SUPPLEMENTARY INFORMATION TO:

The three pillars of natural product dereplication. Alkaloids from the bulbs of *Urceolina peruviana* (C. Presl) J.F. Macbr. as a preliminary test case.

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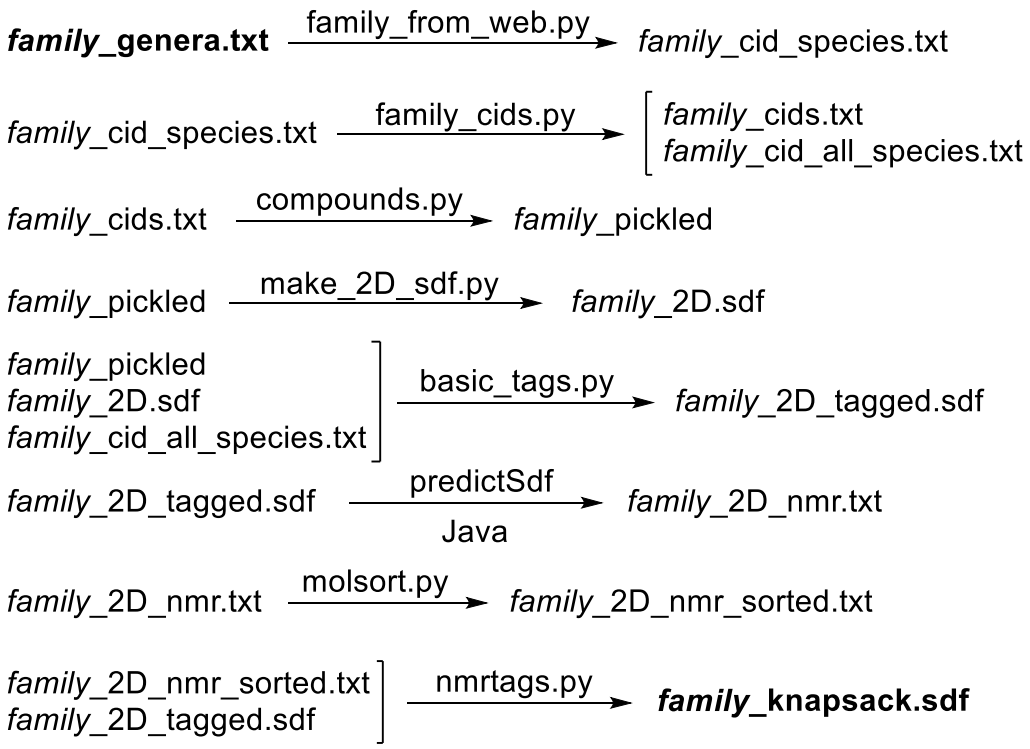
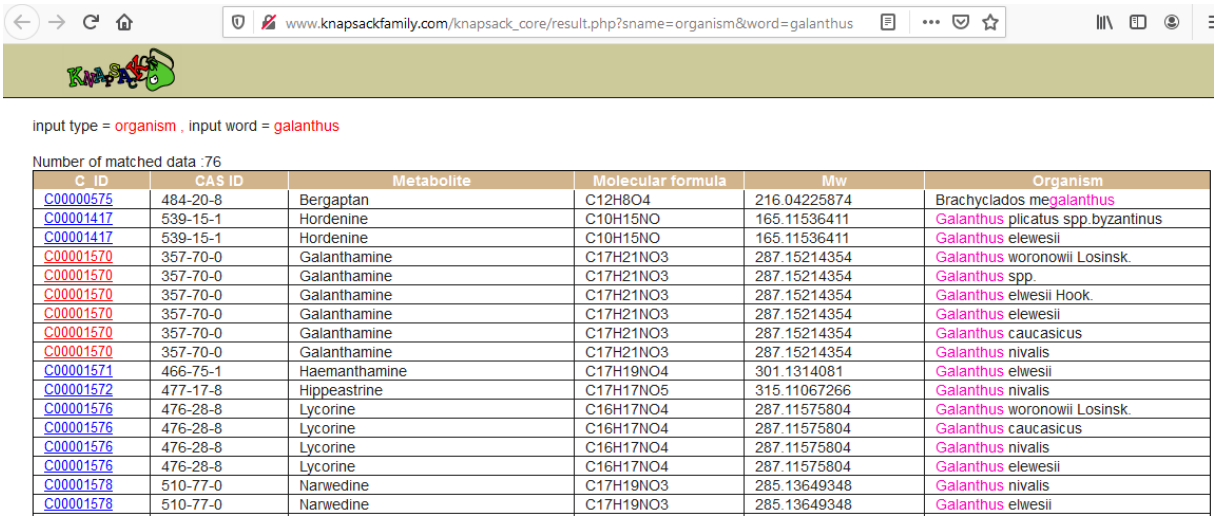


Figure S1. Step-by-step processing by KnapsackSearch of a list of organism genera (*family*_genera.txt, *family* being replaced by an organism family name or an alias, like amaryll standing for Amaryllidaceae) into an SDF file (*family*_knapsack.sdf) with automatically generated 2D structure, basic molecular properties, taxonomic data, and nmrshiftdb2-predicted ^{13}C NMR chemical shifts. All scripts are available from https://github.com/nuzillard/KnapsackSearch.



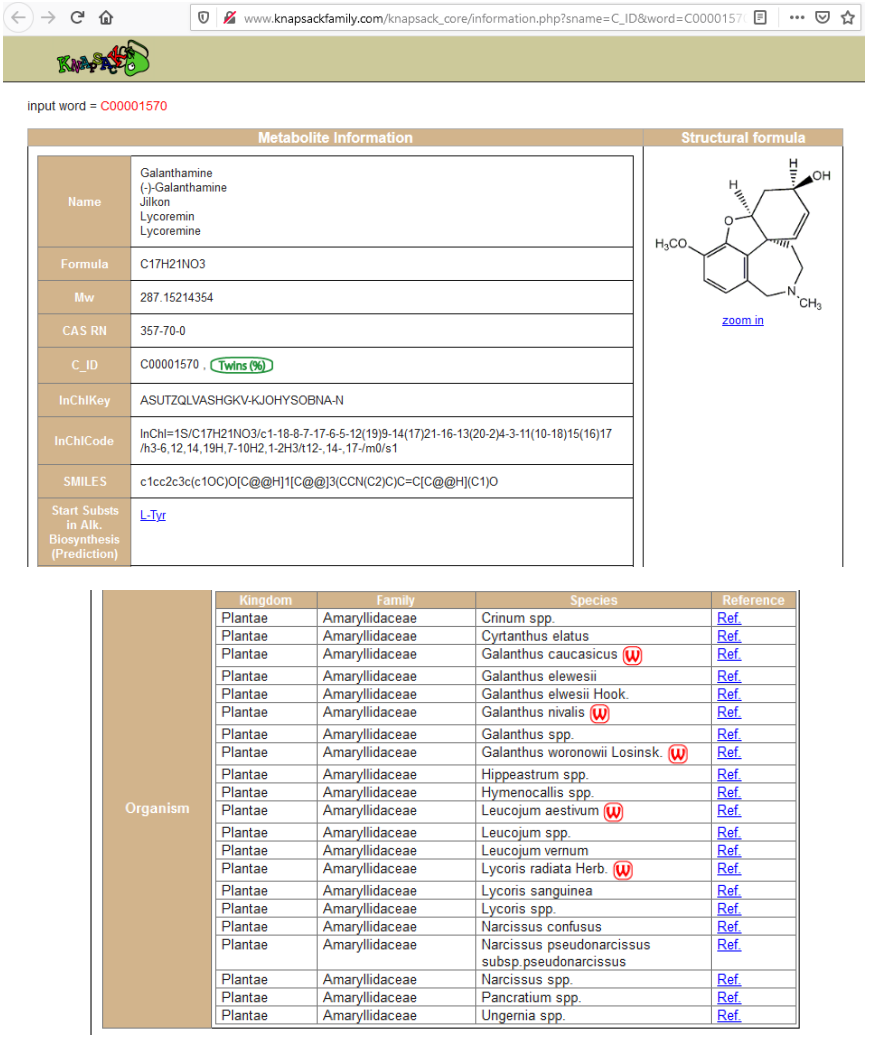
www.knapsackfamily.com/knapsack_core/result.php?sname=organism&word=galanthus

input type = organism , input word = galanthus

Number of matched data :76

C_ID	CAS ID	Metabolite	Molecular formula	Mw	Organism
C00000575	484-20-8	Bergaptan	C12H8O4	216.04225874	Brachyclados megalanthus
C00001417	539-15-1	Hordenine	C10H15NO	165.11536411	Galanthus plicatus spp.byzantinus
C00001417	539-15-1	Hordenine	C10H15NO	165.11536411	Galanthus elewesii
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus woronowii Losinsk.
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus spp.
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus elwesii Hook.
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus elewesii
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus caucasicus
C00001570	357-70-0	Galanthamine	C17H21NO3	287.15214354	Galanthus nivalis
C00001571	466-75-1	Haemanthamine	C17H19NO4	301.1314081	Galanthus elwesii
C00001572	477-17-8	Hippeastrine	C17H17NO5	315.11067266	Galanthus nivalis
C00001576	476-28-8	Lycorine	C16H17NO4	287.11575804	Galanthus woronowii Losinsk.
C00001576	476-28-8	Lycorine	C16H17NO4	287.11575804	Galanthus caucasicus
C00001576	476-28-8	Lycorine	C16H17NO4	287.11575804	Galanthus nivalis
C00001576	476-28-8	Lycorine	C16H17NO4	287.11575804	Galanthus elewesii
C00001578	510-77-0	Narwedine	C17H19NO3	285.13649348	Galanthus nivalis
C00001578	510-77-0	Narwedine	C17H19NO3	285.13649348	Galanthus elwesii

Figure S2a. Screenshot, response of http://www.knapsackfamily.com/knapsack_core/top.php when searching for Organism "Galanthus". The list of data items was truncated.



www.knapsackfamily.com/knapsack_core/information.php?sname=C_ID&word=C0000157

input word = C00001570

Metabolite Information	
Name	Galanthamine (-)-Galanthamine Jilkon Lycoremin Lycoremine
Formula	C17H21NO3
Mw	287.15214354
CAS RN	357-70-0
C_ID	C00001570 , Twins (%)
InChIKey	ASUTZQLVASHGKV-KJOHYSOBNA-N
InChICode	InChI=1S/C17H21NO3/c1-18-8-7-17-6-5-12(19)9-14(17)21-16-13(20-2)4-3-11(10-18)15(16)17/h3-6,12,14,19H,7-10H2,1-2H3/t12-,14-,17-/m0/s1
SMILES	c1cc2c3c(c1OC)O[C@@H]1[C@@]3(CCN(C2)C)C=C[C@@H](C1)O
Start Substs in Alk. Biosynthesis (Prediction)	L-Tyr

Structural formula

zoom in

Organism	Kingdom	Family	Species	Reference
	Plantae	Amaryllidaceae	Crinum spp.	Ref.
	Plantae	Amaryllidaceae	Cyrtanthus elatus	Ref.
	Plantae	Amaryllidaceae	Galanthus caucasicus (W)	Ref.
	Plantae	Amaryllidaceae	Galanthus elewesii	Ref.
	Plantae	Amaryllidaceae	Galanthus elwesii Hook.	Ref.
	Plantae	Amaryllidaceae	Galanthus nivalis (W)	Ref.
	Plantae	Amaryllidaceae	Galanthus spp.	Ref.
	Plantae	Amaryllidaceae	Galanthus woronowii Losinsk. (W)	Ref.
	Plantae	Amaryllidaceae	Hippeastrum spp.	Ref.
	Plantae	Amaryllidaceae	Hymenocallis spp.	Ref.
	Plantae	Amaryllidaceae	Leucojum aestivum (W)	Ref.
	Plantae	Amaryllidaceae	Leucojum spp.	Ref.
	Plantae	Amaryllidaceae	Leucojum vernum	Ref.
	Plantae	Amaryllidaceae	Lycoris radiata Herb. (W)	Ref.
	Plantae	Amaryllidaceae	Lycoris sanguinea	Ref.
	Plantae	Amaryllidaceae	Lycoris spp.	Ref.
	Plantae	Amaryllidaceae	Narcissus confusus	Ref.
	Plantae	Amaryllidaceae	Narcissus pseudonarcissus subsp.pseudonarcissus	Ref.
	Plantae	Amaryllidaceae	Narcissus spp.	Ref.
	Plantae	Amaryllidaceae	Pancratium spp.	Ref.
	Plantae	Amaryllidaceae	Ungernia spp.	Ref.

Figure S2b. Screenshot, response of http://www.knapsackfamily.com/knapsack_core/top.php when searching for C_ID C00001570 (galanthamine), upper part of screen, with molecular data and lower part with botanical data (truncated).

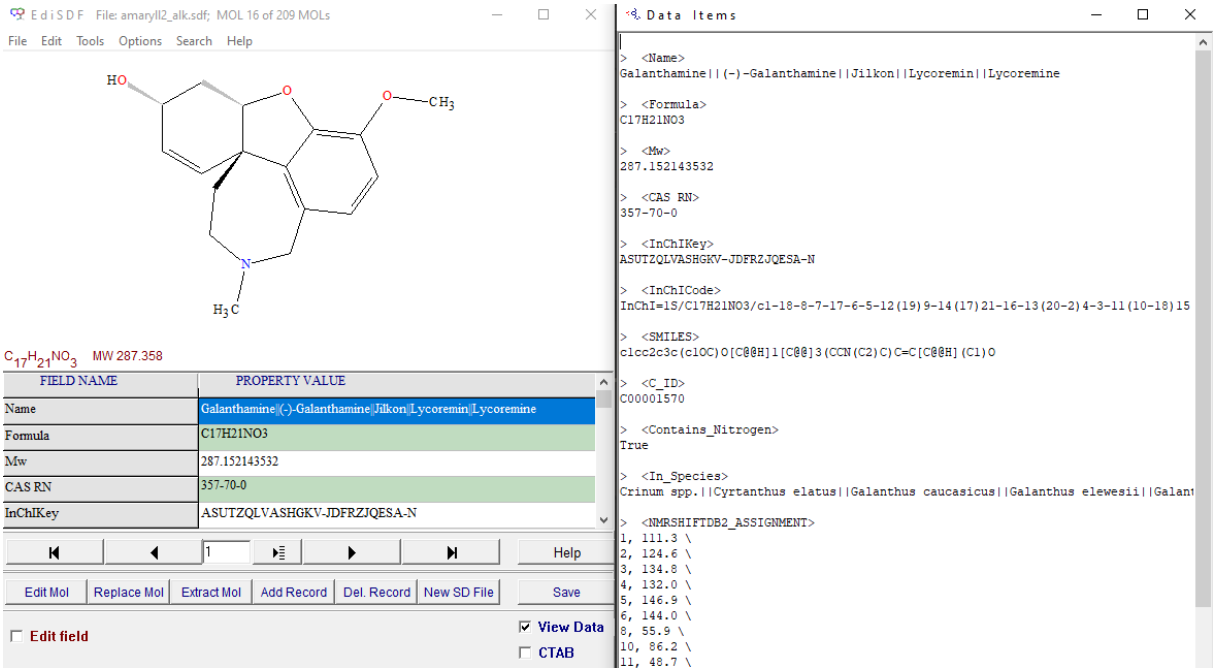


Figure S2c. Screenshot, view of galanthamine by EdiSDF as produced by KnapsackSearch and present in database DB2. The list of chemical shifts was truncated.

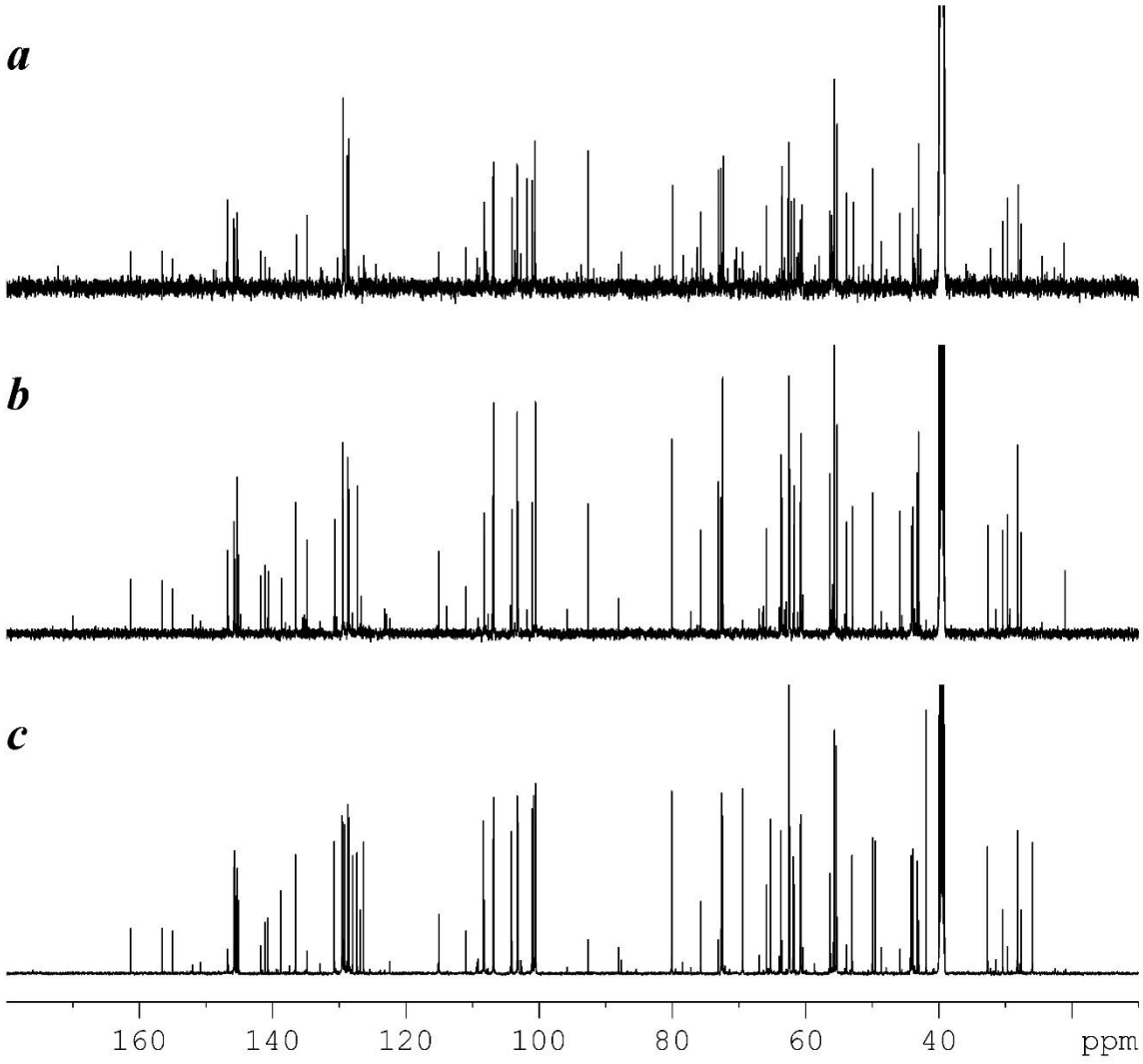


Figure S3. Comparison of the ^{13}C NMR spectra of extracts 1, 2, and 3, drawn in sub-figures *a*, *b*, and *c*, respectively.

1. Launch CNMR Predictor. ChemSketch window appears
2. Switch to Database window, bottom menu bar, item 7-Database. The Database interface appears
3. Create database. Database->New... from top menu bar. The "Create New Database" pop-up appears.
4. Indicate directory and name for the database location. Save. Leave passwords blank. OK.
5. Click "Database->Import" from top menu bar. The "Import" pop-up appears.
6. Indicate .sdf file directory and name. The "Import Options" pop-up appears
7. Check for "Search for Duplicated Chemical Structures" and select "Stop and Prompt". OK.
8. The "Import Information" pop-up apprears. OK. The first structure appears in the left-side panel
9. In the toolbar click on the "Copy Chemical Structure to Editor" button, on the left of the "Delete Record" button, the latter shows a red cross.
10. The ChemSketch window appears with the structure inside. Select All (Ctrl-A) and Copy (Ctrl-C) the structure.
11. Click on the "7-Database" button in the bottom menu bar. Back to the database panel.
12. Click on "ACD/Labs -> Spectrus". The Spectrus windows appears.
13. Paste the structure with Ctrl-V. The structure appears in the right-side panel.
14. Click on the pocket calculator icon at the very right of the tool bar of the right-side panel.
Possibly enlarge this panel to let the icon show up if hidden (This may happen).
15. Select HNMR under the calculator icon. The 1H-NMR spectrum and the parameter table show up in the center panel
16. Click "Database -> Update C+H NMR Database". The "Duplicated Structure" pop-up appears. Click "Update".
17. The database window pops-up with 1H NMR data tables in the center panel.
18. Click on "ACD/Labs -> Spectrus". The Spectrus windows appears.
19. Click on the pocket calculator icon at the very right of the tool bar of the right-side panel and select CNMR.
The 13C-NMR spectrum shows up in the center panel, under the 1H spectrum.
20. Click "Database -> Update C+H NMR Database". The "Duplicated Structure" pop-up appears. Click "Update".
21. The database window pops-up with 1H and 13C NMR data tables in the center panel.
22. Click on >> in the top tool bar to select the next molecule.
23. In the toolbar click on the "Copy Chemical Structure to Editor" button, on the left of the "Delete Record" button.
24. A pop-up appears to ask for deleting the existing structure in ChemSketch. Click the "Yes" button.
25. Select all and copy and go to the database window (7-Database, bottom menu bar). Select "ACD/Labs -> Spectrus"
26. Delete the two spectra, by clicking on the red cross that appears when the mouse hovers above the left-side orange spectrum bar.
Do not save the changes.
27. Copy the structure to the right panel of Spectrus with Ctrl-V and go back to step 14.
28. The process maybe stopped after step 21.
29. Click "Database -> Close" to close the database and "Database -> Exit" to exit the Database. The Spectrus database becomes visible
30. Click "File -> Exit" and then "No All". Spectrus and ChemSketch windows disappear.

Figure S4. Procedure for the semi-automatic supplementation of ACD/Labs databases with predicted chemical shifts. ACD C+H NMR Predictors and DB 2020 and 2019.

Substructure	Type	SMARTS
1	Lycorine	Oc1cc2C~3~C~C~C~C~C~4~C~C~N(~C~3~4)~Cc2cc1O
2	Homolycorine	Oc1cc2C~3~C~4~N~C~C~C~C~4~C~C~C~3OC(~O)c2cc1O
3	Narciclassine	Oc1cc2C~3~C~C~C~C~C~C~3~N~Cc2cc1O
4	Galanthamine	Oc1ccc(c24)C~N~C~C~C2~3~C~C~C~C~C~3Oc14
5	Crinine	Oc1cc2C~N(~C~C~4)~C~3~C~C~C~C~C~C~3~4c2cc1O
6	Tazettine	Oc1cc2COC~3~C~N~C~4~C~C~C~C~C~C~3~4c2cc1O
7	Norbelladine	c1cc(O)c(O)cc1C~N~C~Cc1ccc(O)cc1
8	Montanine	Oc1cc2C~N(~C~3)~C~4~C~C~C~C~C~C~4~C~3c2cc1O

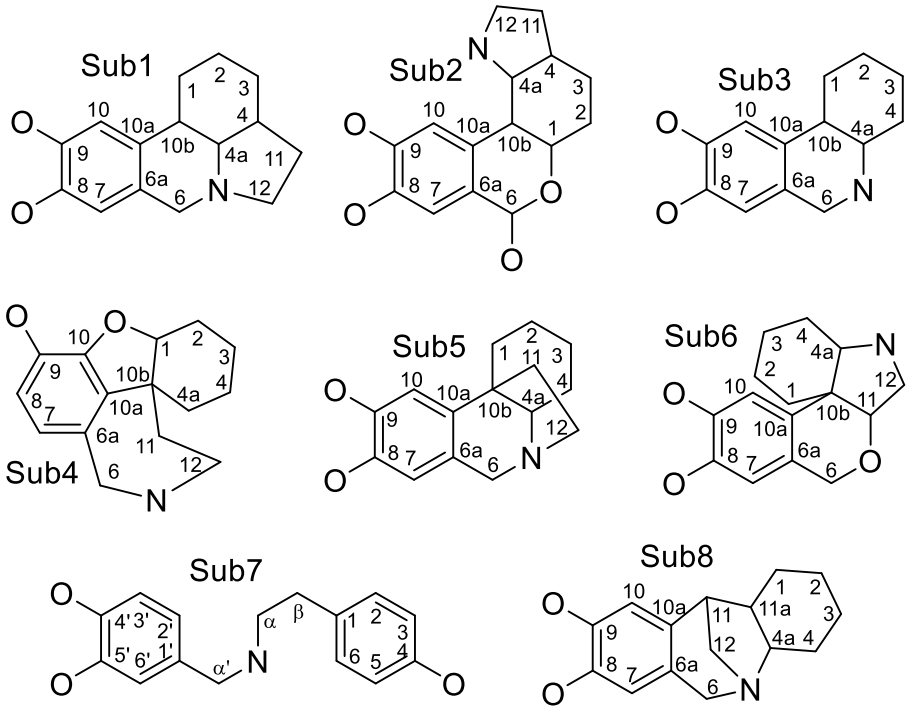


Figure S5. Substructures that define eight classes of Amaryllidaceae alkaloids. Sub3 is a substructure of Sub5 and Sub1, thus reducing to six the effective number of substructures.

A4	A7	A9	A11
145.7380(s)	161.2988(s)	145.7999(s)	145.5792(s)
145.6658(s)	156.5513(s)	145.2919(s)	145.1041(s)
129.5609(d)	155.0277(s)	136.5904(s)	138.8210(s)
129.1635(d)	141.8143(s)	129.5186(d)	130.7921(d)
127.9679(s)	141.1331(s)	128.7362(d)	128.4712(d)
126.3558(s)	140.6848(s)	127.3450(s)	126.9639(s)
108.3809(d)	115.0101(d)	106.8113(d)	106.8801(d)
104.1610(d)	110.9643(s)	103.2841(d)	103.1479(d)
101.0643(s)	108.2002(d)	100.5172(t)	100.4552(t)
100.8134(t)	75.7086(d)	80.0883(d)	62.4607(d)
72.6015(d)	65.8267(d)	72.4080(d)	62.3959(d)
69.4049(d)	61.6679(q)	63.7084(t)	61.9272(t)
65.2038(t)	60.7180(q)	62.4698(d)	53.0113(t)
60.7529(t)	56.3367(q)	60.7084(t)	44.1980(t)
55.3574(q)	55.7209(t)	55.6452(q)	43.8661(s)
49.4757(s)	43.9295(d)	49.8956(s)	32.7112(t)
41.8599(q)	43.2234(q)	28.1847(t)	
25.9311(t)	30.3999(t)		
	27.5896(t)		

Table S1. Lists of ^{13}C NMR chemical shifts drawn from the spectra of fractions A4, A7, A9, and A11. The number of attached protons, or H multiplicity, is given by symbols between parenthesis: s, d, t, and q for quarternary, methine, methylene, and methyl carbons, respectively. H multiplicity was derived from the inspection of the multiplicity-edited HSQC spectra of fractions.

Fraction	Database	Minimum number of matching C atoms	Tolerance (ppm)	Number of solutions	Solutions	Filter 1	Number of solutions	Solutions	Filter 2	Number of solutions	Solutions
	DB1			2	Taezttine, Criwelline						
	DB2			0							
A4	DB3	18	2	22	==>	18 C, 1-2 N	7	isomers of tazettine			
	DB3'			7	isomers of tazettine						
	DB4			1	Tazettine (flat)						
	DB1		2	1	Albomaculine						
			2								
		19	3	0							
	DB2		4								
		18	4	1	Secoplicamine (C26)	19 C, 1-2 N	0				
A7		17		5	==>		1	Albomaculine			
	DB3		4	2750	==>	19 C, 1-2 N	39	==>	$C_{19}H_{23}NO_5$	2	isomers of albomaculine
		17							$C_{19}H_{25}NO_5$	1	1-methylexcentricine
	DB3'		4	10	==>	19 C, 1-2 N	2	isomers of albomaculine			
	DB4			28			1	Albomaculine (flat)			
			2	0							
	DB1		3	1	Varadine (C18)	17 C, 1-2 N	0				
			4	10	==>		5	==>	C17H19NO4	2	isomers of haemanthamine
			2	0							
A9	DB2	17	3	2	isomers of haemanthamine						
	DB3		3	229	==>	17 C, 1-2 N	9	isomers of haemanthamine			
	DB3'		3	9	isomers of haemanthamine						
	DB4		3	18	==>	17C, 1-2 N	2	haemanthamine, haemanthidine	C17H19NO4	1	haemanthamine (flat)
	DB1		2	1	epi-vittatine						
			3	3	==>	16 C, 1-2 N	2	epi-vittatine, caranine			
			2	1	caranine						
	DB2		3	13	==>	16 C, 1-2 N	4	3 isomers of crinine, caranine			
A11		16	2	27	==>	16 C, 1-2 N	0				
	DB3		3	219			6	isomers of crinine			
			2	0							
	DB3'		3	42	==>	16 C, 1-2 N	6	isomers of crinine			
			2	0							
	DB4		3	17	==>	16C, 1-2 N	2	crinine, caranine (flat)			

Table S2. Tentative identification of compounds in DB1, DB2, DB3, DB3' and DB4 that fit with the ^{13}C NMR chemical shifts from fractions F4, F7, F9, and F11.