SUPPORTING INFORMATION

# Antiprotozoal Isoprenoids from *Salvia hydrangea*

Marzieh Tabefam,[†, ‡] Mahdi M. Farimani,*[,†] Ombeline Danton,[‡] Justine Ramseyer,[‡] Samad N. Ebrahimi,[†] Markus Neuburger,[§] Marcel Kaiser,[⊥,O] Peyman Salehi,[†] Olivier Potterat,[‡] and Matthias Hamburger *[,‡]

[†] Department of Phytochemistry, Medicinal Plants and Drugs Research Institute, Shahid Beheshti University, G. C., Evin, Tehran, Iran

[‡] Department of Pharmaceutical Biology, University of Basel, Klingelbergstrasse 50, 4056 Basel, Switzerland

[§] Inorganic Chemistry, Department of Chemistry, University of Basel, 4056 Basel, Switzerland

[⊥] Swiss Tropical and Public Health Institute, Socinstrasse 57, CH-4002 Basel, Switzerland

[O] University of Basel, 4001 Basel, Switzerland

**Corresponding Authors**

*Tel: +41 61 207 14 25. Fax: +41 61 207 14 74. E-mail: matthias.hamburger@unibas.ch

*Tel: +98 21 2990 40 43. Fax: +98 21 2990 26 79. E-mail: m_moridi@sbu.ac.ir

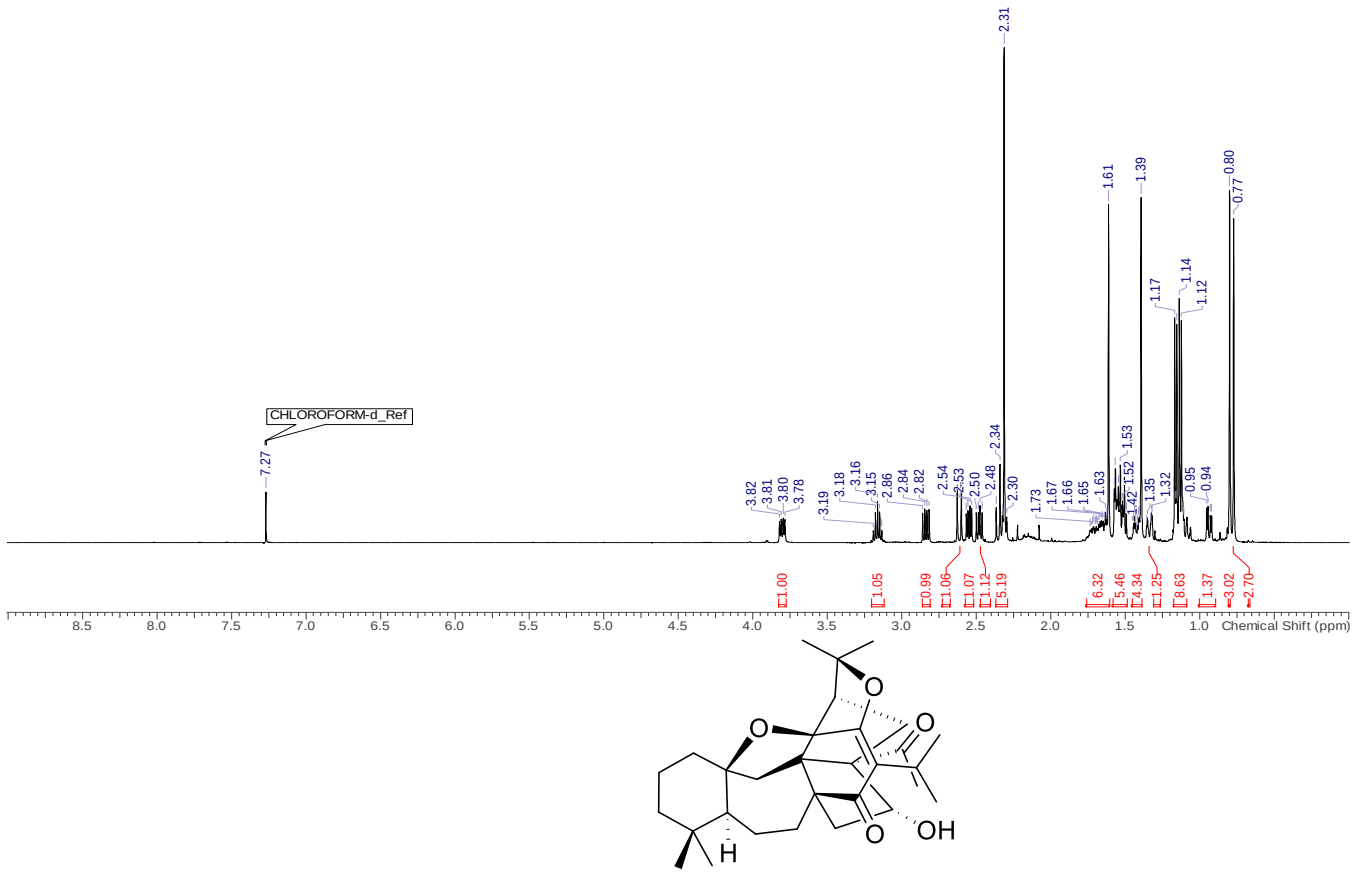
TABLE OF CONTENT

**Table S1.** $^{1}$H and $^{13}$C NMR Spectroscopic Data for Compounds **7** ..... 1
**Figure S1.** $^{1}$H NMR spectrum of compound **1** ..... 2
**Figure S2.** $^{13}$C-DEPTq spectrum of compound **1** ..... 3
**Figure S3.** $^{1}$H-$^{1}$H COSY spectrum of compound **1** ..... 4
**Figure S4.** $^{1}$H-$^{1}$H NOESY spectrum of compound **1** ..... 5
**Figure S5.** HSQC-DEPT spectrum of compound **1** ..... 6
**Figure S6.** HMBC spectrum of compound **1** ..... 7
**Figure S7.** $^{1}$H NMR spectrum of compound **2** ..... 8
**Figure S8.** $^{13}$C-DEPTq spectrum of compound **2** ..... 9
**Figure S9.** $^{1}$H-$^{1}$H COSY spectrum of compound **2** ..... 10
**Figure S10.** $^{1}$H-$^{1}$H NOESY spectrum of compound **2** ..... 11
**Figure S11.** HSQC-DEPT spectrum of compound **2** ..... 12
**Figure S12.** HMBC spectrum of compound **2** ..... 13
**Figure S13.** $^{1}$H NMR spectrum of compound **3** ..... 14
**Figure S14.** $^{13}$C-DEPTq spectrum of compound **3** ..... 15
**Figure S15.** $^{1}$H-$^{1}$H COSY spectrum of compound **3** ..... 16
**Figure S16.** $^{1}$H-$^{1}$H NOESY spectrum of compound **3** ..... 17
**Figure S17.** HSQC-DEPT spectrum of compound **3** ..... 18
**Figure S18.** HMBC spectrum of compound **3** ..... 19
**Figure S19.** $^{1}$H NMR spectrum of compound **4** ..... 20
**Figure S20.** $^{1}$H-$^{1}$H COSY spectrum of compound **4** ..... 21
**Figure S21.** $^{1}$H-$^{1}$H NOESY spectrum of compound **4** ..... 22
**Figure S22.** HSQC-DEPT spectrum of compound **4** ..... 23
**Figure S23.** HMBC spectrum of compound **4** ..... 24
**Figure S24.** $^{1}$H NMR spectrum of compound **5** ..... 25
**Figure S25.** $^{13}$C-DEPTq spectrum of compound **5** ..... 26
**Figure S26.** $^{1}$H-$^{1}$H COSY spectrum of compound **5** ..... 27
**Figure S27.** $^{1}$H-$^{1}$H NOESY spectrum of compound **5** ..... 28
**Figure S28.** HSQC-DEPT spectrum of compound **5** ..... 29
**Figure S29.** HMBC spectrum of compound **5** ..... 30
**Figure S30.** $^{1}$H NMR spectrum of compound **6** ..... 31
**Figure S31.** $^{13}$C-DEPTq spectrum of compound **6** ..... 32
**Figure S32.** $^{1}$H-$^{1}$H COSY spectrum of compound **6** ..... 33
**Figure S33.** $^{1}$H-$^{1}$H NOESY spectrum of compound **6** ..... 34
**Figure S34.** HSQC-DEPT spectrum of compound **6** ..... 35
**Figure S35.** HMBC spectrum of compound **6** ..... 36
Computational methods ..... 37

**Table S1.** $^{1}H$ and $^{13}C$ NMR Spectroscopic Data for Compound **7** ($CDCl_3$; 500 MHz for $^{1}H$ and 125 MHz for $^{13}C$ NMR; $\delta$ in ppm)

| | **7** | |
|---|---|---|
| position | $\delta_H$ (mult *J* in Hz) | $\delta c$ |
| 1 | 1.44[a] | 42.3, $CH_2$ |
| | 2.01[a] | |
| 2 | 1.45[a] | 19.5, $CH_2$ |
| | 1.96[a] | |
| 3 | 1.16[a] | 41.2, $CH_2$ |
| | 1.41[a] | |
| 4 | - | 35.9, C |
| 5 | 1.25 (d, 8.5) | 49.9, C |
| 6 | 1.79 (m) | 20.6, $CH_2$ |
| | 1.95[a] | |
| 7 | 1.19[a] | 31.8, $CH_2$ |
| | 1.94[a] | |
| 8 | - | 51.0, C |
| 9 | - | 49.8, C |
| 10 | - | 90.9, C |
| 11 | - | 99.8, C |
| 12 | - | 203.1, C |
| 13 | - | 71.4, C |
| 14 | - | 211.2, C |
| 15 | 2.02[a] | 25.9, CH |
| 16 | 0.93 (d, 7.0) | 17.0, $CH_3$ |
| 17 | 1.08 (d, 6.7) | 18.9, $CH_3$ |
| 18 | 0.87 (s) | 32.6, $CH_3$ |
| 19 | 0.96 (s) | 21.8, $CH_3$ |
| 20 | 1.88 (d, 6.4) | 40.3, $CH_2$ |
| 21 | 2.43 (m) | 29.2, $CH_2$ |
| 22 | 5.28 (m) | 119.3, $CH_2$ |
| 23 | - | 136.8, C |
| 24 | 2.32 (d, 2.6) | 46.1, CH |
| 25 | 2.64 (dd, 11.3, 2.6) | 50.6, CH |
| 26 | 5.38 (br d, 11.3) | 124.8, CH |
| 27 | - | 131.9, C |
| 28 | 1.65 (d, 1.2) | 18.8, $CH_3$ |
| 29 | 1.68 (d, 0.9) | 26.2, $CH_3$ |
| 30 | 1.71 (d, 1.5) | 22.6, $CH_3$ |
| OH | 2.76 (s) | - |

[a]Overlapping signals

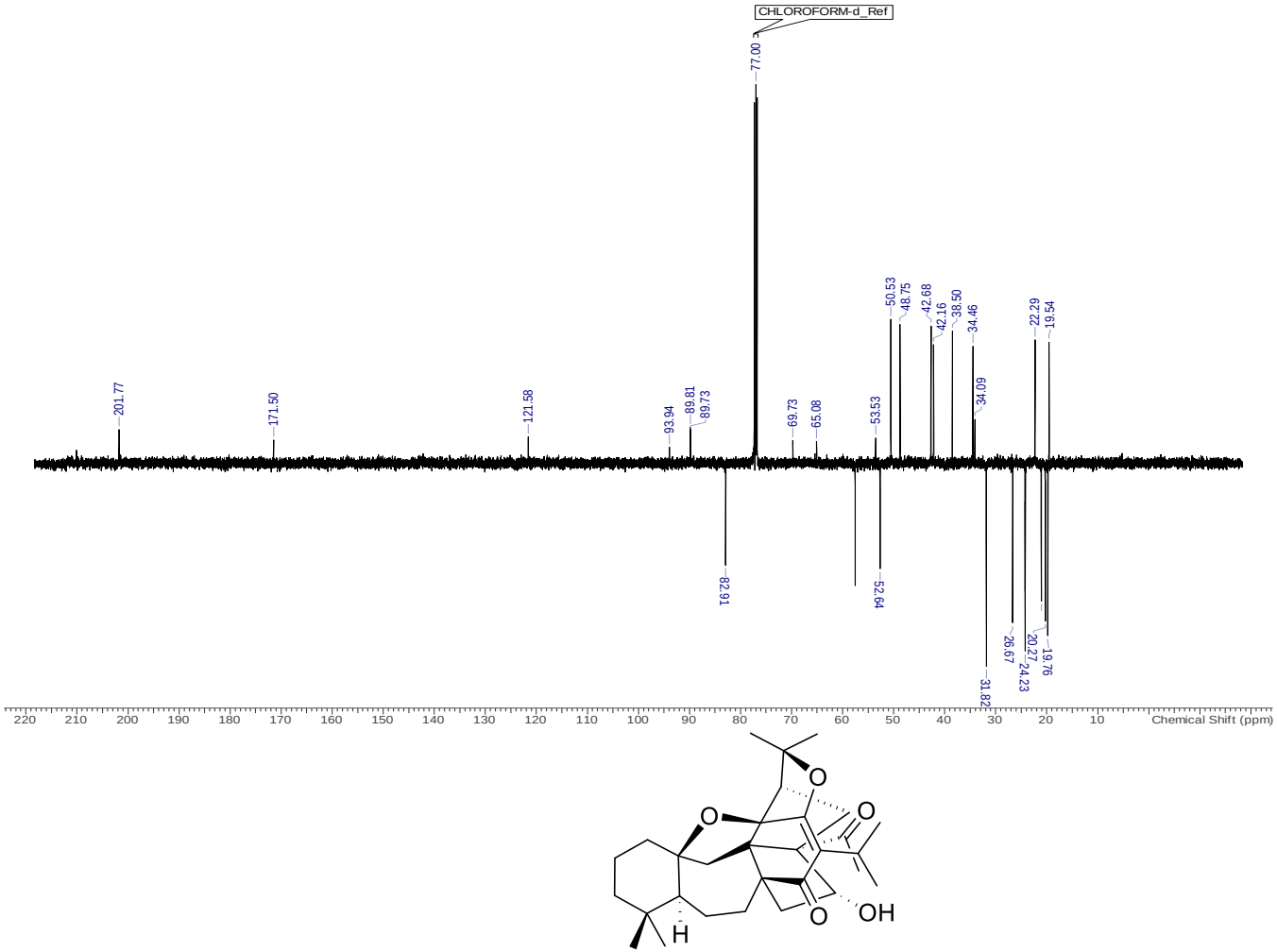






**1**

**Figure S1.** $^{1}$H NMR spectrum of compound **1** (500 MHz, $CDCl_3$)




**1**

**Figure S2.** $^{13}$C-DEPTq spectrum of compound **1**(125 MHz, $CDCl_3$)

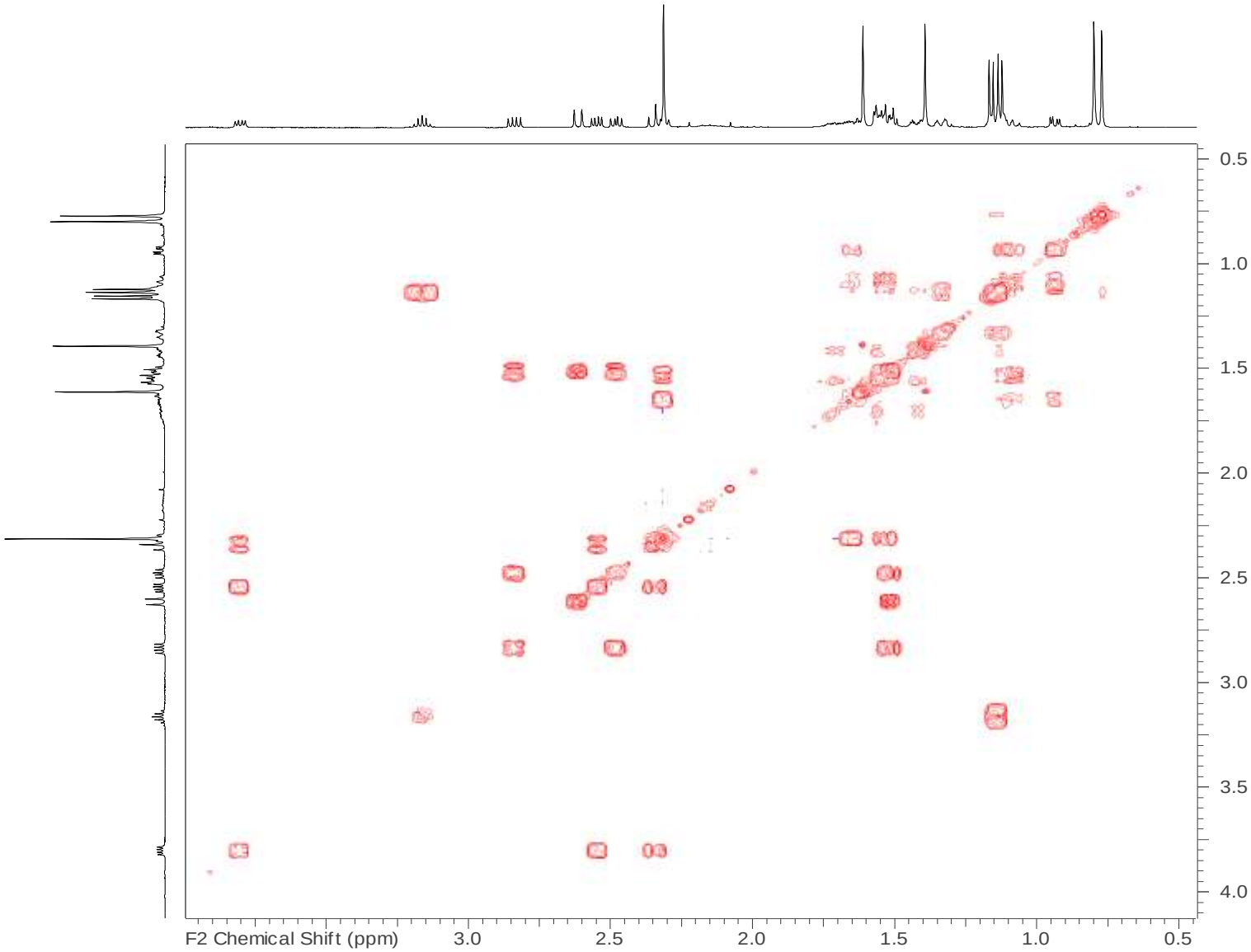



**Figure S3.** $^{1}H$-$^{1}H$ COSY spectrum of compound **1** (500 MHz, $CDCl_3$)

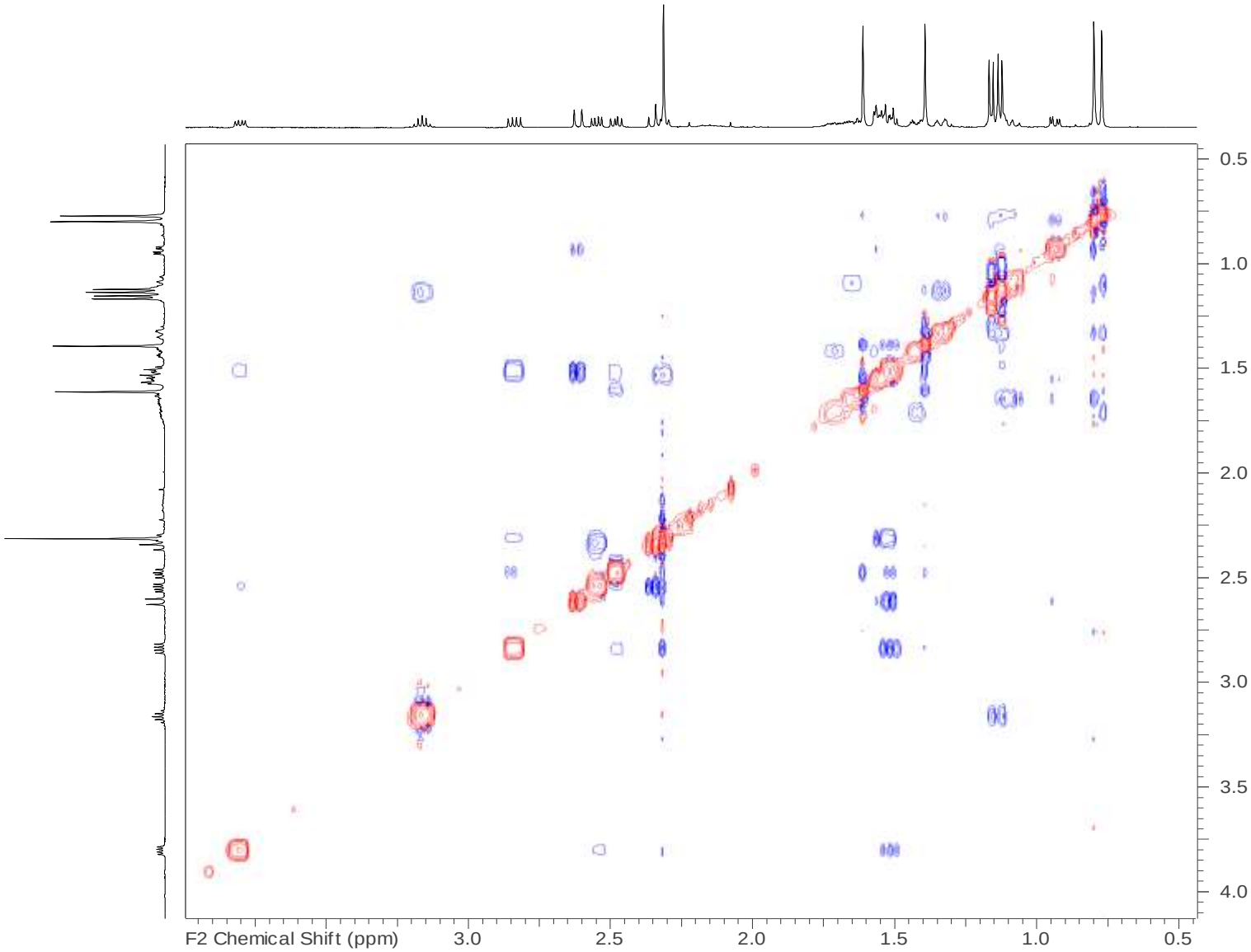



**Figure S4.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **1** (500 MHz, $CDCl_3$)

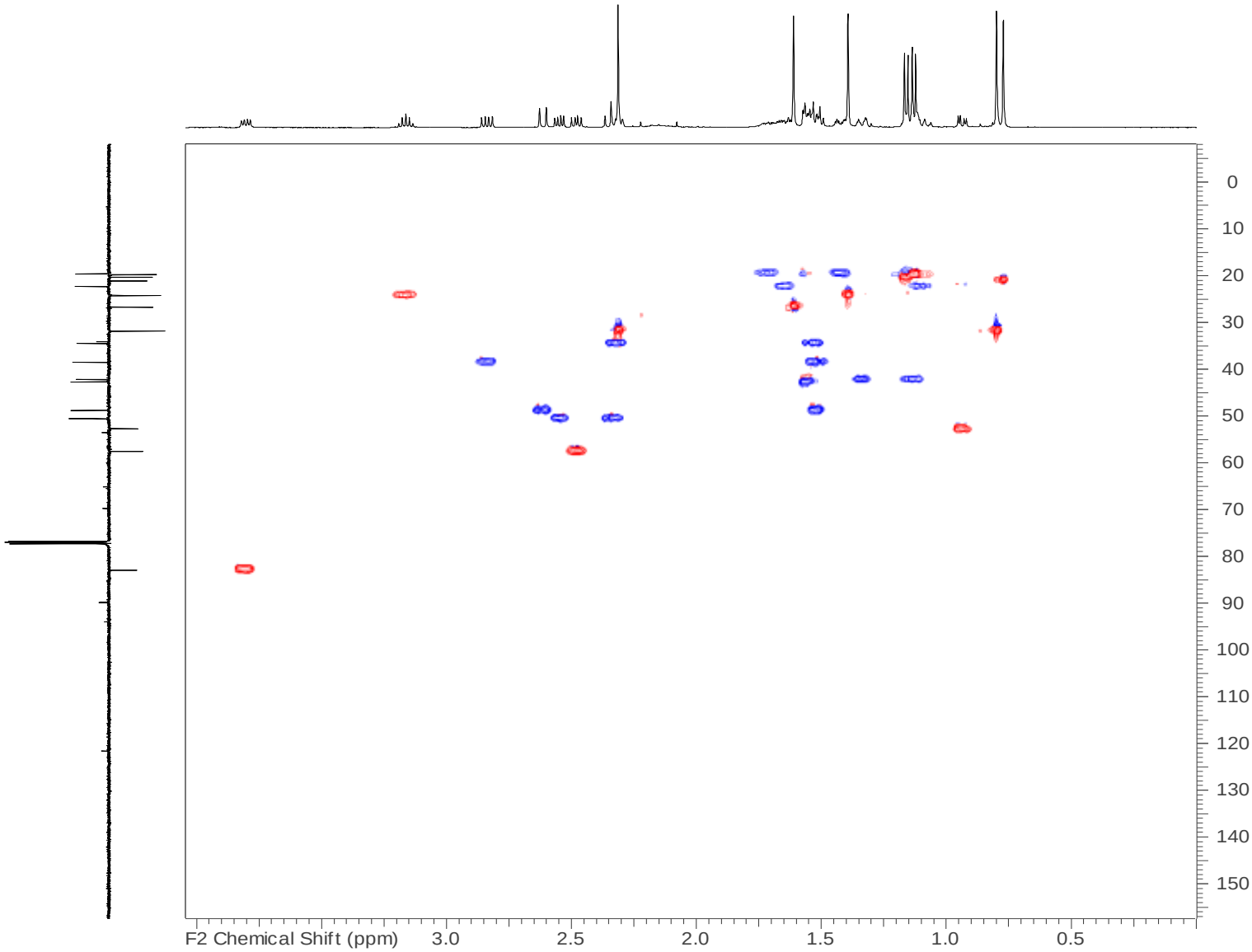



**Figure S5.** HSQC-DEPT spectrum of compound **1** (500 MHz, $CDCl_3$)

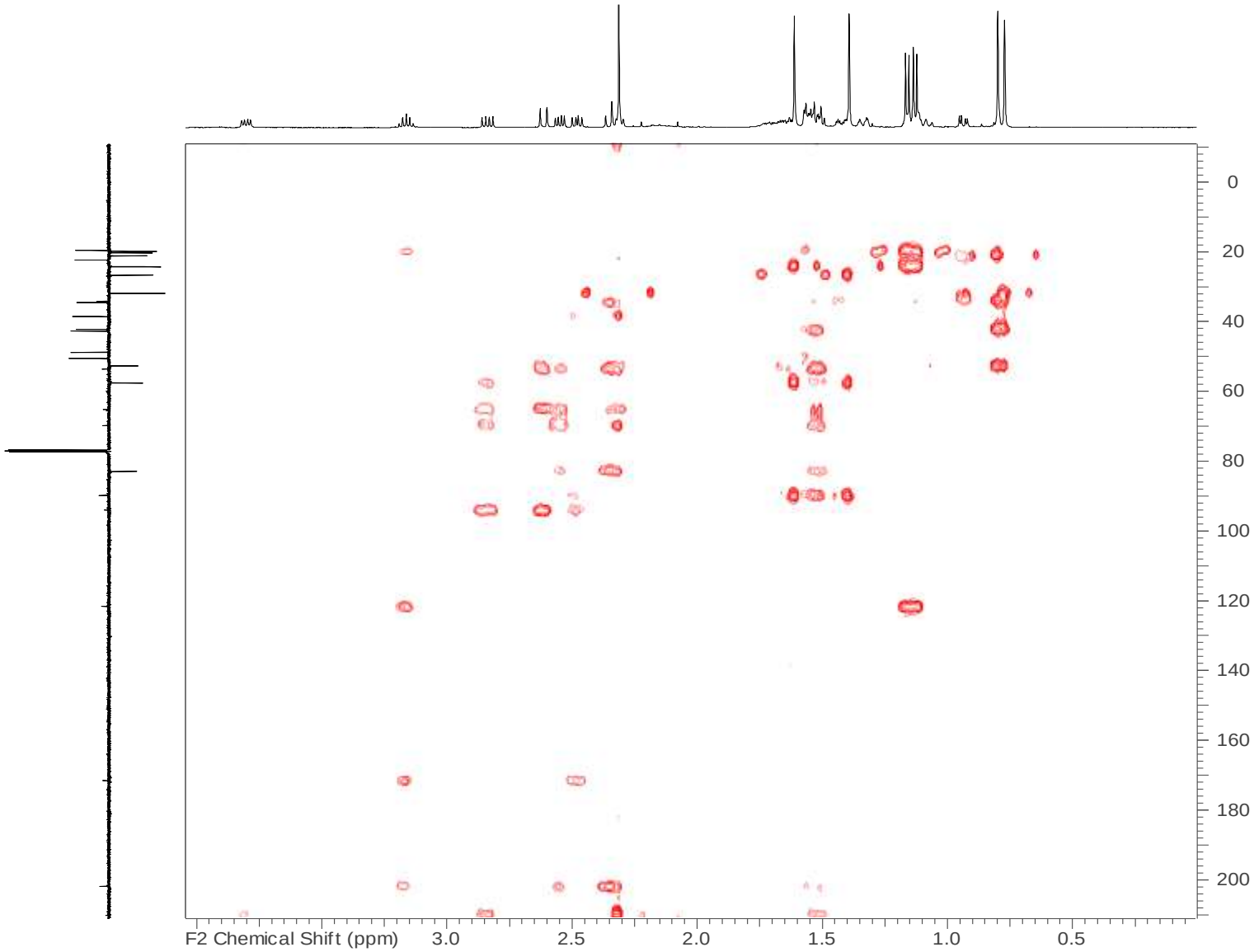
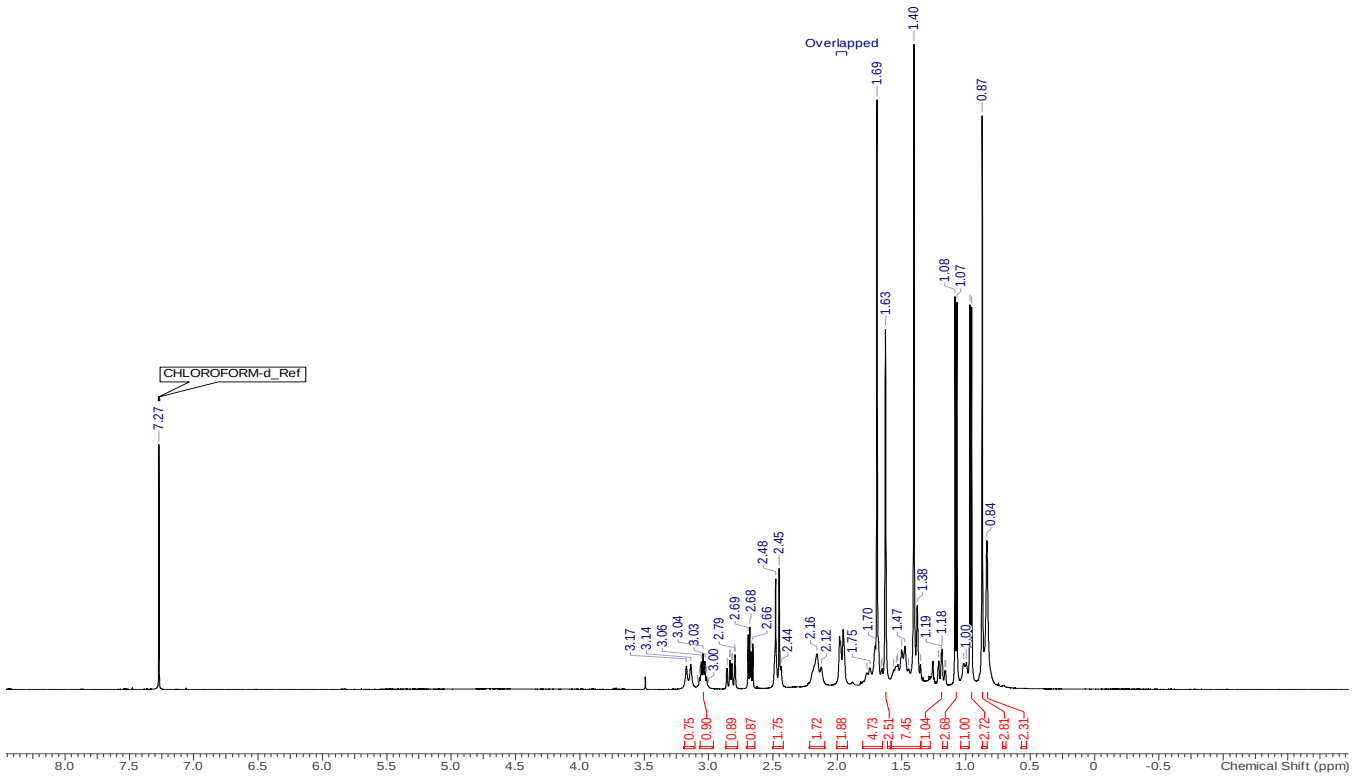
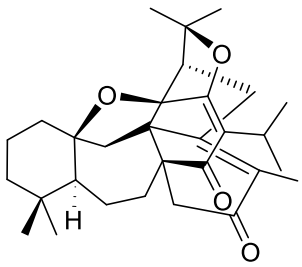


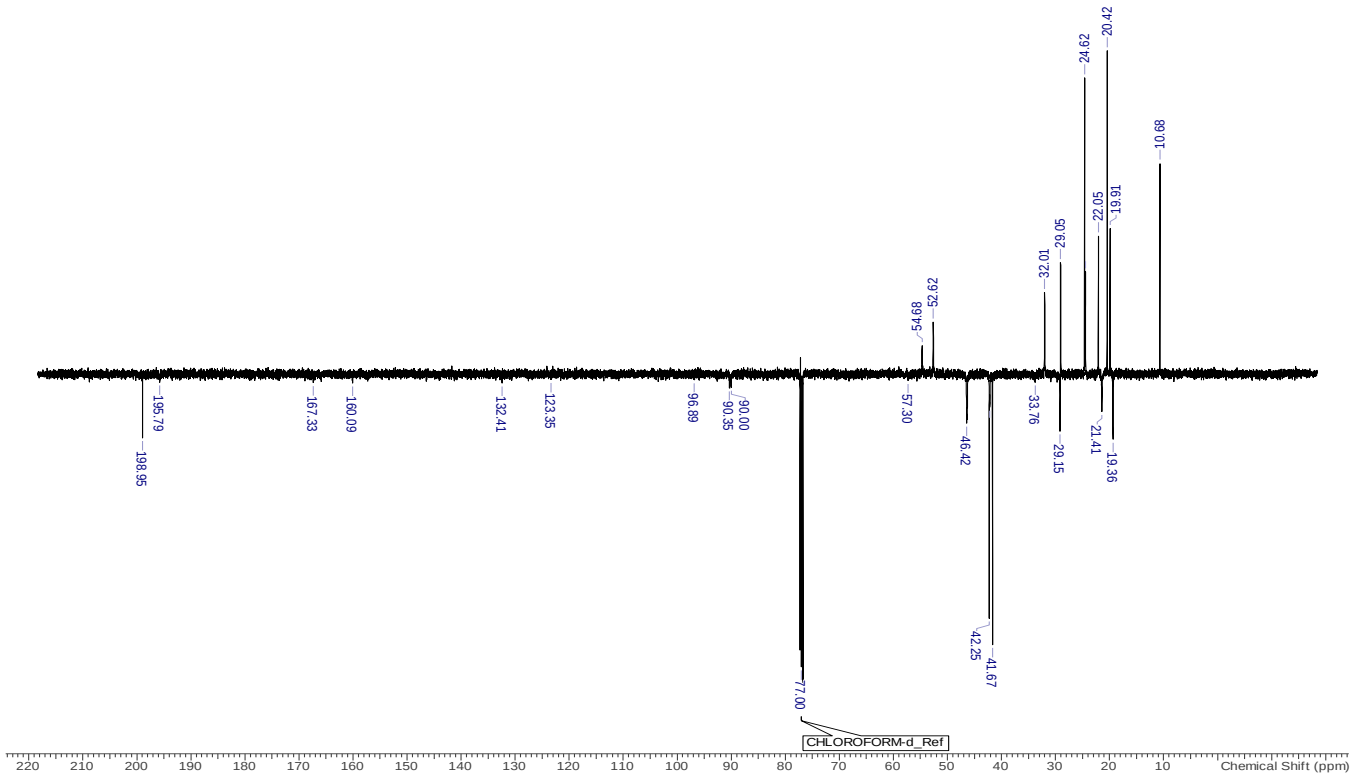

**Figure S6.** HMBC spectrum of compound **1** (500 MHz, $CDCl_3$)

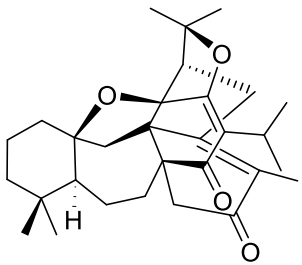



**2**

**Figure S7.** $^{1}$H NMR spectrum of compound **2** (500 MHz, $CDCl_3$)




**2**

**Figure S8.** $^{13}$C-DEPTq spectrum of compound **2** (125 MHz, $CDCl_3$)

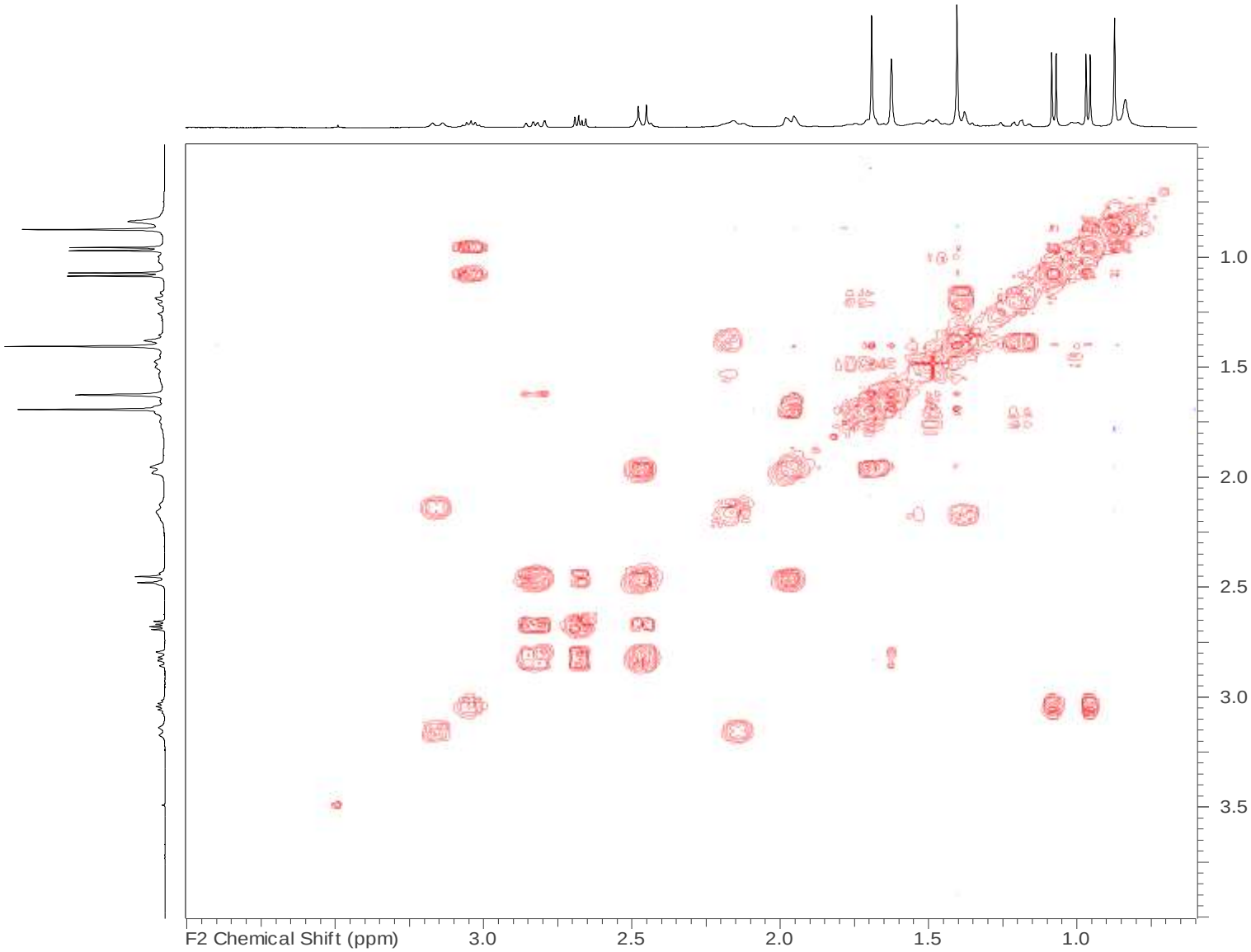



**Figure S9.** $^{1}H$-$^{1}H$ COSY spectrum of compound **2** (500 MHz, $CDCl_3$)

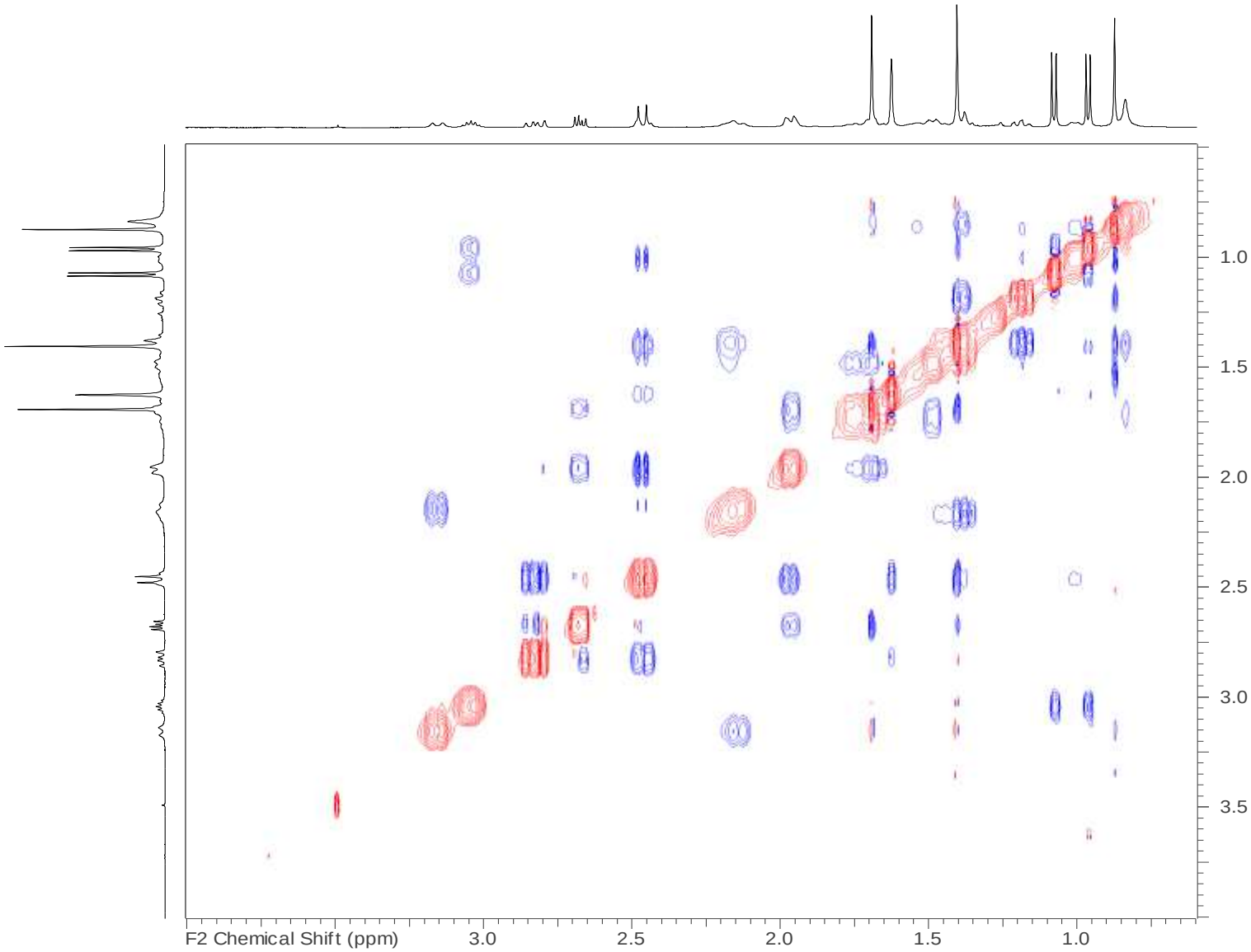



**Figure S10.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **2** (500 MHz, $CDCl_3$)

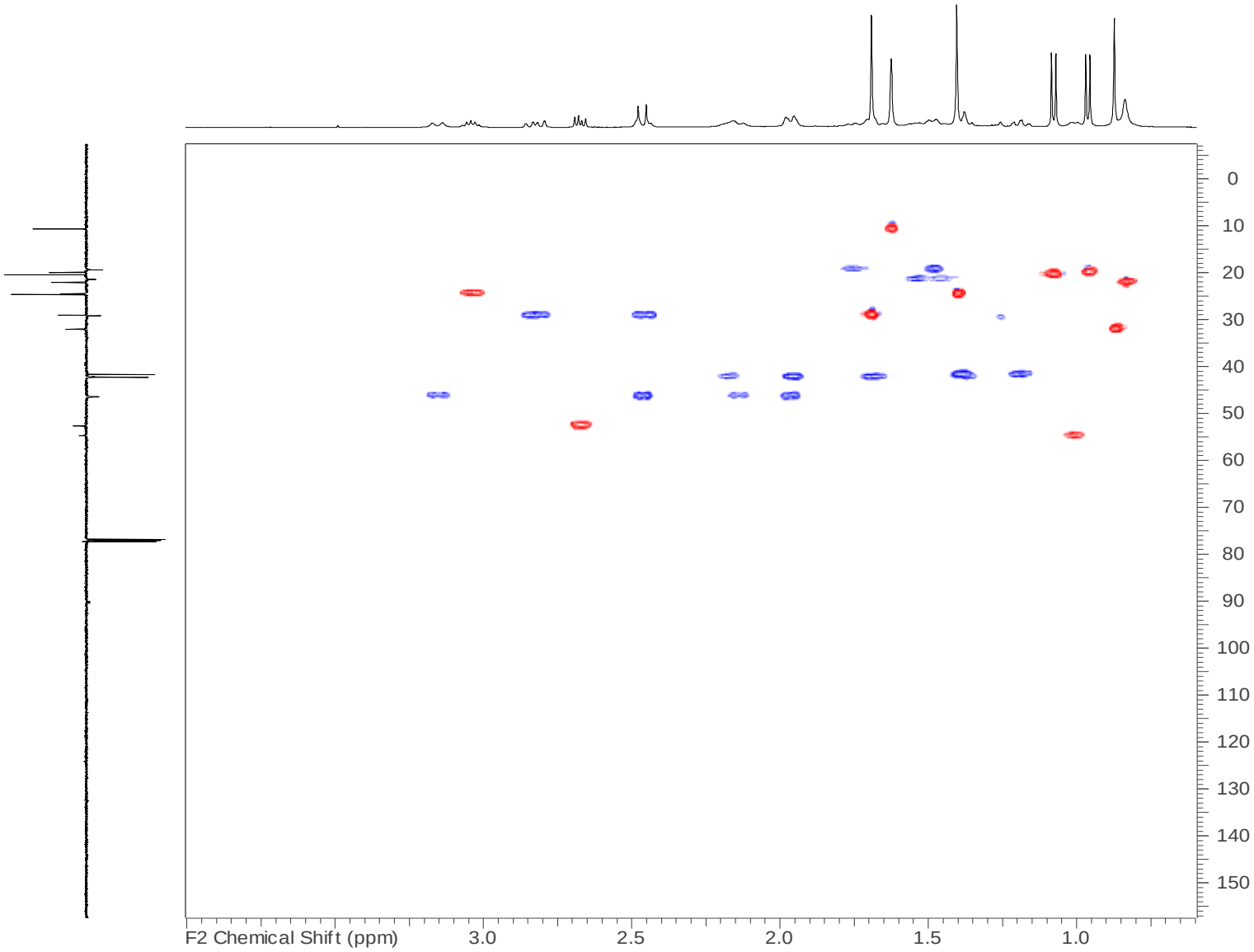



**Figure S11.** HSQC-DEPT spectrum of compound **2** (500 MHz, $CDCl_3$)

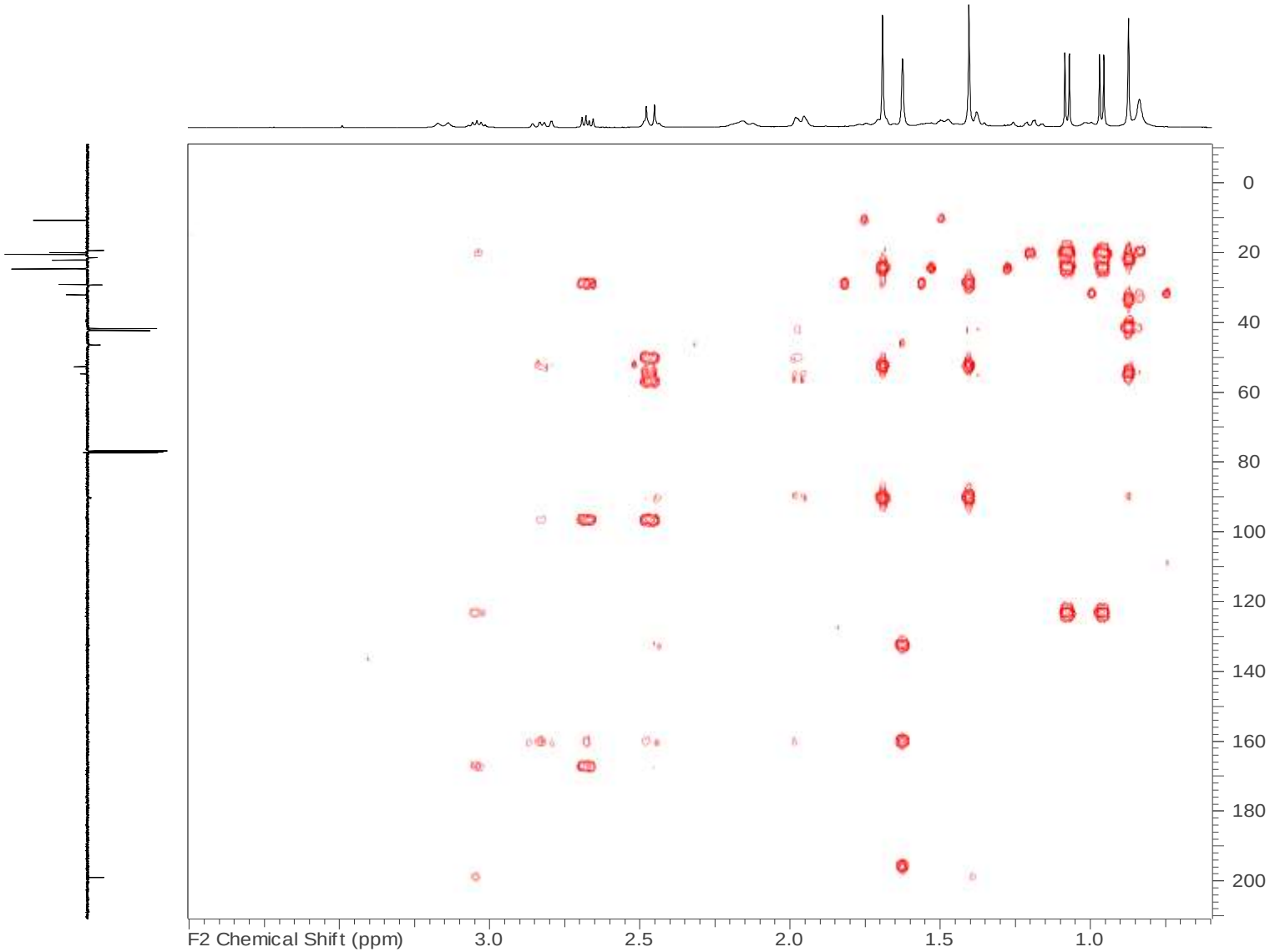
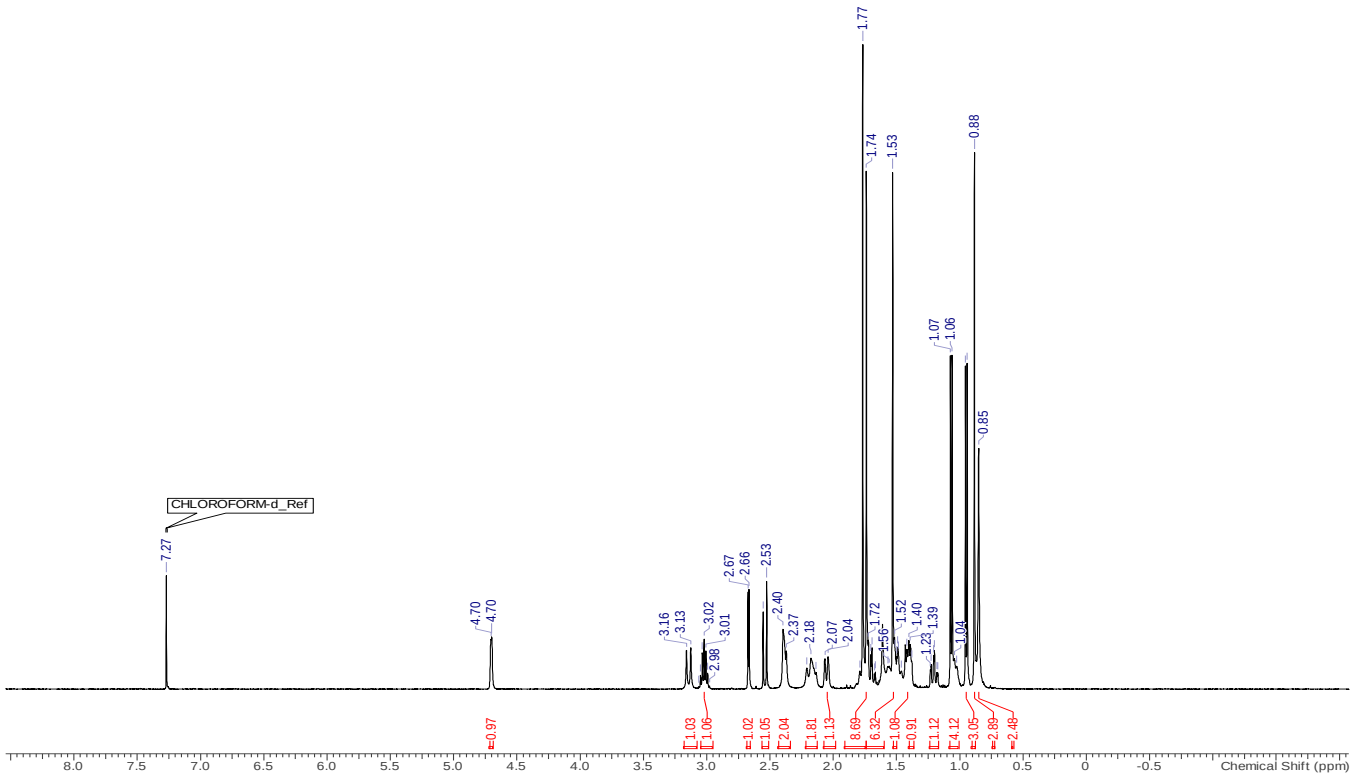
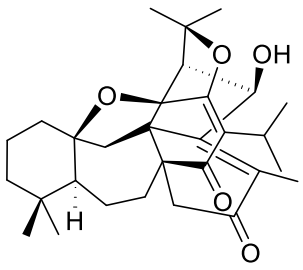


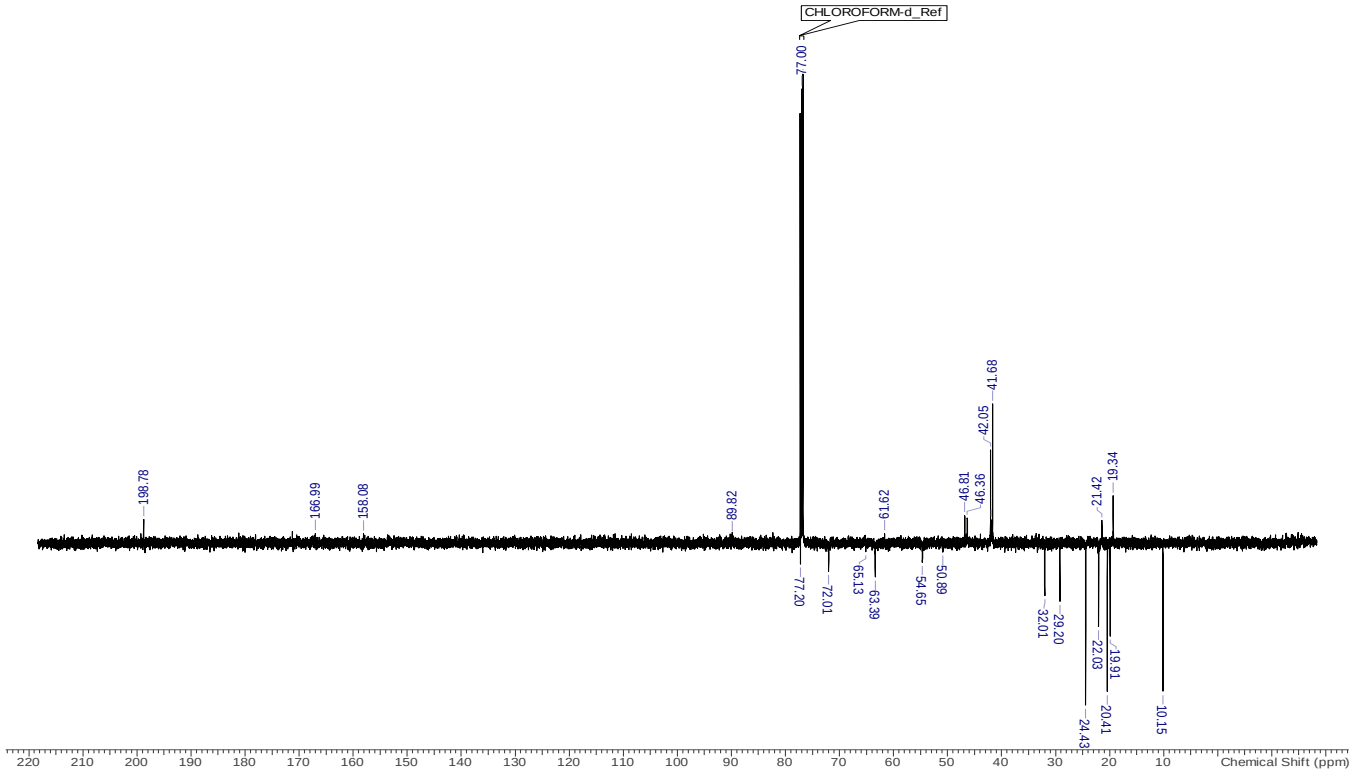

**Figure S12**. HMBC spectrum of compound **2** (500 MHz, $CDCl_3$)

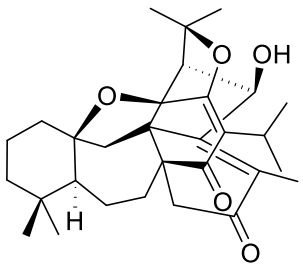



**3**

**Figure S13.** $^{1}$H NMR spectrum of compound **3** (500 MHz, $CDCl_3$)




**3**

**Figure S14.** $^{13}$C-DEPTq spectrum of compound **3** (125 MHz, $CDCl_3$)

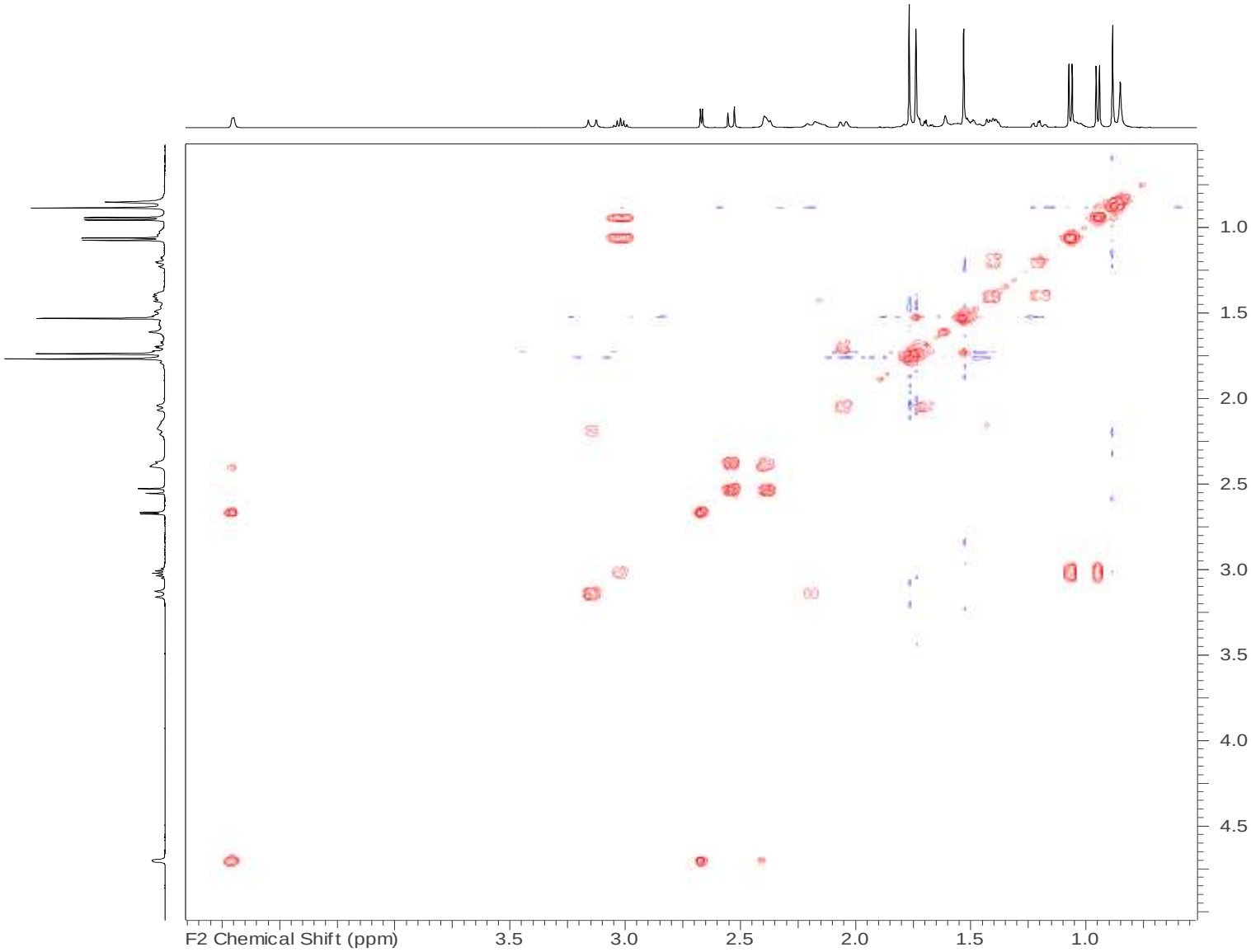



**Figure S15.** $^{1}H$-$^{1}H$ COSY spectrum of compound **3** (500 MHz, $CDCl_3$)

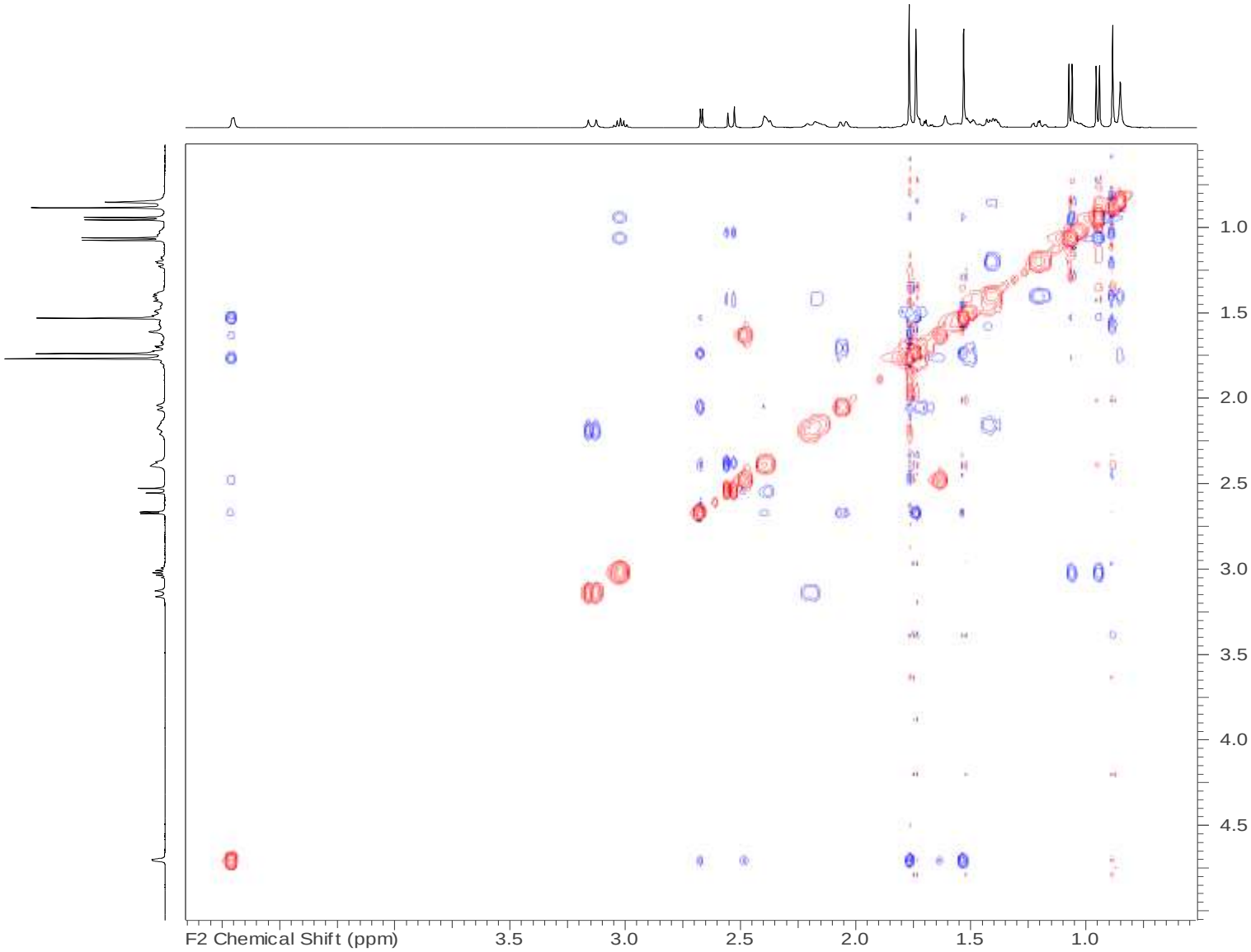



**Figure S16.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **3** (500 MHz, $CDCl_3$)

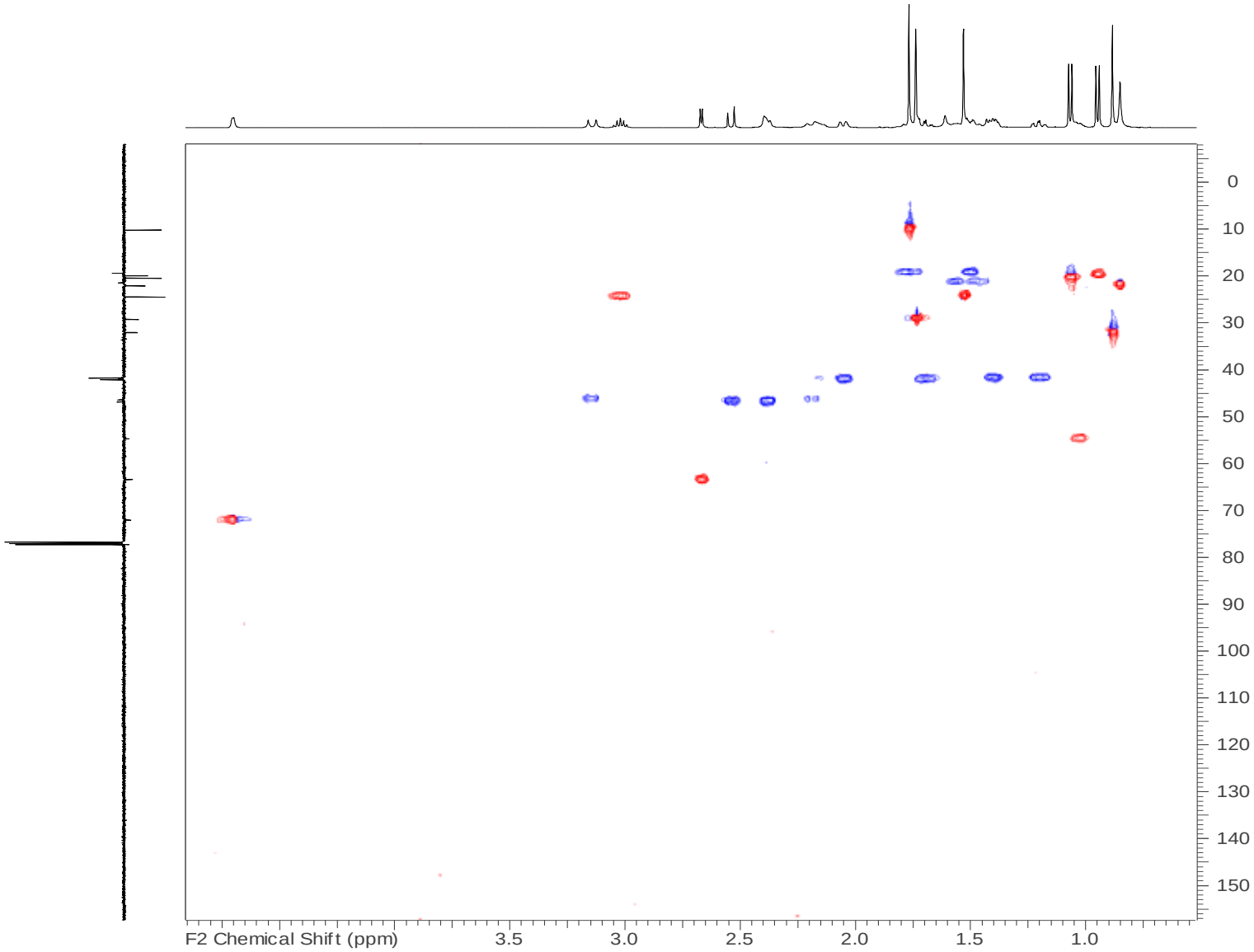



**Figure S17.** HSQC-DEPT spectrum of compound **3** (500 MHz, $CDCl_3$)

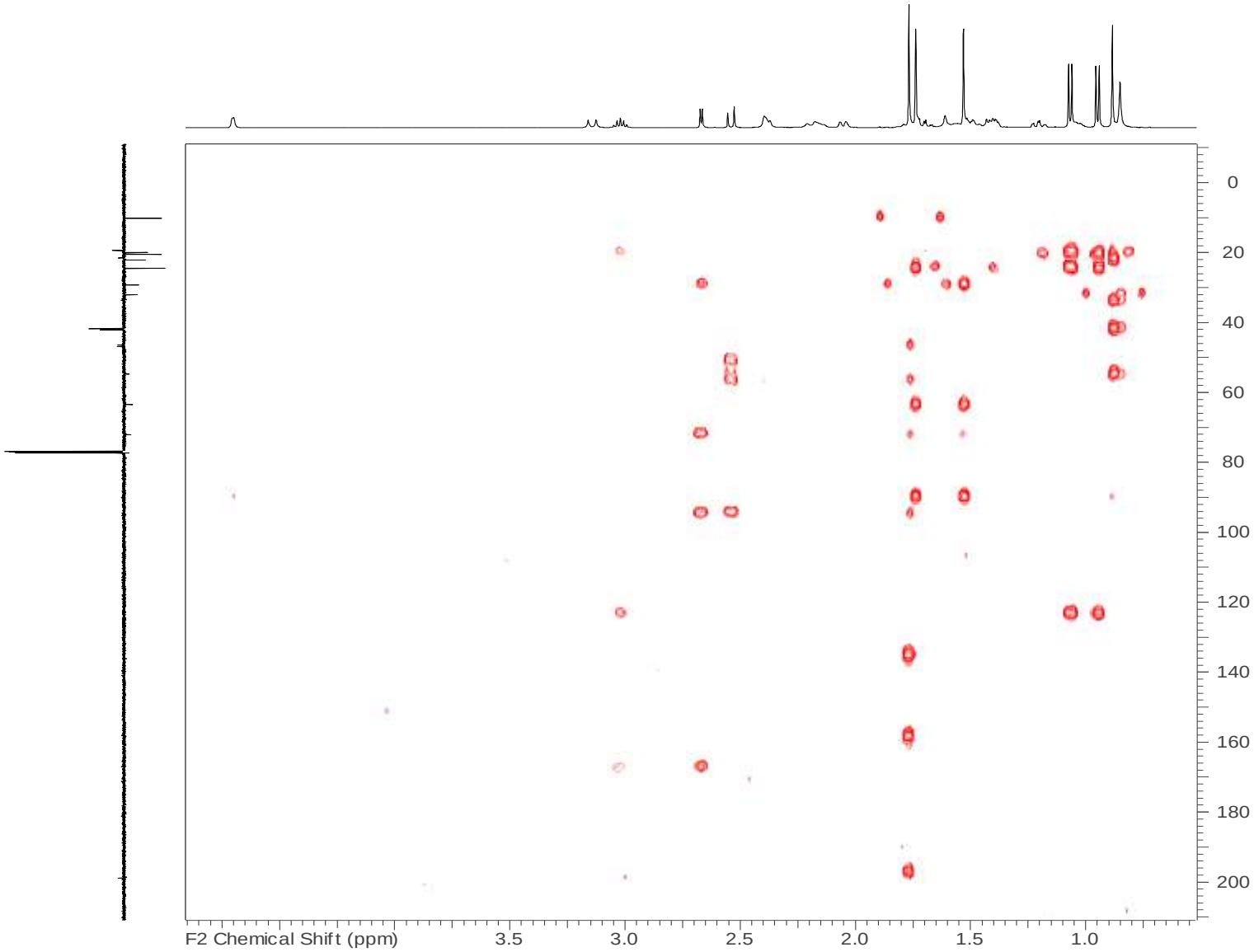
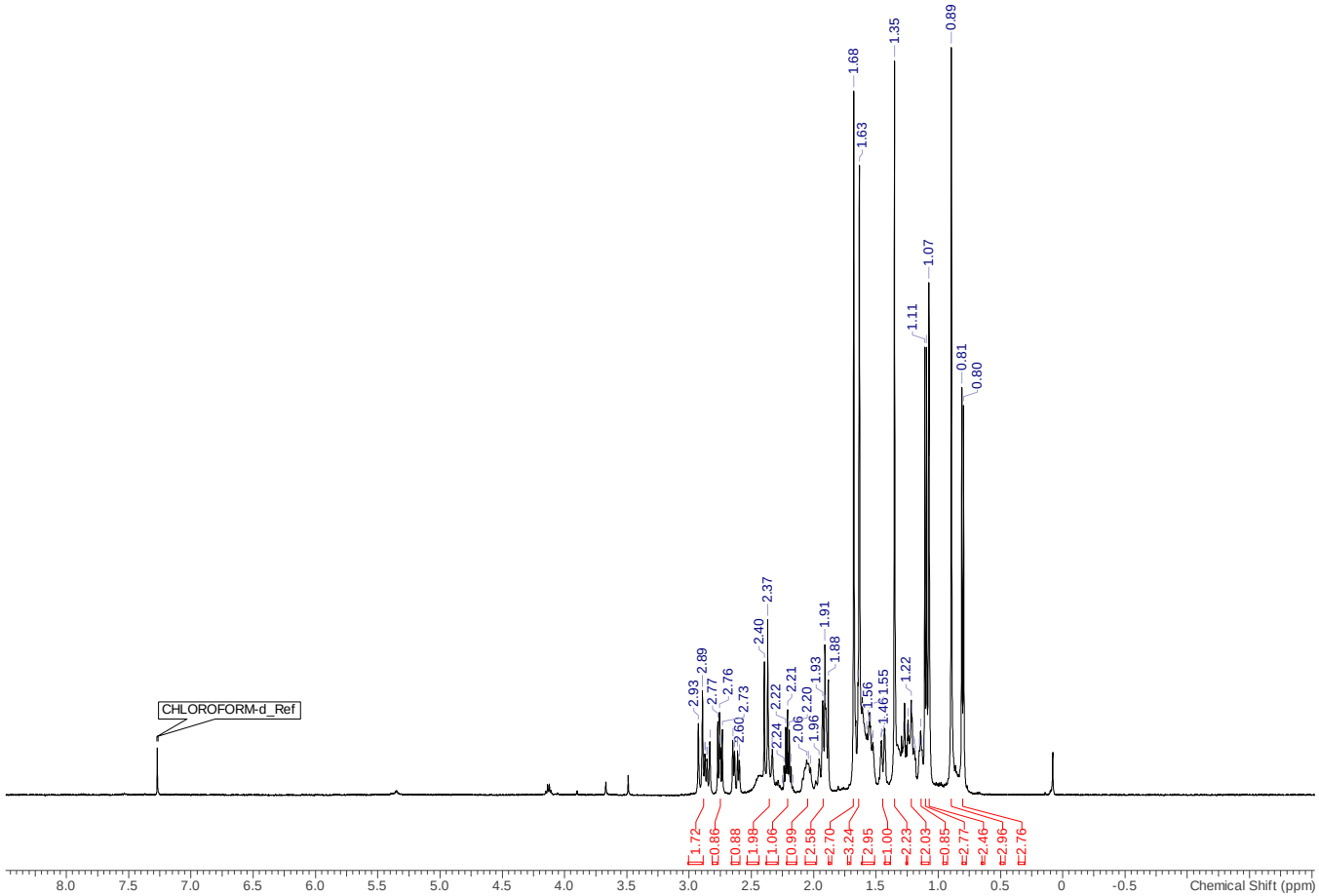
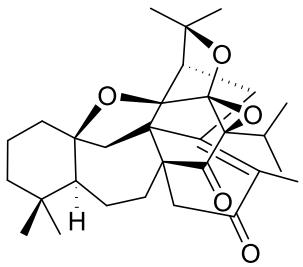



**Figure S18.** HMBC spectrum of compound **3** (500 MHz, $CDCl_3$)




**4**

**Figure S19.** $^{1}$H NMR spectrum of compound **4** (500 MHz, $CDCl_3$)

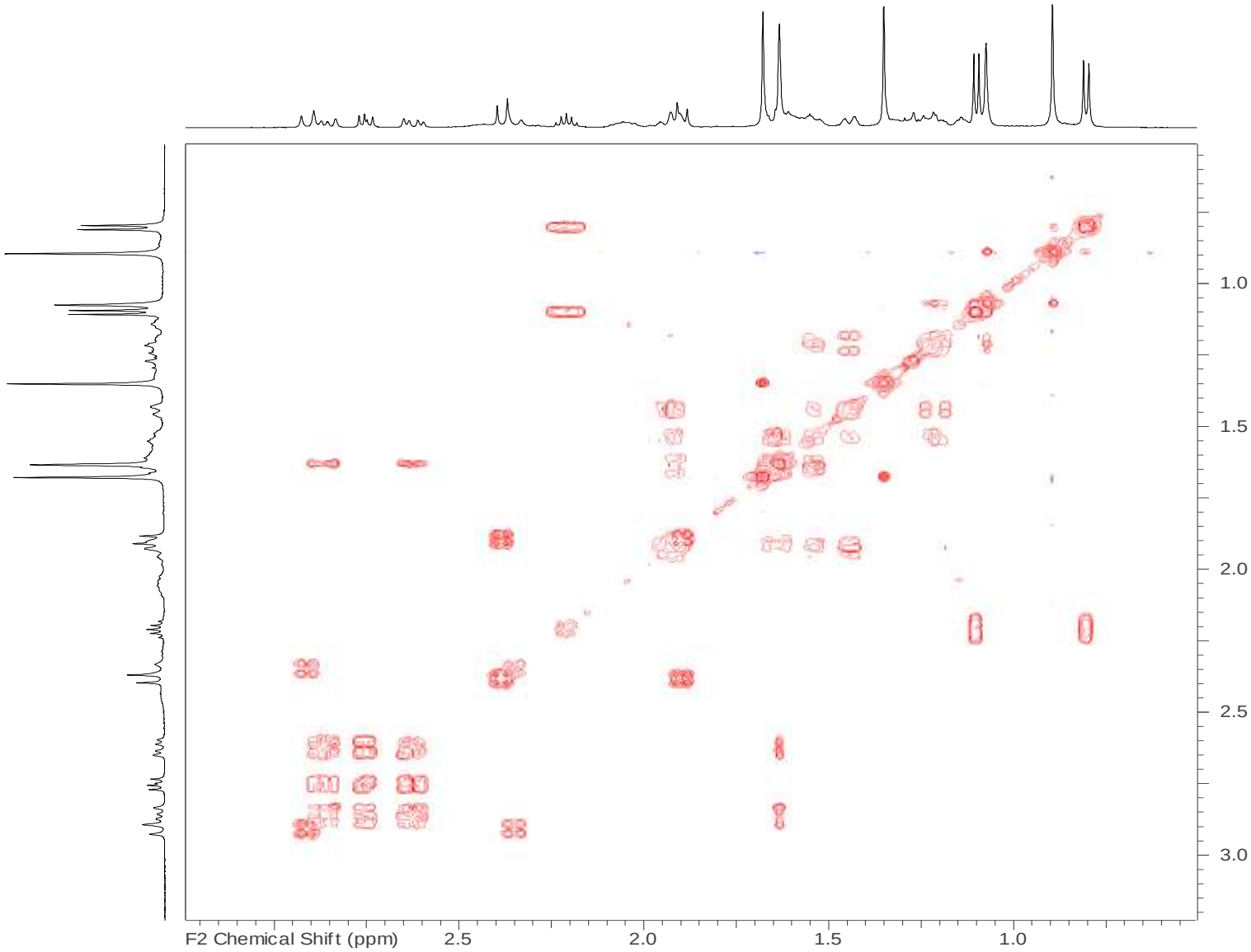



**Figure S20.** $^{1}H$-$^{1}H$ COSY spectrum of compound **4** (500 MHz, $CDCl_3$)

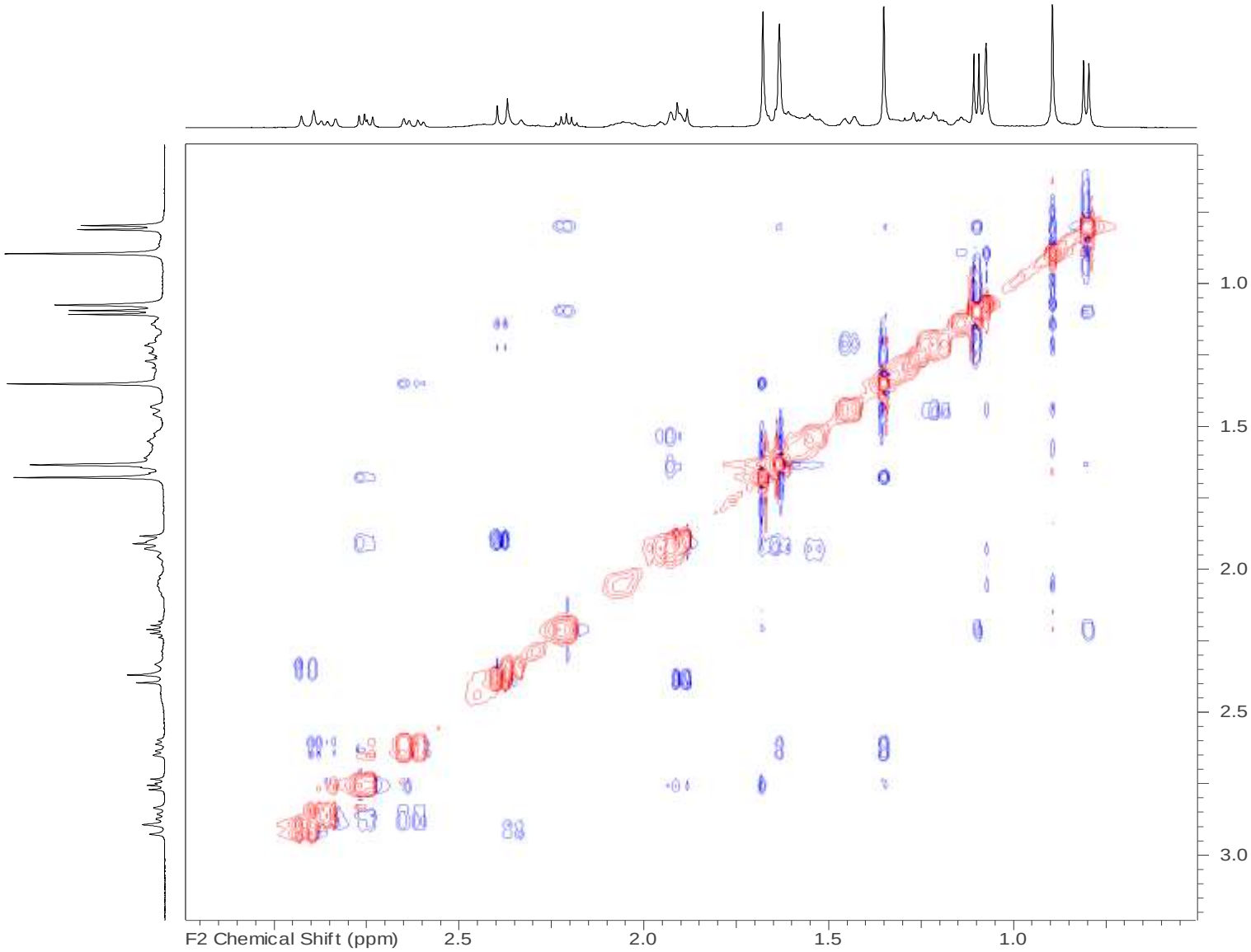



**Figure S21.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **4** (500 MHz, $CDCl_3$)

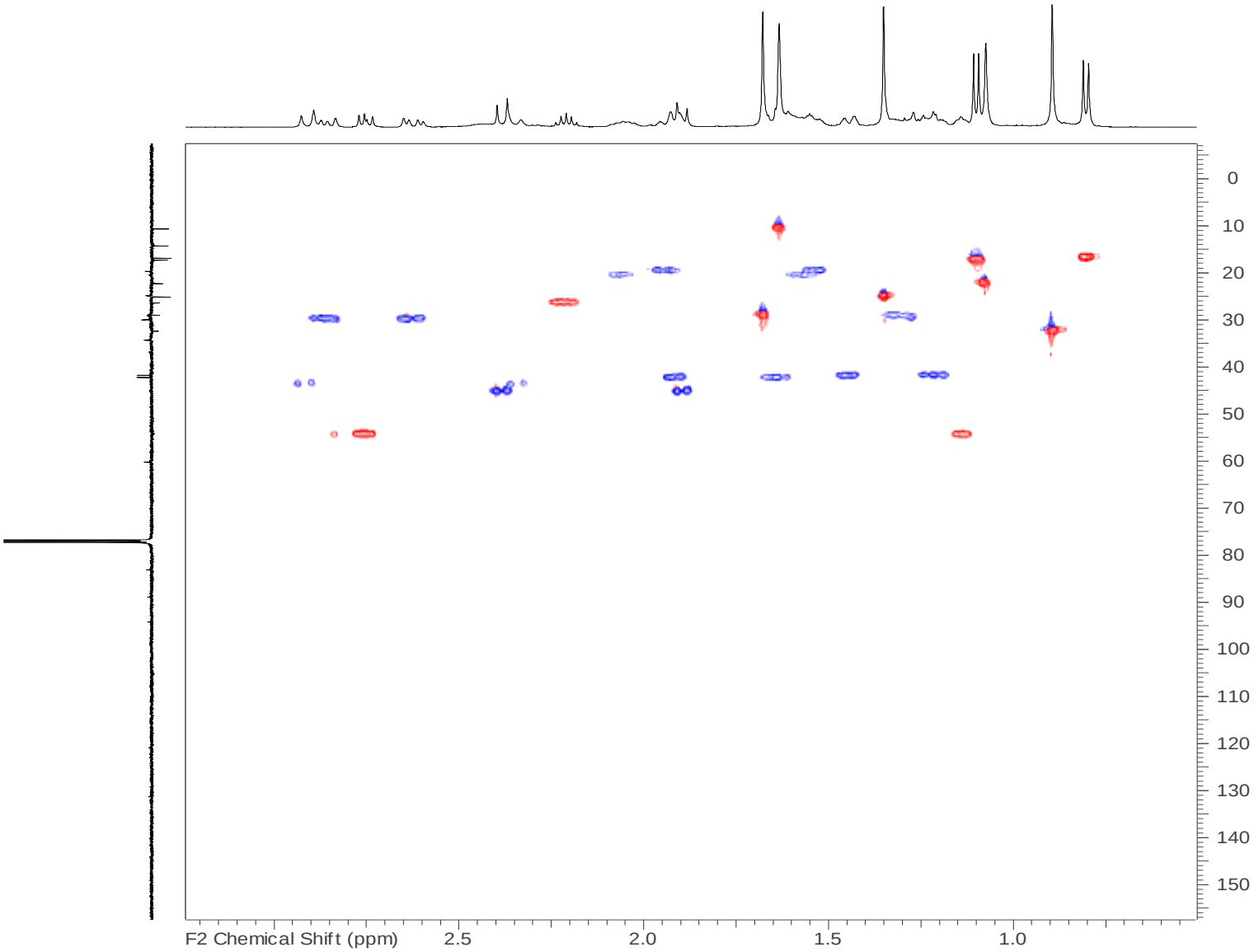



**Figure S22.** HSQC-DEPT spectrum of compound **4** (500 MHz, $CDCl_3$)

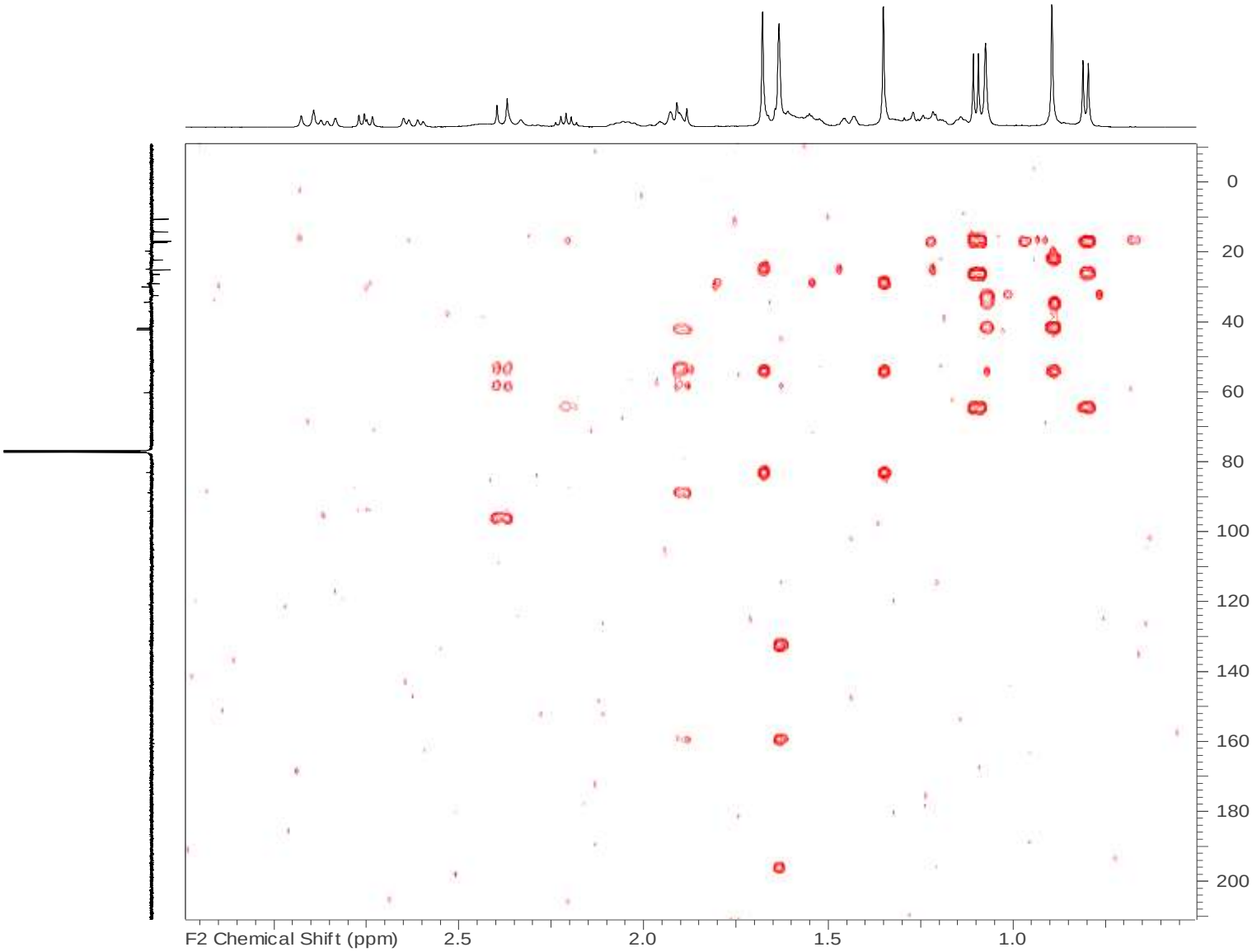
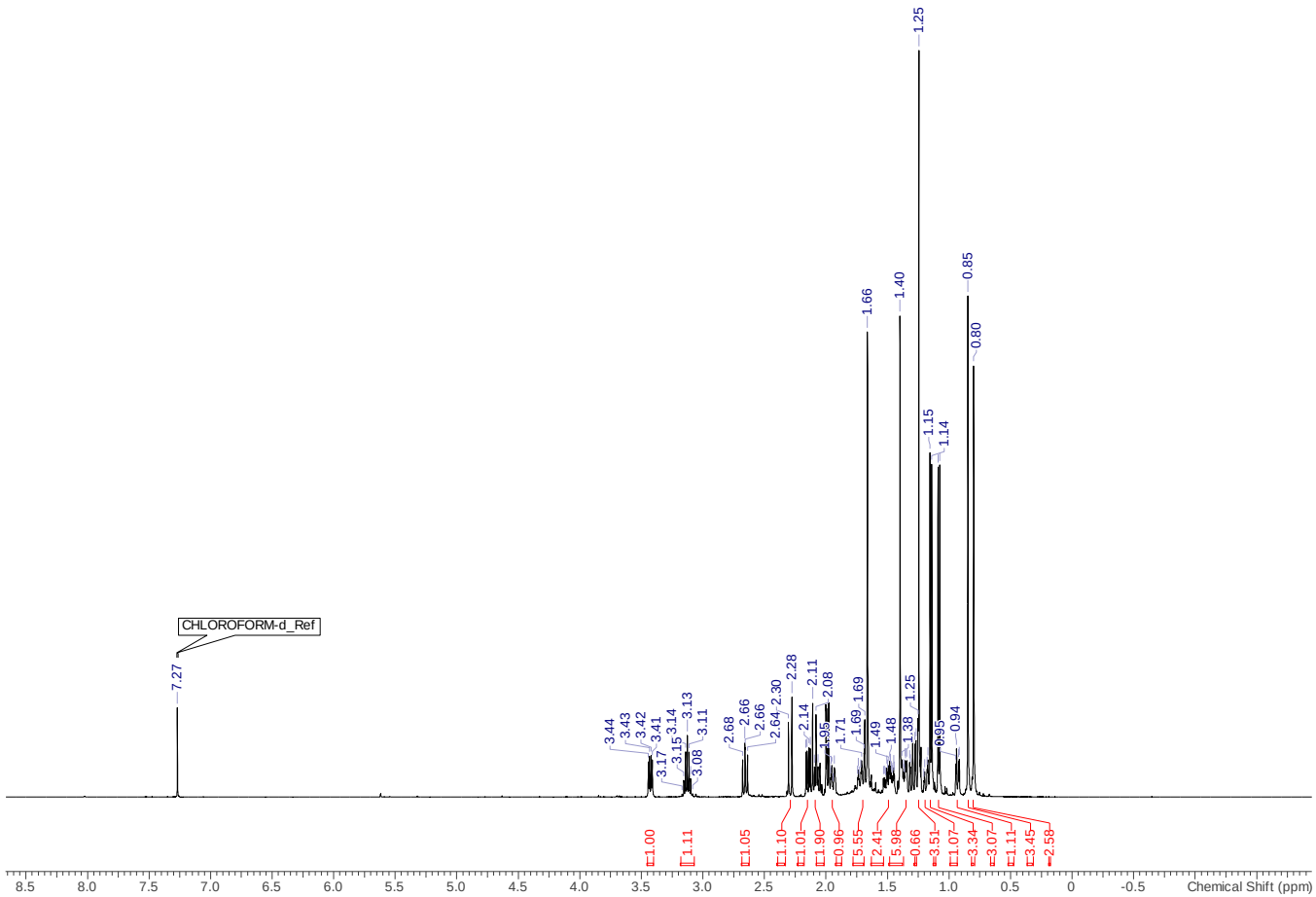
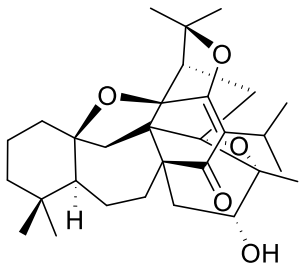


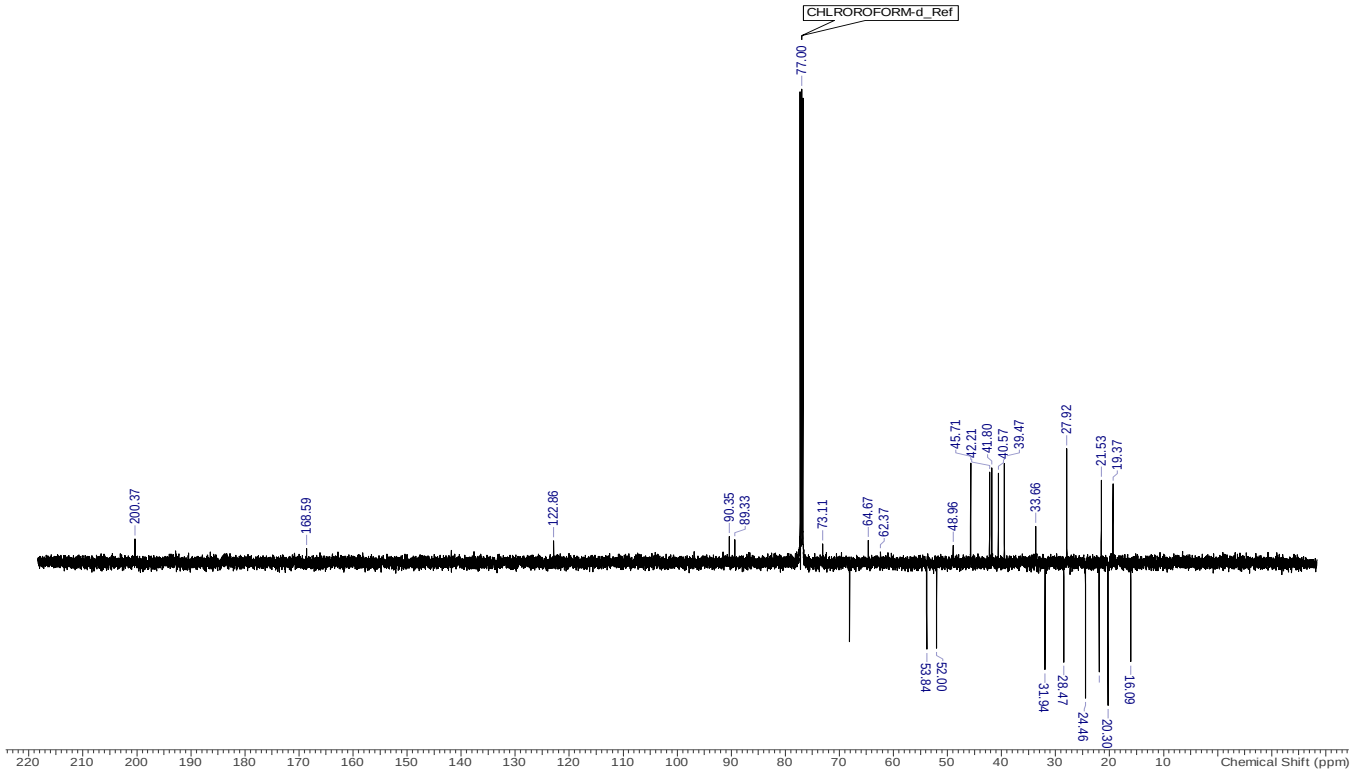

**Figure S23.** HMBC spectrum of compound **4** (500 MHz, $CDCl_3$)

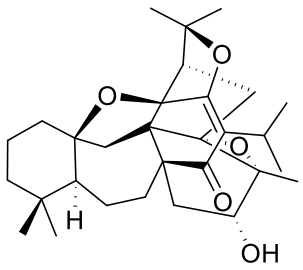



**5**

**Figure S24.** $^{1}$H NMR spectrum of compound **5** (500 MHz, $CDCl_3$)




**5**

**Figure S25.** $^{13}$C-DEPTq spectrum of compound **5** (125 MHz, $CDCl_3$)

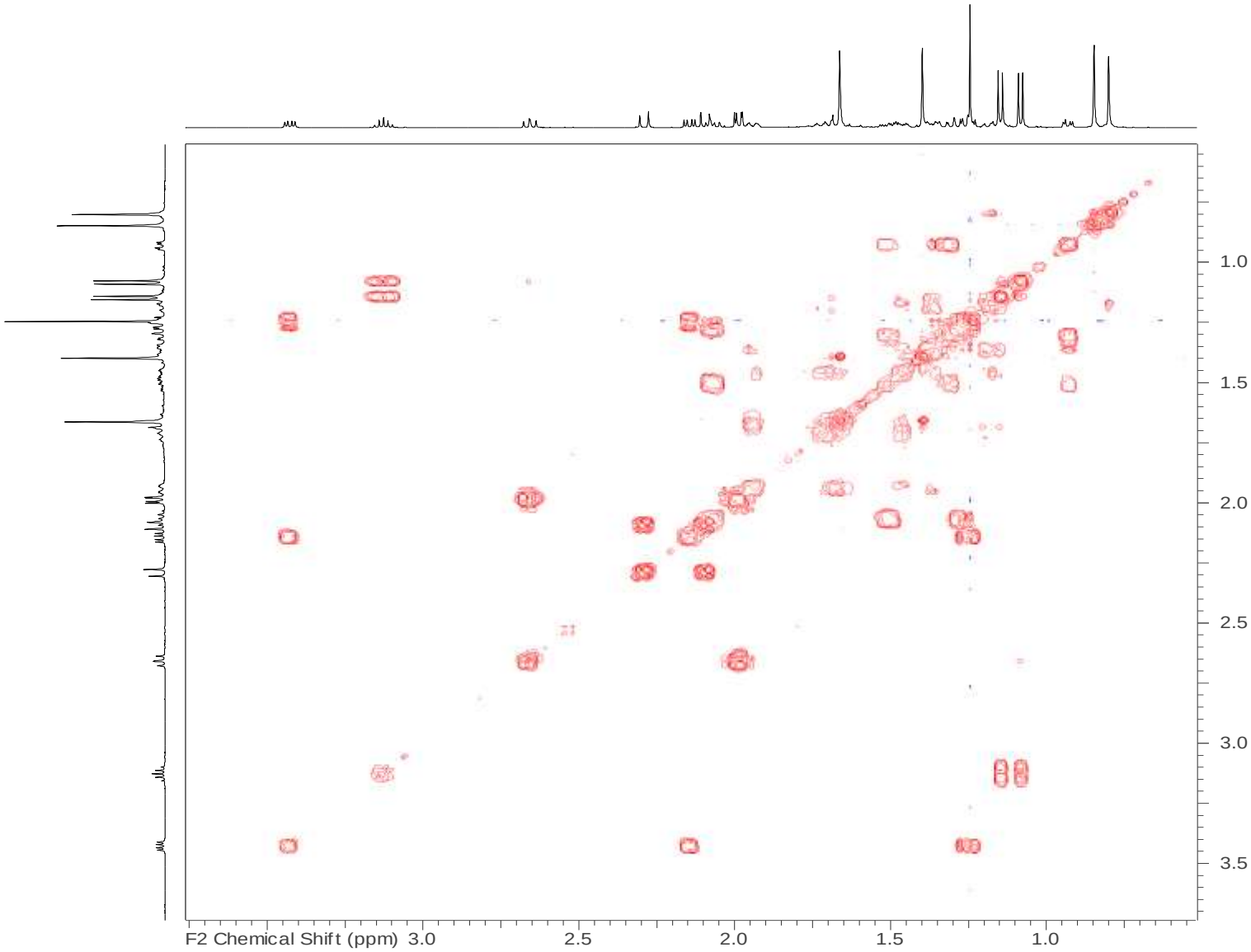



**Figure S26.** $^{1}H$-$^{1}H$ COSY spectrum of compound **5** (500 MHz, $CDCl_3$)

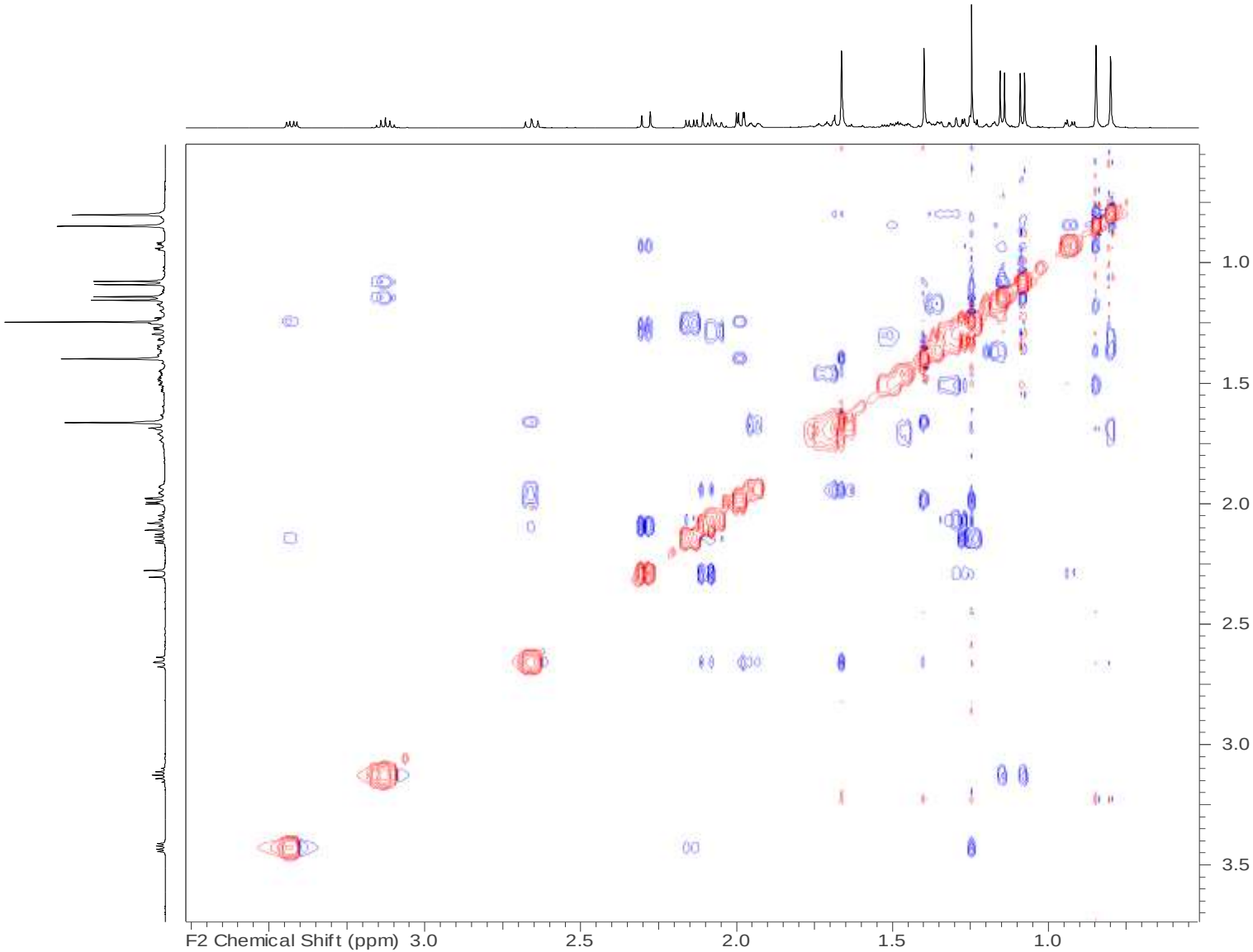



**Figure S27.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **5** (500 MHz, $CDCl_3$)

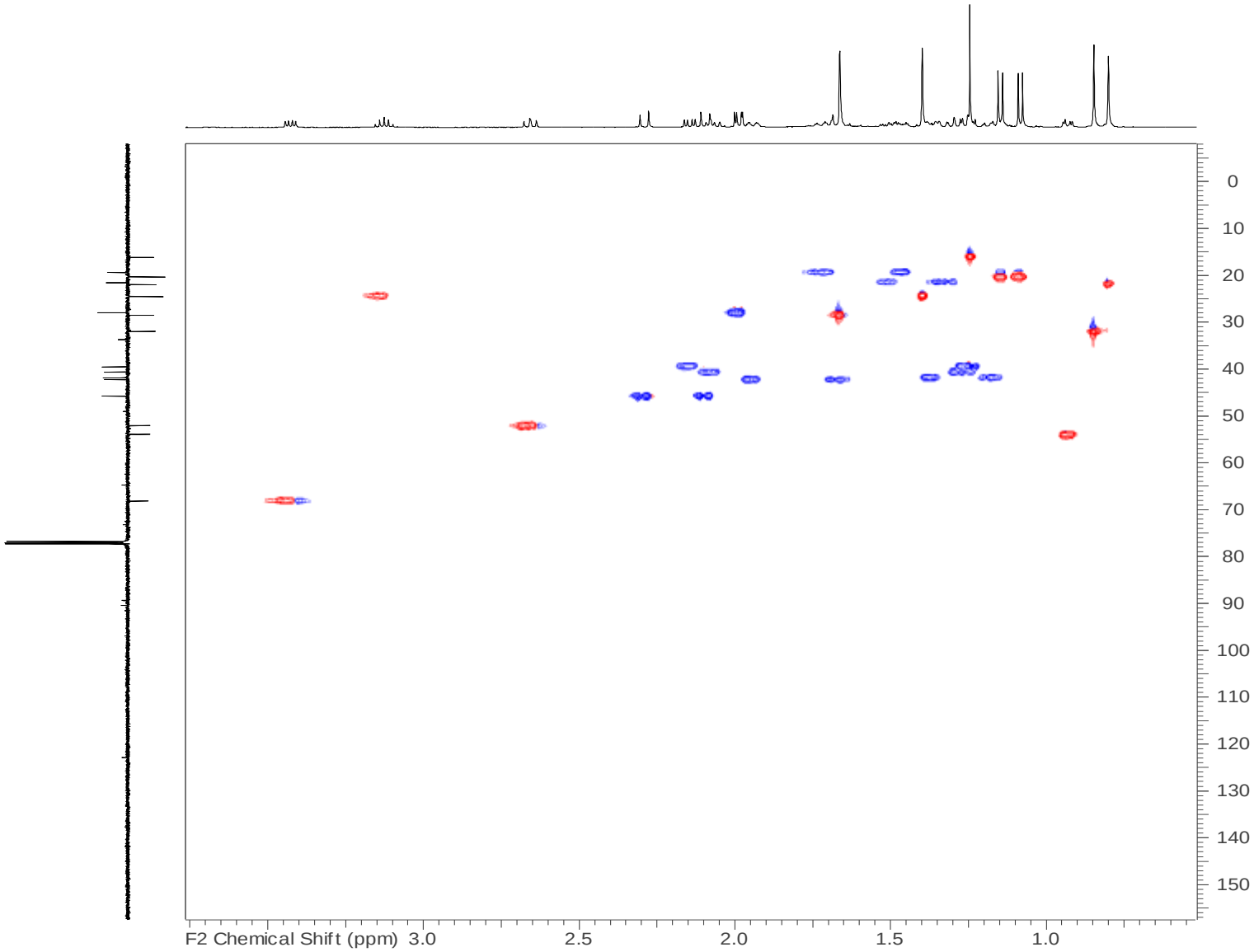



**Figure S28.** HSQC-DEPT spectrum of compound **5** (500 MHz, $CDCl_3$)

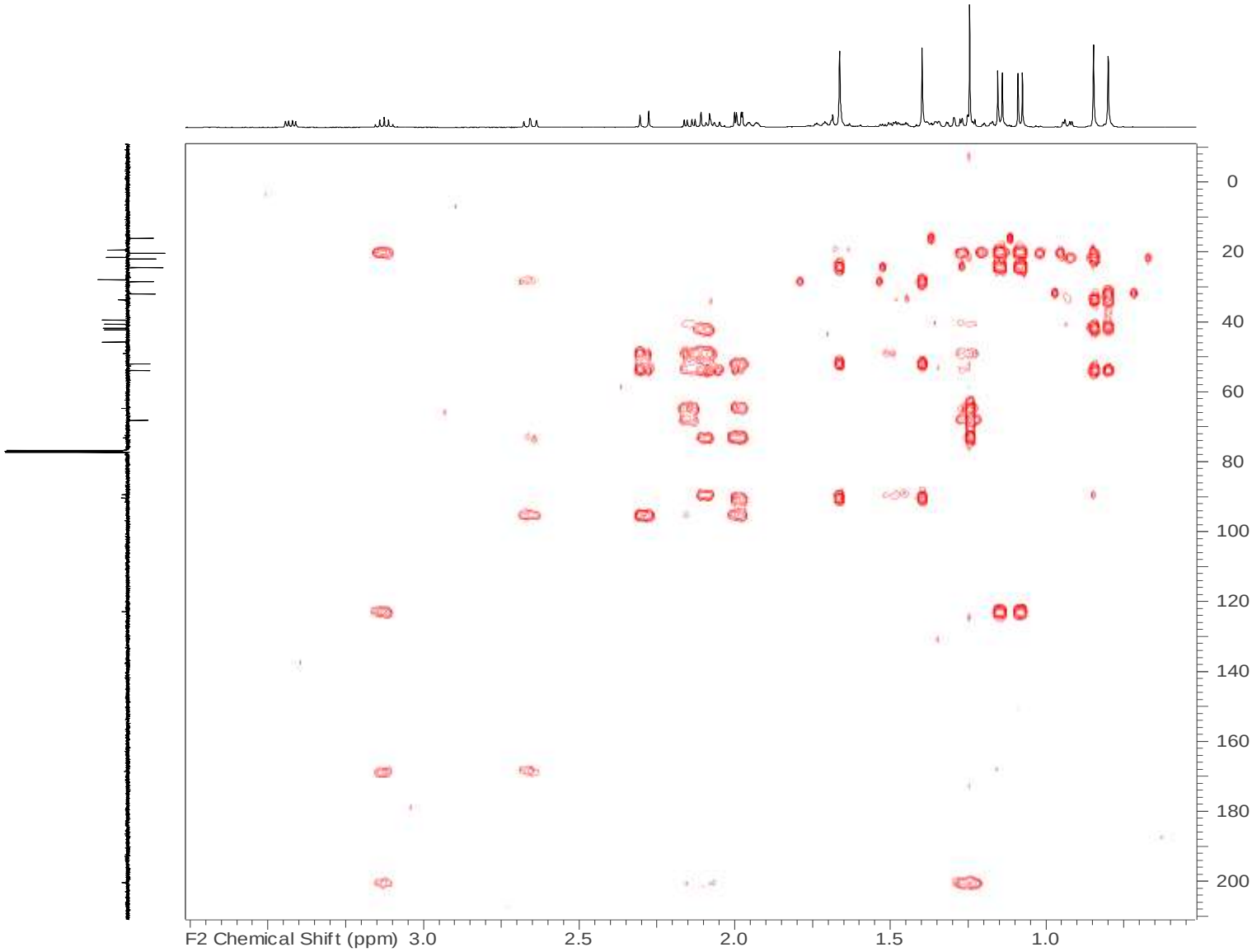
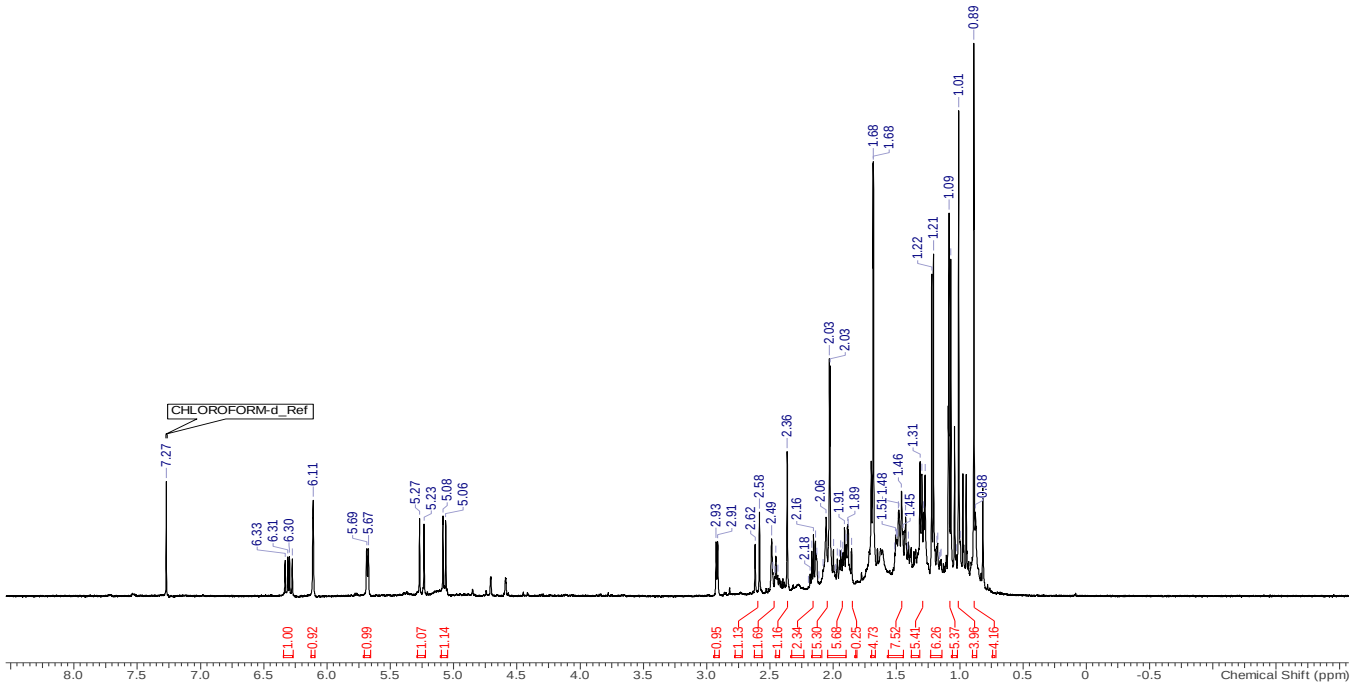
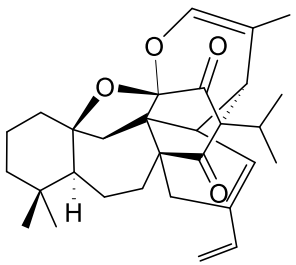


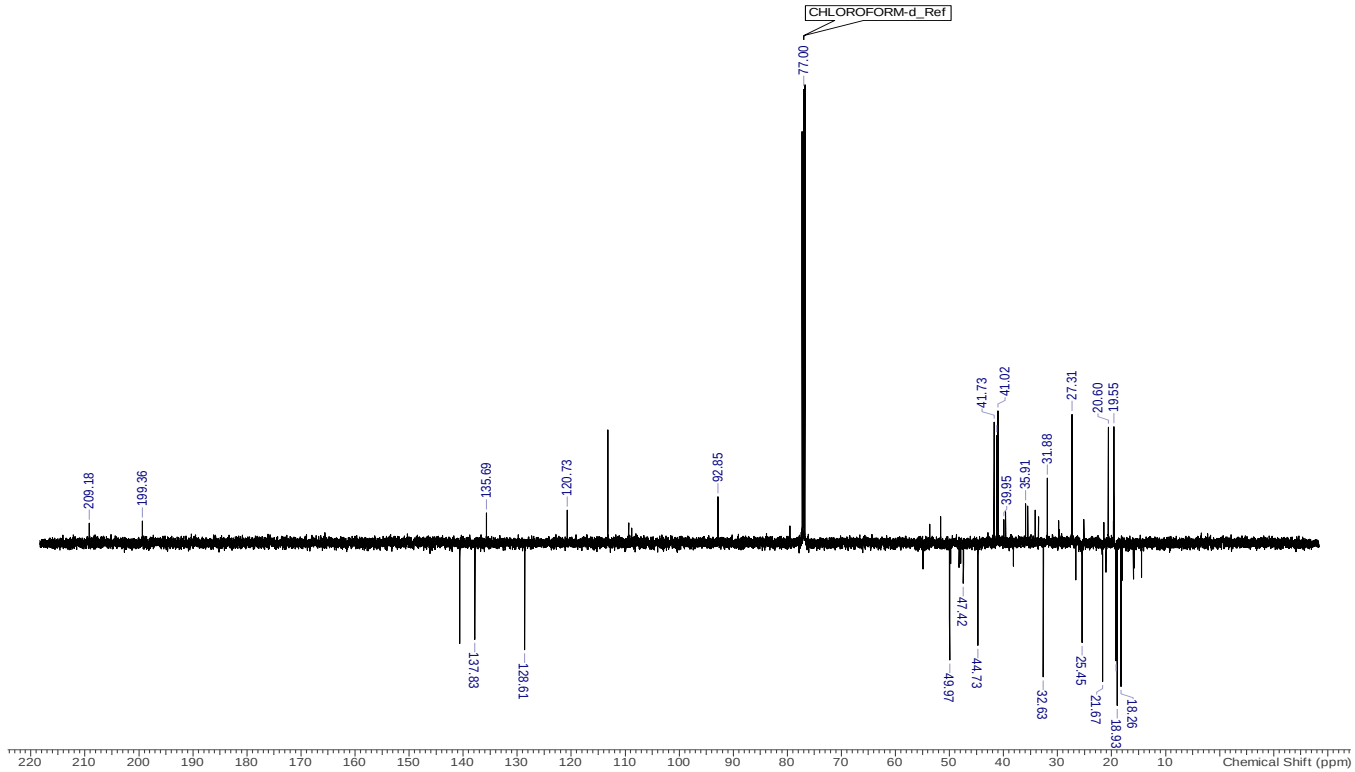

**Figure S29.** HMBC spectrum of compound **5** (500 MHz, $CDCl_3$)

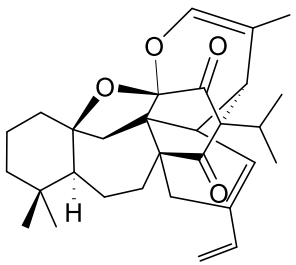



**6**

**Figure S30.** $^{1}$H NMR spectrum of compound **6** (500 MHz, $CDCl_3$)




**6**

**Figure S31.** $^{13}$C-DEPTq spectrum of compound **6** (125 MHz, $CDCl_3$)

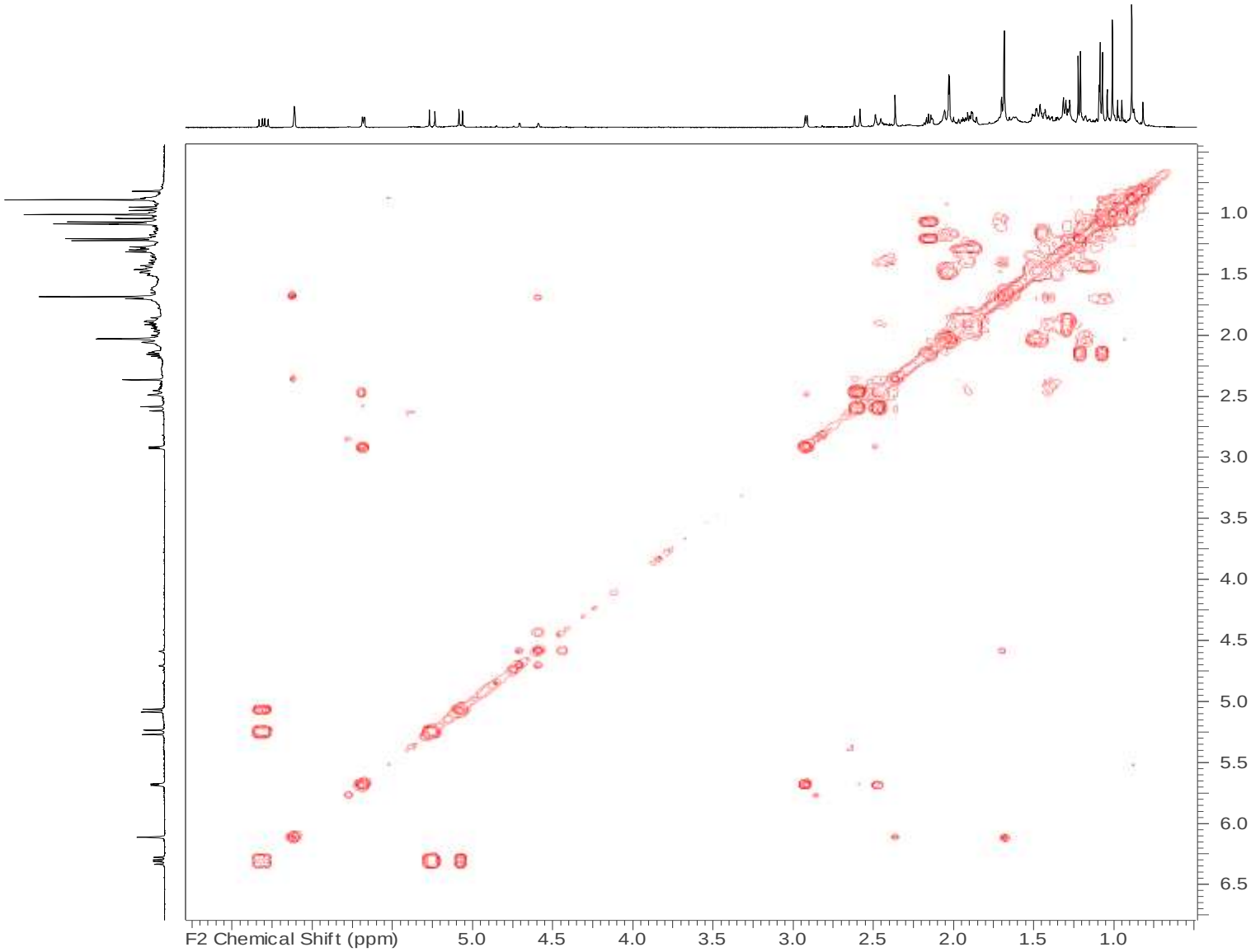



**Figure S32.** $^{1}H$-$^{1}H$ COSY spectrum of compound **6** (500 MHz, $CDCl_3$)

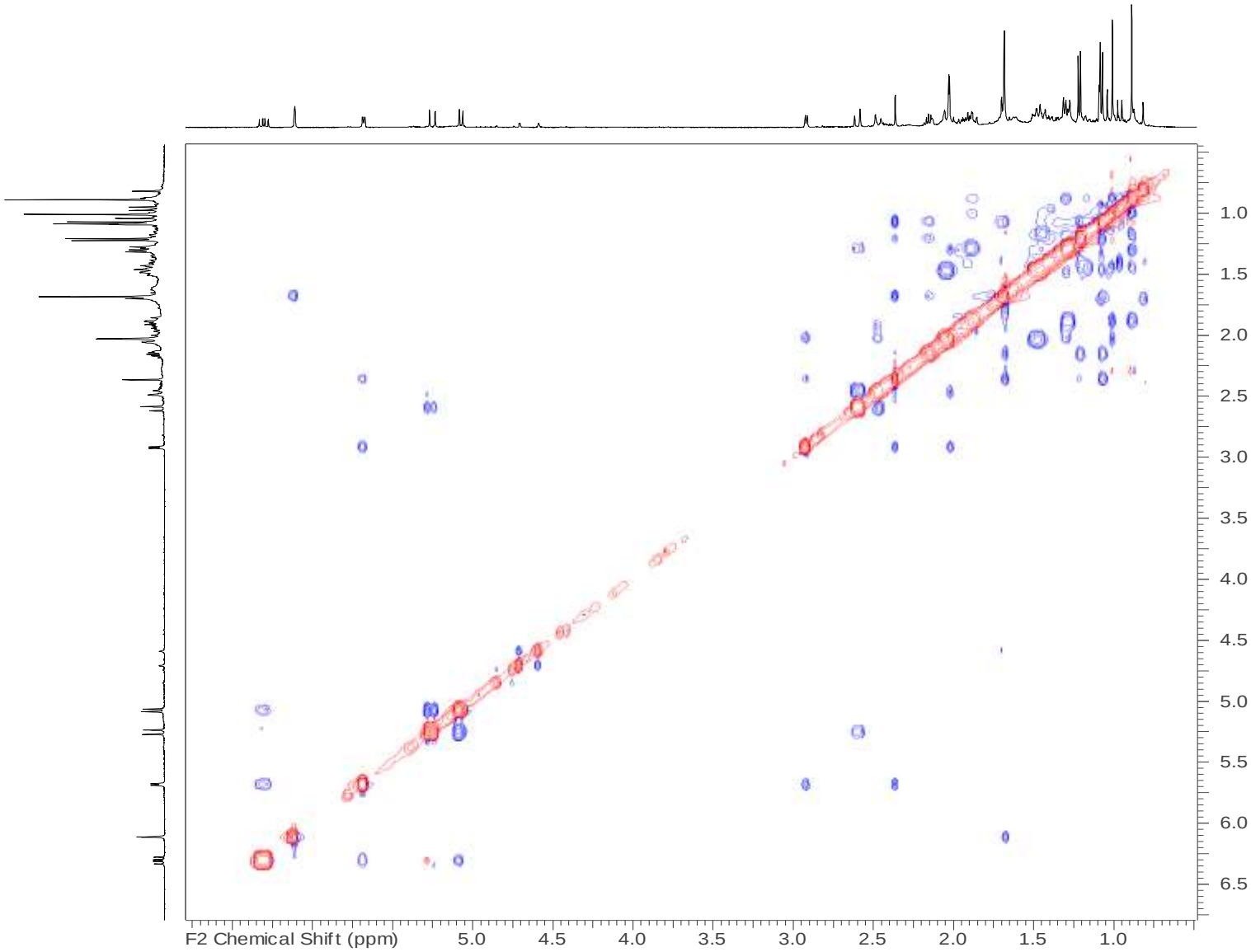



**Figure S33.** $^{1}H$-$^{1}H$ NOESY spectrum of compound **6** (500 MHz, $CDCl_3$)

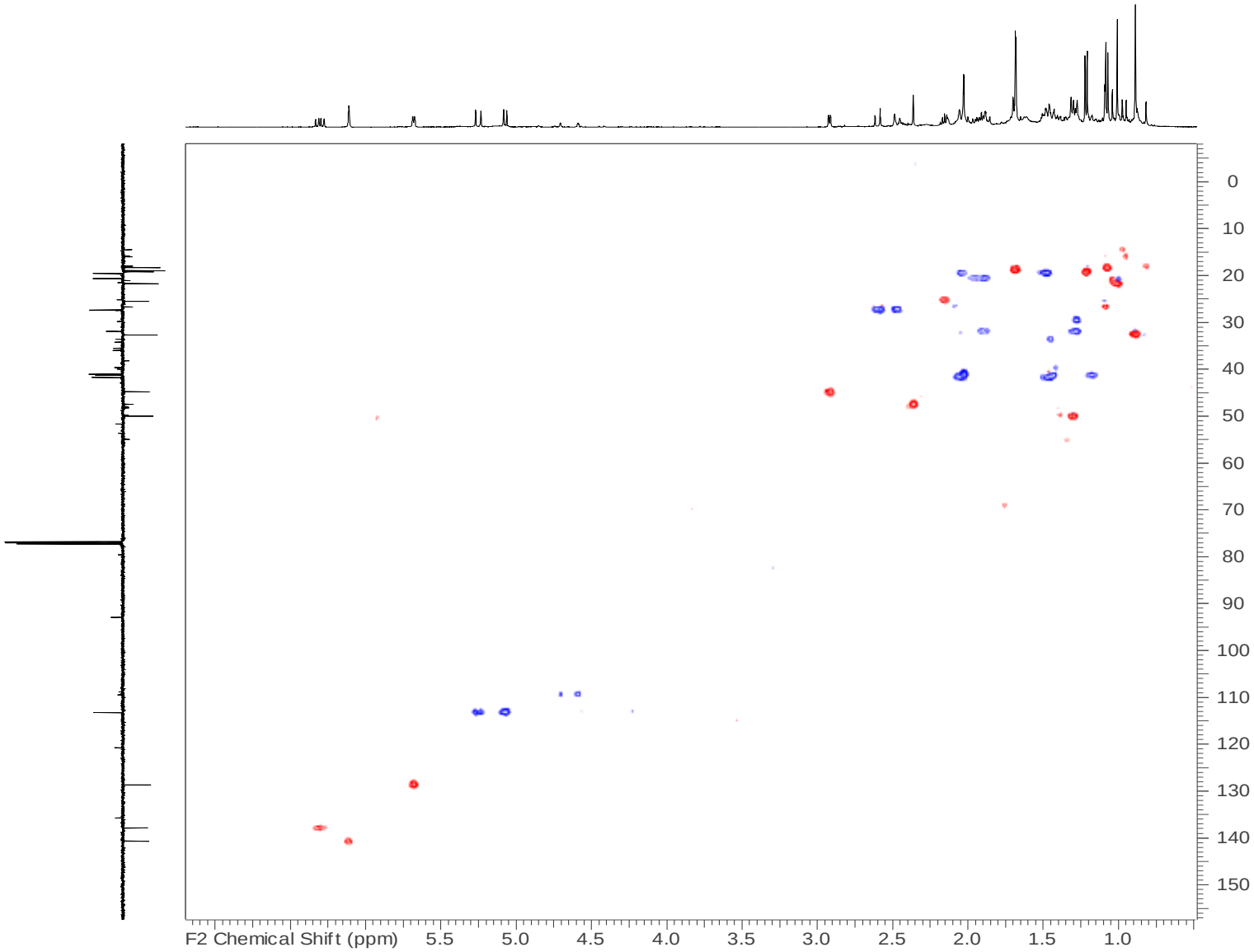



**Figure S34.** HSQC-DEPT spectrum of compound **6** (500 MHz, $CDCl_3$)

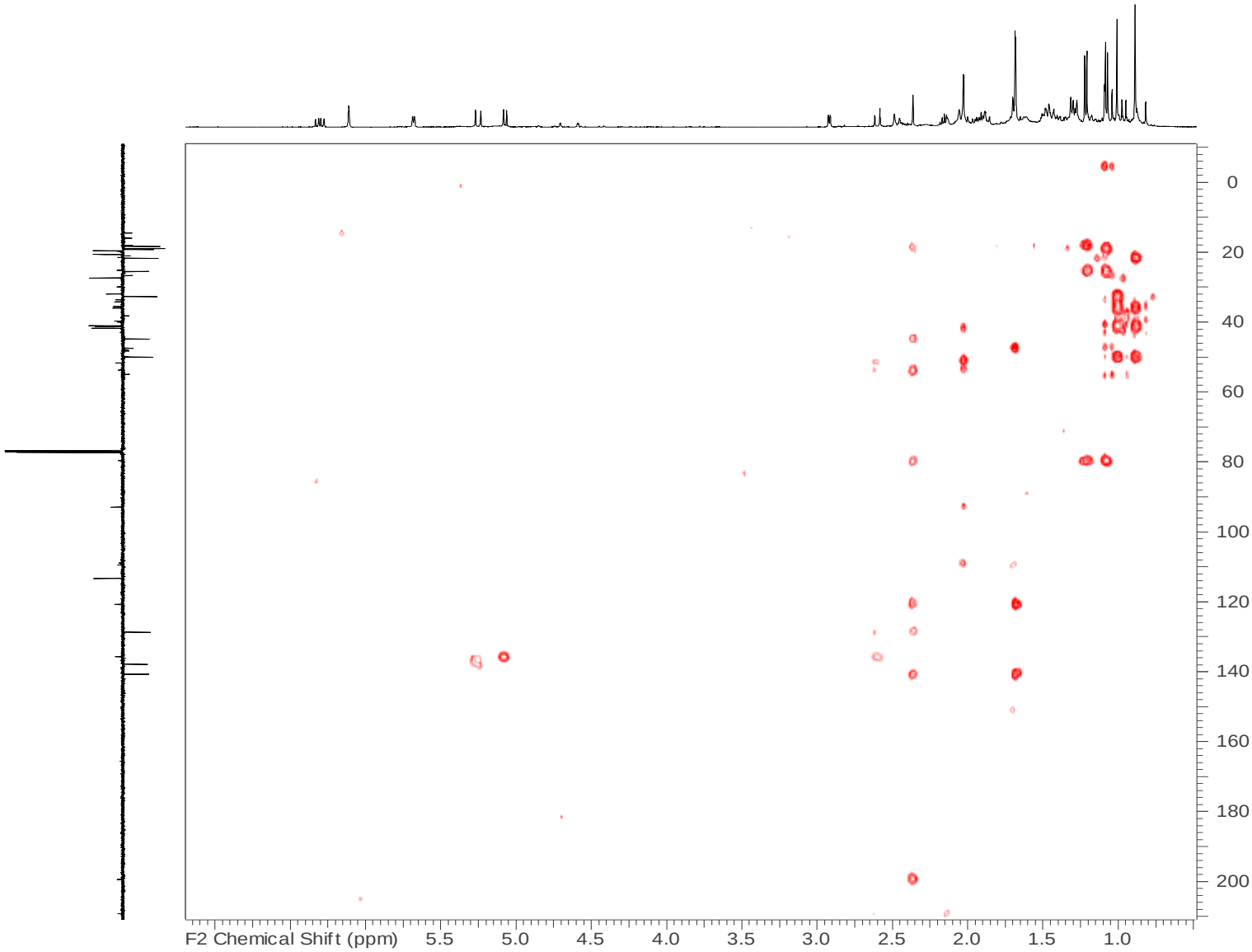



**Figure S35.** HMBC spectrum of compound **6** (500 MHz, $CDCl_3$)

**Computational Methods.** Conformational analysis of compounds **1-7** was performed with MacroModel 9.8 software (Schrödinger LLC) employing the OPLS 2005 (Optimized Potential for Liquid Simulations) force field in $H_2O$. Conformers within a 2 kcal/mol energy window from the global minimum were selected for geometrical optimization and energy calculation using Density Function Theory (DFT) with Becke's nonlocal three-parameter exchange and correlation functional, and the Lee-Yang-Parr correlation functional level (cam-B3LYP) using the B3LYP/6-31G** basis set in the gas phase with the Gaussian 09 program package. Vibrational evaluation was done at the same level to confirm minima. Excitation energy (denoted by wavelength in nm), rotatory strengths dipole velocity ($R_{vel}$) and dipole length ($R_{len}$) were calculated in MeOH by TD-DFT/cam-B3LYP/6-31G**, using the SCRF method, with the CPCM model. ECD curves were obtained on the basis of rotatory strengths with a half-band of 0.3-0.4 eV and UV shift using SpecDis v1.64. ECD spectra were calculated from the spectra of individual conformers according to their contribution calculated by Boltzmann weighting.