

Supporting Information:

Total Synthesis of (+)-Hyacinthacine A₂ Based on Sml₂-Induced Nitron Umpolung

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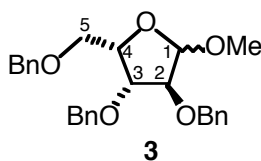
Supporting Information contents:

- General Procedures: **S1**
- Protocole for preparation of methyl 2,3,5-tri-*O*-benzyl- α,β -L-xylofuranoside (**3**): **S2**
- Copies of the spectra for compounds **8-11** and for synthetic (+)-hyacinthacine A₂ (**2**): **S3-S7**
- CIF for compound **11**: see separate file.

General Procedures :

All non-aqueous reactions were performed under a positive pressure of dry argon in oven-dried, or flame-dried glassware equipped with a magnetic stir bar. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents. Toluene and THF were freshly distilled over sodium and under a dry argon atmosphere. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates. TLC spots were viewed under ultraviolet light and by heating the plate after treatment with either a 5% solution of ammonium molybdate in 10% aqueous sulfuric acid (w/v), or a *p*-anisaldehyde staining solution (80 mL 95% ethanol, 2.9 mL sulfuric acid, 0.86 mL acetic acid, 2.1 mL *p*-anisaldehyde). Infrared (IR) spectra were obtained either as neat films, or as a thin film of a dichloromethane solution of the compound on sodium chloride discs, using a Fourier transform infrared spectrometer (FTIR) and the data are reported in reciprocal centimeters (cm⁻¹). All shifts for ¹H spectra are values downfield from tetramethylsilane and are reported as follows: chemical shift (ppm), multiplicity, integration, and coupling constants (Hz). Mass spectra (MS) were recorded on an ion-trap spectrometer using DCI (ammonia/isobutane 63/37).

Methyl 2,3,5-tri-*O*-benzyl- α,β -L-xylofuranoside (**3**)¹



L-xylose (5.0 g, 33.33 mmol) was dissolved in 0.5% HCl in methanol (138 mL) and stirred overnight at room temperature. The mixture was then neutralised with solid Ca(OH)₂. Filtration over celite and methanol evaporation under vacuum afforded α,β -L-methylxylofuranoside as a white foam which is used in the following step without purification.

The crude methyl α,β -L-xylofuranoside (33.33 mmol) in solution in DMF (120 mL) was added to a suspension of NaH (7.5 g, 200 mmol) in THF (40 mL) at 0 °C. The mixture was stirred for 15 min at room temperature, then tetra-butylammonium iodide (cat.) and benzylbromide (24 mL, 200 mmol) were added. The mixture was stirred at room temperature for 48 h. After addition of methanol (20 mL) and concentration under vacuum, water (200 mL) was added to the heterogeneous mixture, that was then extracted with ether (3 x 200 mL). The organic layers were washed with 5% LiCl aqueous solution (3 x 100 mL), then dried over MgSO₄, filtered, and the filtrate was concentrated to give the crude product, which upon column chromatography over silica gel (pentane / AcOEt : 9/1, then 4/1) yielded compounds **3** (β -anomer : 6.5 g; α -anomer : 5.2 g; 90%) as oils.

C₂₇H₃₀O₅

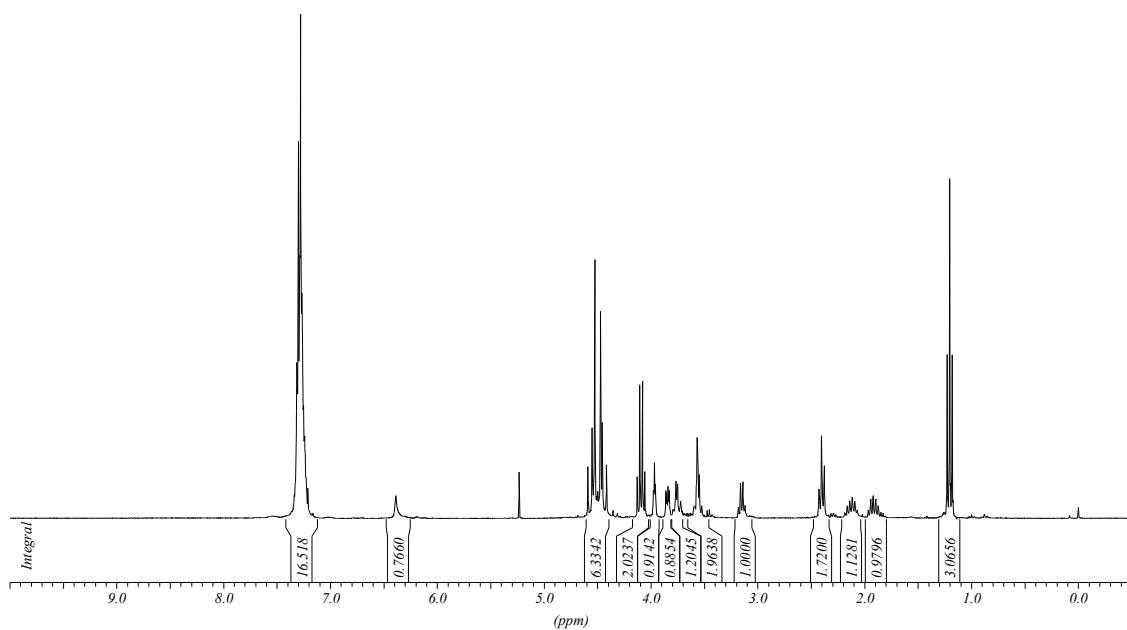
MS (DCI) *m/z* (%) : 452 (100) [M+NH₄]⁺ ; 420 (70) [M+NH₄-CH₃OH]⁺.

α -Anomer : ¹³C NMR (75MHz, CDCl₃) δ 55.1, 69.3, 72.4, 72.5, 73.3, 75.8, 81.4, 83.8, 100.4, 127-129, 137.6, 138.0, 138.1.

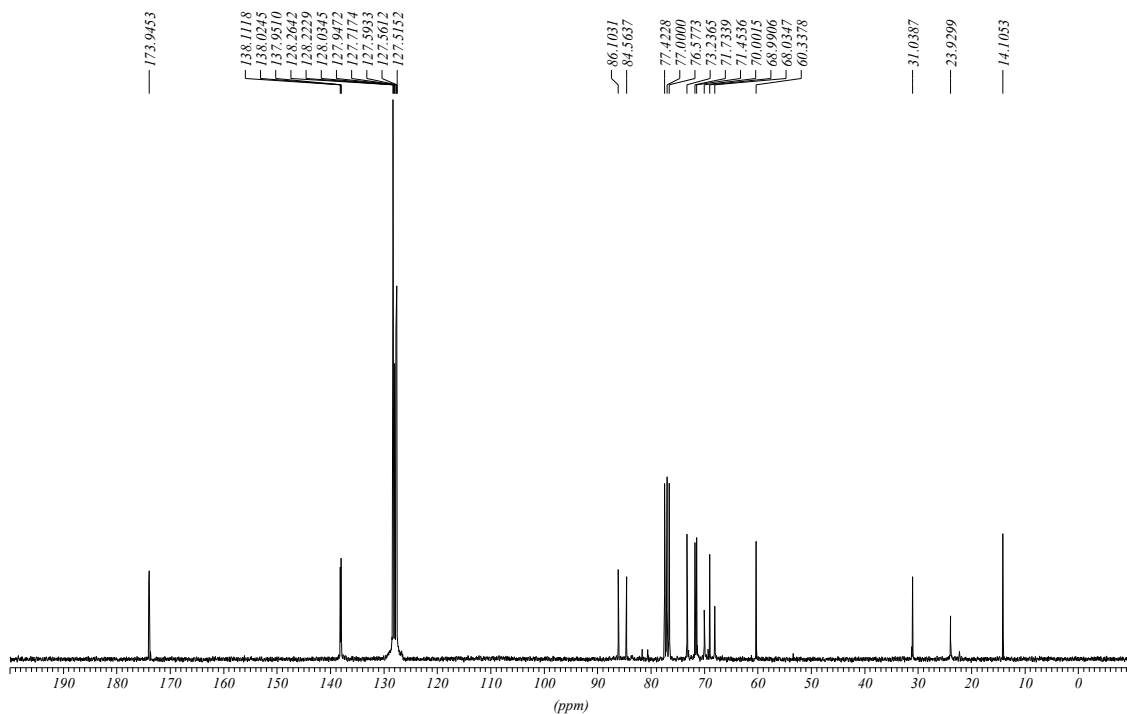
β -Anomer : ¹³C NMR (75MHz, CDCl₃) δ 55.5, 69.7, 71.8, 72.1, 73.1, 80.0, 81.5, 86.8, 108.0, 127-129, 137.5, 137.7, 138.2.

¹ Secrist, J. A., III; Tiwari, K. N.; Shortnacy-Fowler, A. T.; Messini, L.; Riordan, J. M.; Montgomery, J. A.; Meyers, S. C.; Ealick, S. E. *J. Med. Chem.* **1998**, *41*, 3865-3871.

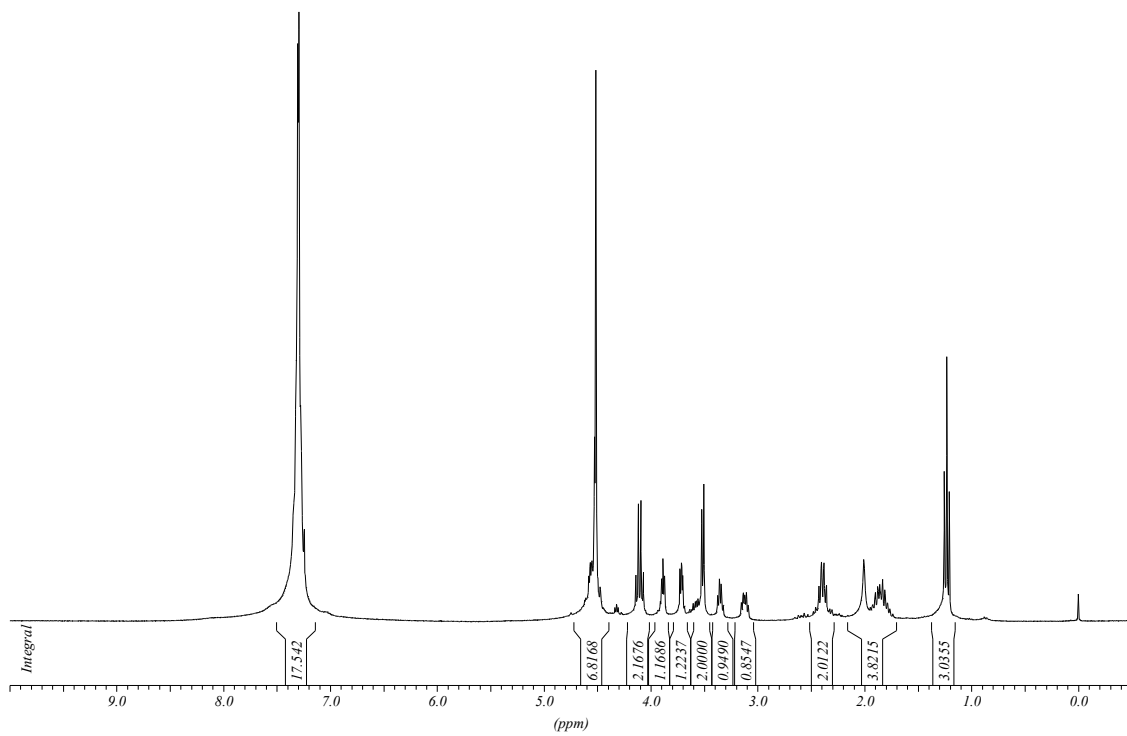
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Compound 8



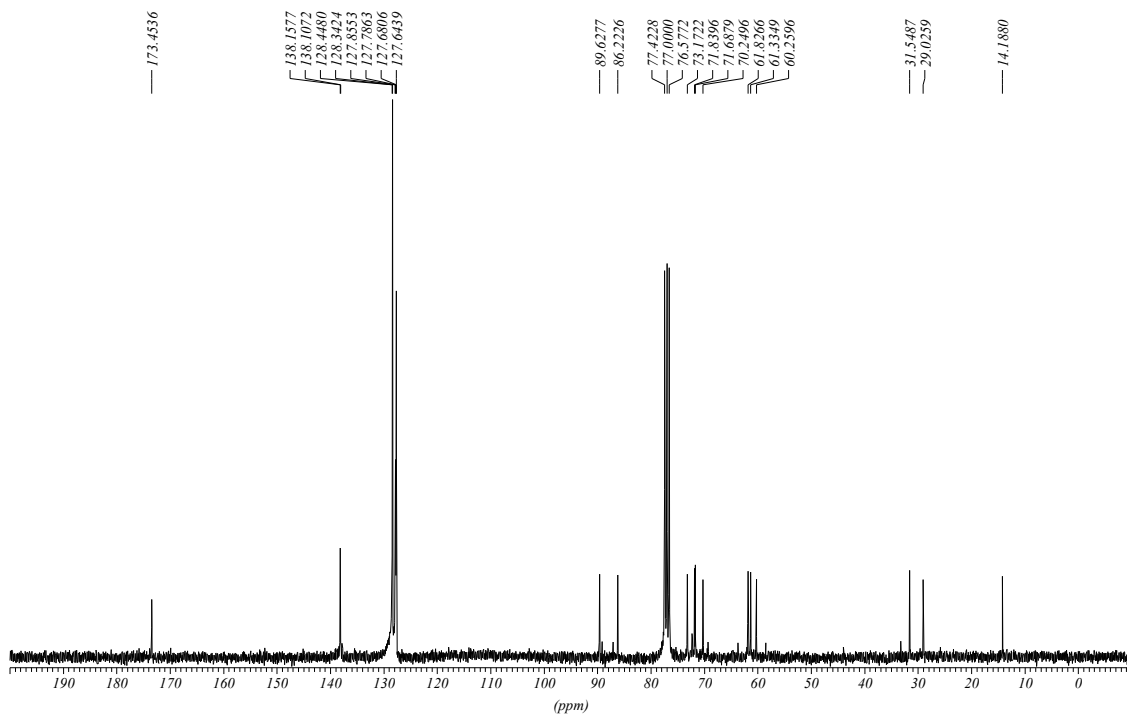
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Compound 8



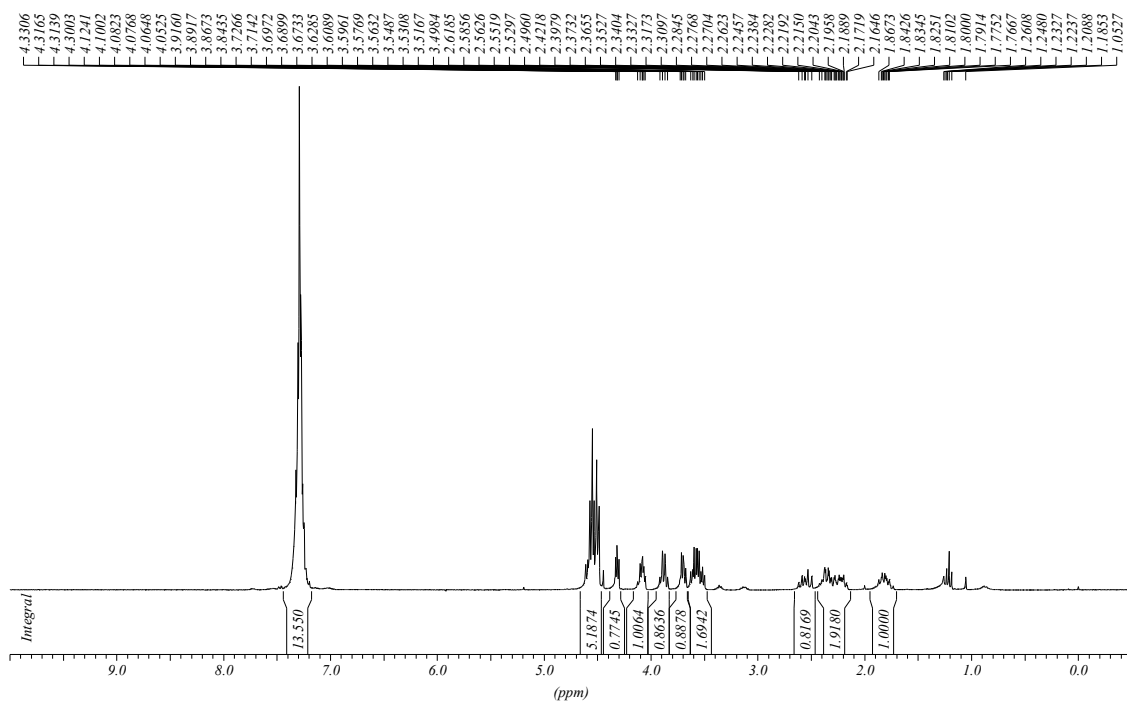
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Compound 9



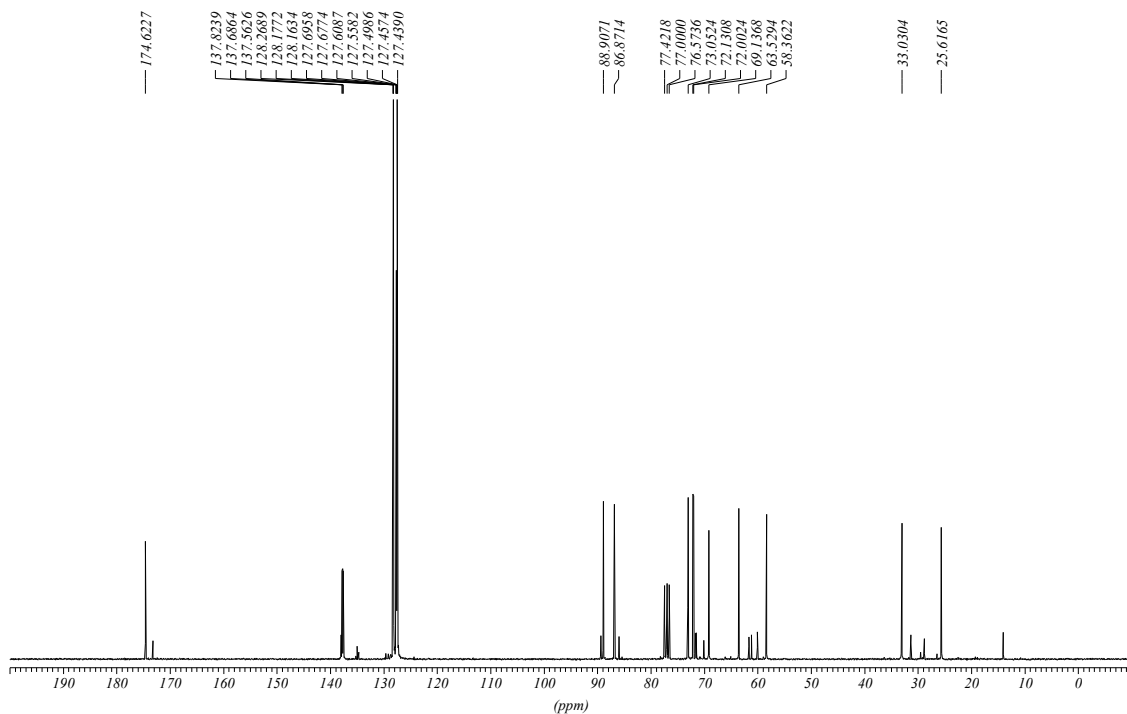
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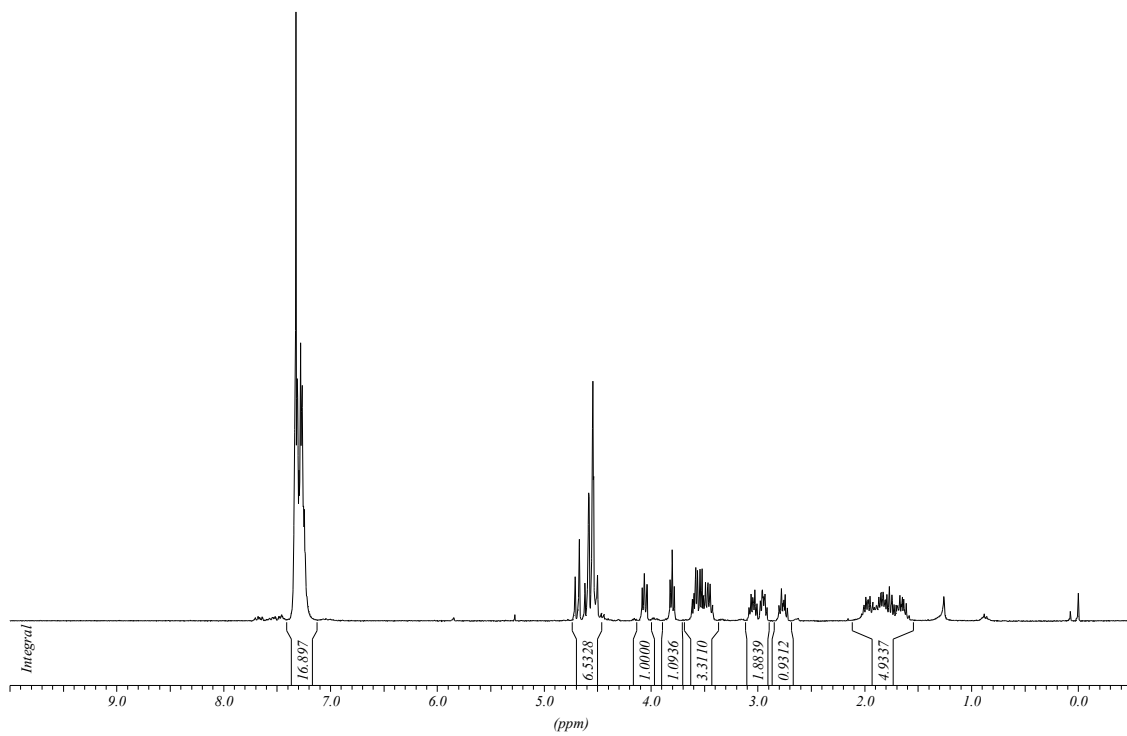
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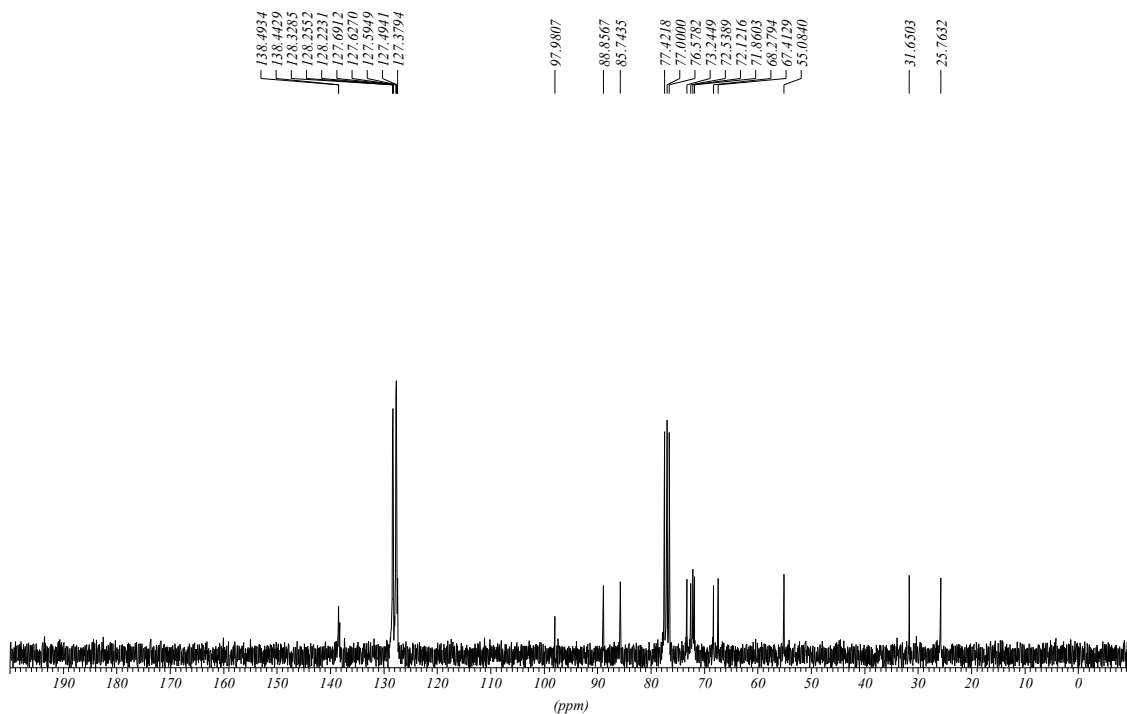
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Compound 10



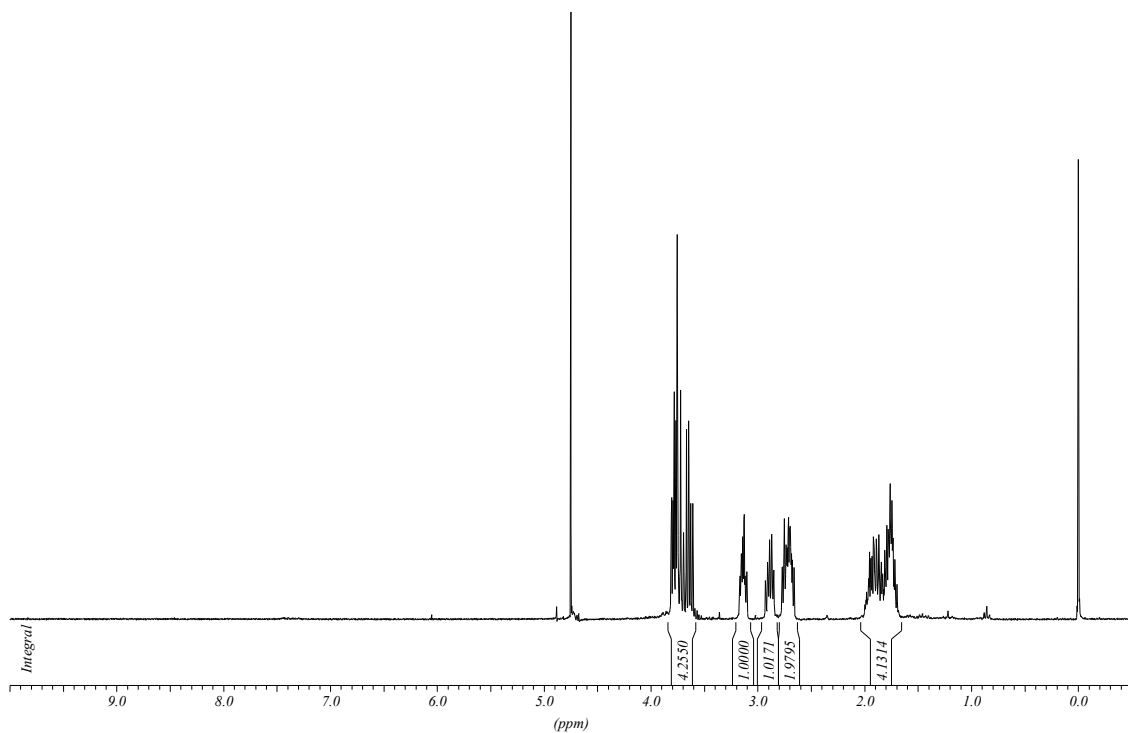
sd030526, CDCl₃, 300 MHz
Compound 11



sd030526, CDCl₃, 75 MHz
Compound 11



sd040715, D2O, 300 MHz
Compound 2 : Hyacinthacine A2



sd040713, D2O, 75 MHz
Compound 2 : Hyacinthacine A2

