Supplementary Information (SI) for Organic & Biomolecular Chemistry.
This journal is © The Royal Society of Chemistry 2025

Supporting Information

for

Total synthesis of Griseocazine D2 and D3

Subhasish Pradhan[1] and Rajesh Viswanathan*

* Corresponding Author: Rajesh Viswanathan

E-mail Address: rajesh@lab.iisertirupati.ac.in

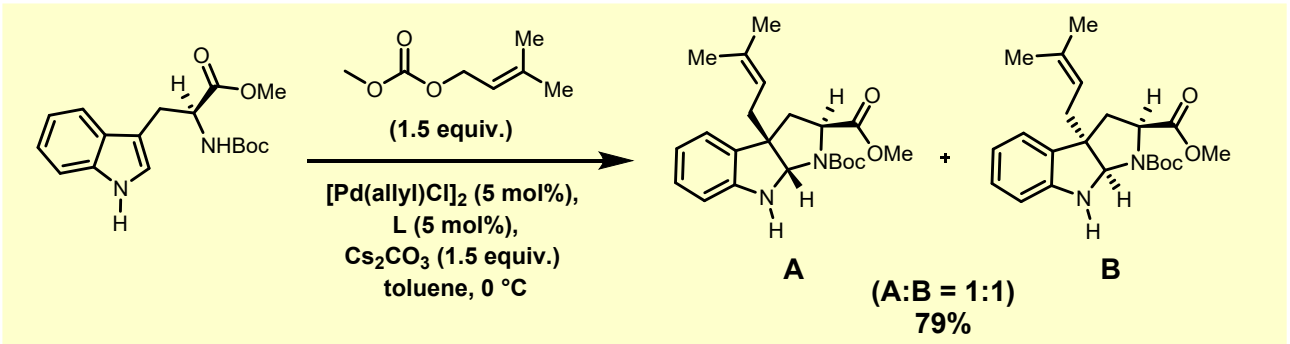
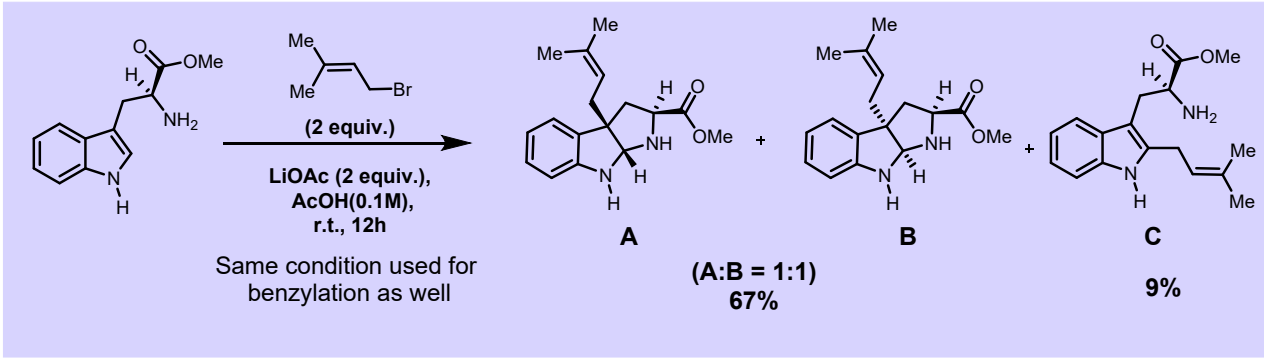
Table of contents

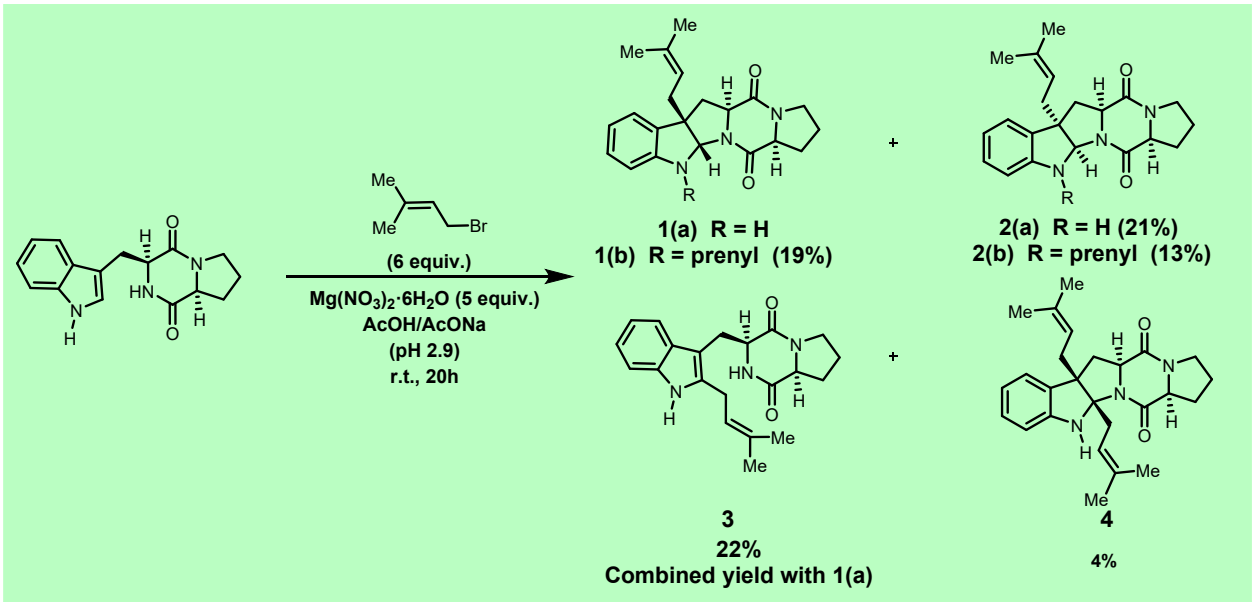
Abbreviations

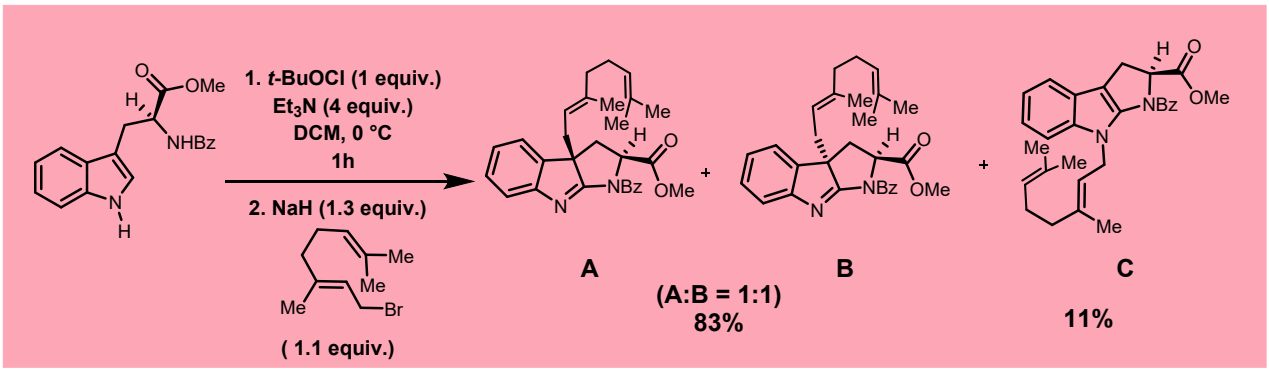
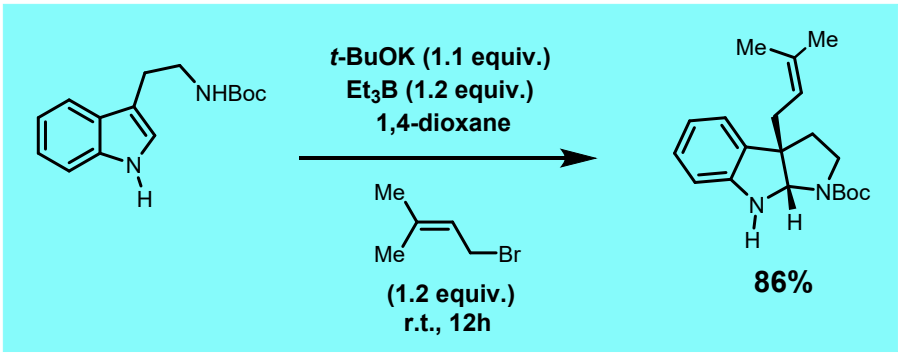
ACN	Acetonitrile
BINOL	1,1′-Bi-2-naphthol
Boc anhydride	tert-butyloxycarbonyl anhydride
BOP-chloride	Bis-(2-oxo-3-oxazolidinyl) phosphinic chloride
$CDCl_3$	Deuterated Chloroform
CD_3OD	Deuterated Methanol
DCM	Dichloromethane
DKP	2,5-Diketopiperazine
EtOAc	Ethyl Acetate
HCl	Hydrochloric Acid
MeOH	Methanol
MHz	MegaHertz
mmol	Millimole
µL	Microlitre
$NaHCO_3$	Sodium Bicarbonate
Na_2SO_4	Sodium Sulphate

NMR	Nuclear Magnetic Resonance
NOESY	Nuclear Overhauser Effect Spectroscopy
$[Pd(allyl)Cl]_2$	Allyl palladium chloride dimer
PMA (stain)	Phosphomolybdic acid
RT	Room temperature
THF	Tetrahydrofuran
TMS	Tetramethyl silane
Trp	Tryptophan
Trp-OMe	Tryptophan methyl ester

Table S1: - Comparative Synthetic methods for achieving C3-normal isoprenylation.

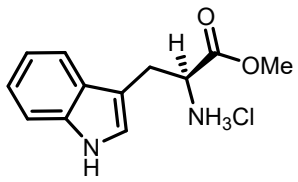
S.No.	Electrophile	Condition	Yields of the Products.	References
				
1	Methyl prenyl carbonate	$[Pd(allyl)Cl]_2$ (5 mol%), L (5 mol%), Cs_2CO_3 (1.5 equiv.) toluene, 0 °C	79% A: B (> 19.:1)	Tu, HF.; Zhang, X.; Zheng, C. *et al*. Enantioselective dearomative prenylation of indole derivatives. *Nat. Catal*. **2018**,*1*, 601–608.
				
2	Prenyl bromide	LiOAc (2 equiv.), AcOH (0.1M),	67% A: B= 1:1	1. Thandavamurthy, K.; Sharma, D.; Porwal, S. K.; Ray,

		r.t., 12h	C 9%	D.; Viswanathan, R. Regioselective Cope Rearrangement and Prenyl Transfers on Indole Scaffold Mimicking Fungal and Bacterial Dimethylallyltryptophan Synthases. *J. Org. Chem.* **2014**, *79*, 10049-10049. 2. Khopade, T. M.; Ajayan, K.; Joshi, S. S.; Lane, A. L.; Viswanathan, R. Bioinspired Brønsted Acid-Promoted Regioselective Tryptophan Isoprenylations. *ACS Omega* **2021**, *6*, 10840– 10858
				
3	Prenyl	$Mg(NO_3)_2$ 6H_2	1(b) 19%	Caballero, E.; Avendañ o,

	bromide	O AcOH/AcONa	2(a) 21% 2(b) 13% 3 with 1(a) 22% (4) 4%	C.;Menéndez, J. C. Brief Total Synthesis of the Cell Cycle InhibitorTryprostatin B and Related Preparation of Its Alanine Analogue. *J.Org. Chem*. **2003**, *68*, 6944−6951.
				
4	Geranyl bromide	1. *t*-BuOCl, Et_3N, DCM, 0 °C, 1h (cyclised product) 2. NaH, THF, 0 °C, 5h	83% (A: B= 47:36) (C3-geranylated product) 11% (N-alkylation of indole nitrogen)	Okada M.; Sato I.; Jeong Cho S.; Dubnau D.; Sakagami Y. 2006. Chemical synthesis of ComX pheromone and related peptides containing isoprenoidal tryptophan residues. *Tetrahedron*, **2006**, *62*, 8907–8918.
				
5	Prenyl	*t*-BuOk (1.1	86%	Lin, A.; Yang, J.; Hashim, M. N-

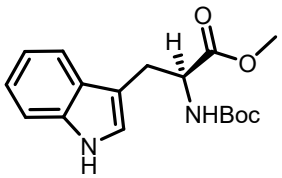
	bromide	equiv.) Et_3B (1.2 equiv.) 1,4-dioxane, r.t., 12h		Indolyltriethylborate: A Useful Reagent for Synthesis of C3-Quaternary Indolenines. *Org. Lett.* **2013**, *15*, 1950−1953.

1. **L-Trp-OMe-HCl:**



To Magnetically stirring solution of L-Trp (20g, 97.93 mmol, 1.0 equiv.) with excess methanol, Thionyl chloride (17.76 ml, 244.82 mmol, 2.5 equiv.) was added dropwise by dropping funnel at 0 °C (under ice bath). After completion of the addition, reflux the solution at 60 °C for 18 h. After complete conversion, evaporate the excess methanol under Rota Vap. This led to the formation of a solid compound (25 g, 98.15 mmol, 100.22% yield) of white colure due to the formation of the hydrochloride salt. Data: mp 204–209 °C. $[\alpha]_D^{20}$ +17.8 (*c* 0.52, CH_3OH). ^1H NMR (400 MHz, CD_3OD) δ 7.44 (dt, *J* = 7.8, 1.0 Hz,1H), 7.29 (dt, *J* = 8.2, 0.9 Hz, 1H), 7.10 (s, 1H), 7.04 (m, 1H), 6.97 (m, 1H), 4.23 (dd, *J* = 7.4, 5.5 Hz,1H), 3.70 (s, 3H), 3.40 – 3.33 (m, 1H), 3.28 (d, *J* = 7.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, CD_3OD) δ 169.4, 136.9, 126.7, 124.1, 121.5, 118.9, 117.4, 111.2, 106.0, 53.2, 52.2, 26.1. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{12}H_{15}N_2O_2$ 219.1128; found 219.1127.

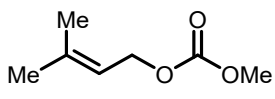
2. **Methyl (tert-butoxy carbonyl)-L-tryptophanate:**



To an ice-cold solution of HCl salt of ester (4g, 15. 17 mmol, 1 equiv.) and triethylamine (2.85 ml, 20.42 mmol, 1.30 equiv.) in 100 ml of DCM, Boc anhydride

(4.33 ml, 18.84 mmol, 1.20 equiv.) was added dropwise. After complete addition, let the reaction mixture stir for 16 h at RT. Excess DCM was evaporated after quenching the reaction mixture with adding 1N HCl solution; the resulting residue was dissolved in ethyl acetate, washed with brine, and dried over anhydrous sodium sulphate. On concentration of organic phase dense honey-type product was observed (4.75 g, 14.92 mmol, 95 % yield). Then, it is directly used for subsequent reactions without purification. Data: mp 150-153 °C. $[\alpha]_D^{20}$ +45.5 (*c* 0.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.23 – 7.15 (m, 1H), 7.16 – 7.07 (m, 1H), 6.99 (d, *J* = 2.1 Hz, 1H), 5.09 (d, *J* = 8.2 Hz, 1H), 4.65 (dd, *J* = 8.4, 5.2 Hz, 1H), 3.68 (s, 3H), 3.29 (dd, *J* = 5.6, 2.8 Hz, 2H), 1.43 (s, 9H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 172.8, 155.2, 136.1, 127.6, 122.7, 122.2, 119.6, 118.7, 111.2, 110.1, 79.8, 54.2, 52.2, 28.3,28.0. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{17}H_{22}N_2O_4$ 319.1653; found 319.1652.

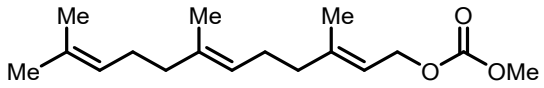
3. **methyl (3-methylbut-2-en-1-yl) carbonate:**



Methyl Chloroformate (2.16ml, 27.86 mmol, 1.2 equiv.) was added dropwise to the solution of prenyl alcohol (2.38 ml, 23.22 mmol, 1 equiv.), pyridine (5.61 ml, 69.66 mmol, 3 equiv.) in 0.2 M dry DCM under ice bath, then the reaction stirred for 5hr

in RT. After that, 100ml of 1N HCl was added to quench the reaction. The organic phase was washed with brine and dried over anhydrous sodium sulphate. The product (3.1g, 21.50 mmol, 92.6% yield) was purified by column chromatography using (10% EtOAc/Hexane) solvent system. Data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.35 (t, *J* = 7.3, 1.4 Hz, 1H), 4.61 (d, *J* = 7.3 Hz, 2H), 3.75 (s, 3H), 1.74 (s, 3H), 1.70 (s,3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 155.8, 140.0, 118.0, 64.6, 54.6, 25.7, 18.0. HRMS(ESI) m/z: [M + H] $^{+}$ calcd. for $C_7H_{12}O_3$ 145.0860; found 145.0866.

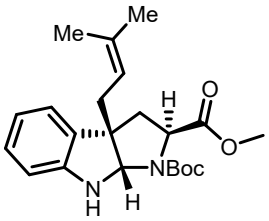
4. **methyl ((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl) carbonate:**



To an ice-cold solution of commercially available pure (E, E)-farnesol (5.64ml, 22.48 mmol, 1equiv.), pyridine (5.43ml, 67.45 mmol, 3 equiv.) in 0.2 M dry DCM, methyl chloroformate (2.09ml, 26.98 mmol,3 equiv.) was added dropwise. Then, the reaction mixture was allowed to stir for 5hr in rt. The reaction was quenched by the addition of 150ml of 1N HCl solution. The organic phase was washed with brine and dried over anhydrous sodium sulphate. The product (5.2g, 18.54mmol, 82.48% yield) was purified by column chromatography (10% EtOAc/Hexane) solvent mixture as eluent. Data: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (tq, *J* = 7.2, 1.4 Hz, 1H), 5.08(tq, *J* = 5.3, 1.5 Hz, 2H), 4.65 (d, *J* = 7.2 Hz, 2H), 3.77 (s, 3H), 2.07 (dq, *J* = 16.2, 7.9 Hz, 6H), 1.97 (dd, *J* = 9.2, 6.1 Hz, 2H), 1.72

(s, 3H), 1.67 (s, 3H), 1.59(s, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 155.8, 143.2, 135.5, 131.3, 124.3, 123.5, 117.7, 64.7, 54.6, 39.6, 39.5, 26.7, 26.1, 25.6, 17.6, 16.5, 16.0. HRMS(ESI) m/z: [M + Na] $^{+}$ calcd. for $C_{17}H_{28}O_3$ 303.1931; found 303.1947.

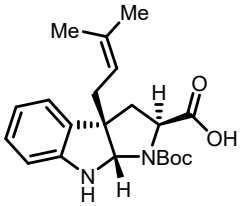
5. **1-(tert-butyl) 2-methyl (3aS,8aS)-3a-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b] indole-1,2(2H)-dicarboxylate:**



Solution of prenyl carbonate (0.67g, 4.71mmol, 1.5 equiv.) in 10 ml of dry toluene was added dropwise to an ice-cold solution of L-Trp-OMe -NHBoc (1g, 3.14 mmol, 1equiv.), ***R***-ligand (84.27mg, 0.15mmol, 0.05equiv.), $[Pd(allyl)Cl]_2$ (57.44mg ,0.15mmol, 0.05 equiv.), Cesium carbonate (1.5g, 4.71 mmol, 1.5 equiv.) in 60ml of dry toluene. The reaction mixture was allowed to stir for 16 hours at 0 °C; after that, the reaction was quenched by the addition of distilled water. The compound was extracted using EtOAc as an organic phase, washed with brine, and dried over anhydrous sodium sulphate. The mixture was loaded to a column and separated by using (10% EtOAc/Hexane) solvent system. Yellow-colored oil of (1g, 2.59mmol, 82% yield) formed under reduced pressure with a trace amount of another isomer **(> 19:1 dr)**. Data: $[\alpha]_D^{20}$ -252.45 (*c* 0.24, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (m, *J* = 15.0, 7.4, 3.5, 1.3 Hz, 1H), 6.75 (m, *J* = 7.5, 3.3, 1.0

Hz, 1H), 6.62 (dd, *J* = 11.0, 7.8 Hz, 1H), 5.20 (d, *J* = 27.5 Hz, 1H), 5.16 – 5.08 (m, 1H), 4.08 – 3.97 (m, 1H), 3.73 (s, 3H), 2.53 (m, *J* = 12.6, 7.5 Hz, 1H), 2.35 (m, *J* = 14.5, 14.0, 7.3 Hz, 2H), 2.17 (ddd, *J* = 12.9, 8.8, 4.2 Hz, 1H), 1.69 (s, 3H), 1.52 (s, 3H), 1.43 (9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 173.6, 153.6, 148.4, 135.3, 132.1, 128.4, 123.2, 119.1, 118.9, 109.7, 80.9, 59.4, 57.0, 56.0, 52.1, 38.9, 28.6, 28.2, 25.9, 17.9. HRMS(ESI) m/z: [M + H] $^{+}$ calcd. for $C_{22}H_{30}N_2O_4$ 387.2279; found 387.2293.

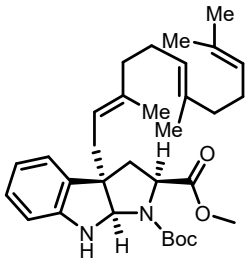
6. **(3aS)-1-(tert-butoxycarbonyl)-3a-(3-methylbut-2-en-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylic acid:**



LiOH (1234g, 5.14mmol, 4equiv.) was added to the solution of C3-Prenylated ester (0.5g, 1.29mmol, 1equiv.) in (1:1:1; by vol.) MeOH: H_2O: THF at 0 °C, then reaction mixture allowed to stir overnight at RT. 1N HCl was added after the completion of the reaction to quench the reaction. The compounds are extracted using DCM as an organic phase, washed with brine, dried over anhydrous sodium sulphate, and loaded into a column. The product spot was isolated by using (2% MeOH/DCM) solvent mixture. A white foamy product (0.3g, 0.805 mmol, 62.3% yield) formed under reduced pressure. Data: $[\alpha]_D^{20}$ - 156.47 (*c* 0.55, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 – 7.05 (m, 2H), 6.80 – 6.71 (m, 1H), 6.63 (dd, *J* = 12.4, 7.8 Hz, 1H), 5.22 (d, *J* = 27.6 Hz,

1H), 5.17 – 5.08 (m, 1H), 4.41-3.99 (m, 1H), 2.59 (ddd, *J* = 19.5, 12.8, 7.7 Hz,1H), 2.38 (m, 2H), 2.30-2.22 (m, 1H), 1.70(3H), 1.53 (s, 3H), 1.45 (9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 179.0, 153.8, 148.6, 135.4, 132.1, 128.5, 123.1, 118.8, 109.7, 81.3, 81.1, 59.3, 56.2, 39.2, 35.4, 28.6, 28.2, 25.9, 17.9. HRMS(ESI) m/z: [M + H] $^{+}$ calcd. for $C_{21}H_{28}N_2O_4$ 373.2122; found 373.2130.

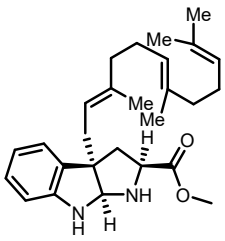
7. **1-(tert-butyl) 2-methyl (2S,3aR,8aR)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate.**



2g (6.28 mmol, 1 equiv.) of L-Trp-OMe-NHBoc was taken in a 250ml flame-dried round RB, into the RB (***S)-*** ligand (0.16g, 0.314 mmol, 0.05 equiv.), $[Pd(prenyl)Cl]_2$ (0.11g, 0.314mmol, 0.0 5equiv.) were added under argon atmosphere. 60 ml of dry toluene was added to the flask under ice bath by maintaining 0 °C. A Solution of farnesyl carbonate (2.63g, 9.42mmol, 1.5equiv.) in 10 ml of dry toluene was added to the same reaction flask dropwise at the same temperature. Then, the reaction was allowed to stir at 0 °C for 16 hours. The reaction was quenched by the addition of distilled water, and the organic phase was extracted using EtOAc and dried over anhydrous sodium sulphate. The required product spot was isolated by column chromatography with a **dr 13.3: 1** using (10%

EtOAc/Hexane) solvent mixture. A colorless liquid (2.1g, 4.11 mmol, 67% yield) formed under reduced pressure. Data: $[\alpha]_D^{20}$ +137.71 (*c* 0.41, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 – 6.99 (m, 1H), 6.95 (dd, *J* = 7.4, 1.3 Hz, 1H), 6.64 (d, *J* = 1.0 Hz, 1H), 6.60 (m, 1H), 5.23 – 5.16 (m, 1H), 5.13 (s, 1H), 5.11 – 5.05 (m, 2H), 4.47 (ddd, *J* = 59.2, 8.8, 1.4 Hz, 1H), 3.15 (3H), 2.43 (m, 4H), 2.13 – 1.92 (m, 8H), 1.67 (s, 3H), 1.59 (s, 6H), 1.55 (s, 3H), 1.46 (9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.2, 154.1, 149.9, 138.9, 135.1, 131.3, 128.5, 124.3, 124.0, 123.4, 118.7, 118.3, 109.3, 80.9, 80.6, 80.3, 59.6, 59.2, 57.2, 56.2, 51.9, 51.7, 39.9, 39.7, 38.5, 35.3, 28.6, 28.3, 26.7, 26.5, 25.7, 17.7, 16.3, 16.0. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{32}H_{47}N_2O_4$ 523.3531; found 523.3549.

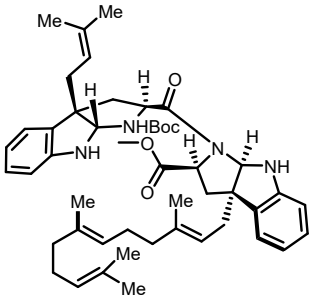
8. **methyl (2S,3aR,8aS)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate.**



3.40ml of CAN, TMSI (15.30 mmol, 8 equiv.) was added dropwise to the ice-cold solution of Boc-protected C3-farnesyl pyrroloindoline methyl-ester (1g, 1.91 mmol, 1 equiv.) over 5 min. After the reaction, it was quenched by dropwise addition of sodium thiosulphate. DCM was used to extract the organic phase, which was dried over anhydrous sodium sulphate. Column chromatography separated the product using 100-200 silica mesh and (5%

MeOH/DCM) solvent mixture. The compound slightly reddish oily nature (0.5g, 1.18 mmol, 61.84% yield) was obtained under reduced pressure. Data: $[\alpha]_D^{20}$ +90.1 (*c* 0.02, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (dd, *J* = 7.2, 3.6 Hz, 2H), 6.69 (t, *J* = 7.4 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 1H), 5.15 (m, 1H),5.08(m, 2H) 4.81 (s, 1H), 3.87 (dd, *J* = 7.7, 3.5 Hz, 1H), 3.33 (s, 3H), 2.41 (m, 5H), 1.99 (m, 9H), 1.68 (s, 3H), 1.60 (s, 3H), 1.58 (s, 3H),1.55(s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 174.5, 149.5, 138.3, 138.2, 135.2, 133.5, 131.4, 128.2, 125.0, 124.4, 124.1, 123.9, 119.8, 119.6, 118.9, 109.6, 82.6, 60.2, 57.8, 52.0, 41.2, 40.3, 40.0, 39.8, 36.5, 26.9, 25.8, 23.5, 17.8, 16.4, 16.1. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{27}H_{39}N_2O_2$ 423.3007; found 423.3011.

9. **tert-butyl (2S,3aS,8aS)-2-((2S,3aR,8aR)-2-(methoxycarbonyl)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1-carbonyl)-3a-(3-methylbut-2-en-1-yl)-1,2,3,3a,8,8a-hexahydro-1l4-pyrrolo[2,3-b]indole-1-carboxylate.**

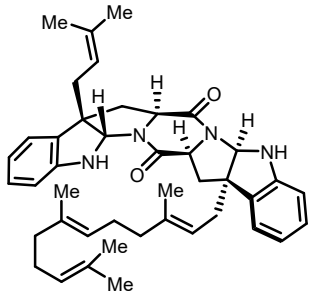


Boc protected-C3′-prenyl pyrroloindoline methyl acid (0.1g, 0.268 mmol, 1 equiv.) was loaded in a syringe pump for slow addition, over 16hr to a flame-dried RB having amine (Boc deprotected-C3-farnesyl-methyl-ester) (0.22g, 0.53 mmol, 2 equiv.), Collidine (80 µl,

0.616 mmol, 2.3 equiv.) and BOP-Cl (0.15g, 0.616 mmol, 2.3 equiv.) in 10 ml of dry DCM. After the addition, the reaction mixture was allowed to stir for more than 6 hours. The reaction mixture was quenched by adding sodium bicarbonate solution, extracted using DCM as the organic phase, and dried over anhydrous sodium sulphate. The required product was isolated using (25%-30% EtOAc/Hexane) solvent mixture a colourless oily compound (0.13g, 0.16 mmol, 65% yield). Data: $[\alpha]_D^{20}$ +6.82 (*c* 0.41, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 – 7.03 (m, 2H), 7.04 – 6.93 (m, 2H), 6.84 – 6.46 (m, 4H), 5.37 – 5.28 (m, 1H), 5.27 – 5.20 (m, 1H), 5.18 – 5.01 (m, 3H), 4.91 (d, *J* = 8.9 Hz, 1H), 4.32 (d, *J* = 7.8 Hz, 1H), 4.06 (m, 1H) 3.26 – 3.07 (m, 3H), 2.60 (m, 1H), 2.39 (m, 4H), 2.31 (d, *J* = 7.1 Hz, 2H), 2.12 – 1.81 (m, 7H), 1.71 – 1.66 (m, 6H), 1.60 (m, 3H), 1.58 – 1.48 (m, 6H), 1.45 (m, 3H), 1.41 (m, 9H). ^{13}C{H} NMR (101 MHz, $CDCl_3$) δ 172.0, 170.9, 154.9, 153.8,149.7, 148.9, 148.5, 139.2, 135.3, 135.1, 132.9,132.7, 132.0, 131.3, 128.8, 128.3, 124.2, 123.9,123.6, 123.1, 120.2, 118.9, 118.6, 118.1, 110.7, 109.7,109.3, 109.0, 81.8, 81.7, 80.6, 59.0, 58.8, 58.3, 58.0, 56.1, 55.4, 54.6, 52.3, 51.9, 40.2, 39.7, 38.8, 37.7, 36.6, 35.6, 35.7, 35.6, 28.6, 28.4, 26.7, 26.5, 25.9, 25.7, 17.9, 17.7, 16.3, 16.0.

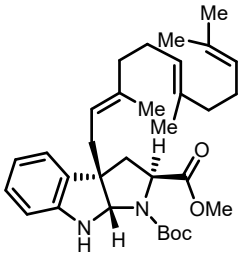
HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{48}H_{65}N_4O_5$ 777.4950; found 777.4963.

10. Griseocazine D2:



A slurry was made up of 0.13g of peptide (0.16 mmol, 1equiv.) with a pinch of 230-400 mesh silica gel in DCM. Then, it was stirred and heated at 170 °C for 30 min. After the reaction (monitored by TLC) the reaction mixture was directly loaded to column chromatography to separate the required product. The product (94mg, 0.14 mmol, 88% yield) was isolated by a 25-30% mixture of EtOAc and Hexane as an eluent. Data: $[\alpha]_D^{20}$ -51.447 (*c* 0.31, DCM). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.16 (d, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 7.2 Hz, 1H), 6.97 (q, *J* = 7.7 Hz, 2H), 6.65 (d, *J* = 7.5 Hz, 1H), 6.61 (dd, *J* = 7.6, 3.6 Hz, 2H), 6.56 (d, *J* = 7.9 Hz, 1H), 6.49 (d, *J* = 7.8 Hz, 1H), 6.47 (s, 1H), 5.21 (s, 1H), 5.14 (s, 1H), 5.12-4.90 (m, 4H), 4.70 – 4.53 (m, 1H), 4.13 – 4.02 (m, 1H), 2.55 (m, 1H), 2.45 (m, 2H), 2.35 (m, 3H), 2.16 (dd, *J* = 12.8, 11.0 Hz, 1H), 2.02 – 1.76 (m, 9H), 1.63 (s, 6H), 1.56 (s, 3H), 1.54 (s, 3H), 1.49 (d, *J* = 2.4 Hz, 6H). ^{13}C{H} NMR (101 MHz, DMSO-d_6) δ 167.2, 166.0, 149.6, 148.5, 137.6, 134.4, 133.9, 132.6, 131.3, 130.5, 128.0, 127.8, 124.1, 123.7, 123.0, 122.3, 119.5, 119.2, 117.7, 117.4, 108.7, 79.7, 78.0, 59.9, 58.5, 55.3, 55.2, 37.5, 35.3, 34.1, 26.1, 26.0, 25.7, 25.4, 17.7, 17.5, 16.1. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{42}H_{53}N_4O_2$ 645.4164 found; 645.4156.

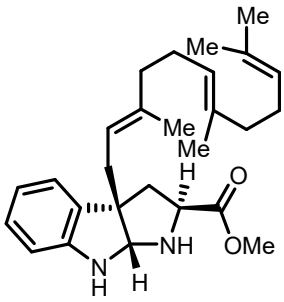
11. **1-(tert-butyl) 2-methyl (2S,3aS,8aS)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate:**



L-Trp-OMe-NHBoc (2g, 6.28mmol, 1equiv.) was taken in 250ml RB with 60ml of dry toluene. Into the RB ***R***-ligand (0.16g, 0.314 mmol, 0.05equiv.), $[Pd(prenyl)Cl]_2$ (0.11g, 0.314mmol, 0.05equiv.) were added under argon atmosphere. Solution of farnesyl carbonate (2.63g, 9.42mmol, 1.5equiv.) in 10 ml of dry toluene was then added to the same reaction flask dropwise in an ice bath. Then, the reaction was allowed to stir for 16 hr at 0 °C. Then, the reaction was quenched by the addition of distilled water. The resulting residue was dissolved in EtOAc, washed with brine, and dried over anhydrous sodium sulphate. The required product spot was isolated by column chromatography using (10% EtOAc/ hexane) solvent mixture. On concentration of organic phase under reduced pressure, a colorless oil of (2.5g, 4.78mmol, 76.2% yield) with a trace quantity of another product formed **(dr > 19:1)**. Data: $[\alpha]_D^{20}$ -213.82 (*c* 0.62, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (ddd, *J* = 7.4, 4.3, 2.8 Hz, 2H), 6.62 (td, *J* = 7.5, 4.9 Hz, 1H), 6.53 – 6.46 (m, 1H), 5.12 (d, *J* = 21.4 Hz, 1H), 5.08 – 5.04 (m, 1H), 5.03 – 4.97 (m, 2H), 4.01 – 3.87 (m, 1H), 3.62 (s, 3H), 2.44 (td, *J* =

12.8, 7.5 Hz, 1H), 2.27 (dq, J = 14.5, 7.3 Hz, 2H), 2.08 (ddd, J = 12.0, 8.7, 3.1 Hz, 1H), 1.92 (m, 8H), 1.57 (s, 3H), 1.50 (s, 6H), 1.43 (3H), 1.33 (9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 172.3, 152.4, 147.4, 137.6, 133.1, 130.9, 130.0, 127.3, 123.3, 123.0, 122.1, 117.8, 117.5, 108.5, 80.2, 79.5, 76.5, 76.2, 75.9, 58.3, 56.0, 55.0, 50.8, 38.7, 38.0, 34.3, 27.4, 27.0, 25.7, 25.5, 24.6, 16.6, 15.1, 14.9. HRMS(ESI) m/z: [M + H] $^{+}$ calcd. for $C_{32}H_{47}N_2O_4$ 523.3531; found 523.3548.

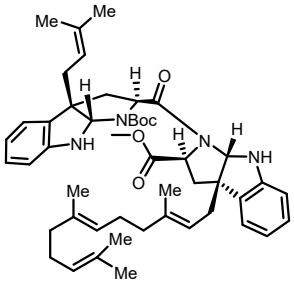
12. methyl (2S,3aS,8aR)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-2-carboxylate:



To an ice-cold solution of the above compound (0.5g, 0.95mmol, 1equiv.) in 30 ml of dry ACN, TMSI (1.08ml, 7.6mmol, 8equiv.) was added dropwise, then the reaction was allowed to stir at 0 °C for 30min. After fully converting the starting material, the reaction was quenched by adding sodium thiosulphate solution. DCM solvent was used as an extracting solvent, washed with brine dried over anhydrous sodium sulphate, and loaded into a column. The product was isolated by using (5% MeOH/DCM) solvent mixture. Slightly red color oily nature compound (0.285g, 0.674mmol, 70% yield) formed under reduced pressure. Data:

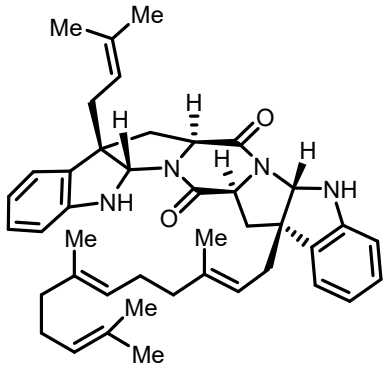
$[\alpha]_D^{20}$ -69.231 (*c* 0.15, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (t, *J* = 7.4 Hz, 2H), 6.72 (t, 1H), 6.57 (d, 3H), 5.16 – 5.03 (m, 2H), 4.91 (s, 1H), 3.71 (s, 4H), 2.45 (d, *J* = 7.3 Hz, 2H), 2.39 (dd, *J* = 12.0, 5.7 Hz, 1H), 2.09 – 2.01 (m, 11H), 1.68 (s, 3H), 1.59 (m, 6H), 1.55 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 174.2, 149.9, 138.2, 135.2, 135.1, 132.9, 131.5, 131.3, 128.1, 124.8, 124.3, 123.6, 119.7, 119.5, 109.0, 82.3,59.6, 59.4, 52.1, 44.2, 39.9, 36.8, 32.0, 26.7, 25.7, 23.4, 17.7, 16.3, 16.0. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{27}H_{39}N_2O_2$ 423.3007; found 423.3009.

13.tert-butyl (2S,3aS,8aS)-2-((2S,3aS,8aS)-2-(methoxycarbonyl)-3a-((2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-yl)-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b]indole-1-carbonyl)-3a-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate:



In a flame-dried RB, amine (223mg, 0.53 mmol, 2equiv.), BOP-Cl (156.5mg, 0.616 mmol, 2.3equiv.), 2,4,6-Collidine (80 µL, 0.616 mmol, 2.3 equiv.) was taken under argon atmosphere. To this RB 10ml dry DCM was added. In separate dried pear-shaped RB, acid (100mg, 0.268, 1equiv.) was taken and dissolved with 5ml dry DCM; then the acid solution was added to the RB containing amine dropwise by syringe pump over 14hr. The reaction mixture was again allowed to stir at room temperature for an extra 6hr after

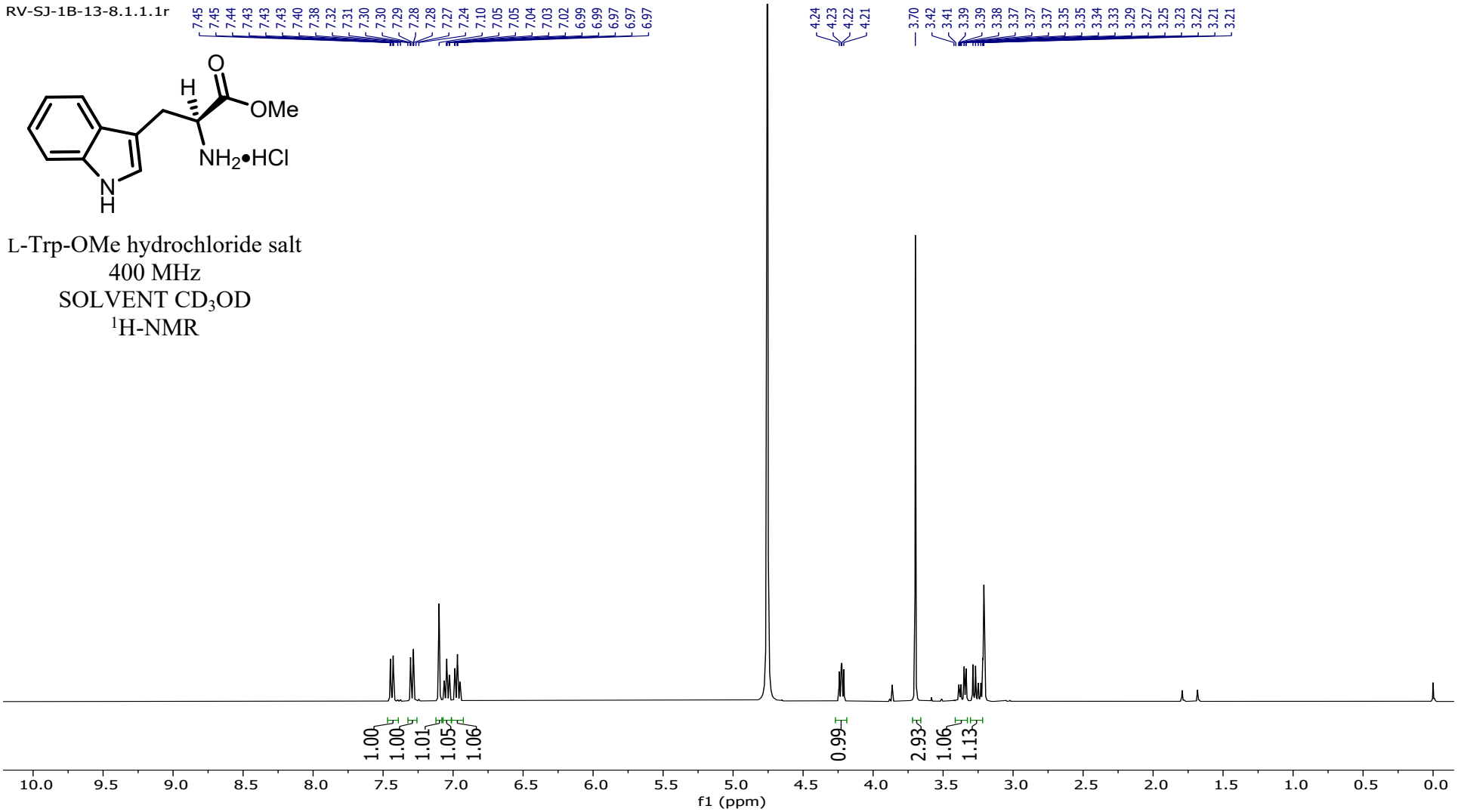
the reaction was quenched by the addition of $NaHCO_3$ solution and extracted through DCM, dried over anhydrous sodium sulphate. The required product spot was isolated through silica-gel chromatography by using (20% EtOAc/Hexane) solvent system. Colorless oily products (0.14g, 0.180 mmol, 67.1% yield) formed under reduced pressure. Data: $[\alpha]_D^{20}$ -256.410 (*c* 0.15, DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 – 6.98 (m, 4H), 6.76 (m, 2H), 6.63 (m, 2H), 6.52 – 6.46 (m, 1H), 5.32 – 5.25 (m, 1H), 5.21 (s, 1H), 5.17 – 5.03 (m, 4H), 4.92 (s, 1H), 4.50 – 4.36 (m, 1H), 4.13 (m, 1H), 3.73 (d, *J* = 19.1 Hz, 3H), 2.60 (m, 2H), 2.51 – 2.32 (m, 4H), 2.37 (m, 1H), 2.26 (m, 1H), 2.06 – 1.94 (m,8H), 1.68 (d, *J* = 5.2 Hz, 6H), 1.63 (s, 6H), 1.59 (m, 3H), 1.51(s, 9H), 1.46 (s, 3H), 1.34 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 172.6, 172.1, 154.2, 149.8, 148.1, 147.5, 138.9, 135.2, 1349, 132.7, 131.2, 128.6, 128.4, 124.3, 124.0, 123.5, 122.9, 119.1, 118.7, 110.3, 109.3, 81.5, 81.4, 81.2, 59.8, 58.4, 58.2, 57.4, 55.9, 52.1, 40.0, 39.7, 39.4, 36.0, 35.8, 28.7, 26.8, 25.9, 25.7, 17.9, 17.7, 16.5, 16.4, 16.0. HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{48}H_{65}N_4O_5$ 777.4950; found 777.4957.



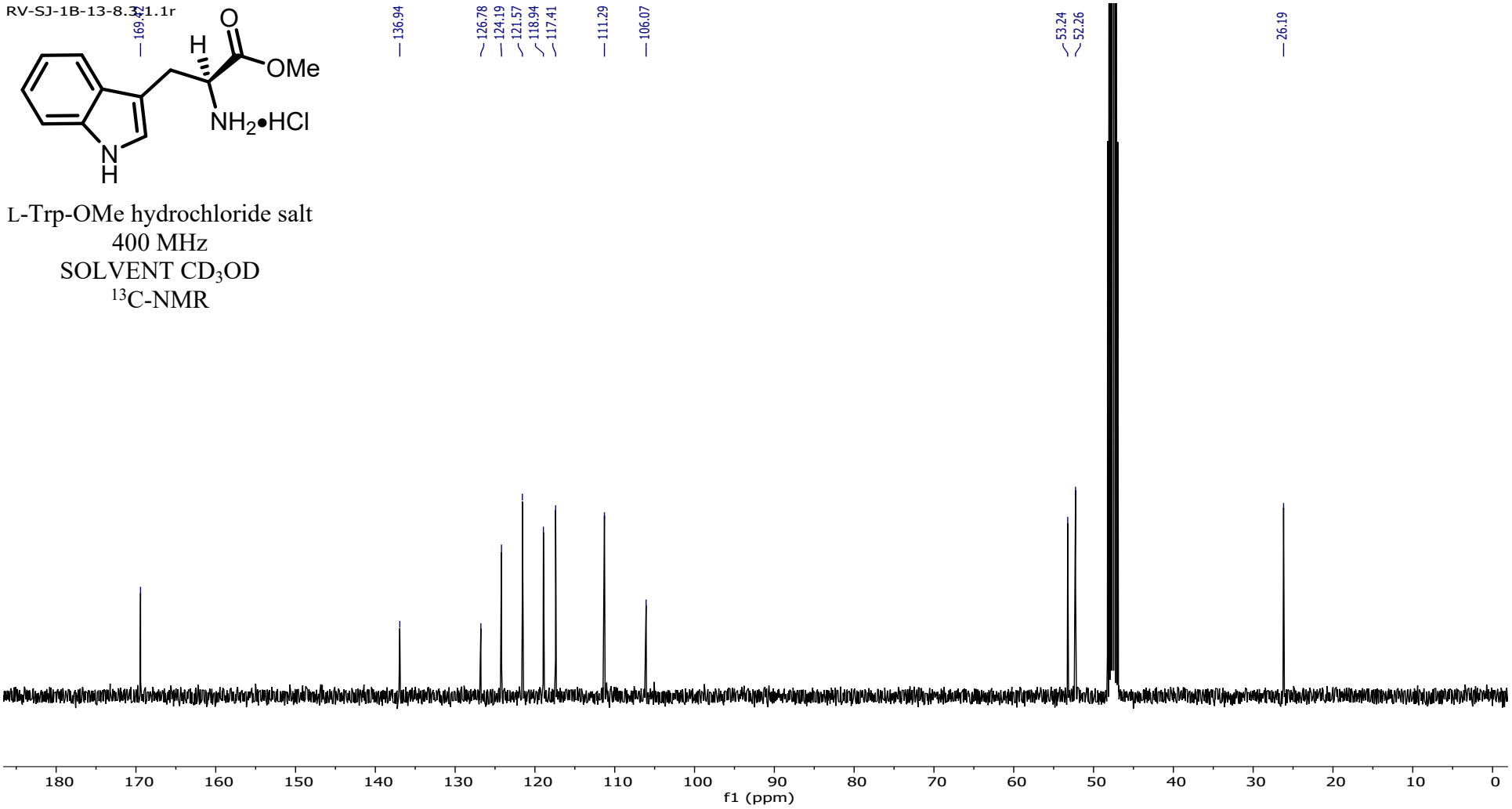
14.Griseocazine D3:

The slurry of peptide (50mg, 0.064 mmol, 1equiv.) was made by using 230-400 mesh silica in 5ml of dry DCM in a 50ml of oven-dried RB and then magnetically

stirred in 170 °C for 30min. (formed powder). After that, directly loaded to silica gel chromatography, the product was isolated by (25% EtOAc/Hexane) solvent mixture. A colorless oil product (37mg, 0.057 mmol, 90.5 % yield) was formed under reduced pressure. Data: $[\alpha]_D^{20}$ -495.667 (*c* 0.6, DCM). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.10 (m, 2H), 6.94 (m, 2H), 6.58 (m, 2H), 6.50 (m, 2H), 6.36 (m, 2H), 5.25 – 5.15 (m, 2H), 5.08 (m, 4H), 3.99 (dd, *J* = 10.8, 6.4 Hz, 2H), 2.46 (dt, *J* = 12.6, 6.6 Hz, 2H), 2.34 (m, 4H), 2.18 (m, 2H), 2.06 – 1.87 (m, 8H), 1.64 (s, 6H), 1.56 (s, 6H), 1.49 (s, 6H). ^{13}C{H} NMR (101 MHz, DMSO-d_6) δ 165.5, 149.8, 137.4, 134.3, 133.8, 131.2, 131.1, 130.6, 128.0, 124.1, 123.9, 122.9, 119.2, 119.1, 117.6, 117.5, 108.5, 78.5, 78.3, 59.4, 59.3, 55.0, 54.9, 39.2, 38.3, 38.2, 35.8, 35.6, 26.2, 26.0, 25.7, 25.4, 17.7, 17.5, 16.0, 15.7.HRMS(ESI) m/z: [M + H] $^+$ calcd. for $C_{42}H_{53}N_4O_2$ 645.4164 found; 645.4156.

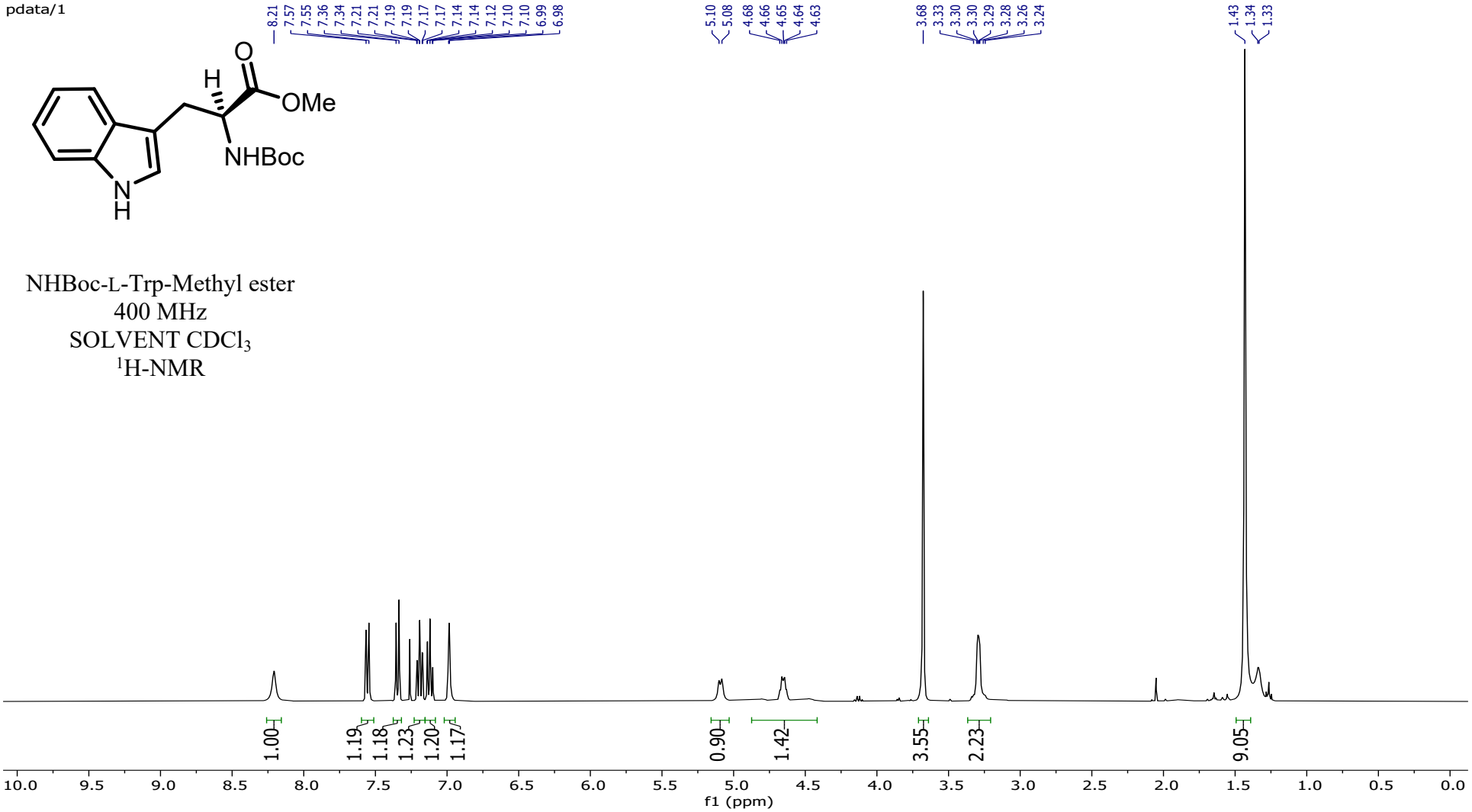


Spectrum-1. ^{1}H NMR of L-Trp-OMe hydrochloride salt.



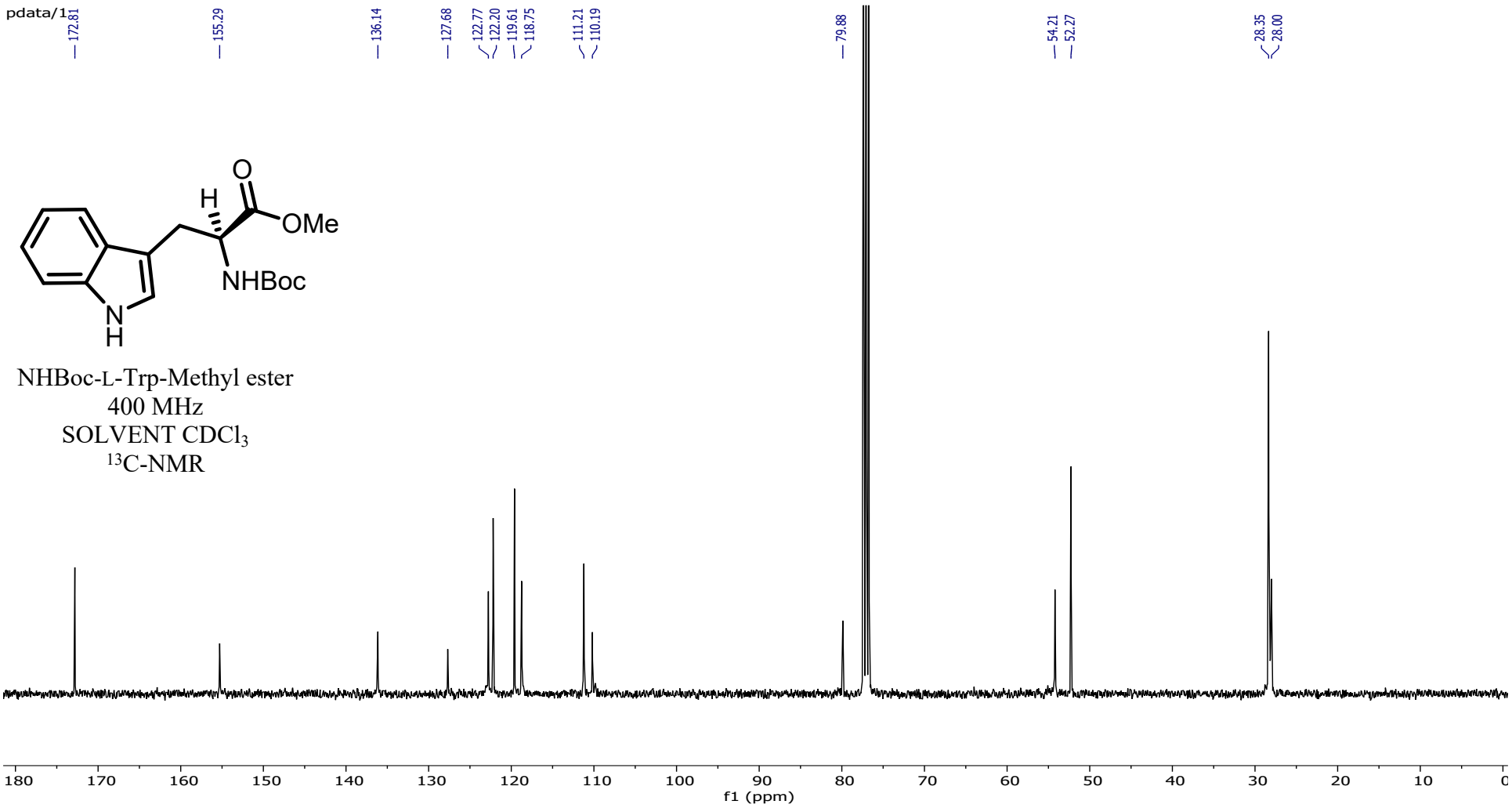
L-Trp-OMe hydrochloride salt
400 MHz
SOLVENT CD_3OD
^{13}C-NMR

Spectrum-2. ^{13}C NMR of L-Trp-OMe hydrochloride salt.

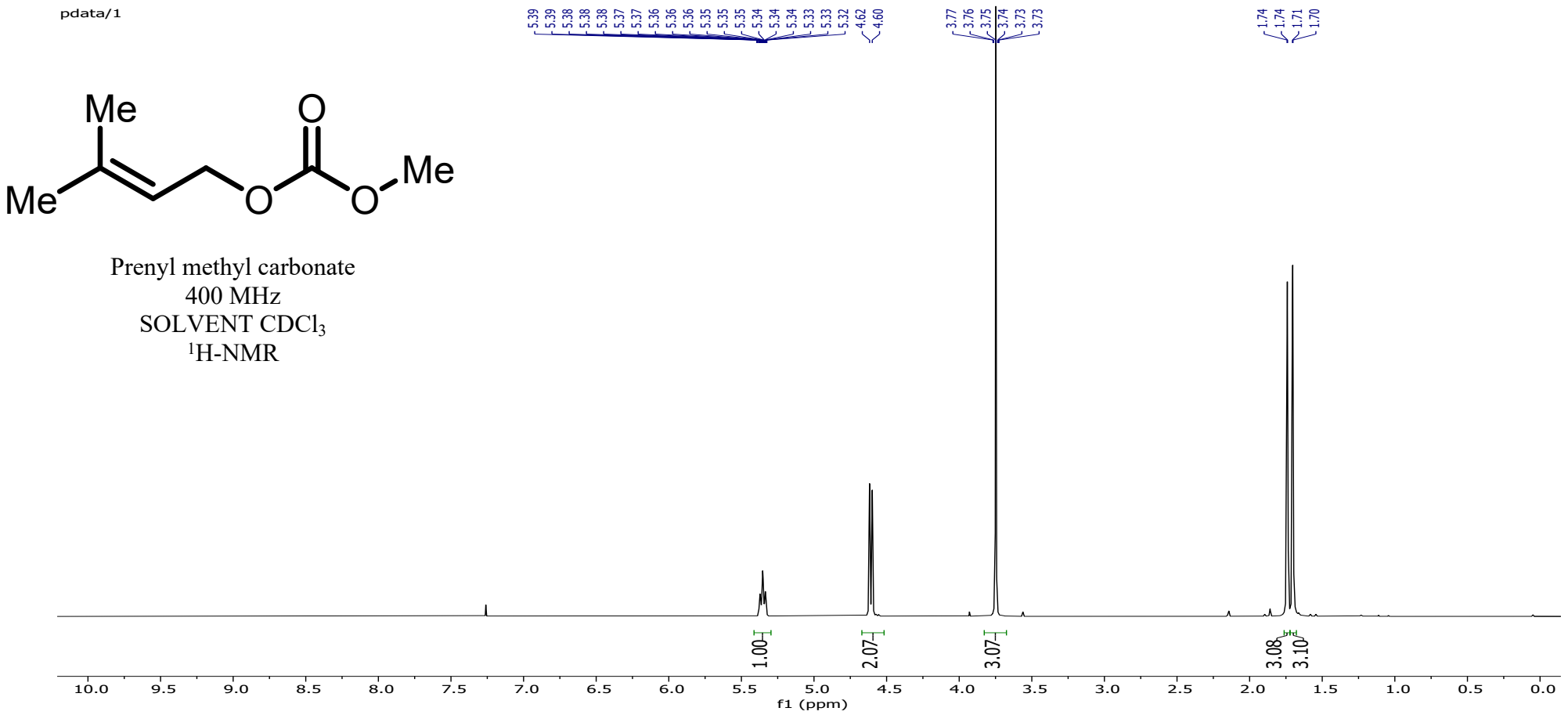


NHBoc-L-Trp-Methyl ester
400 MHz
SOLVENT $CDCl_3$
^{1}H-NMR

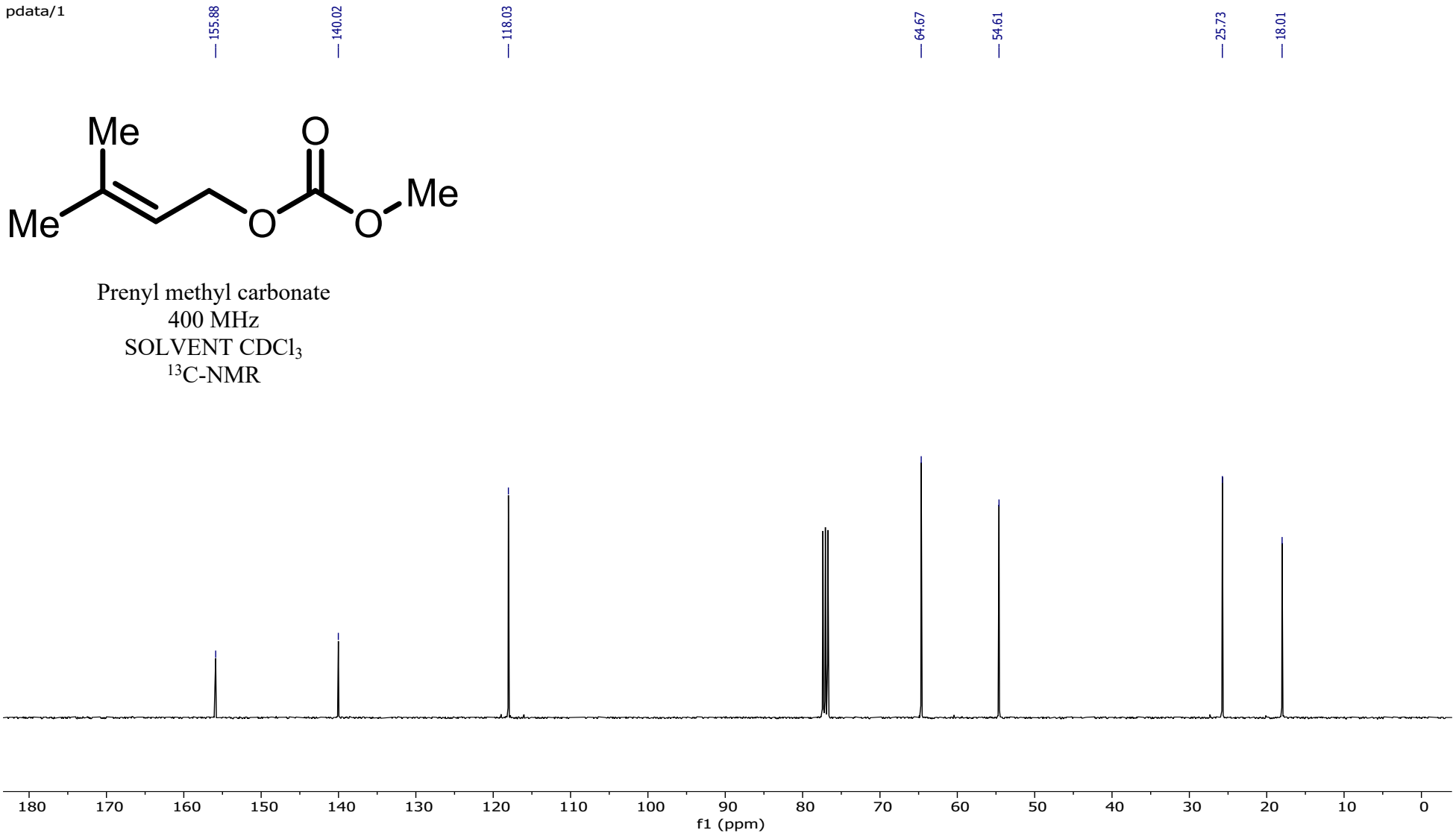
Spectrum-3. ^{1}H NMR of Boc-protected-L-Trp-Methyl-ester.



Spectrum-4. ^{13}C NMR of Boc-protected-L-Trp-Methyl-ester.

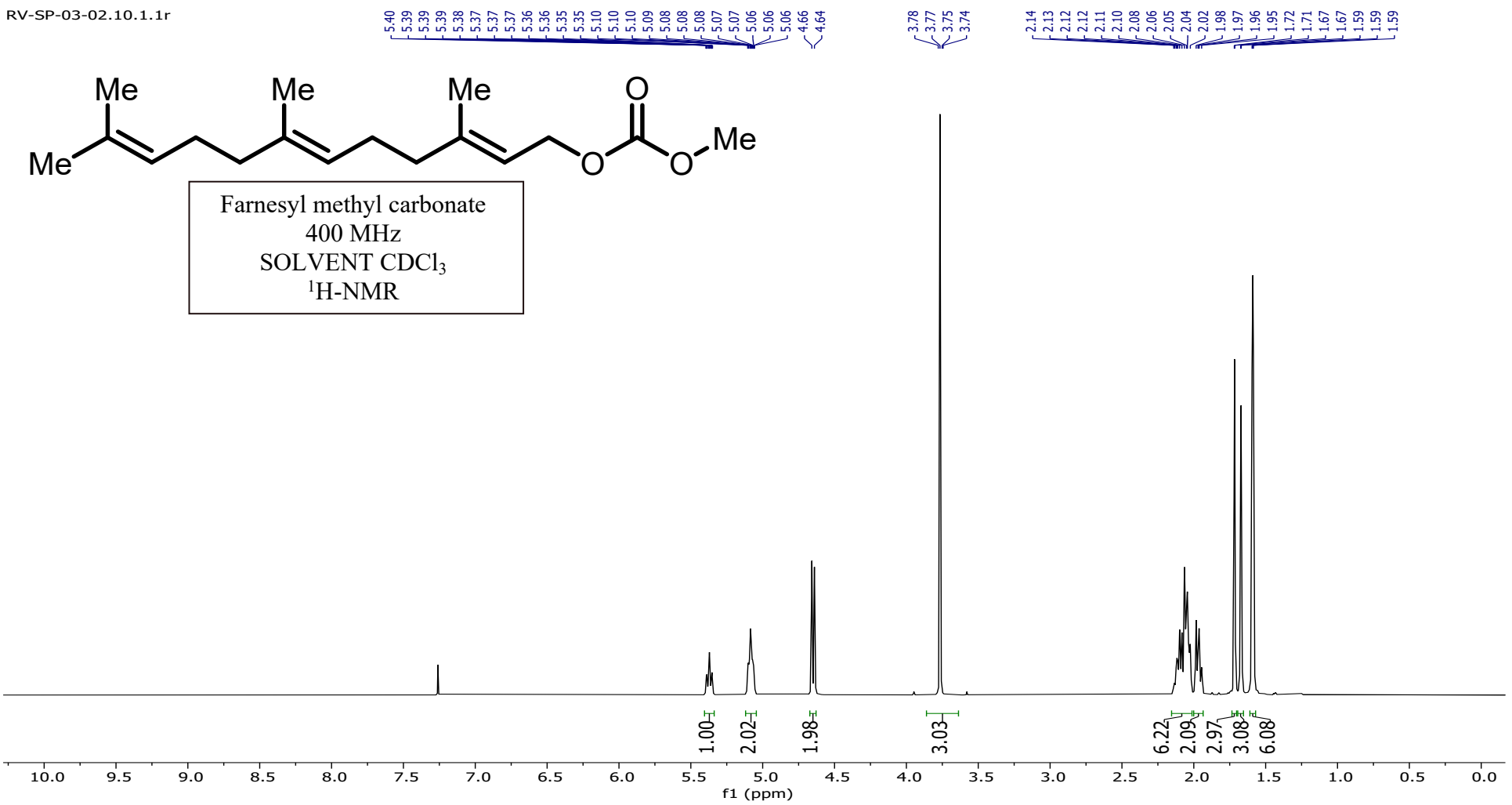


Spectrum-5. ^{1}H NMR of Prenyl methyl carbonate.

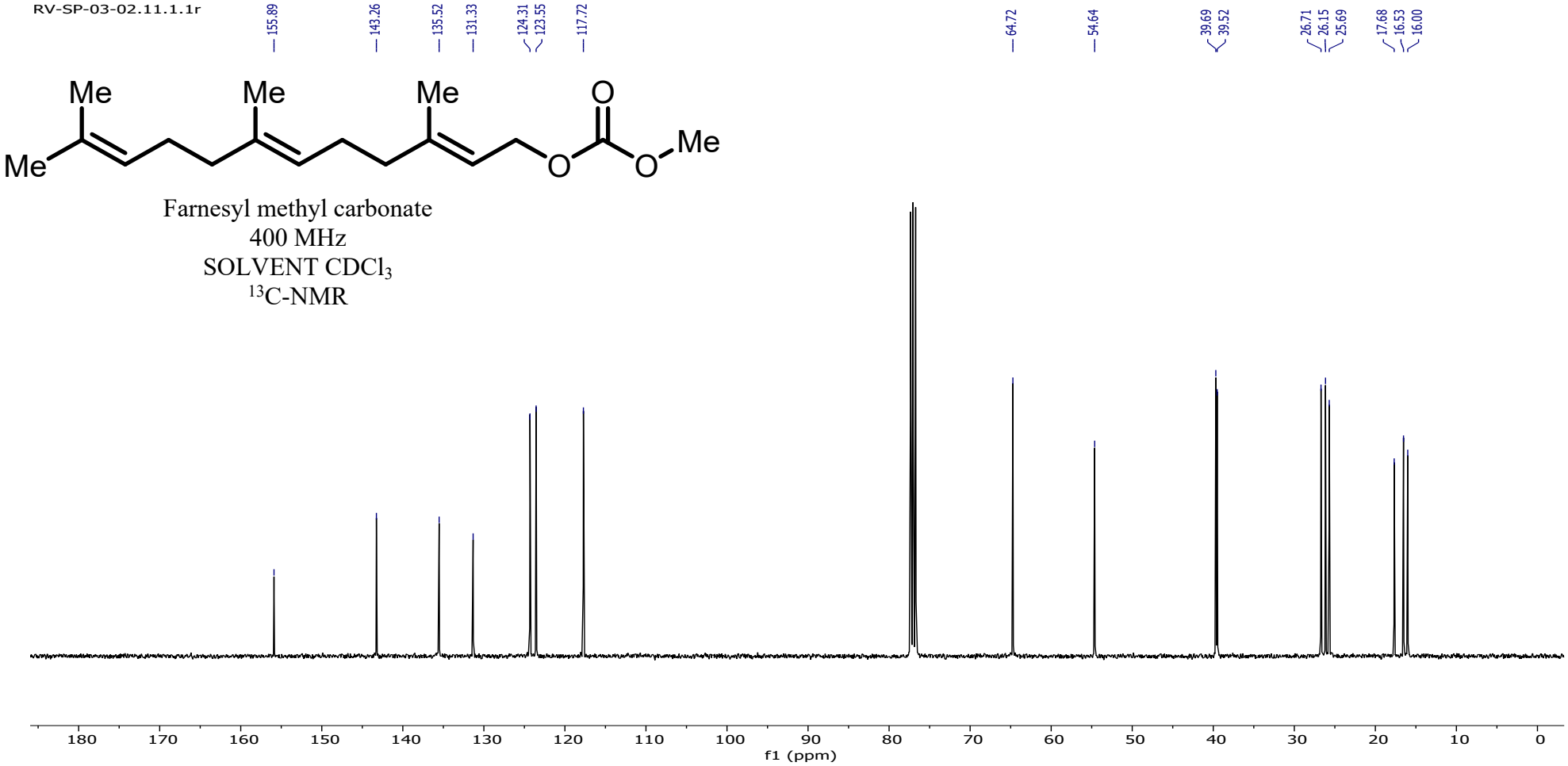


Prenyl methyl carbonate
400 MHz
SOLVENT $CDCl_3$
^{13}C-NMR

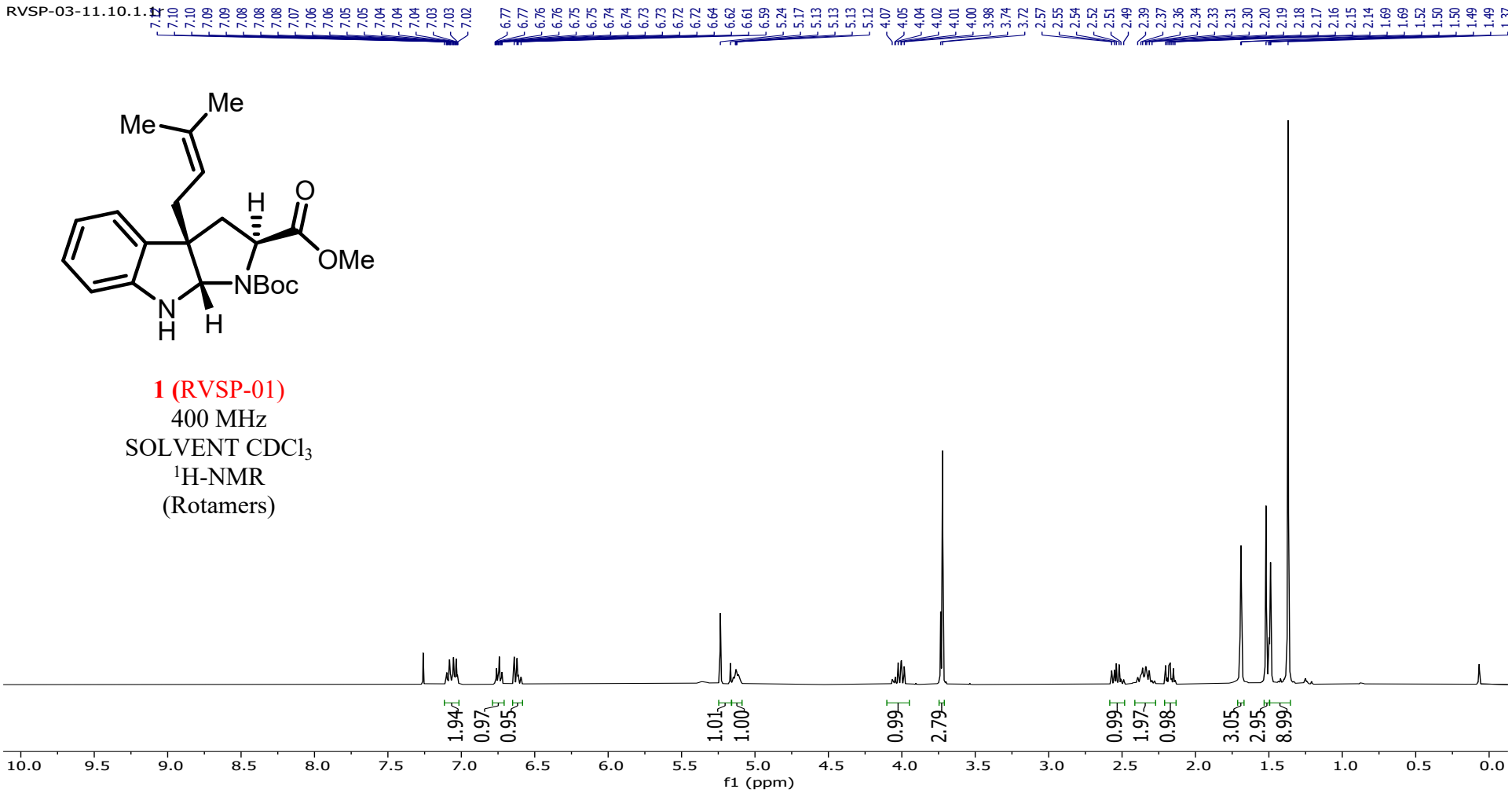
Spectrum-6. ^{13}C NMR of Prenyl methyl carbonate.



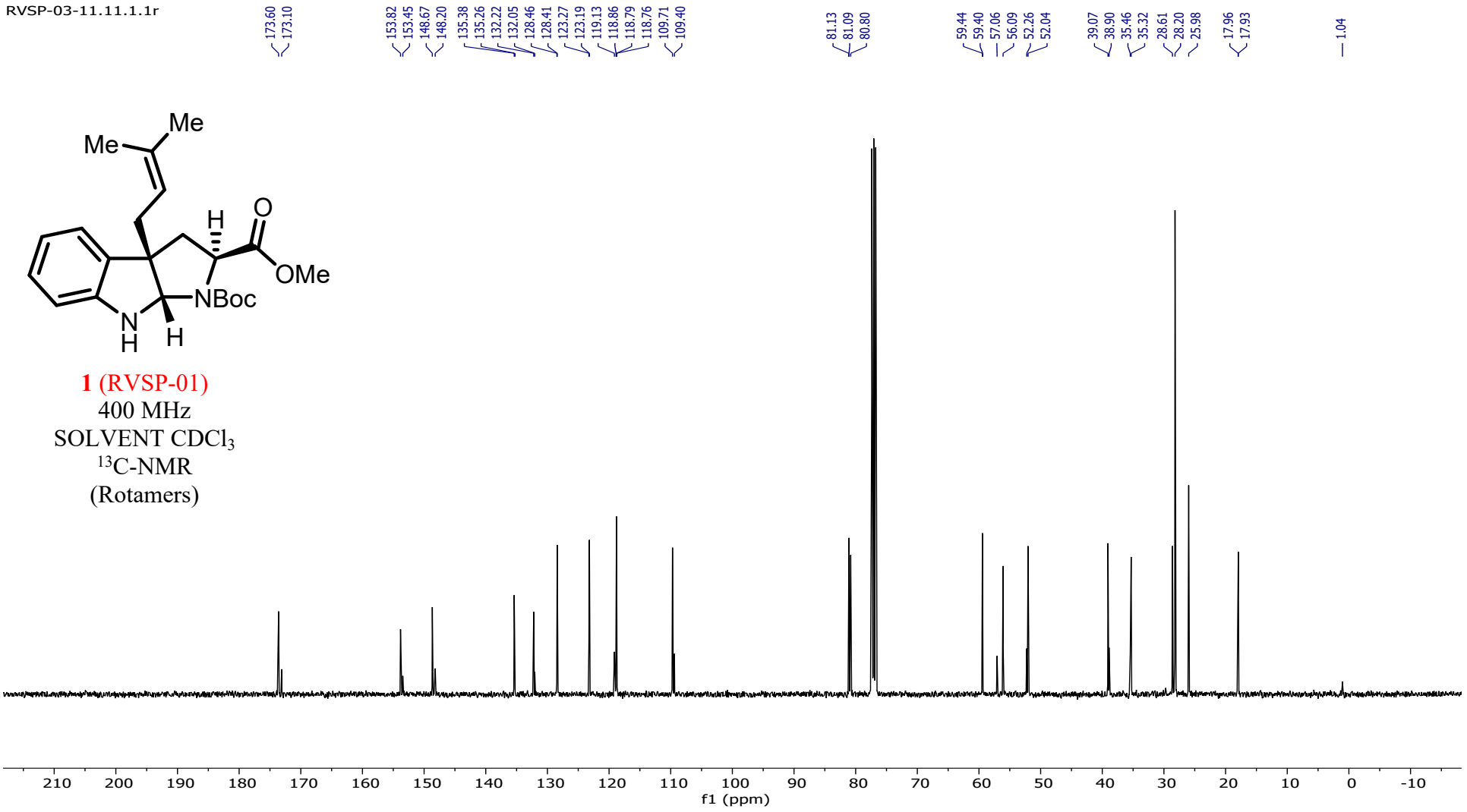
Spectrum-7. ^{1}H NMR of Farnesyl methyl carbonate.



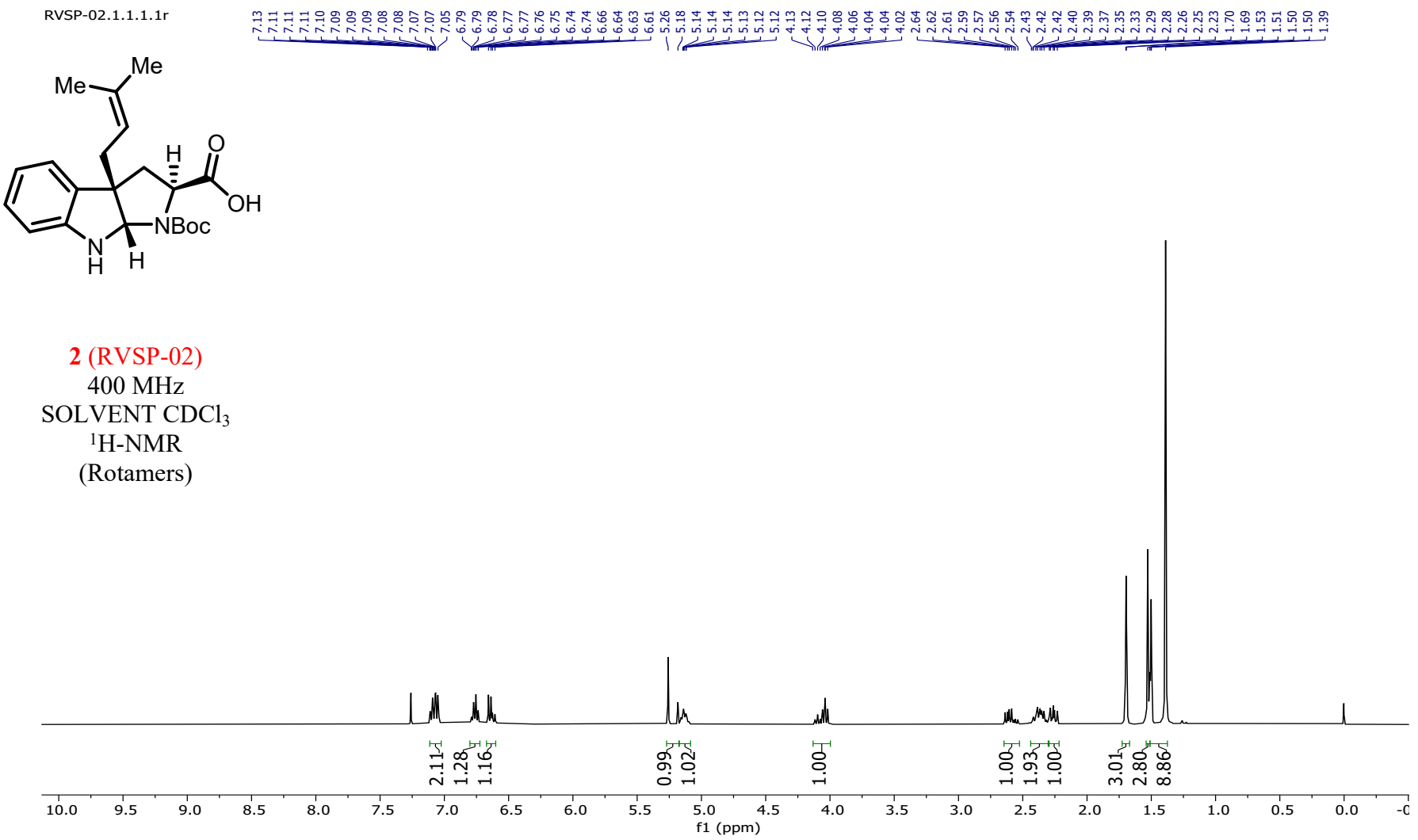
Spectrum-8. ^{13}C NMR of Farnesyl methyl carbonate.



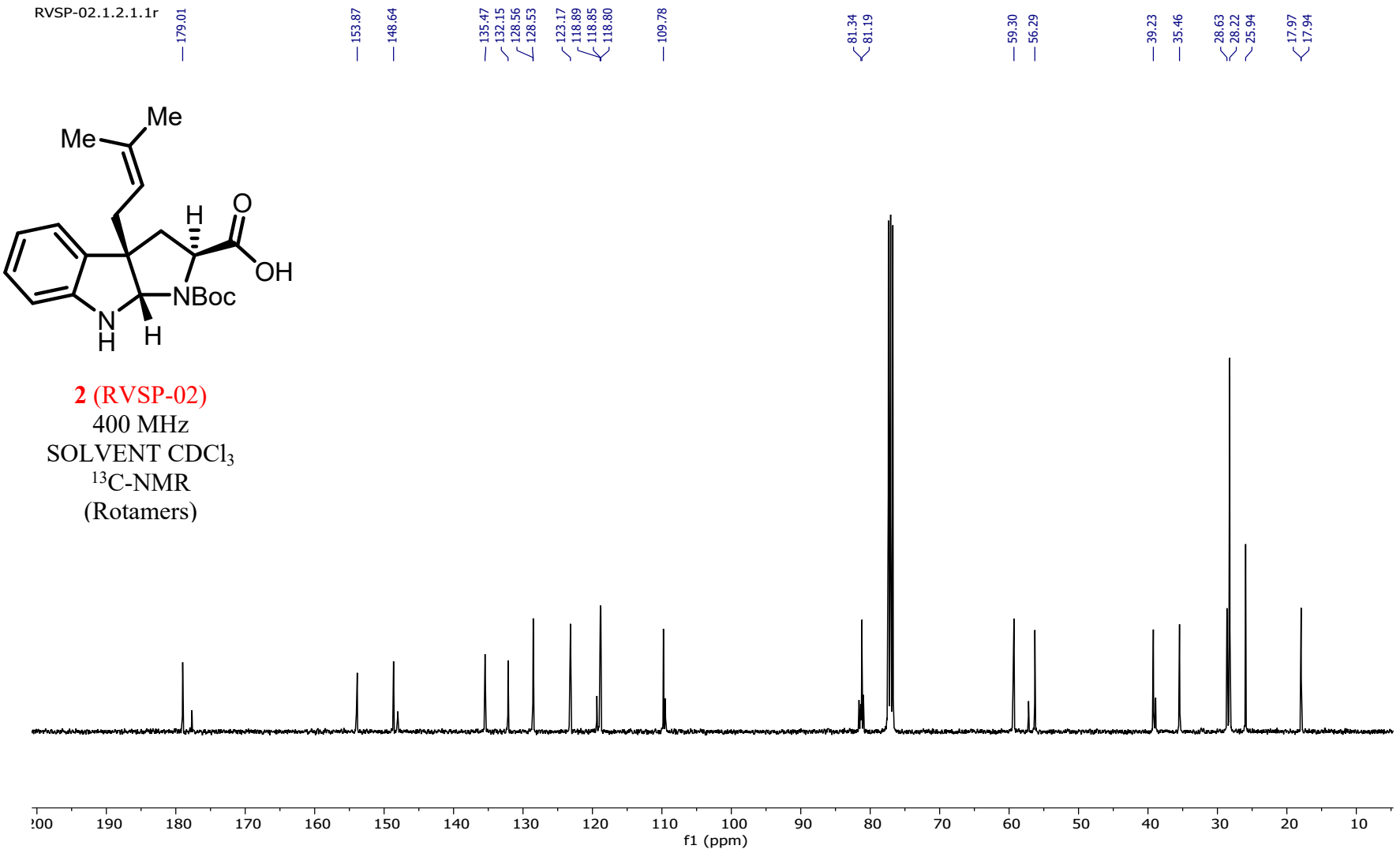
Spectrum-9. ^{1}H NMR of 01: Boc protected C3-Prenyl -L-Trp-pyrroloindoline-methyl-ester.



Spectrum-10. ^{13}C NMR of 01: Boc protected C3-Prenyl -L-Trp-pyrroloindoline-methyl-ester.

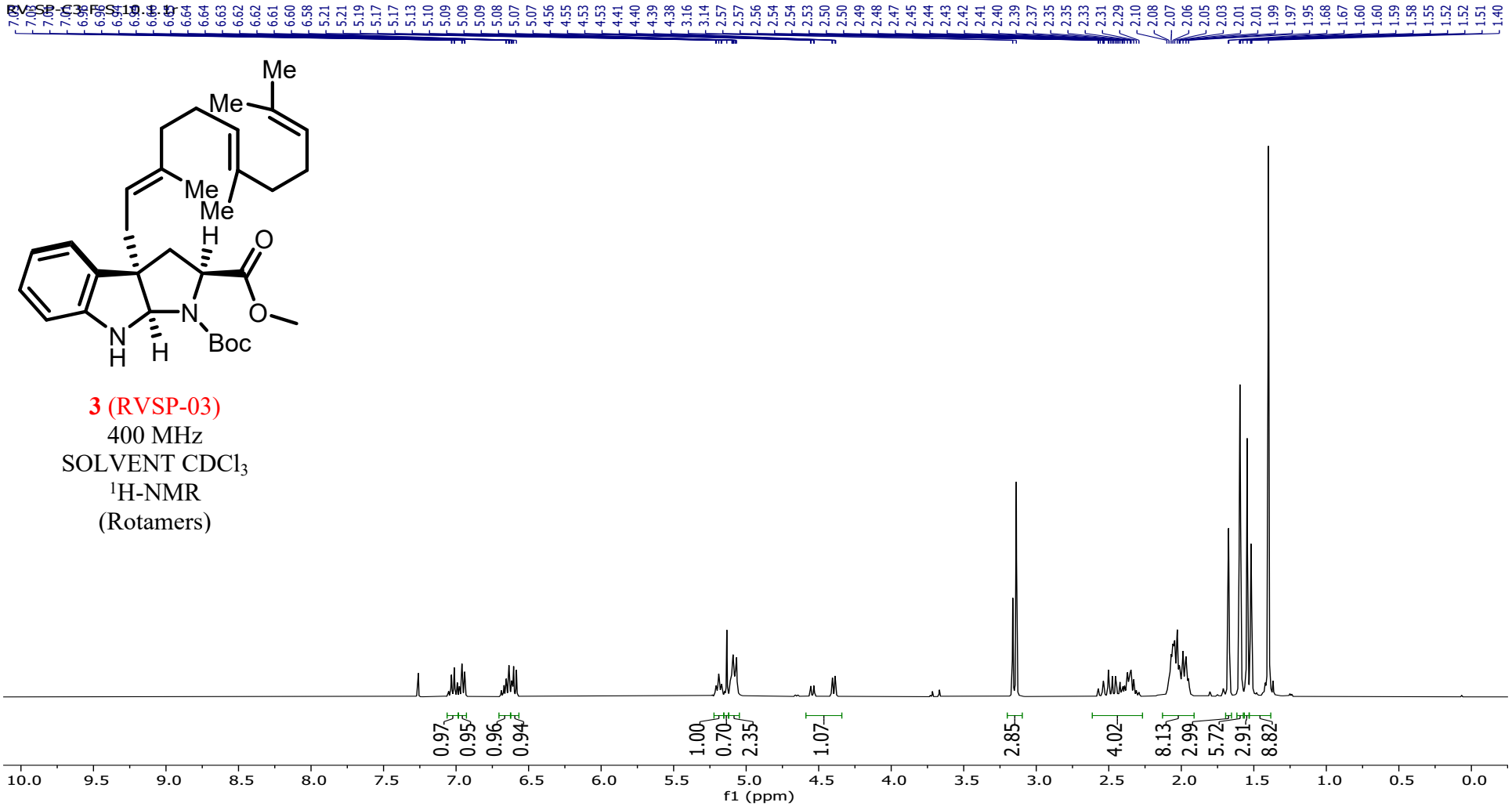


Spectrum-11. [1]H NMR of 02: C3-Prenyl -L-Trp-pyrroloindoline acid.

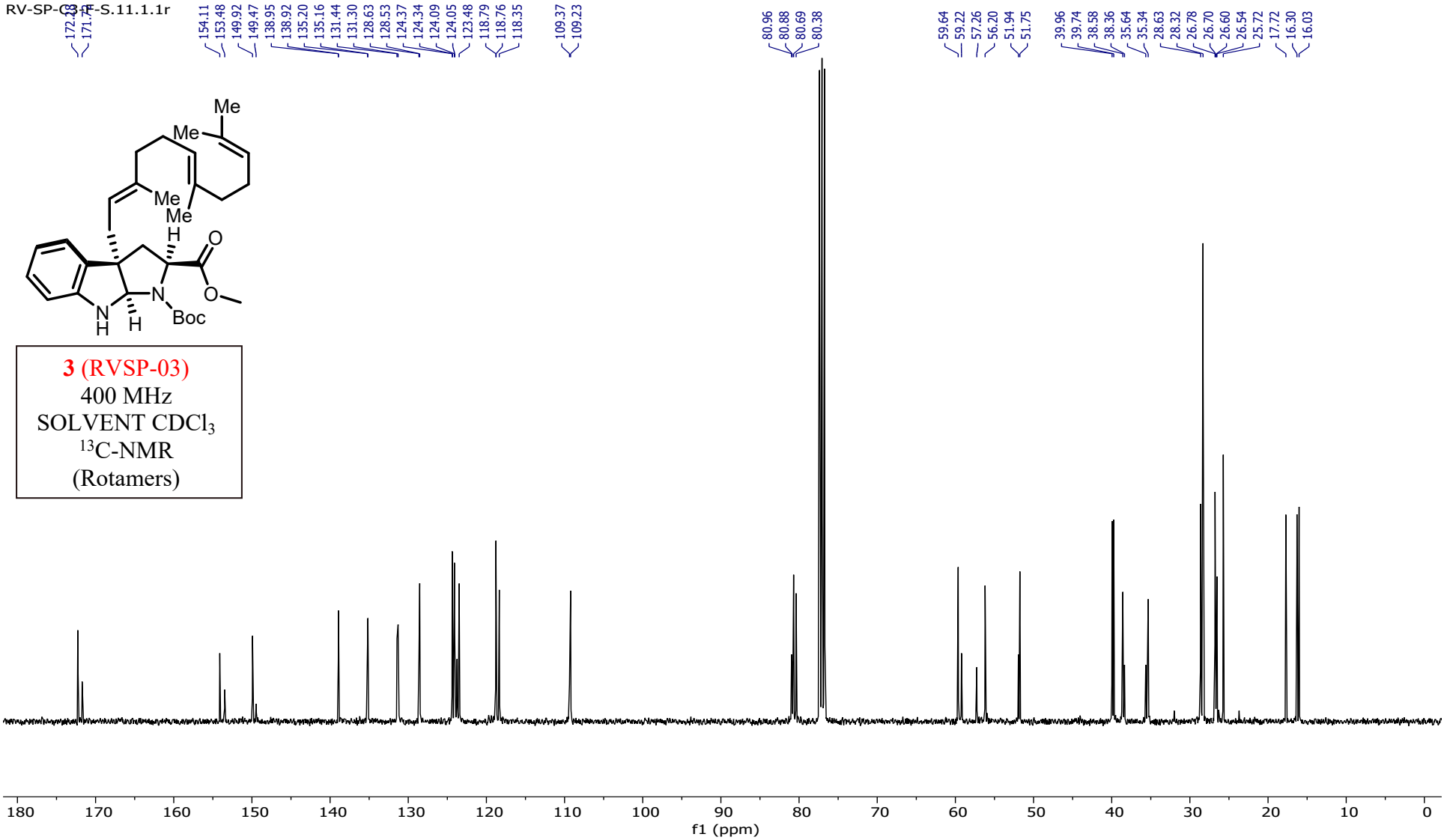


2 (RVSP-02)
400 MHz
SOLVENT $CDCl_3$
^{13}C-NMR
(Rotamers)

Spectrum-12. ^{13}C NMR of 02: C3-Prenyl -L-Trp-pyrroloindoline acid.

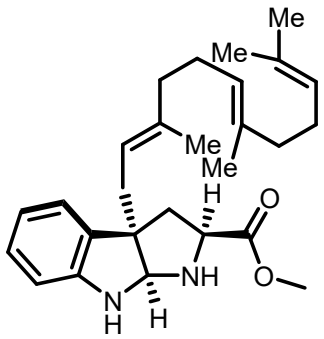


Spectrum-13. ^{1}H NMR of 03: Boc protected-endo- C3′-farnesyl -L-Trp pyrroloindoline methyl-ester.


RV-SP-C13-E-S.11.1.1r
172.43
171.74
154.11
153.48
149.92
149.47
138.95
138.92
135.20
135.16
131.44
131.30
128.63
128.53
124.37
124.34
124.09
124.05
123.48
118.79
118.76
118.35
109.37
109.23
80.96
80.88
80.69
80.38
59.64
59.22
57.26
56.20
51.94
51.75
39.96
39.74
38.58
38.36
35.64
35.34
28.63
28.32
26.78
26.70
26.60
26.54
25.72
17.72
16.30
16.03
Me
Me
Me
Me
H
O
O
N
Boc
N
H
H
3 (RVSP-03)
400 MHz
SOLVENT CDCl3
13C-NMR
(Rotamers)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

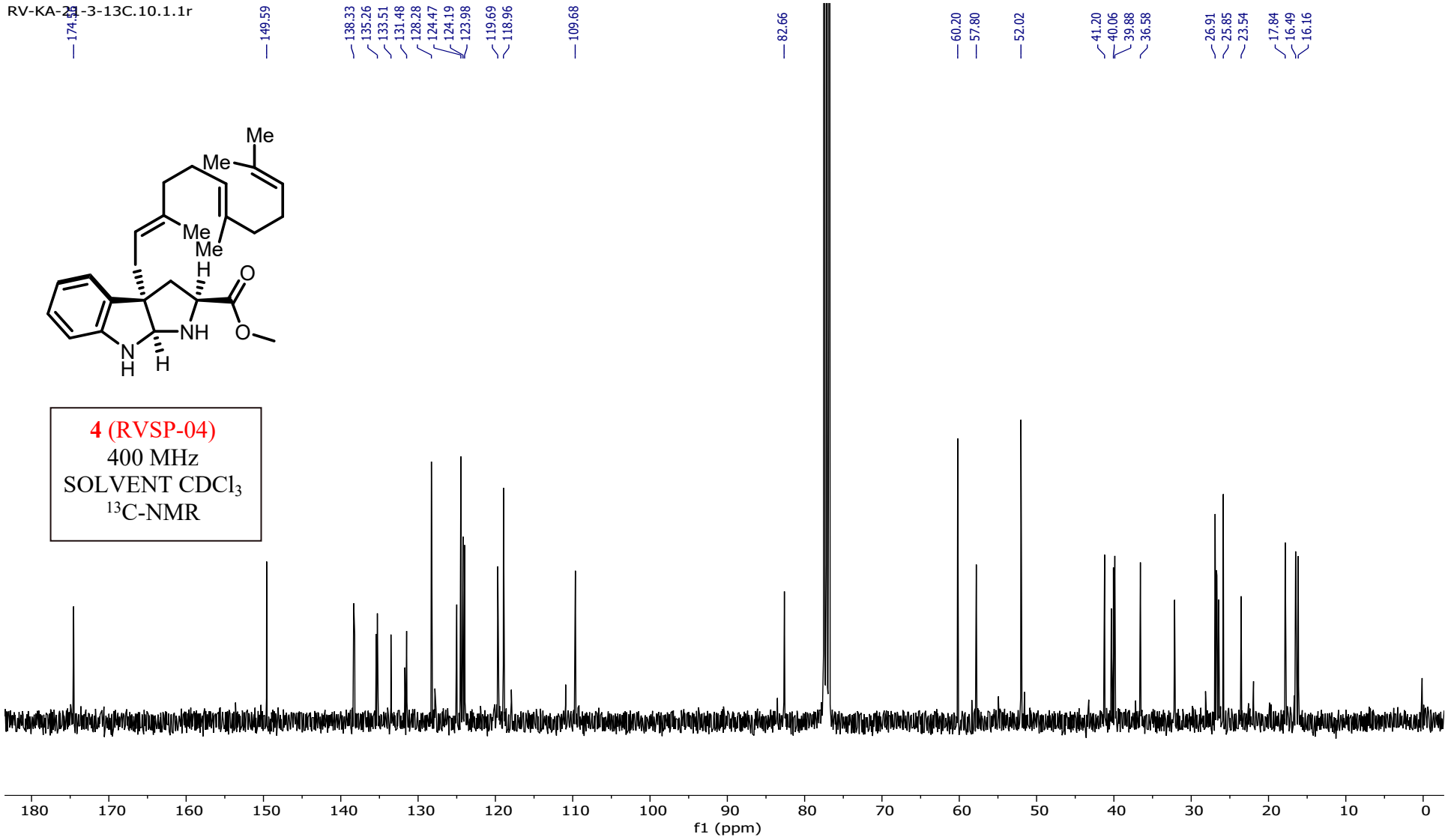
Spectrum-14. ^{13}C NMR of 03: Boc protected-endo- C3′-farnesyl -L-Trp pyrroloindoline methyl-ester.

RVSP-ENDO-A.1.1.1r

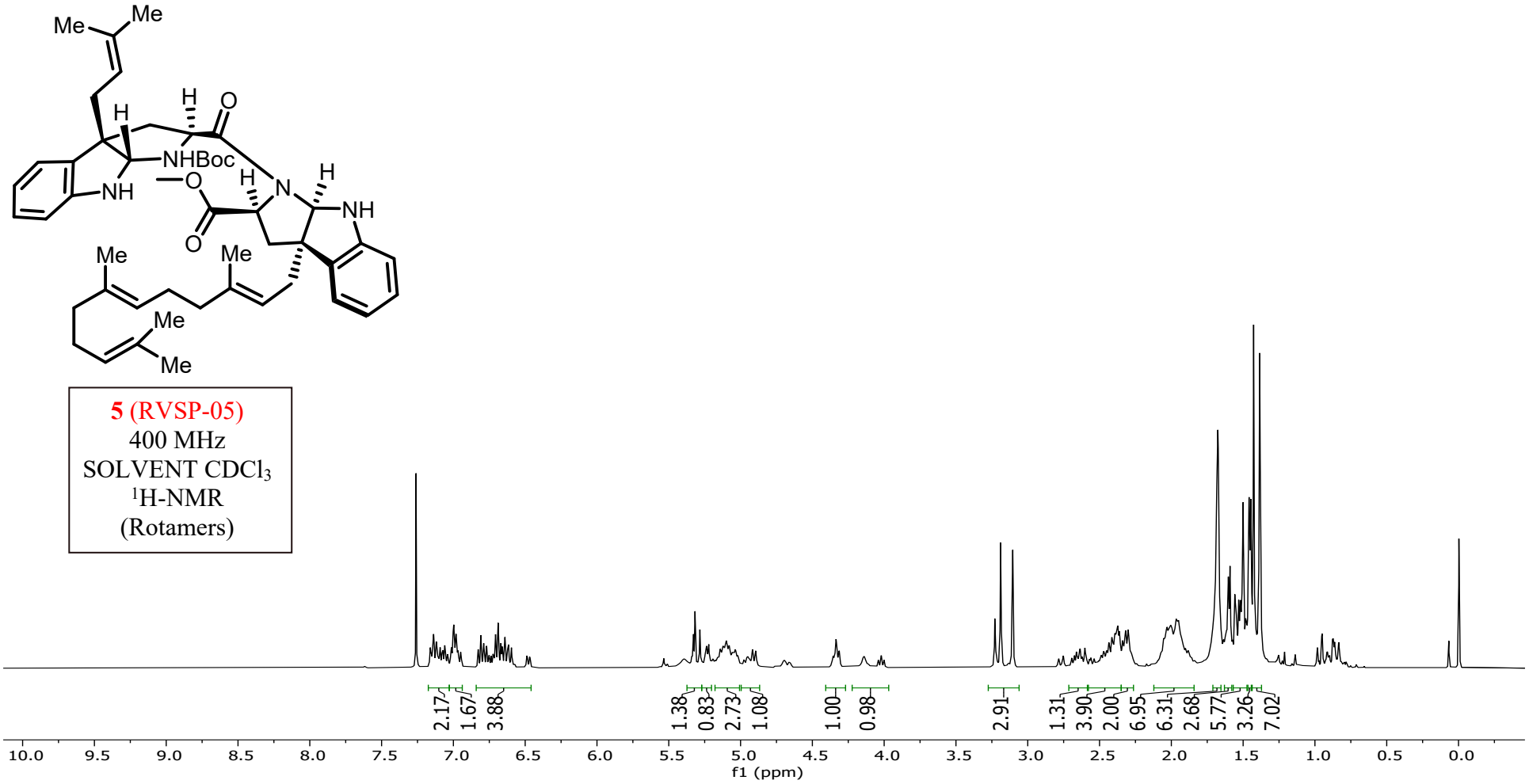


4 (RVSP-04)
400 MHz
SOLVENT $CDCl_3$
^{1}H-NMR

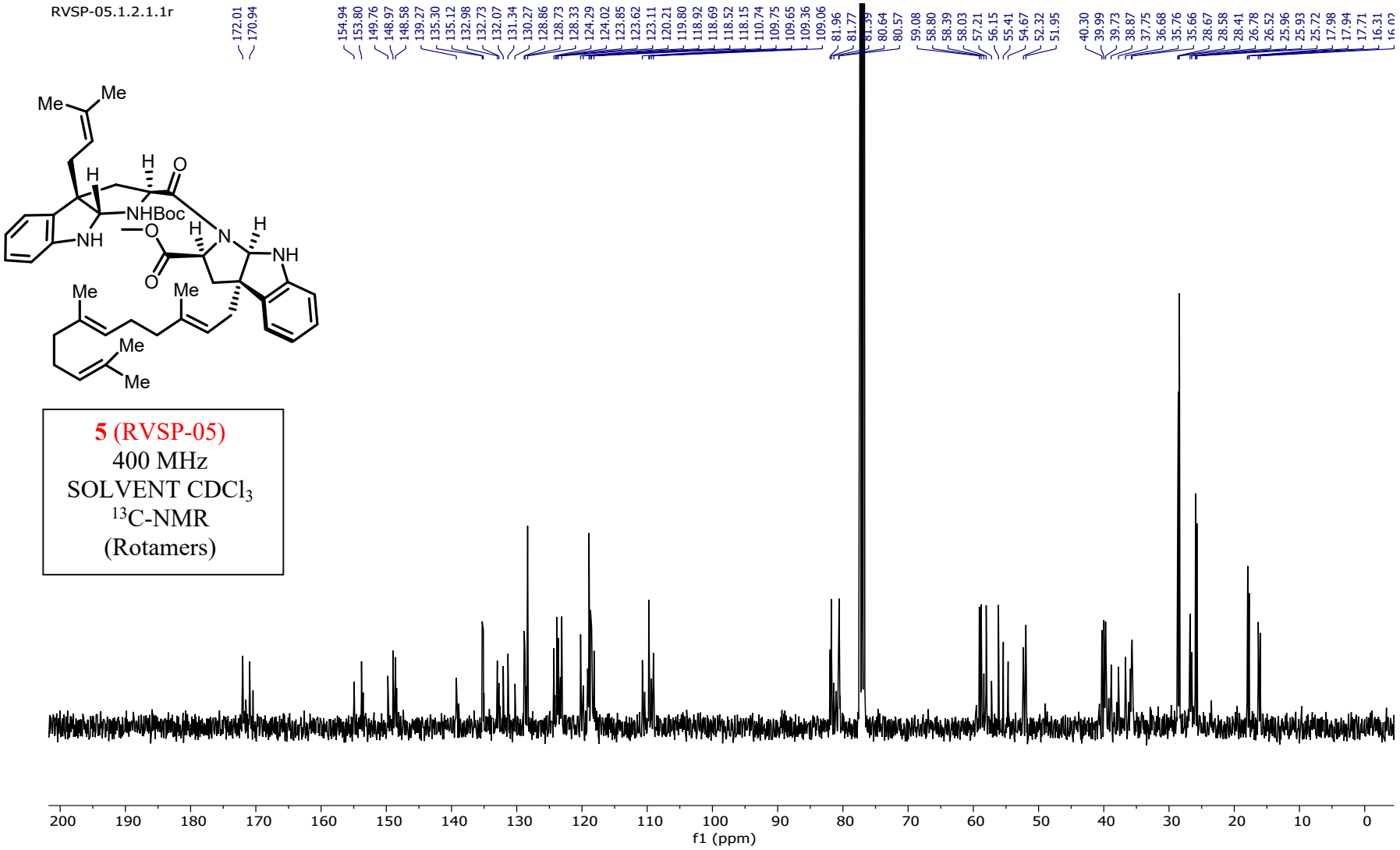
Spectrum-15. ^{1}H NMR of 04: endo-C3′-farnesyl -L-Trp pyrroloindoline methyl-ester.


RV-KA-21-3-13C.10.1.1r
174.44
149.59
138.33
135.26
133.51
131.48
128.28
124.47
124.19
123.98
119.69
118.96
109.68
82.66
60.20
57.80
52.02
41.20
40.06
39.88
36.58
26.91
25.85
23.54
17.84
16.49
16.16
Me
Me
Me
Me
H
O
NH
O
N
H
H
4 (RVSP-04)
400 MHz
SOLVENT CDCl3
13C-NMR
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

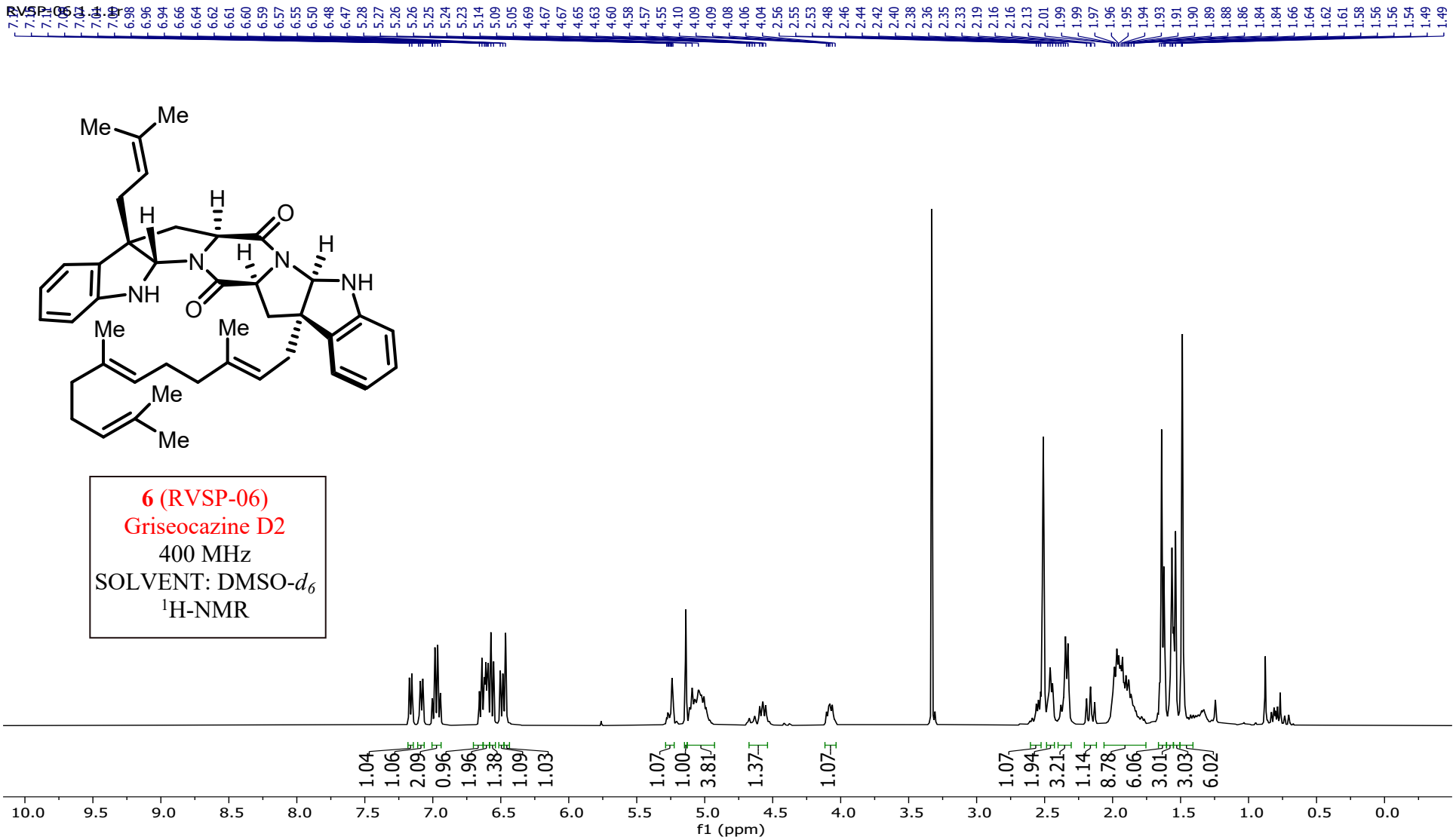
Spectrum-16. ^{13}C NMR of 04: endo-C3′-farnesyl -L-Trp pyrroloindoline methyl-ester.



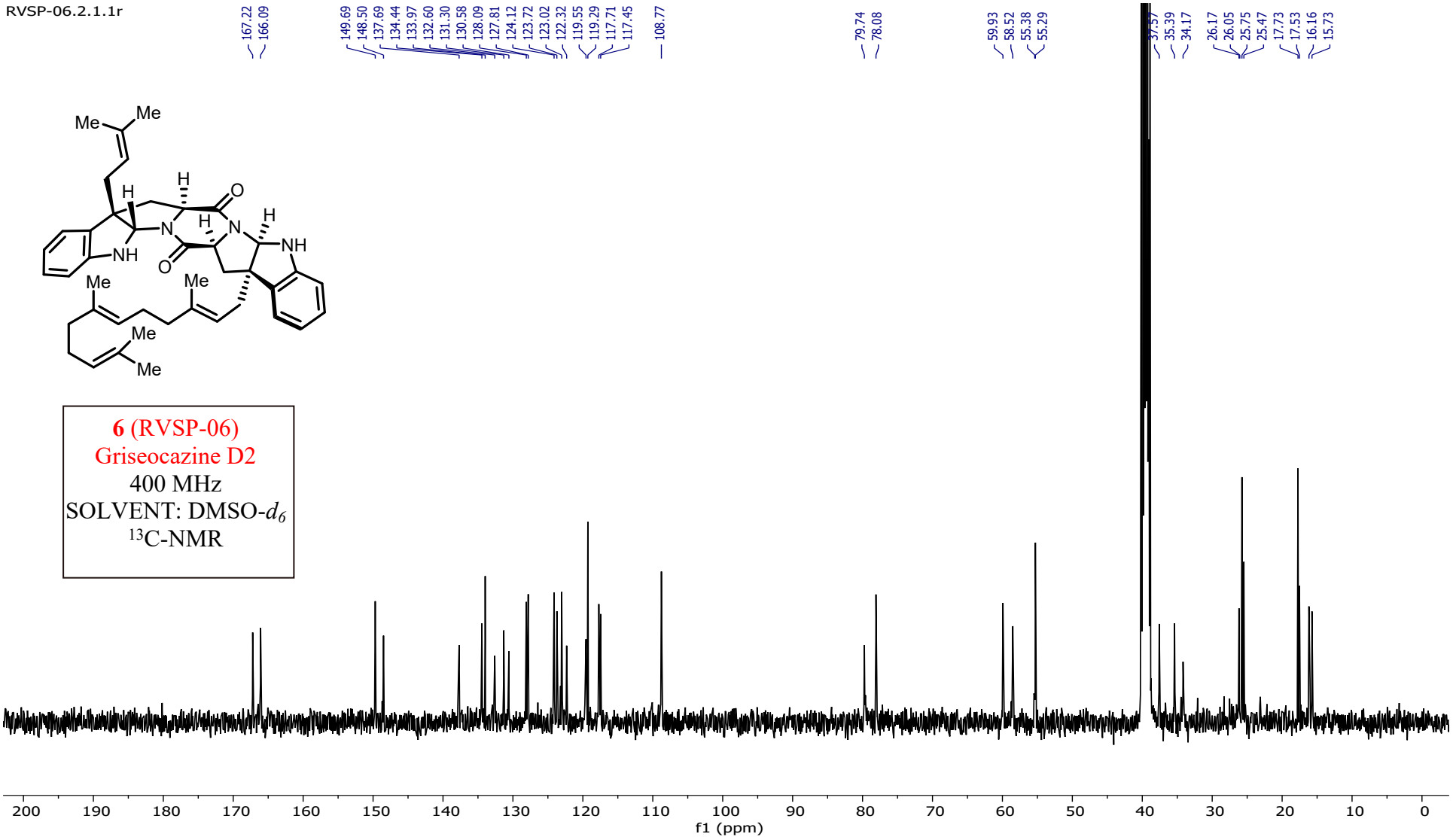
Spectrum-17. ^{1}H NMR of 05: endo- C3′-farnesyl-exo-C3-prenyl -L-Trp-L-Trp pyrroloindoline Peptide.



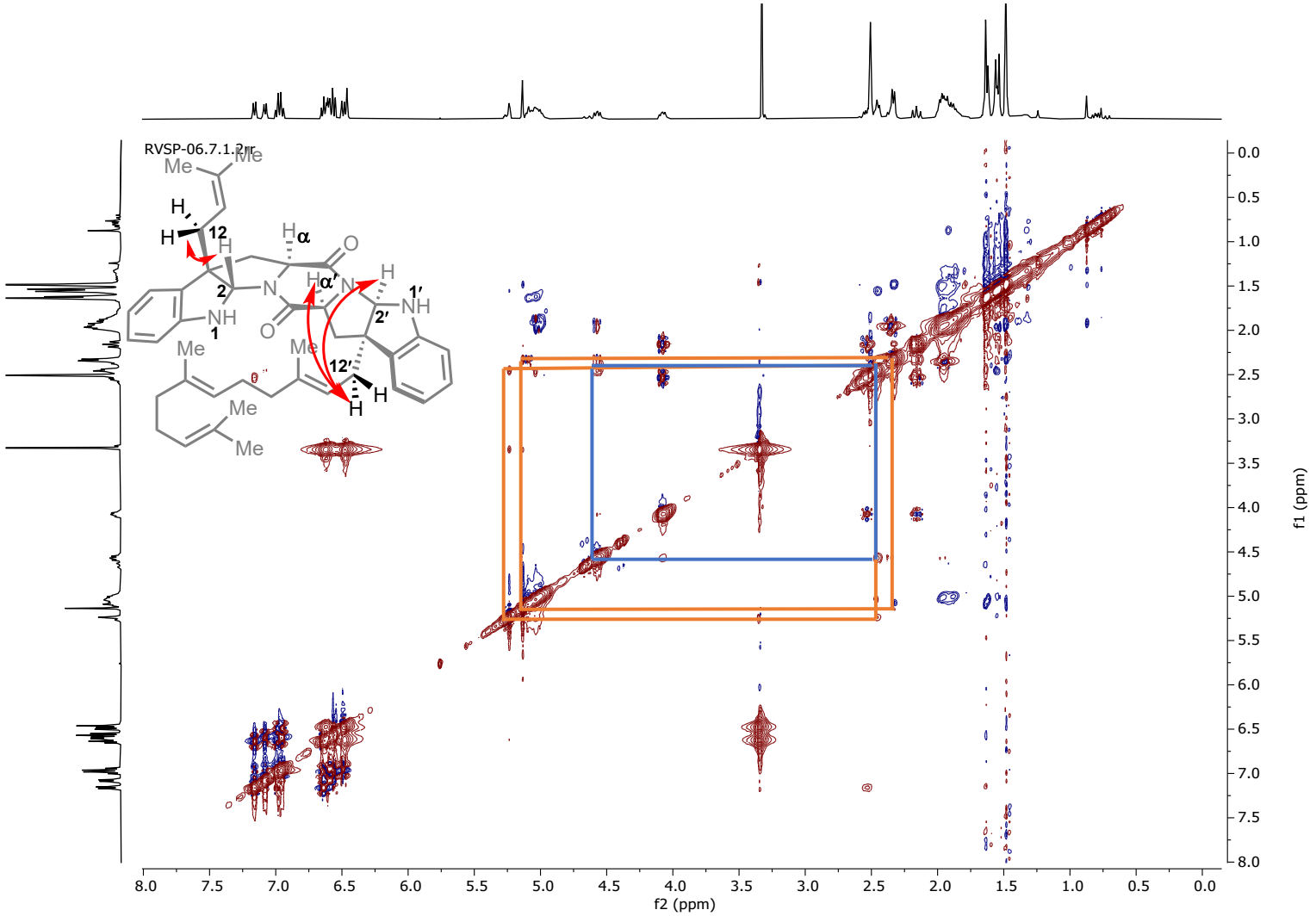
Spectrum-18. ^{13}C NMR of 05: endo-C3′-farnesyl-exo-C3-prenyl -L-Trp-L-Trp pyrroloindoline Peptide.


RVSP-06-1-1-1H
Me
Me
H
H
O
H
N
N
H
NH
NH
O
Me
Me
Me
Me
6 (RVSP-06)
Griseocazine D2
400 MHz
SOLVENT: DMSO-d6
1H-NMR
1.04
1.06
2.09
0.96
1.96
1.38
1.09
1.03
1.07
1.00
3.81
1.37
1.07
1.07
1.94
3.21
1.14
8.78
6.06
3.01
3.03
6.02
10.0
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
0.0
f1 (ppm)

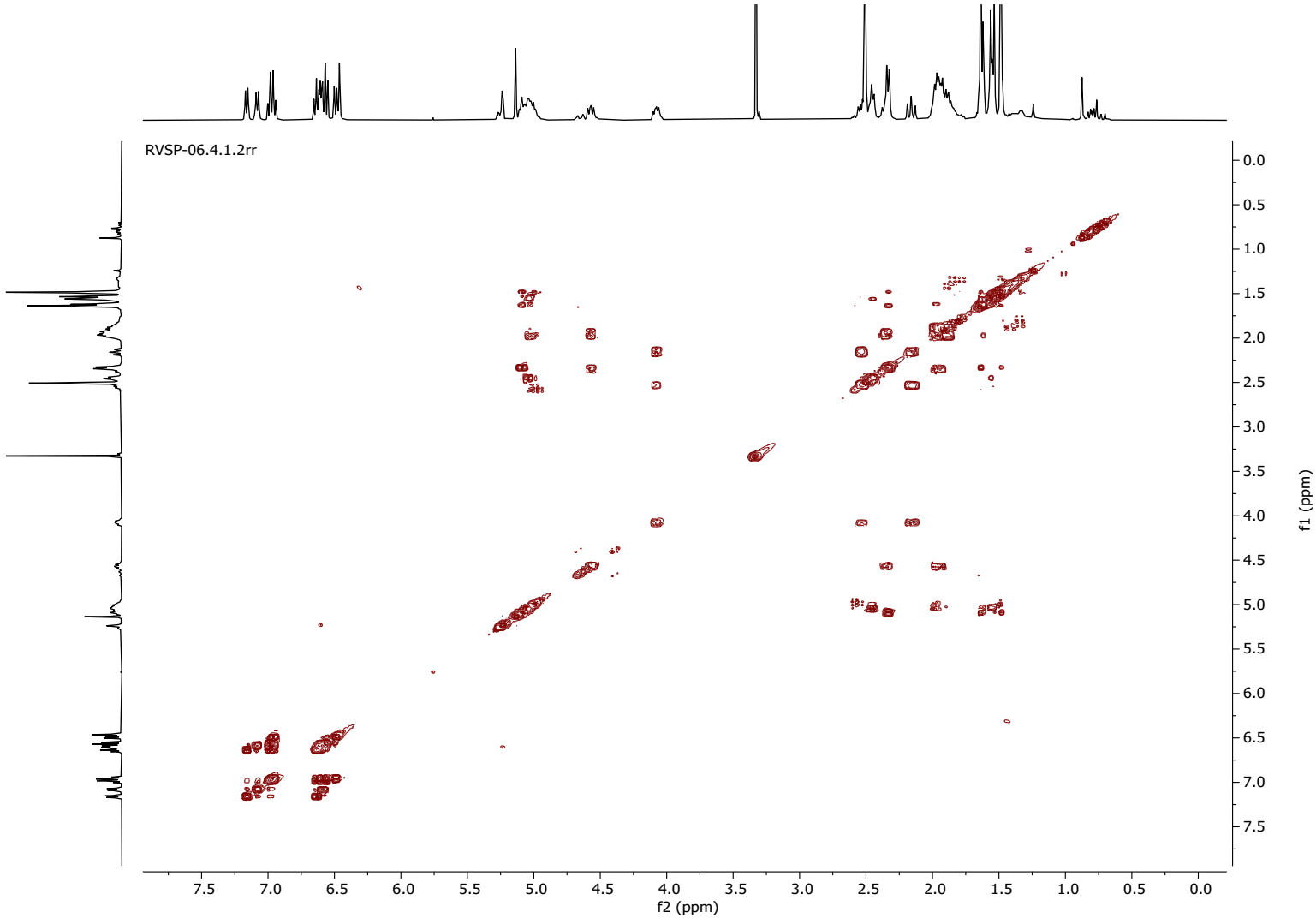
Spectrum-19. ^{1}H NMR of 06: Griseocazine D2.


RVSP-06.2.1.1r
167.22
166.09
149.69
148.50
137.69
134.44
133.97
132.60
131.30
130.58
128.09
127.81
124.12
123.72
123.02
122.32
119.55
119.29
117.71
117.45
108.77
79.74
78.08
59.93
58.52
55.38
55.29
37.57
35.39
34.17
26.17
26.05
25.75
25.47
17.73
17.53
16.16
15.73
Me
Me
H
H
O
N
H
N
H
NH
NH
O
Me
Me
Me
Me
6 (RVSP-06)
Griseocazine D2
400 MHz
SOLVENT: DMSO-d6
13C-NMR
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

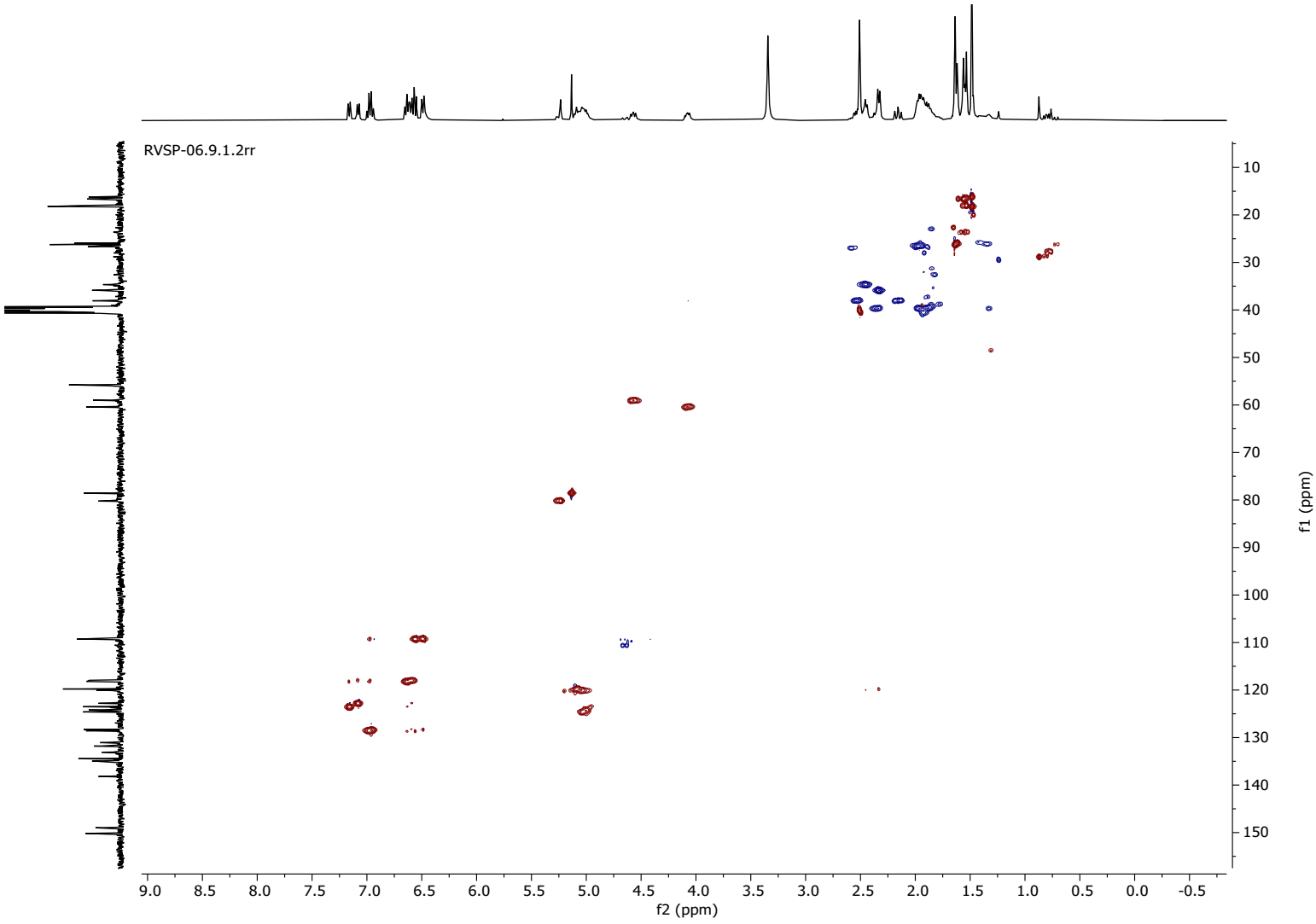
Spectrum-20. ^{13}C NMR of 06: Griseocazine D2.



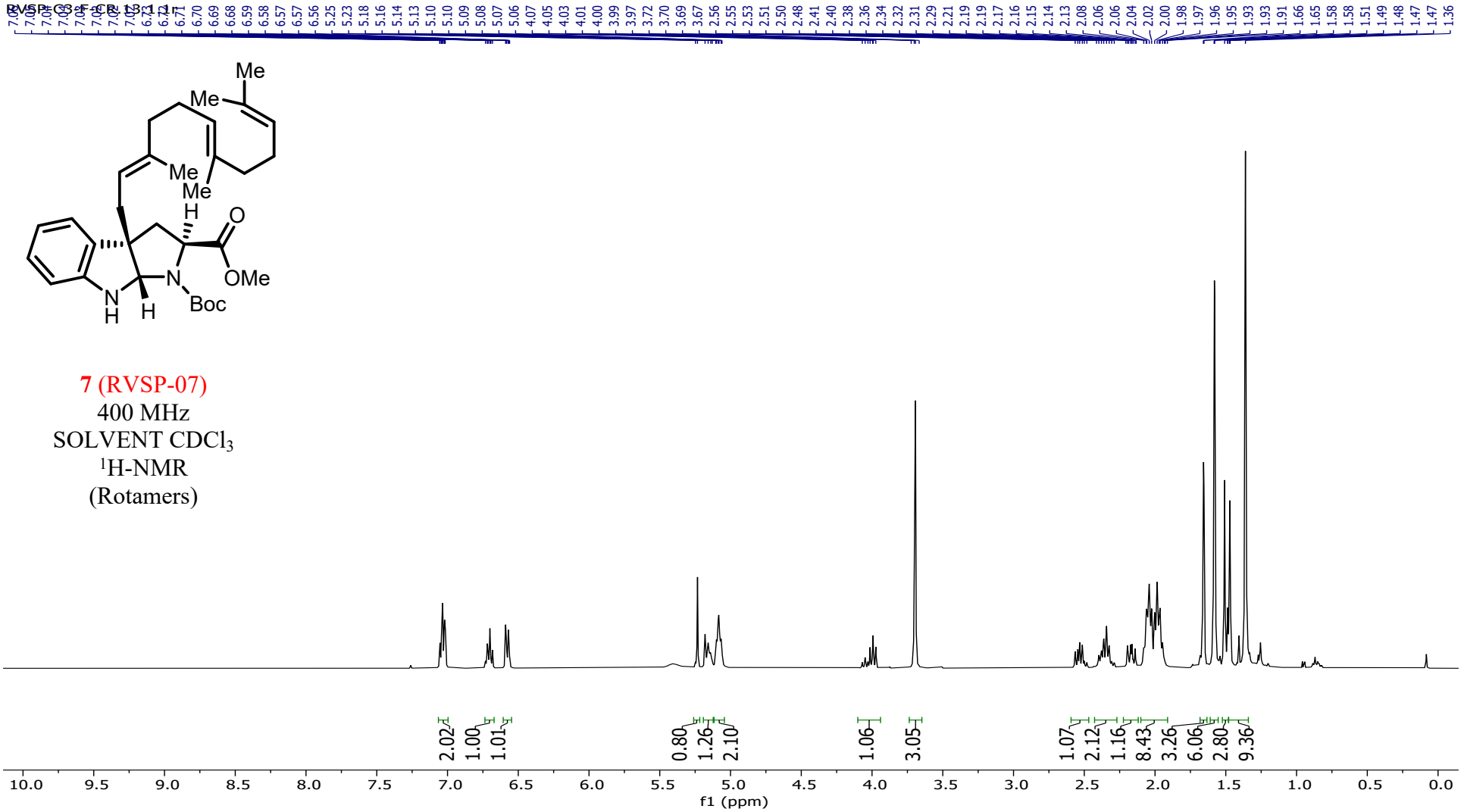
Spectrum-21. NOESY Spectrum of 06: Griseocazine D2



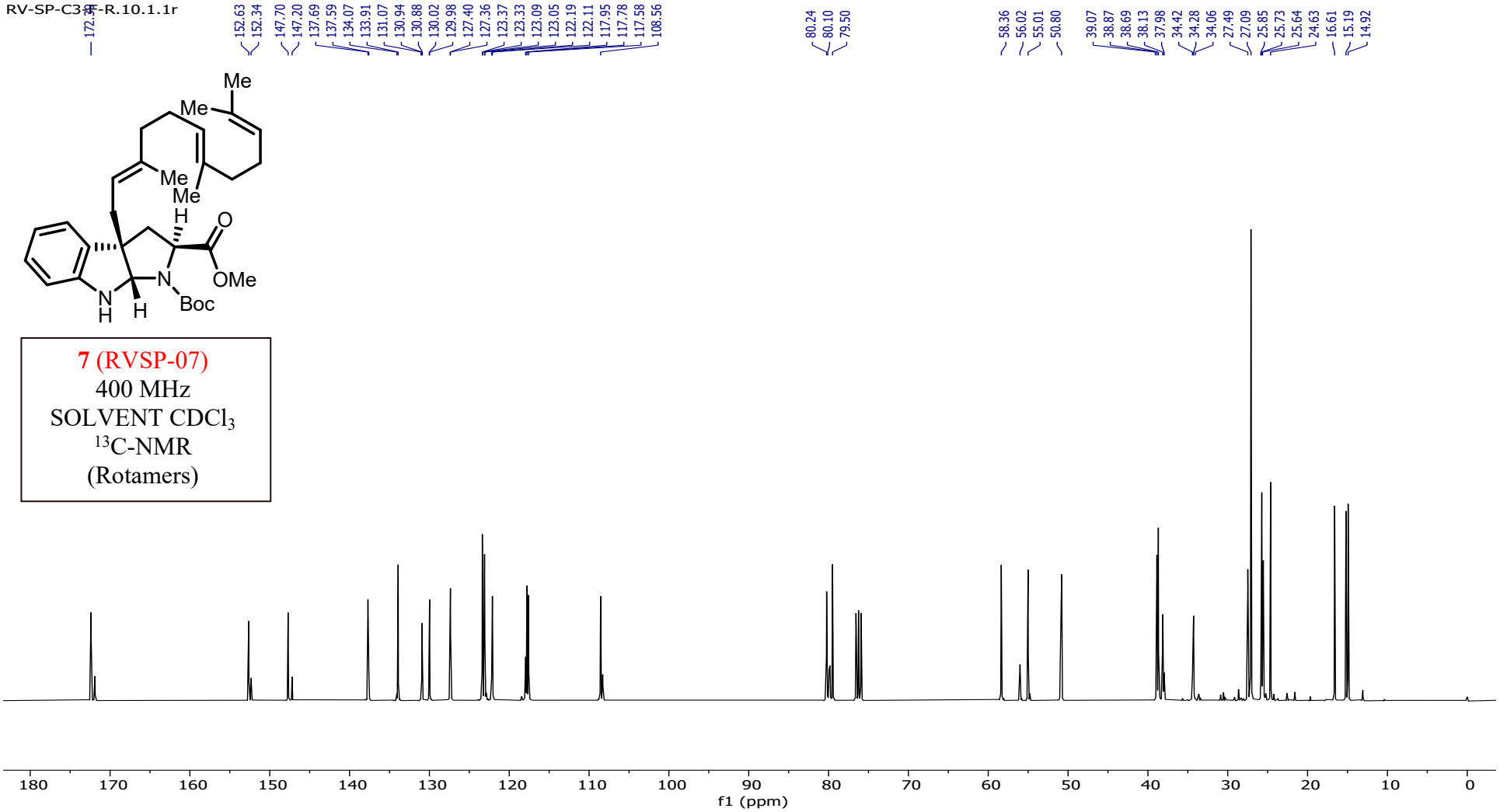
Spectrum-22. COSY Spectrum of 06: Griseocazine D2



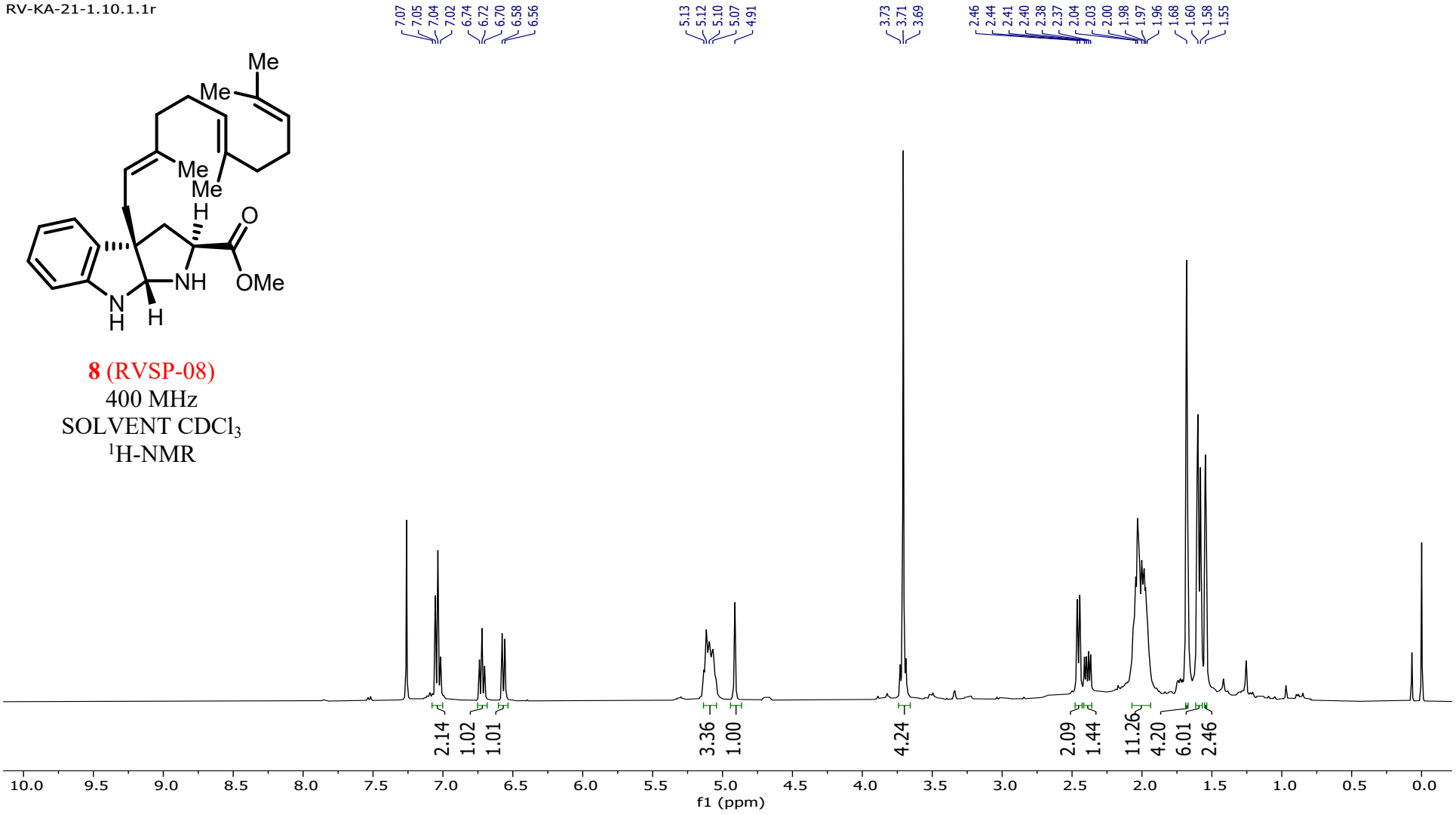
Spectrum-23. HSQC Spectrum of 06: Griseocazine D2



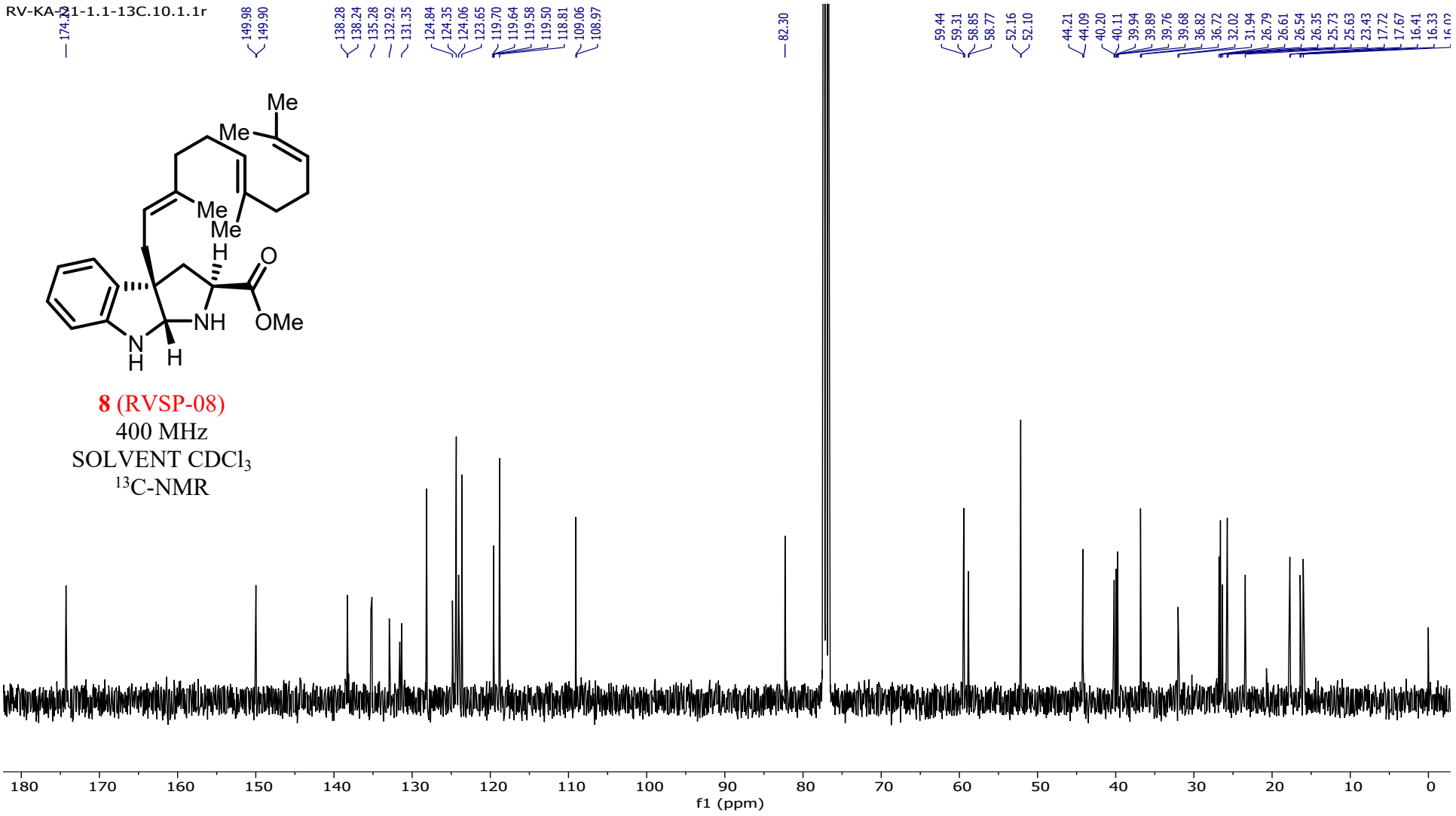
Spectrum-24. ^{1}H NMR of 07: Boc protected-exo-C3′-farnesyl -L-Trp-pyrroloindoline.



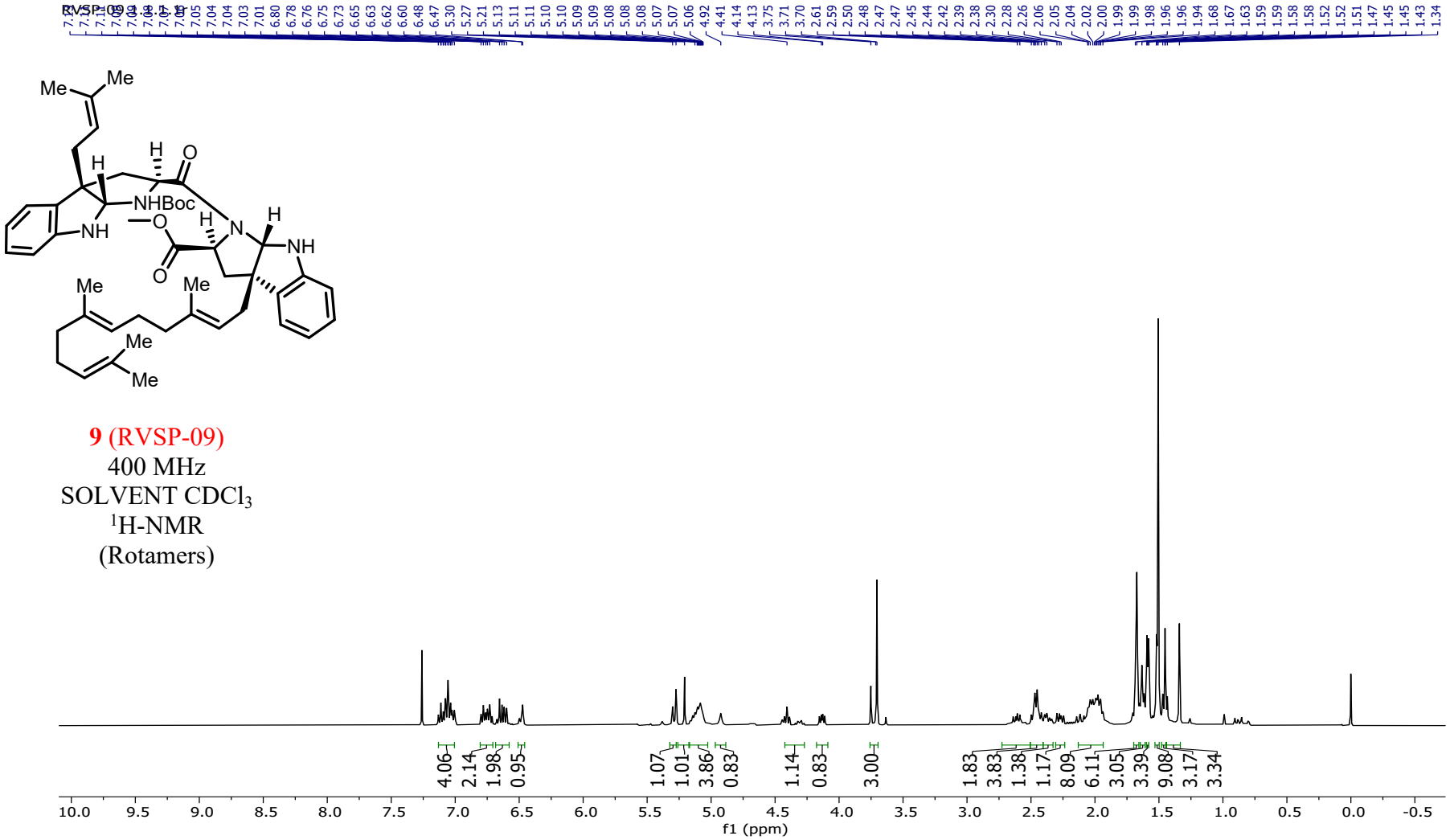
Spectrum-25. ^{13}C NMR of 07: Boc protected-exo-C3′-farnesyl -L-Trp-pyrroloindoline methyl-ester.



Spectrum-26. ^{1}H NMR of 08: exo-C3′-farnesyl -L-Trp-pyrroloindoline methyl-ester.

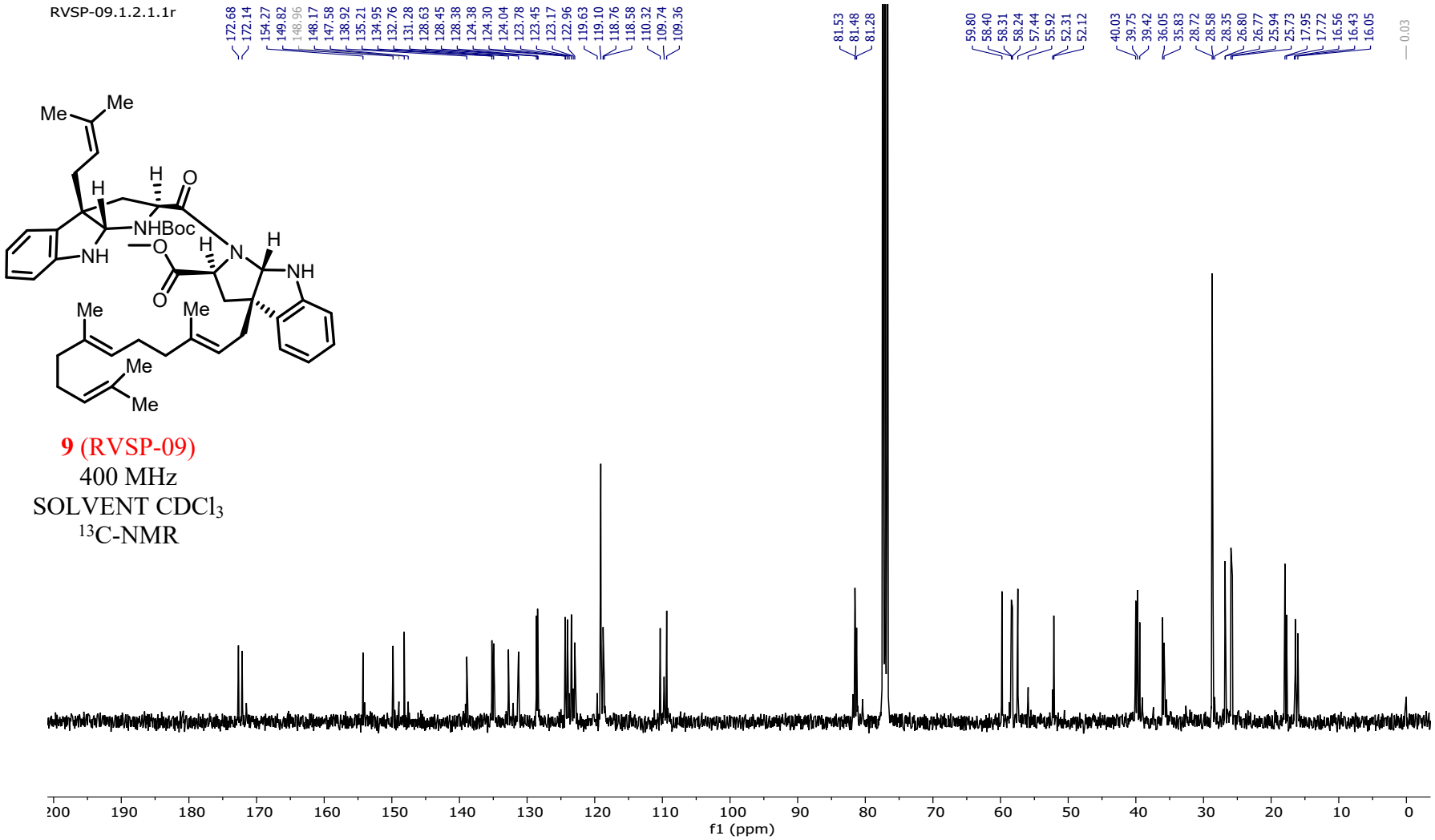


Spectrum-27. ^{13}C NMR of 08: exo-C3′-farnesyl -L-Trp-pyrroloindoline methyl-ester. (solvent peak at δ 77.0 ppm)

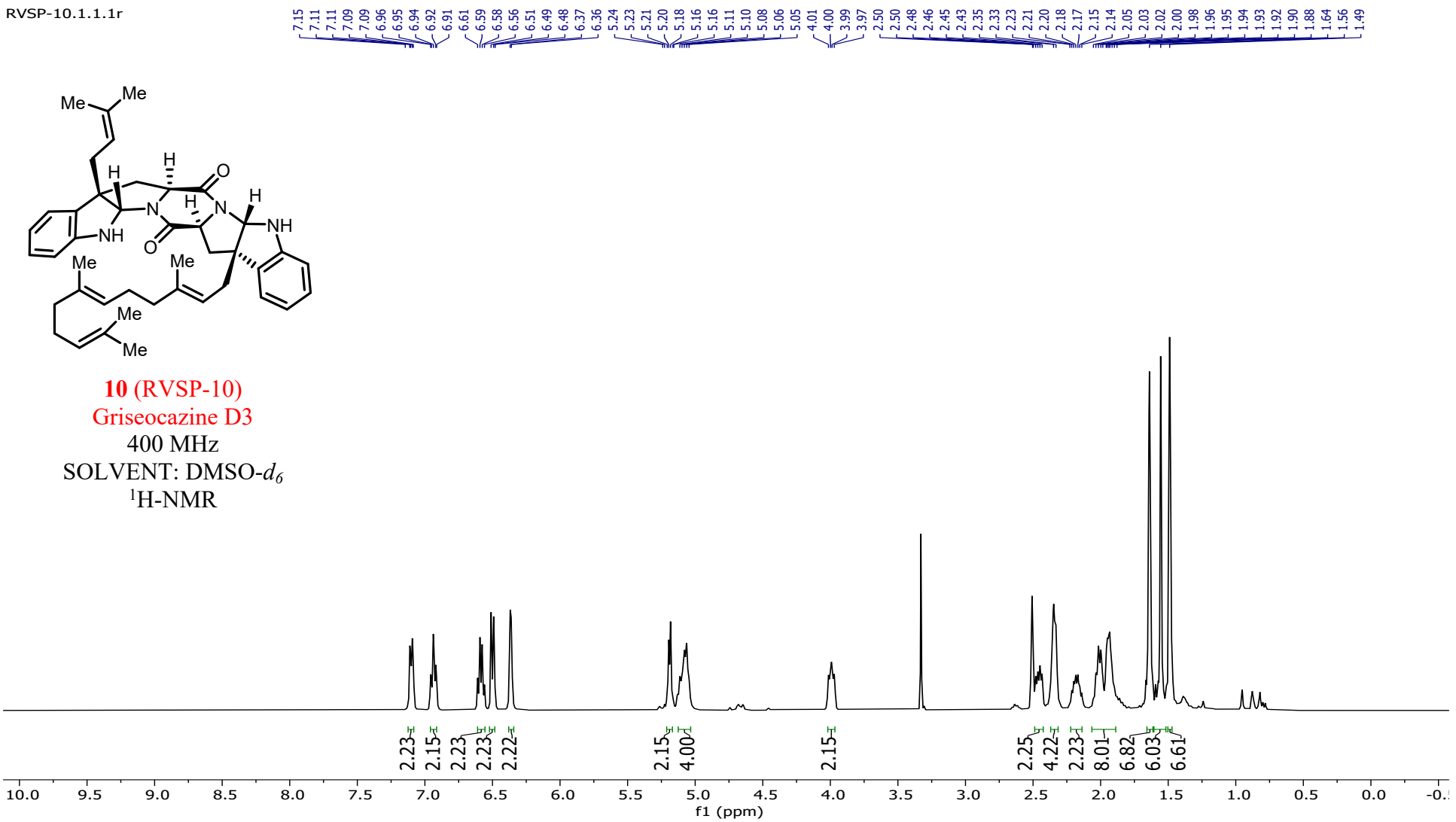


9 (RVSP-09)
400 MHz
SOLVENT $CDCl_3$
^{1}H-NMR
(Rotamers)

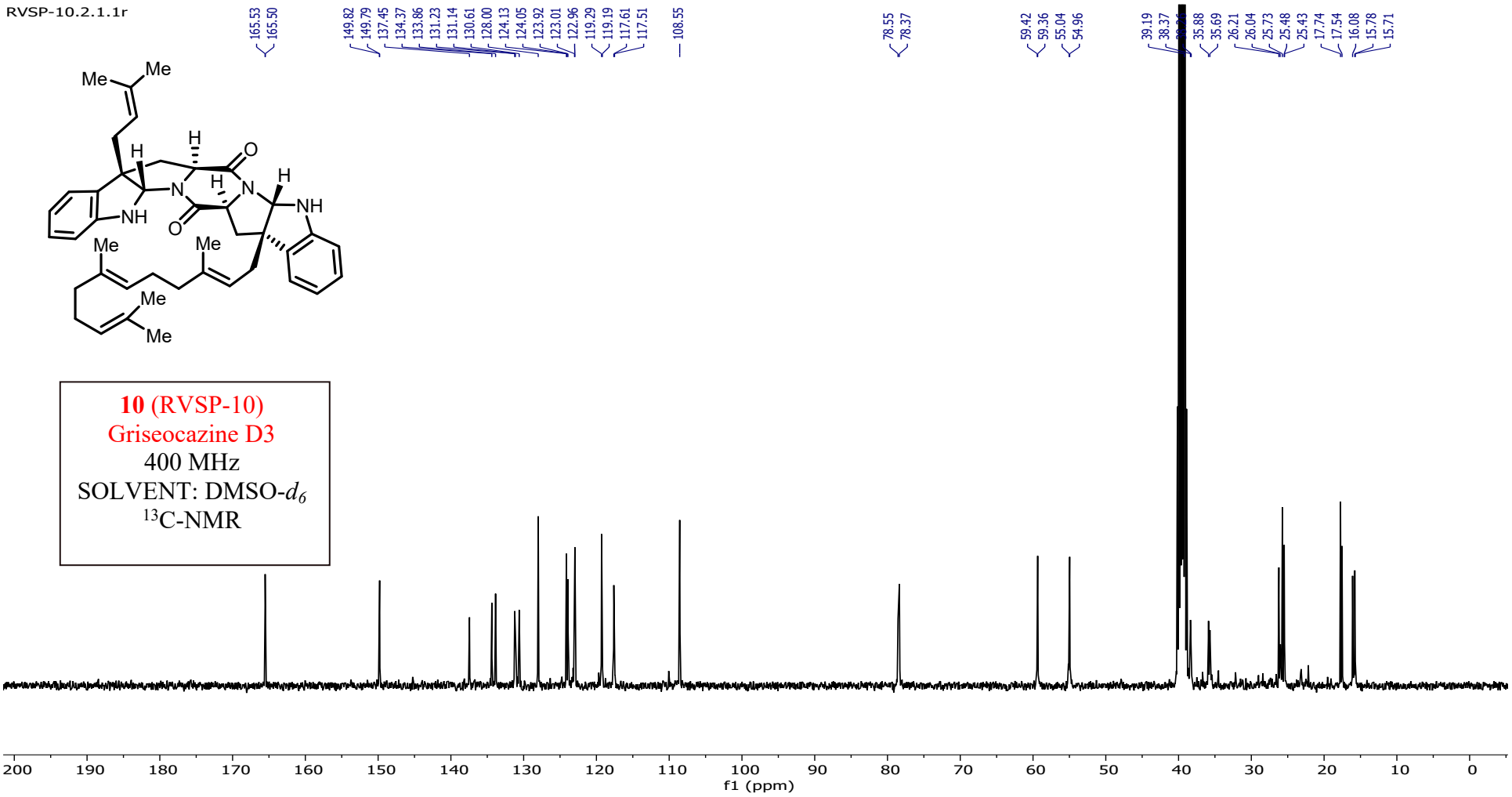
Spectrum-28. ^{1}H NMR of 09: exo-C3′-farnesyl-exo-C3-prenyl -L-Trp-L-Trp-pyrroloindoline Peptide.



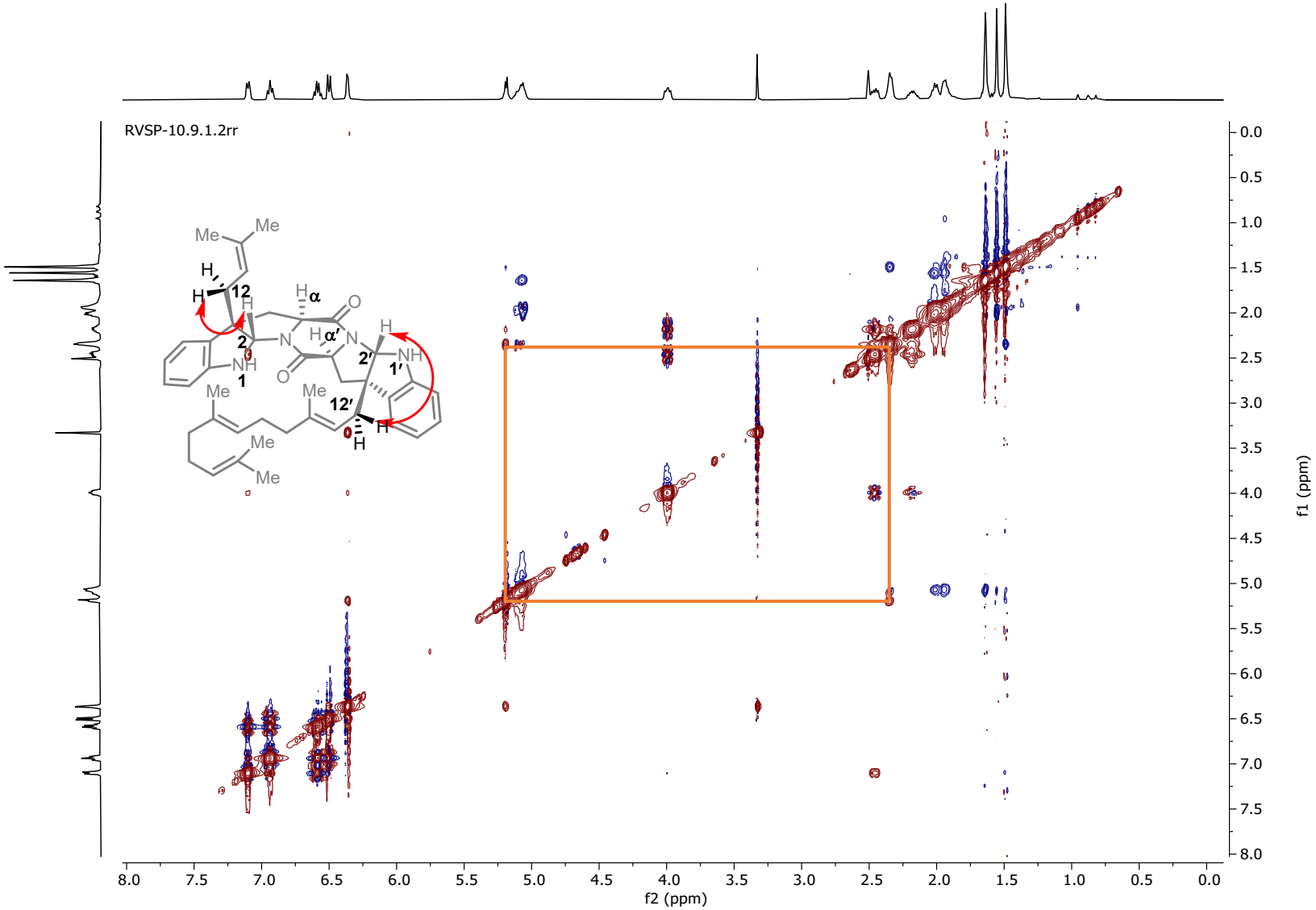
Spectrum-29. ^{13}C NMR of 09: exo-C3′-farnesyl-exo-C3-prenyl -L-Trp-L-Trp pyrroloindoline Peptide.



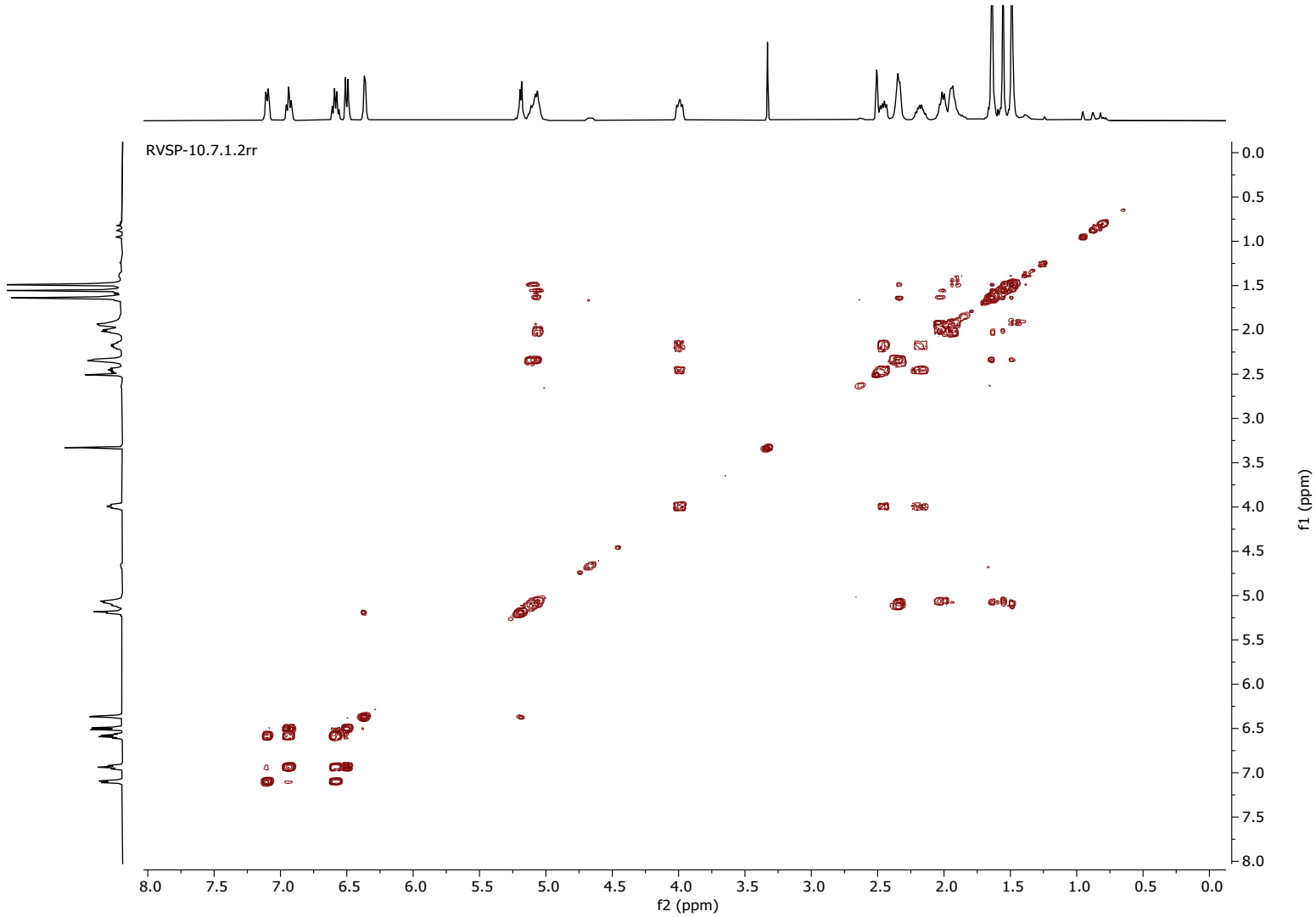
Spectrum-30. ^{1}H NMR of 10: Griseocazine D3



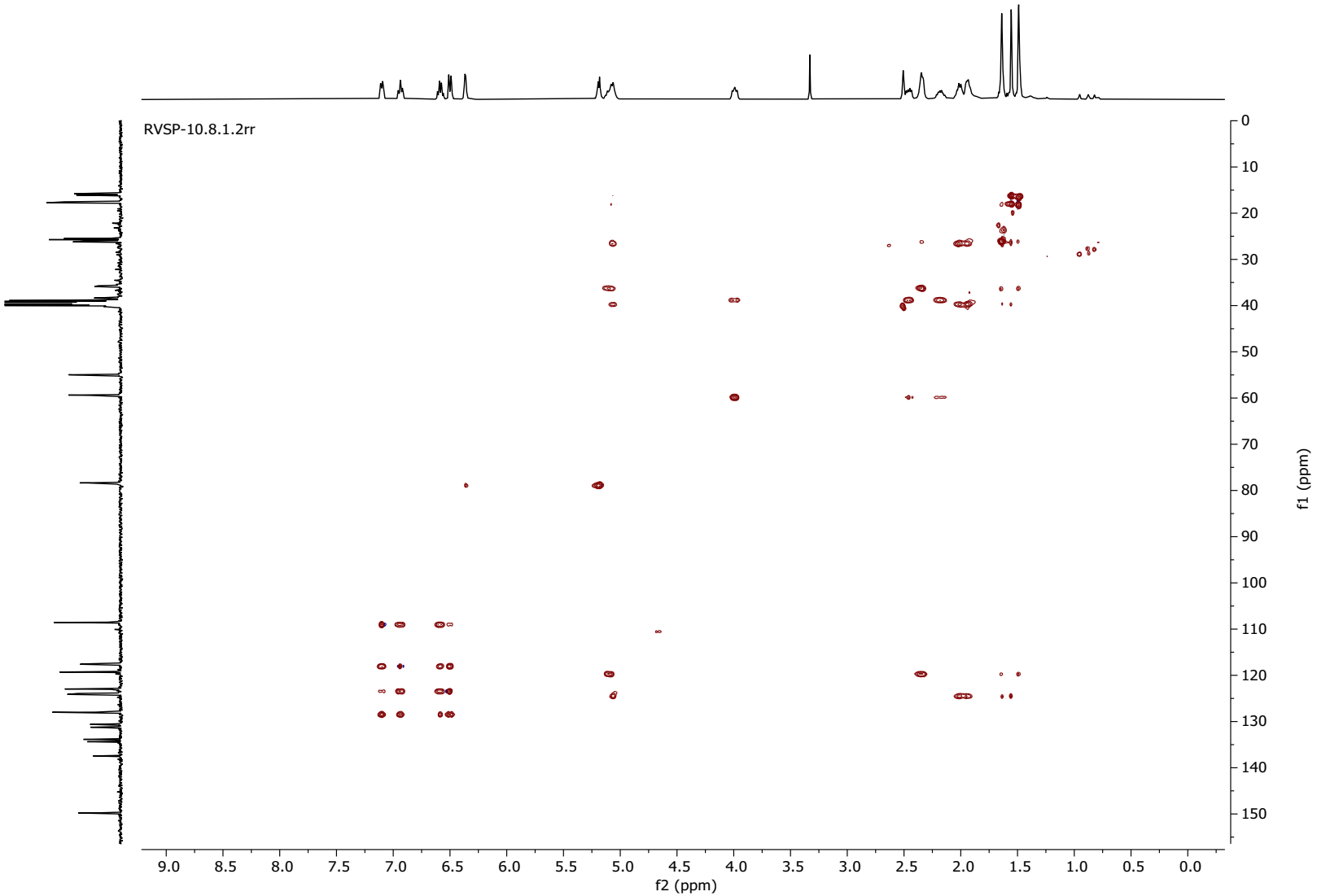
Spectrum-31. ^{13}C NMR of 10: Griseocazine D3



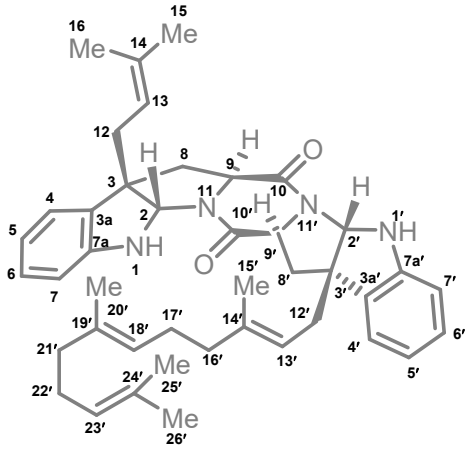
Spectrum-32. NOESY Spectrum of 10: Griseocazine D3



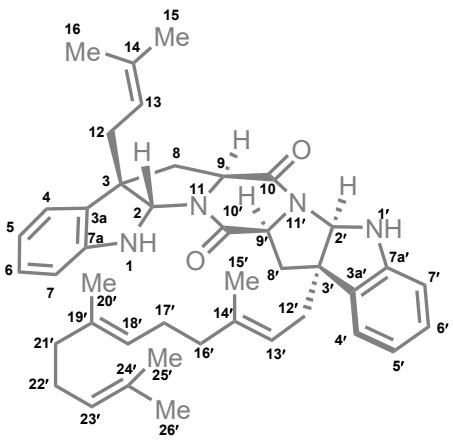
Spectrum-33. COSY Spectrum of 10: Griseocazine D3



Spectrum-34. HSQC Spectrum of 10: Griseocazine D3



Griseocazine D3



Griseocazine D2

Comparison of ^{1}H-NMR for isolated and synthetic Griseocazine D2

S.No.	Carbon No.	Reported (Isolation by Malit *et al.)* DMSO-d_6, (800 MHz) (53-proton)	Observed (Synthetic) This work DMSO-d_6, (400 MHz) (52- proton)
1	N-1	6.46 (s, 1H)	6.47 (s, 1H)
	N-1′	6.60 (d, 1H)	6.61 (dd, 1H)
2	C2 (CH)	5.13 (s, 1H)	5.13 (s, 1H)
	C2′ (CH)	5.22 (d, 1H)	5.21 (s, 1H)
3	C3 (C)	-	-
	C3′ (C)	-	-
	C3a (C)	-	-
	C3a′ (C)	-	-
4	C4 (CH)	7.16 (d, 1H)	7.16 (d, 1H)
	C4′ (CH)	7.07 (d, 1H)	7.08 (d, 1H)
5	C5 (CH)	6.63 (td, 1H)	6.65 (m, 1H)
	C5′ (CH)	6.58 (td, 1H)	6.61 (m, 1H)
6	C6 (CH)	6.97[a] (m, 1H)	6.97 (m, 2H)
	C6′ (CH)	6.95 (m, 1H)	
7	C7 (CH)	6.55 (d, 1H)	6.56 (d, 1H)
	C7′ (CH)	6.48 (d, 1H)	6.49 (d, 1H)
	C7a (C)	-	-
	C7a′ (C)	-	-
8	C8 (CH_2)	2.53 (dd, 2H), 2.15 (dd, 1H)	2.55 (m, 1H), 2.16 (dd, 1H)
	C8′ (CH_2)	2.34[a] (m, 1H), 1.94[a] (m, 1H)	2.35[a] (m, 1H), 2.02[a]-1.76[a] (m, 1H)

9	C9 (CH)	4.07 (ddd, 1H)	4.13-4.02 (m, 1H)
	C9′ (CH)	4.57 (ddd, 1H)	4.70-4.53 (m, 1H)
10	C10 (C)	-	-
	C10′ (C)	-	-
11	N-11	-	-
	N-11′	-	-
12	C12 (CH_2)	2.34[a] (m, 2H)	2.35[a] (m, 2H)
	C12′ (CH_2)	2.44 (m, 2H)	2.45 (m, 2H)
13	C13 (CH) C13′ (CH)	5.08 (t, 1H) 5.04[a] (m, 1H)	5.12-4.90[a] (m, 2H)
14	C14 (C)	-	-
	C14′ (C)	-	-
15	C15 (CH_3)	1.48[a] (m, 3H)	1.49[a] (d, 3H)
	C15′ (CH_3)	1.55 (s, 3H)	1.56 (s, 3H)
16	C16 (CH_3)	1.63 (s, 3H)	1.63 (s, 3H)
	C16′ (CH_2)	1.92[a] (m, 2H)	2.02[a]-1.76[a] (m, 2H)
17	C17′ (CH_2)	1.97[a] (m, 2H)	2.02[a]-1.76[a] (m, 2H)
18	C18′ (CH)	4.99 (t, 1H)	5.12-4.90[a] (m, 1H)
19	C19’ (C)	-	-
20	C20’ (CH_3)	1.48[a] (m, 3H)	1.49[a] (d, 3H)
21	C21′ (CH_2)	1.87 (m, 2H)	2.02[a]-1.76[a] (m, 2H)
22	C22′ (CH_2)	1.97[a] (m, 2H)	2.02[a]-1.76[a] (m, 2H)
23	C23’ (CH)	5.03[a] (m, 1H)	5.12-4.90[a] (m, 1H)
24	C24′ (C)	-	-
25	C25′ (CH_3)	1.53 (s, 3H)	1.54 (s, 3H)
26	C26′ (CH_3)	1.63 (s, 3H)	1.63 (s, 3H)

Table S2. Comparison of chemical shifts (δ) of ^{1}H-NMR between synthesized and isolated and synthetic Griseocazine D2. [a] Signal overlapping with each other.

Comparison of ^{13}C{H}-NMR for isolated and synthetic Griseocazine D2

S.No.	Carbon No.	Reported (Isolation by Malit *et al.)* DMSO-d_6, (800 MHz)	Observed (Synthetic) This work DMSO-d_6, (400 MHz)	Change in chemical shift Δδ (in ppm)
1	N-1	-	-	-
	N-1′	-	-	
2	C2 (CH)	78.1	78.0	0.1
	C2′ (CH)	79.7	79.7	-
3	C3 (C)	55.3	55.2	0.1
	C3′ (C)	55.4	55.3	0.1
	C3a (C)	131.3	131.3	-
	C3a′ (C)	132.6	132.6	-
4	C4 (CH)	123.0	123.0	-
	C4′ (CH)	122.3	122.3	-
5	C5 (CH)	117.7	117.7	-
	C5′ (CH)	117.5	117.4	0.1

6	C6 (CH)	128.1	128.0	0.1
	C6′ (CH)	127.8	127.8	-
7	C7 (CH)	108.8	108.7[a]	0.1
	C7′ (CH)	108.7	108.7[a]	-
	C7a (C)	149.7	149.6	0.1
	C7a′ (C)	148.5	148.5	-
8	C8 (CH_2)	37.6	37.5	0.1
	C8 (CH_2)	39.1	Merged with solvent residual peak	-
9	C9 (CH)	59.9	59.9	-
	C9′ (CH)	58.5	58.5	-
10	C10 (C)	167.2	167.2	-
	C10′ (C)	166.1	166.0	0.1
11	N-11	-	-	-
	N-11′	-	-	-
12	C12 (CH_2)	35.4	35.3	0.1
	C12′ (CH_2)	34.2	34.1	0.1
13	C13 (CH)	119.3	119.2	0.1
	C13′ (CH)	119.6	119.5	0.1
14	C14 (C)	134.0	133.9	0.1
	C14′ (C)	137.7	137.6	0.1
15	C15 (CH_3)	17.7	17.7	-
	C15′ (CH_3)	16.2	16.1	0.1
16	C16 (CH_3)	25.8	25.7	0.1
	C16′ (CH_2)	39.3	Merged with solvent residual peak	-
17	C17′ (CH_2)	26.1	26.1	-
18	C18′ (CH)	123.7	123.7	-
19	C19’ (C)	134.5	134.4	0.1
20	C20’ (CH_3)	17.5	17.5	0.1
21	C21′ (CH_2)	39.2	Merged with solvent residual peak	-
22	C22′ (CH_2)	26.2	26.1	0.1
23	C23’ (CH)	124.1	124.1	-
24	C24′ (C)	130.6	130.5	0.1
25	C25′ (CH_3)	17.5	17.5	-
26	C26′ (CH_3)	25.4	25.4	-

Table S3. Comparison of 13C{H} NMR chemical shifts (δ) and difference in chemical shift (Δδ) between isolated and synthetic Griseocazine D2. [a] Signal overlapping with each other.

Comparison of ^{1}H-NMR for natural and synthetic Griseocazine D3

S.No.	Carbon No.	Reported (Isolation by Malit *et al.)* DMSO-d_6, (800 MHz) (52-Proton)	Observed (Synthetic) This work DMSO-d_6, (400 MHz) (52-Proton)
1	N-1	6.38[a] (m, 1H)	6.36 (m, 2H)
	N-1′	6.37[a] (m, 1H)	
2	C2 (CH)	5.17[a] (m, 1H)	5.25-5.15 (m, 2H)
	C2′ (CH)	5.19[a] (m, 1H)	
3	C3 (C)	-	-
	C3′ (C)	-	-
	C3a (C)	-	-
	C3a′ (C)	-	-
4	C4 (CH)	7.11[a] (m, 1H)	7.10 (m, 2H)
	C4′ (CH)	7.10[a] (m, 1H)	
5	C5 (CH)	6.59[a] (m, 1H)	6.58 (m, 2H)
	C5′ (CH)	6.57[a] (m, 1H)	
6	C6 (CH)	6.93[a] (m, 1H)	6.94 (m, 2H)
	C6′ (CH)	6.93[a] (m, 1H)	
7	C7 (CH)	6.49[a] (d, 1H)	6.50 (m, 2H)
	C7′ (CH)	6.49[a] (d, 1H)	
	C7a (C)	-	-
	C7a′ (C)	-	-
8	C8 (CH_2)	2.45[a] (m, 1H), 2.16[a] (m, 1H)	2.46[a] (m, 1H), 2.18[a] (m, 1H)
	C8′ (CH_2)	2.44[a] (m, 1H), 2.17[a] (m, 1H)	2.46[a] (m, 1H), 2.18[a](m, 1H)
9	C9 (CH)	4.01[a] (m, 1H)	3.99 (m, 2H)
	C9′ (CH)	4.00[a] (m, 1H)	
10	C10 (C)	-	-
	C10′ (C)	-	-
11	N-11	-	-
	N-11′	-	-
12	C12 (CH_2)	2.34[a] (m, 2H)	2.34 (m, 4H)
	C12′ (CH_2)	2.34[a] (m, 2H)	
13	C13 (CH)	5.07[a] (m, 1H)	5.08[a] (m, 2H)
	C13′ (CH)	5.10[a] (m, 1H)	
14	C14 (C)	-	-
	C14′ (C)	-	-
15	C15 (CH_3)	1.49[a] (m, 3H)	1.49 (s, 6H)
	C15′ (CH_3)	1.48[a] (m, 3H)	
16	C16 (CH_3)	1.64[a] (m, 3H)	1.64 (s, 3H)
	C16′ (CH_2)	1.94[a] (m, 2H)	2.06[a]-1.87[a] (m, 2H)
17	C17′ (CH_2)	2.00[a] (m, 2H)	2.06[a]-1.87[a] (m, 2H)
18	C18′ (CH)	5.05[a] (m, 1H)	5.08[a] (m, 1H)
19	C19’ (C)	-	-
20	C20’ (CH_3)	1.55 (s, 3H)	1.56 (s, 3H)
21	C21′ (CH_2)	1.92[a] (m, 2H)	2.06[a]-1.87[a] (m, 2H)

22	C22′ (CH_2)	2.01[a] (m, 2H)	2.06[a]-1.87[a] (m, 2H)
23	C23’ (CH)	5.06[a] (m, 1H)	5.08[a] (m, 1H)
24	C24′ (C)	-	-
25	C25′ (CH_3)	1.56 (s, 3H)	1.56 (s, 3H)
26	C26′ (CH_3)	1.63[a] (m, 3H)	1.64 (s, 3H)

Table S4. Comparison of chemical shifts (δ) of ^{1}H-NMR between synthesized and isolated and synthetic Griseocazine D3. [a] Signal overlapping with each other.

Comparison of ^{13}C{H}-NMR for natural and synthetic Griseocazine D3

S.No.	Carbon No.	Reported (Isolation by Malit *et al.)* DMSO-d_6, (800 MHz)	Observed (Synthetic) This work DMSO-d_6, (400 MHz)	Change in chemical shift Δδ (in ppm)
1	N-1	-	-	-
	N-1′	-	-	-
2	C2 (CH)	78.4	78.3	0.1
	C2′ (CH)	78.6	78.5	0.1
3	C3 (C)	55.0	54.9	0.1
	C3′ (C)	55.1	55.0	0.1
	C3a (C)	131.3	131.2	0.1
	C3a′ (C)	131.2	131.1	0.1
4	C4 (CH)	123.0	122.9	0.1
	C4′ (CH)	123.0	122.9	0.1
5	C5 (CH)	117.6	117.6	-
	C5′ (CH)	117.5	117.5	-
6	C6 (CH)	128.0[a]	128.0[a]	-
	C6′ (CH)	128.0[a]	128.0[a]	-
7	C7 (CH)	108.6[a]	108.5[a]	0.1
	C7′ (CH)	108.6[a]	108.5[a]	0.1
	C7a (C)	149.8	149.8	-
	C7a′ (C)	149.8	149.8	-
8	C8 (CH_2)	38.4	38.3	0.1
	C8 (CH_2)	38.3	38.2	0.1
9	C9 (CH)	59.4	59.3	0.1
	C9′ (CH)	59,4	59.4	-
10	C10 (C)	165.6	165.5	0.1
	C10′ (C)	165.5	165.5	-
11	N-11	-	-	-
	N-11′	-	-	-
12	C12 (CH_2)	35.9	35.8	0.1
	C12′ (CH_2)	35.7	35.6	0.1
13	C13 (CH)	119.3	119.2	0.1
	C13′ (CH)	119.2	119.1	0.1

14	C14 (C)	133.9	133.8	0.1
	C14′ (C)	137.5	137.4	0.1
15	C15 (CH_3)	17.8	17.7	0.1
	C15′ (CH_3)	17.6	17.5	0.1
16	C16 (CH_3)	25.8	25.7	0.1
	C16′ (CH_2)	39.4	Merged with solvent residual peak	-
17	C17′ (CH_2)	26.0	26.0	-
18	C18′ (CH)	123.9	123.9	-
19	C19’ (C)	134.4	134.4	-
20	C20’ (CH_3)	15.8	15.7	0.1
21	C21′ (CH_2)	39.3	39.2	0.1
22	C22′ (CH_2)	26.2	26.2	-
23	C23’ (CH)	124.1	124.1	-
24	C24′ (C)	130.7	130.6	0.1
25	C25′ (CH_3)	17.6	17.5	0.1
26	C26′ (CH_3)	25.5	25.4	-

Table S5. Comparison of 13C{H} NMR chemical shifts (δ) and difference in chemical shift (Δδ) between isolated and synthetic Griseocazine D3. [a] Signal overlapping with each other.