

# Supplementary Information

## **Marine Inspired 2-(5-Halo-1*H*-indol-3-yl)-*N,N*-Dimethylethanamines As Modulators of Serotonin Receptors: An Example Illustrating the Power of Bromine as part of the Uniquely Marine Chemical Space.**

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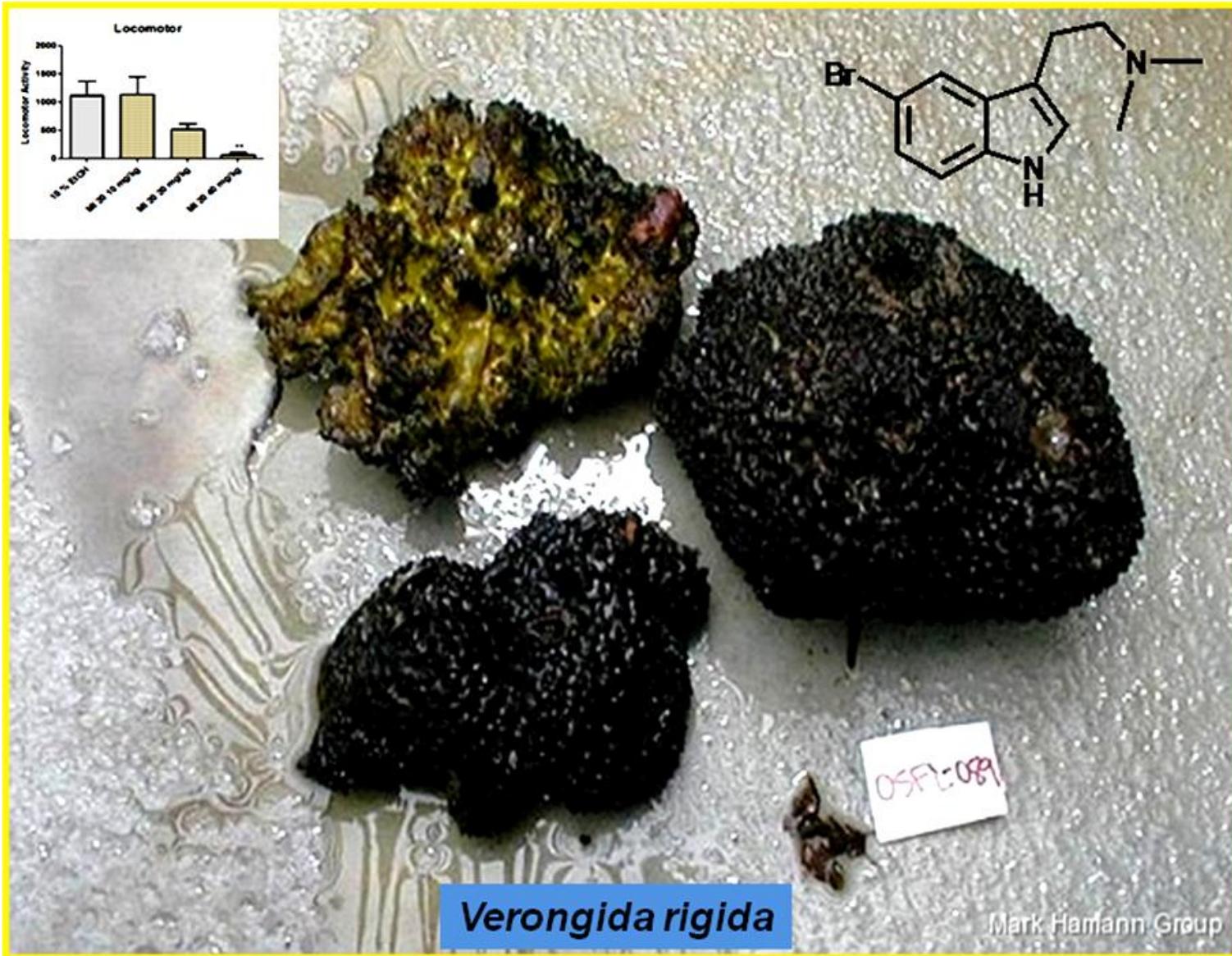
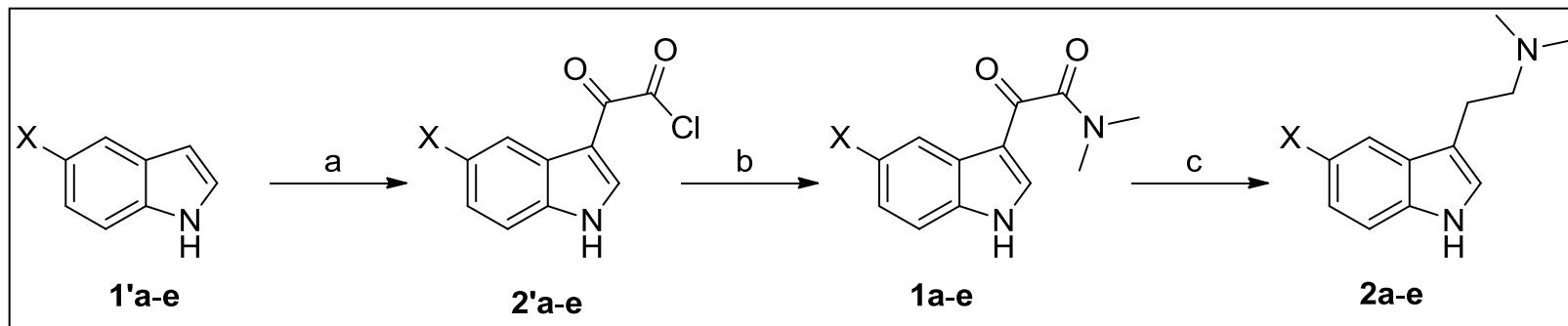
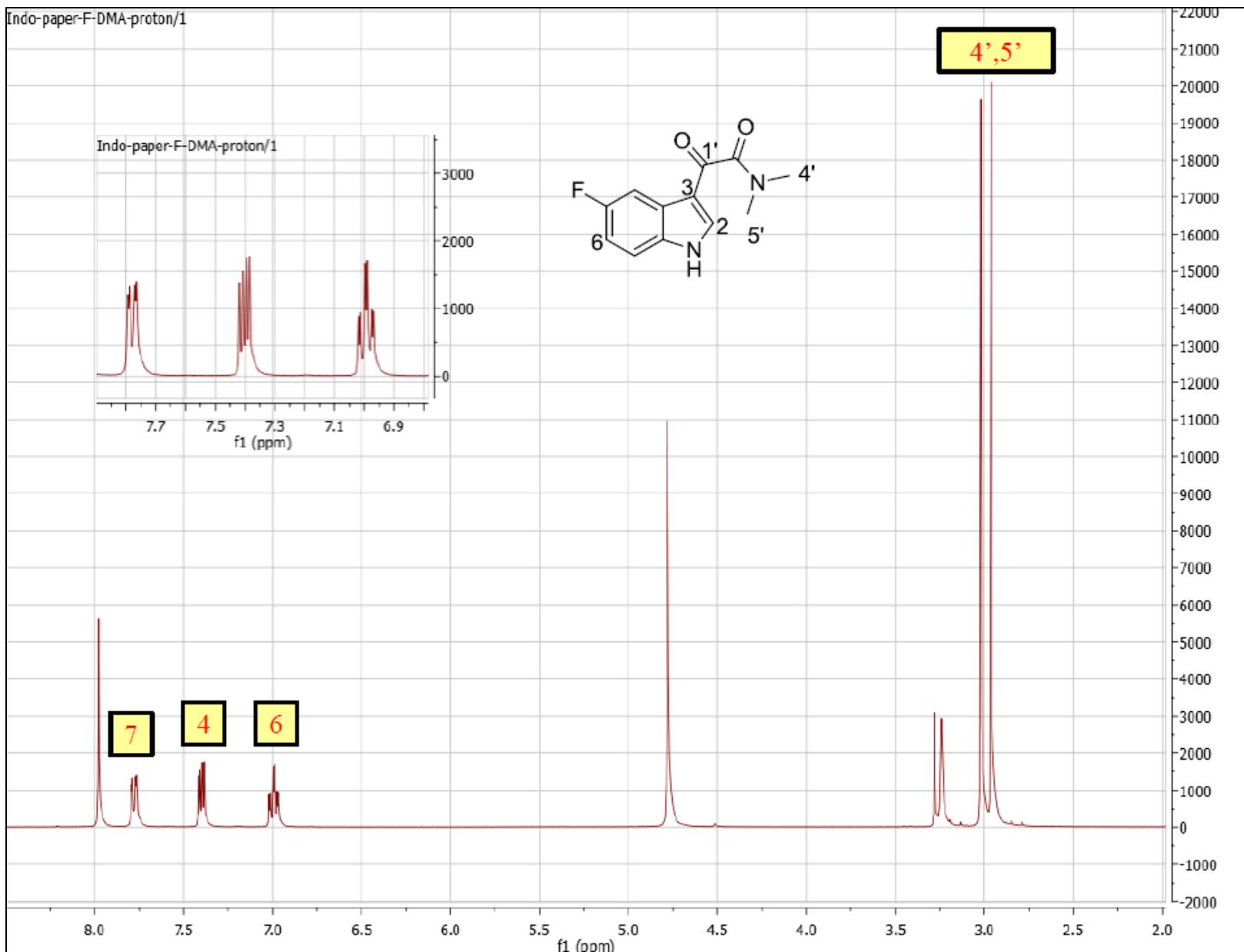


Figure 1. Picture of the sponge *Verongida rigida*



**Figure 2.** The synthesis of 5-haloindoledimethylethanamines. Reagents and reaction conditions: (a) Oxalyl chloride, diethyl ether, 0 °C, 30-60 min, (80-90%); (b) Dimethylamine, 0 °C, 30 min, then rt, 2 h, (80-90%); (c) LiAlH<sub>4</sub>, DME, 0 °C, 1 h, then rt, 2 h, then 80 °C, 2 h, (65-75%)

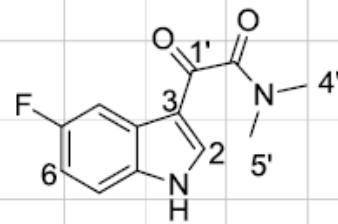


**Figure 3.** <sup>1</sup>H NMR spectrum of 2-(5-fluoro-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1b**) in methanol-*d*<sub>4</sub> (400 MHz)

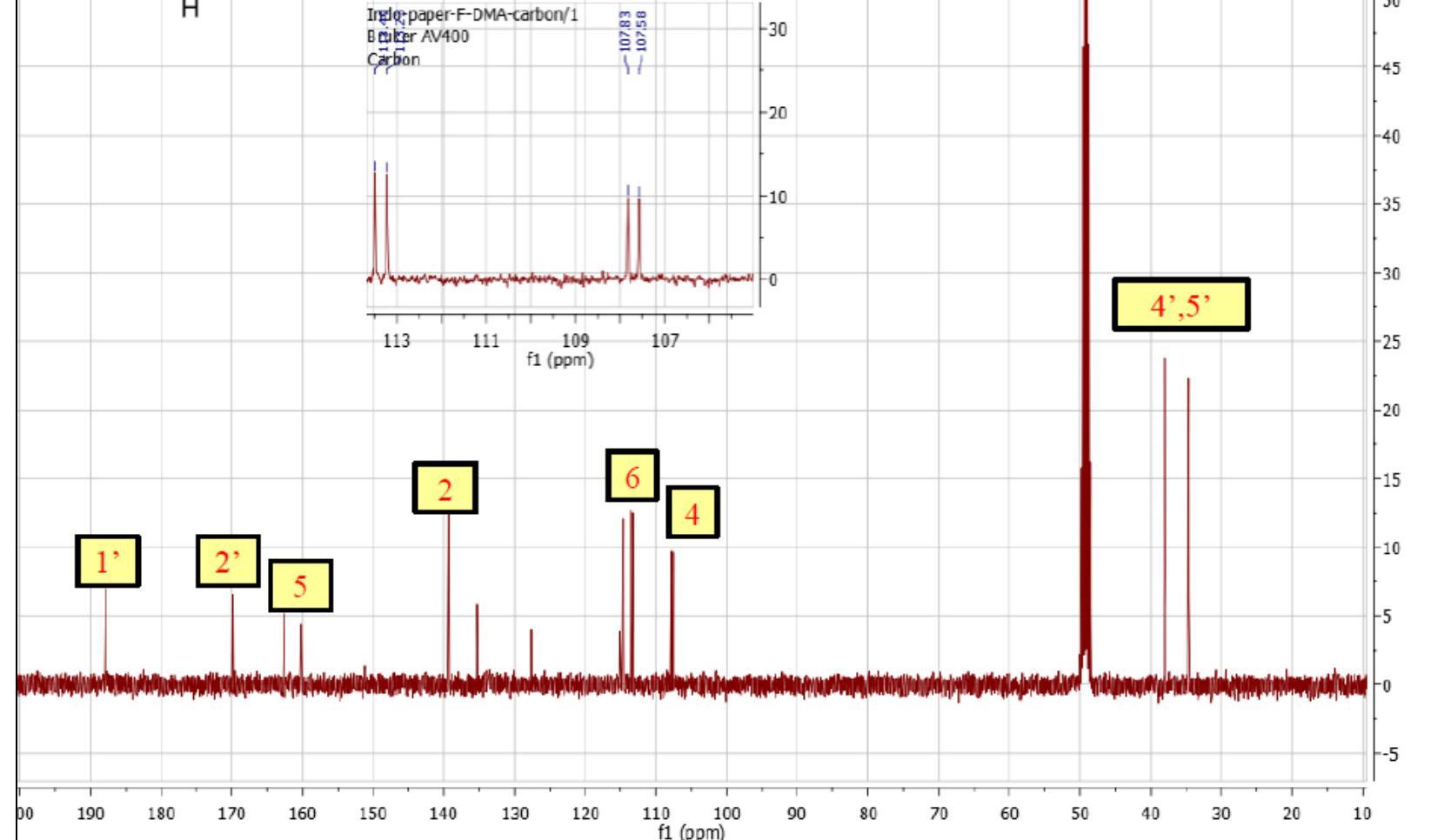
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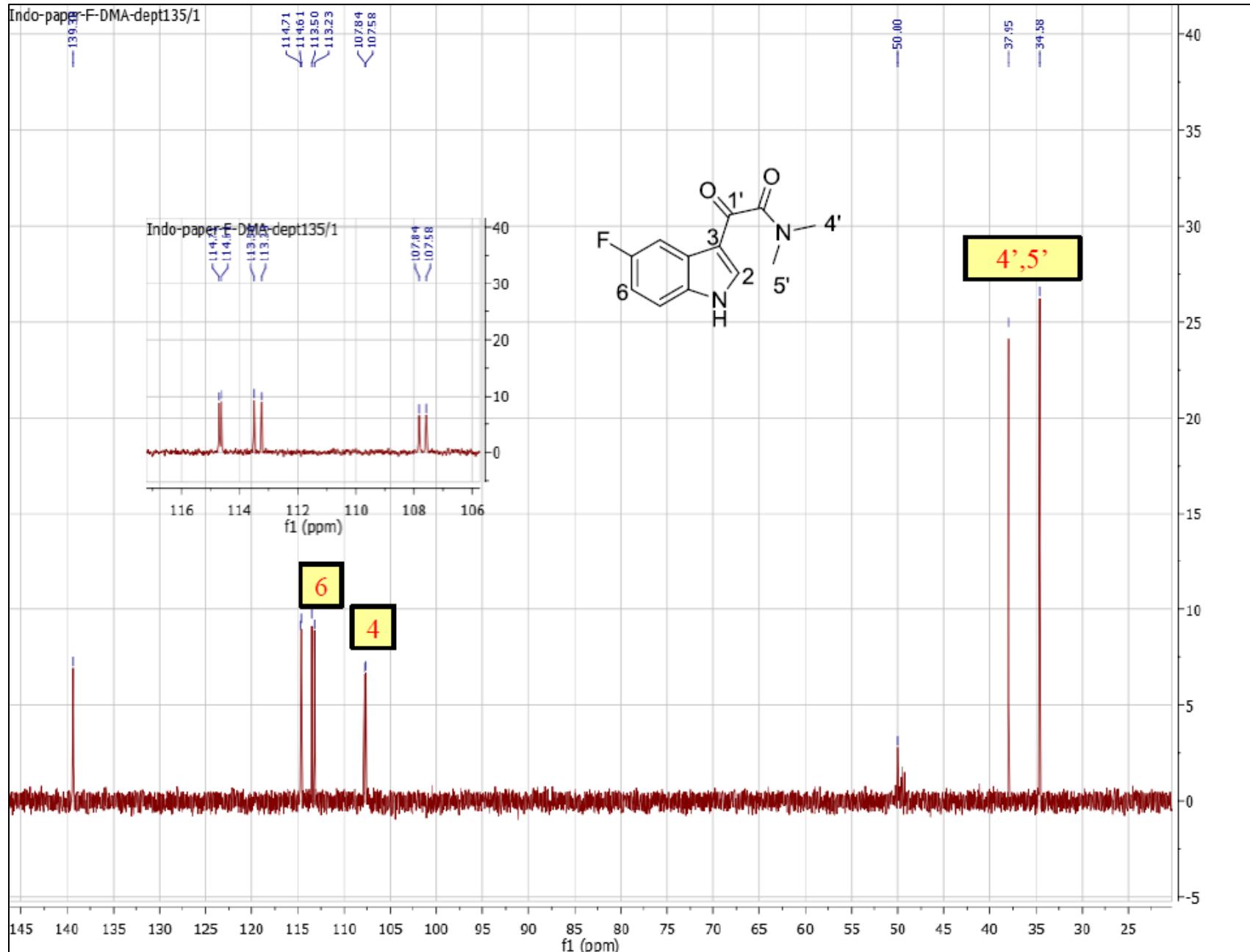
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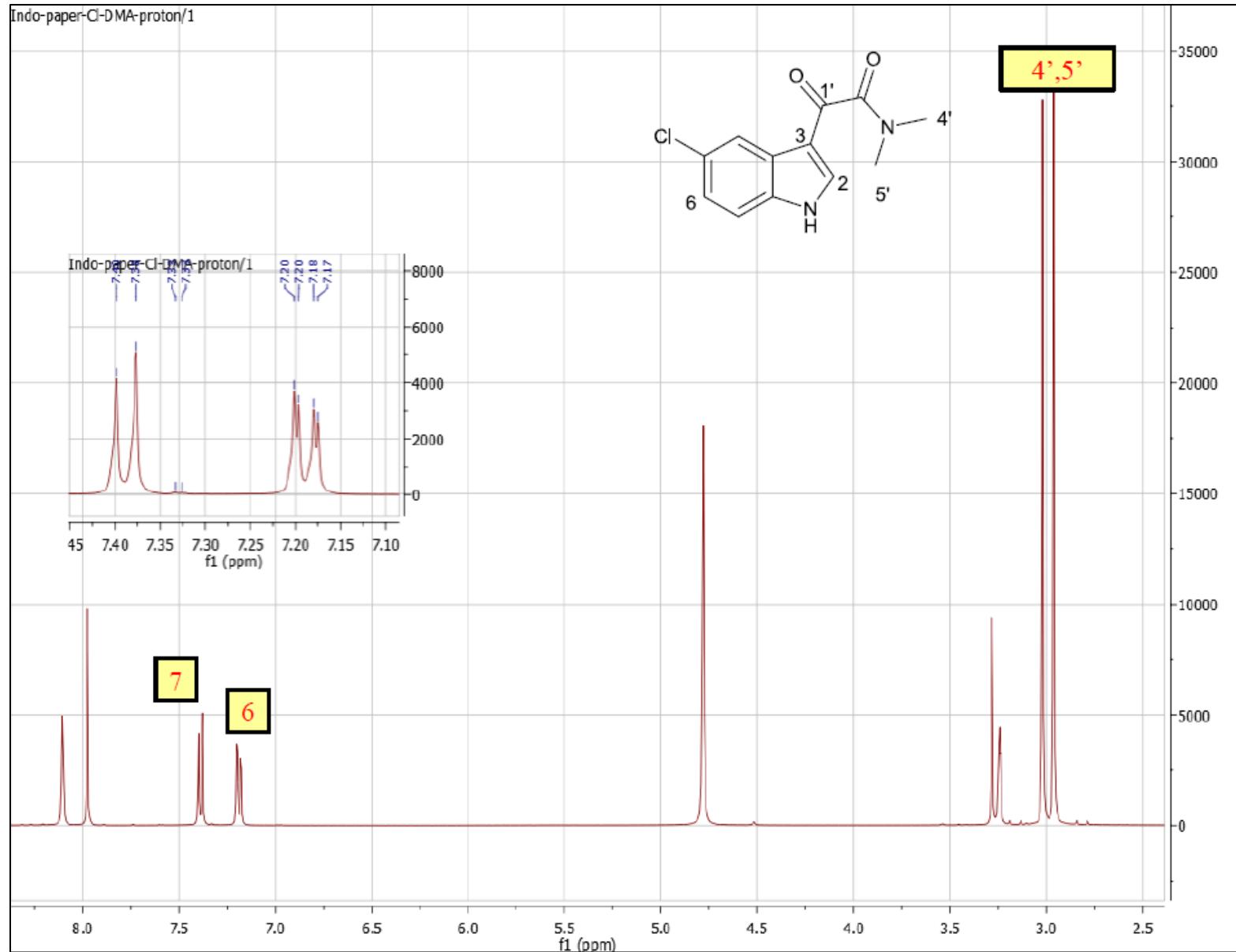
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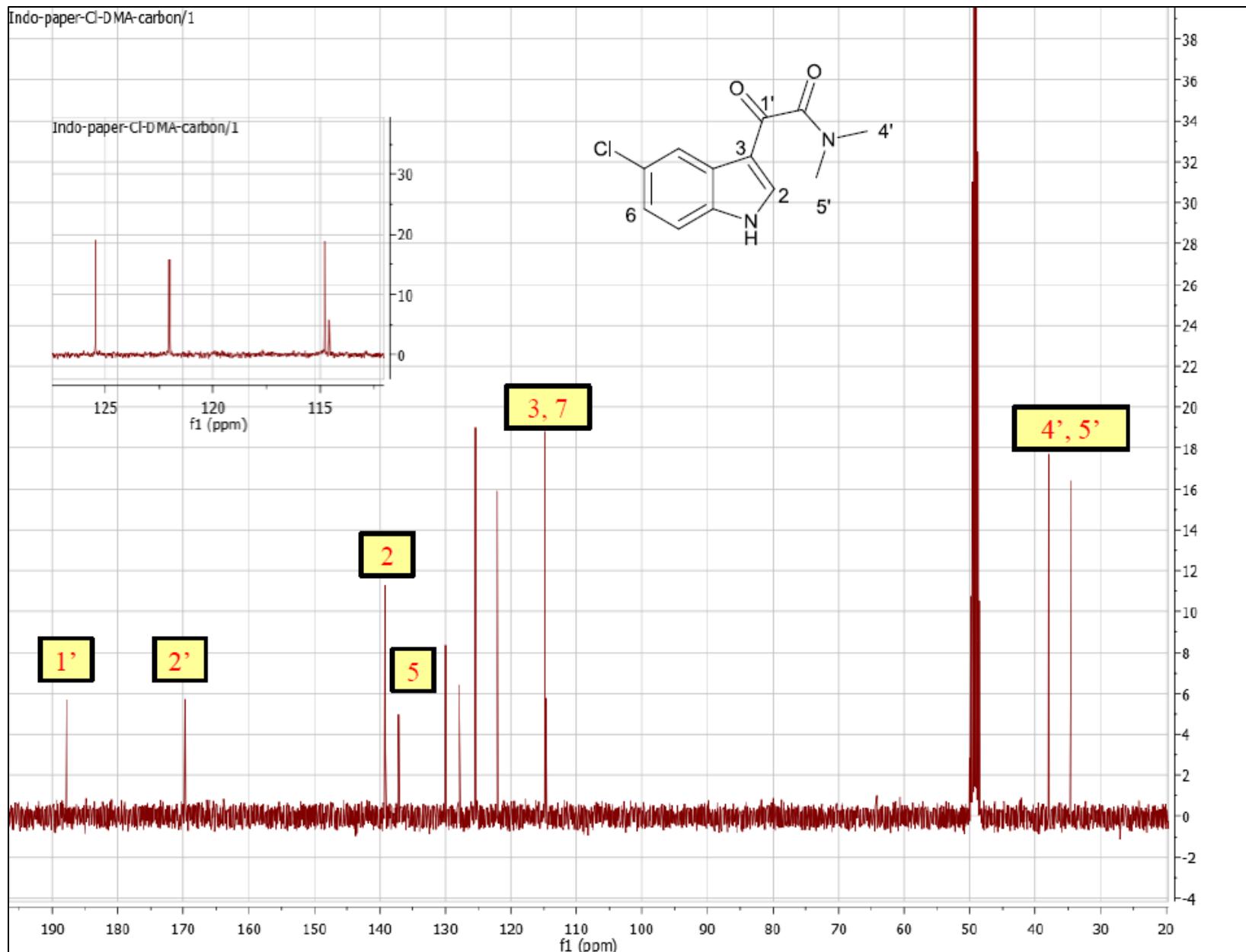
**Figure 4.** 13C NMR spectrum of 2-(5-fluoro-1H-indol-3-yl)-N,N-dimethyl-2-oxoacetamide (**1b**) in methanol-d<sub>4</sub> (400 MHz)



**Figure 5.**  $135^{\circ}$  DEPT spectrum of 2-(5-fluoro-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1b**) in methanol- $d_4$  (400 MHz)



**Figure 6.**  $^1\text{H}$  NMR spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1c**) in methanol- $d_4$  (400 MHz)



**Figure 7.**  $^{13}\text{C}$  NMR spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1c**) in methanol- $d_4$  (400 MHz)

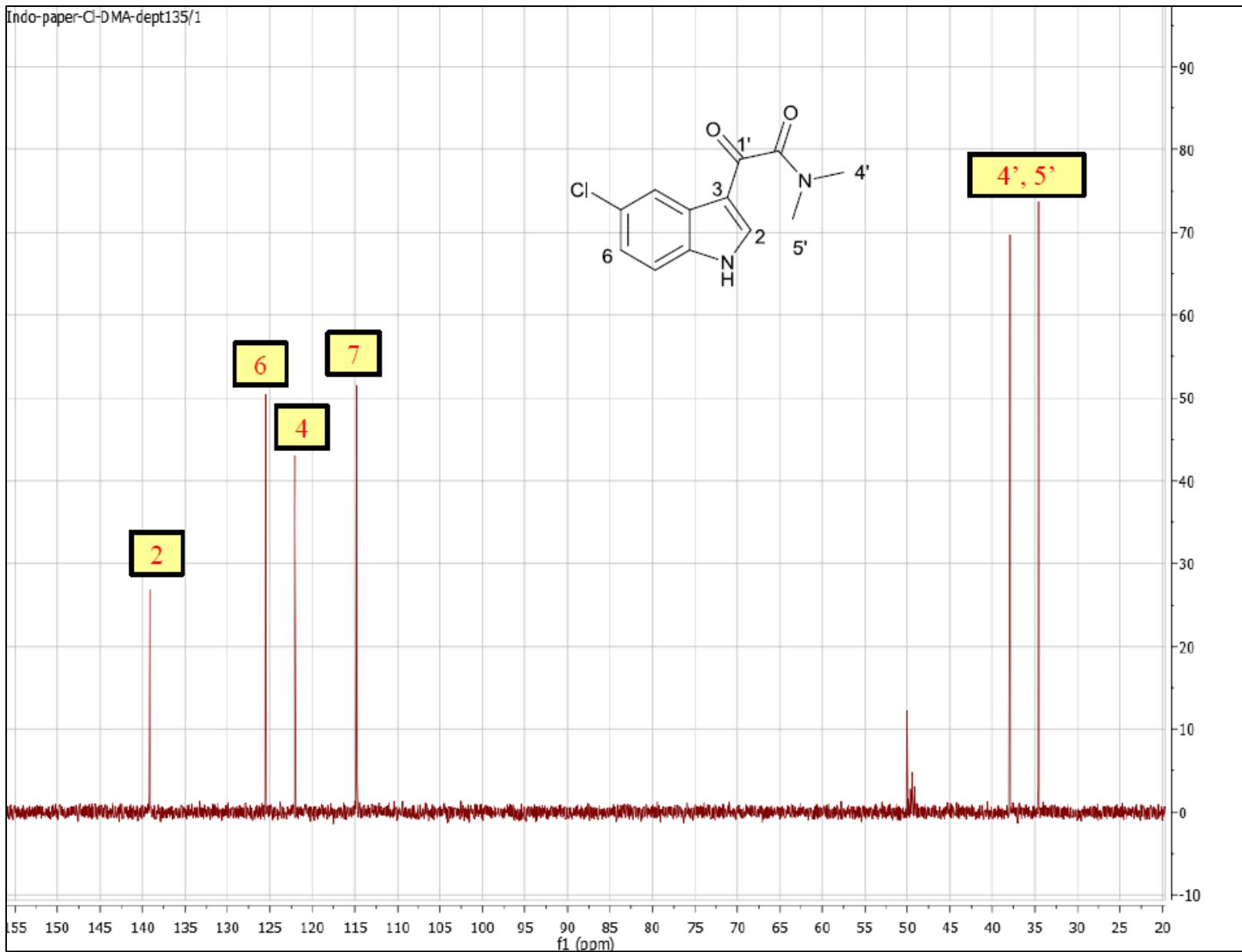


Figure 8.  $135^\circ$  DEPT spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1c**) in methanol-*d*<sub>4</sub> (400 MHz)

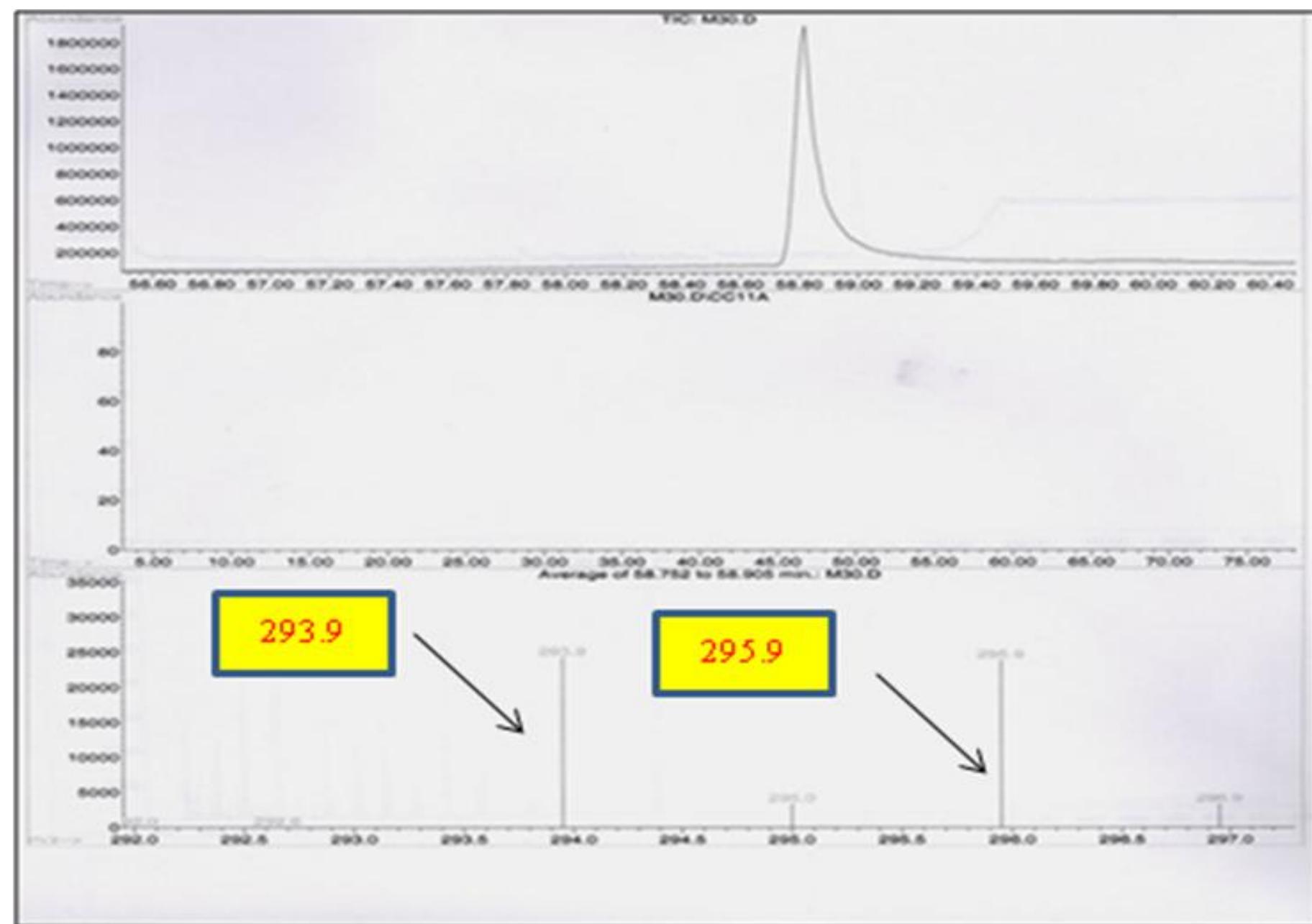
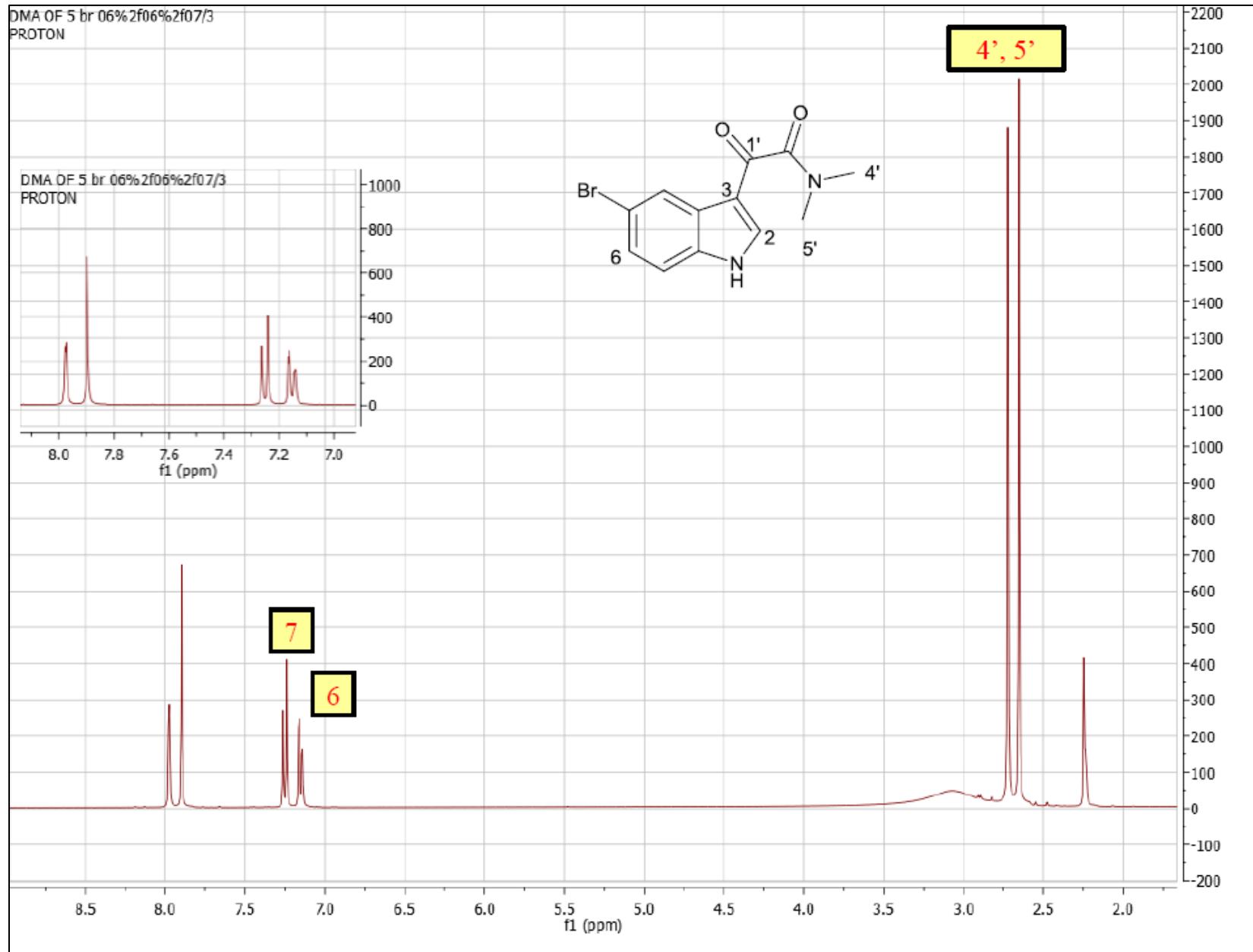
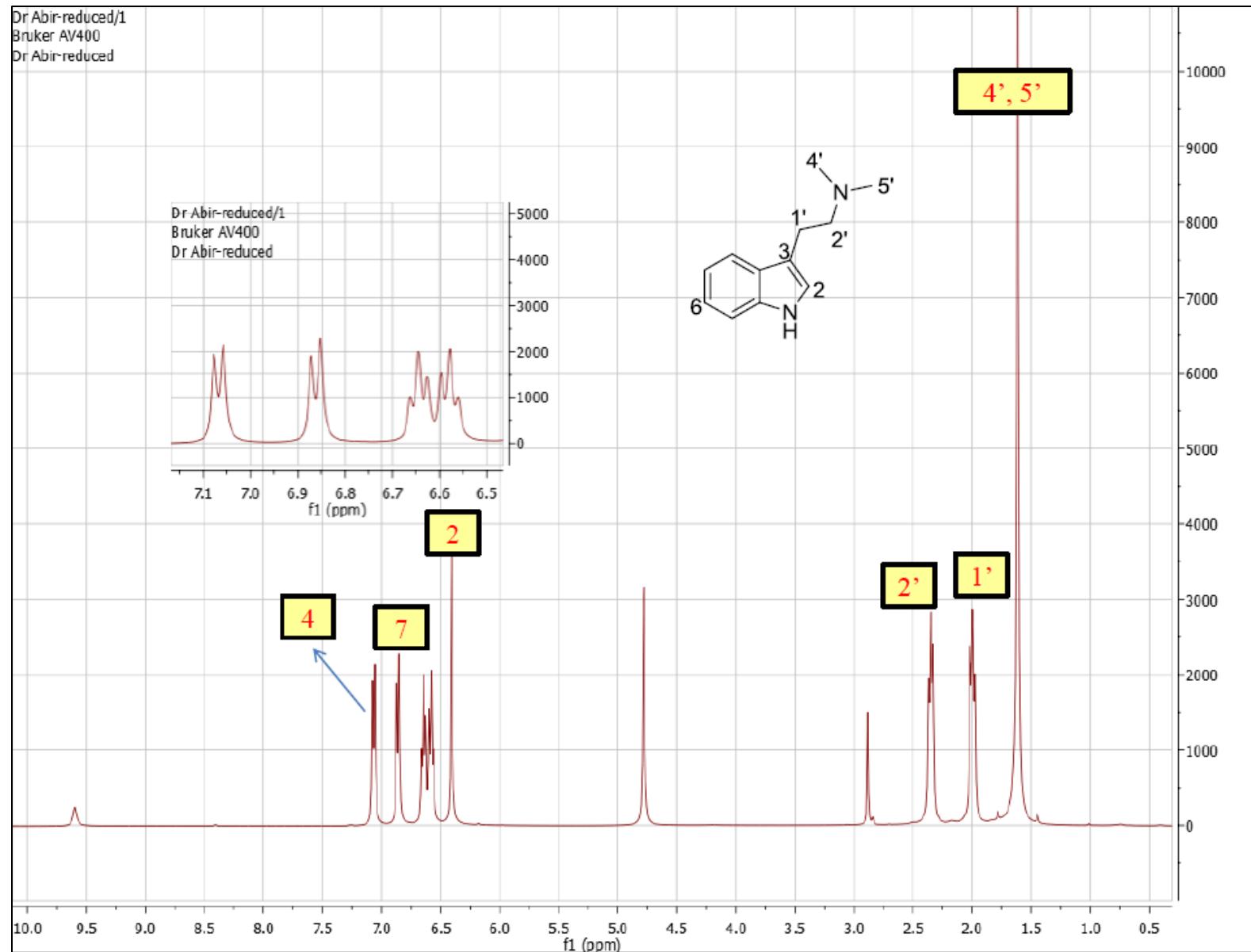


Figure 9. GC/MS chromatogram of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1d**)



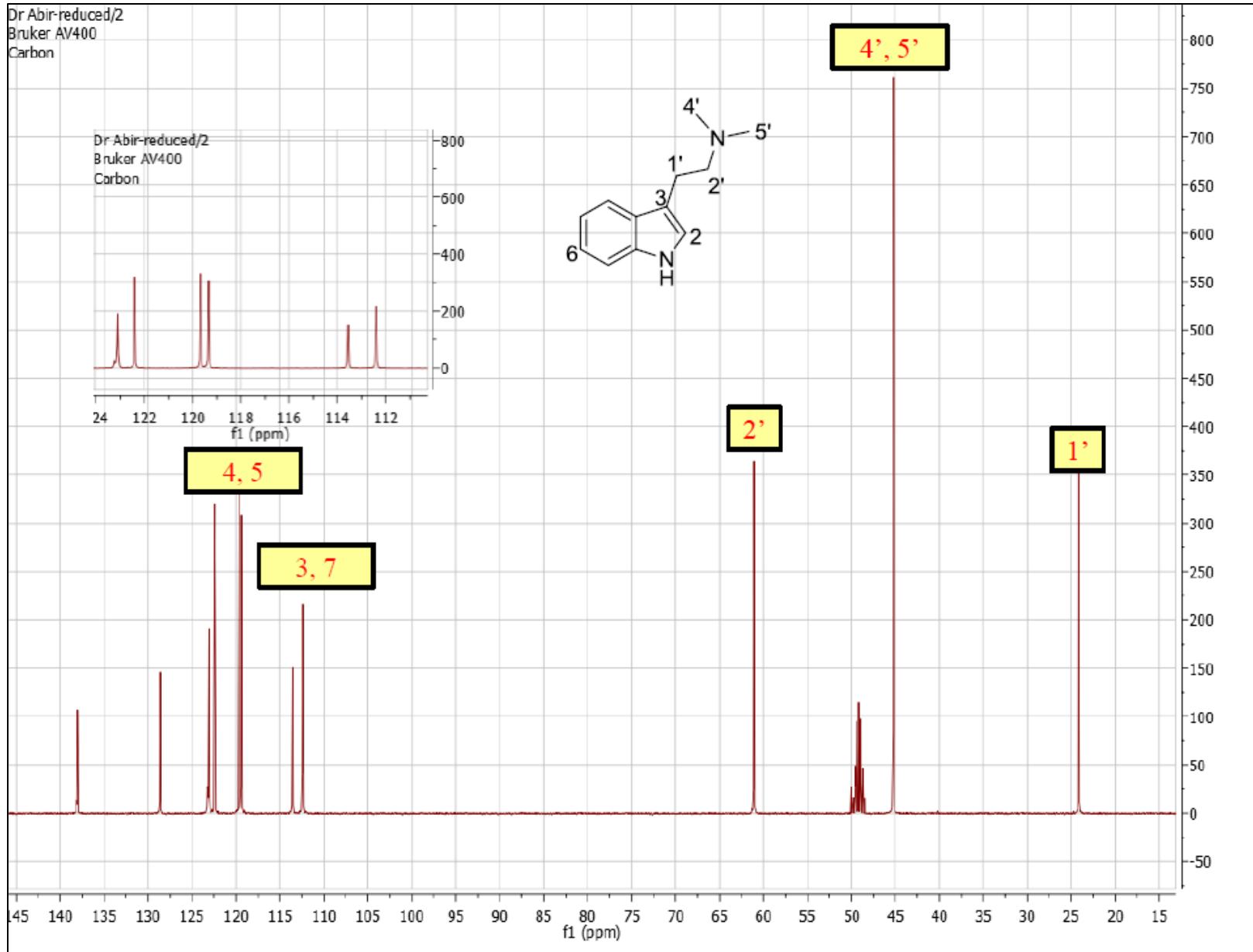
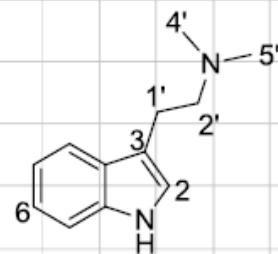
**Figure 10.**  $^1\text{H}$  NMR spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethyl-2-oxoacetamide (**1d**) in  $\text{CDCl}_3$  (400 MHz)



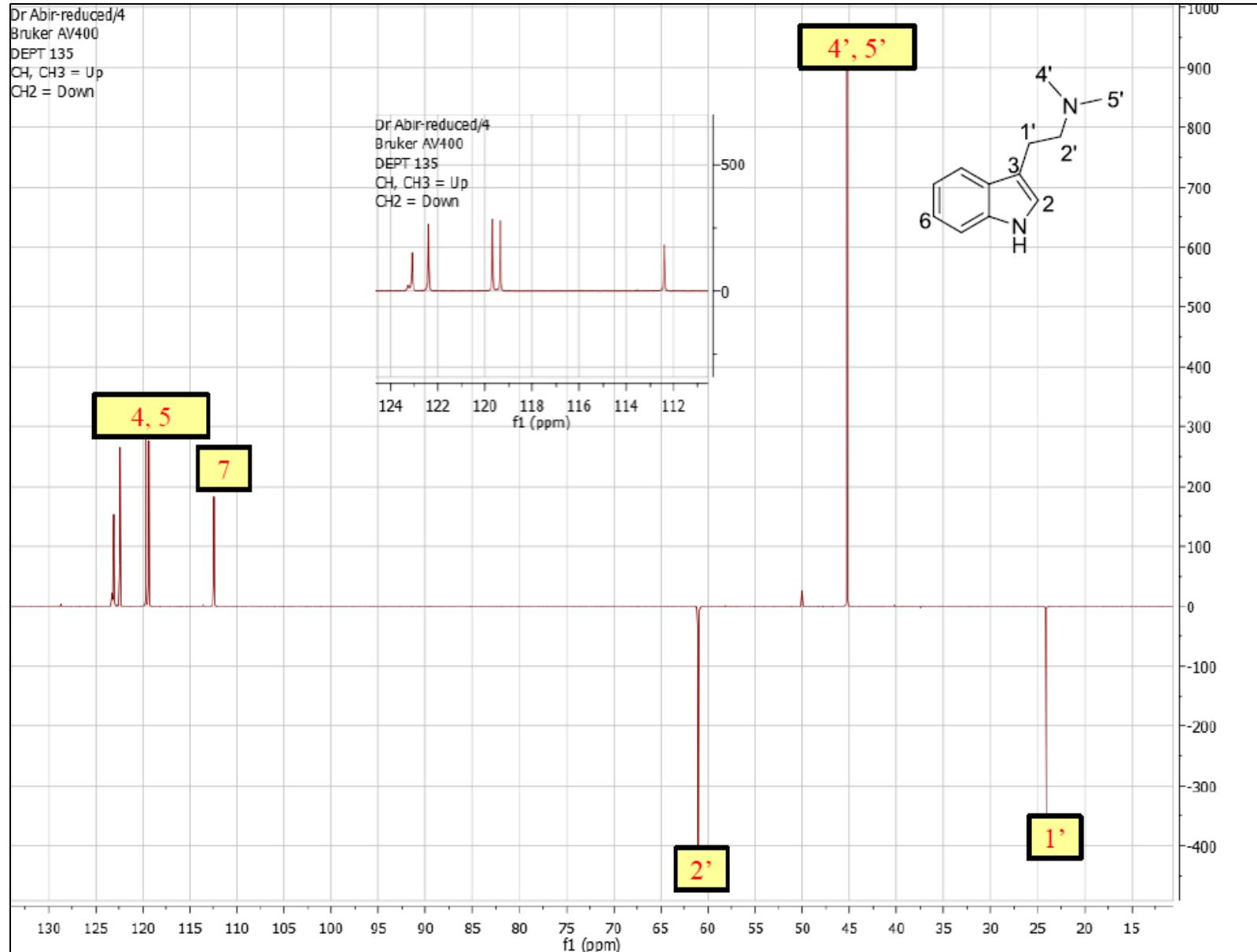
**Figure 11.** <sup>1</sup>H NMR spectrum of 2-(1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2a**) in methanol-*d*<sub>4</sub> (400 MHz)

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Bruker AV400  
Carbon

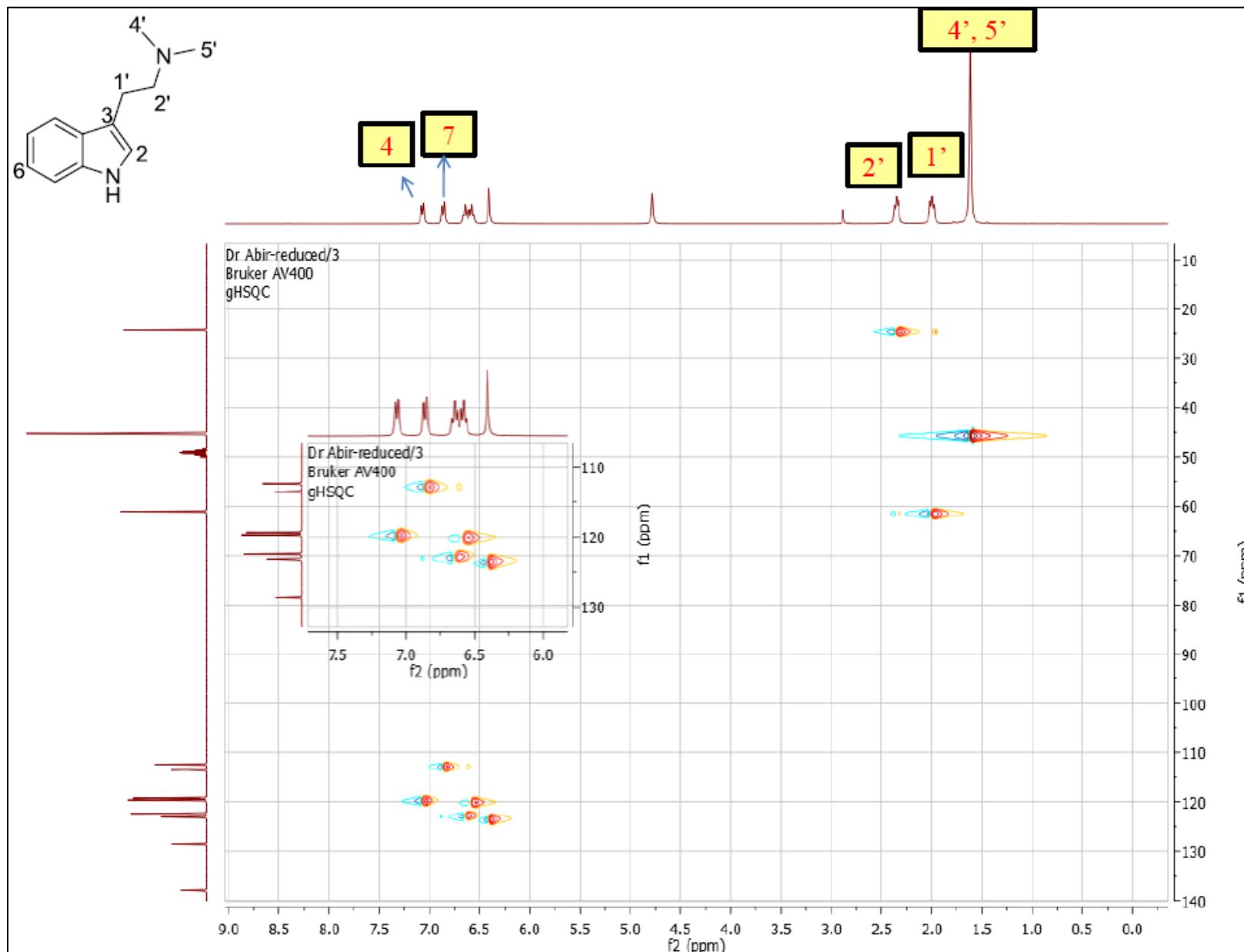
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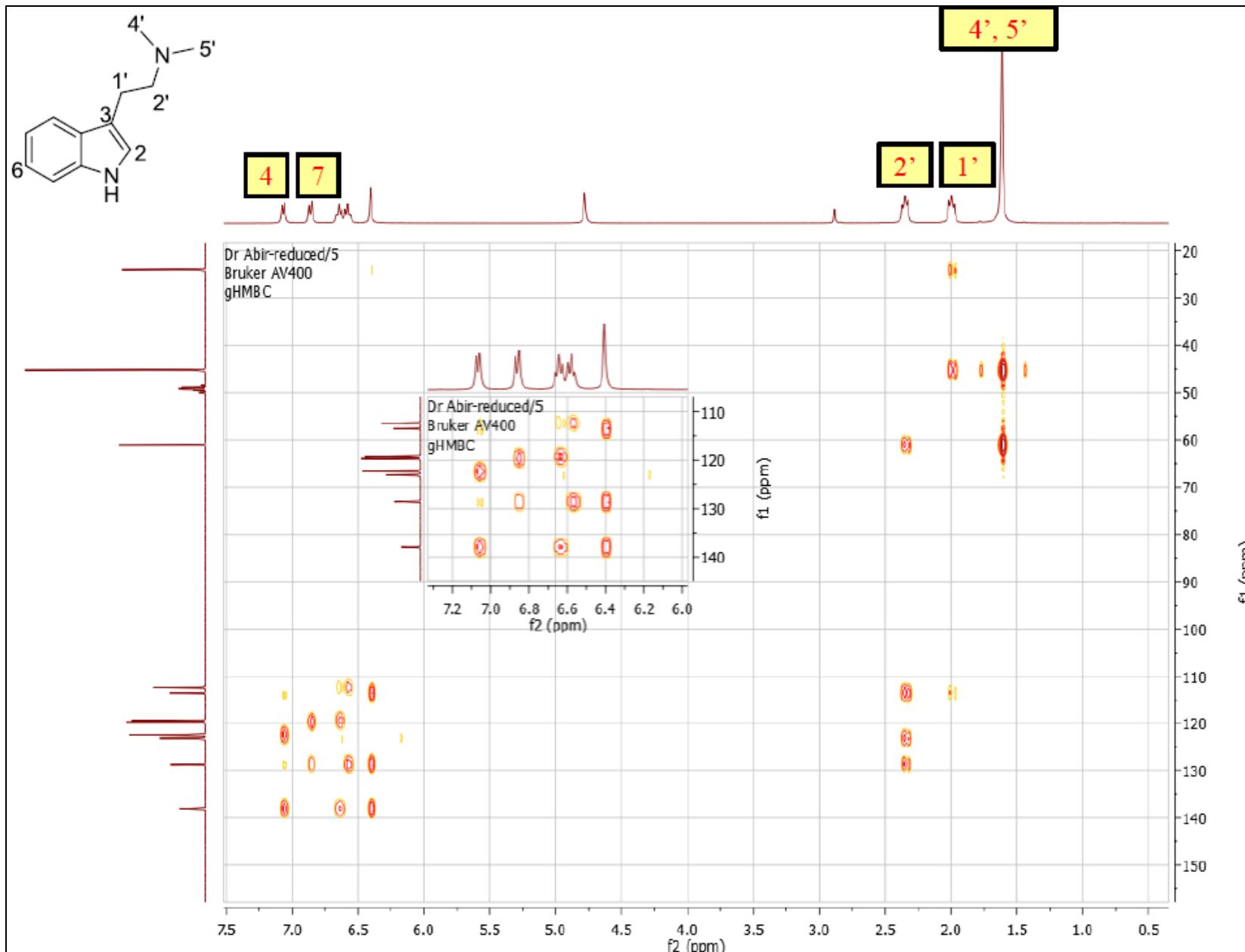
**Figure 12.**  $^{13}\text{C}$  NMR spectrum of 2-(1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2a**) in methanol- $d_4$  (400 MHz)



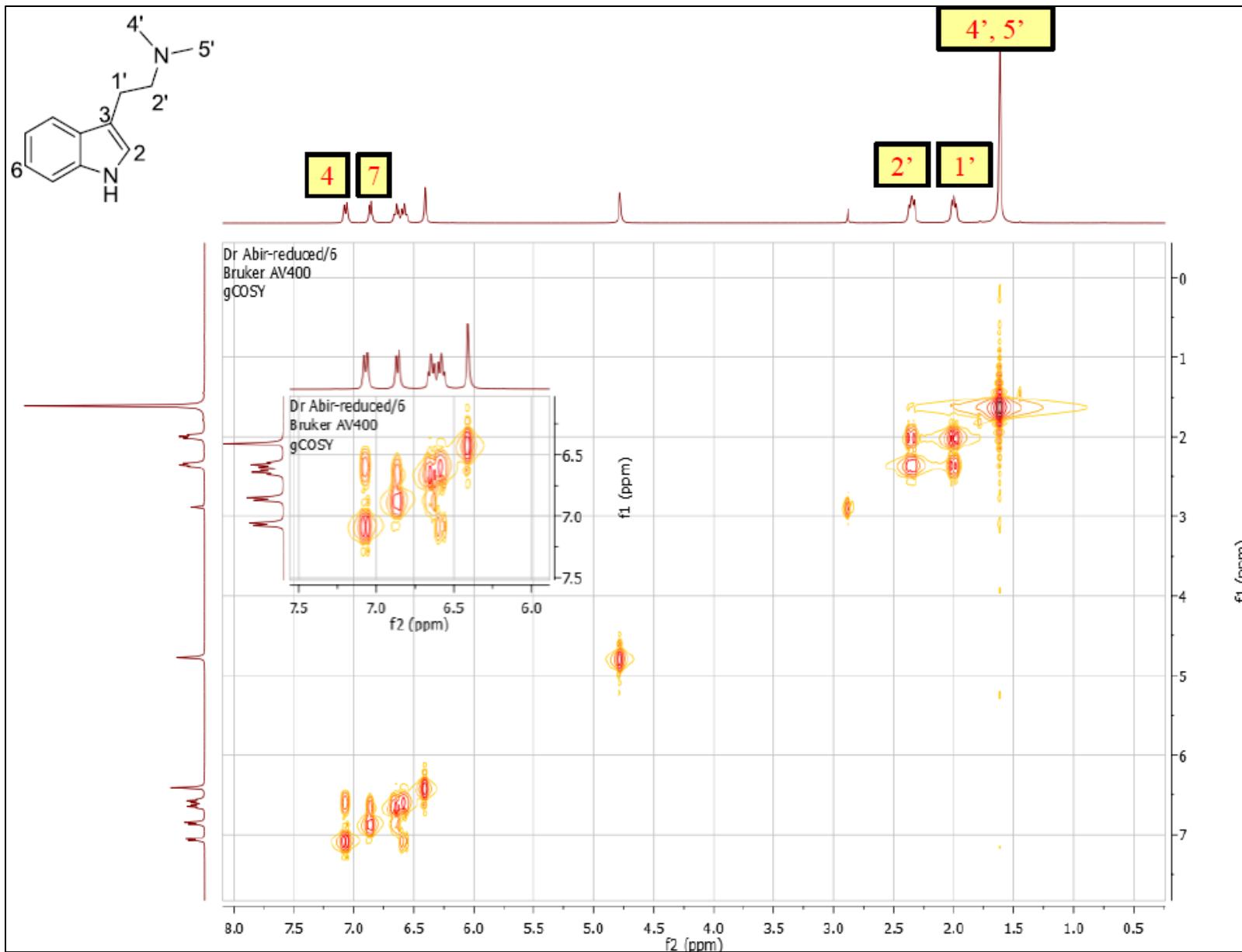
**Figure 13.**  $^{135}\text{^o}$  DEPT spectrum of 2-(1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2a**) in methanol-*d*<sub>4</sub> (400 MHz)



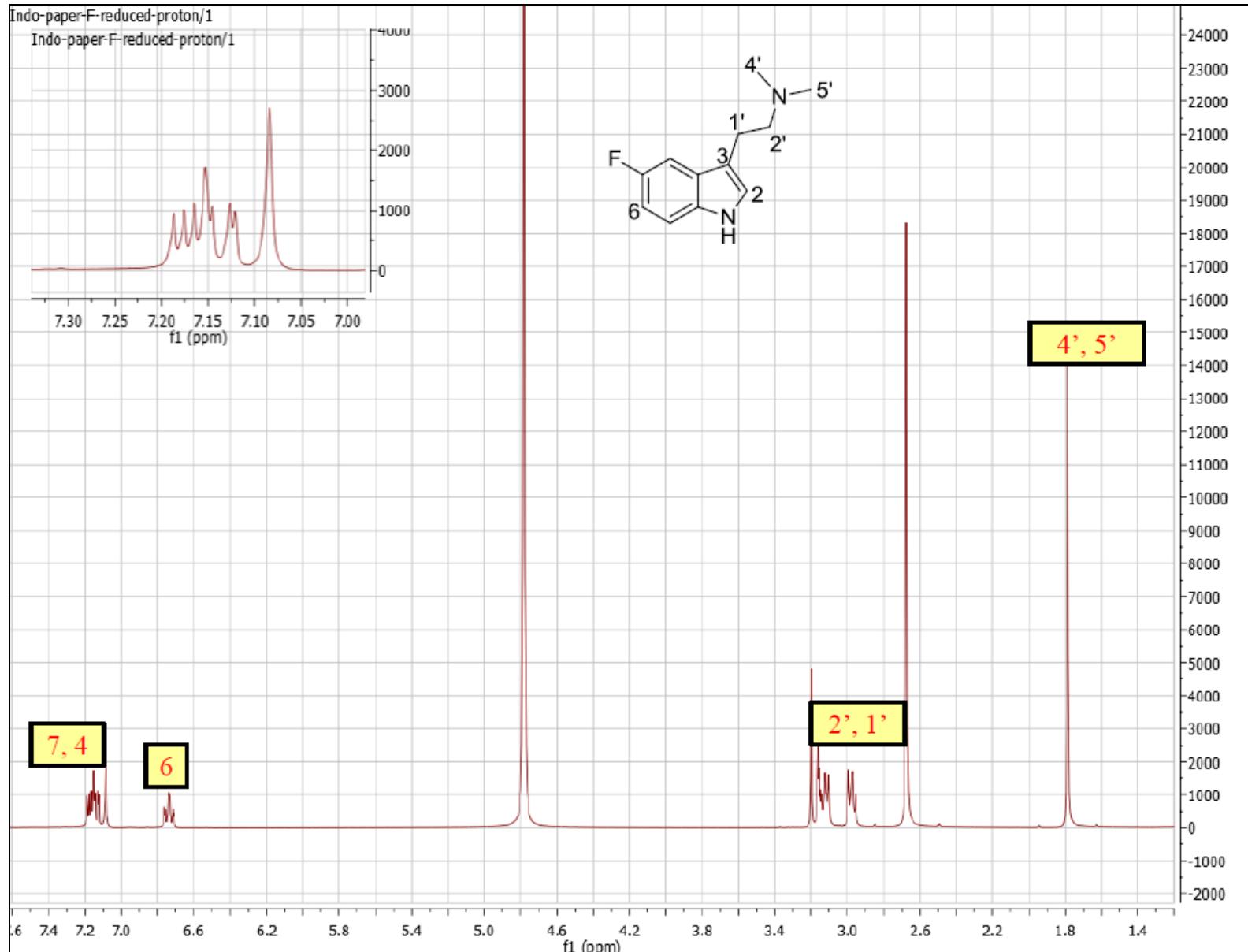
**Figure 14.** HSQC spectrum of 2-(1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2a**) in methanol- $d_4$  (400 MHz)



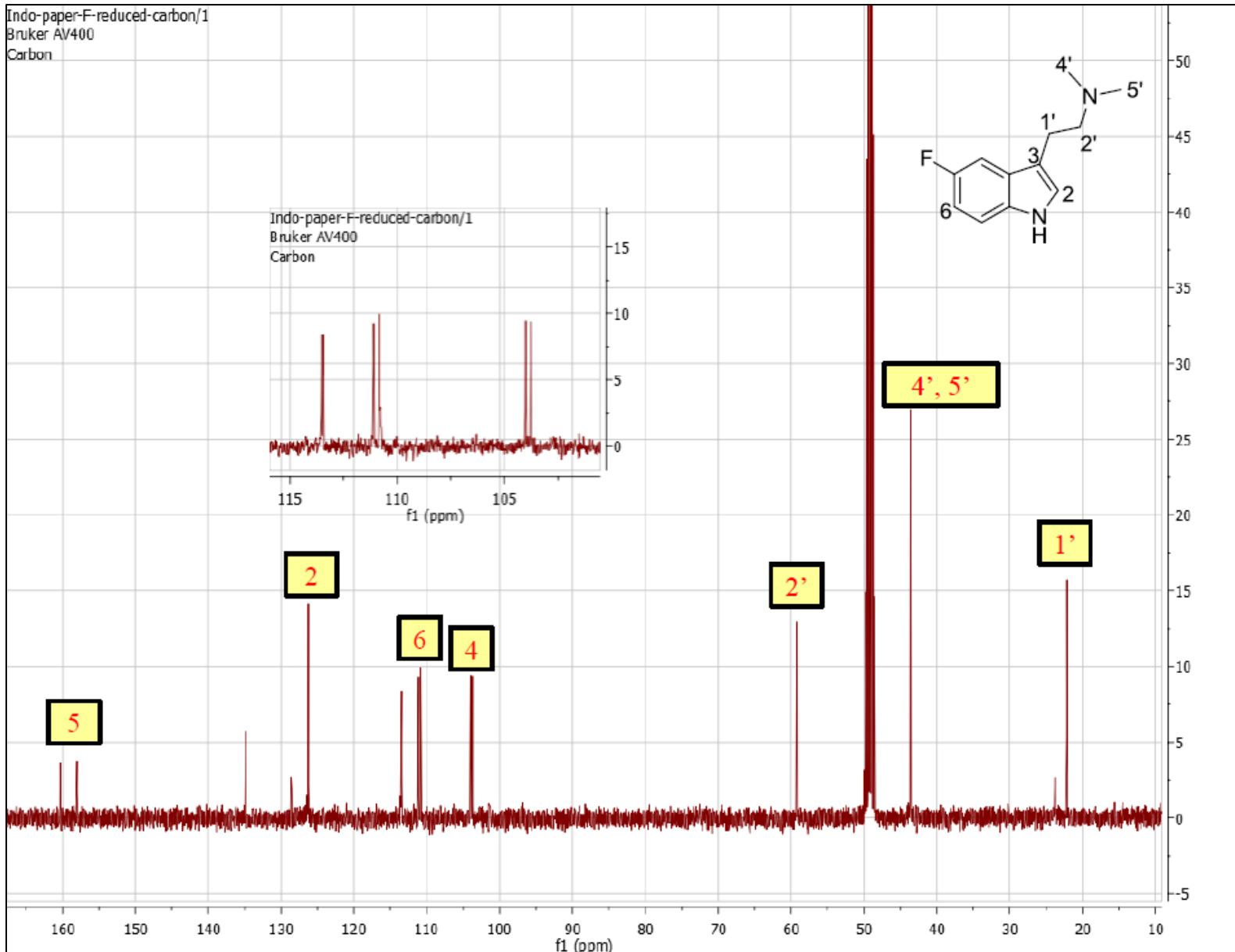
**Figure 15.** HMBC spectrum of 2-(1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2a**) in methanol-*d*<sub>4</sub> (400 MHz)



**Figure 16.** COSY spectrum of 2-(1 $H$ -indol-3-yl)- $N,N$ -dimethylethanamine (**2a**) in methanol- $d_4$  (400 MHz)



**Figure 17.** <sup>1</sup>H NMR spectrum of 2-(5-fluoro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2b**) in methanol-*d*<sub>4</sub> (400 MHz)



**Figure 18.**  $^{13}\text{C}$  NMR spectrum of 2-(5-fluoro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2b**) in methanol- $d_4$  (400 MHz)

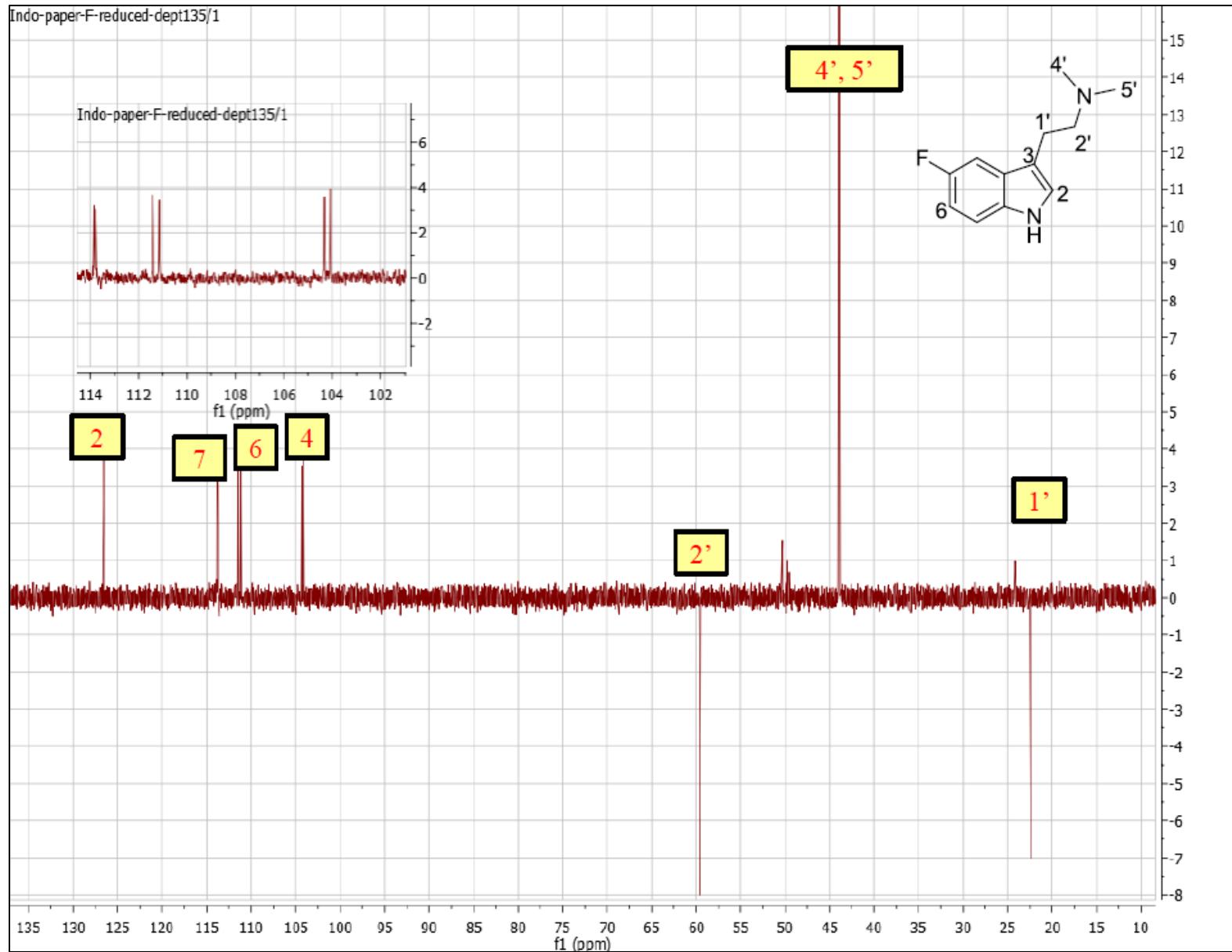
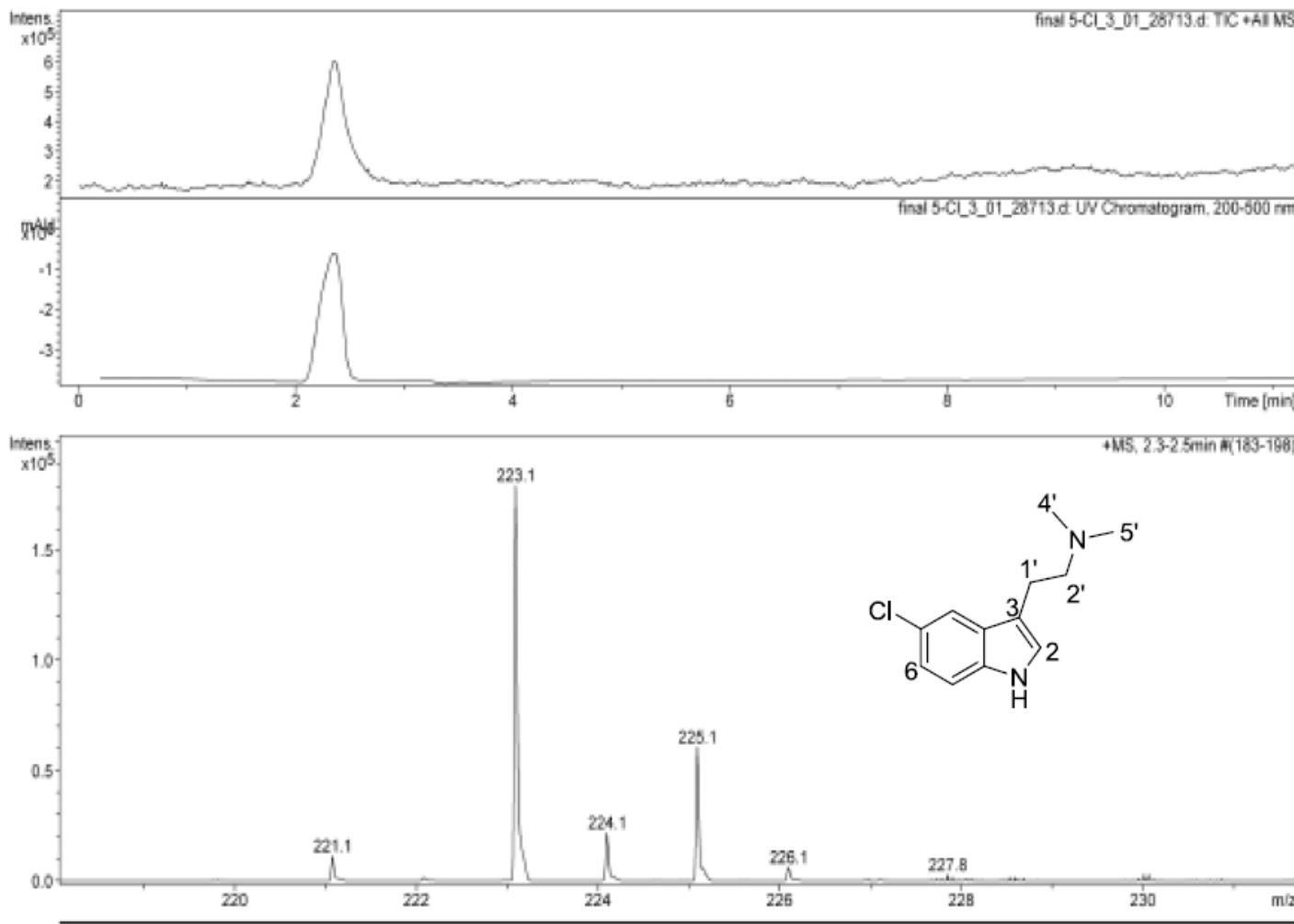
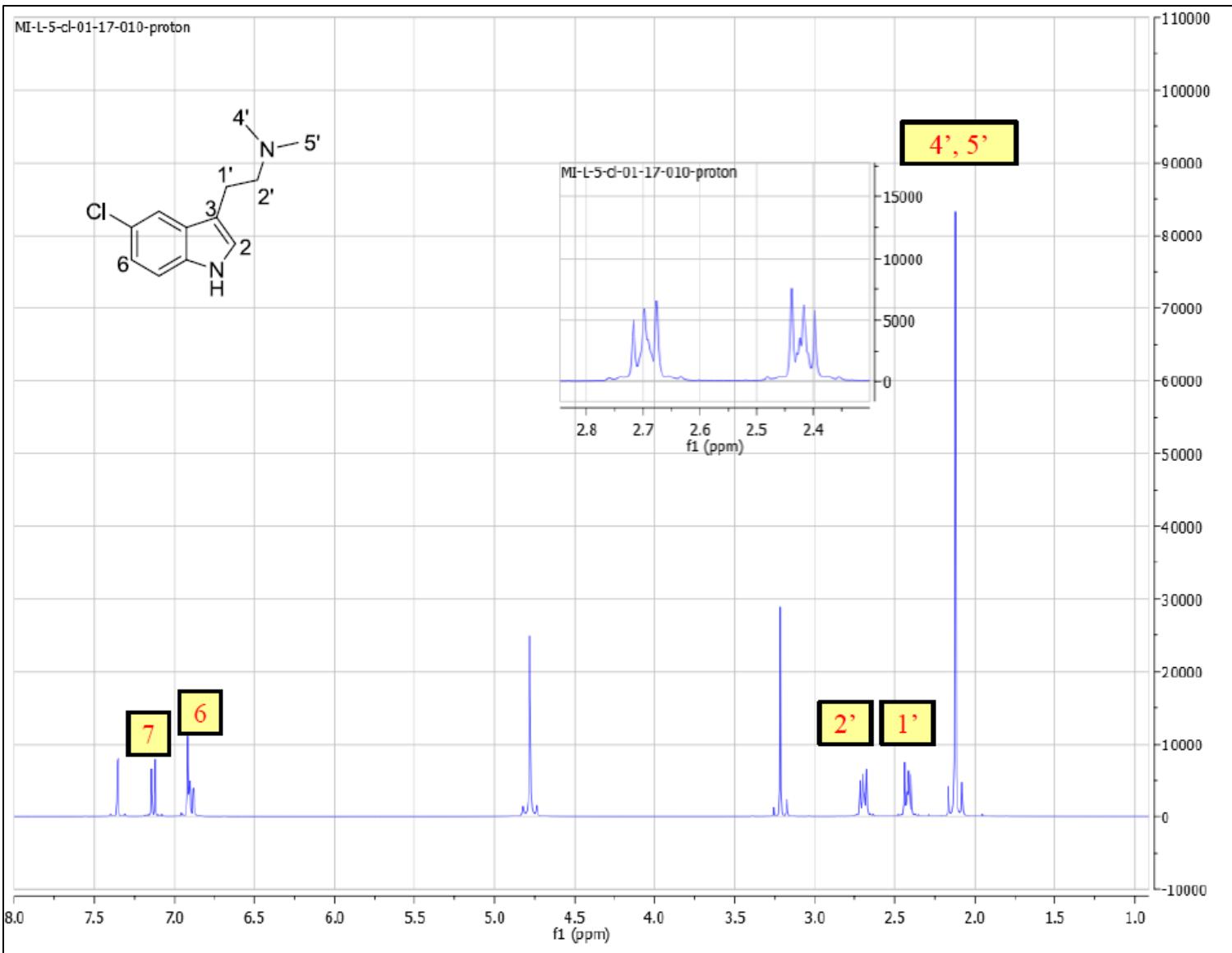


Figure 19.  $135^{\circ}$  DEPT spectrum of 2-(5-fluoro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2b**) in methanol-*d*<sub>4</sub> (400 MHz)

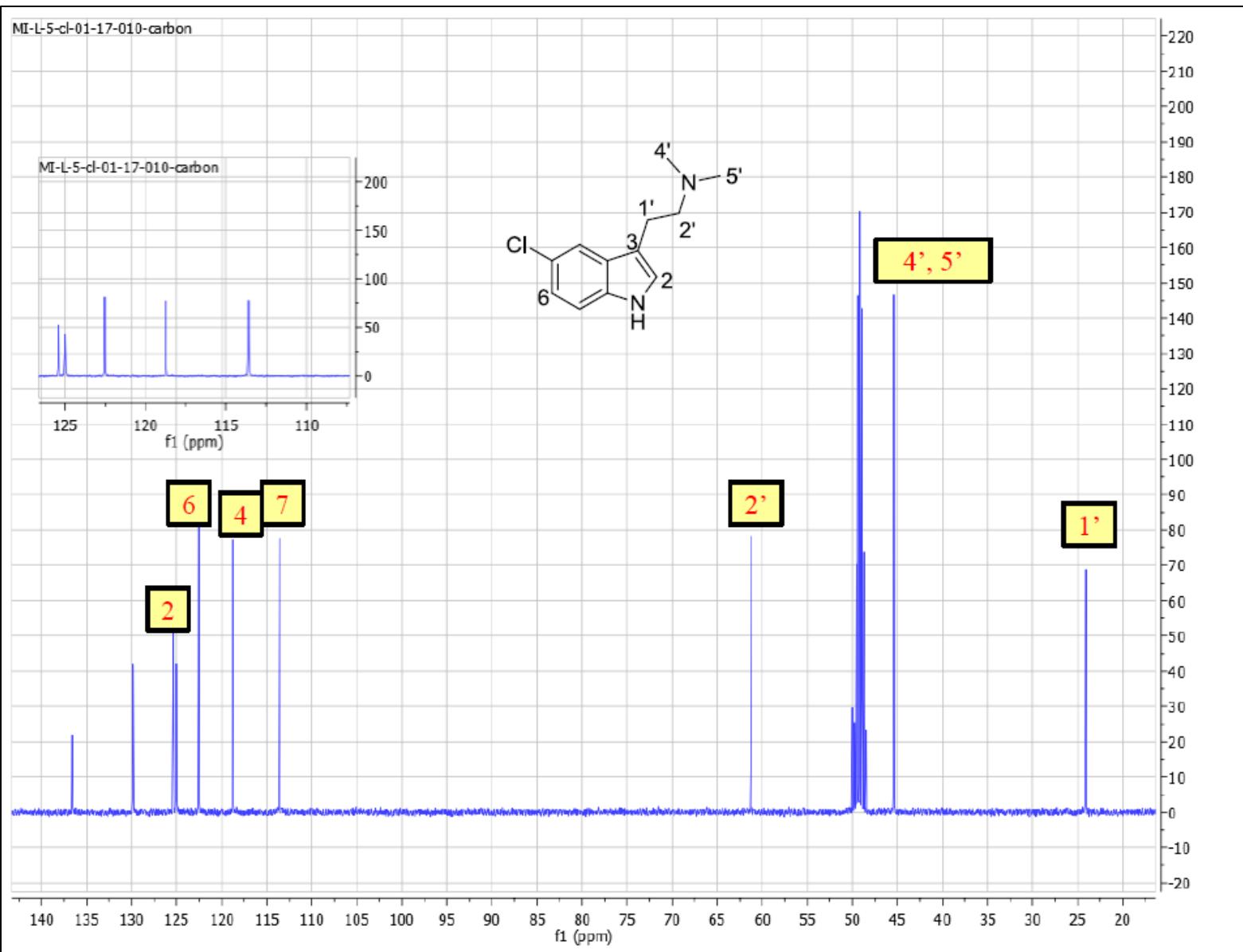
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**Figure 20.** LC/MS chromatogram of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2c**)



**Figure 21.**  $^1\text{H}$  NMR spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2c**) in methanol- $d_4$  (400 MHz)



**Figure 22.**  $^{13}\text{C}$  NMR spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2c**) in methanol- $d_4$  (400 MHz)

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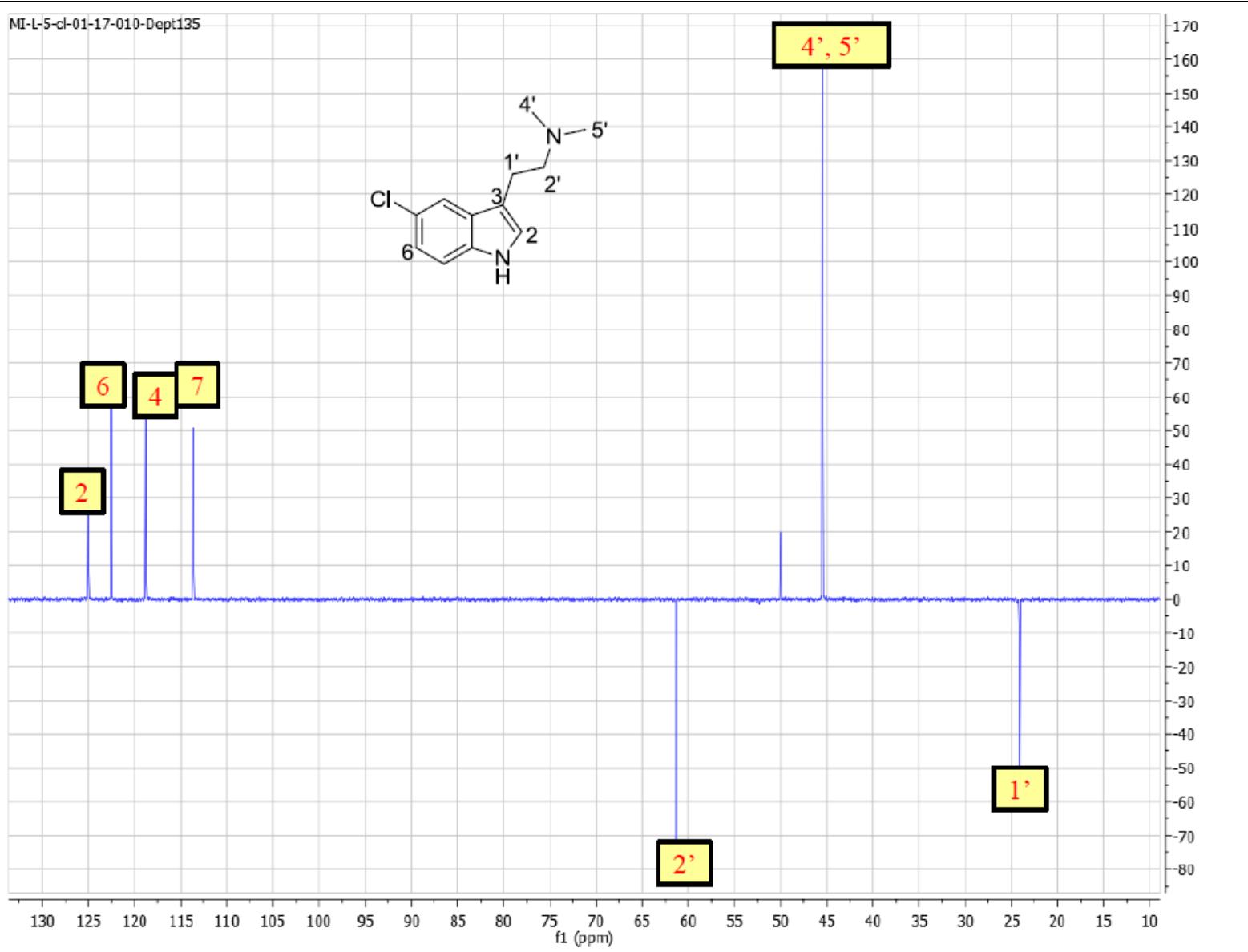
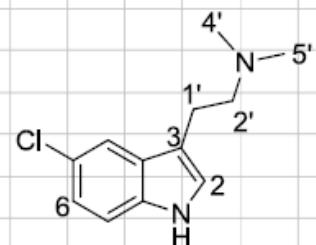
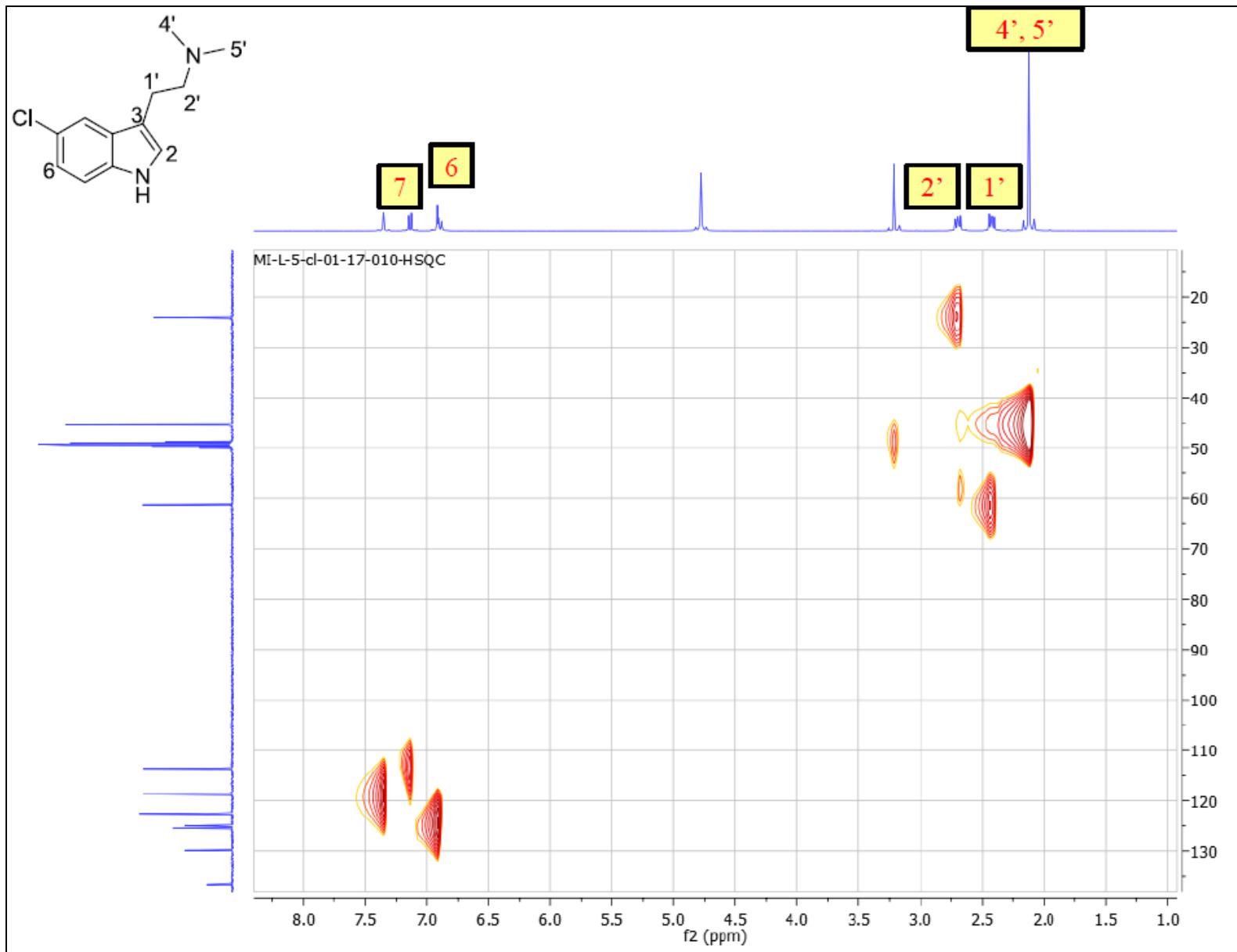


Figure 23. 135° DEPT spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2c**) in methanol-*d*<sub>4</sub> (400 MHz)

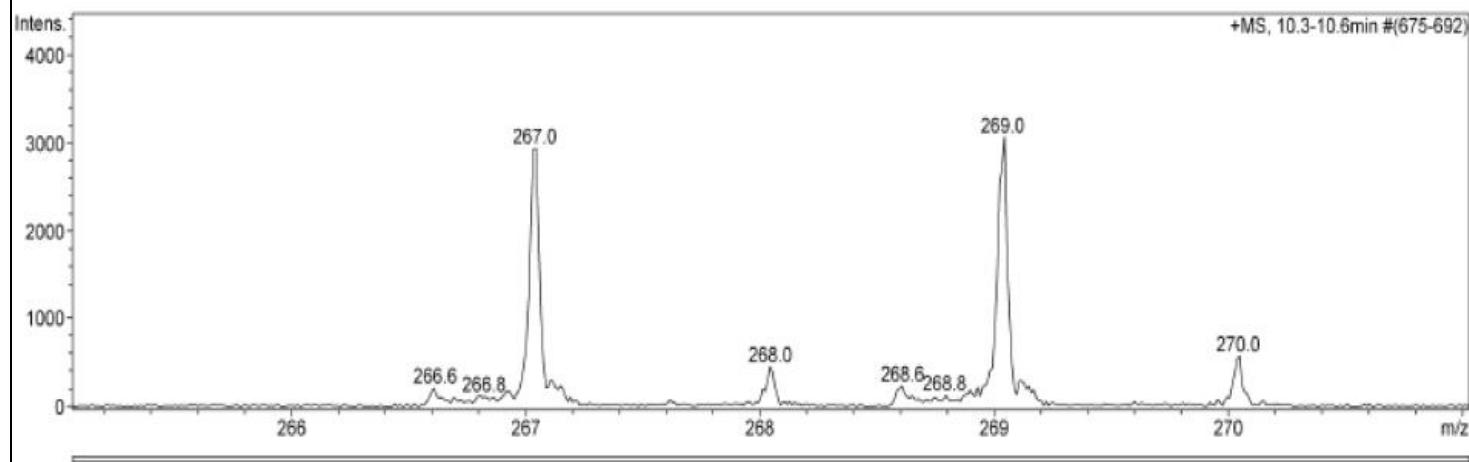
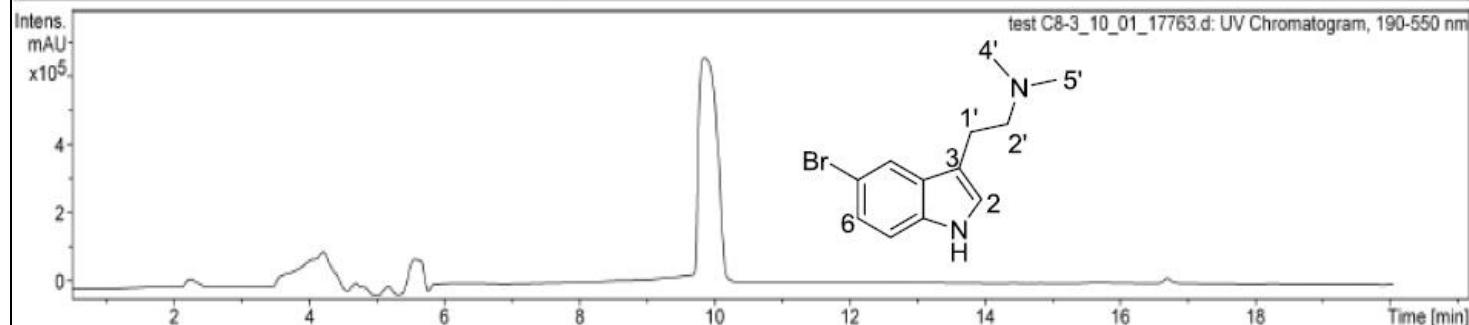


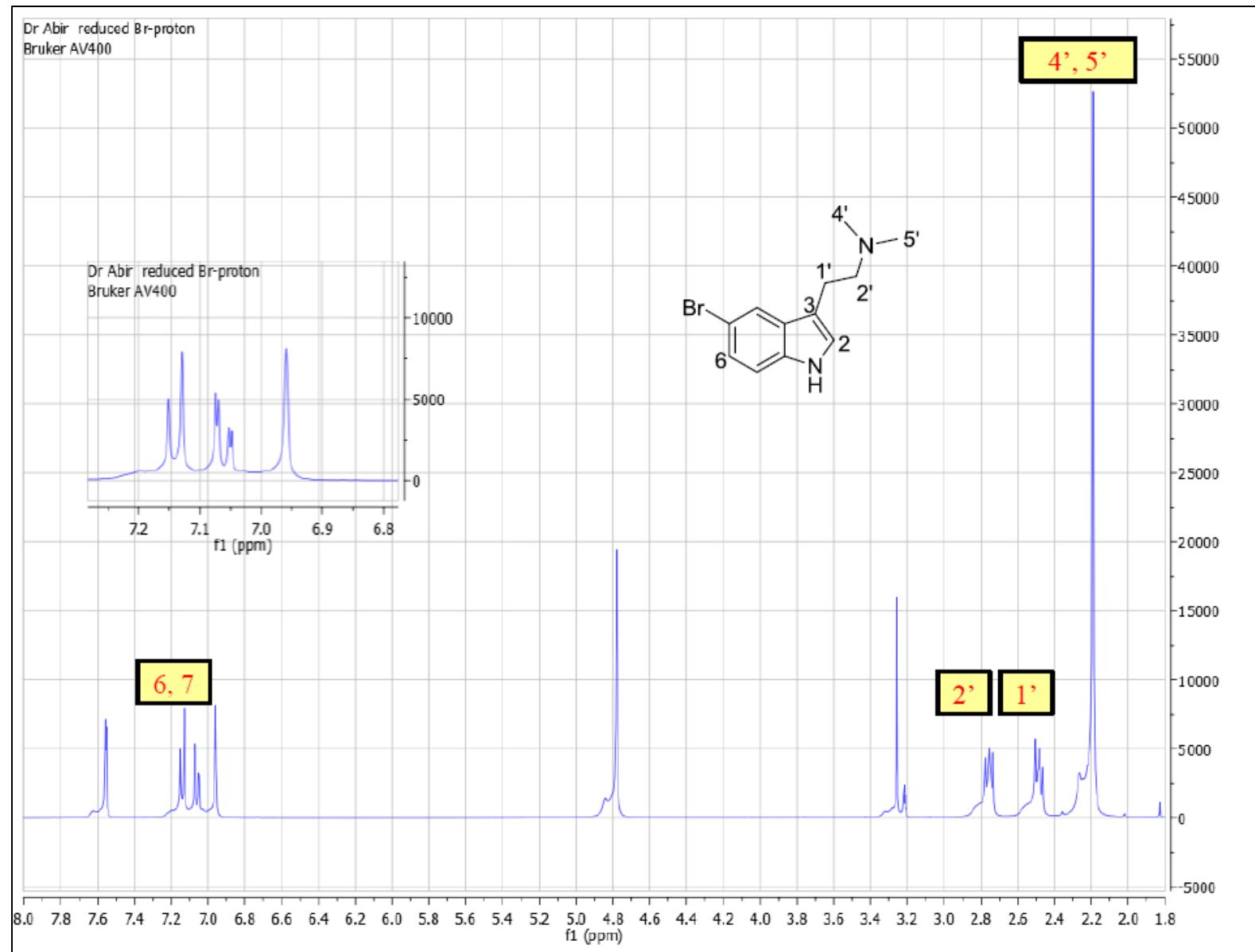
**Figure 24.** HSQC spectrum of 2-(5-chloro-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2c**) in methanol-*d*<sub>4</sub> (400 MHz)

## Comment

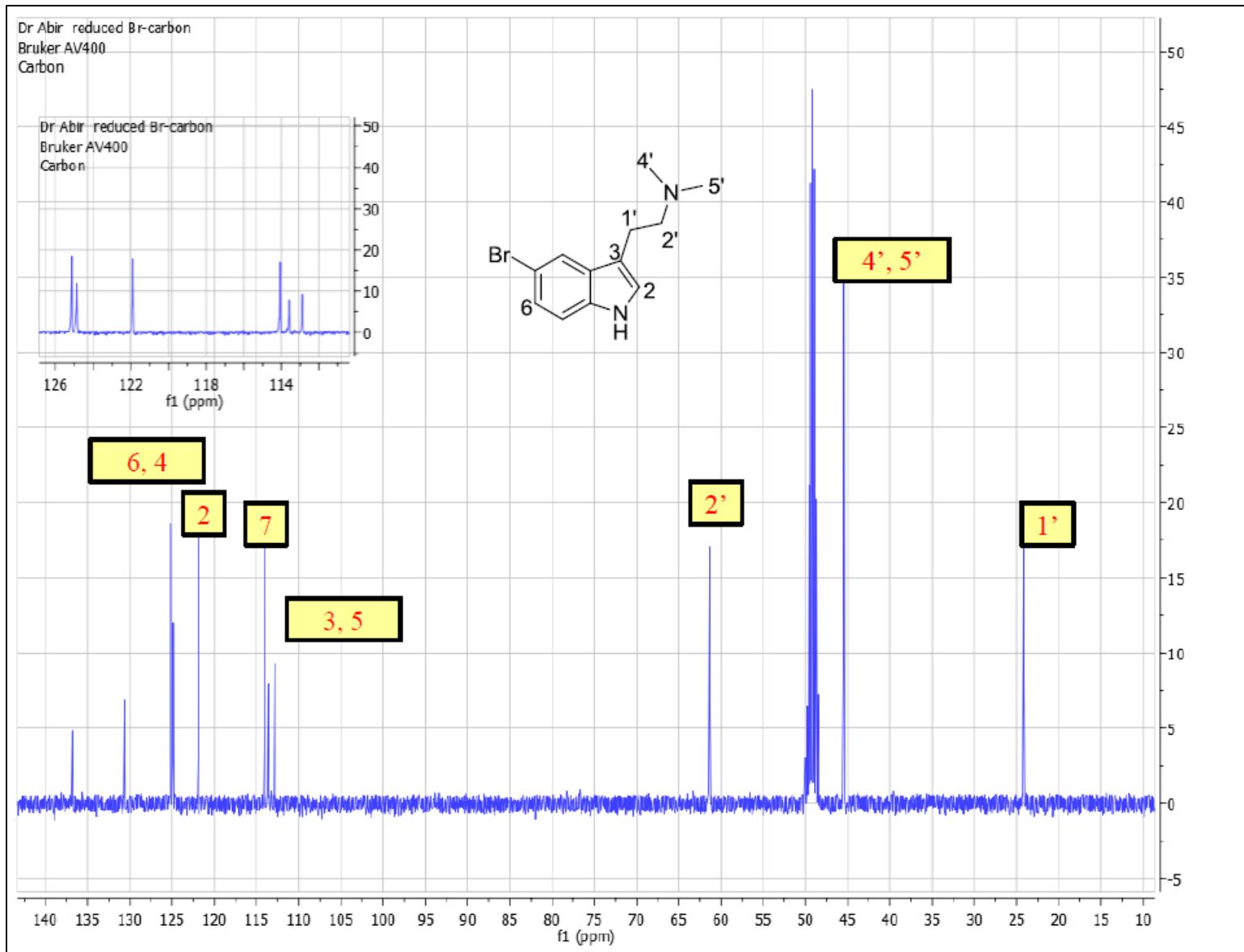
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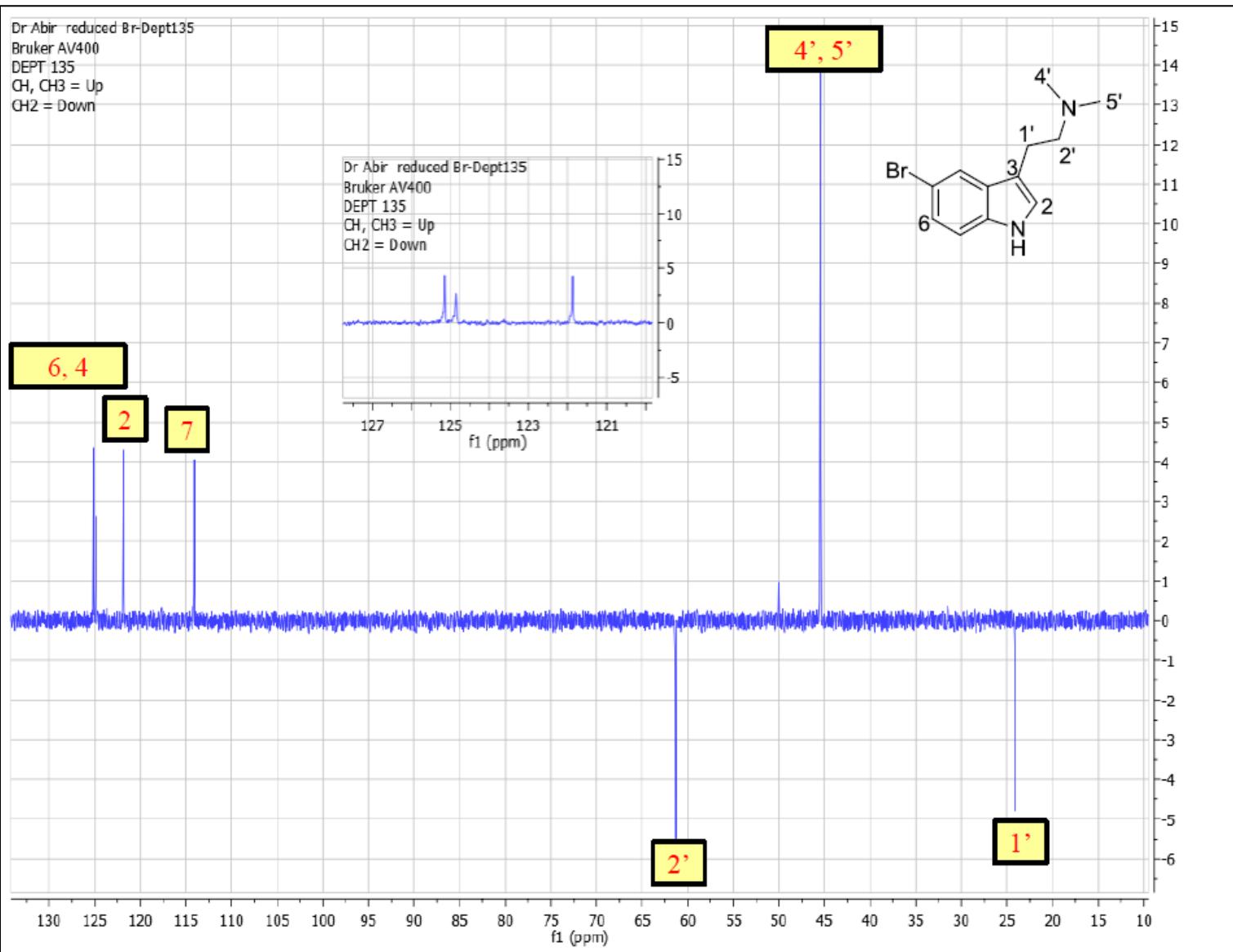
**Figure 25.** LC/MS chromatogram of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**)



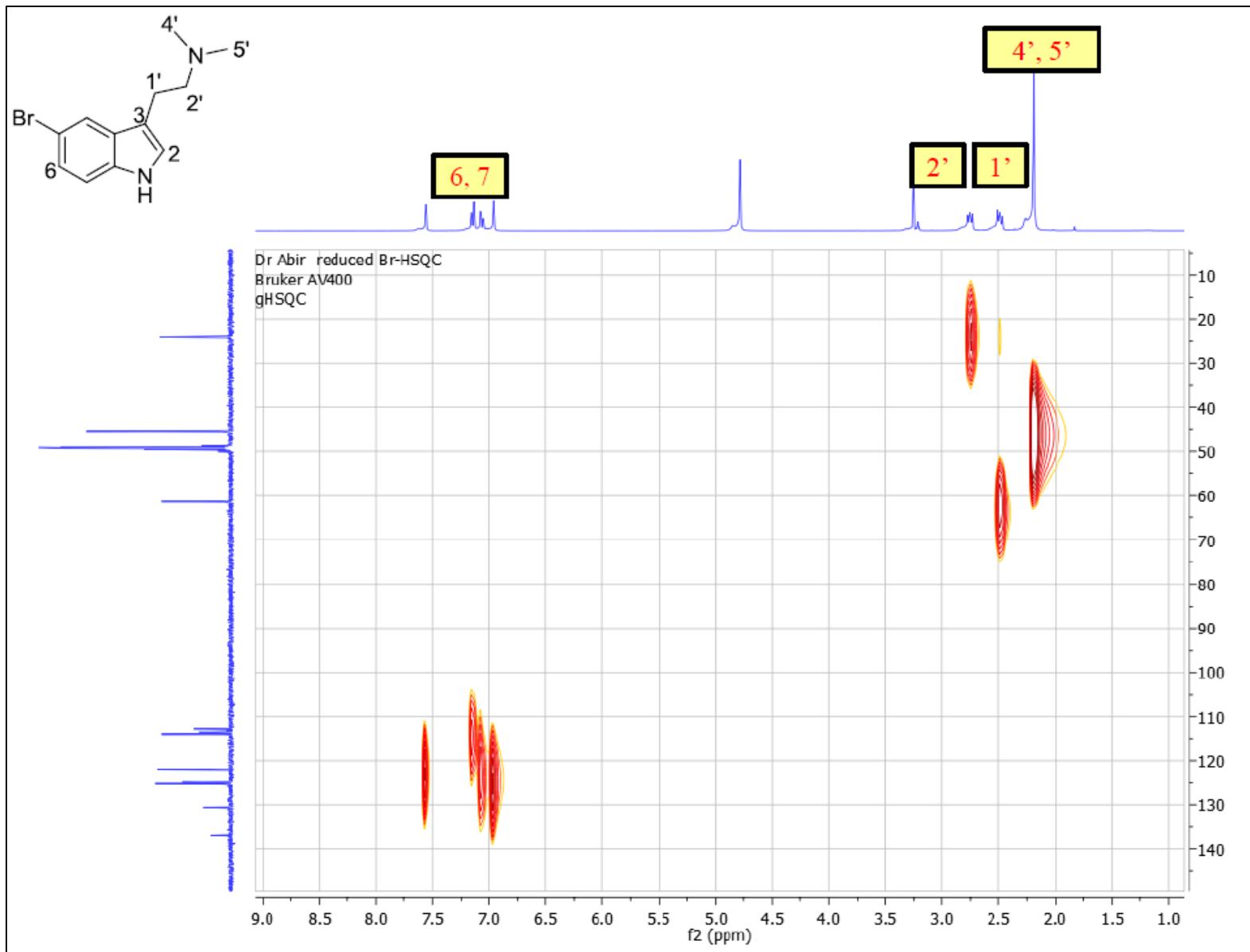
**Figure 26.**  $^1\text{H}$  NMR spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**) in methanol- $d_4$  (400 MHz)



**Figure 27.** <sup>13</sup>C NMR spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**) in methanol-*d*<sub>4</sub> (400 MHz)

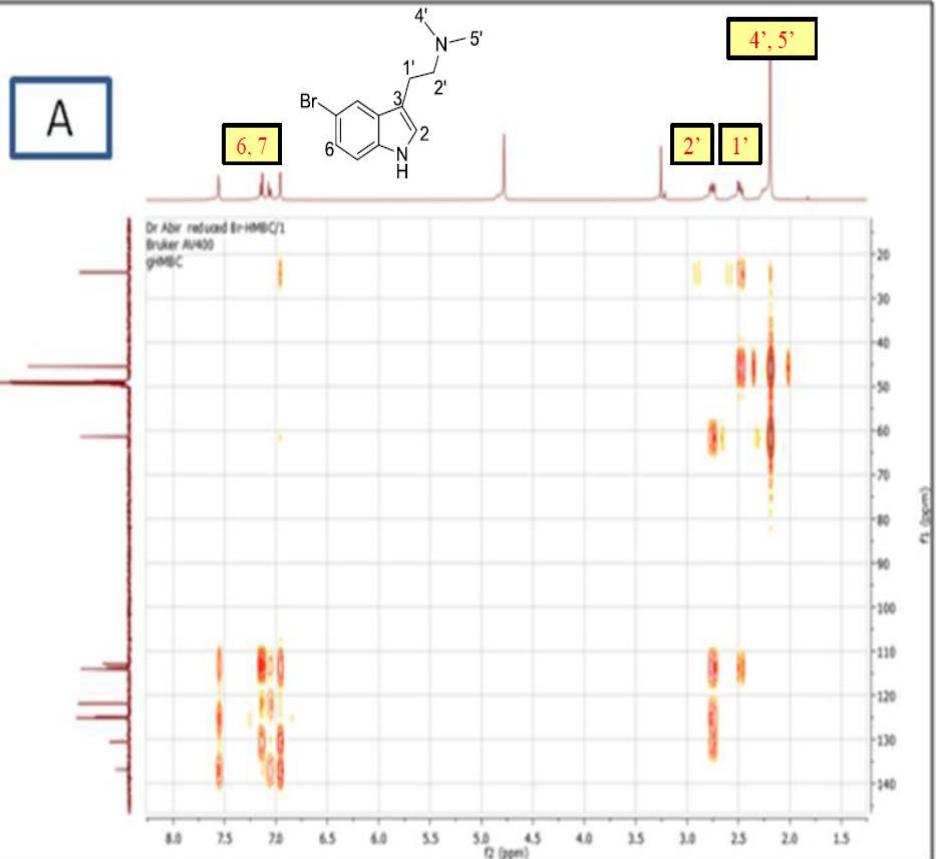


**Figure 28.**  $135^{\circ}$  DEPT spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**) in methanol-*d*<sub>4</sub> (400 MHz)

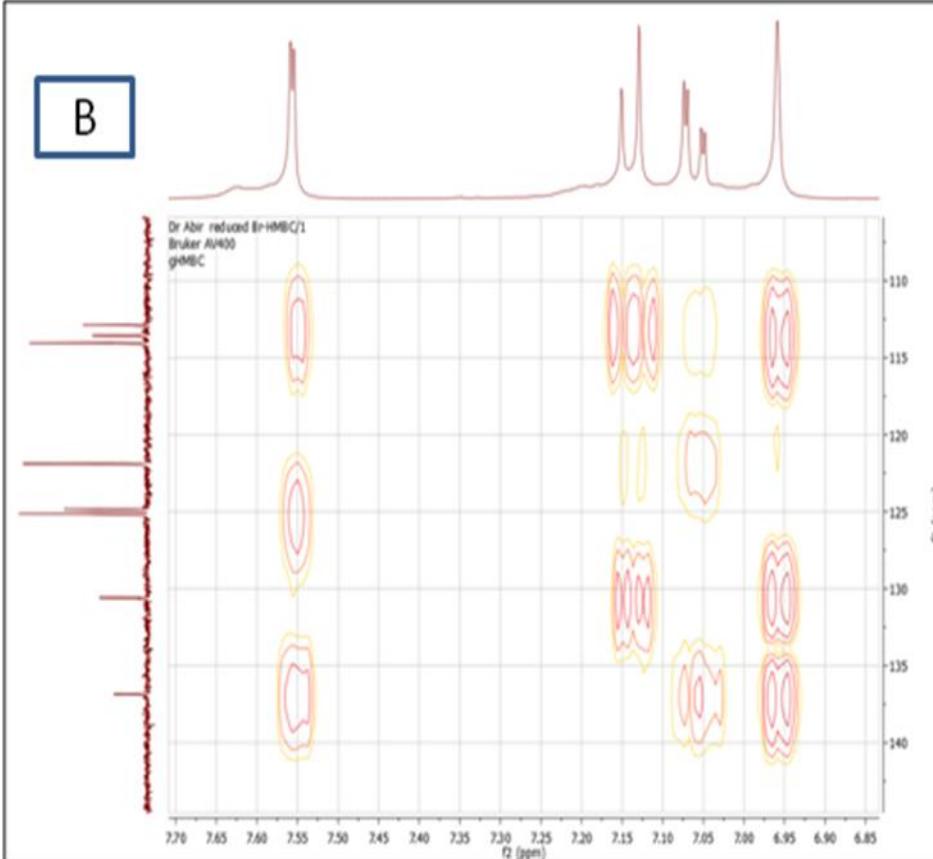


**Figure 29.** HSQC spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**) in methanol-*d*<sub>4</sub> (400 MHz)

A



B



**Figure 30.** HMBC spectrum of 2-(5-bromo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2d**) in methanol-*d*<sub>4</sub> (400 MHz); A) the full spectrum, B) the high field region

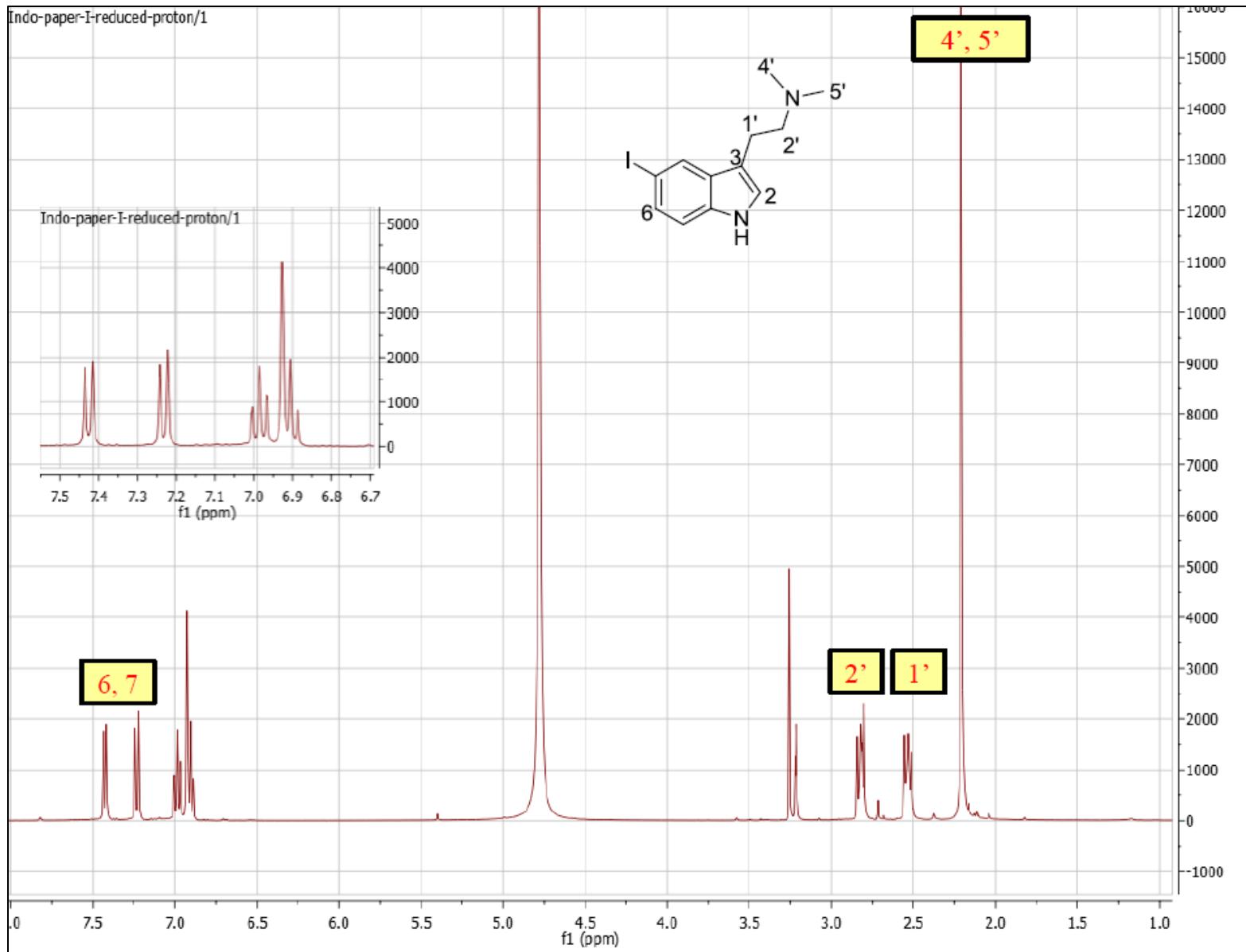
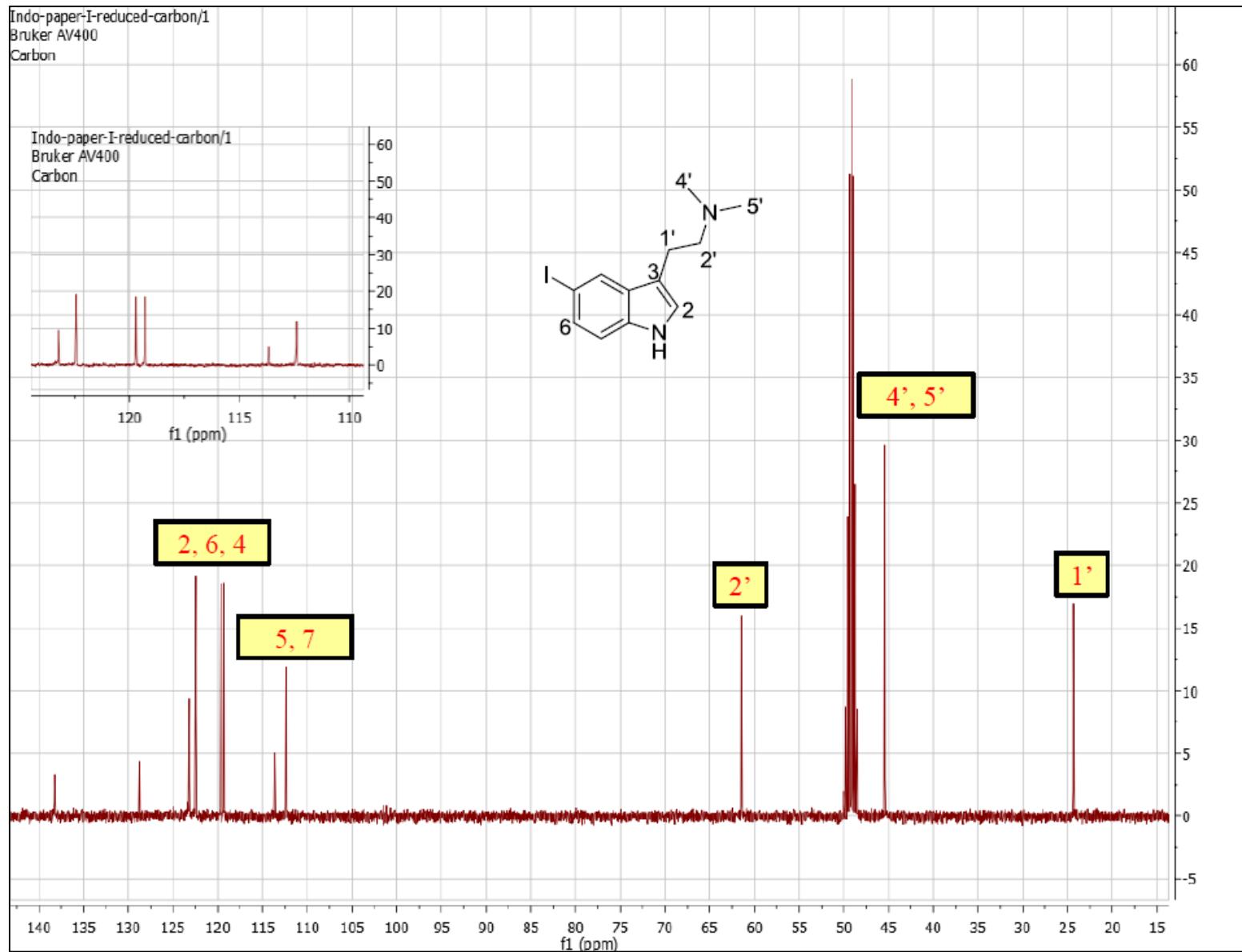


Figure 31. <sup>1</sup>H NMR spectrum of 2-(5-iodo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2e**) in methanol-d<sub>4</sub> (400 MHz)



**Figure 32.**  $^{13}\text{C}$  NMR spectrum of 2-(5-iodo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2e**) in methanol- $d_4$  (400 MHz)

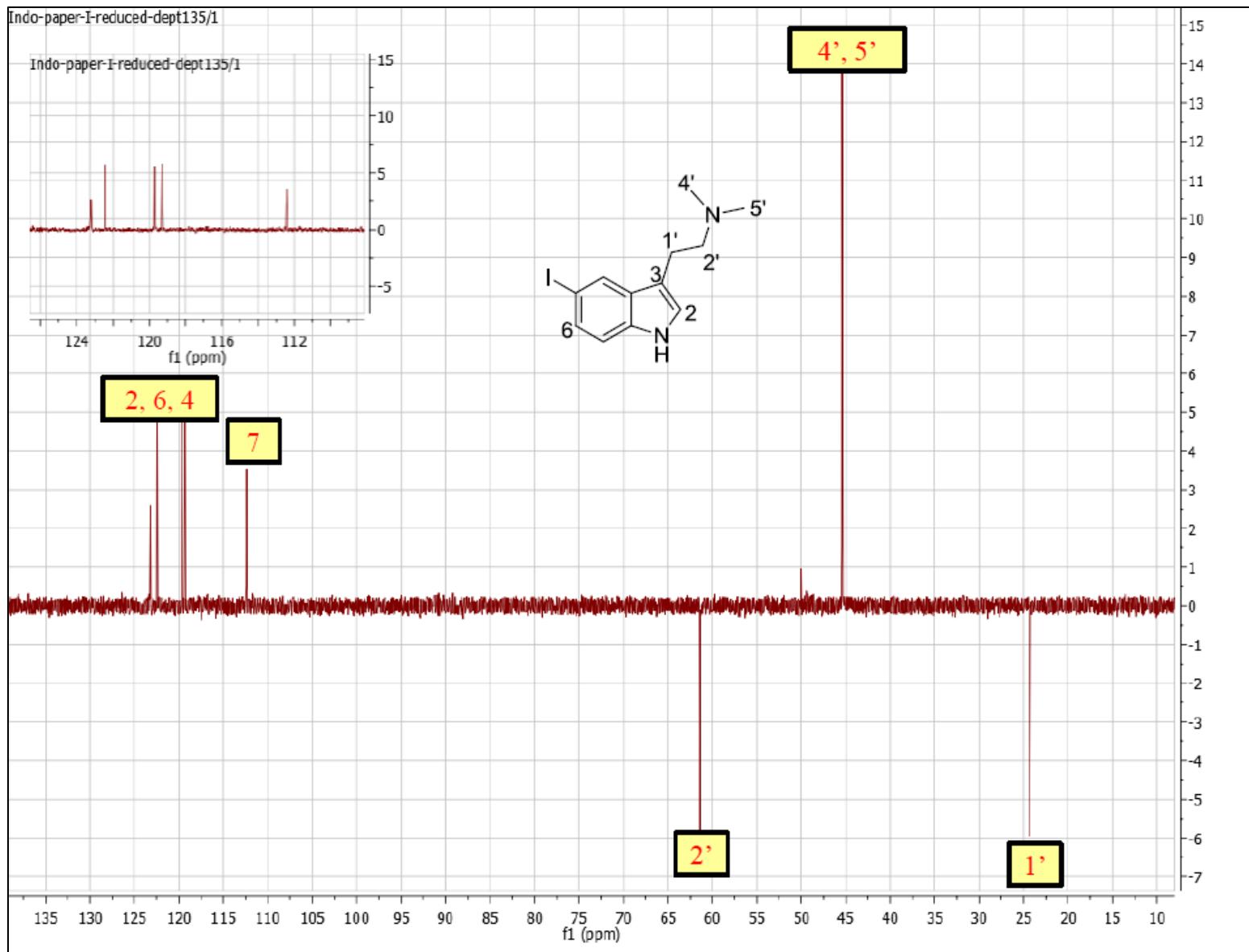


Figure 33.  $135^\circ$  DEPT spectrum of 2-(5-iodo-1*H*-indol-3-yl)-*N,N*-dimethylethanamine (**2e**) in methanol-*d*<sub>4</sub> (400 MHz)