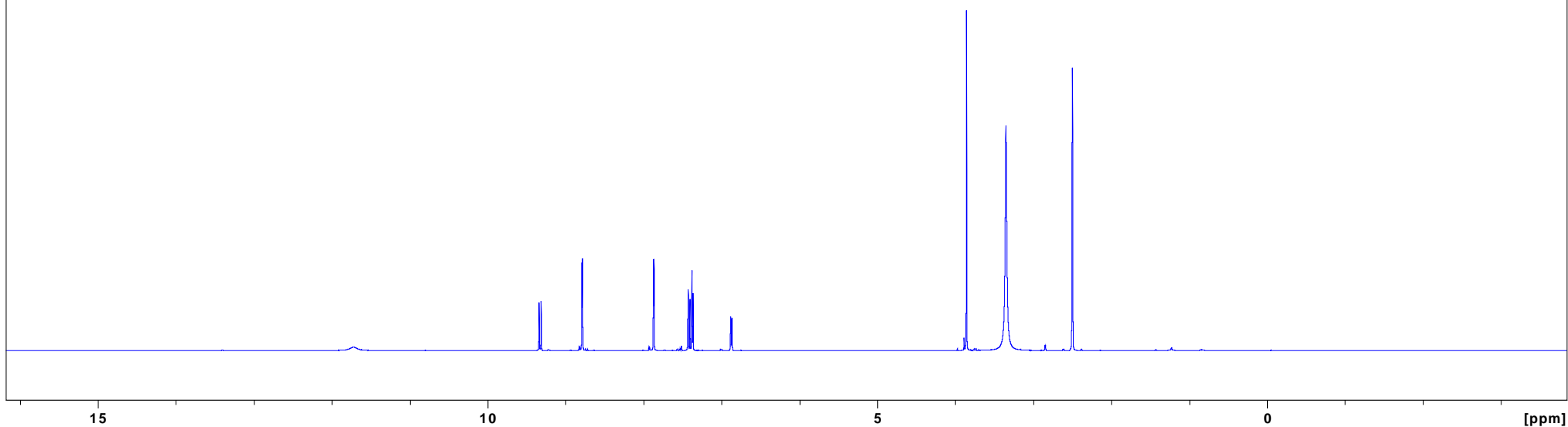
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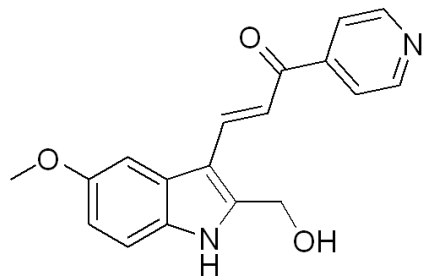




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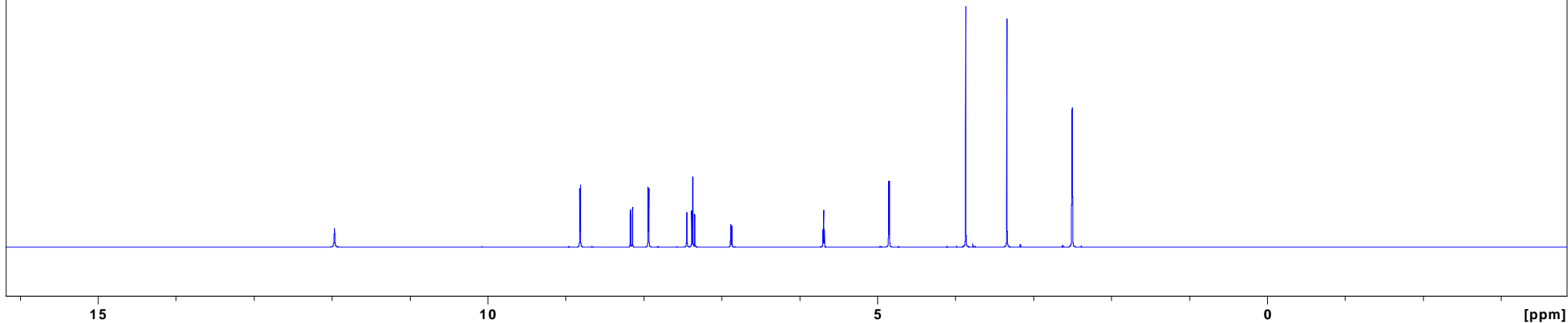
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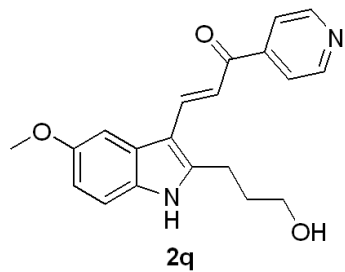




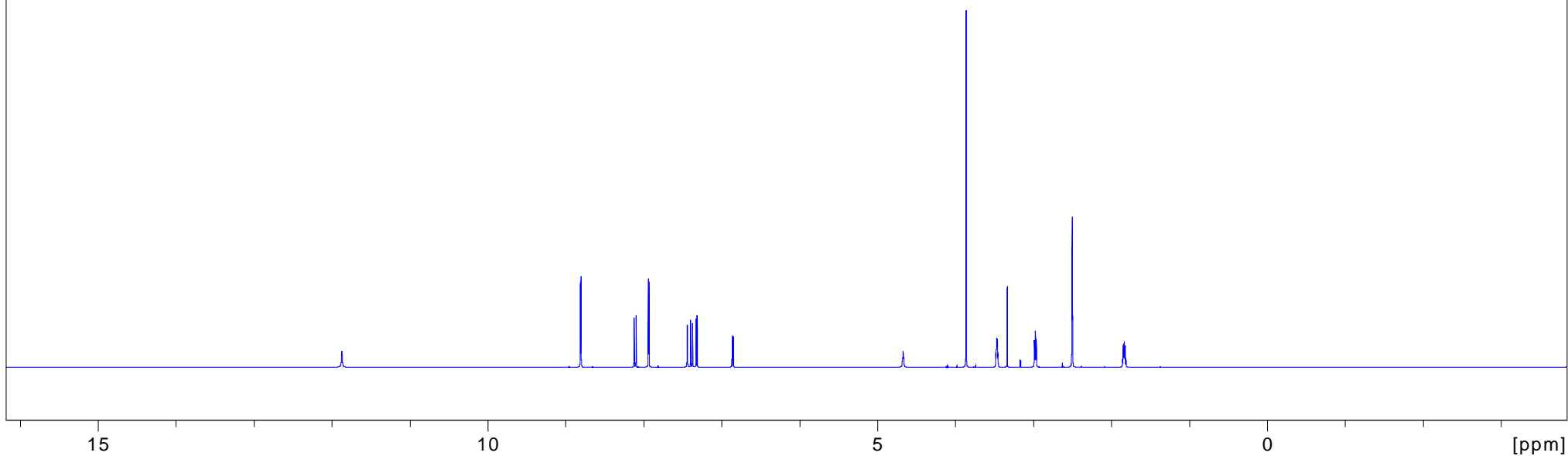
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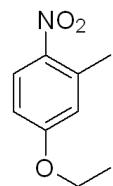
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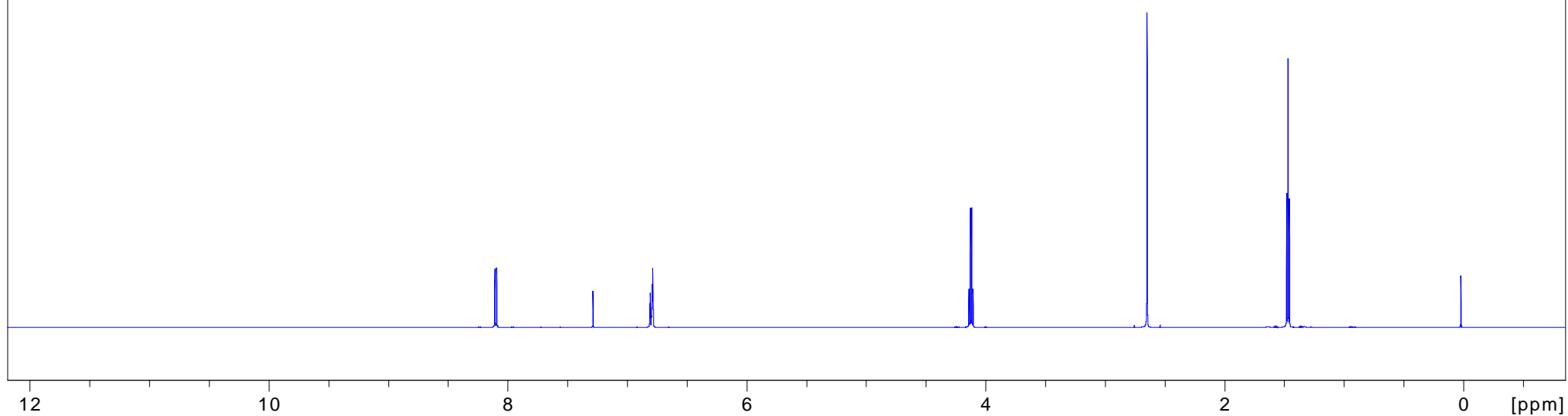
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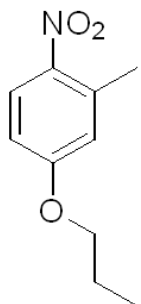




**4a**

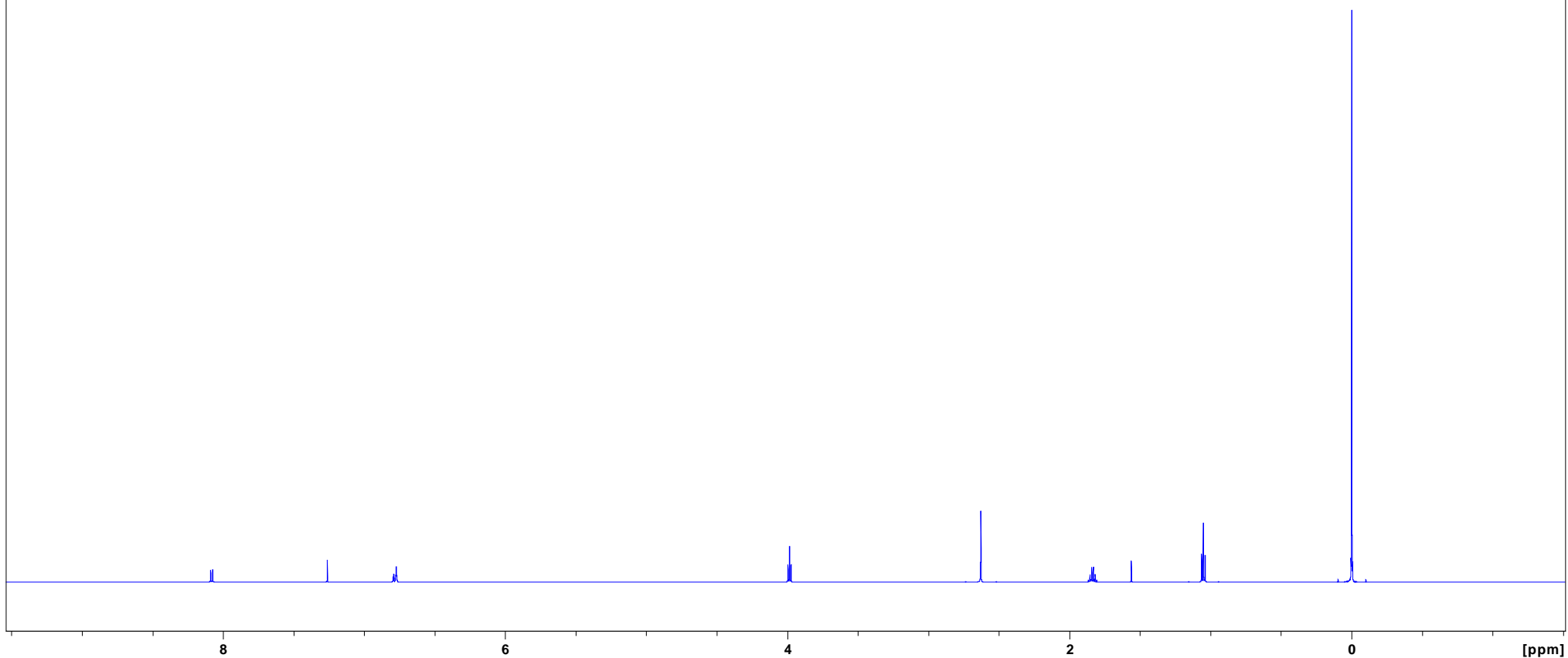
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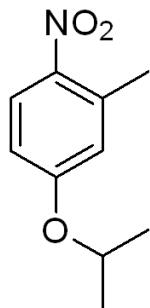


**4b**

$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )

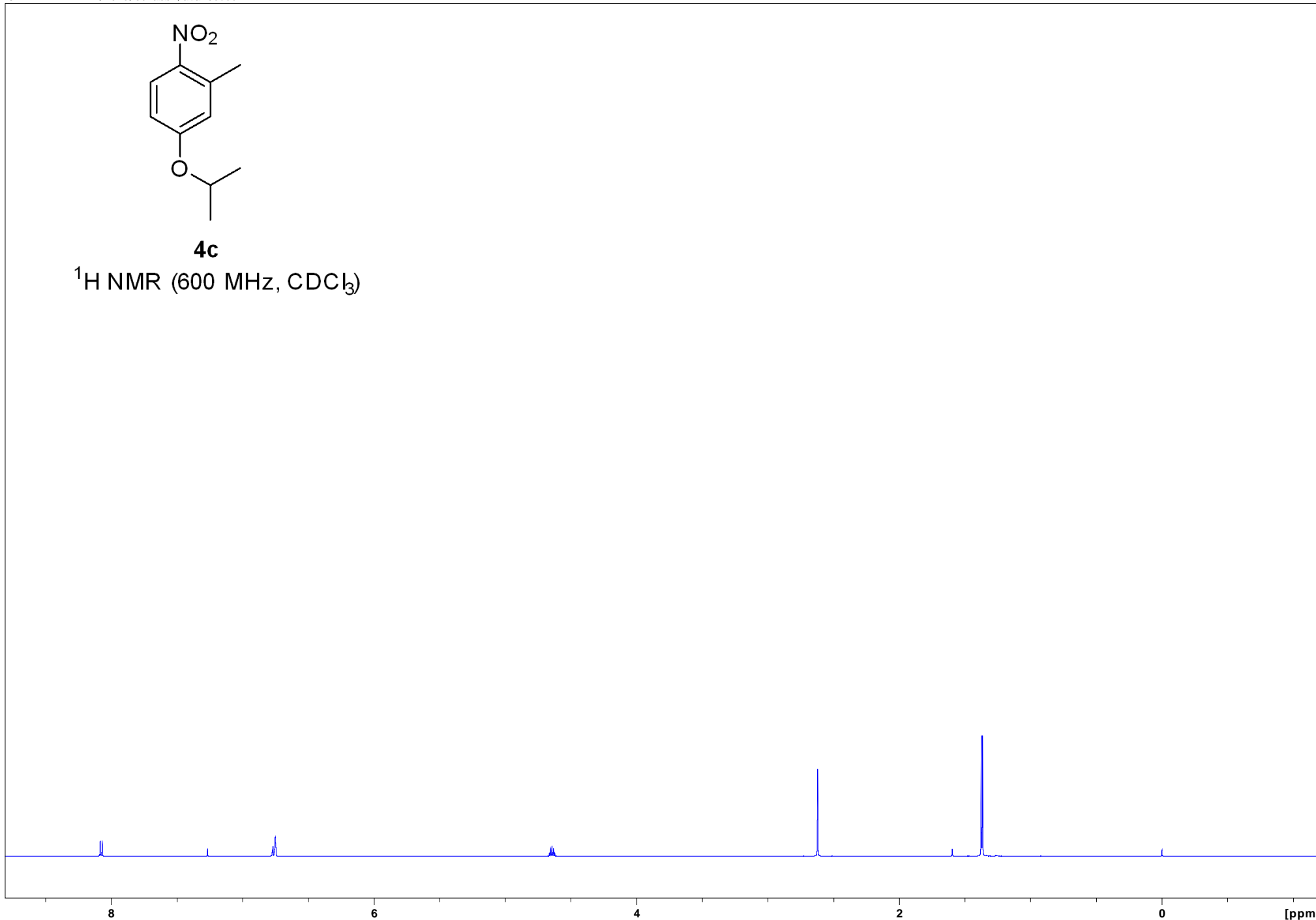


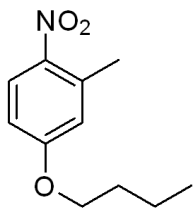




**4c**

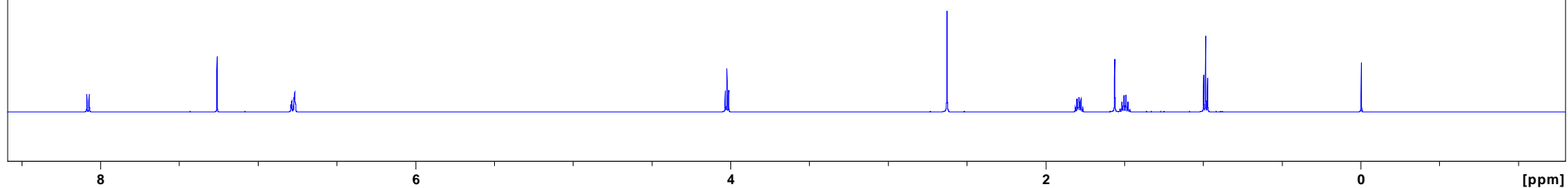
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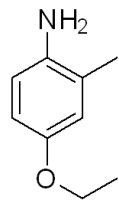




**4d**

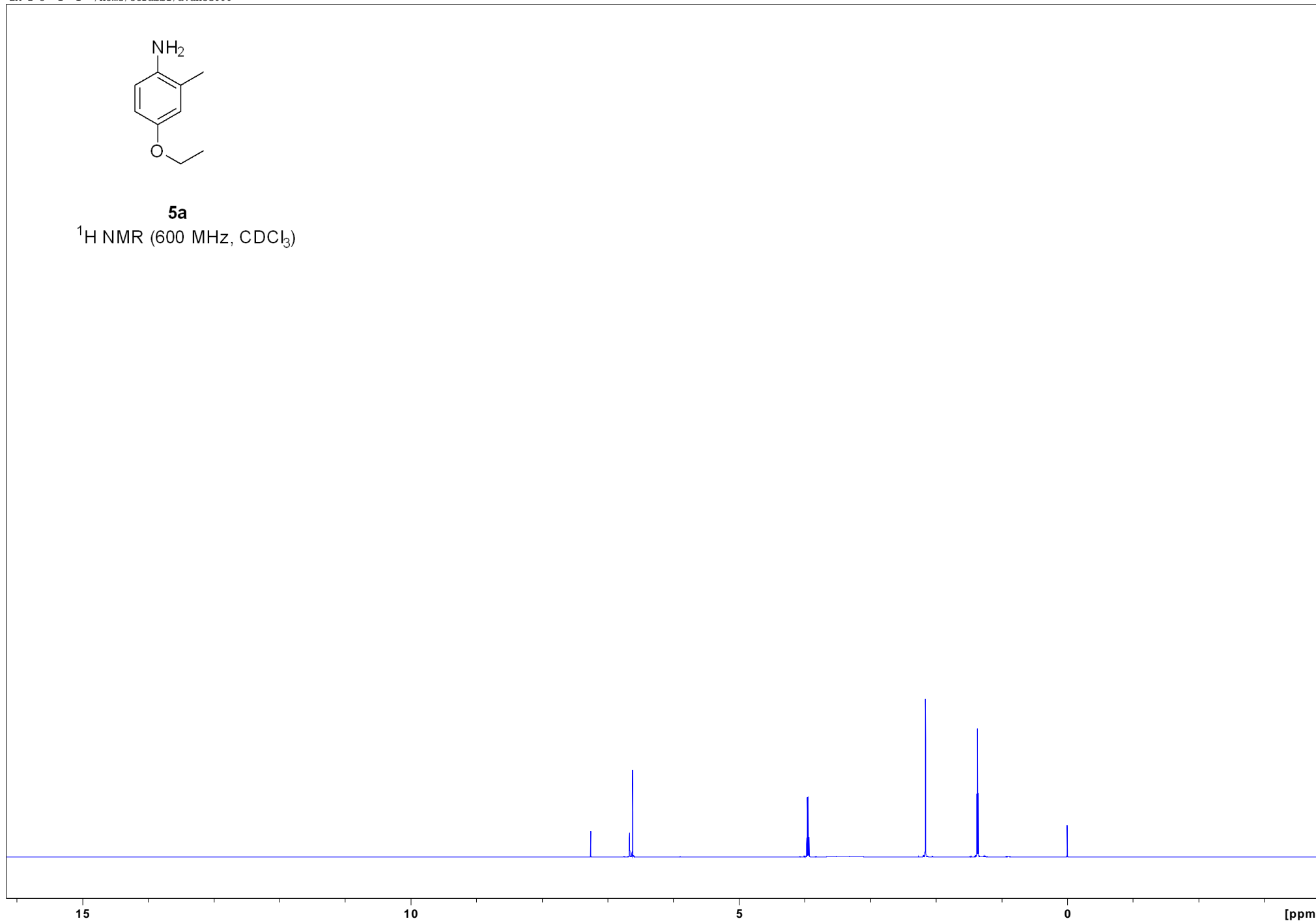
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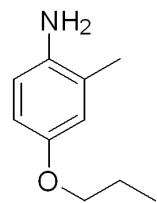




**5a**

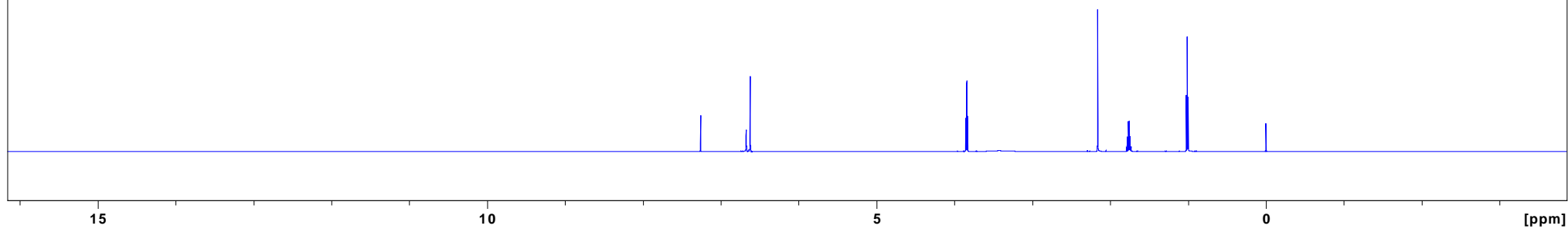
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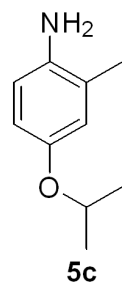




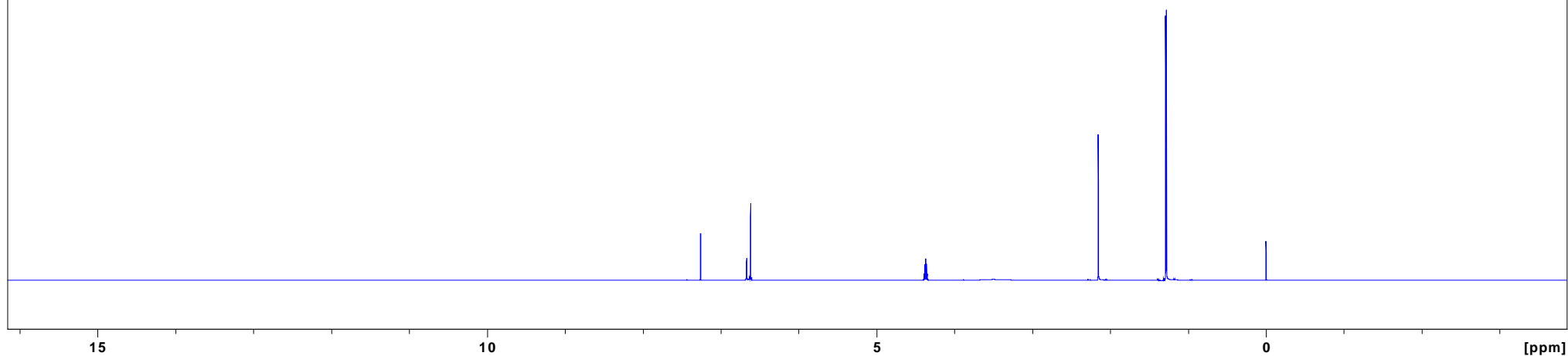
**5b**

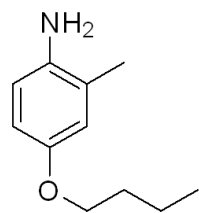
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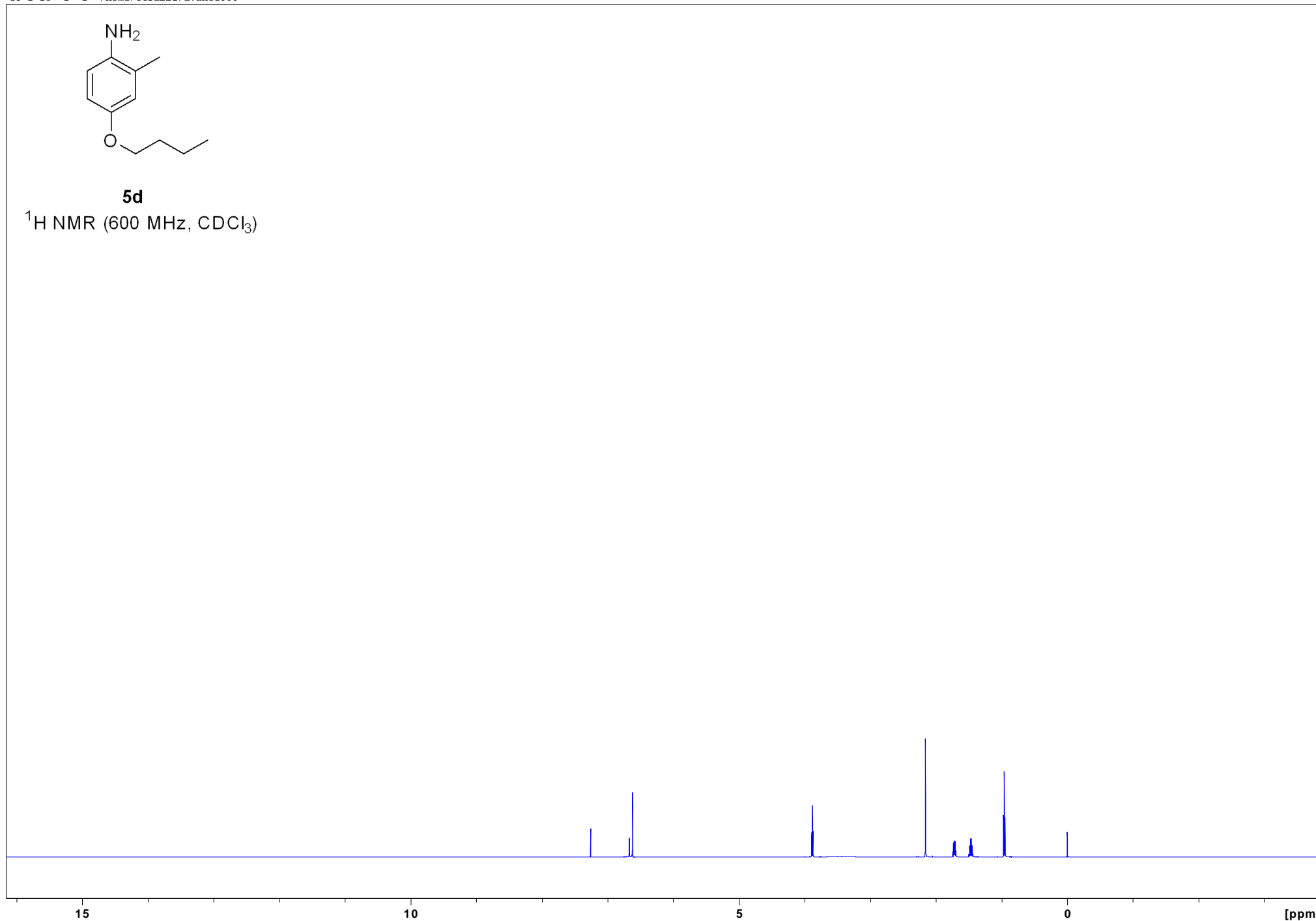
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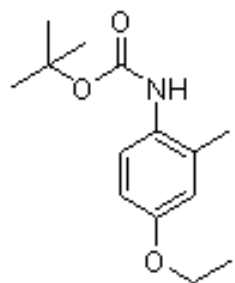




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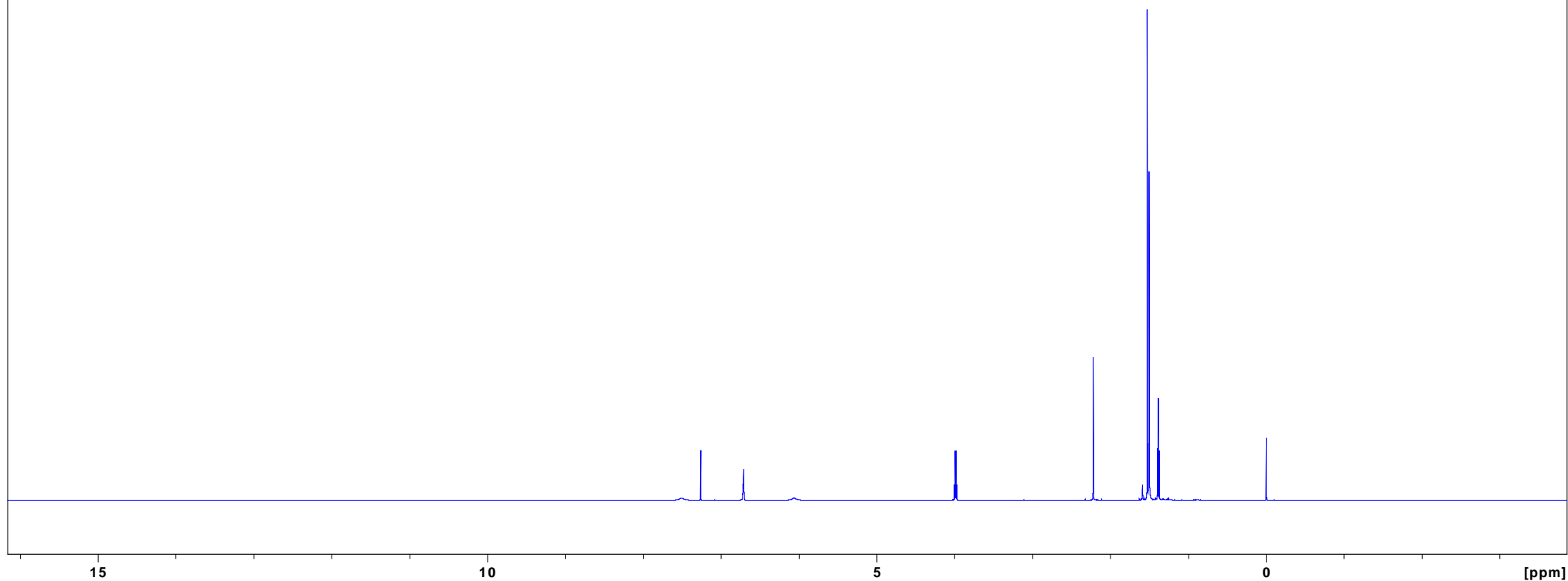
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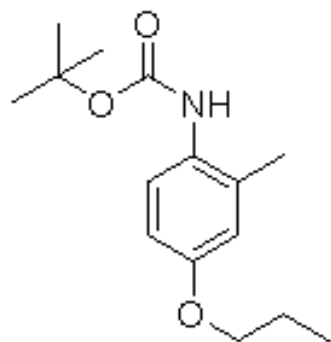




**6a**

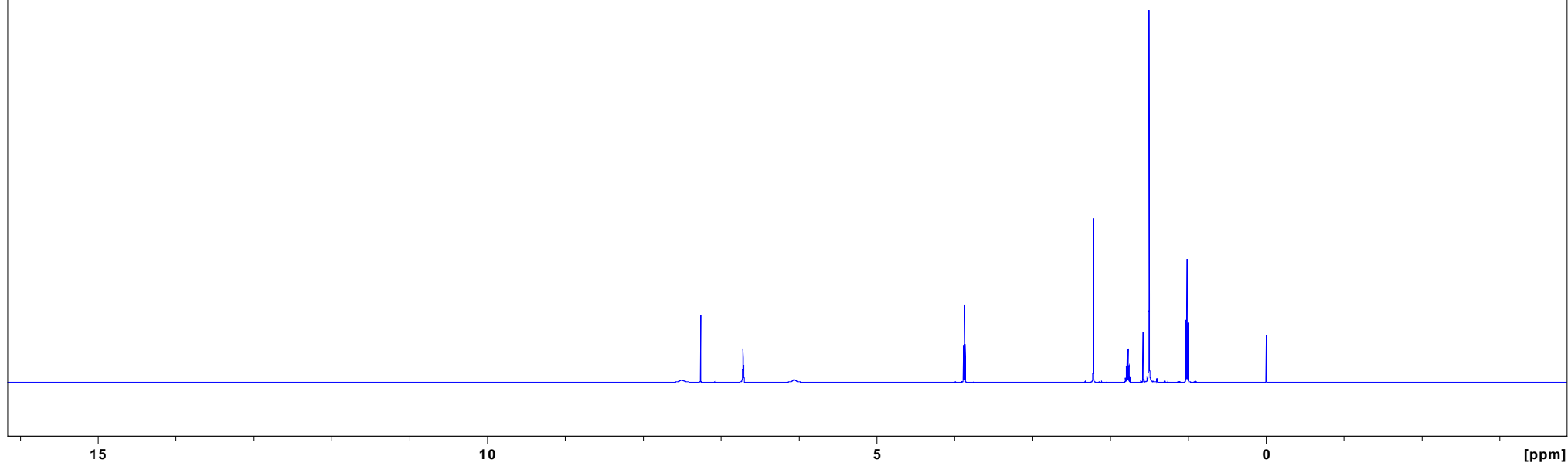
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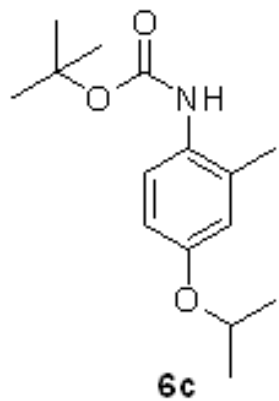


**6b**

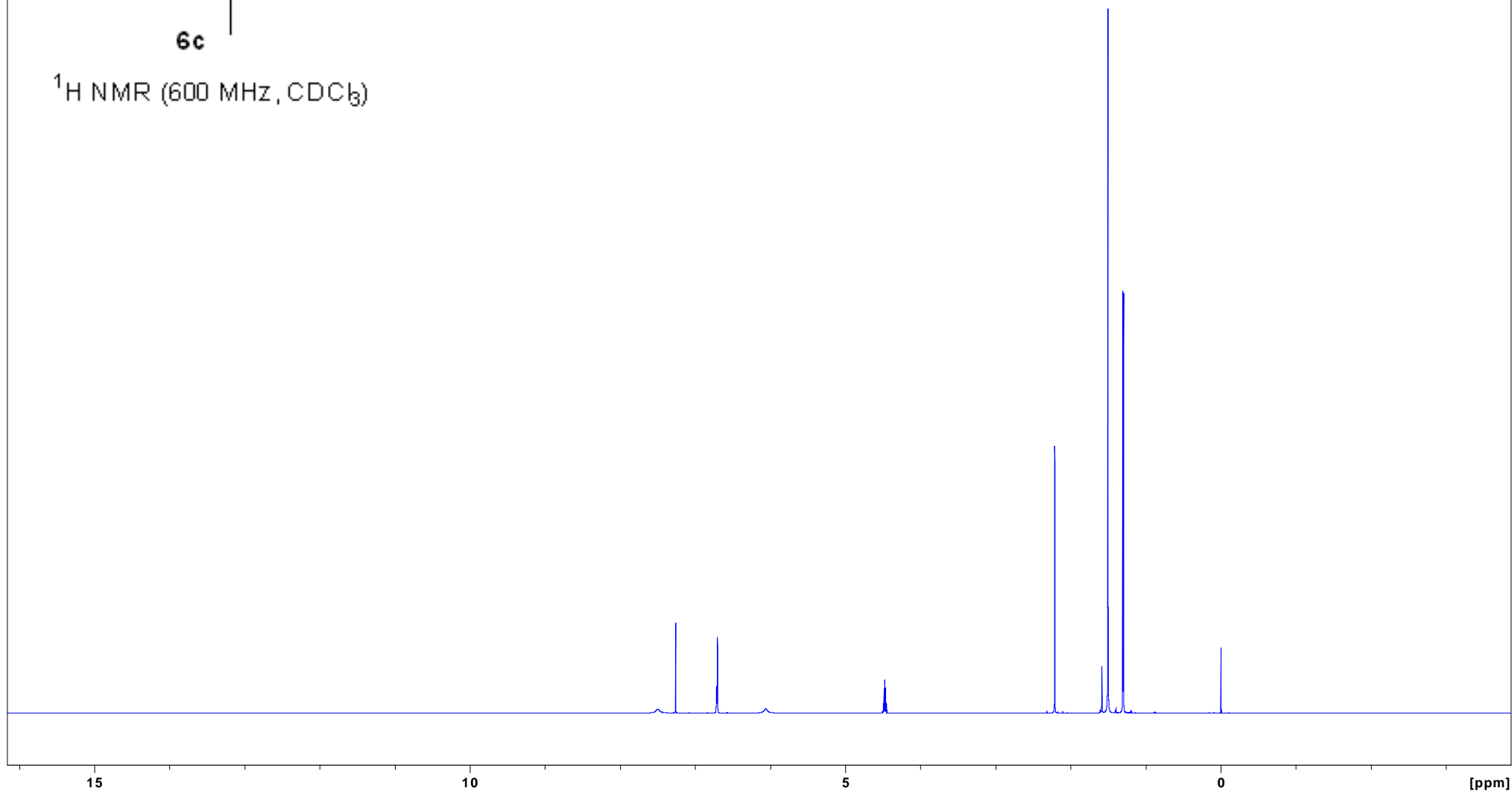
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )

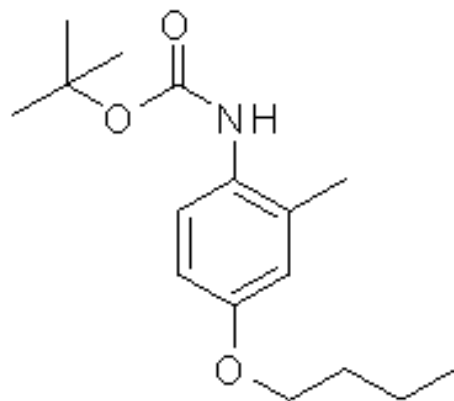






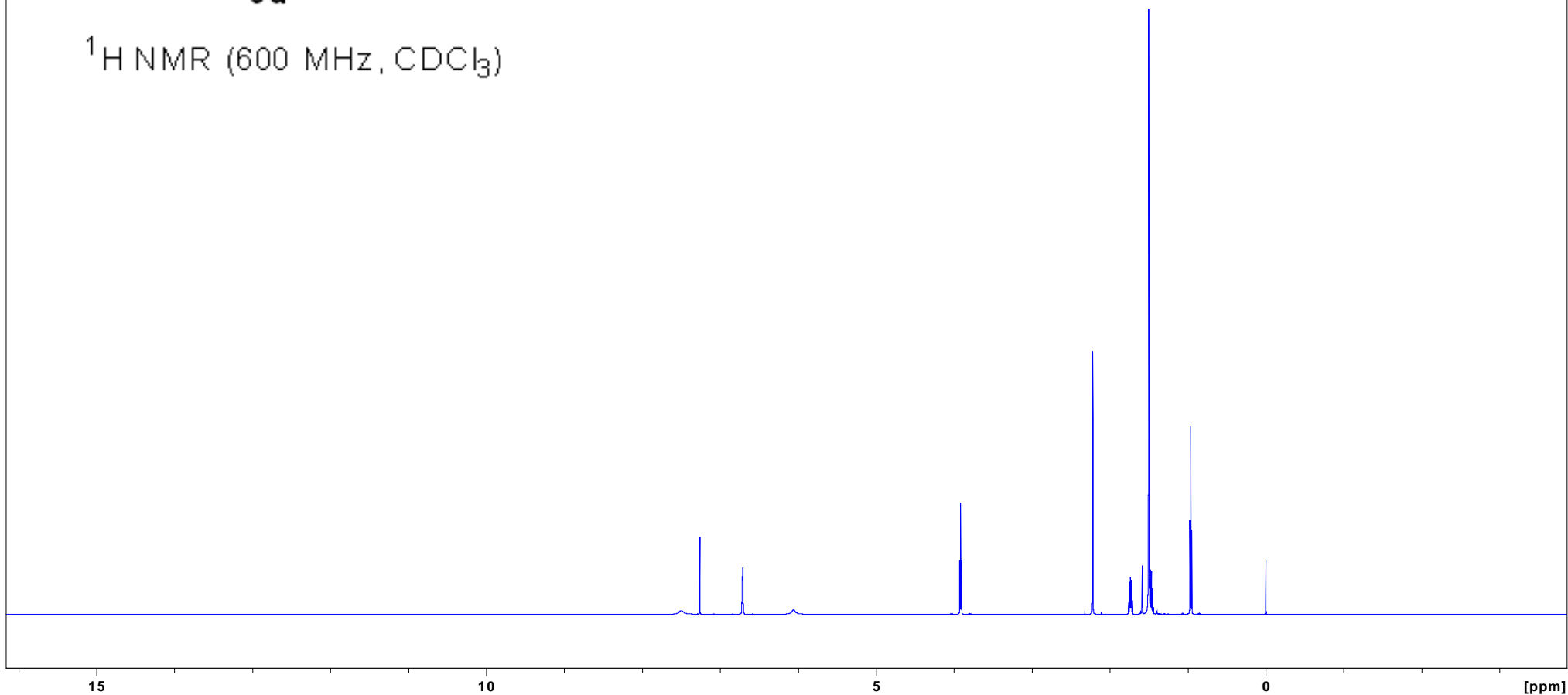
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )

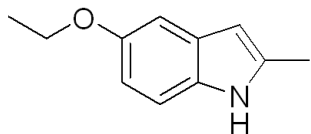




**6d**

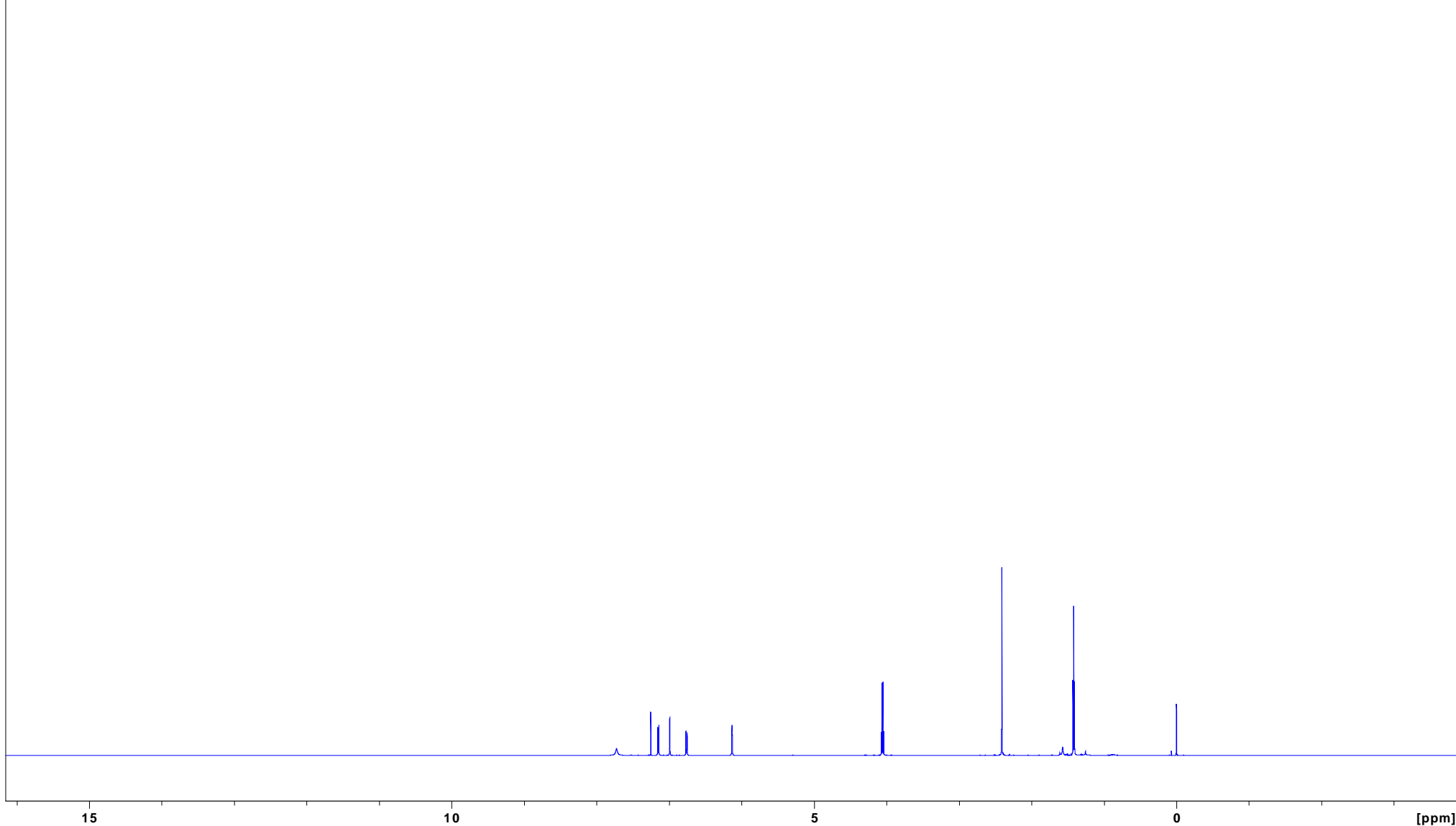
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )

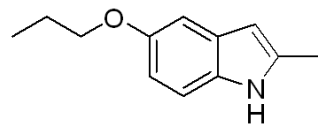




**8a**

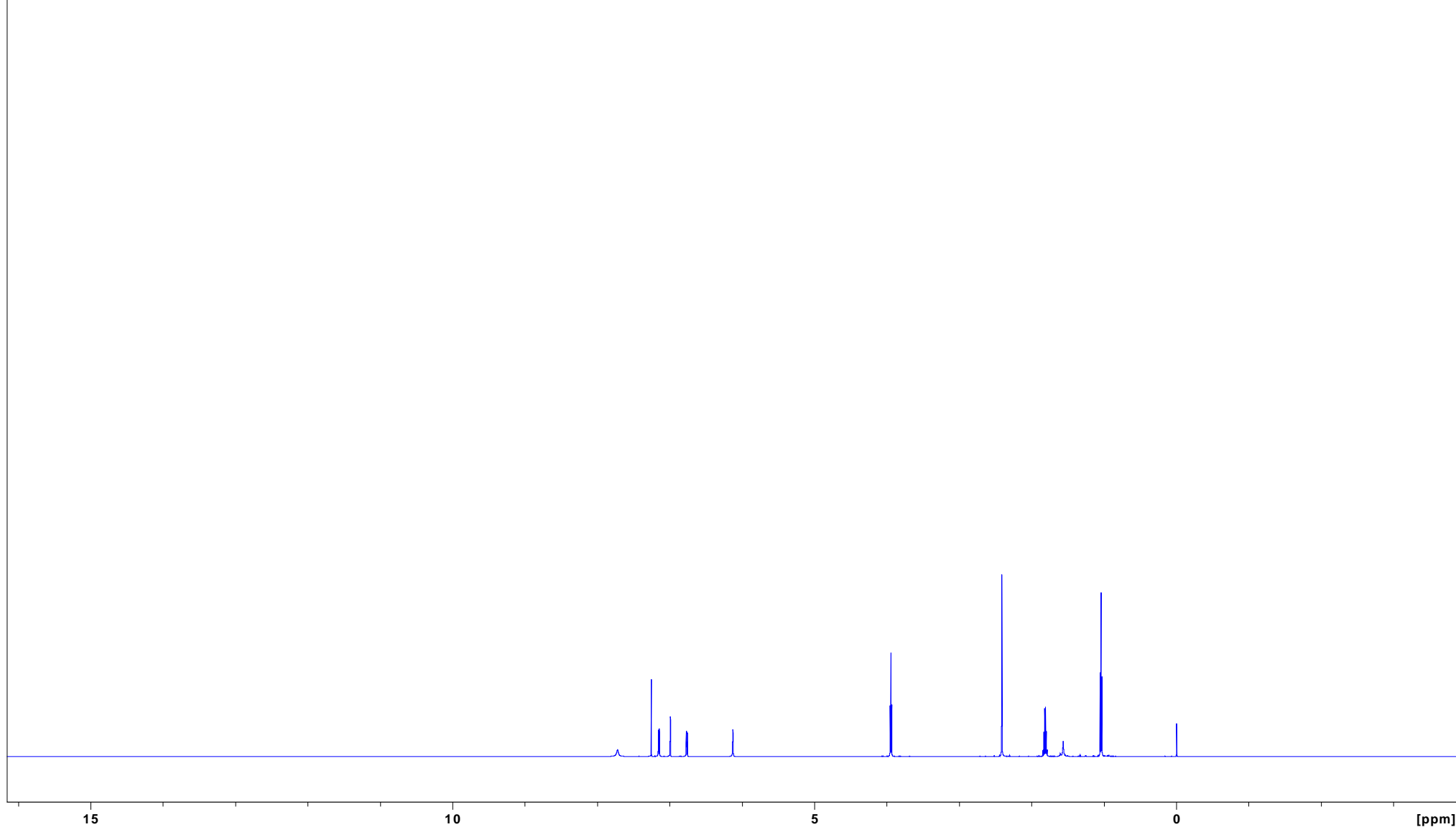
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

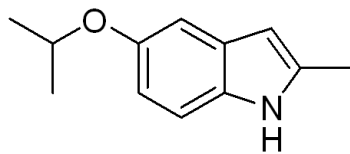




**8b**

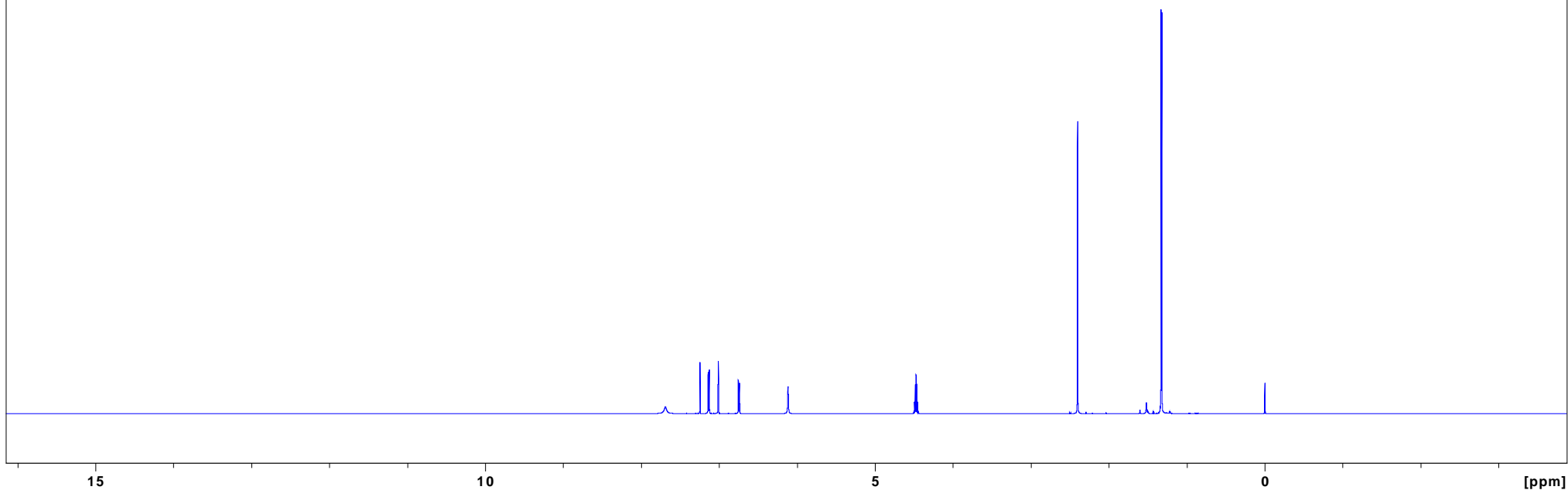
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )

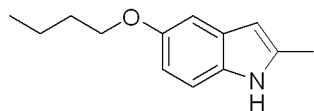




**8c**

$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )

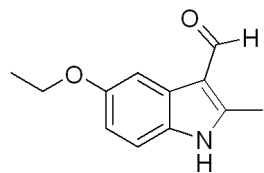




**8d**

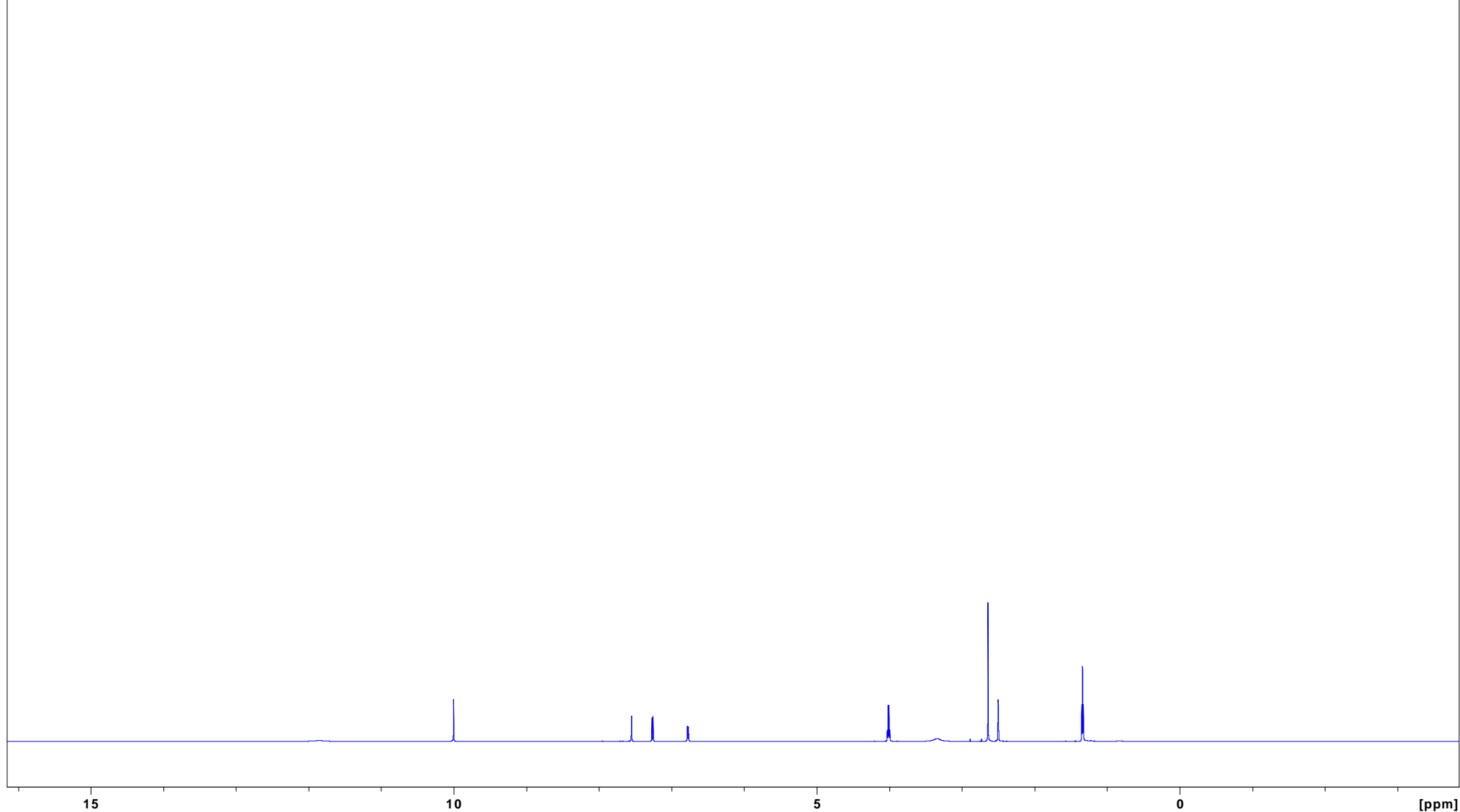
$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )

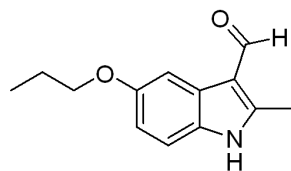




**9a**

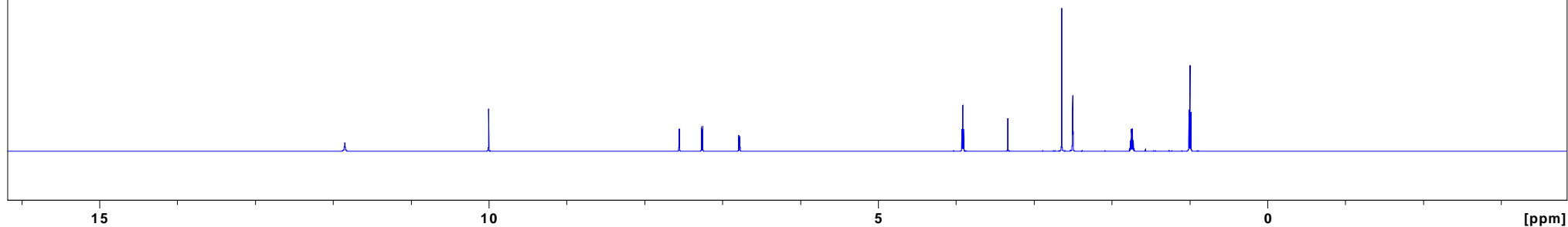
$^1\text{H}$  NMR (600 MHz,  $d_6$ -DMSO)



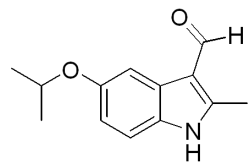
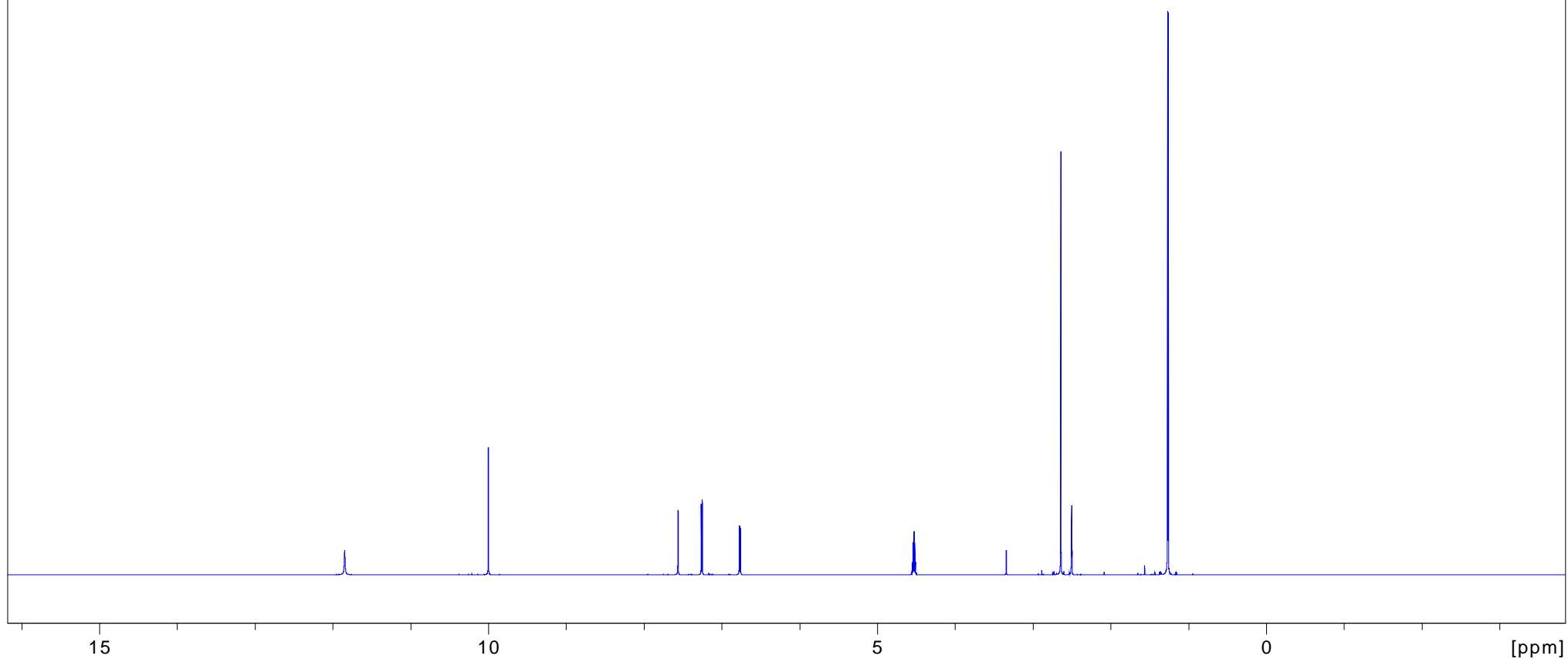


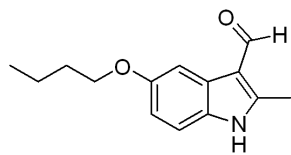
**9b**

$^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)



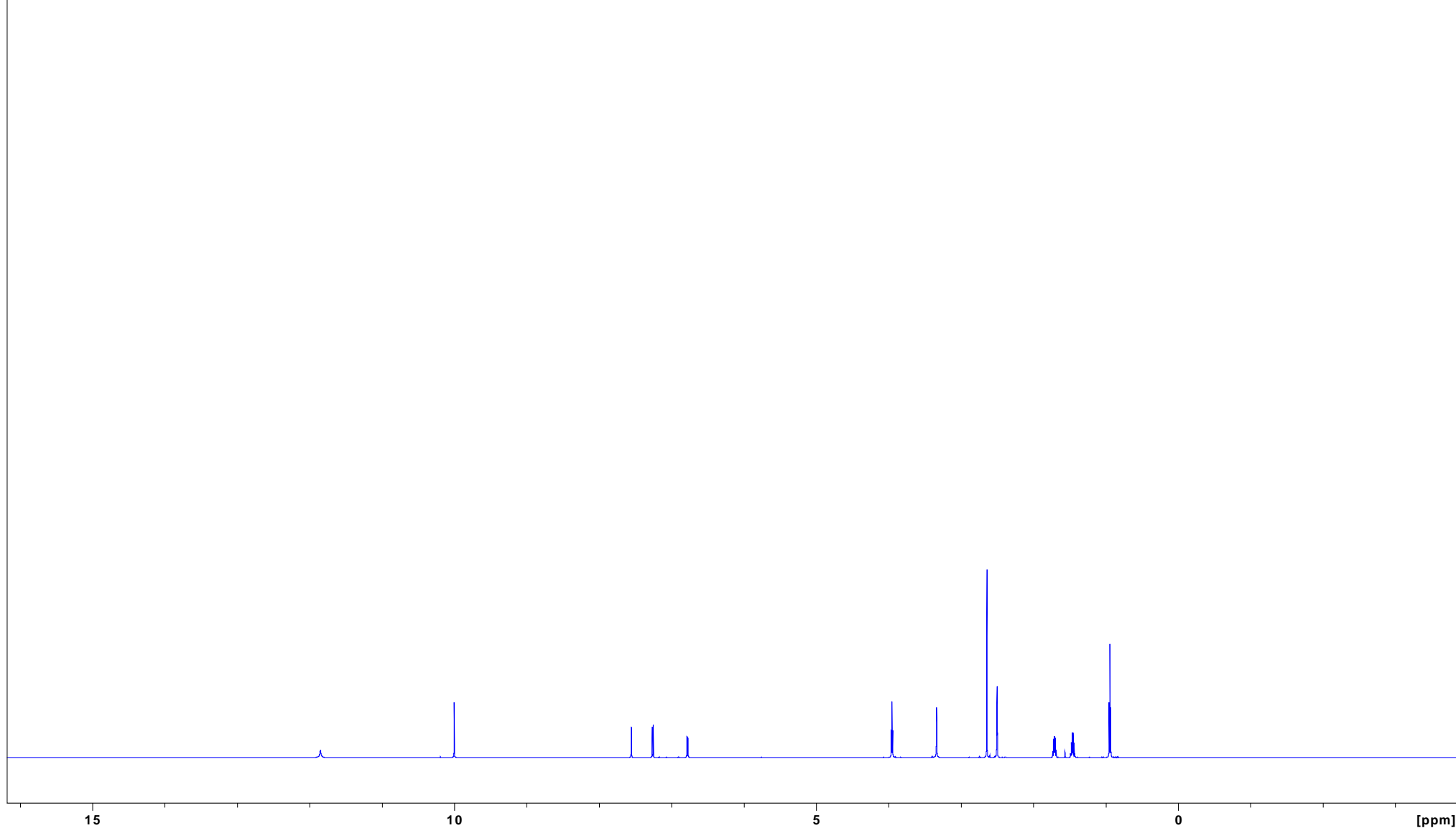


**9c** $^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)



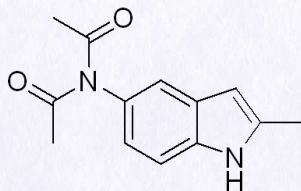
**9d**

$^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)



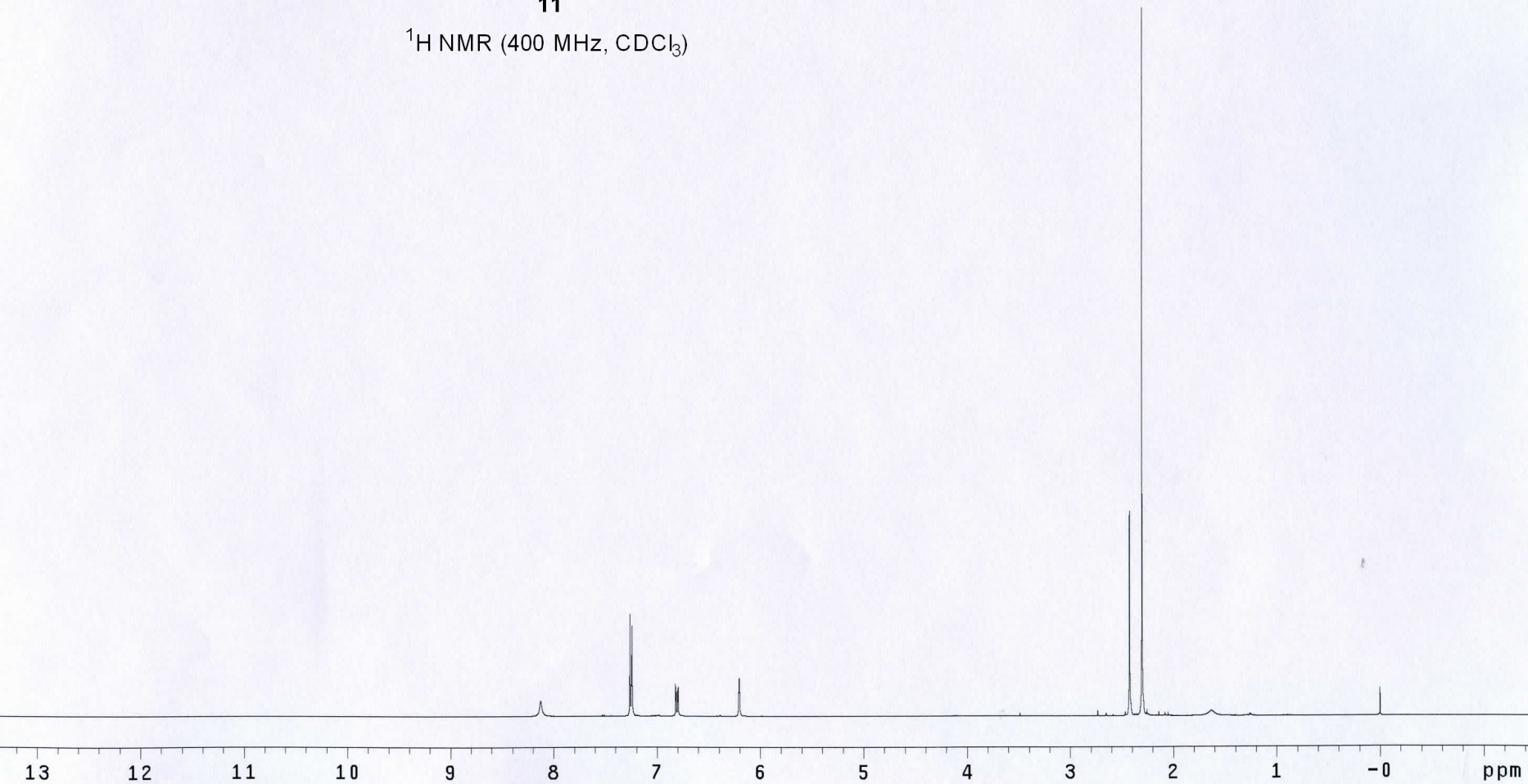
Ambient temperature  
file: MS-1-8  
INOVA-600 "inova-wkst"

Relax delay 2 000 sec  
Pulse 47 4 degrees  
Acq time 2 731 sec  
Width 5999 7 Hz  
32 repetitions  
OBSERVE H1, 399 9486781 MHz  
DATA PROCESSING  
Line broadening 0 5 Hz  
F1 size 65536  
Total time 2 min, 31 sec



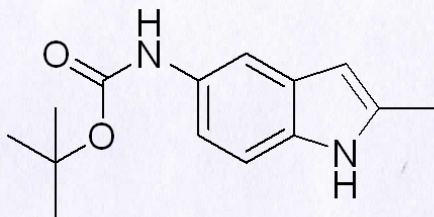
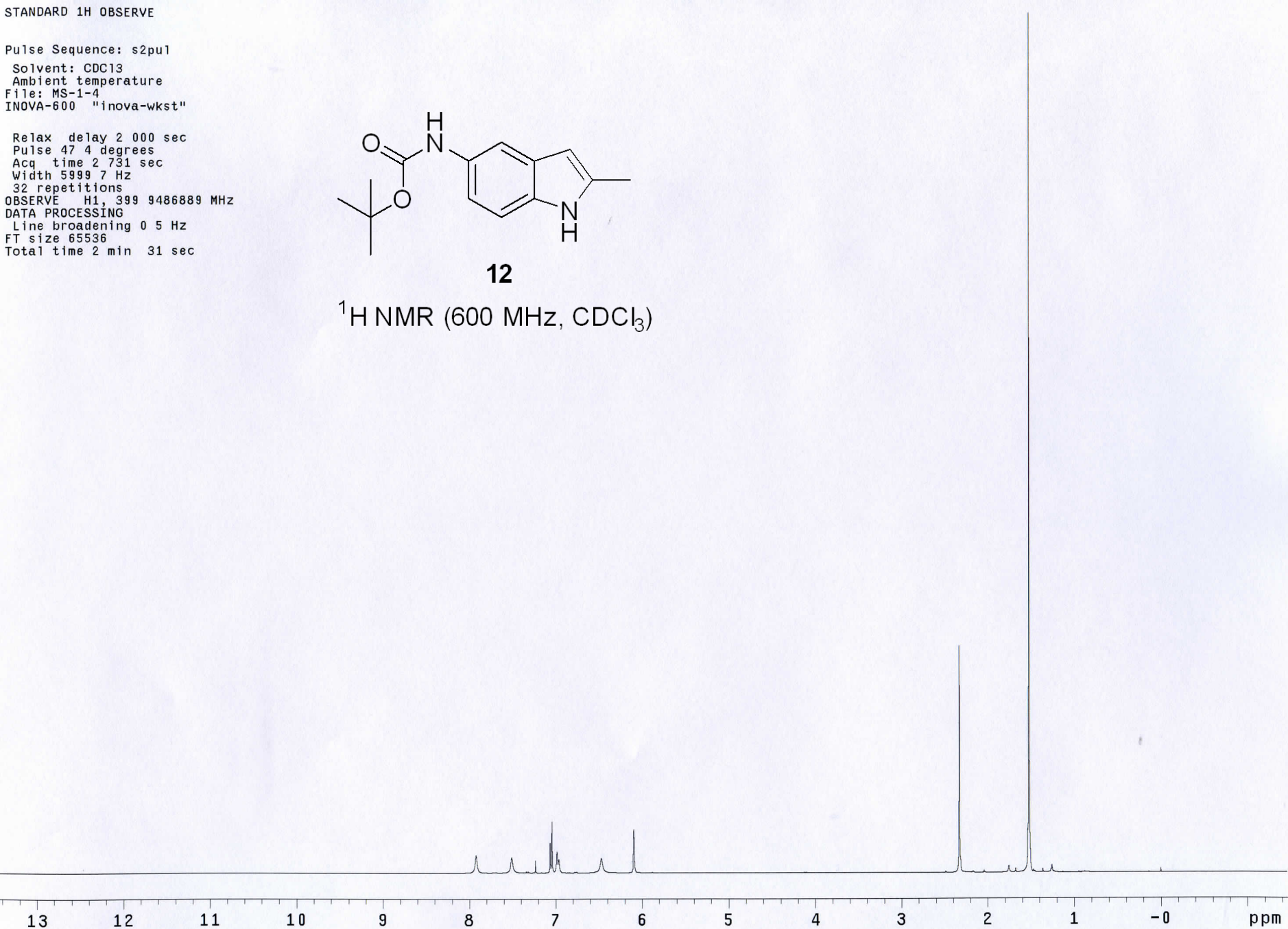
11

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )



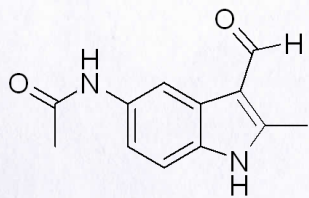
Pulse Sequence: s2pu1  
Solvent: CDCl3  
Ambient temperature  
File: MS-1-4  
INOVA-600 "inova-wkst"

Relax delay 2 000 sec  
Pulse 47 4 degrees  
Acq time 2 731 sec  
Width 5999 7 Hz  
32 repetitions  
OBSERVE H1, 399 9486889 MHz  
DATA PROCESSING  
Line broadening 0 5 Hz  
FT size 65536  
Total time 2 min 31 sec

**12**<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

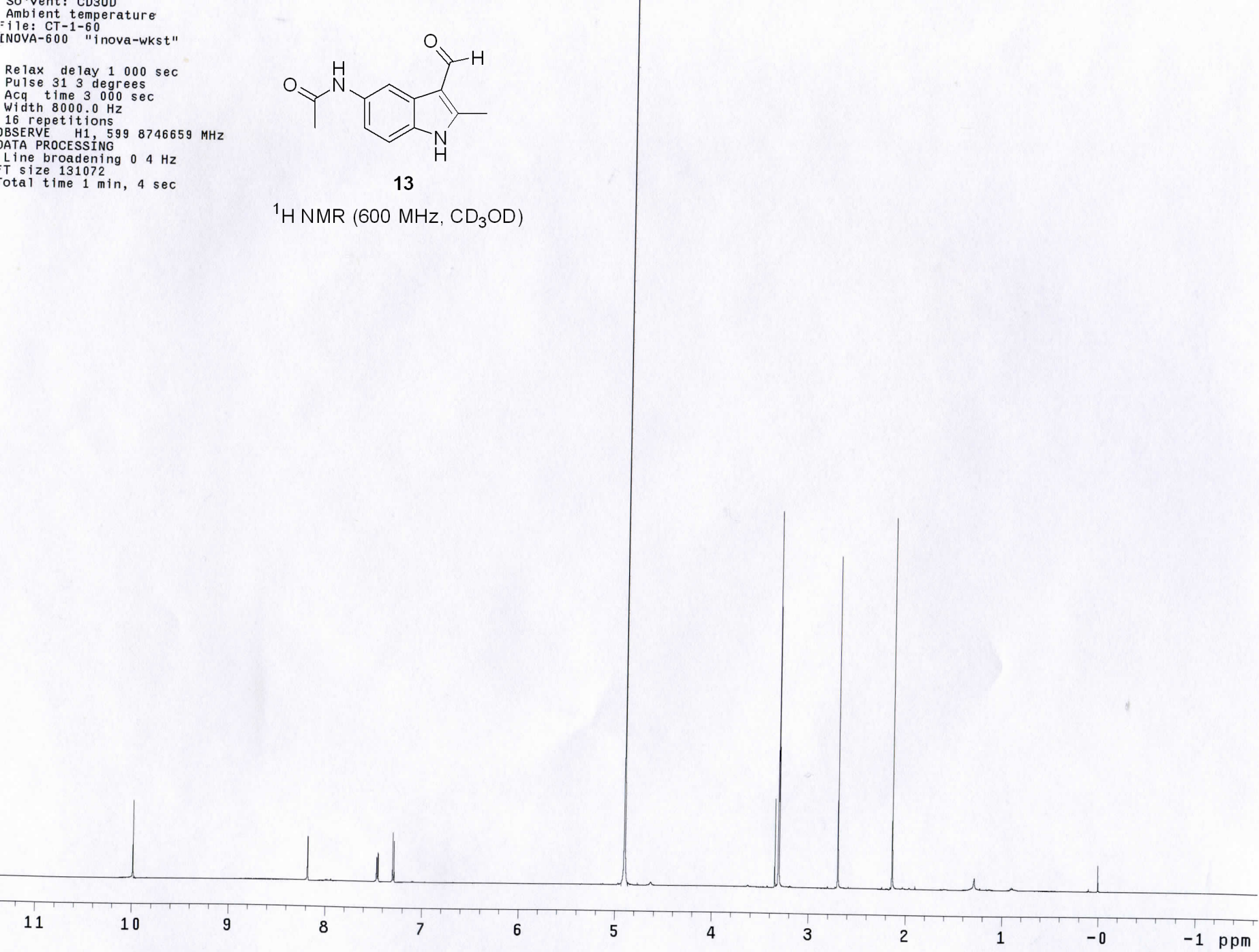
Solvent: CD3OD  
Ambient temperature  
File: CT-1-60  
INOVA-600 "inova-wkst"

Relax delay 1 000 sec  
Pulse 31 3 degrees  
Acq time 3 000 sec  
Width 8000.0 Hz  
16 repetitions  
OBSERVE H1, 599 8746659 MHz  
DATA PROCESSING  
Line broadening 0 4 Hz  
T size 131072  
Total time 1 min, 4 sec



13

<sup>1</sup>H NMR (600 MHz, CD<sub>3</sub>OD)



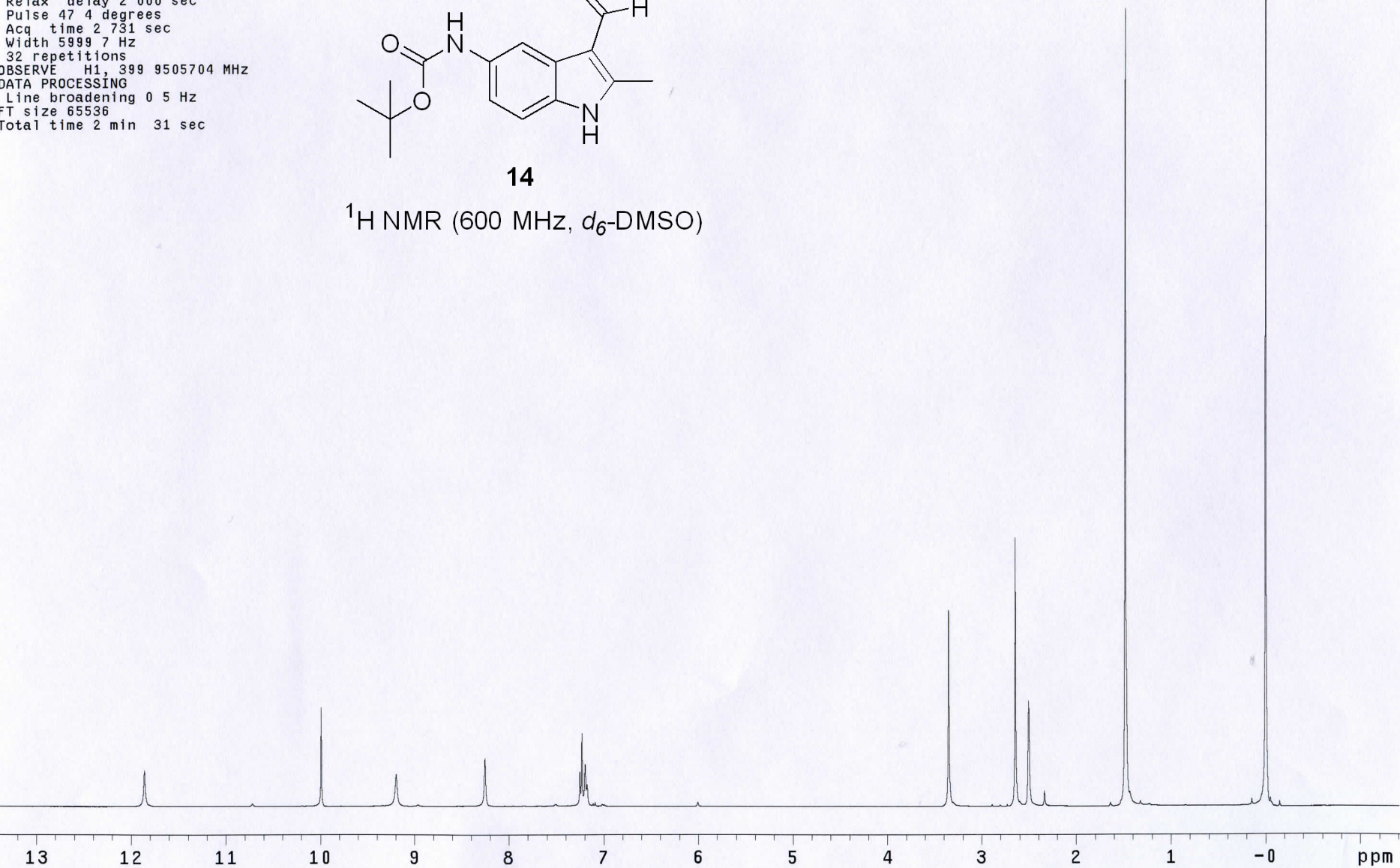
Solvent: DMSO  
Ambient temperature  
File: CT-1-58  
INOVA-600 "inova-wkst"

Relax delay 2 000 sec  
Pulse 47 4 degrees  
Acq time 2 731 sec  
Width 5999 7 Hz  
32 repetitions  
OBSERVE H1, 399 9505704 MHz  
DATA PROCESSING  
Line broadening 0 5 Hz  
FT size 65536  
Total time 2 min 31 sec



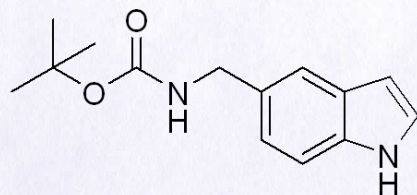
**14**

$^1\text{H}$  NMR (600 MHz,  $d_6$ -DMSO)



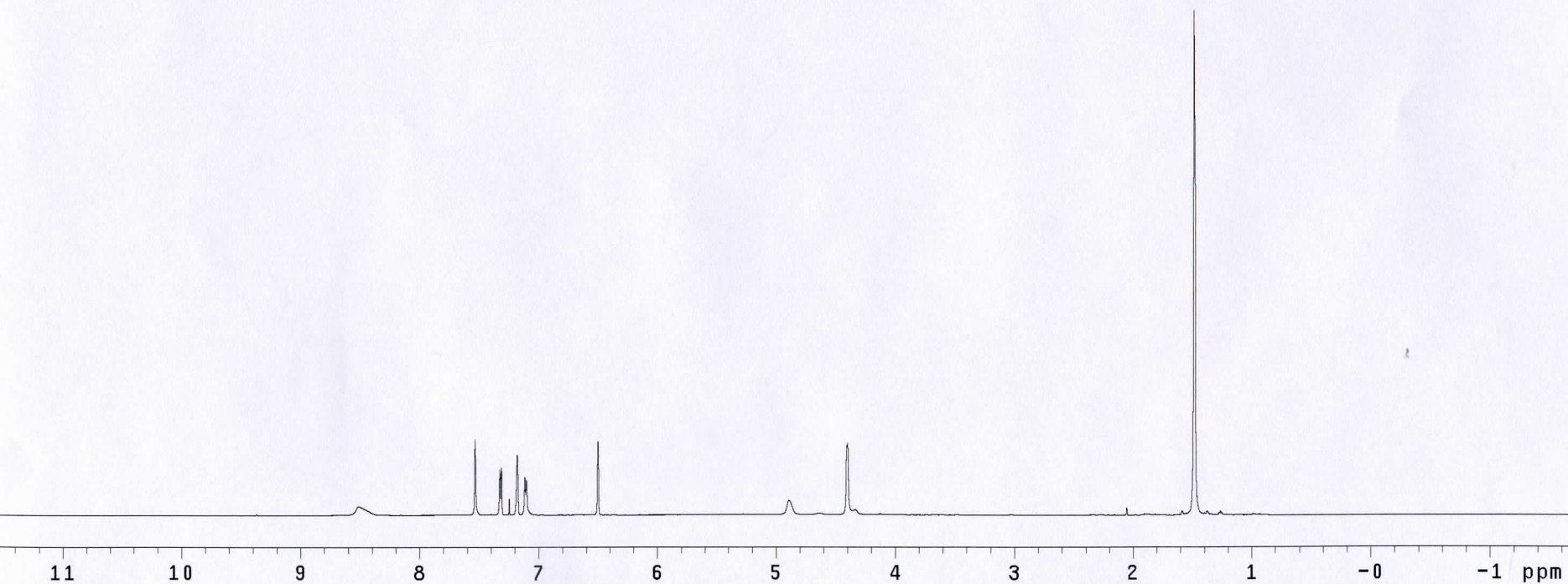
Ambient temperature  
File: CT-1-68  
INOVA-600 "inova-wkst"

Relax delay 1 000 sec  
Pulse 31 3 degrees  
Acq time 3 000 sec  
Width 8000 0 Hz  
16 repetitions  
OBSERVE H1, 599.8723148 MHz  
DATA PROCESSING  
Line broadening 0 4 Hz  
FT size 131072  
Total time 1 min, 4 sec

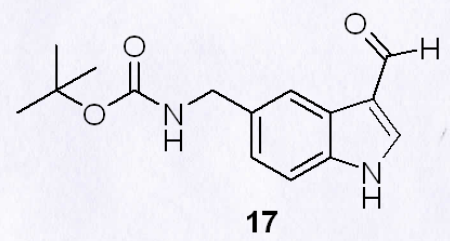


**16**

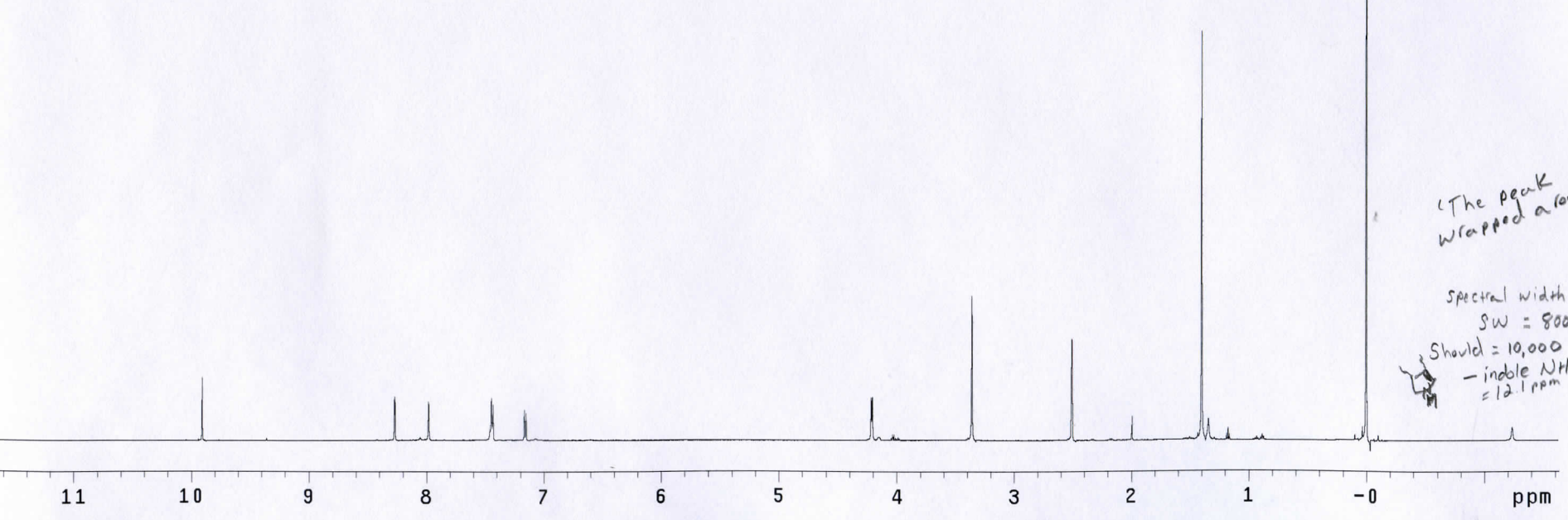
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)



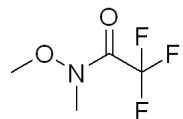
Relax delay 1 000 sec  
Pulse 31 3 degrees  
Acq. time 3 000 sec  
Width 8000.0 Hz  
16 repetitions  
OBSERVE H1, 599.8751435 MHz  
DATA PROCESSING  
Line broadening 0 4 Hz  
FT size 131072  
Total time 1 min, 4 sec



<sup>1</sup>H NMR (600 MHz, d<sub>6</sub>-DMSO)

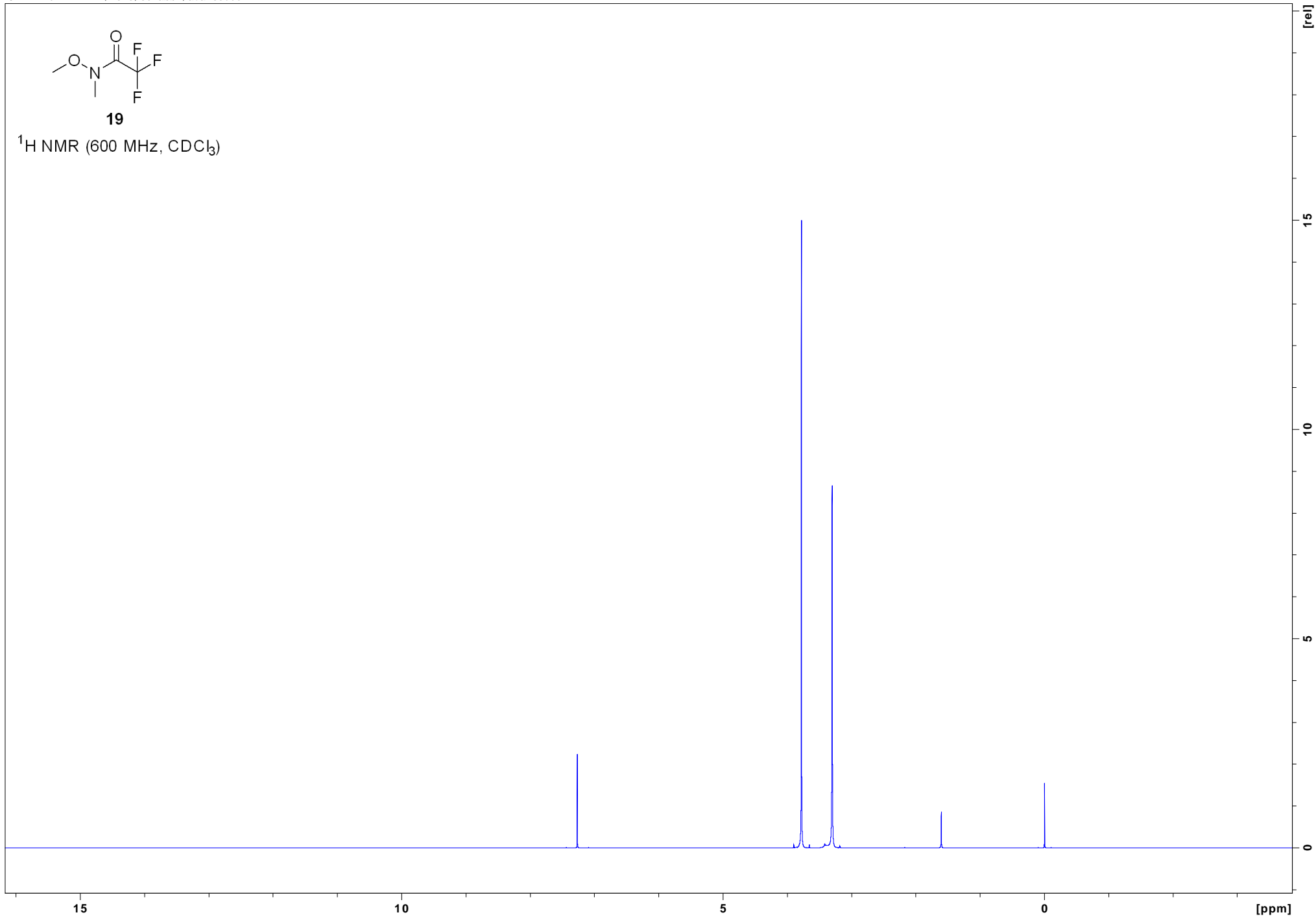


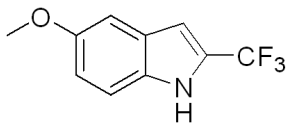




**19**

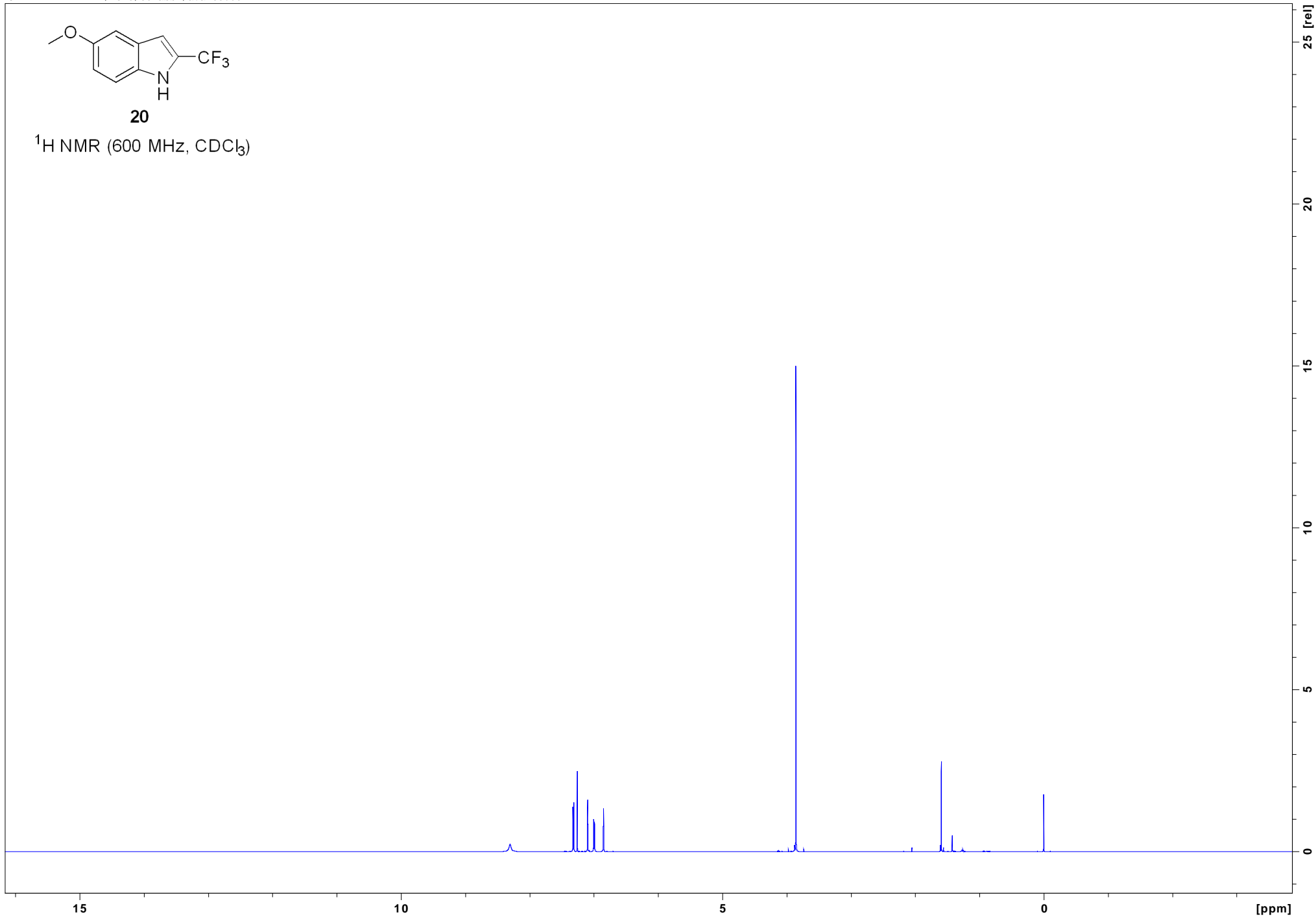
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

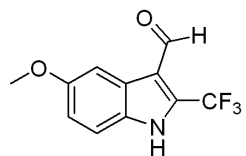




**20**

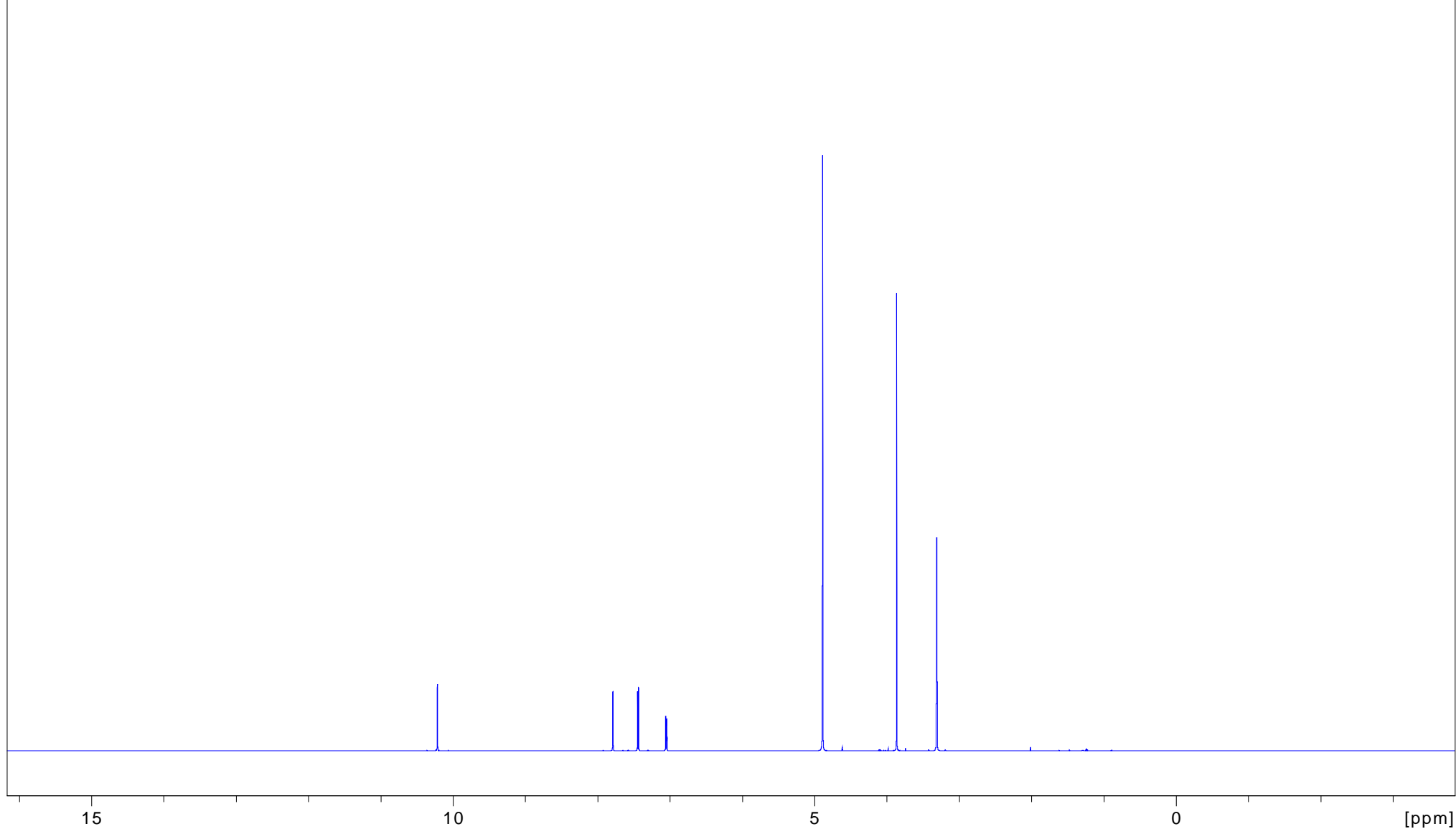
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)





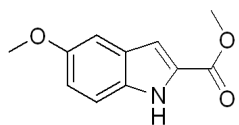
21

<sup>1</sup>H NMR (600 MHz, *d*<sub>4</sub>-MeOH)



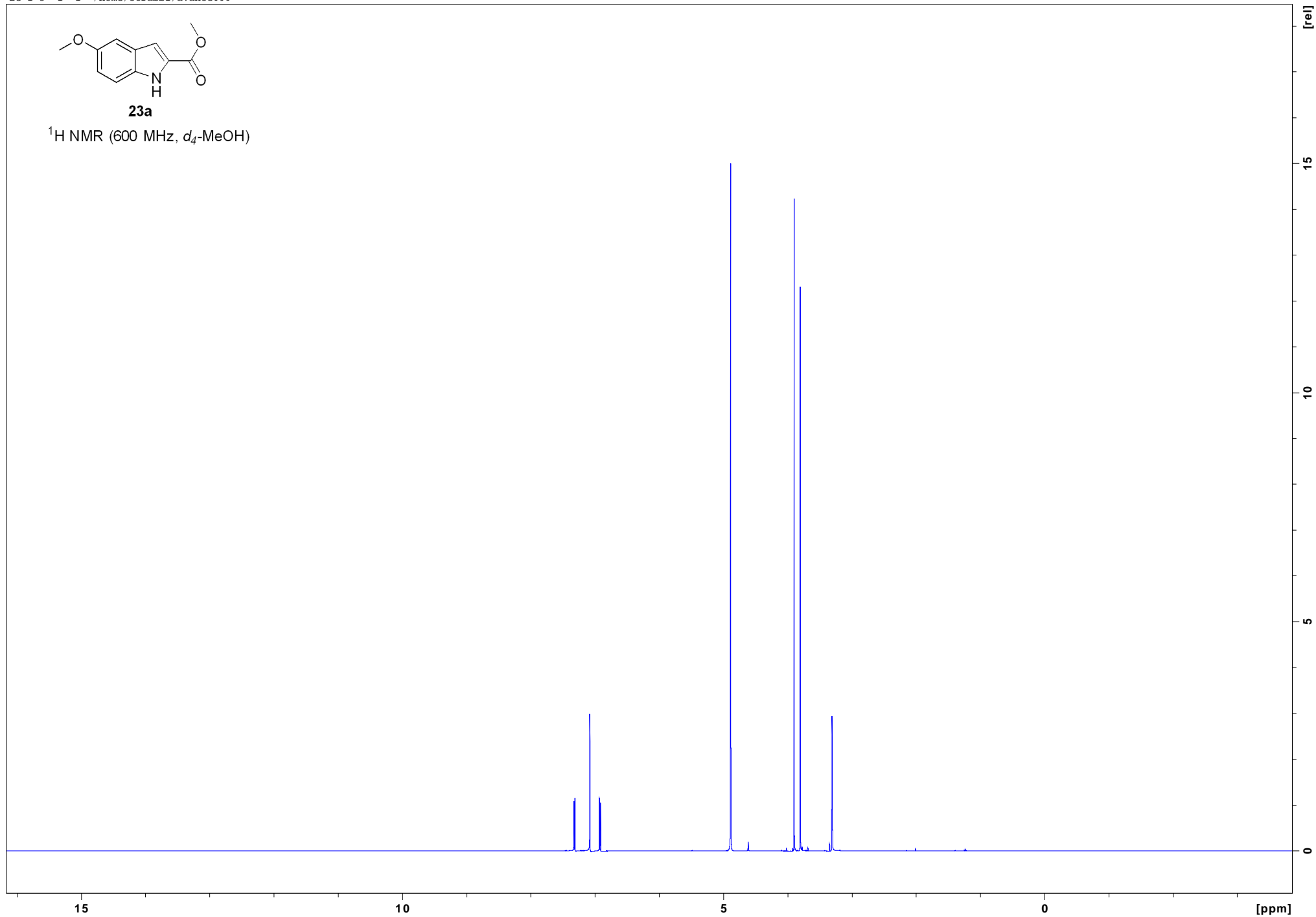
S51

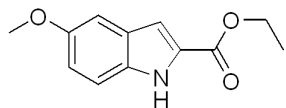
[ppm]



**23a**

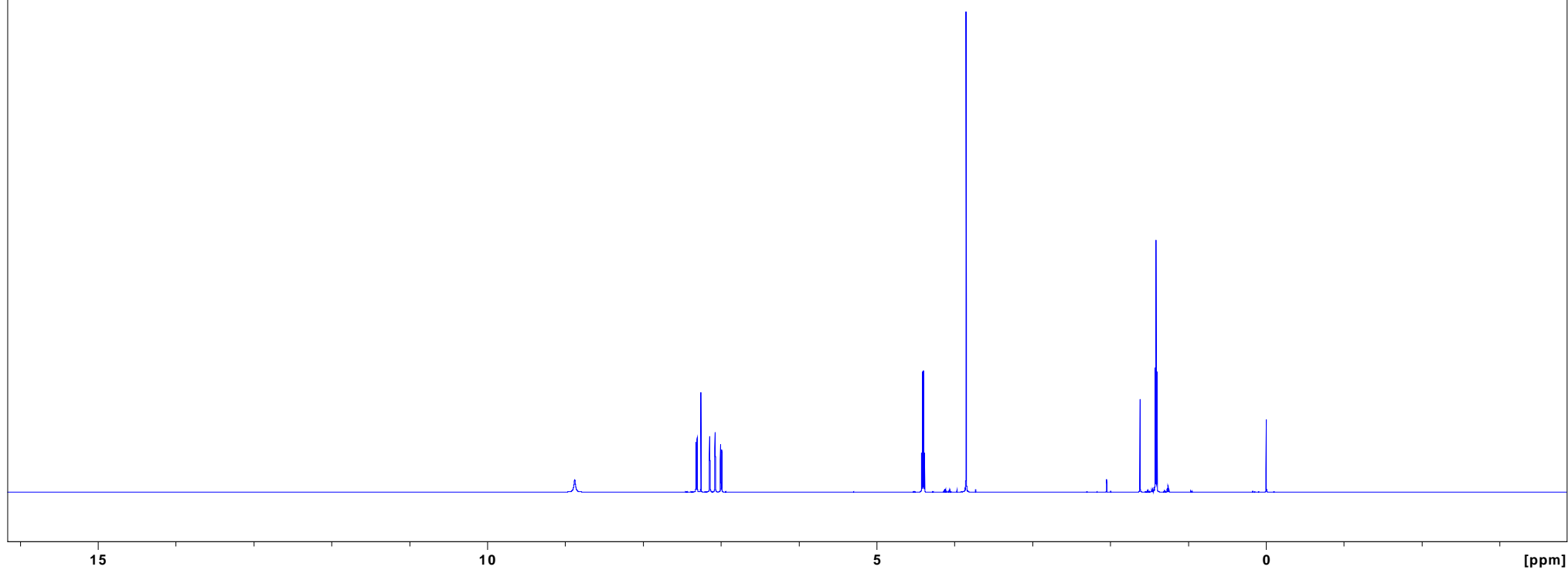
$^1\text{H NMR}$  (600 MHz,  $d_4$ -MeOH)

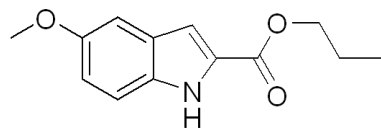




**23b**

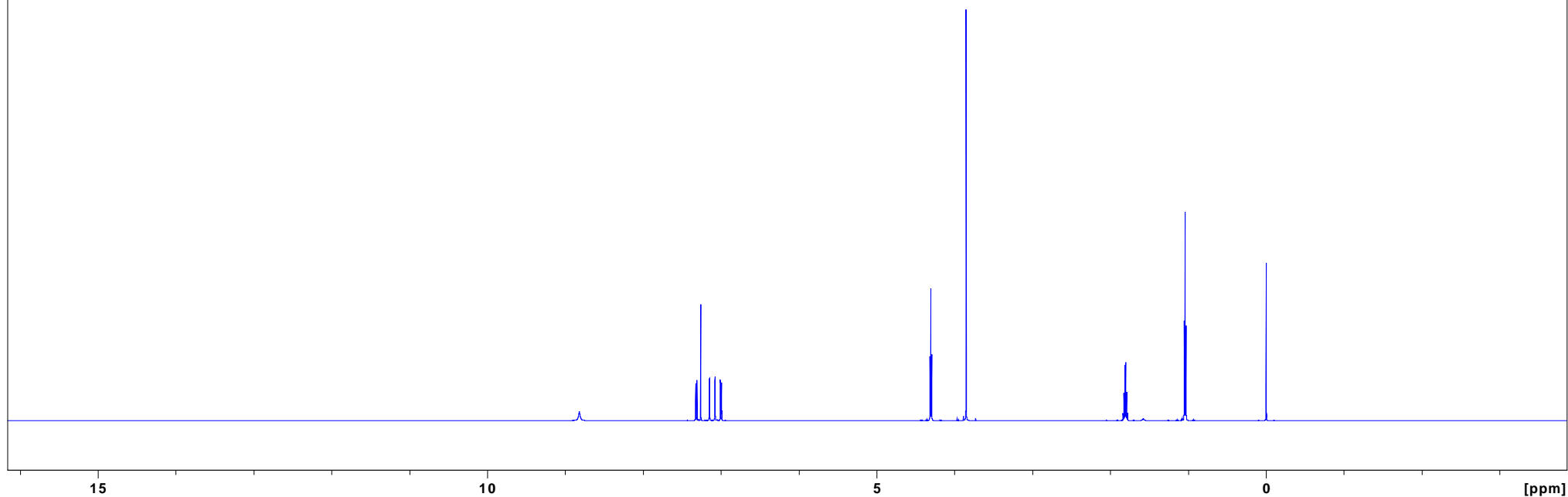
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

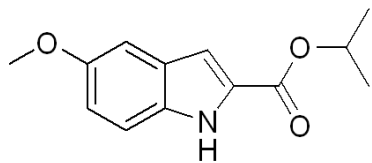




**23c**

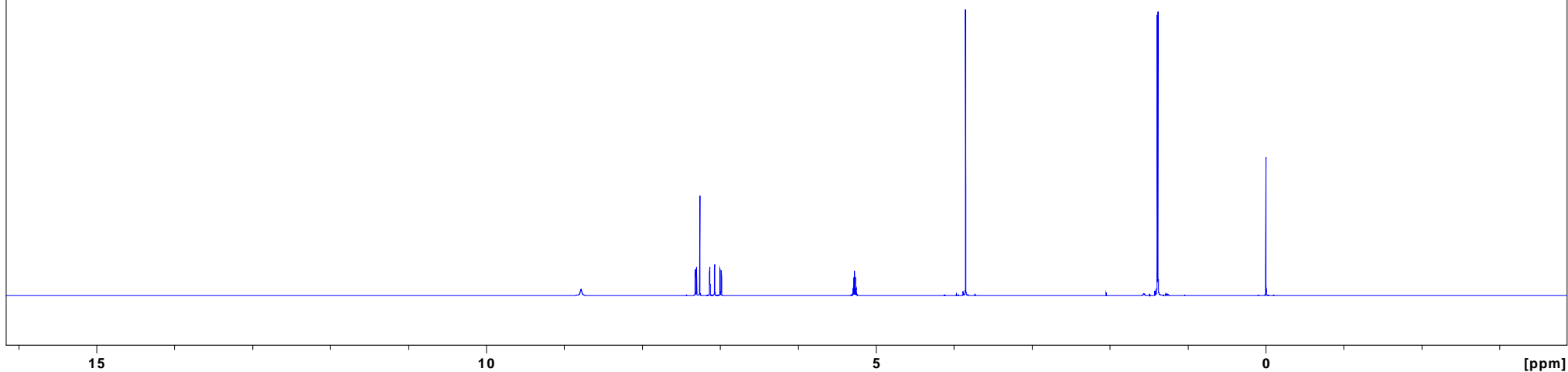
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

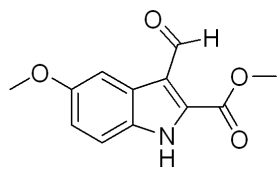




**23d**

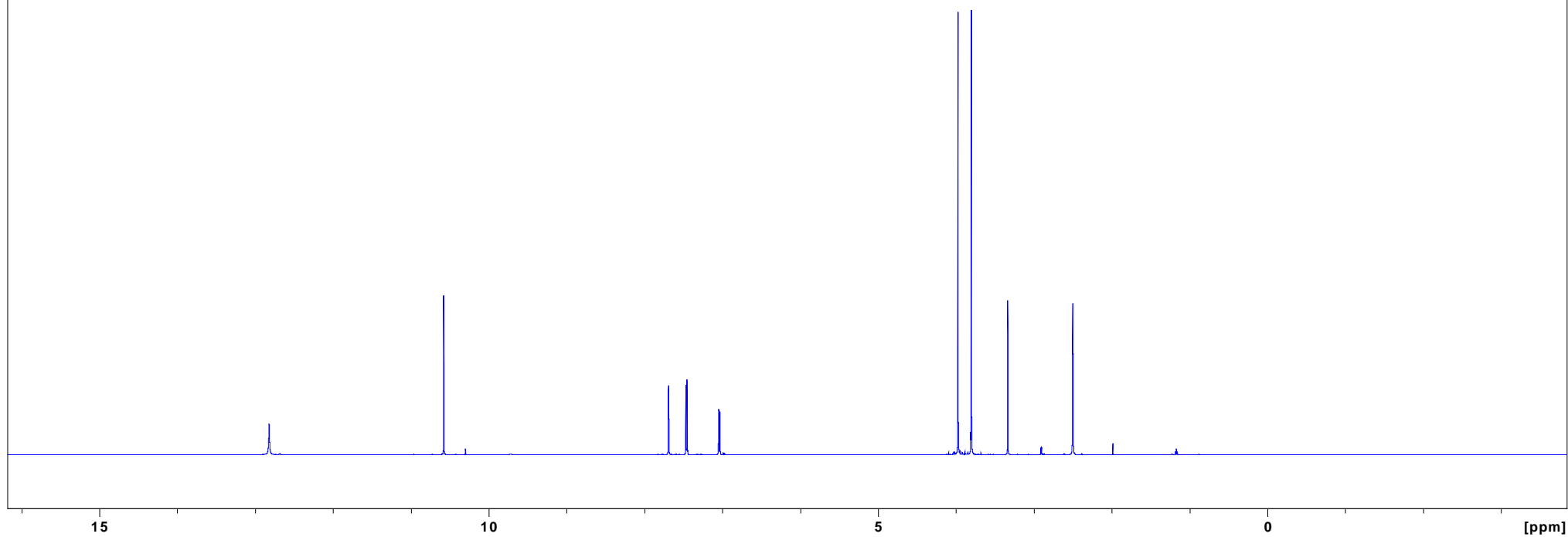
$^1\text{H NMR}$  (600 MHz,  $\text{CDCl}_3$ )



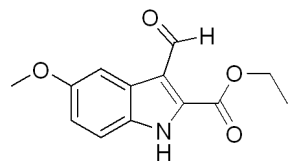


**24a**

$^1\text{H NMR}$  (600 MHz,  $d_6$ -DMSO)

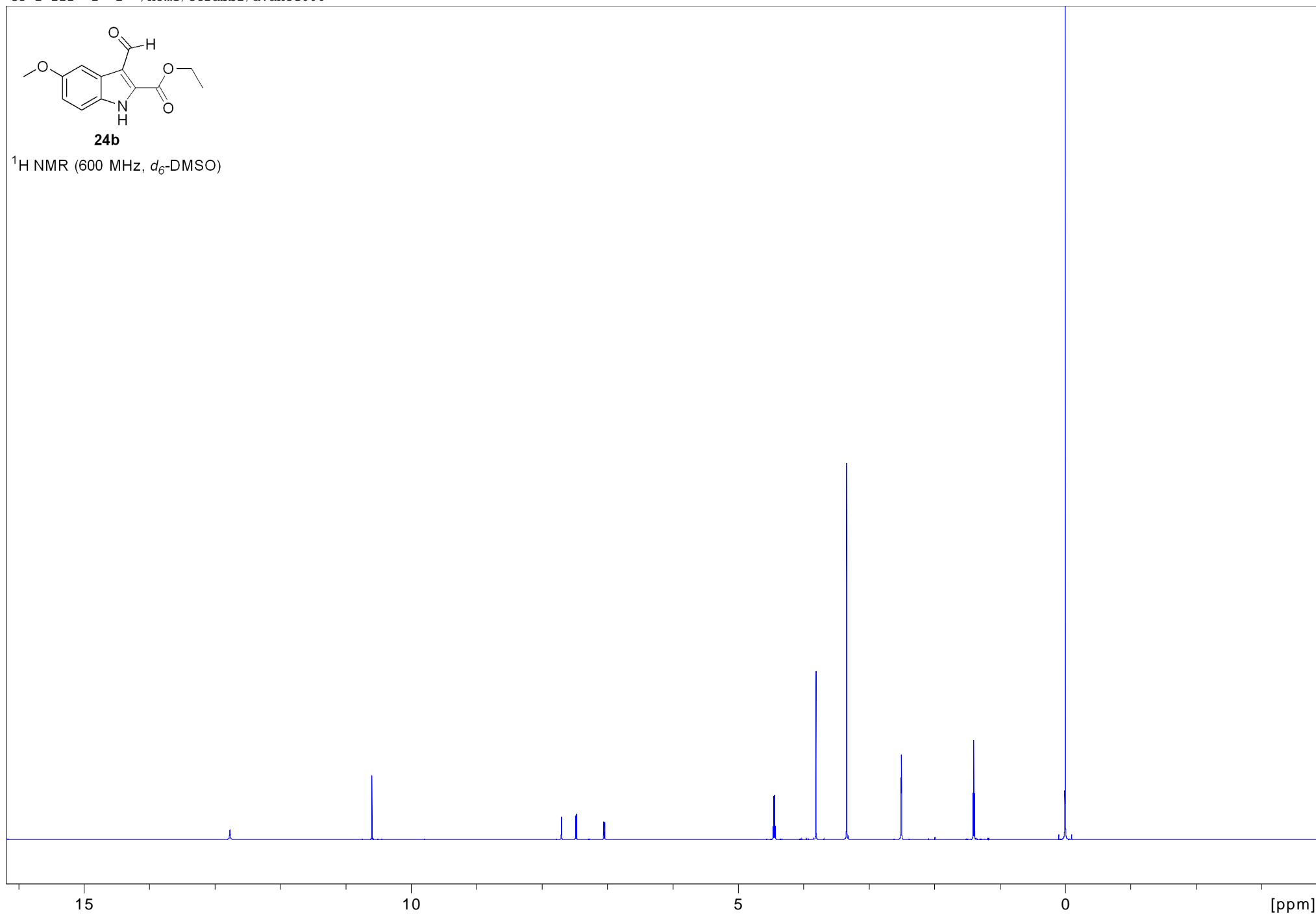


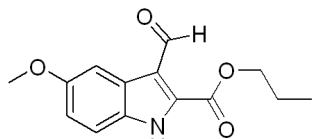




**24b**

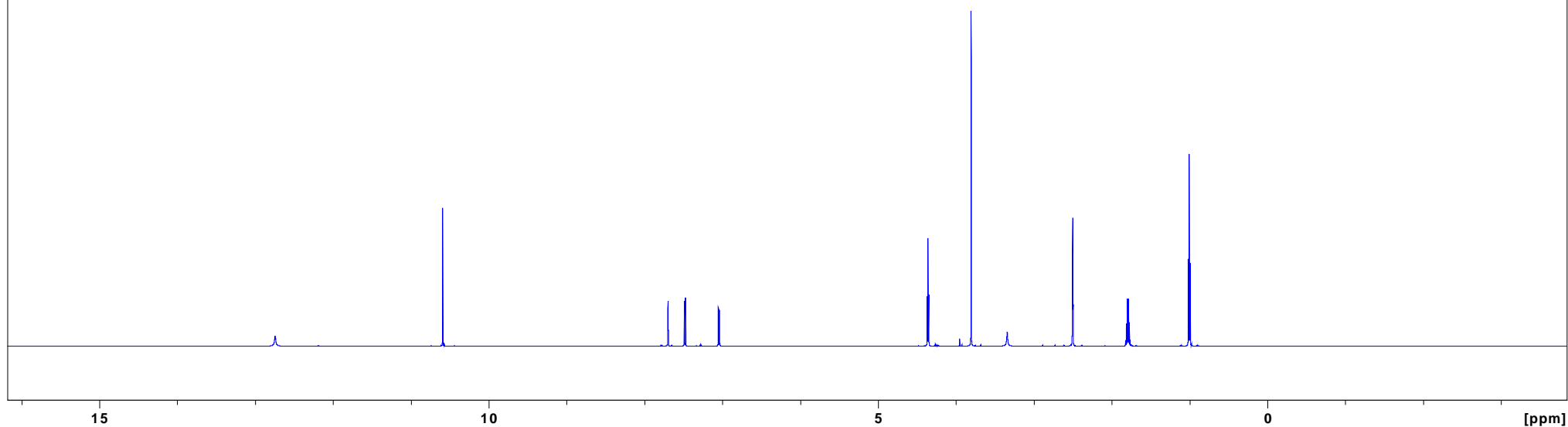
<sup>1</sup>H NMR (600 MHz, d<sub>6</sub>-DMSO)

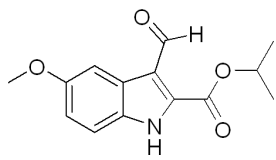




**24c**

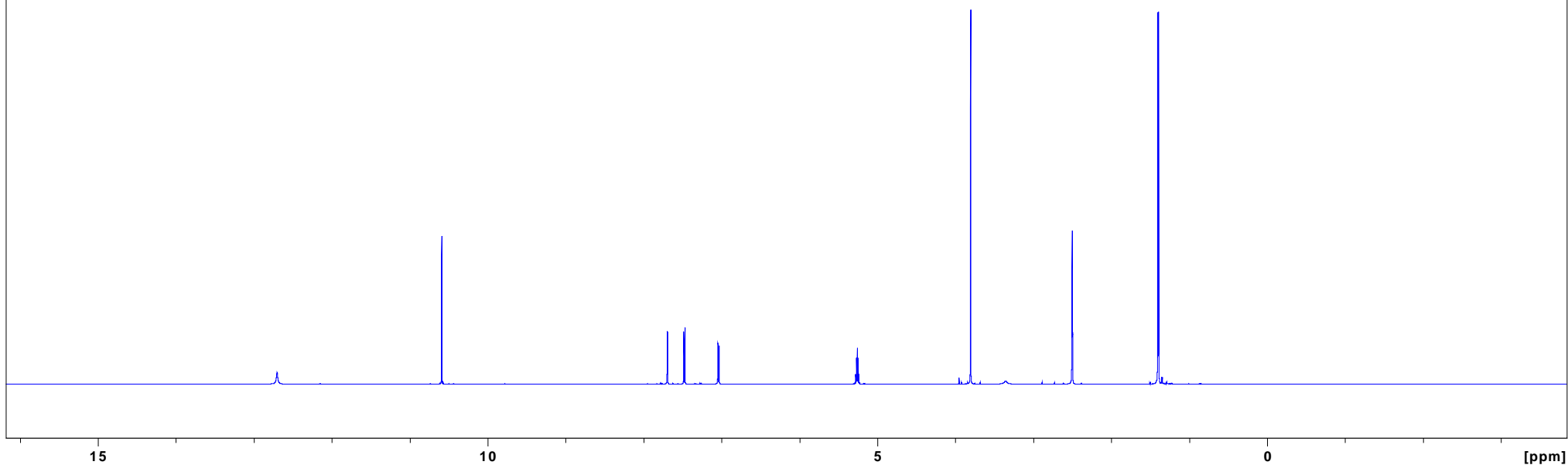
<sup>1</sup>H NMR (600 MHz, *d*<sub>6</sub>-DMSO)

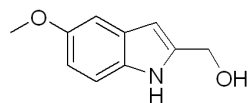




**24d**

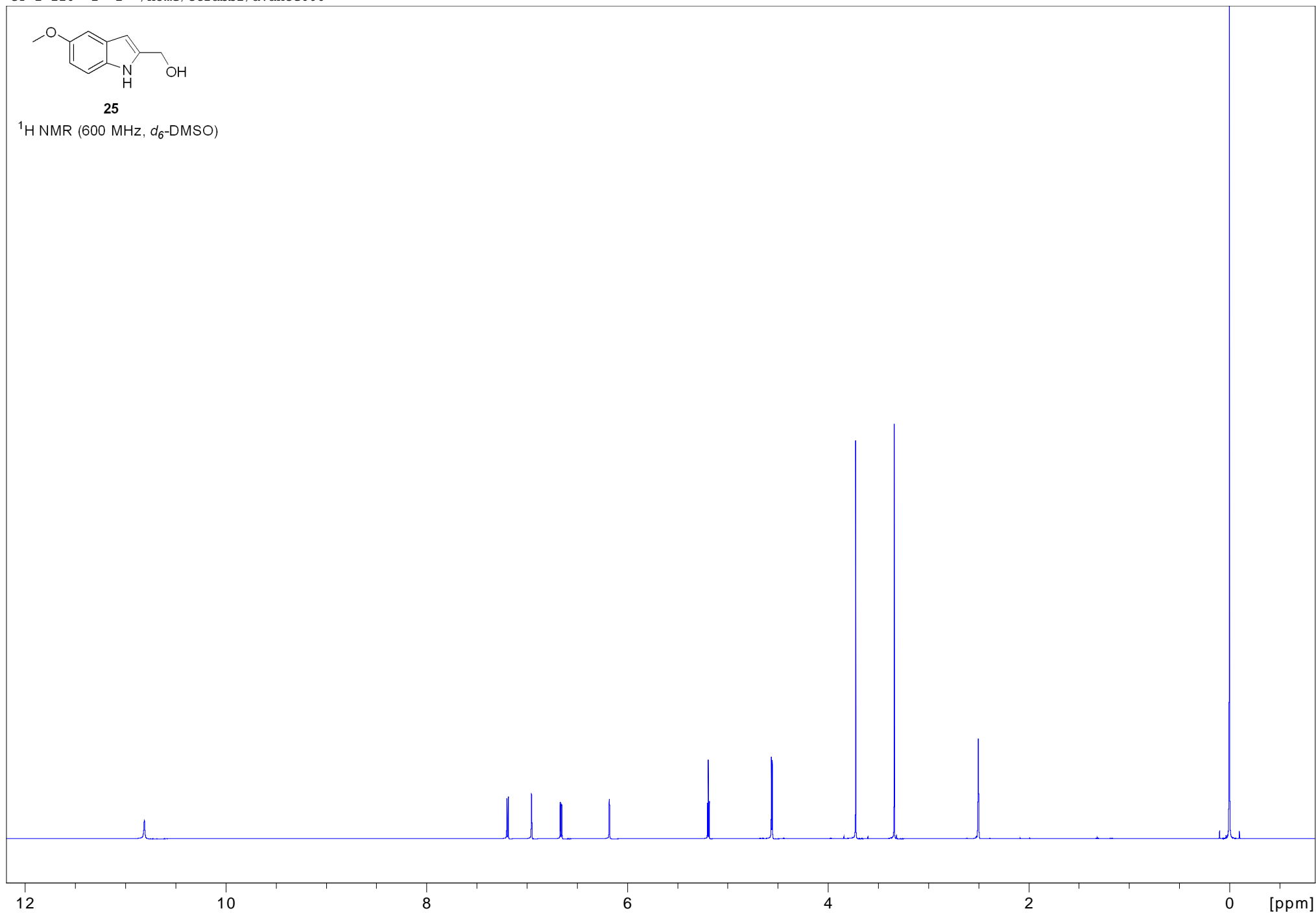
$^1\text{H}$  NMR (600 MHz,  $d_6$ -DMSO)

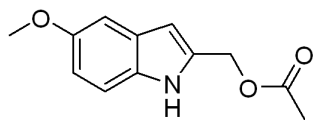




**25**

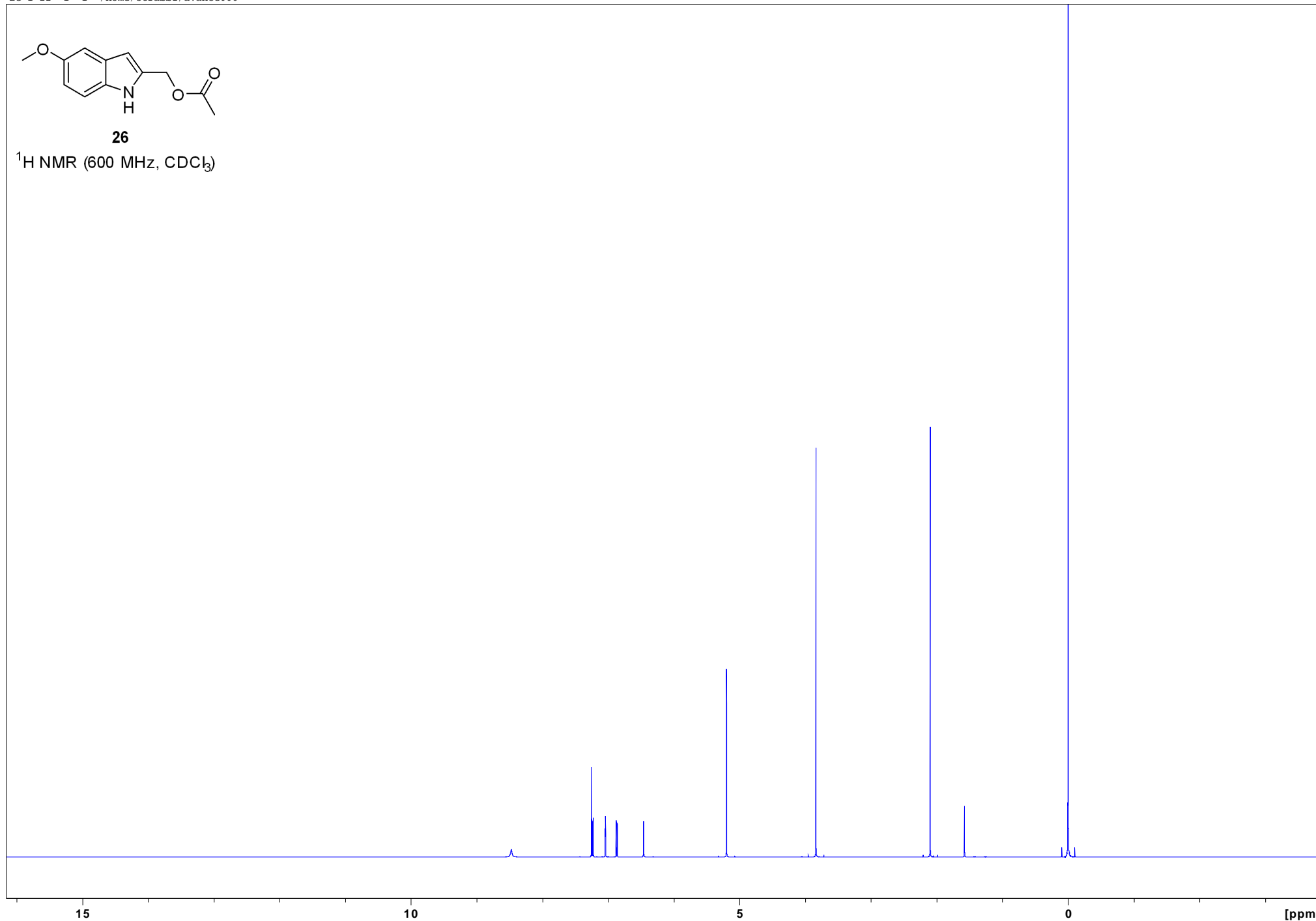
<sup>1</sup>H NMR (600 MHz, d<sub>6</sub>-DMSO)

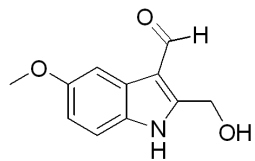




**26**

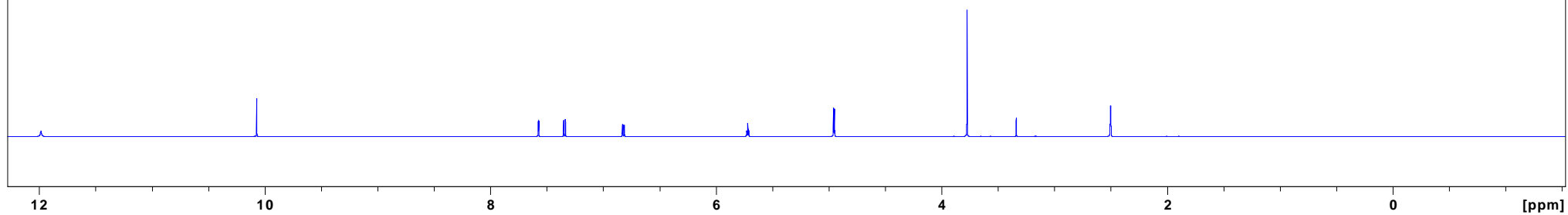
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

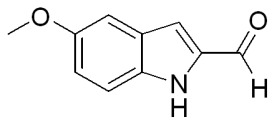




**27**

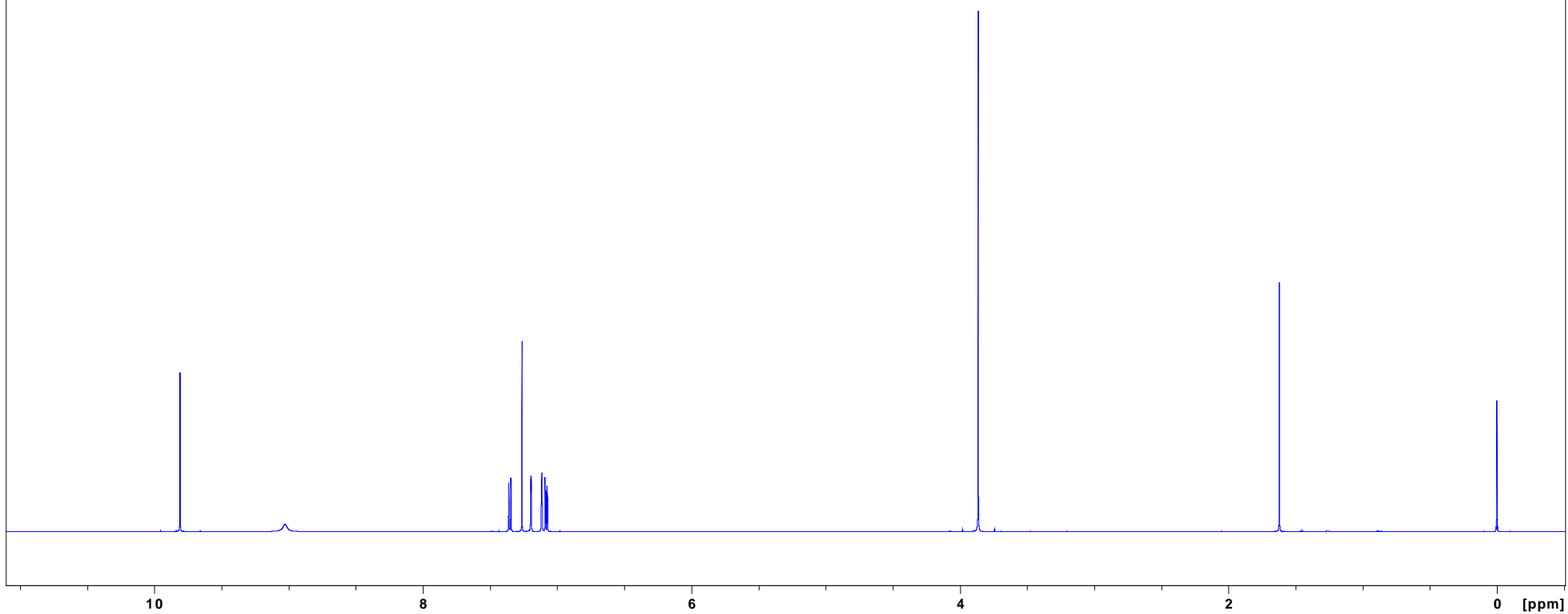
<sup>1</sup>H NMR (600 MHz, d<sub>6</sub>-DMSO)

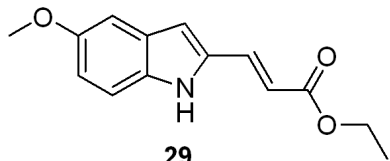




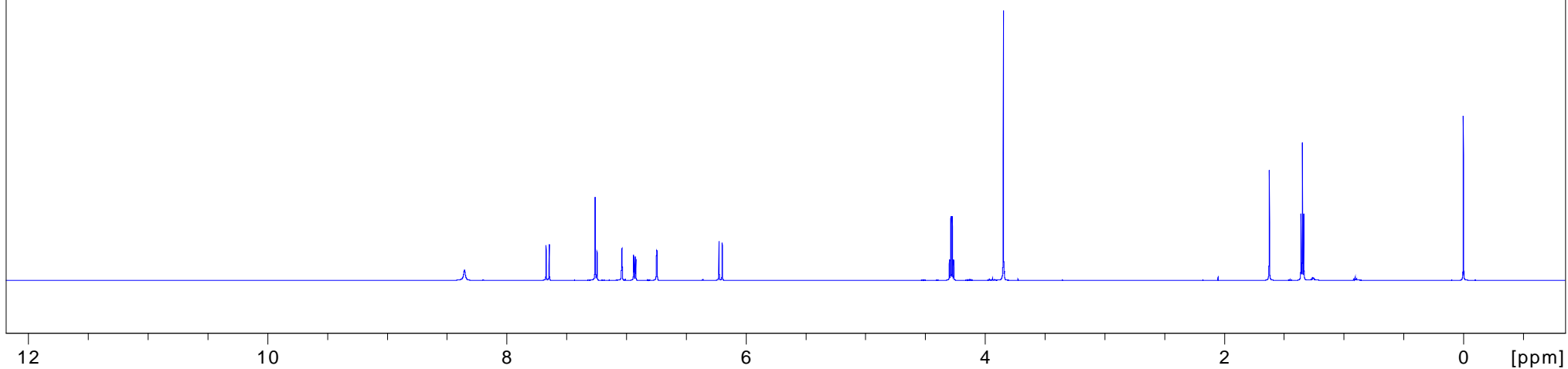
**28**

<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)

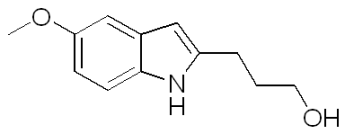




$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )

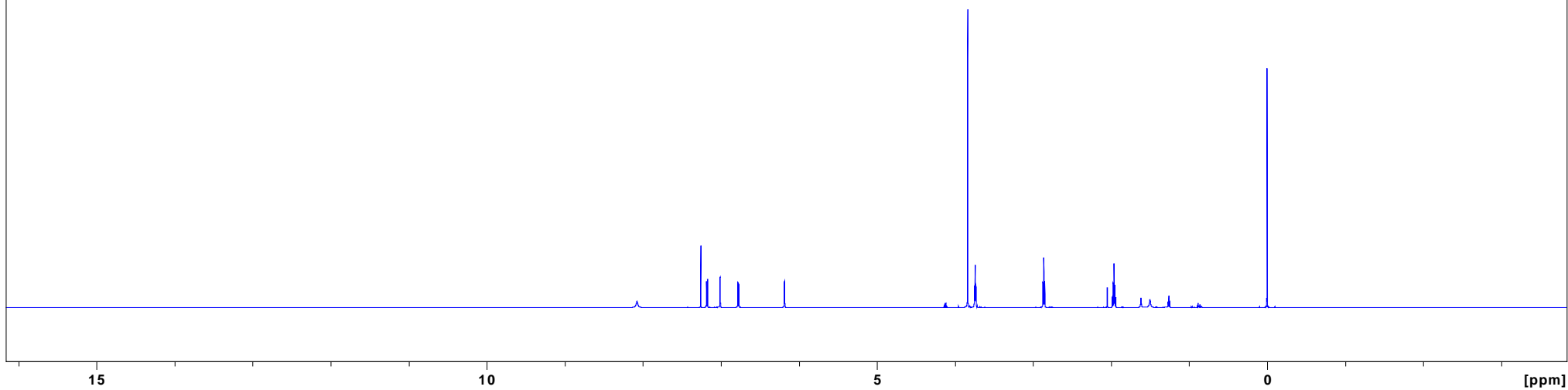


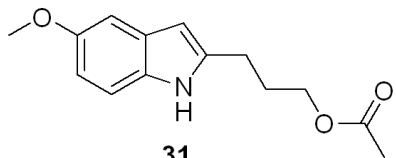




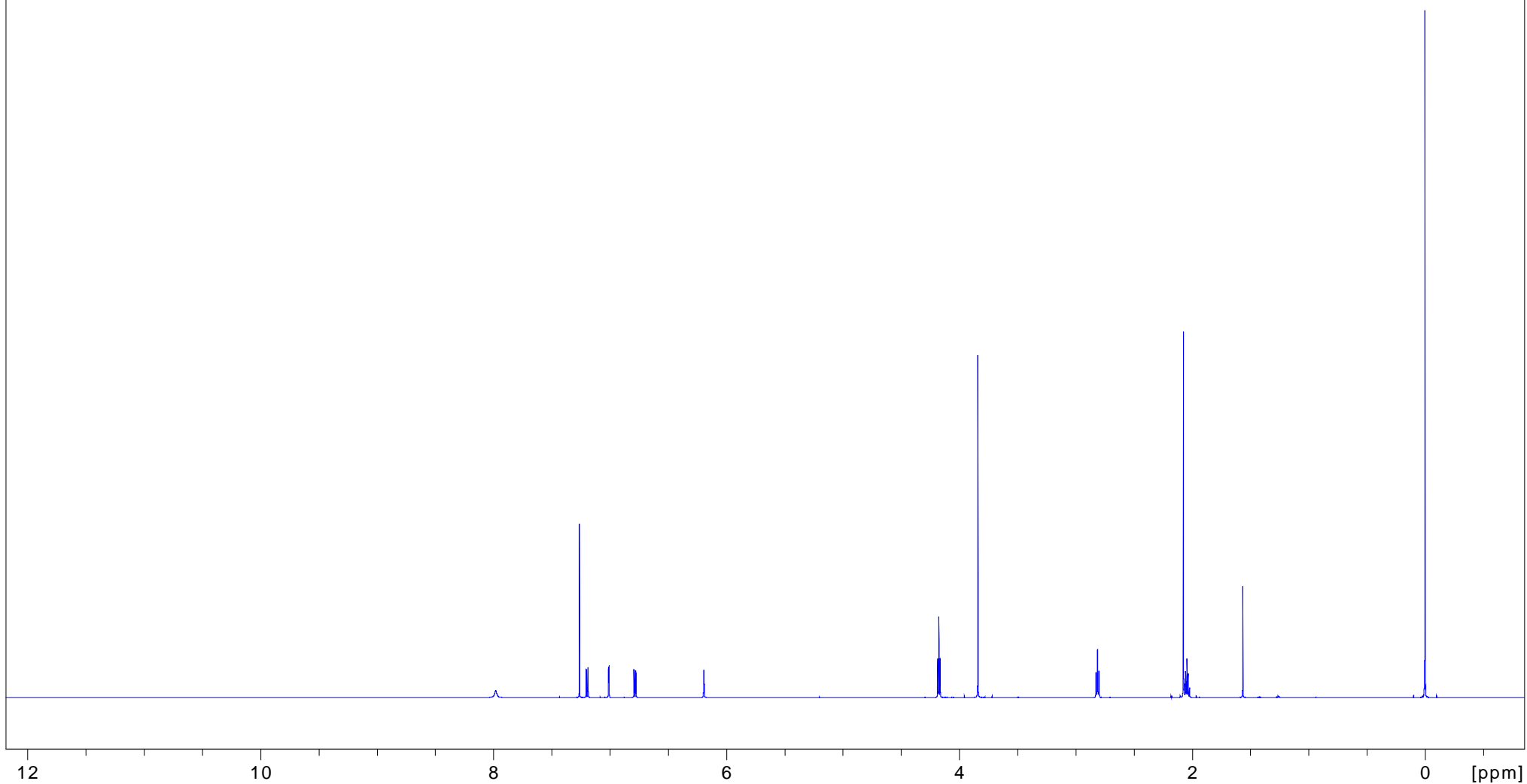
**30**

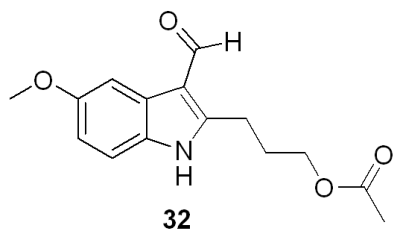
<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)





<sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)





<sup>1</sup>H NMR (600 MHz, d<sub>6</sub>-DMSO)

