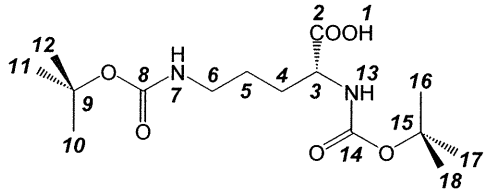
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Synthesis, characterisation and antimicrobial activity of conjugates between fluoroquinolones and staphyloferrin-type siderophores

Stephen J. Milner[a], Alexandra Seve[a], Anna M. Snelling[b], Gavin H. Thomas[c], Kevin G. Kerr[b, d], Anne Routledge[a], Anne-Kathrin Duhme-Klair[a*]*

Data for (2*R*)-2, 5-bis({[(*tert*-butoxy)carbonyl]amino})pentanoic acid (2a).

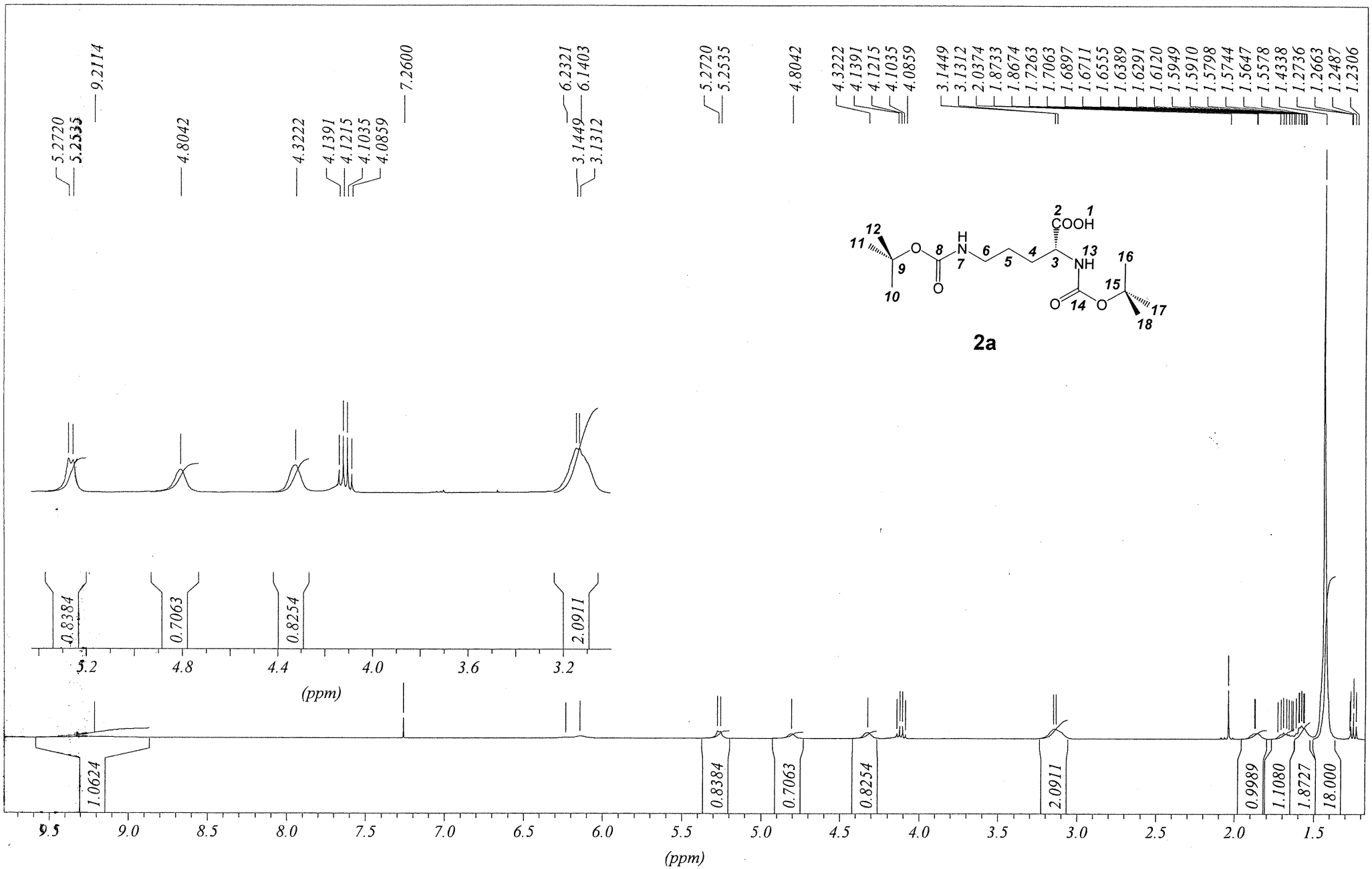


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 9.21 (1H, br s, H-***1***), 5.25 (1H, d, $^3J_{H\text{-}H}$ = 7.40 Hz, H-***13***), 4.80 (1H, br s, H-***7***), 4.32 (1H, br s, H-***3***), 3.14-3.13 (2H, br m, H-***6***), 1.87-1.87 (1H, br m, H-***4***), 1.73-1.61 (1H, br m, H-***4***), 1.59-1.56 (2H, m, H-***5***), 1.43 (18H, s, H-***10***, ***11***, ***12***, ***16***, ***17***, ***18***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 175.93 (C=O, C-***2***), 156.57 (C=O, C-***14***), 155.83 (C=O, C-***8***), 80.25 (4°-C, C-***14***), 79.74 (4°-C, C-***9***), 53.09 (CH, C-***3***), 40.07 (CH_2, C-***6***), 29.96 (CH_2, C-***4***), 28.52 (CH_3, C-***16***, ***17***, ***18***), 28.46 (CH_3, C-***10***, ***11***, ***12***), 26.17 (CH_2, C-***5***).

c8373sjm: SJM-16-04-10 [DBD-Ornithine]

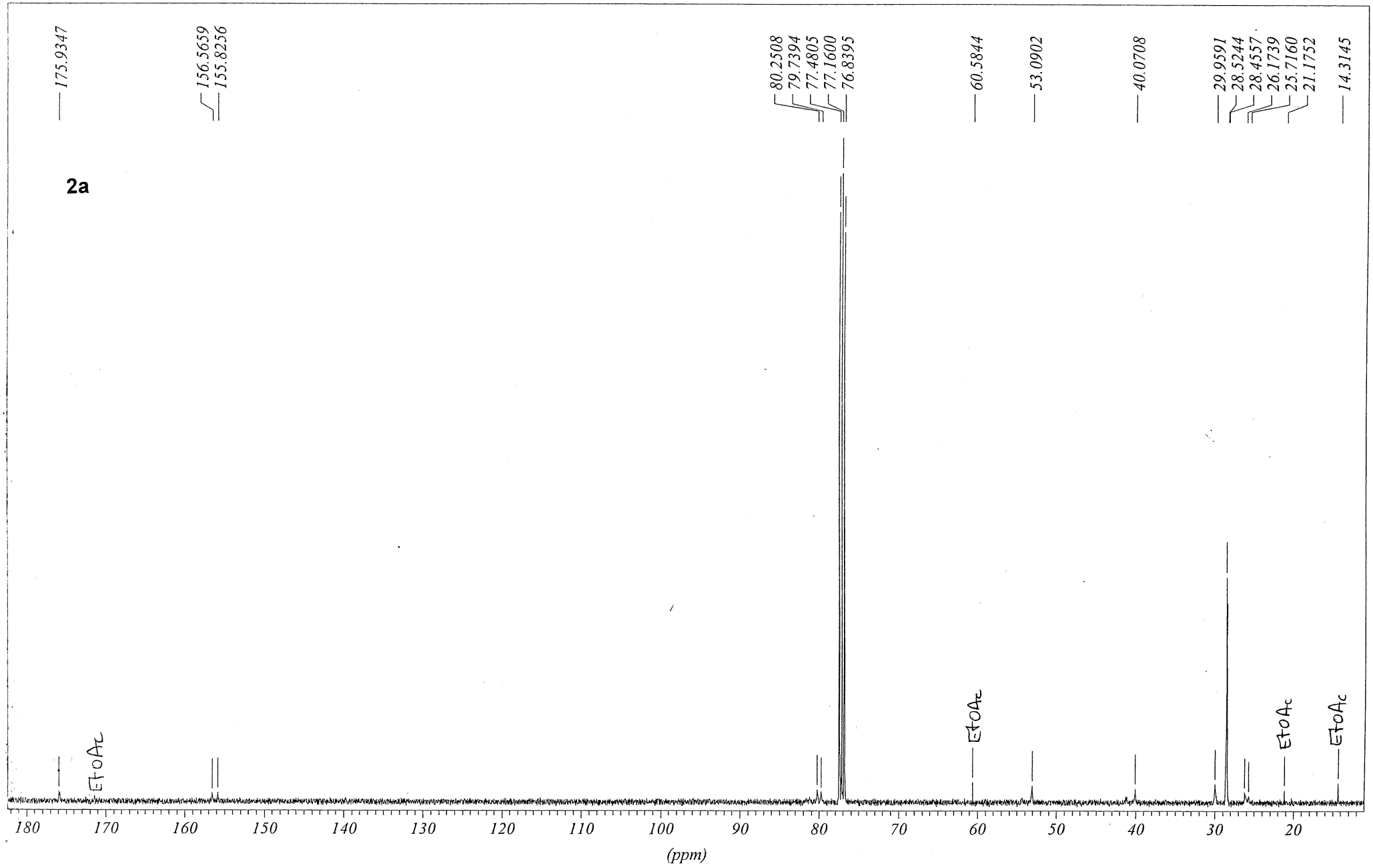
Acquisition Freq. = 399.785 MHz (ECS-spectrometer)



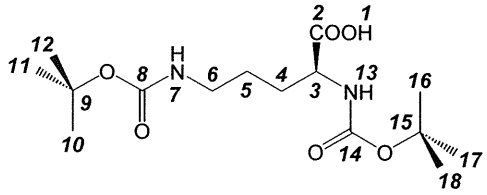
2a

c8388sjm: SJM-16-04-10 [DBD-Ornithine]

Acquisition Freq. = 100.535 MHz (ECS-spectrometer)



Data for (2*S*)-2,5-bis({[(*tert*-butoxy)carbonyl]amino})pentanoic acid (2b).

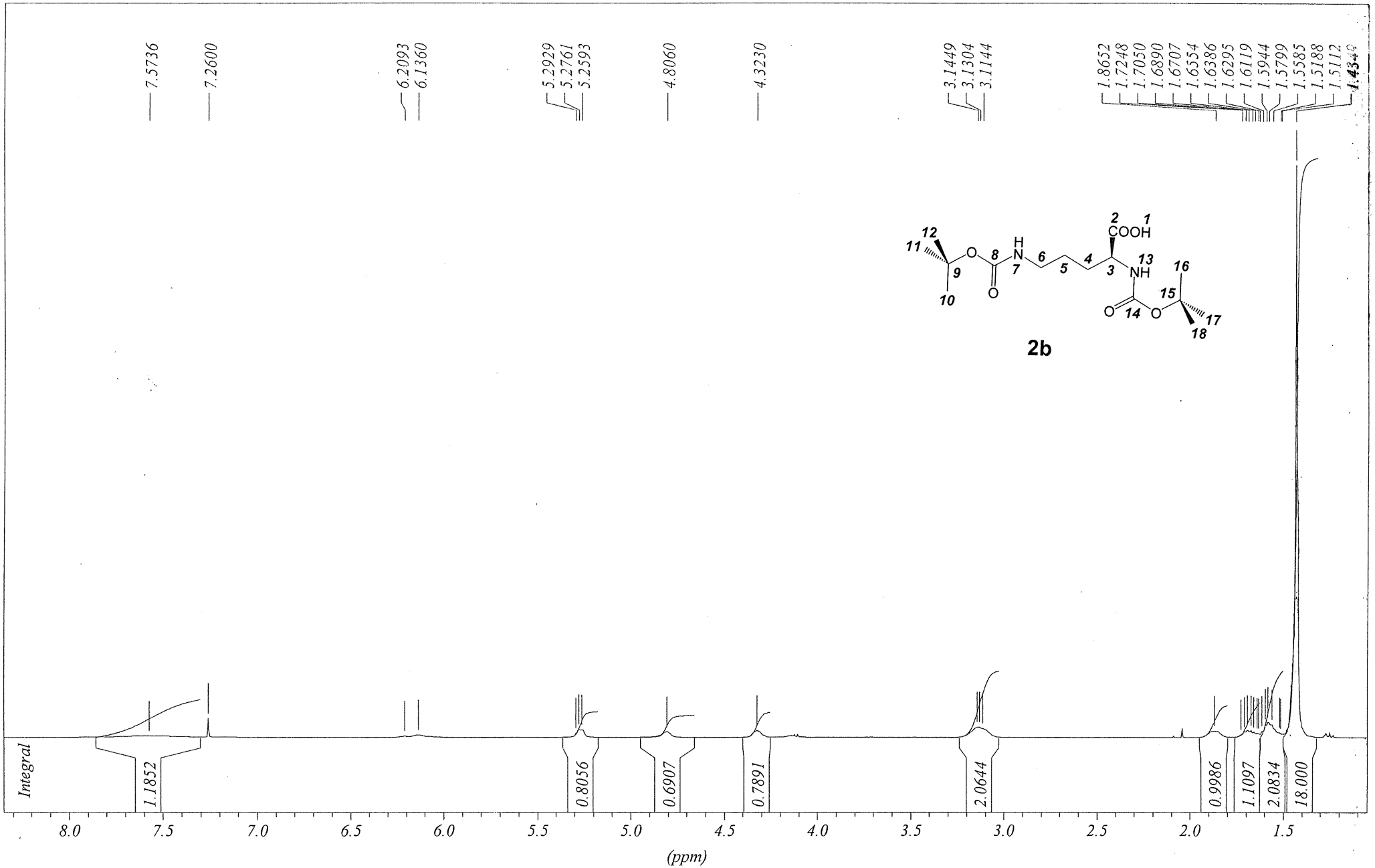


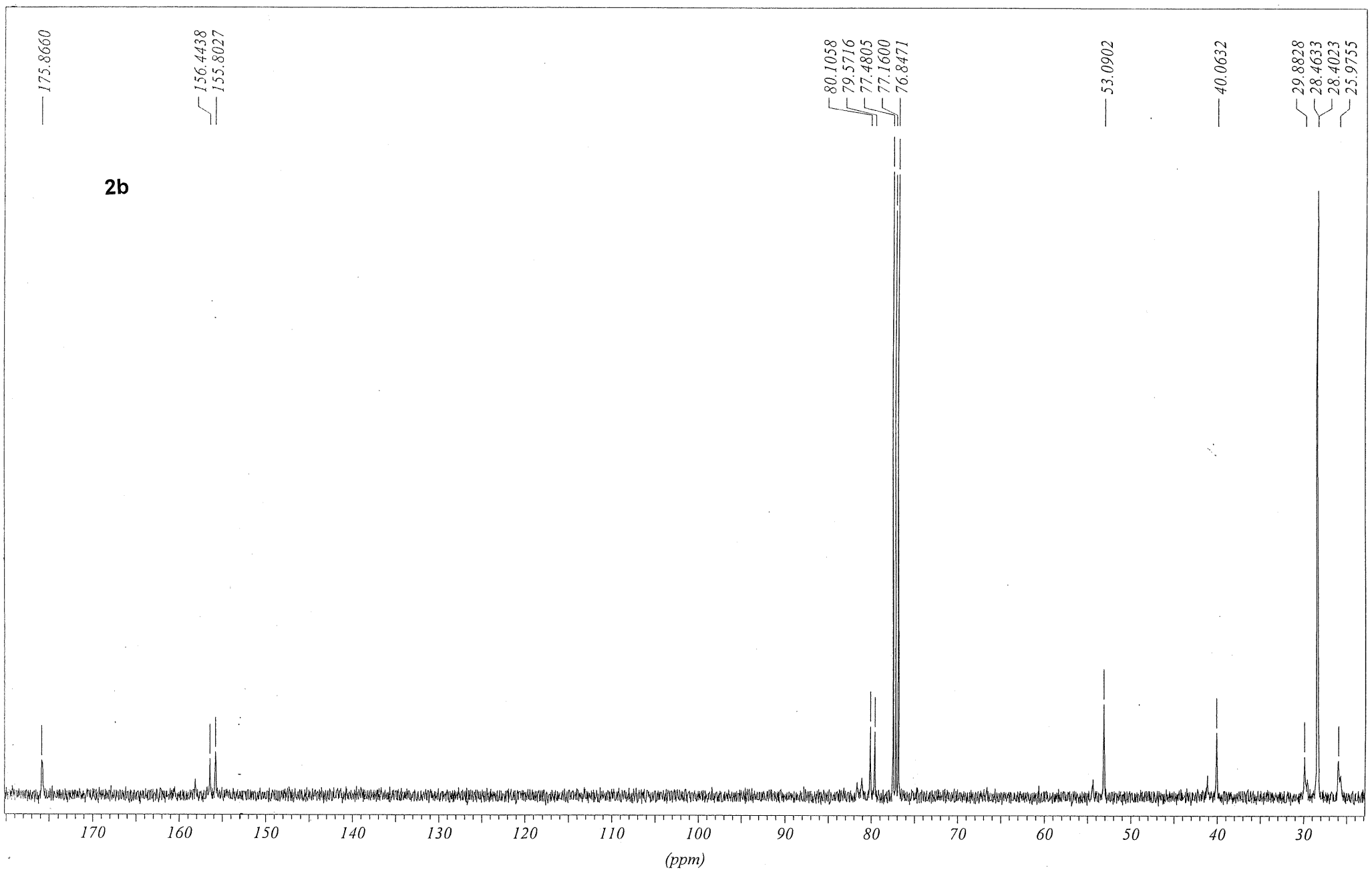
^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 7.57 (1H, br s, H-***1***), 5.27 (1H, d, $^{3}J_{H\text{-}H}$ = 6.72 Hz, H-***13***), 4.81 (1H, br s, H-***7***), 4.32 (1H, br s, H-***3***), 3.14-3.11 (2H, br m, H-***6***), 1.87 (1H, br s, H-***4***), 1.72-1.63 (1H, m, H-***4***), 1.61-1.51 (2H, m, H-***5***), 1.43 (18H, s, H-***10***, ***11***, ***12***, ***16***, ***17***, ***18***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 175.87 (C=O, C-***2***), 156.44 (C=O, C-***14***), 155.80 (C=O, C-***8***), 80.11 (4º-C, C-***15***), 79.57 (4º-C, C-***9***), 53.09 (CH, C-***3***), 40.06 (CH_2, C-***6***), 29.88 (CH_2, C-***4***), 28.46 (CH_3, C-***16***, ***17***, ***18***), 28.40 (CH_3, C-***10***, ***11***, ***12***), 25.98 (CH_2, C-***5***).

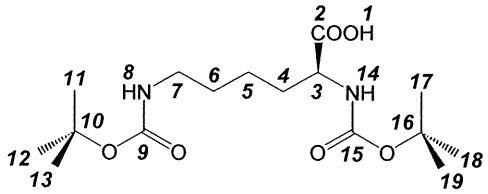
k2981sjm: DBL-Ornithine [SJM-22-06-10]

Acquisition Freq. = 399.785 MHz





Data for (2*S*)-2, 6-bis({[(*tert*-butoxy)carbonyl]amino})hexanoic acid (2c).

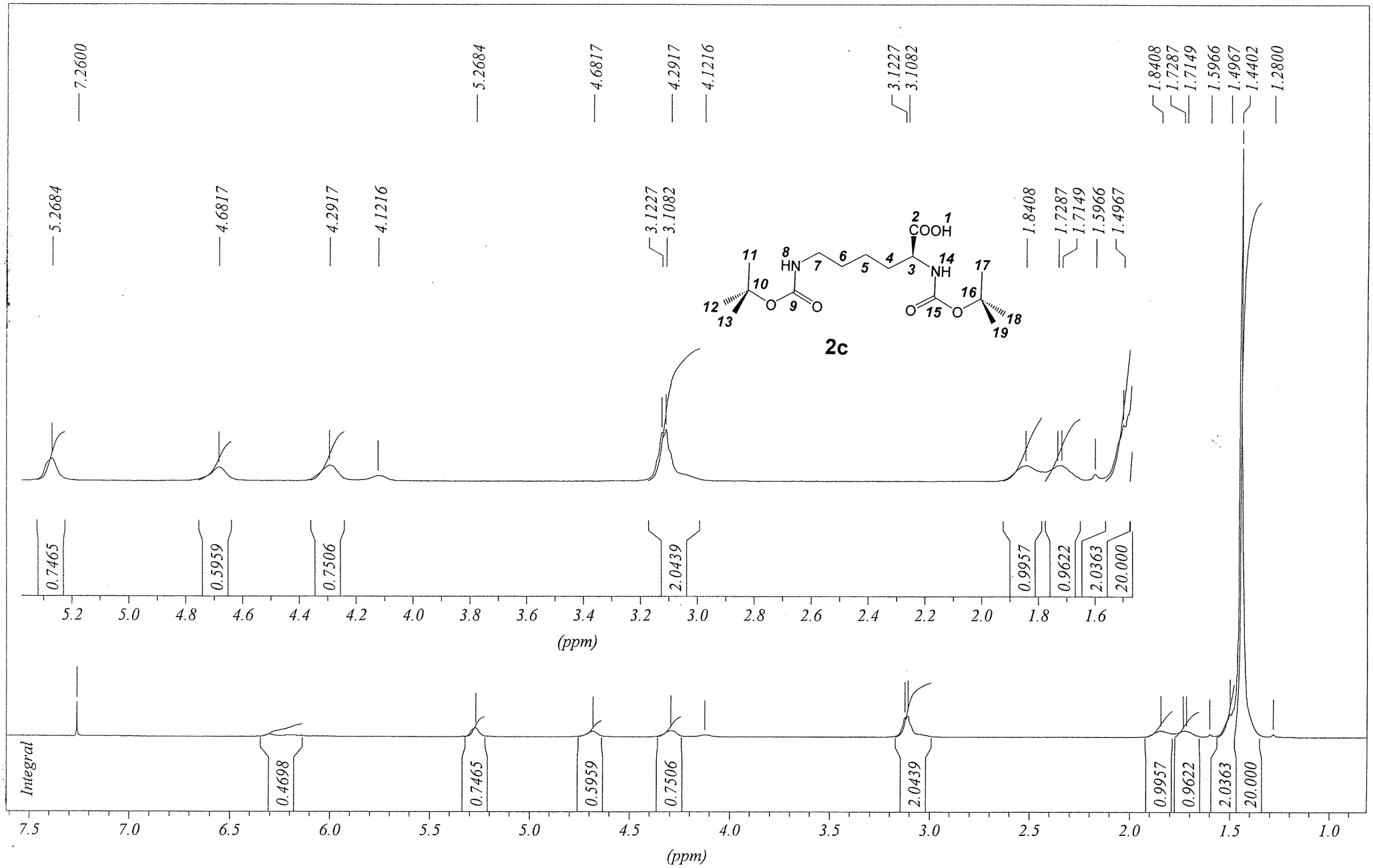


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 5.27 (1H, br s, H-***14***), 4.68 (1H, br s, H-***8***), 4.29 (1H, br s, H-***3***), 3.12-3.11 (2H, br m, H-***7***), 1.84 (1H, br s, H-***4***), 1.73-1.71 (1H, br m, H-***4***), 1.50 (2H, br s, H-***5***), 1.44 (20H, s, H-***6***, ***11***, ***12***, ***13***, ***17***, ***18***, ***19***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 176.37 (C=O, C-***2***), 156.44 (C=O, C-***15***), 155.96 (C=O, C-***9***), 80.14 (4º-C, C-***16***), 79.49 (4º-C, C-***10***), 53.34 (CH, C-***3***), 40.21 (CH_2, C-***7***), 32.13 (CH_2, C-***4***), 29.62 (CH_2, C-***6***), 28.52 (CH_3, C-***17***, ***18***, ***19***), 28.46 (CH_3, C-***11***, ***12***, ***13***), 22.51 (CH_2, C-***5***).

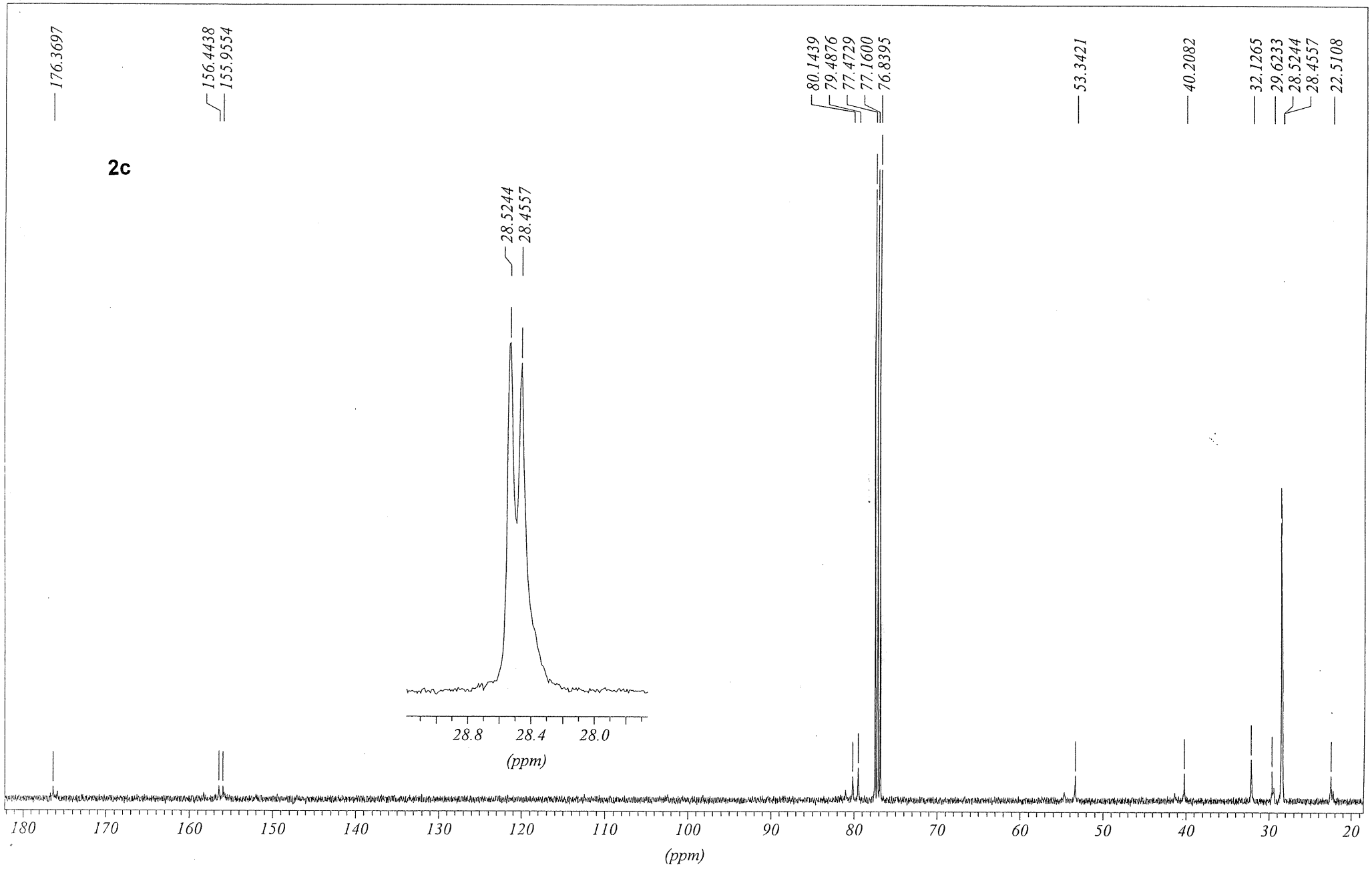
k2997sjm: DBL-Lysine [SJM-23-03-10]

Acquisition Freq. = 399.785 MHz

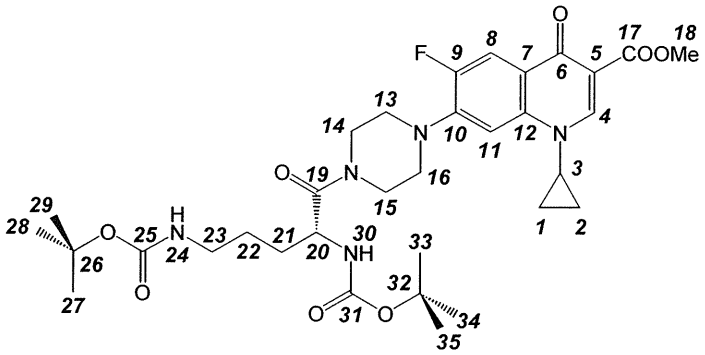


d0942sjm: DBL-Lysine [SJM-23-03-10]

Acquisition Freq. = 100.535 MHz



Data for Methyl 7-{4-[(2*R*)-2,5-bis({[(*tert*-butoxy)carbonyl]amino})pentanoyl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (5a).

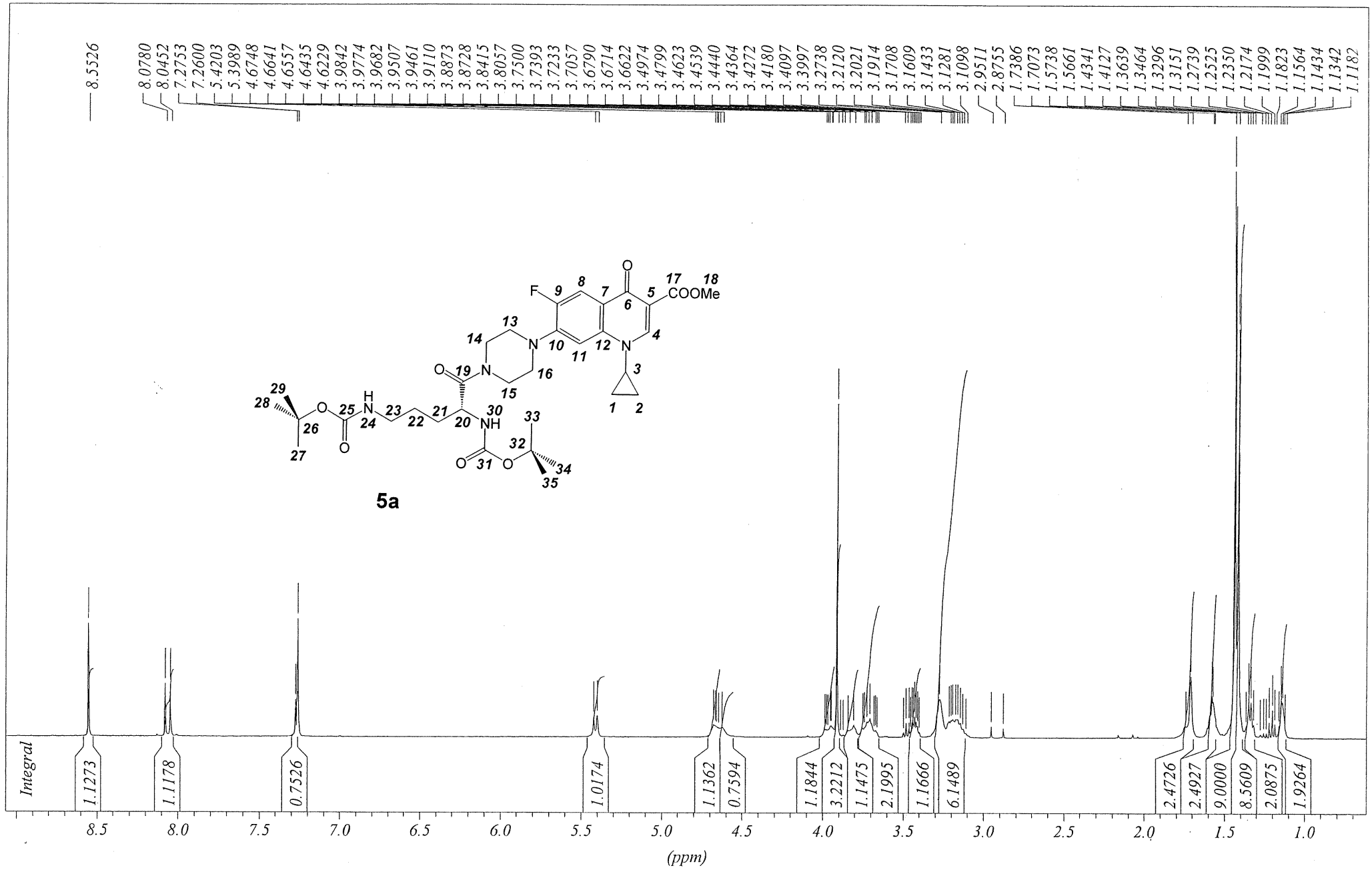


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.55 (1H, s, H-***4***), 8.06 (1H, d, $^3J_{H\text{-}F}$ = 13.1 Hz, H-***8***), 7.27 (1H, d, $^4J_{H\text{-}F}$ = 6.12 Hz, H-***11***), 5.41 (1H, d, $^3J_{H\text{-}H}$ = 8.56 Hz, H-***30***), 4.67-4.64 (1H, m, H-***20***), 4.62 (1H, br s, H-***24***), 3.98-3.95 (1H, m, H-***13***/***16***), 3.91 (3H, s, H-***18***), 3.84-3.81 (1H, m, H-***13***/***16***), 3.75-3.66 (2H, m, H-***13***/***16***), 3.45-3.40 (1H, m, H-***3***), 3.27-3.11 (6H, m, H-***14***, ***15***, ***23***), 1.73-1.71 (2H, br m, H-***21***), 1.57-1.57 (2H, br m, H-***22***), 1.43 (9H, s, H-***33***, ***34***, ***35***), 1.41 (9H, s, H-***27***, ***28***, ***29***), 1.36-1.32 (2H, m, H-***1***/***2***), 1.16-1.12 (2H, m, H-***1***/***2***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 173.07 (C=O, C-***6***), 170.80 (C=O, C-***19***), 166.33 (C=O, C-***17***), 156.15 (C=O, C-***31***), 155.66 (C=O, C-***25***), 153.39 (*ipso*-Ar, d, $^1J_{C\text{-}F}$ = 249 Hz, C-***9***), 148.56 (CH, C-***4***), 143.99 (*ipso*-Ar, d, $^2J_{C\text{-}F}$ = 10.7 Hz, C-***10***), 138.03 (*ipso*-Ar, C-***5***), 123.63 (*ipso*-Ar, d, $^3J_{C\text{-}F}$ = 6.90 Hz, C-***7***), 113.53 (CH, d, $^2J_{C\text{-}F}$ = 23.0 Hz, C-***8***), 110.18 (*ipso*-Ar, C-***12***), 105.34 (CH, C-***11***), 79.94 (4º-C, C-***32***), 79.34 (4º-C, C-***26***), 52.16 (CH_3, C-***18***), 50.36 (CH_2, C-***13***/***16***), 49.86 (CH_2, C-***13***/***16***), 49.64 (CH, C-***20***), 45.51 (CH_2, C-***14***, ***15***), 41.99 (CH_2, C-***23***), 34.67 (CH, C-***3***), 30.78 (CH_2, C-***21***), 28.49 (CH_3, C-***33***, ***34***, ***35***), 28.43 (CH_3, C-***27***, ***28***, ***29***), 25.94 (CH_2, C-***22***), 8.25 (CH_2, C-***1***, ***2***).

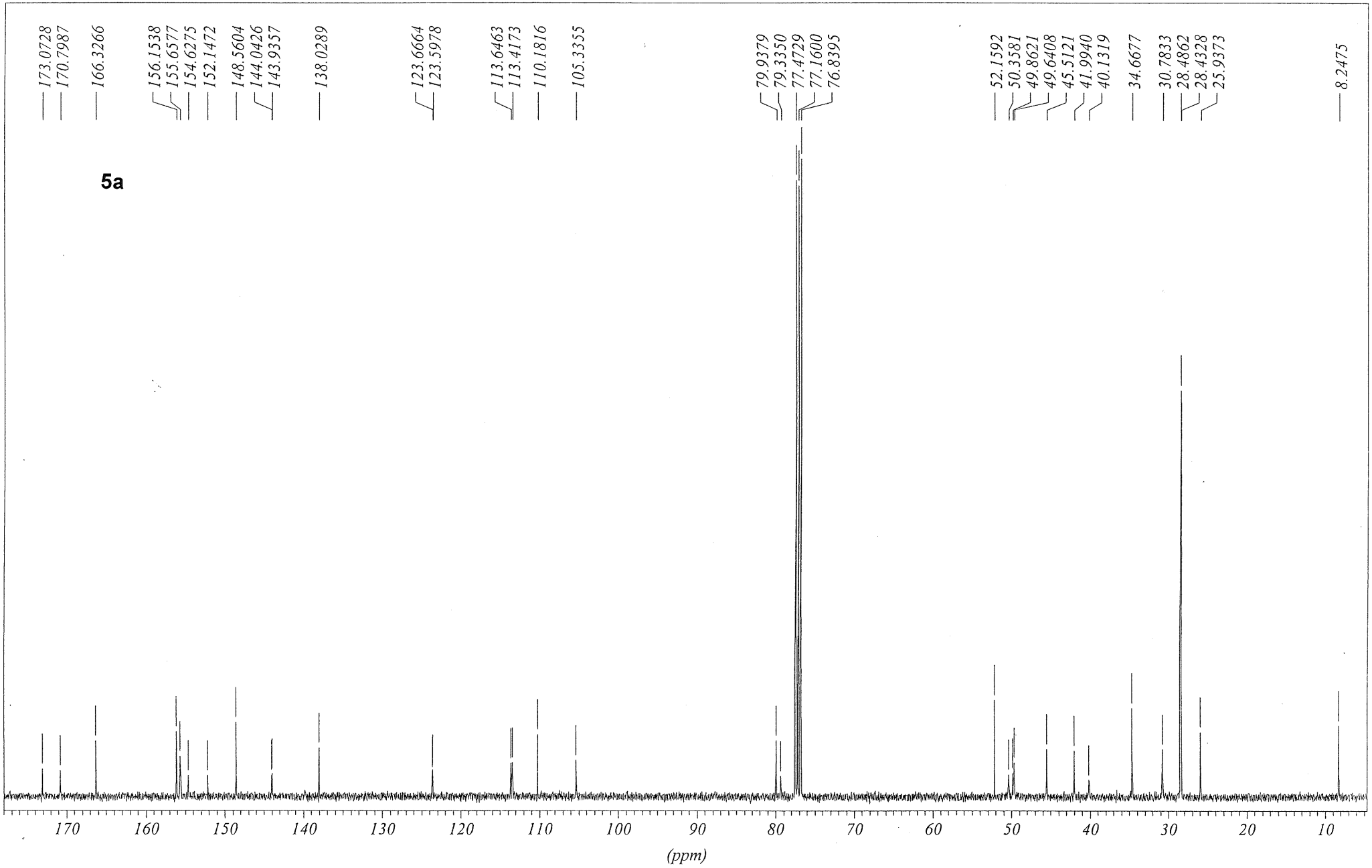
k2364sjm: DBD-Orn-Cpf-Me [SJM-27-04-10-B]

Acquisition Freq. = 399.785 MHz

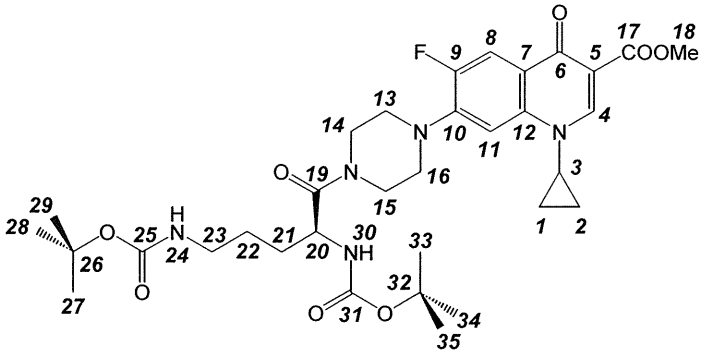


k5189sjm: DBD-Orn-Cpf-Me [SJM-27-04-10-BJ

Acquisition Freq. = 100.535 MHz



Data for methyl 7-{4-[(2*S*)-2,5-bis({[(*tert*-butoxy)carbonyl]amino})pentanoyl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (5b).

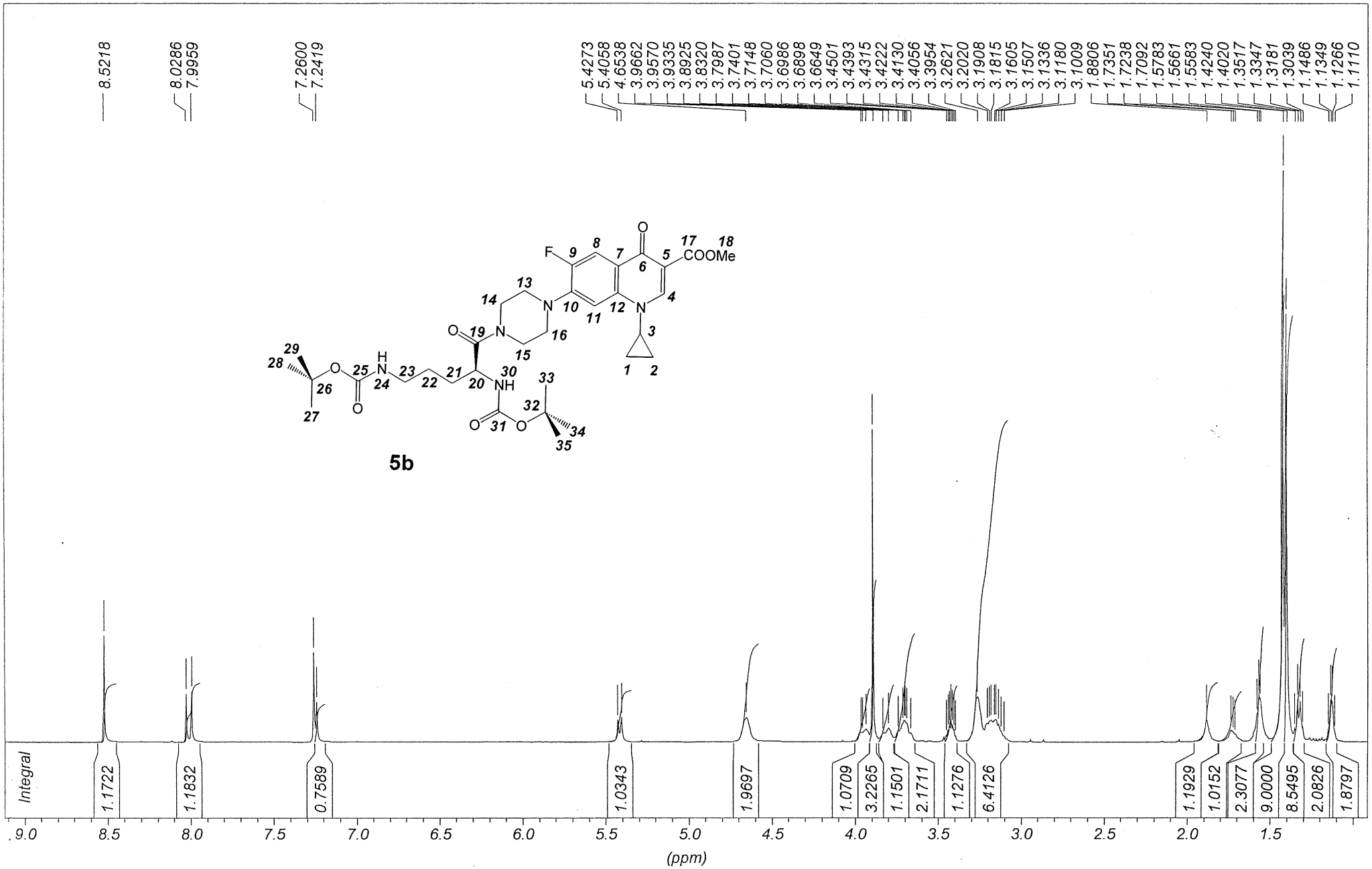


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.52 (1H, s, H-***4***), 8.01 (1H, d, $^{3}J_{H\text{-}F}$ = 13.1 Hz, H-***8***), 7.25 (1H, d, $^{4}J_{H\text{-}F}$ = 7.24 Hz, H-***11***), 5.42 (1H, d, $^{3}J_{H\text{-}H}$ = 8.60 Hz, H-***30***), 4.65 (2H, br s, H-***20***, ***24***), 3.97-3.93 (1H, m, H-***14***/***15***), 3.89 (3H, s, H-***18***), 3.83-3.80 (1H, br m, H-***14***/***15***), 3.74-3.66 (2H, br m, H-***14***/***15***), 3.45-3.40 (1H, m, H-***3***), 3.26-3.10 (6H, br m, H-***13***, ***16***, ***23***), 1.88 (1H, br s, H-***21***), 1.74-1.71 (1H, br m, H-***21***), 1.58-1.56 (2H, br m, H-***22***), 1.42 (9H, s, H-***33***, ***34***, ***35***), 1.40 (9H, s, H-***27***, ***28***, ***29***), 1.35-1.31 (2H, m, H-***1***/***2***), 1.15-1.11 (2H, m, H-***1***/***2***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 173.07 (C=O, C-***6***), 170.80 (C=O, C-***19***), 166.44 (C=O, C-***17***), 156.14 (C=O, C-***31***), 155.66 (C=O, C-***25***), 153.42 (*ipso*-Ar, d, $^{1}J_{C\text{-}F}$ = 249 Hz, C-***9***), 148.59 (CH, C-***4***), 144.01 (*ipso*-Ar, d, $^{2}J_{C\text{-}F}$ = 9.97 Hz, C-***10***), 138.06 (*ipso*-Ar, C-***5***), 123.74 (*ipso*-Ar, d, $^{3}J_{C\text{-}F}$ = 6.91 Hz, C-***7***), 113.63 (CH, d, $^{2}J_{C\text{-}F}$ = 22.2 Hz, C-***8***), 110.29 (*ipso*-Ar, C-***12***), 105.31 (CH, C-***11***), 79.95 (4º-C, C-***32***), 79.35 (4º-C, C-***26***), 52.21 (CH_3, C-***18***), 50.37 (CH_2, C-***13***/***16***), 49.90 (CH_2, C-***23***), 49.66 (CH, C-***20***), 45.54 (CH_2, C-***14***/***15***), 42.01 (CH_2, C-***14***/***15***), 40.14 (CH_2, C-***13***/***16***), 34.66 (CH, C-***3***), 30.84 (CH_2, C-***21***), 28.50 (CH_3, C-***33***, ***34***, ***35***), 28.46 (CH_3, C-***27***, ***28***, ***29***), 25.98 (CH_2, C-***22***), 8.29 (CH_2, C-***1***, ***2***).

d5552sjm: DBL-Orn-Cpf-Me [SJM-05-08-10]

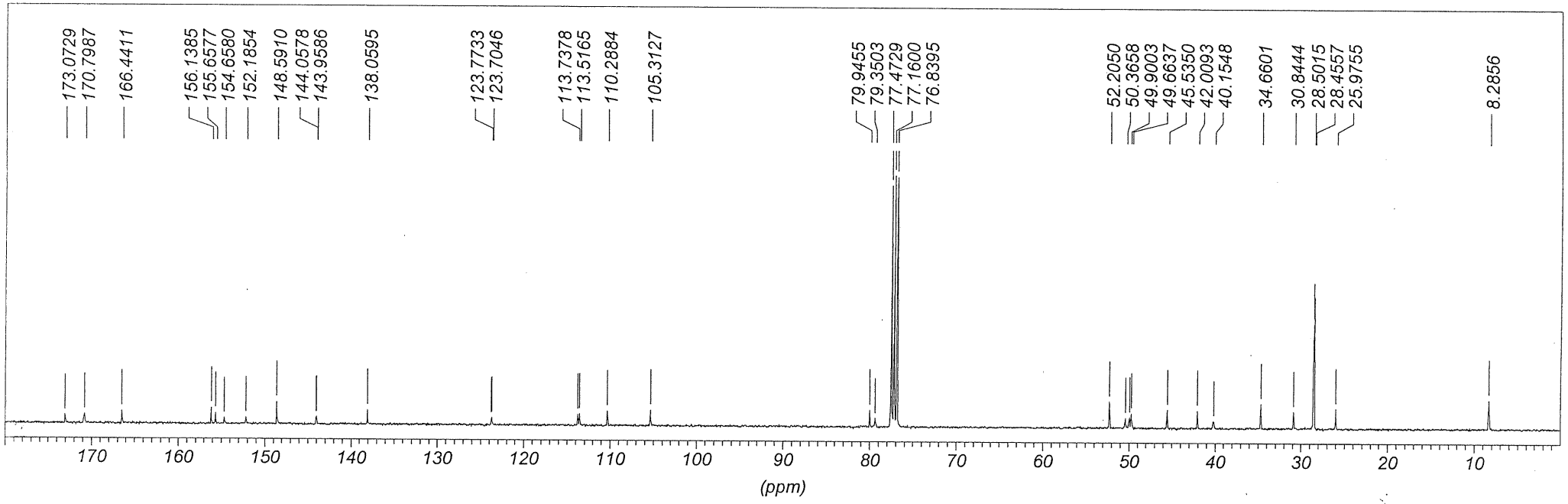
Acquisition Freq. = 399.785 MHz

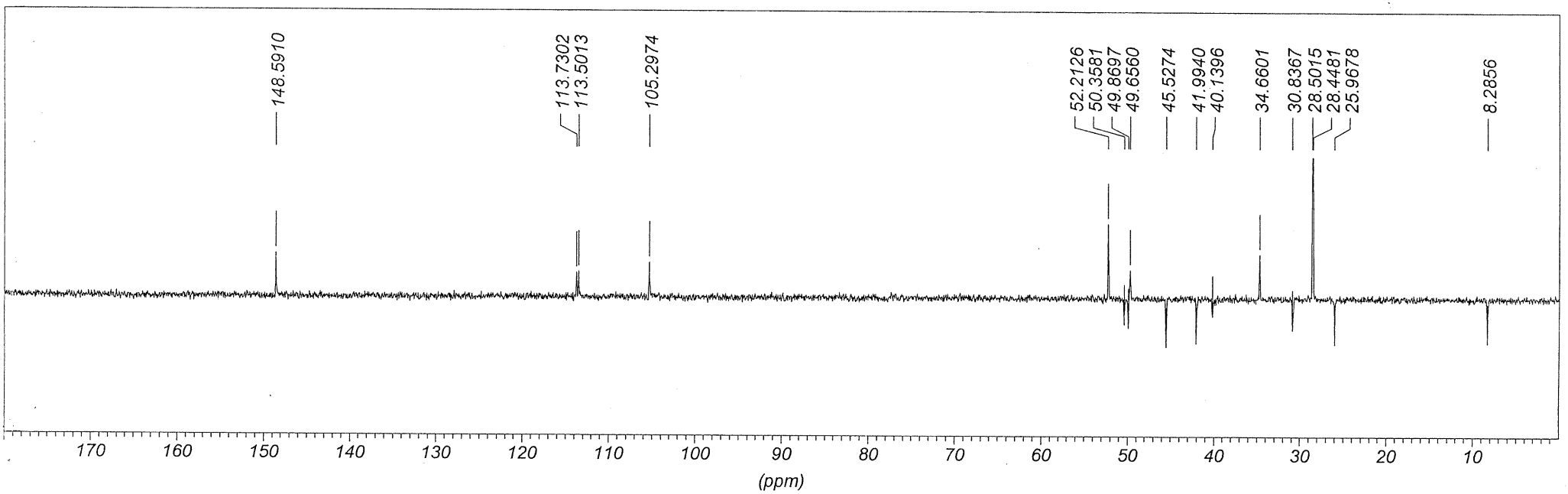


d5587sjm: DBL-Orn-Cpf-Me [SJM-05-08-10]

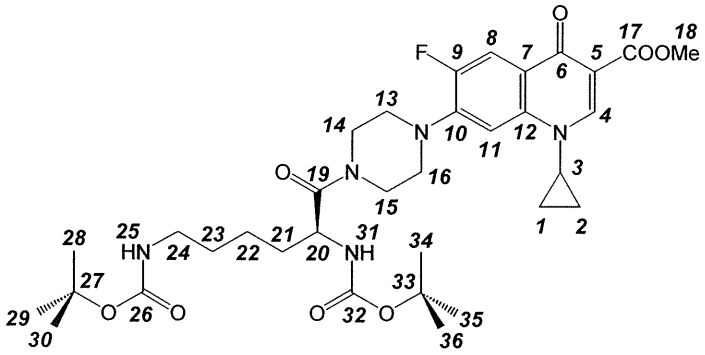
Acquisition Freq. = 399.785 MHz

5b





Data for methyl 7-{4-[(2*S*)-2,6-bis({[(*tert*-butoxy)carbonyl]amino})hexanoyl]piperazin-1-yl}-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (5c).

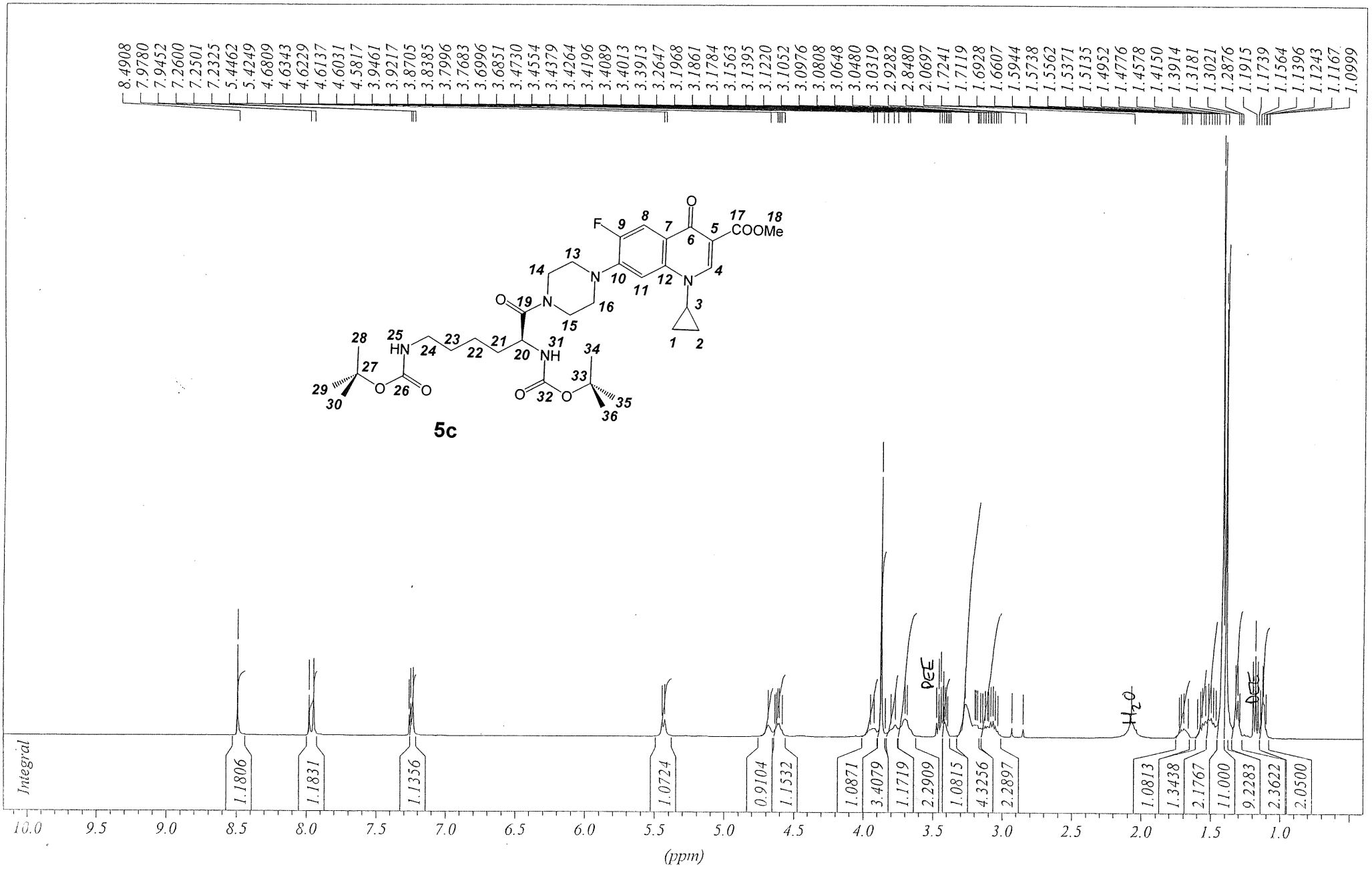


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.49 (1H, s, H-***4***), 7.96 (1H, d, $^3J_{H\text{-}F}$ = 13.1 Hz, H-***8***), 7.24 (1H, d, $^4J_{H\text{-}F}$ = 7.04 Hz, H-***11***), 5.44 (1H, d, $^3J_{H\text{-}H}$ = 8.52 Hz, H-***31***), 4.68 (1H, br s, H-***25***), 4.63-4.58 (1H, m, H-***20***), 3.95-3.92 (1H, br m, H-***13/16***), 3.87 (3H, s, H-***18***), 3.80-3.77 (1H, br m, H-***13/16***), 3.70-3.69 (2H, br m, H-***13/16***), 3.44-3.39 (1H, m, H-***3***), 3.26-3.18 (4H, br m, H-***14***, ***15***), 3.16-3.03 (2H, br m, H-***24***), 1.72-1.66 (1H, m, H-***21***), 1.59-1.54 (1H, m, H-***21***), 1.54-1.46 (2H, m, H-***22***), 1.42 (11H, s, H-***23***, ***34***, ***35***, ***36***), 1.39 (9H, s, H-***28***, ***29***, ***30***), 1.32-1.29 (2H, m, H-***1/2***), 1.14-1.10 (2H, m, H-***1/2***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 173.03 (C=O, C-***6***), 170.91 (C=O, C-***19***), 166.29 (C=O, C-***17***), 156.17 (C=O, C-***32***), 155.74 (C=O, C-***26***), 153.38 (*ipso*-Ar, d, $^1J_{C\text{-}F}$ = 249 Hz, C-***9***), 148.55 (CH, C-***4***), 143.99 (*ipso*-Ar, d, $^2J_{C\text{-}F}$ = 10.7 Hz, C-***10***), 138.01 (*ipso*-Ar, C-***5***), 123.59 (*ipso*-Ar, d, $^3J_{C\text{-}F}$ = 6.91 Hz, C-***7***), 113.47 (CH, d, $^2J_{C\text{-}F}$ = 22.2 Hz, C-***8***), 110.13 (*ipso*-Ar, C-***12***), 105.34 (CH, d, $^3J_{C\text{-}F}$ = 2.30 Hz, C-***11***), 79.88 (4°-C, C-***33***), 79.17 (4°-C, C-***27***), 52.13 (CH_3, C-***18***), 50.33 (CH_2, C-***13/16***), 49.87 (CH_2, C-***12/15***), 49.82 (CH, C-***20***), 45.48 (CH_2, C-***14***, ***15***), 41.94 (CH_2, C-***24***), 34.66 (CH, C-***3***), 33.21 (CH_2, C-***21***), 29.64 (CH_2, C-***23***), 28.49 (CH_3, C-***34***, ***35***, ***36***), 28.44 (CH_3, C-***28***, ***29***, ***30***), 22.43 (CH_2, C-***22***), 8.23 (CH_2, C-***1***, ***2***).

k5176sjm: DBL-Lys-Cpf-Me [SJM-20-04-10]

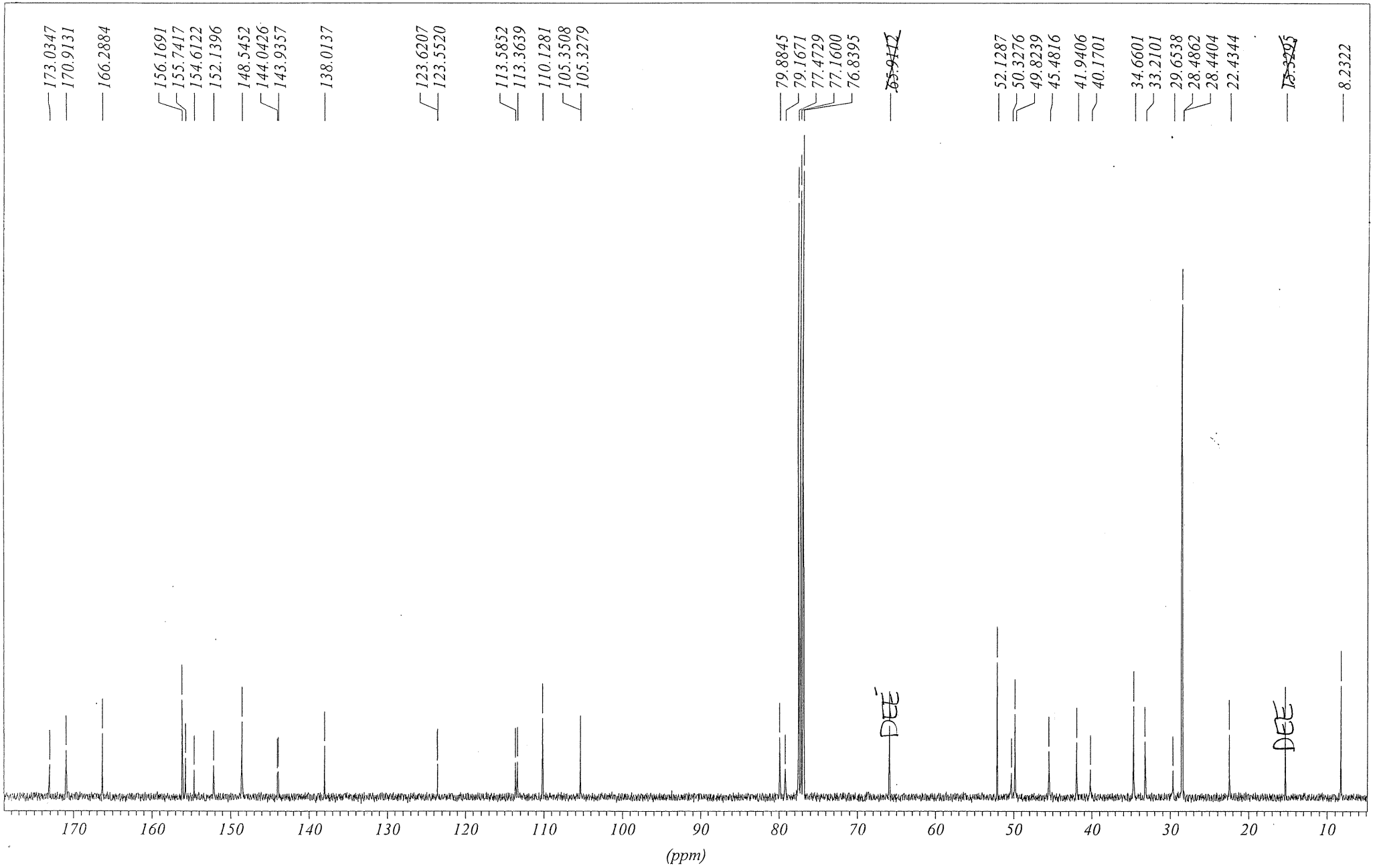
Acquisition Freq. = 399.785 MHz



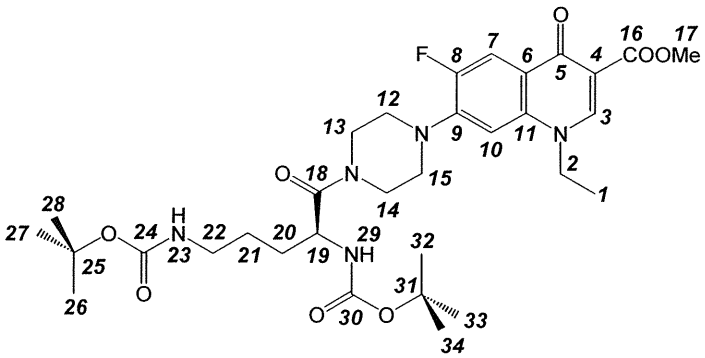
k5190sjm: DBL-Lys-Cpf-Me [SJM-20-04-10]

Acquisition Freq. = 100.535 MHz

5c



Data for methyl 7-{4-[(2*S*)-2,5-bis({[(*tert*-butoxy)carbonyl]amino})pentanoyl]piperazin-1-yl}-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate (5d).

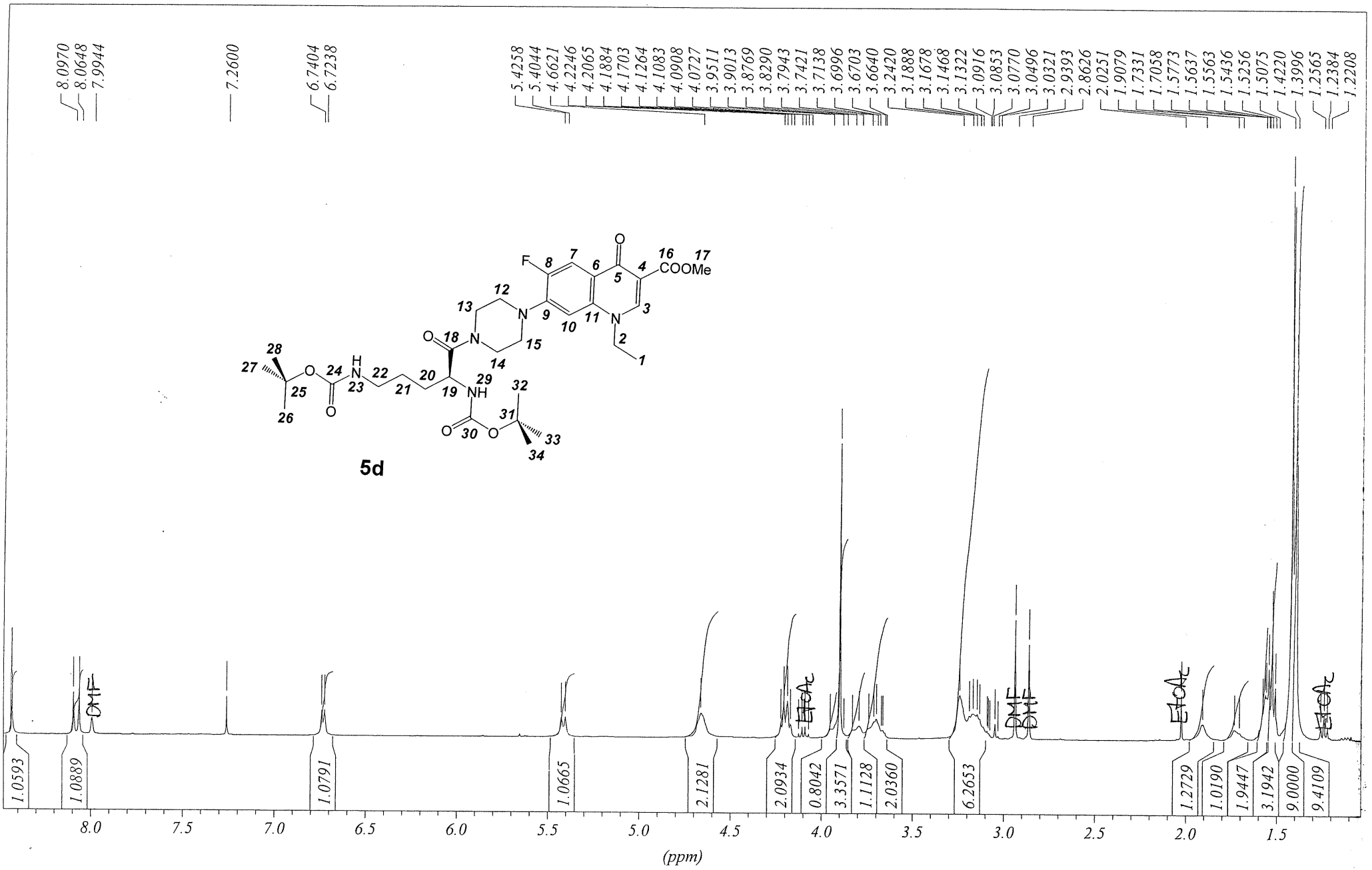


^{1}H NMR ($CDCl_3$, 400 MHz) δ_H 8.43 (1H, s, H-***3***), 8.08 (1H, d, $^3J_{H\text{-}F}$ = 12.9 Hz, H-***7***), 6.73 (1H, d, $^4J_{H\text{-}F}$ = 6.64 Hz, H-***10***), 5.42 (1H, d, $^3J_{H\text{-}H}$ = 8.56 Hz, H-***29***), 4.66 (2H, br s, H-***19***, ***23***), 4.20 (2H, q, $^3J_{H\text{-}H}$ = 7.24 Hz, H-***2***), 3.95 (1H, br s, H-***12***/***15***), 3.90 (3H, s, H-***17***), 3.83-3.79 (1H, br m, H-***12***/***15***), 3.74-3.66 (2H, m, H-***12***/***15***), 3.24-3.13 (6H, m, H-***13***, ***14***, ***22***), 1.91 (1H, br s, H-***20***), 1.73-1.71 (1H, br m, H-***20***), 1.58-1.56 (2H, m, H-***21***), 1.53 (3H, t, $^3J_{H\text{-}H}$ = 7.24 Hz, H-***1***), 1.42 (9H, s, H-***32***, ***33***, ***34***), 1.40 (9H, s, H-***26***, ***27***, ***28***).

^{13}C NMR ($CDCl_3$, 100 MHz) δ_C 173.08 (C=O, C-***5***), 170.81 (C=O, C-***18***), 166.64 (C=O, C-***16***), 156.15 (C=O, C-***30***), 155.67 (C=O, C-***24***), 153.28 (*ipso*-Ar, d, $^1J_{C\text{-}F}$ = 249 Hz, C-***8***), 148.50 (CH, C-***3***), 144.28 (*ipso*-Ar, d, $^2J_{C\text{-}F}$ = 10.7 Hz, C-***9***), 136.15 (*ipso*-Ar, C-***4***), 124.60 (*ipso*-Ar, d, $^3J_{C\text{-}F}$ = 6.90 Hz, C-***6***), 114.08 (CH, d, $^2J_{C\text{-}F}$ = 23.0 Hz, C-***7***), 110.41 (*ipso*-Ar, C-***11***), 104.40 (CH, C-***10***), 79.95 (4º-C, C-***31***), 79.35 (4º-C, C-***25***), 52.24 (CH_3, C-***17***), 50.43 (CH_2, C-***12***/***15***), 50.02 (CH_2, C-***12***/***15***), 49.63 (CH, C-***19***), 49.12 (CH_2, C-***2***), 45.52 (CH_2, C-***13***, ***15***), 42.02 (CH_2, C-***22***), 30.82 (CH_2, C-***20***), 28.51 (CH_3, C-***32***, ***33***, ***34***), 28.46 (CH_3, C-***26***, ***27***, ***28***), 25.98 (CH_2, C-***21***), 14.57 (CH_3, C-***1***).

d0250sjm: DBL-Orn-Nrf-Me [SJM-13-07-10]

Acquisition Freq. = 399.783 MHz

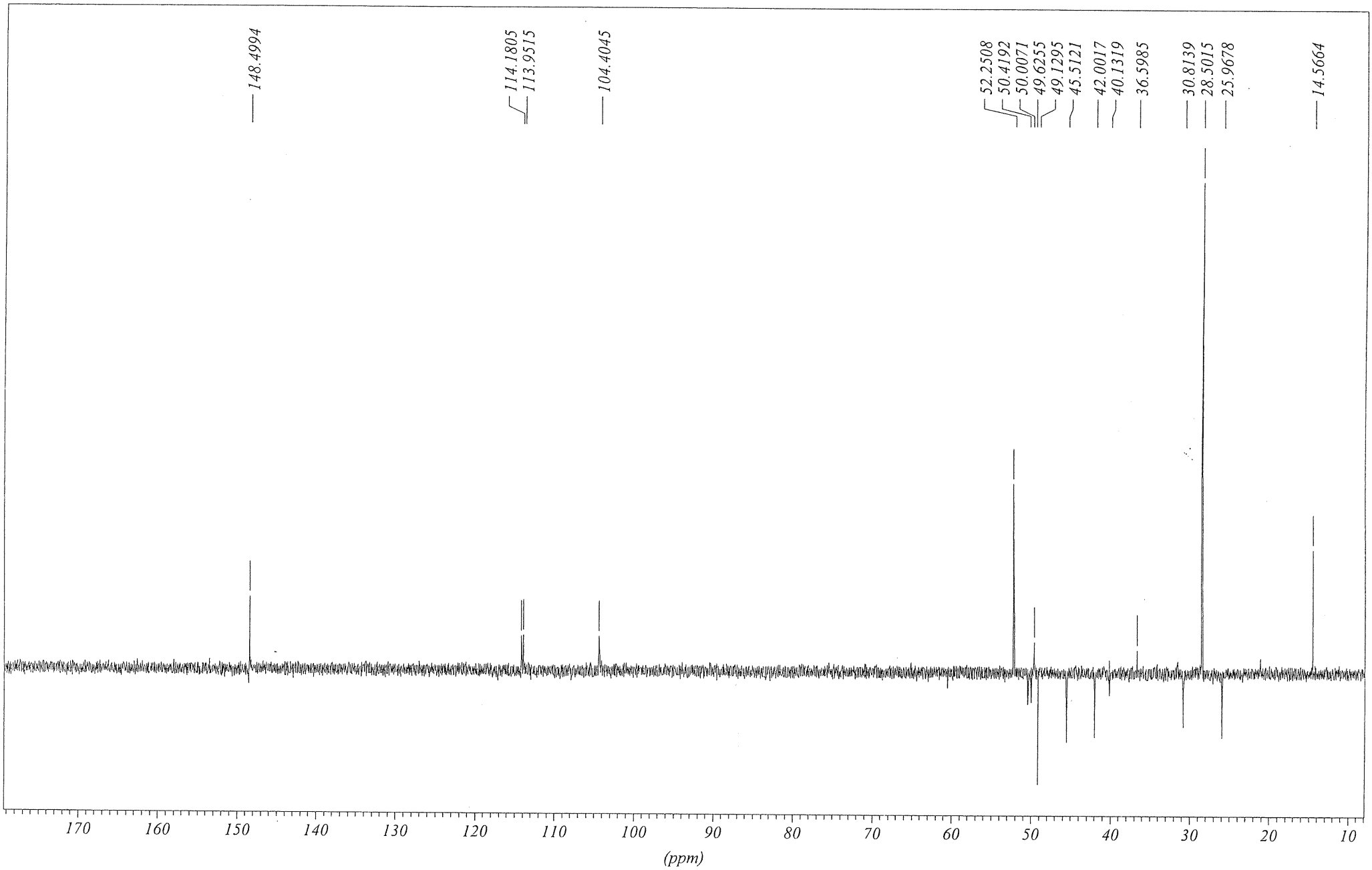


5d

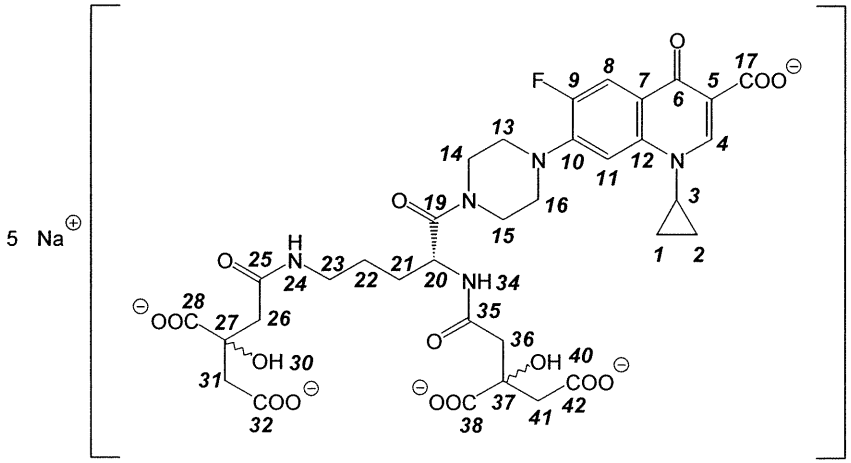
d0273sjm: DBL-Orn-Nrf-Me [SJM-13-07-10]

Acquisition Freq. = 100.535 MHz

5d

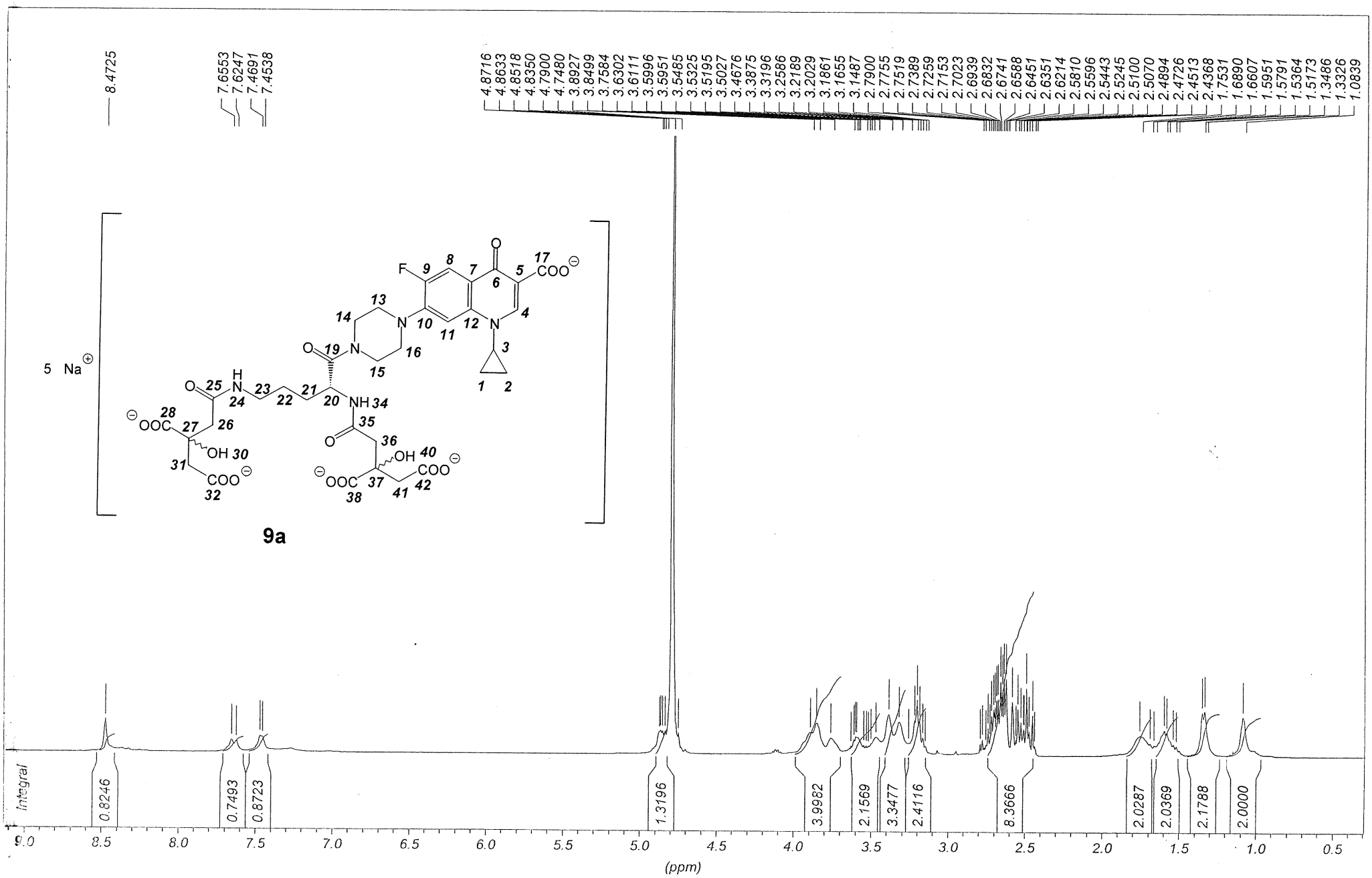


Data for 2-({[(2*R*)-1-[4-(3-carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-yl]-5-(3,4-dicarboxy-3-hydroxybutanamido)-1-oxopentan-2-yl]carbamoyl}methyl)-2-hydroxybutanedioic acid (9a).



^{1}H NMR (D_2O, 400 MHz) δ_H 8.47 (1H, s, H-***4***), 7.64 (1H, d, $^{3}J_{H\text{-}F}$ = 12.2 Hz, H-***8***), 7.46 (1H, d, $^{4}J_{H\text{-}F}$ = 6.12 Hz, H-***11***), 4.87-4.84 (1H, br s, H-***20***), 3.89-3.76 (4H, br m, H-***13***, ***16***), 3.63-3.47 (2H, br m, H-***3***, ***14***/***15***), 3.39-3.26 (3H, br m, H-***14***/***15***), 3.22-3.15 (2H, m, H-***23***), 2.79-2.44 (8H, m, H-***26***, ***31***, ***36***, ***41***), 1.75-1.66 (2H, br m, H-***21***), 1.60-1.52 (2H, br m, H-***22***), 1.34-1.33 (2H, m, H-***1***/***2***), 1.08 (2H, br s, H-***1***/***2***).

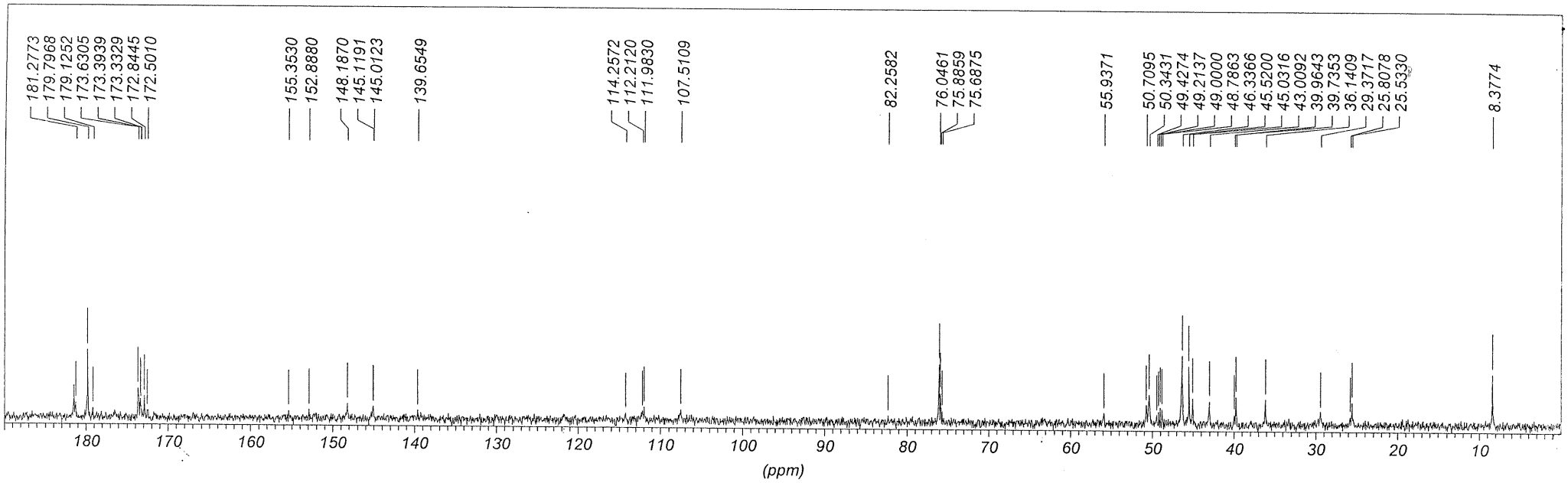
^{13}C NMR (D_2O, 100 MHz) δ_C 181.44 (C=O), 181.28 (C=O), 179.80 (C=O), 173.63 (C=O), 173.39 (C=O), 172.84 (C=O), 154.12 (*ipso*-Ar, $^{1}J_{C\text{-}F}$ = 248 Hz, C-***9***), 148.19 (CH, C-***4***), 145.07 (*ipso*-Ar, d, $^{2}J_{C\text{-}F}$ = 10.7 Hz, C-***10***), 139.65 (*ipso*-Ar, C-***5***), 114.26 (*ipso*-Ar, C-***7***), 112.09 (CH, d, $^{2}J_{C\text{-}F}$ = 23.0 Hz, C-***8***), 107.51 (CH, C-***11***), 76.05 (4º-C, C-***37***), 75.89 (4º-C, C-***27***), 50.71 (CH, C-***20***), 50.34 (CH_2, C-***23***), 46.34 (CH_2, C-***14***/***15***), 45.52 (CH_2, C-***13***/***16***), 45.03 (CH_2, C-***13***/***16***), 43.01 (CH_2, C-***31***, ***41***), 39.96 (CH_2, C-***26***/***36***), 39.73 (CH_2, C-***26***/***36***), 39.15 (CH_2, C-***23***), 36.14 (CH, C-***3***), 28.14 (CH_2, C-***21***), 25.53 (CH_2, C-***22***), 8.38 (CH_2, C-***1***, ***2***).

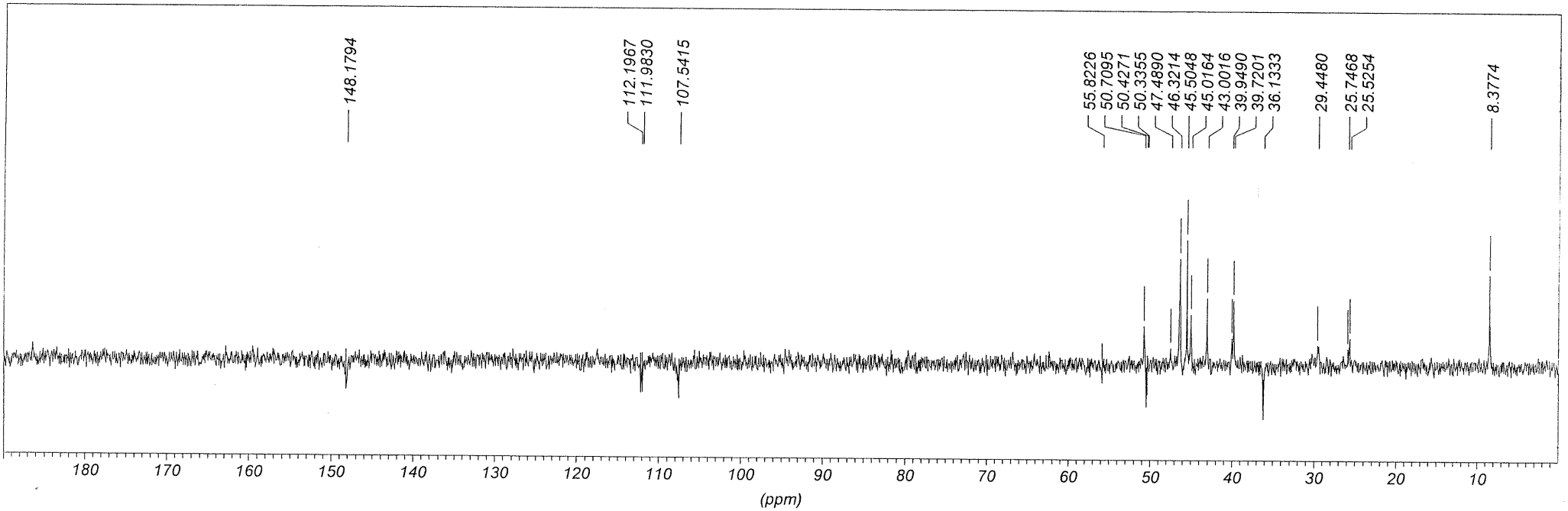


n3570sjm: 2(1,3-C)-D-Orn-Cpf [SJM-22-02-11]

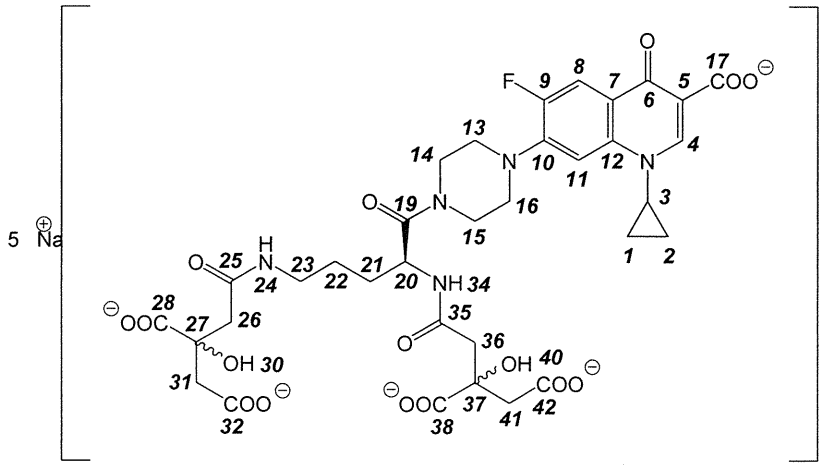
Acquisition Freq. = 100.535 MHz

9a





Data for 2-({[(2*S*)-1-[4-(3-carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-yl]-5-(3,4-dicarboxy-3-hydroxybutanamido)-1-oxopentan-2-yl]carbamoyl}methyl)-2-hydroxybutanedioic acid (9b).

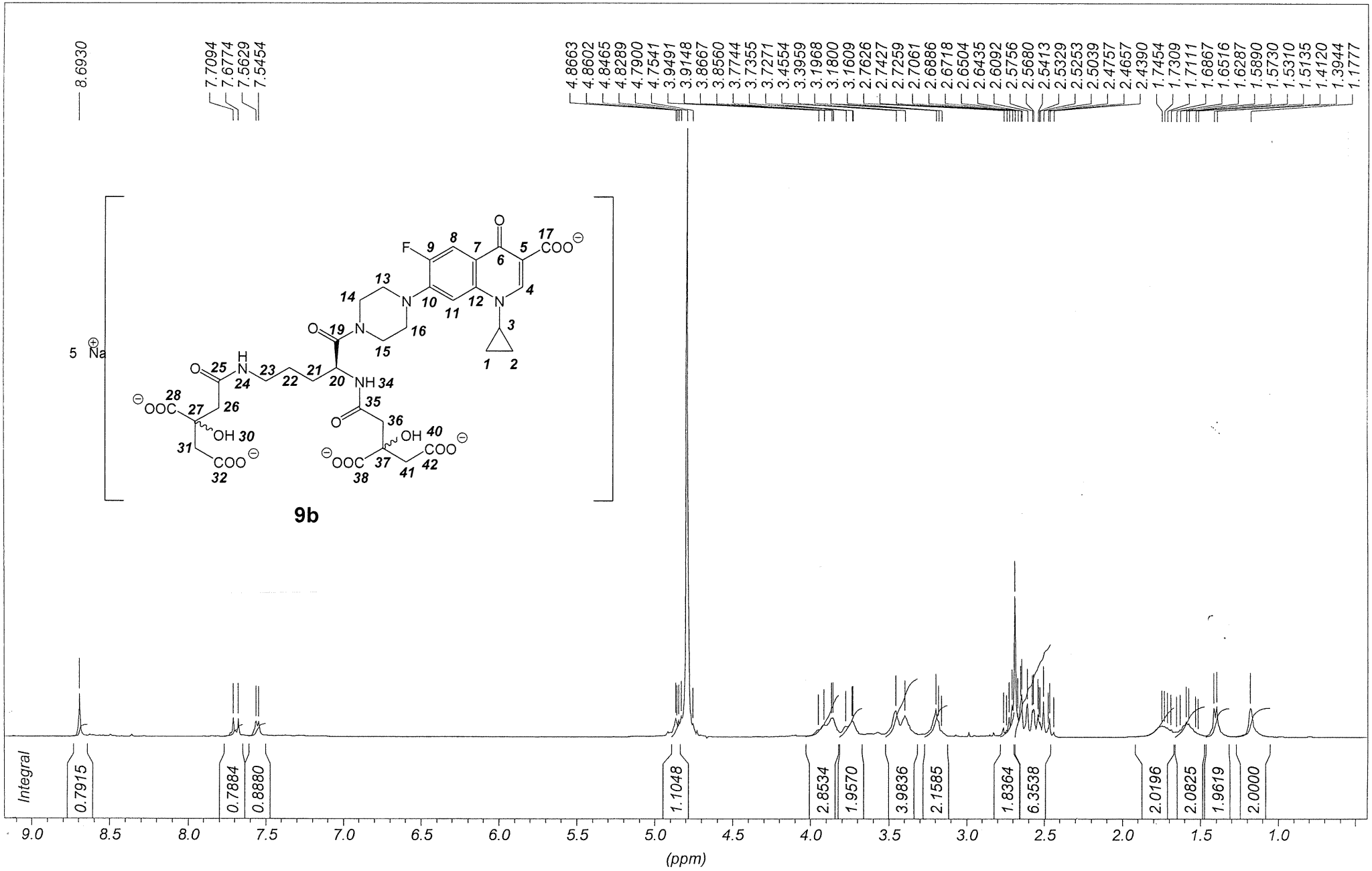


^{1}**H NMR** (D_2O, 400 MHz) δ_H 8.46 (1H, s, H-***4***), 7.64 (1H, d, $^{3}J_{H\text{-}F}$ = 12.2 Hz, H-***8***), 7.46 (1H, d, $^{4}J_{H\text{-}F}$ = 6.12 Hz, H-***11***), 4.85-4.88 (1H, br s, H-***20***), 3.86-3.75 (4H, br m, H-***13***, ***16***), 3.60-3.49 (2H, br m, H-***3***, ***14***/***15***), 3.40-3.27 (3H, br m, H-***14***/***15***), 3.21-3.16 (2H, m, H-***23***), 2.81-2.45 (8H, m, H-***26***, ***31***, ***36***, ***41***), 1.76-1.66 (2H, br m, H-***21***), 1.58-1.52 (2H, br m, H-***22***), 1.34-1.34 (2H, m, H-***1***/***2***), 1.06 (2H, br s, H-***1***/***2***).

^{13}**C NMR** (D_2O, 100 MHz) δ_C 181.56 (C=O), 181.29 (C=O), 179.78 (C=O), 173.61 (C=O), 173.39 (C=O), 172.85 (C=O), 154.16 (*ipso*-Ar, $^{1}J_{C\text{-}F}$ = 248 Hz, C-***9***), 148.23 (CH, C-***4***), 145.05 (*ipso*-Ar, d, $^{2}J_{C\text{-}F}$ = 10.7 Hz, C-***10***), 139.67 (*ipso*-Ar, C-***5***), 114.25 (*ipso*-Ar, C-***7***), 112.11 (CH, d, $^{2}J_{C\text{-}F}$ = 23.0 Hz, C-***8***), 107.52 (CH, C-***11***), 76.06 (4º-C, C-***37***), 75.89 (4º-C, C-***27***), 50.70 (CH, C-***20***), 50.36 (CH_2, C-***23***), 46.35 (CH_2, C-***14***/***15***), 45.54 (CH_2, C-***13***/***16***), 45.05 (CH_2, C-***13***/***16***), 43.02 (CH_2, C-***31***, ***41***), 39.97 (CH_2, C-***26***/***36***), 39.73 (CH_2, C-***26***/***36***), 39.16 (CH_2, C-***23***), 36.16 (CH, C-***3***), 28.16 (CH_2, C-***21***), 25.54 (CH_2, C-***22***), 8.38 (CH_2, C-***1***, ***2***).

m7841sjm: 2(1,3-C)-L-Orn-Cpf [SJM-24-02-11]

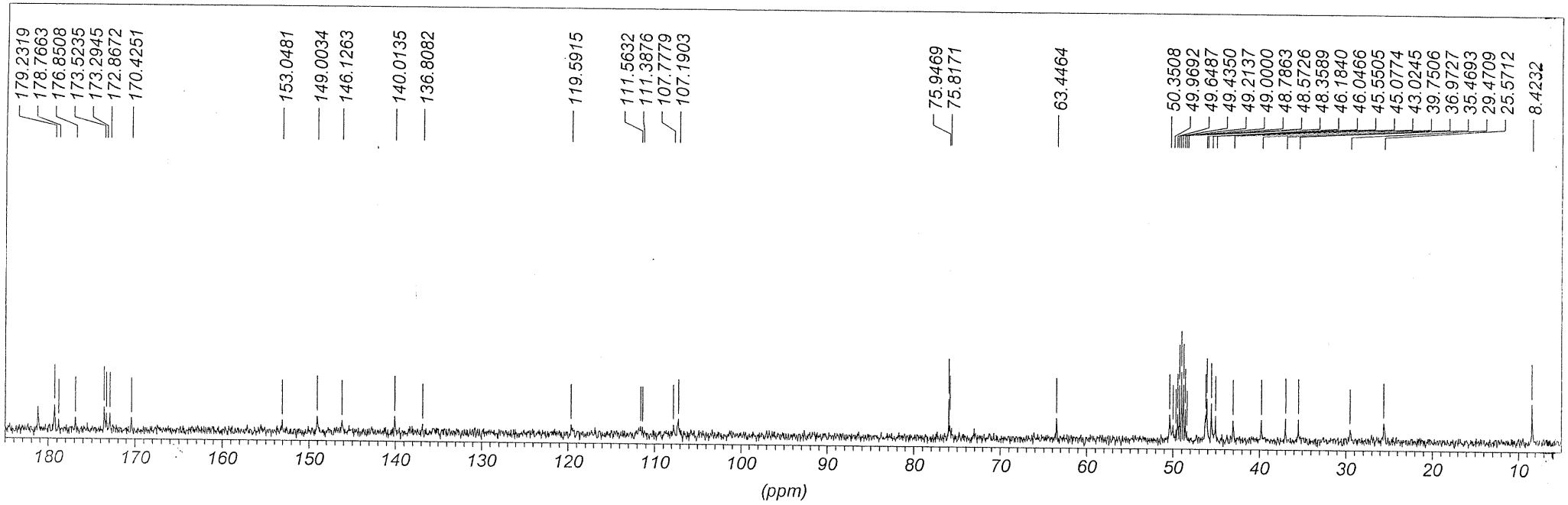
Acquisition Freq. = 399.785 MHz

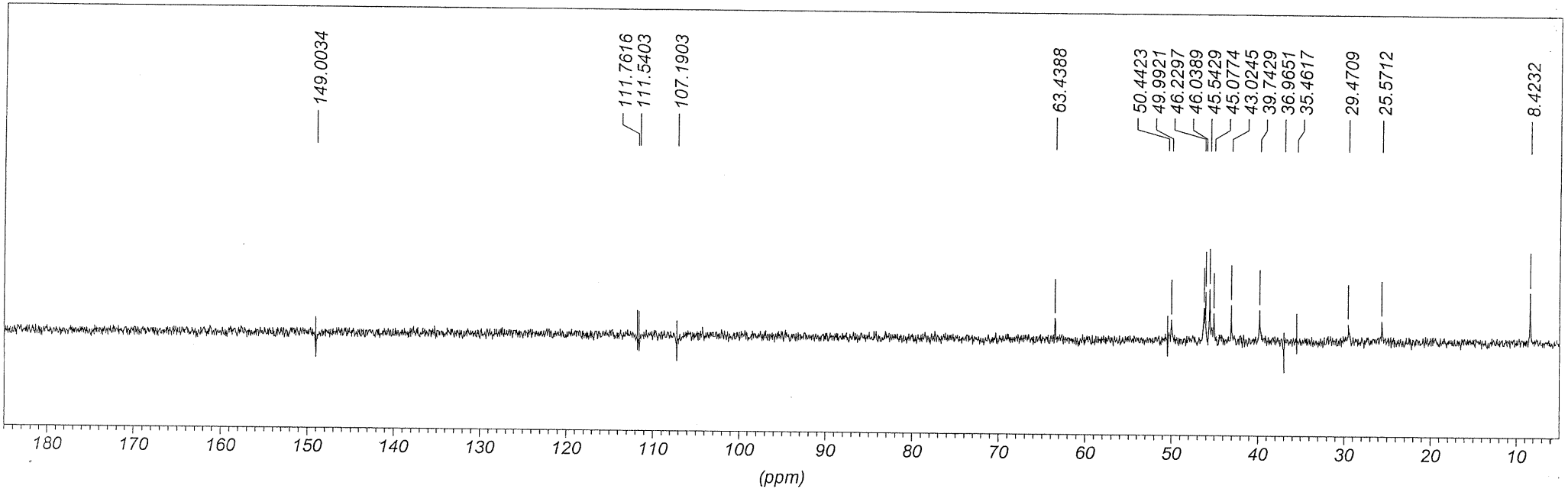


m8606sjm: 2(1,3-C)-L-Orn-Cpf [SJM-24-02-11]

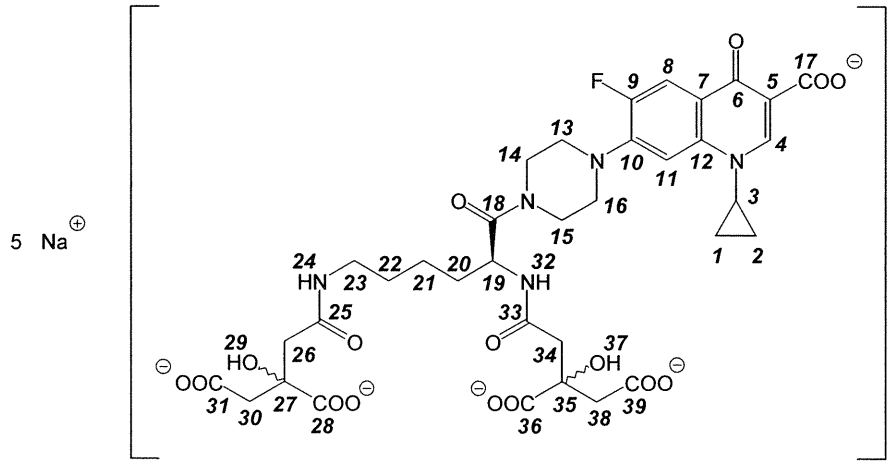
Acquisition Freq. = 100.535 MHz

9b





Data for 2-({[(2*S*)-1-[4-(3-carboxy-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl)piperazin-1-yl]-6-(3,4-dicarboxy-3-hydroxybutanamido)-1-oxohexan-2-yl]carbamoyl}methyl)-2-hydroxybutanedioic acid pentasodium salt (9c).

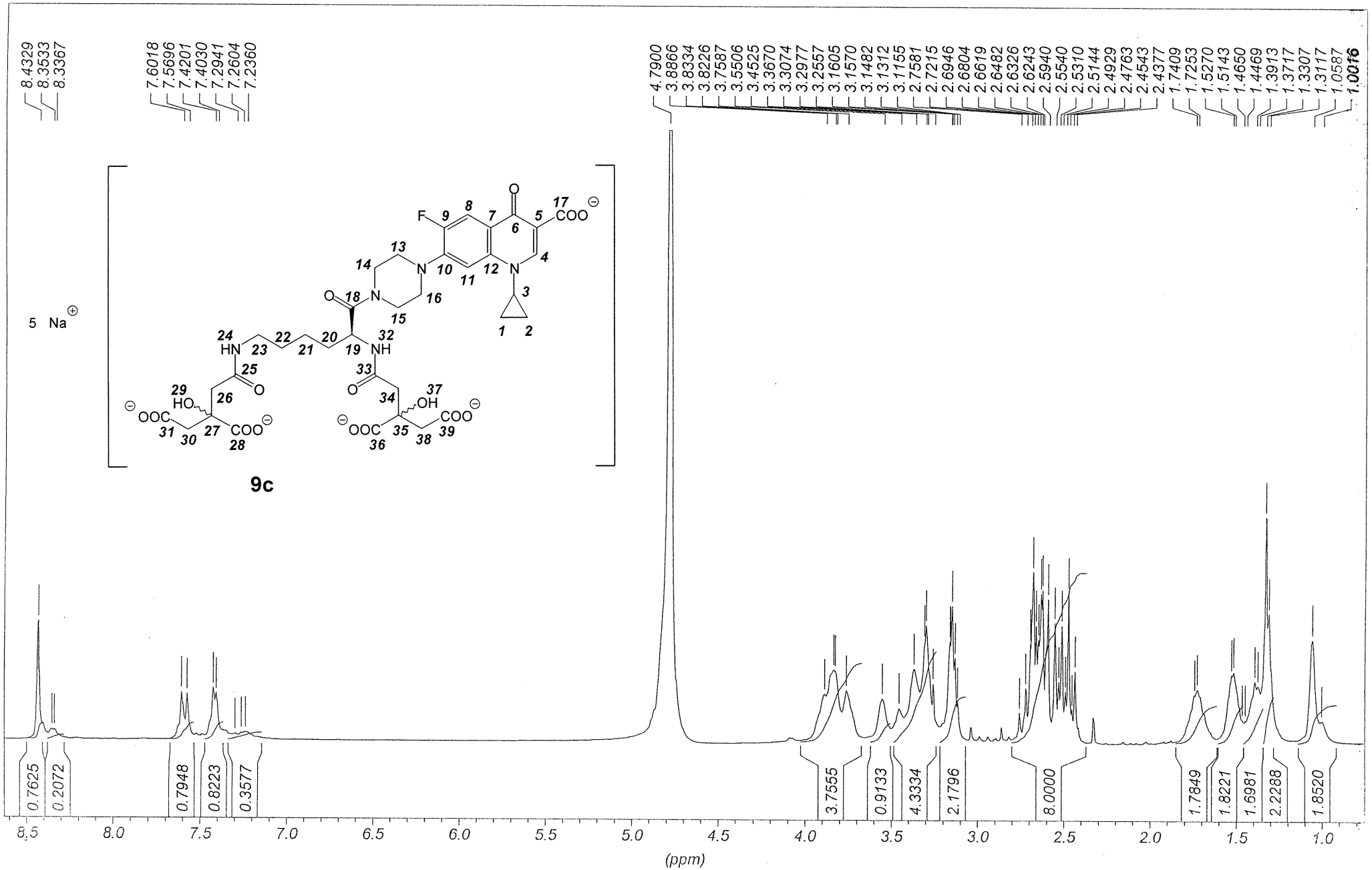


^{1}H NMR (D_2O, 400 MHz) δ_H 8.43 (1H, s, H-***4***), 8.35-8.34 (1H, br m, H-***32***), 7.59 (1H, d, $^{3}J_{H\text{-}F}$ = 12.9 Hz, H-***8***), 7.41 (1H, d, $^{4}J_{H\text{-}F}$ = 6.84 Hz, H-***11***), 7.29-7.24 (1H, br m, H-***24***), 4.79 (1H, br s, H-***19***), 3.89-3.76 (4H, br m, H-***13***, ***16***), 3.55 (1H, br s, H-***3***), 3.45-3.26 (4H, br m, H-***14***/***15***, ***23***), 3.16-3.12 (2H, m, H-***14***/***15***), 2.76-2.44 (8H, m, H-***26***, ***30***, ***34***, ***38***), 1.74-1.73 (2H, br m, H-***20***), 1.53-1.47 (2H, br m, H-***22***), 1.45-1.37 (2H, br m, H-***21***), 1.33-1.31 (2H, m, H-***1***/***2***), 1.06-1.00 (2H, m, H-***1***/***2***).

^{13}C NMR (D_2O, 100 MHz) δ_C 180.60 (C=O), 180.44 (C=O), 179.38 (C=O), 172.64 (C=O), 172.52 (C=O), 172.25 (C=O), 153.20 (*ipso*-Ar, $^{1}J_{C\text{-}F}$ = 249 Hz, C-***9***), 147.28 (CH, C-***4***), 144.14 (*ipso*-Ar, d, $^{2}J_{C\text{-}F}$ = 10.7 Hz, C-***10***), 138.70 (*ipso*-Ar, C-***5***), 120.93 (*ipso*-Ar, C-***7***), 111.19 (CH, d, $^{2}J_{C\text{-}F}$ = 23.0 Hz, C-***8***), 106.57 (CH, C-***11***), 75.19 (4º-C, C-***35***), 75.02 (4º-C, C-***27***), 49.83 (CH, C-***19***), 49.46 (CH_2, C-***23***), 48.79 (CH_2, C-***14***/***15***), 45.46 (CH_2, C-***13***/***16***), 44.62 (CH_2, C-***30***, ***38***), 44.13 (CH_2, C-***26***, ***34***), 42.12 (CH_2, C-***13***/***16***), 39.15 (CH_2, C-***14***/***15***), 35.25 (CH, C-***3***), 30.84 (CH_2, C-***23***), 28.14 (CH_2, C-***22***), 22.40 (CH_2, C-***21***), 7.50 (CH_2, C-***1***, ***2***).

d5104sjm: 2(1,3-C)-L-Lys-Cpf [SJM-07-02-11]

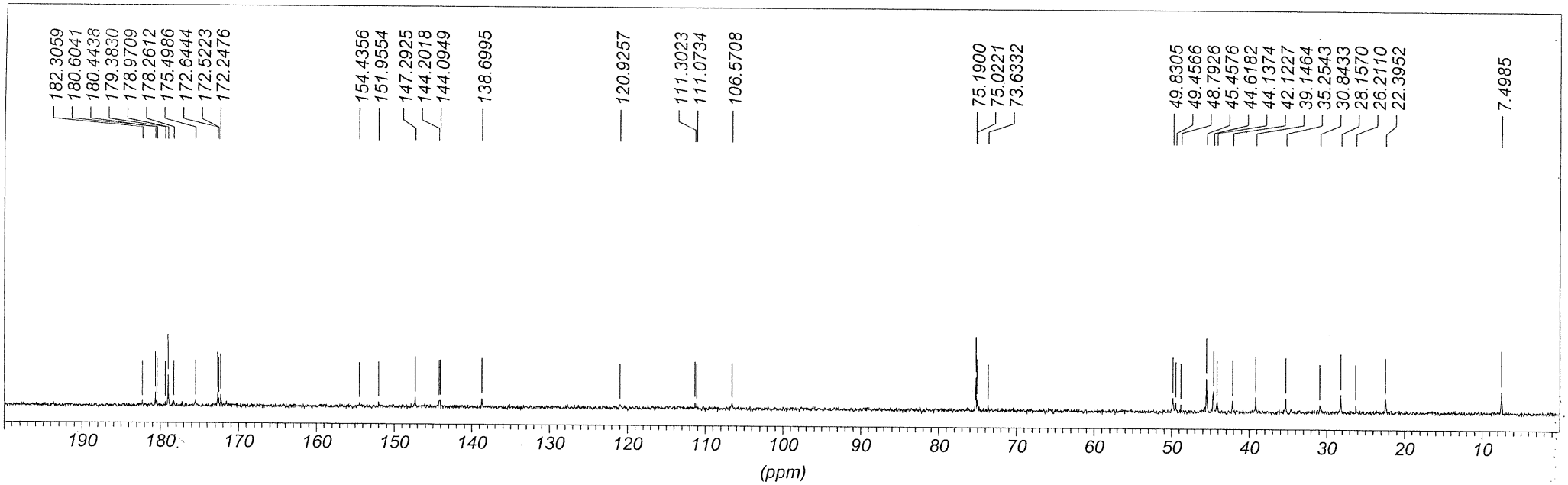
Acquisition Freq. = 399.785 MHz

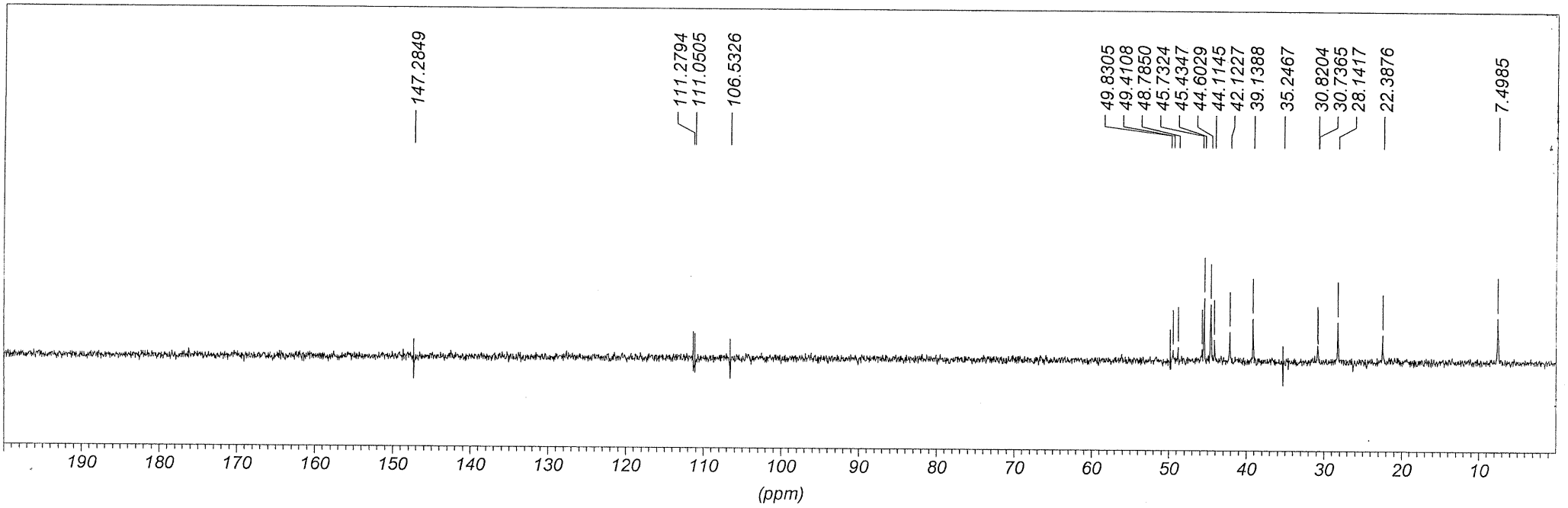


m4018sjm: 2(1,3-C)-L-Lys-Cpf [SJM-07-02-11]

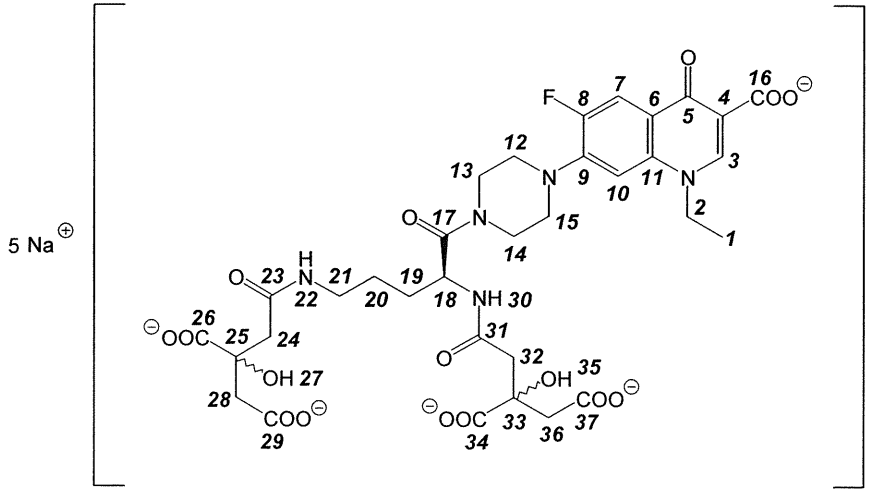
Acquisition Freq. = 100.535 MHz

9c





Data for 2-({[(2*S*)-1-[4-(3-carboxy-1-ethyl-6-fluoro-4-oxo-1,4-dihydroquinolin-7-yl]-5-(3,4-dicarboxy-3-hydroxybutanamido)-1-oxopentan-2-yl]carbamoyl}methyl)-2-hydroxybutanedioic acid pentasodium salt (9d).

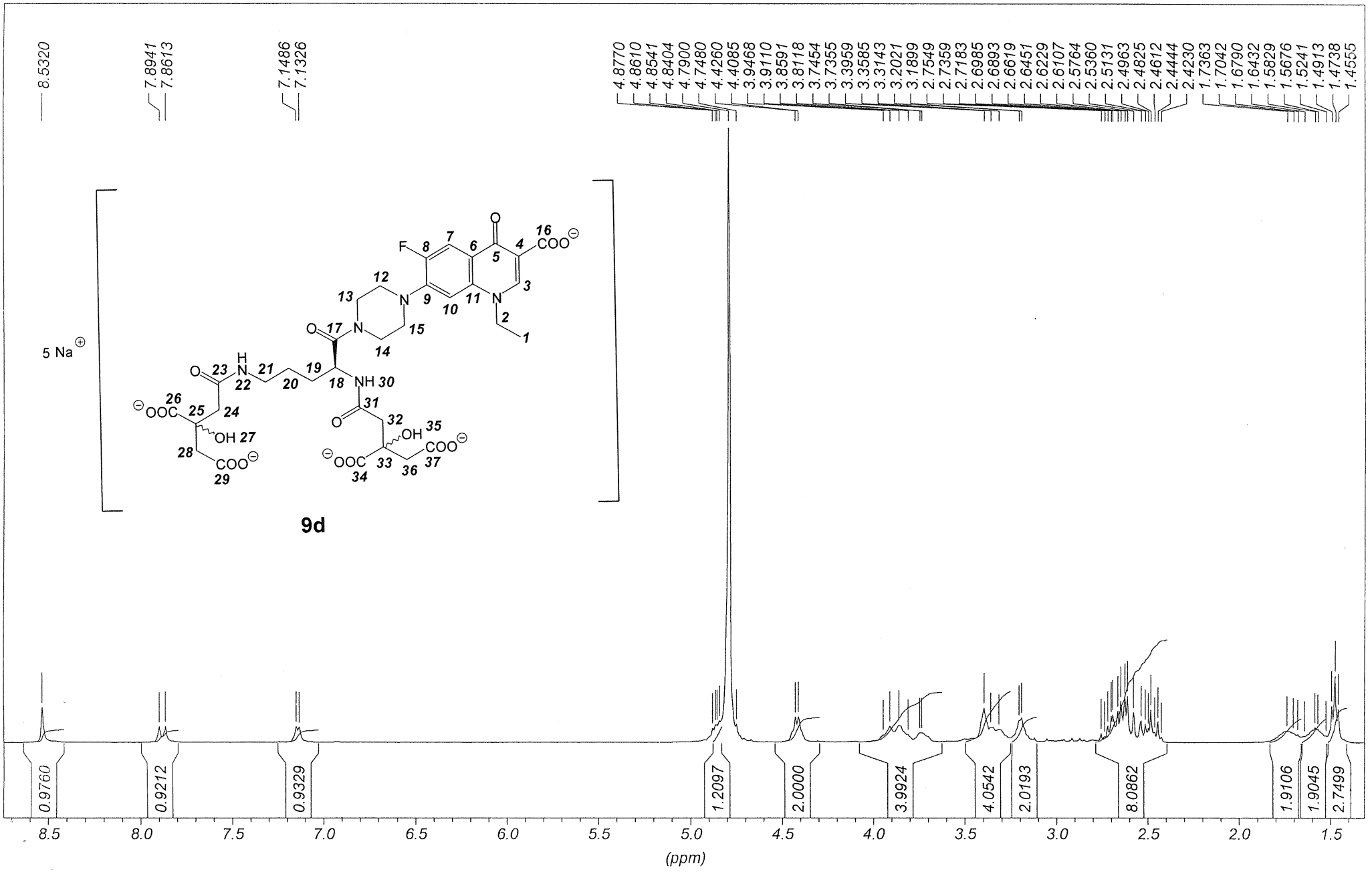


^{1}H NMR (D_2O, 400 MHz) δ_H 8.53 (1H, s, H-***3***), 7.88 (1H, d, $^{3}J_{H\text{-}F}$ = 13.1 Hz, H-***7***), 7.14 (1H, d, $^{4}J_{H\text{-}F}$ = 6.40 Hz, H-***10***), 4.88-4.75 (1H, m, H-***18***), 4.42 (2H, br q, $^{3}J_{H\text{-}H}$ = 13.7, 6.72 Hz, H-***2***), 3.95-3.74 (4H, m, H-***12***, ***15***), 3.40-3.31 (4H, m, H-***13***, ***14***), 3.20-3.19 (2H, m, H-***21***), 2.75-2.42 (8H, m, H-***24***, ***28***, ***32***, ***36***), 1.74-1.68 (2H, m, H-***19***), 1.64-1.52 (2H, m, H-***20***), 1.47 (3H, t, $^{3}J_{H\text{-}H}$ = 7.32 Hz, H-***1***).

^{13}C NMR (D_2O, 100 MHz) δ_C 181.27 (C=O, C-***6***), 179.80 (C=O, C-***16***), 179.12 (C=O, C-***31***), 176.32 (C=O, C-***23***), 173.65 (C=O, C-***34***), 173.41 (C=O, C-***26***), 172.87 (C=O, C-***37***), 172.39 (C=O, C-***29***), 154.09 (*ipso*-Ar, $^{1}J_{C\text{-}F}$ = 249 Hz, C-***8***), 148.03 (CH, C-***3***), 145.50 (*ipso*-Ar, d, $^{2}J_{C\text{-}F}$ = 10.7 Hz, C-***9***), 137.82 (*ipso*-Ar, C-***4***), 122.43 (*ipso*-Ar, C-***6***), 112.40 (CH, d, $^{2}J_{C\text{-}F}$ = 23.8 Hz, C-***7***), 106.77 (CH, C-***10***), 76.05 (4º-C, C-***33***), 75.89 (4º-C, C-***25***), 50.74 (CH_2, C-***13***, ***14***), 50.53 (CH_2, C-***2***), 50.42 (CH, C-***18***), 46.34 (CH_2, C-***12***/***15***), 45.52 (CH_2, C-***32***, ***36***), 45.02 (CH_2, C-***24***, ***28***), 43.06 (CH_2, C-***12***/***15***), 39.73 (CH_2, C-***21***), 29.46 (CH_2, C-***19***), 25.54 (CH_2, C-***20***), 14.60 (CH_3, C-***1***).

m7842sjm: 2(1,3-C)-L-Orn-Nrf [SJM-01-03-11]

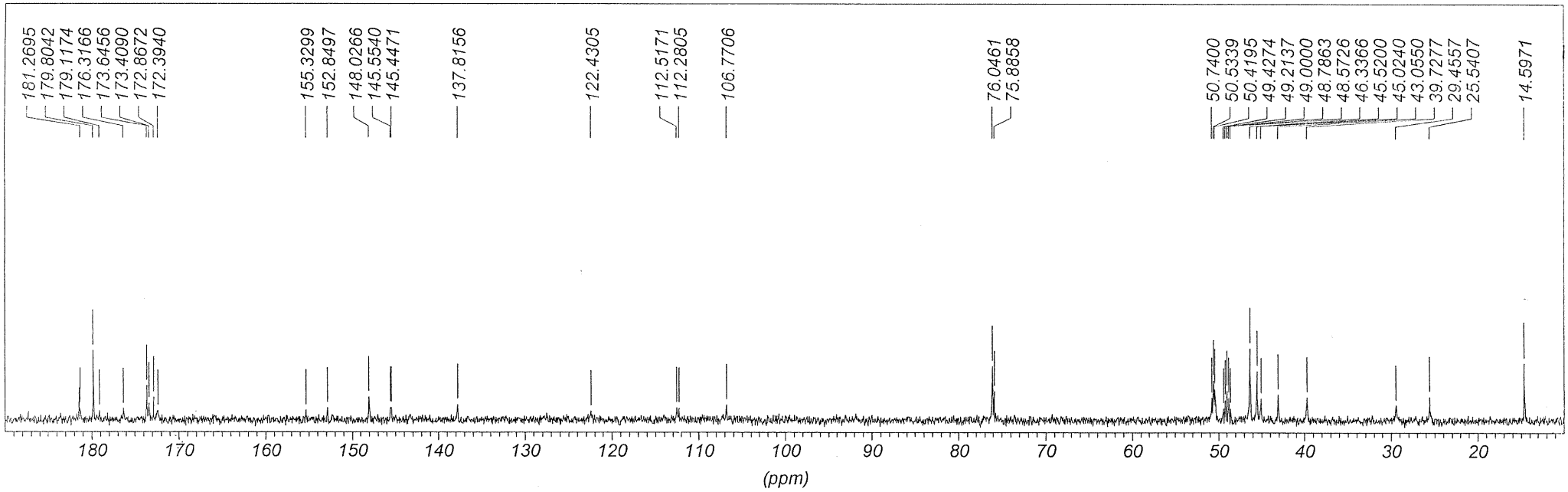
Acquisition Freq. = 399.785 MHz



m8430sjm: 2(1,3-C)-L-Orn-Nrf [SJM-01-03-11]

Acquisition Freq. = 100.535 MHz

9d



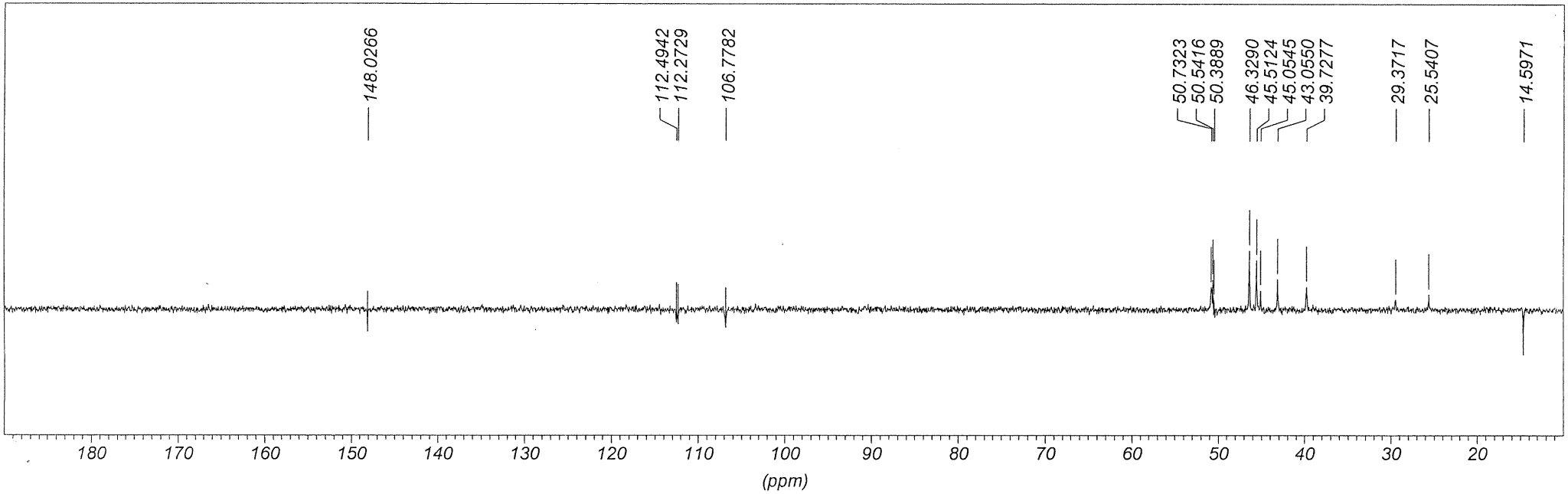


Table S1. Activity of the methyl-ester of ciprofloxacin (**3**), the methyl-ester of norfloxacin (**4**) and conjugates **6c** and **6d** in a disc diffusion assay.

Bacterial Strain	Diameter of zone of inhibition (mm)			
	3[a]	**4**[b]	**6c**[a]	**6d**[b]
Staphylococcus aureus (Oxford) NCTC 6571	R	R	R	R
Staphylococcus aureus NCTC 10399	R	R	R	11
Staphylococcus aureus HG-1[c,d]	R	R	R	R
Staphylococcus aureus NCTC 13142[c]	R	R	R	R
Staphylococcus aureus NCTC 13143[c,d]	R	R	R	R
Staphylococcus aureus BIG 0052[c,d]	R	R	R	R
Staphylococcus epidermidis NCTC 11047	R	R	R	R
Staphylococcus epidermidis NCTC 2749	R	R	R	R
Staphylococcus haemolyticus NCTC 11042	R	R	R	14
Escherichia coli NCTC 10418	R	R	10	8
Escherichia coli BIG 0046[d]	R	R	R	R
Escherichia coli BIG 0051[d]	R	R	R	R
Pseudomonas aeruginosa NCTC 6749	R	R	R	R
Pseudomonas aeruginosa BIG 0039	R	R	R	R
Pseudomonas aeruginosa BIG 0037	R	R	R	R
Pseudomonas aeruginosa NCTC 10662	R	R	R	R
Pseudomonas aeruginosa BIG 0063	R	R	R	R
Serratia marcescens NCTC 1377	R	R	R	R
Burkholderia cepacia NCTC 10744	R	R	R	R

R = resistant, zone of inhibition = 0 mm. [a]Compound discs equimolar with 5 μg ciprofloxacin were used in the assay. [b]Compound discs equimolar with 5 μg norfloxacin were used in the assay. [c]Methicillin-resistant *S. aureus* (MRSA). [d]Strains of clinical origin defined as resistant to ciprofloxacin by CLSI criteria.