**Supplementary Information SI1**

**Phytochemical characterization and biological activities of *Stenomesson miniatum* bulb extract, a medicinal plant of the Andes.**

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The structures of the characterized compounds are reported in Figure 1. Table 1 connects each compound identifier, such as “compound1” with the compound name (tazettine) and with the reference of the fraction (A4) in which it is present and of the set of NMR spectra which was used to carry out structure determination. The raw NMR data, the corresponding spectra, and their interpretation are stored in a zenodo.org archive, https://doi.org/10.5281/zenodo.4574016. This archive contains four zipped directories named “Assignments”, “NMReDATA”, “CDCl3”, and “Tables”.

The Assignments directory contains ChemDraw files, one per compound and a ChemDraw\_PDF directory that shows them once exported as one-page PDF files. The all\_compounds.cdx.pdf file shows them all in a single multi-page PDF file. Each ChemDraw file is named after the related compound identifier and shows the molecular structure of the compound, its name, and the identifier of the fraction from which it was characterized. The values of 13C NMR chemical shifts are reported in the neighborhood of each carbon atom, as well as the 1H NMR chemical shifts of the directly bound hydrogen atoms, if any. The NMR spectra recorded with DMSO-*d*6 as solvent were referenced by means of residual solvent signals, set at 2.5 ppm for 1H and 39.52 ppm for 13C NMR spectra.

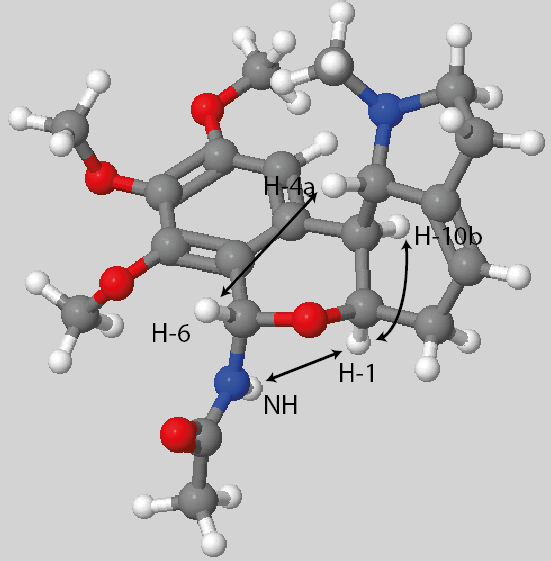
The NMReDATA directory contains zipped directories named NMReDATA records, one per compound, with nmredata.zip file extension. Each archive contains a directory and a file. For example, directory “compound1” contains an SDF file named “compound1.nmredata.sdf” and a directory named compound1\_A4, after the identifiers of the compound and of the fraction. The compound1.nmredata.sdf file reports the features and their interpretation that were extracted from the spectra stored in the corresponding directory. Directory compound1\_A4 contains NMR raw data and spectra produced by the TopSpin4 (TS4) software (Bruker, Rheinstetten, Germany) including 1D and 2D peak picking information. The nmredata.sdf files are text files formatted according to the computer readable NMReDATA template (https://nmredata.org/wiki).

Each NMReDATA file is an SDF file related to a single compound but contains two structures, a first one with 2D coordinates in the style of those usually published in Journals and a second one with 3D coordinates. The 2D structure section, enriched with chirality data at asymmetric centers, is followed by NMReDATA-specific key-value pairs for NMR spectra descriptions and for spectral assignment. An assignment is a triplet such as “c1, 129.1635, 4” that associates an atom name (“4” for the fourth atom in the list of atoms written in the atom block of the SDF file, an NMR signal label (“c1”, for the 13C NMR signal of the biogenetically numbered carbon atom C-1) and the corresponding chemical shift value (129.1635). The biogenetic atom numbering, the one displayed in Scheme 1, is incorporated in signal labels so that 1D NMR spectra descriptions are readily understandable. Assignment data make possible to describe 2D spectra as pairs of signal labels instead of pairs of chemical shift values, thus increasing data readability for humans. Atom numbering is consistent between the 2D and 3D structure descriptions and is standardized using the ALATIS software (Dashti et al., 2017). The 3D structures are produced by the ETKDGv3 procedure implemented in the RDKit library of cheminformatics tools (Wang et al., 2020). The 3D structure with the lowest Merck Molecular Force Field (MMFF) energy is retained as a reasonable guess of what the most stable molecular conformation could be, even this quick exploration procedure of the molecular conformational space is not intended to provide a definitive description of 3D structures. The 2D structures may be easily viewed with EdiSDF (https://vpsolovev.ru/programs/edisdf/) and the 3D structures with Jmol (http://jmol.sourceforge.net/) but any alternative software selection is possible.

The CDCl3 directory contains raw NMR data and the corresponding spectra for pure compounds **1**—**4** dissolved in CDCl3, respectively from fractions A4, A7, A9, A11.

The Tables directory contains MS Excel files for compounds **1**—**4** and MS word files for the other ones. The tables are formatted in the style organic chemists expect to see for NMR spectra descriptions and assignments. They carry the same information as the nmredata.sdf files but the formers are hardly machine-readable.

The difference in the processing of compounds **1**—**4** for the writing of the NMR data tables was motivated considering that the fractions in which they were characterized, A4, A7, A9, A11 contain these compounds at a high purity state. The creation of nmredata.sdf files and of traditional data tables was partly automated while the creation of these files for the other fractions was a fully manual process, meaning that no computer script was involved. The manual peak picking in the 2D NMR spectra of compounds **1**—**4** relies on the peak integration tool of TopSpin while it relies on the peak annotation tool for the other compounds. This choice can be explained, at least in part, by the fact that it seemed complicated to exploit the highly crowded 2D spectra of complex mixtures by means of the integration tool.



Structure of 6-dehydroxy-6-acetamido-nerinine: compound 12

**Structure determination of compound 12**. The planar structure was determined by the thorough analysis of 1D 1H and 13C NMR spectra and of 2D COSY, HSQC, and HMBC spectra. The *cis* ring junction at C-1 and C-10b, the α orientation of the acetamido group, and the *trans*-diaxial positions of H-4a and H-10b were deduced from the observation of the H-1/H-10b, NH/H-1, and H-6/H-4a ROESY correlations.



**6-dehydroxy-6-acetamido-nerinine:** 1H NMR, 13C NMR, COSY and HMBC NMR data (600 MHz, DMSO-*d6*)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Position** | **δH (*J* in Hz)** | **δC** | **COSY** | **HMBC** |
| 1 | 4.153 *m* | 65.57 | H-2a, H-2b, H-6, H-10b | C-2, C-3, C-4a, C-6,  C-10a |
| 2a | 2.586 *m* | 31.47 | H-1, H-2b, H-3 | C-3, C-4, C-10b |
| 2b | 2.042 *m* |  | H-2a, H-3 | C-1, C-3, C-4, C-10b |
| 3 | 5.37 *ddd* (10.4, 1.9, 1.6) | 114.93 | H-2a, H-2b | C-4a |
| 4 |  | 141.55 |  |  |
| 4a | 2.566 *m* | 67.0 | H-1, H-3 |  |
| 6 | 6.248 *d* (8.7) | 71.56 | H-1, H-10, NH | C-1, C-6a, C-7, C-8, C-9, C-10a, CO(Ac) |
| 6a |  | 119.88 |  |  |
| 7 |  | 150.13 |  |  |
| 8 |  | 140.63 |  |  |
| 9 |  | 152.25 |  |  |
| 10 | 6.769 *s* | 109.29 | H-6, H-10b, 9-OMe | C-4a, C-6, C-6a, C-7, C-8, C-9, C-10a, C-10b |
| 10a |  | 133.34 |  |  |
| 10b | 2.274 *dd* (9.4, 2.2) | 43.58 | H-1, H-4a, H-10 | C-4, C-4a, C-6a, C-10, C-10a |
| 11a | 2.392 *m* |  | H-12a, H-12b |  |
| 11b | 2.289 *m* | 28.16 | H-12a |  |
| 12a | 2.998 *ddd* (9.6, 7.6, 3.6) |  | H-11a, H-11b, H-12b | C-4, C-4a, C-11, NMe |
| 12b | 2.174 *m* | 56.2 | H-11a, H-11b, H-12a | C-4, C-4a, C-11, NMe |
| NH | 8.84 *d* (8.7) |  | H-6, Me(Ac) | C-6, C-6a, CO(Ac) |
| Me(Ac) | 1.833 *s* | 22.88 | NH | CO(Ac) |
| CO(Ac) |  | 168.45 |  |  |
| 7-OMe | 3.729 *s* | 60.37 |  | C-7 |
| 8-OMe | 3.726 *s* | 60.17 |  | C-8 |
| 9-OMe | 3.784 *s* | 56.02 | H-10 | C-9 |
| NMe | 1.898 *s* | 44.34 |  | C-4a, C-12 |

ROESY (F2--> F1): H-1 --> H-2a, H-10b, NH; H-2a --> H-1, H-3; H-2b --> H-1; H-3; H-4a --> NMe; H-10 --> NMe; H-10b --> H-1; H-12a --> H-12b, NMe; H-12b --> H-12a, NMe; NH --> H-1, Me(Ac), 7-OMe.

Descriptors for compounds **1**—**12**

Compound **1**

Tazettine C18H21NO5 (Knolker 2020),

13C NMR data reported from (Roberts et al. 1971)

InChI-Key: YLWAQARRNQVEHD-PBZHRCKQSA-N

InChI=1S/C18H21NO5/c1-19-9-18(20)17(4-3-12(21-2)6-16(17)19)13-7-15-14(22-10-23-15)5-11(13)8-24-18/h3-5,7,12,16,20H,6,8-10H2,1-2H3/t12-,16+,17+,18-/m1/s1

SMILES: CN1[C@@H]2[C@@]3(C=C[C@@H](OC)C2)[C@](C1)(O)OCC4=C3C=C5C(OCO5)=C4

Compound **2**

Albomaculine C19H23NO5(de Andrade et al. 2014)

InChI-Key: OXFLPPXWFHSXSK-XNRPHZJLSA-N

InChI=1S/C19H23NO5/c1-20-8-7-10-5-6-12-14(16(10)20)11-9-13(22-2)17(23-3)18(24-4)15(11)19(21)25-12/h5,9,12,14,16H,6-8H2,1-4H3/t12-,14-,16-/m1/s1

SMILES: CN1CCC2=CC[C@@H]3[C@H]([C@@H]21)C4=CC(=C(C(=C4C(=O)O3)OC)OC)OC

Compound **3**

Haemanthamine C17H19NO4(Viet Nguyen et al. 2019)

InChI-Key: YGPRSGKVLATIHT-HSHDSVGOSA-N

InChI=1S/C17H19NO4/c1-20-11-2-3-17-12-6-14-13(21-9-22-14)4-10(12)7-18(8-16(17)19)15(17)5-11/h2-4,6,11,15-16,19H,5,7-9H2,1H3/t11-,15+,16+,17+/m1/s1

SMILES: CO[C@H]1C[C@H]2[C@@]3(C=C1)[C@H](CN2CC4=CC5=C(C=C34)OCO5)O

Compound **4**

Crinine C16H17NO3(Viladomat et al. 1995)

InChI-Key: RPAORVSEYNOMBR-IUIKQTSFSA-N

InChI=1S/C16H17NO3/c18-11-1-2-16-3-4-17(15(16)6-11)8-10-5-13-14(7-12(10)16)20-9-19-13/h1-2,5,7,11,15,18H,3-4,6,8-9H2/t11-,15+,16+/m0/s1

SMILES: C1CN2CC3=CC4=C(C=C3[C@]15[C@H]2C[C@H](C=C5)O)OCO4

Compound **5**

Trisphaeridine C14H9NO2(Viladomat et al. 1997)

RFILRSDHWIIIMN-UHFFFAOYSA-N

InChI=1S/C14H9NO2/c1-2-4-12-10(3-1)11-6-14-13(16-8-17-14)5-9(11)7-15-12/h1-7H,8H2

SMILES: C1OC2=C(O1)C=C3C4=CC=CC=C4N=CC3=C2

Compound **6**

3-Epimacronine C18H19NO5(Viladomat et al. 1990)

InChI-Key: YEISBJOTHHFANE-NJVUAGGXSA-N

InChI=1S/C18H19NO5/c1-19-8-16-18(4-3-10(21-2)5-15(18)19)12-7-14-13(22-9-23-14)6-11(12)17(20)24-16/h3-4,6-7,10,15-16H,5,8-9H2,1-2H3/t10-,15+,16+,18+/m1/s1

SMILES: CN1C[C@H]2[C@]3([C@@H]1C[C@@H](C=C3)OC)C4=CC5=C(C=C4C(=O)O2)OCO5

Compound **7**

3-methoxy-8,9-methylenedioxy-3,4-dihydrophenanthridine C15H13NO3(Hohmann et al., 2002)

InChI-Key: OIOVDHXEPUXTQZ-UHFFFAOYSA-N

InChI=1S/C15H13NO3/c1-17-10-2-3-11-12-6-15-14(18-8-19-15)4-9(12)7-16-13(11)5-10/h2-4,6-7,10H,5,8H2,1H3

SMILES: COC1CC2=C(C=C1)C3=CC4=C(C=C3C=N2)OCO4

Compound **8**

Crinine-3-acetate C18H19NO4(Ali et al. 1986)

InChI-Key: YEIGSYFTXGPBIB-MORSLUCNSA-N

InChI=1S/C18H19NO4/c1-11(20)23-13-2-3-18-4-5-19(17(18)7-13)9-12-6-15-16(8-14(12)18)22-10-21-15/h2-3,6,8,13,17H,4-5,7,9-10H2,1H3/t13-,17+,18+/m0/s1

SMILES: CC(O[C@@H](C=C[C@]12CC3)C[C@H]1N3CC4=C2C=C5C(OCO5)=C4)=O

Compound **9**

6α-Hydroxybuphanisine C17H19NO4 (Frahm et al. 1985)

InChI-Key: VCFGXYUXSWZFDE-CNFIPTJHSA-N

InChI=1S/C17H19NO4/c1-20-10-2-3-17-4-5-18(15(17)6-10)16(19)11-7-13-14(8-12(11)17)22-9-21-13/h2-3,7-8,10,15-16,19H,4-6,9H2,1H3/t10-,15+,16+,17+/m0/s1

SMILES: CO[C@@H]1C[C@@H]2[C@@]3(CCN2[C@@H](C4=CC5=C(C=C43)OCO5)O)C=C1Co

Compound **10**

Nerinine C19H25NO5(de Andrade et al. 2014)

InChI-Key: MNAREALDHXFRFJ-QNDNMDDASA-N

InChI=1S/C19H25NO5/c1-20-8-7-10-5-6-12-14(16(10)20)11-9-13(22-2)17(23-3)18(24-4)15(11)19(21)25-12/h5,9,12,14,16,19,21H,6-8H2,1-4H3/t12-,14-,16-,19+/m1/s1

SMILES: CN1CCC2=CC[C@@H]3[C@H]([C@@H]21)C4=CC(=C(C(=C4[C@H](O3)O)OC)OC)OC

Compound **11A**

Pretazettine (major epimer, 6β-pretazattine) C18H21NO5(Baldwin and Debenham 2000; Kobayashi et al. 1980)

InChI-Key: KLJOYDMUWKSYBP-YNBLHMCPSA-N

InChI=1S/C18H21NO5/c1-19-8-16-18(4-3-10(21-2)5-15(18)19)12-7-14-13(22-9-23-14)6-11(12)17(20)24-16/h3-4,6-7,10,15-17,20H,5,8-9H2,1-2H3/t10-,15+,16+,17-,18+/m1/s1

SMILES: CN1C[C@H]2[C@]3([C@@H]1C[C@@H](C=C3)OC)C4=CC5=C(C=C4[C@@H](O2)O)OCO5

Compound **11B**

Pretazettine (minor epimer, 6α-pretazettine) C18H21NO5(Kobayashi et al. 1980)

InChI-Key: KLJOYDMUWKSYBP-GTQNRYLJSA-N

InChI=1S/C18H21NO5/c1-19-8-16-18(4-3-10(21-2)5-15(18)19)12-7-14-13(22-9-23-14)6-11(12)17(20)24-16/h3-4,6-7,10,15-17,20H,5,8-9H2,1-2H3/t10-,15+,16+,17+,18+/m1/s1

SMILES: CN1C[C@H]2[C@@]3(C4=CC5=C(OCO5)C=C4[C@@H](O)O2)[C@@H]1C[C@H](OC)C=C3

Compound **12**

6-dehydroxy-6-acetamido-nerinine C21H28N2O5

InChI-Key: JPSHDRAJDZKEJG-OQBJRAFVSA-N

InChI=1S/C21H28N2O5/c1-11(24)22-21-17-13(10-15(25-3)19(26-4)20(17)27-5)16-14(28-21)7-6-12-8-9-23(2)18(12)16/h6,10,14,16,18,21H,7-9H2,1-5H3,(H,22,24)/t14-,16-,18-,21+/m1/s1

SMILES: CN1CCC2=CC[C@H]([C@@H]3[C@@H]21)O[C@H](NC(C)=O)C4=C3C=C(OC)C(OC)=C4OC

Comparison of the data recorded by the authors with those from literature, when available

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Tazettine **1** | | | Albomaculine **2** | | | Haemanthamine **3** | | | Crinine **4** | | |
| Our data | Literature | Our data | Our data | Literature | Our data | Our data | Literature | Our data | Our data | Literature | Our data |
| CDCl3 | CDCl3 | DMSO-*d6* | CDCl3 | CDCl3 | DMSO-*d6* | CDCl3 | CDCl3 | DMSO-*d6* | CDCl3 | CDCl3 | DMSO-*d6* |
| 146.75 | 146.60 | 145.74 | 162.39 | 162.40 | 161.30 | 146.60 | 146.50 | 145.80 | 146.25 | 146.10 | 145.58 |
| 146.54 | 146.40 | 145.67 | 157.15 | 157.20 | 156.55 | 146.30 | 146.20 | 145.29 | 145.84 | 145.70 | 145.10 |
| 130.74 | 130.60 | 129.56 | 156.25 | 156.30 | 155.03 | 135.25 | 135.40 | 136.59 | 138.25 | 138.40 | 138.82 |
| 128.74 | 128.60 | 129.16 | 142.57 | 142.70 | 141.81 | 132.25 | 132.00 | 129.52 | 131.87 | 132.20 | 130.79 |
| 127.94 | 128.00 | 127.97 | 140.77 | 140.80 | 141.13 | 127.30 | 127.40 | 128.74 | 127.83 | 127.40 | 128.47 |
| 125.60 | 125.50 | 126.36 | 140.42 | 140.60 | 140.68 | 126.62 | 126.90 | 127.35 | 126.02 | 126.50 | 126.96 |
| 109.48 | 109.30 | 108.38 | 115.62 | 115.60 | 115.01 | 106.97 | 106.90 | 106.81 | 107.06 | 106.90 | 106.88 |
| 104.13 | 104.00 | 104.16 | 111.44 | 111.60 | 110.96 | 103.45 | 103.30 | 103.28 | 102.98 | 102.70 | 103.15 |
| 102.10 | 102.10 | 101.06 | 107.30 | 107.40 | 108.20 | 100.98 | 100.80 | 100.52 | 100.91 | 100.60 | 100.46 |
| 101.09 | 100.90 | 100.81 | 76.29 | 76.30 | 75.71 | 80.13 | 80.20 | 80.09 | 63.86 | 64.10 | 62.46 |
| 72.94 | 72.90 | 72.60 | 65.95 | 66.00 | 65.83 | 72.81 | 72.80 | 72.41 | 62.92 | 62.80 | 62.40 |
| 70.22 | 70.00 | 69.40 | 62.08 | 62.10 | 61.67 | 63.54 | 63.60 | 63.71 | 62.16 | 62.40 | 61.93 |
| 65.54 | 65.60 | 65.20 | 61.30 | 61.30 | 60.72 | 62.79 | 62.70 | 62.47 | 53.57 | 53.60 | 53.01 |
| 62.18 | 62.10 | 60.75 | 56.57 | 56.60 | 56.34 | 61.35 | 61.40 | 60.71 | 44.34 | 44.20 | 44.20 |
| 56.30 | 56.20 | 55.36 | 56.45 | 56.50 | 55.72 | 56.78 | 56.70 | 55.65 | 44.09 | 44.20 | 43.87 |
| 49.98 | 49.90 | 49.48 | 45.35 | 45.50 | 43.93 | 50.23 | 50.10 | 49.90 | 32.76 | 32.70 | 32.71 |
| 42.22 | 41.90 | 41.86 | 43.68 | 43.70 | 43.22 | 28.23 | 28.30 | 28.18 |  |  |  |
| 26.72 | 26.70 | 25.93 | 30.97 | 31.00 | 30.40 |  |  |  |  |  |  |
|  |  |  | 27.98 | 28.10 | 27.59 |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Literature** |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |
| Tazettine **1** |  |  | (Pham et al. 1999) | | | | |  |  |  |  |
| Albomaculine **2** | |  | (de Andrade et al. 2014) | | | | |  |  |  |  |
| Haemanthamine **3** | |  | (Viet Nguyen et al. 2019) | | | | |  |  |  |  |
| Crinine **4** |  |  | (Frahm et al. 1985) | | | | | |  |  |  |

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Trisphaeridine **5** | | 3-epimacronine **6** | | Crinine acetate **8** | | 6α-hydroxybuphanisine **9** | | Nerinine **10** | |
| Our data | Literature | Our data | Literature | Our data | Literature | Our data | Literature | Our data | Literature |
| DMSO-*d6* | CDCl3 | DMSO-*d6* | CDCl3 | DMSO-*d6* | CDCl3 | DMSO-*d6* | CDCl3 | DMSO-*d6* | CDCl3 |
| 151.85 | 151.80 | 164.89 | 168.50 | 169.93 | 170.00 | 146.59 | 147.30 | 152.00 | 153.10 |
| 151.51 | 148.20 | 152.18 | 152.30 | 145.67 | 146.20 | 145.05 | 145.80 | 150.80 | 151.30 |
| 148.14 | 148.10 | 146.83 | 147.10 | 145.31 | 145.90 | 139.15 | 138.50 | 141.62 | 141.20 |
| 143.74 | 143.80 | 142.11 | 142.20 | 138.07 | 138.20 | 132.95 | 131.80 | 140.71 | 141.10 |
| 129.57 | 130.30 | 131.76 | 131.30 | 135.25 | 134.50 | 129.13 | 127.40 | 132.92 | 133.60 |
| 129.51 | 129.90 | 125.94 | 126.00 | 126.85 | 126.40 | 125.35 | 125.70 | 122.42 | 121.20 |
| 128.04 | 128.10 | 118.07 | 118.60 | 123.15 | 123.70 | 109.42 | 109.30 | 115.06 | 115.80 |
| 126.72 | 126.70 | 109.91 | 111.00 | 106.99 | 107.00 | 102.54 | 102.30 | 109.20 | 109.10 |
| 124.02 | 124.30 | 104.06 | 103.80 | 103.09 | 102.00 | 100.63 | 100.70 | 88.04 | 89.80 |
| 123.07 | 122.00 | 102.41 | 102.10 | 100.54 | 100.00 | 88.05 | 88.70 | 66.90 | 67.50 |
| 122.87 | 123.10 | 79.29 | 80.10 | 66.33 | 66.60 | 72.03 | 72.10 | 63.98 | 66.30 |
| 105.39 | 105.50 | 72.37 | 72.70 | 62.86 | 63.30 | 56.49 | 56.40 | 60.81 | 61.40 |
| 102.25 | 101.90 | 62.50 | 63.30 | 61.66 | 62.40 | 55.69 | 56.20 | 60.36 | 61.00 |
| 100.35 | 99.90 | 55.37 | 56.20 | 52.95 | 53.60 | 47.87 | 47.60 | 56.19 | 57.10 |
|  |  | 52.98 | 53.50 | 44.03 | 44.30 | 43.97 | 44.20 | 55.86 | 56.30 |
|  |  | 45.68 | 46.20 | 43.94 | 44.10 | 40.76 | 40.60 | 44.32 | 44.60 |
|  |  | 42.53 | 42.80 | 29.28 | 29.90 | 28.29 | 27.70 | 43.72 | 44.50 |
|  |  | 28.95 | 29.80 | 20.97 | 21.20 |  |  | 31.39 | 31.90 |
|  |  |  |  |  |  |  |  | 28.14 | 28.40 |
|  |  |  |  |  |  |  |  |  |  |
| **Literature** |  |  |  |  |  |  |  |  |  |
| Trisphaeridine **5** | |  | (Viladomat et al. 1997) | | | |  |  |  |
| 3-Epimacronine **6** | |  | (Viladomat et al. 1990) | | | | |  |  |
| Crinine acetate **8** | |  | (Ali et al. 1986) | | | | |  |  |
| 6α-OH-Buphanisine **9** | |  | (Frahm et al. 1985) | | | | | |  |
| Nerinine **10** |  |  | (de Andrade et al. 2014) | | | | |  |  |

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|  |  |  |  | |  |  |  |  |  |  |
| Pretazettine **11A** | |  | Compound **7** | |  | Pretazettine **11B** |  | Compound **12** |  |  |
| Our data | Literature |  | Our data | |  | Our data |  | Our data |  |  |
| DMSO-*d6* | CDCl3 |  | DMSO-*d6* | |  | DMSO-*d6* |  | DMSO-*d6* |  |  |
| 146.77 | 147.70 |  | 151.35 | |  | 146.62 |  | 168.45 |  |  |
| 145.76 | 146.50 |  | 148.21 | |  | 145.92 |  | 152.24 |  |  |
| 134.80 | 135.30 |  | 147.40 | |  | 134.98 |  | 150.13 |  |  |
| 129.43 | 129.10 |  | 147.07 | |  | 130.80 |  | 141.55 |  |  |
| 129.41 | 128.80 |  | 130.02 | |  | 130.37 |  | 140.63 |  |  |
| 128.60 | 127.40 |  | 128.36 | |  | 128.02 |  | 133.34 |  |  |
| 108.28 | 108.10 |  | 124.81 | |  | 107.65 |  | 119.88 |  |  |
| 104.11 | 104.80 |  | 124.15 | |  | 104.30 |  | 114.93 |  |  |
| 101.02 | 101.20 |  | 120.53 | |  | 101.02 |  | 109.29 |  |  |
| 92.64 | 93.90 |  | 103.20 | |  | 95.78 |  | 71.56 |  |  |
| 73.08 | 73.80 |  | 101.94 | |  | 77.24 |  | 67.00 |  |  |
| 72.69 | 73.10 |  | 98.06 | |  | 72.69 |  | 65.57 |  |  |
| 63.48 | 64.10 |  | 72.01 | |  | 63.86 |  | 60.37 |  |  |
| 55.25 | 56.10 |  | 54.94 | |  | 55.25 |  | 60.17 |  |  |
| 53.81 | 54.00 |  | 35.93 | |  | 54.09 |  | 56.20 |  |  |
| 45.80 | 46.20 |  |  | |  | 45.52 |  | 56.02 |  |  |
| 43.02 | 43.30 |  |  | |  | 42.95 |  | 44.34 |  |  |
| 29.65 | 30.20 |  |  | |  | 29.68 |  | 43.58 |  |  |
|  |  |  |  | |  |  |  | 31.47 |  |  |
|  |  |  |  | |  |  |  | 28.16 |  |  |
|  |  |  |  | |  |  |  | 22.88 |  |  |
|  |  |  |  | |  |  |  |  |  |  |
| **Literature** |  |  |  | |  |  |  |  |  |  |
| 3-methoxy-8,9-methylenedioxy-3,4-dihydrophenanthridine **7** | | | | | | (Hohmann et al. 2002) | | | | |
| Pretazettine (major epimer) **11A** | | |  | |  | (Baldwin and Debenham 2000) | | | |  |
| Pretazettine (major epimer) **11B** | | |  | |  | no reference found | |  |  |  |
| 6-dehydroxy-6-acetamido-Nerinine **12** | | | |  |  |  |  |  |  |  |

**References**

Ali, A.A., El Saved, H.M., Abdalliah, O.M., Steglich, W., 1986. Oxocrinine and other alkaloids from *Crinum americanum*. Phytochemistry 25, 2399–2401. https://doi.org/10.1016/S0031-9422(00)81704-5

Baldwin, S.W., Debenham, J.S., 2000. Total Syntheses of (−)-Haemanthidine, (+)-Pretazettine, and (+)-Tazettine. Org. Lett. 2, 99–102. https://doi.org/10.1021/ol9911472

Dashti, H., Westler, W.M., Markley, J.L., Eghbalnia, H.R., 2017. Unique identifiers for small molecules enable rigorous labeling of their atoms. Sci. Data 4, 170073. https://doi.org/10.1038/sdata.2017.73

de Andrade, J.P., Guo, Y., Font-Bardia, M., Calvet, T., Dutilh, J., Viladomat, F., Codina, C., Nair, J.J., Zuanazzi, J.A.S., Bastida, J., 2014. Crinine-type alkaloids from *Hippeastrum aulicum* and *H. calyptratum*. Phytochemistry 103, 188–195. https://doi.org/10.1016/j.phytochem.2014.03.007

Frahm, A.W., Ali, A.A., Ramadan, M.A., 1985. 13C nuclear magnetic resonance spectra of amaryllidaceae alkaloids. I—alkaloids with the crinane skeleton. Magn. Reson. Chem. 23, 804–808. https://doi.org/10.1002/mrc.1260231004

Hohmann, J., Forgo, P., Szabó, P., 2002. A new phenanthridine alkaloid from *Hymenocallis × festalis*. Fitoterapia 73, 749–751. https://doi.org/10.1016/S0367-326X(02)00240-X

Knolker, H., 2020. The Alkaloids. Elsevier.

Kobayashi, S., Kihara, M., Shingu, T., Shingu, K., 1980. Transformation of Tazettine to Pretazettine. Chem. Pharm. Bull. (Tokyo) 28, 2924–2932. https://doi.org/10.1248/cpb.28.2924

Pham, L.H., Gründemann, E., Wagner, J., Bartoszek, M., Döpke, W., 1999. Two novel Amaryllidaceae alkaloids from *Hippeastrum equestre* Herb.: 3-O-demethyltazettine and egonine. Phytochemistry 51, 327–332. https://doi.org/10.1016/S0031-9422(98)00743-2

Roberts, J.D., Crain, W.O., Wildman, W.C., 1971. Nuclear magnetic resonance spectroscopy. Carbon-13 spectra of nicotine, quinine, and some Amaryllidaceae alkaloids. J. Am. Chem. Soc. 93, 990–994. https://doi.org/10.1021/ja00733a035

Viet Nguyen, K., Laidmäe, I., Kogermann, K., Lust, A., Meos, A., Viet Ho, D., Raal, A., Heinämäki, J., Thi Nguyen, H., 2019. Preformulation Study of Electrospun Haemanthamine-Loaded Amphiphilic Nanofibers Intended for a Solid Template for Self-Assembled Liposomes. Pharmaceutics 11, 499. https://doi.org/10.3390/pharmaceutics11100499

Viladomat, F., Bastida, J., Tribo, G., Codina, C., Rubiralta, M., 1990. Alkaloids from *Narcissus bicolor*. Phytochemistry 29, 1307–1310. https://doi.org/10.1016/0031-9422(90)85448-O

Viladomat, F., Codina, C., Bastida, J., Mathee, S., Campbell, W.E., 1995. Further alkaloids from *Brunsvigia josephinae*. Phytochemistry 40, 961–965. https://doi.org/10.1016/0031-9422(95)00375-H

Viladomat, F., Sellés, M., Cordina, C., Bastida, J., 1997. Alkaloids from *Narcissus asturiensis*. Planta Med. 63, 583–583. https://doi.org/10.1055/s-2006-957781

Wang, S., Witek, J., Landrum, G.A., Riniker, S., 2020. Improving Conformer Generation for Small Rings and Macrocycles Based on Distance Geometry and Experimental Torsional-Angle Preferences. J. Chem. Inf. Model. 60, 2044–2058. https://doi.org/10.1021/acs.jcim.0c00025