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The Rhoeadine Alkaloids

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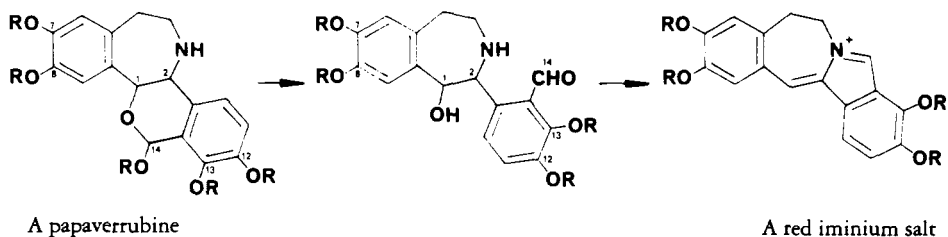
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THE RHOEADINE ALKALOIDS

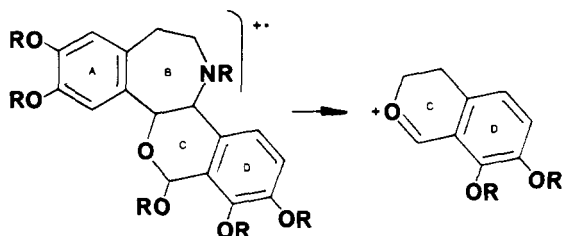
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University Park, PA 16802*

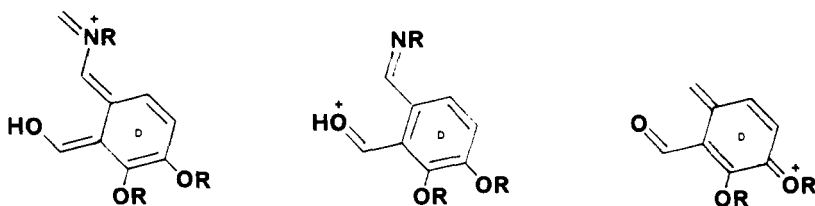
Although rhoeadine, the first member of the rhoeadine-papaverrubine group of alkaloids, was originally isolated more than one hundred years ago, the structures of these compounds were only elucidated after ^1H -nmr and ms became commonly available in the 1960s. It is interesting to note that the norrhoeadines or papaverrubines are responsible for the red color developed by opium upon treatment with strong acids, a reaction discovered as far back as 1837 (1). Their acid-catalyzed rearrangement and dehydration can be formulated as follows (5):



All these alkaloids are cyclic acetals or hemiacetals, and this functional distinction is reflected in their mass spectra, which serve as a basis for their classification (13). The acetals give abundant molecular ions and intense ($M^+ - 15$) and m/z 177 or 193 (base) mass spectral peaks due to a stable fragment incorporating rings C and D:



On the other hand, the mass spectra of the hemiacetals are characterized by fairly weak molecular ion peaks, and prominent signals at m/z 206, 192, and 163 (when ring D is methoxylated at C-12 and -13), or 190, 176, and 147 (when ring D bears a methylenedioxy group), attributed to ions with the structures:



Rhoeadines and papaverrubines have only been found among the Papaveraceae, where they are concentrated in the closely related genera *Papaver* and *Meconopsis*, with an isolated occurrence in *Bocconia* (1,2). All the sections of *Papaver* contain rhoeadines and/or papaverrubines, but the abundance and distribution of the different alkaloids varies considerably from one section to another. Thus, the relative abundance of rhoeadines and papaverrubines *vs.* morphine alkaloids in the species of the morphologically heterogeneous section *Mecones* Bernh. has led to the segregation of the new section *Glaucia* J. Novák, supported by chromosome counts and a reevaluation of morphological features (46).

Twenty-one of the compounds are known as natural products, and no new ones have been reported in recent years. Four *O*-ethyl acetals have been isolated and are probably artifacts formed in ethanol solution. Only 11 members of the group have been prepared by modification of naturally occurring alkaloids involving *N*- or *O*-methylation, acetal hydrolysis, C-14 epimerization, or *trans* to *cis* isomerization around C-1 and C-2.

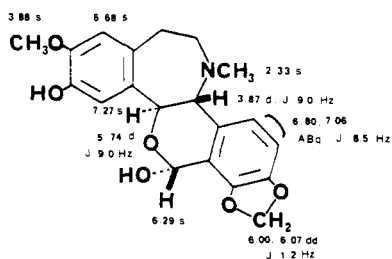
All the rhoeadines and papaverubines have the (*R*) configuration at C-2 and are dextrorotatory; C-1 and C-14 can have either stereochemistry. The problem of the absolute configuration was solved by application of the aromatic chirality rule (5), and the assignment was confirmed by X-ray diffraction analysis of rhoeagenine methiodide (48). The *cis* or *trans* relationship of the hydrogen atoms at C-1 and C-2 is readily apparent in the ^1H -nmr spectra from their coupling constants of *ca.* 2 Hz or 9 Hz, respectively.

The rhoeadine alkaloids are biogenetic derivatives of protopines, and direct evidence exists of the incorporation of labeled protopine into rhoeadine in *Papaver rhoeas* L. (48). All compounds bear oxygen substituents at C-7, C-8, C-12, and C-13 and may be derived from protopine, cryptopine, muramine, or the hitherto unknown 2-*O*-demethylcryptopine. It is noteworthy that no rhoeadine alkaloids have been found with an oxygen substituent at C-9 (corresponding to C-1 of the protopines and to C-8 of the closely related phthalideisoquinolines). Surprisingly, the widely distributed allocryptopine has no counterpart in the rhoeadine series.

The tabulated data specifically referring to the occurrence of the alkaloids in nature frequently quote secondary literature sources, especially Šantavý's monumental reviews on the papaveraceous alkaloids in Manske's series (1,2), in order to reduce the necessarily large number of literature references.

All uv data are in nm with log ϵ values in parentheses; nmr chemical shifts (δ values) are quoted for CDCl_3 solutions unless specified otherwise. The ms m/z figures are followed by the relative abundances of the ions (in parentheses), when these have been reported. The botanical names have been transcribed from the literature with only minor spelling corrections in a few cases, but no attempt has been made to achieve uniformity regarding the rank of certain taxa, which are mentioned as species by some authors and as subspecies by others.

1. N-METHYL-14-O-DEMETHYL-EPIPORPHYROXINE



$\text{C}_{20}\text{H}_{21}\text{NO}_6$: 371.1369

MP: 217-218° (MeOH) (17)

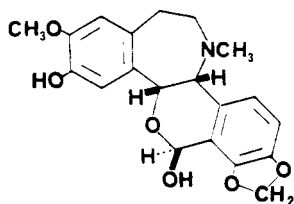
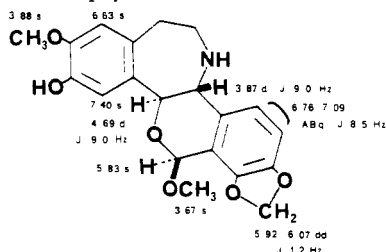
UV: (EtOH) 238, 288 (17)

^1H -NMR: (17)

MS: m/z 371 (M^+), 206, 192, 163 (17)

$[\alpha]_D$: +340° (c 0.2, MeOH) (17)

Sources: *Papaver somniferum* L. (17,1,46)

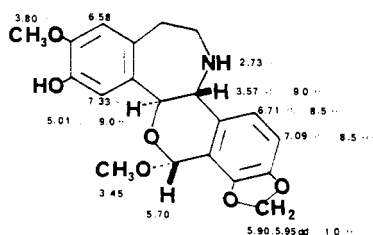
2. *cis*-N-METHYL-14-O-DEMETHYL-
EPIPORPHYROXINE $C_{20}H_{21}NO_6$: 371.1369Sources: Semi-synthetic (from *N*-methyl-14-O-demethylepiporphyroxine) (27)3. PAPAVERRUBINED
(Porphyroxine) $C_{20}H_{21}NO_6$: 371.1369

MP: 237-239° (MeOH) (15)

UV: 232 (3.90), 287 (3.83) (15)

 1H -NMR: (6)MS: m/z 371, 206, 192, 179 (13,22)[α]D: +391° (CHCl₃) (26)

Sources: *Meconopsis betonicifolia* Franch. (2), *M. borridula* Hook. f. & Thoms. (2), *M. napaulensis* DC. (2), *M. paniculata* (D. Don.) Prain (2), *M. robusta* Hook. f. & Thoms. (2), *M. rudis* Prain (2), *M. sinuata* Prain (2), *Papaver albiflorum* subsp. *austromoravicum* Kubát (43), *P. alboroseum* Hulten (1,2), *P. alpinum* subsp. *alpinum* (1,2), subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (2), subsp. *rhaeticum* (2), subsp. *sendtneri* (2), subsp. *tatricum* Nyár. (1), *P. anomalum* Fedde (1), *P. argemone* L. (1), *P. atlanticum* Ball. (1), *P. bracteatum* Lindl. (1,2), *P. californicum* A. Gray (2), *P. caucasicum* Marsch.-Bieb. (1), *P. commutatum* Fisch. & Mey. (2), *P. decaisnei* Hochst. (39), *P. feddei* Schwz. (1), *P. fugax* Poir. (1,2), *P. glaucum* Boiss. & Hauskn. (1,2,46), *P. heldreichii* Boiss. (1), *P. hybridum* L. (1), *P. latericum* C. Koch. (1), *P. lecoquii* Lamotte (43), *P. litwinowii* Fedde ex Bornm. (42), *P. macrostomum* Boiss. & Huet. (1), *P. nudicaule* L. (1), *P. orientale* L. (1,2), *P. oreophilum* Rupr. (1,41), *P. paeoniflorum* (1), *P. pavoninum* Fisch. & Mey. (1), *P. persicum* Lindl. (1), *P. pilosum* Sibth. & Smith (1), *P. polychaetum* Schott & Kotschy (1), *P. pseudocanescens* M. Pop. (2), *P. rhoeades* L. (1), *P. rupifragum* Boiss. & Reut. (1,2,37), *P. setigerum* DC. (1,46), *P. somniferum* L. (1,46), *P. strigosum* Schur. (1), *P. syriacum* Boiss. & Blanche (2), *P. triniaefolium* Boiss. (2)

4. PAPAVERRUBINE C
(Epiporphyroxine) $C_{20}H_{21}NO_6$: 371.1369

MP: 190-191.5° (15)

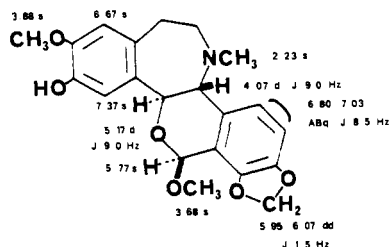
UV: 232 (3.97), 285 (3.85) (15)

 1H -NMR: (15)MS: m/z 371 (m^+), 356, 179 (15)[α]D: +282° (c 1.47, CHCl₃) (12,28)

Sources: *Meconopsis betonicifolia* Franch. (2), *Papaver albiflorum* subsp. *austromoravicum* Kubát (43), *P. alboroseum* Hulten (1,2), *P. alpinum* subsp. *alpinum* (2), *P. anomalum* Fedde (1), *P. atlanticum* Ball. (1), *P. caucasicum* Marsch.-Bieb. (1), *P. commutatum* Fisch. & Mey. (2), *P. decaisnei* Hochst. (3), *P. fugax* Poir. (1), *P. glaucum* Boiss. & Hauskn. (1,2,46), *P. lecoquii* Lamotte (43), *P. litwinowii* Fedde ex Bornm. (42), *P. oreophilum* F.J.

Rupr. (41), *P. orientale* L. (2), *P. pseudocanescens* M. Pop. (2), *P. rhoeas* L. (1,2), *P. rupifragum* Boiss. & Reut. (2,37), *P. somniferum* L. (1,46)

5. N-METHYLPORPHYROXINE

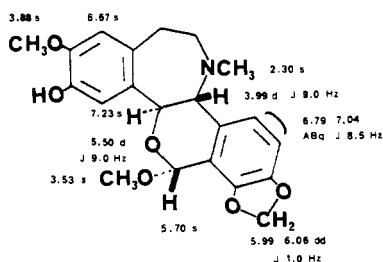


C₂₁H₂₃NO₆: 385.1525

¹H-NMR: (6)

Sources: Semi-synthetic (from porphyroxine=papaverubine D) (27), may occur in *Papaver somniferum* L. (17)

6. N-METHYLEPIPORPHYROXINE

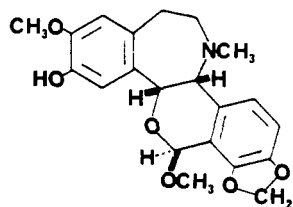


C₂₁H₂₃NO₆: 385.1525

¹H-NMR: (17)

Sources: Semi-synthetic (from N-methylporphyroxine) (17,27)

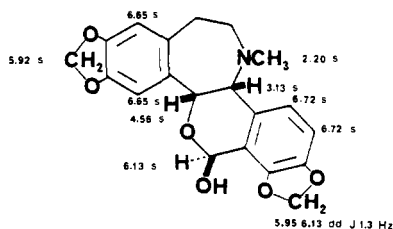
7. cis-N-METHYLEPIPORPHYROXINE



C₂₁H₂₃NO₆: 385.1525

Sources: Semi-synthetic (from N-methylepiporphyroxine) (27)

8. RHOEAGENINE



C₂₀H₁₉NO₆: 369.1681

MP: 236-238° (36)

UV: 243 (3.97), 290 (3.96) (36)

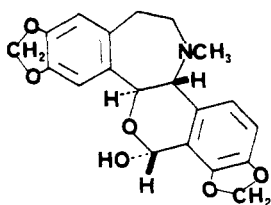
¹H-NMR: (CDCl₃ + DMSO-d₆) (16)

MS: m/z 369 (M⁺, 11), 314 (4), 311 (2), 206 (100), 192 (64), 177 (11), 163 (96), (13,14,16)

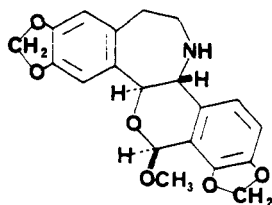
[α]_D²²: +130±5° (c 0.20, pyridine) (36)

Sources: *Papaver arenarium* Marsch.-Bieb. (1), *P. argemone* L. (1), *P. armeniacum* (L.) DC. (45), *P. atlanticum* Ball. (1), *P. californicum* A. Gray (1,2), *P. commutatum* Fisch. & Mey (1), *P. dubium* L. (1), *P. hispidum* Lam. (1), *P. latericum* C. Koch (1), *P. nudicaule* L. subsp. *rubroaurantiacum* (DC.) Fedde (1), *P. oreophilum* Rupr. (1,41), *P. pilosum* Sibth. & Smith (1), *P. rhoeas* L. (1), var. *decaisnei* Hochst. & Stend. (1), var. *flore pleno* (1), *P. rupifragum* Boiss. & Reut. (2,38), *P. strigosum* Schur. (1), *P. syriacum* Boiss. & Blanche (2), *P. tauricola* Boiss. (16)

9. ISORHOEAGENINE

C₂₀H₁₉NO₆: 369.1681[α]_D: +153° (1:1 MeOH-CHCl₃) (11)Sources: *Papaver commutatum* Fisch. & Mey (1,2), *P. rhoeas* L. (2)

10. PAPAVERRUBINE A

C₂₀H₁₉NO₆: 369.1213

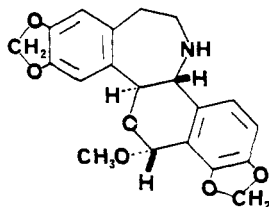
MP: 223-224° (8)

UV: 240 (3.91), 289 (4.03) (24)

MS: *m/z* 354 (97), 206 (4), 192 (8), 178 (22), 177 (100), 176 (20) (13,22)[α]_D²²: +406 ± 2° (c 0.978, CHCl₃) (31)

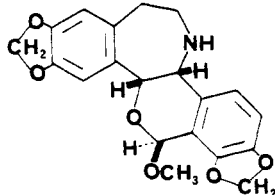
Sources: *Meconopsis betonicifolia* Franch. (2), *Papaver albiflorum* subsp. *austromoravicum* Kubát (43), *P. arenarium* Marsch.-Bieb. (1), *P. atlanticum* Ball. (1), *P. californicum* A. Gray (2), *P. caasicum* Marsch.-Bieb. (1), *P. commutatum* Fisch. & Mey (2), *P. decaisnei* Hochst. (39), *P. dubium* L. (1), *P. glaucum* Boiss. & Hausskn. (2), *P. heldreichii* Boiss. (1), *P. latericum* C. Koch (1), *P. lecoquii* Lamotte (43), *P. litwinowii* Fedde ex Bornm. (42), *P. macrostomum* Boiss. & Huet. (1), *P. oreophilum* Rupr. (1,41), *P. pilosum* Sibth. & Smith (1), *P. rhoeas* L. (1,2), var. *flore albo* (1), var. *flore pleno* (1), *P. rupifragum* Boiss. & Reut. (1,2,38), *P. setigerum* DC. (1,46), *P. strigosum* Schur. (1), *P. syriacum* Boiss. & Blanche (2)

11. EPIPAPAVERRUBINE A

C₂₀H₁₉NO₆: 369.1213

Sources: Semi-synthetic (from papaverrubine A) (27)

12. PAPAVERRUBINE E

C₂₀H₁₉NO₆: 369.1213

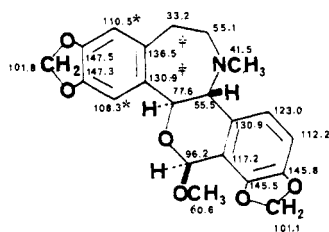
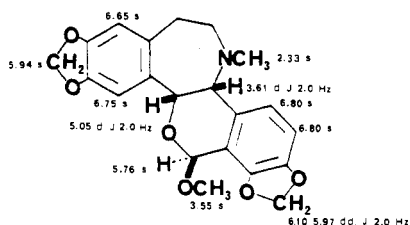
MP: 230-231° (8)

UV: (MeOH) 289 (21)

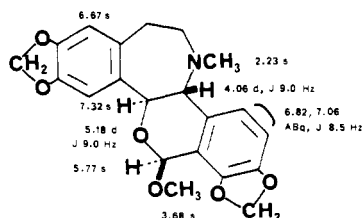
MS: *m/z* 354 (100), 206 (4), 192 (8), 178 (22), 177 (100), 176 (20) (13,22)[α]_D: +331° (CHCl₃) (11)

Sources: *Bocconia frutescens* L. (2), *Meconopsis betonicifolia* Franch. (2), *M. borridula* Hook. f. & Thoms. (2), *M. napaulensis* DC. (2), *M. paniculata* (D. Don) Prain (2), *M. rudis* Prain (2), *Papaver albiflorum* subsp. *austromoravicum* Kubát (43), *P. alpinum* subsp. *kernerii* Fedde (1,2), *P. argemone* L. (1), *P. atlanticum* Ball. (1), *P. bracteatum* Lindl. (1,2), *P. californicum* A. Gray (2), *P. caasicum* Marsch.-Bieb. (1), *P. commutatum* Fisch. & Mey (2), *P. decaisnei* Hochst. (39), *P. dubium* L. (1), *P. feddei* Schwz. (1), *P. fugax* Poir. (1,2), *P. heldreichii* Boiss. (1), *P. hybridum* L. (1), *P. latericum* C. Koch (1), *P. lecoquii* Lamotte (43), *P. litwinowii* Fedde ex Bornm. (42), *P. macrostomum* Boiss. & Huet. (1), *P. oreophilum* Rupr. (1,41), *P. orientale*

13. RHOEADINE



14. ISORHOEADINE



Methylene doublets: 5.95 and 6.08

L. (1), *P. pavoninum* Fisch. & Mey (1), *P. pilosum* Sibth. & Smith (1), *P. polychaetum* Schott & Kotschy (1), *P. pseudocanescens* M. Pop. (2), *P. radiculatum* Rottb. (2), *P. rhoeas* L. (1,2), *P. rupifragum* Boiss. & Reut. (1,2,38), *P. strigosum* Schur. (1), *P. syriacum* Boiss. & Blanche (2), *P. tauricola* Boiss. (2)

 $C_{21}H_{21}NO_6$: 383.1369

MP: 251-253° (3)

UV: 205 (4.91), 240 (3.96), 292 (3.94) (3)

 1H -NMR: (3,16)MS: m/z 383 (M^+ , 50), 368 (50), 352 (14), 206 (50), 192 (36), 290 (28), 177 (100), 163 (50) (13,14,16,22) $[\alpha]^{22}_D$: $+235 \pm 2^\circ$ (c 1.01, $CHCl_3$) ^{13}C -NMR: (30)

Sources: *Bocconia frutescens* L. (2,38), *Meconopsis betonicifolia* Franch. (2), *M. horridula* Hook. f. & Thoms. (?) (2), *M. napaulensis* DC. (2), *M. paniculata* (D. Don) Prain (2), *M. rudis* Prain (2), *Papaver albiflorum* subsp. *austromoravicum* Kubát (44), *P. anomalum* Fedde (1), *P. argemone* L. (1), *P. armeniacum* (L.) DC. (45), *P. arenarium* Marsch.-Bieb. (1), *P. atlanticum* Ball. (1), *P. californicum* A. Gray (1,2), *P. commutatum* Fisch. & Mey (1), *P. decaisnei* Hochst. (39), *P. dubium* L. (1), subsp. *lecoquii* (Lamotte) Fedde (1), *P. fugax* Poir. (2,45), *P. glaucum* Boiss. & Hauskn. (1,46), *P. gracile* Auch. (1,46), *P. hispidum* Lam. (1), *P. intermedium* Bedker O. Ktze. (1), *P. latericum* C. Koch (1), *P. lecoquii* Lamotte (43), *P. macrostomum* Boiss. & Huet. (1), *P. monanthum* Trautv. (1), *P. nudicaule* L. subsp. *leiocarpum* (Turcz.) Fedde (1), subsp. *rubroaurantiacum* (DC.) Fedde (1), subsp. *xanthopetalum* (Trautv.) Fedde (1), *P. oreophilum* Rupr. (1,42), *P. paeoniflorum* (1), *P. pavoninum* Fisch. & Mey (1), *P. pilosum* Sibth. & Smith (1), *P. pseudocanescens* M. Pop. (2), *P. rhoeas* L. (1,2,44), var. *decaisnei* Hochst. & Stend. (1), var. *flore albo* (1), var. *flore pleno* (1), *P. rupifragum* Boiss. & Reut. (2), *P. strigosum* Schur. (1), *P. syriacum* Boiss. & Blanche (2), *P. tauricola* Boiss. (16)

 $C_{21}H_{21}NO_6$: 383.1369

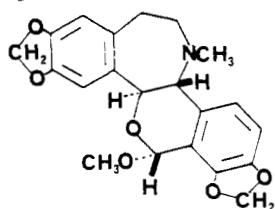
MP: 159-161° (3)

UV: 241, 292 (12)

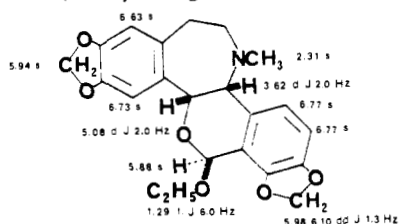
 1H -NMR: (3,35)MS: m/z 383 (M^+), 368, 352, 177 (13) $[\alpha]_D$: $+314 \pm 3^\circ$ (c 0.576, $CHCl_3$)

Sources: *Meconopsis betonicifolia* Franch. (2), *Papaver arenarium* Marsch.-Bieb. (1), *P. argemone* L. (1), *P. commutatum* Fisch. & Mey (1,2), *P. decaisnei* Hochst. & Stend. (46), *P. dubium* L. subsp. *lecoquii* (Lamotte) Fedde (1), *P. oreophilum* Rupr. (1,41), *P. rhoeas* L. (1,2), var. *decaisnei* Hochst. & Stend. (1), var. *flore albo* (1), var. *flore pleno* (1), *P. rupifragum* Boiss. & Reut. (38), *P. syriacum* Boiss. & Blanche (2)

15. EPIISORHOEADINE

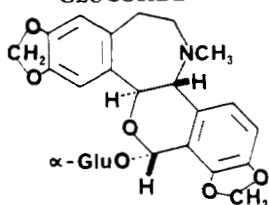
 $C_{21}H_{21}NO_6$: 383.1369

Sources: Semi-synthetic (from epipaverrubine A) (27)

16. DUBIRHEINE
(*O*-Ethylrhoeagenine) $C_{22}H_{23}NO_6$: 397.1525

MP: 236-237° (23)

UV: 242 (3.90), 293 (3.97) (45)

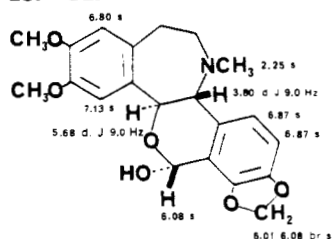
 1H -NMR: (16)MS: m/z 397 (M^+ , 50), 368 (83), 352 (20), 192 (16), 190 (20), 177 (100), 163 (16), (23, 16, 45) $[\alpha]^{24}_D$: +236° (23)Sources: *Papaver armeniacum* (L.) DC. (45), *P. dubium* L. (23, 16), *P. tauricola* Boiss. (16), probably an artifact (23, 16, 45)17. ISORHOEAGENINE α -D-GLUCOSIDE $C_{26}H_{29}NO_{11}$: 531.1740

MP: 242° (24)

UV: 240 (3.90), 293 (4.00) (24)

 $[\alpha]_D$: +250° (1:1 MeOH-CHCl₃) (11)Sources: *P. commutatum* Fisch. & Mey. (2), *P. rhoeas* L. (1, 2), *P. rhoeas* var. *decaisnei* Hochst. & Stend. (1)

18. GLAUCAMINE

 $C_{21}H_{23}NO_6$: 385.1525

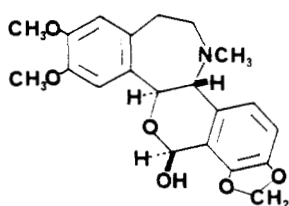
MP: 222-223° (20)

UV: 238 (4.0), 286 (3.8) (20)

 1H -NMR: (DMSO- d_6) (16, 17)MS: m/z 385 (M^+ , 100), 370 (20), 354 (10), 209 (12), 206 (12), 193 (24), 179 (23), 148 (100) (13, 16) $[\alpha]^{22}_D$: +298 \pm 3° (c 0.25, CHCl₃) (20)Sources: *Papaver anomalum* Fedde (1), *P. fugax* Poir. (45), *P. glaucum* Boiss. & Hauskn. (1, 2, 46), *P. nudicaule* L. var. *leiocarpum* (Turcz.) Fedde (1), *P. rhoeas* L. (1, 2), *P. tauricola* Boiss. (16)

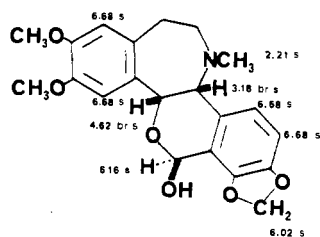
Methoxyl singlets: 3.70 and 3.73

19. EPIGLAUCAMINE

 $C_{21}H_{23}NO_6$: 385.1525 $[\alpha]^{21}_D$: +126 \pm 3° (c 0.27, CHCl₃) (20)

Sources: Semi-synthetic (from glaupavine and glaucamine) (20)

20. OREOGENINE



Methoxyl singlets: 3.80 and 3.88

$C_{21}H_{23}NO_6$: 385.1525

MP: indefinite, MeI salt 173-175° (36)

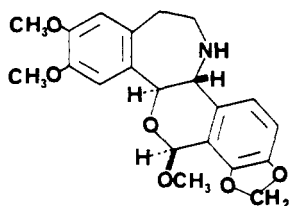
UV: (MeOH) 237 (4.08), 286 (3.83) (36)

1H -NMR: (16)

MS: m/z 385 (M^+ , 18), 370 (22), 354 (11), 209 (11), 206 (11), 193 (22), 148 (100) (36, 16)

Sources: *Papaver fugax* Poir. (45), *P. oreophilum* Rupr. (36, 1, 41), *P. tauricola* Boiss. (16)

21. PAPAVERRUBINE B



$C_{21}H_{23}NO_6$: 385.1525

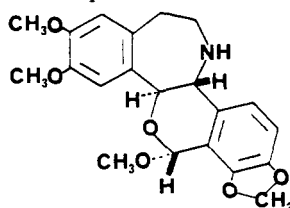
MP: 201-203° (MeOH) (33)

UV: 235, 286 (33)

MS: m/z 385 (M^+ , 370, 206, 193 (100), 192, 178 (13, 21, 22)

$[\alpha]_D$: +398° (CHCl₃) (28)

Sources: *Papaver alpinum* subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (1), subsp. *tatricum* Nyár (1), *P. atlanticum* Ball. (1), *P. bracteatum* Lindl. (1, 2), *P. californicum* A. Gray (2), *P. caucasicum* Marsch.-Bieb. (1), *P. commutatum* Fisch. & Mey (2), *P. dubium* L. (1), *P. feddei* Schwz. (1), *P. fugax* Poir. (2), *P. glaucum* Boiss. & Hauskn. (2, 46), *P. beldreichii* Boiss. (1, 2), *P. latericum* C. Koch. (1), *P. macrostomum* Boiss. & Huet. (1), *P. nudicaule* L. (1), *P. oreophilum* Rupr. (1), *P. orientale* L. (1), *P. persicum* Lindl. (1), *P. pilosum* Sibth. & Smith (1), *P. polychaetum* Schott & Kotschy (1), *P. rhoeas* L. (1), *P. rupifragum* Boiss. & Reut. (1, 37), *P. setigerum* DC. (1, 46), *P. strigosum* Schur. (1), *P. triniaefolium* Boiss. (1), *P. urbanianum* Fedde (1)

22. EPIPAPAVERRUBINE B
(Papaverubine H)

$C_{21}H_{23}NO_6$: 385.1525

MP: 70-71° (21)

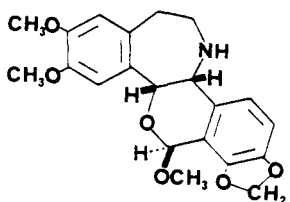
UV: (MeOH) 285 (21)

MS: m/z 385 (M^+ , 370, 206, 193 (100), 192, 178 (21)

$[\alpha]_D$: +308° (CHCl₃) (28)

Sources: Semi-synthetic (from papaverubine B) (21)

23. PAPAVERRUBINE F



$C_{21}H_{23}NO_6$: 385.1525

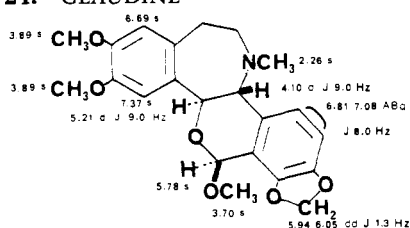
MP: 223-225° (acetone) (9, 36), MeI salt 186-189° (9)

UV: (MeOH) 237 (4.11), 287 (3.84) (9, 36)

MS: m/z 385 (M^+ , 370, 193 (36)

Sources: *Papaver commutatum* Fisch. & Mey (2), *P. oreophilum* Rupr. (1, 9, 36)

24. GLAUDINE

 $C_{22}H_{25}NO_6$: 399.1681

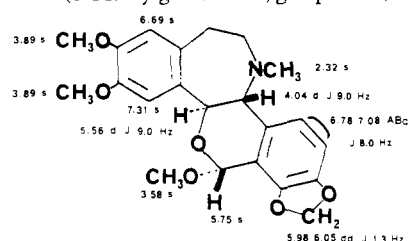
MP: 103-105° (32)

UV: 237, 287 (32)

 1H -NMR: (16,18)MS: m/z 399 (M^+ , 73), 384 (80), 220 (4), 206 (34), 193 (100), 192 (12) (16)[α]_D: +455 \pm 5° (c 0.5, $CHCl_3$) (32)Sources: *Papaver armeniacum* (L.) DC. (45), *P. fugax* Poir. (45), *P. glaucum* Boiss. & Hauskn. (12,46), *P. rhoeas* L. (1), *P. somniferum* L. (1,46), *P. tauricola* Boiss. (16)

25. EPIGLAUDINE

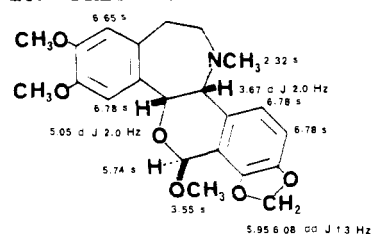
(O-Methylglaucamine, glaupavine?)

 $C_{22}H_{25}NO_6$: 399.1681

UV: (MeOH) 237 (4.18), 287 (4.06) (36)

 1H -NMR: (16,17,18)MS: m/z 399 (M^+ , 73), 384 (80), 220 (4), 306 (34), 193 (100), 192 (12) (13,16)[α]_D²²: +293 \pm 5° (c 0.1, $CHCl_3$) (36)Sources: *Papaver glaucum* Boiss. & Hauskn. (as glaupavine) (20,1), *P. tauricola* Boiss. (16)

26. OREODINE

 $C_{22}H_{25}NO_6$: 399.1681

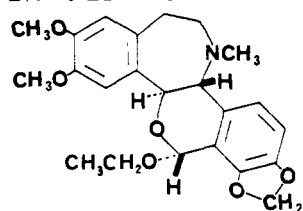
MP: 184-186° (36)

UV: 235 (4.19), 285 (3.94) (36)

 1H -NMR: (16,36)MS: m/z 399 (M^+ , 83), 384 (72), 368 (20), 356 (7), 206 (37), 193 (100), 178 (8), 175 (10) (13,16,36)[α]_D: +224 \pm 5° (c 0.1, $CHCl_3$) (36)Sources: *Papaver fugax* Poir. (45), *P. oreophilum* Rupr. (36,1), *P. tauricola* Boiss. (16)

Methoxyl singlets: 3.82 and 3.87

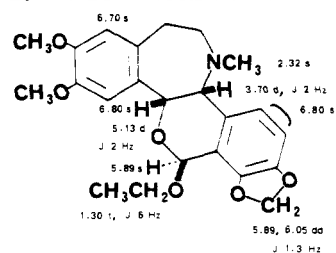
27. O-ETHYLGLAUCAMINE

 $C_{23}H_{27}NO_6$: 413.1838

UV: 235, 285 (45)

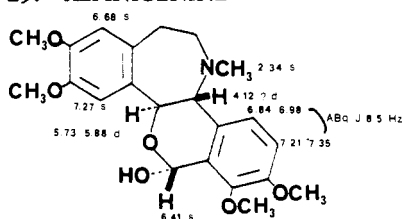
MS: m/z 413 (M^+ , 74), 384 (80), 234 (6), 220 (35), 206 (11), 193 (100) (45)Sources: *Papaver fugax* Poir. (= *P. causicum* Marsch.-Bieb.), probably an artifact (45)

28. O-ETHYLOREOGENINE

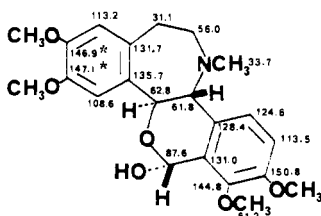
 $C_{23}H_{27}NO_6$: 413.1838 1H -NMR: (16)MS: m/z 413 (M^+ , 74), 384 (80), 234 (6), 220 (35), 206 (11), 193 (100) (16)Sources: *Papaver fugax* Poir. (= *P. causicum* Marsch.-Bieb.) (45), *P. tauricola* Boiss. (16), probably an artifact (16,45)

Methoxyl singlets: 3.82 and 3.89

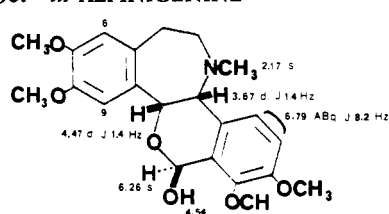
29. ALPINIGENINE



Methoxyl singlets: 3.86 and 3.94

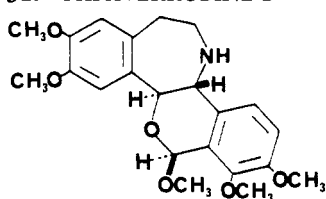


Other methoxyl signals between 56.0 and 56.4 ppm

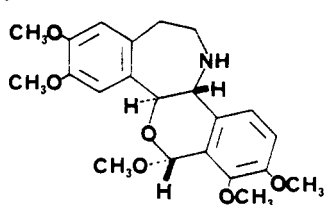
30. *cis*-ALPINIGENINE

Methoxyl singlets: 3.85, 3.83 and 3.75.
AB quartet at 6.60, $J=2.4$ Hz (C-6, C-9),
collapsing to triplet?

31. PAPAVERRUBINE G



32. EPIPAPAVERRUBINE G



$C_{22}H_{27}NO_6$: 401.1838

MP: 193-195° (35)

UV: 230 (4.19), 284 (3.79) (35)

1H -NMR: (35)

^{13}C -NMR: (29)

MS: m/z 401 (M^+ , 6), 383 (14), 340 (18), 222 (100), 208 (22), 206 (3), 179 (68), 164 (14) (7, 13, 28)

$[\alpha]^{22}_D$: $+268 \pm 5^\circ$ (c 0.63, MeOH) (35)

Sources: *Papaver alpinum* L. subsp. *alpinum* (2), subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (1, 2), subsp. *rhaeticum*, (2), subsp. *sendtneri* (2), subsp. *tatricum* Nyár. (1), *P. bracteatum* Lindl. (1, 2, 29, 40), *P. fugax* Poir. (= *P. caucasicum* Marsch.-Bieb.) (45), *P. orientale* L. (47), *P. pseudo-orientale* (Fedde) Medw. (47)

$C_{22}H_{27}NO_6$: 401.1838

MP: 175-176° (MeOH) (34)

1H -NMR: (34)

MS: m/z 401 (M^+), 222 (100), 208 (22), 206 (18), 176 (87) (13, 34)

$[\alpha]^{22}_D$: $+110^\circ$ (c 0.851, MeOH) (34)

Sources: Semi-synthetic (from alpinigenine) (18, 34)

$C_{22}H_{27}NO_6$: 401.1838

MP: indefinite, MeI salt 165-166° (25)

UV: (MeOH) 230, 281 (25)

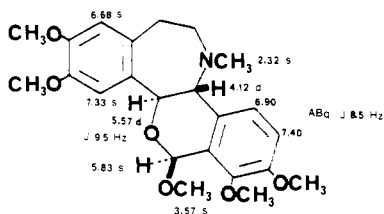
MS: m/z 401 (M^+), 396, 208, 193 (100), 192 (21)

$[\alpha]_D$: $+397 \pm 10^\circ$ (c 0.12, MeOH) (19)

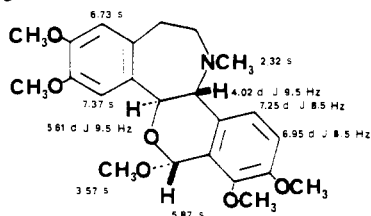
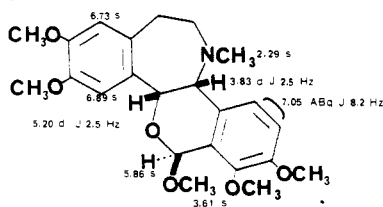
Sources: *P. alpinum* L. subsp. *alpinum* (25, 21), subsp. *rhaeticum* (2), subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (21, 1), subsp. *sendtneri* (21, 1, 2), subsp. *tatricum* Nyár. (1), *P. anomalum* Fedde (= *P. nudicaule* subsp. *amurense* N. Busch) (21, 1)

$C_{22}H_{27}NO_6$: 401.1838

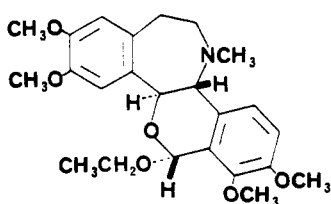
Sources: Semi-synthetic (from papaverrubine G) (27)

33. ALPININE

Methoxyl singlets: 3.87, 3.88, and 3.90.

34. EPIALPININE**35. *cis*-ALPININE**

Methoxyl singlets: 3.88, 3.89, 3.90, 3.90, and 3.93

36. *O*-ETHYLALPINIGENINE

$C_{23}H_{29}NO_6$: 415.1994

MP: indefinite (35)

UV: 231 (4.19), 286 (3.80) (35)

1H -NMR: (35)

MS: m/z 236, 222, 208 (35, 13)

$[\alpha]^{22}_D$: $+288 \pm 10^\circ$ (c 0.82, $CHCl_3$) (35)

Sources: *Papaver alpinum* L. subsp. *alpinum* (2), subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (1, 2), subsp. *rhaeticum* (2), subsp. *sendtneri* (2), subsp. *taticum* Nyár. (1), *P. bracteatum* Lindl. (2), *P. pseudo-orientale* (Fedde) Medw. (47)

$C_{23}H_{29}NO_6$: 415.1994

MP: 122-123° (MeOH- H_2O) (28)

UV: (MeOH) 230 (4.20), 284 (3.85) (28, 19)

1H -NMR: (28)

MS: m/z 415 (M^+ , 90), 400 (72), 383 (14), 311 (15), 222 (43), 206 (37), 204 (10), 193 (100), 179 (18) (28)

$[\alpha]_D$: $+293 \pm 10^\circ$ (c 0.1, MeOH) (19)

Sources: *Papaver alpinum* L. subsp. *burseri* (Crantz) Fedde (1), subsp. *kernerii* (Hayek) Fedde (1), subsp. *taticum* Nyár. (1)

$C_{23}H_{29}NO_6$: 415.1994

MP: 106-107° (34)

1H -NMR: (34)

$[\alpha]_D$: $+193.3^\circ$ (c 0.794, MeOH) (34)

Sources: Semi-synthetic (from alpinine) (4, 18)

$C_{24}H_{31}NO_6$: 429.2141

UV: 231 (4.19), 286 (3.80) (45)

MS: m/z 429 (M^+ , 73), 400 (79), 250 (3), 236 (33), 208 (25), 193 (100) (45)

Sources: *Papaver fugax* Poir. (= *P. caucasicum* Marsch.-Bieb.), probably an artifact (45)

Alphabetical Listing of the Rhoeadines and Papaverrubines

Alpinigenine (29)

cis-Alpinigenine (30)

Alpinine (33)

cis-Alpinine (35)

Dubirheine (*O*-Ethylrhoeadine) (16)

Epialpinine (34)

Epiglaucamine (19)

Epiglaudine (*O*-Methylglaucamine) (25)

Epiisorrhoeadine (15)

Epipapaverrubine A (11)

Epipapaverrubine B (Papaverrubine H) (22)

Epipapaverrubine G (32)

O-Ethylalpinigenine (36)

O-Ethylglaucamine (27)

O-Ethylrhoeadine (28)

Glaucamine (18)

Glaudine (24)

Isorrhoeadine (14)

Isorrhoeagenine (9)

Isorrhoeagenine α -D-glucoside (17)

N-Methyl-14-*O*-demethylepiporphyroxine (1)

cis-*N*-Methyl-14-*O*-demethylepiporphyroxine (2)

N-Methylepiporphyroxine (6)

cis-*N*-Methylepiporphyroxine (7)

N-Methylporphyroxine (5)

Oreodine (26)

Oreogenine (20)

Papaverrubine A (10)

Papaverrubine B (21)

Papaverrubine C (Epiporphyroxine) (4)

Papaverrubine D (Porphyroxine) (3)

Papaverrubine E (12)

Papaverrubine F (23)

Papaverrubine G (31)

Rhoeadine (13)

Rhoeadine (8)

Molecular Weights and Molecular Compositions.

369.1213	$C_{20}H_{19}NO_6$	397.1525	$C_{22}H_{23}NO_6$
	Papaverrubine A (10)		Dubirheine (16)
	Epipapaverrubine A (11)		
	Papaverrubine E (12)	399.1681	$C_{22}H_{25}NO_6$
	Rhoeagenine (8)		Glaudine (24)
	Isorhoeagenine (9)		Epiglaudine (25)
371.1369	$C_{20}H_{21}NO_6$		Oreodine (26)
	N-Methyl-14-O-demethylepi-	401.1838	$C_{22}H_{27}NO_6$
	porphyroxine (1)		Alpinigenine (29)
	cis-N-Methyl-14-O-demethylepi-		cis-Alpinigenine (30)
	porphyroxine (2)		Papaverrubine G (31)
	Papaverrubine D (3)		Epipapaverrubine G (32)
	Papaverrubine C (4)		
383.1369	$C_{21}H_{21}NO_6$	413.1838	$C_{23}H_{27}NO_6$
	Rhoeadine (13)		O-Ethylglauamine (27)
	Isorhoeadine (14)		O-Ethylroegenine (28)
	Epiisorhoeadine (15)		
385.1525	$C_{21}H_{23}NO_6$	415.1994	$C_{23}H_{29}NO_6$
	Papaverrubine B (21)		Alpinine (33)
	Epipapaverrubine B (22)		Epialpinine (34)
	Papaverrubine F (23)		cis-Alpinine (35)
	N-Methylporphyroxine (5)	429.2141	$C_{24}H_{31}NO_6$
	N-Methylepiporphyroxine (6)		O-Ethylalpinigenine (36)
	cis-N-Methylepiporphyroxine (7)		
	Glauamine (18)	531.1740	$C_{26}H_{29}NO_{11}$
	Epiglauamine (19)		Isorhoeagenine α -D-glucoside (17)
	Oreogenine (20)		

ACKNOWLEDGMENTS

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