Supporting Information

A Tetrachloro Polyketide Hexahydro-1*H*-isoindolone, Muironolide A, from the Marine Sponge *Phorbas* sp. Natural Products at the Nanomole-Scale

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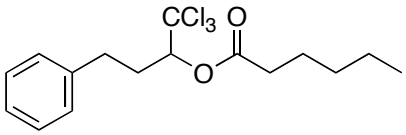
General Procedures. HPLC grade solvent used for purification of sub-micromole samples was redistilled from glass. CD spectra were recorded on a Jasco J810 spectropolarimeter in 0.1 cm quartz cells at 23 ˚C unless otherwise stated. UV-Vis spectra were recorded in a dual beam Jasco V630 spectrometer in 0.1 cm quartz cells. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (99.8/% D) using either a Varian Mercury-400 (400 MHz), Varian Unity-500 (500 MHz), Bruker DMX-600 (600 MHz) equipped with a 1.7-mm $\{^{13}C\}^{1}H$ cryoprobe (Bruker 1.7 mm CPTCI probe). NMR spectra were measured in $CDCl_3$ and referenced to residual solvent signals (^{1}H, δ 7.26 ppm; ^{13}C, δ 77.16 ppm). IR spectra were recorded using attenuated total reflectance (ATR, 3 mm ZnSe plate) with a Jasco 4100 FTIR on samples deposited as thin films. LR LCMS was carried out on a ThermoFisher Accela UPLC coupled to an MSQ single quadrupole mass spectrometer operating in positive ion mode, unless otherwise stated. HRMS measurements were measured at the Scripps Research Institute (TOF-MS or ICR-FTMS) mass spectrometry facility. Semi-preparative HPLC was carried out on a Varian SD200 system equipped with a dual-pump and UV-1 detector (variable λ's) under specified conditions.

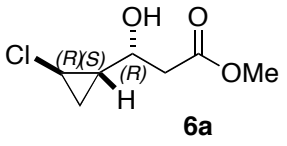
Isolation of 1. The sponge *Phorbas* sp. (sample ID: 93-054) was collected at –10 m by scuba near Muiron Island, Western Australia in 1993. The single specimen was immediately frozen and stored at –20 ˚C until extraction (~2 months). The CCl_4-soluble fraction (93-054-B-1, 350 mg) of the MeOH extract[1] was separated by flash chromatography (silica cartridge, Analogix RS-12, 12 g, 2 cm x 7.5 cm) and elution by step-gradient of solvent (0-100% EtOAc in hexane) to yield seven fractions. Fraction 5 (93-054-B1-5, 12.5 mg) was further purified twice by reversed phase HPLC (Phenylhexyl column, 250 × 10 mm, 1:9 H_2O-MeOH, followed by Phenylhexyl column, 250 × 4.6 mm, 2:3 H_2O-CH_3CN) to yield pure **1** (t_R = 34 min), 90 μg (yield = 4.1×10^{-5} % dry weight of sponge). The yield was calculated using NMR quantitation by solvent ^{13}C-satellites (QSCS).[2]

(1) Searle, P. A.; Molinski, T. F. *J. Am. Chem. Soc.* **1995**, *117*, 8126.
(2) Dalisay, D. S.; Molinski, T. F. *J. Nat. Prod.* **2009**, *11*, 1967.

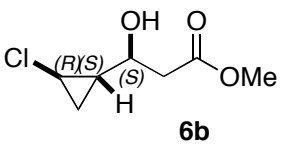


(±)-1,1,1-trichloro-4-phenylbutan-2-yl hexanoate, 4. A solution of (±)-1,1,1-trichloro-4-phenylbutan-2-ol (130 mg, 0.516 mmol, prepared from hydrocinnamaldehyde, Cl_3COOH and Cl_3COONa in DMF[3]) in dry CH_2Cl_2 (5mL) was treated with DMAP (63 mg, 0.516 mmol) and DCC (106.7 mg, 0.516 mmol) and the mixture stirred for 5 min. Hexanoic acid (72.2 mg, 0.621 mmol) was added and the mixture stirred at r.t. under N_2 until TLC indicated completion of the reaction (3 h). The solvent was removed under reduced pressure and the solid residue was dissolved in EtOAc (10 mL) and chilled at 0 ˚C for 10 min whereupon a colorless solid precipitated. The solid was removed by filtration and the supernatant washed with sat. NH_4Cl (3 × 6 mL) and sat. NaCl (3 × 4 mL). The organic layer was passed through a short column of anhydrous Na_2SO_4 and the filtrate was concentrated under reduced pressure to give a crude product which was purified by flash chromatography (silica, 2:3 CH_2Cl_2-hexane) to give (±)-**4** (71.6 mg, 72 %) as a colorless oil. FTIR (ATR): ν 2956, 2933, 2861, 1751, 1496, 1455, 1372, 1265, 1222, 1148, 1093, 785, 735, 699 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.28 m (2H), 7.24 m (4 H), 5.57 (dd, J = 10.3, 1.4 Hz, 1H), 2.70 m (1H), 2.47 m (1H), 2.41 m (1H), 2.21 m (1H), 1.70 m (1H), 1.35 m (1H), 0.92 (t, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 172.6 (C), 140.4 (CH), 128.7 (CH), 128.5 (CH), 126.5 (CH), 100.1(C), 80.3 (C), 34.1 (CH_2), 32.4 (CH_2), 31.9 (CH_2), 31.4 (CH_2), 24.5 (CH_2), 22.4 (CH_2), 14.0 (CH_3). HREIMS *m/z* 373.0503 $[M+Na]^+$; calc. 373.0499 for $C_{16}H_{21}Cl_3O_2Na$.

Preparation of (2-Chloro-1-cyclopropyl)-3-hydroxypropanoate esters, 6a and 6b



6a



6b

Aldehyde. A solution of alcohol (–)-**5** (200 mg, 1.88 mmol, 86% ee)[4] in CH_2Cl_2 (5 mL) was added to a mixture of pyridinium chlorochromate (2.83 g, 13 mmol) and Celite (2.83 g) in anhydrous CH_2Cl_2 (11 mL) at room temperature. After stirring 3.5 h, the mixture was filtered through a bed of Florisil (elution with 2:3 Et_2O/pentane). Fractions containing the aldehyde were combined and carefully concentrated under reduced pressure maintaining a bath temperature of 0 °C to give *aldehyde* (~ 100 mg, *volatile!*)[5] as a clear, colorless oil which was used in the next step without further purification.

(3) Corey, E. J.; Link, J. O.; Shao, Y. *Tetrahedron Lett*. **1992**, *33*, 3435

(4) Masuno, M. N.; Young, D. M.; Hoepker, A. C.; Skepper, C. K.; Molinski, T. F. *J. Org. Chem*. **2005**, *70*, 4162

(5) (a) Paterson, I.; Davies, R. D. M.; Marquez, R. *Angew. Chem., Int. Ed*. **2001**, *40*, 603. (c) Huang, H.; Panek, J. S. *Org. Lett*. **2004**, *6*, 4383. (c) Olivo, H. F.; Velaquez, F.; Trevisan, H. C. *Org. Lett*. **2000**, *2*, 4055

Reformatsky Reaction.[6] Zn dust (1.26 g, 19.3 mmol) was suspended in anhydrous THF (8 mL) and the mixture heated to 40 °C. TMSCl (260 mg, 2.4 mmol) was added and the temperature elevated to 55 °C. After 15 minutes, the pressure of the reaction flask was reduced to 250-260 mm Hg to produce a steady reflux. Methyl bromoacetate (2.70 g, 17.7 mmol) was added dropwise over approximately 10 minutes at which time the mixture turned a yellow-green color. The mixture was stirred an additional 5 minutes then cooled to room temperature. After excess solids had settled, the supernatant was transferred under nitrogen through a nylon syringe filter (0.45 μm) into a clean, dry scintillation vial.

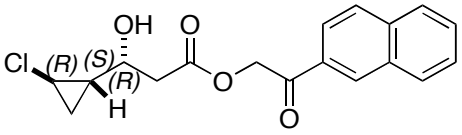
The resulting bromozincate reagent (~0.57 mmol) was added dropwise to a mixture of *aldehyde* (50 mg, 0.48 mmol) in THF (2 mL) at 0 °C and the pale yellow mixture stirred 20 minutes then allowed to warm to room temperature over 2 hours. The mixture was quenched with a mixture of concentrated $NH_4OH_{(aq)}$ (2.3 mL) and saturated $NH_4Cl_{(aq)}$ (23 mL) and extracted with Et_2O (3 × 10 mL). The combined Et_2O extracts were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Flash chromatography (silica, 2:3 Et_2O-pentane) gave an inseparable mixture of **6a** and **6b** (56 mg, 66 %, *dr* ~1:1) as a clear, colorless oil which was used immediately in the next step.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.78 (ddd, 1H, 9.0, 6.2, 3.2 Hz), 3.71 (s, 3H), 3.62 (ddd, 1H, 7.8, 6.6, 3.9 Hz), 3.04 (ddd, 1H, 7.2, 4.0, 3.9 Hz), 2.97 (ddd, 1H, 7.6, 3.6, 3.6 Hz), 2.67-2.52 (m, 2H, *overlap)*, 1.37-1.29 (m, 1H, *overlap*), 1.08 (q, 1H, 6.7 Hz), 1.01-0.94 (m, 2H ***6a**** and 1H ***6b****); LR-ESI-MS m/*z* 211.20 $[M+Na]^+$ * arbitrary assignment.

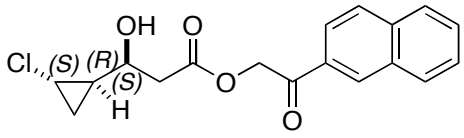
2-Napthone Ester Standards: 7a, 7b, 7c and 7d

A mixture of diastereomers **6a** and **6b** (1:1, *ee* 86%) (5.8 mg, 0.035 mmol) was dissolved in 250 μL of LiOH (1.45 mg, 0.053) and then stirred for 3 min, then added with 250 μL solution of α-bromo-2-acetonaphthalene (88 mg, 0.355 mmol) in THF and stirred vigorously at RT for 24 h. The reaction mixture was neutralized with 250 μL HCl (1.90 mg, 0.053) to pH 6.0 the extracted with 1 mL $CHCl_3$ (3x). The organic layer was dried under reduced pressure to form a yellow solid residue which then purified by flash chromatography 8:2 EtOAc:hexane to yield the mixture of diastereomers (5.4 mg, 23 % yield) as colorless oil. Individual diastreomers were separated by HPLC (3:7 *i*-PrOH-hexane, chiral column, Chiralpak® AD, 250 × 4.6 mm) to afford pure samples of **7a** ($t_{R\ min}$ = 11.68), **7c** (t_R = 13.05), **7d** (t_R = 13.74) and **7b** (t_R = 14.83) in the ratios 10:0.9:0.6:7.5 respectively.

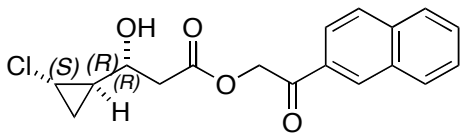
(6) (a) Reformatsky, S. *Chem. Ber.* **1887**, *20*, 1210. (b) Kloetzing, R. J.; Thaler, T.; Knochel, P. *Org. Lett.* **2006**, *8*, 1125.



(*R*)-2-(naphthalen-2-yl)-2-oxoethyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoate, 7a, colorless solid. FTIR (ATR): ν 3571 (broad peak), 2973, 2254, 1625, 1281, 952, 674, 648, 615. UV (hexane:*i*-PrOH, 70:30) λ 209 nm (ε 5700) 248 (34300), 284 (6487). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.2 Hz, 1H), 5.64 (d, *J* = 16.3 Hz, 1H), 5.54 (d, *J* = 16.3 Hz, 1H), 4.03 (m, 1H), 3.65 (d, *J* = 3.7 Hz, 1H), 3.09 (ddd, *J* = 7.2, 3.7, 3.0 Hz, 1H), 2.85 (dd, *J* = 14.8, 3.0 Hz, 1H), 2.74 (dd, *J* = 14.8, 9.4 Hz, 1H), 1.43 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.19 (q, *J* = 13.8, 6.5 Hz, 1H), 1.03 (m,1H). ^{13}C NMR[7]: δ 192.2 (C), 171.0 (C), 136.0 (C), 132.1 (C), 130.7 (C), 130.1 (CH), 130.0 (CH), 129.5 (CH), 129.1 (CH), 127.9 (CH), 127.4 (CH), 123.2 (CH), 67.7 (CH), 66.2 (CH_2), 42.3 (CH_2), 30.3 (CH), 27.4 (CH), 13.1 (CH_2). HREIMS *m/z* 355.0712 $[M+Na]^+$; calcd. 355.0708 for $C_{18}H_{17}ClNaO_4$.



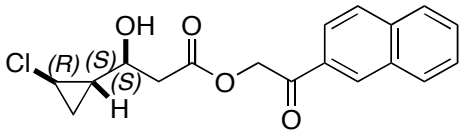
(*S*)-2-(naphthalen-2-yl)-2-oxoethyl 3-((1*R*,2*S*)-2-chlorocyclopropyl)-3-hydroxypropanoate, 7c, colorless solid. FTIR (ATR): ν 3571 (broad peak), 2973, 2254, 1625, 1281, 952, 674, 648, 615. UV (hexane:*i*-PrOH, 70:30) λ 209 nm (ε 5700) 248 (34300), 284 (6487). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.2 Hz, 1H), 5.64 (d, *J* = 16.3 Hz, 1H), 5.54 (d, *J* = 16.3 Hz, 1H), 4.03 (m, 1H), 3.65 (d, *J* = 3.7 Hz, 1H), 3.09 (ddd, *J* = 7.2, 3.7, 3.0 Hz, 1H), 2.85 (dd, *J* = 14.8, 3.0 Hz, 1H), 2.74 (dd, *J* = 14.8, 9.4 Hz, 1H), 1.43 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.19 (q, *J* = 13.8, 6.5 Hz, 1H), 1.03 (m,1H). ^{13}C NMR[7]: δ 192.2 (C), 171.0 (C), 136.0 (C), 132.1 (C), 130.7 (C), 130.1 (CH), 130.0 (CH), 129.5 (CH), 129.1 (CH), 127.9 (CH), 127.4 (CH), 123.2 (CH), 67.7 (CH), 66.2 (CH_2), 42.3 (CH_2), 30.3 (CH), 27.4 (CH), 13.1 (CH_2). HREIMS *m/z* 355.0716 $[M+Na]^+$; calcd. 355.0708 for $C_{18}H_{17}ClNaO_4$.



(*R*)-2-(naphthalen-2-yl)-2-oxoethyl 3-((1*R*,2*S*)-2-chlorocyclopropyl)-3-hydroxypropanoate, 7d, colorless solid. FTIR (ATR): ν 3571 (br), 2973, 2254, 1625, 1281, 952, 674, 648, 615. UV (hexane:*i*-PrOH, 70:30) λ 209 nm (ε 5700) 248 (34300), 284 (6487). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J*

(7) Measured indirectly and assigned by HSQC and HMBC (600 MHz,$CDCl_3$).

= 8.2 Hz, 1H), 5.64 (d, *J* = 16.3 Hz, 1H), 5.54 (d, *J* = 16.3 Hz, 1H), 3.84 (m, 1H), 3.67 (d, *J* = 3.7 Hz, 1H), 3.16 (ddd, *J* = 7.2, 3.7, 3.0 Hz, 1H), 2.84 (dd, *J* = 14.8, 3.0 Hz, 1H), 2.78 (dd, *J* = 14.8, 9.4 Hz, 1H), 1.45 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.07 (q, *J* = 13.8, 6.5 Hz, 1H), 1.03 (m,1H). HREIMS *m/z* 355.0710 $[M+Na]^+$; calcd. 355.0708 for $C_{18}H_{17}ClNaO_4$.



(*S*)-2-(naphthalen-2-yl)-2-oxoethyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoate, 7b, colorless solid. FTIR (ATR): ν 3571 (broad peak), 2973, 2254, 1625, 1281, 952, 674, 648, 615. UV (hexane:*i*-PrOH, 70:30) λ 209 nm (ε 5700) 248 (34300), 284 (6487). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.59 (t, *J* = 8.2 Hz, 1H), 5.64 (d, *J* = 16.3 Hz, 1H), 5.54 (d, *J* = 16.3 Hz, 1H), 3.84 (m, 1H), 3.67 (d, *J* = 3.7 Hz, 1H), 3.16 (ddd, *J* = 7.2, 3.7, 3.0 Hz, 1H), 2.84 (dd, *J* = 14.8, 3.0 Hz, 1H), 2.78 (dd, *J* = 14.8, 9.4 Hz, 1H), 1.45 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.07 (q, *J* = 13.8, 6.5 Hz, 1H), 1.03 (m,1H). ^{13}C NMR[7]: δ 192.2 (C), 171.0 (C), 136.0 (C), 132.1 (C), 131.7 (C), 130.1 (CH), 130.0 (CH), 129.5 (CH), 129.1 (CH), 127.9 (CH), 127.4 (CH), 123.2 (CH), 68.7 (CH), 66.2 (CH_2), 42.0 (CH_2), 30.3 (CH), 27.5 (CH), 13.5 (CH_2). HREIMS *m/z* 355.0710 $[M+Na]^+$; calcd. 355.0708 for $C_{18}H_{17}ClNaO_4$.

Preparation of (*R*)- and (*S*)-MTPA esters of (*R*)-2-(naphthalen-2-yl)-2-oxoethyl 3-((1*S*,2*R*)-2-chlorocyclopropyl)-3-hydroxypropanoate. Separate solutions of **7a** (100 μg) in dry pyridine (100 μL) were treated with added (*R*)- or (*S*)-MTPACl (5 μL) and the mixture stirred vigorously at r.t. for 2 h. The reaction mixtures were concentrated by under reduced pressure and each residue purified by silica gel chromatography (pencil column) with elution by 9:1 EtOAc:hexanes to afford pure (*S*)-**8** (white solid; 100 μg, 85%) or (*R*)-**9** (white solid; 100 μg; 86%).

(*S*)-MTPA Ester of **7a** (**S8**): ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 8.1 Hz, 1H), 7.52 (m, 2H), 7.41 (m, 4H), 5.53 (d, *J* = 16.1 Hz, 1H), 5.48 (d, *J* = 16.1 Hz, 1H), 5.16 (m, 1H), 3.54 (s, 3H), 3.09 (dd, *J* = 16.4, 8.2 Hz, 1H), 3.03 (dd, *J* = 16.4, 4.9 Hz, 1H), 3.00 (m, 1H), 1.43 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.19 (q, *J* = 13.8, 6.5 Hz, 1H), 1.08 (m,1H). HREIMS *m/z* 571.1102 $[M+Na]^+$; calc. 571.1106 for $C_{28}H_{24}ClNaF_3O_6$.

(*R*)-MTPA Ester of **7a** (**S9**): ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.95 (m, 3H), 7.90 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 8.1 Hz, 1H), 7.52 (m, 2H), 7.41 (m, 4H), 5.42 (d, *J* = 16.2 Hz, 1H), 5.39 (d, *J* = 16.2 Hz, 1H), 5.14 (m, 1H), 3.55 (s, 3H), 3.10 (m, 1H), 3.03 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.98 (dd, *J* = 16.0, 5.4 Hz, 1H), 1.43 (dddd, *J* = 9.4, 9.4, 6.5, 3.1 Hz, 1H), 1.19 (q, *J* = 13.8, 6.5 Hz, 1H), 1.15 (m,1H). HREIMS *m/z* 571.1120 $[M+Na]^+$; calc. 571.1106 for $C_{28}H_{24}ClNaF_3O_6$.

Hydrolysis-Derivatization of 1 with α-Bromo-2-Acetonaphthalene

Muironolide A (**1**, 30 μg, 0.050 mmole) was dissolved in THF (50 μL) and treated with aqueous LiOH solution (0.002 M, 50 μL), and the mixture stirred at r.t. for 1.5 h before neutralization with aqueous HCl (0.002 M, 50 μL). The mixture was dried under the stream of N_2 and the residue re-dissolved in a mixture of H_2O (25 μL, HPLC grade) and aqueous LiOH (0.001 M, 50 μL), stirred for 5 min, then treated with solution of α-bromo-2-acetonaphthalene (3M, 50 μL, 0.151 mmol,) in THF and stirred vigorously at rt for 24 h. The reaction mixture was diluted with H_2O (500 μL) and extracted with $CHCl_3$ (3 × 500 μL). The combined organic layers were concentrated under reduced pressure and the residue purified by flash chromatography (silica, pencil column, 30 mm) eluting with 1:4 EtOAc-hexane. Fractions corresponding to the product were pooled and dried under reduced pressure and dissolved in 20 μL of CH_3CN (HPLC grade) for LCMS analysis.

LC-ESI-MS Analysis

The acetonapthone derivative of **1** was analysed by LC-MS using a ThermoElectron Accela series ultra-high pressure liquid chromatograph (UPLC) and a ChiralPak AD-RH column (2.1 x 150 mm, 5 μ) connected to a PDA and ThermoFinnigan MSQ quadrupole mass spectrometer. LC parameters were as follows; isocratic 1:4 HCOOH (0.1% aq)–CH_3CN, 80% (0.2 mL/min, over 20 min. Injection volume was 3 μL. PDA parameters were as follows; channel A; 210 nm; channel B, 248 nm; channel C, 284 nm. MSQ parameters were as follows; ESI-MS, selected ion monitoring at *m/z* 355.07 $[M+Na]^+$, span 1.5 amu; dwell, 0.6 sec; cone voltage, 75V; probe temperature 450 °C. Retention times (min) for the naphthone ester derivatives were as follows: **7a**, t_R = 13.84; **7c**, t_R = 9.05; **7d**, t_R = 9.90; **7b**, t_R = 11.13. The naphthone ester, derived from hydrolysis-derivation of **1**, eluted at t_R = 11.13 min. and was confirmed by co-injections with standard naphthone ester **7b** that co-eluted as a single peak (t_R = 11.11 min). See Figure S20.

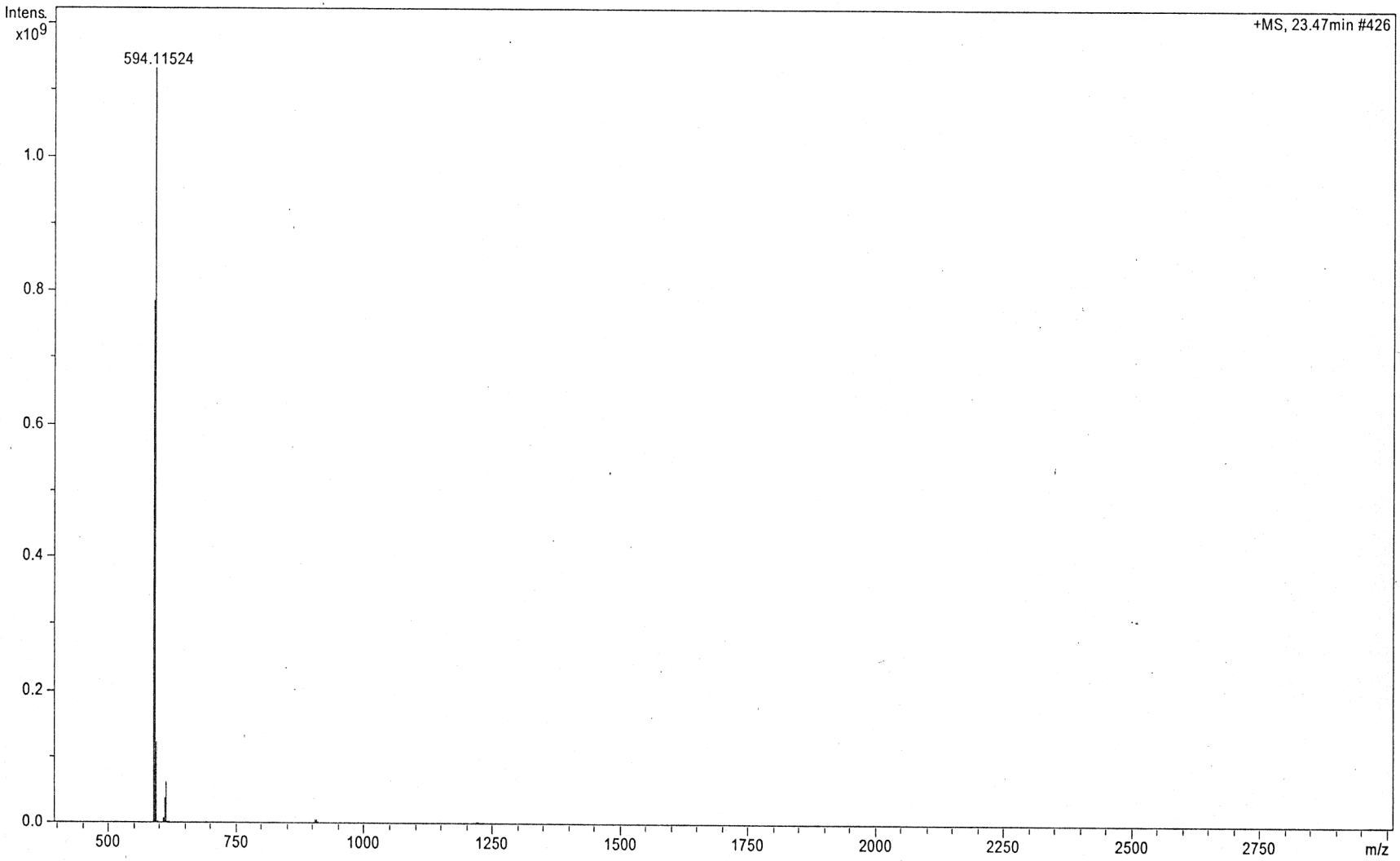


Fig. S4. LC-ESI-FT-ICR HRMS (+ve ion mode). 7.0T Bruker q-FT-ICR interfaced with an Agilent 1200 capillary LC (500 μ ID x 15 cm Zorbax, 10 μL/min).

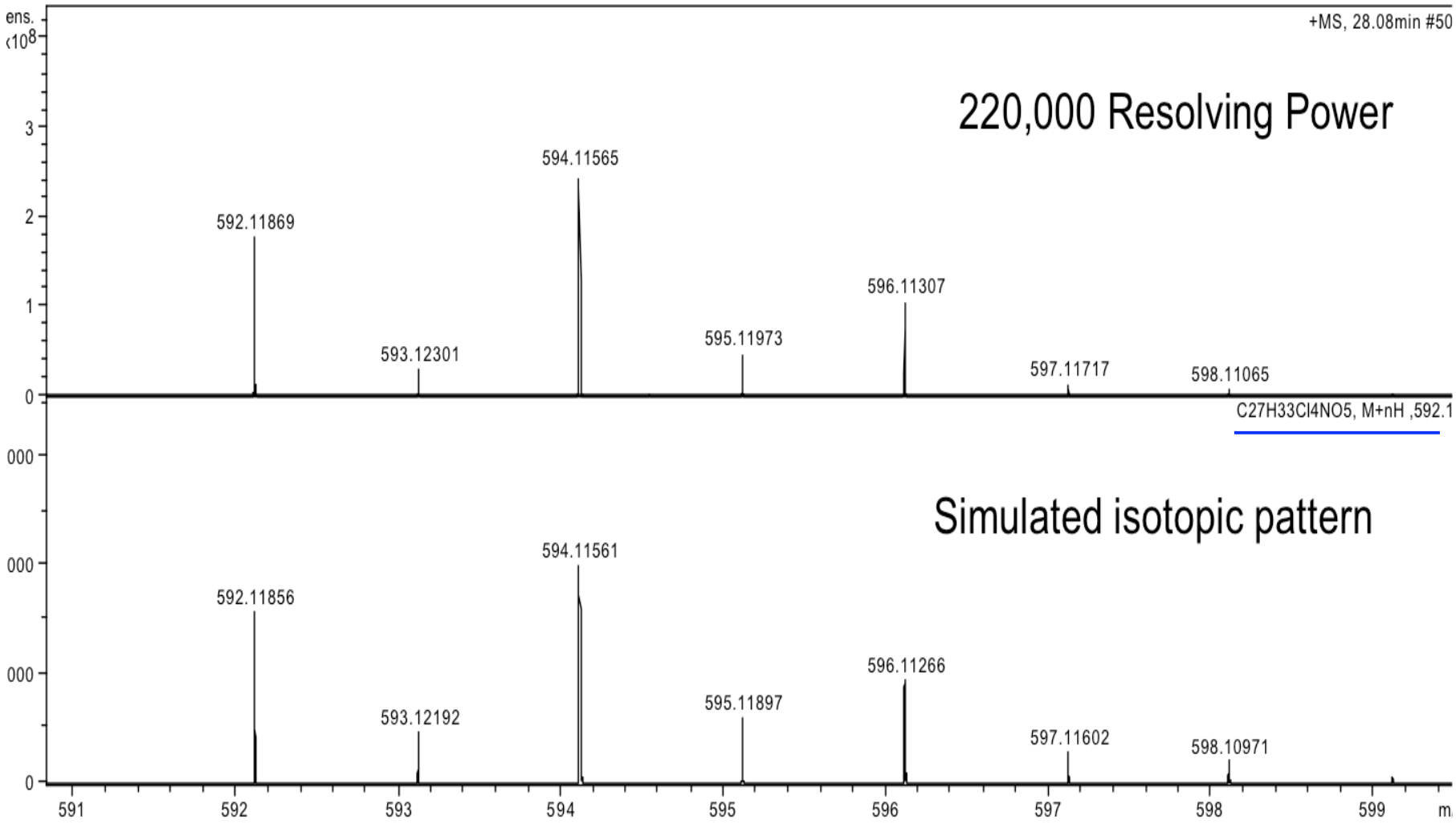


Figure S5. LC-ESI-FT-ICR HRMS (+ve ion mode). Expansion of Figure S4 and simulated isotopic pattern.

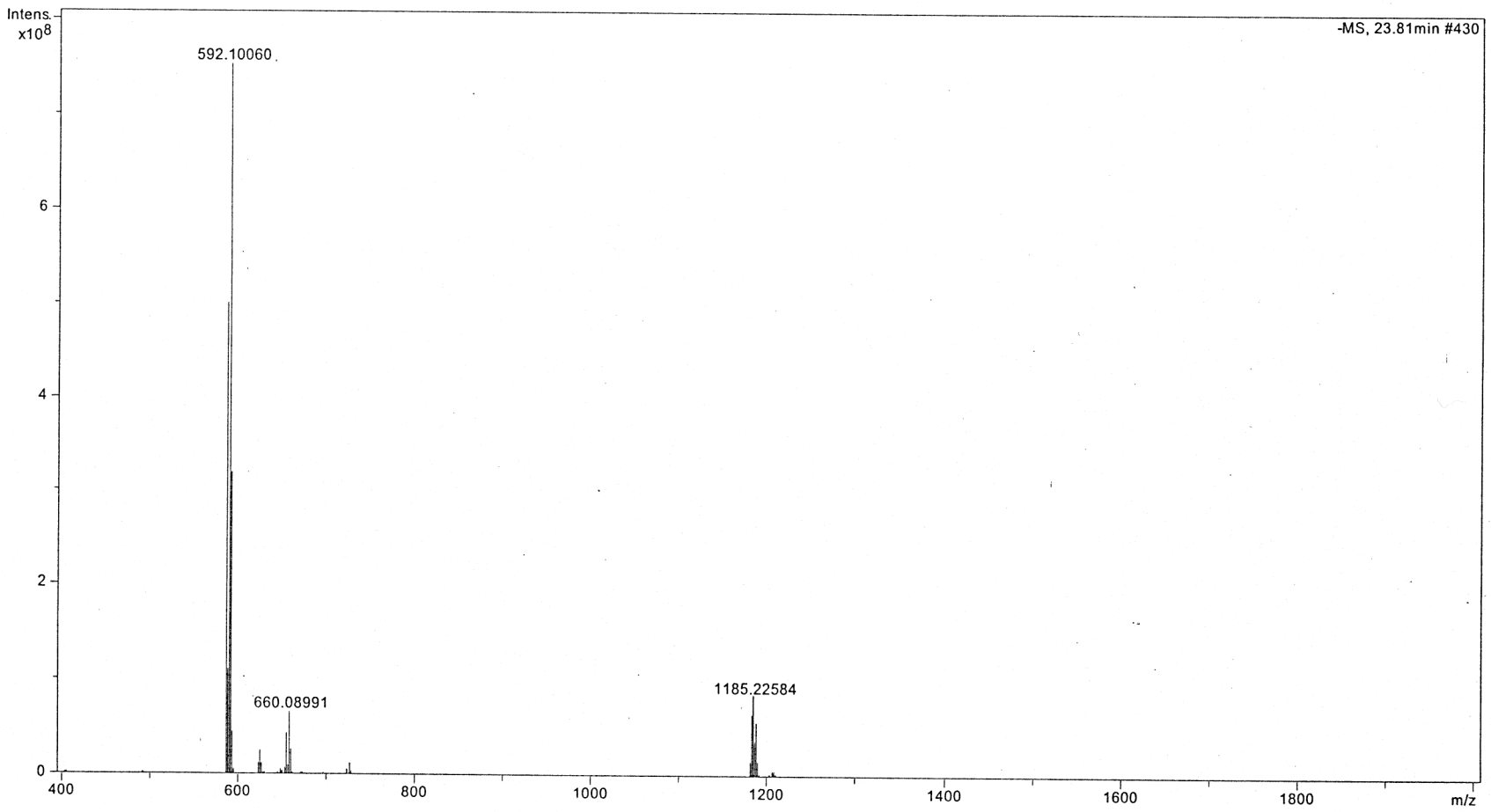


Figure S6. LC-ESI-FT-ICR HRMS (–ve ion mode). 7.0T Bruker q-FT-ICR interfaced with an Agilent 1200 capillary LC (500 μ ID x 15 cm Zorbax, 10 μL/min).

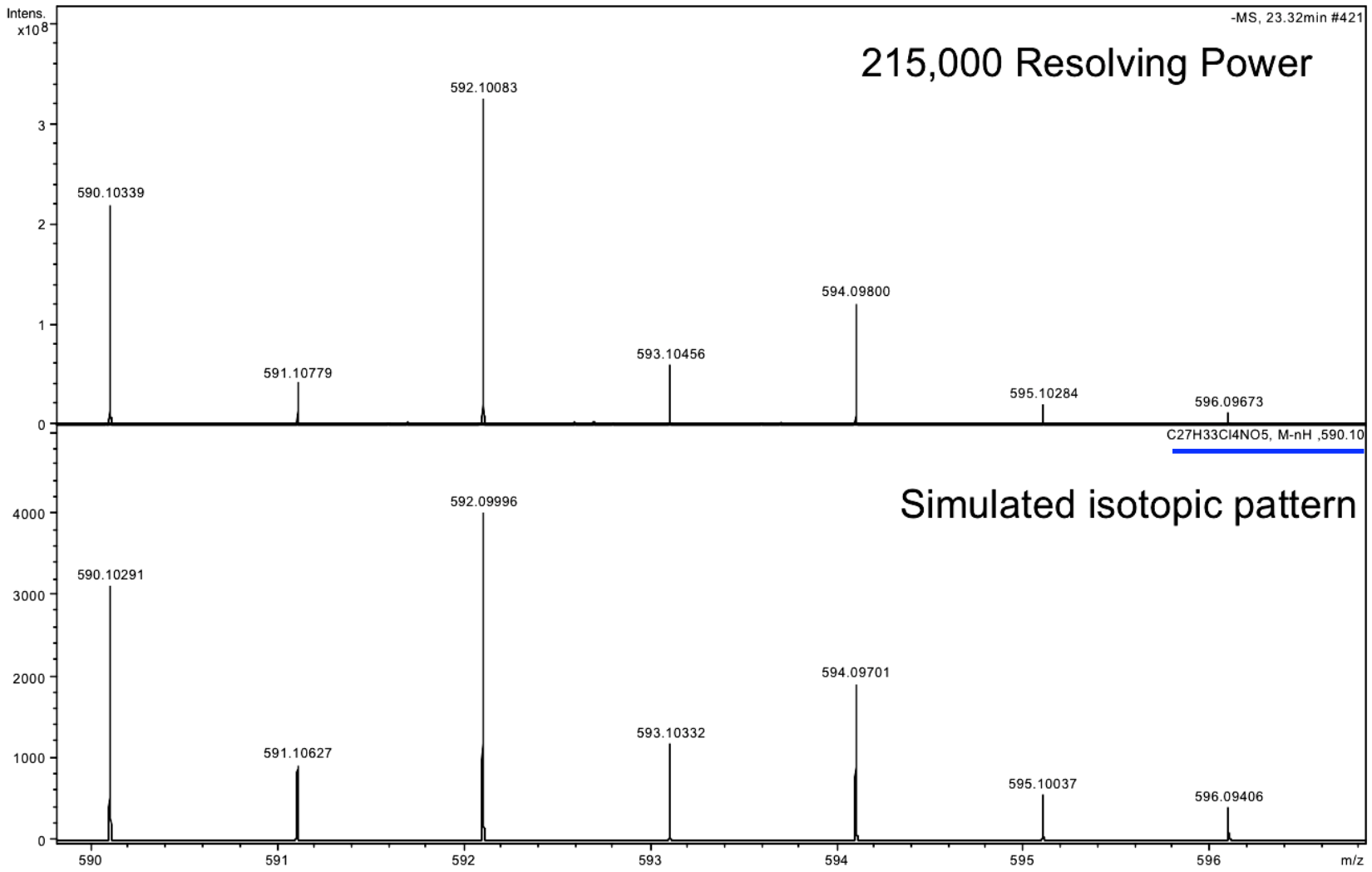


Figure S7. LC-ESI-FT-ICR HRMS (–ve ion mode). Expansion of Figure **S6** and simulated isotopic pattern.

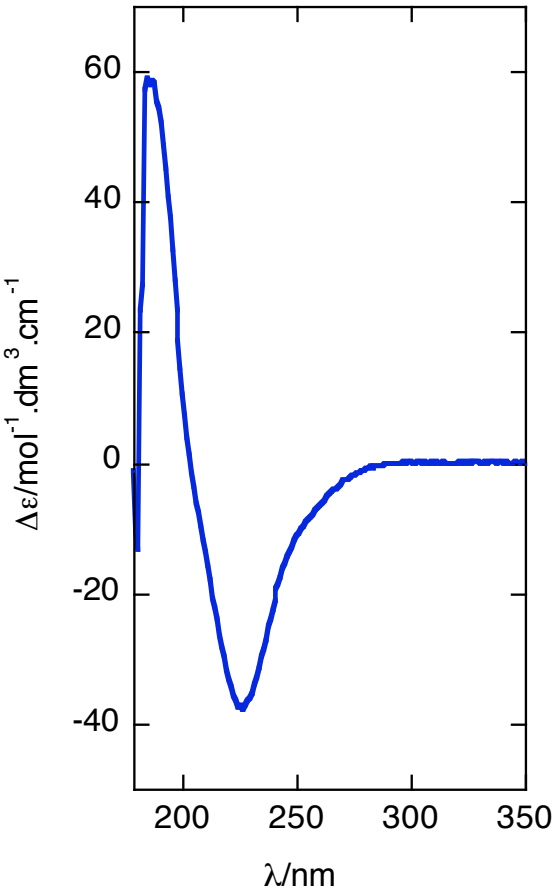


Figure S8. Circular dichroism (CD) spectrum of **1**. Concentration 2.5 x 10^{-4} M in CH_3CN. λ_{max} ($\Delta\varepsilon$) 186 (58.5), 225 (-37.2).

Table S1. ^{1}H and ^{13}C data of muironolide A, **1** (600 MHz, 1.7 mm cryoprobe, $CDCl_3$)

Position	^{1}H (m, J = Hz)	^{13}C[a] (m, J_{CH} = Hz)	COSY	HMBC [a]	NOESY[b]
1		164.4			
2	5.77 (d, 15.5)	124.8 (CH, 161.5)	H3	C1, C4	H4, H13
3	6.53 (dd, 15.5, 11.6)	146.9 (CH, 164.5)	H2, H4	C1, C2, C4, C5, C11	H6, H11
4	2.45 (t, 11.6)	53.6 (CH, 128.4)	H3, H11	C2, C3, C5, C6, C10, C11, C12, C25	H2, H10, H13, H25
5		44.0			
6	3.33 (d, 8.8)	49.0 (CH_2, 141.6)	H6'	C4, C5, C25	H3, H6', H11, -NH
	2.84 (br d, 8.8)	49.0 (CH_2, 147.6)	H6, -NH	C5, C7, C8, C25	H6, H25, -NH
7		169.7			
8		139.7			
9	6.73 (dd, 7.8, 2.5)	130.0 (CH, 165.0)	H10, H10'	C7, C10, C11	H10, H10'
10	1.92 (m)	31.3 (CH_2, 136.8)	H9, H10', H11	C4, C8, C9, C11	H9, H10', H13,
	2.40 (m)	31.3 (CH_2, 134.4)	H9, H10, H11	C8, C9, C11, C12	H9, H10, H11
11	1.70 (ddd, 11.6, 8.7, 2.8)	46.2 (CH, 131.4)	H4, H10, H10'	C3, C4, C5, C9, C12, C13, C15, C26,	H3, H6, H10'
12		133.8			
13	4.88 (d, 9.12)	131.6 (CH, 150.0)	H14, H26	C11, C15, C26	H2, H15
14	2.42 (m)	30.8 (CH, 137.4)	H13, H15, H15', H27	C15	H15', H16', H26, H27
15	1.16 (m)	31.4 (CH_2, 131.4)	H14, H15', H16	C13, C14, C17,	H14, H15, H16, H17
	1.05 (m)	31.4 (CH_2, 131.4)	H14, H15, H16	C13, C14, C16, C17, C27	H13, H15', H16, H16'
16	1.95 (m)	27.1 (CH_2, 131.4)	H15, H15', H16', H17	C14, C15, C18	H15', H16'
	2.04 (m)	27.1 (CH_2, 131.4)	H15, H15', H16, H17	C14, C15, C18	H14, H15, H17
17	5.55 (dd, 10.8, 2.4)	80.3 (CH, 157.5)	H16, H16'	C15, C16, C19, C18	H14, H15', H16'
18		99.3			
19		168.9			
20	2.90 (dd, 16.2, 3.0)	39.4 (CH_2, 123.0)	H20', H21	C19, C21, C22	H21
	2.94 (dd, 16.2, 11.6)	39.4 (CH_2, 123.0)	H20, H21	C19, C21, C22	H21
21	5.03 (ddd, 11.6, 9.4, 3.2)	70.8 (CH, 153.6)	H20, H20', H22	C1, C19, C20, C22, C23, C24	H20, H20', H23, H24'
22	1.44 (dddd, 9.4, 9.4, 6.3, 3.2)	25.6 (CH, 177.0)	H21, H23, H24, H24'	C23	H24
23	2.98 (ddd, 6.5, 3.7, 3.2)	30.0 (CH, 200.4)	H22, H24, H24'	C21, C22	H21, H24'
24	1.09 (ddd, 9.4, 6.5, 3.7)	14.7 (CH_2, 173.4)	H22, H23, H24'	C21, C22, C23	H22, H24
	1.25 (q, 6.5)	14.7 (CH_2, 173.4)	H22, H23, H24	C21, C22	H21, H23, H24
25	1.28 (s)	27.7 (CH_3, 130.0)		C4, C5, C6, C8	H4, H6
26	1.56 (s)	19.1 (CH_3, 128.4)	H13	C11, C12, C13	H14

[a.] Assigned by HSQC ($^{1}J_{CH}$ = 190 Hz) and HMBC ($^{1}J_{CH}$ = 6 Hz). [b.] Mixing time = 400 ms.

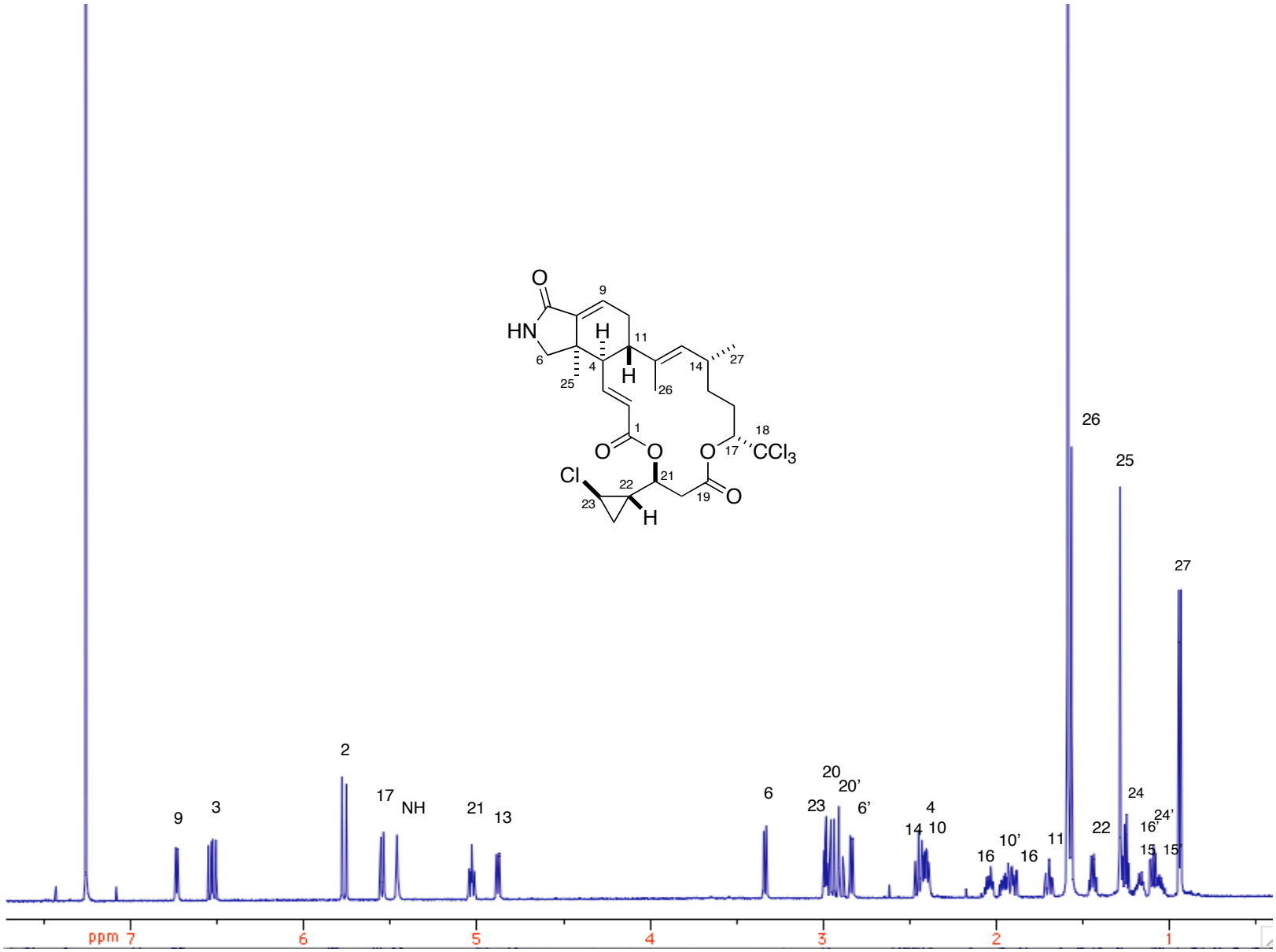


Figure S9 ^{1}H NMR spectrum of **1** (90 μg, 152 nmole) (600 MHz, $CDCl_3$)

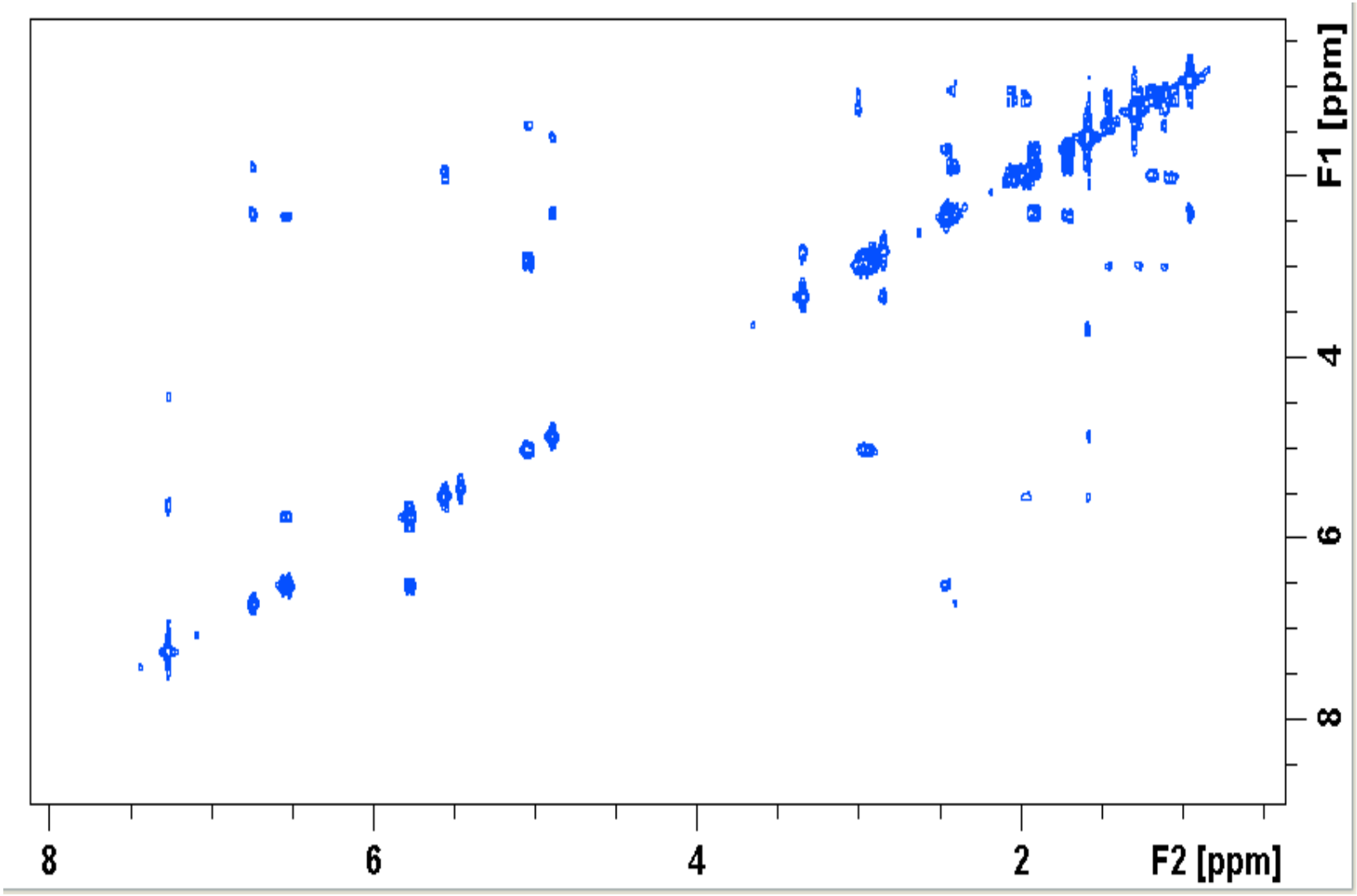


Figure S10. COSY NMR spectrum of **1** (90 μg, 152 nmole) (600 MHz, $CDCl_3$)

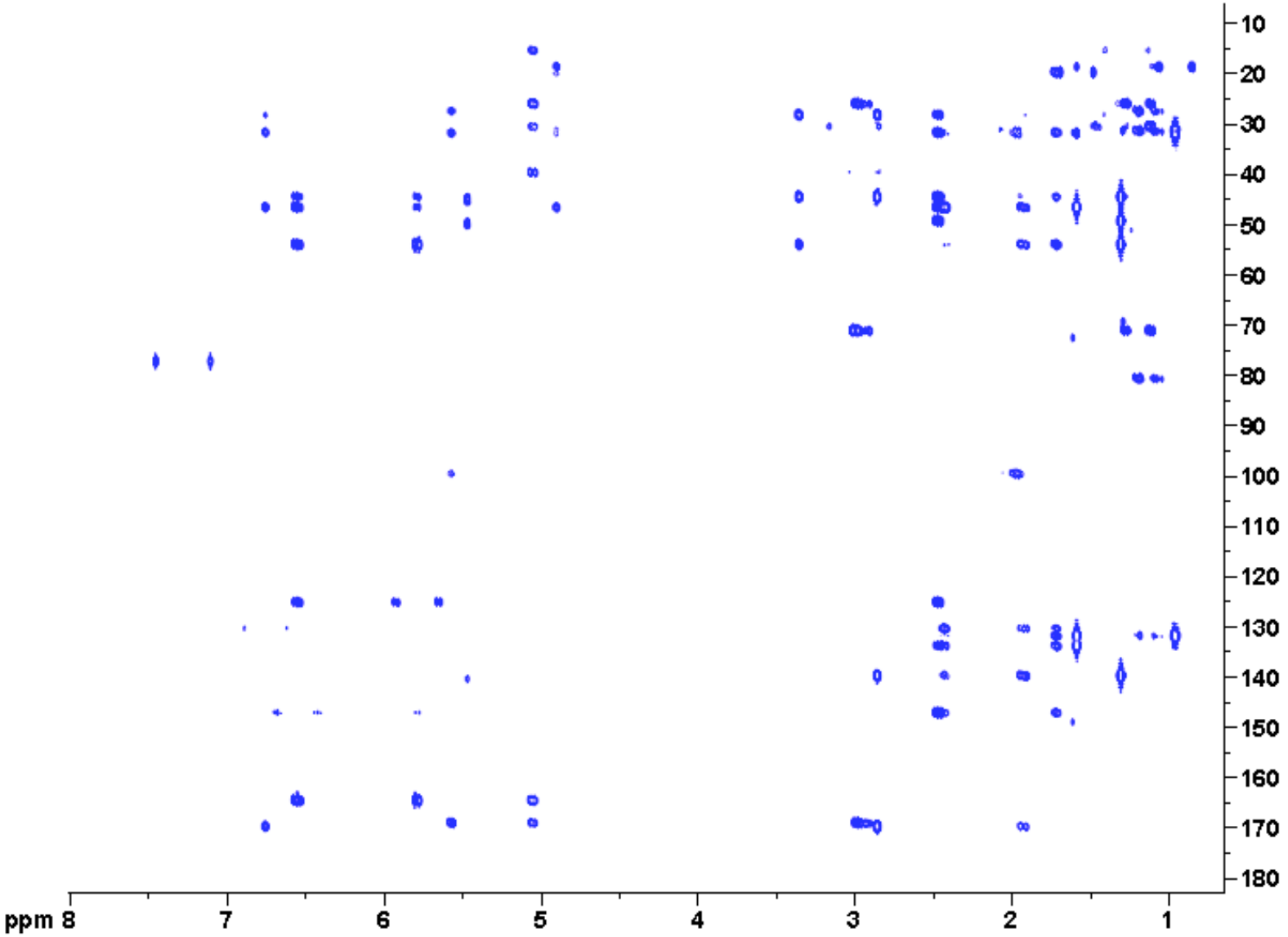


Figure S11. HMBC NMR spectrum of **1** (90 μg, 152 nmole) (600 MHz, $CDCl_3$). Optimized for $^{1}J_{CH}$= 6 Hz.

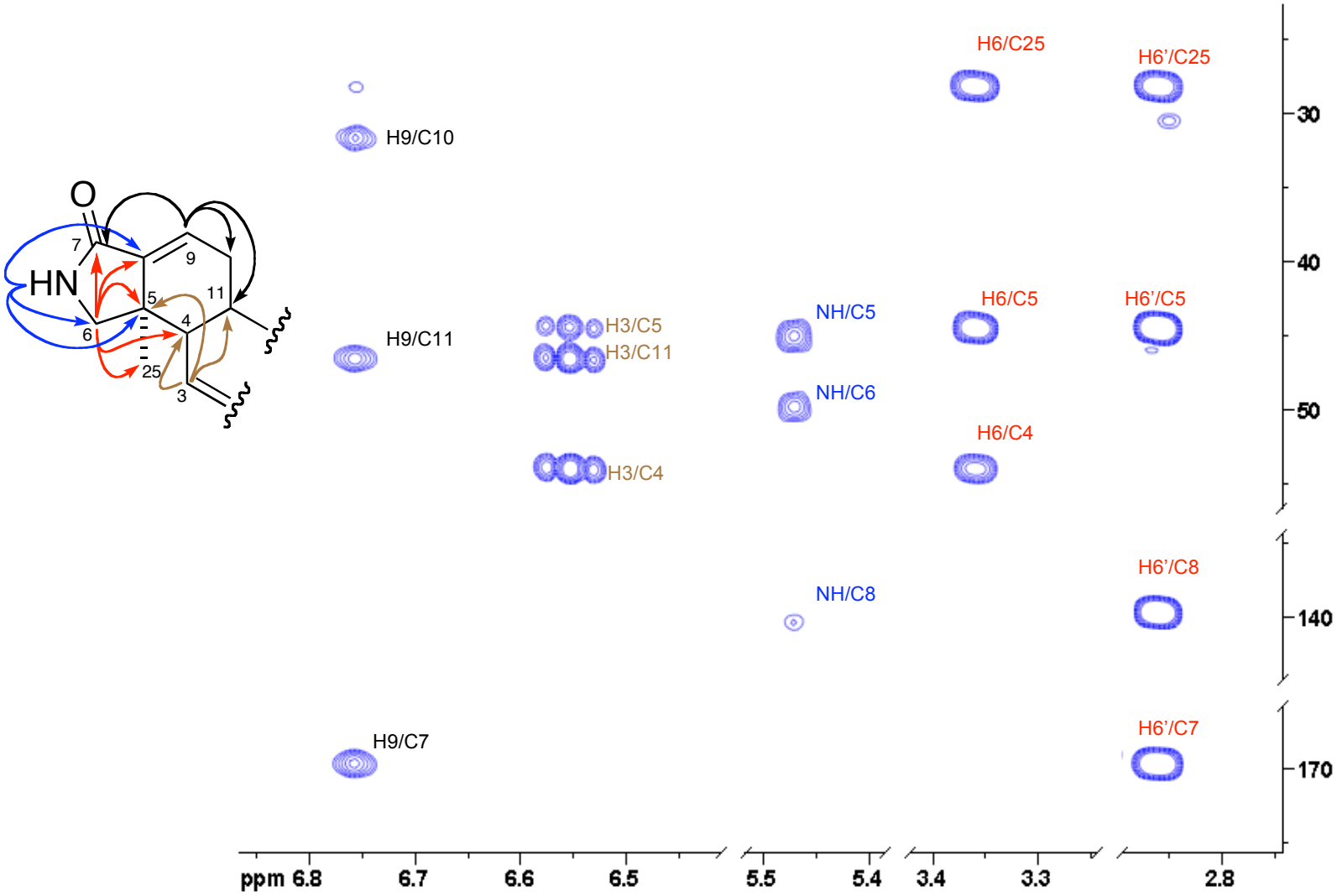


Figure S12. HMBC spectrum of **1** (600 MHz, $CDCl_3$), expansion. Optimized for $^{1}J_{CH}$= 6 Hz.

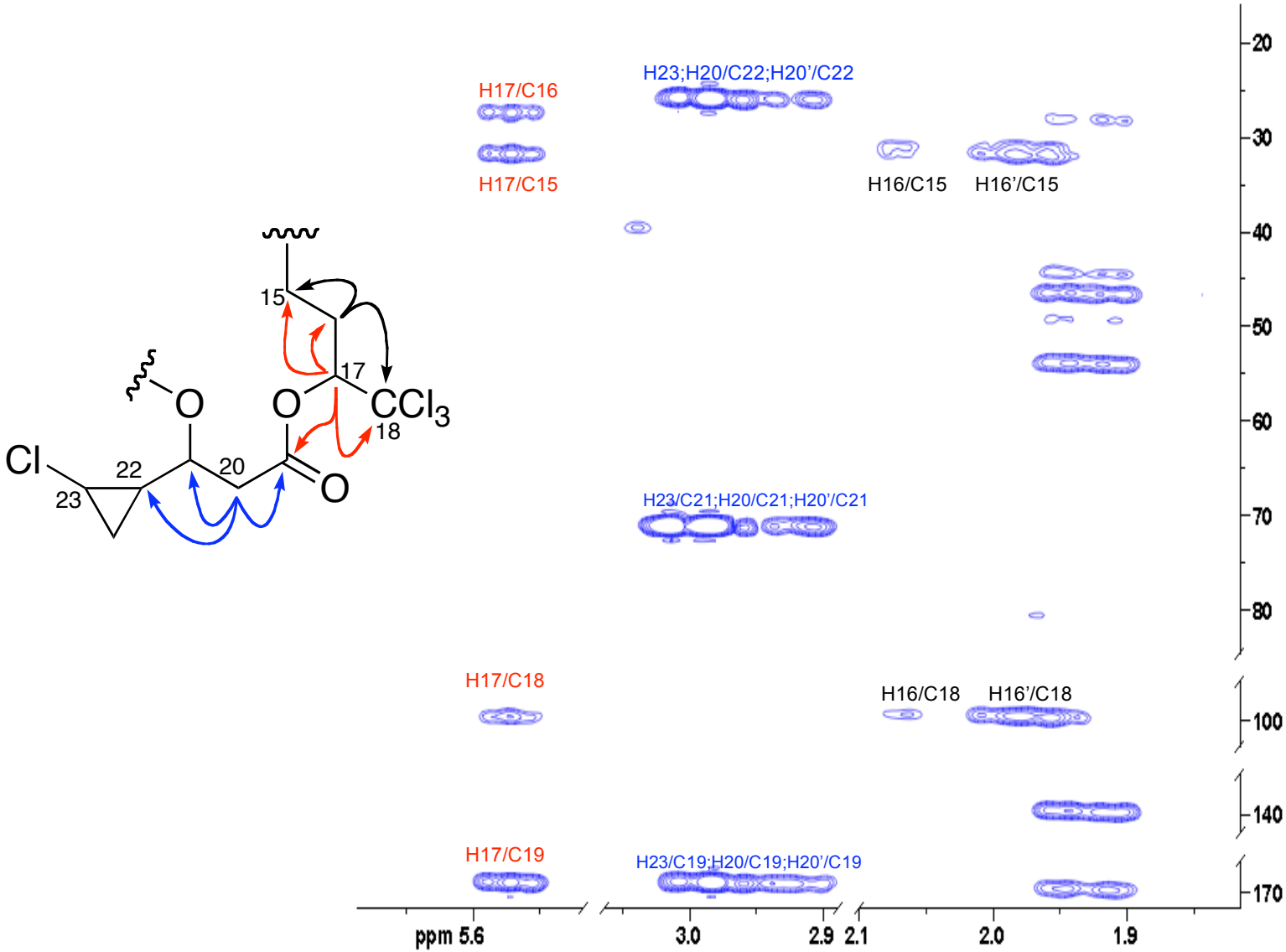


Figure S13. HMBC spectrum of **1** (600 MHz, $CDCl_3$, expansion. Optimized for $^{1}J_{CH}$= 6 Hz.

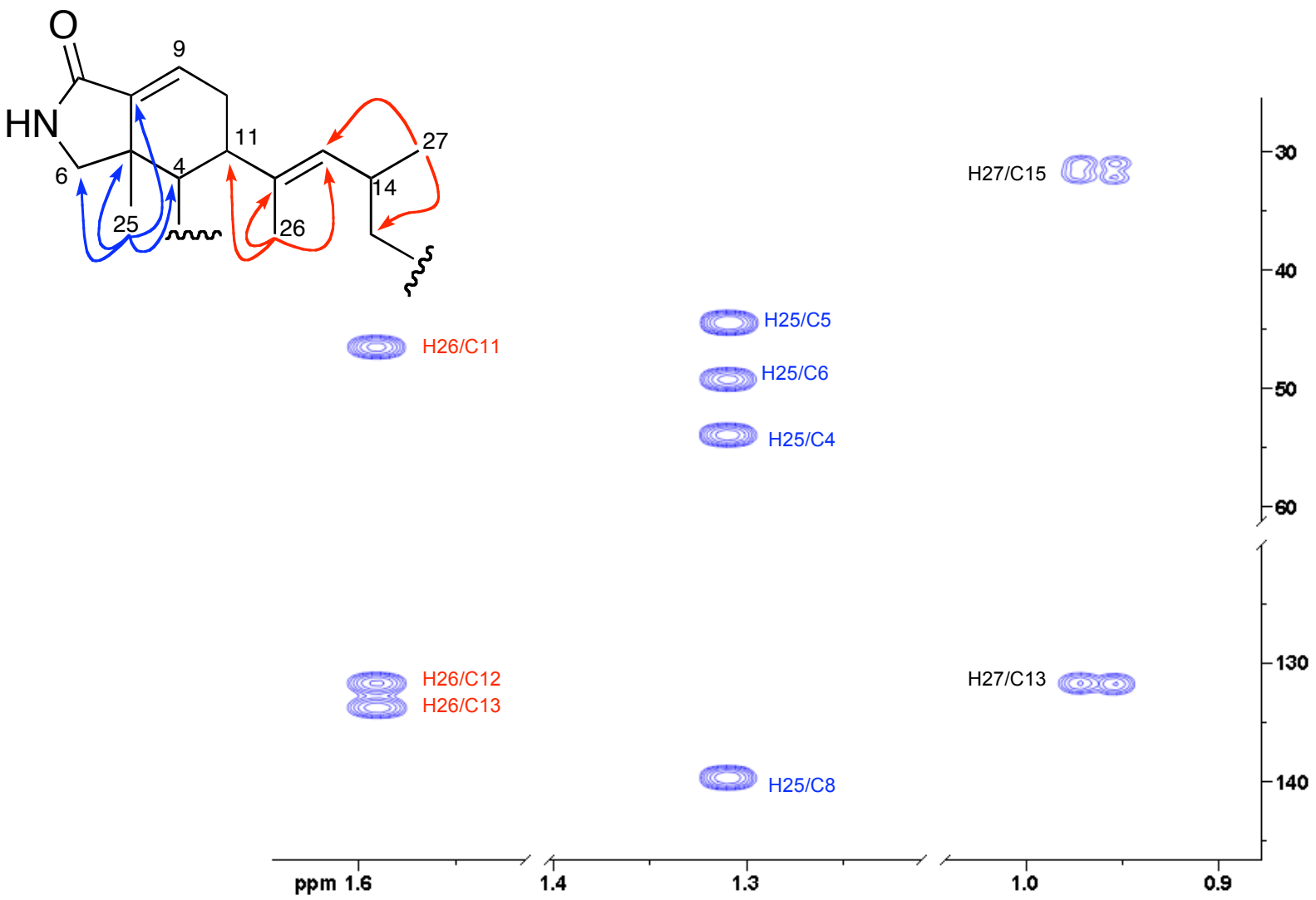


Figure S14 HMBC NMR spectrum expansion of **1** (600 MHz, $CDCl_3$). Optimized for $^{1}J_{CH}$= 6 Hz.

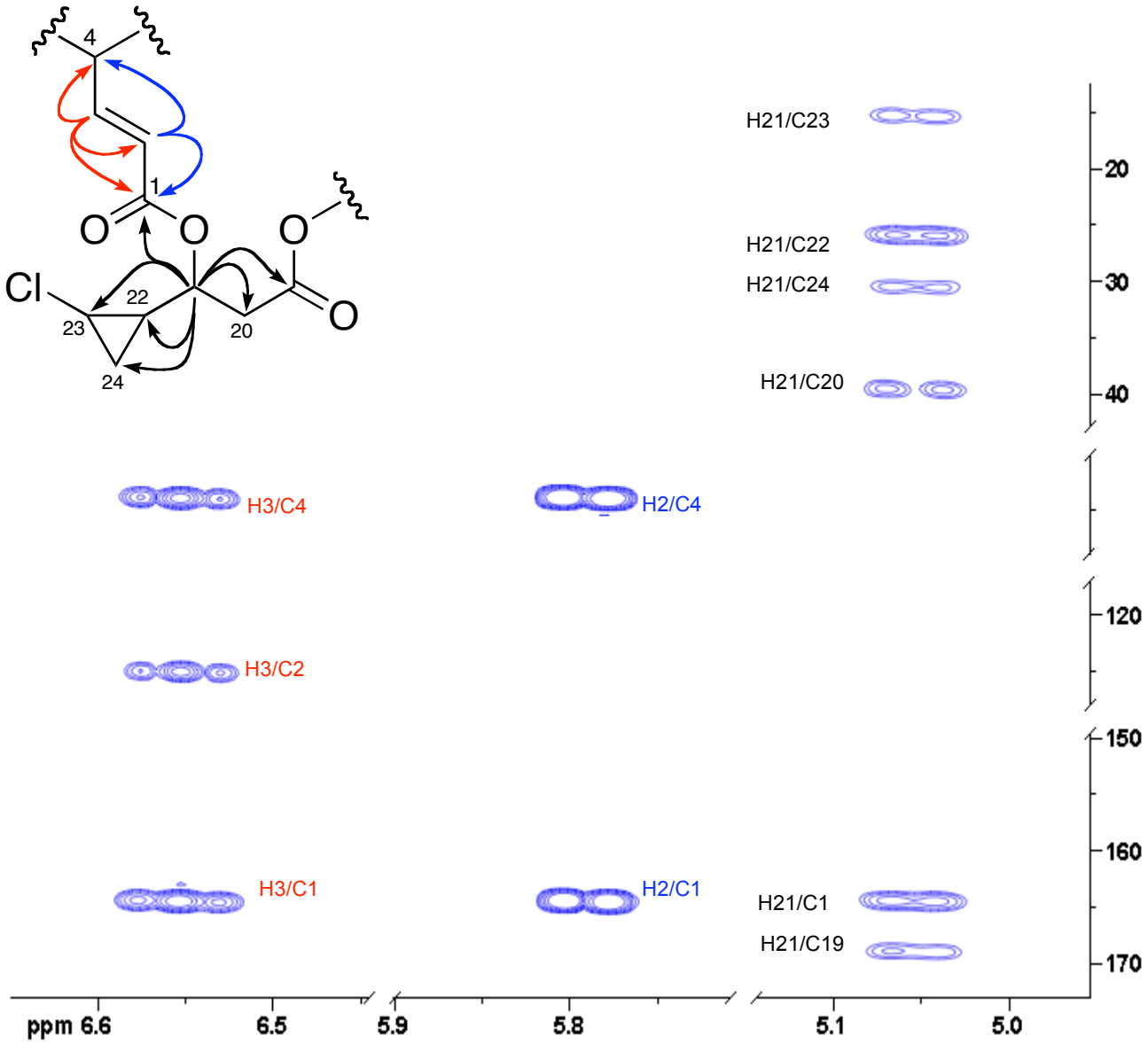


Figure S15. HMBC NMR spectrum expansion of **1** (600 MHz, $CDCl_3$). Optimized for $^{1}J_{CH}$= 6 Hz.

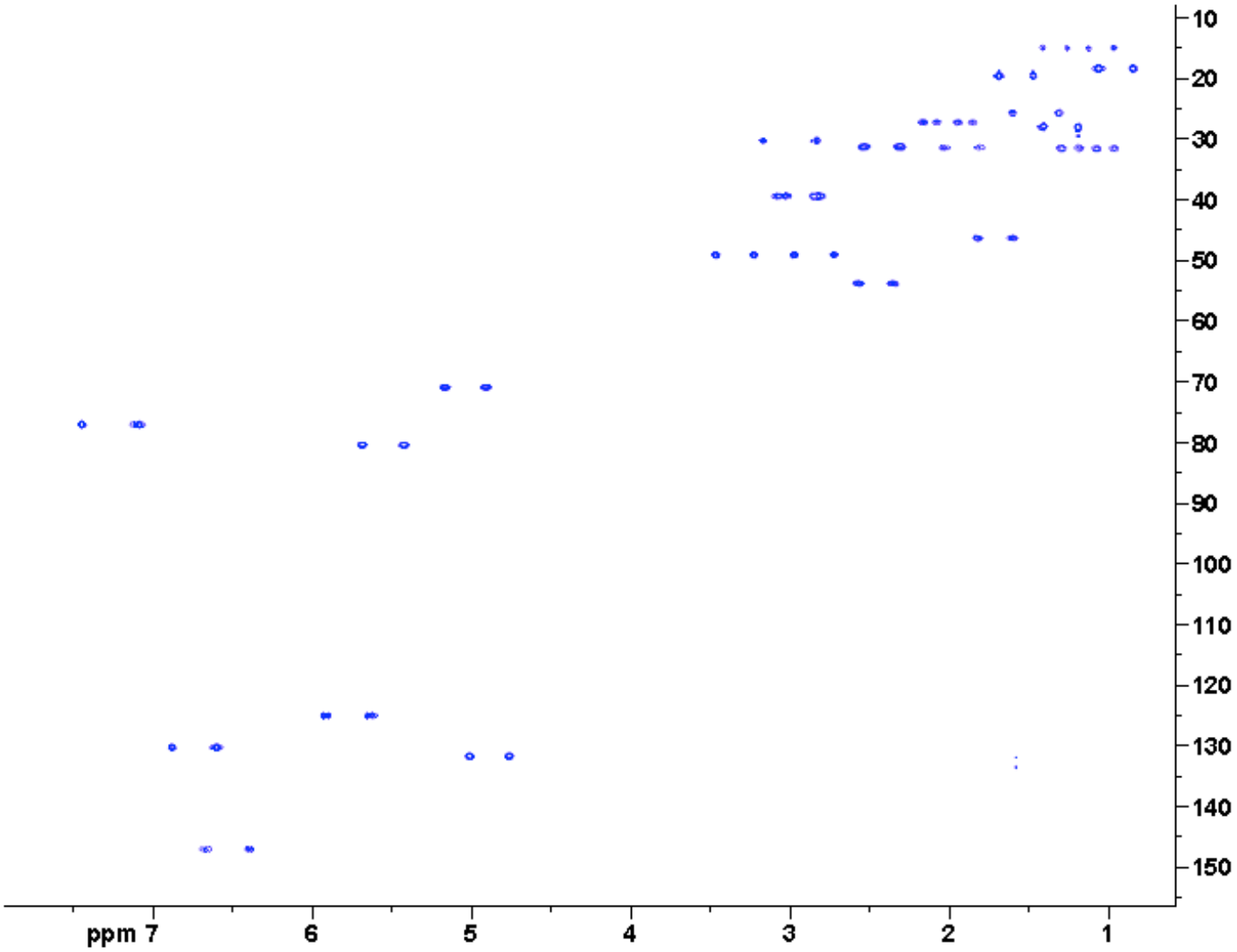


Figure S16. ^{1}H-coupled HSQC spectrum of **1** (90 μg, 152 nmole) (600 MHz, $CDCl_3$). Optimized for $^{1}J_{CH}$= 190 Hz.

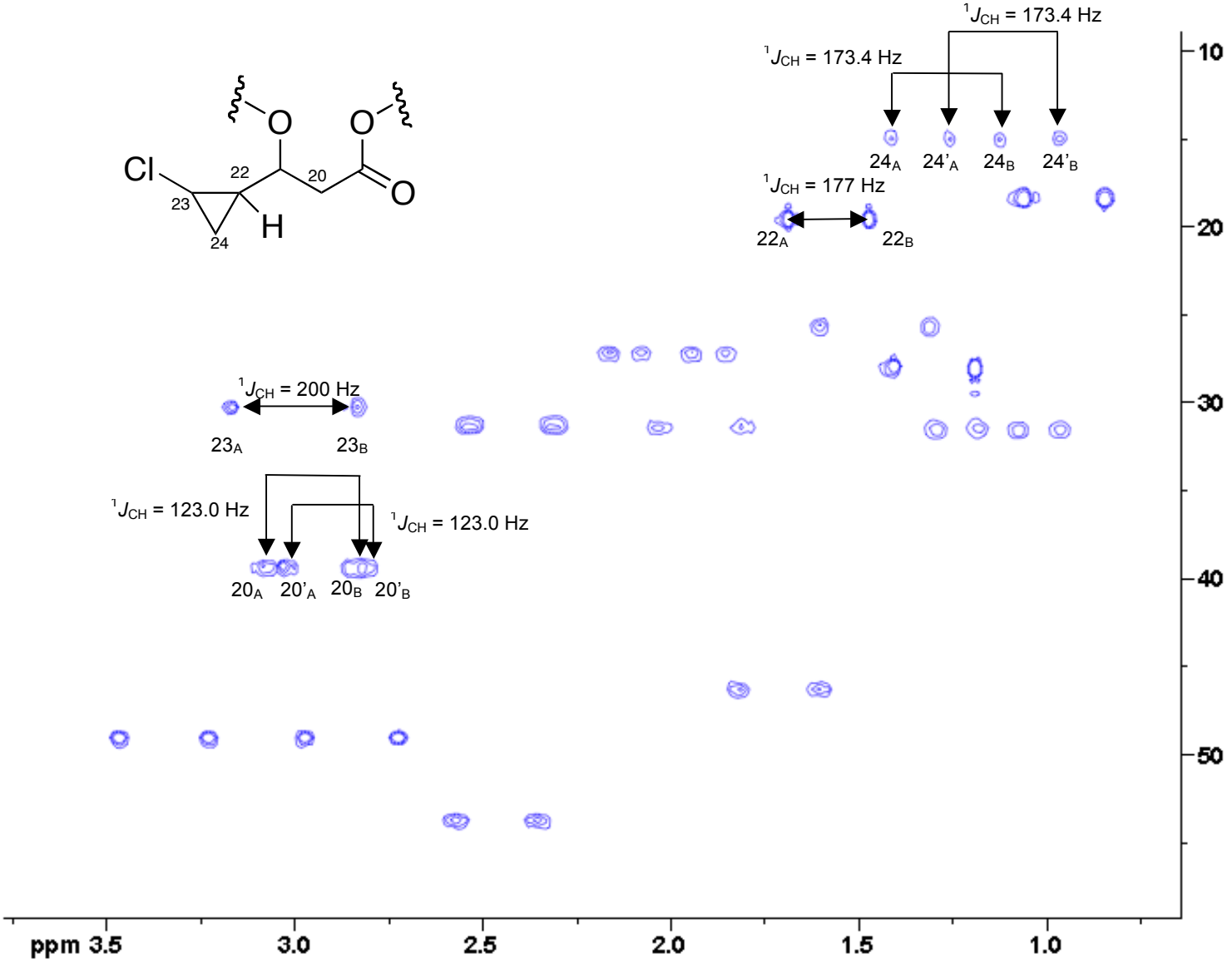


Figure S17. ^{1}H-coupled HSQC spectrum of **1** (90 μg, 152 nmole) (600 MHz, $CDCl_3$), expansion. Optimized for $^1J_{CH}$= 190 Hz.

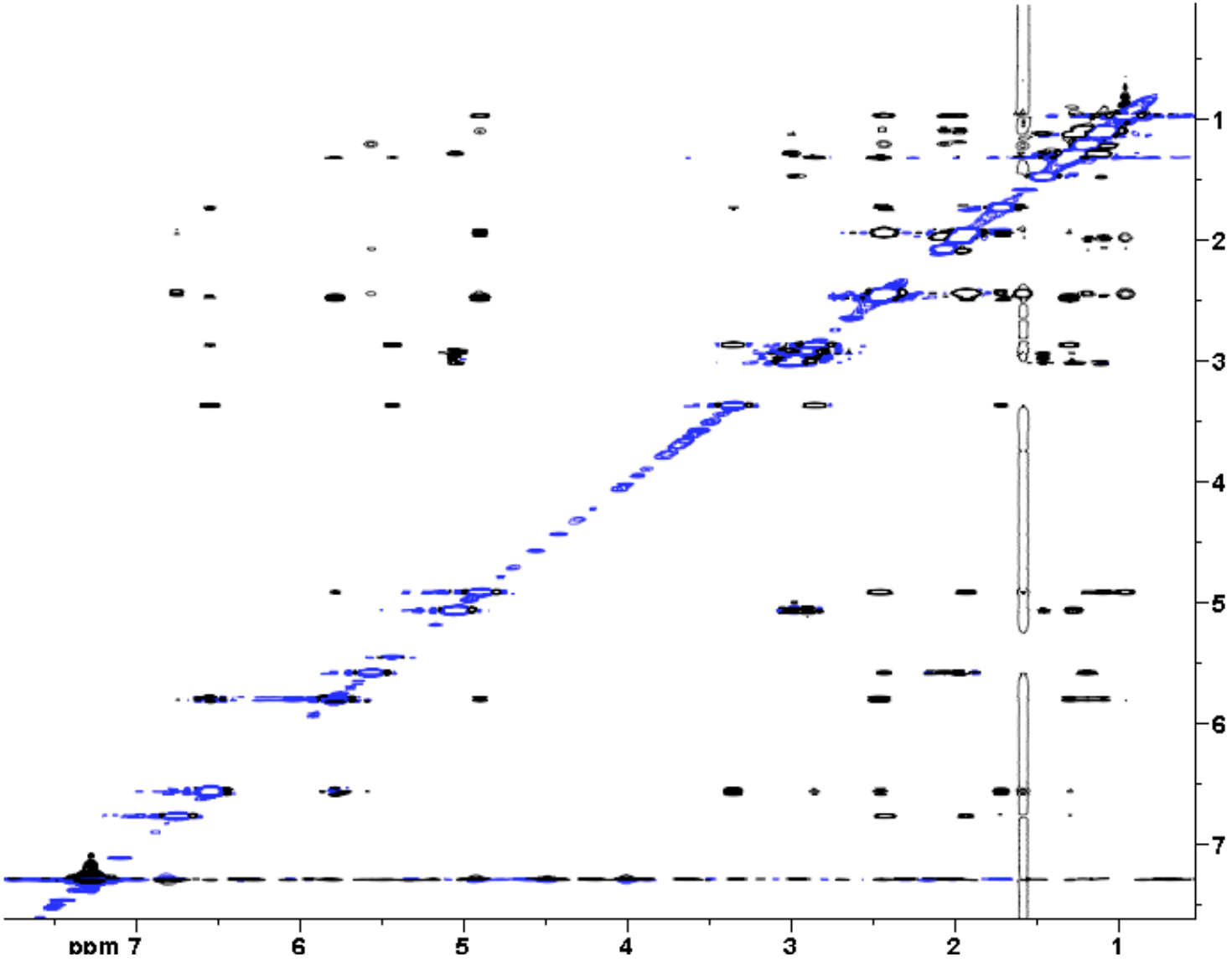


Figure S18. NOESY **1** (600 MHz, $CDCl_3$). t_m = 400 ms.

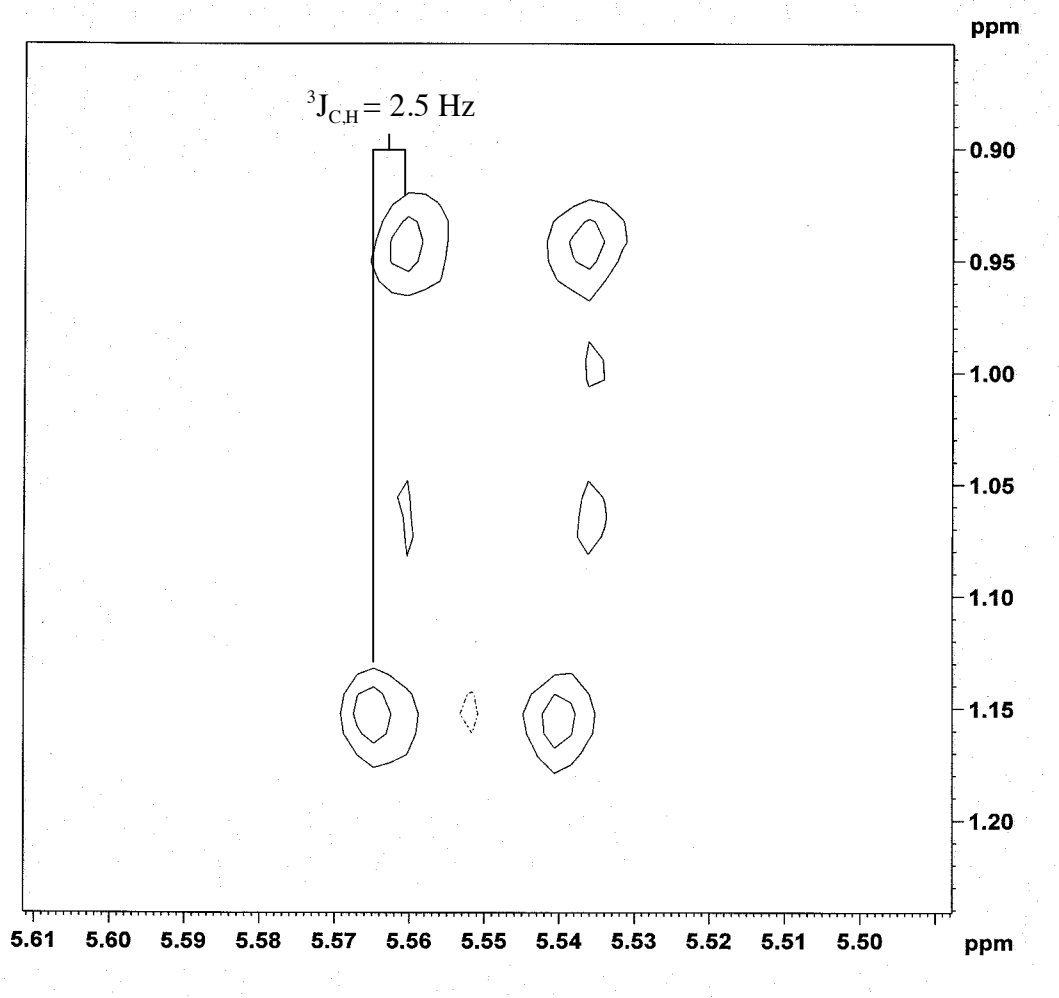


Figure S19. Expansion of HETLOC spectrum showing H17/H15 cross peak (600 MHz, $CDCl_3$).

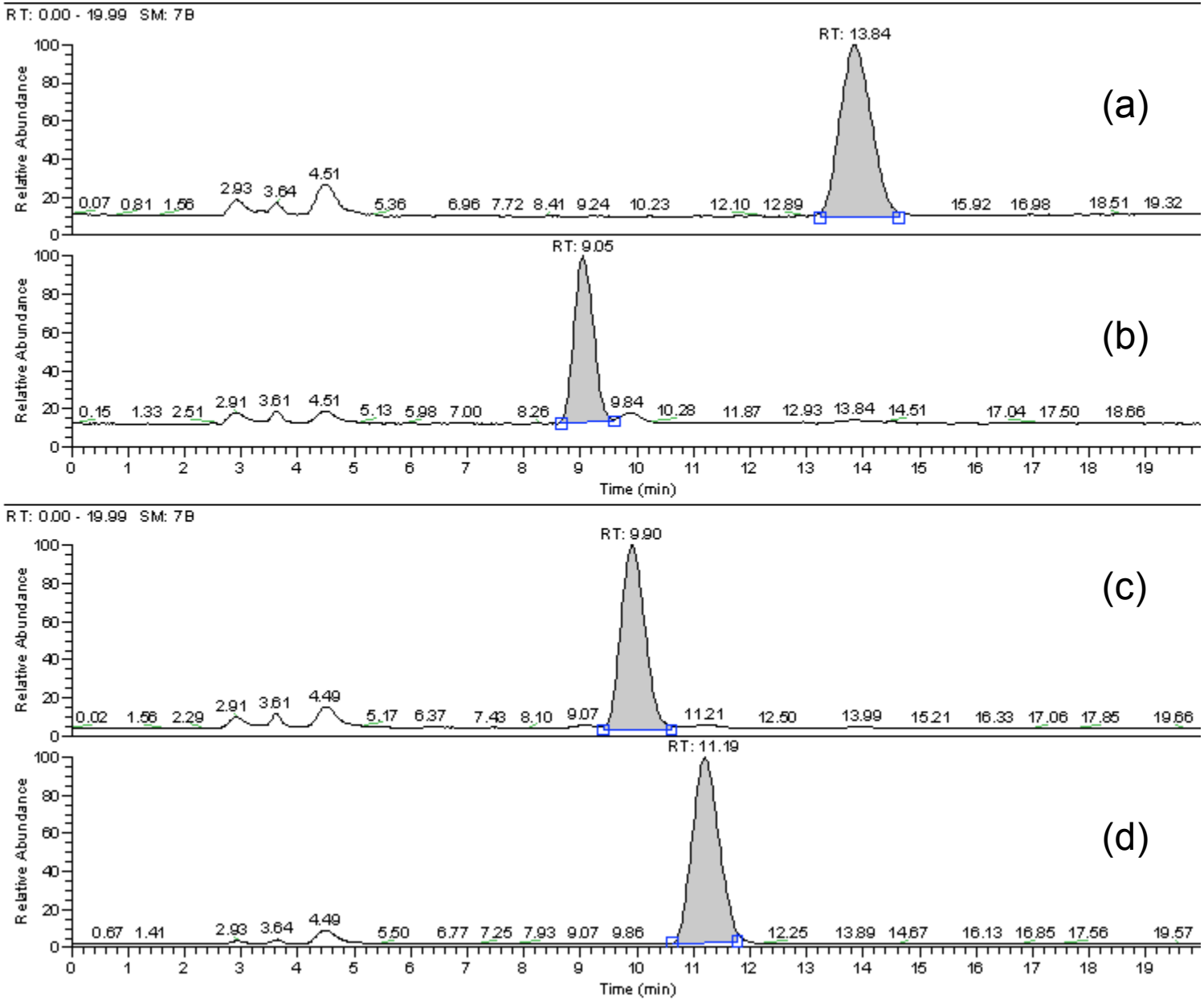


Figure S20. ESI LCMS chromatograms (single ion monitoring, *m/z* 355.2, $M+Na^+$). Chiralpak AD-RH (2.1 x 150 mm, 5 µ; 1:4 HCOOH (aq. 0.1%)–CH_3CN, 0.2 mL/min). (a) **7a** (b**) 7c** (c) **7d** (d) **7b**.

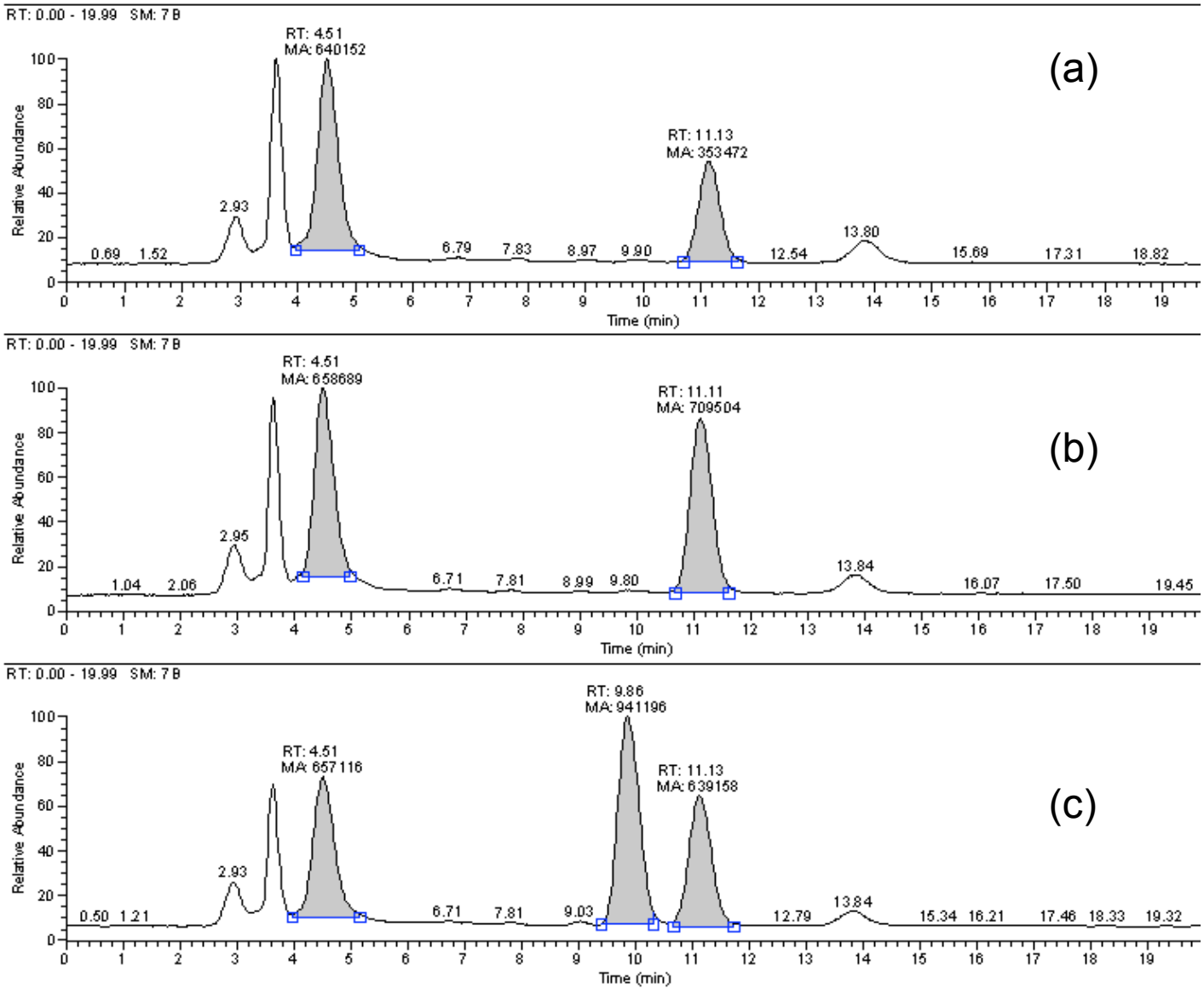


Figure S21. ESI LCMS chromatograms (single ion monitoring, *m/z* 355.2, $M+Na^+$). Chiralpak AD-RH (2.1 x 150 mm, 5 µ; 1:4 HCO_2H (0.1% aq.)–CH_3CN, 0.2 mL/min). (a) 2-naphthone derivative of hydrolysate of **1** (see text). (b**)** co-injection of (a) and authentic (3*S*,4*S*,5*R*)-**7b**. (a). (c) co-injection of (a) + **7b** + **7d**.

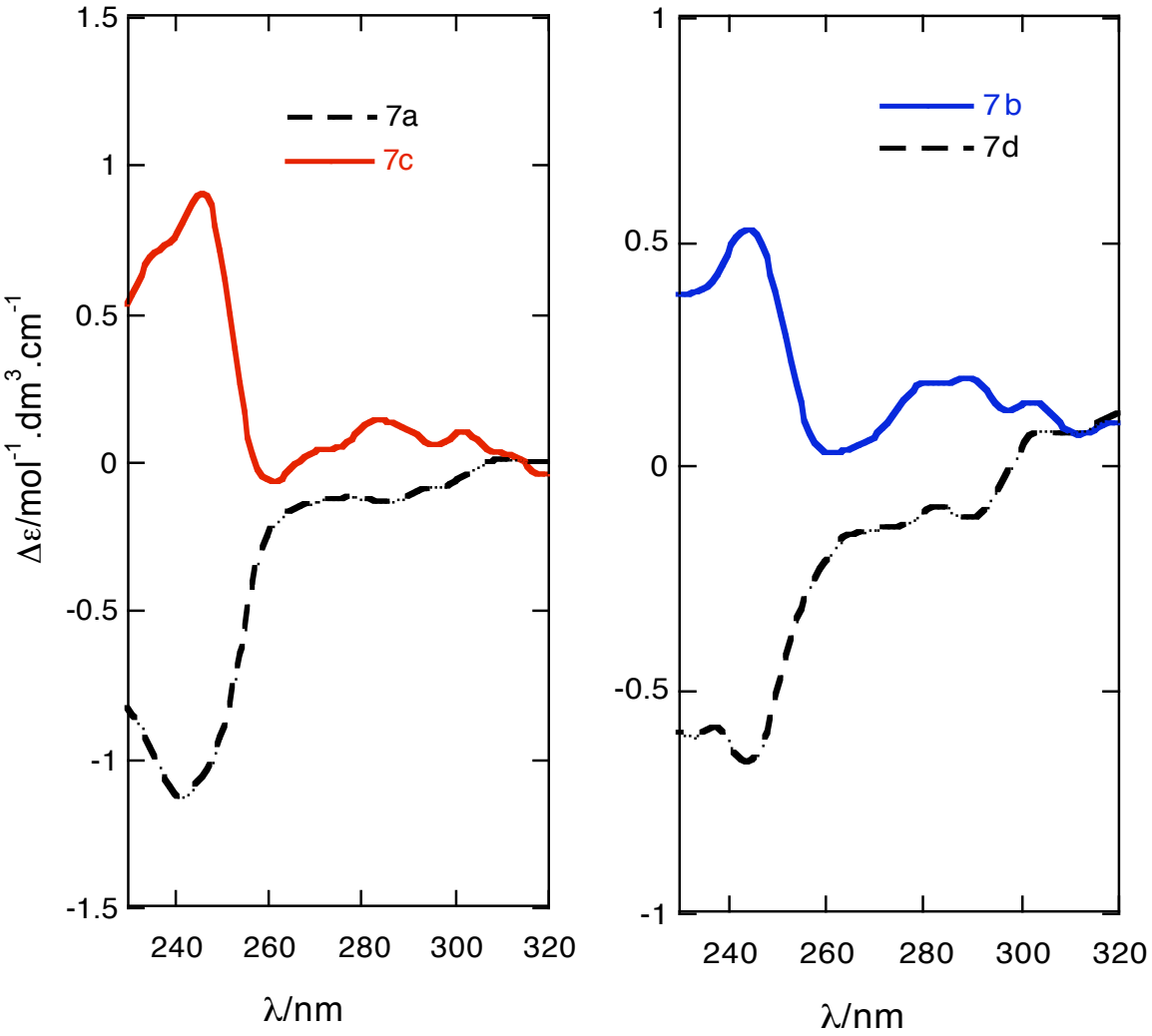


Figure S22. CD spectra of **7a-d** (3:7 *i*-PrOH:hexane). **7a**, conc. 2.4 x 10^{-4} M; **7c**, conc. 1.28 x 10^{-4} M; **7b**, conc. 2.4 x 10^{-4} M **7d**, conc. 1.26 x 10^{-4} M.

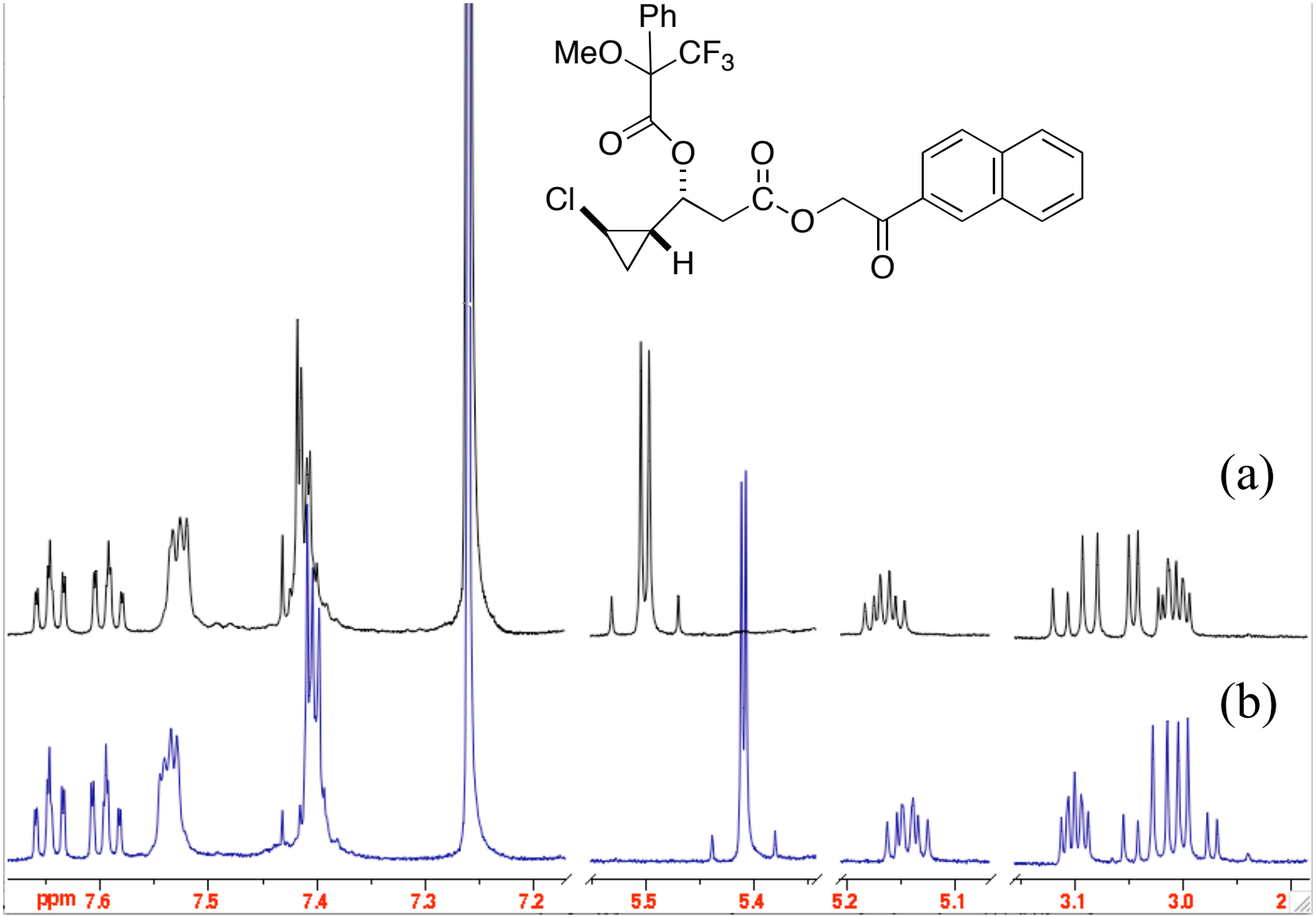


Figure S23. Expansion of ^{1}H NMR spectra of (a) (*S*)-MTPA and (b) (*R*)-MTPA esters of **7a**. ($CDCl_3$, 600 MHz).