Supporting Information

Structure diversification of vancomycin through peptide-catalyzed, site-selective lipidation: A catalysis-based approach to combat glycopeptide-resistant pathogens

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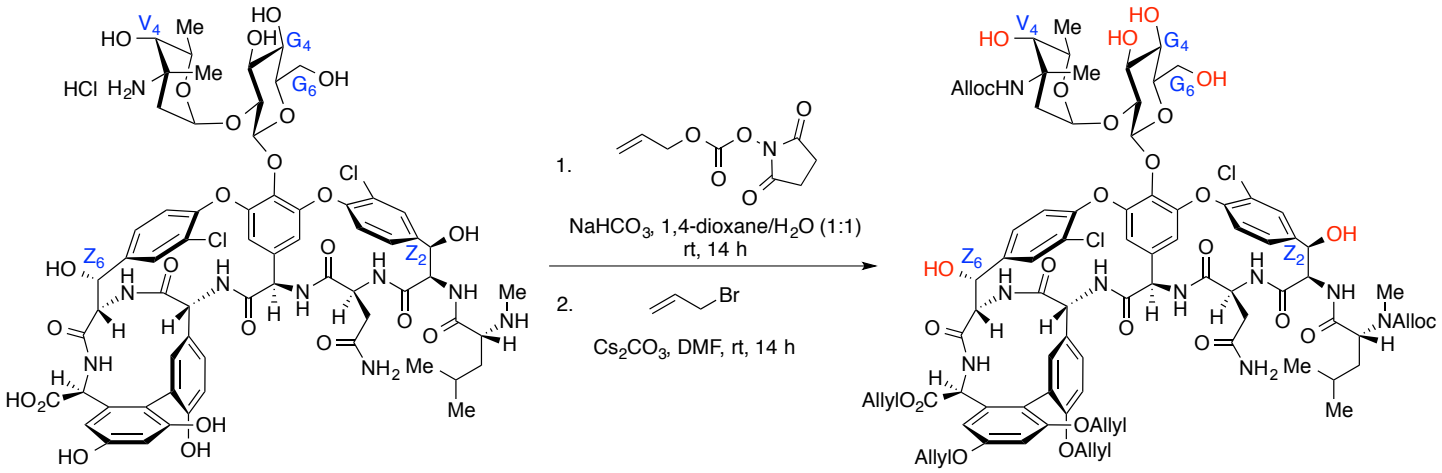
[b] current address

Supporting Information Contents:

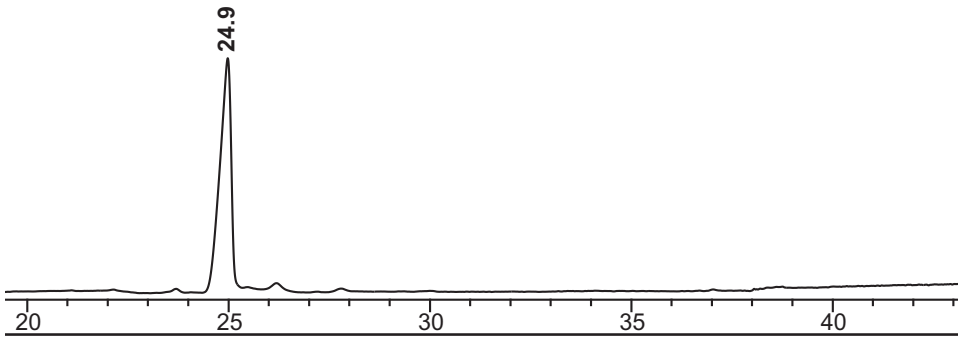
I. Synthesis of partially protected vancomycin derivative 3



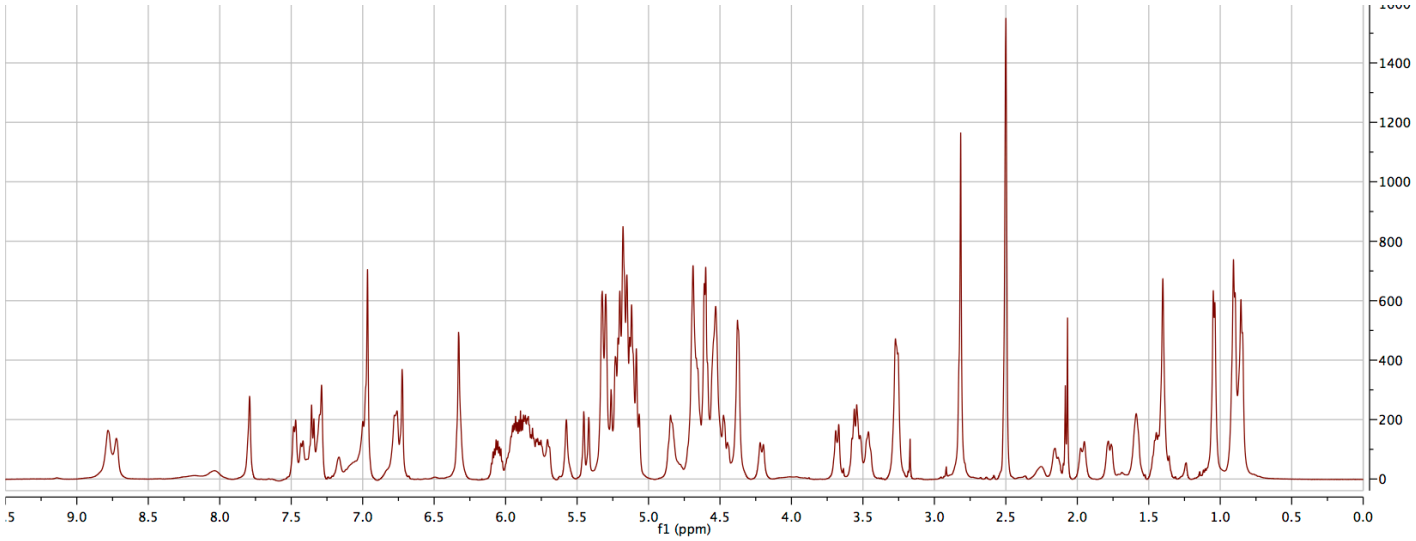
Vancomycin•HCl

Partially protected vancomycin (**3**)

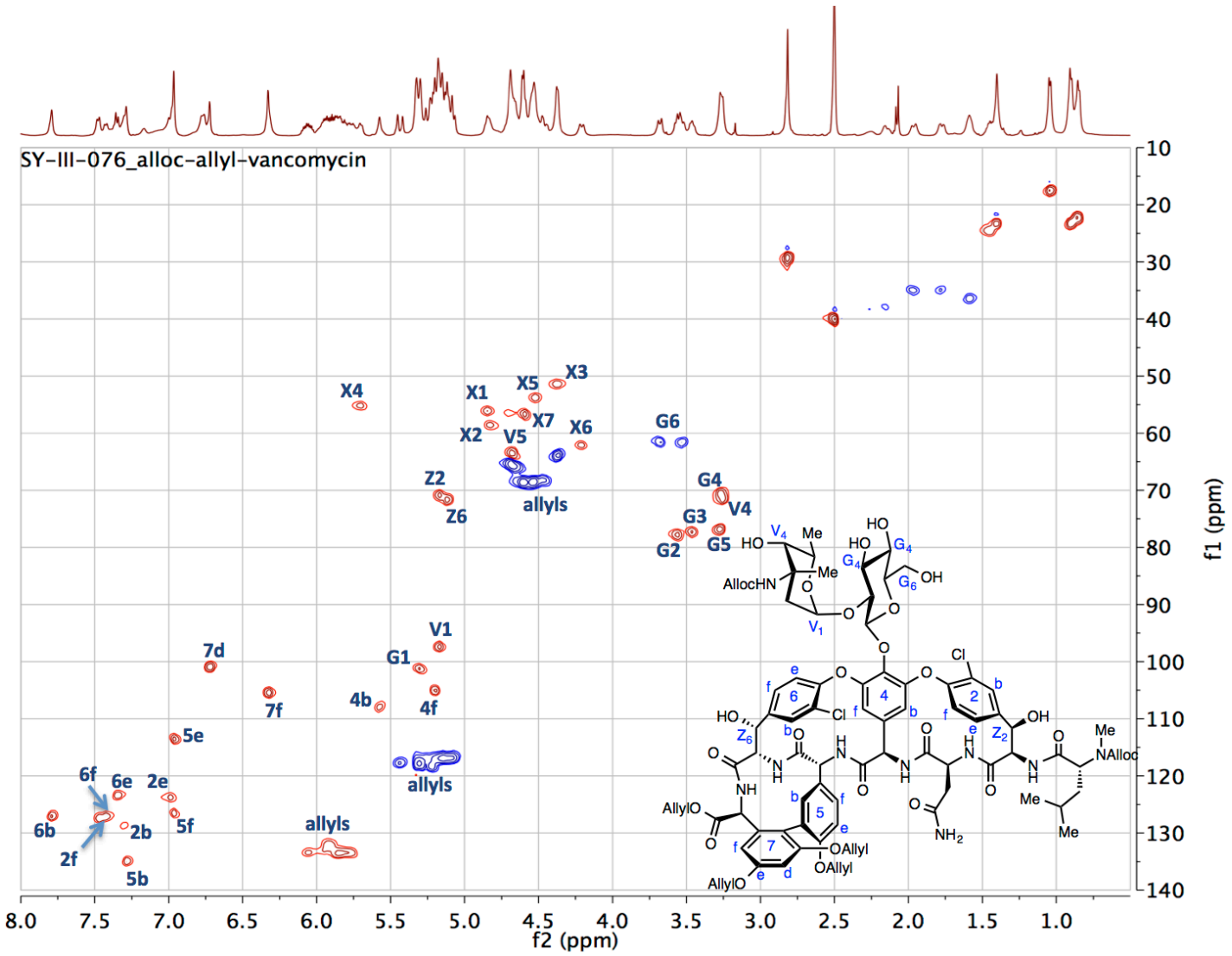
Partially protected vancomycin **3** was synthesized using reported literature procedures.[1,2] Compound **3** was purified using Biotage (RP-MPLC, Method 6). RP-HPLC retention time (Method 3): 24.9 min; LC-MS (ESI$^+$) for $C_{86}H_{100}Cl_2N_9O_{28}$ $[M+H]^+$: Calc'd = 1776.605; found = 1776.615.



HPLC Trace of alloc/allyl protected vancomycin (3): RP-HPLC Method 3, λ = 220 nm, t_R = 24.8 min.

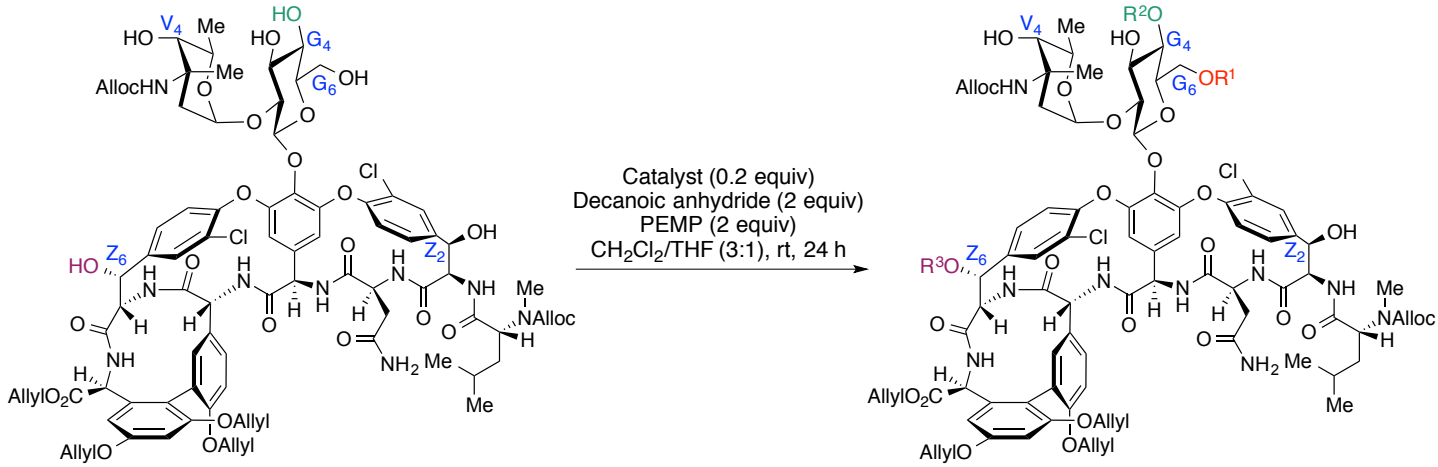


^{1}H NMR spectrum of alloc/allyl-protected vancomycin in DMSO-d_6



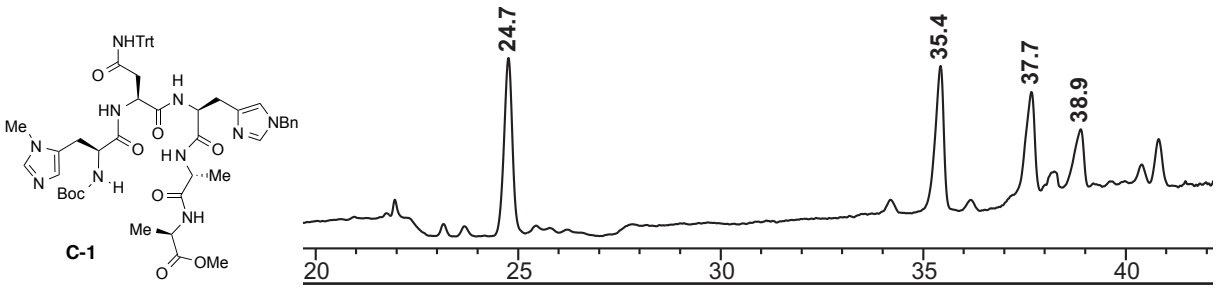
HSQC-NMR spectrum of alloc/allyl-protected vancomycin in DMSO-d_6

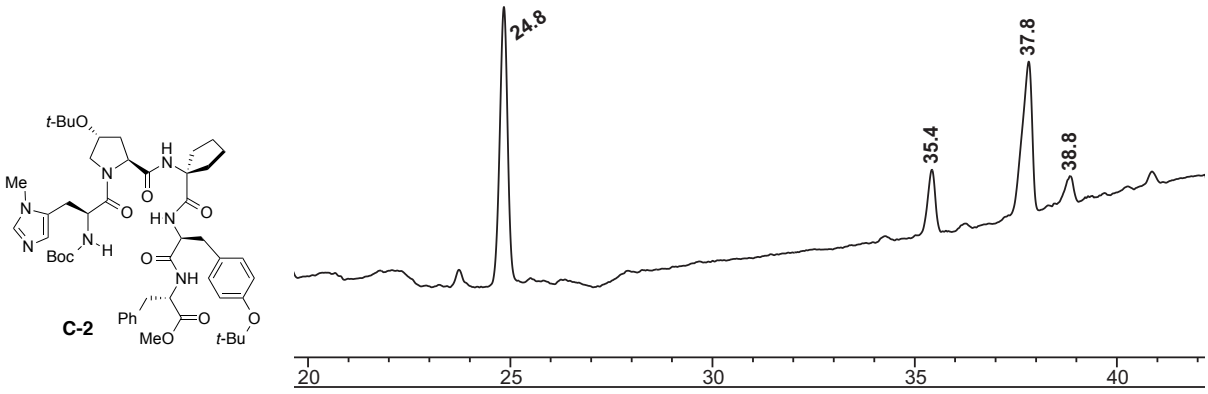
II. Screening of peptide catalysts for the decanoylation of 3

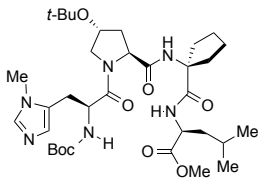


3

4a: $R^1 = CO(CH_2)_8CH_3$, $R^2 = H$, $R^3 = H$
4b: $R^1 = H$, $R^2 = CO(CH_2)_8CH_3$, $R^3 = H$
4c: $R^1 = H$, $R^2 = H$, $R^3 = CO(CH_2)_8CH_3$







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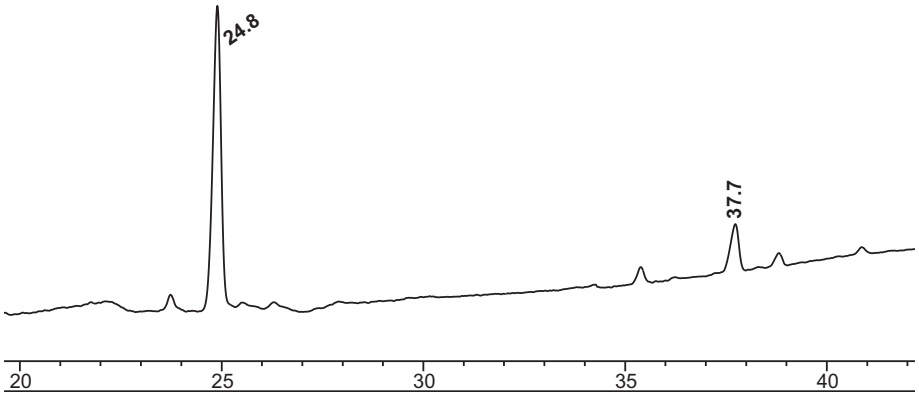
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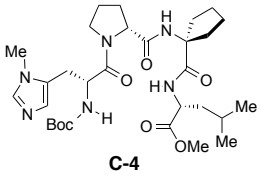

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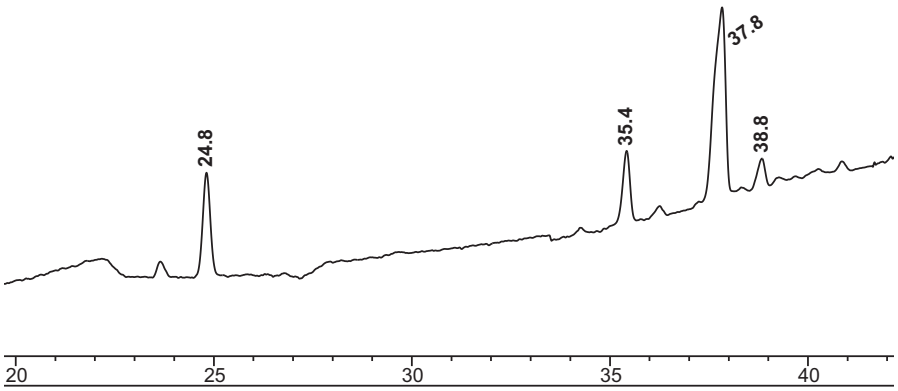
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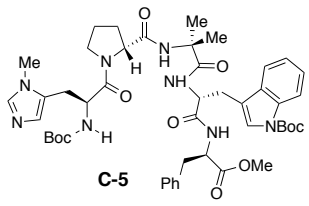

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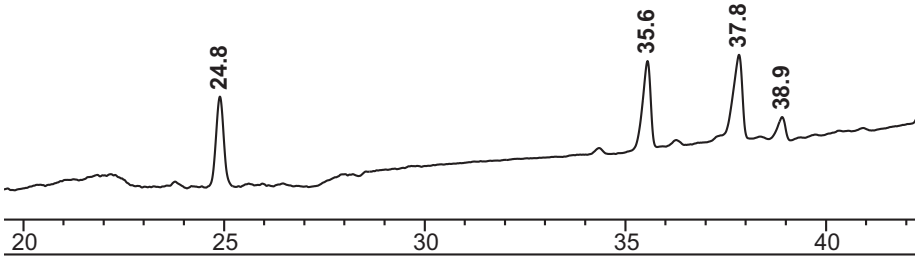
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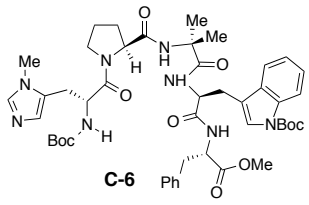

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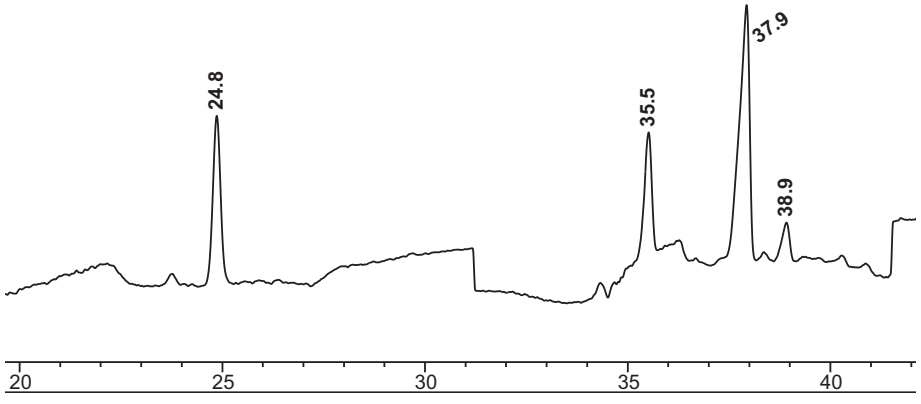
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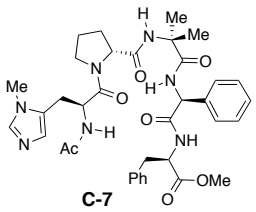

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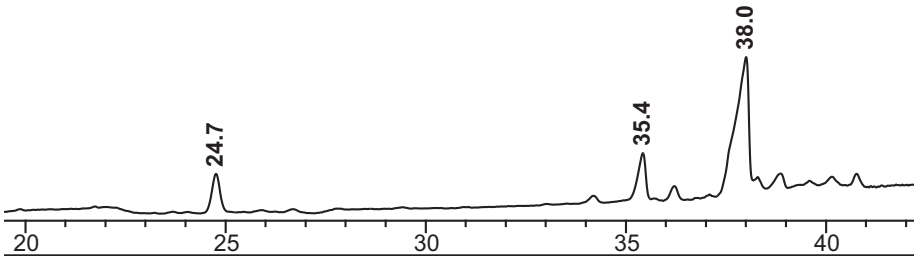
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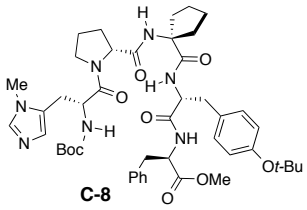

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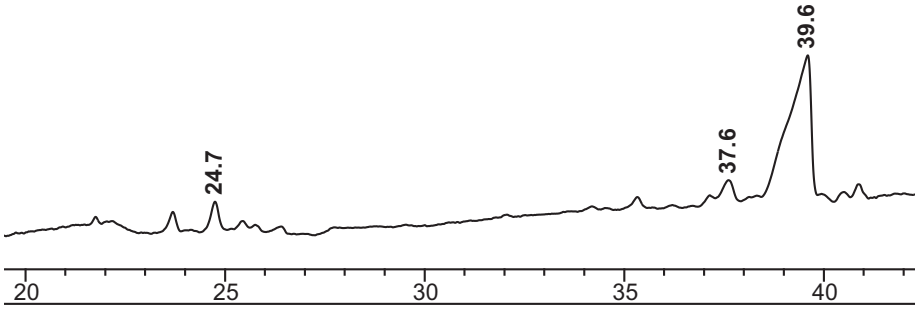
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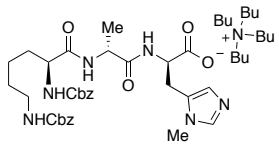

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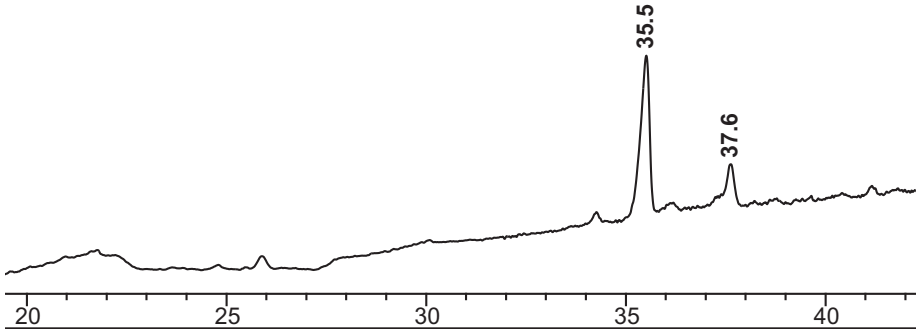
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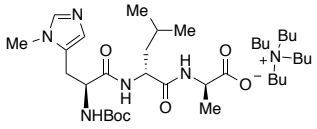

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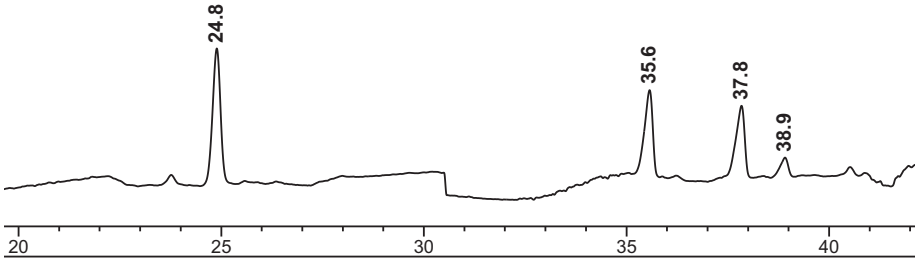
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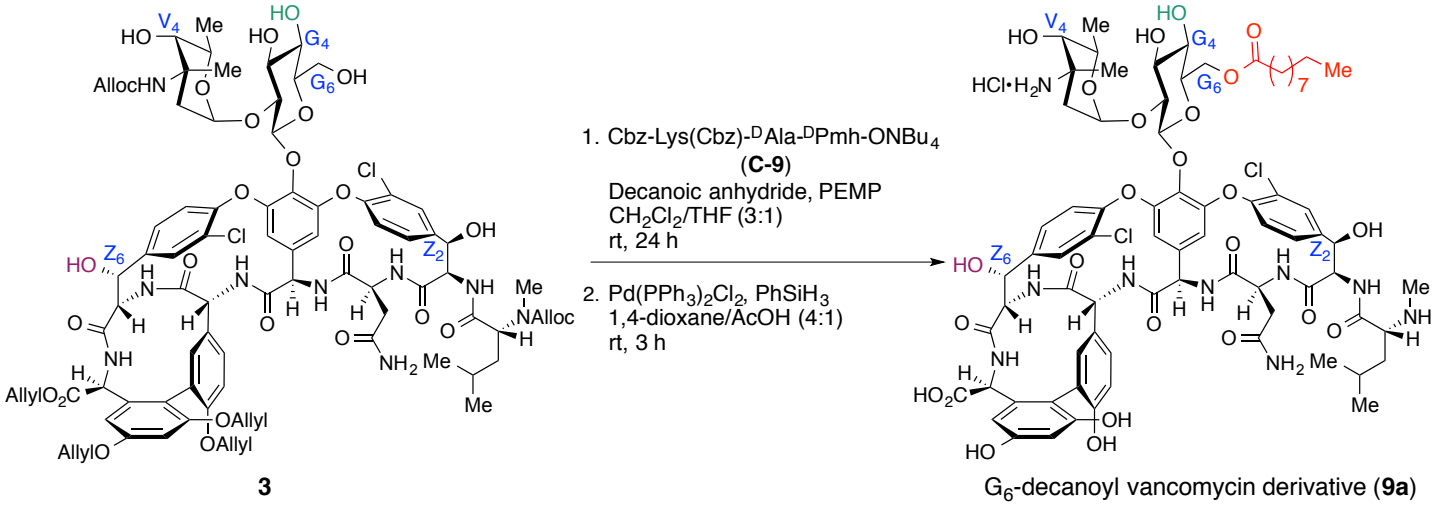
III. Synthesis of G_6-decanoyl vancomycin derivative 9a



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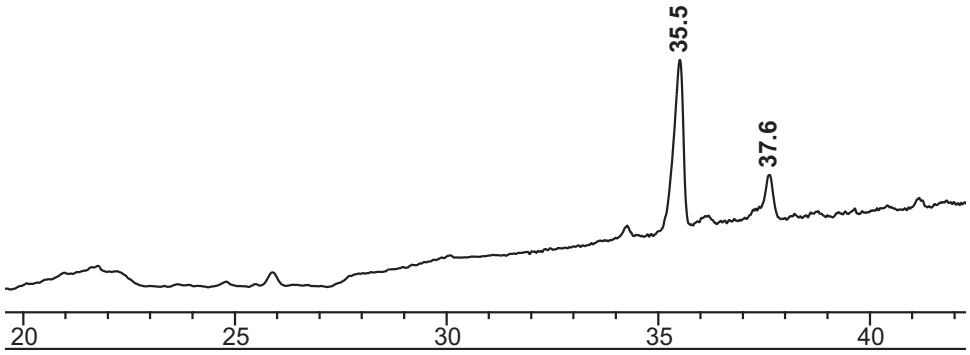
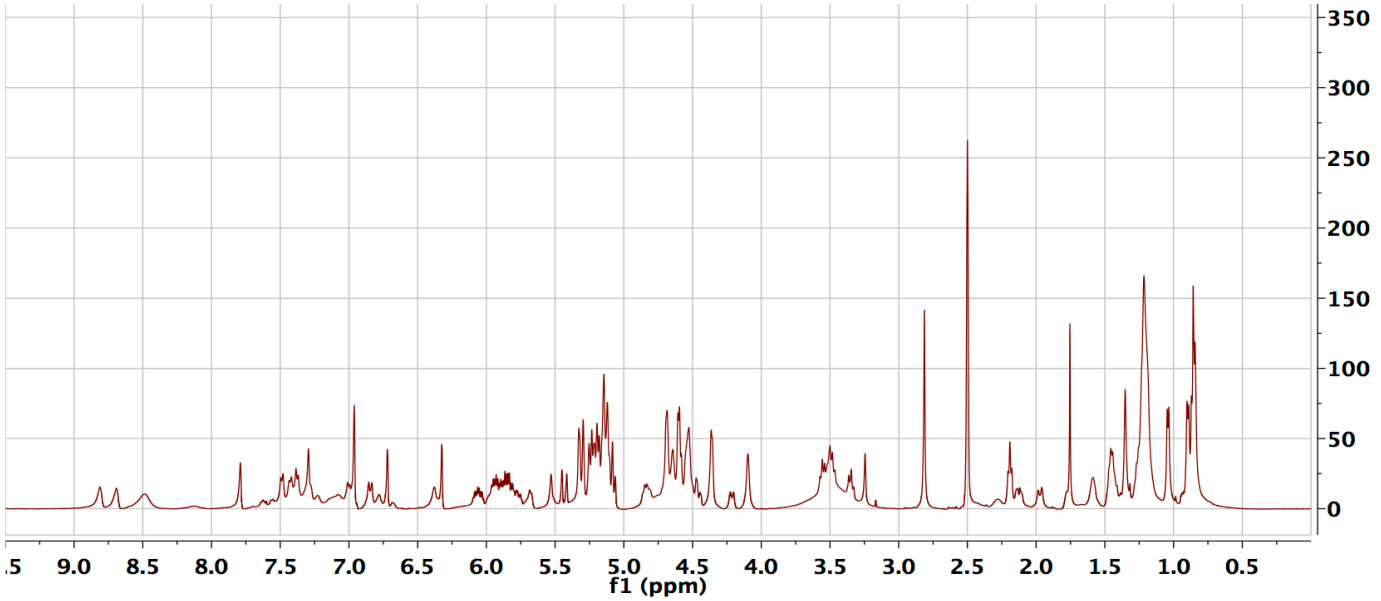
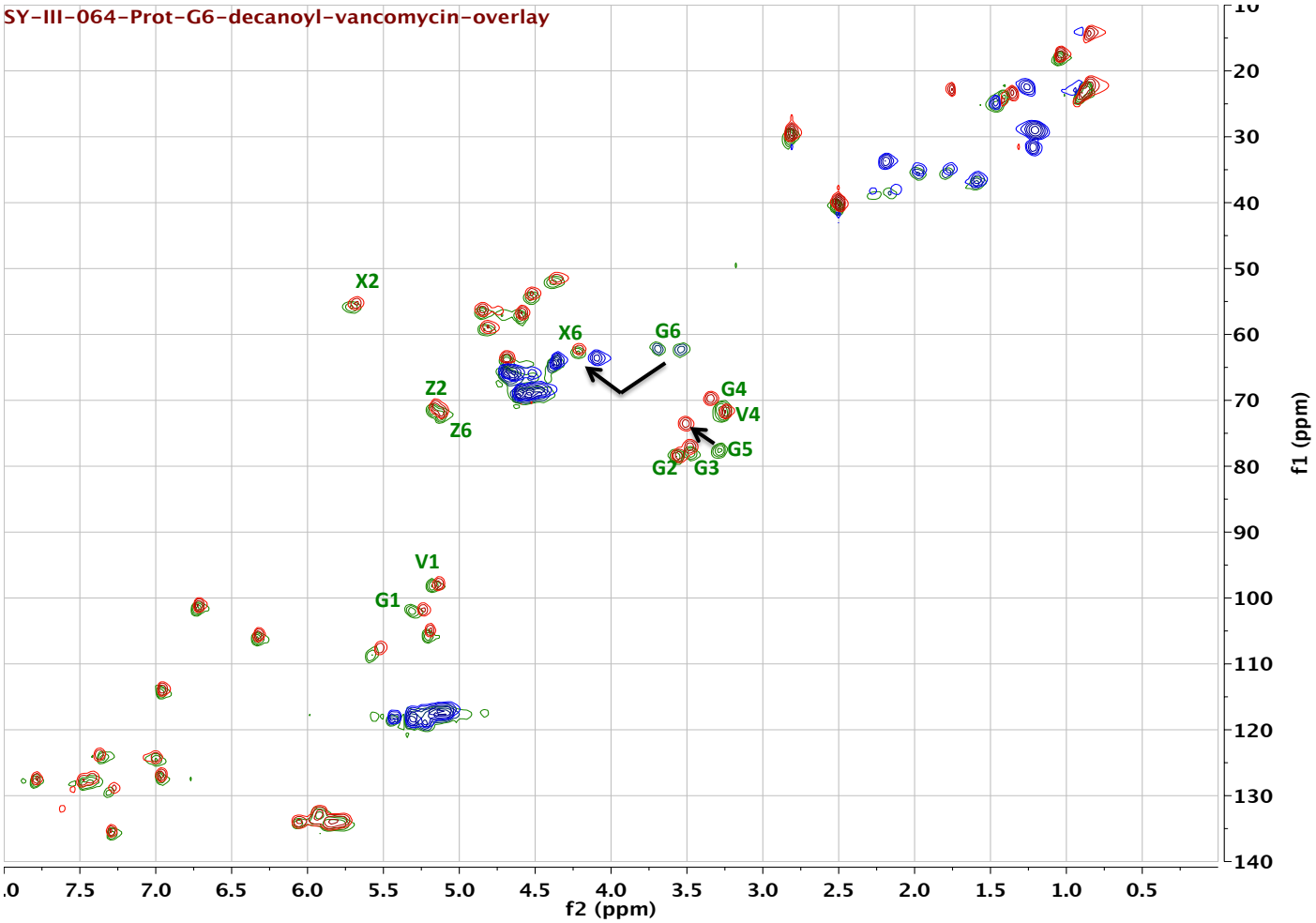
G_6-decanoyl vancomycin derivative (**9a**)



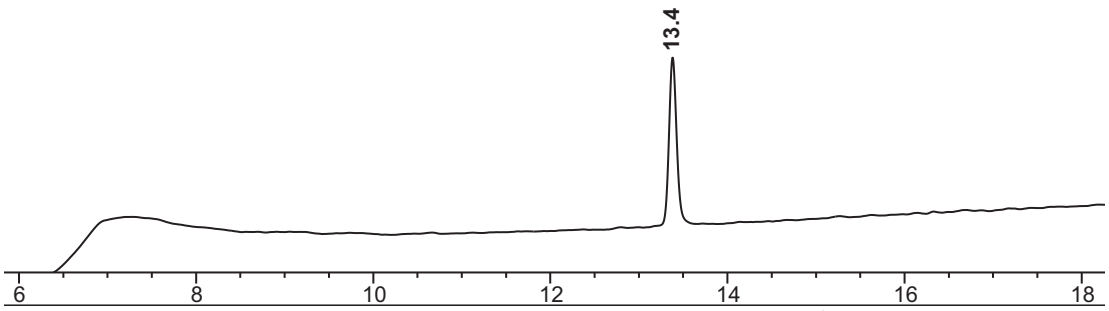
HPLC Trace of G_6-selective decanoylation reaction: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.5 min; t_R (protected G_4-decanoyl vancomycin, **4b**) = 37.6 min.



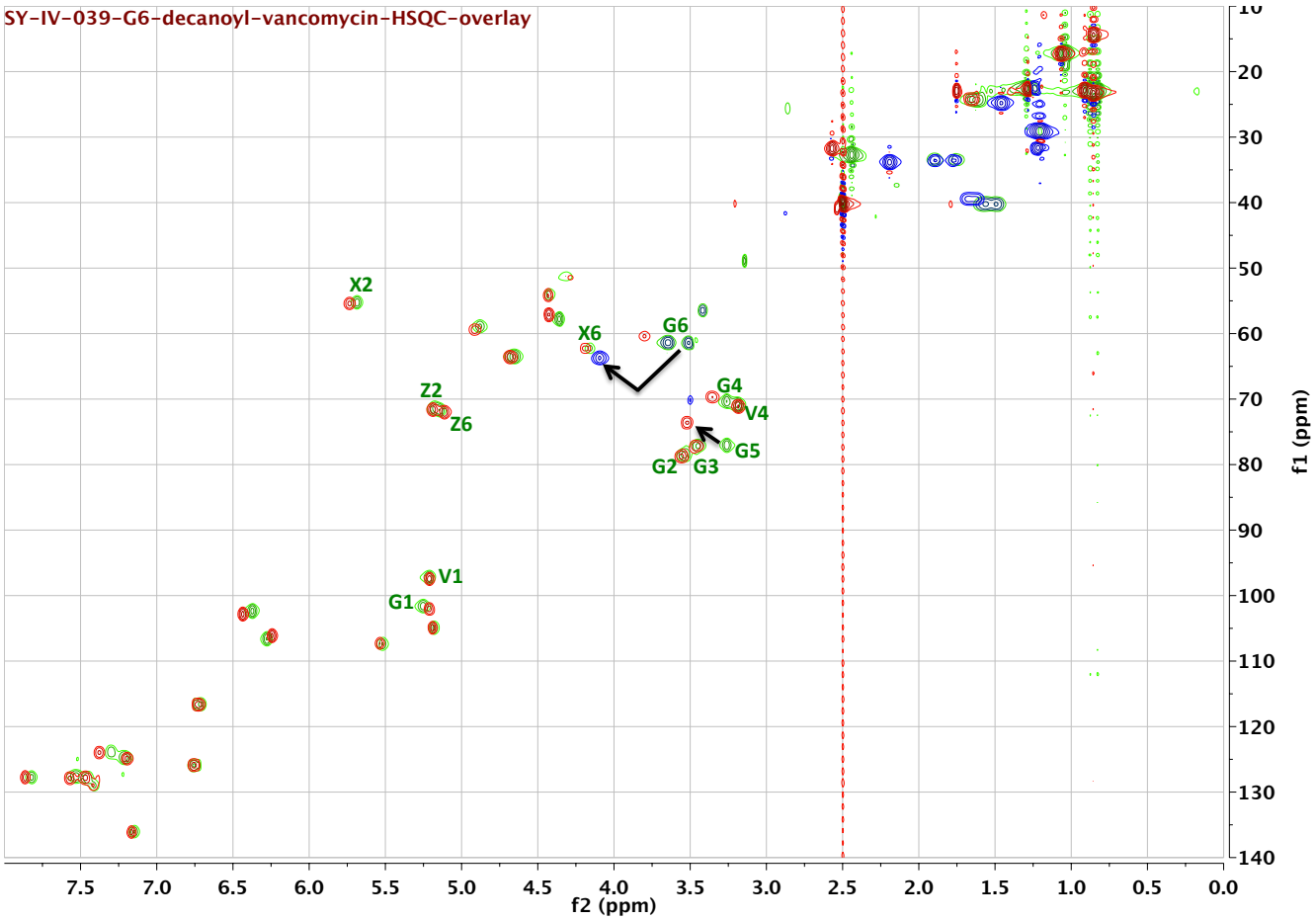
^{1}H NMR spectrum of protected G_6-decanoyl vancomycin in DMSO-d_6



HSQC-NMR spectrum of protected G_6-decanoyl vancomycin in DMSO-d_6. [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]

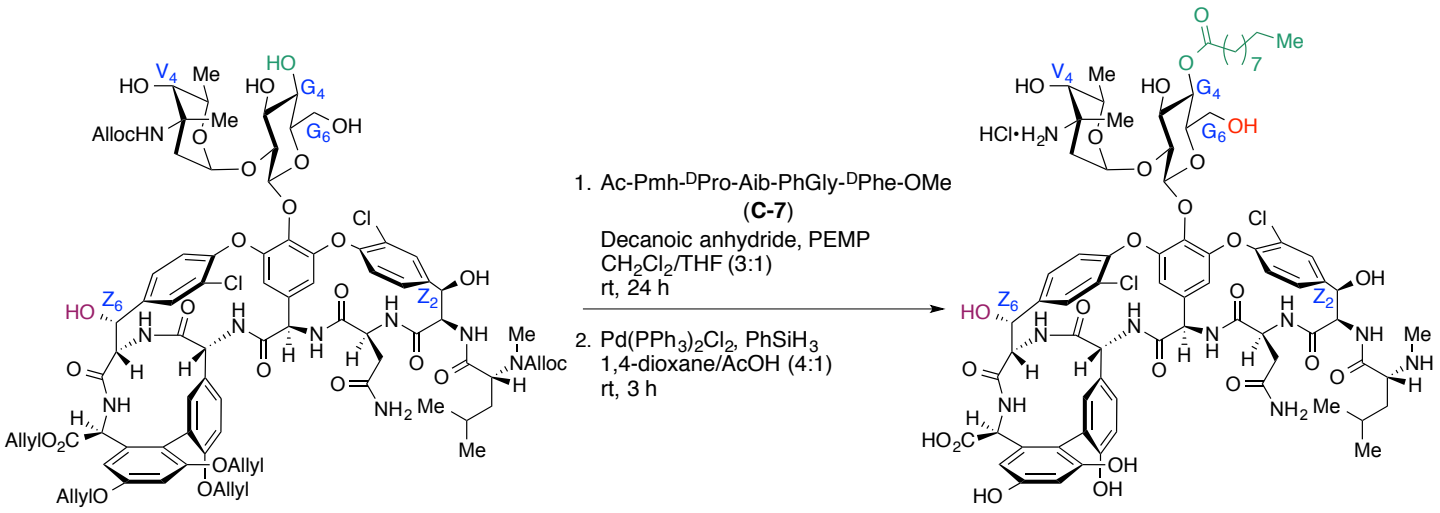


HPLC Trace of G_6-decanoyl-vancomycin (9a): RP-HPLC Method 3, λ = 220 nm, t_R = 13.4 min.

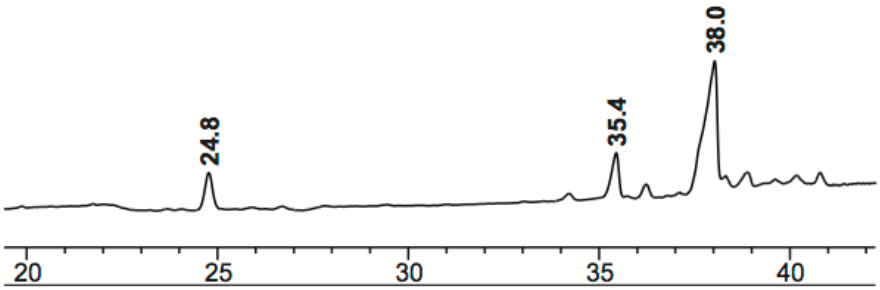


HSQC-NMR spectrum of G_6-decanoyl vancomycin (9a) in DMSO-d_6. [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]

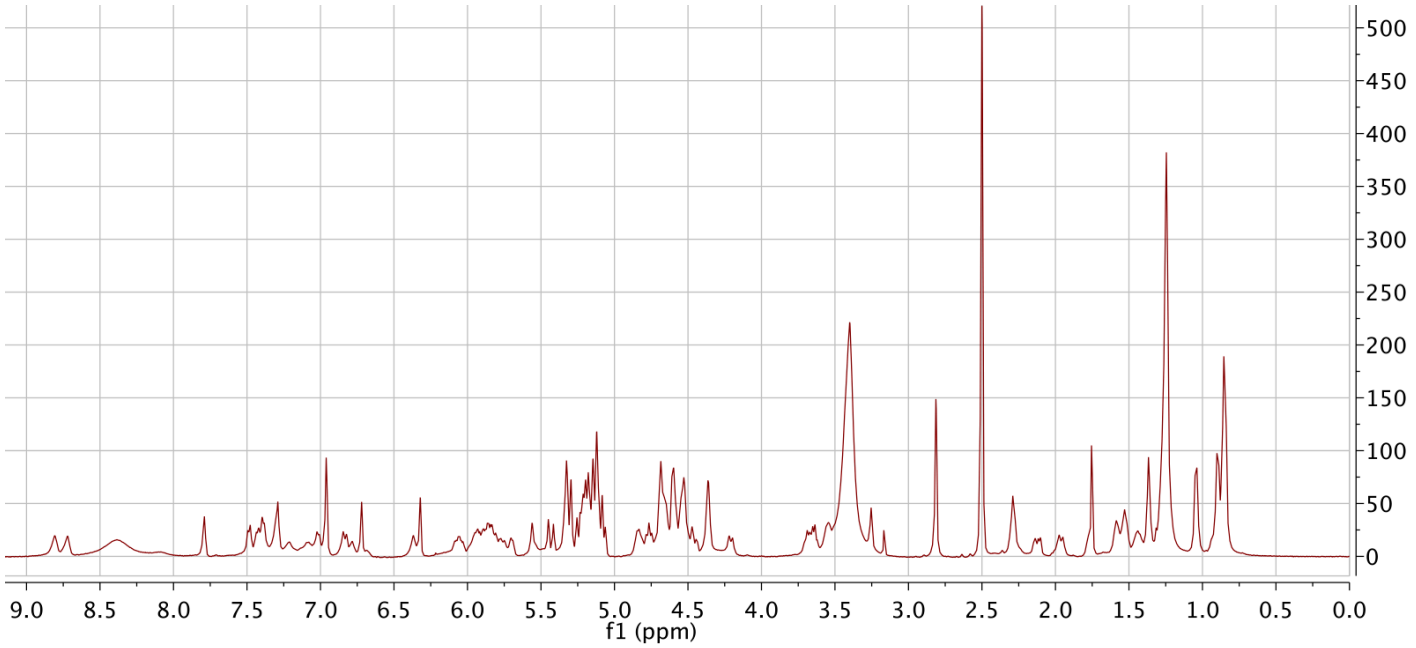
IV. Synthesis of G_4-decanoyl vancomycin derivative 9b



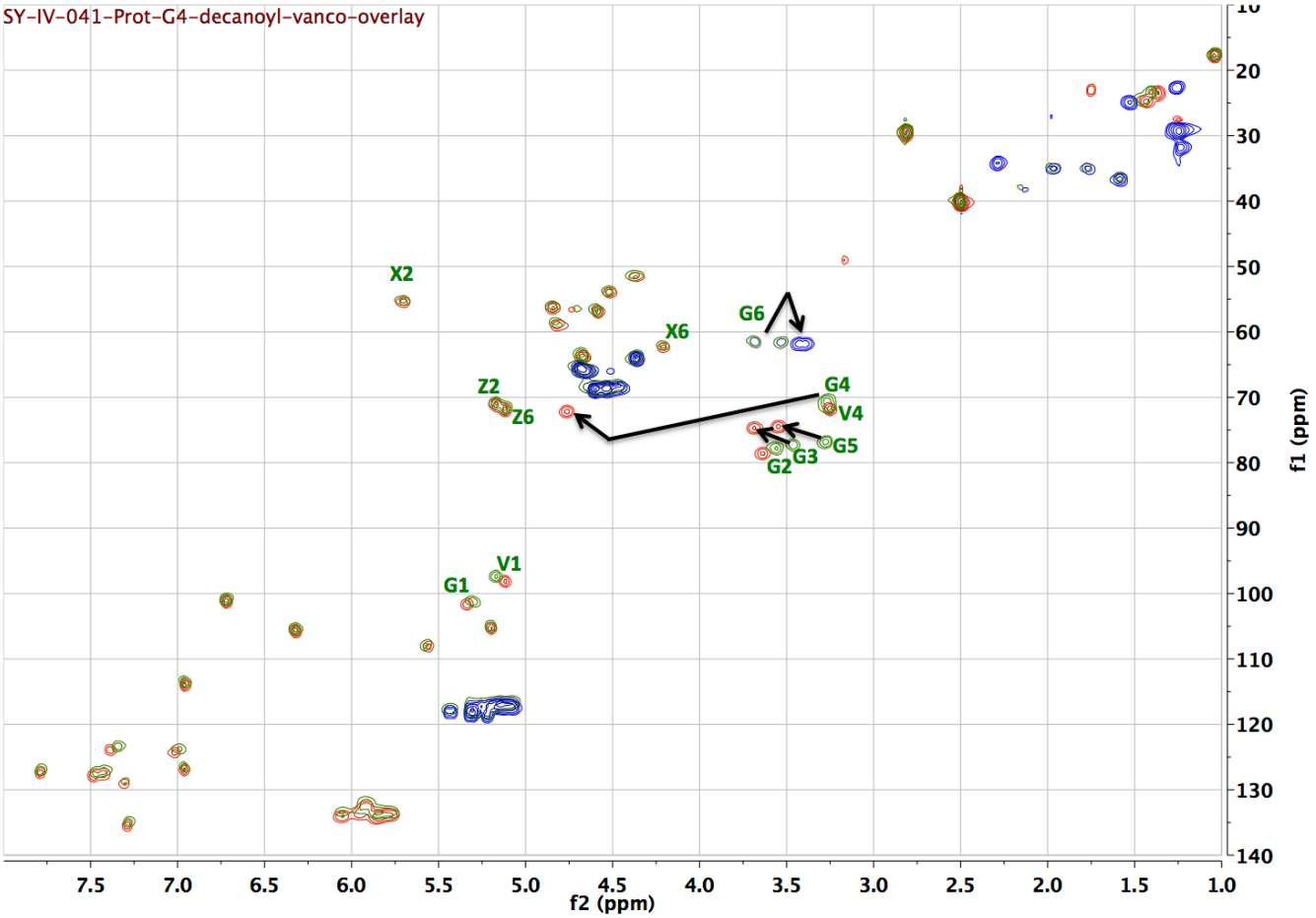
3 G_4-decanoyl vancomycin derivative (**9b**)



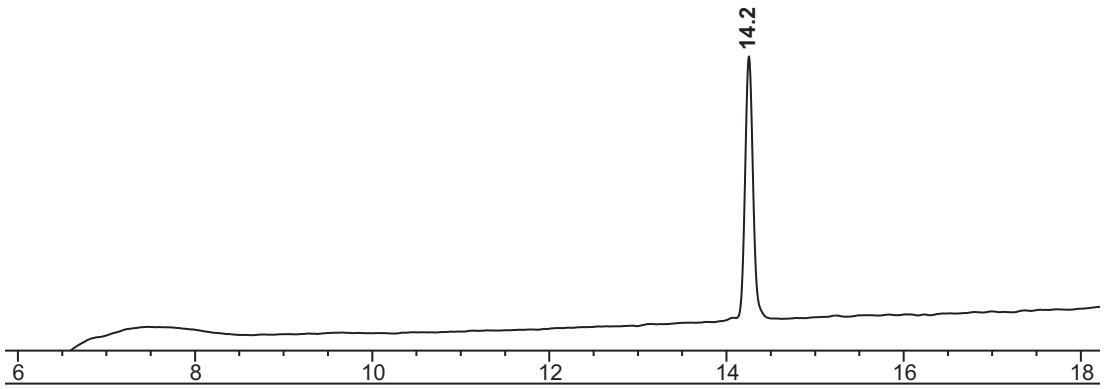
HPLC Trace of G_4-selective decanoylation reaction: RP-HPLC Method 3, λ = 220 nm, t_R (**3**) = 24.8 min; t_R (G_6-decanoyl vancomycin, **4a**) = 35.4 min; t_R (protected G_4-decanoyl vancomycin, **4b**) = 38.0 min.



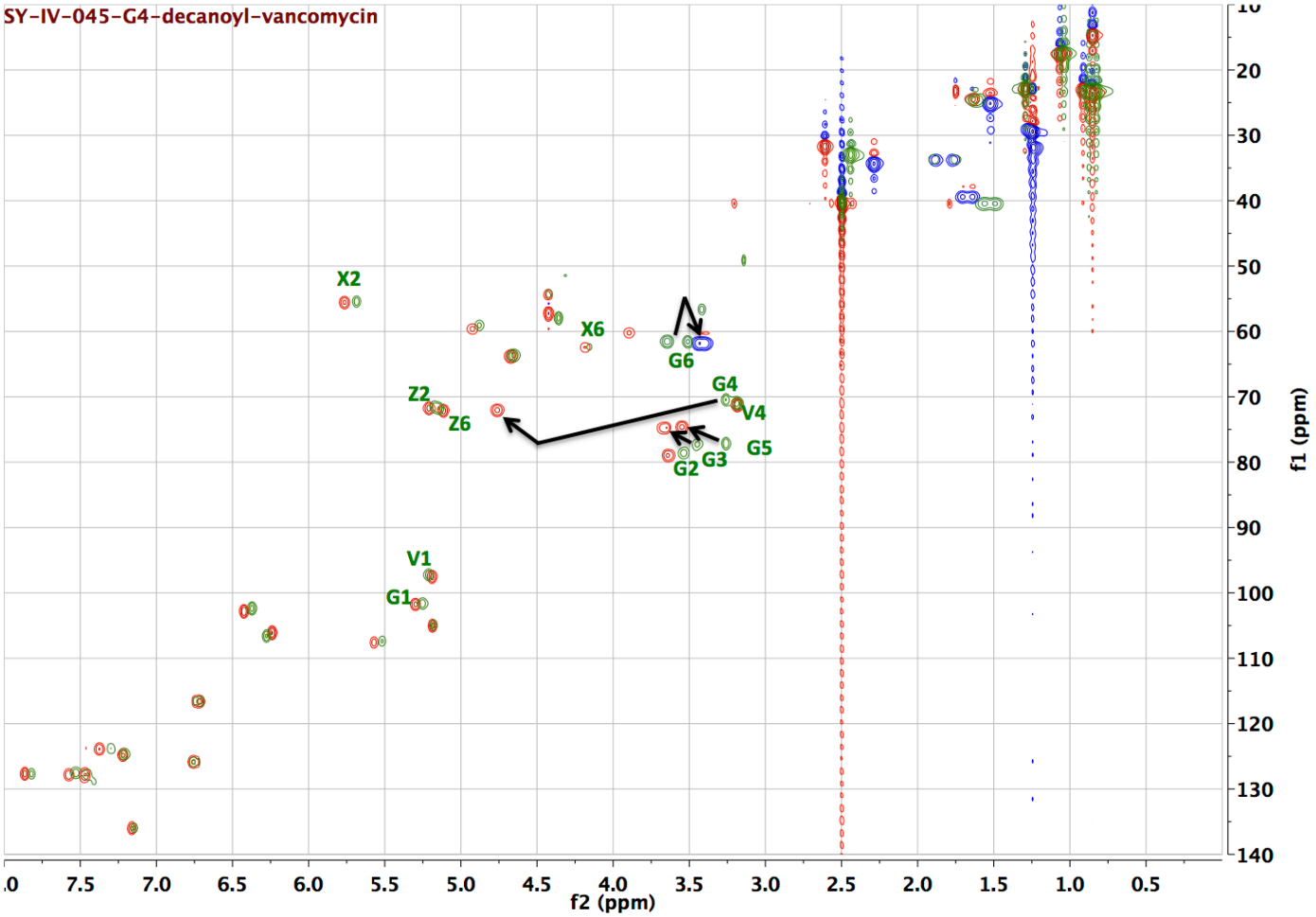
^{1}H NMR spectrum of protected G_4-decanoyl vancomycin in DMSO-d_6



HSQC-NMR spectrum of protected G_4-decanoyl vancomycin in DMSO-d_6. [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]

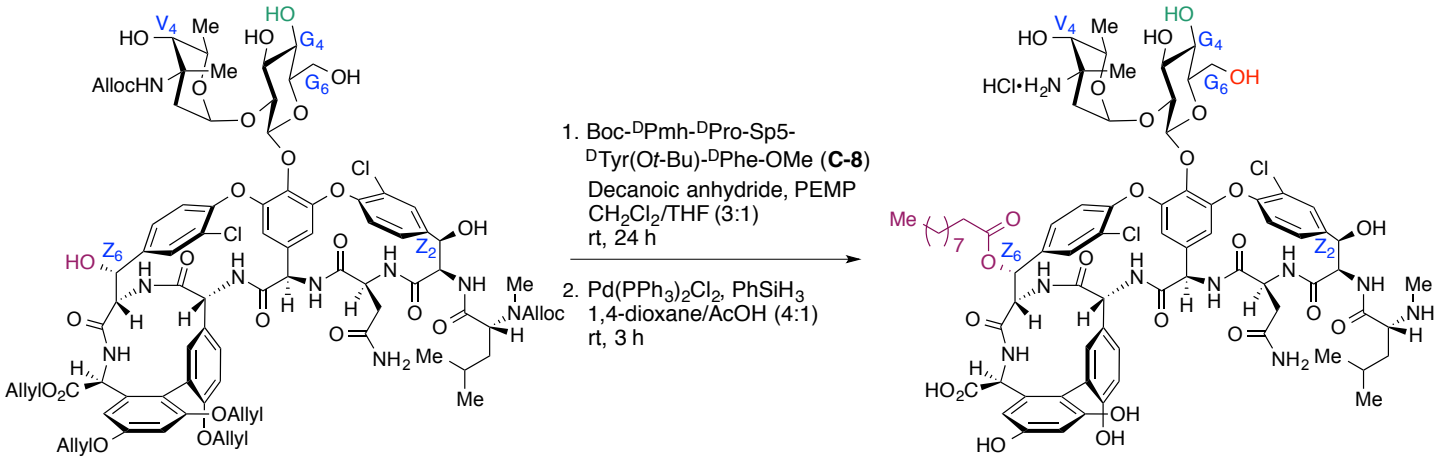


HPLC Trace of G_4-decanoyl-vancomycin (9b): RP-HPLC Method 3, λ = 220 nm, t_R = 14.2 min..



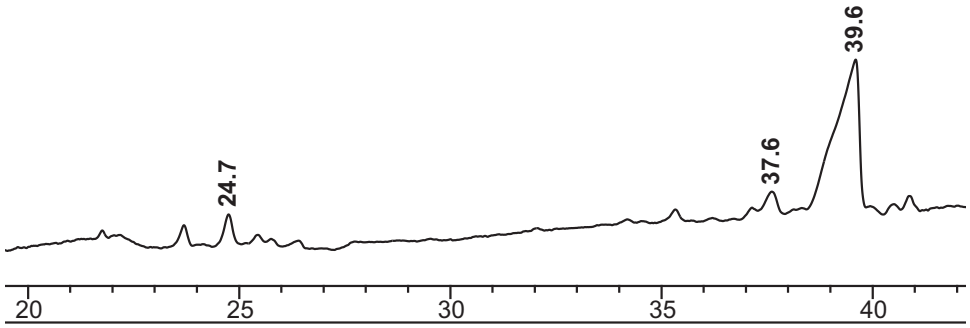
HSQC-NMR spectrum of G_4-decanoyl vancomycin (9b) in DMSO-d_6. [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]

V. Synthesis of Z_6-decanoyl vancomycin derivative 9c

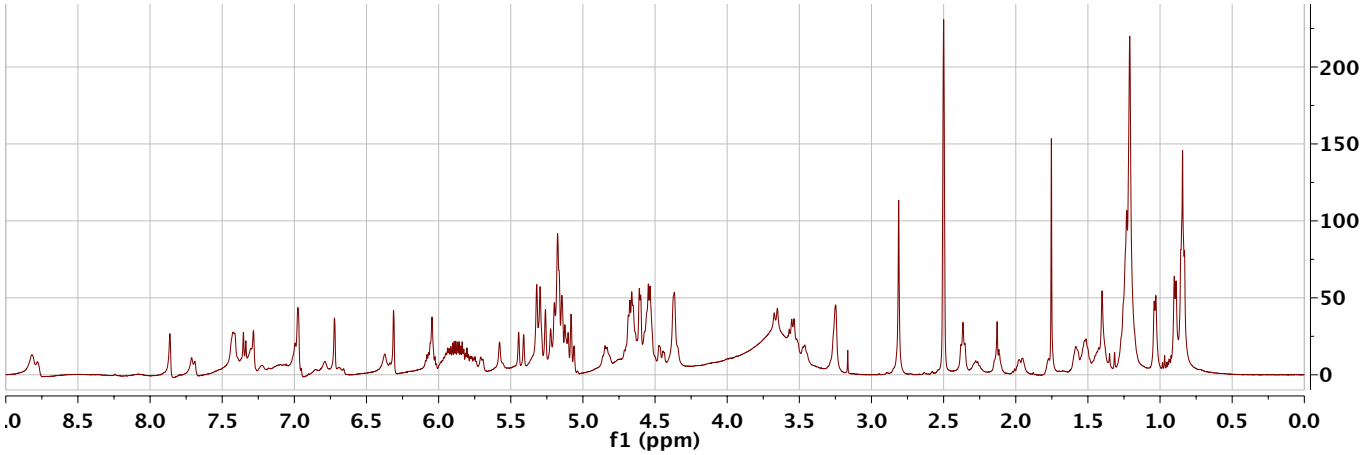


1

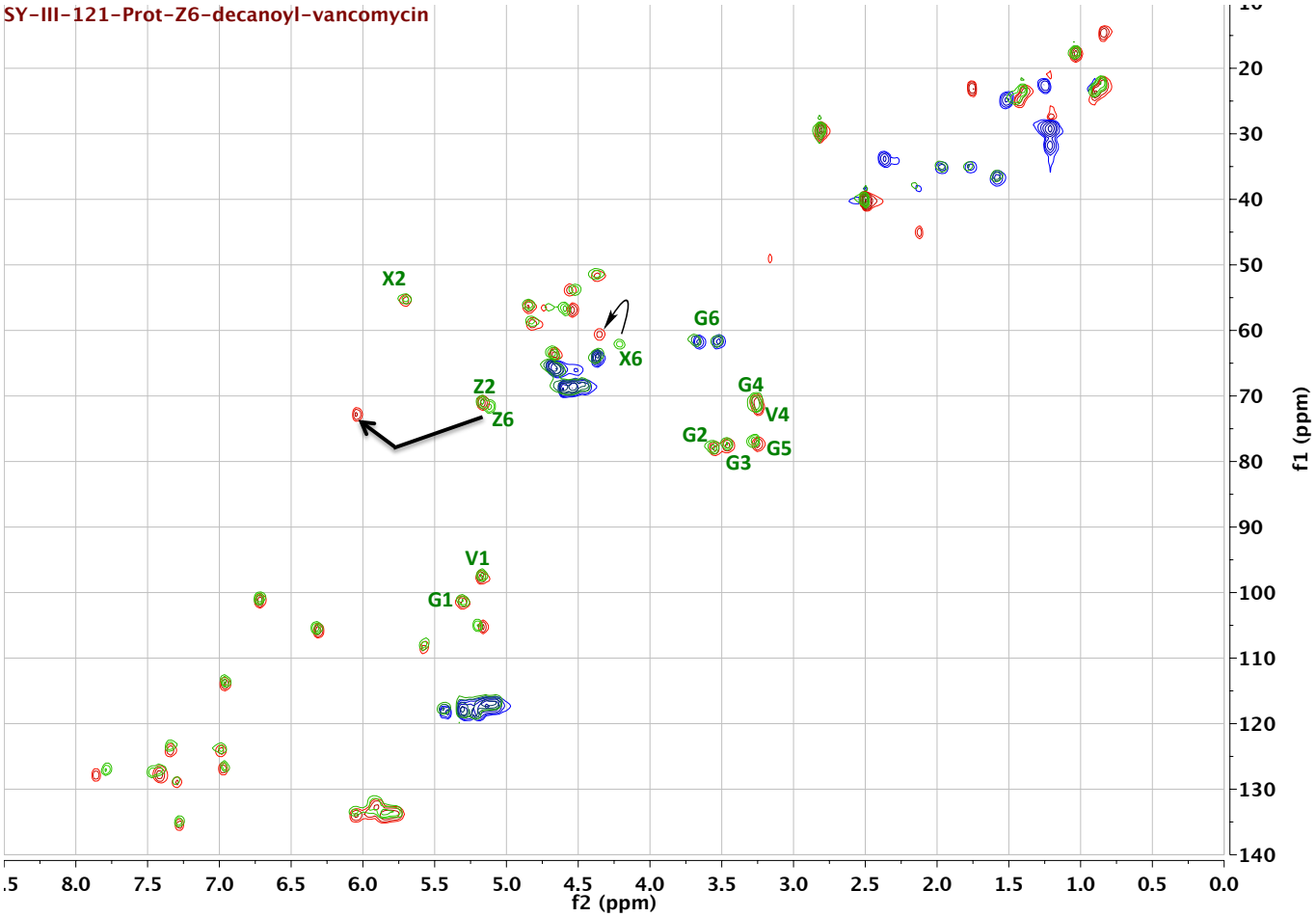
Z_6-decanoyl vancomycin derivative (**9c**)



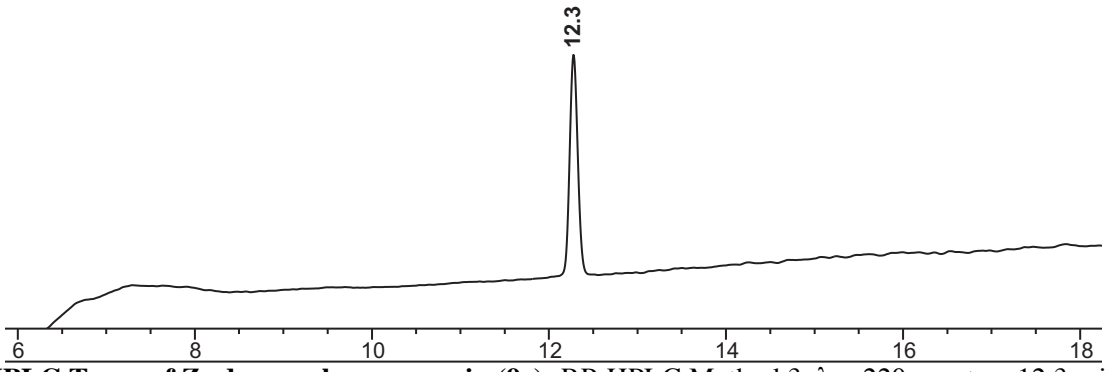
HPLC Trace of Z_6-selective decanoylation reaction: RP-HPLC Method 3, λ = 220 nm, t_R = 24.7 min; t_R (protected Z_6-decanoyl vancomycin) = 39.6 min.



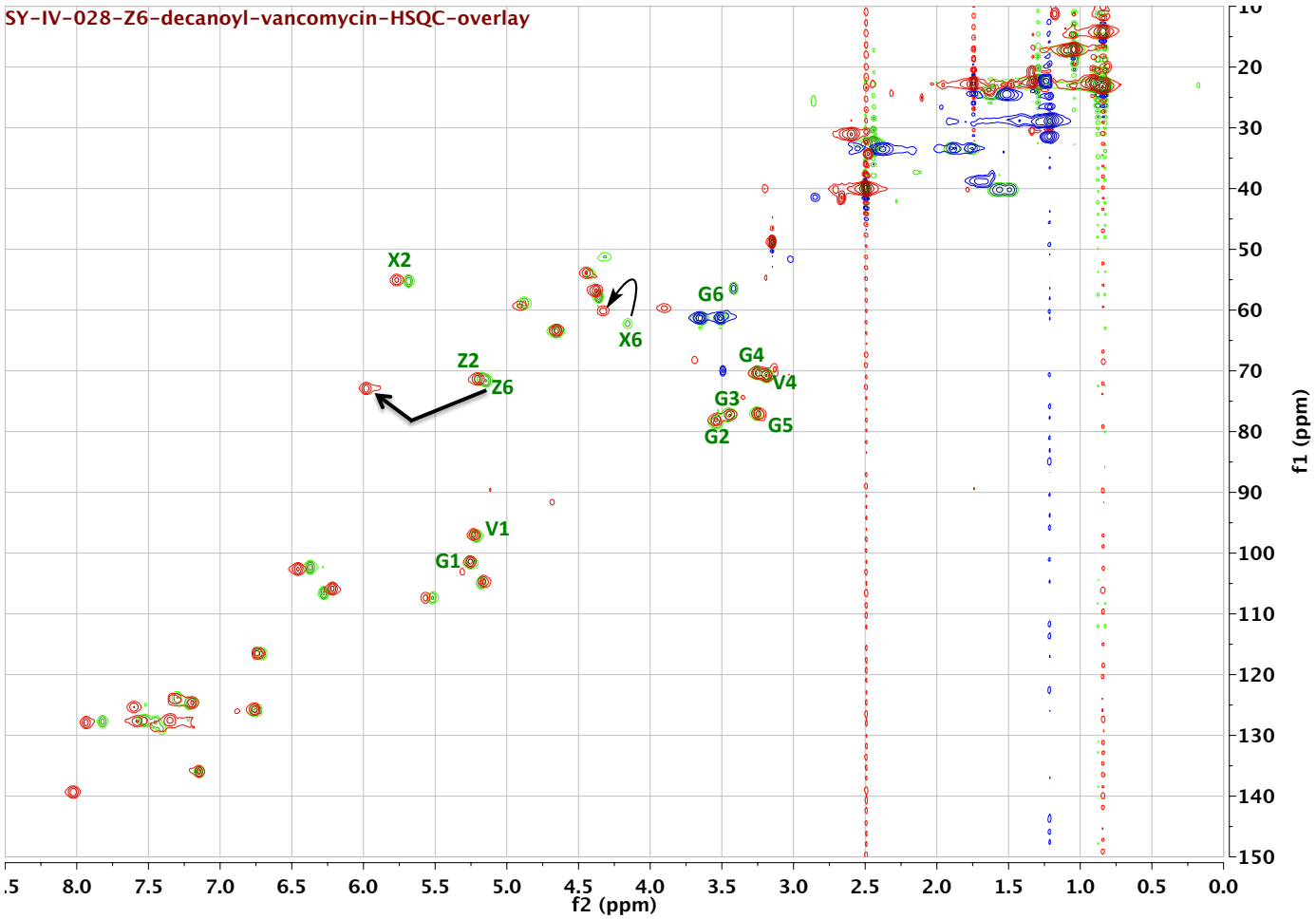
^{1}H NMR spectrum of protected Z_6-decanoyl vancomycin in DMSO-d_6



HSQC-NMR spectrum of protected Z_6-decanoyl vancomycin in DMSO-d_6 [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]



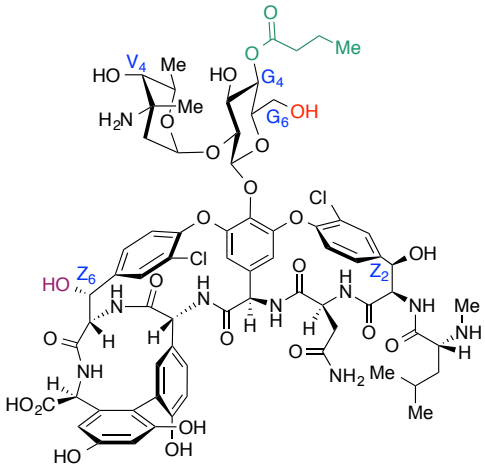
HPLC Trace of Z_6-decanoyl-vancomycin (9c): RP-HPLC Method 3, λ = 220 nm, t_R = 12.3 min.



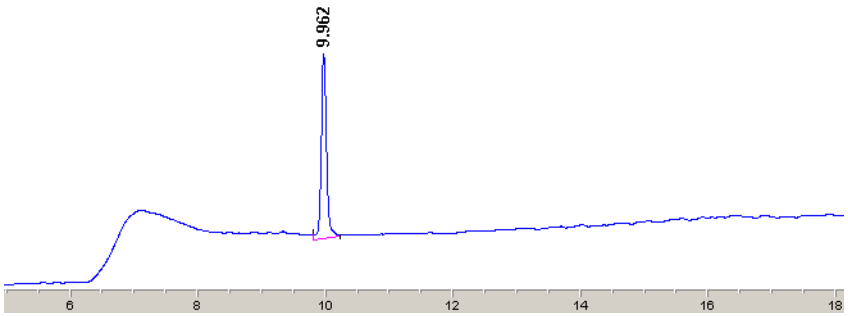
HSQC-NMR spectrum of Z_6-decanoyl vancomycin in DMSO-d_6. [HSQC spectrum of native vancomycin is colored in green, and HSQC spectrum of decanoyl-vancomycin derivative is colored in red and blue]

VI. Synthesis of G_4-acyl vancomycin derivatives 10-15

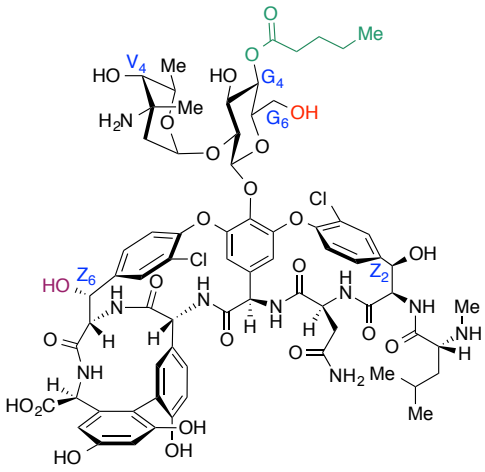
VIa. G_4-butyryl-vancomycin derivative (10): Analog **10** was synthesized using the general procedure 2 and isolated as a white solid (14.5 mg, 17% over two steps). RP-HPLC retention time (Method 3): 9.7 min; LC-MS (ESI^+) for $C_{71}H_{84}Cl_2N_9O_{25}$ $[M+H]^+$: Calc'd = 1518.479; found = 1518.469.



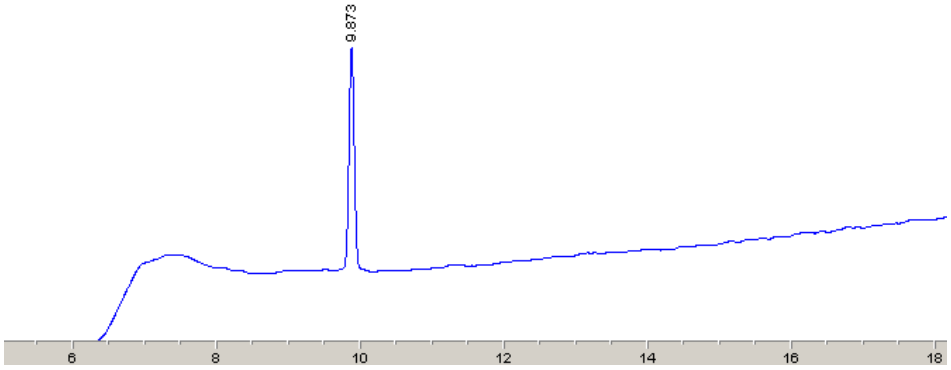
G_4-butyrylvancomycin derivative (**10**)



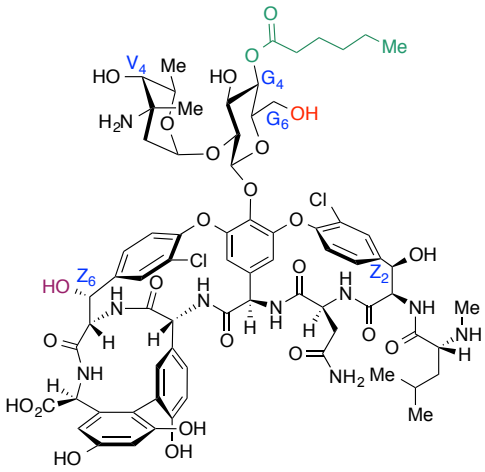
VIb. G_4-pentanoyl vancomycin derivative (11): Analog **11** was synthesized using the general procedure 2 and isolated as a white solid (10 mg, 23% over two steps). RP-HPLC retention time (Method 3): 9.8 min; LC-MS (ESI^+) for $C_{71}H_{84}Cl_2N_9O_{25}$ $[M+H]^+$: Calc'd = 1532.495; found = 1532.526.



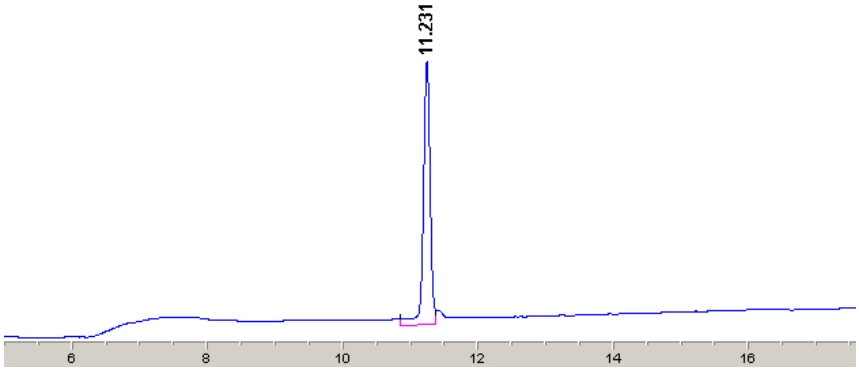
G_4-pentanoylvancomycin derivative (**11**)



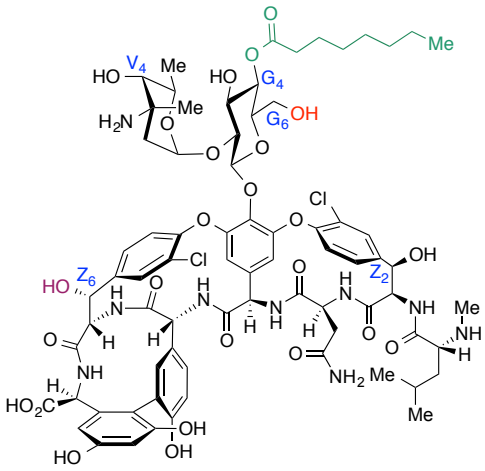
VIc. G_4-hexanoyl vancomycin derivative (12): Analog **12** was synthesized using the general procedure 2 and isolated as a white solid (11 mg, 25% over two steps). RP-HPLC retention time (Method 3): 11.2 min; LC-MS (ESI^+) for $C_{72}H_{86}Cl_2N_9O_{25}$ $[M+H]^+$: Calc'd = 1546.511; found = 1546.510.



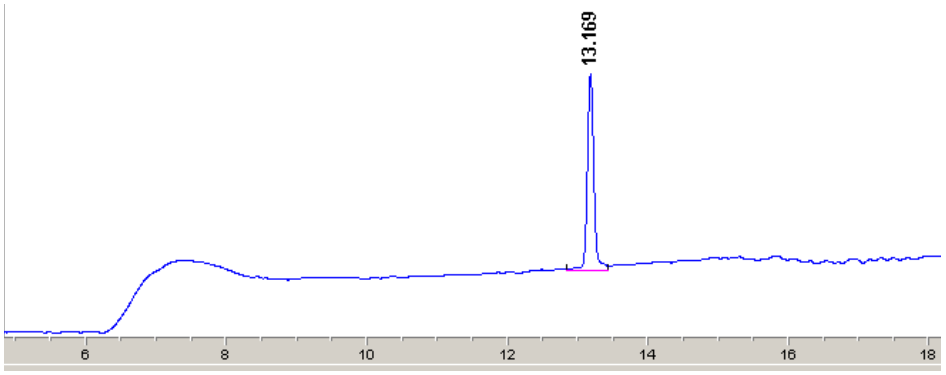
G_4-hexanoyl vancomycin derivative (**12**)



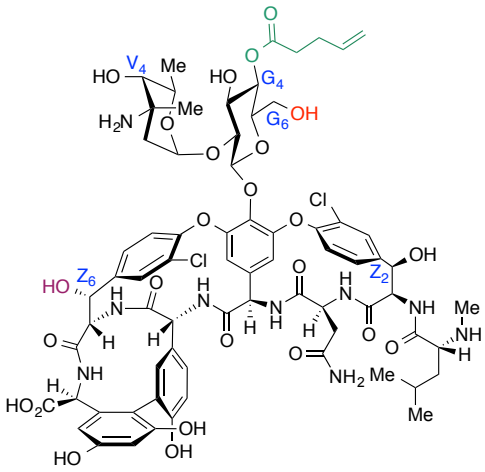
VId. G_4-octanoyl vancomycin derivative (13): Analog **13** was synthesized using the general procedure 2 and isolated as a white solid (14 mg, 32% over two steps). RP-HPLC retention time (Method 3): 13.2 min; LC-MS (ESI^+) for $C_{74}H_{90}Cl_2N_9O_{25}$ $[M+H]^+$: Calc'd = 1574.542; found = 1574.540.



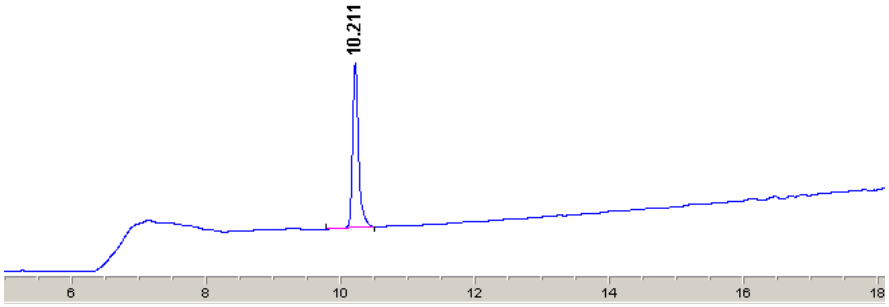
G_4-octanoyl vancomycin derivative (**13**)



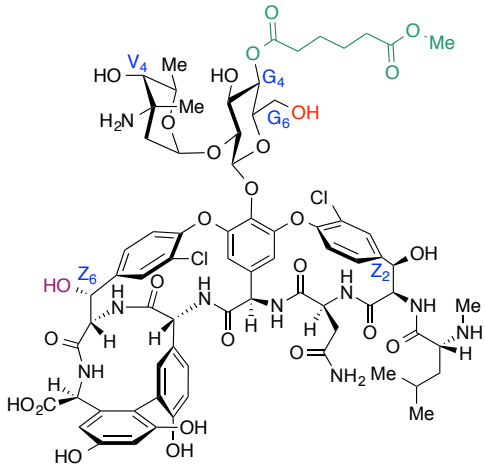
VIe. G_4-pentenoyl-vancomycin derivative (14): Analog **14** was synthesized using the general procedure 2 and isolated as a white solid (18 mg, 21% over two steps). RP-HPLC retention time (Method 3): 10.2 min; LC-MS (ESI^+) for $C_{71}H_{82}Cl_2N_9O_{25}$ $[M+H]^+$: Calc'd = 1530.479; found =1530.476.



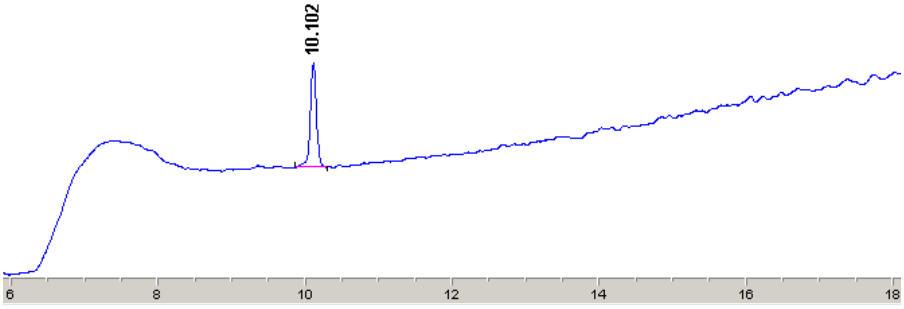
G_4-pentenoyl-vancomycin derivative (**14**)



VIf. G_4-methyladipoyl-vancomycin derivative (15): Analog **15** was synthesized using the general procedure 2 and isolated as a white solid. RP-HPLC retention time (Method 3): 10.1 min; LC-MS (ESI^+) for $C_{73}H_{86}Cl_2N_9O_{27}$ $[M+H]^+$: Calc'd = 1590.500; found = 1590.529.



G_4-methyl-adipoyl-vancomycin derivative (**15**)

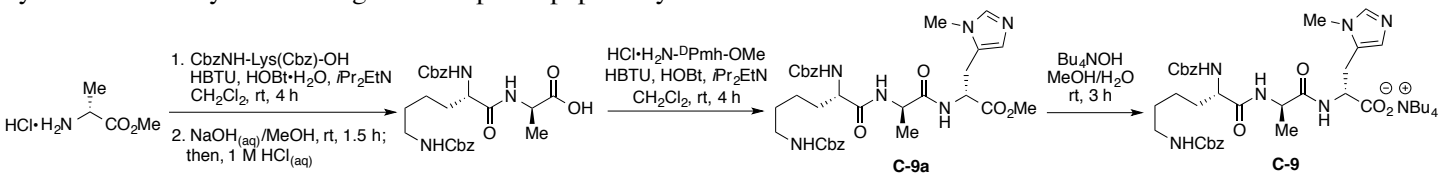


VII. Synthesis of peptide catalysts: Previously reported peptide catalysts were synthesized using either an Fmoc-based solid phase peptide synthetic strategy using commercially available Wang resin or 2-chlorotrityl resins, or a Boc-based solution phase peptide synthetic strategy. Please see original reports for details.[2]

Synthesis of catalyst **C-1** using solution phase peptide synthesis:

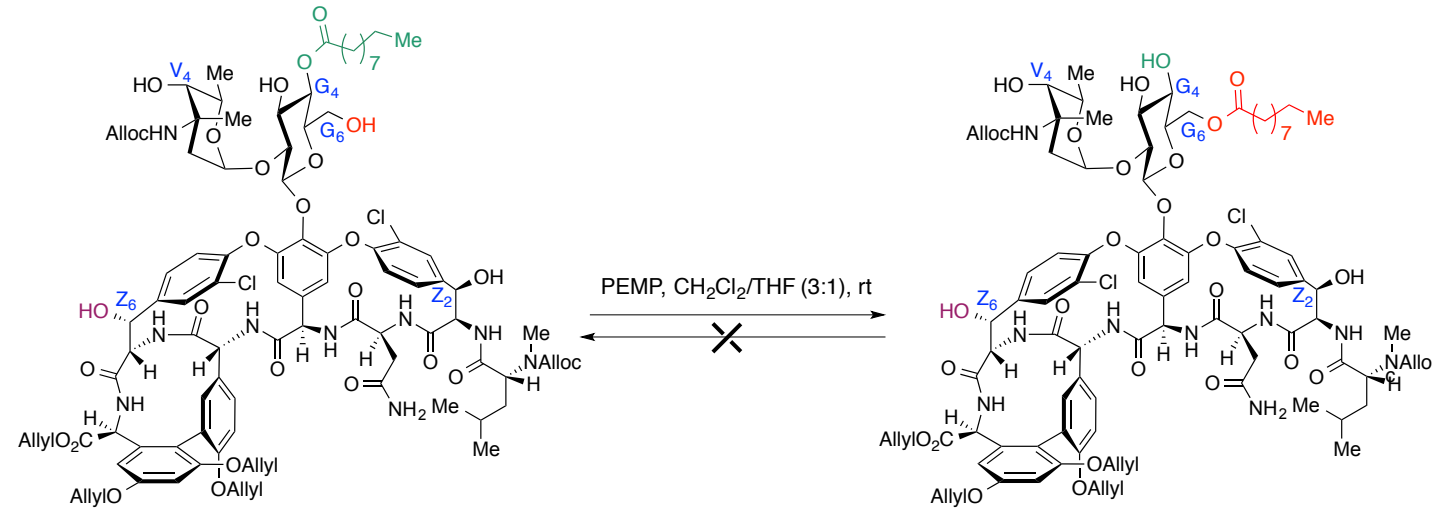
Boc-Pmh-Asn(Trt)-His(Bn)-^{D}Ala-^{D}Ala-OMe (C-1): white solid, 400 mg, 76%. **^{1}H NMR:** (500 MHz, Chloroform-*d*) δ 8.10 (d, *J* = 6.7 Hz, 1H), 7.74 (d, *J* = 6.5 Hz, 1H), 7.39 – 7.07 (m, 22 H), 6.76 (s, 1H), 6.62 (d, *J* = 1.3 Hz, 1H), 5.26 (d, *J* = 8.1 Hz, 1H), 4.93 (s, 2H), 4.59 (m, 1H), 4.53 – 4.44 (m, 2H), 4.35 (m, 1H), 3.67 (s, 3H), 3.66 (m, 1H), 3.51 (s, 3H), 3.09 (dd, *J* = 15.4, 5.6 Hz, 1H), 3.04 – 2.90 (m, 2H), 2.93 – 2.82 (m, 4H), 1.46 – 1.30 (m, 2H), 1.34 (s, 9H), 1.29 (d, *J* = 7.3 Hz, 3H), 1.15 (d, *J* = 7.2 Hz, 3H). **^{13}C NMR:** (126 MHz, Chloroform-*d*) δ 171.87, 170.99, 170.41, 169.70, 155.40, 144.26, 138.45, 137.87, 136.97, 129.03, 128.72, 128.36, 128.28, 128.00, 127.96, 127.49, 127.18, 117.60, 80.48, 70.93, 54.42, 53.82, 52.30, 50.88, 50.81, 49.42, 47.81, 38.05, 31.43, 28.97, 28.26, 26.91, 17.95, 16.78. **LC-MS:** (ESI) calculated for $C_{55}H_{65}N_{10}O_9$ $[M+H]^+$ 1009.40, observed 1009.46.

Synthesis of catalyst **C-9** using solution phase peptide synthesis:[2c]



Catalyst **C-9** was synthesized using reported literature procedure.[2c] **Cbz-Lys(Cbz)-DAla-DPmh-OMe (C-9a):** white solid, 139 mg, 87%. **^{1}H NMR:** (500 MHz, Chloroform-*d*) δ 7.32 – 7.28 (m, 10H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.68 (s, 1H), 6.28 (d, *J* = 8.0 Hz, 1H), 5.15 (s, 1H), 5.09 (s, 2H), 5.06 (s, 2H), 4.76 (m, 1H), 4.47 (m, 1H), 4.15 (dd, *J* = 7.0, 7.0 Hz, 1H), 3.74 (s, 3H), 3.49 (s, 3H), 3.17 – 3.06 (m, 3H), 2.93 (dd, *J* = 15.6, 8.9 Hz, 1H), 1.97 – 1.86 (m, 4H), 1.51 (m, 2H), 1.38 (m, 2H), 1.25 (d, *J* = 6.8 Hz, 3H). **^{13}C NMR:** (126 MHz, Chloroform-*d*) δ 172.01, 171.94, 171.29, 156.85, 156.67, 138.46, 136.68, 136.32, 128.58, 128.52, 128.42, 128.23, 128.11, 128.07, 126.53, 67.10, 66.63, 54.81, 52.73, 50.92, 48.70, 40.45, 31.35, 29.36, 26.68, 22.59, 17.30. **LC-MS:** (ESI) calculated for $C_{33}H_{43}N_6O_8$ $[M+H]^+$ 651.31, observed 651.34.

VIII. Evaluation of acyl-migration

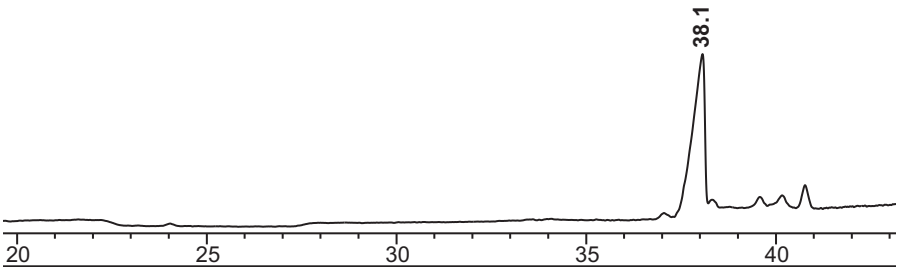


Protected G_4-decanoyl vancomycin derivative (**4b**)

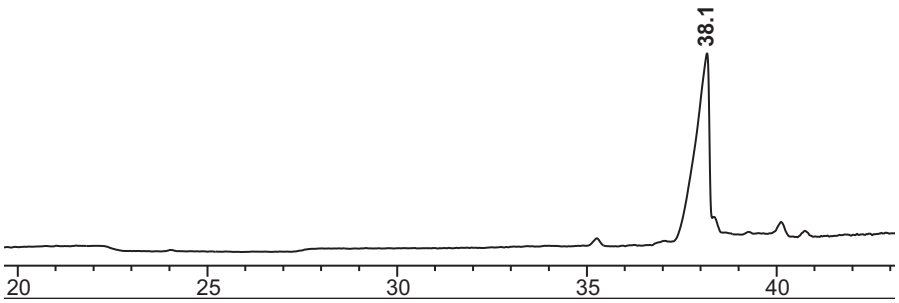
Protected G_6-decanoyl vancomycin derivative (**4a**)

VIIIa: Treatment of 4b under reaction condition:

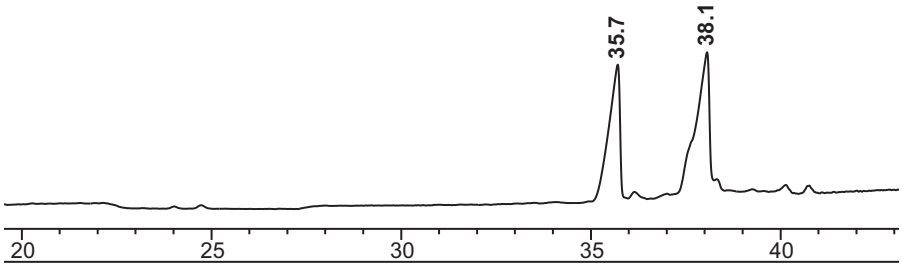
In a flame-dried vial containing a stir bar, compound **4b** (5.4 mg, 2.79 μmol, 1 equiv) was dissolved in THF (100 μL), and then CH_2Cl_2 (300 μL) was added to the vial. To the solution, PEMP (1.0 μL, 5.58 μmol, 2 equiv) was added and reaction was monitored using RP-HPLC (Method 3). Compound **4b** was stable at t = 5 h; however after 20 h, **4b** is converted to **4a** (1:1 mixture, see HPLC traces below). The results indicate that acyl migration occurs from G_4-position to G_6-position only under strong basic conditions with prolonged reaction time.



HPLC Trace of a standard sample of 4b: RP-HPLC Method 3, λ = 220 nm, t_R (**4b**) = 38.1 min.

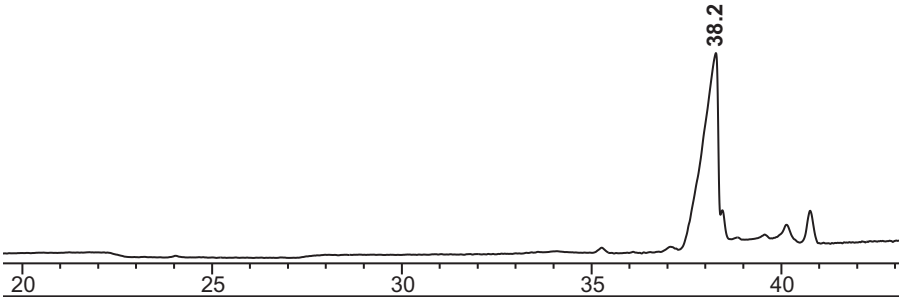


HPLC Trace of 4b in the presence of PEMP (2 equiv) after 5 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4b**) = 38.1 min.

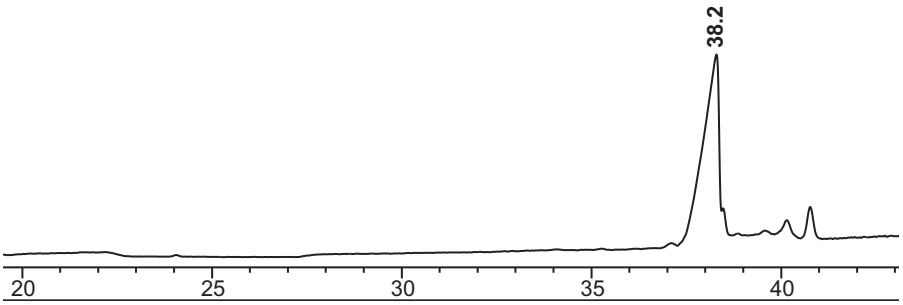


HPLC Trace of 4b in the presence of PEMP (2 equiv) after 20 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4b**) = 38.1 min t_R (**4a**) = 35.7 min.

In a flame-dried glass vial containing a stir bar, compound **4b** (4.5 mg, 2.33 μmol, 1 equiv) was dissolved in THF (100 μL), and then CH_2Cl_2 (300 μL) was added to the vial. To the solution, PEMP (0.2 μL, 1.16 μmol, 0.5 equiv) was added and reaction was monitored using RP-HPLC (Method 3). Compound **4b** was stable up to 23 h (see HPLC traces below). The observations suggest that under mild basic conditions protected G_4-decanoyl-vancomycin derivative does not undergo acyl migration.



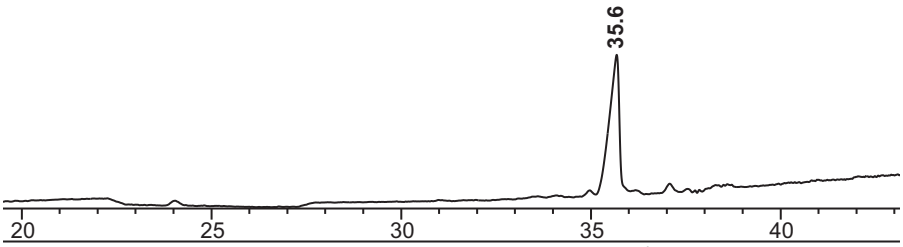
HPLC Trace of 4b in the presence of PEMP (0.5 equiv) after 5 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4b**) = 38.2 min.



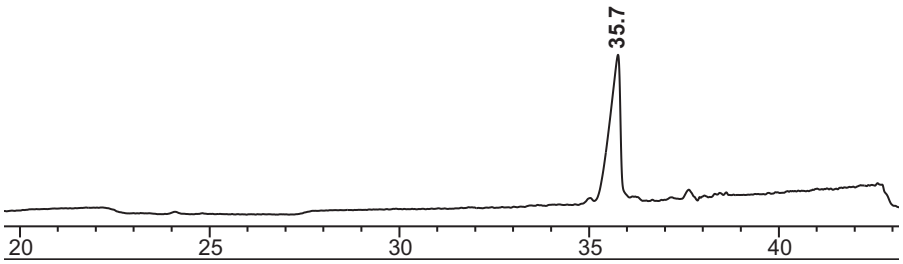
HPLC Trace of 4b in the presence of PEMP (0.5 equiv) after 23 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4b**) = 38.2 min.

VIIIb: Treatment of 4a under reaction condition:

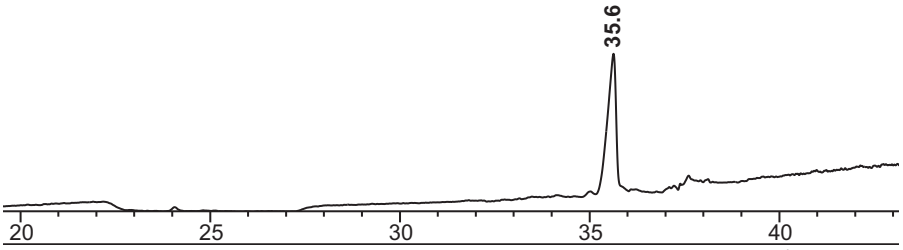
In a flame-dried glass vial containing a stir bar, compound **4a** (4.5 mg, 2.33 μmol, 1 equiv) was dissolved in THF (100 μL) and then CH_2Cl_2 (300 μL) was added to the vial. To the solution, PEMP (0.85 μL, 4.66 μmol, 2 equiv) was added and reaction was monitored using RP-HPLC (Method 3). Compound **4a** was stable up to 20 h (see RP-HPLC traces below). The results indicate that there is no acyl-migration from G_6-position to G_4-position occurring under basic conditions. This supports our hypothesis that the formation of G_4-acyl product is exclusively assisted by the catalyst, and not due to an internal acyl migration.



HPLC Trace of a standard sample of 4a: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.6 min.

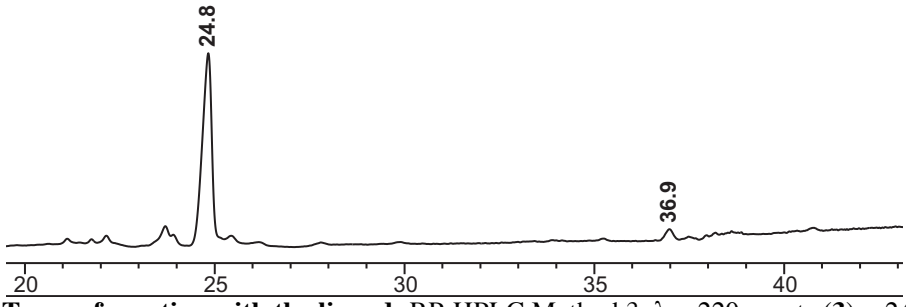


HPLC Trace of 4a in the presence of PEMP (2 equiv) after 5 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.7 min.

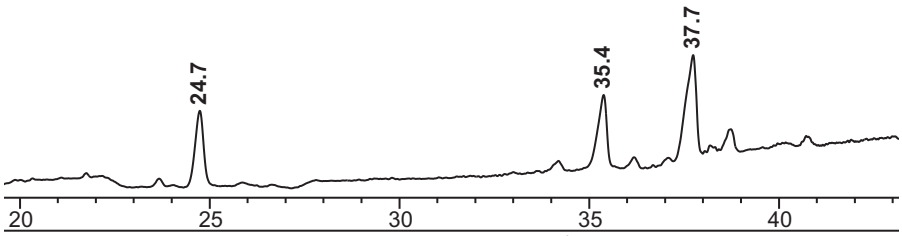


HPLC Trace of 4a in the presence of PEMP (2 equiv) after 20 h: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.6 min.

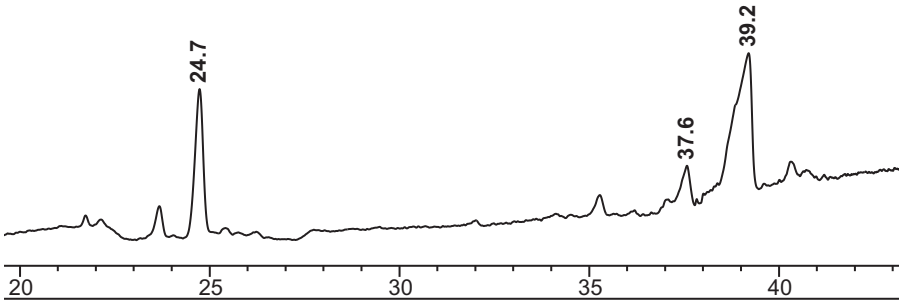
IX. Competition studies using Boc-Leu-^{D}Ala-^{D}Ala-OH, a tripeptide ligand for vancomyin



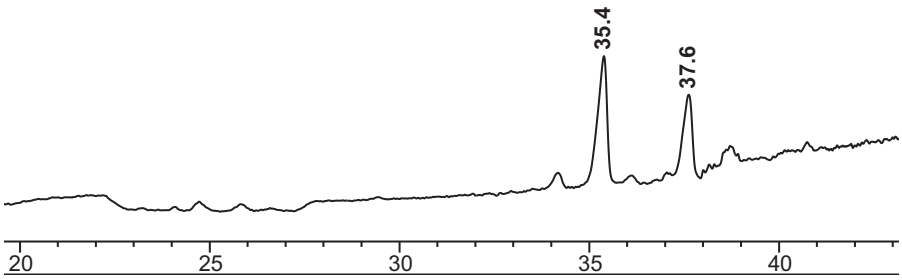
HPLC Trace of reaction with the ligand: RP-HPLC Method 3, λ = 220 nm, t_R (**3**) = 24.8 min.



HPLC Trace of reaction with C-7 and ligand: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.4 min, t_R (**4b**) = 37.7 min.



HPLC Trace of reaction with C-8 and ligand: RP-HPLC Method 3, λ = 220 nm, t_R of protected Z_6-decanoyl-vancomycin (**4c**) = 39.2 min.



HPLC Trace of reaction with C-9 and ligand: RP-HPLC Method 3, λ = 220 nm, t_R (**4a**) = 35.6 min, t_R (**4b**) = 37.6 min.

X. Antimicrobial evaluation of acyl-vancomycin derivatives & Minimum inhibitory concentration (MIC) data:

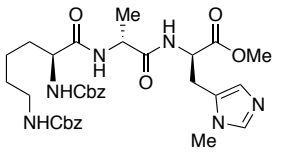
MSSA = methicillin-susceptible *S. aureus*; **MRSA** = methicillin-resistant *S. aureus*; **VSE** = vancomycin- susceptible enterococci (*E. faecalis*); **VRE (VanB)** = vancomycin-resistant enterococci (*E. faecalis*, teicoplanin susceptible); **VRE (VanA)** = vancomycin-resistant enterococcus (*E. faecalis*, teicoplanin resistant). **ATCC #:** American Type Culture Collection isolate. **MMX #:** Micromyx, LLC isolate. Minimum inhibitory concentrations (MICs) were determined by Micromyx, LLC (Kalamazoo, MI) in accordance with CLSI guidelines.

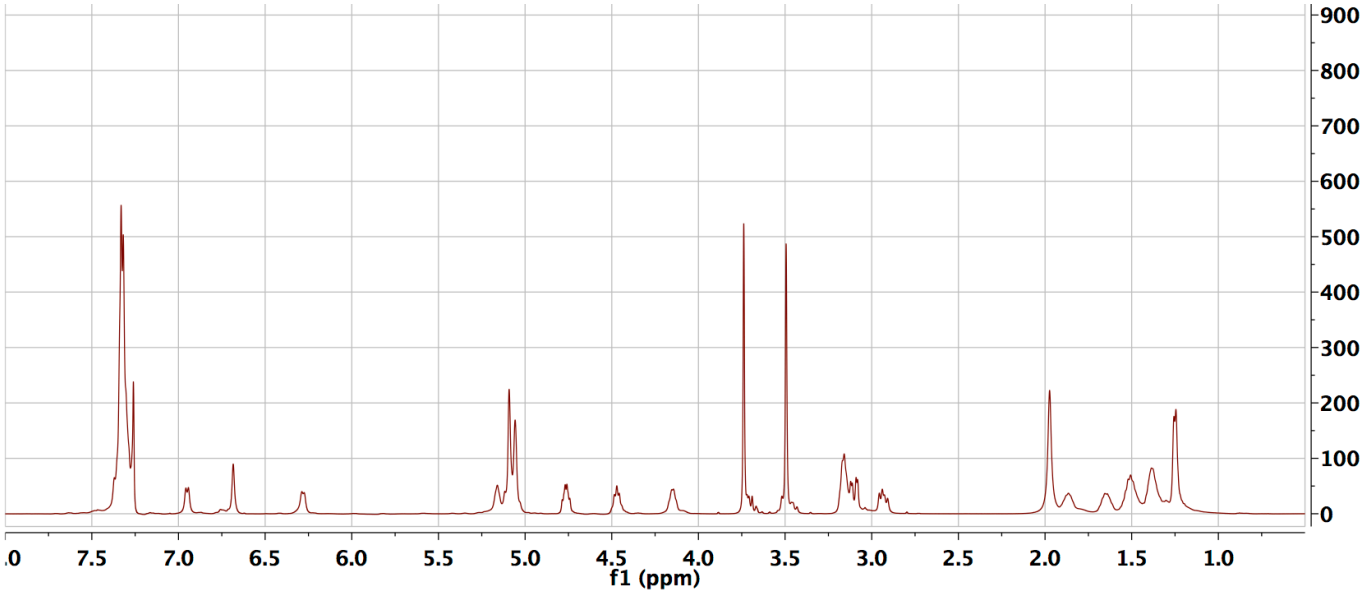
Compound	*S. aureus* (MSSA) ATCC 29213	*S. aureus* (MRSA) ATCC 43300	*E. faecalis* (Van S) ATCC 29212	*E. faecalis* (Van B) ATCC 51299	*E. faecalis* (Van A) MMX 486[a]
9a	0.25	0.25	0.5	1	16
9b	0.12	0.12	0.25	0.25	16
9c	0.25	0.5	0.25	0.5	16
10	4	4	8	32	>64
11	2	4	4	32	>32
12	2	2	4	16	>64
13	0.5	0.5	1	8	>64
14	4	4	8	32	>32
15	4	4	8	64	>64
Vancomycin	1	1	2	16	>64[b]
Teicoplanin	1	0.5	0.25	0.25	>64[b]
Linezolid	4	4	2	2	2

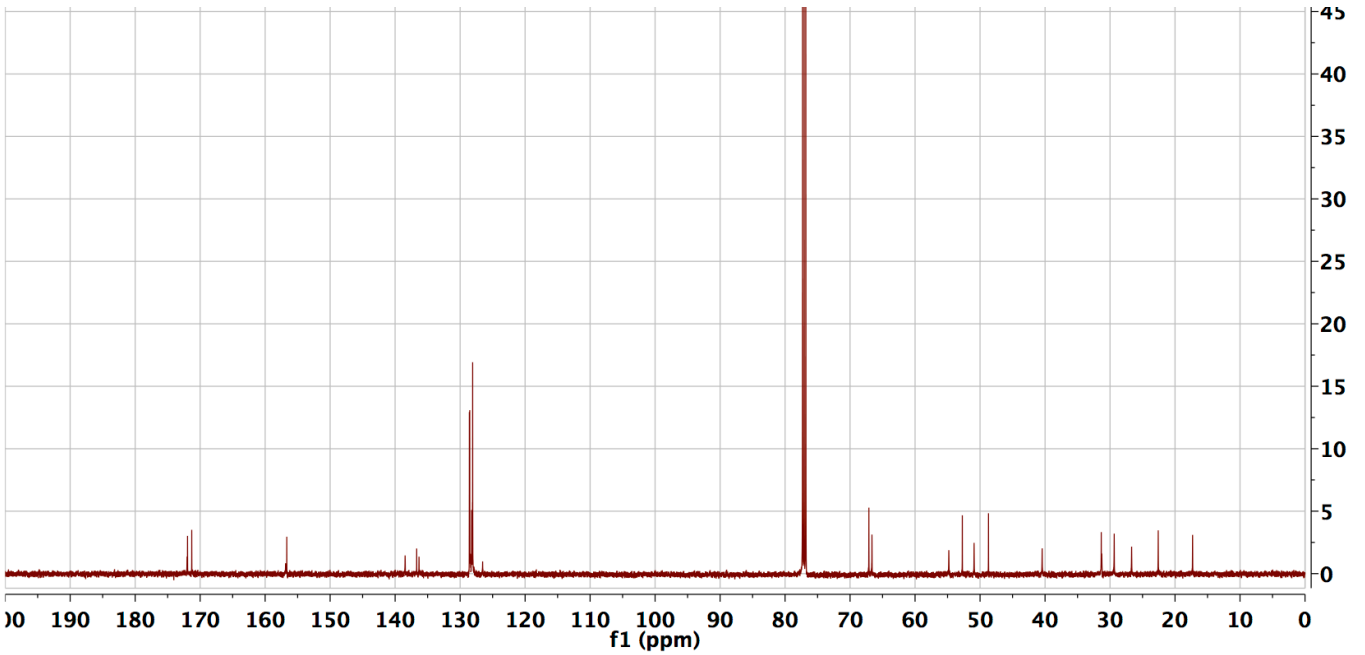
[a]MMX: Micromyx isolate number. [b]Vancomycin exhibits an MIC of 512 μg/mL and teicoplanin A_2-2 exhibits an MIC of 128 μg/mL against Van A phenotype VRE strain, based on a literature report.[3]

XI. NMR Spectra

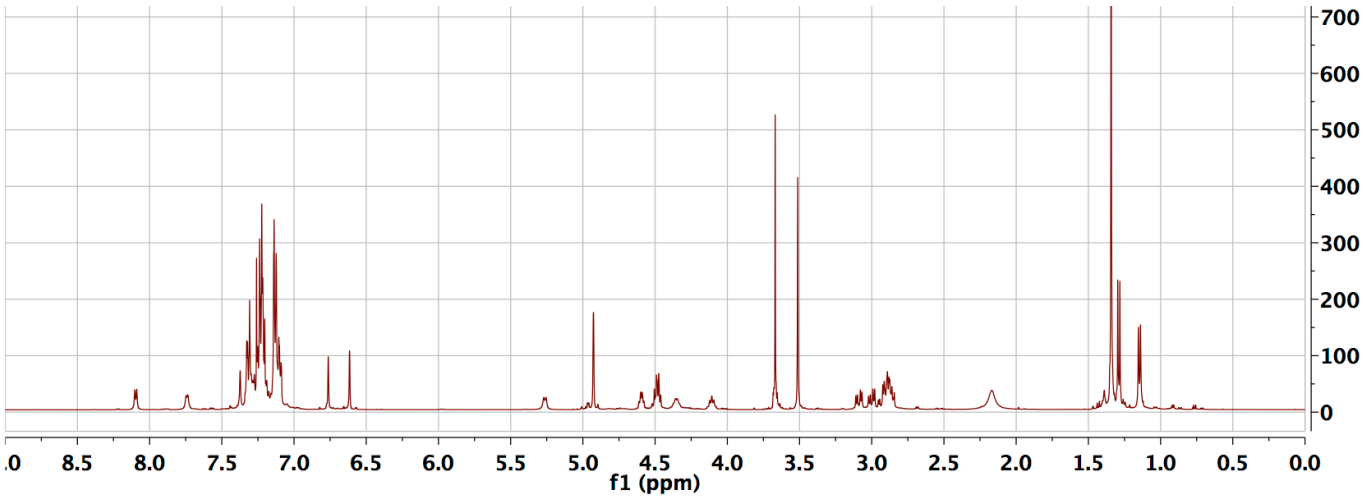
NMR spectra of catalyst Cbz-Lys(Cbz)-^{D}Ala-^{D}Pmh-OMe:

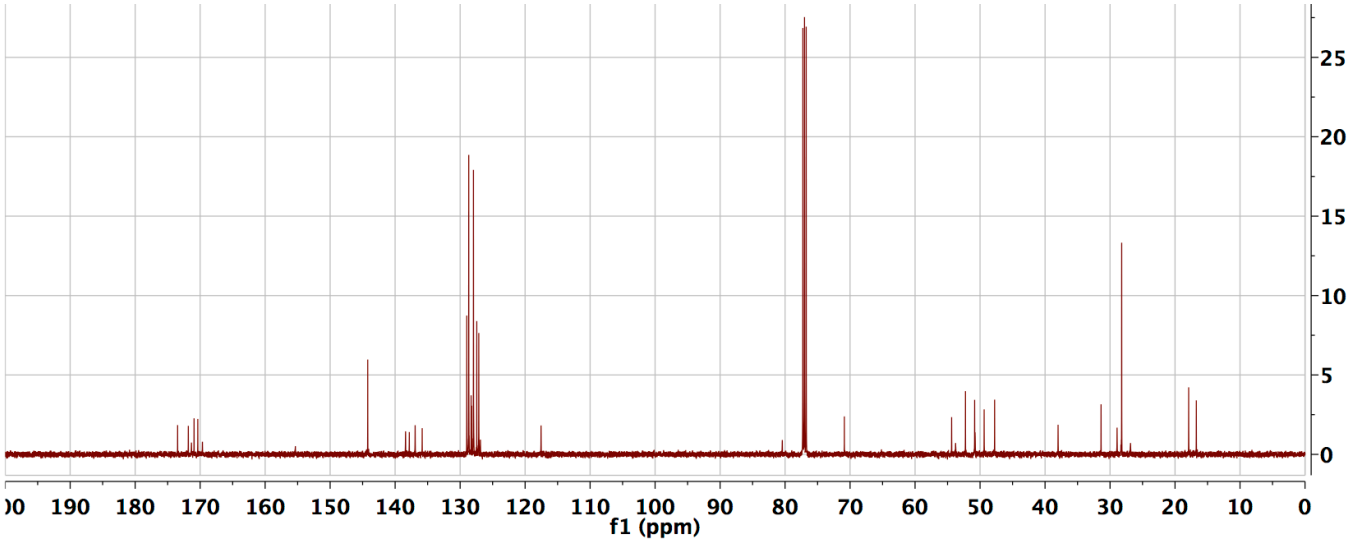






NMR spectra of catalyst Boc-Pmh-Asn(Trt)-His(Bn)-^{D}Ala-^{D}Ala-OMe:

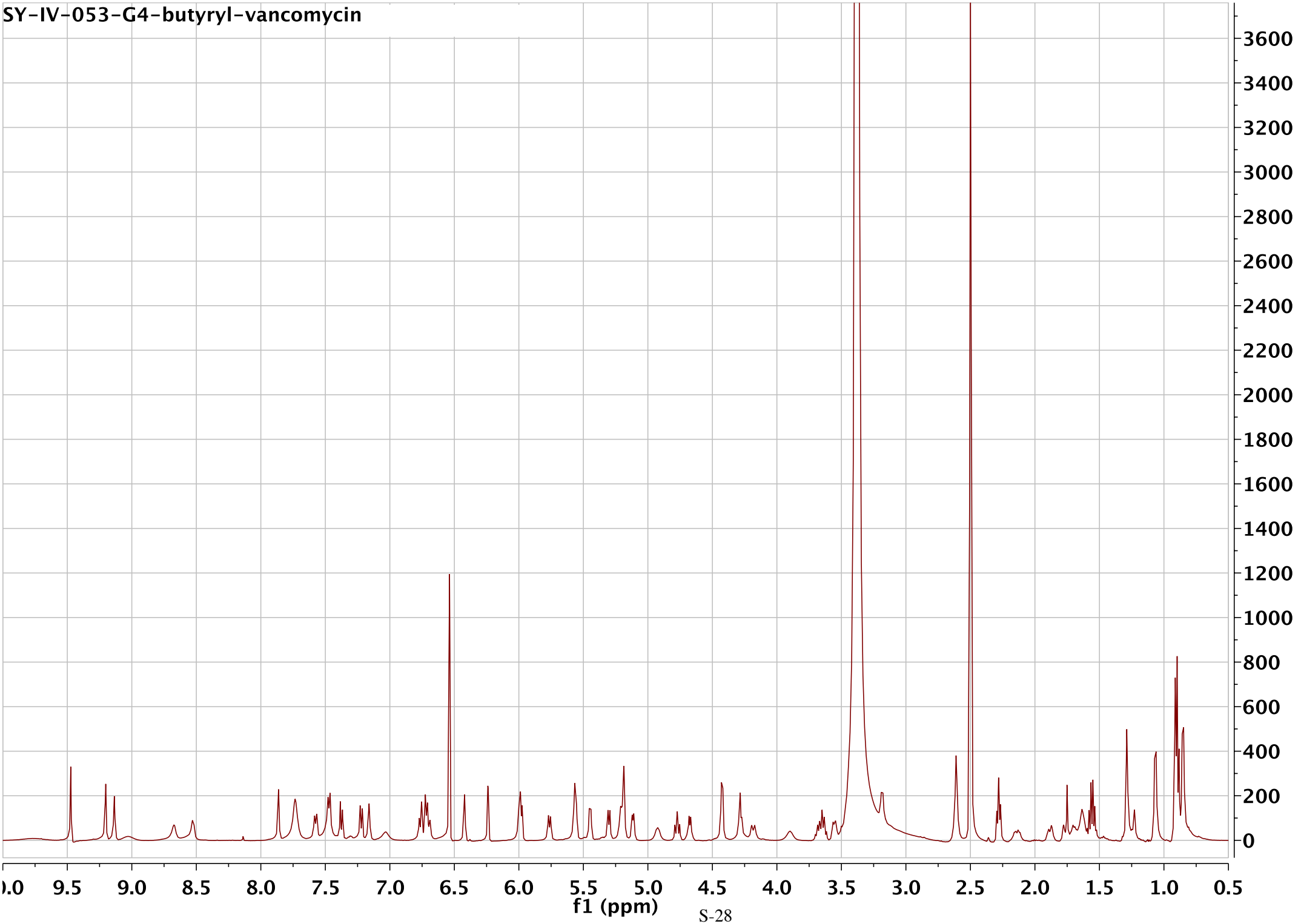


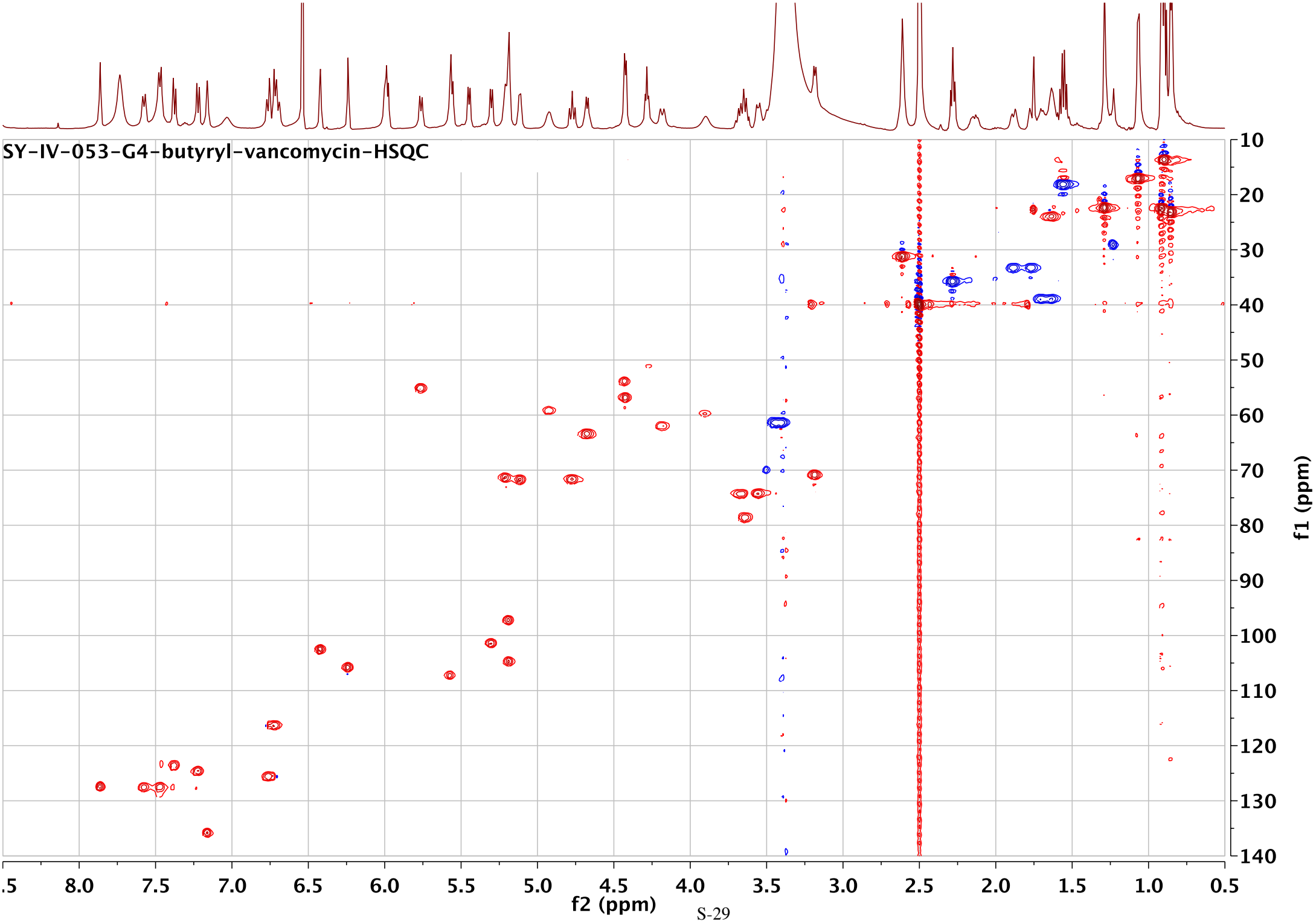


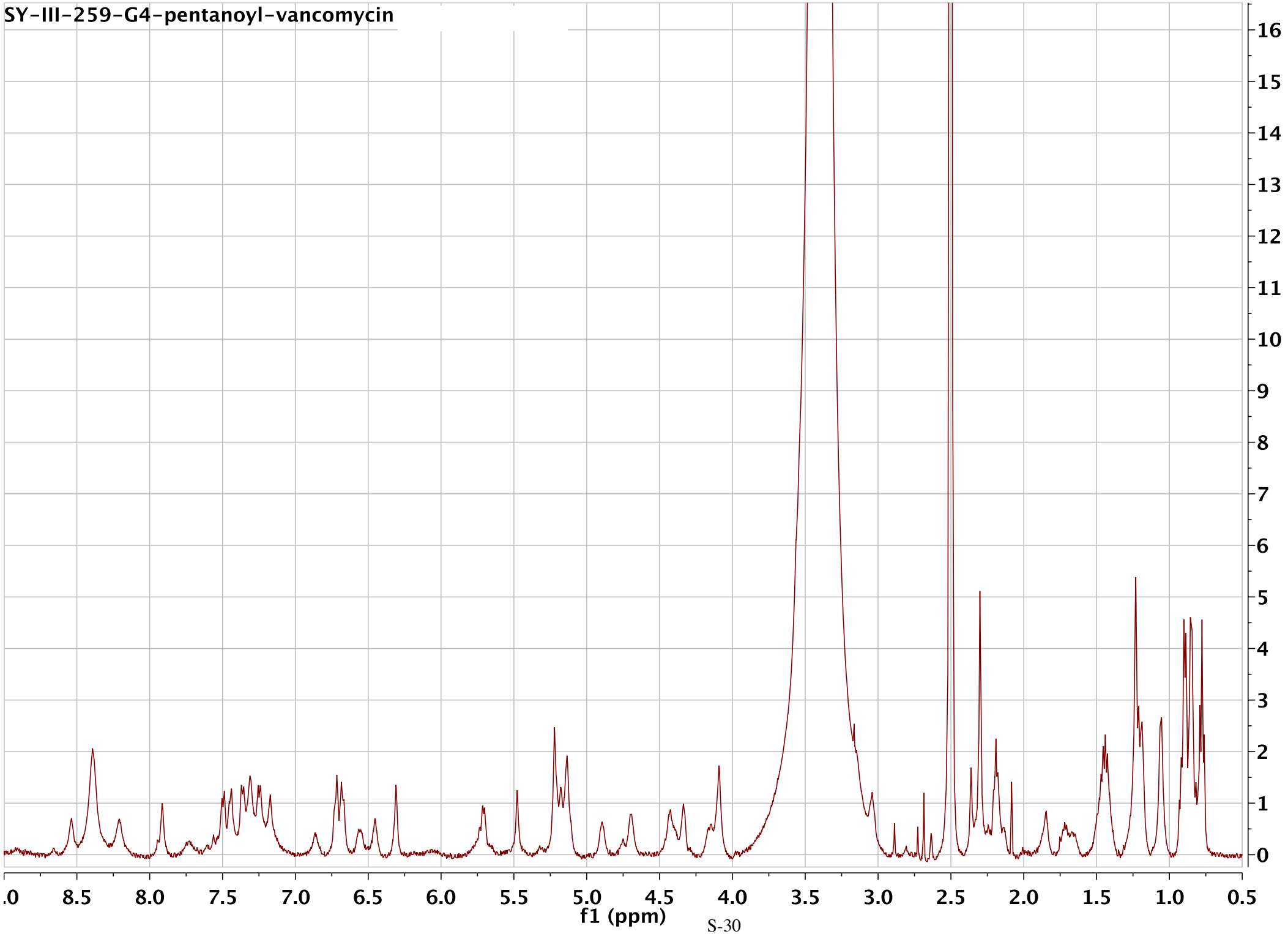
[1] (a) Thompson, C.; Ge, M.; Kahne, D. Synthesis of vancomycin from the aglycon. *J. Am. Chem. Soc.* **1999**, *121*, 1237. (b) Griffith, B. R.; Krepel, C.; Fu, X.; Blanchard, S.; Ahmed, A.; Edmiston, C. E.; Thorson, J. S. Model for antibiotic optimization via neoglycosylation: Synthesis of liponeoglycopeptides active against VRE. *J. Am. Chem. Soc.* **2007**, *129*, 8150.

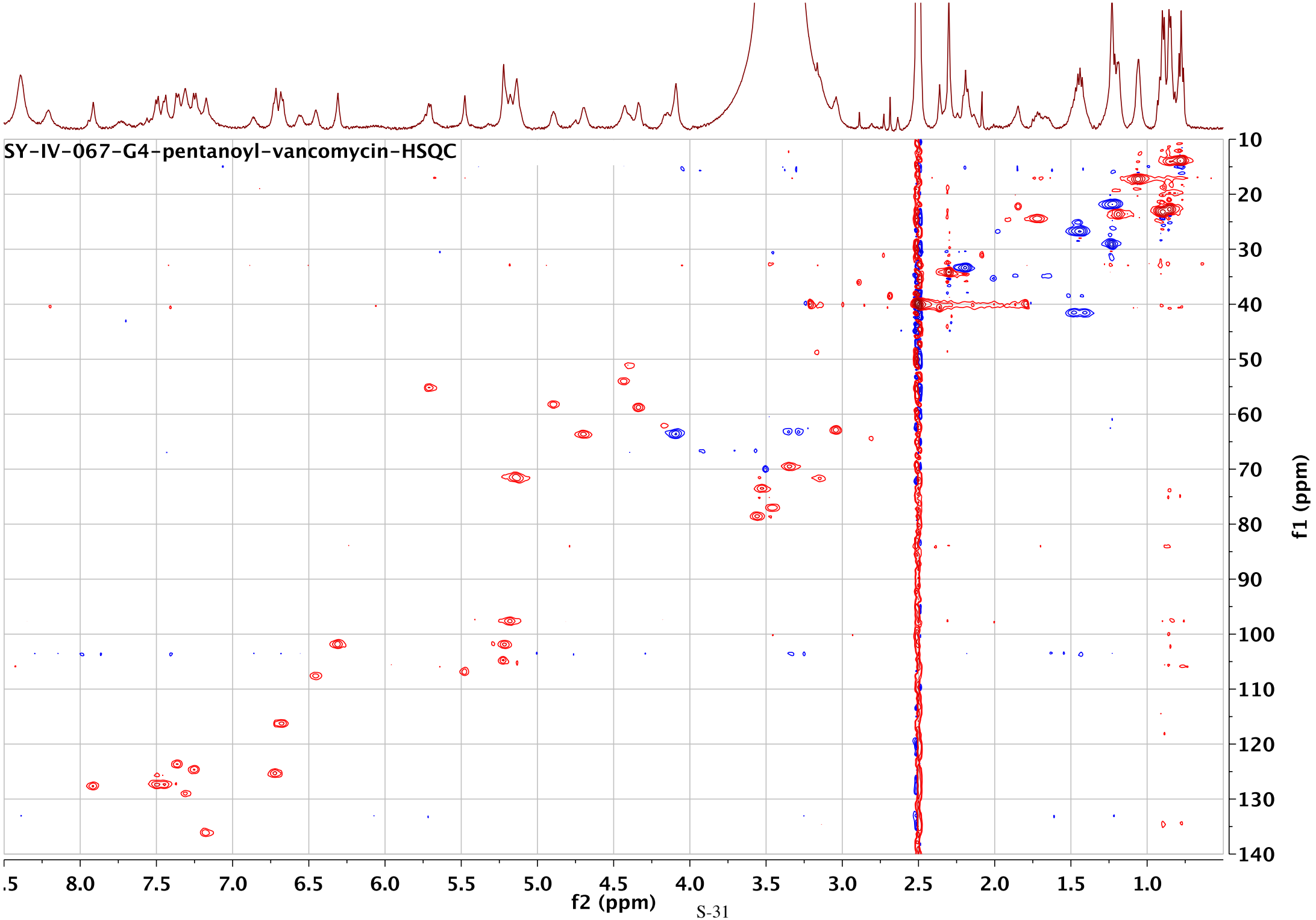
[2] Fowler, B. S.; Laemmerhold, K. M.; Miller, S. J. Catalytic Site-Selective Thiocarbonylations and Deoxygenations of Vancomycin Reveal Hydroxyl-Dependent Conformational Effects. *J. Am. Chem. Soc.* **2012**, *134*, 9755.; Fowler, B. S.; Mikochik, P. J.; Miller, S. J. Peptide-Catalyzed Kinetic Resolution of Formamides and Thioformamides as an Entry to Nonracemic Amines. *J. Am. Chem. Soc.* **2010**, *132*, 2870.; Sculimbrene, B. R.; Morgan, A. J.; Miller, S. J. Enantiodivergence in small-molecule catalysis of asymmetric phosphorylation: Concise total syntheses of the enantiomeric D-myo-inositol-1-phosphate and D-myo-inositol-3-phosphate. *J. Am. Chem. Soc.* **2002**, *124*, 11653.; Fiori, K. W.; Puchlopek, A. L. A.; Miller, S. J. Enantioselective sulfonylation reactions mediated by a tetrapeptide catalyst. *Nat. Chem.* **2009**, *1*, 630.

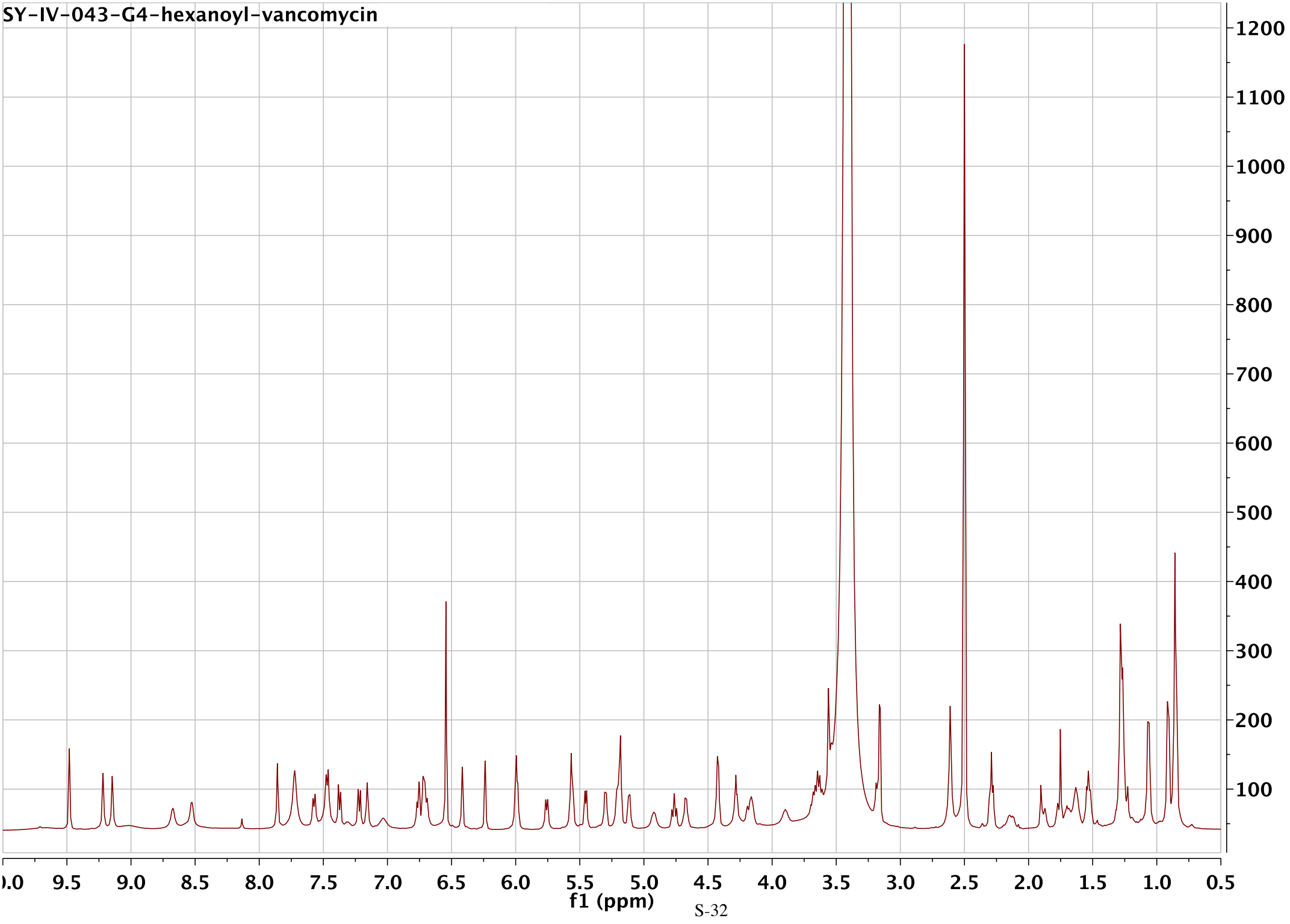
[3] Kerns, R.; Dong, S. D.; Fukuzawa, S.; Carbeck, J.; Kohler, J.; Silver, L.; Kahne, D. The role of hydrophobic substituents in the biological activity of glycopeptide antibiotics. *J. Am. Chem. Soc.* **2000**, *122*, 12608.

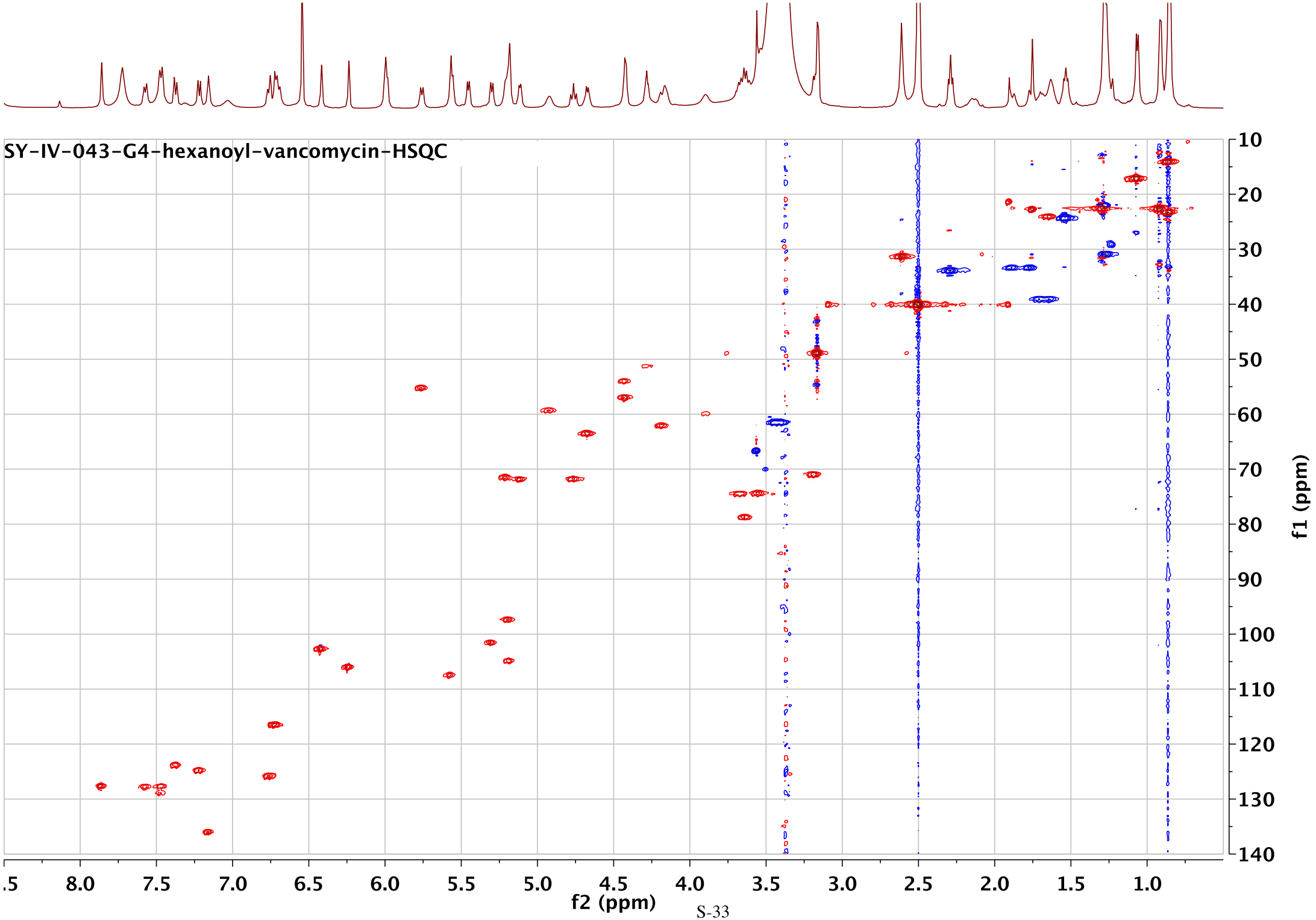

SY-IV-053-G4-butyryl-vancomycin
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

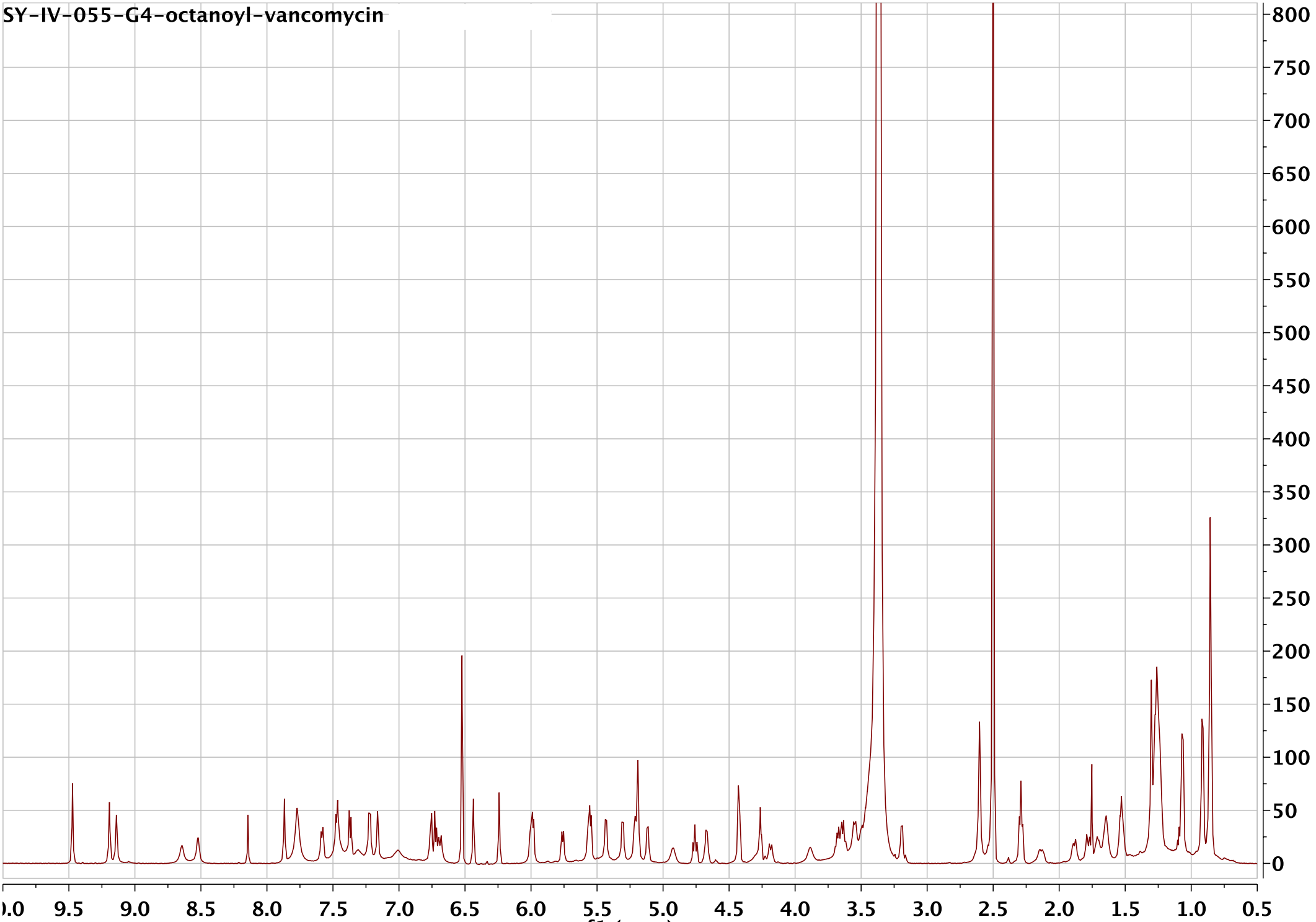

SY-IV-053-G4-butyryl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
10
20
30
40
50
60
70
80
90
100
110
120
130
140

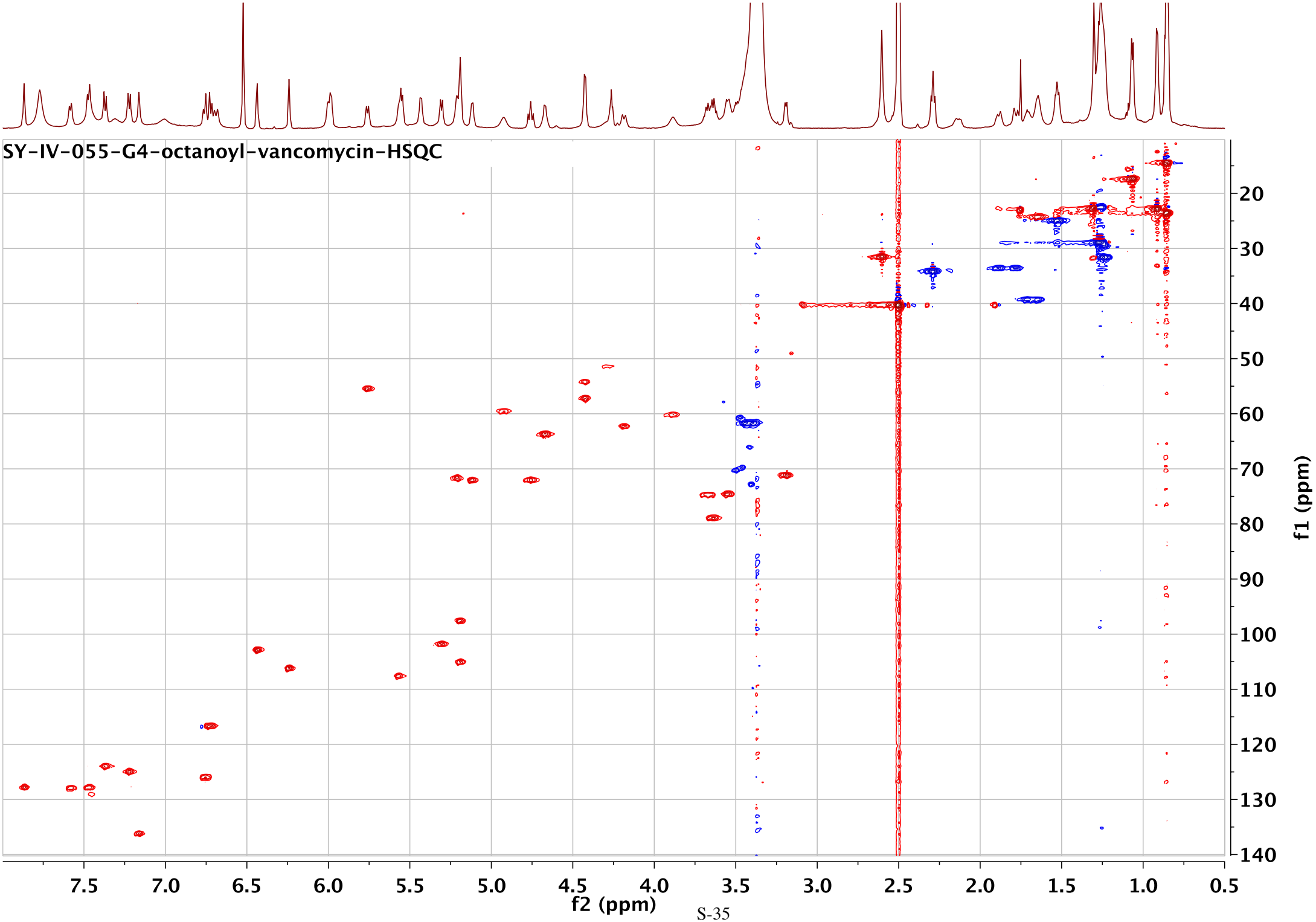

SY-III-259-G4-pentanoyl-vancomycin
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

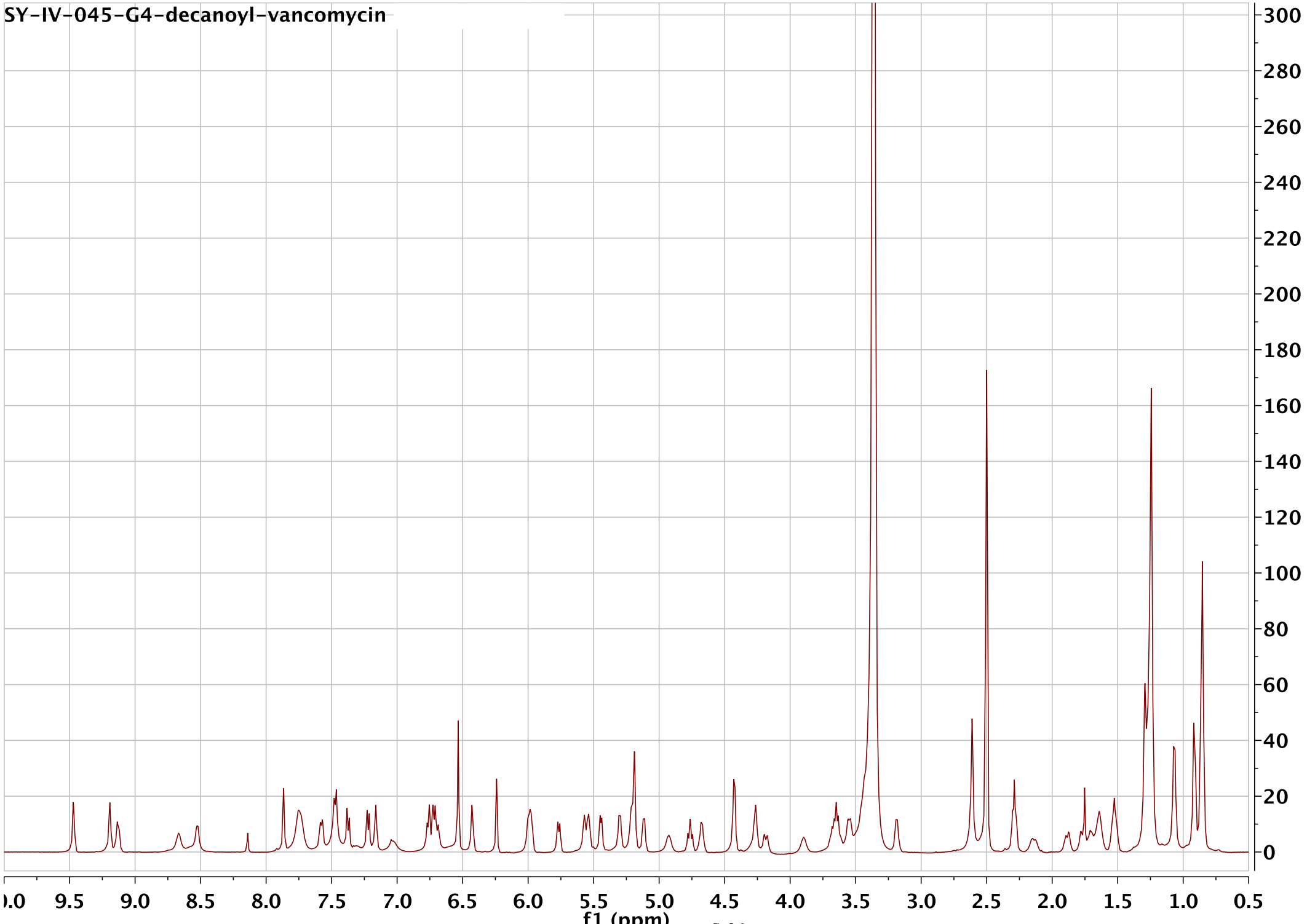

SY-IV-067-G4-pentanoyl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
10
20
30
40
50
60
70
80
90
100
110
120
130
140

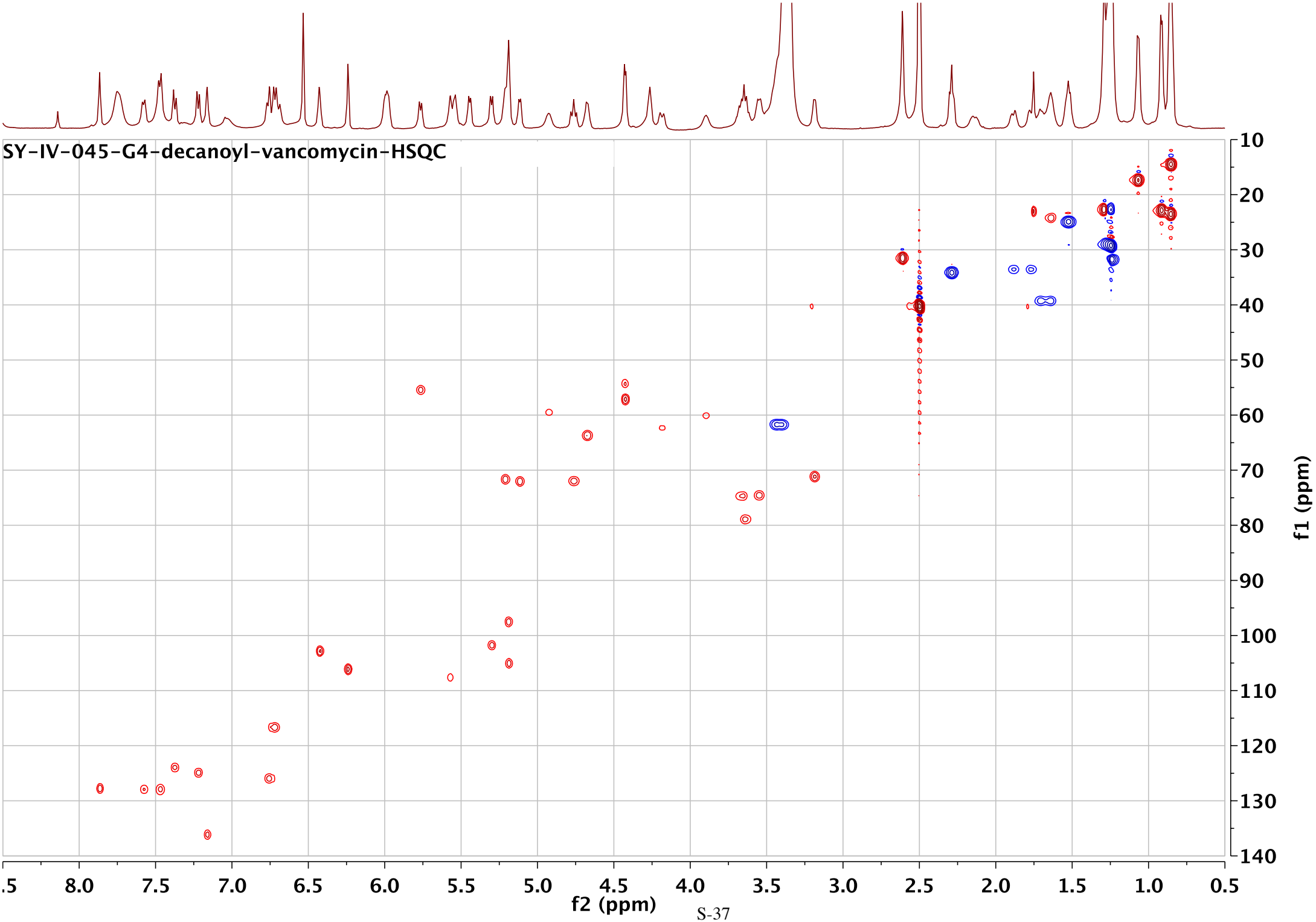

SY-IV-043-G4-hexanoyl-vancomycin
1200
1100
1000
900
800
700
600
500
400
300
200
100
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

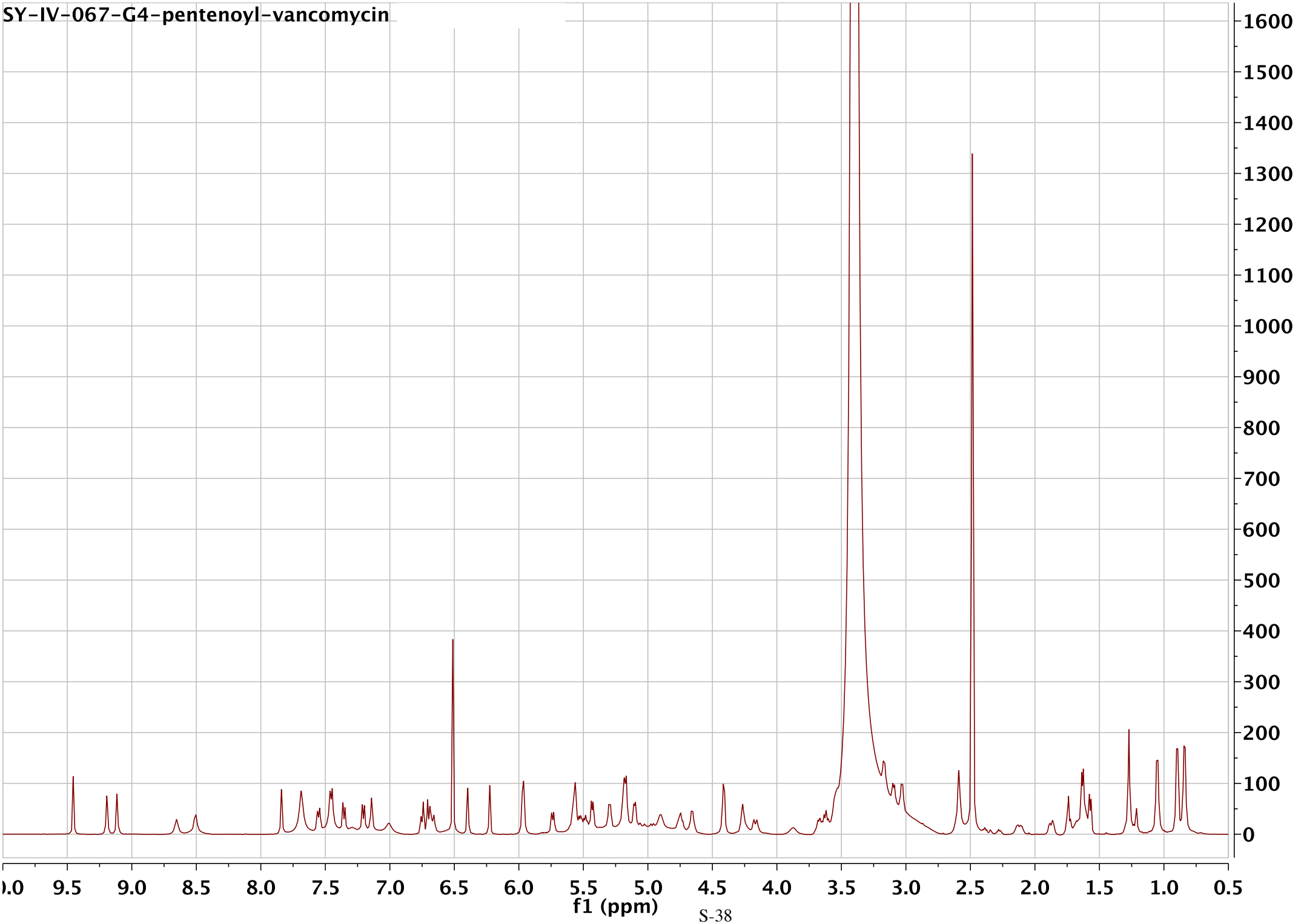

SY-IV-043-G4-hexanoyl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
10
20
30
40
50
60
70
80
90
100
110
120
130
140

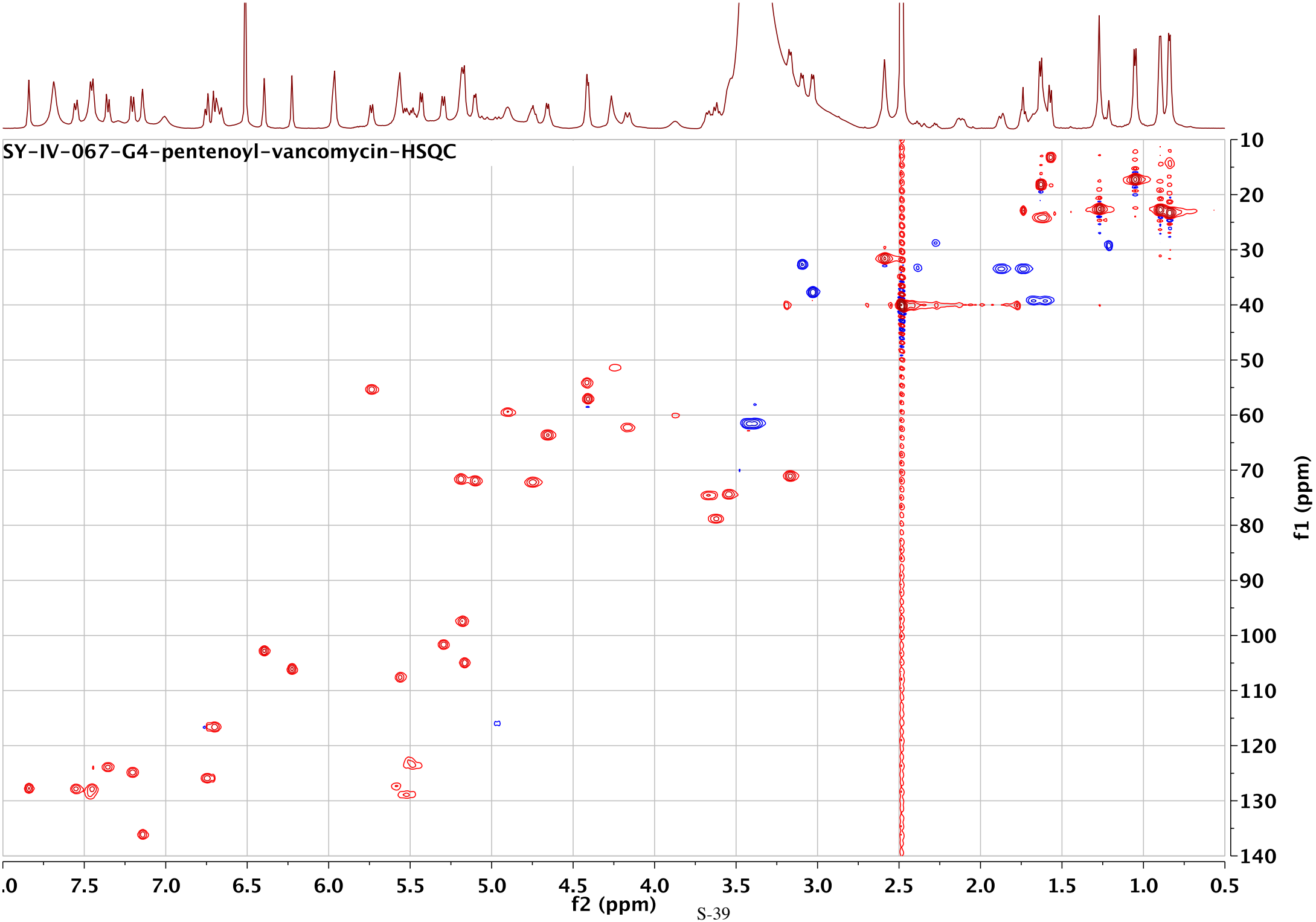

SY-IV-055-G4-octanoyl-vancomycin
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

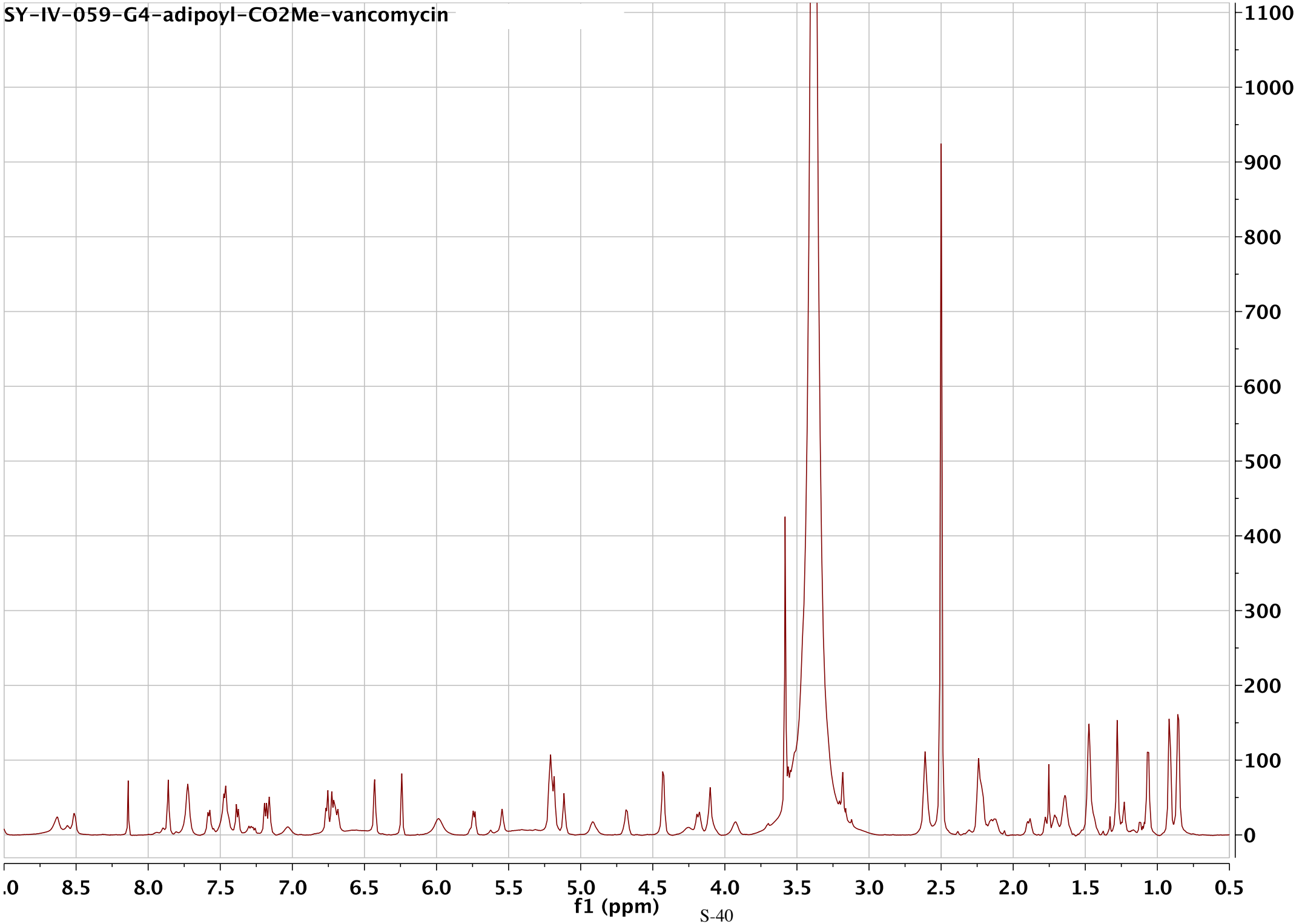

SY-IV-055-G4-octanoyl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
20
30
40
50
60
70
80
90
100
110
120
130
140

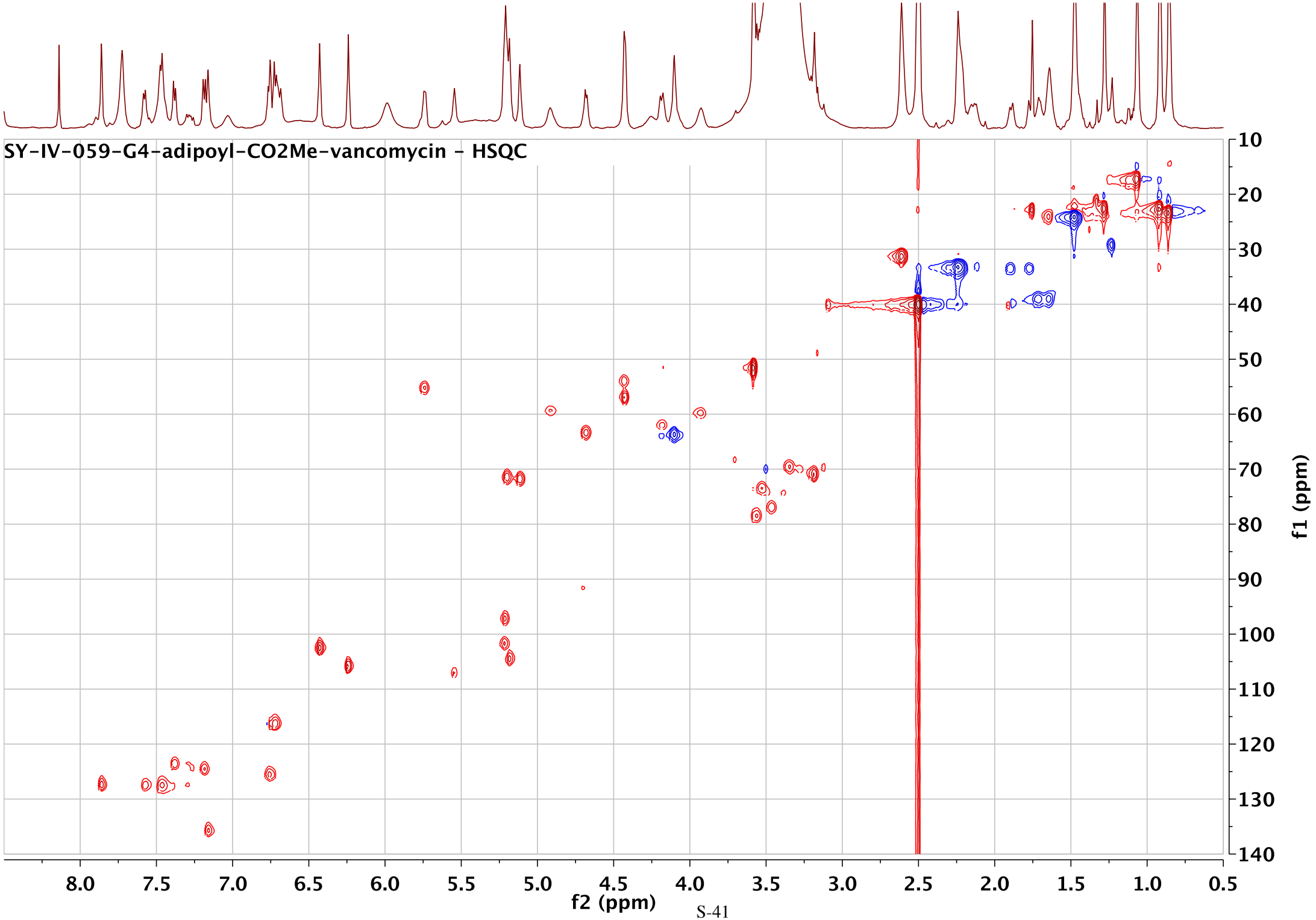

SY-IV-045-G4-decanoyl-vancomycin
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


SY-IV-045-G4-decanoyl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
10
20
30
40
50
60
70
80
90
100
110
120
130
140


SY-IV-067-G4-pentenoyl-vancomycin
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


SY-IV-067-G4-pentenoyl-vancomycin-HSQC
f2 (ppm)
f1 (ppm)
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
10
20
30
40
50
60
70
80
90
100
110
120
130
140


SY-IV-059-G4-adipoyl-CO2Me-vancomycin
1100
1000
900
800
700
600
500
400
300
200
100
0
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


SY-IV-059-G4-adipoyl-CO2Me-vancomycin - HSQC
f2 (ppm)
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
10
20
30
40
50
60
70
80
90
100
110
120
130
140