Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

Ψ[CH(CF_3)NH]Gly-Peptides: Synthesis and Conformation Analysis

Marco Molteni, Maria Cristina Bellucci, Serena Bigotti, Stefania Mazzini, Alessandro Volonterio,* Matteo Zanda*

Dipartimento di Chimica, Materiali ed Ingegneria Chimica "G. Natta" del Politecnico di Milano, via Mancinelli 7, I-20131 Milano, Italy, and C.N.R.- Istituto di Chimica del Riconoscimento Molecolare, Sezione "A. Quilico", via Mancinelli 7, I-20131 Milano, Italy.

alessandro.volonterio@polimi.it; matteo.zanda@polimi.it;

Table of Contents:

4a: $[\alpha]^{23}_{D}$ = - 17.2° (*c* = 1.2, $CHCl_3$); FT IR (film): ν_{max} = 3363, 2966, 1732, 1566, 1382 cm^{-1} ; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.41-7.33 (m, 5H), 5.18 (d, *J* = 12.2 Hz, 1H), 5.15 (d, *J* = 12.2 Hz, 1H), 4.64 (dd, *J* = 13.5, 4.3 Hz, 1H), 4.52 (dd, *J* = 13.5, 7.5 Hz, 1H), 3.91 (m, 1H), 3.32 (d, *J* = 5.3 Hz, 1H), 2.04 (m, 1H), 1.94 (br s, 1H), 0.97 (d, *J* = 6.5 Hz, 3H), 0.87(d, *J* = 6.5 Hz, 3H); ^{19}F NMR (470.6 MHz, $CDCl_3$): δ = - 75.8 (d, *J* = 7.7 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 174.1, 135.4, 128.62, 128.60, 128.5, 124.5 (q, *J* = 281.7 Hz), 74.3, 67.1, 66.6, 58.29 (q, *J* = 29.8 Hz), 31.9, 19.1, 17.3; MS (70 eV): *e/z* (%): 349 [M^+ + 1] (20), 213 (100), 91 (40).

4b: $[\alpha]^{23}_{D}$ = - 12.9° (*c* = 1.8, $CHCl_3$); FT IR (film): ν_{max} = 3362, 2972, 2930, 1716, 1567 cm^{-1} ; ^1H NMR (250 MHz, $CDCl_3$): δ = 4.67 (dd, *J* = 13.9, 4.2 Hz, 1H), 4.57 (dd, *J* = 13.9, 7.4 Hz, 1H), 3.88 (m, 1H), 3.14 (d, 4.9 Hz, 1H), 1.98(m, 1H), 1.95 (br s, 1H), 1.46 (s, 9H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = - 76.4 (d, *J* = 6.9 Hz, 3F); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.4, 124.6 (q, *J* = 282.3 Hz), 81.9, 74.4, 66.9, 58.5 (q, *J* = 29.7 Hz), 31.9, 27.8, 19.0, 17.1.

4c: $[\alpha]^{23}_{D}$ = - 24.0° (*c* = 1.6, $CHCl_3$); FT IR (film): ν_{max} = 3360, 2980, 2936, 1728, 1642, 1567, 1382 cm^{-1} ; ^1H NMR (250 MHz, $CDCl_3$): δ = 4.67 (dd, *J* = 13.3, 4.9 Hz, 1H), 4.59 (dd, *J* = 13.3, 7.5 Hz, 1H), 3.95 (m, 1H), 3.47 (q, *J* = 6.9 Hz, 1H), 2.00 (br s, 1H), 1.45 (s, 9H), 1.30 (d, *J* = 6.9 Hz, 3H); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = - 76.3 (d, *J* = 7.3 Hz, 3F); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.9, 124.7 (q, *J* = 282.2 Hz), 82.0, 74.4, 57.3 (q, *J* = 29.7 Hz), 56.7, 27.9, 19.7; MS (70 eV): *e/z* (%): 287 [M^+ + 1] (1), 185 (100).

4e: $[\alpha]^{23}_{D}$ = - 14.1° (*c* = 1.2, $CHCl_3$); FT IR (film): ν_{max} = 3355, 2932, 1725, 1570, 1370, 1153 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.17 (m, 5H), 4.60 (dd, *J* = 13.3, 4.7 Hz, 1H), 4.47 (dd, *J* = 13.3, 7.7 Hz, 1H), 3.95 (m, 1H), 3.65 (dd, *J* = 7.2, 6.1 Hz 1H), 2.98 (dd, *J* =13.5, 6.1 Hz, 1H), 2.88 (dd, *J* =13.5, 7.2 Hz, 1H), 1.83 (br s, 1H), 1.40 (s, 9H); ^{19}F NMR (470.6 MHz, $CDCl_3$): δ = - 76.0 (d, *J* = 7.3 Hz, 3F); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 172.6, 136.4, 129.4, 128.4, 126.9, 124.5 (q, *J* = 281.0 Hz), 82.3, 74.2, 61.9, 57.6 (q, *J* = 29.3 Hz), 40.1, 27.8.

4g: $[\alpha]^{23}_{D}$ = + 13.8° (*c* = 1.2, $CHCl_3$); FT IR (film): ν_{max} = 3359, 2957, 1740, 1563, 1382, 1267, 1030 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 7.33-7.15 (m, 5H), 4.60 (dd, *J* = 13.1, 4.3 Hz, 1H), 4.44 (dd, *J* = 13.1, 8.14 Hz, 1H), 3.95 (m, 1H), 3.79 (dd, *J* = 7.4, 5.3 Hz, 1H), 3.70 (s, 3H), 3.06

(dd, *J* =13.5, 5.3 Hz, 1H), 2.90 (dd, *J* = 13.5, 7.4 Hz, 1H), 1.86 (br s, 1H); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = - 76.1 (d, *J* = 6.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.6, 136.0, 129.2, 128.6, 127.1, 124.1 (q, *J* = 283.3 Hz), 74.3, 61.4, 57.5 (q, *J* = 29.7 Hz), 52.3, 39.6; MS (70 eV): *e/z* (%): 321 [M^+ + 1] (20), 261 (98), 229 (100), 91 (35).

5a: $[\alpha]^{23}_D$ = + 22.9° (*c* = 1.0, $CHCl_3$); FT IR (film): ν_{max} = 3345, 2967, 2919, 1733, 1567, 1382 cm^{-1} ; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41-7.31 (m, 5H), 5.15 (s, 2H), 4.59 (dd, *J* = 12.9, 3.6 Hz, 1H), 4.40 (dd, *J* = 12.9, 10.1 Hz, 1H), 3.94 (m, 1H), 3.20 (d, *J* = 4.6 Hz, 1H), 2.20 (br s, 1H), 1.90(m, 1H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.80(d, *J* = 6.5 Hz, 3H); ^{19}F NMR (470.6 MHz, $CDCl_3$): δ = - 74.8 (d, *J* = 7.6 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.5, 135.4, 128.6, 124.7 (q, *J* = 285.5 Hz), 74.7, 67.1, 66.3, 59.4 (q, *J* = 29.5 Hz), 32.7, 19.0, 17.2; MS (70 eV): *e/z* (%): 349 [M^+ + 1] (20), 213 (100), 91 (40).

5b: this diastereoisomer was not isolated in analytically pure form; ^{19}F NMR (235.4 MHz $CDCl_3$): δ = -75.1 (d, *J* = 7.0 Hz).

5c: $[\alpha]^{23}_D$ = + 19.0° (*c* = 1.3, $CHCl_3$); FT IR (film): ν_{max} = 3340, 2969, 1722, 1570, 1371, 1124 cm^{-1} ; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.62 (dd, *J* = 13.1, 3.9 Hz, 1H), 4.41 (dd, *J* = 13.1, 9.3 Hz, 1H), 4.03 (m, 1H), 3.40 (q, *J* = 6.8 Hz, 1H), 2.27 (br s, 1H), 1.46 (s, 9H), 1.23 (d, *J* = 6.8 Hz, 3H); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = - 75.1 (d, *J* = 7.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.4, 124.5 (q, *J* = 284.5 Hz), 81.9, 74.7, 57.4 (q, *J* = 29.5 Hz), 55.8, 27.9, 19.8; MS (70 eV): *e/z* (%): 287 [M^+ + 1] (1), 185 (100), 57 (30).

5e: this diastereoisomer was not isolated in analytically pure form. ^{19}FNMR (470.6 MHz, $CDCl_3$): δ = -74.6 (d, *J* = 7.3 Hz).

5g: $[\alpha]^{23}_D$ = - 35.5° (*c*= 0.6, $CHCl_3$); FT IR (film): ν_{max} = 2956, 3354, 2924, 1736, 1566, 1382 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.30 (m, 3H), 7.10 (m, 2H), 4.51 (dd, *J* = 13.1, 4.2 Hz, 1H), 4.29 (dd, *J* = 13.1, 9.2 Hz, 1H), 3.91 (m, 1H), 3.70 (s, 3H), 3.65 (dd, *J* = 6.9, 5.4 Hz, 1H), 2.95 (dd, *J* = 13.5, 5.4 Hz, 1H), 2.81 (dd, *J* = 13.5, 6.9 Hz, 1H), 2.03 (br s, 1H); ^{19}F NMR (235.4 MHz, $CDCl_3$): δ = - 75.3 (d, *J* = 6.6 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 173.6, 136.3, 129.3, 128.5, 127.0, 124.7 (q, *J* = 283.9 Hz), 74.4, 61.9, 58.5 (q, *J* = 29.5 Hz), 40.7; MS (70 eV): *e/z* (%): 321 [M^+ + 1] (38), 261 (85), 229 (100), 91 (38).

8b: $[\alpha]^{23}_{D}$ = - 8.5° (c = 2.7, CH_3COCH_3); FT IR (microscope): ν_{max} = 3300, 2956, 2924, 1724, 1687, 1654, 1539, 1368 cm^{-1} ; ^{1}H NMR: (250 MHz, CD_3COCD_3): δ = 7.69 (br s, 1H), 7.36-7.16 (m, 10H), 6.40 (br d, *J* = 8.3 Hz, 1H), 5.05 (d, *J* = 12.8 Hz, 1H), 4.95 (d, *J* = 12.8 Hz, 1H), 4.49 (m, 1H), 3.49 (m, 2H), 3.29 (dd, *J* = 13.7, 5.1 Hz, 1H), 3.21 (m, 1H), 3.16 (d, *J* = 4.2 Hz, 1H), 2.98 (m, 1H), 2.36 (br s, 1H), 1.97 (m, 1H), 1.47 (s, 9H), 0.98 (d, *J* = 6.5, 3H), 0.89 (d, *J* = 6.5 Hz, 3H); ^{19}F NMR: (235.4 MHz, $CDCl_3$): δ = -74.0 (d, *J* = 6.9 Hz); ^{13}C NMR (62.9 MHz, CD_3COCD_3): δ = 175.9, 173.7, 157.4, 139.6 138.7 130.9, 129.8, 129.7, 129.2, 129.1, 127.9, 127.8 (q, *J* = 282.7 Hz), 82.6, 67.9, 67.3, 60.6 (q, *J* = 27.7 Hz), 58.0, 39.3, 33.0, 29.0, 20.4, 18.6; MS (70 eV): *e/z* (%): 566 [M^+ + 1] (60), 464 (30), 91 (100).

8d: $[\alpha]^{23}_{D}$ = - 12.2° (*c* = 1.8, CH_3COCH_3); FT IR (film): ν_{max} = 3305, 2966, 1735, 1688, 1656, 1540, 1382 cm^{-1} ; ^{1}H NMR: (400 MHz, CD_3COCD_3): δ = 7.69 (br s, 1H), 7.36-7.17 (m, 10H), 6.44 (m, 1H), 5.06 (d, *J* = 12.5 Hz, 1H), 4.98 (d, *J* = 12.5 Hz, 1H), 4.52 (m, 1H), 3.69 (s, 3H), 3.49 (m, 2H), 3.30 (m, 2H), 3.21 (m, 1H), 3.0 (m, 1H), 2.44 (br s, 1H), 1.71 (m, 1H), 1.53 (m, 1H), 1.21 (m, 1H), 0.92 (d, *J* = 6.7 Hz), 0.88 (t, *J* = 7.6 Hz); ^{19}F NMR: (235.4 MHz, CD_3COCD_3): δ = -74.2 (d, *J* = 7.3 Hz); ^{13}C NMR (62.9 MHz, CD_3COCD_3): δ = 176.2, 173.2, 156.8, 138.8, 138.0, 130.2, 129.1, 129.0, 128.5, 128.4, 127.2, 127.1 (q, *J* = 281.5 Hz), 66.6, 66.3, 59.8 (q, *J* = 27.6 Hz), 57.4, 52.1, 39.2, 38.7, 25.6, 16.1, 11.7; MS (70 eV): *e/z* (%): 538 [M^+ + 1] (60), 478 (90), 91 (100).

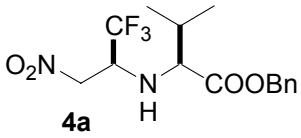
8g: $[\alpha]^{23}_{D}$ = - 11.6° (*c* = 0.4, CH_3COCH_3); FT IR (film): ν_{max} = 3324, 2952, 1731, 1648, 1654, 1531, 1263, 1171 cm^{-1}; ^{1}H NMR: (400 MHz, CD_3COCD_3): δ = 7.55 (br s, 1H), 7.23 (m, 15H), 6.36 (br d, *J* = 7.0 Hz, 1H), 5.03 (d, *J* = 12.6 Hz, 1H), 4.97 (d, *J* = 12.6 Hz, 1H), 4.44 (m, 1H), 3.74 (m, 1H), 3.63 (s, 3H), 3.52 (m, 1H), 3.32 (m, 2H), 3.21 (dd, *J* = 14.0, 5.0 Hz, 1H), 2.93 (m, 3H), 2.41 (br d, *J* = 8.2 Hz, 1H); ^{19}F NMR: (235.4 MHz, CD_3COCD_3): δ = -74.2 (d, *J* = 7.2 Hz); ^{13}C NMR (62.9 MHz, CD_3COCD_3): δ = 176.1, 173.6, 157.5, 139.5, 138.9, 138.7, 130.8, 130.7, 129.8, 129.7, 129.6, 129.2, 129,1, 128.0, 127.9, 67.3, 63.5, 59.8 (q, *J* = 28.1 Hz), 58.0, 52.9, 41.0, 39.3; the CF_3 signal was obscured due to its low intensity.

12: $[\alpha]^{23}_{D}$ = +4.4 (*c* = 1.6, $CHCl_3$); FT IR (film): ν_{max} = 3453, 1634, 1543, 1437, 1262, 1131, 754cm^{-1} ^{1}HNMR (400 MHz, $CDCl_3$): δ = 7.44 (br t, *J* = 4.0 Hz, 1H), 6.91(br d, *J* = 8.0 Hz, 1H), 4.49 (m, 2H), 3.82 (m, 1H), 3.71 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.55 (m, 1H), 3.41(m, 2H), 3.17(m, 1H), 3.02(s, 3H), 2.95(s, 3H), 2.40 (br s, 1H), 2.28(m, 1H), 2.19-1.90 (overlap, 8H), 1.47(ddd, *J* =

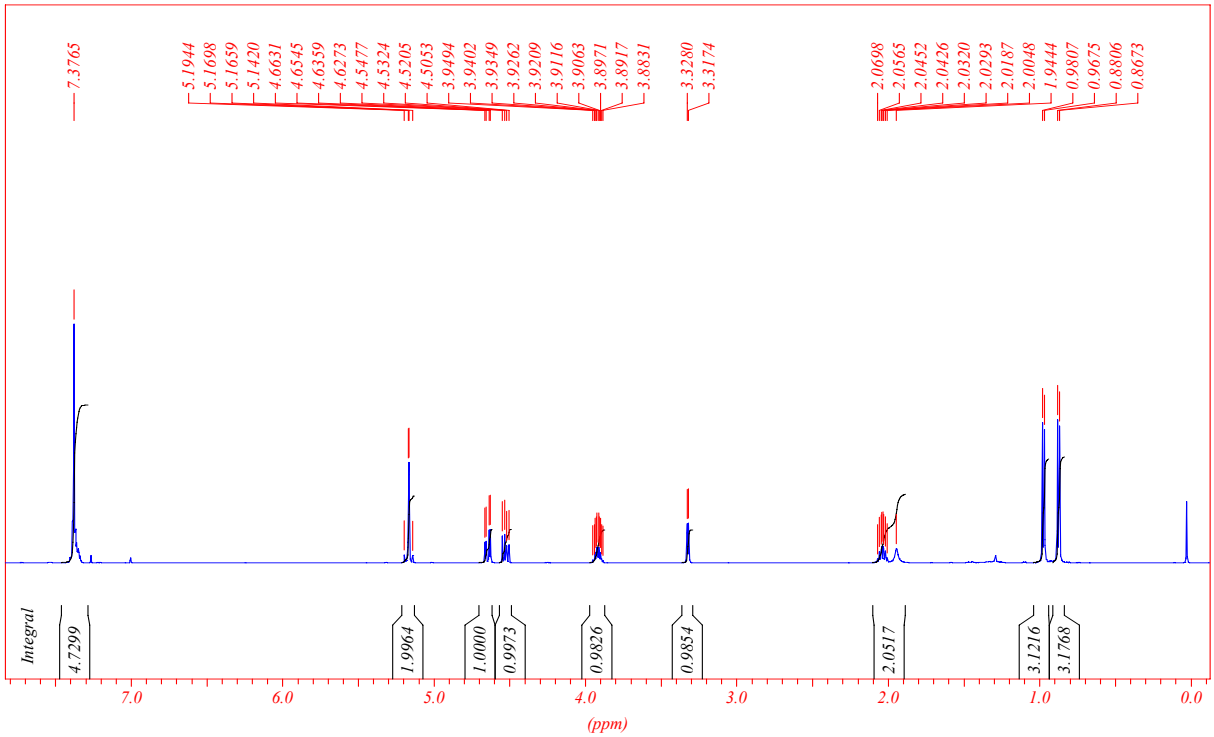
13.6, 9.4, 4.2 Hz, 1H), 1.23(ddd, *J* = 13.6, 8.7, 4.2 Hz, 1H), 0.97 (m, 12H); ^{13}C NMR (62.3 MHz, $CDCl_3$): δ = 172.0, 171.5, 170.8, 60.4, 58.01(q, *J* = 26.7 Hz), 56.4, 55.5, 47.5, 42.6, 37.8, 36.8, 36.0, 30.5, 29.7, 28.3, 24.7, 24.4, 23.4, 22.8, 21.8, 19.6, 18.4; ^{19}F NMR (235.3 MHz, $CDCl_3$): δ = -74.2 (br s). MS (70 eV): *e/z* (%): 508[M^+ + 1] (20), 435 (38), 294 (80), 84 (80), 70 (100), 43 (40). The CF_3 signal was obscured due to its low intensity.

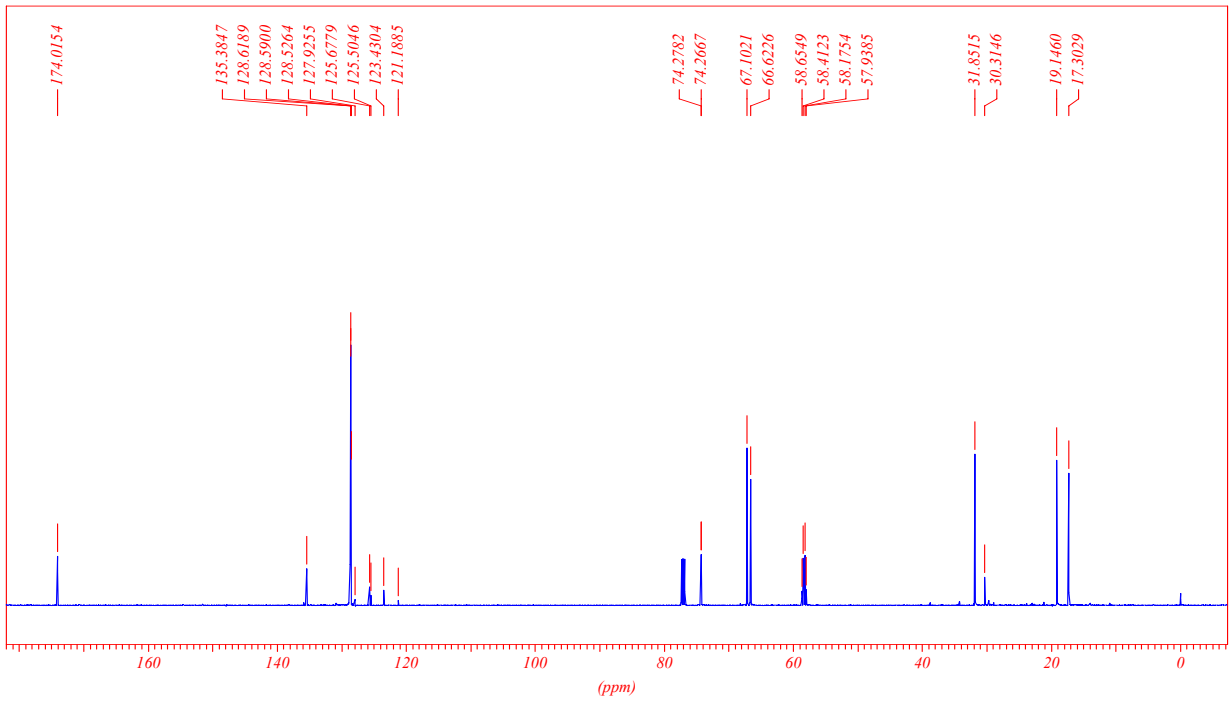
13: $[\alpha]^{23}_D$ = -47.1° (*c* = 0.7, $CHCl_3$); FT IR (film): ν_{max} = 3411, 2960, 1634, 1543, 1431, 1262, cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ = 7.02 (br t, *J* = 5.6 Hz, 1H), 6.23 (br d, *J* = 8.8 Hz, 1H), 4.61 (m, 1H), 4.40 (m, 1H), 3.78 (m, 2H), 3.58 (m, 2H), 3.21 (m, 2H), 3.03 (s, 3H), 2.96 (s, 3H), 2.30 (m, 2H), 2.20 (m, 1H), 2.10 (m, 2H), 2.00 (s, 3H), 1.87 (m, 1H), 1.39(ddd, *J* = 13.6, 9,5, 4.8 Hz, 1H), 1.27 (ddd, *J* = 13.6, 8.9,4.1 Hz, 1H), 0.96 (m, 13H); ^{13}C NMR (150.9 MHz, $CDCl_3$): δ =175.0, 172.3, 171.9, 60.7, 58.63 (q, J=26.8 Hz), 55.8, 54,2, 48.0, 43.8, 38.0, 37.0, 36.3, 31.8, 30.0, 28.3, 25.4, 24.9, 23.9, 23.6, 22.1, 19.7, 18.0 ; ^{19}F NMR (235.3 MHz, CDCl3): δ = -74.3 (br s) ; MS (70 eV): *e/z* (%): 508 [M^+ + 1] (10), 367 (30), 294 (98), 70 (100).

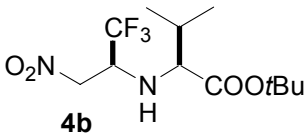
14: $[\alpha]^{23}_D$ = +10.4° (*c* = 1.2, $CHCl_3$); FT IR (film): ν_{max} = 3411, 2960, 1634, 1543, 1431, 1262, cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$): δ = 7.89 (br s, 1H), 6.42(d, *J* = 8.7Hz, 1H), 4.60(dd, *J* = 7.8, 6.1 Hz, 1H), 4.46(dd, *J* = 7.5, 2.6 Hz, 1H), 4.00(m, 1H), 3.75(dd, *J* = 10.5, 2.7 Hz, 1H), 2.98(s, 3H), 2.95(s, 3H), 2.89(m, 1H), 2.00(m, 10H), 1.21 (m, 2H), 0.92 (m, 12H); ^{13}C NMR (62.3 MHz, CDCl3): δ = 174.7, 172.3, 171.3, 170.0, 125.5(Q, *J* = 283.8 Hz), 60.9, 57.7(q, *J* = 27.6 Hz), 56.1, 47.4, 42.3, 38.5, 36.7, 36.3, 31.0, 29.5, 24.5, 24.4, 23.6, 21.0, 19.7, 17.7; ^{19}F NMR (235.3 MHz, CDCl3): δ = -74.2 (br s). MS (70 eV): *e/z* (%): 508[M^+ + 1] (20), 435 (35), 367(40), 294 (80), 70 (100), 43 (20).


CF3
O2N
N
H
COOBn

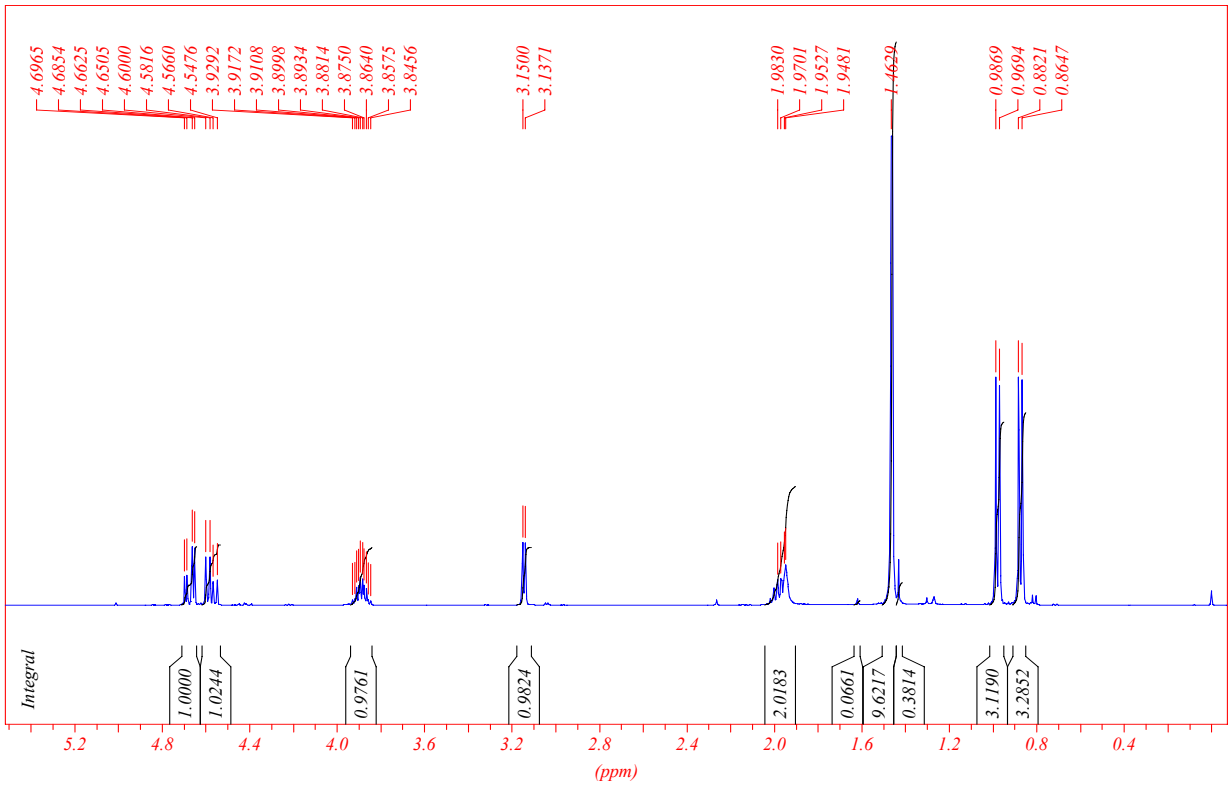
4a

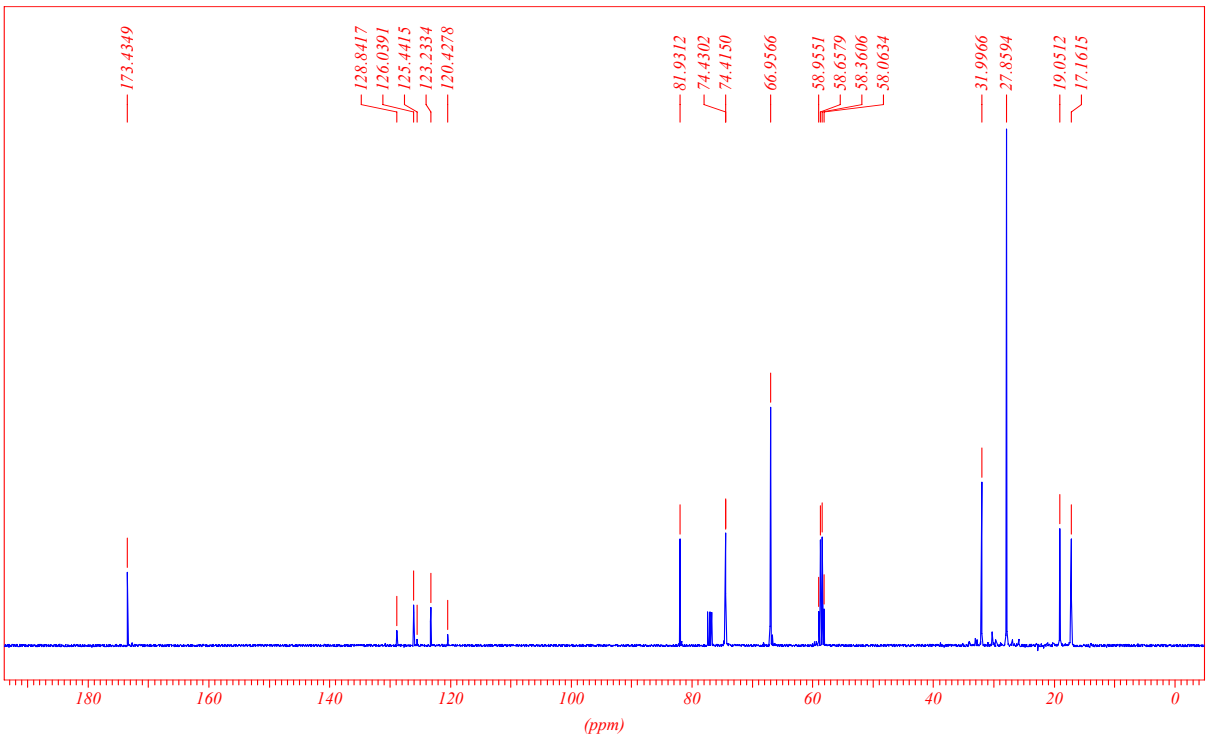

7.3765
5.1944
5.1698
5.1659
5.1420
4.6631
4.6545
4.6359
4.6273
4.5477
4.5324
4.5205
4.5053
3.9494
3.9402
3.9349
3.9262
3.9209
3.9116
3.9063
3.8971
3.8917
3.8831
3.3280
3.3174
2.0698
2.0565
2.0452
2.0426
2.0320
2.0293
2.0187
2.0048
1.9444
0.9807
0.9675
0.8806
0.8673
Integral
4.7299
1.9964
1.0000
0.9973
0.9826
0.9854
2.0517
3.1216
3.1768
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

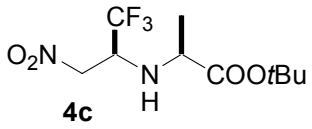

174.0154
135.3847
128.6189
128.5900
128.5264
127.9255
125.6779
125.5046
123.4304
121.1885
74.2782
74.2667
67.1021
66.6226
58.6549
58.4123
58.1754
57.9385
31.8515
30.3146
19.1460
17.3029
160
140
120
100
80
60
40
20
0
(ppm)


CF3
O2N
N
H
COOtBu

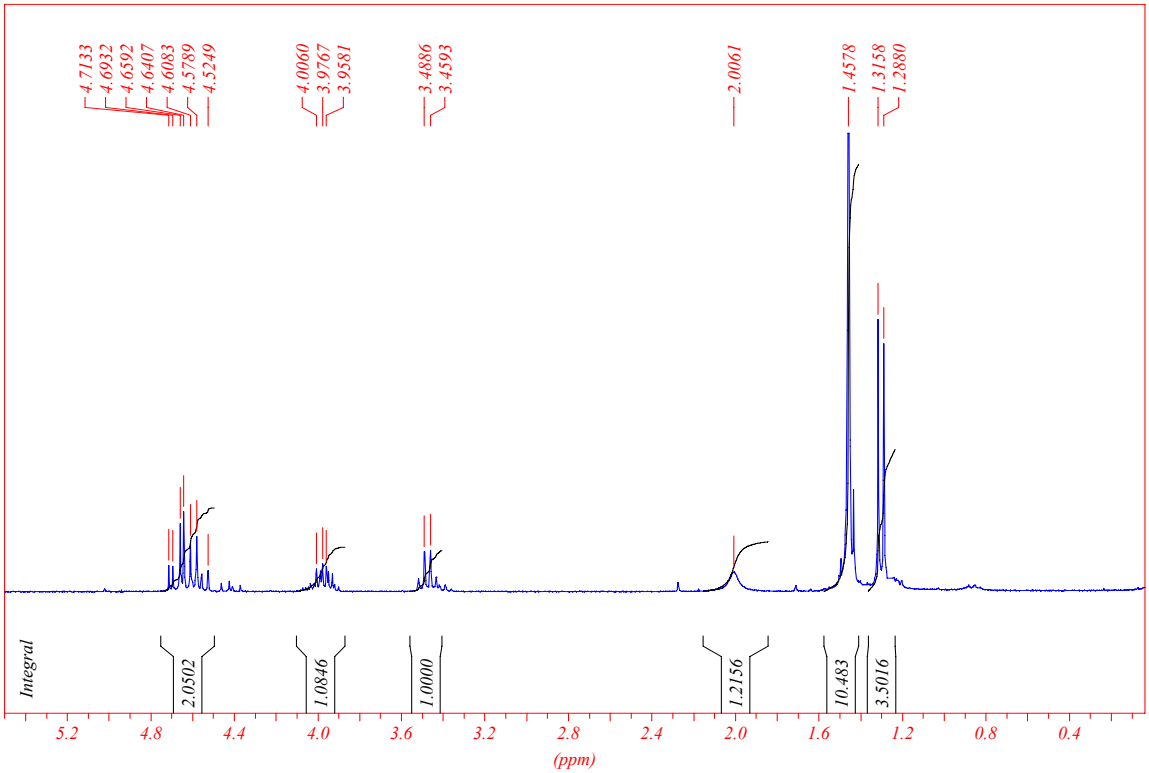
4b

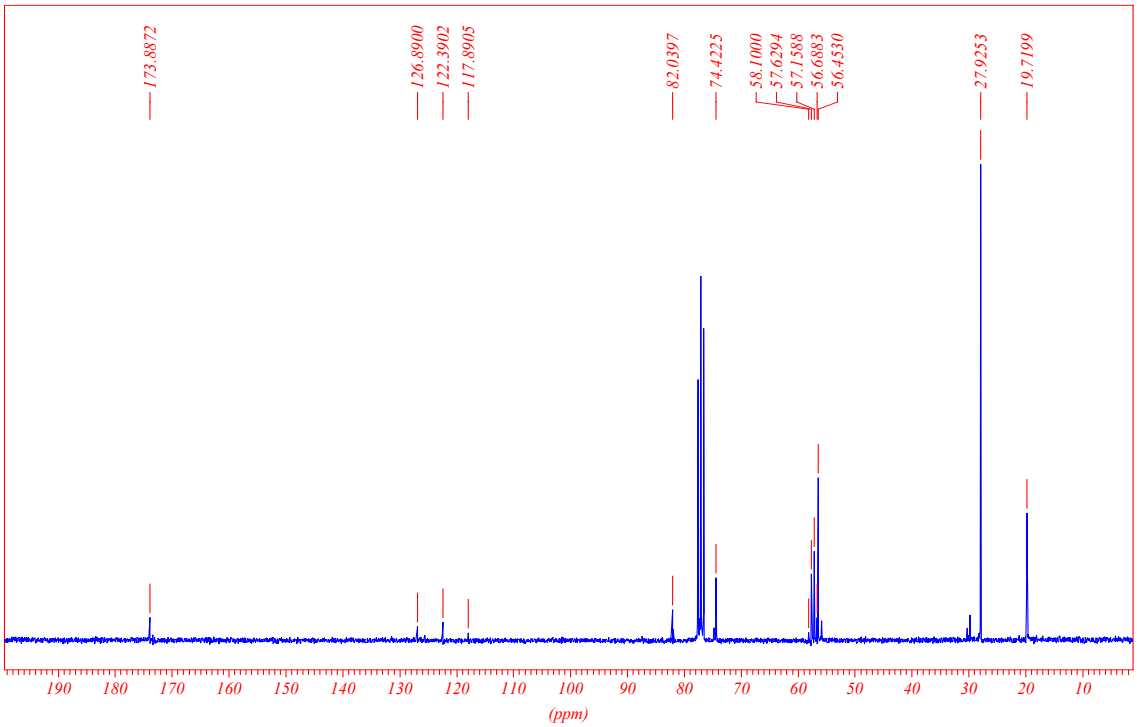

4.6965
4.6854
4.6625
4.6505
4.6000
4.5816
4.5660
4.5476
3.9292
3.9172
3.9108
3.8998
3.8934
3.8814
3.8750
3.8640
3.8575
3.8456
3.1500
3.1371
1.9830
1.9701
1.9527
1.9481
1.4639
0.9869
0.9694
0.8821
0.8647
Integral
1.0000
1.0244
0.9761
0.9824
2.0183
0.0661
9.6217
0.3814
3.1190
3.2852
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
(ppm)

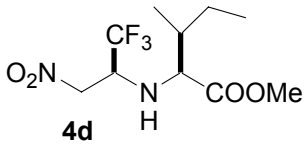

173.4349
128.8417
126.0391
125.4415
123.2334
120.4278
81.9312
74.4302
74.4150
66.9566
58.9551
58.6579
58.3606
58.0634
31.9966
27.8594
19.0512
17.1615
180
160
140
120
100
80
60
40
20
0
(ppm)


CF3
O2N
N
H
COOtBu

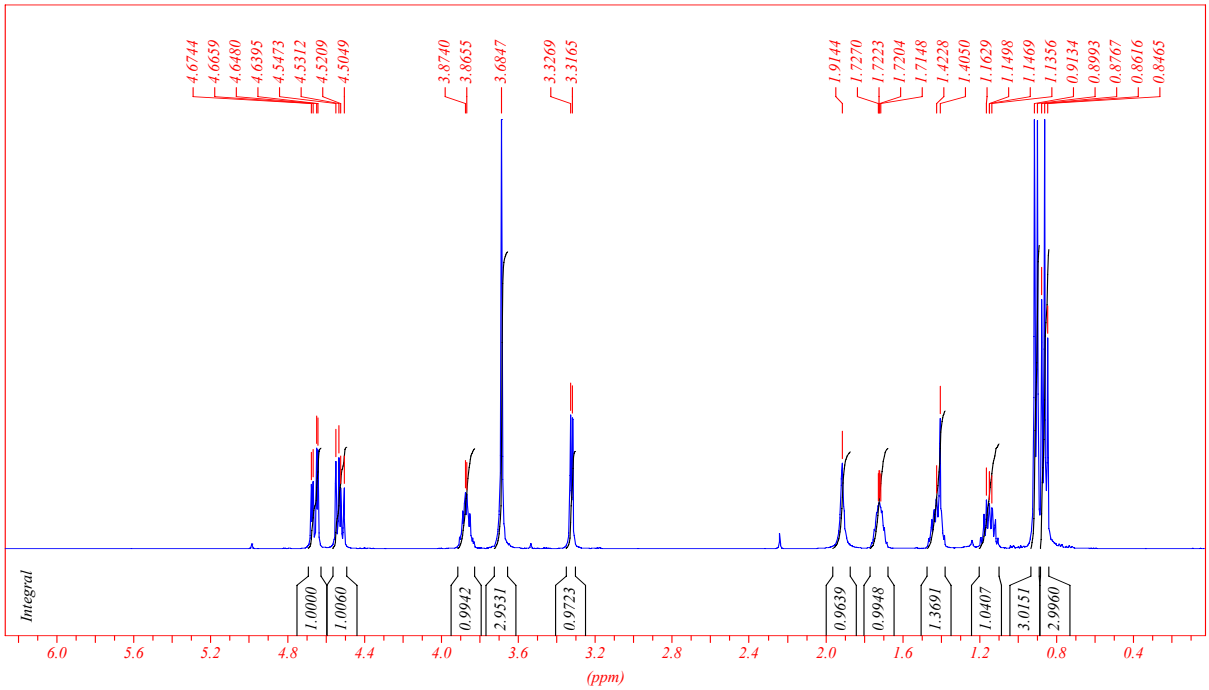
4c

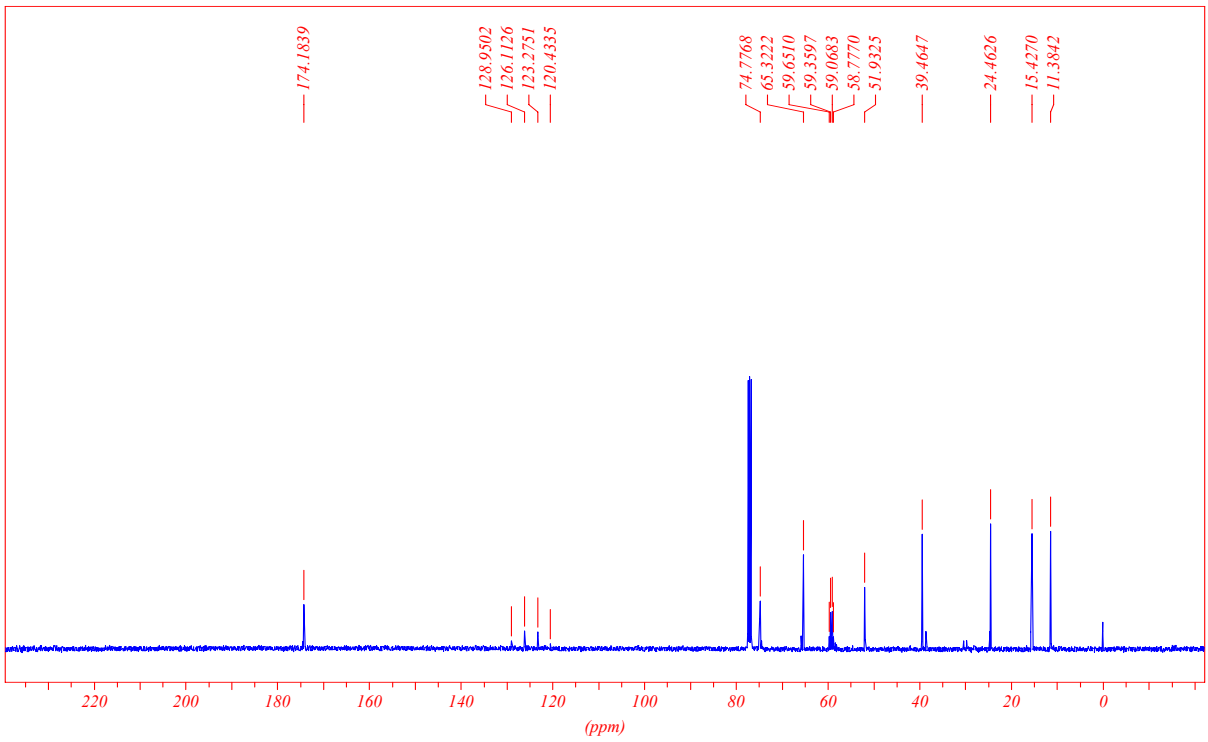

4.7133
4.6932
4.6592
4.6407
4.6083
4.5789
4.5249
4.0060
3.9767
3.9581
3.4886
3.4593
2.0061
1.4578
1.3158
1.2880
Integral
2.0502
1.0846
1.0000
1.2156
10.483
3.5016
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
(ppm)

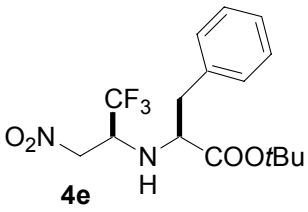

173.8872
126.8900
122.3902
117.8905
82.0397
74.4225
58.1000
57.6294
57.1588
56.6883
56.4530
27.9253
19.7199
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)


CF3
O2N
N
H
COOMe

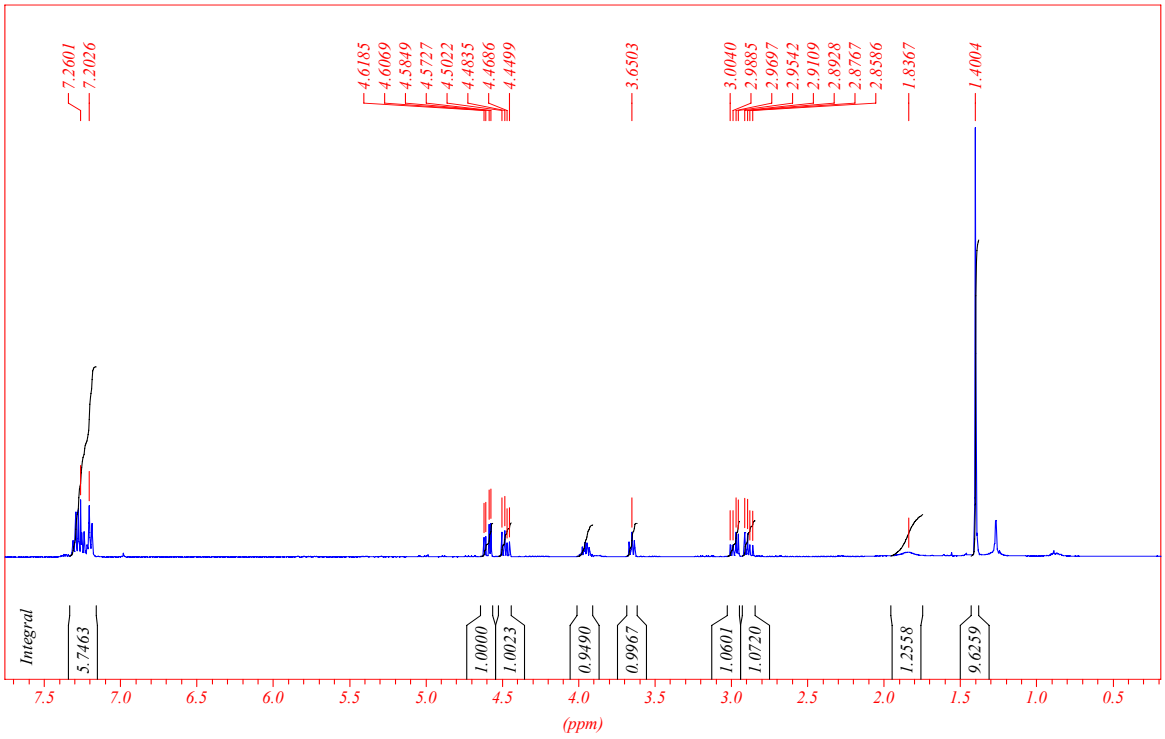
4d

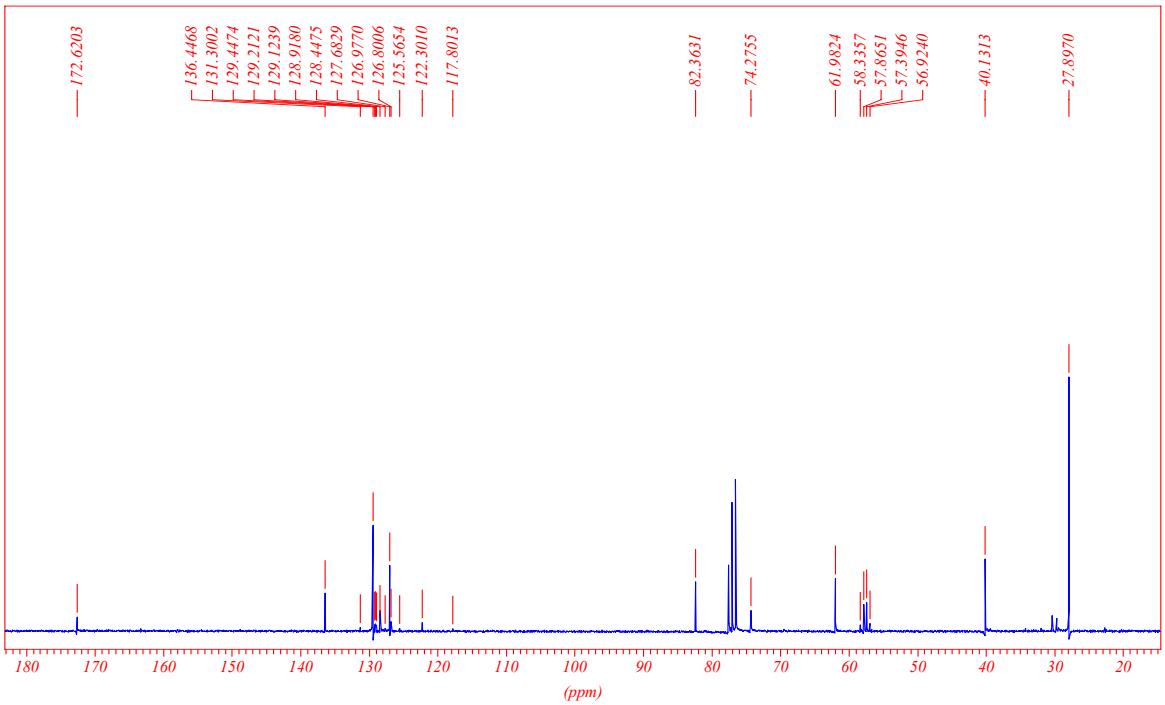

4.6744
4.6659
4.6480
4.6395
4.5473
4.5312
4.5209
4.5049
3.8740
3.8655
3.6847
3.3269
3.3165
1.9144
1.7270
1.7223
1.7204
1.7148
1.4228
1.4050
1.1629
1.1498
1.1469
1.1356
0.9134
0.8993
0.8767
0.8616
0.8465
Integral
1.0000
1.0060
0.9942
2.9531
0.9723
0.9639
0.9948
1.3691
1.0407
3.0151
2.9960
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
0.8
0.4
(ppm)

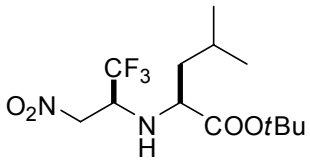

174.1839
128.9502
126.1126
123.2751
120.4335
74.7768
65.3222
59.6510
59.3597
59.0683
58.7770
51.9325
39.4647
24.4626
15.4270
11.3842
220
200
180
160
140
120
100
80
60
40
20
0
(ppm)


CF3
O2N
N
H
COOtBu

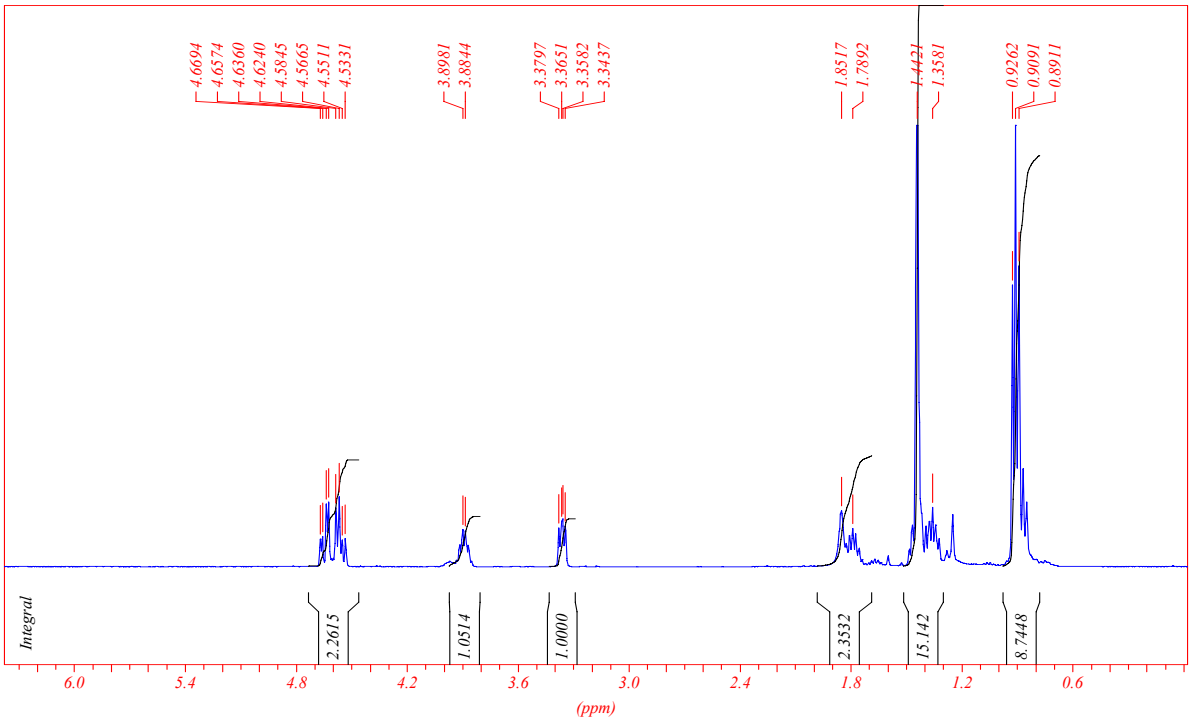
4e

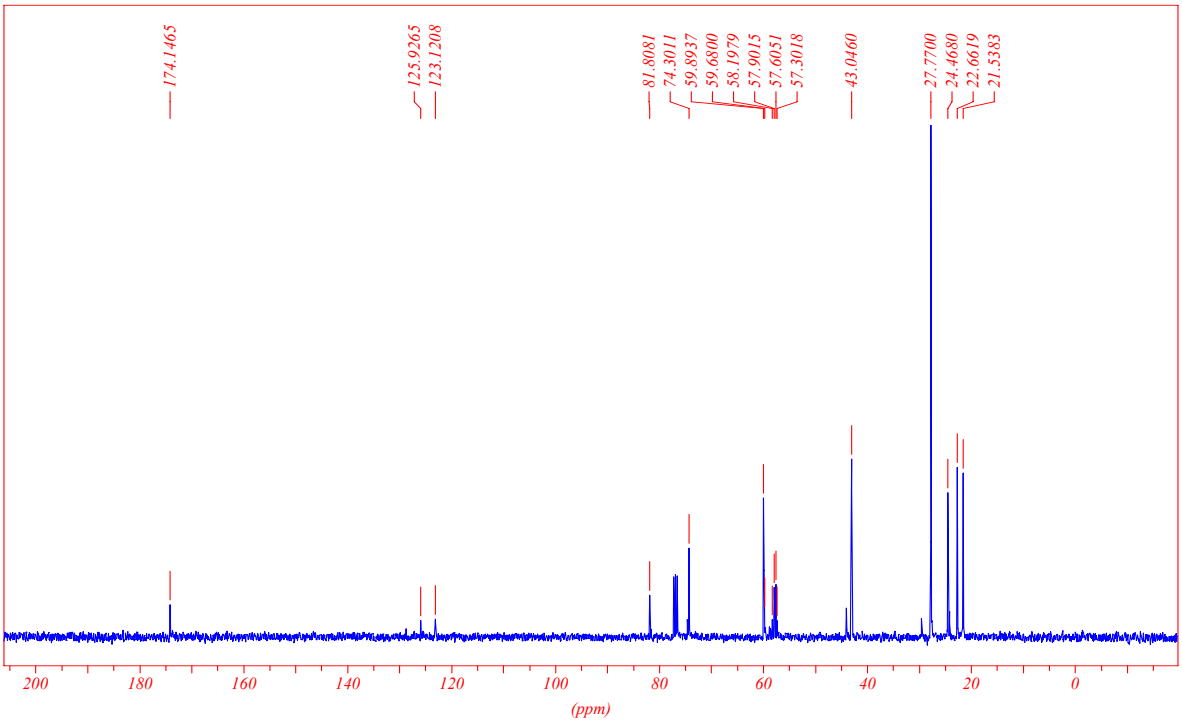

7.2601
7.2026
4.6185
4.6069
4.5849
4.5727
4.5022
4.4835
4.4686
4.4499
3.6503
3.0040
2.9885
2.9697
2.9542
2.9109
2.8928
2.8767
2.8586
1.8367
1.4004
Integral
5.7463
1.0000
1.0023
0.9490
0.9967
1.0601
1.0720
1.2558
9.6259
(ppm)

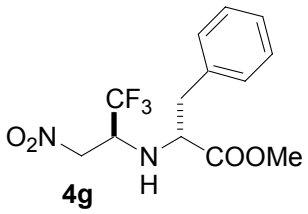

172.6203
136.4468
131.3002
129.4474
129.2121
129.1239
128.9180
128.4475
127.6829
126.9770
126.8006
125.5654
122.3010
117.8013
82.3631
74.2755
61.9824
58.3357
57.8651
57.3946
56.9240
40.1313
27.8970
(ppm)


CF3
O2N
N
H
COOtBu

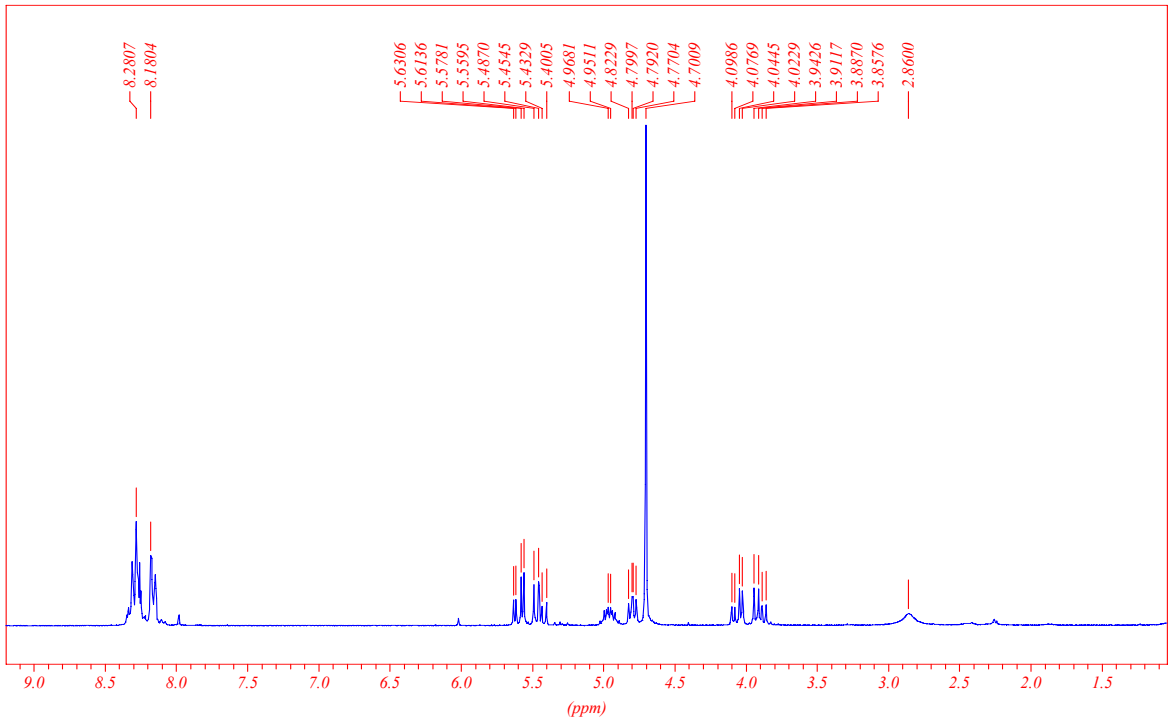
4f

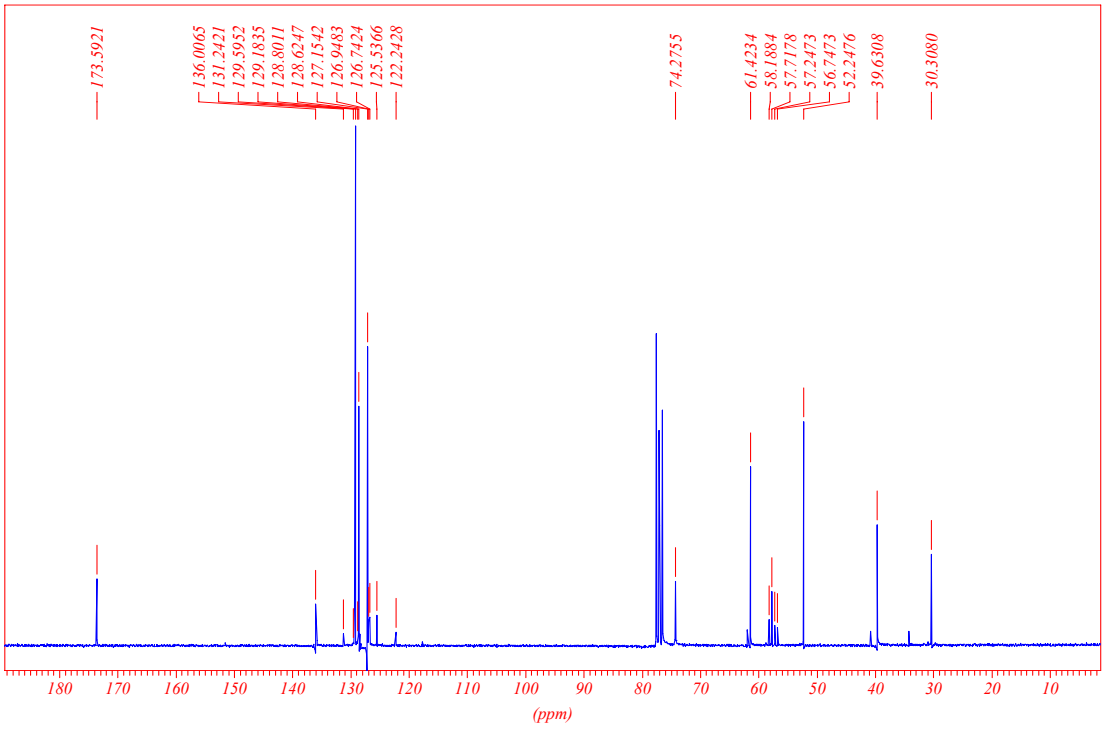

4.6694
4.6574
4.6360
4.6240
4.5845
4.5665
4.5511
4.5331
3.8981
3.8844
3.3797
3.3651
3.3582
3.3437
1.8517
1.7892
1.4421
1.3581
0.9262
0.9091
0.8911
Integral
2.2615
1.0514
1.0000
2.3532
15.142
8.7448
6.0
5.4
4.8
4.2
3.6
3.0
2.4
1.8
1.2
0.6
(ppm)

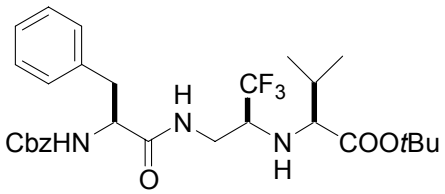

174.1465
125.9265
123.1208
81.8081
74.3011
59.8937
59.6800
58.1979
57.9015
57.6051
57.3018
43.0460
27.7700
24.4680
22.6619
21.5383
200
180
160
140
120
100
80
60
40
20
0
(ppm)


CF3
O2N
N
H
COOMe

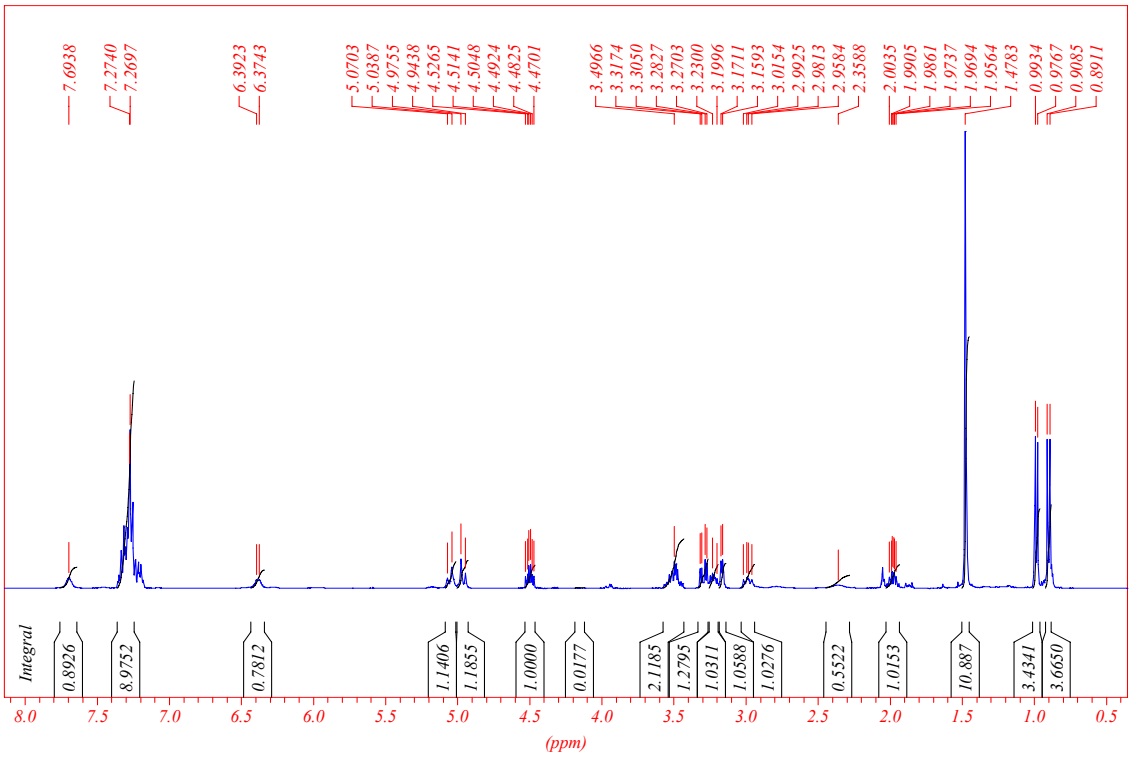
4g

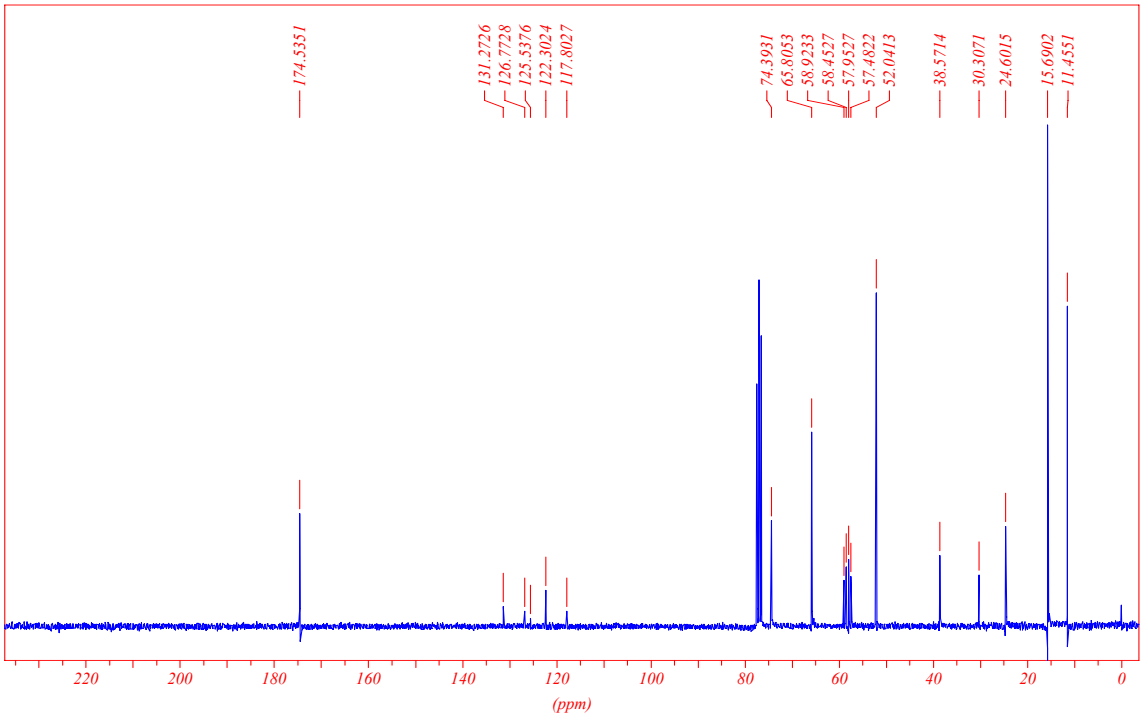

8.2807
8.1804
5.6306
5.6136
5.5781
5.5595
5.4870
5.4545
5.4329
5.4005
4.9681
4.9511
4.8229
4.7997
4.7920
4.7704
4.7009
4.0986
4.0769
4.0445
4.0229
3.9426
3.9117
3.8870
3.8576
2.8600
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
(ppm)

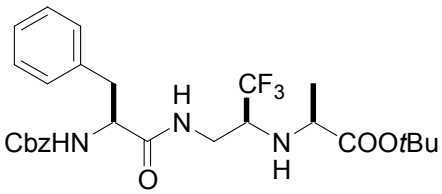

173.5921
136.0065
131.2421
129.5952
129.1835
128.8011
128.6247
127.1542
126.9483
126.7424
125.5366
122.2428
74.2755
61.4234
58.1884
57.7178
57.2473
56.7473
52.2476
39.6308
30.3080
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)


CbzHN
H
N
O
CF3
N
H
COOtBu

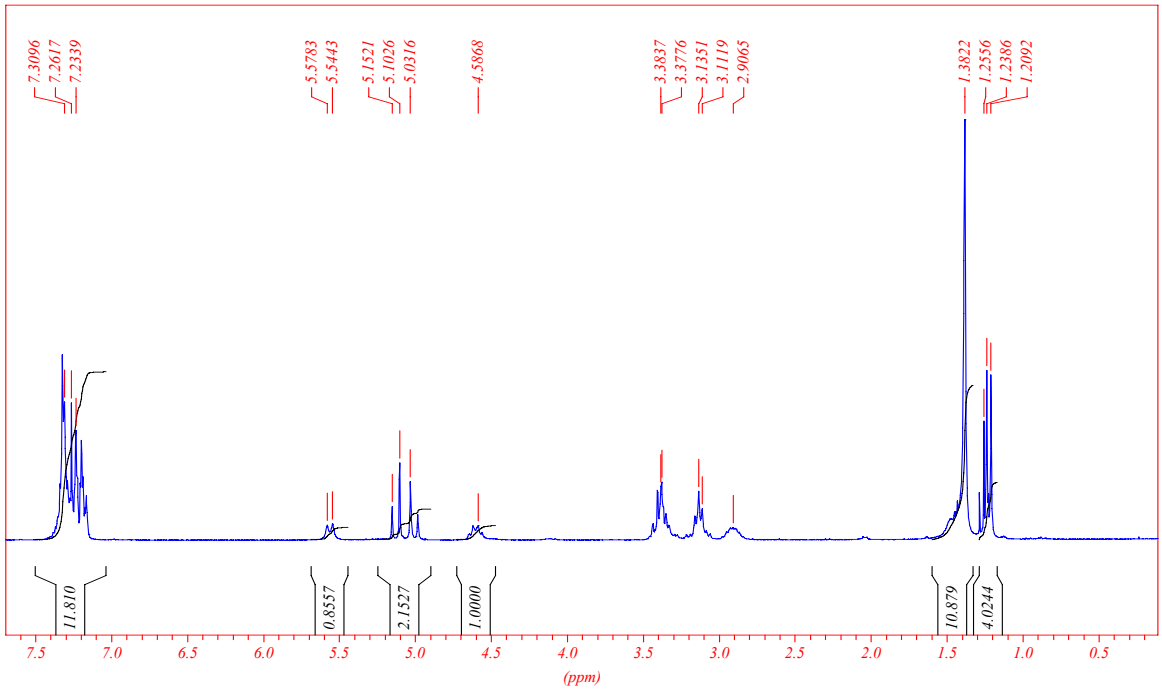
8b

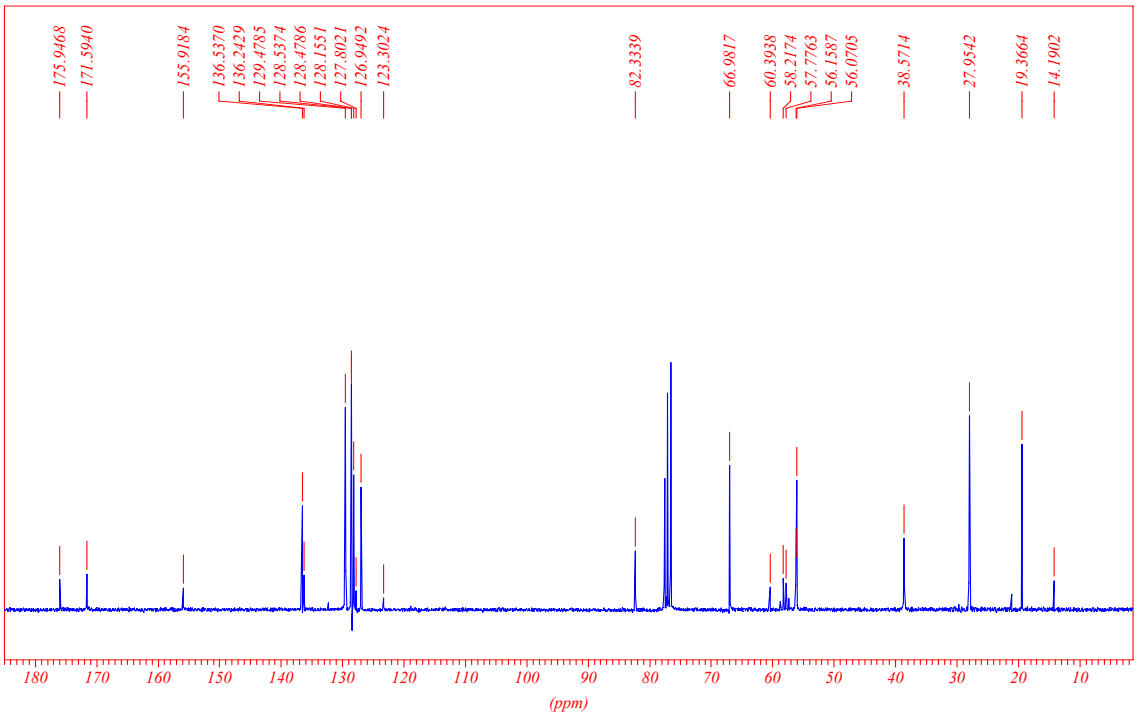

7.6938
7.2740
7.2697
6.3923
6.3743
5.0703
5.0387
4.9755
4.9438
4.5265
4.5141
4.5048
4.4924
4.4825
4.4701
3.4966
3.3174
3.3050
3.2827
3.2703
3.2300
3.1996
3.1711
3.1593
3.0154
2.9925
2.9813
2.9584
2.3588
2.0035
1.9905
1.9861
1.9737
1.9694
1.9564
1.4783
0.9934
0.9767
0.9085
0.8911
Integral
0.8926
8.9752
0.7812
1.1406
1.1855
1.0000
0.0177
2.1185
1.2795
1.0311
1.0588
1.0276
0.5522
1.0153
10.887
3.4341
3.6650
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

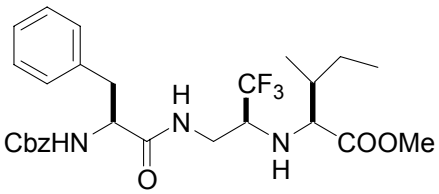

174.5351
131.2726
126.7728
125.5376
122.3024
117.8027
74.3931
65.8053
58.9233
58.4527
57.9527
57.4822
52.0413
38.5714
30.3071
24.6015
15.6902
11.4551
220
200
180
160
140
120
100
80
60
40
20
0
(ppm)


CbzHN
H
N
O
CF3
N
H
COOtBu

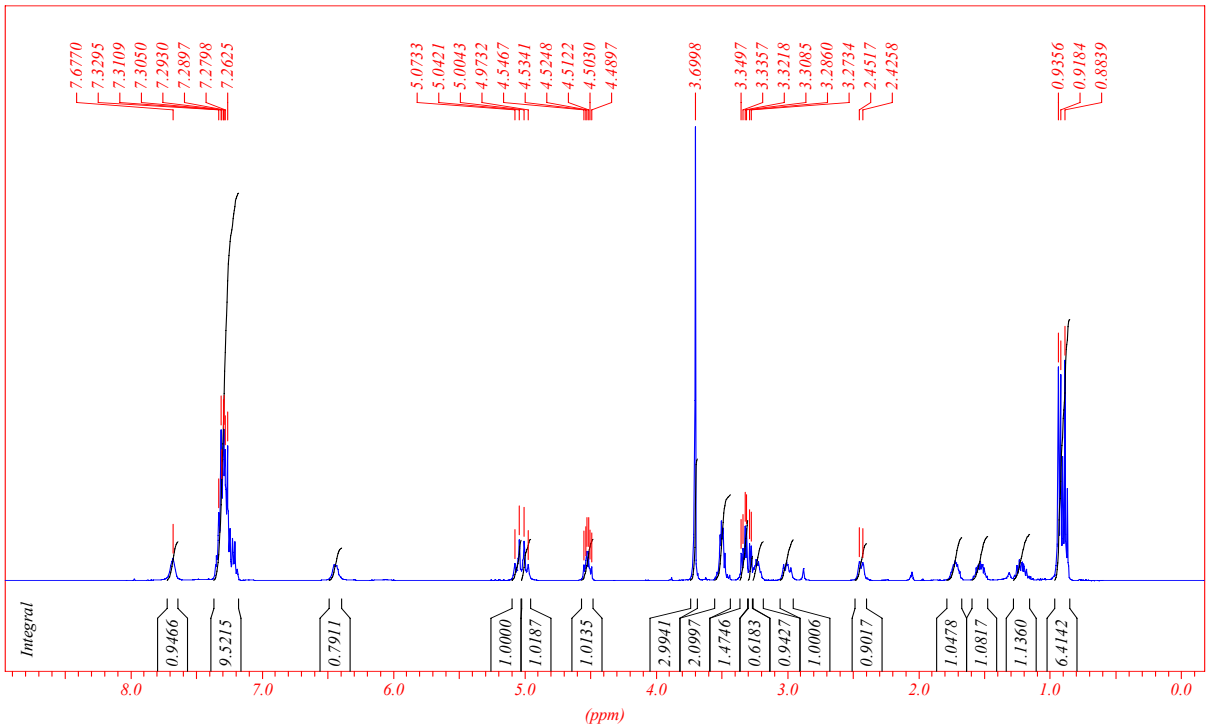
8c

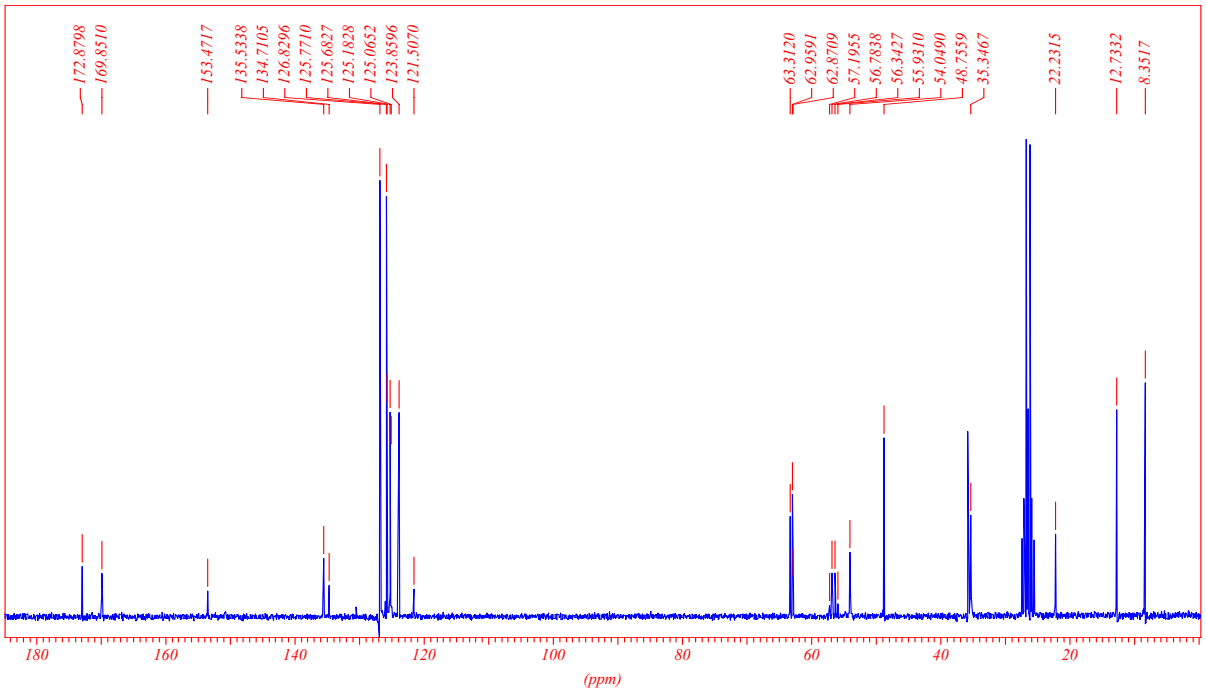

7.3096
7.2617
7.2339
5.5783
5.5443
5.1521
5.1026
5.0316
4.5868
3.3837
3.3776
3.1351
3.1119
2.9065
1.3822
1.2556
1.2386
1.2092
11.810
0.8557
2.1527
1.0000
10.879
4.0244
(ppm)

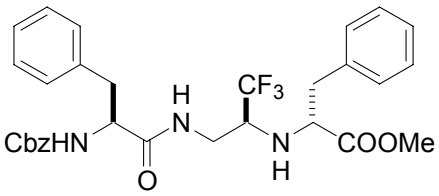

175.9468
171.5940
155.9184
136.5370
136.2429
129.4785
128.5374
128.4786
128.1551
127.8021
126.9492
123.3024
82.3339
66.9817
60.3938
58.2174
57.7763
56.1587
56.0705
38.5714
27.9542
19.3664
14.1902
(ppm)


CbzHN
H
N
O
CF3
N
H
COOMe

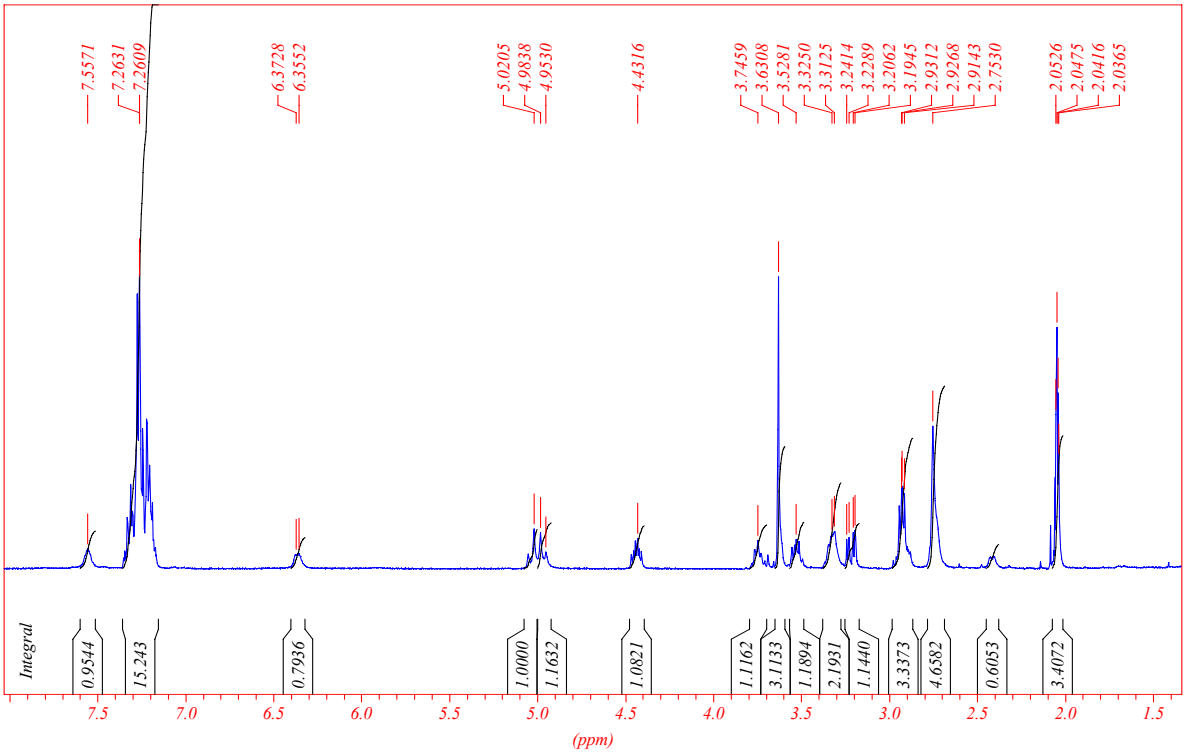
8d

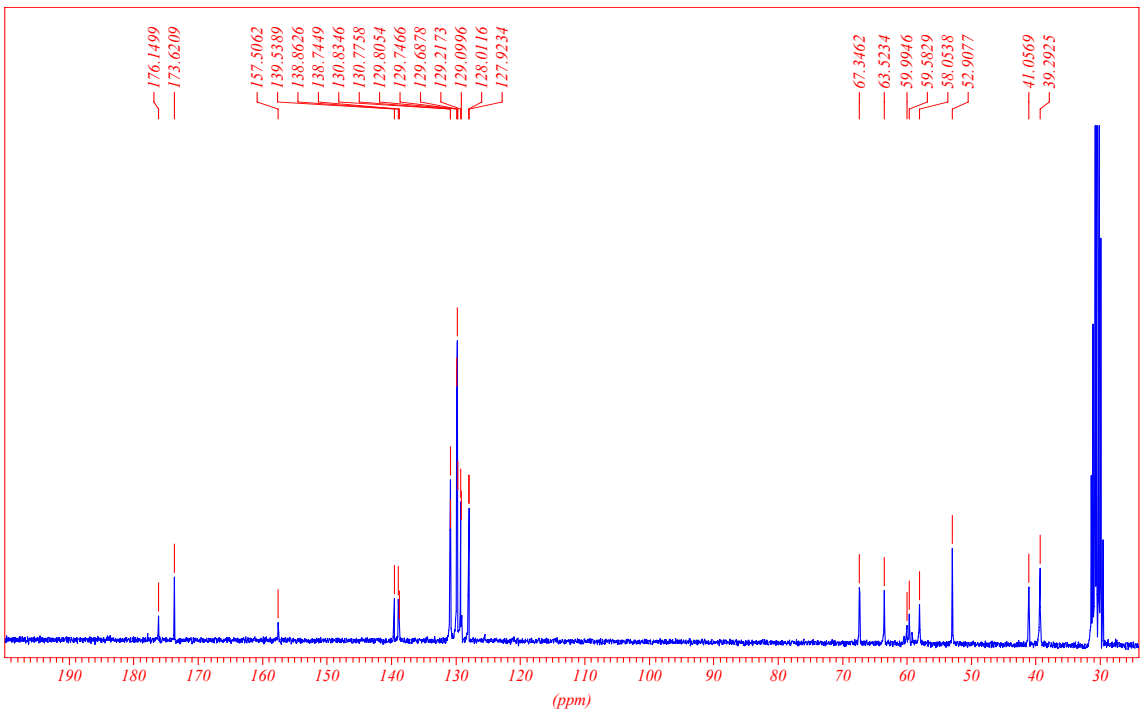

7.6770
7.3395
7.3109
7.3050
7.2930
7.2897
7.2798
7.2625
5.0733
5.0421
5.0043
4.9732
4.5467
4.5341
4.5248
4.5122
4.5030
4.4897
3.6998
3.3497
3.3357
3.3218
3.3085
3.2860
3.2734
2.4517
2.4258
0.9356
0.9184
0.8839
Integral
0.9466
9.5215
0.7911
1.0000
1.0187
1.0135
2.9941
2.0997
1.4746
0.6183
0.9427
1.0006
0.9017
1.0478
1.0817
1.1360
6.4142
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

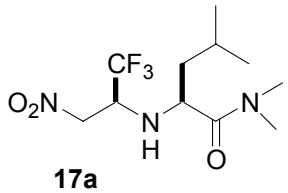

172.8798
169.8510
153.4717
135.5338
134.7105
126.8296
125.7710
125.6827
125.1828
125.0652
123.8596
121.5070
63.3120
62.9591
62.8709
57.1955
56.7838
56.3427
55.9310
54.0490
48.7559
35.3467
22.2315
12.7332
8.3517
180
160
140
120
100
80
60
40
20
(ppm)


CbzHN
H
N
O
CF3
N
H
COOMe

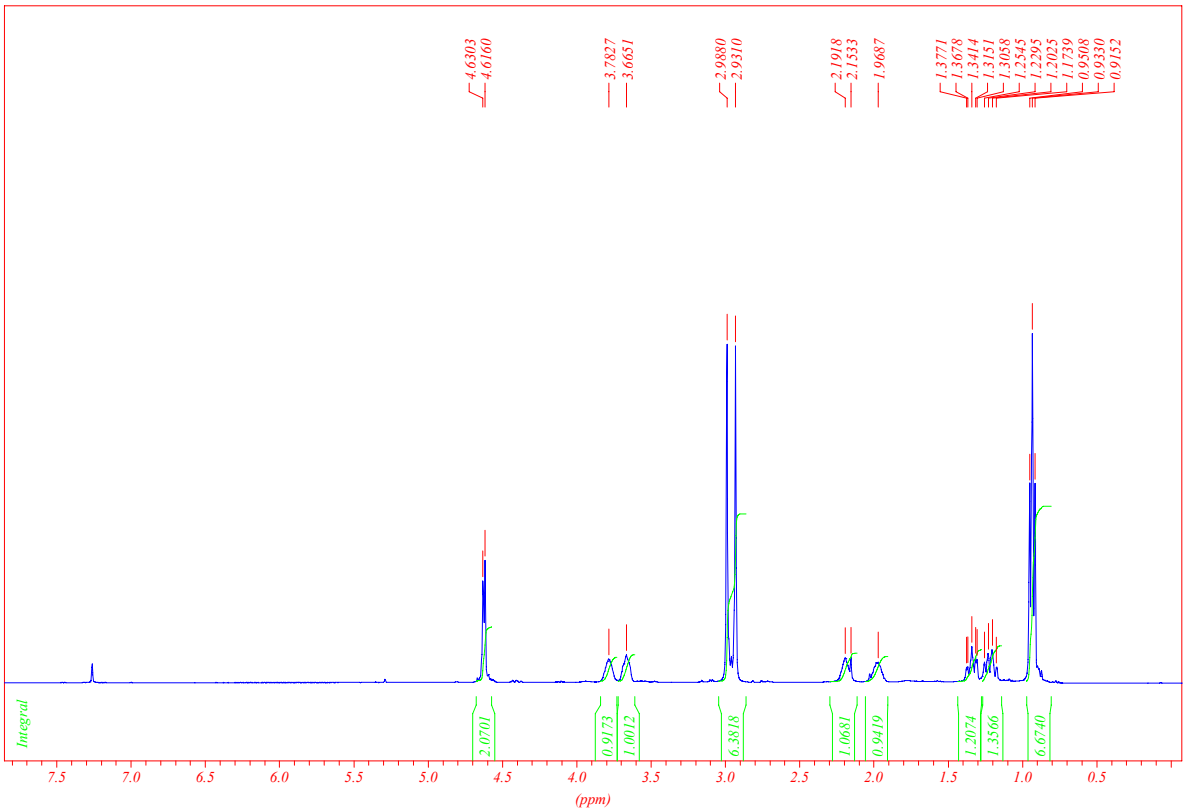
8g

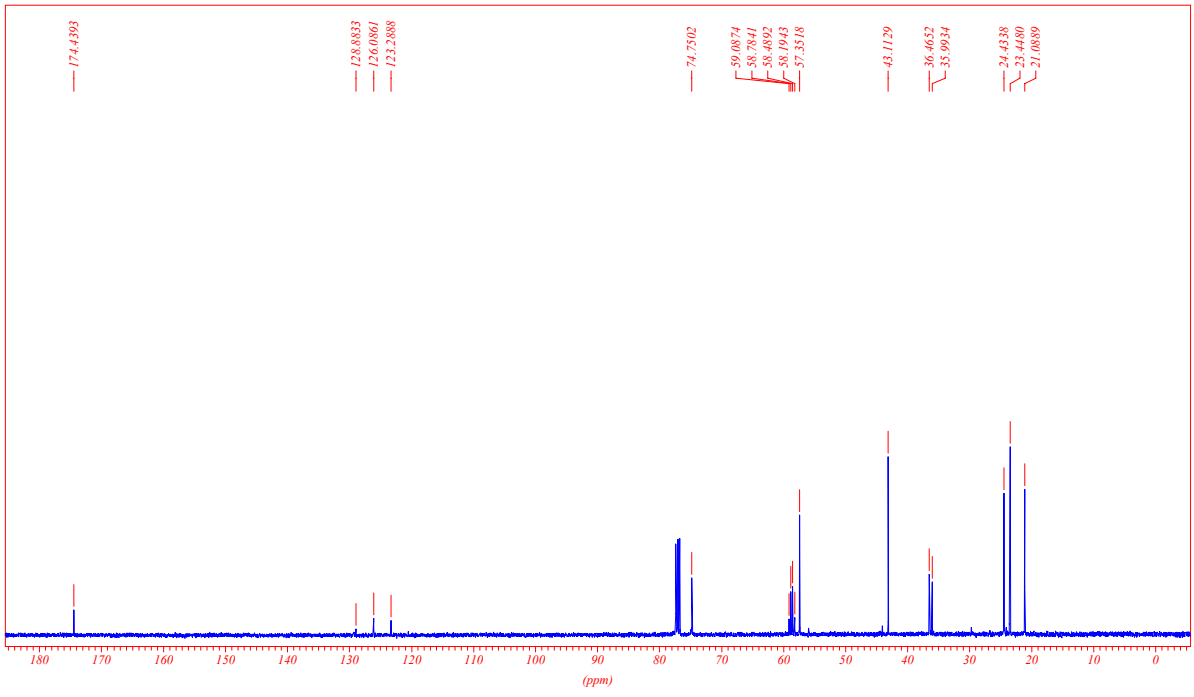

7.5571
7.2631
7.2609
6.3728
6.3552
5.0205
4.9838
4.9530
4.4316
3.7459
3.6308
3.5281
3.3250
3.3125
3.2414
3.2289
3.2062
3.1945
2.9312
2.9268
2.9143
2.7530
2.0526
2.0475
2.0416
2.0365
Integral
0.9544
15.243
0.7936
1.0000
1.1632
1.0821
1.1162
3.1133
1.1894
2.1931
1.1440
3.3373
4.6582
0.6053
3.4072
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
(ppm)

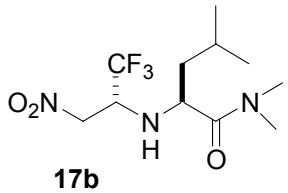

176.1499
173.6209
157.5062
139.5389
138.8626
138.7449
130.8346
130.7758
129.8054
129.7466
129.6878
129.2173
129.0996
128.0116
127.9234
67.3462
63.5234
59.9946
59.5829
58.0538
52.9077
41.0569
39.2925
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
(ppm)


CF3
O2N
N
H
N
O

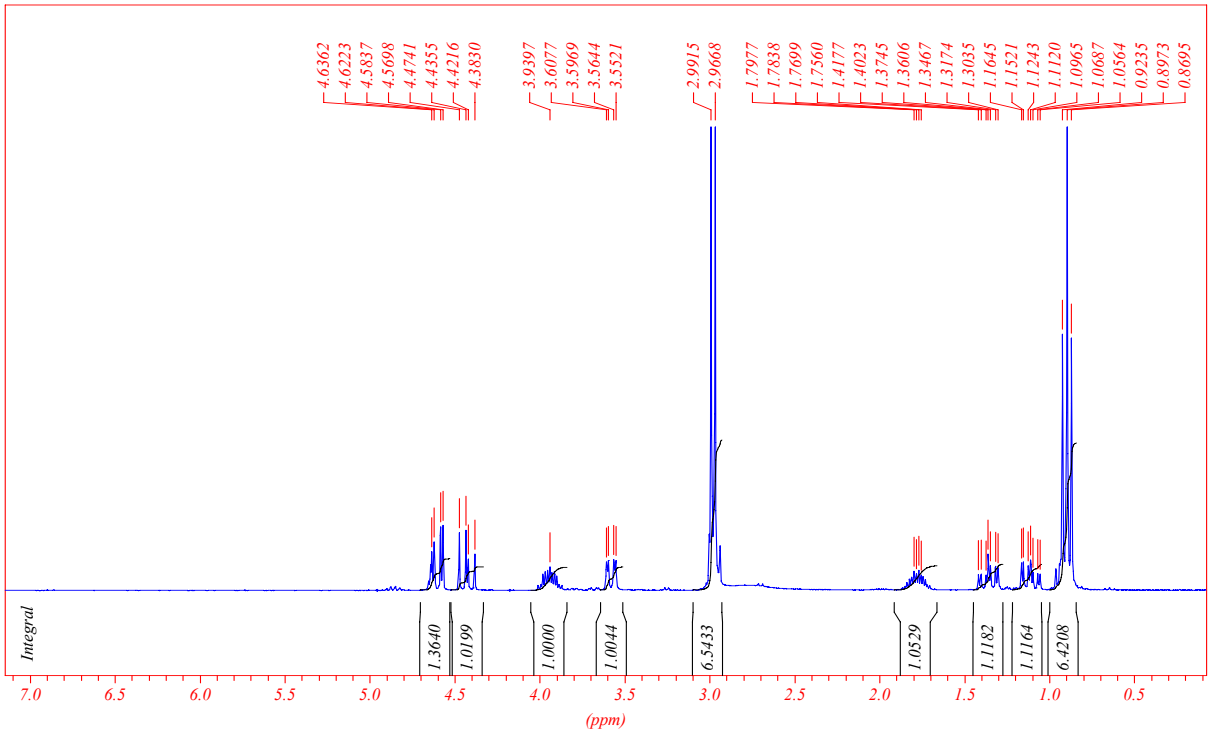
17a

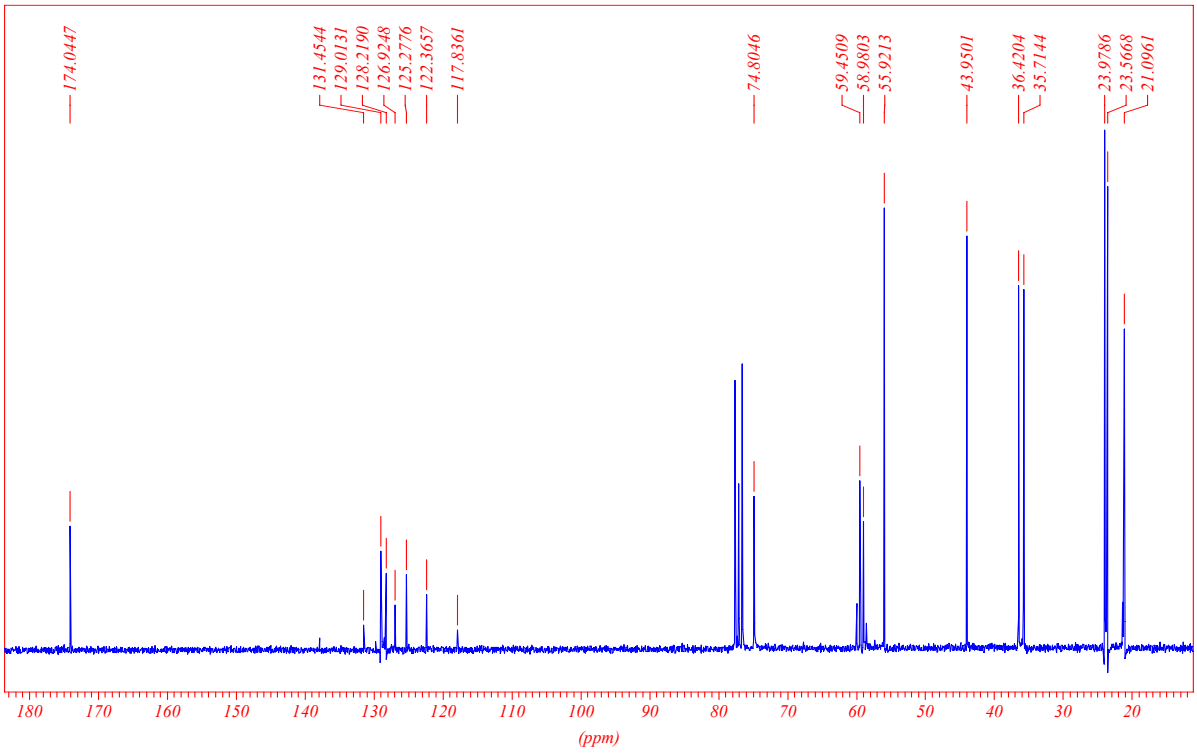

4.6303
4.6160
3.7827
3.6651
2.9880
2.9310
2.1918
2.1533
1.9687
1.3771
1.3678
1.3414
1.3151
1.3058
1.2345
1.2295
1.2025
1.1739
0.9508
0.9330
0.9152
Integral
2.0701
0.9173
1.0012
6.3818
1.0681
0.9419
1.2074
1.3566
6.6740
(ppm)

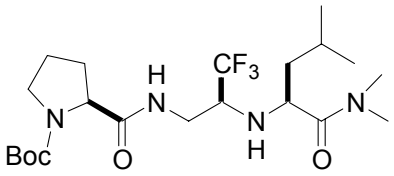

174.4393
128.8833
126.0861
123.2888
74.7502
59.0874
58.7841
58.4892
58.1943
57.3518
43.1129
36.4652
35.9934
24.4338
23.4480
21.0889
(ppm)


CF3
O2N
N
H
N
O

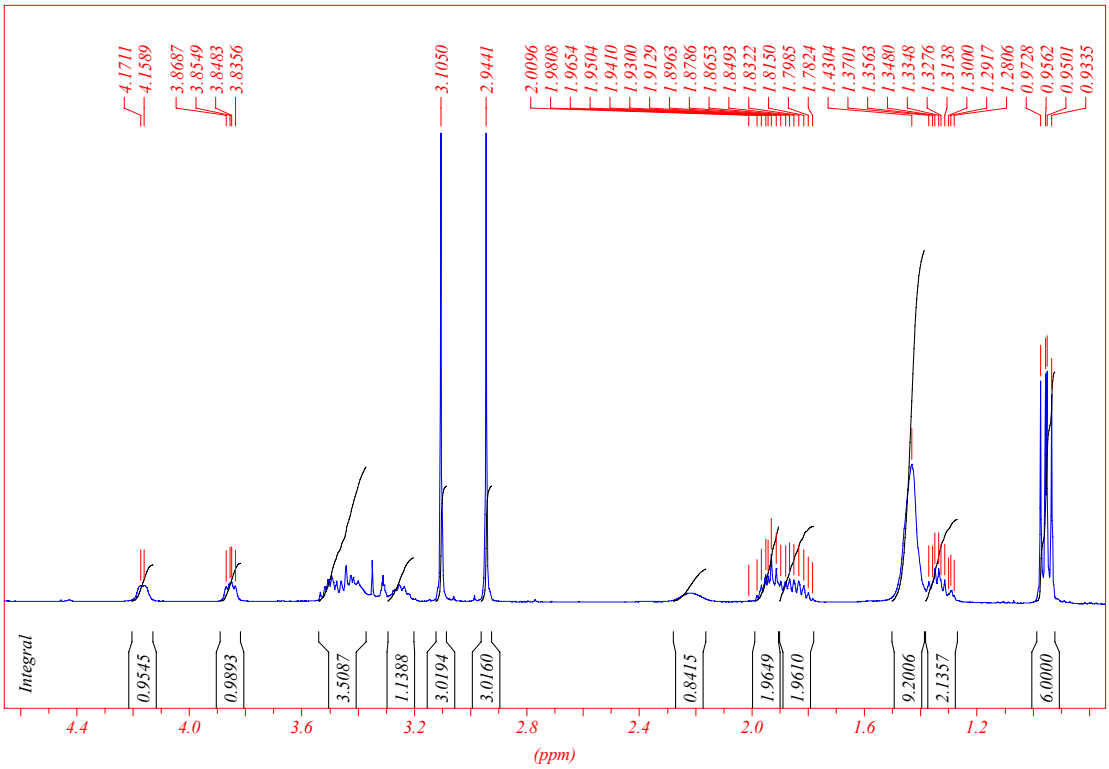
17b

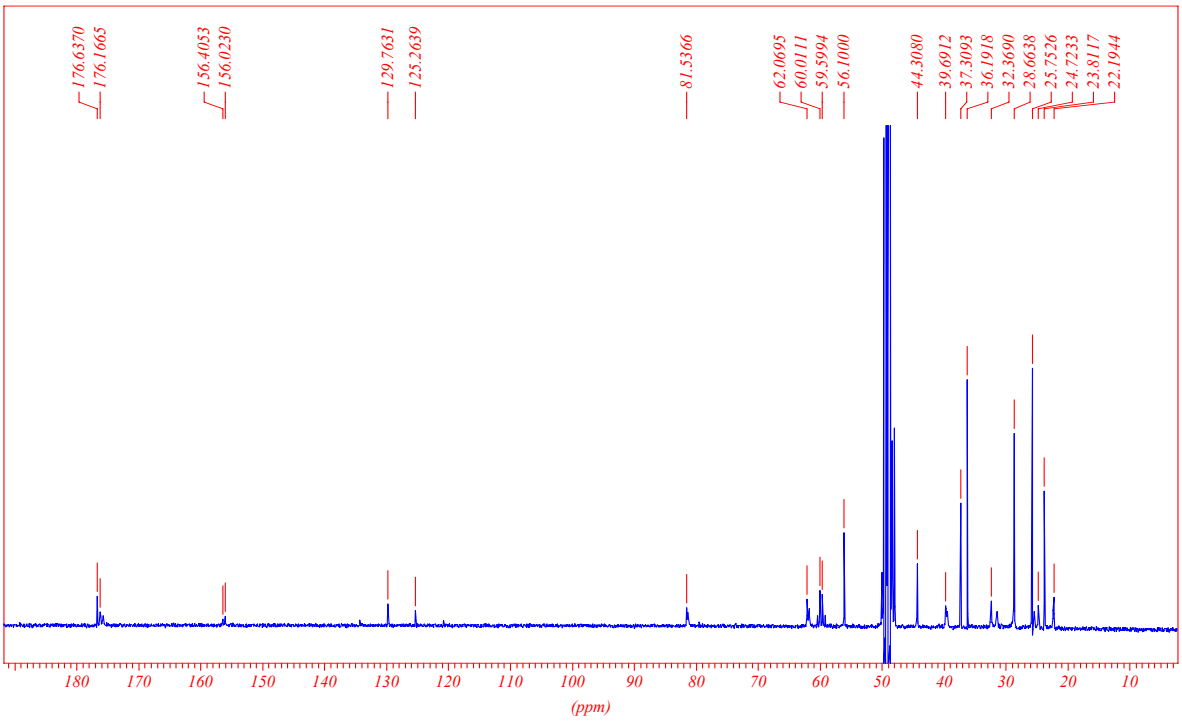

4.6362
4.6223
4.5837
4.5698
4.4741
4.4355
4.4216
4.3830
3.9397
3.6077
3.5969
3.5644
3.5521
2.9915
2.9668
1.7977
1.7838
1.7699
1.7560
1.4177
1.4023
1.3745
1.3606
1.3467
1.3174
1.3035
1.1645
1.1521
1.1243
1.1120
1.0965
1.0687
1.0564
0.9235
0.8973
0.8695
Integral
1.3640
1.0199
1.0000
1.0044
6.5433
1.0529
1.1182
1.1164
6.4208
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

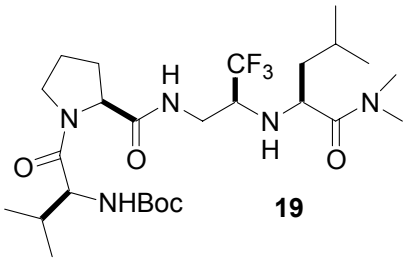

174.0447
131.4544
129.0131
128.2190
126.9248
125.2776
122.3657
117.8361
74.8046
59.4509
58.9803
55.9213
43.9501
36.4204
35.7144
23.9786
23.5668
21.0961
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
(ppm)


Boc
N
O
H
N
CF3
N
H
N
O

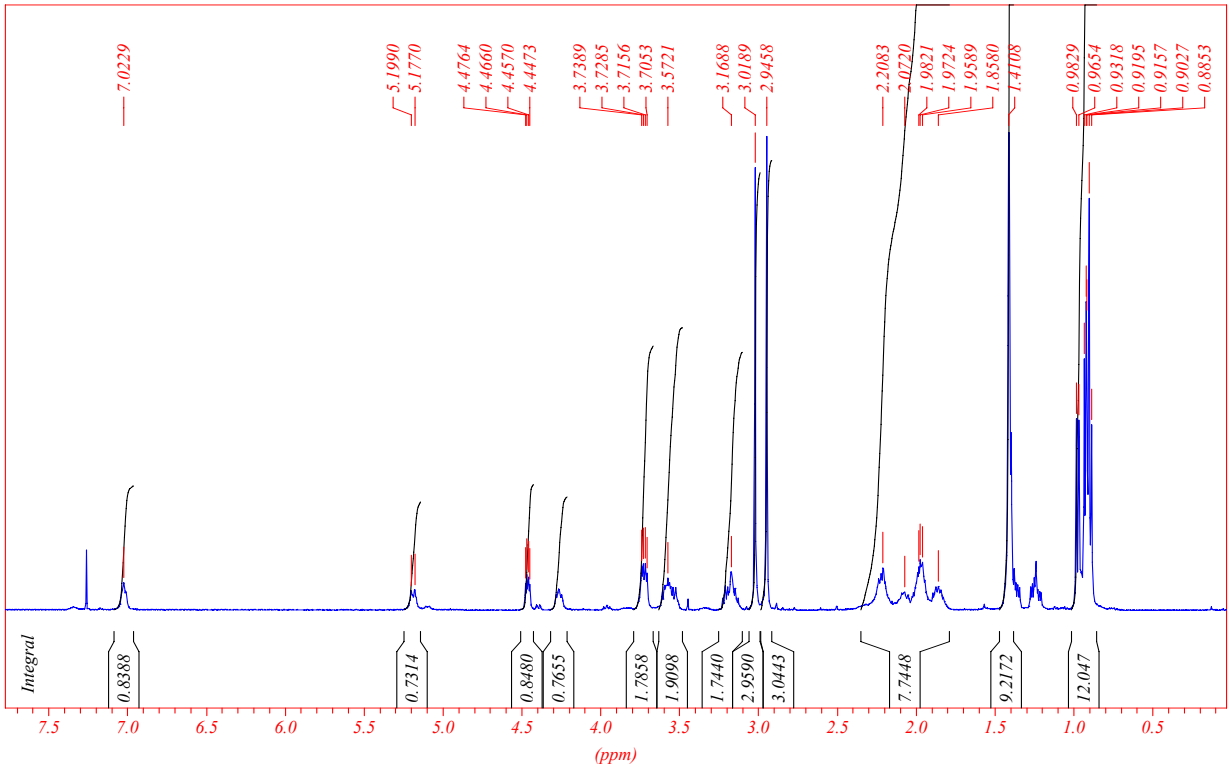
18

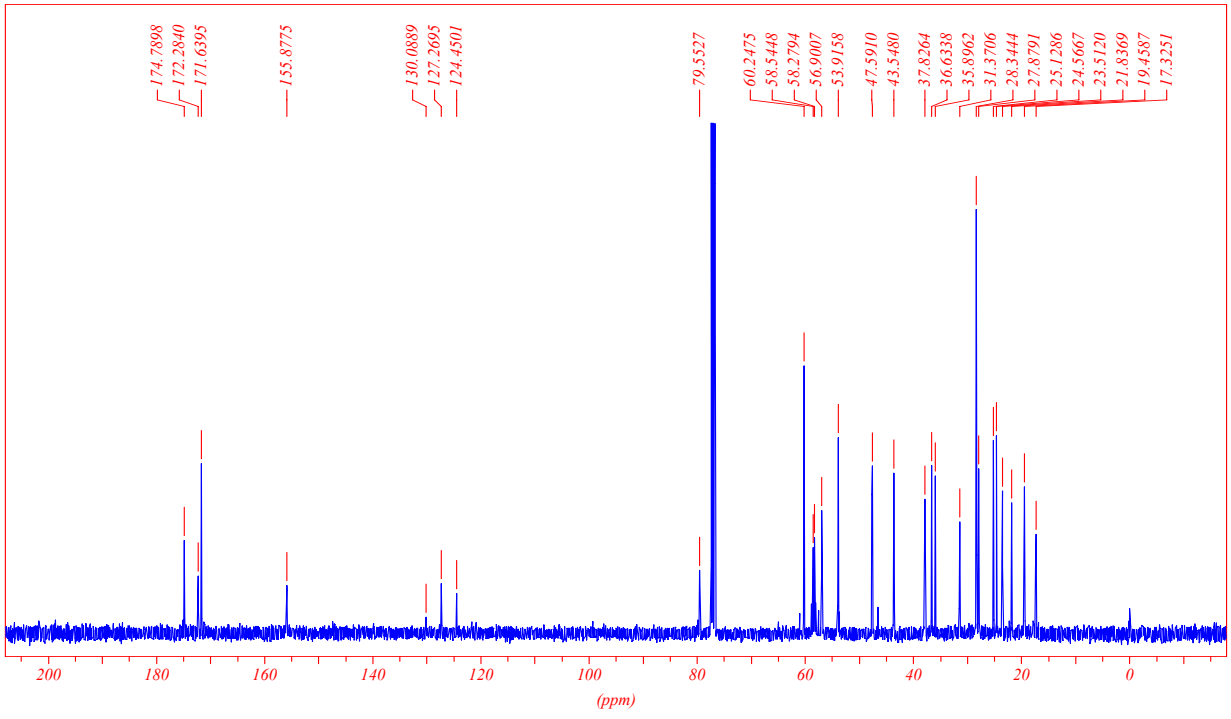

4.1711
4.1589
3.8687
3.8549
3.8483
3.8356
3.1050
2.9441
2.0096
1.9808
1.9654
1.9504
1.9410
1.9300
1.9129
1.8963
1.8786
1.8653
1.8493
1.8322
1.8150
1.7985
1.7824
1.4304
1.3701
1.3563
1.3480
1.3348
1.3276
1.3138
1.3000
1.2917
1.2806
0.9728
0.9562
0.9501
0.9335
Integral
0.9545
0.9893
3.5087
1.1388
3.0194
3.0160
0.8415
1.9649
1.9610
9.2006
2.1357
6.0000
4.4
4.0
3.6
3.2
2.8
2.4
2.0
1.6
1.2
(ppm)

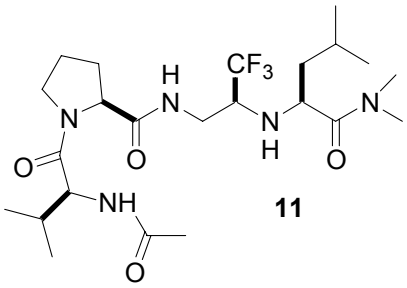

176.6370
176.1665
156.4053
156.0230
129.7631
125.2639
81.5366
62.0695
60.0111
59.5994
56.1000
44.3080
39.6912
37.3093
36.1918
32.3690
28.6638
25.7526
24.7233
23.8117
22.1944
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)


H
N
CF3
N
H
N
N
O
O
O
NHBoc

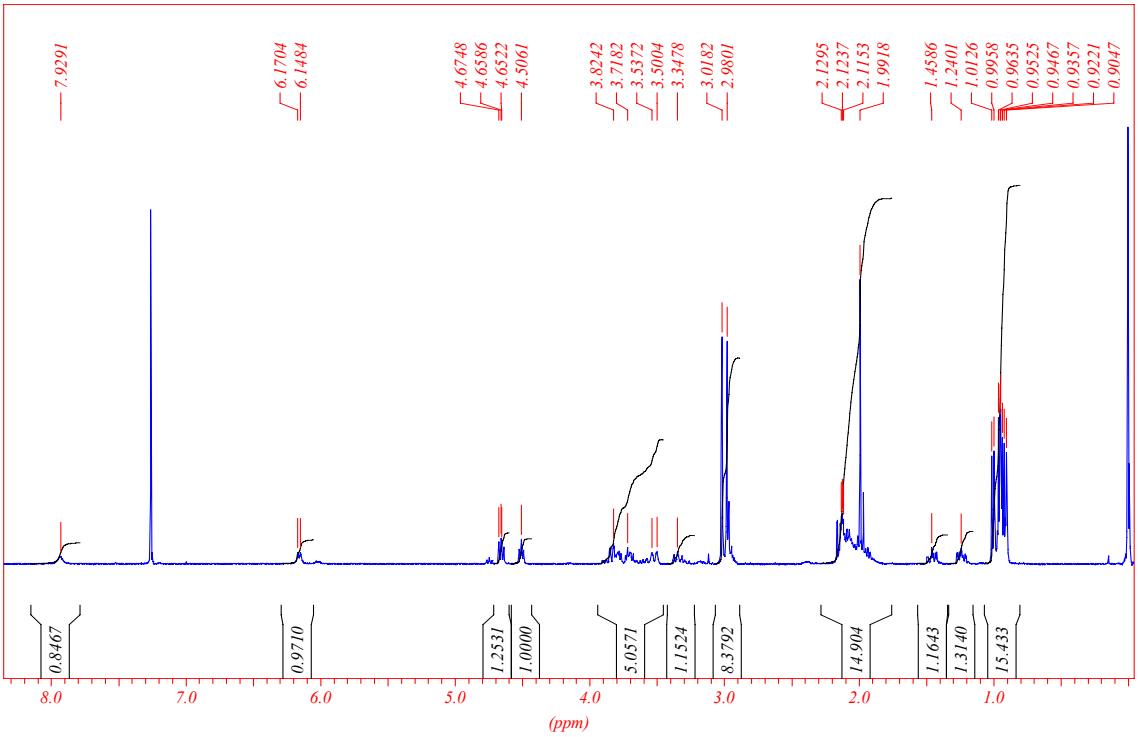
19

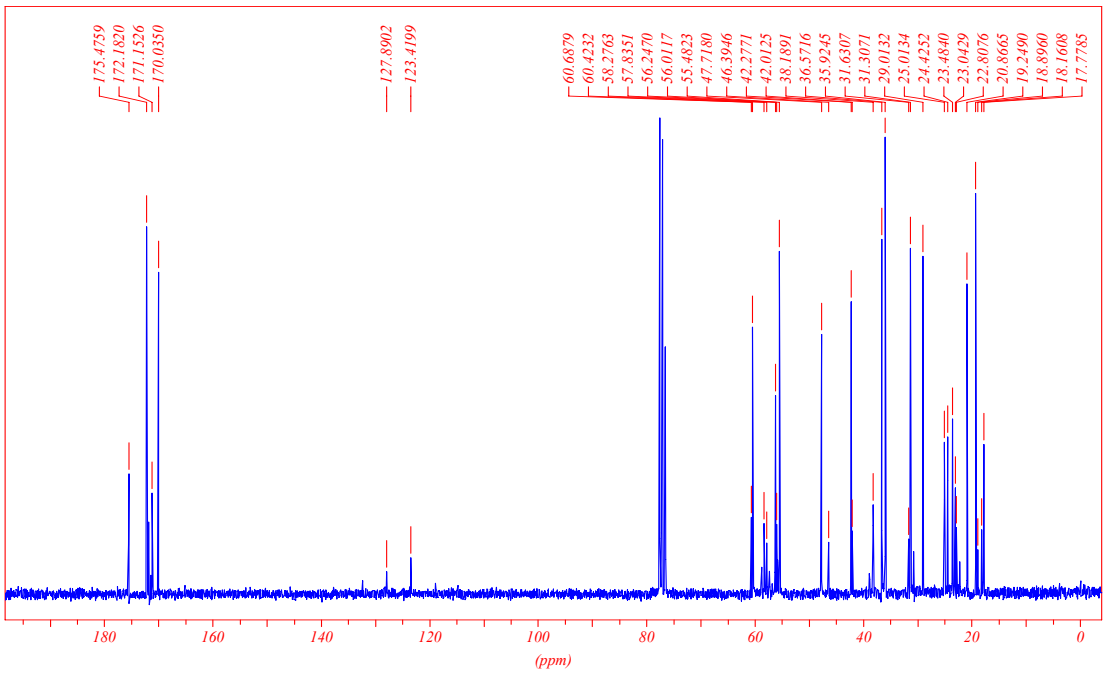

7.0229
5.1990
5.1770
4.4764
4.4660
4.4570
4.4473
3.7389
3.7285
3.7156
3.7053
3.5721
3.1688
3.0189
2.9458
2.2083
2.0220
1.9821
1.9724
1.9589
1.8580
1.4708
0.9829
0.9654
0.9318
0.9195
0.9157
0.9027
0.8853
Integral
0.8388
0.7314
0.8480
0.7655
1.7858
1.9098
1.7440
2.9590
3.0443
7.7448
9.2172
12.047
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
(ppm)

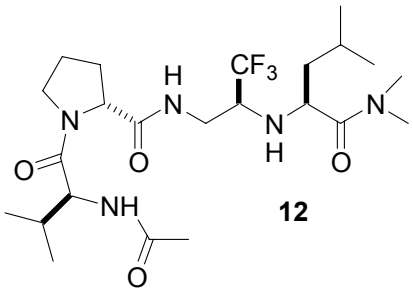

174.7898
172.2840
171.6395
155.8775
130.0889
127.2695
124.4501
79.5527
60.2475
58.5448
58.2794
56.9007
53.9158
47.5910
43.5480
37.8264
36.6338
35.8962
31.3706
28.3444
27.8791
25.1286
24.5667
23.5120
21.8369
19.4587
17.3251
200
180
160
140
120
100
80
60
40
20
0
(ppm)


H
N
CF3
N
H
N
N
O
O
O
NH
O

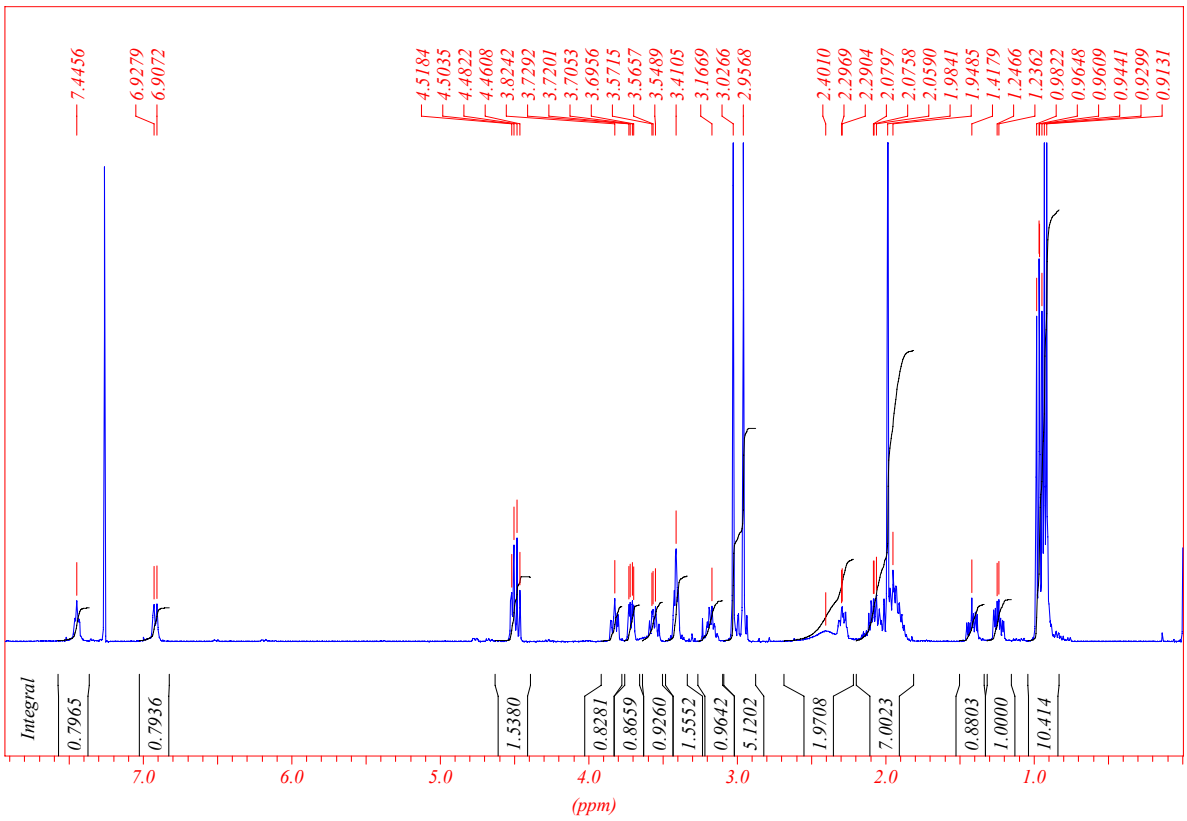
11

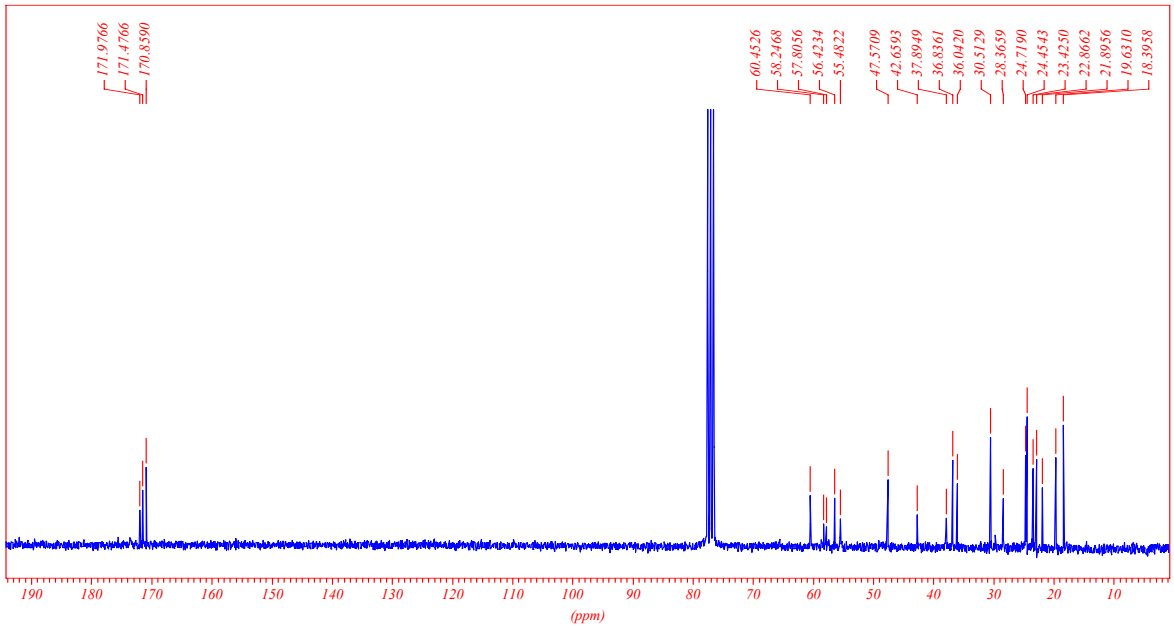

7.9291
6.1704
6.1484
4.6748
4.6586
4.6522
4.5061
3.8242
3.7182
3.5372
3.5004
3.3478
3.0182
2.9801
2.1295
2.1237
2.1153
1.9918
1.4586
1.2401
1.0126
0.9958
0.9635
0.9525
0.9467
0.9357
0.9221
0.9047
0.8467
0.9710
1.2531
1.0000
5.0571
1.1524
8.3792
14.904
1.1643
1.3140
15.433
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

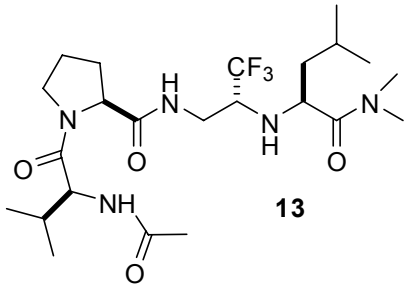

175.4759
172.1820
171.1526
170.0350
127.8902
123.4199
60.6879
60.4232
58.2763
57.8351
56.2470
56.0117
55.4823
47.7180
46.3946
42.2771
42.0125
38.1891
36.5716
35.9245
31.6307
31.3071
29.0132
25.0134
24.4252
23.4840
23.0429
22.8076
20.8665
19.2490
18.8960
18.1608
17.7785
180
160
140
120
100
80
60
40
20
0
(ppm)


H
N
CF3
N
N
H
O
O
O
NH
O

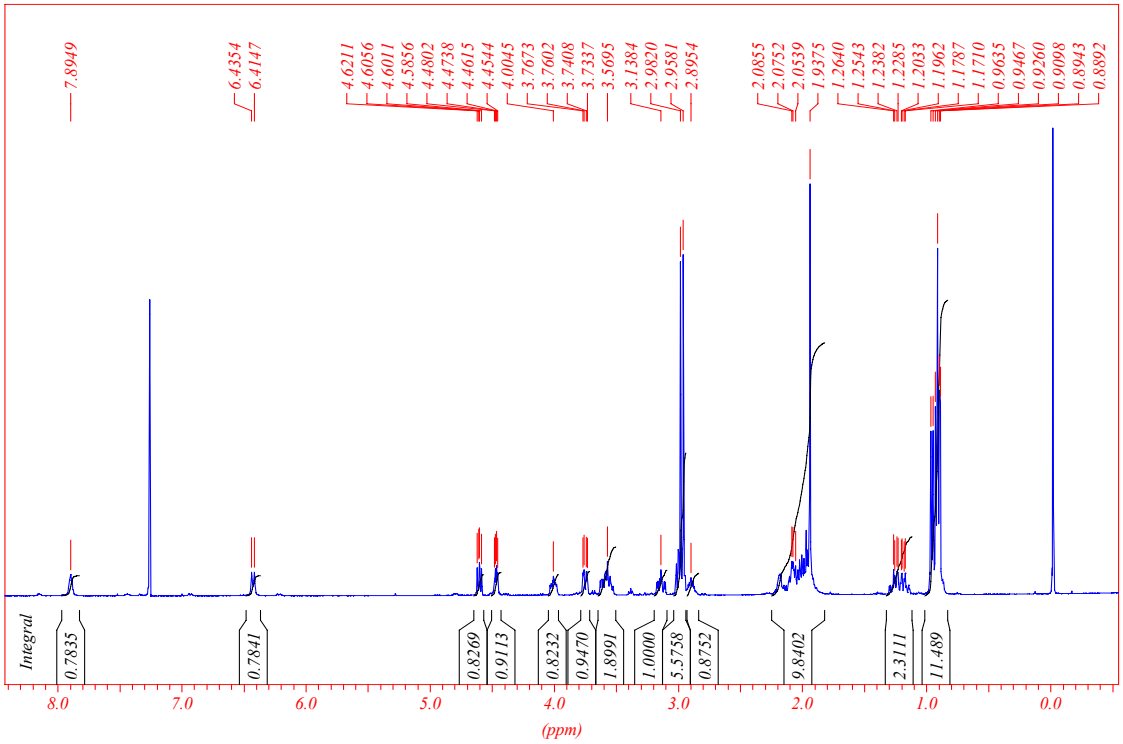
12

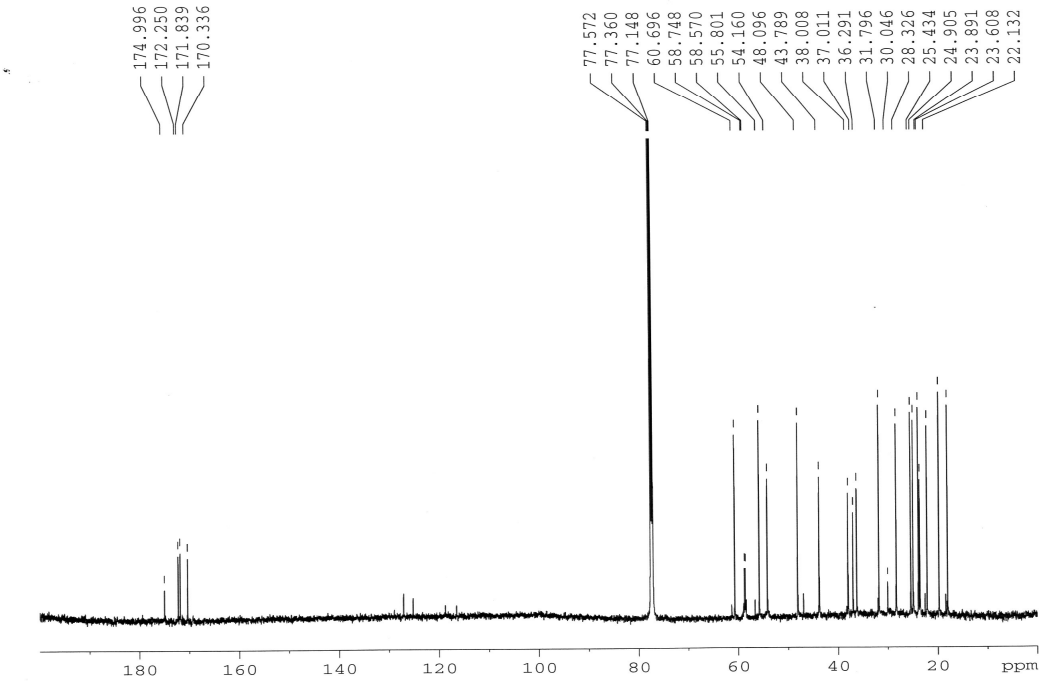

7.4456
6.9279
6.9072
4.5184
4.5035
4.4822
4.4608
3.8242
3.7292
3.7201
3.7053
3.6956
3.5715
3.5657
3.5489
3.4105
3.1669
3.0266
2.9568
2.4010
2.2969
2.2904
2.0797
2.0758
2.0590
1.9841
1.9485
1.4179
1.2466
1.2362
0.9822
0.9648
0.9609
0.9441
0.9299
0.9131
Integral
0.7965
0.7936
1.5380
0.8281
0.8659
0.9260
1.5552
0.9642
5.1202
1.9708
7.0023
0.8803
1.0000
10.414
7.0
6.0
5.0
4.0
3.0
2.0
1.0
(ppm)

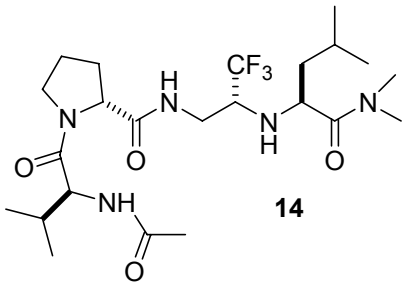

171.9766
171.4766
170.8590
60.4536
58.2468
57.8056
56.4234
55.4822
47.5709
42.6593
37.8949
36.8361
36.0420
30.5129
28.3659
24.7190
24.4543
23.4250
22.8662
21.8956
19.6310
18.3958
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)


CF3
H
N
N
H
N
O
O
O
O
NH
O

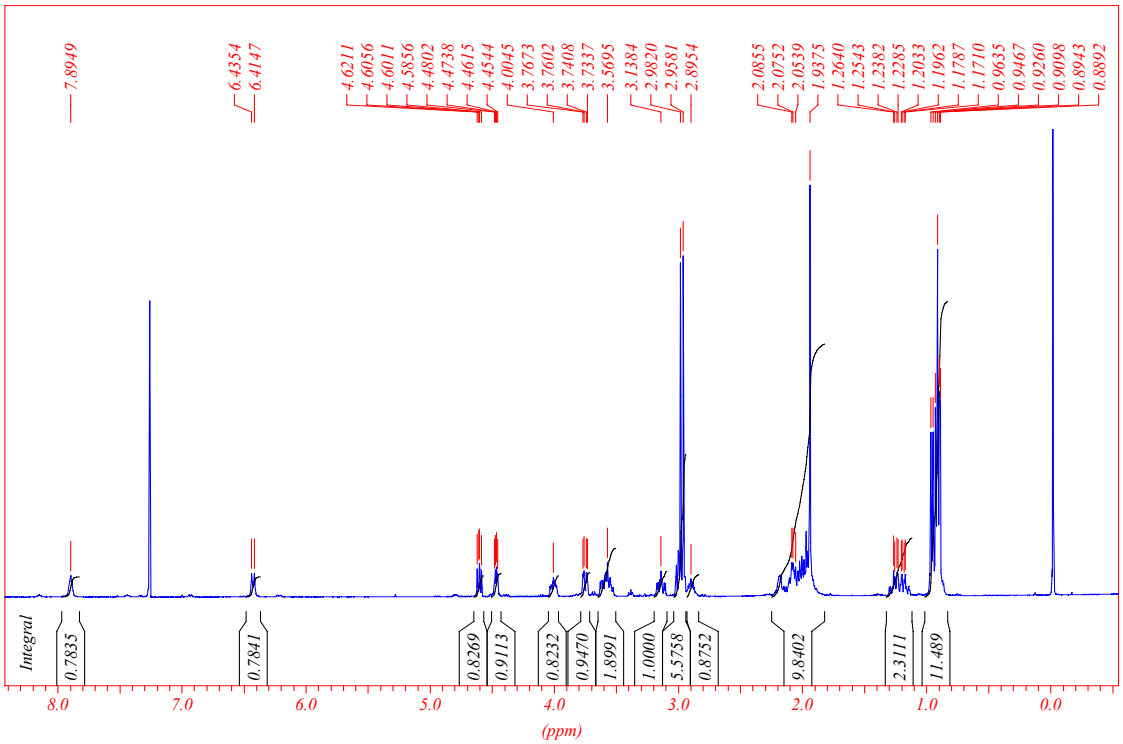
13

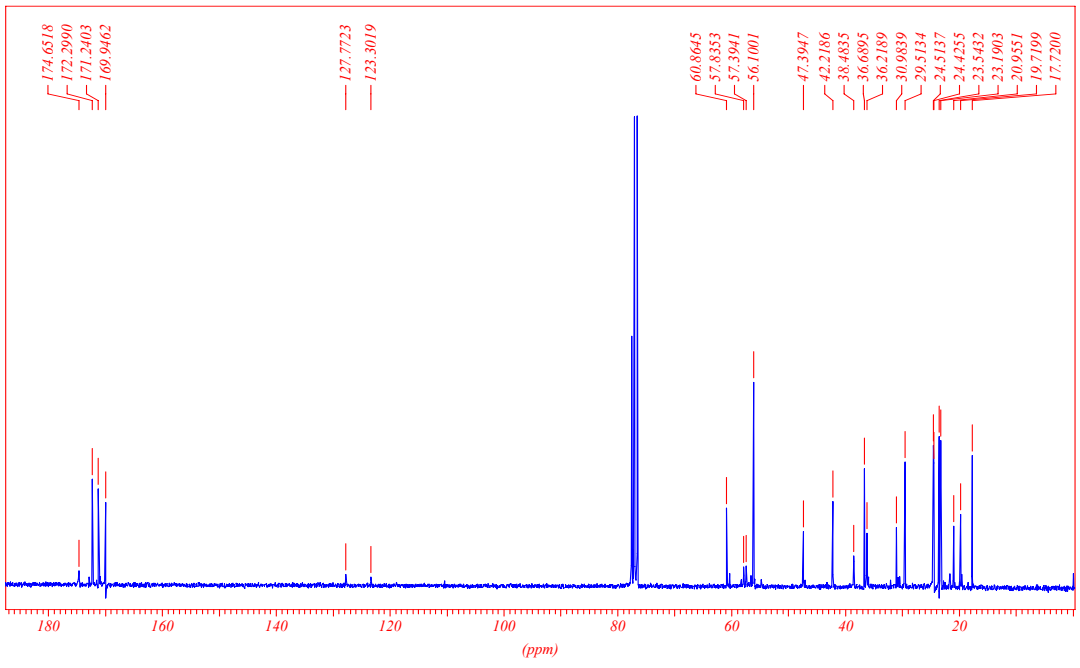

7.8949
6.4354
6.4147
4.6211
4.6056
4.6011
4.5856
4.4802
4.4738
4.4615
4.4544
4.0045
3.7673
3.7602
3.7408
3.7337
3.5695
3.1384
2.9820
2.9581
2.8954
2.0855
2.0752
2.0539
1.9375
1.2640
1.2543
1.2382
1.2285
1.2033
1.1962
1.1787
1.1710
0.9635
0.9467
0.9260
0.9098
0.8943
0.8892
Integral
0.7835
0.7841
0.8269
0.9113
0.8232
0.9470
1.8991
1.0000
5.5758
0.8752
9.8402
2.3111
11.489
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

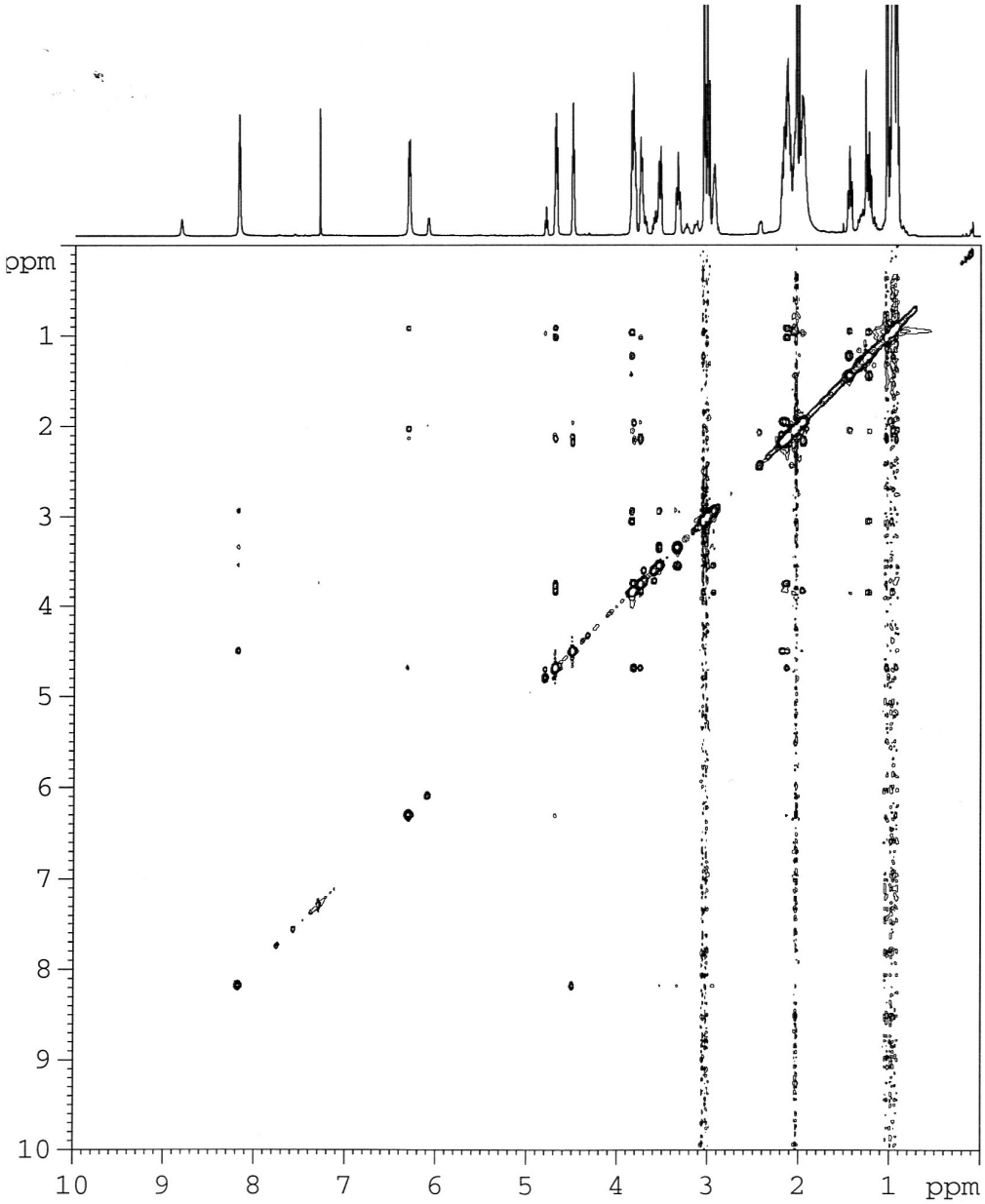

174.996
172.250
171.839
170.336
77.572
77.360
77.148
60.696
58.748
58.570
55.801
54.160
48.096
43.789
38.008
37.011
36.291
31.796
30.046
28.326
25.434
24.905
23.891
23.608
22.132
180
160
140
120
100
80
60
40
20
ppm


CF3
H
N
N
H
N
O
O
O
N
NH
O

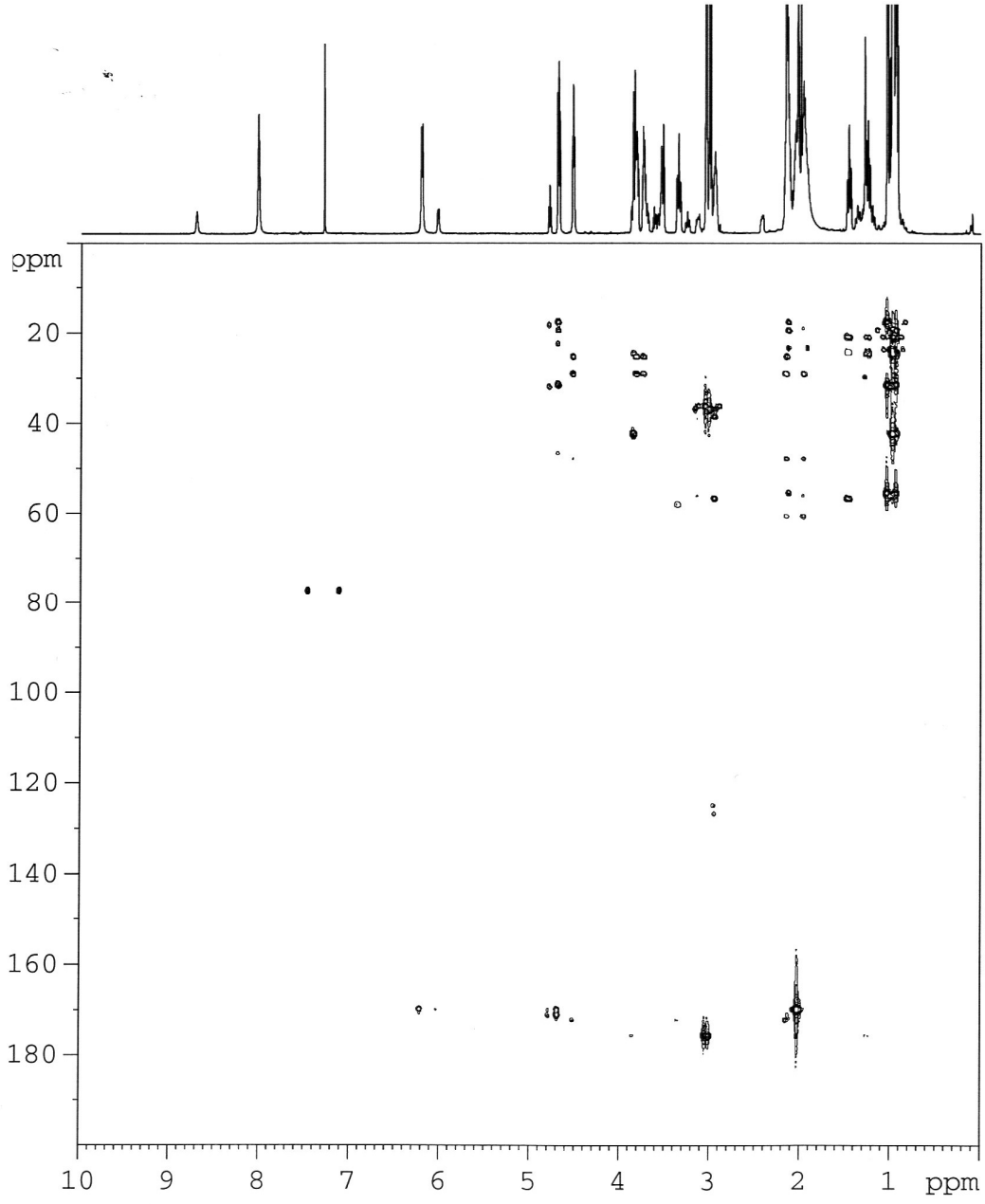
14


7.8949
6.4354
6.4147
4.6211
4.6056
4.6011
4.5856
4.4802
4.4738
4.4615
4.4544
4.0045
3.7673
3.7602
3.7408
3.7337
3.5695
3.1384
2.9820
2.9581
2.8954
2.0855
2.0752
2.0539
1.9375
1.2640
1.2543
1.2382
1.2285
1.2033
1.1962
1.1787
1.1710
0.9635
0.9467
0.9260
0.9098
0.8943
0.8892
Integral
0.7835
0.7841
0.8269
0.9113
0.8232
0.9470
1.8991
1.0000
5.5758
0.8752
9.8402
2.3111
11.489
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

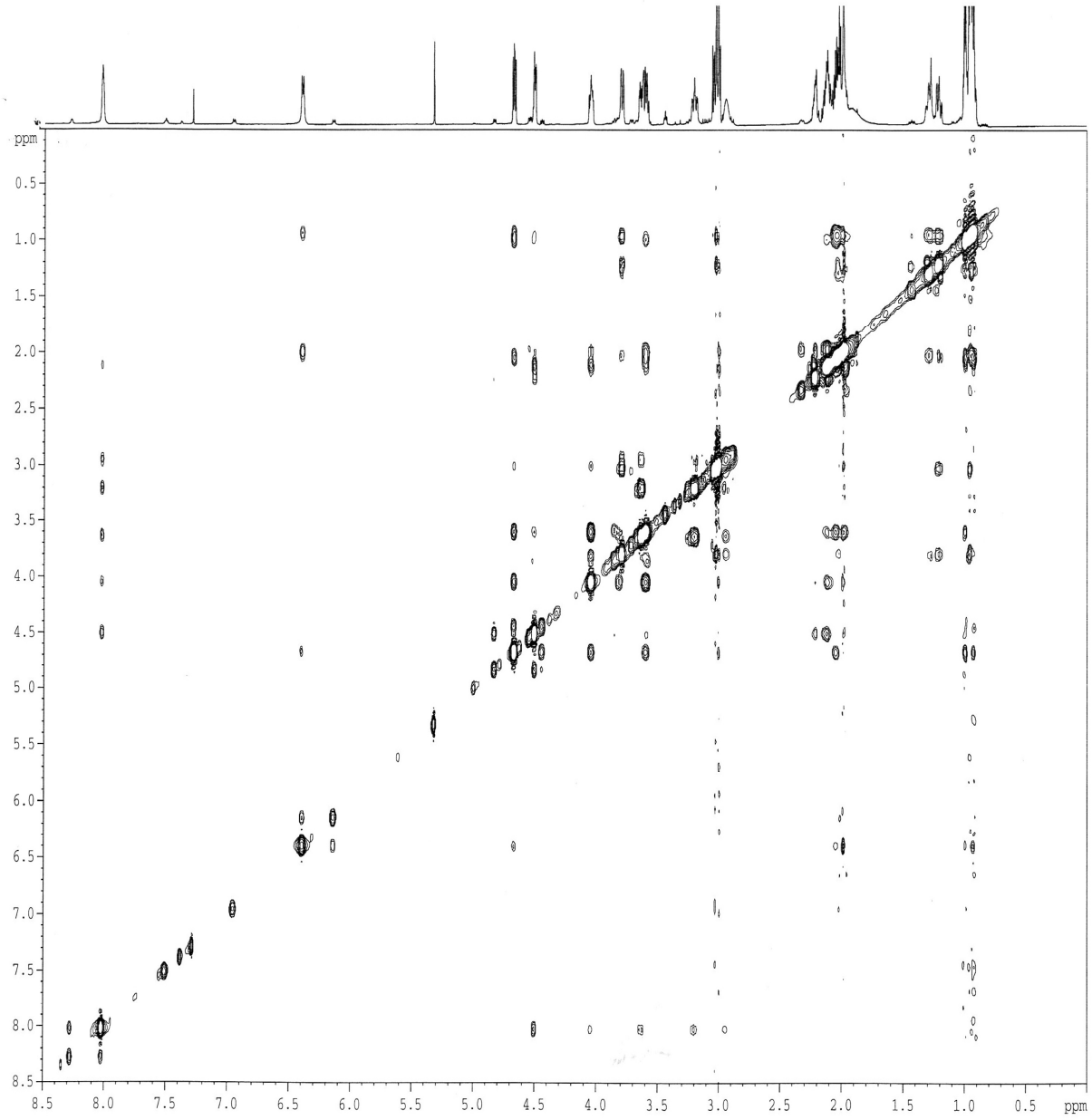

174.6518
172.2990
171.2403
169.9462
127.7723
123.3019
60.8645
57.8353
57.3941
56.1001
47.3947
42.2186
38.4835
36.6895
36.2189
30.9839
29.5134
24.5137
24.4255
23.5432
23.1903
20.9551
19.7199
17.7200
180
160
140
120
100
80
60
40
20
(ppm)



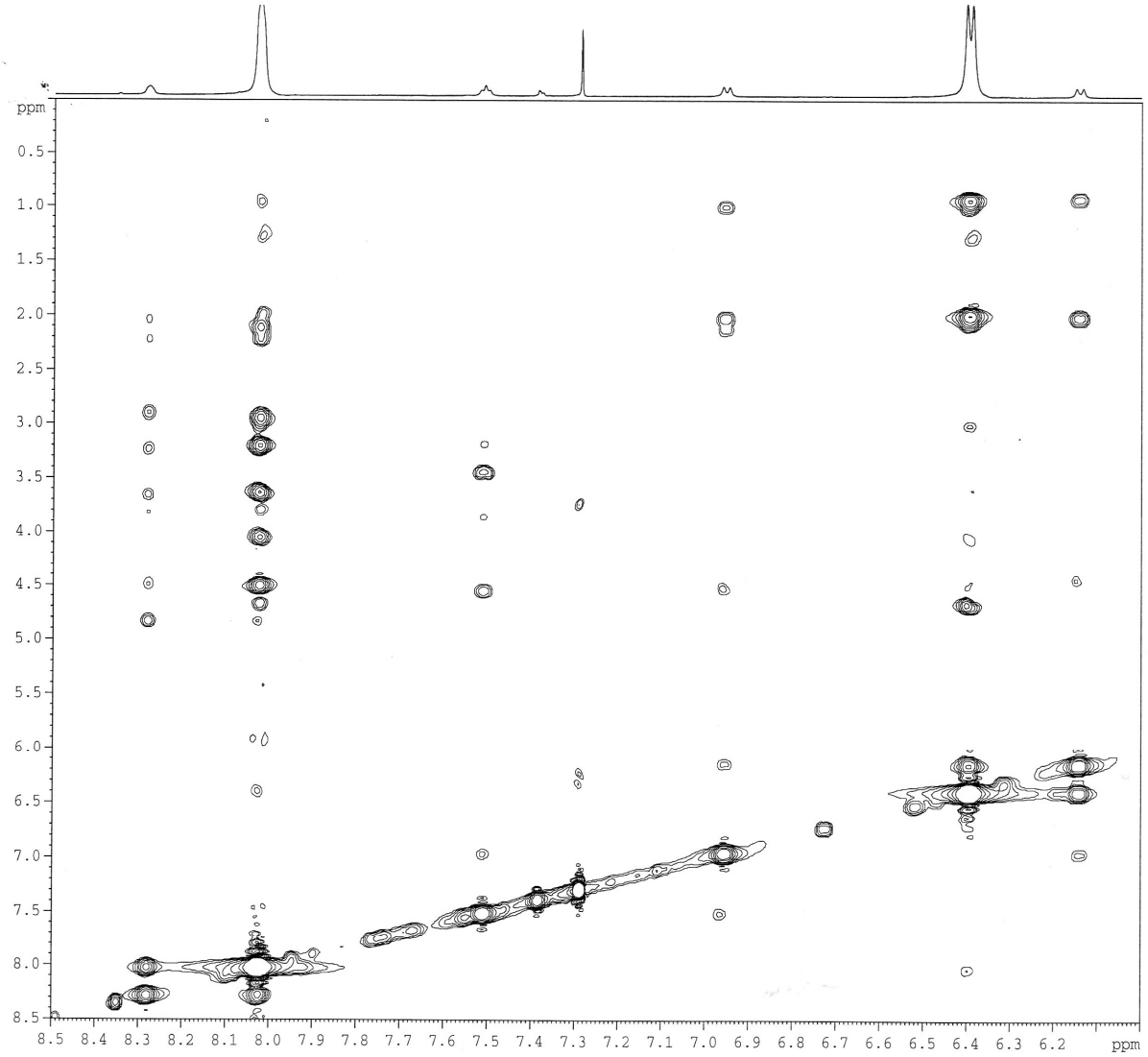
2D ROESY of **11** at 298 K



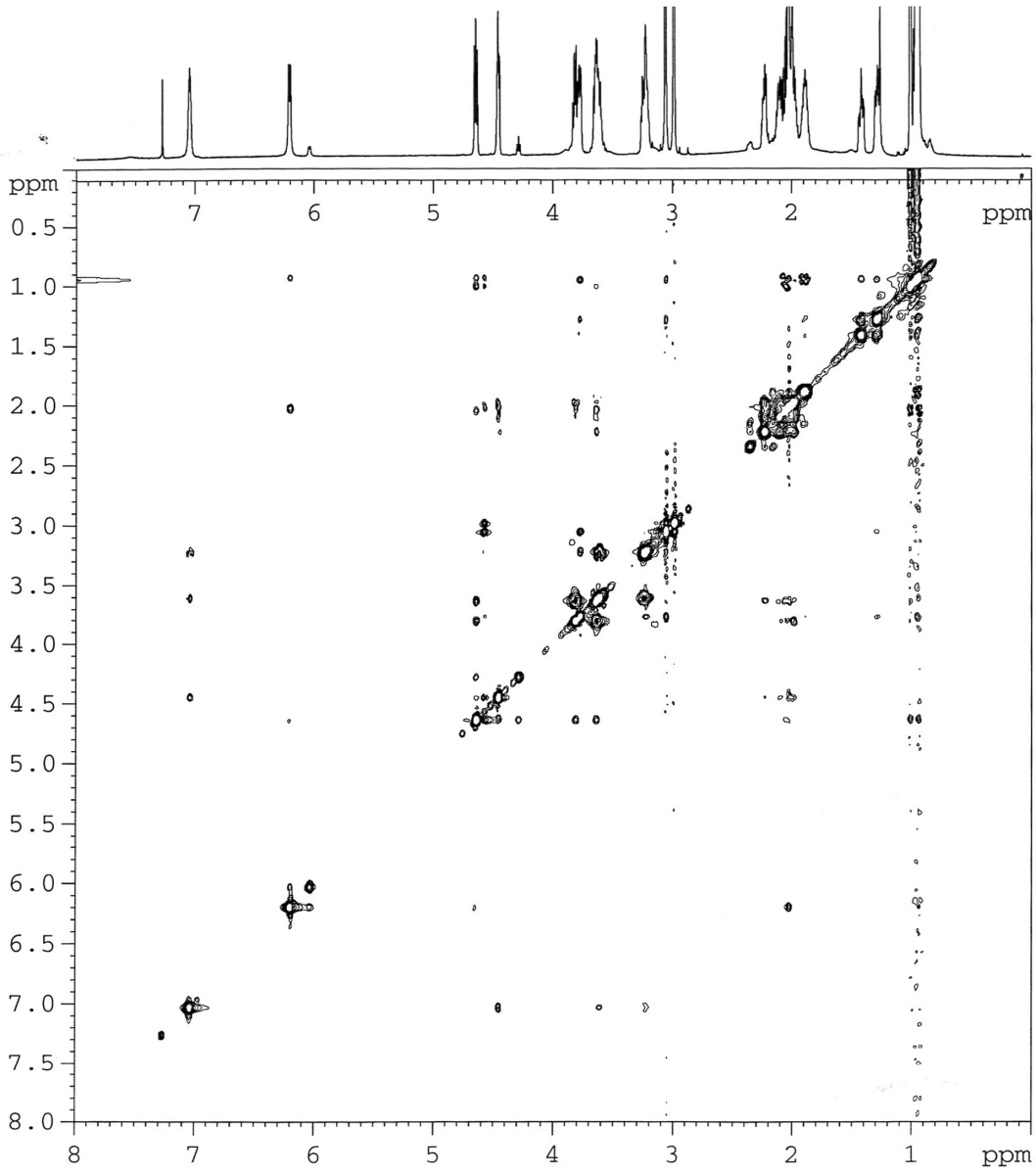
^{1}H-^{13}C 2D HMBC of **11**



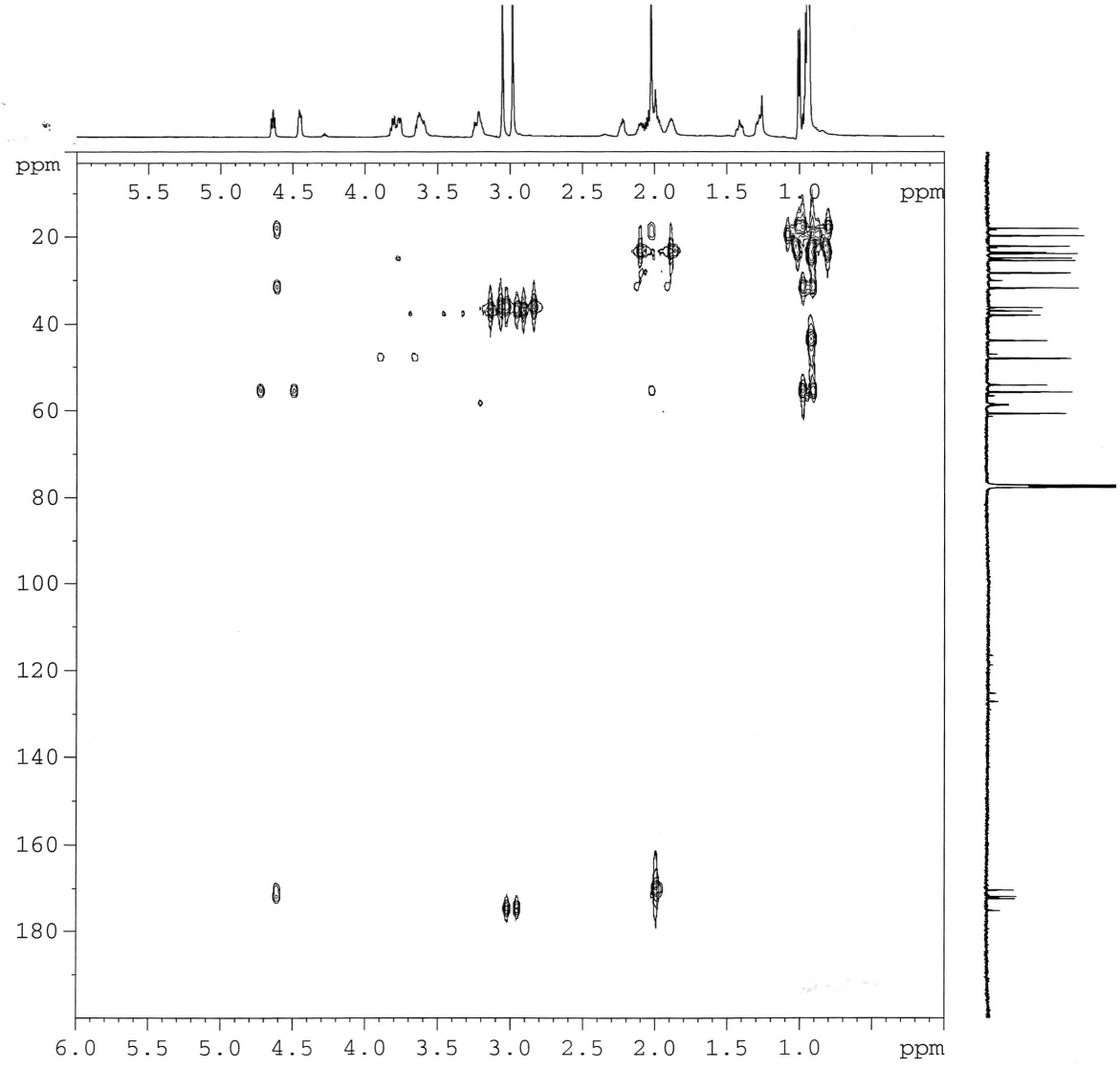
2D ROESY of **12** at 298 K



Expansion of the 2D ROESY of **12** at 298 K



2D ROESY of **13** at 298 K



^{1}H-^{13}C 2D HMBC of **13**