

**Development of selective steroid inhibitors for the glucose-6-phosphate dehydrogenase from
*Trypanosoma cruzi***

Fabício Fredo Naciuk, Jéssica do Nascimento Faria, Amanda Gonçalves Eufrazio, Artur Torres Cordeiro* and Marjorie Bruder*

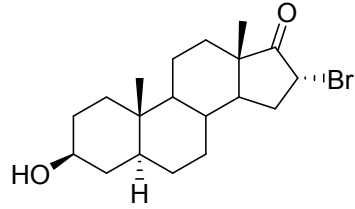
Brazilian Biosciences National Laboratory, Brazilian Center for Research in Energy and Materials, Campinas-SP, Brazil

SUPPORTING INFORMATION - ANNEX

NMR spectra for compounds 3-42 and 45-50

BrEA (3) – ¹H – CDCl₃ – 250 MHz

— 7.26

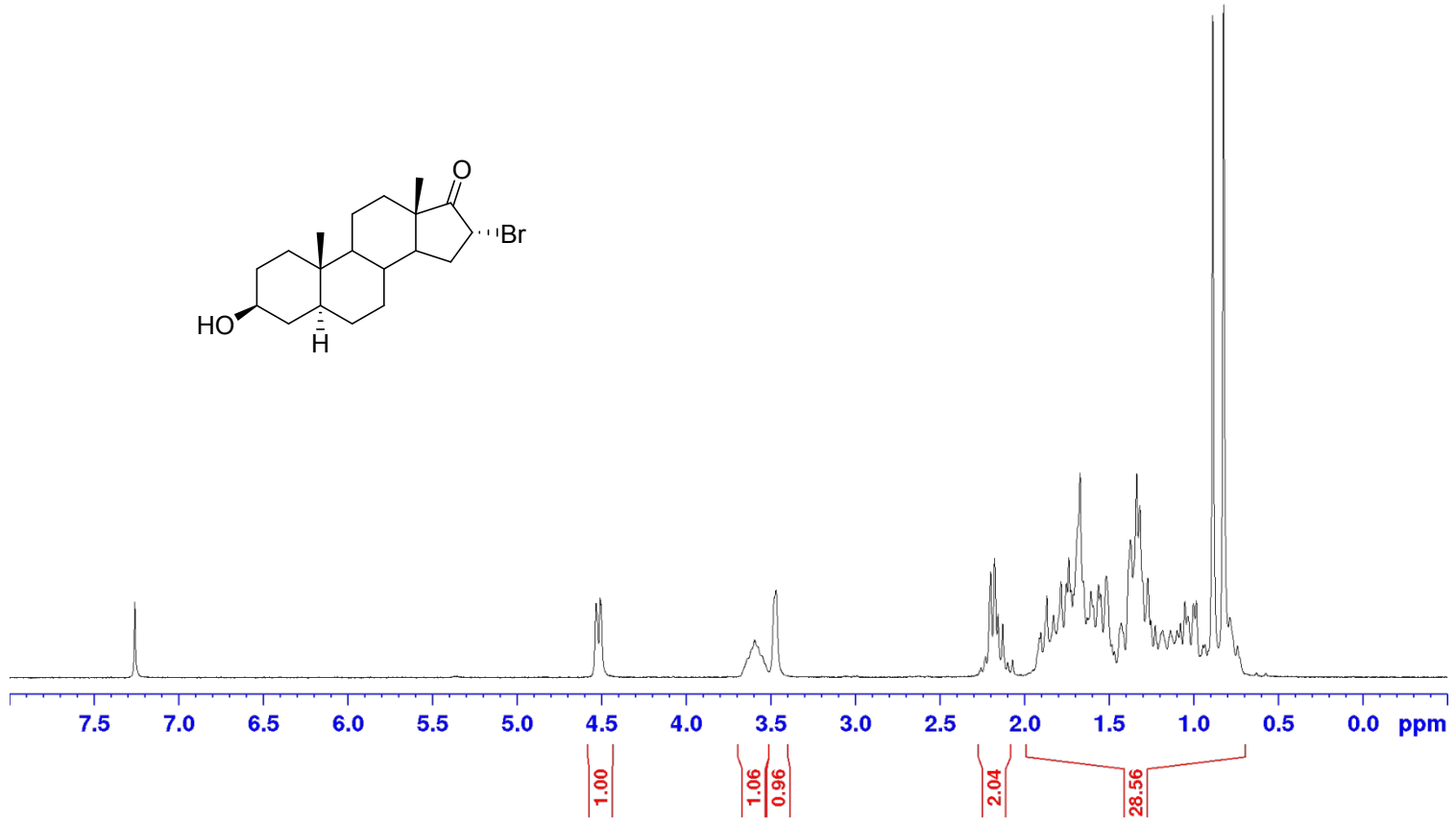


4.53
4.51

3.68
3.60
3.52
3.47

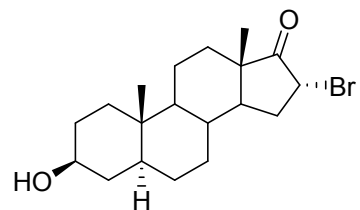
2.26
2.23
2.20
2.18
2.16
2.13
2.10
2.07
1.90

0.89
0.82
0.74

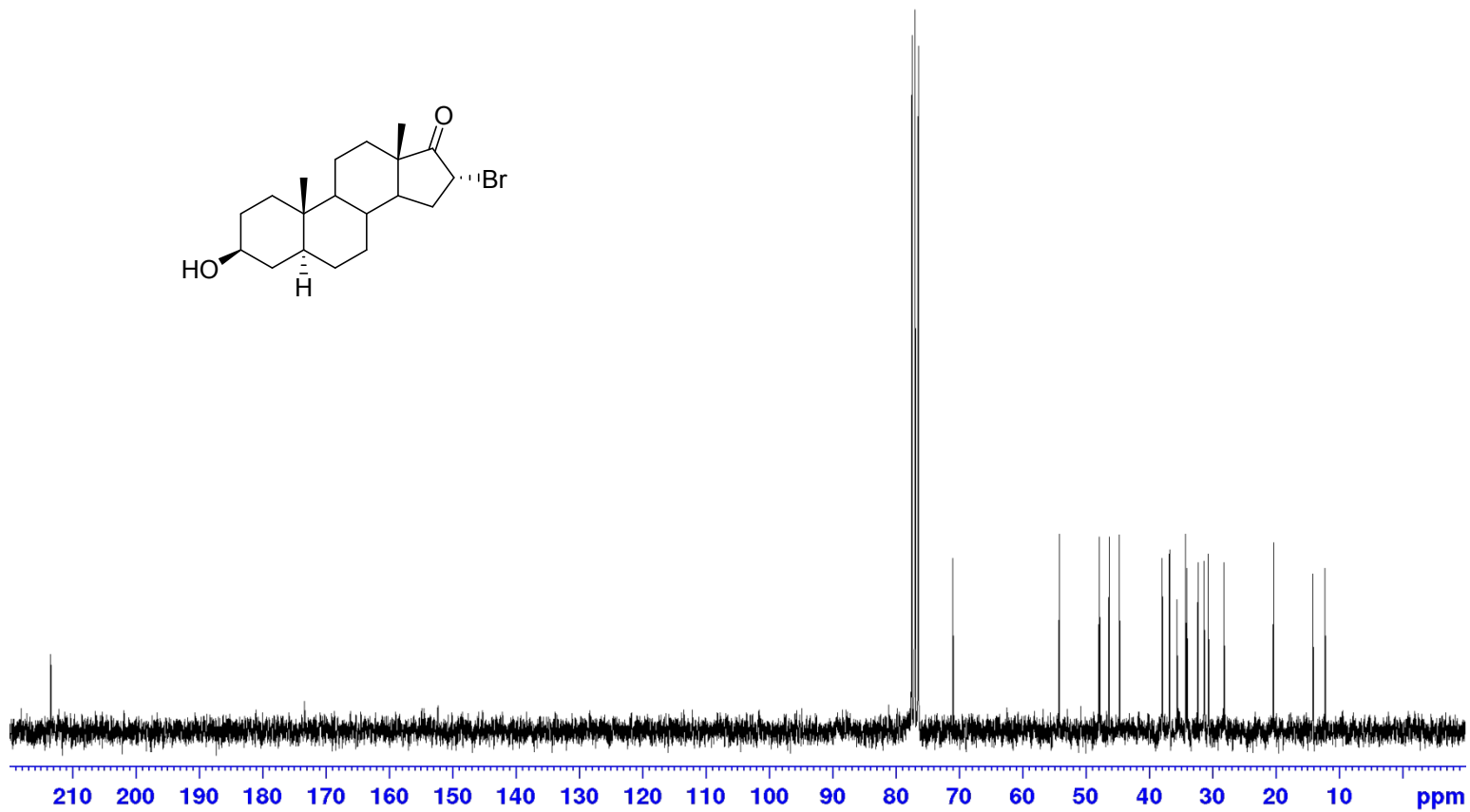


— 213.5

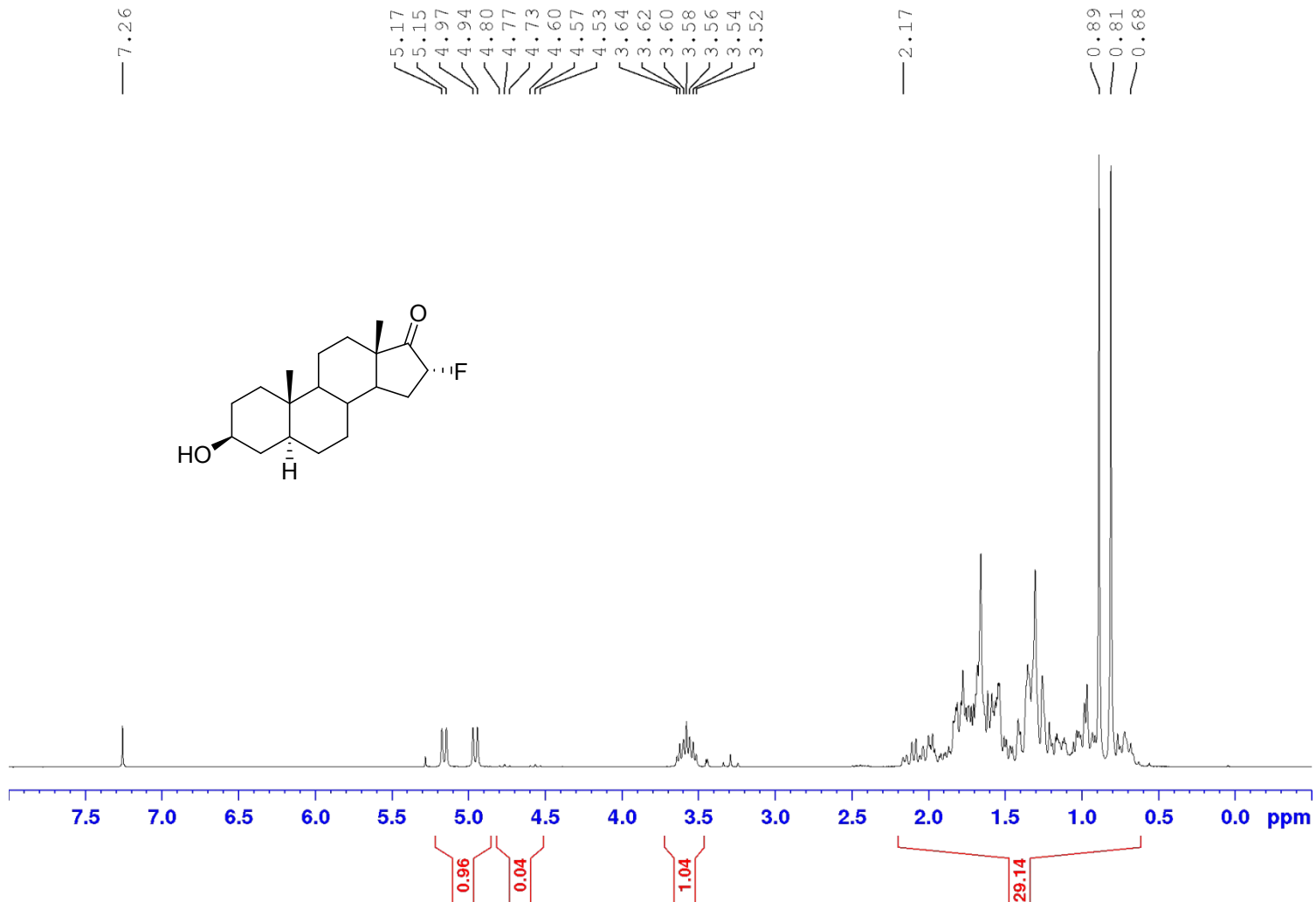
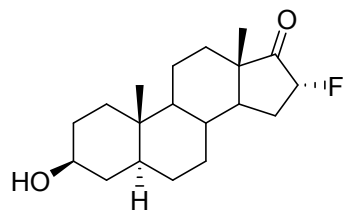
BrEA (3) — ^{13}C — CDCl_3 — 62.5 MHz



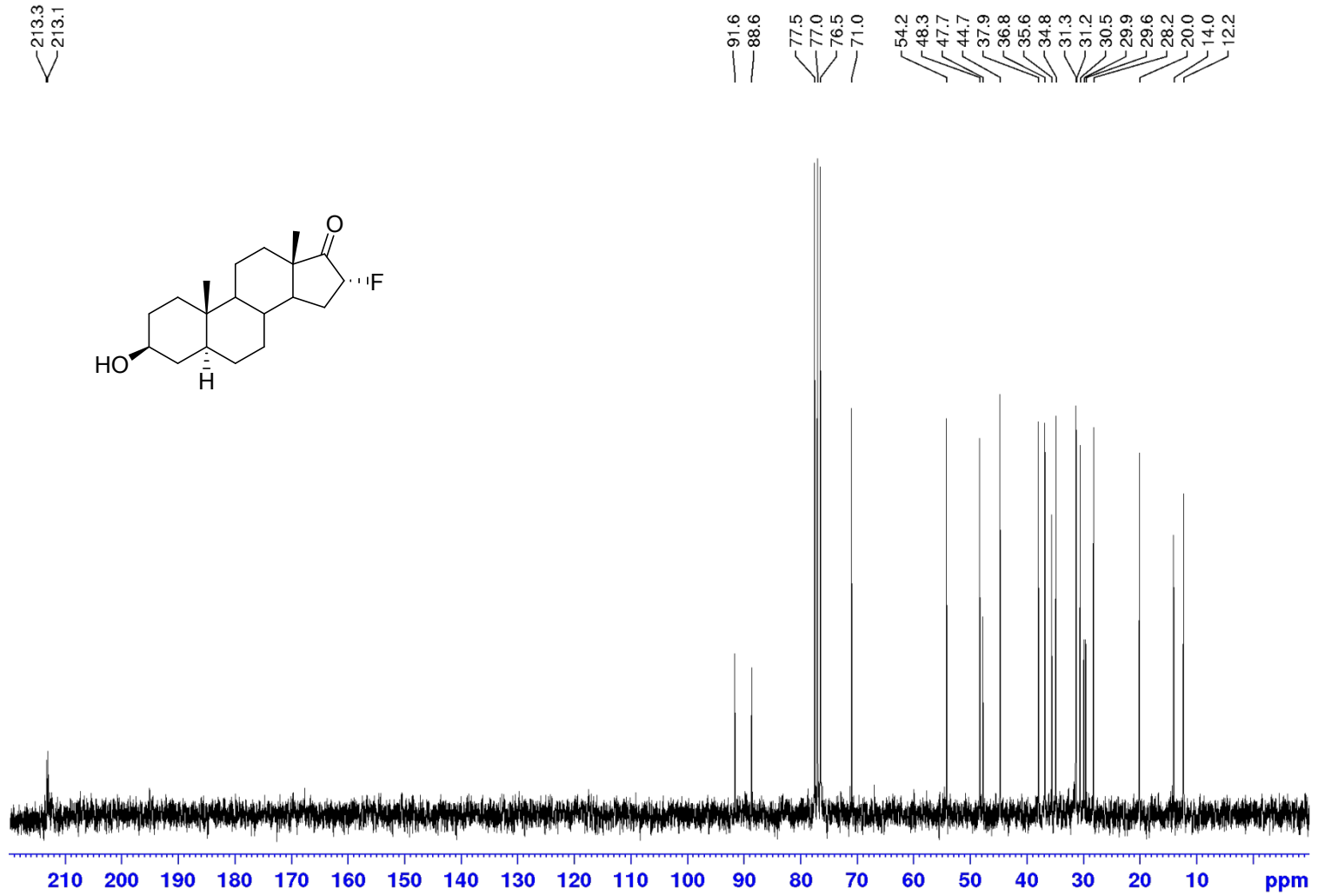
77.5
77.0
76.5
71.0
54.2
47.9
47.8
46.3
44.7
37.9
36.8
35.6
34.3
34.0
32.3
31.3
30.7
28.2
20.3
14.2
12.2

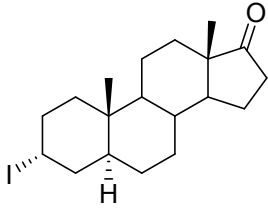


FEA (4) – ¹H – CDCl₃ – 250 MHz

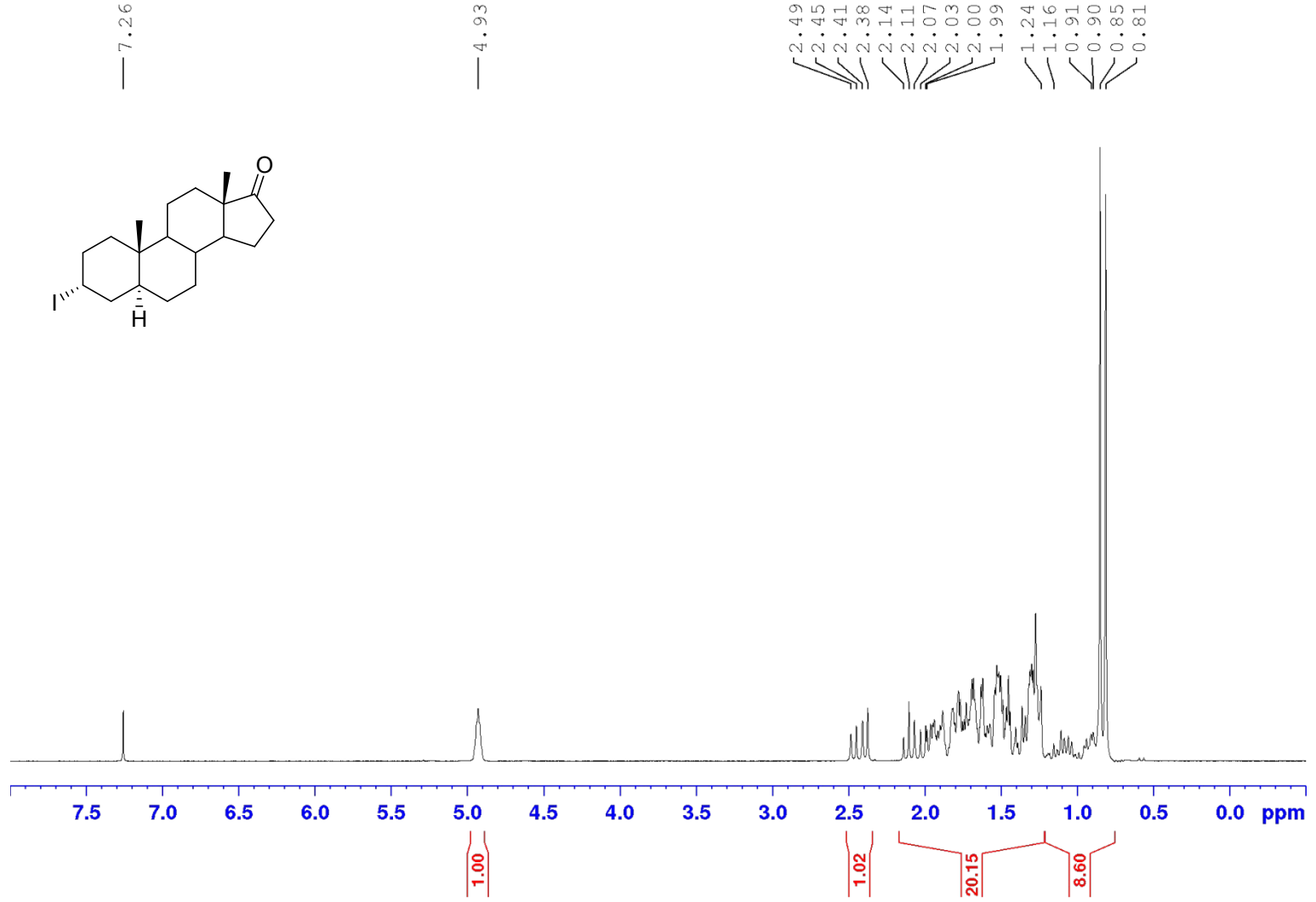


FEA (4) – ^{13}C – CDCl_3 – 62.5 MHz



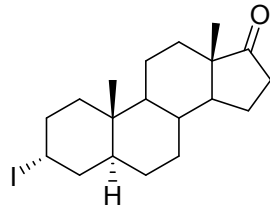


3-IEA - ¹H - CDCl₃ - 250 MHz

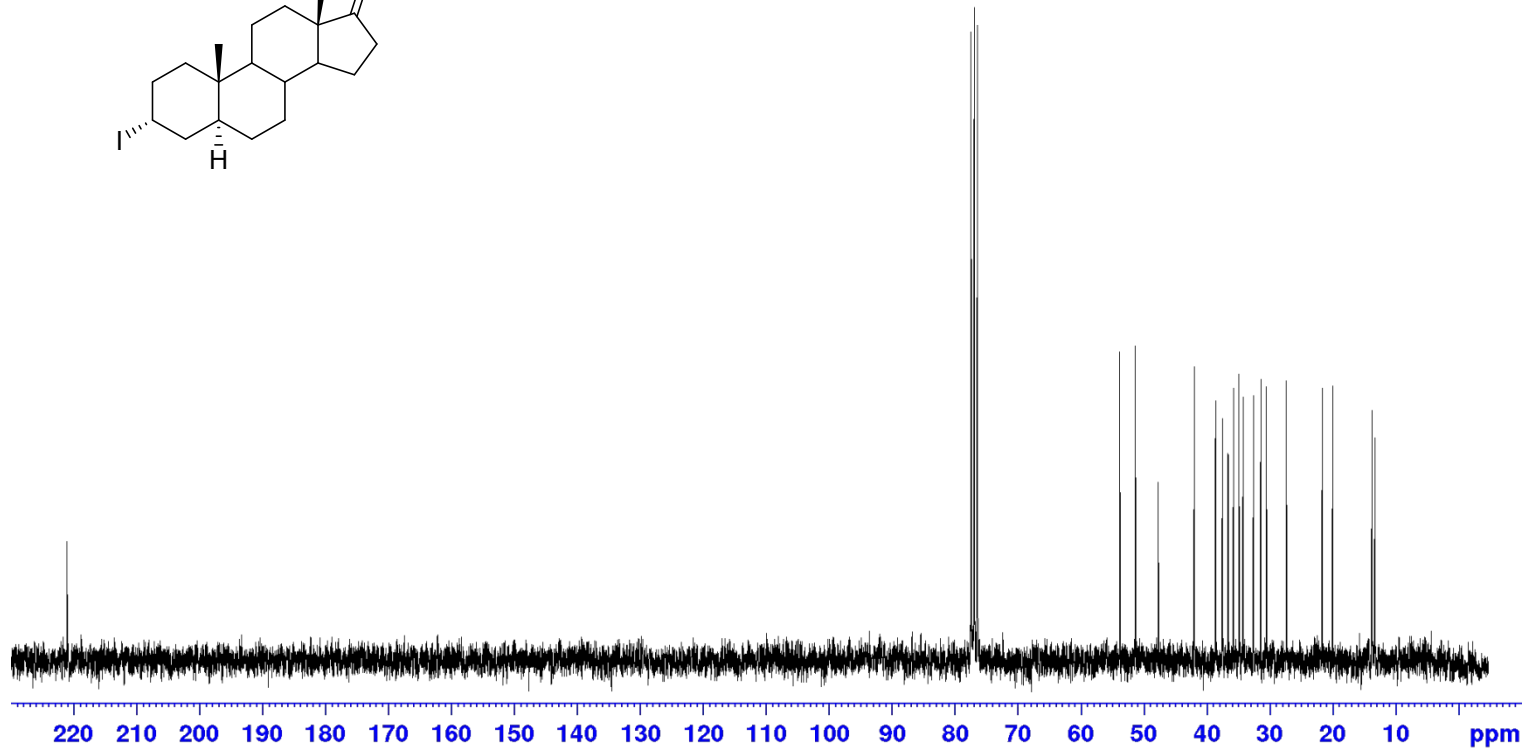


3-IEA - ¹³C - CDCl₃ - 62.5 MHz

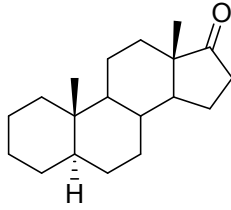
—221.1



77.5
77.0
76.5
53.9
51.4
47.7
42.0
38.6
37.6
36.6
35.8
34.9
34.3
32.6
31.5
30.6
27.4
21.7
20.0
13.8
13.3

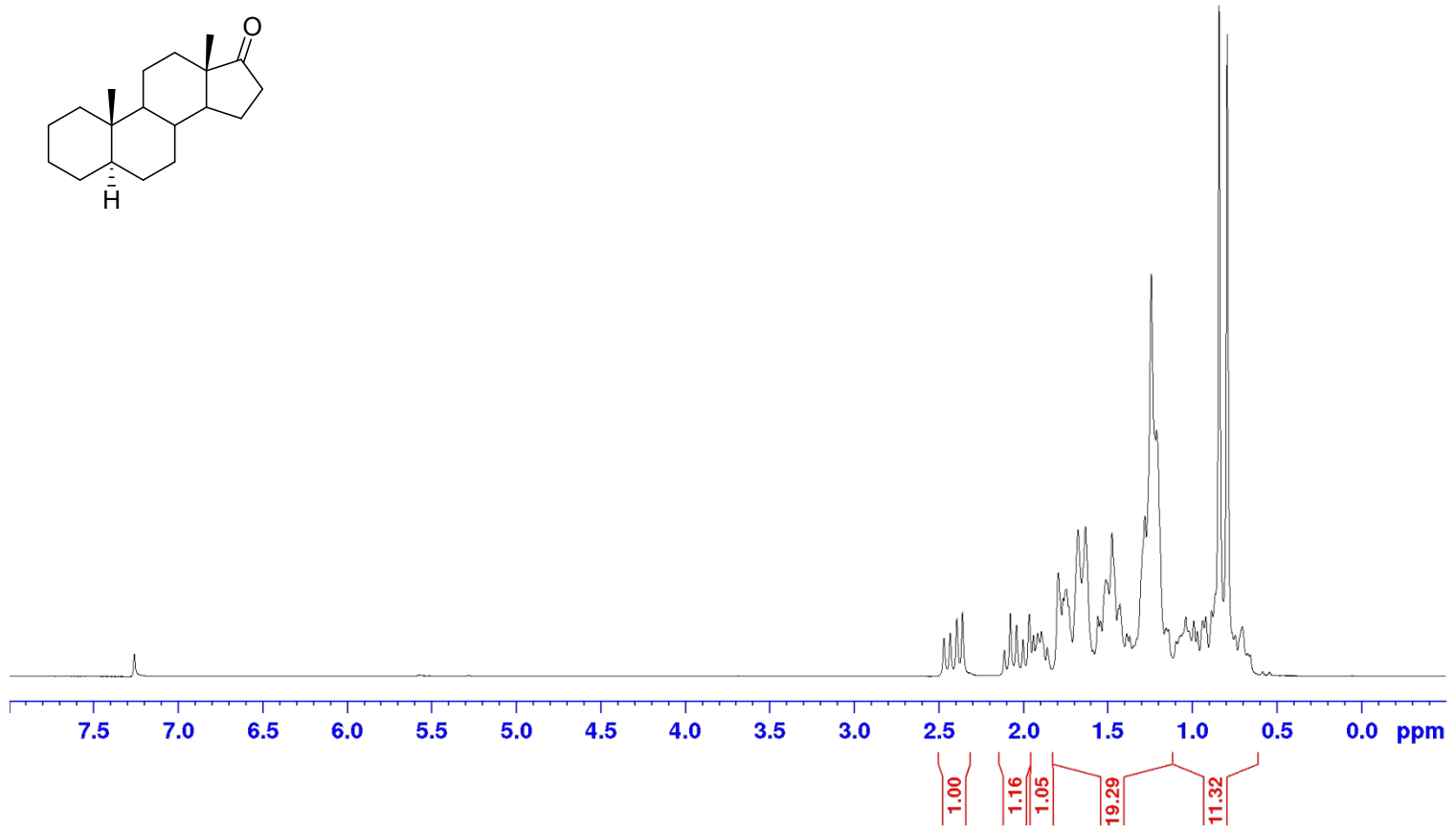


dEA (5) – ¹H – CDCl₃ – 250 MHz

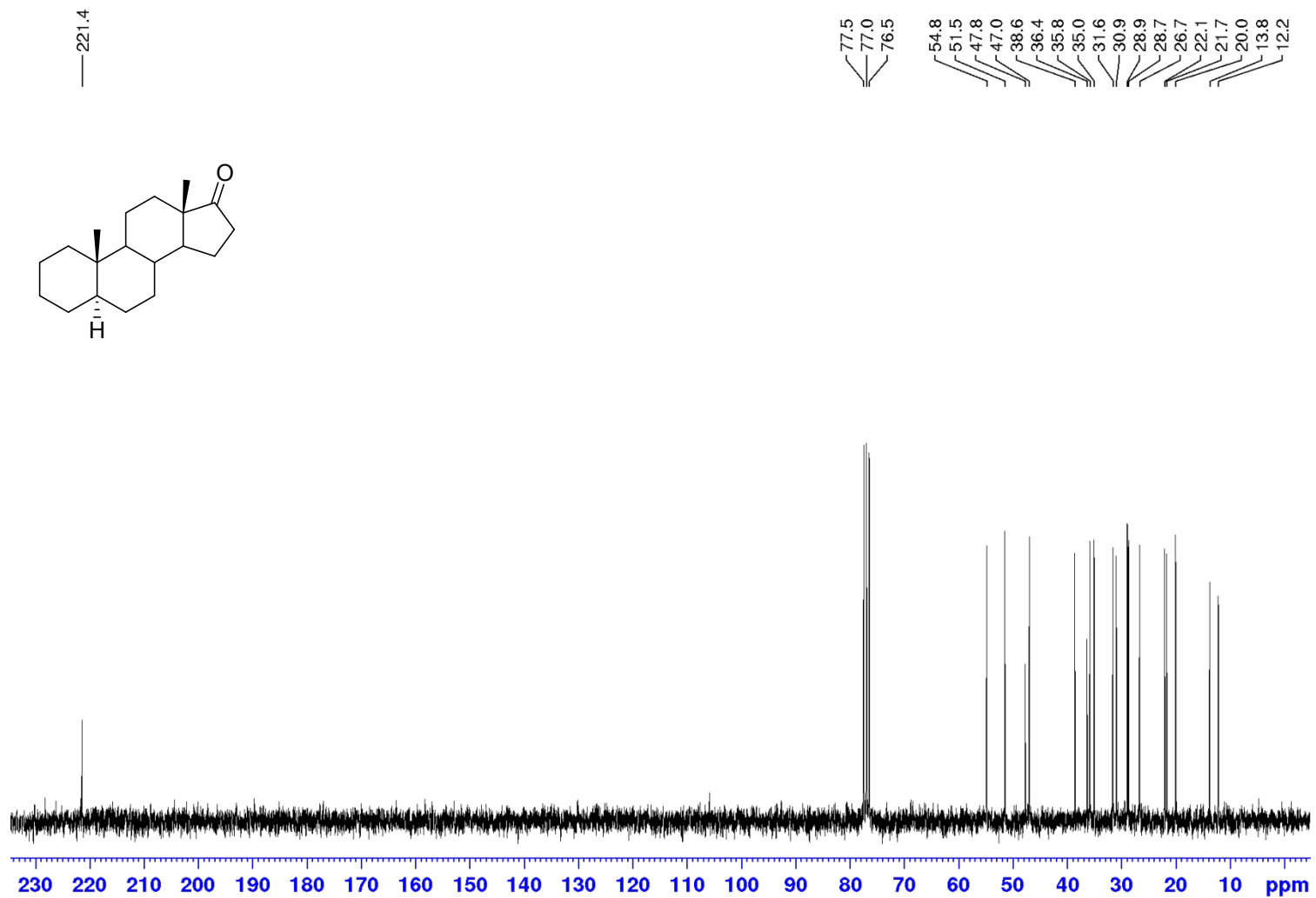
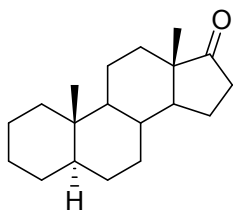


— 7.26

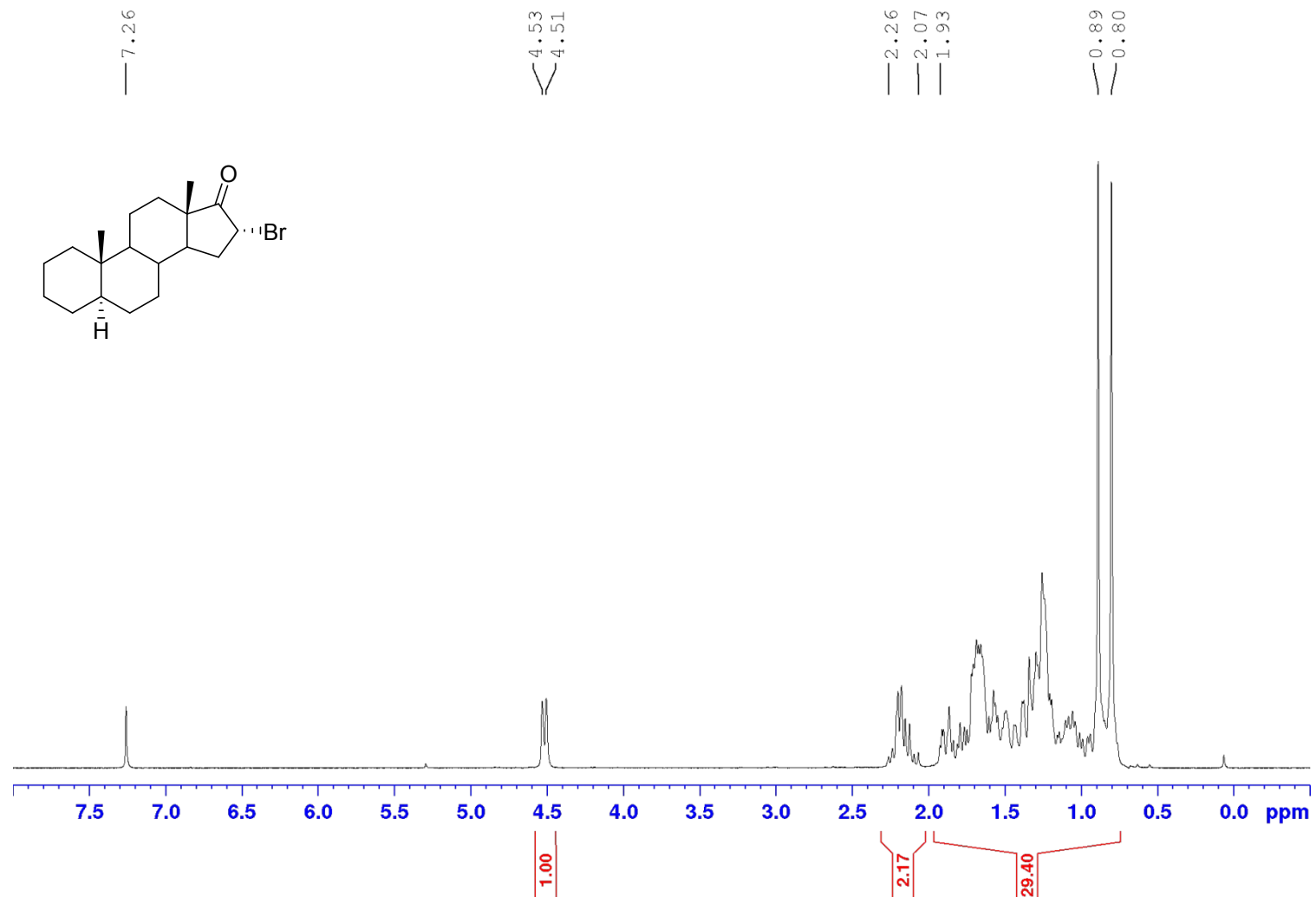
2.47
2.36
2.11
1.96
1.86
1.79
1.14
1.10
0.84
0.79
0.66



dEA (5) – ^{13}C – CDCl_3 – 62.5 MHz

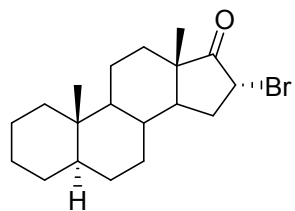


dBrEA (6) – ¹H – CDCl₃ – 250 MHz

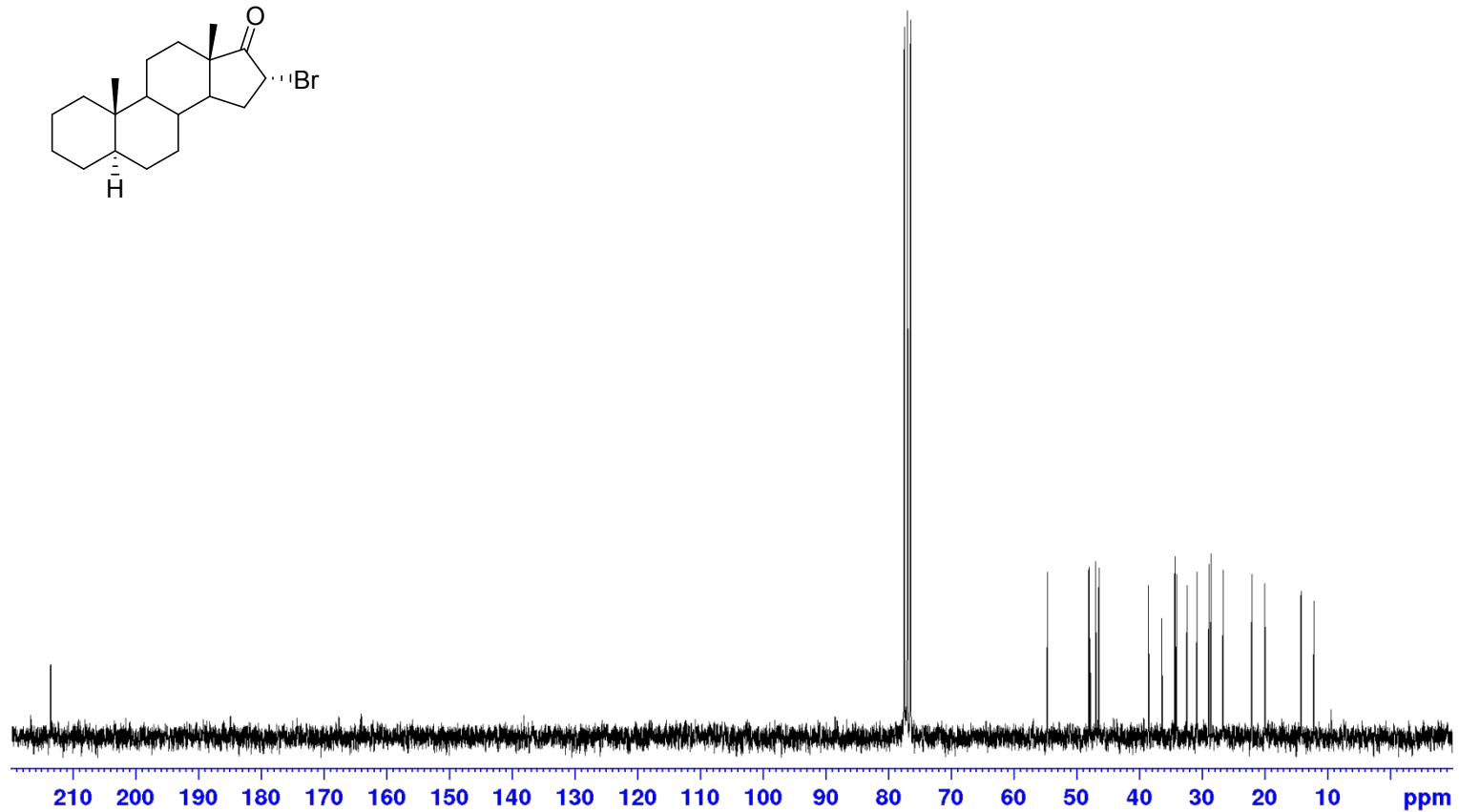


dBrEA (6) – ^{13}C – CDCl_3 – 62.5 MHz

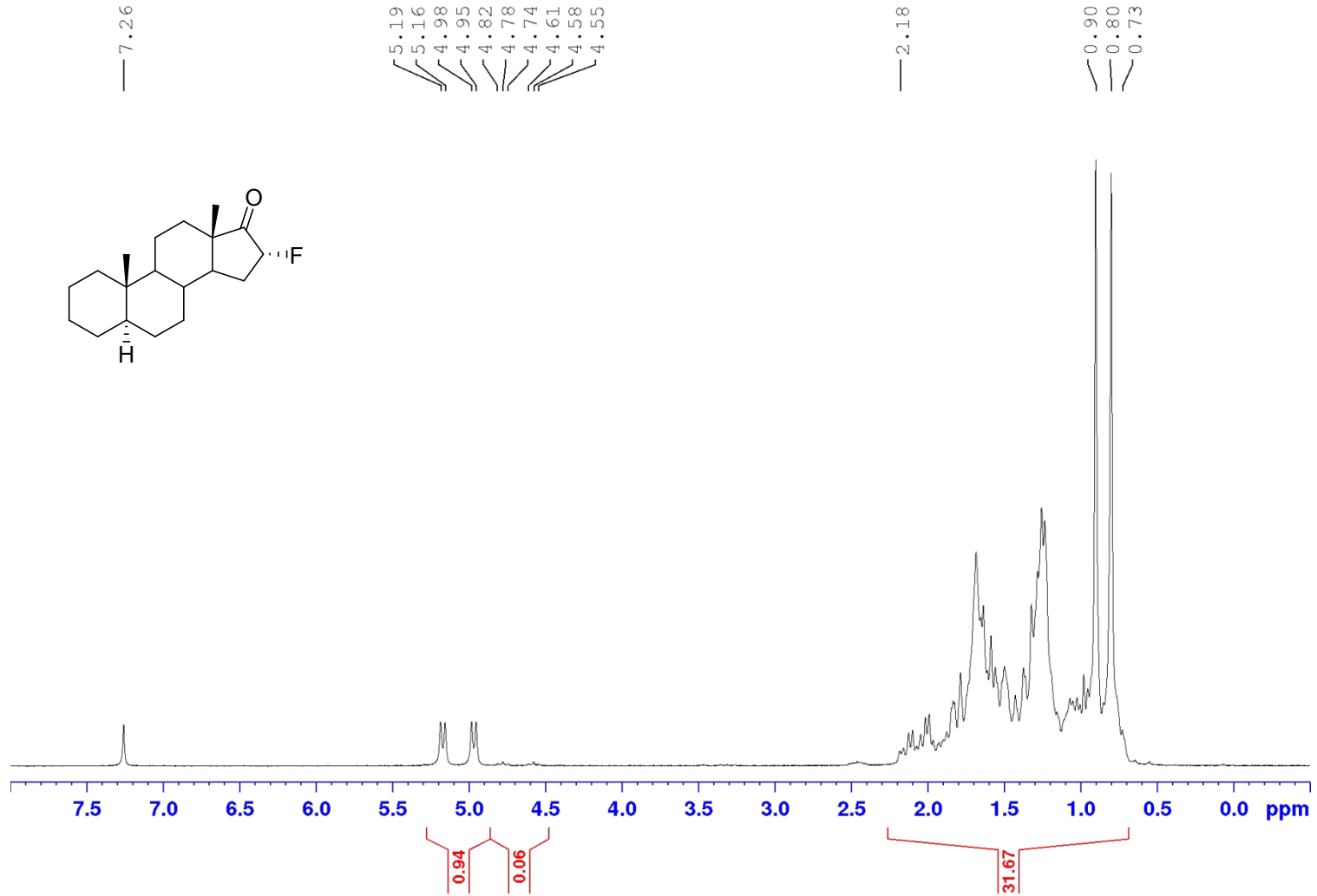
— 213.6



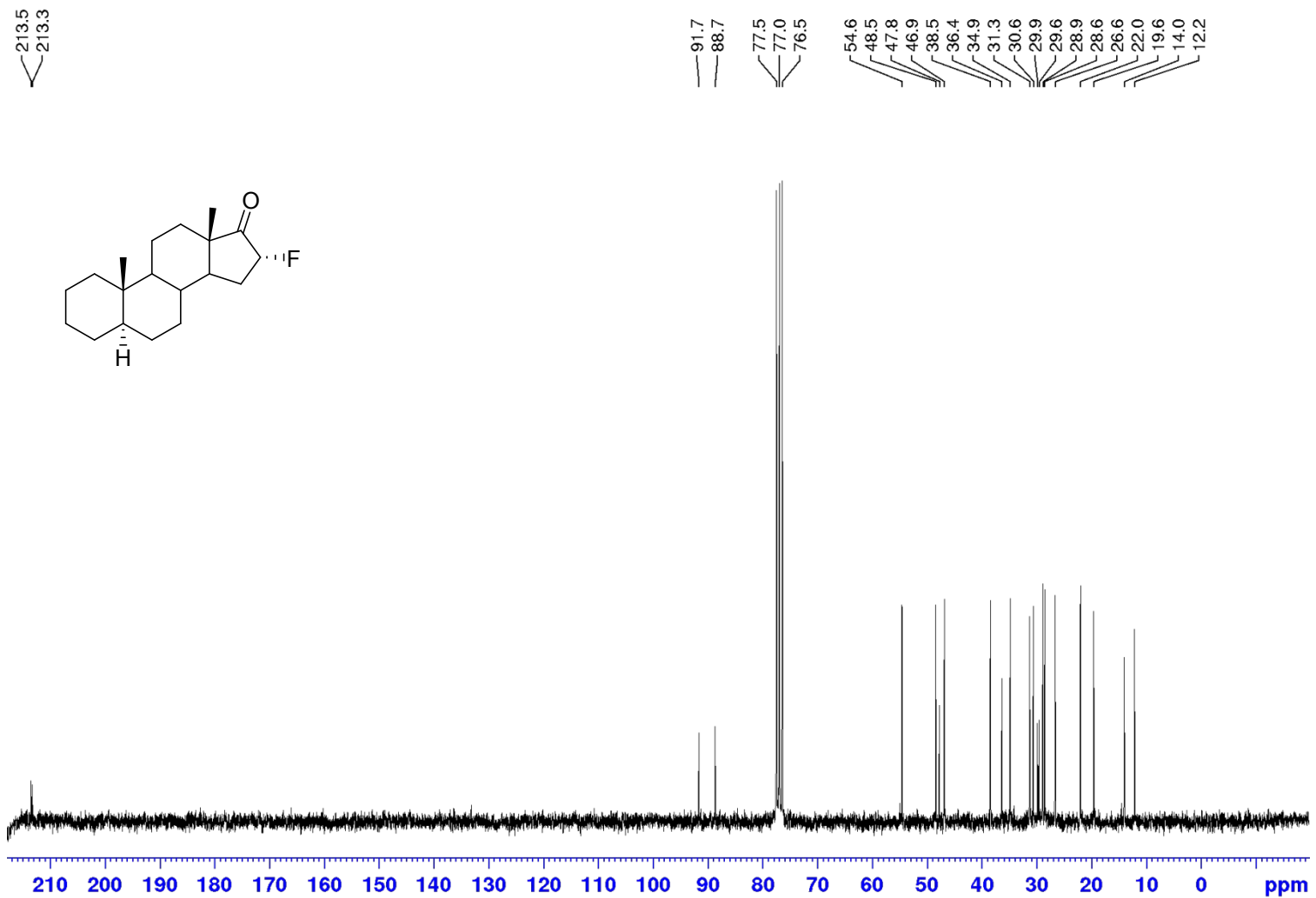
77.5
77.0
76.5
54.6
48.0
47.8
46.9
46.5
38.5
36.4
34.3
34.1
32.4
30.8
28.9
28.6
26.7
22.1
19.9
14.2
12.1



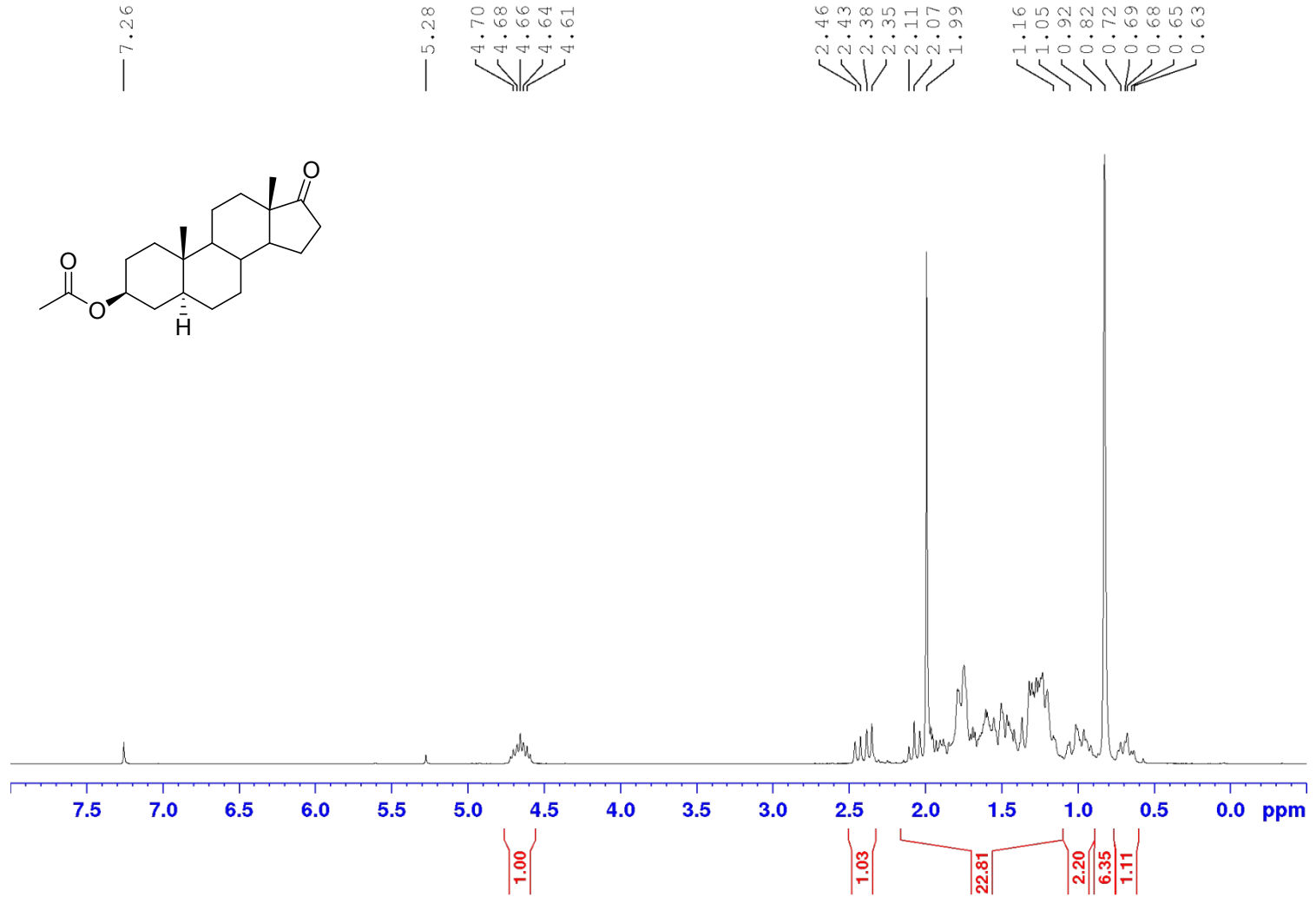
dFEA (7) - ¹H - CDCl₃ - 250 MHz



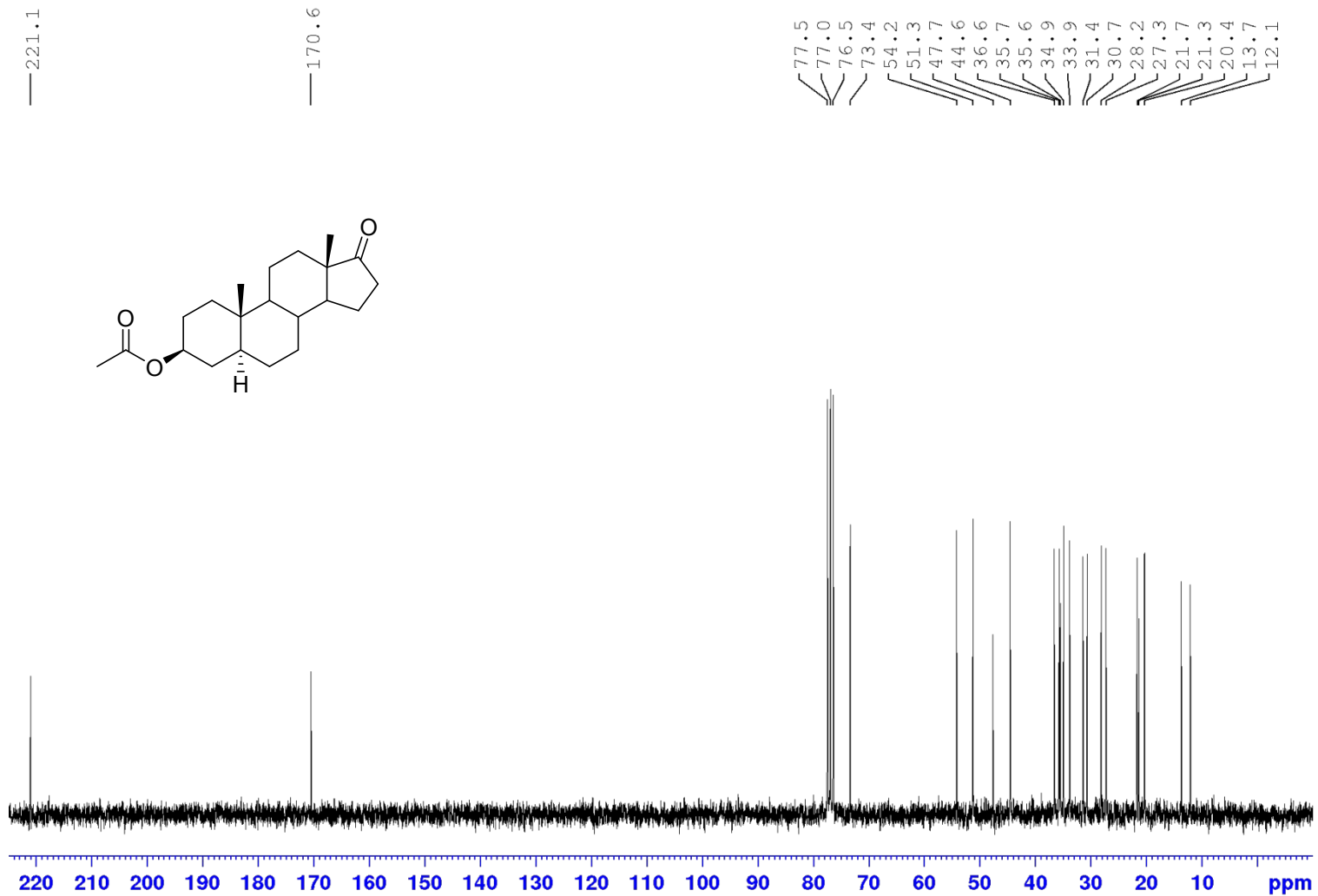
dFEA (7) – ¹³C – CDCl₃ – 62.5 MHz



Epiandrosterone acetate (8) – ¹H – CDCl₃ – 250 MHz



Epiandrosterone acetate (8) – ^{13}C – CDCl_3 – 62.5 MHz

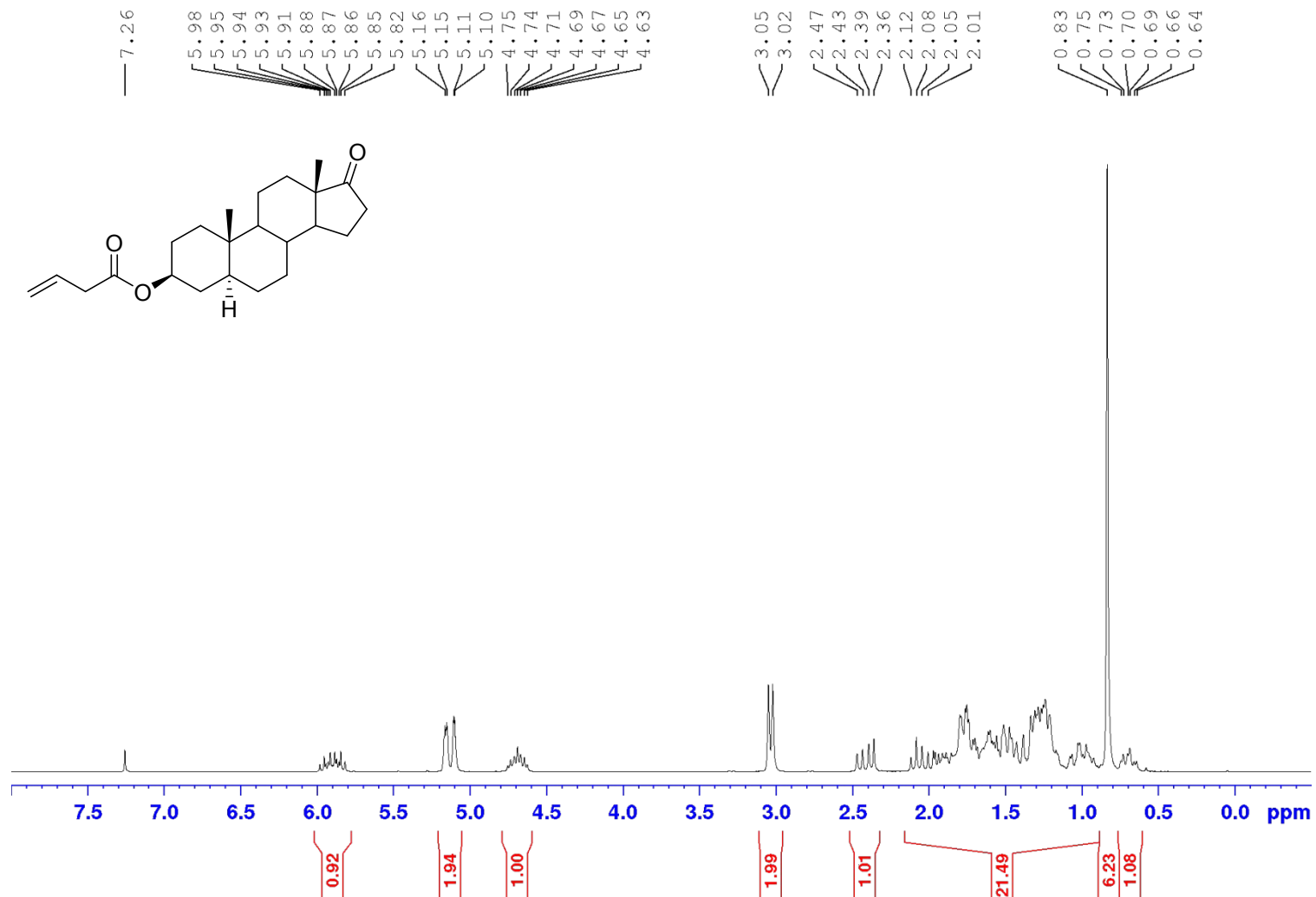


—221.1

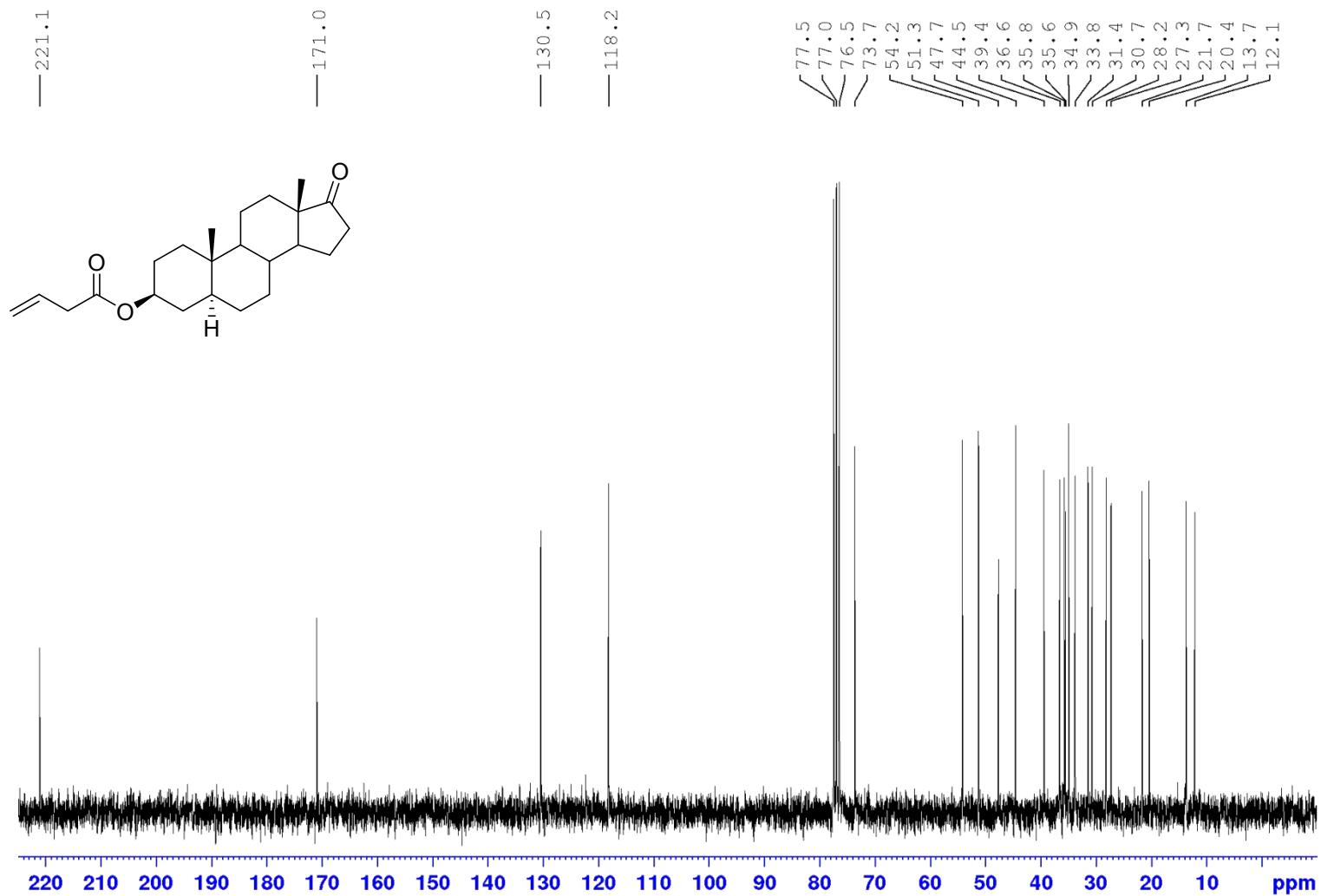
—170.6

77.5
77.0
76.5
73.4
54.2
51.3
47.7
44.6
36.6
35.7
35.6
34.9
33.9
31.4
30.7
28.2
27.3
21.7
21.3
20.4
13.7
12.1

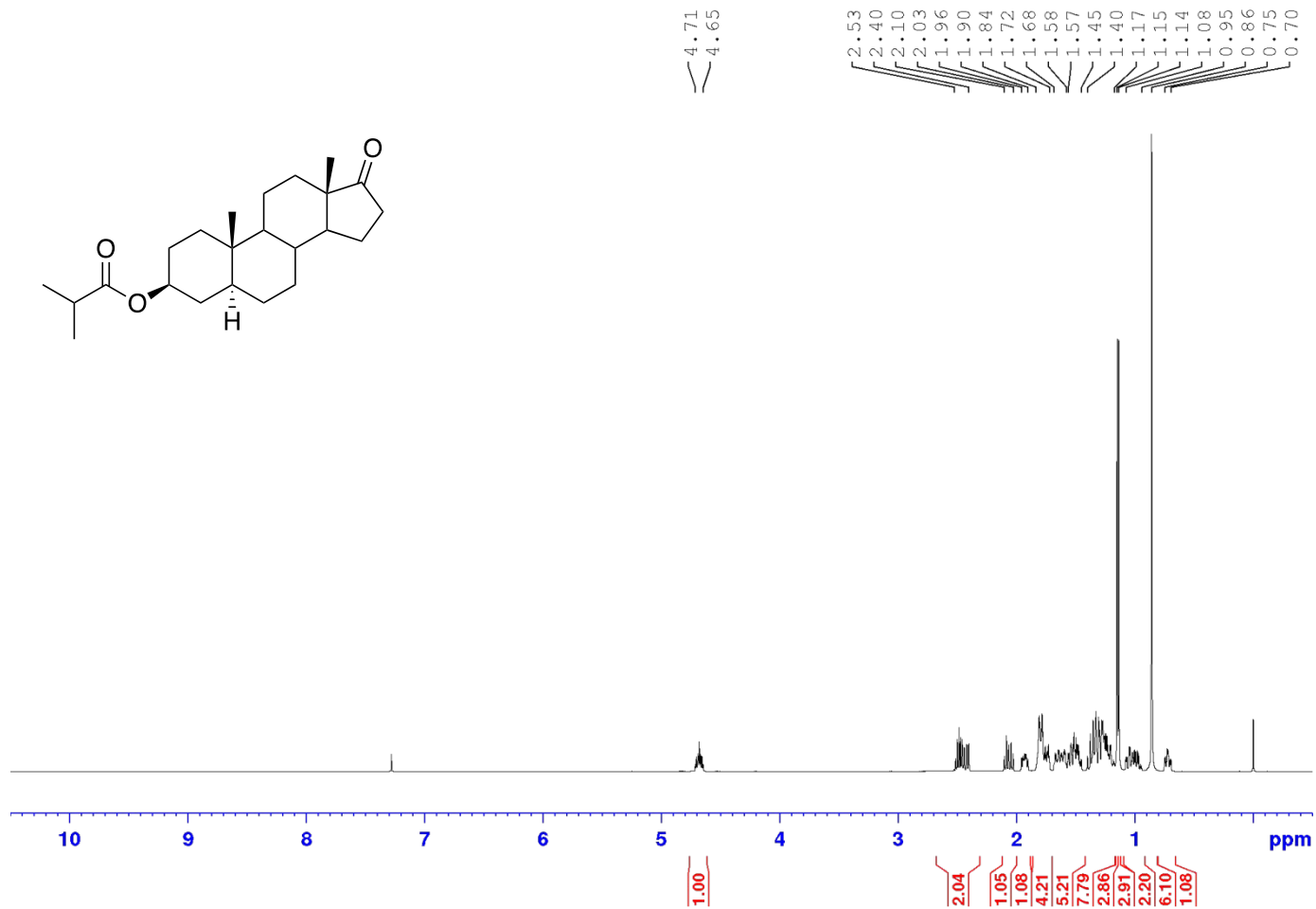
Epiandrosterone but-3-enoate (9) – ¹H – CDCl₃ – 250 MHz



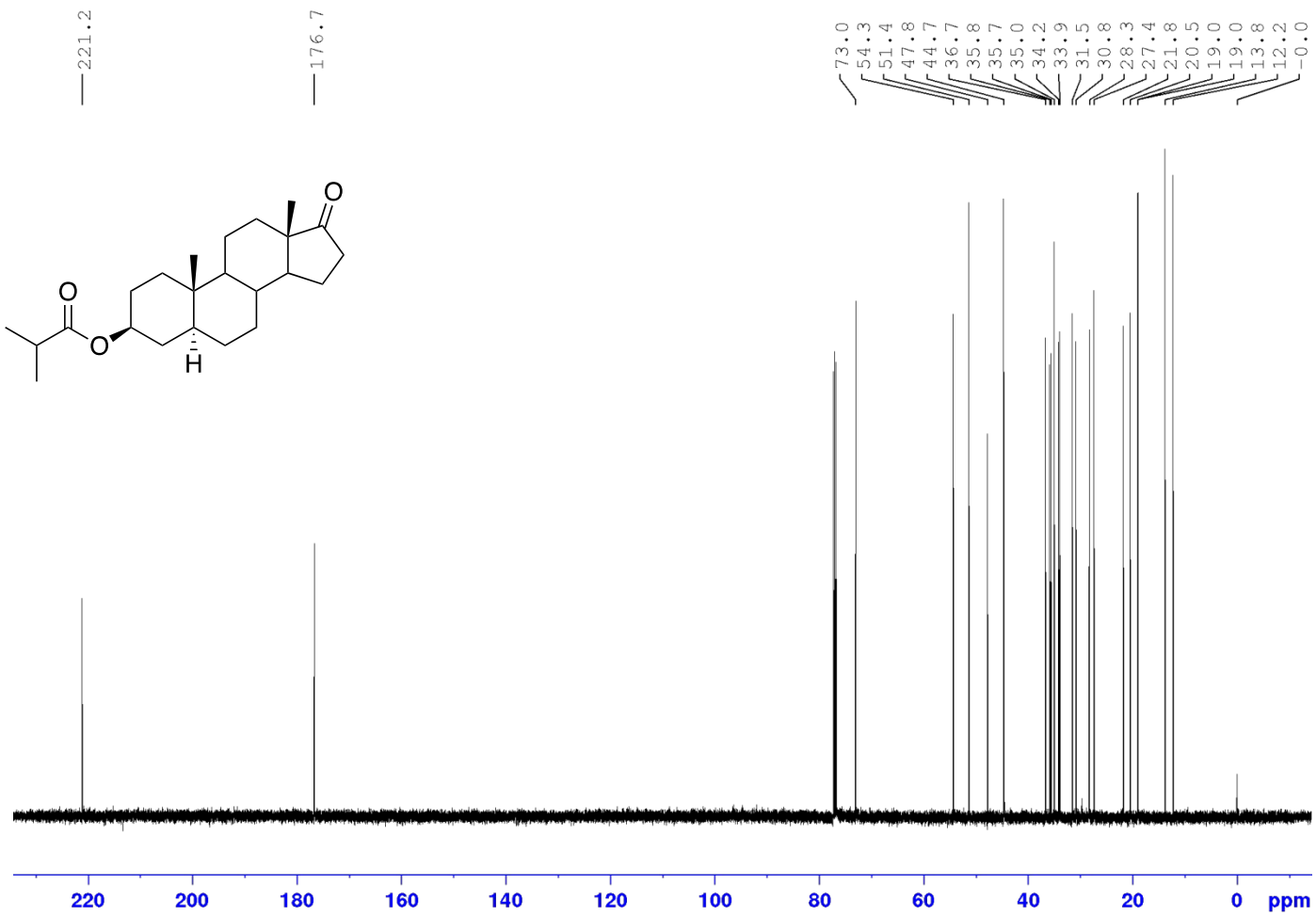
Epiandrosterone but-3-enoate (9) – ^{13}C – CDCl_3 – 62.5 MHz



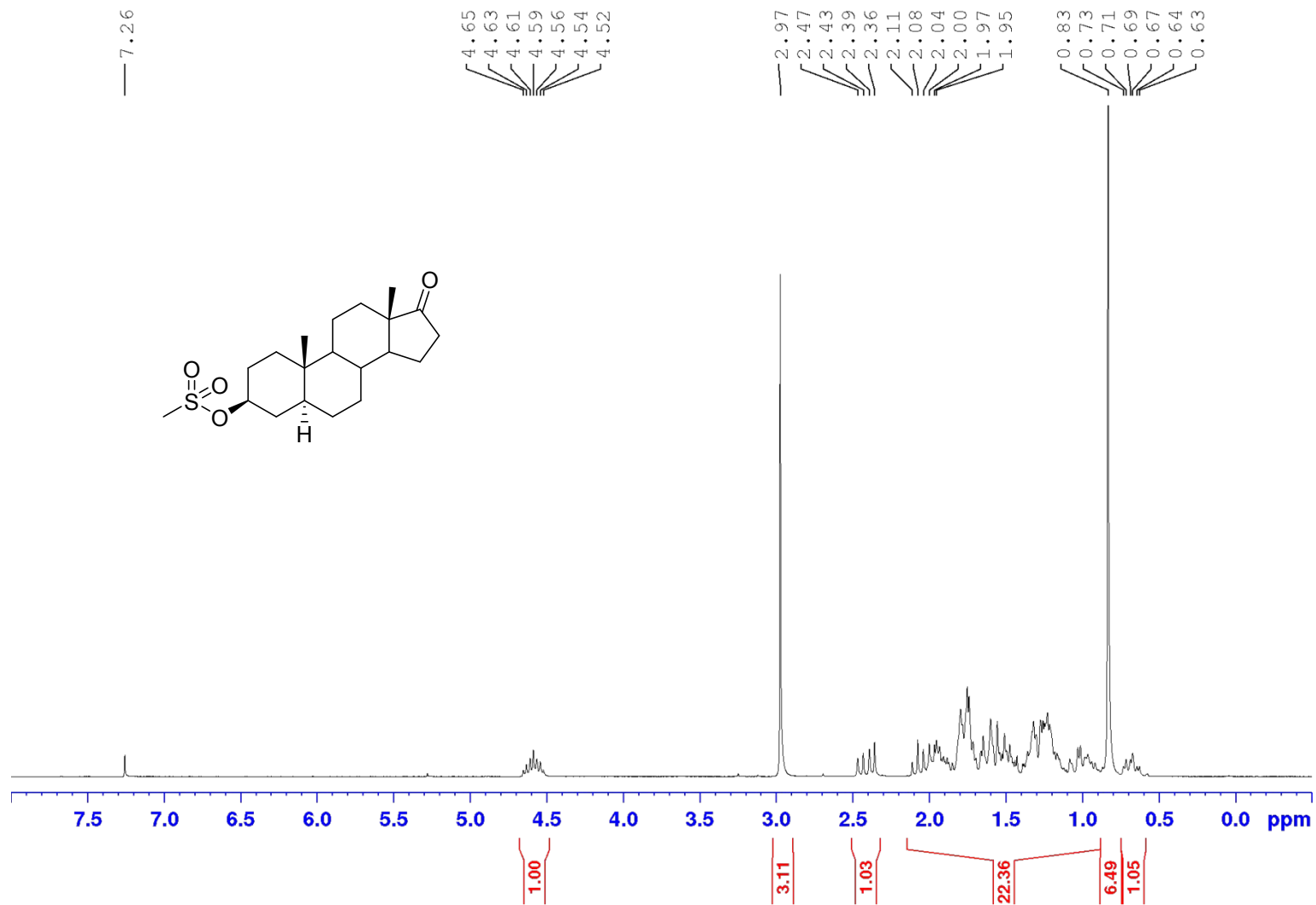
Epiandrosterone isobutyrate (10) – ^1H – CDCl_3 – 500 MHz



Epiandrosterone isobutyrate (10) – ^{13}C – CDCl_3 – 125 MHz



Epiandrosterone methanesulfonate (11) – ¹H – CDCl₃ – 250 MHz



— 7.26

4.65
4.63
4.61
4.59
4.56
4.54
4.52

2.97
2.47
2.43
2.39
2.36
2.11
2.08
2.04
2.00
1.97
1.95

0.83
0.73
0.71
0.69
0.67
0.64
0.63

1.00

3.11

1.03

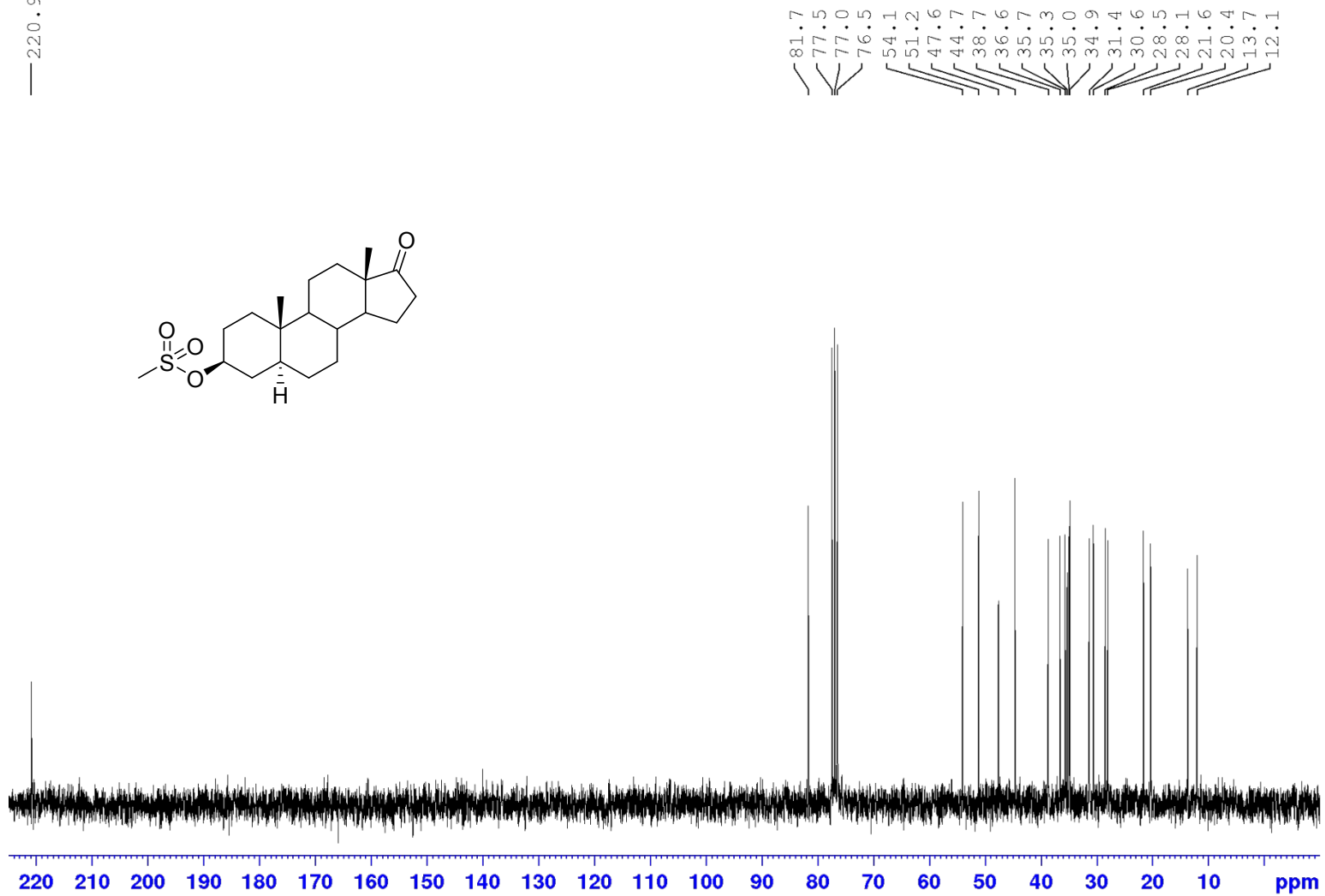
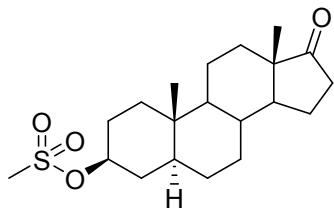
22.36

6.49

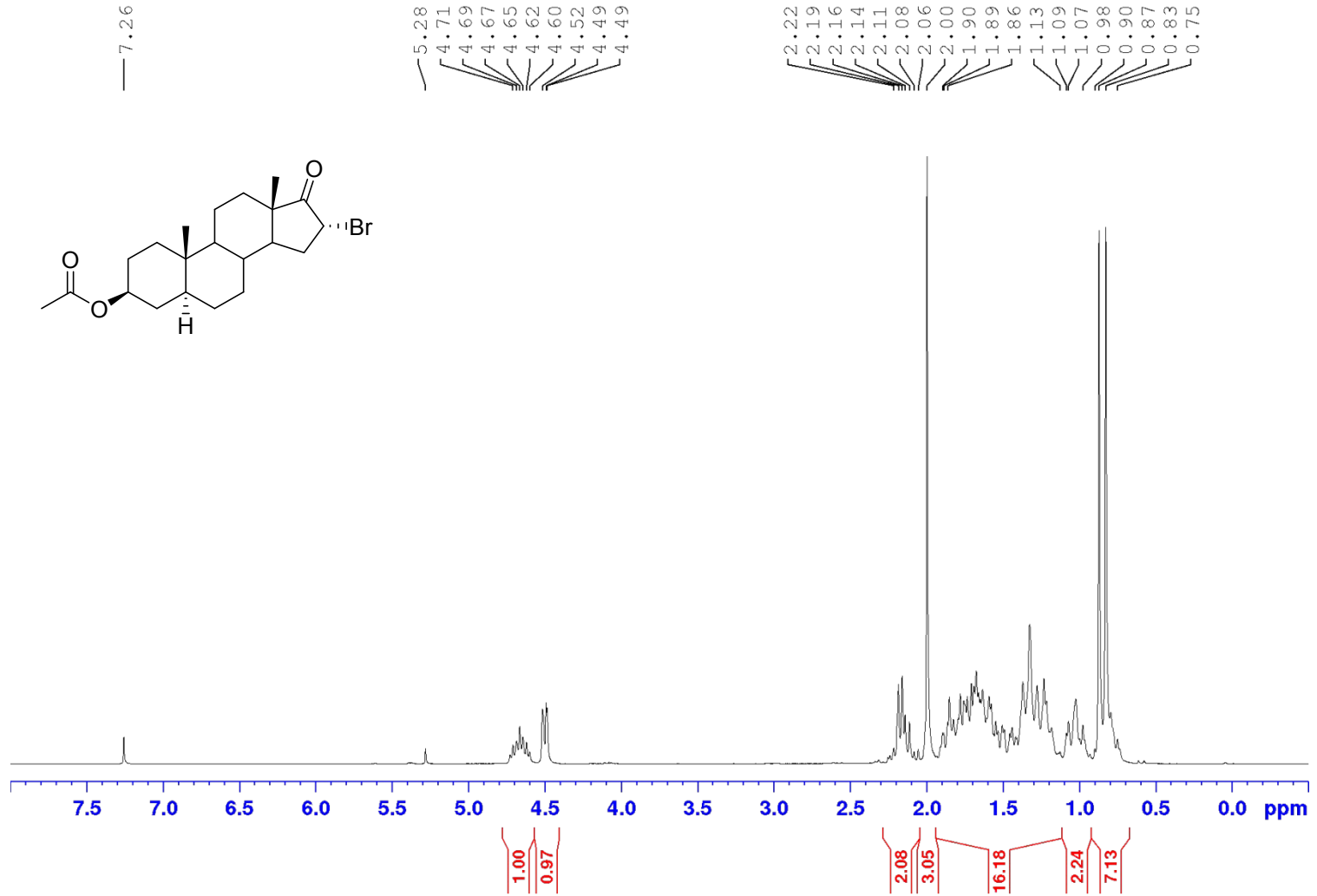
1.05

— 220.9

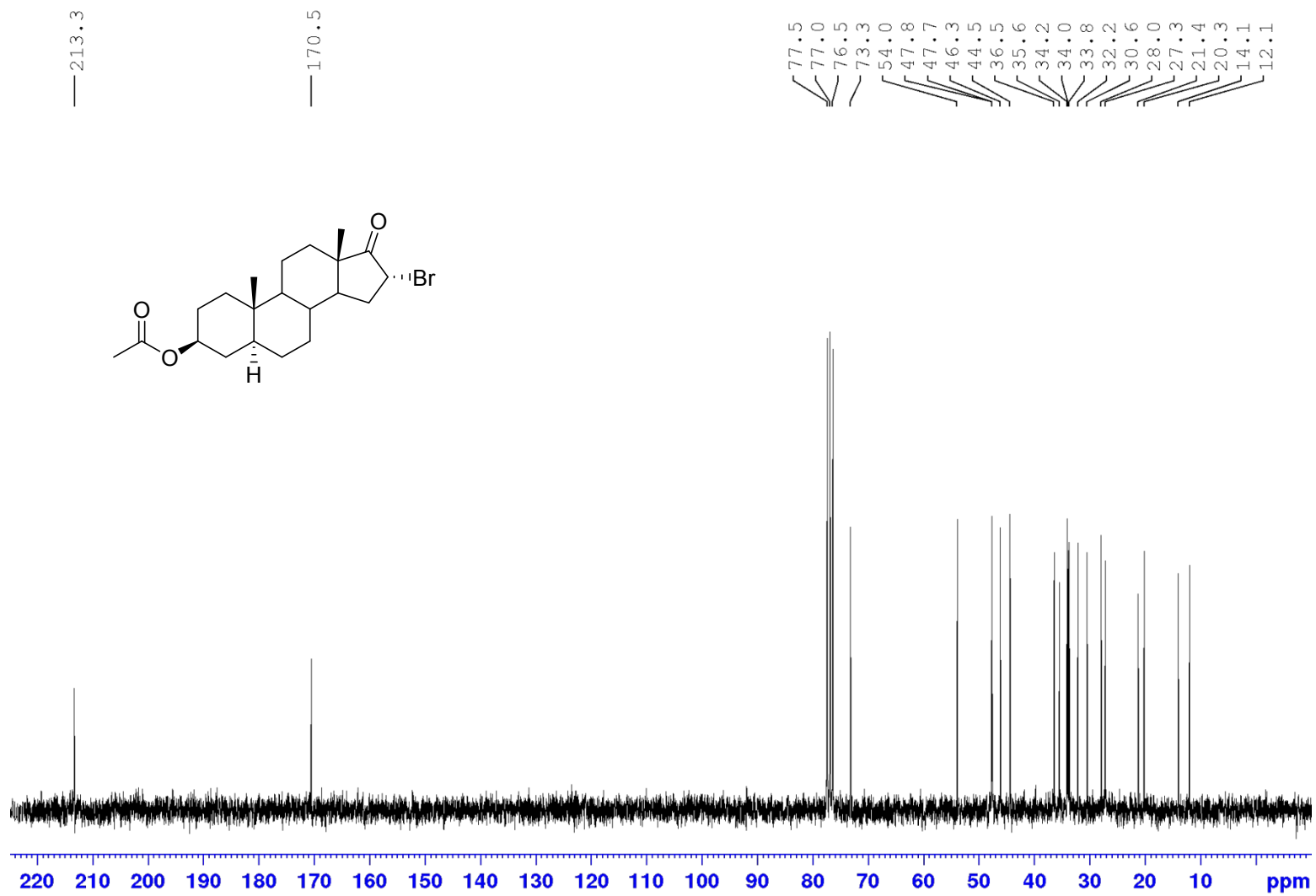
Epiandrosterone methanesulfonate (11) – ^{13}C – CDCl_3 – 62.5 MHz



16 α -Bromoepiandrosterone acetate (12) – ^1H – CDCl_3 – 250 MHz



16 α -Bromoepiandrosterone acetate (12) – ^{13}C – CDCl_3 – 62.5 MHz

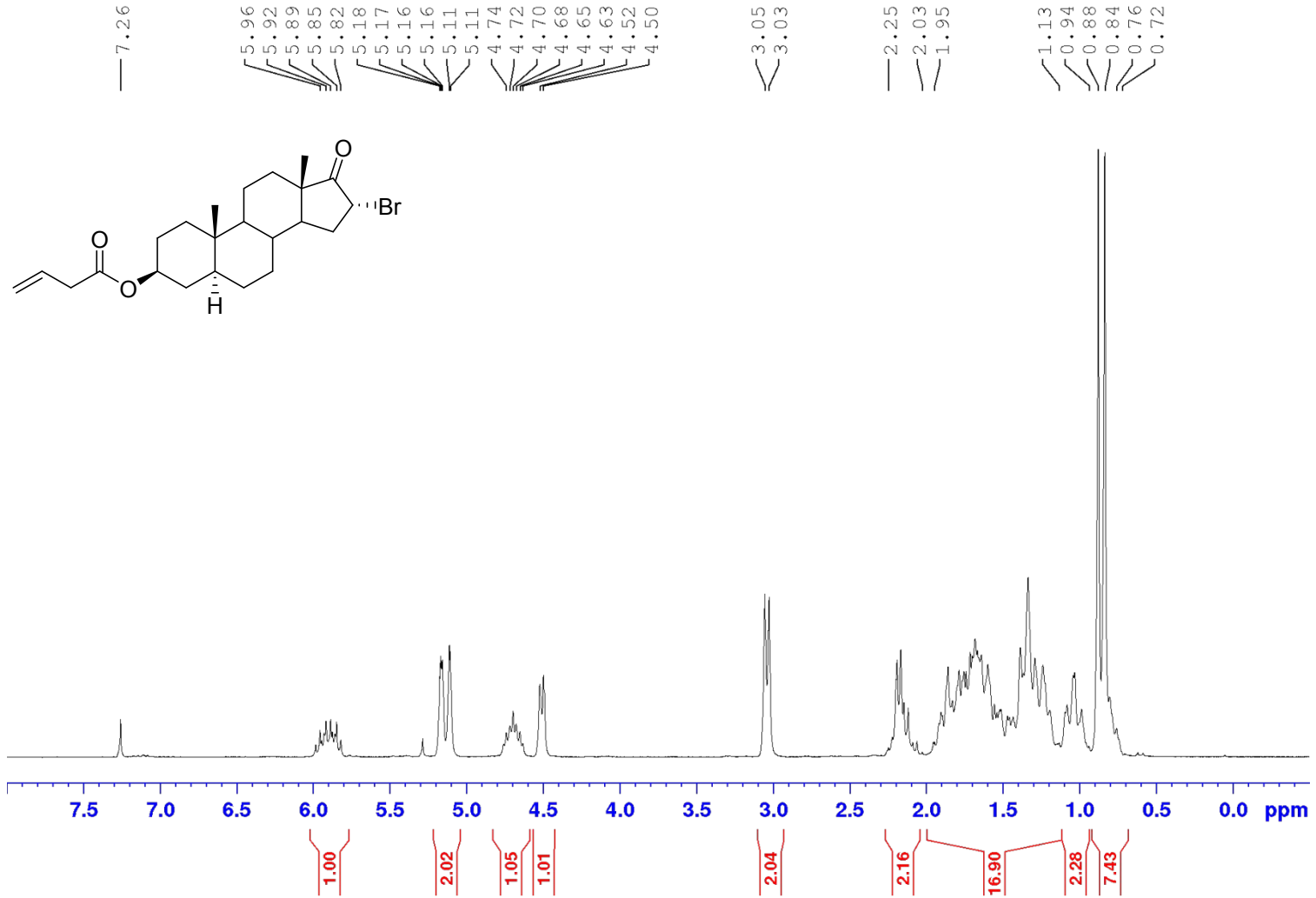


—213.3

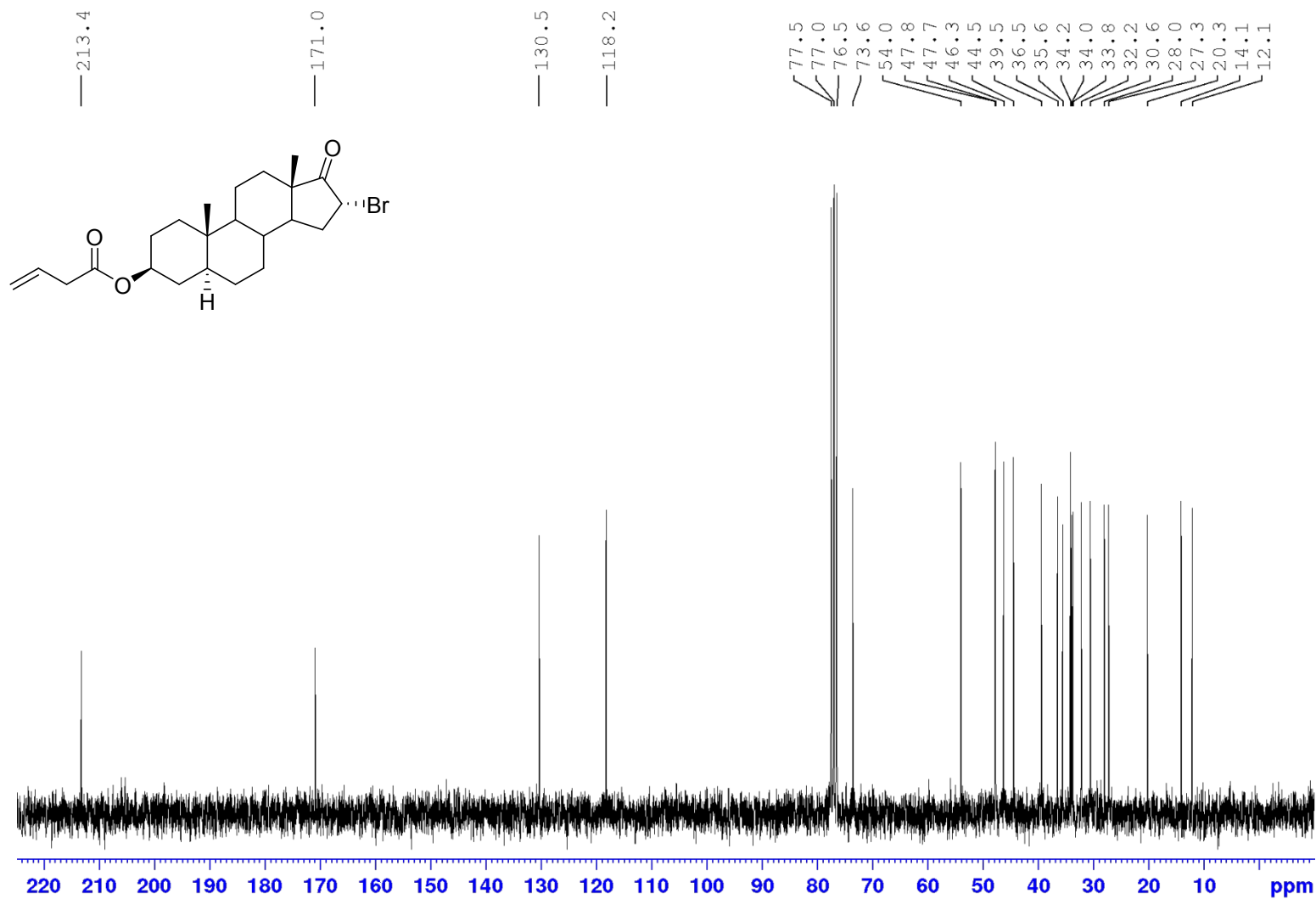
—170.5

77.5
77.0
76.5
73.3
54.0
47.8
47.7
46.3
44.5
36.5
35.6
34.2
34.0
33.8
32.2
30.6
28.0
27.3
21.4
20.3
14.1
12.1

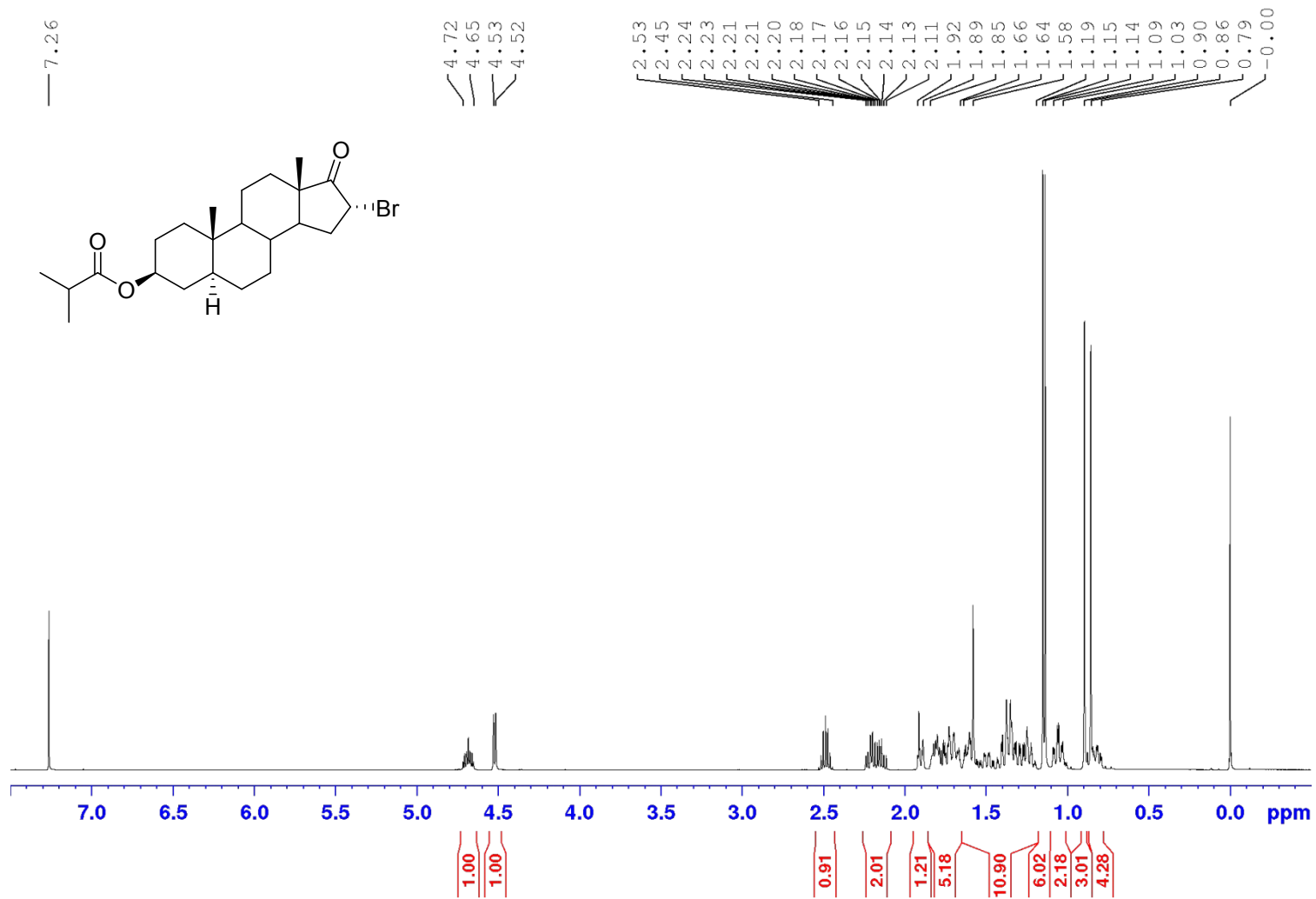
16 α -Bromoepiandrosterone but-3-enoate (13) – ^1H – CDCl_3 – 250 MHz



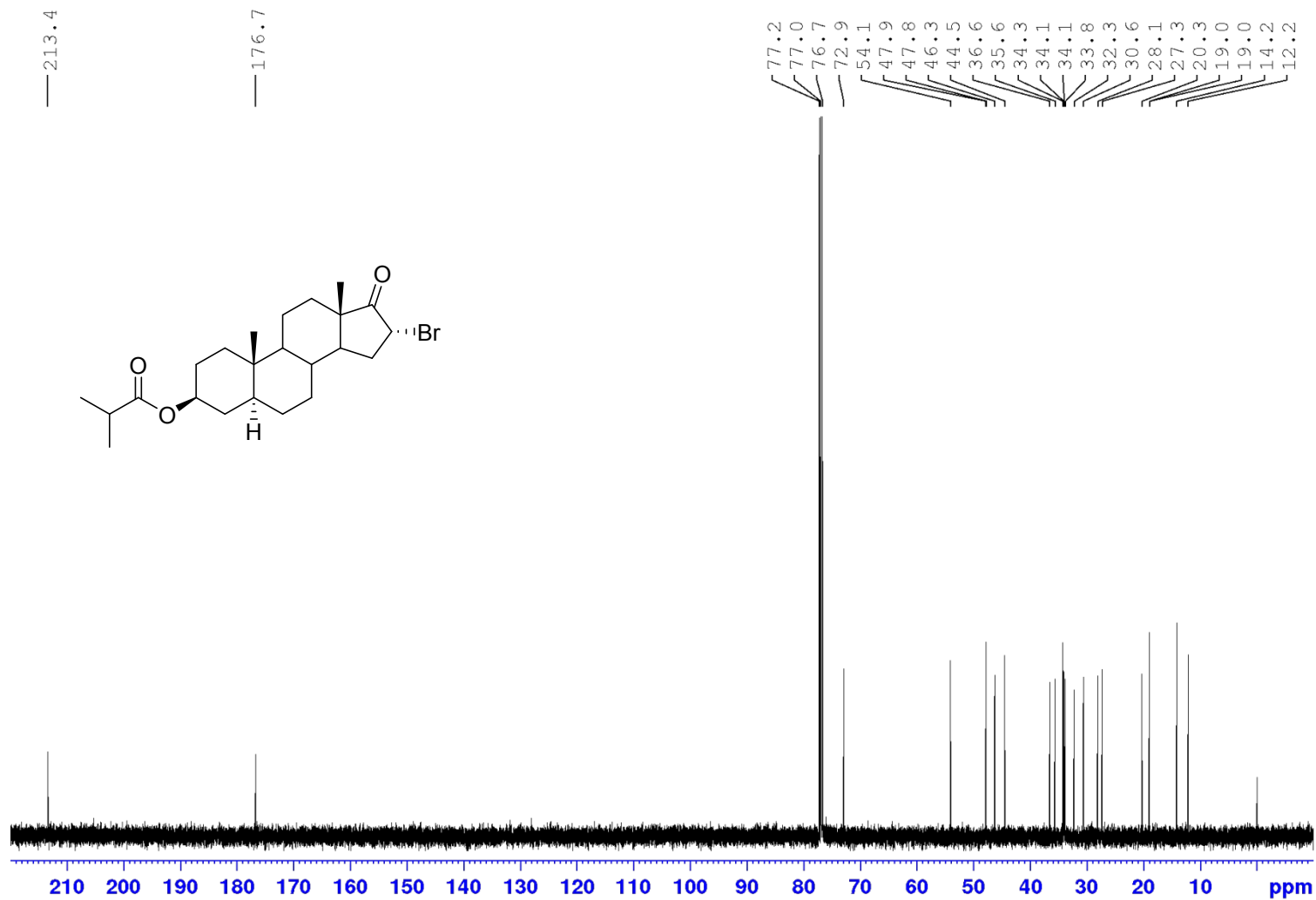
16 α -Bromoepiandrosterone but-3-enoate (13) – ^{13}C – CDCl_3 – 62.5 MHz



16 α -Bromoepiandrosterone isobutyrate (14) – ^1H – CDCl_3 – 500 MHz

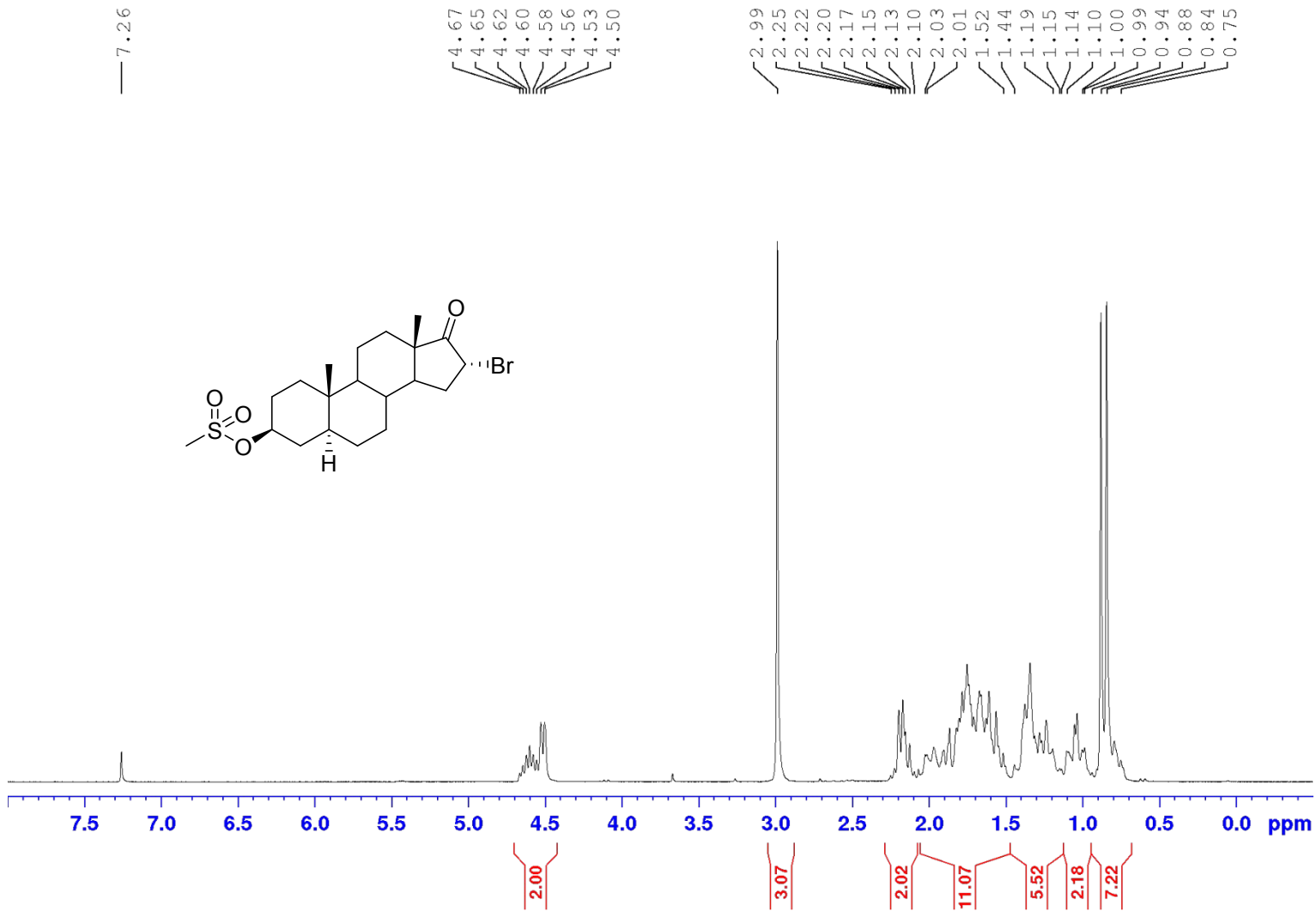
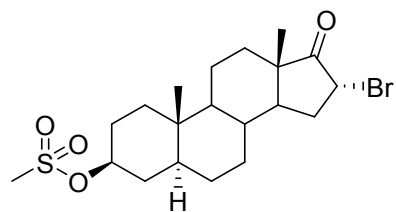


16 α -Bromoepiandrosterone isobutyrate (14) – ^{13}C – CDCl_3 – 125 MHz



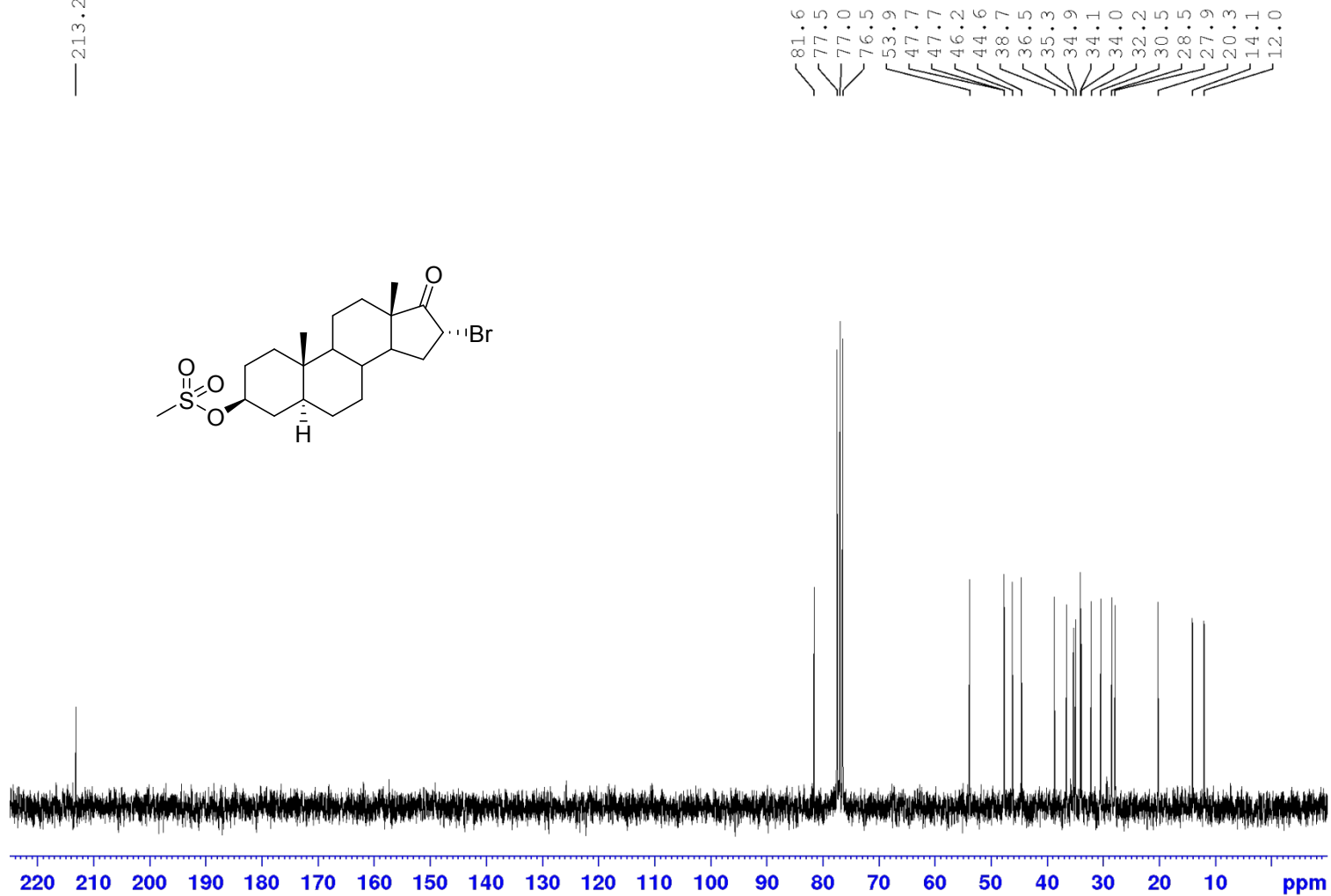
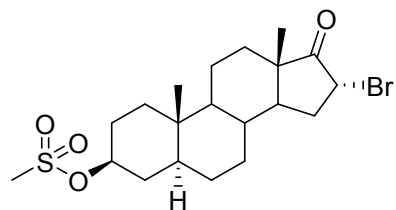
16 α -Bromoepiandrosterone methanesulfonate (15) – ^1H – CDCl_3 – 250 MHz

— 7.26

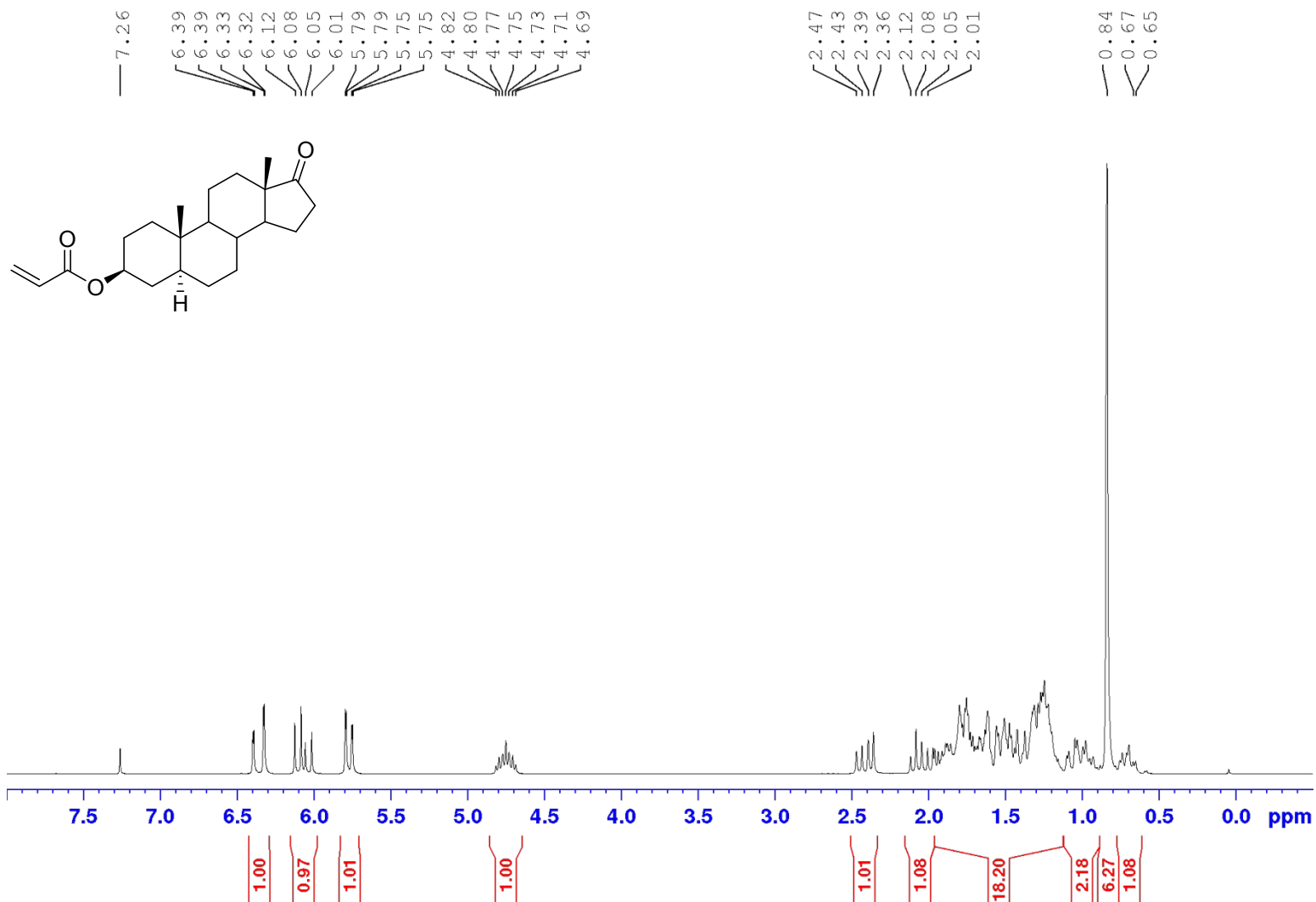


16 α -Bromoepiandrosterone methanesulfonate (15) – ^{13}C – CDCl_3 – 62.5 MHz

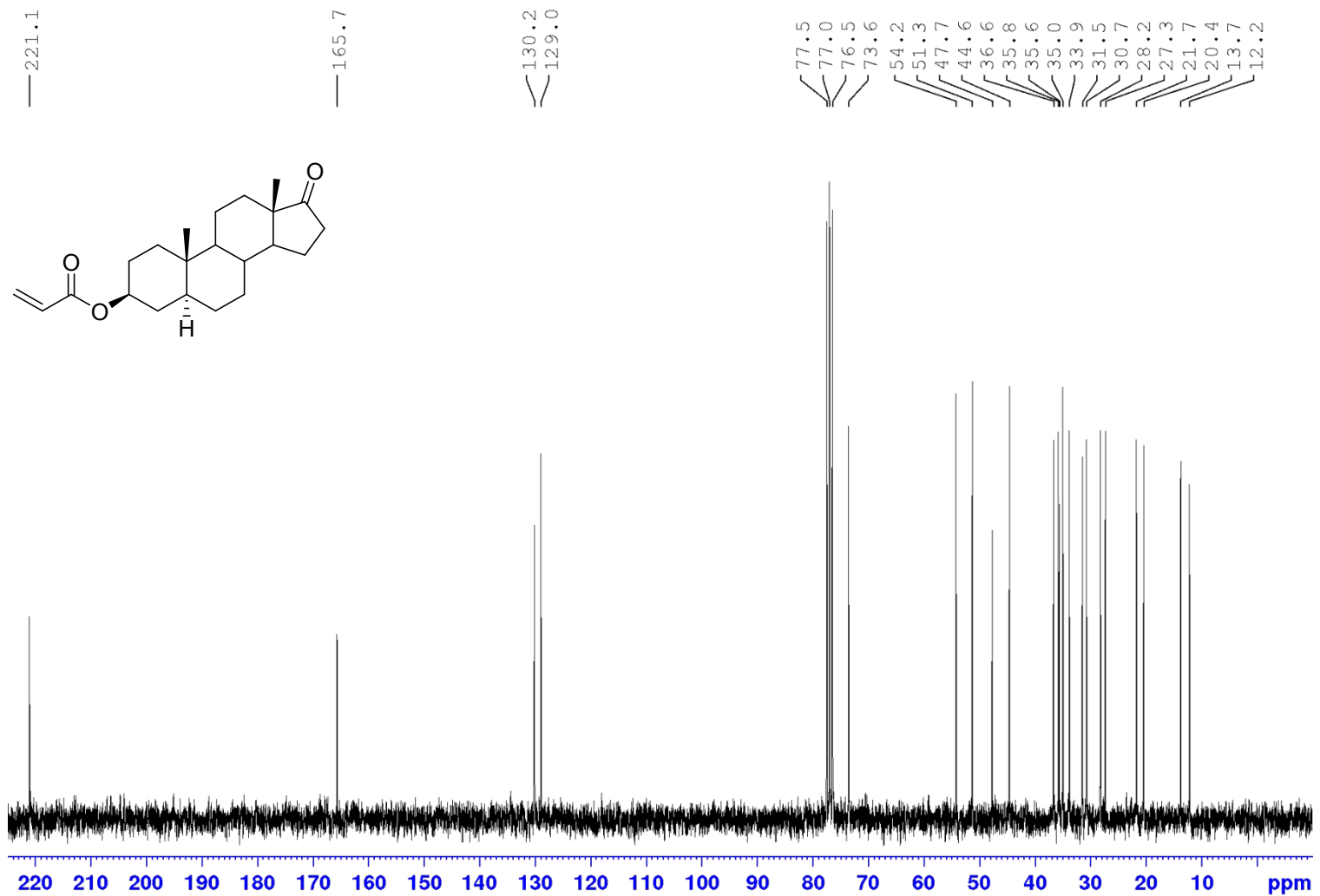
— 213.2



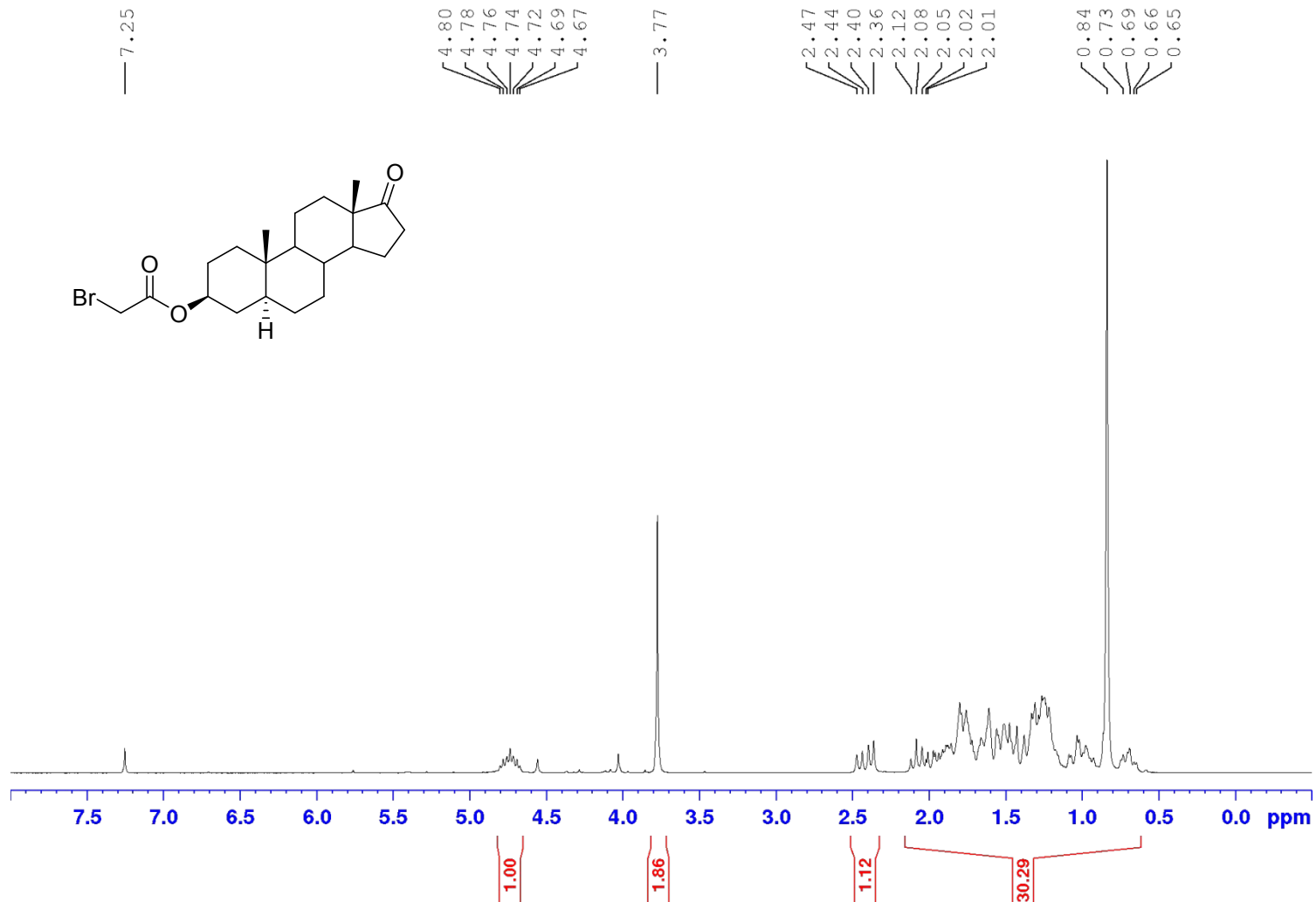
Epiandrosterone acrylate (16) – ^1H – CDCl_3 – 250 MHz



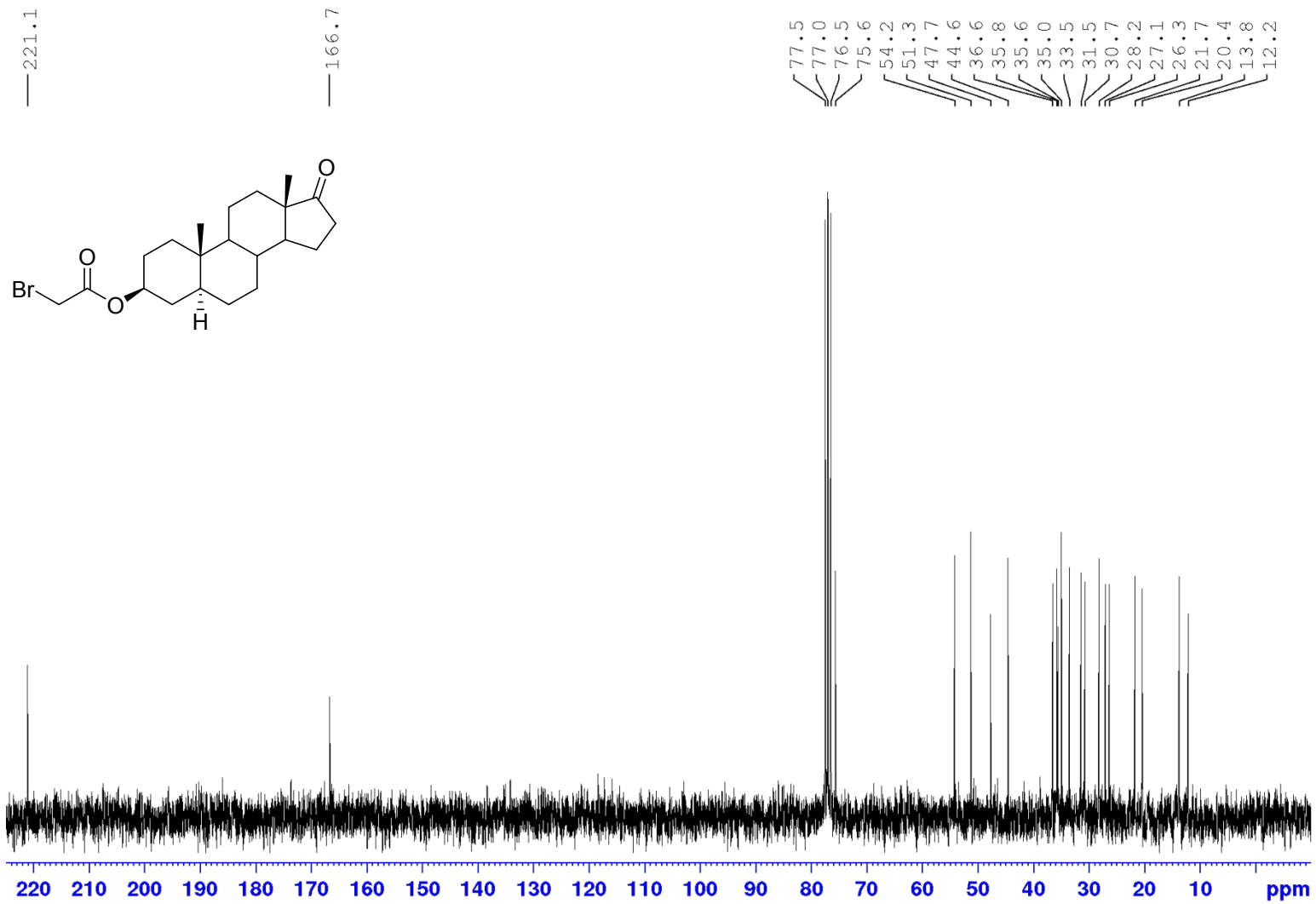
Epiandrosterone acrylate (16) – ^{13}C – CDCl_3 – 62.5 MHz



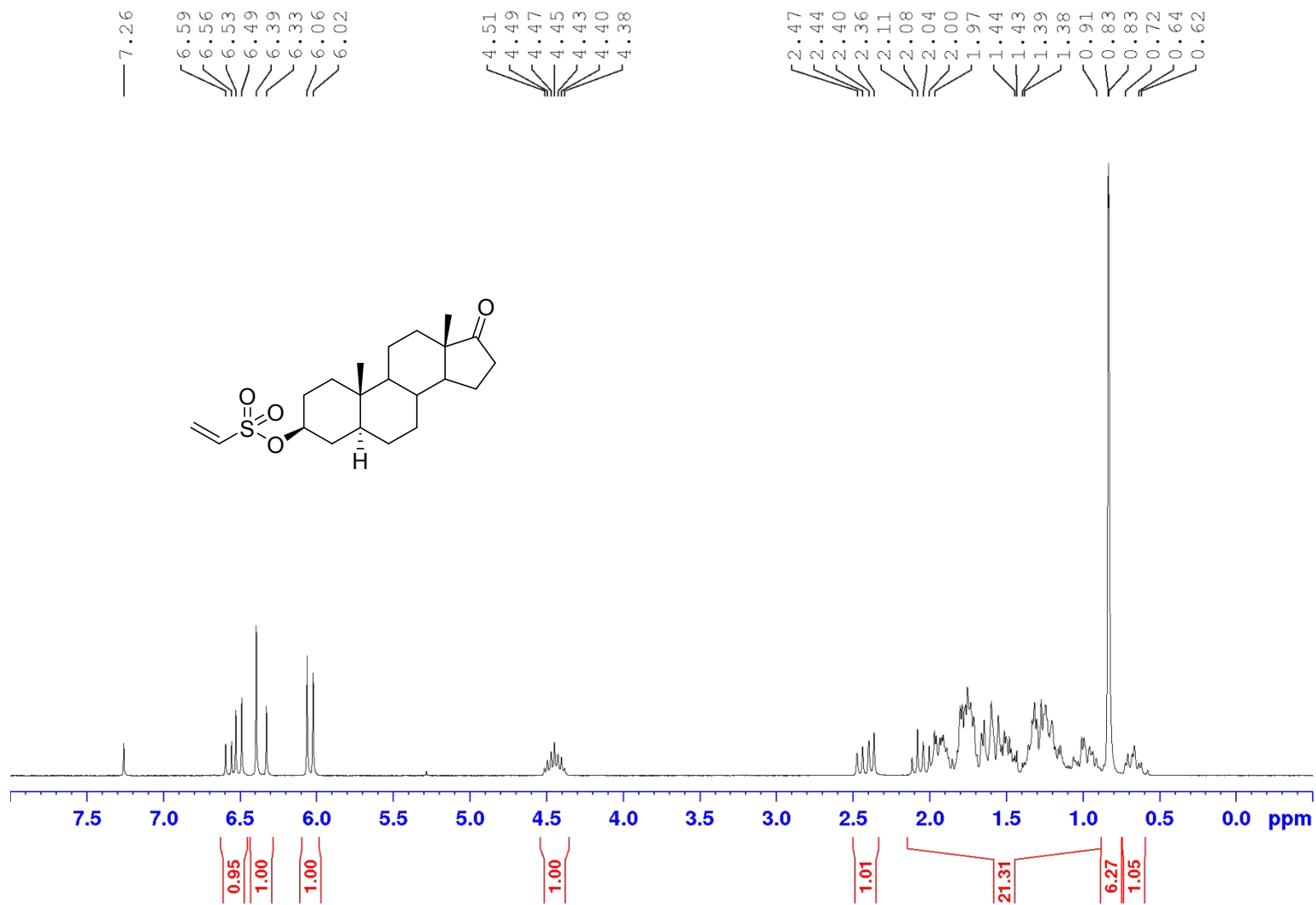
Epiandrosterone α -bromoacetate (17) – ^1H – CDCl_3 – 250 MHz



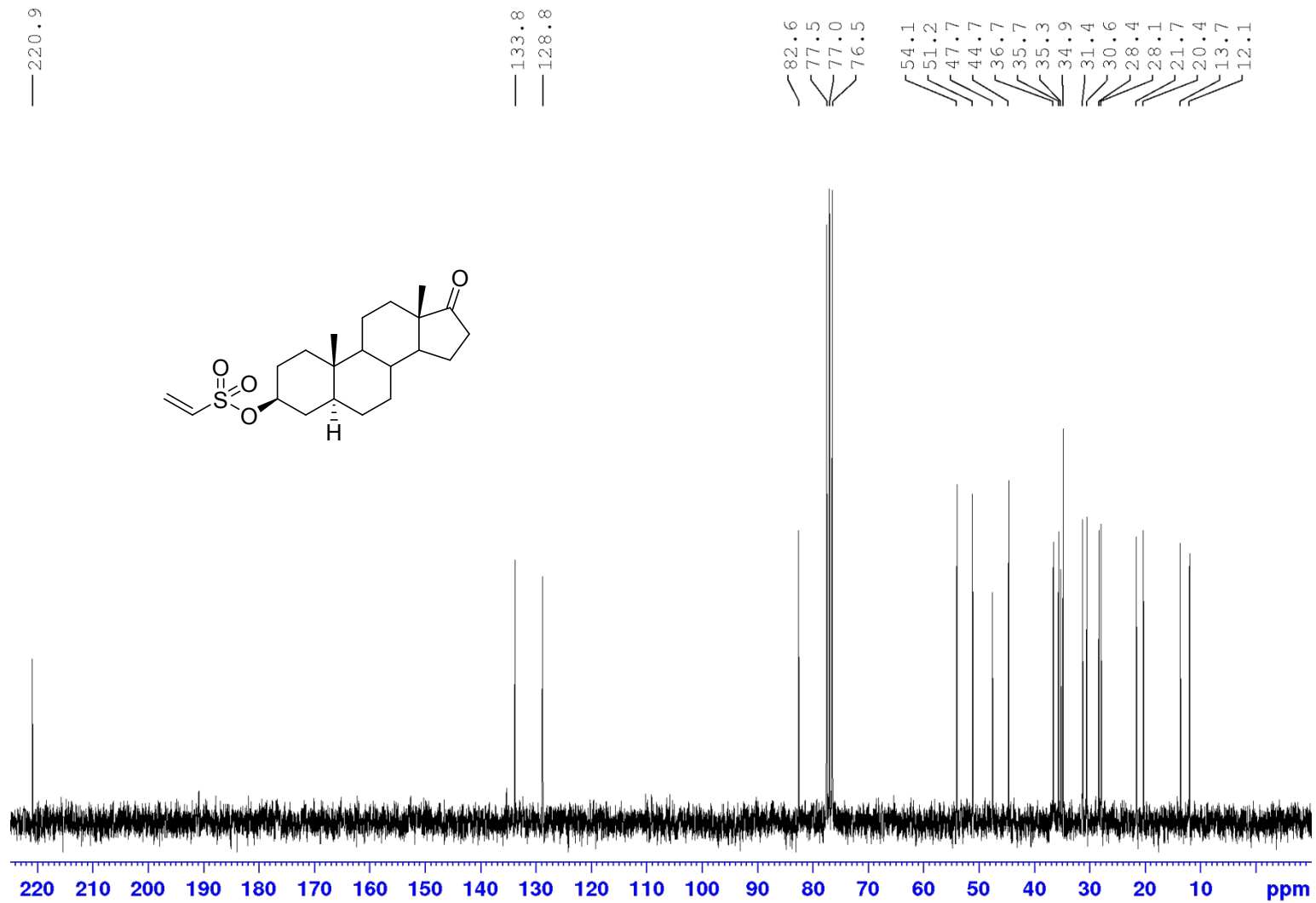
Epiandrosterone α -bromoacetate (17) – ^{13}C – CDCl_3 – 62.5 MHz



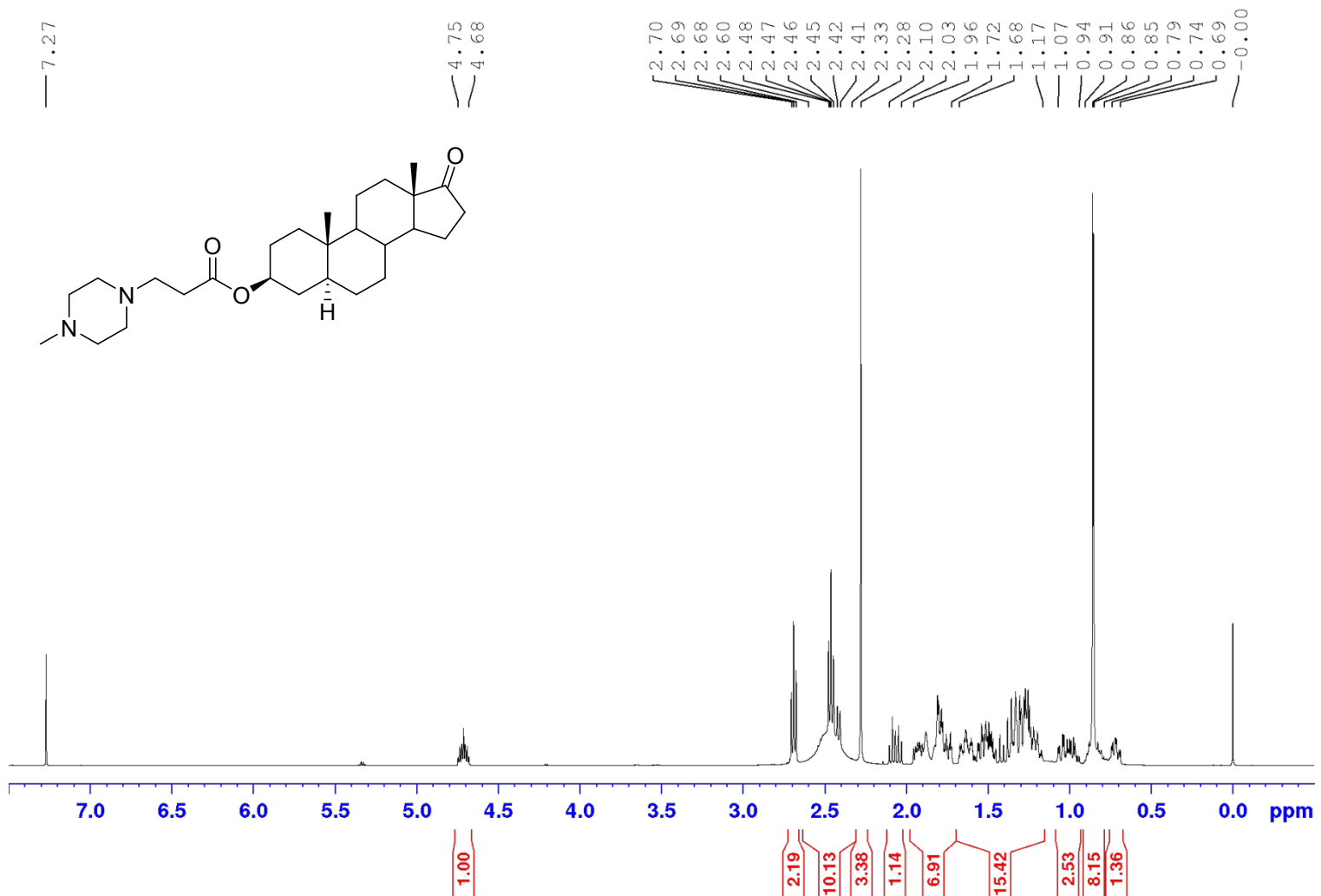
Epiandrosterone vinylsulfonate (18) – ^1H – CDCl_3 – 250 MHz



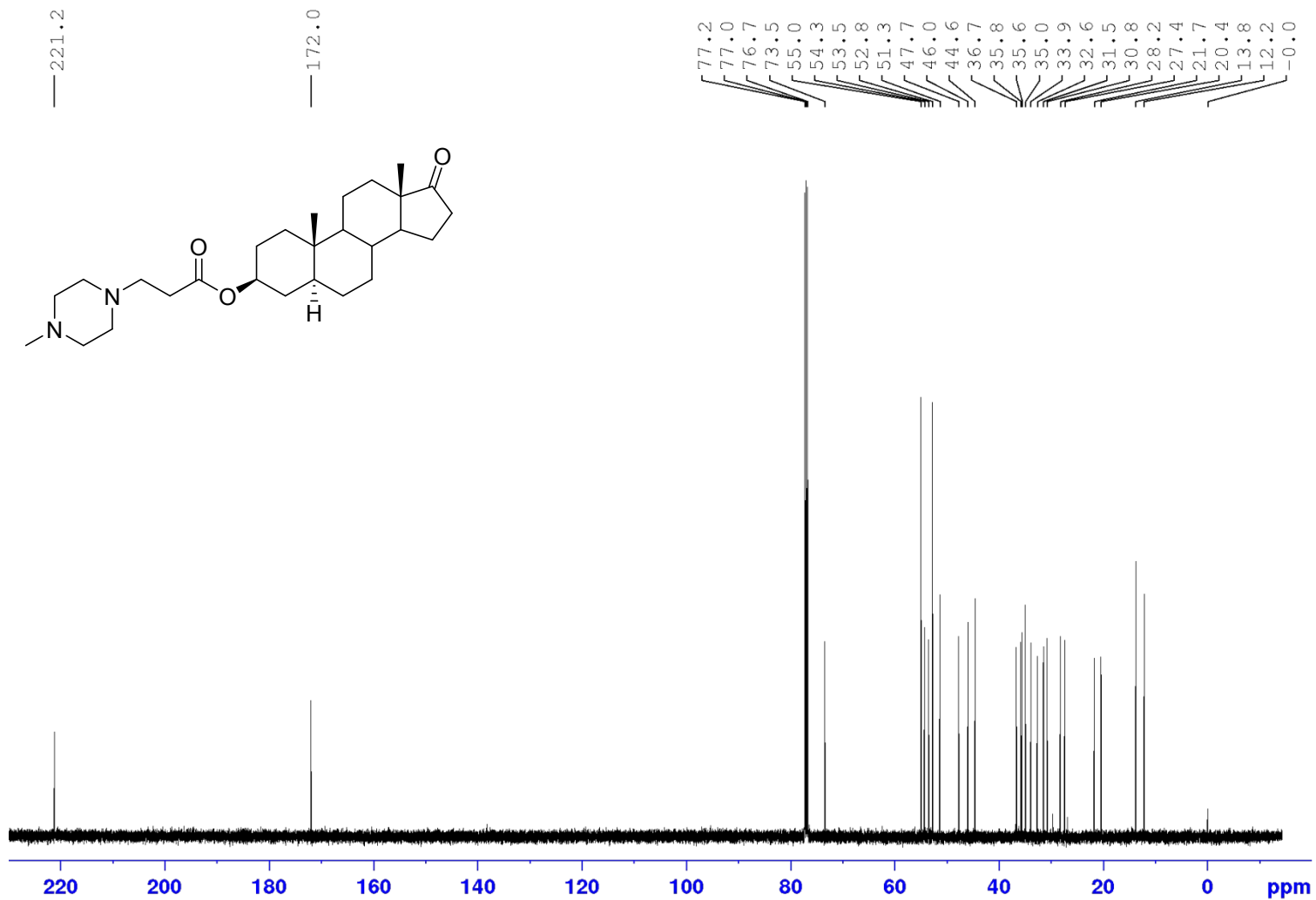
Epiandrosterone vinylsulfonate (18) – ^{13}C – CDCl_3 – 62.5 MHz



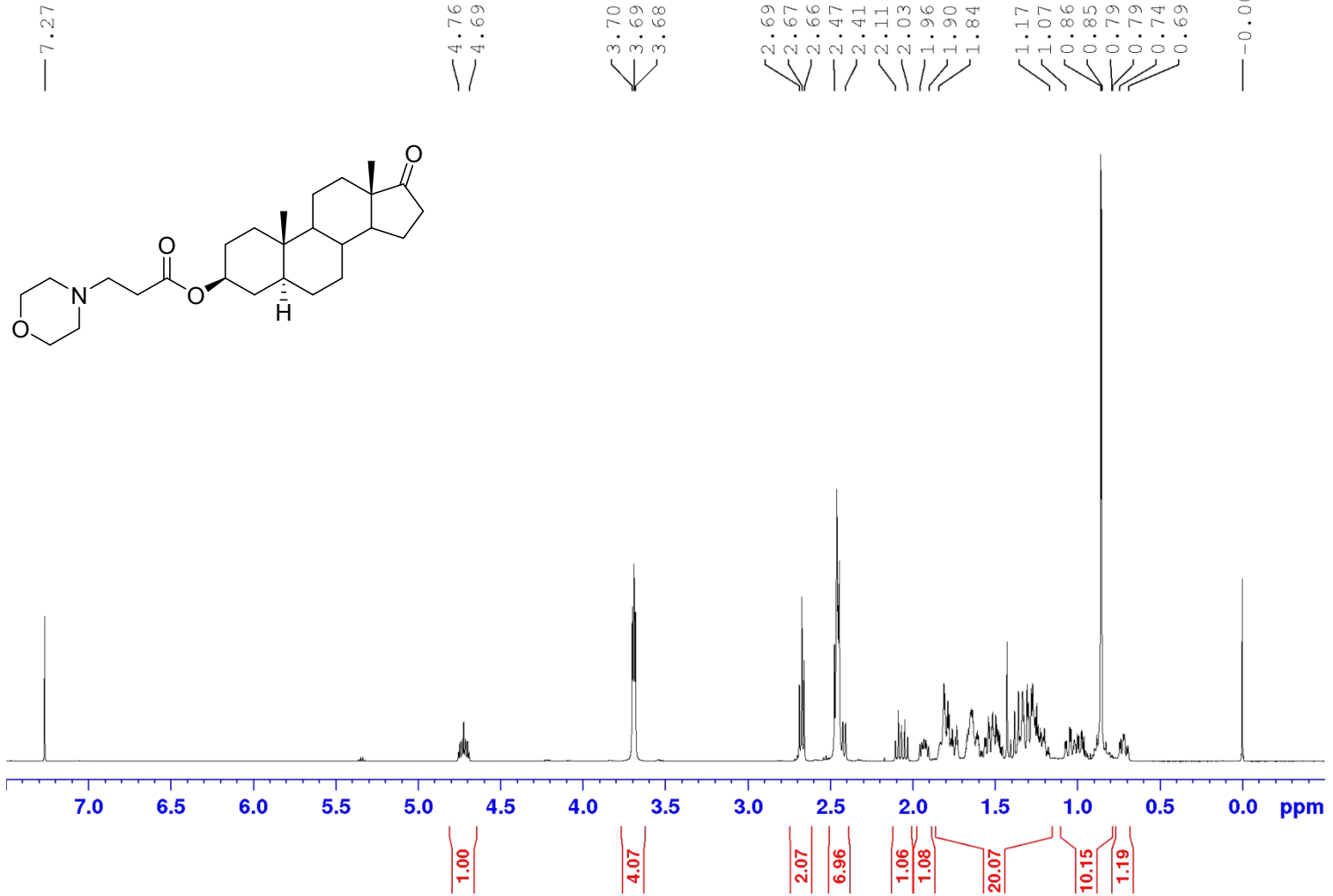
Epiandrosterone 3-(4-methylpiperazin-1-yl)propanoate (19) – ^1H – CDCl_3 – 500 MHz



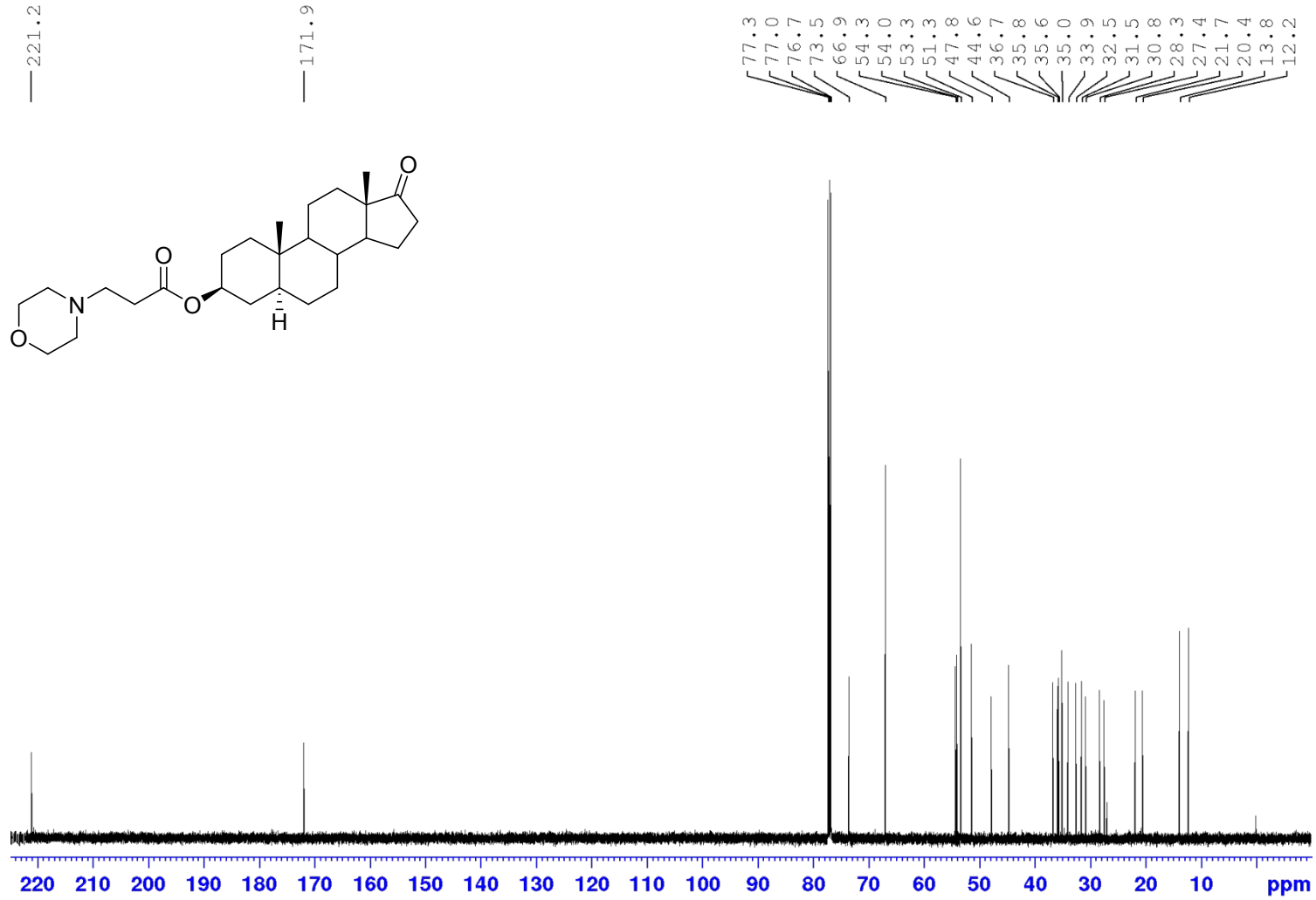
Epiandrosterone 3-(4-methylpiperazin-1-yl)propanoate (19) – ^{13}C – CDCl_3 – 125 MHz



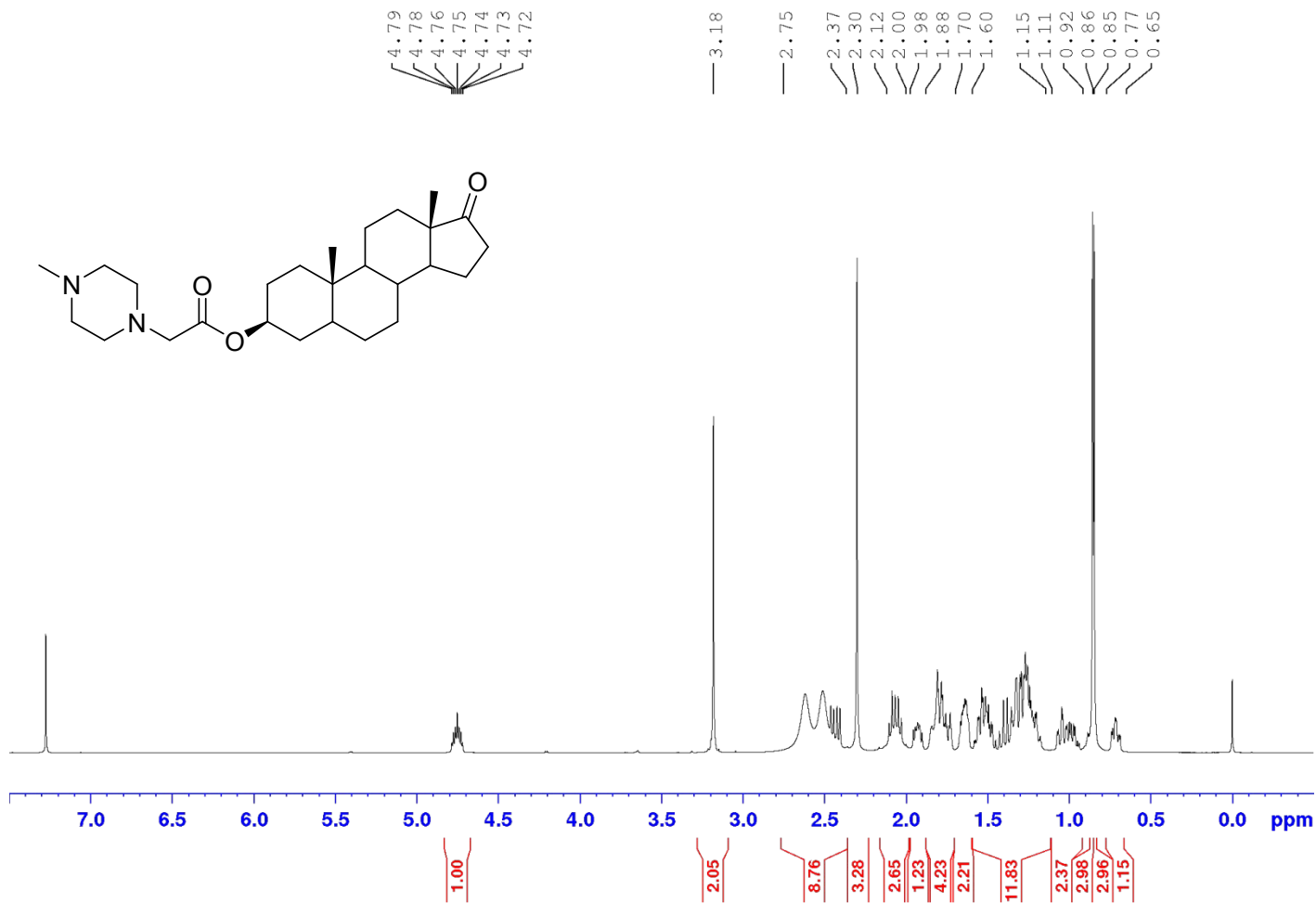
Epiandrosterone 3-morpholinopropanoate (20) – ^1H – CDCl_3 – 500 MHz



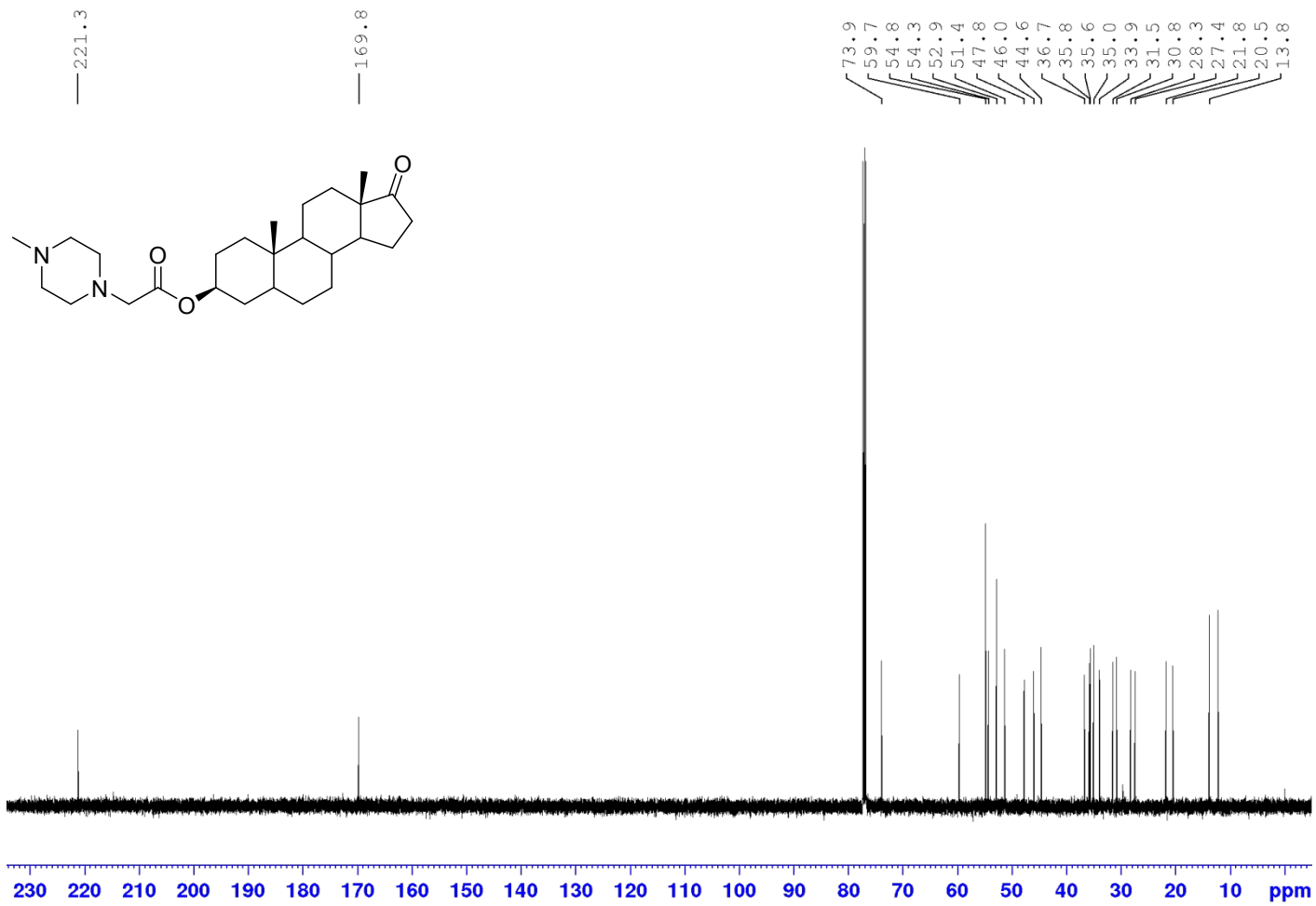
Epiandrosterone 3-morpholinopropanoate (20) – ^{13}C – CDCl_3 – 125 MHz



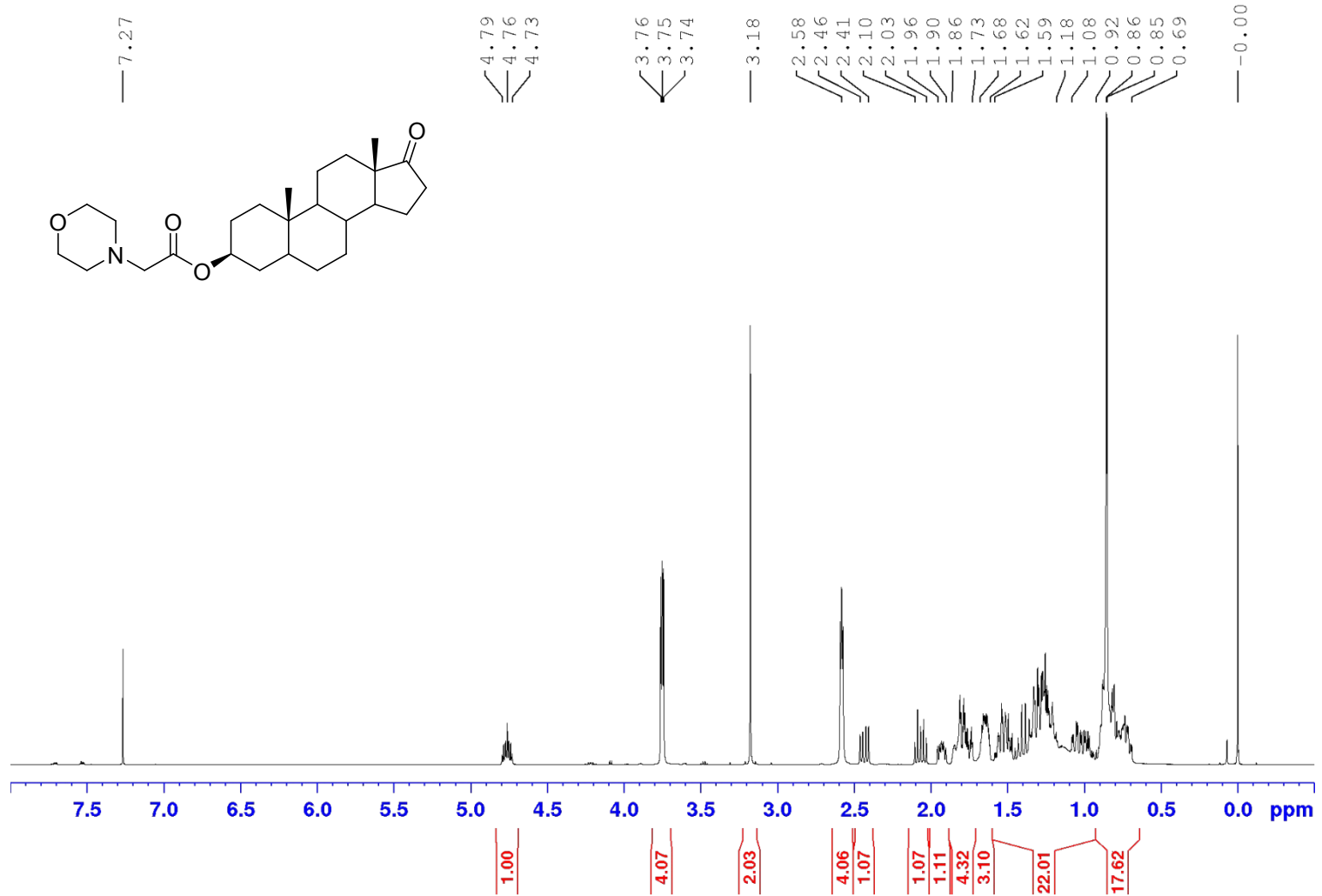
Epiandrosterone 2-(4-methylpiperazin-1-yl)acetate (21) – ^1H – CDCl_3 – 500 MHz



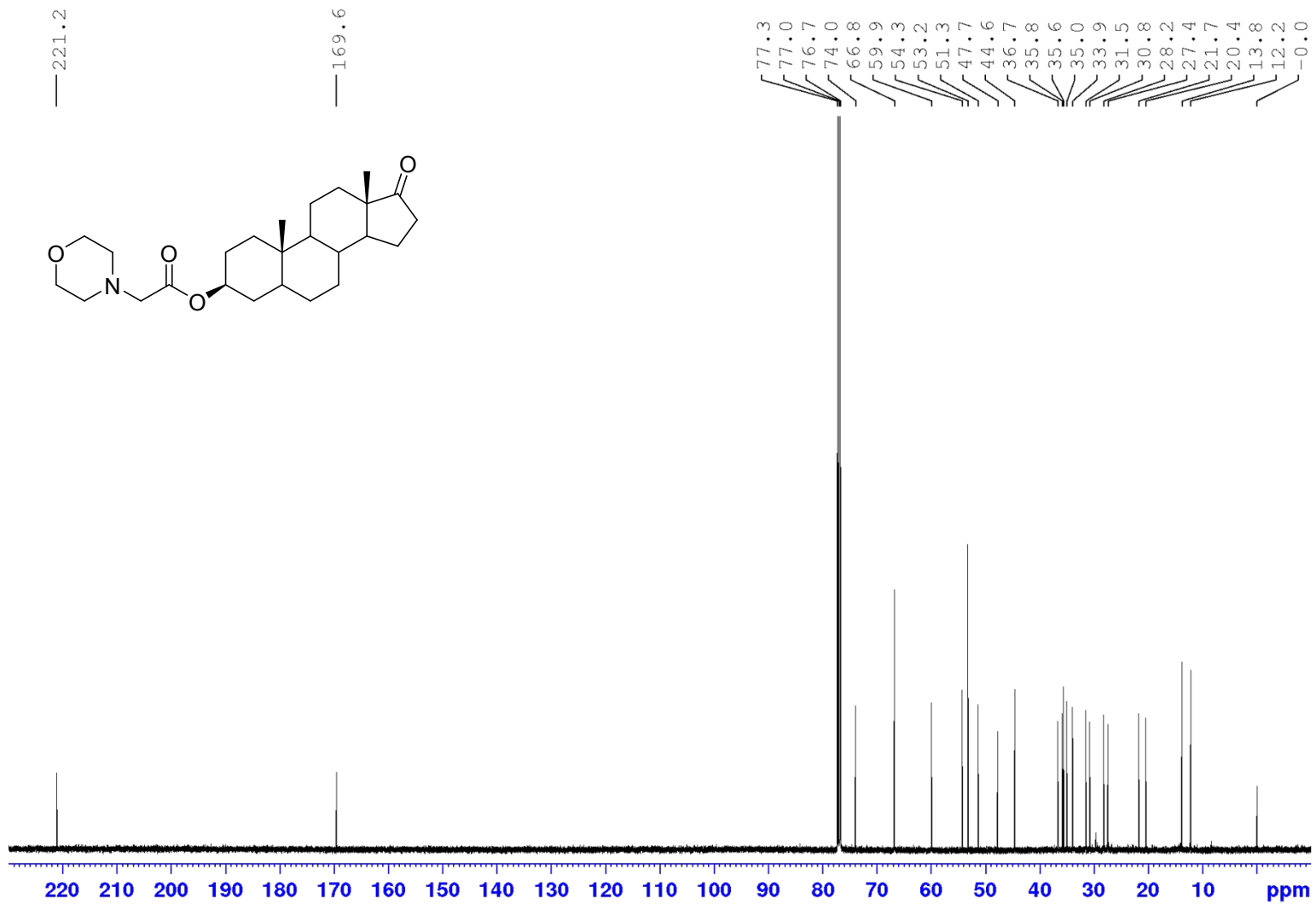
Epiandrosterone 2-(4-methylpiperazin-1-yl)acetate (21) – ^{13}C – CDCl_3 – 125 MHz



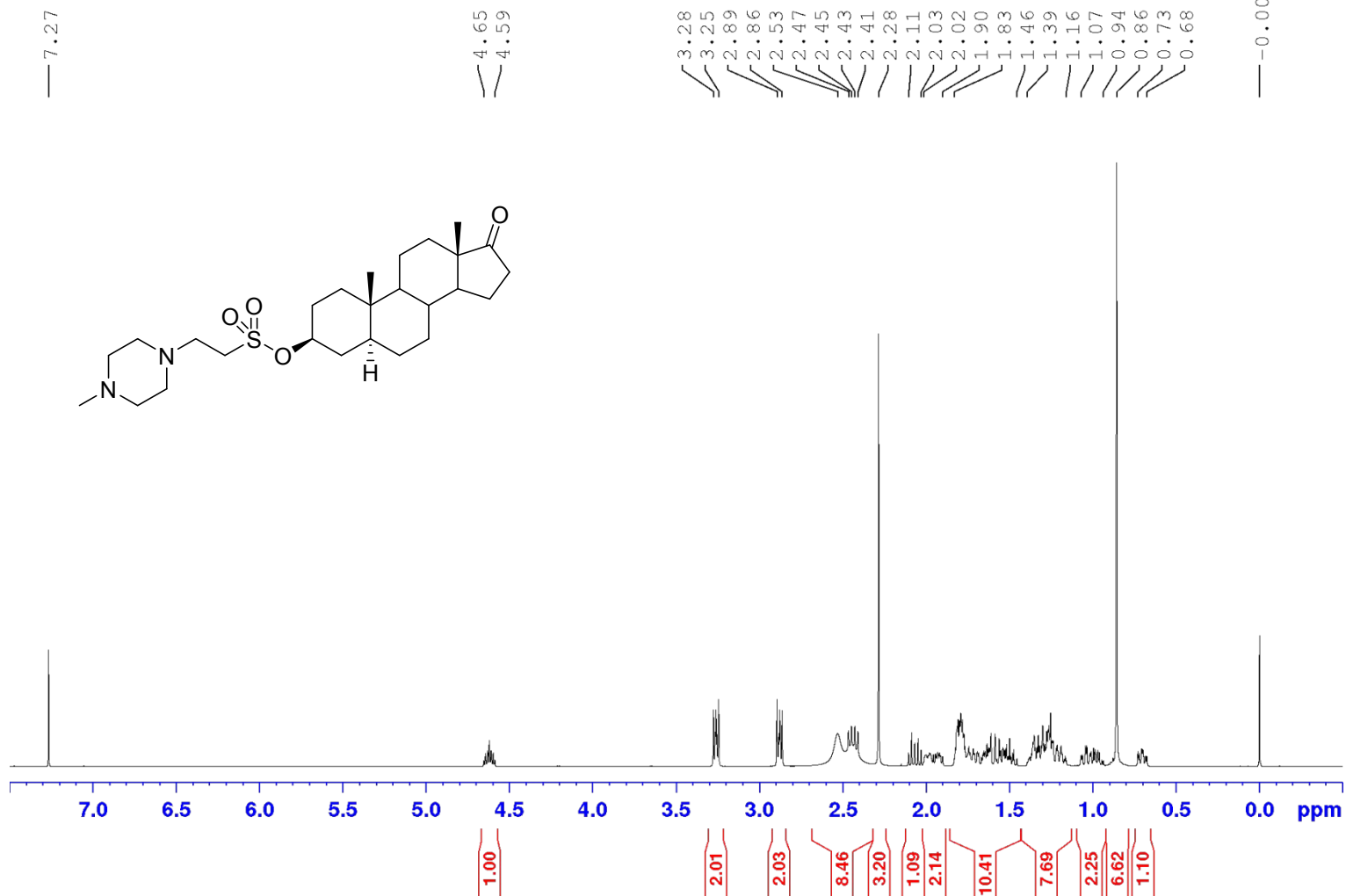
Epiandrosterone 2-morpholinoacetate (22) – ^1H – CDCl_3 – 500 MHz



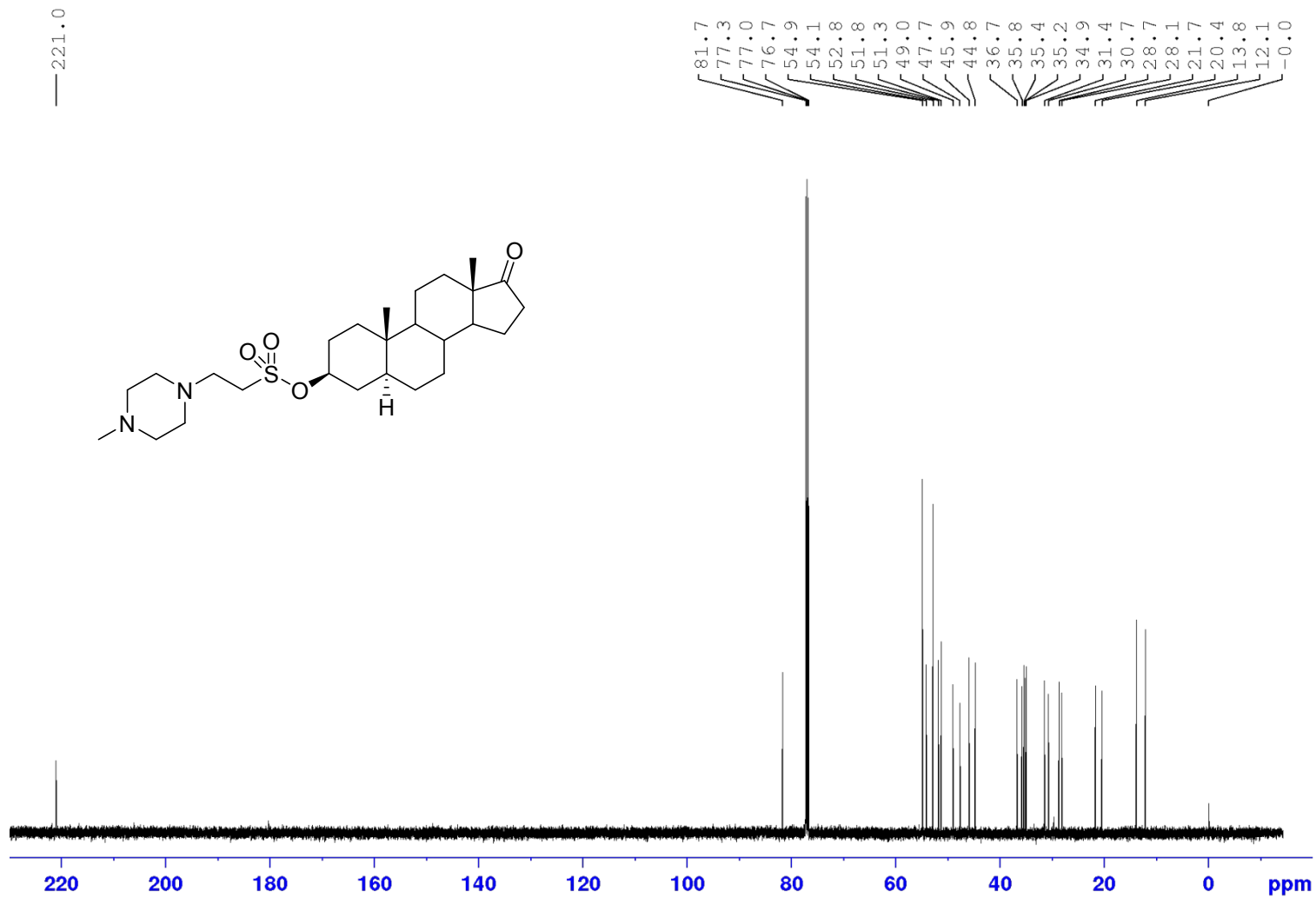
Epiandrosterone 2-morpholinoacetate (22) – ^{13}C – CDCl_3 – 125 MHz



Epiandrosterone 2-(4-methylpiperazin-1-yl)ethane-1-sulfonate (23) – ¹H – CDCl₃ – 500 MHz

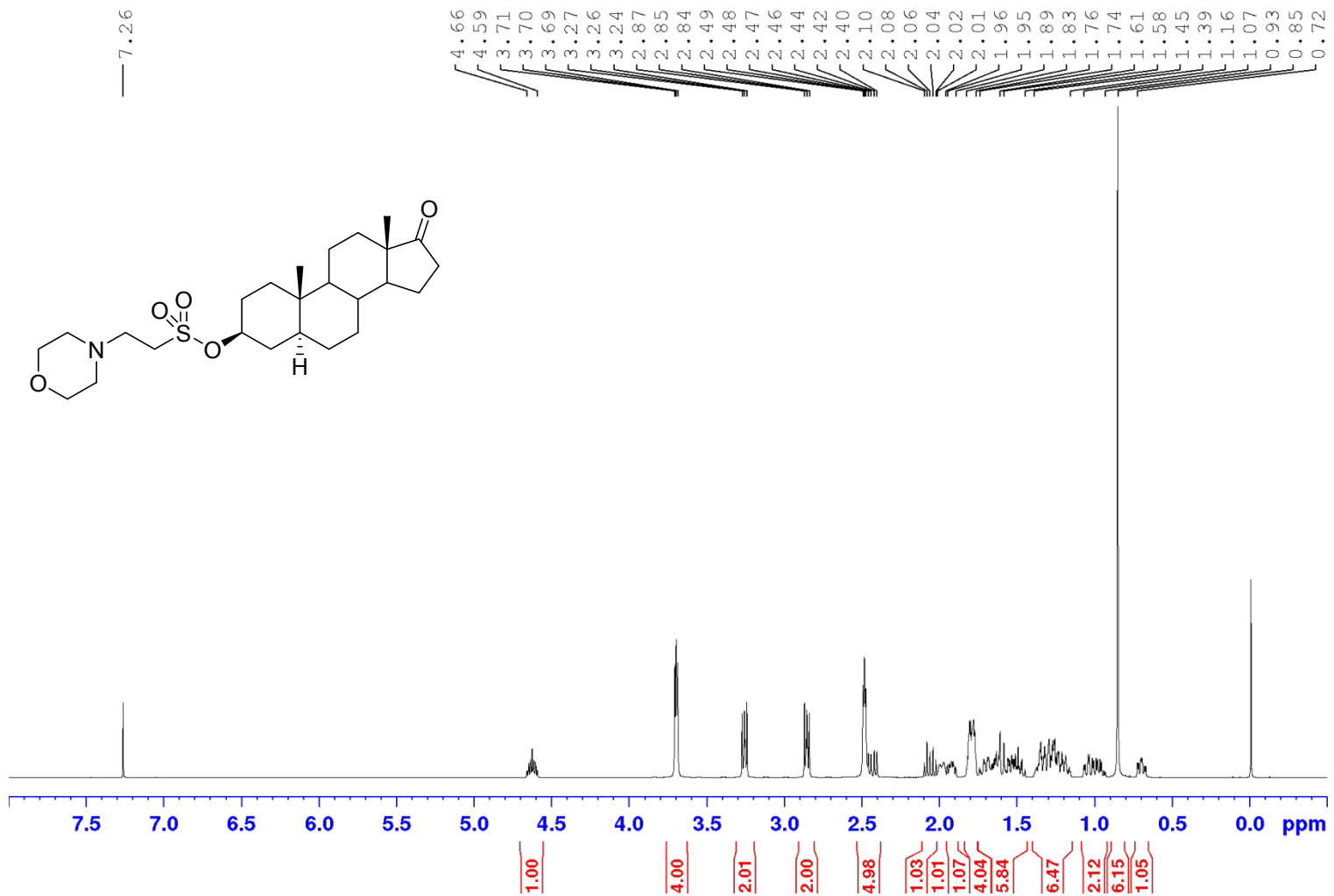


Epiandrosterone 2-(4-methylpiperazin-1-yl)ethane-1-sulfonate (23) – ^{13}C – CDCl_3 – 125 MHz



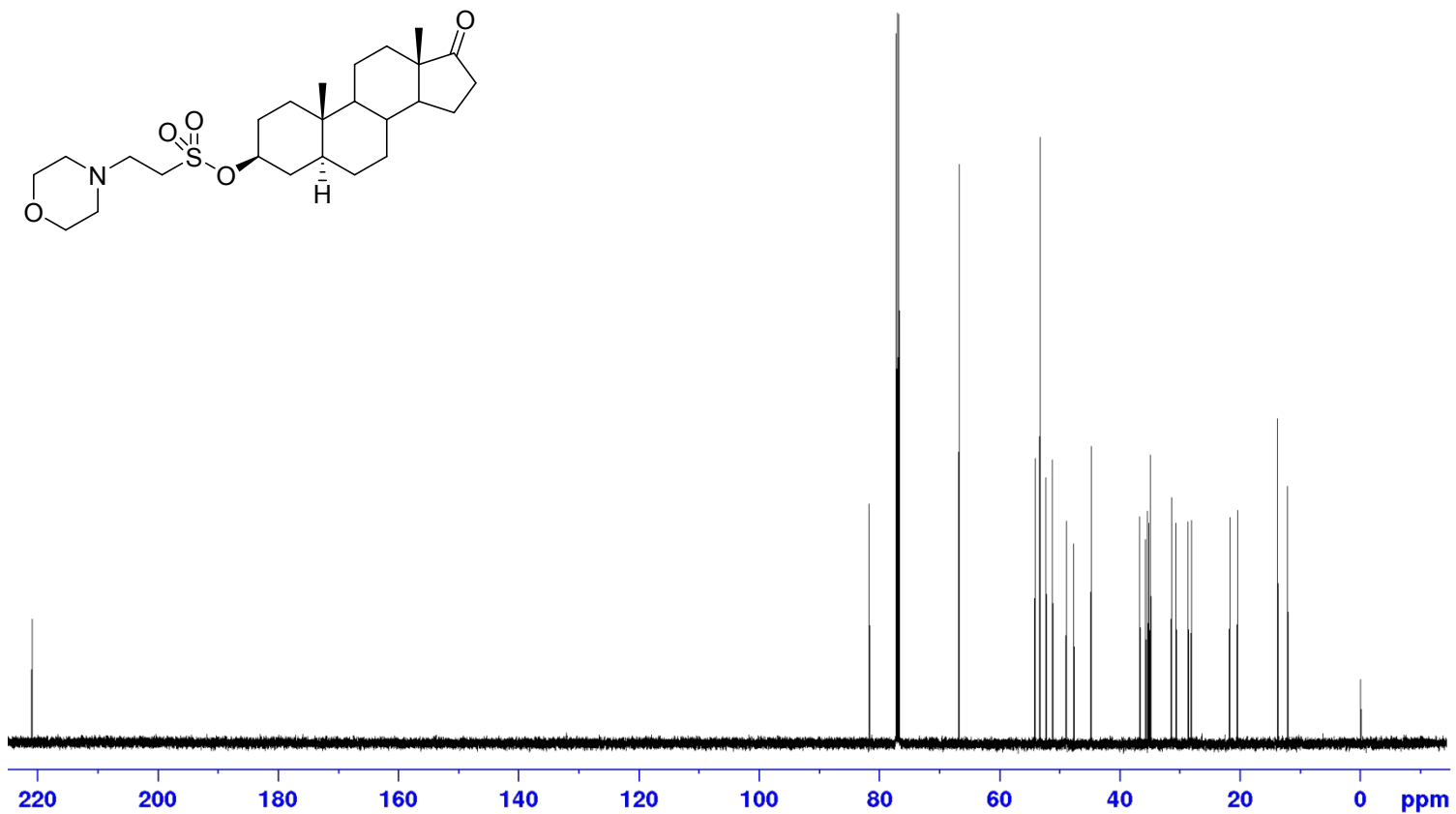
— 221.0

Epiandrosterone 2-morpholinoethanesulfonate (24) – ^1H – CDCl_3 – 500 MHz

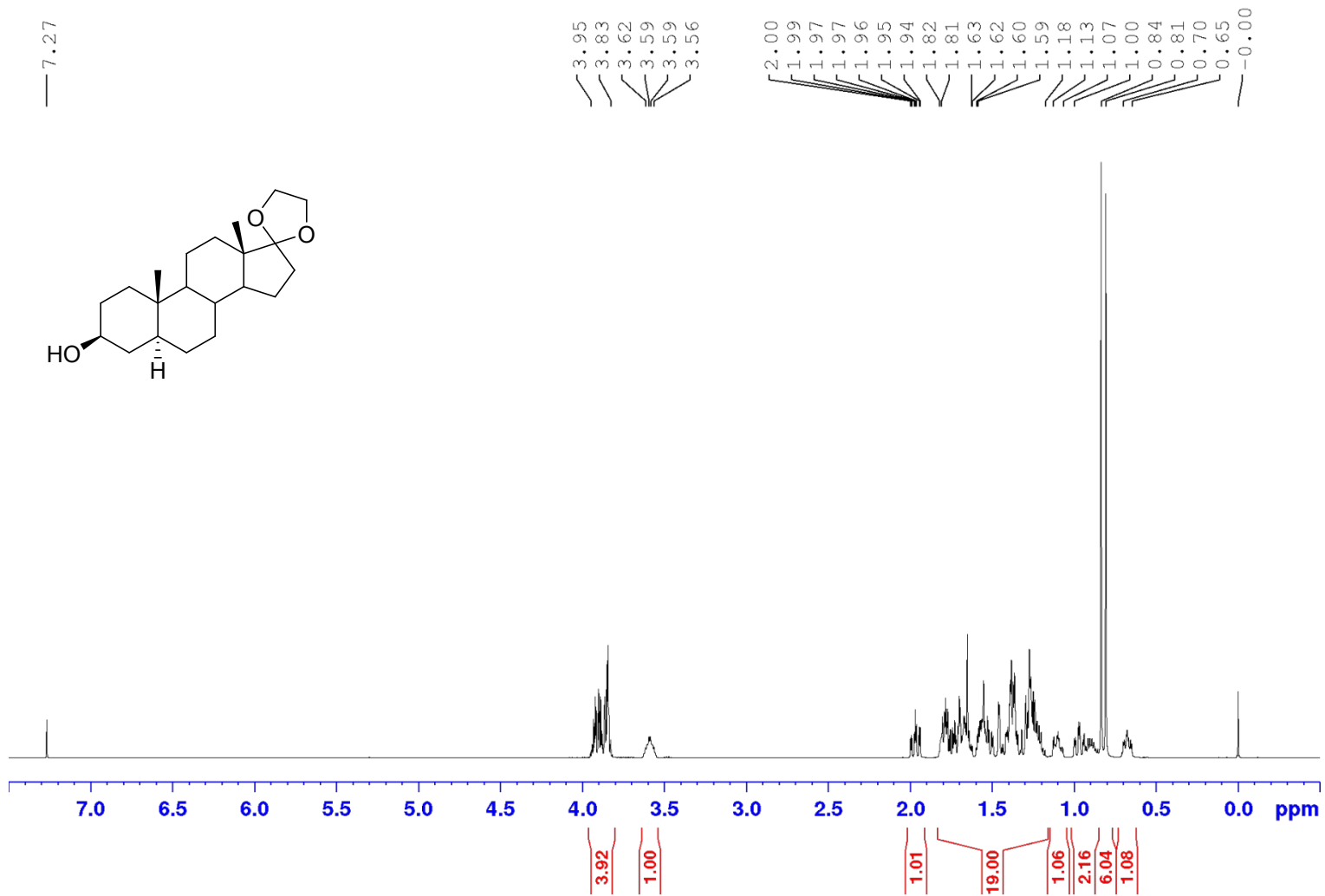
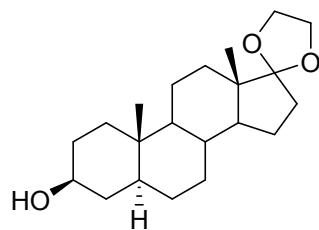


— 221.0

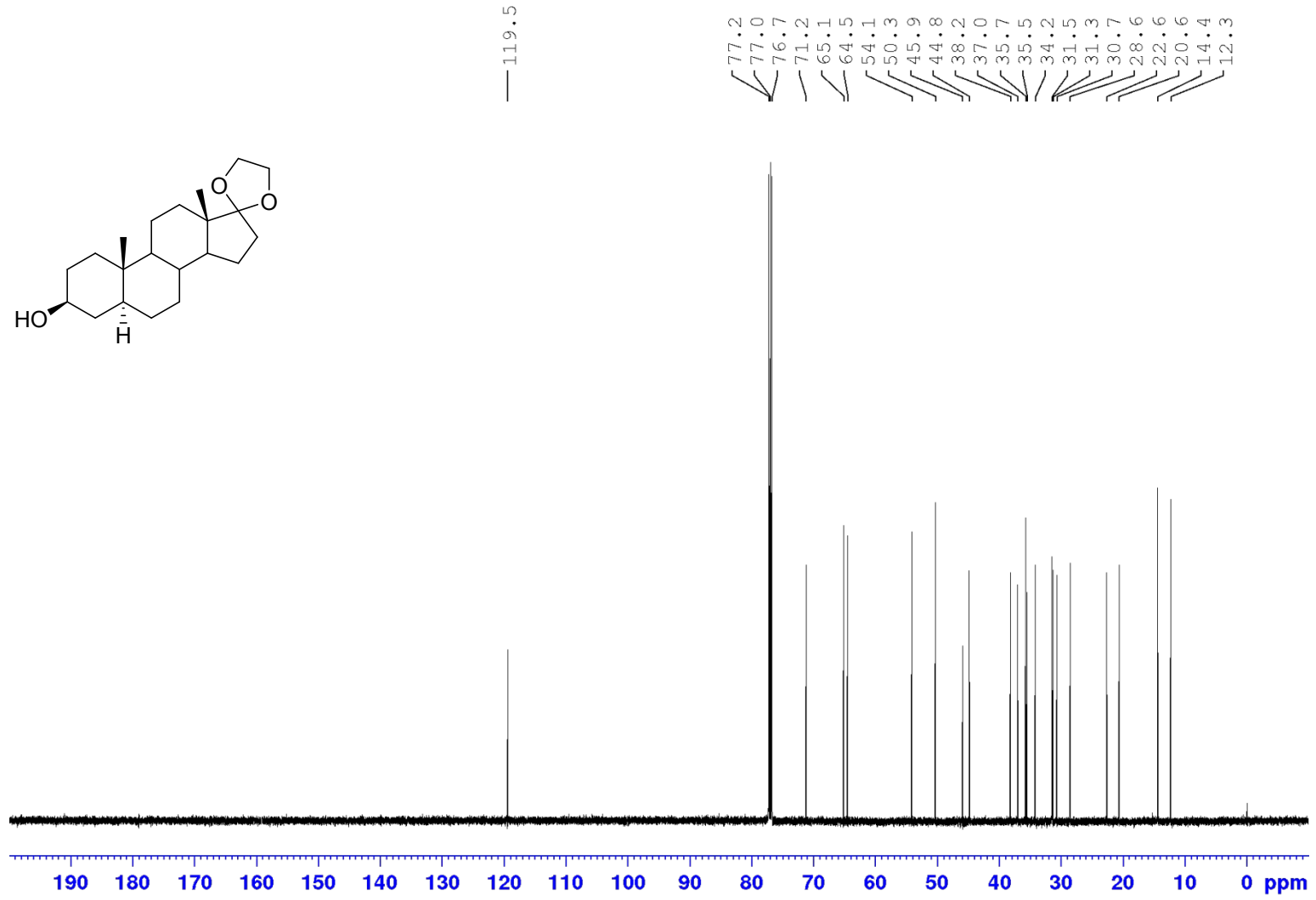
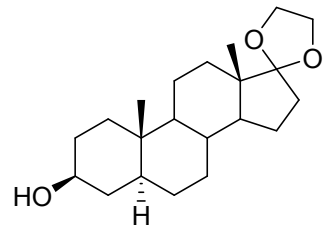
Epiandrosterone 2-morpholinoethanesulfonate (24) — ^{13}C — CDCl_3 — 125 MH



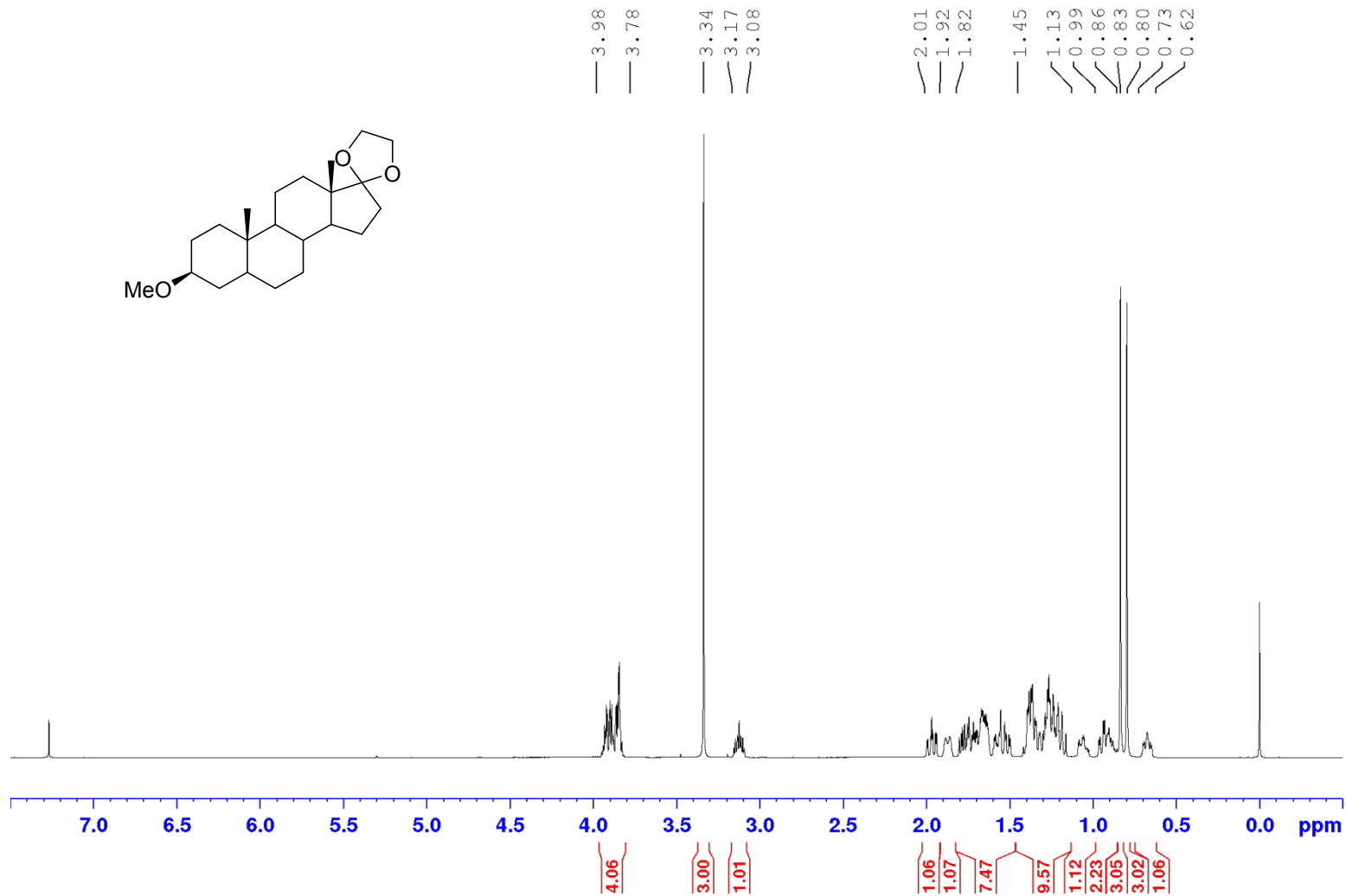
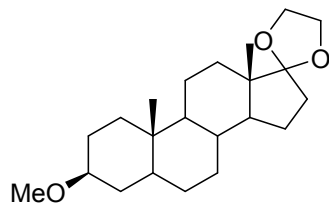
Epiandrosterone 17-acetal (25) – ^1H – CDCl_3 – 500 MHz



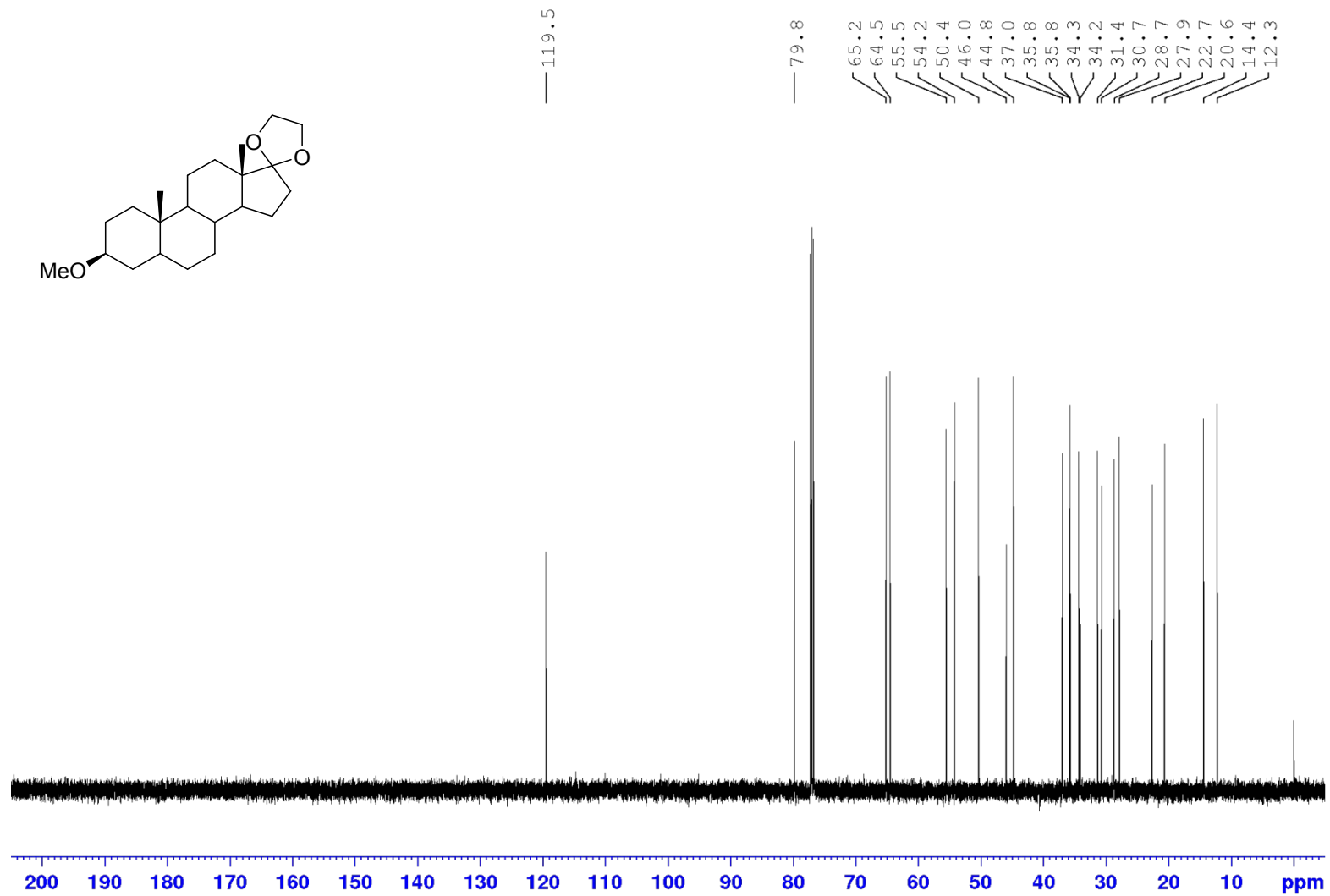
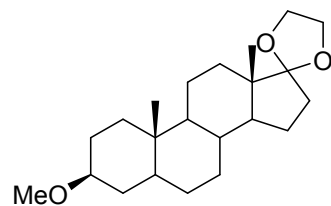
Epiandrosterone 17-acetal (25) – ^{13}C – CDCl_3 – 125 MHz



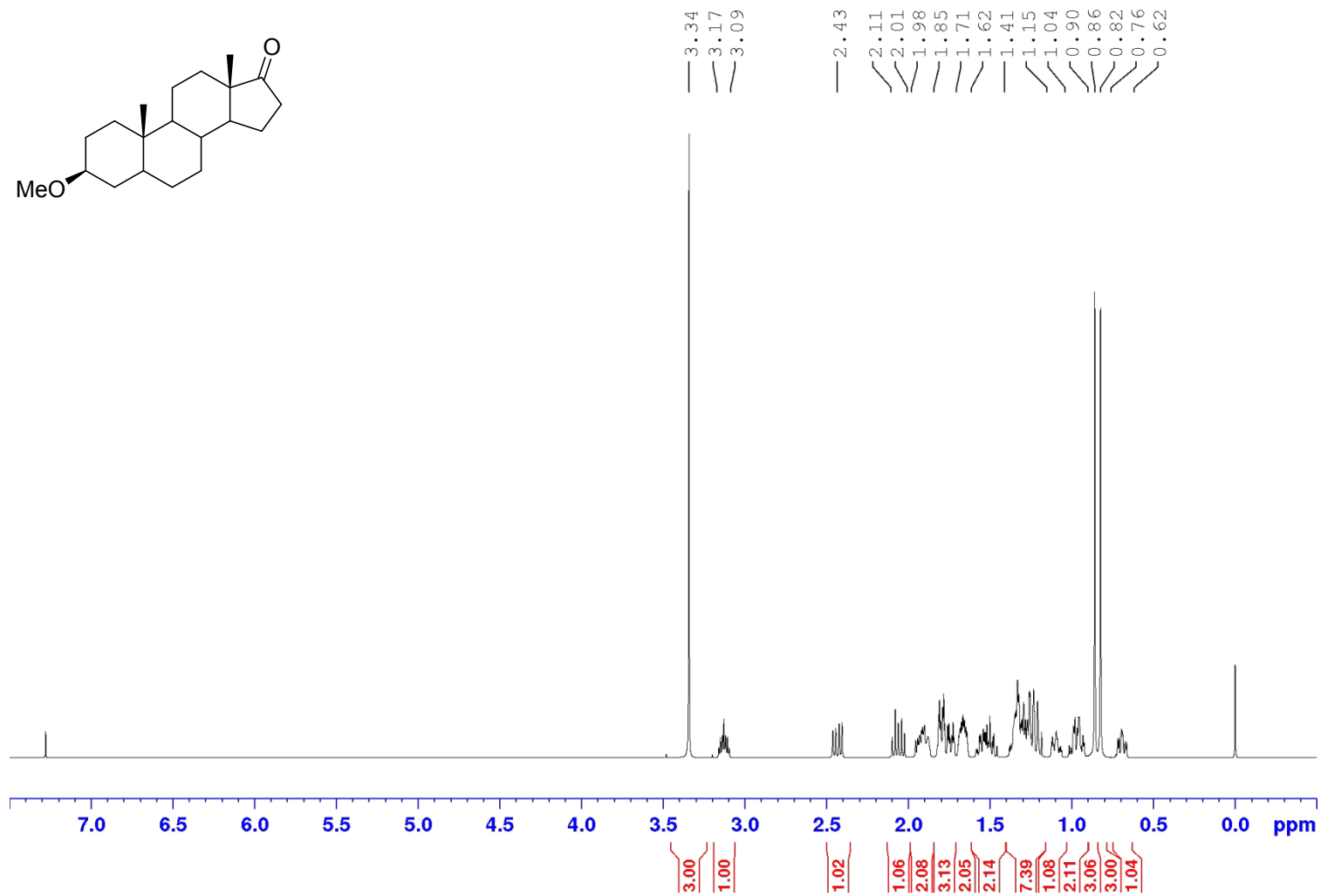
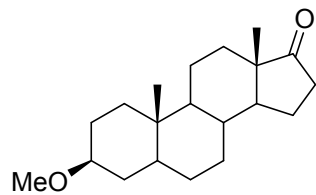
Epiandrosterone 17-acetal methyl ether (26) – ^1H – CDCl_3 – 500 MHz



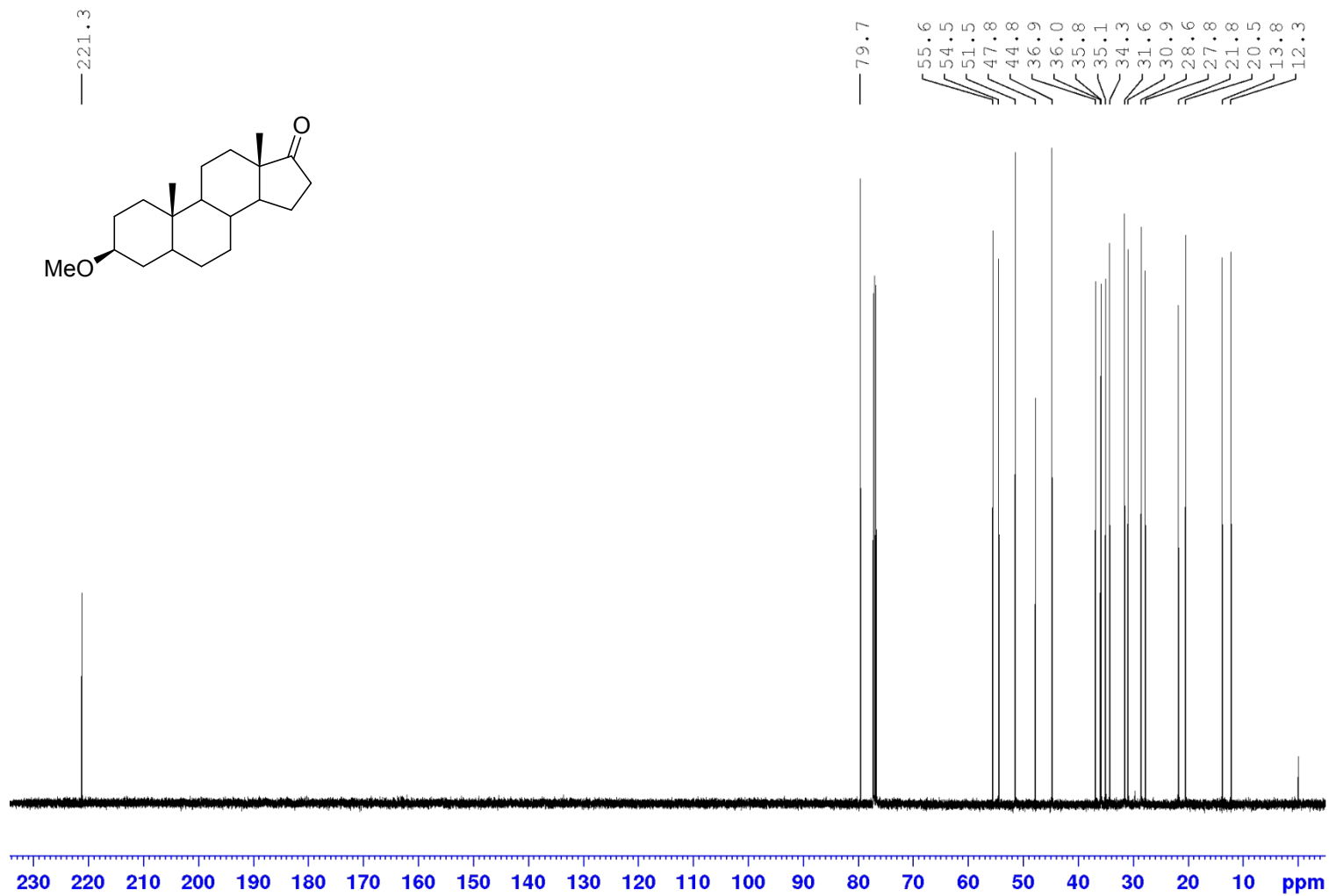
Epiandrosterone 17-acetal methyl ether (26) – ^{13}C – CDCl_3 – 125 MHz



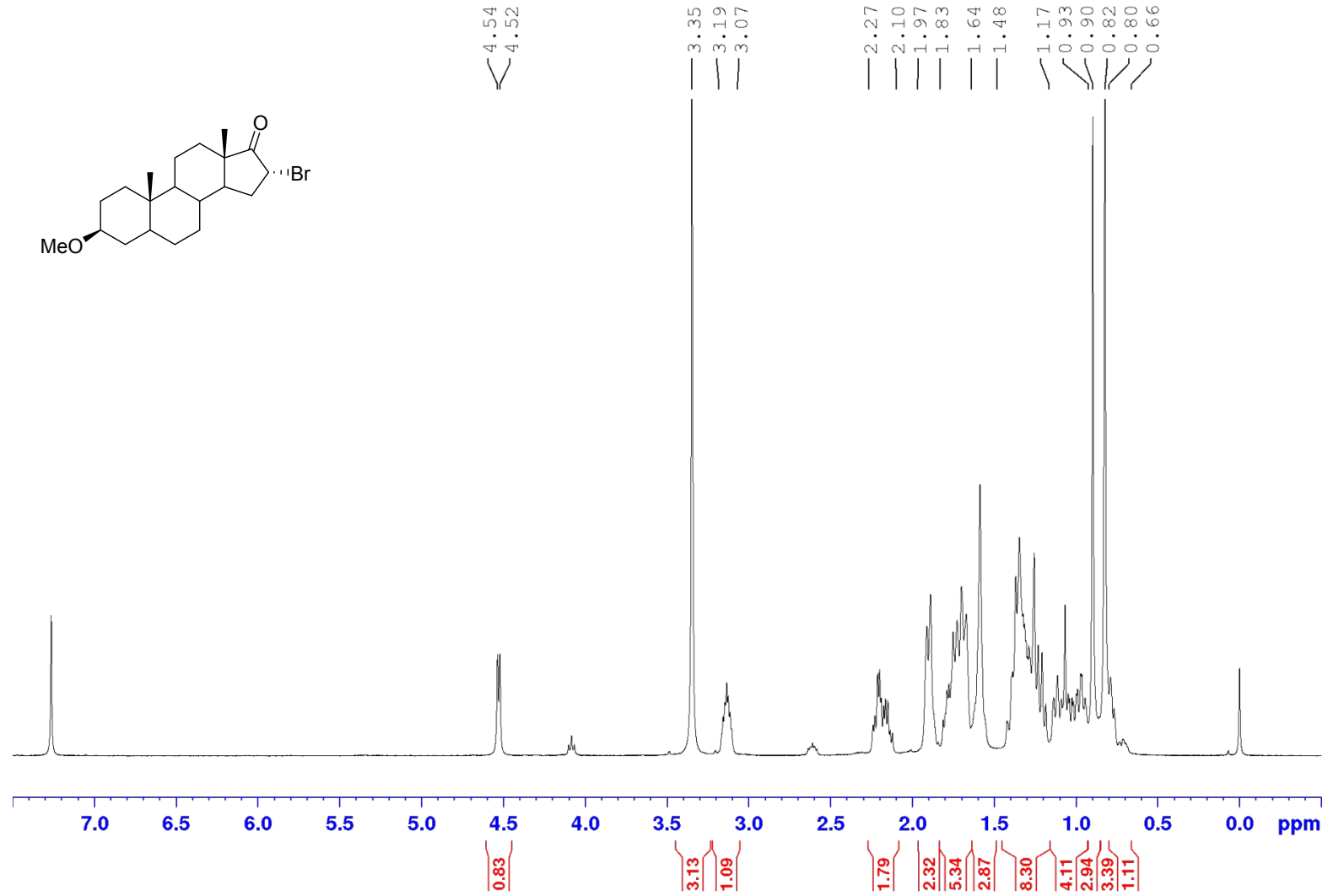
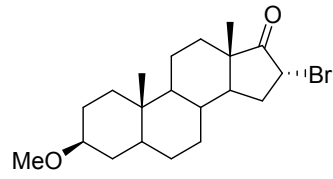
Epiandrosterone methyl ether (27) – ¹H – CDCl₃ – 500 MHz



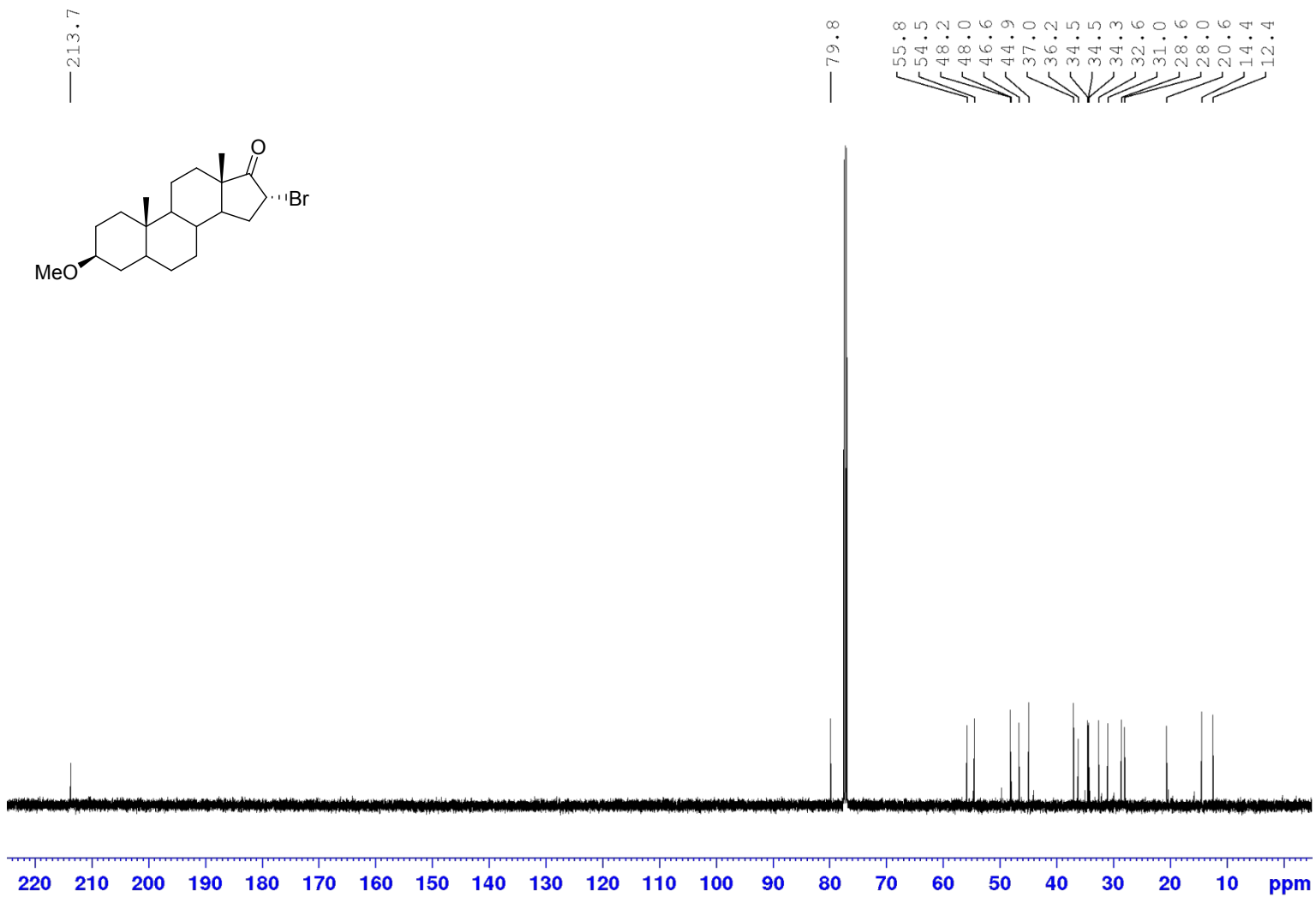
Epiandrosterone methyl ether (27) – ^{13}C – CDCl_3 – 125 MHz



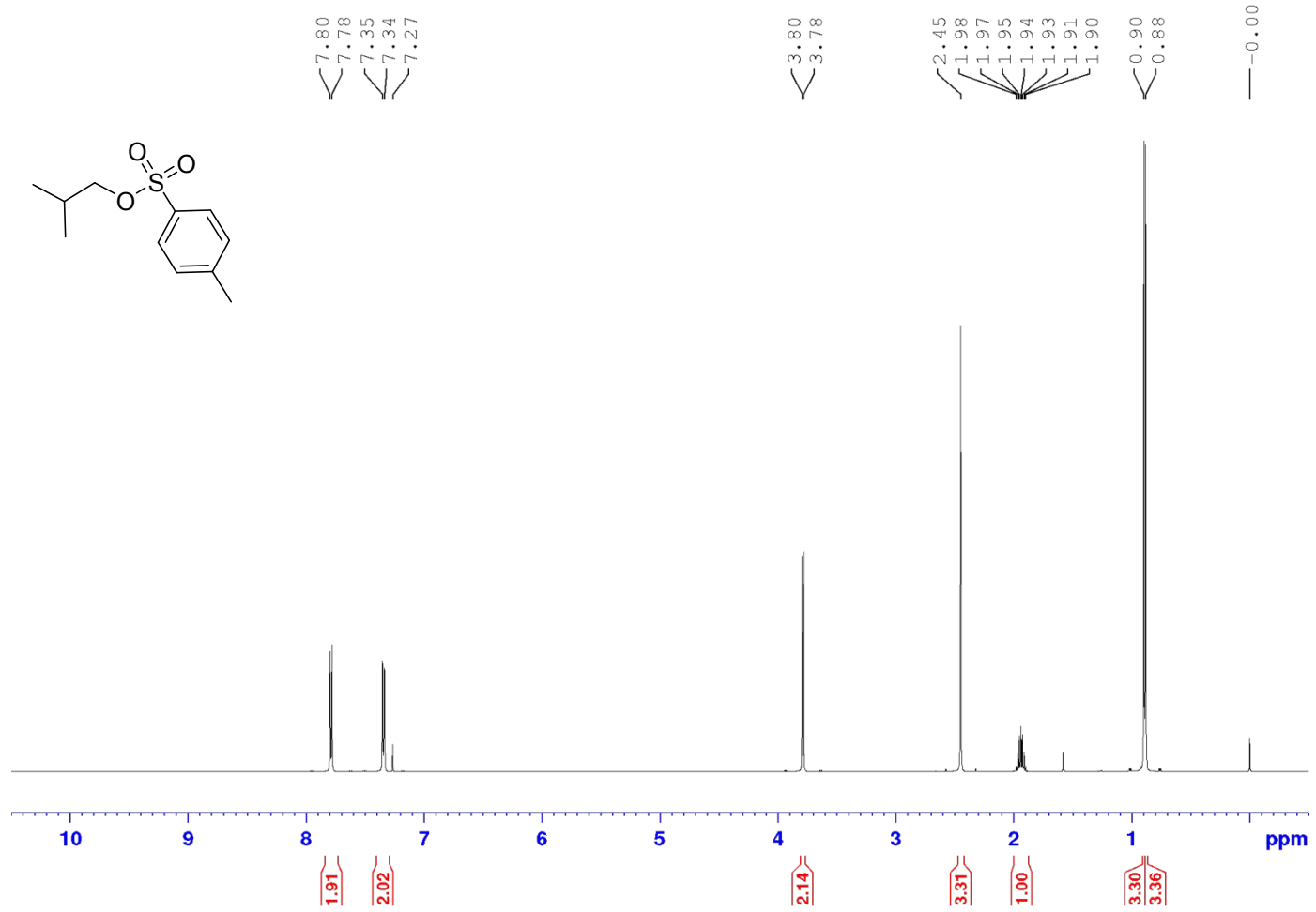
16 α -Bromoepiandrosterone methyl ether (28) – ^1H – CDCl_3 – 500 MHz



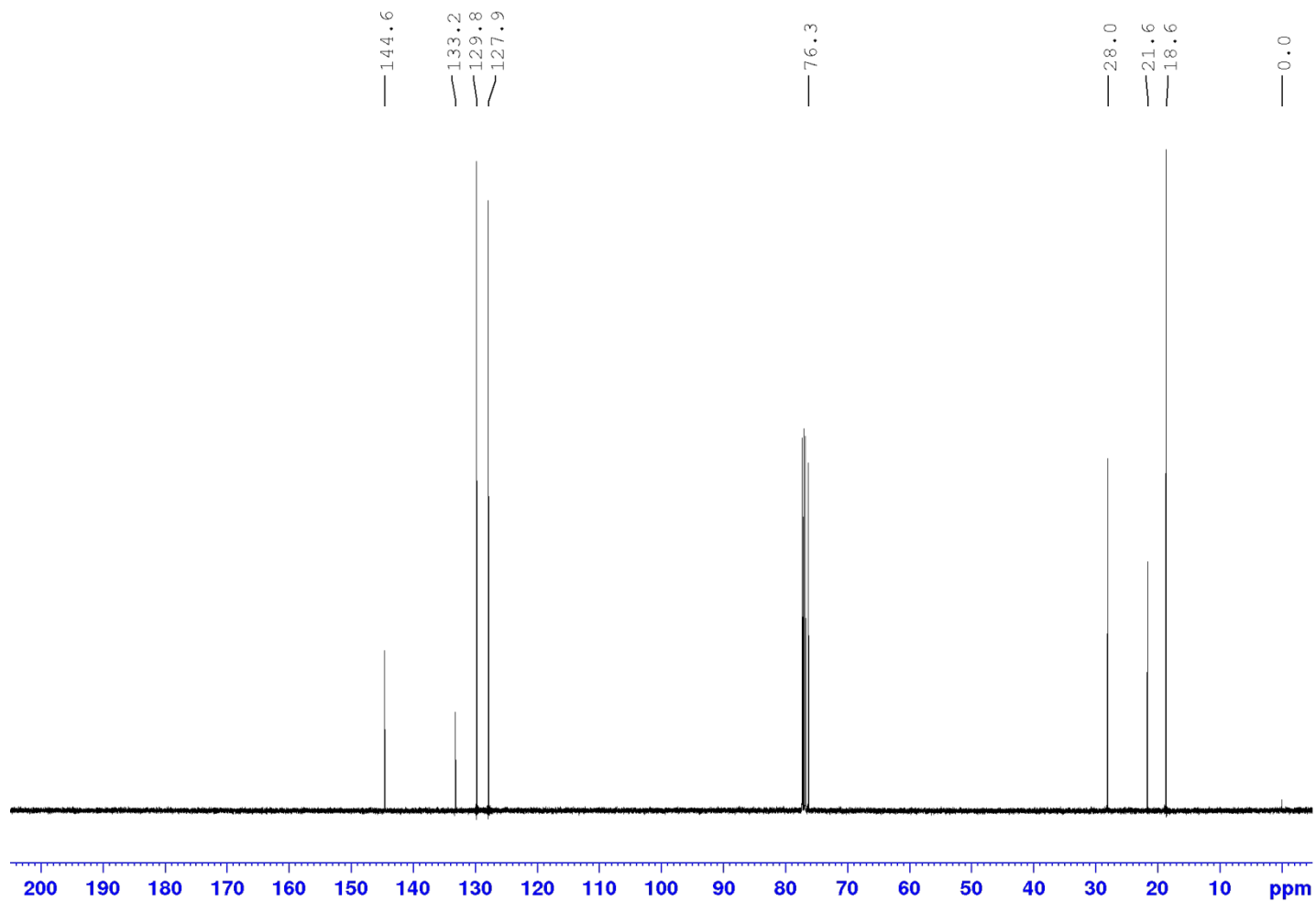
16 α -Bromoepiandrosterone methyl ether (28) – ^{13}C – CDCl_3 – 125 MHz



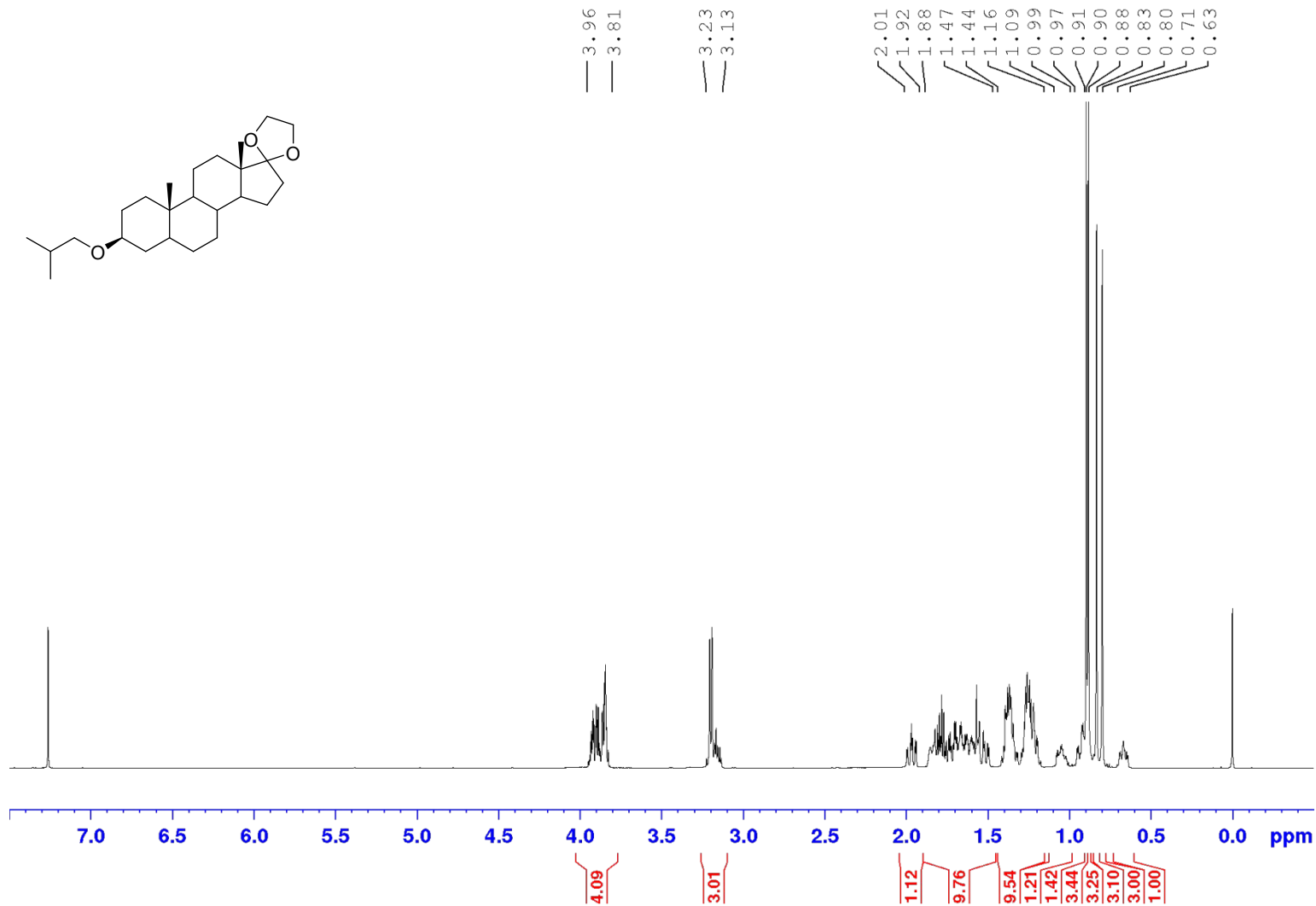
Isobutyl-4-toluenesulfonate (29) – ^1H – CDCl_3 – 500 MHz



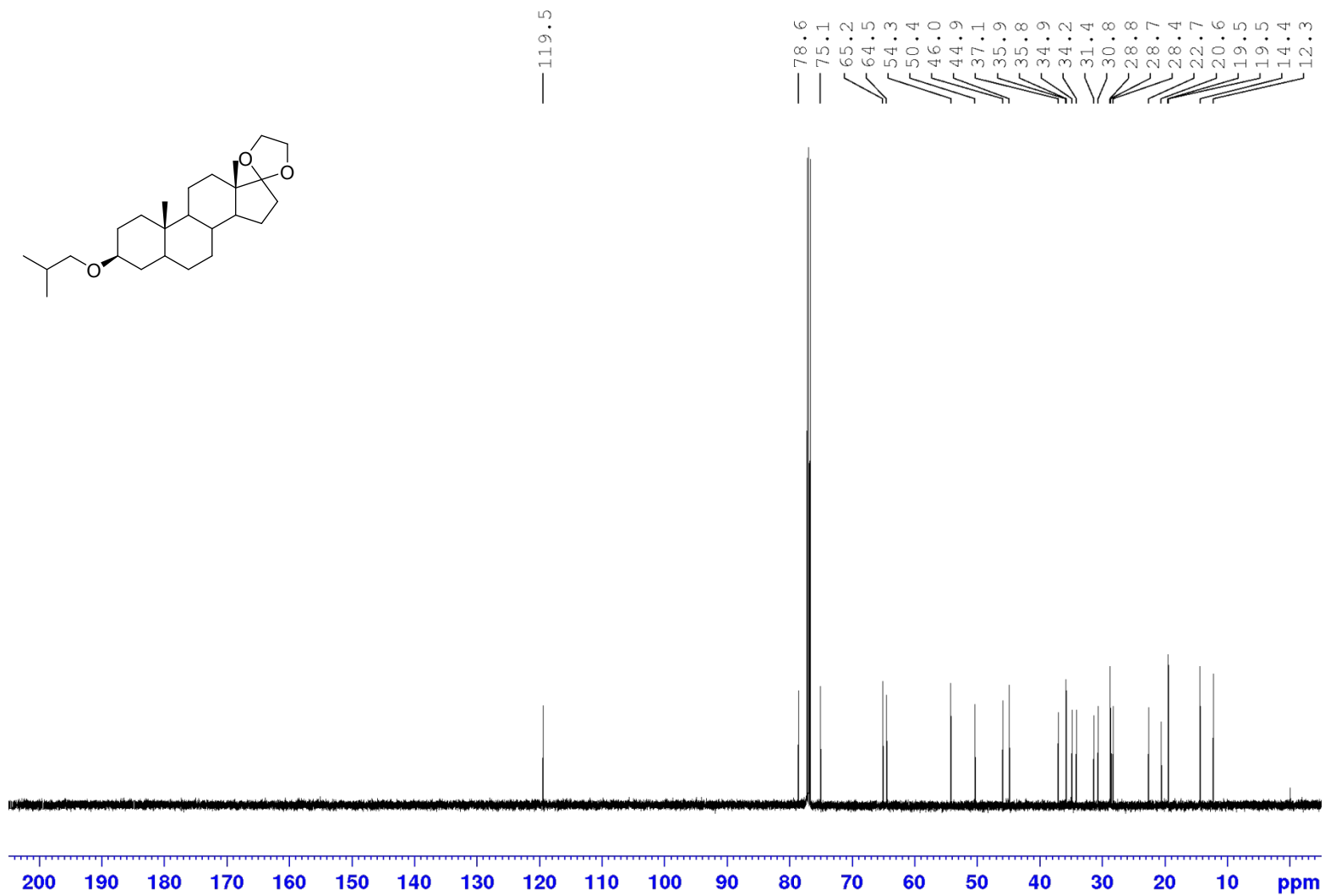
Isobutyl-4-toluenesulfonate (29) – ^{13}C – CDCl_3 – 125 MHz



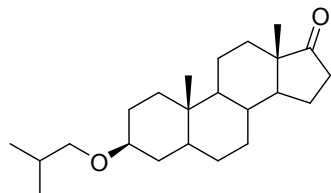
Epiandrosterone 17-acetal isobutyl ether (30) – ^1H – CDCl_3 – 500 MHz



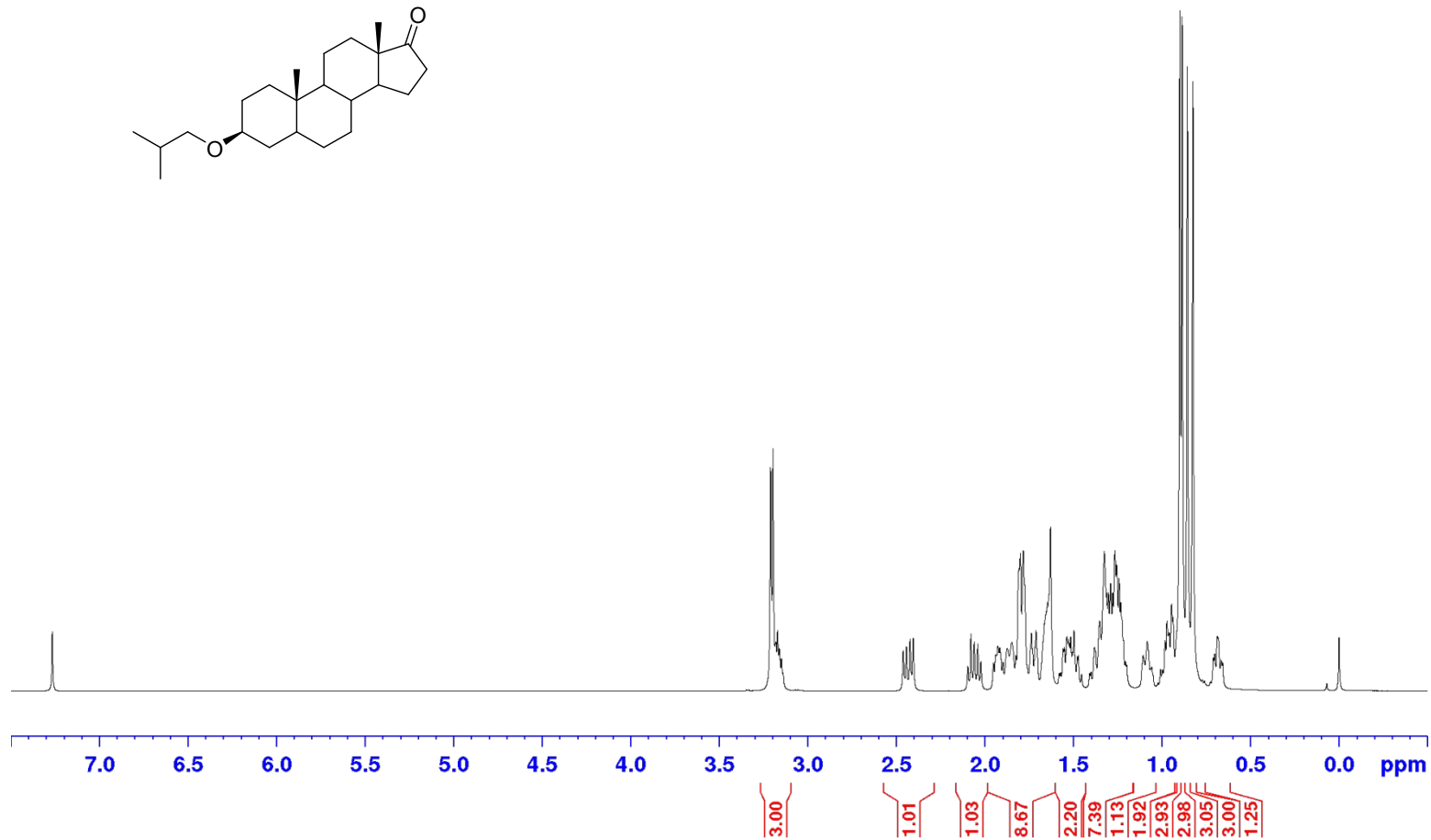
Epiandrosterone 17-acetal isobutyl ether (30) – ^{13}C – CDCl_3 – 125 MHz



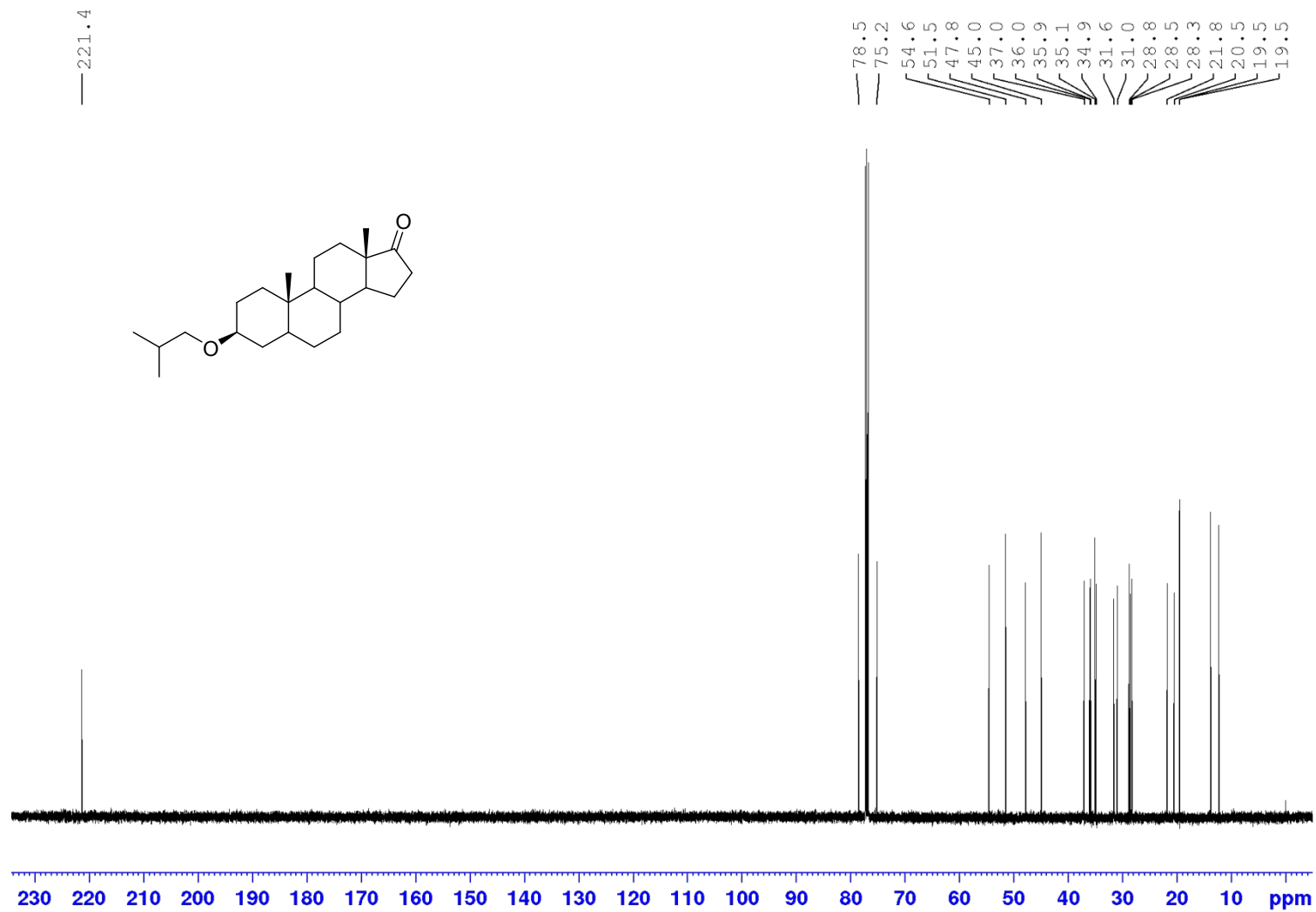
Epiandrosterone isobutyl ether (31) – ¹H – CDCl₃ – 500 MHz



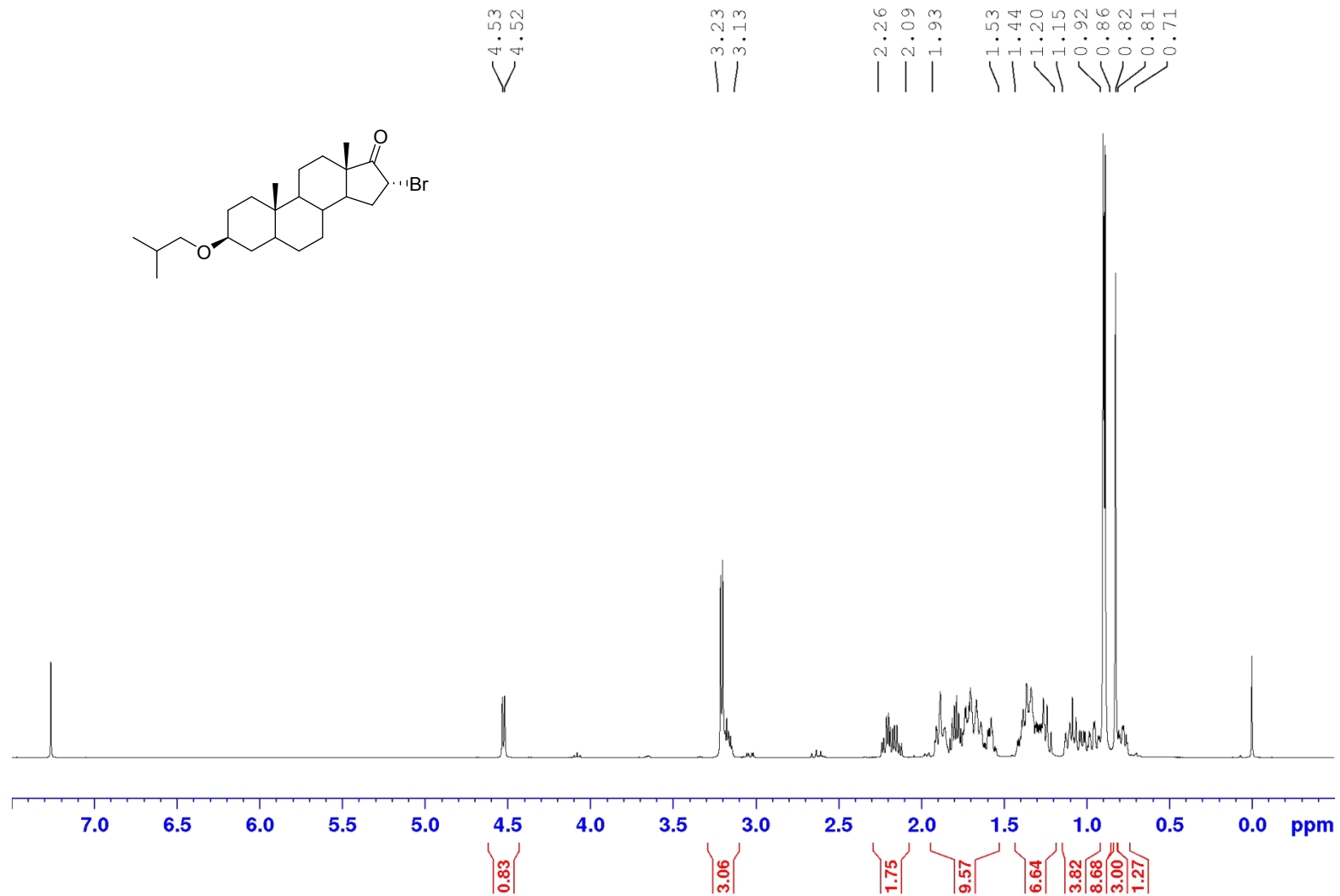
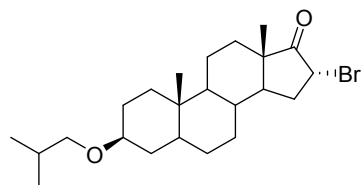
— 3.26
— 3.10
2.46
2.44
2.42
2.40
2.12
2.00
1.98
1.60
1.43
1.17
1.14
1.03
0.93
0.90
0.89
0.86
0.83
0.74
0.64



Epiandrosterone isobutyl ether (31) – ^{13}C – CDCl_3 – 125 MHz

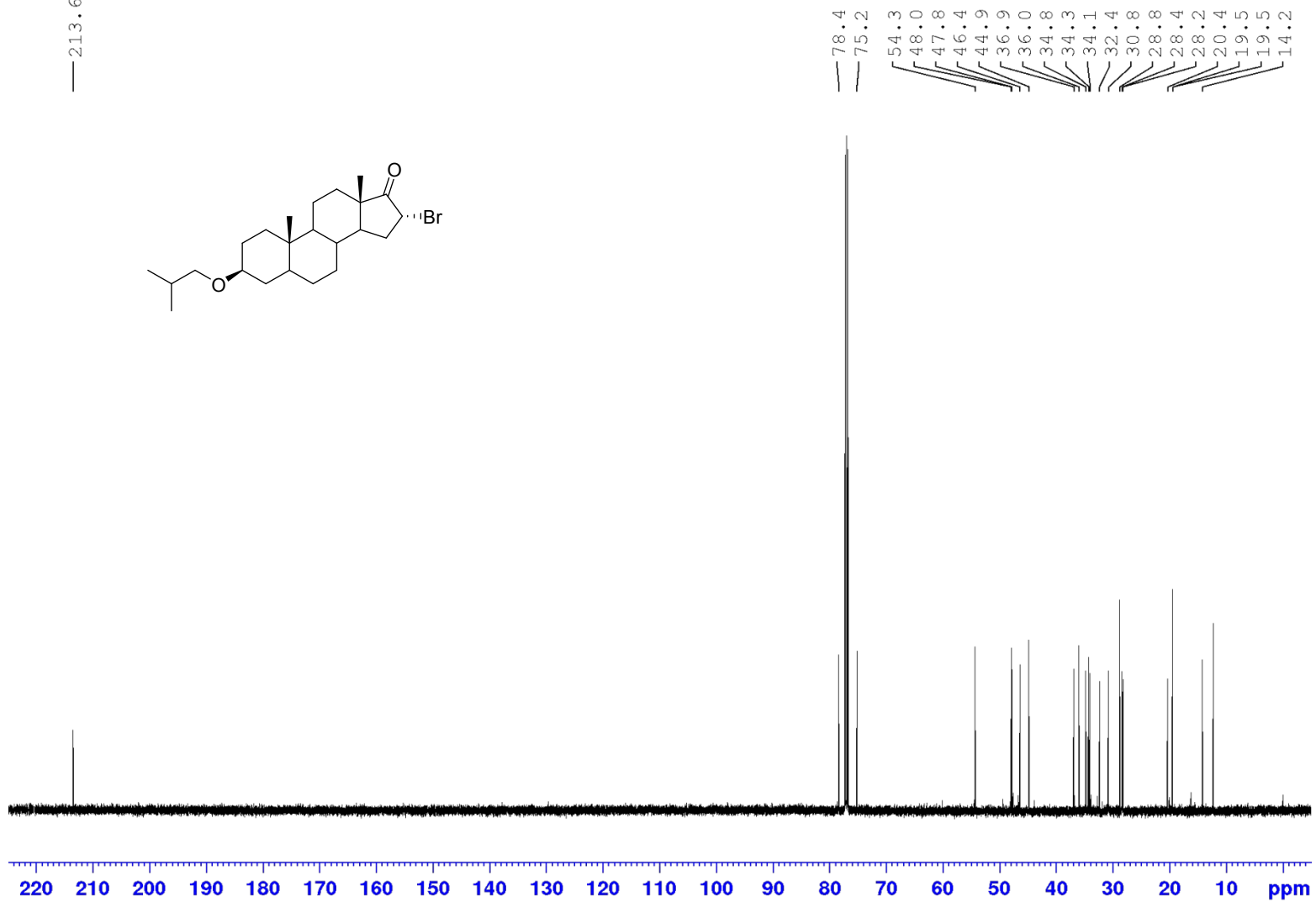
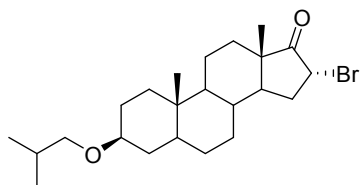


16 α -Bromoepiandrosterone isobutyl ether (32) – ^1H – CDCl_3 – 500 MHz

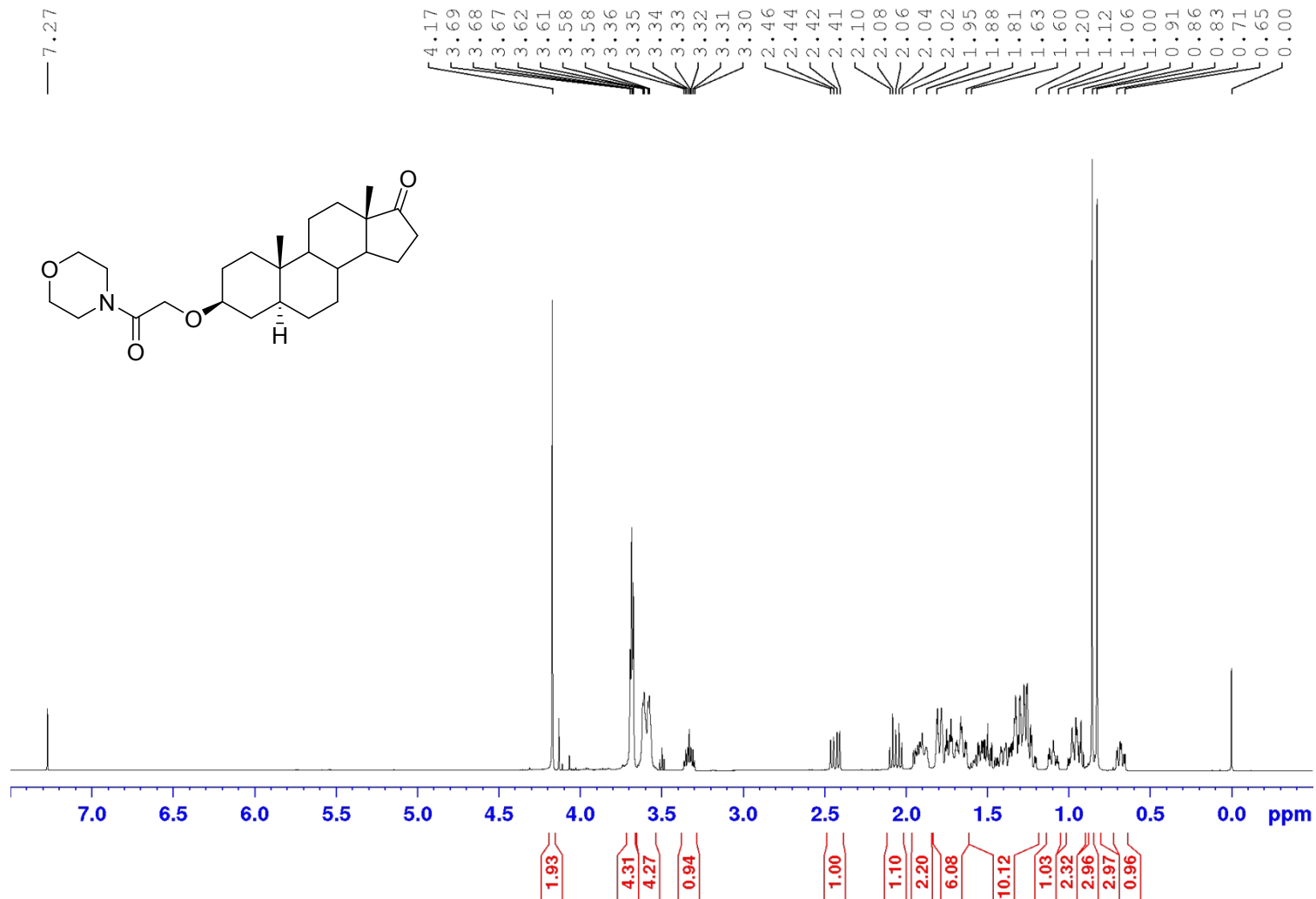


16 α -Bromoepiandrosterone isobutyl ether (32) – ^{13}C – CDCl_3 – 125 MHz

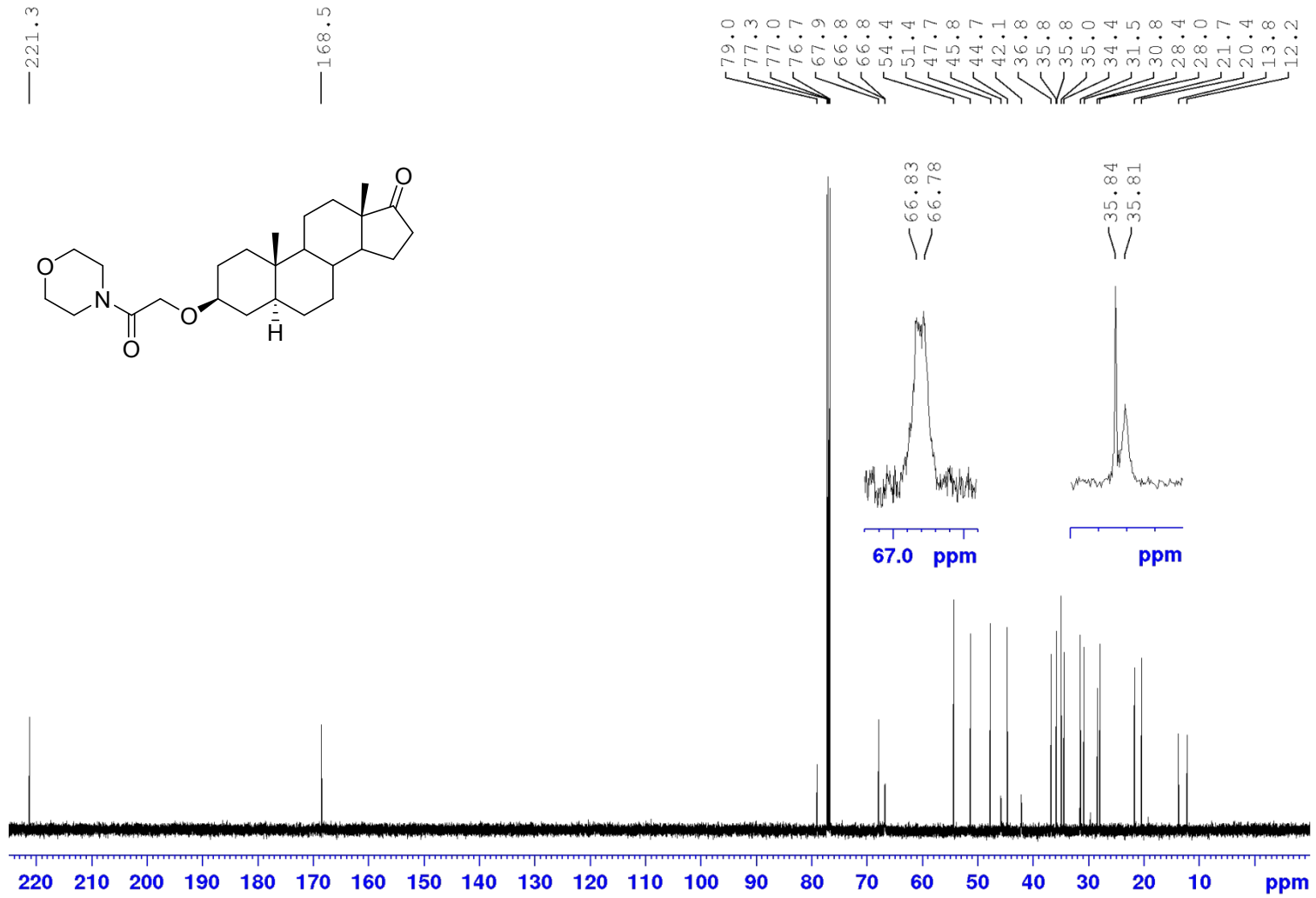
— 213.6



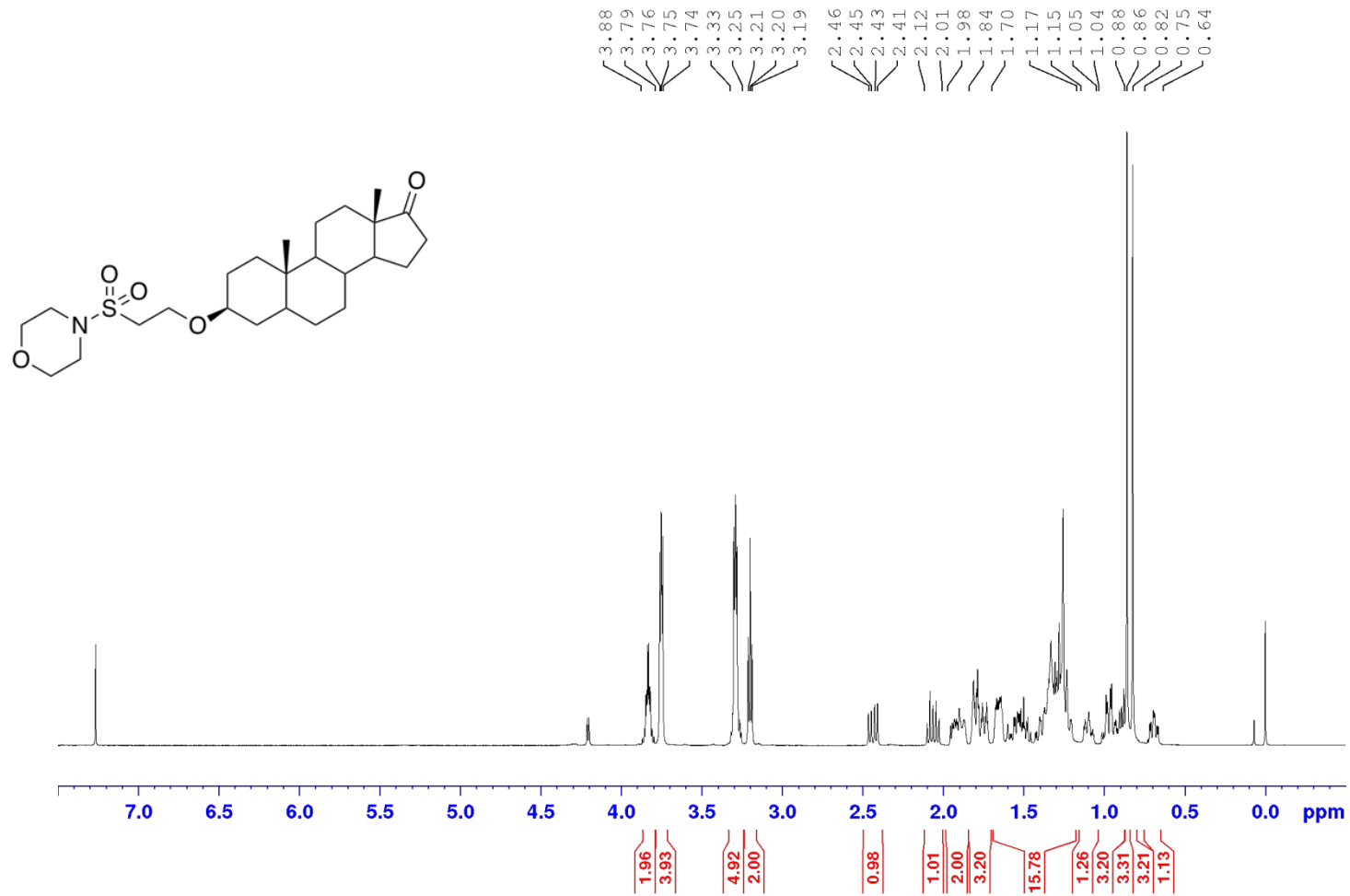
Epiandrosterone 2-morpholino-2-oxoethoxy ether (33) – ¹H – CDCl₃ – 500 MHz



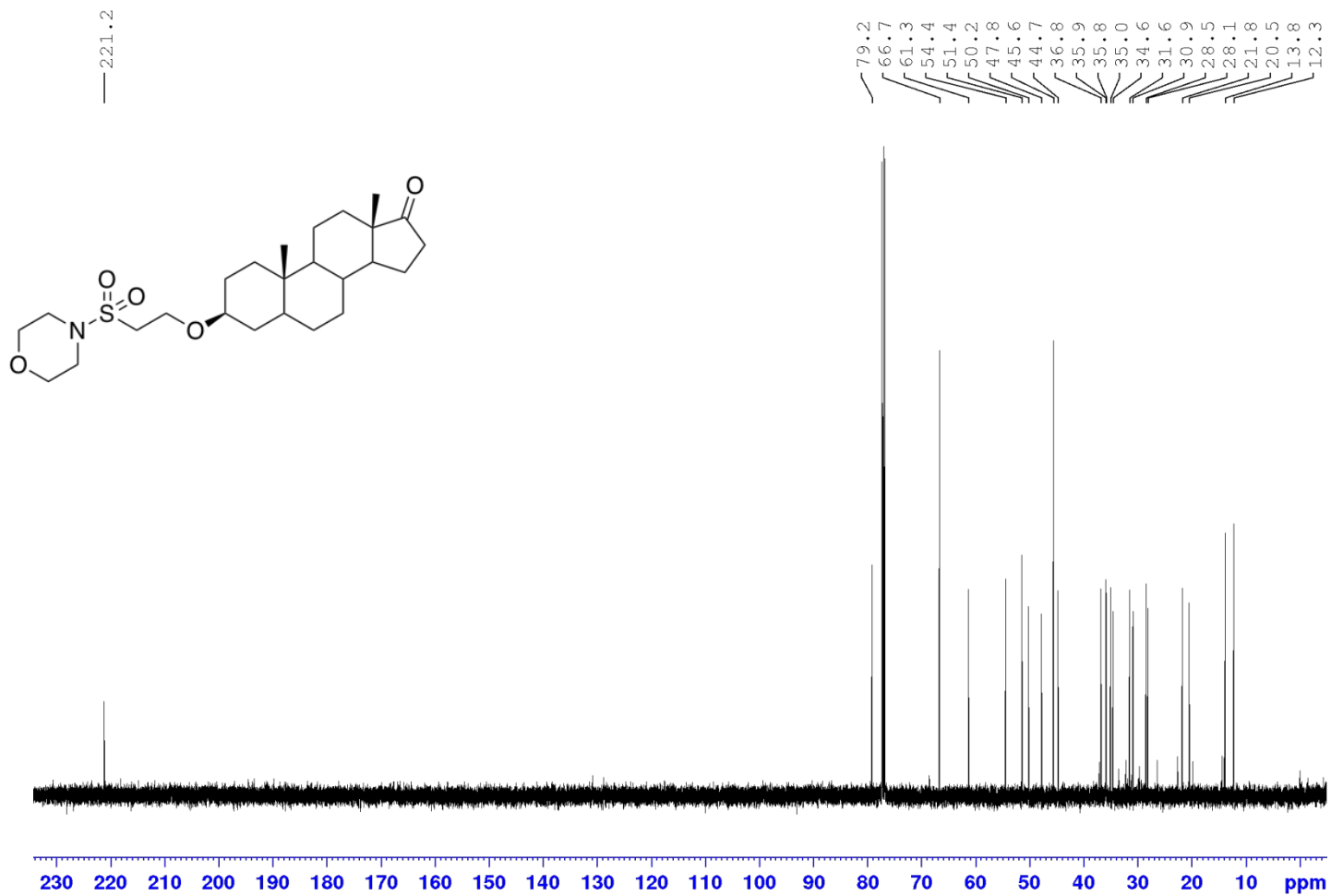
Epiandrosterone 2-morpholino-2-oxoethoxy ether (33) – ^{13}C – CDCl_3 – 125 MHz



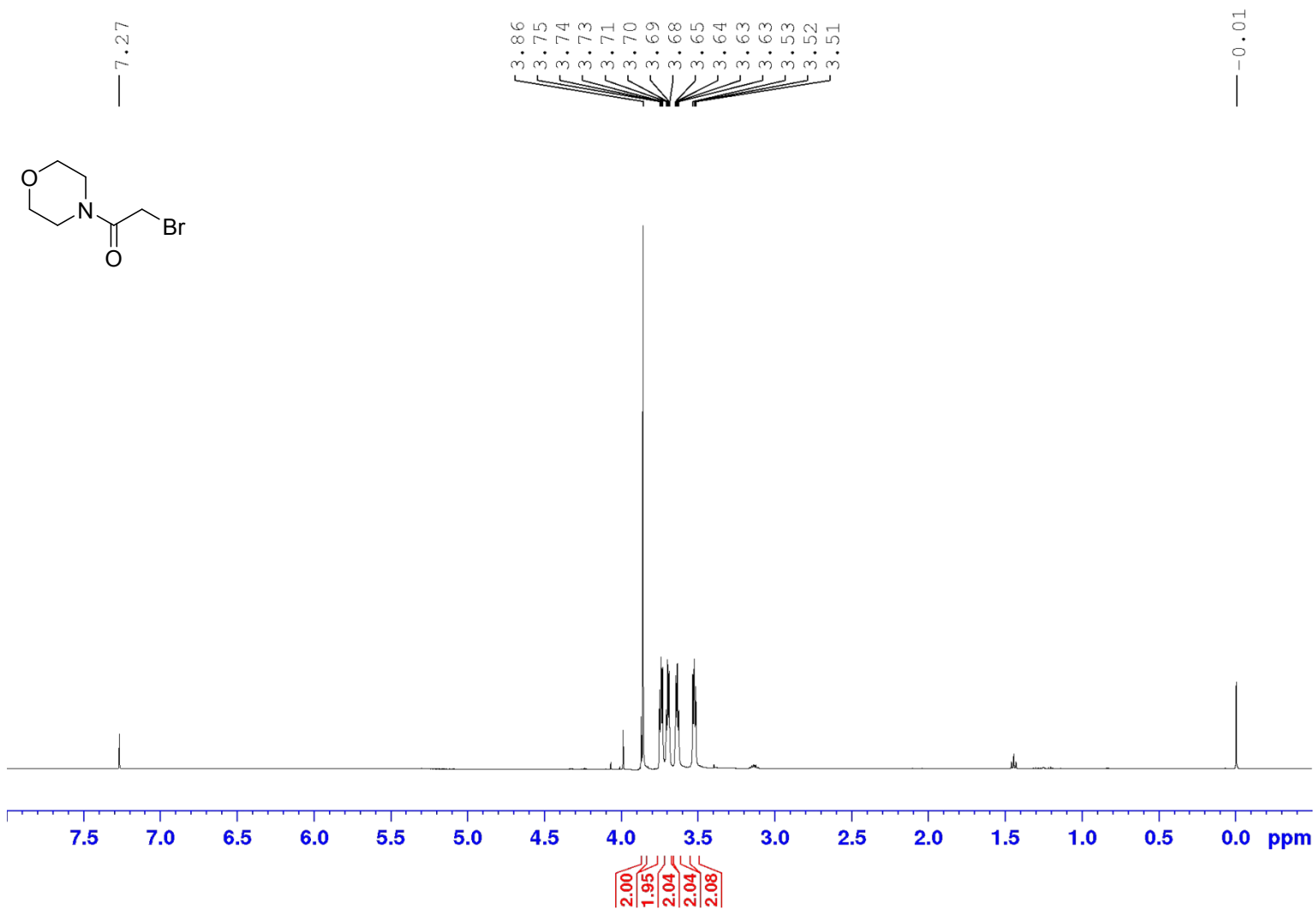
Epiandrosterone 2-(morpholinosulfonyl)ethyl ether (34) – ^1H – CDCl_3 – 500 MHz



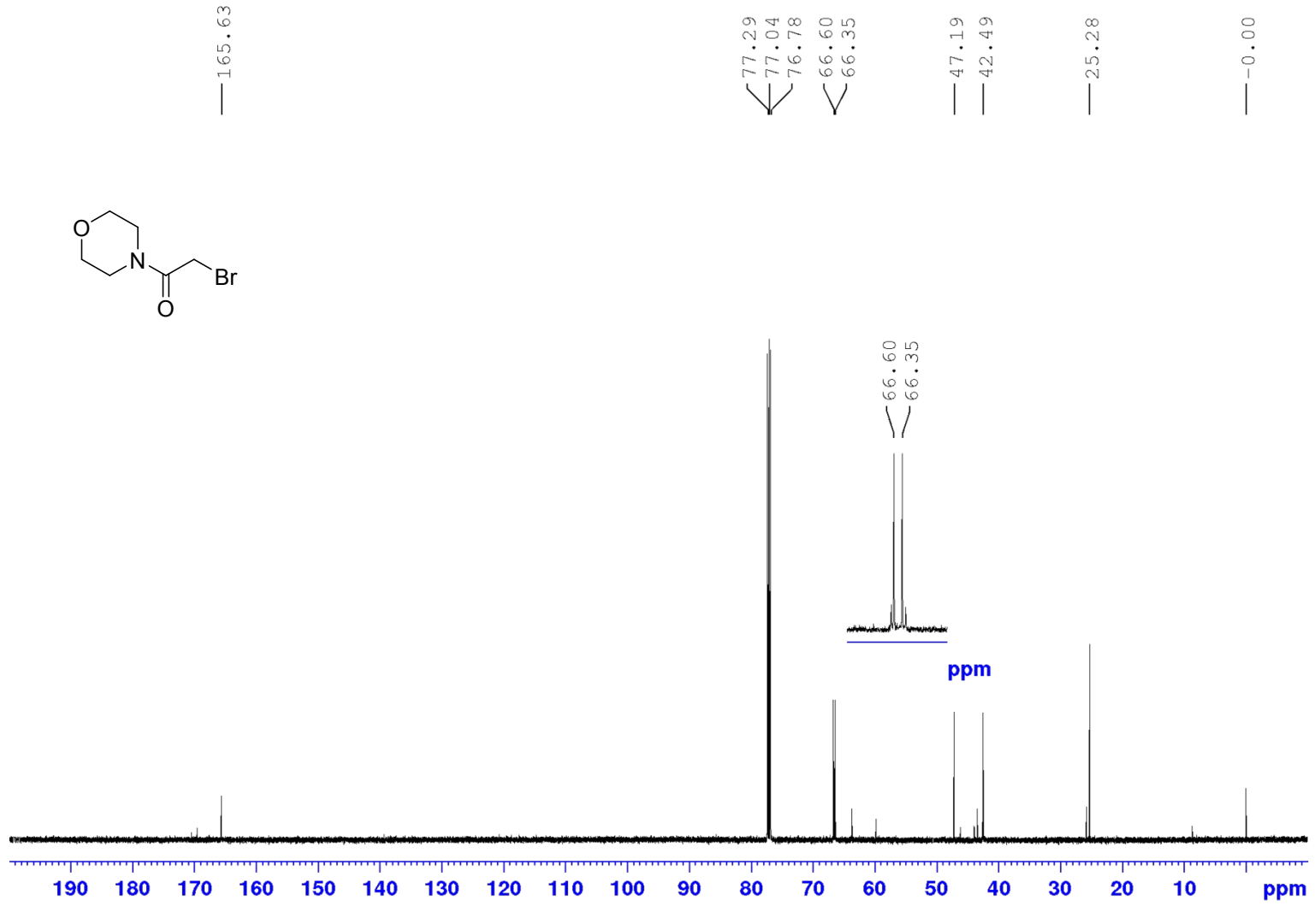
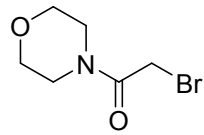
Epiandrosterone 2-(morpholinosulfonyl)ethyl ether (34) – ^{13}C – CDCl_3 – 125 MHz



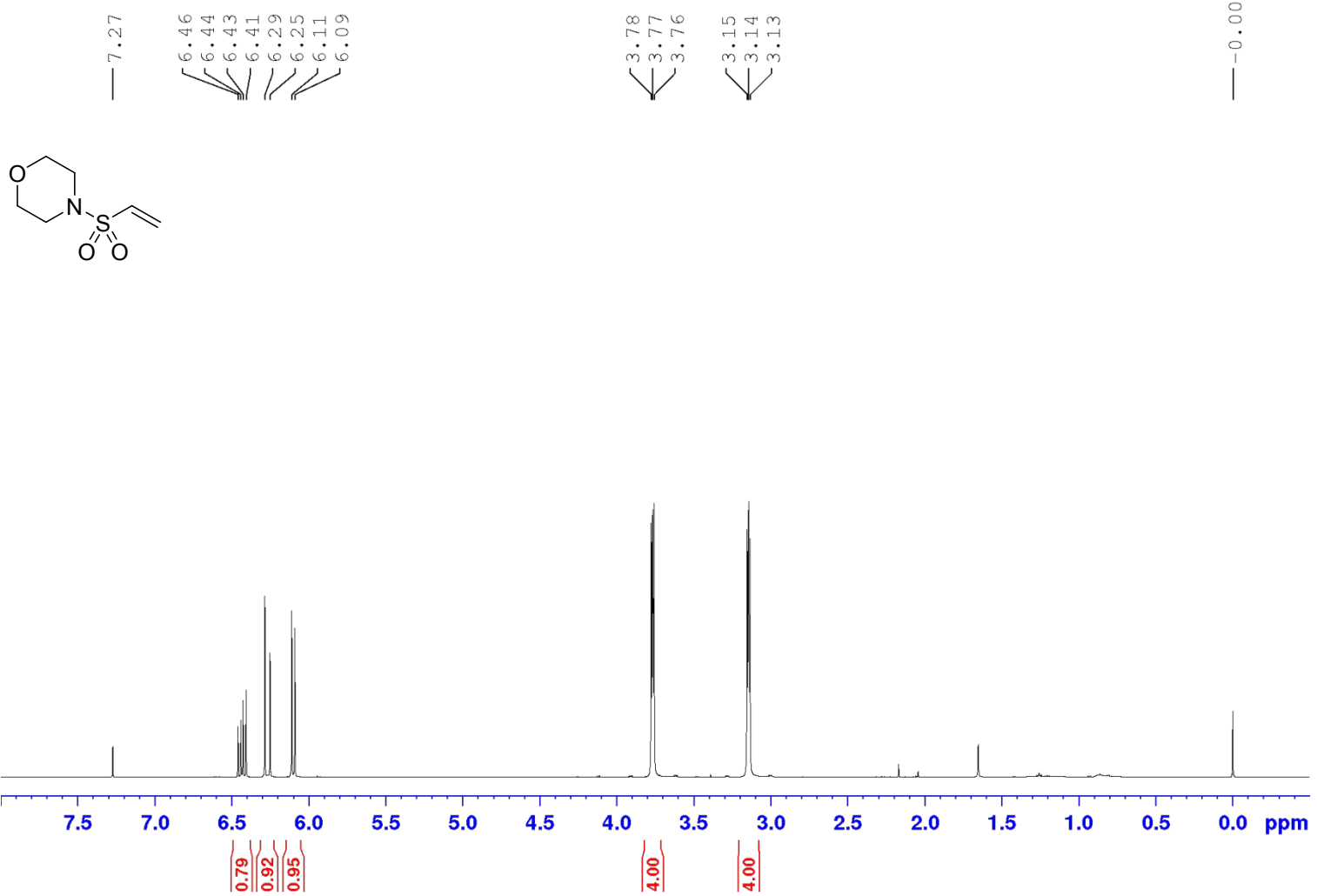
2-Bromo-1-morpholinoethan-1-one (35) – ^1H – CDCl_3 – 500 MHz



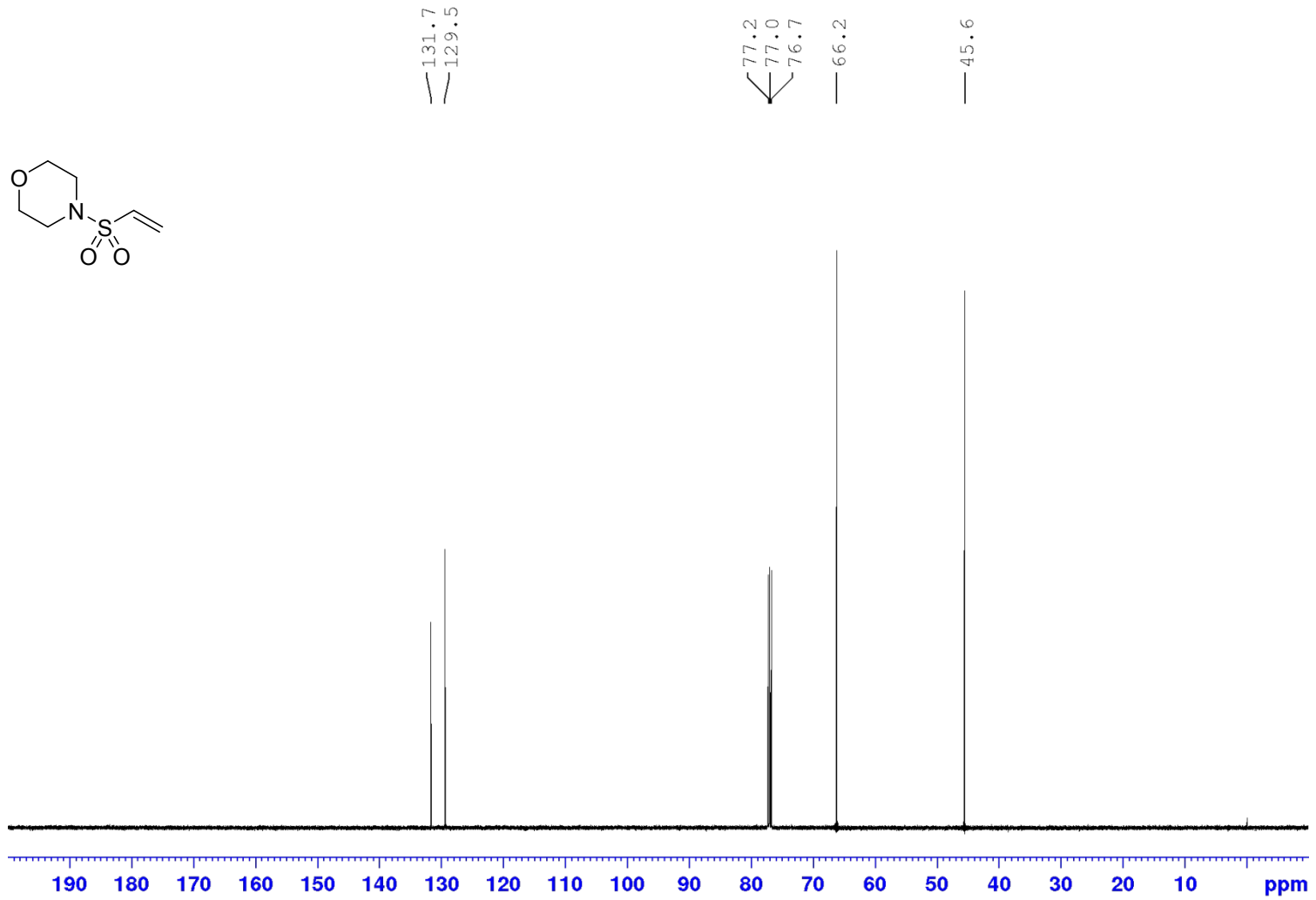
2-Bromo-1-morpholinoethan-1-one (35) – ^{13}C – CDCl_3 – 125 MHz



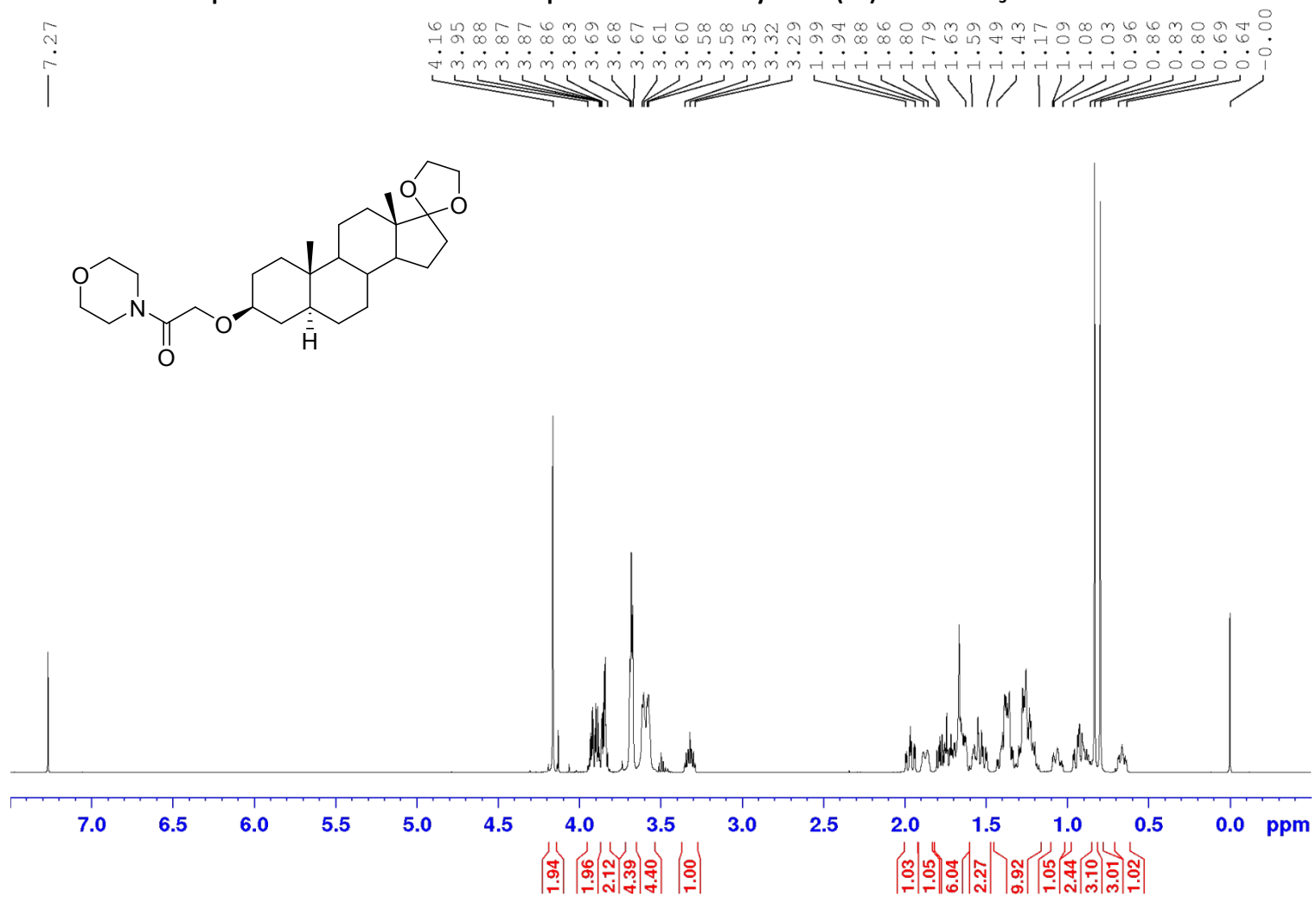
4-(Vinylsulfonyl)morpholine (36) – ^1H – CDCl_3 – 500 MHz



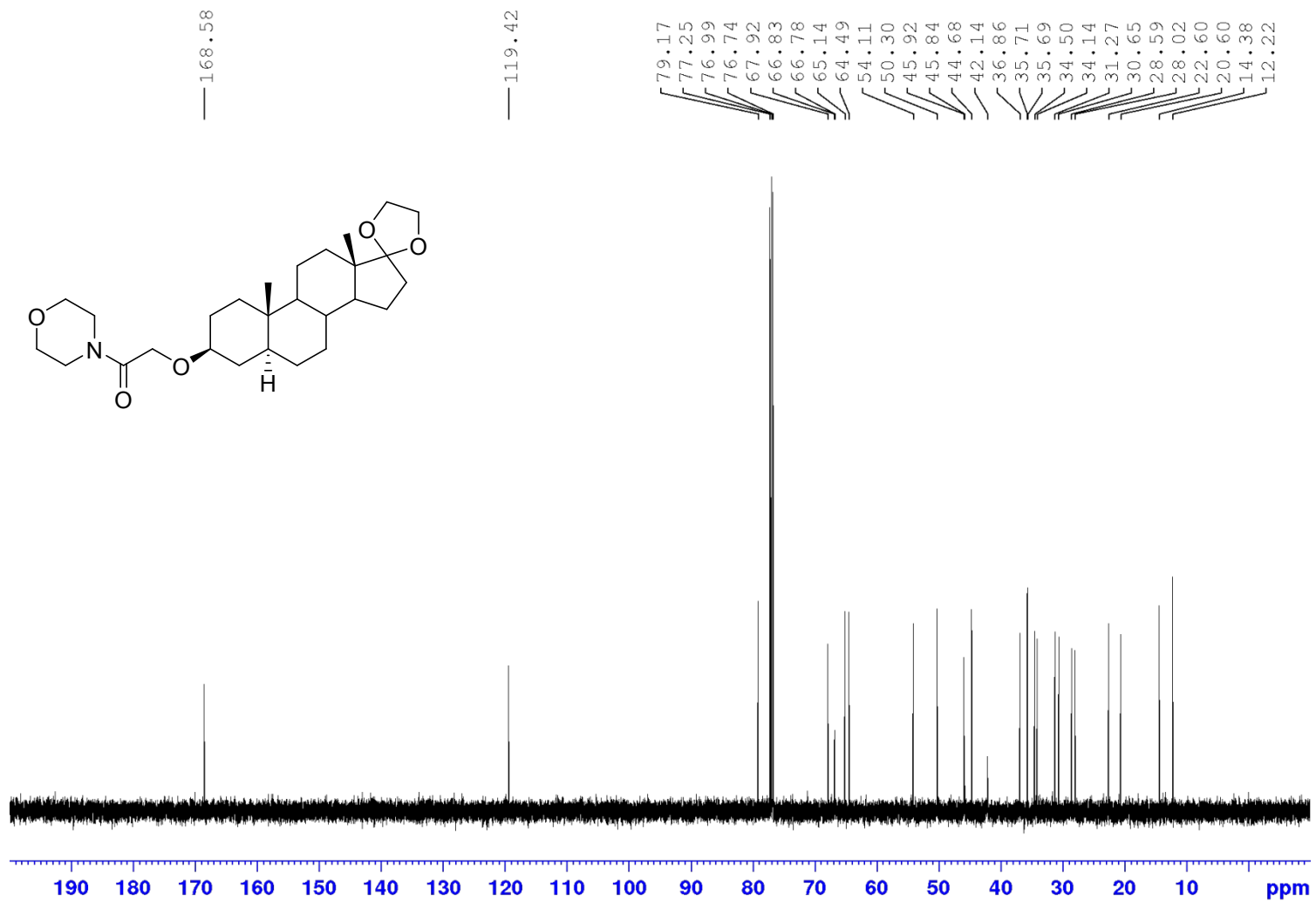
4-(Vinylsulfonyl)morpholine (36) – ^{13}C – CDCl_3 – 125 MHz



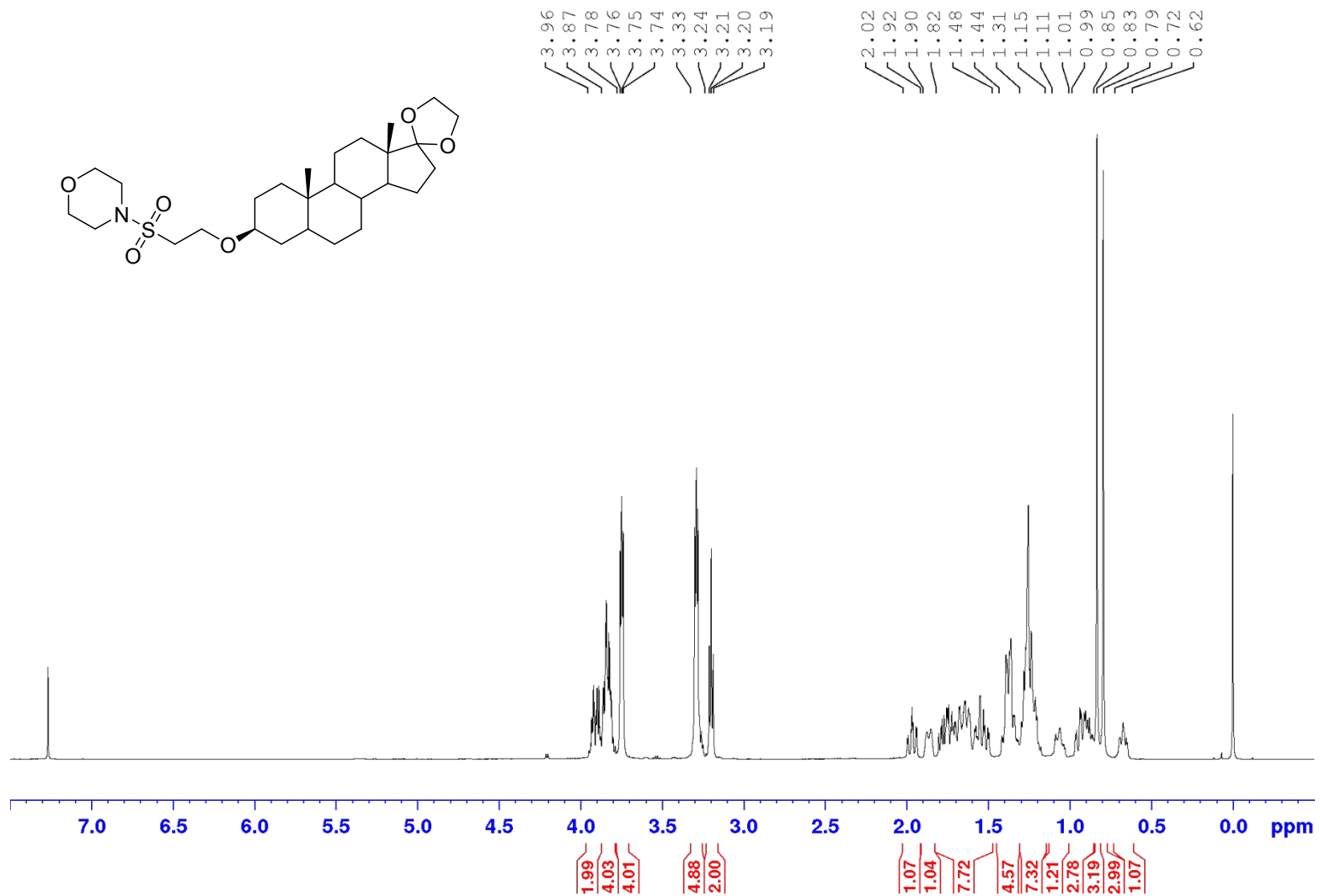
Epiandrosterone 17-acetal 2-morpholino-2-oxoethoxy ether (37) – ^1H – CDCl_3 – 500 MHz



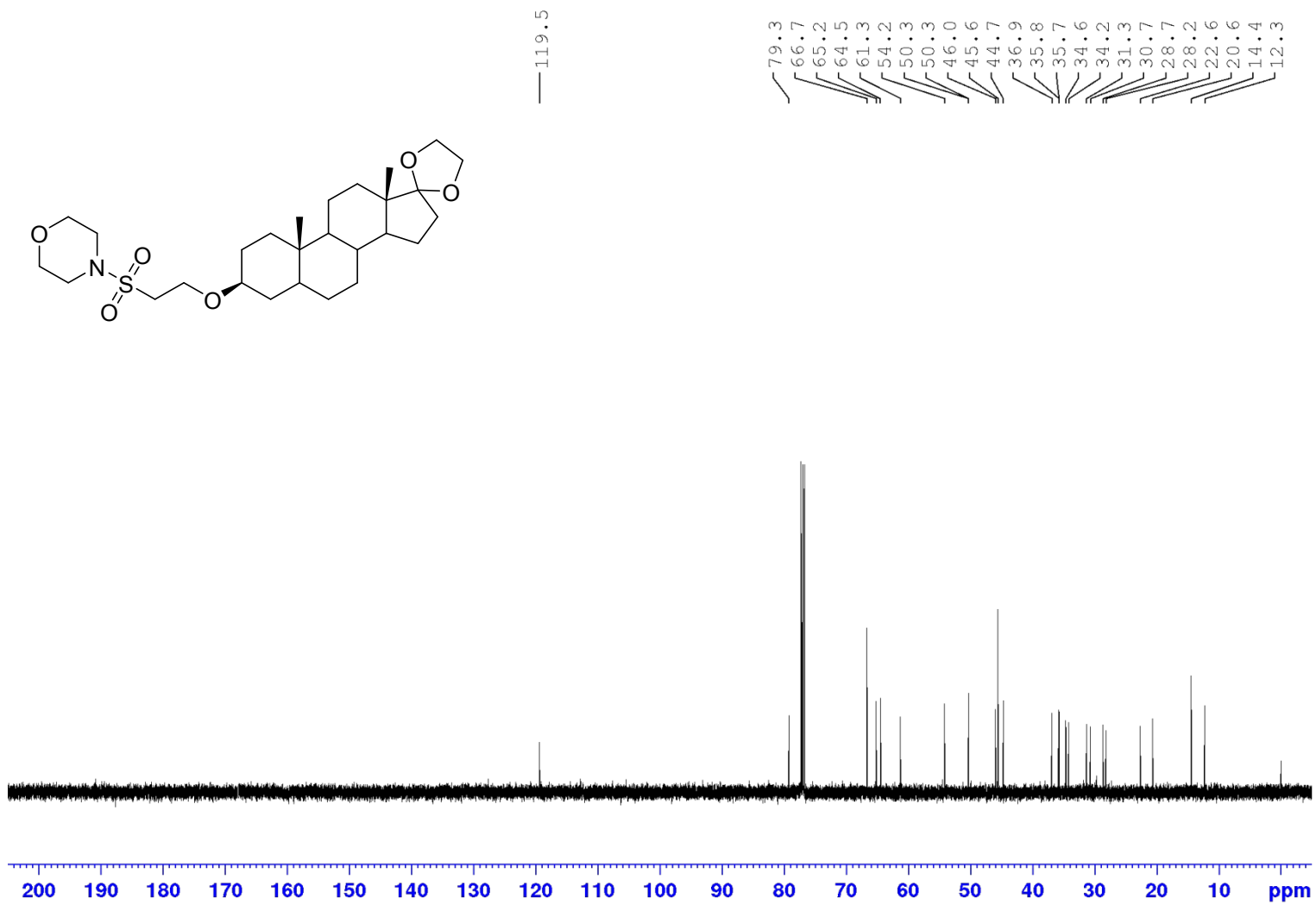
Epiandrosterone 17-acetal 2-morpholino-2-oxoethoxy ether (37) – ^{13}C – CDCl_3 – 125 MHz



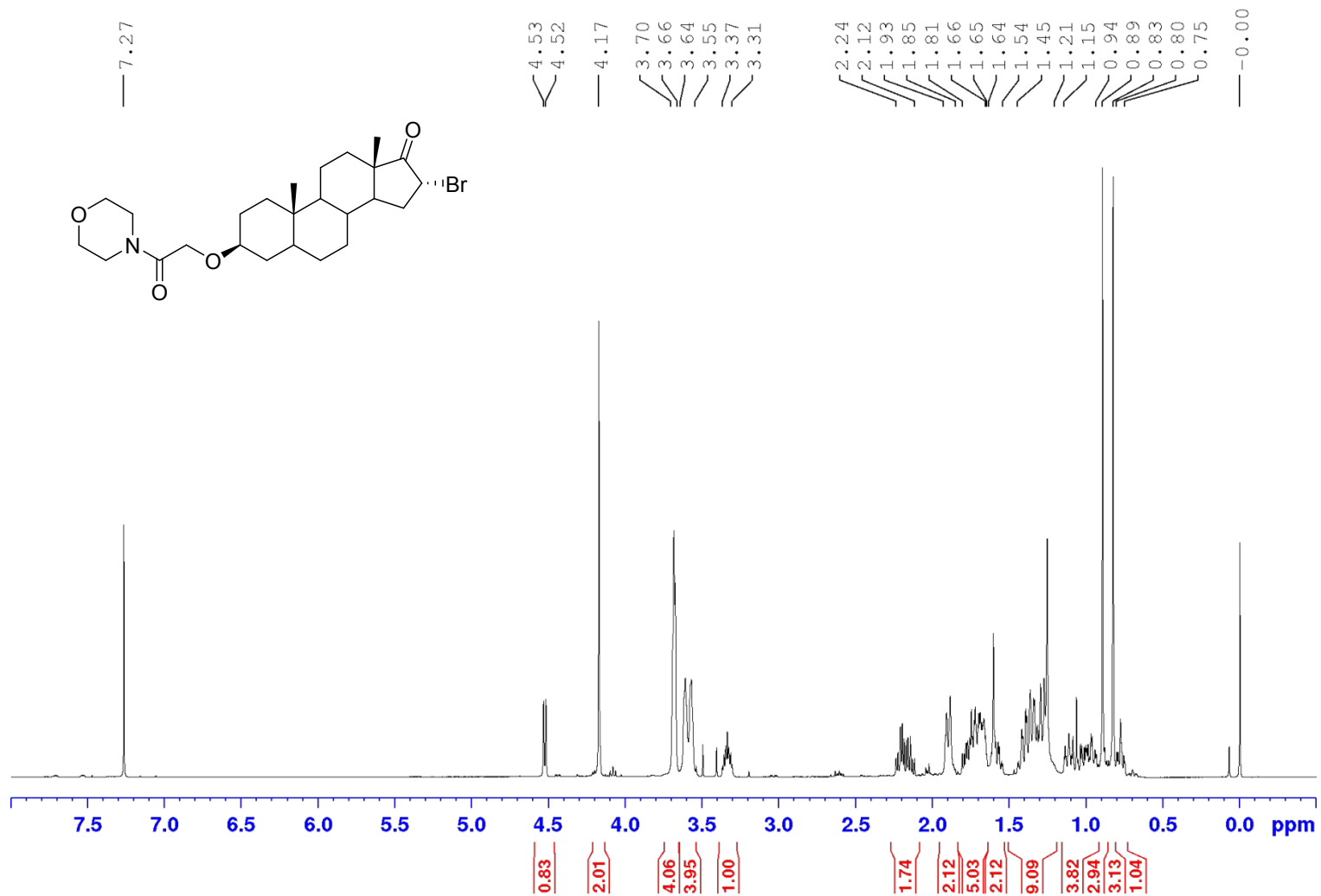
Epiandrosterone 17-acetal 2-(morphinosulfonyl)ethyl ether (38) – ^1H – CDCl_3 – 500 MHz



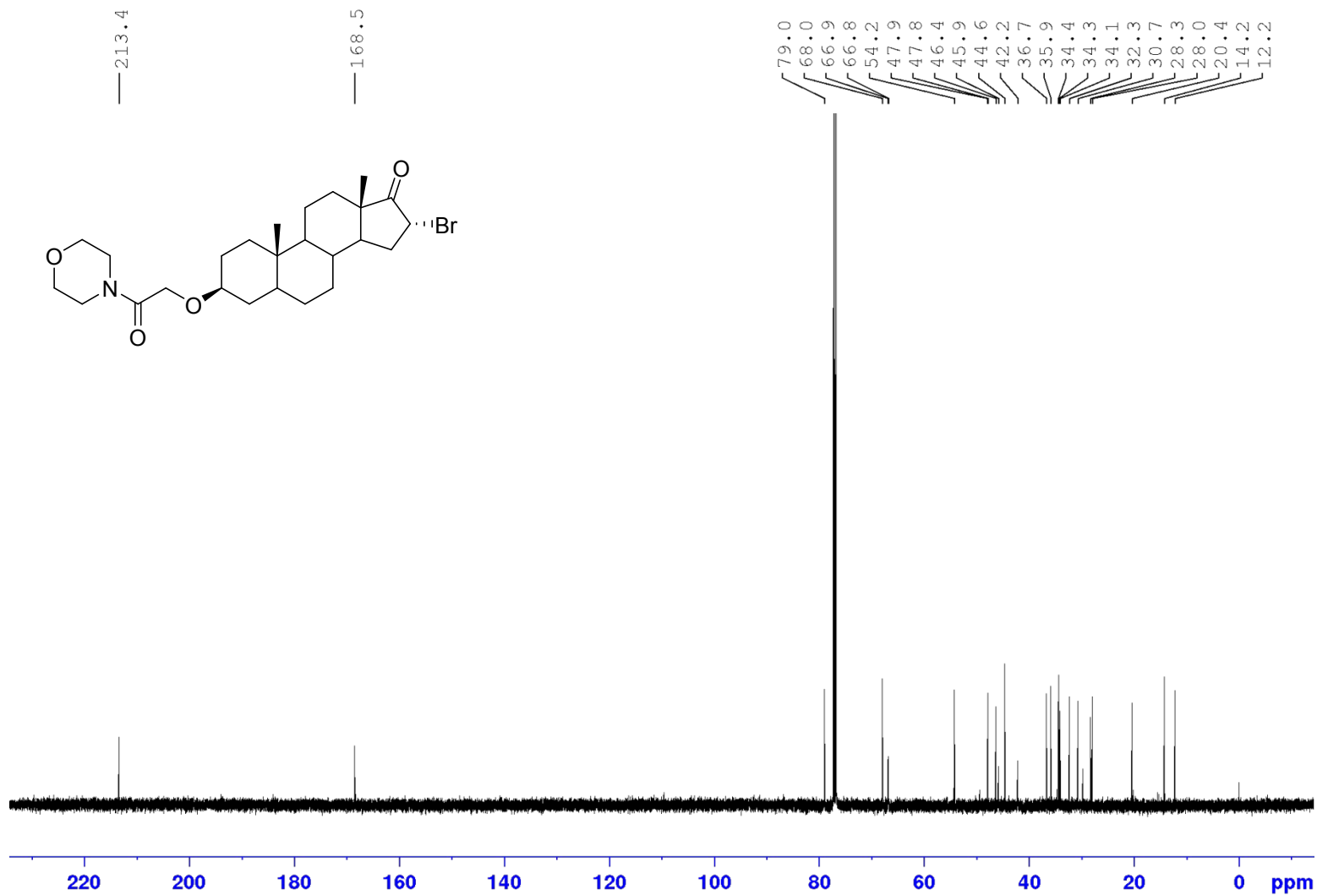
Epiandrosterone 17-acetal 2-(morpholinosulfonyl)ethyl ether (38) – ^{13}C – CDCl_3 – 125 MHz



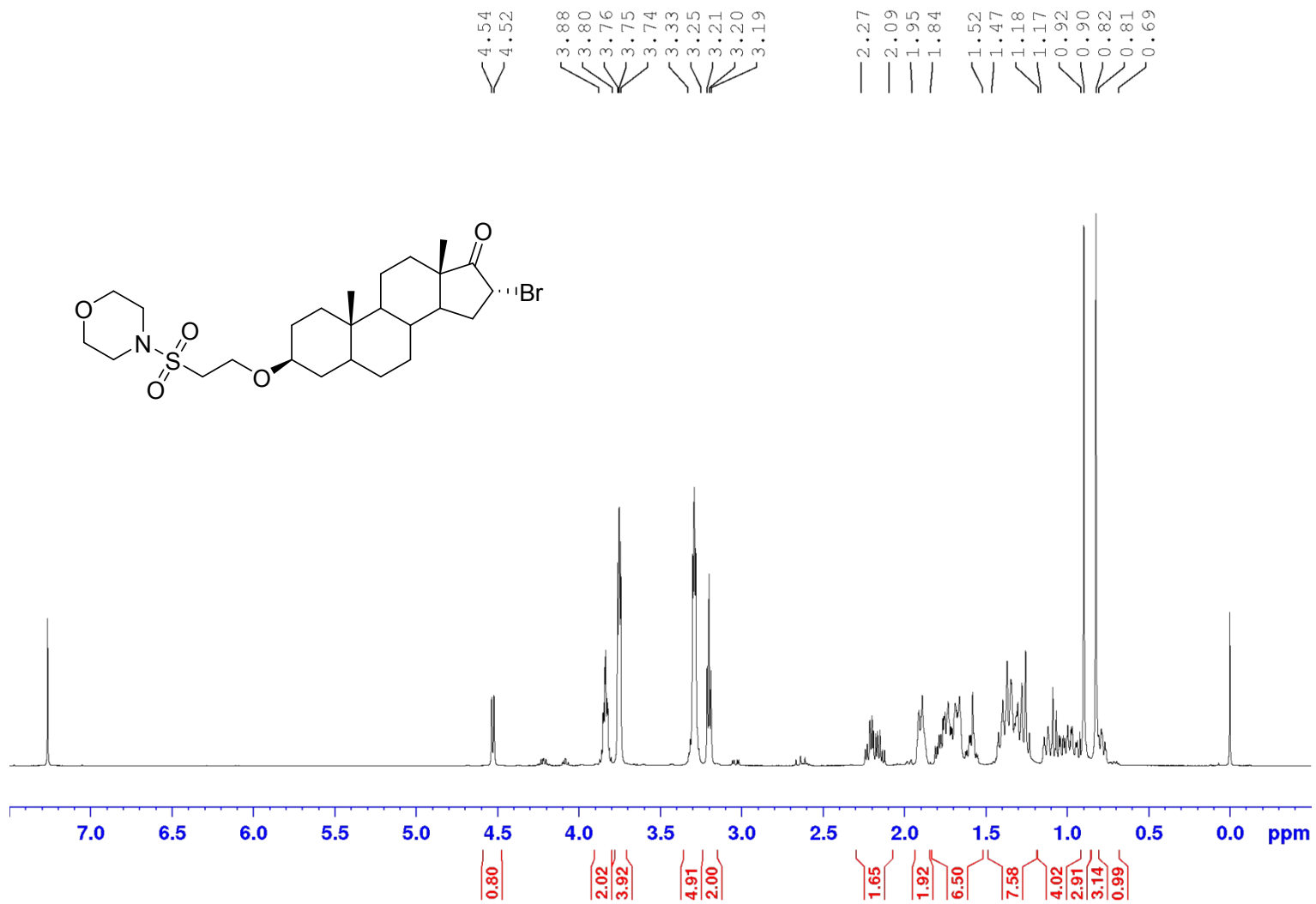
16 α -Bromoepiandrosterone 2-morpholino-2-oxoethoxy ether (39) – ^1H – CDCl_3 – 500 MHz



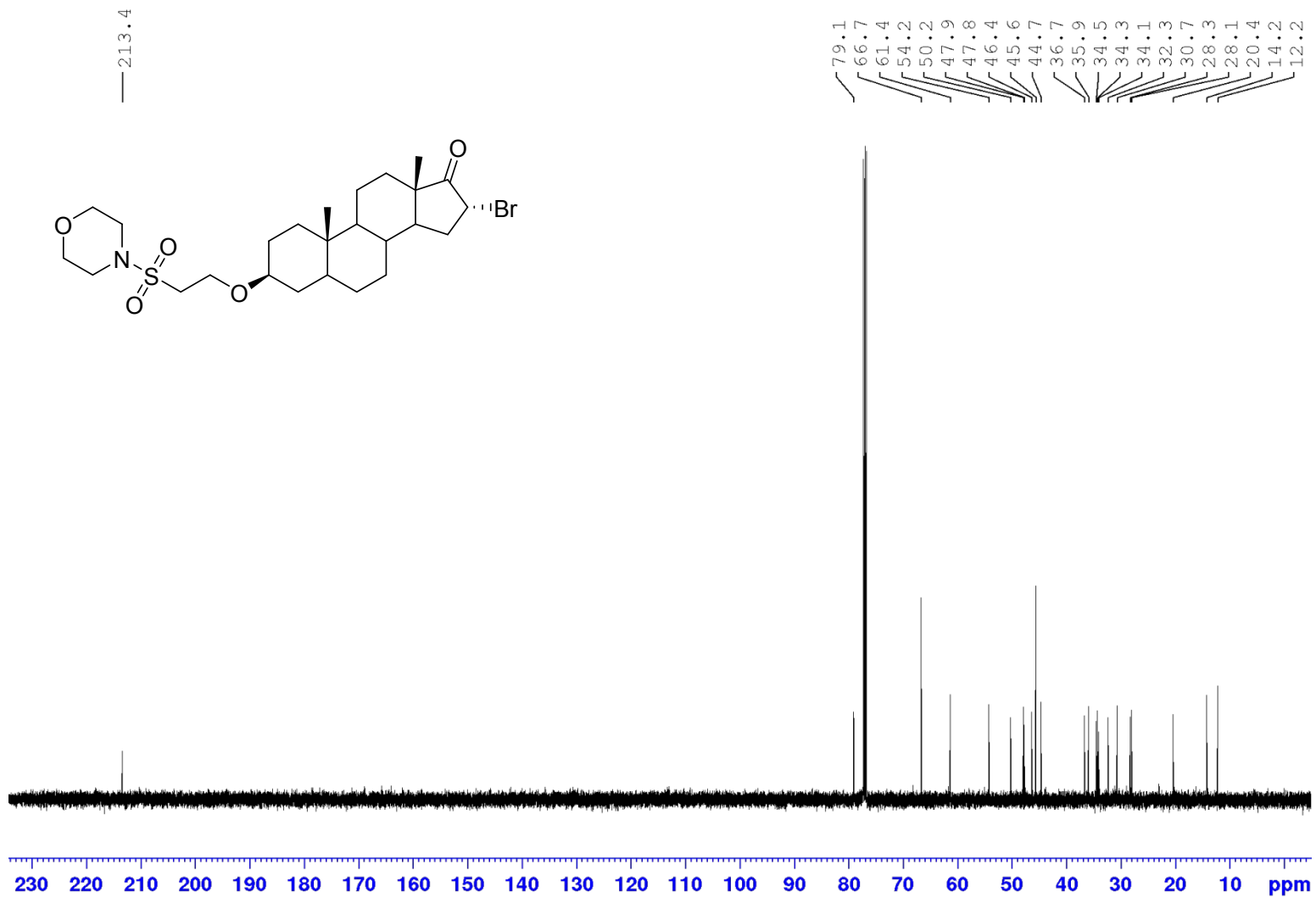
16 α -Bromoepiandrosterone 2-morpholino-2-oxoethoxy ether (39) – ^{13}C – CDCl_3 – 125 MHz



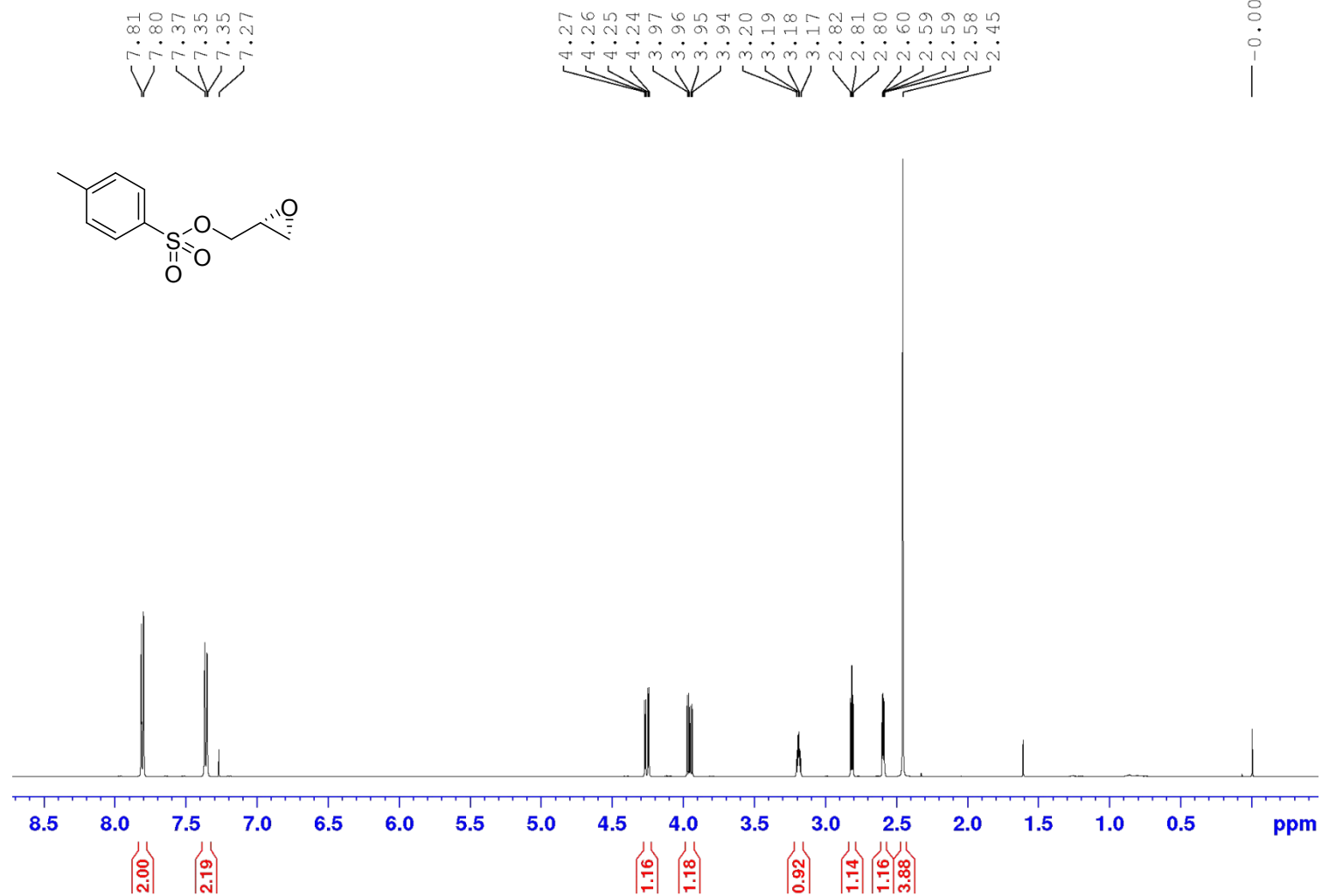
16 α -Bromoepiandrosterone 2-(morpholinosulfonyl)ethyl ether (40) – ^1H – CDCl_3 – 500 MHz



16 α -Bromoepiandrosterone 2-(morpholinosulfonyl)ethyl ether (40) – ^{13}C – CDCl_3 – 125 MHz

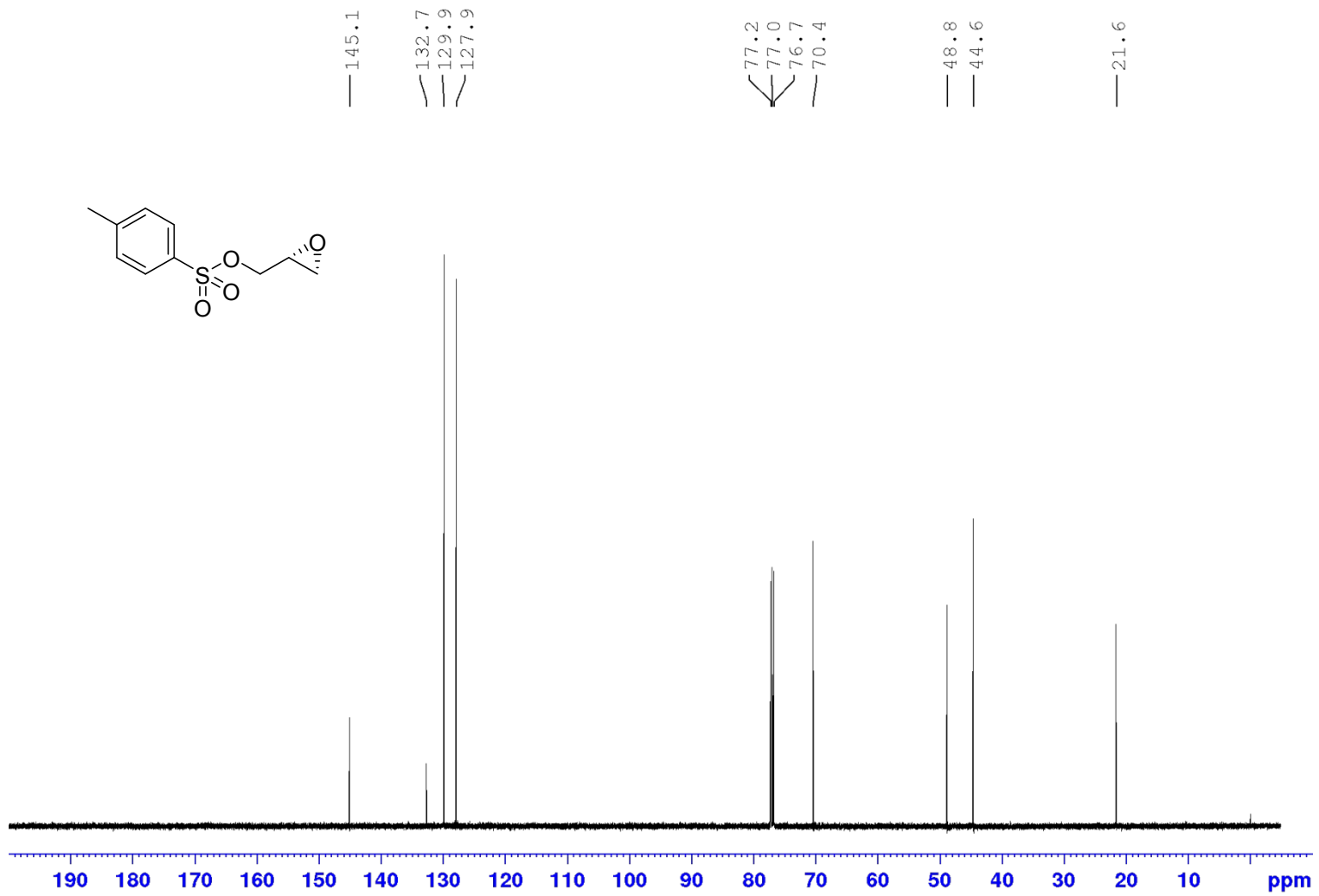


(R)-Oxiran-2-ylmethyl 4-methylbenzenesulfonate (41) – ^1H – CDCl_3 – 500 MHz

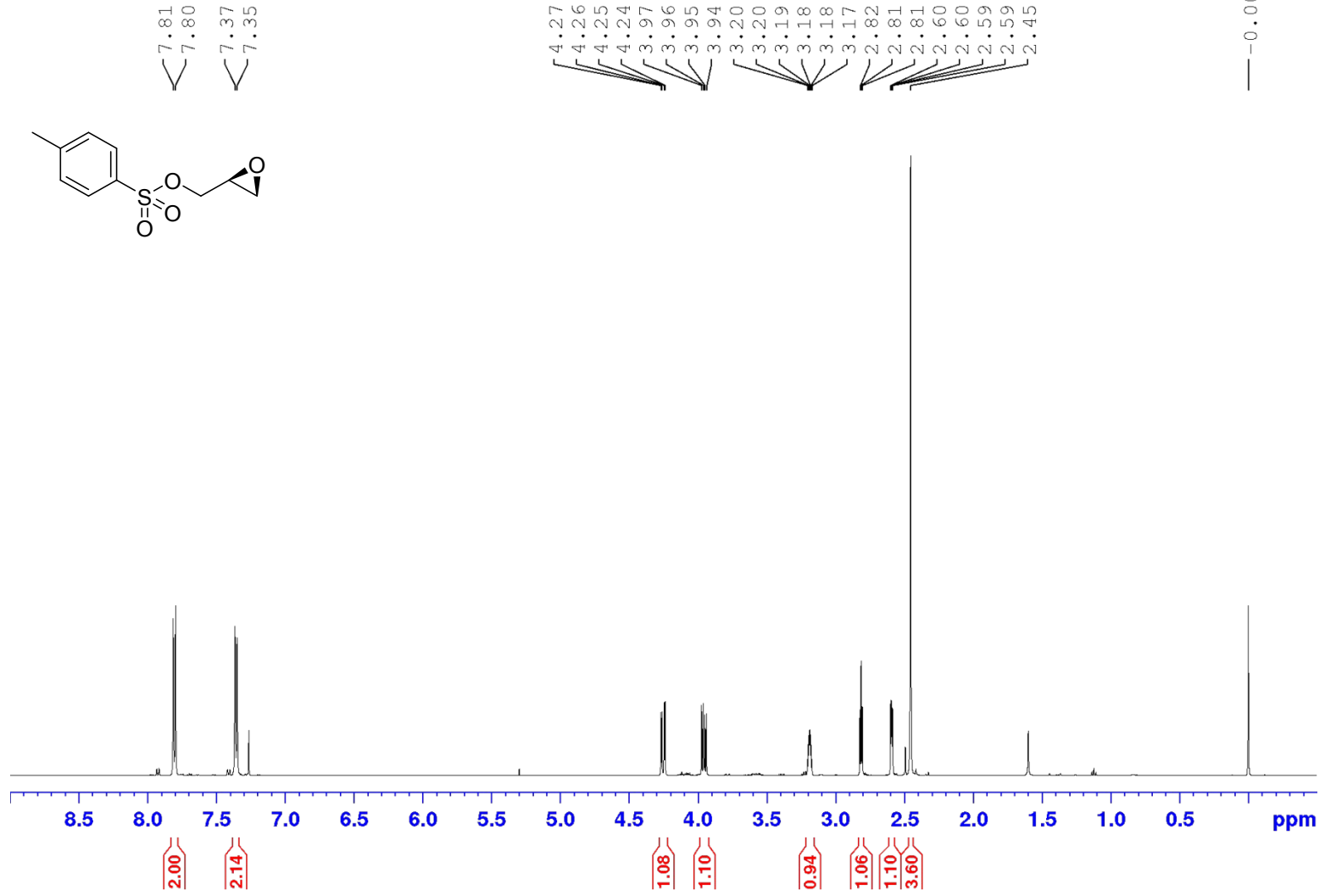


— — 0.00

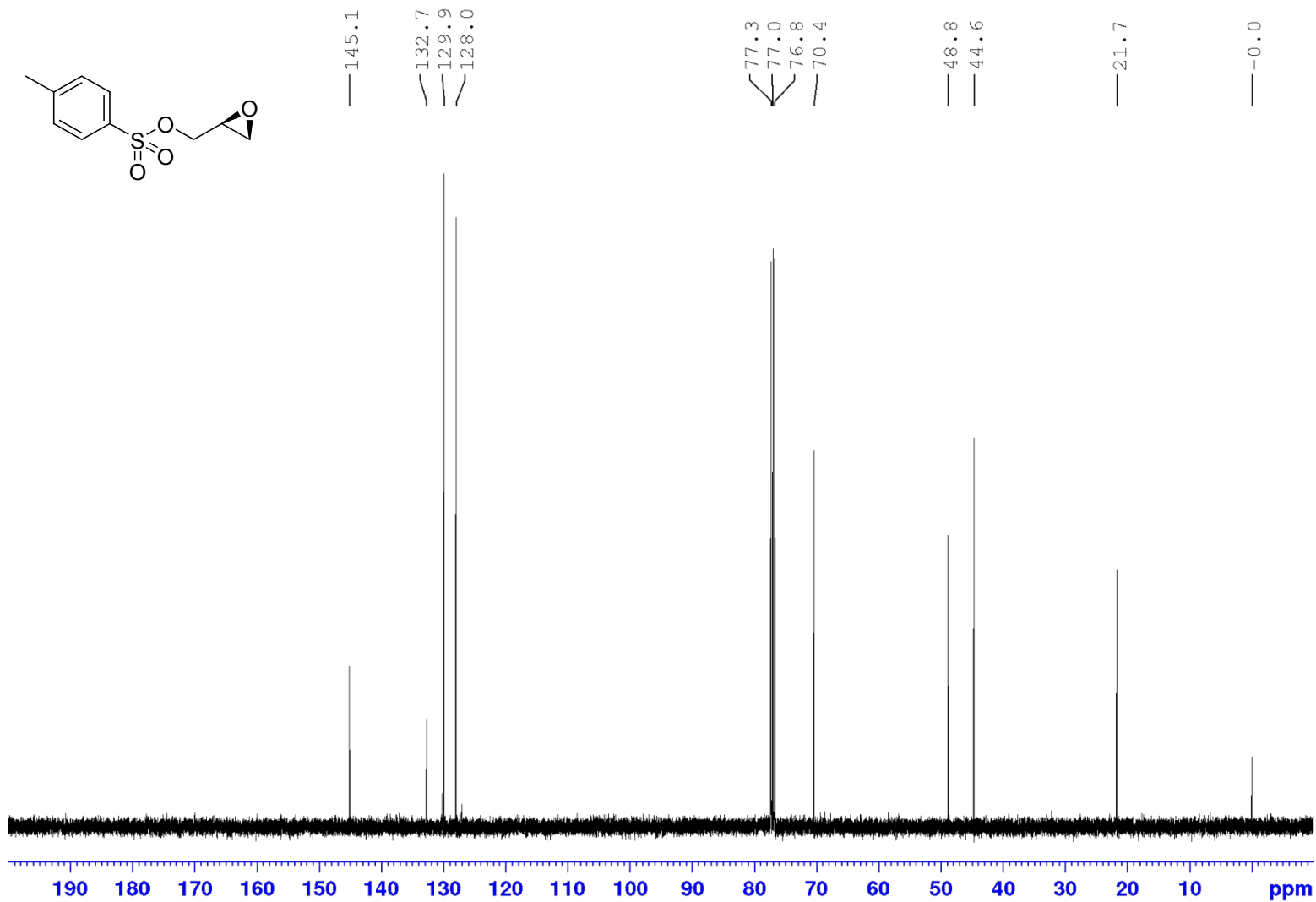
(R)-Oxiran-2-ylmethyl 4-methylbenzenesulfonate (41) – ^{13}C – CDCl_3 – 125 MHz



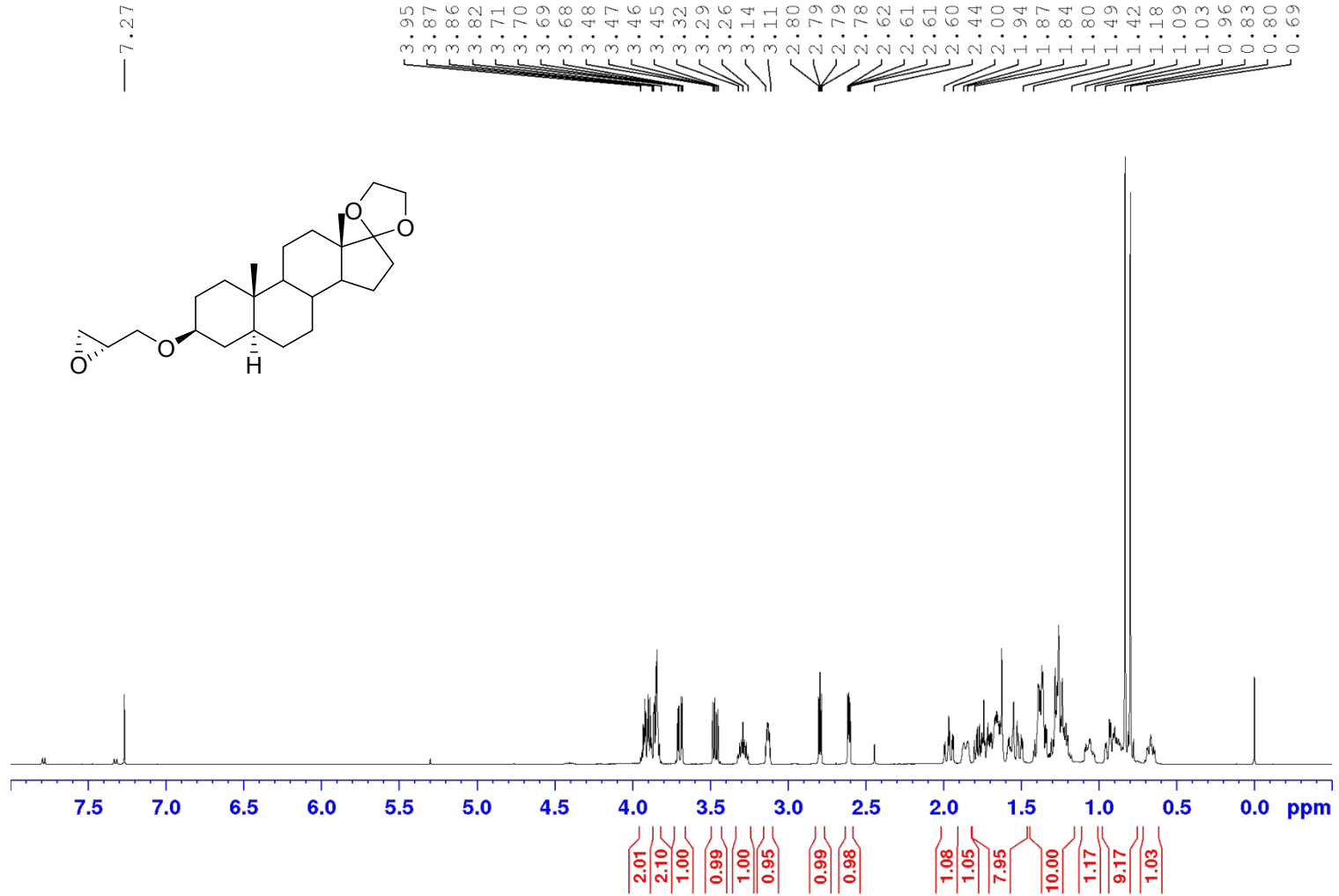
(S)-Oxiran-2-ylmethyl 4-methylbenzenesulfonate (42) – ^1H – CDCl_3 – 500 MHz



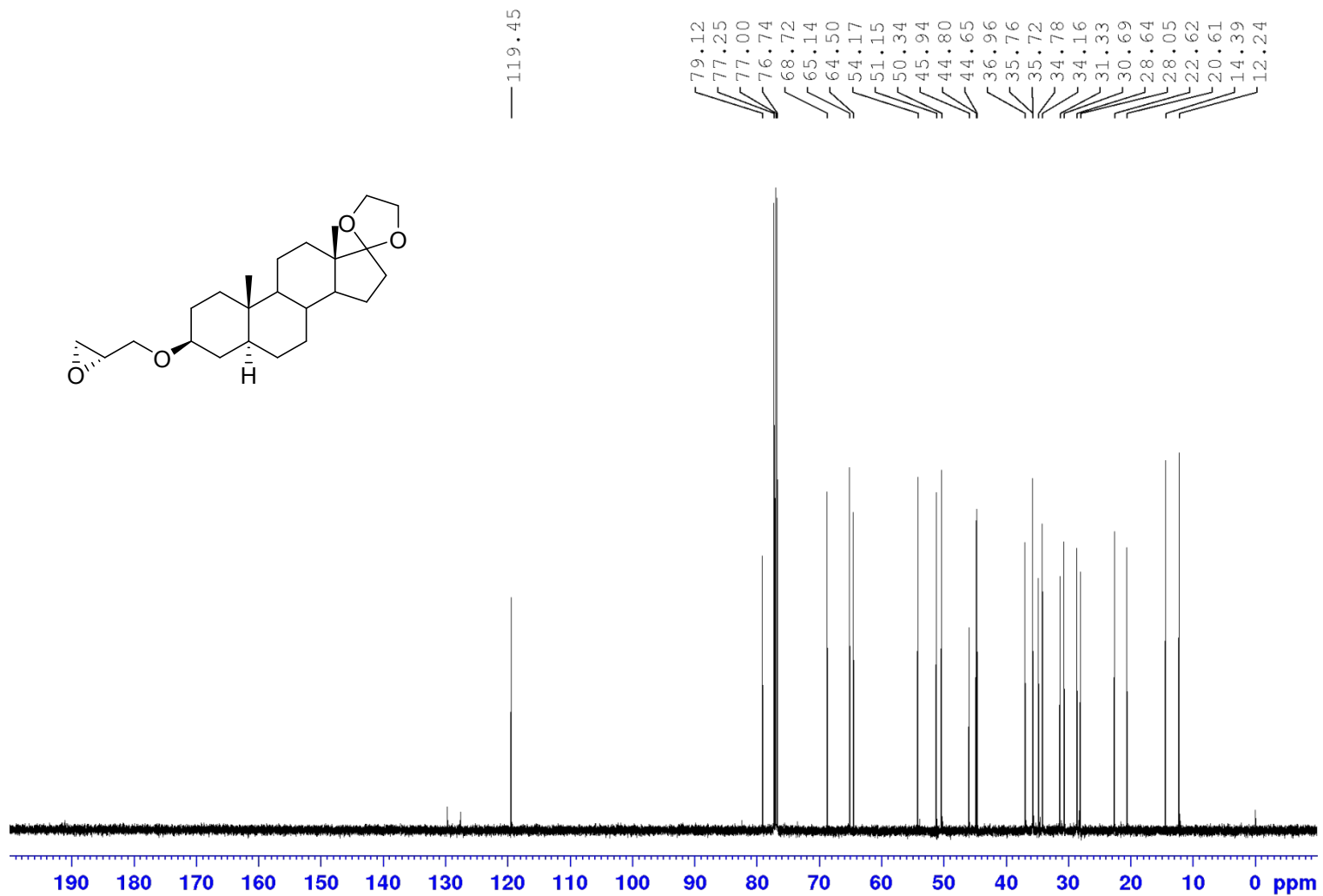
(S)-Oxiran-2-ylmethyl 4-methylbenzenesulfonate (42) – ^{13}C – CDCl_3 – 125 MHz



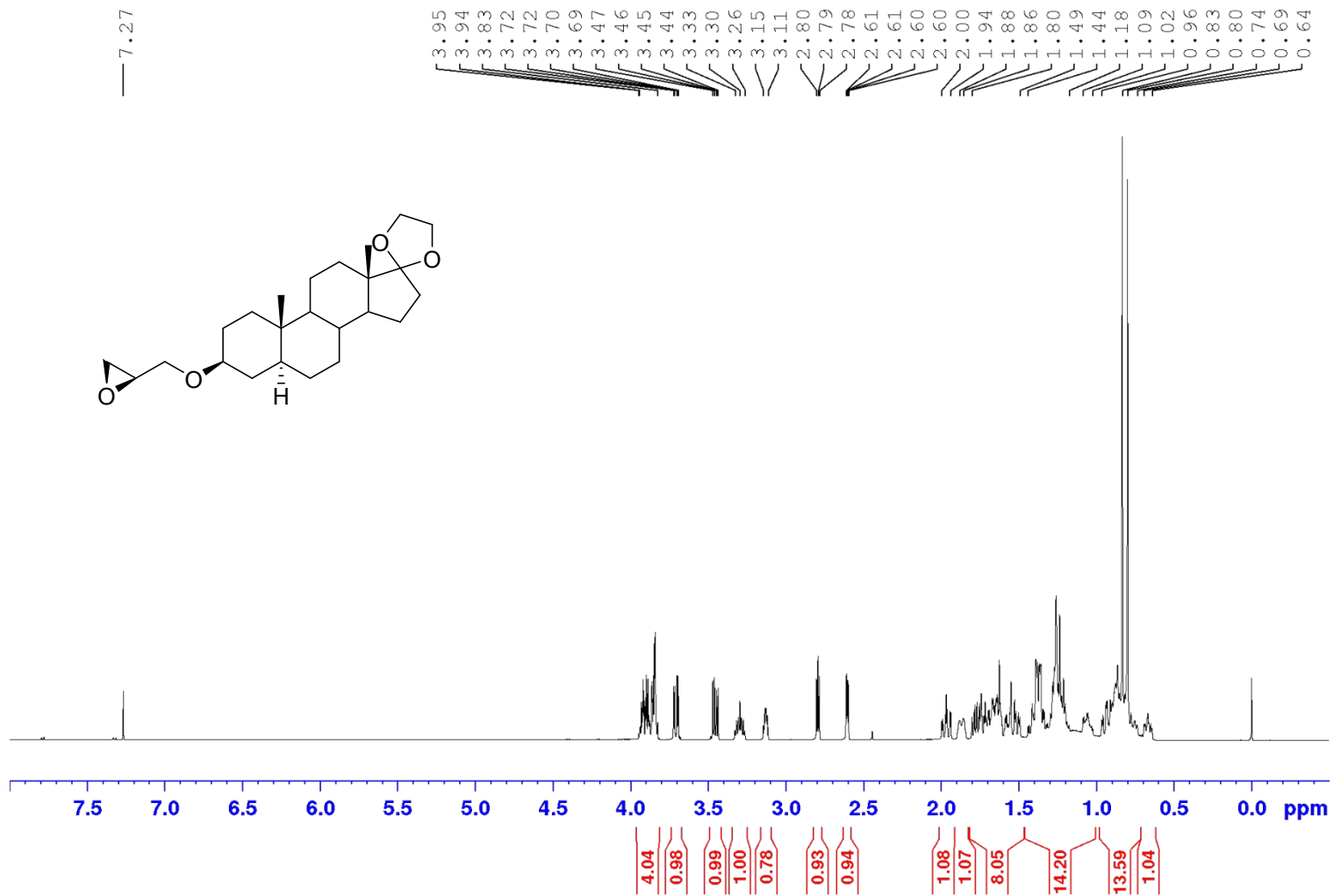
Epiandrosterone 17-acetal (*R*-oxiran-2-yl)methyl ether (45) - ^1H - CDCl_3 - 500 MHz



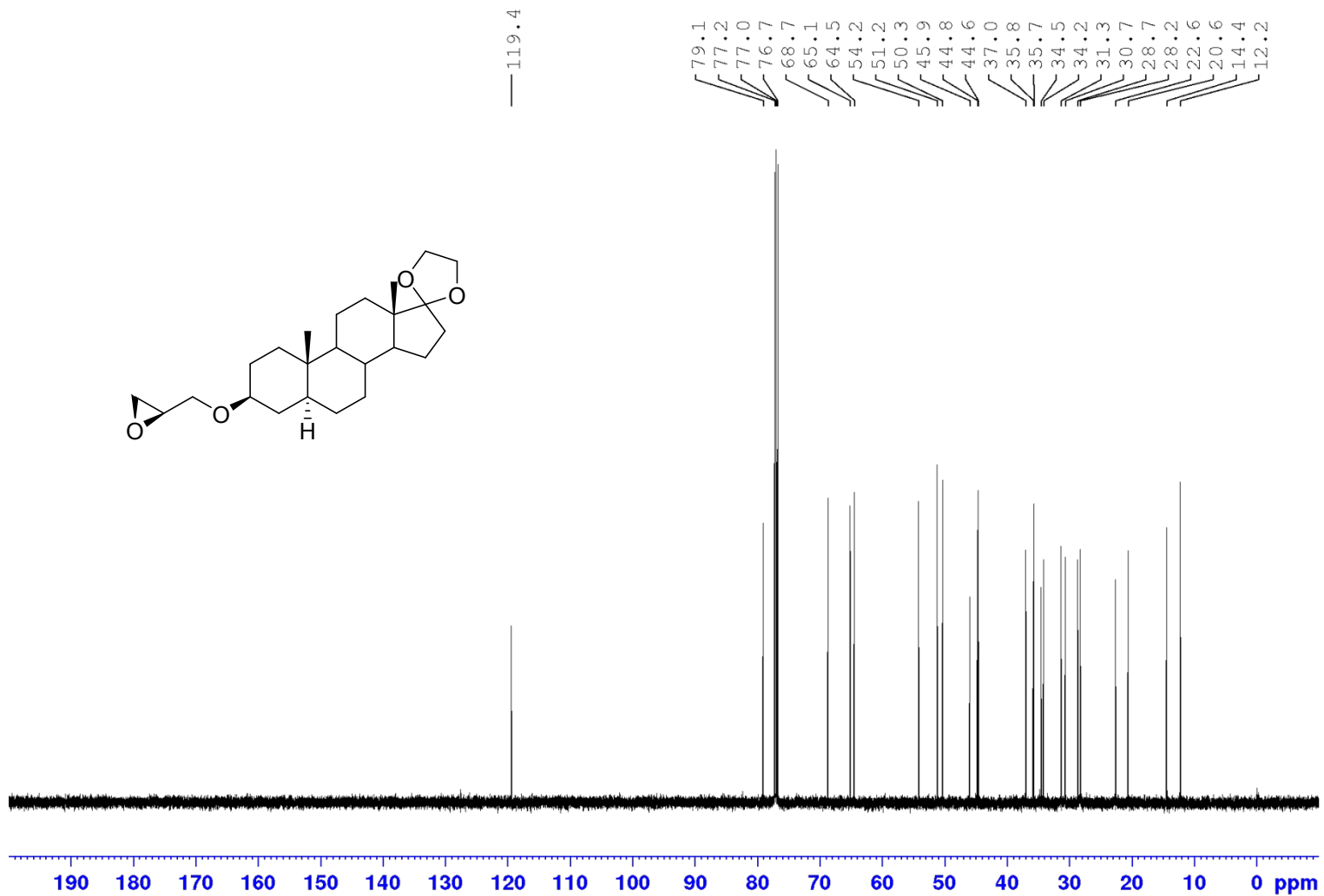
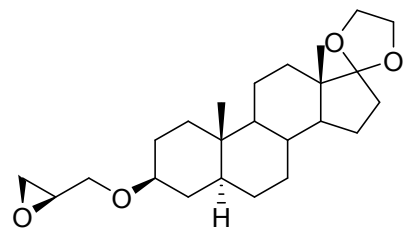
Epiandrosterone 17-acetal (*R*-oxiran-2-yl)methyl ether (45) – ^{13}C – CDCl_3 – 125 MHz



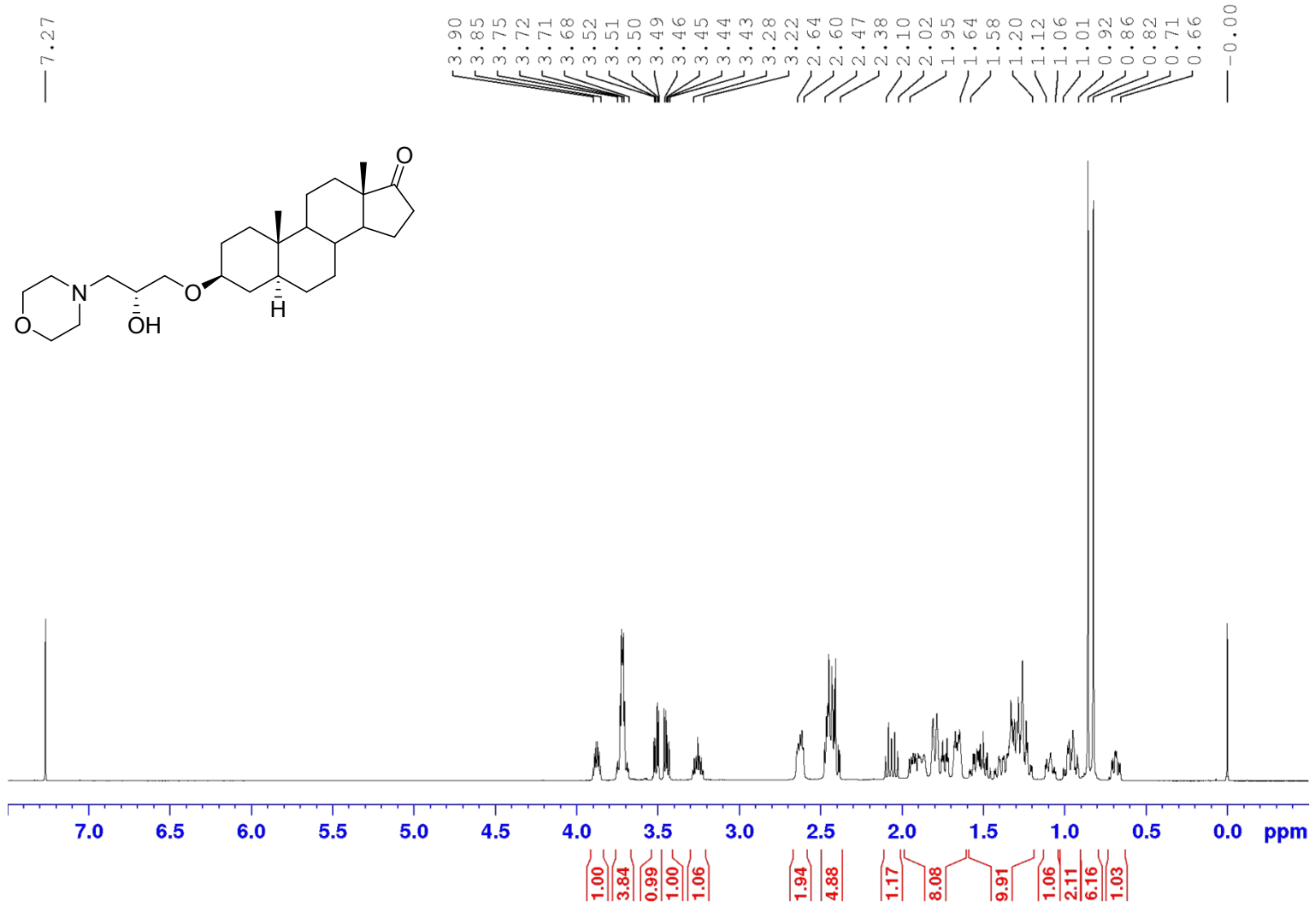
Epiandrosterone 17-acetal (*S*-oxiran-2-yl)methyl ether (46) – ^1H – CDCl_3 – 500 MHz



Epiandrosterone 17-acetal (*S*-oxiran-2-yl)methyl ether (46) – ^{13}C – CDCl_3 – 125 MHz



Epiandrosterone (*R*)-2-hydroxy-3-morpholinopropyl ether (47) – ¹H – CDCl₃ – 500 MHz

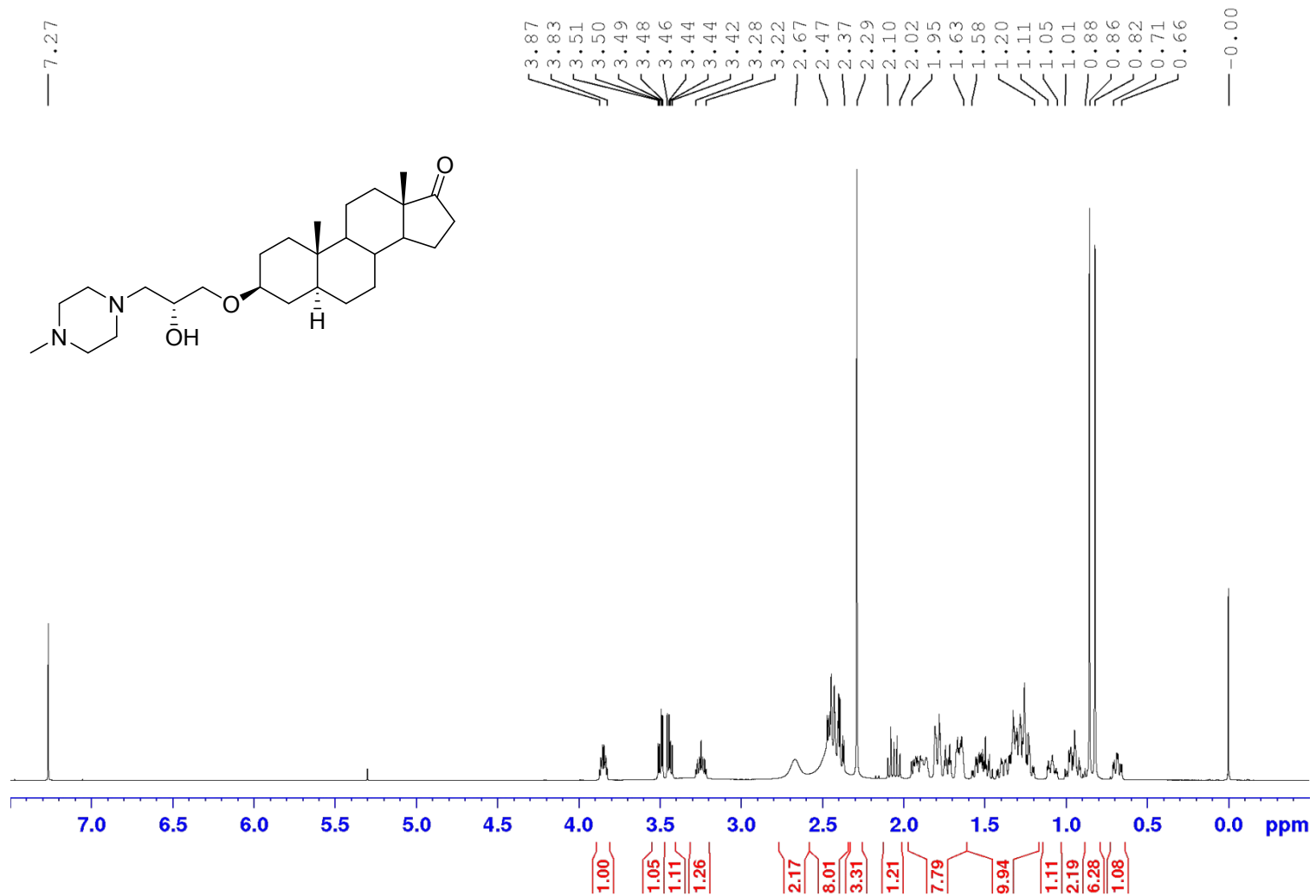


Epiandrosterone (*R*)-2-hydroxy-3-morpholinopropyl ether (47) – ^{13}C – CDCl_3 – 125 MHz



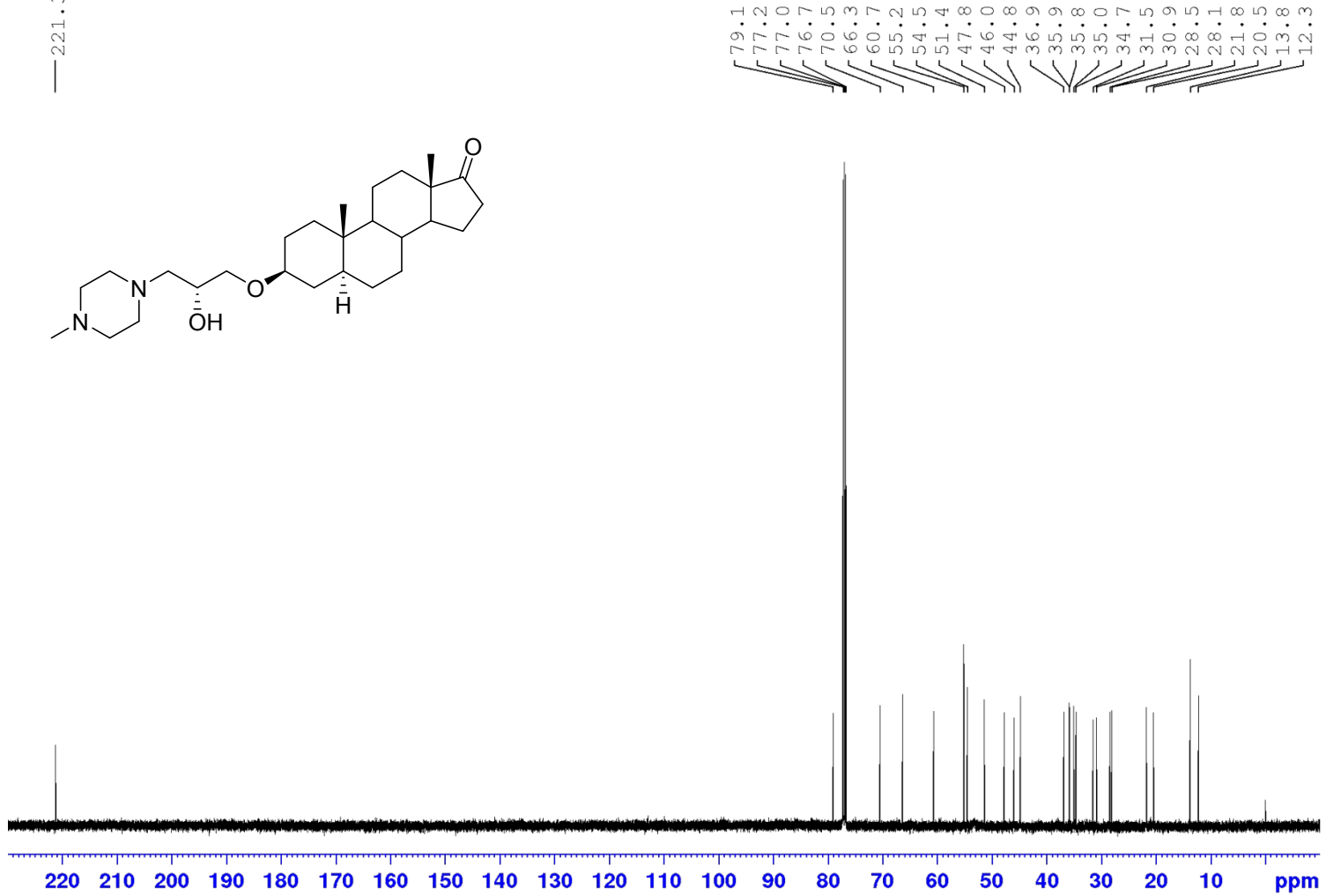
— 221.3

Epiandrosterone (*R*)-2-hydroxy-3-(4-methylpiperazin-1-yl)propyl ether (48) – ^1H – CDCl_3 – 500 MHz

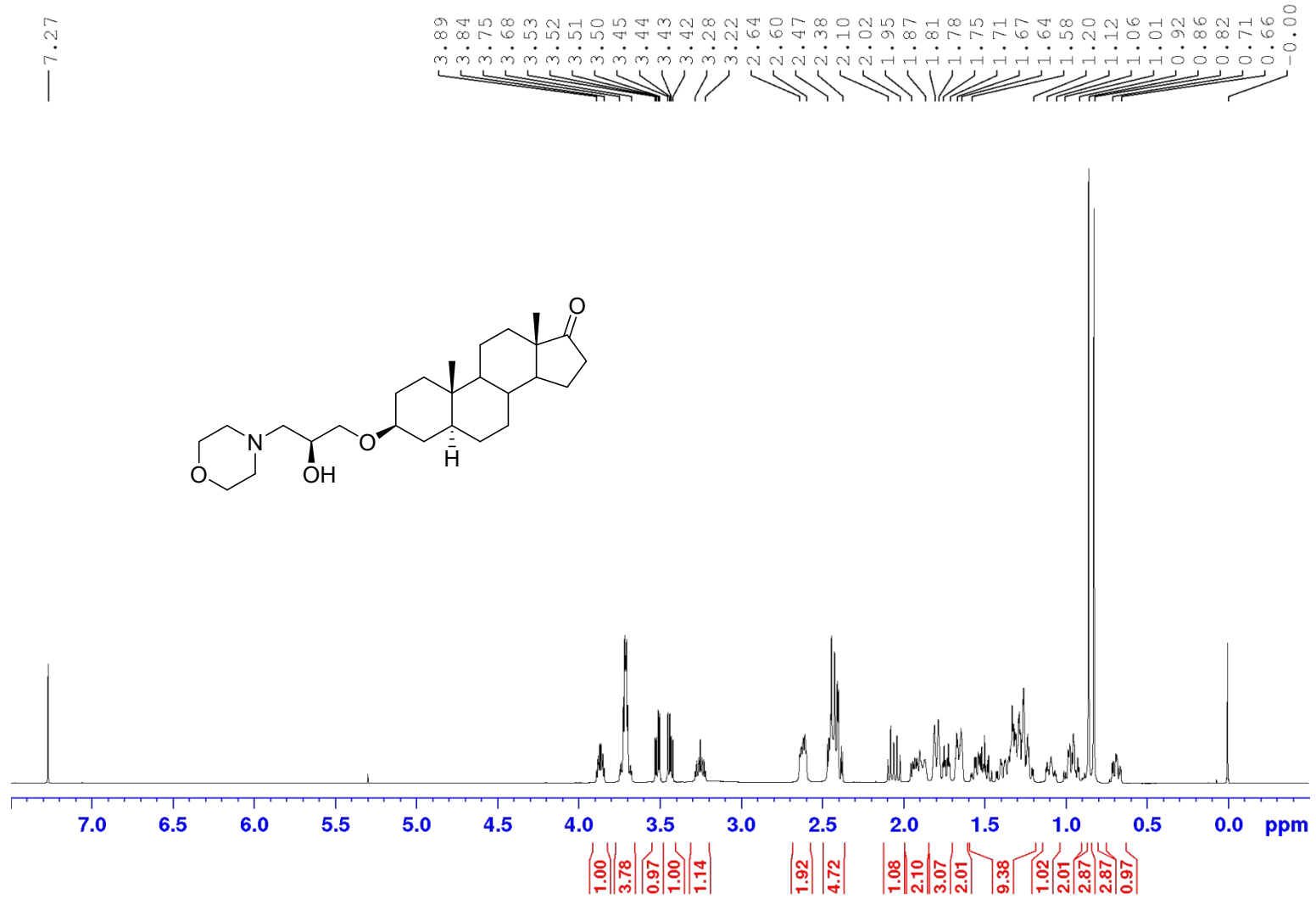


— 221.3

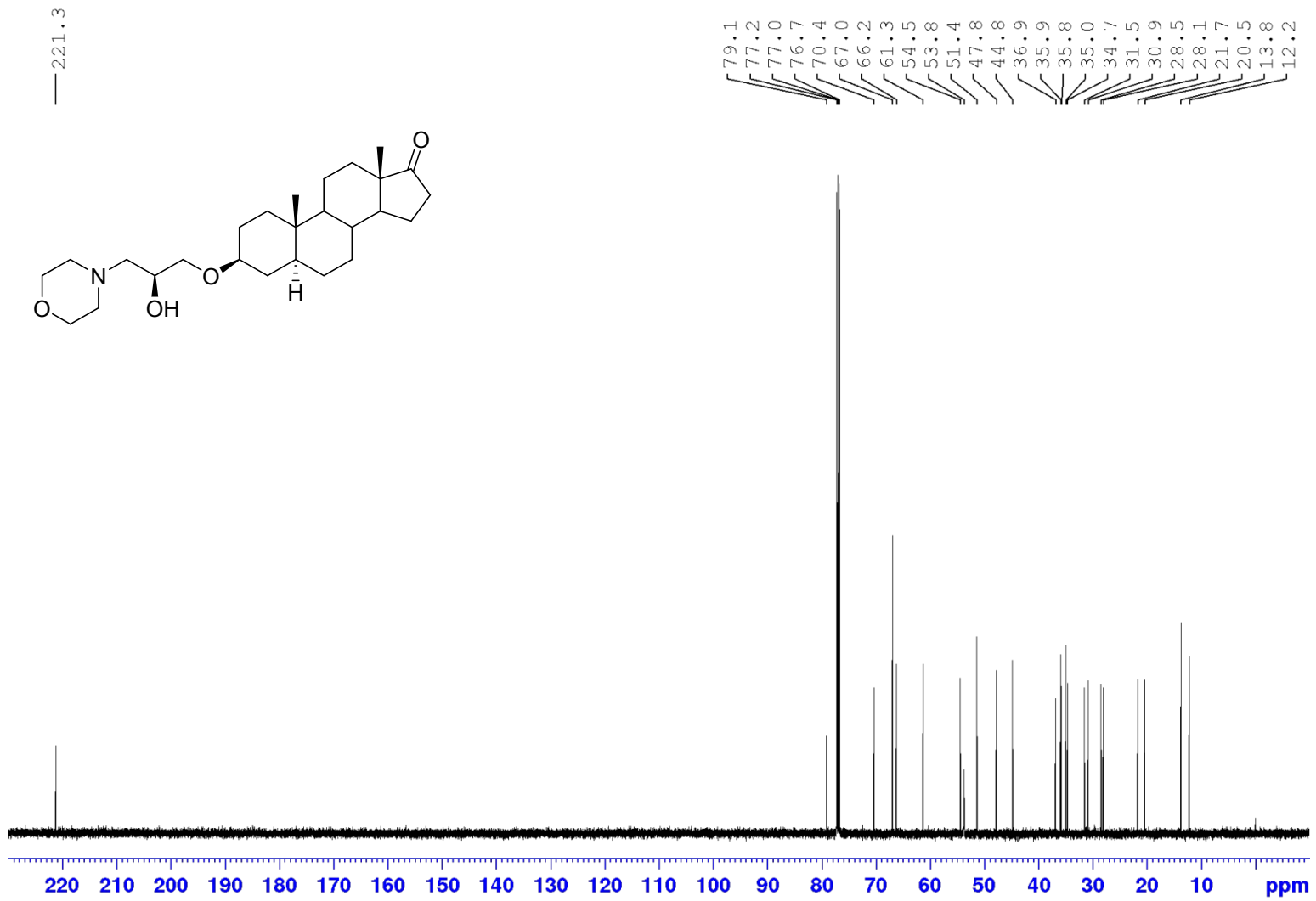
Epiandrosterone (*R*)-2-hydroxy-3-(4-methylpiperazin-1-yl)propyl ether (48) – ^{13}C – CDCl_3 – 125 MHz



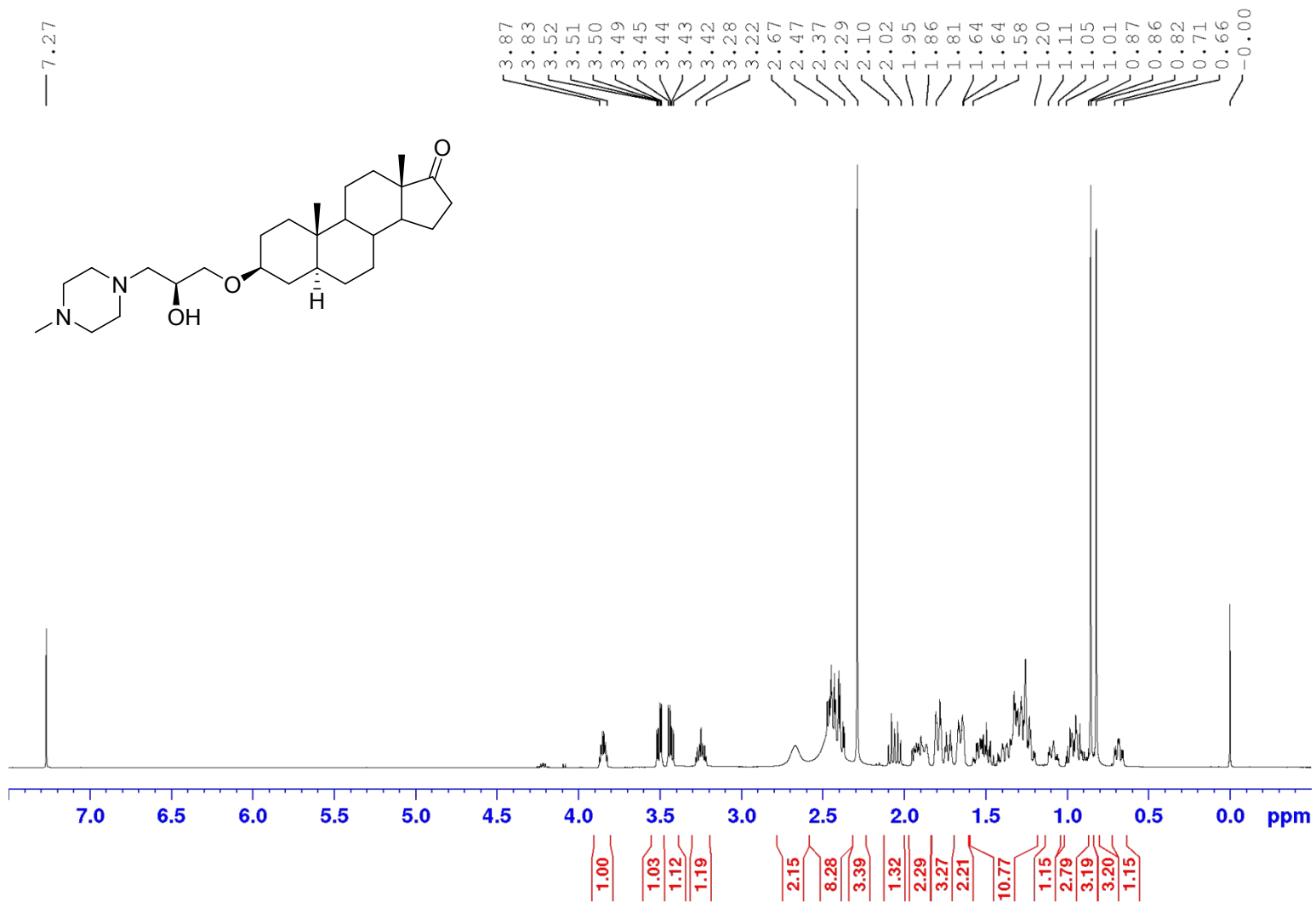
Epiandrosterone (S)-2-hydroxy-3-morpholinopropyl ether (49) – ¹H – CDCl₃ – 500 MHz



Epiandrosterone (S)-2-hydroxy-3-morpholinopropyl ether (49) – ^{13}C – CDCl_3 – 125 MHz



Epiandrosterone (S)-2-hydroxy-3-(4-methylpiperazin-1-yl)propyl ether (50) – ^1H – CDCl_3 – 500 MHz



— 221.3

Epiandrosterone (S)-2-hydroxy-3-(4-methylpiperazin-1-yl)propyl ether (50) – ^{13}C – CDCl_3 – 125 MHz

