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# Supporting Information



69451 Weinheim, Germany

# Total Synthesis of (-)-Reidispongiolide A, an Actin-Targeting Marine Macrolide

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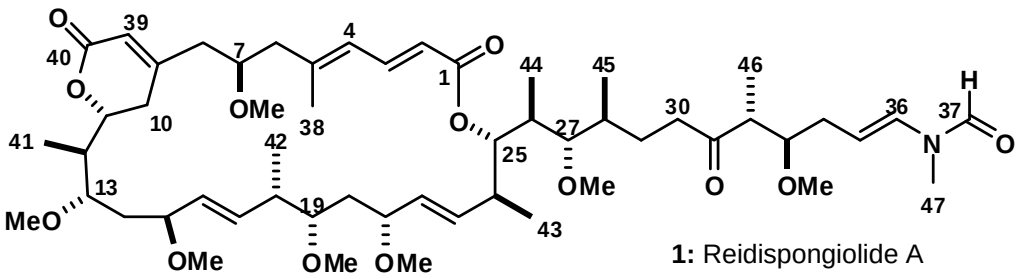
**The following data is included as supporting information:**

$^{1}$H NMR data for natural and synthetic reidispongiolide A ($CDCl_3$)
$^{13}$C NMR data for natural and synthetic reidispongiolide A ($CDCl_3$)
CD spectra for natural and synthetic reidispongiolide A (MeOH)
HPLC chromatograms for natural and synthetic reidispongiolide A

NMR spectra were recorded in deuterochloroform ($CDCl_3$). Signal positions ($\delta$) are given in parts per million from tetramethylsilane ($\delta$ 0) and were measured relative to the signal of the solvent in which the sample was analyzed ($CDCl_3$: $\delta$ 7.26, $^{1}$H NMR; $\delta$ 77.0, $^{13}$C NMR). Coupling constants (*J* values) are given in Hertz (Hz) and are reported to the nearest 0.1 Hz. $^{1}$H NMR spectral data are tabulated in the order: multiplicity (br, broad; s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet), coupling constant. Due to restricted rotation around the amide bond in the N-vinyl formamide terminus, doubling of some signals in the $^{1}$H and $^{13}$C NMR spectra is observed. The ratio of rotamers in $CDCl_3$ solution was determined as 2:1.

CD spectra were recorded on an Applied Photophysics Chirascan circular dichroism spectropolarimeter using a 1-mm path length quartz cuvette. Scans were performed at 20°C over a wavelength range of 220-320 nm with response time of 0.5 s, 1 nm pitch and 1 nm bandwidth. Blank spectra of samples (MeOH) were subtracted from collected data. The CD spectra represent an average of three scans and are zero-corrected at 320 nm ($\theta$ quoted in mdeg).

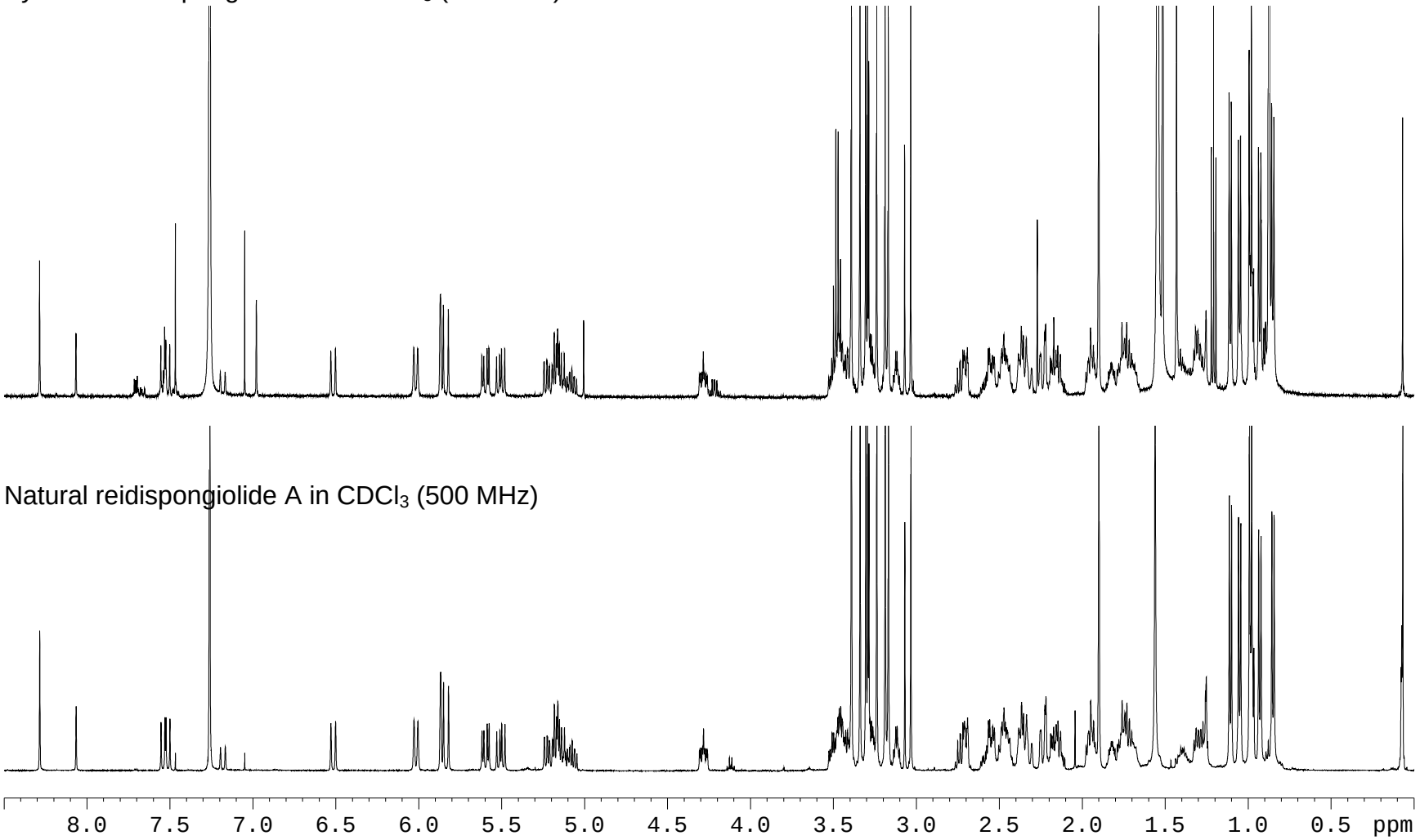



**1:** Reidispongiolide A

**Figure 1:** Numbering system for reidispongiolide A

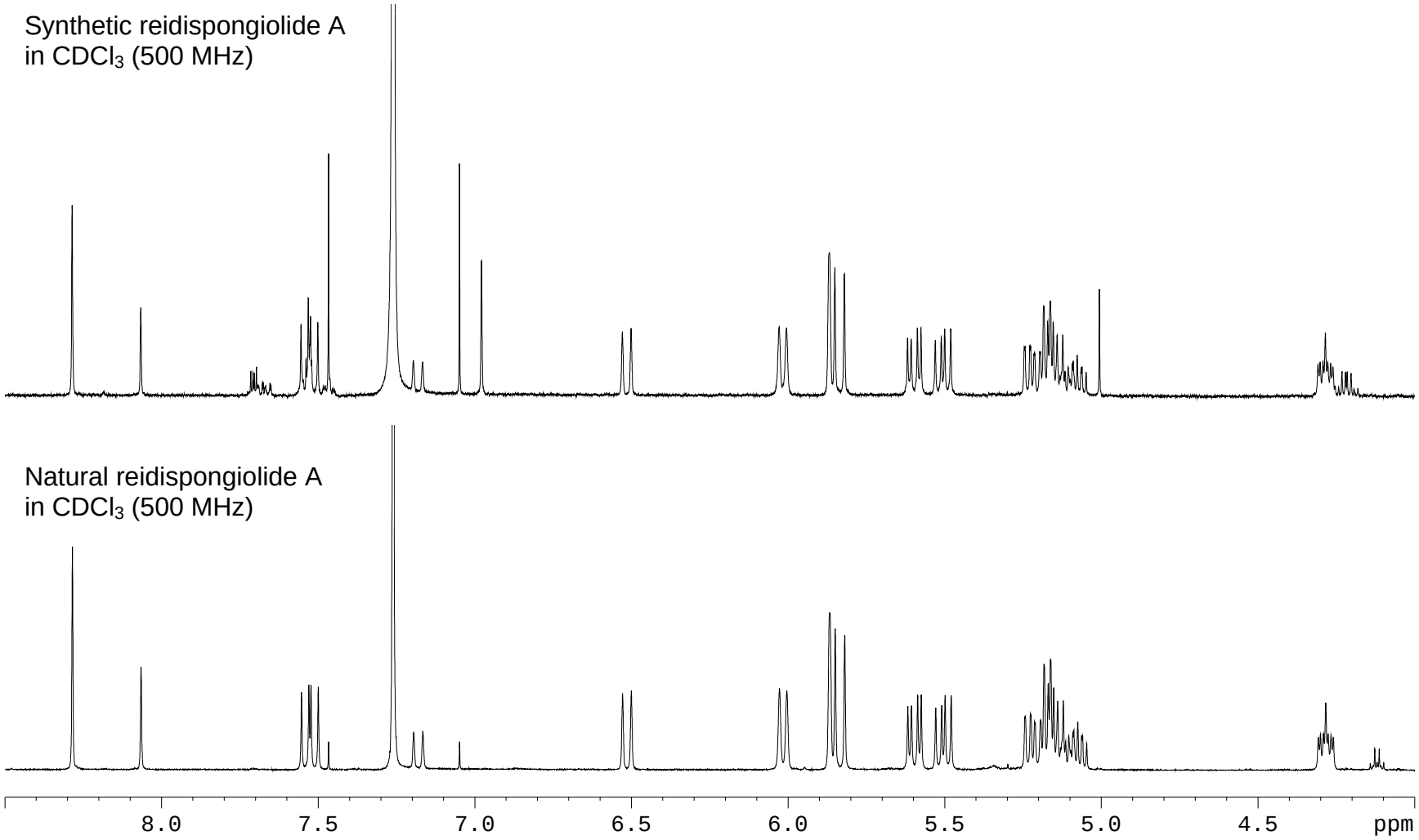
# $^{1}$H NMR spectra for natural and synthetic reidispongiolide A

Synthetic reidispongiolide A in $CDCl_3$ (500 MHz)

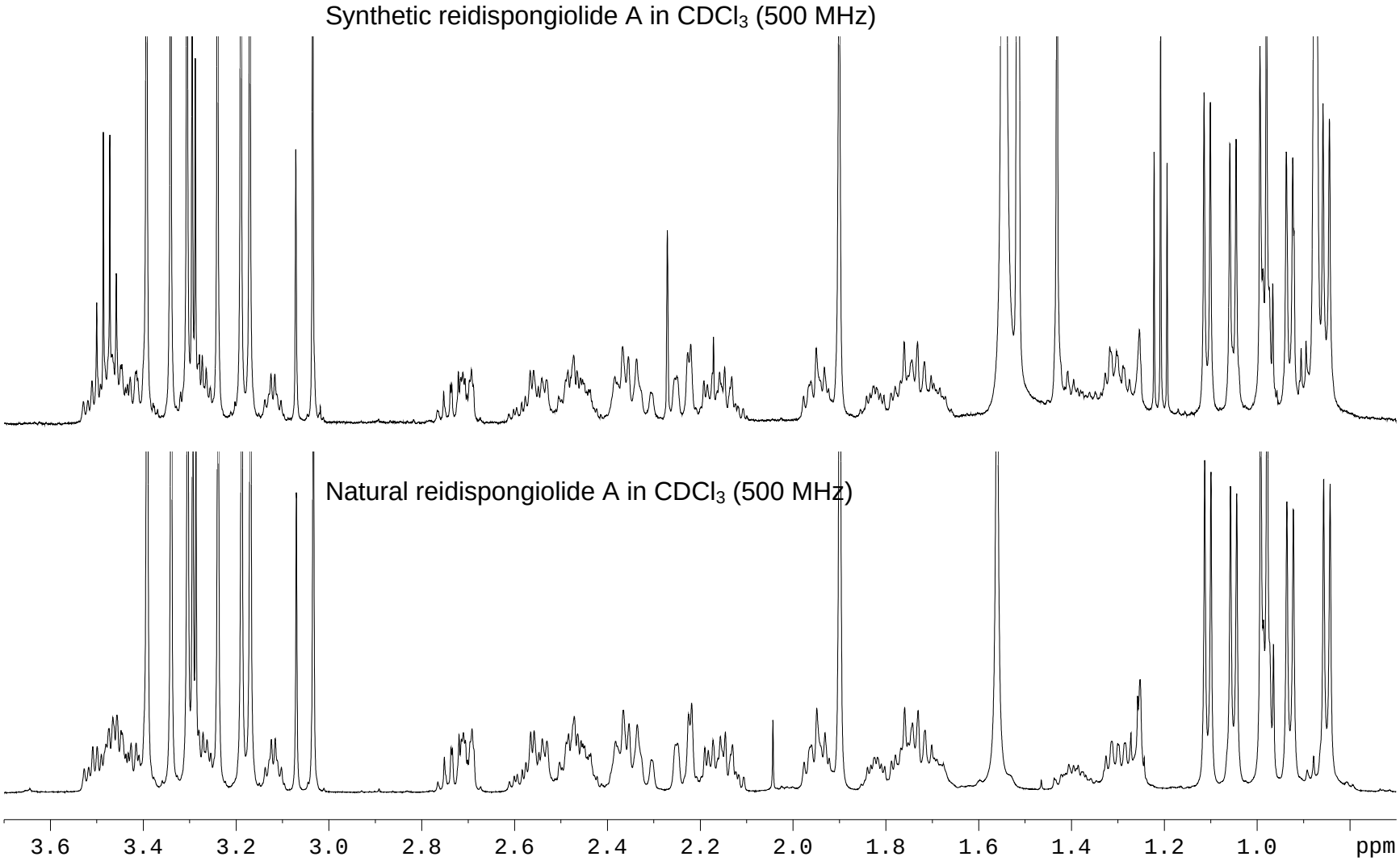



Natural reidispongiolide A in $CDCl_3$ (500 MHz)

# $^{1}$H NMR spectra for natural and synthetic reidispongiolide A



# $^{1}$H NMR spectra for natural and synthetic reidispongiolide A



# $^{1}$H NMR data for natural and synthetic reidispongiolide A ($CDCl_3$)

| Proton No. | natural reidispongiolide A[1] ($\delta_H$) | natural reidispongiolide A[2] ($\delta_H$) | synthetic reidispongiolide A[3] ($\delta_H$) |
|---|---|---|---|
| 2 | 5.79 d (15.3) | 5.83 d (15.2) | 5.84 d (15.2) |
| 3 | 7.50 dd (15.3, 11.8) | 7.53 dd (15.2, 11.8) | 7.53 dd (15.2, 11.6) |
| 4 | 6.00 d (11.8) | 6.02 d (11.7) | 6.02 d (11.7) |
| 5-Me (38) | 1.87 s | 1.90 s | 1.90 s |
| 6a | 2.48 dd | 2.54 m | 2.54 m |
| 6b | 2.08 dd | 2.16 m | 2.17 m |
| 7 | 3.45 m | 3.47 m | 3.47 m |
| 8a | 2.30 m | 2.37 m | 2.37 m |
| 8b | 2.20 dd (14.7, 3.16) | 2.24 m | 2.24 m |
| 10a | 2.29 m | 2.33 m | 2.33 m |
| 10b | 2.19 m | 2.23 m | 2.24 m |
| 11 | 4.22 m | 4.28 ddd (12.0, 8.4, 3.6) | 4.28 ddd (12.0, 8.4, 3.5) |
| 12 | 1.78 dd | 1.82 m | 1.82 m |
| 12-Me (41) | 1.10 d (6.9) | 1.11 d (6.8) | 1.11 d (6.8) |
| 13 | 3.20 m | 3.28 m | 3.28 m |
| 14a | 1.89 m | 1.94 m | 1.95 m |
| 14b | 1.72 m | 1.77 m | 1.77 m |
| 15 | 3.48 m | 3.50 m | 3.51 m |
| 16 | 5.18 dd (15.4, 8.5) | 5.22 ddd (15.7, 9.0, 1.1) | 5.22 ddd (15.6, 9.0, 1.2) |
| 17 | 5.52 dd (15.4, 7.8) | 5.60 dd (15.7, 5.8) | 5.60 dd (15.7, 5.8) |
| 18 | 2.32 dd | 2.38 m | 2.38 m |
| 18-Me (42) | 0.84 d (6.9) | 0.85 d (6.8) | 0.85 d (6.9) |
| 19 | 3.08 m | 3.12 m | 3.12 m |
| 20a | 1.66 m | 1.73 m | 1.73 m |
| 20b | 1.23 m | 1.30 m | 1.31 m |
| 21 | 3.38 m | 3.42 m | 3.42 m |
| 22 | 5.10 dd (15.1, 10.0) | 5.15 dd (15.1, 8.9) | 5.15 dd (15.1, 8.8) |
| 23 | 5.42 dd (15.1, 10.0) | 5.50 dd (15.2, 9.7) | 5.51 dd (15.2, 9.6) |
| 24 | 2.42 dd | 2.48 m | 2.49 m |
| 24-Me (43) | 1.03 d (6.9) | 1.05 d (6.8) | 1.05 d (6.8) |
| 25 | 5.12 dd | 5.17 d (10.3) | 5.17 d (10.5) |
| 26 | 1.89 dd | 1.95 m | 1.96 m |
| 26-Me (44) | 0.91 d (6.9) | 0.93 d (7.0) | 0.93 d (6.9) |
| 27 | 2.66 dd | 2.70 dd (7.2, 2.1) | 2.70 dd (7.1, 2.3) |
| 28 | 1.63 m | 1.69 m | 1.69 m |
| 28-Me (45) | 0.97 d (6.9) | 0.99 d (7.0) | 0.99 d (6.9) |
| 29a | 1.65 m | 1.75 m | 1.75 m |
| 29b | 1.32 m | 1.40 m | 1.40 m |
| 30a | 2.55 m | 2.58 m | 2.58 m |
| 30b | 2.45 m | 2.46 m | 2.46 m |
| 32 | 2.70 d | 2.73 m | 2.73 m |
| 32-Me (46) | 0.97 d (6.9) | 0.98 m | 0.98 m |
| 33 | 3.41 m | 3.46 m | 3.46 m |
| 34a | 2.42 m | 2.46 m | 2.46 m |
| 34b | 2.11 m | 2.14 m | 2.14 m |
| 35 | 5.11-5.06[a] m | 5.12[a]-5.08 m | 5.12[a]-5.08 m |
| 36 | 6.47-7.18[a] d (15.0) | 6.51 d (14.1)-7.18[a] d (14.6) | 6.52 d (14.1)-7.18[a] d (14.8) |
| 37 | 8.28-8.02[a] s | 8.28-8.06[a] s | 8.29-8.07[a] s |
| 47-N-Me | 3.03-3.08[a] s | 3.07[a]-3.03 s | 3.07[a]-3.03 s |
| 39 | 5.83 s | 5.87 s | 5.87 s |
| 7-OMe | 3.26 s | 3.30 s | 3.31 s |
| 13-OMe | 3.13 s | 3.17 s | 3.17 s |
| 15-OMe | 3.20 s | 3.24 s | 3.24 s |
| 19-OMe | 3.15 s | 3.19 s | 3.19 s |
| 21-OMe | 3.27 s | 3.34 s | 3.34 s |
| 27-OMe | 3.30 s | 3.39 s | 3.39 s |
| 33-OMe | 3.30-3.25[a] s | 3.29-3.28[a] s | 3.29-3.28[a] s |

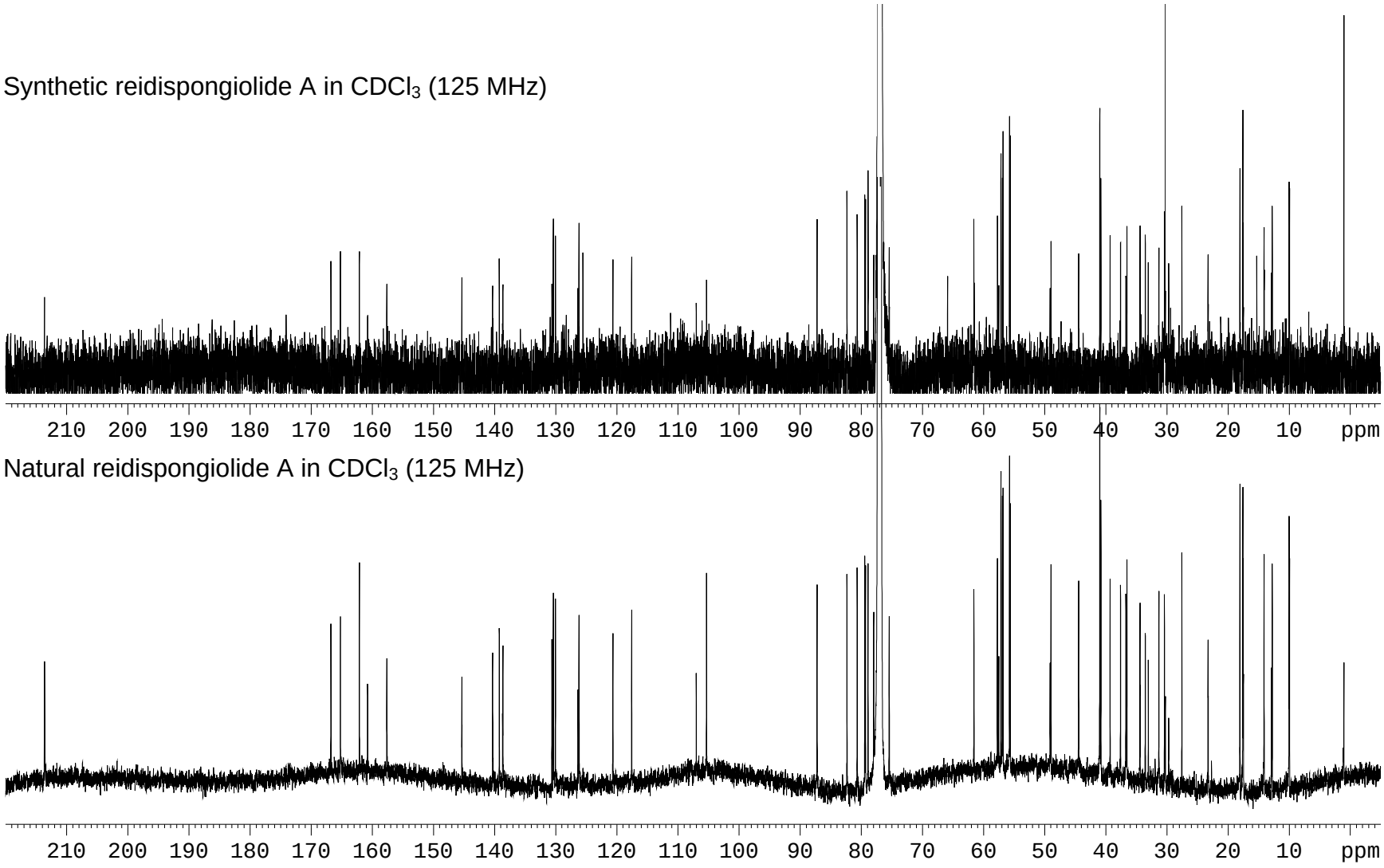
[a] Signals for minor conformer. The coupling constants are given in Hz and shown in parentheses. [1]D'Auria, M. V. et al. *Tetrahedron* **1994**, *16*, 4829. Data recorded at 500 MHz. [2]A natural sample of reidispongiolide A was kindly provided by Professor D'Auria. Data recorded at 500 MHz and chemical shifts for obscured resonances were assigned based upon the appropriate COSY data. [3]Data recorded at 500 MHz.

# $^{13}$C NMR data for natural and synthetic reidispongiolide A ($CDCl_3$)

| Carbon No. | natural reidispongiolide A[1] ($\delta_C$) | natural reidispongiolide A[2] ($\delta_C$) | synthetic reidispongiolide A[3] ($\delta_C$) |
|---|---|---|---|
| 1 | 166.7 | 166.76 | 166.76 |
| 2 | 120.5 | 120.61 | 120.61 |
| 3 | 140.2 | 140.30 | 140.30 |
| 4 | 126.1 | 126.16 | 126.16 |
| 5 | 145.5 | 145.33 | 145.33 |
| 6 | 44.5 | 44.42 | 44.42 |
| 7 | 76.9 | N.D. | N.D. |
| 8 | 40.8 | 40.97 | 40.97 |
| 9 | 157.6 | 157.60 | 157.59 |
| 10 | 31.2 | 31.29 | 31.28 |
| 11 | 79.3 | 79.42 | 79.42 |
| 12 | 39.2 | 39.28 | 39.27 |
| 13 | 77.8 | 77.94 | 77.94 |
| 14 | 33.4 | 33.52 | 33.52 |
| 15 | 79.2 | 79.29 | 79.29 |
| 16 | 129.9 | 130.02 | 130.02 |
| 17 | 139.2 | 139.21 | 139.22 |
| 18 | 37.5 | 37.57 | 37.57 |
| 19 | 80.6 | 80.66 | 80.65 |
| 20 | 36.6 | 36.70 | 36.70 |
| 21 | 78.8 | 78.88 | 78.88 |
| 22 | 130.3 | 130.37 | 130.38 |
| 23 | 138.6 | 138.62 | 138.63 |
| 24 | 40.6 | 40.79 | 40.79 |
| 25 | 75.3 | 75.41 | 75.41 |
| 26 | 36.4 | 36.52 | 36.52 |
| 27 | 87.1 | 87.21 | 87.21 |
| 28 | 34.3 | 34.39 (34.36)[a] | 34.39 (34.35)[a] |
| 29 | 23.2 | 23.25 (23.22)[a] | 23.25 (23.22)[a] |
| 30 | 40.8 | 40.97 | 40.97 |
| 31 | 213.5 | 213.60 | 213.60 |
| 32 | 49.0 (48.8)[a] | 48.94 (49.09)[a] | 48.94 (49.09)[a] |
| 33 | 82.2 | 82.33 | 82.33 |
| 34 | 30.6 (30.3)[a] | 30.38 (30.23)[a] | 30.38 (30.22)[a] |
| 35 | 105.4 (107.1)[a] | 105.31 (106.98)[a] | 105.31 (106.98)[a] |
| 36 | 130.5 (126.3)[a] | 130.61 (126.34)[a] | 130.61 (126.34)[a] |
| 37 | 162.1 (160.8)[a] | 162.10 (160.75)[a] | 162.10 (160.75)[a] |
| 38 (5-Me) | 17.9 | 18.03 | 18.03 |
| 39 | 117.4 | 117.55 | 117.55 |
| 40 | 164.0 | 165.20 | 165.20 |
| 41 (12-Me) | 9.8 | 9.92 | 9.92 |
| 42 (18-Me) | 14.0 | 14.08 | 14.07 |
| 43 (24-Me) | 17.4 | 17.49 (17.46)[a] | 17.49 |
| 44 (26-Me) | 9.9 | 9.99 | 9.99 |
| 45(28-Me) | 17.5 | 17.56 | 17.56 |
| 46 (32-Me) | 12.7 (12.8)[a] | 12.75 (12.88)[a] | 12.75 (12.88)[a] |
| 47 (N-Me) | 27.5 (32.9)[a] | 27.54 (33.02)[a] | 27.54 (33.02)[a] |
| 7-OMe | 56.8 | 56.80 | 56.80 |
| 13-OMe | 55.5 | 55.61 | 55.61 |
| 15-OMe | 55.6 | 55.74 | 55.74 |
| 19-OMe | 57.4 | 57.14 | 57.14 |
| 21-OMe | 57.0 | 56.91 | 56.91 |
| 27-OMe | 61.5 | 61.56 (61.53)[a] | 61.57 (61.53)[a] |
| 33-OMe | 57.6 | 57.71 (57.49)[a] | 57.71 (57.50)[a] |

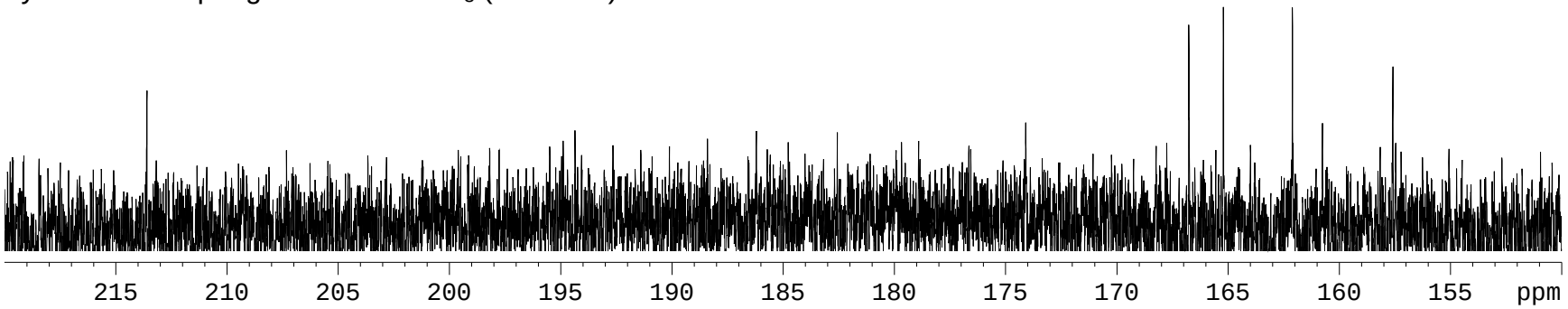
[a] Signals for minor conformer shown in parentheses. [1]D'Auria, M. V. et al. *Tetrahedron* **1994**, *16*, 4829. Data recorded at 125 MHz. [2]A natural sample of reidispongiolide A was kindly provided by Professor D'Auria. Data recorded at 125 MHz. [3]Data recorded at 125 MHz.

# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

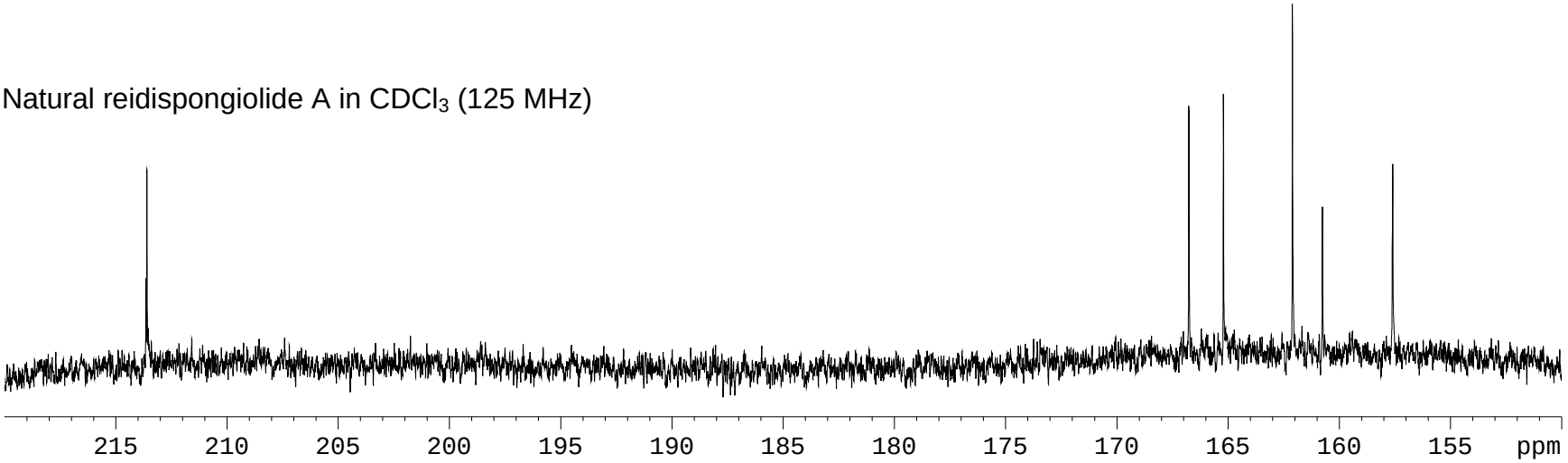


# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

Synthetic reidispongiolide A in $CDCl_3$ (125 MHz)

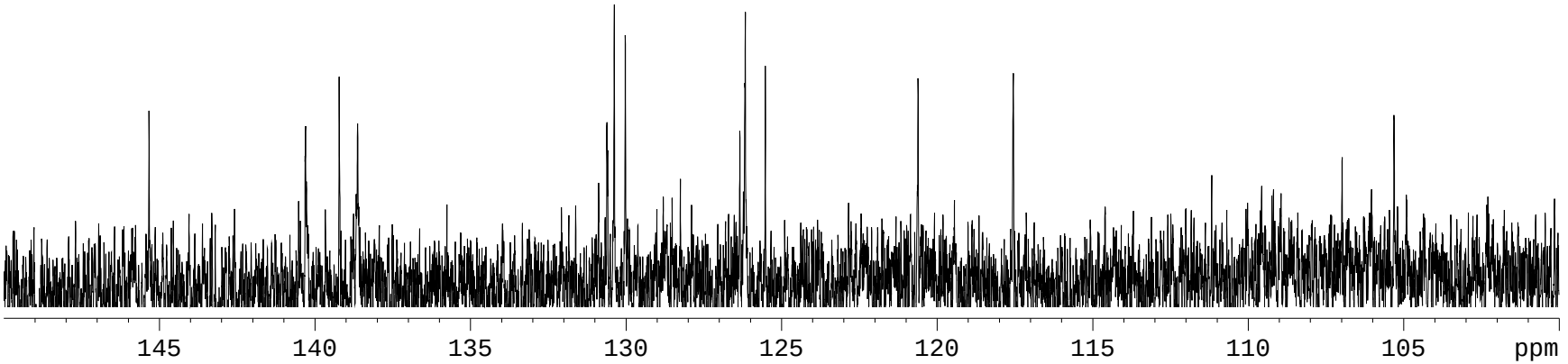



Natural reidispongiolide A in $CDCl_3$ (125 MHz)

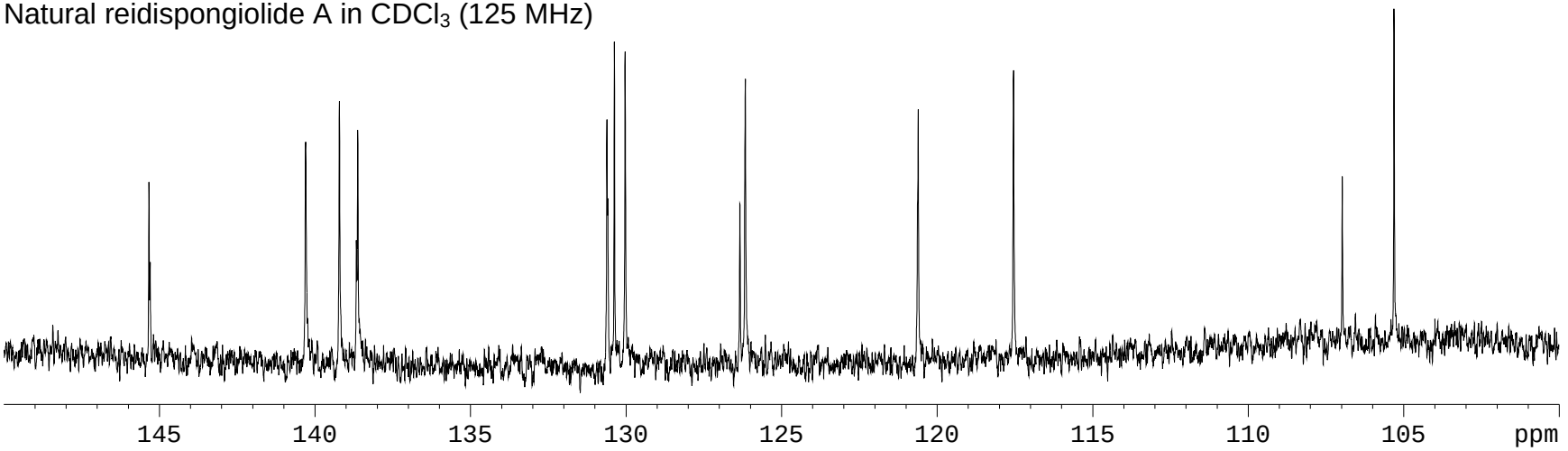


# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

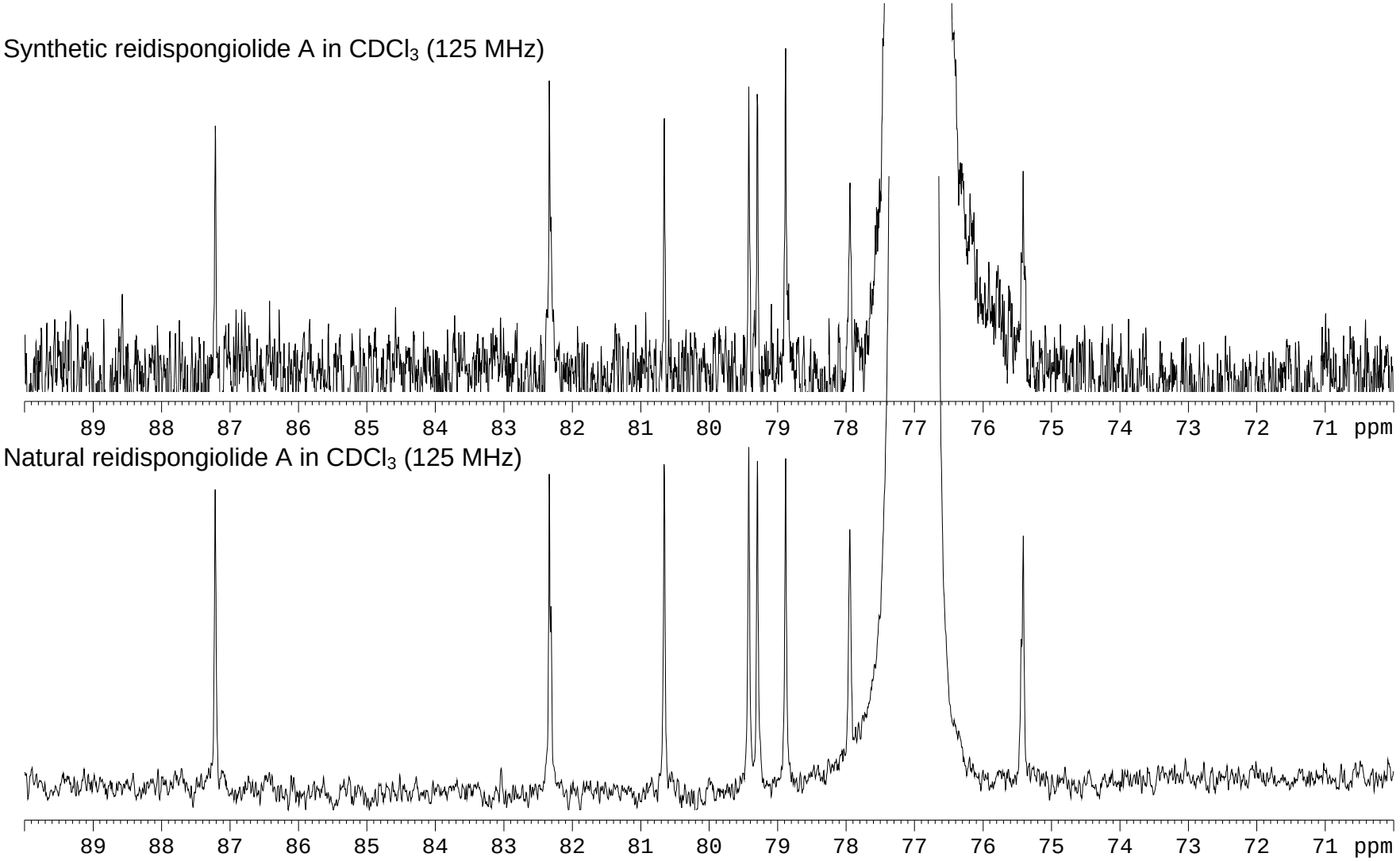
Synthetic reidispongiolide A in $CDCl_3$ (125 MHz)




Natural reidispongiolide A in $CDCl_3$ (125 MHz)

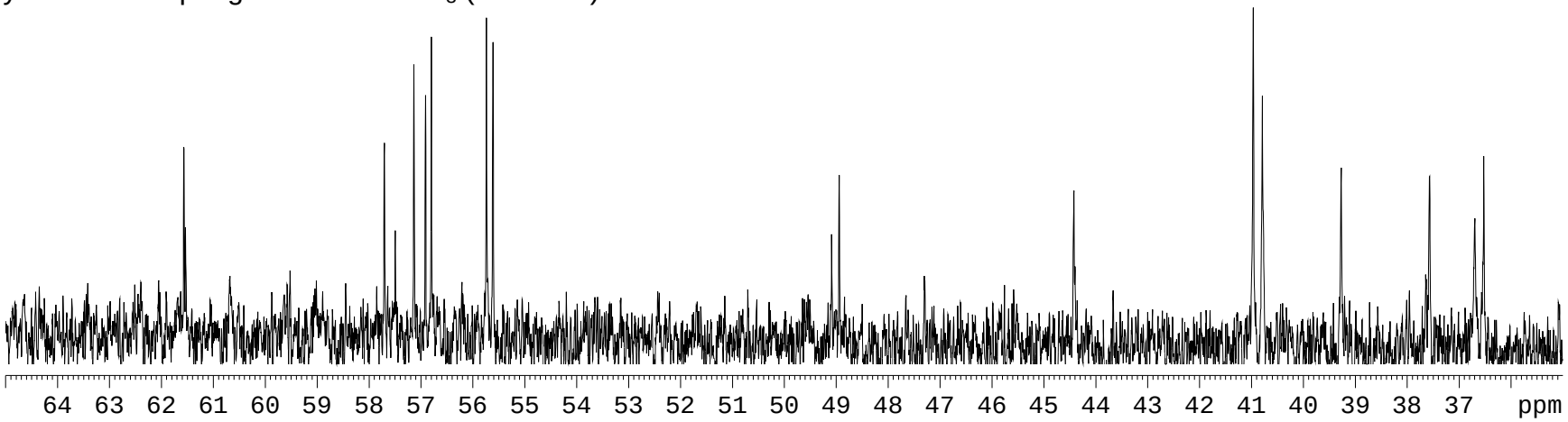


# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

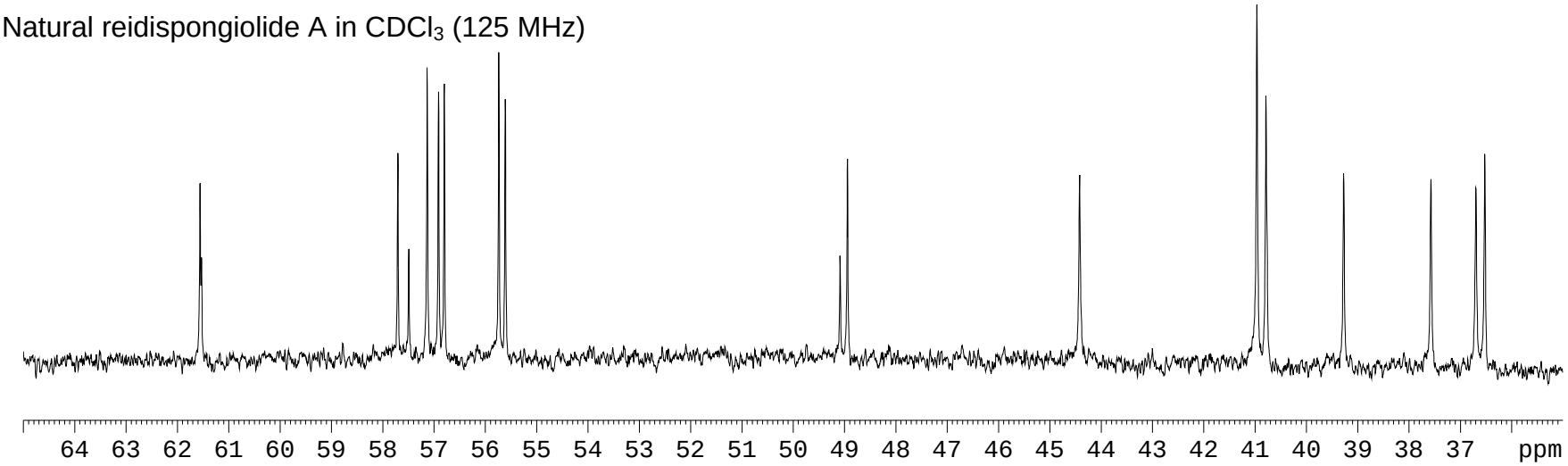


# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

Synthetic reidispongiolide A in $CDCl_3$ (125 MHz)

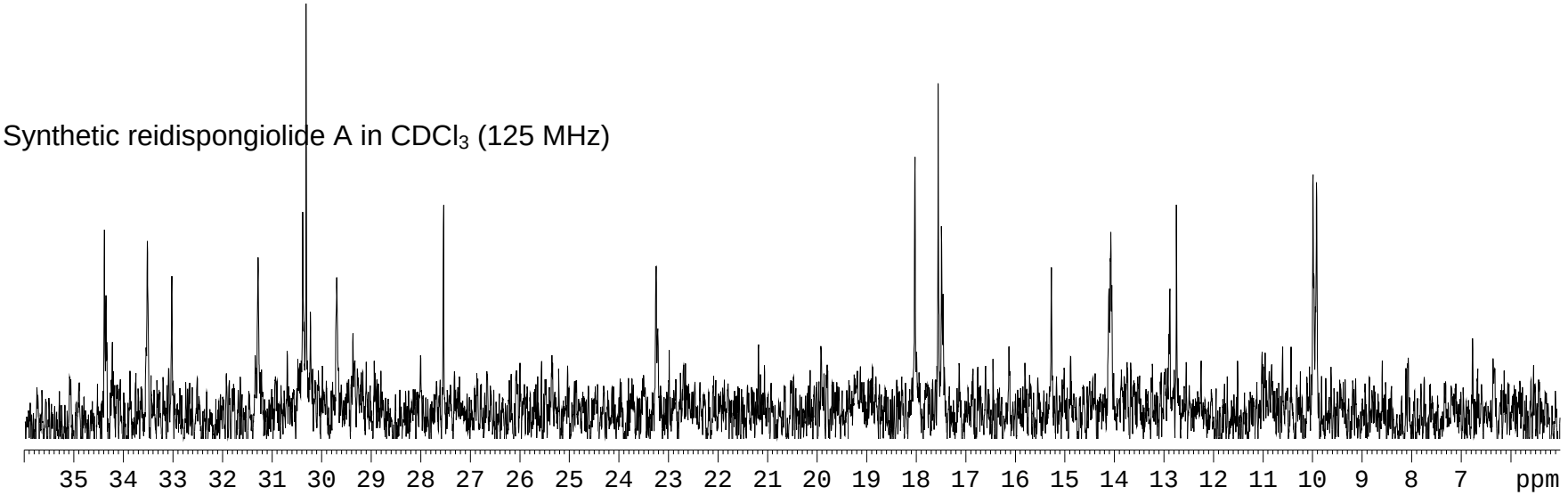



Natural reidispongiolide A in $CDCl_3$ (125 MHz)

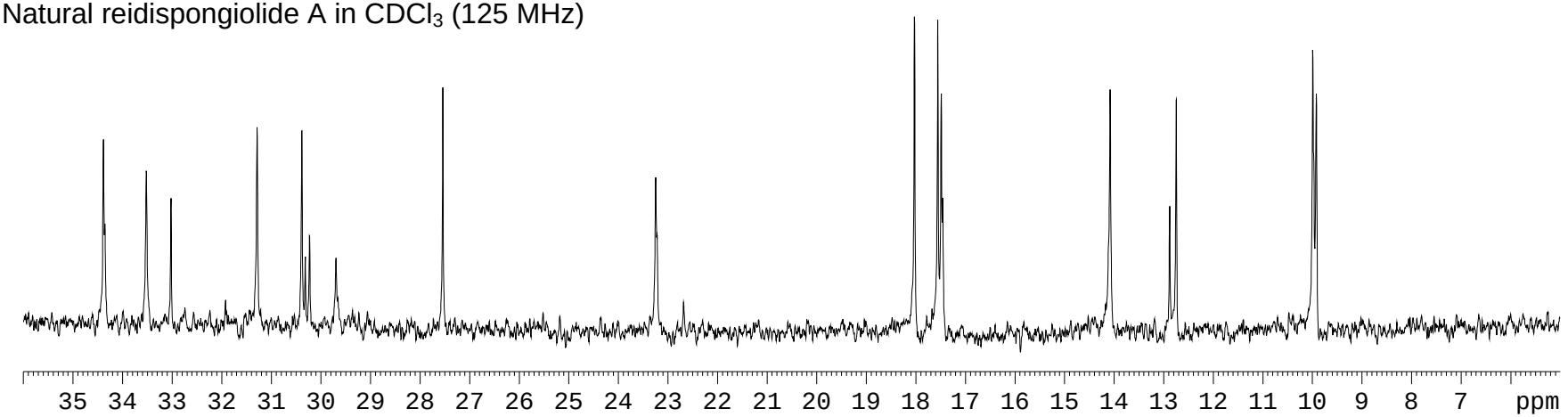


# $^{13}$C NMR spectra for natural and synthetic reidispongiolide A

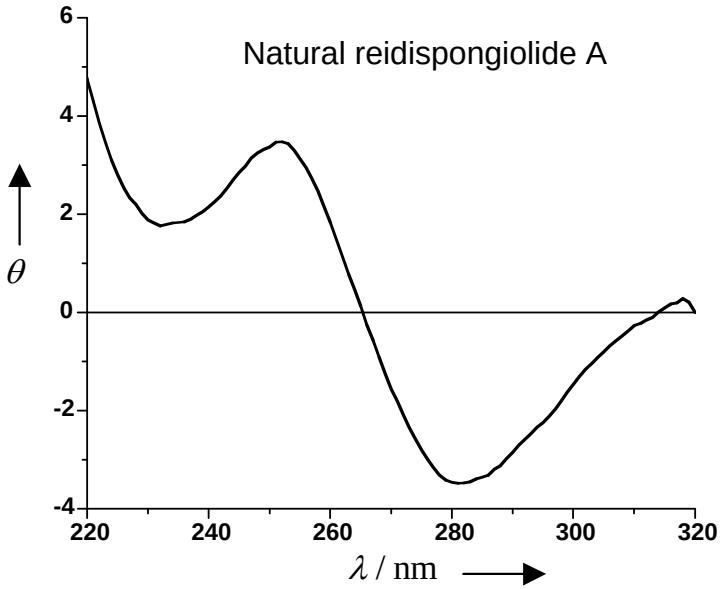
Synthetic reidispongiolide A in $CDCl_3$ (125 MHz)



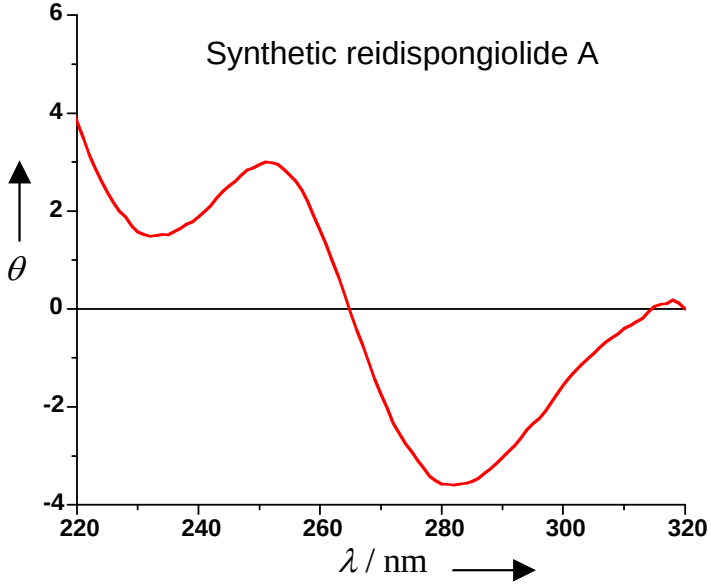

Natural reidispongiolide A in $CDCl_3$ (125 MHz)



# CD spectra for natural and synthetic reidispongiolide A




c = 0.000355 M in MeOH

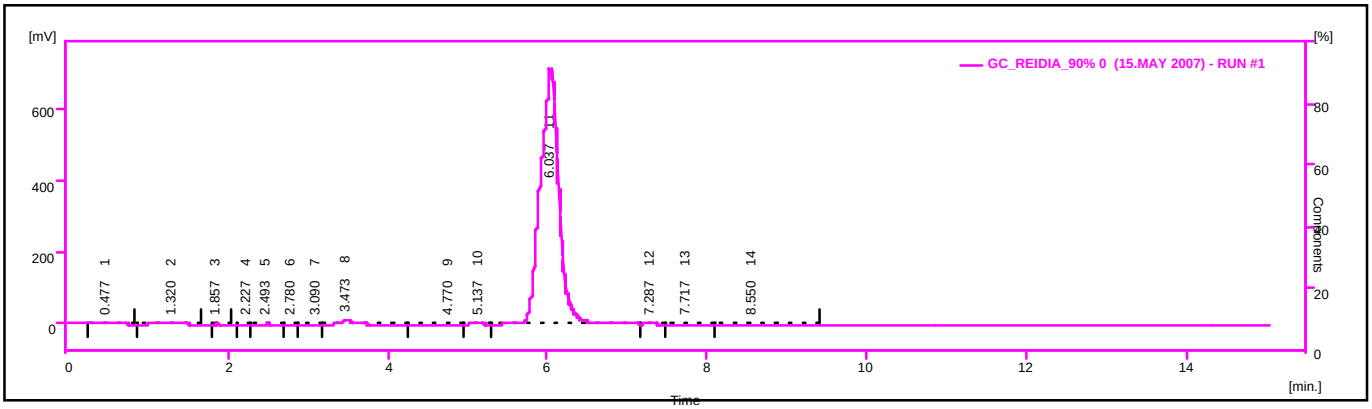



c = 0.000417 M in MeOH

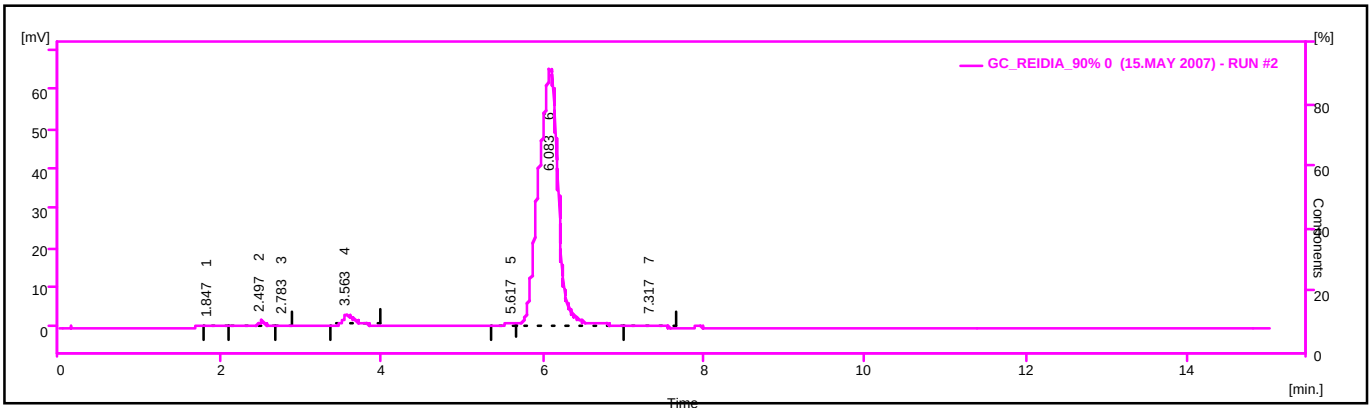
# HPLC chromatograms of synthetic and natural reidispongiolide A

Column: Jones Chromatography® Hypersil (reversed phase C-18) ODS 5μ, 250 x 4.6 mm
Flow rate: 1 mL/min
Solvent: 10% $H_2O$ in MeOH

Natural reidispongiolide A




Synthetic reidispongiolide A




Combined natural and synthetic reidispongiolide A