6a,7-Dehydro-2-hydroxy-4,5-dioxonoraporphine and Other Alkaloids from Monocyclanthus vignei: C-nmr Studies on 4,5-Dioxoaporphines

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6a,7-DEHYDRO-2-HYDROXY-4,5-DIOXONORAPORPHINE AND OTHER ALKALOIDS FROM *MONOCYCLANTHUS VIGNEI*: ^{13}C-NMR STUDIES ON 4,5-DIOXOAPORPHINES[1,2]

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ABSTRACT.—The new and unusually substituted 4,5-dioxonoraporphine **1** was isolated, among other aporphines and phenanthrene-type alkaloids, from *Monocyclanthus vignei*. The ^{13}C-nmr spectra of 4,5-dioxoaporphines were studied for the first time.

In the course of our phytochemical investigations on tropical plants, we studied the constituents of *Monocyclanthus vignei* Keay. This plant of the Annonaceae grows endemically in West Africa (1).

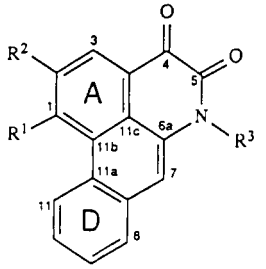
From the basic fraction of the MeOH extract the individual alkaloids **1–12**, reticuline, and *N*-feruloyltyramine were isolated by chromatographic procedures.

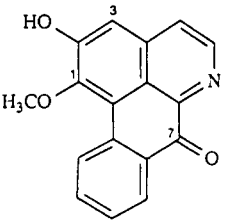
The approximate concentrations of these compounds are summarized in Table 1.

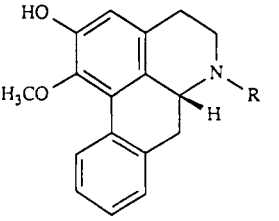
The structures given mainly result from spectroscopic studies. Compounds **1**, **3**, **9**, and possibly, **10–12** represent new genuine natural products.

Compounds **1** and **2** show electron spectra and eims typical for 4,5-dioxoaporphines (9). The eims of **2** exhibits significant ions at $[M + 14]^+$ and $[M - 14]^+$ caused by intermolecular methyl transfer. The position of the only hydroxy substituent in **1** at C-2 is indicated by the *m*-coupling between H-1 and H-3.

Because no ^{13}C-nmr data of 4,5-dioxoaporphines have yet been published, we studied the ^{13}C nmr of **1** and **2**. In this study are included their methylation products **13** and **14** and the dioxoaporphines **15** and **16**, available to us from other sources (10,11). Due to poor solubility in the usual solvents, all spectra were run in pyridine-d_5. The assignments presented in Table 2 are based on heteronuclear ^1J- and $^{2,3}J$-COSY measurements.







1 R^1=H, R^2=OH, R^3=H
2 R^1=OMe, R^2=OH, R^3=H
13 R^1=H, R^2=OMe, R^3=Me
14 R^1=R^2=OMe, R^3=Me
15 R^1=R^2=OMe, R^3=H
16 R^1+R^2=OCH_2O, R^3=Me

3

4 R=H
5 R=Me

[1]Dedicated to Prof. Dr. H. Oelschläger, Frankfurt, on the occasion of his 70th birthday.

[2]Part 47 in the series "Constituents of Tropical Medicinal Plants." For Part 46, see H. Achenbach, W. Utz, A. Usubillaga, and H.A. Rodriguez, *Phytochemistry*, in press.

TABLE 1. Nitrogen-containing Constituents Isolated from the MeOH Extract of *Monocyclanthus vignei*.

Compound	Content [%][a]	References
1-Desmethoxy-4,5-dioxodehydroasimilobine [**1**]	0.06	—
4,5-Dioxodehydroasimilobine [**2**]	0.17	(2)
7-Oxodehydroasimilobine [**3**]	0.025	—
Asimilobine [**4**]	0.046	(3)
N-Methylasimilobine [**5**]	0.005	(3)
Aristololactam A II [**6**]	0.016	(4)
Argentinine [**7**]	0.026	(5)
Stephenanthrine [**8**]	0.23	(6)
8-Hydroxystephenanthrine [**9**]	0.13	—
Reticuline	0.076	(7)
N-trans-Feruloyltyramine	0.047	(8)
Argentinine-*N*-oxide [**10**]	0.007	—
Stephenanthrine-*N*-oxide [**11**]	0.043	—
8-Hydroxystephenanthrine-*N*-oxide [**12**]	0.016	—

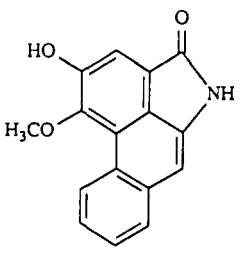
[a]Dry weight of total MeOH extract = 100%.

Among the four hydrogen-bearing carbons of ring D the signal of C-8 always appears at lowest field. As far as the influence of substituents is concerned, *N*-methylation does not significantly affect the resonances of the α-carbons (C-5, C-6a) but shifts C-4 about 2 ppm to higher and C-7 the same amount to lower field. Replacement of the two methoxy-substituents (in **14**) by a methylenedioxy group shifts the resonance of C-3 to higher field (Δδ ca. −4 ppm) and C-11b to lower field (Δδ ca. +1 ppm).

Structure **3** (7-oxodehydroasimilobine) was deduced by comparison of its spectra (eims, ^{1}H nmr) with those of **4** and lysicamine (2-*O*-methyl-**3**). Consequently, **3** was methylated with MeI to give lysicamine (10,12). The position of the original OMe group in **3** at C-1 was corroborated by an nOe experiment.

The phenanthrene-type alkaloids **7–9** exhibit eims with characteristic fragment ions at $[M-58]^+$ and the base peak at *m/z* 58 (=dimethyl methylene iminium) (13); further structure information comes from ^{1}H and ^{13}C nmr. The position of the OH-substituent in **9** at C-8 is based on ^{1}H-nmr arguments: in **7**, **8**, and **9** the signal of H-5 appears at lowest field due to deshielding by the oxygen-substituent at C-4; but in **9** H-5 is part of a system of only three vicinal protons at ring C, and in addition, it shows characteristic long-range coupling (ca. 1 Hz) with H-9, which was demonstrated by decoupling.

The eims of the *N*-oxides **10–12** does not exhibit molecular ions, but at highest mass the base fragments characteristically appear at $[M-61]^+$ (14). Structures **10–12**



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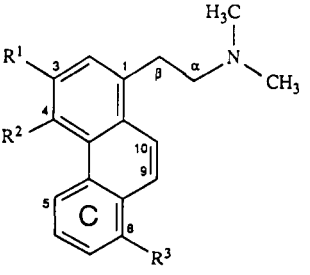
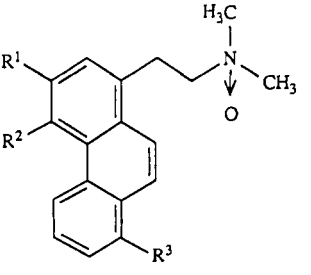


7 R^1=OH, R^2=OMe, R^3=H
8 R^1+R^2=OCH_2O, R^3=H
9 R^1+R^2=OCH_2O, R^3=OH



10 R^1=OH, R^2=OMe, R^3=H
11 R^1+R^2=OCH_2O, R^3=H
12 R^1+R^2=OCH_2O, R^3=OH

TABLE 2. ^{13}C-nmr Data of 4,5-Dioxoaporphines **1**, **2**, and **13–16** (in C_5D_5N).

Carbon	Compound					
	1	**2**	**13**	**14**	**15**	**16**
C-1	117.1[a]	154.1	115.7	154.9	154.9	151.4
C-2	159.3	152.8	159.6	153.2	153.4	148.2
C-3	117.0[a]	118.4	114.6	112.9	113.2	108.5
C-3a	131.2[b]	126.4	130.2	124.8[a]	124.8[a]	123.0
C-4	179.0	178.3	176.8	176.0	178.0	175.0
C-5	157.2	157.0	156.7	156.5	156.9	156.7
C-6a	132.1[b]	131.8	133.1[a]	132.7	131.5	132.4
C-7	110.6	112.3	112.4	114.3	113.2	114.2
C-7a	133.5[b]	133.6	133.3[a]	133.3	133.5	133.1
C-8	128.7	128.9	129.4	129.6	129.0	129.0
C-9	128.4	128.2[a]	128.7	128.4[b]	128.3[b]	127.4[a]
C-10	126.3	126.9	127.1	127.7[b]	127.2[b]	127.0[a]
C-11	123.0	128.1[a]	123.6	128.1[b]	128.3[b]	128.5[a]
C-11a	127.2	127.2	127.2	127.2	127.2	128.3
C-11b	133.2[b]	125.3	133.1[a]	124.7[a]	125.8[a]	125.7
C-11c	116.4	118.4	117.8	119.9	119.5	121.3
1-OMe	—	59.9	—	60.3	60.3	—
2-OMe	—	—	56.0	56.3	56.3	—
OCH_2O	—	—	—	—	—	103.8
N-Me	—	—	30.1	30.2	—	30.1

[a,b]Assignments in the same column with the same superscript may be interchanged.

were corroborated by *N*-oxidation of compounds **7** to **9** using *m*-chloroperbenzoic acid (15).

The structural types of alkaloids isolated from *M. vignei* have also been found in other Annonaceae and so far corroborate the botanical classification of the plant from a chemotaxonomic point of view (16, 17). In spite of the fact that the *N*-oxides **10–12** might be genuine natural products (18), corresponding experiments performed with **7–9** show that *N*-oxidation easily occurs in the presence of air. Therefore, it cannot be excluded that **10–12** are artifacts.

The isolation of **1** is of major importance from a biogenetic point of view, since according to our knowledge no natural aporphines are known without an oxygen substituent at C-1. Biogenetically the oxygen at C-1 comes from the incorporation of tyrosine, which is the precursor of ring A, together with C-4, C-5, and N-6 in the isoquinoline and aporphine-type alkaloids (19). Therefore, we suppose a joint biogenetic aporphinoid intermediate for **1** and **2** and a subsequent deoxygenation process at C-1 in the formation of **1**.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—The mp's were obtained on a Kofler hot-stage apparatus and are uncorrected. Optical rotations and uv/vis measurements were made in MeOH. Nmr spectra, if not otherwise stated, were recorded in C_5D_5N with TMS as the internal standard for ^{1}H nmr at 360 MHz and for ^{13}C nmr at 90 MHz on an AM 360 Bruker instrument. For ^1J-correlation the sequence according to Bax and Subramanian (20) was used, and for long range correlation the sequence according to Bax and Subramanian (21). NOe's were measured by the difference method. Ms were run by ei at 70 eV on a Finnigan 4500 instrument, and high resolution measurements on a MAT 311. Characteristic ions usually are given with intensities >10% and *m/z* >100. If not otherwise stated, Si gel for cc was obtained from Macherey-Nagel (no. 81538) and Al_2O_3 from Woelm. Analytical tlc was performed on precoated Si gel plates (Macherey-Nagel, no. 811023) using solvent systems S-1 = $CHCl_3$-MeOH (9:1) and S-2 = $CHCl_3$-MeOH (8:2) with detection by uv and ceric ammonium sulfate reagent (22).

PLANT MATERIAL.—*M. vignei* was collected in March 1985, at Ankasa Forest Reserve, Ghana and identified by Mr. A.A. Enti (Forestry Enterprises, Legon, Ghana). A voucher specimen is kept at the herbarium of our institute under no. 8507.

EXTRACTION AND ISOLATION.—Stem bark (360 g) was extracted at room temperature with petroleum ether (4.6 g extract) and then with MeOH (24 g extract).

Workup of the MeOH extract with 5% HOAc in the usual manner (23) yielded 2.8 g of crude alkaloid mixture. This was chromatographed on Sephadex LH 20 (Pharmacia) with MeOH. Repeated cc of the resulting eight fractions on SiO_2 and/or Al_2O_3 (neutral, activity III) with $CHCl_3$/MeOH mixtures gave the crude alkaloids **1–12**, reticuline, and *N-trans*-feruloyl-tyramine. Final purification was achieved by cc on Fractogel PVA-500 (Merck) with MeOH-$CHCl_3$ (7:3) as the eluent.

6a,7-Dehydro-2-hydroxy-4,5-dioxonoraporphine (=1-demethoxy-4,5-dioxodehydroasimilobine) [**1**].—Orange needles (14 mg): mp 283–285° (from MeOH); tlc R_f 0.44 (S-1), 0.64 (S-2), brownish-orange with Ce-IV reagent; ir (KBr) ν max cm^{-1} 3370 (broad), 1691, 1680; uv/vis λ max nm (log ϵ) 218 (4.33), 244 (sh), 257 (4.39), 305 (sh), 314 (3.83), 326 (3.86), 464 (3.78); λ max (+KOH) nm 221 (4.85), 255 (sh), 267 (4.32), 326 (3.82), 338 (3.82), 513 (3.76); ^{1}H nmr δ ppm 8.96 (1H, d, J = 2.5 Hz, H-1), 8.79 (1H, br d, J = 8 Hz, H-11), 8.55 (1H, d, J = 2.5 Hz, H-3), 7.96 (1H, dd, J_1 = 8 Hz, J_2 = 2 Hz, H-8), 7.68 (1H, s, H-7), 7.65 (1H, ddd, J_1 = J_2 = 8 Hz, J_3 = 1.5 Hz, H-9), 7.62 (1H, ddd, J_1 = J_2 = 8 Hz, J_3 = 2 Hz, H-10); ^{13}C nmr see Table 2; eims *m/z* (%) $[M]^+$ 263.0581 (100) (calcd for $C_{16}H_9NO_3$, 263.0582), 236 (11), 235 (64), 206 (16), 152 (16), 151 (11).

4,5-Dioxodehydroasimilobine [**2**].—Orange needles (41 mg): mp 299–303° (from C_5H_5N) [lit. (2) 310–312° (from $CHCl_3$/MeOH)]; tlc R_f 0.47 (S-1), 0.73 (S-2), brownish-orange with Ce-IV reagent; ir and uv/vis in accordance with published data (2); ^{1}H nmr δ ppm 9.79 (1H, m, H-11), 8.63 (1H, s, H-3), 7.95 (1H, m, H-8), 7.73 (1H, s, H-7), 7.63–7.71 (2H, m, H-9 and H-10), 4.20 (3H, s, 1-OMe); important ^{1}H nmr nOe 1-OMe to H-11; ^{13}C nmr see Table 2; eims *m/z* (%) 307 (45), $[M]^+$ 293.0689 (100) (calcd for $C_{17}H_{11}NO_4$, 293.0688), 279 (18), 265 (22), 264 (11), 250 (41), 222 (17), 166 (21), 164 (10).

7-Oxodehydroasimilobine [**3**].—Brown amorphous powder (6 mg): tlc R_f 0.32 (S-1), brownish-orange with Ce-IV reagent; ir (KBr) ν max cm^{-1} 3470, 1660; uv/vis λ max nm (log ϵ) 221 (sh), 236 (4.92), 267 (4.82) 274 (sh), 310 (4.28), 380 (4.26), 411 (4.28); λ max (+KOH) nm 246 (4.88), 273 (4.80), 301 (4.64), 400 (4.45), 479 (3.86); λ max (+HCl) nm 249 (4.87), 275 (4.89), 338 to 350 (4.25), 389 (4.27), 462 (3.99); ^{1}H nmr δ ppm 9.41 (1H, d, J = 8 Hz, H-11), 8.95 (1H, d, J = 5 Hz, H-5), 8.80 (1H, dd, J_1 = 8 Hz, J_2 = 1.5 Hz, H-8), 7.795 (1H, d, J = 5 Hz, H-4), 7.790 (1H, ddd, J_1 = J_2 = 8 Hz, J_3 = 1.5 Hz, H-10), 7.63 (1H, s, H-3), 7.57 (1H, br dd, J_1 = J_2 = 8 Hz, H-9), 4.16 (3H, s, 1-OMe); eims *m/z* (%) $[M]^+$ 277.0740 (90) (calcd for $C_{17}H_{11}NO_3$, 277.0739, 234 (100), 206 (11), 177 (14), 151 (22), 150 (11); important ^{1}H nmr nOe 1-OMe to H-11.

Lysicamine by methylation of **3**.—Compound **3** (1.8 mg) was dissolved in dry Me_2CO (2 ml), MeI (0.1 ml) and K_2CO_3 (10 mg) were added, and the reaction mixture was stirred for 12 h at room temperature. Usual workup and cc over Si gel yielded lysicamine (=2-*O*-methyl-7-oxodehydroasimilobine) (12) (1.3 mg); tlc R_f 0.61 (S-1), orange with Ce-IV reagent; identical with an authentic sample (10).

Asimilobine [**4**].—Colorless oil (11 mg): tlc R_f 0.32 (S-2), violet with Ce-IV reagent; $[\alpha]^{21}D$ −200° (c = 0.23, $CHCl_3$) [lit. (3) $[\alpha]^{14}D$ −213° (c = 0.64, $CHCl_3$)]; identical with an authentic sample (24).

N-*Methylasimilobine* [**5**].—Colorless oil (1.3 mg): tlc R_f 0.37 (S-1), 0.50 (S-2), violet with Ce-IV reagent; $[\alpha]^{21}D$ −177° (c = 0.08, $CHCl_3$) [lit. (3) $[\alpha]^{20}D$ −220° (c = 0.40, $CHCl_3$)]; identical with an authentic sample (10).

Aristololactam A II [**6**].—Colorless needles (4 mg): mp 268° (from MeOH) [lit. (4) mp 271° (from HOAc)]; tlc R_f 0.49 (S-1), 0.66 (S-2), pale violet with Ce-IV reagent; ir, uv, ^{1}H nmr, eims in accordance with published data (4).

Argentinine [**7**].—Colorless oil (6 mg): tlc R_f 0.23 (S-2), yellowish-brown with Ce-IV reagent; identical with an authentic sample (10).

Stephenanthrine [**8**].—Colorless crystals (55 mg): mp 80–81° (from MeOH); tlc R_f 0.42 (S-2), green with Ce-IV reagent; ir, uv, eims in accordance with published data (6); ^{1}H nmr ($CDCl_3$) δ ppm 9.08 (1H, br d, J = 8 Hz, H-5), 7.84 (1H, d, J = 9 Hz, H-10), 7.82 (1H, dd, J_1 = 6.5 Hz, J_2 = 2 Hz, H-8), 7.62–7.54 (3H, m, H-6, H-7, H-9), 7.14 (1H, s, H-2), 6.22 (2H, s, OCH_2O), 3.24 (2H, m, CH_2-β), 2.65 (2H, m, CH_2-α), 2.37 (6H, s, NMe_2); ^{13}C nmr ($CDCl_3$) δ ppm 145.0 (C-3), 142.2 (C-4), 132.0 (C-8a), 130.8 (C-1), 128.8 (C-4b), 127.6 (C-8), 127.3 (C-5), 126.7 (C-7), 126.2 (C-6), 126.0 (C-10a), 125.1 (C-9), 122.7 (C-10), 117.1 (C-4a), 110.5 (C-2), 101.0 (OCH_2O), 61.0 (CH_2-α), 45.3 (NMe_2), 31.9 (CH_2-β) (assignments by COSY).

8-Hydroxystephenanthrine [**9**].—Colorless oil (30 mg): tlc R_f 0.26 (S-2), yellow with Ce-IV reagent; ir (KBr) ν max cm^{-1} 3435 (bd), 2954, 1594, 1445, 1370, 1288, 1064, 1051, 809, 758; uv λ max nm (log ϵ) 218 (4.46), 239 (sh), 246 (sh), 254 (4.70), 297 (4.26), 314 (4.11), 327 (4.13), 338 (sh), 356 (3.68), 375 (3.71); λ max (+KOH) nm 228 (4.55), 248 (sh), 255 (4.61), 302 (4.16), 337 (4.01), 368 (3.84), 387 (3.82); ^{1}H nmr (CD_3OD) δ ppm 8.58 (1H, ddd, $J_1 = 8$ Hz, $J_2 = J_3 = 1$ Hz, H-5), 8.03 (1H, dd, $J_1 = 9.5$ Hz, $J_2 = 1$ Hz, H-9), 7.80 (1H, d, $J = 9.5$ Hz, H-10), 7.37 (1H, dd, $J_1 = J_2 = 8$ Hz, H-6), 7.17 (1H, s, H-2), 6.98 (1H, dd, $J_1 = 8$ Hz, $J_2 = 1$ Hz, H-7), 6.20 (2H, s, OCH_2O), 3.24 (2H, m, CH_2-β), 2.66 (2H, m, CH_2-α), 2.41 (6H, s, NMe_2); ^{13}C nmr (CD_3OD) δ ppm 153.6 (C-8), 145.5 (C-3), 143.1 (C-4), 130.6, 130.4 (C-1, C-4b), 127.2 (C-6), 126.8 (C-10a), 122.7 (C-8a), 121.5, 119.7, 119.3 (C-5, C-9, C-10), 117.9 (C-4a), 111.4, 111.2 (C-2, C-7), 101.6 (OCH_2O), 61.2 (CH_2-α), 45.2 (NMe_2), 31.7 (CH_2-β); eims *m/z* (%) $[M]^+$ 309.1364 (9) (calcd for $C_{19}H_{19}NO_{31}$, 309.1365), 251 (2), 165 (2), 58 (100).

Reticuline.—Colorless oil (18 mg): tlc R_f 0.42 (S-1), brownish-orange with Ce-IV reagent; $[\alpha]^{21}_D$ +94° (*c* = 1.1) [lit. (25) $[\alpha]_D$ +100° (*c* = 0.78)]; ir, uv, ^{1}H nmr, ^{13}C nmr, cims in accordance with published data (25,26).

N-trans-*Feruloyltyramine*.—Colorless oil (11 mg): tlc R_f 0.33 (S-2), yellow with Ce-IV reagent; ir, uv, ^{1}H nmr, ^{13}C nmr, eims in accordance with published data (8,27).

Argentinine-N-*oxide* [**10**].—Colorless oil (1.3 mg): tlc R_f 0.14 (S-2), yellowish-brown with Ce-IV reagent; ir (KBr) ν max cm^{-1} 3390 (bd, weak), 2953, 1600, 1444, 1298, 1003, 819, 756; uv λ max nm (log ϵ) 231 (4.00), 249 (sh), 255 (4.21), 277 (sh), 300 (sh), 310 (3.62), 345 (3.00), 362 (2.96); λ max (+KOH) nm 244 (4.14), 253 (4.14), 267 (sh), 289 (3.58), 335 (3.64), 376 (sh); ^{1}H nmr ($CDCl_3$) δ ppm 9.46 (1H, br d, $J = 8$ Hz, H-5), 7.86–7.82 (2H, m, H-8, H-10), 7.66–7.56 (3H, m, H-6, H-7, H-9), 7.40 (1H, s, H-2), 3.86 (3H, s, 4-OMe), 3.76–3.69 (4H, m, CH_2-α, CH_2-β), 3.49 (6H, s, NMe_2); eims *m/z* (%) $[M-61]^+$ 250.0997 (100) (calcd for $C_{17}H_{14}O_{21}$, 250.0994), 235 (12), 217 (64), 189 (51), 178 (18), 94 (16), 61 (12), 60 (16), 58 (21).

Stephenanthrine-N-*oxide* [**11**].—Colorless oil (10 mg): tlc R_f 0.14 (S-2), green with Ce-IV reagent; ir (KBr) ν max cm^{-1} 2922, 1598, 1455, 1284, 1049, 818, 753; uv λ max nm (log ϵ) 238 (4.47), 248 (4.52), 257 (sh), 283 (4.07), 314 (sh), 320 (3.87), 350 (3.38), 369 (3.35); ^{1}H nmr ($CDCl_3$) δ ppm 9.08 (1H, br d, $J = 7.5$ Hz, H-5), 7.92 (1H, d, $J = 9$ Hz, H-10), 7.84 (1H, m, H-8), 7.65–7.57 (3H, m, H-6, H-7, H-9), 7.20 (1H, s, H-2), 6.25 (2H, s, OCH_2O), 3.76–3.56 (4H, m, CH_2-α, CH_2-β), 3.40 (6H, s, NMe_2); eims *m/z* (%) $[M-61]^+$ 248.0835 (100) (calcd for $C_{17}H_{12}O_2$, 248.0837), 218 (18), 217 (25), 189 (70), 188 (28), 94 (32), 58 (20).

8-Hydroxystephenanthrine-N-*oxide* [**12**].—Colorless oil (2 mg): tlc R_f 0.07 (S-2), yellow with Ce-IV reagent; ir (KBr) ν max cm^{-1} 3400 (bd), 2923, 1595, 1456, 1285, 1057, 829, 758; uv λ max nm (log ϵ) 216 (4.23), 240 (sh), 247 (sh), 254 (4.36), 297 (3.90), 313 (3.76), 327 (3.78), 356 (3.32), 375 (3.35); λ max (+KOH) nm 226 (sh), 248 (sh), 255 (4.27), 290 (sh), 301 (3.83), 338 (3.72), 370 (3.50), 388 (3.49); ^{1}H nmr (CD_3OD) δ ppm 8.60 (1H, br d, $J = 8$ Hz, H-5), 8.10 (1H, dd, $J_1 = 9.5$ Hz, $J_2 = 1$ Hz, H-9), 7.89 (1H, d, $J = 9.5$ Hz, H-10), 7.40 (1H, dd, $J_1 = J_2 = 8$ Hz, H-6), 7.28 (1H, s, H-2), 7.01 (1H, dd, $J_1 = 8$ Hz, $J_2 = 1$ Hz, H-7), 6.24 (2H, s, OCH_2O), 3.69–3.57 (4H, m, CH_2-α, CH_2-β), 3.32 (6H, s, NMe_2); eims *m/z* (%) $[M-61]^+$ 264.0796 (100) (calcd for $C_{17}H_{12}O_3$, 264.0783), 247 (7), 233 (14), 217 (6), 205 (12), 176 (23), 58 (22).

COMPOUNDS **10**, **11**, AND **12** BY *N*-OXIDATION OF **7**, **8** AND **9**.—The basic alkaloid (**7**, **8**, or **9**) (ca. 2 mg) was dissolved in $CHCl_3$ (2 ml), treated with *m*-chloroperbenzoic acid (3 mg) and worked up according to the procedure of Craig and Purushothaman (15). This procedure yielded the corresponding *N*-oxides (ca. 1.5 mg), which were proved to be identical with **10**, **11**, and **12**, respectively.

METHYLATION OF **1**.—Compound **1** (3 mg) was subjected to the methylation procedure described above for **3**. Purification by cc on Fractogel PVA-500 yielded 2.5 mg of *N*,O-dimethyl-1-desmethoxy-4,5-dioxodehydroasimilobine [**13**]: orange, amorphous; tlc R_f 0.71 (S-1), brownish-orange with Ce-IV reagent; ir (KBr) ν max cm^{-1} 1666; uv/vis λ max nm (log ϵ) 232 (sh), 244 (4.39), 288 (sh), 300 (3.81), 311 (3.84), 444 (3.73); ^{1}H nmr δ ppm 8.81 (1H, br d, $J = 8$ Hz, H-11), 8.57 (1H, d, $J = 2.5$ Hz, H-1), 8.34 (1H, d, $J = 2.5$ Hz, H-3), 8.06 (1H, dd, $J_1 = 8$ Hz, $J_2 = 2$ Hz, H-8), 7.72 (1H, ddd, $J_1 = J_2 = 8$ Hz, $J_3 = 1.5$ Hz, H-9), 7.68 (1H, ddd, $J_1 = J_2 = 8$ Hz, $J_3 = 2$ Hz, H-10), 7.65 (1H, s, H-7), 3.96 (3H, s, 2-OMe), 3.76 (3H, s, N-Me); ^{13}C nmr see Table 2; eims *m/z* (%) $[M]^+$ 291.0902 (100) (calcd for $C_{18}H_{13}NO_3$, 291.0895), 264 (16), 263 (93), 248 (16), 220 (6), 192 (7), 179 (9), 165 (20), 163 (13), 132 (8).

CEPHARADIONE B [**14**] BY METHYLATION OF **2**.—Compound **2** (10 mg) was subjected to the methylation procedure described above for **3**. Purification by cc on Fractogel PVA-500 yielded **14** (8.4 mg): orange needles; mp 264–267° (from MeOH) [lit. (9) mp 267–268° (from EtOH)]; tlc R_f 0.68 (S-1),

brownish-orange with Ce-IV reagent; ir, uv/vis, and eims in accordance with Akasu *et al.* (9); ^{1}H nmr (C_5D_5N) δ ppm 9.76 (1H, m, H-11), 8.39 (1H, s, H-3), 8.09 (1H, m, H-8), 7.72 (1H, s, H-7), 7.78–7.70 (2H, m, H-9, H-10), 4.11 (3H, s, 2-OMe), 3.92 (3H, s, 1-OMe), 3.80 (3H, s, N-Me); ^{13}C nmr (C_5D_5N) see Table 2; ^{13}C nmr ($CDCl_3$) δ ppm 175.5 (C-4), 156.3 (C-5), 155.0 (C-1), 152.8 (C-2), 132.3 (C-7a), 131.8 (C-6a), 129.0 (C-8), 128.0 (C-9), 127.6 (C-10, C-11), 126.9 (C-11a), 124.6, 123.7 (C-3a, C-11b), 119.5 (C-11c), 114.3 (C-7), 112.6 (C-3), 60.4 (1-OMe), 56.5 (2-OMe), 30.5 (N-Me).

NORCEPHARADIONE B [**15**].—Compound **15** was isolated by chromatography of the MeOH extract of *Oxymitra velutina* (10) as orange needles (3 mg): mp 302° (from MeOH) [lit. (28) 304–307° (dec)]; tlc R_f 0.51 (S-1), brownish-orange with Ce-IV reagent; ^{1}H nmr (C_5D_5N) δ ppm 9.77 (1H, m, H-11), 8.42 (1H, s, H-3), 7.99 (1H, m, H-8), 7.78 (1H, s, H-7), 7.74–7.67 (2H, m, H-9, H-10), 4.12 (3H, s, 2-OMe), 3.94 (3H, s, 1-OMe); ^{13}C nmr see Table 2; eims *m/z* (%) $[M]^+$ 307 (100), 279 (30), 264 (10), 236 (10), 221 (10), 193 (13), 181 (11), 165 (11), 164 (13).

CEPHARADIONE A [**16**].—The reference material (9) was kindly provided by Dr. H. Jaggy (11).

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