Supporting Information for

A Flexible Approach for the Asymmetric Syntheses of Hyacinthacines A_2 and A_3 and Structural Confirmation of Hyacinthacine A_3

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Contents (27 pages):

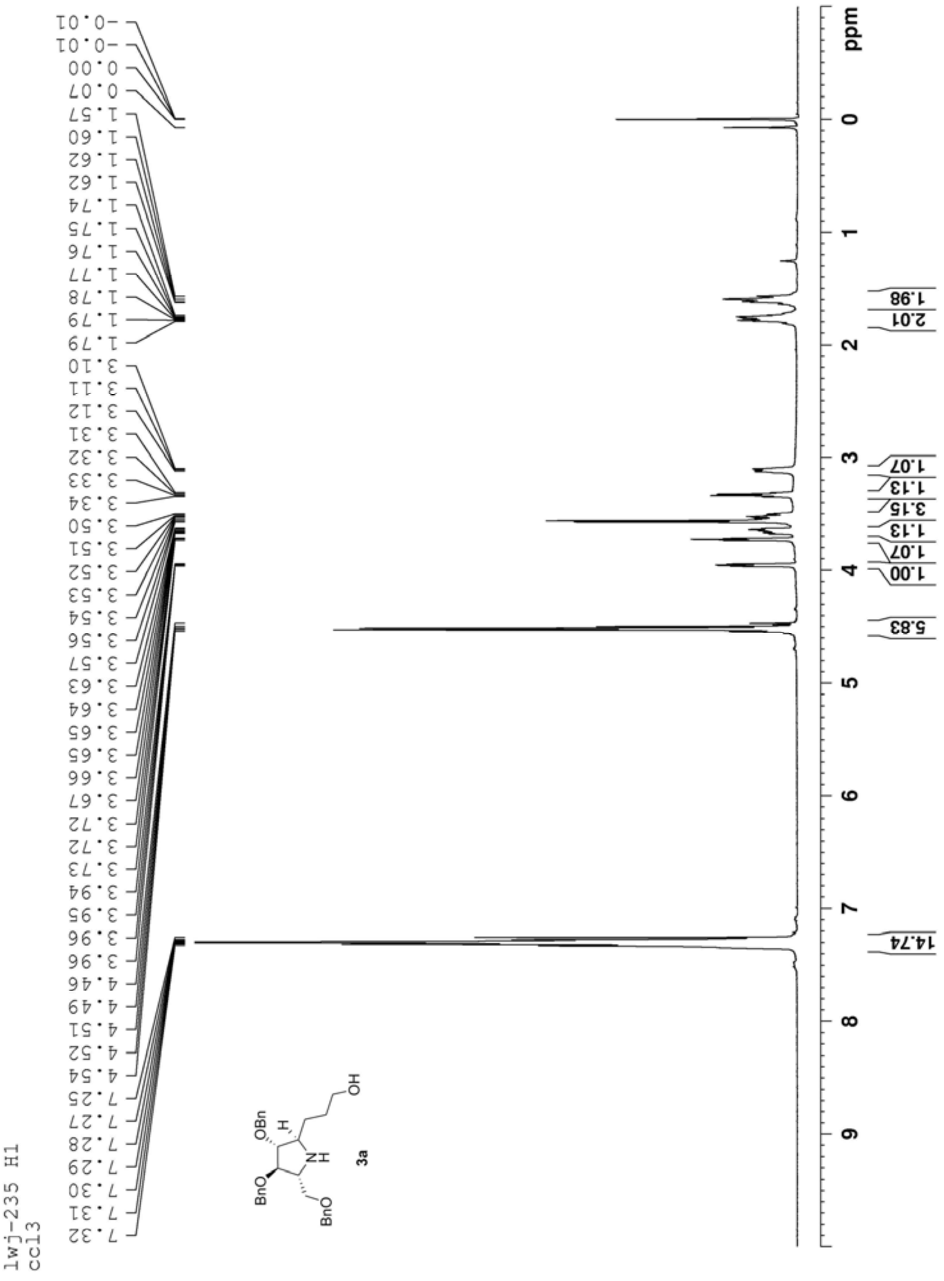
- ^{1}H and ^{13}C NMR spectra of compounds **3a**, **10**, **1**, **13a**, **13b**, **14**, **6**, **15a** (pp. 2-17) and **2** (pp. 21-22).
- Compared ^{1}H and ^{13}C NMR data of natural and synthetic hyacinthacine A_3. (pp. 19-20)
- Compared ^{1}H and ^{13}C NMR data in D_2O and in CD_3OD of hyacinthacine $\mathbf{A_3}$ (data from this work). (pp.20-21)
- Structural verification and assignment for compound **2**. (pp. 22-24)
- ^{1}H and ^{13}C NMR spectra of natural hyacinthacine A_3 provided by Asano, the mixture of synthetic hyacinthacine A_3 (**2**) and natural hyacinthacine A_3 provided by Asano (pp. 24-27).
- GC-MS results of the mixture of the natural hyacinthacine A_3 and synthetic compound (pp. 27)

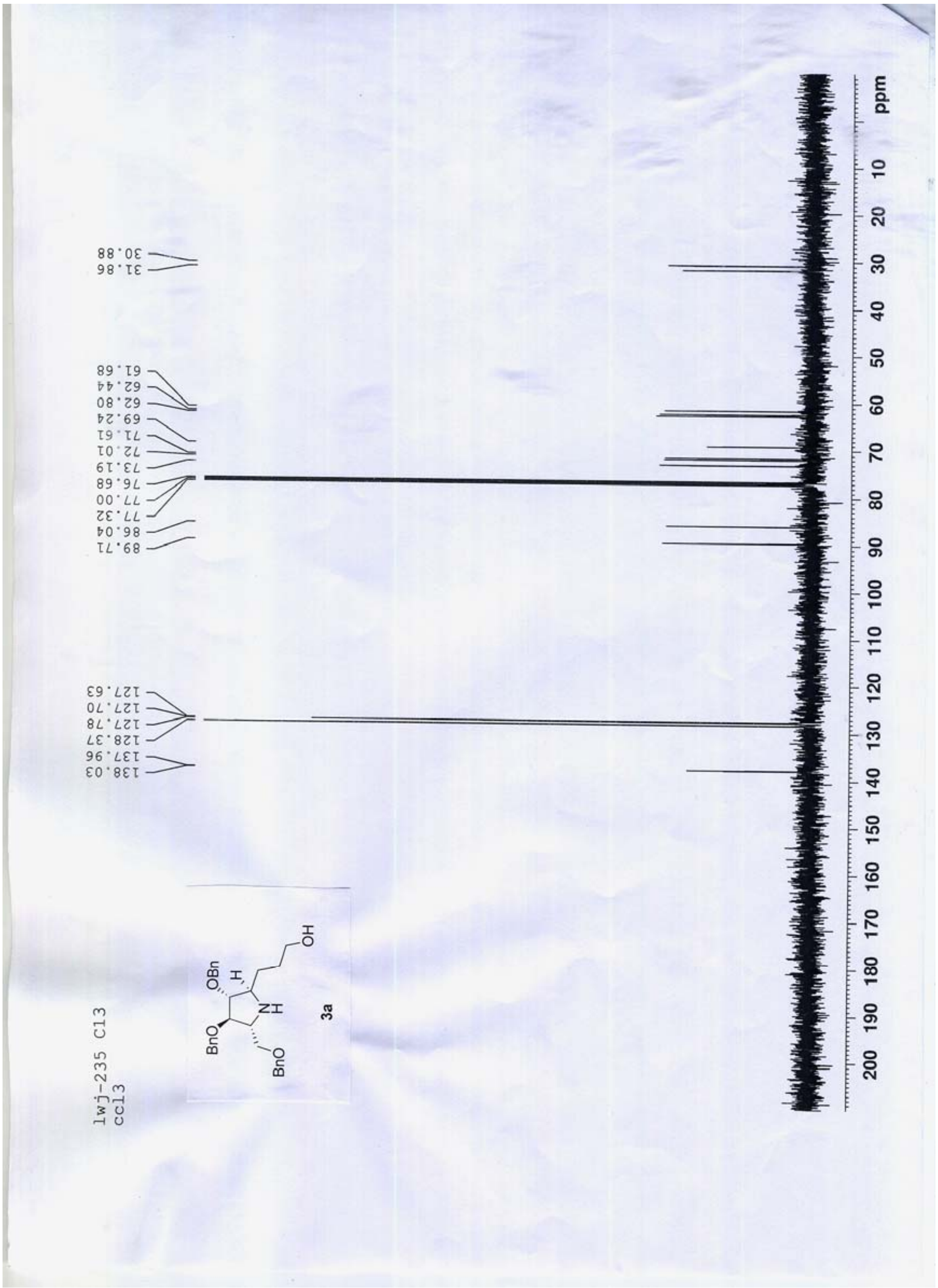
General Methods Optical rotations were recorded on a Perkin-Elmer 341 automatic polarimeter. NMR spectra were recorded in $CDCl_3$ or D_2O (^{1}H at 400, 500 or 600 MHz and ^{13}C at 100, 125 MHz) on Bruker spectrometer. Chemical shifts are expressed in parts per million (δ) relative to internal Me_4Si (in $CDCl_3$) or TSP (trimethylsilyl-2,2,3,3-tetradeuteropropionic acid, sodium salt) (in D_2O). IR spectra were recorded on a Nicolet Avatar 360 RT-IR spectrophotometer. Mass spectra were recorded by Bruker Dalton Esquire 3000 plus and Finnigan Mat-LCQ (ESI direct injection), HRFABMS spectra were recorded by a Bruker APEX-FTMS apparatus. Elemental analyses were performed using a Vario RL analyzer. Melting points were determined on a Yanaco MP-500 melting point apparatus and are uncorrected.

In the GC-MS analyses, the mixture of the natural hyacinthacine A_3 and synthetic compound were dried and silylated at 20 °C for 60 min using 100 μL of Sigma Sil-A [HMDS (hexamethyldisilazane)/ TMSCl (trimethylchlorosilane) in pyridine (3:1:9)] per milligram of sample. A 30 m × 0.25 mm HP-5MS (film thickness, 0.25 μm) capillary column (SGE) column was used. The chromatograph was performed with a 25 min temperature program ran from 160 to

250 °C with an initial rate of increase of 20 °C/ min and then held at 250 °C. The mass spectrometer used is an Agilent 5975C set at 70 eV with a mass range of 45–500 amu.

Tetrahydrofuran was distilled prior to use from sodium benzophenone ketyl. Methylene chloride was distilled from phosphorus pentoxide. Dimethylformamide was distilled from calcium hydride. Silica gel (zhifu, 300-400 mesh) from Yantai silica gel factory (China) was used for column chromatography, eluting (unless otherwise stated) with ethyl acetate/petroleum ether (PE) (60-90 °C) mixture.

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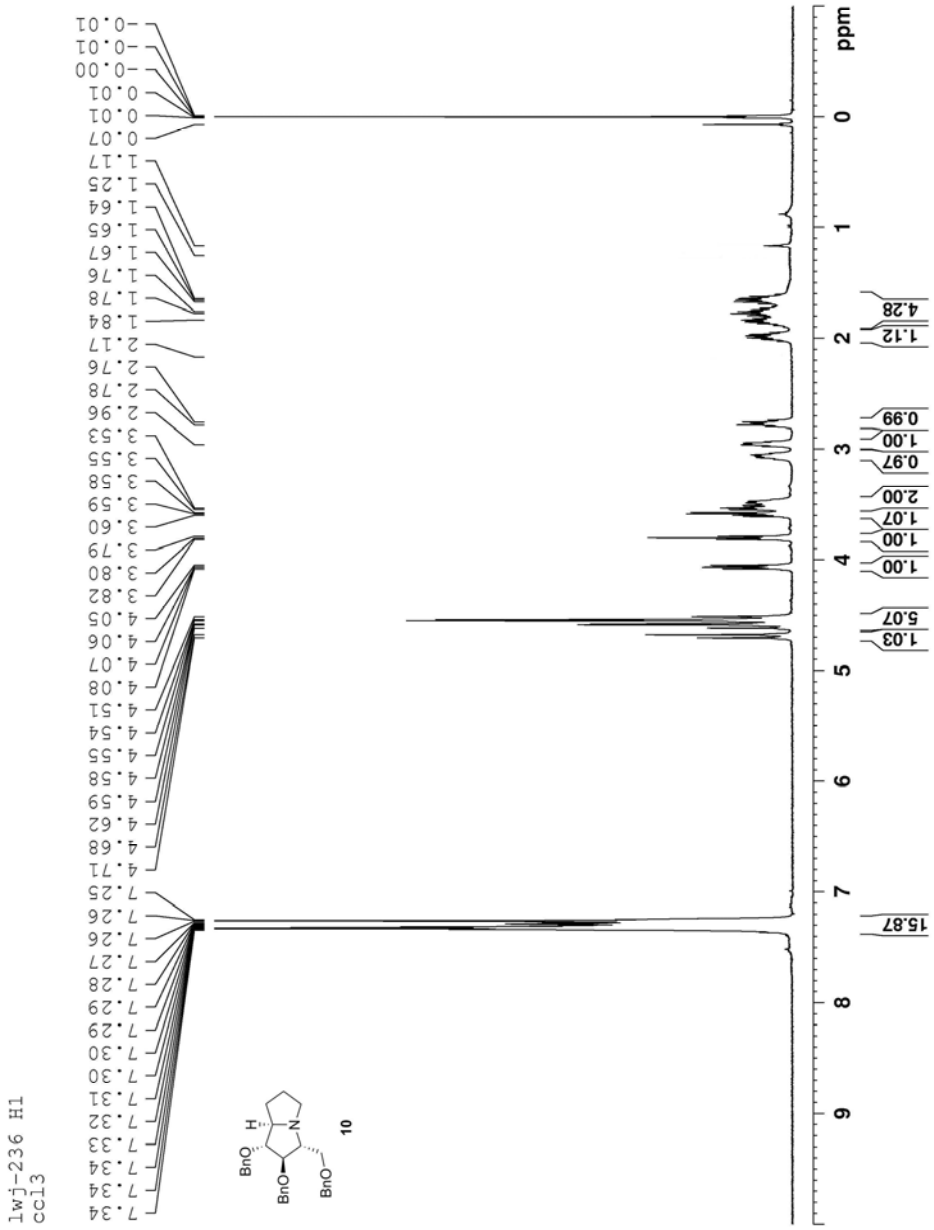
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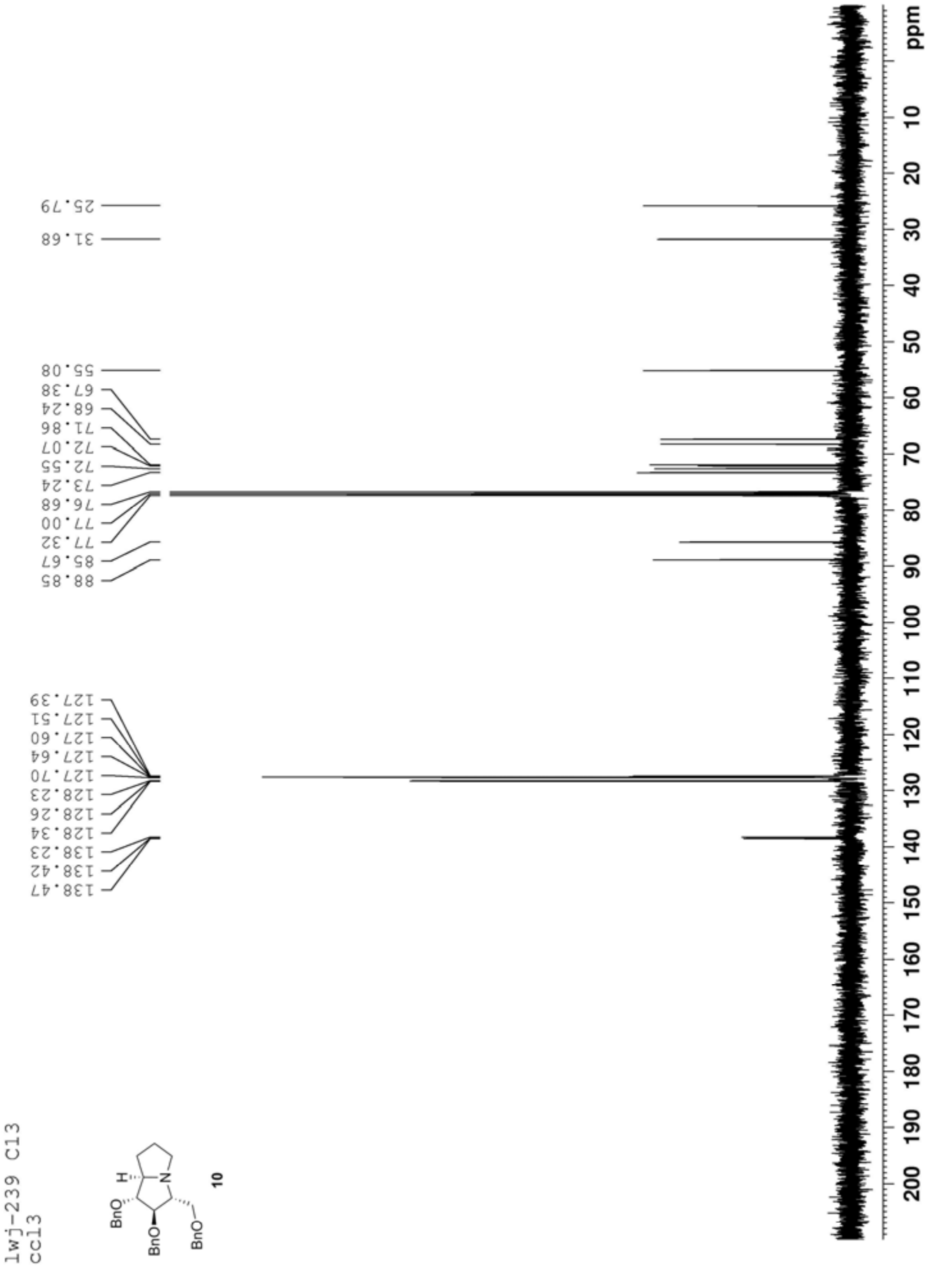
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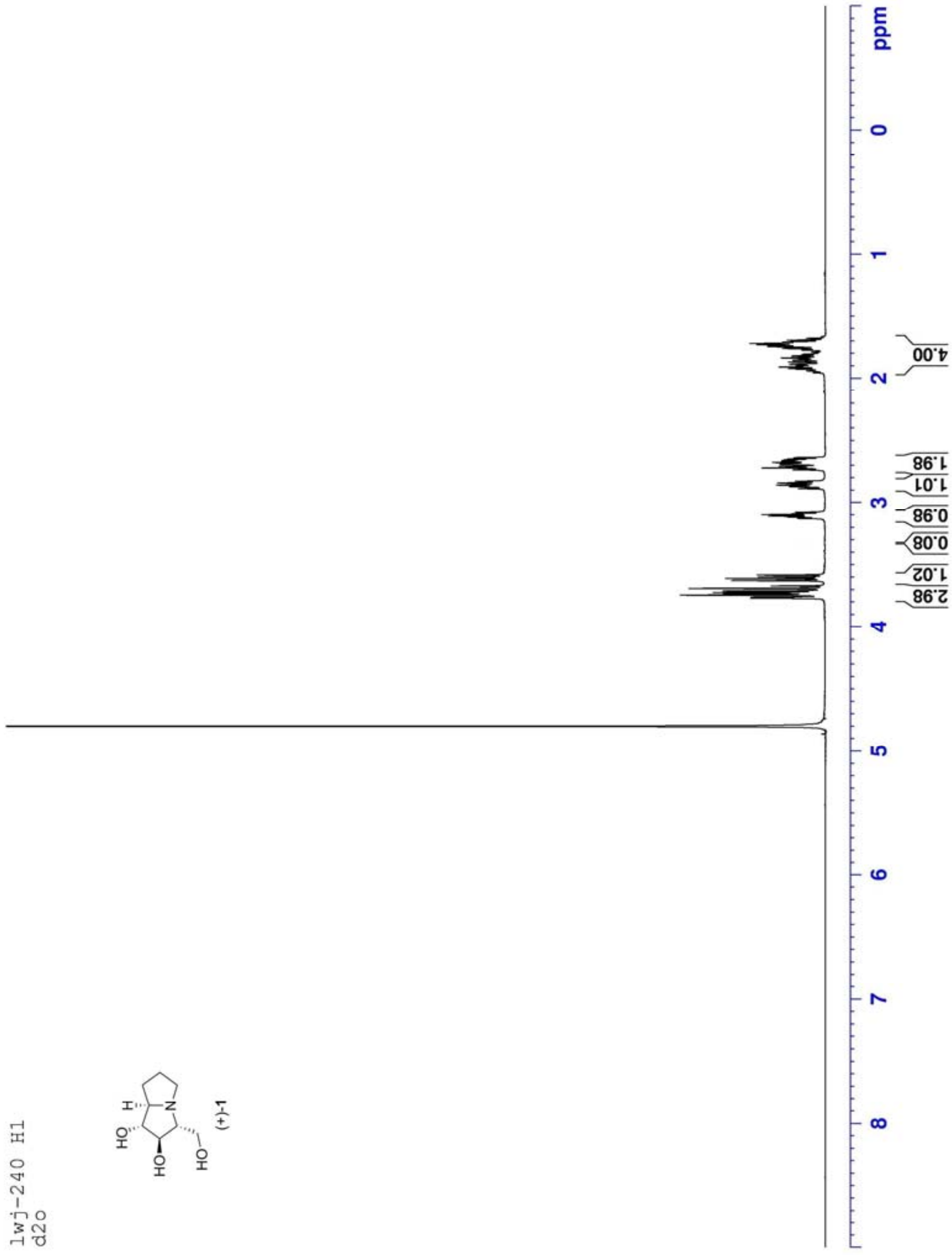
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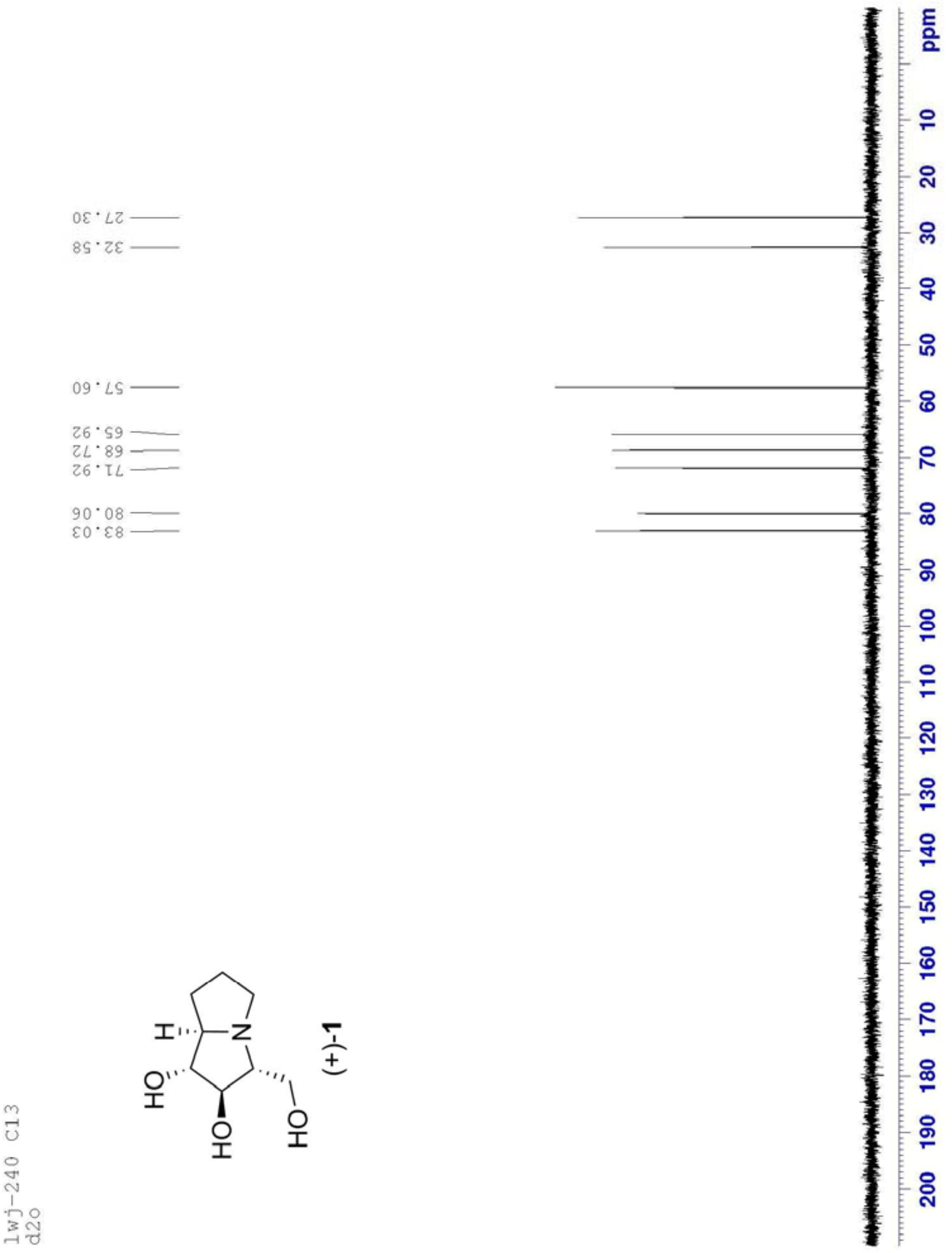
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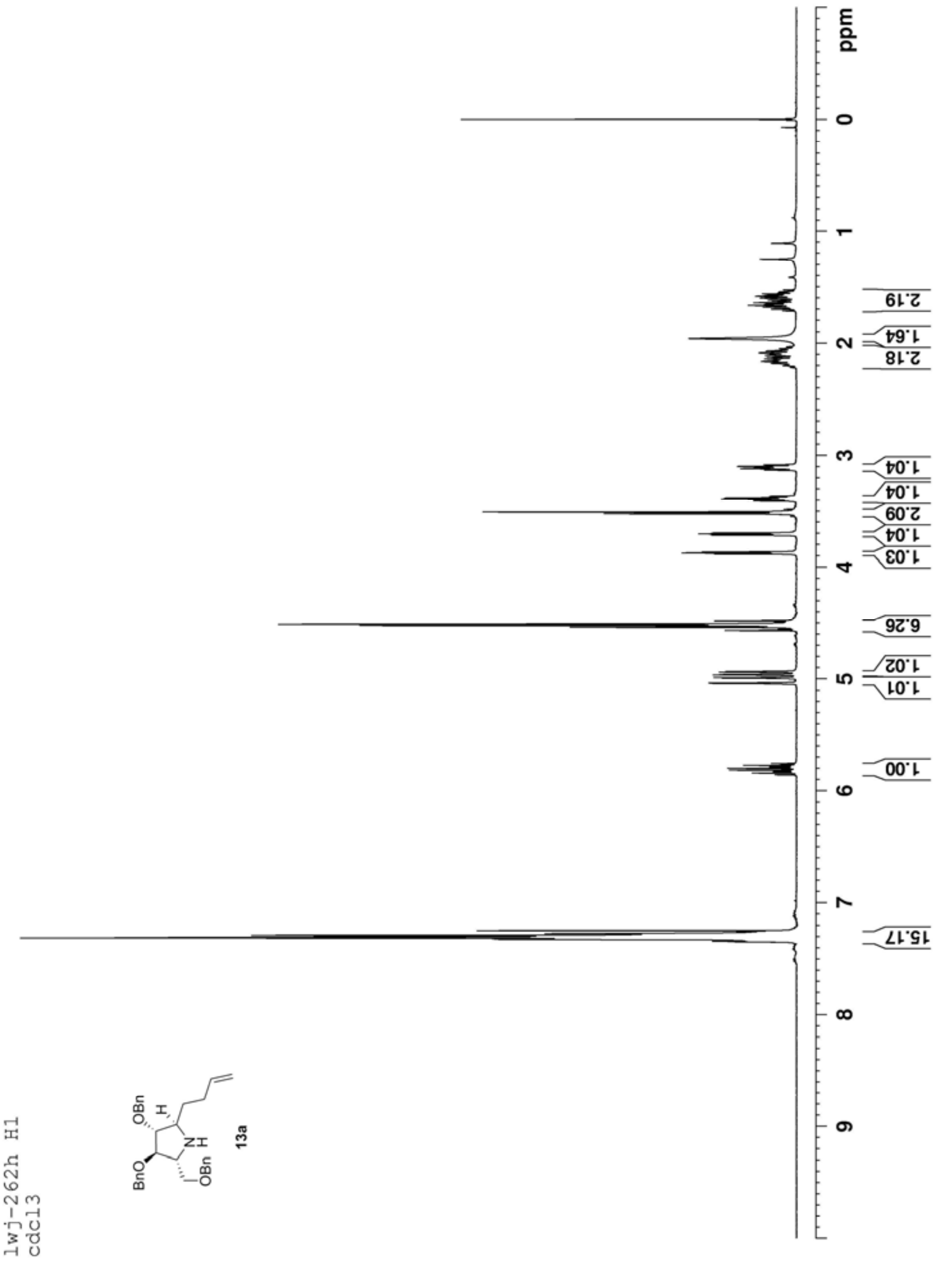
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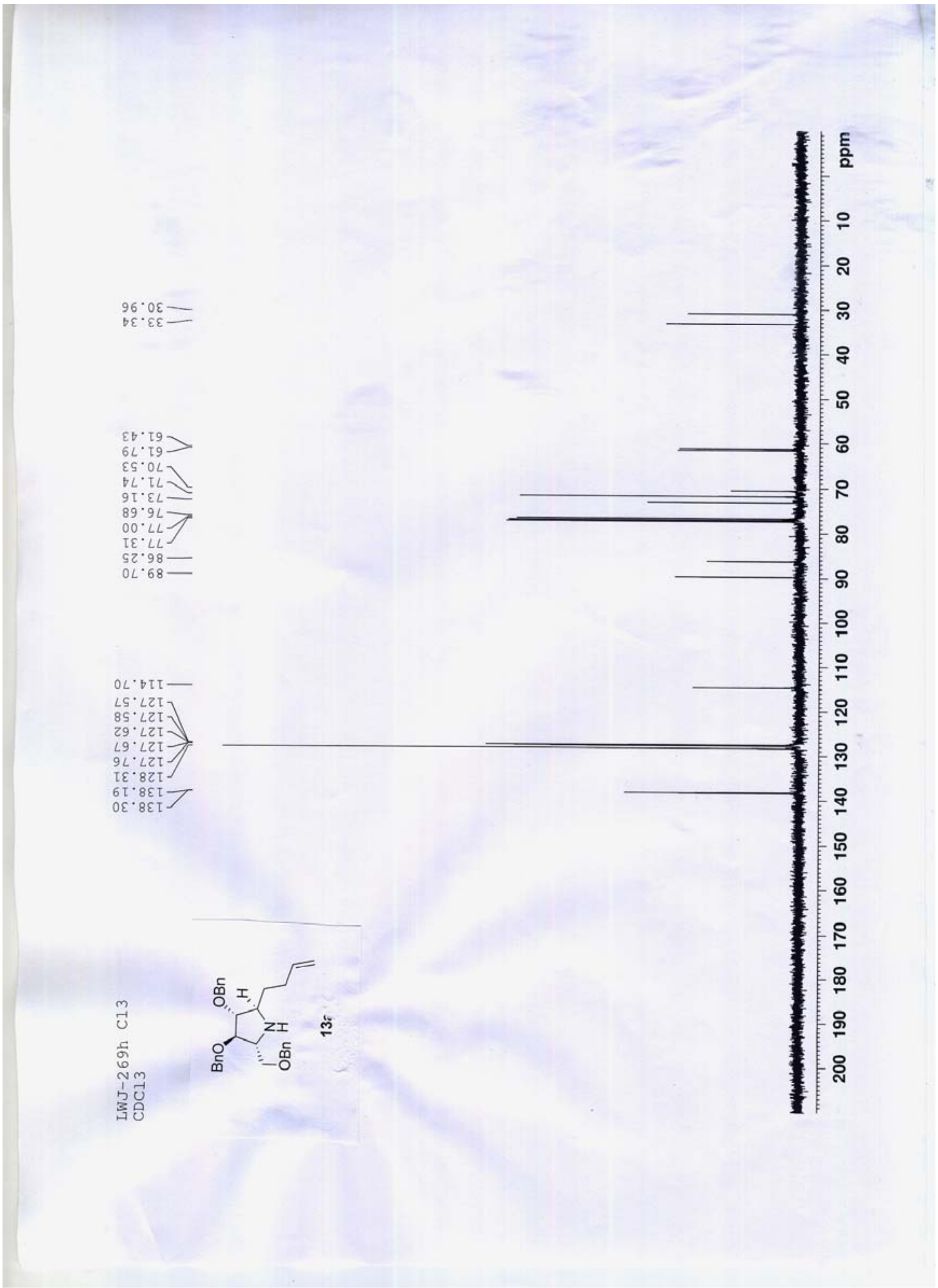
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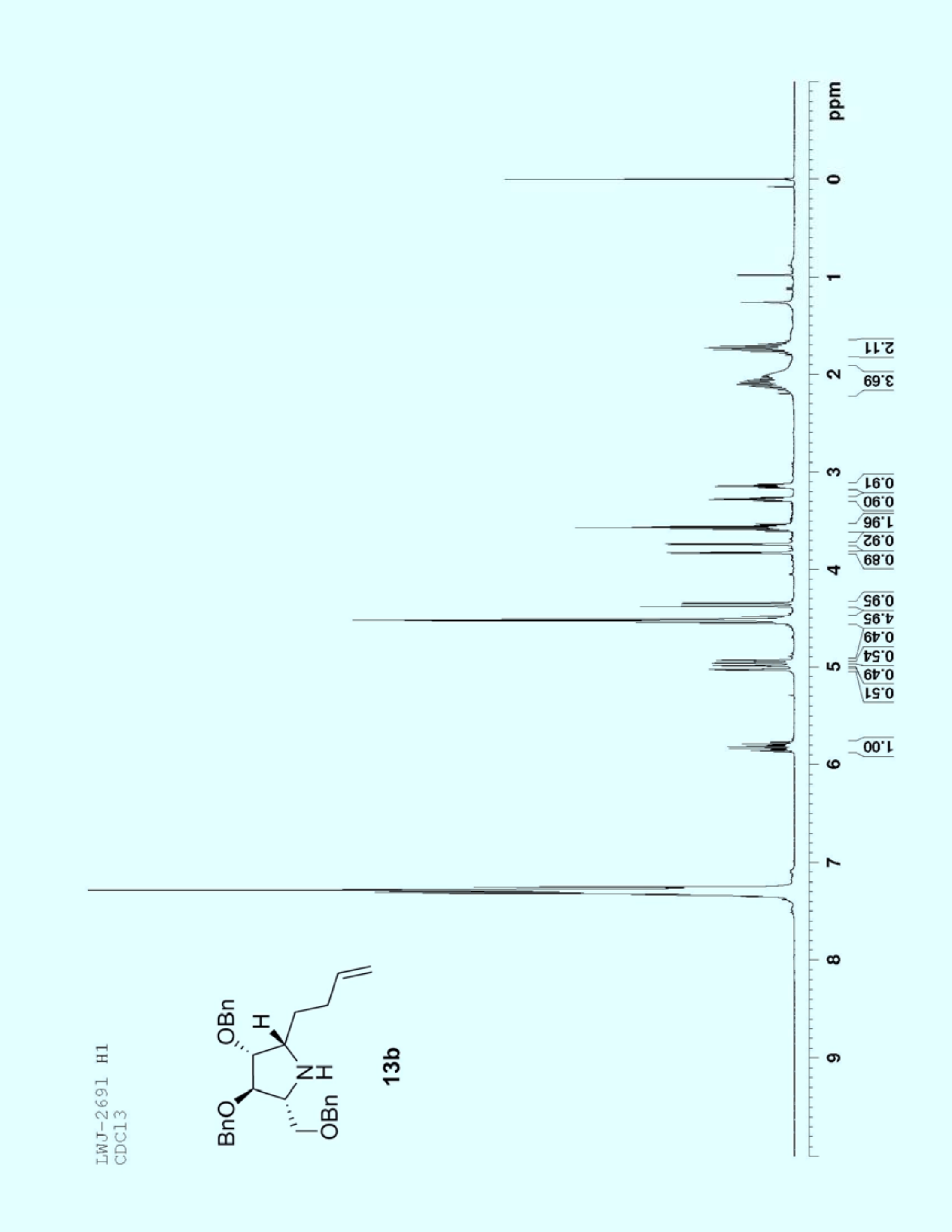
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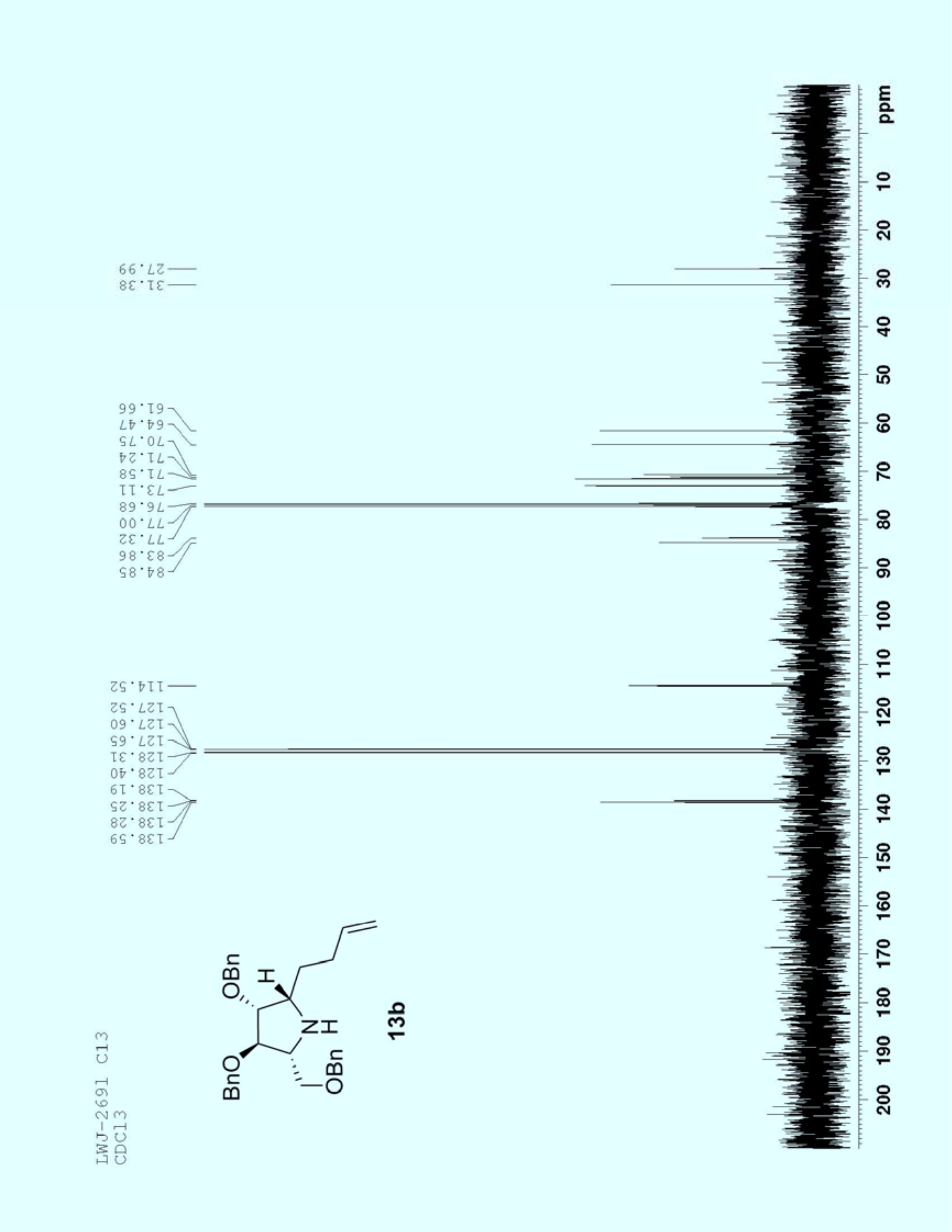
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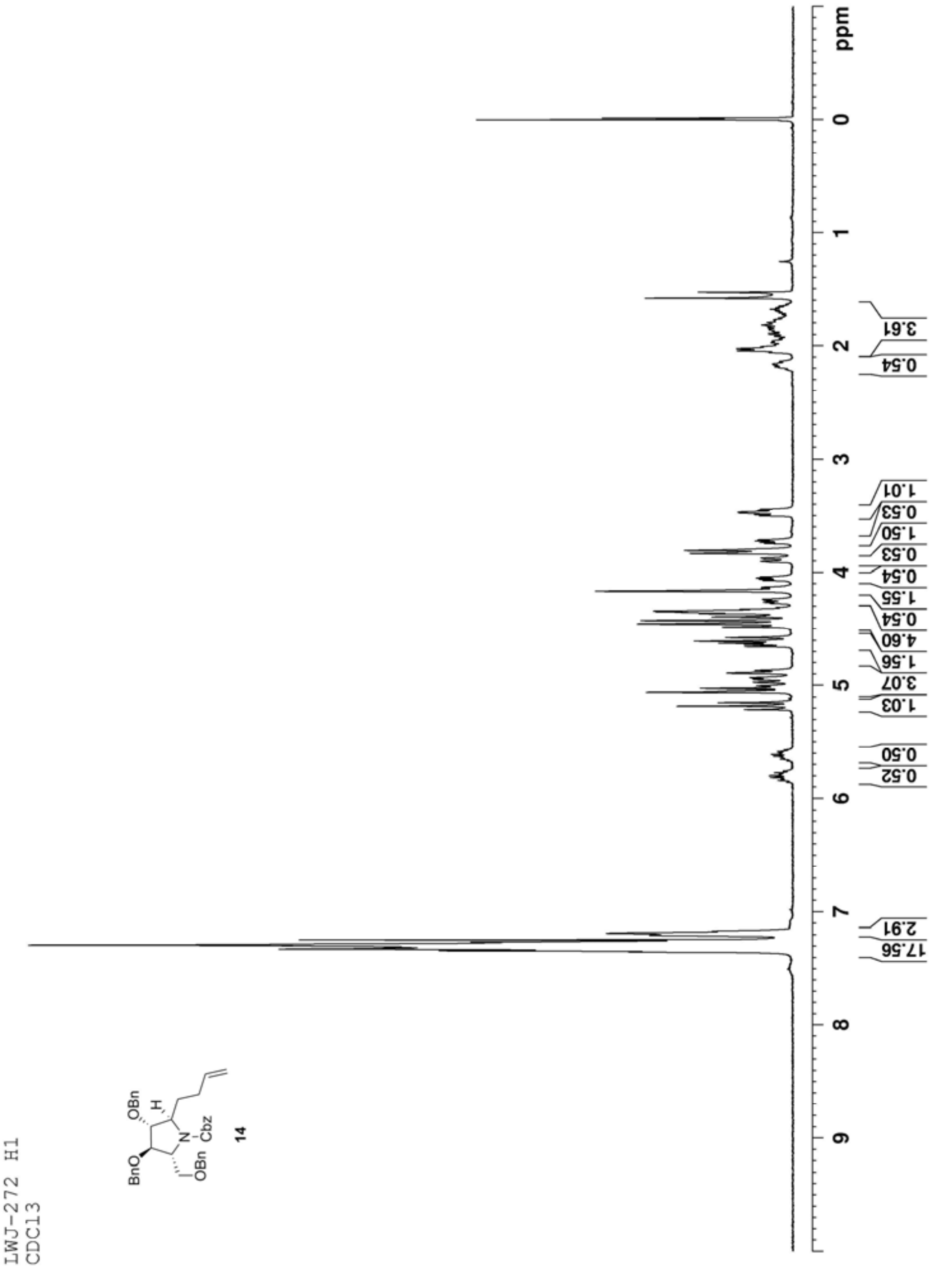
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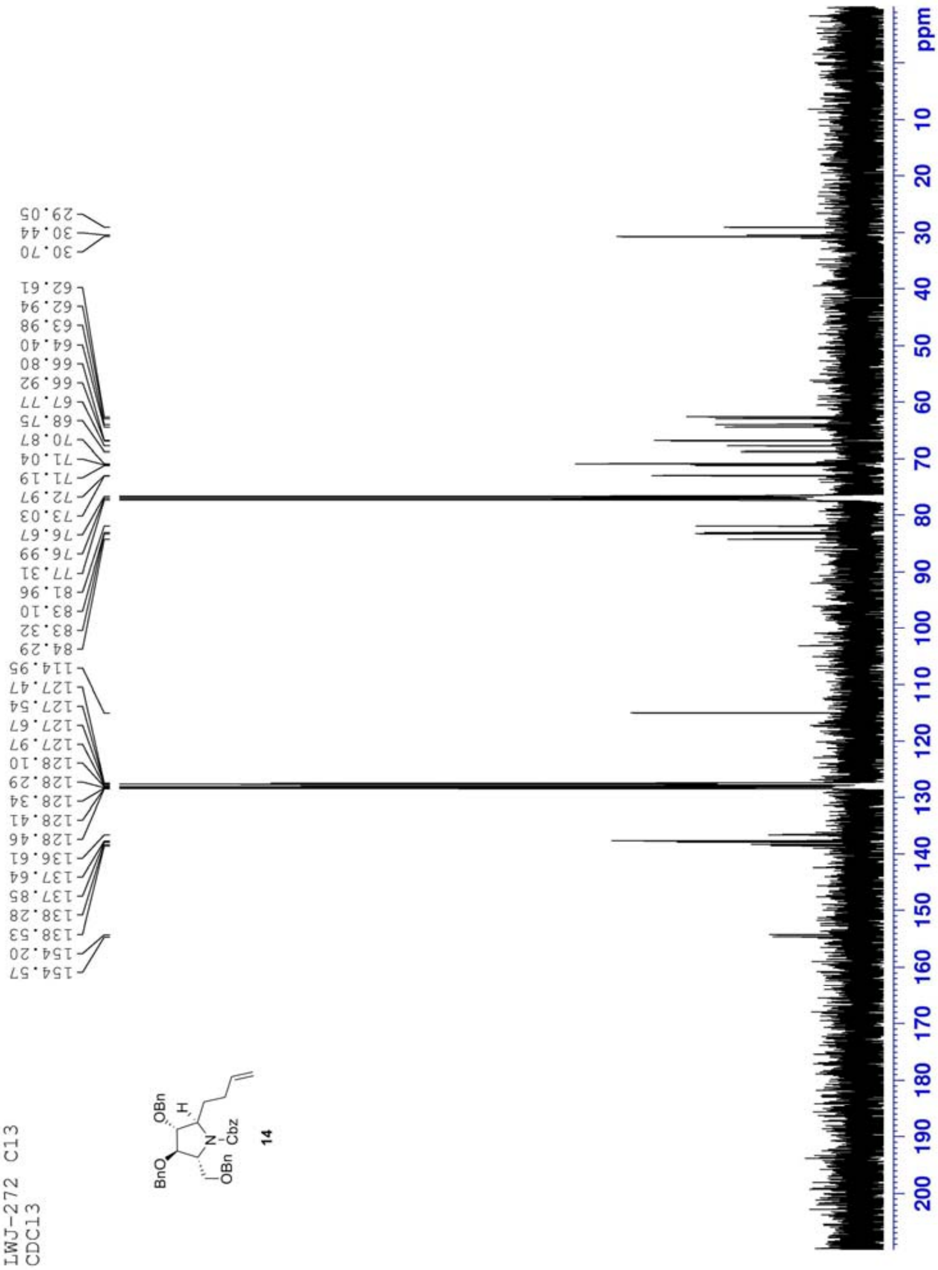
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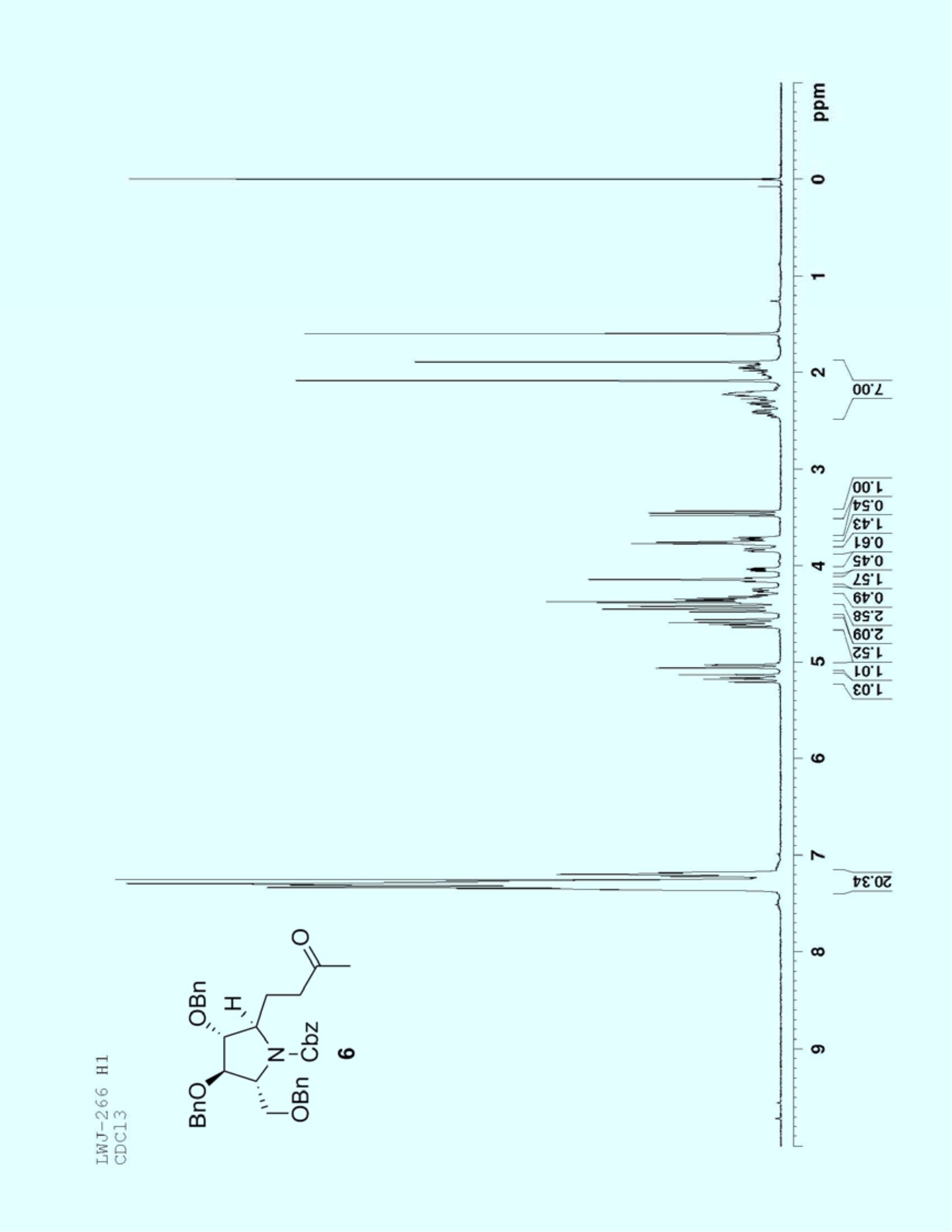
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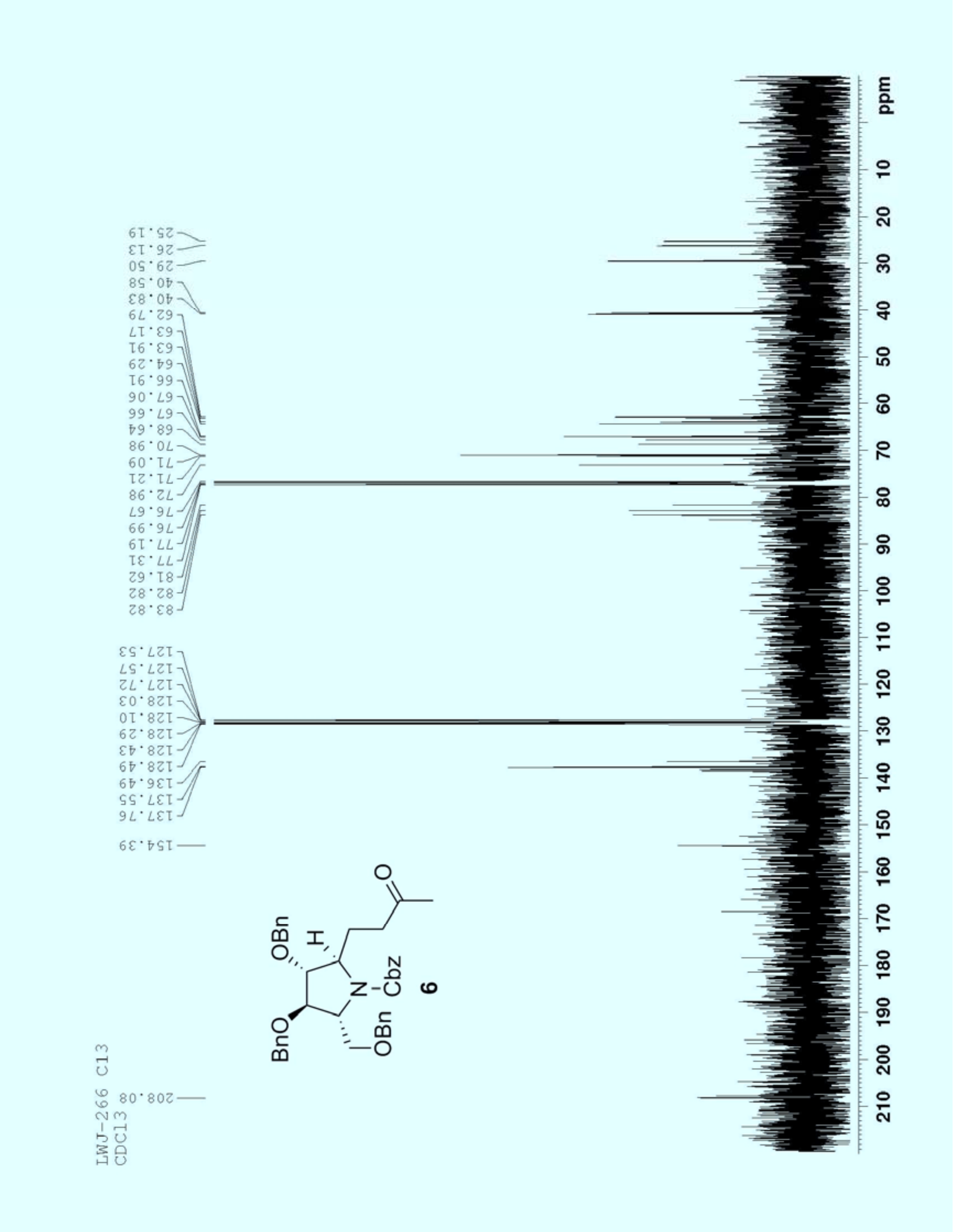
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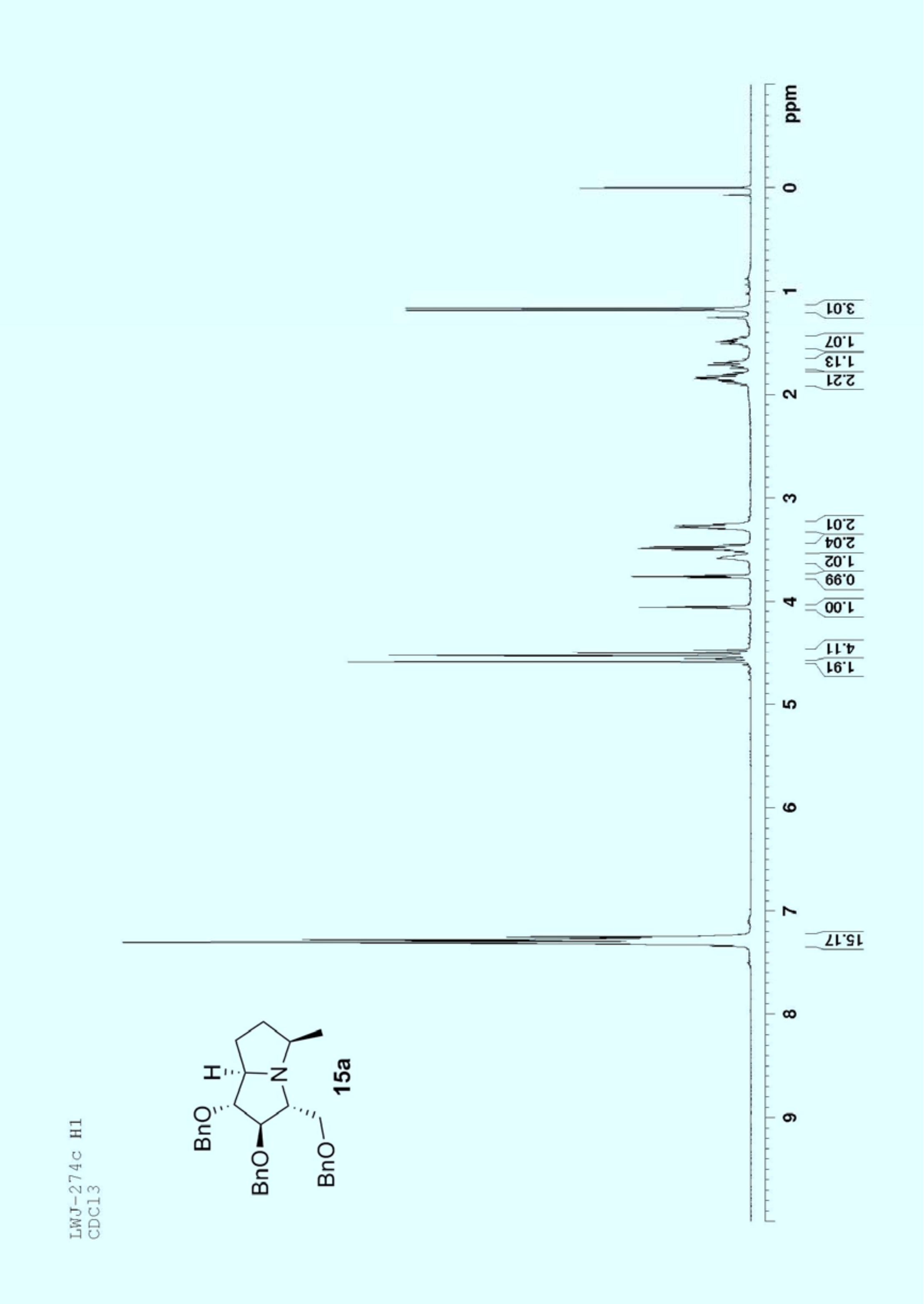
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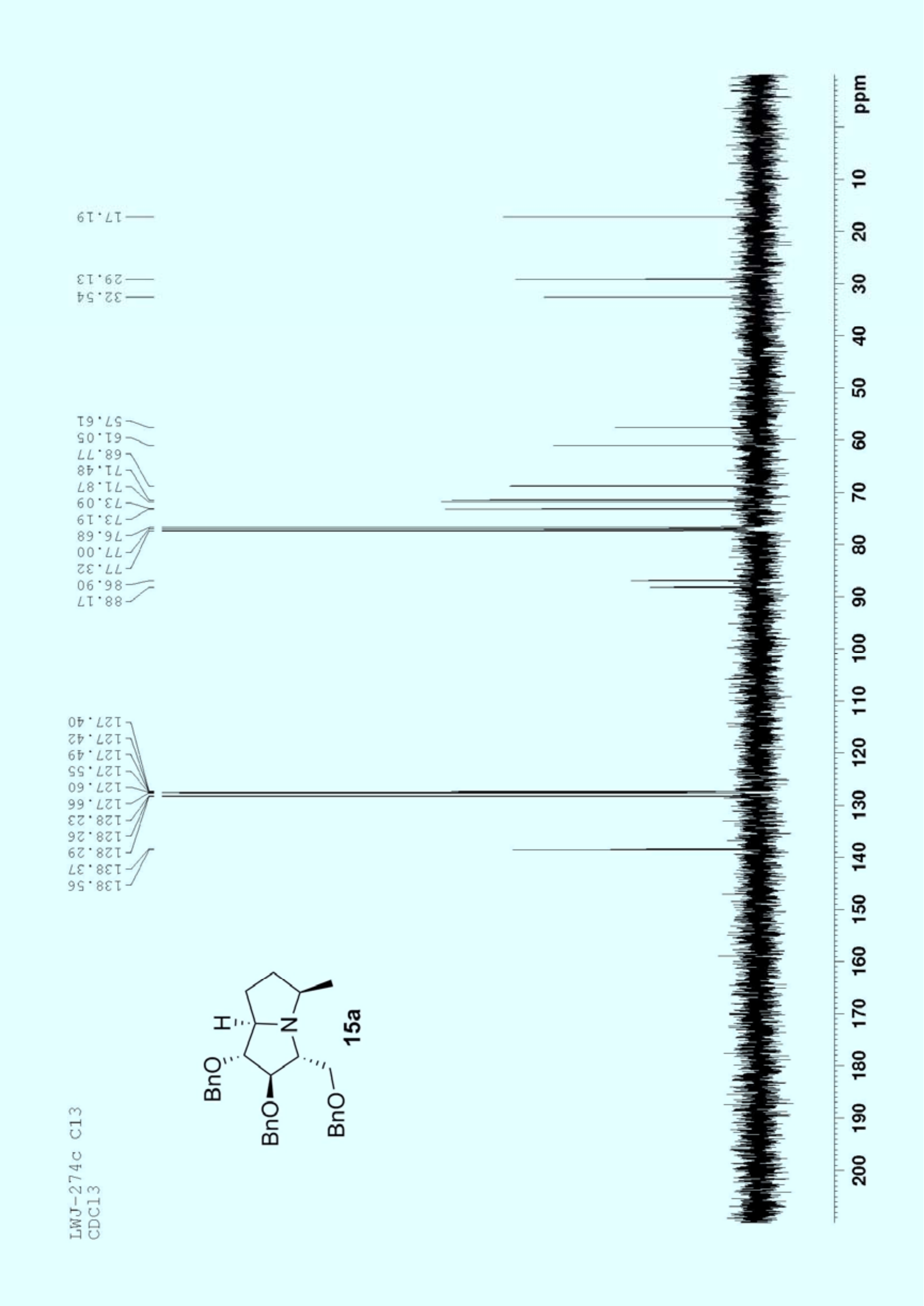
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15a

Hyacinthacine A_3 (2) Structural Verification and Assignment

The ^1H NMR, ^1H-^1H COSY, ^1H-^1H NOESY spectra of hyacinthacine A_3 (**2**) were recorded on a Bruker AV III 600 spectrometer. The ^{13}C NMR, HSQC, HMBC, DEPT-135 spectra of hyacinthacine A_3 (**2**), ^1H and ^{13}C NMR of **A_3** provided by Asano and mixture of compound **2** and **A_3** provided by Asano were recorded on a Bruker AV III 500 spectrometer.

Table 1. ^{1}H NMR data (in D_2O) for synthetic and natural hyacinthacine $\mathbf{A_3}$

H	δ_H of synthetic $\mathbf{A_3}$ reported by Izquierdo[1]	δ_H of synthetic $\mathbf{A_3}$ reported by Marco[2]	δ_H of natural $\mathbf{A_3}$ reported by Asano[3]	δ_H re-recorded data of natural $\mathbf{A_3}$ provided by Asano[2]	δ_H of Synthetic $\mathbf{A_3}$ (**2**) of this work	δ_H of mixture of Synthetic $\mathbf{A_3}$ (**2**) and natural $\mathbf{A_3}$ provided by Asano[2]
Me-5	1.26 (d, 3H, J = 6.8 Hz)	1.19 (d, 3H, J = 6.8 Hz)	1.24 (d, 3H, J = 6.8 Hz,)	1.27 (d, 3H, J = 6.8 Hz,)	1.20 (d, 3H, J = 6.81 Hz)	1.31 (d, 3H, J = 6.8 Hz,)
H-6α	1.68 (1H, m, H-6α)	1.65-1.55 (m, 1H)	1.73–1.63 (m, 1H),	1.74–1.63 (m, 1H),	1.65-1.55 (m, 1H)	1.79–1.68 (m, 1H),
H-7α	1.85 (1H, m)	1.80-1.75 (m, 1H)	1.88–1.80 (m, 1H)	1.90–1.81 (m, 1H)	1.81-1.72 (m, 1 H)	1.94–1.86 (m, 1H)
H-6β	1.95 (1H, m)	1.95-1.85 (overl, m, 1H)	2.03–1.92 (m, 2H)	2.06–1.91 (m, 2H)	1.97-1.84 (m, 1H)	2.09–1.97 (m, 2H)
H-7β	2.00 (1H, m)	1.95-1.85 (overl, m, 1H)			1.97-1.84 (m, 1H)	
H-3	3.19 (1H, dt, J = 8.1, 4.9 Hz, H-3)	3.10 (dt, 1H, J= 7.8, 5 Hz)	3.24 (m, 1H)	3.21 (m, 1H)	3.09 (dt, 1H, J = 7.95, 5.26 Hz)	3.26 (dt, 1H, J = 8.03, 4.82 Hz)
H-5	3.36 (1H, m)	3.24 (br, q,, J = ~ 7 Hz)	3.46 (m, 1H,)	3.24 (m, 1H,)	3.17-3.24 (m, 1H)	3.43 (m, 1H,)
H-7a	3.44 (1H, m)	3.30 (td, 1H, J = 7.8, 5 Hz)	3.59 (dt, 1H, $J_{7,7a}$ = $J_{7',7a}$ = 4 Hz)	3.46 (m, 1H)	3.31-3.24 (m, 1H)	3.52 (m)
H-8	3.74 (2H, d, J = 4.9 Hz)	3.68 (d, 2H, J = 5 Hz)	3.71 (d, 2H, J = 4.5 Hz)	3.75 (d, 2H, J = 4.9 Hz)	3.69 (d, 2H , J = 5.0 Hz)	3.79 (d, 2H, J = 4.9 Hz)
H-1	3.77 (1H, t, $J_{1,2}$ = $J_{1,7a}$ = 7.3 Hz, H-1)	3.70 (t, 1H, J = 7.8 Hz,)	3.76 (bt, 1H, $J_{1,7a}$ = 7.2 Hz,)	3.77 (bt, 1H, J = 7.5 Hz,)	3.71 (t, 1H, J = 7.5 Hz)	3.82 (bt, 1H, J = 7.4 Hz,)
H-2	3.95 (1H, dd, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 8.8 Hz)	3.90 (t, 1H, J = 7.8 Hz)	3.91 (bt, 1H, J = 7.5 Hz)	3.95 (bt, 1H, J = 7.8 Hz)	3.91 (bt, 1H, J = 7.8 Hz)	3.91 (bt, 1H, J = 7.6 Hz)

Table 2. Comparison of the ^{13}C NMR data (in D_2O) for synthetic and natural hyacinthacine **A$_3$**

C	δ_C of synthetic **A$_3$** reported by Izquierdo[1]	δ_C of synthetic **A$_3$** reported by Marco[2]	δ_C of natural **A$_3$** reported by Asano[3]	δ_C re-recorded data of **A$_3$** provided by Asano[2]	δ_C of Synthetic **A$_3$** of this work	δ_C of mixture of Synthetic **A$_3$** **(2)** and natural **A$_3$** provided by Asano[2]
C-1	80.86	83.0	82.6	82.6	83.3	82.6
C-2	78.21	81.1	80.4	80.4	81.5	80.5
C-7a	71.26	70.1	70.8	70.9	70.1	71.2
C-8	64.96	60.6	64.8	64.9	66.1	65.1
C-3	62.65	65.6	64.6	64.6	64.4	64.5
C-5	61.82	64.4	61.6	61.8	60.4	62.1
C-6	32.87	34.6	34.3	34.4	34.8	34.4
C-7	29.26	30.5	30.4	30.5	30.7	30.5
Me-5	16.49	18.1	17.9	17.9	18.4	17.9

Table 3. ^{1}H NMR data in D_2O and in CD_3OD of hyacinthacine **A$_3$** (data from this work)

	^{1}H NMR (D_2O) δ_H	^{1}H NMR (CD_3OD) δ_H
Me-5	1.20 (d, 3H, J = 6.81 Hz)	1.14 (d, 3H, J = 6.81 Hz)
H-6α	1.65-1.55 (m, 1H)	1.45-1.52 (m, 1H)
H-7α	1.81-1.72 (m, 1 H)	1.68-1.74 (m, 1 H)
H-6β	1.97-1.84 (m, 1H)	1.75-1.81 (m, 2 H)
H-7β	1.97-1.84 (m, 1H)	
H-3	3.09 (dt, 1H, J = 7.95, 5.26 Hz)	2.95 (dt, 1H, J = 7.1, 4.8 Hz)
H-5	3.17-3.24 (m, 1H)	3.12-3.18 (m, 1H)
H-7a	3.31-3.24 (m, 1H)	3.19-3.24 (m, 1H)
H-8	3.69 (d, 2H , J = 5.0 Hz)	3.51 (dd, 1H, $J_1 = J_2$ = 6.8 Hz)
H-1	3.71 (t, 1H, J = 7.5 Hz)	3.55 (dd, 1H, J = 4.1, 4.6 Hz)
H-2	3.91 (bt, 1H, J = 7.8 Hz)	3.82 (dd, 1H, $J_1 = J_2$ = 6.9 Hz)

Table 4. ^{13}C NMR data in D_2O and in CD_3OD of hyacinthacine **A_3** (data from this work)

^{13}C NMR δ_H in D_2O		^{13}C NMR δ_H in CD_3OD
83.3	**C-1**	81.7
81.5	**C-2**	79.3
70.1	**C-7a**	69.0
66.1	**C-8**	63.6
64.4	**C-3**	63.0
60.4	**C-5**	57.7
34.8	**C-6**	32.5
30.7	**C-7**	28.8
18.4	**Me-5**	15.9

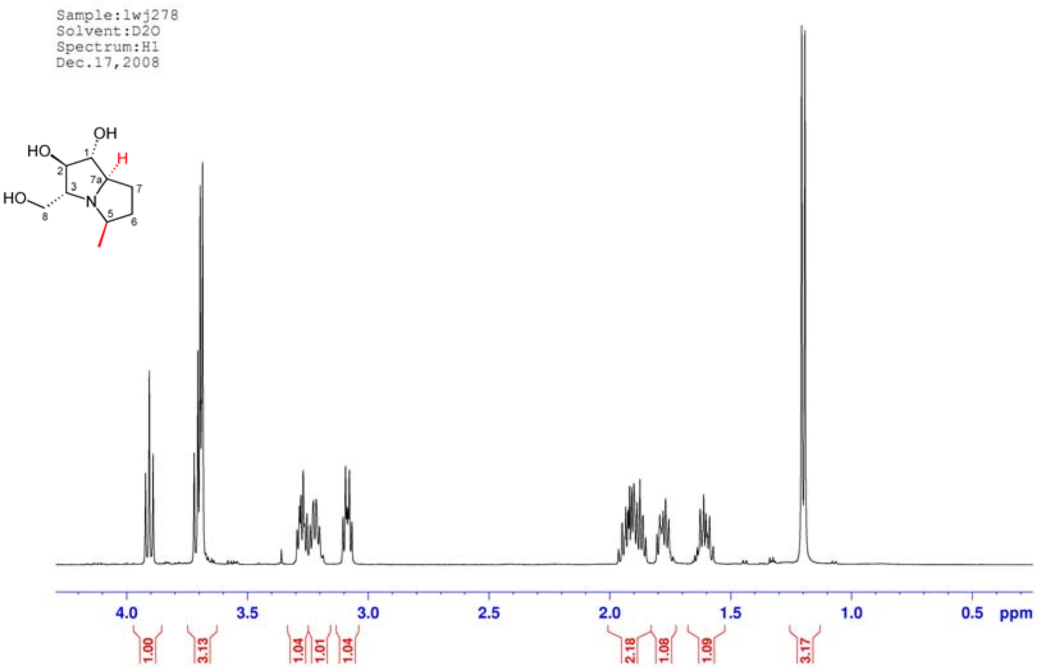

Figure 1. ^{1}H NMR spectrum of synthetic hyacinthacine A_3 (**2**)

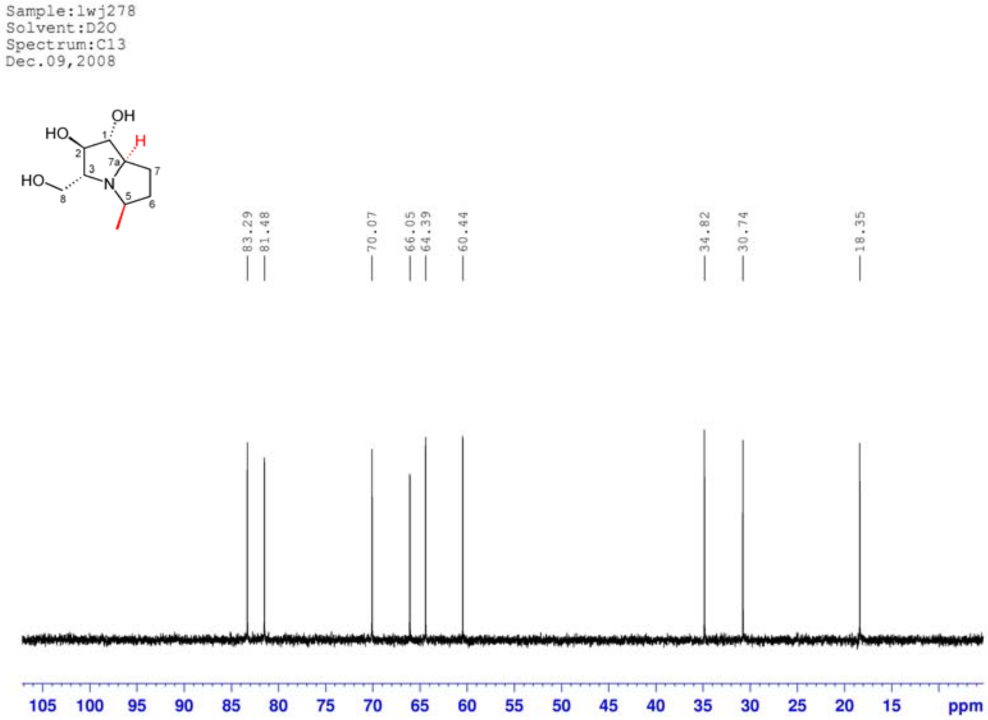

Figure 2. ^{13}C NMR spectrum of synthetic hyacinthacine A_3 (**2**)

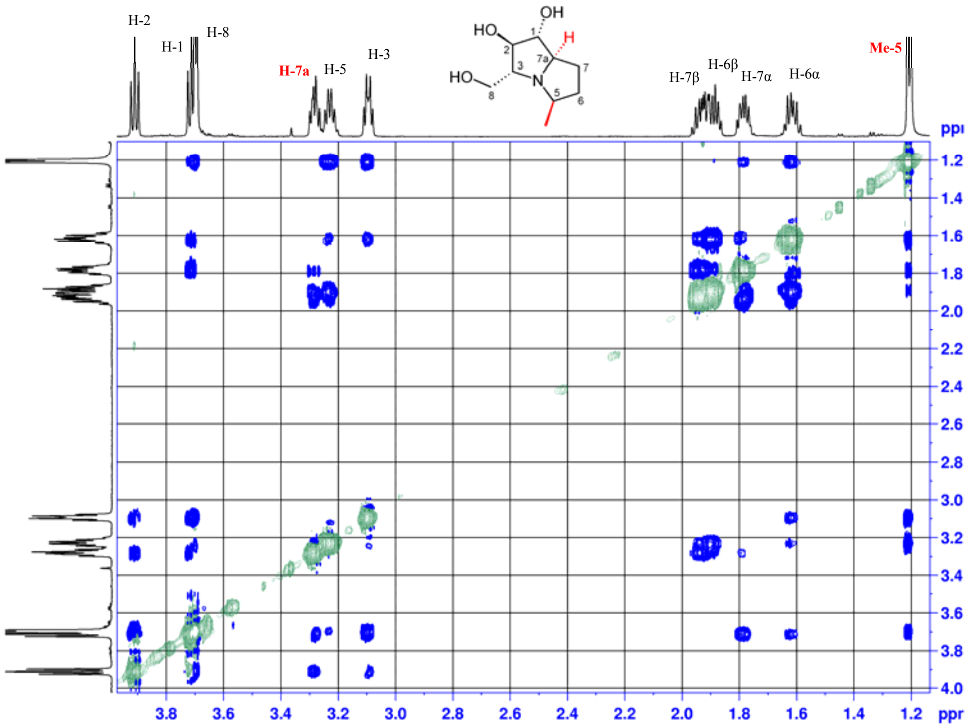

Figure 3. ^{1}H-^{1}H NOESY spectrum of synthetic hyacinthacine A_3 (**2**)

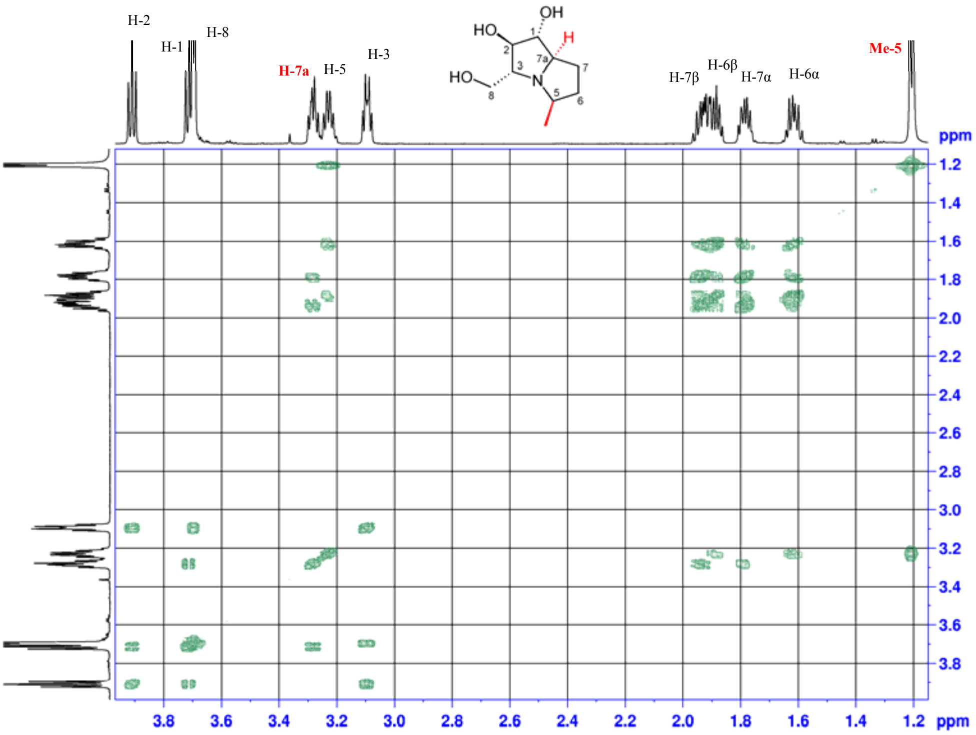

Figure 4. ^1H-^1H COSY spectrum of synthetic hyacinthacine A_3 (**2**)

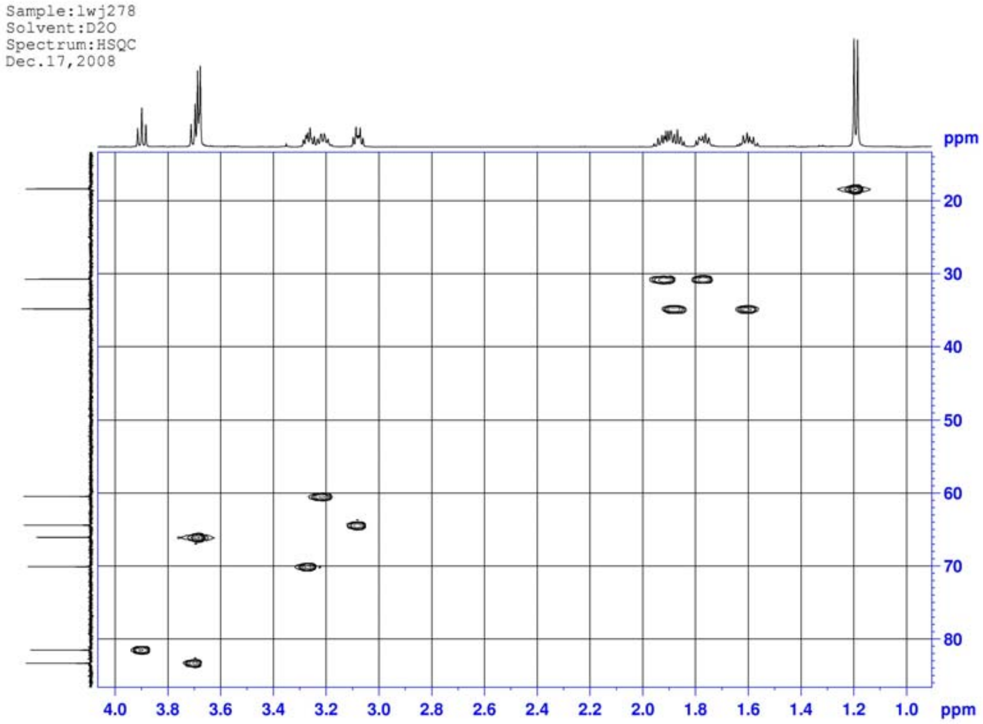

Figure 5. HSQC spectrum of synthetic hyacinthacine A_3 (**2**)

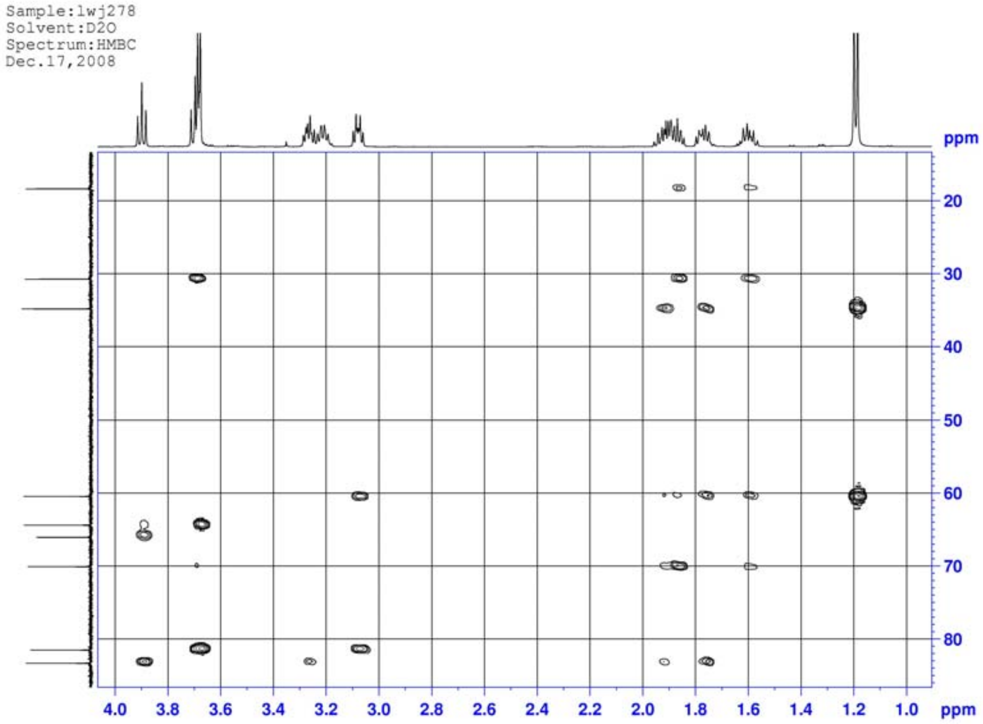

Figure 6. HMBC spectrum of synthetic hyacinthacine A_3 (**2**)

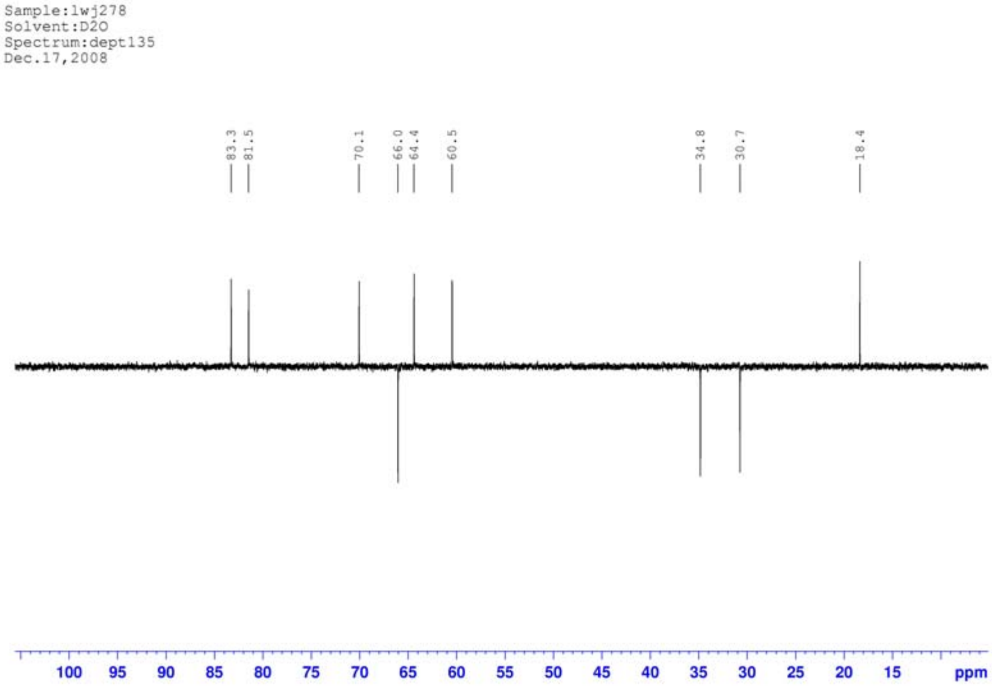

Figure 7. DEPT-135 spectrum of synthetic hyacinthacine A_3 (**2**)

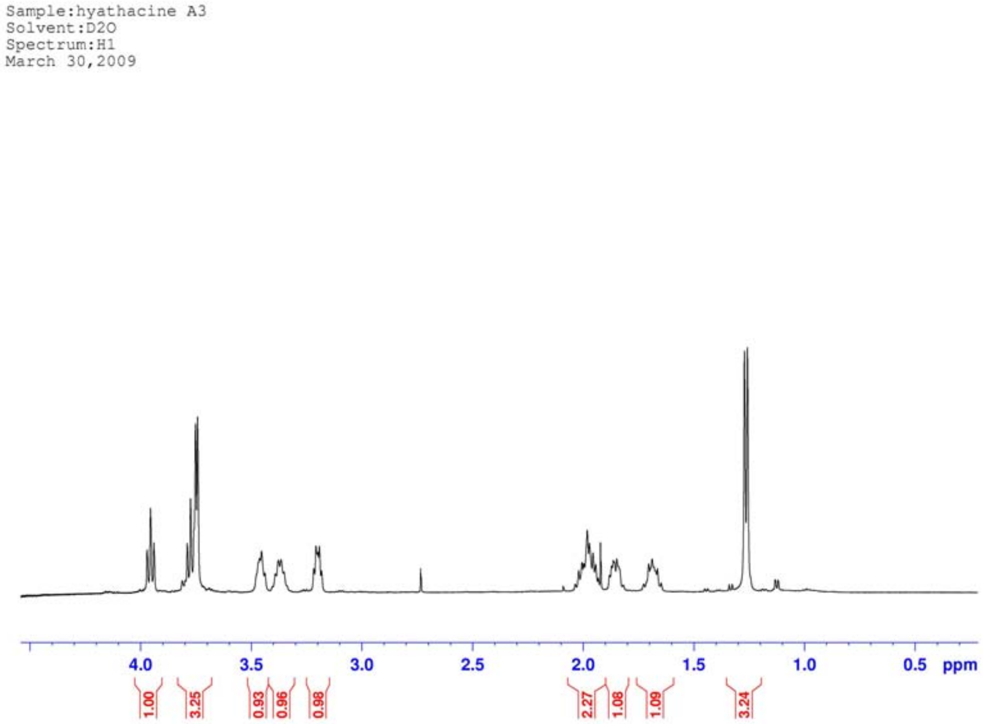

Figure 8. Re-recorded ^{1}H NMR spectrum of natural hyacinthacine A_3 provided by Asano

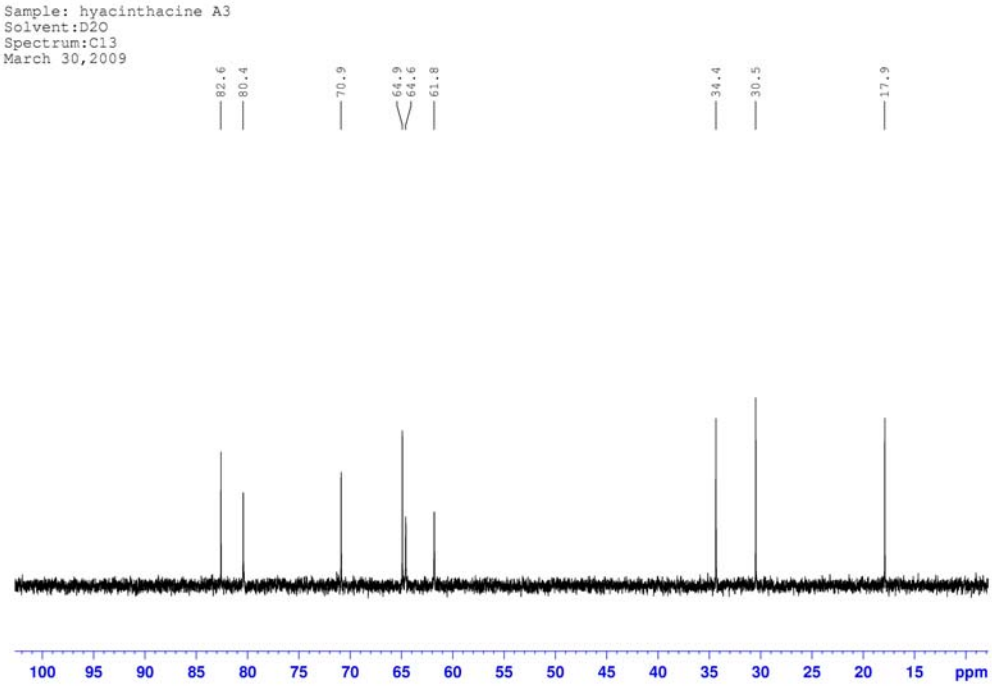

Figure 9. Re-recorded ^{13}C NMR spectrum of natural hyacinthacine A_3 provided by Asano

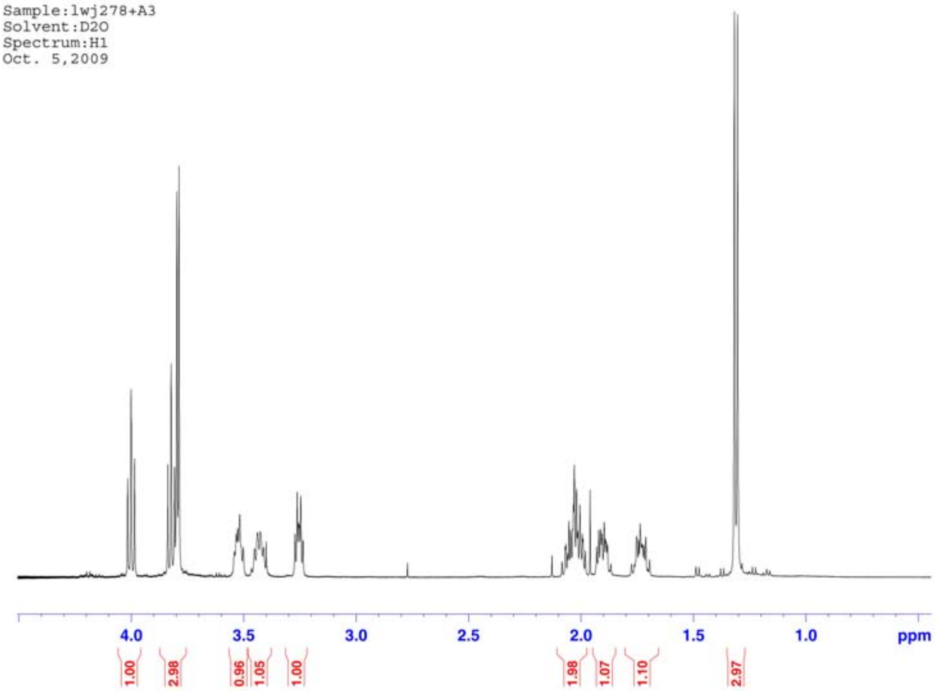

Figure 10. ^{1}H NMR spectrum of the mixture of synthetic hyacinthacine A_3 (**2**) and natural hyacinthacine A_3 provided by Asano

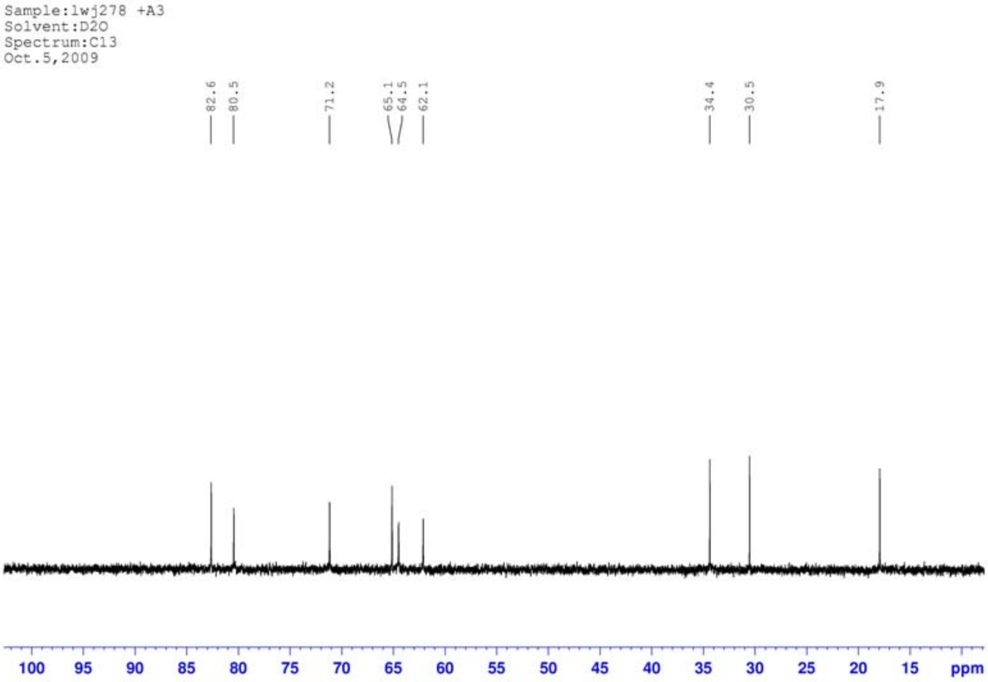

Figure 11. Re-recorded ^{13}C NMR spectrum of the mixture of synthetic hyacinthacine A_3 (**2**) and natural hyacinthacine A_3 provided by Asano

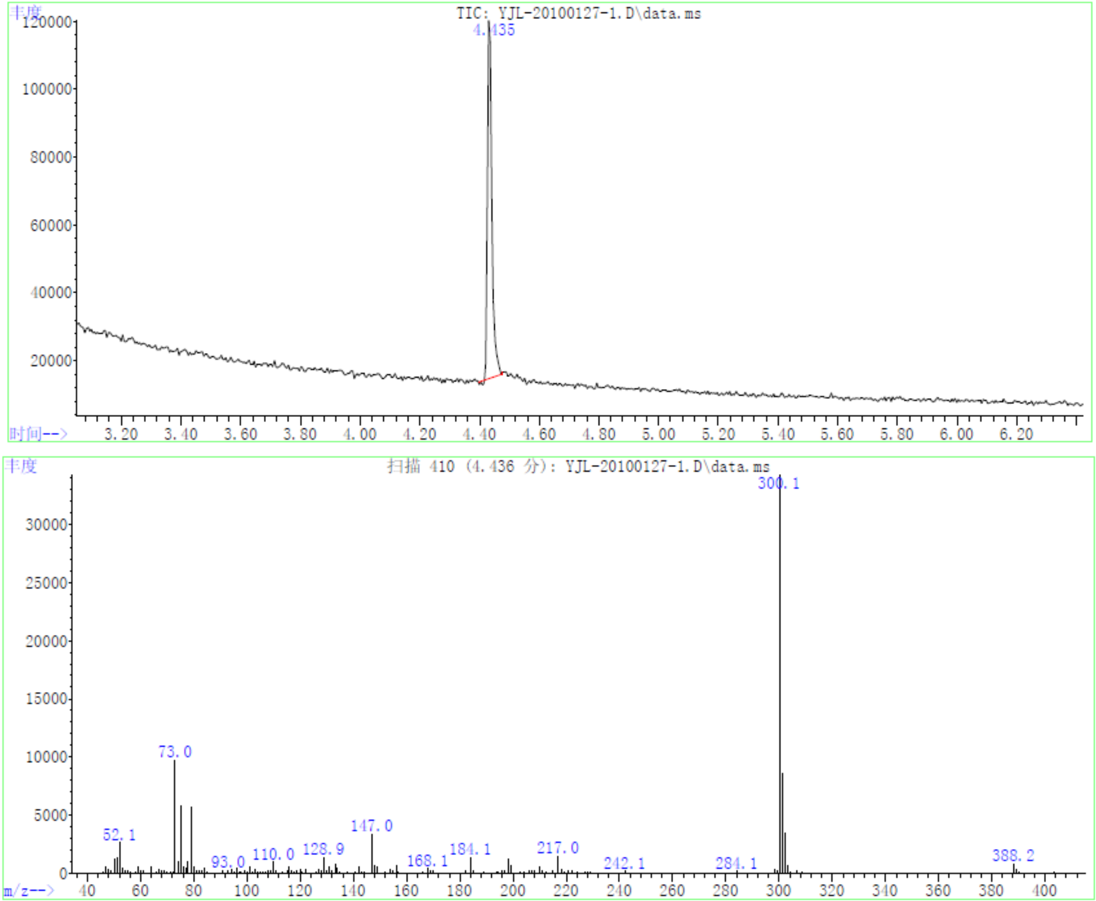

Figure 12. GC-MS spectrum of the mixture of synthetic hyacinthacine A_3 (**2**) and natural hyacinthacine A_3 provided by Asano

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