Supplementary Data

Cyclopeptide alkaloids: Stereochemistry and Synthesis of the Precursors of Discarine C, D and Myrianthine A

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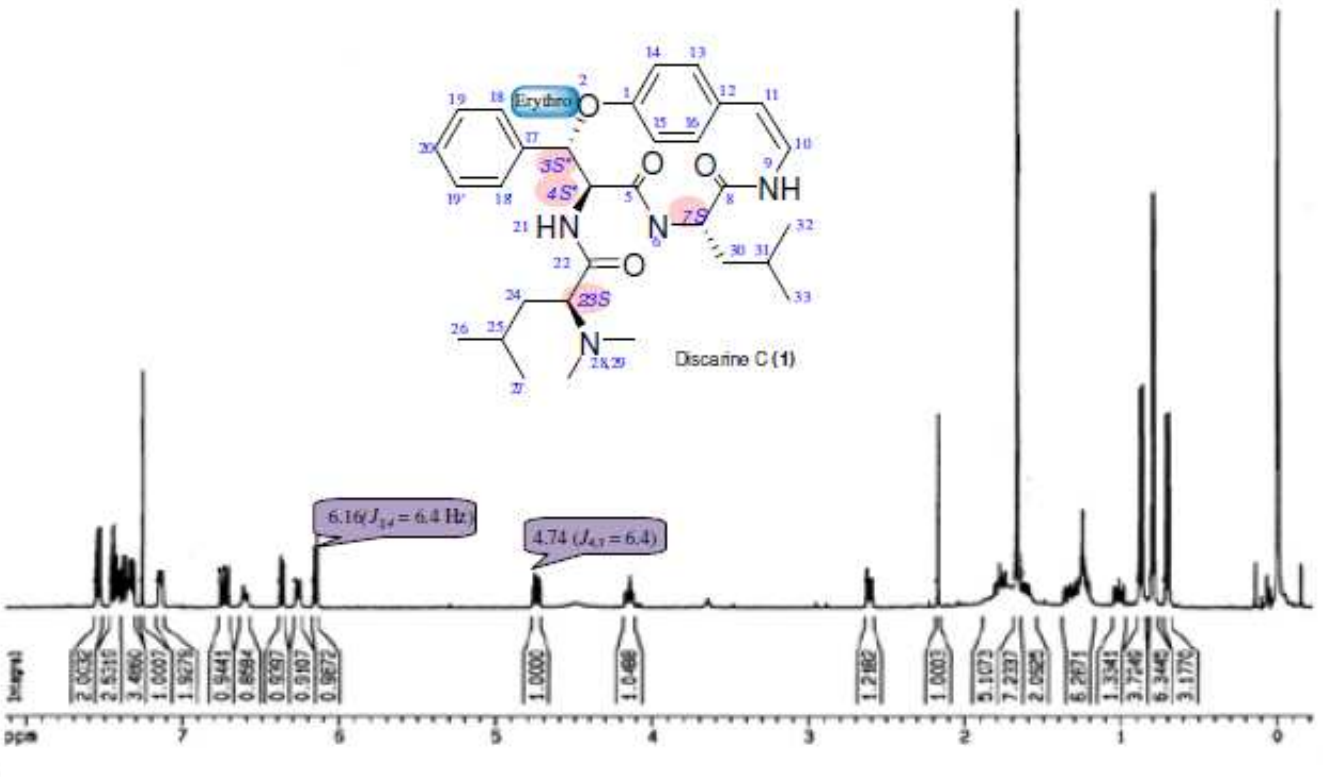
Discarine C (**1**): white powder; mp 240–241 °C, TLC Rf = 0.57 ($CHCl_3$-MeOH 98:2), $[\alpha]_D^{25}$= -239 (c 0.1, $CHCl_3$), was determined by direct comparison with authentic samples and ^{1}H NMR ($CDC1_3$, 400.1 MHz): δ 7.32 (1H, bs), 7.12-7.55 (5H, m, overlap), 7.12-7.55 (4H, m, overlap), 6.73 (1H, dd, $J_{10,11}$ = 7.6, $J_{10,9}$ = 10.4 Hz), 6.61 (1H, d, $J_{9,10}$ = 10.4 Hz), 6.37 (1H, d, $J_{11,10}$ = 7.6 Hz), 6.16 (1H, d, $J_{3,4}$ = 6.4 Hz), 6.26 (1H, d, $J_{6,7}$ = 8.0 Hz), 4.74 (1H, dd, $J_{4,3}$ = 6.4, $J_{4,21}$ = 8.8 Hz), 4.14 (1H, m), 2.61 (1H, dd, $J_{23,24}$ = 4.8, $J_{23,24'}$ = 5.2 Hz), 1.66 (6H, s), 1.77 (1H, m), 1.27 (1H, m), 1.61 (1H, m), 1.31 (1H, m), 1.00 (1H, m), 1.23 (1H, t), 0.87 (3H, d, $J_{33,31}$ = 6.4 Hz), 0.79 (3H, d, $J_{27,25}$ = 6.8 Hz), 0.79 (3H, d, $J_{32,31}$ = 6.8 Hz), 0.71 (3H, d, $J_{26,25}$ = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.8, 171.1, 167.5,155.3, 137.2, 132.7, 132.1-123.6 (C13-16), 127.8-129.0 (C-18-20), 125.6, 115.0, 81.9 (C-3), 65.4(C-7), 55.9 (C-4), 54.0 (C-23), 40.9, 39.1, 33.7, 26.1, 24.4, 23.2, 22.8, 21.8, 20.5.

Discarine D (**2**): white powder; mp 211-212°C, TLC Rf = 0.54 ($CHCl_3$-MeOH 98:2), $[\alpha]_D^{25}$= -148 (c 0.1, $CHCl_3$), was determined by direct comparison with authentic samples and ^{1}H NMR ($CDC1_3$, 400.1 MHz): δ 7.21 (1H, bs), 6.74 (1H, dd, $J_{10,11}$ = 7.6, $J_{10,9}$ = 12.4 Hz), 7.12-7.55 (4H, overlap), 7.12-755 (5H, overlap), 7.05-7.50 (5H, overlap), 6.52 (1H, d, $J_{9,10}$ = 12.4 Hz), 6.49 (1H, d, $J_{6,7}$ = 8.0 Hz), 6.39 (1H, d, $J_{11,10}$ = 7.6 Hz), 6.11 (1H, d, $J_{3,4}$ = 6.4 Hz, H-3), 4.66 (1H, dd, $J_{4,3}$ = 6.4, $J_{4,21}$ = 8.8 Hz), 4.57 (1H, m), 2.86/3.19 (2H, dd, $J_{30,31}$ = 9.2, $J_{30,7}$ = 4.0 Hz), 2.26 (1H, dd, $J_{23,24}$ = 6.0, $J_{23,24'}$ = 5.8 Hz), 1.57 (6H, s), 1.48 (1H, m), 1.09 (1H, m), 0.96 (1H, m), 0.85 (3H, d, $J_{27,25}$ = 6.8 Hz), 0.79 (3H, d, $J_{26,25}$ = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.7, 171.1, 166.7, 155.3, 137.3, 136.3, 132.5, 132.0-123.4 (C13-16), 126.7-129.0 (C32-34), 127.8-128.8 (C-18-20), 125.5, 115.7, 81.9 (C-3), 64.8 (C-7), 55.9 (C-4), 54.0 (C-23), 40.8, 36.3, 34.6, 26.0, 22.9, 22.2.

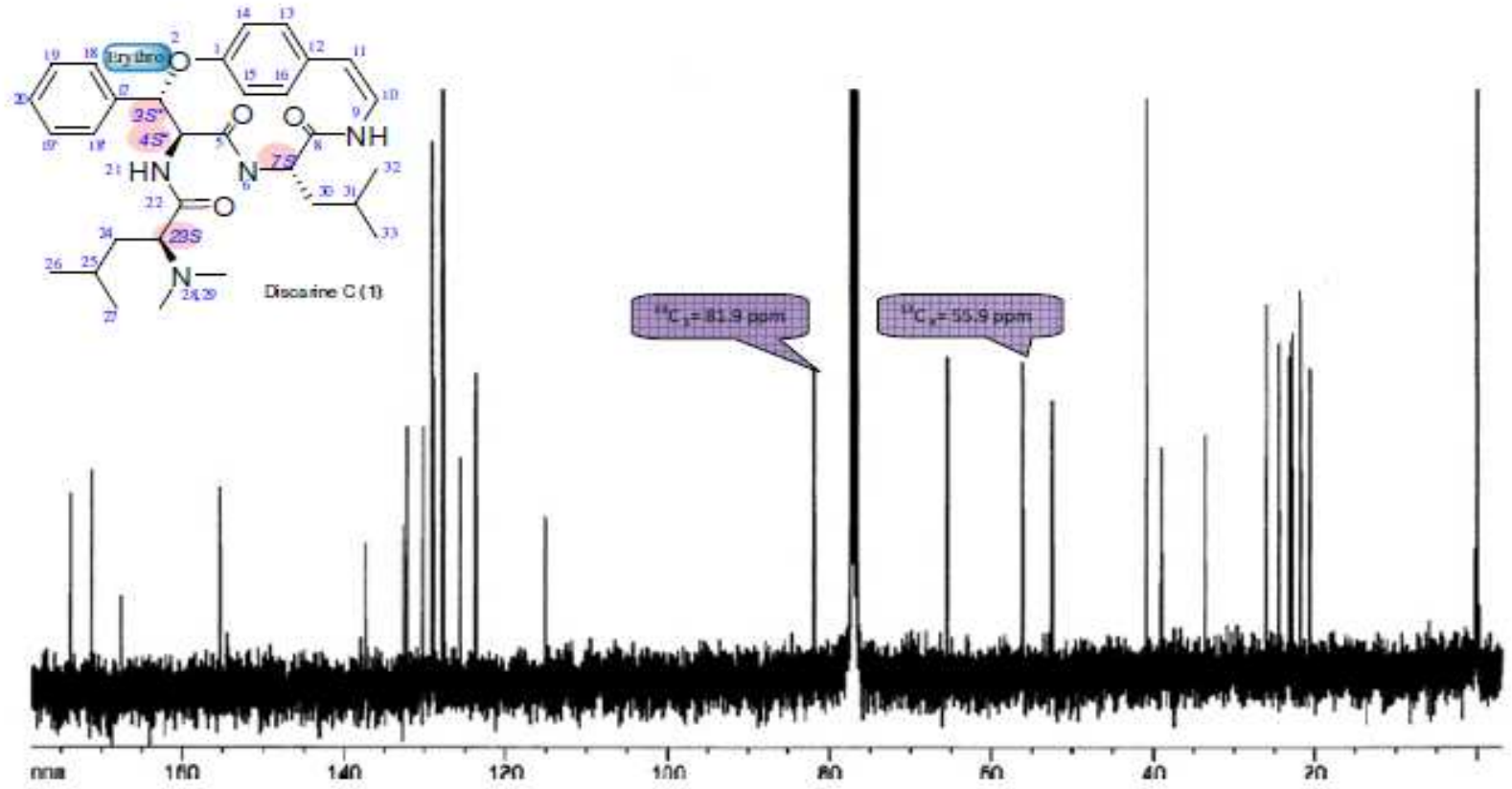
Myrianthine A (**3**): white powder; mp 206–207 °C, TLC Rf = 0.51 ($CHCl_3$-MeOH 98:2), $[\alpha]_D^{25}$= -263 (c 0.1, $CHCl_3$), was determined by direct comparison with authentic samples and ^{1}H NMR ($CDC1_3$, 400.1 MHz): δ 7.54-7.12 (4H, overlap), 7.54-7.12 (5H, overlap), 7.26 (1H, overlap), 6.73 (1H, dd, $J_{10,11}$ = 7.6,

$J_{10,9}$ = 10.4 Hz), 6.61 (1H, d, $J_{9,10}$ = 10.4 Hz), 6.40 (1H, d, $J_{6,7}$ = 8.4 Hz), 6.38 (1H, d, $J_{11,10}$ = 7.6 Hz), 6.21 (1H, d, $J_{3,4}$ = 6.4 Hz), 4.71 (1H, dd, $J_{4,3}$ = 6.4, $J_{4,21}$= 8.4 Hz), 4.09 (1H, dd, $J_{7,30}$ = 3.2, $J_{7,21}$ = 8.4 Hz), 2.63 (1H, dd, $J_{23,24}$ = 8.4, $J_{23,24'}$ =5.8 Hz), 2.19 (1H, m), 1.68 (6H, s), 1.62 (1H, m), 1.08 (1H, m), 1.02 (1H, m), 1.21 (1H, m), 0.97(1H, m), 0.86 (3H, d, $J_{27,25}$ = 6.8 Hz), 0.78 (3H, d, $J_{26,25}$ = 6.8 Hz), 0.81 (3H, t), 0.66 (3H, d, $J_{33,30}$ = 7.2 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.8, 171.6, 166.9, 155.4, 137.4, 132.7, 132.3-123.6 (C-13- 16), 129.1-127.7 (C-18-20), 125.7, 115.3, 81.8 (C-3), 65.8 (C-7), 59.3 (C-4), 56.4 (C-23), 33.8, 41.2, 35.2 , 33.8, 26.1, 23.0, 21.7, 20.3,15.9.

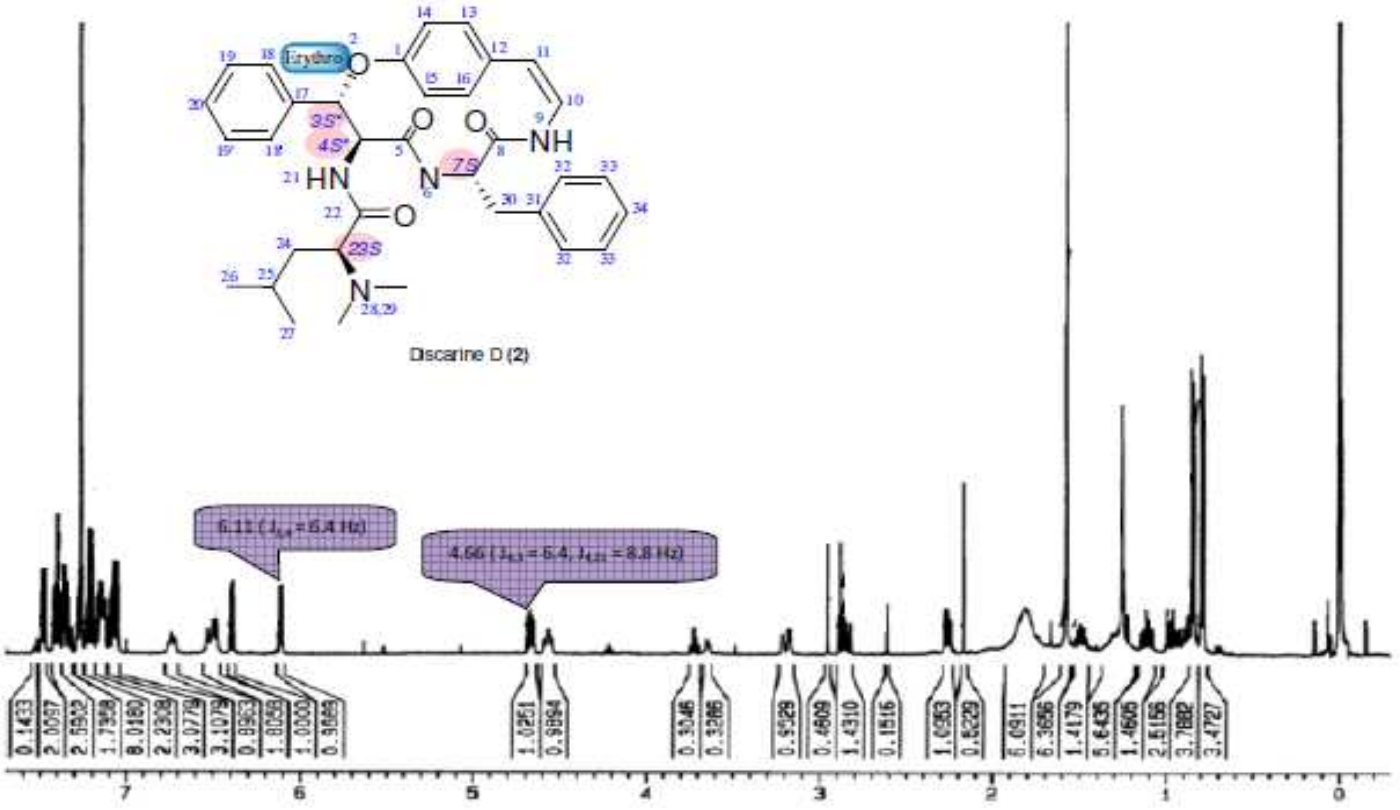
NMR Selected Spectra for Compounds



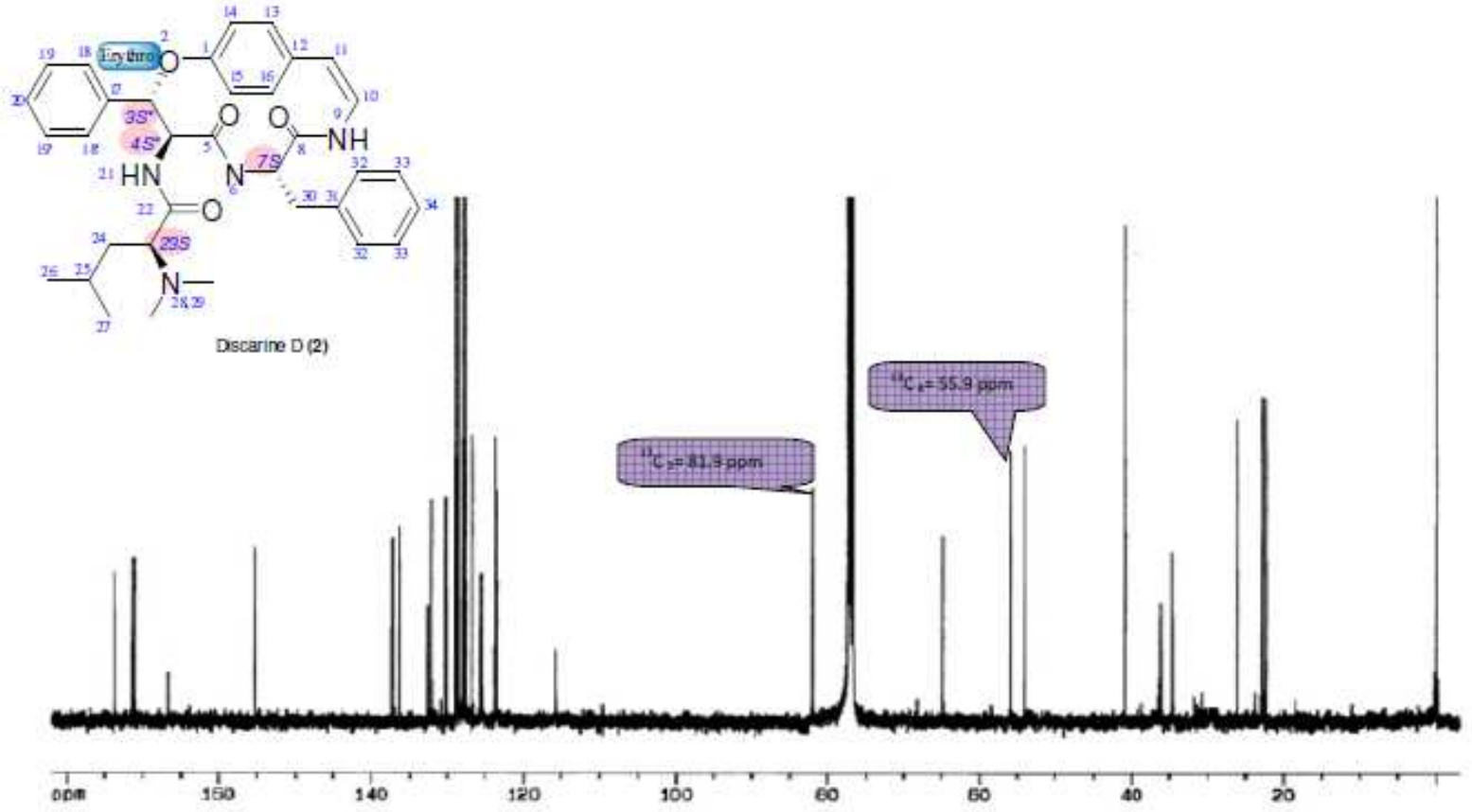
S1. ^{1}H NMR spectrum of Discarine C (1) in $CDCl_3$



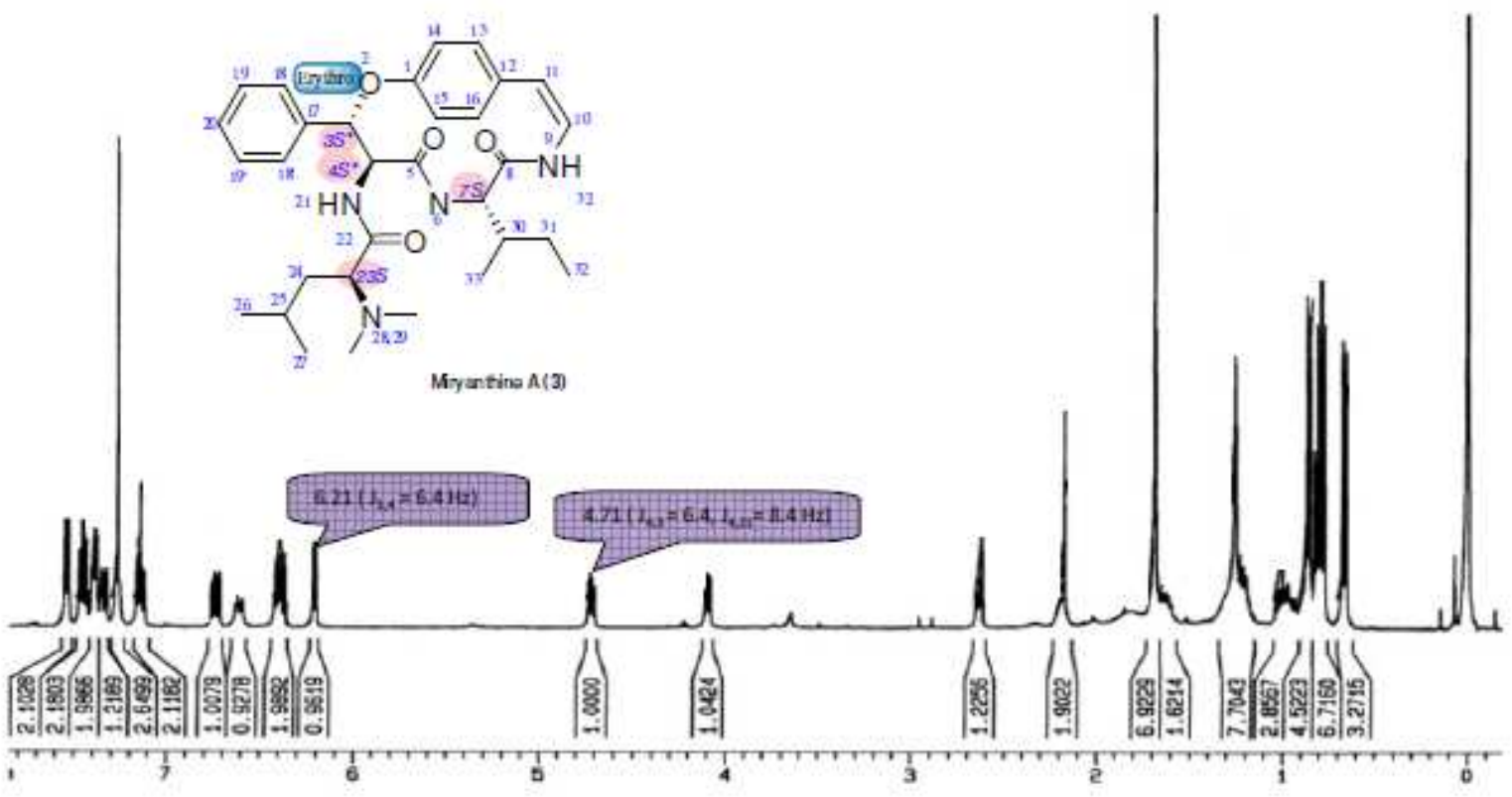
S2. ^{13}C NMR spectrum of Discarine C (1) in $CDCl_3$



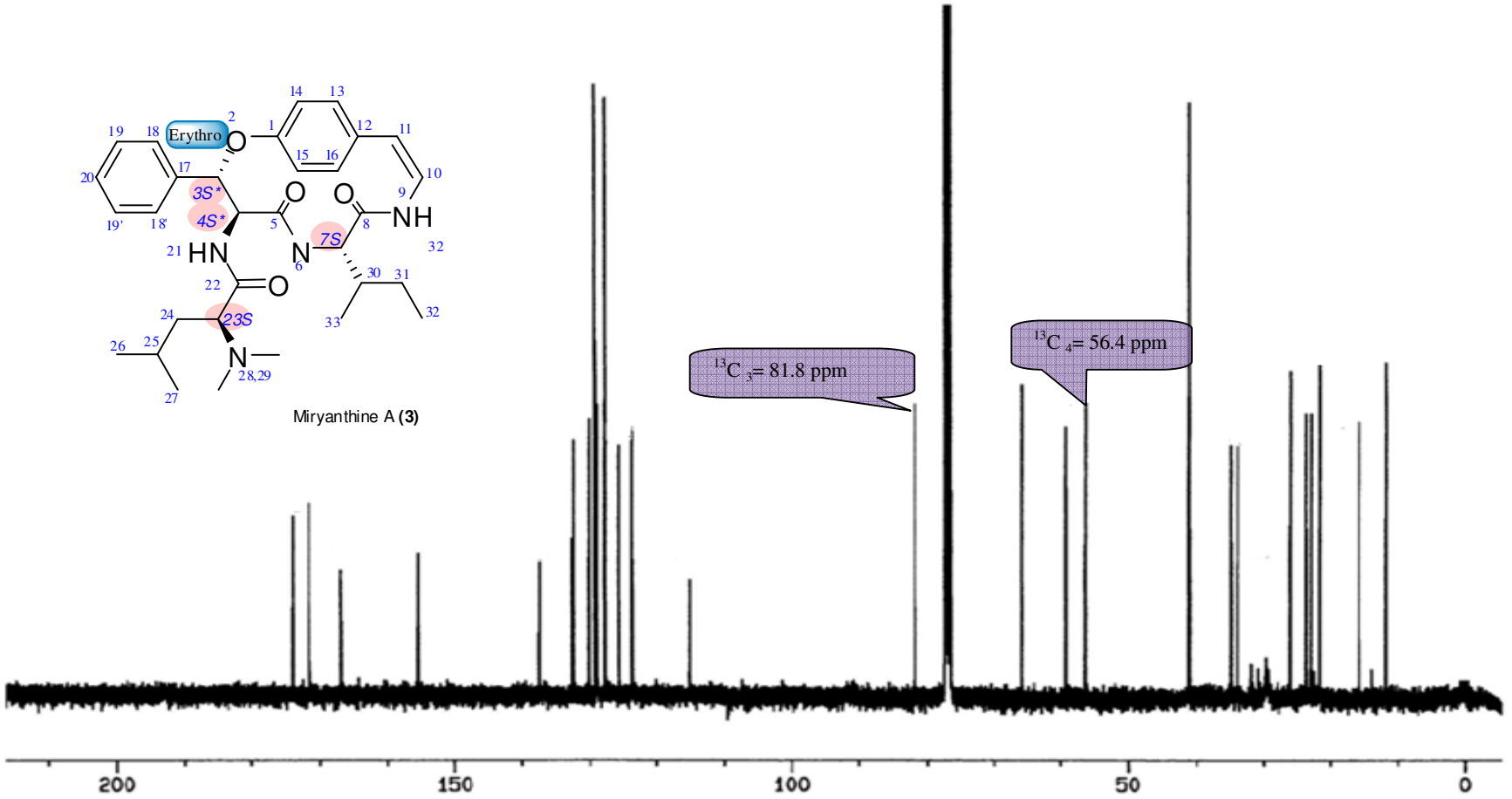
S3. ^{1}H NMR spectrum of Discarine D (2) in $CDCl_3$



S4. ^{13}C NMR spectrum of Discarine D (2) in $CDCl_3$



S5. ^{1}H NMR spectrum of Miryanthine A (3) in $CDCl_3$



S6. ^{13}C NMR spectrum of Miryanthine A (3) in $CDCl_3$

1. General Procedure for the Synthesis of Tripeptides Fragments 5-7:

In a round-bottom flask, a mixture of the corresponding protected dipeptide **4** (2.36 g, 5.53 mmol), 1-hydroxybenzotriazol (0.75 g, 5.53 mmol), N-methylmorpholine (0.61 mL, 5.53 mmol) and the respective amino acid ester (5.53 mmol) in dry THF (5 mL). The solution was kept and cooling in an ice water bath and stirred vigorously with a magnetic stirrer. The carbodiimide (DCCI, 1.14 g, 5.80 mmol) was added and stirring at 0 °C in a ice bath. After about 1 hour, the ice- water in the bath is replaced by water of room temperature and stirring continued for more 0.5 hours. The DCCU formed was removed by filtration and thoroughly washed with ethyl acetate (3 x 25mL). The filtrate and washing are combined and concentrated in vacuo. The residue was dissolved in ethyl acetate, washings with a saturated aq. $NaHCO_3$ (3 x 50 mL), aq. citric acid 10% (w/v), followed by water. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was crystallized from a small volume of ethyl ether-ether petroleum, yielding pure diastereoisomeric forms of **5**-**7**.

1.1. (5S,8S,11S)-methyl 8-((R)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**5a**): yield 50%; yellow solid; mp. 90-91.3 °C; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.25 (1H, d, overlap), 7.16 (1H, overlap), 7.14-7.08 (10H, m, overlap), 5.35 (1H, d, *J* = 6.1 Hz), 5.32 (1H, bs, H-3), 5.03/4.94(2H, d, *J* = 12.0 Hz), 4.72 (1H, dd, *J* = 8.0, 3.6 Hz, H-4), 4.44 (1H, bs, H-7), 4.12 (1H, m, H-23), 3.61 (3H, s), 1.48 (2H, m), 1.48 (1H, m), 1.48 (1H, m), 1.36/1.25 (2H, m), 0.88 (3H, d, *J* = 6.4 Hz), 0.88 (3H, d, *J* = 6.4 Hz), 0.85 (3H, d, *J*= 6.6 Hz), 0.85 (3H, d, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 172.9, 172.7, 169.6, 156.2, 139.1, 136.0, 128.5, 128.5, 128.1, 127.9, 127.7, 126.0, 72.1(C-3), 67.1, 57.8 (C-4), 53.7 (C-23), 52.2, 51.0 (C-7), 41.0, 41.0, 24.7, 24.5, 22.7, 22.6, 21.8.

1.2. (5S,8R,11S)-methyl 8-((S)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**5b**): yield 48%; yellowish viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.30 (1H, sb), 7.3 (1H, d, overlap), 7.08-7.14 (5H, overlap), 6.98 (1H, d, *J* = 7.9 Hz), 5.47 (1H, bs), 5.27 (1H, d, *J* = 6.7 Hz, H-3), 5.10/4.98 (2H, d, *J* =12.2 Hz), 4.75 (1H, d, *J* = 7.04 Hz, H-4), 4.50 (1H, dd, *J* = 7.9, 4.8 Hz, H-7), 3.99 (1H, dd, *J* = 7.16, 6.7 Hz, H-23), 3.67 (3H, s), 1.91 (2H, m), 1.39 (1H, m), 1.33 (1H, m), 1.25/1.09 (2H, m), 0.87 (3H, d, *J* = 6.9 Hz), 0.87(3H, d, *J* = 6.9 Hz), 0.71 (3H, d, *J* = 6.3 Hz), 0.71 (3H, d, *J* = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 172.5, 171.6, 170.0, 156.2, 139.6, 135.9, 128.5, 128.2, 128.2, 127.9, 127.4, 125.6, 71.8 (C-3), 67.2, 58.8 (C-4), 54.1 (C-23), 52.3, 51.3 (C-7), 40.5, 40.2, 33.7, 25.2, 24.3, 22.2, 21.7, 21.5.

1.3. (5S,8S,11S)-methyl 11-benzyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**6a**): yield 51%; white powder solid; mp 139.8-140.8 ºC; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.17-7.34 (15H, bs), 7.09 (1H, d, *J* = 8.0 Hz), 7.00 (1H, d, *J* = 8.3 Hz), 5.29 (1H, d,

J = 3.0 Hz, H-3), 5.12 (1H, bs), 5.10/5.03 (2H, d, *J* = 12.3 Hz), 4.77 (1H, dd, *J* = 8.2, 6.8, 4.4 Hz, H-7), 4.70 (1H, dd, *J* = 8.0, 3.0 Hz, H-4), 4.11 (1H, m, H-23), 3.72 (3H, s), 3.10, 3.03 (2H, dd, *J* = 6.8, 4.4 Hz), 1.50 (1H, m), 1.41, 1.28 (2H, m), 0.85 (3H, d, *J* = 6.4 Hz), 0.85 (3H, d, *J* = 6.4 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 172.7, 171.3, 169.7, 156.2, 139.0, 135.9, 135.7, 129.2, 128.5, 128.5, 128.5, 128.2, 128.0, 127.7, 127.1, 125.8, 71.9 (C-3), 67.2, 57.7 (C-4), 53.7 (C-7), 53.5 (C-23), 52.3, 40.9, 37.6, 24.5, 22.8, 21.1; FAB-M^+ (m/z): 591.

1.4. (5S,8R,11S)-methyl 11-benzyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**6b**): yield 46%; white powder solid; mp 166 ºC; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.48 (1H, d, *J* = 7.56 Hz), 7.10-7.25 (15H, m, overlap), 6.98 (1H, d, *J* = 7.9 Hz), 5.42 (1H, sb, H-3), 5.31 (1H, d, *J* = 7.3 Hz), 5.04/4.94 (2H, d, *J* = 12.1 Hz), 4.75 (1H, dd, *J* = 7.9 Hz, H-7), 4.50 (1H, dd, *J* = 7.9, 7.6, 4.8 Hz, H-4), 4.00 (1H, m, H-23), 3.61 (3H, s), 3.08/3.00 (2H, dd, *J* = 14.0, 7.6, 6.0 Hz), 1.36/1.30 (2H, m), 1.32 (1H, m), 0.72 (3H, d, *J* = 6.4 Hz), 0.72 (3H, d, *J* =6.4 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.5, 171.0, 171.0, 139.4, 136.7, 135.6, 134.9, 129.1, 128.4, 127.9, 127.6, 127.4, 127.0, 126.6, 126.0, 125.6, 71.8 (C-3), 65.3, 58.7 (C-4), 57.2 (C-7), 53.0 (C-23), 52.1, 40.8, 36.9, 24.2, 22.2, 21.3.

1.5. (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**7a**): yield 53%; yellowish solid; mp 81,8-82,5 ºC; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.33 (5H, overlap), 7.23 (1H, m, overlap), 7.18-7.24 (5H, overlap), 7.10 (1H, d, *J* =7.7 Hz), 5.32 (1H, d, *J* = 3.0 Hz, H-3), 5.18 (1H, d, *J* = 6.5 Hz), 5.10/5.07 (2H, d, *J* = 11.8 Hz), 4.74 (1H, dd, *J* =7.90, 3.0 Hz, H-4), 4.49 (1H, dd, *J* = 8.2, 5.3 Hz, H-7), 4.17 (1H, m, H-23), 3.72 (3H, s), 1.86 (1H, m), 1.53 (1H, m), 1.47 (2H, m), 1.38/1.15 (2H, m), 0.88 (3H, t, overlap), 0.88 (d, overlap), 0.85 (3H, d, *J* = 6.6 Hz), 0.85 (3H, d, *J* =6.6 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.1, 171.6, 170.2, 156.1, 139.0, 136.0, 128.5, 128.3, 128.2, 128.0, 127.8, 125.9, 71.9 (C-3), 67.2, 57.6 (C-4), 56.8 (C-7), 53.7 (C-23), 52.1, 41.0, 37.6, 25.0, 24.6, 22.7, 21.8, 15.3, 11.4.

1.6. (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (**7b**): yield 45%; yellowish viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.36 (1H, m, overlap), 7.31-7.35 (5H, m, overlap), 7.31 (5H, bs), 6.98 (1H, d, *J* = 7.9 Hz), 5.47 (1H, bs, H-3), 5.31 (1H, d, *J* = 6.7 Hz), 4.99/4.51(2H, d, *J* = 12.1 Hz), 4.75 (1H, d, *J* = 7.9 Hz, H-4), 4.50 (1H, dd, *J* = 7.9, 4.8 Hz, H-7), 3.99 (1H, dd, *J* = 14.3, 7.0 Hz, H-23), 3.67 (3H, s), 1.90 (1H, m), 1.38 (2H, m), 1.15 (2H, m), 1.11 (1H, m) 0.90 (3H, d, *J* = 6.8 Hz), 0.85 (3H, t, *J* = 7.4 Hz), 0.72 (3H, m), 0.72 (3H, m); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 173.2, 172.4, 170.8, 156.2, 139.4, 136.0, 128.5, 128.3, 128.2, 127.9, 127.5, 125.6, 71.8 (C-3), 67.0, 58.7 (C-4), 57.2 (C-7), 54.0 (C-23), 52.1, 40.8, 36.9, 25.2, 24.3, 22.2, 22.2, 15.5, 11.5.

2. General procedure for the removal of the benzyloxycarbonyl-group:

The individual tripeptides (**5**-**7**) were dissolved in absolute methanol in two neck round bottom flask, provide with a magnetic stirrer, a gas inlet-outlet tube then were added catalytic amount of 10% palladium-on-charcoal and H_2 was bubbling up the resulting mixture, continually stirred at room temperature for 3 h and monitored to completion by TLC. After the reaction was filtered and the catalyst is washed with methanol, the filtrate were combined and concentrated in vacuo to give crude products purify from silica-gel column chromatography.

2.1. (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (**8a**): yield 90%; colorless viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 8.11 (1H, d, *J* = 7.9 Hz), 7.36 (2H, d, *J* = 7.4 Hz), 7.30 (2H, m, overlap), 7.30 (1H, overlap), 7.24 (1H, m), 5.36 (1H, d, *J* = 2.7 Hz, H-3), 4.66 (1H, dd, *J* = 7.9, 2.7 Hz, H-4), 4.53 (1H, dt, *J* = 7.8, 5.4 Hz, H-7), 3.73 (3H, s), 3.36 (1H, m, H-23), 1.60 (2H, m, overlap), 1.60 (1H, m, overlap), 1.54 (1H, m), 1.37 (1H, m), 1.35-1.05 (1H, m) 0.91 (3H, d, *J* = 5.4 Hz), 0.88 (3H, d, *J* = 5.4 Hz), 0.83 (3H, d, *J* = 5.9 Hz), 0.81 (3H, d, *J* = 5.9 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 176.5, 172.7, 170.9, 139.2, 128.2, 127.6, 125.9, 71.9 (C-3), 57.2 (C-4), 53.4 (C-23), 52.3, 51.0 (C-7), 43.5, 41.0, 24.9, 24.5, 23.4, 22.6, 21.7, 21.0.

2.2. (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (**8b**): yield 91%; colorless viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 8.05 (1H, bs), 7.45 (1H, d, *J* = 8.4 Hz), 7.37 (2H, m), 7.29 (2H, m), 7.22 (1H, m), 5.36 (1H, d, *J* = 2.8 Hz, H-4), 4.68 (1H, d, *J* = 2.8 Hz, H-3), 4.50 (1H, m, H-7), 3.68 (3H, s), 3.44(1H, m, overlap, H-23), 1.56 (2H, m, overlap), 1.56 (1H, m, overlap), 1.56 (1H, m, overlap), 1.42/1.30 (2H, m), 0.89 (3H, d, *J* = 6.0 Hz), 0.88 (3H, overlap), 0.82 (3H, d, *J* = 6.0 Hz), 0.80 (3H, d, *J* = 6.0 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 175.5, 173.5, 171.0, 139.2, 128.3, 127.6, 125.8, 72.1 (C-3), 58.4 (C-4), 53.2 (C-23), 52.4, 51.0 (C-7), 43.1, 40.5, 24.7, 24.5, 22.9, 22.7, 21.6, 21.4.

2.3. (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (**9a**): yield 94%; colorless viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 8.01 (1H, d, *J* = 8.2 Hz), 7.25 (1H, overlap), 7.19-7.73 (5H, overlap), 7.19-7.73 (5H, overlap), 5.36 (1H, d, *J* = 2.5 Hz, H-3), 4.82(1H, dd, *J* = 7.6, 5.4 Hz, H-7), 4.58 (1H, dd, *J* = 8.2, 2.5 Hz, H-4), 3.21 (1H, m, H-23), 3.72 (3H, s), 3.17/ 2.99 (2H, dd, *J* = 14.0, 7.6, 5.4 Hz), 1.48 (1H, m), 1.29/0.94 (2H, m), 0.79 (3H, d, *J* = 6.6 Hz), 0.79 (3H, d, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 176.5, 171.0, 170.9, 139.3, 135.9, 129.2, 128.4, 128.2, 127.6, 126.9, 125.8, 71.7 (C-3), 57.1 (C-4), 53.3 (C-7), 53.2 (C-23), 52.4, 43.4, 37.6, 24.5, 23.0, 21.4.

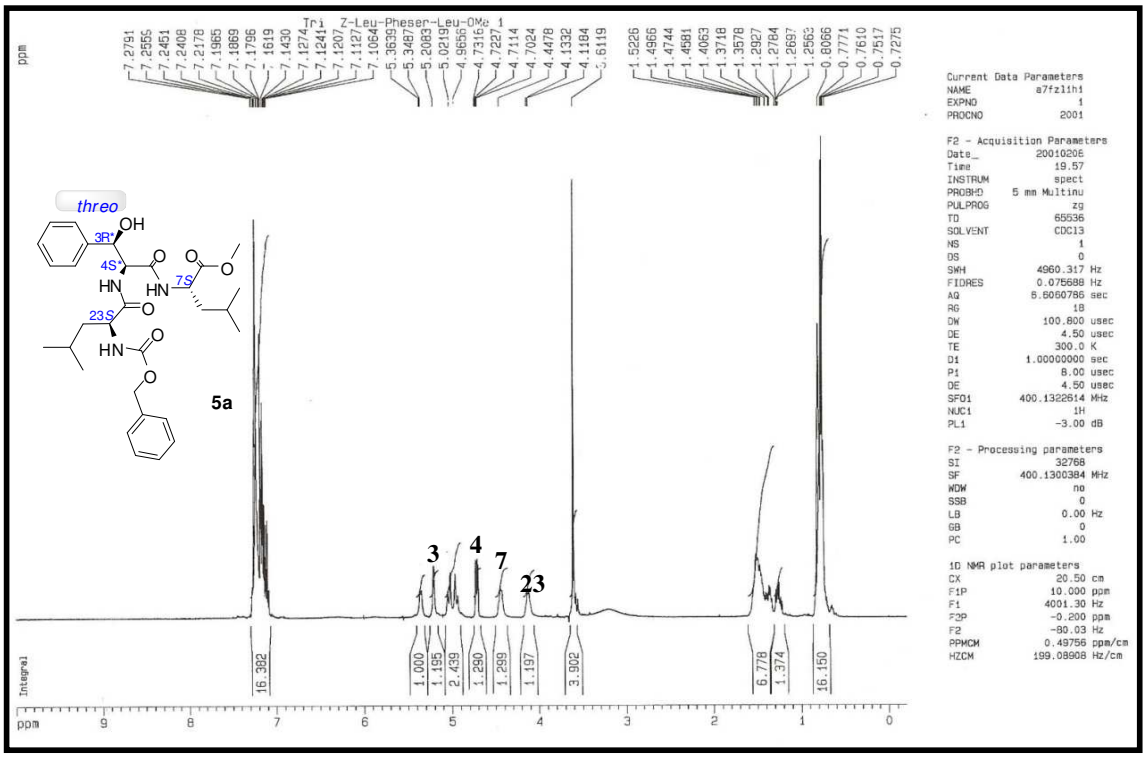
2.4. (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (**9b**): yield 93%; colorless viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 8.03 (1H, d, J = 8.2 Hz), 7.25 (1H, overlap), 7.20-7.73 (5H, overlap), 7.20-7.73 (5H, overlap), 5.36 (1H, d, J = 2.5 Hz, H-3), 4.81 (1H, dd, J = 7.6, 5.4 Hz, H-7), 4.57 (1H, dd, J = 8.2, 2.5 Hz, H-4), 3.70 (3H, s), 3.22 (1H, m, H-23), 3.00/3.17 (2H, dd, J = 14.0, 7.6, 5.4 Hz), 1.49 (1H, m), 0.93 (1H, m), 1.29 (1H, m), 0.80 (3H, d, J = 6.6 Hz), 0.79 (3H, d, J = 6.6 Hz);^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 176.7, 171.2, 171.1, 139.5, 135.9, 129.4, 128.6, 128.4, 127.8, 127.1, 126.0, 71.9 (C-3), 57.3 (C-4), 53.5 (C-7), 53.4 (C-23), 52.6, 43.6, 37.6, 24.5, 23.0, 21.5.

2.5. *(2S,3S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate* (**10a**): yield 94%; colorless viscous mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 8.12 (1H, d, J = 7.8 Hz), 7.37 (2H, m), 7.35 (1H, overlap), 7.22 (2H, m), 5.37 (1H, d, J = 2.2 Hz, H-3), 4.63 (1H, dd, J = 7.8, 2.2 Hz, H-4), 4.50 (1H, dd, J = 8.3, 5.6 Hz, H-7), 3.74 (3H, s), 3.34 (1H, m, H-23), 1.89 (1H, m), 1.52 (1H, m), 1.39 (1H, m), 1.03 (1H, m), 1.39 (1H, m), 1.15 (1H, m), 0.89 (3H, d, J = 7.40 Hz), 0.88 (3H, t, J = 6.9 Hz), 0.83 (3H, d, J = 2.8 Hz), 0.81 (3H, d, J = 2.8 Hz); ^{13}C NMR ($CDCl_3$,100.6 MHz): δ 176.7, 171.6, 139.2, 128.2, 127.6, 125.8, 71.8 (C-3), 57.2 (C-4), 56.7 (C-7), 53.4 (C-23), 52.1, 43.5, 37.5, 25.0, 24.5, 23.0, 21.4, 15.4, 11.5.

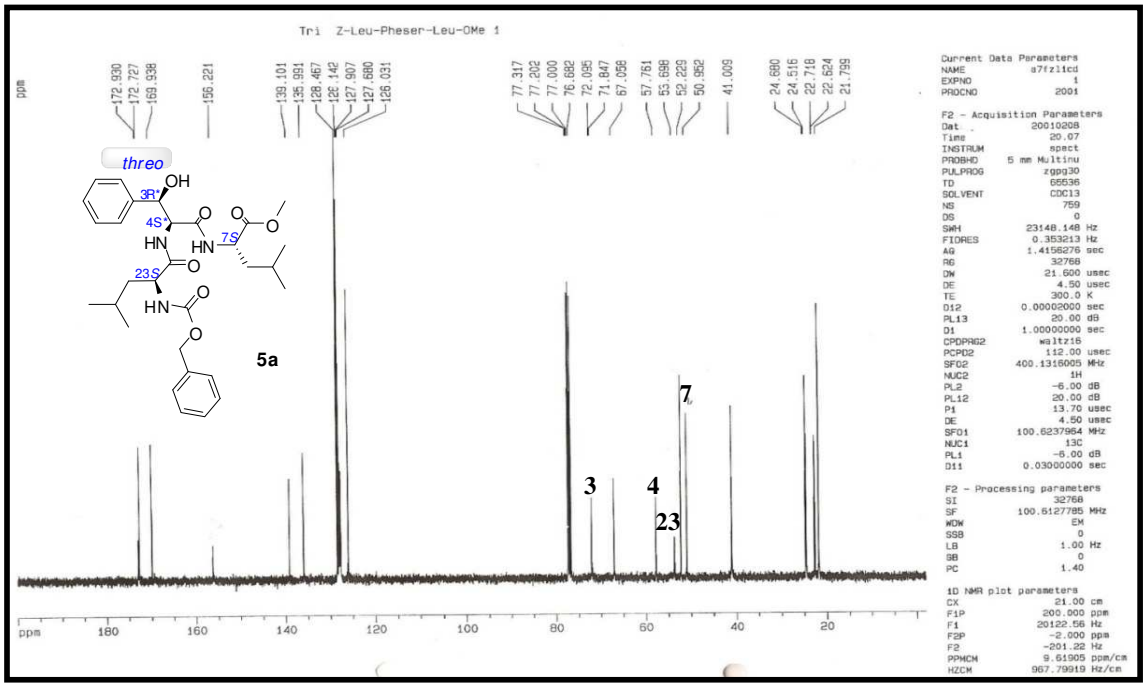
2.6. (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (**10b**): yield 95%; colorless semisolid mass; ^{1}H NMR ($CDC1_3$, 400.1 MHz) δ 7.99 (1H, d, J = 7.8 Hz), 7.39 (2H, m), 7.32 (2H, m), 7.32 (1H, overlap), 7.30 (1H, m), 5.43 (1H, d, J =2.4 Hz, H-3), 4.61 (1H, dd, J = 7.8, 2.4 Hz, H-4), 4.49 (1H, dd, J = 8.4, 4.8 Hz, H-7), 3.71 (3H, s), 3.28 (1H, d, J = 9.5, 4.4 Hz, H-23), 1.90 (1H, m), 1.56 (1H, m), 1.55 (1H, m), 1.38 (1H, m), 1.31 (1H, m), 1.17 (1H, m), 0.92 (3H, t, J = 7.4 Hz), 0.91 (3H, d, J = 6.9 Hz), 0.88 (3H, d, J = 6.1 Hz), 0.85 (3H, d, J = 6.1 Hz); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 177.4, 171.9, 171.5, 139.4, 128.3, 127.6, 125.7, 71.6 (C-3), 57.6 (C-4), 56.8 (C-7), 53.5 (C-23), 52.1, 43.9, 37.2, 25.0, 24.7, 23.1, 21.3, 15.6, 11.5.

3. General procedure for the reductive methylation using sodium cyanoborohydride:

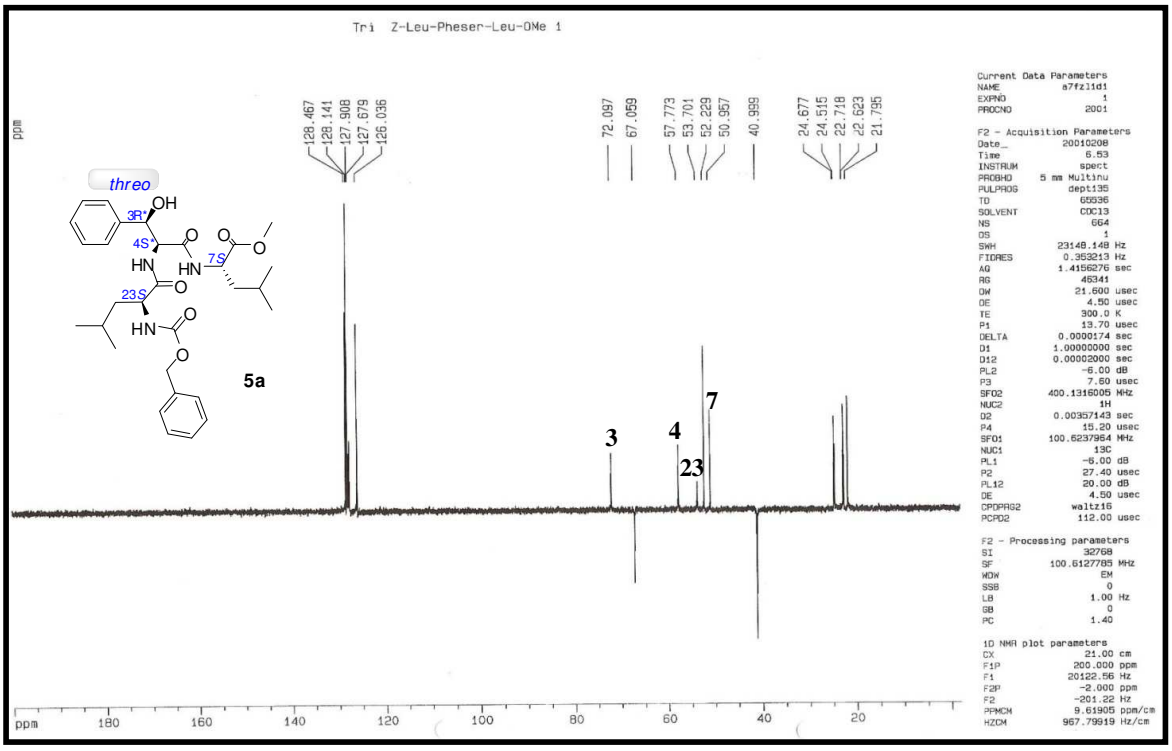
On an individual diastereomeric tripeptides solution (3.0 mmol) in methanol (10 mL) was added formaldehyde (6.0 mmol) at room temperature and in a single portion. After 1 h of stirring, $NaBH_3CN$ (6.0 mmol) was added and allowed to stir at room temperature overnight. The reaction was monitored for completion by TLC analysis. The solution was evaporated to dryness in vacuo and the crude product was purified by column chromatography.



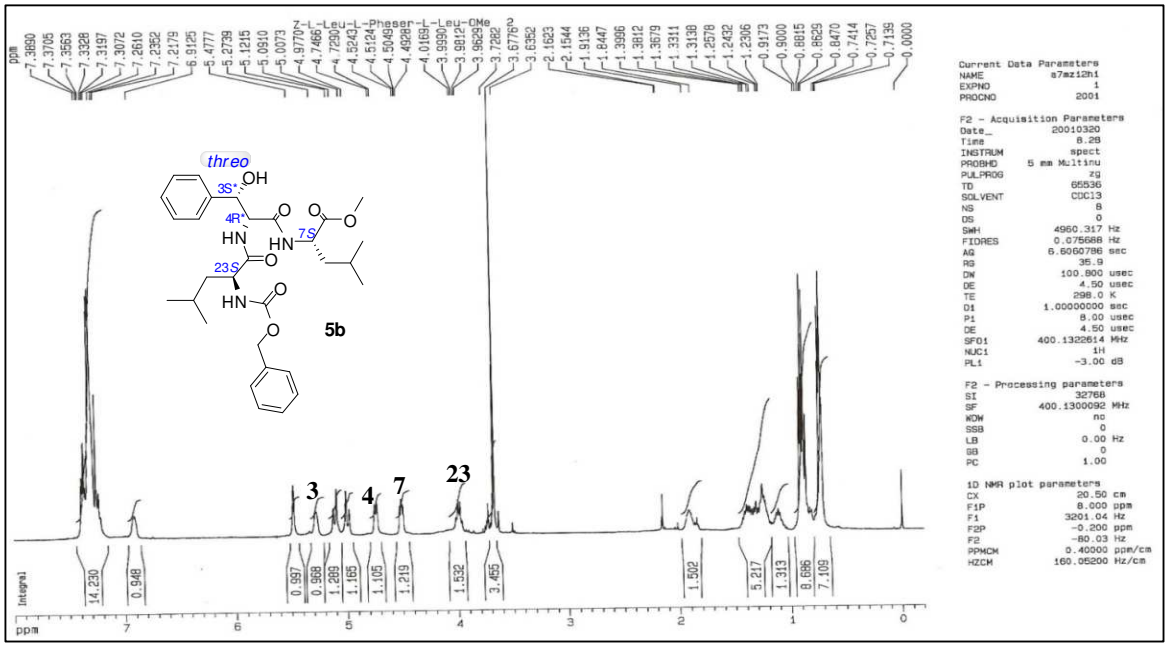
S7. ^{1}H NMR spectrum of (5S,8S,11S)-methyl 8-((R)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5a) in $CDCl_3$



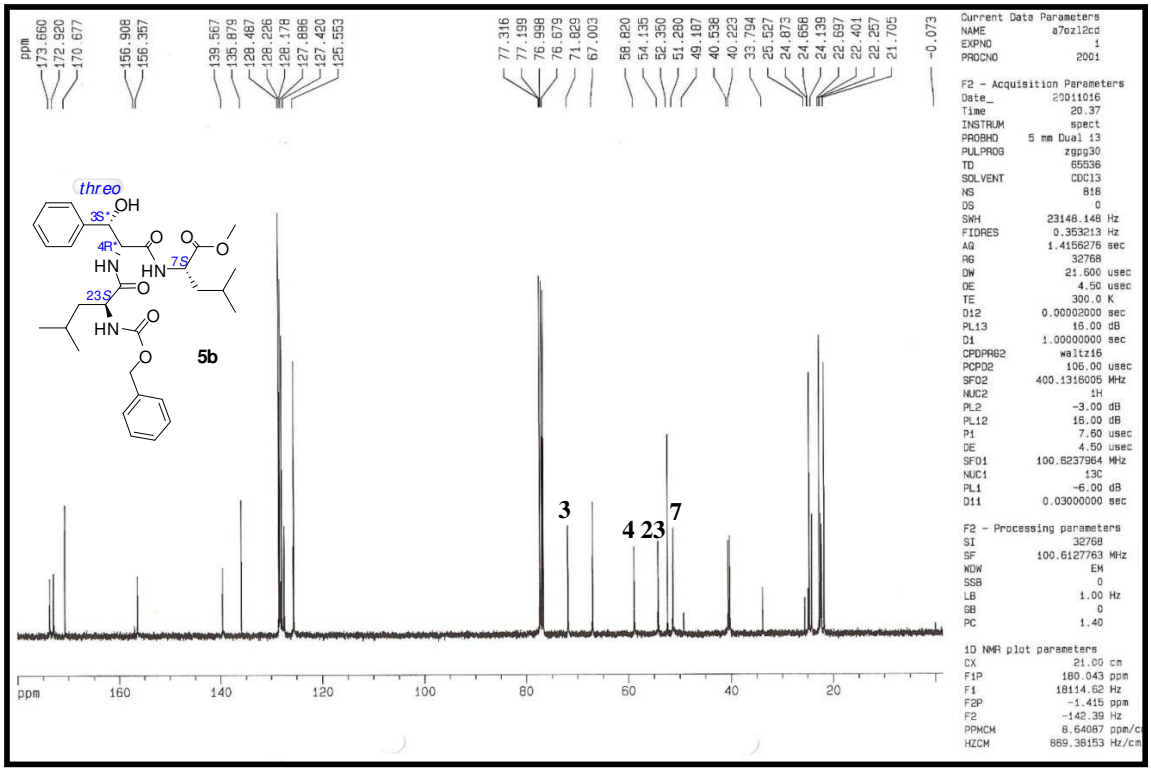
S8. ^{13}C NMR spectrum of (5S,8S,11S)-methyl 8-((R)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5a) in $CDCl_3$



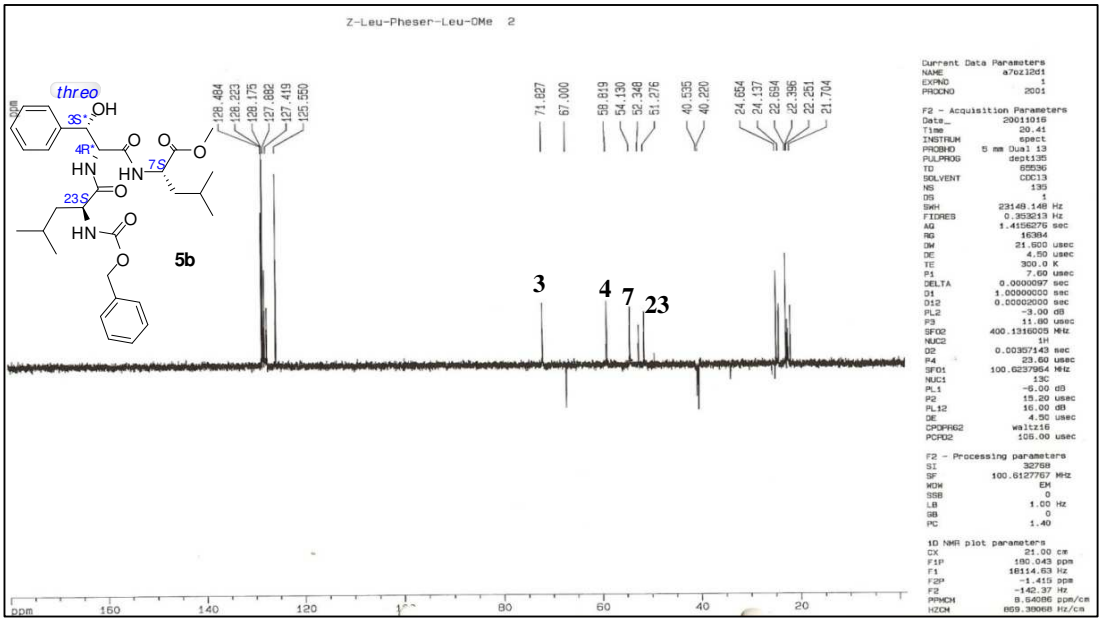
S9. DEPT 135 spectrum of (5S,8S,11S)-methyl 8-((R)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5a) in $CDCl_3$



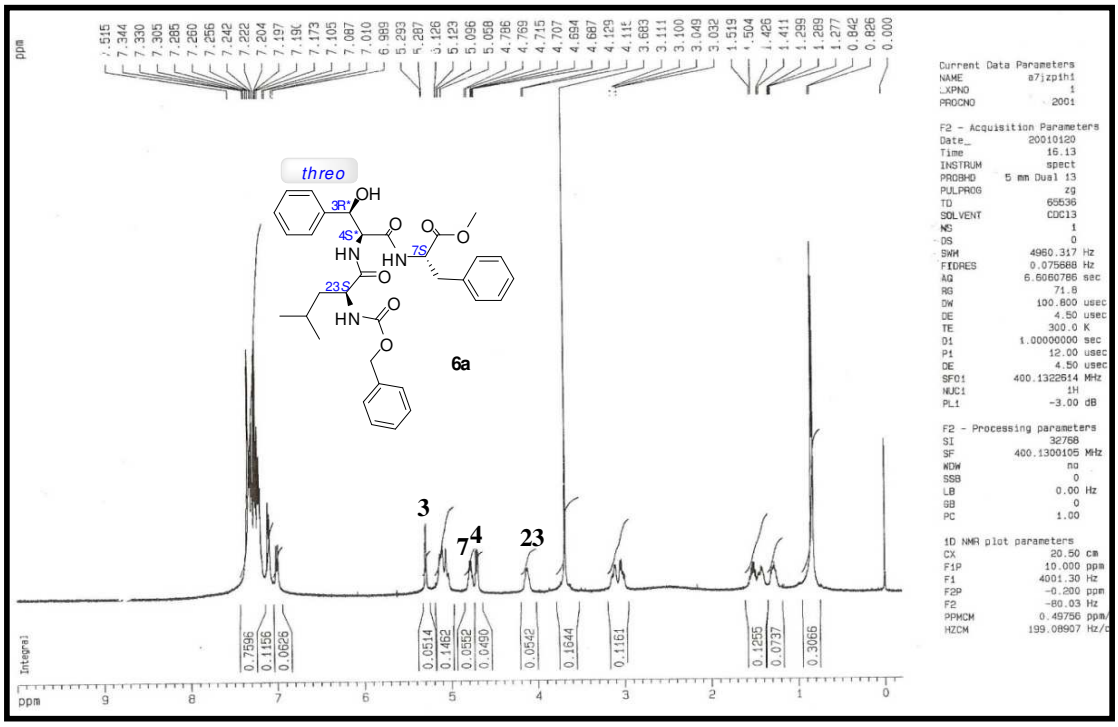
S10. ^{1}H NMR spectrum of (5S,8R,11S)-methyl 8-((S)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5b) in $CDCl_3$



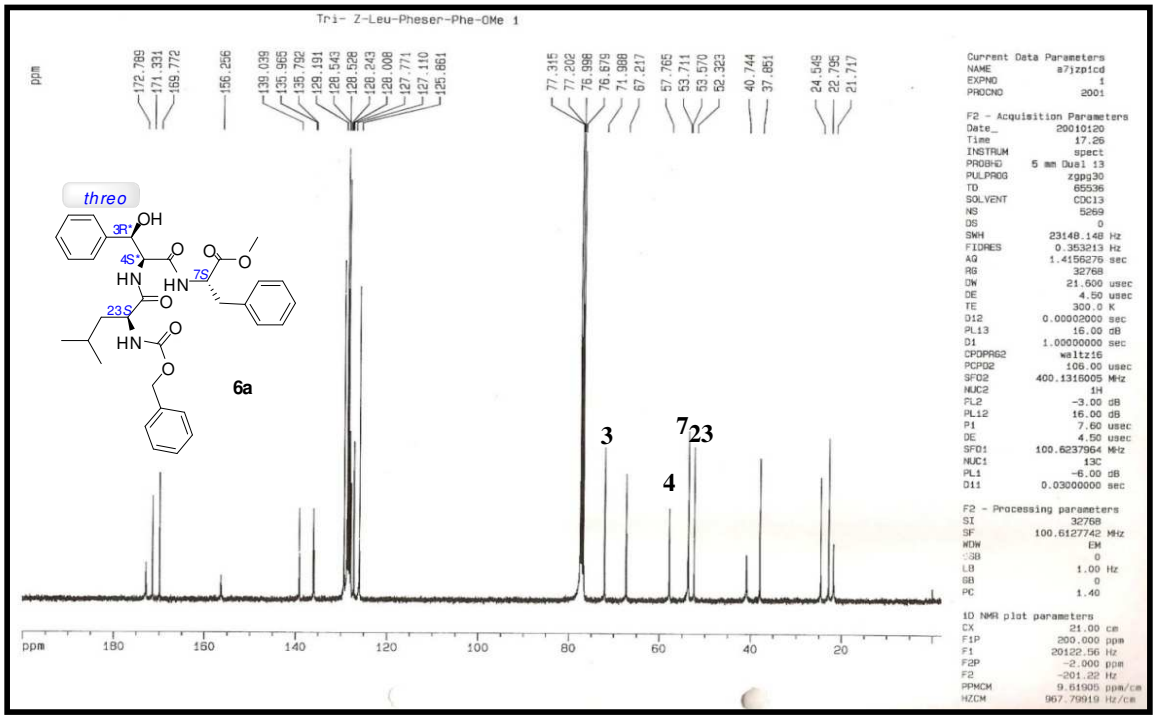
S11. ^{13}C NMR spectrum of (5S,8R,11S)-methyl 8-((S)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5b) in $CDCl_3$



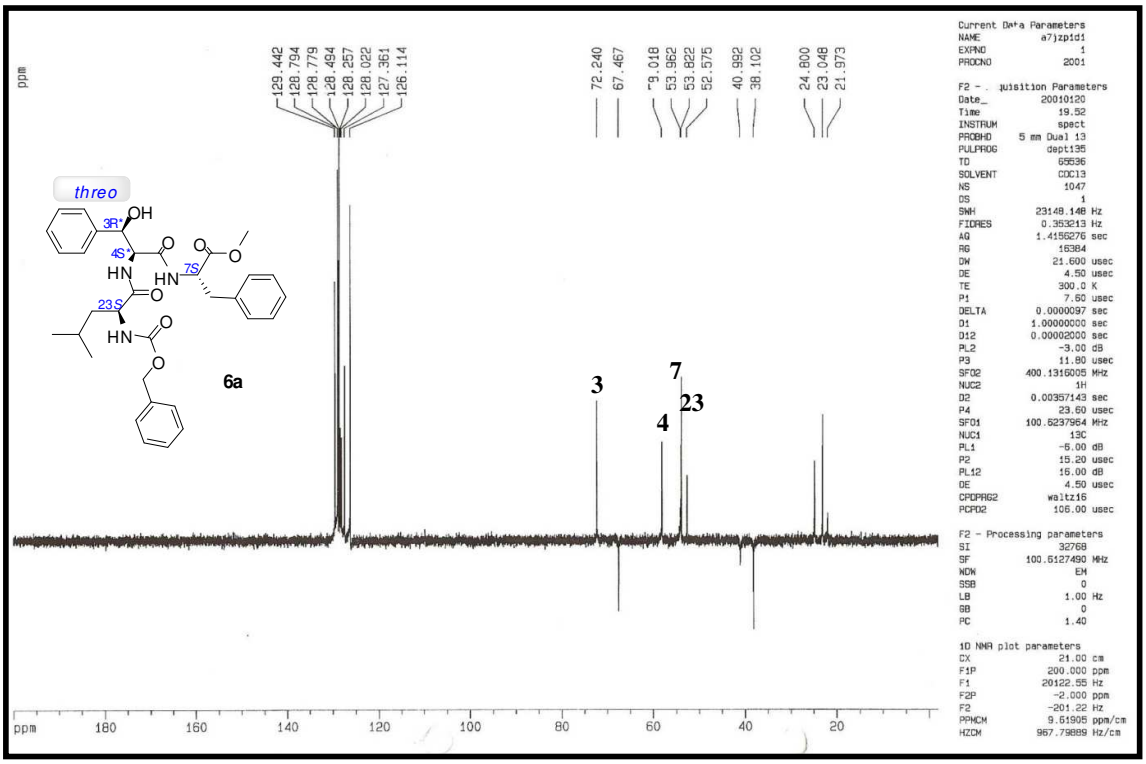
S12. DEPT135 NMR spectrum of (5S,8R,11S)-methyl 8-((S)-hydroxy(phenyl)methyl)-5,11-diisobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (5b) in $CDCl_3$



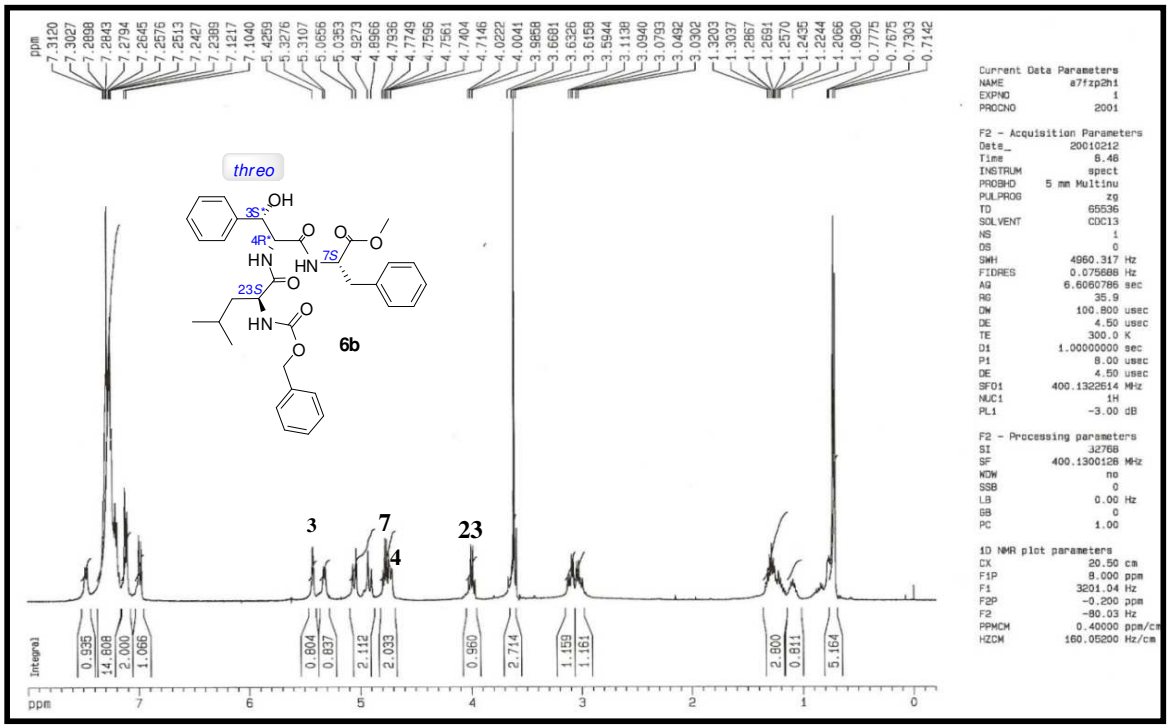
S13. ^{1}H NMR spectrum of (5S,8S,11S)-methyl 11-benzyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (6a) in $CDCl_3$



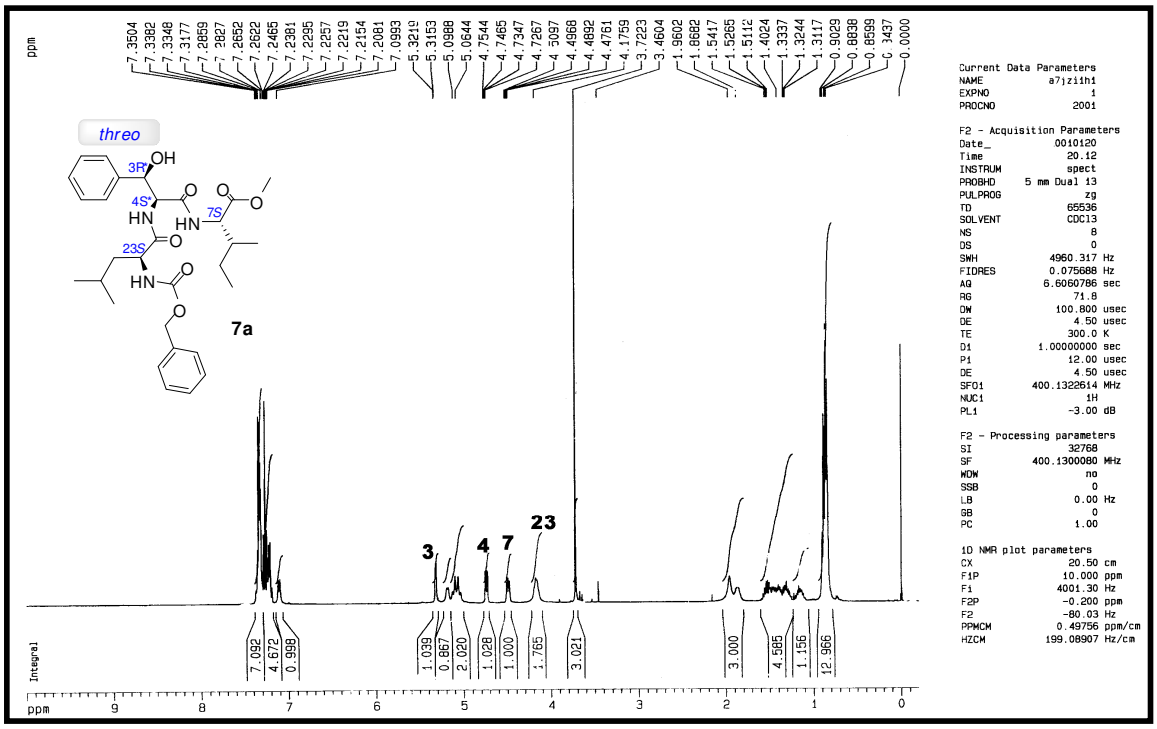
S14. ^{13}C NMR spectrum of (5S,8S,11S)-methyl 11-benzyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (6a) in $CDCl_3$



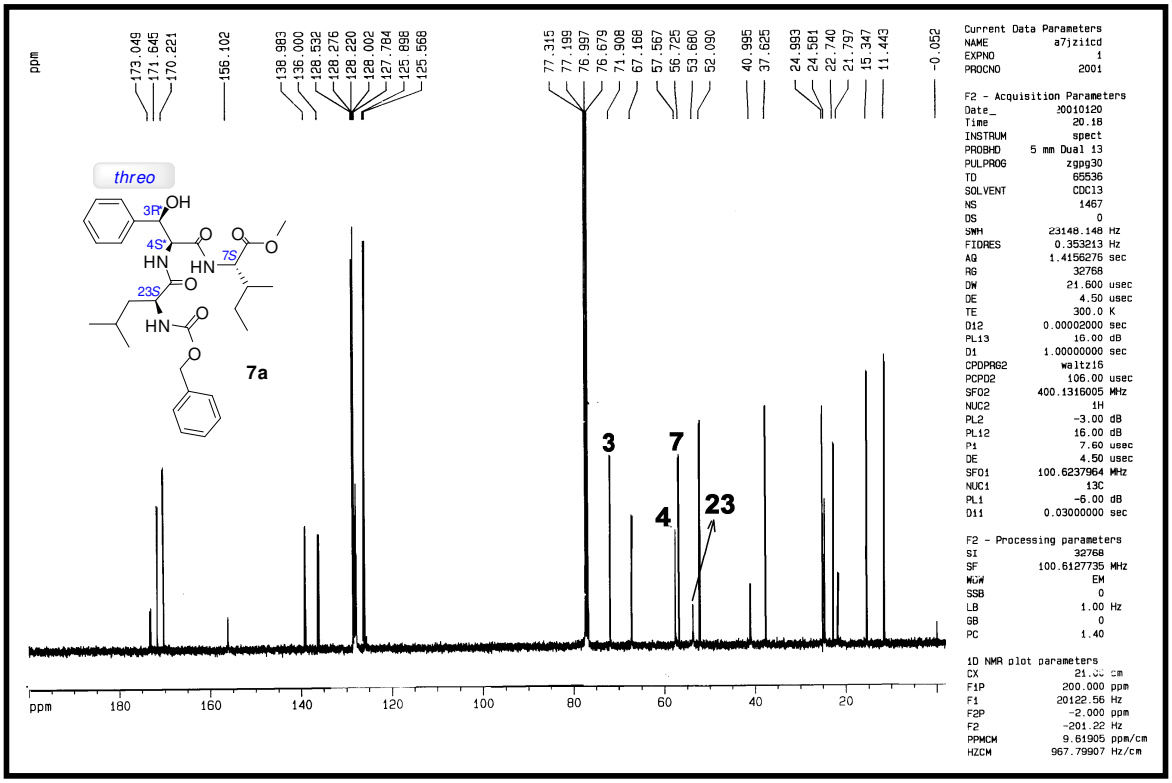
S15. DEPT 135 spectrum of (5S,8S,11S)-methyl 11-benzyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (6a) in $CDCl_3$



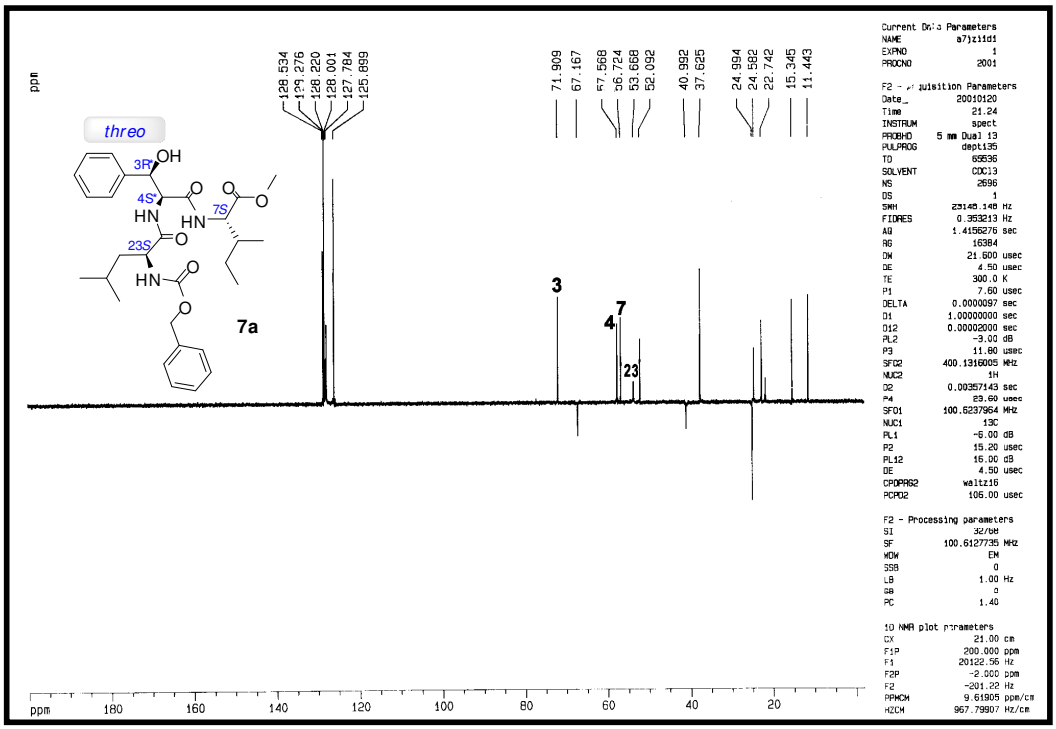
S16. ^{1}H NMR spectrum of (5S,8R,11S)-methyl 11-benzyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (6b)in $CDCl_3$



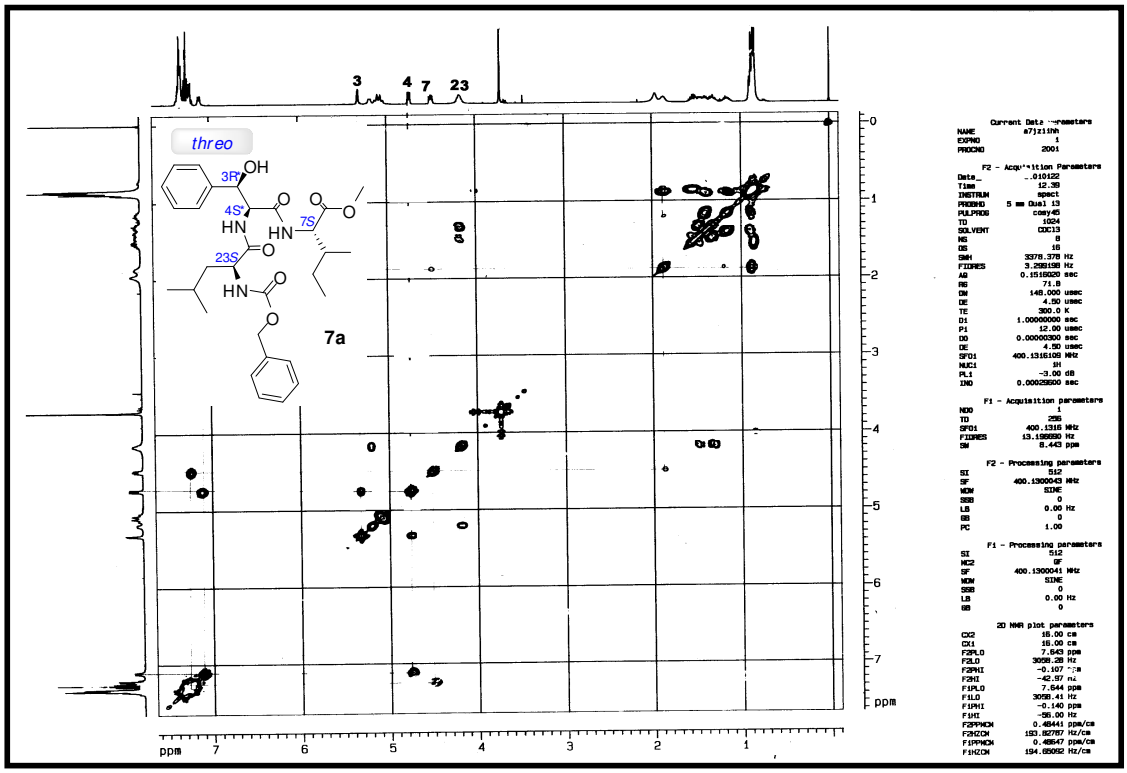
S17. ^{1}H NMR spectrum of (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7a) in $CDCl_3$



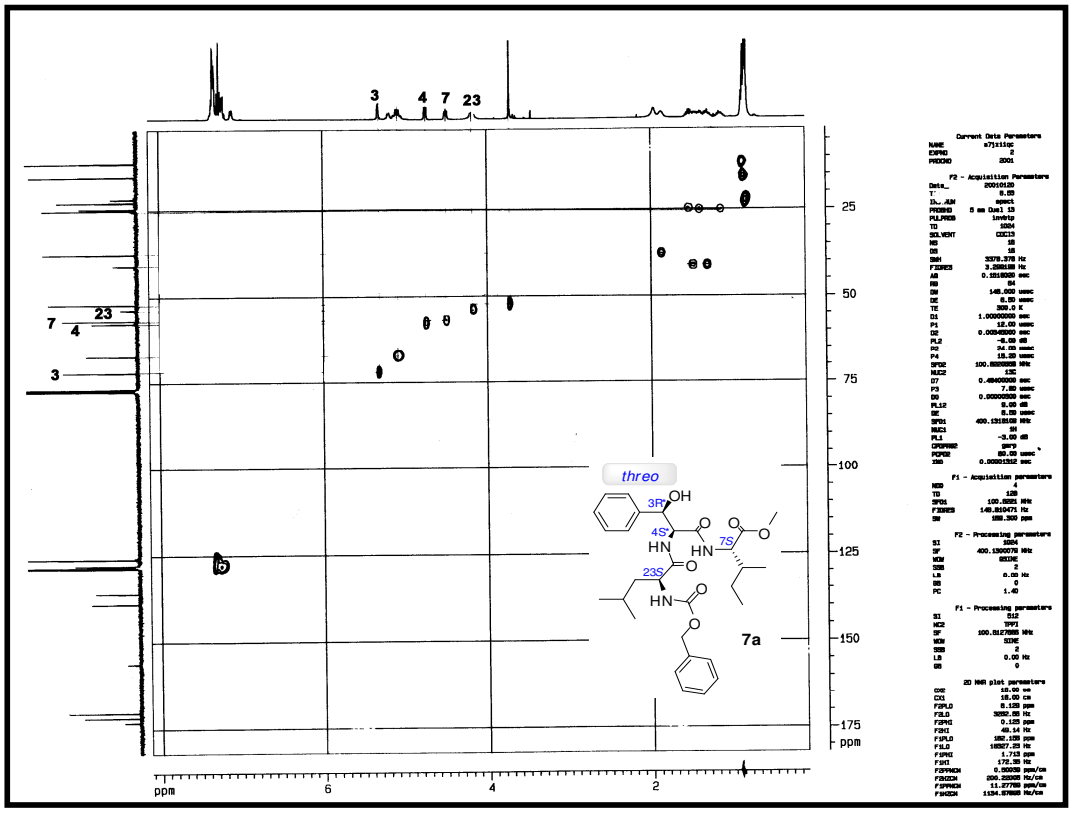
S18. ^{13}C NMR spectrum of (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7a) in $CDCl_3$



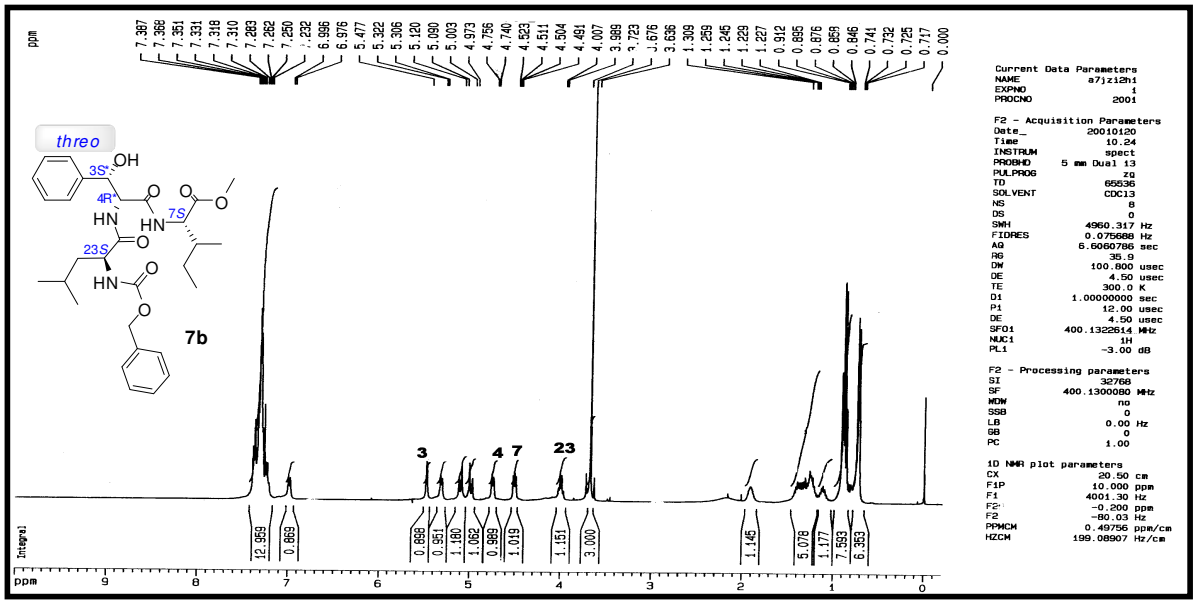
S19. DEPT 135 NMR spectrum of (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7a) in $CDCl_3$



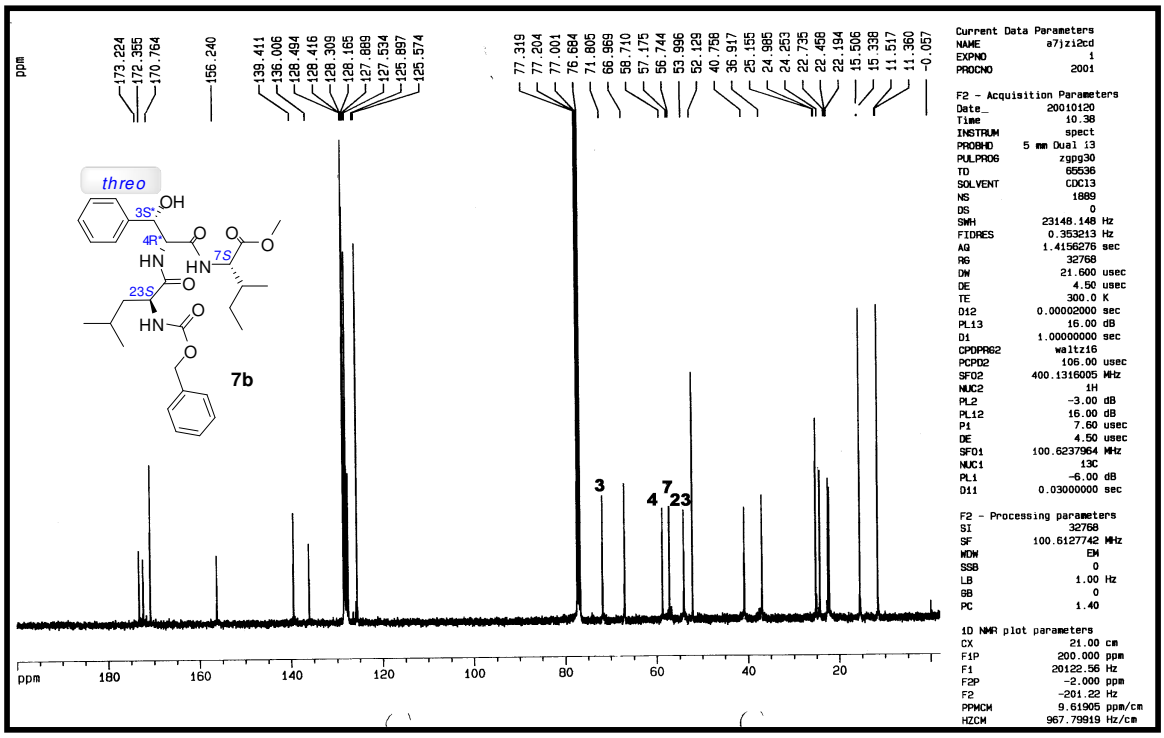
S20. COSY 45 NMR spectrum of (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7a) in $CDCl_3$



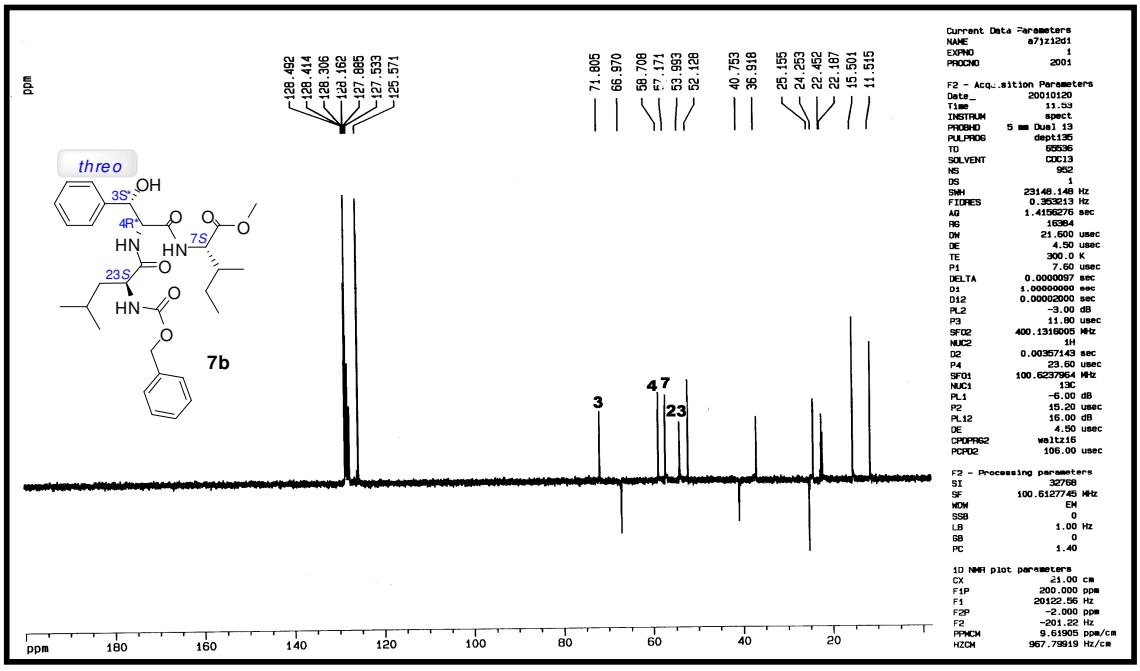
S21. HMQC NMR spectrum of (5S,8S,11S)-methyl 11-sec-butyl-8-((R)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7a) in $CDCl_3$



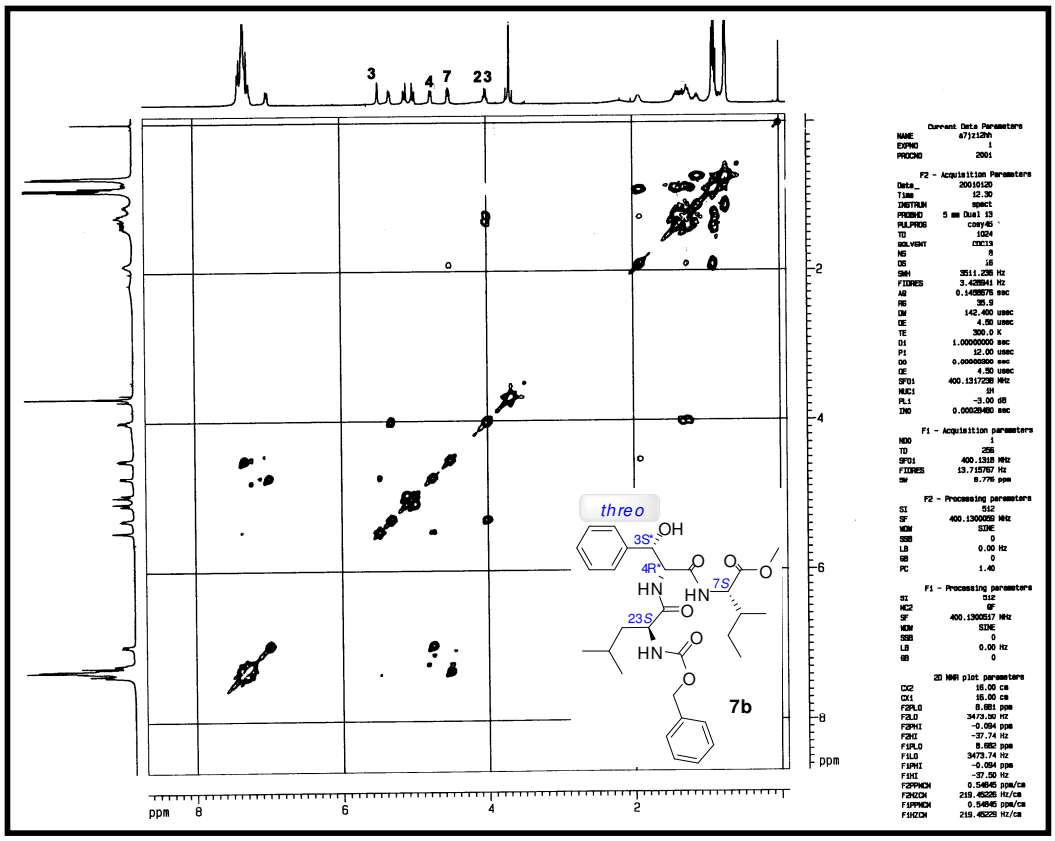
S22. ^{1}H NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



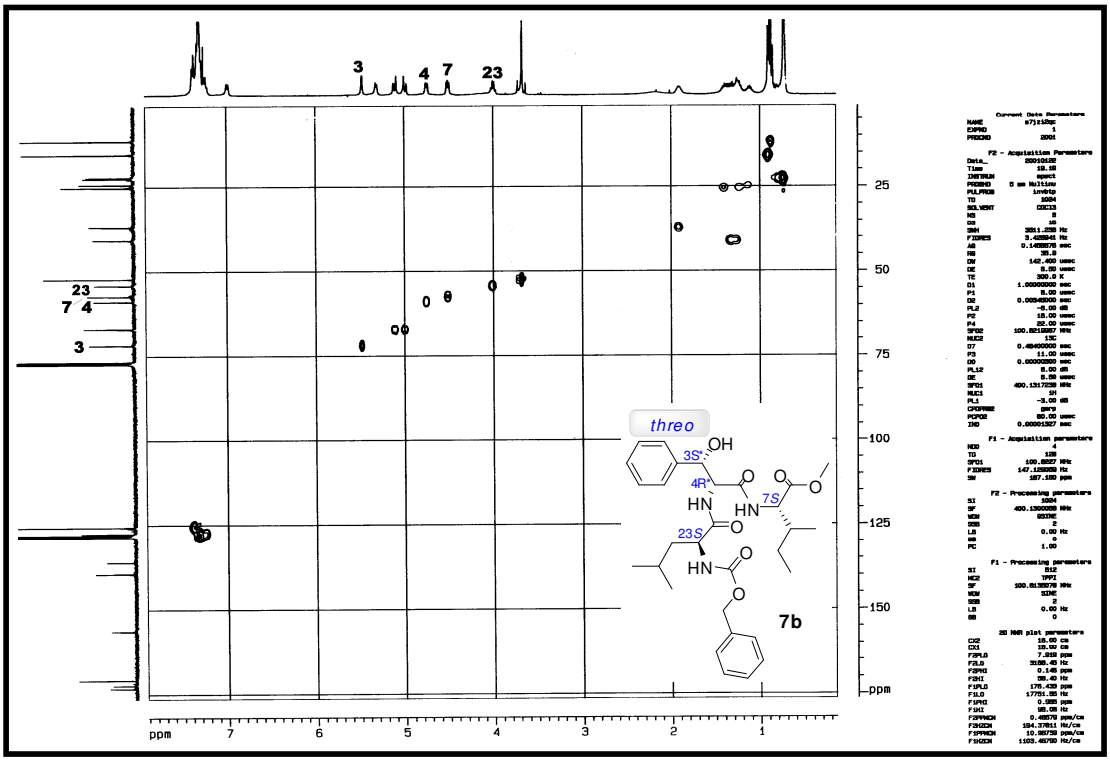
S23. ^{13}C NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



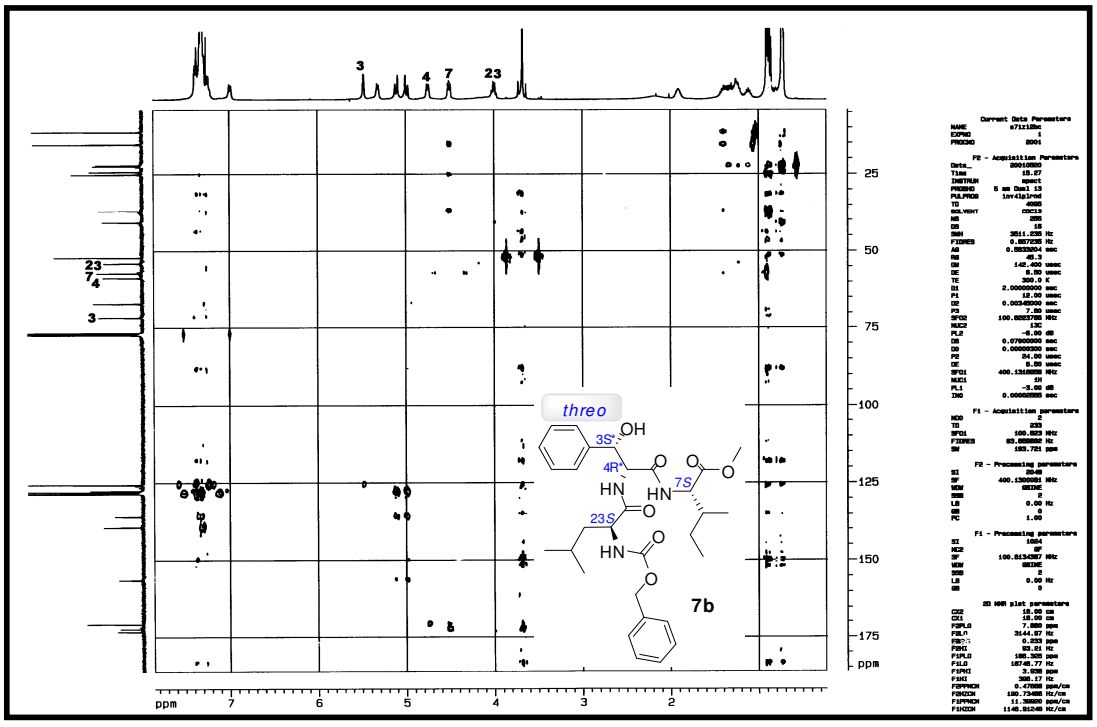
S24. DEPT 135 NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



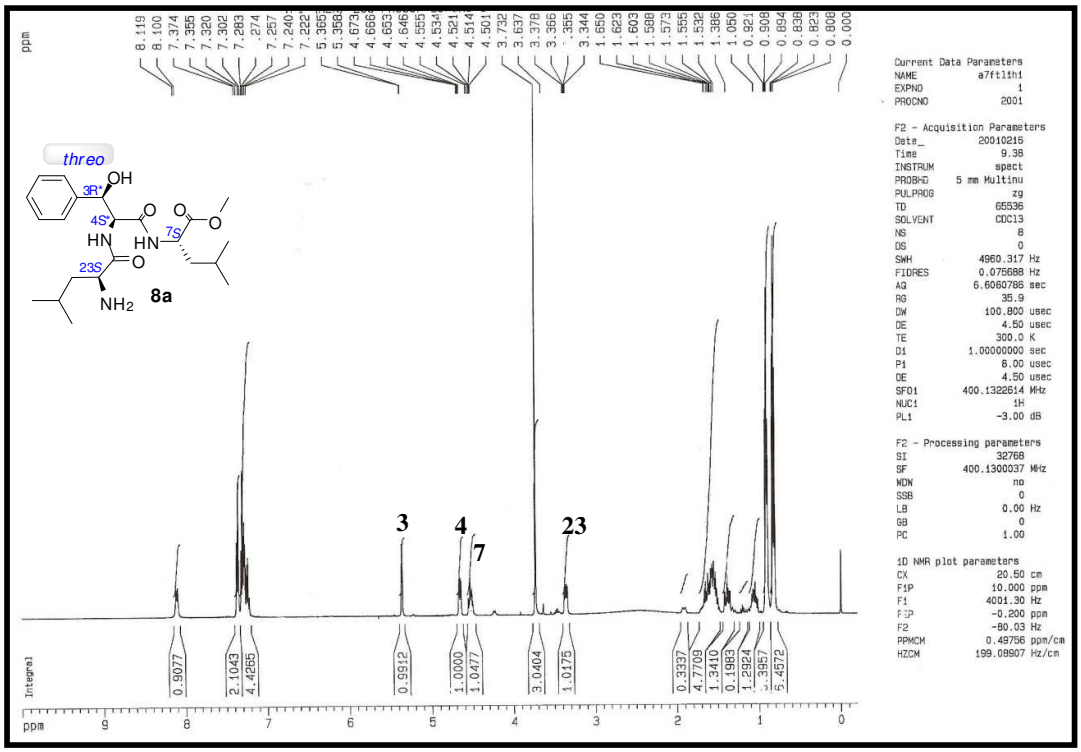
S25. COSY 45 NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



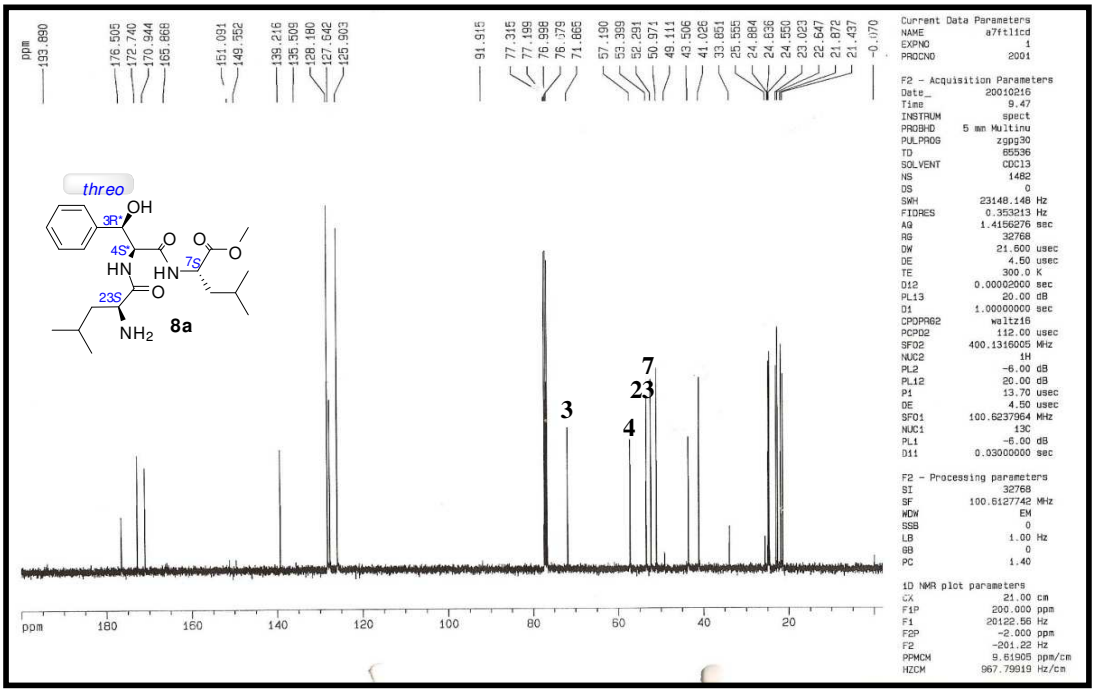
S26. HMQC NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



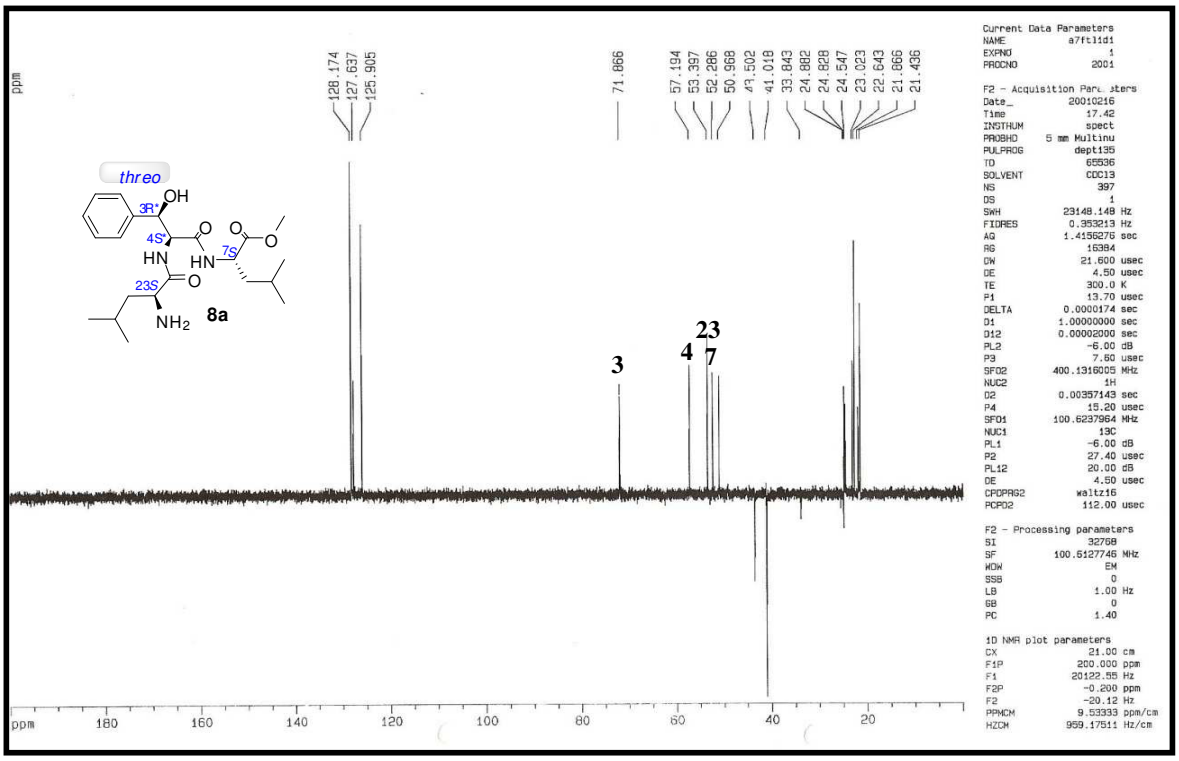
S27. HMBC NMR spectrum of (5S,8R,11S)-methyl 11-sec-butyl-8-((S)-hydroxy(phenyl)methyl)-5-isobutyl-3,6,9-trioxo-1-phenyl-2-oxa-4,7,10-triazadodecan-12-oate (7b) in $CDCl_3$



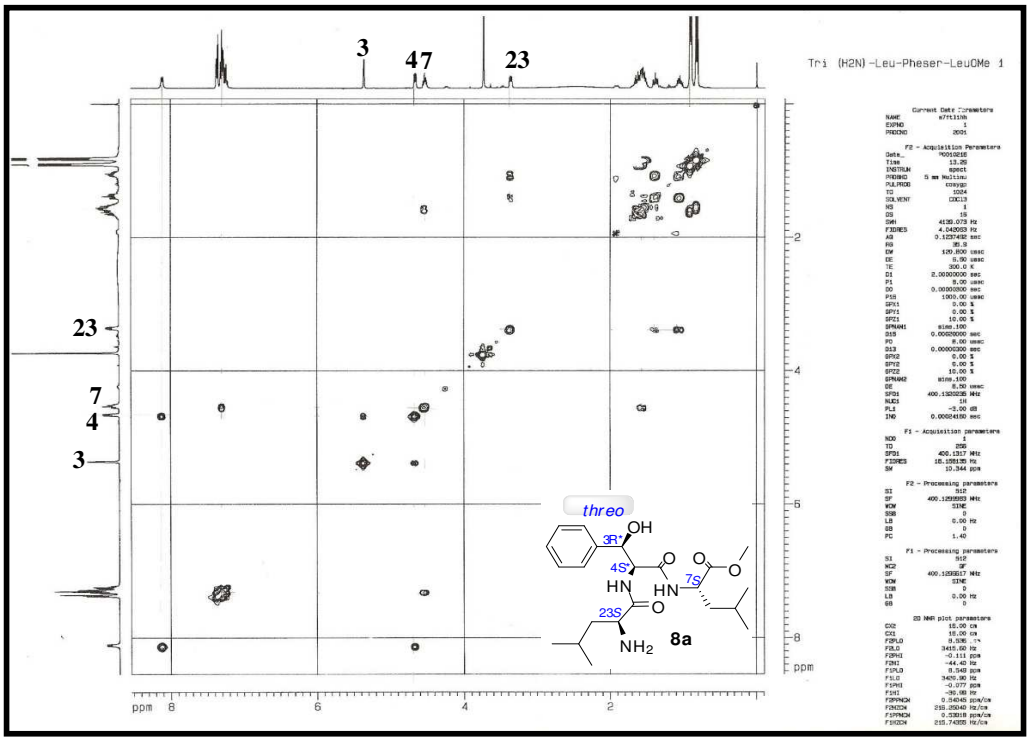
S28. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8a) in $CDCl_3$



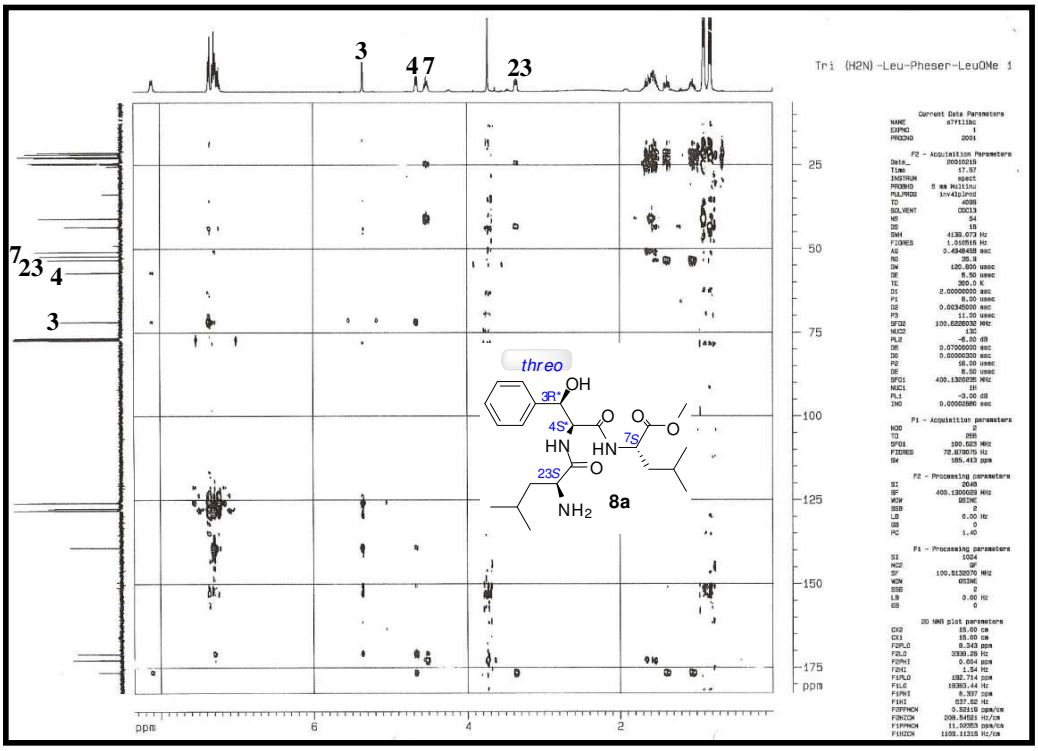
S29. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8a) in $CDCl_3$



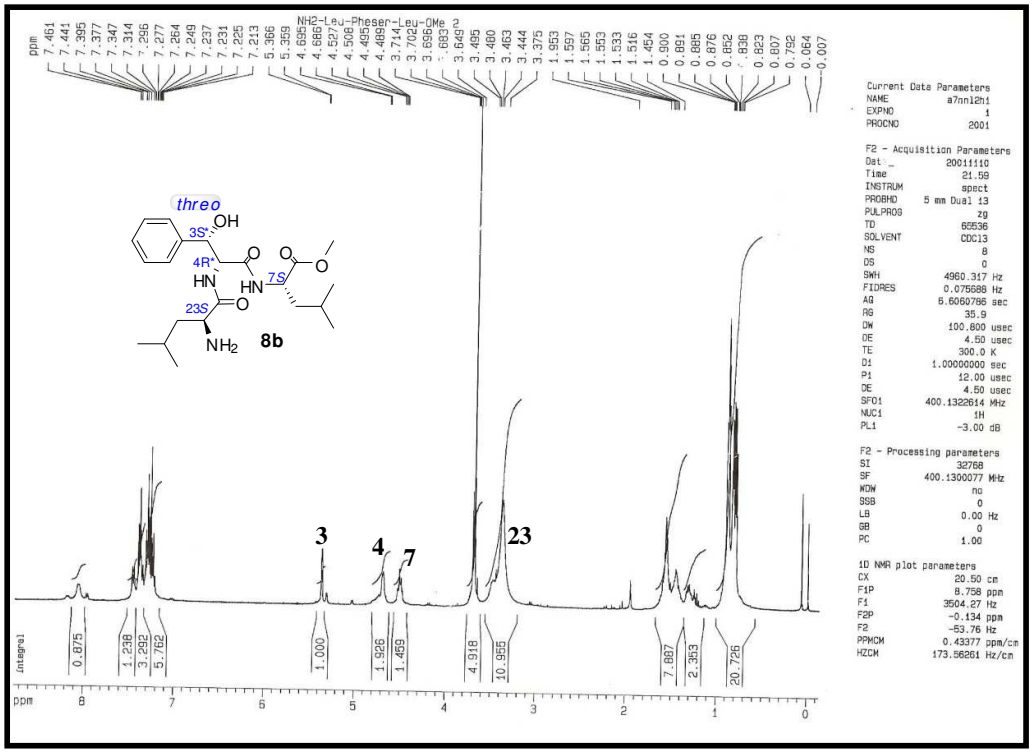
S30. DEPT 135° NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8a) in $CDCl_3$



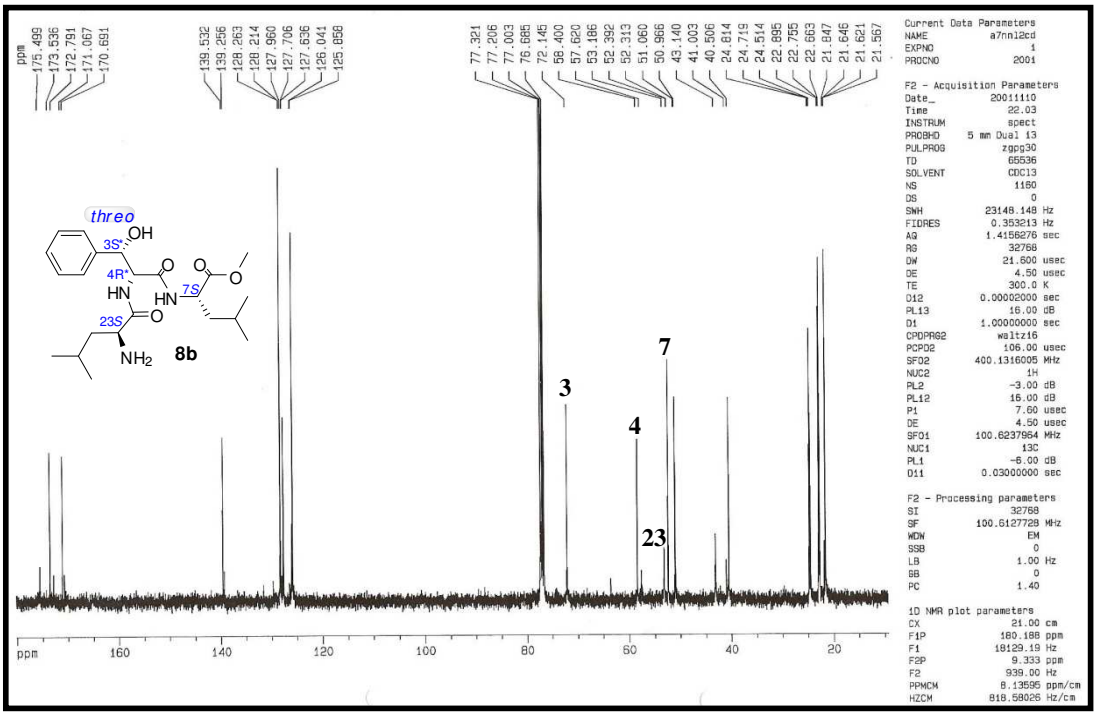
S31. COSY 45° NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8a) in $CDCl_3$



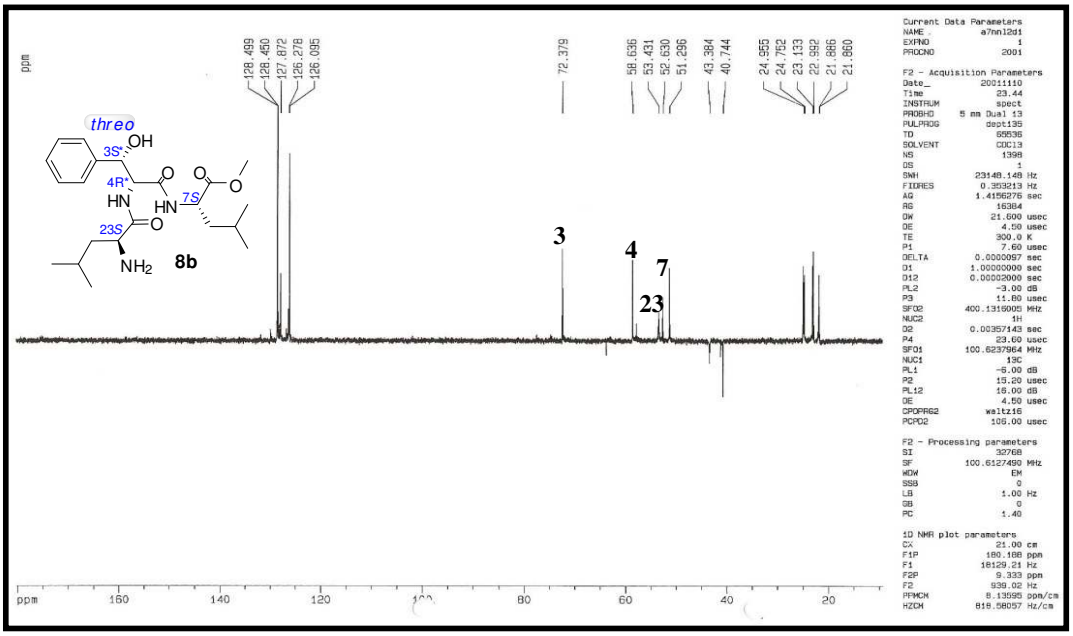
S32. HMBC NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8a) in $CDCl_3$



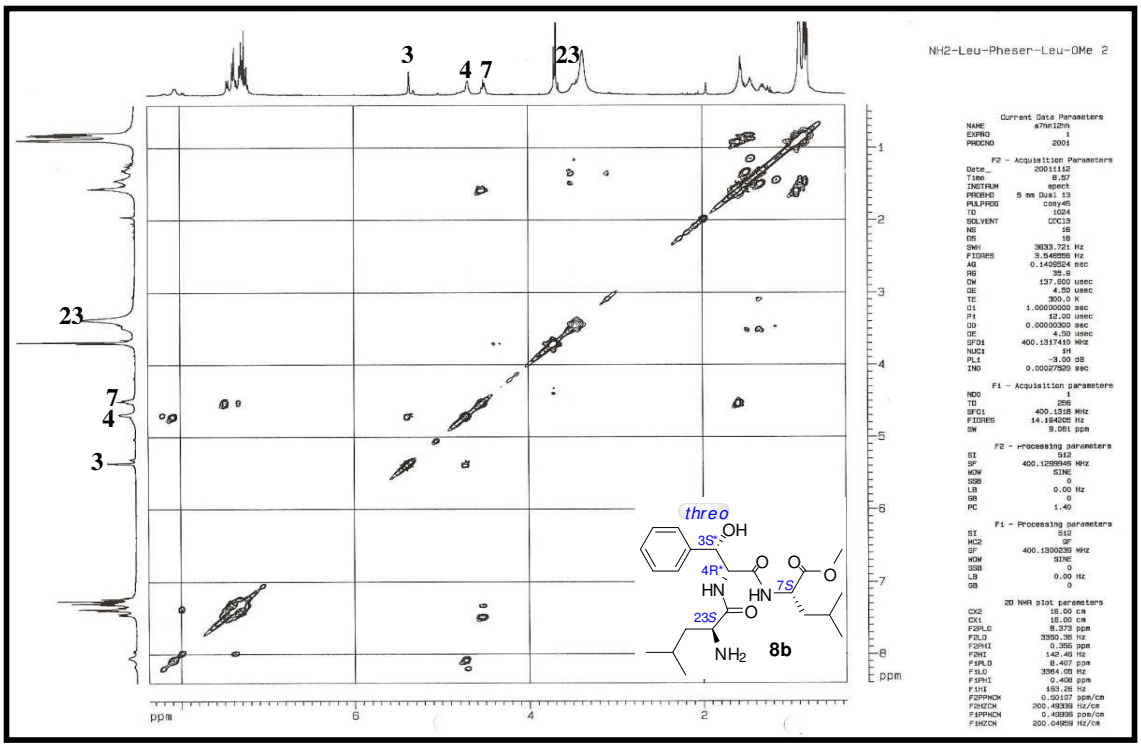
S33. ^{1}H NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8b) in $CDCl_3$



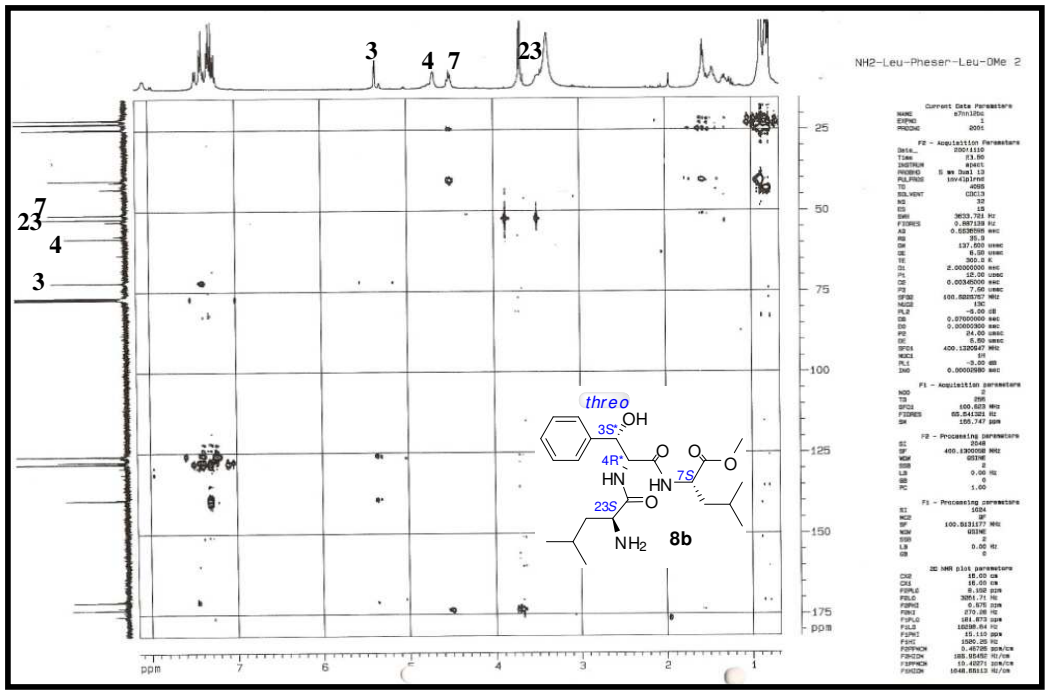
S34. ^{13}C NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8b)in $CDCl_3$



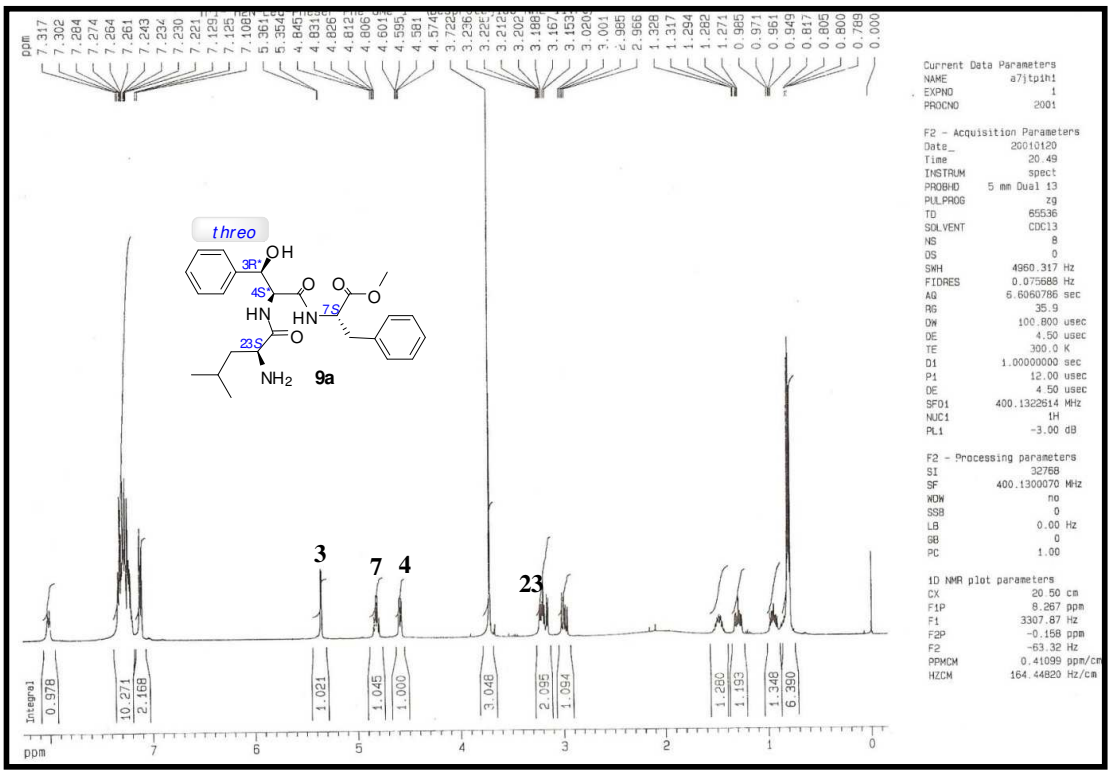
S35. DEPT 135 NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8b) in $CDCl_3$



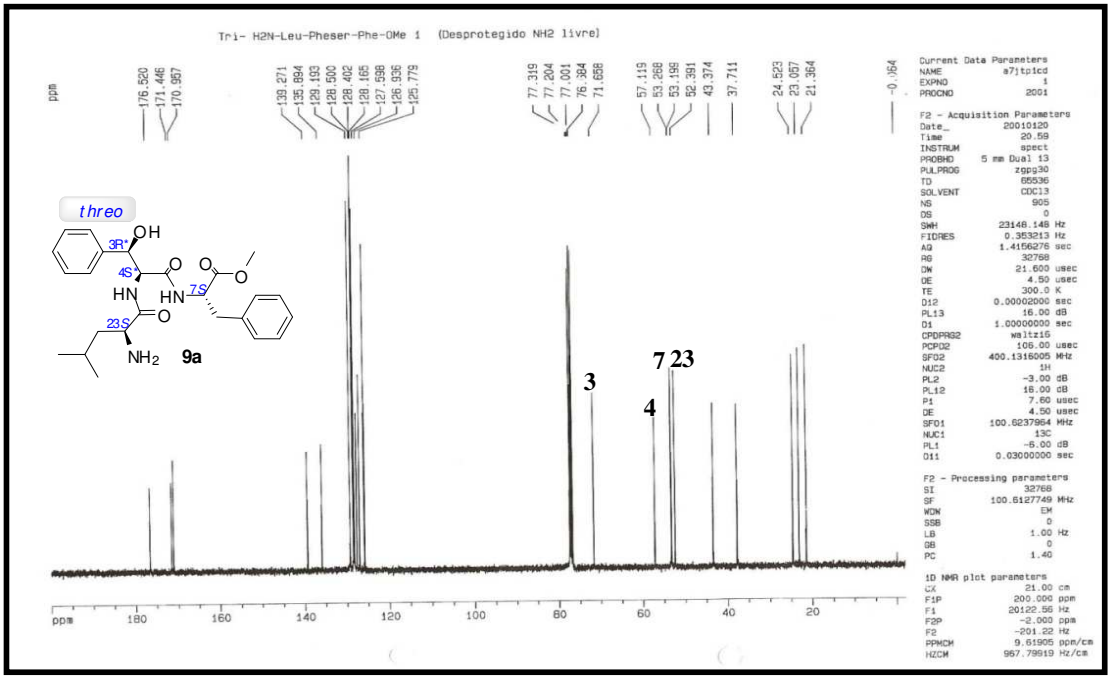
S36. ^{1}H-^{1}H COSY 45° NMR spectrum of of (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8b) in $CDCl_3$



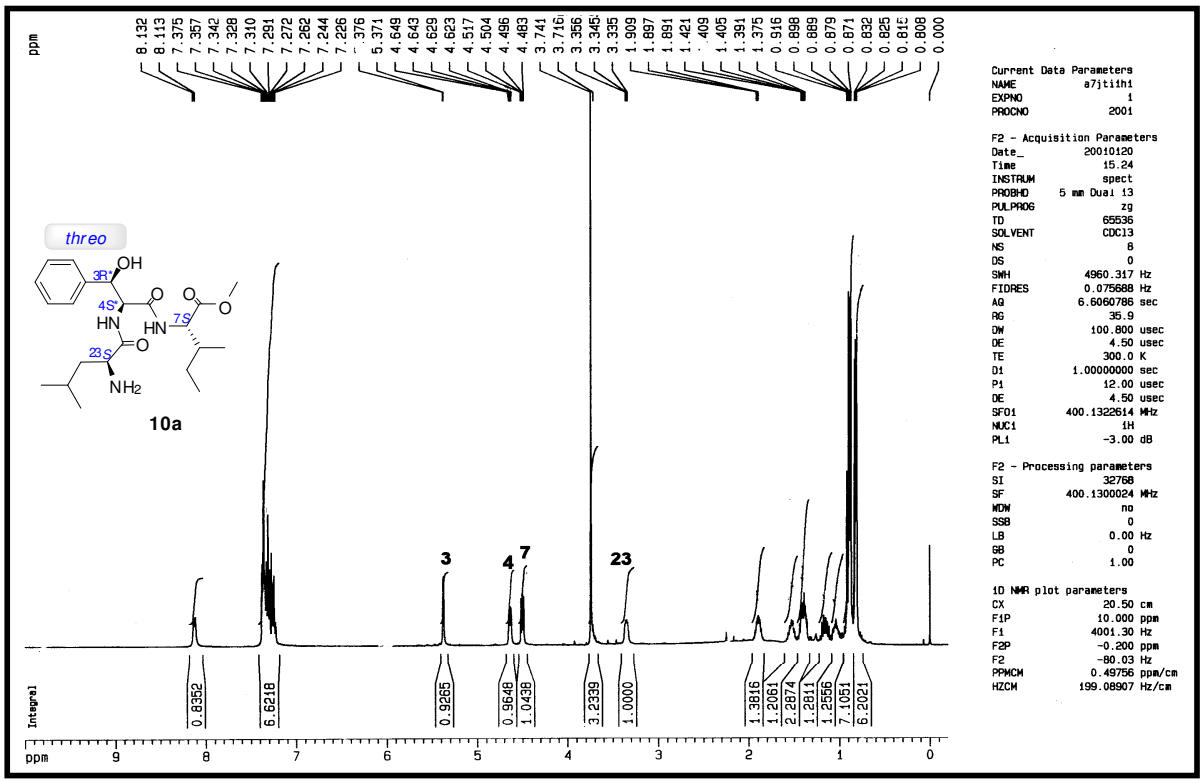
S37. HMBC NMR spectrum of of (S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (8b) in $CDCl_3$



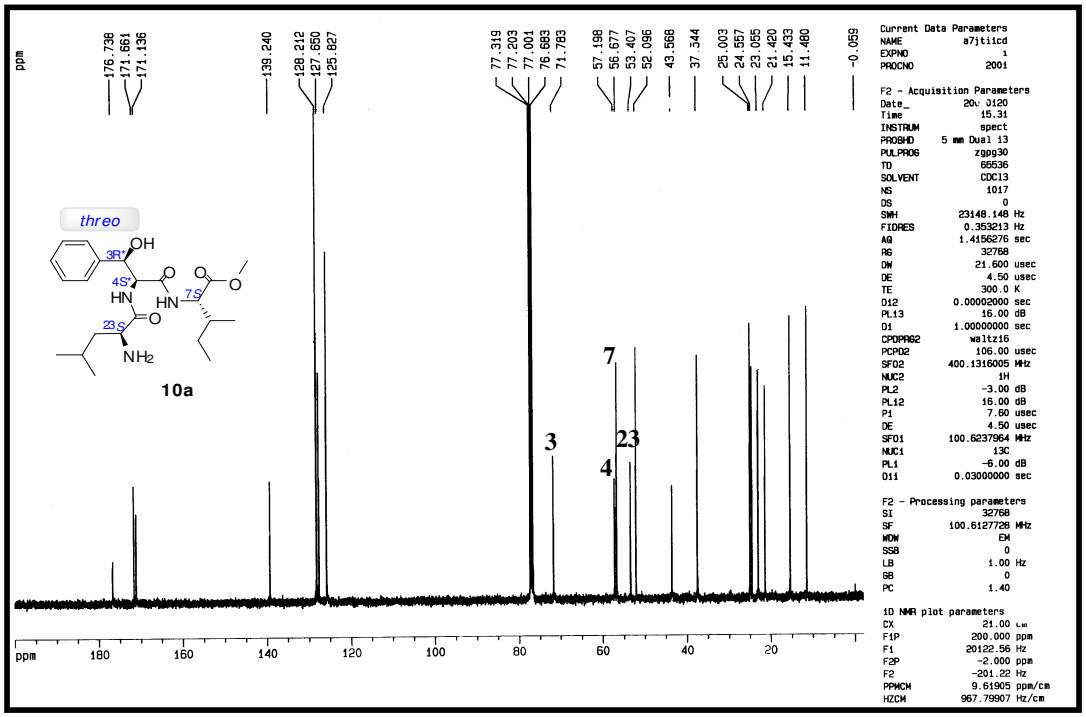
S38. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (9a) in $CDCl_3$



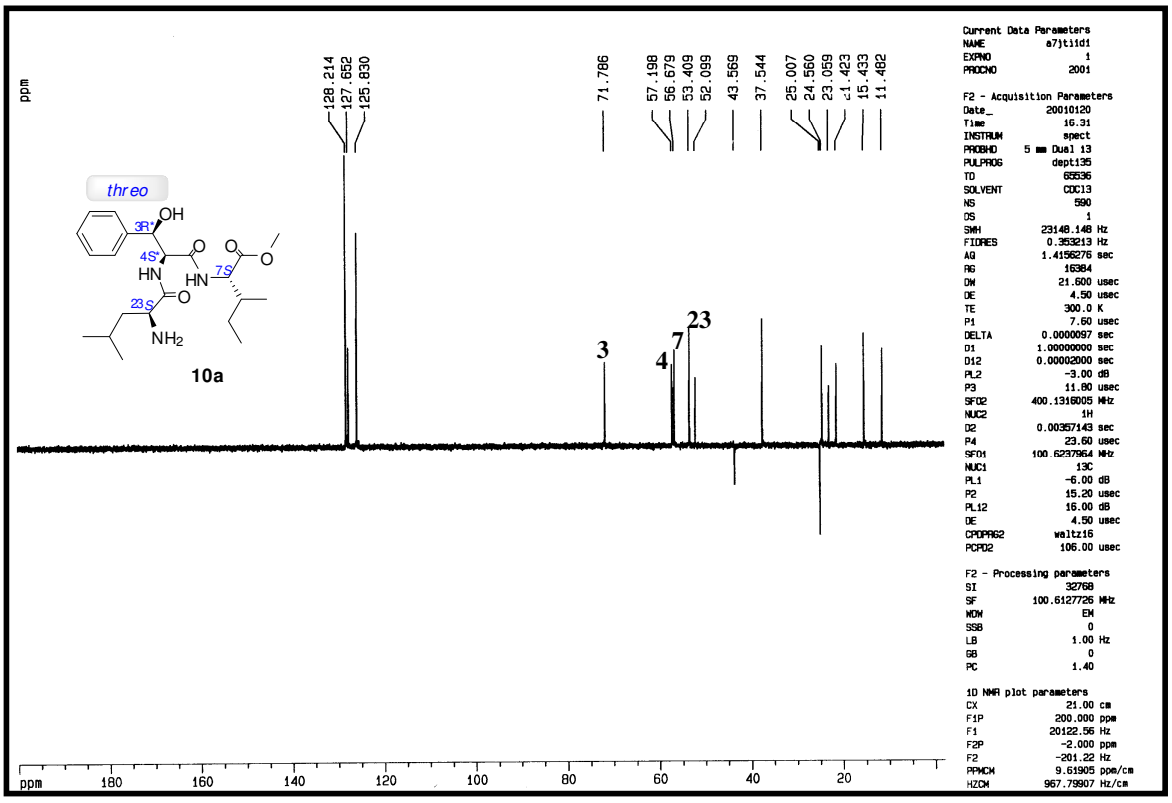
S39. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (9a) in $CDCl_3$



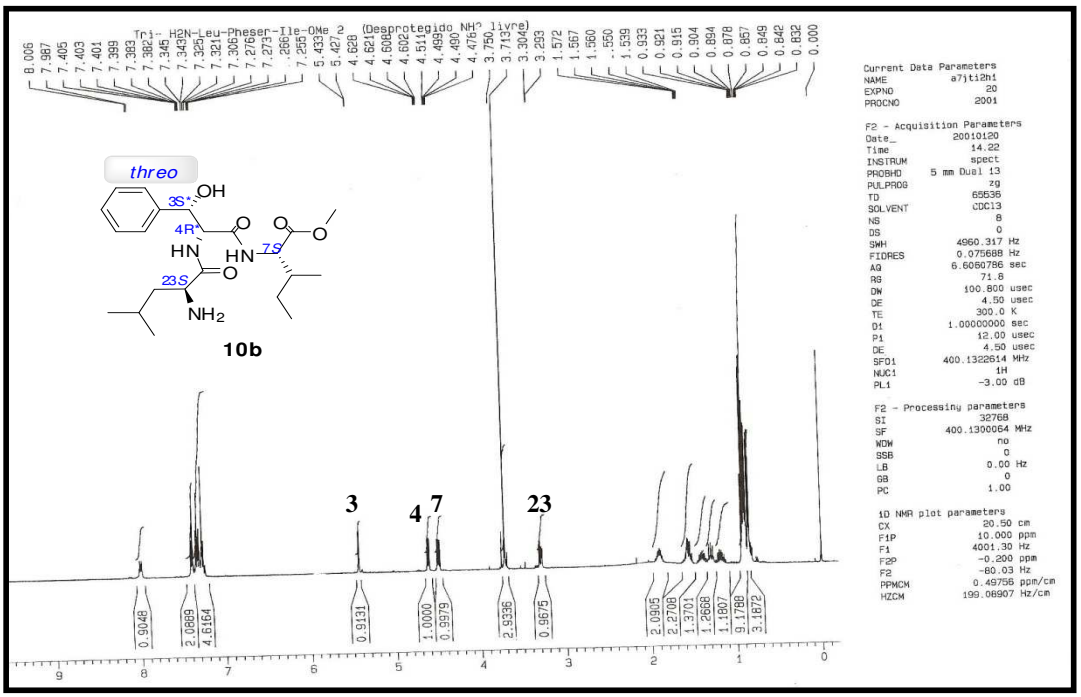
S40. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10a) in $CDCl_3$



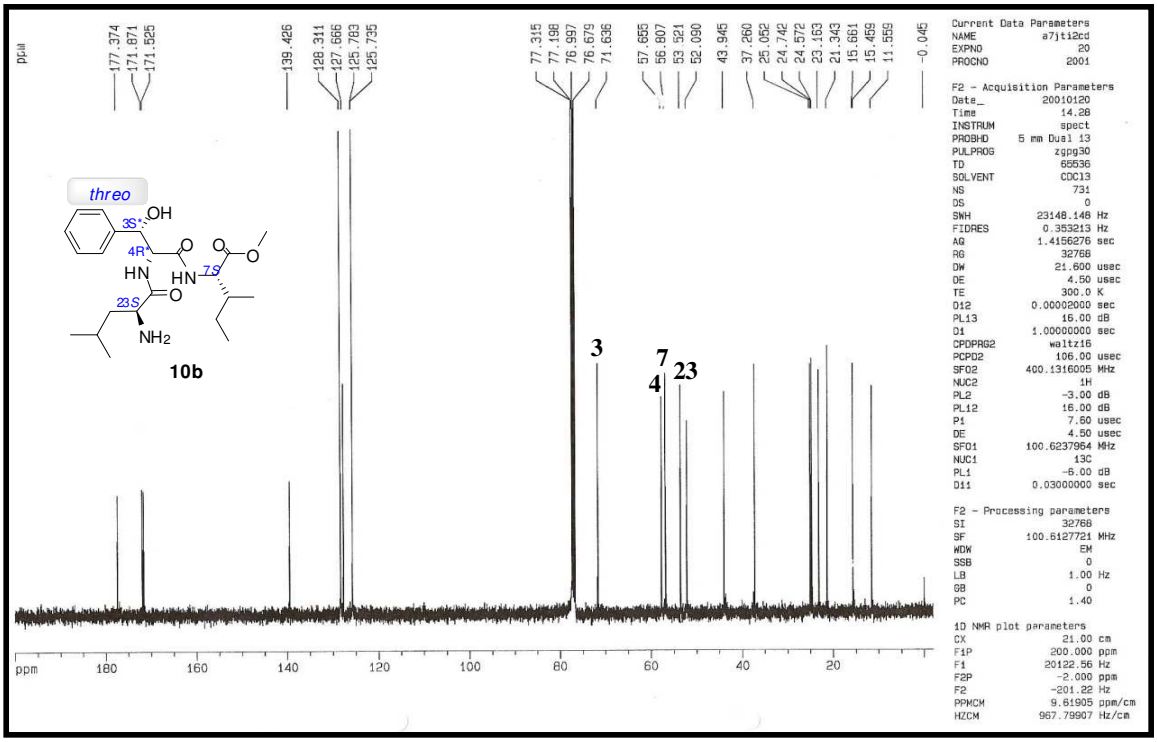
S41. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10a) in $CDCl_3$



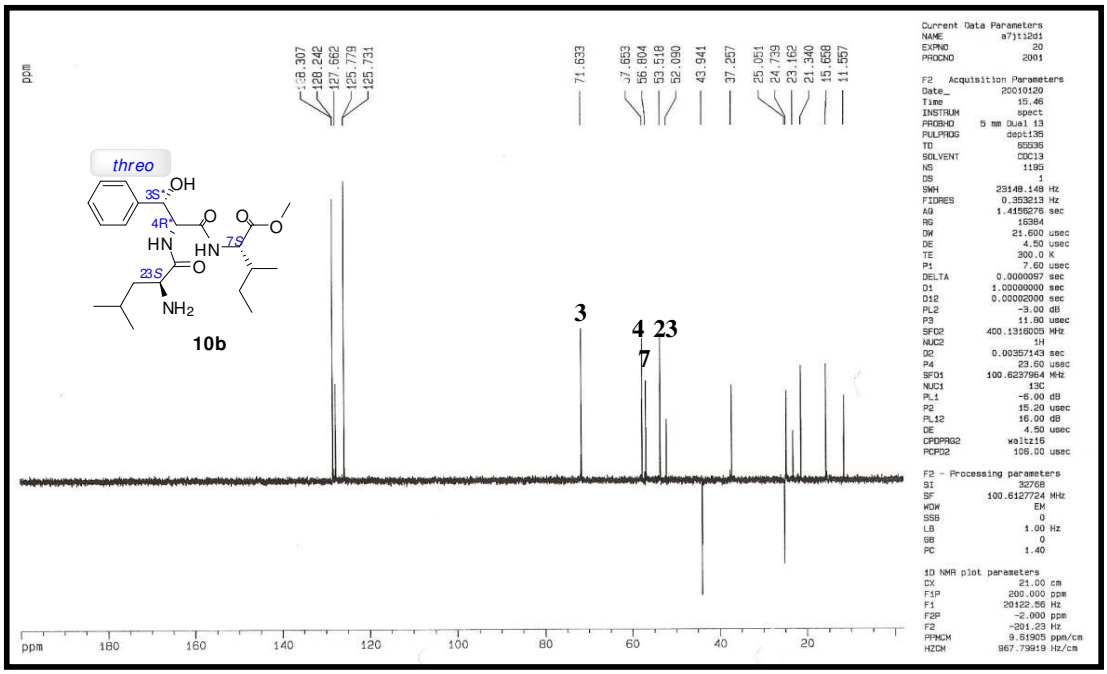
S42. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10a) in $CDCl_3$



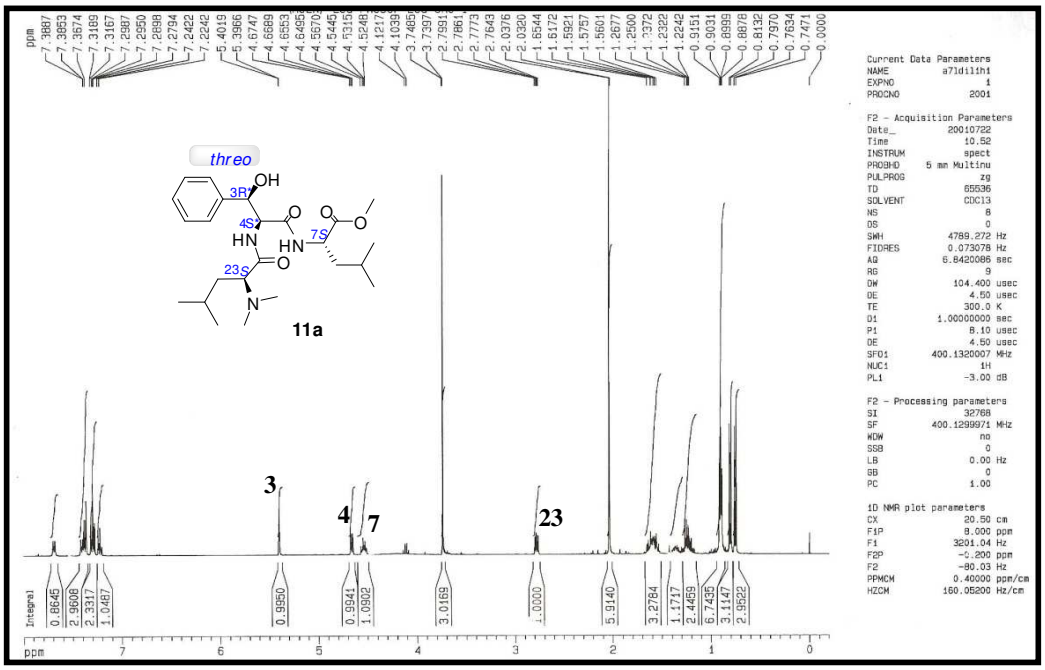
S43. ^1H NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10b) in $CDCl_3$



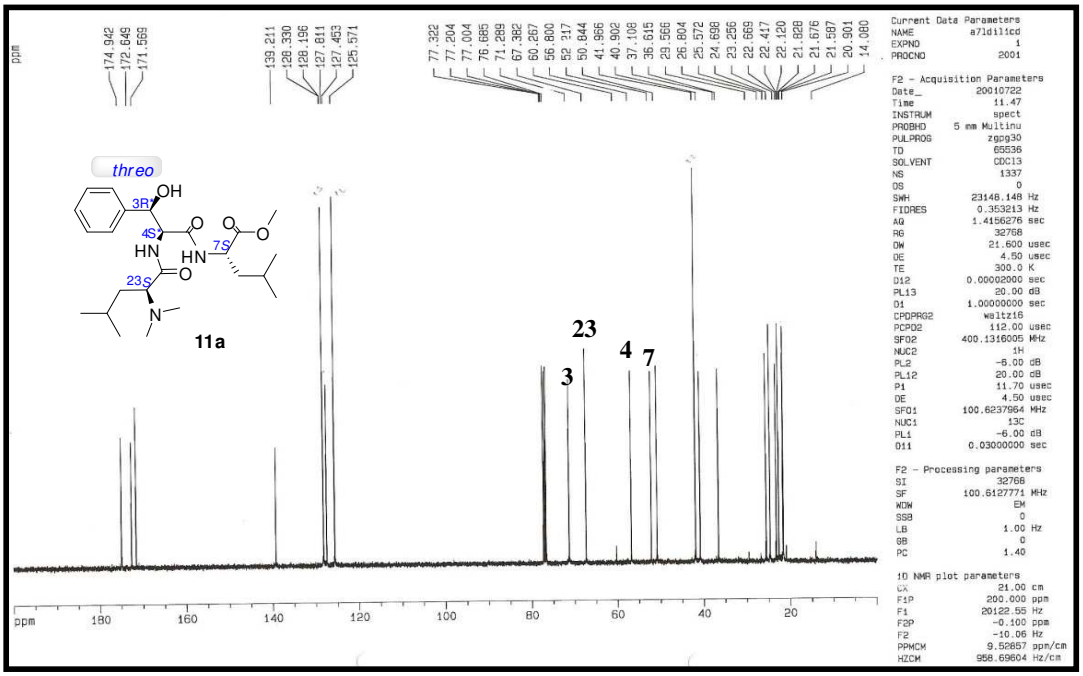
S44. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10b) in $CDCl_3$



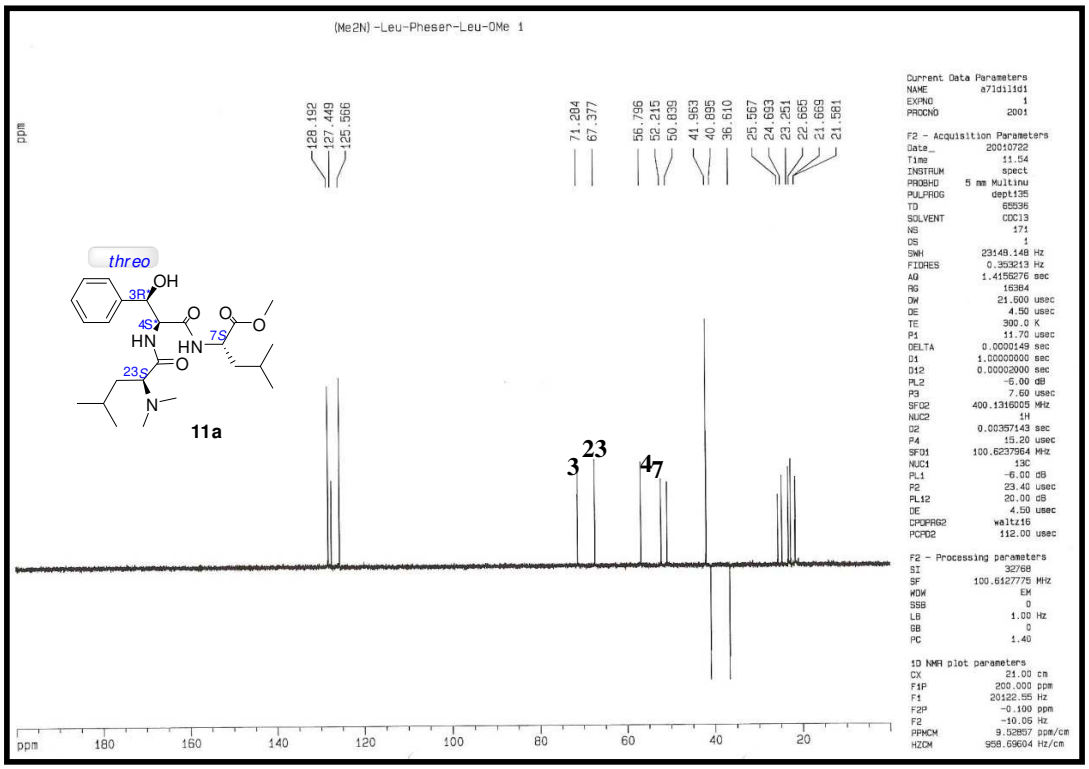
S45. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-amino-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (10b) in $CDCl_3$



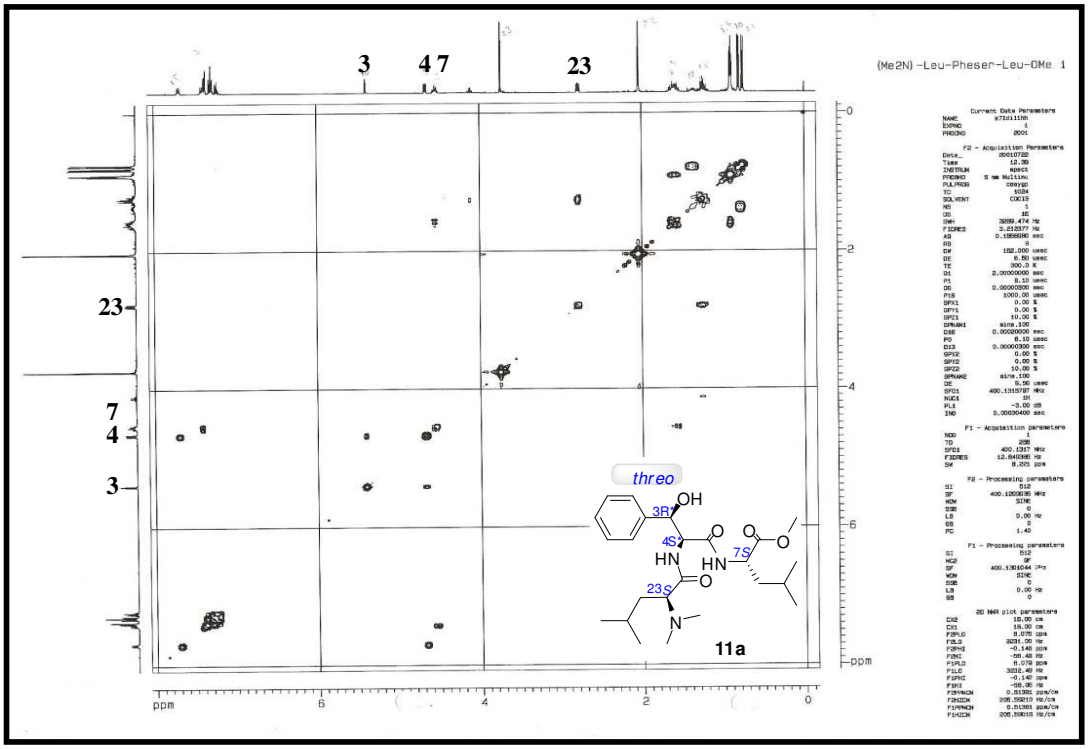
S46. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



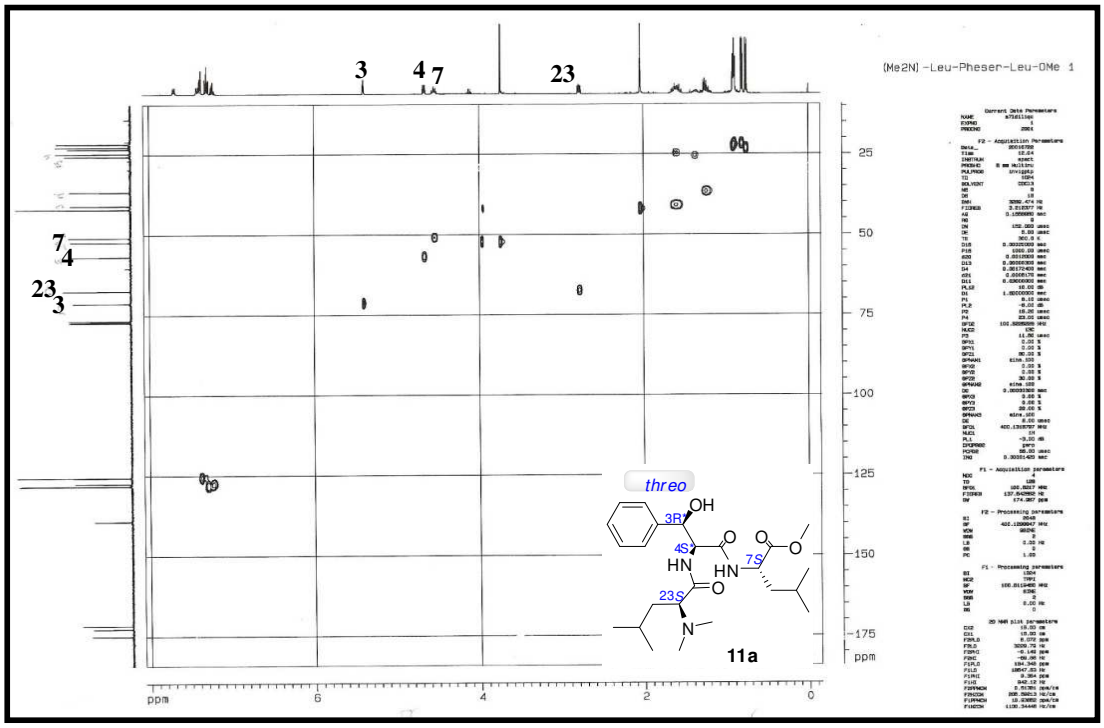
S47. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



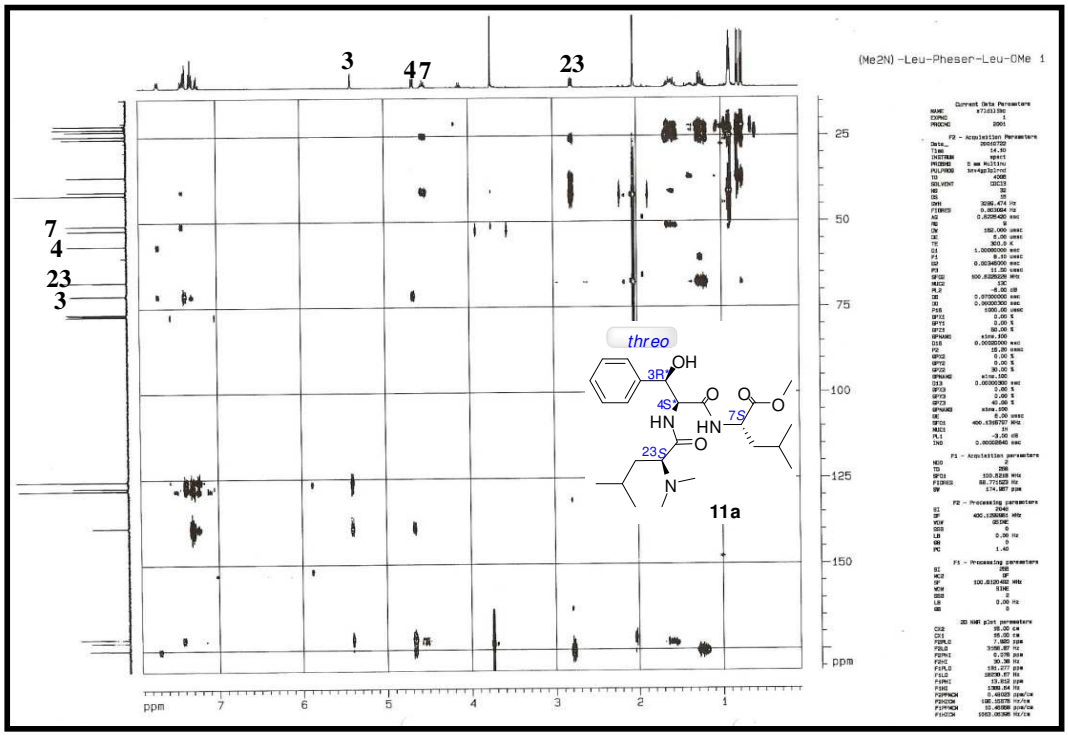
S48. DEPT 135 NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



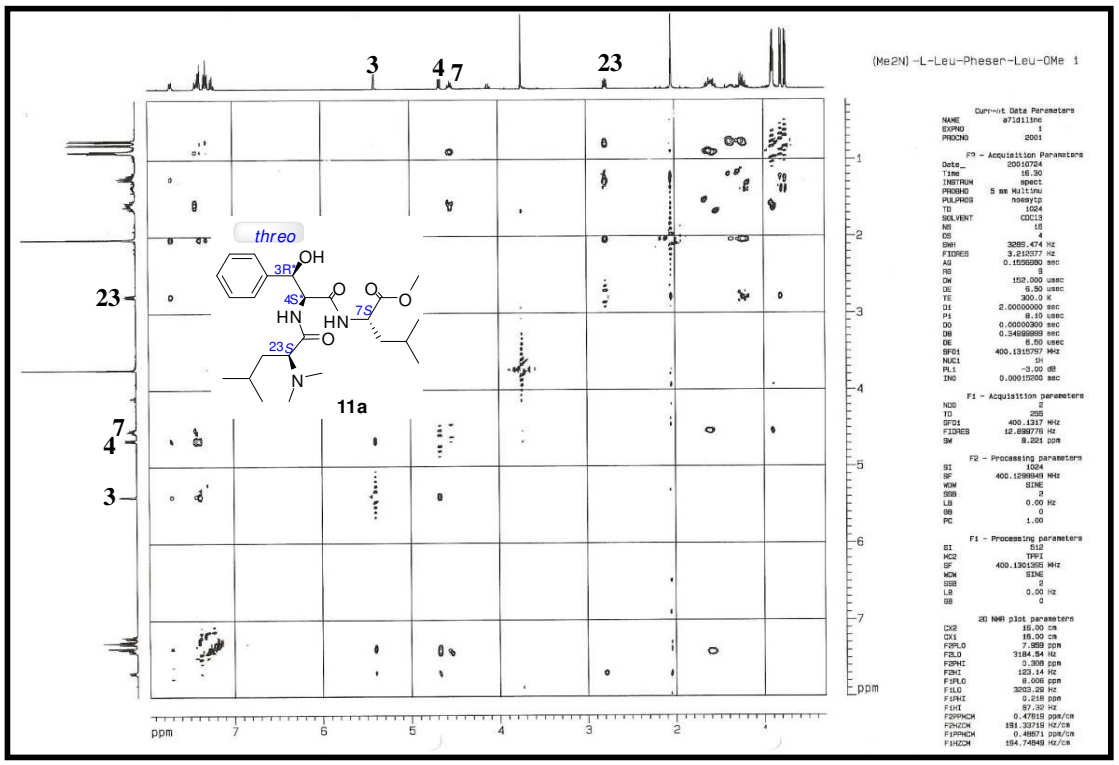
S49. COSY 45° NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



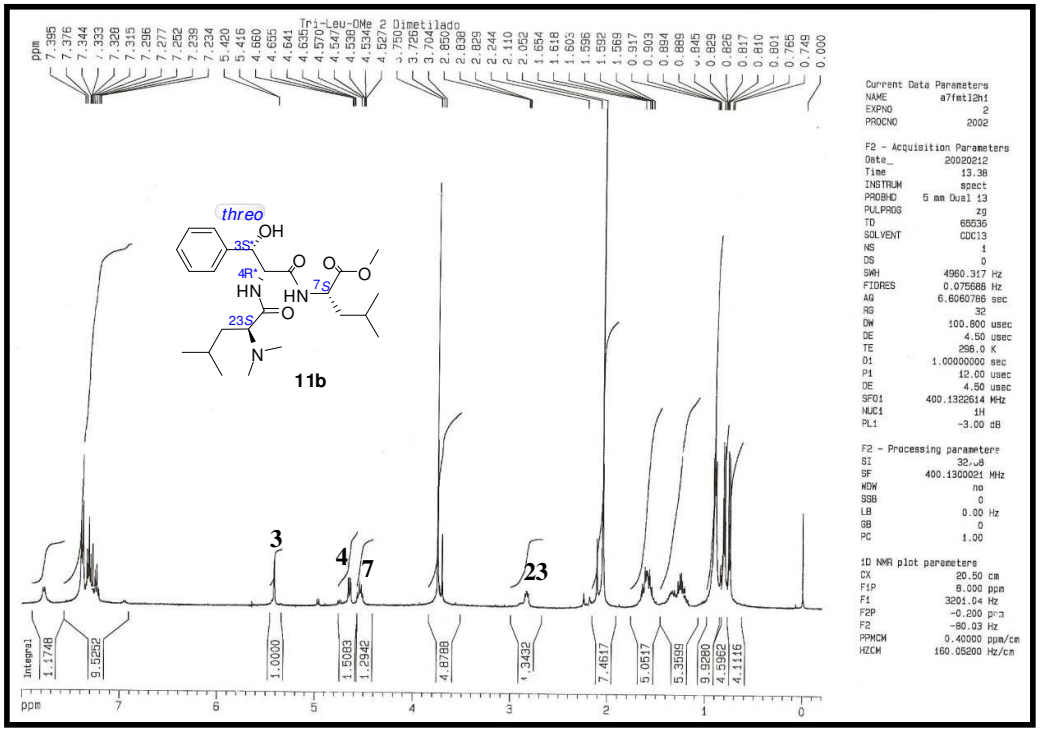
S50. HMQC NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



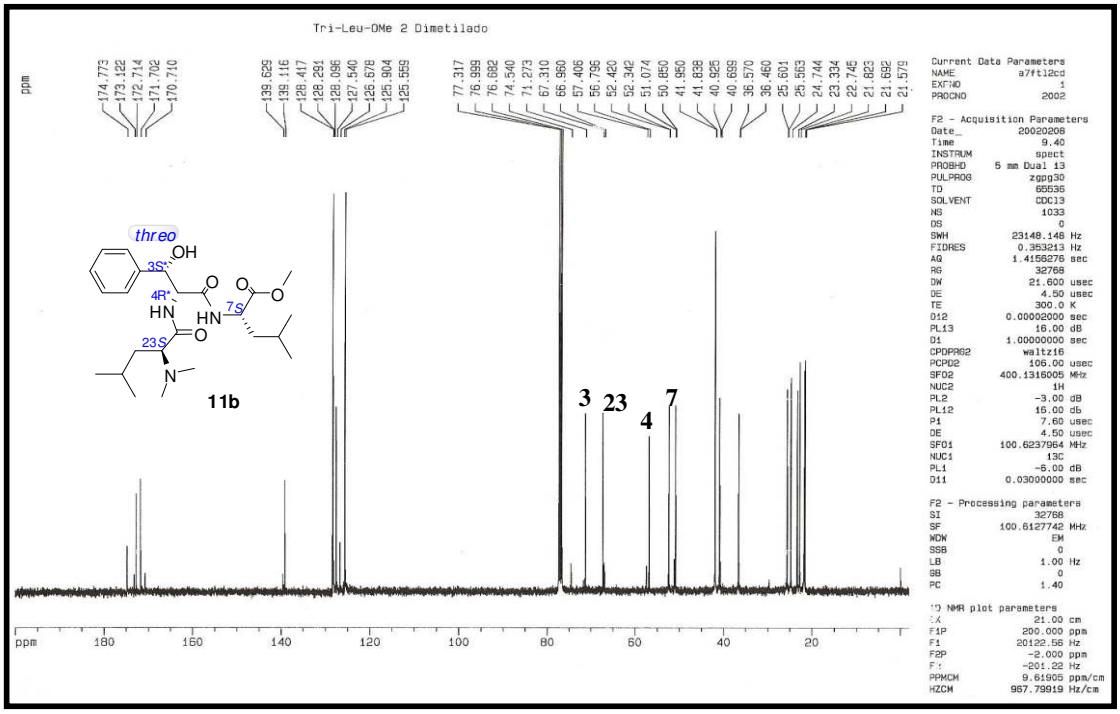
S50. HMBC NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



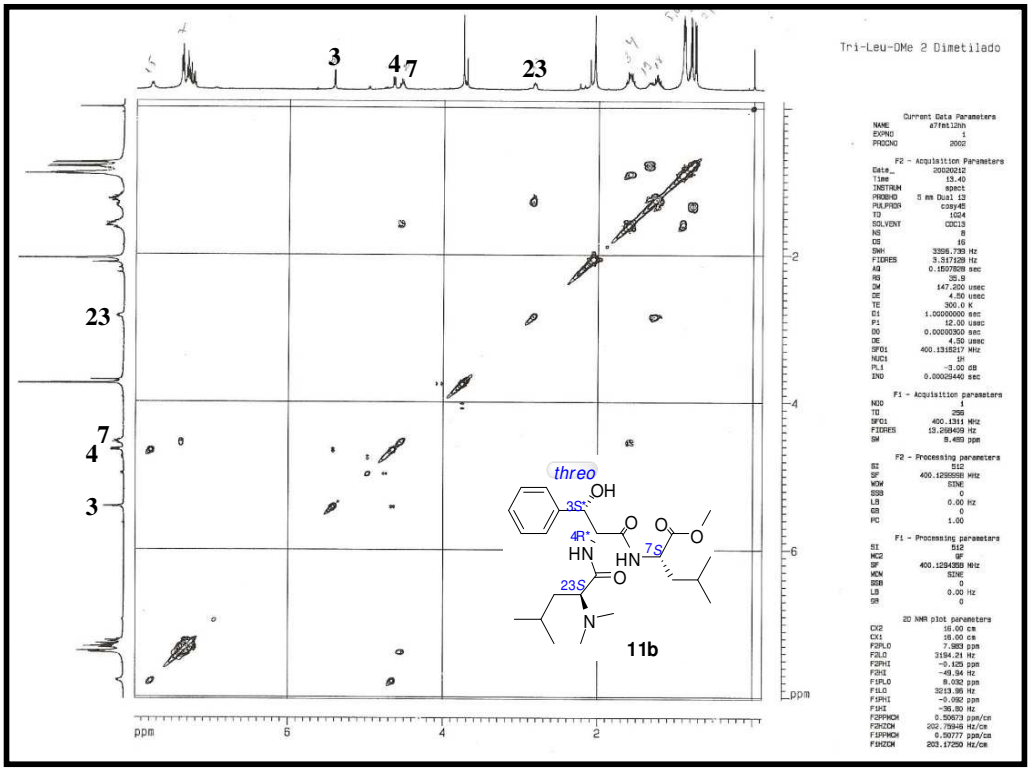
S51. NOESY NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11a) in $CDCl_3$



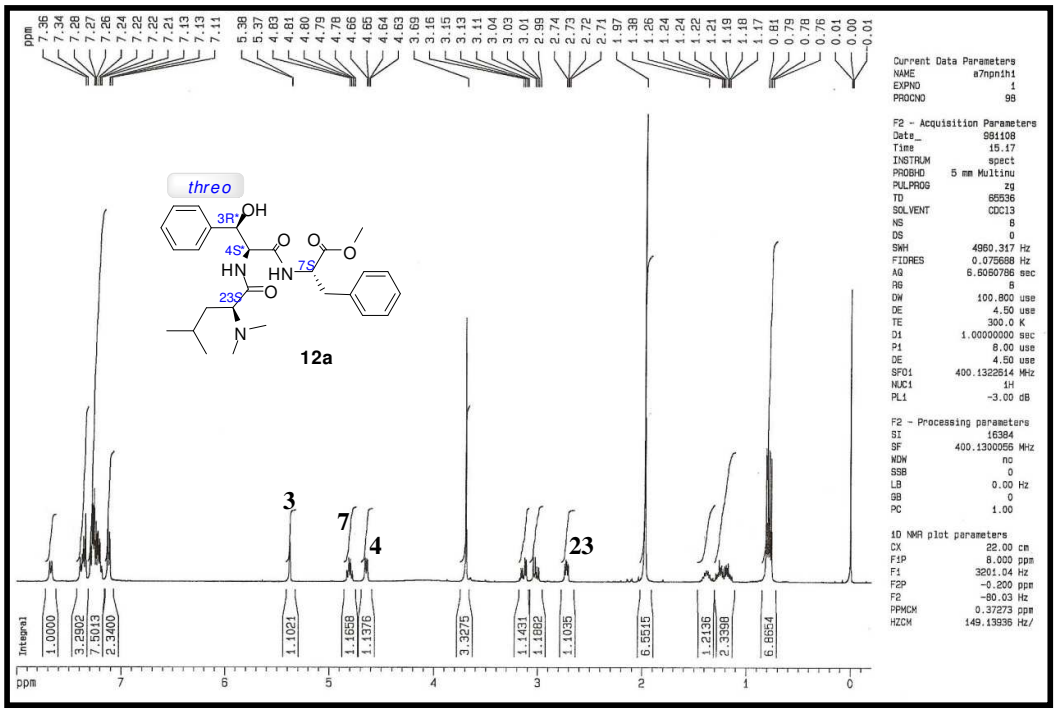
S52. ^{1}H NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11b) in $CDCl_3$



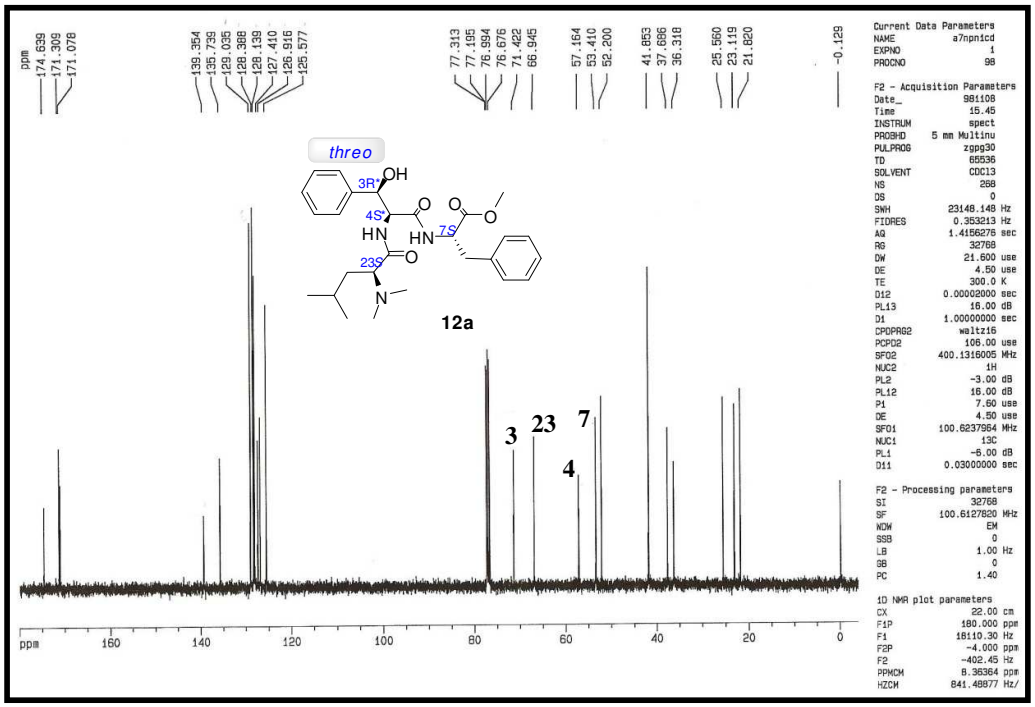
S53. ^{13}C NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11b) in $CDCl_3$



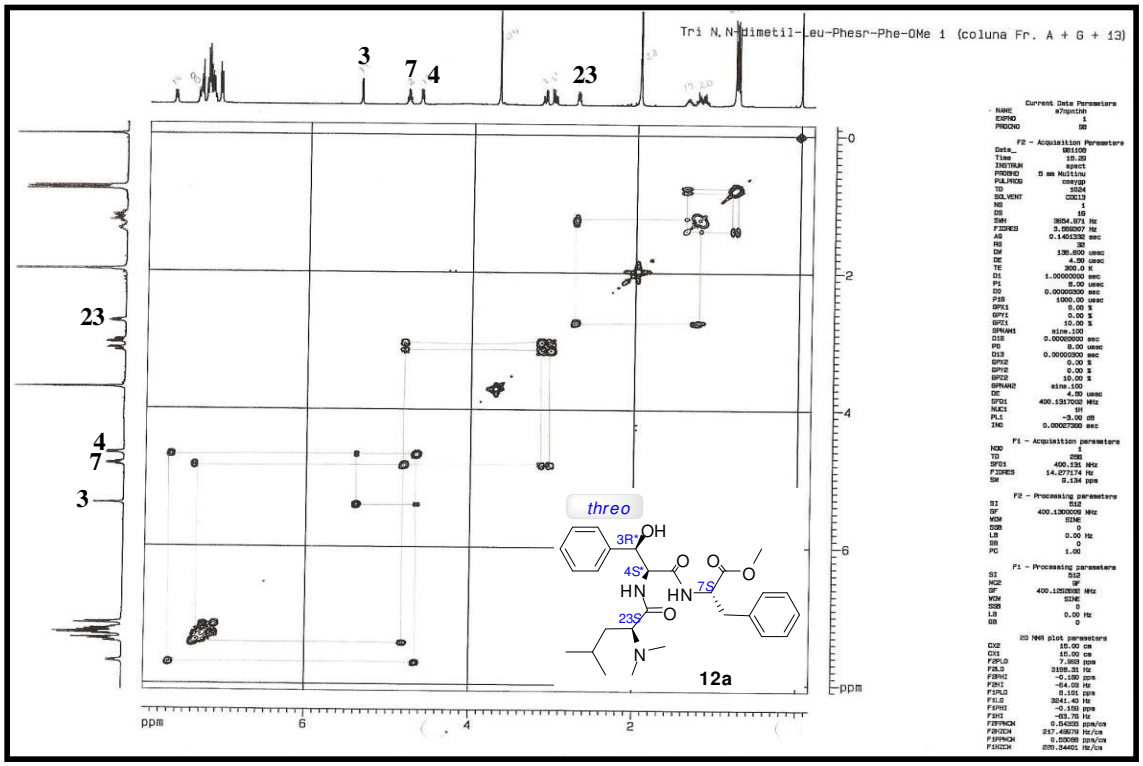
S54. ^{1}H-^{1}H COSY 45° NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-4-methylpentanoate (11b) in $CDCl_3$



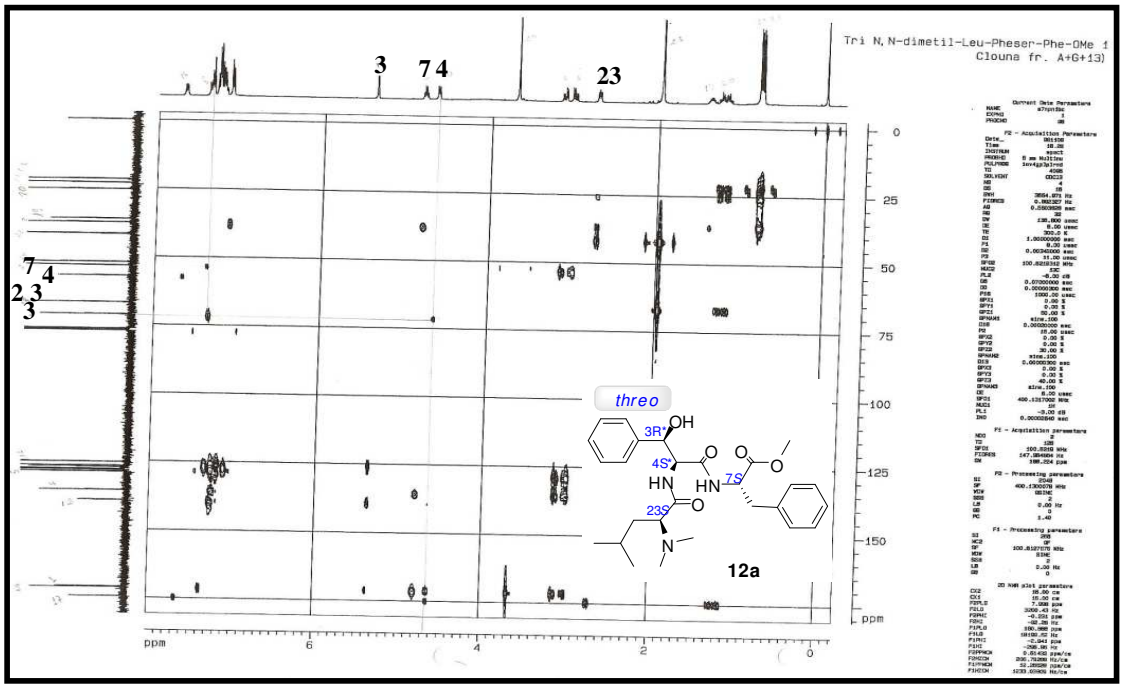
S55. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12a) in $CDCl_3$



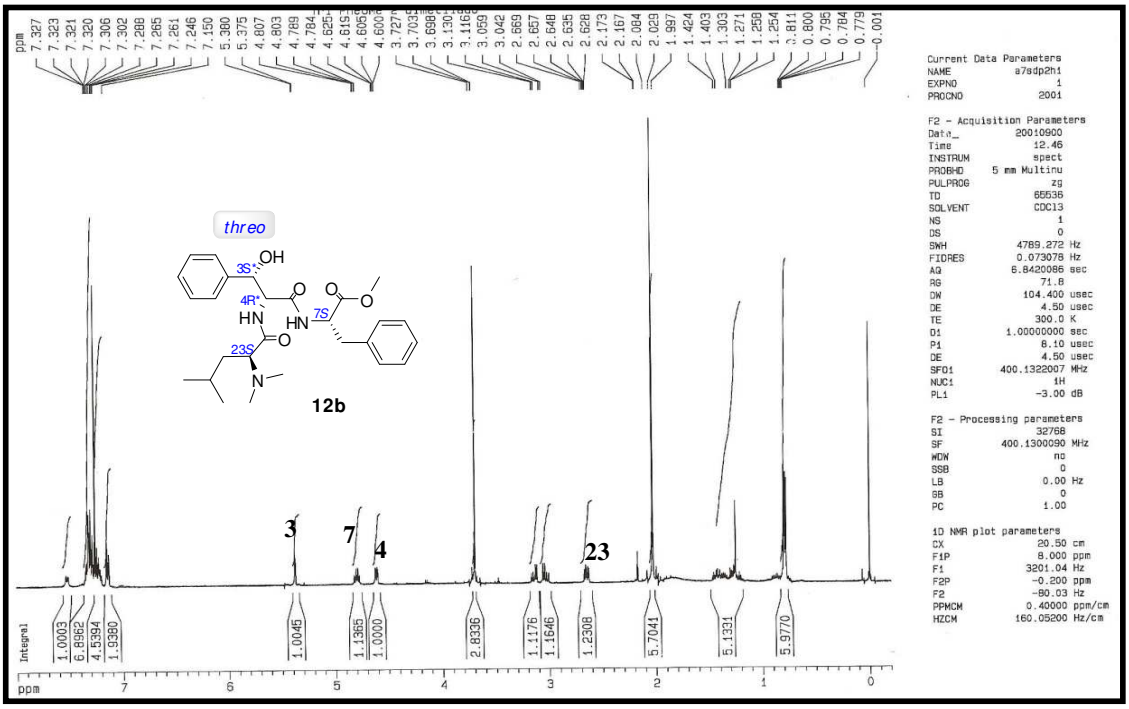
S56. ^{13}H NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12a) in $CDCl_3$



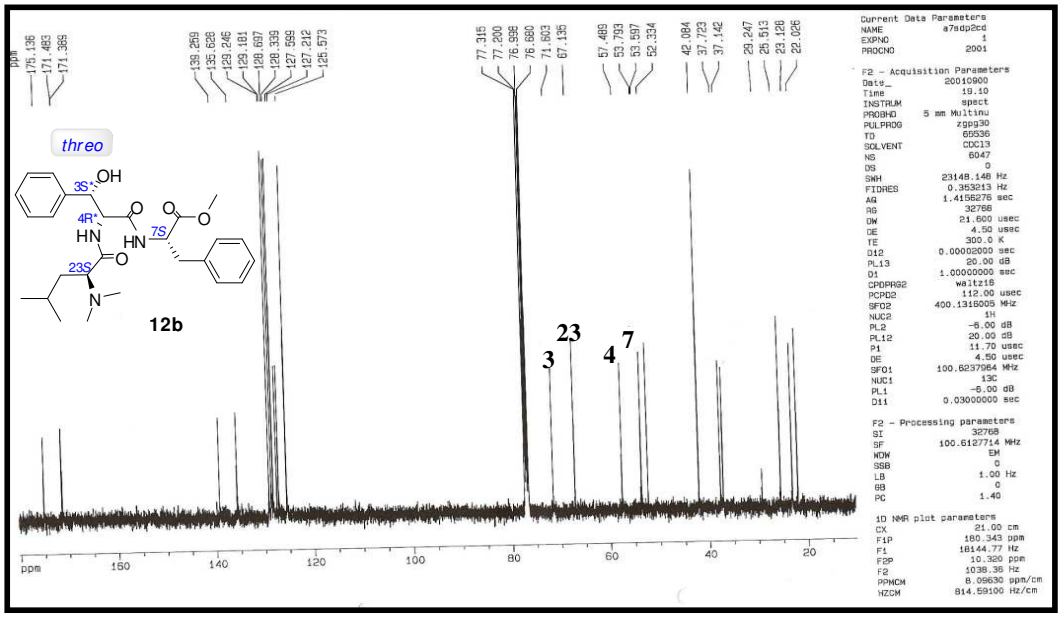
S57. ^{1}H-^{1}H COSY 45° NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12a) in $CDCl_3$



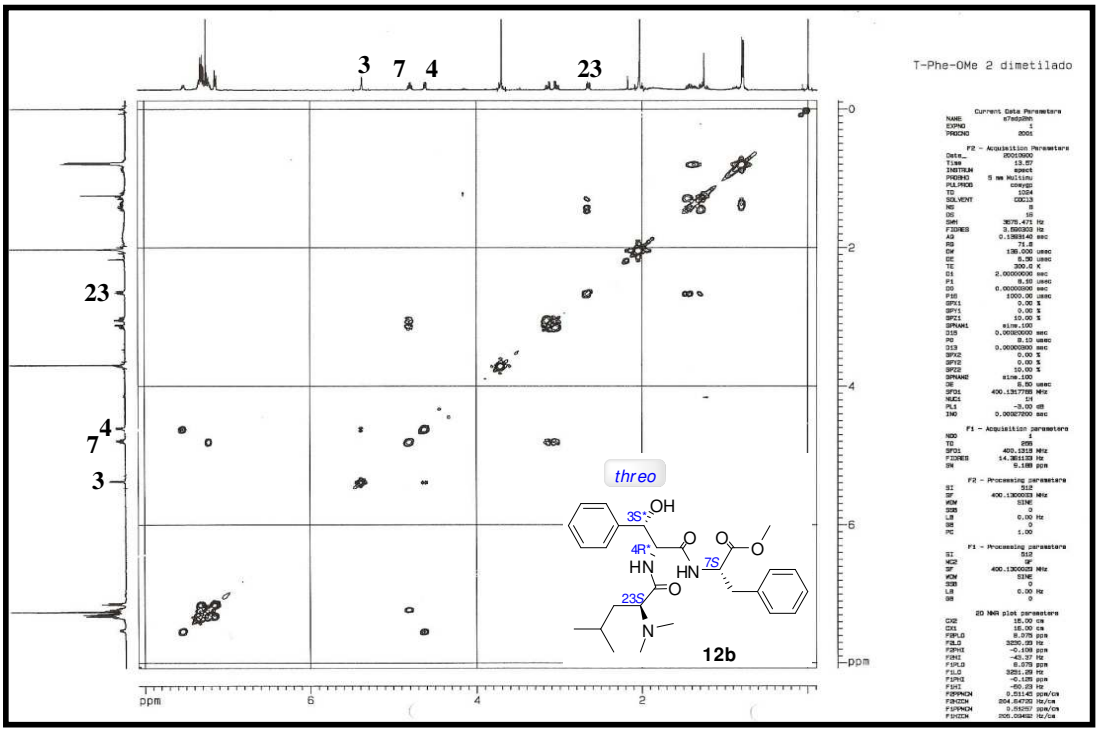
S58. HMBC NMR spectrum of (S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12a) in $CDCl_3$



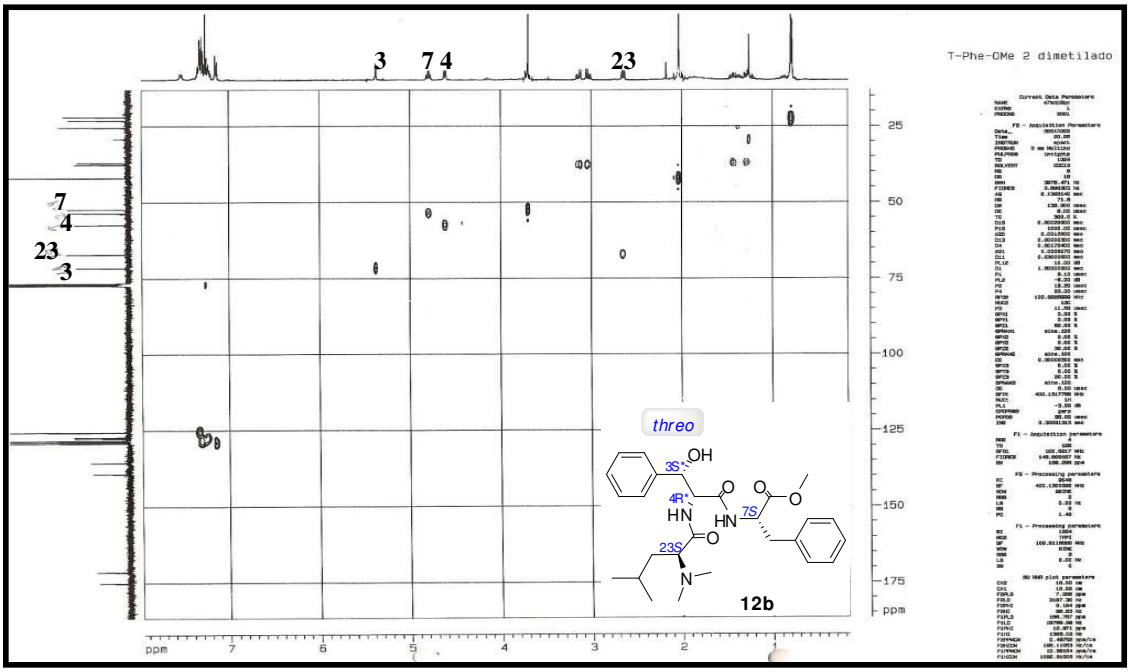
S59. ^{1}H NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12b) in $CDCl_3$



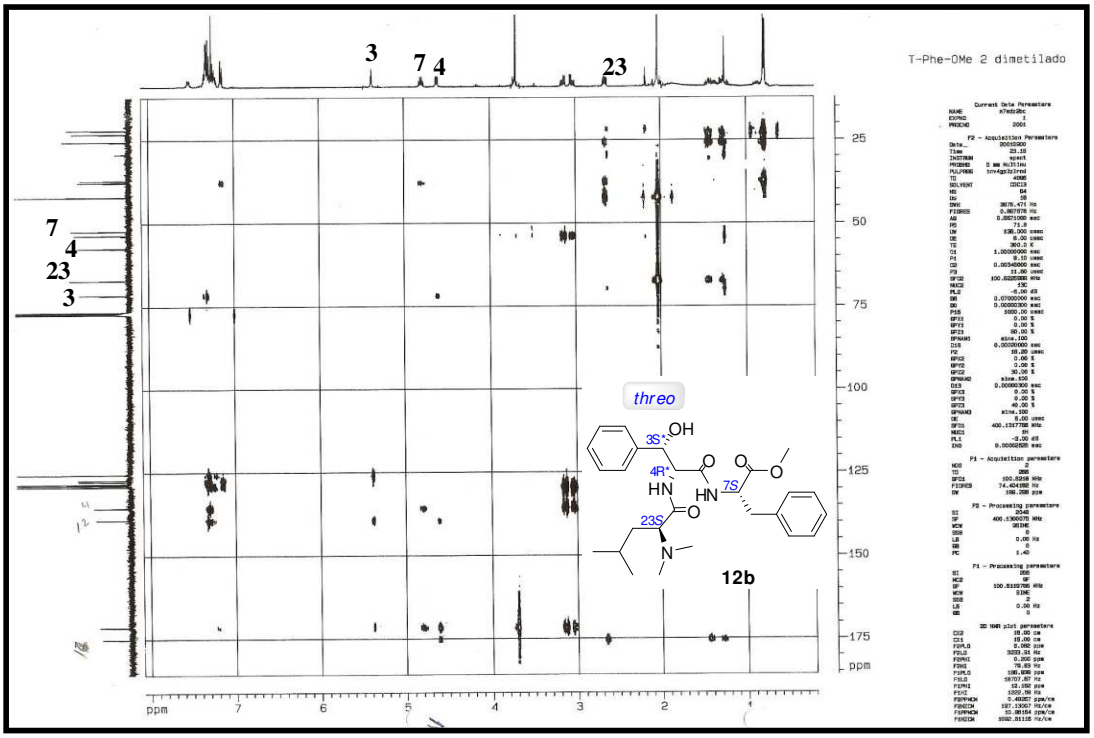
S60. ^{13}C NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12b) in $CDCl_3$



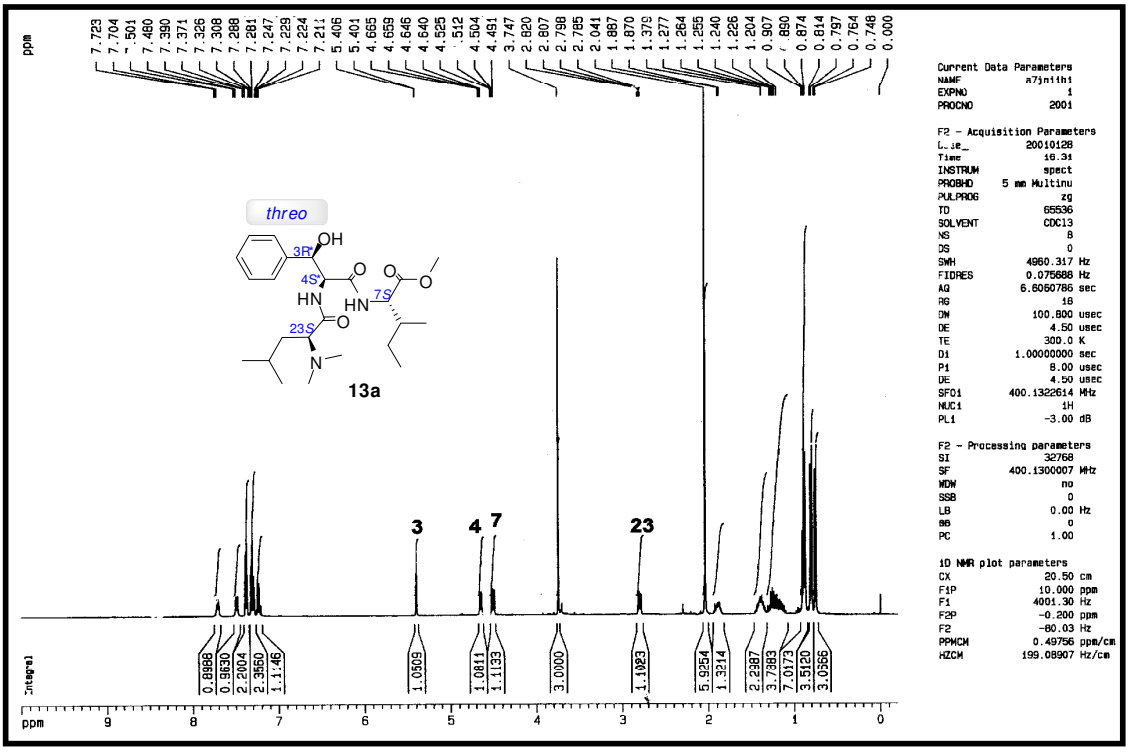
S61. ^{1}H-^{1}H COSY 45° NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12b) in $CDCl_3$



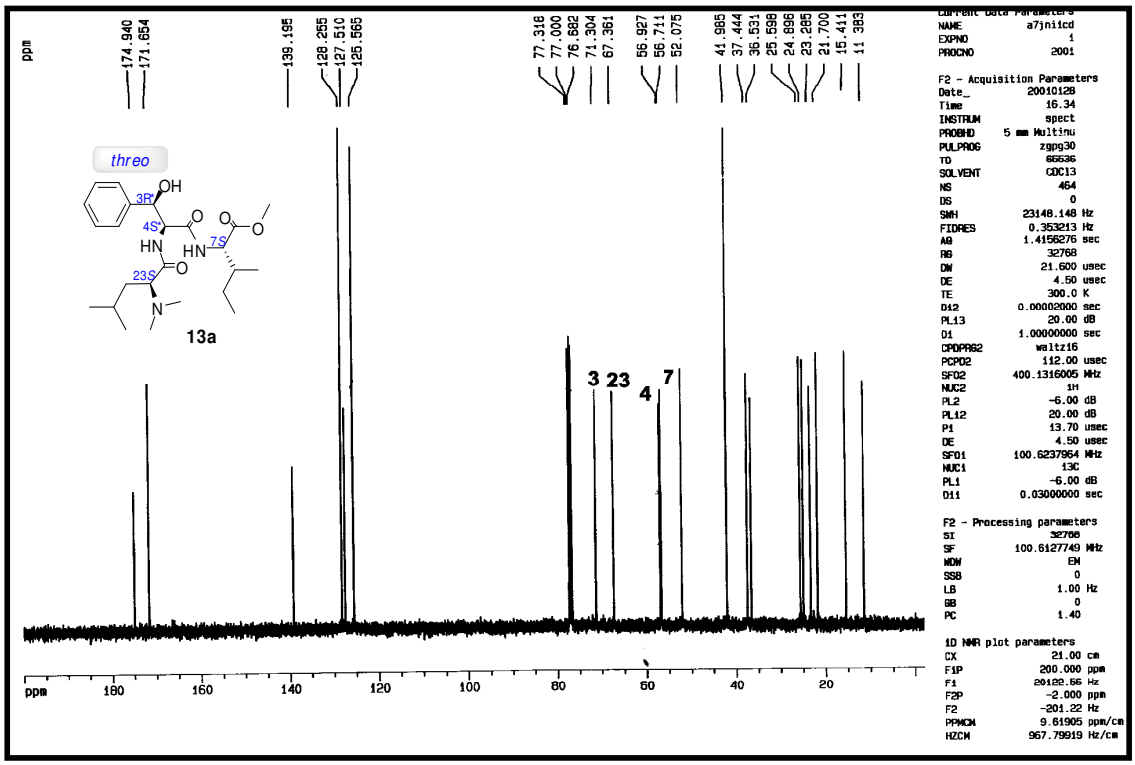
S62. HMQC NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12b) in $CDCl_3$



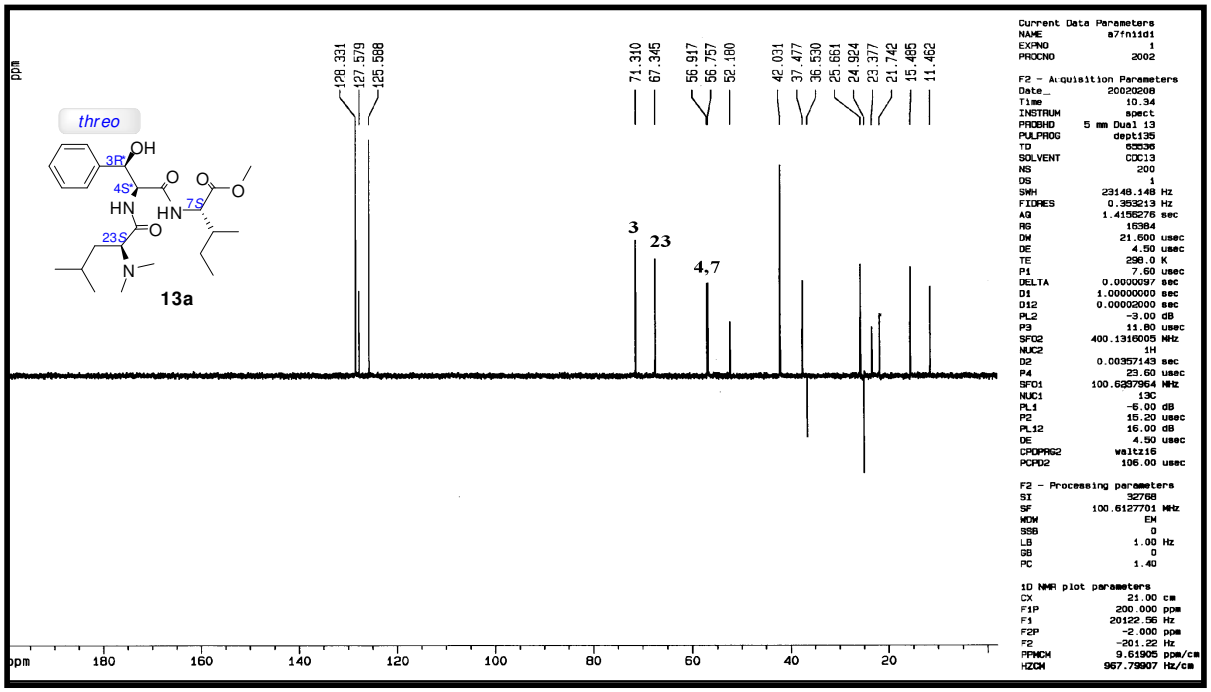
S63. HMBC NMR spectrum of (S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-phenylpropanoate (12b) in $CDCl_3$



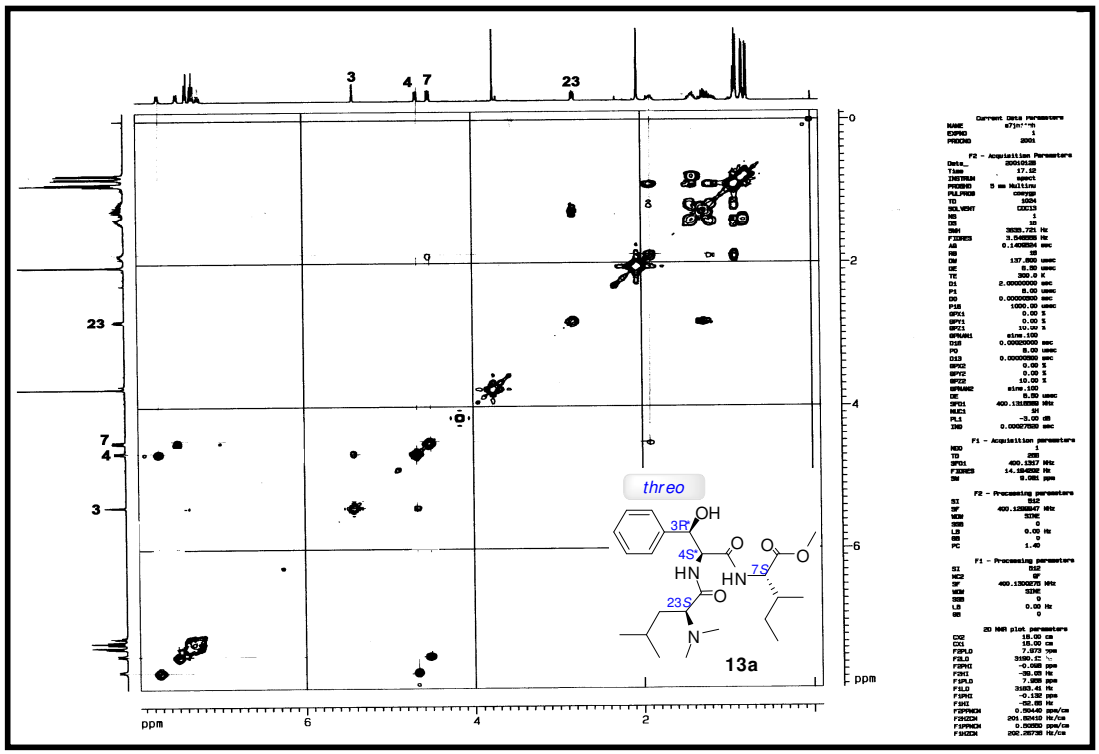
S64. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



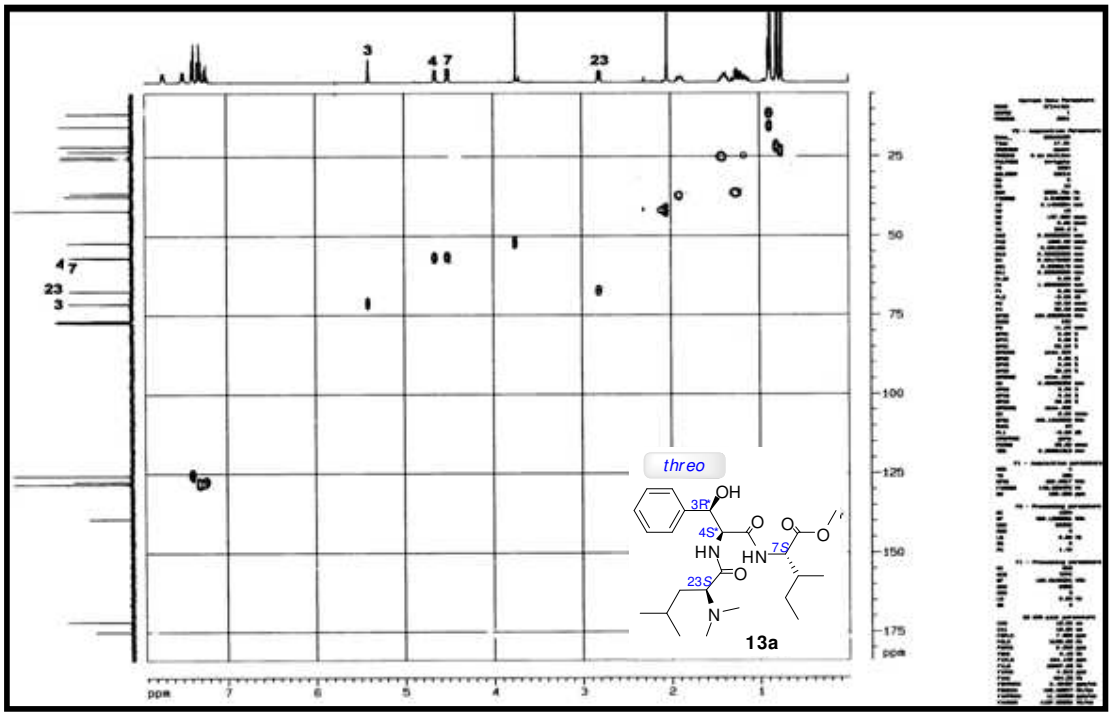
S65. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



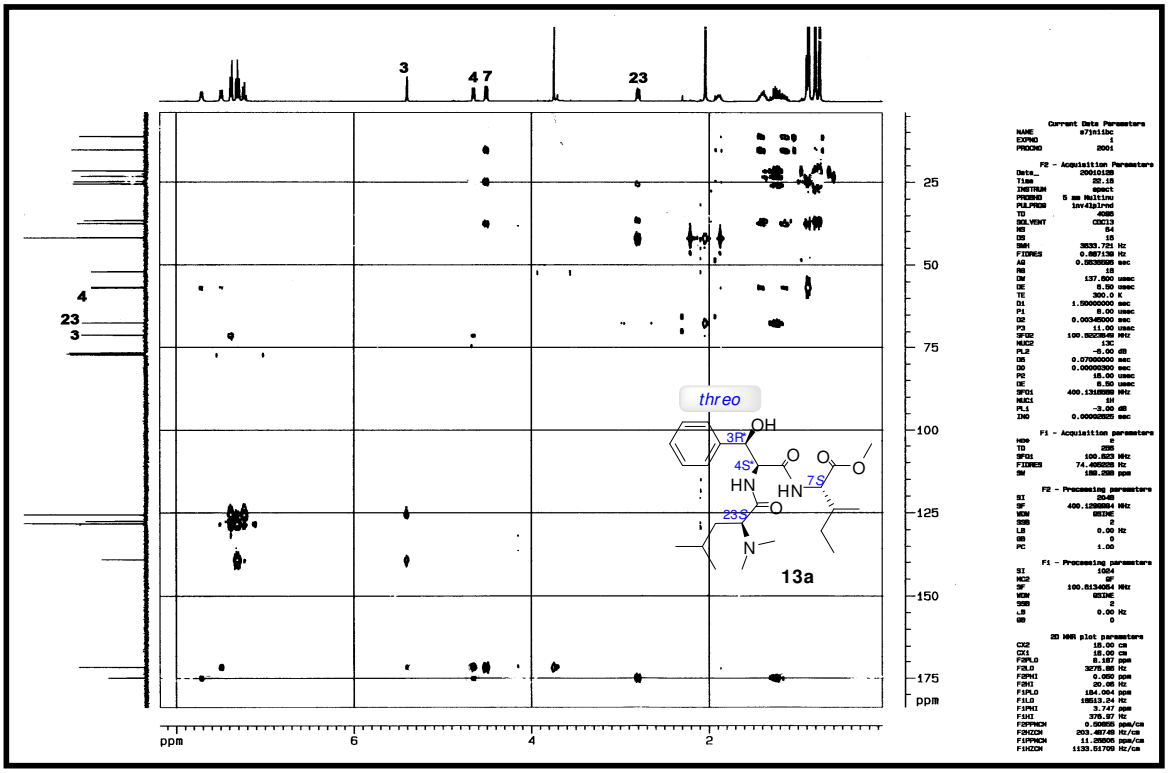
S66. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



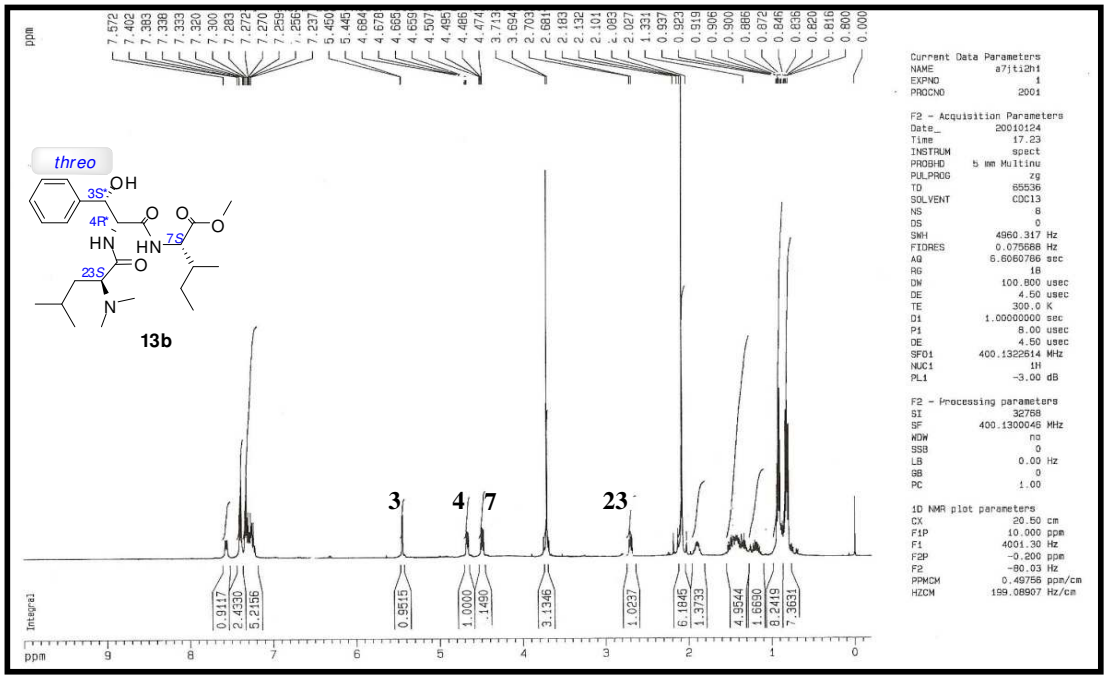
S67. ^{1}H-^{1}H COSY 45° NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



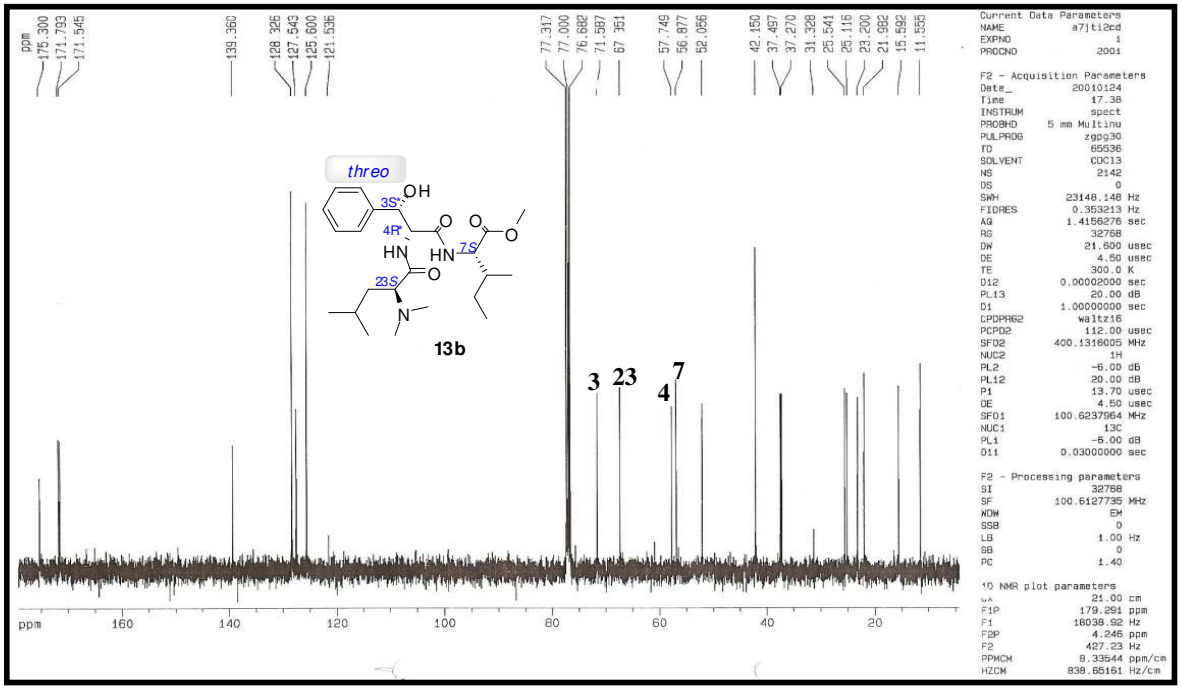
S68. HMQC NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



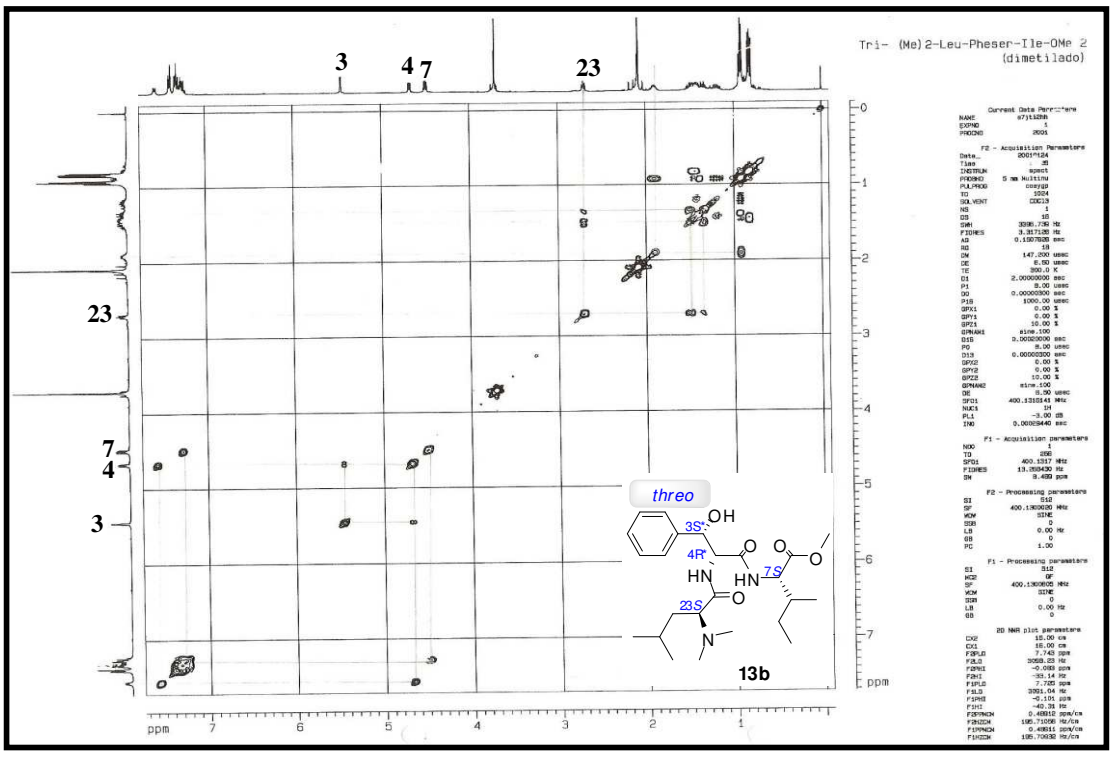
S69. HMBC NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13a) in $CDCl_3$



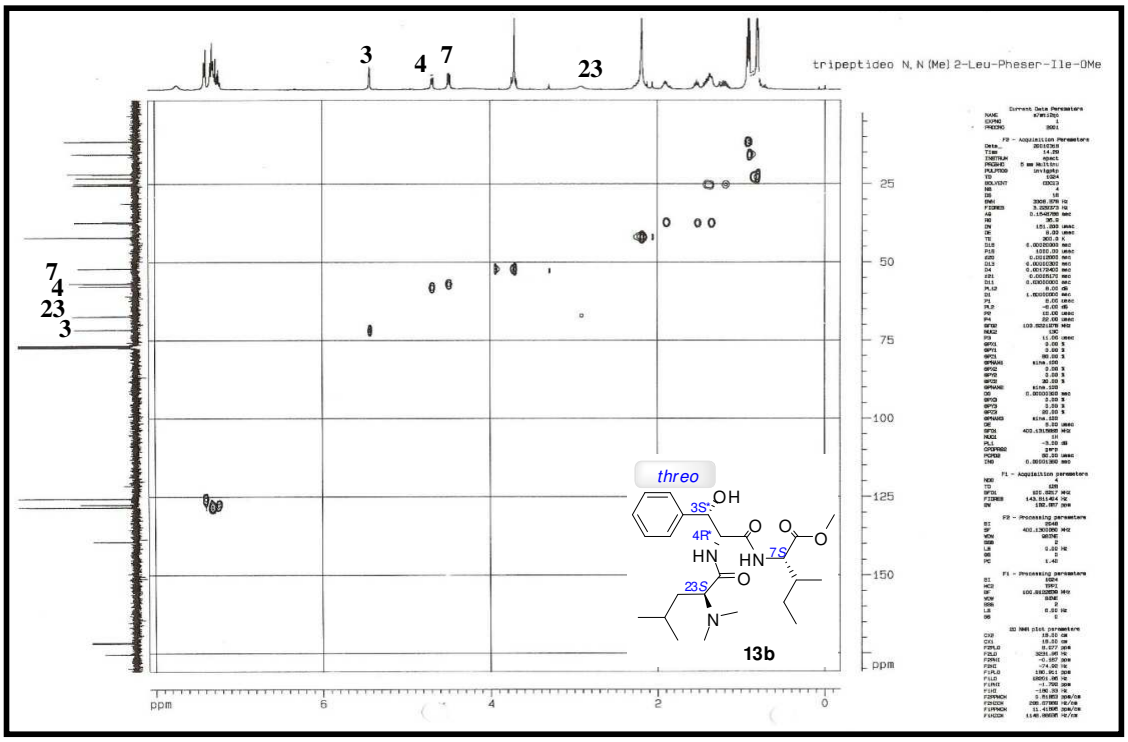
S70. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13b) in $CDCl_3$



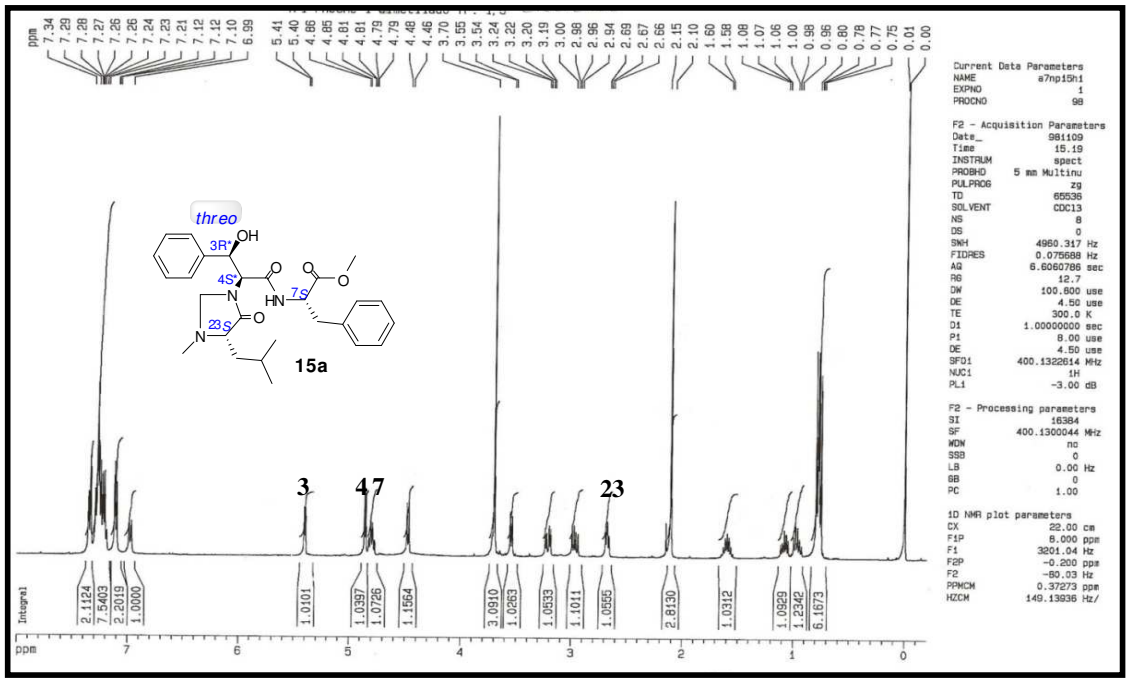
S71. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13b) in $CDCl_3$



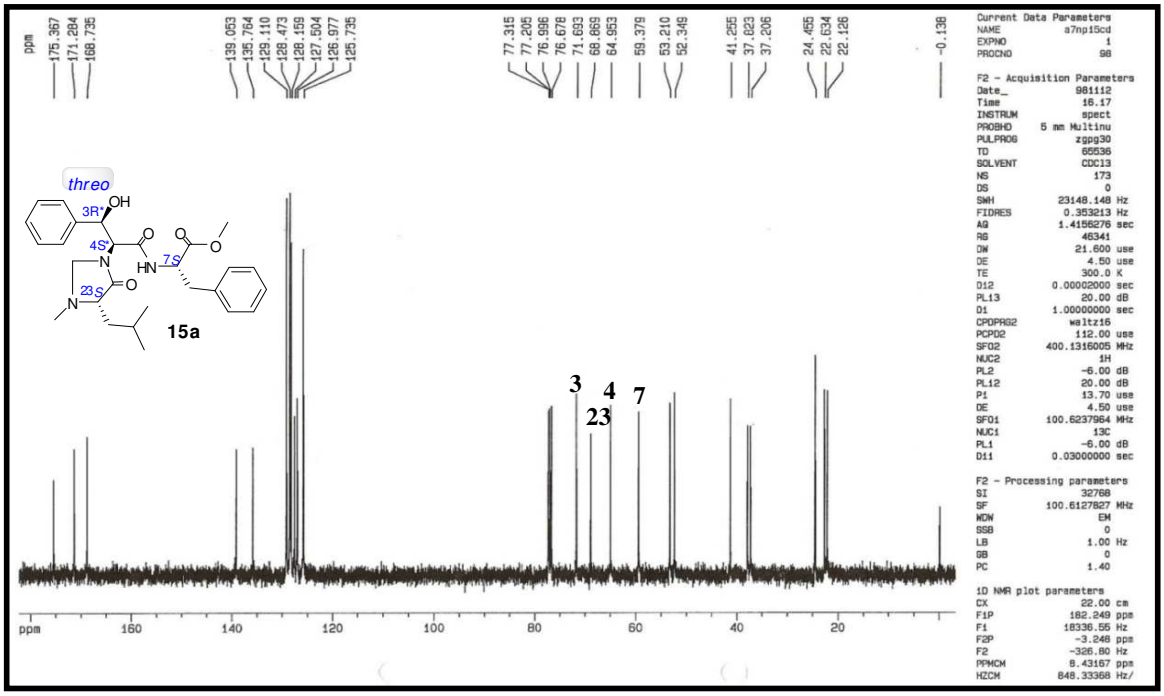
S71. ^{1}H-^{1}H COSY 45° NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13b) in $CDCl_3$



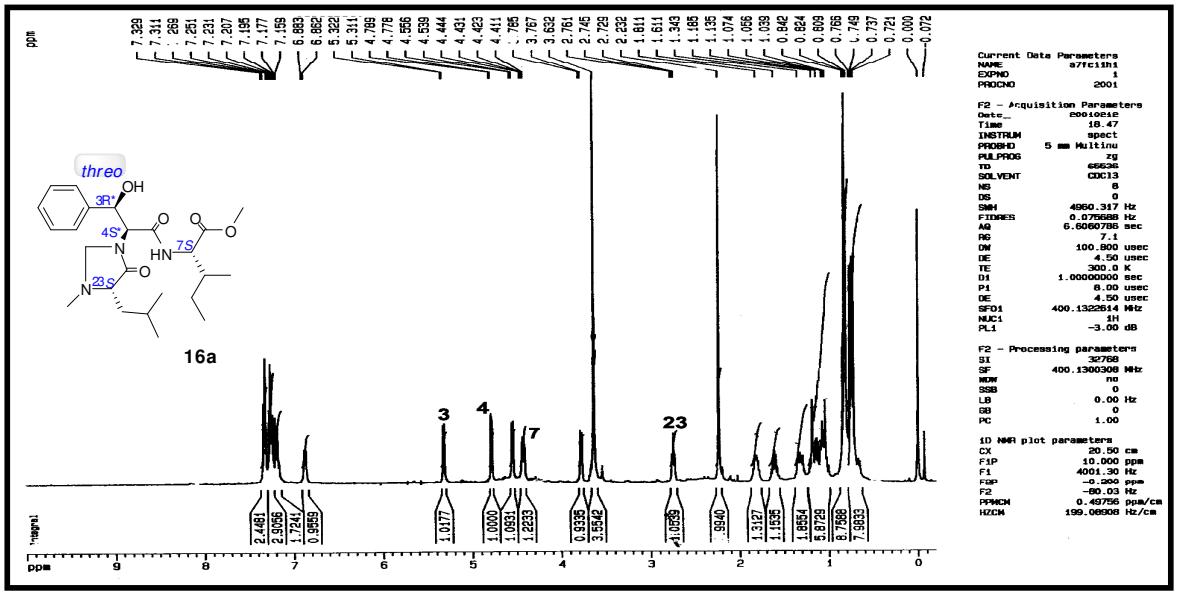
S72. HMQC NMR spectrum of (2S,3S)-methyl 2-((2R,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-hydroxy-3-phenylpropanamido)-3-methylpentanoate (13b) in $CDCl_3$.



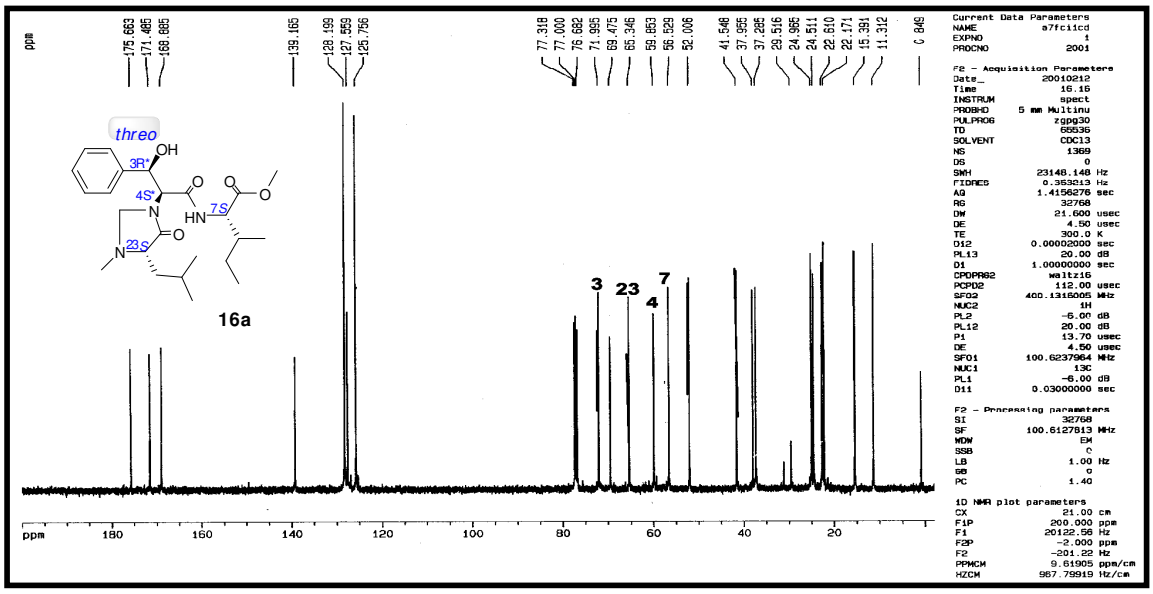
S73. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3R)-3-hydroxy-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (15a) in $CDCl_3$



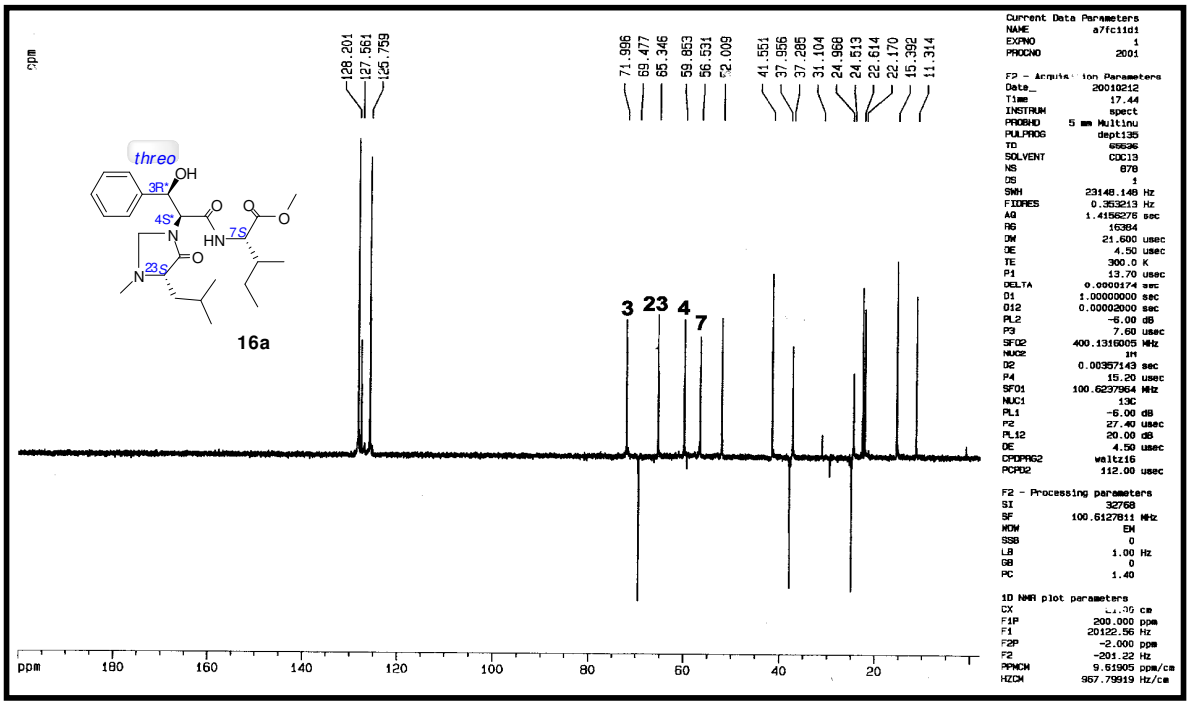
S74. ^{13}C NMR spectrum of (S)-Methyl 2-((2S.3R)-3-hydroxy-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (15a) in $CDCl_3$



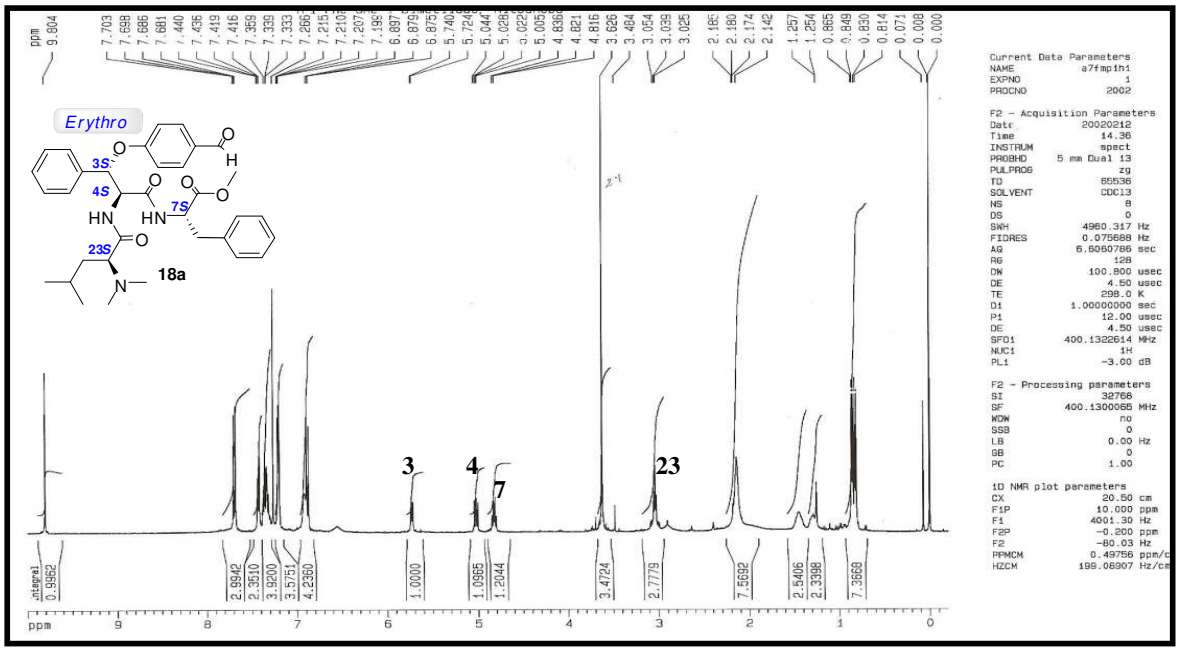
S75. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-3-hydroxy-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (16a) in $CDCl_3$.



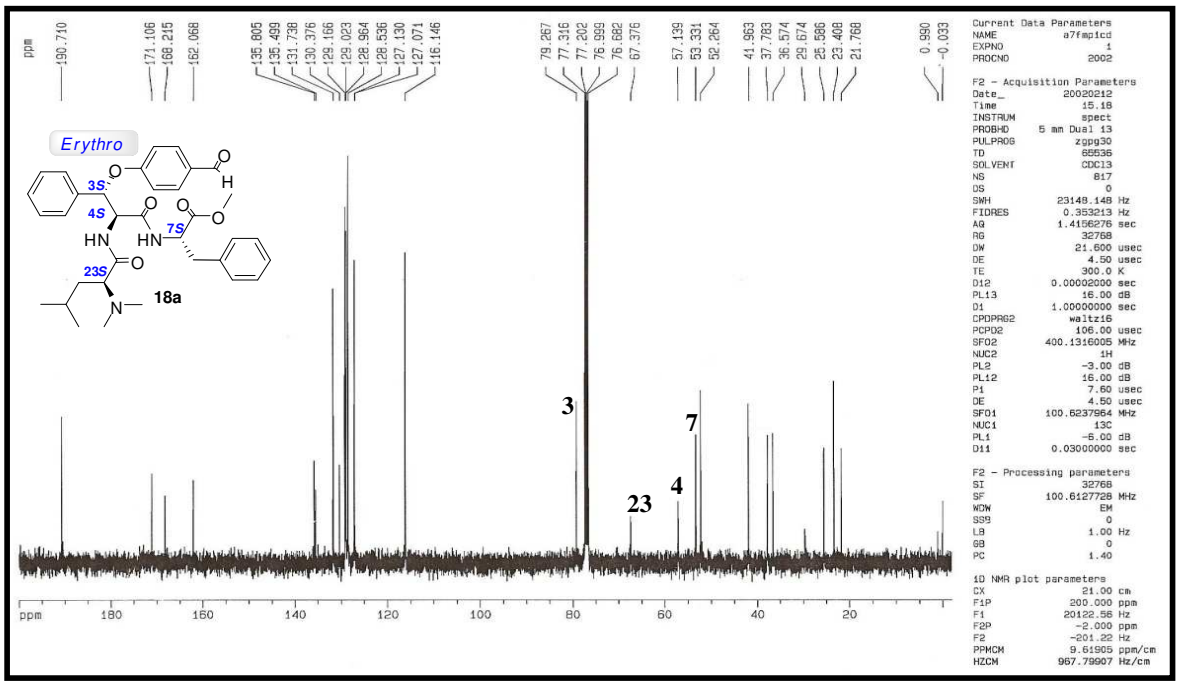
S76. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-3-hydroxy-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (16a) in $CDCl_3$.



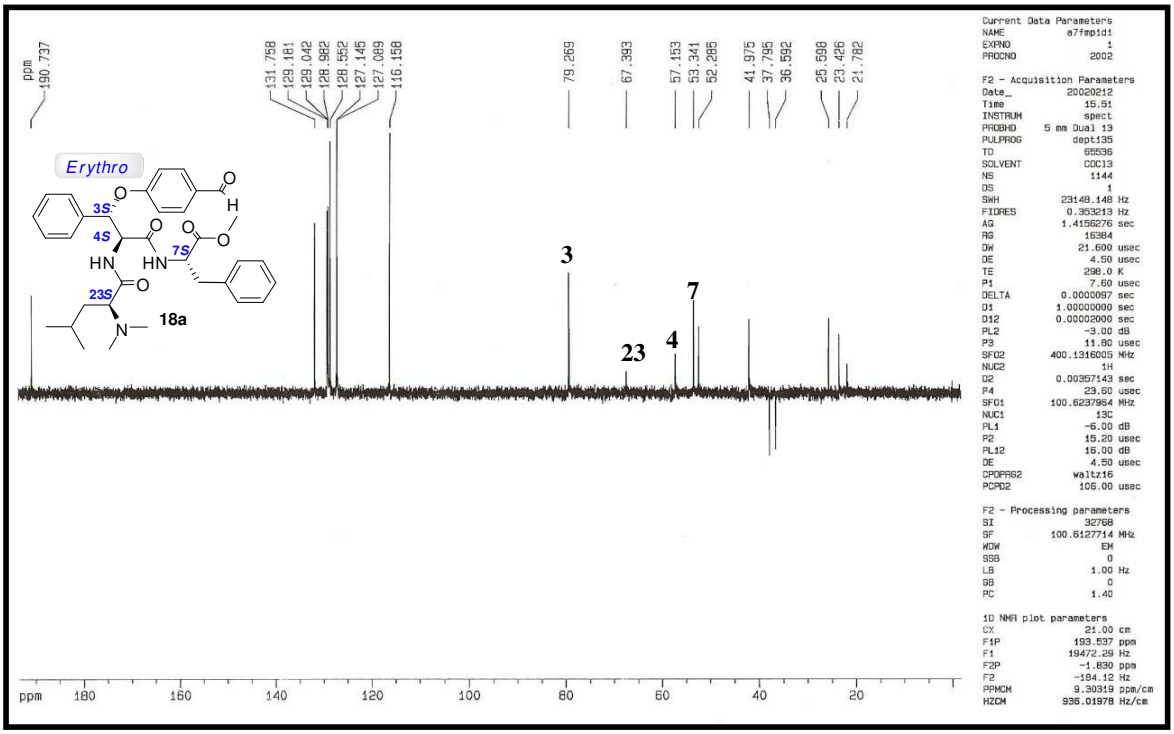
S77. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2S,3R)-3-hydroxy-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (16a) in $CDCl_3$



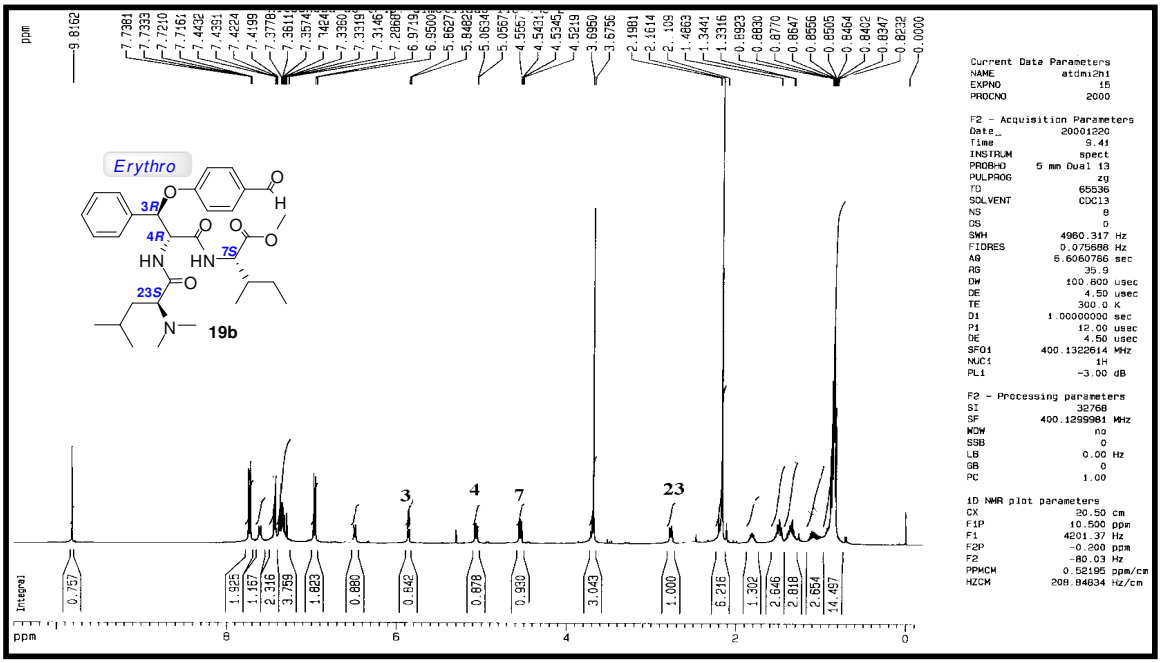
S78. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-phenylpropanoate (18a) in $CDCl_3$



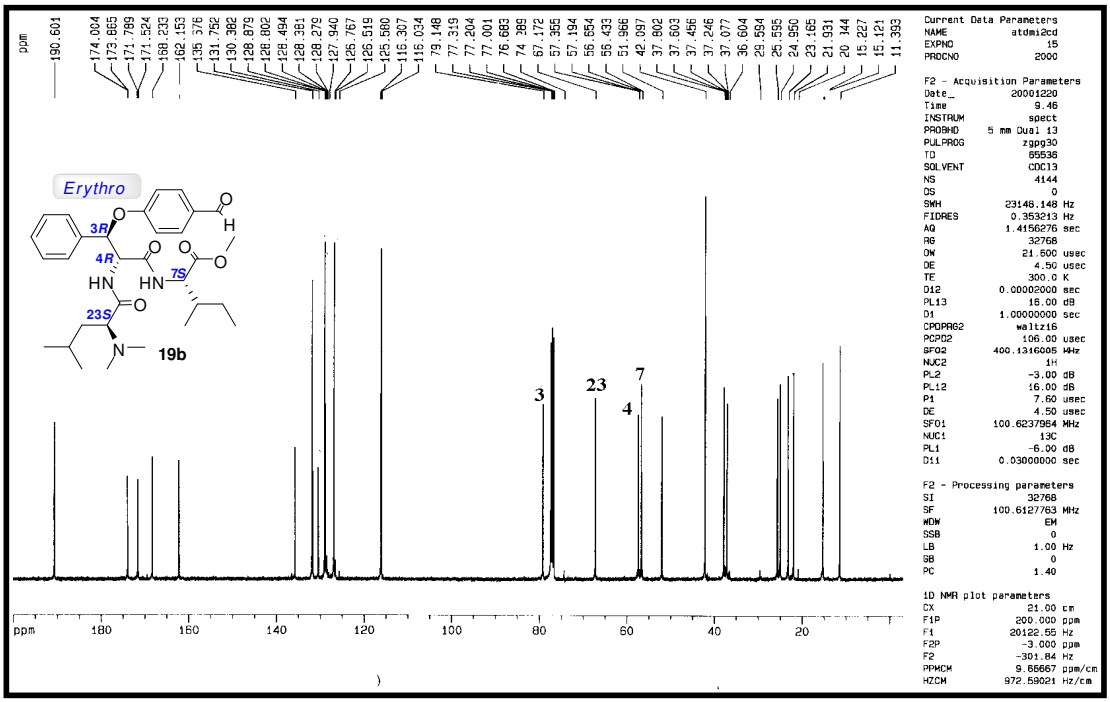
S79. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-phenylpropanoate (18a) in $CDCl_3$



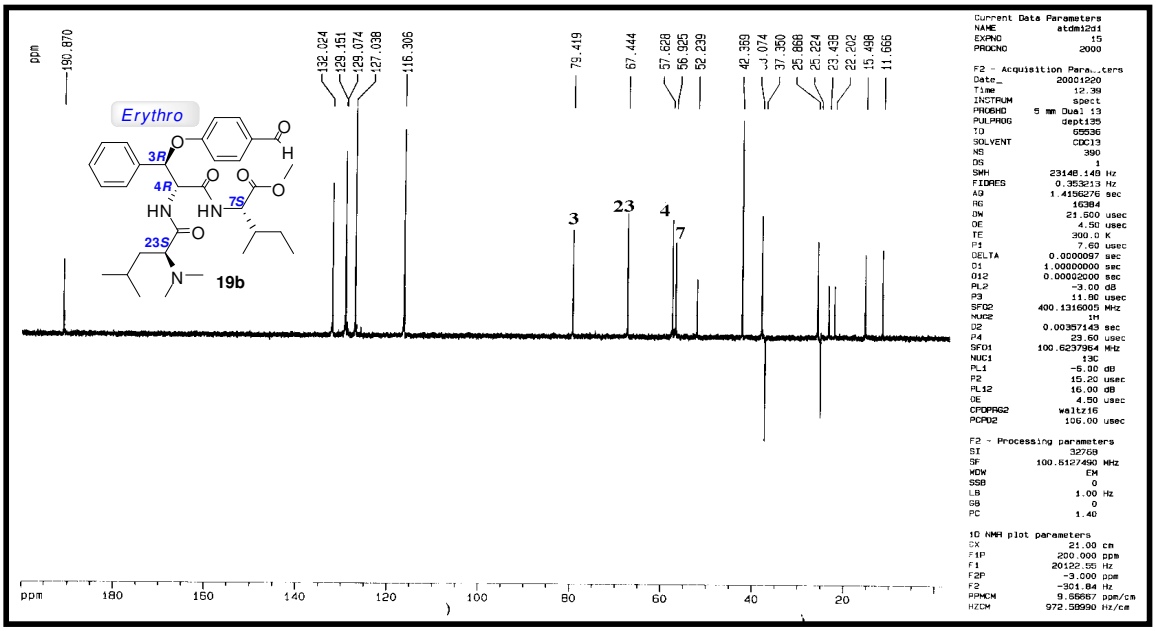
S80. DEPT 135 NMR spectrum of (S)-methyl 2-((2S,3S)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-phenylpropanoate (18a) in $CDCl_3$



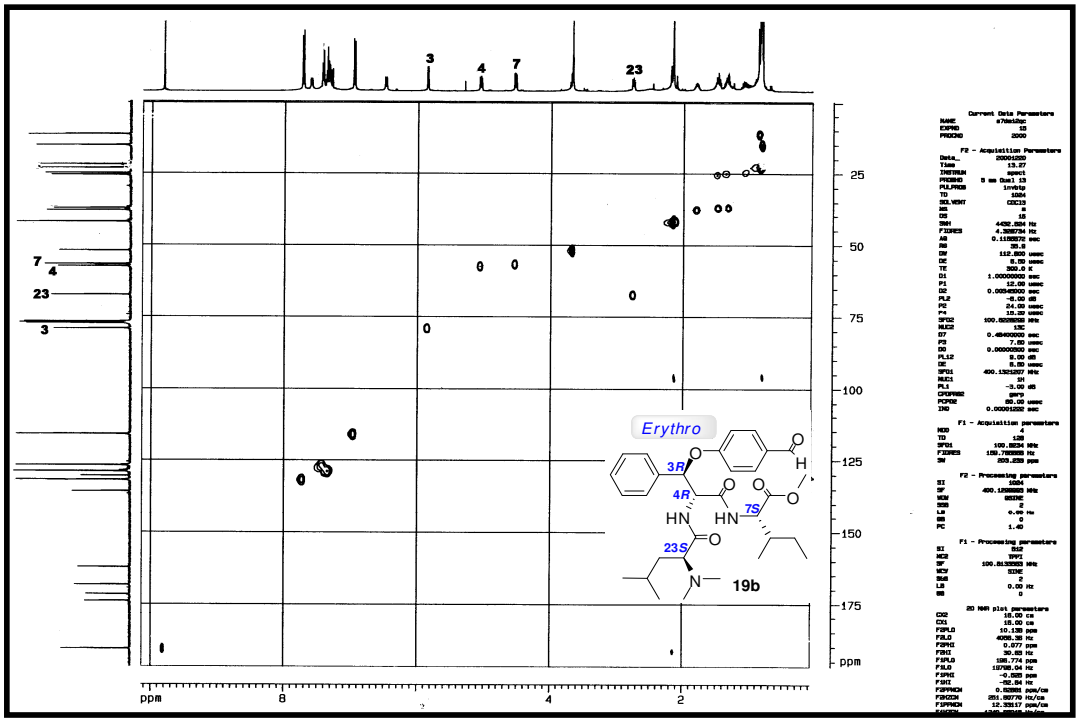
S81. ^1H NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-methylpentanoate (19b) in $CDCl_3$



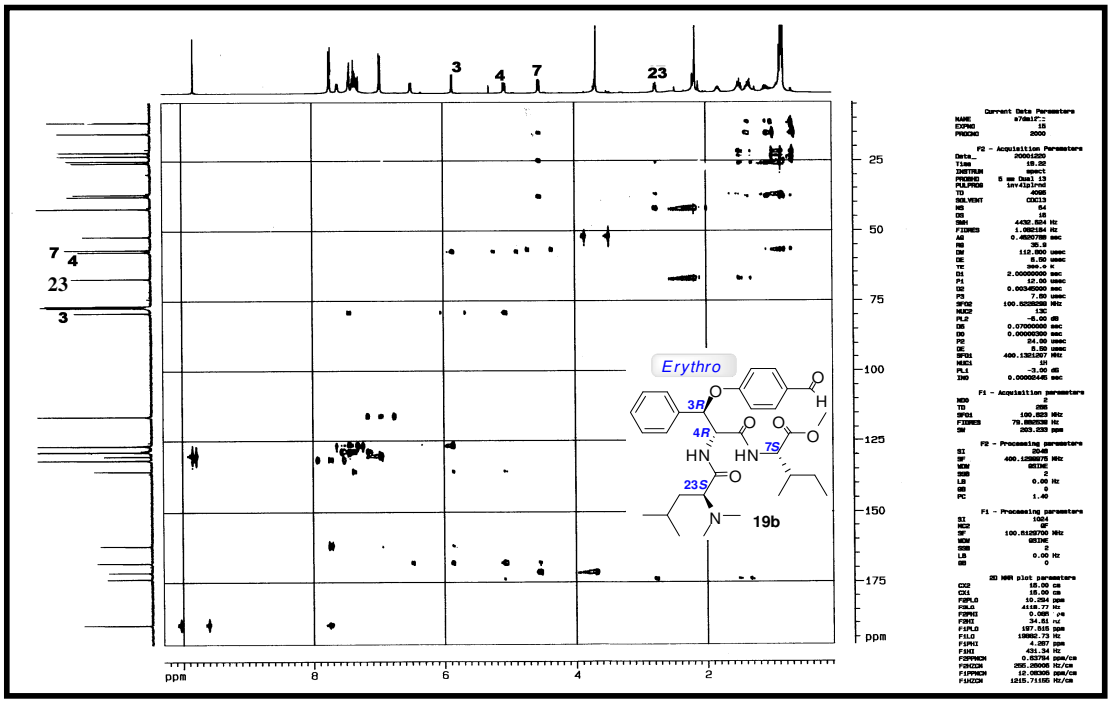
S82. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-methylpentanoate (19b) in $CDCl_3$



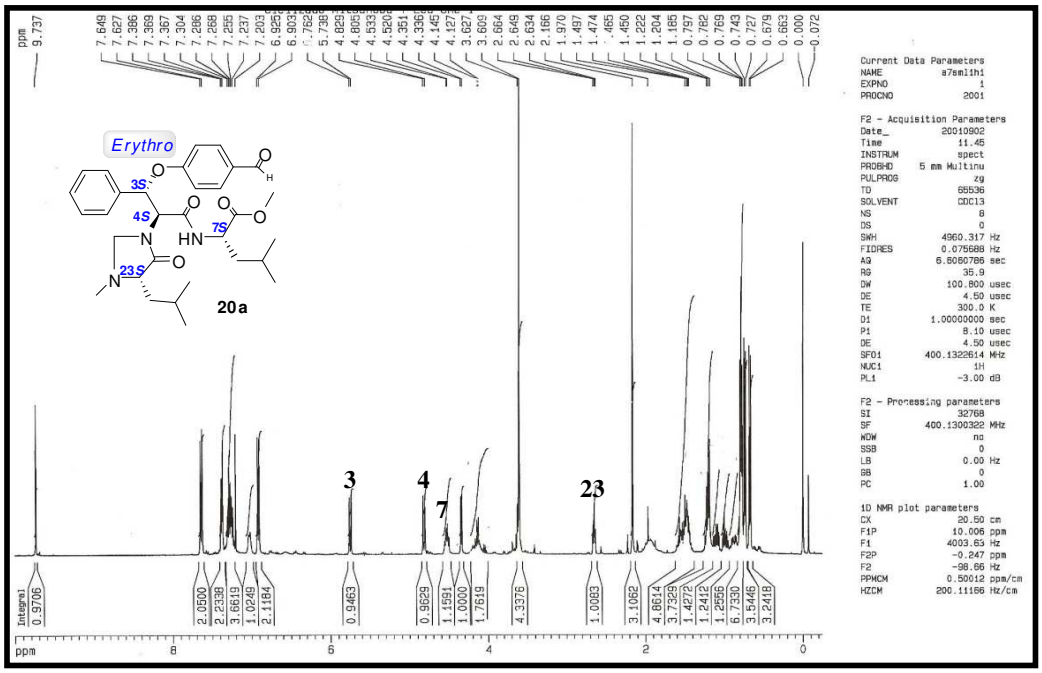
S83. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-methylpentanoate (19b) in $CDCl_3$



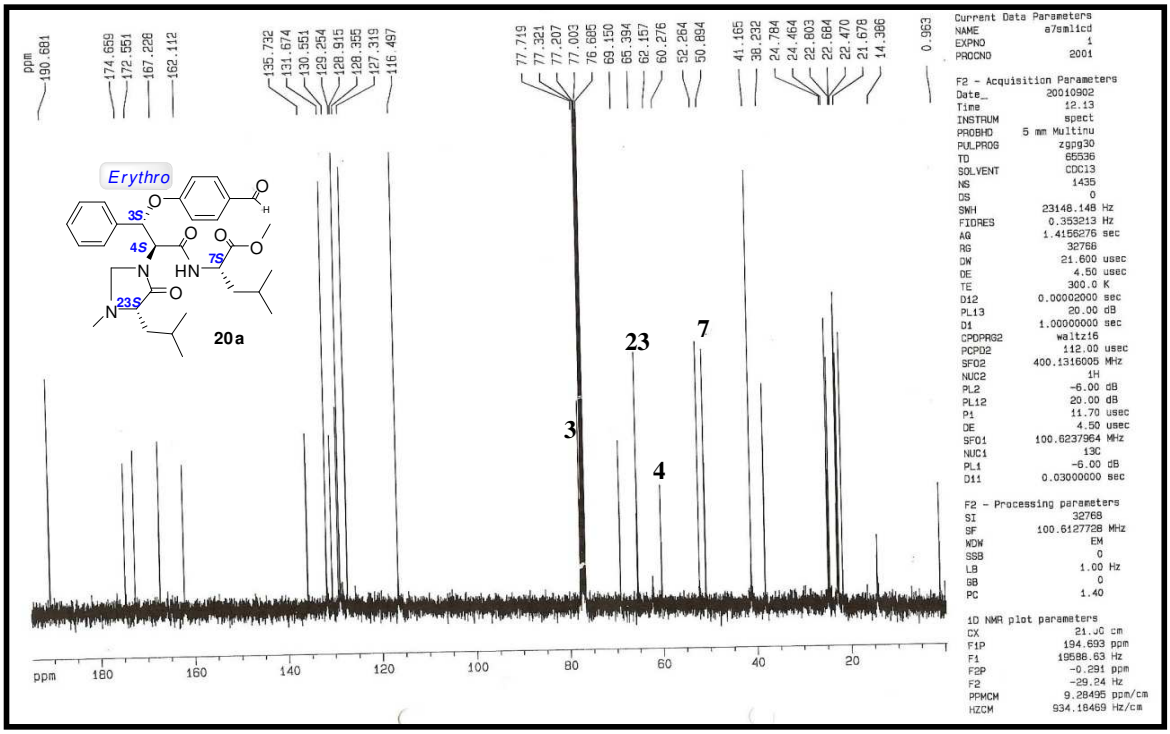
S84. HMQC NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-methylpentanoate (19b) in $CDCl_3$



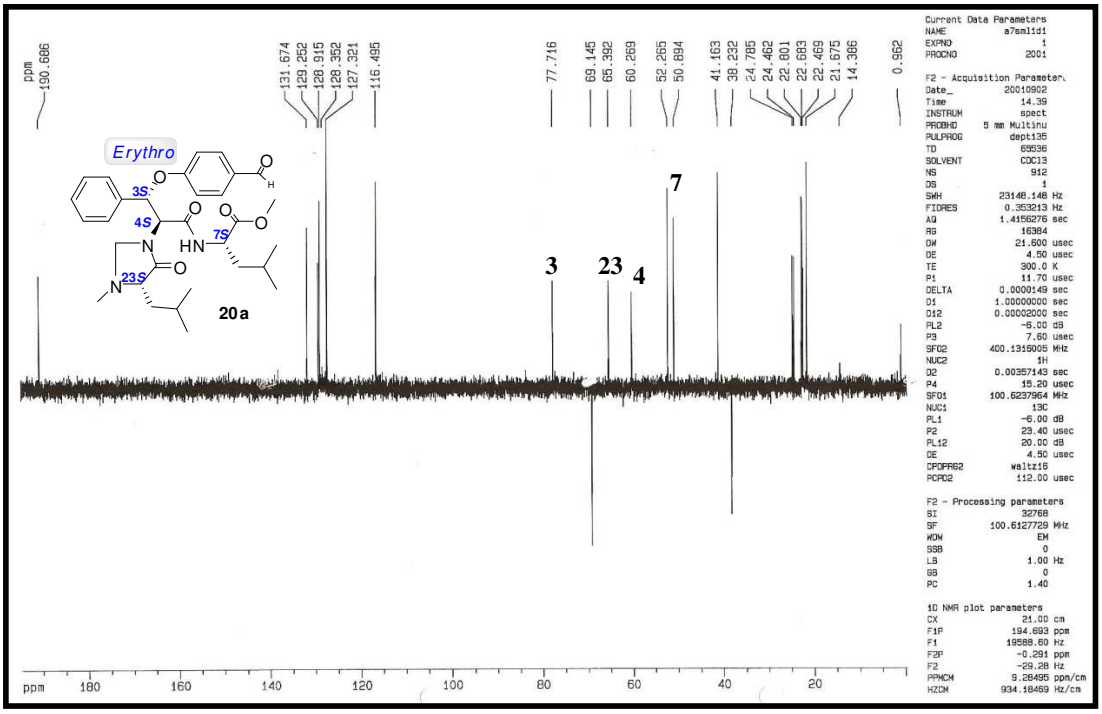
S85. HMBC NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-2-((S)-2-(dimethylamino)-4-methylpentanamido)-3-(4-formylphenoxy)-3-phenylpropanamido)-3-methylpentanoate (19b) in $CDCl_3$



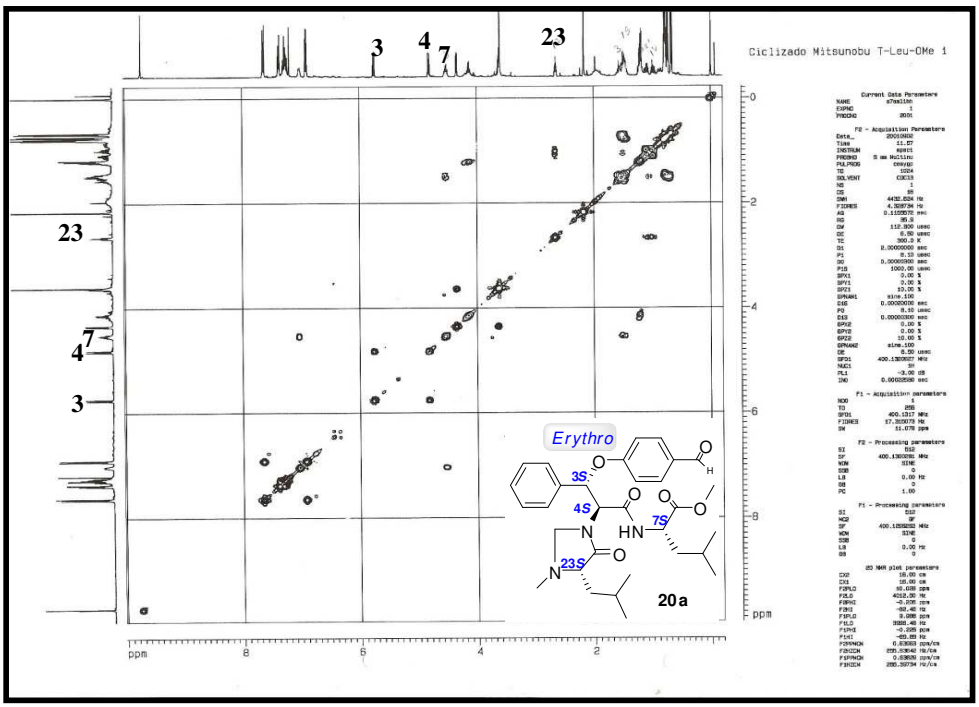
S86. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-4-methylpentanoate (20a) in $CDCl_3$



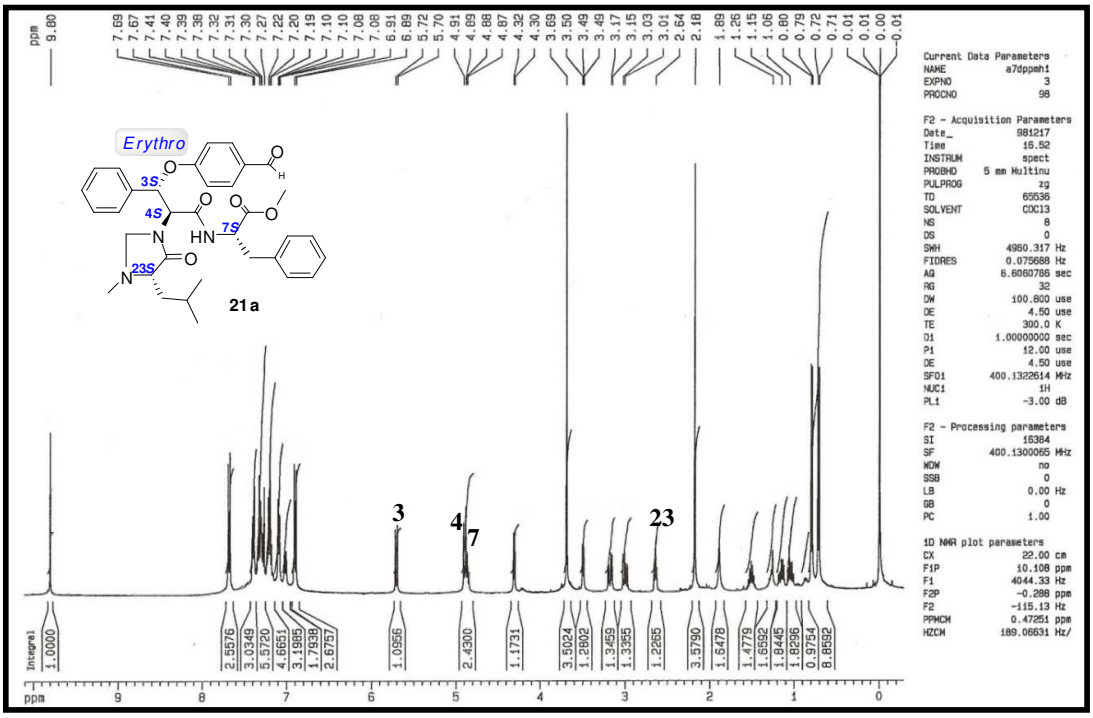
S87. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-4-methylpentanoate (20a) in $CDCl_3$.



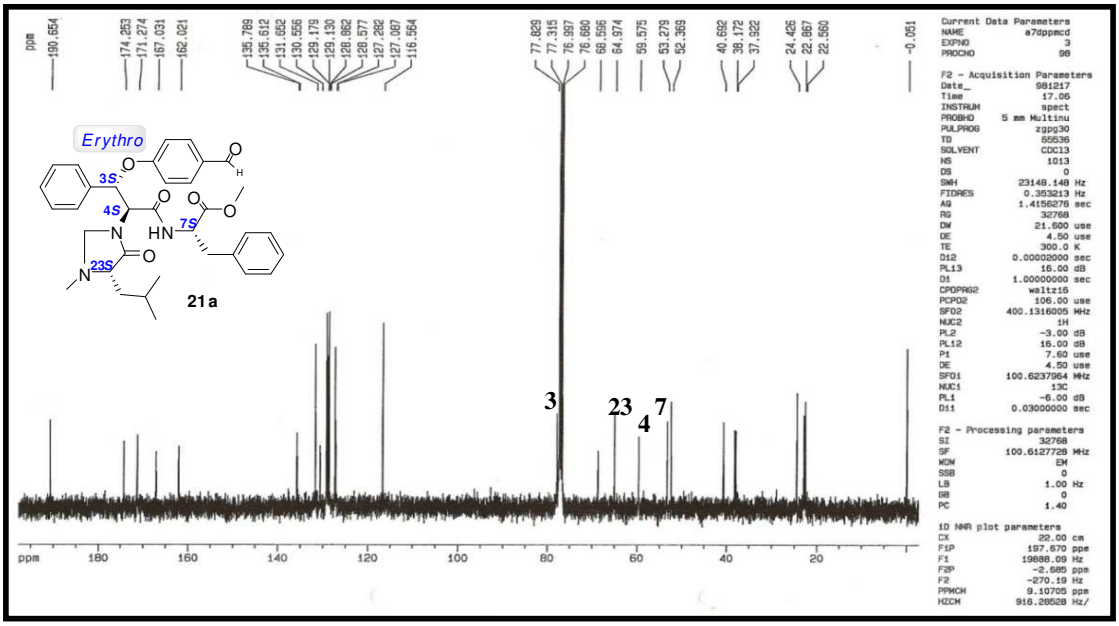
S88. DEPT 135 NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-4-methylpentanoate (20a) in $CDCl_3$



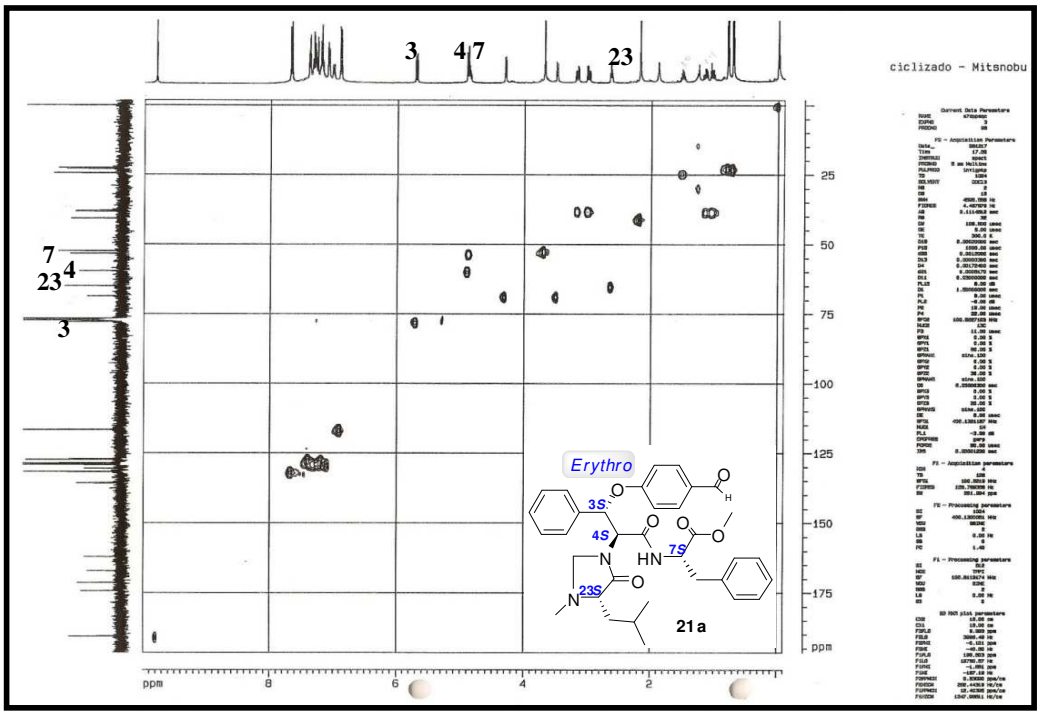
S89. ^{1}H-^{1}H COSY 45 NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-4-methylpentanoate (20a) in $CDCl_3$



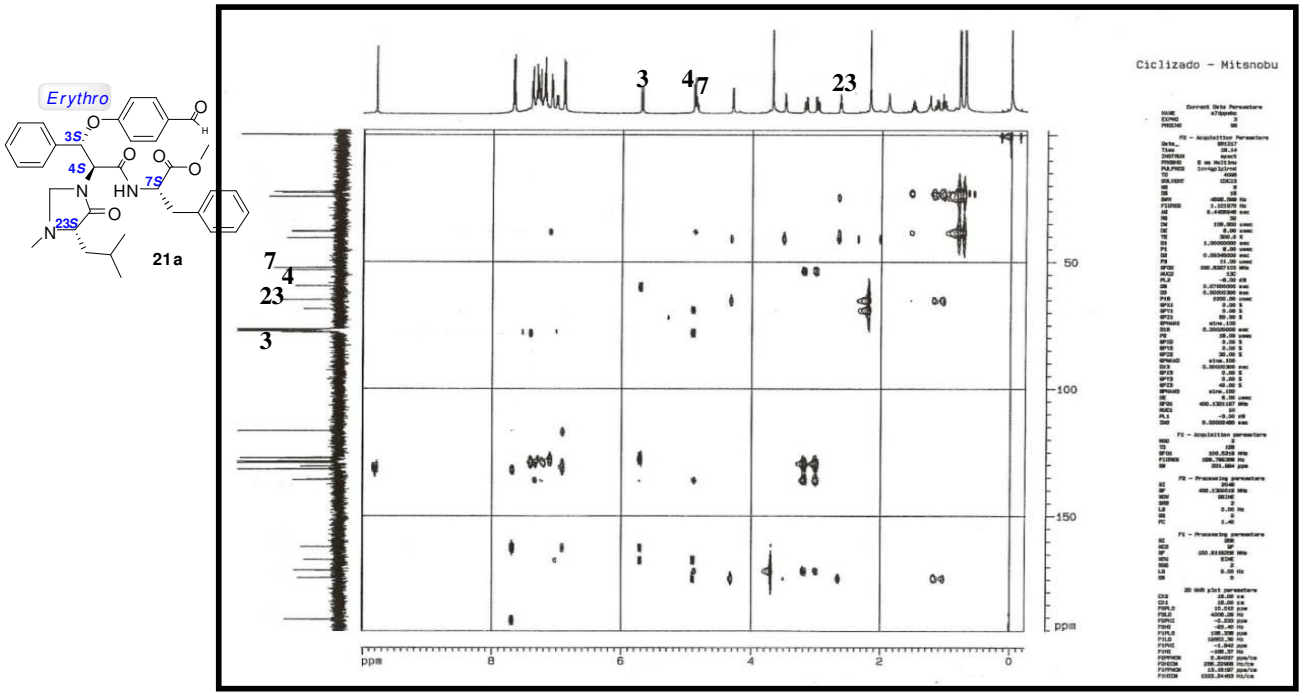
S90. ^{1}H NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (21a) in $CDCl_3$



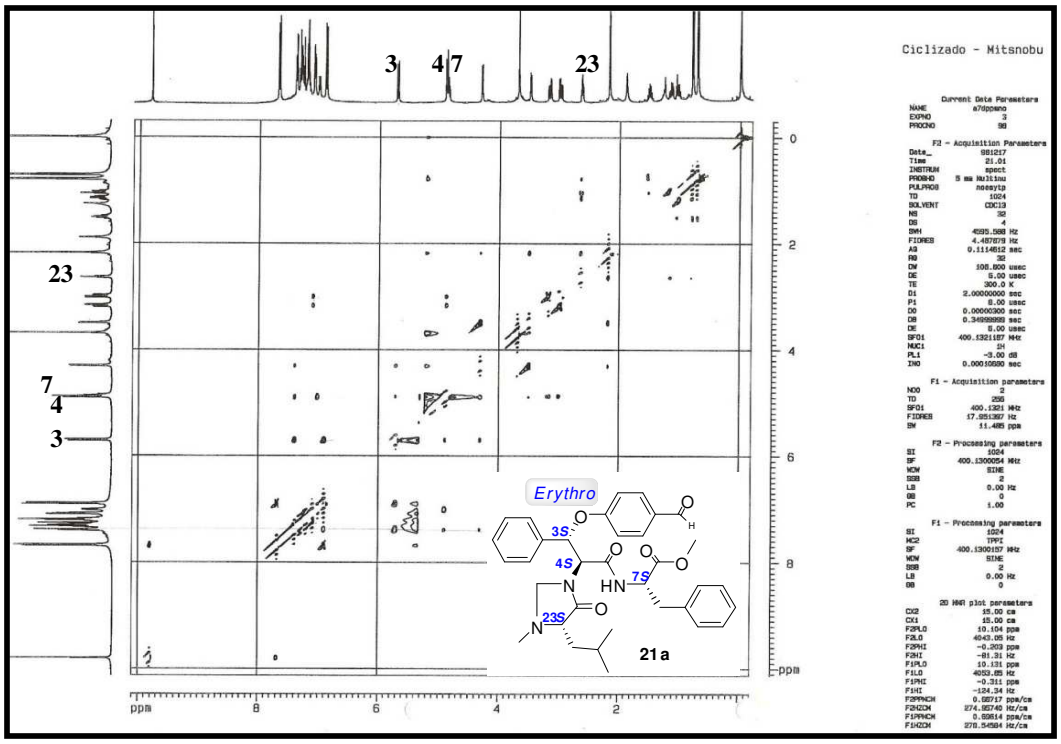
S91. ^{13}C NMR spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (21a) in $CDCl_3$



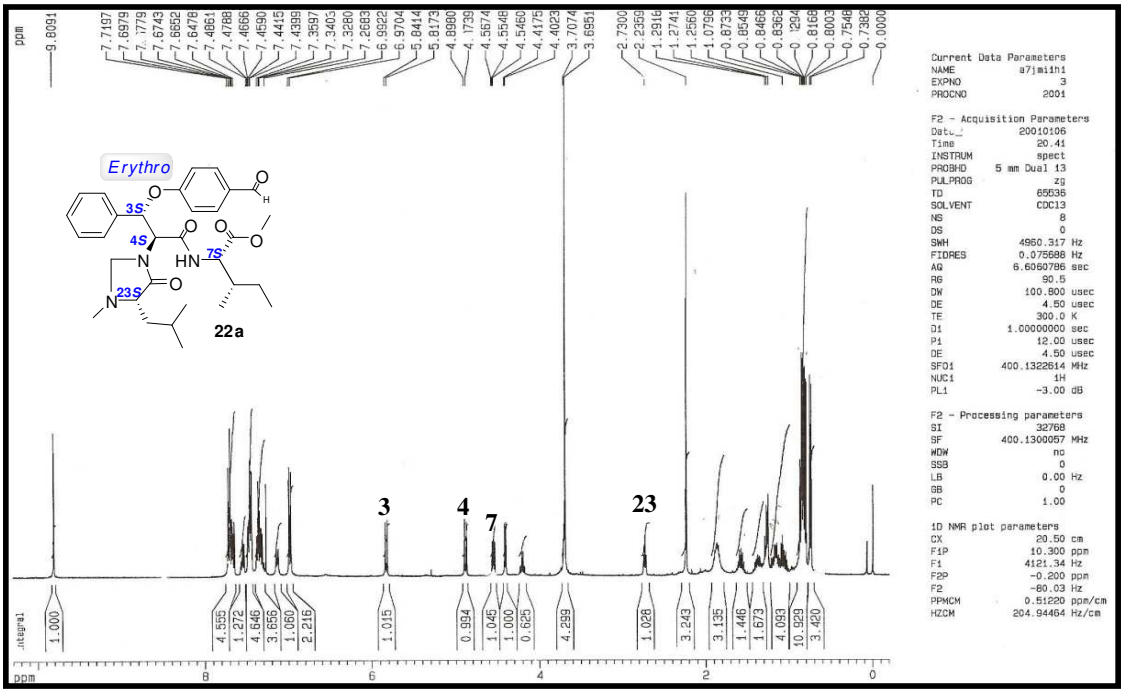
S92. HMQC spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (21a) in $CDCl_3$



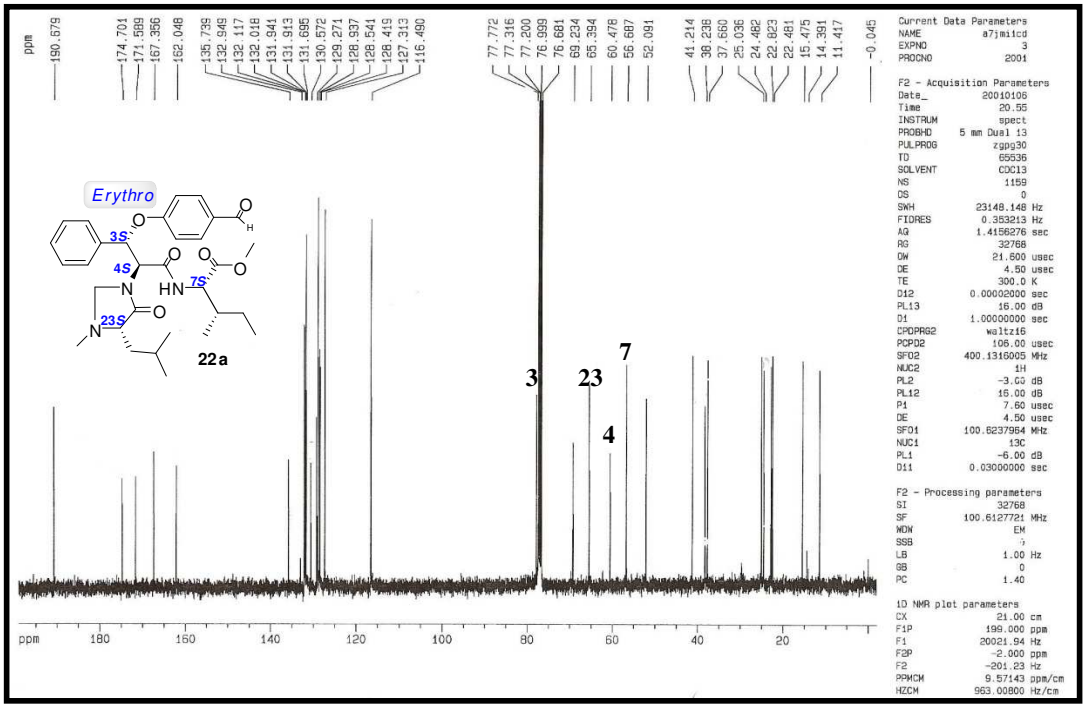
S93. HMBC spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (21a) in $CDCl_3$



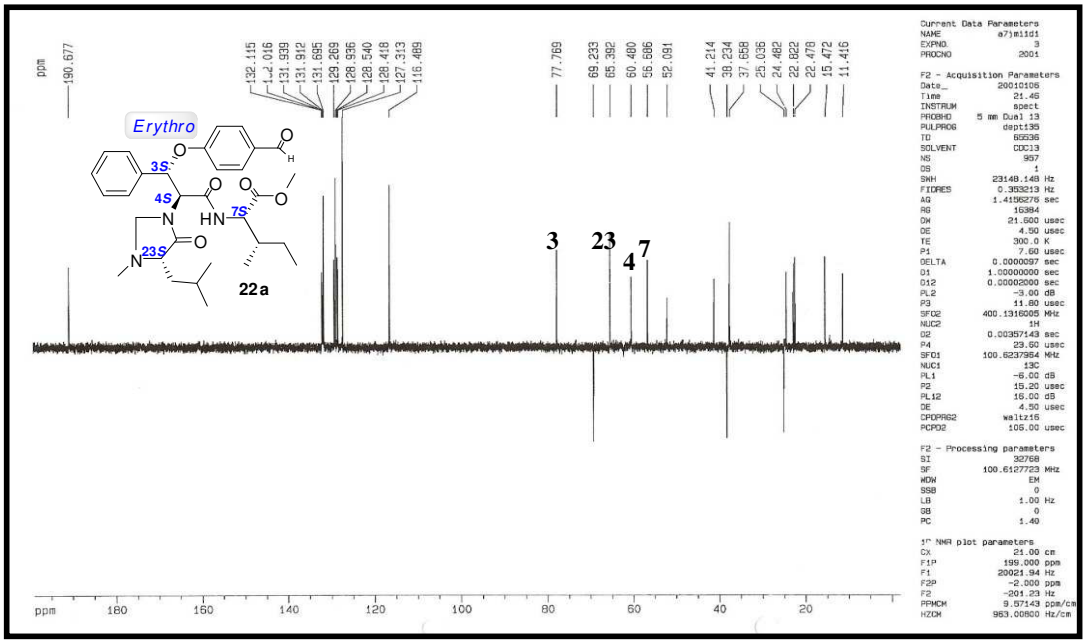
S94. NOESY spectrum of (S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-phenylpropanoate (21a) in $CDCl_3$



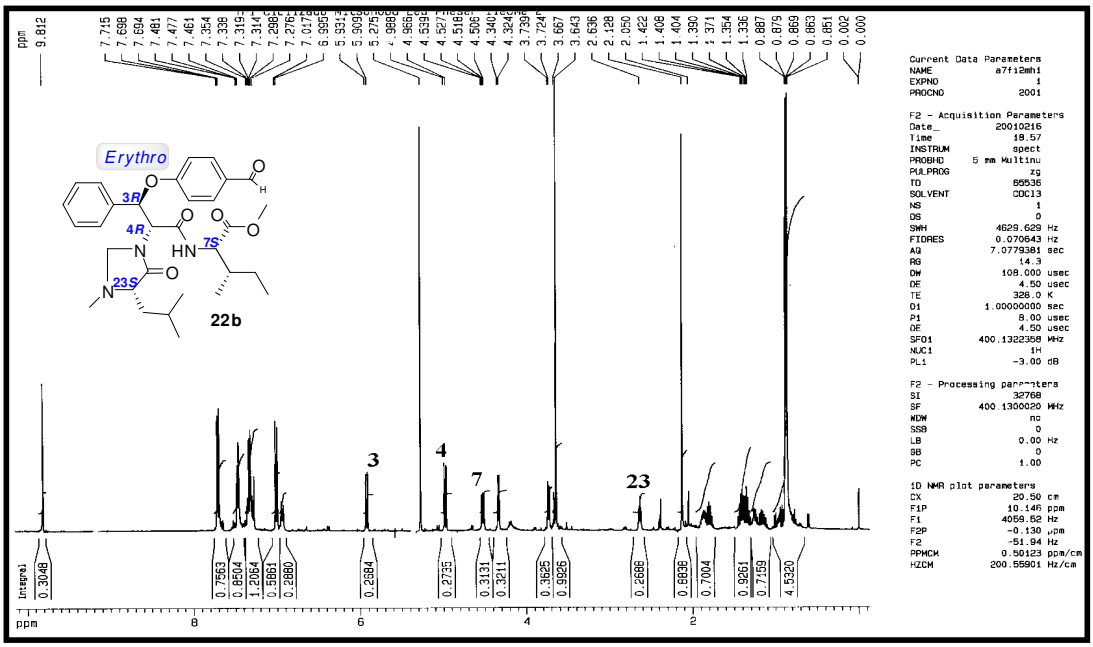
S95. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22a) in $CDCl_3$



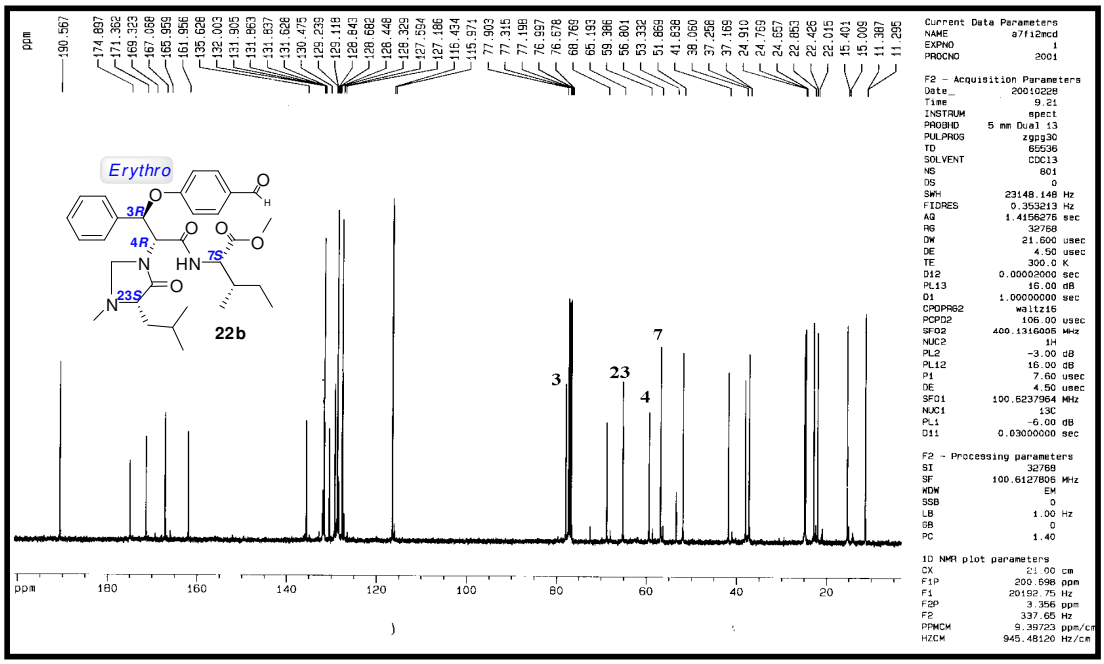
S96. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22a) in $CDCl_3$



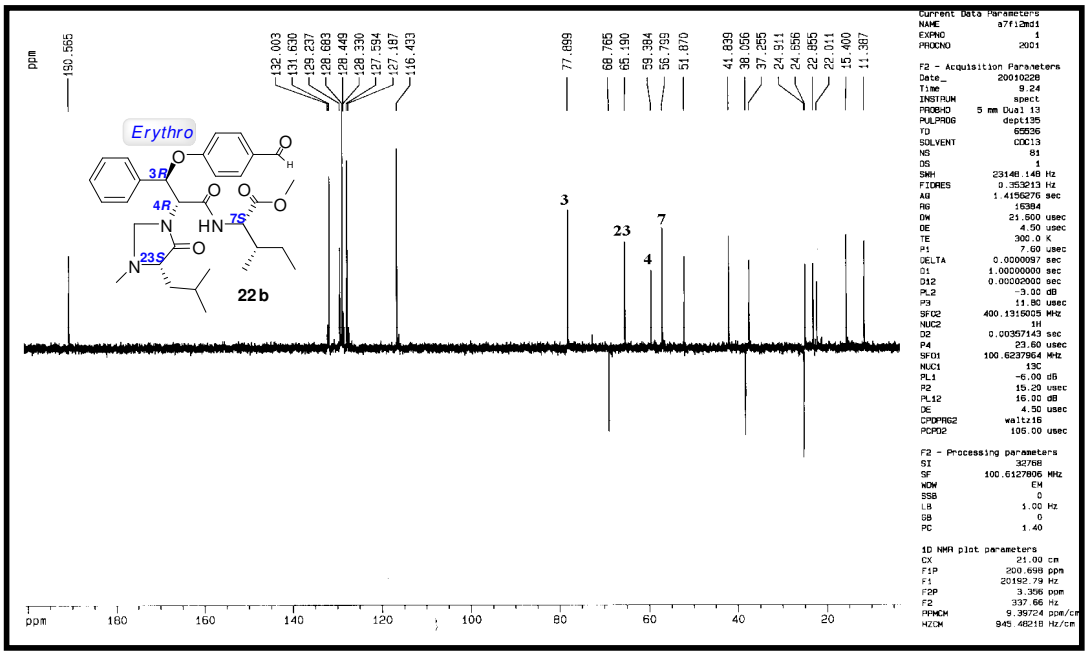
S97. DEPT 135 spectrum of (2S,3S)-methyl 2-((2S,3S)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22a) in $CDCl_3$



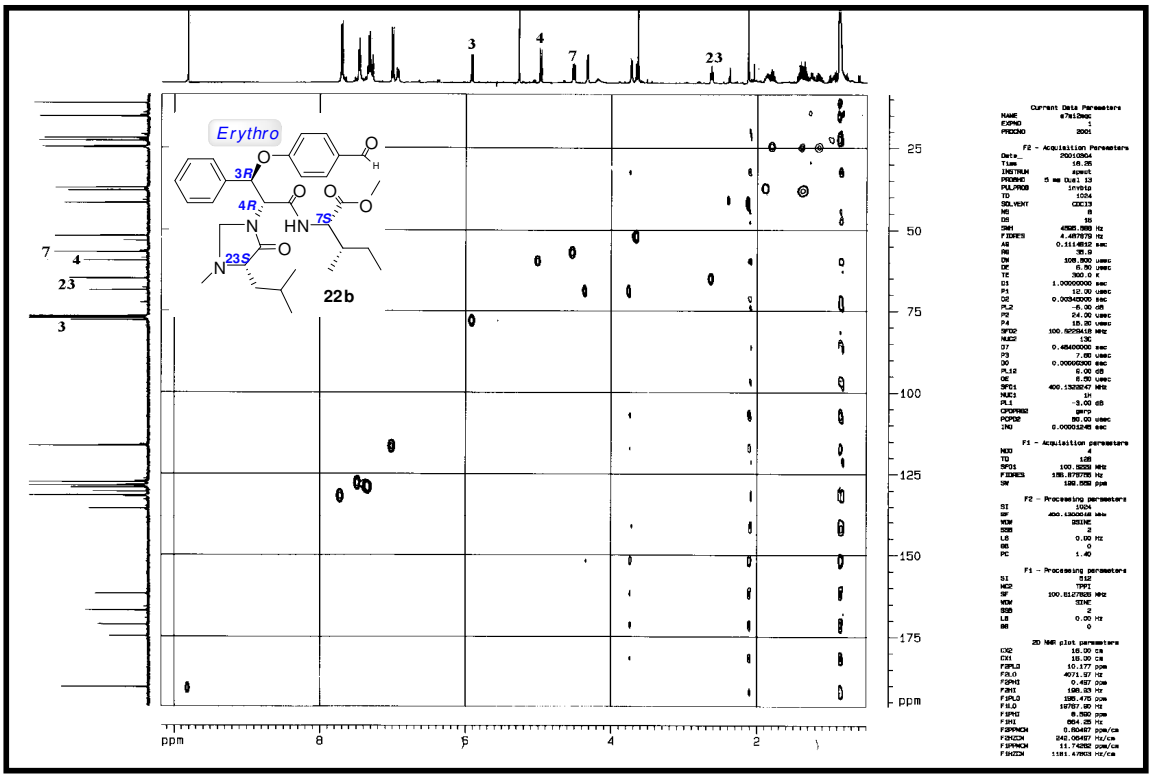
S98. ^{1}H NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22b) in $CDCl_3$



S99. ^{13}C NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22b) in $CDCl_3$



S100. DEPT 135 NMR spectrum of (2S,3S)-methyl 2-((2R,3R)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22b) in $CDCl_3$

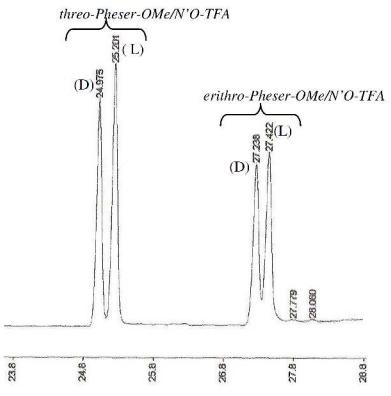


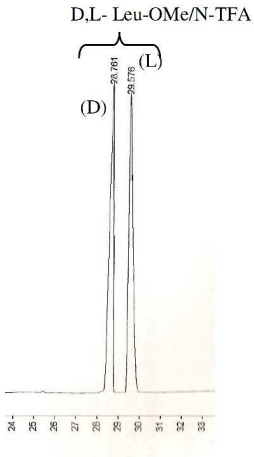
S101. HMQC spectrum of (2S,3S)-methyl 2-((2R,3R)-3-(4-formylphenoxy)-2-((S)-4-isobutyl-3-methyl-5-oxoimidazolidin-1-yl)-3-phenylpropanamido)-3-methylpentanoate (22b) in $CDCl_3$

Data of the GC Analysis

Table 1. Conditions to Amino acid Stereochemistry Determination by Enantioselective Gas Chromatography analysis:

Amino acid (*COOMe/N-TFA*)	Conditions	Separation Factor (α) = t_2/t_1	Order of Elution
N,N-(dimethyl)-D,L-Leucine	Column: 6-Me-2,3-Pe-γ-CD, 60%/OV1701, Temperature: 50°C Pressure: 50 kPa H_2	1.06	D,L
D,L-Leucine	Column: 2,6-Pe-3-Bu-γ-CD, 50%/OV1701, Temperature: 50-155°C at 2°C/min Pressure: 50 kPa H_2	1.02	D,L
D,L-Phenylalanine	Column: 2,6-Me-3-Pe-β-CD, 20%/OV1701, Temperature: 105°C Pressure: 50 kPa H_2	1.05	L,D
D,L-*Iso*-leucine	Column: 2,6-Pe-3-Bu-γ-CD, 50%/OV1701, Temperature: 80-160°C at 2°C/min Pressure: 50 kPa H_2	1.11	D,L
D,L-*threo*- Phenylserine	Column: 2,6-Pe-3-Bu-γ-CD, 50%/OV1701, Temperature: 80-160°C at 2°C/min Pressure: 50 kPa H_2	1.00	D,L
D,L-*erithro*- Phenylserine	Column: 2,6-Pe-3-Bu-γ-CD, 50%/OV1701, Temperature: 80-160°C at 2°C/min Pressure: 50 kPa H_2	1.00	D,L





Data of Antimicrobial activities

Table 2. Quantity Minimum Inhibitory for Anti-bacterial Activity of Compounds.

Peptides	Microorganism				
	S. aureus	*S. epidermidis*	*E. coli*	*K. pneumoniae*	*S. setubal*
Z-L-Leu-D-*threo*- Pheser-L-Leu-OMe **(5b)**	-	1.5 µg	-	-	-
Z-L-Leu-D-*threo*-Pheser-L-Ile-OMe **(7b)**	-	6.2 µg	-	-	-
H_2N-L-Leu-L-*threo*-Pheser-L-Leu-OMe **(8a)**	-	25.0 µg	12.5 µg	25.0 µg	-
H_2N-L-Leu-L-*threo*-Pheser- L-Phe-OMe **(9a)**	-	3.1 µg	12.5 µg	12.5 µg	NT
H_2N-L-Leu-D-*threo*-Pheser-L-Phe-OMe **(9b)**	-	-	1.5 µg	-	-
Me_2N-L-Leu-D-*threo*-Pheser-L-Phe-OMe **(12b)**	30.0 µg	-	>50.0µg	>50.0µg	-
MeN-L-Leu-*L-threo*-Pheser-L-Phe-OMe (**15a**)	25.0 µg	50.0 µg	-	50.0 µg	25.0 µg
MeN-L-Leu-D-*threo*-Pheser-L-Phe-OMe (**15b**)	-	6.2 µg	3.1 µg	6.2 µg	12.5 µg
Me_2N-L-Leu-L-*erythro*-Pheser(OPheCHO)-L-Phe-OMe **(18a)**	-	12.5 µg	-	-	25.0 µg
Me_2N-L-Leu-L-*erythro*-Pheser(OPheCHO)-L-Ile-OMe **(19a)**	25.0 µg	12.5 µg	-	25.0 µg	50.0 µg
Me_2N-L-Leu-D-*erythro*-Pheser(OPheCHO)-L-Ile-OMe **(19b)**	6,2 µg	6,2 µg	1,5 µg	1,5 µg	12,5 µg