



# High-Affinity Alkynyl Bisubstrate Inhibitors of Nicotinamide N-Methyltransferase (NNMT)

## Citation

Policarpo, R. L., L. Decultot, E. May, P. Kuzmic, S. Carlson, D. Huang, V. Chu, et al. 2019. "High-Affinity Alkynyl Bisubstrate Inhibitors of Nicotinamide N-Methyltransferase (Nnmt)." *J Med Chem* 62, no. 21: 9837-73. <https://doi.org/10.1021/acs.jmedchem.9b01238>.

## Published Version

<http://doi.org/10.1021/acs.jmedchem.9b01238>

## Permanent link

<https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37369014>

## Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Open Access Policy Articles, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#OAP>

## Share Your Story

The Harvard community has made this article openly available.  
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

# High-Affinity Alkynyl Bisubstrate Inhibitors of Nicotinamide N-Methyltransferase (NNMT)

## Supporting Information Part 2: NMR Spectra

Rocco L. Policarpio\*, Ludovic Decultot\*, Elizabeth May<sup>†</sup>, Petr Kuzmič<sup>§</sup>, Samuel Carlson<sup>†</sup>,  
Danny Huang\*, Vincent Chu\*, Brandon Wright\*, Saravanakumar Dhakshinamoorthy<sup>‡</sup>,  
Aimo Kann<sup>t</sup>\*, Shilpa Rani<sup>‡</sup>, Sreekanth Dittakavi<sup>‡</sup>, Joseph Panarese\*, Rachelle Gaudet<sup>†</sup>,  
and Matthew D. Shair\*

*\*Department of Chemistry & Chemical Biology, Harvard University, Cambridge MA 02138, USA*

*<sup>†</sup>Department of Molecular & Cellular Biology, Harvard University, Cambridge MA 02138, USA*

*<sup>§</sup>BioKin Ltd., Watertown MA 02472, USA*

*<sup>‡</sup>Jubilant Biosys Ltd., Yeshwantpur Bangalore - 560 022, Karnataka, India*

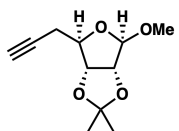
*\*Sanofi Research and Development, Industriepark Hoechst, H823, D-65926, Frankfurt am Main, Germany*

## List of NMR Spectra

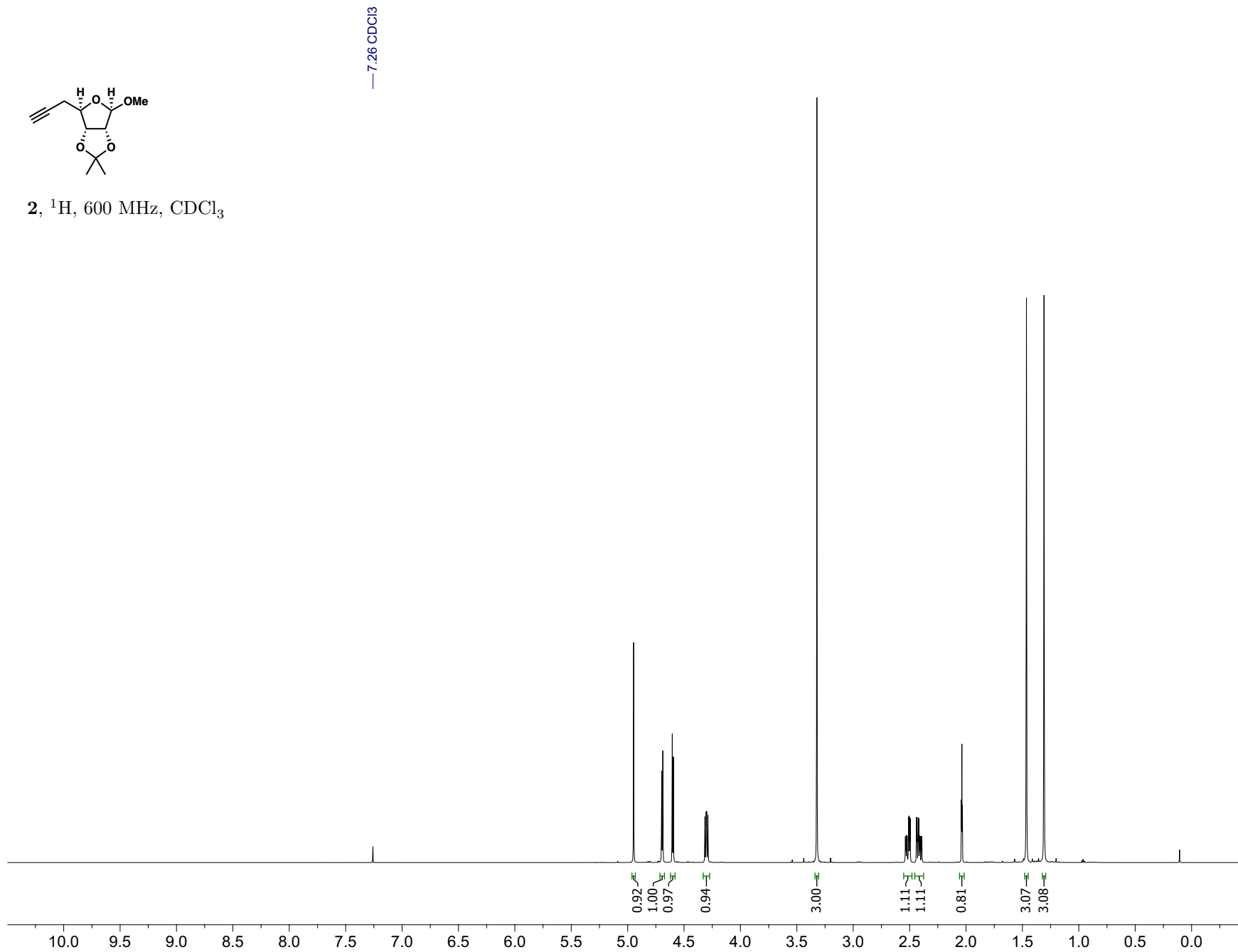
<b>2</b> NS1: Terminal Alkyne . . . . .	S5
<b>3</b> NS1: Terminal Alkene . . . . .	S7
<b>4</b> NS1: Enal . . . . .	S9
<b>5</b> NS1: Aldehyde . . . . .	S11
<b>S2</b> NS1: Phosphonate . . . . .	S13
<b>6</b> NS1: Enamide . . . . .	S15
<b>7</b> NS1: Protected Amino Acid . . . . .	S17
<b>S3</b> TIPS Cleavage Product . . . . .	S19
<b>S4</b> NS1: Triacetate . . . . .	S21
<b>8</b> NS1: Nucleoside . . . . .	S23
<b>9</b> NS1: Benzamide . . . . .	S25
<b>10</b> NS1 . . . . .	S27
<b>S6</b> Desthia-SAH: Methyl Ester . . . . .	S29
<b>S7</b> Desthia-SAH: Aldehyde . . . . .	S31
<b>S8</b> Desthia-SAH: Enamide . . . . .	S33
<b>S9</b> Desthia-SAH: Protected Amino Acid . . . . .	S35
<b>S10</b> Desthia-SAH: Triacetate . . . . .	S37
<b>S11</b> Desthia-SAH: Nucleoside . . . . .	S39
<b>11</b> Desthia-SAH . . . . .	S41
<b>12</b> NS1-Alkyne . . . . .	S43
<b>S12</b> NS1-Phenyl: Benzamide . . . . .	S45
<b>13</b> NS1-Phenyl . . . . .	S47
<b>S13</b> NS1-6'Epi: Aldehyde . . . . .	S49
<b>S14</b> NS1-6'Epi: Enamide . . . . .	S51
<b>S15</b> NS1-6'Epi: Protected Amino Acid . . . . .	S53
<b>S16</b> NS1-6'Epi: Alkyne . . . . .	S55
<b>S17</b> NS1-6'Epi: Triacetate . . . . .	S57
<b>S18</b> NS1-6'Epi: Nucleoside . . . . .	S59
<b>S19</b> NS1-6'Epi: Benzamide . . . . .	S61
<b>14</b> NS1-6'Epi . . . . .	S63
<b>15</b> NS1-Alkane . . . . .	S65
<b>16</b> NS1-Alkane 6'Epi . . . . .	S67
<b>S21</b> Mini-NS1: Alcohol . . . . .	S69
<b>S22</b> Mini-NS1: Aldehyde . . . . .	S71
<b>S23</b> Mini-NS1: Alkyne . . . . .	S73
<b>S24</b> Mini-NS1: Triacetate . . . . .	S75
<b>S25</b> Mini-NS1: Nucleoside . . . . .	S77
<b>S26</b> Mini-NS1: Benzamide . . . . .	S79
<b>17</b> Mini-NS1 . . . . .	S81
<b>S28</b> NS1-Cyclopropyl: Alcohol . . . . .	S83
<b>S29</b> NS1-Cyclopropyl: Aldehyde . . . . .	S85
<b>S30</b> NS1-Cyclopropyl: Alkyne . . . . .	S87

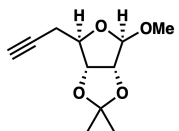
<b>S31</b> NS1-Cyclopropyl: Triacetate . . . . .	S89
<b>S32</b> NS1-Cyclopropyl: Nucleoside . . . . .	S91
<b>S33</b> NS1-Cyclopropyl: Benzamide . . . . .	S93
<b>18</b> NS1-Cyclopropyl . . . . .	S95
<b>S34</b> NS1-Desadenine: Benzamide . . . . .	S97
<b>S35</b> NS1-Desadenine: 1,2-Diol . . . . .	S99
<b>19</b> NS1-Desadenine . . . . .	S101
<b>S36</b> NS1-Carboxylic Acid: Enoate . . . . .	S103
<b>S37</b> NS1-Carboxylic Acid: Methyl Ester . . . . .	S105
<b>S38</b> NS1-Carboxylic Acid: Alkyne . . . . .	S107
<b>S39</b> NS1-Carboxylic Acid: Triacetate . . . . .	S109
<b>S40</b> NS1-Carboxylic Acid: Nucleoside . . . . .	S111
<b>S41</b> NS1-Carboxylic Acid: Benzamide . . . . .	S113
<b>20</b> NS1-Carboxylic Acid . . . . .	S115
<b>S42</b> NS1-Amine: Nitro-olefin . . . . .	S117
<b>S43</b> NS1-Amine: Trifluoroacetamide . . . . .	S119
<b>S44</b> NS1-Amine: Alkyne . . . . .	S121
<b>S45</b> NS1-Amine: Triacetate . . . . .	S123
<b>S46</b> NS1-Amine: Nucleoside . . . . .	S125
<b>S47</b> NS1-Amine: Benzamide . . . . .	S127
<b>21</b> NS1-Amine . . . . .	S129
<b>22</b> NS1-Amide . . . . .	S131
<b>S48</b> NS1-MethylEster: Carbamate . . . . .	S133
<b>S49</b> NS1-MethylEster: Triacetate . . . . .	S135
<b>S50</b> NS1-MethylEster: Nucleoside . . . . .	S137
<b>S51</b> NS1-MethylEster: Benzamide . . . . .	S139
<b>23</b> NS1-MethylEster . . . . .	S141
<b>24</b> NS1-AminoAmide . . . . .	S143
<b>S52</b> NS1-Urea: TIPS alkyne Alcohol . . . . .	S145
<b>S53</b> NS1-Urea: Alkynyl Alcohol . . . . .	S147
<b>S54</b> NS1-Urea: Nosyl Amine . . . . .	S149
<b>S55</b> NS1-Urea: Triacetate . . . . .	S151
<b>S56</b> NS1-Urea: Nucleoside . . . . .	S153
<b>S57</b> NS1-Urea: Benzamide . . . . .	S155
<b>S58</b> NS1-Urea: Urea . . . . .	S157
<b>25</b> NS1-Urea . . . . .	S159
<b>S59</b> Homo-NS1: Nitrile . . . . .	S161
<b>S61</b> Homo-NS1: Enamide . . . . .	S163
<b>S62</b> Homo-NS1: Protected Amino Acid . . . . .	S165
<b>S63</b> Homo-NS1: Alkyne . . . . .	S167
<b>S64</b> Homo-NS1: Triacetate . . . . .	S169
<b>S65</b> Homo-NS1: Nucleoside . . . . .	S171
<b>S66</b> Homo-NS1: Benzamide . . . . .	S173

<b>26</b> Homo-NS1 . . . . .	S175
<b>S67</b> NS1- <i>p</i> Benzamide: <i>p</i> -Benzamide . . . . .	S177
<b>27</b> NS1- <i>p</i> Benzamide . . . . .	S179
<b>S68</b> NS1- <i>o</i> Benzamide: <i>o</i> -Benzamide . . . . .	S181
<b>28</b> NS1- <i>o</i> Benzamide . . . . .	S183
<b>S69</b> NS1-Sulfonamide: Benzenesulfonamide . . . . .	S185
<b>29</b> NS1-Sulfonamide . . . . .	S187
<b>S70</b> NS1-12'F: 2-Fluoro-5-iodobenzamide . . . . .	S189
<b>S71</b> NS1-12'F: Fluorobenzamide . . . . .	S191
<b>30</b> NS1-12'F . . . . .	S193
<b>S72</b> NS1-12'Me: 5-Iodo-2-methylbenzamide . . . . .	S195
<b>S73</b> NS1-12'Me: Methylbenzamide . . . . .	S197
<b>31</b> NS1-12'Me . . . . .	S199
<b>S74</b> NS1-12'CF <sub>3</sub> : 5-Iodo-2-(trifluoromethyl)benzamide . . . . .	S201
<b>S75</b> NS1-12'CF <sub>3</sub> : (Trifluoromethyl)benzamide . . . . .	S203
<b>32</b> NS1-12'CF <sub>3</sub> . . . . .	S205
<b>S76</b> NS1-12'Cl: 2-Chloro-5-iodobenzamide . . . . .	S207
<b>S77</b> NS1-12'Cl: Chlorobenzamide . . . . .	S209
<b>33</b> NS1-12'Cl . . . . .	S211
<b>S78</b> NS1-Benzolactam6: Dihydro Isoquinolinone . . . . .	S213
<b>34</b> NS1-Benzolactam6 . . . . .	S215
<b>35</b> NS1-Benzolactam5 . . . . .	S217
<b>S80</b> NS1-Methylenedioxy: Iodobenzamide . . . . .	S219
<b>S81</b> NS1-Methylenedioxy: Benzamide . . . . .	S221
<b>36</b> NS1-Methylenedioxy . . . . .	S223
<b>S82</b> NS1-Pyr10': Picolinamide . . . . .	S225
<b>37</b> NS1-Pyr10' . . . . .	S227
<b>S83</b> NS1-Pyr12': Picolinamide . . . . .	S229
<b>38</b> NS1-Pyr12' . . . . .	S231
<b>S84</b> NS1-Pyr13': Nicotinamide . . . . .	S233
<b>39</b> NS1-Pyr13' . . . . .	S235
<b>S85</b> NS1-Pyr14': Isonicotinamide . . . . .	S237
<b>40</b> NS1-Pyr14' . . . . .	S239
<b>S86</b> NS1-Aminonaphthalene: Naphthalene . . . . .	S241
<b>41</b> NS1-Aminonaphthalene . . . . .	S243

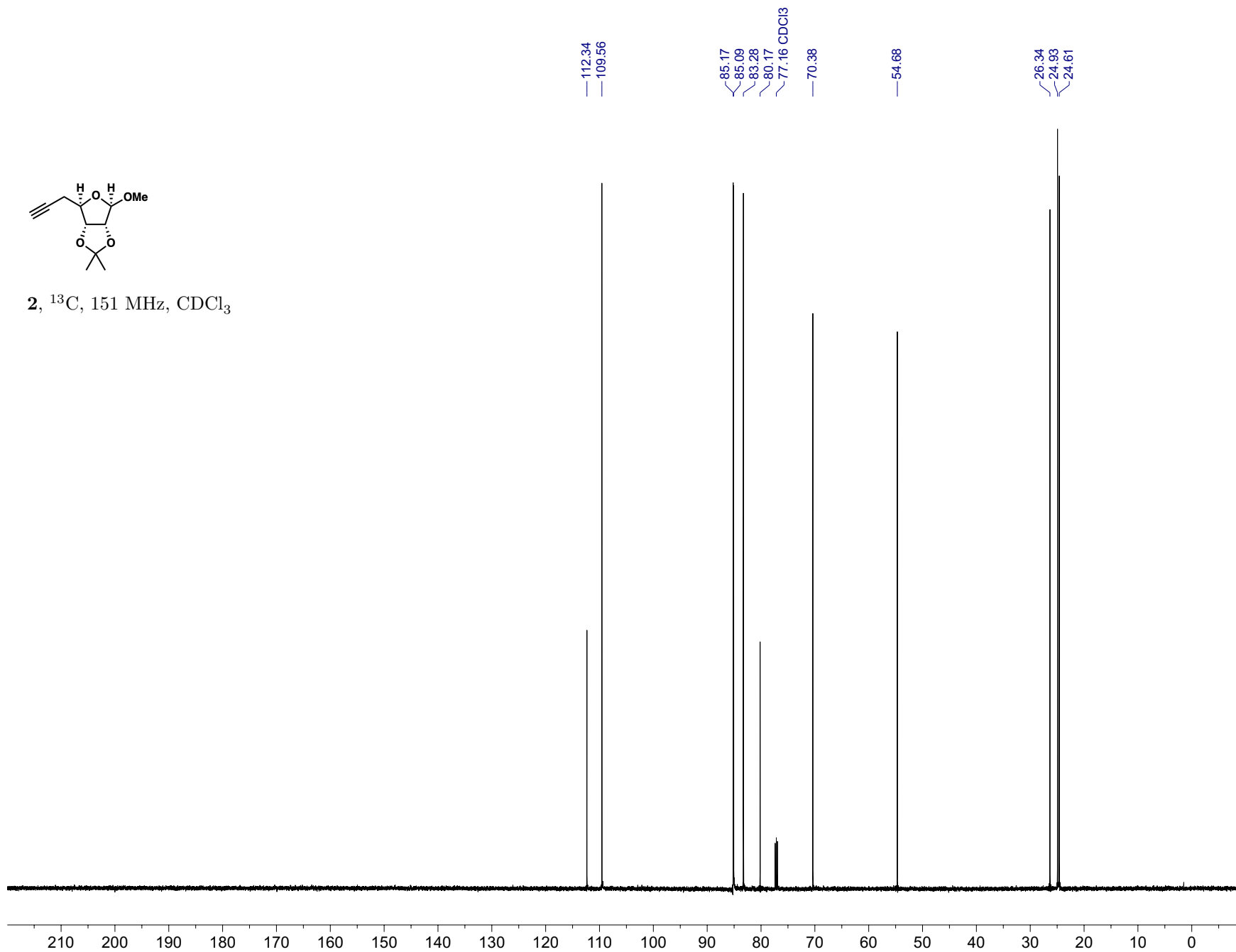


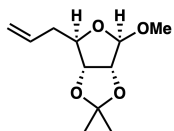
2,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$



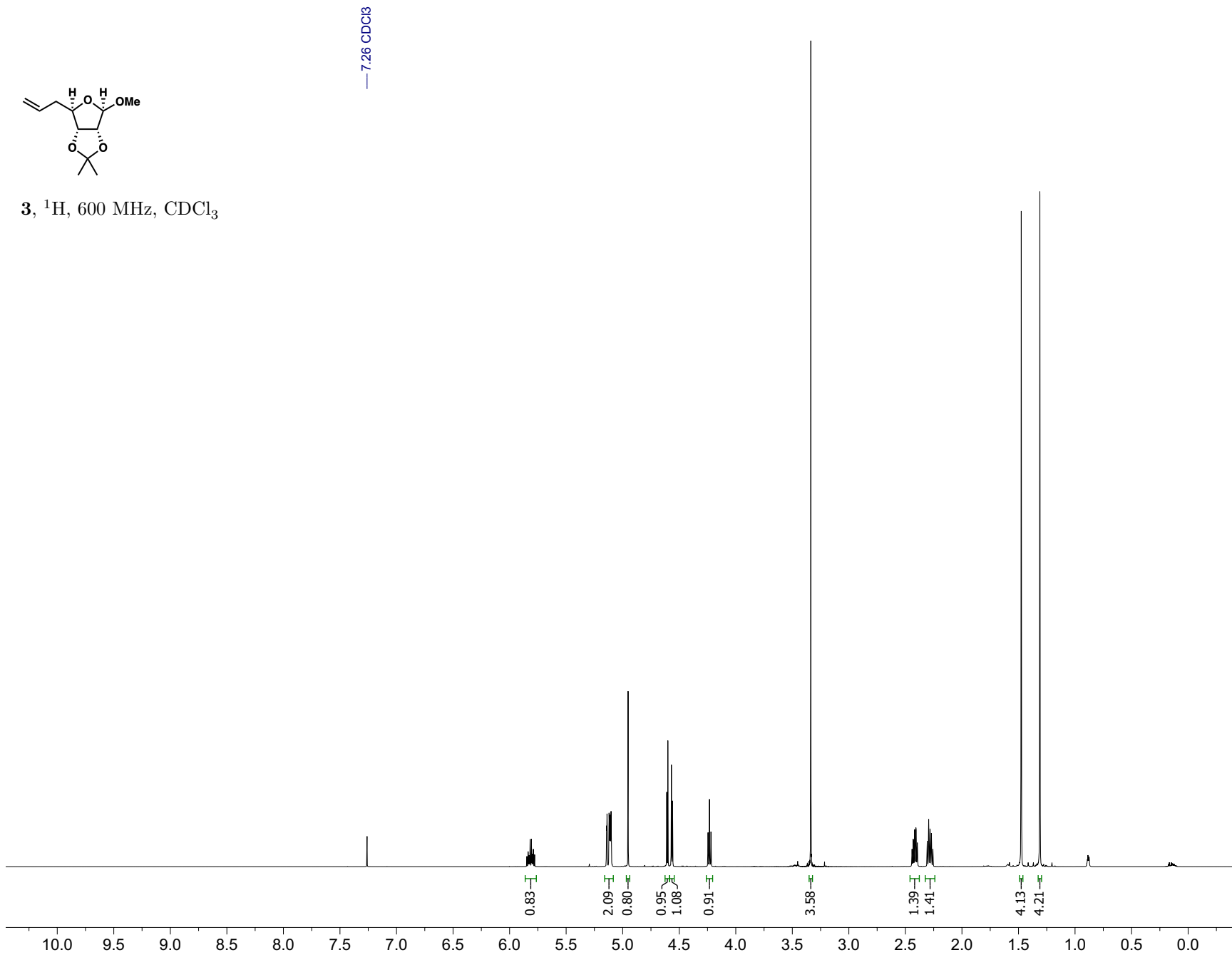


**2**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

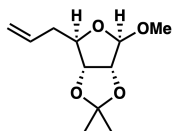




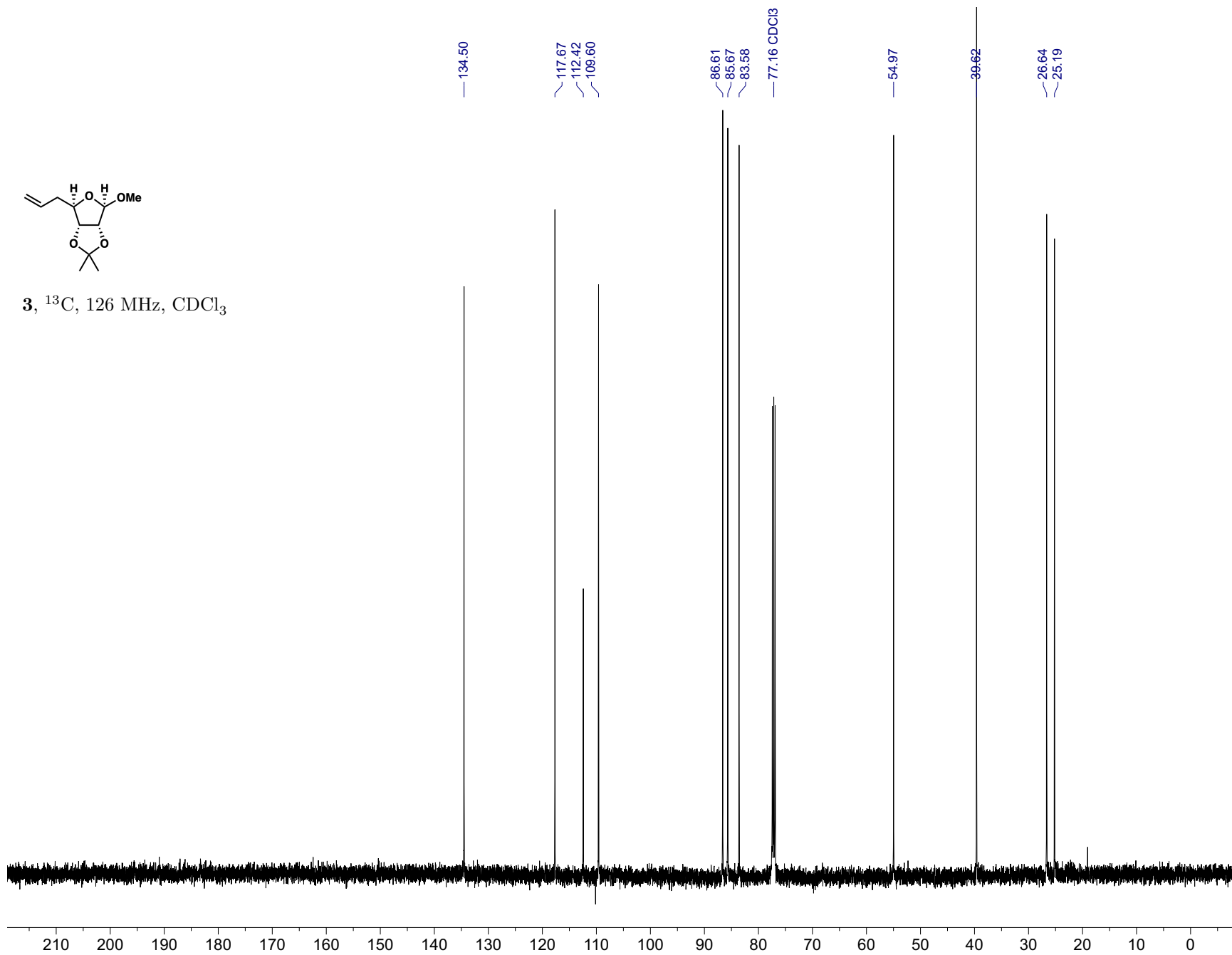
**3**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

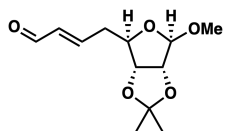






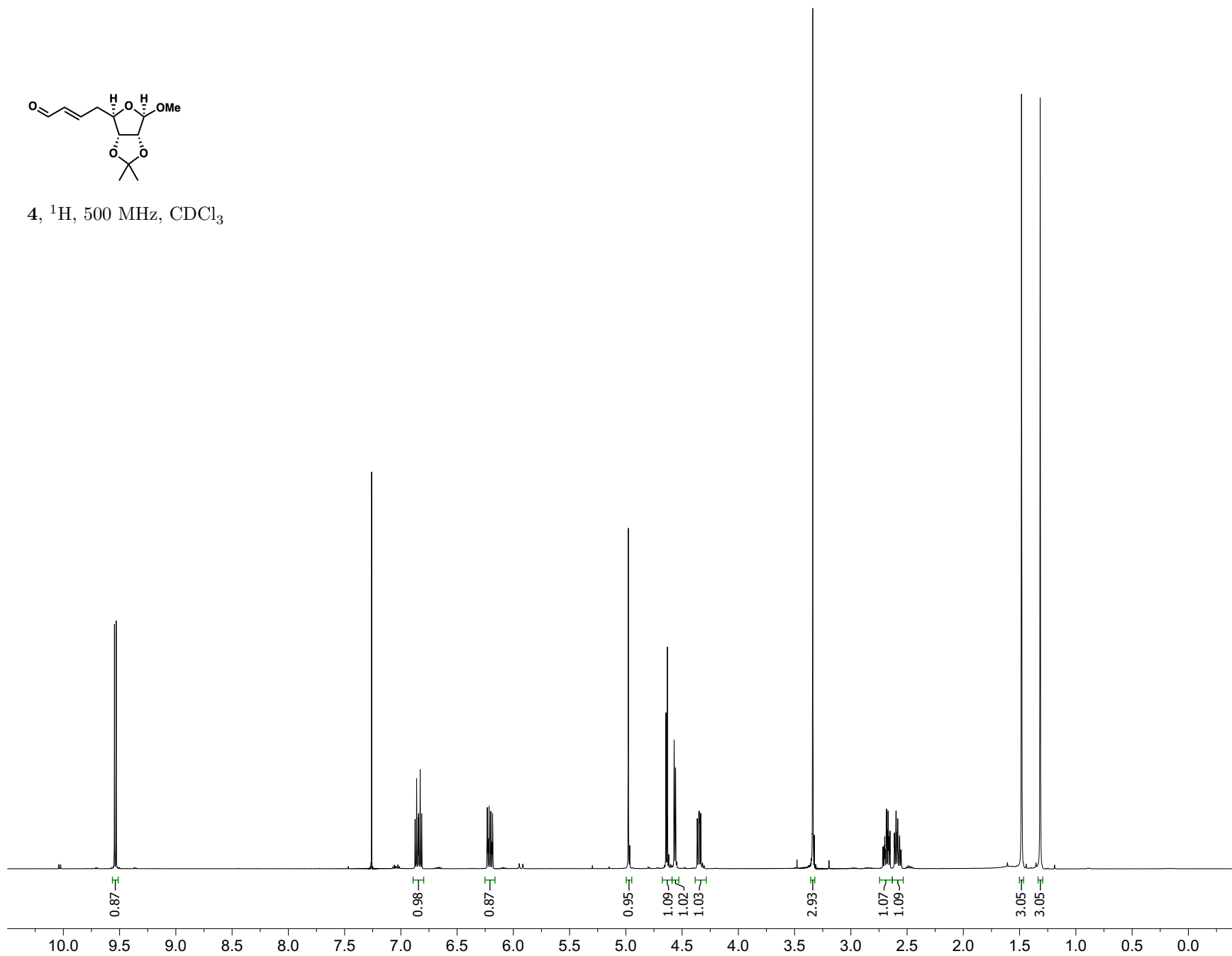
**3**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



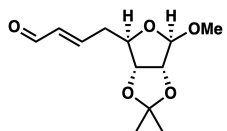


4,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

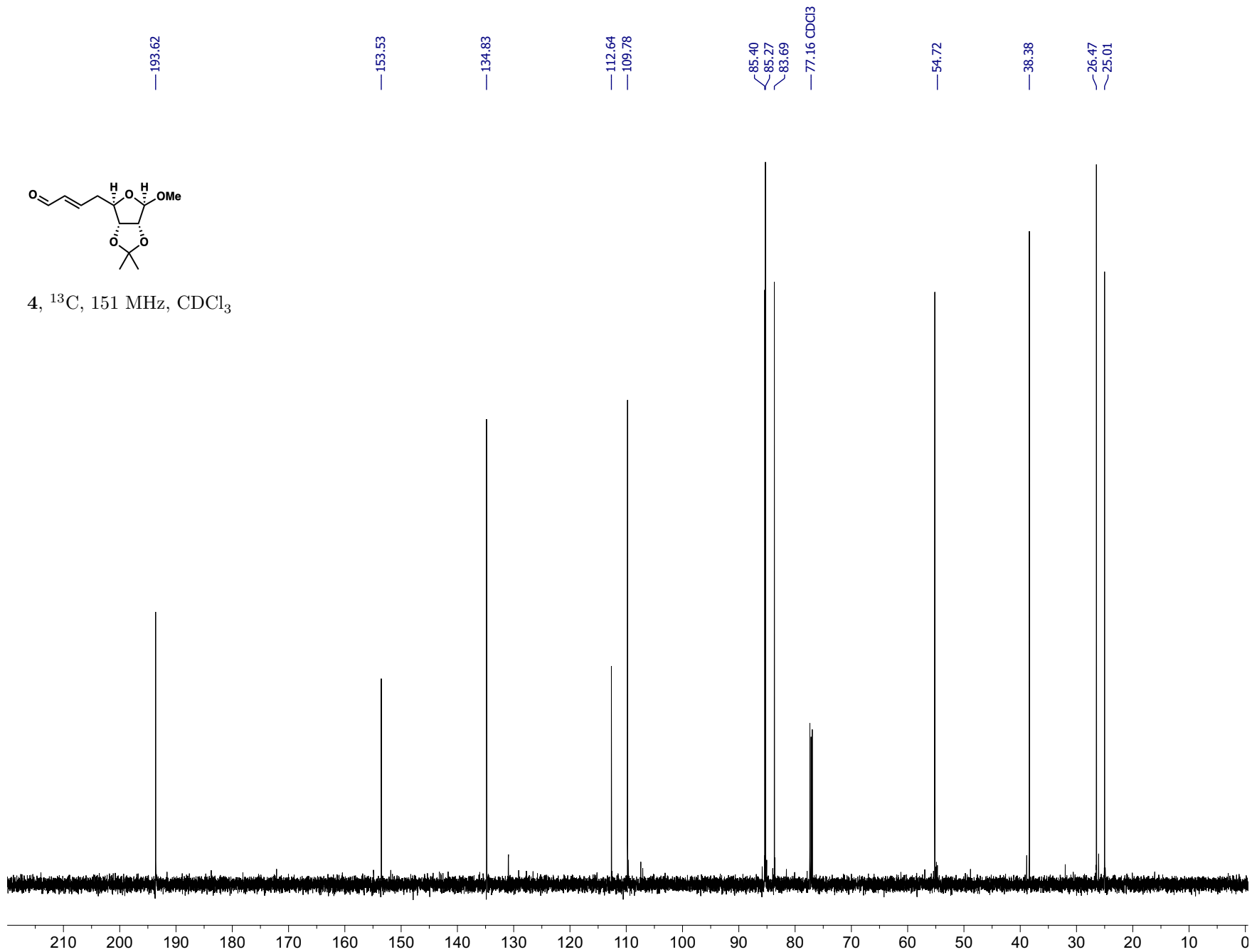
69



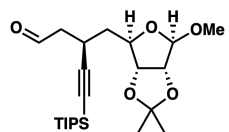
S10



4,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

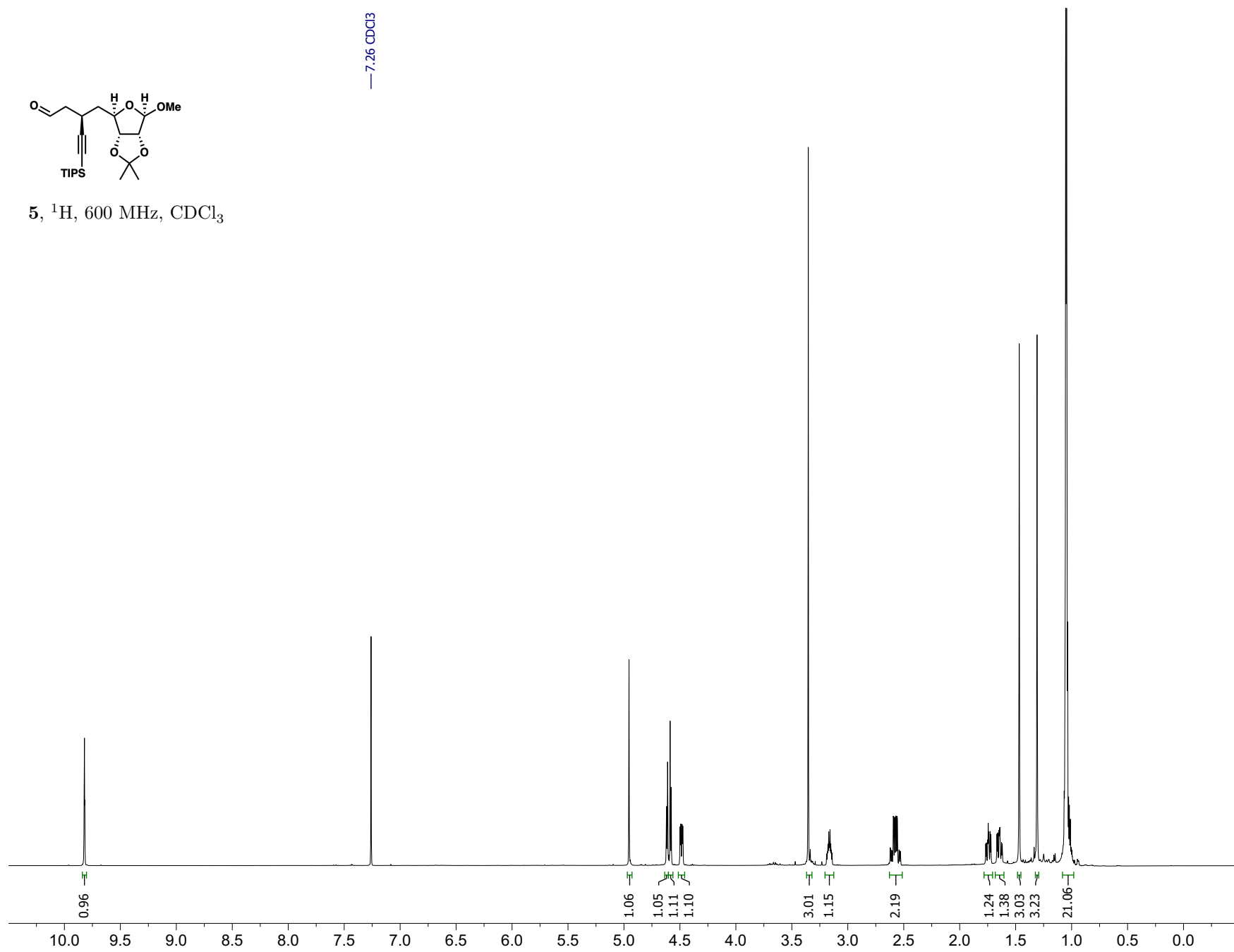


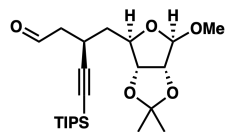
—7.26 CDCl<sub>3</sub>



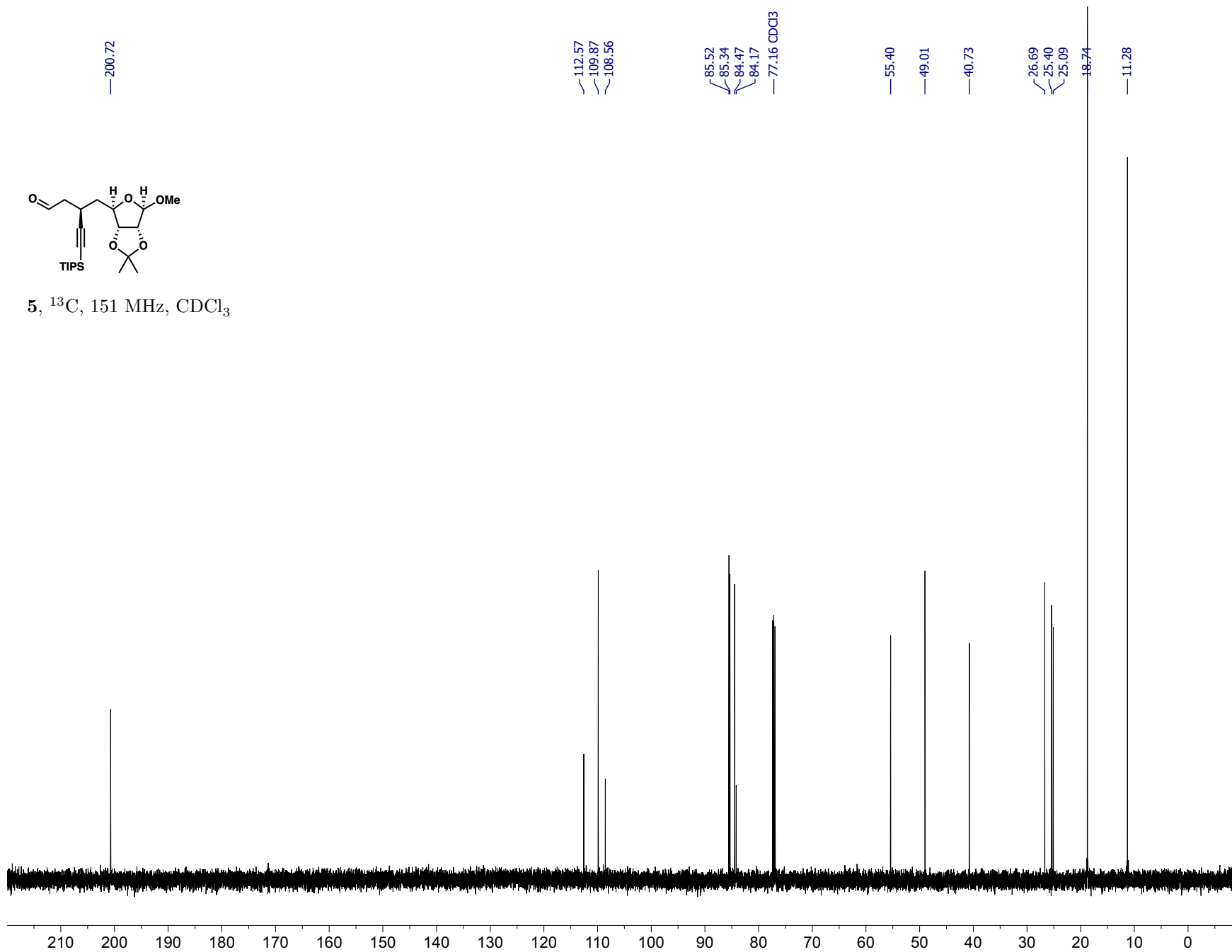
5, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

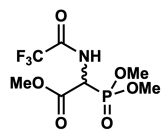
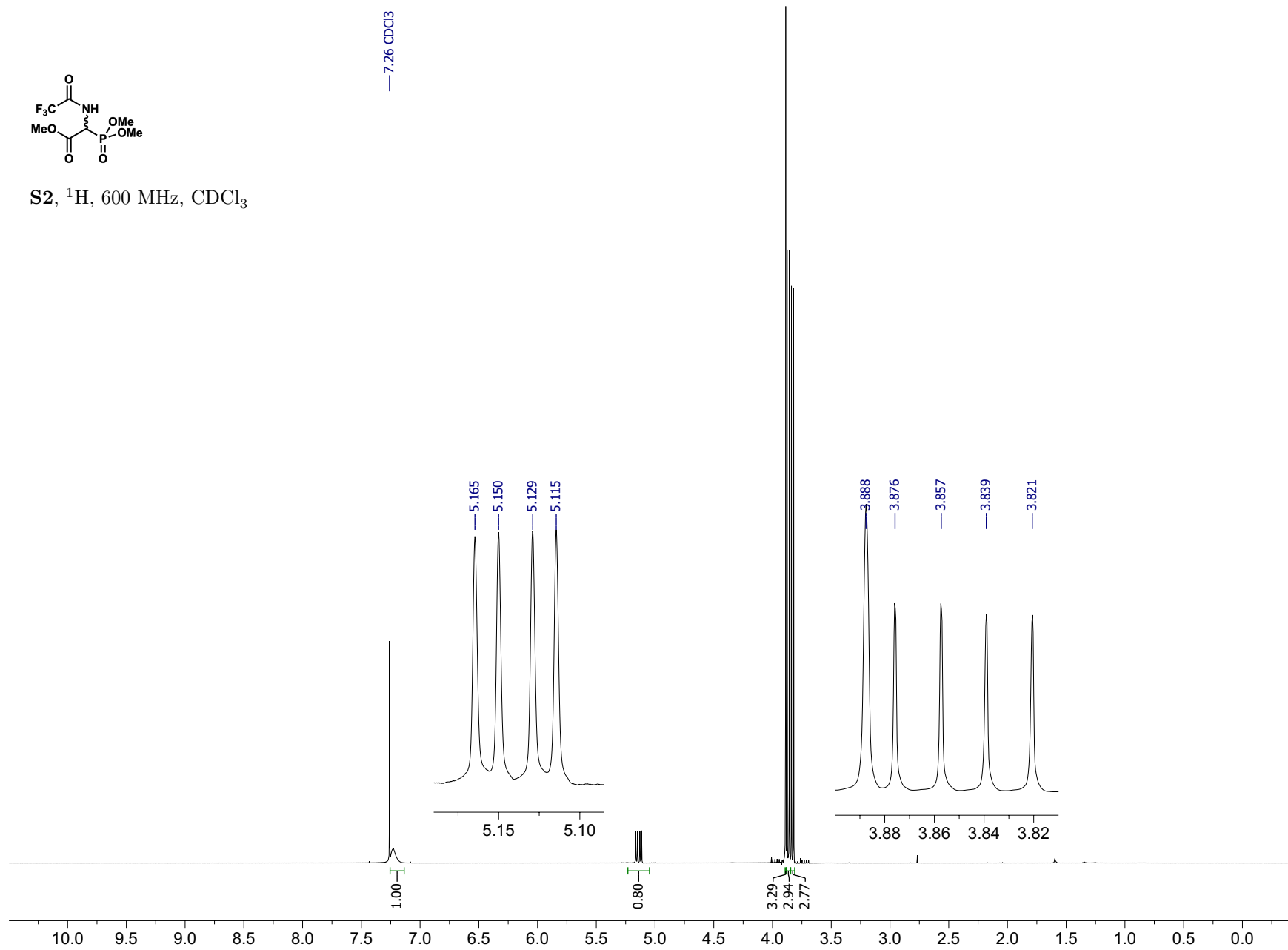
TTS

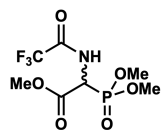
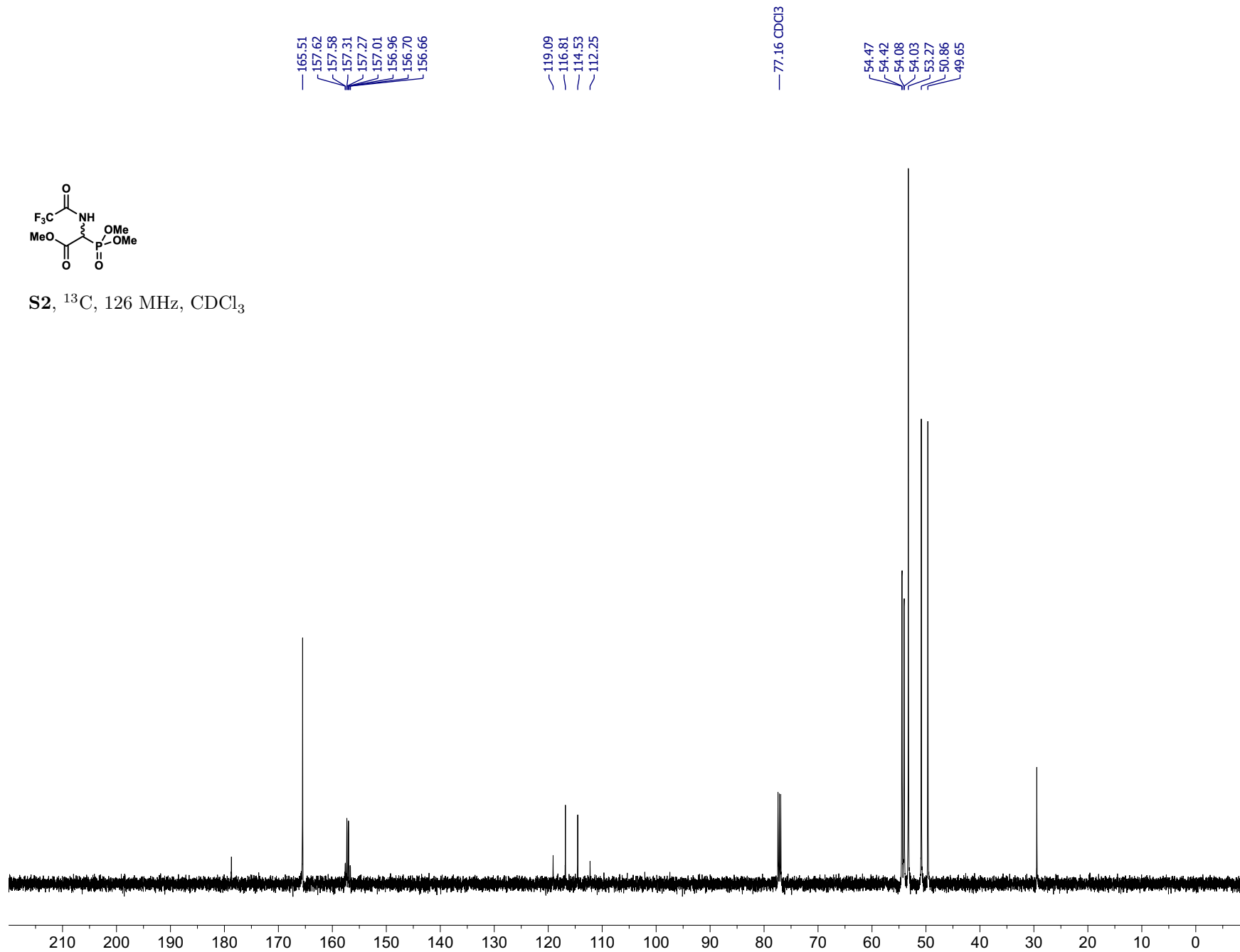


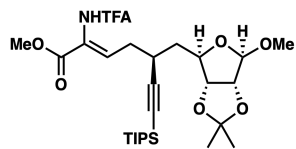


**5**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

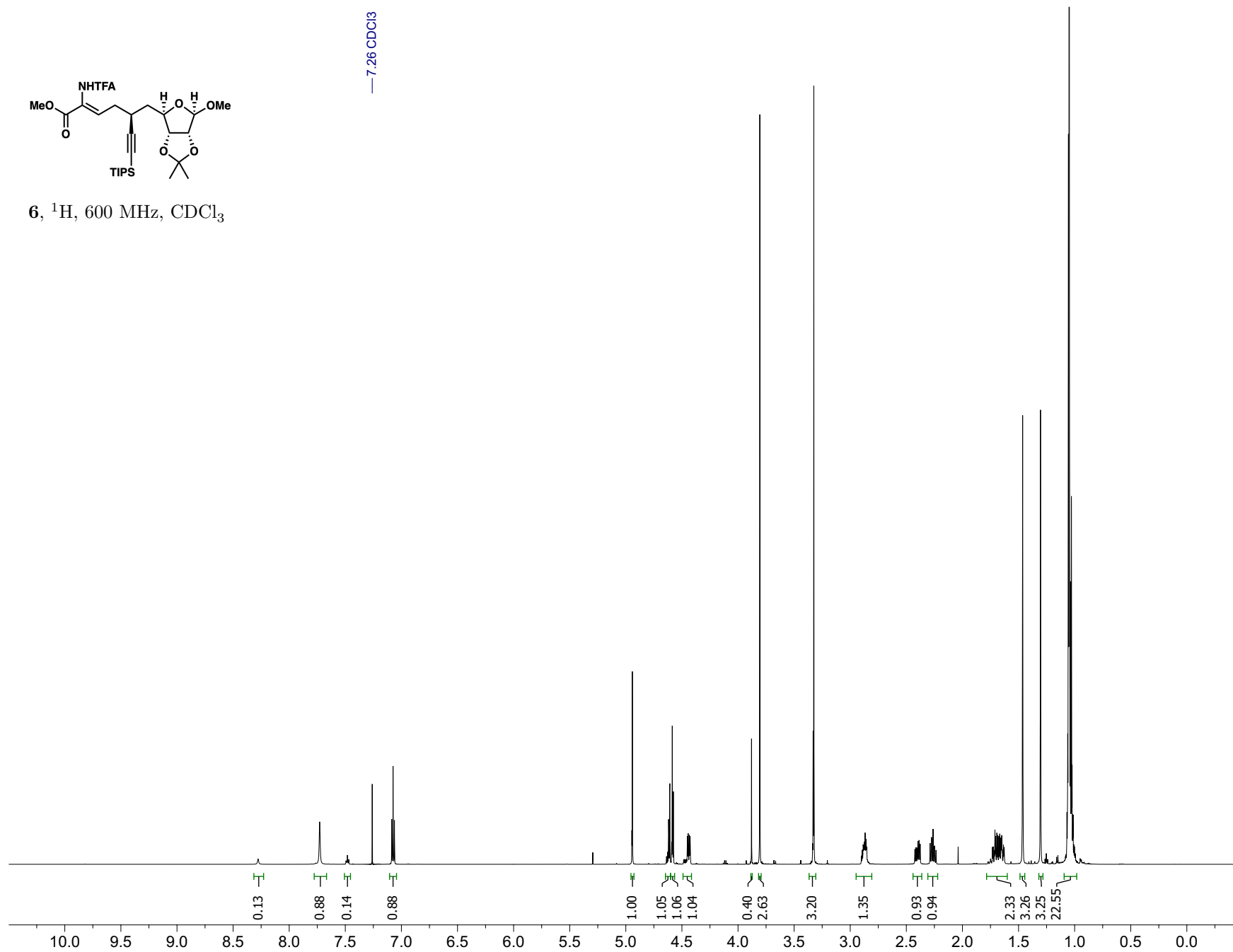


S2,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ 

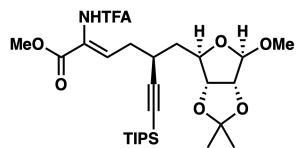
**S2**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$ 



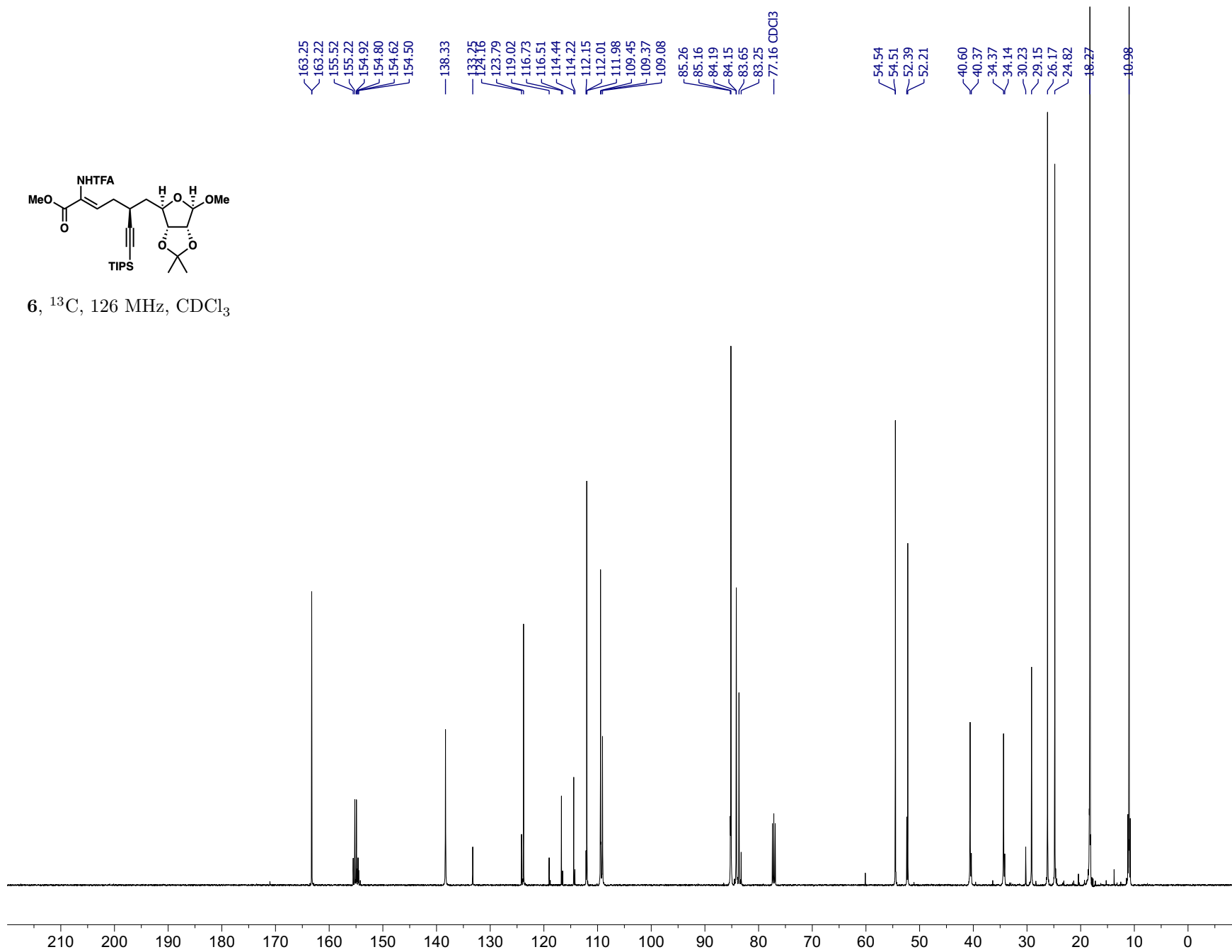
**6**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

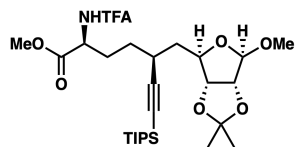




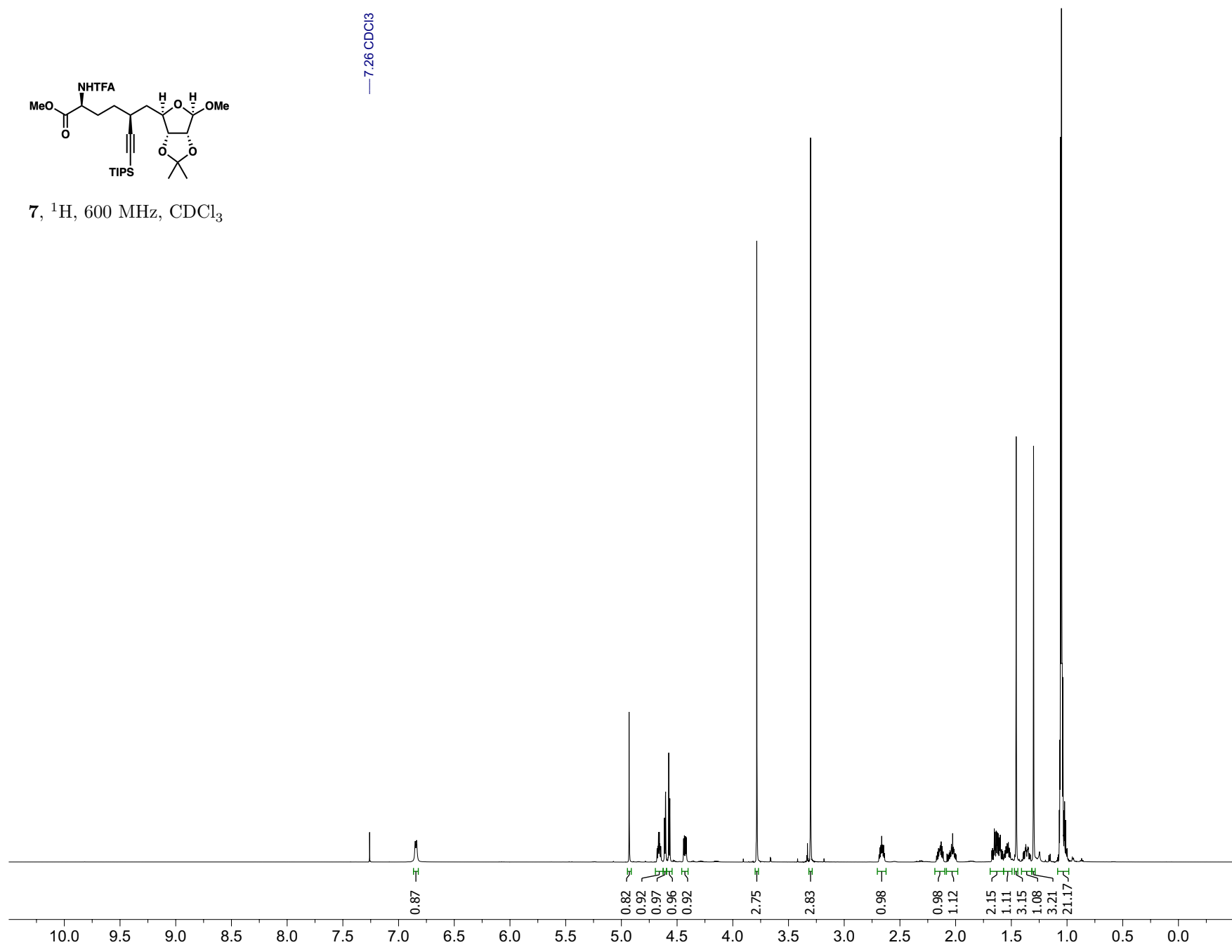


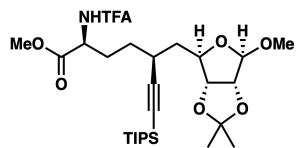
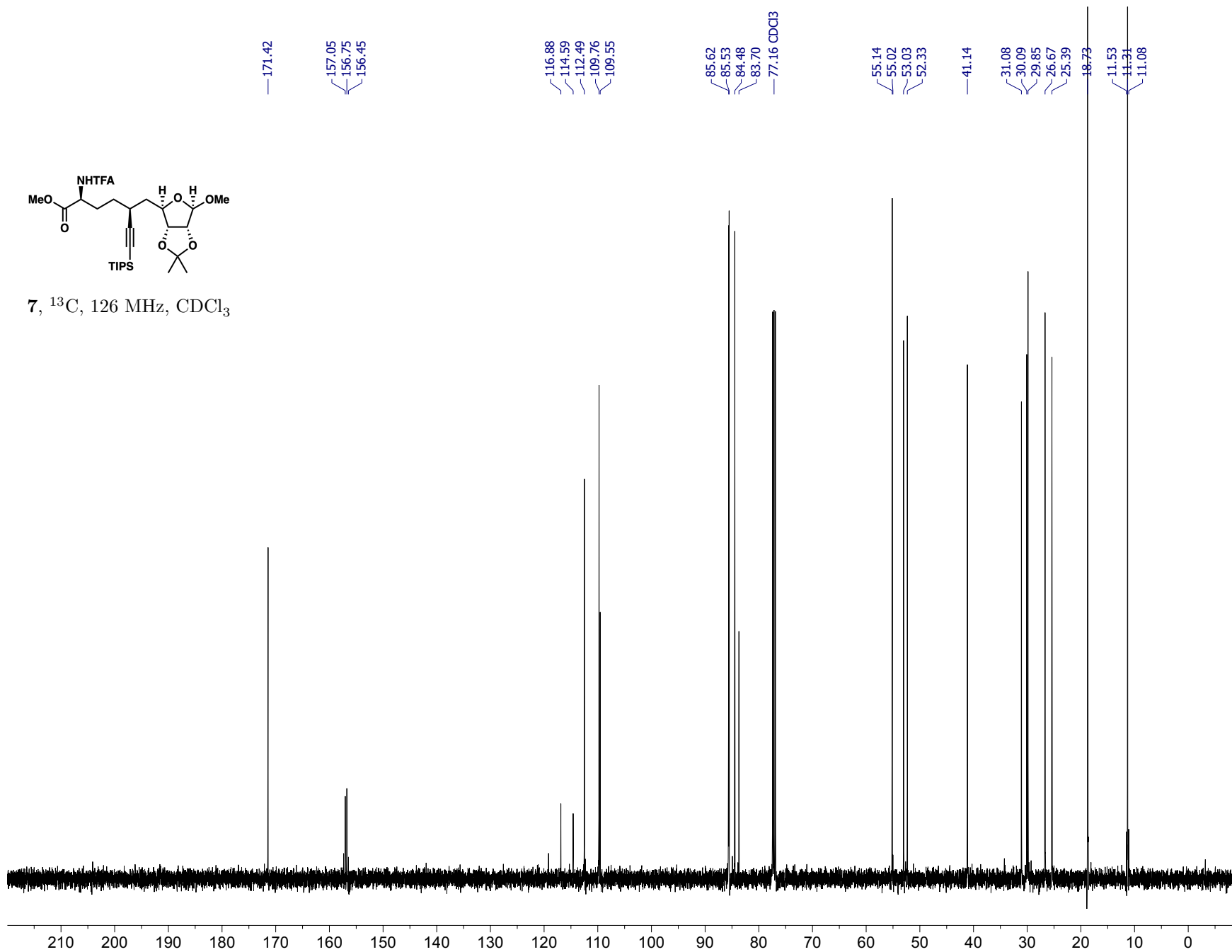
**6**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

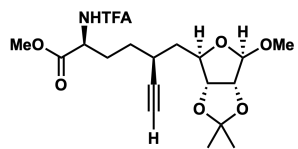




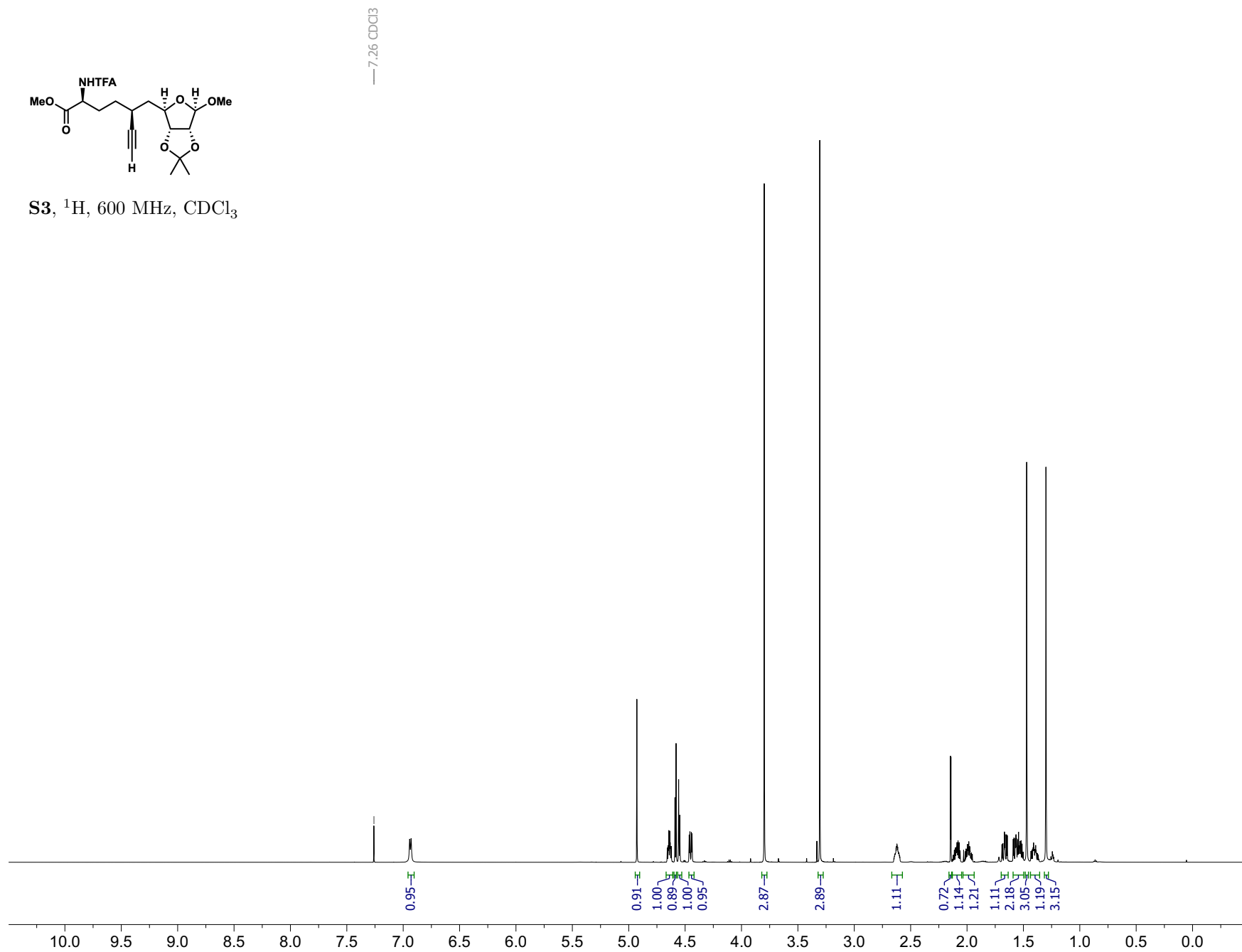
7, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

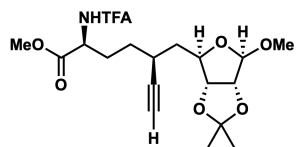


7,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$ 

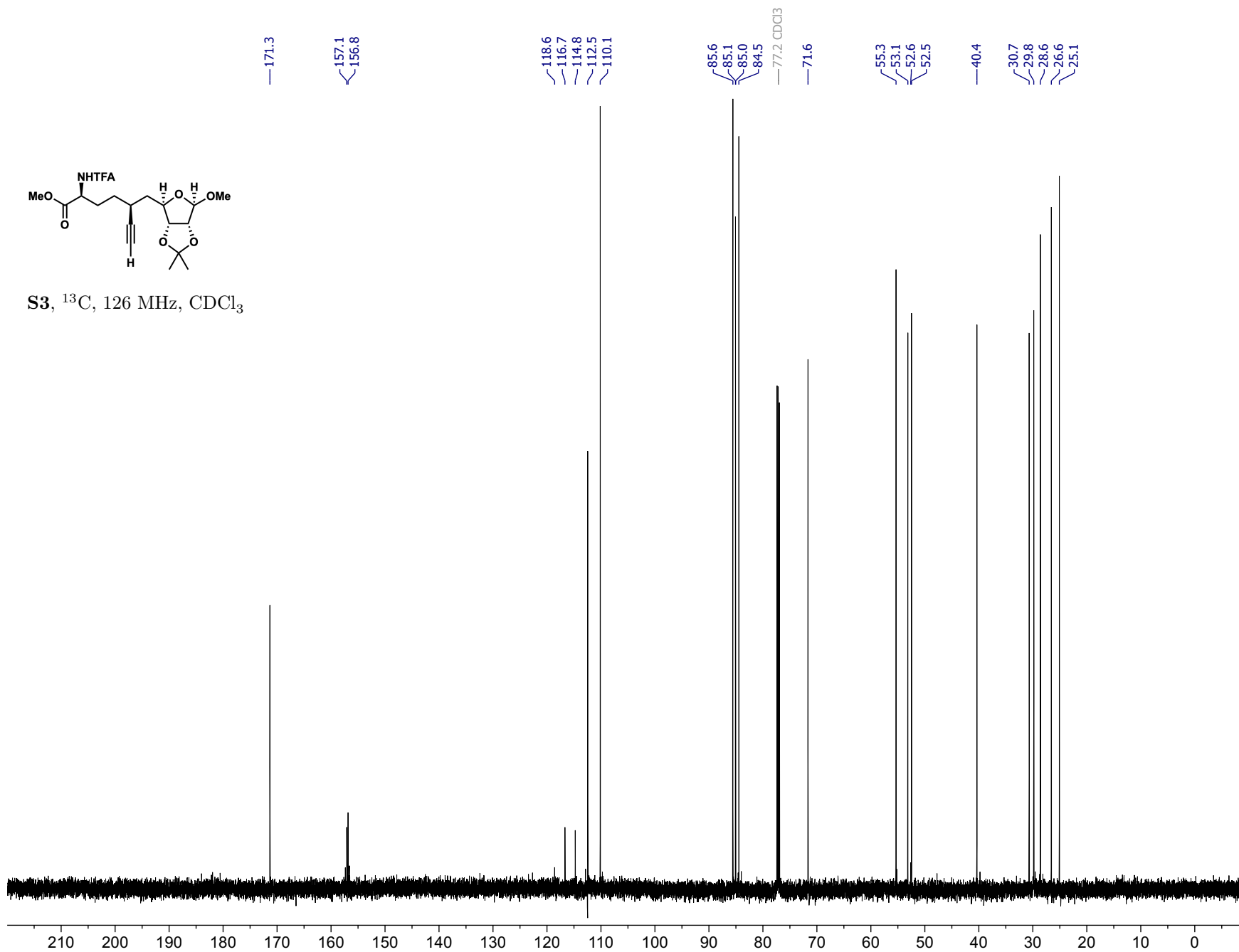


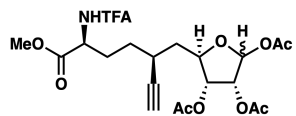
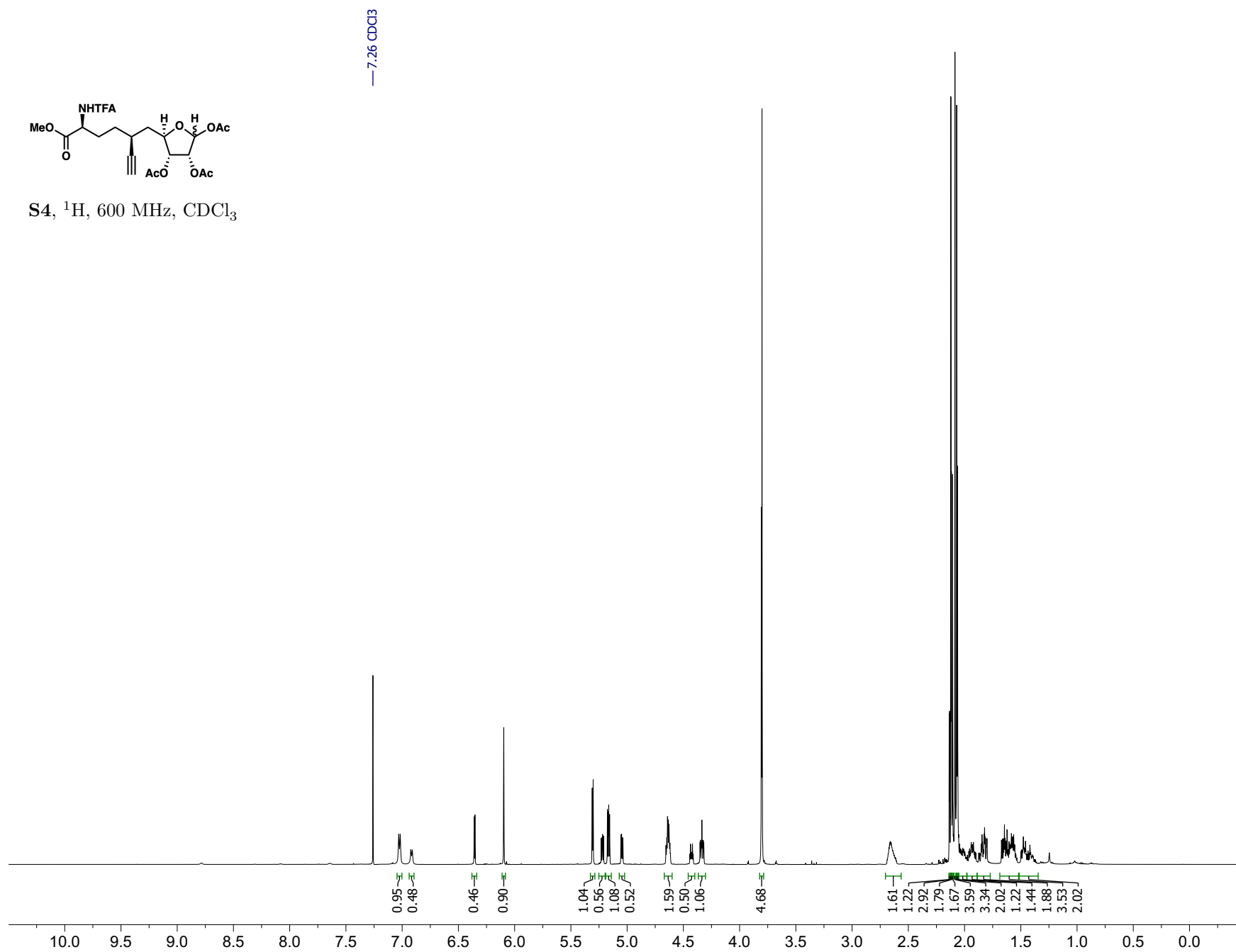
S3, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

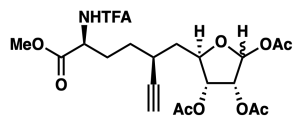




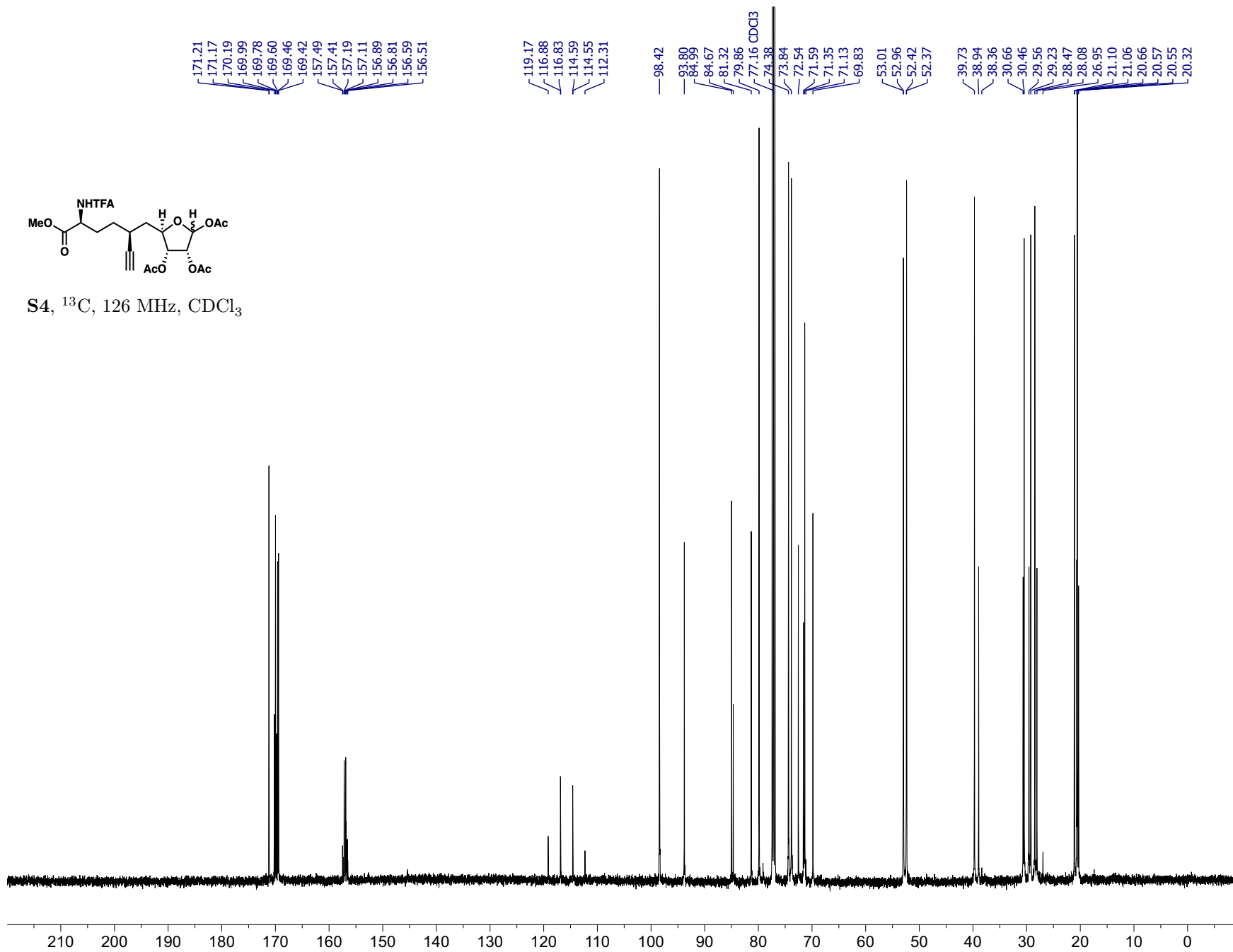
**S3**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

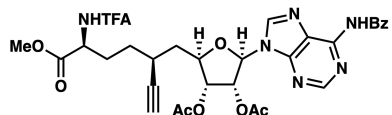


S4,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ — 7.26  $\text{CDCl}_3$



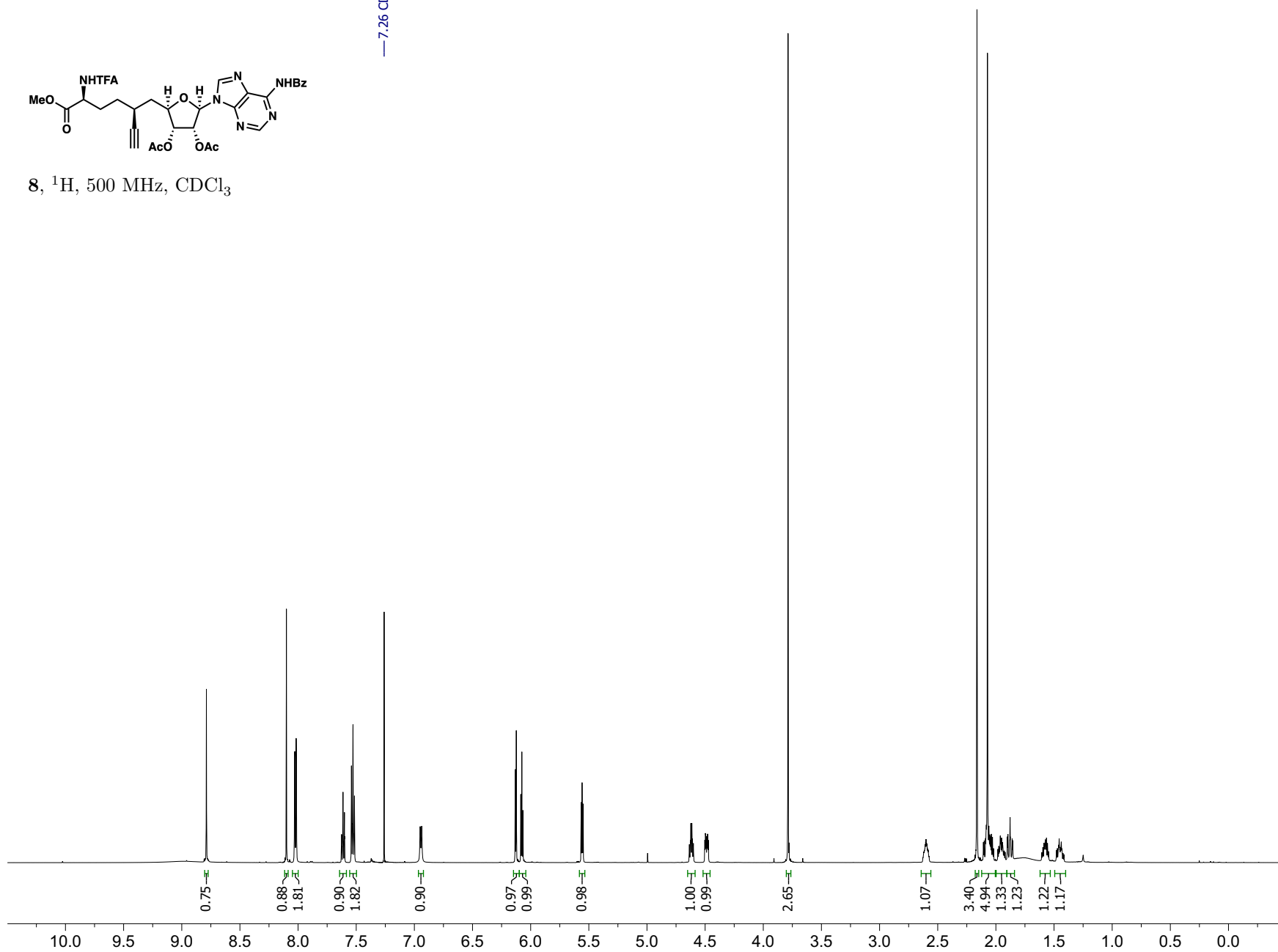
S4,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



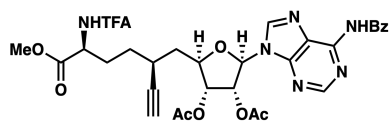


8, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>

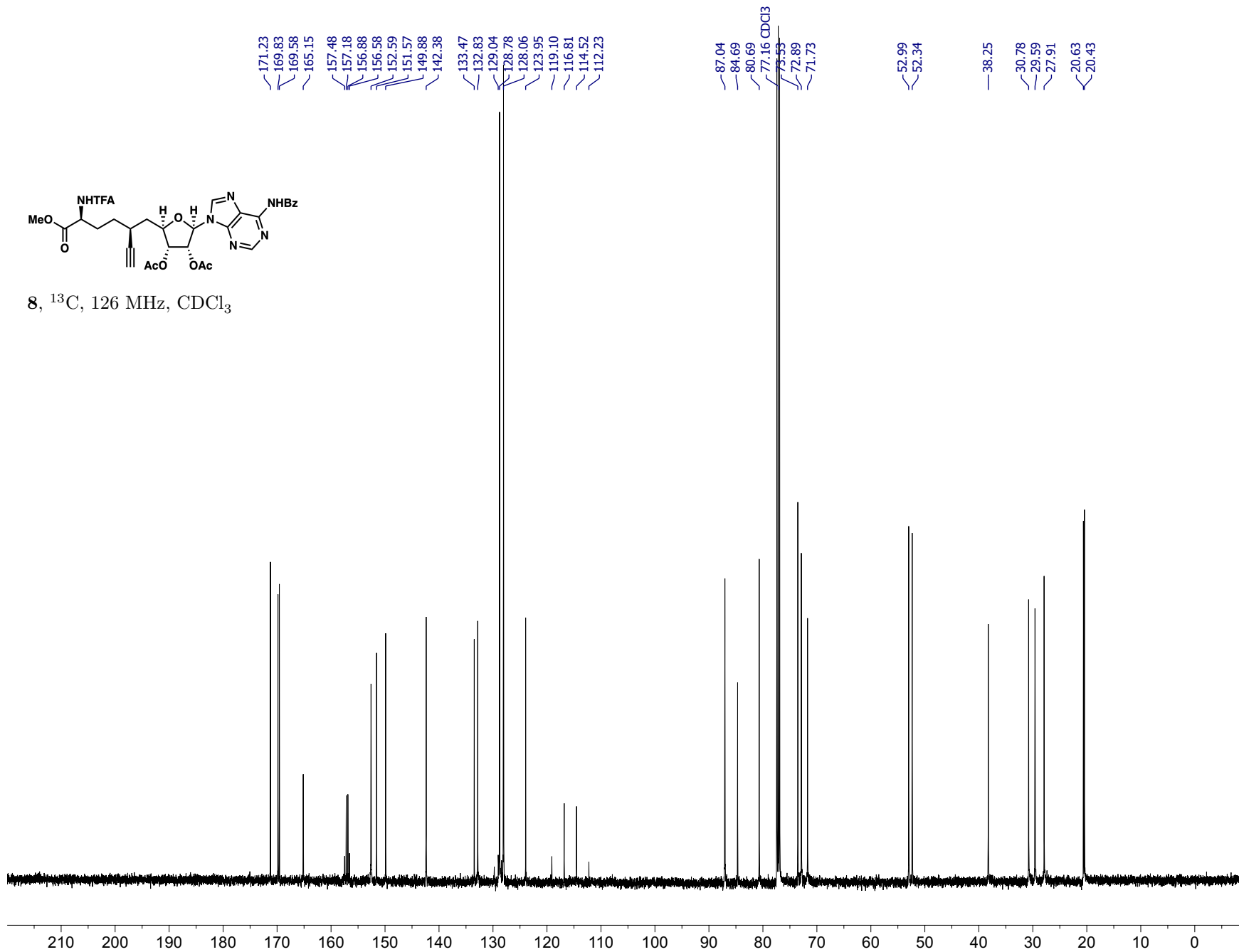
— 7.26 CDCl<sub>3</sub>

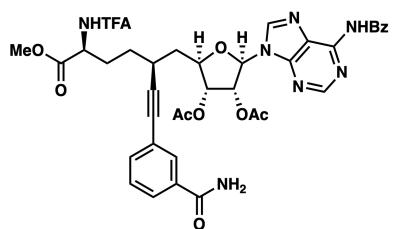






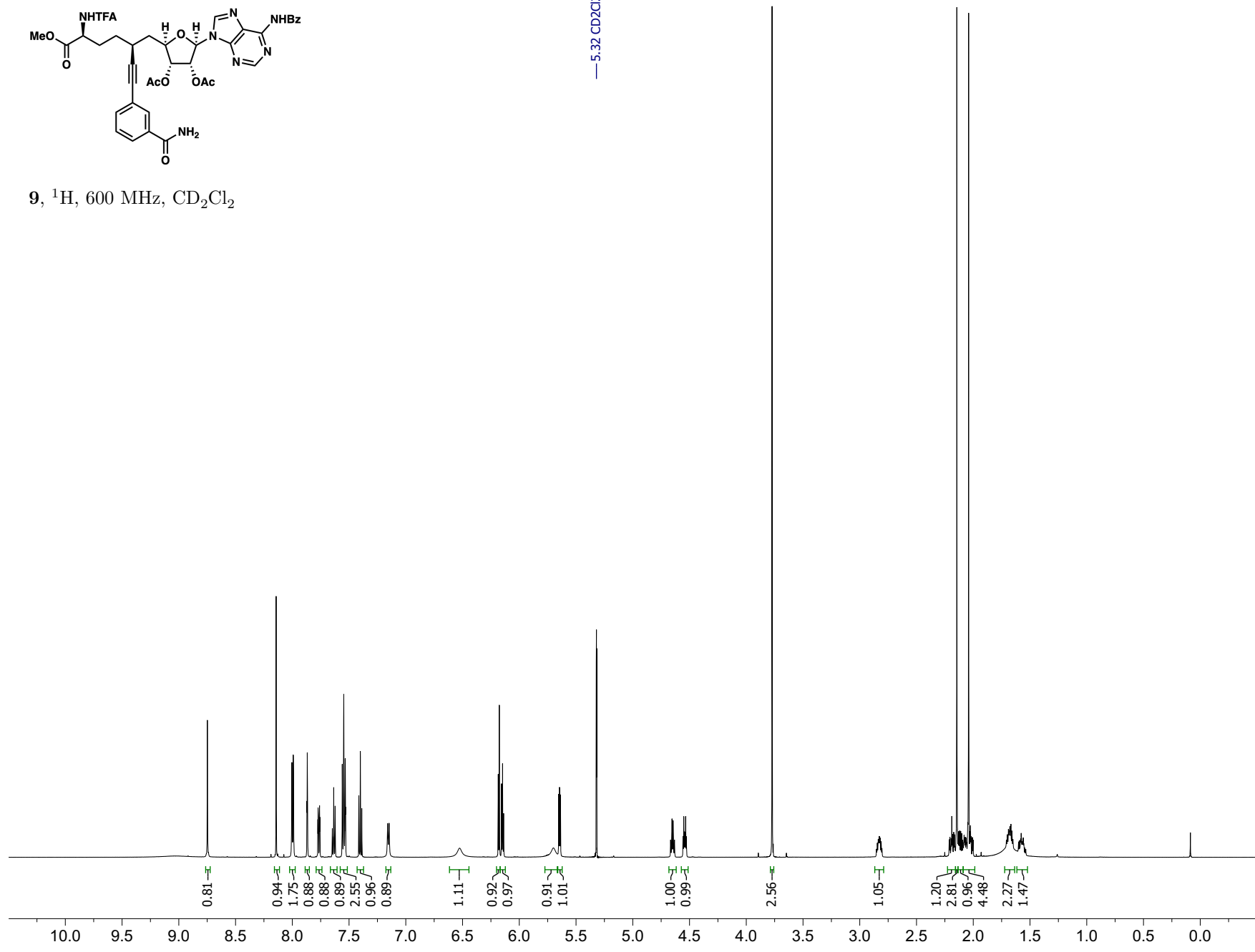
**8**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

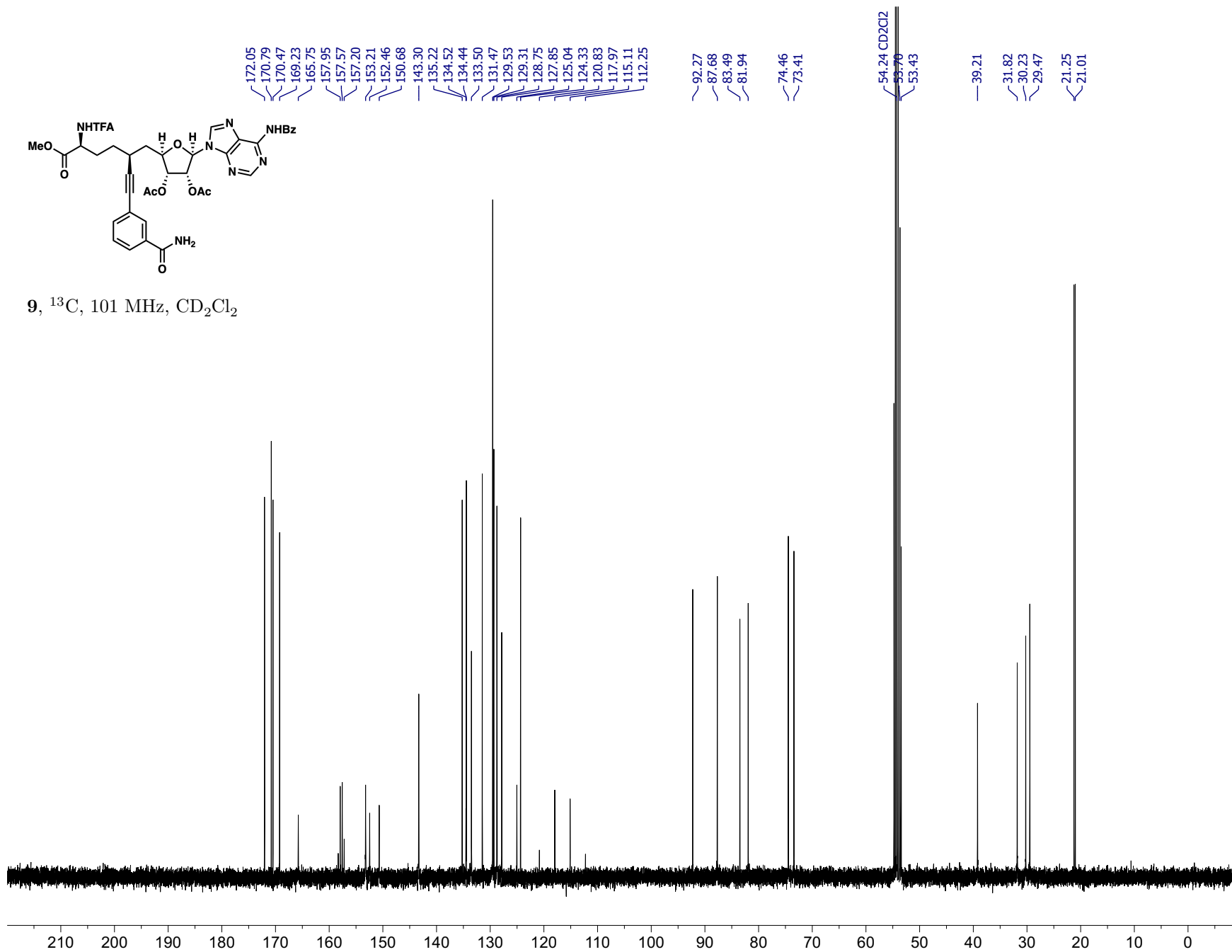


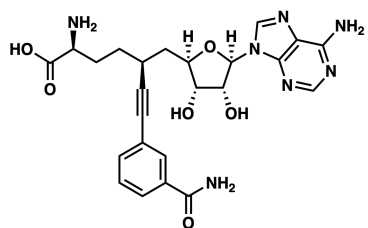


9,  $^1\text{H}$ , 600 MHz,  $\text{CD}_2\text{Cl}_2$

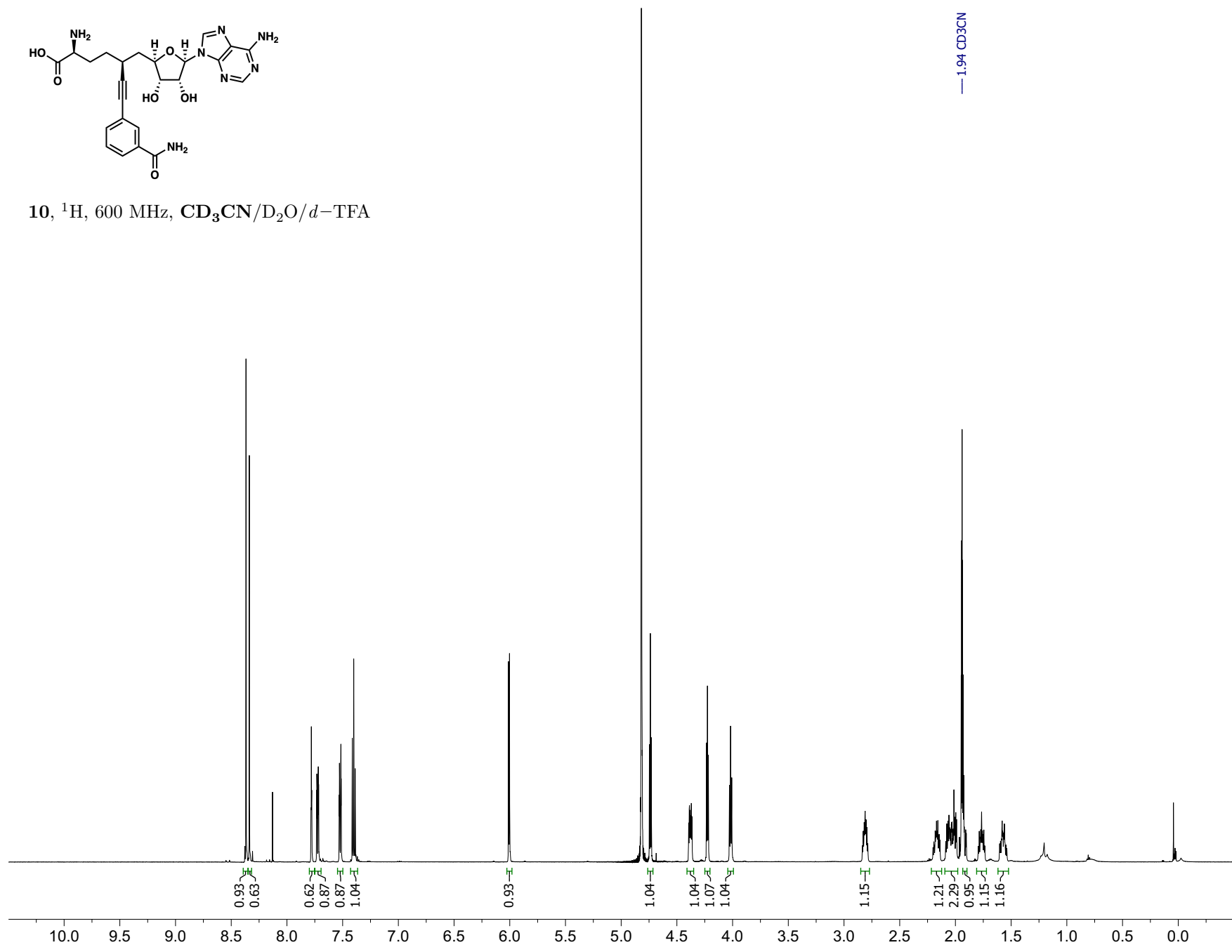
— 5.32  $\text{CD}_2\text{Cl}_2$

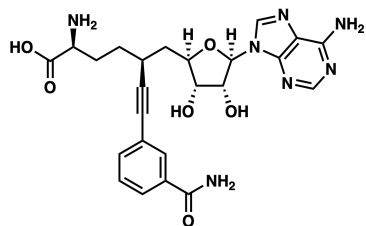




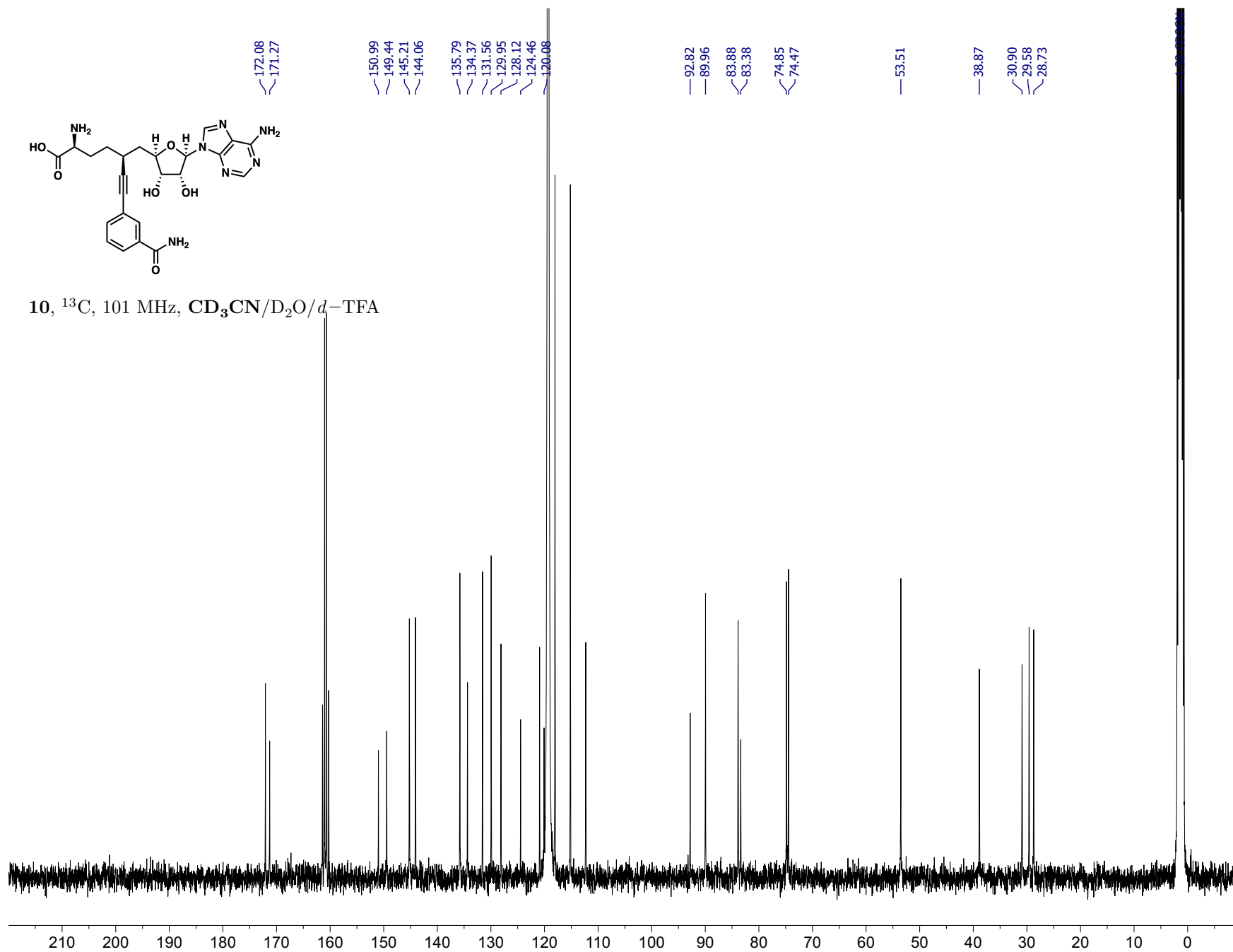


10,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

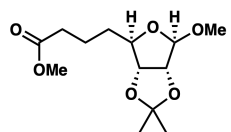




10,  $^{13}\text{C}$ , 101 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

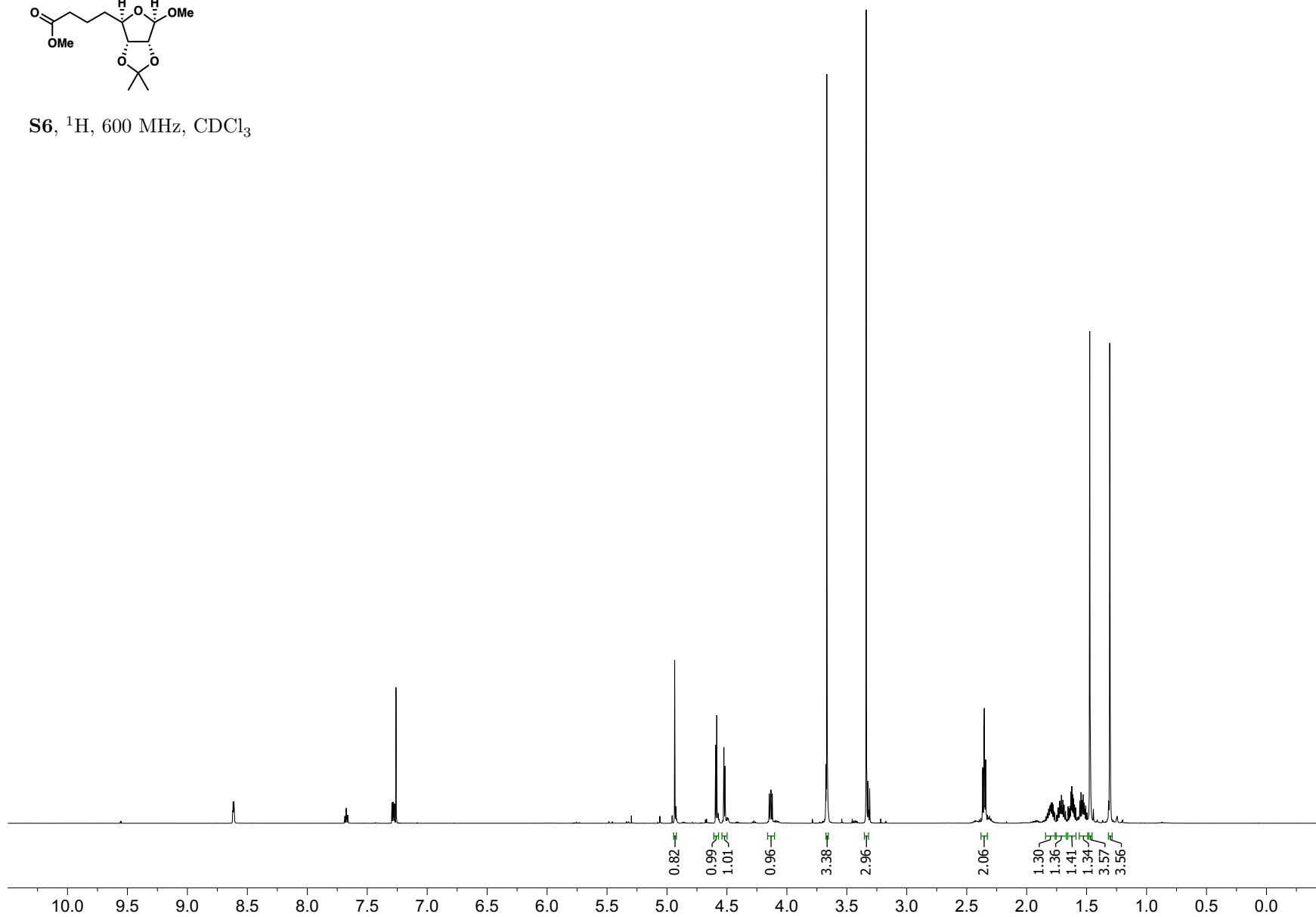


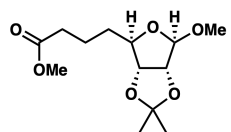
—7.26 CDCl<sub>3</sub>



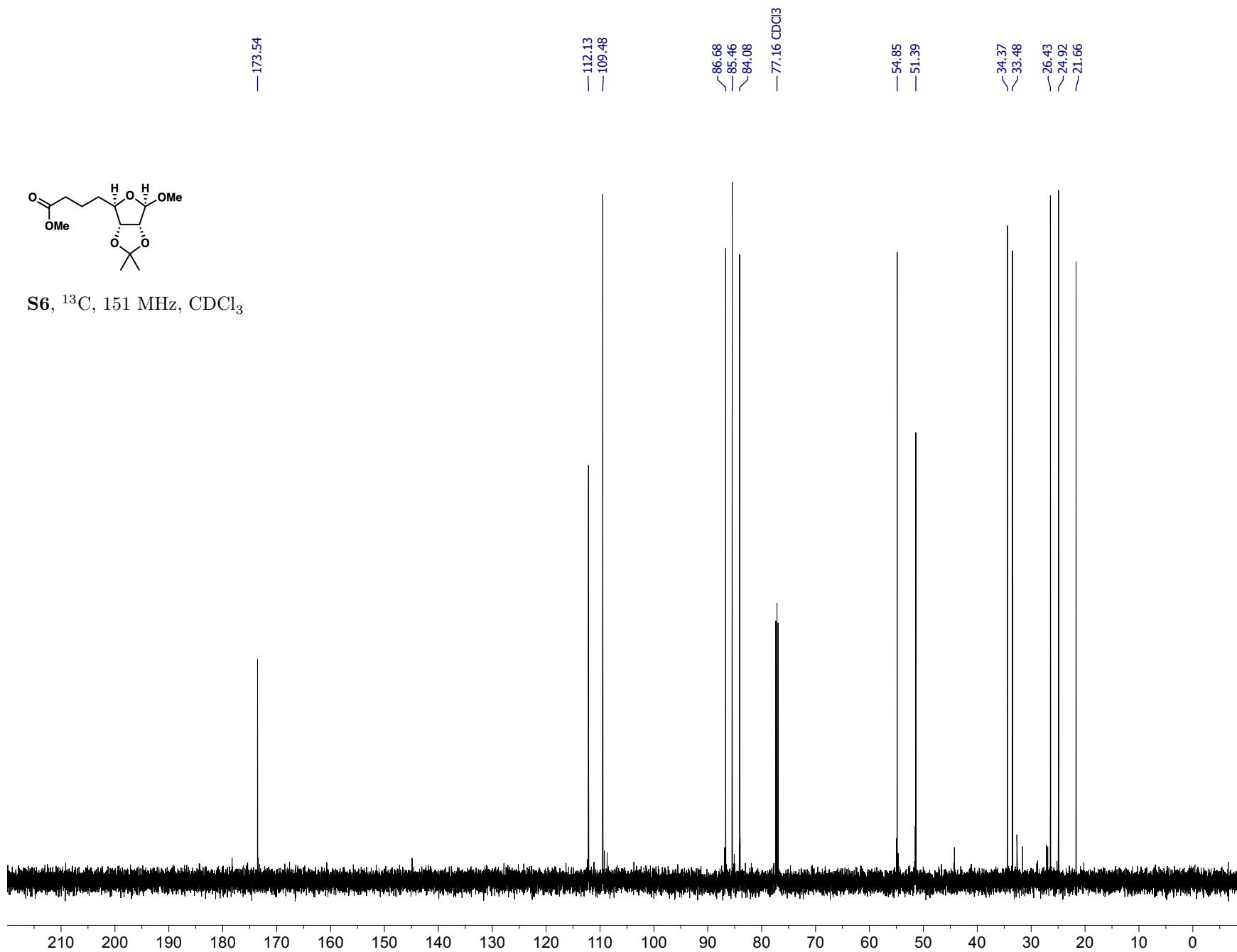
S6, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

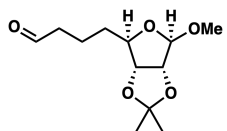
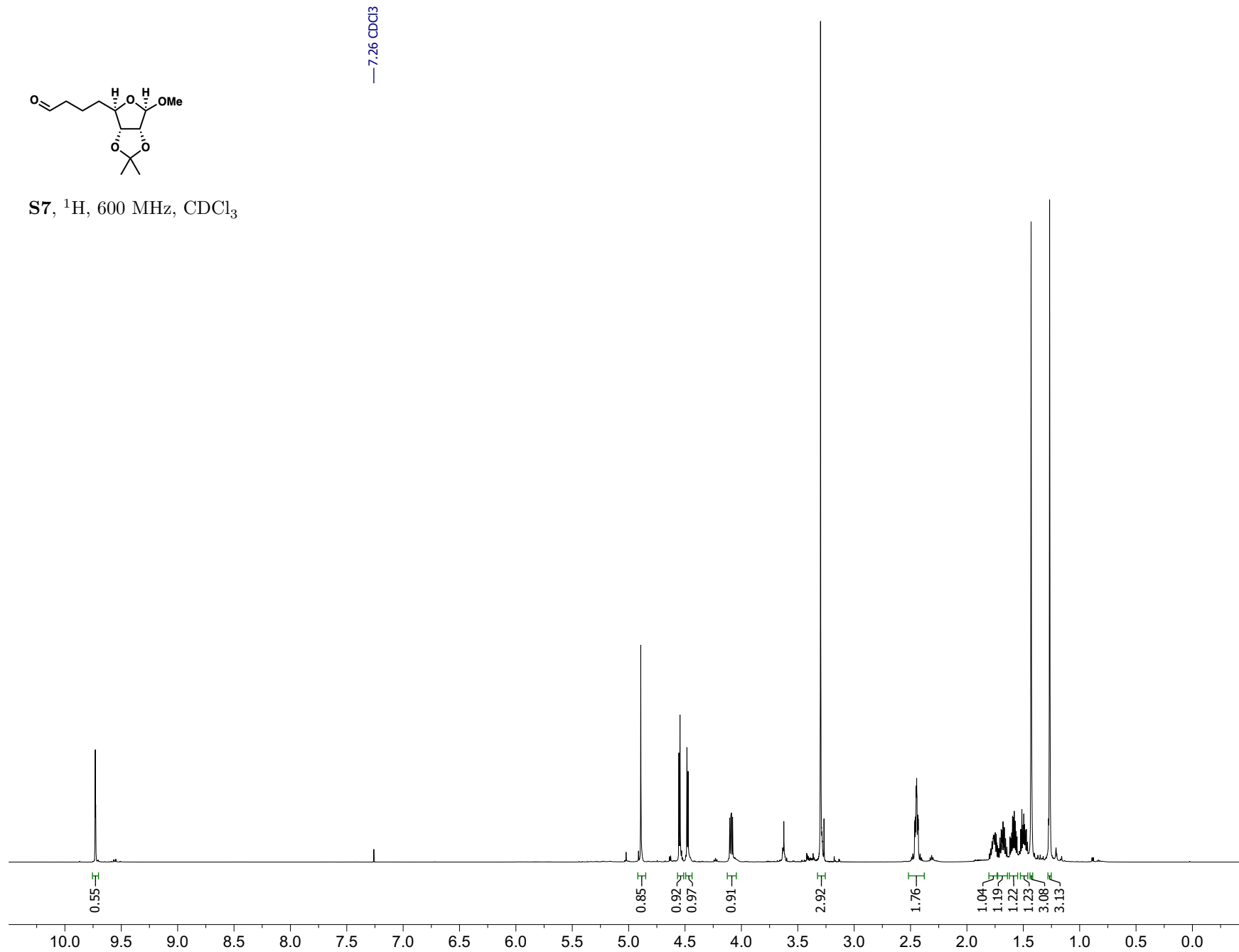
S29



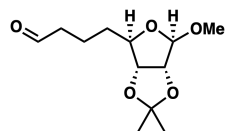
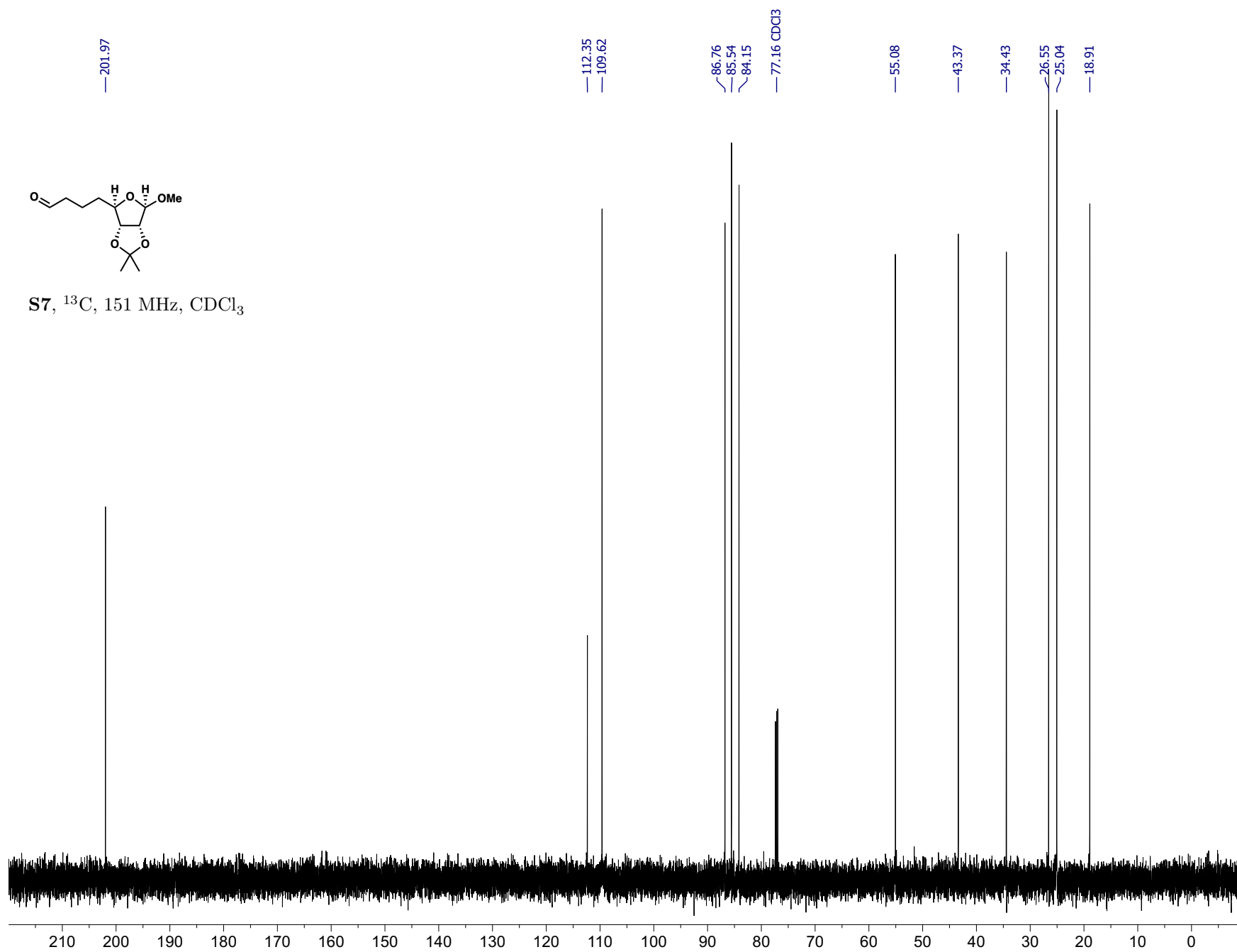


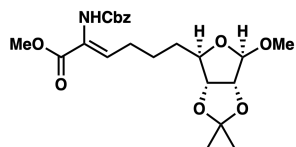
S6,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$



S7,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ 

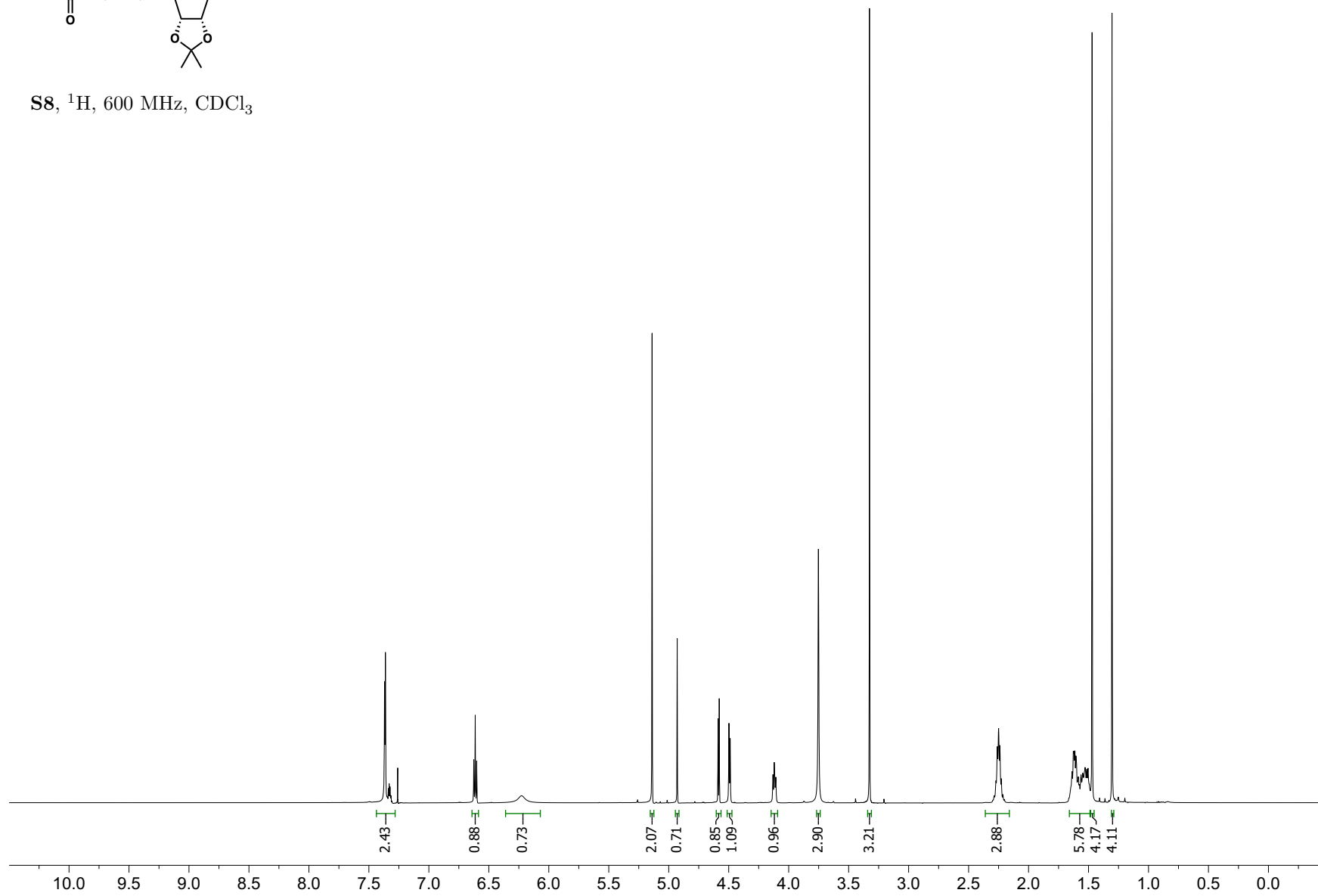


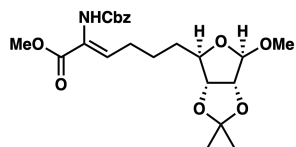
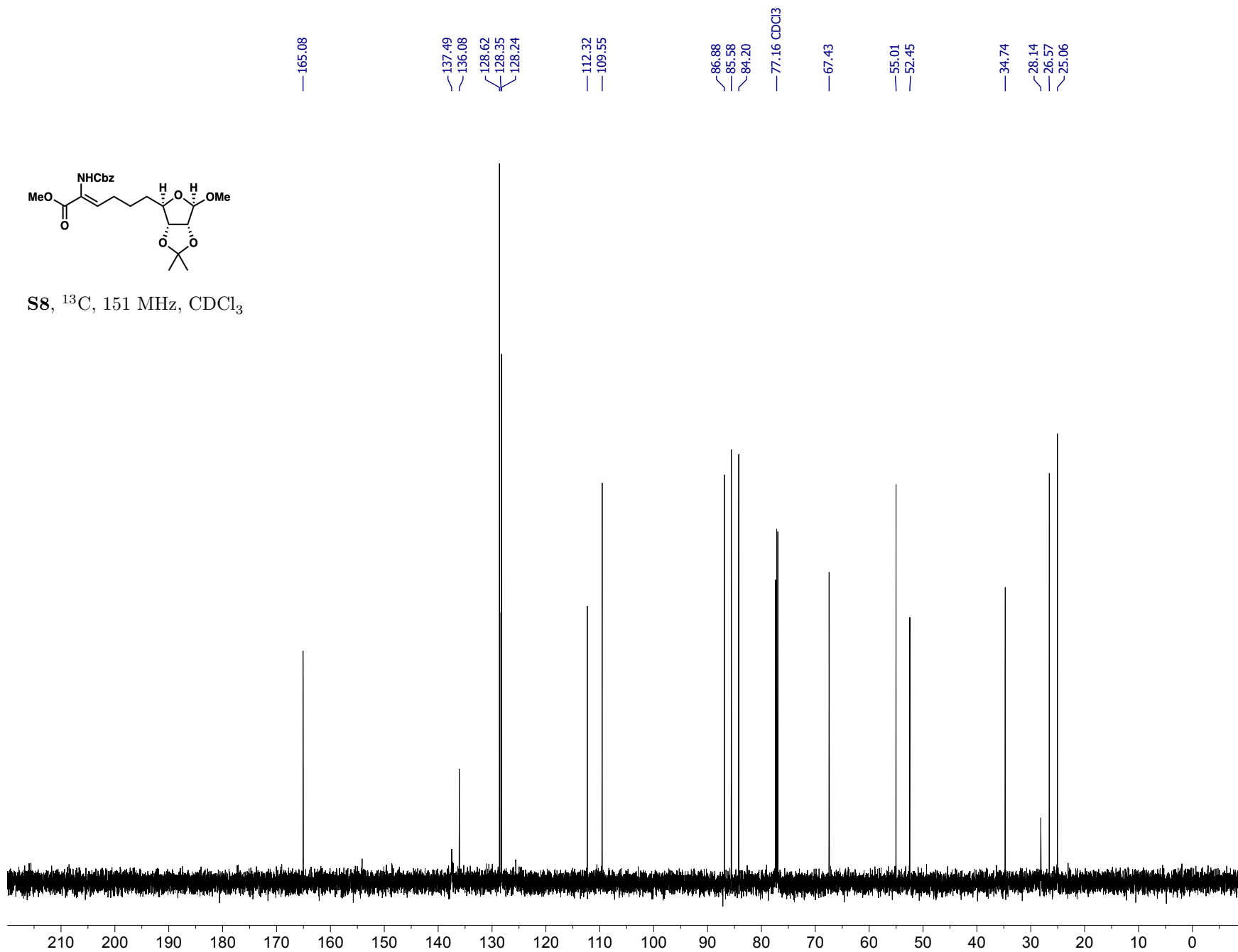
S7,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 

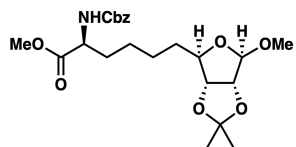
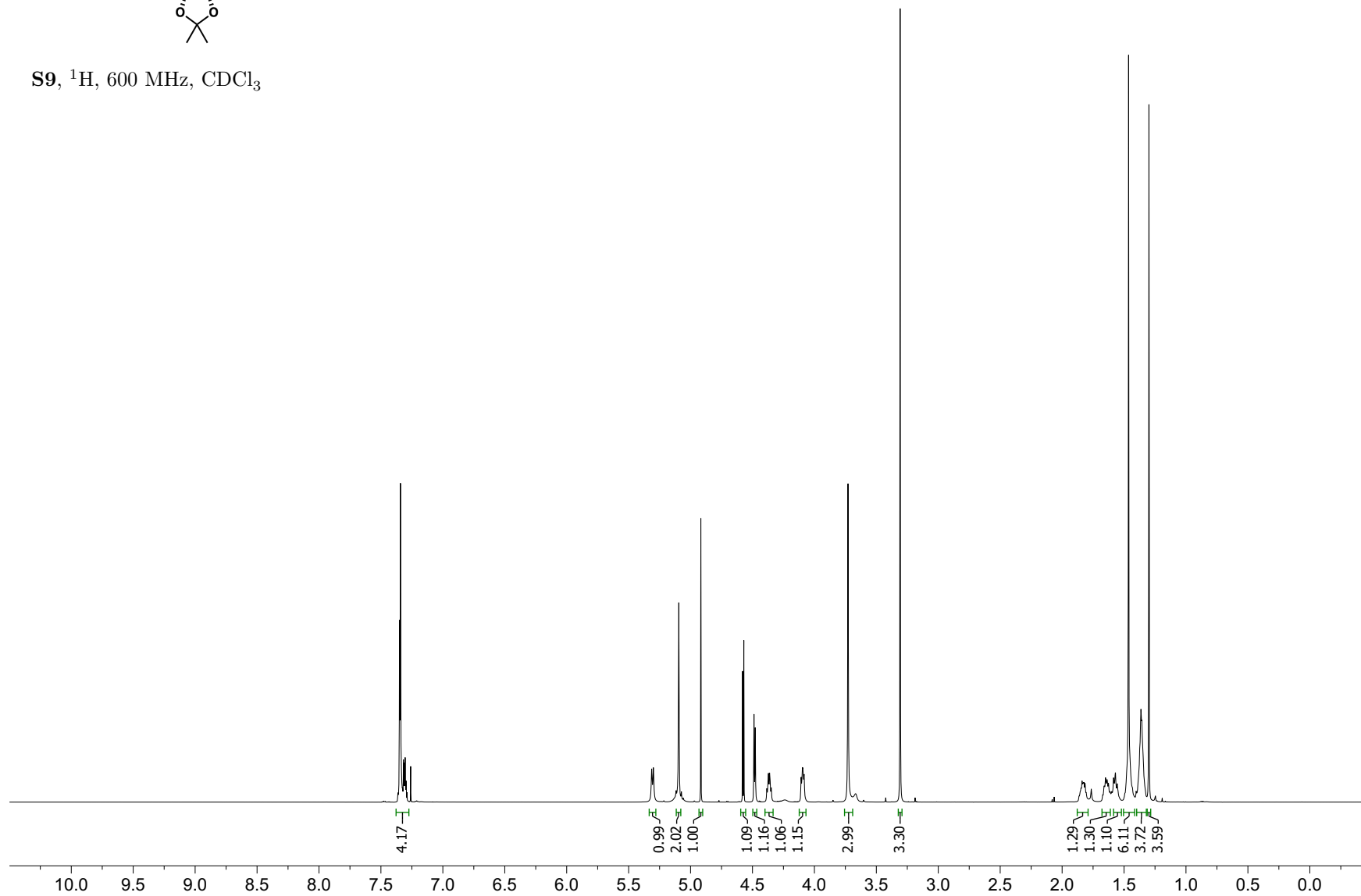


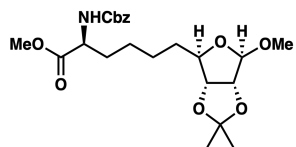
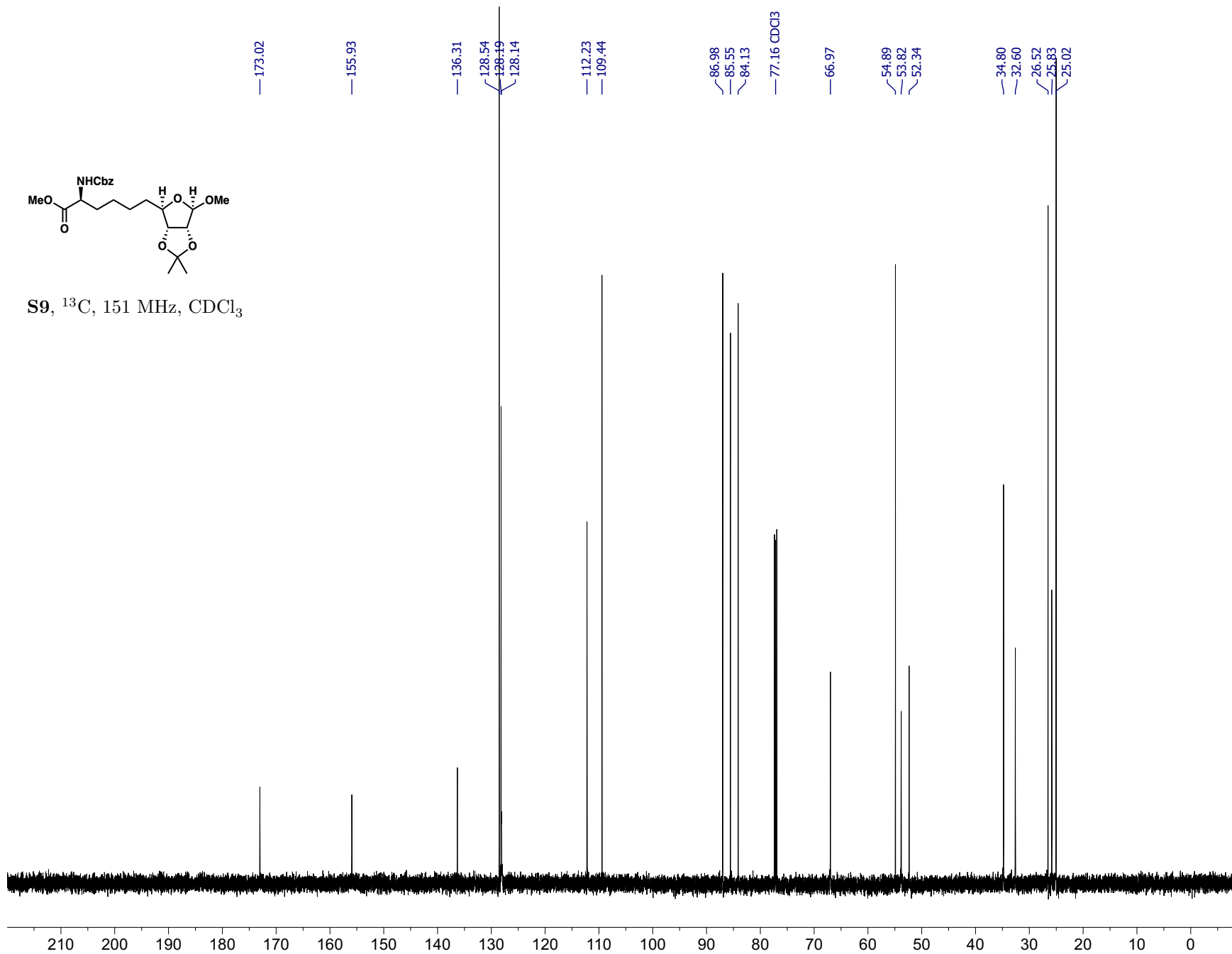
**S8**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

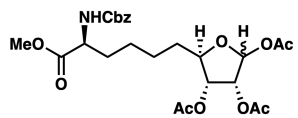
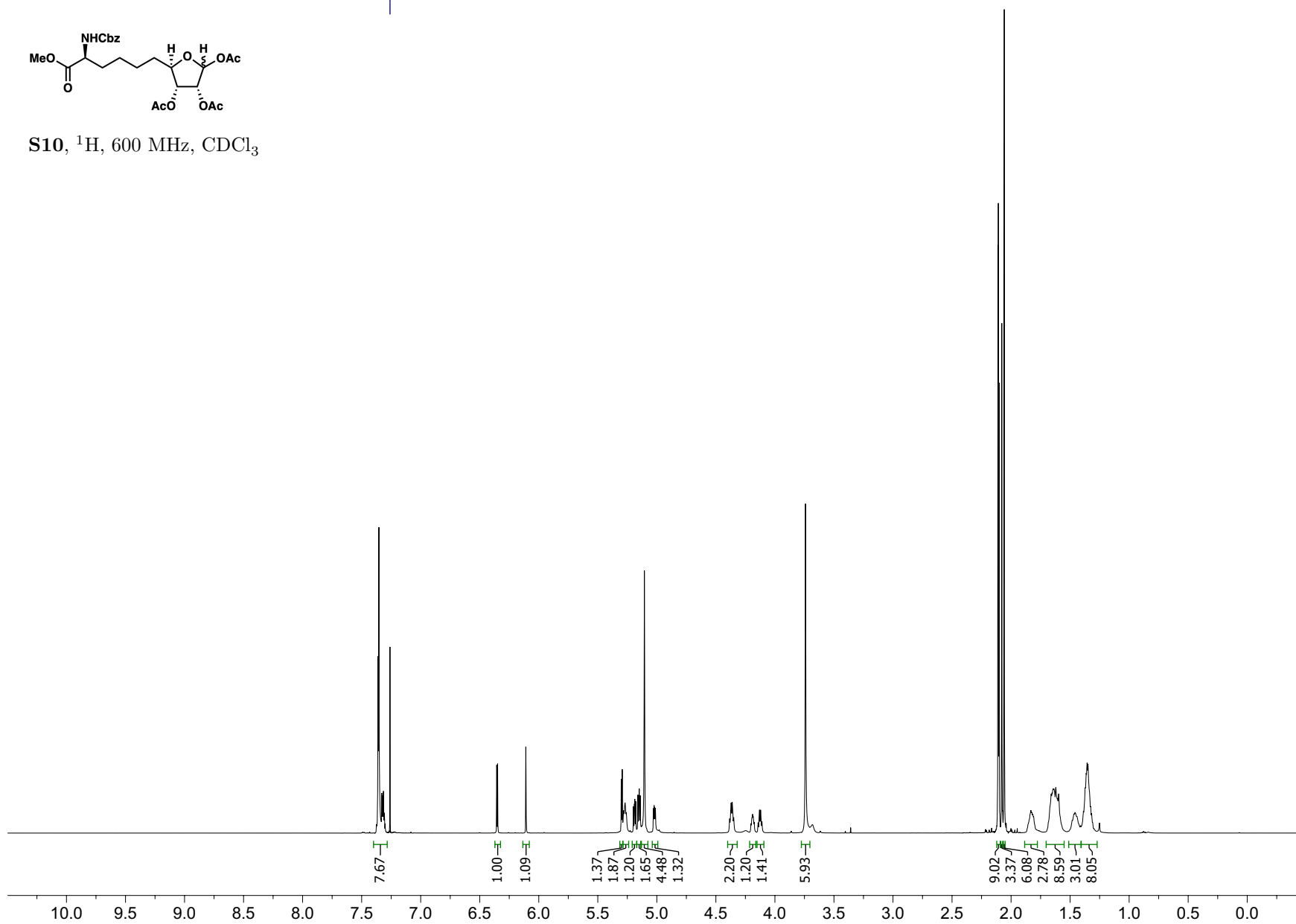
— 7.26  $\text{CDCl}_3$

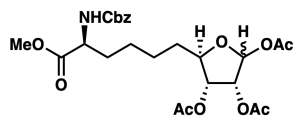


S8,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 

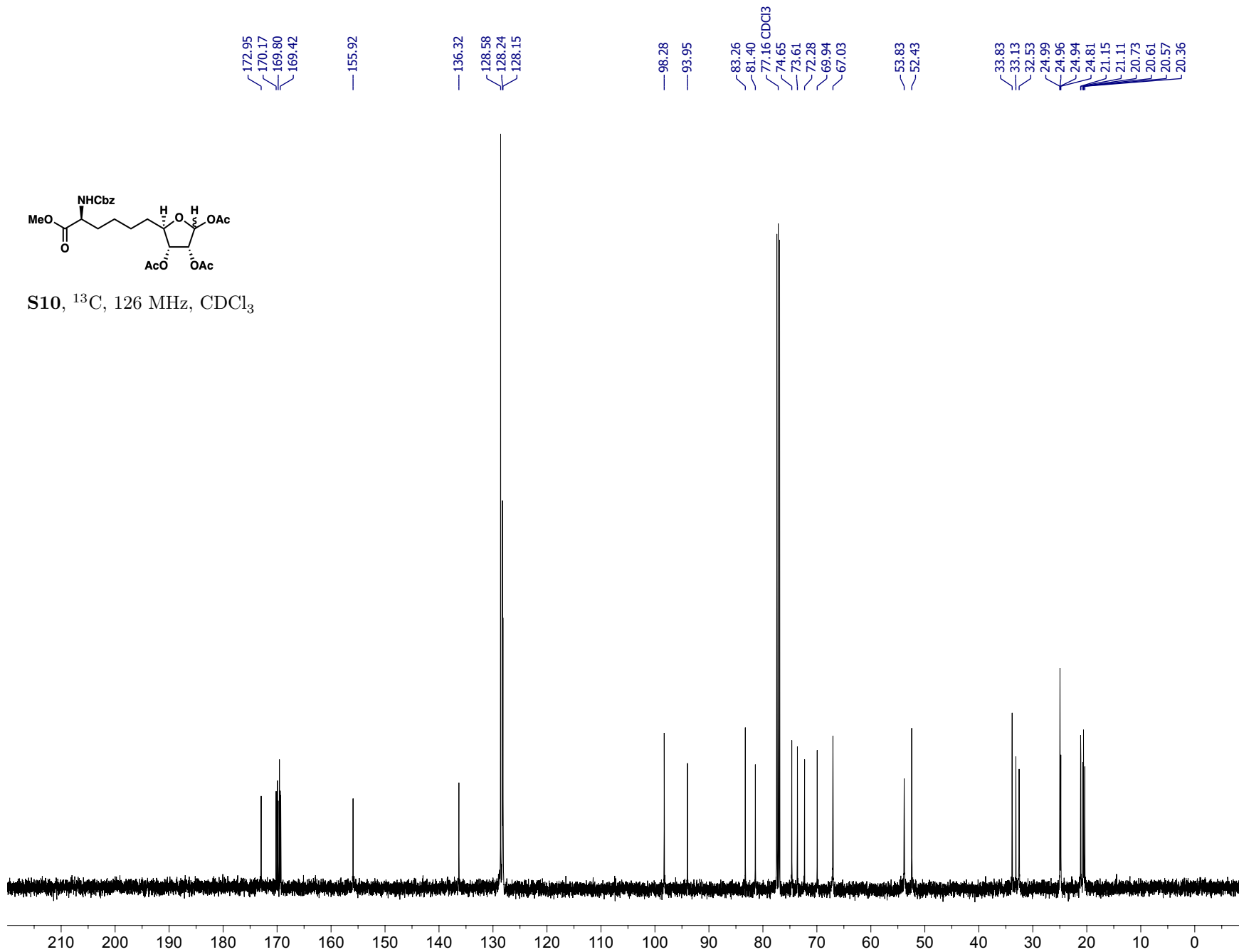
S9,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ 

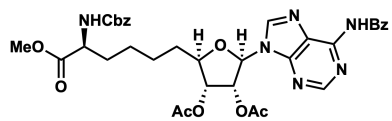
**S9**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 

S10,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ 

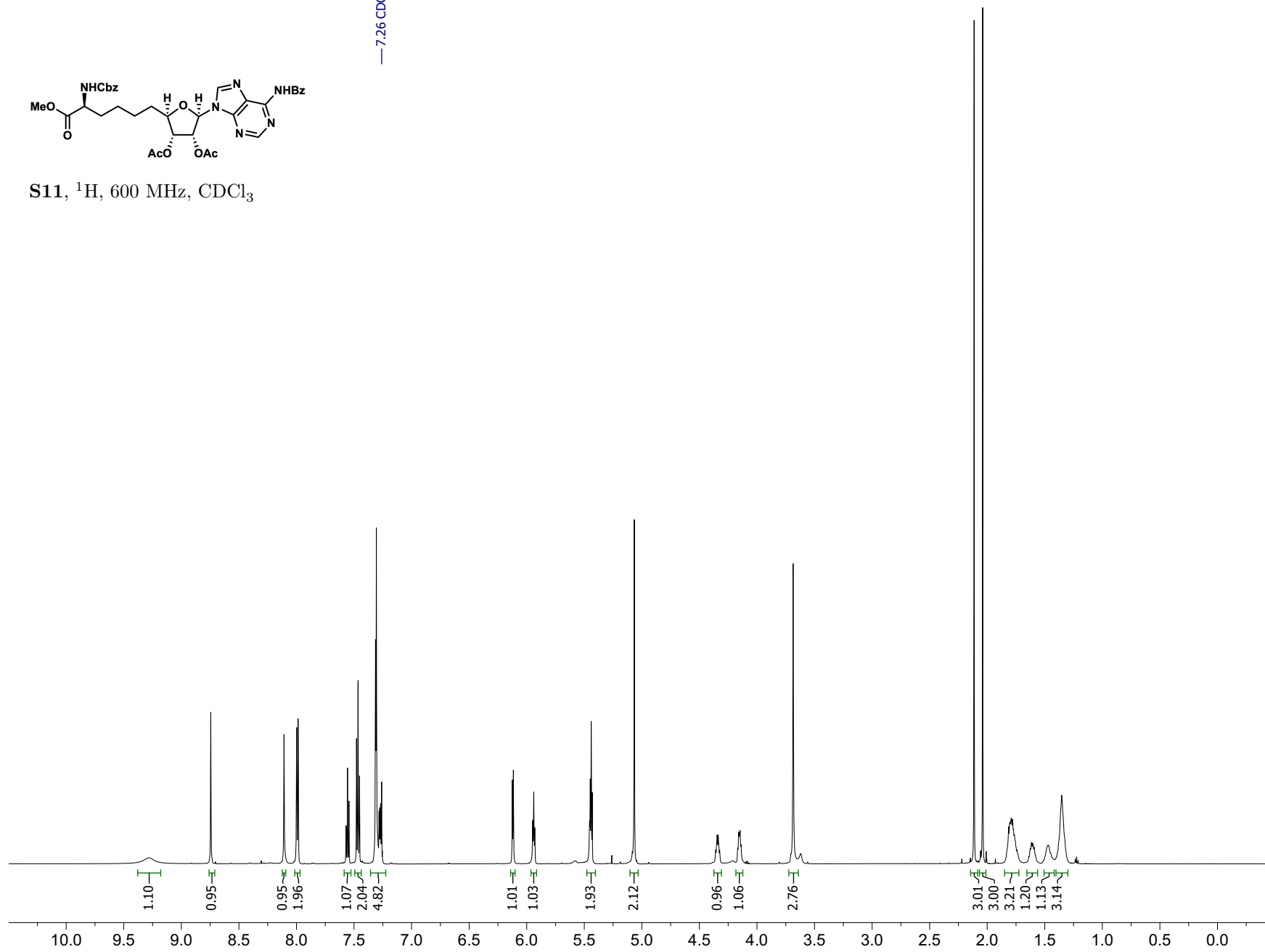


S10,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



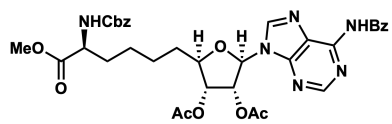


S11,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

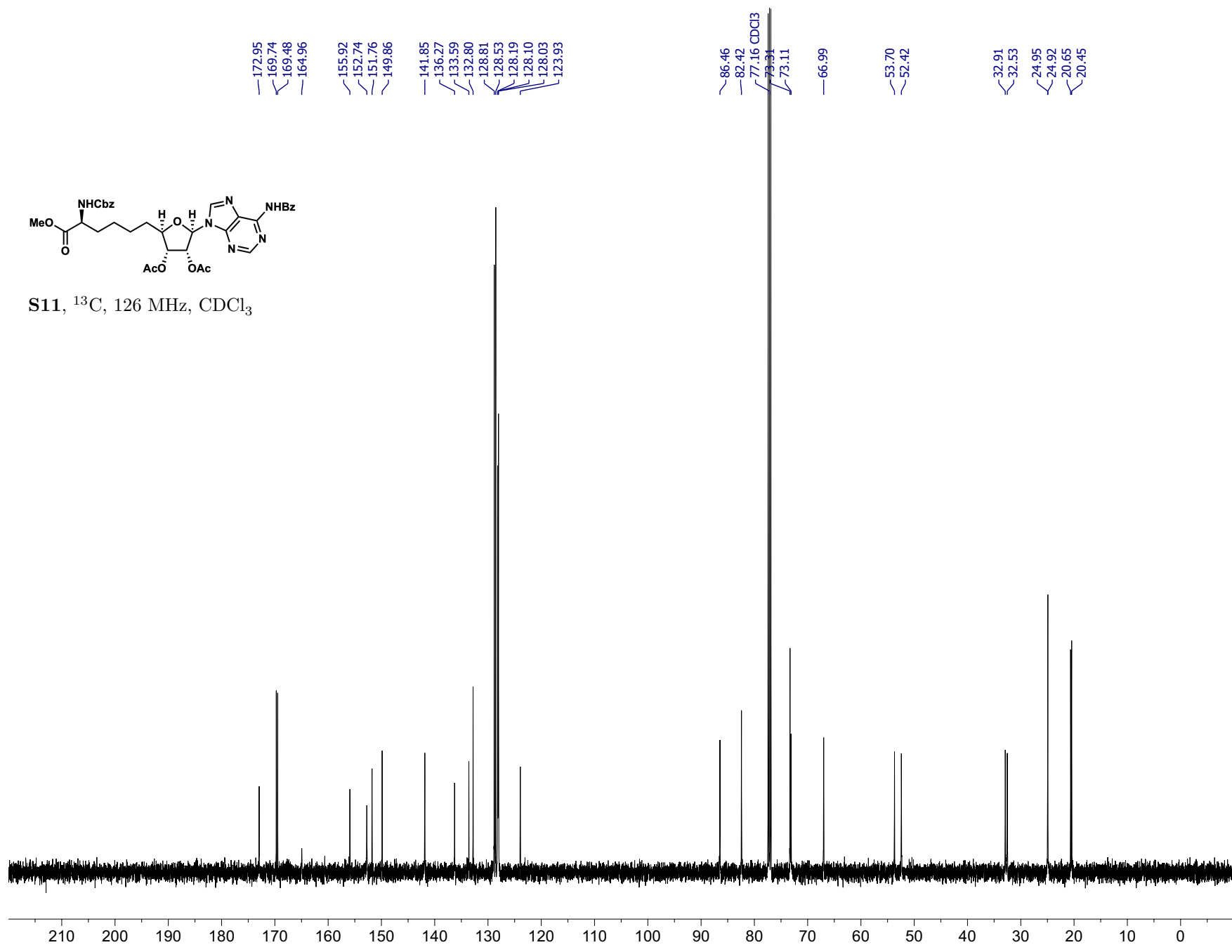


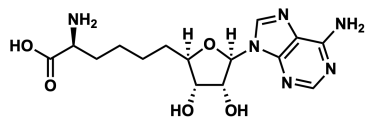
— 7.26  $\text{CDCl}_3$





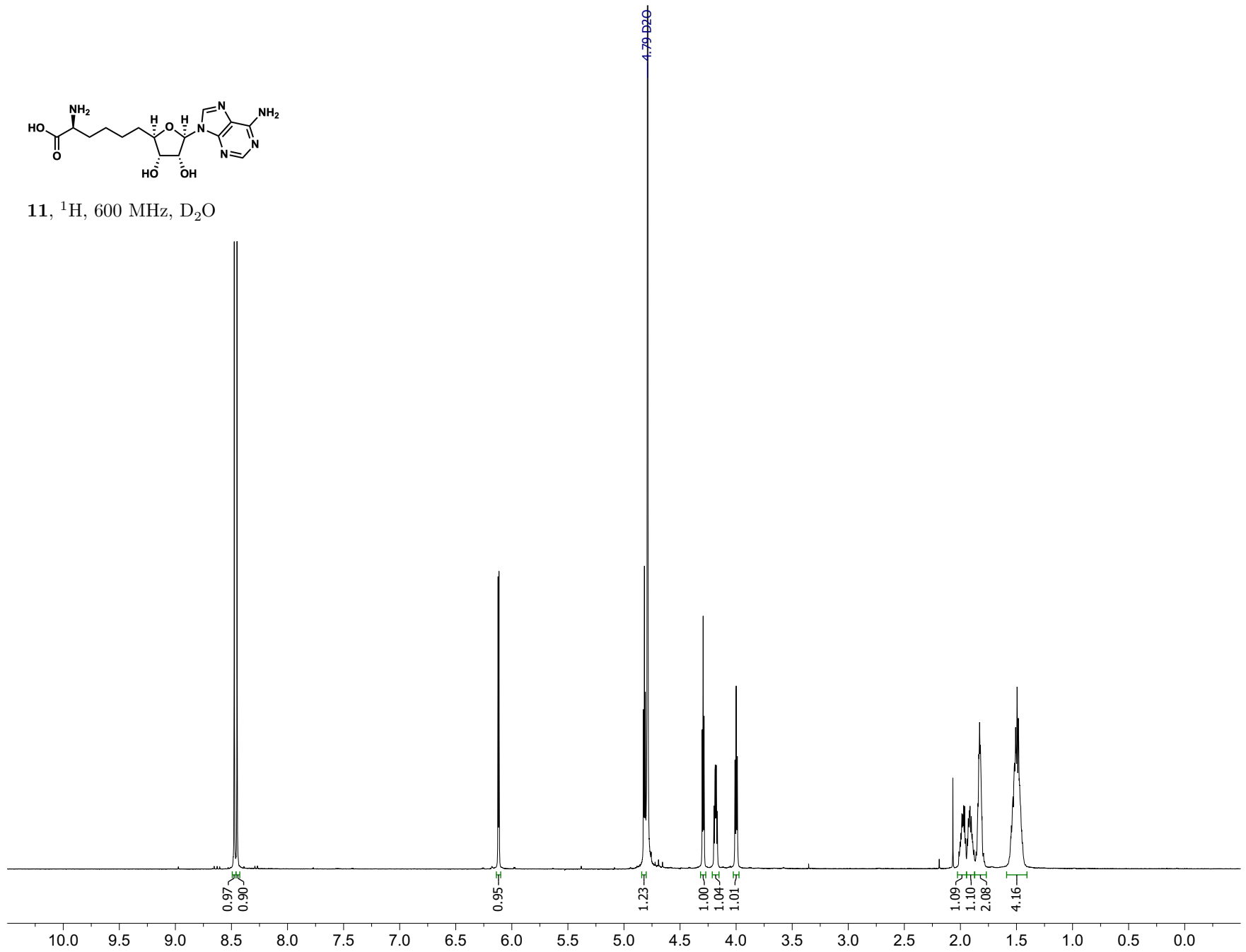
S11,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

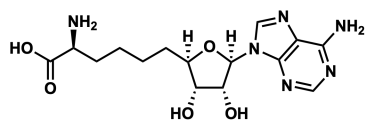
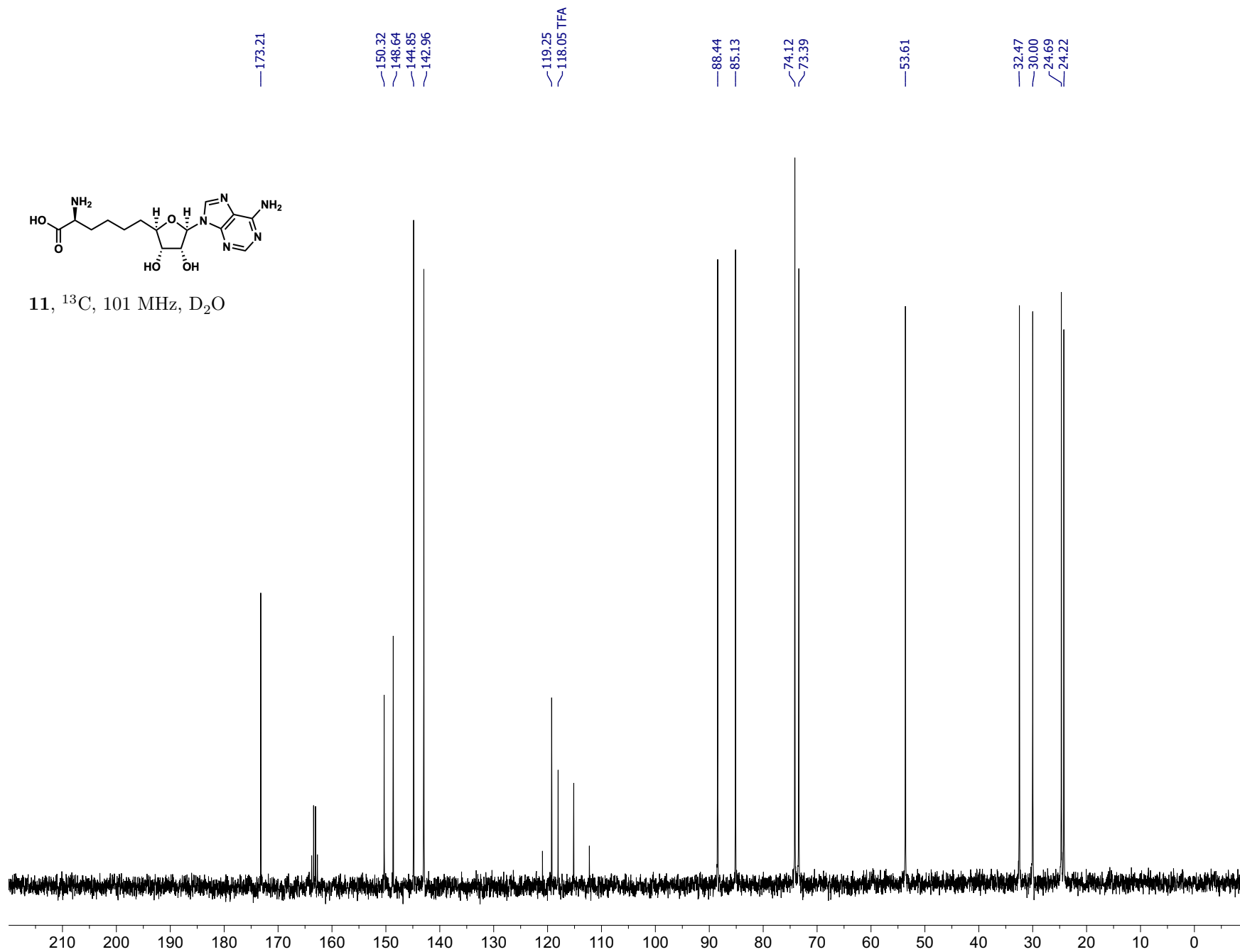


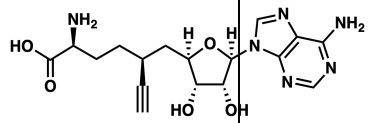


11,  $^1\text{H}$ , 600 MHz,  $\text{D}_2\text{O}$

S41

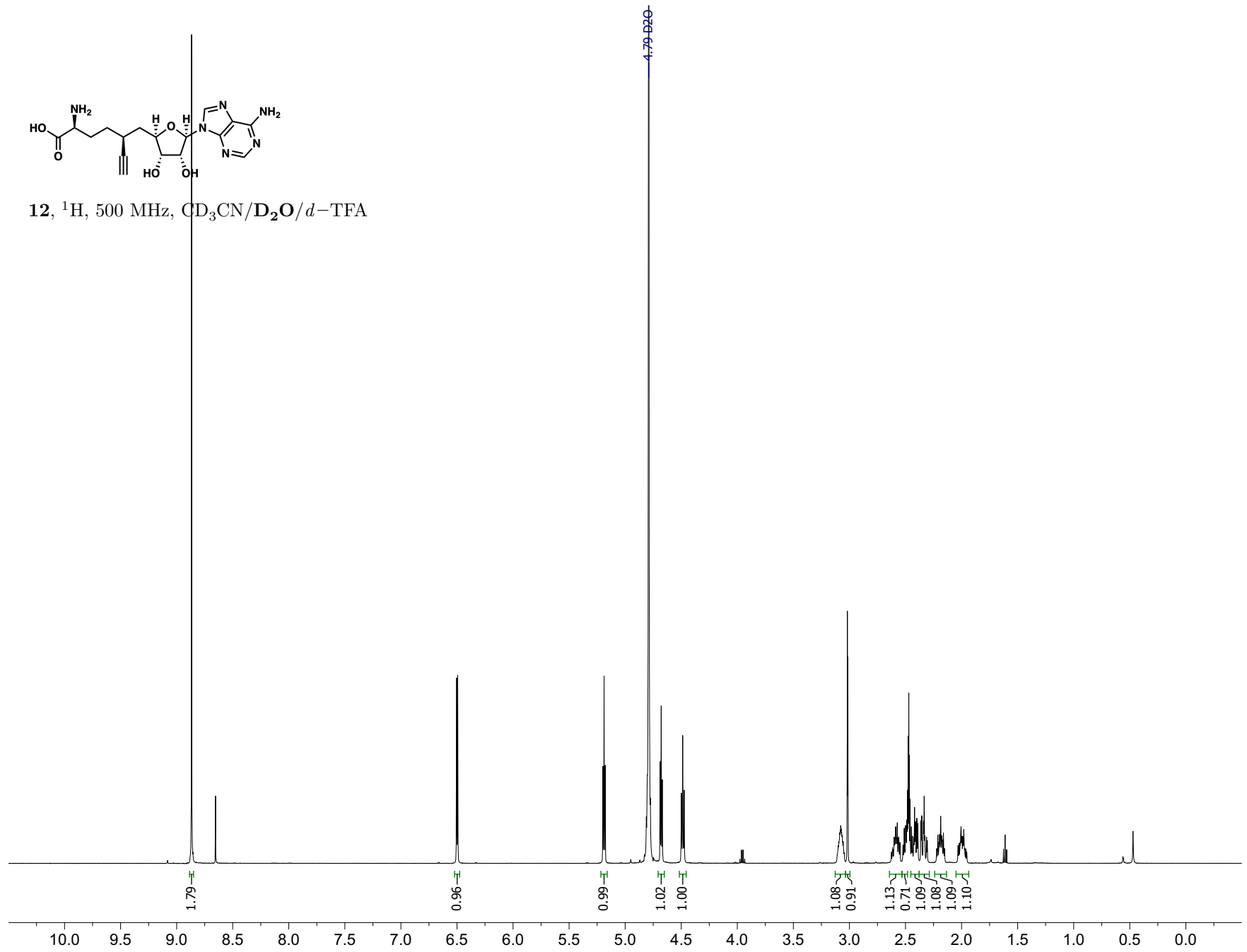


11,  $^{13}\text{C}$ , 101 MHz,  $\text{D}_2\text{O}$ 

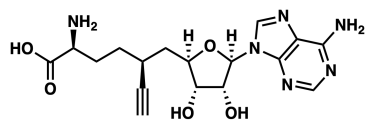


12,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

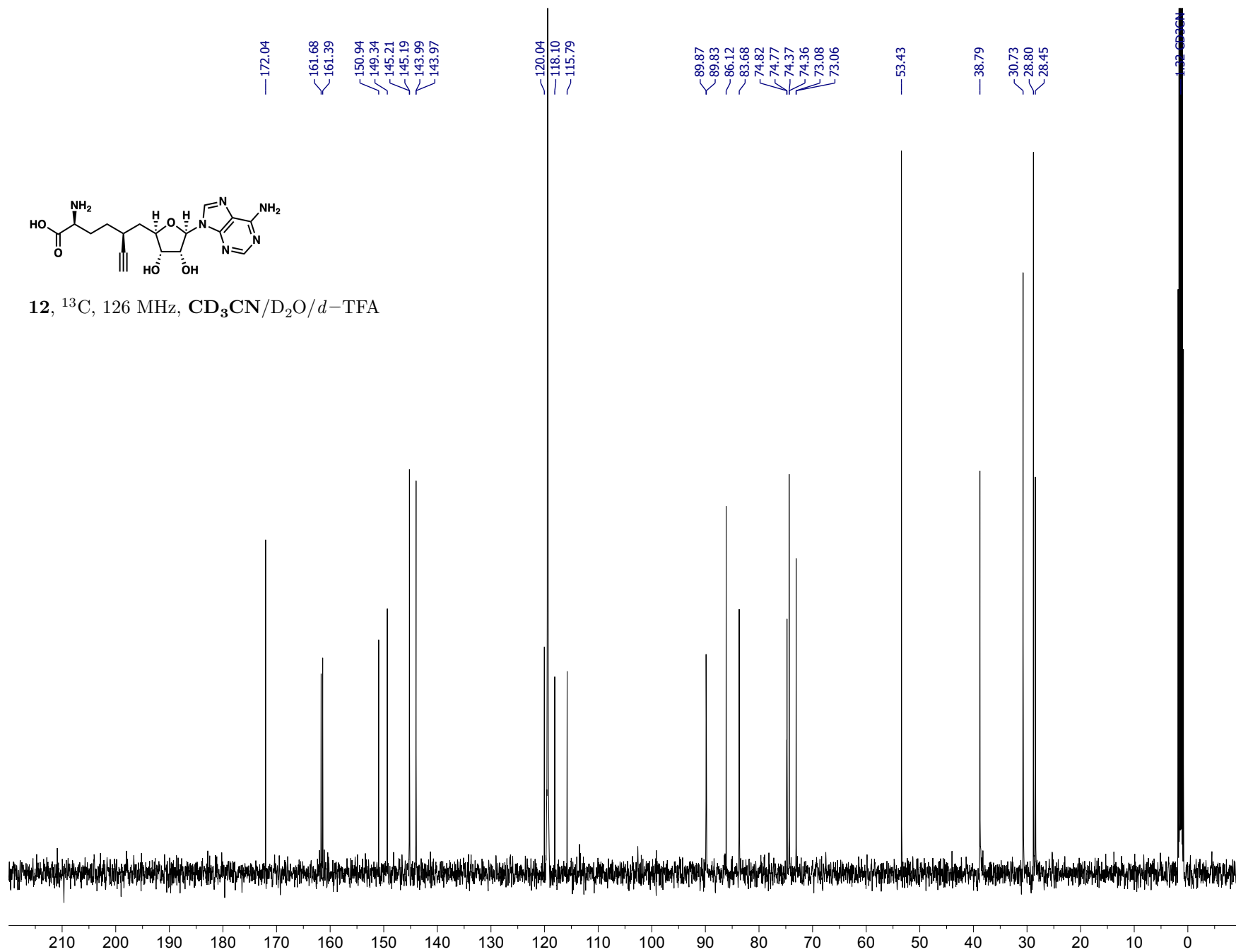
S13

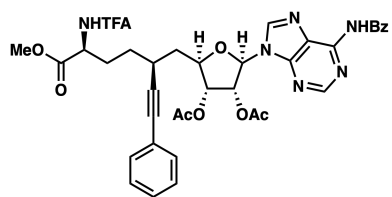


F1S



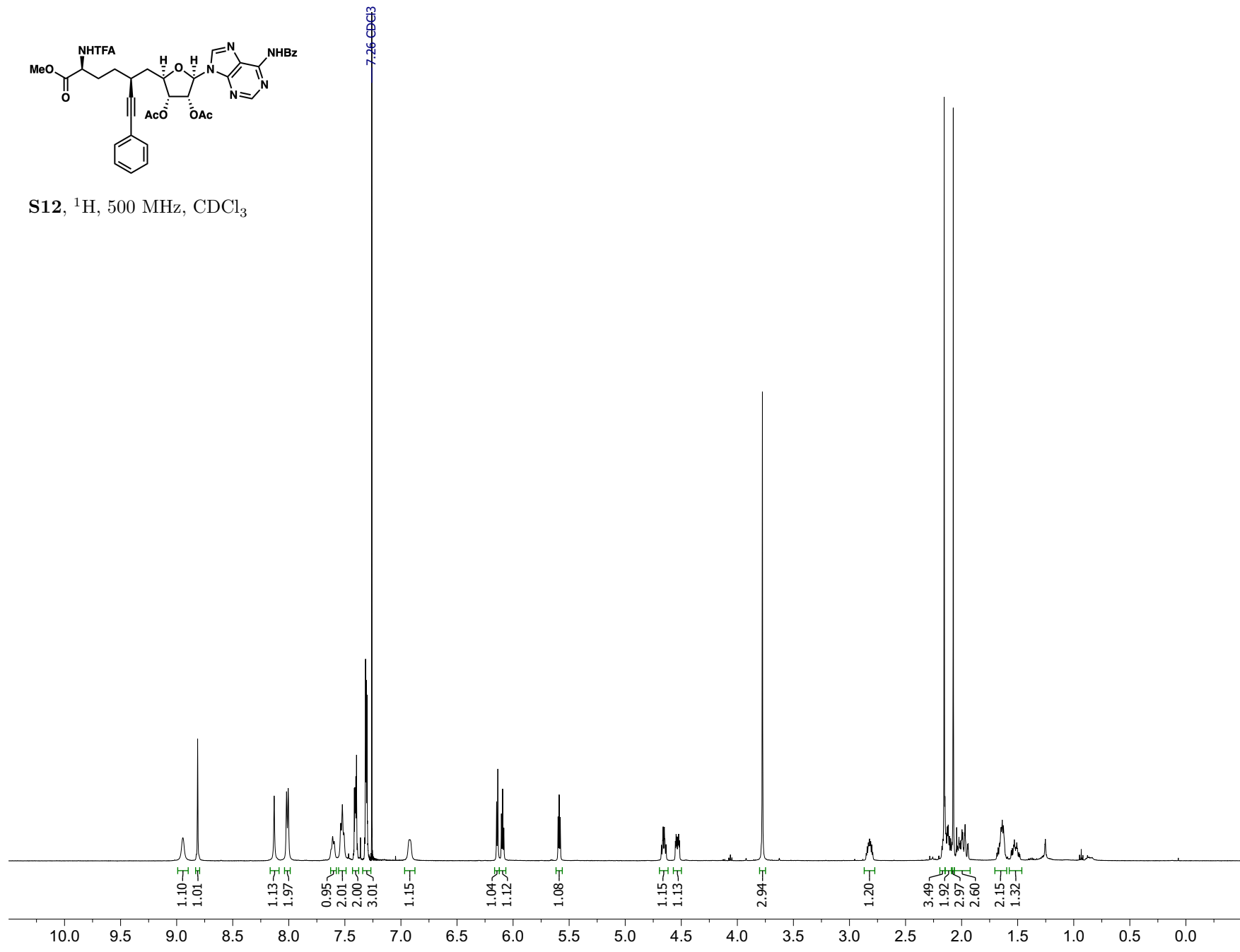
12,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

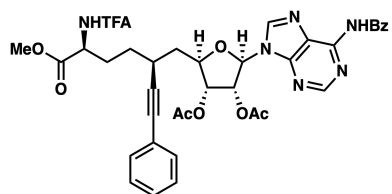




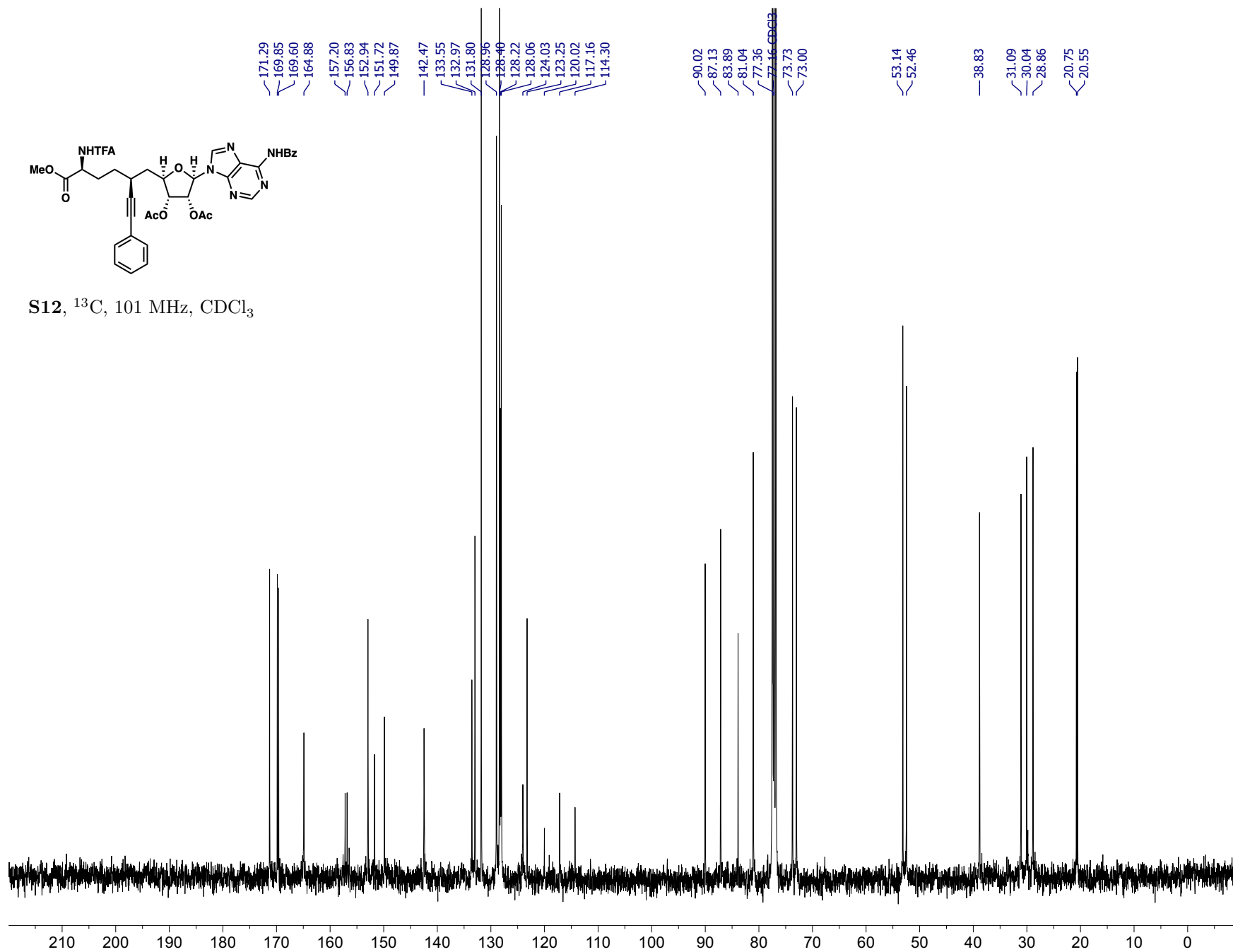
S12, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>

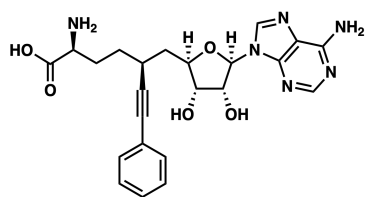
S15





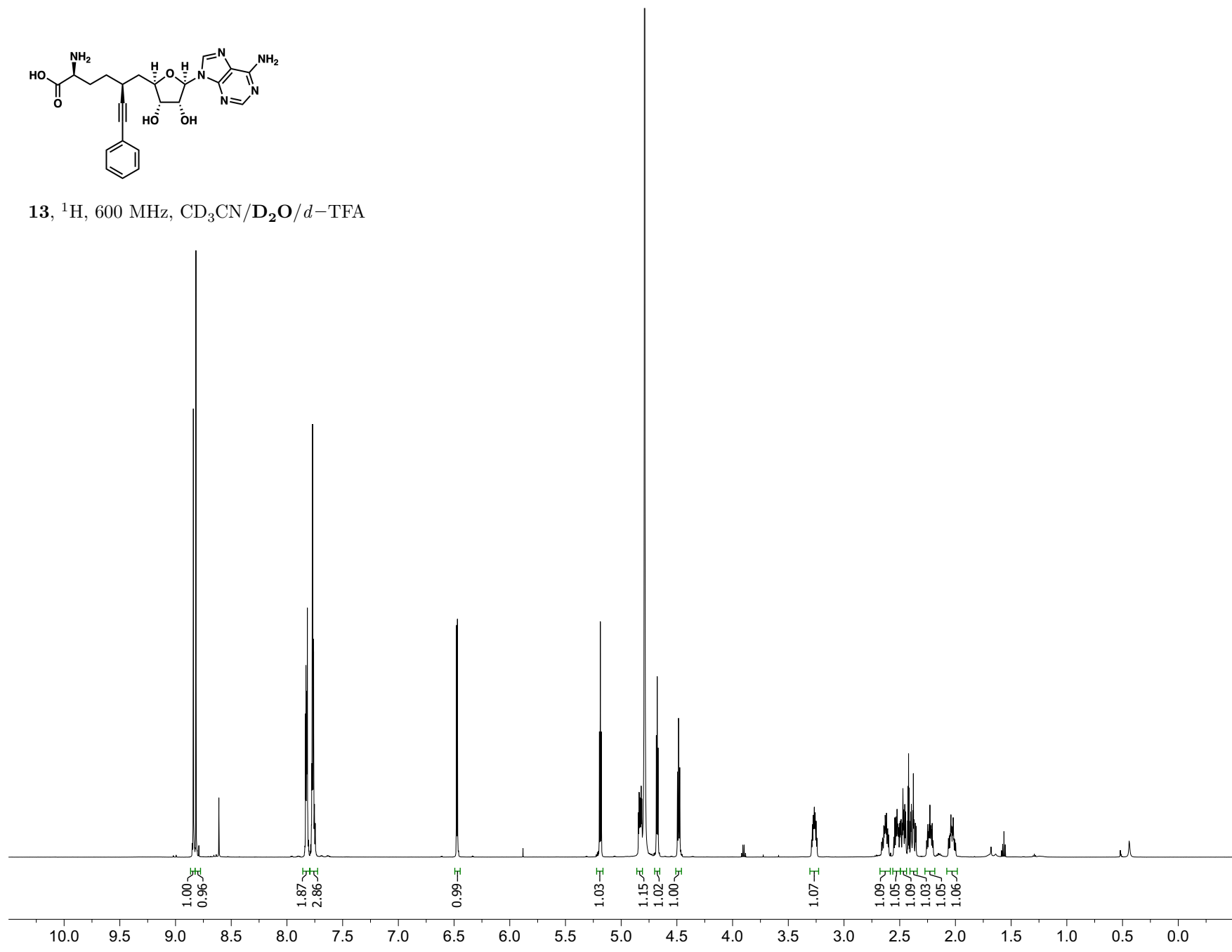
S12,  $^{13}\text{C}$ , 101 MHz,  $\text{CDCl}_3$





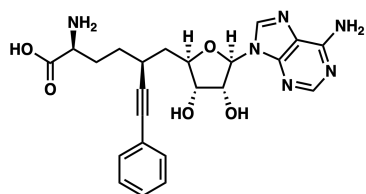
13, <sup>1</sup>H, 600 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA

S47

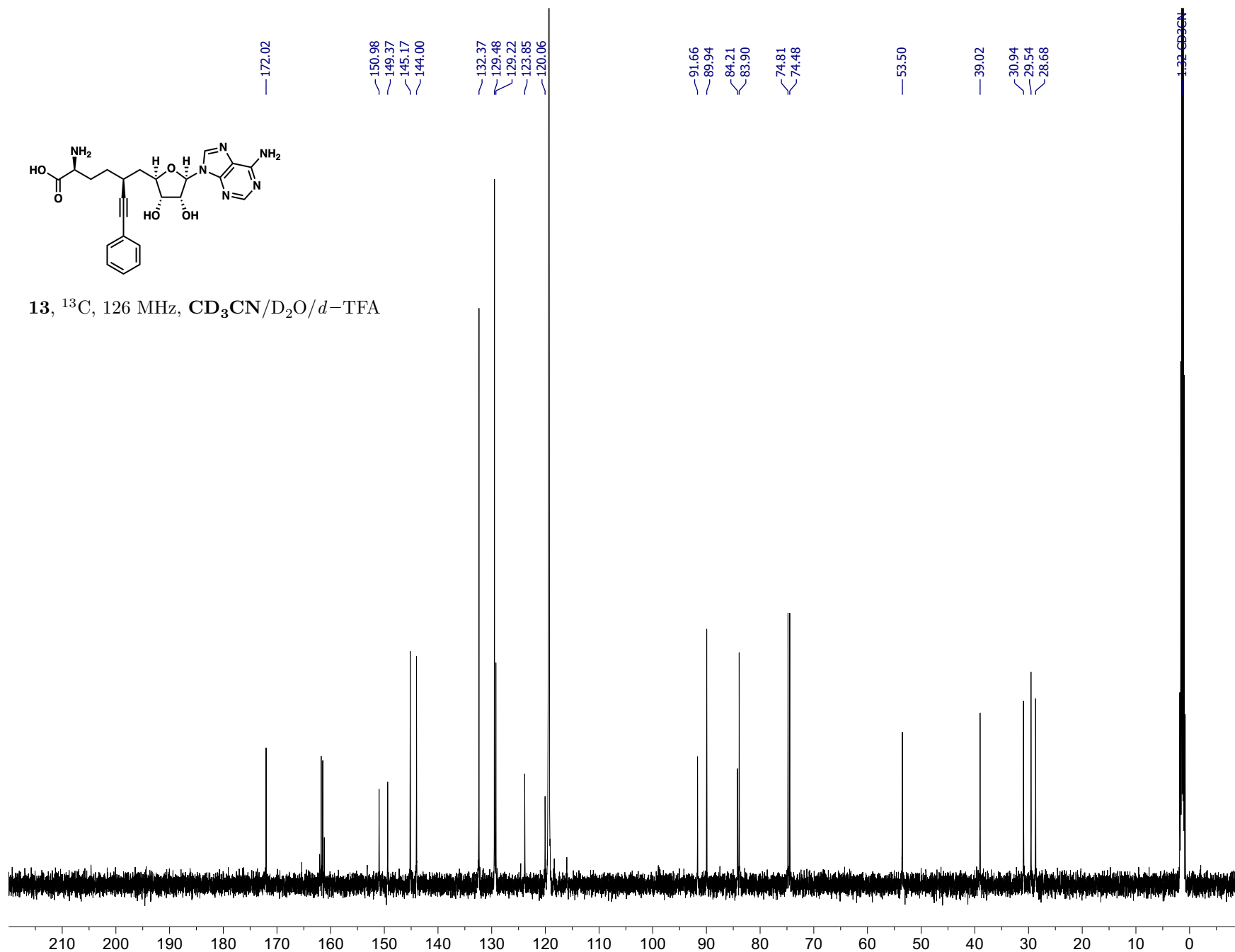


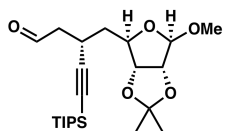


SFS



**13**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

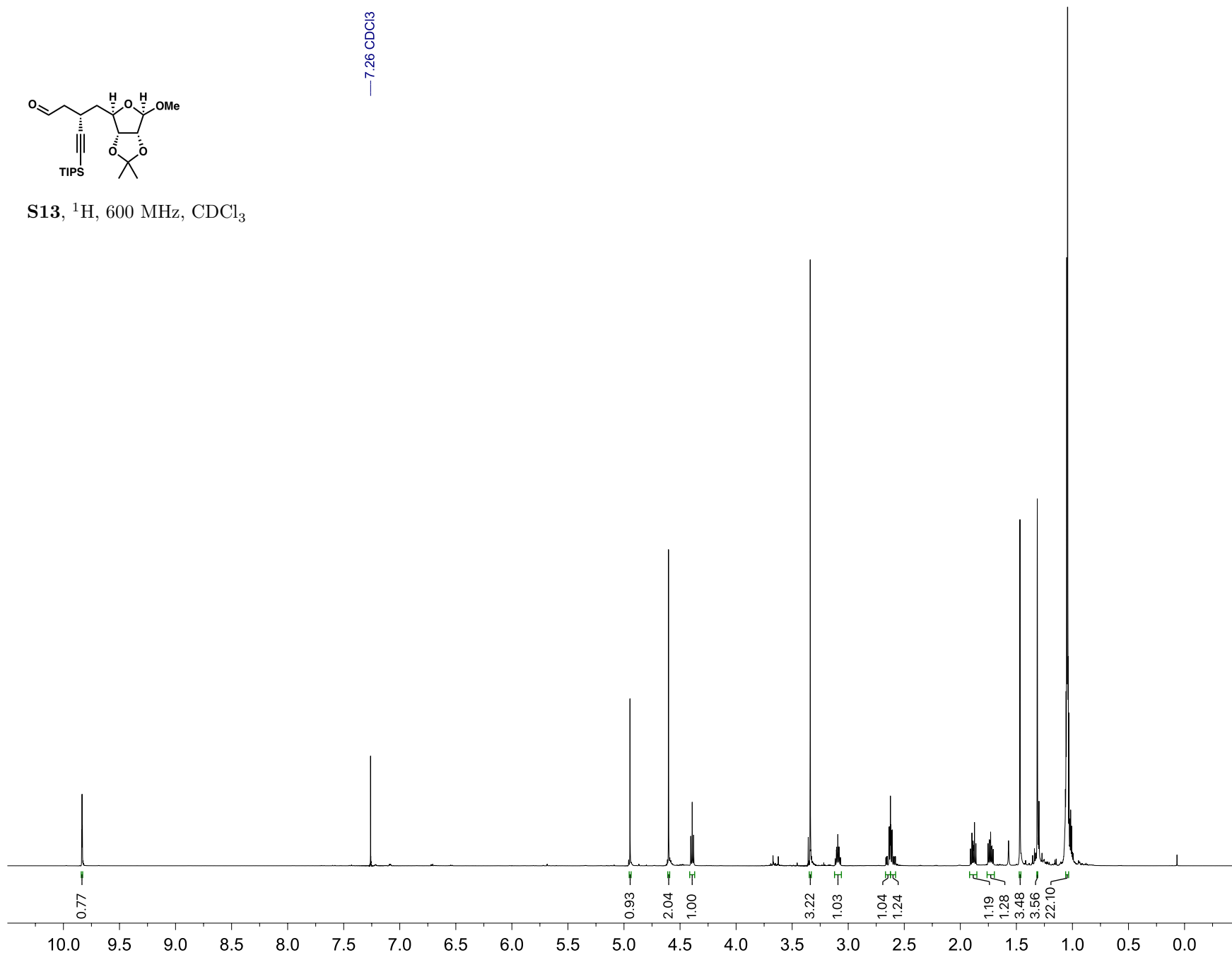


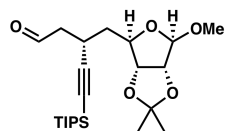


S13,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

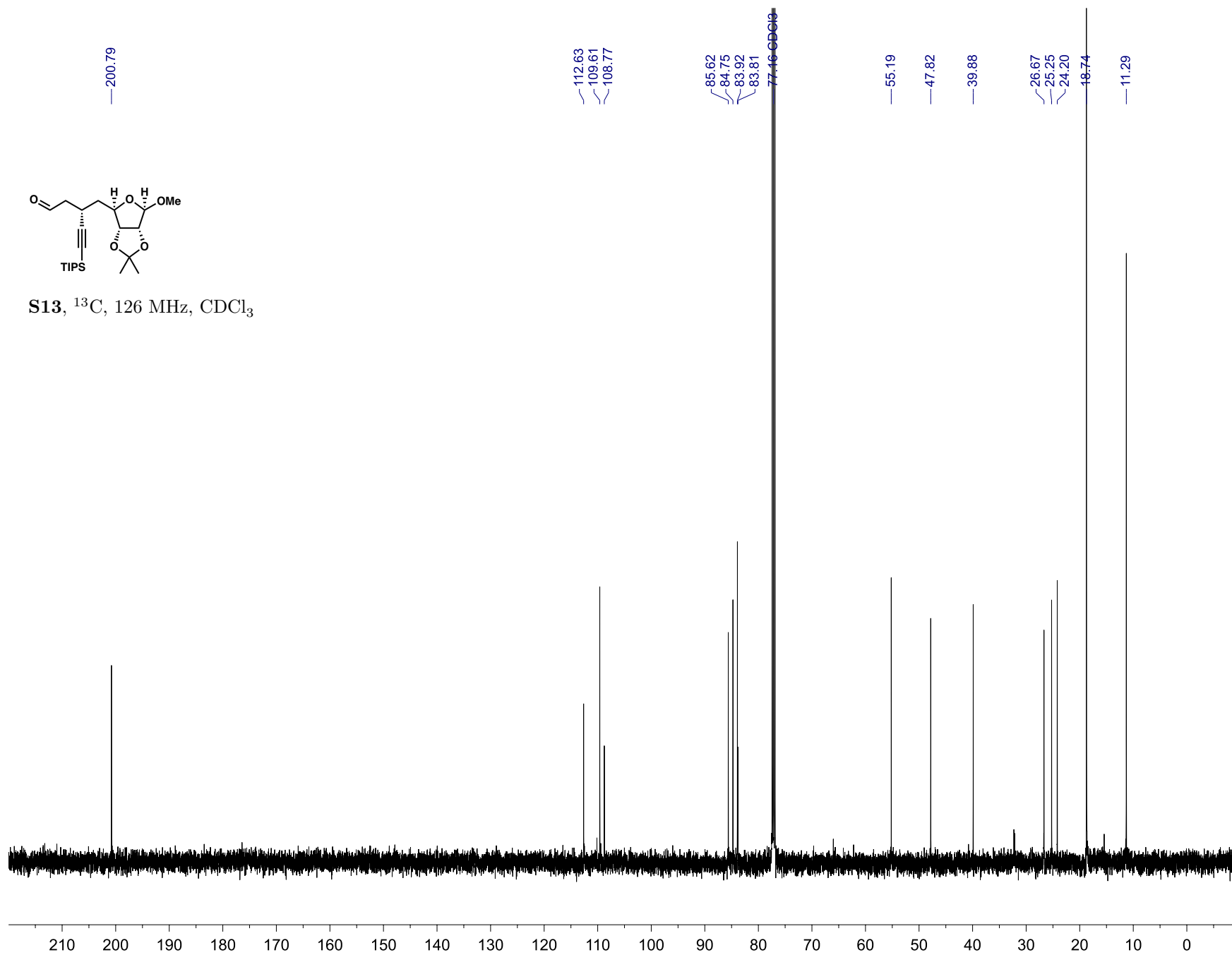
— 7.26  $\text{CDCl}_3$

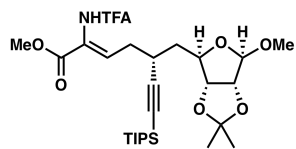
6FS



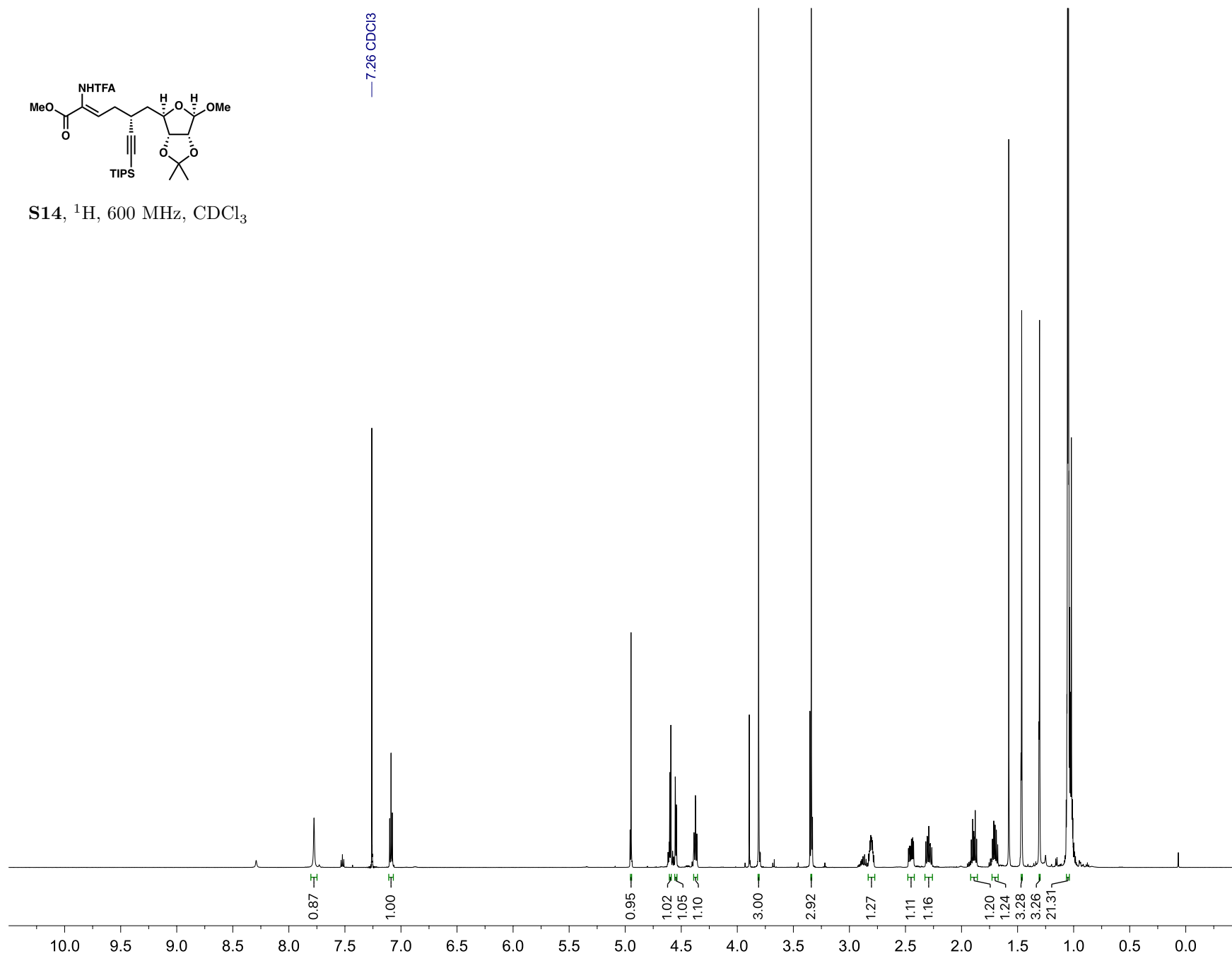


**S13**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

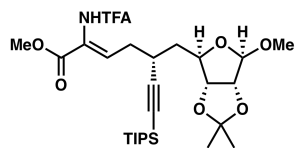




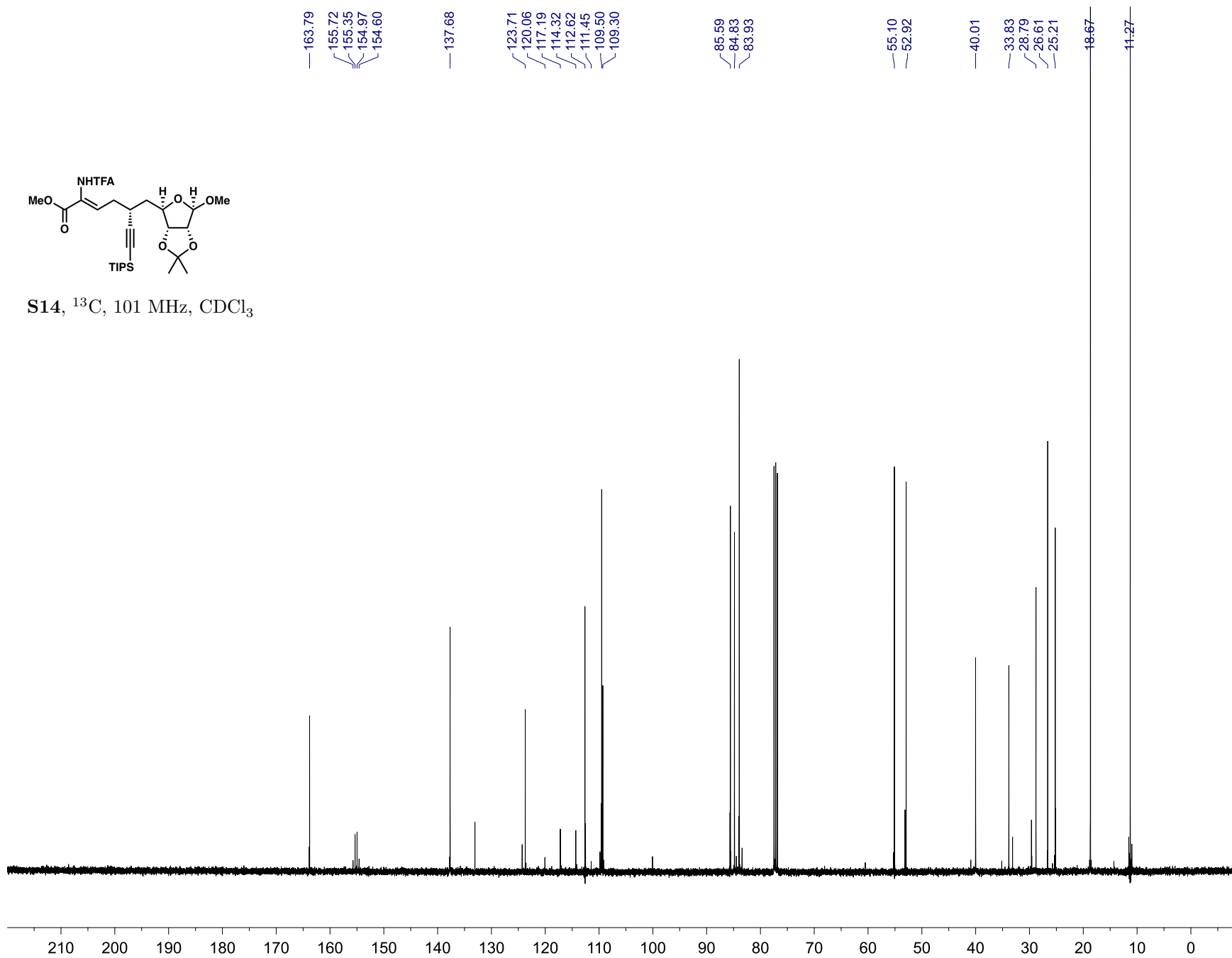
S14,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

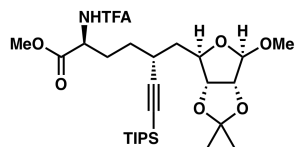


— 7.26  $\text{CDCl}_3$

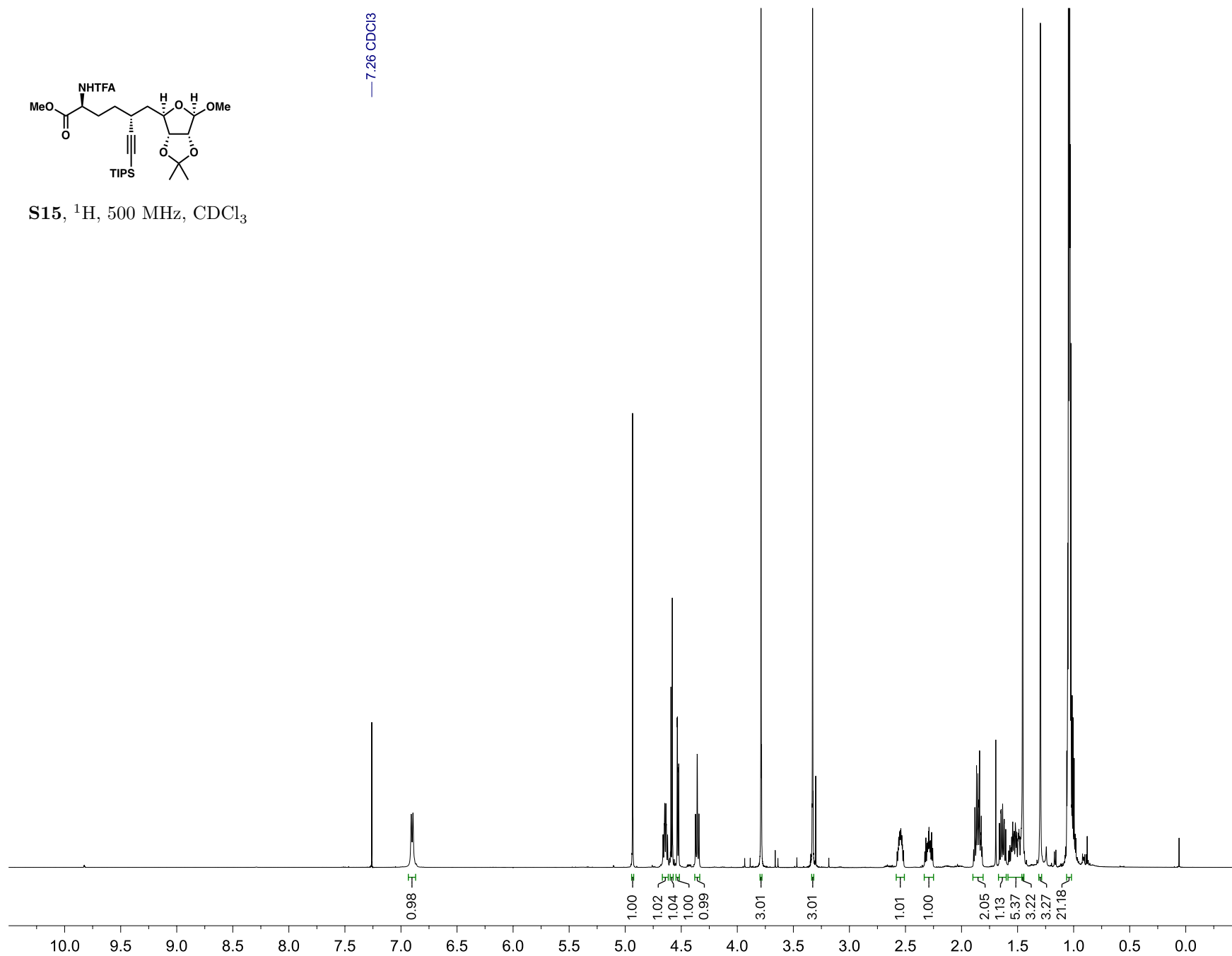


S14,  $^{13}\text{C}$ , 101 MHz,  $\text{CDCl}_3$

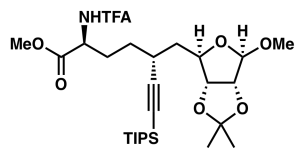




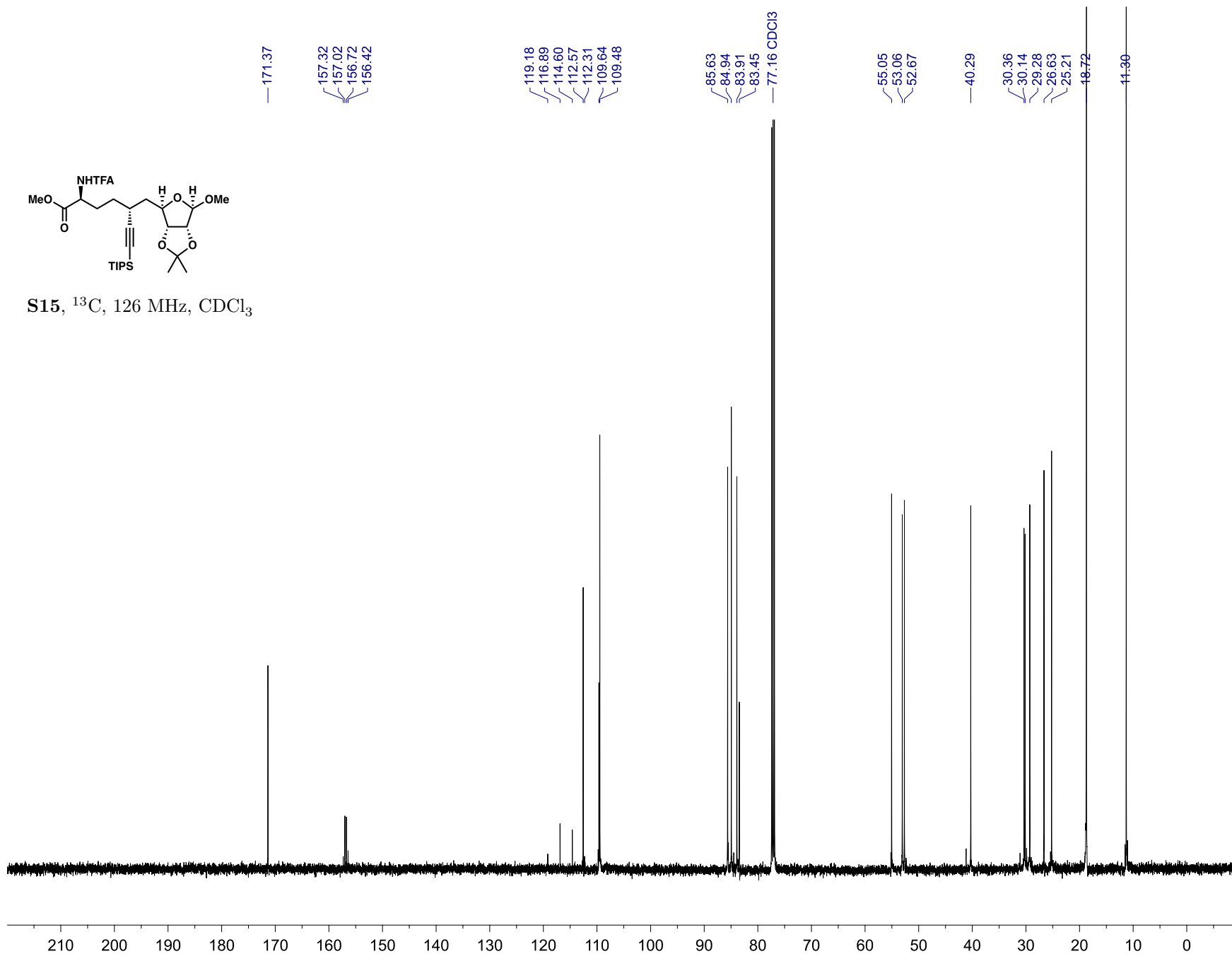
S15,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

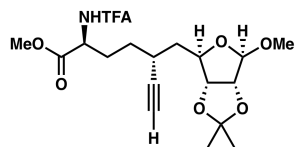


F5S

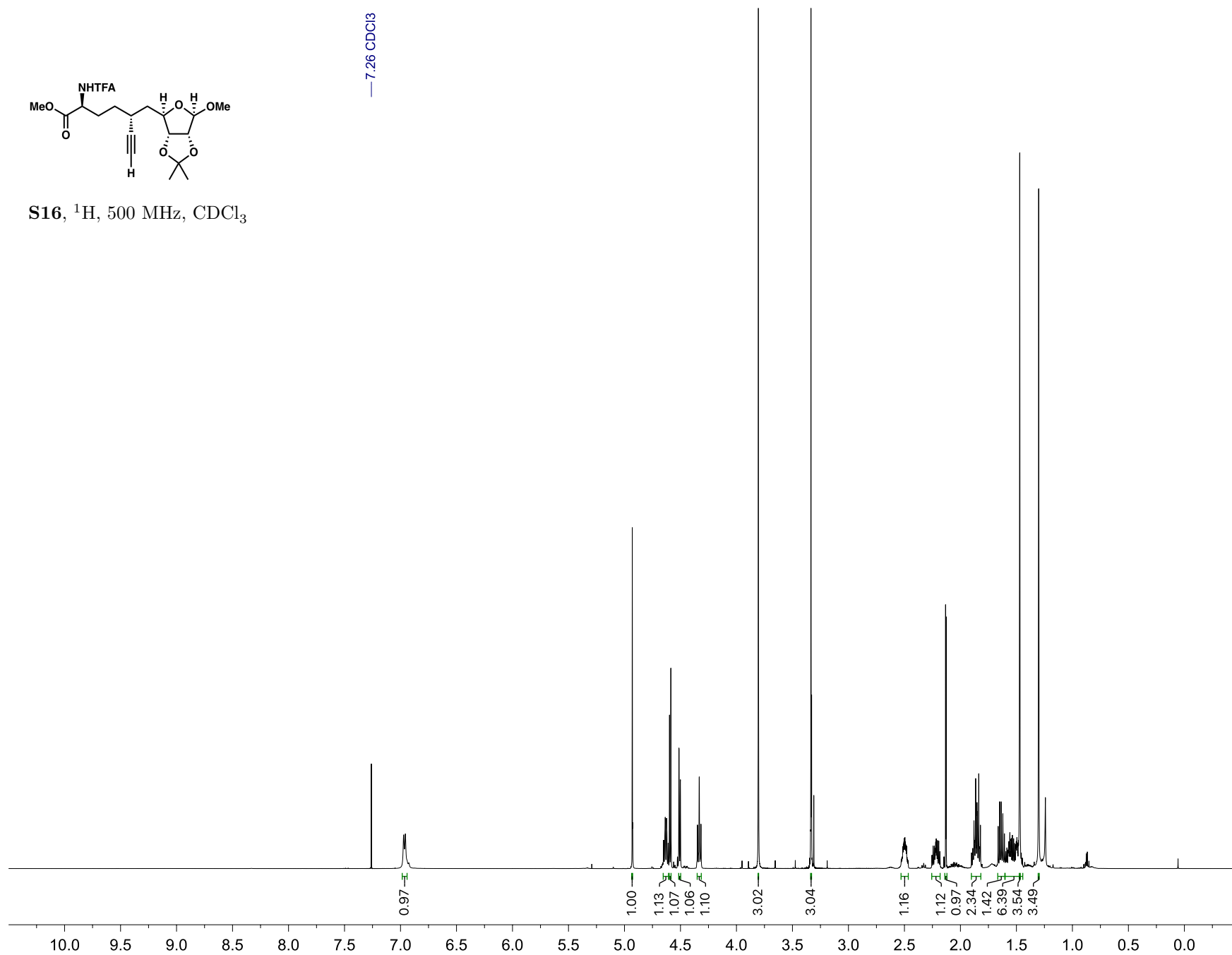


S15,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

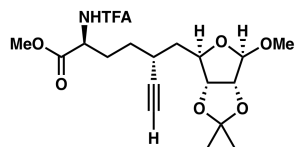




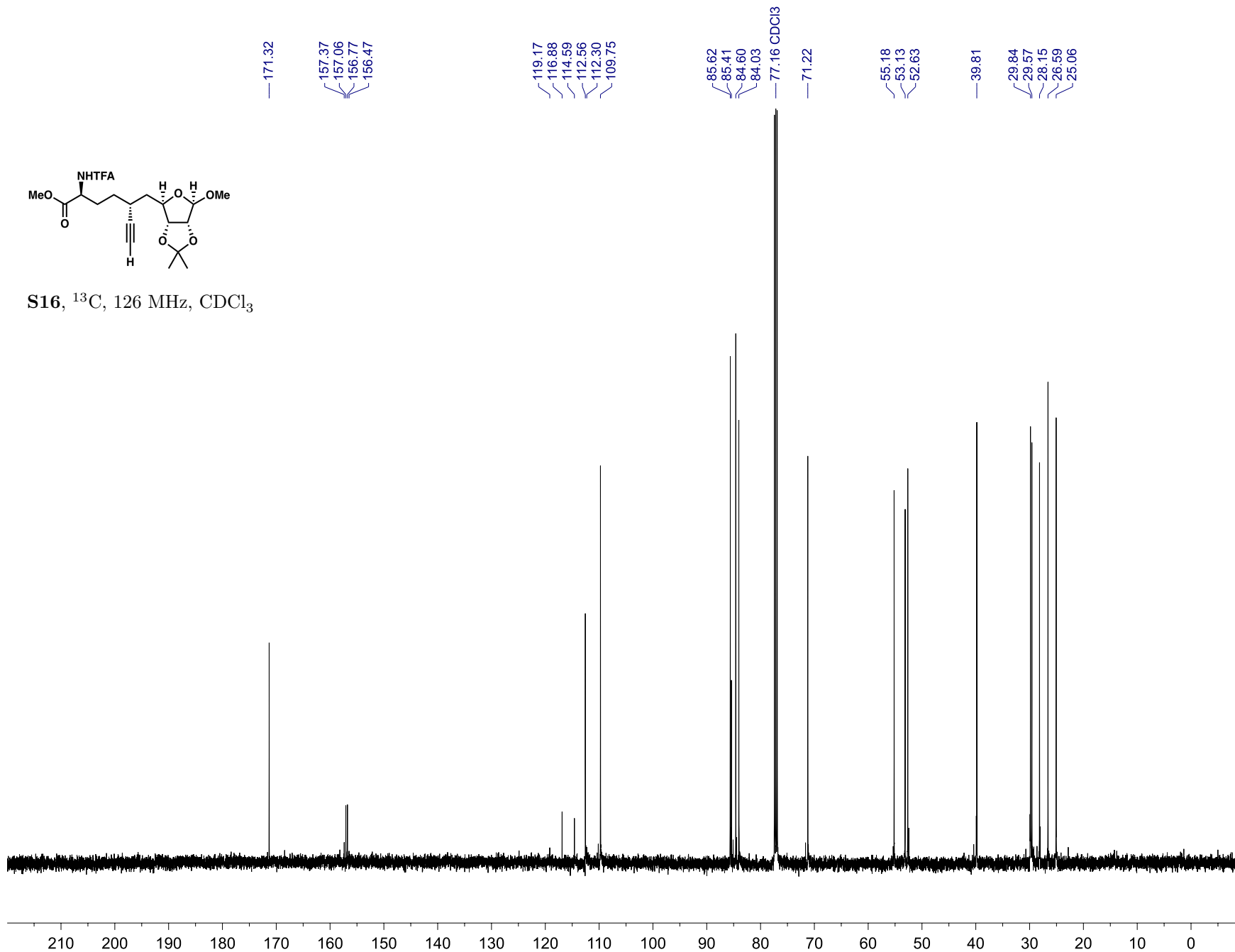
S16,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

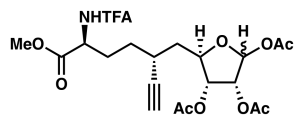




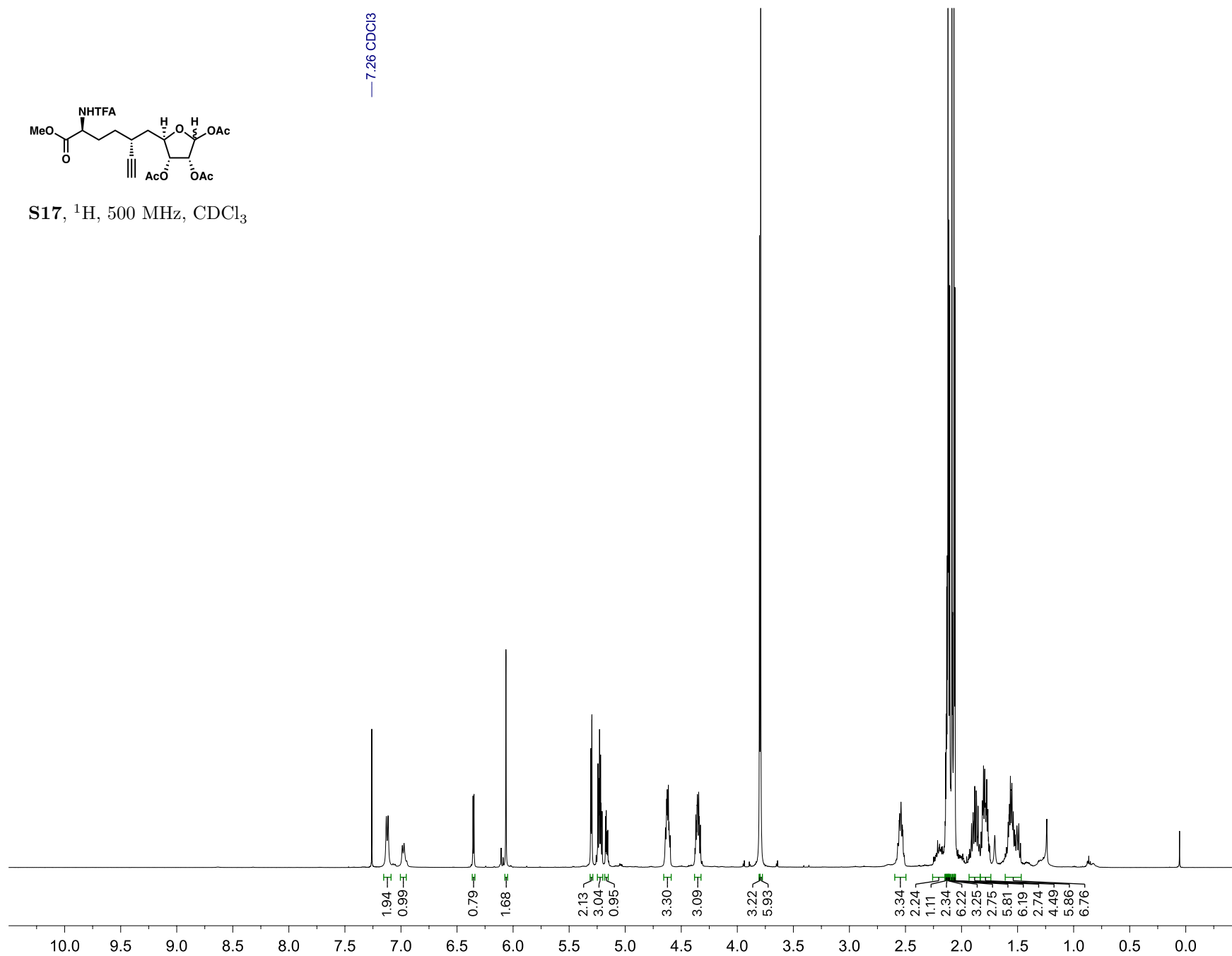


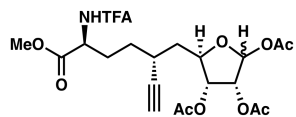
S16,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



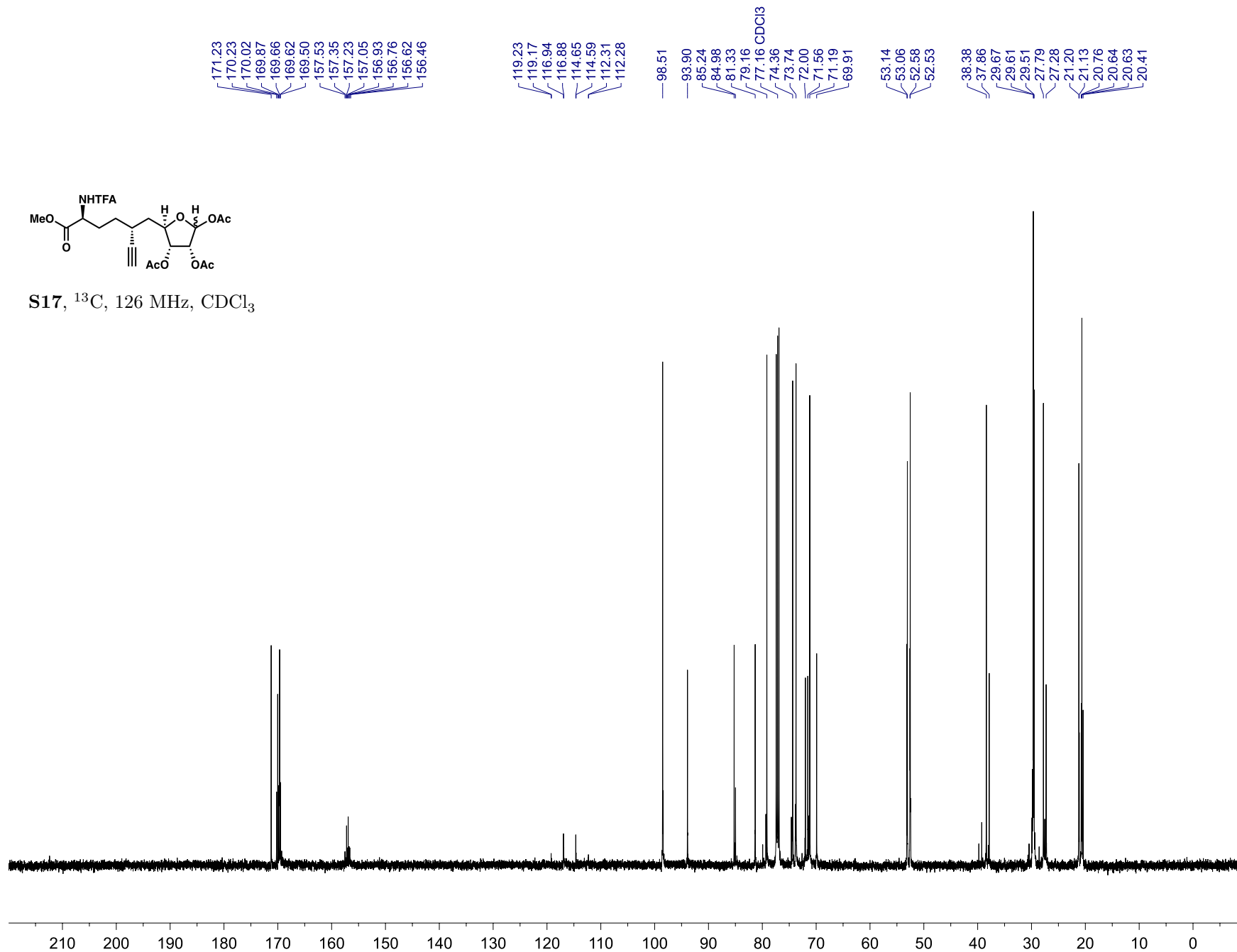


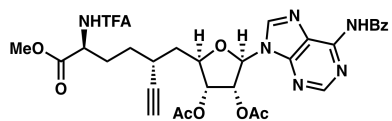
S17,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



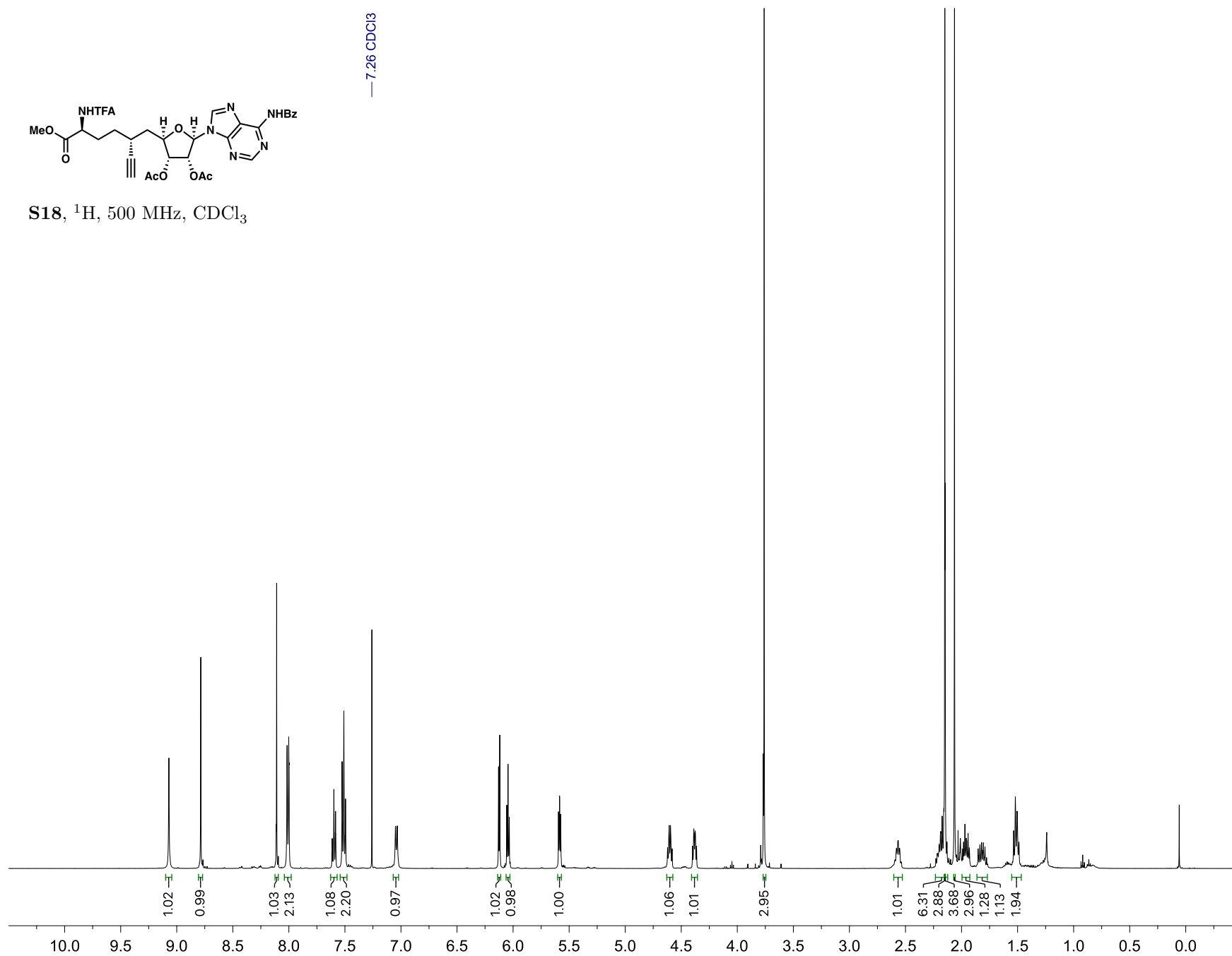


S17,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

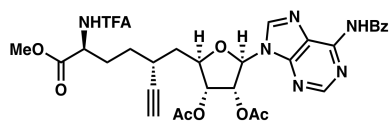




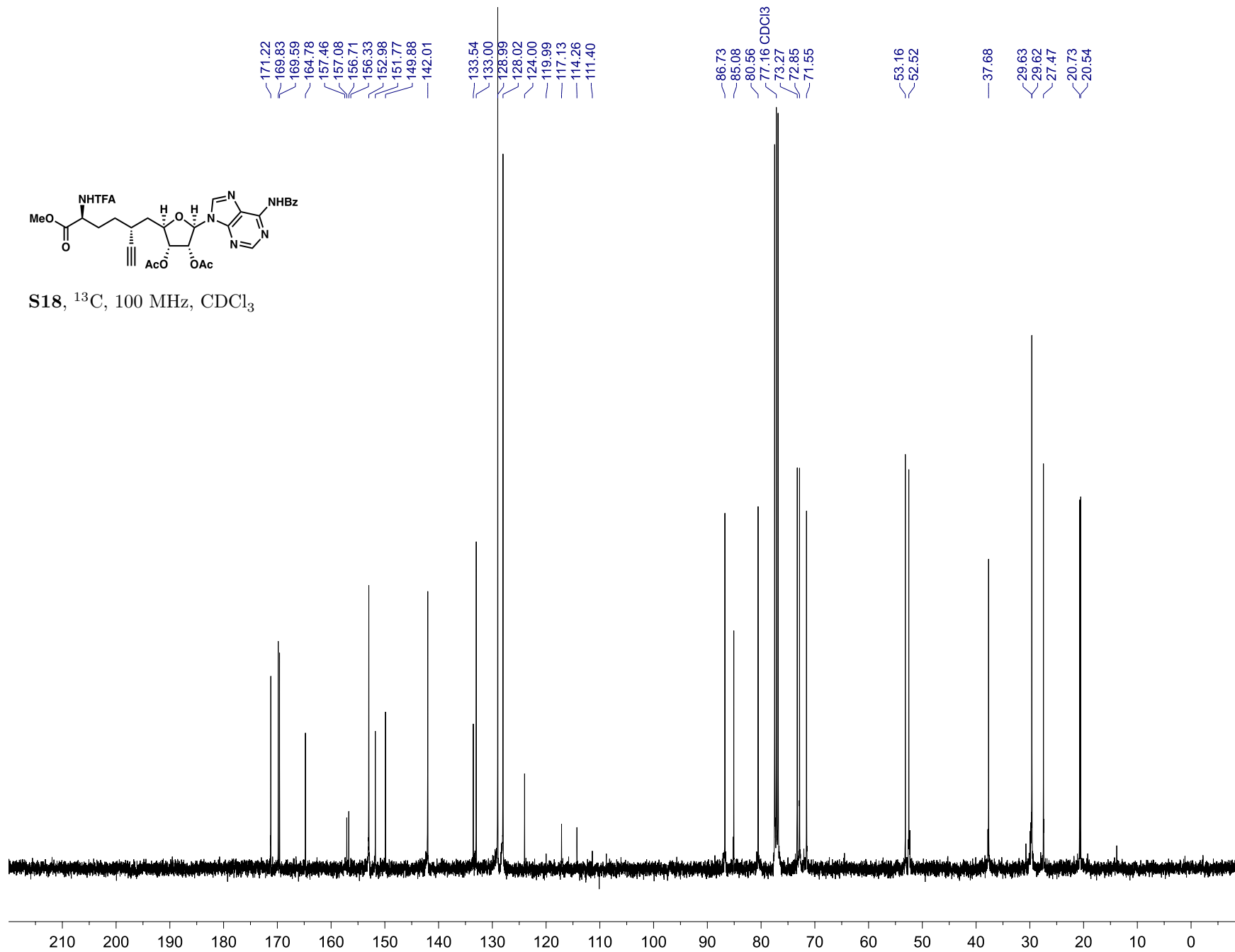
S18,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

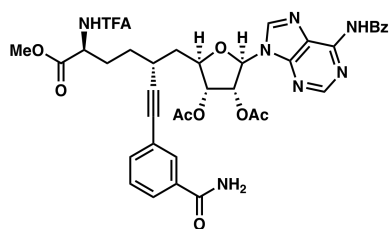


— 7.26  $\text{CDCl}_3$



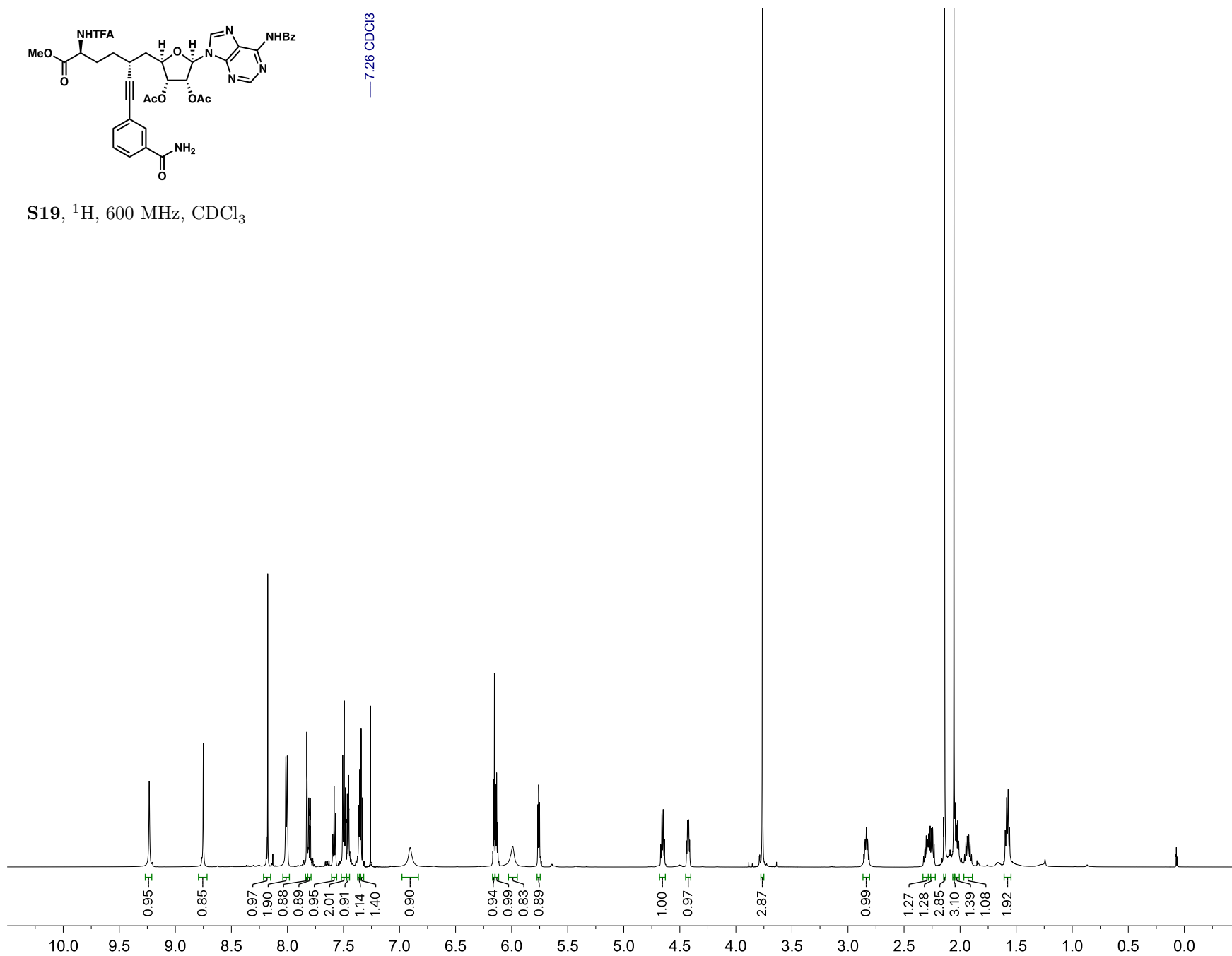
S18,  $^{13}\text{C}$ , 100 MHz,  $\text{CDCl}_3$

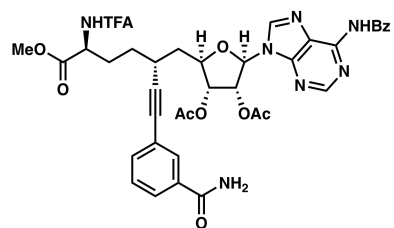




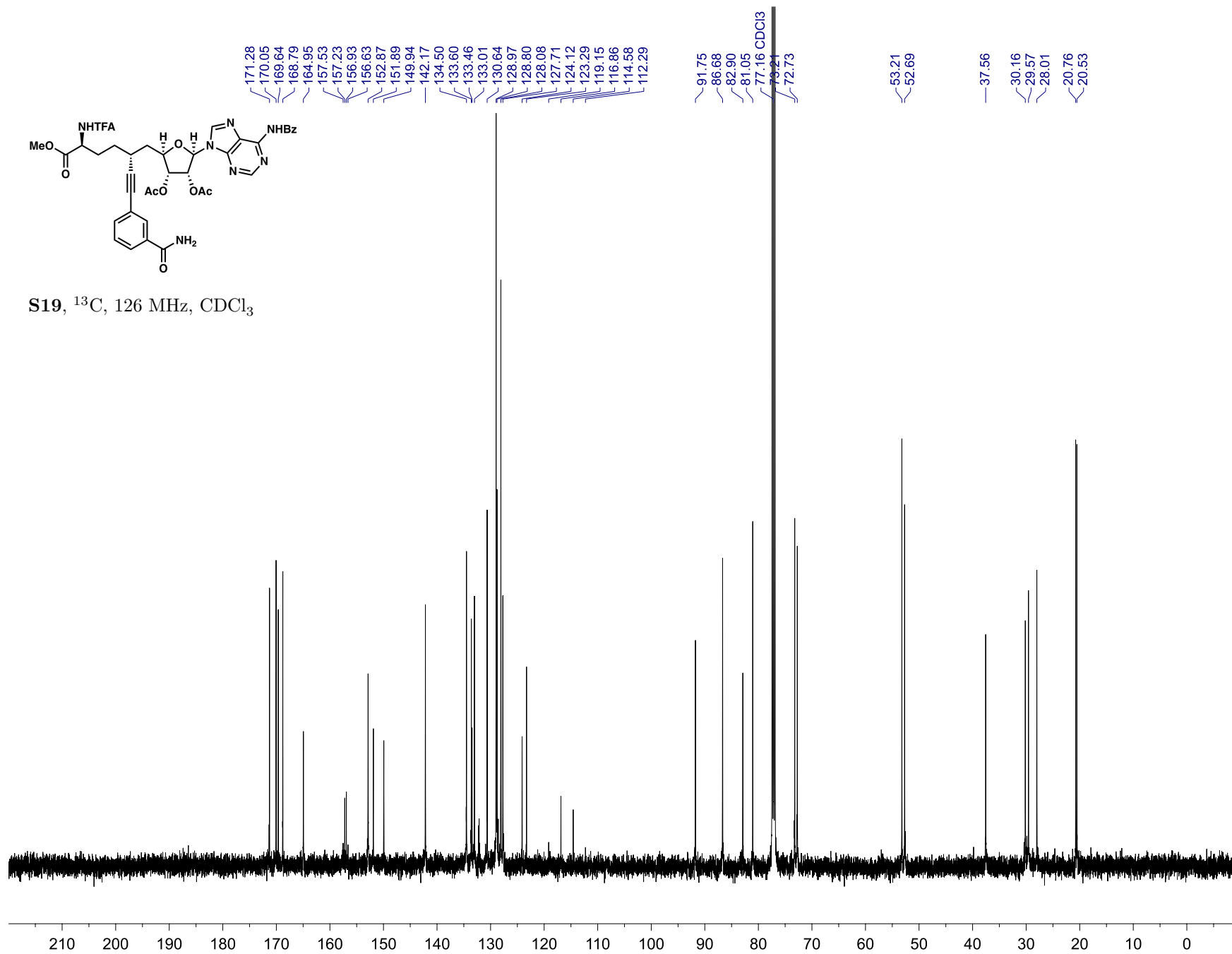
— 7.26 CDCl<sub>3</sub>

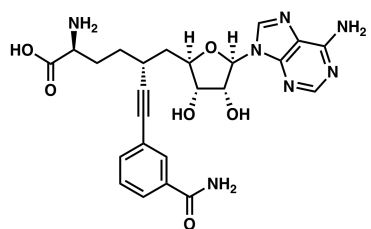
S19, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





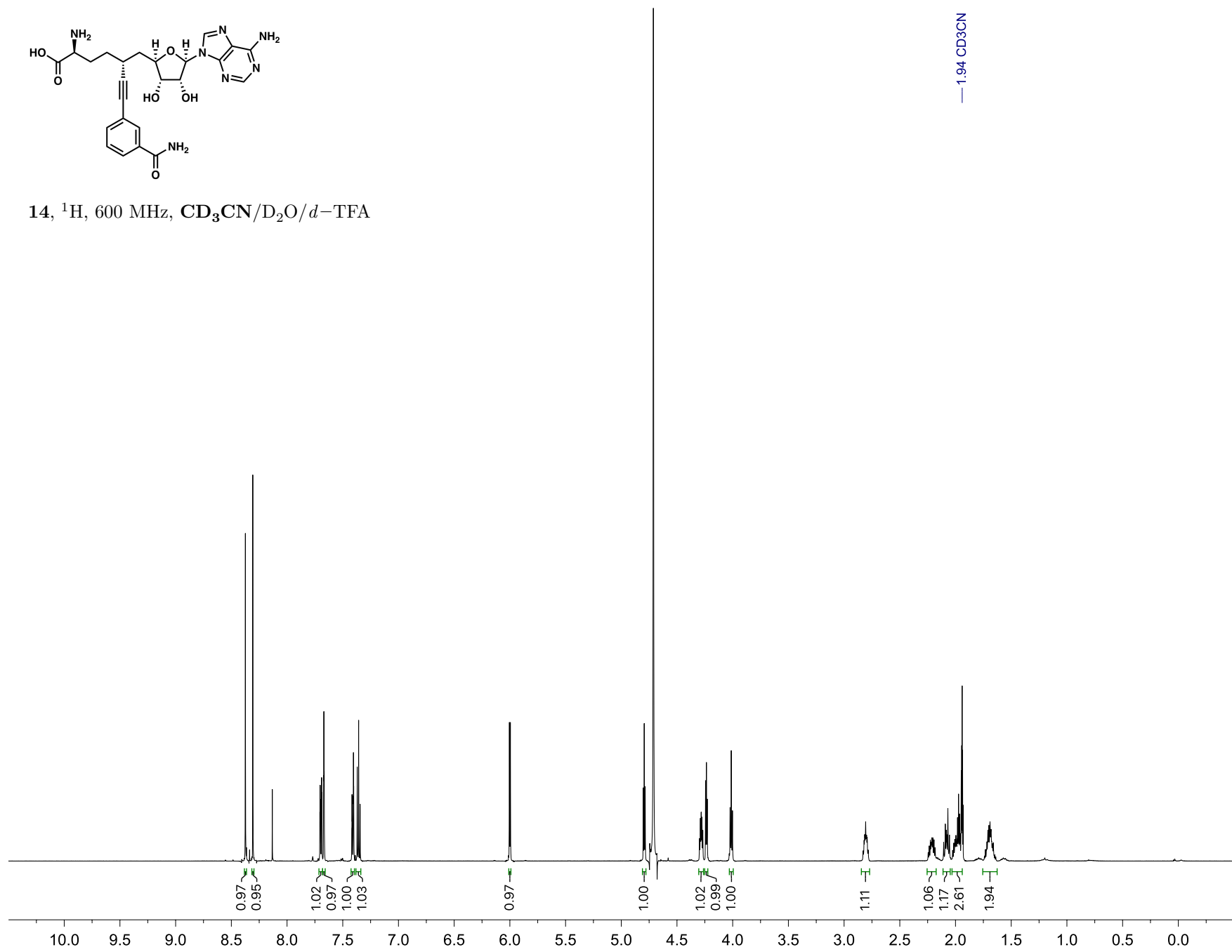
**S19**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$





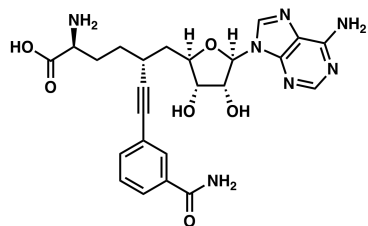
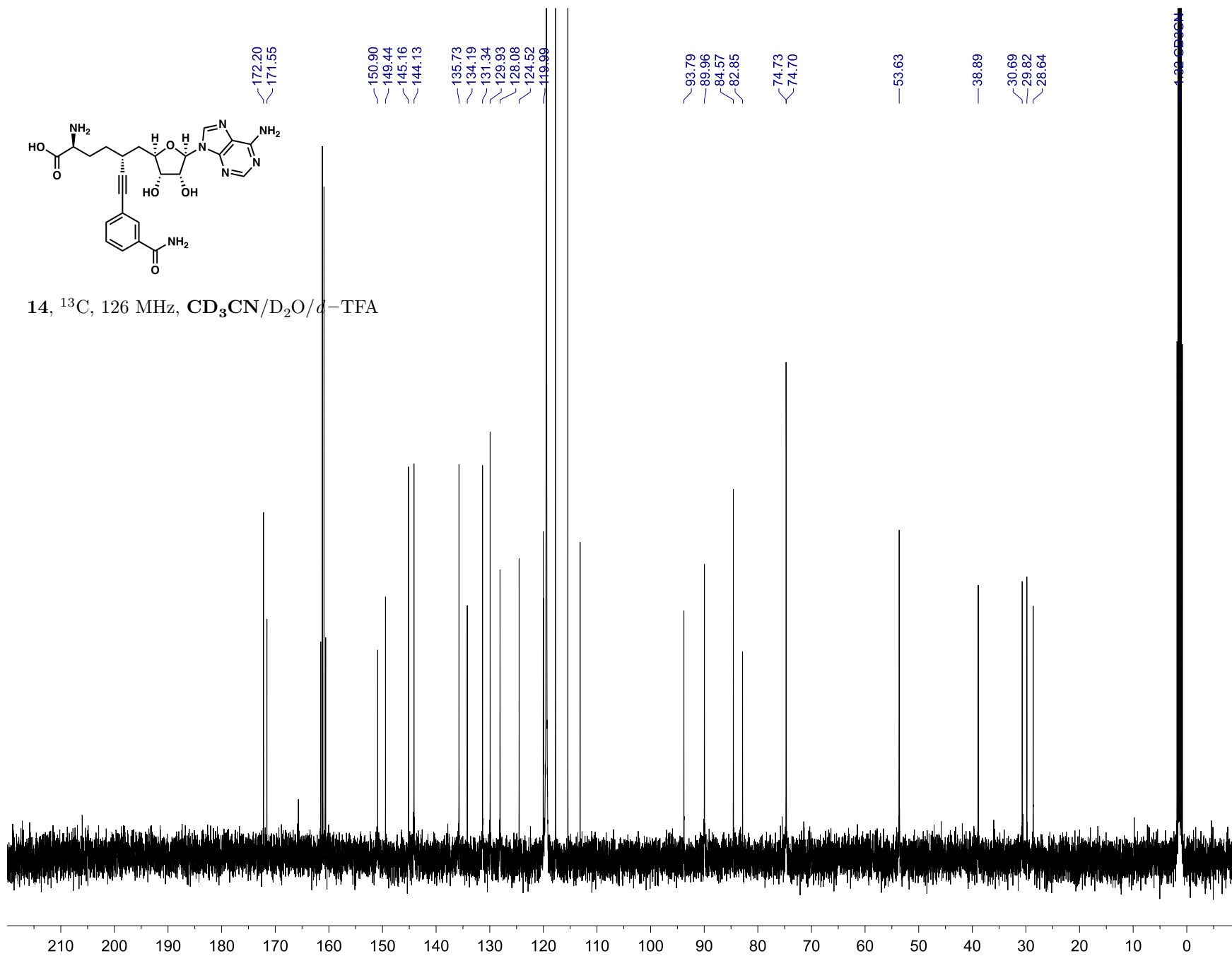
14, <sup>1</sup>H, 600 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA

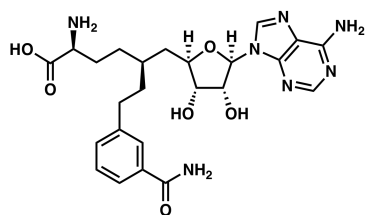
S63



— 1.94 CD3CN

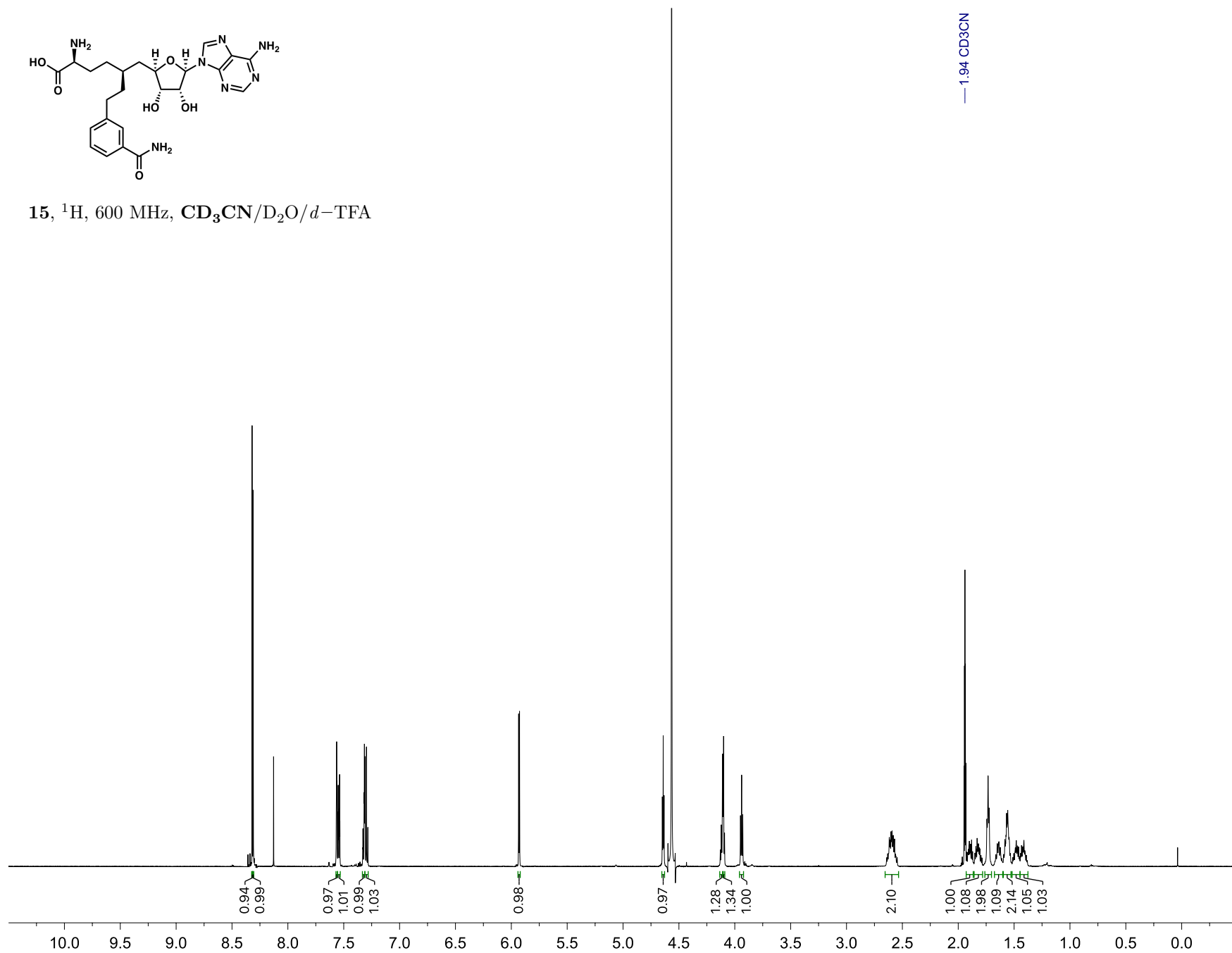


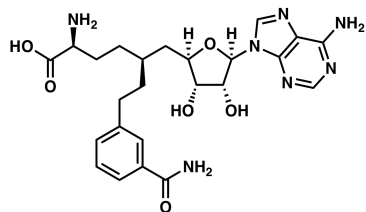
14,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$ 



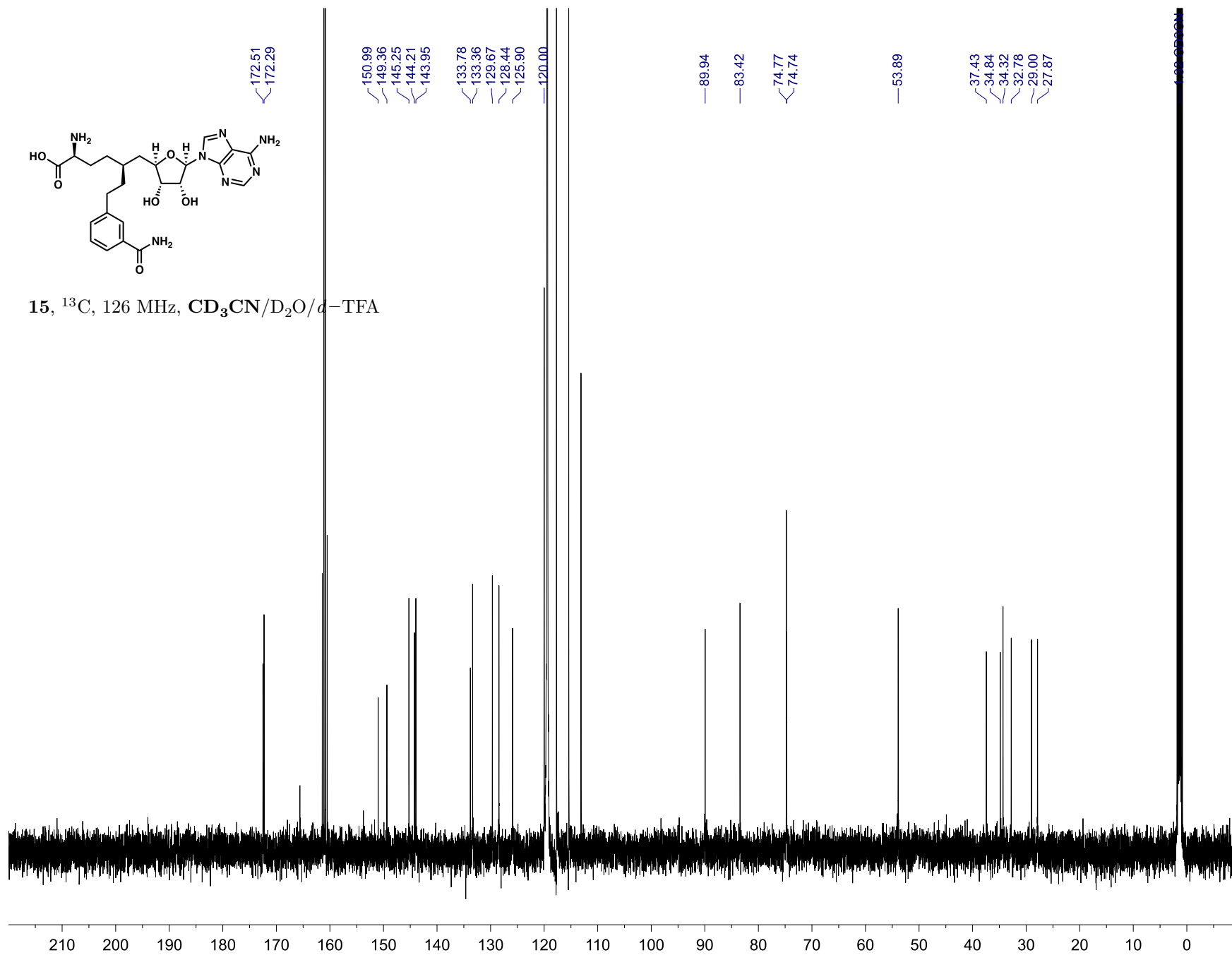
15,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

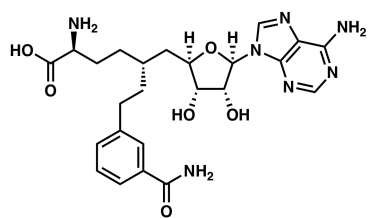
595





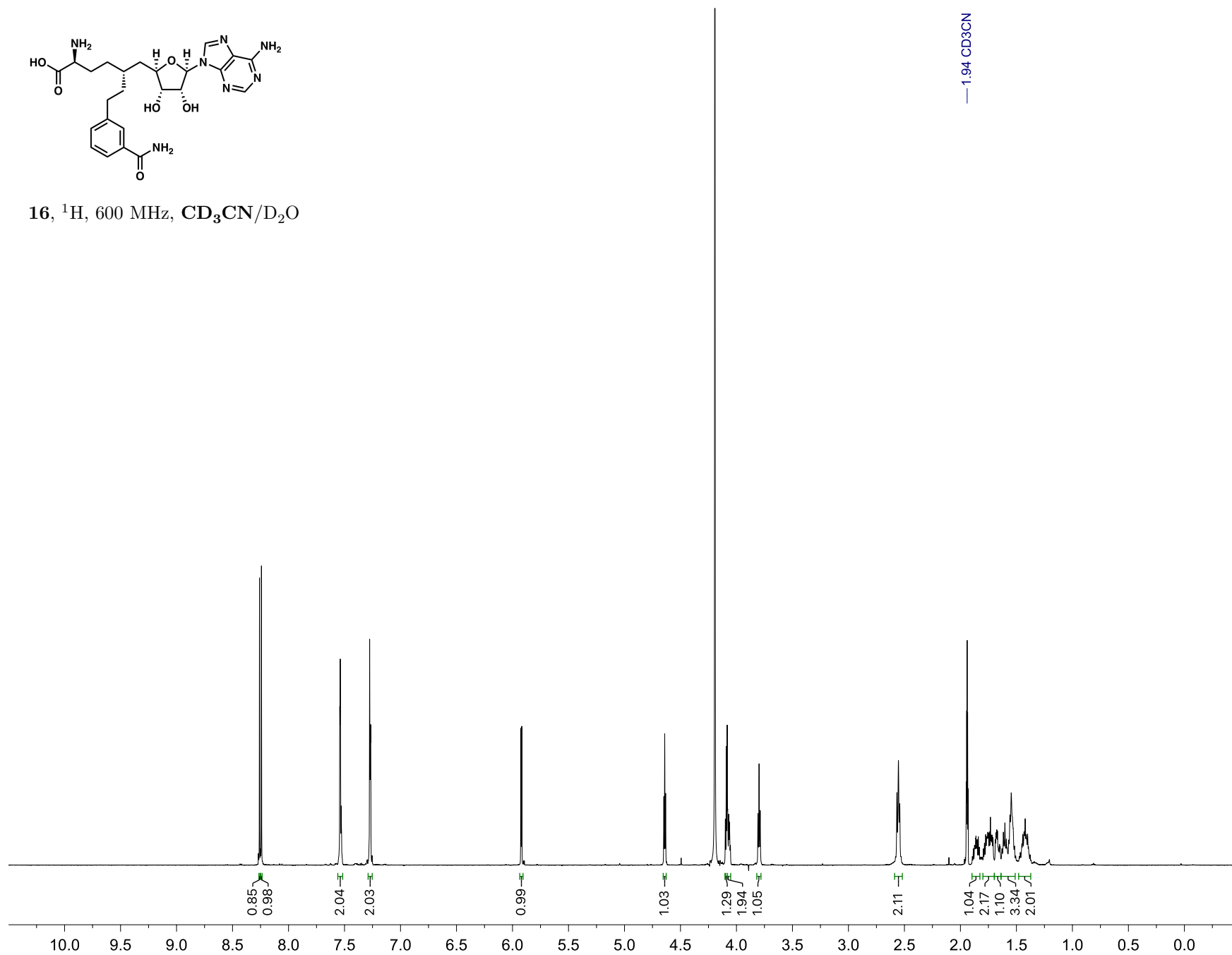
15, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA

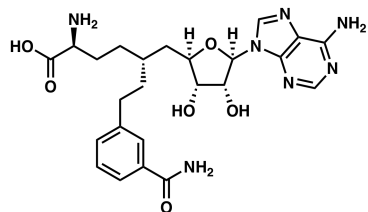




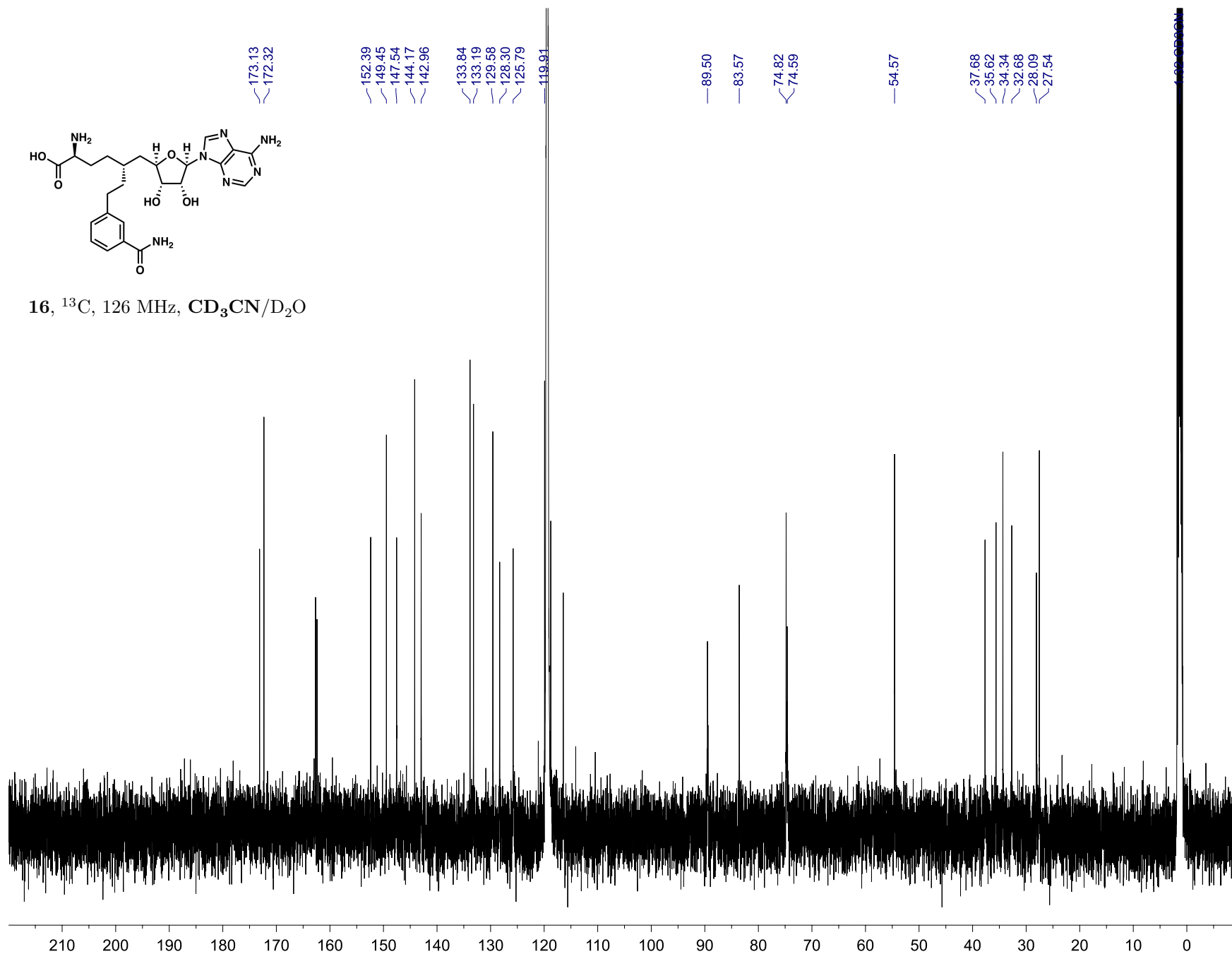
16,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

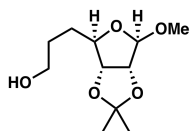
795



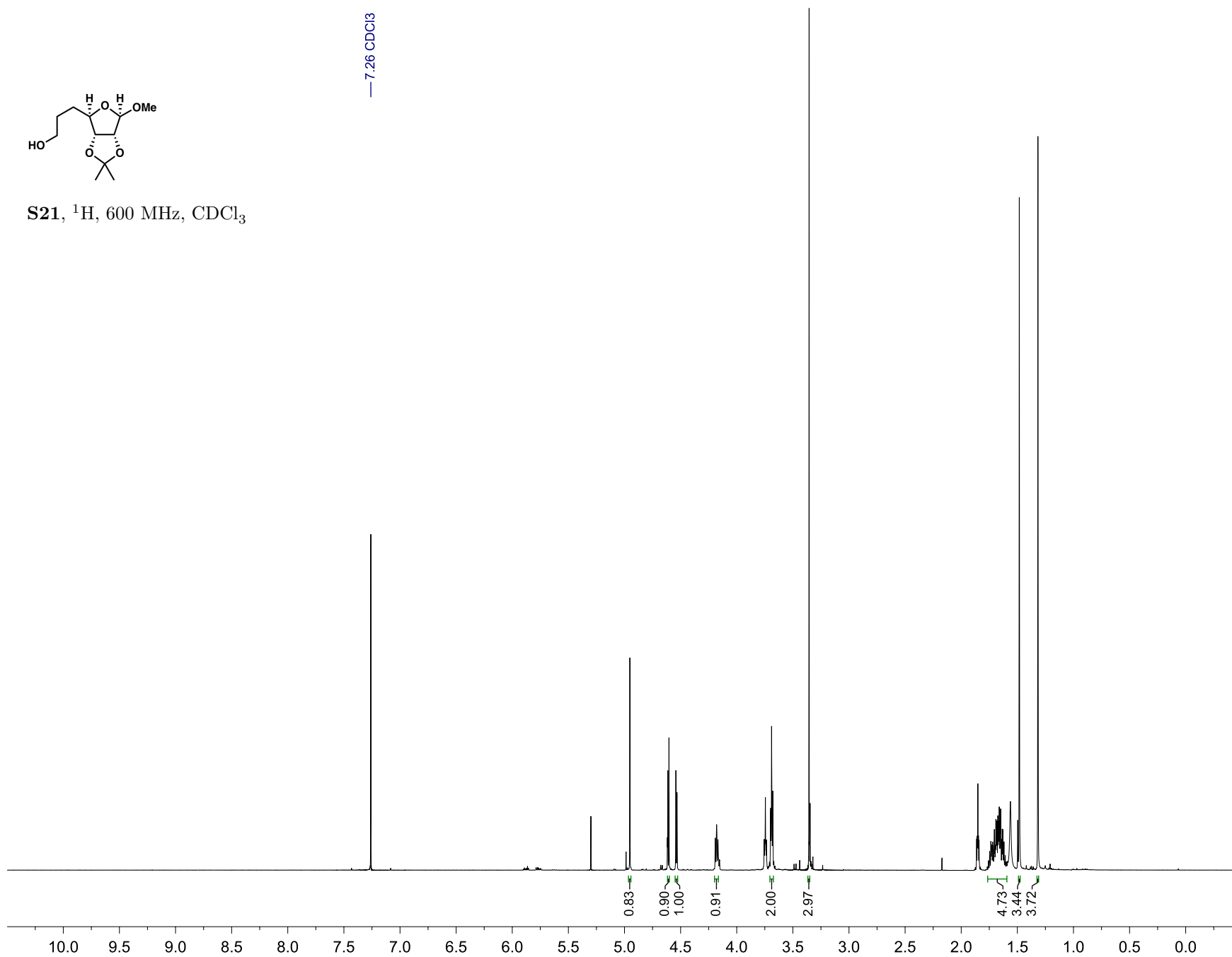


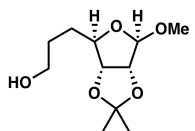
16,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$





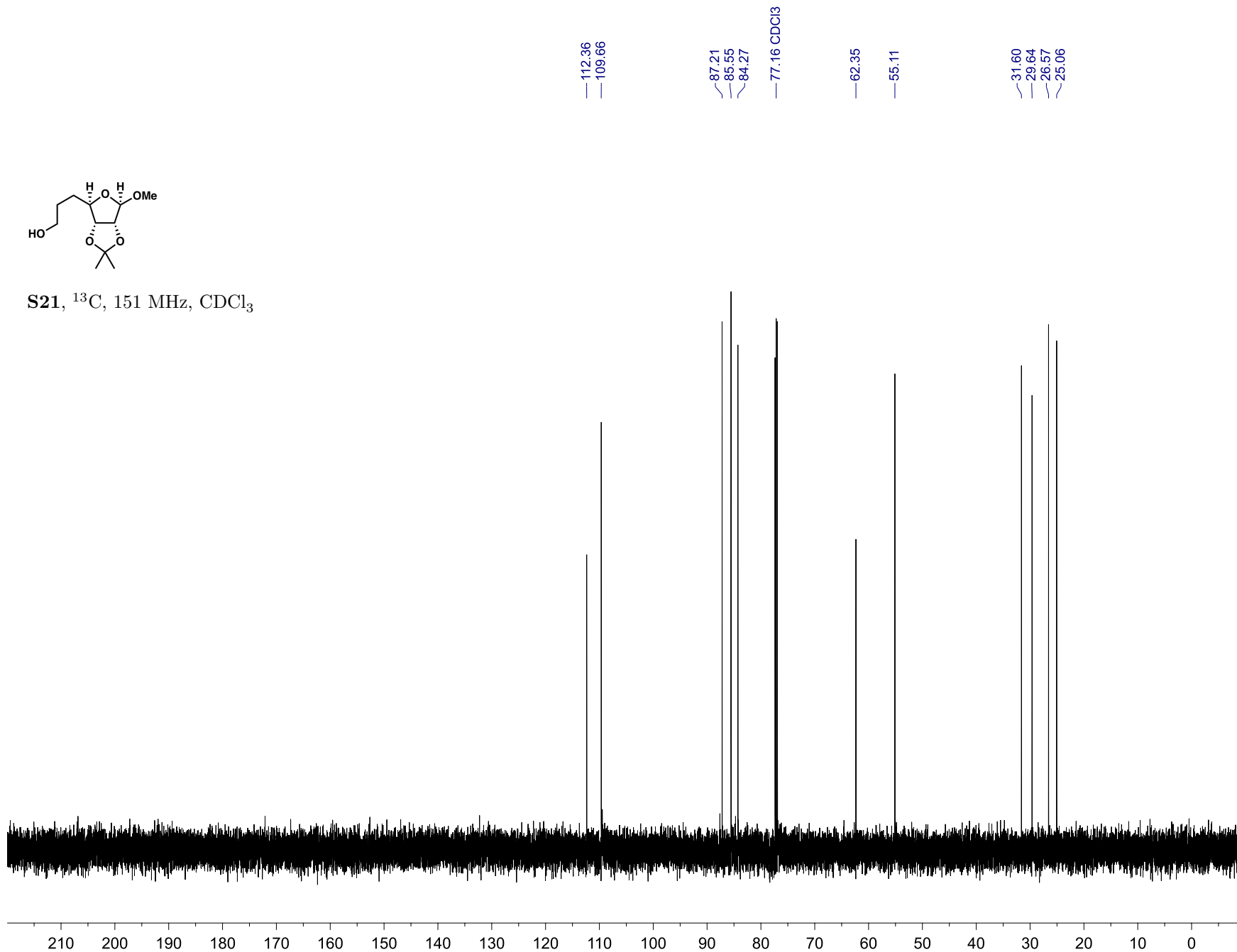
S21,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

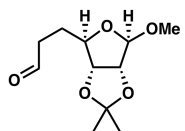




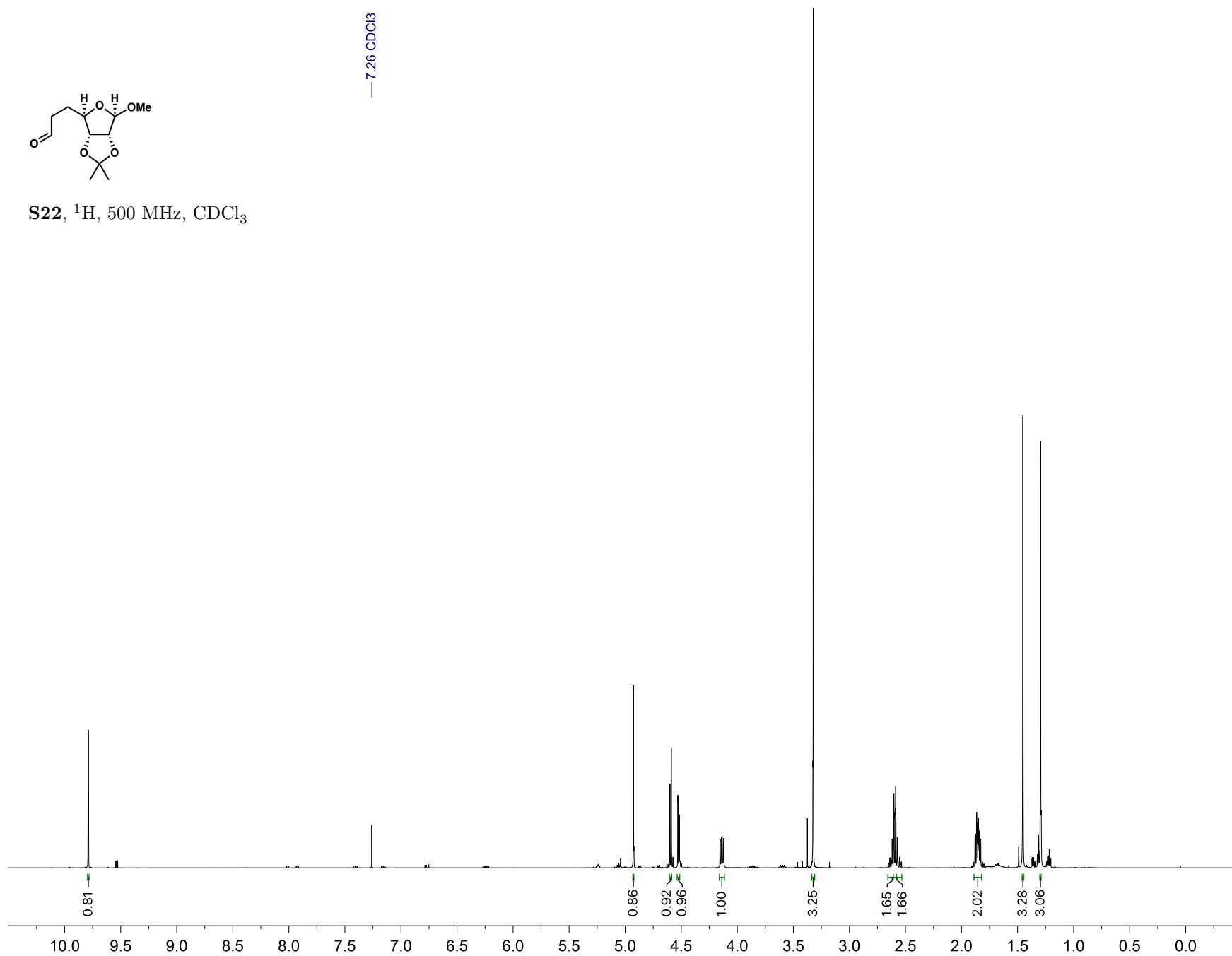
S21,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

0.25

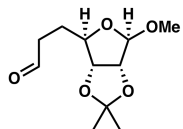
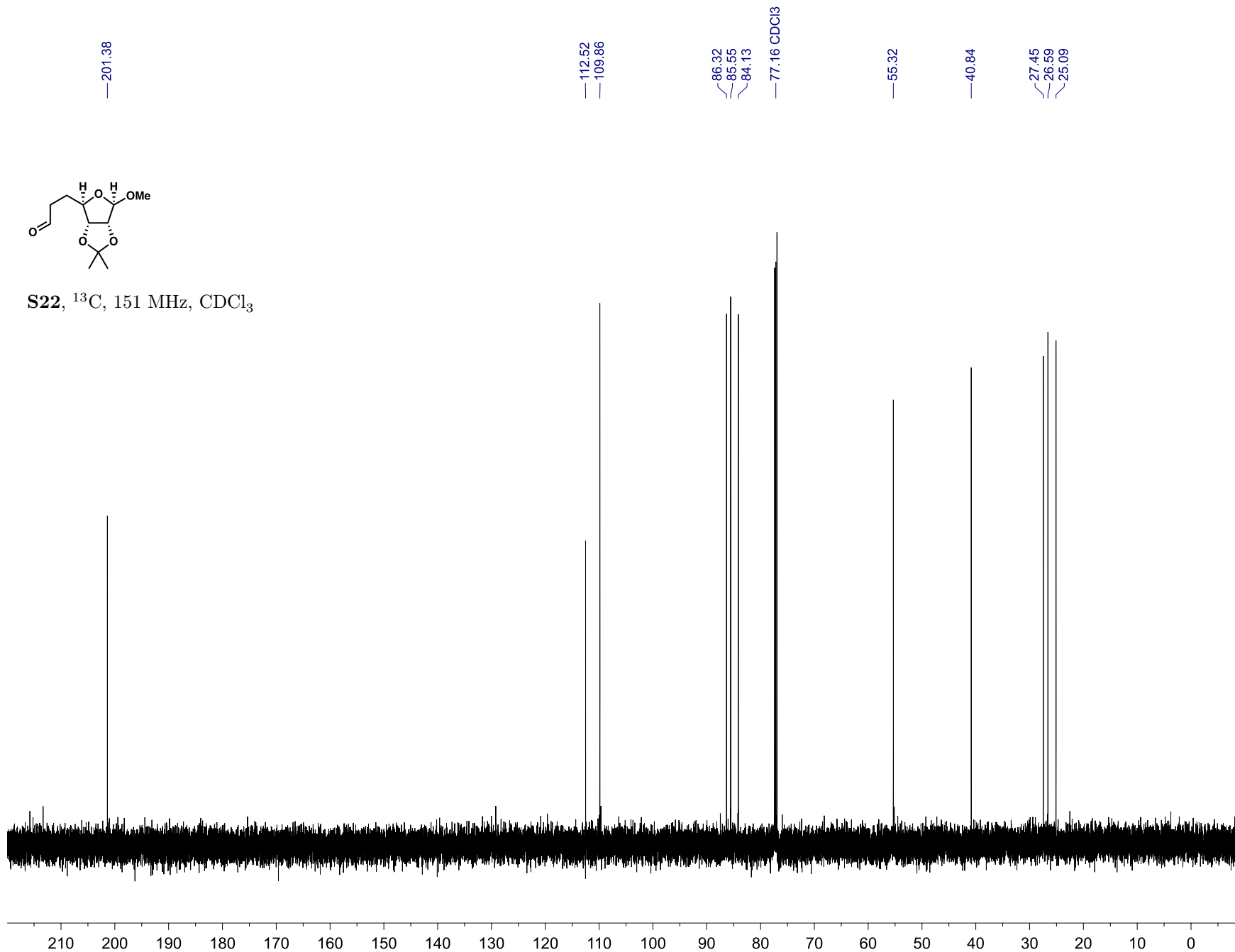


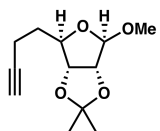


S22,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

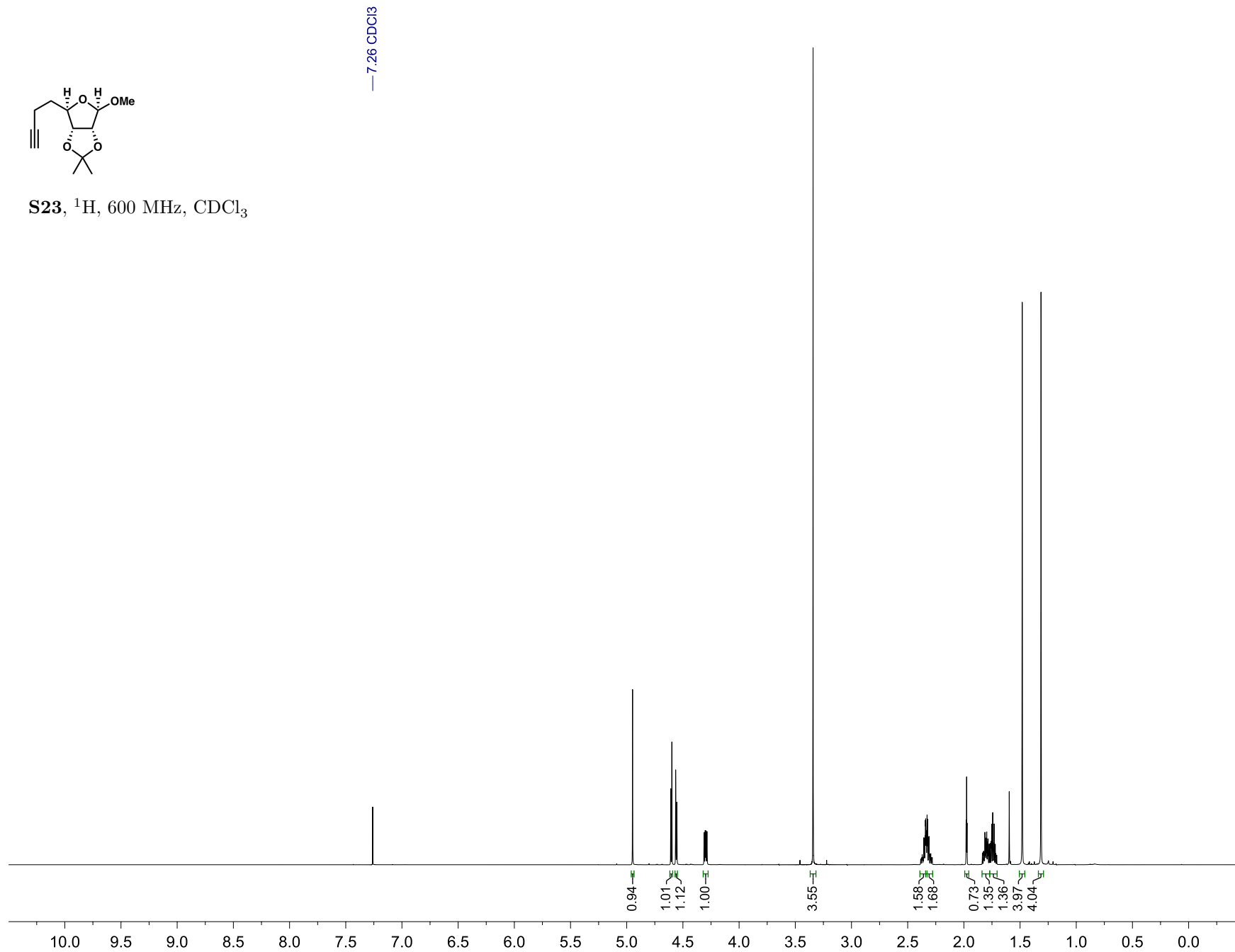


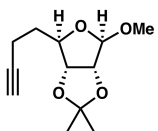


**S22**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 



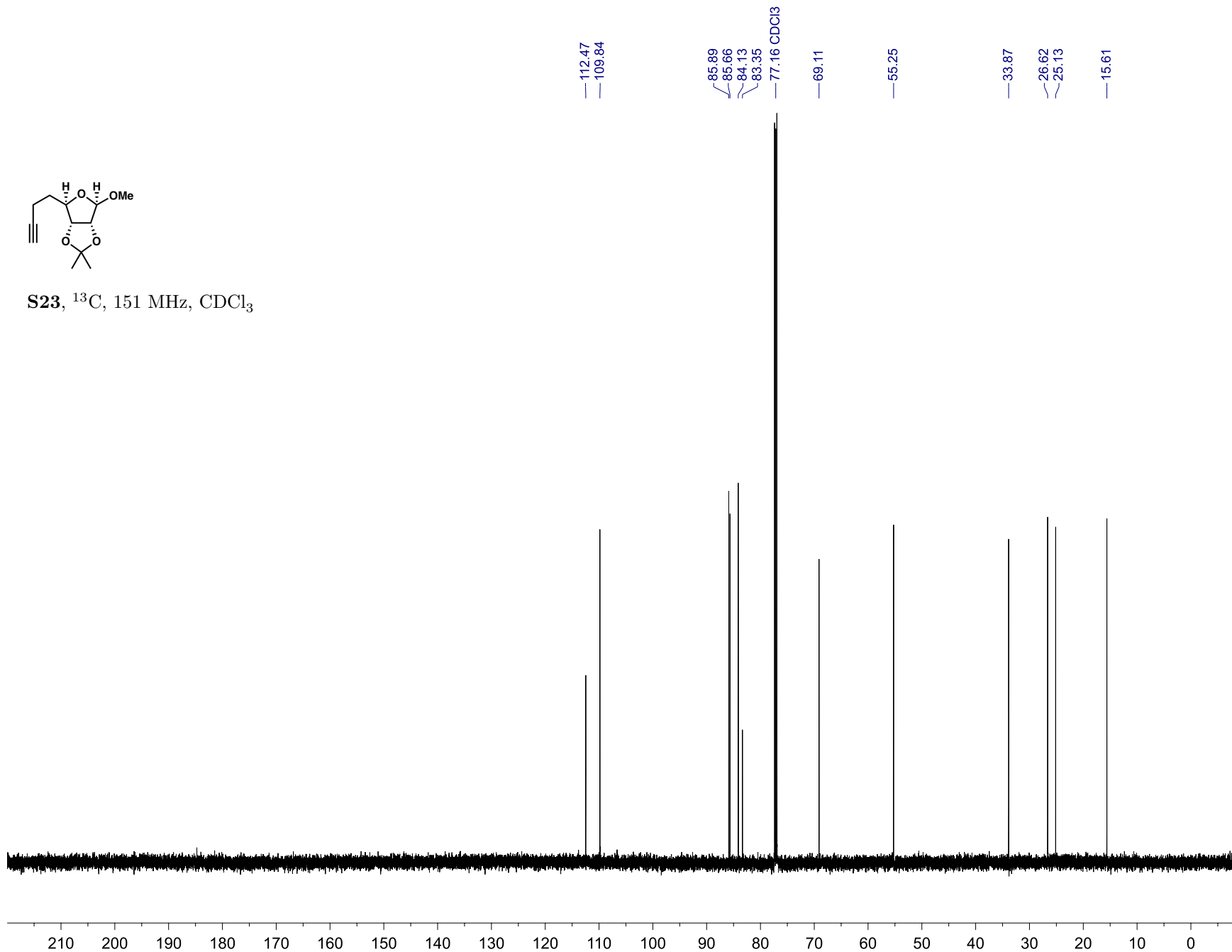
S23,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

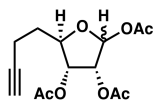
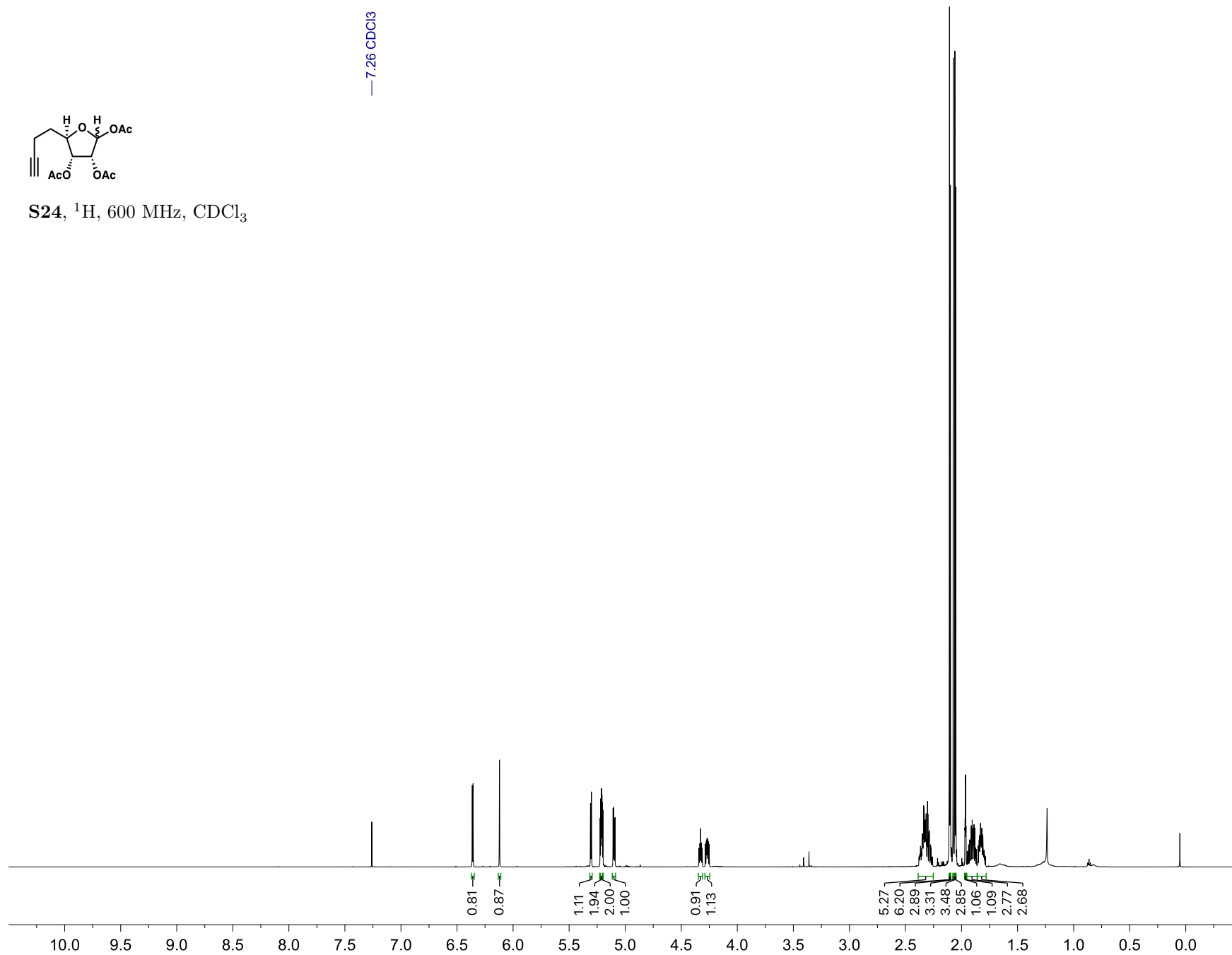


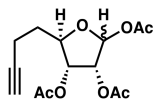
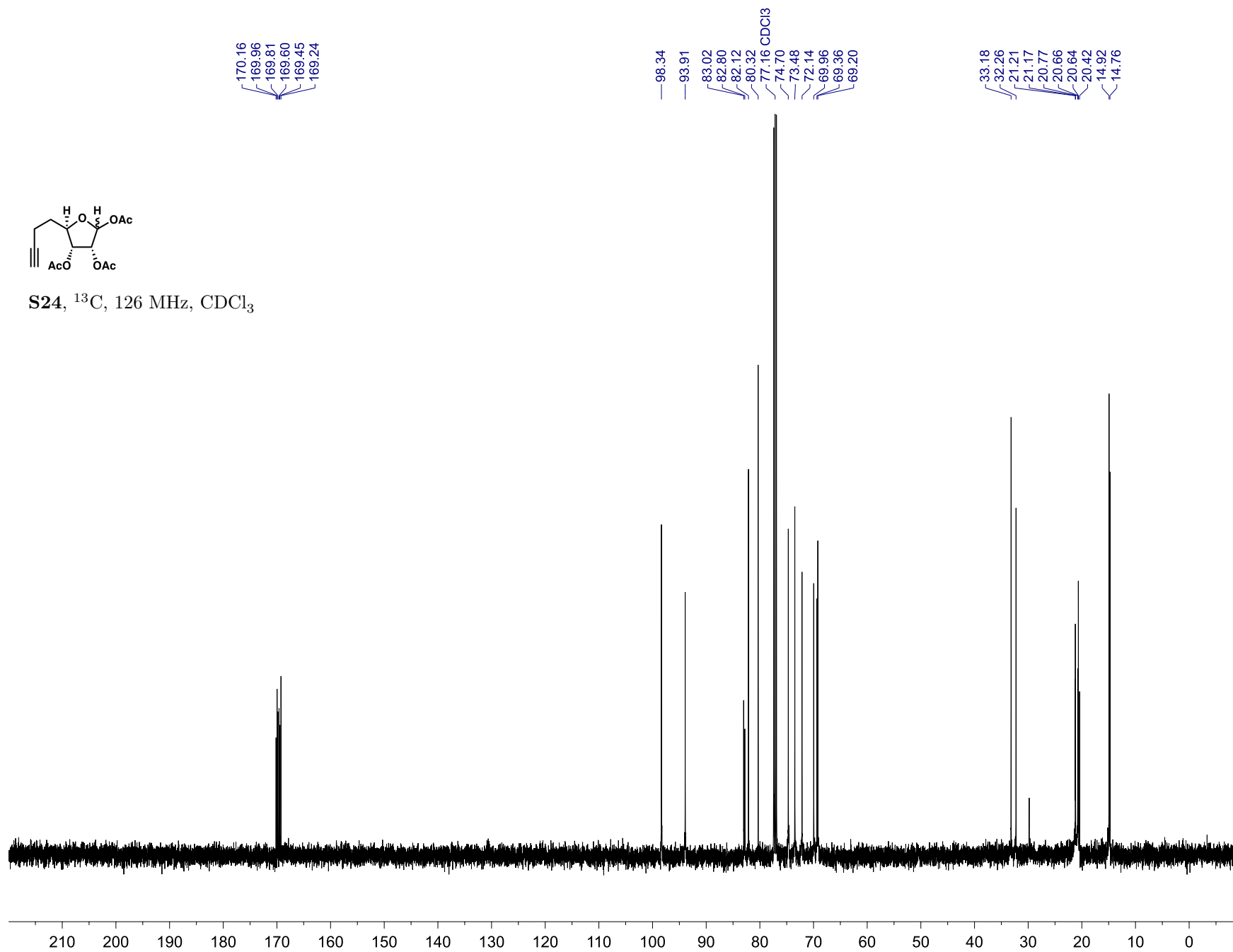


**S23**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

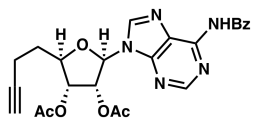
F2S



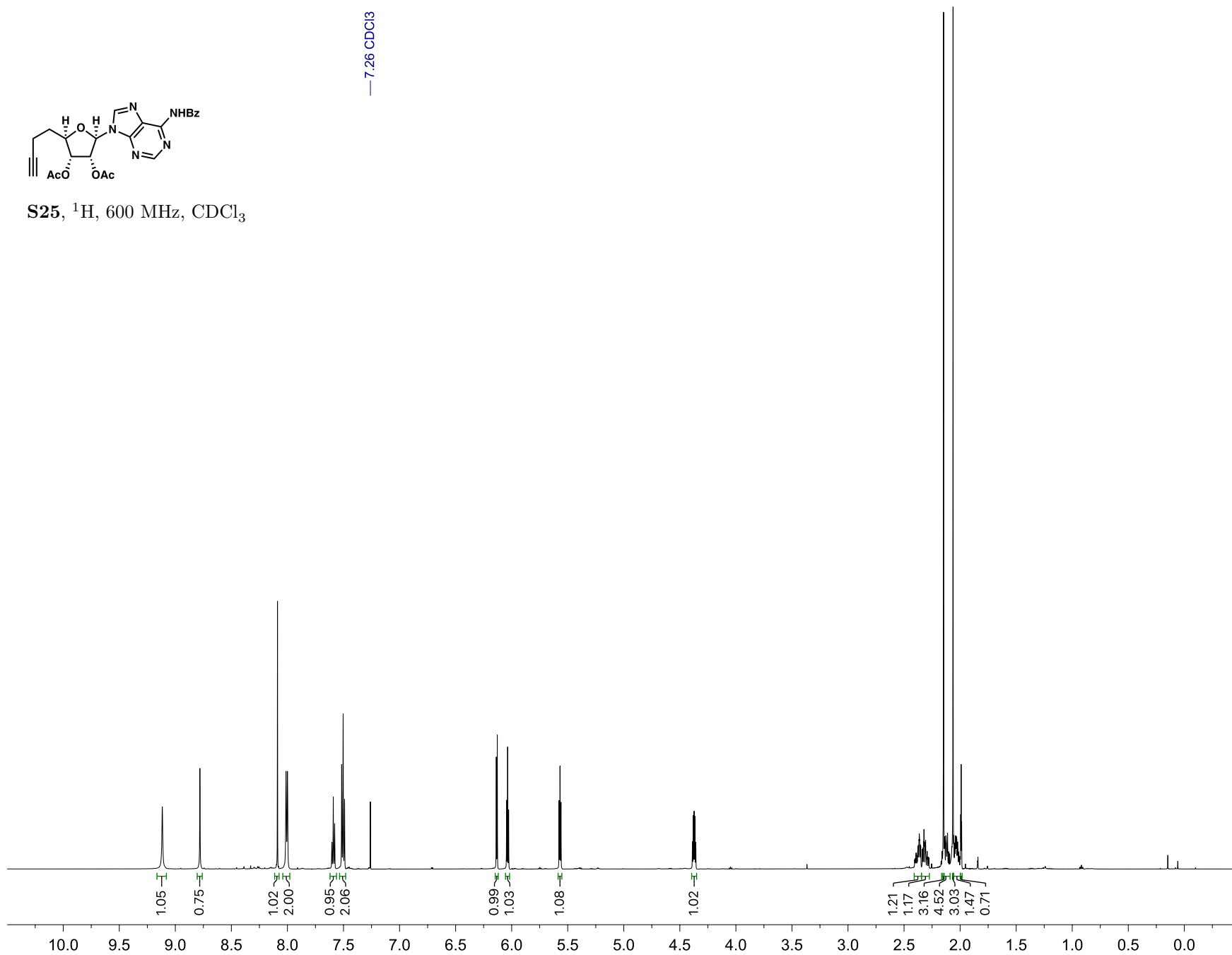
**S24**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ — 7.26  $\text{CDCl}_3$ 

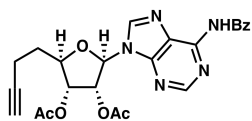
**S24**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$ 

— 7.26 CDCl<sub>3</sub>

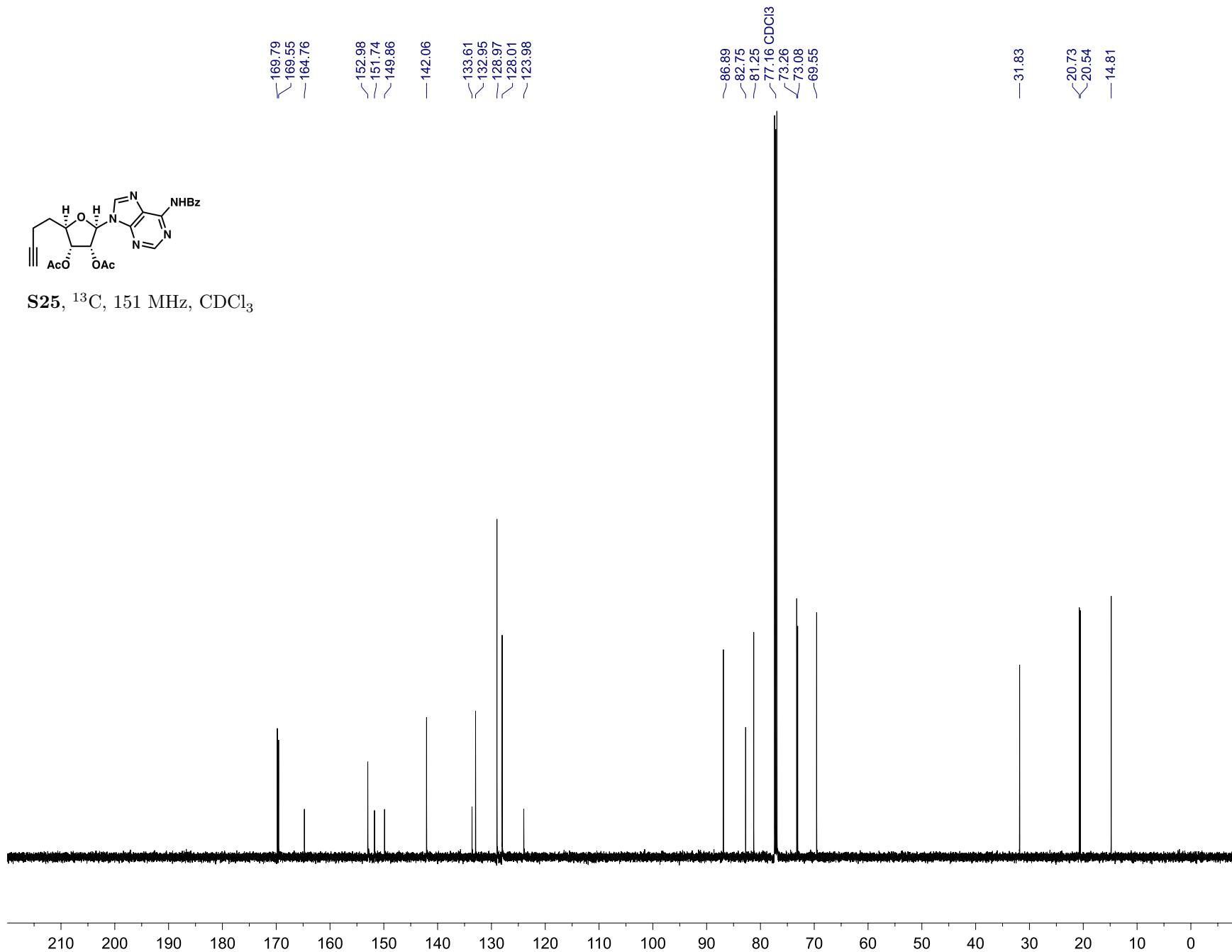


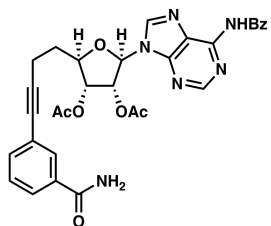
**S25**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





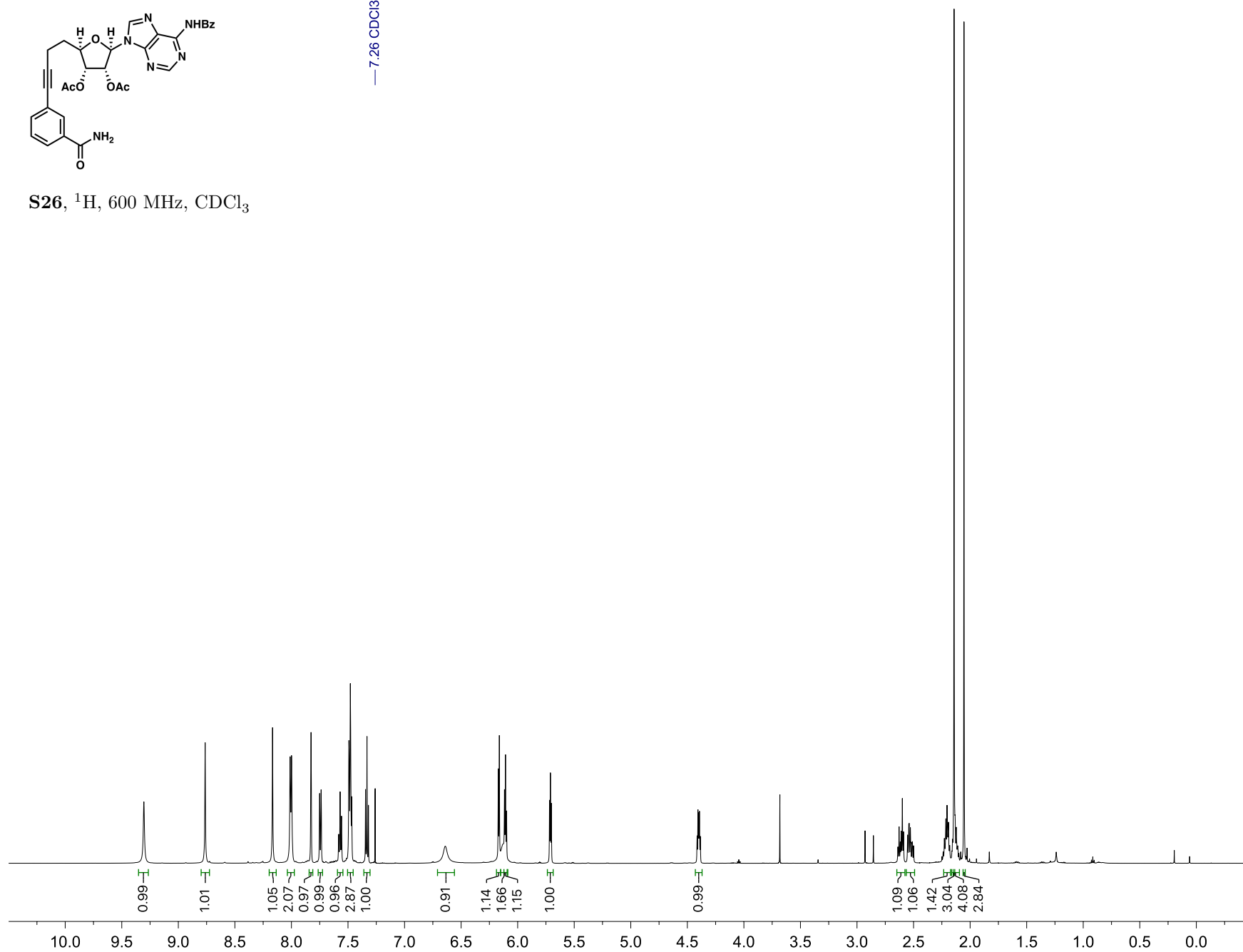
**S25**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$



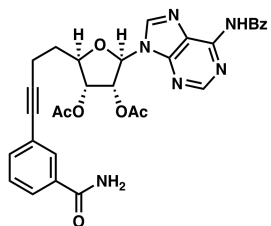


**S26**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

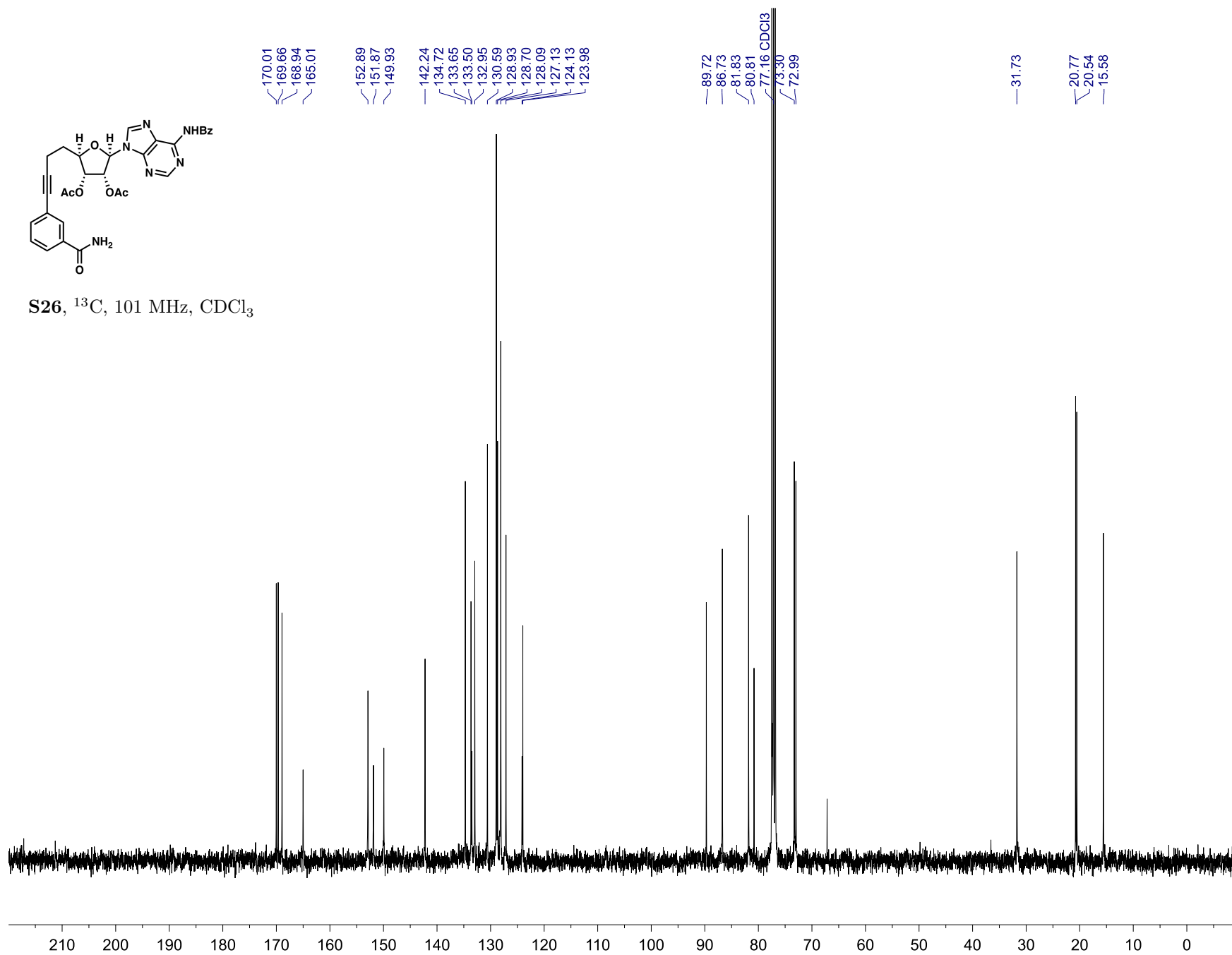
— 7.26  $\text{CDCl}_3$

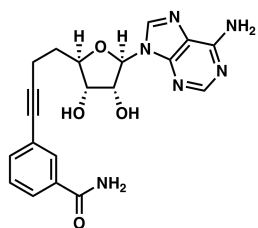






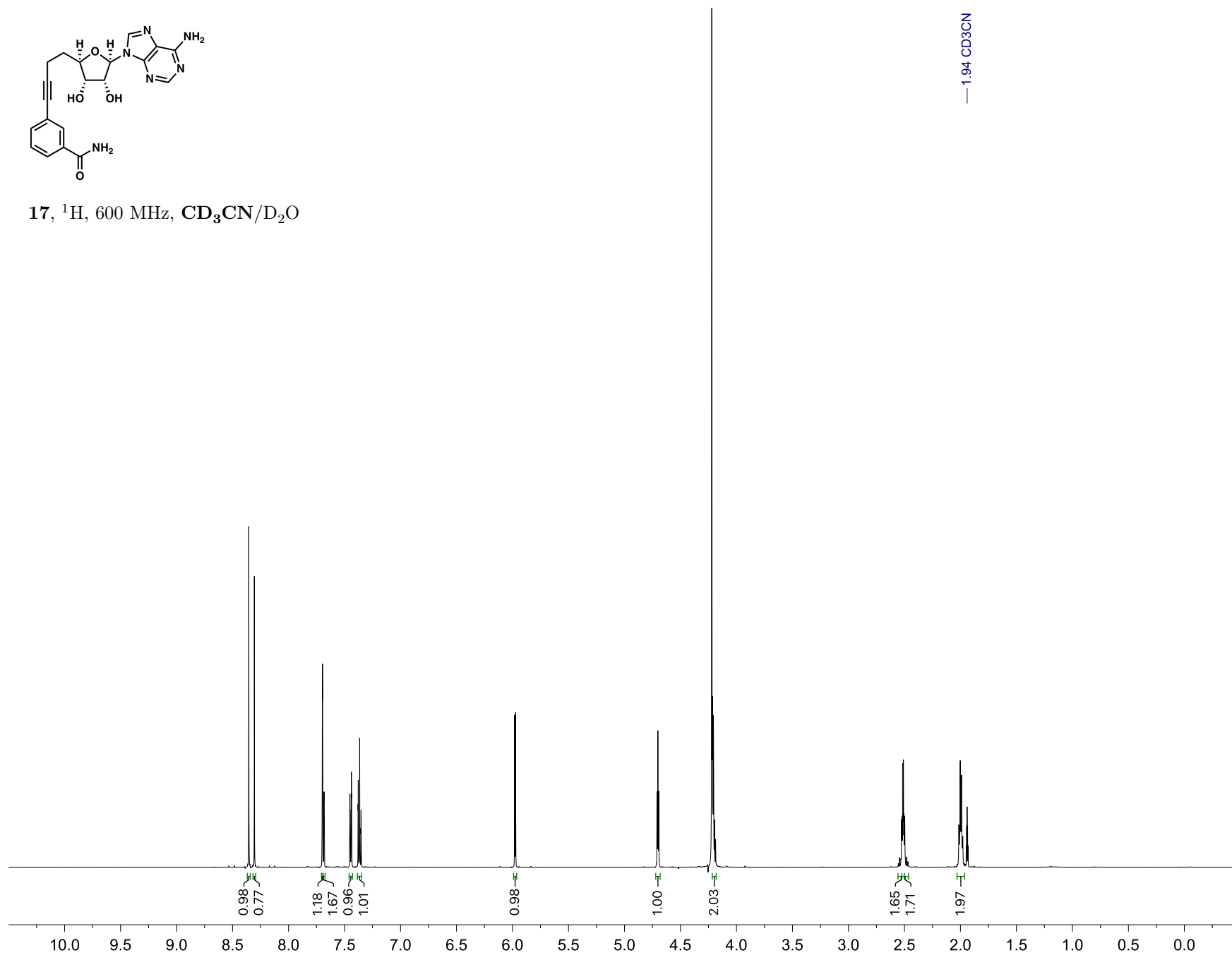
S26,  $^{13}\text{C}$ , 101 MHz,  $\text{CDCl}_3$

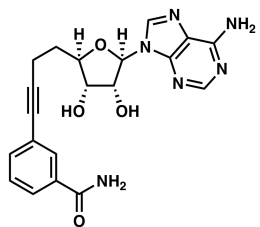




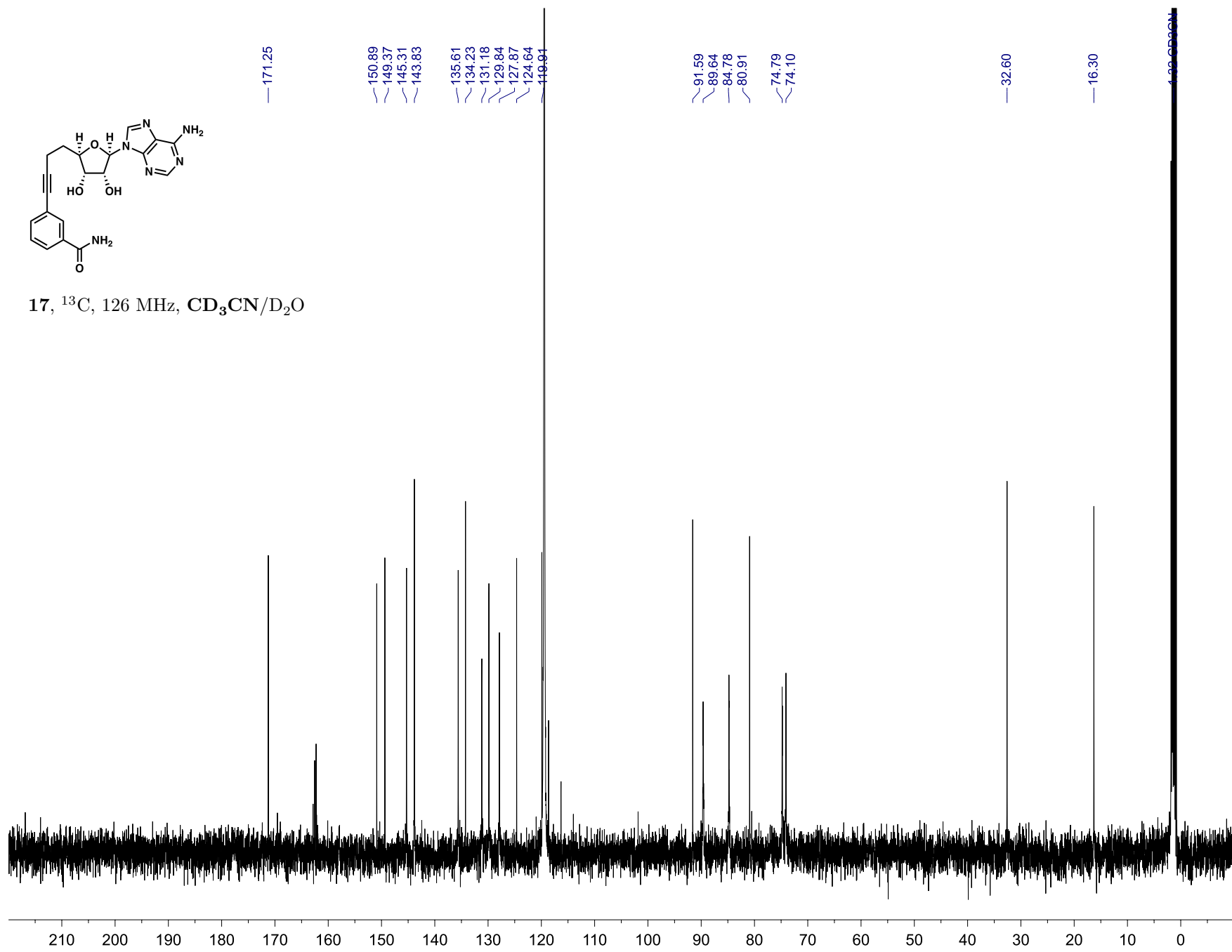
17,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

188

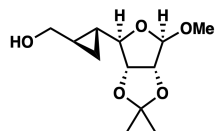




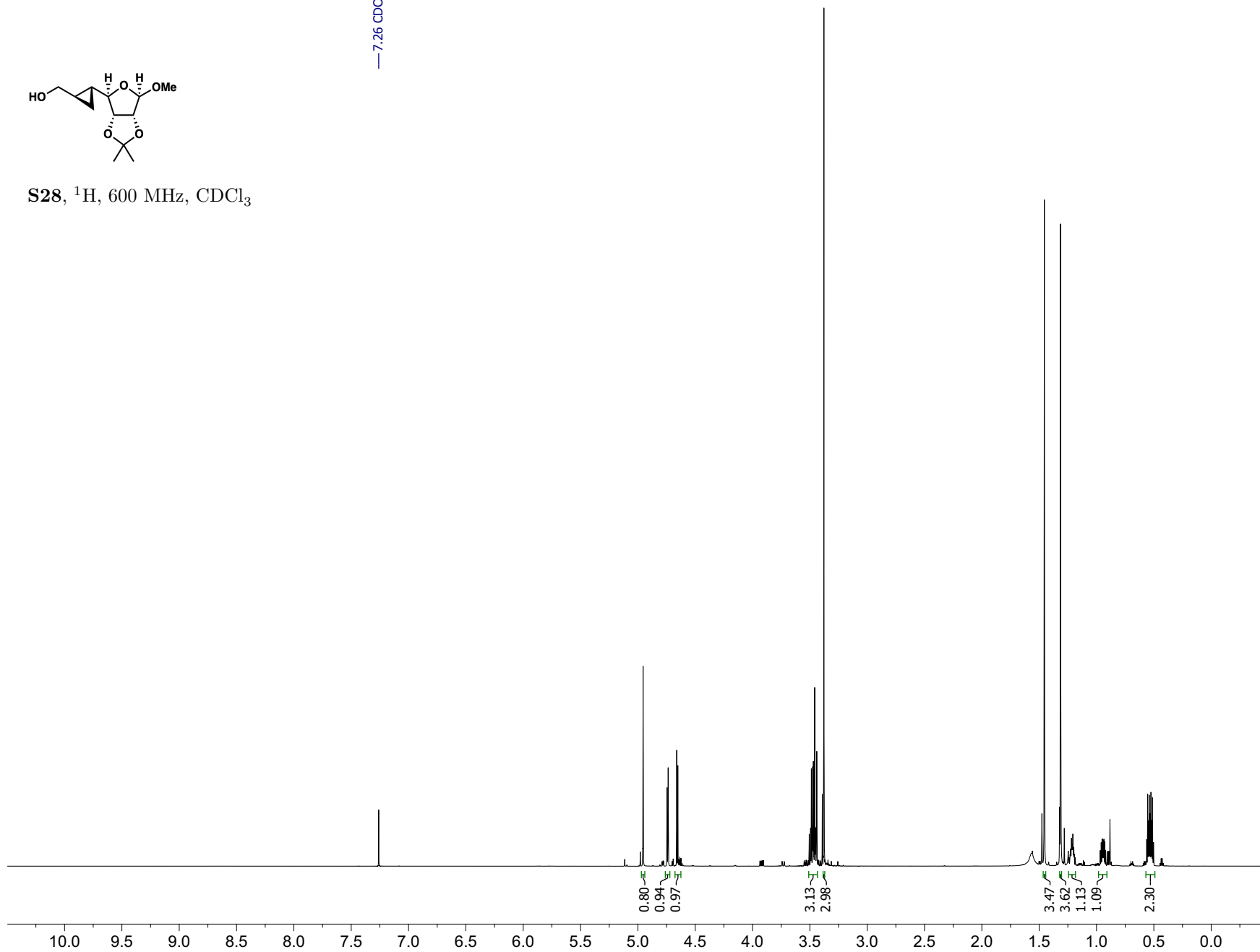
17, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O

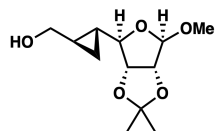


— 7.26 CDCl<sub>3</sub>

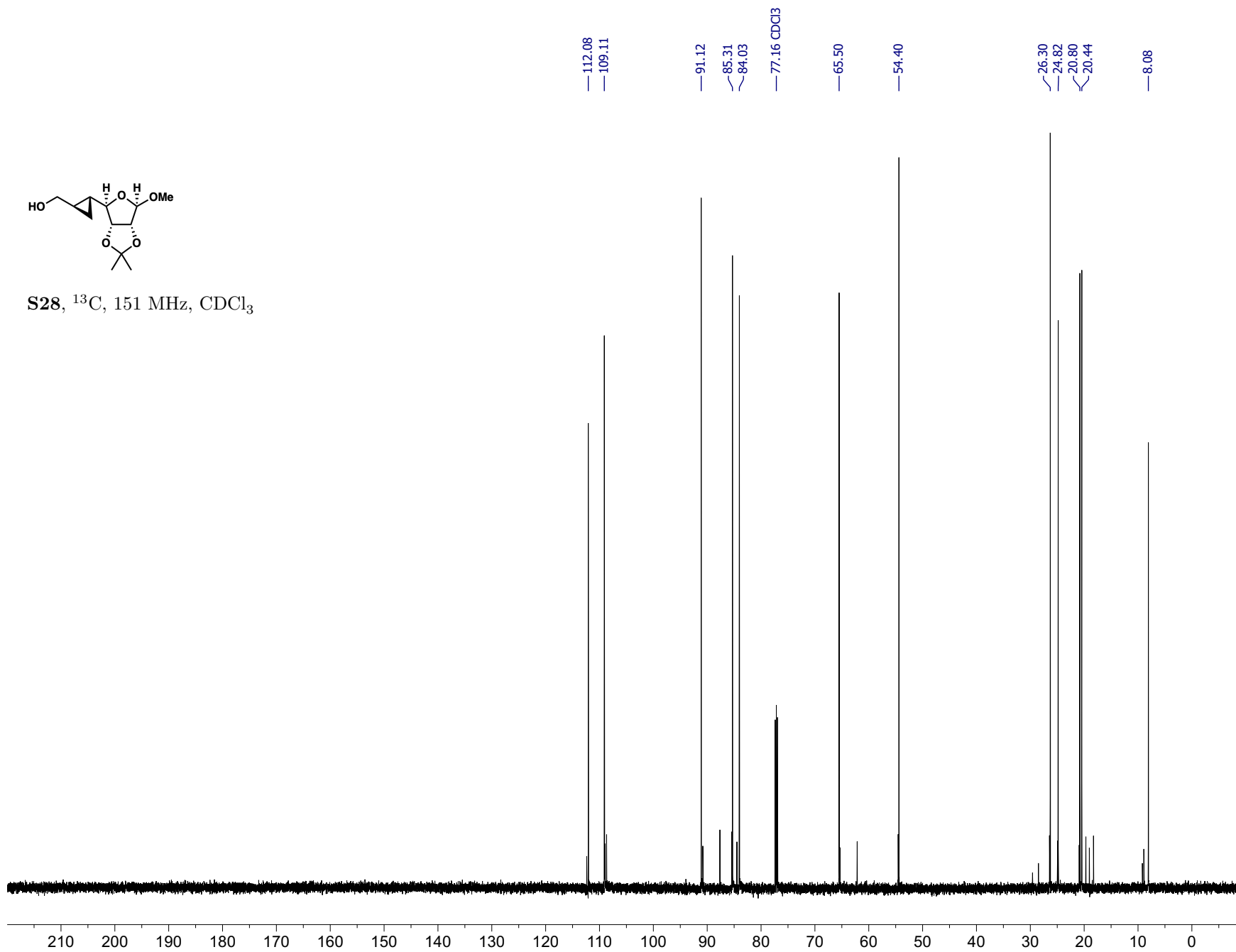


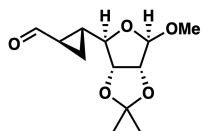
**S28**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





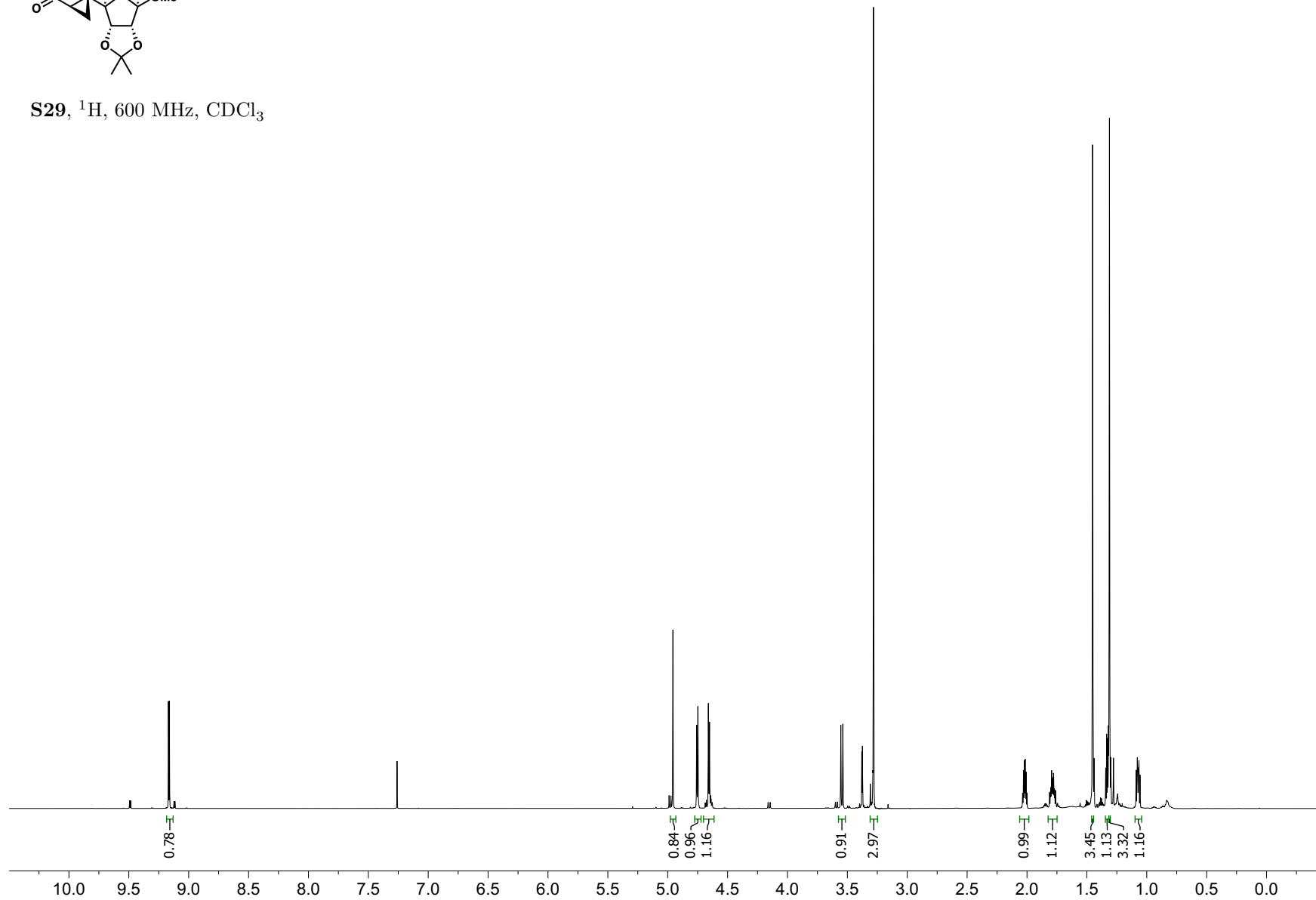
**S28**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

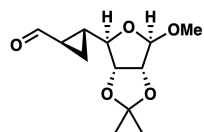
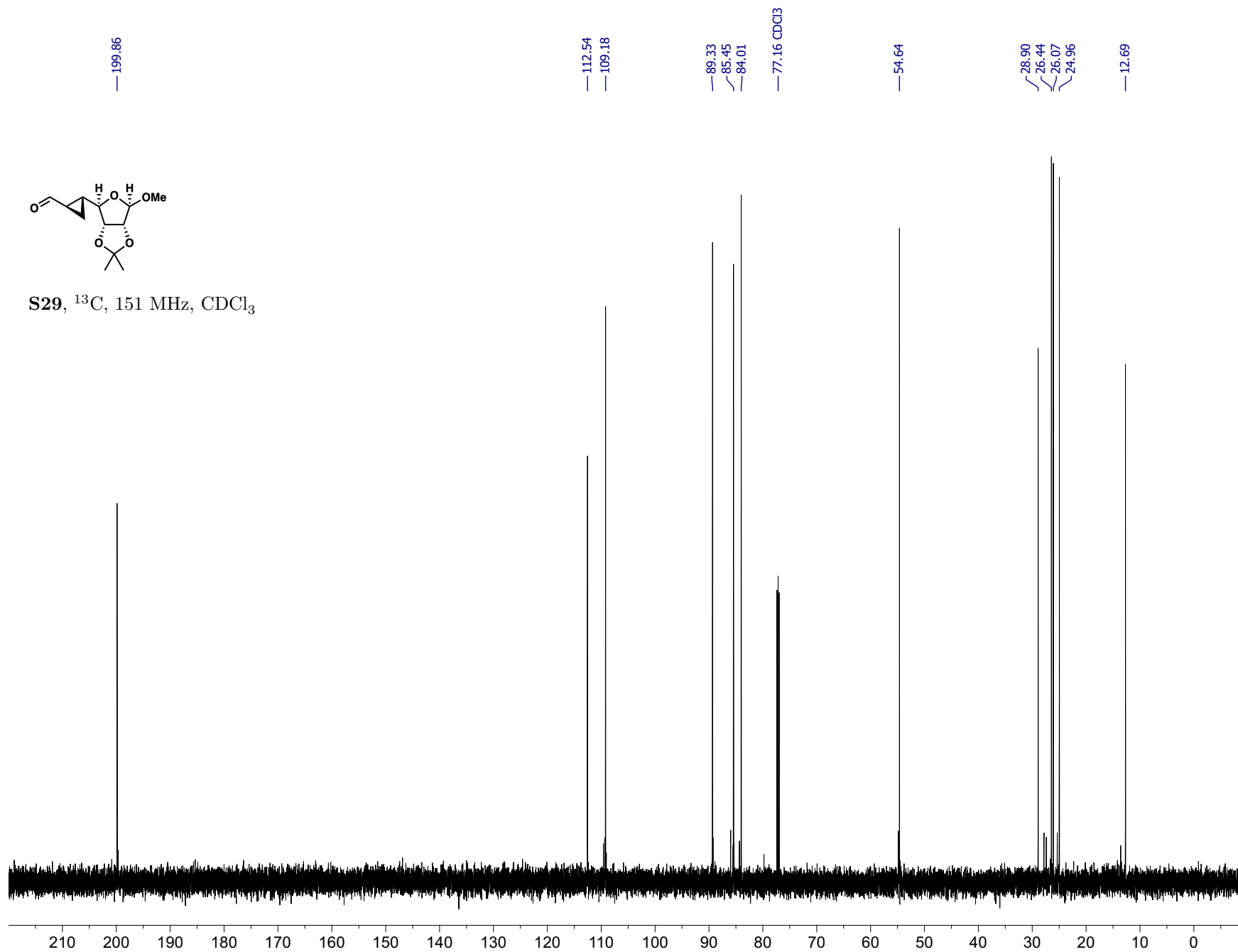




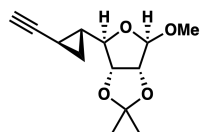
S29,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

—7.26  $\text{CDCl}_3$

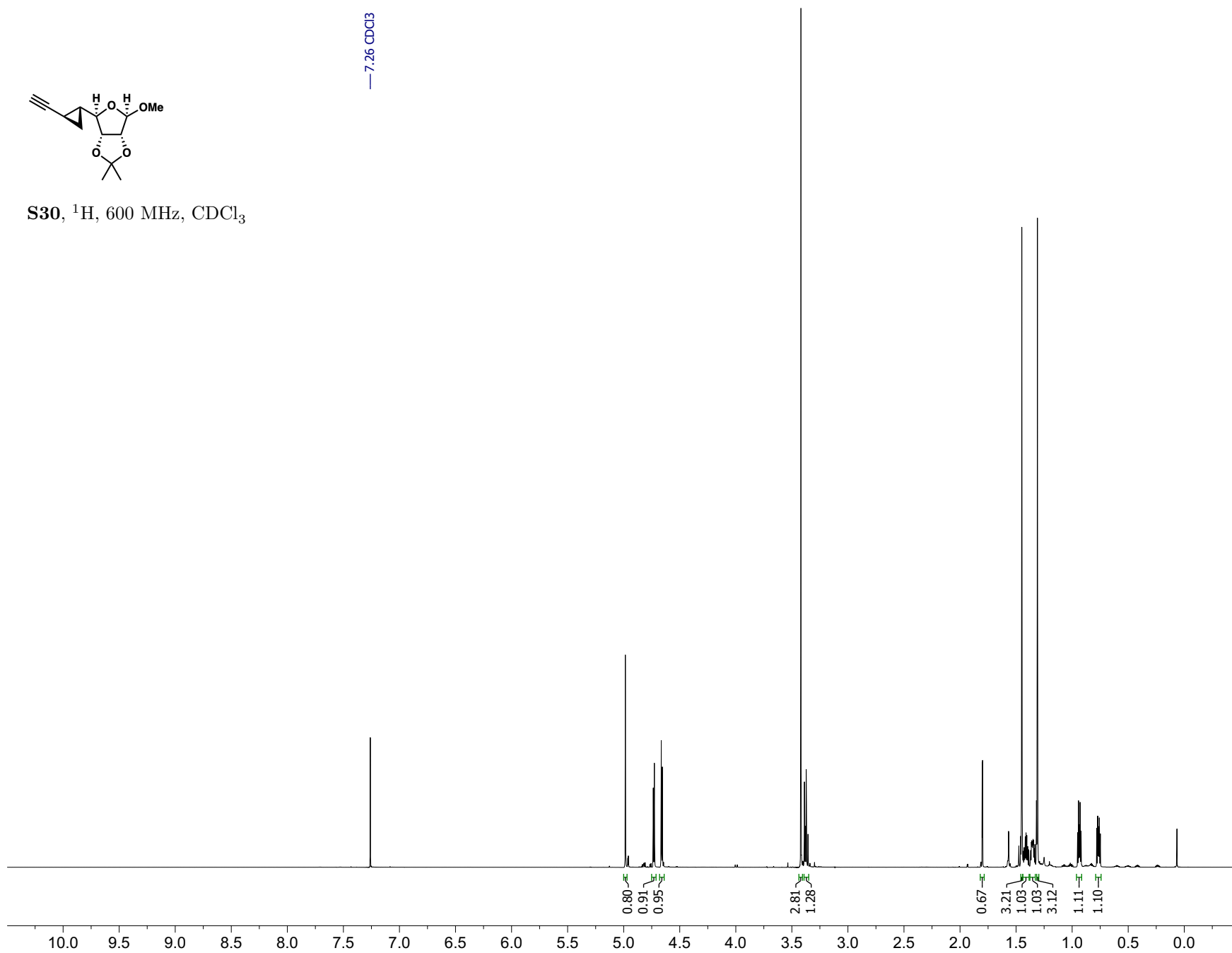


**S29**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 

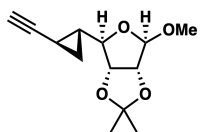
—7.26 CDCl<sub>3</sub>



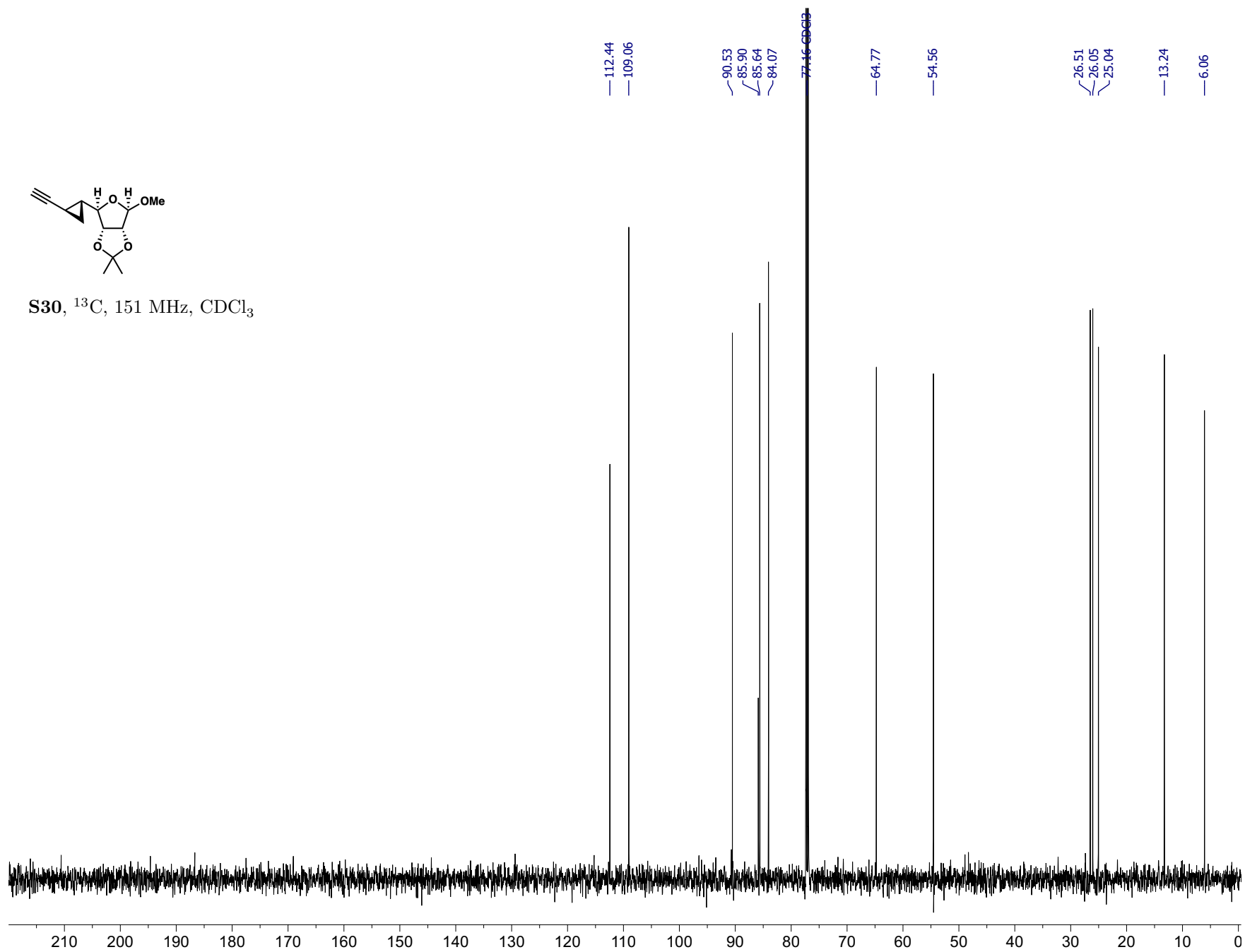
**S30**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

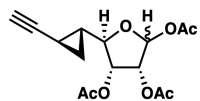






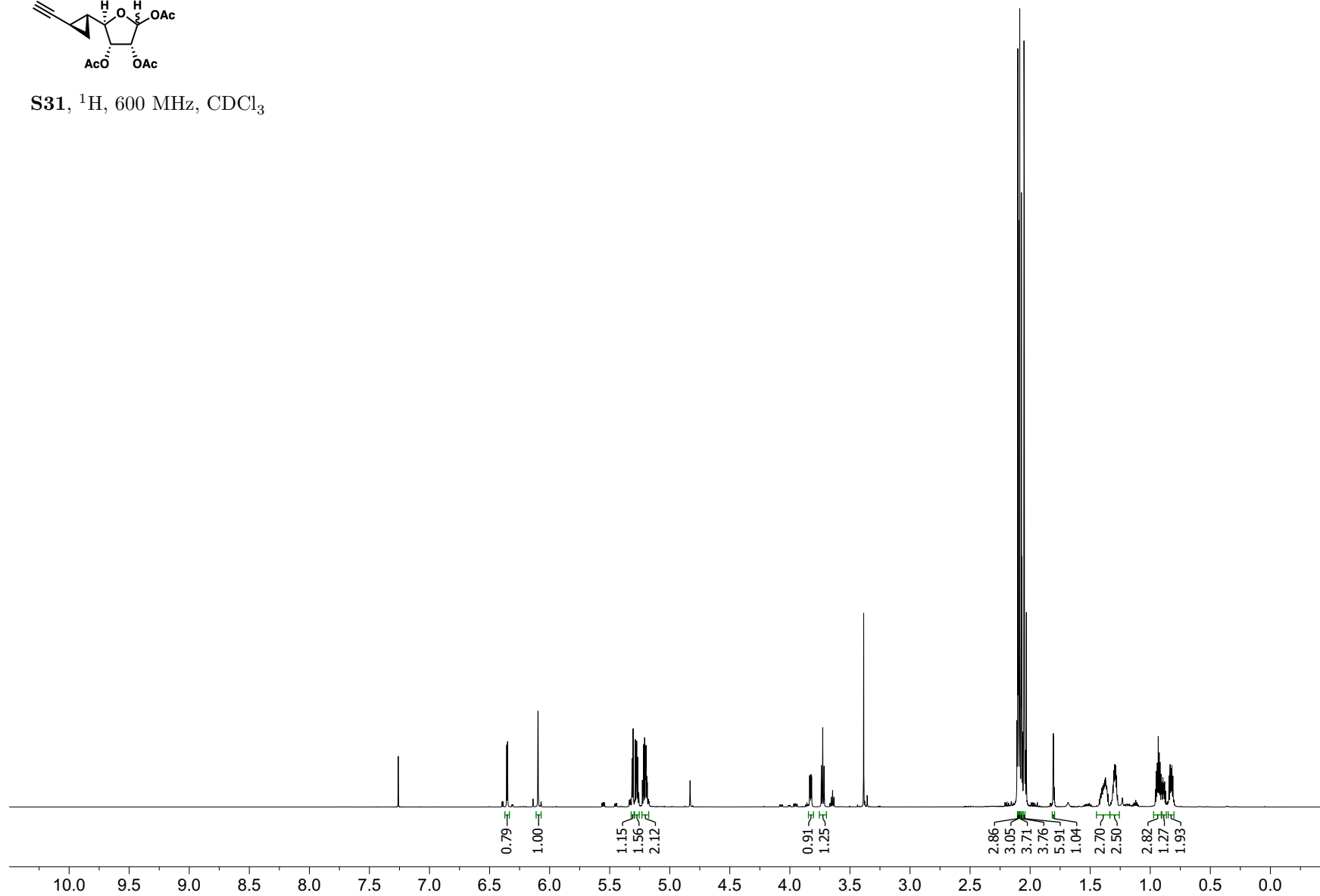
**S30**, <sup>13</sup>C, 151 MHz, CDCl<sub>3</sub>

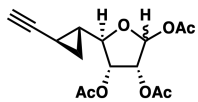




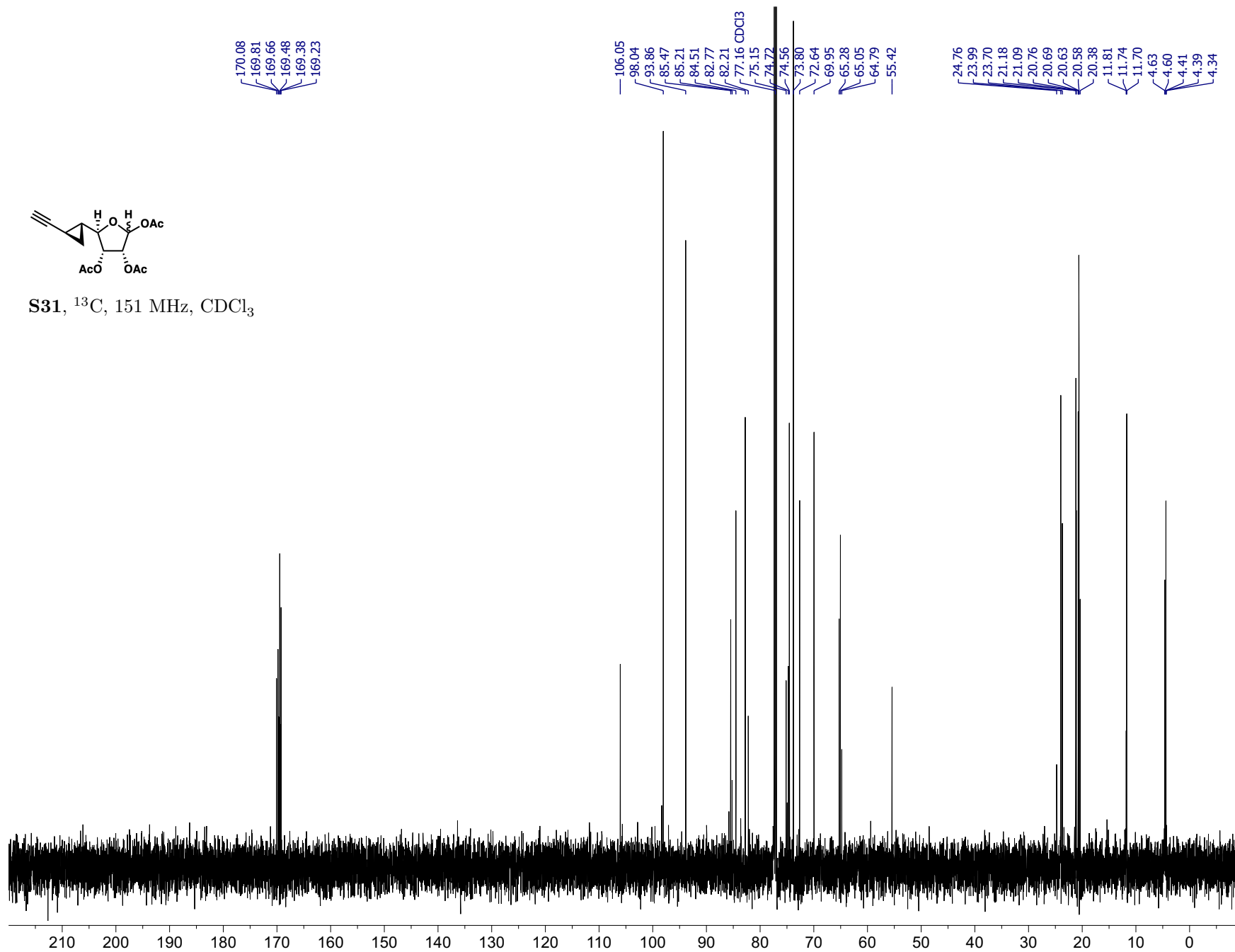
S31,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

—7.26  $\text{CDCl}_3$

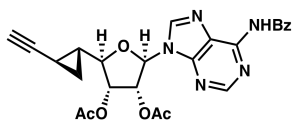




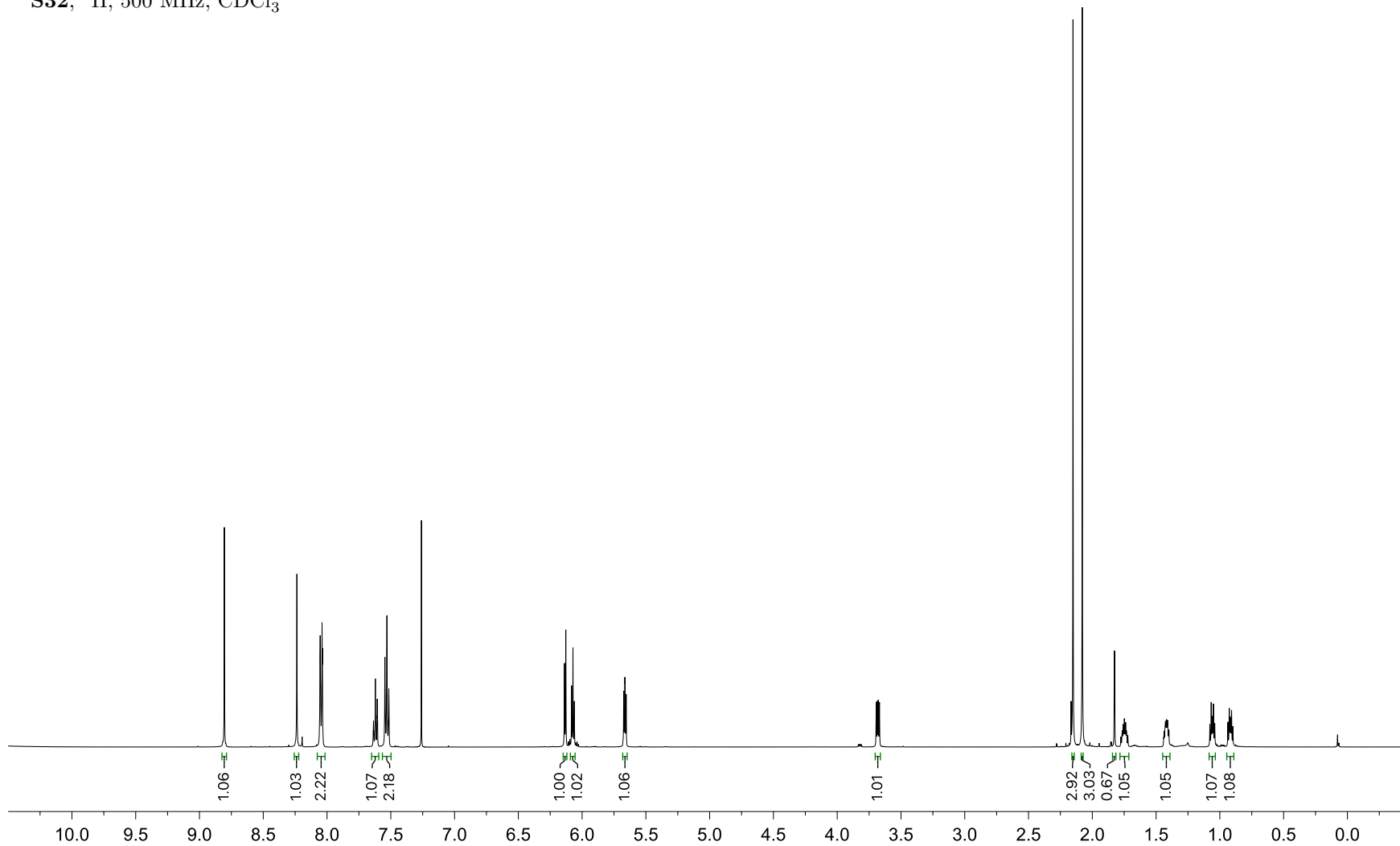
**S31**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

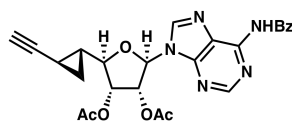


— 7.26 CDC13

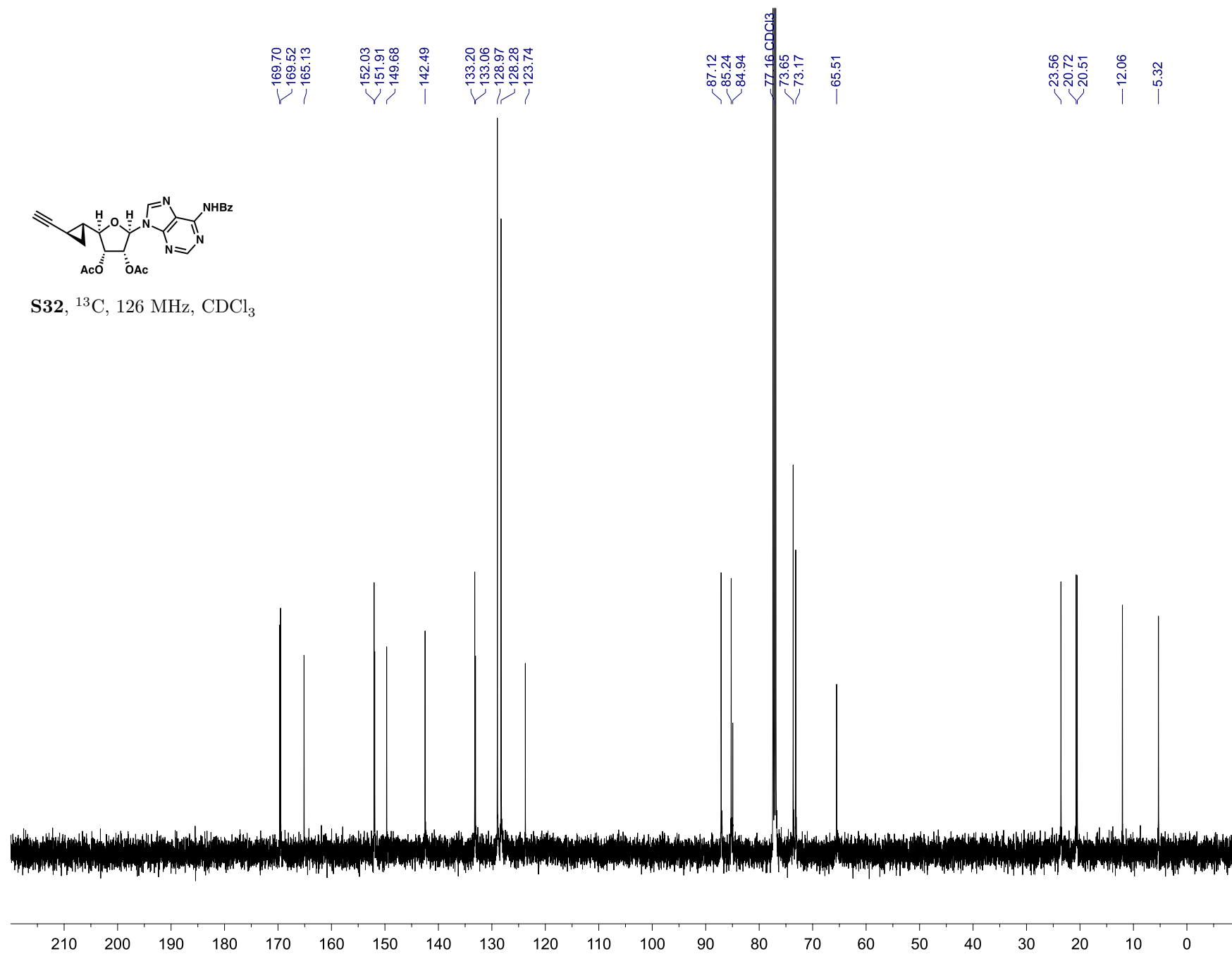


S32,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

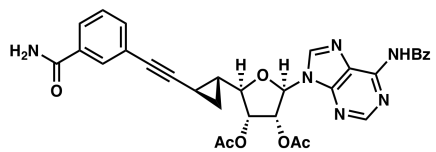




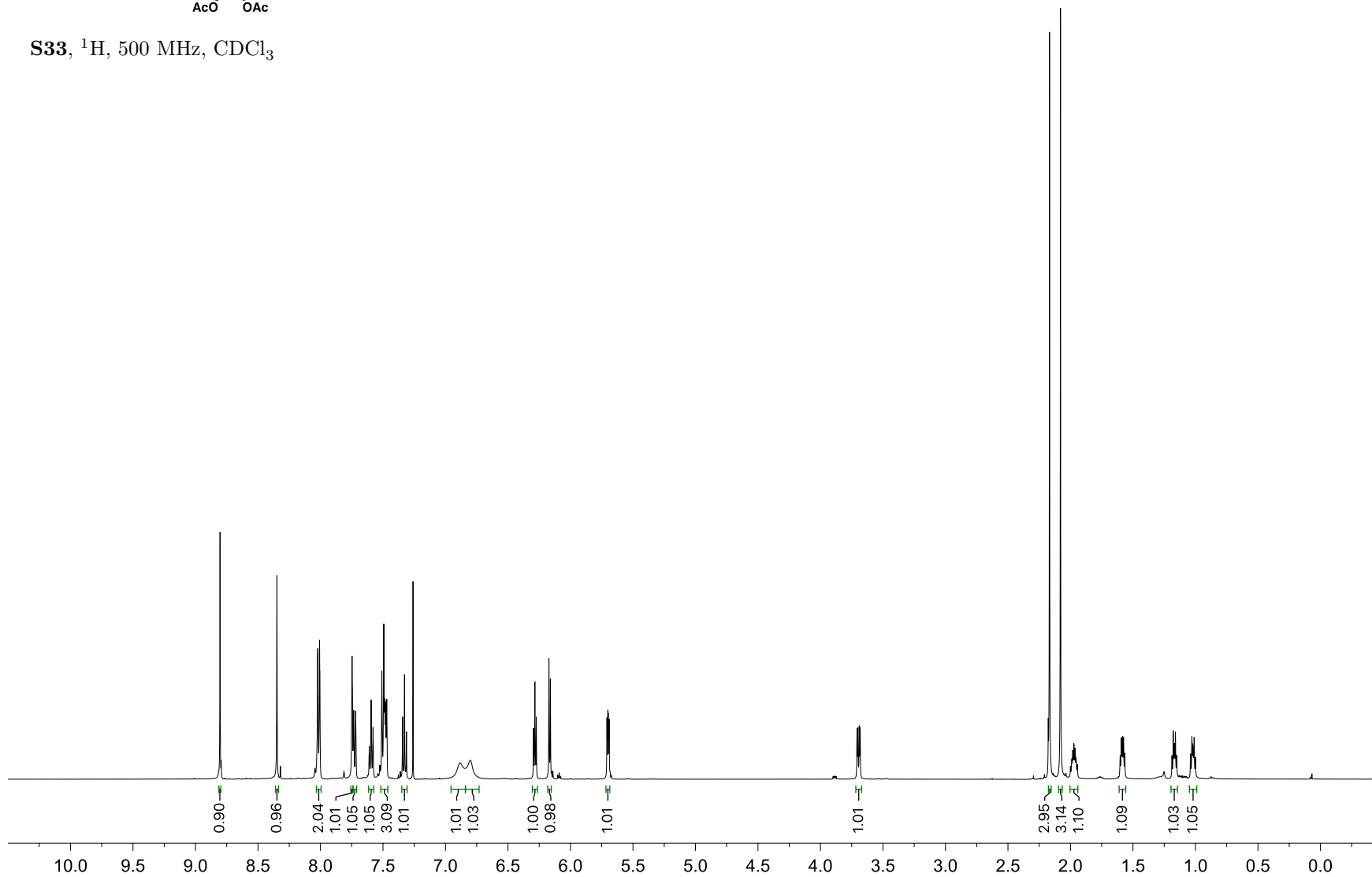
S32,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

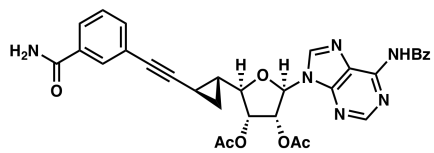


— 7.26 CDCl<sub>3</sub>

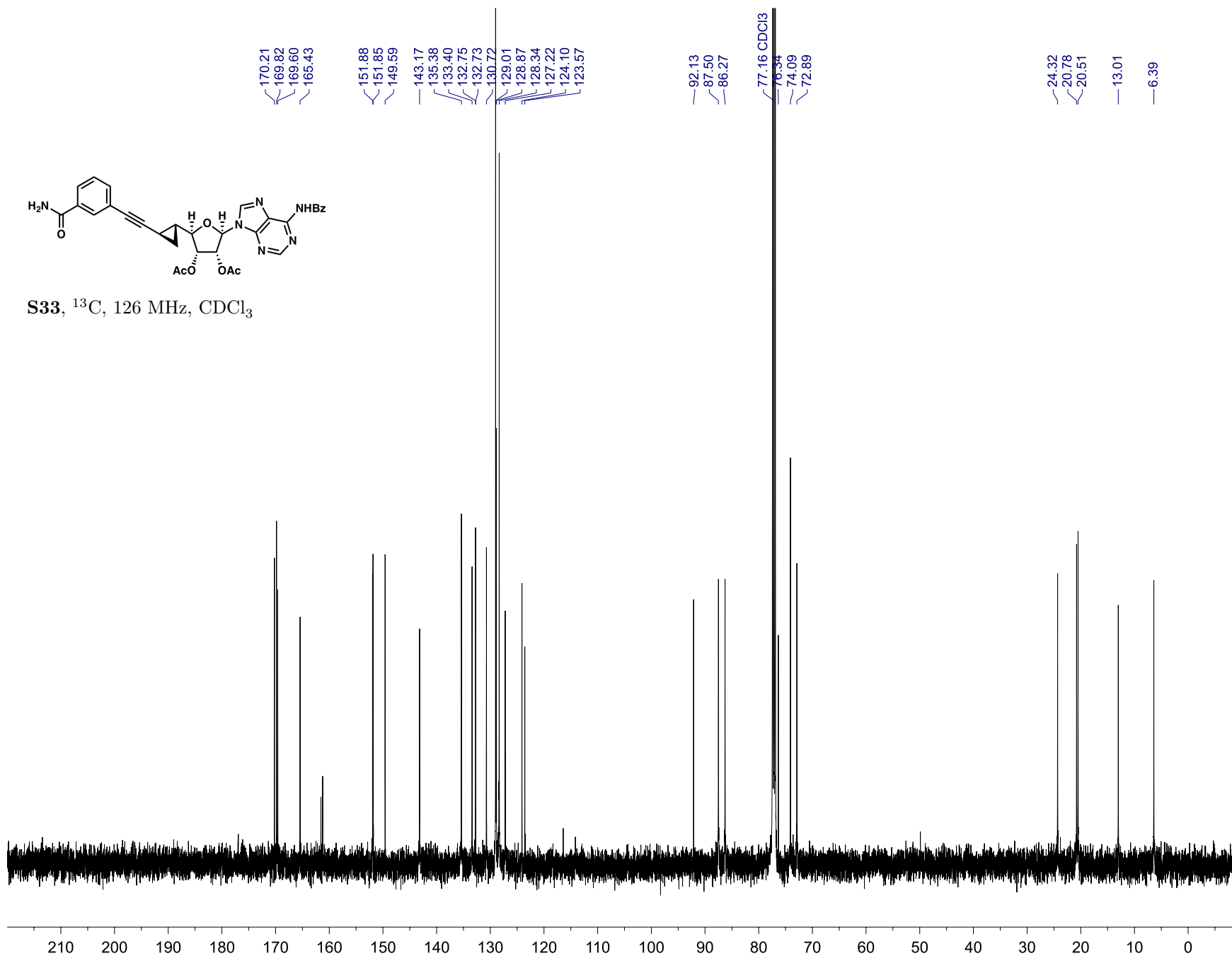


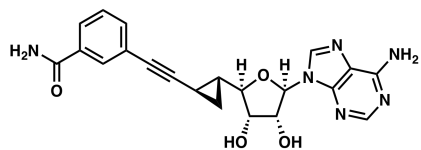
**S33**, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>



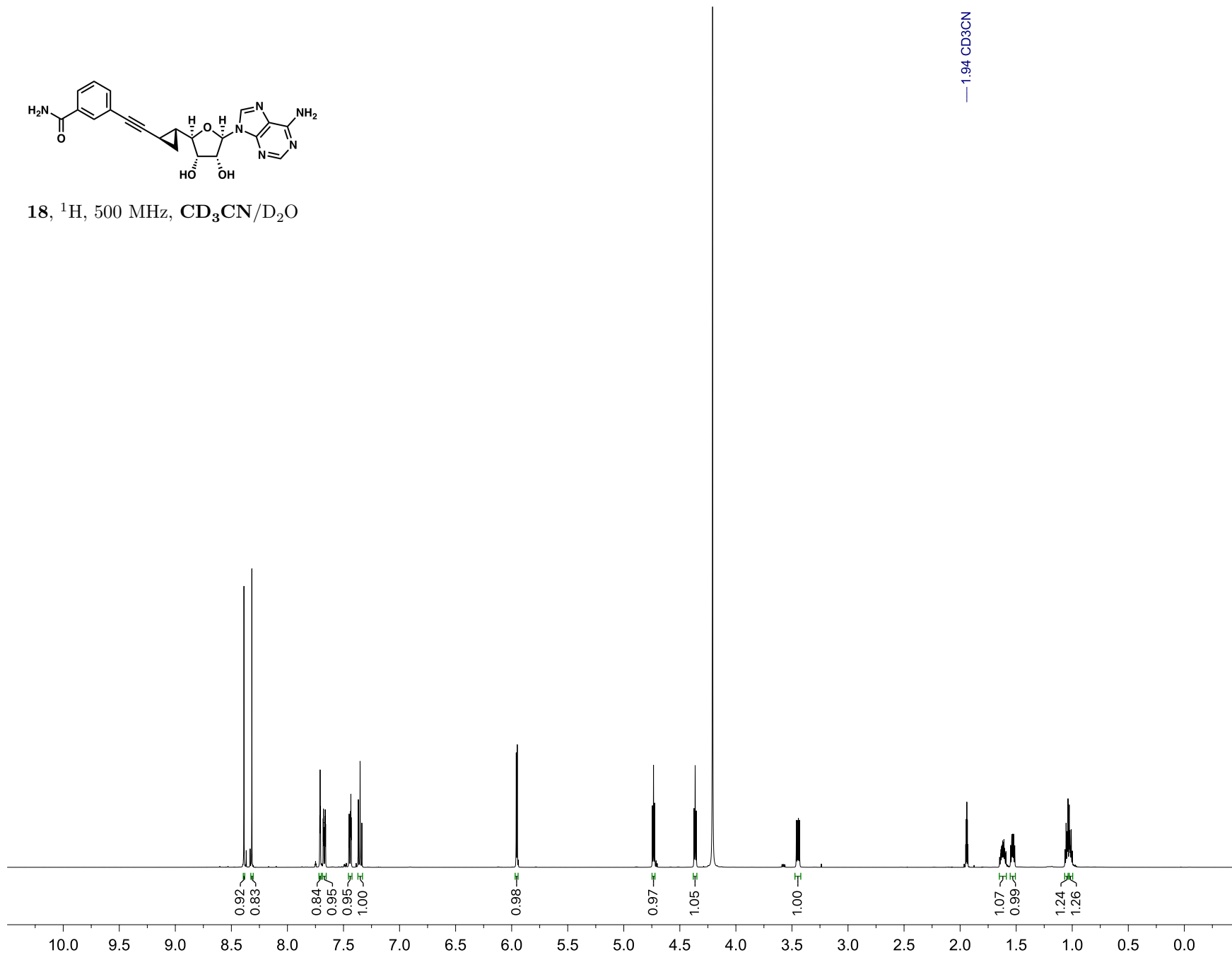


S33,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

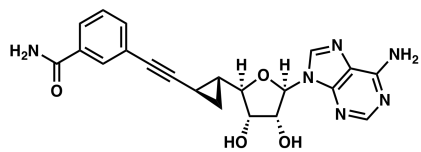




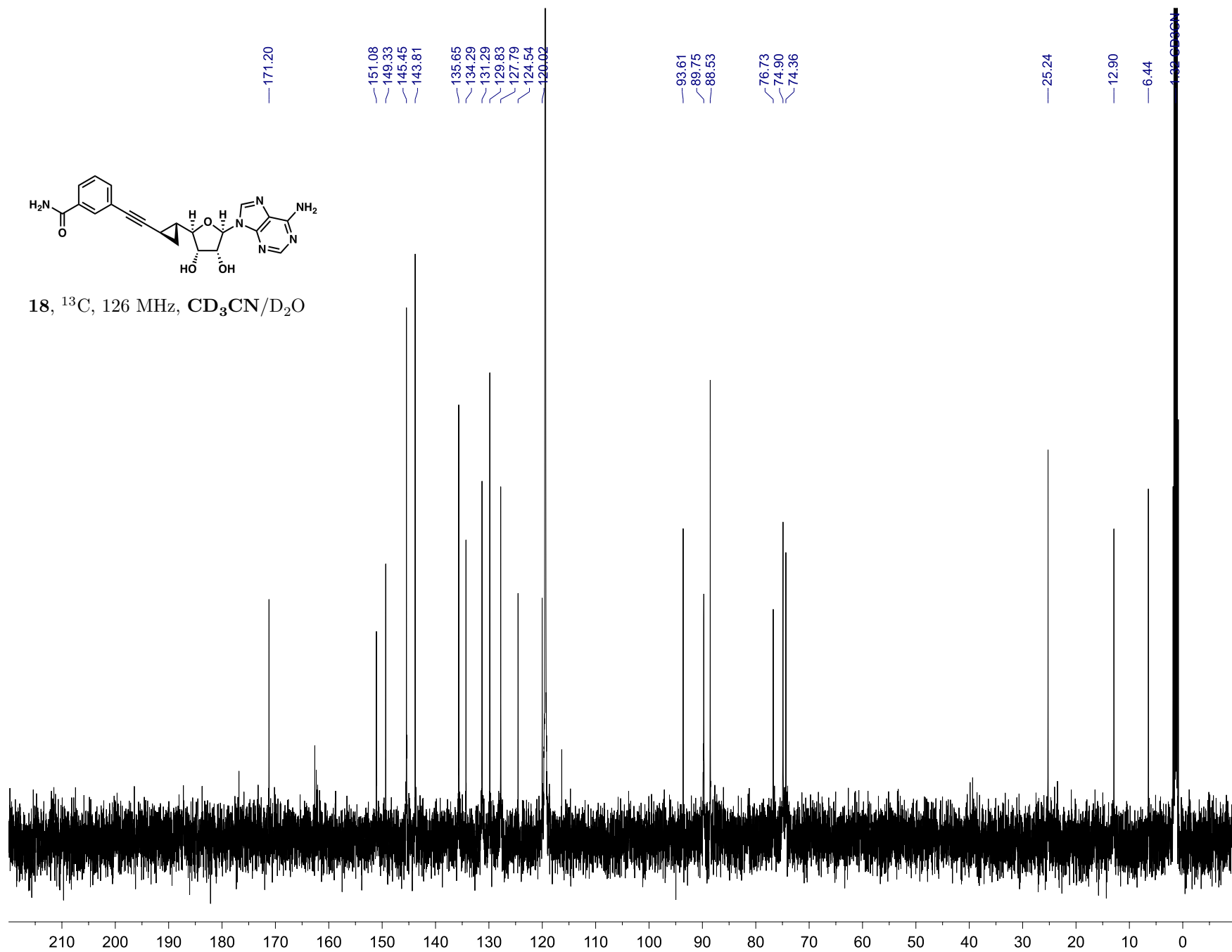
18,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

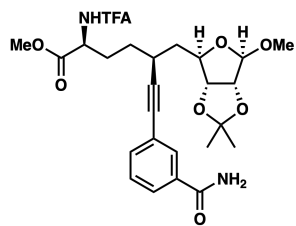




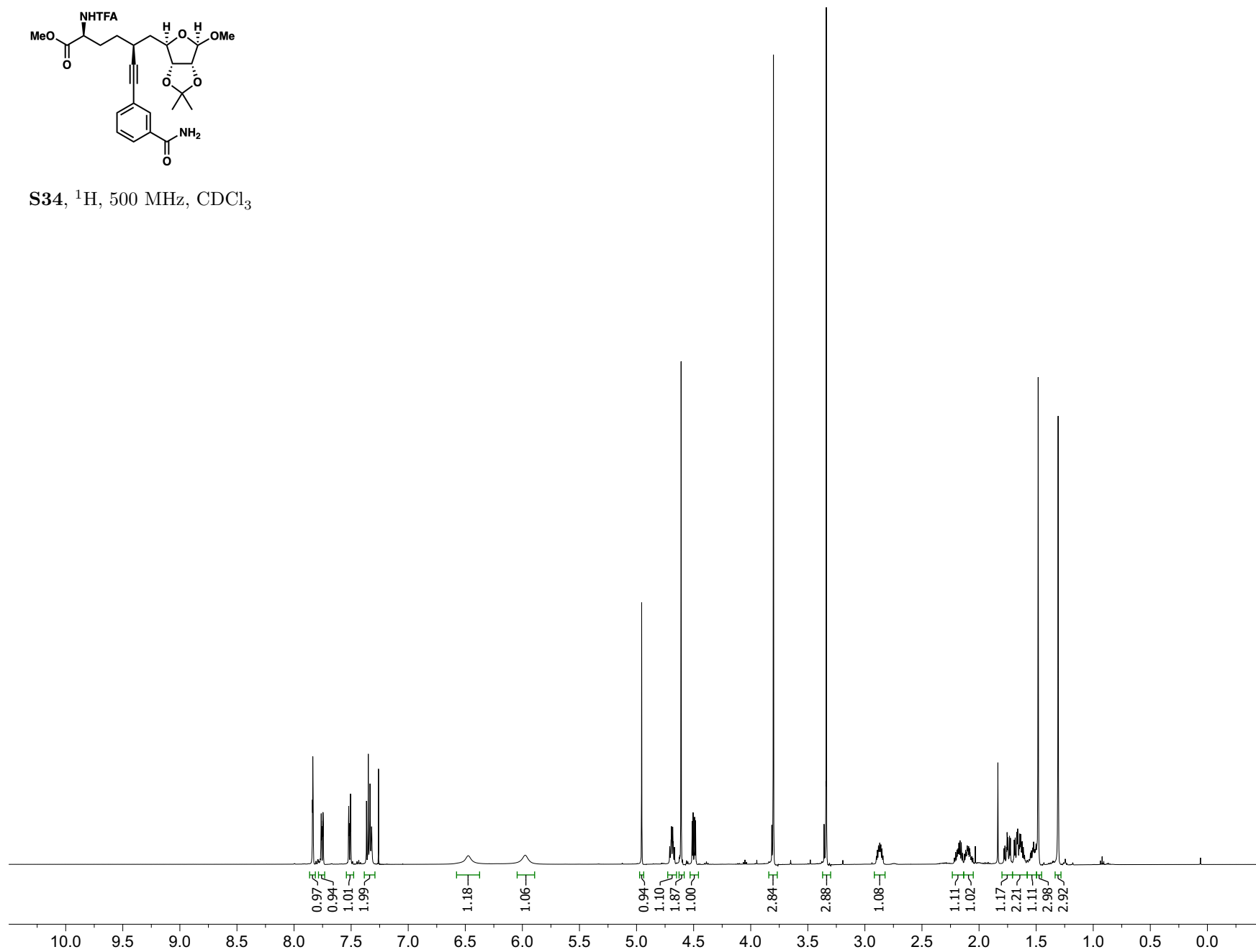


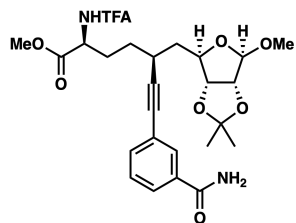
18,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$



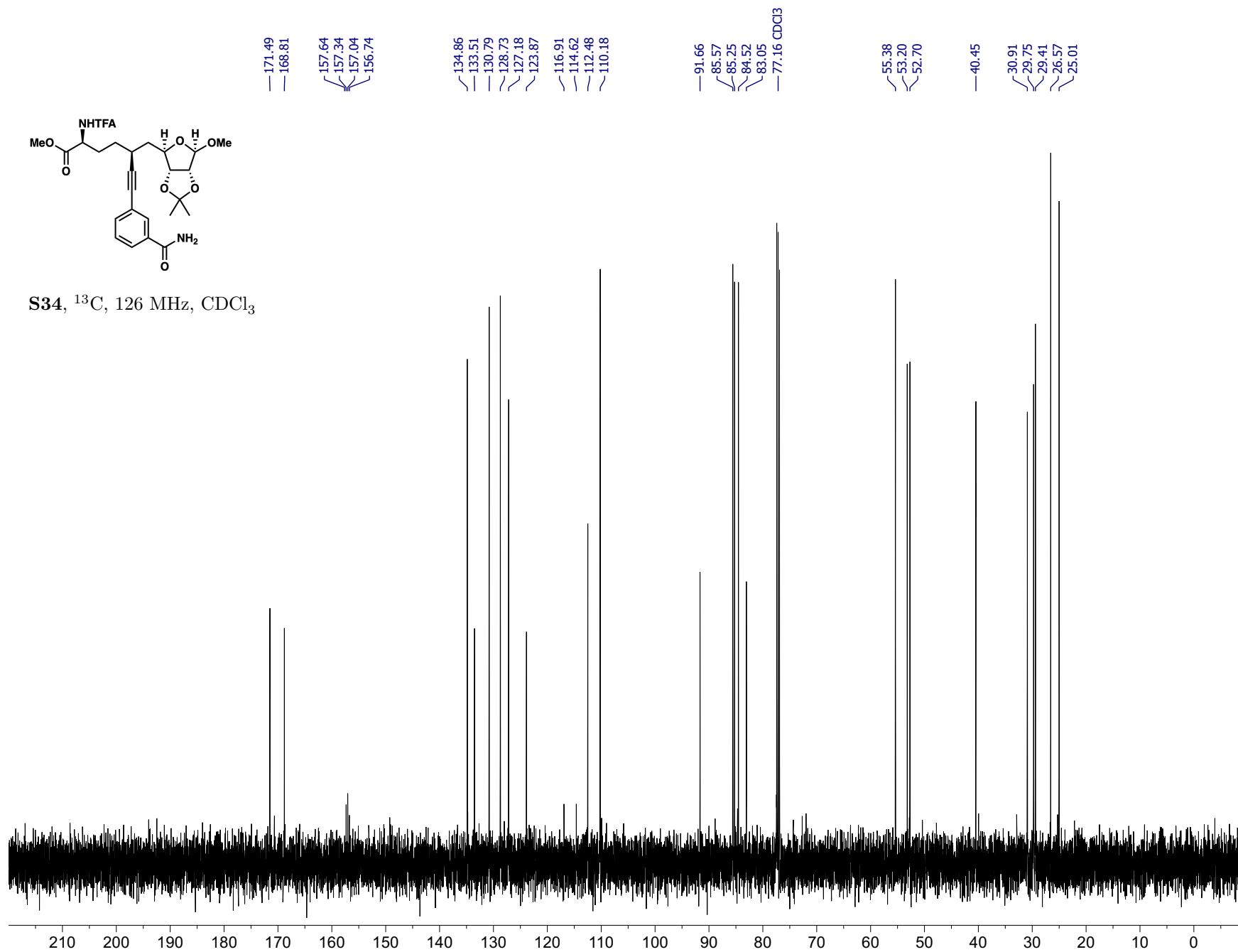


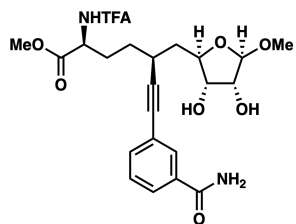
S34,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



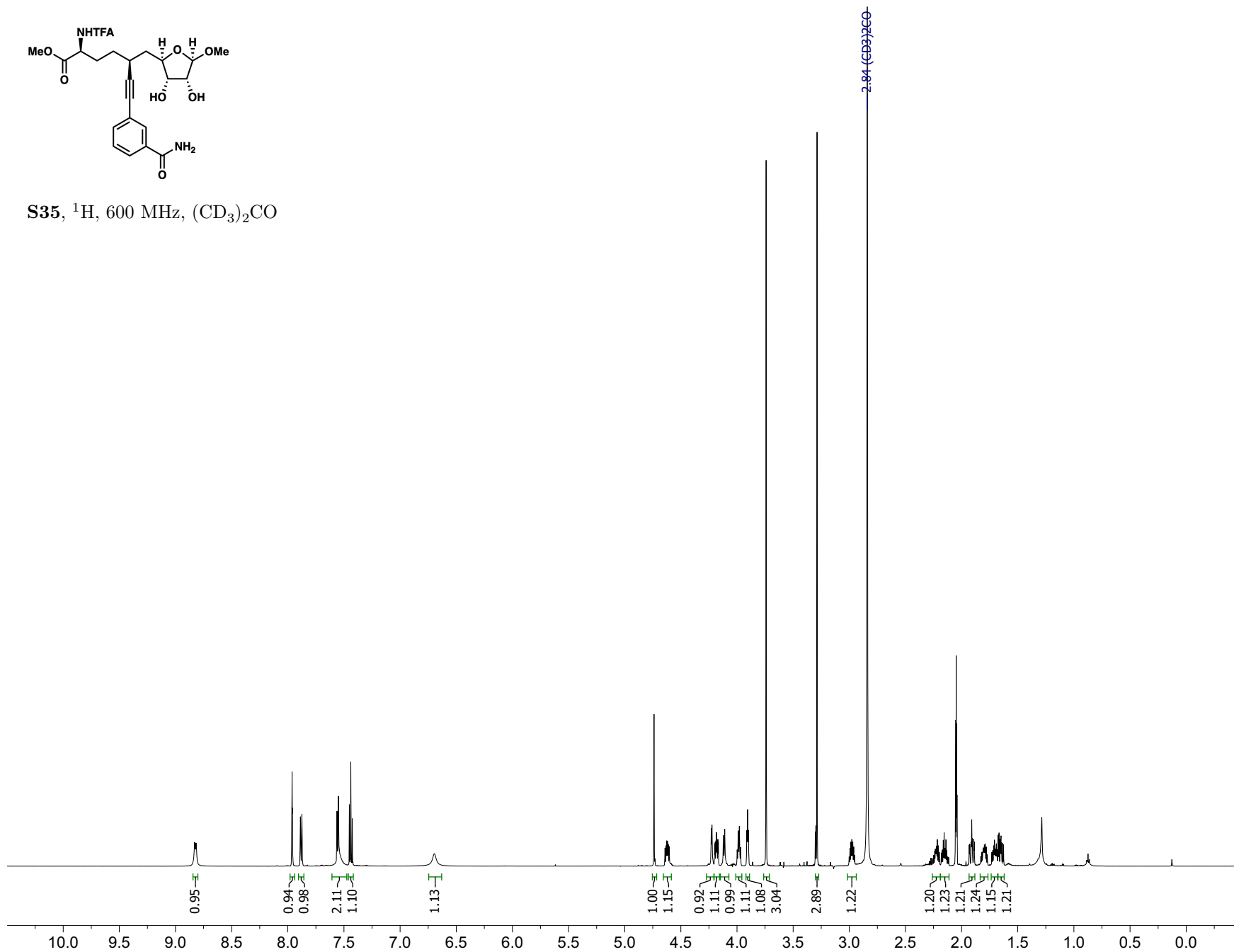


S34,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

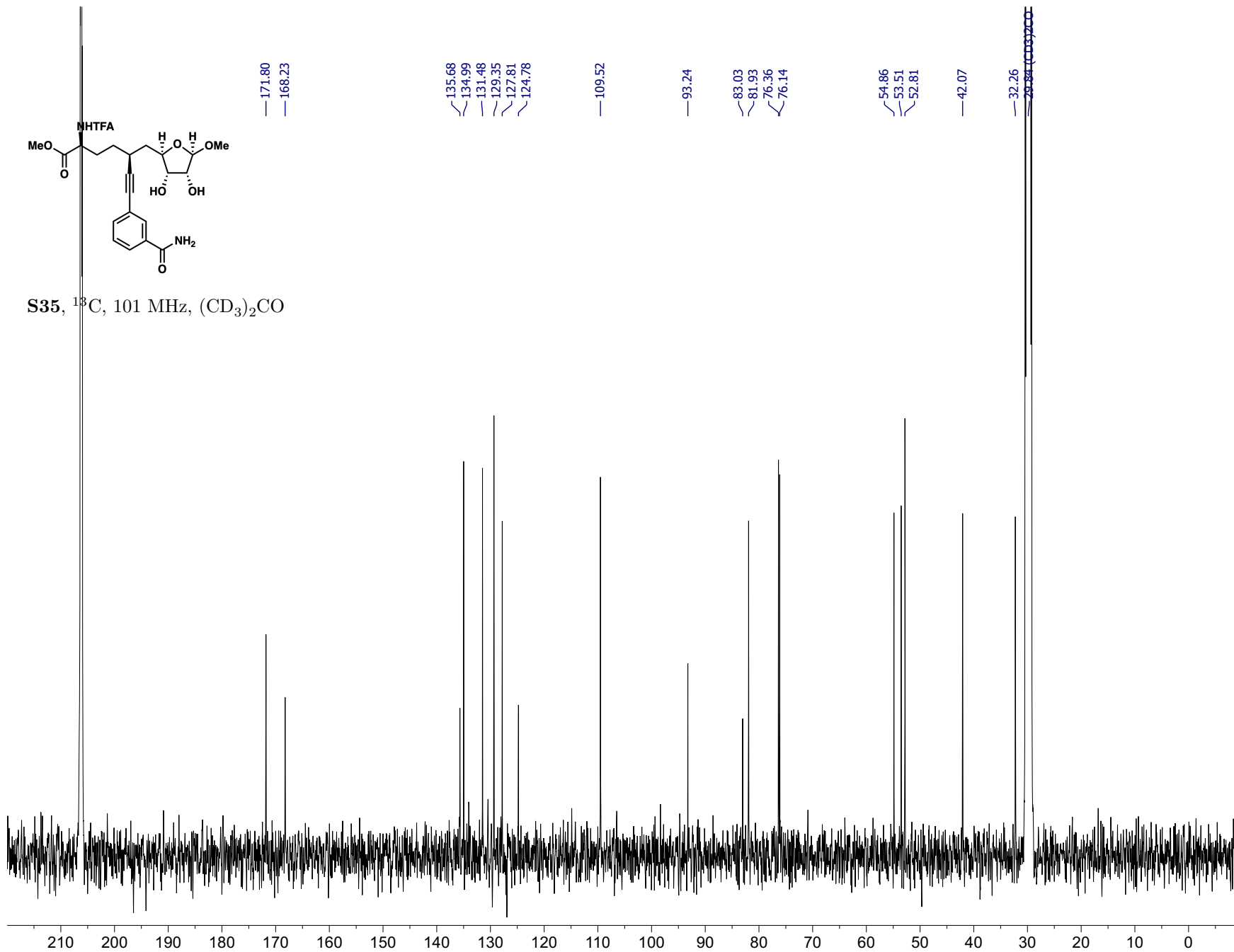


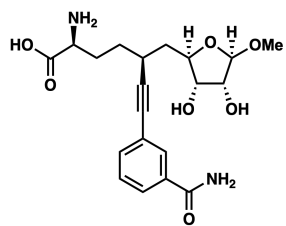


S35,  $^1\text{H}$ , 600 MHz,  $(\text{CD}_3)_2\text{CO}$

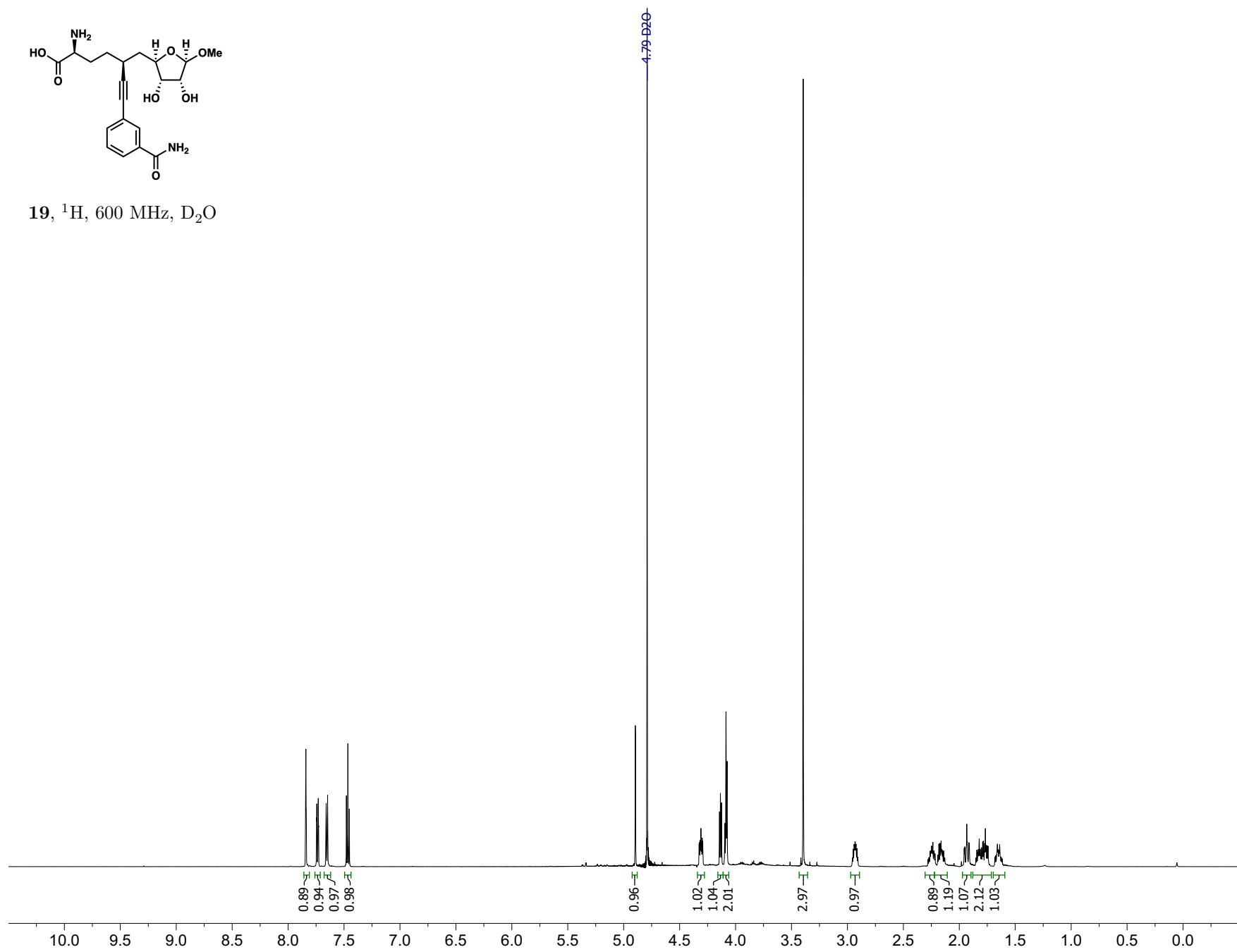


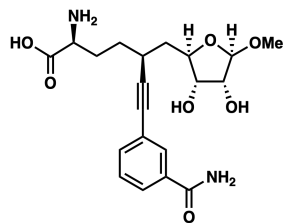
001S



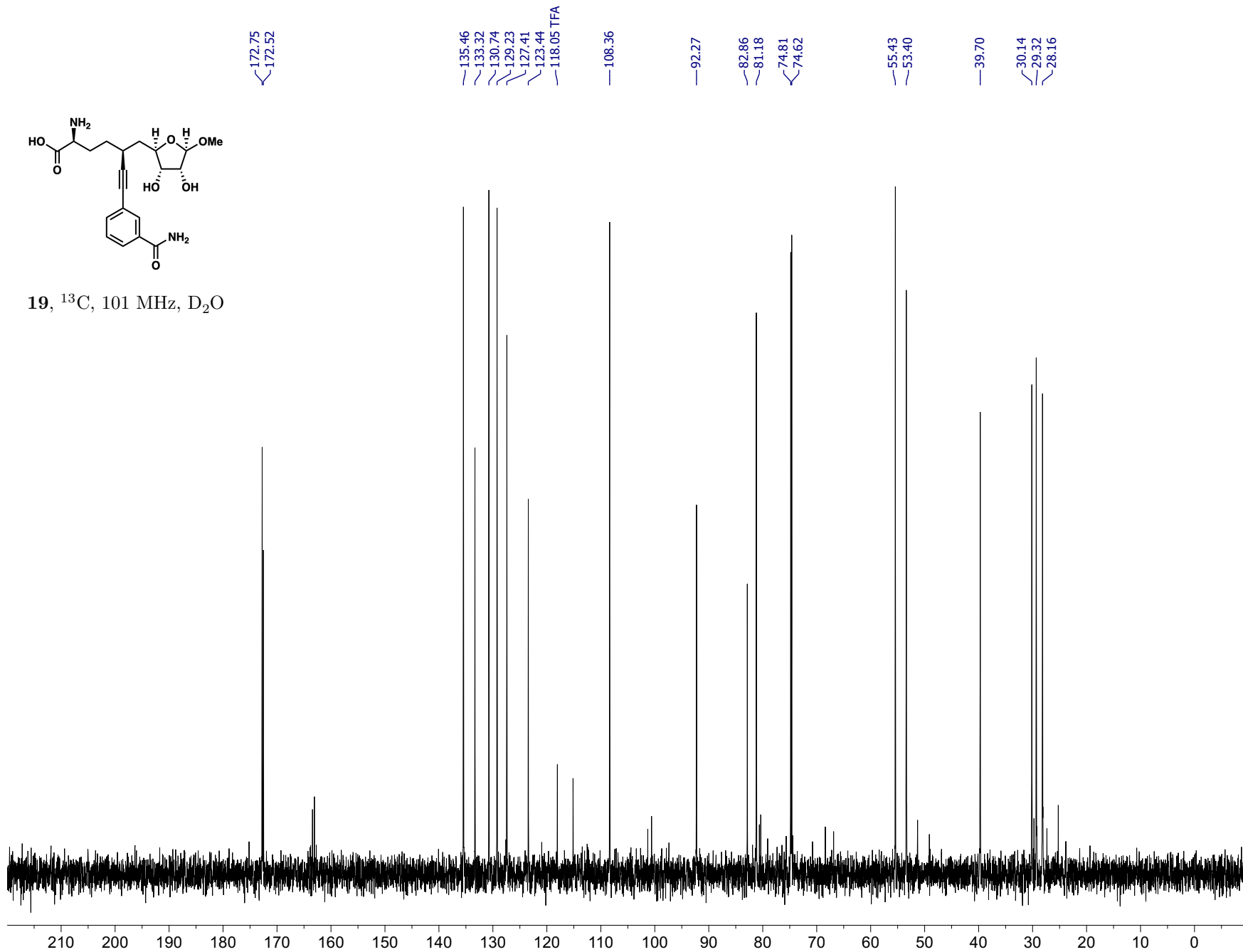


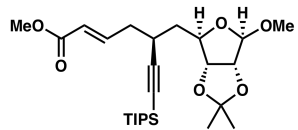
19,  $^1\text{H}$ , 600 MHz,  $\text{D}_2\text{O}$



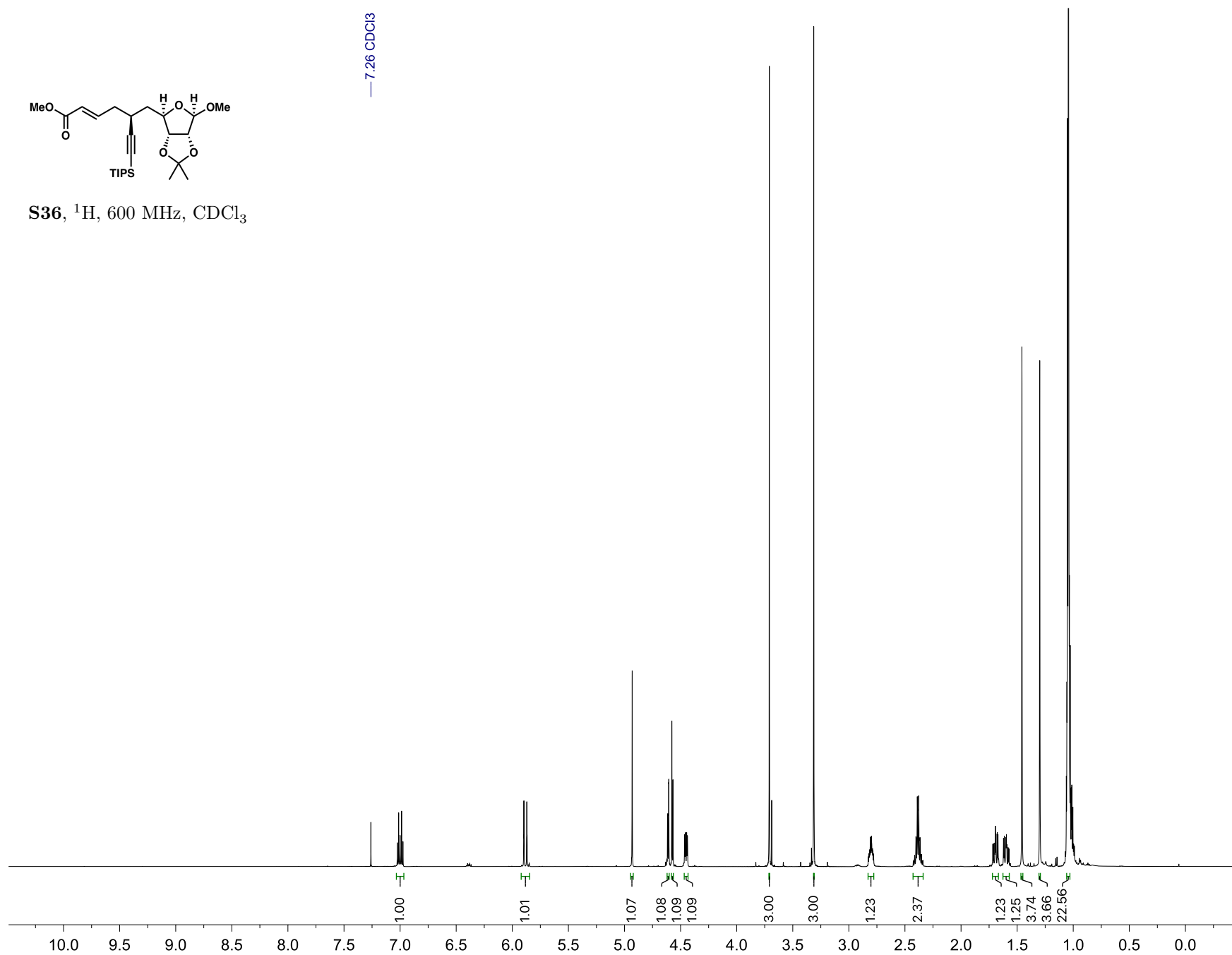


**19**,  $^{13}\text{C}$ , 101 MHz,  $\text{D}_2\text{O}$

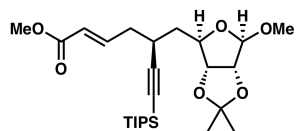




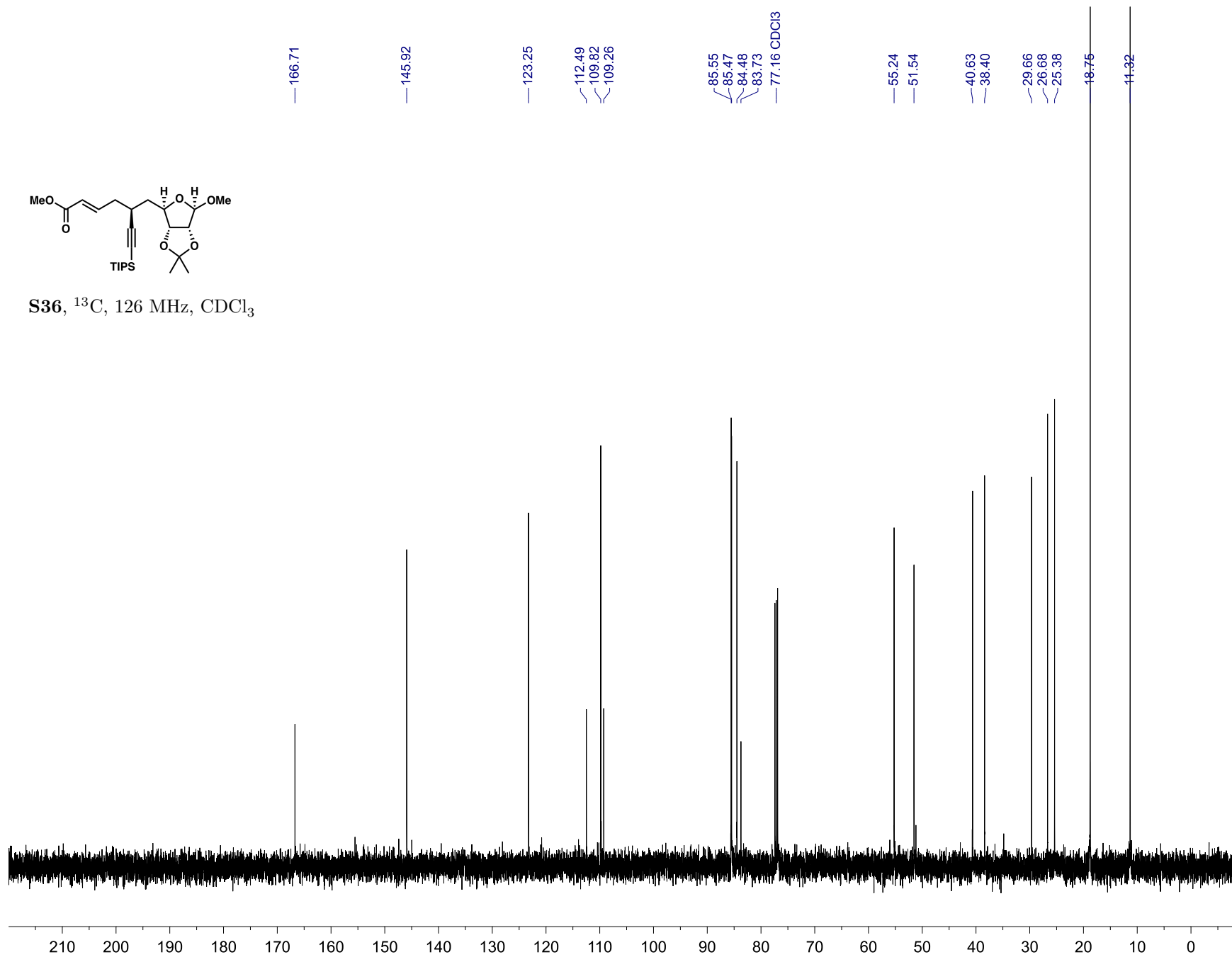
**S36**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

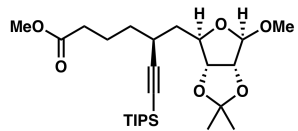




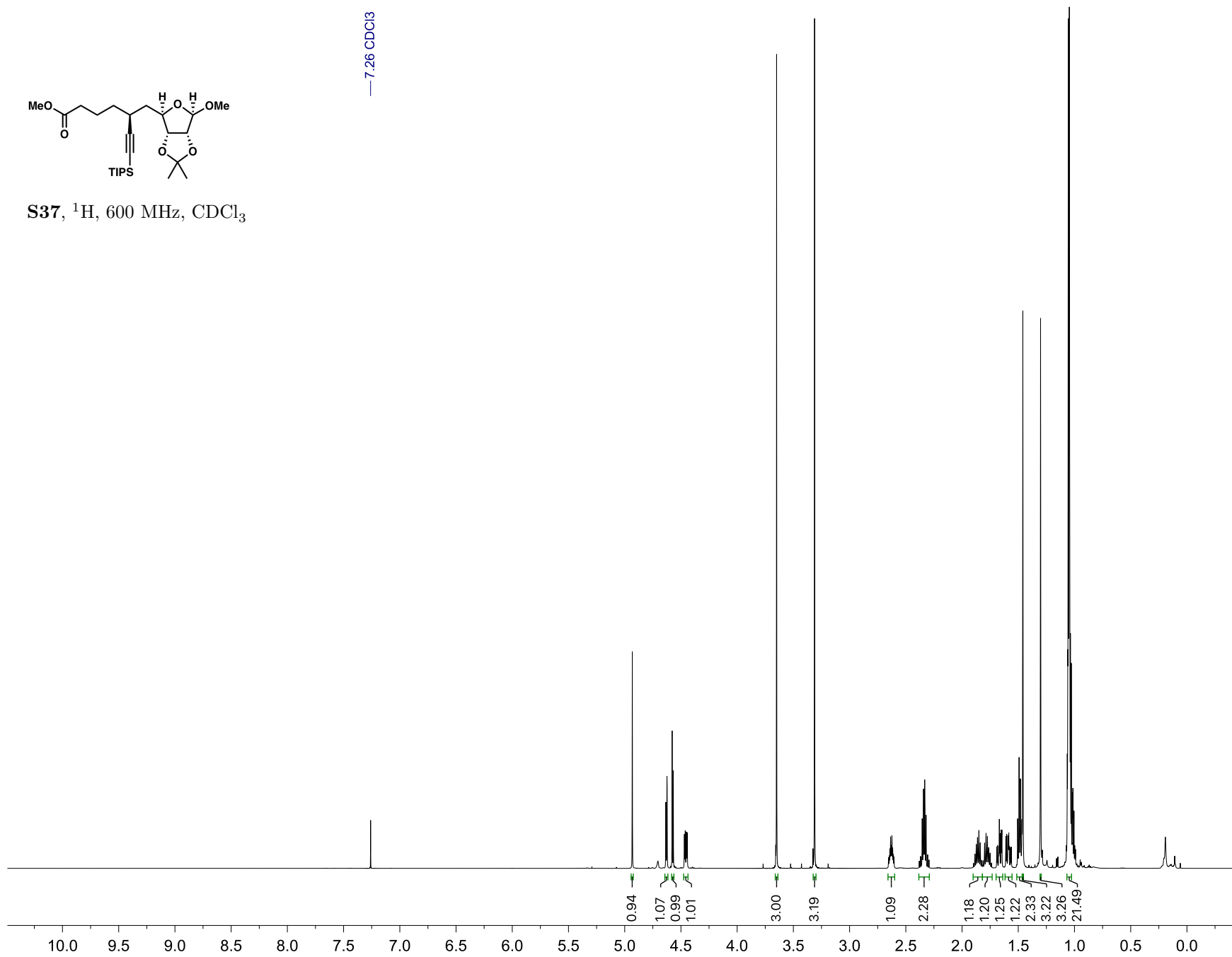


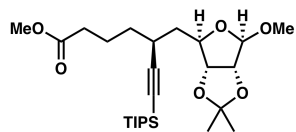
**S36**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



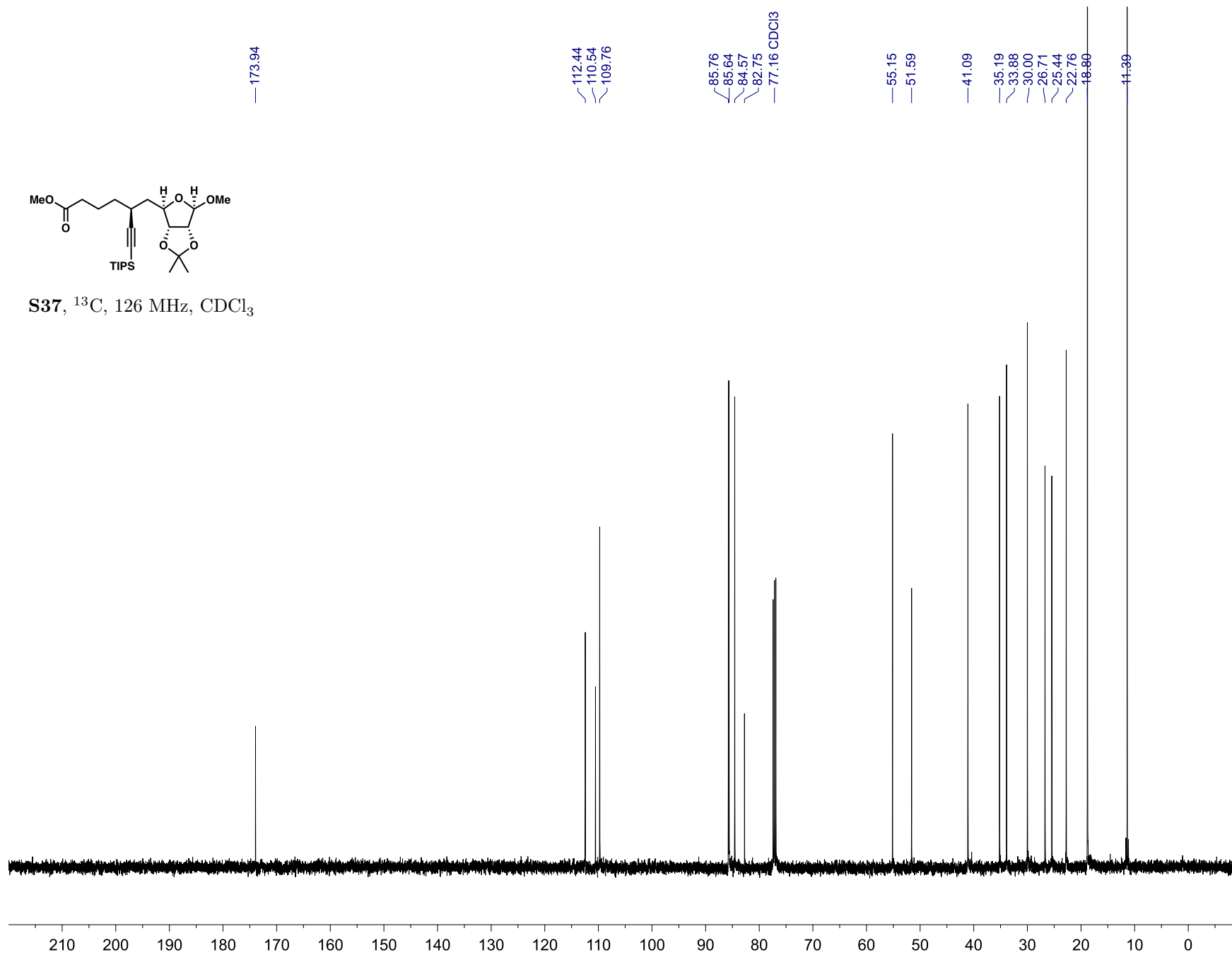


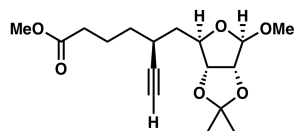
**S37**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$



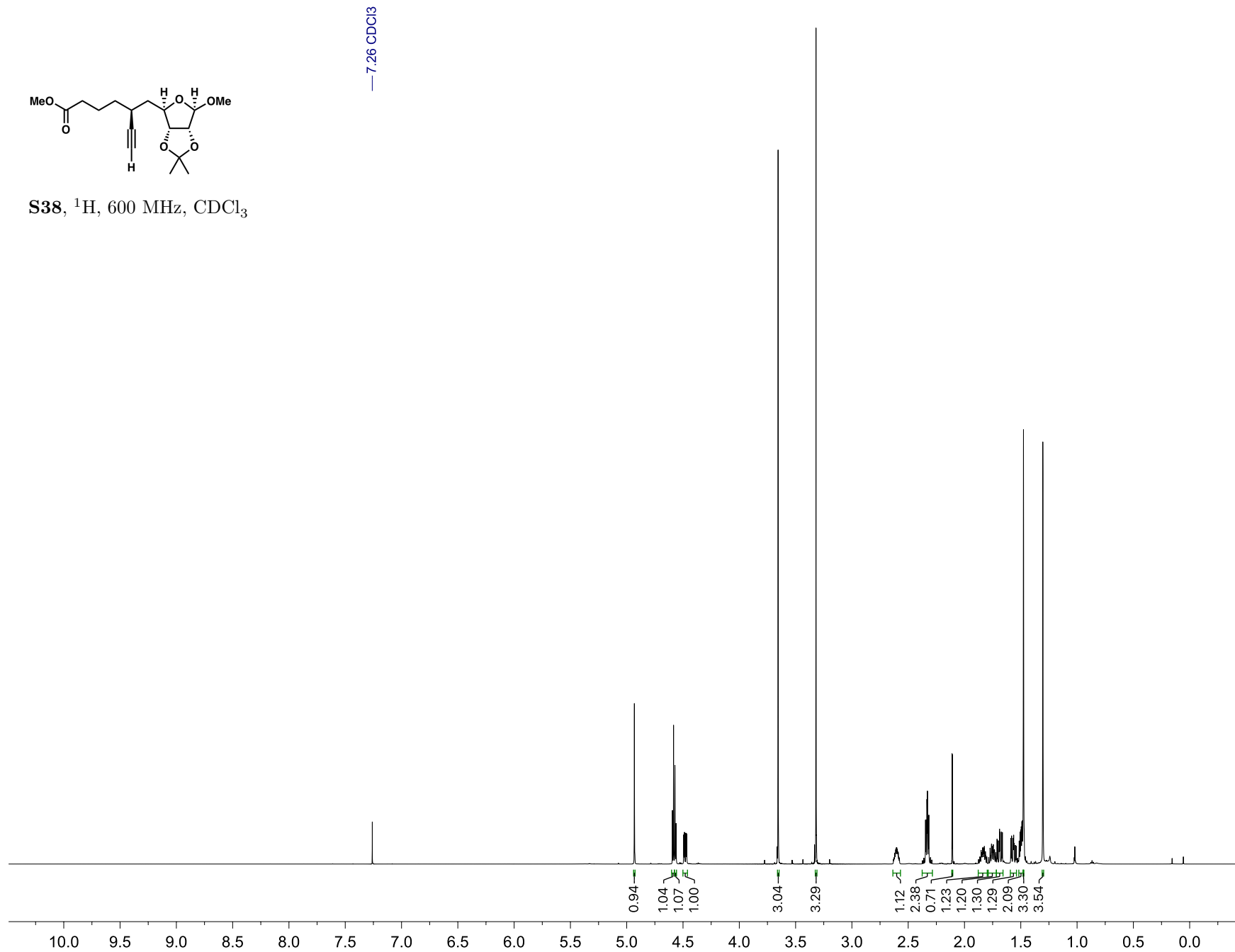


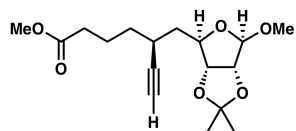
S37,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



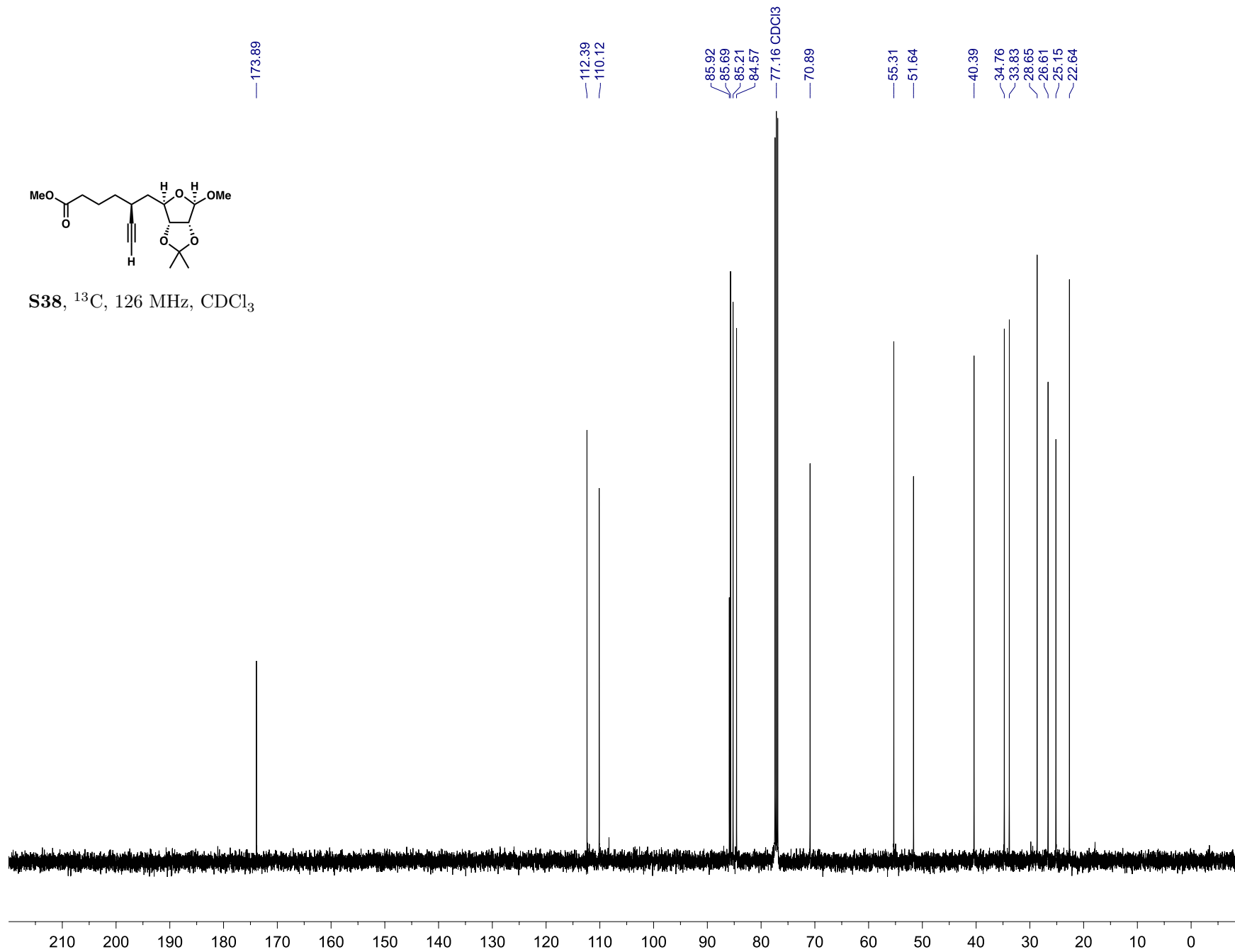


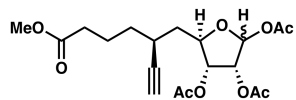
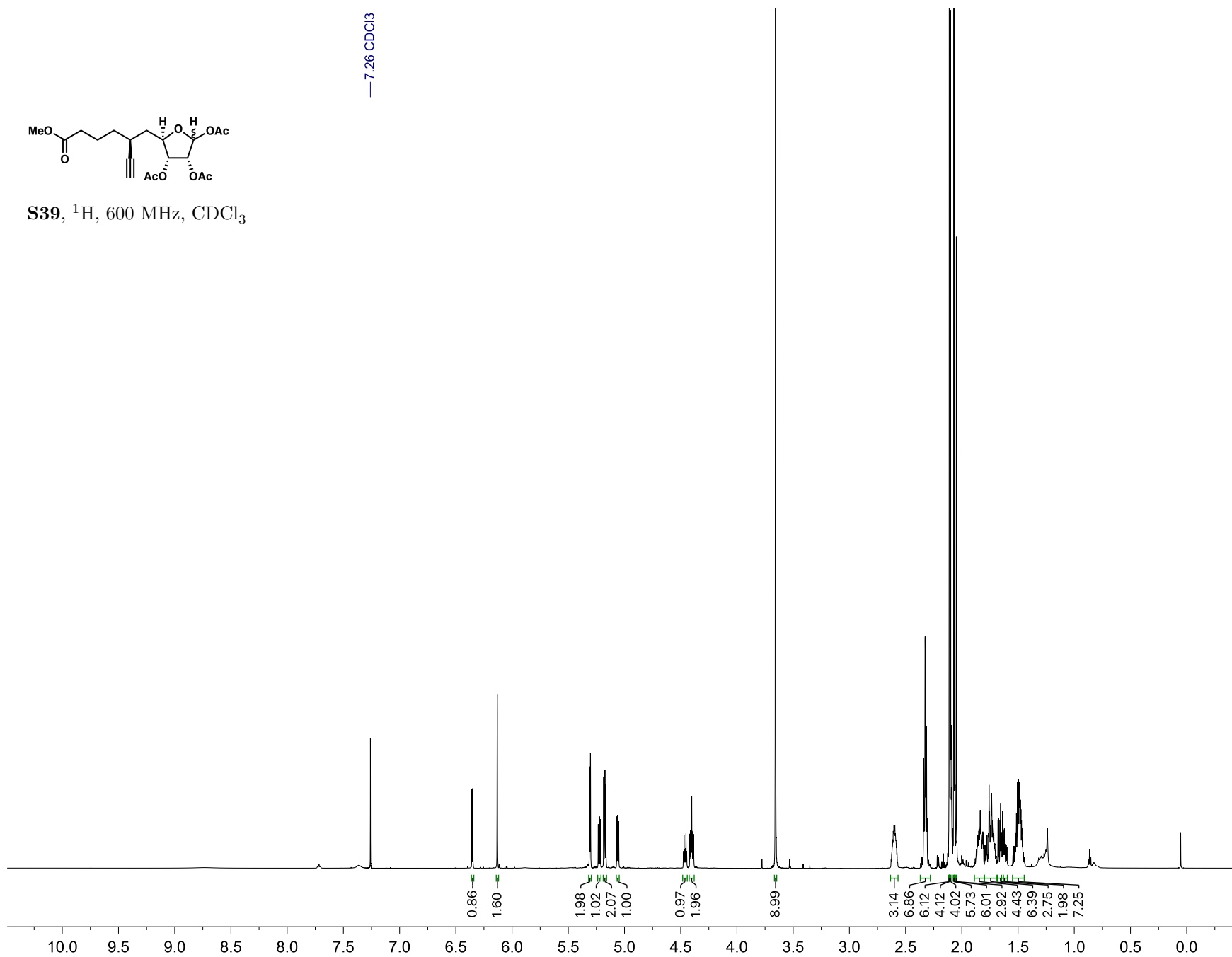
**S38**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

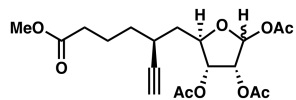




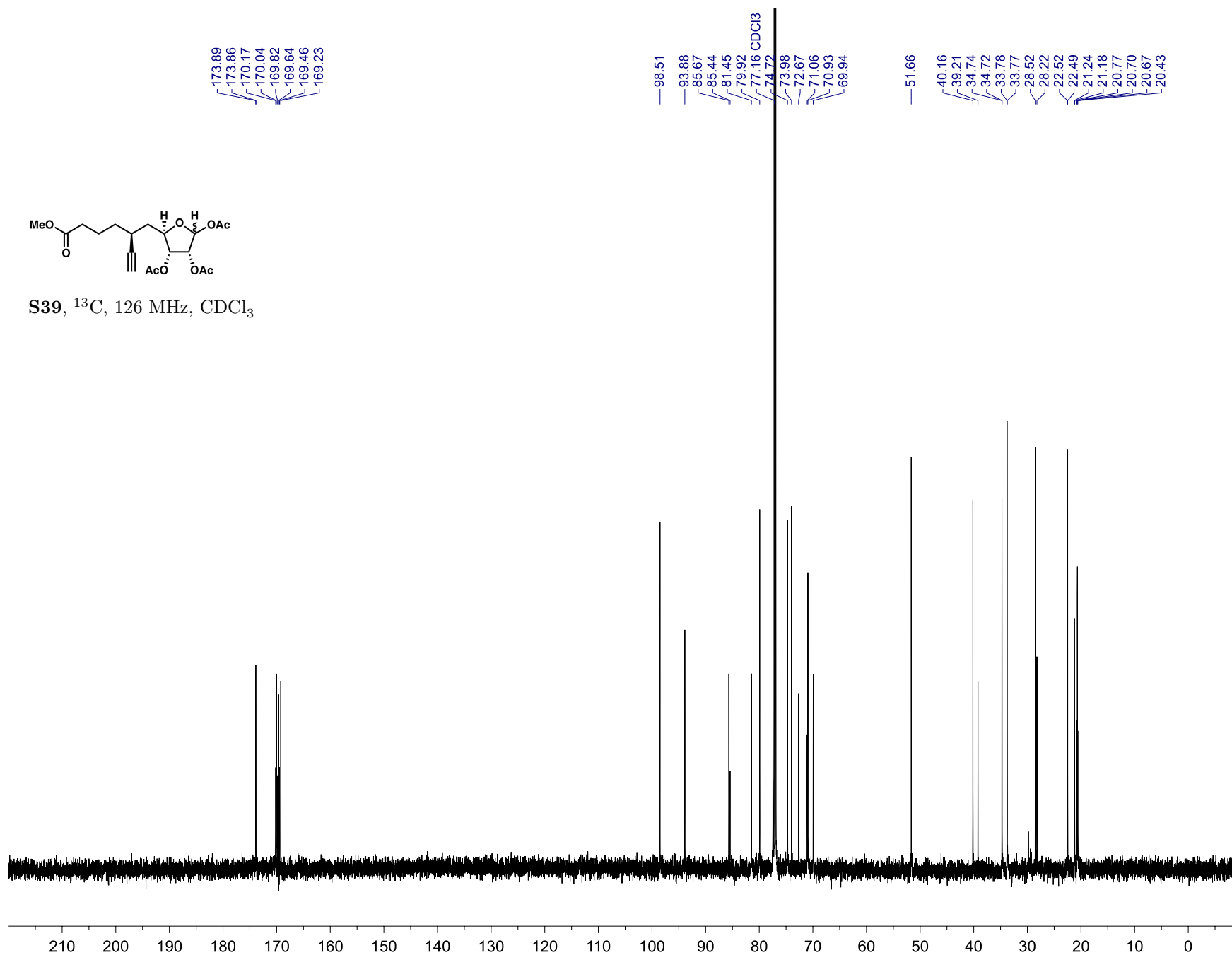
**S38**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



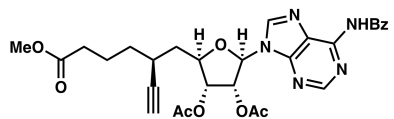
**S39**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ — 7.26  $\text{CDCl}_3$ 



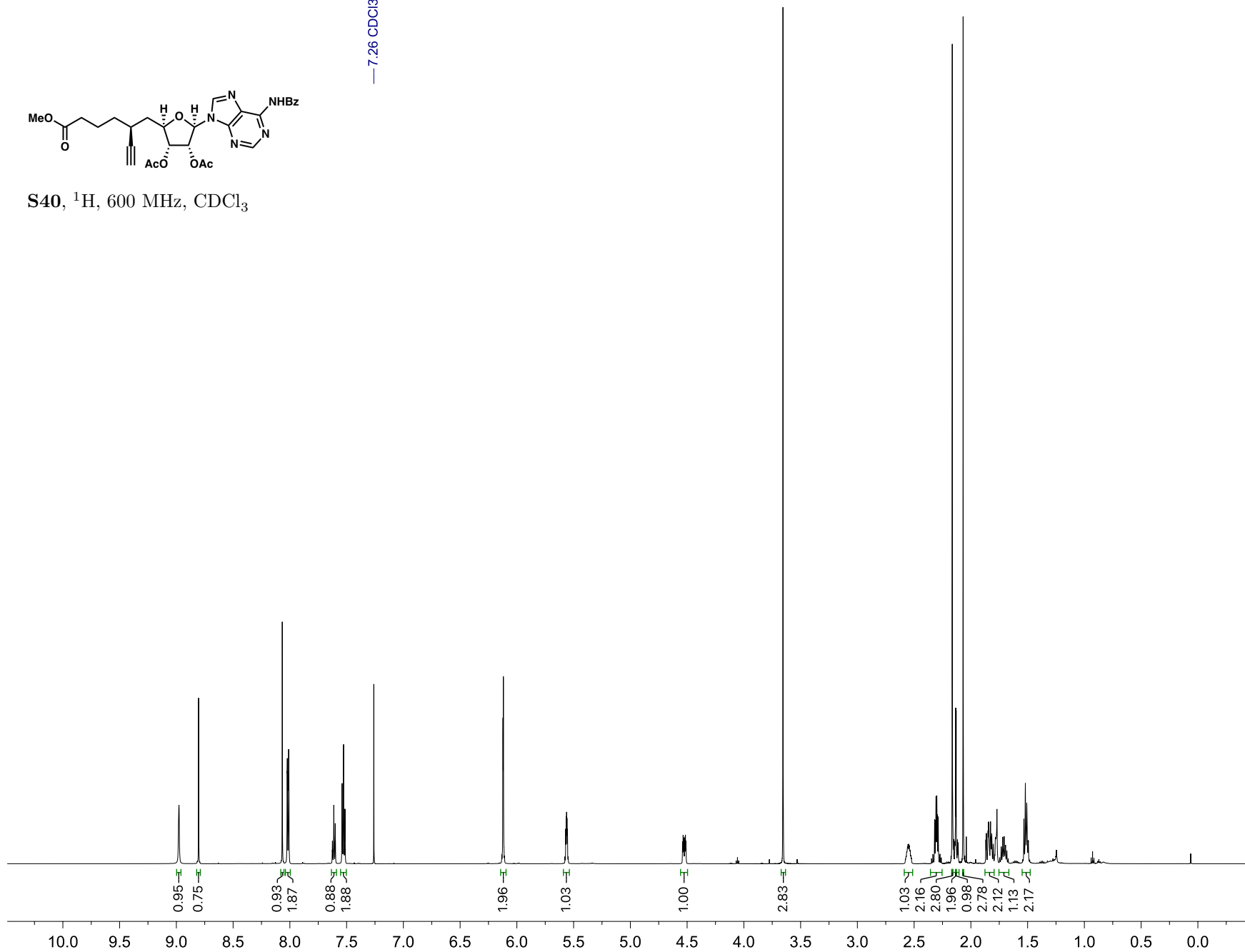
**S39**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



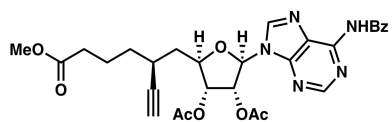
— 7.26 CDCl<sub>3</sub>



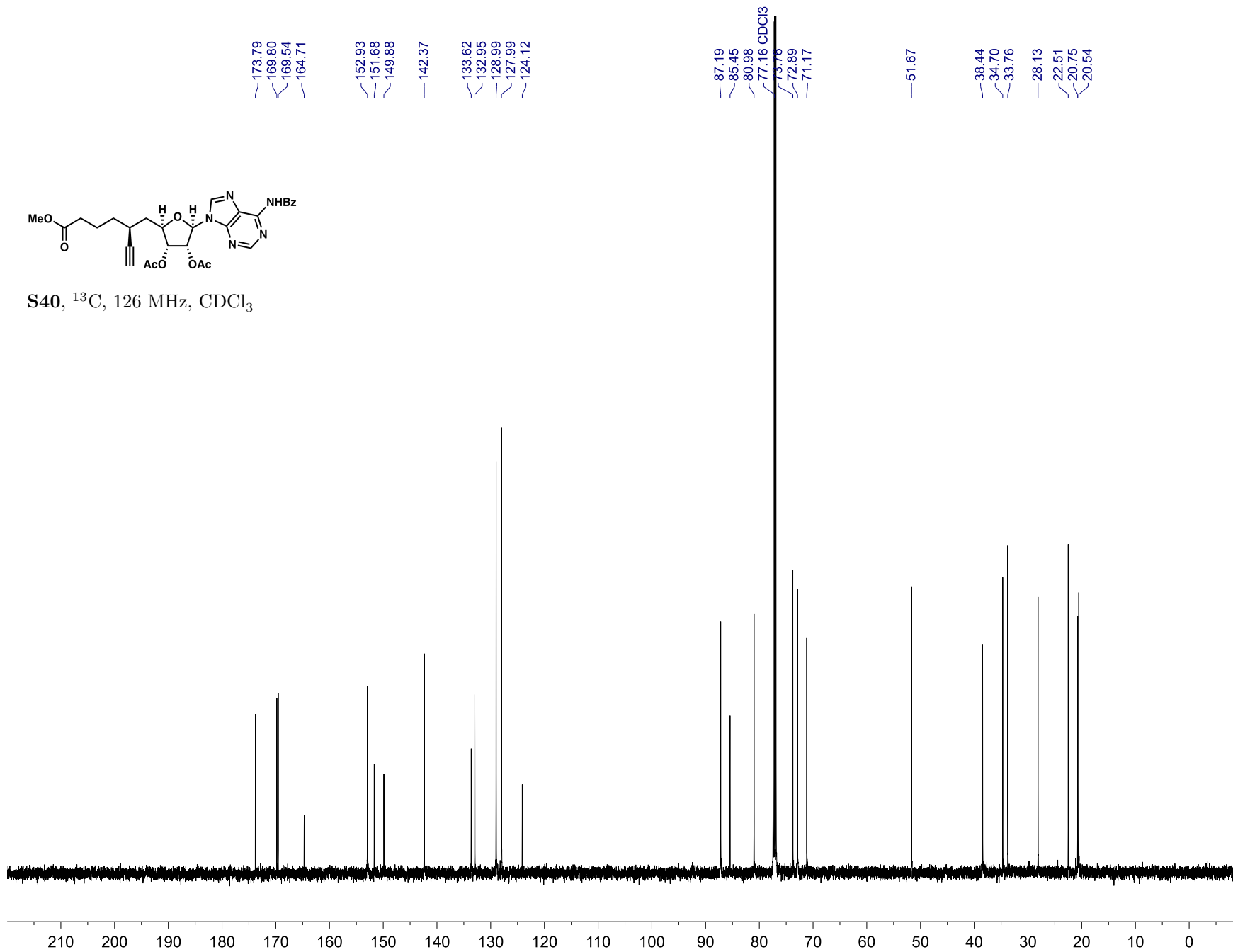
**S40**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

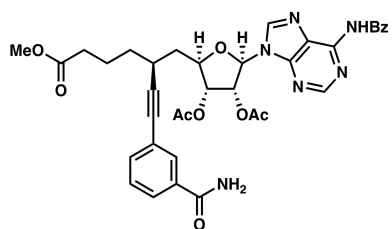
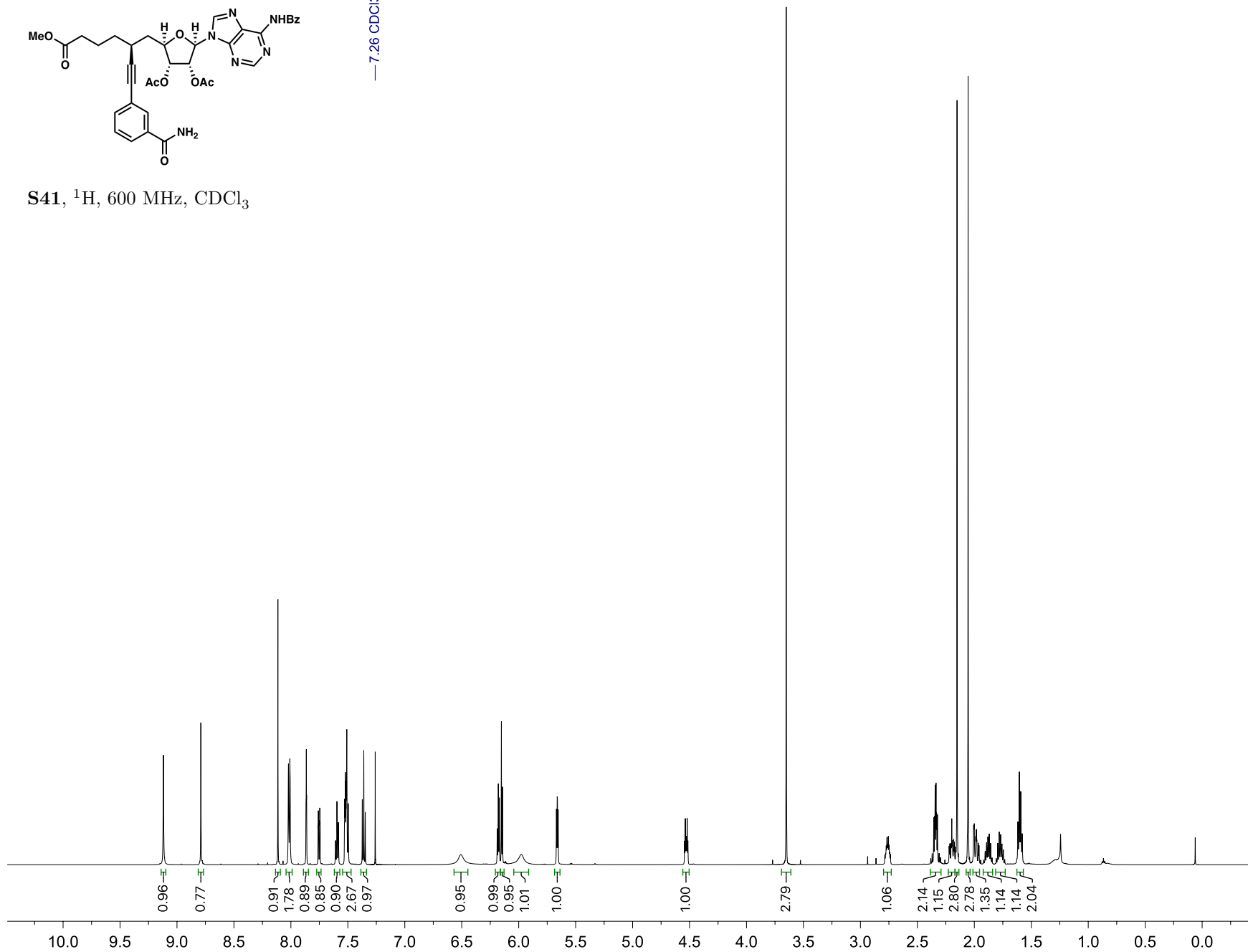


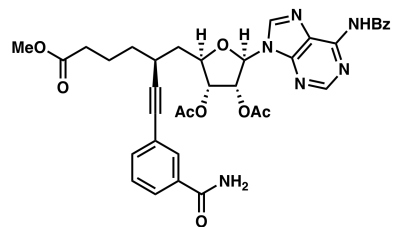




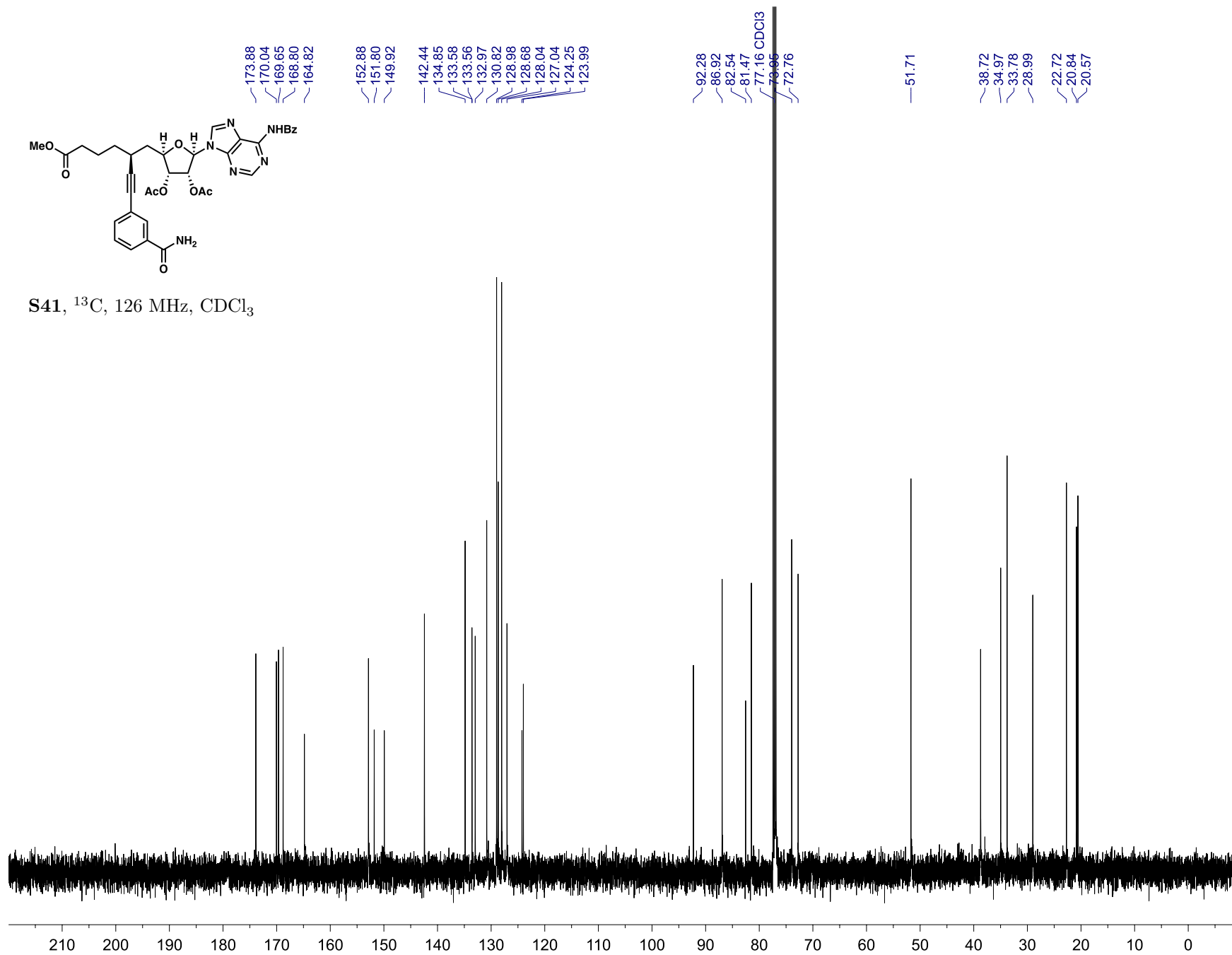
S40,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

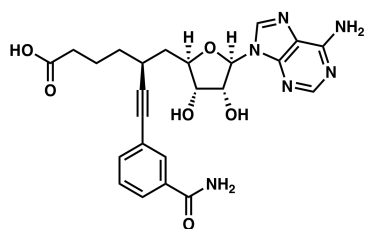


— 7.26 CDCl<sub>3</sub>**S41**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>



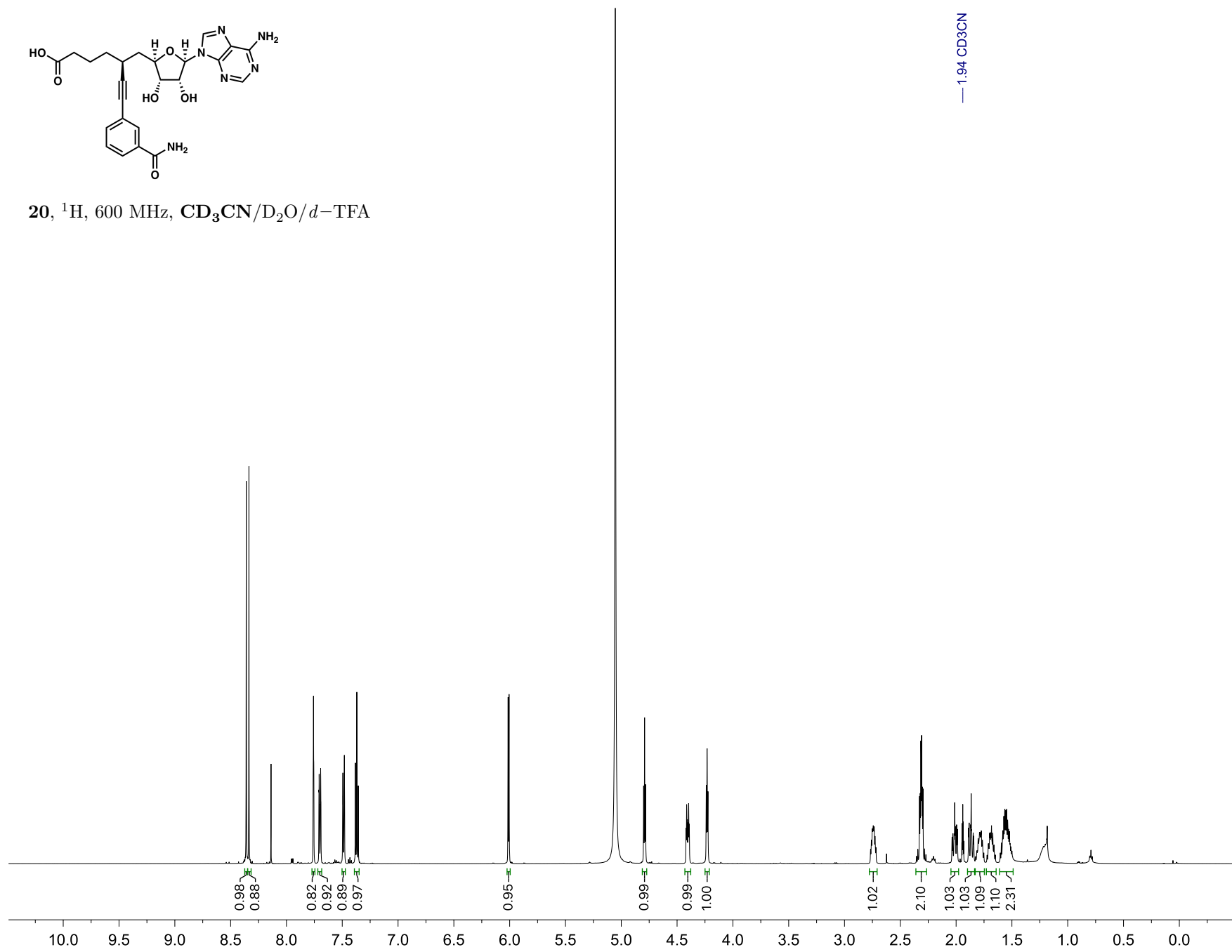
S41,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

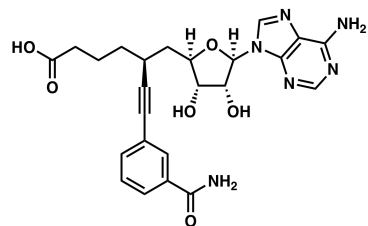




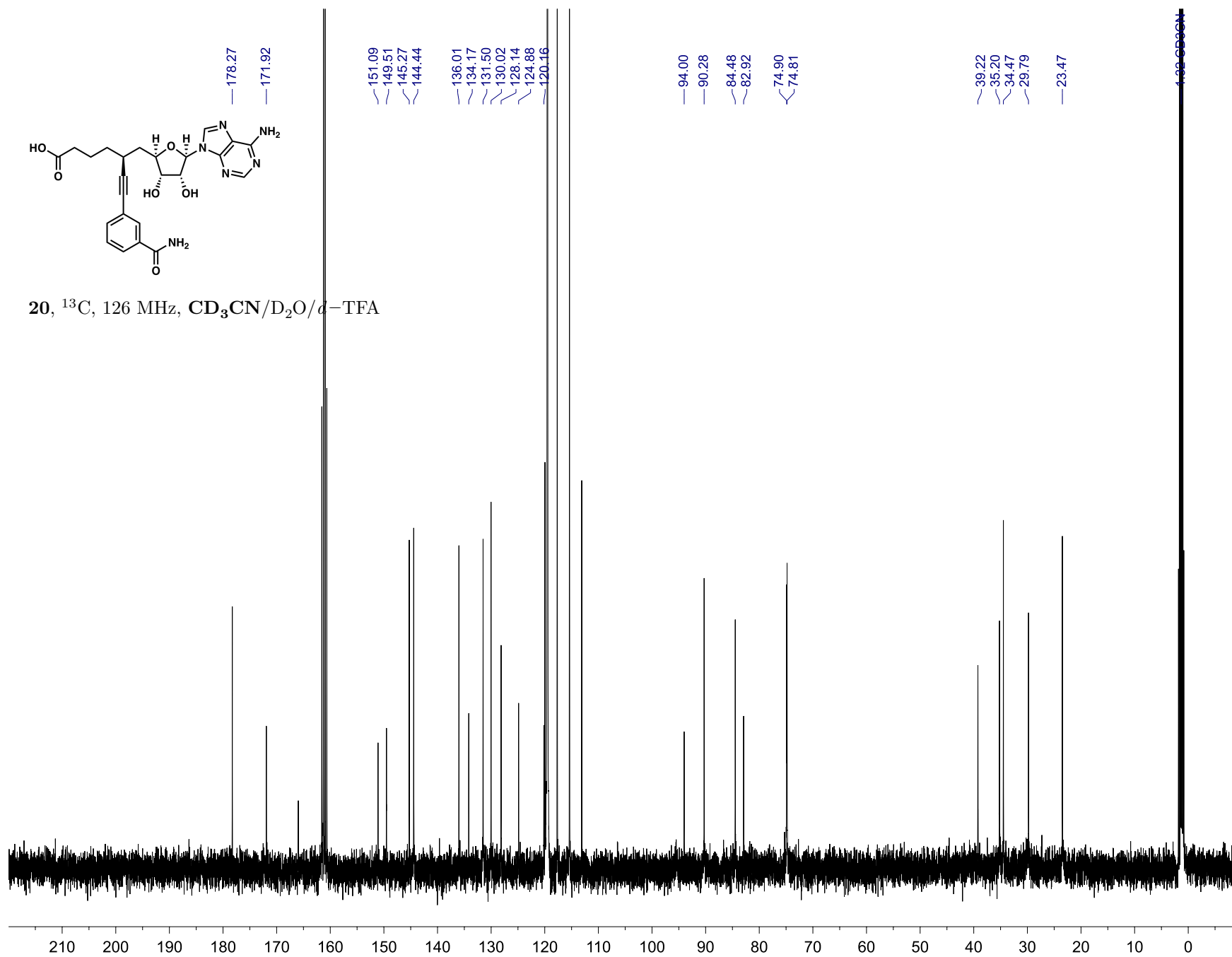
20, <sup>1</sup>H, 600 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA

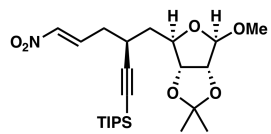
S115



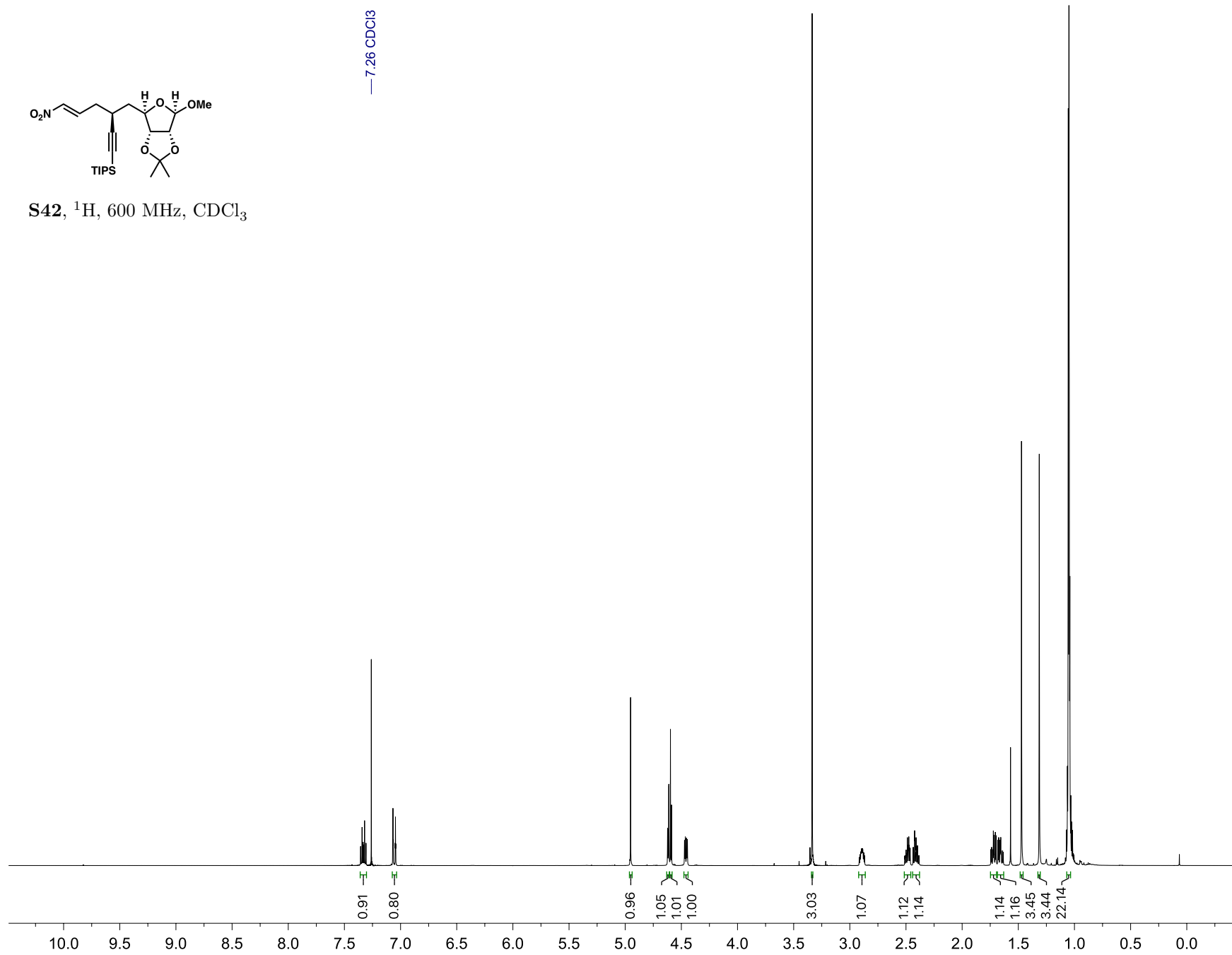


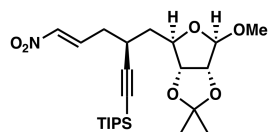
**20**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$



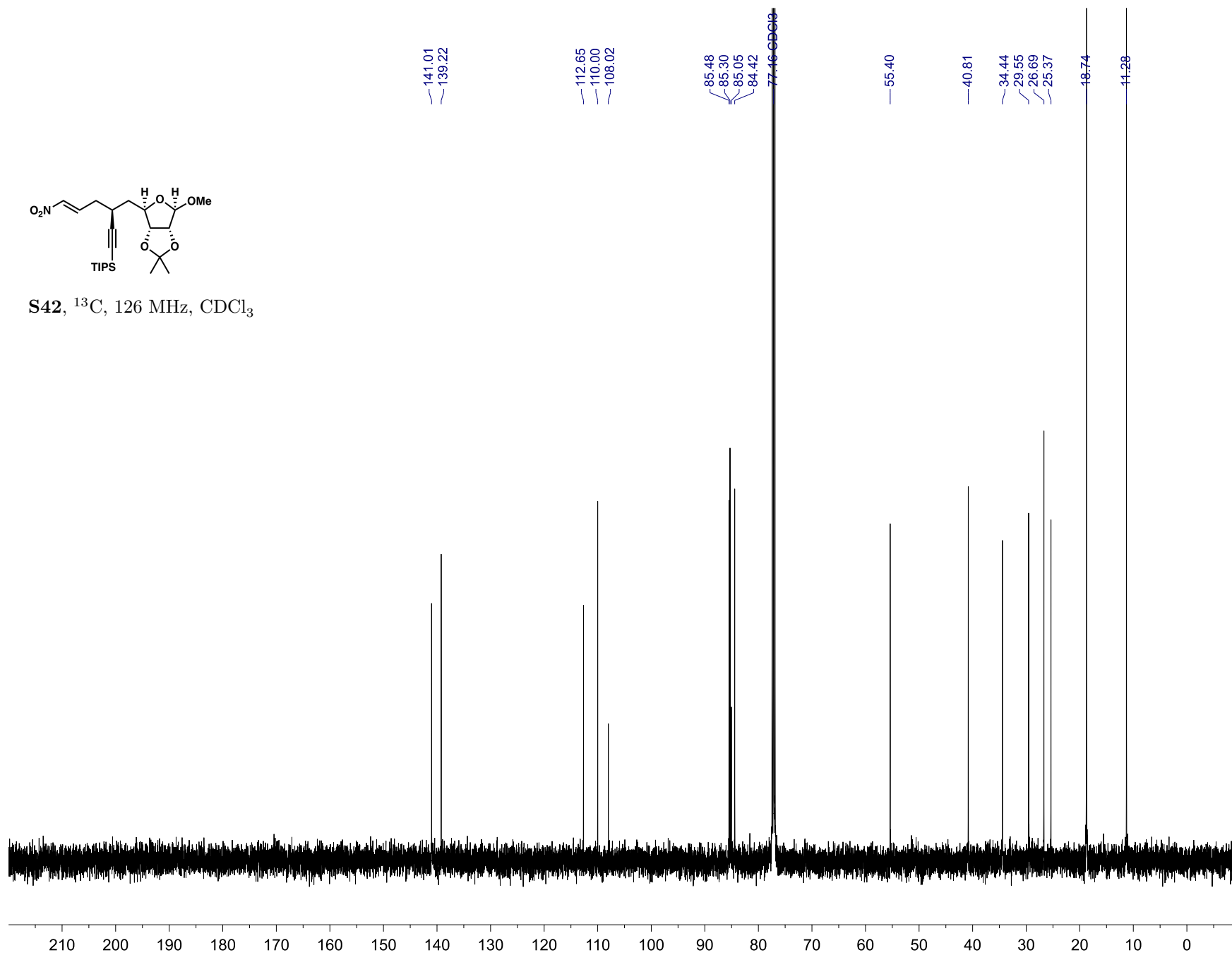


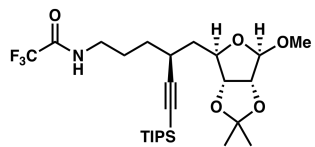
S42, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>



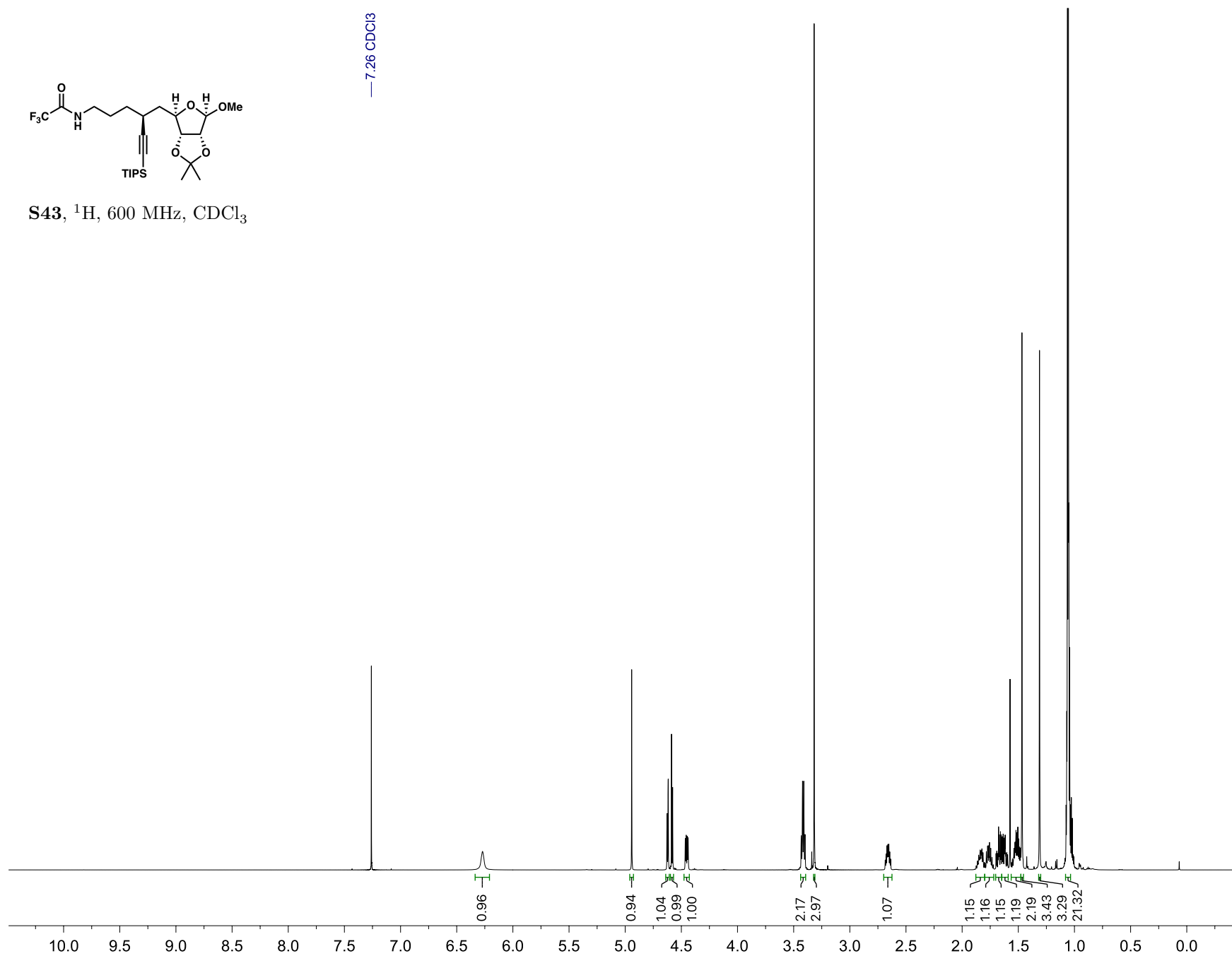


S42, <sup>13</sup>C, 126 MHz, CDCl<sub>3</sub>

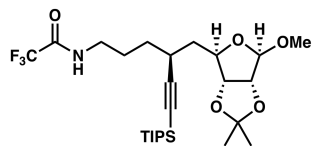




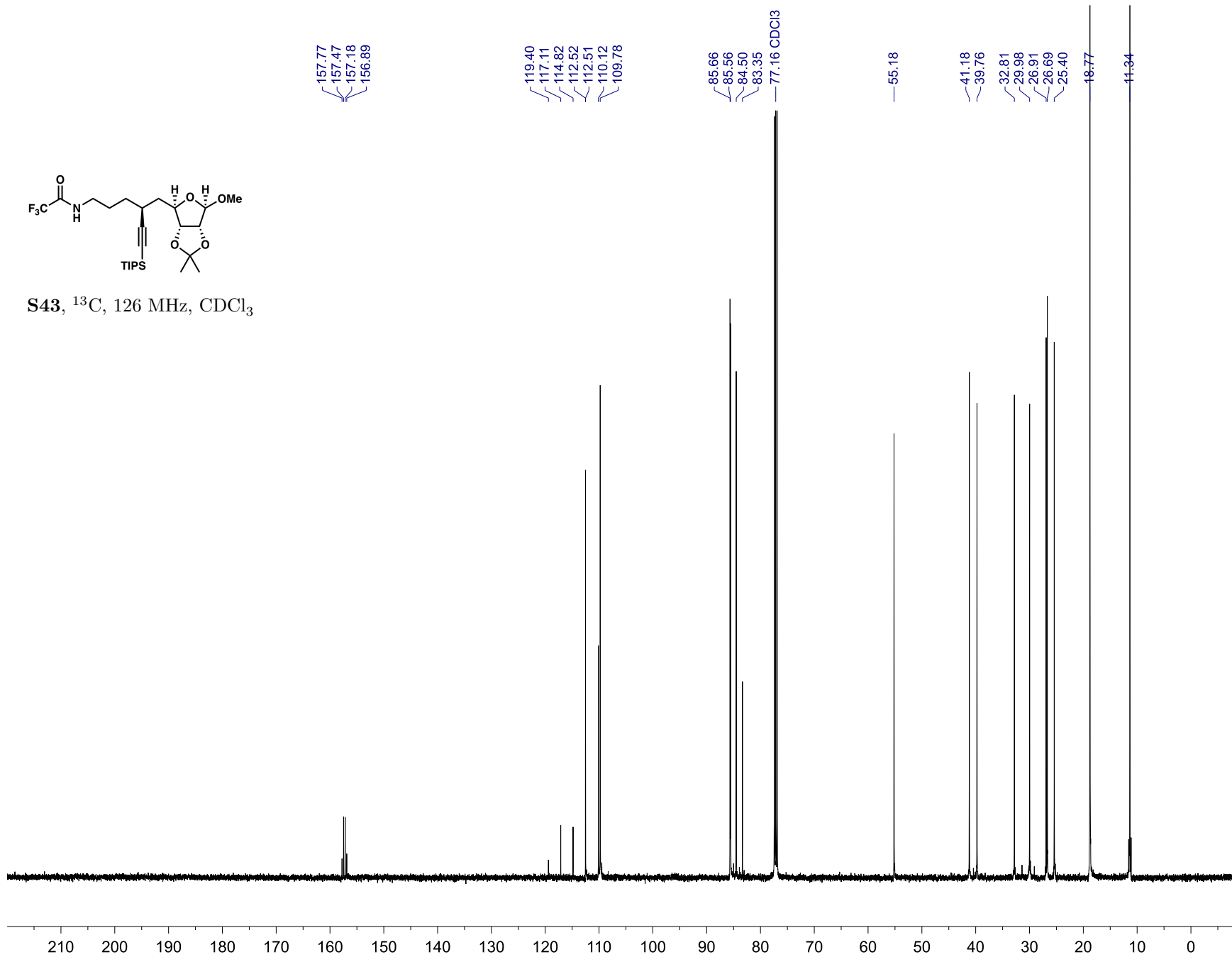
**S43**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$



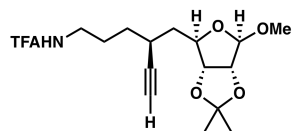




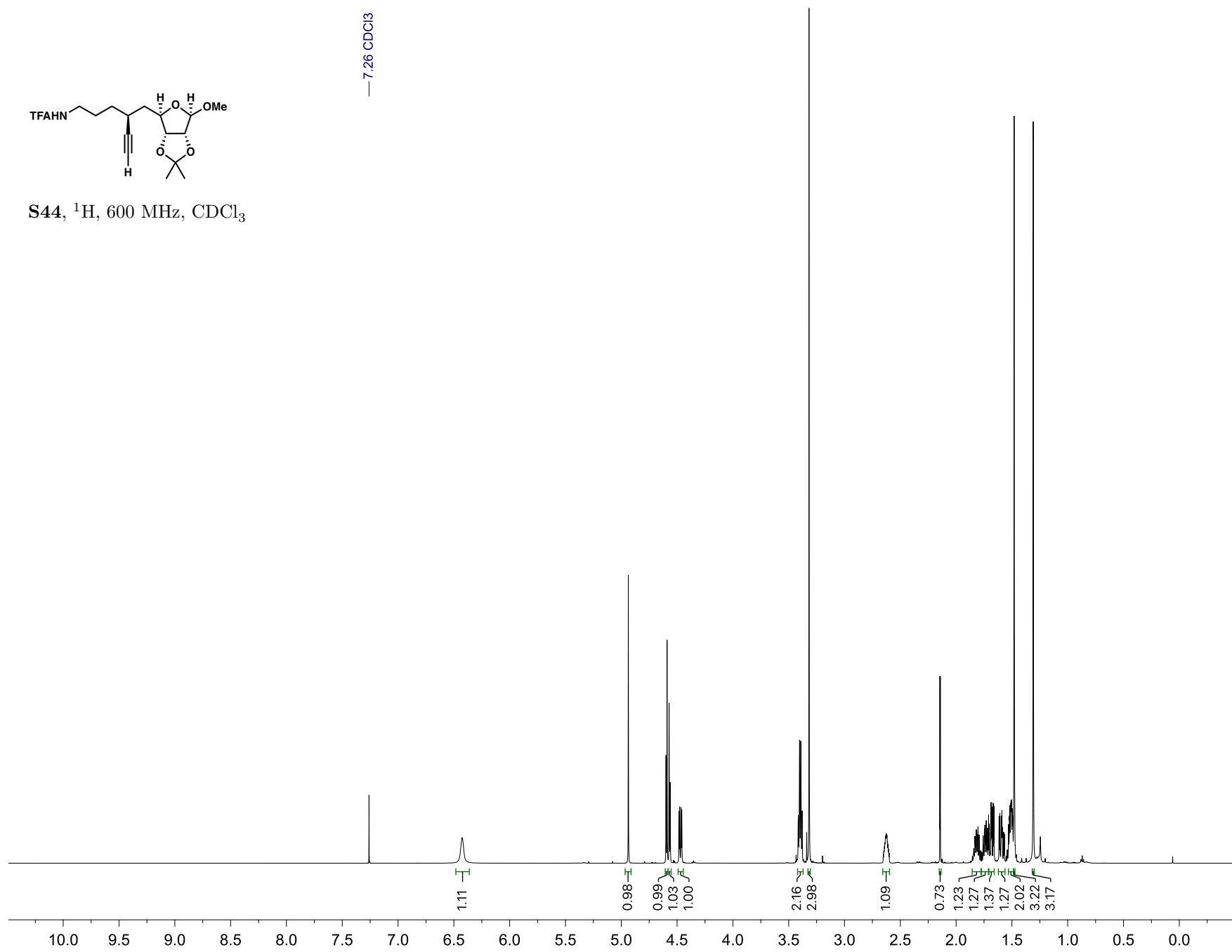
S43, <sup>13</sup>C, 126 MHz, CDCl<sub>3</sub>

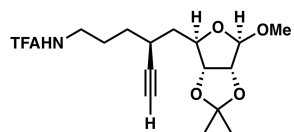


— 7.26 CDCl<sub>3</sub>

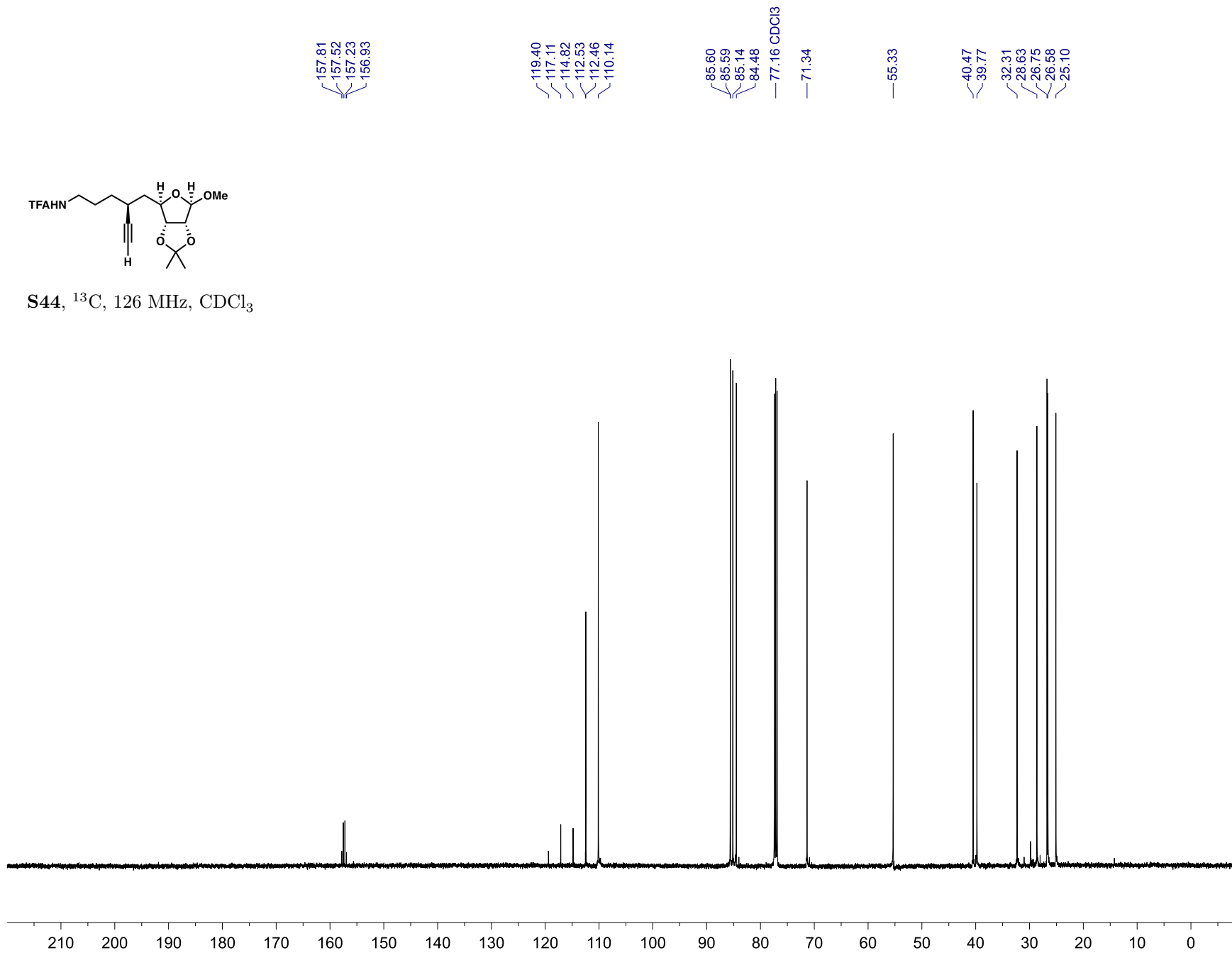


S44, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

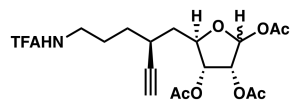




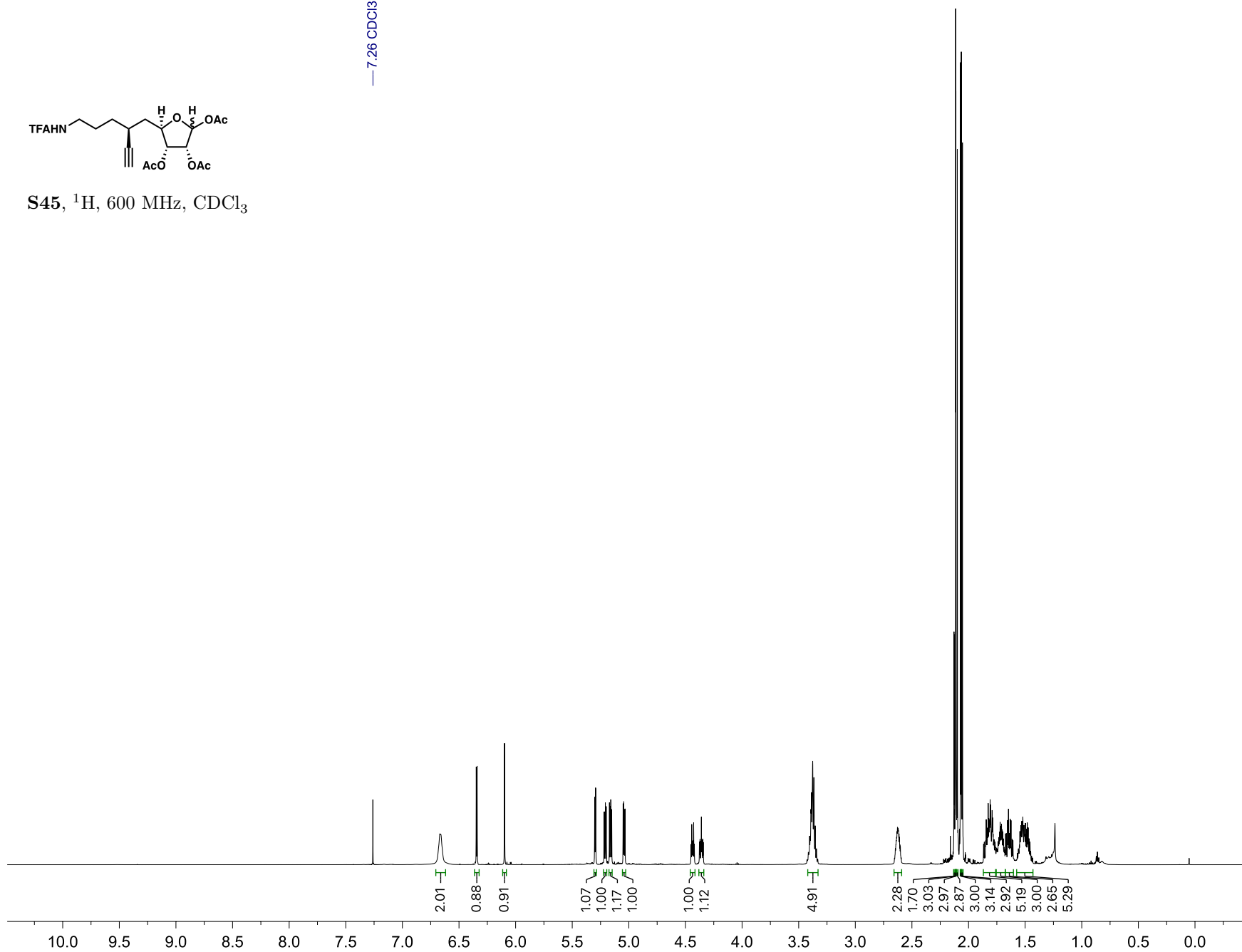
S44,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

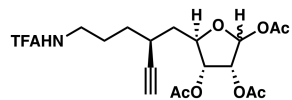


— 7.26 CDCl<sub>3</sub>

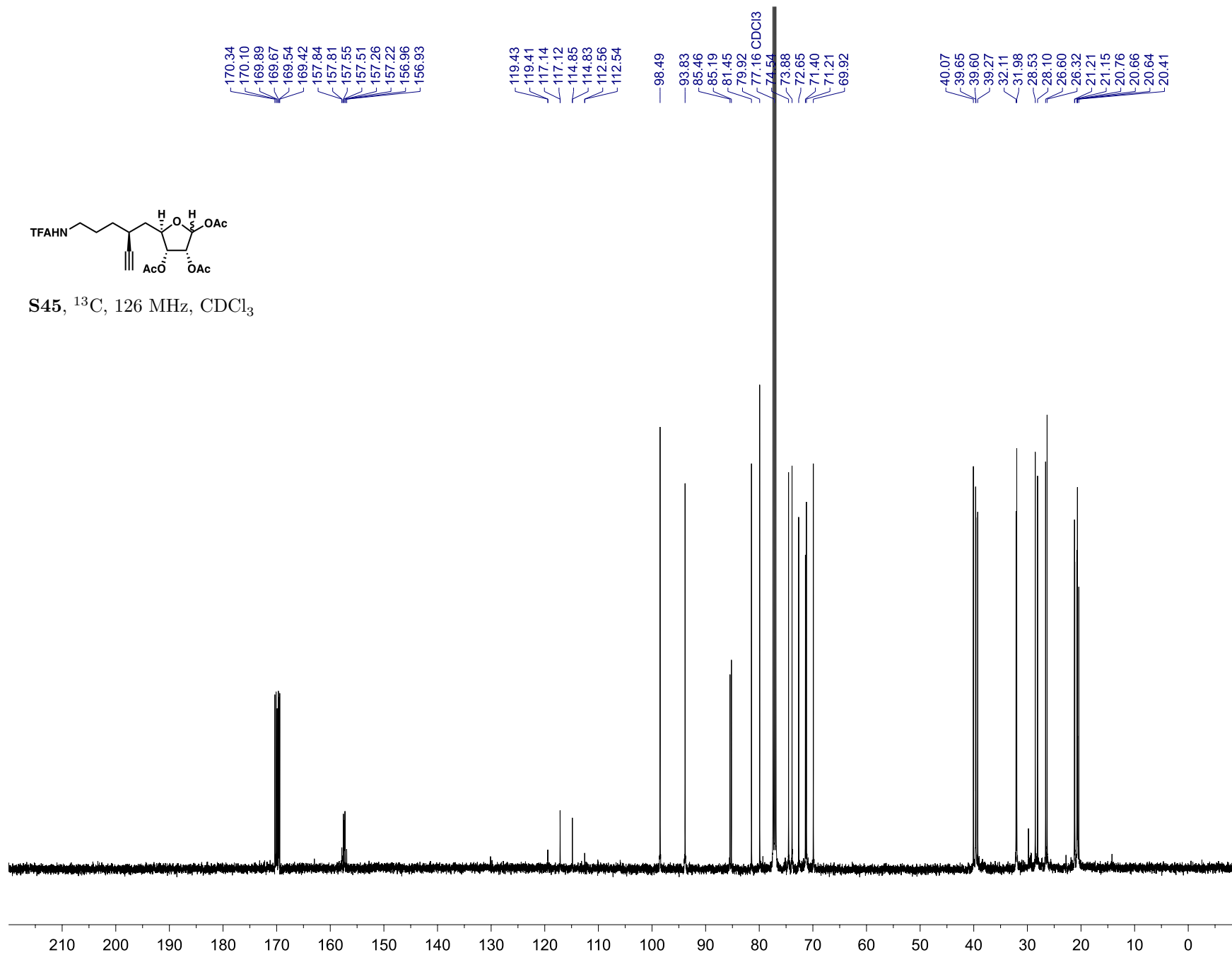


S45, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

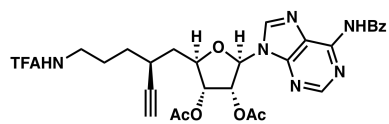




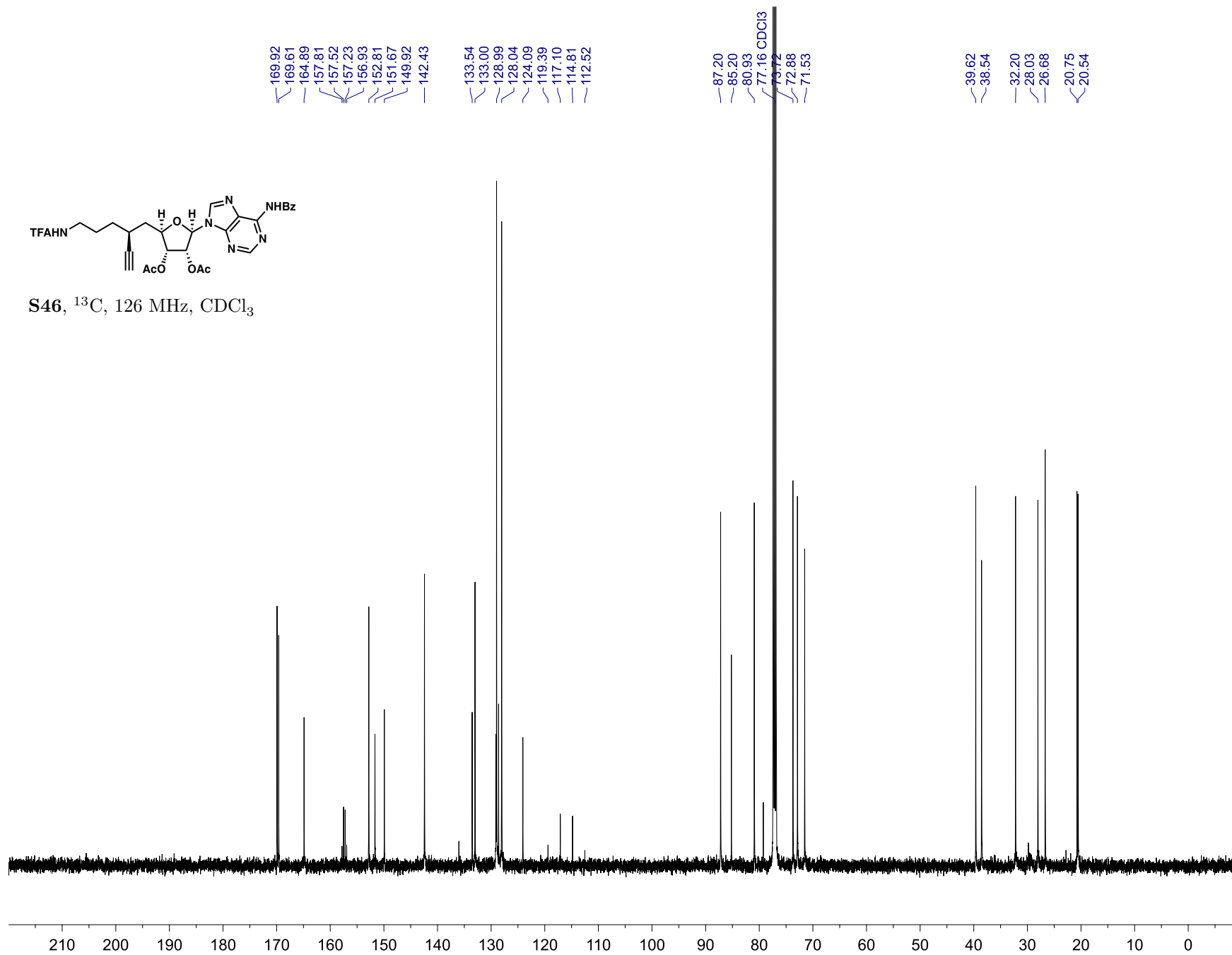
**S45**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

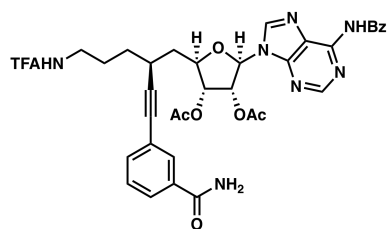






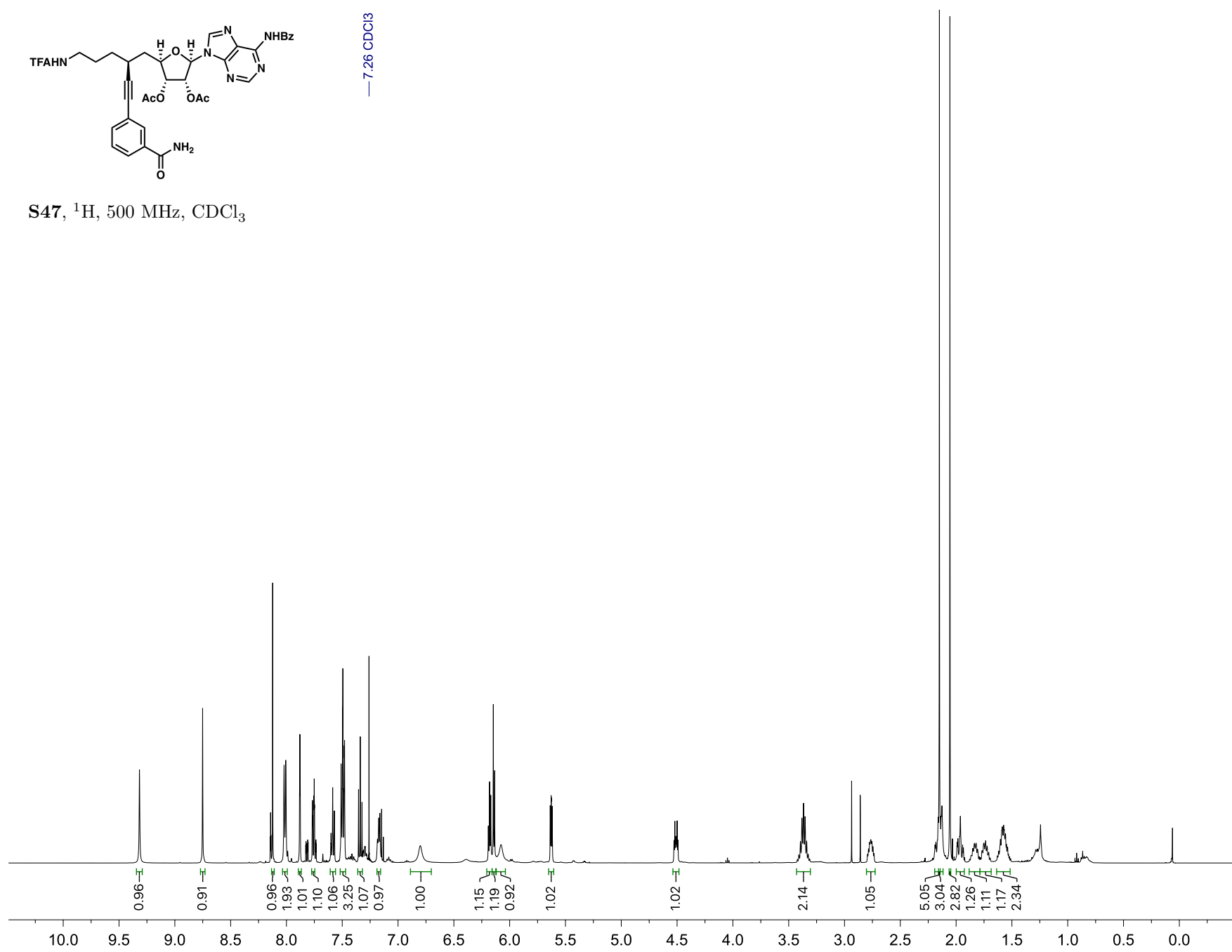
**S46**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



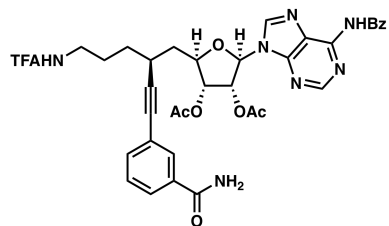


— 7.26 CDCl<sub>3</sub>

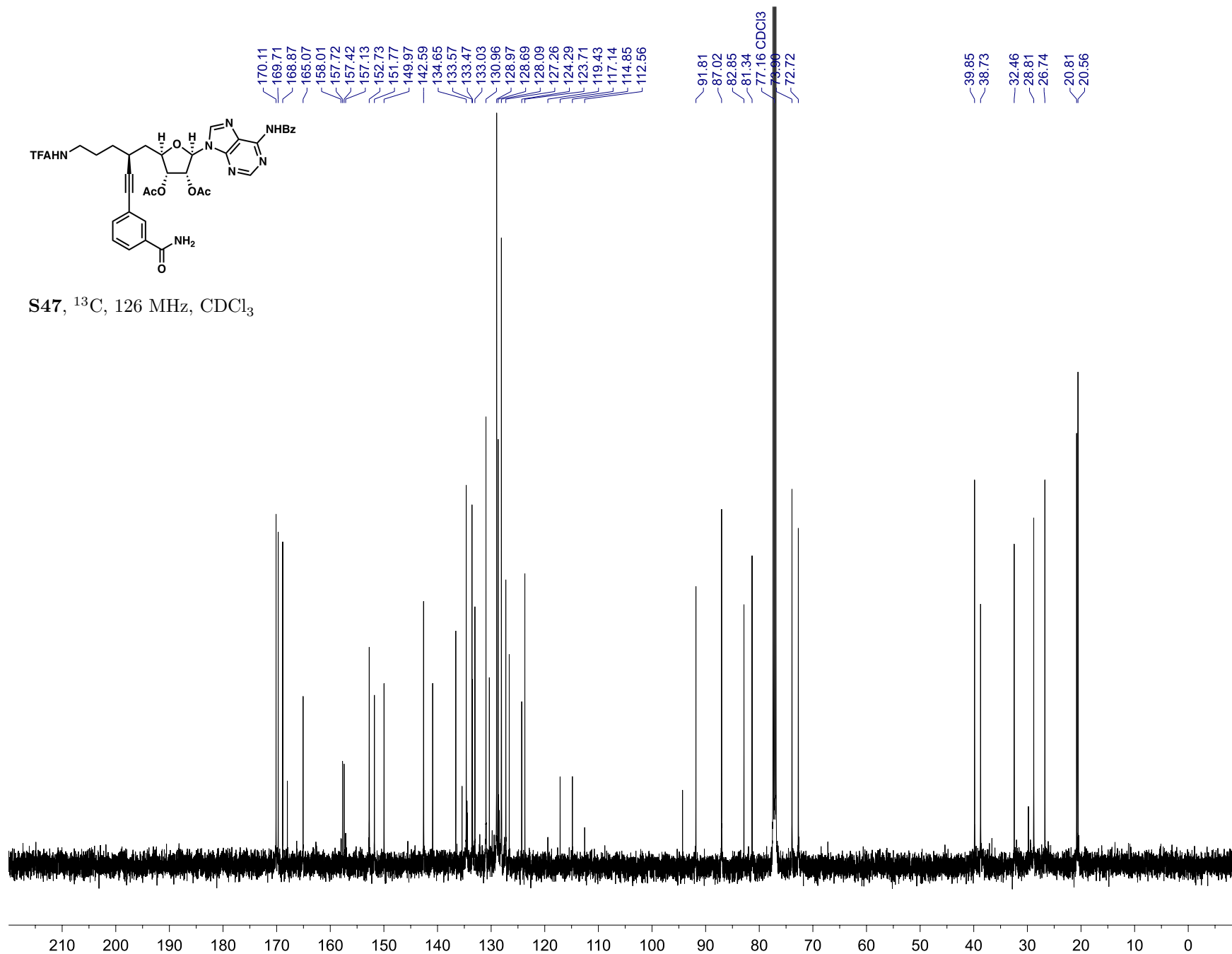
S47, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>

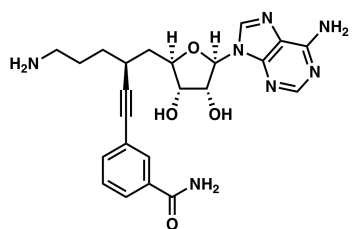






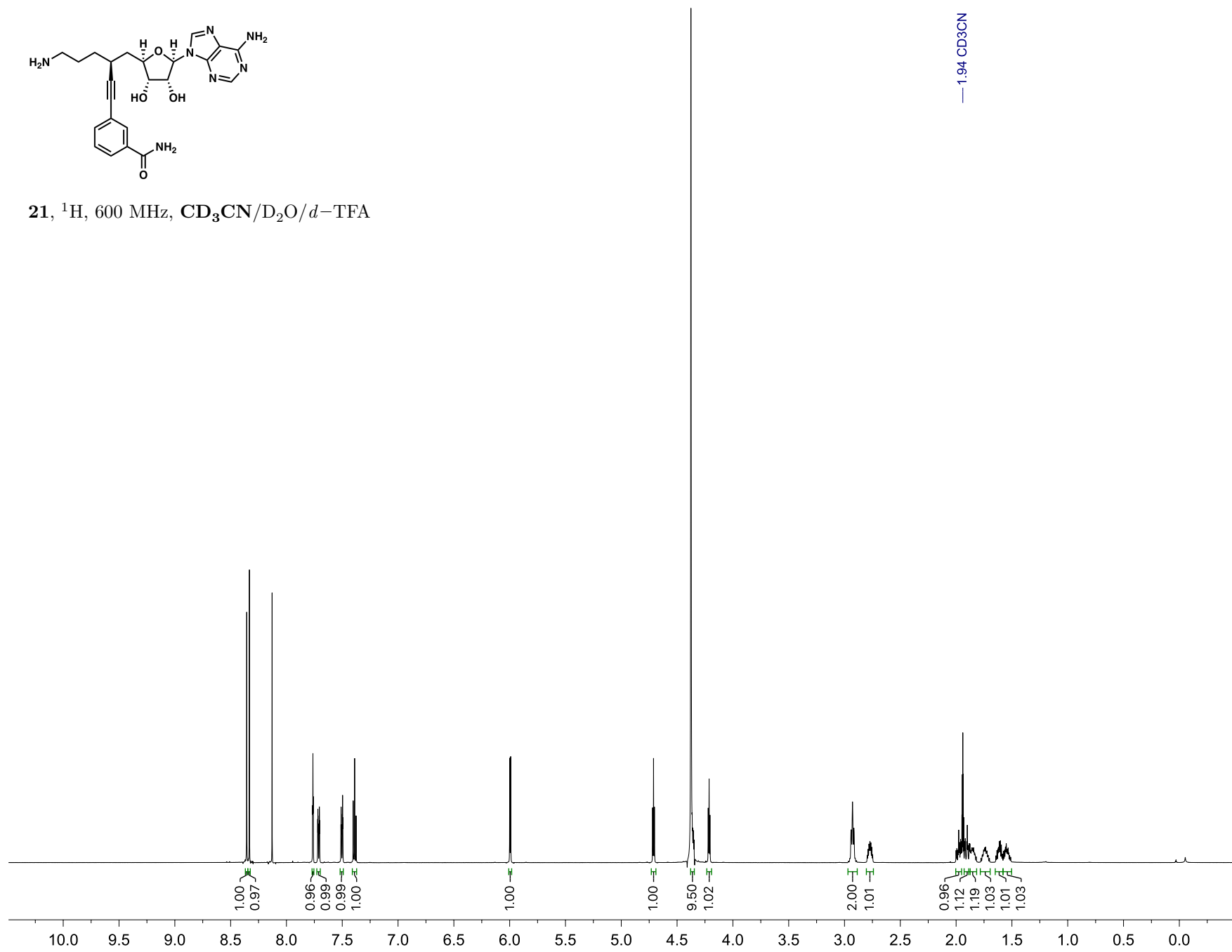
S47, <sup>13</sup>C, 126 MHz, CDCl<sub>3</sub>

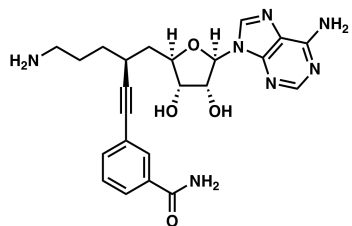




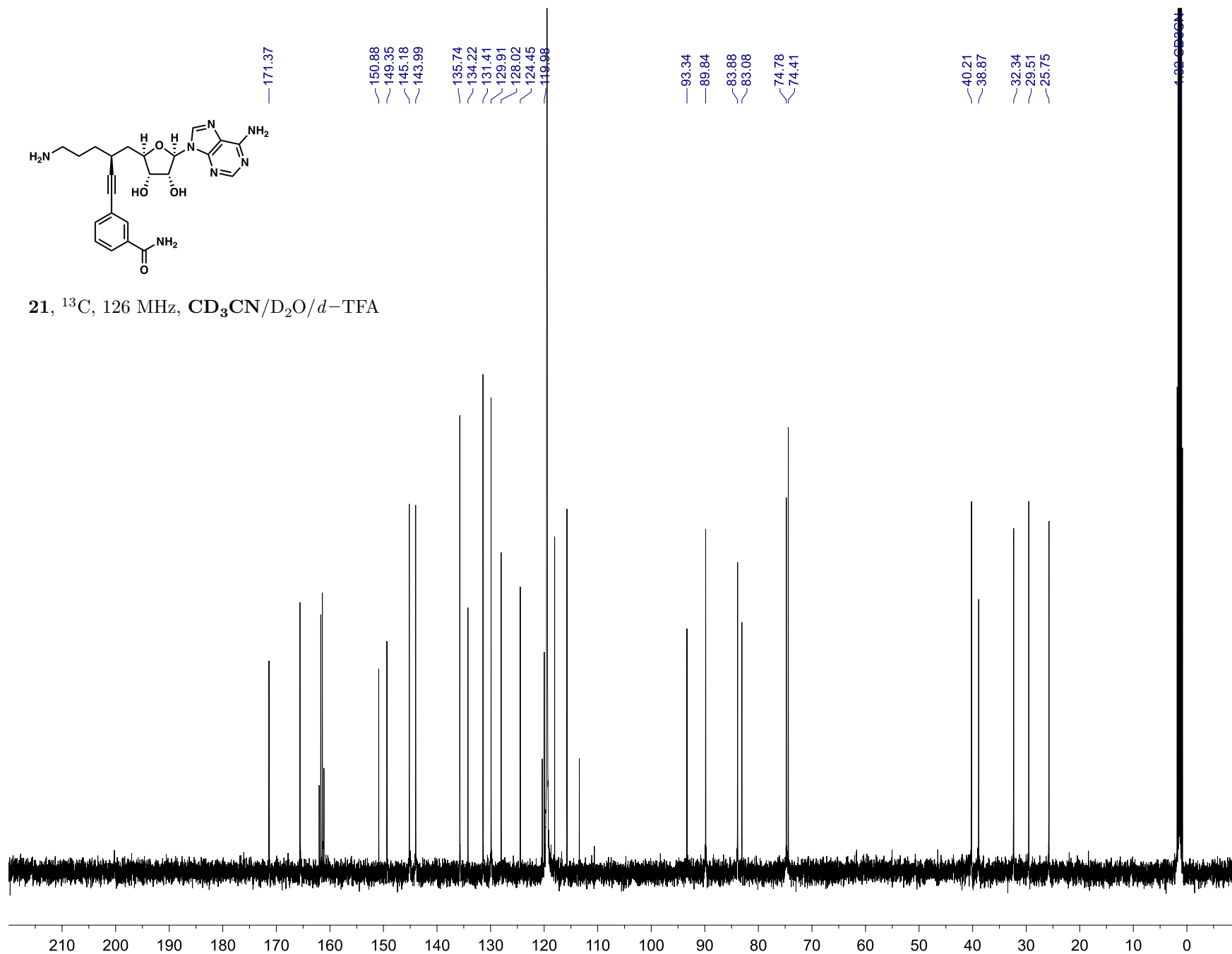
21,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

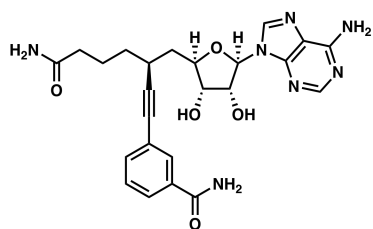
— 1.94  $\text{CD}_3\text{CN}$





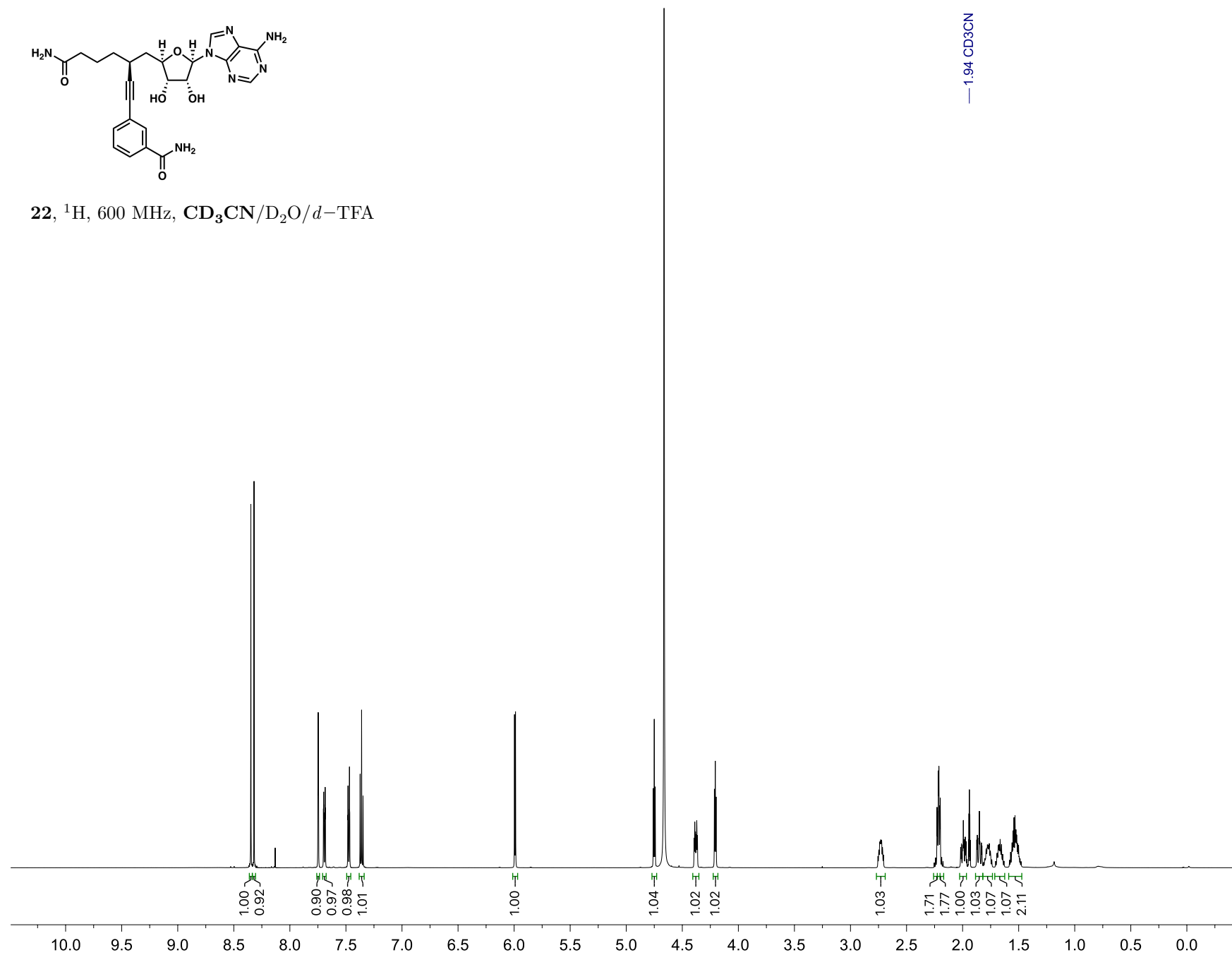
**21**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

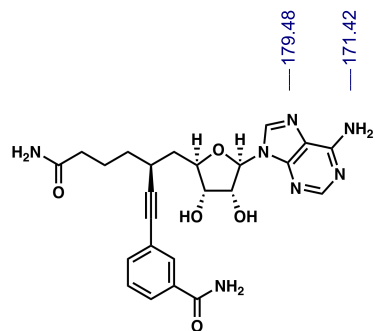




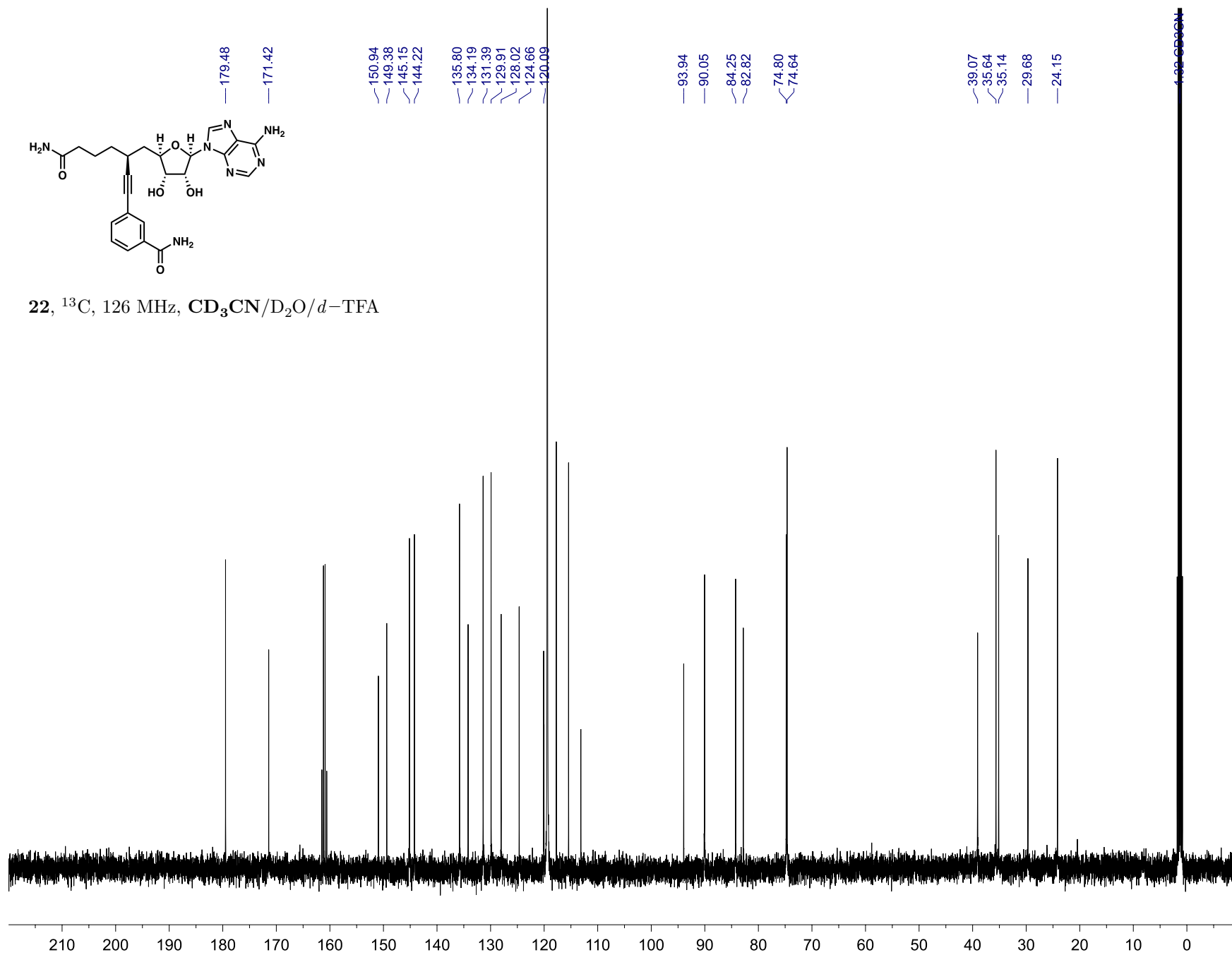
22,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

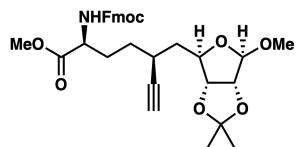
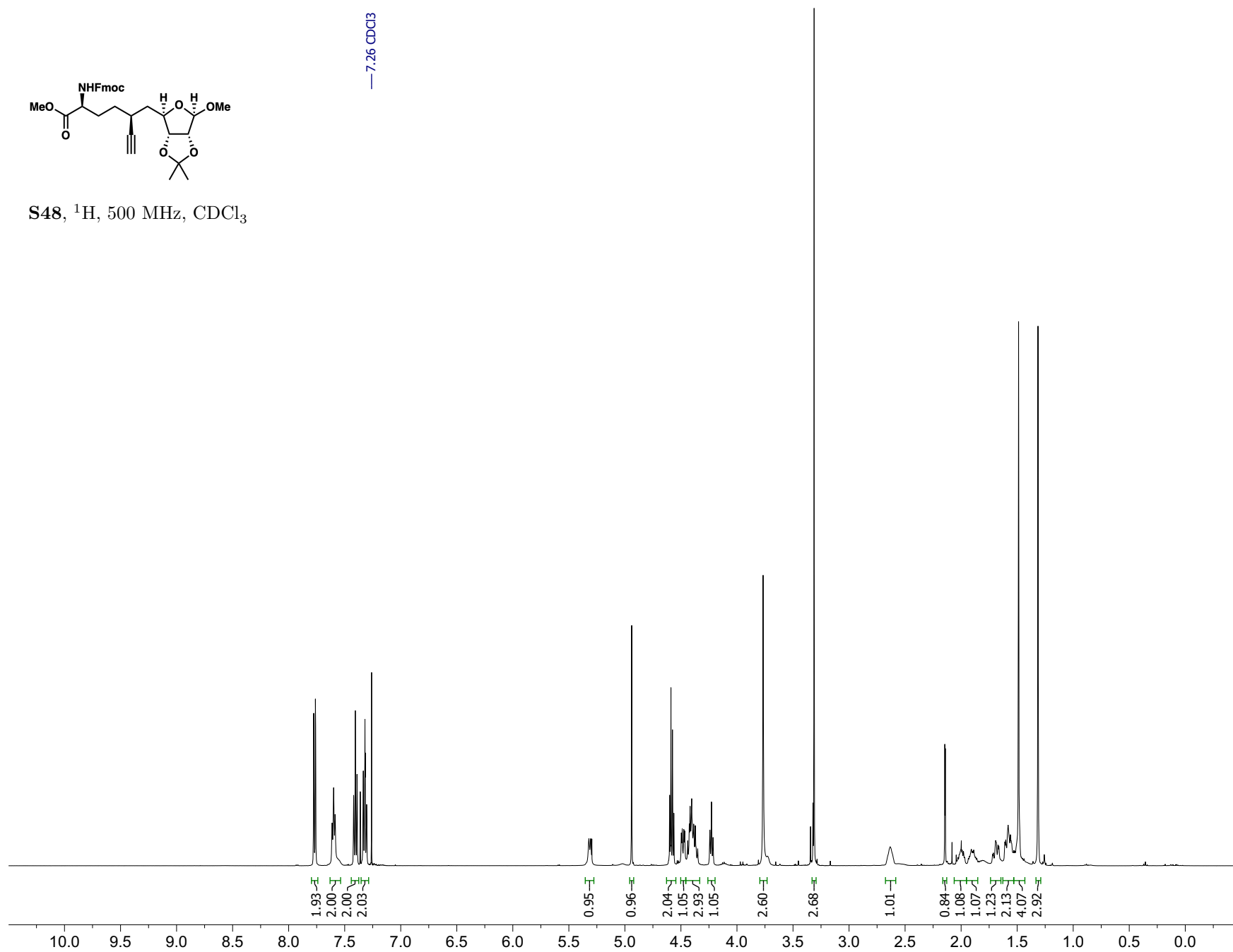
1818

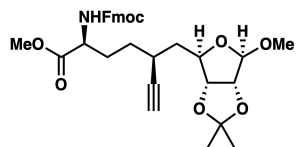




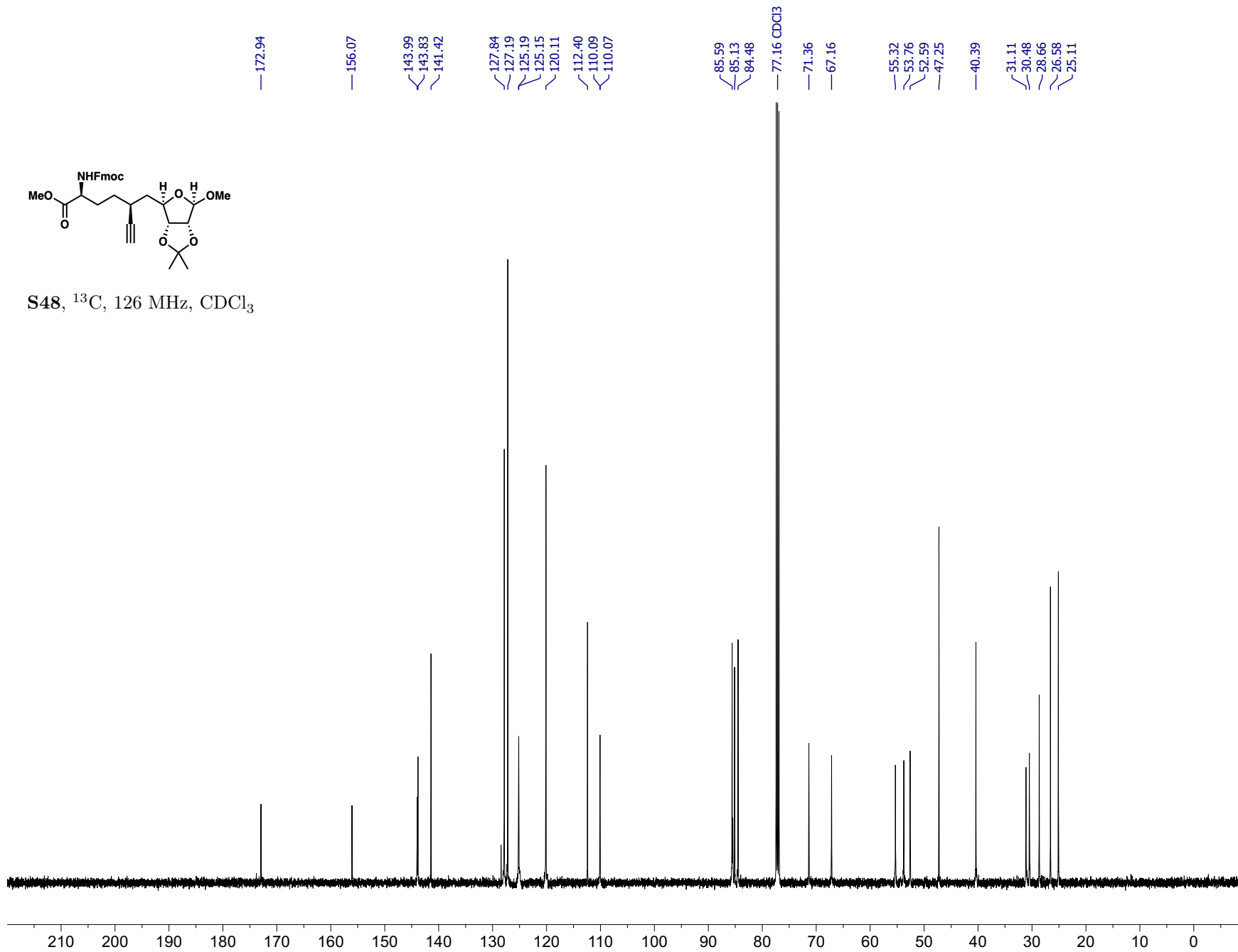
**22**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

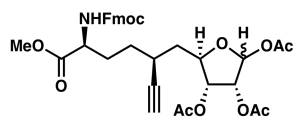


S48,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$ 

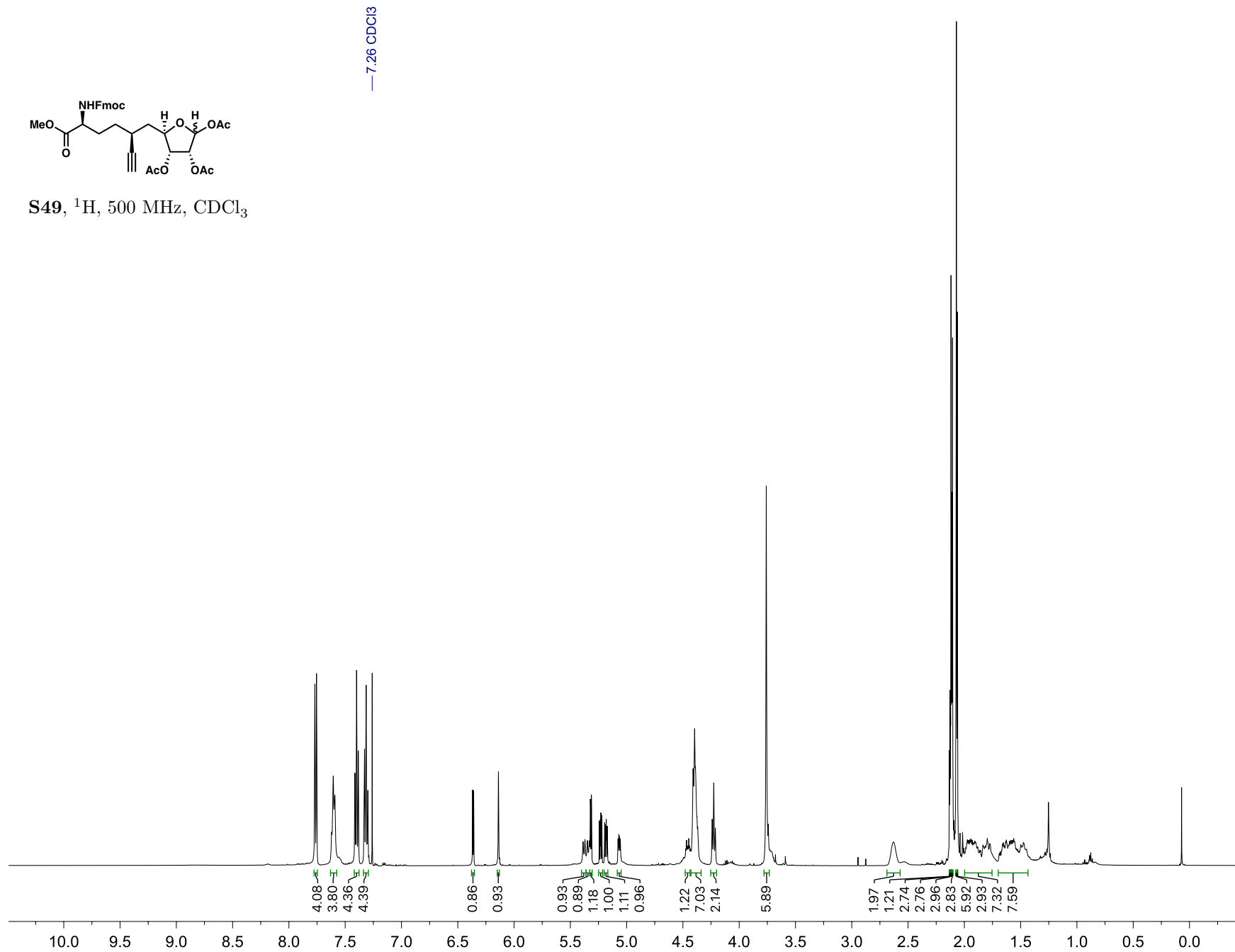


S48,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



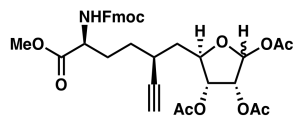
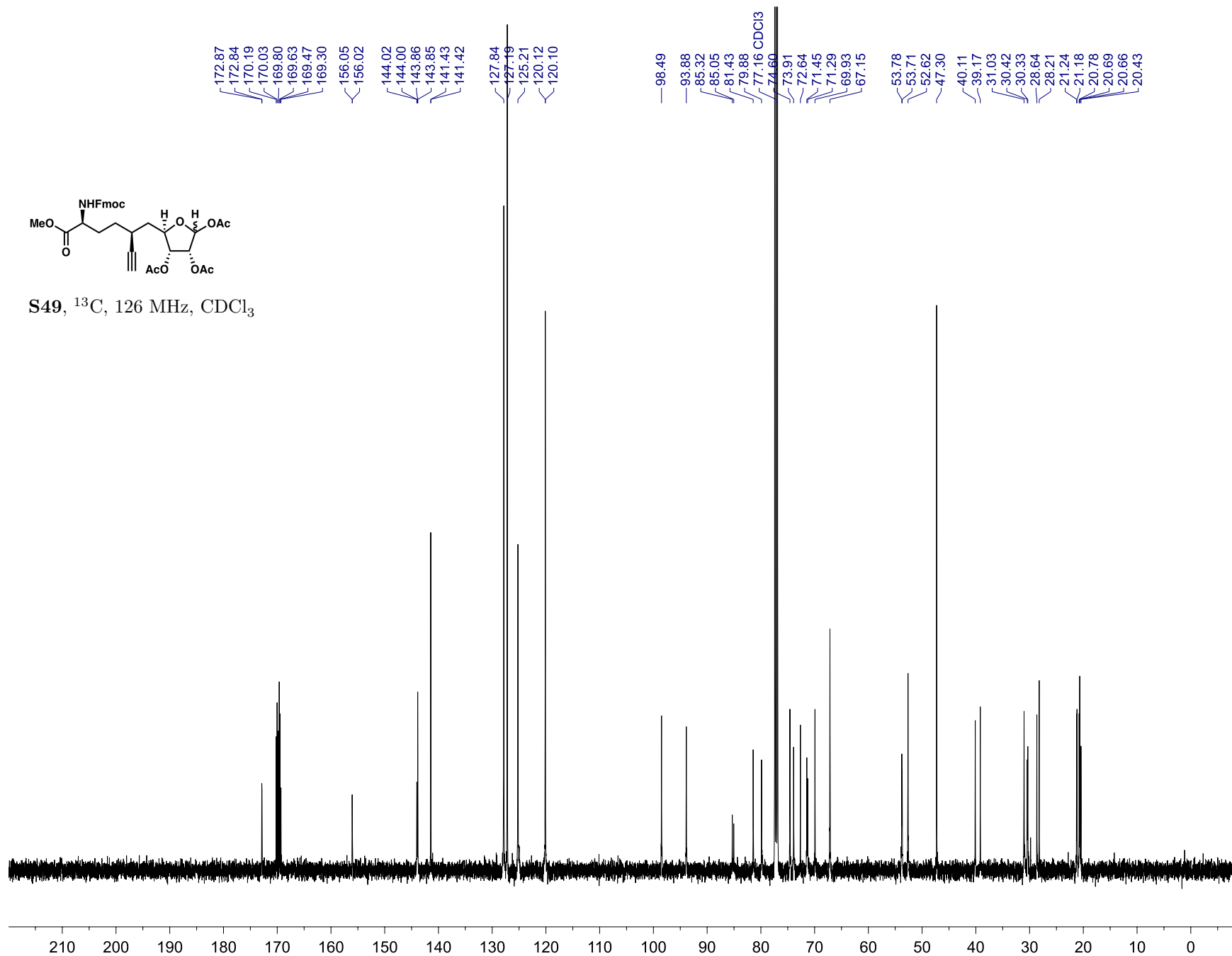


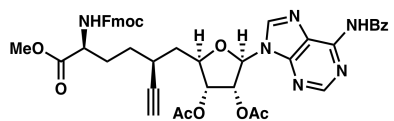
S49,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



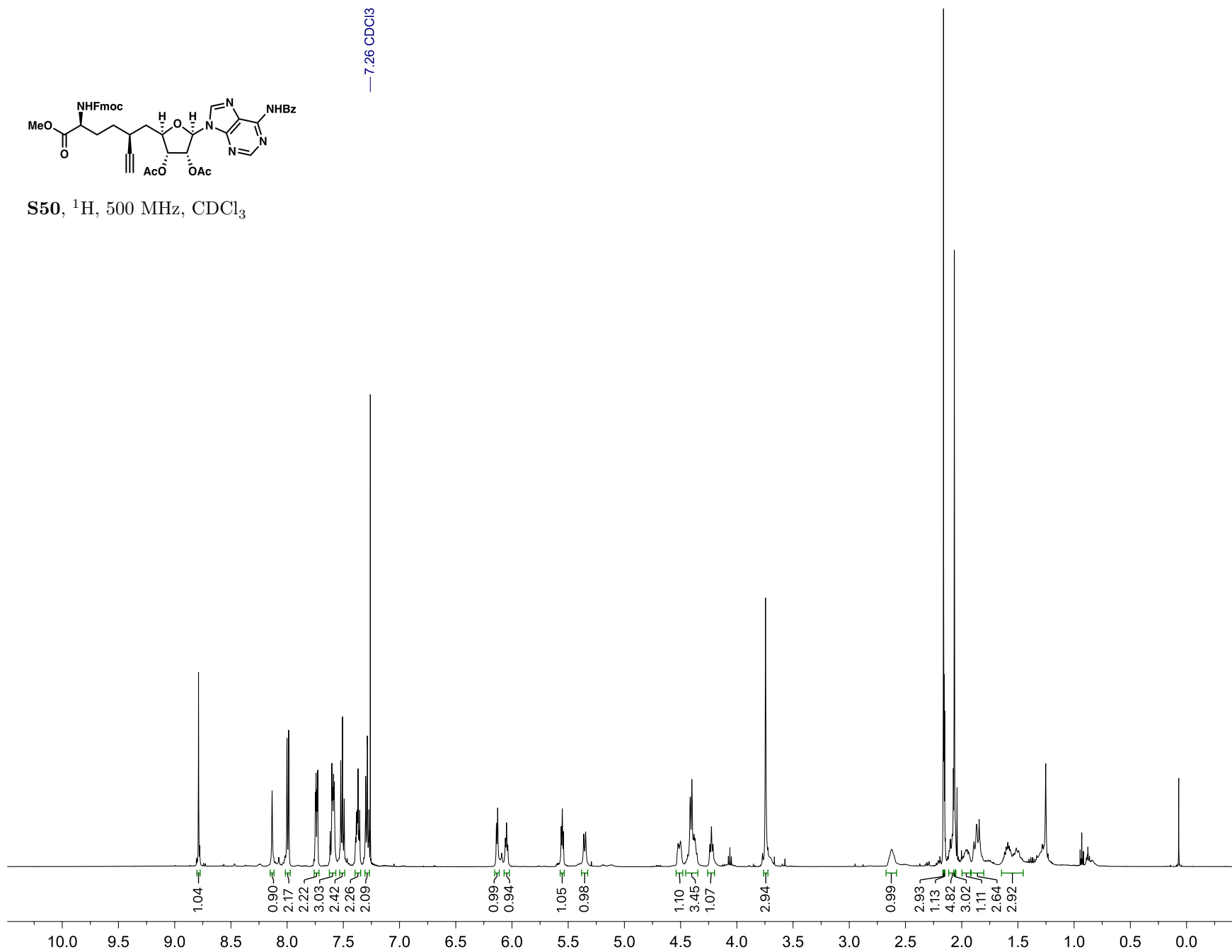
— 7.26  $\text{CDCl}_3$

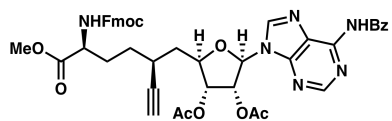


**S49**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$ 

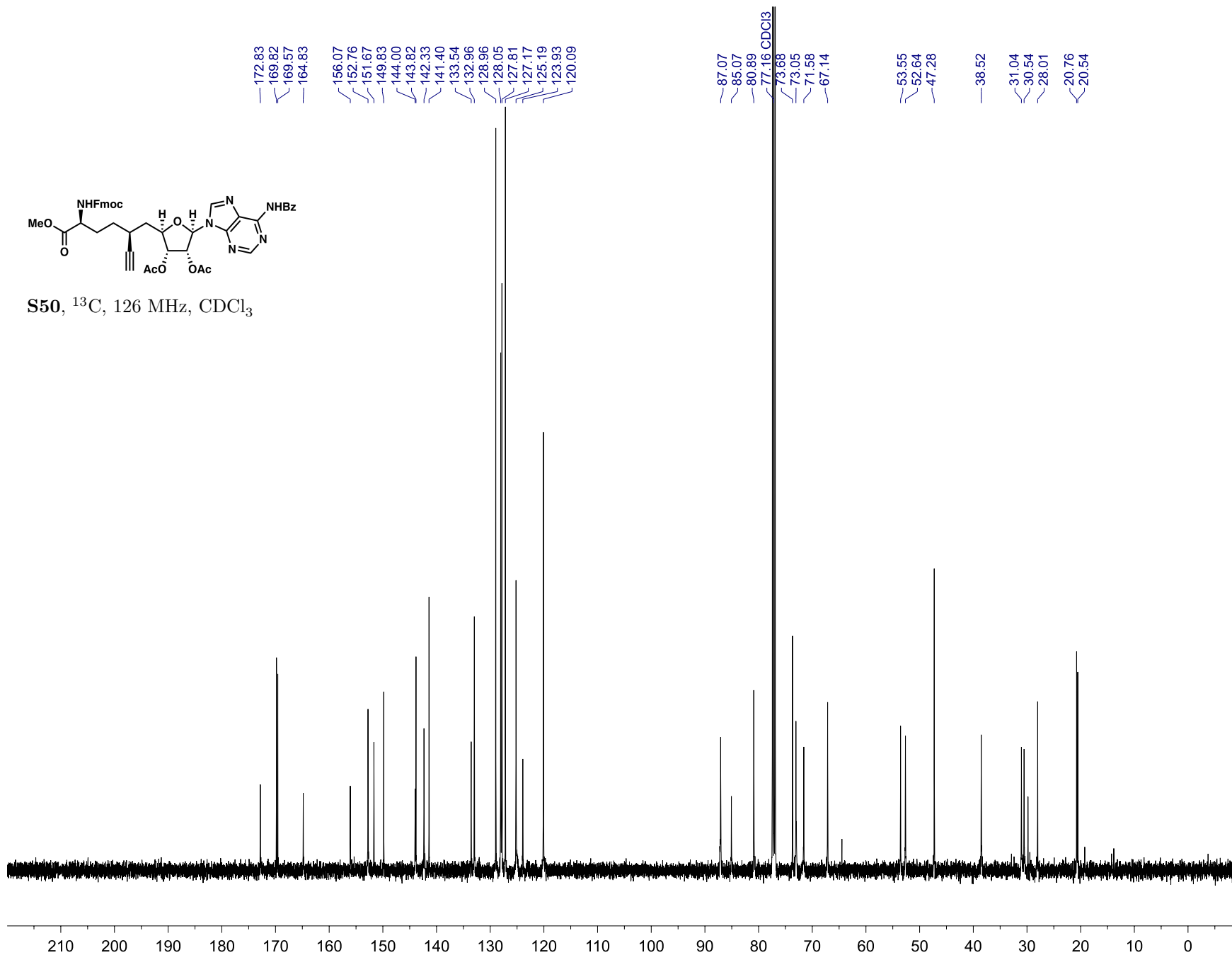


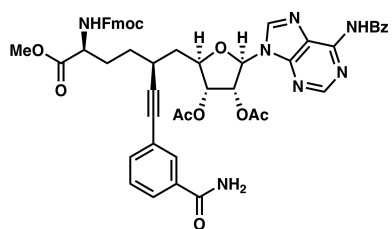
S50,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



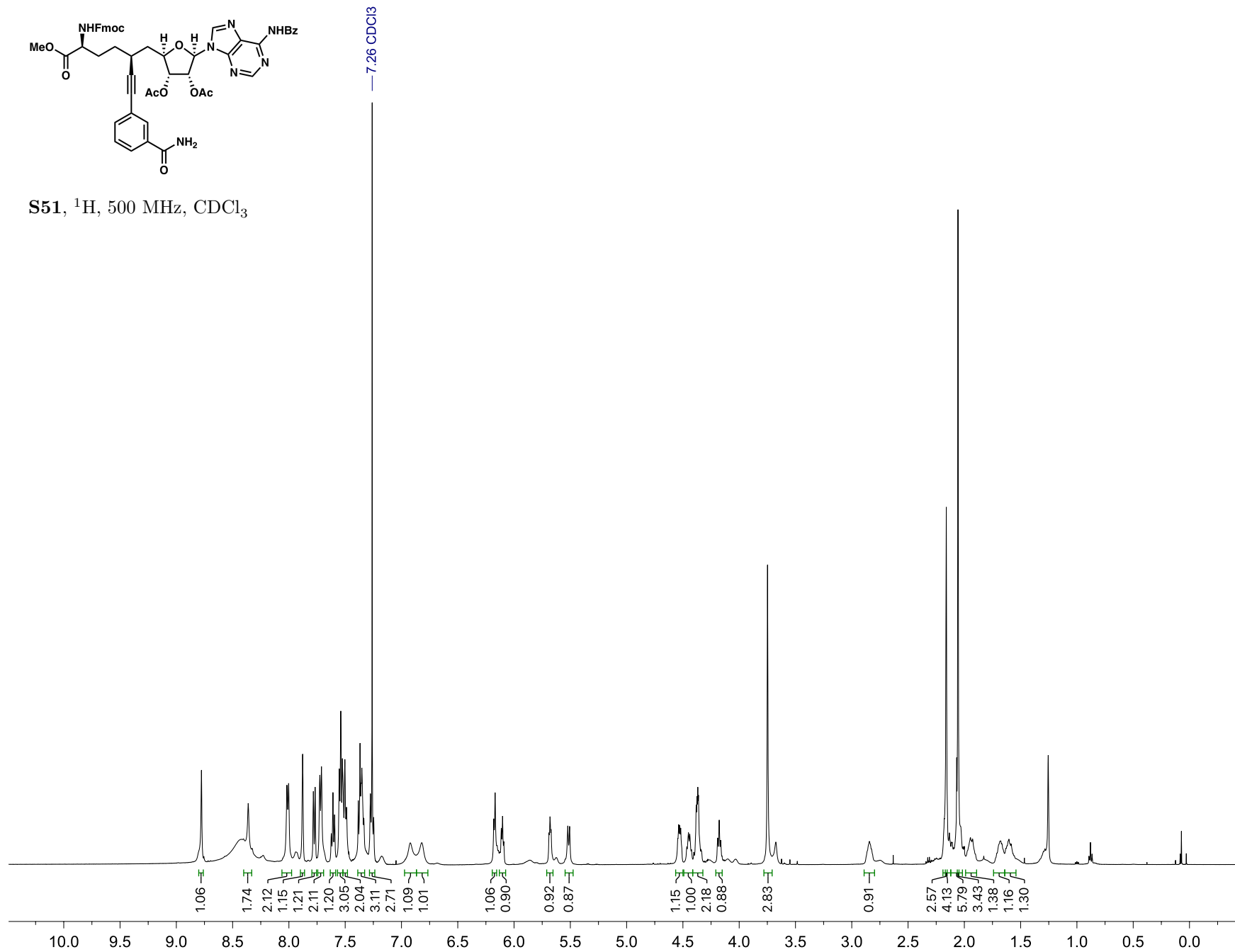


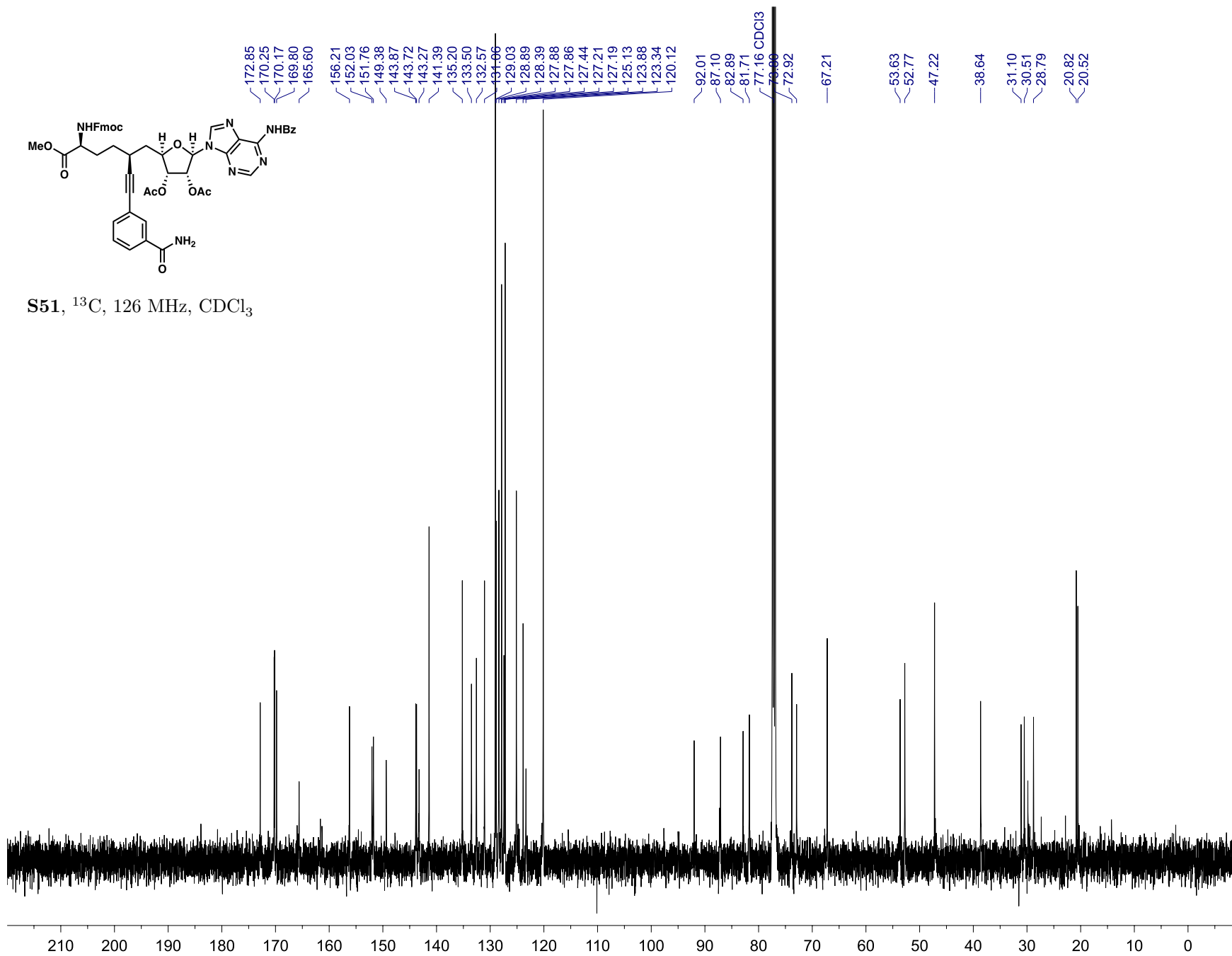
**S50**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

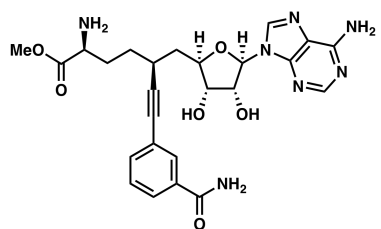




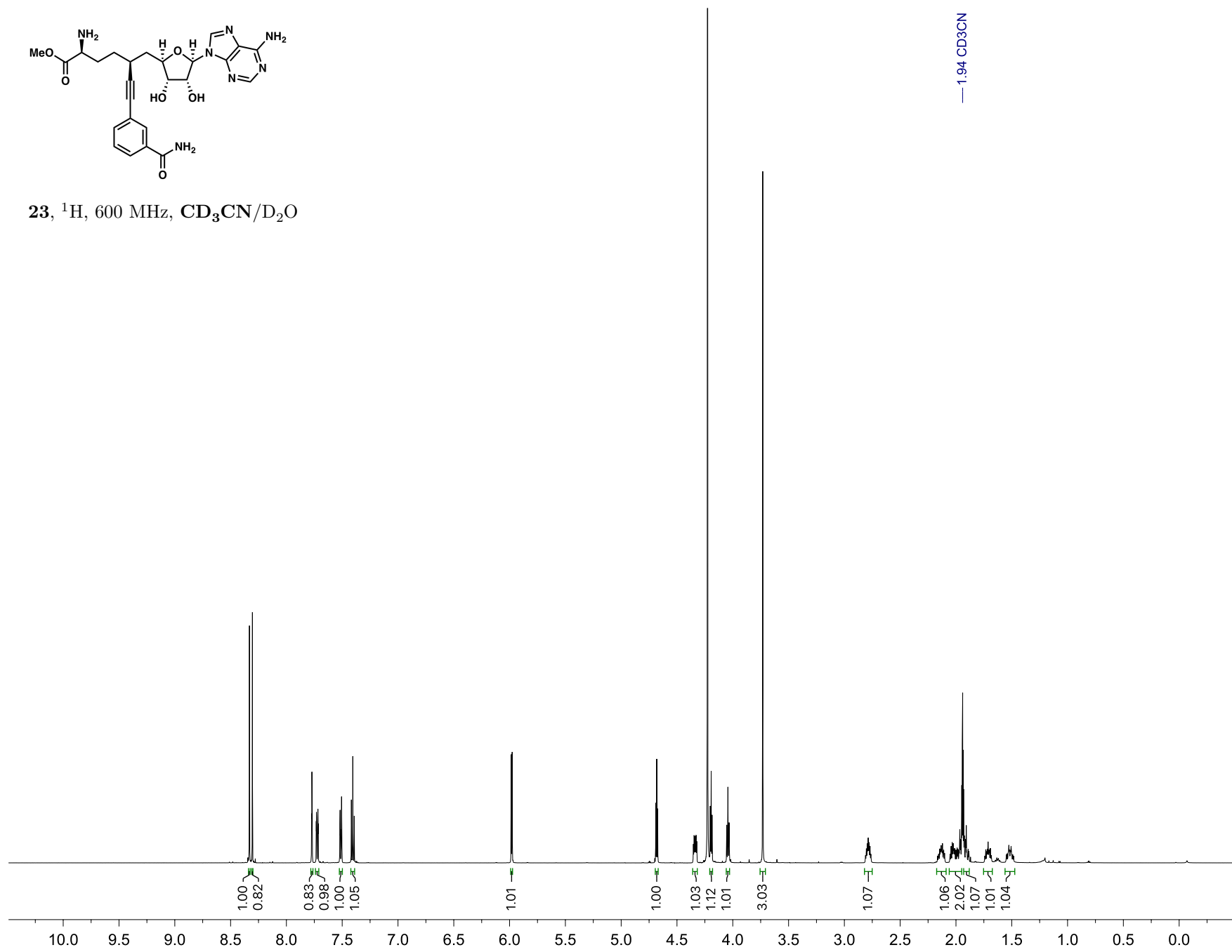
S51,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

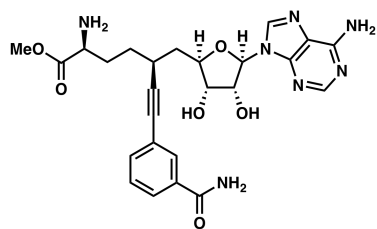




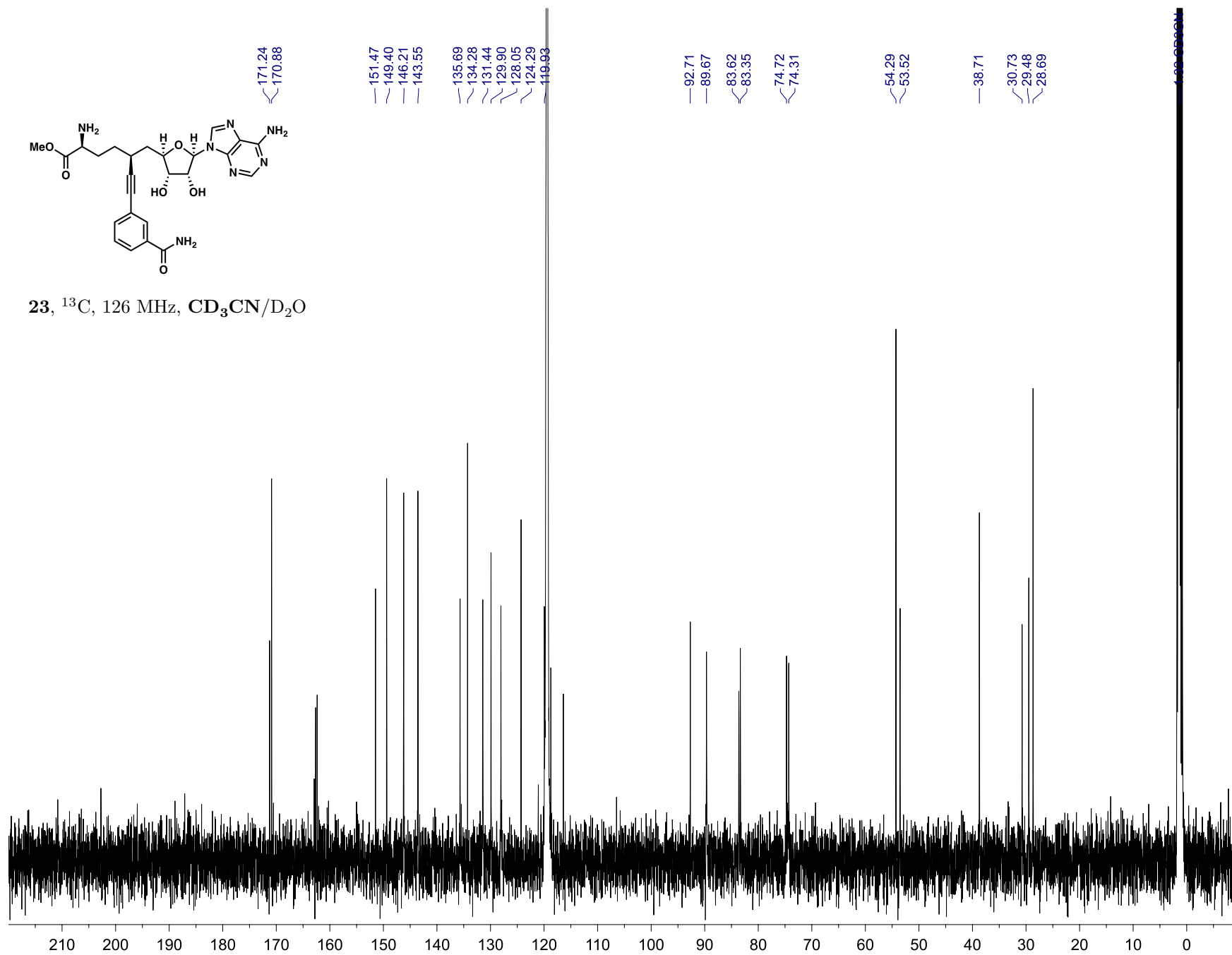


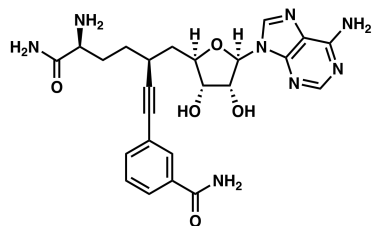
**23**,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$





**23**, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O

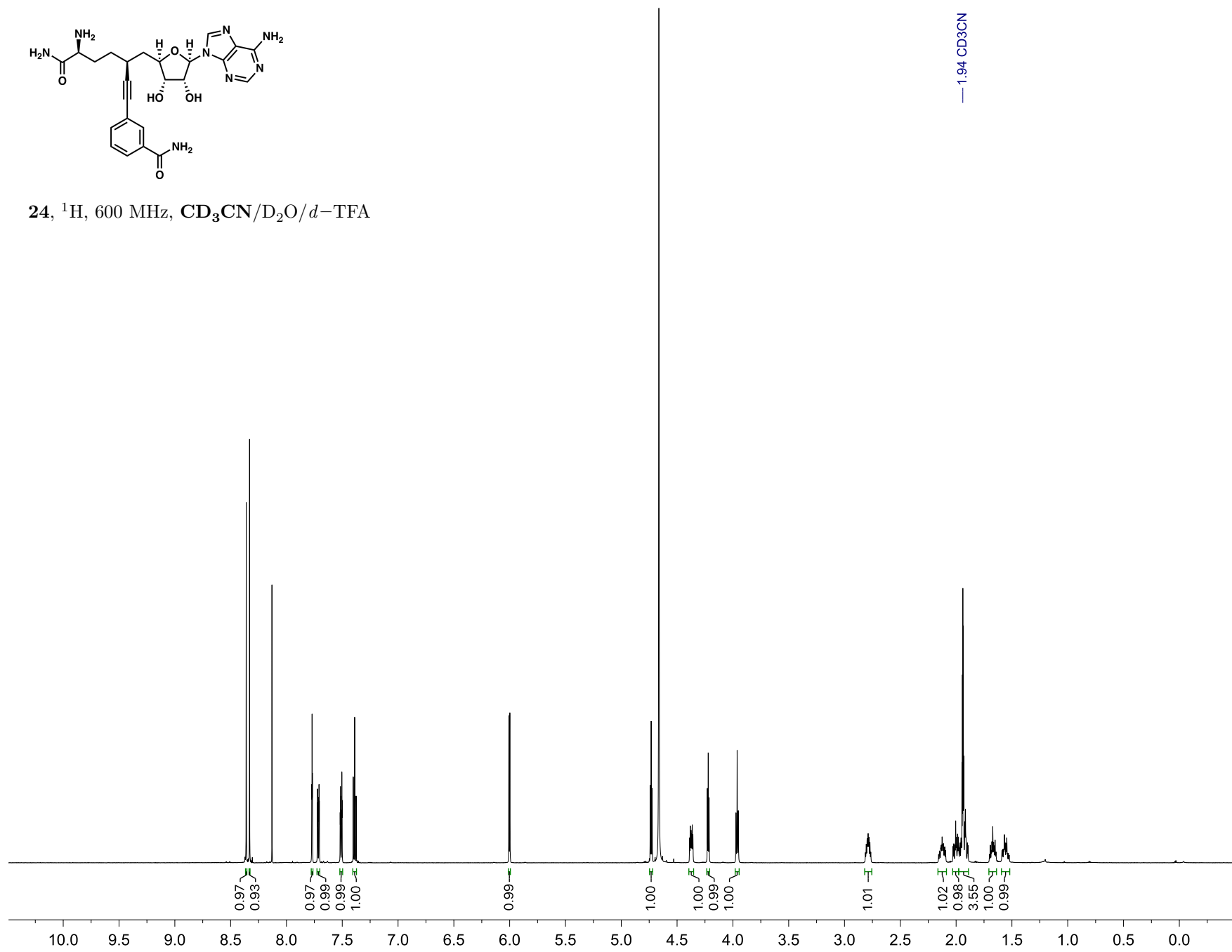




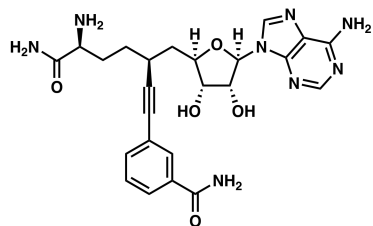
24,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

— 1.94  $\text{CD}_3\text{CN}$

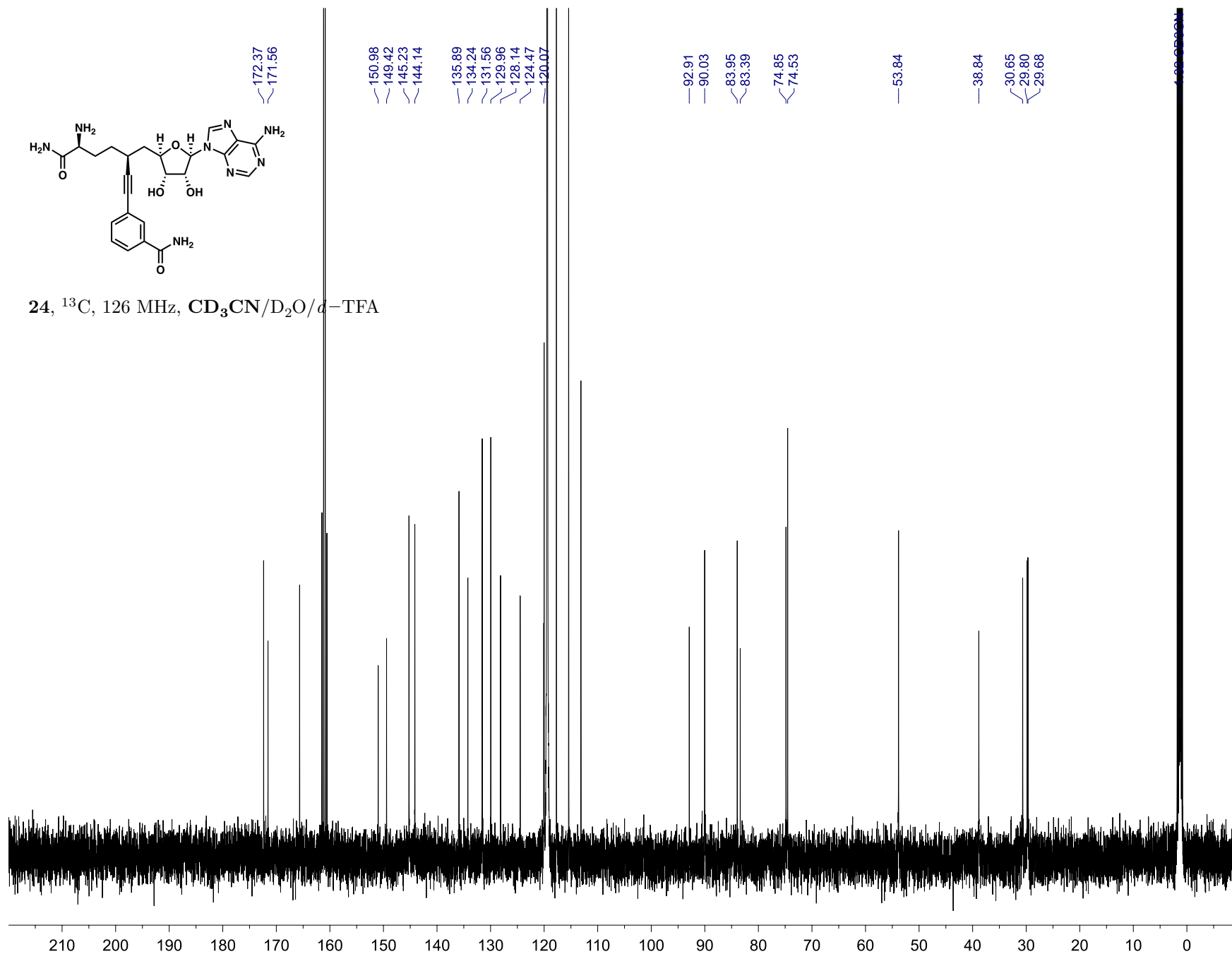
S143

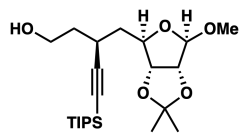




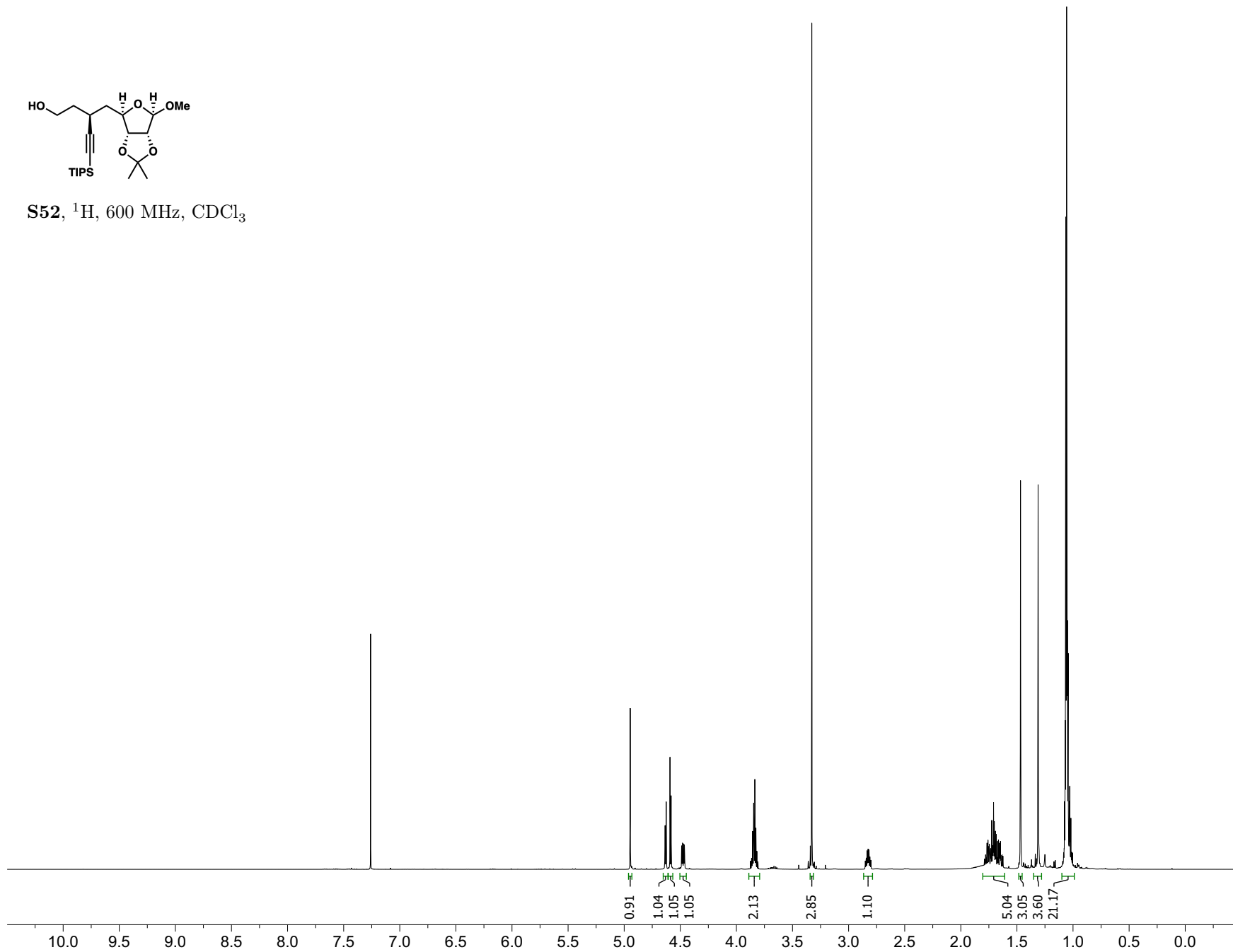


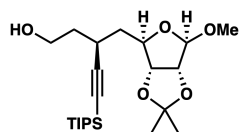
24,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$



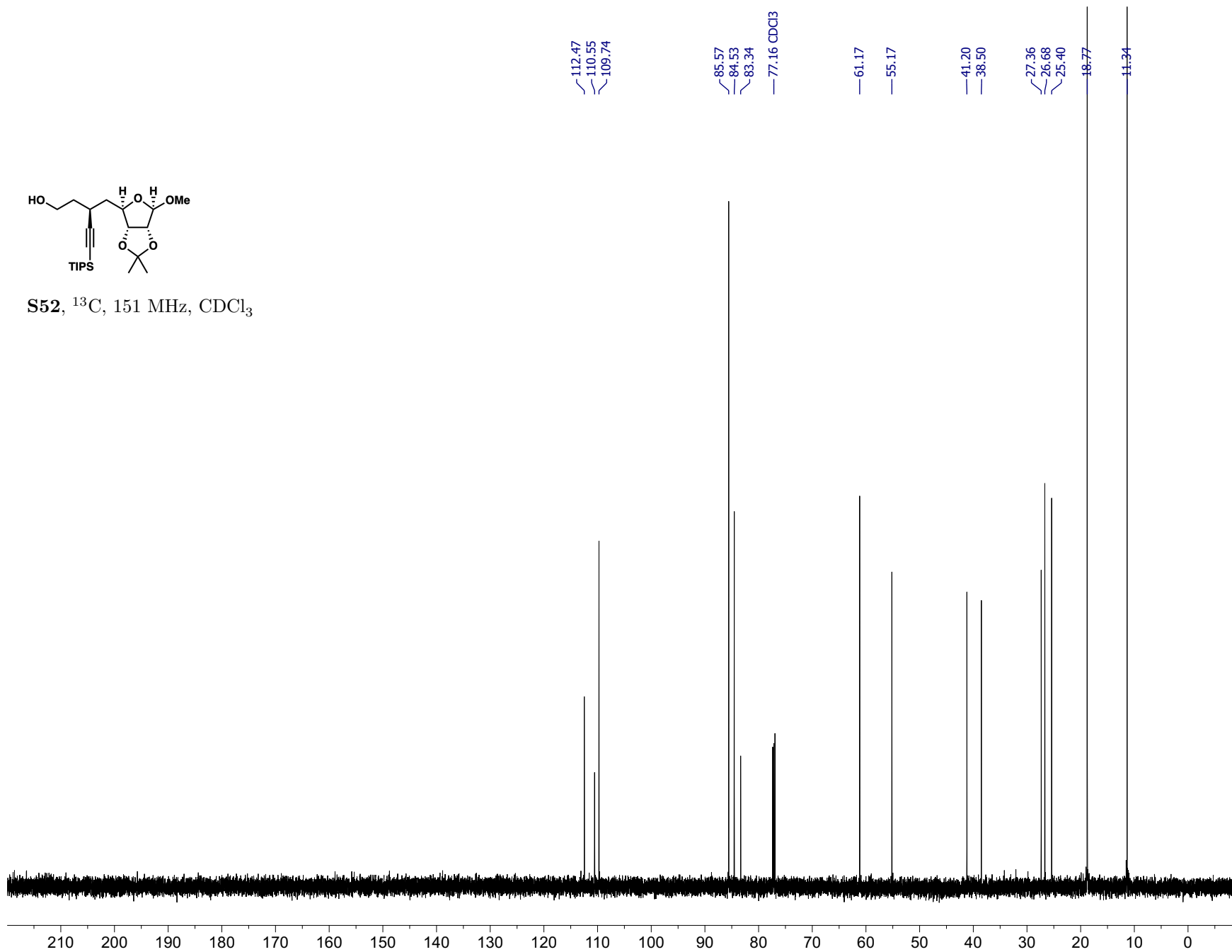


S52,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

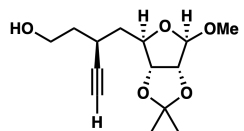




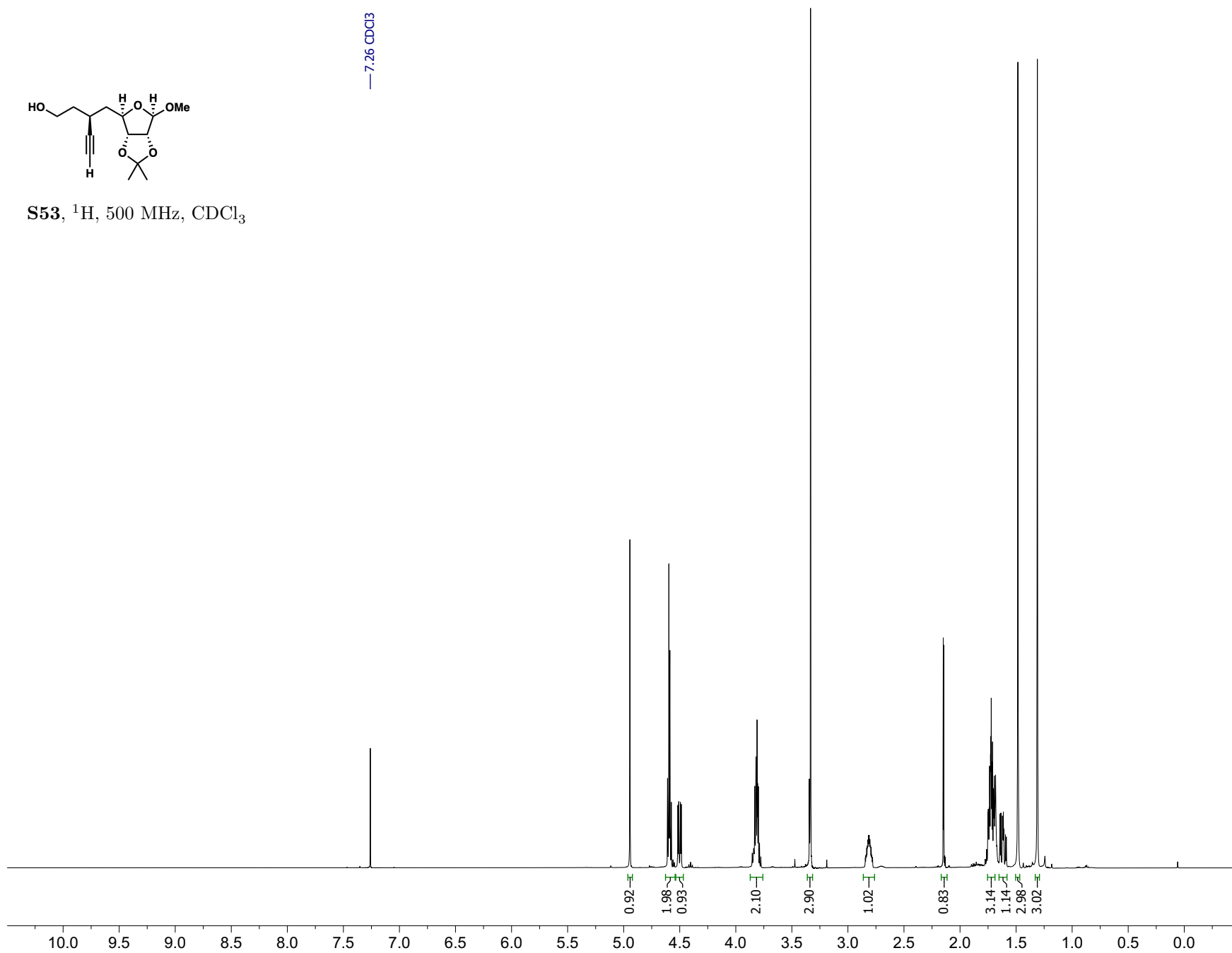
**S52**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$

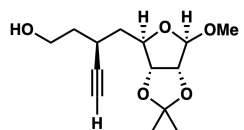


— 7.26 CDCl<sub>3</sub>

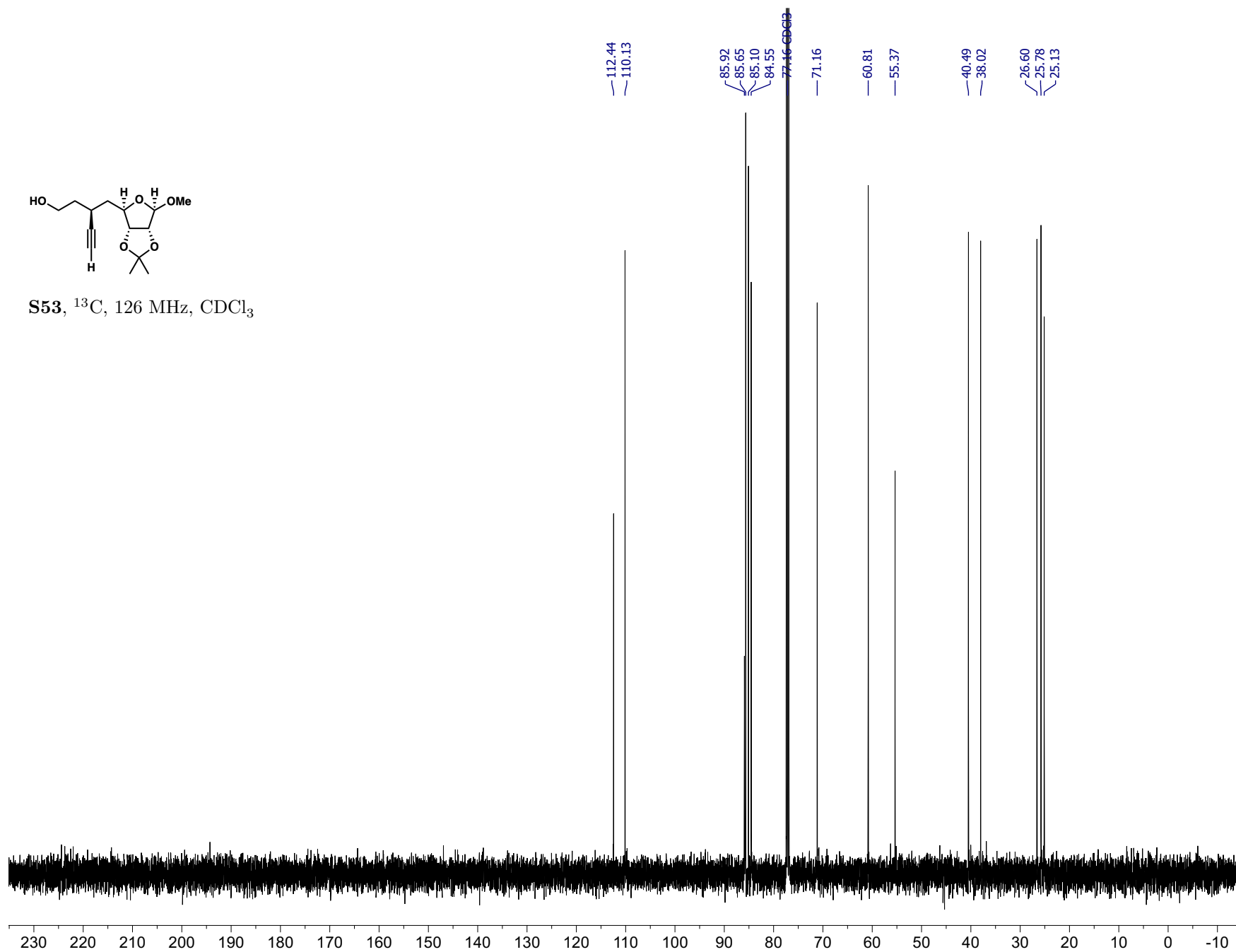


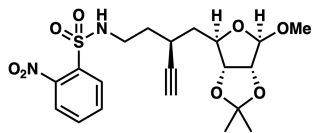
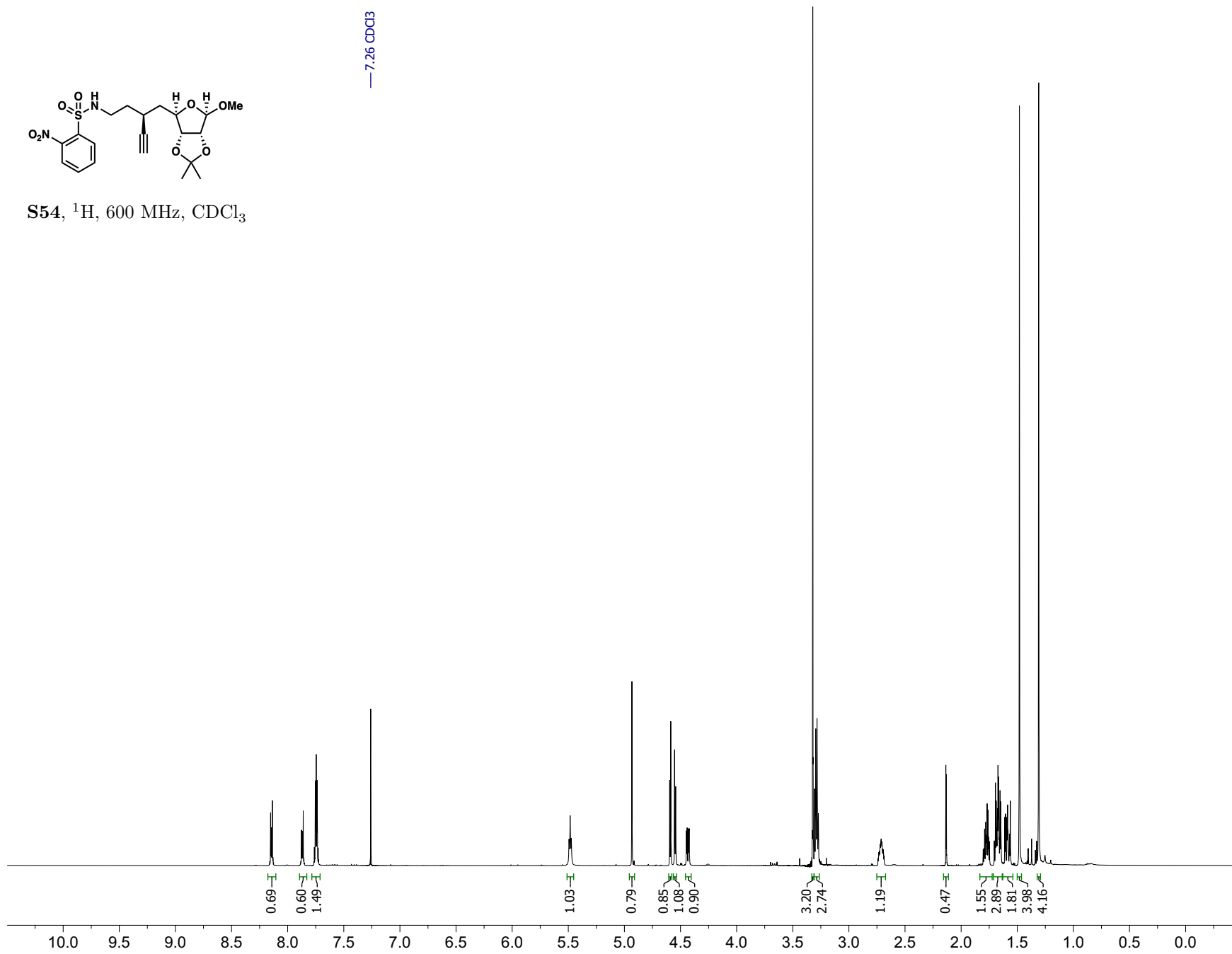
S53, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>

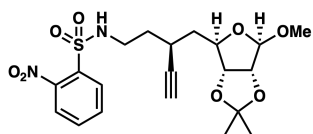
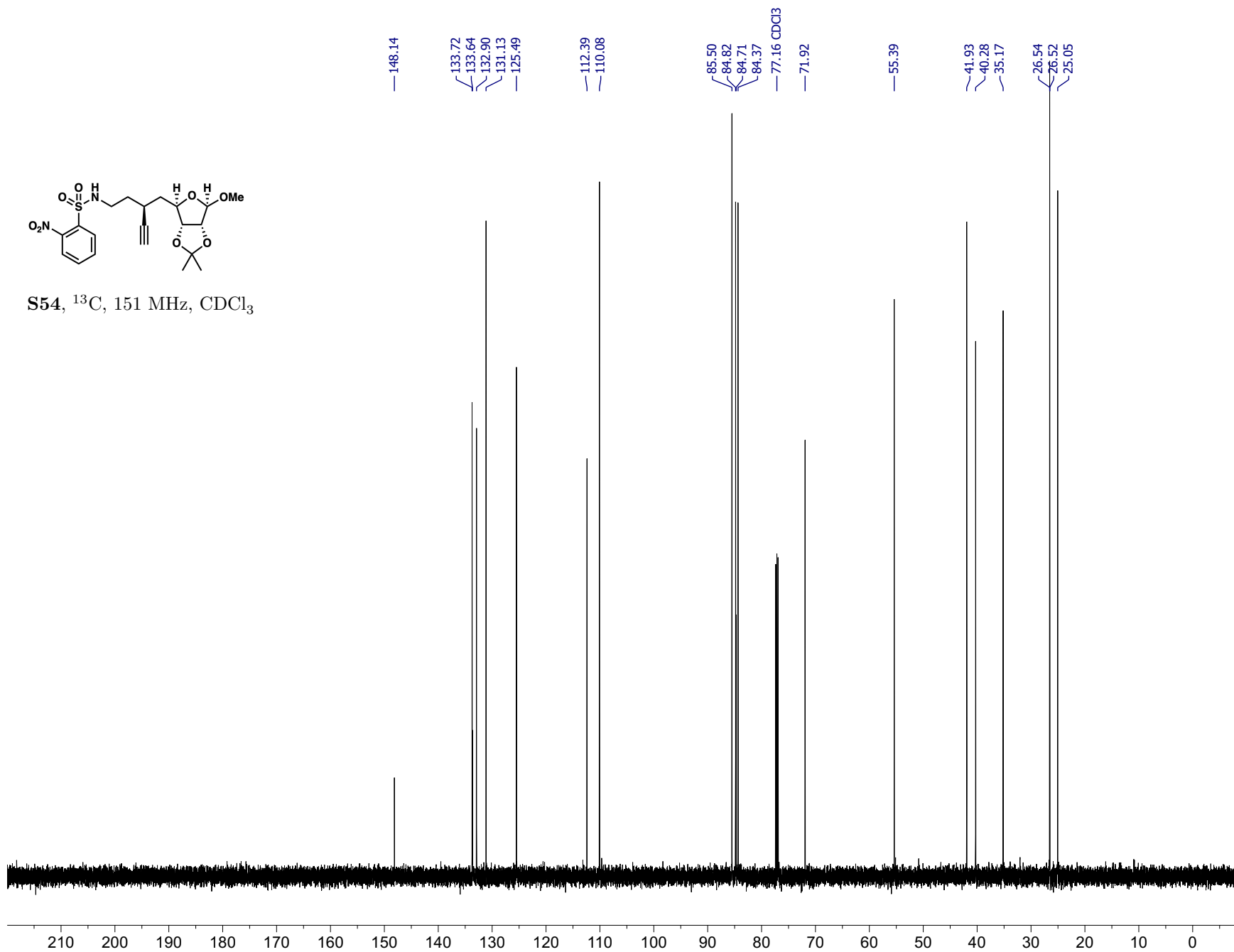




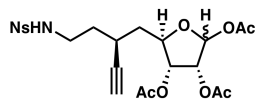
S53,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



**S54**,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$ 

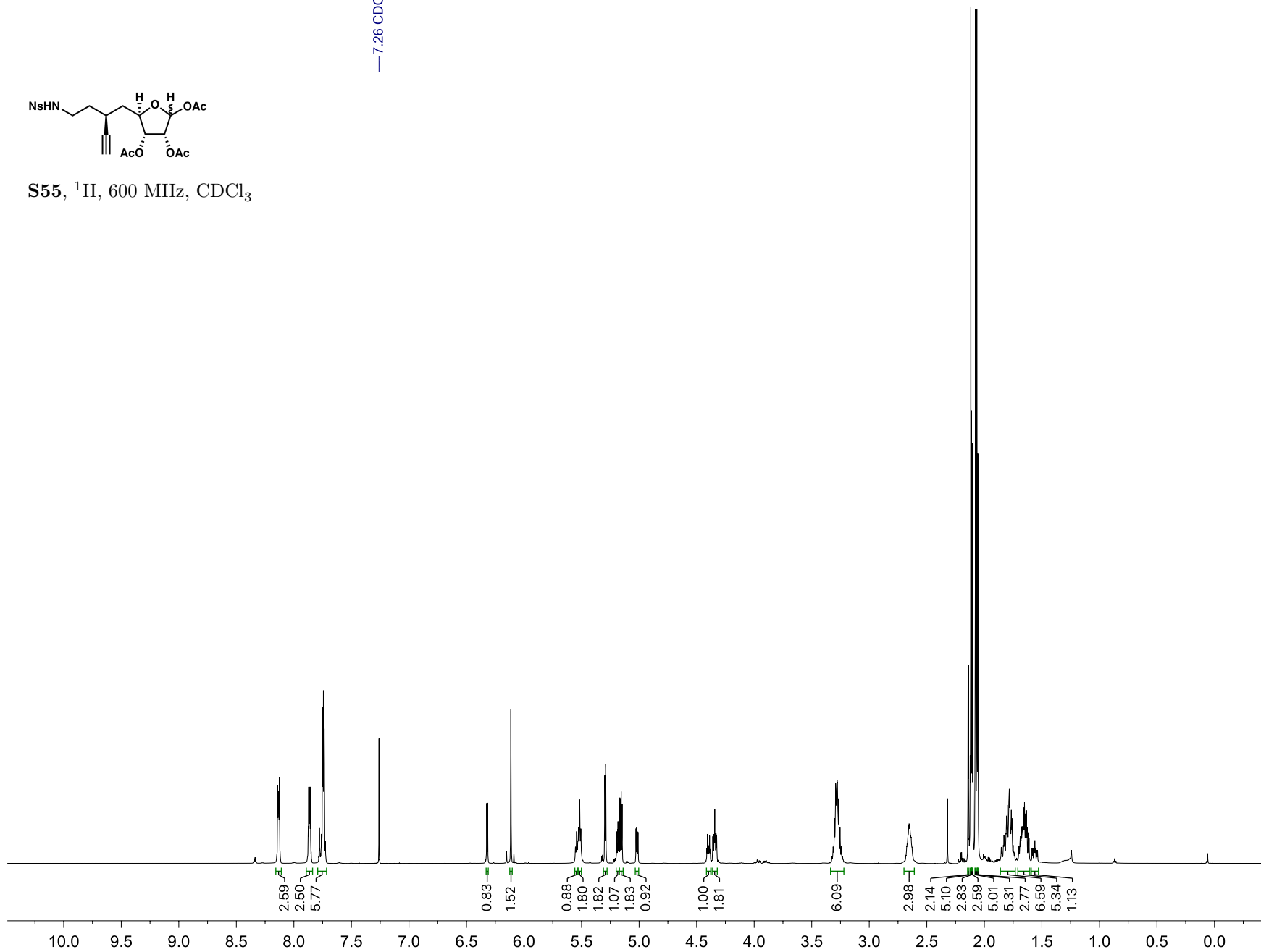
**S54**,  $^{13}\text{C}$ , 151 MHz,  $\text{CDCl}_3$ 

— 7.26 CDCl<sub>3</sub>

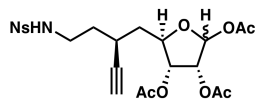


**S55**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

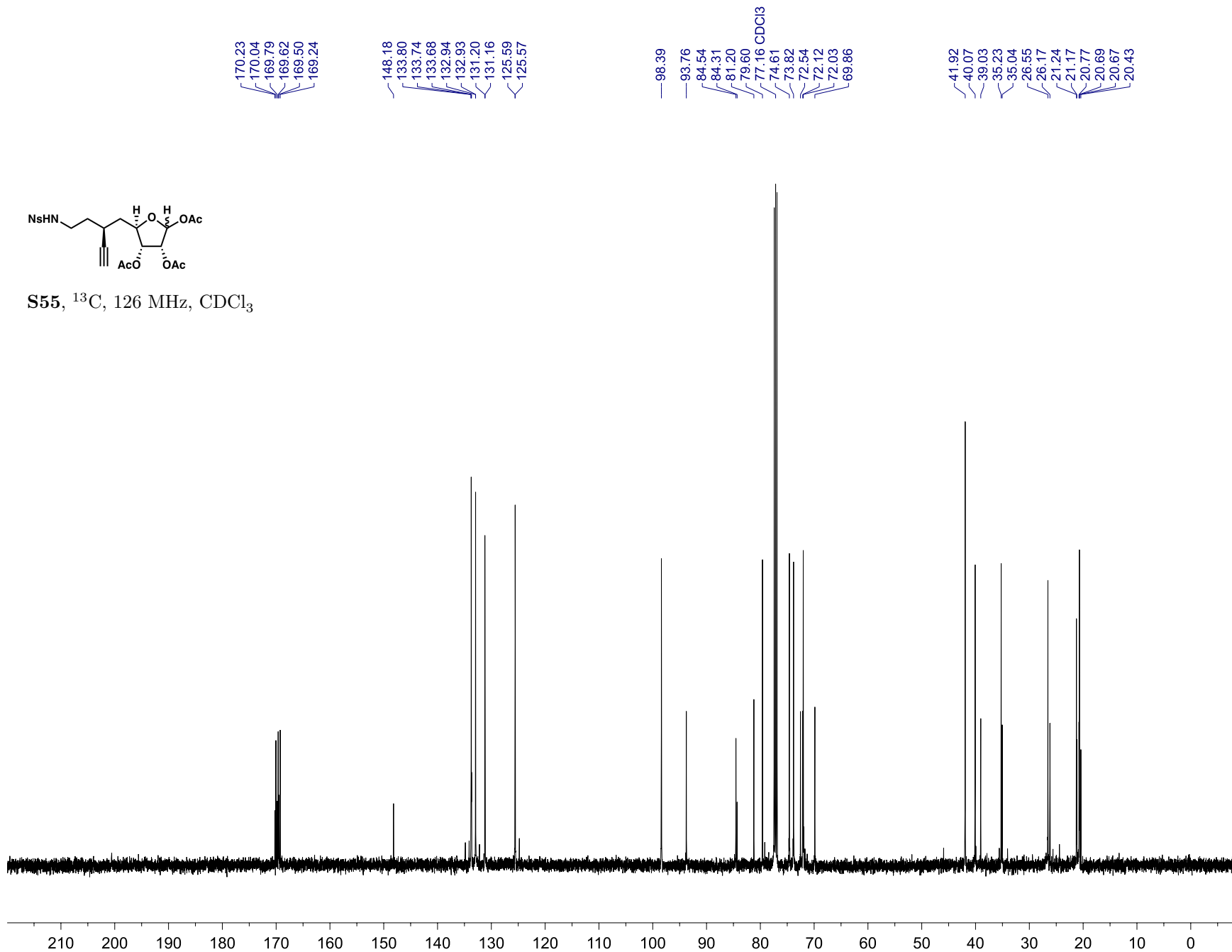
S151

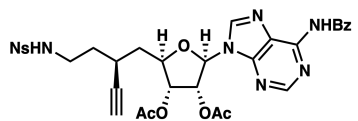






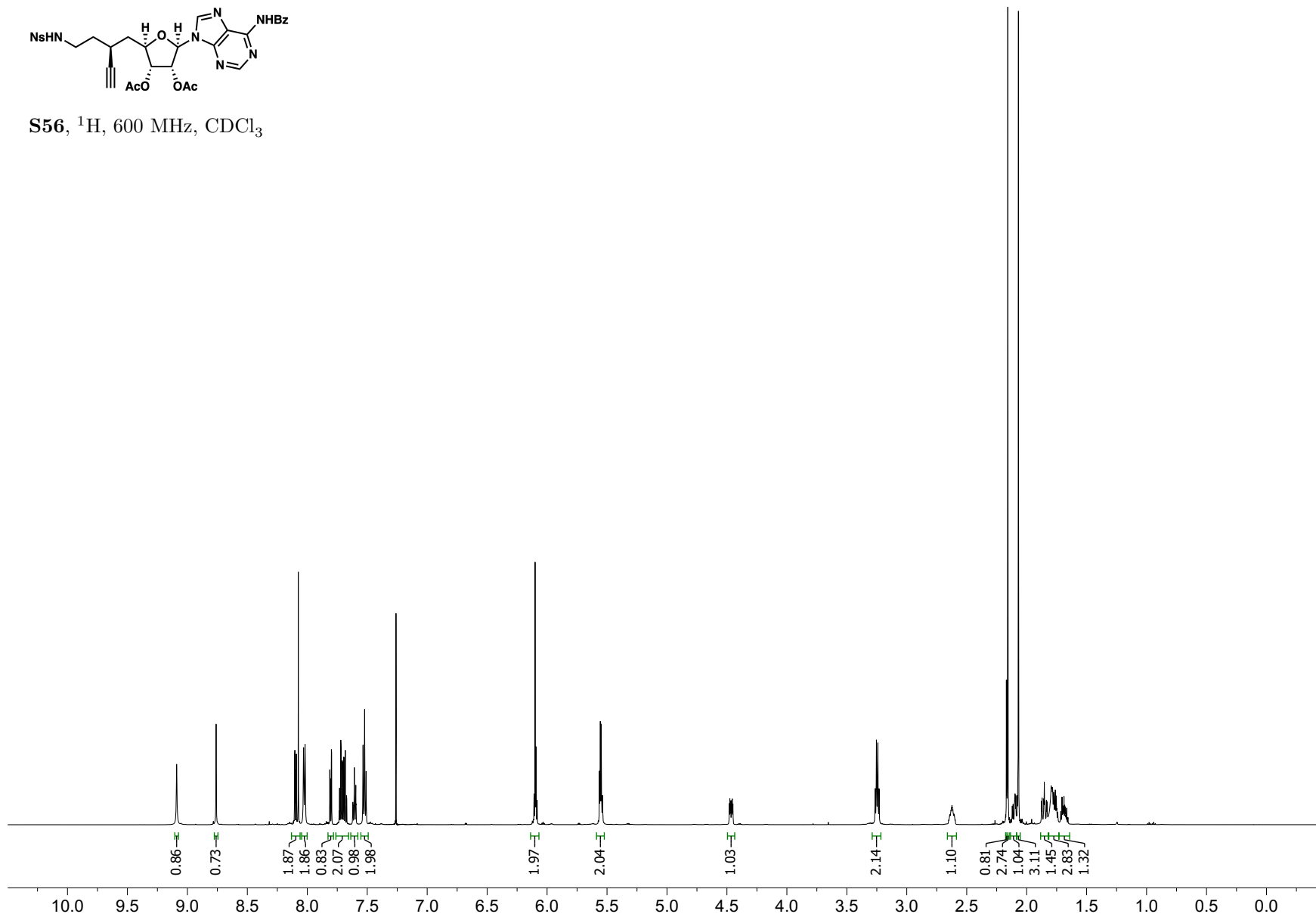
S55,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

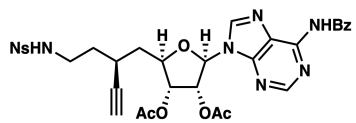




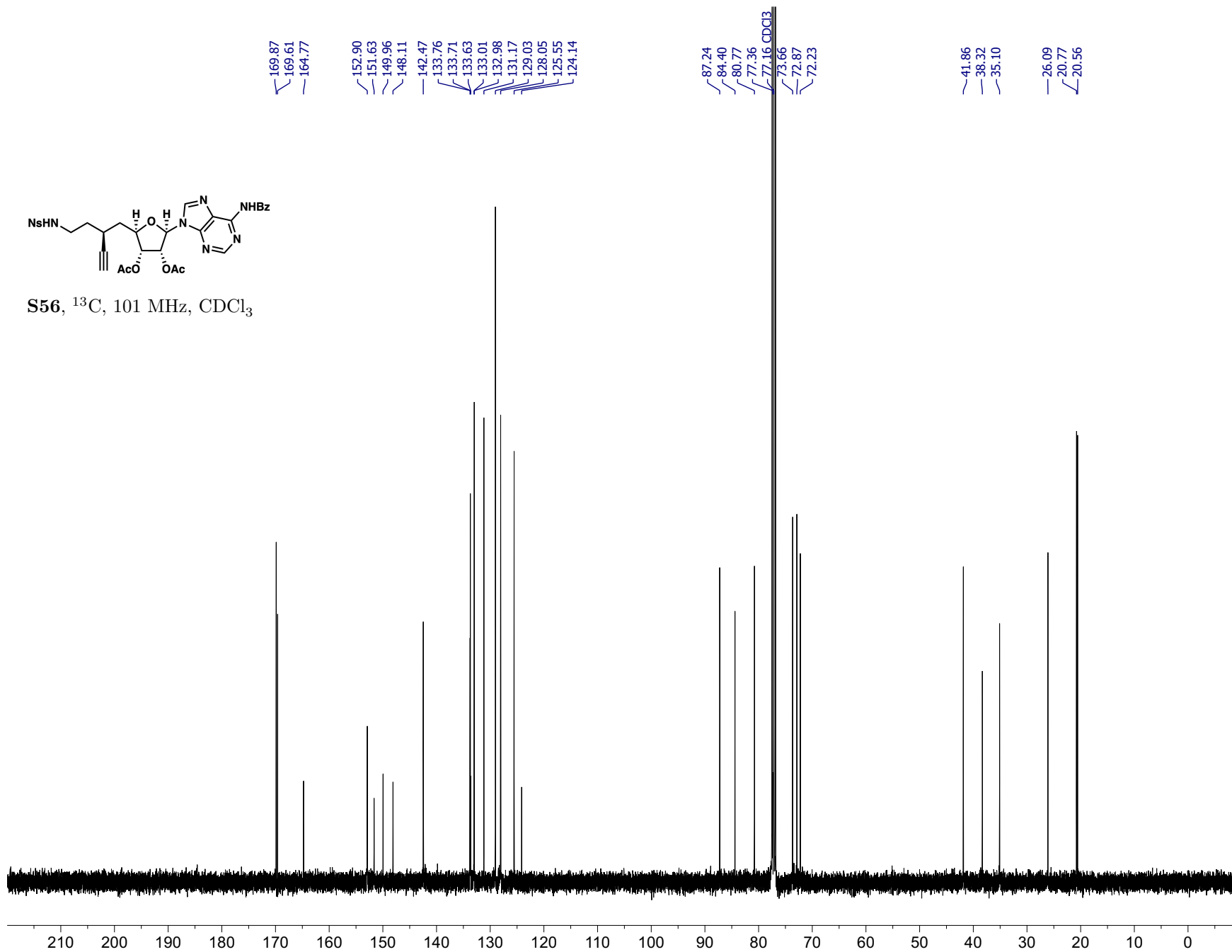
S56,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

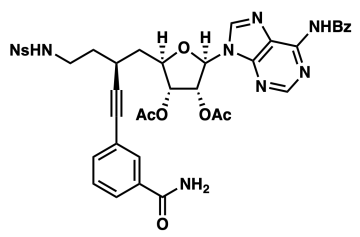
— 7.26  $\text{CDCl}_3$





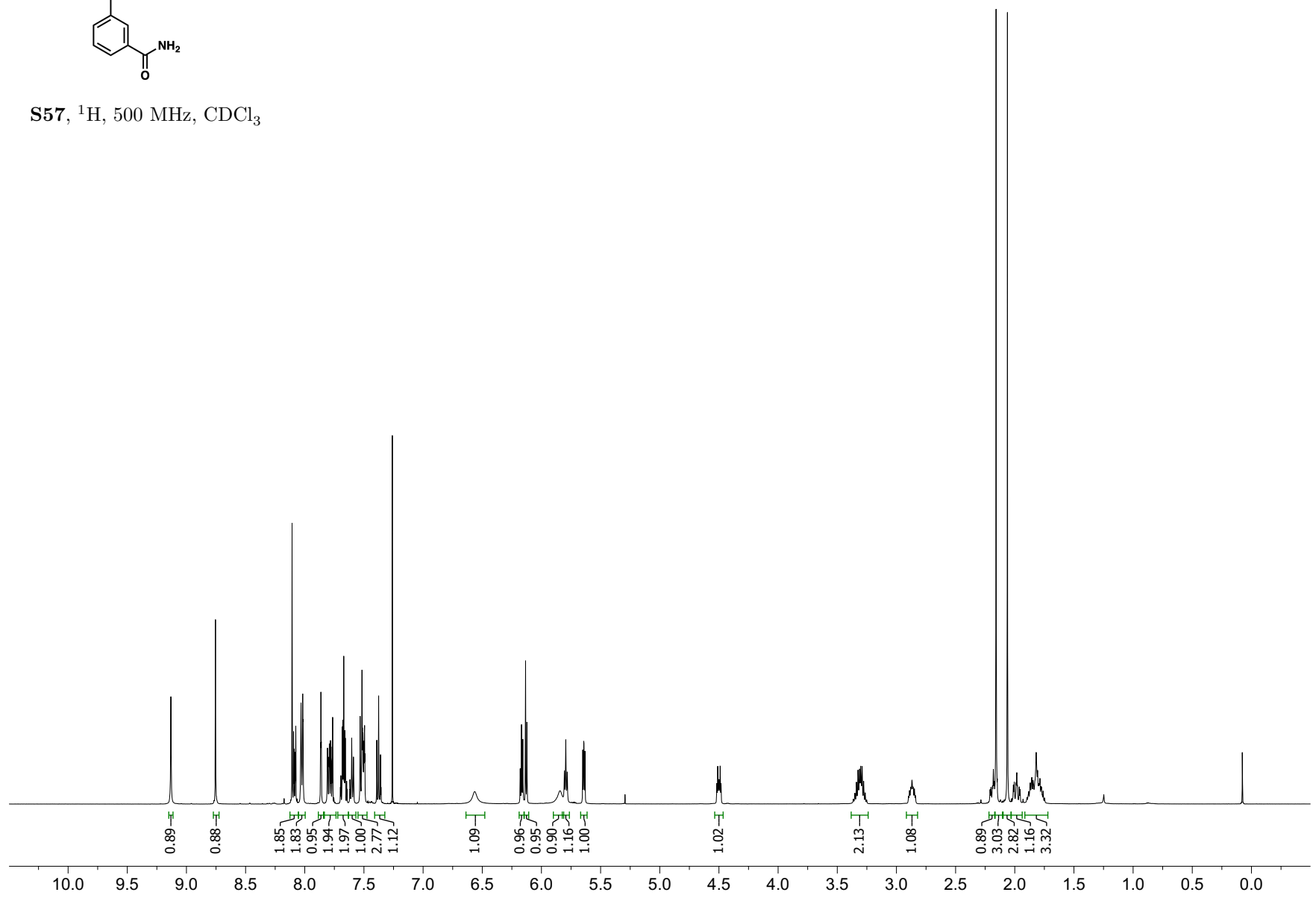
S56,  $^{13}\text{C}$ , 101 MHz,  $\text{CDCl}_3$

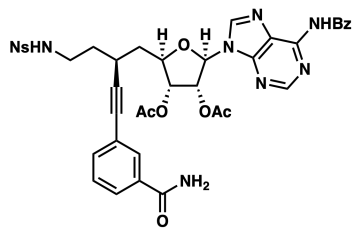




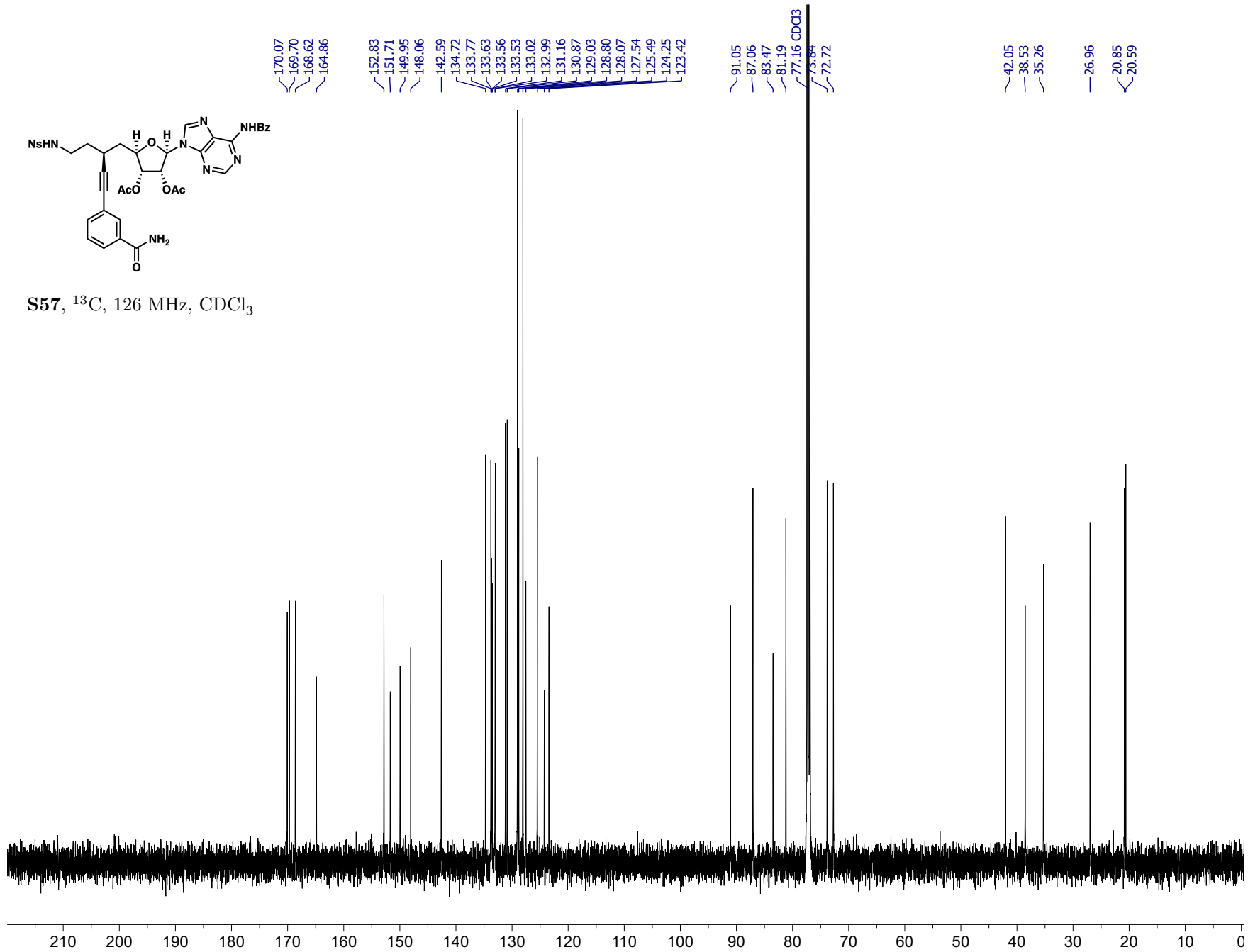
— 7.26 CDCl<sub>3</sub>

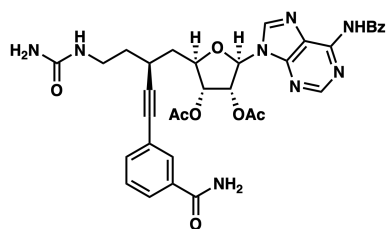
S57, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>



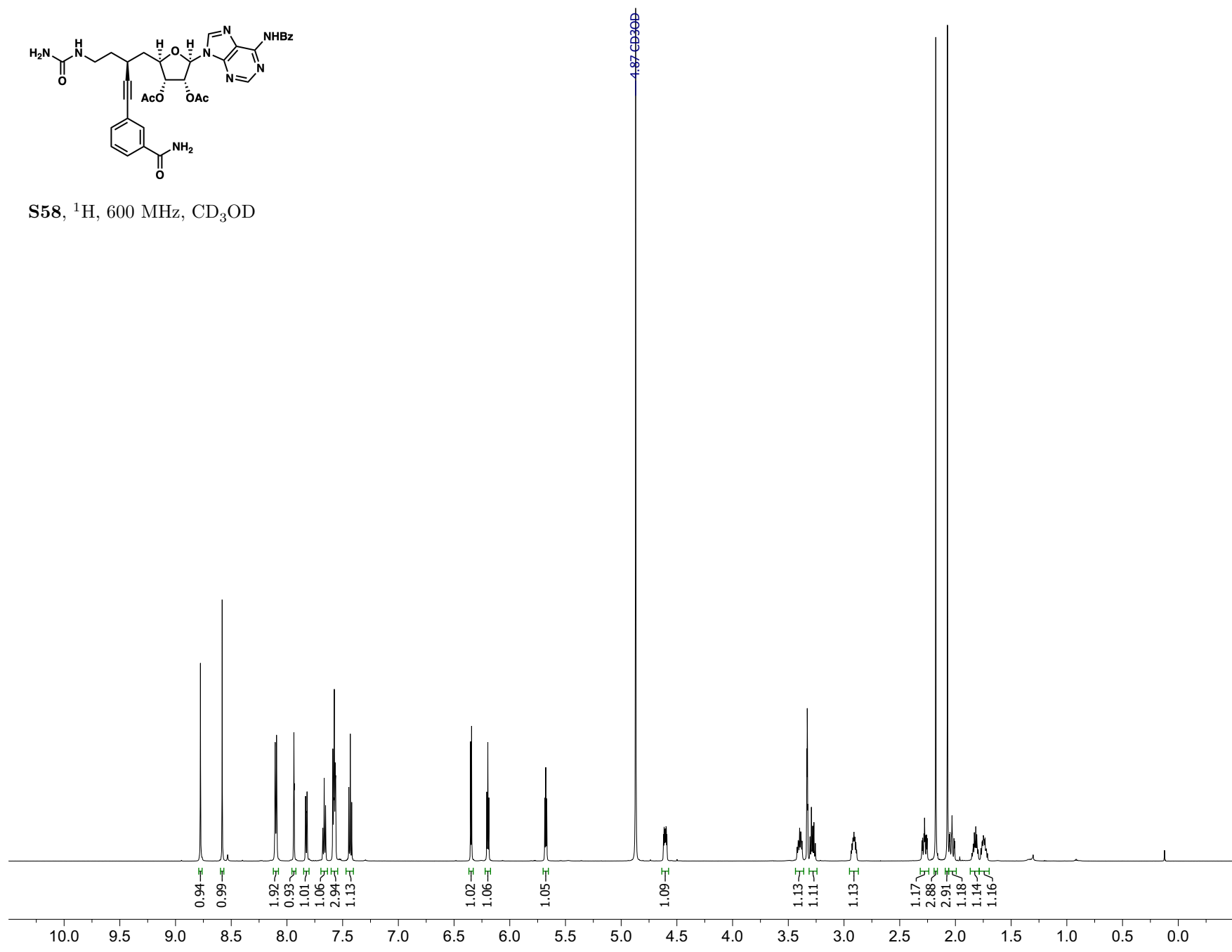


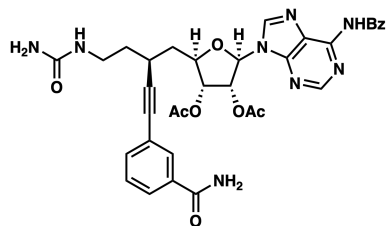
S57,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



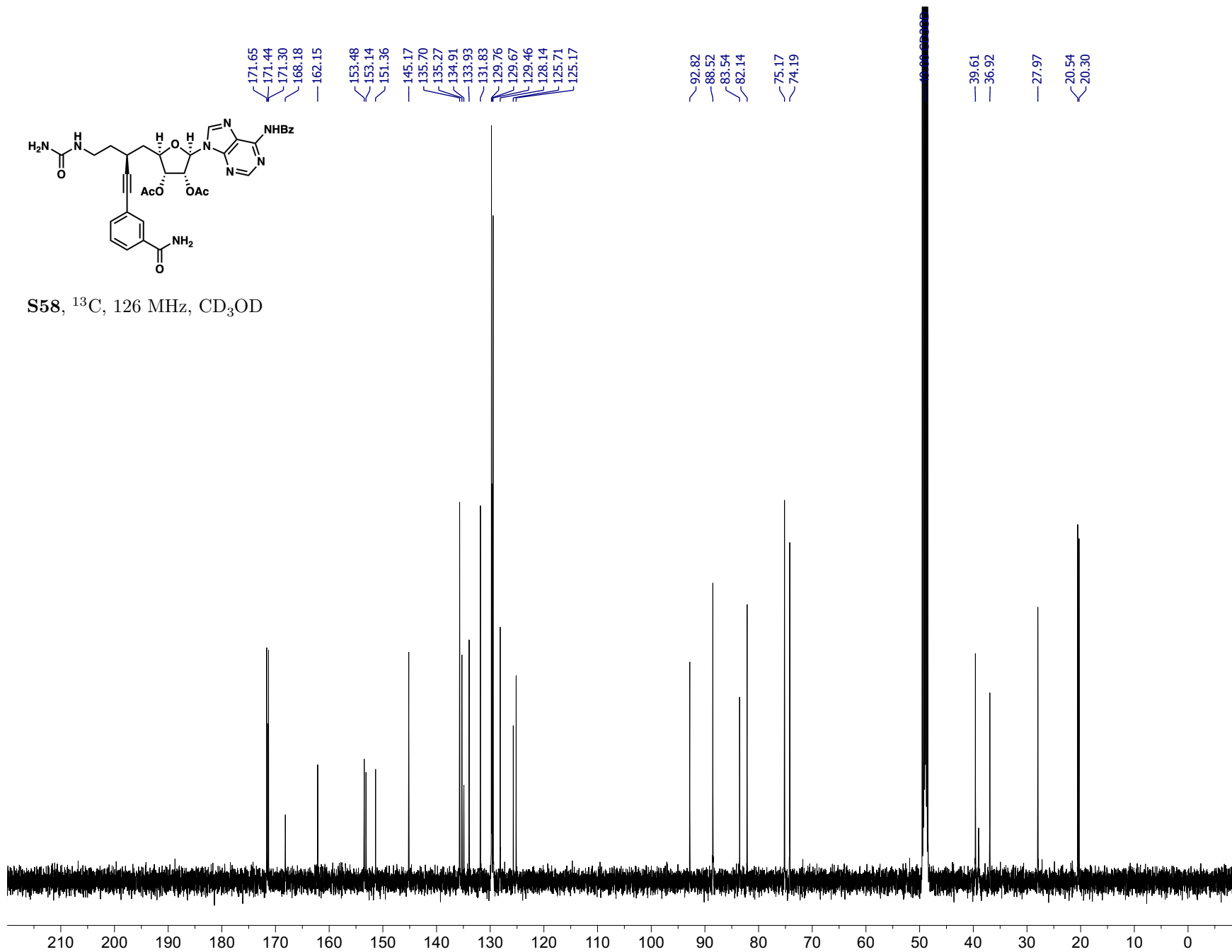


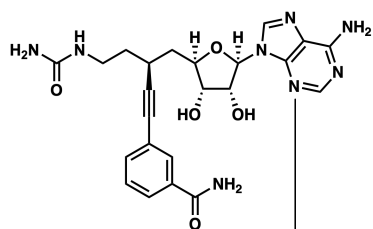
S58, <sup>1</sup>H, 600 MHz, CD<sub>3</sub>OD



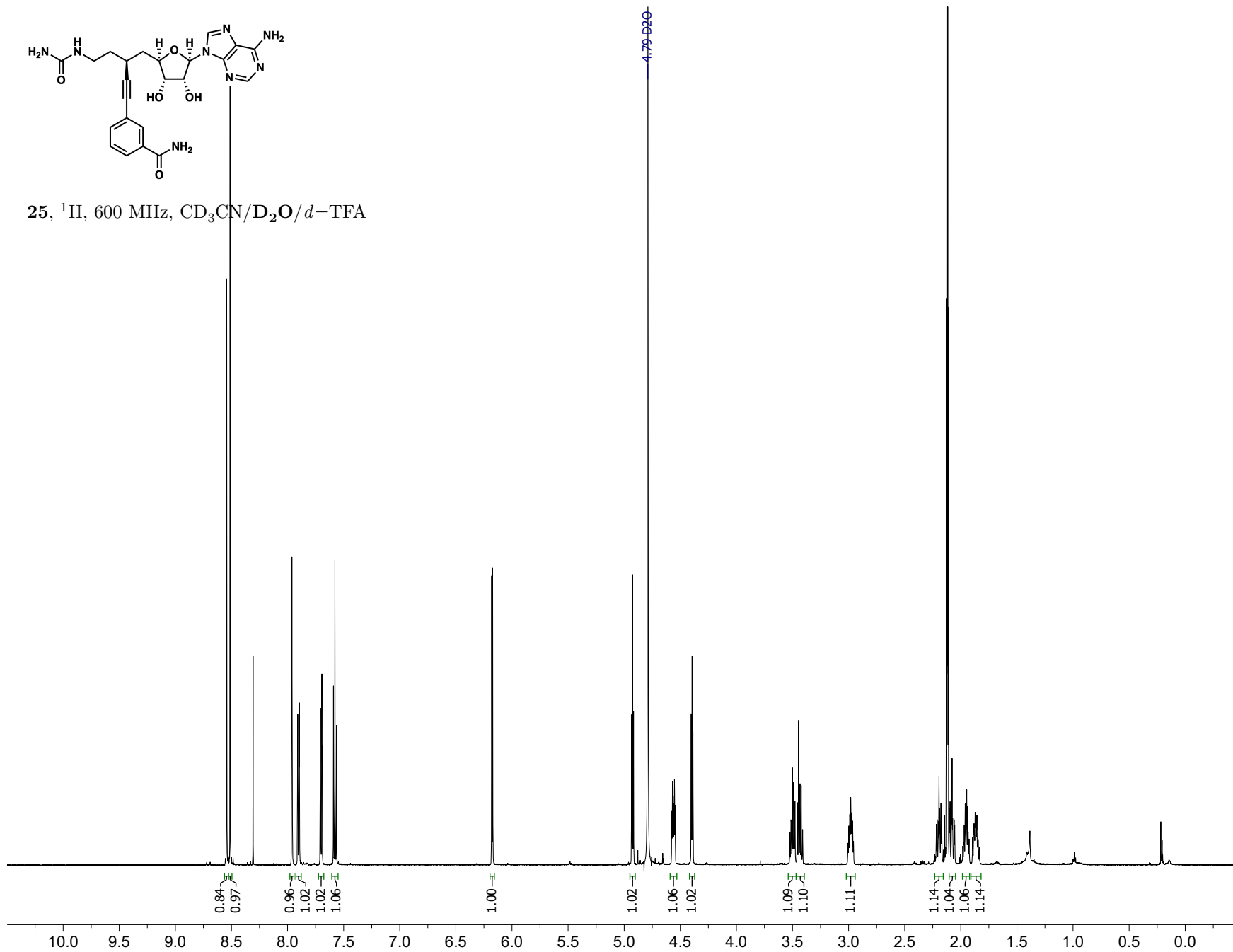


S58,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{OD}$

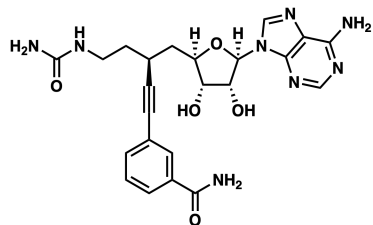




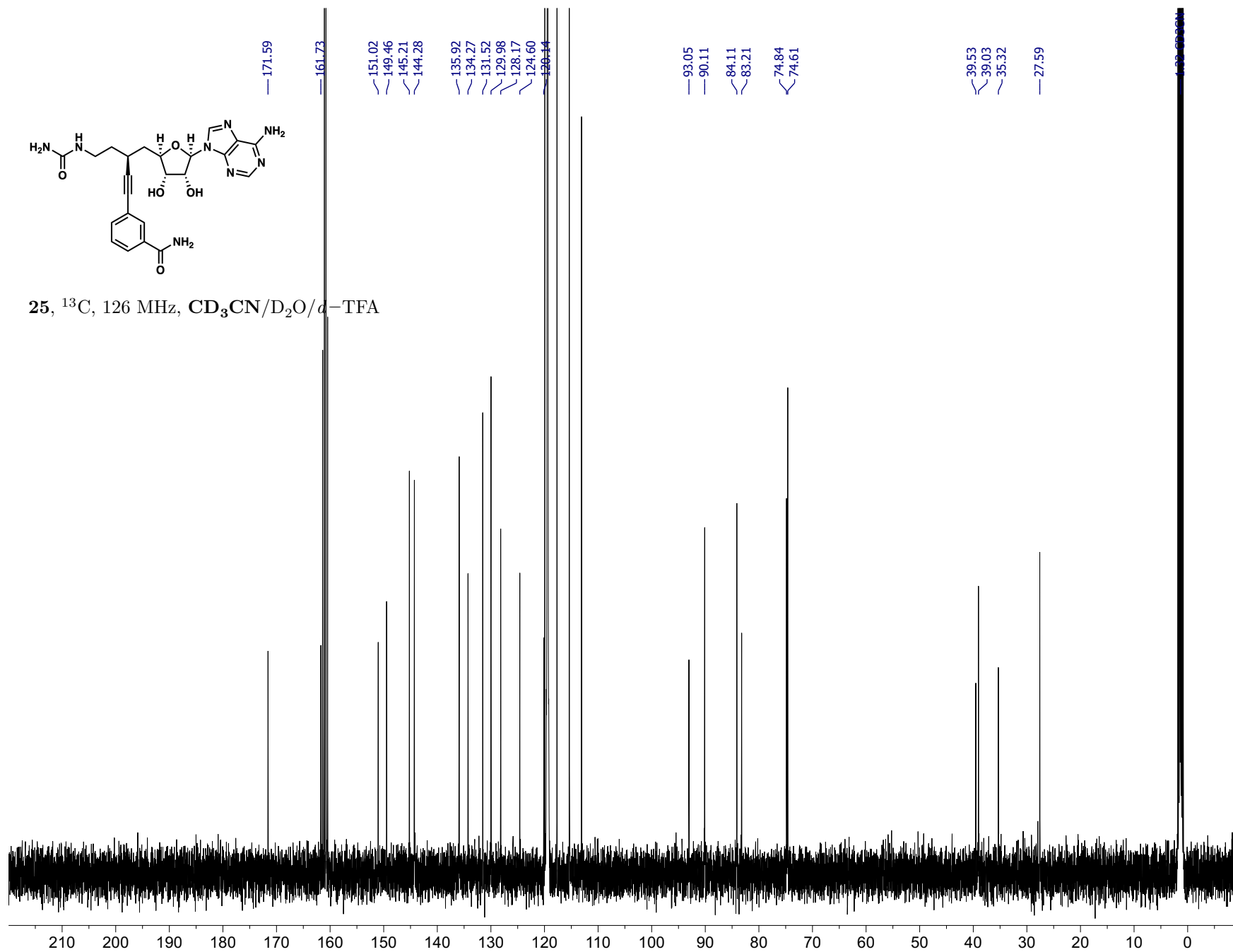
25,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

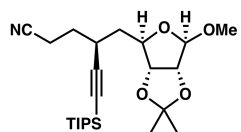






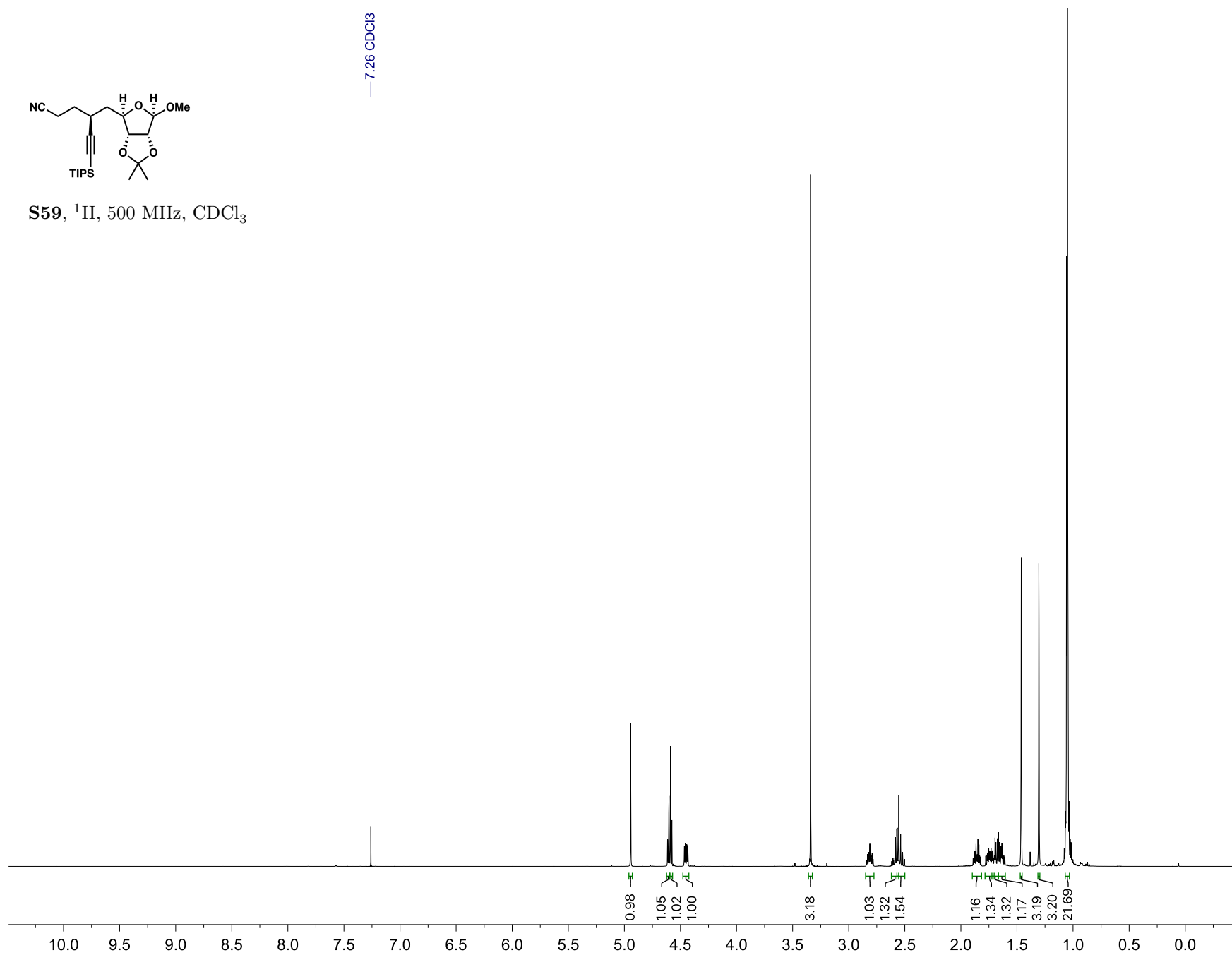
25,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

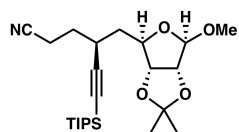




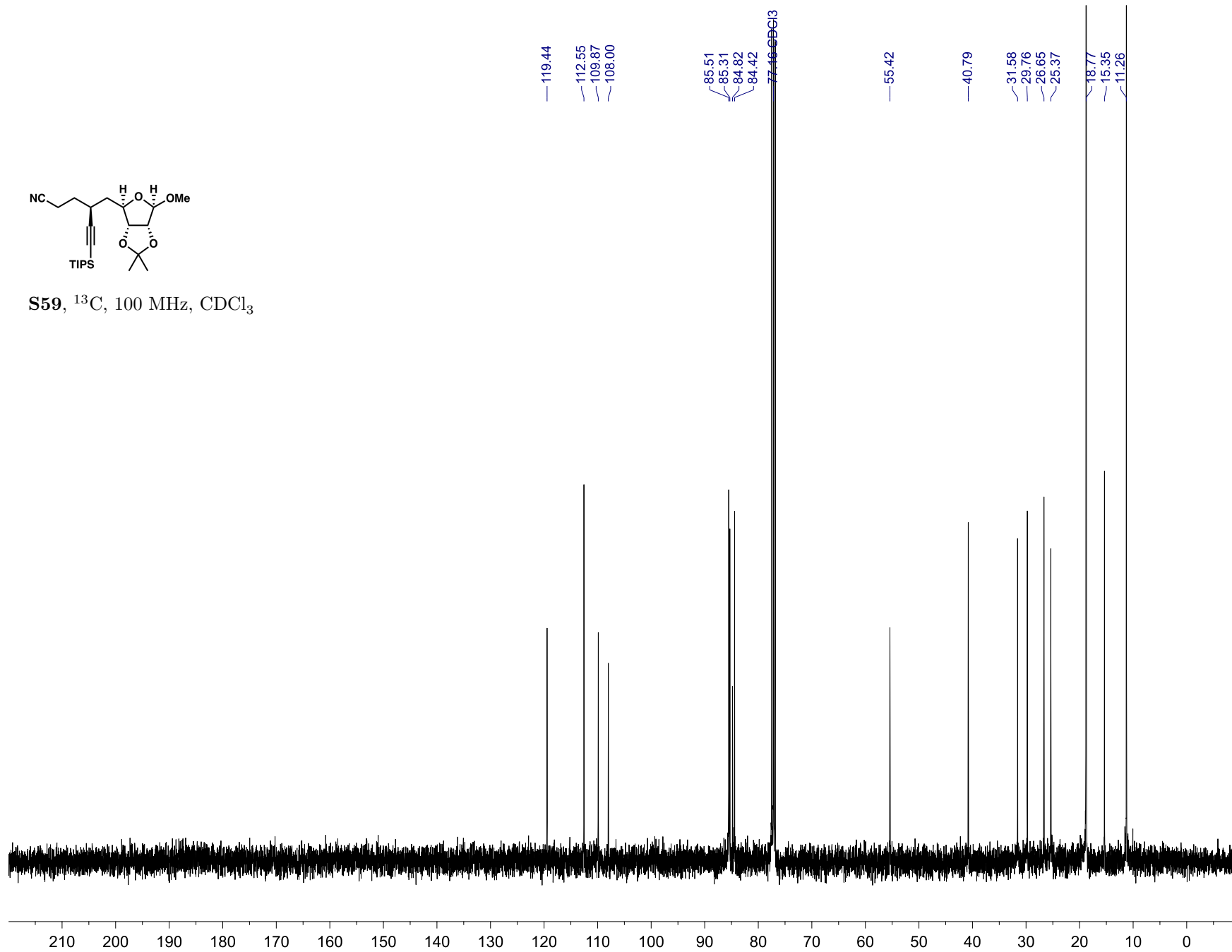
S59,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$

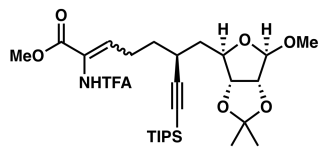
— 7.26  $\text{CDCl}_3$



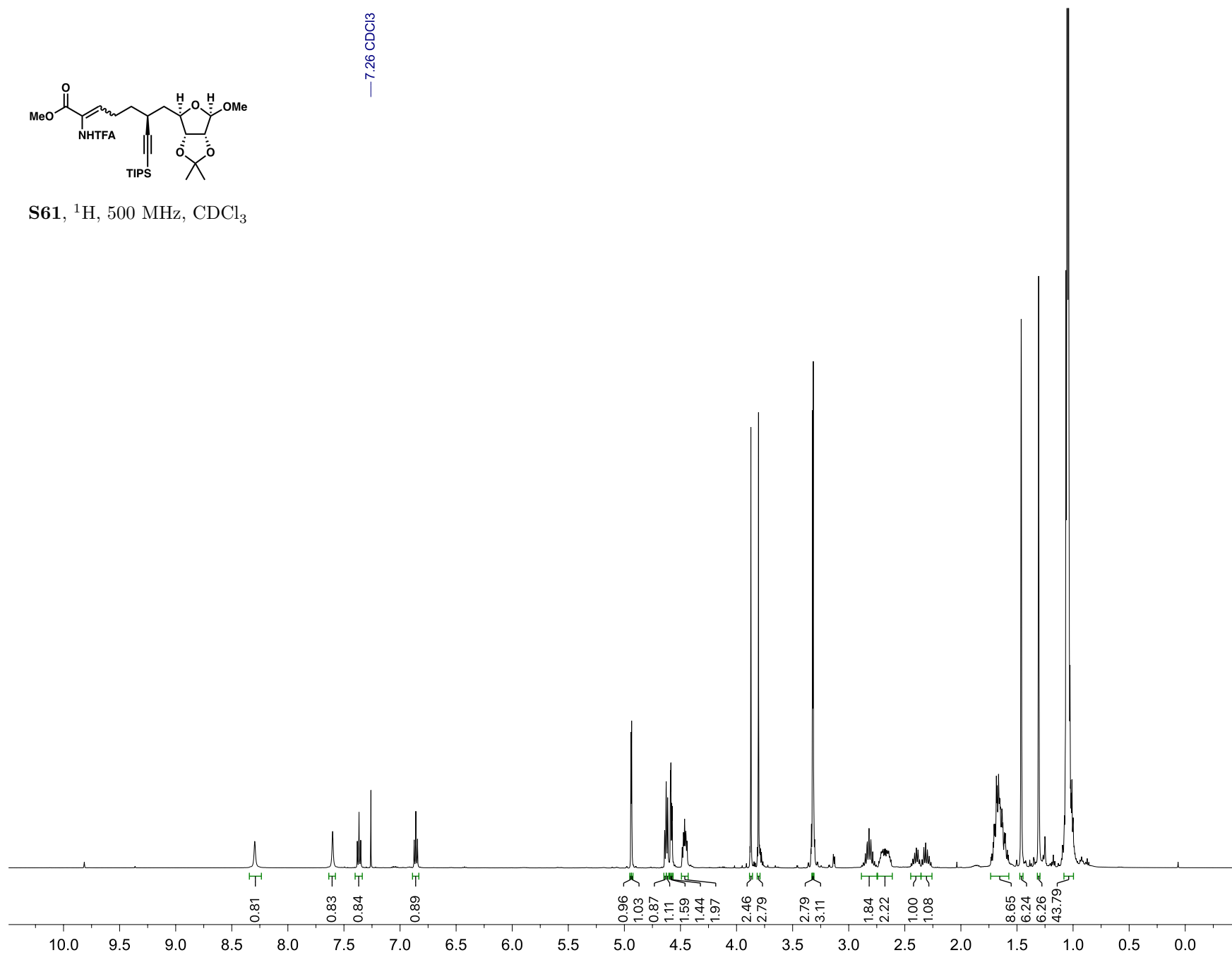


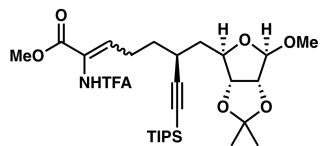
**S59**,  $^{13}\text{C}$ , 100 MHz,  $\text{CDCl}_3$



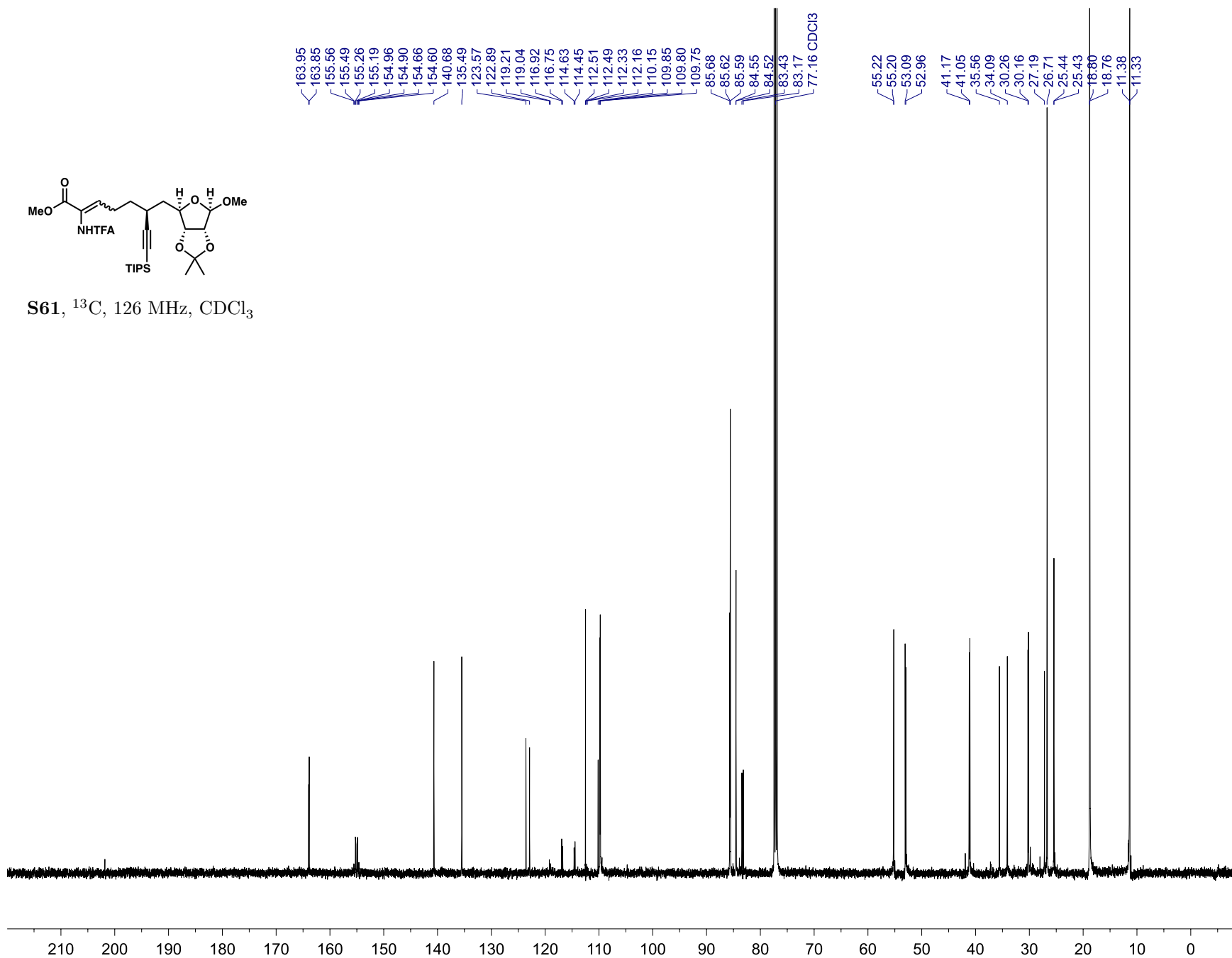


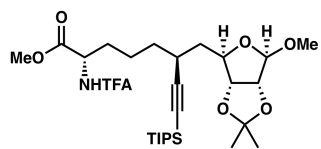
S61,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



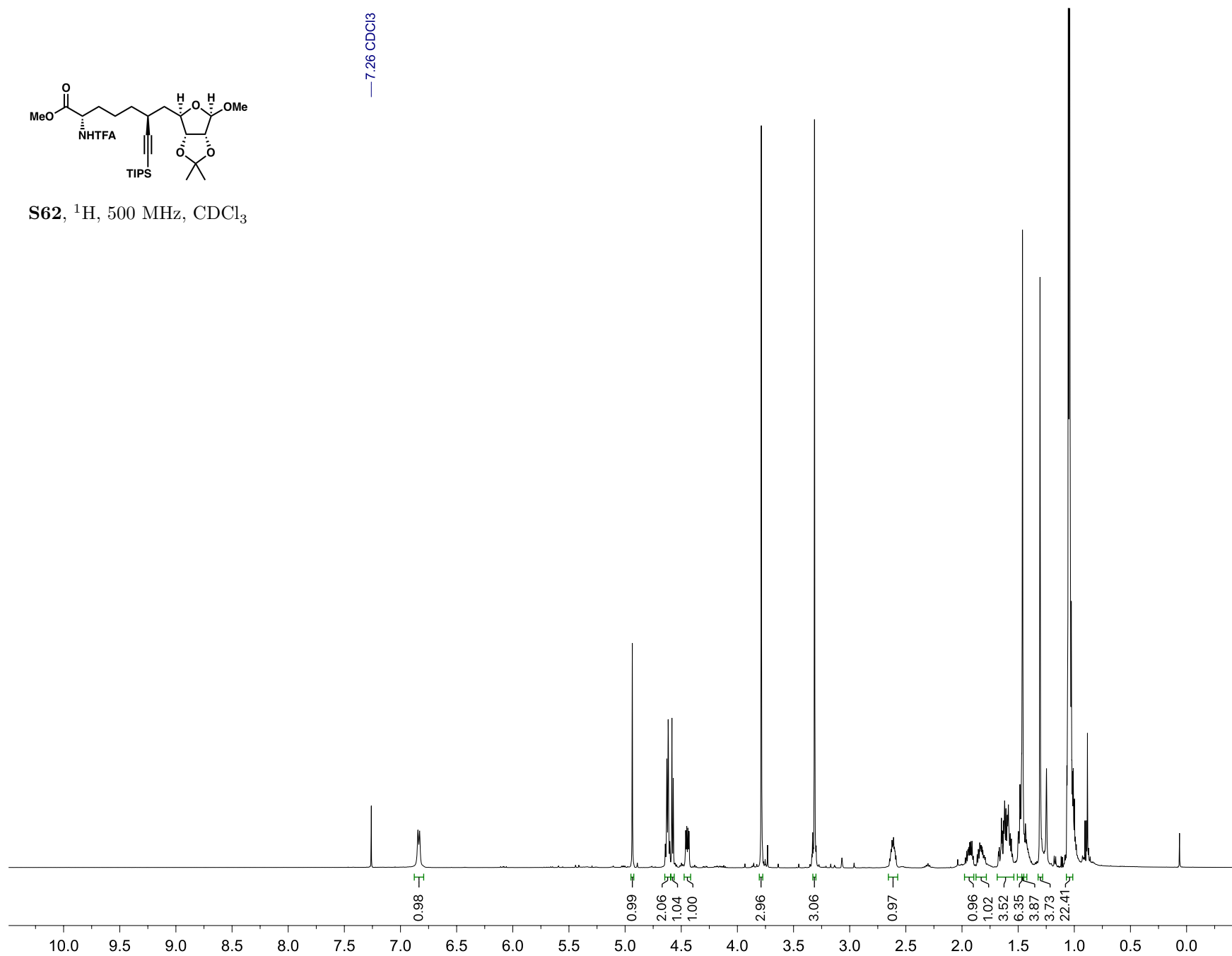


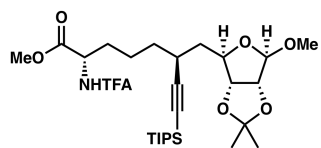
S61,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



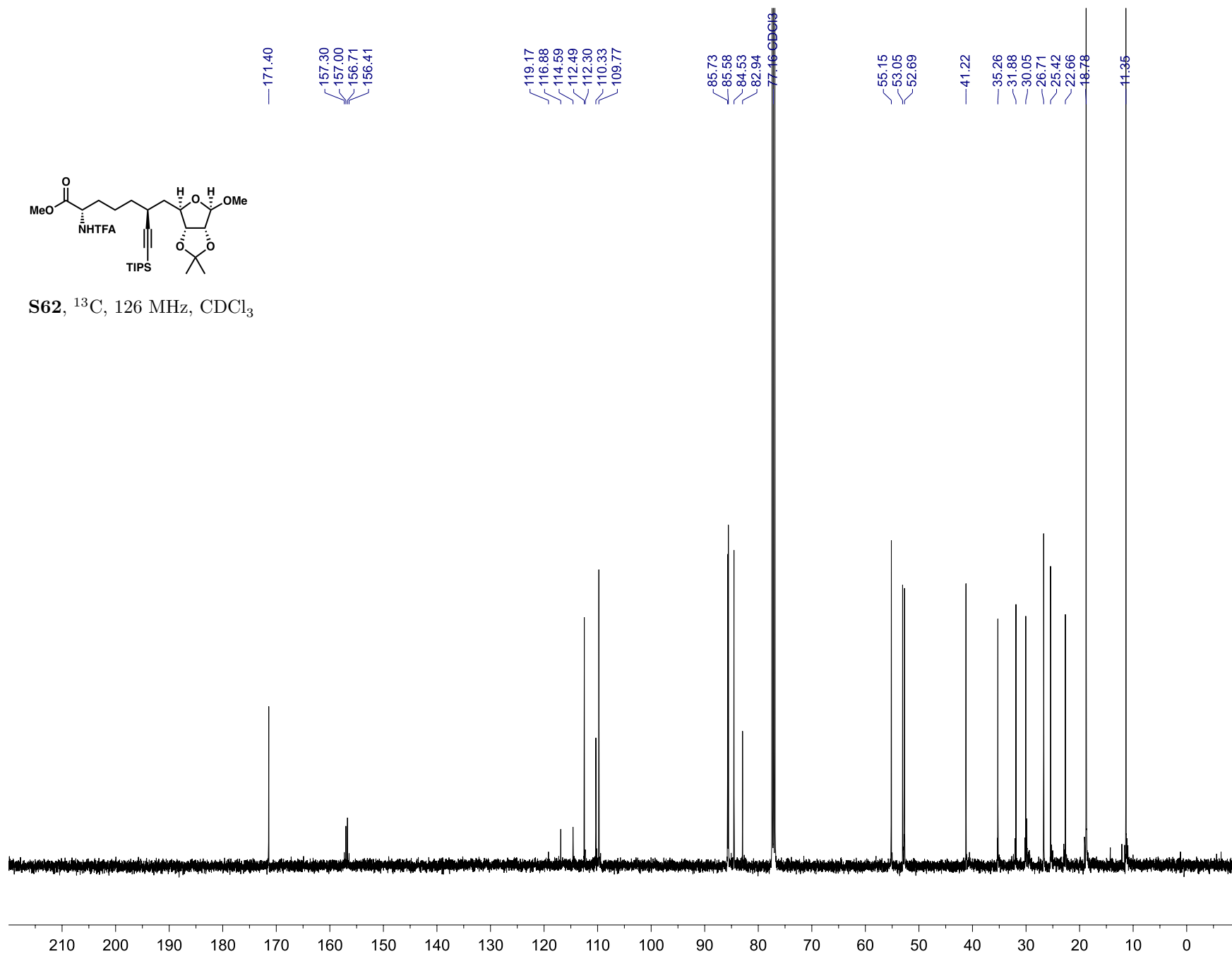


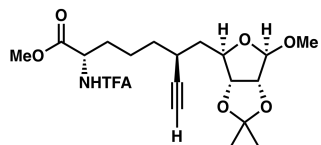
**S62**,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



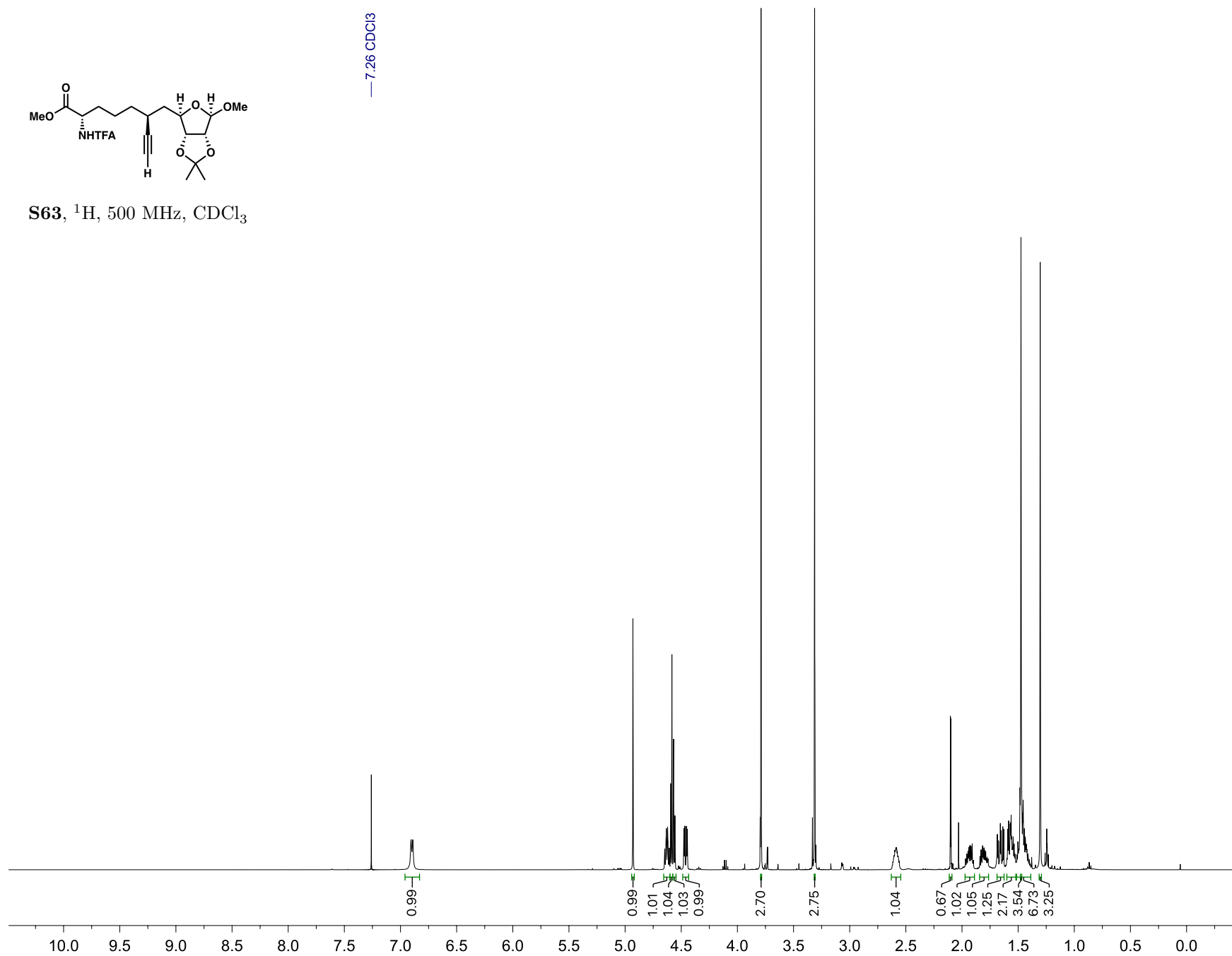


**S62**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



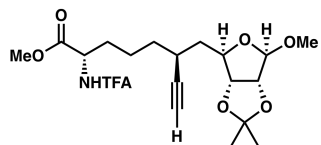


**S63**, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>

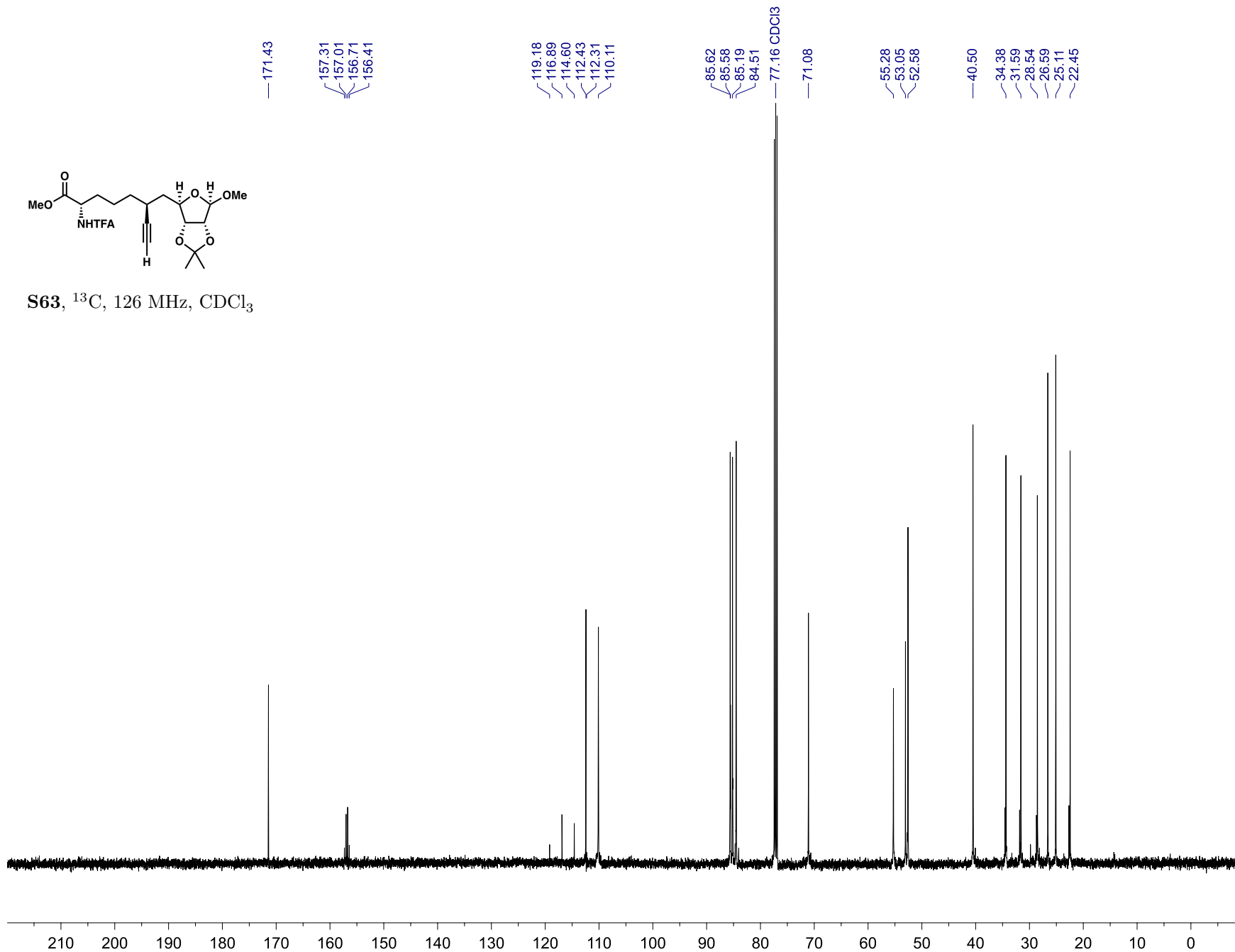


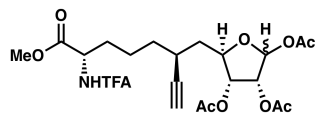
— 7.26 CDCl<sub>3</sub>



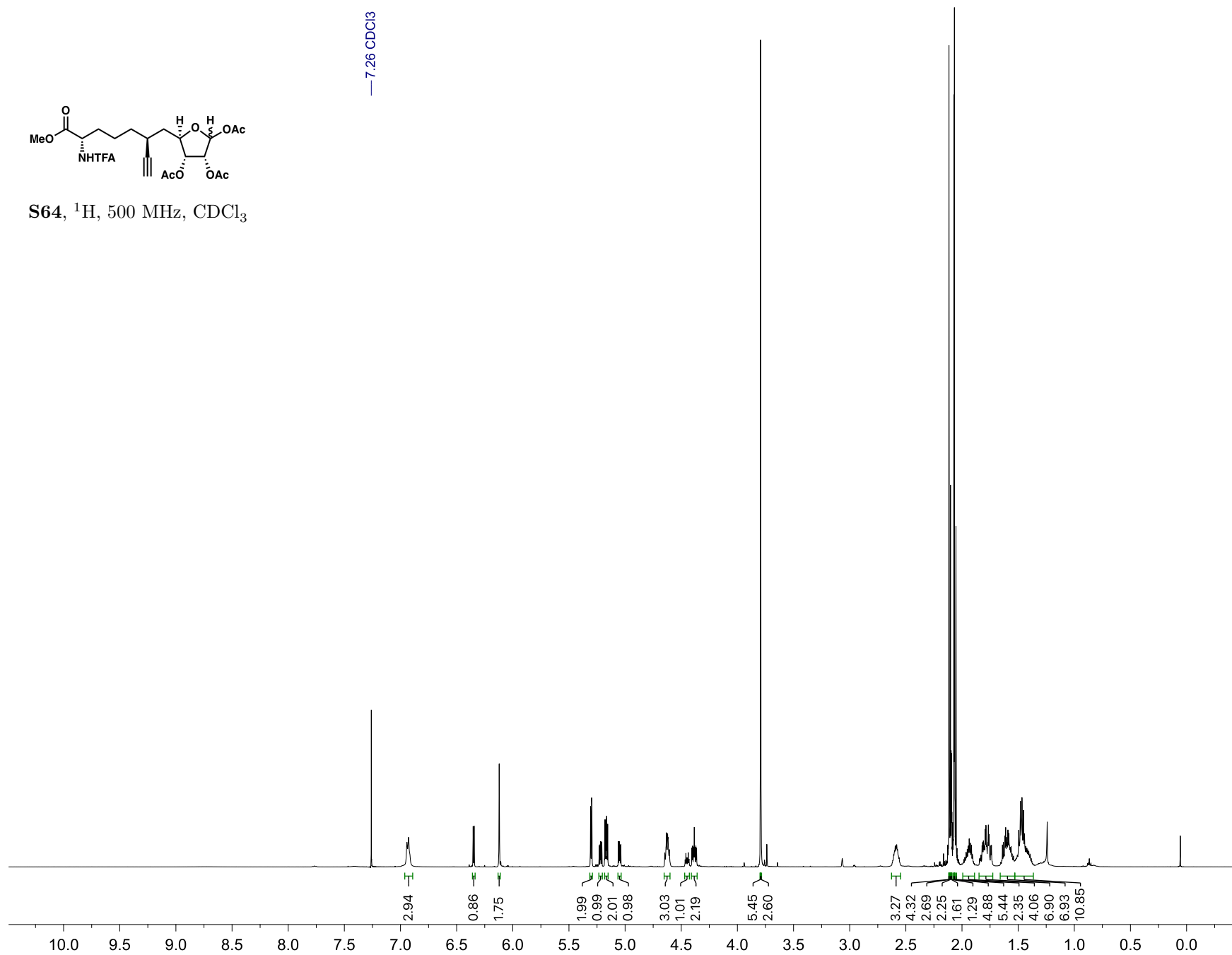


**S63**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

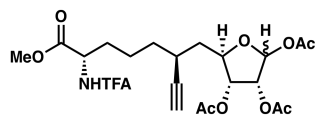
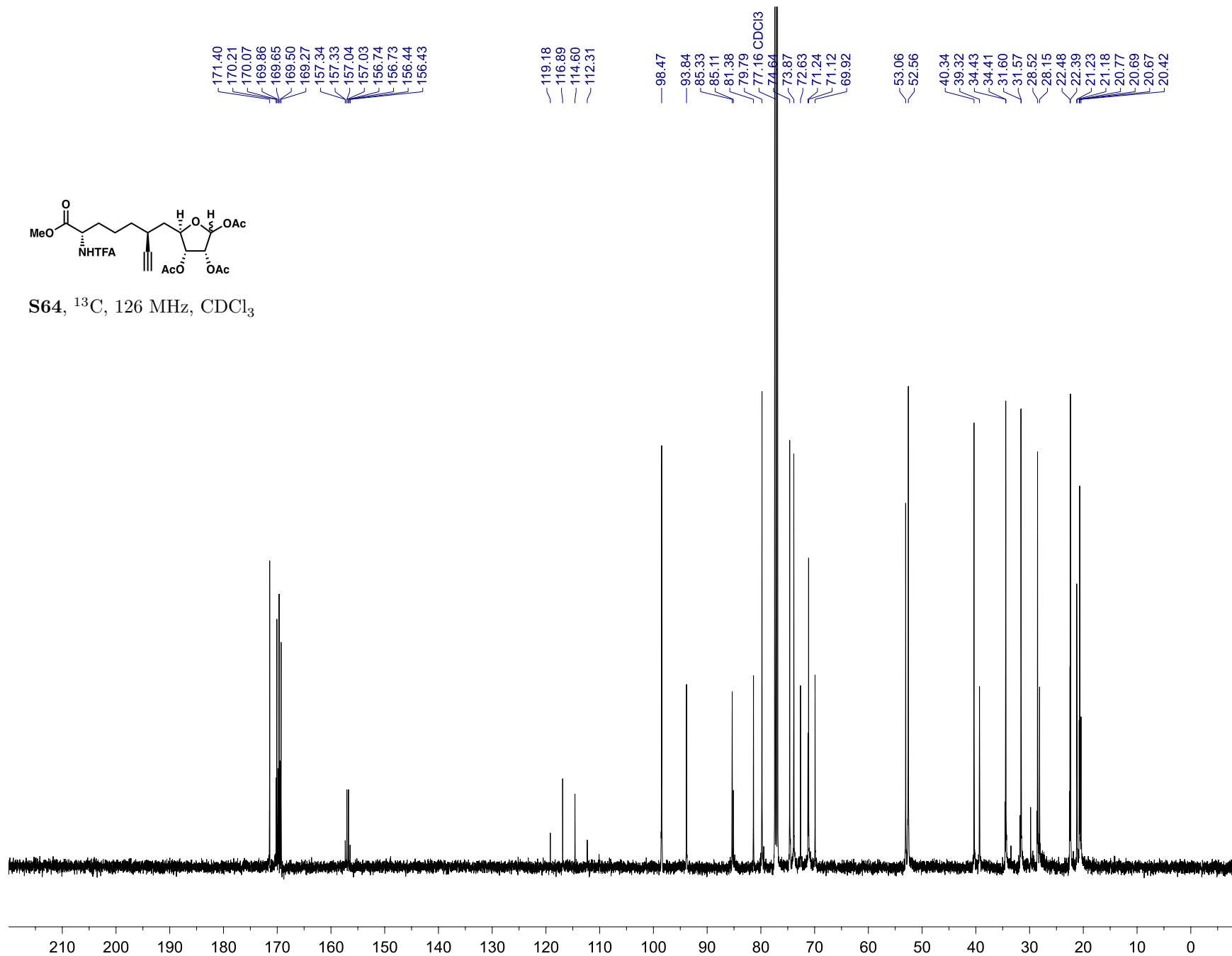


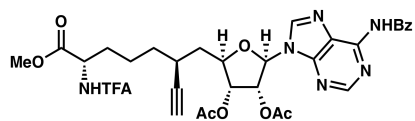


S64,  $^1\text{H}$ , 500 MHz,  $\text{CDCl}_3$



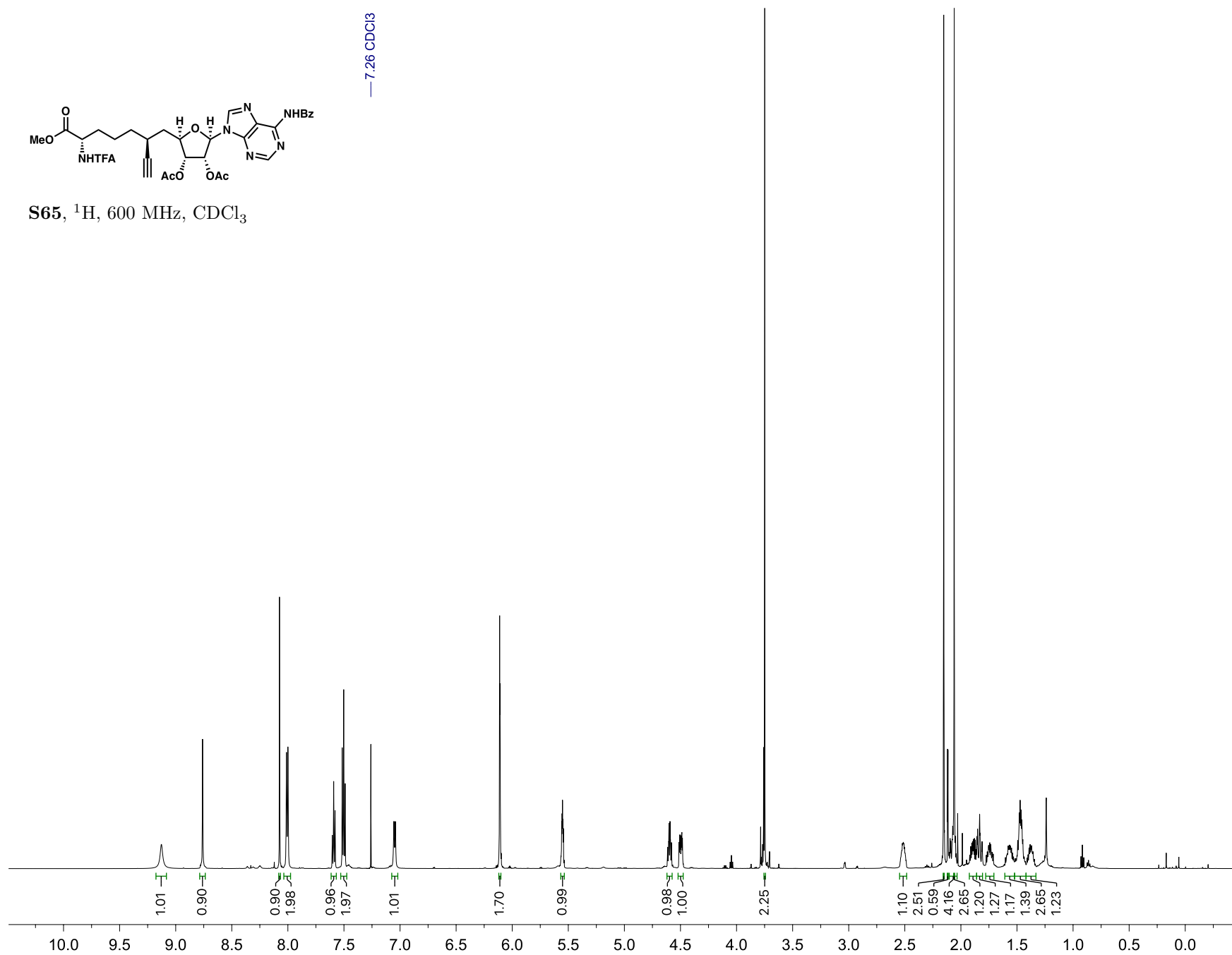
— 7.26  $\text{CDCl}_3$

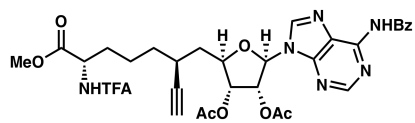
**S64**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$ 



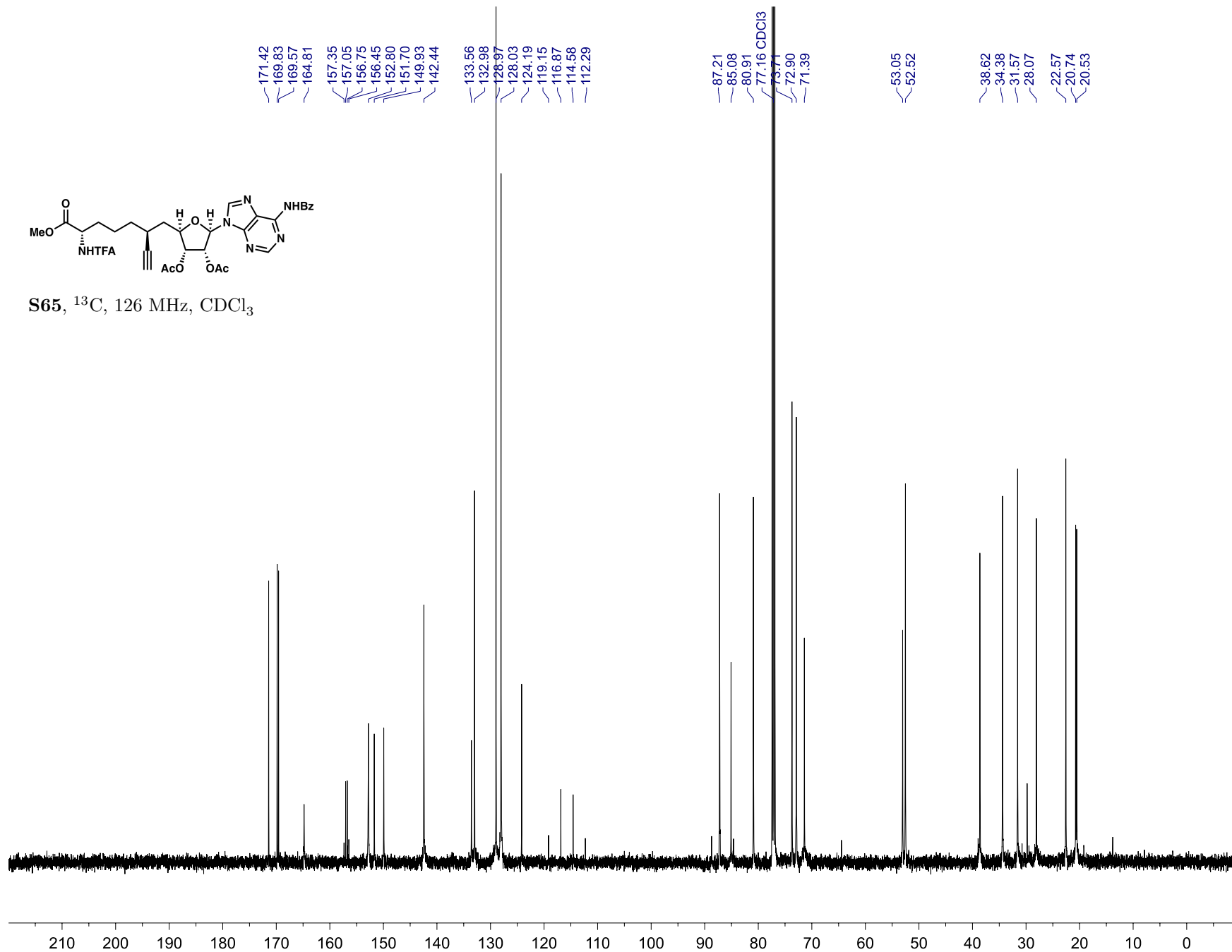
S65,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

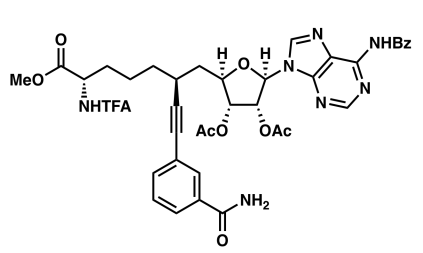
— 7.26  $\text{CDCl}_3$





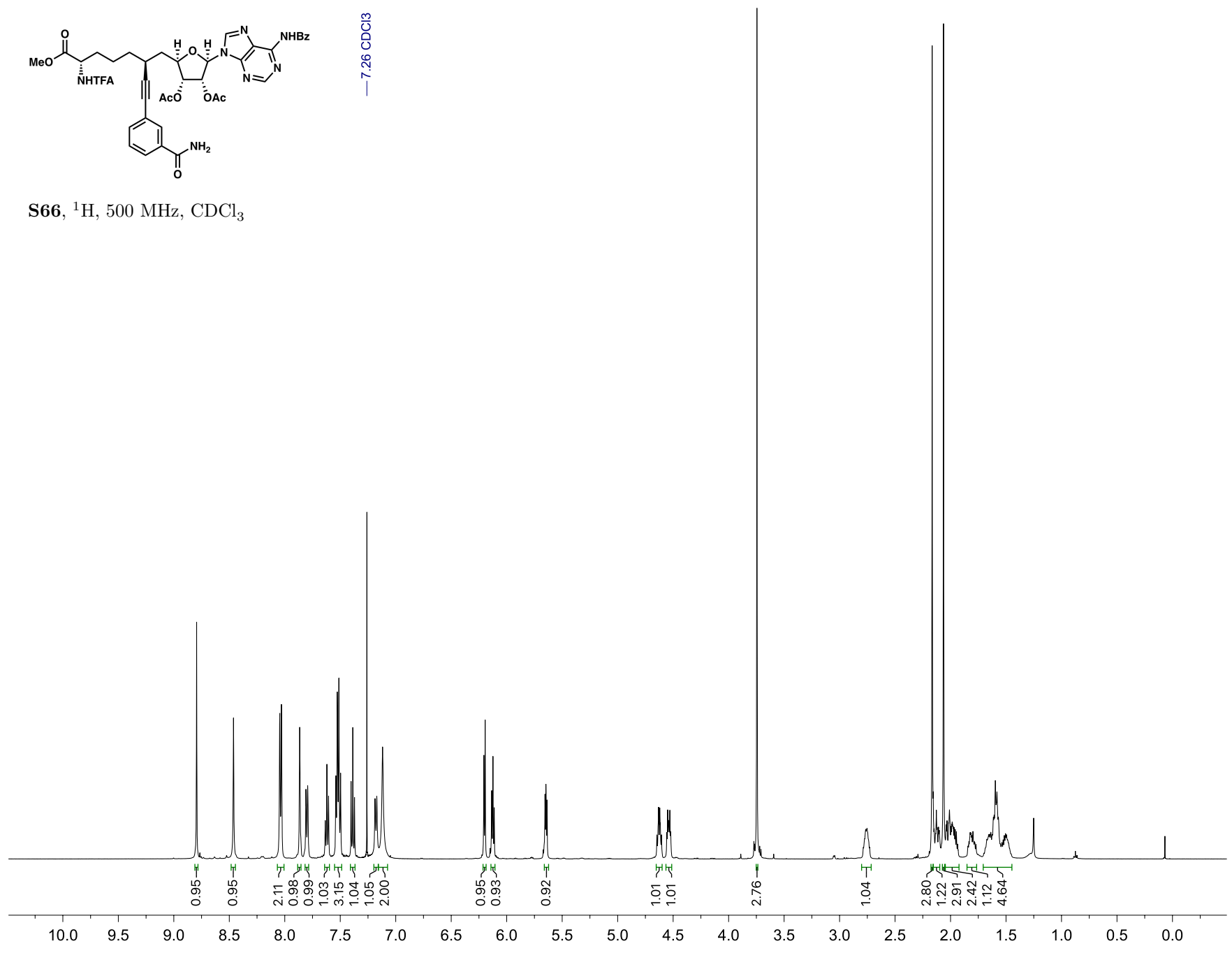
S65,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

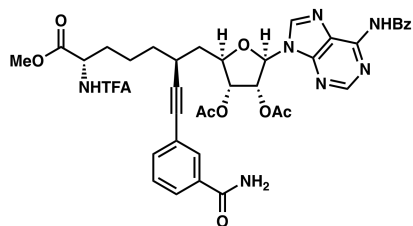




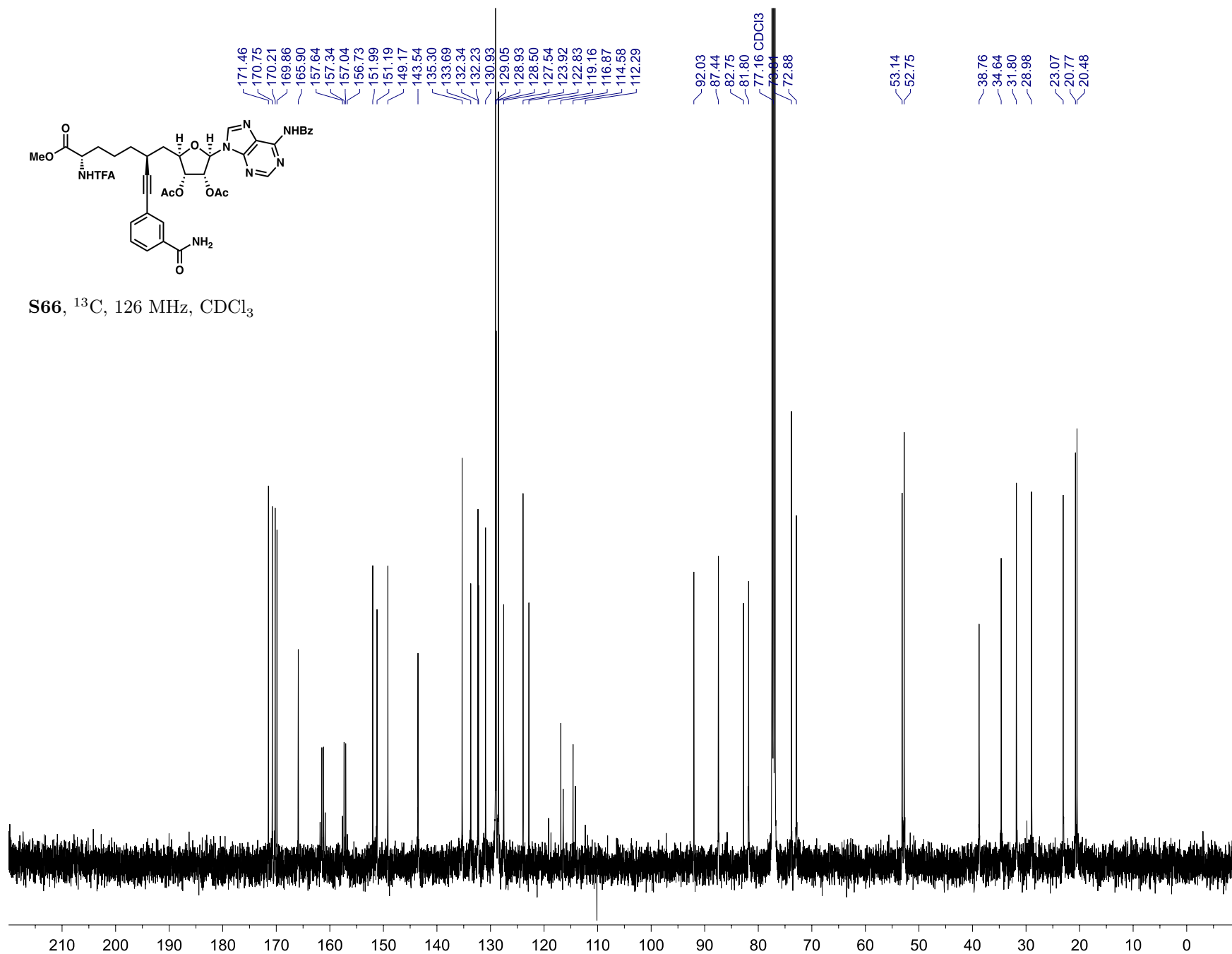
— 7.26 CDCl<sub>3</sub>

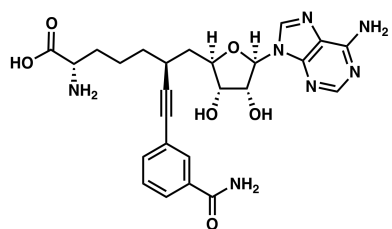
S66, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>



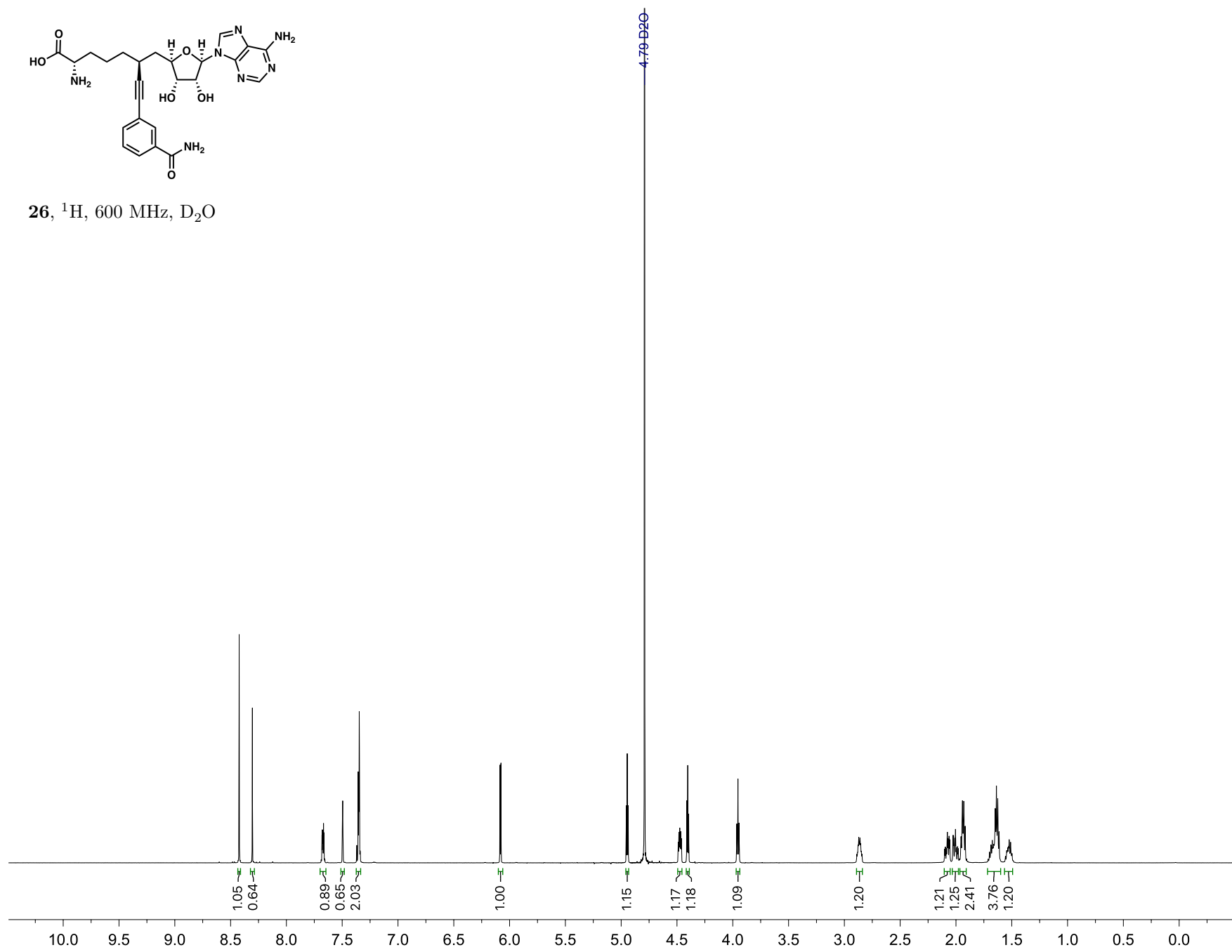


S66,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

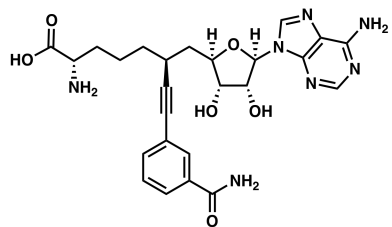




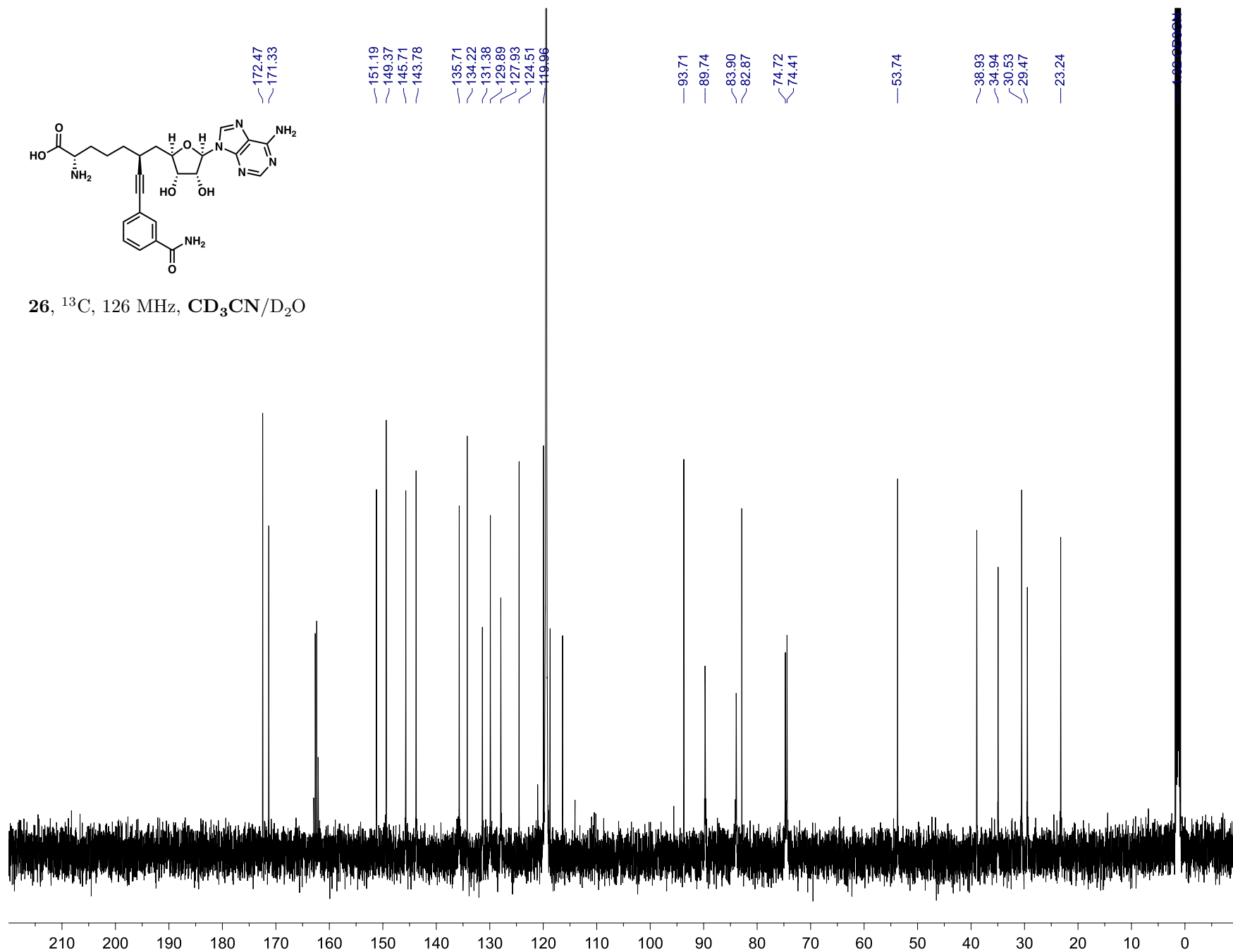
26, <sup>1</sup>H, 600 MHz, D<sub>2</sub>O

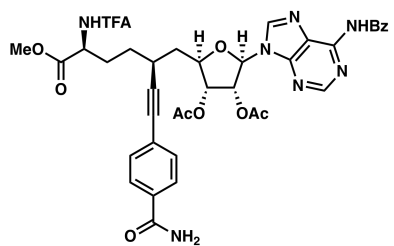




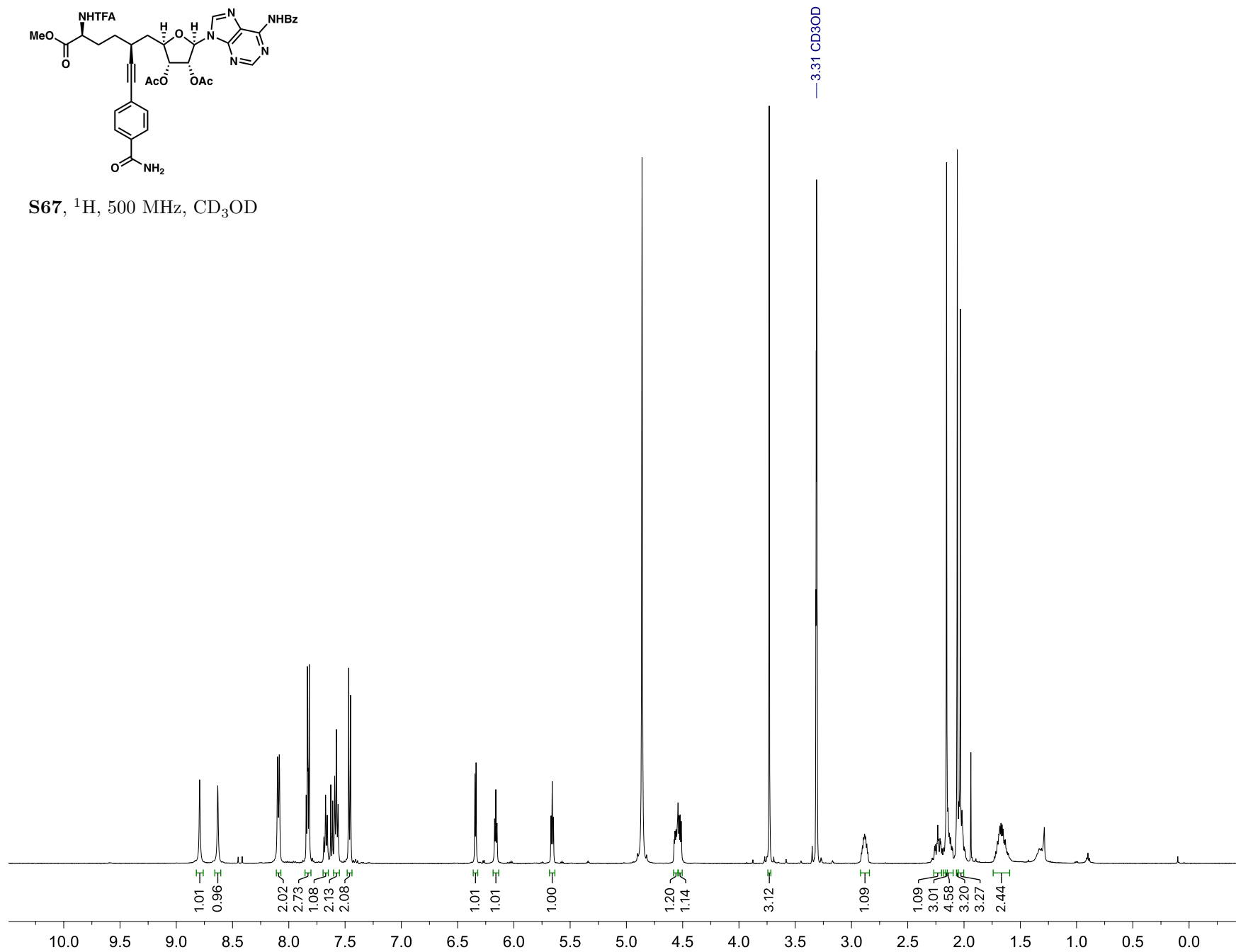


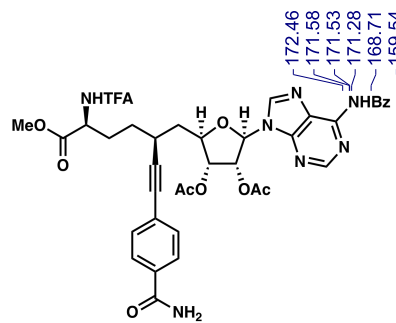
**26**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$



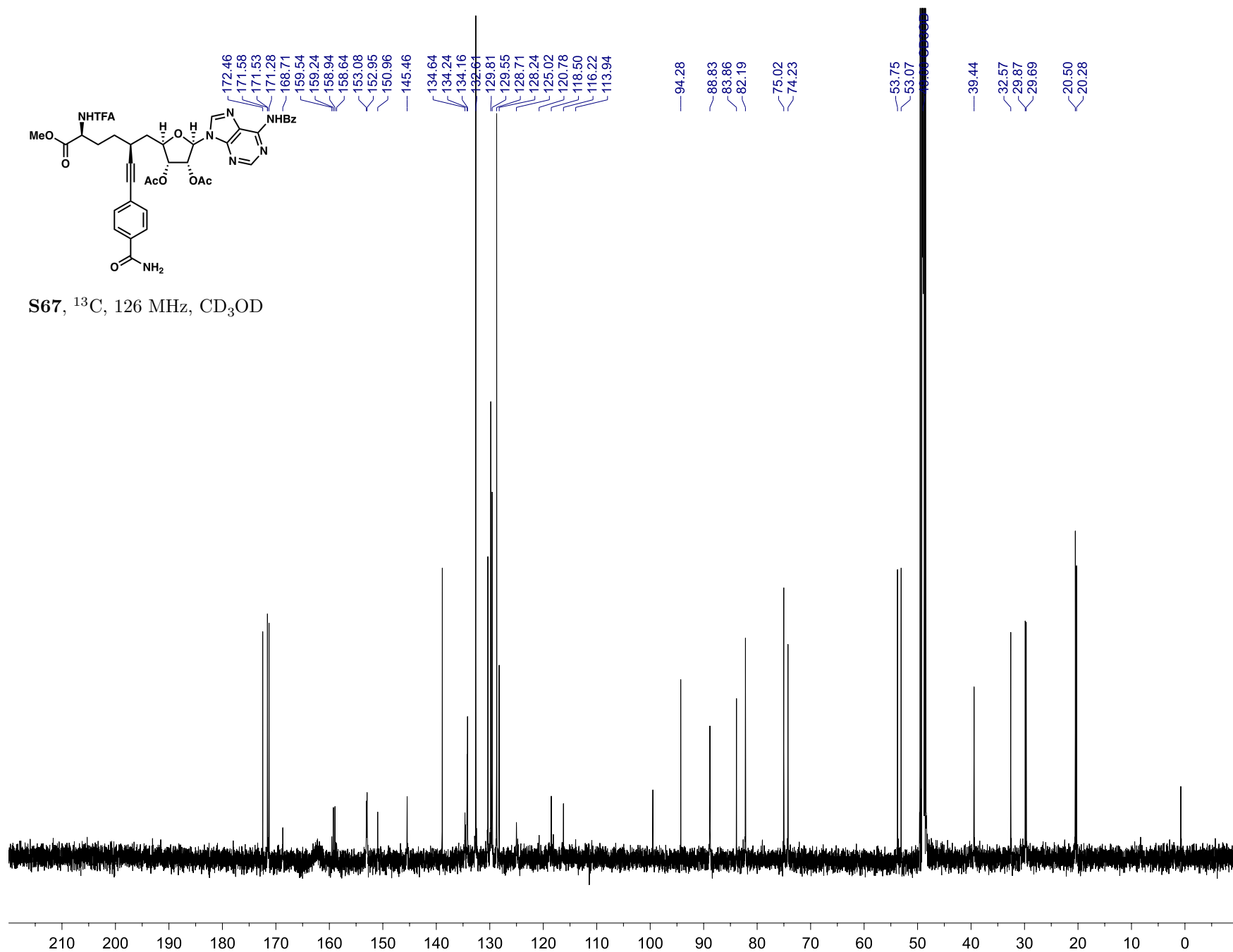


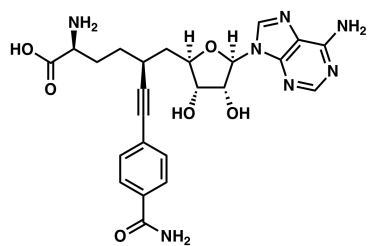
S67, <sup>1</sup>H, 500 MHz, CD<sub>3</sub>OD





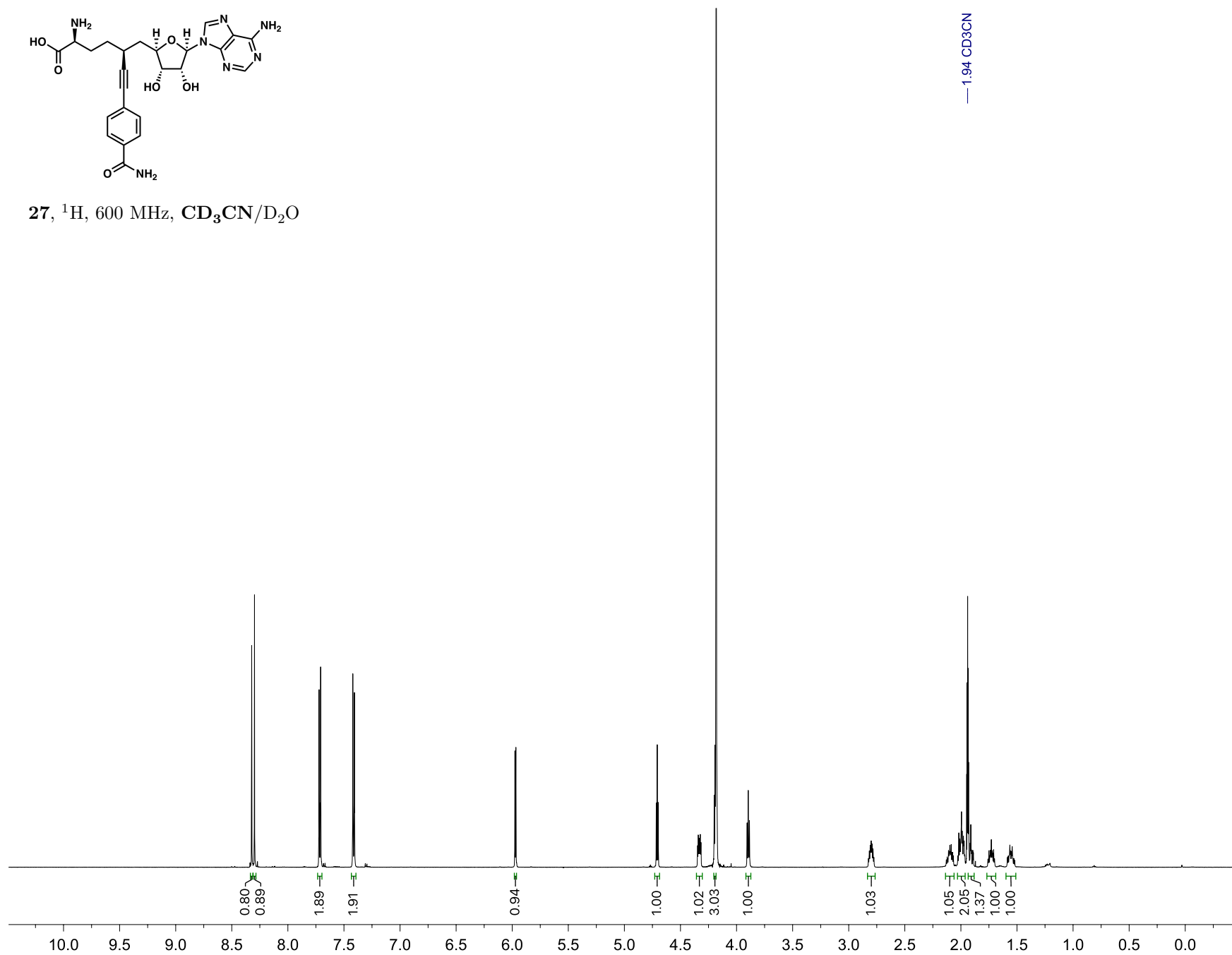
S67, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>OD



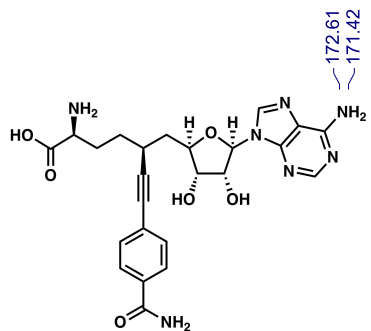


27,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

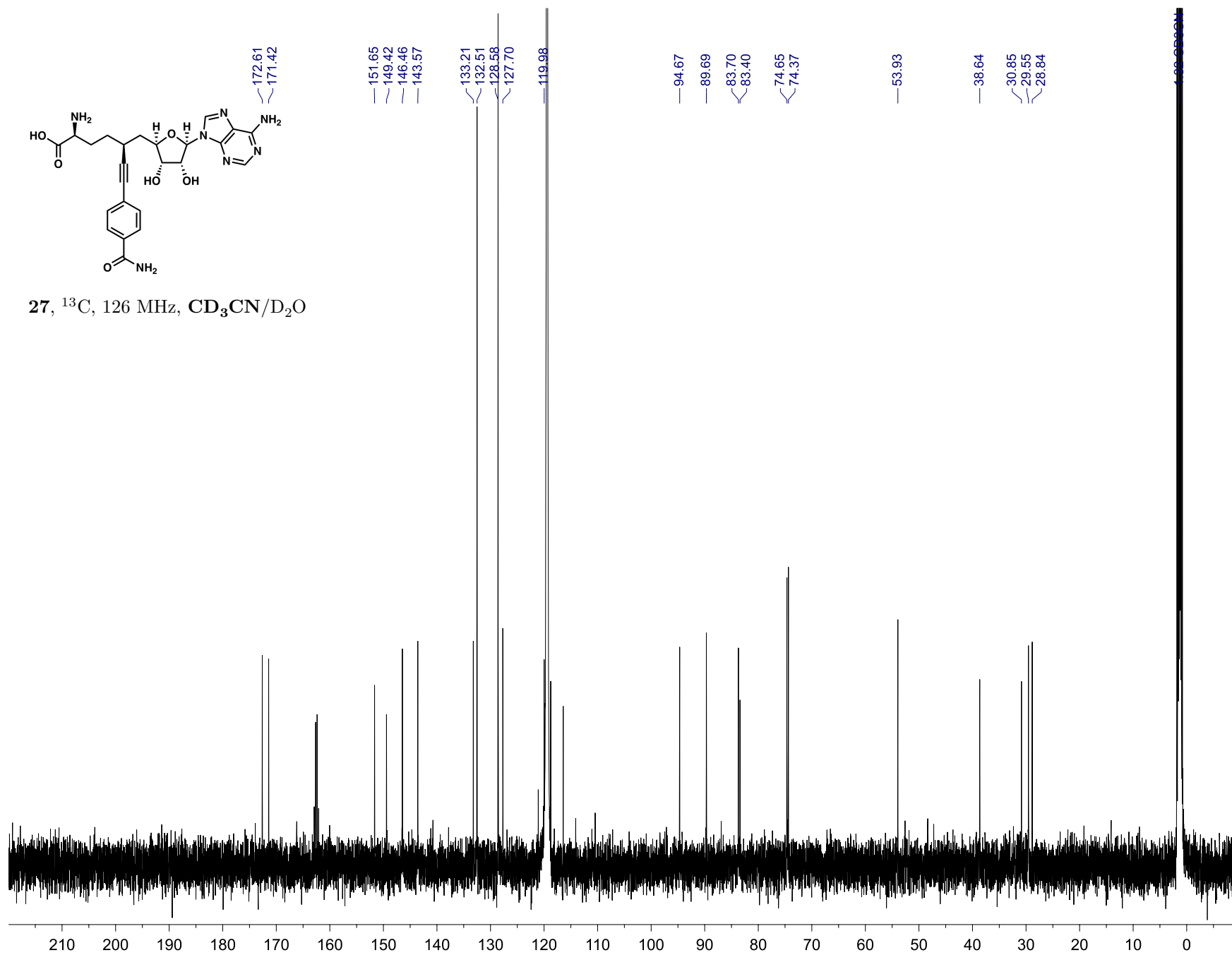
67 IS

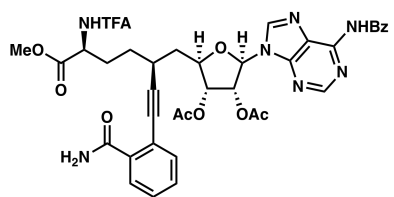


— 1.94  $\text{CD}_3\text{CN}$

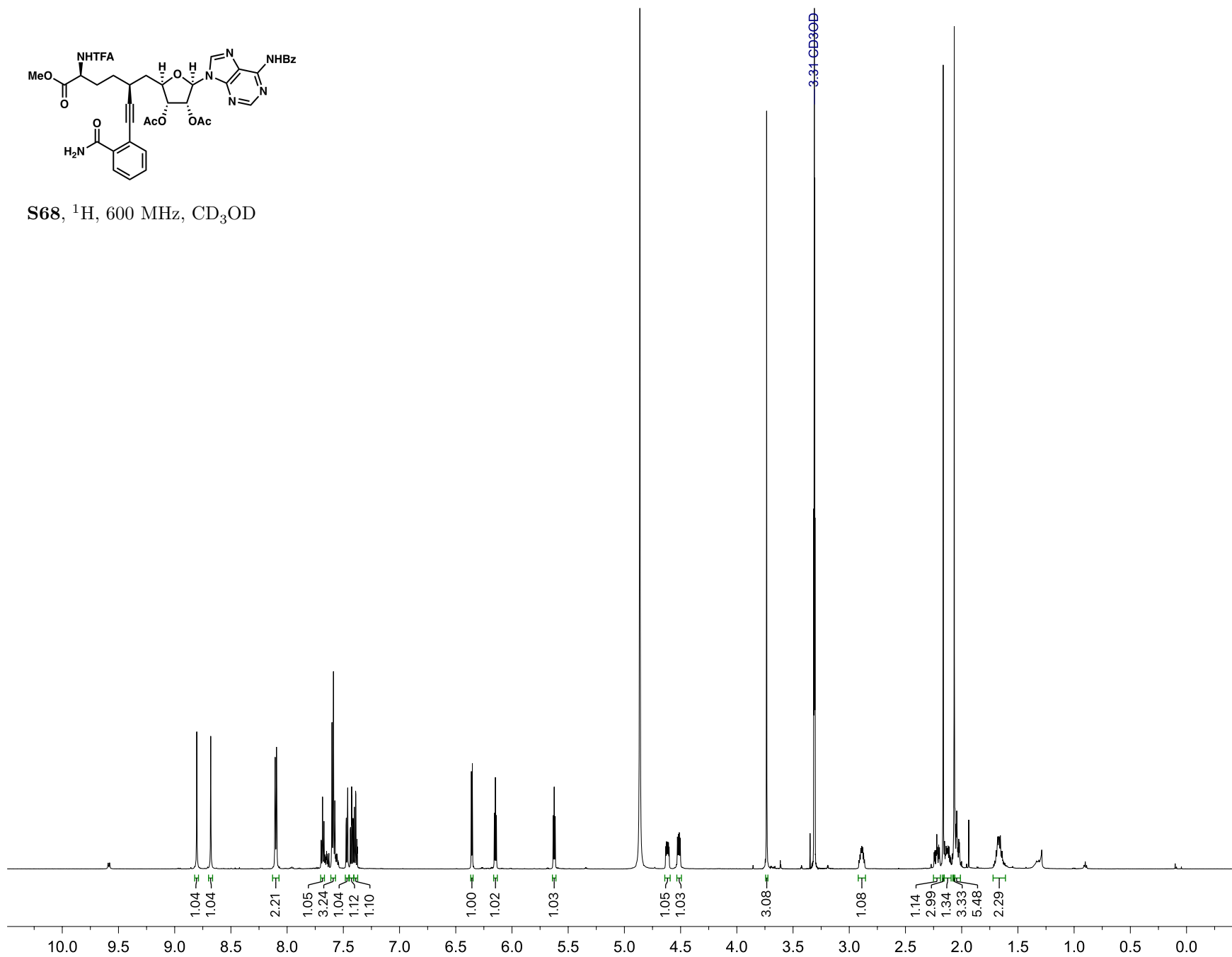


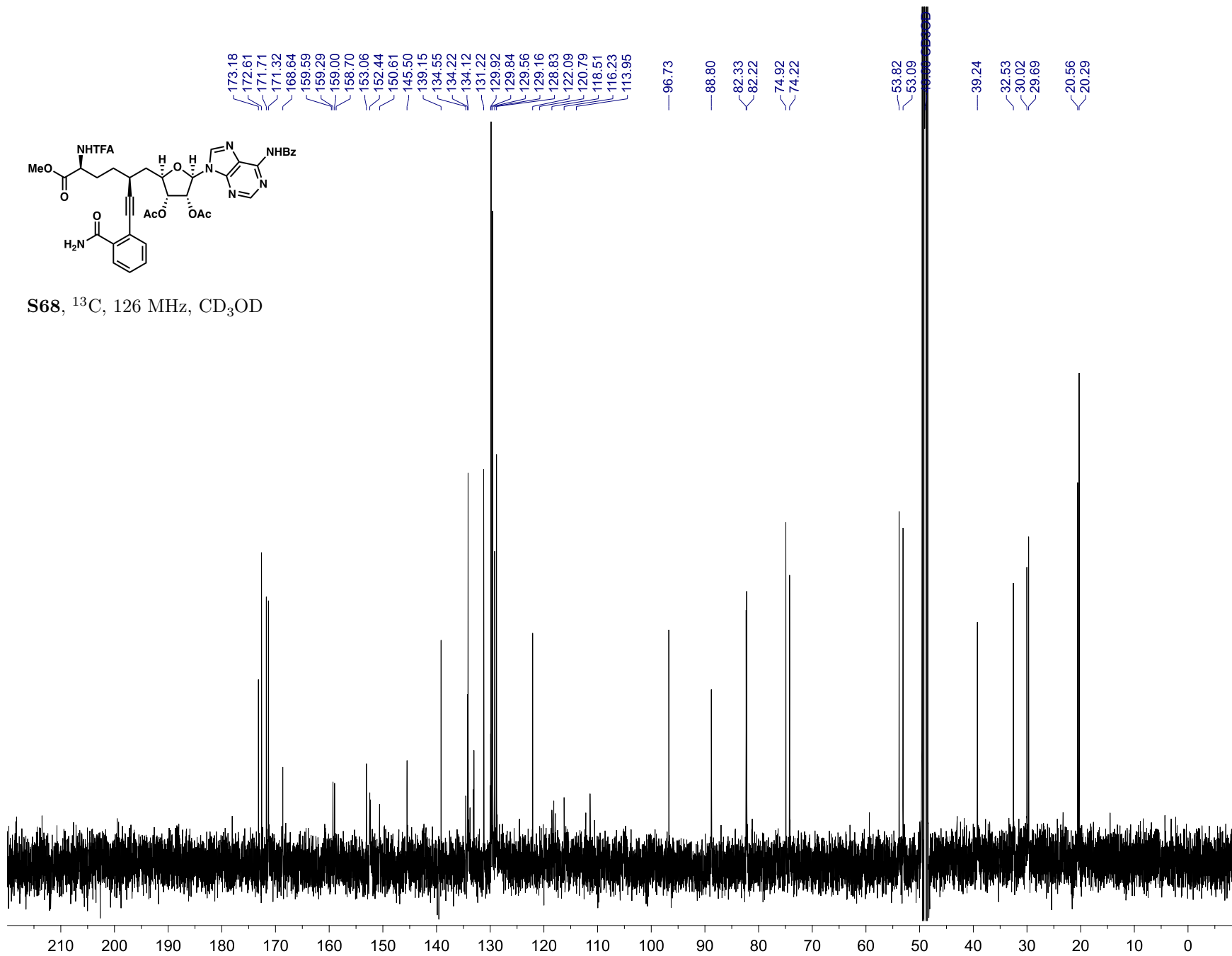
27, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O

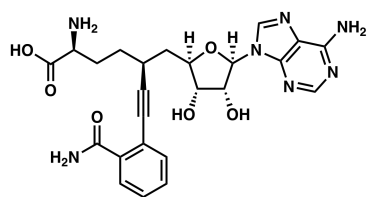




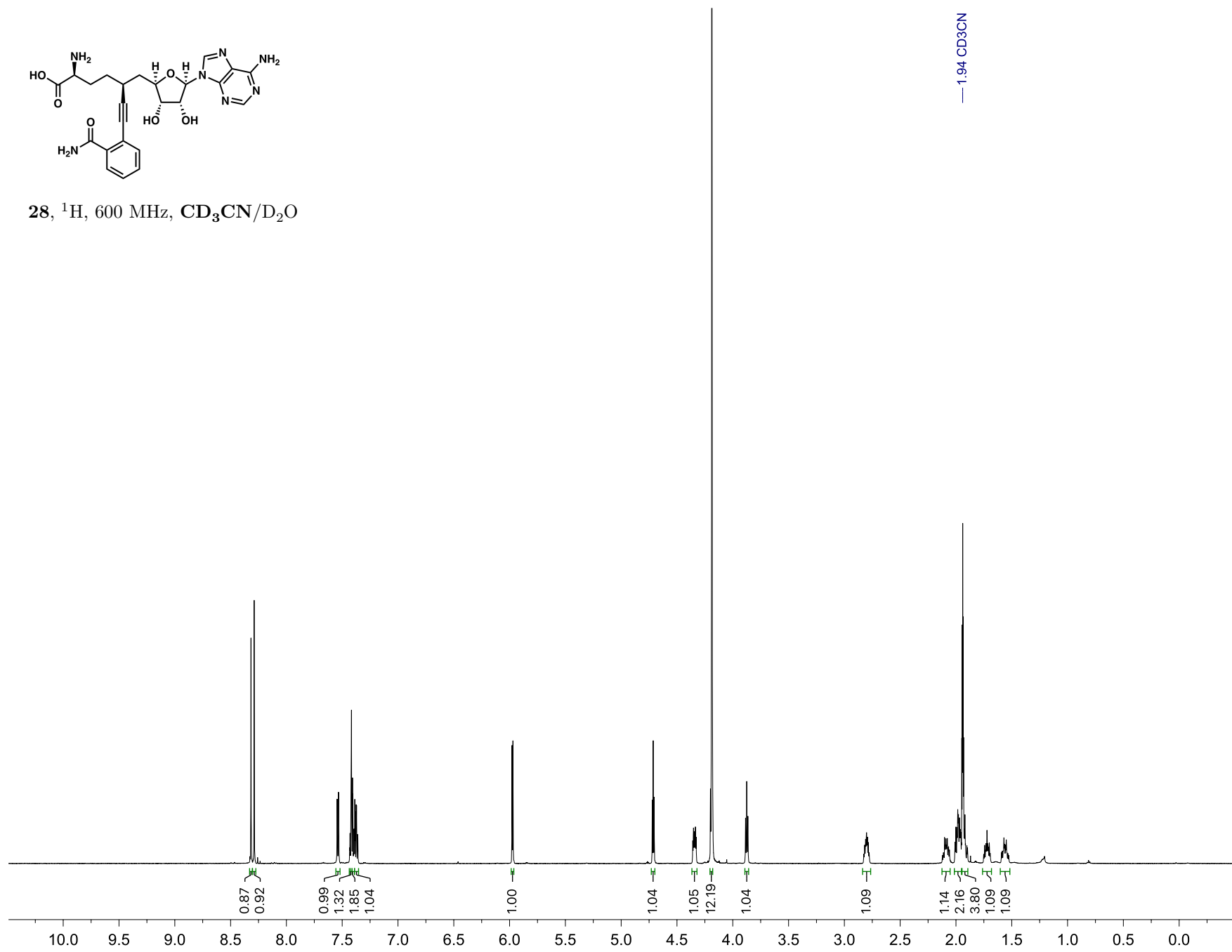
S68,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{OD}$



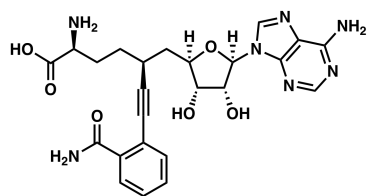




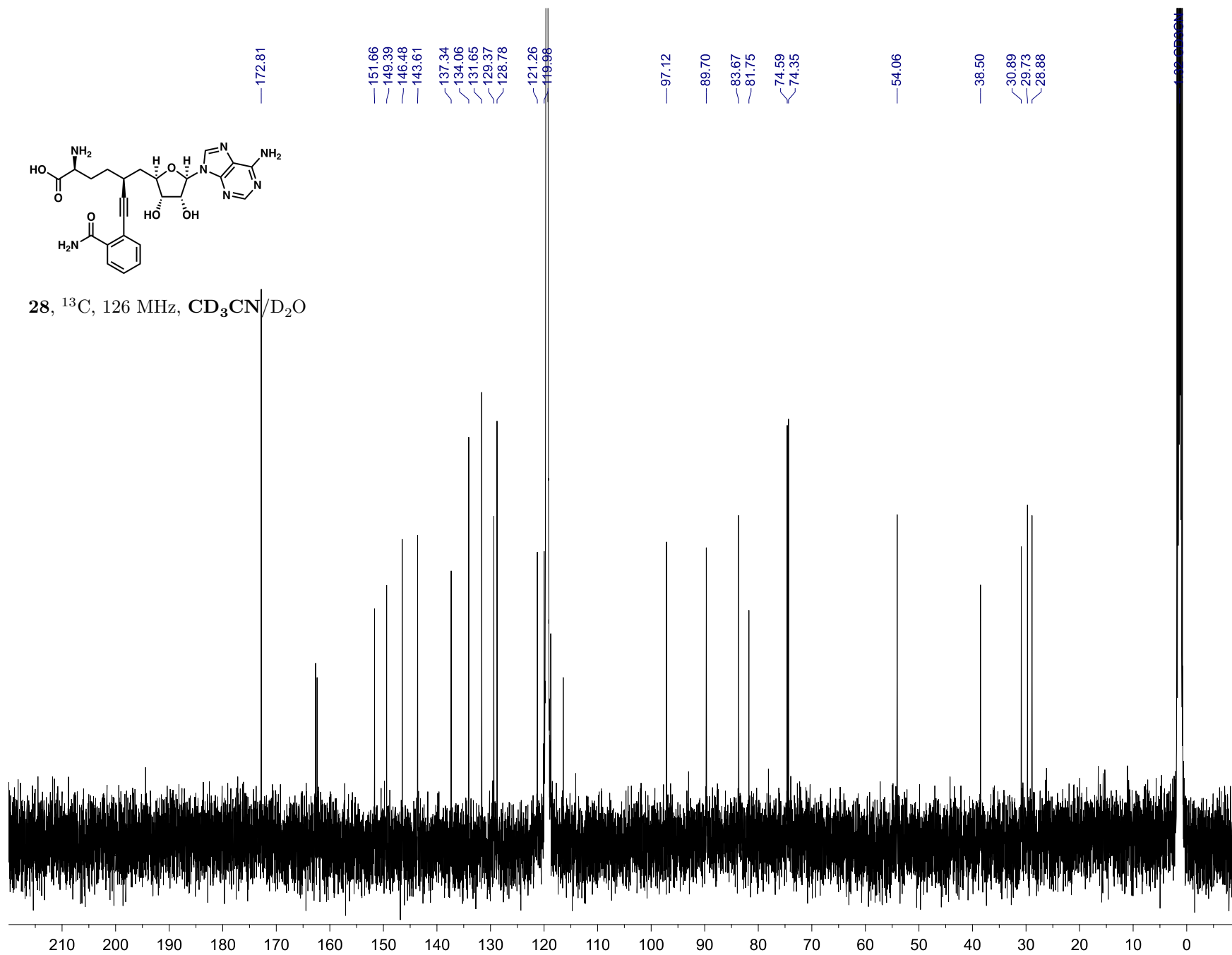
28,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

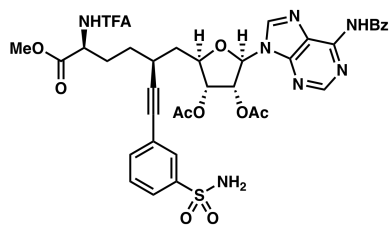






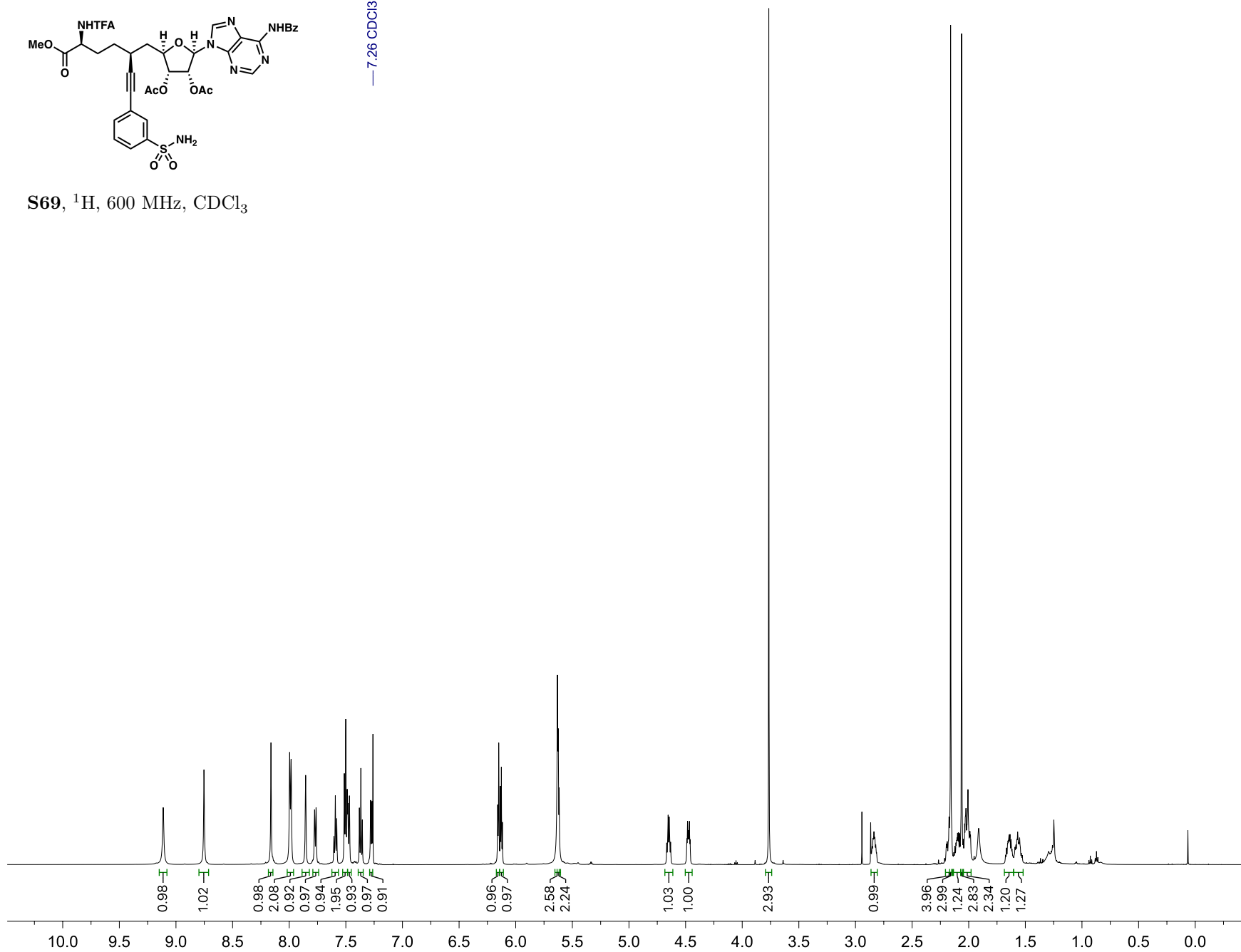
28,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

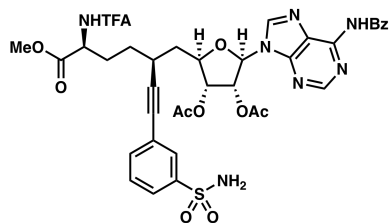




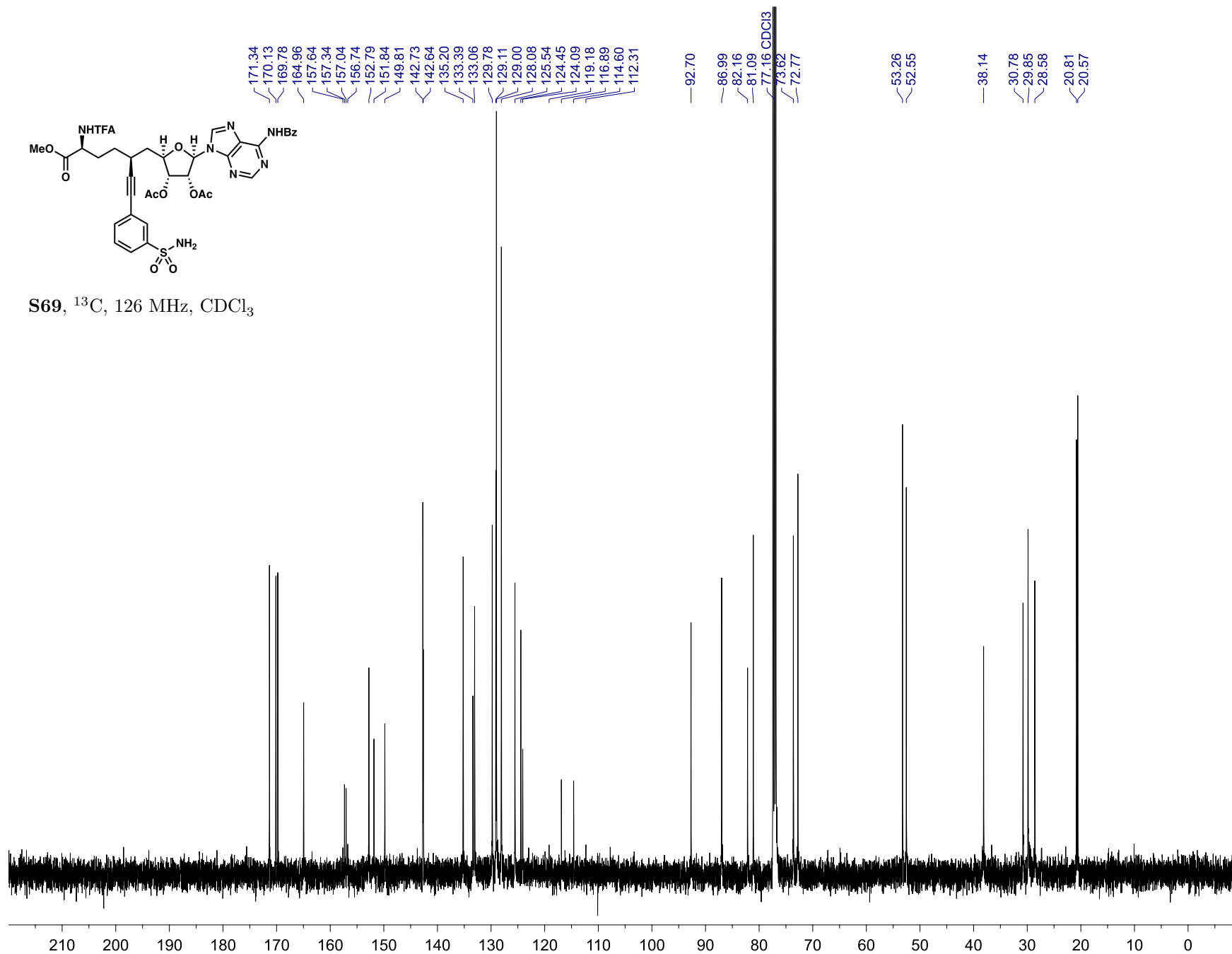
S69, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

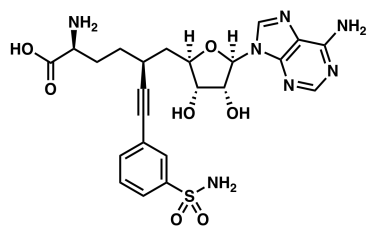
— 7.26 CDCl<sub>3</sub>





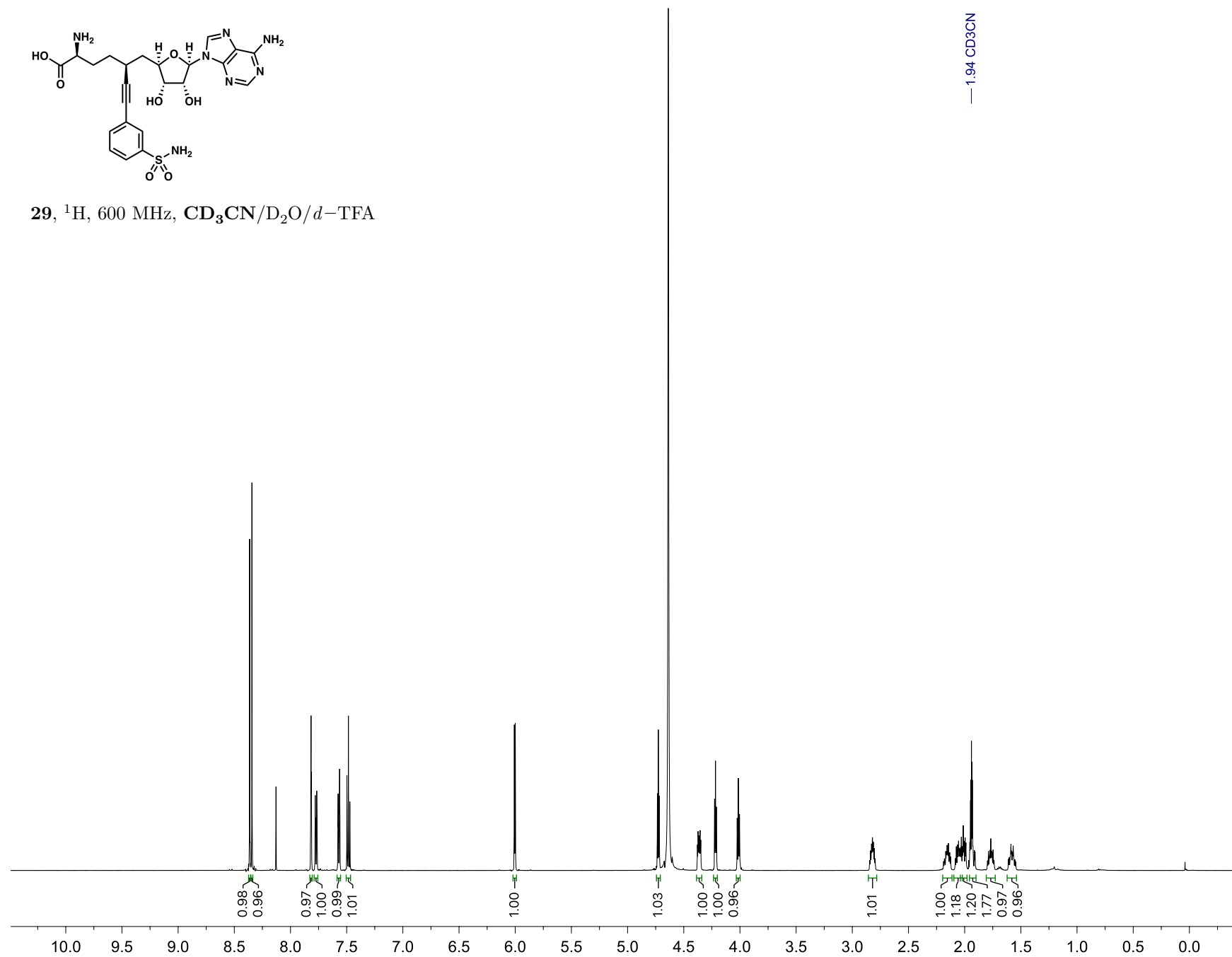
**S69**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

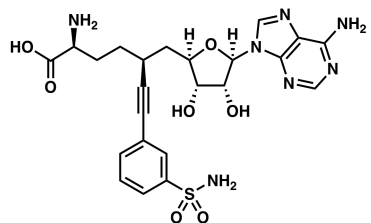




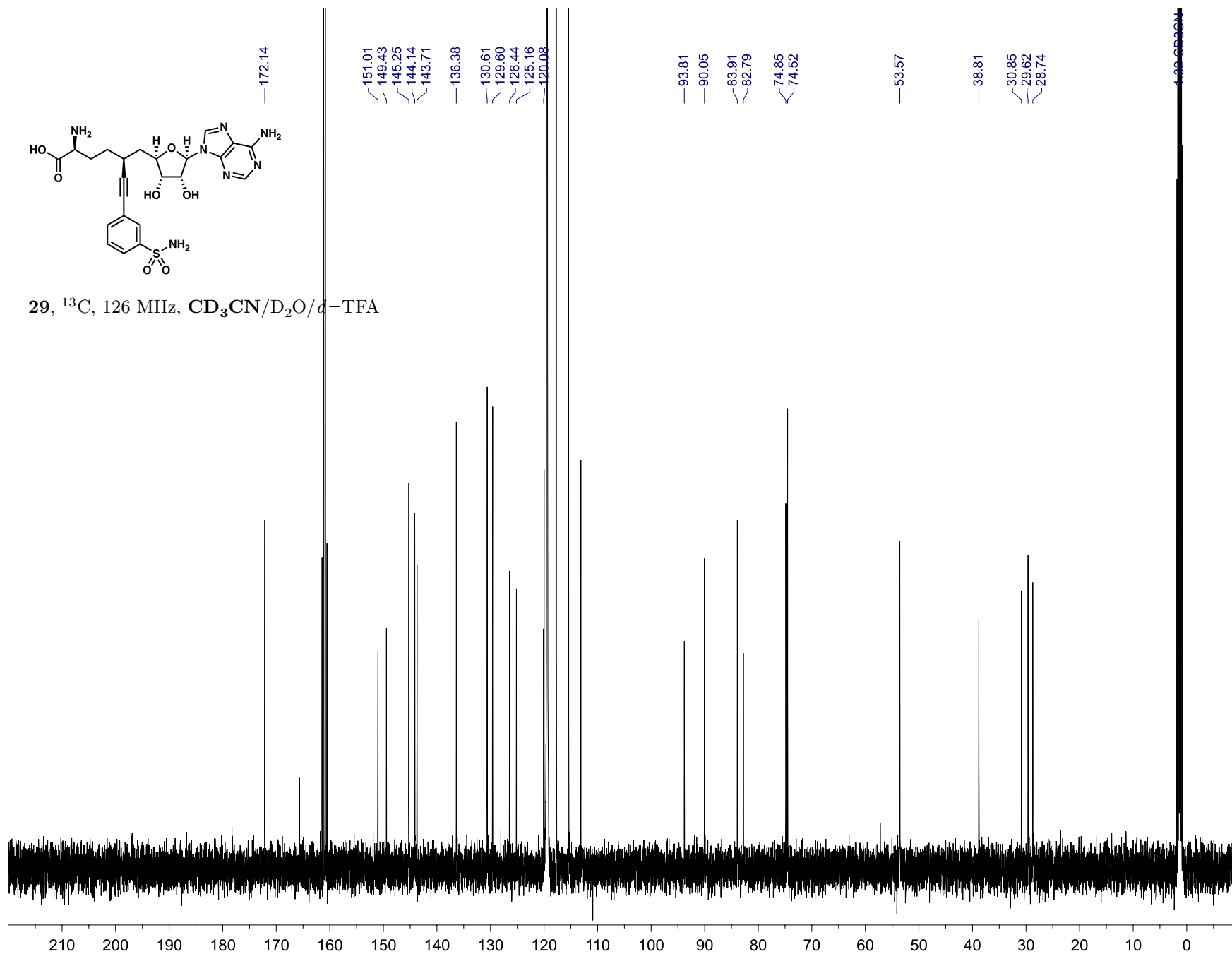
29,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

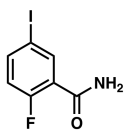
7818





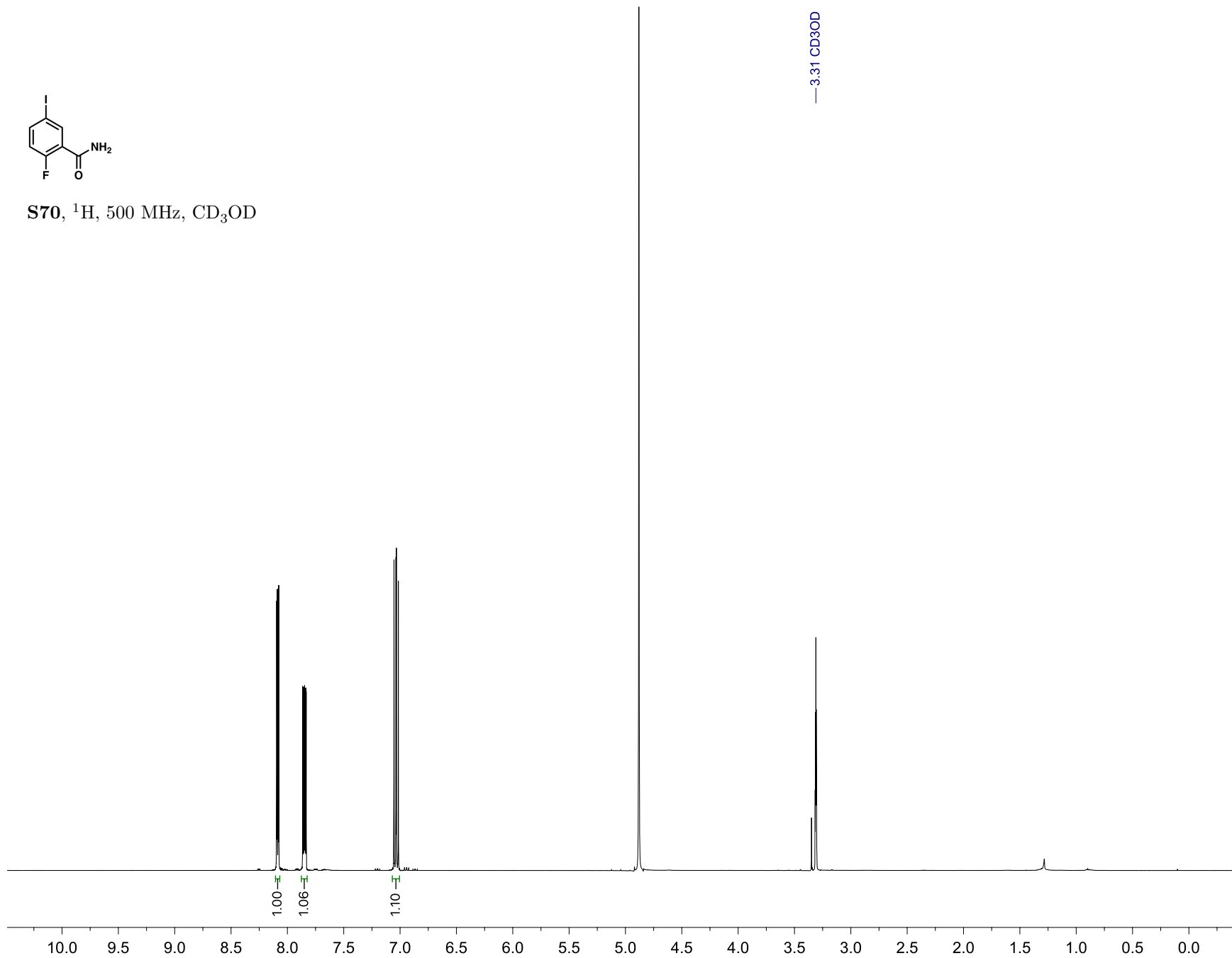
29, <sup>13</sup>C, 126 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA



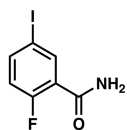


S70,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{OD}$

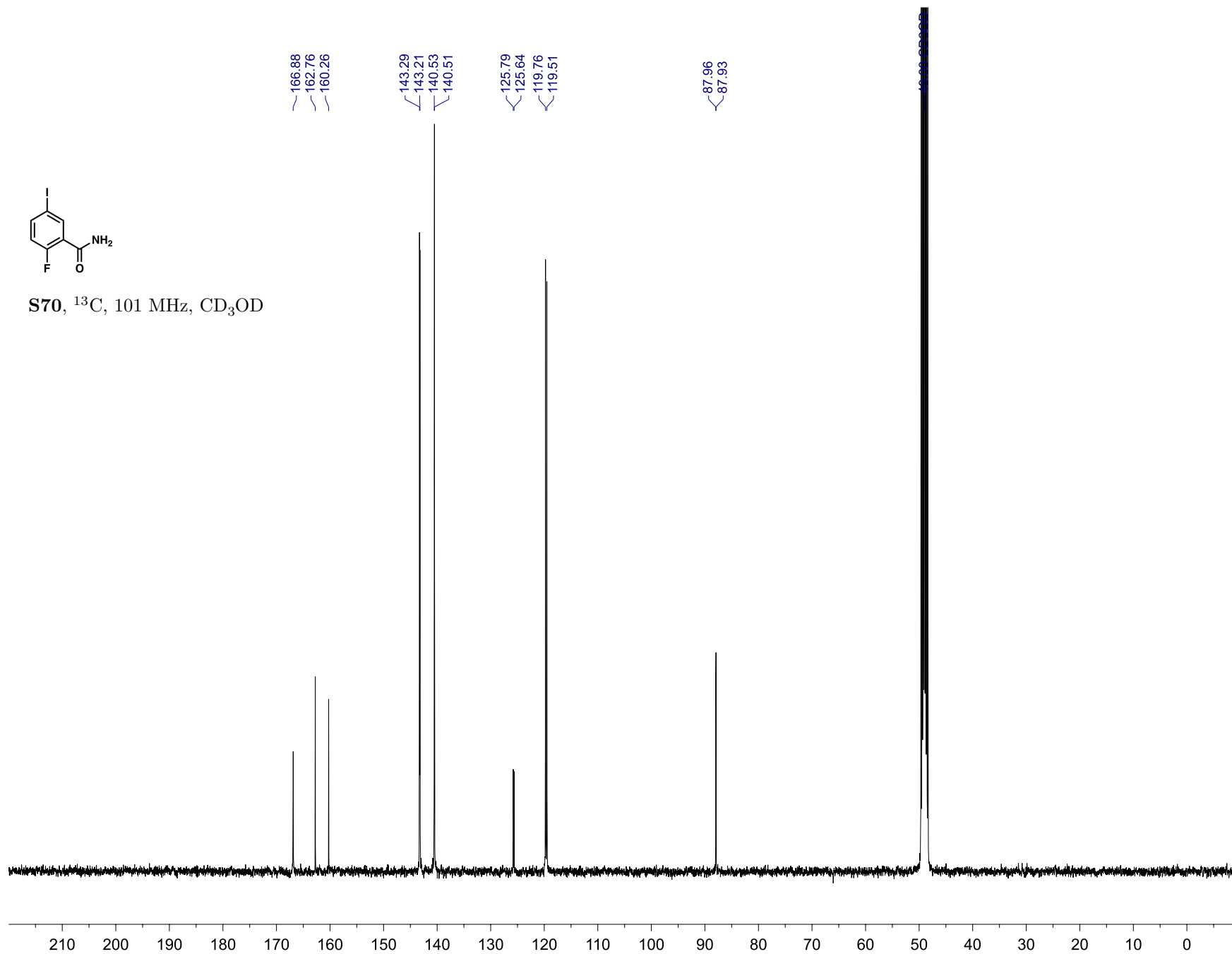
681S

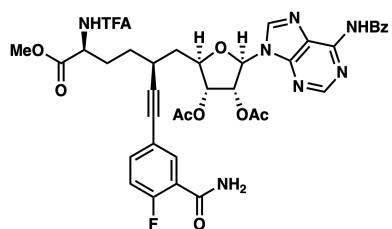


061S



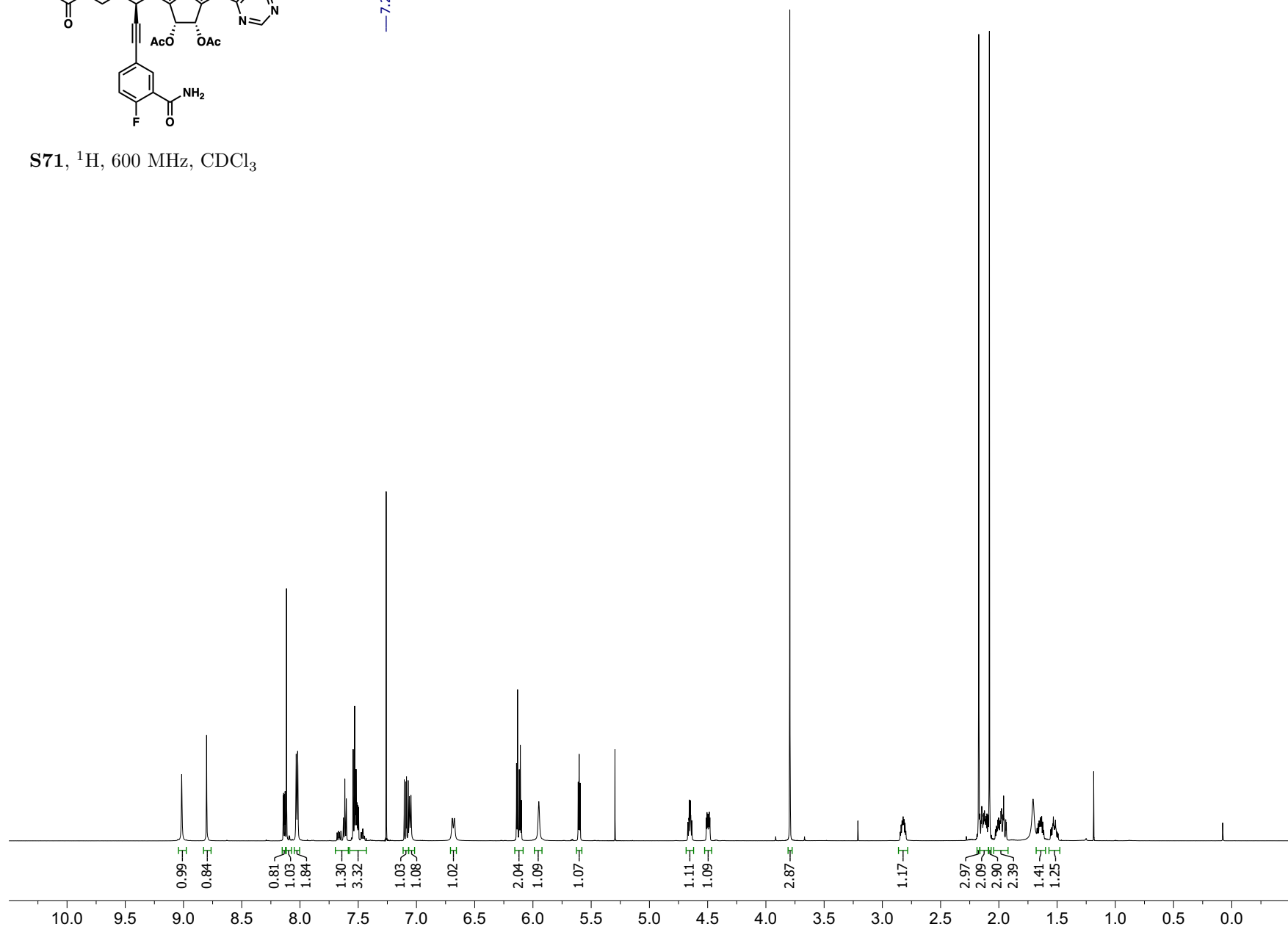
S70,  $^{13}\text{C}$ , 101 MHz,  $\text{CD}_3\text{OD}$



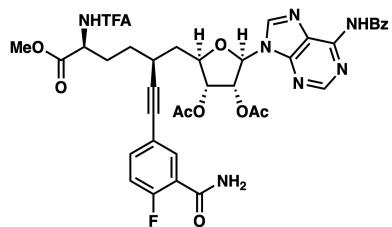
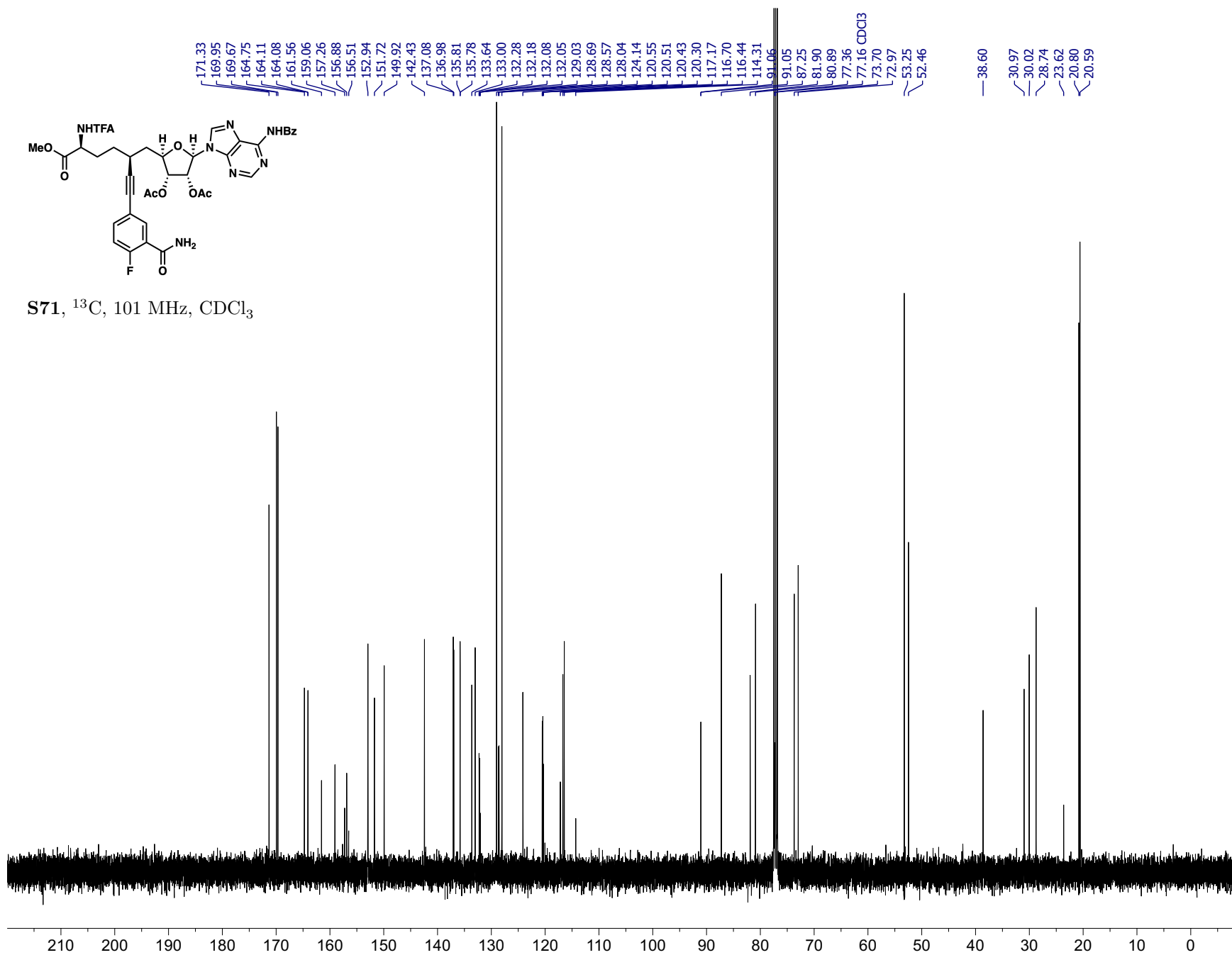


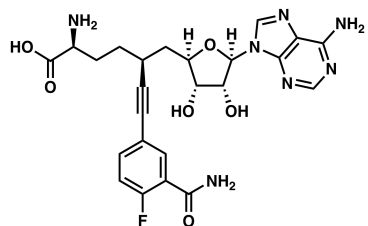
— 7.26 CDCl<sub>3</sub>

S71, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





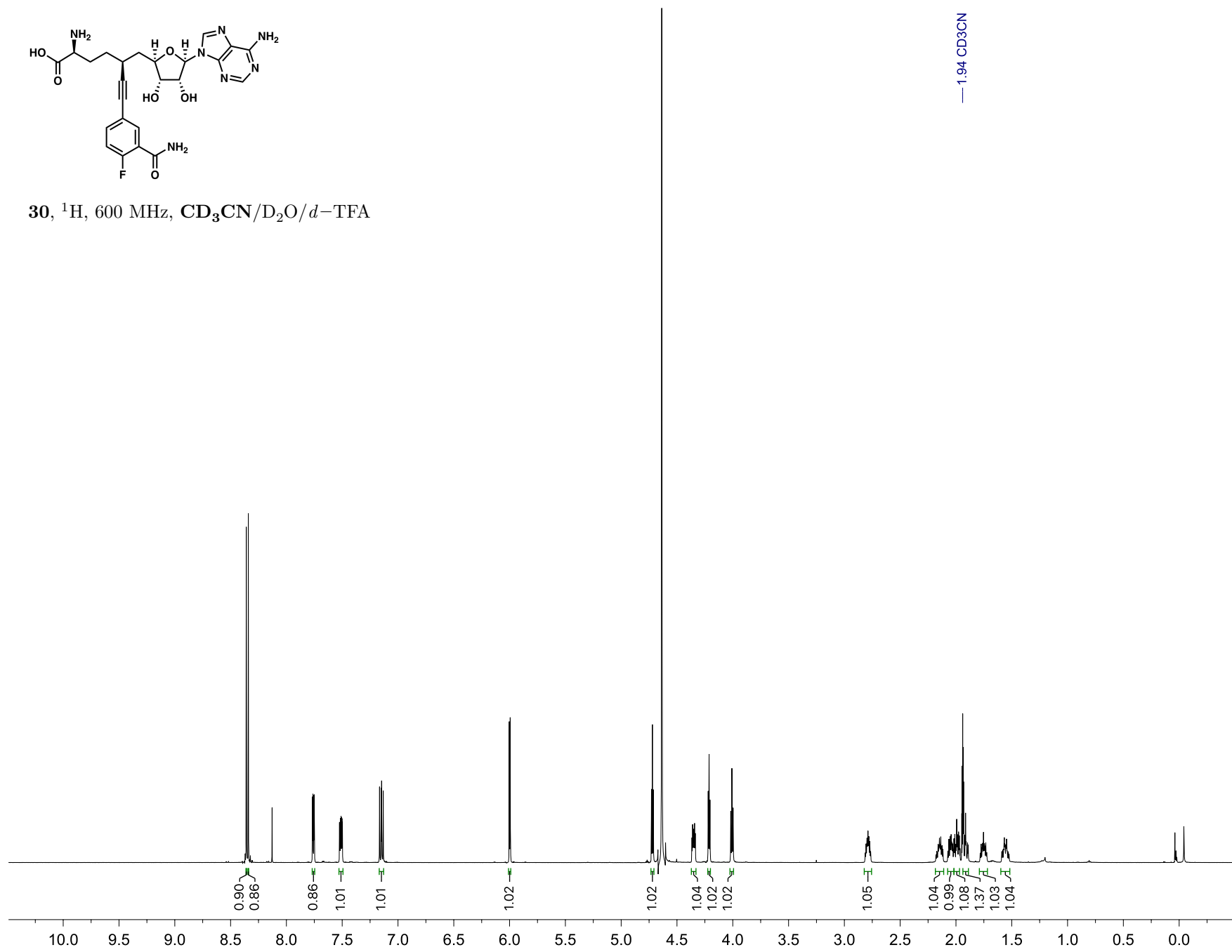
S71, <sup>13</sup>C, 101 MHz, CDCl<sub>3</sub>

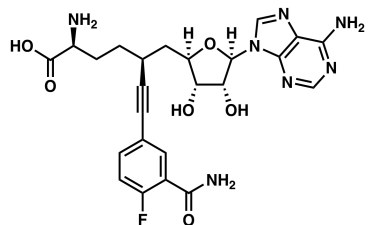


30,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

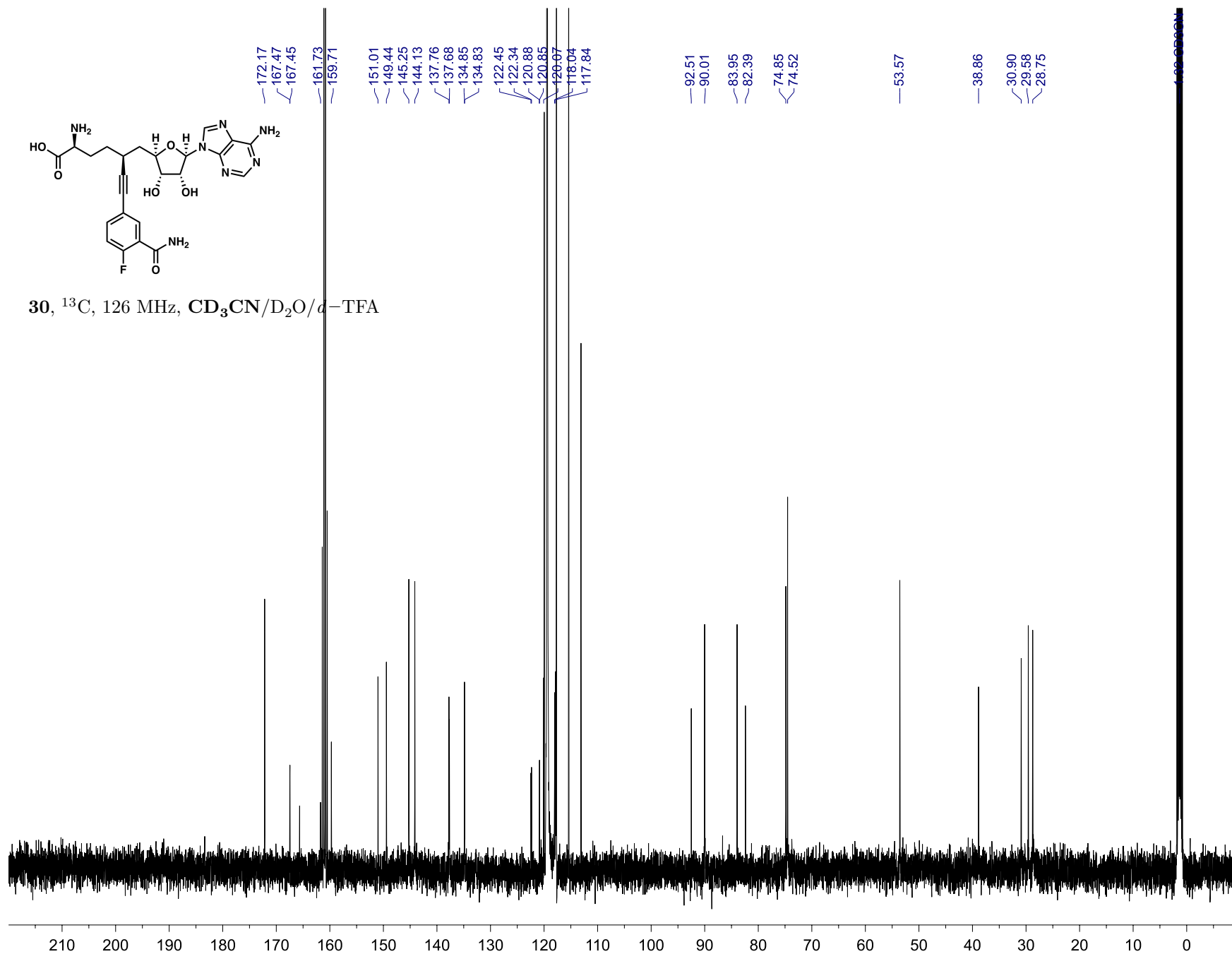
— 1.94  $\text{CD}_3\text{CN}$

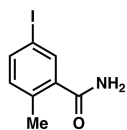
S193





**30**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

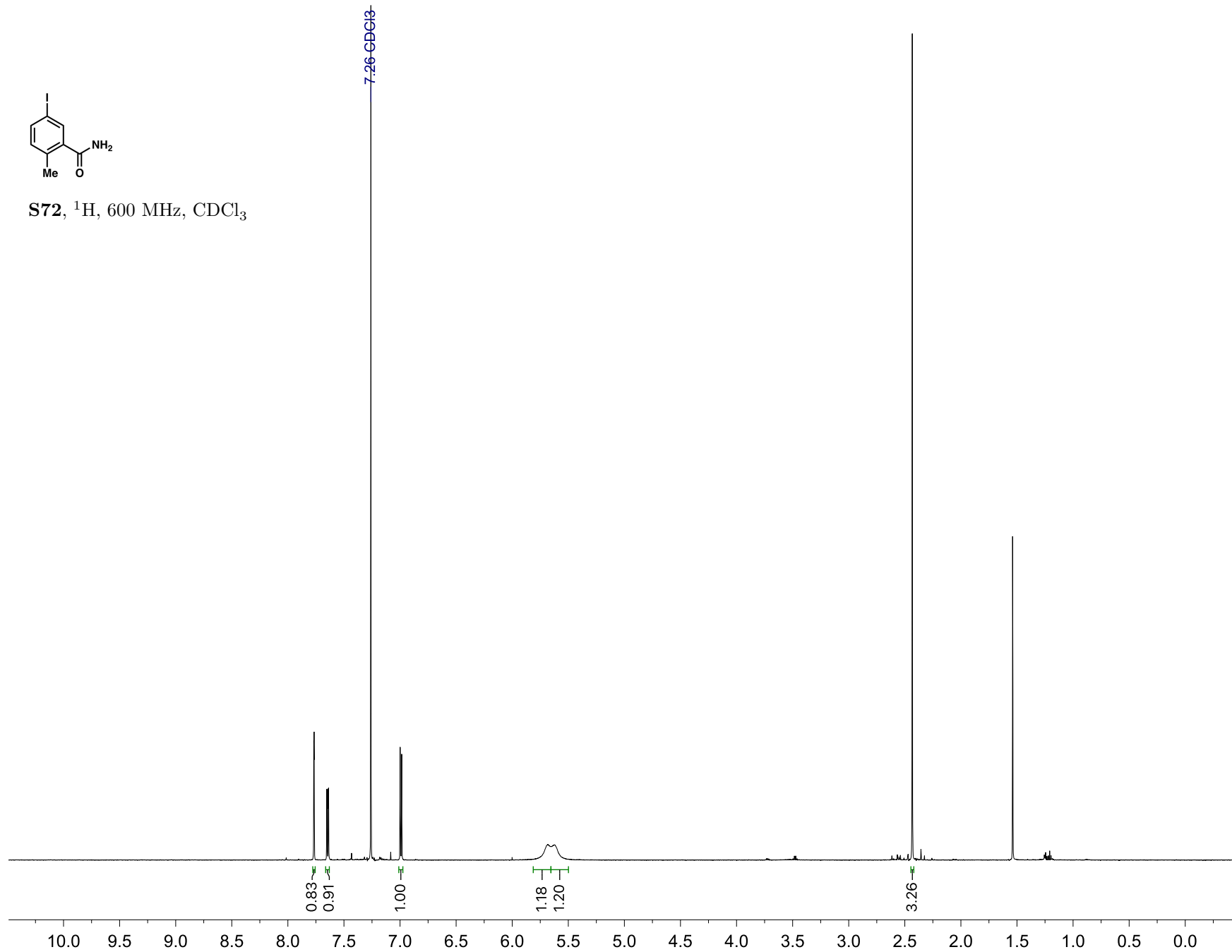




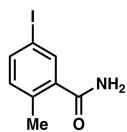
S72,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

7.26  $\text{CDCl}_3$

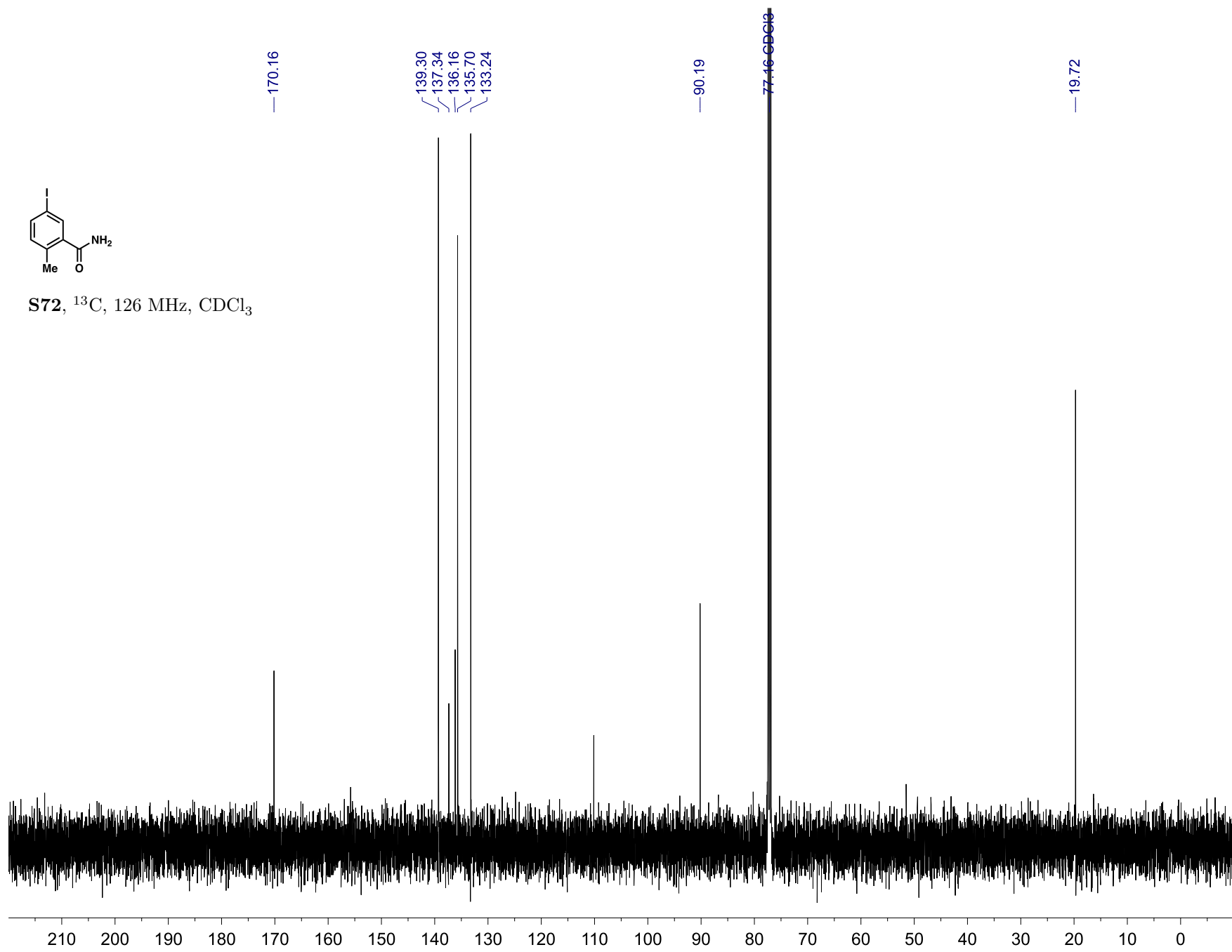
S195

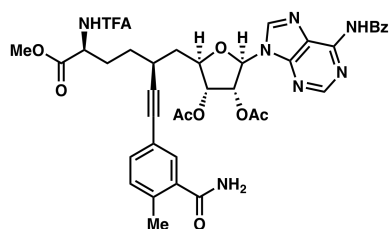


96IS



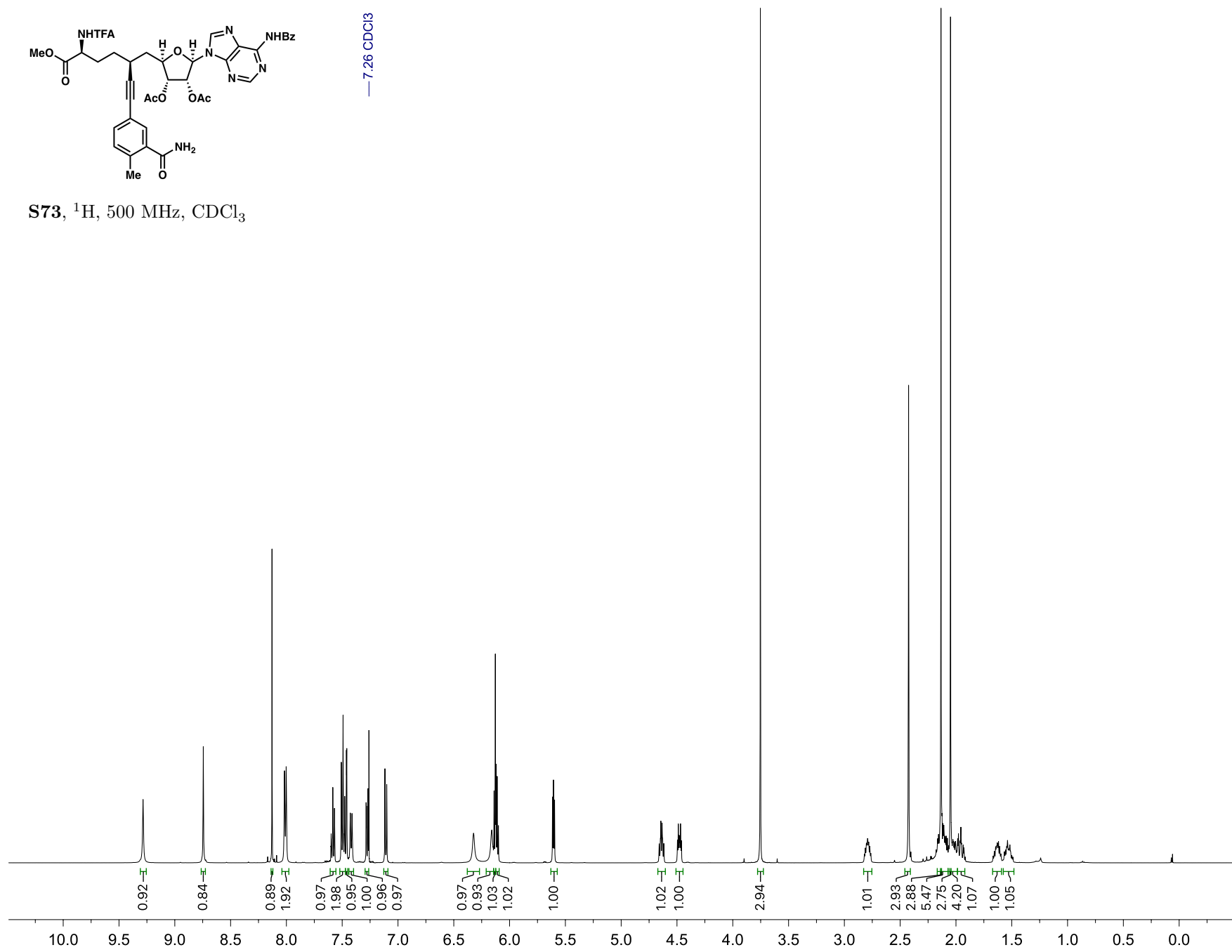
S72,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

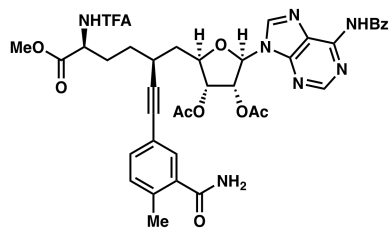




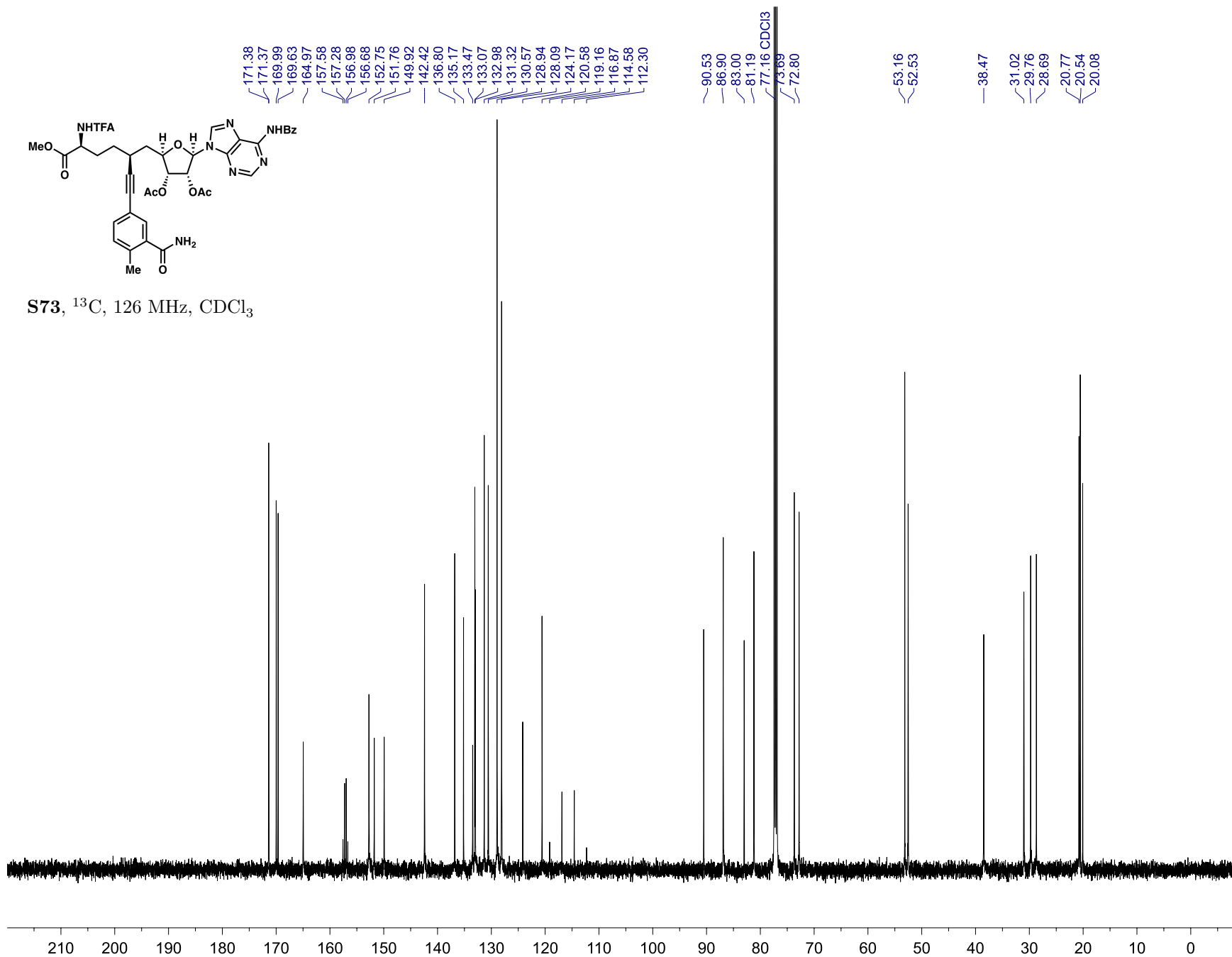
— 7.26 CDCl<sub>3</sub>

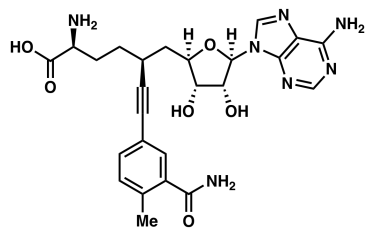
**S73**, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>



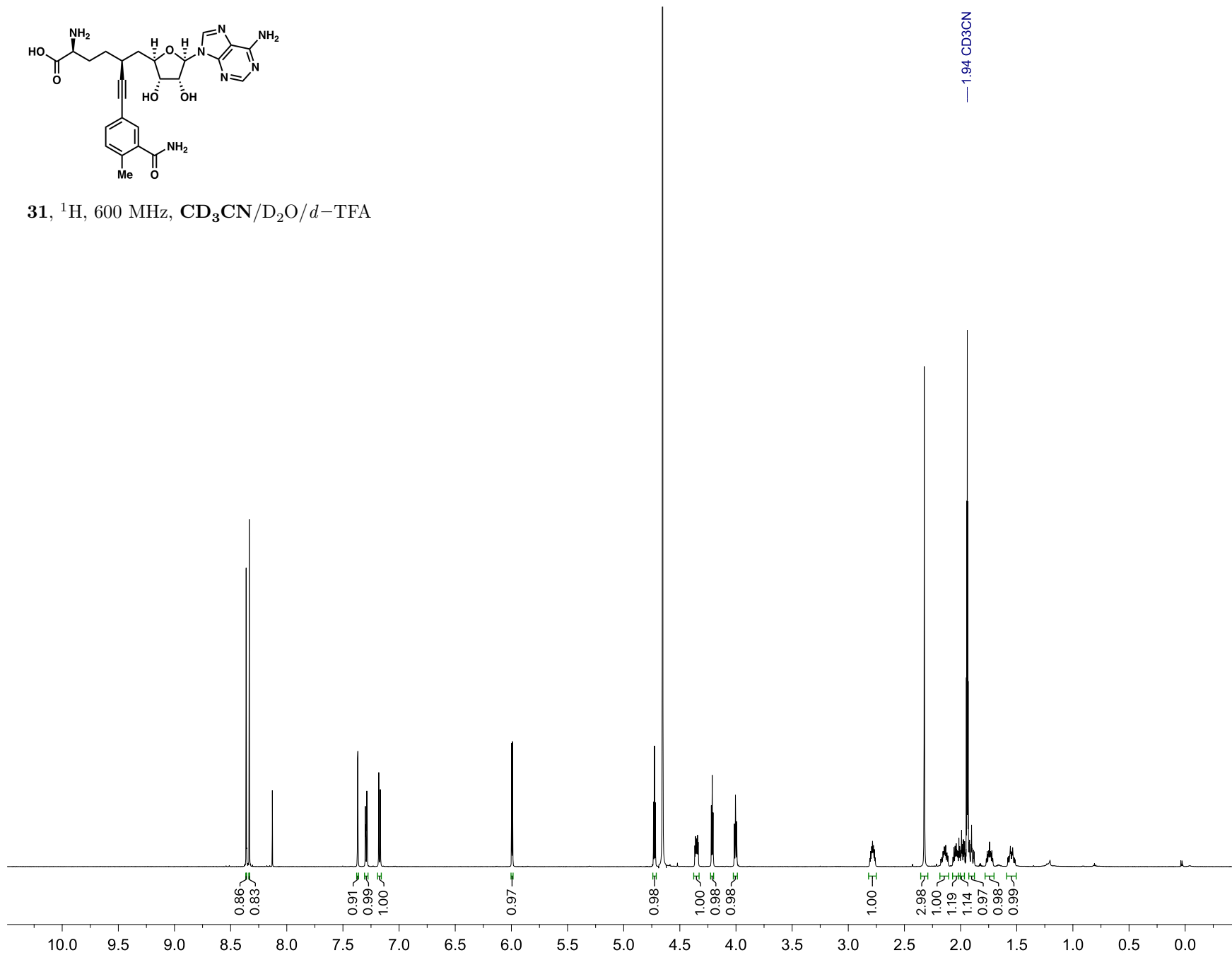


**S73**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



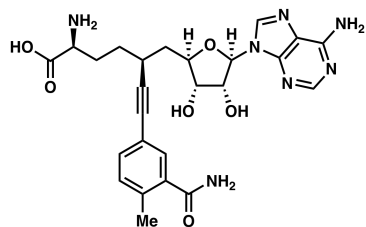


31,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

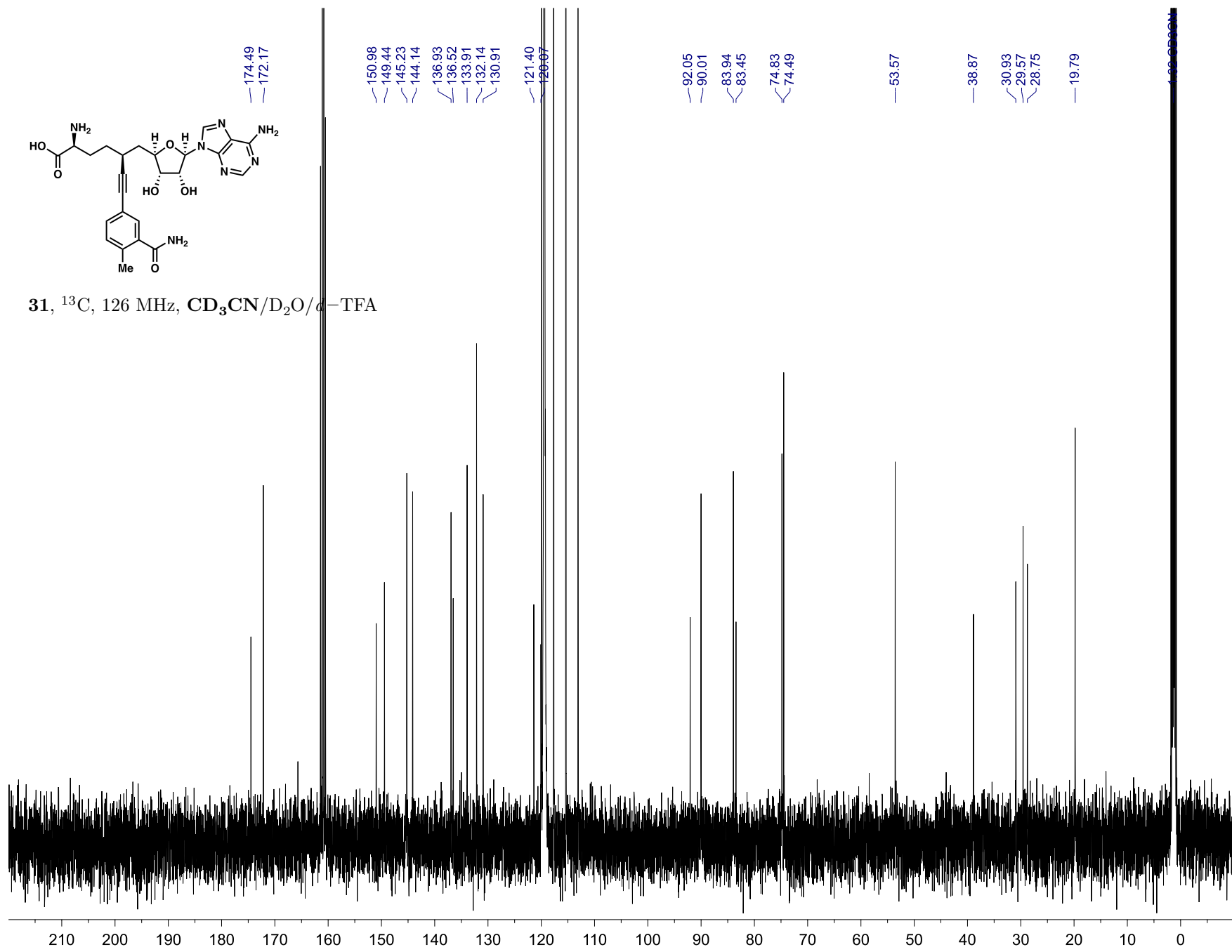


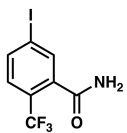


S200



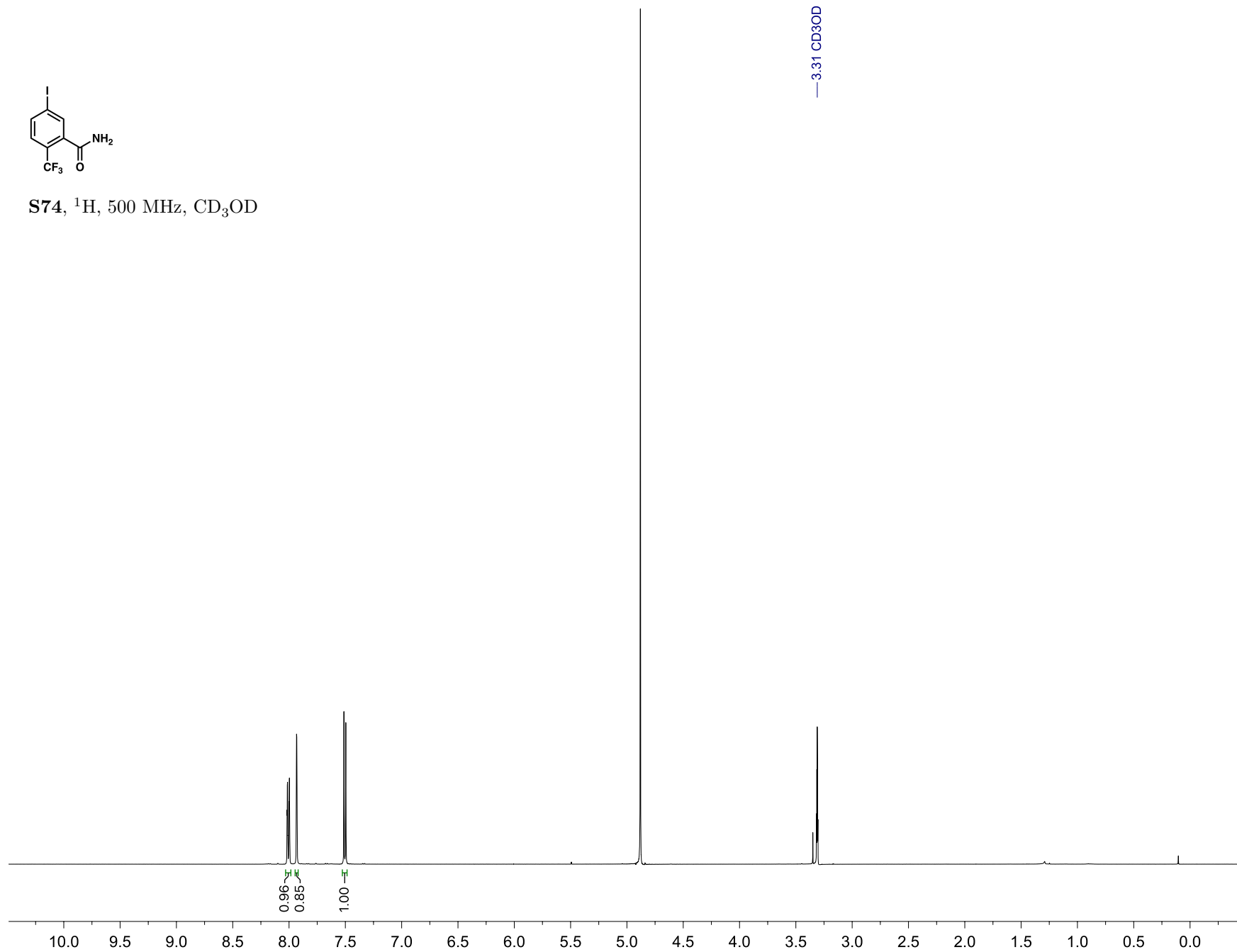
31,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

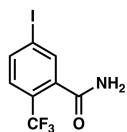




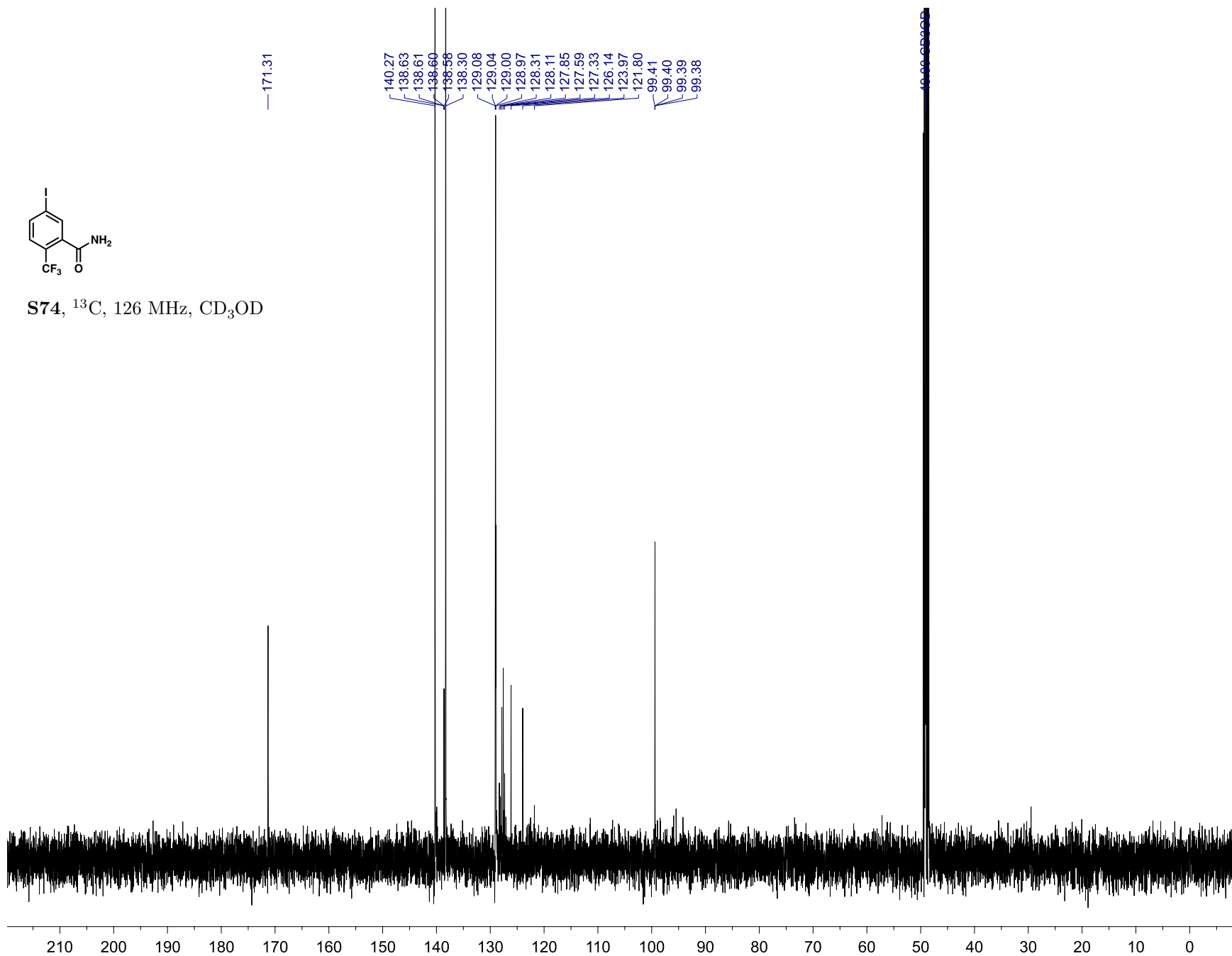
S74,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{OD}$

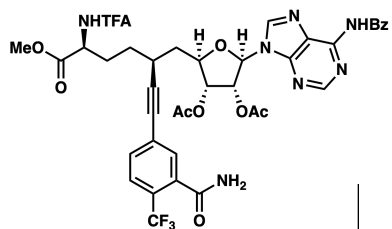
S201



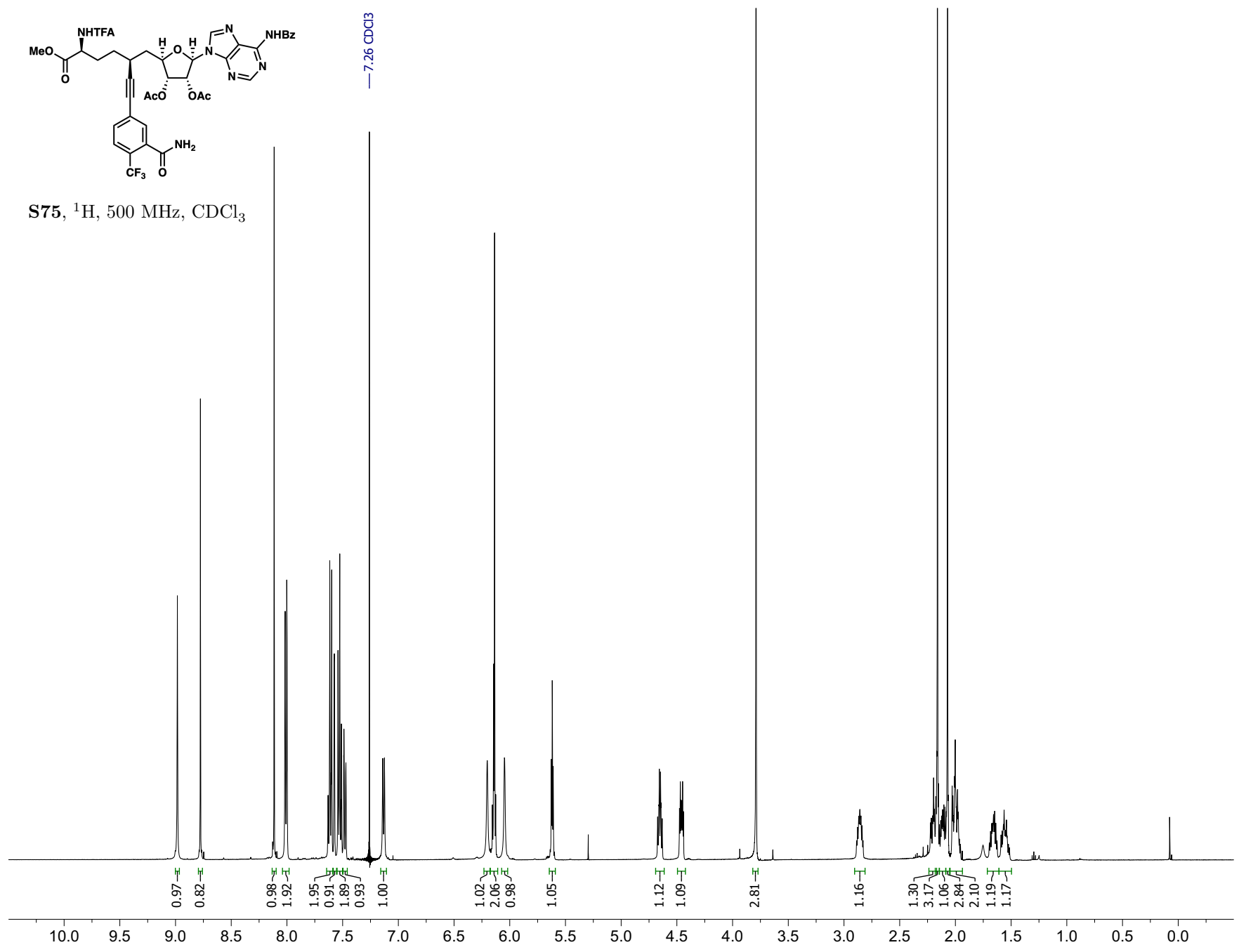


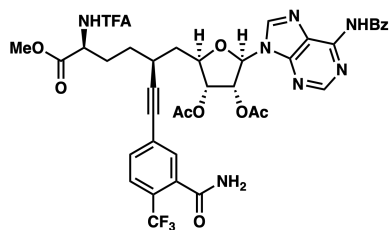
S74,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{OD}$



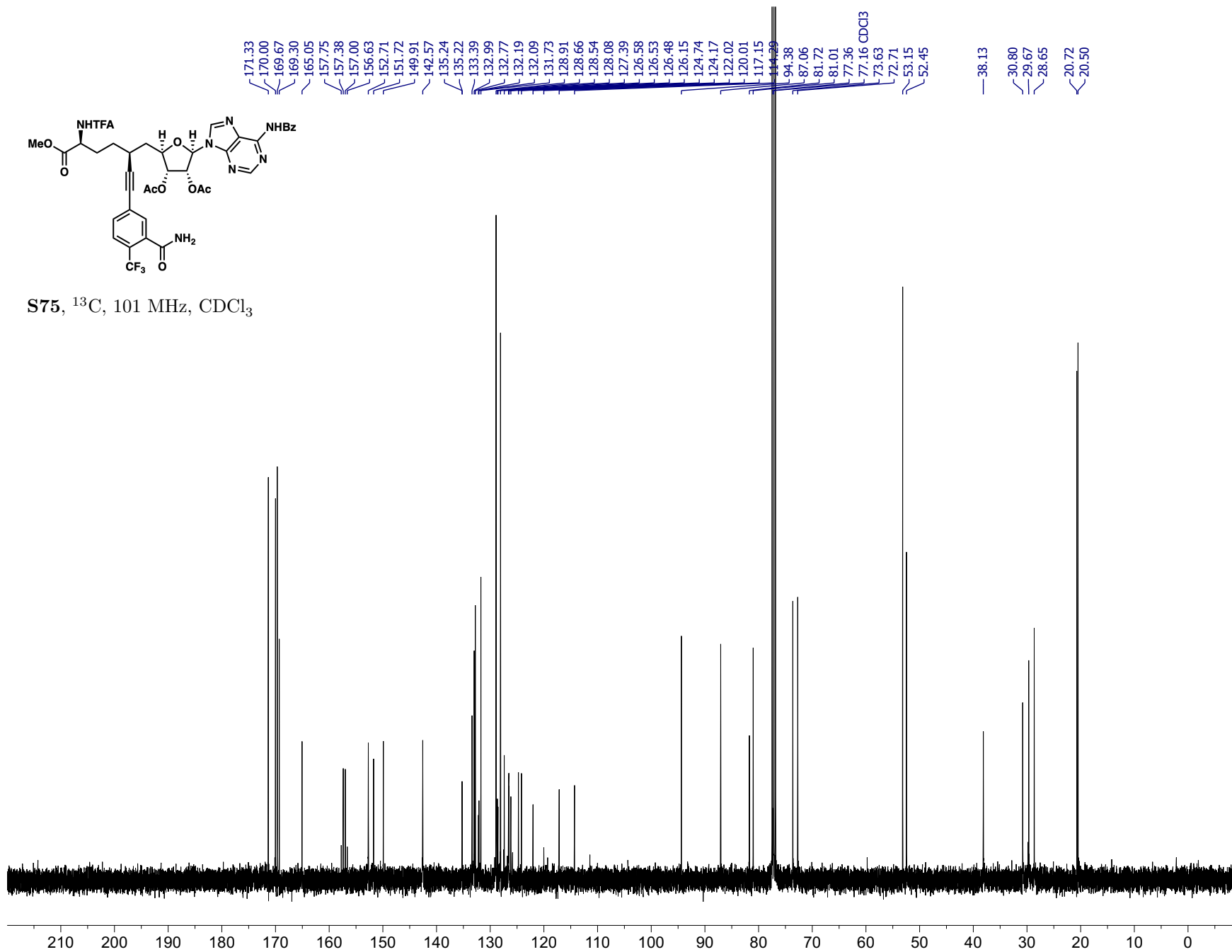


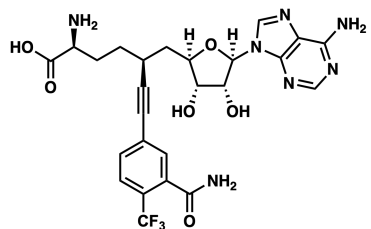
S75, <sup>1</sup>H, 500 MHz, CDCl<sub>3</sub>



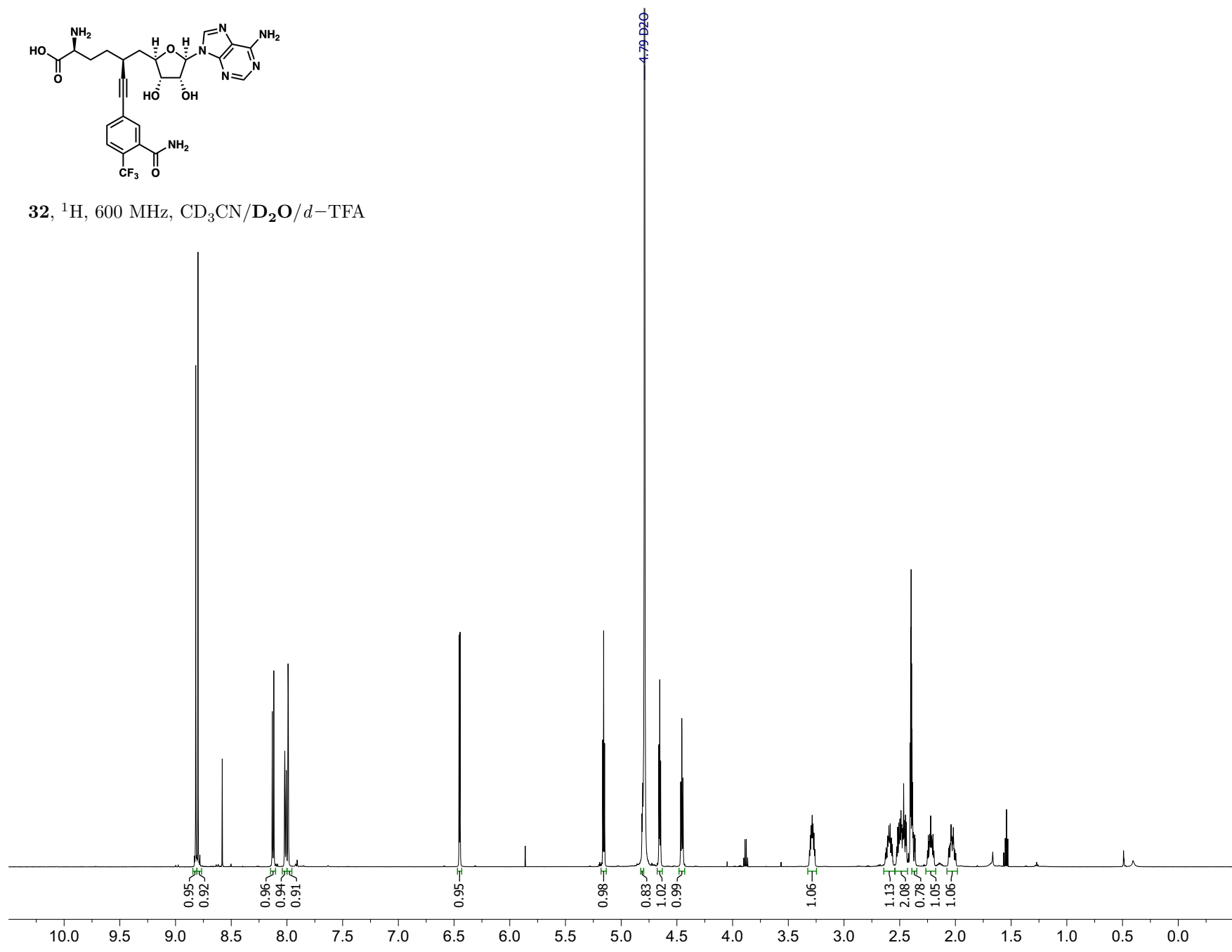


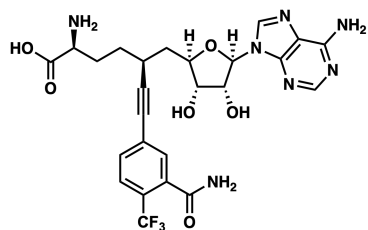
S75,  $^{13}\text{C}$ , 101 MHz,  $\text{CDCl}_3$



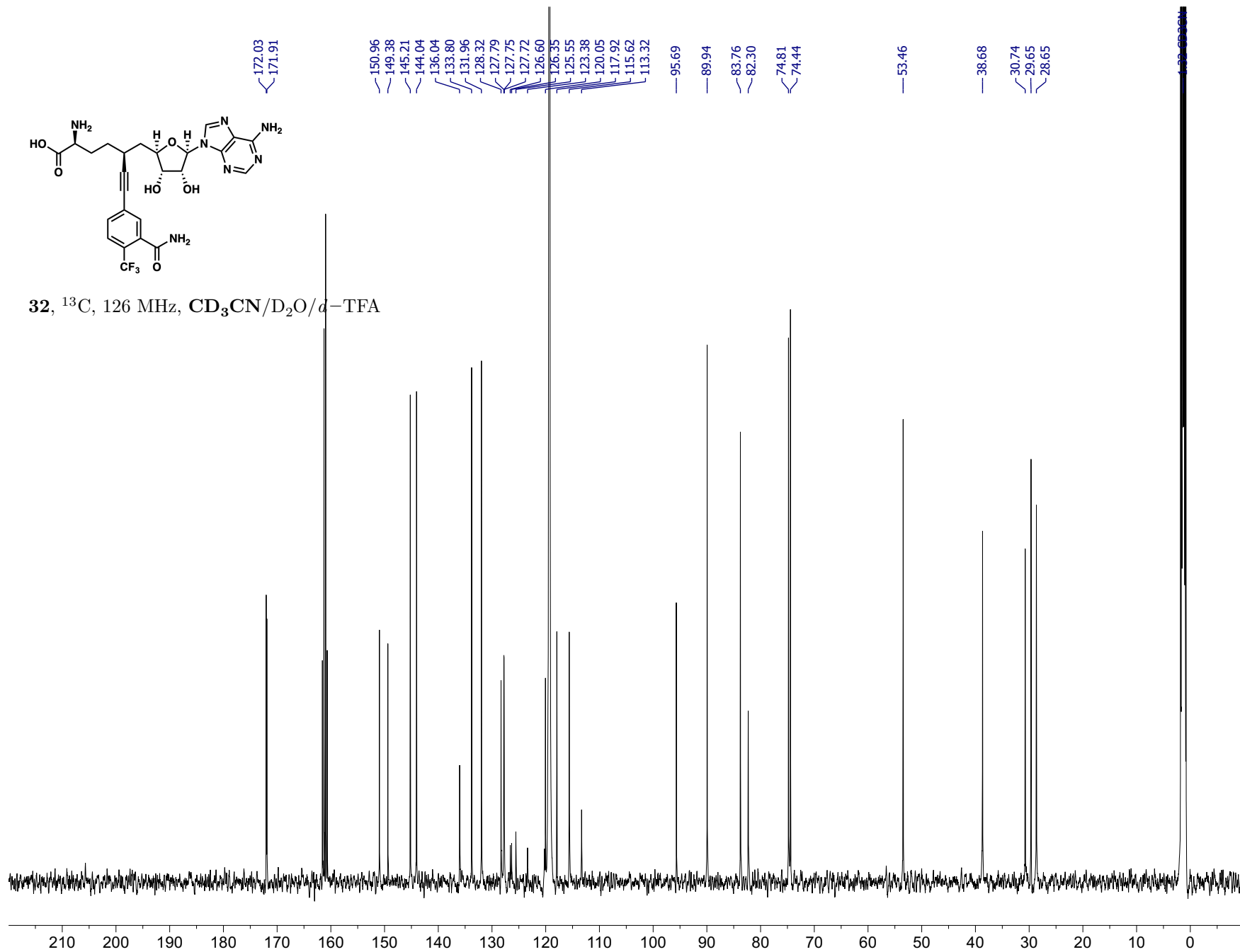


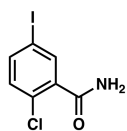
32, <sup>1</sup>H, 600 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA





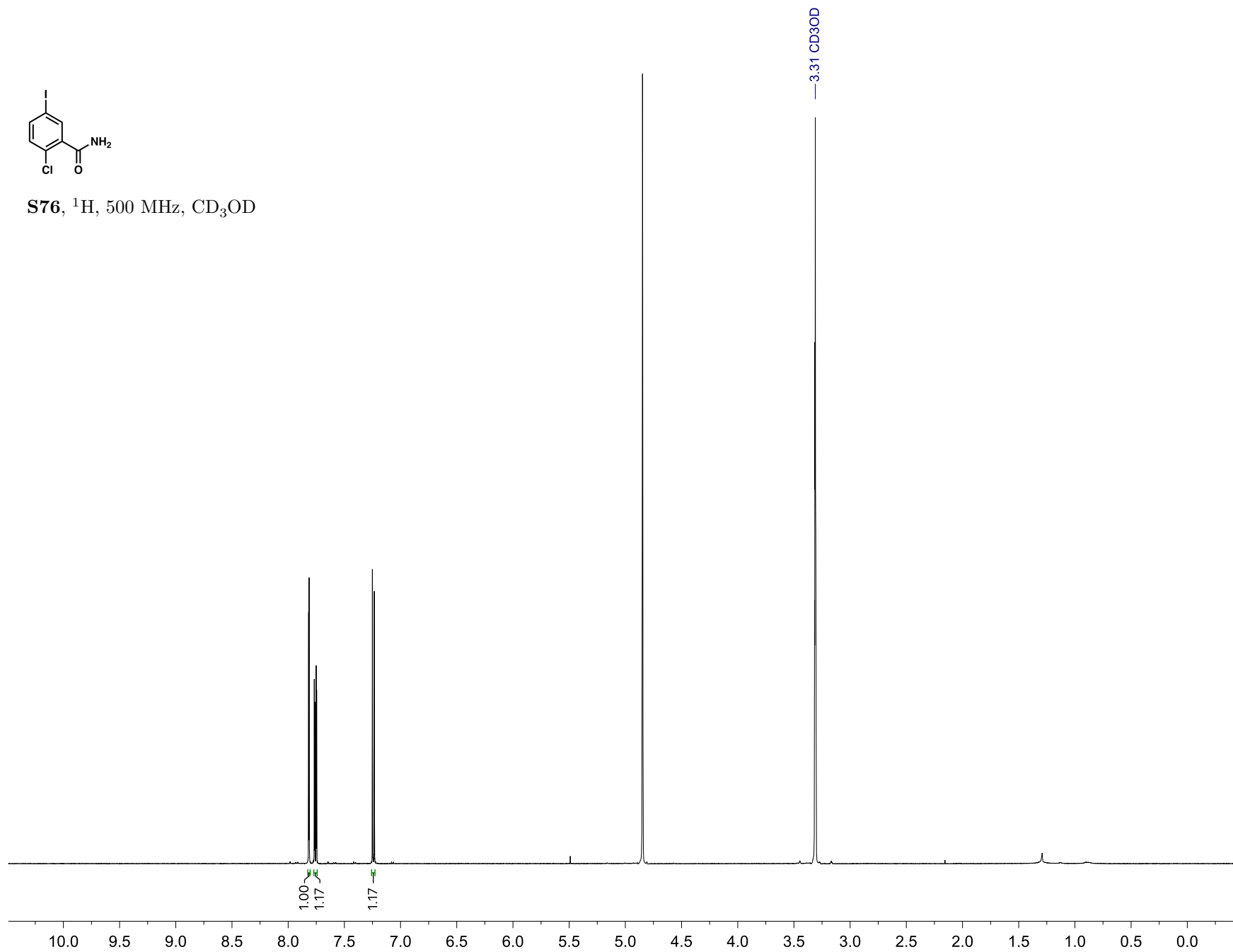
**32**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$





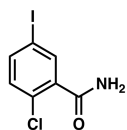
S76,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{OD}$

S207

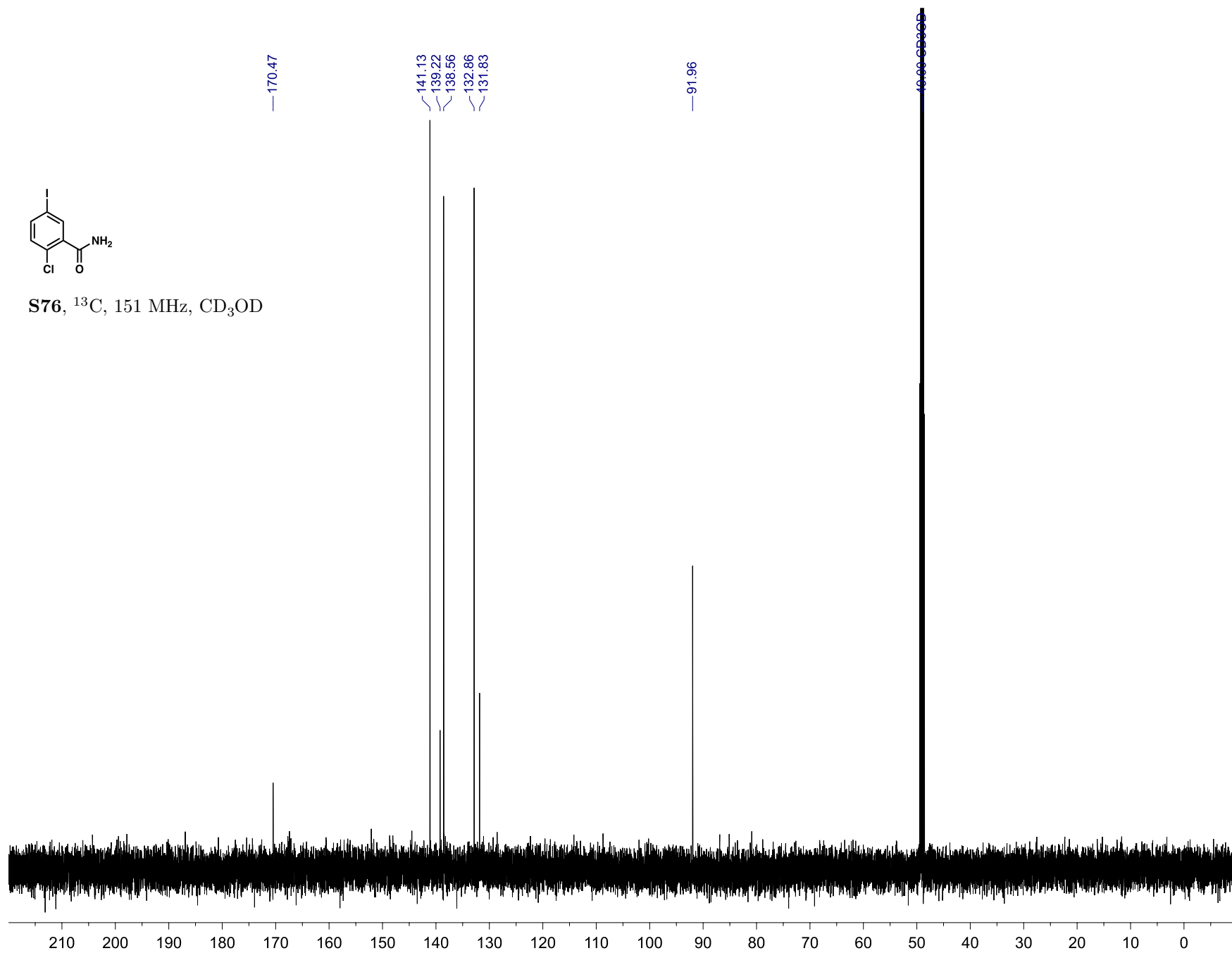


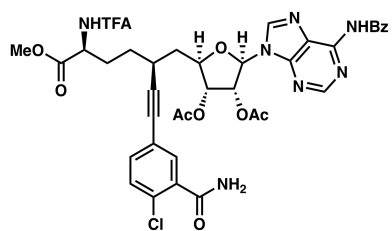


S208



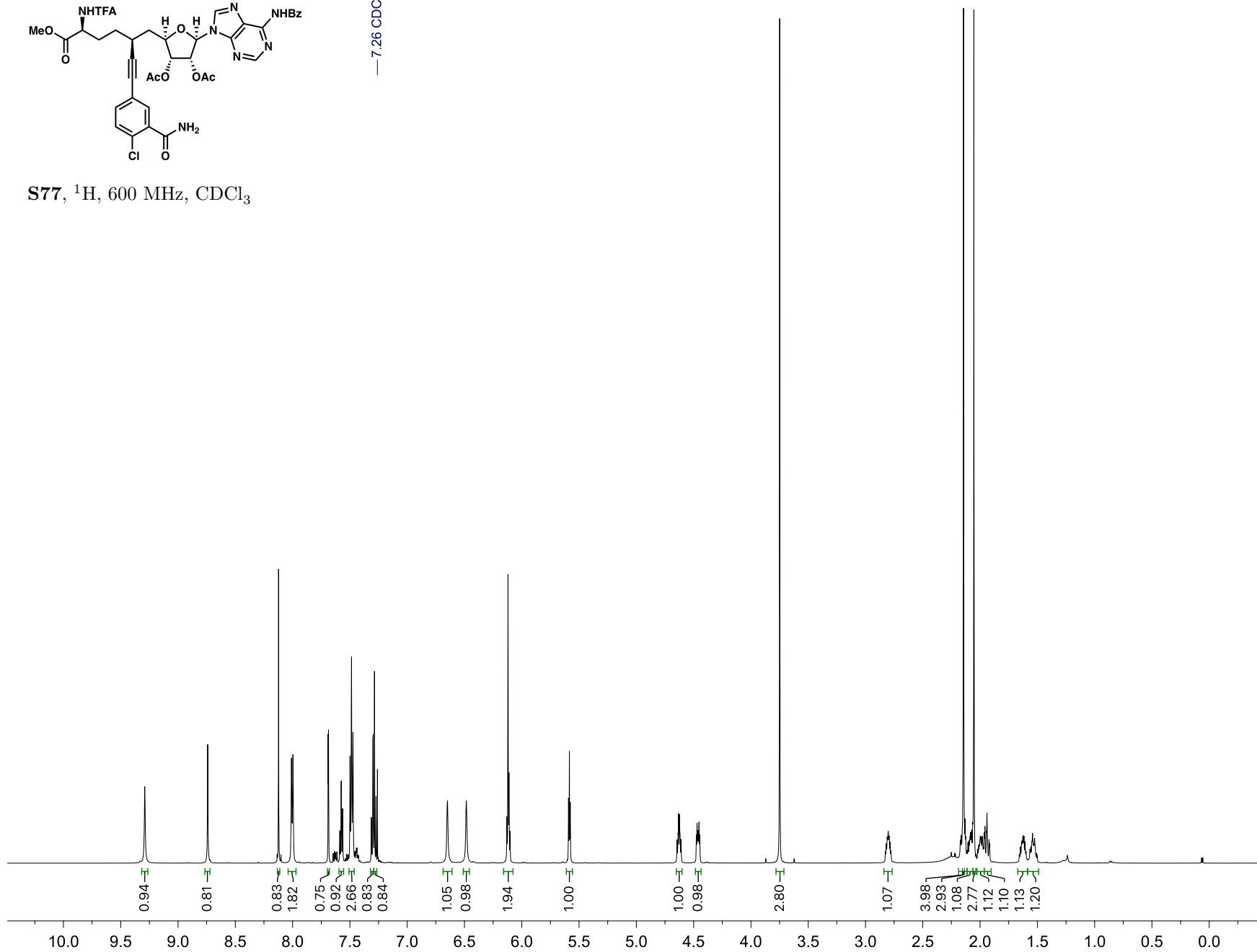
S76,  $^{13}\text{C}$ , 151 MHz,  $\text{CD}_3\text{OD}$

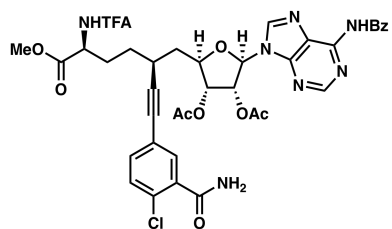




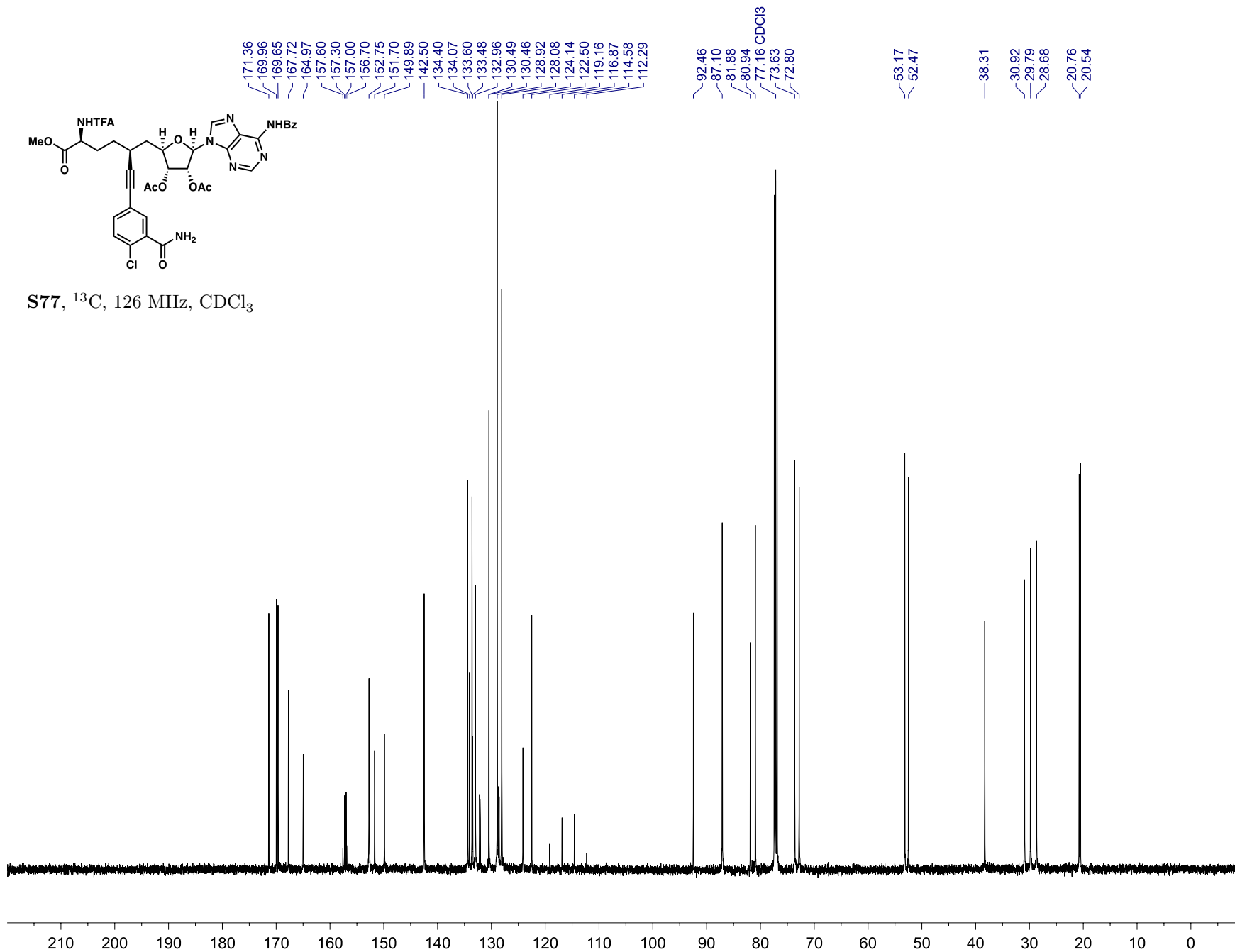
— 7.26 CDCl<sub>3</sub>

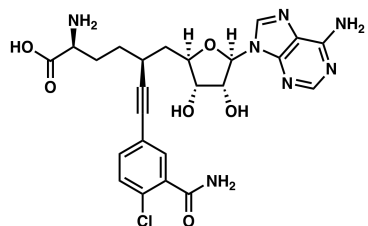
S77, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>



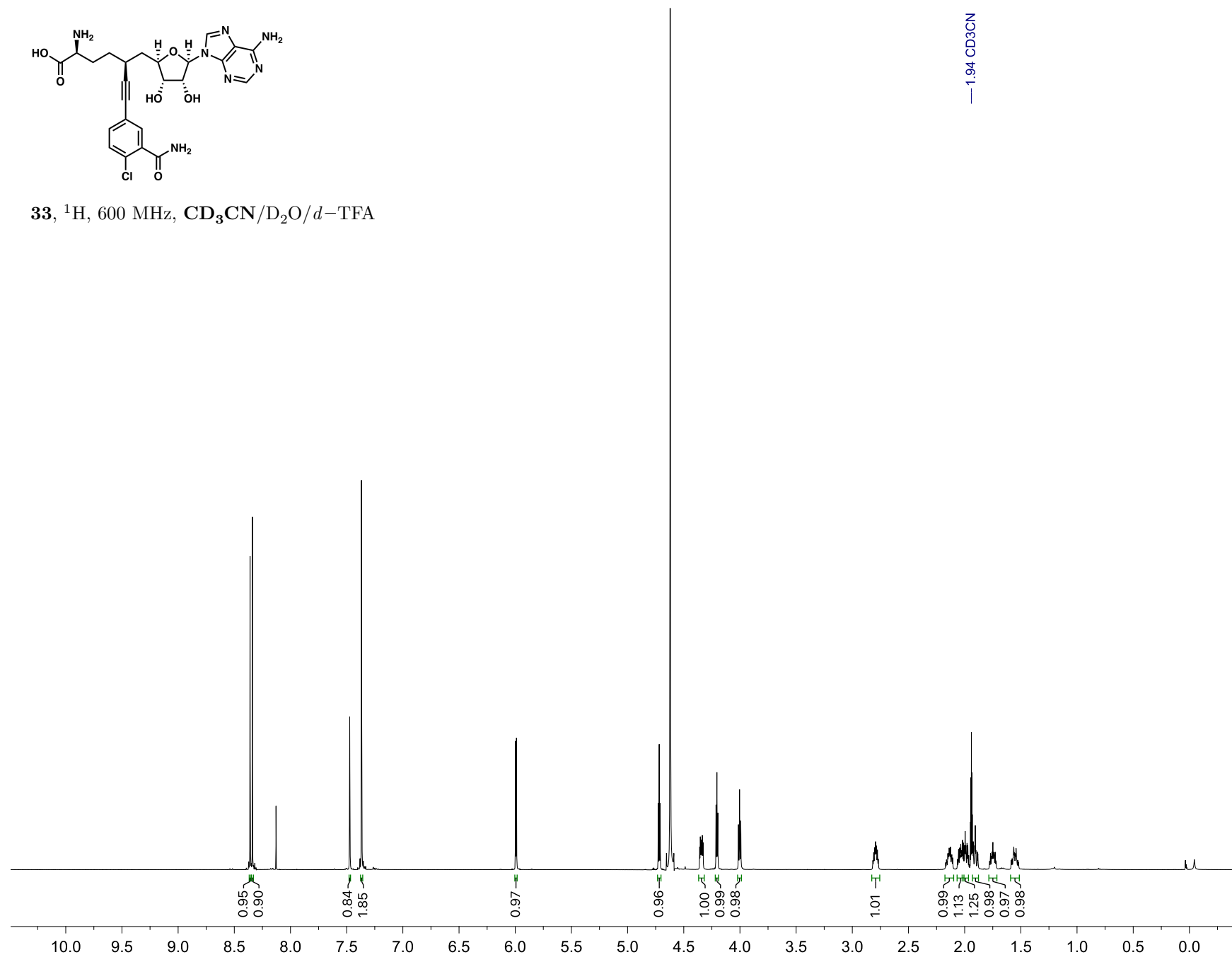


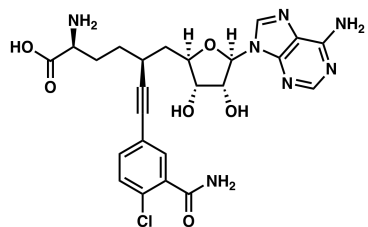
S77,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



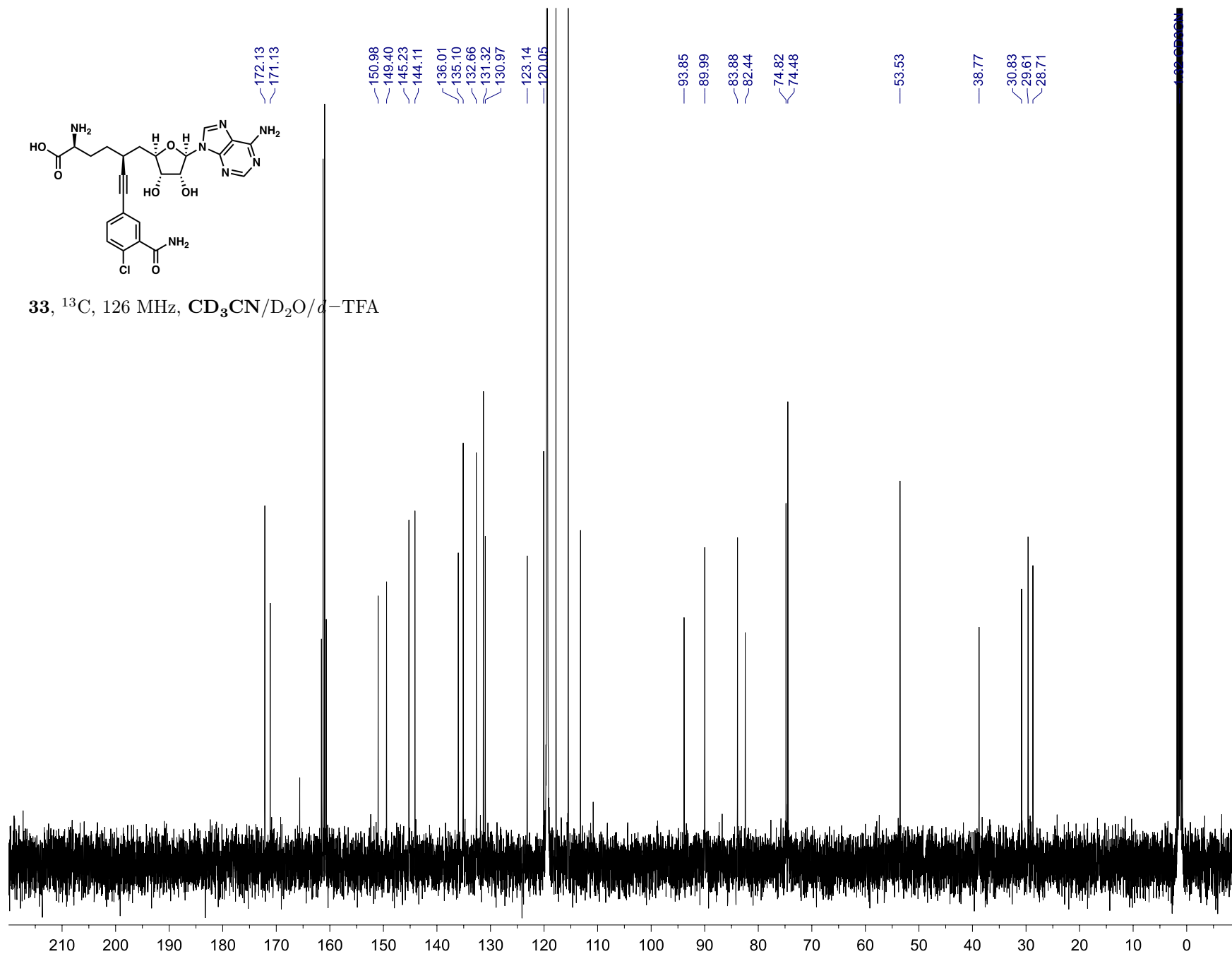


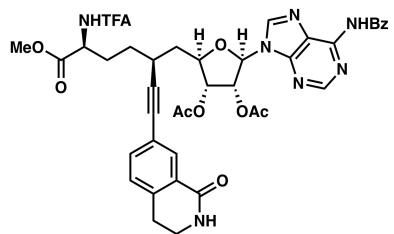
**33**,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$





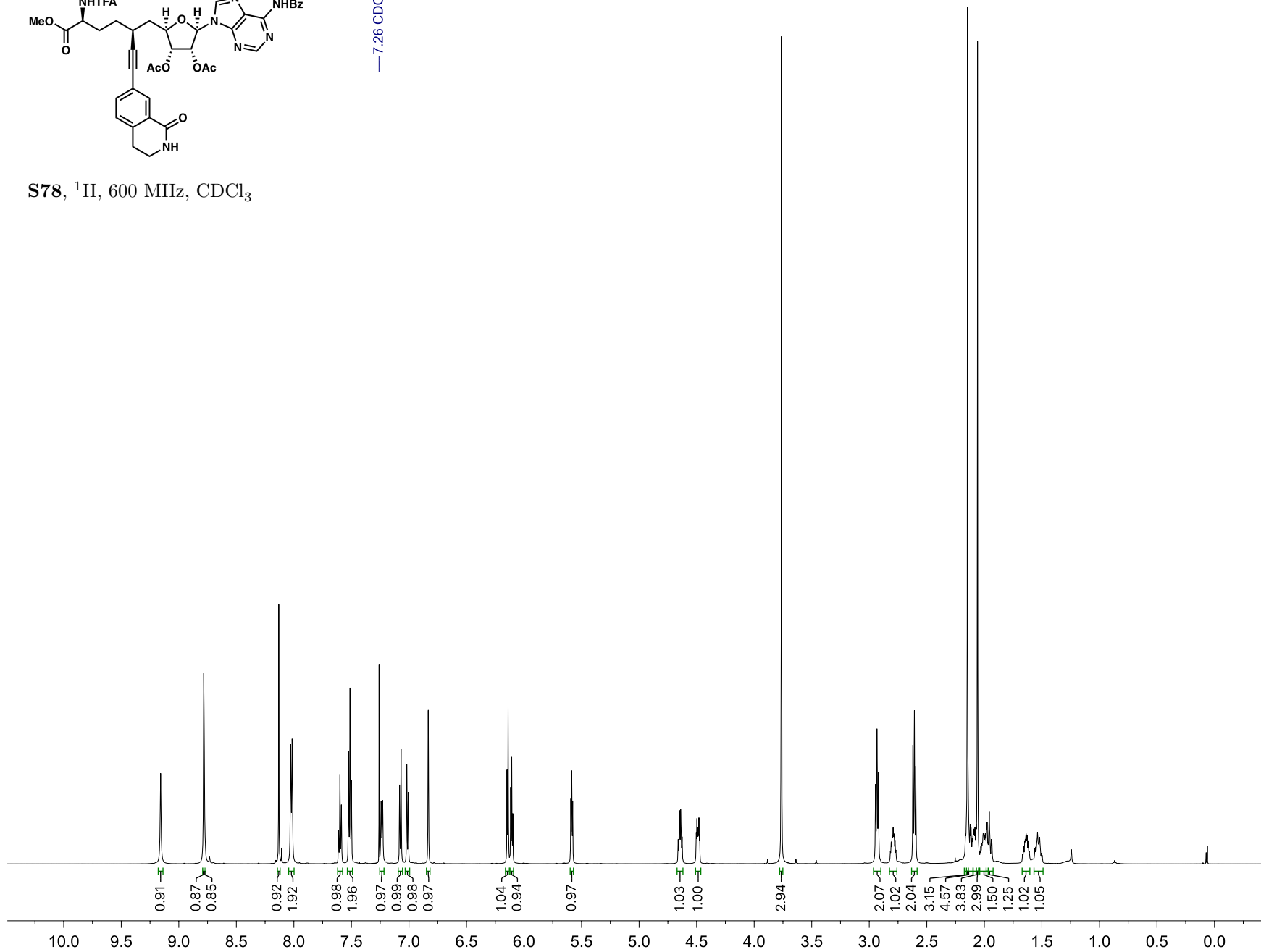
**33**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

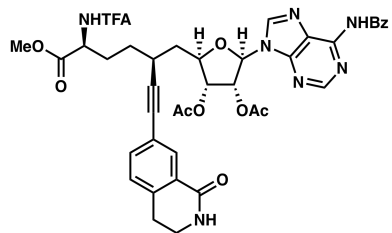




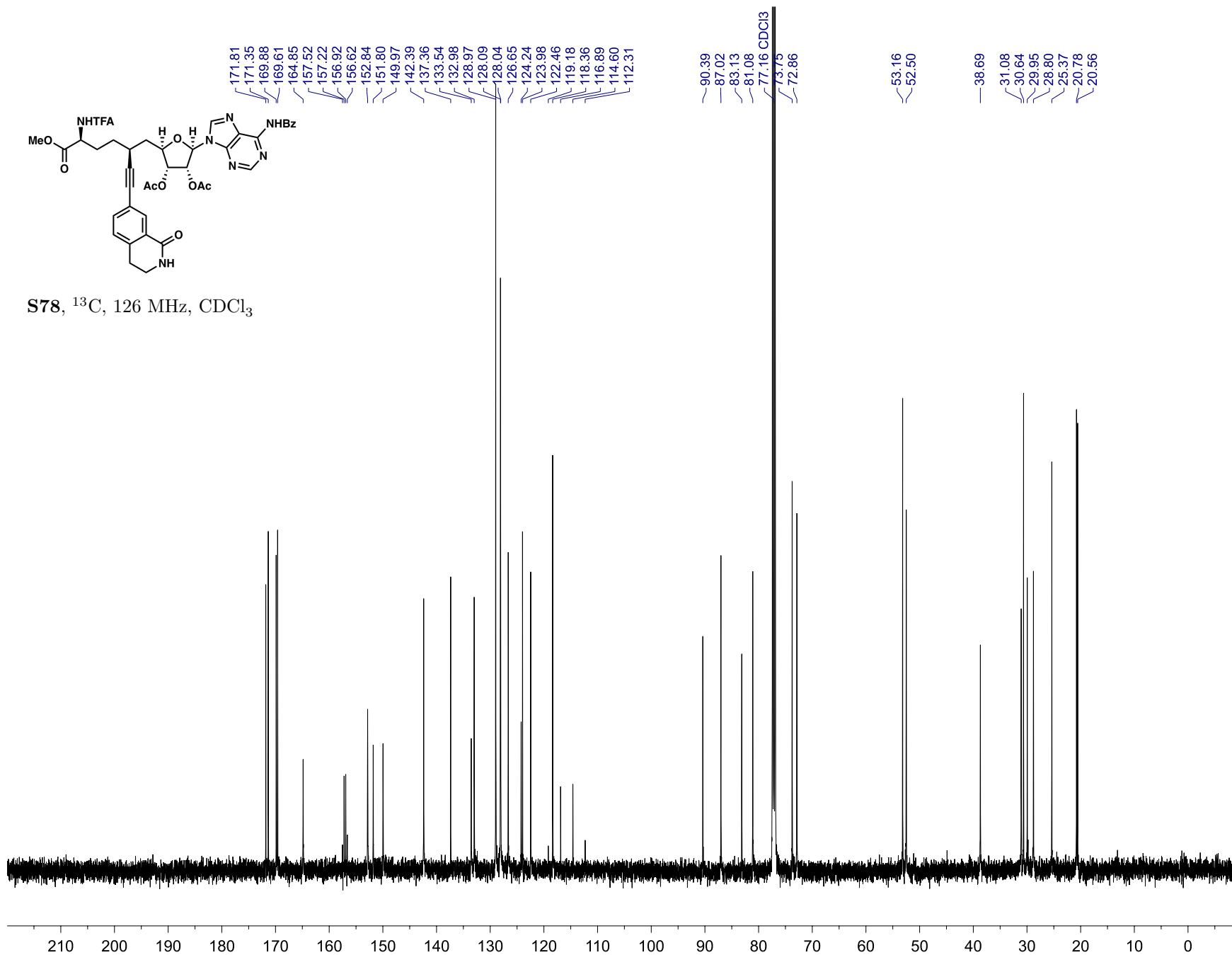
S78,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$

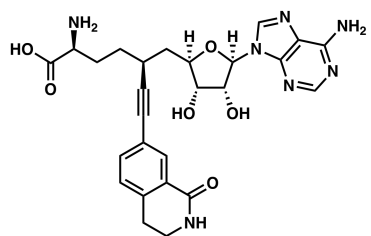
— 7.26  $\text{CDCl}_3$





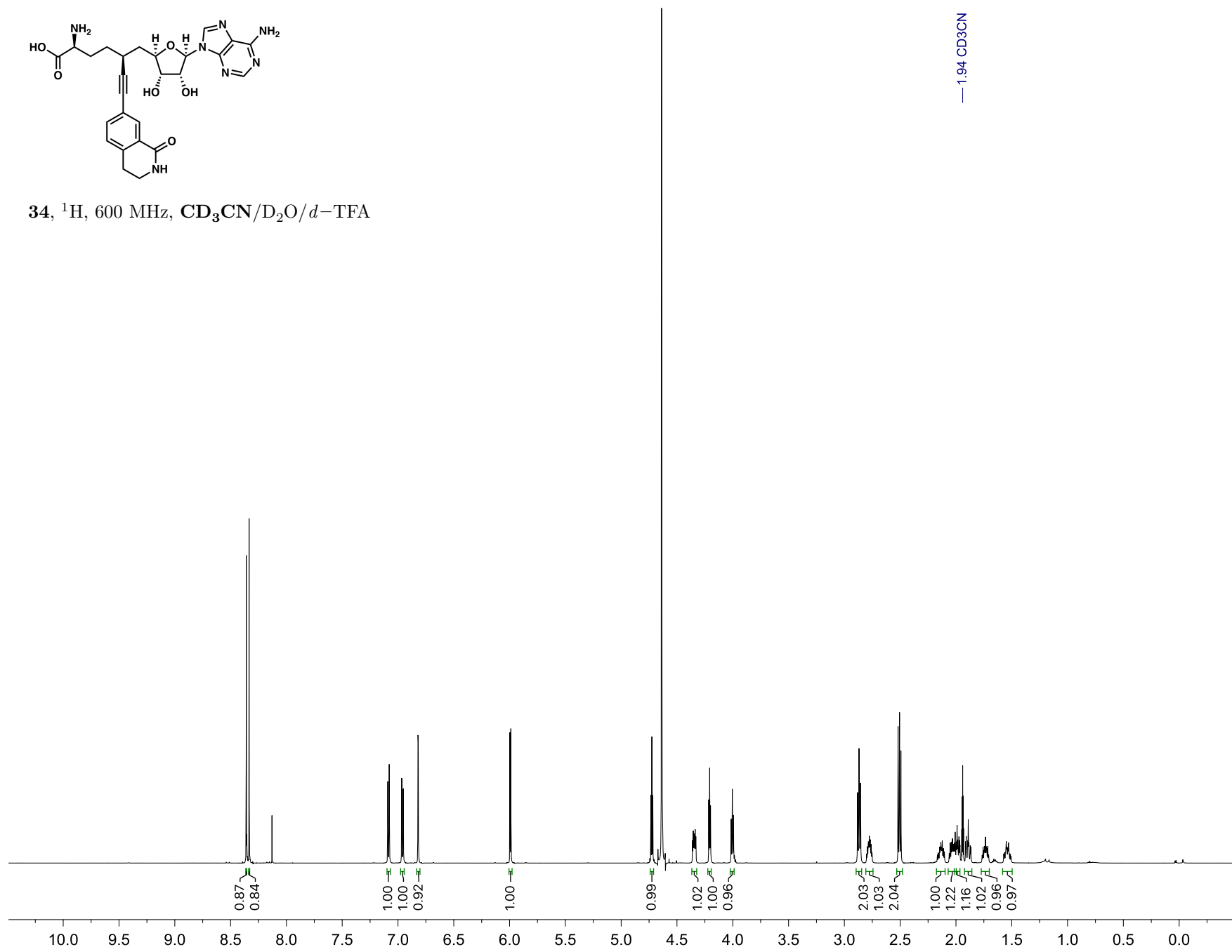
S78,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$



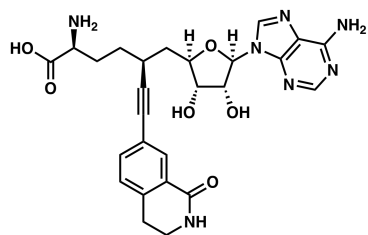


**34**,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

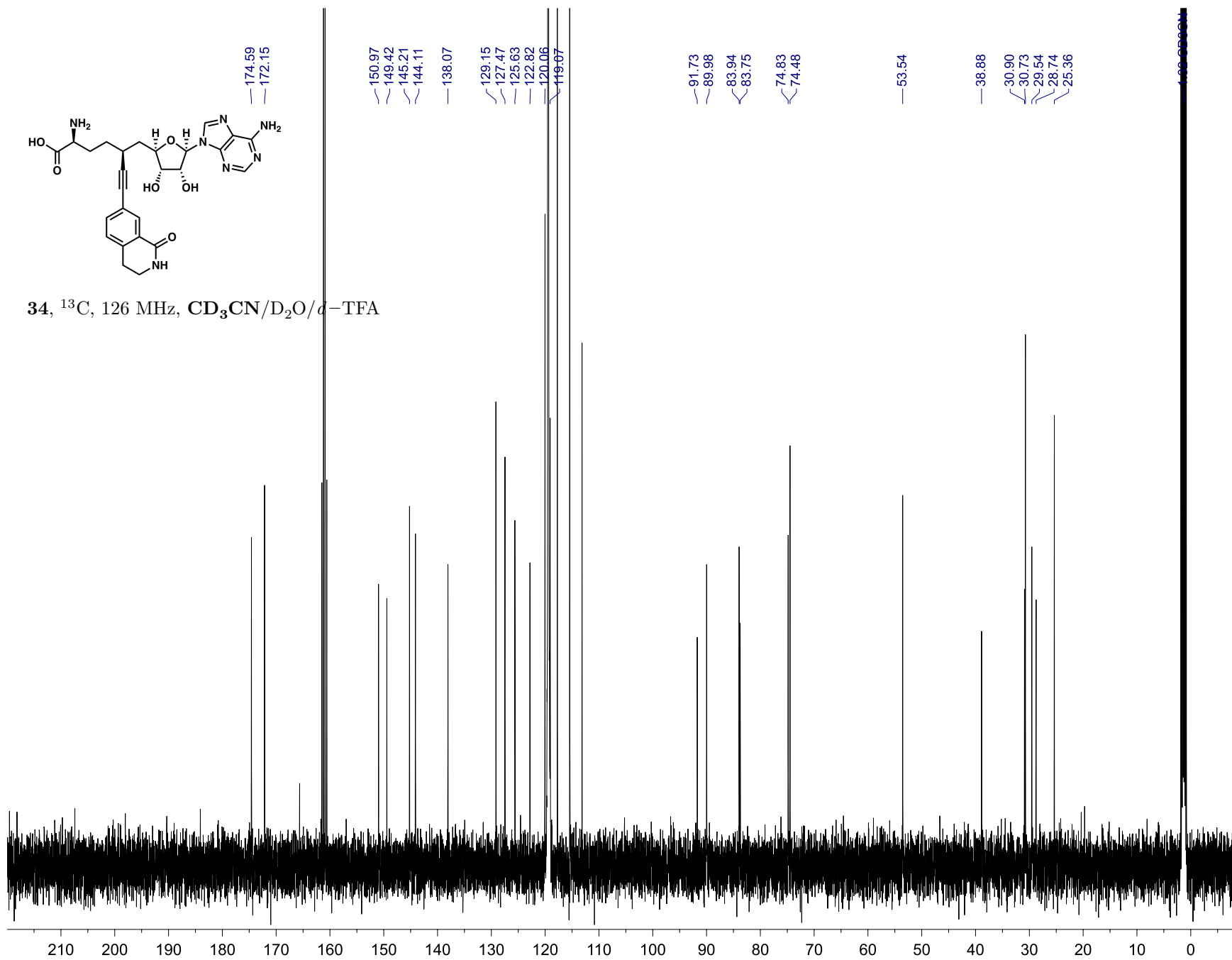
— 1.94  $\text{CD}_3\text{CN}$

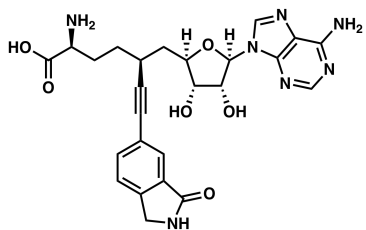




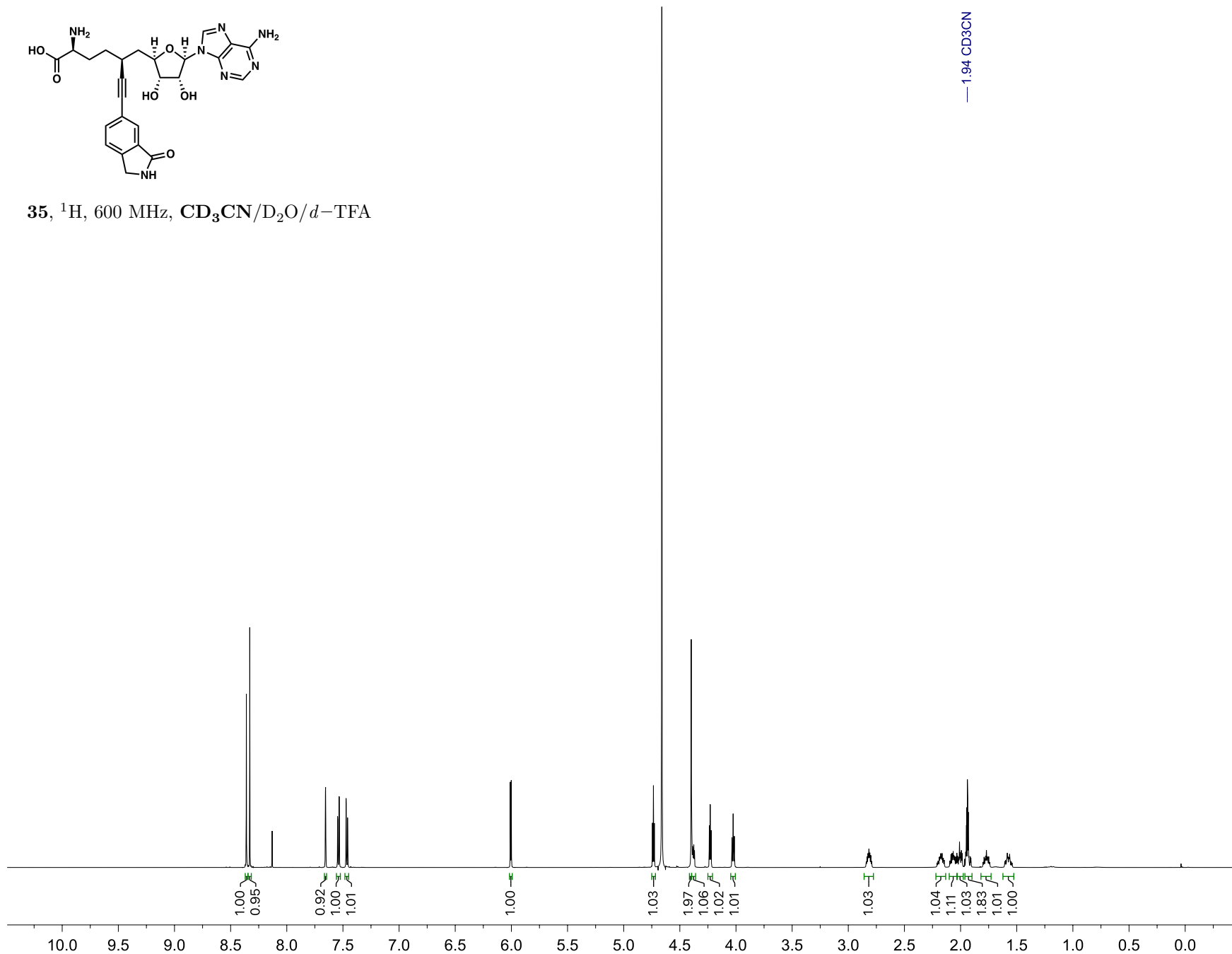


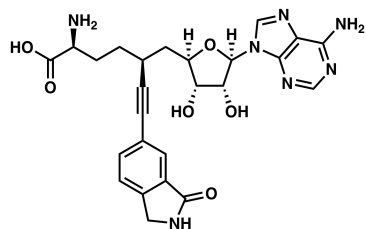
34,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$



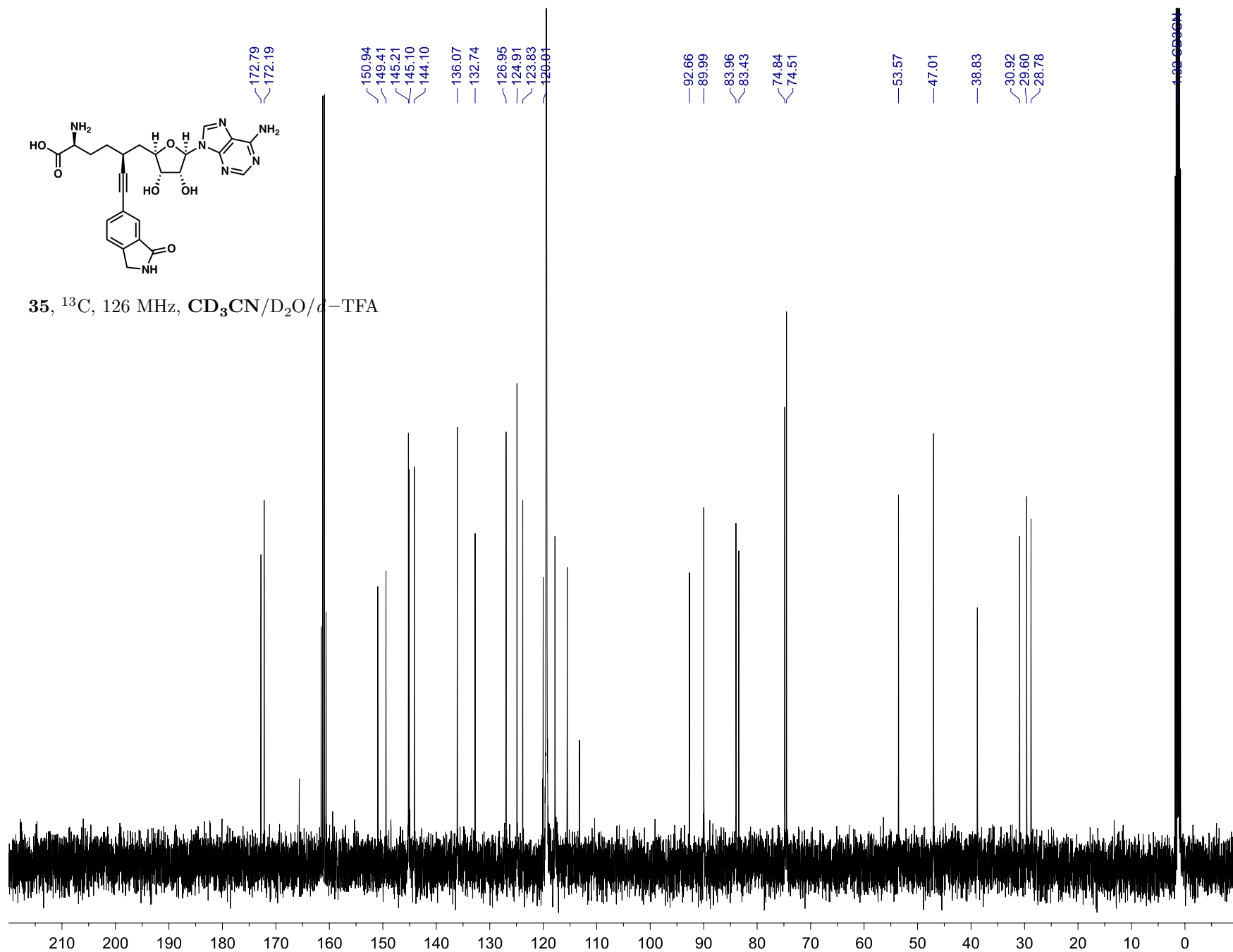


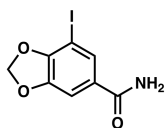
35,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$





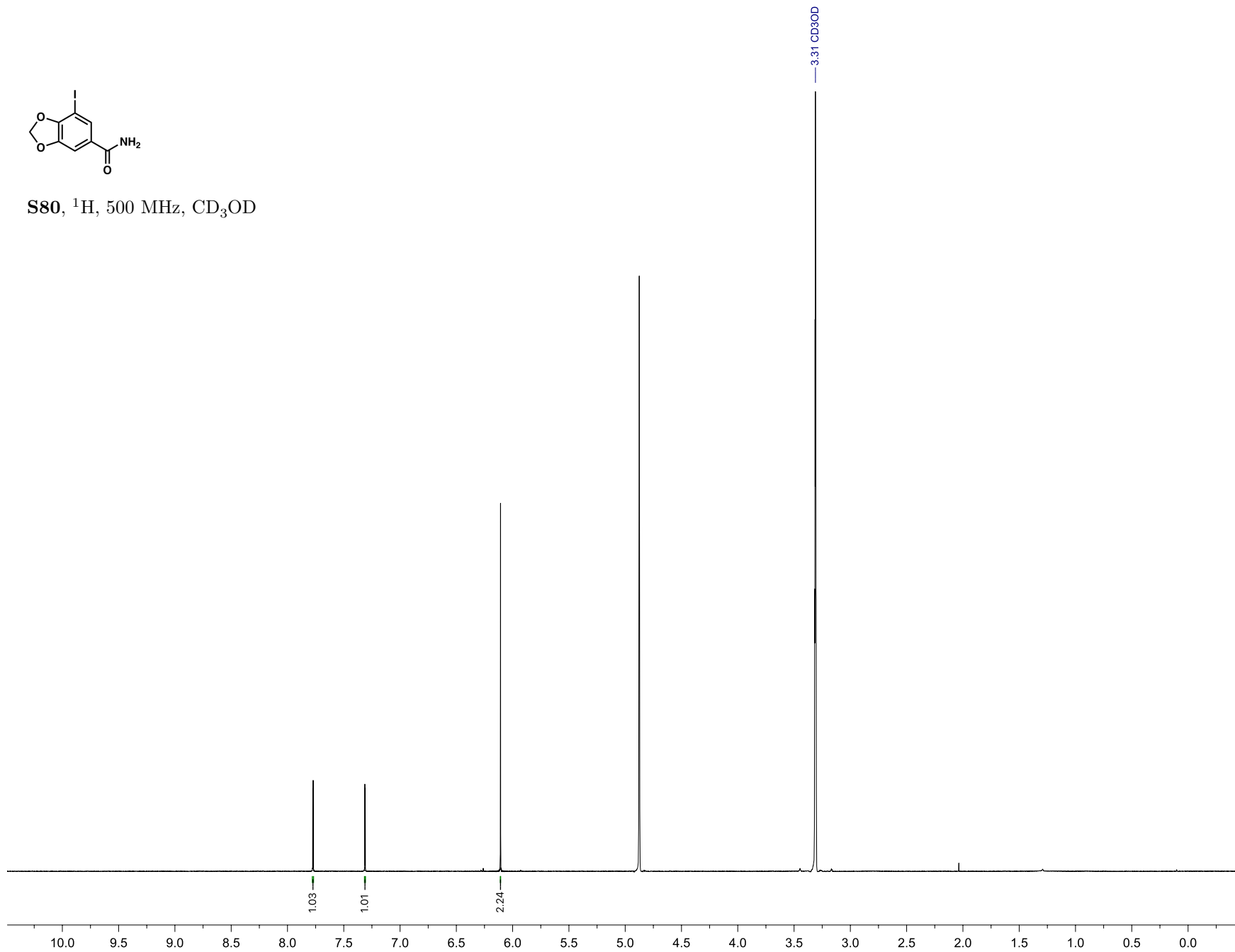
35,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

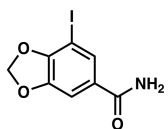




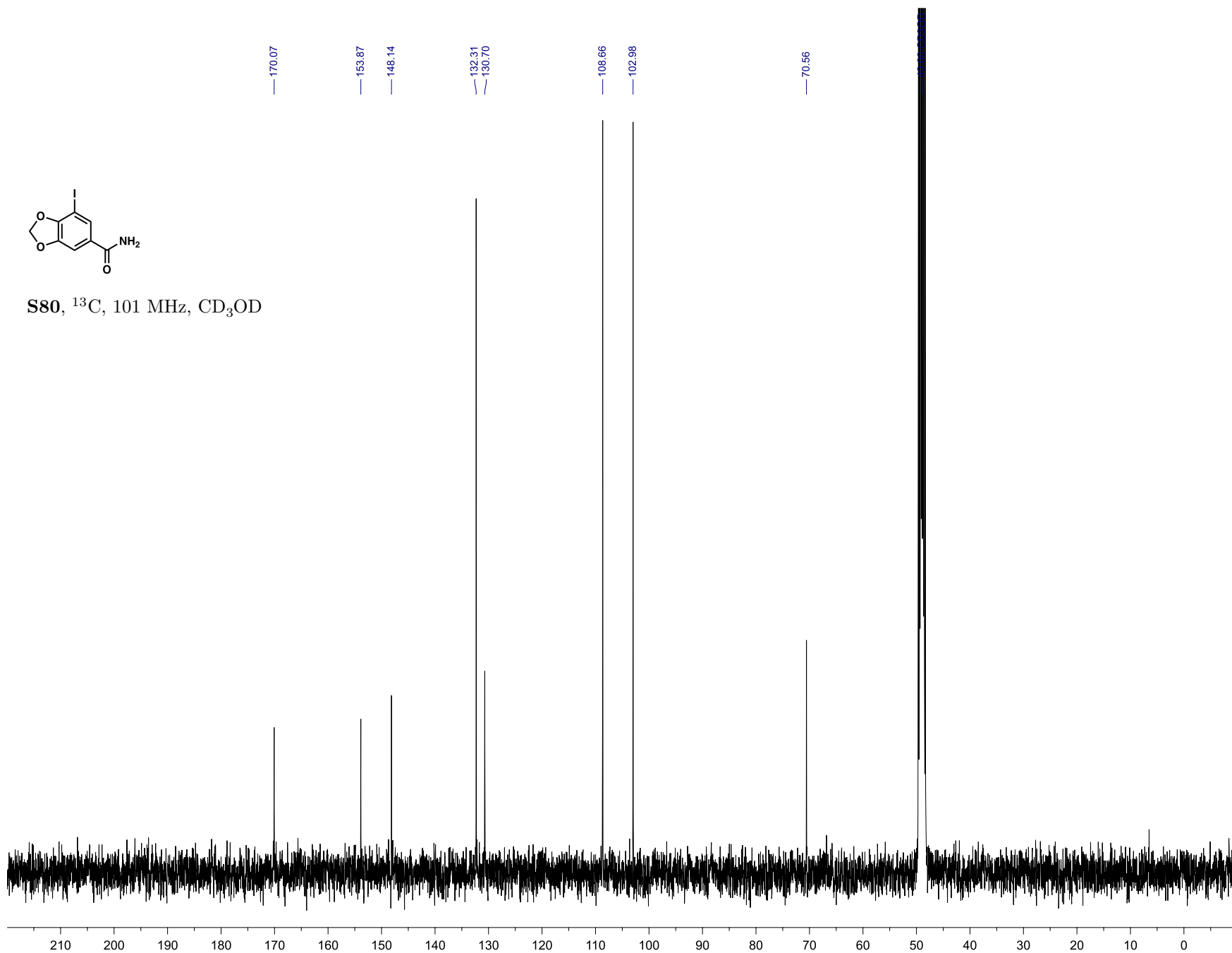
S80,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{OD}$

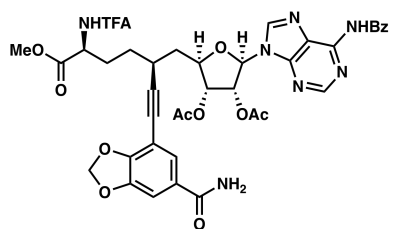
S219



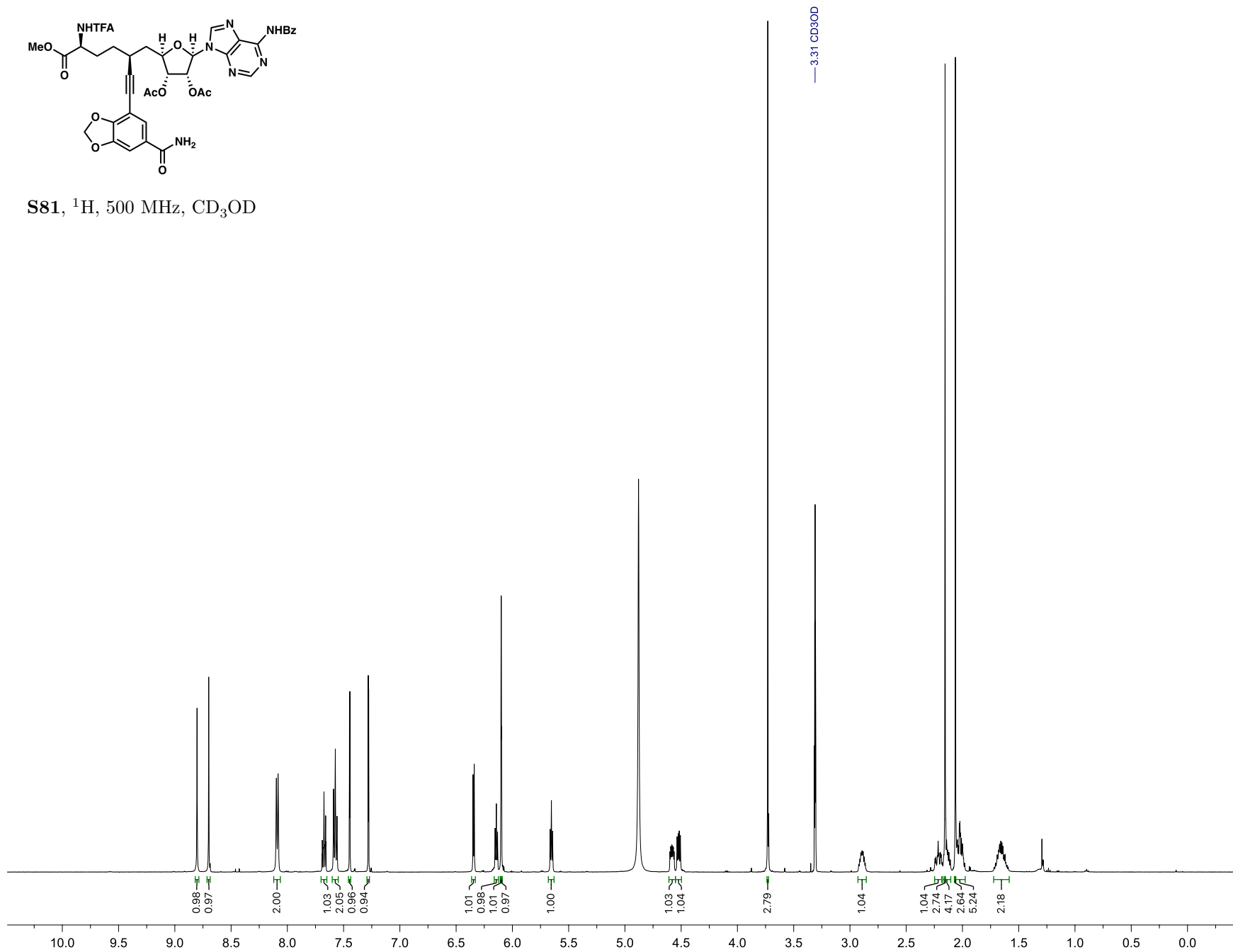


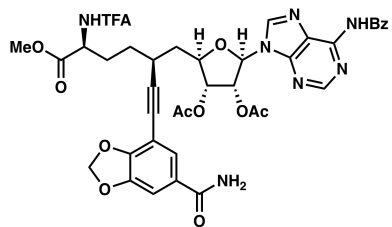
S80,  $^{13}\text{C}$ , 101 MHz,  $\text{CD}_3\text{OD}$



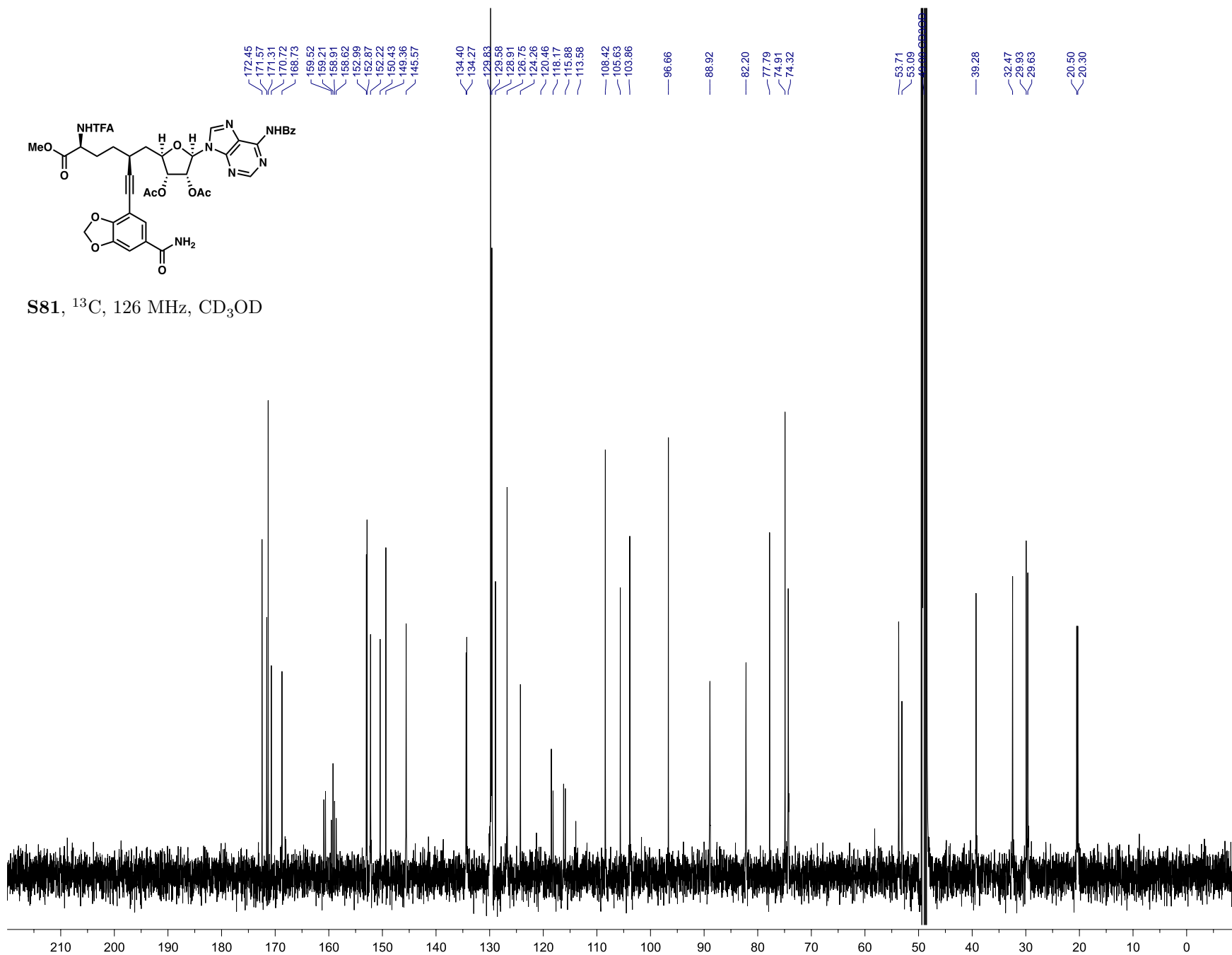


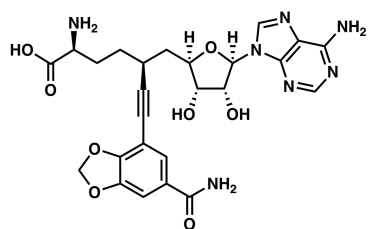
S81,  $^1\text{H}$ , 500 MHz,  $\text{CD}_3\text{OD}$





S81,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{OD}$

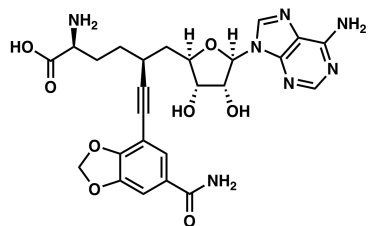




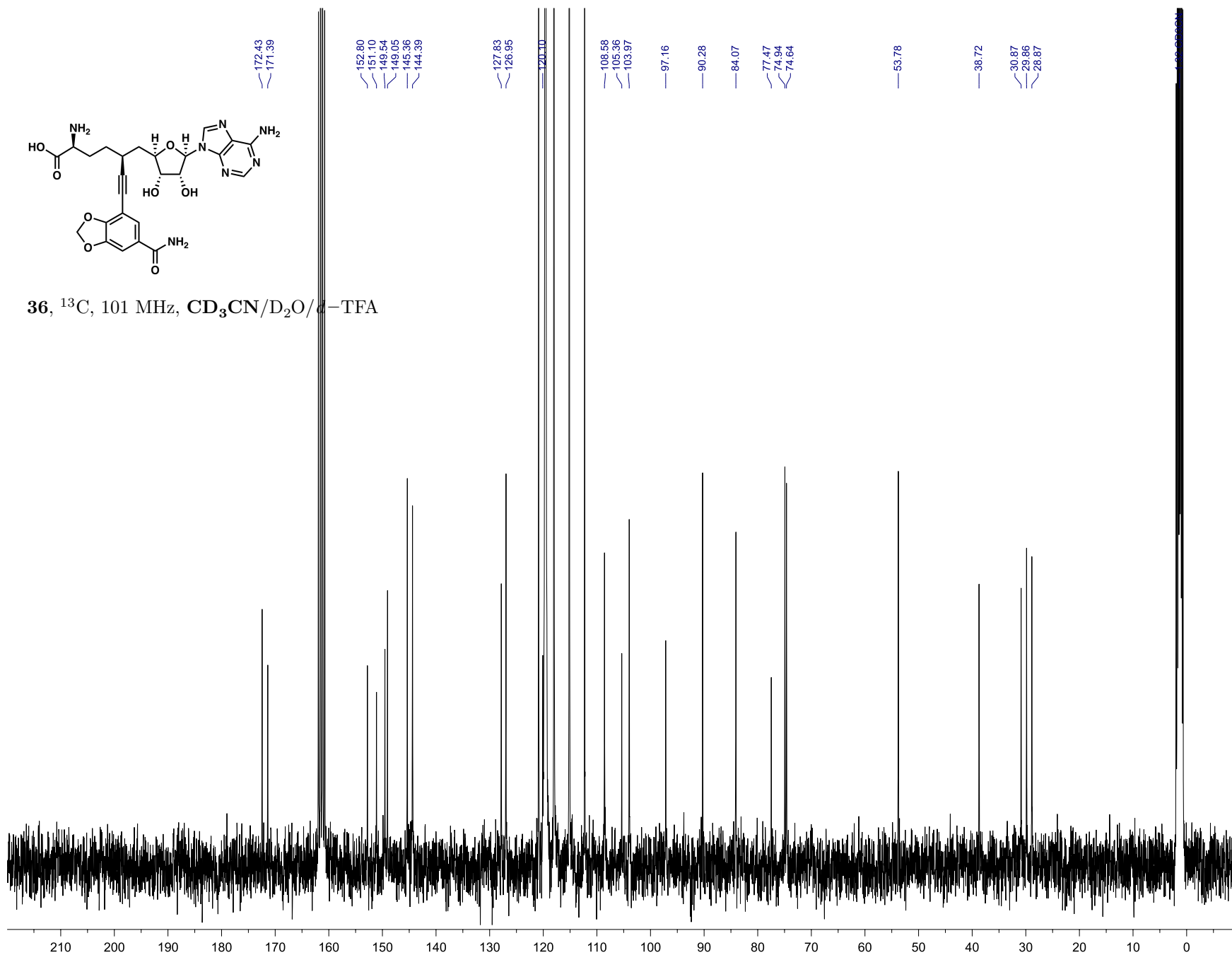
36,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}$

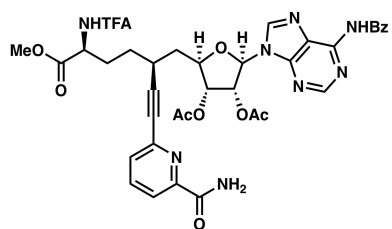






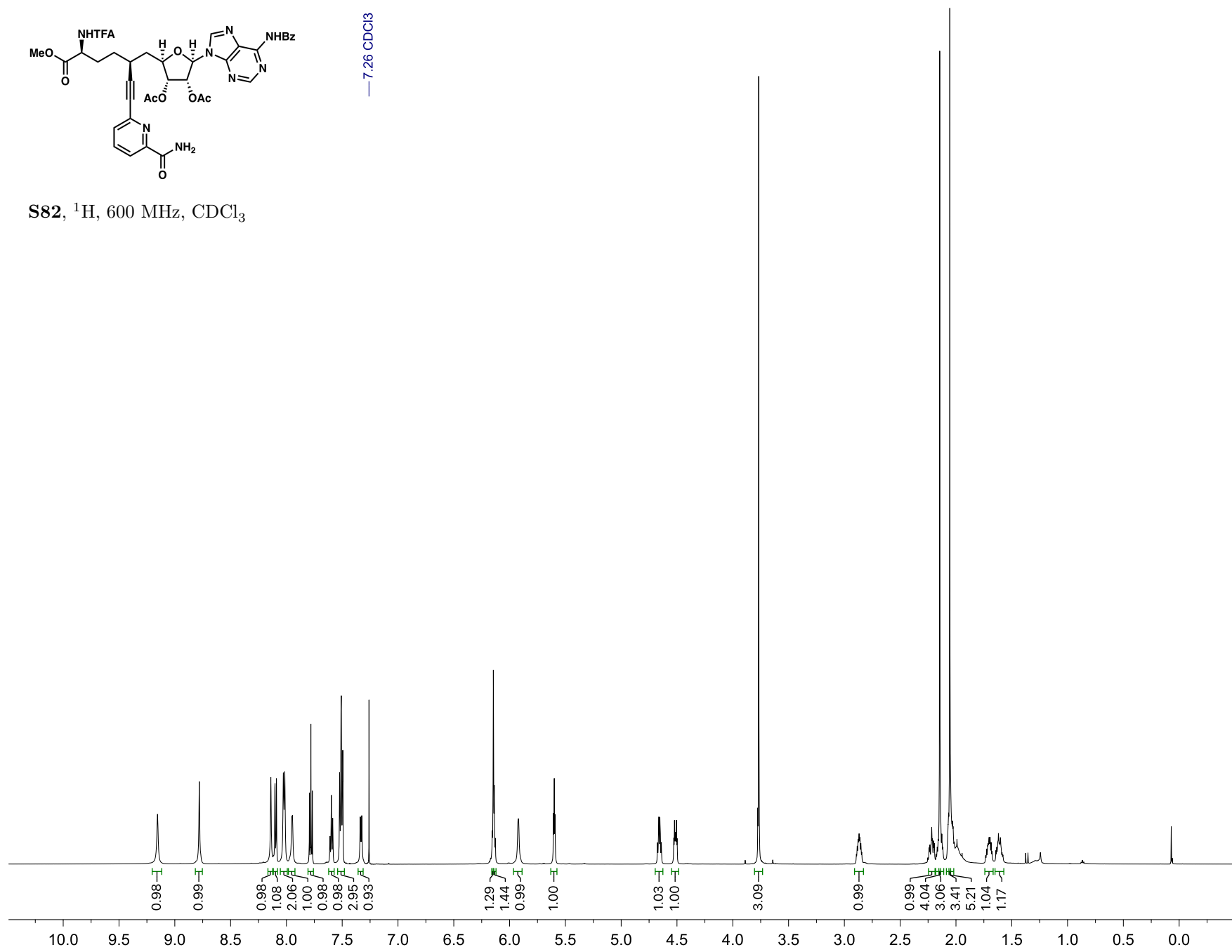
**36**,  $^{13}\text{C}$ , 101 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

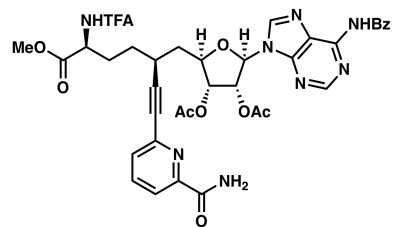




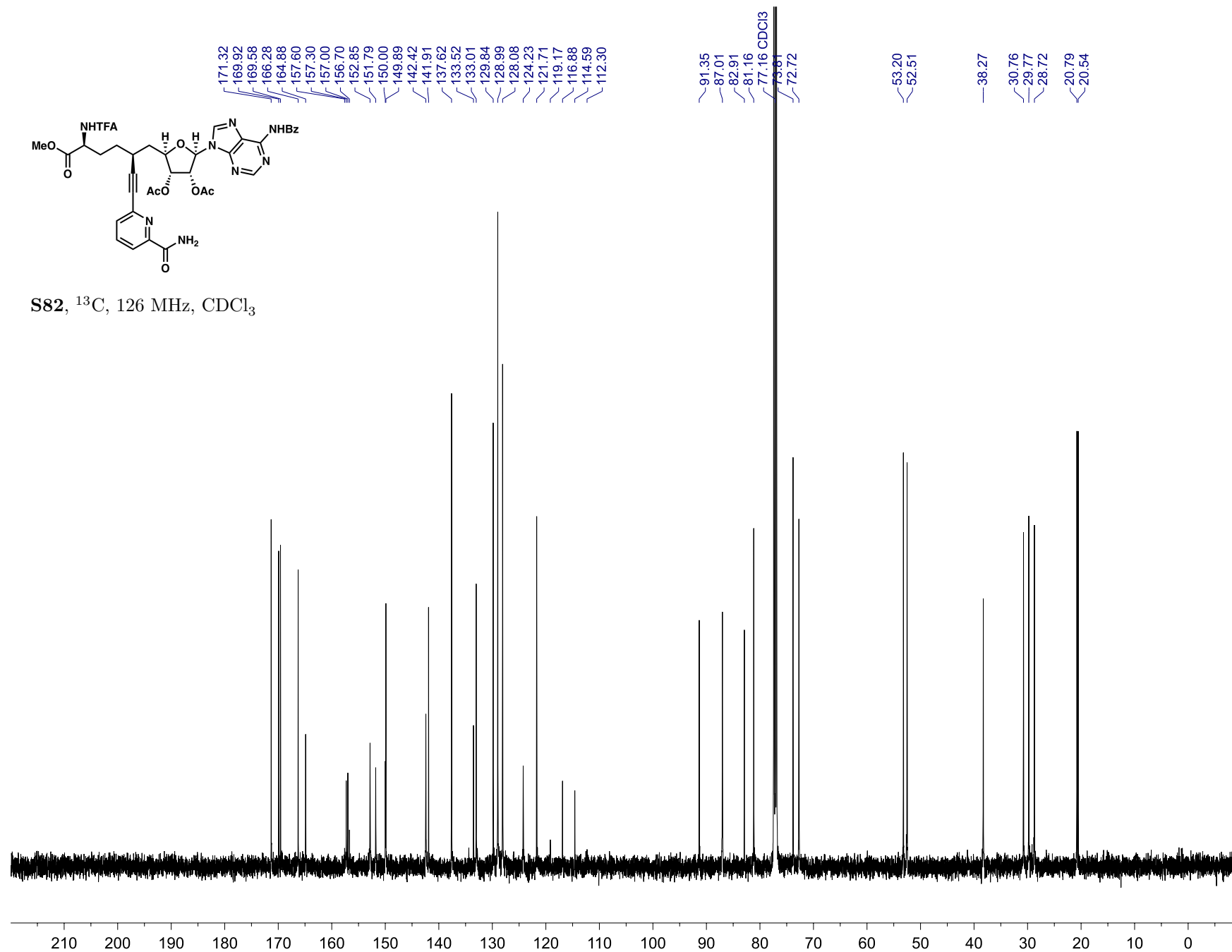
— 7.26 CDCl<sub>3</sub>

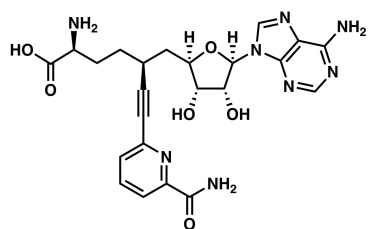
S82, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





**S82**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

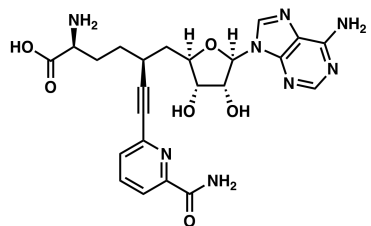




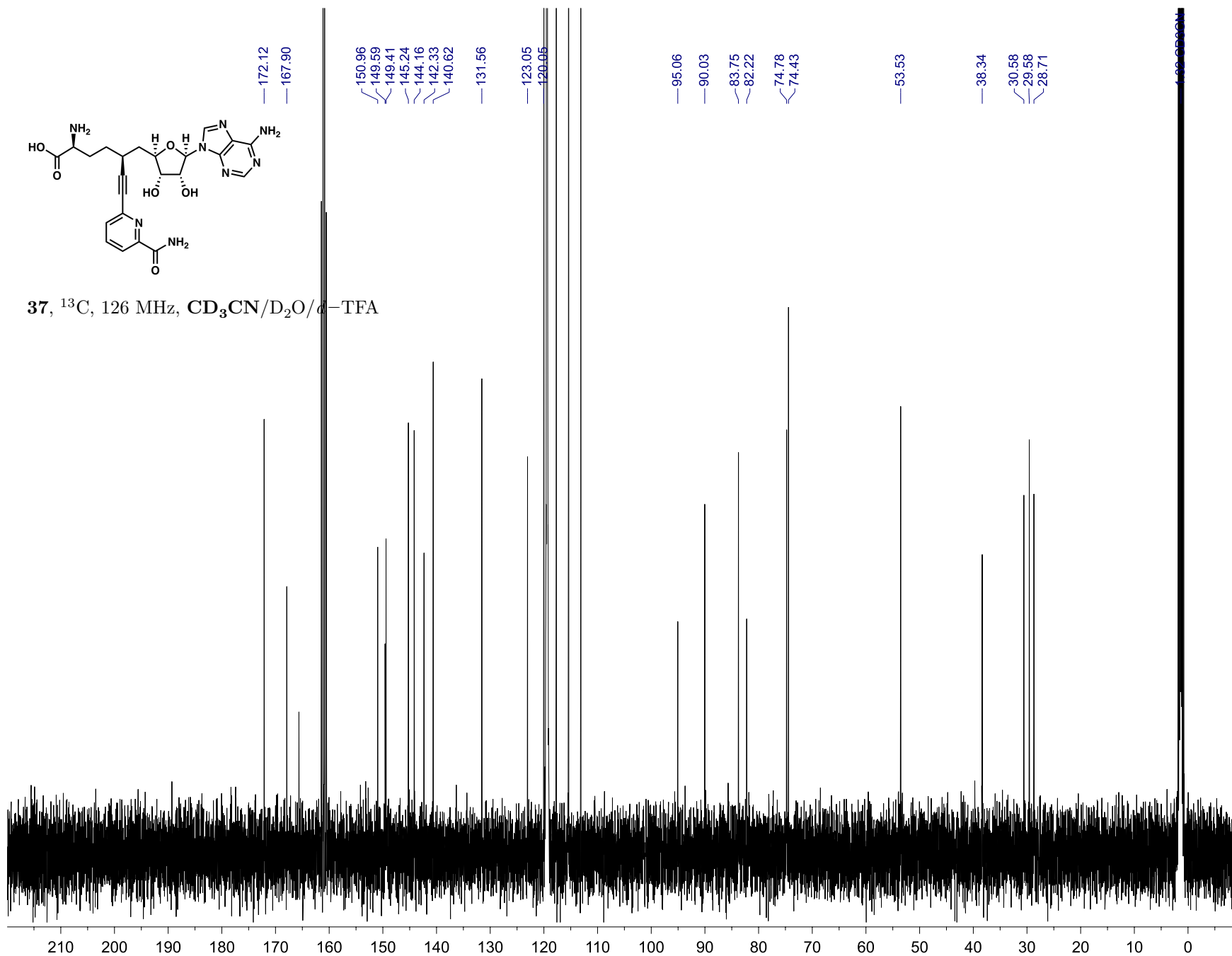
37,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

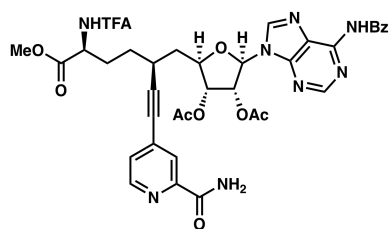


— 1.94  $\text{CD}_3\text{CN}$



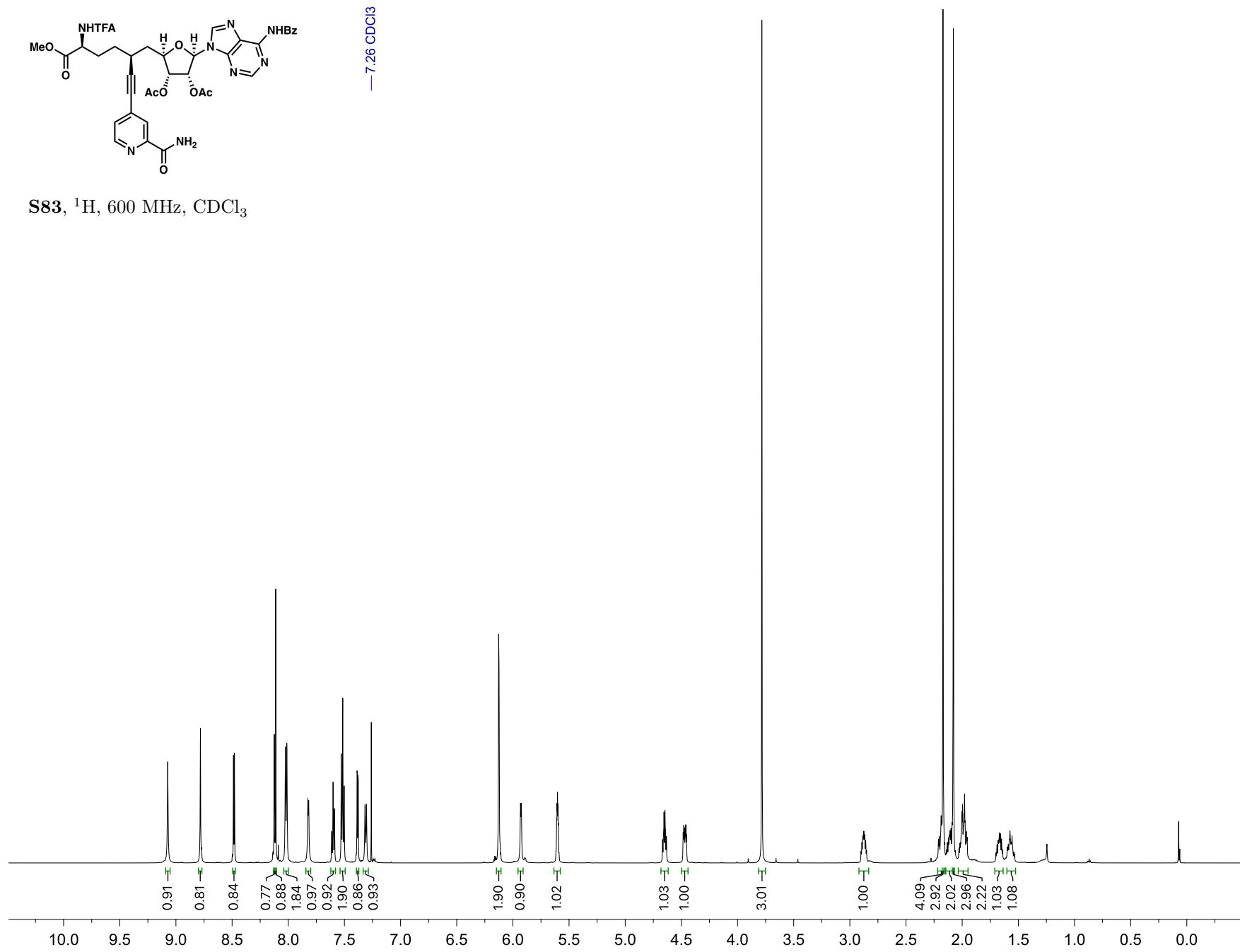
37,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

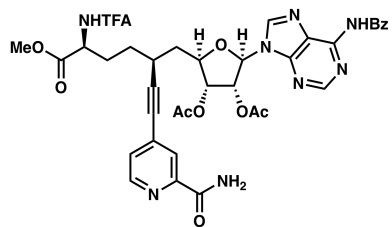




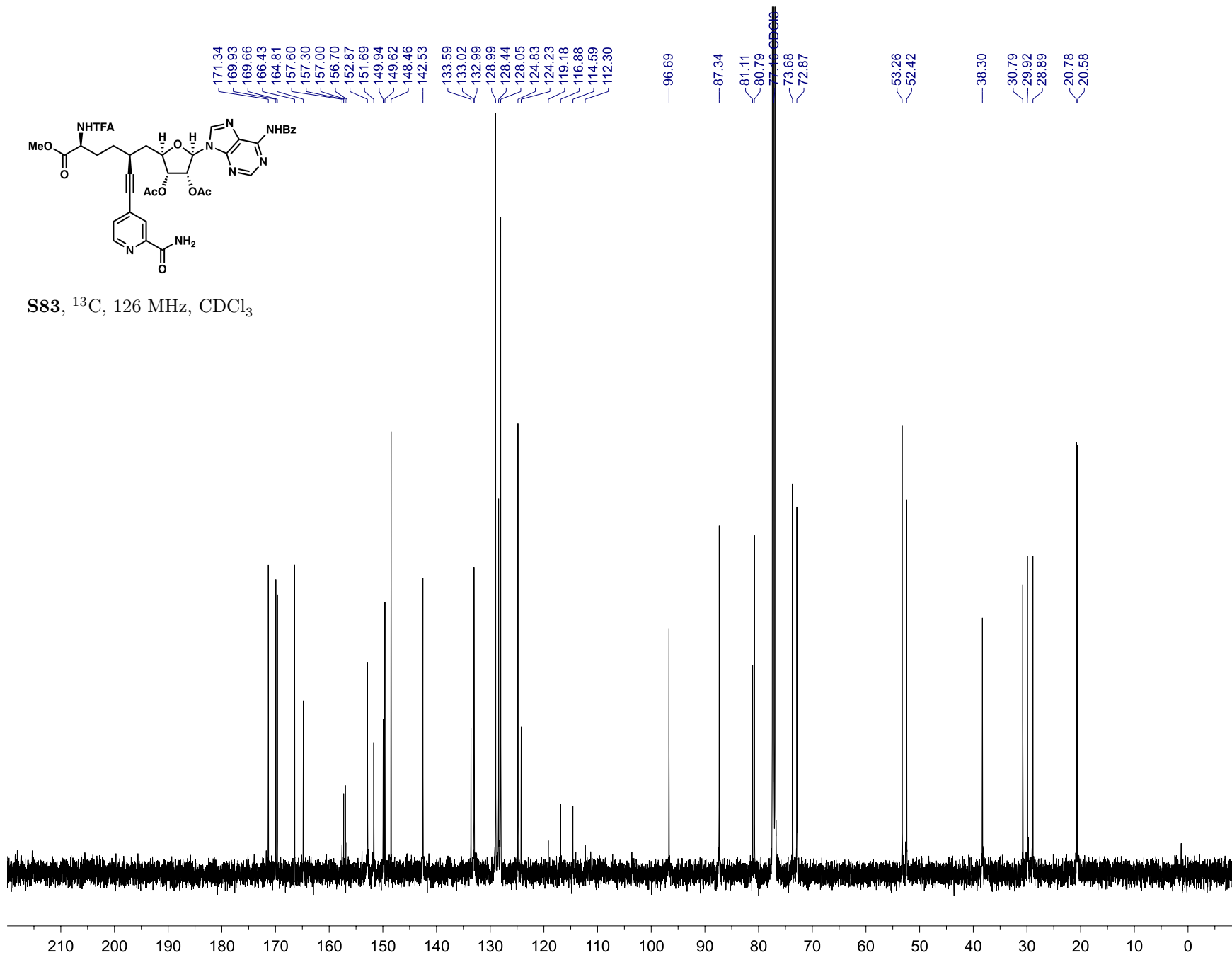
— 7.26 CDCl<sub>3</sub>

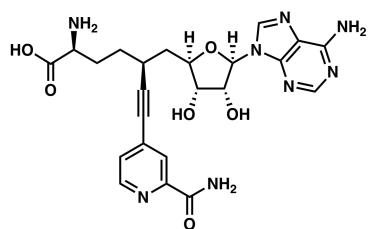
**S83**, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>



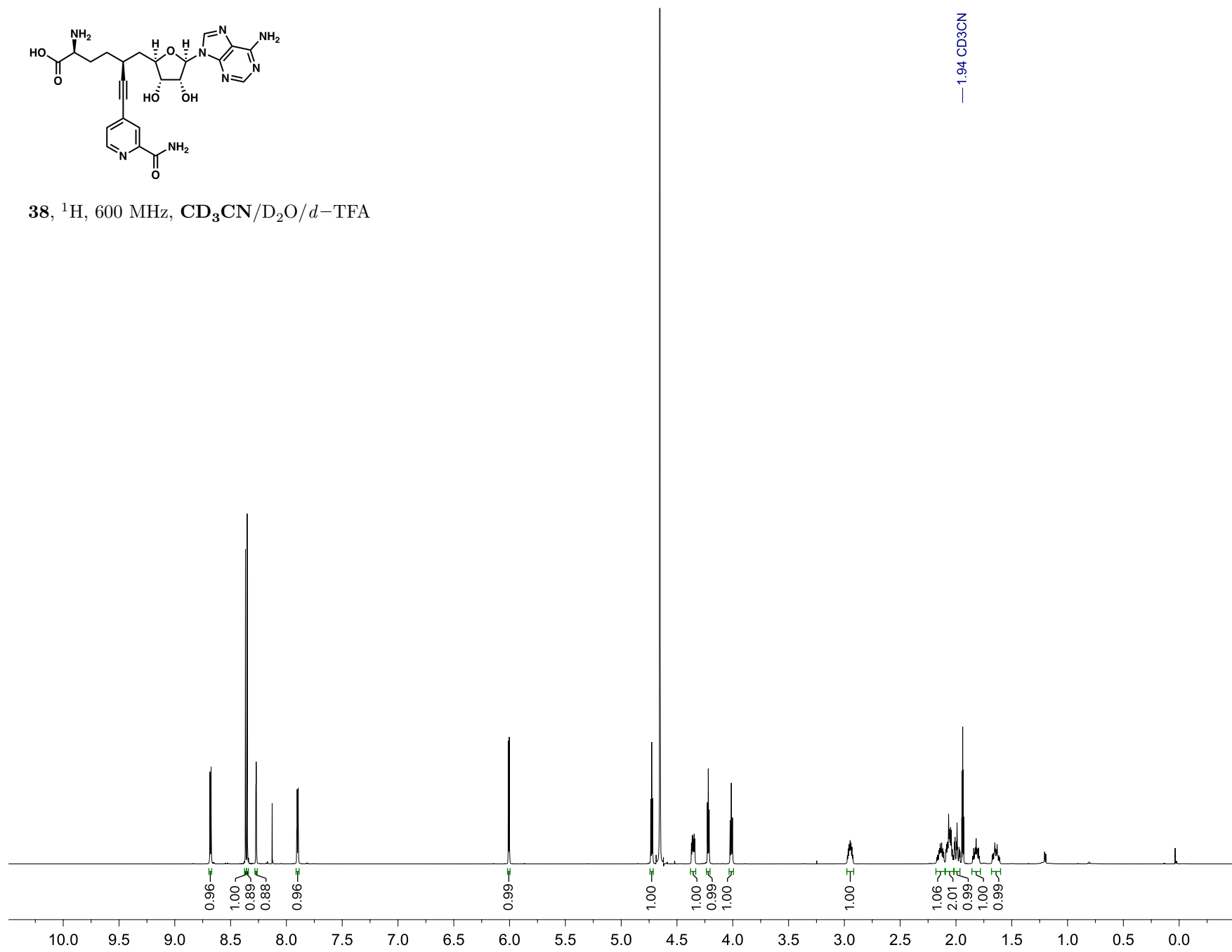


**S83**,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

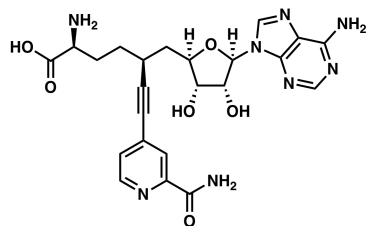




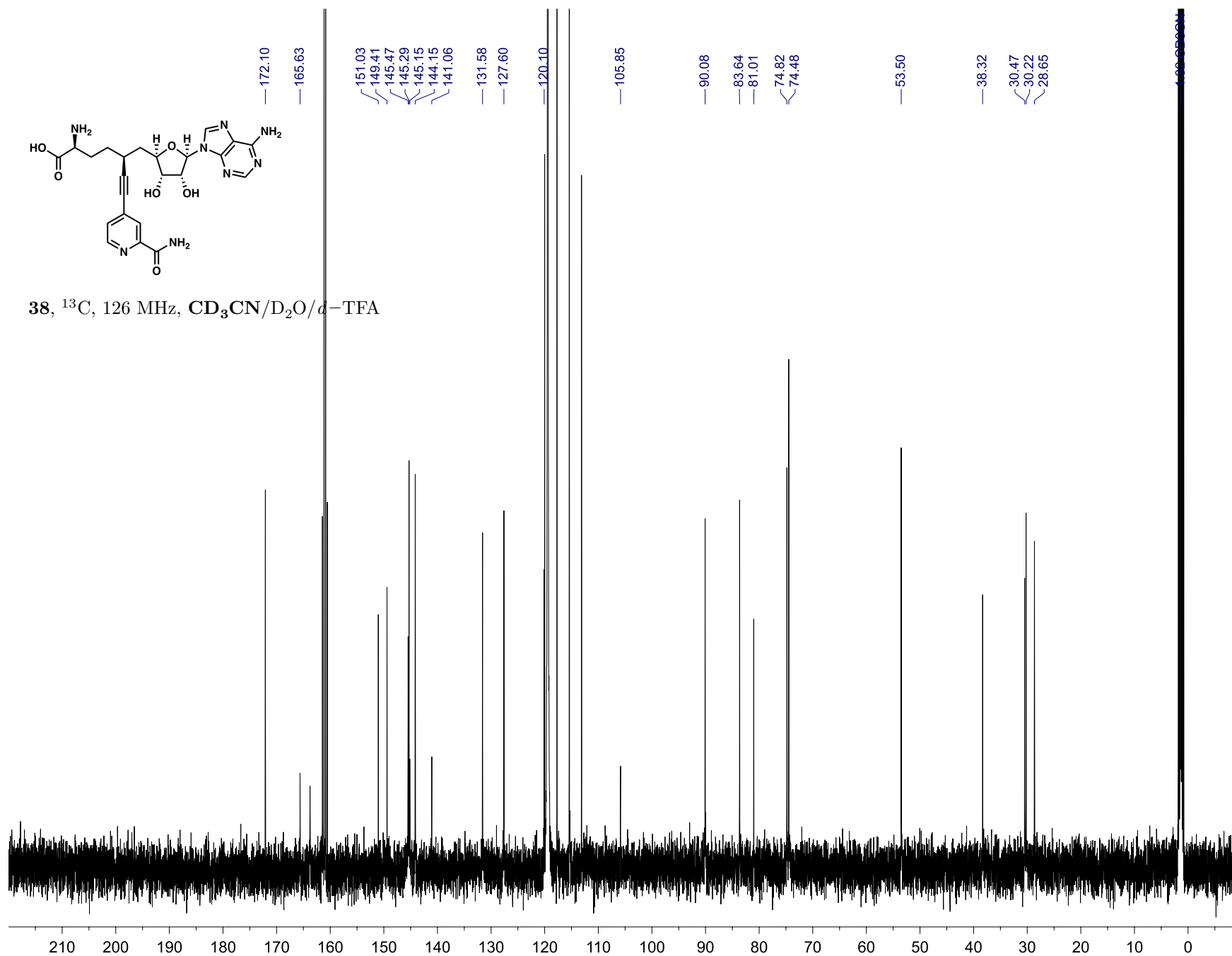
**38**,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

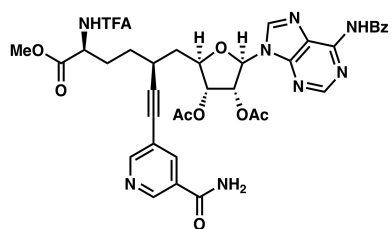






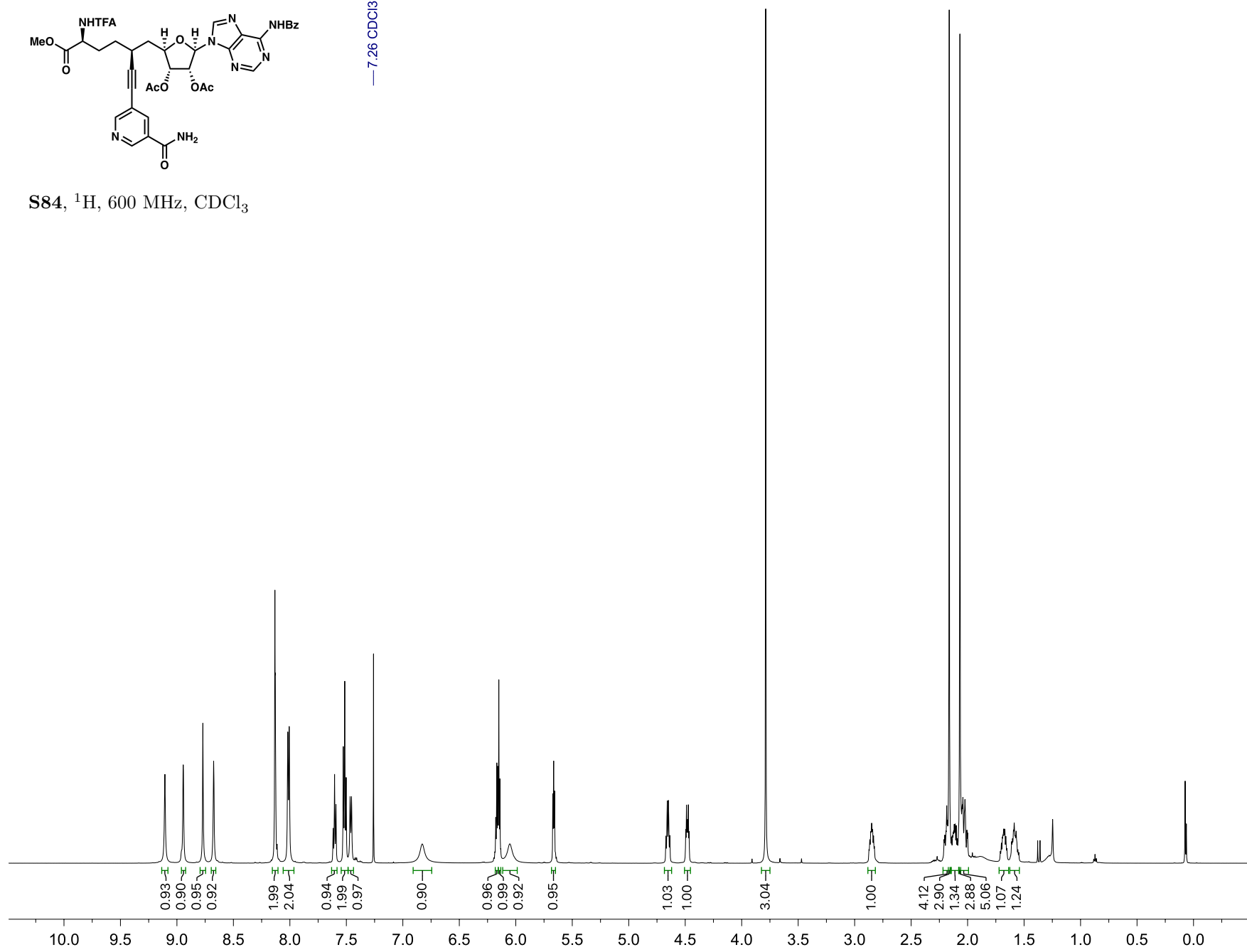
38,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$



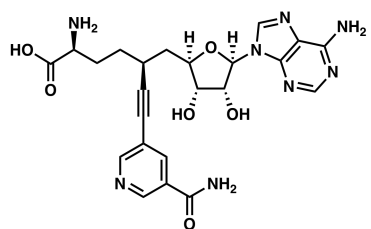


— 7.26 CDCl<sub>3</sub>

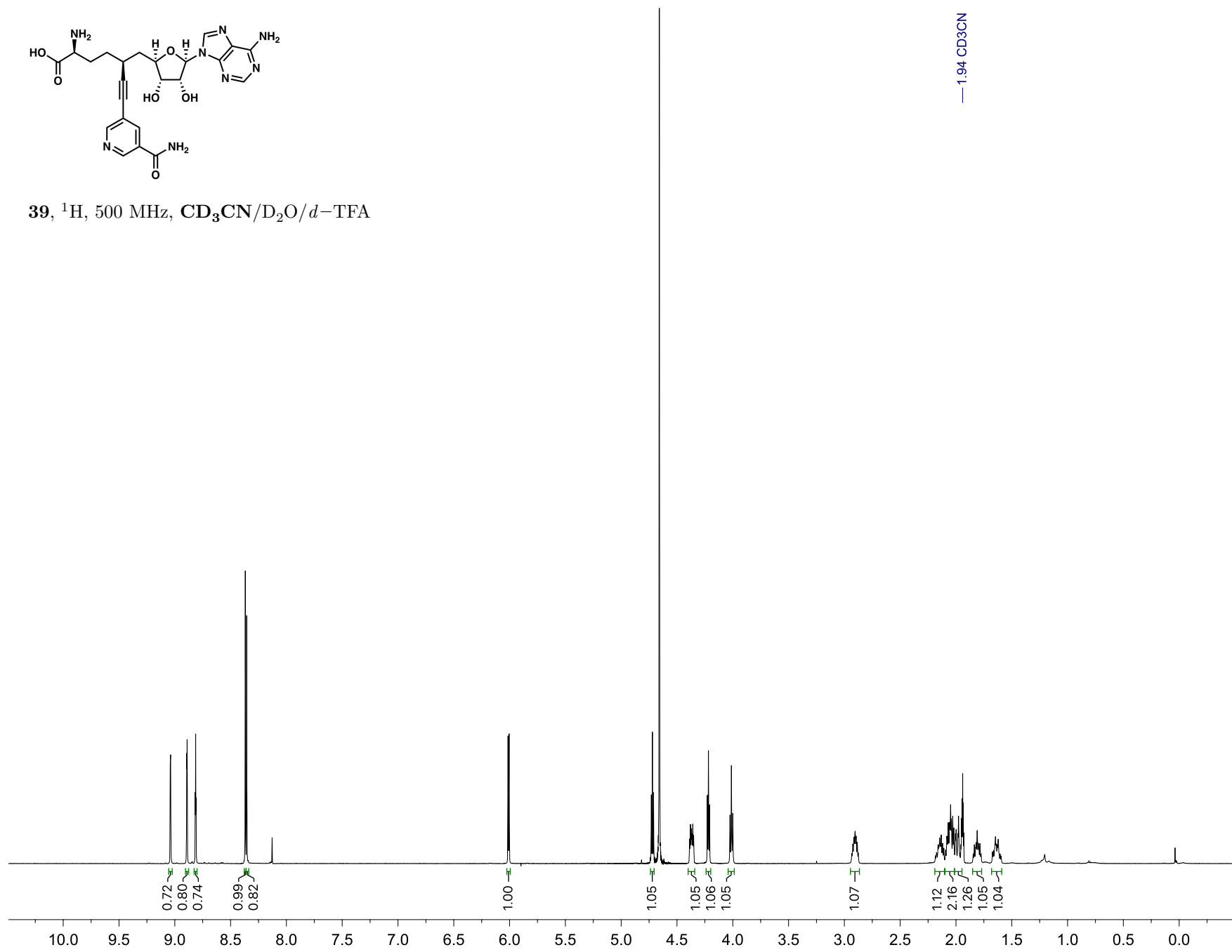
S84, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>

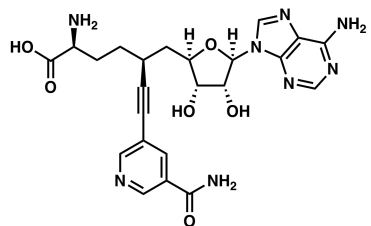




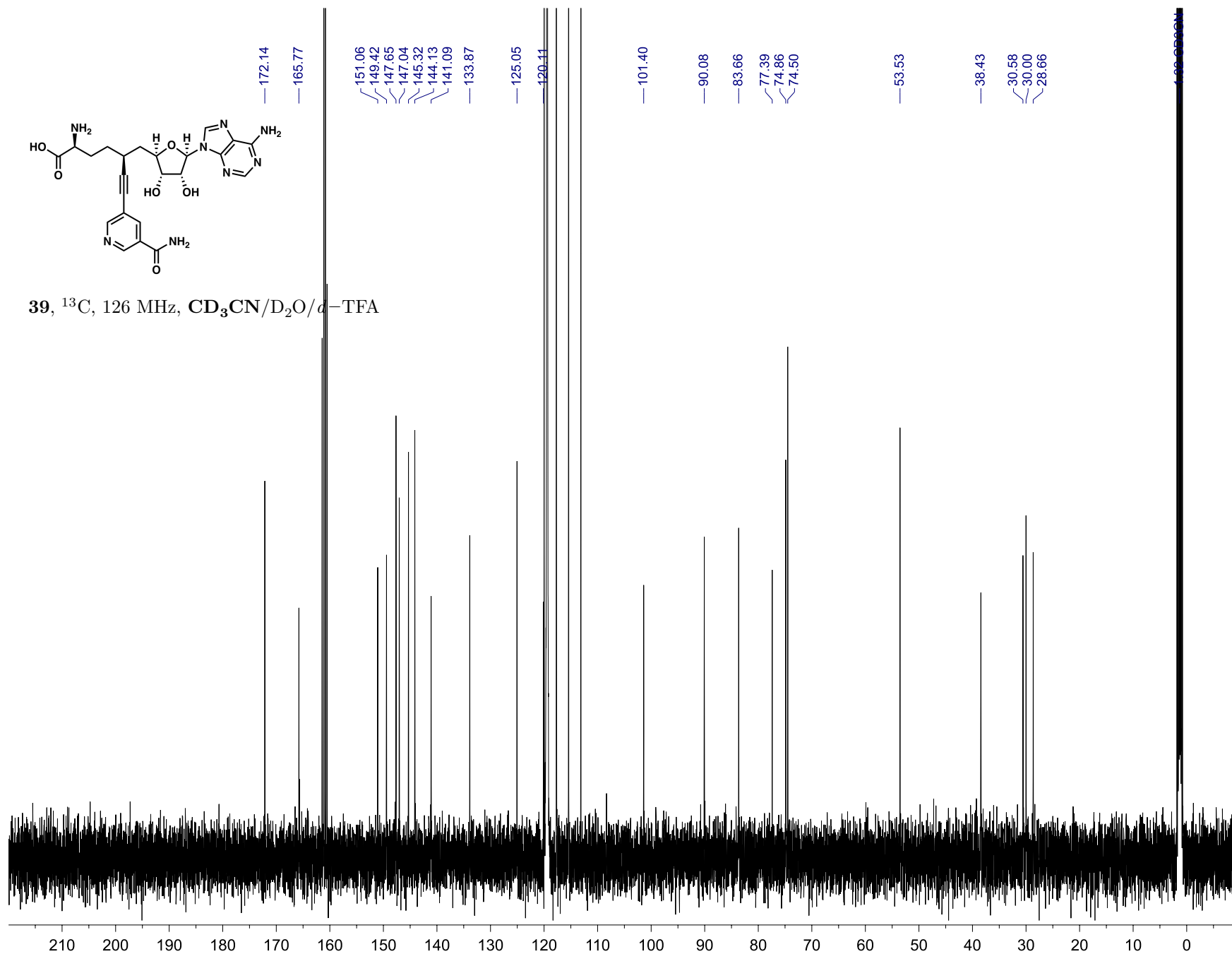


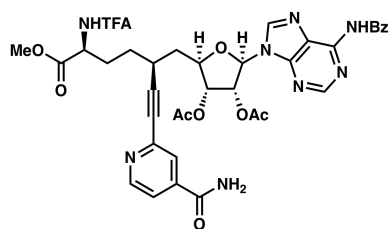
39, <sup>1</sup>H, 500 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA





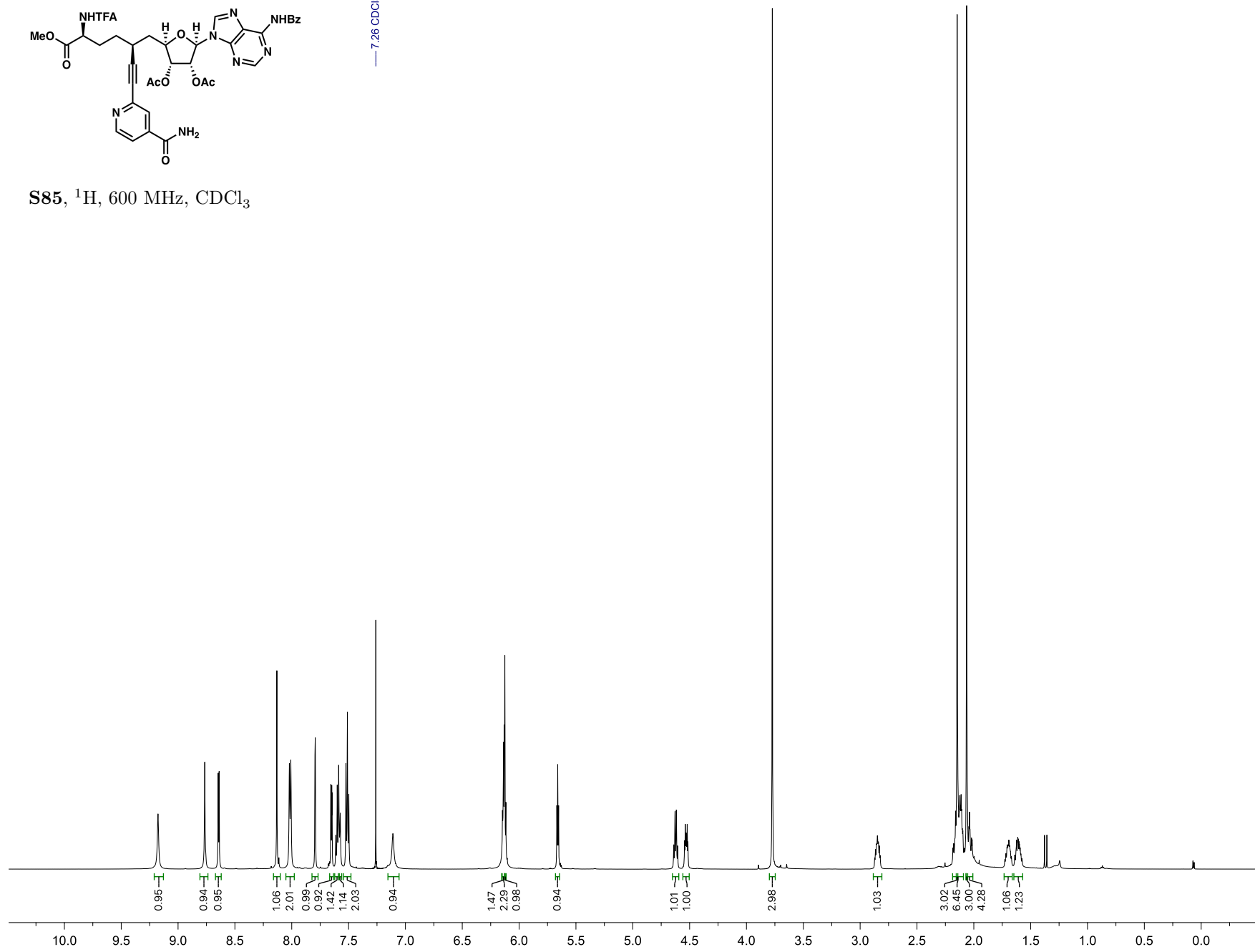
**39**,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

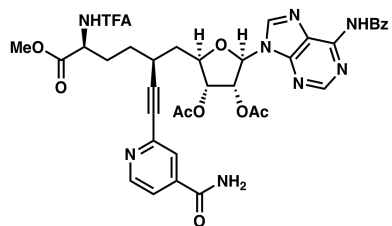




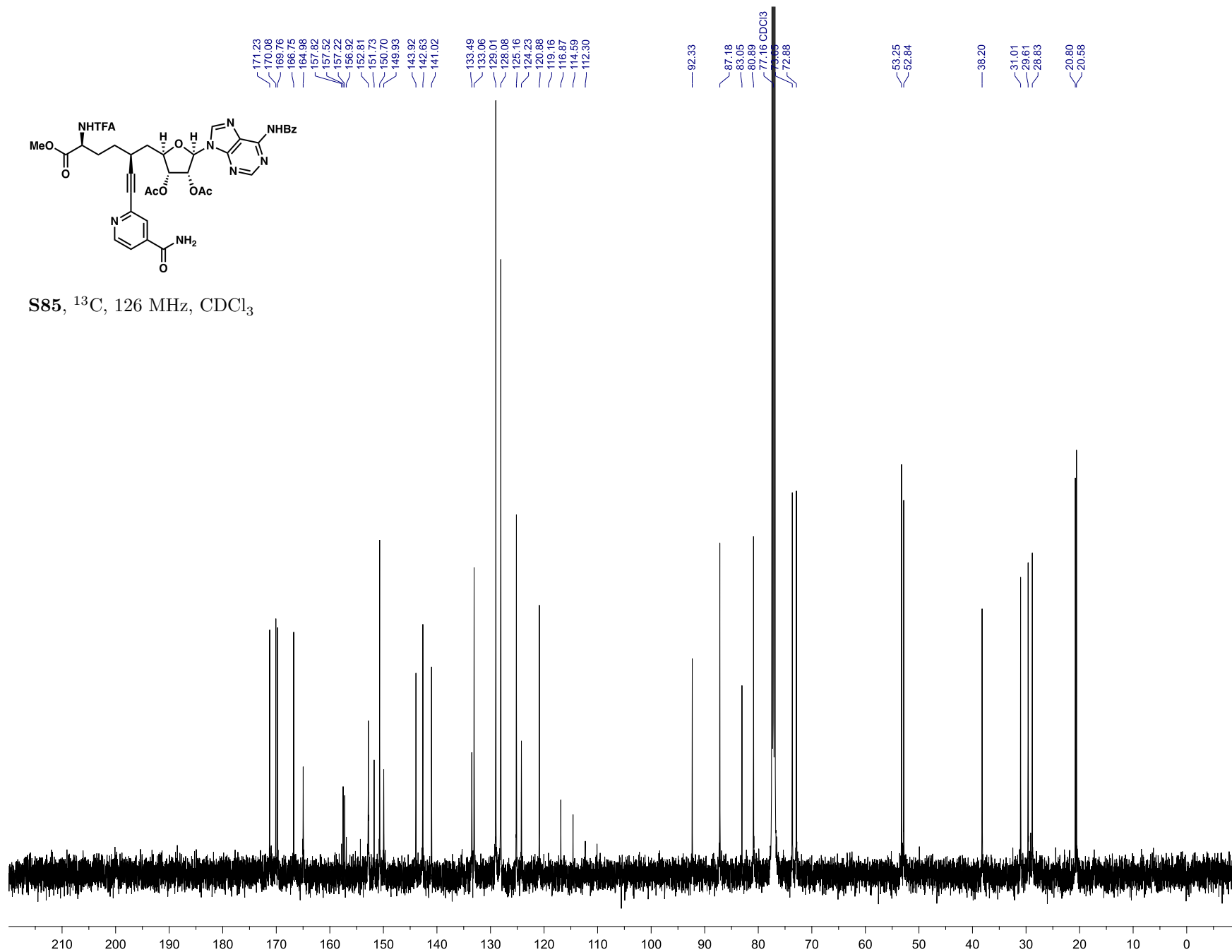
— 7.26 CDCl<sub>3</sub>

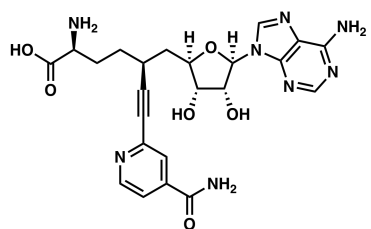
S85, <sup>1</sup>H, 600 MHz, CDCl<sub>3</sub>





S85,  $^{13}\text{C}$ , 126 MHz,  $\text{CDCl}_3$

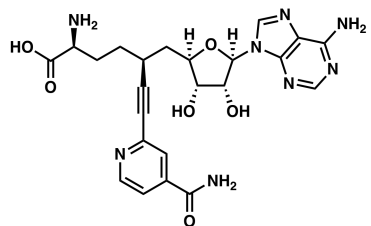




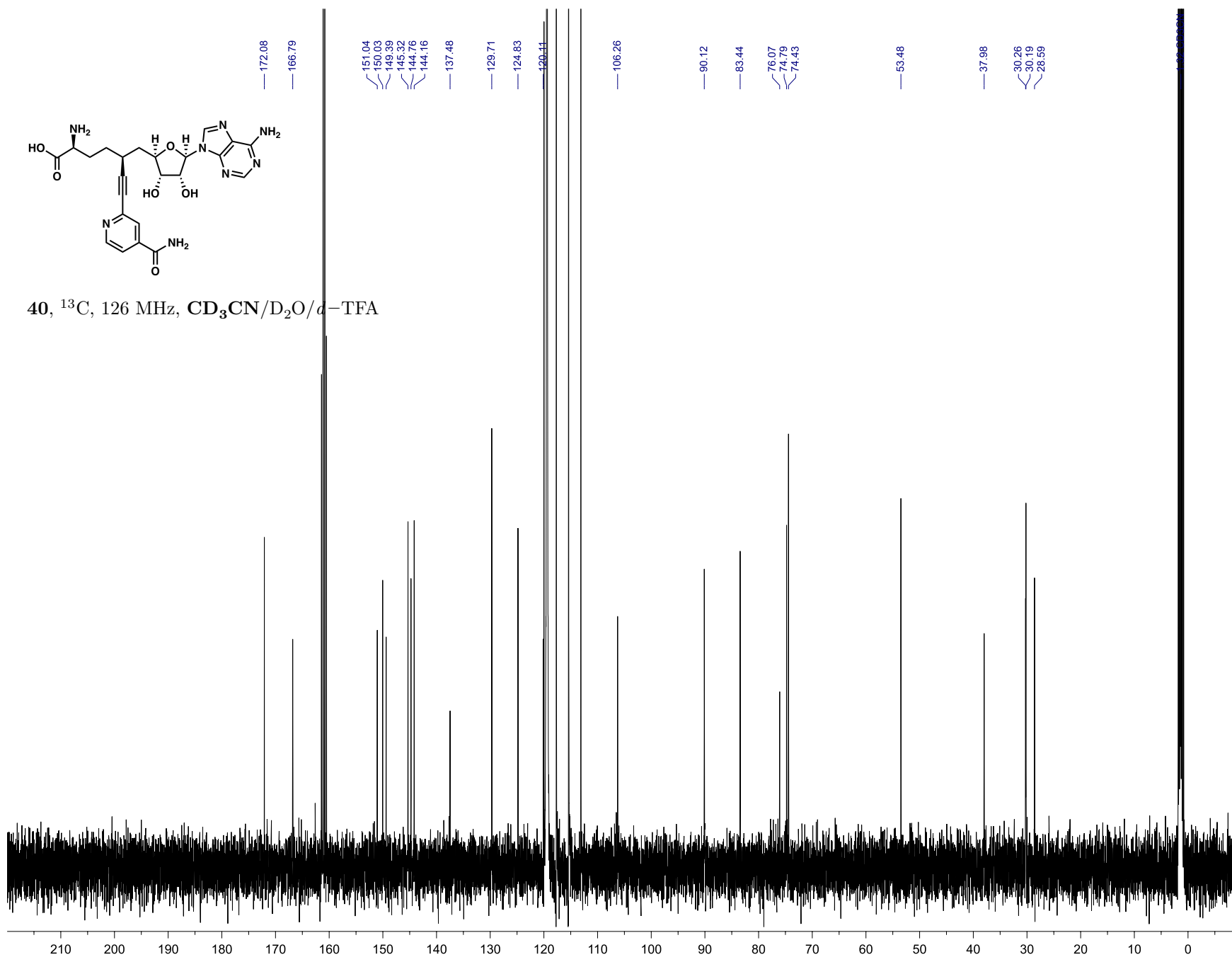
40, <sup>1</sup>H, 500 MHz, CD<sub>3</sub>CN/D<sub>2</sub>O/*d*-TFA

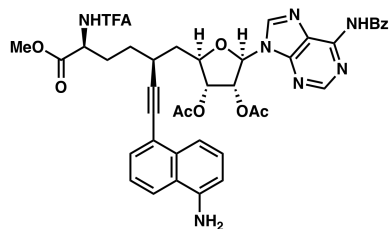






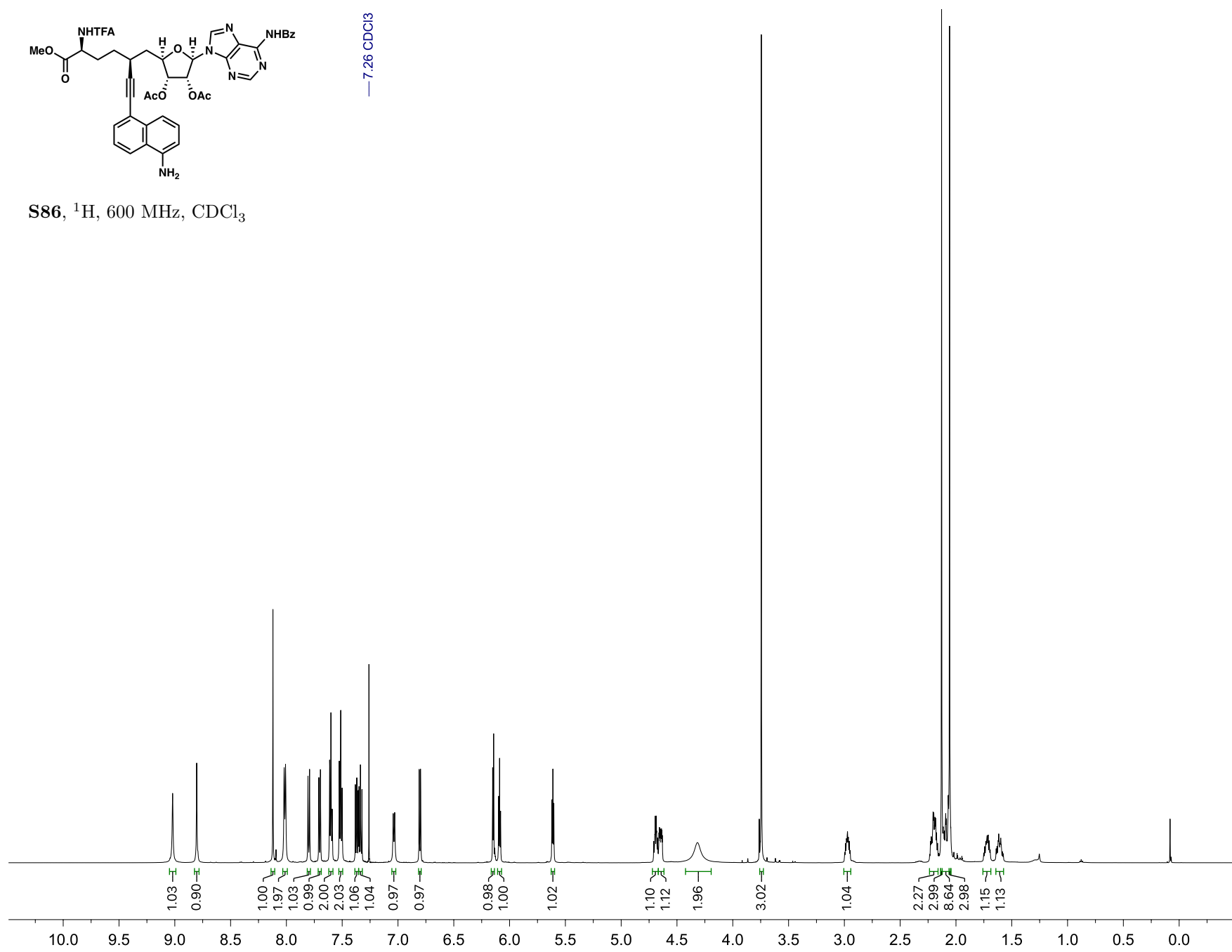
40,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$

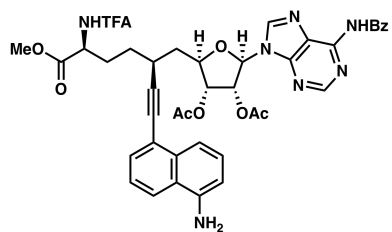




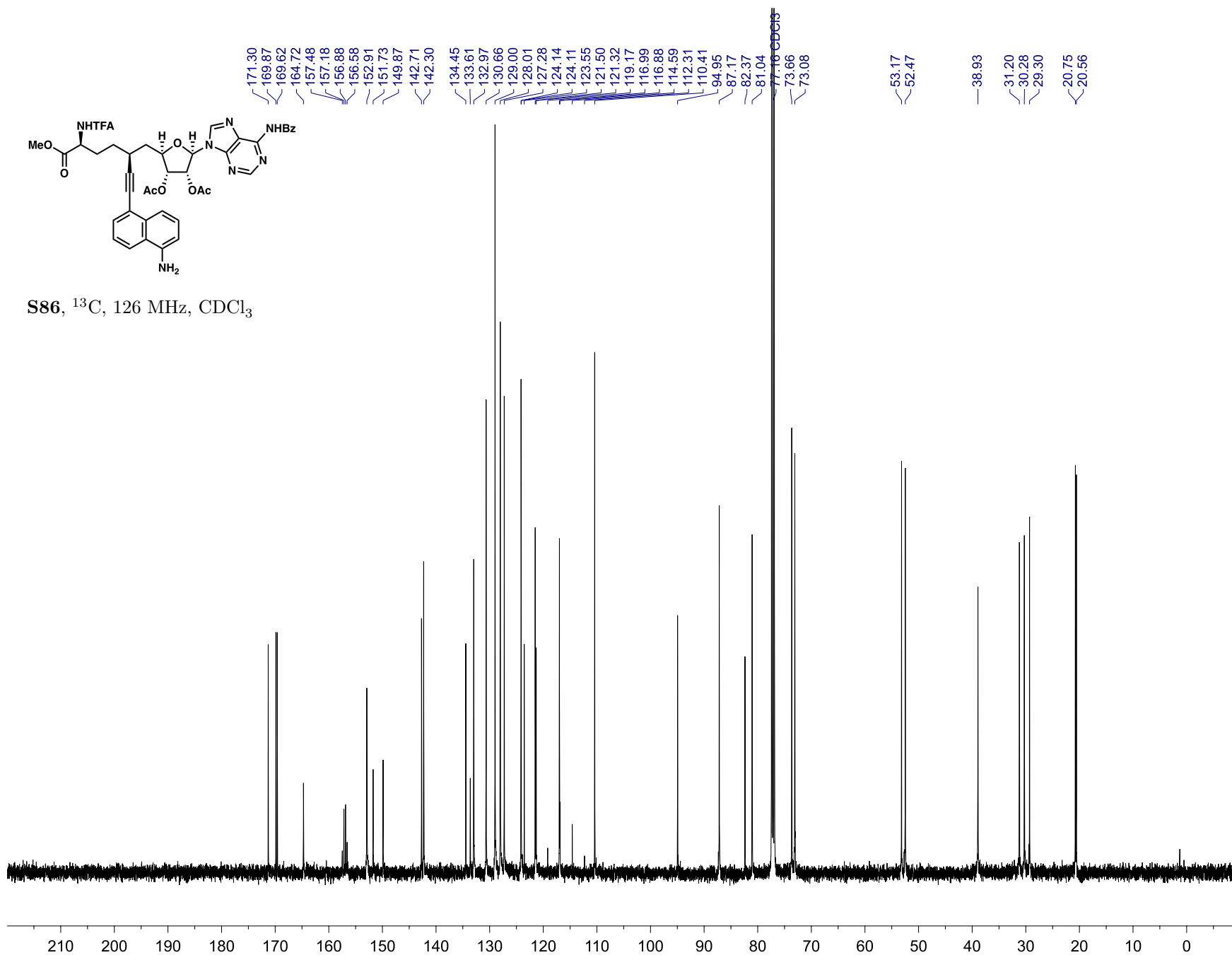
— 7.26  $\text{CDCl}_3$

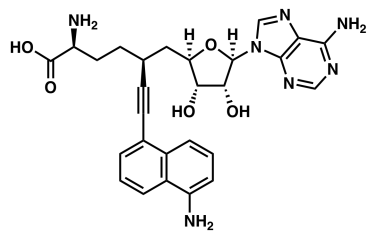
S86,  $^1\text{H}$ , 600 MHz,  $\text{CDCl}_3$



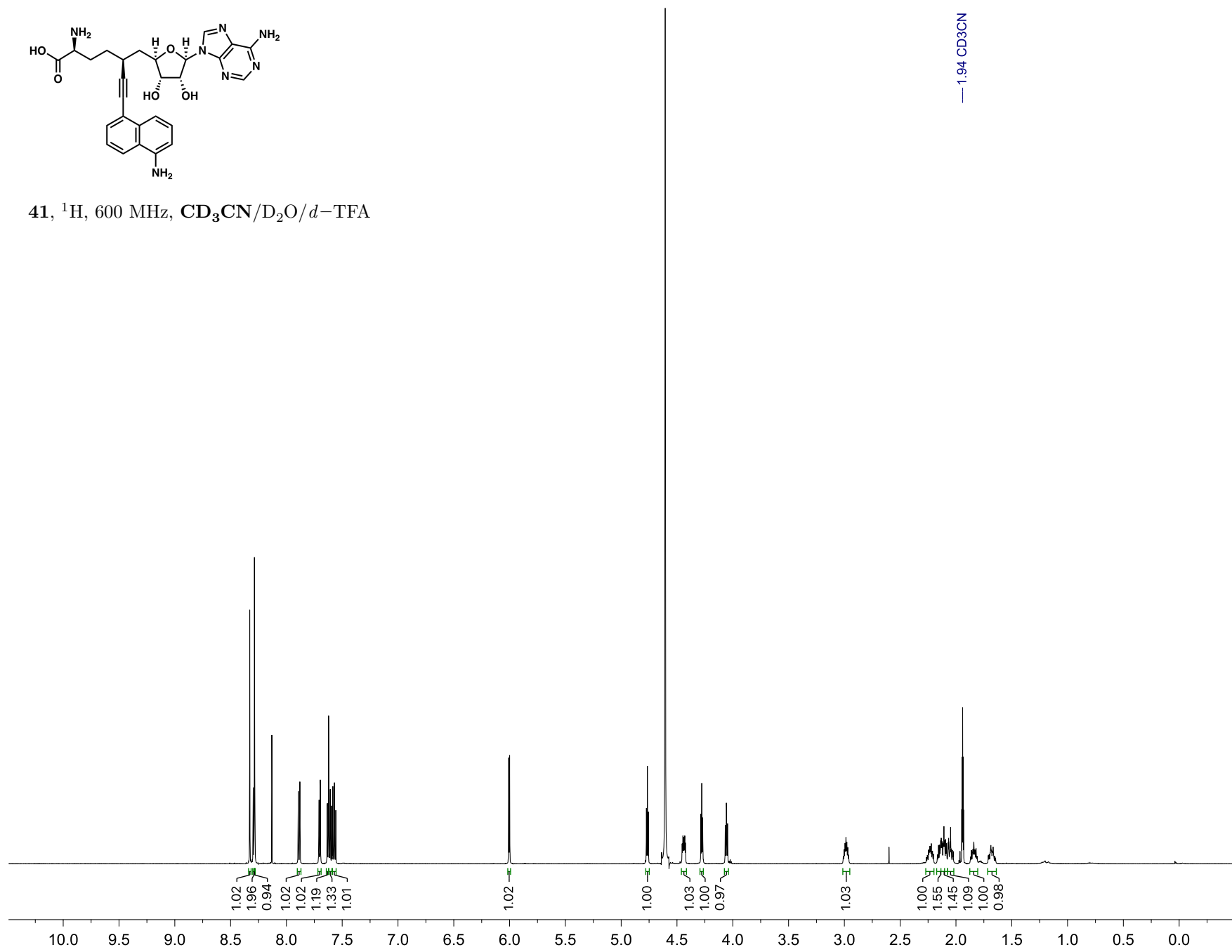


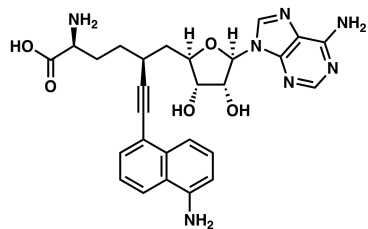
S86, <sup>13</sup>C, 126 MHz, CDCl<sub>3</sub>





41,  $^1\text{H}$ , 600 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$



41,  $^{13}\text{C}$ , 126 MHz,  $\text{CD}_3\text{CN}/\text{D}_2\text{O}/d\text{-TFA}$ 