

OXIDATIVE FRAGMENTATION OF CYTISINE AS AN ENTRY TO THE BIS(PIPERIDINE) SCAFFOLD OF VIRGIDIVARINE

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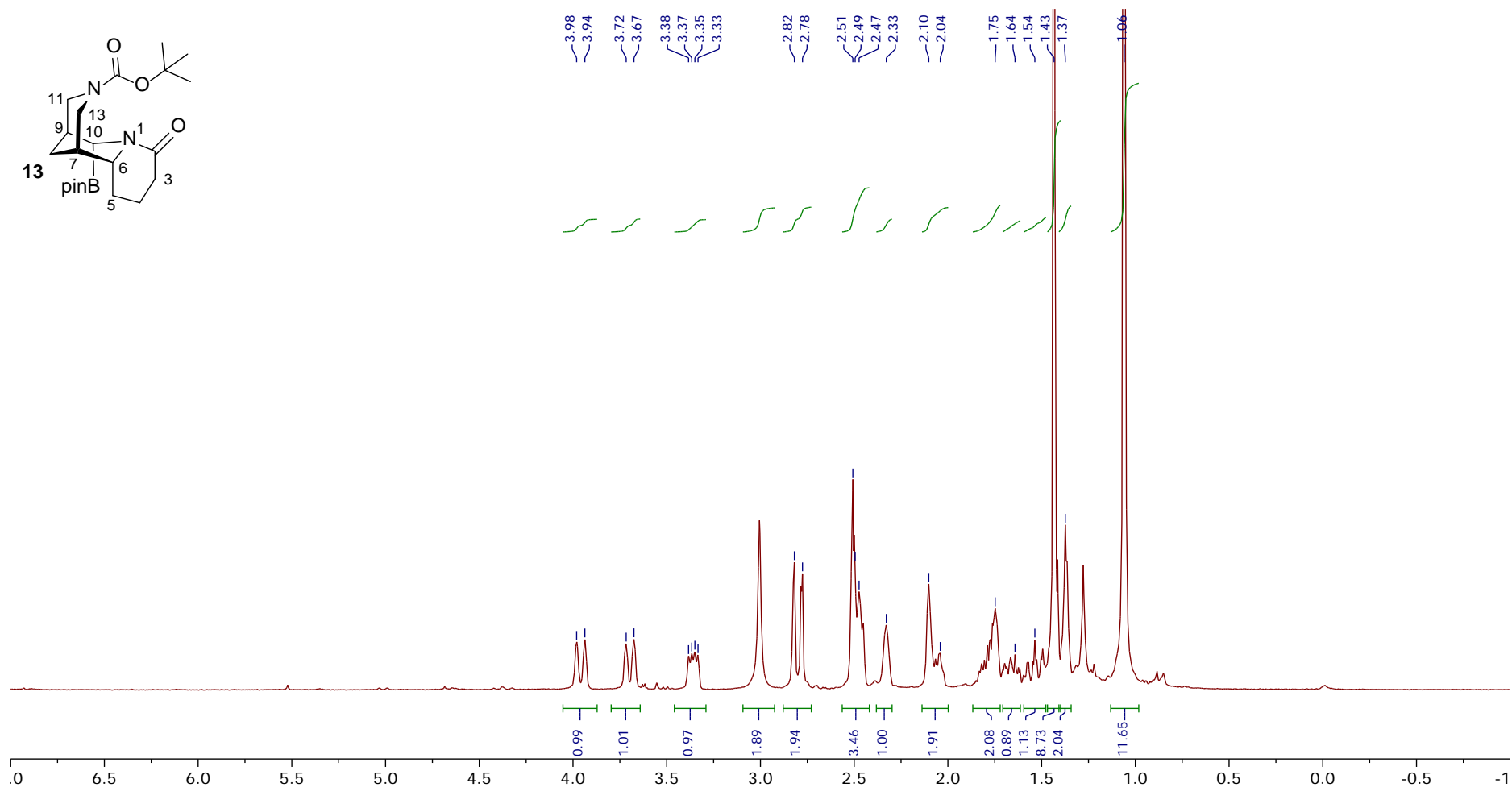
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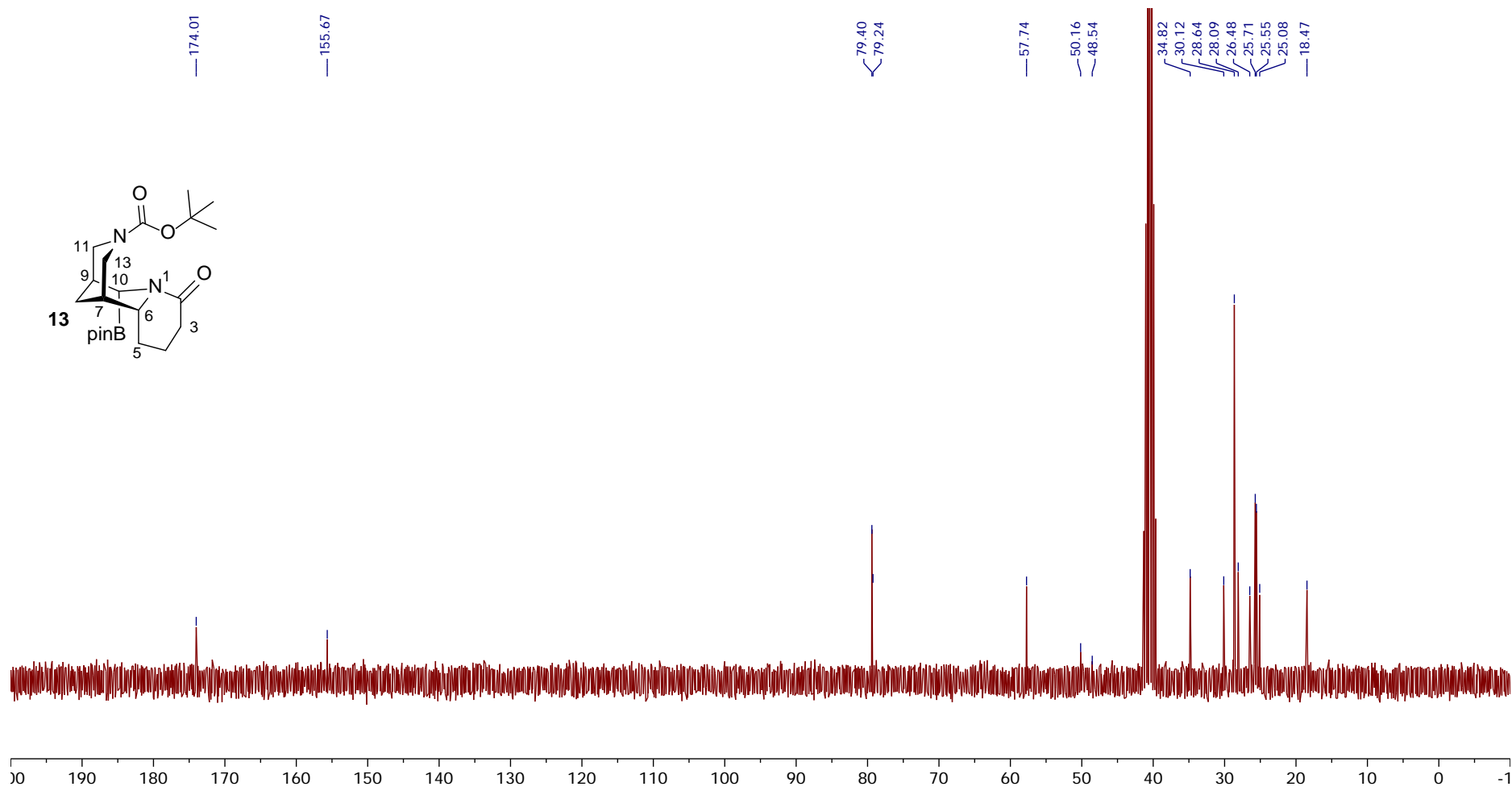
Supporting Information

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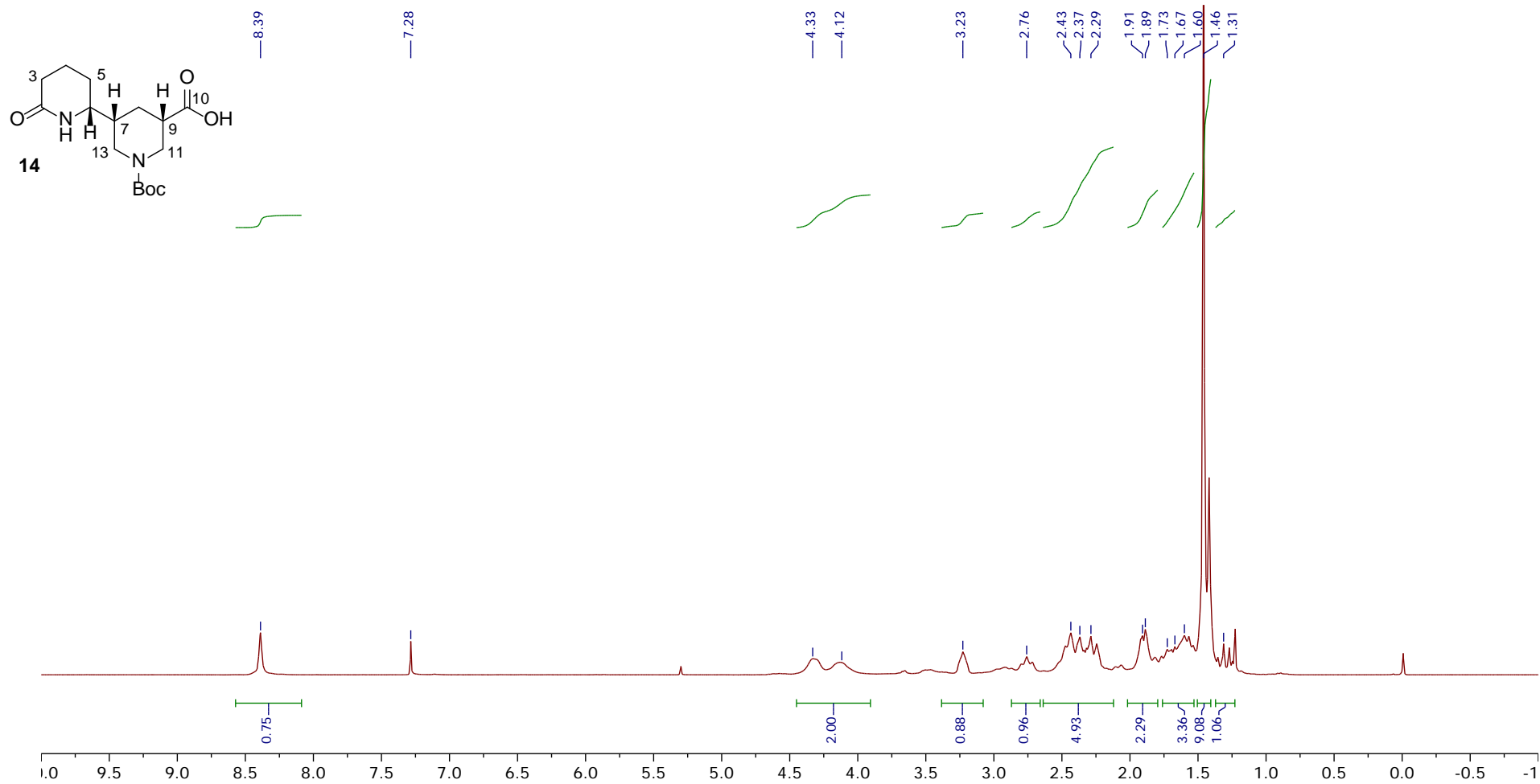
¹H and ¹³C NMR spectra

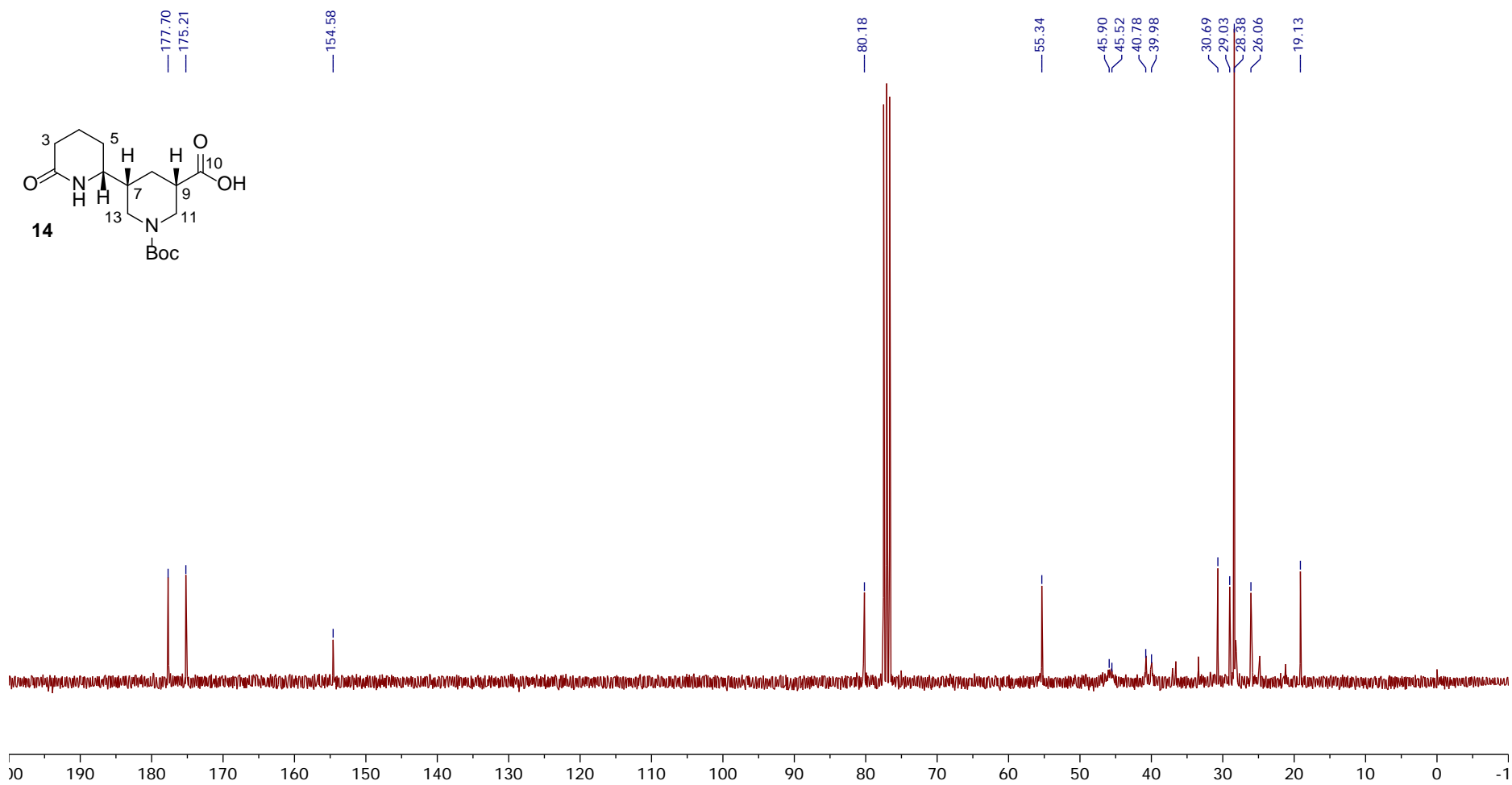
tert-Butyl (6*S*,11*aS*)-8-oxo-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)octahydro-2*H*-1,5-methanopyrido[1,2-*a*][1,5]diazocine-3(4*H*)-carboxylate (**13**)



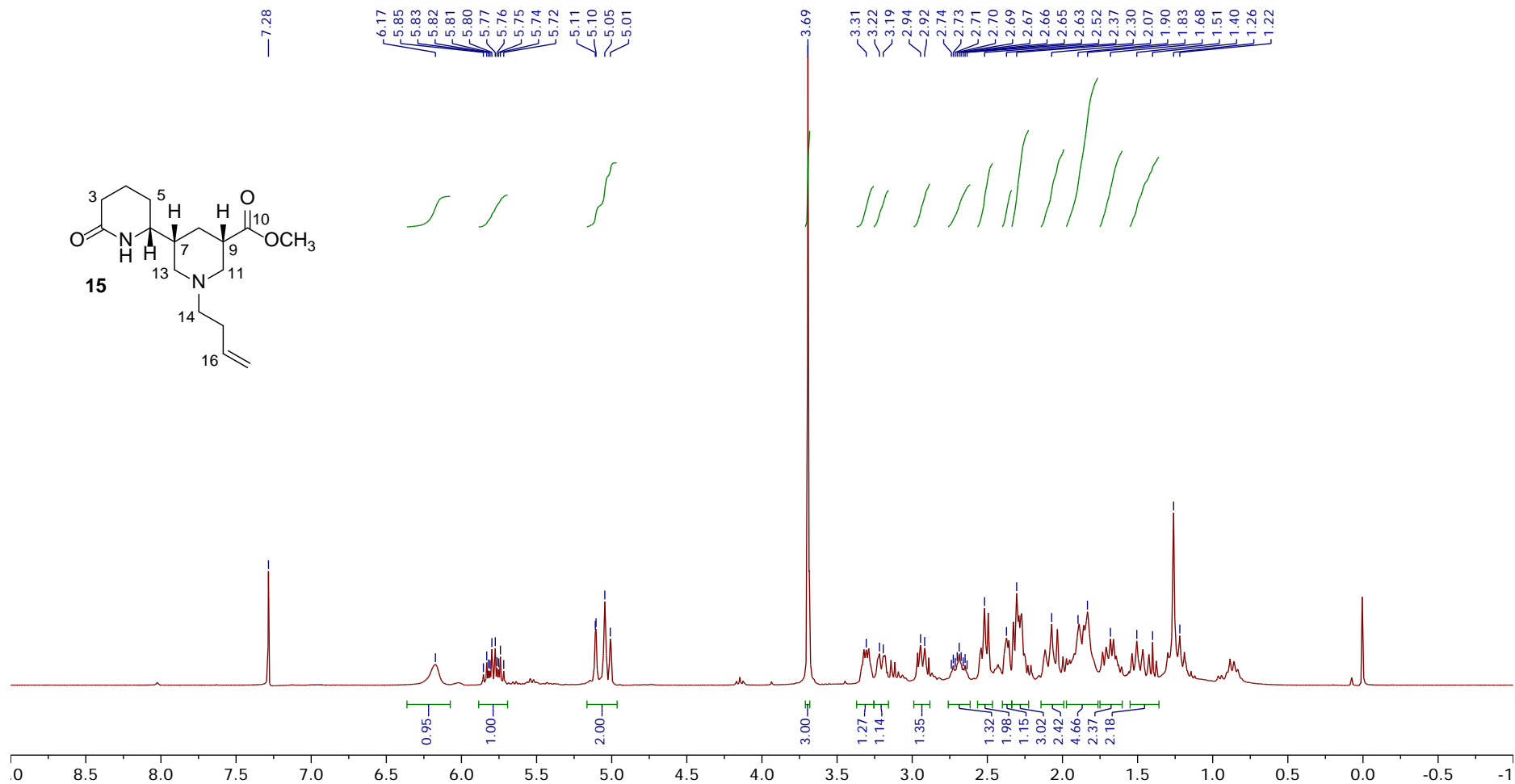


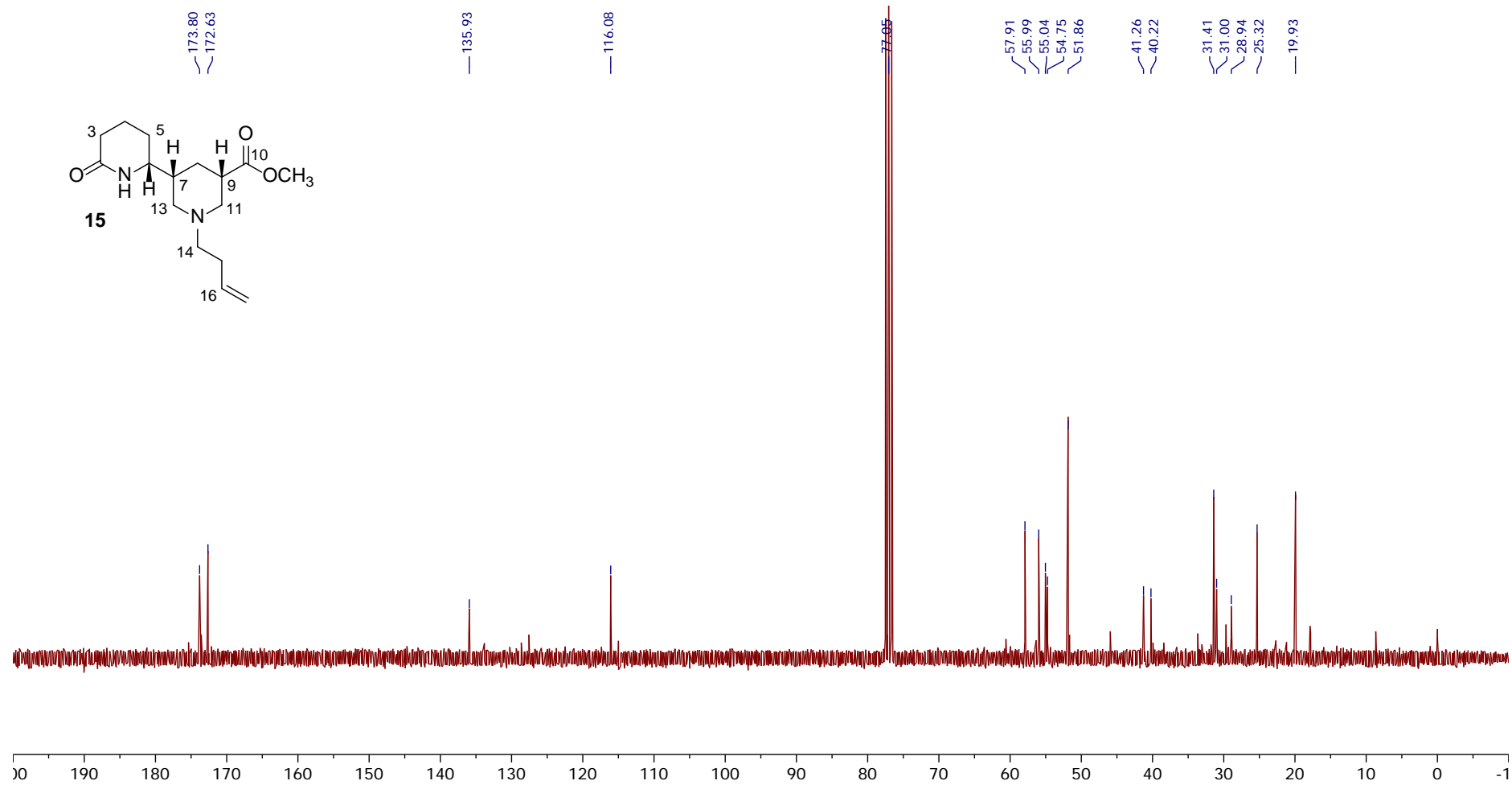
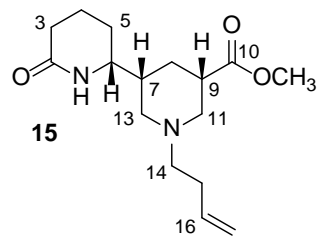
(2S,3'R,5'S)-1'-(*tert*-Butoxycarbonyl)-6-oxo-[2,3'-bipiperidine]-5'-carboxylic acid (14)



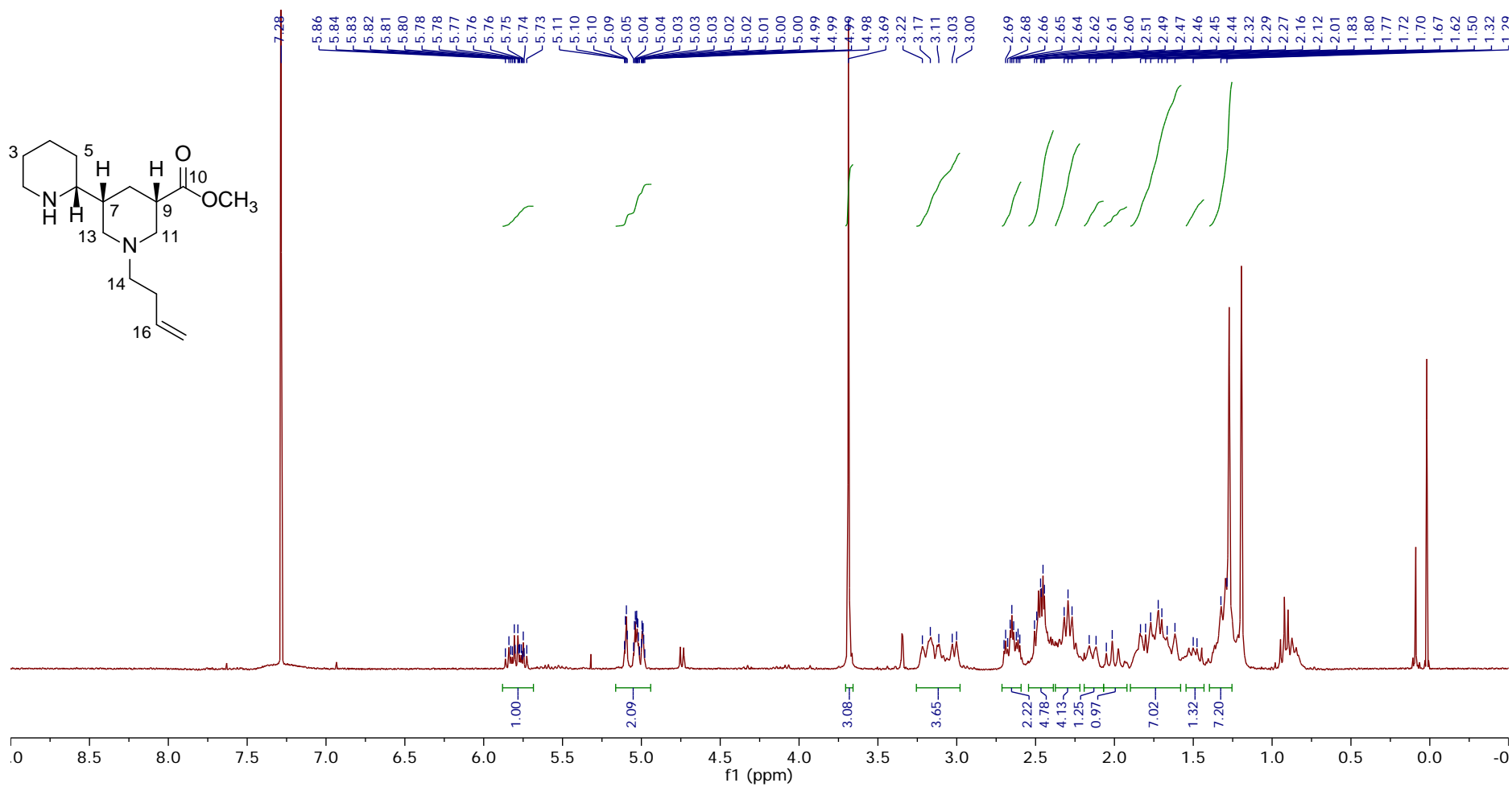


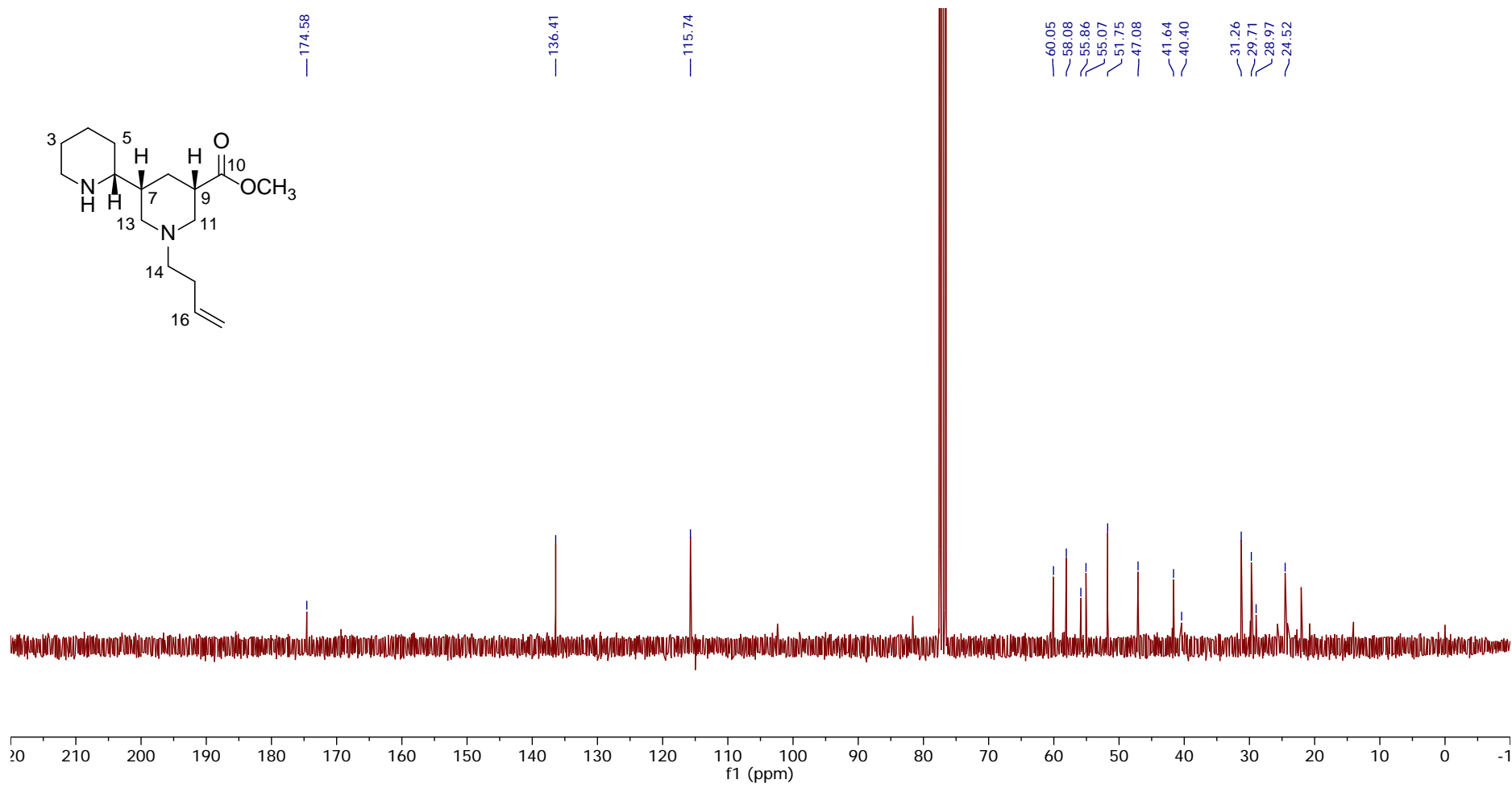
Methyl (2*S*,3'*R*,5'*S*)-1'-(but-3-en-1-yl)-6-oxo-[2,3'-bipiperidine]-5'-carboxylate (15)



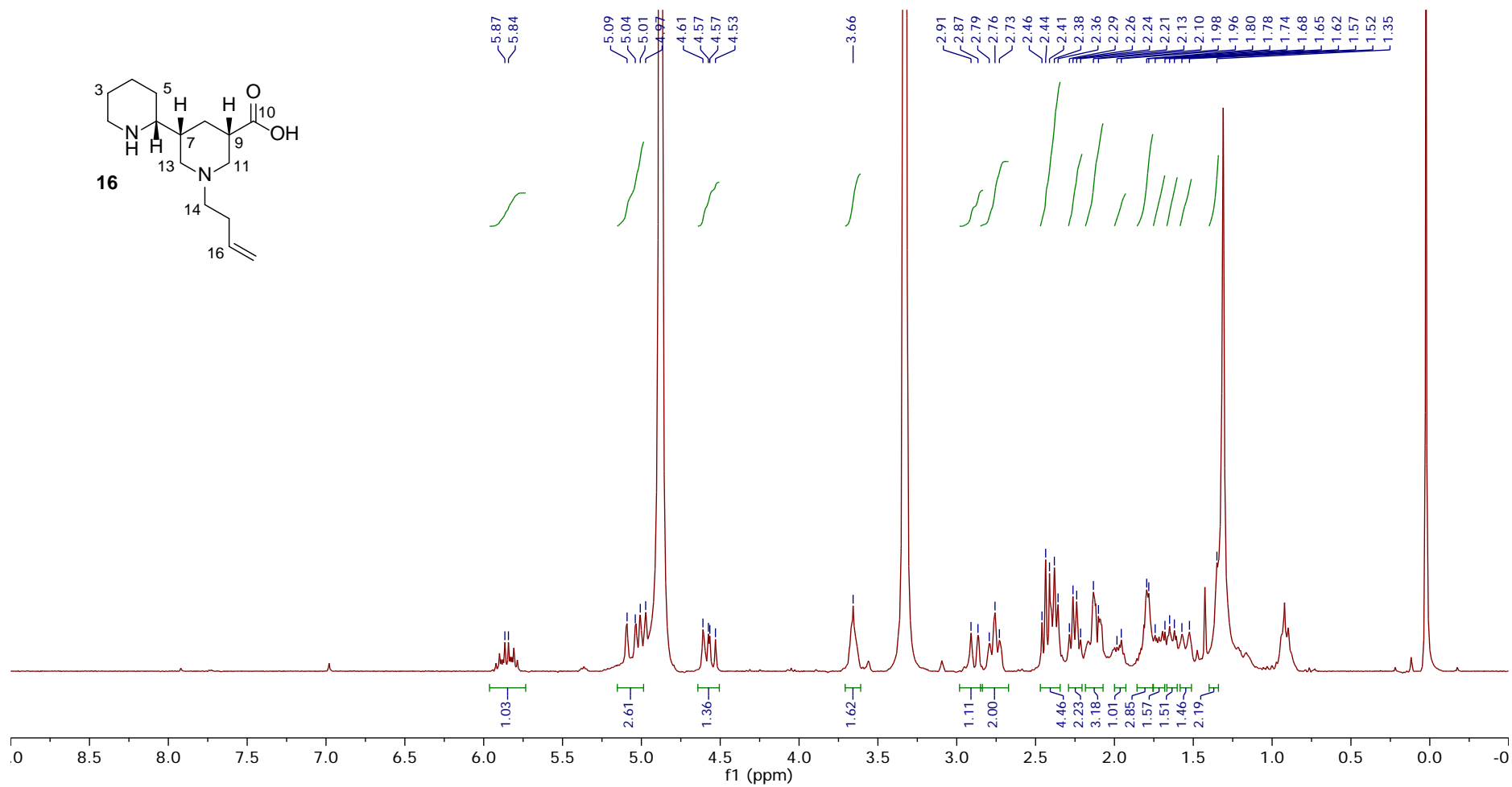


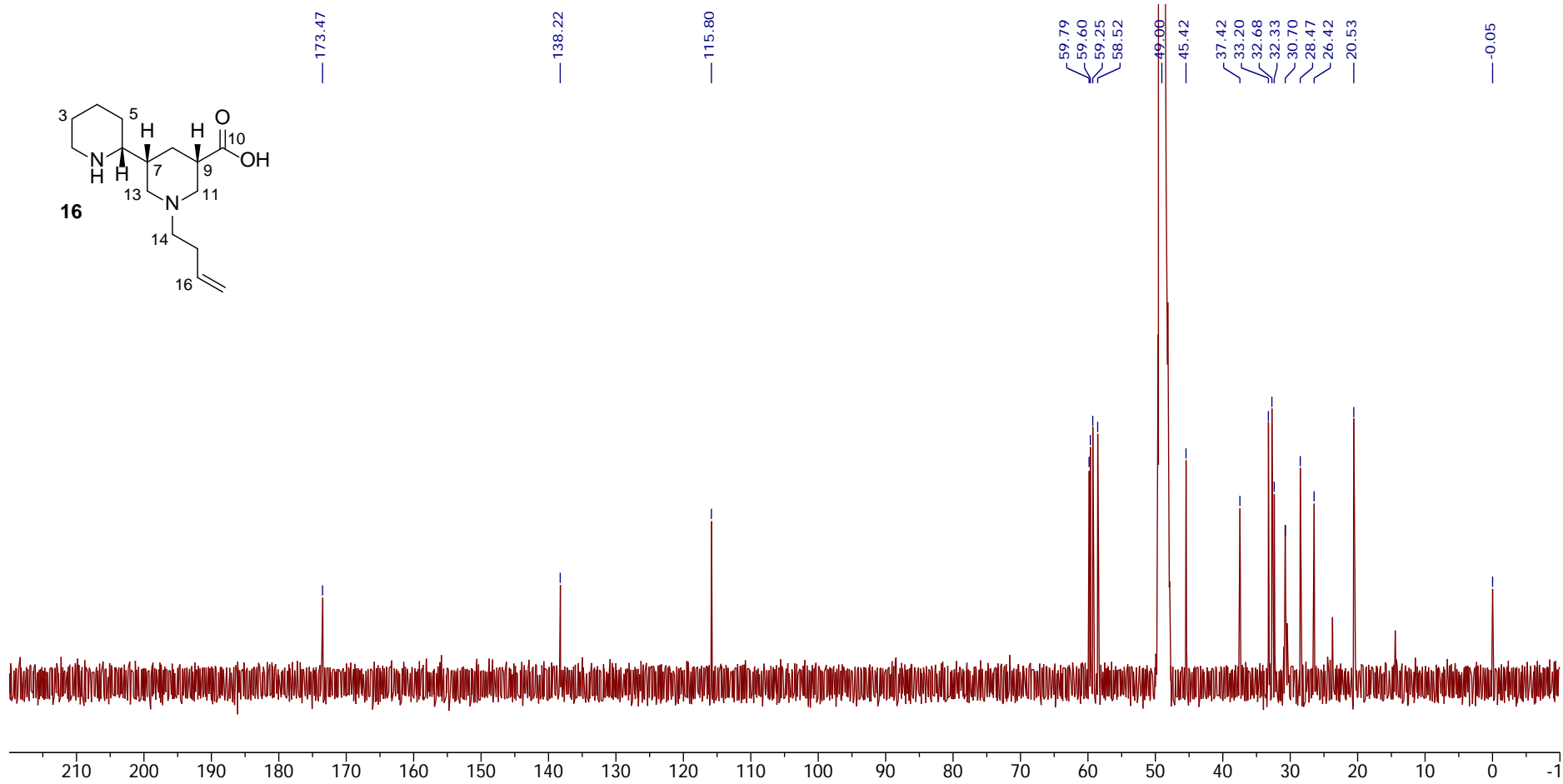
Methyl (2S,3'R,5'S)-1'-(but-3-en-1-yl)-[2,3'-bipiperidine]-5'-carboxylate





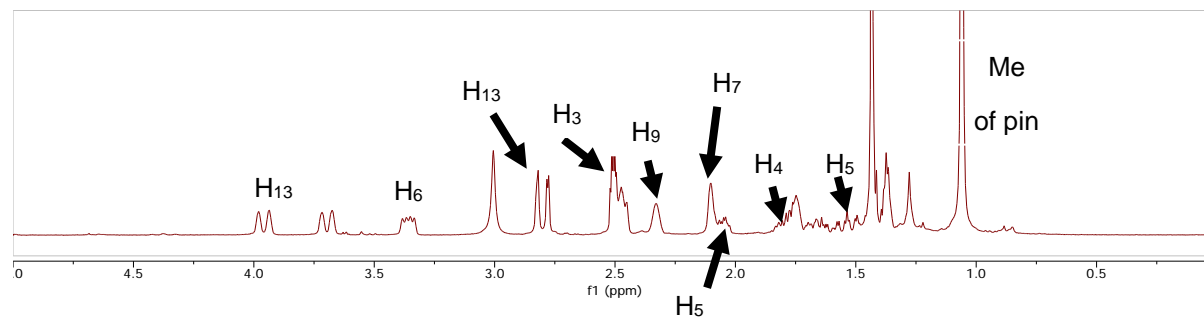
(2*S*,3'*R*,5'*S*)-1'-(But-3-en-1-yl)-[2,3'-bipiperidine]-5'-carboxylic acid (16)



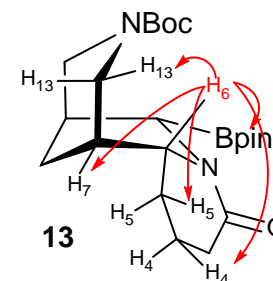
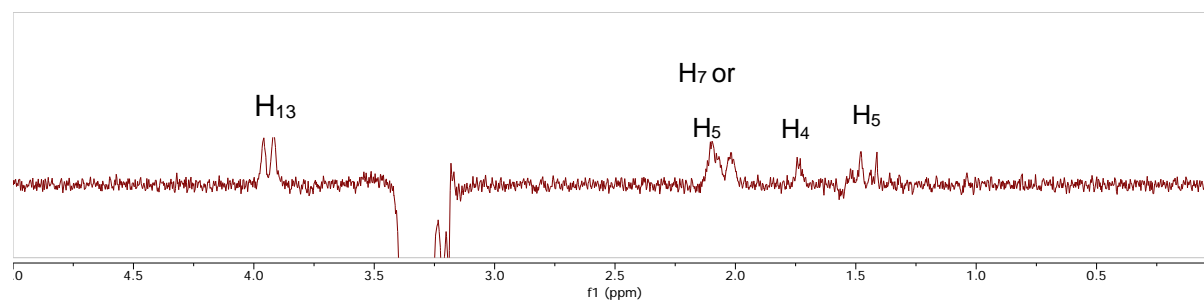


1D NOE experiments on boronic ester **13**

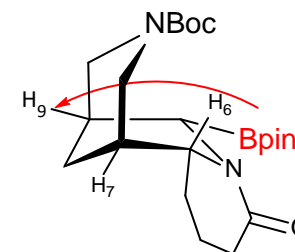
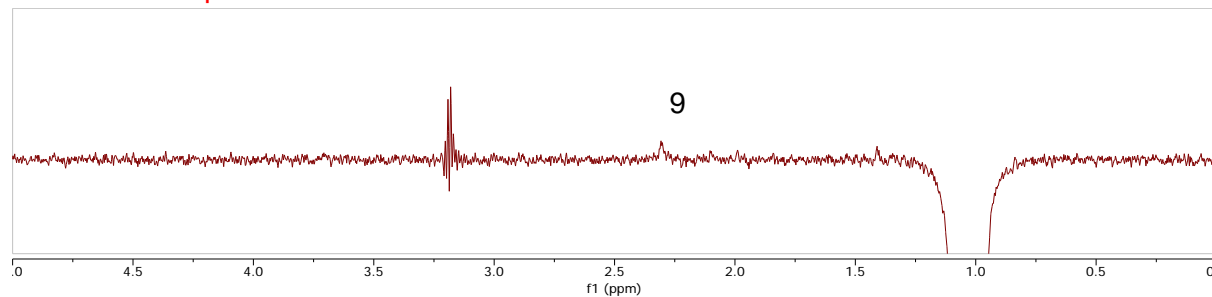
300 MHz ¹H NMR of **13**



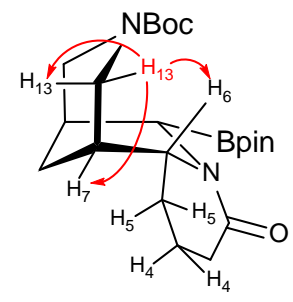
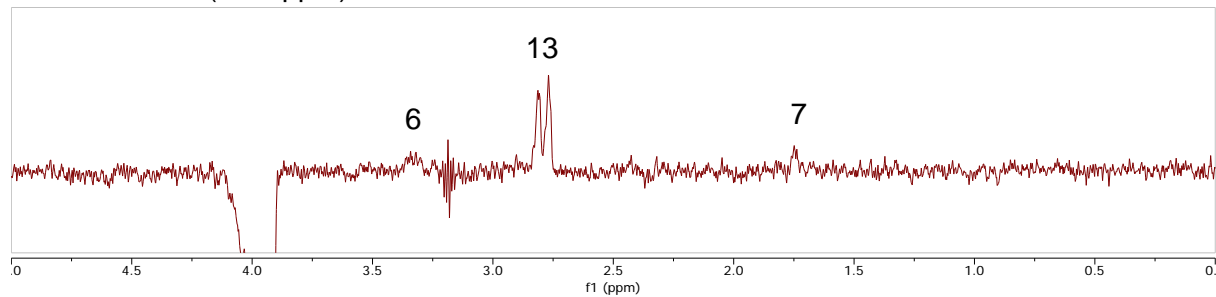
Irradiation of **H₆**



Irradiation of **B-pinacol Me** residues



Irradiation of H_{13} (3.96 ppm)



3. Comparison of ^1H & (selected) ^{13}C NMR data for 2'-epivirgdivarine **16** and virgdivarine **7**

| Numbering system used | | | | |
|--|---|---|---|---|
| | | | | |
| position | δ_{H} (ppm) ^a | | δ_{C} (ppm) (selected signals) | |
| | 16 (600 MHz, CD_3OD) | Virgdivarine free base 7 (700 MHz, CD_3OD) [‡] | Compound 16 (151 MHz, CD_3OD) | Virgdivarine free base 7 (175 MHz, CDCl_3 , CD_3OD) [‡] |
| 2 | 2.92 – 2.71 (m); 2.20 – 2.06 (m) | 3.23 – 3.21 (m); 2.04 (t) | | |
| 3 | 2.39 – 2.32 (m) | 2.45 – 2.41 (m) | 28.5 | 46.5 |
| 4 | 1.56 – 1.50 (m); 1.36 – 1.30 (m) | 2.09 – 2.06 (m) 1.22-1.17 (m)‡ | 26.4 | 31.9 |
| 5 | 1.85 – 1.67 (m) | 1.85 (m) | 37.4 | 41.3 |
| 6 | 2.92 – 2.71 (m); 2.20 – 2.06 (m) | 3.07 – 3.04 (m) 1.81 – 1.50 (br, m) | | |
| 2' | 3.70 – 3.58 (m) | 2.92 – 2.91 (m) | 59.8 | 62.1 |
| 3' | 2.00 – 1.93 (m); 1.67 – 1.58 (m) | 1.96 – 1.91 (m) 1.50 – 1.44 (m) | 32.7 | 28.4 |
| 4' | 1.85 – 1.67 (m) | 1.81 – 1.50 (br, m); 1.57 – 1.51 (m) | | |
| 5' | 2.39 – 2.32 (m); 2.20 – 2.06 (m) | 1.96 – 1.91 (m); 1.70 – 1.64 (m) | | |
| 6' | 4.54 – 4.52 (m); 2.92 – 2.71 (m); | <i>under solvent peak</i> ; 2.95 (dt); | | |
| 8 | | | 173.5 | 182.4 |
| 1'' | 2.44 (t) | 2.55 – 2.53 (m) | | |
| 2'' | 2.29 – 2.21 (m) | 2.36 – 2.33 (m) | | |
| 3'' | 5.83 (ddt) | 5.84 (ddt) | | |
| 4'' | 5.08 – 5.02 (m) | 5.12 (d); 5.03 (d) | | |
| [‡] Data from Blechert et al ¹ [‡] While Hb was presented, the other proton (Ha) was extracted from SI ¹) ¹ S. Kress, J. Weckesser, S. R. Schulz, and S. Blechert, <i>Eur. J. Org. Chem.</i> , 2013 , 1346. | | | | |
| | Signals associated with differences in stereochemistry in the region of the bis(piperidine) link C5-C2' using the numbering system applied here | | | |