HETISANE-TYPE DITERPENOID ALKALOIDS

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UDC 547.944/945

Data in the literature up to 1998 on hetisane-type diterpenoid alkaloids isolated from plants of the genera Aconitum, Consolida, Delphinium, Thalictrum, *and* Spirea *are reviewed and systematized. Data on the chemistry and physicochemical methods of studying the structures and pharmacology of hetisane alkaloids are generalized. An alphabetical list of 107 hetisane alkaloids with an indication of the plant source, structure, characteristic derivatives, physicochemical data, and references to the original literature is presented.*

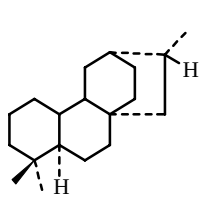
Key words: *Aconitum*, *Consolida*, *Delphinium*, *Thalictrum* (Ranunculaceae), *Spirea* (Rosaceae), hetisane-type C_{20}-diterpenoid alkaloids (chemical properties, spectral data, pharmacology).

A new group of natural compounds, hetisane-type alkaloids, has been clearly identified in recent decades in the chemistry of diterpenoid alkaloids (DA). The first representatives of this group, paniculatine (**81**) [1], hetisine (**32**), and kobusine (**68**) [2] were isolated in the 1930s and 1940s. However, their structures were elucidated much later, in the 1980s, owing to the development of instrumental methods and the ability to perform x-ray structure analysis (XSA).

Since the time when the structure of hetisine was established, many studies have been devoted to the isolation of this type of compounds from plants of the genera *Aconitum*, *Delphinium*, *Thalictrum*, *Consolida* (Ranunculaceae), and *Spirea* (Rosaceae). The unwavering interest in hetisane alkaloids, like other DA, is due to their complicated structures, interesting and unique chemistry, valuable pharmacological properties, and widespread popularity of plants containing these compounds in the folk medicine. At this time (1998), more than 100 hetisane-type representatives are known (Table 1). Hetisane itself (Fig. 1) has not been isolated from plants or synthesized.

The latest progress in the chemistry and pharmacology of DA has been reviewed [3-9].

The chemical structures of hetisane alkaloids are similar to those of atisane diterpenoids **108**, which contain the bicyclo-[2,2,2]-octane system [3]. In 1955, Wenkert [83] hypothesized that the precursors of atisane diterpenoids, like those of atisane-caurane alkaloids, are tricyclic pymarane diterpenoids **109**. Schemes have been proposed for the formation of the heterocyclic rings of atisine alkaloids **110**, from which a logical succession of forming the bridge bonds C14–C20 (**111**) and N–C6 (**112**) produces the hetisane carbon framework (**113**) [84]. The formation of the N–C6 bond is based on the structures of the natural alkaloids miyaconitine and miyaconitinone [84], which are analogs of the intermediate **112**.



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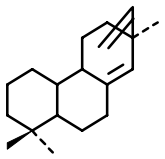

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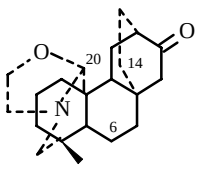

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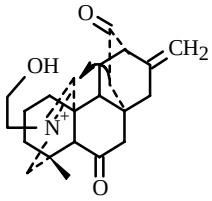

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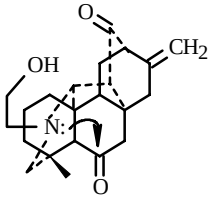
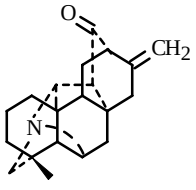


112



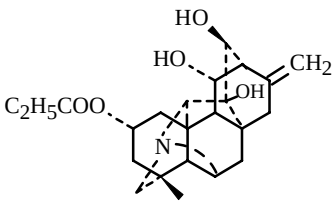
113

Aspects of the biogenesis of DA have been reviewed [85]. Alternate methods of forming the N–C6 bond, e.g., from talasamine-type alkaloids, were proposed.

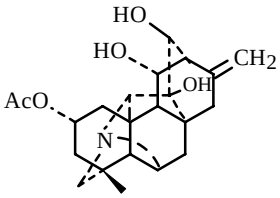
S. Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (99871) 120 64 75, e-mail: cnc@icps.org.uz. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 345-376, September-October, 2000. Original article submitted June 26, 2000.

0009-3130/00/3605-0419$25.00

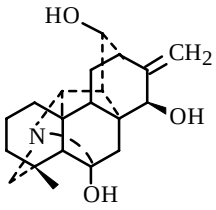
TABLE 1. Physical Properties and Spectral Data of Hetisane Alkaloids*



1. Acoridine [10a]



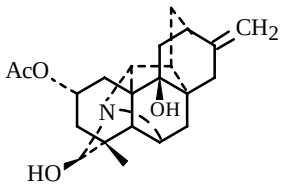
2. Acorine (guan-fu base Y) [10b]



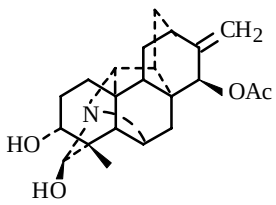
3. Acorientine

Aconitum orientale [11]
$C_{20}H_{27}NO_3$: 329
$[\alpha]_D$ +13.5° ($CHCl_3$)
IR: 3360, 2940, 2820, 1660, 1560, 1450, 1410, 1220, 1100, 1040, 1020, 910, 760
Mass: 329 (M^+, 23), 314 (7), 301 (7), 284 (5), 162 (100), 127 (50), 63 (75)
PMR: 1.42 (3H, s, 18-CH_3), 2.45 (1H, br. s, H-14), 3.86 (1H, s, H-20), 3.98 (1H, d, J = 5.0, H-13), 4.02 (1H, s, H-15α), 5.16, 5.27 (1H each, br. s, H-17)
^{13}C NMR:

C-1	39.3	C-8	40.9	C-15	73.6
2	18.9	9	54.1	16	150.3
3	35.1	10	49.6	17	116.1
4	35.9	11	37.6	18	29.9
5	59.3	12	39.5	19	57.3
6	100.9	13	72.0	20	67.2
7	46.7	14	40.7		



4. Acsinatine [10c]



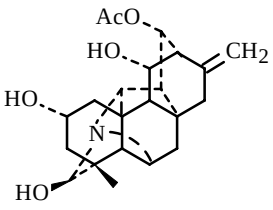
5. Andersobine

Delphinium andersonii Gray [12]
$C_{22}H_{29}NO_4$: 371
mp: 310° (CH_3OH) (dimethylaminobenzoate, 204-207°C)
IR: 3470, 1730, 1460, 1375, 1235, 1027, 960, 908, 870

*^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with the exception of cases mentioned in the Table (δ ppm, J Hz).

Mass: 371 (M^+, 1), 353 (100), 311 (8), 209 (22), 189 (10), 172 (10), 161 (20), 133 (18), 117 (18), 105 (25), 91 (30), 43 (70)
PMR (C_5D_5N): 1.08 (1H, td, J = 13.0, 3.0, 3.0, H-13α), 1.42 (1H, m, H-1β), 1.50 (1H, s, H-5), 1.64 (3H, s, 18-CH_3), 1.68 (1H, m, H-11β), 1.71 (1H, m, H-13β), 1.78 (1H, m, H-7β), 1.82 (2H, m, H-1α, H-9), 1.84 (1H, m, H-2α), 1.91 (1H, m, H-11α), 2.08 (2H, m, H-2β, H-14), 2.14 (1H, m, H-12), 2.16 (3H, s, OAc), 2.72 (1H, s, H-20), 3.83 (1H, dd, J = 11.4, 5.5, H-3), 3.86 (1H, s, H-6), 4.89 (1H, s, H-19), 4.94 (1H, s, 19-OH), 5.00, 5.18 (1H each, t, J = 1.6, H-17), 5.67 (1H, t, J = 1.0, H-15α), 6.08 (1H, d, J = 4.5, 3-OH)
^{13}C NMR:

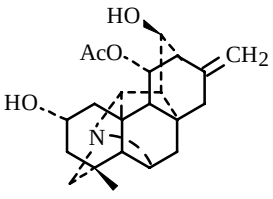
C-1	26.7	C-9	45.1	C-17	110.5
2	29.4	10	50.1	18	20.4
3	74.5	11	27.0	19	89.3
4	49.4	12	34.3	20	71.4
5	63.0	13	33.7	C=O	171.2
6	62.1	14	44.1	|	
7	33.0	15	73.0	CH_3	21.2
8	44.7	16	152.8		



6. 13-Acetylvakhmatine

Consolida ambigua L. P. W. Ball and V. H. Heywood [13]
$C_{22}H_{29}NO_5$: 387
mp: amorph.
$[\alpha]_D$ -20° ($CHCl_3$)
IR: 3450, 1720, 1455, 1375, 1250, 1030, 960, 880
PMR: 1.00 (3H, s, 18-CH_3), 1.45 (1H, s, H-5), 1.55 (1H, dd, J = 7.8, 2.1, H-3β), 1.56 (1H, m, H-7β), 1.71 (1H, dd, J = 14.0, 2.7, H-7α), 1.82 (1H, dd, J = 15.0, 4.0, H-1β), 1.91 (1H, d, J = 9.0, H-9), 1.98 (1H, br. d, J = 7.8, H-3α), 2.03, 2.18 (2H, AB, J = 18.0, H-15), 2.22 (3H, s, OAc), 2.38 (1H, d, J = 9.0, H-14), 2.42 (1H, d, J = 2.5, H-12), 2.66 (1H, br. d, J = 15.0, H-1α), 3.28 (1H, s, H-20), 3.55 (1H, br. s, $W_{1/2}$ = 4.0, H-6), 4.18 (1H, br. s, $W_{1/2}$ = 8.0, H-2β), 4.23 (1H, d, J = 9.0, H-11β), 4.70 (1H, s, H-17), 4.71 (1H, s, H-19), 4.86 (1H, s, H-17), 5.00 (1H, br. d, J = 9.0, H-13β)
^{13}C NMR:

C-1	32.8	C-9	55.1	C-17	108.7
2	66.1	10	50.2	18	22.7
3	40.7	11	75.8	19	90.9
4	42.0	12	48.5	20	65.0
5	61.6	13	76.6	C=O	172.8
6	60.2	14	49.9	|	
7	35.6	15	33.7	CH_3	21.1
8	44.2	16	144.8		

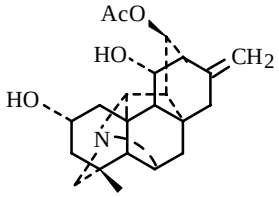


7. 11-Acetylhetisine

Delphinium nuttallianum Pritz [14]
$C_{22}H_{29}NO_4$: 371
mp: 264-266°C (acetone-hexane) [15]
IR: 3420, 3090, 1730, 1650, 1460, 1435, 1420, 1375, 1340, 1310, 1300, 1250, 1215, 1180, 1152, 1140, 1115, 1085, 1070, 1055, 1030, 990, 975, 960, 940, 910, 880, 850, 815 [15]
Mass: 371 (M^+, 20), 354 (18), 328 (15), 294 (6), 282 (5), 43 (100) [15]
PMR: 1.00 (3H, s, 18-CH_3), 2.10 (3H, s, OAc), 3.82 (1H, br. s, H-20), 4.19 (1H, br. d, J = 8.0, H-13α), 4.71, 4.91 (1H each, br. s, H-17), 5.13 (1H, d, J = 9.0, H-11β) [15]

^{13}C NMR [15]:

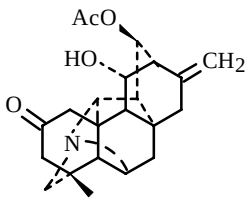
C-1	32.6	C-9	53.3	C-17	108.1
2	66.8	10	50.4	18	29.8
3	39.1	11	76.7	19	63.6
4	36.5	12	48.1	20	67.9
5	61.3	13	70.9	C=O	171.1
6	64.4	14	52.8	|	
7	36.5	15	34.1	CH_3	21.6
8	43.9	16	146.1		



8. 13-Acetylhetisine

Delphinium nuttallianum Pritz [16]
$C_{22}H_{29}NO_4$: 371
mp: 241-243°C [15] (perchlorate 273°C) [16]
IR: 3410, 3070, 1730, 1650, 1460, 1435, 1420, 1375, 1360, 1340, 1300, 1250, 1215, 1180, 1155, 1140, 1115, 1085, 1070, 1055, 1030, 990, 980, 960, 940, 910, 880, 850, 820 [15]
Mass: 371 (M^+, 10), 354 (3), 312 (18), 282 (5), 43 (100) [15]
PMR: 0.97 (3H, s, 18-CH_3), 2.17 (3H, s, OAc), 3.23 (1H, br. s, H-6β), 3.49 (1H, s, H-20), 4.19 (1H, br. s, $W_{1/2}$ = 10.0, H-2β), 4.24 (1H, br. d, J = 8.5, H-11β), 4.72, 4.88 (1H each, br. s, H-17), 5.13 (1H, br. d, J = 9.0, H-13α) [15]
^{13}C NMR:

C-1	33.8	C-9	55.2	C-17	108.7
2	66.7	10	50.6	18	29.7
3	40.3	11	75.6	19	63.2
4	36.6	12	48.5	20	68.6
5	61.5	13	74.5	C=O	170.3
6	64.3	14	50.4	|	
7	36.0	15	33.5	CH_3	21.2
8	43.6	16	144.8		

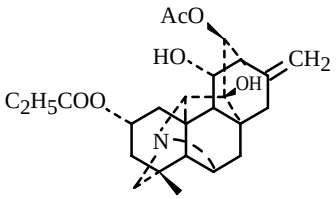


9. 13-Acetylhetisinone

Delphinium cardiopetalum DC. [15], *D. gracile* DC. [17], *D. peregrinum* var. elongatum Boiss [18]
$C_{22}H_{27}NO_4$: 369

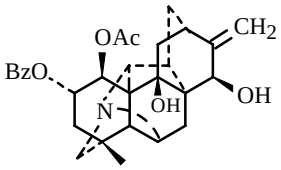
^{13}C NMR [19]:

C-1	45.2	C-9	54.7	C-17	109.9
2	213.0	10	55.5	18	28.7
3	50.2	11	74.4	19	64.7
4	42.8	12	48.4	20	70.7
5	60.9	13	73.6	C=O	170.3
6	65.3	14	49.9	|	
7	36.0	15	33.7	CH_3	21.1
8	44.7	16	144.5		



10. 13-Acetyl-14-hydroxy-2-propionylhetisine

Aconitum coreanum (Levl.) Rapaics [6]
$C_{25}H_{33}NO_6$: 443

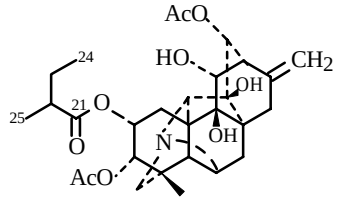


11. 1-Acetylhypognavine

Aconitum sanyoense Nakai var. tonense Nakai [20]
$C_{29}H_{33}NO_6$: 491
mp: 127-128°C (dec., acetone)
$[\alpha]_D$ +116.7° ($CHCl_3$)
IR: 3450, 2950, 1730, 1272, 1239
Mass: 491 (M^+, 1), 432 (100)
PMR: 1.10 (3H, s, 18-CH_3), 2.13 (3H, s, OAc), 2.72 (1H, s, H-5), 3.18 (1H, s, H-20), 3.47 (1H, br. s, H-6), 4.07 (1H, s, H-15), 5.02, 5.05 (1H each, s, H-17), 5.26 (1H, m, H-2), 5.44 (1H, d, J = 2.0, H-1), 7.44-8.00 (5H, H-Ar)
^{13}C NMR:

C-1*	70.2	C-9	79.8	C-17	109.9	4	133.3
2*	70.3	10	54.4	18	29.2	1β-CO	169.6
3	33.5	11	39.3	19	63.5	|	
4	35.7	12	34.8	20	72.2**	CH_3	21.2
5	51.5	13	33.1	Ar-CO	165.0		
6	64.7	14	42.2	Ar-1	129.7		
7	28.9	15	72.6**	2,6	129.6		
8	44.7	16	154.5	3,5	128.7		

*,**Assignments may be interchanged.

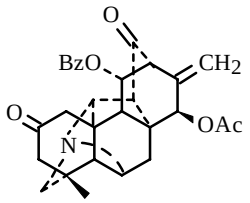


12. 13-Acetylglanduline

Consolida glandulosa (Boiss. et Huet), Bornm. [21]
$C_{29}H_{39}NO_9$: 545
mp: 110-115°C
$[\alpha]_D$ +15.2°
IR: 3393, 2930, 1731, 1657, 1578, 1460, 1368, 1233, 1184, 1147, 1098, 1036, 1024, 975, 883
Mass: 545 (M^+, 3), 528 (2), 503 (10), 502 (15), 487 (30), 486 (100), 475 (5), 474 (6), 472 (12), 458 (5), 445 (9), 444 (33), 430 (5), 426 (5), 402 (21), 384 (13), 360 (15), 342 (21), 324 (31), 314 (10), 312 (7), 297 (10), 296 (7), 174 (10), 144 (12), 131 (9), 105 (11), 91 (10), 85 (11), 83 (10), 81 (10), 71 (11), 57 (69)
PMR ($CDCl_3$—CD_3OD, 9:1): 0.89 (3H, t, J = 7.4, H-24), 1.03 (3H, s, 18-CH_3), 1.23 (3H, d, J = 7.0, H-25), 1.48, 1.68 (1H each, ddq, J = 14.6, 7.3, 7.3, H-23), 1.70 (1H, dd, J = 13.4, 3.0, H-7α), 1.75 (1H, dd, J = 13.8, 2.2, H-7β), 1.99 (1H, d, J = 18.0, H-15β), 1.99 (3H, s, OAc), 2.02 (3H, s, OAc), 2.04 (1H, d, J = 18.0, H-15α), 2.09 (1H, dd, J = 16.6, 4.7, H-1β), 2.36 (1H, sext., J = 7.0, H-22), 2.54 (1H, d, J = 12.5, H-19β), 2.59 (1H, s, H-5), 2.65 (1H, d, J = 2.2, H-12), 3.10 (1H, br. s, $W_{1/2}$ = 6.1, H-6), 3.13 (1H, dd, J = 16.6, 2.0, H-1α), 3.38 (1H, d, J = 12.5, H-19α), 3.62 (1H, s, H-20), 4.10 (1H, s, H-11β), 4.78 (1H, s, H-17), 4.90 (1H, d, J = 4.7, H-3β), 4.96 (1H, d, J = 2.2, H-13β), 4.97 (1H, s, H-17), 5.50 (1H, m, $W_{1/2}$ = 14.0, H-2β)

^{13}C NMR ($CDCl_3$—CD_3OD, 9:1):

C-1	28.8	C-9	80.9	C-17	109.5	C-25	17.1
2	68.1	10	47.3	18	25.7	3αC=O	170.6
3	74.2	11	84.0	19	59.9	|	
4	41.8	12	48.4	20	68.0	CH_3	20.7
5	55.7	13	80.4	21	175.9	3αC=O	169.8
6	61.8	14	77.3	22	41.3	|	
7	26.4	15	27.9	23	26.1	CH_3	21.4
8	50.6	16	143.1	24	11.5		

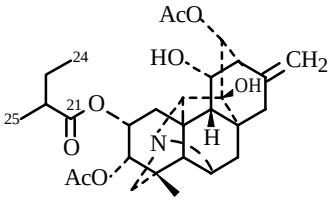


13. 15-Acetyl-13-dehydrocardiopetamine

Aconitum napellus L. s. Str. (*A. anglicum* Stapf) [22]
$C_{29}H_{29}NO_6$: 487
mp: 253-255°C
$[\alpha]_D$ -46°
IR: 1725, 1705, 1240, 1225, 1090, 1020, 710 [22]
Mass: 487 (M^+, 24), 366 (12), 338 (7), 278 (6), 233 (8), 105 (100), 77 (35), 43 (35) [22]
PMR: 1.12 (3H, s, 18-CH_3), 1.87, 1.93 (1H each, dd, J = 10.0, 2.2, H-7), 2.08 (1H, s, H-5), 2.17 (3H, s, OAc), 2.21 (1H, d, J = 13.7, H-19β), 2.41 (1H, d, J = 14.0, H-1β), 2.56 (1H, d, J = 1.8, H-14), 2.71 (1H, d, J = 13.2, H-19α), 2.75 (1H, d, J = 14.0, H-1α), 2.80 (1H, s, H-12), 2.91 (1H, dd, J = 8.5, 2.1, H-9), 3.16 (1H, s, H-20), 3.40 (1H, br. s, $W_{1/2}$ = 7.0, H-6), 5.34, 5.52 (1H each, s, H-17), 5.50 (1H, s, H-15), 5.68 (1H, d, J = 8.4, H-11), 7.48-7.95 (5H, m, H-Ar) [22]
^{13}C NMR [19]:

C-1	45.7	C-9	49.8	C-17	121.3	Ar-1	129.9
2	209.6	10	54.5	18	28.7	2,6	128.9
3	49.7	11	71.9	19	64.2	3,5	128.9
4	42.6	12	57.7	20	71.9	4	133.9
5	60.0	13	204.9	Ar-CO	166.2	CO	170.8
6	65.5	14	58.8			|	
7	31.6	15	71.7			CH_3	21.3
8	48.2	16	138.7				

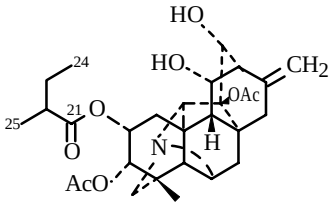
14. 13-Acetyl-9-deoxyglanduline



Consolida glandulosa (Boiss. et Huet) Bornm. [21]
$C_{29}H_{39}NO_8$: 529
mp: 154-156°C
$[\alpha]_D$ +46.6°
IR: 3406, 2919, 2840, 1736, 1636, 1573, 1549, 1512, 1436, 1369, 1236, 1179, 1142, 1092, 1062, 1029, 975, 925, 883
Mass: 529 (M^+, 7), 512 (7), 498 (6), 486 (24), 471 (30), 470 (100), 456 (12), 446 (18), 444 (1), 440 (2), 428 (3), 410 (7), 386 (17), 368 (9), 342 (5), 326 (13), 308 (28), 298 (22), 174 (15), 144 (10), 105 (9), 91 (8), 85 (9), 69 (10), 57 (52), 55 (15)
PMR: 0.89 (3H, t, J = 7.4, H-24), 1.02 (3H, s, 18-CH_3), 1.25 (3H, d, J = 7.0, H-25), 1.41 (1H, dd, J = 14.0, 2.5, H-7β), 1.48, 1.69 (1H each, ddq, J = 14.0, 7.0, 7.0, H-23), 1.79 (1H, s, H-5), 1.89 (1H, dd, J = 14.0, 3.4, H-7α), 1.99 (3H, s, OAc), 2.01 (3H, s, OAc), 2.02 (1H, m, H-15β), 2.04 (1H, d, J = 8.9, H-9), 2.07 (1H, dd, J = 16.2, 4.4, H-1β), 2.17 (1H, d, J = 17.9, H-15α), 2.35 (1H, sext., J = 7.0, H-22), 2.50 (1H, d, J = 12.5, H-19β), 2.64 (1H, d, J = 2.5, H-12), 3.07 (1H, dd, J = 16.2, 2.2, H-1α), 3.13 (1H, br. s, $W_{1/2}$ = 6.4, H-6), 3.35 (1H, d, J = 12.5, H-19α), 3.54 (1H, s, H-20), 4.28 (1H, d, J = 8.9, H-11β), 4.77, 4.97 (1H each, s, H-17), 4.98 (1H, d, J = 4.4, H-3β), 5.06 (1H, t, J = 2.2, H-13β), 5.50 (1H, m, $W_{1/2}$ = 14.0, H-2β)

^{13}C NMR:

C-1	29.7	C- 13	81.1	C-25	17.2
2	68.0	14	78.8	3αC=O	170.3
3	74.1	15	30.7	|	
4	42.2	16	143.3	CH_3	20.7
5	61.6	17	109.5	13αC=O	169.6
6	62.6	18	25.4	|	
7	31.6	19	59.6	CH_3	21.4
8	44.7	20	69.5		
9	53.2	21	175.7		
10	45.9	22	41.4		
11	74.7	23	26.1		
12	49.7	24	11.6		

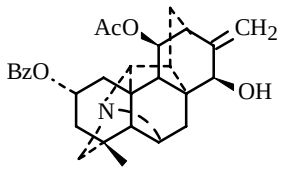


15. 14-Acetyl-9-deoxyglanduline

Consolida glandulosa (Boiss. et Huet) Bornm. [21]
$C_{29}H_{39}NO_8$: 529
mp: 145-148°C
$[\alpha]_D$ +20°

IR: 3409, 2951, 2929, 1735, 1652, 1567, 1457, 1237, 1183, 1148, 1091, 1061, 1040, 975, 896, 872
Mass: 529 (M^+, 0.1), 503 (1), 487 (18), 473 (9), 470 (10), 459 (10), 458 (7), 456 (5), 445 (6), 444 (8), 442 (10), 431 (8), 430 (9), 429 (29), 428 (100), 415 (11), 414 (42), 410 (8), 396 (3), 386 (6), 344 (9), 326 (9), 308 (4), 174 (5), 146 (2), 144 (2), 105 (2), 94 (2), 85 (2), 60 (8), 57 (14), 45 (8), 43 (11)
PMR: 0.94 (3H, t, J = 7.4, H-24), 1.12 (3H, s, 18-CH_3), 1.21 (3H, d, J = 7.0, H-25), 1.49 (1H, m, J = 14.0, 7.0, 7.0, H-23), 1.50 (1H, br. d, J = 14.0, H-7β), 1.70 (1H, ddq, J = 14.0, 7.0, 7.0, H-23), 1.98 (1H, s, H5), 1.99 (3H, s, OAc), 2.00 (3H, s, OAc), 2.04 (1H, d, J = 17.7, H-15β), 2.08 (1H, d, J = 8.7, H-9), 2.11 (1H, dd, J = 14.5, 5.5, H-1β), 2.15 (1H, d, J = 17.7, H-15α), 2.16 (1H, dd, J = 14.0, 3.5, H-7α), 2.46 (1H, sext. J = 7.0, H-22), 2.56 (1H, s, H-12), 2.73 (1H, d, J = 12.5, H-19β), 3.03 (1H, br. d, J = 15.5, H-1α), 3.51 (1H, br. s, $W_{1/2}$ = 6.3, H-6), 3.65 (1H, d, J = 12.5, H-19α), 4.14 (1H, s, H-13β), 4.21 (1H, s, H-20), 4.24 (1H, d, J = 8.8, H-11β), 4.73, 4.93 (1H each, s, H-17), 4.95 (1H, d, J = 4.6, H-3β), 5.46 (1H, m, $W_{1/2}$ = 14.0, H-2β)
^{13}C NMR:

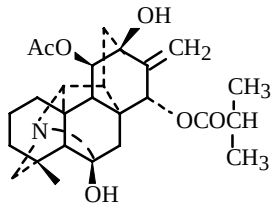
C-1	31.1	C-9	53.3	C-17	108.7	C-25	17.0
2	67.2	10	46.1	18	22.5	3αC=	170.0
3	73.1	11	75.6	19	58.6	|	
4	41.1	12	51.6	20	69.2	CH_3	20.7
5	60.4	13	80.8	21	175.6	14βC=O	177.6
6	63.2	14	80.2	22	41.5	|	
7	31.3	15	30.5	23	26.6	CH_3	20.6
8	44.0	16	143.0	24	11.5		



16. 11-Acetylisohypognavine

Aconitum japonicum Thunb [23]
$C_{29}H_{33}NO_5$: 475
mp: 187-188.5°C (dec., acetone)
$[\alpha]_D$ +74.1° ($CHCl_3$)
UV: 230, 274.5 (4.03, 2.84)
IR: 3420, 1735, 1720, 1280, 1250, 715

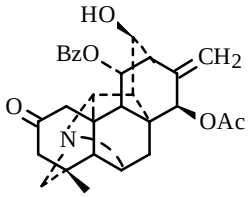
Mass: 475 (M^+, 21), 432 (8), 354 (100)
PMR: 1.02 (3H, s, 18-CH_3), 1.98 (3H, s, OAc), 3.94 (1H, d, J = 8.0, H-15), 5.06 (1H, d, J = 5.0, H-11), 5.00, 5.19 (1H each, s, H-17), 5.50 (1H, m, H-2), 7.40-7.58 (3H, H-Ar), 7.98 (2H, dd, J = 6.0, 2.0, H-Ar)



17. 11-Acetylcardionine

Delphinium gracile DC [24]
$C_{26}H_{35}NO_6$: 457
mp: amorph.
$[\alpha]_D$ -5.71° ($CHCl_3$)
IR: 3540, 3380, 2895, 1710, 1230, 1140, 1050, 895
Mass: 457 (M^+, 79), 414 (24), 397 (29), 370 (12), 369 (19), 326 (22), 310 (35), 309 (27), 308 (21), 298 (14), 188 (12), 163 (38), 162 (41), 161 (28), 160 (36), 137 (20), 105 (18), 91 (27), 79 (18), 77 (15), 71 (16), 55 (18), 43 (100), 41 (46)
PMR: 1.20 (6H, d, J = 7.0, H-23, H-24), 1.33 (3H, s, 18-CH_3), 1.56 (1H, s, H-5), 1.65 (1H, d, J = 2.0, H-9), 2.04 (3H, s, OAc), 2.32 (1H, br. d, J = 10.8, $W_{1/2}$ = 7.5, H-14), 2.37 (1H, d, J = 12.2, H-19α), 2.59 (1H, s, H-20), 2.63 (1H, J = 7.0, H-22), 3.08 (1H, d, J = 12.2, H-19β), 4.99 (1H, s, H-11α), 5.01, 5.34 (1H each, d, J = 2.5, H-17), 5.68 (1H, t, J = 2.2, H-15β)
^{13}C NMR:

C-1	35.6	C-9	56.3	C-17	109.4	11βC=O	172.2
2	19.4	10	50.4	18	30.6	|	
3	27.7	11	76.3	19	60.3	CH_3	21.4
4	38.2	12	73.1	20	73.4		
5	61.3	13	36.2	21	177.1		
6	99.0	14	40.9	22	34.3		
7	39.6	15	71.1	23	19.2		
8	45.8	16	148.0	24	19.3		

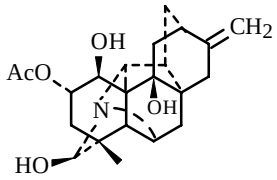


18. 15-Acetylcardiopetamine

Aconitum napellus L. s. Str., (*A. anglicum* Stapf) [22], *Delphinium cardiopetalum* DC [25]
$C_{29}H_{31}NO_6$: 489
mp: 236-237°C [25]
$[\alpha]_D$ +12° (alcohol) [25], {aminoalcohol 306-308°C (dec.)} [25]
IR: 3425, 1735, 1710, 1650, 1285, 1230, 720 [25]
Mass: 489 (M^+, 100), 430 (11), 385 (10), 384 (41), 369 (13), 368 (53), 340 (18), 308 (14), 105 (100), 77 (52), 43 (25) [22]
PMR: 1.10 (3H, s, 18-CH_3), 1.82 (2H, m, H-7), 2.02 (1H, s, H-5), 2.10 (3H, s, OAc), 2.22 (1H, d, J = 12.0, H-19β), 2.28 (1H, d, J = 13.3, H-1β), 2.29 (1H, d, J = 10.0, H-14), 2.58 (1H, d, J = 2.5, H-12), 2.71 (1H, d, J = 12.0, H-19α), 2.71 (1H, d, J = 9.0, H-9), 3.11 (1H, s, H-20), 3.37 (1H, br. s, $W_{1/2}$ = 8.0, H-6), 3.48 (1H, d, J = 13.2, H-1α), 4.18 (1H, br. d, J = 9.7, $W_{1/2}$ = 6.0, H-13), 5.15 (1H, s, H-15), 5.26, 5.34 (1H each, s, H-17), 5.57 (1H, d, J = 9.0, H-11), 7.42-8.08 (5H, m, H-Ar) [22]
^{13}C NMR [19]:

C-1	44.1	C-9	49.4*	C-17	116.5	4	133.9
2	212.0	10	55.0	18	28.6	CO	171.0
3	50.0	11	75.1	19	64.6	|	
4	42.6	12	47.8	20	70.1	CH_3	21.3
5	60.2	13	69.6	Ar-CO	166.6		
6	65.2	14	49.6*	Ar-1	129.8		
7	32.9	15	72.0	2,6	129.8		
8	48.1	16	144.7	3,5	128.7		

*Assignments may be interchanged.

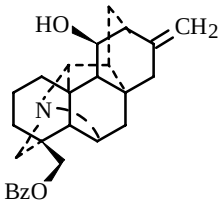


19. 2-Acetylseptentriosine

Aconitum septentrionale [26]
$C_{22}H_{29}NO_5$: 387
mp: 182-184°C (ether—hexane)
$[\alpha]_D$ +6.4° (alcohol)
{1,19-diAc, 210.5-212.5°C (acetone), aminoalcohol (septentriosine) 259-262°C (methanol)}
IR: 3560, 3470, 3440, 3320, 1730, 1705, 1650
Mass: 387 (M^+, 3), 370 (3), 345 (1), 327 (6), 309 (5), 105 (7), 91 (2), 56 (16), 43 (100)
PMR: 1.08 (3H, s, 18-CH_3), 2.07 (3H, s, OAc), 2.76 (1H, br. s, H-20), 3.60 (1H, br. s, H-6), 4.18 (1H, s, H-19), 4.52 (1H, s, H-1), 4.59, 4.74 (1H each, d, J = 1.5, H-17), 5.00 (1H, t, J = 1.5, H-2)
^{13}C NMR:

C-1	67.9	C-9	79.6	C-17	104.7
2	73.2	10	53.7	18	21.15
3	39.2	11	33.8	19	91.7
4	42.1	12	36.1	20	67.9
5	50.7	13	32.9	C=O	169.9
6	60.5	14	43.7	|	
7	30.9	15	30.7	CH_3	22.5
8	42.1	16	150.4		

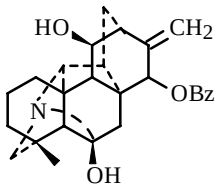
XSA: [26]



20. 18-Benzoyldavisinol

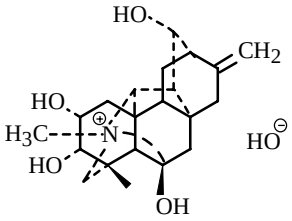
Delphinium davisii Munz [27]
$C_{27}H_{31}NO_3$: 417
mp: amorph.
$[\alpha]_D$ +42.3° ($CHCl_3$)
IR: 1720, 1465, 1455, 1375, 1336, 1270
PMR: 1.02, 1.95 (1H each, m, H-13), 1.45 (1H, s, H-9), 1.51, 1.79 (1H each, m, H-2), 1.51, 1.92 (1H each, m, H-1), 1.61, 1.76 (1H each, m, H-7), 1.62 (2H, m, H-3), 1.88 (1H, m, H-5), 1.90 (1H, m, H-14), 2.20, 2.27 (1H each, m, H-15), 2.33 (1H, br. s, $W_{1/2}$ = 9.0, H-12), 2.44, 2.72 (1H each, AB, J = 17.9, H-19), 2.51 (1H, s, H-20), 3.27 (1H, br. s, H-6), 4.06, 4.24 (1H each, AB, J = 12.8, 18-CH_2), 4.07 (1H, d, J = 4.8, H-11), 4.89 (2H, br. s, H-17), 7.46 (2H, dd, J = 7.6, H-Ar), 7.58 (1H, dd, J = 7.4, H-Ar), 8.02 (2H, d, J = 7.5, H-Ar)
^{13}C NMR:

C-1	26.4	C-9	59.6	C-17	110.7
2	18.8	10	49.5	18	70.8
3	28.9	11	67.5	19	58.4
4	42.3	12	41.9	20	75.9
5	56.3	13	29.5	Ar-CO	166.1
6	65.2	14	44.3	Ar-1	130.1
7	35.8	15	33.6	2,6	129.6
8	40.5	16	145.6	3,5	128.5
				4	133.1



21. 15-Benzoylpseudokobusine

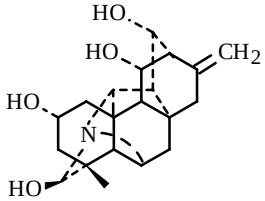
Aconitum yesoense var. macroyesoense (Nakai) Tamura [28]
$C_{27}H_{31}NO_4$: 433
mp: amorph.
$[\alpha]_D$ -6.9° (alcohol)
UV: 229 (3.87)
IR: 3550, 1715, 1580, 1265
Mass: 433 (M^+, 100), 312
PMR: 1.33 (3H, s, 18-CH_3), 4.07 (1H, d, J = 4.6, H-11), 5.27, 5.48 (1H each, s, H-17), 5.82 (1H, s, H-15), 7.34-7.63 (3H, m, H-Ar), 7.91-8.03 (2H, m, H-Ar)



22. Vakhmadine

Aconitum palmatum Don. [29]
$C_{21}H_{30}NO_4^+OH^-$: 359
mp: 263-273°C (alcohol)
$[\alpha]_D$ -37.8° (methanol)
{2,3,13-tri-OAc-secovakhmadine 261-262°C (acetone)}
IR: 3340, 3060, 1650, 1110, 1090, 1075, 1050, 1020, 990, 870
Mass: 359 (M^+, 3.9), 342 (8), 44 (100)
PMR (D_2O): 1.40 (3H, s, 18-CH_3), 2.58 (3H, s, N–CH_3), 2.97, 4.05 (1H each, d, J = 11.7, H-19), 3.33 (1H, d, J = 4.3, H-3β), 3.93 (1H, d, J = 11.0, H-13β), 3.97 (1H, br. m, H-2β), 4.22 (1H, s, H-20), 4.59, 4.73 (1H each, s, H-17)
^{13}C NMR (D_2O):

C-1	30.0	C-8	41.5	C-15	31.8
2	69.3	9	45.3	16	148.1
3	73.5	10	45.2	17	107.2
4	40.6	11	21.4	18	25.3
5	58.9	12	41.5	19	66.7
6	105.0	13	67.8	20	73.2
7	40.1	14	48.1	N-CH_3	36.3

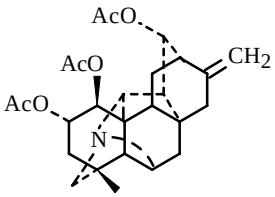


23. Vakhmatine

Aconitum palmatum Don. [29], *Consolida ambigua* L.P.W. Ball and V. H. Heywood [13]
$C_{20}H_{27}NO_4$: 345
mp: 170.5-174.5°C (methanol) [29]
$[\alpha]_D$ +12.6° (methanol) [29]
IR: 3550, 3320, 3060, 1650, 1205, 1080, 1035, 950, 875 [29]
Mass: 345 (M^+, 4.6), 327 (7.4), 309 (14), 281 (13.8), 222 (7.5), 173 (13.6), 144 (14.2), 128 (18.4), 115 (17.4), 105 (27.3), 91 (47.1), 77 (30.6), 55 (45.2), 43 (67.5), 41 (100) [29]
PMR (CD_3OD): 1.04 (3H, s, 18-CH_3), 1.55 (1H, dd, J = 15.2, 4.8, H-3β), 1.91 (1H, dd, J = 9.0, 2.1, H-9), 1.99, 2.25 (1H each, br. d, J = 17.7, H-15), 2.12 (1H, dd, J = 9.3, 1.8, H-14), 2.35 (1H, d, J = 2.6, H-12), 3.00 (1H, br. d, J = 15.3, H-1α), 3.38 (1H, br. s, H-6), 4.02 (1H, br. m, H-2β), 4.11 (1H, dt, J = 9.3, 2.3, H-13β), 4.18 (1H, s, H-19), 4.22 (1H, d, J = 9.1, H-11β), 4.67, 4.84 (1H each, br. s, H-17) [29]

^{13}C NMR (CD_3OD) [29]:

C-1	35.1	C-8	45.3	C-15	34.5
2	62.9	9	56.8	16	148.2
3	38.5	10	51.5	17	107.6
4	42.4	11	76.9	18	27.5
5	60.6	12	52.4	19	95.5
6	61.6	13	73.0	20	66.1
7	36.8	14	53.2		

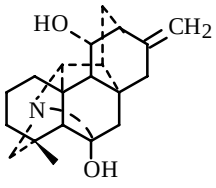


24. Venudelphine

Delphinium venulosum Boiss. [30]
$C_{26}H_{33}NO_6$: 455
$[\alpha]_D$ 0° ($CHCl_3$)

IR: 3070, 3020, 2970, 2930, 2880, 1737, 1730, 1650, 1450, 1430, 1365, 1240, 1020
Mass: 455 (M^+, 10.2), 440 (8), 412 (60), 395 (100), 352 (27), 292 (5), 105 (18), 91 (10)
PMR: 1.05 (3H, s, 18-CH_3), 1.98, 2.01, 2.09 (3H each, s, 3×OAc), 2.55, 2.82 (1H each, br. d, J = 14.0, H-19), 3.32 (1H, br. s, H-6), 3.86 (1H, s, H-20), 4.82, 4.99 (1H each, br. s, H-17), 5.07 (1H, dt, J = 10.0, 1.5, 1.5, H-13β), 5.31 (1H, dd, J = 3.5, 5.0, H-2β), 5.72 (1H, d, J = 3.5, H-1α)
^{13}C NMR:

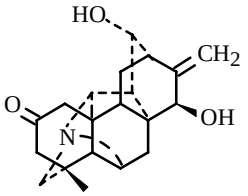
C-1	73.1	C-9	63.2	C-17	110.6	CO	169.9
2	71.1	10	52.8	18	29.2	|	
3	36.7	11	29.2	19	64.1	CH_3	21.2
4	37.4	12	49.4	20	60.3	CO	169.7
5	54.7	13	74.9	CO	170.8	|	
6	67.1	14	51.6	|		CH_3	21.5
7	35.7	15	34.1	CH_3	21.0		
8	43.9	16	142.1				



25. Venulol

Delphinium venulosum Boiss. [31]
$C_{20}H_{27}NO_2$: 313
$[\alpha]_D$ +19.7° (methanol)
IR: 3440, 3340, 3060, 2950, 1640, 1600, 1460, 1250, 1150, 1120, 1100, 965, 900, 820
Mass: 313 (M^+, 100), 298 (15), 285 (52), 105 (36), 91 (54)
PMR: 1.37 (3H, s, 18-CH_3), 2.30 (1H, d, J = 4.5, H-9), 2.50 (1H, br. d, J = 4.5, H-12), 2.86, 3.28 (1H each, d, J = 12.5, H-19), 3.97 (1H, d, J = 4.5, H-11β), 4.70, 4.77 (1H each, br. s, H-17)
^{13}C NMR:

C-1	30.2	C-8	43.2	C-15	36.1
2	19.6	9	42.9	16	146.3
3	38.6	10	57.9	17	109.8
4	42.3	11	72.6	18	29.2
5	59.4	12	42.8	19	59.8
6	102.2	13	27.3	20	68.1
7	35.9	14	47.7		

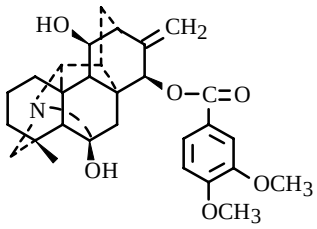


26. Venuluson

Delphinium venulosum Boiss. [31]
$C_{20}H_{25}NO_3$: 327
$[\alpha]_D$ +27.3° (methanol)
IR: 3450, 3070, 2960, 2925, 1720, 1650, 1570, 1450, 1410, 1380, 1230, 1180, 1140, 1040, 1020, 940, 880, 820

Mass: 327 (M^+, 5.8), 313 (72), 296 (100), 131 (1.5), 91 (7.8), 57 (3.2)
PMR: 1.02 (3H, s, 18-CH_3), 2.75 (1H, d, J = 9.0, H-14), 3.10 (1H, s, H-20), 4.05 (1H, br. s, H-15α), 4.20 (1H, br. d, J = 9.0, H-13), 4.71, 4.90 (1H each, br. s, H-17)
^{13}C NMR:

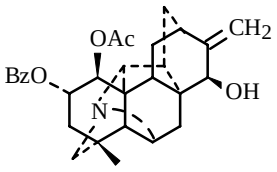
C-1	31.5	C-8	44.2	C-15	75.4
2	212.5	9	45.1	16	155.3
3	41.5	10	60.7	17	109.3
4	42.7	11	27.8	18	28.7
5	59.9	12	42.1	19	60.7
6	63.7	13	70.1	20	70.2
7	35.7	14	49.6		



27. 15-Veratroylpseudokobusine

Aconitum yesoense var. macroyesoense (Nakai) Tamura [28]
$C_{29}H_{35}NO_6$: 493
mp: amorph.
$[\alpha]_D$ -6.7° (alcohol)
UV: 260, 290 (3.91, 3.62)
IR: 3550, 1710, 1605, 1270

Mass: 493 (M^+), 312, 165 (100)
PMR: 1.35 (3H, s, 18-CH_3), 3.92, 3.94 (3H each, s, 2×OCH_3), 4.06 (1H, d, J = 4.6), 5.27, 5.45, 5.86 (1H each, s), 6.82 (1H, d, J = 8.3), 7.53 (1H, d, J = 2.0), 7.62 (1H, dd, J = 8.3, 2.0)

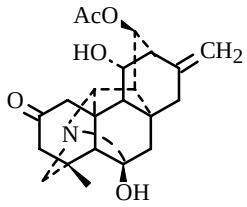


28. Hanamisine

Aconitum sanyoense Nakai, *A. sanyoense* var. tonense Nakai [32]
$C_{29}H_{33}NO_5$: 475
mp: 124-127°C (acetone)
$[\alpha]_D$ +122.6° (methanol)
{iodomethylate 253-256°C (ethylacetate—acetone)} [32]
Mass: 475 (M^+)
PMR (CD_3OD): 1.08 (3H, s, 18-CH_3), 2.10 (3H, s, OAc), 3.98 (1H, br. s, H-15), 4.96 (2H, m, H-17), 5.30 (2H, m, H-1, H-2) [32]
^{13}C NMR [20]:

C-1	69.8	C-9	42.4	C-17	108.8	Ar-1	129.8
2	69.9	10	52.1	18	29.0	2,6	129.6
3	33.7	11	26.8	19	63.5	3,5	128.6
4	36.4	12	33.4	20	73.8	4	133.2
5	56.9	13	33.2	Ar-CO	165.1	1β-CO	169.8
6	65.1	14	43.9			|	
7	32.7	15	71.4			CH_3	20.9
8	44.7	16	156.1				

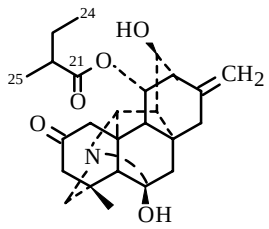
XSA {iodomethylate}: [32]



29. Geyeridine

Delphinium geyeri [33]
$C_{22}H_{27}NO_5$: 385
mp: tar
UV: 250, 289
IR: 3610, 3055, 2930, 1727, 1709, 1368, 1294, 1263, 1257, 1242, 1164, 1092, 1044, 863
Mass: 385 (M^+, 35), 367 (7), 342 (17), 327 (23), 326 (100), 325 (22), 308 (14), 298 (15), 296 (18), 269 (16), 252 (9), 223 (10), 209 (8), 192 (9), 176 (16), 175 (25), 96 (35), 91 (21), 55 (24)
PMR: 1.48 (3H, s, 18-CH_3), 1.79 (1H, d, J = 13.0), 2.00 (1H, s), 2.04 (3H, s, OAc), 2.09 (1H, br. s), 2.17-2.28 (6H, m), 2.35-2.43 (5H, m), 2.98 (1H, s, H-20), 3.20 (1H, d, J = 12.0, H-3α), 3.34 (1H, dd, J = 13.0, 2.0, H-1α), 4.17 (1H, ddd, J = 9.0, 3.0, 1.0, H-11), 4.79, 4.94 (1H each, br. s, H-17), 5.14 (1H, br. d, J = 9.0, 1.0, 1.0, H-13)
^{13}C NMR:

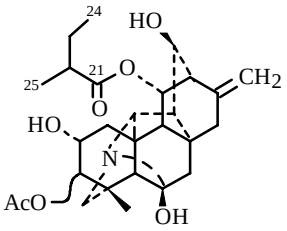
C-1	43.2	C-8	42.8	C-15	42.9
2	209.9	9	52.2	16	143.2
3	51.4	10	55.7	17	109.9
4	45.9	11	69.8	18	30.1
5	59.2	12	48.6	19	59.9
6	100.2	13	75.3	20	68.4
7	32.9	14	49.7	CO	170.6
				|	
				CH_3	21.3



30. Geyerine

Delphinium geyeri [33]
$C_{25}H_{33}NO_5$: 427
mp: amorph.
$[\alpha]_D$ +9.6° (alcohol)
UV: 252, 297
IR: 3360, 2930, 1725, 1705, 755
Mass: 427 (M^+, 16), 410 (5), 342 (10), 327 (22), 326 (100), 325 (20), 298 (25), 269 (7)
PMR: 0.96 (3H, dd, J = 7.0, 7.0, H-24), 1.20 (3H, d, J = 7.0, H-25), 1.49-1.53 (1H, m, J = 7.0, H-23), 1.55 (3H, s, 18-CH_3), 1.70-1.78 (1H, m, J = 7.0, H-23), 1.96-2.14 (6H, m), 2.23-2.34 (4H, m), 2.43-2.48 (2H, m), 2.50 (1H, dd, J = 3.0, 1.0, H-12), 2.58 (1H, m, J = 7.0, H-22), 2.65 (1H, d, J = 14.0, H-1β), 2.88 (1H, s, H-20), 3.36 (1H, br. d, J = 12.0, H-3α), 3.54 (1H, dd, J = 15.0, 2.0, H-1α), 4.36 (1H, ddd, J = 9.0, 1.0, 1.0, H-13), 4.80, 4.98 (1H each, br. s, H-17), 5.14 (1H, ddd, J = 10.0, 3.0, 1.0, H-11)
^{13}C NMR:

C-1	44.4	C-9	53.7	C-17	109.8
2	211.2	10	56.1	18	30.3
3	51.5	11	74.0	19	61.2
4	45.8	12	48.1	20	69.2
5	60.3	13	72.1	21	176.0
6	99.2	14	48.4	22	40.9
7	33.1	15	43.8	23	26.5
8	42.9	16	143.6	24	11.7
				25	16.7



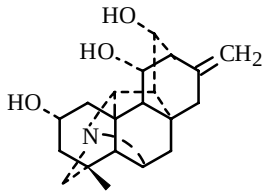
31. Geyerinine

Delphinium geyeri [33]
$C_{27}H_{37}NO_7$: 487
mp: tar
UV: 230, 257, 285

IR: 3595, 2910, 1727, 1360, 1225, 1065, 1040, 845
SIMS (NH_3): 488 (MH^+, 48), 486 (16), 470 (12), 428 (57), 426 (33), 414 (42), 412 (25), 410 (22), 386 (84), 384 (78), 382 (30), 368 (22), 366 (16), 326 (100), 324 (61), 308 (37), 296 (19)
Mass: 428 (9), 427 (8), 386 (20), 385 (10), 368 (11), 356 (9), 342 (8), 326 (43), 325 (28), 308 (17), 298 (16), 297 (20), 296 (30), 268 (9), 176 (14), 132 (13), 105 (24), 91 (22), 74 (46), 57 (100)
PMR: 0.95 (3H, t), 1.21 (3H, d, J = 7.0), 1.32 (1H, s), 1.40 (3H, s, 18-CH_3), 1.48-1.60 (2H, m), 1.73 (1H, m), 1.82-2.10 (6H, m), 2.15 (3H, s), 2.20-2.50 (4H, m), 2.64 (1H, m), 3.02 (1H, d, J = 12.0, H-19), 3.12 (1H, dd, J = 15.0, 2.0, H-1α), 3.48 (1H, d, J = 12.0, H-19), 3.76 (1H, s, H-20), 4.13 (1H, m, $W_{1/2}$ = 12.0, H-2β), 4.32 (1H, br. d, J = 9.0, 1.0, 1.0, H-13), 4.78 (1H, br. s, H-17), 4.86 (1H, d, J = 4.0, H-3), 4.94 (1H, br. s, H-17), 5.13 (1H, dd, J = 9.0, 3.0, 1.0, H-11)
^{13}C NMR:

C-1	31.6	C-11	75.1	C-21	175.9
2	67.4	12	48.7	22	41.4
3	77.4	13	73.5	23	26.5
4	51.5	14	49.4	24	11.6
5	63.4	15	44.7	25	16.8
6	96.9	16	144.3	CO	170.2
7	33.6	17	109.2	|	
8	44.9	18	26.8	CH_3	21.1
9	54.3	19	77.4		
10	57.8	20	67.7		

32. Hetisine

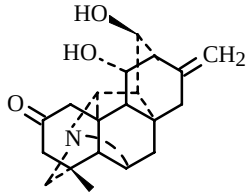


Aconitum heterophyllum Wall [23], *A. palmatum* Don. [29], *Delphinium cardinale* Hook [34], *D. davisii* Munz [27], *D. delavayi* Franch var. pogonanthum (H.-M.) Wang [35], *D. elatum* L. [23], *D. fissum* subsp. anatolicum [36], *D. nudicaule* Torr. and Gray [37], *D. nuttalianum* [38], *D. occidentale* S. Wats [39], *D. tatsienense* Franch [40], *D. venulosum* Boiss. [31]
$C_{20}H_{27}NO_3$: 329

mp: 256-259°C (acetone) [35]
$[\alpha]_D$ +10° ($CHCl_3$) [35]
IR: 3390, 3030, 1653, 1379, 900 [23]
Mass: 329 (M^+, 100), 312 (50), 300 (10), 283 (20) [15]
PMR ($CDCl_3$ + CD_3OD): 0.99 (3H, s, 18-CH_3), 3.80 (1H, br. s, H-20), 4.00-4.15 (3H, m, H-2, H-11, H-13), 4.65, 4.90 (1H each, br. s, H-17) [15]
^{13}C NMR [19]:

C-1	34.5	C-8	43.6	C-15	34.5
2	67.0	9	55.8	16	146.4
3	39.4	10	51.2	17	107.7
4	36.7	11	76.7	18	30.3
5	61.7	12	50.8	19	63.7
6	64.5	13	72.4	20	68.4
7	36.6	14	52.9		

XSA: [41, 42]



33. Hetisinone (2-dehydrohetisine)

Aconitum heterophyllum Wall [23], *Delphinium cardinale* Hook [34], *D. cardiopetalum* DC. [15], *D. davisii* Munz [27], *D. delavayi* Franch var. pogonanthum (H.-M.) Wang [35], *D. denudatum* [43], *D. fissum* subsp. anatolicum [36], *D. gracile* DC. [17], *D. nudicaule* Torr. and Gray [37], *D. nuttalianum* Pritz [38]. *D. occidentale* S. Wats [39], *D. tatsienense* Franch [40], *D. venulosum* Boiss. [31]

$C_{20}H_{25}NO_3$: 327

mp: 268-270°C (acetone) [40]

$[\alpha]_D$ +40° ($CHCl_3$) [35]

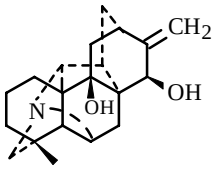
IR: 3570, 1710, 1650, 890 [23]

Mass: 327 (M^+, 45) [35]

PMR: 1.17 (3H, s, 18-CH_3), 3.29 (2H, br. s, OH), 4.21 (2H, d, J = 8.6, H-13α, H-11β), 4.70, 4.88 (1H each, s, H-17) [15]

^{13}C NMR [19]:

C-1	45.3	C-8	44.3	C-15	33.8
2	213.0	9	54.9	16	145.2
3	49.7	10	55.4	17	108.2
4	42.3	11	75.8	18	28.8
5	60.4	12	50.7	19	64.3
6	65.2	13	71.6	20	70.4
7	36.1	14	52.4		



34. 9-Hydroxynominine

Aconitum ibukiense Nakai [44]

$C_{20}H_{27}NO_2$: 313

mp: 287-291°C (dec., acetone)

$[\alpha]_D$ +68.5° (methanol)

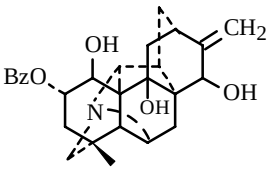
IR: 3470

Mass: 313 (M^+, 50), 296 (100)

PMR: 1.02 (3H, s, 18-CH_3), 2.22, 2.44 (1H each, d, J = 17.0, H-19), 4.02 (1H, s, H-15α), 5.00, 5.01 (1H each, s, H-17)

^{13}C NMR:

C-1	28.9	C-8	45.1	C-15	73.2
2	19.6	9	79.2	16	154.6
3	33.4	10	52.8	17	109.9
4	37.3	11	38.5	18	29.0
5	54.6	12	35.1	19	62.4
6	64.8	13	33.4	20	72.3
7	24.5	14	41.5		



35. Hypognavine

Aconitum sanyoense Nakai (Sanyobushi) [45]

$C_{27}H_{31}NO_5$: 449

mp: 239-241°C [46]

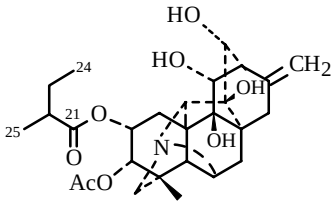
$[\alpha]_D$ +127.1° (methanol) [46]

{hypognavinol 307-308°C, hypognavinol iodomethylate 309-310°C [47], 1-acetyl-15-dehydrohypognavine 265°C [45]}

^{13}C NMR [48]:

C-1	68.1	C-8	44.3	C-15	72.4
2	73.2	9	80.3	16	154.6
3	33.0	10	54.9	17	110.0
4	35.8	11	39.2	18	29.3
5	50.6	12	34.8	19	63.5
6	64.1	13	33.5	20	71.8
7	29.0	14	42.4		

XSA {hypognavinol iodomethylate} [47], {1-acetyl-15-dehydrohypognavine} [45]

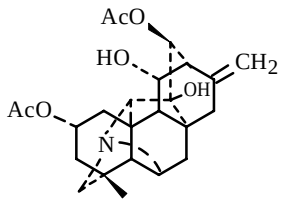


36. Glanduline

Consolida glandulosa (Boiss. et Huet) Bornm. [21]
$C_{27}H_{37}NO_8$: 503
mp: 134-137°C
$[\alpha]_D$ +24°

IR: 3351, 2938, 2924, 2853, 1736, 1720, 1657, 1461, 1373, 1258, 1231, 1176, 1139, 1113, 1088, 1075, 1031, 968
Mass: 503 (M^+, 17), 487 (11), 486 (30), 475 (14), 474 (15), 472 (18), 470 (9), 459 (8), 458 (14), 445 (27), 444 (94), 430 (15), 428 (18), 426 (5), 418 (2), 414 (5), 402 (11), 386 (5), 360 (41), 342 (27), 324 (24), 296 (9), 174 (9), 144 (17), 105 (16), 95 (13), 94 (14), 91 (18), 85 (18), 71 (17), 69 (18), 57 (100), 55 (27)
PMR: 0.92 (3H, t, J = 7.4, H-24), 1.10 (3H, s, 18-CH_3), 1.18 (3H, d, J = 7.0, H-25), 1.49 (1H, ddq, J = 14.0, 7.0, 7.0, H-23), 1.70 (1H, ddq, J = 14.0, 7.0, 7.0, H-23), 1.80 (1H, d, J = 18.0, H-7α), 1.85 (1H, d, J = 18.0, H-7β), 2.00 (1H, d, J = 16.0, H-15β), 2.01 (3H, s, OAc), 2.10 (1H, d, J = 16.0, H-15α), 2.15 (1H, dd, J = 16.0, 3.7, H-1β), 2.45 (1H, sext. J = 7.0, H-22), 2.51 (1H, d, J = 1.8, H-12), 2.70 (1H, d, J = 12.5, H-19β), 2.72 (1H, br. s, H-5), 3.04 (1H, br. d, J = 16.0, H-1α), 3.34 (1H, br. s, $W_{1/2}$ = 6.4, H-6), 3.59 (1H, d, J = 12.5, H-19α), 4.06 (1H, s, H-20), 4.09 (1H, br. s, H-13β), 4.12 (1H, s, H-11β), 4.74, 1H, s, H-17), 4.90 (1H, d, J = 4.7, H-3β), 4.91 (1H, s, H-17), 5.45 (1H, m, $W_{1/2}$ = 14.0, H-2β)
^{13}C NMR:

C-1	29.7	C-11	85.3	C-21	175.9
2	67.9	12	51.0	22	41.6
3	73.5	13	79.7	23	26.6
4	41.2	14	78.5	24	11.6
5	55.0	15	28.0	25	17.0
6	62.6	16	143.6	3αCO	170.2
7	26.1	17	108.8	|	
8	50.7	18	25.8	CH_3	20.7
9	81.0	19	59.4		
10	46.7	20	67.7		

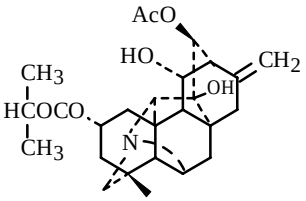


37. Guan-fu base A

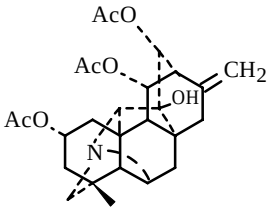
Aconitum bullatifolium var. homotorichum [49], *A. coreanum* (Levl.) Rapaics [49]
$C_{24}H_{31}NO_6$: 429
mp: 198°C [50]
$[\alpha]_D$ +49° ($CHCl_3$) [50]

{nitrate 265°C (acetone), chl-hydr. 290°C (acetone), br-hydr. 293°C (methanol), perchlorate 272-273°C (aq. alcohol), iodomethylate 284.5-285.5°C (alcohol), di-OAc 154-155°C (ether—petroleum ether), aminoalcohol 243-244°C

(acetone—ether), $[\alpha]_D$ +30.7° (methanol)} [50]
PMR: 0.96 (3H, s, 18-CH_3), 2.00 (1H, H-12), 3.38 (1H, s, H-20), 4.20 (1H, d, J = 8.0, H-11β), 4.60 (1H, br. s, H-13α), 4.79, 4.85 (1H each, br. s, H-17), 5.06 (1H, m, H-2) [51]

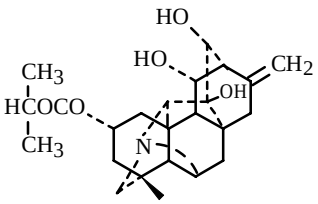


38. Guan-fu base F [10d]

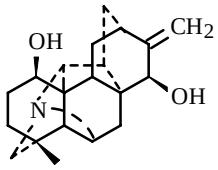


39. Guan-fu base G

A. coreanum (Levl.) Rapaics [49, 51, 52]
$C_{26}H_{33}NO_7$: 471
mp: 178°C
$[\alpha]_D$ +97.3° ($CHCl_3$)
Mass: 471 (M^+, 21), 454 (7), 429 (20), 428 (22), 412 (23), 385 (10), 370 (23), 369 (100), 352 (9), 342 (40), 43 (24) [52]
PMR (CCl_4): 0.96 (3H, s, 18-CH_3), 1.87, 1.90, 1.93 (3H each, s, 3OAc), 3.30 (1H, s, H-20), 4.80 (1H, br. s, H-13), 4.88, 4.94 (1H each, br. s, H-17), 5.04 (2H, m, H-2, H-11) [51, 52]
XSA: [49]



40. Guan-fu base Z [10e]



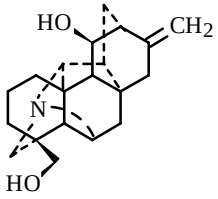
41. Davisine (cossonidine [53])

Delphinium cardiopetalum DC., *D. cossonianum* Batt [53], *D. davisii* Munz [27]
$C_{20}H_{27}NO_2$: 313 [53]
mp: 130-132°C (acetone—hexane) [27]
$[\alpha]_D$ +29.9° ($CHCl_3$) [27]
IR: 3650, 2950, 2900, 1650, 1450, 1380, 1150, 1080, 1050, 1010, 990 [53]
Mass: 313 (M^+, 100), 297 (12), 296 (45), 286 (12), 285 (55), 284 (27), 270 (15), 242 (8), 202 (4), 162 (26), 146 (53), 91 (27) [53]
PMR: 1.01 (3H, s, 18-CH_3), 1.09 (1H, dd, J = 13.0, 2.5, H-13α), 1.25 (1H, m, H-3α), 1.65 (1H, dd, J = 13.0, 3.0, H-7α), 1.71 (1H, m, H-11β), 1.76 (2H, m, H-2), 1.78 (1H, m, H-3β), 1.80 (1H, m, H-13β), 1.85 (1H, m, H-14), 1.86 (1H, s, H-5), 1.93 (1H, dd, J = 14.0, 4.0, H-11α), 2.00 (1H, d, J = 12.0, H-9), 2.02 (1H, dd, J = 13.0, 2.5, H-7β), 2.21 (1H, br. d, $W_{1/2}$ = 5.0, H-12), 2.37, 2.50 (1H each, dd, J = 12.8, H-19), 2.43 (1H, s, H-20), 3.33 (1H, br. s, H-6), 3.99 (1H, s, H-15), 4.20 (1H, br. s, H-1α), 4.94, 4.97 (1H each, s, H-17) [27]

^{13}C NMR [27]:

C-1	66.1	C-8	45.8	C-15	71.3
2	27.1	9	41.3	16	156.2
3	27.8	10	55.0	17	108.8
4	37.5	11	26.8	18	28.4
5	56.5	12	33.7	19	62.8
6	65.7	13	33.1	20	75.6
7	32.5	14	43.4		

42. Davisinol

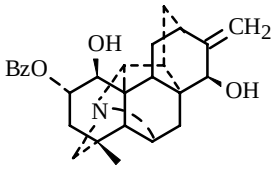


Delphinium davisii Munz [27]
$C_{20}H_{27}NO_2$: 313
mp: amorph.
$[\alpha]_D$ +27.5° ($CHCl_3$)
IR: 3345, 1100, 750, 725

PMR: 0.91, 1.90 (1H each, m, H-13), 1.38 (1H, s, H-9), 1.40-1.50, 1.70 (1H each, m, H-2), 1.40, 1.80 (1H each, m, H-1), 1.48 (2H, m, H-3), 1.57, 1.65 (1H each, d, H-7), 1.72 (1H, s, H-5), 1.78 (1H, m, H-14), 2.10 (2H, m, H-15), 2.23, 2.55 (1H each, dd, J = 12.5, H-19), 2.28 (1H, d, J = 4.8, H-12), 2.40 (1H, s, H-20), 3.14 (1H, br. s, H-6), 3.28, 3.48 (1H each, dd, J = 10.8, H-18), 4.01 (1H, d, J = 4.8, H-11), 4.83 (2H, d, J = 1.8, H-17)
^{13}C NMR:

C-1	26.5	C-8	40.5	C-15	33.6
2	18.9	9	59.5	16	145.8
3	28.4	10	49.6	17	110.1
4	43.5	11	67.4	18	69.2
5	56.0	12	41.9	19	58.2
6	64.8	13	29.6	20	75.7
7	35.8	14	44.0		

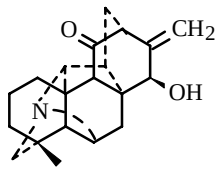
43. Deacetylhanamisine (hanamiyama base)



Aconitum sanyoense Nakai var. tonense Nakai [20, 32]
$C_{27}H_{31}NO_4$: 433
mp: 243-244.5°C (acetone—methanol) [20]
$[\alpha]_D$ +130.0° (methanol) [20]
IR: 3505, 1705, 1270 [20]

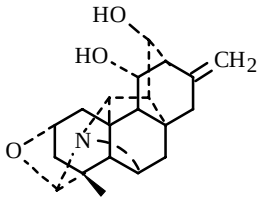
Mass: 433 (M^+, 21), 416 (100), 311 (62) [20]
PMR (C_5D_5N): 1.00 (3H, s, 18-CH_3), 2.68, 3.21 (1H each, d, J = 12.1, H-19), 3.45 (1H, s, H-20), 3.47 (1H, br. s, H-6), 4.32 (1H, s, H-15), 4.68 (1H, s, H-1), 5.01, 5.21 (1H each, d, J = 1.6, H-17), 5.88 (1H, m, H-2) [20]
^{13}C NMR (C_5D_5N) [20]:

C-1	66.7	C-9	43.4	C-17	108.0
2	75.3	10	54.0	18	29.1
3	33.9	11	27.6	19	64.3
4	36.9	12	34.8	20	74.1
5	57.2	13	34.1	Ar-CO	165.9
6	65.6	14	44.8	Ar-1	130.9
7	33.7	15	71.2	2,6	129.8
8	45.2	16	157.7	3,5	129.0
				4	133.4



44. 11-Dehydrokobusine [10f]

mp: 283.5-285.5°C [54]

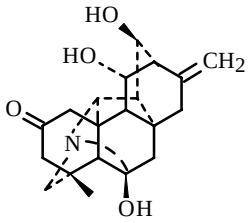


45. Delatisine

Delphinium elatum L. [55]
$C_{20}H_{25}NO_3$: 327
mp: 274.5-276.5°C (acetone)
$[\alpha]_D$ +8.6° ($CHCl_3$)
IR: 3460
Mass: 327 (M^+)
PMR: 1.15 (3H, s, 18-CH_3), 1.57 (1H, d, J = 11.2, H-3β), 1.63 (2H, m, H-7), 1.64 (1H, dd, J = 11.2, 5.7, H-3α), 1.70 (1H, d, J = 13.1, H-1β), 1.74 (1H, s, H-5), 1.87 (1H, dd, J = 9.1, 2.1, H-14), 2.01, 2.16 (1H each, AB, J = 18.0, H-15), 2.18 (1H, dd, J = 8.6, 2.1, H-9), 2.46 (1H, br. s, $W_{1/2}$ = 6.2, H-12), 2.52 (1H, dd, J = 13.1, 5.4, H-1α), 3.44 (1H, br. s, $W_{1/2}$ = 7.6, H-6), 4.11 (1H, br. d, J = 8.6, H-11), 4.25 (1H, m, H-13), 4.26 (1H, s, $W_{1/2}$ = 4.5, H-20), 4.50 (1H, br. t, J = 5.4, 5.7, H-2), 4.67 (2H, br. s, H-17, H-19), 4.88 (1H, br. s, H-17)
^{13}C NMR:

C-1	34.3	C-8	45.7	C-15	33.9
2	79.6	9	55.4	16	145.7
3	41.6	10	52.7	17	108.2
4	50.5	11	75.7	18	20.9
5	62.0	12	50.2	19	100.2
6	66.3	13	72.2	20	64.4
7	37.3	14	50.0		

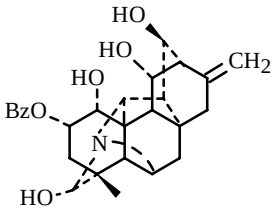
XSA: [55]



46. Delbidine

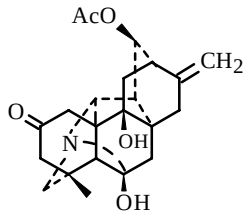
Delphinium occidentale (S. Wats) S. Wats, *D. barbeyi* (Huth) Huth [56]
$C_{20}H_{25}NO_4$: 343
mp: >360°C (methanol)
$[\alpha]_D$ +22.3° (methanol)
IR: 3508, 3360, 1685, 1660, 1460, 1370, 1350, 1332, 1315, 1295, 1280, 1265, 1220, 1200, 1180, 1085, 1065, 1040, 1030, 1000, 960, 940, 910, 880, 860, 810
Mass: 343 (M^+, 10), 326 (5), 287 (7), 269 (20), 176 (19), 91 (49), 55 (100)
PMR (DMSO-d_6): 1.36 (3H, s, 18-CH_3), 4.50, 4.70 (1H each, br. s, H-17)
^{13}C NMR (CD_3SOCD_3):

C-1	44.2	C-8	45.2	C-15	44.0
2	212.9	9	51.3	16	148.1
3	51.5	10	55.6	17	106.1
4	42.3	11	69.9	18	30.2
5	60.9	12	53.7	19	62.7
6	97.9	13	73.3	20	68.9
7	33.3	14	51.1		



47. Delgramine

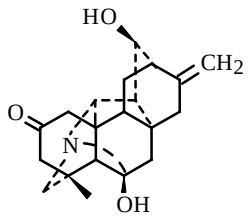
Delphinium grandiflorum [6]
$C_{27}H_{31}NO_6$: 465



48. Delnuttalline

Delphinium nuttallianum [14]
$C_{22}H_{27}NO_5$: 385
mp: 269-271°C
IR: 3409, 1740, 1710, 1237, 1043
Mass: 385 (M^+, 53), 368 (78), 357 (9), 342 (9), 325 (23), 43 (100)
PMR (C_5D_5N): 1.68 (3H, s, 18-CH_3), 1.79 (1H, d, J = 14.5, H-11β), 1.90 (1H, d, J = 12.7, H-7), 1.92 (1H, d, J = 17.8, H-15), 2.27 (3H, s, OAc), 2.34 (1H, d, J = 13.9, H-3α), 2.38 (1H, d, J = 12.2, H-19), 2.41 (1H, br. s, H-12), 2.49 (1H, d, J = 13.9, H-3β), 2.55 (1H, s, H-20), 2.58 (1H, d, J = 17.8, H-15), 2.60 (1H, d, J = 14.2, H-11α), 2.62 (1H, d, J = 9.6, H-14), 2.68 (1H, d, J = 13.0, H-1β), 2.77 (1H, d, J = 12.7, H-7), 2.87 (1H, d, J = 13.0, H-1α), 3.08 (1H, s, H-5), 3.55 (1H, d, J = 12.2, H-19), 4.70 (1H, br. s, H-17), 4.91 (1H, br. s, H-17), 5.09 (1H, br. d, J = 9.6, H-13α)
^{13}C NMR (C_5D_5N):

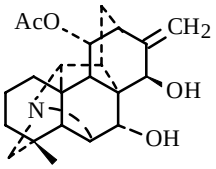
C-1	41.6	C-8	46.2	C-15	30.9
2	212.2	9	78.4	16	147.9
3	52.8	10	57.5	17	108.1
4	43.5	11	34.4	18	30.8
5	56.0	12	41.6	19	63.9
6	99.1	13	73.2	20	67.5
7	40.7	14	48.5	CO	170.2
				CH_3	20.9



49. Delnuttidine

Delphinium nuttallianum [14]
$C_{20}H_{25}NO_3$: 327
Mass: 327 (M^+, 90), 310 (13), 309 (14), 299 (31), 271 (23), 241 (89), 157 (30), 91 (41), 55 (61), 43 (100)
PMR (C_5D_5N): 1.49 (1H, dd, J = 8.7, 14.5, H-11β), 1.65 (3H, s, 18-CH_3), 1.91 (1H, d, J = 8.7, H-9), 1.95 (1H, d, J = 17.4, H-15), 2.12 (1H, d, J = 14.5, H-11α), 2.17 (1H, d, J = 17.4, H-15), 2.25 (1H, s, H-5), 2.27 (1H, d, J = 13.7, H-7), 2.35 (1H, d, J = 13.7, H-1), 2.40, 252 (1H each, d, J = 14.5, H-3), 2.74 (1H, d, J = 13.7, H-7), 2.83 (1H, d, J = 12.1, H-19), 3.29 (1H, d, J = 13.7, H-1), 3.37 (1H, d, J = 9.3, H-14), 3.85 (1H, d, J = 12.1, H-19), 3.90 (1H, s, H-20), 4.24 (1H, d, J = 9.3, H-13α), 4.61, 4.80 (1H each, br. s, H-17)
^{13}C NMR (C_5D_5N):

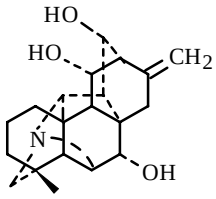
C-1	41.7	C-8	43.8	C-15	33.0
2	209.5	9	49.1	16	148.1
3	51.8	10	53.1	17	107.3
4	42.8	11	22.6	18	29.7
5	58.0	12	42.9	19	59.1
6	101.9	13	69.1	20	68.9
7	42.5	14	49.5		



50. Delnuttine

Delphinium nuttallianum [14]
$C_{22}H_{29}NO_4$: 371
IR: 3400, 1730, 1666, 1246
Mass: 371 (M^+, 57), 354 (8), 328 (42), 312 (19), 146 (87), 105 (12), 91 (23), 77 (15), 55 (21), 43 (100)
PMR ($CDCl_3$ + CD_3OD): 0.93 (3H, s, 18-CH_3), 1.20 (1H, m, H-1), 1.33-1.40 (4H, m, H-1, H-2, H-3, H-13β), 1.50 (1H, s, H-5), 1.50-1.55 (1H, m, H-2), 1.73 (1H, m, H-13α), 1.99 (3H, s, OAc), 2.07 (1H, br. d, J = 10.5, H-14), 2.17-2.26 (3H, m, H-3, H-9, H-12), 2.39 (2H, s, H-19), 2.58 (1H, s, H-20), 3.20 (1H, br. s, H-6), 3.87 (1H, d, J = 2.8, H-7β), 4.37 (1H, s, H-15α), 4.97, 5.02 (1H each, br. s, H-17), 5.18 (1H, d, J = 8.3, H-11β)
^{13}C NMR ($CDCl_3$ + CD_3OD)

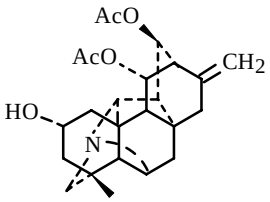
C-1	27.9	C-8	50.8	C-15	65.4
2	19.6	9	46.4	16	152.0
3	33.0	10	53.0	17	111.3
4	37.5	11	75.6	18	28.7
5	59.0	12	40.0	19	61.9
6	70.3	13	28.9	20	73.4
7	66.8	14	37.6	CO	170.7
				|	
				CH_3	21.2



51. Delfissinol

Delphinium fissum subs. anatolicum [36]
$C_{20}H_{27}NO_3$: 329
mp: amorph.
$[\alpha]_D$ -39.1° (methanol)
IR: 3350, 2960, 2860, 1650, 1570, 1360, 1330, 1215, 1110, 1090, 1042, 950, 880, 750
Mass: 329 (M^+, 22), 311 (12), 298 (52), 283 (15), 239 (8), 176 (10), 129 (10), 83 (18), 71 (27), 57 (40)
PMR: 2.72, 3.07 (1H each, d, J = 12.5, H-19), 4.16 (1H, br. d, J = 7.0, H-11), 4.26 (1H, br. d, J = 8.6, H-13), 4.48 (1H, t, J = 5.0, H-7), 4.68, 4.86 (1H each, br. s, H-17)
^{13}C NMR:

C-1	34.4	C-8	44.3	C-15	35.4
2	19.2	9	50.5	16	145.2
3	32.3	10	51.5	17	108.2
4	38.7	11	75.8	18	29.9
5	56.7	12	50.8	19	62.0
6	65.6	13	73.2	20	70.1
7	70.1	14	52.0		



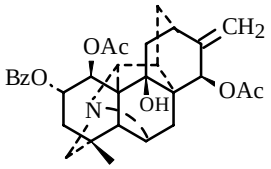
52. 11,13-Diacetylhetisine

Delphinium nuttallianum Pritz [38]
$C_{24}H_{31}NO_5$: 413
mp: 225-227°C [15]
$[\alpha]_D$ +26.1° ($CHCl_3$) [15]
IR: 3250, 1735, 1660, 1460, 1430, 1360, 1340, 1312, 1280, 1250, 1225, 1165, 1140, 1130, 1110, 1090, 1060, 1030, 1000, 980, 970, 948, 930, 900, 890, 860, 850 [15]

Mass: 413 (M^+, 19), 396 (13), 370 (6), 354 (7), 310 (3), 294 (8), 276 (3), 43 (100) [15]
PMR: 1.00 (3H, s, 18-CH_3), 2.12, 2.23 (3H each, s, OAc), 3.62 (1H, s, H-20), 4.20 (1H, br. s, H-2β), 4.82, 5.00 (1H each, br. s, H-17) [15]
^{13}C NMR [15]:

C-1	32.0	C-10	50.6	C-19	63.6
2	66.5	11	75.9	20	68.5
3	40.6	12	45.1	CO	179.8
4	36.8	13	73.0	|	
5	61.4	14	50.2	CH_3	21.5
6	64.3	15	34.0	CO	170.5
7	36.1	16	144.0	|	
8	43.9	17	109.6	CH_3	21.2
9	53.1	18	29.8		

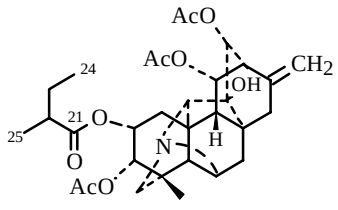
53. 1,15-Diacetylhypognavine



Aconitum sanyoense Nakai var. tonense Nakai [20]
$C_{31}H_{35}NO_7$: 533
mp: amorph.
$[\alpha]_D$ +83.0° ($CHCl_3$)
{picr. 233-239°C (dec.)}
IR: 3575, 1735, 1720, 1272, 1232
Mass: 474 (30), 473 (23), 414 (100)
PMR: 1.09 (3H, s, 18-CH_3), 2.13 (6H, s, 2×OAc), 2.37 (1H, s, H-5), 2.58, 2.93 (1H each, d, J = 12.4, H-19), 3.21 (1H, s, H-20), 3.41 (1H, br. s, H-6), 4.98, 5.10 (1H each, s, H-17), 5.24 (1H, m, H-2), 5.46 (1H, d, J = 2.0, H-1), 5.56 (1H, s, H-15), 7.44-8.00 (5H, H-Ar)
^{13}C NMR [20]:

C-1	69.5	C-9	79.1	C-17	111.7	Ar-1	129.5
2	70.2	10	54.4	18	29.1	2,6	129.4
3	33.4	11	39.7	19	63.1	3,5	128.7
4	35.6	12	34.9	20	71.8	4	133.3
5	51.3	13	32.5	Ar-CO	164.9	1β-CO	169.6
6	64.3	14	42.4			|	
7	28.3	15	73.1			CH_3	21.1
8	44.4	16	149.4			15β-CO	170.3
						|	
						CH_3	21.1

54. 11,13-Diacetyl-9-deoxyglanduline



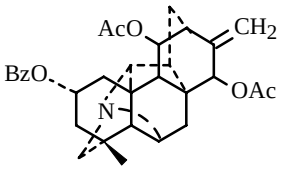
Consolida glandulosa (Boiss. et Huet) Bornm. [21]
$C_{31}H_{41}NO_9$: 571
mp: 195-198°C
$[\alpha]_D$ +36°
IR: 3205, 3089, 2925, 2845, 1737, 1652, 1459, 1369, 1229, 1145, 1045, 951, 884, 847
Mass: 571 (M^+, 4), 556 (1), 528 (10), 513 (20), 512 (59), 498 (3), 486 (2), 470 (2), 468 (2), 452 (3), 428 (4), 410 (3), 368 (5), 340 (3), 326 (4), 324 (3), 308 (7), 280 (5), 174 (4), 144 (24), 105 (29), 92 (24), 85 (31), 57 (100)

PMR: 0.92 (3H, t, J = 7.4, H-24), 1.02 (3H, s, 18-CH_3), 1.24 (3H, d, J = 7.0, H-25), 1.44 (1H, dd, J = 14.0, 2.0, H-7β), 1.50, 1.70 (1H each, ddq, J = 14.8, 7.4, 7.4, H-23), 1.80 (1H, s, H-5), 1.83 (1H, dd, J = 15.3, 4.5, H-1β), 1.91 (1H, dd, J = 14.0, 3.3, H-7α), 1.99 (3H, s, OAc), 2.00 (3H, s, OAc), 2.02 (3H, s, OAc), 2.12 (1H, d, J = 14.0, H-15β), 2.20 (1H, d, J = 14.0, H-15α), 2.23 (1H, d, J = 9.0, H-9), 2.38 (1H, sext, J = 7.4, H-22), 2.50 (1H, d, J = 12.5, H-19β), 2.68 (1H, d, J = 2.4, H-12), 2.85 (1H, dd, J = 15.3, 1.8, H-1α), 3.14 (1H, br. s, $W_{1/2}$ = 6.2, H-6), 3.34 (1H, d, J = 12.5, H-19α), 3.57 (1H, s, H-20), 4.83 (1H, br. s, H-17), 4.92 (1H, d, J = 4.7, H-3β), 5.02 (1H, br. s, H-17), 5.02 (1H, br. s, H-13β), 5.11 (1H, d, J = 9.0, H-11β), 5.47 (1H, m, $W_{1/2}$ = 14.0, H-2β)

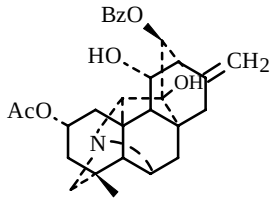
^{13}C NMR:

C-1	29.9	C-11	75.1	C-21	175.7	13αCO	169.3
2	67.9	12	46.1	22	41.4	|	
3	73.9	13	80.5	23	26.2	CH_3	21.4
4	42.2	14	78.6	24	11.6		
5	61.1	15	30.6	25	17.1		
6	62.5	16	141.8	3αCO	170.2		
7	31.3	17	110.6	|			
8	44.9	18	25.4	CH_3	20.7		
9	51.3	19	59.6	11αCO	170.4		
10	45.6	20	69.3	|			
				CH_3	21.2		

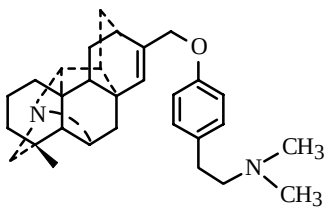
55. Diacetylisohypognavine



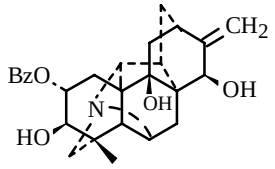
Aconitum japonicum Thunb [23]
$C_{31}H_{35}NO_6$: 517
mp: 181-183°C (ether—hexane)
$[\alpha]_D$ +55.3° ($CHCl_3$)
UV: 231, 274.5 (4.11, 2.96)
IR: 1735, 1725, 1710
Mass: 517 (M^+, 100), 474 (18), 396 (69)
PMR: 1.98, 2.06 (3H each, s, 2×OAc), 5.00, 5.17 (1H each, s, H-17), 5.03 (1H, d, J = 5.0, H-11), 5.45 (1H, s, H-15), 5.54 (1H, m, H-2)



56. Zeravschanizine [10g]

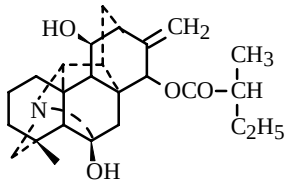


57. Zeraconine [10h]



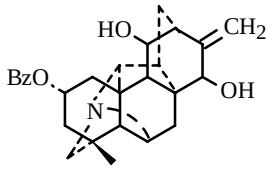
58. Ignavine

Aconitum carmichaeli Debeaux [23], *A. ibukiense* Nakai [44], *A. japonicum* Thnb [57], *A. sanyoense* [23], *A. tasiromontanum* Nakai [46, 58]
$C_{27}H_{31}NO_5$: 449
mp: 216.5-218°C (acetone) [44]
$[\alpha]_D$ +47° (methanol) [23]
{ignavine iodomethylate 300-304°C (dec.) [57], aminoalcohol (anhydroignavinol) 302-304°C, anhydroignavinol iodomethylate 285-287°C (methanol) [58]}
IR: 3350, 1725, 1260 [23]
Mass: 449 (M^+) [23]
PMR: 1.17 (3H, s, 18-CH_3), 4.99 (2H, br. s, H-17) 5.39 (1H, br. s, H-3), 7.54 (3H, m), 7.99 (2H, dd, J = 8.0, 2.0) [23]
^{13}C NMR: 166.8, 155.6, 134.4, 130.4, 130.2, 129.8, 110.2, 80.1, 75.8, 74.7, 73.0, 71.3, 65.7, 62.4, 52.1, 51.5, 45.4, 43.2, 42.2, 39.7, 36.3, 34.3, 30.0, 25.7, 25.7 [23]
XSA: {iodomethylate} [57] {anhdyroignavinol iodomethylate} [58]



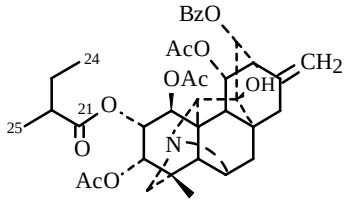
59. Yesodine

Aconitum yesoense var. macroyesoense (Nakai) Tamura [59]
$C_{25}H_{35}NO_4$: 413
mp: amorph.
$[\alpha]_D$ -9.4° ($CHCl_3$)
IR: 3548, 1729, 1216
Mass: 413 (M^+), 328, 312, 310
PMR: 0.91 (3H, t, J = 7.3), 1.16 (3H, d, J = 6.9), 1.34 (3H, s), 4.00 (1H, d, J = 4.6), 5.23, 5.33 (1H each, s), 5.59 (1H, s)
^{13}C NMR: 175.8, 144.2, 118.7, 100.0, 72.3, 70.3, 67.3, 60.0, 58.4, 55.4, 49.9, 44.8, 41.3, 41.1, 40.4, 39.5, 37.7, 35.3, 30.0, 28.0, 27.1, 26.8, 19.1, 16.6, 11.6



60. Isohypognavine

Aconitum japonicum Thunb [23], *A. majimai* Nakai [60]
$C_{27}H_{31}NO_4$: 433
mp: 189-191.5C (dec., methanol) [23]
IR: 3400, 1710, 1640 [23]
Mass: 433 (M^+, 100), 312 (98) [23]
PMR: 1.04 (3H, s, 18-CH_3), 3.30, 3.46 (1H each, 2×OH), 3.89 (1H, s, H-15), 4.00 (1H, d, J = 5.0, H-11), 5.00, 5.14 (1H each, s, H-17), 5.48 (1H, br. s, $W_{1/2}$ = 8.0, H-2), 7.42-7.58 (3H, H-Ar), 7.98 (2H, dd, J = 6.0, 2.0) [23]



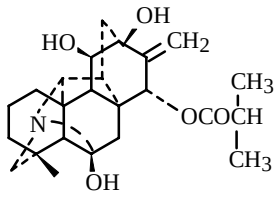
61. Cardiodine

Delphinium cardiopetalum DC. [61]
$C_{38}H_{45}NO_{11}$: 691
mp: amorph.
$[\alpha]_D$ -26°
IR: 3400, 2900, 1745, 1740, 1730, 1725, 1650, 1370, 1270, 1240, 1140, 1040, 910
Mass: 691 (M^+, 3), 632 (96), 590 (6), 586 (6), 574 (6), 570 (8), 560 (12), 548 (12), 530 (6), 510 (11), 498 (6), 488 (8), 470 (6), 366 (22), 324 (18), 306 (13), 280 (4), 105 (100), 77 (18), 57 (44)
PMR: 0.57 (3H, t, J = 7.4, H-24), 0.88 (3H, d, J = 7.4, H-25), 1.05 (3H, s, 18-CH_3), 1.20 (2H, m, H-23), 1.30 (1H, m, H-22), 1.49 (1H, dd, J = 13.9, 2.2, H-7β), 1.87 (3H, s, 3α-OAc), 1.90 (3H, s, 11α-OAc), 2.00 (1H, m, H-7α), 2.09 (3H, s, 1β-OAc),

2.18, 2.30 (1H each, dt, J = 18, 2, H-15), 2.23 (1H, s, H-5), 2.40 (1H, d, J = 9.4, H-9), 2.41 (1H, d, J = 12.5, H-19β), 2.47 (1H, d, J = 2.8, H-12), 3.21 (1H, br. s, $W_{1/2}$ = 6, H-6), 3.23 (1H, d, J = 12.5, H-19α), 3.68 (1H, s, H-20), 4.87, 5.01 (1H each, br. s, H-17), 5.12 (1H, d, J = 4.9, H-3β), 5.40 (1H, d, J = 9.4, H-11β), 5.55 (1H, t, J = 2.4, H-13β), 5.70 (1H, dd, J = 5.0, 3.1, H-2β), 6.08 (1H, d, J = 3.2, H-1α), 7.45 (2H, t, J = 7.6, H-Ar), 7.56 (1H, t, J = 7.6, H-Ar), 8.11 (2H, dd, J = 7.6, 1.6, H-Ar)

^{13}C NMR:

C-1	72.4	C-11	74.9	C-21	174.5	11αCO	171.0
2	65.8	12	47.9	22	39.6	|	
3	70.9	13	80.4	23	24.9	CH_3	21.4
4	42.5	14	78.6	24	10.7	Ar-CO	165.6
5	58.0	15	30.7	25	15.8	Ar-1	130.0
6	62.5	16	141.5	1βCO	170.0	2.6	129.6
7	31.3	17	110.6	|		3.5	128.7
8	44.9	18	25.3	CH_3	21.2	4	133.5
9	49.7	19	59.1	3αCO	169.9		
10	49.5	20	67.0	|			
				CH_3	20.6		



62. Cardionine

Delphinium cardiopetalum DC. [24]

$C_{24}H_{33}NO_5$: 415

mp: 235°C (dec., ethylacetate)

$[\alpha]_D$ -4.68° (alcohol)

IR: 3340, 2900, 1720, 1260, 1195, 1160, 910, 860

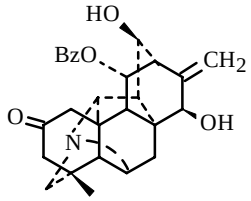
Mass: 415 (M^+, 100), 344 (13), 329 (13), 328 (55), 327 (21), 298 (13), 162 (18), 160 (10), 137 (22), 91 (10), 60 (15), 45 (20), 43 (39), 41 (18)

PMR ($CDCl_3$ + CD_3OD): 1.22 (6H, d, J = 7.0, H-23, H-24), 1.39 (3H, s, 18-CH_3), 1.62 (1H, s, H-5), 1.66 (1H, d, J = 1.7, H-9), 2.36 (1H, br. d, J = 10.7, $W_{1/2}$ = 7.5, H-14), 2.51 (1H, d, J = 11.8, H-19α), 2.63 (1H, J = 7.0, H-22), 2.73 (1H, s, H-20), 3.18 (1H, d, J = 11.8, H-19β), 3.86 (1H, s, H-11α), 5.07, 5.36 (1H each, d, J = 2.0, H-17), 5.73 (1H, t, J = 2.0, H-15β)

^{13}C NMR ($CDCl_3$ + CD_3OD):

C-1	35.7	C-9	58.2	C-17	110.3
2	19.6	10	-	18	30.4
3	27.7	11	71.9	19	59.5
4	38.3	12	74.6	20	72.8
5	60.9	13	35.8	21	177.9
6	99.0	14	41.1	22	34.7
7	38.8	15	71.1	23	19.5
8	45.8	16	148.6	24	19.5

63. Cardiopetamine



Aconitum napellus L. s. str., (*A. anglicum* Stapf) [22], *Delphinium cardiopetalum* DC. [25], *D. gracile* DC. [17]

$C_{27}H_{29}NO_5$: 447

mp: 302-305°C (dec.) [25]

$[\alpha]_D$ +65° (alcohol) [25]

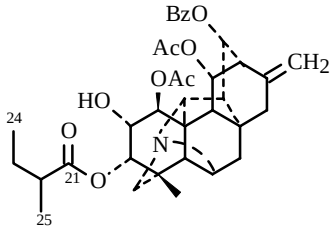
{aminoalcohol 306-308°C, 15-ketoderiv. 275-278°C, 13-ketoderiv. 252-255°C} [25]

UV: 299 [25]
IR: 3440, 1710, 1700, 1650, 1285, 870, 720 [25]
Mass: 447 (M^+, 100), 419 (4), 342 (33), 326 (46), 298 (15), 296 (12), 105 (72), 77 (31) [22]
PMR: 1.13 (3H, s, 18-CH_3), 2.04 (1H, s, H-5), 2.31 (1H, d, J = 13.0, H-1β), 2.62 (1H, d, J = 2.5, H-12), 2.70 (1H, d, J = 13.0, H-19β), 2.75 (1H, dd, J = 8.3, 2.0, H-9), 3.07 (1H, s, H-20), 3.37 (1H, br. s, $W_{1/2}$ = 7.0, H-6), 3.50 (1H, d, J = 13.0, H-1α), 3.94 (1H, s, H-15), 4.15 (1H, br. d, J = 10.8, $W_{1/2}$ = 6.5, H-13), 5.18 (2H, s, H-17), 5.61 (1H, d, J = 8.5, H-11), 7.42-8.08 (5H, m, H-Ar) [22]
^{13}C NMR [19]:

C-1	44.0	C-9	48.7*	C-17	112.1
2	212.1	10	54.5	18	28.3
3	49.6	11	75.1	19	65.0
4	42.1	12	47.7	20	69.8
5	59.7	13	69.0	Ar-CO	165.8
6	64.9	14	48.9*	Ar-1	130.1
7	33.1	15	69.8	2,6	129.6
8	49.3	16	150.5	3,5	128.9
				4	133.5

*Assigments may be interchanged

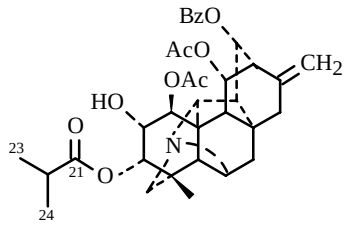
XSA: [25]



64. Cardiopidine

Delphinium cardiopetalum DC. [61]
$C_{36}H_{43}NO_9$: 633
mp: amorph.
$[\alpha]_D$ -22.5°
IR: 3371, 2935, 1729, 1653, 1451, 1371, 1272, 1240, 1090, 710
Mass: 633 (M^+, 3), 574 (45), 532 (100), 490 (10), 472 (15), 410 (13), 308 (32), 280 (11), 278 (11), 105 (70), 77 (16), 71 (15)
PMR: 0.87 (3H, t, J = 7.4, H-24), 0.99 (3H, s, 18-CH_3), 1.12 (3H, d, J = 6.9, H-25), 1.25 (2H, m, H-23), 1.70 (1H, dd, J = 13.6, 2.2, H-7β), 1.89 (1H, dd, J = 13.6, 3.1, H-7α), 1.97 (3H, s, 11α-OAc), 2.02 (3H, s, 1β-OAc), 2.15 (1H, br. d, J = 18.0, H-15α), 2.20 (1H, s, H-5), 2.30 (1H, dd, J = 9.6, 2.2, H-9), 2.40 (1H, br. d, J = 18.0, H-15β), 2.40 (1H, d, J = 12.6, H-19β), 2.50 (1H, dd, J = 9.0, 2.1, H-14), 2.53 (1H, d, J = 2.5, H-12), 2.65 (1H, m, H-22), 3.27 (1H, br. s, $W_{1/2}$ = 6.5, H-6), 3.39 (1H, d, J = 12.6, H-19α), 3.91 (1H, s, H-20), 4.28 (1H, dd, J = 4.6, 3.4, H-2β), 4.85 (1H, br. s, H-17), 4.94 (1H, d, J = 4.8, H-3β), 5.01 (1H, br. s, H-17), 5.36 (1H, dt, J = 9.5, 2.0, H-13β), 5.41 (1H, d, J = 9.2, H-11β), 6.05 (1H, d, J = 3.2, H-1α), 7.50 (2H, t, J = 7.5, H-Ar), 7.56 (1H, t, J = 7.5, H-Ar), 8.23 (2H, d, J = 8.0, H-Ar)
^{13}C NMR:

C-1	74.1	C-11	75.2	C-21	175.7	11αCO	171.0
2	67.1	12	46.0	22	41.2	|	
3	73.3	13	73.9	23	26.6	CH_3	21.4
4	41.8	14	50.2	24	11.6	Ar-CO	165.7
5	59.5	15	33.7	25	16.7	Ar-1	130.1
6	63.6	16	142.7	1βCO	170.4	2,6	130.0
7	35.7	17	110.4	|		3,5	128.5
8	43.6	18	25.6	CH_3	21.3	4	133.2
9	51.5	19	60.0				
10	53.7	20	66.1				

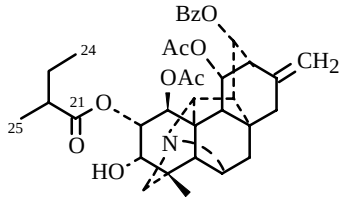


65. Cardiopimine

Delphinium cardiopetalum DC. [61]
$C_{35}H_{45}NO_9$: 619
mp: amorph.
$[\alpha]_D$ -81.3°
IR: 3367, 3029, 1729, 1657, 1272, 1239, 1151, 1110, 776
Mass: 619 (M^+, 2), 560 (69), 532 (76), 490 (15), 472 (12), 396 (12), 308 (30), 280 (11), 105 (100), 77 (25)
PMR: 1.01 (3H, s, 18-CH_3), 1.12 (3H, d, J = 6.8, H-23), 1.15 (3H, d, J = 6.8, H-24), 1.67 (1H, dd, J = 13.8, 2.4, H-7β), 1.91 (1H, dd, J = 13.8, 3.3, H-7α), 1.97 (3H, s, 11α-OAc), 2.02 (3H, s, 1β-OAc), 2.15 (1H, br. d, J = 17.5, H-15α), 2.21 (1H, s, H-5), 2.30 (1H, br. d, J = 9.6, 2.2 H-9), 2.39 (1H, br. d, J = 17.5, H-15β), 2.41 (1H, d, J = 12.6, H-19β), 2.55 (3H, m, H-12, H-14, H-22), 3.33 (1H, br. s, $W_{1/2}$ = 6.3, H-6), 3.43 (1H, d, J = 12.6, H-19α), 3.95 (1H, s, H-20), 4.28 (1H, dd, J = 4.7, 3.2, H-2β), 4.85 (1H, br. s, H-17), 4.91 (1H, d, J = 4.7, H-3β), 5.01 (1H, br. s, H-17), 5.33 (1H, dt, J = 9.6, 3.0, H-13β), 5.41 (1H, d, J = 9.6, H-11β), 6.04 (1H, d, J = 3.2, H-1α), 7.50 (2H, t, J = 7.2, H-Ar), 7.57 (1H, t, J = 7.0, H-Ar), 8.23 (2H, dd, J = 8.0, 1.0, H-Ar)
^{13}C NMR:

C-1	74.2	C-11	75.2	C-21	176.3	11αCO	171.0
2	67.0	12	46.0	22	34.1	|	
3	73.3	13	73.7	23	18.8	CH_3	21.4
4	41.8	14	50.2	24	19.2	Ar-CO	165.8
5	59.6	15	33.7	1βCO	170.4	Ar-1	130.1
6	63.7	16	142.7	|		2,6	129.9
7	35.7	17	110.4	CH_3	21.3	3,5	128.5
8	43.6	18	25.5			4	133.2
9	51.6	19	60.0				
10	53.9	20	66.1				

66. Cardiopine

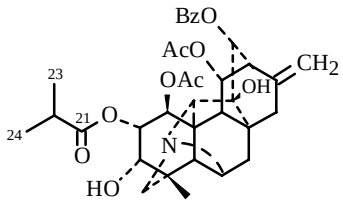


Delphinium cardiopetalum DC. [61]
$C_{36}H_{43}NO_9$: 633
mp: 194-197°C
$[\alpha]_D$ -26.3°
IR: 3367, 3026, 2931, 1733, 1693, 1601, 1451, 1361, 1292, 1245, 1141, 1107, 1034, 979, 712
Mass: 633 (M^+, 1), 574 (100), 560 (4), 532 (2), 490 (14), 472 (8), 452 (3), 430 (2), 410 (2), 308 (5), 105 (28), 77 (5), 57 (7), 43 (3)
PMR: 0.57 (3H, t, J = 7.5, H-24), 0.85 (3H, d, J = 6.5, H-25), 1.08 (2H, m, H-23), 1.10 (1H, m, H-22), 1.14 (3H, s, 18-CH_3), 1.66 (1H, dd, J = 13.6, 2.6, H-7β), 1.88 (1H, dd, J = 13.6, 3.6, H-7α), 2.00 (3H, s, 11α-OAc), 2.06 (3H, s, 1β-OAc), 2.15 (1H, s, H-5), 2.18 (1H, dt, J = 17.8, 2.1, H-15α), 2.33 (1H, dd, J = 9.6, 2.1, H-9), 2.37 (1H, d, J = 12.8, H-19β), 2.38 (1H, d, J = 2.7, H-12), 2.39 (1H, dt, J = 17.8, 2.1, H-15β), 2.53 (1H, dd, J = 9.9, 1.9, H-14), 3.10 (1H, d, J = 12.8, H-19α), 3.30 (1H, br. s, $W_{1/2}$ = 6.0, H-6), 3.67 (1H, s, H-20), 3.87 (1H, d, J = 5.0, H-3β), 4.87, 4.97 (1H each, br. s, H-17), 5.42 (1H, d, J = 9.5, H-11β), 5.51 (1H, dt, J = 9.7, 2.6, H-13β), 5.60 (1H, dd, J = 5.2, 2.9, H-2β), 6.09 (1H, d, J = 2.9, H-1α), 7.47 (2H, t, J = 7.0, H-Ar), 7.57 (1H, t, J = 7.4, H-Ar), 8.14 (2H, d, J = 7.2, H-Ar)

^{13}C NMR:

C-1	73.2	C-11	75.4	C-21	177.2	11αCO	171.5
2	68.9	12	46.6	22	39.6	|	
3	70.8	13	73.8	23	25.0	CH_3	21.5
4	42.7	14	50.4	24	10.8	Ar-CO	165.9
5	59.5	15	33.9	25	15.7	Ar-1	130.1
6	63.9	16	142.7	1βCO	171.0	2,6	129.9
7	35.9	17	110.3	|		3,5	128.7
8	44.2	18	25.7	CH_3	21.2	4	133.4
9	51.7	19	59.5				
10	53.9	20	66.2				

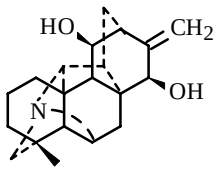
67. Cardiopinine



Delphinium cardiopetalum DC. [61]
$C_{35}H_{45}NO_9$: 619
mp: 218-220°C
$[\alpha]_D$ -26.6°
IR: 3411, 3025, 2980, 1734, 1719, 1657, 1450, 1370, 1272, 1237, 1149, 1109, 1069, 1034, 980, 901, 713
Mass: 619 (M^+, 2), 560 (100), 532 (5), 490 (17), 472 (5), 438 (6), 396 (6), 368 (4), 326 (6), 308 (16), 296 (4), 280 (10), 250 (3), 208 (3), 196 (3), 121 (3), 105 (71), 77 (15)
PMR: 0.59 (3H, d, J = 7.0, H-23), 0.90 (3H, d, J = 7.0, H-24), 1.14 (3H, s, 18-CH_3), 1.25 (1H, J = 6.6, H-22), 1.69 (1H, dd, J = 13.4, 2.4, H-7β), 1.90 (1H, dd, J = 13.4, 3.2, H-7α), 1.99 (3H, s, 11α-OAc), 2.05 (3H, s, 1β-OAc), 2.16 (1H, s, H-5), 2.19 (1H, br. d, J = 17.5, H-15α), 2.30 (1H, dd, J = 9.6, 2.0, H-9), 2.35 (1H, d, J = 12.8, H-19β), 2.39 (1H, br. d, J = 17.5, H-15β), 2.40 (1H, d, J = 2.6, H-12), 2.54 (1H, dd, J = 9.9, 2.0, H-14), 3.10 (1H, d, J = 12.8, H-19α), 3.32 (1H, br. s, $W_{1/2}$ = 6.4, H-6), 3.67 (1H, s, H-20), 3.85 (1H, d, J = 5.1, H-3β), 4.84, 4.97 (1H each, br. s, H-17), 5.43 (1H, d, J = 10.4, H-11β), 5.48 (1H, dt, J = 10.0, 2.0, H-13β), 5.59 (1H, dd, J = 5.1, 2.8, H-2β), 6.08 (1H, d, J = 2.9, H-1α), 7.47 (2H, t, J = 7.6, H-Ar), 7.55 (1H, t, J = 8.0, H-Ar), 8.15 (2H, dd, J = 8.0, 1.0, H-Ar)
^{13}C NMR:

C-1	73.1	C-11	75.3	C-21	177.7	11αCO	171.0
2	68.9	12	46.2	22	33.1	|	
3	70.6	13	73.7	23	17.9	CH_3	21.4
4	42.7	14	50.4	24	19.3	Ar-CO	165.8
5	59.3	15	33.7	1βCO	170.2	Ar-1	130.0
6	63.8	16	142.8	|		2,6	129.8
7	35.7	17	110.3	CH_3	21.2	3,5	128.7
8	44.1	18	25.7			4	133.4
9	51.7	19	59.3				
10	53.9	20	66.1				

68. Kobusine [10i]



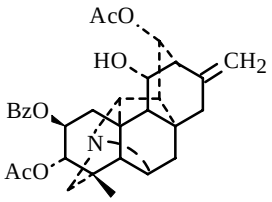
Aconitum japonicum var. montanum Nakai [62], *A. kamtscaticum* Pall (fischeri) [60], *A. luciduscul*um Nakai [60], *A. sachalininse* Fr. Schmid [60], *A. yesoense* var. macroyesoense (Nakai) Tamura [28]
$[\alpha]_D$ +104.4° (methanol) [23]
{11-OBz 214-215°C, 15-OBz 125-134°C, 11-deoxykobusine (nominine) 251-254°C, iodomethylate 294-297°C (methanol—acetone)} [54, 63]

PMR: 0.89 (1H, m, H-13β), 0.94 (3H, s, 18-CH_3), 1.25 (1H, td, J = 2.5, 14.0, H-3β), 1.40 (1H, dt, J = 3.0, 14.0, H-3α), 1.45 (1H, m, H-1β), 1.47 (1H, m, H-2β), 1.49 (1H, s, H-5), 1.62 (1H, m, H-2α), 1.63 (1H, dd, J = 13.6, 2.6, H-7α), 1.67 (1H, dd, H-9), 1.76 (1H, m, H-1α), 1.77 (1H, dd, J = 9.7, 2.4, H-13α), 1.79 (1H, m, H-14), 2.10 (1H, dd, J = 13.6, 2.3, H-7β), 2.32 (1H, AB, J = 12.4, H-19α), 2.43 (1H, m, H-12), 2.44 (1H, s, H-20), 2.47 (1H, AB, J = 12.4, H-19β), 3.20 (1H, br. s, $W_{1/2}$ = 2.3, H-6), 3.85 (1H, s, H-15α), 4.00 (1H, d, J = 4.7, H-11α), 5.05 (1H, s, H-17α), 5.15 (1H, s, H-17β) [27]

^{13}C NMR [27]:

C-1	26.9	C-8	45.9	C-15	70.9
2	19.5	9	54.9	16	150.7
3	33.8	10	49.1	17	114.3
4	37.8	11	67.5	18	28.8
5	61.0	12	41.4	19	62.4
6	65.1	13	30.3	20	75.0
7	32.4	14	41.6		

XSA: {iodomethylate} [63].



69. Cossonine

Delphinium cossonianum Batt. [64]

$C_{31}H_{35}NO_7$: 533

mp: amorph.

$[\alpha]_D$ +45° ($CHCl_3$)

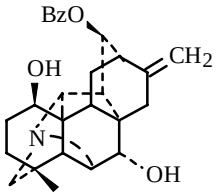
IR: 3432, 2935, 1735, 1720, 1659, 1632, 1606, 1583, 1450, 1384, 1375, 1280, 1236, 1117, 1069, 1042, 716

Mass: 533 (M^+, 7), 474 (100), 472 (8), 454 (7), 432 (7), 414 (8), 386 (4), 372 (3), 370 (2), 368 (3), 367 (2), 352 (13), 331 (6), 325 (5), 310 (19), 292 (9), 280 (8), 105 (58), 77 (13)

PMR: 1.01 (3H, s, 18-CH_3), 1.57 (1H, dd, J = 13.4, 2.4, H-7β), 1.77 (1H, dd, J = 13.4, 3.1, H-7α), 1.81 (1H, dd, J = 14.6, 11.6, H-1β), 1.84 (1H, s, H-5), 1.86 (3H, s, OAc), 1.96 (1H, dd, J = 9.3, 2.1, H-9), 2.01 (1H, d, J = 16.0, H-15α), 2.18 (1H, d, J = 16.0, H-15β), 2.20 (3H, s, OAc), 2.31 (1H, dd, J = 9.6, 2.0, H-14), 2.39 (1H, d, J = 2.3, H-12), 2.51, 2.82 (1H each, d, J = 13.3, H-19), 3.01 (1H, s, H-20), 3.14 (1H, br. s, H-6), 3.24 (1H, dd, J = 14.6, 5.1, H-1α), 4.22 (1H, d, J = 9.3, H-11β), 4.68, 4.86 (1H each, br. s, H-17), 5.10 (2H, m, H-2α, H-13β), 5.21 (1H, d, J = 10.1, H-3β), 7.41, 7.53, 7.96 (5H, m, H-Ar)

^{13}C NMR:

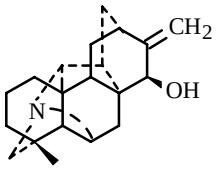
C-1	31.9	C-11	74.8	Ar-CO	165.8
2	72.3	12	48.3	Ar-1	129.9
3	77.2	13	73.6	2,6	129.6
4	43.6	14	49.9	3,5	128.4
5	62.2	15	33.6	4	130.0
6	64.1	16	144.2	3αCO	170.8
7	35.8	17	109.3	|	
8	44.0	18	24.9	CH_3	20.8
9	54.3	19	61.2	13αCO	170.8
10	51.9	20	69.2	|	
				CH_3	21.1



70. Crassicauline B

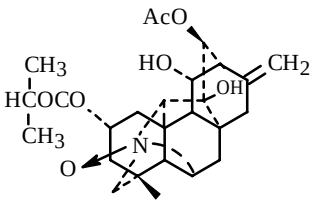
Aconitum crassicaule [65, 66]
$C_{27}H_{31}NO_4$: 433 [65]
mp: 311-315°C (dec.) [65]
{di-OAc 119-121°C (hexane)} [66]

UV: 228, 273, 280 [65]
IR: 3333, 1715, 1660, 1471, 1280, 877, 714 [65]
Mass: 433 (M^+, 65), 416 (100), 312 (12) [66]
PMR: 1.10 (3H, s, 18-CH_3), 3.58 (1H, d, J = 3.0, CHOH), 4.27 (1H, m, CHOH), 4.65, 4.76 (1H each, s, H-17), 5.34 (1H, m, H-13), 7.55, 7.67, 8.06 (5H, m, H-Ar) [66]

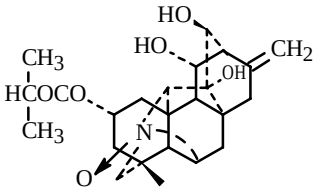


71. Nominine [10j]

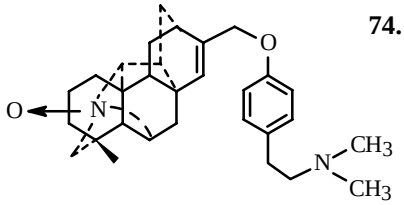
Aconitum sanyoense Nakai [54]
$C_{20}H_{27}NO$: 297
{15-dehydronominine 136-138°C} [67]



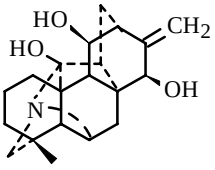
72. Guan-fu base F N-oxide [10k]



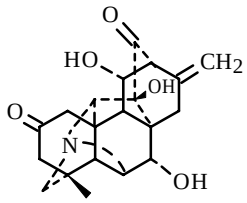
73. Guan-fu base Z N-oxide [10l]



74. Zeraconine-N-oxide [10m]



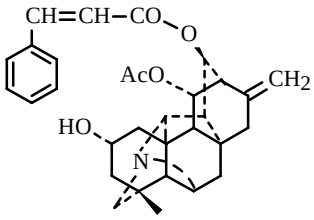
75. Orgetine [10n]



76. Orientinine

Acontium orientale [11]
$C_{20}H_{23}NO_5$: 357
$[\alpha]_D$ +42° ($CHCl_3$)
IR: 3400, 2930, 2850, 1725, 1717, 1650, 1570, 1460, 1400, 1380, 1170, 1100, 1070, 1050, 1030, 890, 760
Mass: 357 (M^+, 47), 340 (62), 321 (25), 314 (30), 300 (15), 284 (25), 274 (45), 256 (30), 213 (17), 185 (15), 115 (37), 97 (55), 83 (60)
PMR: 1.02 (3H, s, 18-CH_3), 1.53, 2.03 (1H each, H-1), 1.60, 1.75 (1H each, H-3), 2.00 (1H, d, J = 9.0, H-9), 2.03 (1H, H-5), 2.30 (2H, H-15), 2.31, 2.62 (1H each, d, J = 11.0, H-19), 2.90 (1H, br. s, H-12), 3.47 (1H, br. s, H-6), 3.64 (1H, H-20), 4.24 (1H, br. d, J = 9.0, H-11β), 4.50 (1H, t, J = 2.0, H-7β), 4.86, 4.98 (1H each, br. s, H-17)
^{13}C NMR:

C-1	46.0	C- 7	69.8	C-14	79.1
2	214.1	8	44.2	15	37.0
3	51.5	9	54.9	16	146.1
4	40.3	10	48.2	17	108.2
5	60.0	11	70.0	18	24.2
6	65.3	12	49.5	19	62.7
		13	211.4	20	68.6

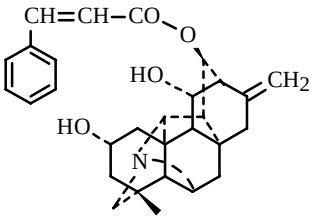


77. Palmadine

Aconitum palmatum Don. [68]
$C_{31}H_{35}NO_5$: 501
mp: 269-271°C (acetone)
$[\alpha]_D$ +11.2° ($CHCl_3$)
PMR: 0.99 (3H, s, 18-CH_3), 2.02 (3H, s, OAc), 2.20 (1H, d, J = 8.6, H-9), 2.42 (1H, d, J = 9.7, H-14), 3.27 (1H, br. s, H-6), 3.84 (1H, s, H-20), 4.24 (1H, br. m, $W_{1/2}$ = 10.8, H-2β), 4.82, 5.00 (1H each, s, H-17), 6.61, 7.86 (1H each, d, J = 16.1, CH=CH), 7.39 (3H, m, H-Ar), 7.53 (2H, m, H-Ar)
^{13}C NMR:

C-1	32.0*	C-11	75.9	Ar-1	134.7
2	67.2	12	45.0	2,6	128.9**
3	40.3	13	73.4	3,5	128.0**
4	36.6	14	50.1	4	130.2
5	61.1	15	33.9*	CO	170.6
6	64.3	16	143.6	|	
7	35.9	17	109.9	CH_3	21.5
8	43.9	18	29.7	=CH	118.7
9	53.2	19	63.4	=CH	144.7
10	50.6	20	68.5	O-C=O	166.1

*,**Assignments may be interchanged



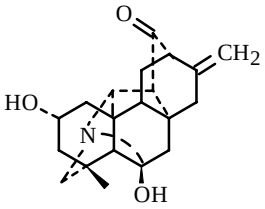
78. Palmasine

Aconitum palmatum Don. [68]
$C_{29}H_{33}NO_4$: 459
mp: 252-254°C (acetone)

PMR: 0.98 (3H, s, 18-CH_3), 3.38 (1H, br. s, H-6), 3.82 (1H, s, H-20), 4.24 (1H, br. m, $W_{1/2}$ = 10.5, H-2β), 4.32 (1H, d, J = 8.4, H-11β), 4.70, 4.91 (1H each, s, H-17), 5.21 (1H, d, J = 9.3, H-13α), 6.57 (1H, d, J = 16.0, CH=CH), 7.39 (3H, m, H-Ar), 7.49 (2H, m, H-Ar), 7.79 (1H, d, J = 16.0, CH=CH)
^{13}C NMR ($CDCl_3$ + CD_3OD):

C-1	33.4*	C-11	75.2	Ar-1	134.6
2	66.5	12	46.9	2,6	128.7**
3	39.9	13	74.4	3,5	128.0**
4	36.4	14	50.0	4	130.1
5	61.2	15	33.7*	=CH	118.3
6	64.3	16	144.9	=CH	145.1
7	35.8	17	108.6	O-C=O	166.5
8	43.7	18	29.5		
9	55.2	19	62.9		
10	50.8	20	68.4		

*,**Assignments may be interchanged



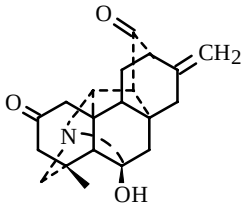
79. Panicudine

Aconitum paniculatum Lam. [69]
$C_{20}H_{25}NO_3$: 327
mp: 249-250°C (alcohol—$CHCl_3$—hexane)
UV: 205, 300

IR: 3405, 2931, 1718, 1650, 1423, 1342, 1278, 1219, 1171, 1143, 1066, 1037, 1015, 965, 947, 902, 867, 822
Mass: 327 (M^+, 100), 310 (32), 299 (14), 282 (6), 254 (12), 240 (7), 224 (7), 191 (15), 190 (13), 178 (15), 176 (16), 160 (60), 148 (10), 128 (12), 118 (32), 105 (18), 91 (30), 84 (11), 77 (18), 55 (18)
PMR (CD_3OD): 1.29 (3H, s, 18-CH_3), 2.20 (1H, s, $W_{1/2}$ = 5.0, H-14), 2.22, 2.52 (1H each, dt, J = 18.0, 1.5, H-15), 2.74 (1H, br. d, J = 4.0, H-12), 2.95, 3.12 (1H each, d, J = 11.5, H-19), 3.49 (1H, s, H-20), 4.02 (1H, m, $W_{1/2}$ = 10.0, H-2β), 4.76, 4.87 (1H each, s, $W_{1/2}$ = 4.0, H-17)
^{13}C NMR (C_5D_5N):

C-1	34.9*	C-8	44.2	C-15	34.0*
2	66.1	9	49.7	16	144.9
3	43.3	10	49.7	17	110.3
4	37.7	11	23.4	18	32.0
5	62.5**	12	54.0	19	61.9
6	99.7	13	210.8	20	70.2
7	44.4	14	61.9**		

*,**Assignments may be interchanged



80. Paniculadine

Aconitum paniculatum Lam. [70]
$C_{20}H_{23}NO_3$: 325
mp: 276-278°C (acetone)
UV: 301 (5.11)

IR: 3194, 2952, 2941, 2923, 2907, 2877, 1717, 1708, 1651, 1458, 1421, 1352, 1339, 1293, 1268, 1218, 1164, 1032, 1010, 915, 862

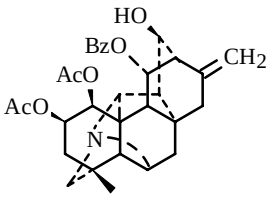
Mass: 325 (M^+, 100), 310 (5), 308 (4), 297 (26), 282 (5), 270 (13), 269 (28), 254 (10), 242 (14), 240 (11), 224 (25), 192 (10), 191 (17), 190 (10), 176 (25), 175 (10)

PMR (C_5D_5N): 1.50 (3H, s, 18-CH_3), 1.59 (2H, m), 1.88 (2H, s), 1.97 (1H, s), 2.00 (2H, s), 2.05 (1H, s), 2.17 (2H, s), 2.20 (3H, s), 2.25-2.45 (3H, m), 2.63 (1H, s), 2.85 (1H, t, J = 4.0, H-12), 3.32 (1H, d, J = 12.0, H-19α), 4.62, 4.79 (1H each, s, H-17)

^{13}C NMR (C_5D_5N):

C-1	43.7	C-8	44.7	C-15	33.2
2	210.1*	9	48.6	16	143.7
3	52.4	10	54.8	17	110.6
4	43.9	11	23.2	18	30.4
5	61.0*	12	53.2	19	63.2
6	99.0	13	210.0*	20	71.8
7	44.1	14	61.1**		

*,**Assignments may be interchanged



81. Paniculatine

Aconitum paniculatum Lam. [1, 71]
$C_{31}H_{35}NO_7$: 533
mp: 263°C [23]
UV: 230, 270 (4.02, 2.98) [71]

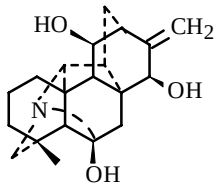
IR: 3150, 1730, 1720, 1650, 1600 [71]

Mass: 533 (M^+), 490, 474 (100), 444, 430, 414, 368, 352, 310, 292, 282, 264, 252, 207, 181, 141, 122, 105 [71]

PMR: 1.03 (3H, s, 18-CH_3), 1.63 (1H, br. s, OH-13), 1.63-1.70, 1.77-1.83 (1H each, m, H-7), 1.78-1.84, 1.88-1.97 (1H each, m, H-3), 2.03 (6H, s, 2×OAc), 2.05 (1H, s, H-5), 2.08 (1H, d, J = 20.0, H-15), 2.27 (1H, H-14), 2.29 (1H, H-12), 2.32 (1H, H-9), 2.35 (1H, d, J = 20.0, H-15), 2.51, 2.88 (1H each, d, J = 15.0, H-19), 3.29 (1H, m, $W_{1/2}$ = 7.0, H-6), 4.19 (1H, m, $W_{1/2}$ = 16.0, H-13), 4.30 (1H, s, H-20), 4.77, 4.90 (1H each, s, H-17), 5.37 (1H, m, H-11), 5.55 (1H, m, $W_{1/2}$ = 9.0, H-2), 5.84 (1H, d, J = 3.0, H-1), 7.46 (2H, t, H-Ar), 7.58 (1H, t, H-Ar), 8.13 (2H, d, H-Ar) [1, 23, 71]

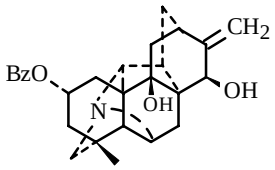
^{13}C NMR [71]:

C-1	71.6	C-11	68.7	Ar-CO	165.8
2	70.9	12	51.8	Ar-1	130.3
3	34.1	13	75.3	2,6	129.9
4	36.9	14	50.0	3,5	128.6
5	51.7	15	36.3	4	133.0
6	65.6	16	144.3	CO	170.1
7	33.1	17	109.0	|	
8	44.0	18	29.4	CH_3	21.3
9	64.2	19	64.0	CO	171.4
10	54.6	20	58.1	|	
				CH_3	21.8



82. Pseudokobusine [10o]

*Aconitum luciduscul*um Nakai [2],
A. yesoense var. macroyesoense (Nakai) Tamura [2, 28]
$C_{20}H_{27}NO_3$: 329
mp: 273-274°C (dec.) [28]
$[\alpha]_D$ +50° ($CHCl_3$) [2]
{6-OBz 238-239°C, 6,11-di-OBz 211-213°C, 6,15-di-OBz 249-251°C, br-hydr. 300 (dec.), $[\alpha]_D$ +23°, perchlorate 260°C, iodomethylate 287°C} [2, 23, 28]

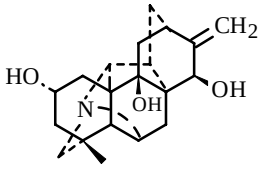


83. Ryosenamine

Aconitum ibukiense Nakai [48]
$C_{27}H_{31}NO_4$: 433
mp: 213-215°C (acetone)
$[\alpha]_D$ +96.8° (methanol)
{mono-Ac 184-185°C (acetone), 15-dehydroryosenamine 275-278°C (dec.)}
UV: 230, 273.5, 281
IR: 3450, 1710
Mass: 433 (M^+, 20), 416 (100), 312 (21)
PMR: 1.06 (3H, s, 18-CH_3), 2.62, 3.04 (1H each, d, J = 13.0, H-19), 3.31 (1H, br. s, H-20), 3.33 (1H, br. s, H-6), 4.12 (1H, s, H-15α), 4.97, 5.00 (1H each, s, H-17), 5.54 (1H, m, H-2β), 7.43-8.03 (5H, H-Ar)
^{13}C NMR:

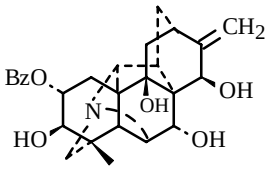
C-1	29.2*	C-11	37.2	Ar-CO	166.0
2	70.8	12	35.0	Ar-1	130.4
3	38.8	13	33.6	2,6	129.4
4	35.9	14	42.0	3,5	128.6
5	54.3	15	72.5	4	133.0
6	64.1	16	155.2		
7	29.1*	17	109.6		
8	44.1	18	29.5		
9	79.3	19	63.7		
10	50.5	20	74.2		

*Assigments may be interchanged



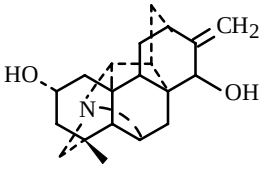
84. Ryosenaminol

Aconitum ibukiense Nakai [44, 48]
$C_{20}H_{27}NO_3$: 329
mp: 287-290°C (dec., methanol) [48]
$[\alpha]_D$ +66.8° (methanol) [48]
{2,15-di-OAc 195-198°C} [44]
IR: 3420 [48]
XSA: [48]



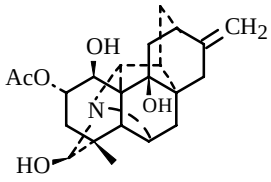
85. Sadosine

Aconitum japonicum Thunb [72]
$C_{27}H_{31}NO_6$: 465
mp: 222-224°C (acetone)
$[\alpha]_D$ +53.1° (methanol)
{iodomethylate 279-281°C (acetone)}
Mass: 465 (M^+)
PMR (CD_3OD): 1.19 (3H, s, 18-CH_3), 3.67 (1H, d, J = 3.0, H-3), 4.44 (1H, d, J = 4.0, H-7), 4.52 (1H, br. s, H-15), 5.00 (2H, br. s, H-17), 5.40 (1H, m, H-2)
^{13}C NMR (CD_3OD): 166.5, 155.4, 134.2, 131.0, 130.1, 129.5, 110.1, 80.6, 75.6, 74.6, 71.3, 71.1, 67.7, 65.0, 62.3, 51.4, 50.0, 48.3, 41.7, 39.9, 37.6, 36.1, 34.0, 25.7, 25.6
XSA: [72]

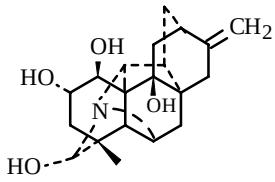


86. Sanyonamine

Aconitum sanyoense Nakai, *A. sanyoense* var. tonense Nakai [67]
$C_{20}H_{27}NO_2$: 313
mp: 276-278°C
$[\alpha]_D$ +62.9°
{15-dehydrosanyonamine 296-300°C}
IR: 3350, 3305
Mass: 313 (M^+, 100), 296 (50)
PMR: 1.06 (3H, s, 18-CH_3), 2.77, 3.50 (1H each, d, J = 12.0, H-19), 3.63 (1H, br. s, H-6), 3.67 (1H, s, H-20), 4.07 (1H, s, H-15), 4.31 (1H, br. s, H-2), 4.96, 4.98 (1H each, s, H-17)
XSA: [67]

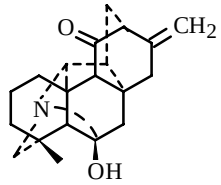


87. Septenine [10p]



88. Septentriosine [10q]

{1,2,19-tri-OAc 210.5-212.5°C} [26]



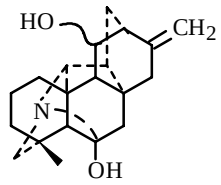
89. Spiradine A [10r]

Spiraea japonica L. fil. [75], *Thalictrum sessile* Hayata [73, 74]
$C_{20}H_{25}NO_2$: 311
mp: 281-282°C [75]
$[\alpha]_D$ +51.7° ($CHCl_3$) [73]
{OAc 215-216°C, NAc 173-175°C, dihydroderiv. 291-292°C, iodomethylate >330°C (dec.), N-methyldiketone 167°C, 11-dihydroderiv. (spiradine B) 259-260°C} [75]
UV: 205, 300 (3.71, 2.27) [23]

IR: 3100, 1710, 1655 [75]
Mass: 311 (M^+, 100), 296 (7), 283 (75), 268 (9), 161 (20) [23]
PMR: 1.41 (3H, s, 18-CH_3), 4.86, 5.00 (1H each, s, H-17)
^{13}C NMR [23]:

C-1	35.6	C-8	44.5	C-15	29.2
2	19.2	9	65.2	16	143.5
3	33.8	10	51.8	17	110.9
4	37.7	11	211.0	18	30.6
5	61.9	12	53.3	19	60.8
6	98.7	13	27.6	20	74.6
7	45.2	14	43.9		

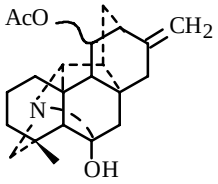
XSA {iodomethylate}: [75]



90. Spiradine B

Spiraea japonica L. fil. [75]
$C_{20}H_{27}NO_2$: 313
mp: 259-260°C
{dehydroderiv. (spiradine A) 281-282°C}

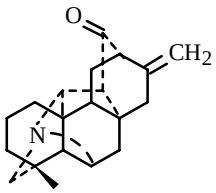
IR: 3250, 1655
Mass: 313 (M^+)



91. Spiradine C

Spiraea japonica L. fil. [75]
$C_{22}H_{29}NO_3$: 355
mp: 248-249°C
{11-deacetylderiv. (spiradine B) 259-260°C}

IR: 3200, 1730, 1655, 1240
Mass: 355 (M^+)

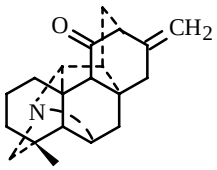


92. Spirasine IV

Spiraea japonica L. fil. var. fortunei (Planchon) Rehd [23]
$C_{20}H_{25}NO$: 295
$[\alpha]_D$ -95.7°C ($CHCl_3$)
UV: 212, 300 (2.81, 2.09)

IR: 1720, 1650, 890
Mass: 295 (M^+, 100), 280 (6), 267 (9), 175 (15), 146 (47)
PMR: 1.04 (3H, s, 18-CH_3), 2.46, 2.72 (1H each, d, J = 11.5, H-19), 3.40 (1H, br. s, H-6), 4.84, 4.96 (1H each, br. s, H-17)
^{13}C NMR:

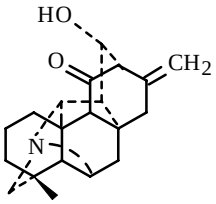
C-1	34.9	C-8	43.0	C-15	26.0
2	19.3	9	48.9	16	142.7
3	33.7	10	49.8	17	110.4
4	38.0	11	22.7	18	28.8
5	61.2	12	53.3	19	62.7
6	65.4	13	213.0	20	70.0
7	33.9	14	60.9		



93. Spirasine IX

Spiraea japonica L. fil. var. fortunei (Planchon) Rehd [23]
$C_{20}H_{25}NO$: 295
mp: 157-158°C
$[\alpha]_D$ +135.5° ($CHCl_3$)
UV: 210, 300 (3.27, 1.95)
IR: 3100, 1720, 1651, 898
Mass: 295 (M^+, 68), 283 (3), 267 (100), 252 (7), 146 (12)
PMR: 1.08 (3H, s, 18-CH_3), 2.72, 2.89 (1H each, d, J = 11.5, H-19), 3.72 (1H, br. s, H-6), 4.82, 4.94 (1H each, br. s, H-17)
^{13}C NMR:

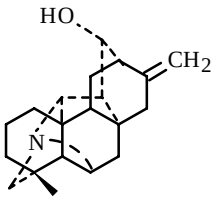
C-1	35.2	C-8	44.2	C-15	28.4
2	19.3	9	65.3	16	144.1
3	33.9	10	51.0	17	110.1
4	38.0	11	211.2	18	28.8
5	61.0	12	53.4	19	63.1
6	65.6	13	28.3	20	75.7
7	35.2	14	45.0		



94. Spirasine X

Spiraea japonica L. fil. var. fortunei (Pl.) Rehd [76]
$C_{20}H_{25}NO_2$: 311
mp: 224-227°C (acetone)
$[\alpha]_D$ +51° ($CHCl_3$)
IR: 3584, 1714, 1640, 891
Mass: 311 (M^+, 100), 266 (79)
PMR: 1.01 (3H, s, 18-CH_3), 1.68, 1.87 (1H each, dd, H-7), 2.04 (1H, d, H-20), 2.26, 2.32 (1H each, br. d, H-15), 2.41 (1H, q, H-14), 2.47, 2.58 (1H each, d, H-19), 2.94 (1H, d, H-12), 3.25 (1H, s, H-9), 3.30 (1H, br. s, H-6), 4.24 (1H, q, H-13β), 4.85, 5.02 (1H each, br. s, H-17)
^{13}C NMR:

C-1	33.5	C-8	44.9	C-15	33.7
2	19.2	9	67.2	16	140.5
3	25.7	10	50.3	17	112.4
4	37.9	11	211.0	18	28.8
5	60.1	12	62.5	19	62.5
6	65.1	13	67.7	20	65.1
7	34.8	14	51.6		

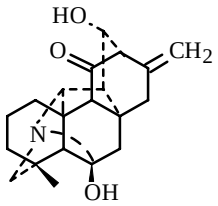


95. Spirasine XI

Spiraea japonica L. fil. var. fortunei (Planchon) Rehd [23]
$C_{20}H_{27}NO$: 297
$[\alpha]_D$ -23.8° ($CHCl_3$)
IR: 3350, 1650, 885
Mass: 297 (M^+, 100), 272 (3), 270 (4), 269 (8), 254 (3), 226 (12), 146 (29)
PMR: 1.13 (3H, s, 18-CH_3), 2.86, 3.06 (1H each, d, J = 11.5, H-19), 4.13 (1H, q, J = 9.4, 3.0, H-13β), 4.68, 4.85 (1H each, br. s, H-17)

^{13}C NMR:

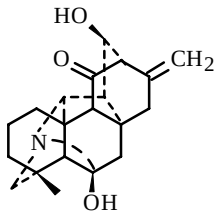
C-1	34.6	C-8	42.2	C-15	24.0
2	19.1	9	49.1	16	147.2
3	33.6	10	50.1	17	107.0
4	37.1	11	21.8	18	28.5
5	58.1	12	49.8	19	59.8
6	65.7	13	67.7	20	69.1
7	33.3	14	41.9		



96. Spirasine XII

Spiraea japonica L. var. fortunei (Pl.) Rehd [77]
$C_{20}H_{25}NO_3$: 327
mp: 226-228°C (CH_2Cl_2—methanol)
$[\alpha]_D$ +17.9° ($CHCl_3$)
UV: 305 (2.1)
IR: 3380, 1720
Mass: 327 (M^+, 100), 299 (90), 282 (89), 161 (33)
PMR: 1.32 (3H, s, 18-CH_3), 1.89 (2H, d, J = 1.5), 2.02 (1H, d, J = 2.0), 2.28 (1H, d, J = 2.0), 2.40 (1H, q, J = 2.0, 10.0, H-14), 2.42 (1H, d, J = 11.5), 2.83 (1H, d, J = 3.5, H-12), 3.08 (1H, d, J = 11.5), 4.12 (1H, q, J = 3.5, 10.0, H-13β), 4.86, 4.96 (1H each, br. s, H-17)
^{13}C NMR (C_5D_5N):

C-1	36.4	C-8	46.6	C-15	33.9
2	19.8	9	65.7	16	142.8
3	27.3	10	51.2	17	111.3
4	38.4	11	210.8	18	31.2
5	62.3	12	64.3	19	61.9
6	98.5	13	67.3	20	68.9
7	44.3	14	51.7		

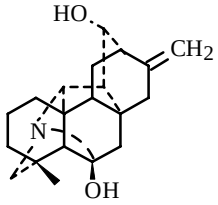


97. Spirasine XIII

Spiraea japonica L. var. fortunei (Pl.) Rehd [77]
$C_{20}H_{25}NO_3$: 327
mp: 188-189°C (CH_2Cl_2)
$[\alpha]_D$ +25.7° ($CHCl_3$)
UV: 305 (2.27)
IR: 3420, 1710, 1650
Mass: 327 (M^+, 100), 299 (95), 282 (35), 161 (26)
PMR: 1.38 (3H, s, 18-CH_3), 1.87, 1.92 (1H each, H-7), 1.95 (1H, s, H-9), 2.38, 2.48 (1H each, br. d, H-15), 2.39, 3.11 (1H each, d, J = 12.0, H-19), 2.94 (1H, s), 3.05 (1H, d, J = 4.0, H-12), 3.65 (1H, d, J = 4.0, H-13α), 4.57 (OH, s), 4.97, 5.02 (1H each, br. s, H-17)

^{13}C NMR:

C-1	35.3	C-8	45.1	C-15	32.8
2	19.0	9	73.9	16	137.6
3	28.6	10	52.3	17	114.9
4	37.6	11	209.2	18	30.5
5	60.7	12	61.9	19	61.1
6	98.9	13	67.4	20	72.0
7	43.3	14	56.0		

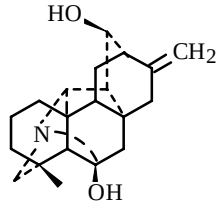


98. Spirasine XIV

Spiraea japonica L. var. fortunei (Pl.) Rehd [77]
$C_{20}H_{27}NO_2$: 313
mp: 244-246°C (CH_2Cl_2—ethylacetate)
$[\alpha]_D$ -18.8° (alcohol)

IR: 3350, 1660, 890
Mass: 313 (M^+, 100)
PMR: 1.36 (3H, s, 18-CH_3), 2.08, 2.30 (1H each, d, J = 12.6, H-19), 3.96 (1H, br. d, J = 10.0, H-13β), 4.62, 4.77 (1H each, br. s, H-17)
^{13}C NMR:

C-1	35.4	C-8	43.1	C-15	33.0
2	18.6	9	48.8	16	147.1
3	24.2	10	49.4	17	106.6
4	37.2	11	21.6	18	29.6
5	59.1	12	48.2	19	58.0
6	99.5	13	65.9	20	69.0
7	42.5	14	41.6		

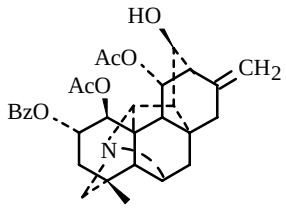


99. Spirasine XV

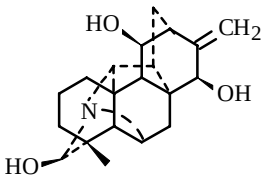
Spiraea japonica L. var. fortunei (Pl.) Rehd [77]
$C_{20}H_{27}NO_2$: 313
mp: 156-158°C (CH_2Cl_2—ethylacetate)
$[\alpha]_D$ 0° (alcohol)

IR: 3450-3200, 1665
Mass: 313 (M^+, 100)
PMR: 1.49 (3H, s, 18-CH_3), 4.85 (2H, br. s, H-17)
^{13}C NMR ($CDCl_3$ + CD_3OD):

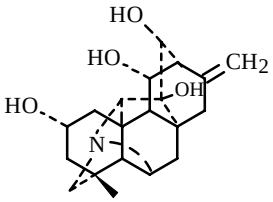
C-1	35.1	C-8	41.2	C-15	32.3
2	18.3	9	47.5	16	143.1
3	26.1	10	49.4	17	109.4
4	37.3	11	23.3	18	29.4
5	58.2	12	53.7	19	56.7
6	101.5	13	69.3	20	71.0
7	41.2	14	41.1		



100. Tadzhaconine [10s] (anthoroidine) [78]



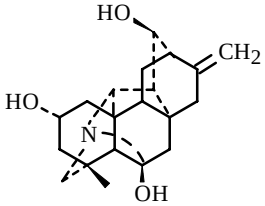
101. Talatizine [10t]



102. Tangutisine

Aconitum coreanum (Levl.) Rapaics [52], *A. tanguticum* (Maxim) Stapf, W. T. Wang [79]
$C_{20}H_{27}NO_4$: 345
{chl-hydr. 310-315°C (dec., H_2O)} [79]
IR: 3380, 3300, 3260, 3220, 1657 [79]
Mass: 345 (M^+, 34), 330 (60), 328 (100), 316 (34), 300 (65) [79]
PMR: 1.16 (3H, s, 18-CH_3), 1.62 (1H, dd, J = 15.4, 4.3, H-3β), 1.76 (1H, dd, J = 15.4, 4.1, H-1β), 1.77 (1H, br. d, J = 15.3, H-7β), 1.92 (1H, br. d, J = 15.4, 1.7, 2.1, H-3α), 2.06 (1H, AB, J = 18.1, H-15α), 2.10 (1H, dd, J = 15.3, 3.4, H-7α), 2.19 (1H, s, $W_{1/2}$ = 4.0, H-5), 2.26 (1H, AB, J = 18.1, H-15β), 2.31 (1H, d, J = 8.8, H-9), 2.55 (1H, d, J = 3.0, <1.0, H-12), 2.97 (1H, br. d, J = 15.4, 1.7, 1.7, H-1α), 3.01, 3.74 (1H each, d, J = 11.6, H-19), 4.05 (2H, br. s, $W_{1/2}$ = 6.8, H-6, H-13β), 4.21 (1H, br. s, $W_{1/2}$ = 10.4, H-2β), 4.33 (1H, d, J = 8.8, 1.8, <1.0, H-11β), 4.50 (1H, s, $W_{1/2}$ = 3.9, H-20), 4.78, 4.99 (1H each, br. s, $W_{1/2}$ = 7.0, H-17) [79]
^{13}C NMR [79]:

C-1	33.2	C-8	44.9	C-15	30.4
2	66.7	9	53.7	16	145.2
3	38.1	10	46.9	17	109.6
4	36.4	11	74.6	18	29.2
5	57.4	12	51.7	19	60.6
6	66.0	13	81.8	20	70.3
7	30.3	14	81.4		



103. Tatsirine

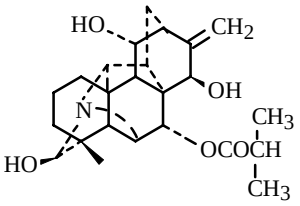
Delphinium tatsienense Franch [80]
$C_{20}H_{27}NO_3$: 329
mp: 260-263°C
{isotatsirine, ^{1}H and ^{1}$_3$C NMR}
Mass: 329 (M^+, 75), 312 (29), 301 (34), 294 (19), 242 (37), 193 (9), 178 (34), 160 (49), 119 (17), 84 (100)
PMR (C_5D_5N): 1.55 (3H, s, 18-CH_3), 4.72, 4.85 (1H each, br. s, H-17)
^{13}C NMR ($CDCl_3$ + CD_3OD): 149.1 (C-16), 106.6 (C-17), 97.9 (C-6), 70.6, 67.4, 66.7, 60.9 (2C), 51.8, 49.4, 48.5, 44.8, 42.9, 42.3, 41.6, 36.8, 33.9, 32.4, 31.2, 22.4

Isotatsirine:

PMR (CD_3OD): 1.10 (1H, br. t, J = 11.6, H-11β), 1.40 (3H, s, 18-CH_3), 1.46 (1H, H-9), 1.50 (1H, H-14), 1.52 (1H, m, H-1β), 1.56 (1H, m, H-3β), 1.66 (1H, s, H-5), 1.70 (1H, m, H-11α), 1.83 (2H, s, H-17), 1.86 (1H, m, H-3α), 1.96 (1H, br. d, J = 14.2, H-1α), 2.22, 2.35 (1H each, d, J = 13.7, H-7), 2.42 (1H, br. s, H-12), 3.20, 3.48 (1H each, d, J = 11.4, H-19), 3.53 (1H, br. s, $W_{1/2}$ = 8.2, H-13α), 3.83 (1H, s, H-20), 4.14 (1H, br. s, $W_{1/2}$ = 13.0, H-2β), 5.54 (2H, br. s, H-15)

^{13}C NMR (CD_3OD):

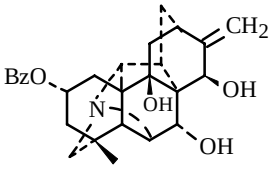
C-1	35.0	C-8	-	C-15	124.1
2	66.9	9	49.8	16	144.1
3	42.4	10	45.9	17	21.8
4	37.6	11	26.3	18	31.1
5	61.0	12	44.0	19	60.3
6	100.7	13	75.4	20	70.8
7	41.8	14	59.1		



104. Ternatine [10u]

IR: 3500, 1710, 1100 [81]

Mass: 415 (M^+, 37), 397 (25), 387 (75), 327 (44), 309 (100), 300 (47), 291 (31), 280 (44), 264 (25) [81]



105. Torokonine (Toroko-base I)

Aconitum subcuneatum Nakai [82]

$C_{27}H_{31}NO_5$: 449

mp: 198.5-199°C (acetone)

$[\alpha]_D$ +71.7° (methanol)

{15-dehydroderiv. 248-250°C (methanol)}

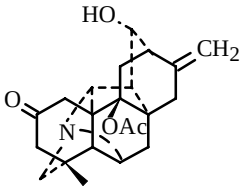
IR: 3400, 1720

Mass: 449 (M^+)

PMR (CD_3OD): 1.11 (3H, s, 18-CH_3), 2.96 (1H, s, H-20), 2.60, 3.11 (1H each, d, J = 12.5, H-19), 3.41 (1H, br. s, H-6), 4.42 (1H, d, J = 2.6, H-7), 4.53 (1H, br. s, H-15), 5.00, 5.03 (1H each, t, J = 1.3, H-17), 5.52 (1H, m, H-2), 7.47-8.02 (5H, H-Ar)

^{13}C NMR:

C-1	28.9	C-9	79.6	C-17	110.5
2	70.2	10	49.8	18	29.3
3	39.2	11	36.9	19	62.2
4	35.4	12	34.6	20	73.3
5	51.5	13	32.7	Ar-CO	165.9
6	69.7	14	36.0	Ar-1	130.1
7	64.3	15	66.6	2,6	129.4
8	48.9	16	153.6	3,5	128.8
				4	133.3

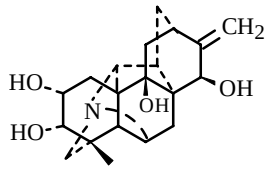


106. Fissumine

Delphinium fissum subsp. anatolicum [36]
$C_{22}H_{27}NO_4$: 369
mp: amorph.
$[\alpha]_D$ -33.8° ($CHCl_3$)

IR: 3450, 2960, 2850, 1730, 1715, 1640, 1600, 1450, 1240, 1150, 1100, 1080, 925, 860
Mass: 369 (M^+, 5), 327 (100), 310 (37), 281 (86), 253 (40), 242 (16), 204 (12), 176 (30), 115 (27), 91 (42), 55 (48)
PMR: 2.05 (3H, s, OAc), 2.52 (1H, d, J = 9.0, H-14), 2.75 (1H, s, H-20), 2.75, 3.04 (1H each, d, J = 13.0, H-19), 4.24 (1H, d, J = 9.0, H-13β), 4.69, 4.88 (1H each, br. s, H-17)
^{13}C NMR:

C-1	44.4	C-8	43.7	C-16	143.8
2	210.6	9	75.1	17	108.5
3	48.9	10	54.4	18	29.4
4	41.2	11	28.3	19	61.6
5	58.3	12	50.3	20	69.3
6	64.7	13	70.8	CO	176.9
7	28.3	14	55.1	|	
		15	34.5	CH_3	22.6



107. 3-Epiignavinol

Aconitum japonicum var. montanum Nakai [62]
$C_{20}H_{27}NO_4$: 345
mp: 292-293.5°C (dec.)
$[\alpha]_D$ +49.1° (methanol)

IR: 3520, 3350, 3280
PMR: 1.14 (3H, s, 18-CH_3), 3.37 (1H, d, J = 4.6, H-3), 3.98 (1H, br. s, H-15α), 4.08 (1H, m, H-2), 4.99 (2H, d, J = 1.7, H-17)
^{13}C NMR (CD_3OD):

C-1	31.6	C-8	45.1	C-15	73.8
2	70.5	9	80.5	16	156.1
3	75.3	10	51.9	17	110.1
4	43.0	11	39.9	18	26.8
5	56.7	12	36.6	19	60.7
6	64.9	13	34.1	20	73.2
7	30.1	14	43.2		

XSA: [62]

Thus, the rigid ring system of the hetisane framework forms from atisine by forming C14–C20 and N–C6 bridges. This results in the formation of three new five-membered rings. According to XSA, the six-membered cyclohexane rings *A* (C1, C2, C3, C4, C5, C10) and *B* (C5, C6, C7, C8, C9, C10) have the chair conformation; piperidine ring *F* (C4, C5, C10, C20, N, C19), the boat conformation. Rings *C* (C8, C9, C11, C12, C13, C14), *D* (C8, C9, C11, C12, C16, C15), and *E* (C8, C14, C13, C12, C16, C15) form the bicyclo-[2,2,2]-octane system, which is fixed in the boat form. The five-membered ring *G* (C4, C5, C6, N, C19) adopts the twist-form; *H* (C5, C6, N, C20, C10), the envelope; and *I* (C8, C9, C10, C20, C14), an equal mixture of the twist and envelope conformations [55]. The fusion of rings *ABC* is identical for all hetisane alkaloids: *A/B*, *trans*; *B/C*, *cis* (Fig. 1).

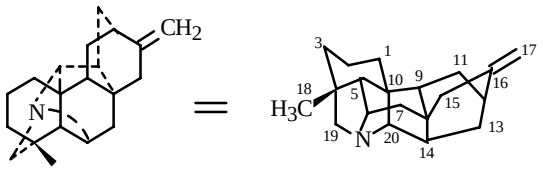


Fig. 1. Carbon framework of hetisane.

Substituents have practically no effect on the conformation of rings *A* and *B*. A small distortion of rings *B*, *C*, and *D* is observed with substituents (OH, OBz, OAc) in the C11 and C13 positions and with the presence of OH...O H-bonds [86-89].

The term "hetisane" alkaloids (sometimes hetisine) is considered commonly accepted. It is derived from the alkaloid hetisine. The determination of the structure of these alkaloids by chemical methods was very complicated owing to their tendency to rearrange. Therefore, the structures of many alkaloids and their transformation products were elucidated by XSA.

The presence of carbonyls, hydroxyls, and esters gives rise to a variety of hetisane alkaloids. Hydroxyls are frequently esterified with acetic, benzoic, and isobutyric acids and less frequently with propionic, 2-methylbutyric, cinnamic, and veratric acids. Almost all alkaloids contain the 18-methyl and 17-exomethylene groups. The exceptions are zeraconine (**57**) and its N-oxide (**74**) [90], which contain a C15=C16 double bond and a *p*-hydroxy-β-aminophenethyl moiety on C17, and davisinol (**42**) and 18-benzoyldavisinol (**20**) [27], which have hydroxymethyl and benzoyloxymethyl, respectively, instead of methyl on C4. Delatisine (**45**) [55] is known to contain a furan ring and represents a new furanohetisane-type DA. The O atom in delatisine is bonded to C2 and C19.

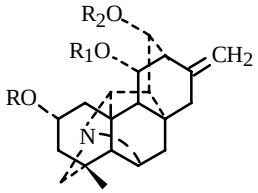
These alkaloids can be subdivided according to the number of functional groups into mono-, di-, tri-, tetra-, penta-, and hexasubstituted hetisanes. The quaternary base **22** [29] and quaternary forms as the N-oxides **72-74** [86, 90, 91] have been isolated from plants in addition to tertiary bases. A small group of N/C19 secocompounds is also known [68, 92-94].

CHEMICAL PROPERTIES

Dehydration was previously widely used to elucidate the type of C framework in DA. It was performed with heating and catalysts such as Se or Pd. This produces a complex mixture, from which phenanthrene and its alkyl derivatives were isolated [2, 46, 60]. It is impossible to distinguish hetisane alkaloids of different structures among the dehydration products because the reaction produces identical products. Dehydration has currently lost its initial attraction.

Chemical methods of elucidating alkaloid structures enable the determination of the nature and number of functional groups. Thus, one peculiarity of the hetisane alkaloids is the exomethylene group, which is observed by the production of formaldehyde upon ozonolysis and the dihydroderivative upon catalytic hydrogenation [60, 75].

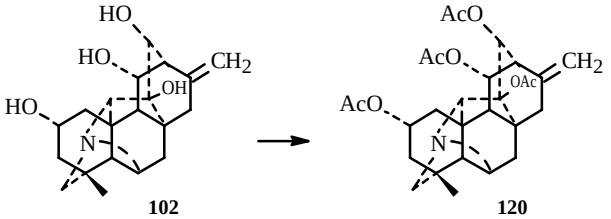
The nature of the functional groups containing O is determined via acylation, oxidation, saponification, etc. Thus, acetylation of hetisine (**32**) in $CHCl_3$ by acetic anhydride in pyridine at -6°C for 53 h forms the 11,13-diacetate (**114**), the 13-acetate (**115**), and the 11-acetate (**116**) of hetisine. The yields after purification by chromatography are 5, 10.6, and 14.3%, respectively. Acetylation of hetisine by acetic anhydride in $CHCl_3$ with heating for 15 h produces the 2,11,13-triacetate (**117**), the 11,13-diacetate (**114**), the 2,11-acetate (**118**), the 2-acetate (**119**), the 11-acetate (**116**), and the 13-acetate (**115**) in yields of 5.6, 44, 6, 3.4, 9, and 14%, respectively, after chromatographic purification [15].



114. R=H, R_1=R_2=Ac
115. R=R_1=H, R_2=Ac
116. R=R_2=H, R_1=Ac
117. R=R_1=R_2=Ac
118. R=R_1=Ac, R_2=H
119. R=Ac, R_1=R_2=H

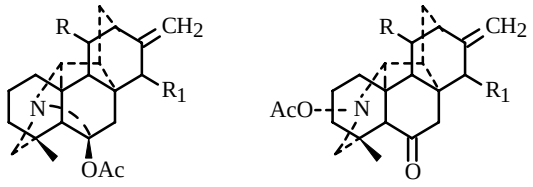
Acetylation of tangutisine (**102**) by acetic anhydride in the presence of *p*-toluenesulfonic acid produces tangutisine

tetraacetate (**120**) [52, 79].



102 **120**

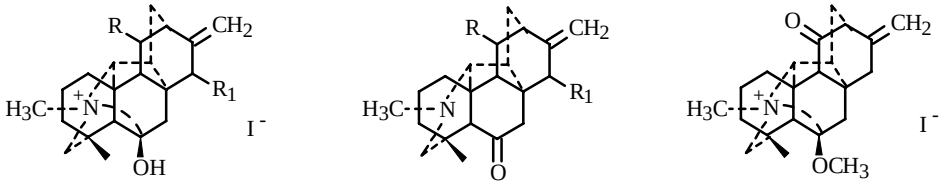
The hydroxyls have different reactivities. Their different positions and stereochemical environments enable the necessary derivatives to be prepared by selecting the reagents. Thus, hetisane alkaloids containing a C6 hydroxyl, which are carbinolamines, can react in two tautomeric forms, the carbinolamine and the aminoketone. For example, acetylation of spiradine A (**89**) and pseudokobusine (**82**) produces both the O-acetyl (**121** and **122**) and N-acetyl (**123** and **124**) derivatives [60, 75].



121. R=O, R_1=H
122. R=R_1=β-OH

123. R=O, R_1=H
124. R=R_1=β-OH

Alkaloids **89** and **82** react with methyl iodide in methanol to give the iodomethylates **125** and **126**, which are converted by aqueous ammonia or silver oxide in 50% aqueous methanol to the N-methylsecoderivatives **127** and **128**. Heating **127** with methyl iodide at 100°C in a sealed ampul gives the iodomethylate **129**, subsequent Hofmann degradation of which gives **129a** [75].

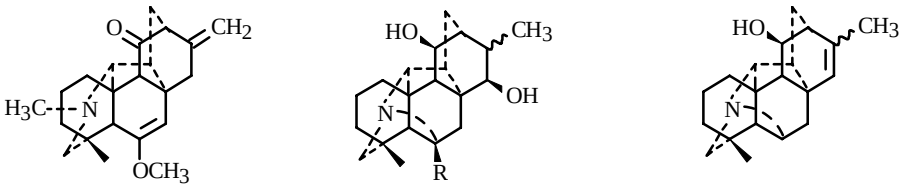


125. R=O, R_1=H
126. R=R_1=β-OH

127. R=O, R_1=H
128. R=R_1=β-OH

129

N-Methylsecopseudokobusine (**128**) can be converted back into pseudokobusine iodomethylate (**126**) by HI. Reduction by sodium in methanol occurs selectively at the C6 hydroxyl, converting dihydropseudokobusine (**130**) into dihydrokobusine (**131**).



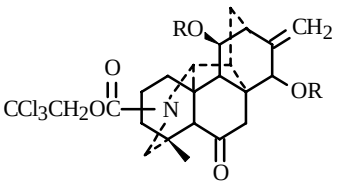
129a

130. R=OH
131. R=H

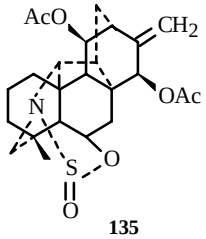
132

Under these conditions kobusine (**68**) and pseudokobusine (**82**), in which the C15 hydroxyl is allylic, give the same product **132** [60].

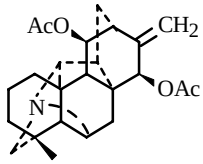
The conversion of pseudokobusine into kobusine in six steps has been reported [95]. The Schotten—Baumann reaction was used first to prepare ketocarbamate **133**, which is formed from **82** and the trichloroethyl ester of chloroformic acid in CH_2Cl_2 under alkaline conditions. Acetylation of **133** gives the diacetate **134**, the reaction of which with thionylchloride in CH_2Cl_2 in the presence of pyridine gives the cyclic sulfinyl derivative **135** (14%) and kobusine diacetate (**136**, 37%).



133. R=H
134. R=Ac



135



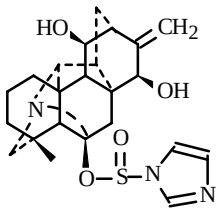
136

Elimination of SO_2 forms **136** in 80% yield upon sublimation of **135** at 180-191°C (2 mm Hg). Hydrolysis of **136** gives kobusine. The method used to prepare the cyclic sulfinyl derivative and to eliminate subsequently SO_2 is a new reaction that can be used to form the N–C6 bond.

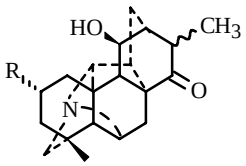
A shorter route to the conversion of pseudokobusine into kobusine was developed later [96] via the thioimidazole **137**, which is prepared by shaking **82** with N,N′-thiocarbonyldiimidazole in CH_2Cl_2 at room temperature for 21 h with subsequent treatment of **137** with tri-*n*-butyltinhydride.

Alkaloids with a C15 hydroxyl react owing to its allylic position relative to the exomethylene.

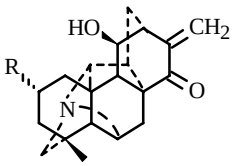
It was mentioned above that kobusine and pseudokobusine are reduced by sodium in propanol to the 15-dehydroxycompound **132**. Catalytic hydrogenation of **68** over Pd-black in acidic medium causes isomerization to methylketones **138** that are epimeric at C16. Oxidation of kobusine by pyridinium dichromate or active MnO_2 gives the conjugated enone **139**. The analogous methylketones **140** and enone **141** are obtained from isohypognavine (**60**) [60].



137



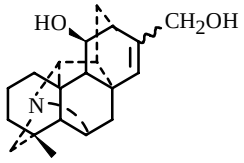
138. R=H
140. R=OBz



139. R=H
141. R=OBz

Heating kobusine with dilute HCl produces the isomers **138**, **142**, and **143** [60].

The correlation between isohypognavine (**60**) and kobusine (**68**) was inferred by oxidation of 15-ketodihydroisohypognavine (**140**) by chromic anhydride in acetic acid to 11,15-diketodihydroisohypognavine (**144**) with subsequent hydrolysis of the benzoylhydroxy group, mesylation of the resulting alcohol **145**, and hydrogenation of the mesylate **146** to 11,15-diketodihydrokobusine (**147**) [60].



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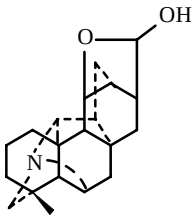

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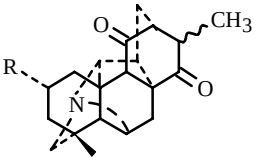
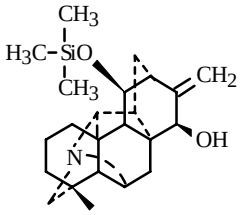


144. R=OBz
145. R=OH
146. R=OSO_2CH_3
147. R=H

Whereas benzoylation of kobusine gives a mixture of three products (11-benzoyl-, 15-benzoyl-, and 11,15-dibenzoylkobusine), silylation in the presence of pyridine at -(42-36)°C occurs stereospecifically to form 11-trimethylsilylkobusine (**148**) in 60% yield. Subsequent benzoylation and removal of the silyl group produces 15-benzoylkobusine (**149**) in quantitative yield. Oxidation of **149** by pyridinium chlorochromate in CH_2Cl_2 in the presence of sodium acetate gives 11-dehydro-15-benzoylkobusine (**150**) in 80% yield. Wolff—Kishner reduction of **150** using the literature method [97] gives nominine (**71**) (22%) and the cyclopropane derivative **151** (46%), the structure of which was found by XSA [54].



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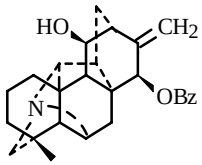

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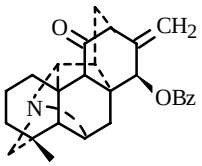
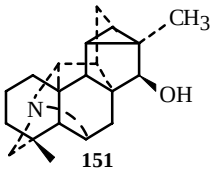
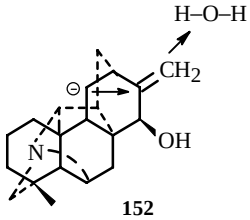


150

It was suggested that the unusual product (**151**) that is isomeric with nominine may be formed under Wolff—Kishner conditions using hydrazine hydrate and hydrazine hydrochloride via the intermediate carbanion **152**. The reduction products **71** and **151** were not obtained upon Wolff—Kishner reduction in the absence of hydrazine hydrochloride. This is a rare instance of the formation of a C–C bond during Wolff—Kishner reduction.

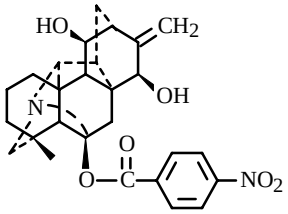


151



152

15-Benzoylpseudokobusine (**21**) [28] can be synthesized by benzoylation of pseudokobusine. The following derivatives of pseudokobusine were isolated by chromatographic purification on silica gel: 6-benzoate, 11-benzoate, 15-benzoate, 6,11-dibenzoate, and 6,15-dibenzoate in the ratio 21:3:1:49:19, i.e., benzolyation is most facile at the C6 hydroxyl and most difficult at C15. 15-Benzoylpseudokobusine was synthesized using selective protection of the C6 hydroxyl via reaction with *p*-nitrobenzoylchloride in pyridine at room temperature for 5 min with subsequent benzoylation of **153**. Compound **154** was obtained in 30% yield from the benzoylation products. Removal of the protecting group of **154** by 28% aqueous ammonia in CH_3OH—$CDCl_3$ gave 15-benzoylpseudokobusine (**21**).



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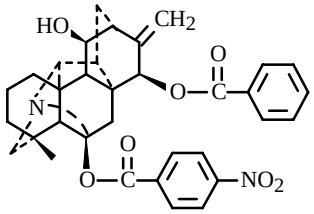
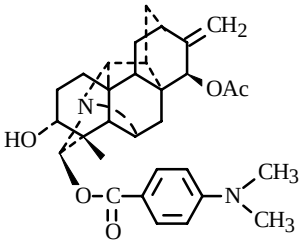


154

Esterification of andersobine (**5**) with 4-dimethylaminobenzoylchloride in dry pyridine in the presence of 4-dimethylaminopyridine at room temperature for four days acylates selectively the C19 hydroxyl to give **155** [12].



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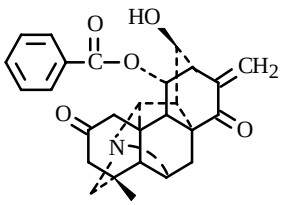

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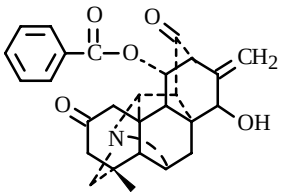
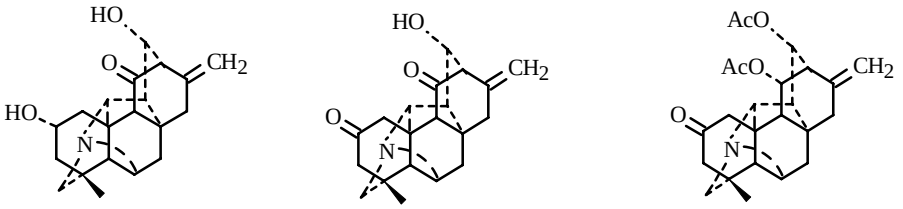


157

Oxidation of cardiopetamine (**63**) by Cornforth reagent at 25°C gives α,β-unsaturated ketone **156** in 48% yield and β,γ-unsaturated ketone **157** in 36% yield [25].

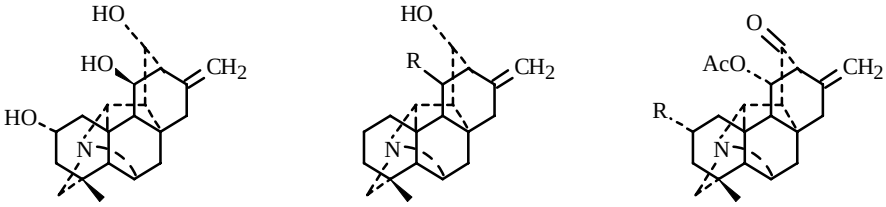
Sarett oxidation of hetisine (**32**) in CH_2Cl_2 at -5°C and chromatographic purification on Al_2O_3 give 11-dehydrohetisine (**158**) in 36% yield and 2,11-didehydrohetisine (**159**) in 21% yield.



158 **159** **160**

Oxidation of 11,13-diacetylhetisine (**114**) by this same reagent gives the 2-dehydroderivative **160**, alkaline hydrolysis of which gives hetisinone (**33**). Reduction of **158** by $NaBH_4$ produces 11-epihetisine (**161**) [15].

Wolff-Kishner reduction of **33** gives 2-dehydroxyhetisine (**162**), selective Sarett oxidation of which produces 2-dehydroxy-11-ketohetisine (**163**) [98].



161

162. R=α-OH
163. R=O

164. R=O
165. R=OAc

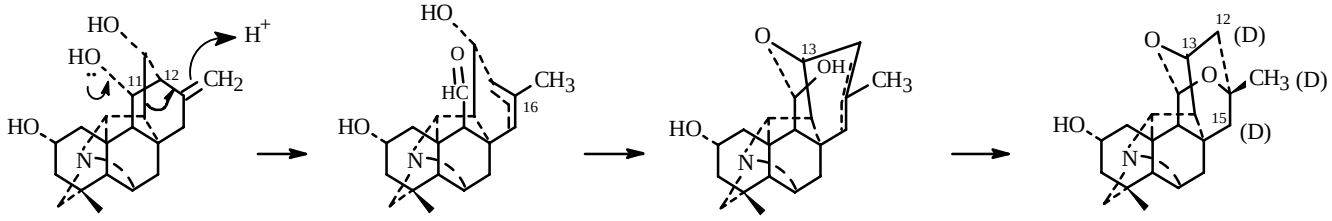
Sarett oxidation of 11-acetylhetisine (**116**) and 2,11-diacetylhetisine (**118**) gives 11-acetyl-2,13-didehydrohetisine (**164**) and 13-dehydro-2,11-diacetylhetisine (**165**), respectively [15].

Hetisine and its derivatives **33**, **158**, **159**, **161**, **163**, **164**, and **165** were then used to study rearrangements [3].

REARRANGEMENTS OF HETISINE AND ITS DERIVATIVES

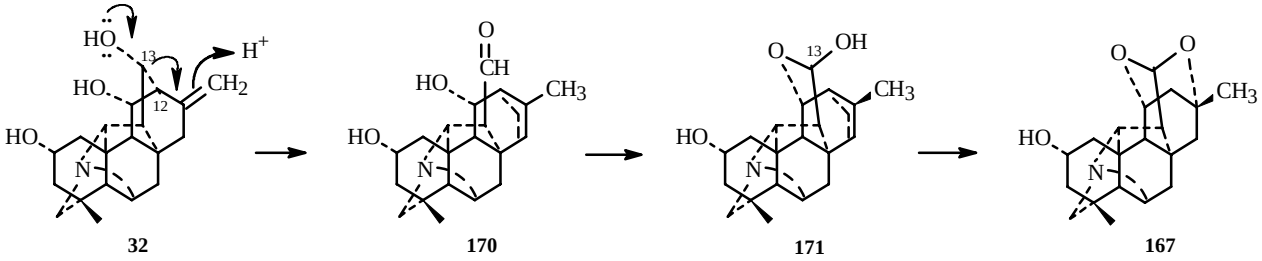
Studies of the structure of hetisine (**32**) were hindered by extensive changes in the C framework that often occur during its chemical conversions. Thus, as long ago as 1959 [99], **166** with the same formula as hetisine was obtained during treatment of hetisine with aqueous H_2SO_4. However, only in 1981 [100] it was demonstrated using XSA of **166** that an unusual rearrangement of the dihydroxybicyclo-[2,2,2]-octane into an adamantane-type framework occurs. Brief heating of hetisine (10 min) with aqueous acid (10% HCl or 5% H_2SO_4) gives adamantane-type rearrangement products **166** and **167** in yields of 95 and 5%, respectively. The structure of **167** was elucidated by comparative analysis of spectral data with those of **166**.

Facile cleavage of the C11–C12 bond leads to the main rearrangement product **166**. Less favorable cleavage of the C12–C13 bond gives the minor product **167**.



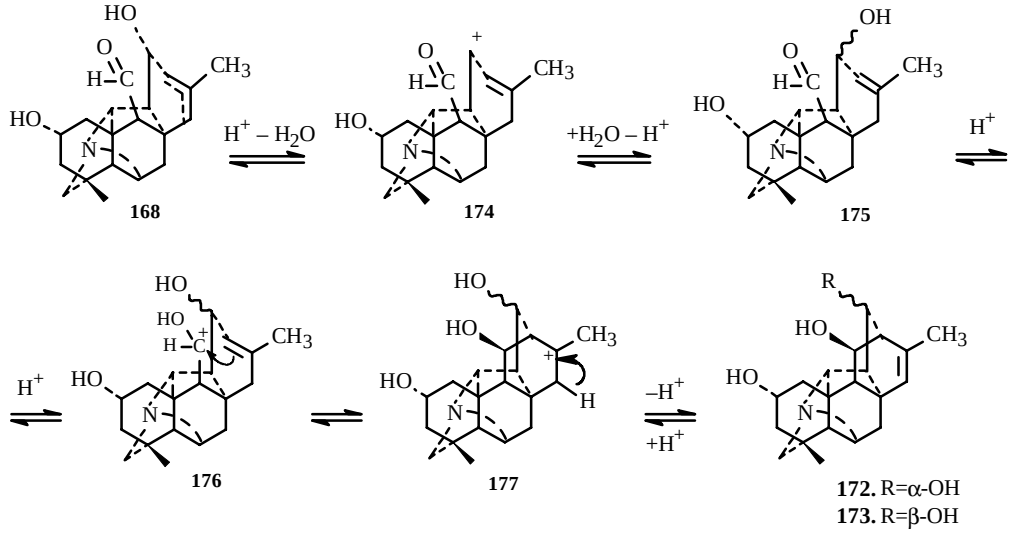
32 **168** **169** **166**

The following mechanism for the transformation of hetisine into the rearrangement product **166** was proposed [100]. Protonation of the exocyclic double bond and retroaldol reaction involving the 11-OH group give aldehyde **168**. Cyclization of hemiacetal **169**, which forms from the aldehyde and 13-OH, gives acetal **166**. It was suggested that intermediate **169** cannot be a dihydroxyaldehyde formed by hydration of **168** at C16, on one hand, owing to the ease of forming **166** and, on the other, because hydration of **168** to the dihydroxyaldehyde would not occur stereospecifically to give the single isomer that would then cyclize into **166**.



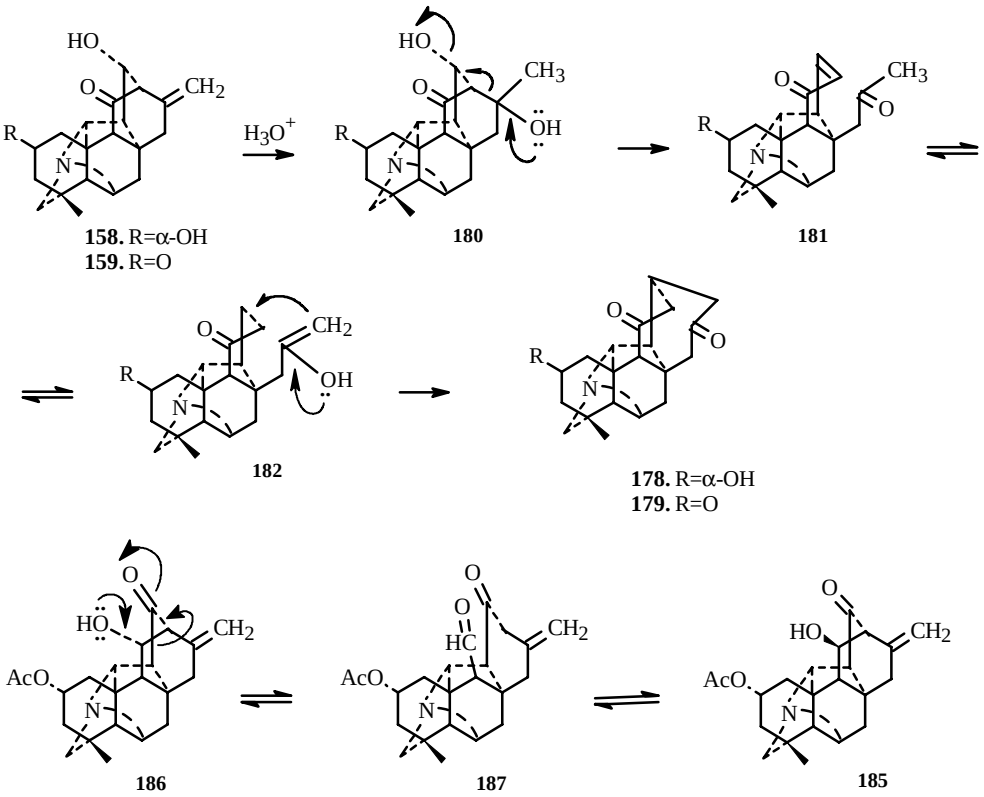
The proposed mechanism of hetisine rearrangement agrees with results obtained by heating **32** with 10% DCl in D_2O under a N_2 atmosphere. The main product **166** contained D atoms on C12, C15, and C17. It was proposed [100] that the minor rearrangement product **167** forms from hetisine by a mechanism analogous to that for **166** via the less preferred cleavage of the C12–C13 bond and intermediates **170** and **171**

Heating 11-epihetisine (**161**) in 5% aqueous H_2SO_4 for 10 min gives the same products **166** and **167** but in a 1:3 ratio. This indicates that cleavage of the C11–C12 bond becomes less preferred upon changing the configuration of the C11 hydroxyl from α to β [101].



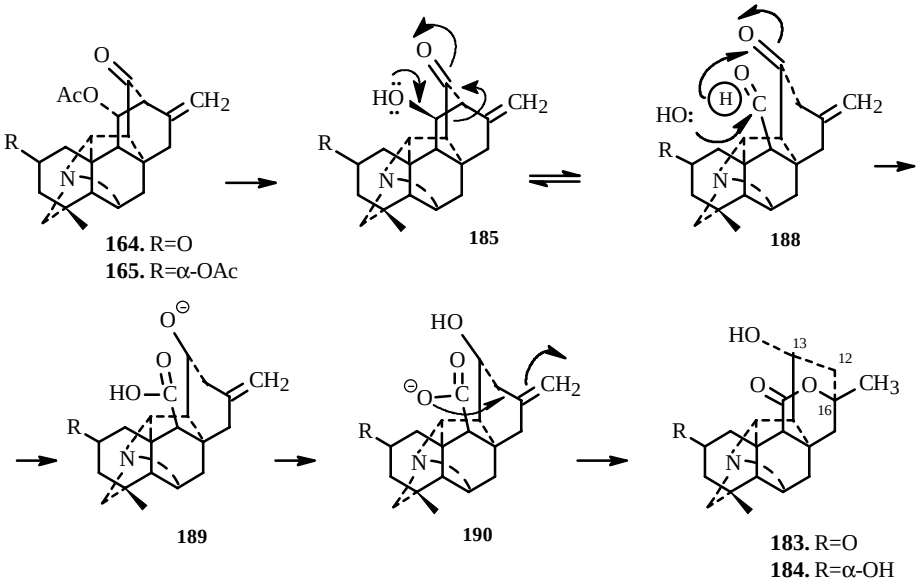
If the acid-catalyzed rearrangement of hetisine is carried out for longer time, isomerization products **172** and **173** form in 20% yield in a 1:1 ratio in addition to **166** and **167** (overall yield 70%). Compounds **172** and **173** are epimers at C13. The mixture of epimers could not be separated. Their structures were established by spectral means and XSA. The electron-density map showed the co-existence of both epimers in the crystal [101]. It was proposed that the epimeric products of hetisine isomerization, which have the same β-configuration for the C-11 hydroxyl, may be formed from intermediate aldehyde **168** via the carbocation **174**. The configuration of the C13 hydroxyl may be either α or β because a water molecule can add to the stable allylic carbocation **174** from both sides. The formation mechanism of **172** and **173** from **174** includes reactions **174** ↔ **175** ↔ **176** ↔ **177**, which are reversible in acidic medium. The fact that rearrangement products **166** and **167** are formed in small amounts upon heating a mixture of **172** and **173** in 5% aqueous H_2SO_4 for 6 h is consistent with the above reactions being reversible [101].

The unique rearrangement products **178** and **179** are obtained upon heating 11-dehydrohetisine (**158**) and 2,11-didehydrohetisine (**159**) with 45% H_2SO_4 for 1.5 h. The structure of **178** was elucidated by XSA; of **179**, by spectral methods and oxidation of **178** by pyridinium chlorochromate to **179**. The proposed mechanism of this rearrangement [102] includes hydration of **158** and **159** at C16 to give the intermediate **180**. Subsequent dehydration and enolization of **181** produces **182**, Michael cycloaddition of which gives rearrangement products **178** and **179**. XSA showed that the carbonyls on C11 and C16 in the eight-membered ring of **178** are situated almost parallel.

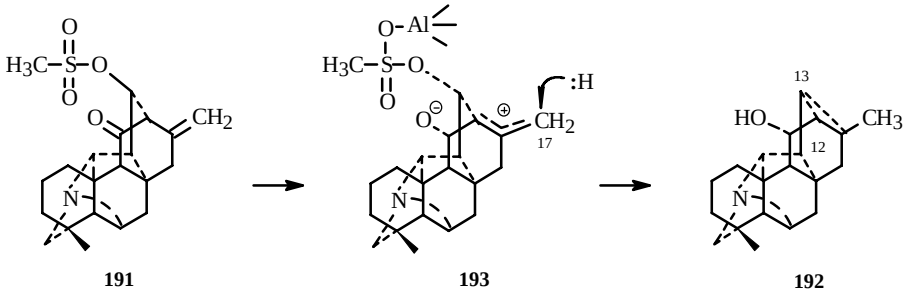


Reaction of 11-acetyl-2,13-didehydrohetisine (**164**) and 2,11-diacetyl-13-dehydrohetisine (**165**) with aqueous methanolic K_2CO_3 gives the new rearrangement products **183** and **184**, which contain a lactone ring. The structure of **183** was found by XSA; of **184**, by oxidation with chromic anhydride in pyridine to **183**. If the reaction of **165** with aqueous methanolic K_2CO_3 is carried out at room temperature, 2-acetyl-11-epi-13-dehydrohetisine (**185**) forms. The 11-OH group in **185** epimerizes through hydrolysis of the C11-acetate in **165** to give **186**. Subsequent retroaldol reaction of **186** to aldehyde **187** and aldol condensation give the 11β-OH epimer **185** [3].

The following mechanism for the **164** → **183** and **165** → **184** rearrangements was proposed [103]. The first step includes saponification of the acetyl group by the mechanism described above to form the 11-OH epimer **185**. Cannizzaro intramolecular reaction, including attack of hydroxide ion at the formyl C atom and transfer of a hydride in **188** from the aldehyde to the carbonyl, occurs under more forcing conditions with heating. The carboxyl and alcohol anion that are formed in **189** convert via proton exchange into the more stable acid anion **190**, cyclization of which leads to rearrangement product **183** or **184**.



2-Dehydroxy-11-dehydrohetisine (**163**) was obtained from hetisine in an attempt to correlate it to kobusine [98]. Mesylation of **163** and reduction of mesylate **191** by $LiAlH_4$ give instead of the expected kobusine the unusual rearrangement product **192**, which contains a cyclopropane ring. The structure of **192** was solved by XSA. It was proposed that **192** forms via intermediate **193**, in which Al as the oxide or hydride coordinates to one of the O atoms of the mesylate, producing partial ionization. Hydride attack at C17 of **193** produces cyclopropyl derivative **192**.



191 **193** **192**

This was the first example of such framework rearrangements of DA. However, similar rearrangements are known for other systems [104-106]. Rearrangements of DA have been reviewed [3].

The data presented above indicate that hetisine and its derivatives that contain functional groups on C11 and C13 in the bicyclo-[2,2,2]-octane portion are capable, depending on the conditions, of rearranging into unique compounds with new C frameworks. Certain of these compounds are found in plants. For example, **166** with the adamantane framework was isolated from *Aconitum heterophyllum* [100]. The hetisane alkaloids zeraconine (**57**) and zeraconine N-oxide (**74**), which have been isolated from *A. zeravschanicum* [90], have a C15=C16 double bond like the isomeric compounds **172** and **173**.

PHYSICAL METHODS

Physical methods have been applied to the determination of DA structures for the last three decades. This reduced the required volume of studies by chemical methods, accelerated structure elucidation, and sharply decreased the amount of a substance needed for its analysis.

IR and UV Spectroscopy. Whereas the IR spectra of hetisane-type DA typically contain absorptions in the ranges 1640-1665, 3100-3020, and 900-870 cm^{-1} (C16=C17 double bond) [23], their UV spectra in the visible region are transparent. Only alkaloids with β,γ-unsaturated carbonyls absorb in the ranges 205-212 and 300-305 nm [1, 23, 54, 69-71].

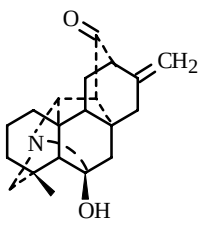
Circular Dichroism. Chiroptical methods have been applied to hetisane-type DA mainly to determine the position of a β,γ-unsaturated carbonyl group and the absolute configuration by comparing circular dichroism (CD) spectra with those of an alkaloid for which the absolute configuration has been established by XSA.

A relation between the position of a β,γ-unsaturated carbonyl and the sign of the Cotton effect (CE) in the range 304-305 nm has been found in the CD spectra of hetisane alkaloids.

The CD spectra of **94** [76], **96** and **97** [77], which have a C11 carbonyl, and 11-ketoderivatives, e.g., **158** [15], exhibit a positive CE. If the β,γ-unsaturated carbonyl is located on C13, then the CE is negative, for example, in the CD spectra of 13-dehydro-2,11-diacetylhetisine (**165**) [15] and 13-ketoderivative **194** that is obtained from spirasine XIV (**98**) and spirasine XV (**99**), which are epimeric at C13 [77].

A positive CE is also observed in the CD spectrum of 2,11-didehydrohetisine (**159**) at 304 nm. The CD spectrum of 2-dehydrohetisine (**33**) does not exhibit a CE for the C2 carbonyl in this region but does have a weak negative CE at 220 nm, which is also observed in the spectrum of **159** [15].

This principle was used to correct the structure **195** that was proposed earlier for paniculatine [1]. Comparison of the CD spectrum of dehydropaniculatine (**196**), which exhibits a negative CE at 303.5 nm, with those of the 11- and 13-ketoderivatives showed that paniculatine has structure **81** and, therefore, the hydroxyl is located on C13 and the benzoyl is on C11, and not the reverse, as in **195** [71].



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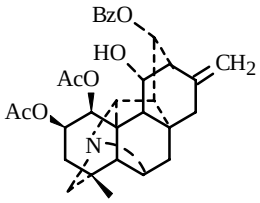

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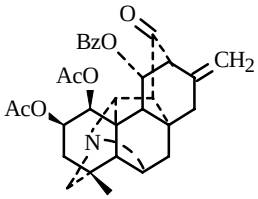
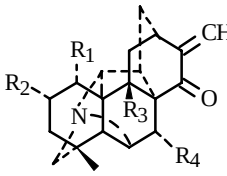


196

The CD spectra of 15-ketoderivatives of nominine (**197**), sanyonamine (**198**), ryosenamine (**199**), 1-acetylhypognavine (**200**), and torokonine (**201**), which were prepared by oxidation of the corresponding alkaloids by freshly prepared MnO_2 or pyridinium dichromate, were also studied.



197. $R_1=R_2=R_3=R_4=H$ [67]
198. $R_1=R_3=R_4=H$, $R_2=OH$ [67]
199. $R_1=R_4=H$, $R_2=OBz$, $R_3=OH$ [44, 48]
200. $R_1=OAc$, $R_2=OBz$, $R_3=OH$, $R_4=H$ [44, 48, 67]
201. $R_1=H$, $R_2=OBz$, $R_3=R_4=OH$ [82]

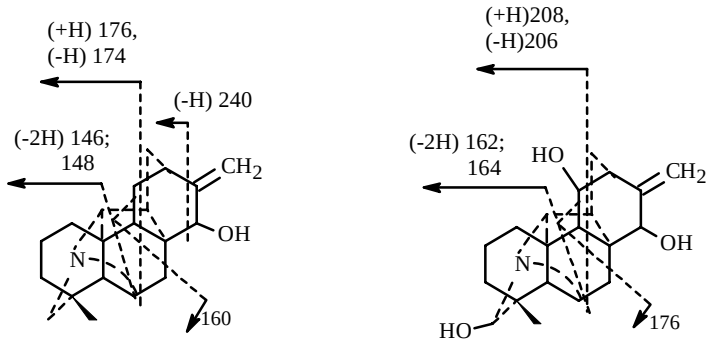
The UV spectra of α,β-unsaturated ketones exhibit strong absorption maxima in the range 220-260 nm and weak absorptions above 300 nm. Therefore, they give more complicated CD spectra. Thus, the spectra of α,β-unsaturated ketoderivatives **197**, **198**, and **200** contain positive CEs at 235, 260, 330 (sh), 337 (sh), 353, 368, and 388 (sh) nm [67]. Analogous curves with positive CEs are obtained for **199** and **201** [44, 82]. The structures and absolute configurations of ryosenamine (**83**) and hypognavine (**35**) were established by XSA [44, 45]. The absolute configurations of nominine, sanyonamine, and torokonine were established based on the very close similarity of the CD spectra of **197**, **198**, and **200** to those of **199** and **201**. The space structure of kobusine (**68**) was established by correlation with the CD curves of 11-dehydrokobusine (**44**) and spiradine A (**89**), the absolute configurations of which were elucidated by XSA [54].

Mass spectrometry is not as effective as NMR spectroscopy in the structural analysis of hetisane alkaloids. The mass numbers and elemental compositions of the molecular ions [32, 55, 72, 75, 77, 82] are given in publications on hetisane alkaloids. Sometimes fragment ions are indicated without noting the relative intensity [28, 71, 88]. Most studies report the mass numbers and relative intensities of the maximum and principal ion peaks. The first attempt to study in detail mass spectra of this type of alkaloids [107] involved an analysis of literature data on the mass spectra of >20 compounds and detailed investigations of the mass spectra of nominine (**71**), hetisine (**32**), and talatizine (**101**).

The molecular ions of 15-acetylcardiopetamine (**18**), diacetylhypognavine (**55**), isohypognavine (**60**), cardiopetamine (**63**), nominine (**71**), and sanyonamine (**86**) are the base peaks in their mass spectra despite the presence in some of these of esters on C2 and C11. The stability of the molecular ions decreases significantly if an OR group is present on C1, C6, and C9. The fragmentation patterns are variable and depend on the position of the O-containing substituent. If the OR is on C1 [1-acetyl-15-ketohypognavine (**200**) and crassicauline-B] and C9 (ryosenamine), formation of $[M - OR]^+$ ions with maximum intensity becomes characteristic. If C6 has a hydroxyl, the role of competing decomposition—elimination of acyloxy radicals from C11 (geyerine, geyerinine) or C13 (geyeridine) increases.

The mass spectra of nominine (**71**), hetisine (**32**), and talatizine (**101**) indicate that the M^+ peaks have the maximum intensity. The decomposition features of these alkaloids were found using high-resolution mass spectra (HRMS) and metastable defocusing spectra (MD). The hydroxyl is preferentially lost from C13 after cleavage of the C14–C20 bond in **32** during the generation of the $[M - OH]^+$ (39%) ion. The formation of stable $[M - OH]^+$ suppresses other decomposition pathways, which are represented in the spectrum by medium or low intensity peaks (from 12 to 2%).

The spectra of nominine and talatizine are consistent with several common decomposition pathways that begin with cleavage of the bridge C14–C20 bond. Subsequent decomposition of ring *B* gives ions with *m*/*z* 146, 148, and 160 (nominine) and 162, 164, and 176 (talatizine). Decomposition of rings *B* and *C* forms ions with *m*/*z* 174 and 176 (nominine) and 206 and 208 (talatizine) (Fig. 2).



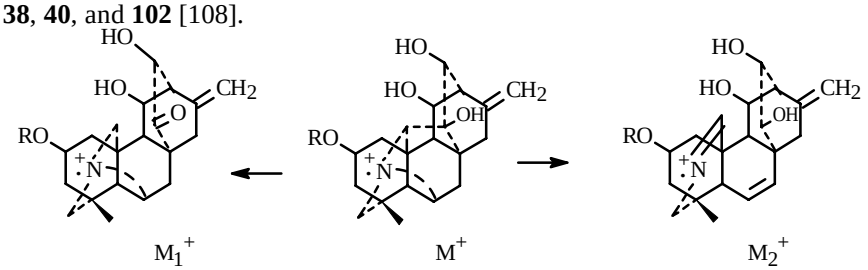
71. M^+ 297 **101.** M^+ 329

Fig. 2. Fragmentation patterns of nominine (**71**) and talatizine (**101**).

The formation of fragments that do not contain N is an interesting and unusual feature of the mass spectra of hetisane alkaloids. Nominine has one ion in this series ($[M - C_3H_7N]^+$) with *m*/*z* 240. The spectrum of talatizine exhibits several peaks for fragments without N with *m*/*z* 253 ($[M - C_2H_6NO_2]^+$) and 226 ($[M - C_4H_9NO_2]^+$).

Mass spectra of zeraconine (**57**) and its N-oxide (**74**) have also been measured. The spectrum of **57** has a rather strong peak for the molecular ion and a base peak with *m*/*z* 58, which is consistent with the presence of a dimethylaminoethyl group.

The mass spectra of 2-acetyl-14-hydroxyhetisine (**3**) and 2-isobutyryl-14-hydroxyhetisine (**40**) and their fragmentation patterns have been reported [51]. It was proposed that $[M - 28]^+$ ions form by loss of CH_2N or ethylene from ring *B*. However, HRMS and a comparison of V/E coupled scanning and MD spectra [108] showed that $[M - 28]^+$ ions form by loss of CO_2 from **3** and **40** under the mass-spectrometry conditions. Mass spectrometry of 14-hydroxyhetisine (**102**) and its acyl derivatives **1**, **3**, **38**, and **40** showed that adding a C14-OH decreases sharply the stability of the M^+ ion. This OH activates α-cleavage of the C14–C20 bond, after which the molecular ion isomerizes into M_1^+ and M_2^+, which are the sources of the principal fragments in the spectra of **1**, **3**, **38**, **40**, and **102** [108].



M_1^+ M^+ M_2^+

The spectra of **1**, **3**, **40**, and **102** have intense $[M - 15]^+$ peaks, which are practically absent in the spectrum of hetisine. These ions further decompose via loss of ROH. The peaks of the corresponding ions $[M - 33]^+$ in **102**, $[M - 75]^+$ in **3**, $[M - 89]^+$ in **1**, and $[M - 103]^+$ in **38** and **40** with *m*/*z* 312 are rather strong (from 11 to 35%).

Another fragmentation pathway for alkaloids with a C13–C14 diol is loss of hydroxyl. Peaks of $[M - OH]^+$ ions (intensities from 84 to 100%) are precursors of the strong fragments $[M - 45]^+$. The composition of the lost fragment, CHO_2, corresponds to loss of OH and CO. Loss of two CO fragments gives a $[M - 56]^+$ peak, which is formed from the C13–C14 diol. This is consistent with the absence of this peak in the spectrum of **38**. The spectra of **1**, **3**, and **40** have strong $[M - OR]^+$ peaks. However, loss of an acyloxy radical is possible only for **3** and **40**, $[M - 59]^+$ and $[M - 87]^+$, respectively. For acoridine (**1**), $[M - 73]^+$ is formed by loss of a propionyl radical and loss of two CO fragments and OH.

The spectrum of **38** exhibits distinct selectivity. It contains $[M - 43]^+$ (100%) and $[M - 59]^+$ (46%) peaks that are formed via loss of acetyl and acetoxy radicals from the 13-OAc.

Thus, the principal fragmentation pathways of **1**, **3**, **38**, **40**, and **102** are determined by the presence of OH on C14. In contrast with other hetisane alkaloids, loss of elements from rings *A*, *B*, and *C* and formation of fragments without N are not characteristic.

Mass spectra of N-oxides **72-74** contain a strong triplet of peaks with *m*/*z* $[M - 16]^+$, $[M - 17]^+$, and $[M - 18]^+$, which are characteristic of such compounds [86, 91, 107]. Their molecular ions are weak.

Thus, mass spectrometry is used to determine the elemental composition of alkaloids and to elucidate their structures.

In several instances the position of individual fragments, especially acyl residues, can be determined and the proposed structures can be verified.

NMR Spectroscopy. Proton and C magnetic resonance (^{1}H and ^{13}C NMR) in most instances enables the structure of hetisane alkaloids to be determined.

Two broad 1H singlets, more rarely triplets or a doublet of doublets (J = 1.2-2 Hz), at 4.48-5.52 ppm are characteristic in the ^{1}H NMR spectra of these alkaloids for the protons of the exocyclic methylene. Signals for protons of the methoxyl and N-methyl groups are absent. The position and nature of the substituents have a significant effect on the chemical shifts (CS) of the methylidene protons. Without substituents on C11, C13, and C15, the signals for these protons appear at 4.48-4.74 ppm [26, 109]. However, they are more often observed at 4.70-5.00 ppm because most hetisane alkaloids have substituents in at least one of these positions. These protons resonate at weaker field at 5.00-5.52 ppm in the spectra of compounds with hydroxyl and acyl substituents on C15 [11, 12] and other substituents in the other positions [22, 24, 25, 59].

Protons of the tertiary 4-CH_3 resonate at 0.86-1.20 ppm. A distinguishing feature of alkaloids with a C6 OH is the absence in their spectra of the characteristically broadened H-6 singlet at 3.07-4.05 ppm and a weak-field shift of the 4-CH_3 singlet to 1.29-1.68 ppm [14, 69]. An analogous shift of this signal is observed in the spectrum of andersobine, which has 3α- and 19β-OH groups [12].

Protons of the C19 methylene resonate as two 1H doublets at 2.21-3.02 and 2.61-3.85 ppm (J = 11.5-14 Hz) [14, 21, 22, 30]. The gem-hydroxy proton appears as a singlet at 4.08-4.89 ppm if C19 contains OH [12, 112].

The spectra of all hetisane alkaloids, with the exception of orgetine that have a C20 OH, contain the signal for H-20 as a broad singlet at 2.04-4.30 ppm. The spectra also have a characteristic 1H signal for H-12, which is observed at 2.14-2.94 ppm as a broad singlet, a doublet, or doublet of doublets with J = 1-4.8 Hz [12, 13, 76].

The overwhelming majority of hetisane alkaloids contain hydroxy or acyloxy groups on C2, C11, C13, and C15. Valuable information about their orientation can be obtained from ^{1}H NMR spectra. Thus, the gem-hydroxy proton H-2β resonates at 4.02-4.31 ppm as a broad singlet or multiplet with a half-width of 8-12 Hz if C2 contains an OH, which as a rule has the α-orientation [13, 67, 69]. In acyl derivatives, OCOR-2α and OCOAr-2α, the signal for H-2β shifts to 4.95-5.17 [109, 113] and 5.40-5.54 ppm, respectively [23, 44, 82]. The signals for H-2α of paniculatine and cossonine, which contain 2β-acetoxy and 2β-benzoyloxy, respectively, are observed at 5.55 [1, 71] and 5.10 ppm [64]. However, paniculatine has an OAc-1β substituent; cossonine, OAc-3α. These affect the CS of the H-2α signals.

The orientation of the C11 OH can be determined from the CS and the splitting constant [3]. The signal of H-11α in spectra of alkaloids containing a C11 β-OH appears as a doublet at 3.92-4.07 ppm ($J_{9,11}$ = 4.6-5 Hz) [23, 27, 59]. In those with α-OH, H-11β is observed at 4.15-4.46 ppm as a broad doublet with a large splitting constant ($J_{9,11}$ = 8-10 Hz) [11, 13, 15, 29, 64, 79]. In 11-O-acyl derivatives, H-11α and H-11β are observed at weaker field at 4.99-5.06 (d, J = 5 Hz) [23] and 5.04-5.26 ppm (d, J = 8.3-10 Hz) [15, 21, 33], respectively. In O-benzoyl derivatives, H-11β appears at 5.57-5.68 ppm (d, J = 8.4-9 Hz) [22].

The signal for a proton geminal to C13 OH is observed at 3.98-4.36 ppm as a broad doublet with SSCC $J_{13,14}$ = 8.6-11 or 4.5-5 Hz [11, 14, 29, 31, 33, 36, 77, 110].

The use of the α and β designations for the stereochemistry of C13 substituents is not consistent in the literature. Some authors [14] designate the farther substituents on C13 in the hetisine ring as α (J = 4-5 Hz, H-13β) and the closer ones β (J = 8-10 Hz, H-13α), as was accepted earlier [15, 16, 46]. Others [12, 27, 29, 55, 80] define the orientation of C13 substituents based on studies of the ^{1}H NMR spectra and Dreiding models, starting with the twist—boat conformation for ring *C* formed by C8, C9, C11, C12, C13, and C14. The protons on C13 oriented pseudoaxially are designated α; pseudoequatorially, β [12, 80]. Using the dihedral angles between the vicinal protons H-13 and H-14 that are determined from Dreiding models to determine the theoretical coupling constants and comparing them with those obtained experimentally makes it possible to determine the stereochemistry of the substituent on C-13 from the coupling constant of the 13-geminal hydroxy proton. If $J_{13,14}$ = 8-10 Hz, then the substituent has the α-orientation [13, 30, 31, 61]; if $J_{13,14}$ = 4.5-5 Hz, then it has the β-orientation [11, 76, 80]. Therefore, the stereochemistry of the C13 substituent in hetisine and its derivatives is changed from β to α [3, 12, 55]. For alkaloids in which C11, C13, and C14 have O-containing groups, H-13β appears as a broad singlet. The α-orientation of the substituent on C13 is determined from the W-coupling between H-11β and H-13β [21, 79]. Thus, substituents on C13 in guan-fu bases A, Y (acorine) [51], Z [110], F, G [52, 111], and the N-oxides of bases Z and F [86, 91] have the α and not the β-orientation.*

*We did not correct the stereochemistry of C-13 in the formulae of these alkaloids with the exception of hetisine.

With the exception of cardionine and 15-acetylcardionine, the O-containing substituents on C15 of all hetisane alkaloids have the β-orientation. The signal of a geminal hydroxy proton H-15α is observed as a broad singlet or triplet (J = 1-2 Hz) at 3.82-4.07 ppm; of a geminal acyloxy proton, 5.20-5.67 ppm. The signal of the geminal hydroxy proton H-15α in the presence of hydroxyls on C7 and C9 appears at 4.37-4.53 ppm [14, 72, 82]. The spectra of cardionine and 11-acetylcardionine, in which the isobutyryloxy on C15 is α-oriented, exhibit H-15β at 5.73 (t, J = 2.0 Hz) and 5.68 ppm (t, J = 2.2 Hz), respectively [24].

The C7 hydroxyl group in all alkaloids, as a rule, has the α-orientation. The signal for H-7β is observed as a doublet (multiplet) at 3.87-4.50 ppm (J = 2.6-4.1 Hz) [11, 14, 72, 82].

The spectra of 3-epiignavinol and sadosine, which have α- and β-oriented hydroxyls, respectively, on C3, exhibit a signal for H-3β at 3.37 ppm (d, J = 4.6 Hz) [62]; H-3α, at 3.67 ppm (d, J = 3.0 Hz) [72].

The ^{13}C NMR spectra of hetisane DA exhibit signals for 20 C atoms of the hetisane framework. Their assignments, which were made previously based on the multiplicity of the signals, consideration of substituent effects, and comparison with model compounds, were confirmed later, with a rare exception, by modern NMR methods.

The hetisane framework contains four C atoms without protons, C4, C10, C8, and C16. If neighboring C atoms lack O-containing substituents, the signals for C4 and C10 are observed at 35.9-38.7 [36, 48] and 46.0-52.0 ppm [81, 110], respectively.

A hydroxyl (O-acyl) on C3, C18, and C19 causes a weak-field shift of the signal for C4 (β-effect) to 41.2-51.2 [21, 33], 42.3-43.5 [27], and 39.7-53.2 ppm [81, 112], respectively. An analogous shift to 52.8-55.0 and 50.4-54.4 ppm is observed for the signal for C10 as a result of the β-effect of the OH (acyl) group on C1 [27] and C9 [36, 113]. A carbonyl group on C2 causes a weak-field shift of the signals for C4 and C10 to 40.3-45.9 [11, 33] and 54.8-60.7 ppm [31, 70], respectively.

A singlet for C8 appears at 40.5-44.2 ppm without O-containing substituents on C7, C9, C14, and C15 [13, 27]. A hydroxyl and carbonyl on C15 have the greatest influence on its signal. In this instance, the signal for C8 is observed at 45.0-48.9 [62, 82] and 55.8-56.1 ppm [19]. A carbonyl on C11 causes an insignificant weak-field shift to 45.1-46.6 ppm [19, 77]. This signal shifts to 48.9 [82], 50.8 [14], and 50.6 ppm [21] with OH groups on C7, C9, and C15; C7 and C15; and C9 and C14, respectively.

A singlet for C16 is observed at 138.0-147.0 ppm [77]. A hydroxyl on C15, which shifts the signal to 150.3-156.8 ppm, has the greatest effect on this signal [11, 44].

The hetisane framework contains six methine C atoms: C5, C6, C9, C12, C14, and C20.

The signal for C5 is usually observed at 58.0-62.3 ppm [21, 77]. It shifts to weak field at 50.6-55.7 ppm if C1 [48, 109], C9 [21, 44], or C7 [82] has an OH (γ-effects).

In most alkaloids, a doublet for C6 appears at 60.2-65.5 ppm. The C7 OH causes a weak-field shift of this signal to 65.6-70.3 ppm [14, 36]. The signal for the carbinolamine C6 in 6-OH substituted alkaloids is observed at 96.8-102.2 ppm [31, 33].

The C9 doublet, in the absence of substituents on neighboring C atoms, is observed at 41.2-42.9 ppm [31, 77]. A C13 carbonyl shifts this signal to weak field at 48.6-48.9 ppm [23, 70]. The simultaneous presence of C11- and C13- [13, 19] or C11- and C12-substituents [24] causes a larger weak-field shift to 55.0-58.2 ppm. The greatest weak-field shift of the signal for C9 to 65.2-65.3 ppm is observed with a carbonyl on C11 [23]. With a carbonyl on C11 and a hydroxyl on C13, the signal for C9 is observed at 65.7-67.2 ppm if the OH is 13α [76, 77]; at 73.9 ppm, if 13β [77]. The signal shifts to 78.8-81.0 ppm (α-effect) with a C9 OH [21, 113].

A doublet for C12 is observed at 36.1-36.9 ppm [26, 109, 112, 113]; with a C12 OH, at 73.1-74.6 ppm [24]. Hydroxyls on C11 or C13 shift the signal to 39.5-42.9 ppm [11, 14]. If they are both present, it shifts to 50.8-53.7 ppm (β-effects) [19, 56]. The signal for C12 is observed in approximately this same region if C11 or C13 has a carbonyl (53.2-54.0 ppm) [23, 69, 70]. A hydroxyl on C15 causes a strong-field shift by ~2 ppm [27, 48, 82]. An acetyl on C11 and C13 (β-effects) has the same effect.

A doublet for C14 is usually observed at 40.9-44.4 ppm [24, 81]; with a C14 OH, at 78.6-81.4 ppm [21, 79]. In N-oxides, this signal is observed at 85.5 ppm owing to the β-effect of the N-oxide [91]. A C13 OH causes a weak-field shift of the signal for C14 to 49.6-56.0 ppm (β-effect) [31, 77]; a carbonyl, 58.8-61.9 ppm [19, 69]. The signal for C14 undergoes a strong-field shift to 36.0 [82] and 37.6 ppm [14] owing to γ-effects of OH groups on C7, C9, and C15 or C7 and C15, respectively.

The doublet for C20 in spectra of all hetisane alkaloids resonates at 65.0-75.0 ppm, with the exception of alkaloids with

a C1 hydroxyl (acetoxy) (58.1-60.5 ppm) [30, 71, 112]. An N-oxide shifts this signal to 82.2 ppm (α-effect) [91]. A hydroxyl on C14 has an insignificant β-effect (1.3-2.2 ppm) on the signal for C20 [15, 21, 79].

A triplet for C2, which resonates in the narrow range 18.3-19.8 ppm, is a diagnostic sign that ring *A* contains no substituents. The signals for C1 and C3 appear in the broad ranges 26.4-39.3 and 24.2-38.6 ppm [11, 23, 27, 31]. As a rule, the signal for C1 is observed at stronger field (28.9-31.8 ppm) if C9 has a OH [21, 44, 113]. Hydroxyls on C18 and C19 have an analogous γ-effect on C3, which appears in these instances at 20.6-28.4 ppm [27, 81]. A hydroxyl on C1 has a β-effect on the signal for C2 (27.1 ppm) and a γ-effect on the signal for C3 (27.8 ppm) [27].

If a doublet is present at 66.1-67.2 ppm [68, 69] or 69.5-70.8 ppm [48, 110] instead of the triplet at 18.3-19.8 ppm, then C2 contains OH or acyloxy groups, respectively. The signal for C3 shifts to 36.5-43.3 ppm whereas the CS for C1 changes insignificantly (Δ = 0.5-1 ppm) (β-effects).

A carbonyl on C2 causes a weak-field shift of the signals for C1 and C3, which appear at 41.6-46.0 and 41.5-52.8 ppm, respectively [11, 14, 31].

When all three C atoms have acyl substituents, the signal for C1 is observed at 72.4; C2, 65.8; and C3, 70.9 ppm [61].

A triplet for C7 appears at 33.3-36.6 ppm [19, 23]; with a OH group on it, at 70.1 ppm [36]. A hydroxyl on C6 causes a weak-field shift of the signal for C7 to 42.5-46.7 ppm (β-effect) [11, 14]. A strong-field shift to 27.0-32.1 [44, 114], 64.3-69.8 [11, 82], and 38.8-40.7 ppm [14, 24] is noted for all signals mentioned above if C9, C14, and C15, respectively, have hydroxyls.

A triplet for C11 without substituents on C9, C12, and C13 appears at 26.8-27.1 ppm [23, 27, 44]; a doublet at 67.3-67.5 ppm, with a C11 β-OH [27, 59]; and at 72.6-74.0 ppm [31, 81], with a C11 α-OH.

The signal for C11 undergoes a weak-field shift to 33.5-39.2 ppm (β-effect) [109, 112] with a hydroxyl on C9; to 21.6-23.3 ppm (γ-effect) [14, 77], on C13.

A triplet for C13 without substituents on C11, C12, and C14 appears at 32.7-34.3 ppm [82, 109]. A doublet appears at 65.9-72.0 ppm with a OH on C13 [11, 77]. A hydroxyl on C11 causes a strong-field shift to 27.3-30.3 ppm [27, 31]. If C11 has a OH (acyloxy) (γ-effect) and C12 has a OH (β-effect), the signal for C13 is observed at 35.8-36.2 ppm [24].

The signal for C13 is observed at 27.6-28.3 ppm if C11 contains a carbonyl [23, 77] (β-effect). A carbonyl on C13 causes an analogous strong-field shift of the signal for C11 (22.7-23.4 ppm) [23, 69]. Therefore, the position of a β,γ-unsaturated carbonyl can be determined from the CS of the triplet [70].

If C11 and C13 contain OH groups, then the C11 doublets are observed at 75.6-76.9; C13, at 71.5-73.2 ppm [19, 29, 36]. The signal for C13 shifts to weak-field (79.8-81.8 ppm) if C14 has a OH [21, 51, 79]. A C9 OH shifts the signal for C11 to weak field (84.0-85.3 ppm) (β-effect) [21]. If C11 and C13 contain O-acyls, the signal for C11 is observed at 75.2-76.1; for C13, at 73.0-73.9 ppm [15, 19, 61].

A triplet for C15 appears at 32.3-36.1 ppm [31, 77]. It appears as a doublet at 70.3-75.4 ppm with a OH (acyloxy) on C15 [31, 59]. Hydroxyls on C9 [21, 113] and C14 [21, 110] cause a strong-field shift of the signal for C15 to 30.4-31.8 ppm. Hydroxyls on both C9 and C14 shift the signal to 27.9-28.0 ppm (γ-effects) [21].

The triplet for C17 in all hetisane alkaloids is observed at 104.3-114.4 ppm. An O-acyl on C15 causes a weak-field shift to 116.5-121.3 ppm [19, 59].

A triplet for C19 in most hetisane alkaloids appears at 62.7-65.0 ppm or at 90.9-95.2 if C19 contains a OH [13, 112]. An N-oxide shifts the signal for C19 to 76.2 ppm (α-effect) [91]. Hydroxyls (acyloxys) on C3 [21, 61, 62] and C18 [27] shift the signal to strong field at 58.2-60.7 ppm.

A quartet for C18 is observed in most alkaloids at 28.5-32.0 ppm. The signal shifts to strong field at 22.5-26.8 [21, 62] and 21.5-23.5 ppm [26, 81] with O-containing substituents on C3 and C19, respectively; to 20.4 ppm, with these groups on C3 and C18 [12].

Currently, ^{1}H and ^{13}C NMR data that are interpreted using 2M $^{1}H—^{1}H$ (homonuclear $^{1}H—^{1}H$ COSY correlation) and $^{1}H—^{13}C$ CS correlations (heteronuclear $^{1}H—^{13}C$ COSY or HMQC correlation) and distant $^{1}H—^{13}C$ couplings (HMBC) and NOE measurements with a rotating coordinate system (ROESY) have made it possible to determine the structures of very complicated polyfunctional hetisane alkaloids without invoking XSA.

Pharmacology. Studies of the pharmacological properties and structure—activity relationships of DA revealed [115] that hetisane alkaloids from *A. zeravschanicum* possess antiarhythmic (AA) properties. Their AA activity is greater than that of a mixture of alkaloids from this plant and its main component, heteratisine. Tadzhaconine has the highest AA activity, followed by zeravschanizine and hetisine. Nominine has the weakest activity. Increasing toxicity is observed in the order nominine < zeravschanizine < hetisine < tadzhaconine.

Hetisine exceeds songorine in its ability to block spontaneous release of Ca^{2+} from sarcoplasmatic reticulum during Ca transfer. However, it is inferior to dihydroatisine, benzoylnapelline, and benzoylheteratisine [116].

The alkaloids acsinatine, septenine, septentriosine, and tangutisine and its acyl derivatives (guan-fu base Z, acorine, acoridine) have been reported to have moderate AA activity. The toxicity decreases in the order acorine > guan-fu base F > guan-fu base Z > acoridine. The least toxic are the N-oxides of guan-fu bases F and Z. The N-oxide of guan-fu base Z (**73**) exhibits slight hypotensive and H-choline-blocking effects [101].

The total alkaloids from *D. geyerii* and one of the components, geyerine, have been reported [33] to be toxic to insect larvae and act as insecticides for locust.

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