SYNTHESIS OF NOVEL 7,7'-BIS-6*a*,7-DEHYDRONORAPORPHINES

Akino Jossang, Michel Lebœuf, and André Cavé *

Laboratoire de Pharmacognosie, U.A.496 CNRS,Faculté de Pharmacie, Université Paris XI

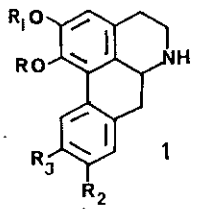
92296 Châtenay-Malabry Cedex, France

Abstract- New dimers, (±)-bisdehydroanonaine **5a**, (±)-bisdehydroxylopine **5c**, (±)-bisdehydronornantenine **5d** and (±)-7-dehydroxylopinyl-7'-dehydronornantenine **8**, and the previously described (±)-urabaine **5b**, were prepared from dehydroxylopine **3c** and known dehydronoraporphines **3a**, **3b**, and **3d** *via* dimerization at the β-carbon of cyclic secondary enamines.

In the last few years, a number of 7,7'-bis-6a,7-dehydroaporphines have been isolated from different Annonaceous plants in our laboratory [1-3]. These compounds, named bipowine, bipowinone[1], urabaine, *N*-methylurabaine, *N,N'*-dimethylurabaine [2], and 7,7'-bisdehydroanonaine[3], are the first representatives of a new class of dimeric alkaloids. Related substances have been reported as oxidation products of 6*a*,7-dehydroaporphines, using iodine[4] or mercuric nitrate or acetate[5].

Previously described methods for the preparation of 6*a*,7-dehydronoraporphines involve photochemical oxidation of noraporphines[6] and total synthesis[7-9]. We have now found that oxidation of noraporphines by *N*-chlorosuccinimide and sodium ethoxide leads to monomeric 6*a*,7-dehydronoraporphines and their 7,7'-dimers[1]. Thus this previously undescribed dimerization at the *β*–carbon of a cyclic secondary enamine allowed us to synthesize several dimers from 6*a*,7-dehydroxylopine **3c** and the known monomers **3a**, **3b** and **3d**. The new dimers were (±)-7,7'-bis-6*a*,7-dehydroanonaine **5a**, (±)-7,7'-bis-6*a*,7-dehydroxylopine **5c**, (±)-7,7'-bis-6*a*,7-dehydronornantenine **5d**, and the asymmetrical (±)-7-dehydroxylopinyl-7'-dehydronornantenine **8**; the previously isolated (±)-urabaine **5b** was also prepared.

Reaction of the noraporphine **1** with *N*-chlorosuccinimide produced the chloramine **2** (yield 95%) which, when treated with sodium ethoxide at 70 °C, afforded a mixture containing dehydronoraporphine **3** (23-46%), 7-chlorodehydronoraporphine **4** (3-6%), 7,7'-bisdehydronoraporphine **5** (1-16%) and oxoaporphine **6** (12-21%). The dehydronoraporphine **3** was converted in turn into the corresponding dimer **5** (20-60%) and the oxoaporphine **6** (30%), by passing air through a solution of **3** in a mixture of



1

Anonaine **1a** : R,R_1=CH_2, R_2=R_3=H

Nornuciferine **1b** : R=R_1=CH_3, R_2=R_3=H

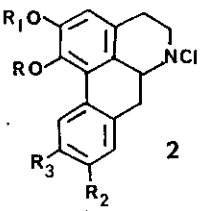
Xylopine **1c** : R,R_1=CH_2, R_2=OCH_3, R_3=H

Nornantenine **1d** : R=R_1=CH_3, R_2,R_3=OCH_2O

Norglaucine **1e** : R=R_1=CH_3, R_2=R_3=OCH_3

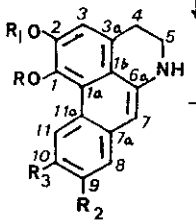
Wilsonirine **1f** : R=H, R_1=CH_3, R_2=R_3=OCH_3

NCS

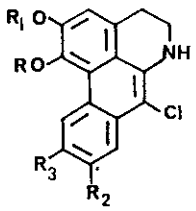


2

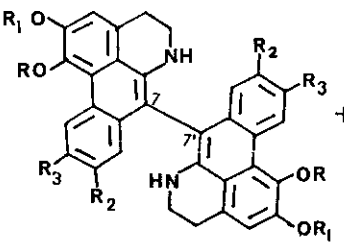
EtONa



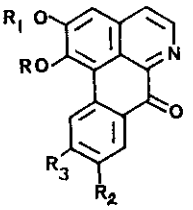
3



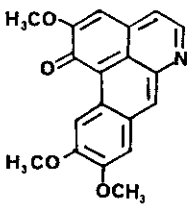
4



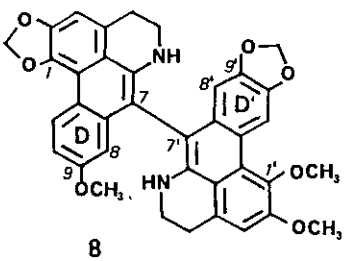
5



6



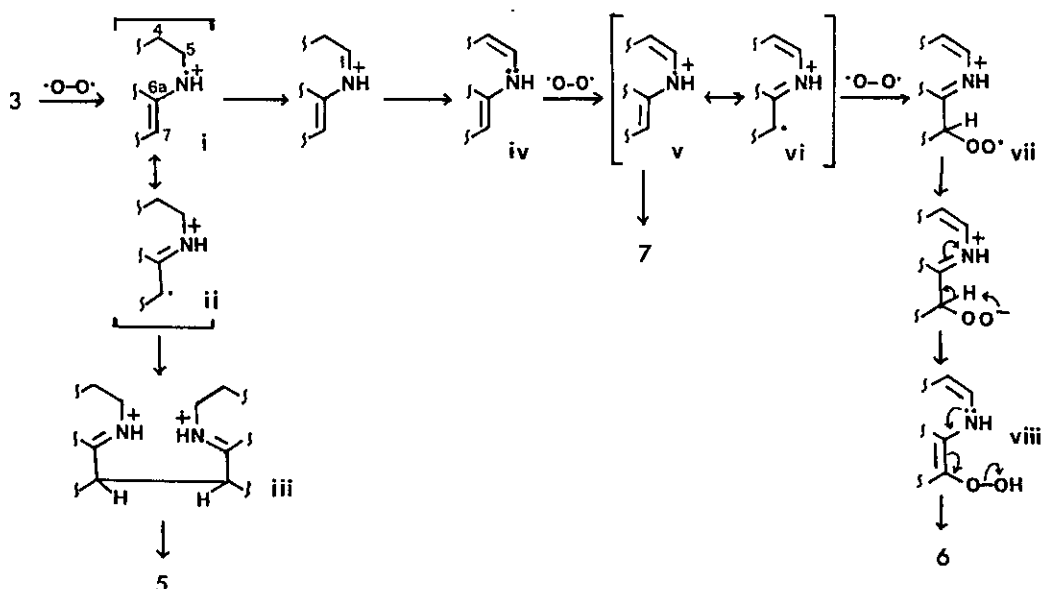
7



8

dichloromethane and methanol. By heating with sodium ethoxide, **3** formed an unidentified water-soluble red product and gave only trace of oxidized compounds, except in the case of dehydronorglaucine **3e**, which dimerized very smoothly[1].

The variety of reaction products observed may be explained by an autoxidation mechanism of the enamine [10], which is probably a free-radical chain process as outlined in Scheme 1. The chloramine **2** may be converted first into an imine, which would then isomerize to a more stable cyclic enamine, forming at the same time the phenanthrene aromatic system of the dehydronoraporphine **3**. Alkaloid **3** may produce a radical cation **I** by transferring one electron of the unshared pair of the nitrogen on an oxygen molecule. Two identical radicals **II**, the immonium form of **I**, may couple to produce a dimer **III**, followed by isomerization into β,β'-bisenamine, 7,7'-bis-6*a*,7-dehydronoraporphine **5**. By another way, **I** may form the 4,5,6*a*,7- dienamine **Iv** after H˙ transfer at C-5 and isomerization. The very instable **Iv** may be immediately converted into the radical cation **v** by abstraction of an electron from the nitrogen with oxygen. The immonium radical **vI** and an oxygen molecule may combine to give the free radical **vII**, followed by extraction of an electron (the propagation step) and by internal proton transfer at C-7, thus producing β-hydroperoxylenamine **vIII**. Compound **vIII** may decompose into an iminoketone, oxoaporphine **6**. In the case of the 1-hydroxynoraporphine wilsonirine **1f**, **v** led to pancoridine **7**[1] through transfer of H˙ from the phenol.



Scheme 1

The first synthetic example of an asymmetrical 7,7'-dimer, 7-dehydroxylopinyl-7'-dehydronornantenine **8**, was prepared from the mixture of 6*a*,7-dehydroxylopine **3c** and 6*a*,7-dehydronornantenine **3d** under the same conditions.

The 7,7'-bisdehydronoraporphines as well as the 7,7'-bisdehydroaporphines[2,4,5] and the 4,7'-bisaporphinoids[11] were the atropisomeric compounds, because rotation about single C-7-C-7' bond is prevented. The atropisomerism of these dimers **5a-5e** appeared in the ^{1}H nmr spectrum[12] (table 1) by the fact that the protons at C-8, C-8' (δ 6.52 to 7.13 ppm) and those of methoxyls at C-9, C-9' (δ 3.5 to 3.6

Table 1. ^{1}H Nmr spectral data of 6*a*,7-dehydronoraporphines **3**, their dimers **5**, and the asymmetrical dimer **8**. ($CDCl_3$, 250MHz)

Proton	Compounds											
	3a	**5a**[2]	**3b**	**5b**	**3c**	**5c**[2]	**3d**[1]	**5d**[1]	**8**		**3e**[1]	**5e**[1]
OCH_3-1	-	-	3.87	3.94	-	-	3.86	3.96	-	4.00	3.85	3.99
OCH_3-2	-	-	3.98	4.01	-	-	3.96	4.04	-	4.08	3.92	4.02
OCH_2O-1,2	6.17	6.30	-	-	6.19	6.32	-	-	6.28	-	-	-
H-3	6.93	7.07	7.02	7.08	6.92	7.04	6.90	7.04	6.99	7.08	6.85	7.02
CH_2-4[3]	3.18t	3.25m	3.23t	3.30m	3.21t	3.30m	3.20t	3.24m	3.20m		3.15t	3.22m
CH_2-5[3]	3.43t		3.50t		3.48t		3.44t				3.40t	
H-7[4]	6.57	-	6.73	-	6.56	-	6.55	-	-	-	6.52	-
H-8[5]	7.50d	7.13d	7.53d	7.13d	6.97d	6.69d	6.96	6.52	6.54d	6.62	6.81	6.61
H-9[5]	7.39t	7.26t	7.41t	7.22t	-	-	-	-	-	-	-	-
H-10[5]	7.27t	7.37t	7.31t	7.35t	6.95dd	7.13dd	-	-	6.98dd	-	-	-
H-11[5]	8.85d	9.07d	9.42d	9.63d	8.08d	9.04d	8.96	9.12	8.98d	9.19	8.95	9.26
OCH_3-9	-	-	-	-	3.92	3.58	-	-	3.59	-	3.95	3.48
OCH_3-10	-	-	-	-	-	-	-	-	-	-	3.96	4.02
OCH_2O-9,10	-	-	-	-	-	-	6.00	5.90	-	5.94d[6]	-	-
										5.96d[6]		
NH		4.05	3.60	4.32	3.80		3.50	3.80			3.10	3.80

1: 90 MHz. *2*: $CDCl_3$ + 5% CD_3OD. *3*: J = 5 Hz. *4*: Disappeared by addition of D_2O or CD_3OD.

5: Jo = 8 Hz, Jm = 2.5 Hz *6*: J = 1 Hz.

ppm) produced signals at unusually high field, shielded about 0.4 ppm and 0.3 ppm respectively in comparison to the corresponding monomers **3a**-**3e** (δ 6.81 to 7.53 ppm and δ 3.92 to 3.95 ppm). Consequently, it appeared that they were located in the field of the anisotropic effect of D and D' cycles. On the other hand, the feature of the four protons of the methylenes at C-4 and C-5 allowed also to distinguish between the dehydronoraporphine monomers and their 7,7'-dimers. Thus two triplets were found at about δ 3.2 ppm and δ 3.4 to 3.5 ppm in the monomers and multiplets centered around δ 3.25 ppm in the 7,7'-dimers.

Determination of the specific optical rotation of the naturally occurring 7,7'- and 4,7'-dimers[1,2,11] was often quite difficult : solutions are strongly coloured due to the instability of these compounds and their $[\alpha]_D$ values are particularly low[3].

Also noteworthy are the high reactivity and the presence of tautomerism of 6*a*,7-dehydronoraporphine **3** demonstrated in the ^1H nmr spectrum, which showed instantaneous and reversible deuterium exchange of the C-7 proton and NH. Thus, one proton singlet near by δ 6.55 ppm (doublet of C-7 at δ 102 ppm of in the ^{13}C nmr spectrum) in $CDCl_3$ disappeared by addition of D_2O or CD_3OD. Contrary, the dehydroaporphines, *N*-methyl derivatives, did not exchange deuterium under the same conditions, but incorporation of deuterium at C-7 occurred slowly, reaching a maximum after 32 hours and only partially (30%) in CF_3COOD by acid-catalyzed reaction[13].

Glaucine, the *N*-methylated derivative of **1e**, reacted with *N*-bromosuccinimide to give 28% yield of 7-bromo-6*a*,7-dehydroglaucine and 10% 6*a*,7-dehydroglaucine as previously reported[14]. Nuciferine, however, did not reacted with *N*-chlorosuccinimide under the above mentioned conditions. The intermediate dienamine **Iv** could not been detected, but such dienamines derived from 6*a*,7-dehydroaporphines were more stable than **Iv** and have been prepared by electrochemical oxidation [15] and photooxidation[16]. 6*a*,7-Dehydronuciferine, *N*-methylated **3b**, was more stable toward oxygen under similar conditions without catalyst and light[17]. In the presence of mercuric nitrate, 6*a*,7-dehydroaporphines reacted to produce the corresponding 7,7'-dimers[2,5], but 6*a*,7-dehydroxylopine **3c** was oxidized further to an oxoaporphine, lanuginosine **6c**. The intermediate **III** could not be isolated, but a related dimeric immonium salt has been obtained from an aporphine through oxidation with iodine[4]. Thus, it is interesting to point out that important differences of reactivity are found between 6*a*,7-dehydronoraporphines and their *N*-methyl derivatives, the 6*a*,7-dehydroaporphines, concerning oxidation with air.

EXPERIMENTAL

All melting points were uncorrected. ^{1}H and ^{13}C nmr spectra (δ ppm) were measured on a Varian HA-90, a Brüker 250 MHz or a Varian CFT20 in $CDCl_3$ using TMS as internal standard. Uv spectra were recorded with a Philips Unicam SP1800 and mass spectra were determined with a Varian MAT311. Spectral data of known aporphines and aporphinoids are described in[18].

Oxidation of anonaine **1a**.– A solution of **1a** (107 mg, 0.4 mmol) and *N*-chlorosuccinimide (46 mg, 0.4 mmol) in CH_2Cl_2 (30 ml) was stirred for 30 min at room temperature. The mixture was washed with water and dried over Na_2SO_4 and solvent removed *in vacuo* at maximum 30°C. The solution of residue in EtOH (20 ml) containing Na (9.2 mg, 0.4 mmol) was heated for 10 min at 70°C under nitrogen. After evaporation of EtOH the reaction mixture was dissolved in water, taken up into CH_2Cl_2 and worked up as usual. The chromatography on silica gel of the residue eluted with 0.2% MeOH in CH_2Cl_2 afforded fraction 1: 4 mg **4a** (4.1% yield), fraction 2: 4 mg **5a** (4.6%), fraction 3: 20 mg **3a** (23%), fraction 4: 12 mg unidentified, fraction 5: 10 mg liriodenine **6a** (12%) and fraction 6: 20 mg **1a** unreacted.

7-Chloro-6*a*,7-dehydroanonaine **4a**.– Amorphous. $C_{17}H_{12}ClNO_2$. Ms *m/z* (%): 299 ($M^{+\cdot}$ +2, 35), 298 ($M^{+\cdot}$ +1, 27), 297 ($M^{+\cdot}$, 100). Uv λmax MeOH nm (log ε): 212 (3.64), 253 (4.13), 261sh (4.12), 326 (3 43), 397 (3.13). ^{1}H nmr, $CDCl_3$, 250 MHz: 3.22 (2H, t, J = 5 Hz , CH_2-4), 3.55 (2H, t, J = 5 Hz, CH_2-5), 3.60 (NH), 6.22 (2H, s, OCH_2O), 6.99 (1H, s, C-3 H), 8.05 (1H, d, C-8 H), 7.57 (1H, t, C-9 H), 7.37 (1H, t, C-10 H), 8.94 (1H, d, C-11 H), J_o = 8 Hz.

(±)-7,7'-Bis-6*a*,7-dehydroanonaine **5a**.– Amorphous. $C_{34}H_{24}N_2O_4$. Ms *m/z*: 525 ($M^{+\cdot}$ +1, 12), 263 ($M^{+\cdot}/2$ +1, 16), 43(100). Uv λmax MeOH nm (log ε): 214 (3.78), 252sh (4.14), 260 (4.14), 328 (3.25), 380 (3.17); MeOH+HCl: 214, 252, 260, 288, 328, 372, 390.

6*a*,7-Dehydroanonaine **3a**.– Mp 125 - 128°C (acetone) (lit. 8: 135 - 6°C). Ms *m/z* : 263 ($M^{+\cdot}$, 100), 248 (17), 232 (12).

Oxidation of nornuciferine **1b**.– 200 mg **1b** were treated in the same manner as **1a** to give 5 mg **4b** (3% yield), 56 mg **3b** (28%), 2 mg **5b** (1%) and 25 mg lysicamine **6b** (13%).

7-Chloro-6*a*,7-dehydronornuciferine **4b**.– Amorphous. $C_{18}H_{16}ClNO_2$. Ms *m/z* : 315 ($M^{+\cdot}$ +2, 23), 314 ($M^{+\cdot}$ +1, 11), 313 ($M^{+\cdot}$, 99), 279 (9), 263 (45), 254 (100), 235 (51), 220 (23). Uv λmax MeOH nm (log ε): 212 (3.61), 255 (4.13), 262 (4.13), 327 (3.24), 395 (2.88). ^{1}H nmr, $CDCl_3$, 250 MHz: 3.22 (2H, t, J = 5Hz, CH_2-4), 3.54 (2H, t, J = 5Hz, CH_2-5), 3.85 (3H, s, OCH_3-1), 3.97 (3H, s, OCH_3-2), 4.10 (NH), 7.02 (1H, s, C-3 H), 8.05 (1H, d, C-8 H), 7.53 (1H, t, C-9 H), 7.35 (1H, t, C-10 H), 9.50 (1H, d, C-11 H), J_o = 8Hz.

6*a*,7-Dehydronornuciferine **3b**. – Mp 147 - 149°C (acetone) (lit. 8: 149.5 - 150.5°C). Ms *m/z* : 279 ($M^{+\cdot}$,100), 264 (36), 236 (25), 220 (32).

(±)-7,7'-Bis-6*a*,7-dehydronornuciferine **5b** [= (±)-urabaine].– Amorphous. $C_{36}H_{32}N_2O_4$. Ms *m/z* : 557 ($M^{+\cdot}$ +1, 65), 279 ($M^{+\cdot}$ +1/2, 50), 263 (60), 41 (100). ^1H nmr and uv spectra as well as Rf were identical with those of natural urabaine[2].

Oxidation of xylopine **1c**.– A similar treatment of **1c** 300 mg afforded **4c** 18 mg (6% yield), **3c** 125 mg (46%), lanuginosine **6c** 60 mg (21%) and **1c** 31 mg unreacted.

7-Chloro-6*a*,7-dehydroxylopine **4c**.– Mp 131 - 133°C (acetone). $C_{18}H_{14}ClNO_3$. Ms (ci - NH_3) *m/z* : 330 (M^+ +3, 35), 329 (M^++2, 22), 328 (M^+ +1, 100). Uv λmax MeOH nm (log ε): 212 (3.71), 355sh (4.14), 269 (4.16), 290sh (3.36), 336 (3.27), 385 (3.15). ^1H nmr, $CDCl_3$, 90MHz: 3.13 (2H, t, J = 5Hz, CH_2-4), 3 52 (2H, t, J = 5Hz, CH_2-5), 3.92 (3H, s, OCH_3-9), 5.00 (NH), 6.14 (2H, s, OCH_2O), 6.85 (1H, s, C-3 H), 7.42 (1H, d, C-8 H), 6.95 (1H, dd, C-10 H), 8.79 (1H, d, C-11 H), J_o = 9Hz, J_m = 2.5Hz.

6*a*,7-Dehydroxylopine **3c**.– Mp 125 - 126°C (acetone). $C_{18}H_{15}NO_3$. Ms (ci - NH_3) *m/z* : 294 (M^+ +1, 100). Uv λmax MeOH nm (log ε): 208 (4.14), 244sh (4.14), 258sh (4.18), 267 (4.21), 290sh (3.63), 338 (3.48), 380sh (3.20); MeOH - HCl: 208, 240, 254, 272, 292, 324, 350, 370. ^{13}C nmr ($CDCl_3$): 141.1 (C-1), 117.8(C-1*a*), 117.4 (C-1*b*), 142.4 (C-2), 111.9 (C-3), 135.5 (C-3*a*), 30.7 (C-4), 41.2 (C-5), 145.2 (C-6*a*), 101.9 (C-7), 127.6 (C-7*a*), 106.6 (C-8), 158.5 (C-9), 105.8 (C-10), 128.5 (C-11), 127.6 (C-11*a*), 100.7 (OCH_2O), 55.1 (OCH_3).

(±)-7,7'-Bis-6*a*,7-dehydroxylopine **5c**.– Amorphous. $C_{36}H_{28}N_2O_6$. Ms (ci - NH_3) *m/z* : 585 (M^++1, 100), 294 (10), 292 (10). Uv λmax MeOH nm (log ε): 210 (4.16), 258sh (4.19), 268 (4.21), 330 (3.75), 380sh (3.29).

Oxidation of nornantenine **1d**.– Treatement of **1d** 50 mg furnished **3d** 19 mg (38%), **5d** 8 mg (16%) and oxonantenine **6d** 10 mg (20%).

6*a*,7-Dehydronornantenine **3d**.– Mp 204 - 205°C (acetone) (lit.8: 208.5 - 9.5°C). Ms (ci - NH_3) *m/z* : 324 (M^+ +1, 100).

(±)-7,7'-Bis-6*a*,7-dehydronornantenine **5d**.– Mp 285 - 290°C (decomp, acetone). $C_{38}H_{32}N_2O_8$. Ms (ci- NH_3) *m/z* : 645 (M^+ +1, 100), 324 (8), 322 (6). Uv λmax MeOH nm (log ε): 212 (3.64), 257 (4.14), 280sh (3.89), 336sh (3.28), 395 (3.16).

Oxidation of norglaucine **1e**.– *cf.* lit. 1.

N-Chloronorglaucine **2e**.– ^1H nmr, $CDCl_3$, 90MHz: 2.60 - 3.90 (4H, m, CH_2-4 and CH_2-7), 3.63 (3H, s, OCH_3-1), 3.84 (3H, s, OCH_3), 3.88 (6H, s, 2 OCH_3), 4.00 - 4.90 (3H, m, CH_2-5 and CH-6*a*), 6.58 (1H, s, C-3 H), 6.72 (1H, s, C-8 H), 8.05 (1H, s, C-11 H).

7-Chloro-6*a*,7-dehydronorglaucine **4e**.– Amorphous. $C_{20}H_{20}ClNO_4$. Ms *m/z* : 375 ($M^{+\cdot}$ +2, 36), 376 ($M^{+\cdot}$

+1, 28), 373 ($M^{+\cdot}$, 100). ^1H nmr, $CDCl_3$, 90MHz: 3.16 (2H, t, J = 5Hz, CH_2-4), 3.51 (2H, t, J = 5Hz, CH_2-5), 3.83 (3H, s, OCH_3-1), 3.97, 3.98 and 4.00 (9H; 3s, 3 OCH_3), 4.60 (NH), 6.92 (1H, s, C-3 H), 7.37 (1H, s, C-8 H), 9.06 (1H, s, C-11 H).

Dimerization of dehydronoraporphines **3**.– Air was passed through a solution of **3** 10 mg in a mixture of CH_2Cl_2 and MeOH (4/1) 50 ml at room temperature untill disappearance of **3** on tlc (7 to 10 days). After evaporation of solvent, the residue was submitted to preparative silicagel tlc (CH_2Cl_2/MeOH = 99.7/0.3) and afforded dimer **5** and oxoaporphine **6**. Thus, **3a** gave 30% yield of **5a** and 30% of **6a**, **3b** furnished 60% of **5b** and 30% of **6b**, **3c** produced 20% of **5c** and 30% of **6c**. All the compounds were identified by comparison with authentic samples (ms, ^1H nmr, tlc).

The mixture of **3c** (18 mg) and **3d** (12 mg), treated in the same manner, afforded **5c** (2 mg), **5d** (4 mg)and the asymmetrical dimer **8** (4 mg).

7-(6*a*,7-Dehydroxylopinyl)-7'-(6'*a*,7'-dehydronornantenine) **8**.– Amorphous. $C_{37}H_{30}N_2O_7$. Ms (ci-NH_3) *m/z* : 615 (M^++1, 100), 324 (5), 322 (5), 294 (18), 292 (10). Uv λmax MeOH nm (log ε): 210 (4.13), 260sh (4.15), 269 (4.16), 338 (3.27), 385 (3.15).

REFERENCES

1. A. Jossang, M. Lebœuf, A. Cavé, and T. Sévenet, *J. Nat. Prod.*, 1986, **49**, 1028.
2. G. Arango, D. Cortes, and A. Cavé, *Phytochemistry*, 1987, **26**, 1227.
3. G. Arango, D. Cortes, and A. Cavé, to be published.
4. M. Gerecke, R. Borer, and A. Brossi, *Helv. Chim. Acta.*, 1975, **58**, 185.
5. L. Castedo, R. Riguera, J.M. Saá, and R. Suau, *Heterocycles*, 1977, **6**, 677.
6. L. Castedo, T. Iglesias, A. Puga, J.M. Saá, and R. Suau, *Heterocycles*, 1981, **15**, 915.
7. M.P. Cava, I. Noguchi, and K.T. Buck, *J. Org. Chem.*, 1973, **38**, 2394.
8. G.R. Lenz and F.J. Koszyk, *J. Chem. Soc. Perkin Trans. I*, 1984, 1273.
9. C. Saá, E. Guitian, L. Castedo, and J.M. Saá, *Tetrahedron Lett.*, 1985, **26**, 4559.
10. S.K. Malhotra, J.J. Hostynek, and A.F. Lundin, *J. Am. Chem. Soc.*, 1968, **90**, 6565.
11. A. Jossang, M. Lebœuf, A. Cavé, T. Sévenet, and K. Padmawinata, *J. Nat. Prod.*, 1984, **47**, 504.
12. L.M. Jackman, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon Press, , New York, 2nd impression 1962.
13. A. Venkateswarlu and M.P. Cava, *Tetrahedron.*, 1976, **32**, 2079.
14. S. Philipov, *Arch. Pharm.*, 1985, **318**, 673.
15. R. Gottlieb and J.L. Neumeyer, *J. Am. Chem. Soc.*, 1976, **98**, 7108.
16. L. Castedo, T. Iglesias, A. Puga, J.M. Saá, and R. Suau, *Heterocycles*, 1982, **19**, 245.
17. M.P. Cava, A. Venkateswarlu, M. Srinivasan, and D.L. Edie, *Tetrahedron*, 1972, **28**, 4299.
18. H. Guinaudeau, M. Lebœuf, and A. Cavé, *Lloydia*, 1975, **38**, 275, and references therein.

Received, 17th April, 1987