SYNTHESIS OF VINCA ALKALOIDS AND RELATED COMPOUNDS. PART LXIX[1]. SYNTHESIS OF 15-SUBSTITUTED EBURNANE DERIVATIVES

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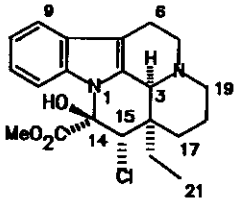
Abstract - Starting from 15α-chlorovincamine (**1**), 15β-hydroxy-14-epivincamine (**2a**) and its 14-*O*-alkyl derivatives (**2b**, **2c**) have been prepared *via* 14,15β-epoxyvincamine (**3**). The latter compound was transformed into (+)-15-oxodihydroeburnamine (**6**). The structures of **2-3** were established *via* detailed nmr investigations.

In a previous communication we described the formation of (+)-15α-chlorovincamine (1) from (+)-apovincamine and its transformation into (+)-vincamine by reducing **1** catalytically.[2] In order to explore further reduction methods, we have treated 1 with $NaBH_4$. The reaction was carried out in methanol, and depending on the work-up conditions of the mixture, two different compounds were



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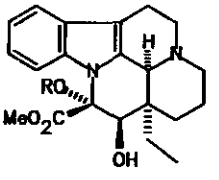
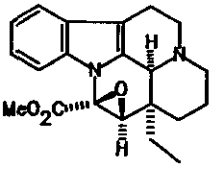


2 a R = H
b R = Me
c R = Et



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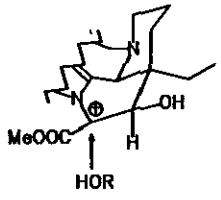
obtained as main products. When the reaction mixture was quenched with acetic acid in aqueous medium, 15β-hydroxy-14-epivincamine (**2a**) was isolated in 22% yield after chromatography. On the other hand, when using a large excess of methanol in the course of the acidic work-up, the 14-O-methyl derivative (**2b**) was obtained in 17 % yield.

To rationalize the formation of these compounds, we have to assume the epoxy derivative (**3**) to be an intermediate. In order to verify this hypothesis, we prepared the epoxy compound by reacting **1** or its hydrochloride salt with different bases (NaOMe, NaH, KO^{t}Bu) in dry benzene. After work-up, **3** was obtained as a crude product in excellent yield (91-96 %).

Compound (**3**) was previously prepared in low (*10 %*) yield, and its structure was elucidated by a French group.[3]

A plausible explanation for the regio- and stereoselectivity of the cleavage of the epoxide ring is as follows: The opening of the protonated epoxy-ring gives the stabilized C-14 carbocation (**4**) which is favored over the C-15 carbocation. This effect determines the position and the β orientation of the C-15 hydroxyl group. In the final step the nucleophile (H_2O or R-OH) attacks **4** from the α face. A direct attack of OR at C-14 in the protonated epoxide is of course also possible.

Starting from the epoxy derivative (**3**) (as a crude product), different 15-hydroxy-14-epivincamine derivatives were prepared. When **3** was treated with diluted sulfuric acid for 4 h at room temperature, after chromatographic work-up **2a** was isolated in *48 % yield. The 14 α-alkoxy derivatives were* prepared by treating **3** with the appropriate alcohol in the presence of concentrated sulfuric acid at room temperature. After 4 h the desired salts (**2b**$\cdot H_2SO_4$ or **2c**$\cdot H_2SO_4$) were precipitated in 46-53 % yield. When chlorohydrine (**1**) was reduced with $NaBH_4$ in DMSO instead of methanol, the dihydroxy compound (**5**) was obtained in 38 % yield. Once again, the intermediate epoxy compound (**3**) is likely to be attacked by the hydride anion in a similar fashion as discussed above regarding the formation of **2**. Finally, the ester group was reduced to give the alcohol (**5**).



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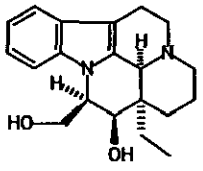

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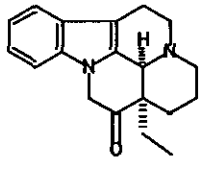

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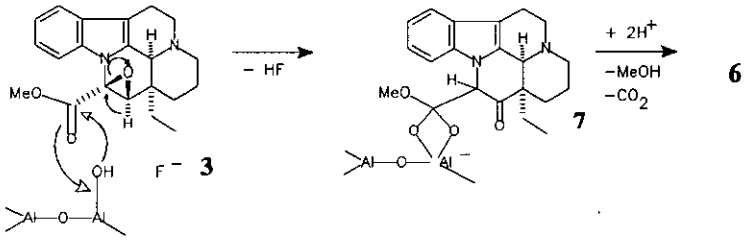
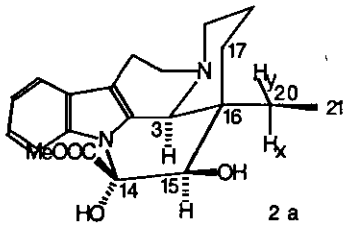
We also tried to convert chlorohydrine (**1**) into the respective 15-fluoro derivative by halogen exchange. When **1** was allowed to react with potassium fluoride in different solvents (benzene, acetone, methanol), only the starting material could be detected by tlc in the reaction mixture. On the other hand, chlorohydrine (**1**) gave unexpected reactions when heated at reflux in benzene in the presence of KF on alumina[4] (6 equivalents of reagent). After a few minutes, as monitored by tlc, **1** had already disappeared and was converted into an intermediate which proved to be epoxide (**3**). The reaction mixture was heated for further 2 h. After a simple work-up (filtration, washing with water, crystallization) compound (**6**)[5] was obtained in 83 % yield. The presumed intermediate (**3**) was also allowed to react with KF on alumina, and this reaction also gave the ketone (**6**). It should be noted that the presence of alumina alone does not result in the formation of **6**, only the starting material (**1**) or epoxide (**3**) can be detected in the reaction mixture.

Epoxide (**3**) can react with the oxide anion of the alumina generated via deprotonation by the fluoride anion. The complex formed can probably be depicted by structure (**7**). After protonation the orthoester can easily lose alcohol and CO_2. In the final step the anion formed is protonated to give the endproduct (**6**). When starting from **6**, several unusual reactions have been observed which will be published elsewhere.



The structures of compounds (**2**, **3**, **5** and **6**) were confirmed by detailed ^1H and ^{13}C nmr studies. ^1H And ^{13}C chemical shifts are collected in Table 1 and Table 2, respectively. The assignments presented here were secured by the concerted use of 2D ^1H-^1H and ^{13}C-^1H correlation experiments and homonuclear 1D $^1H\{^1H\}$ NOE measurements. Below is a brief account of the main nmr spectroscopic features that verify the most significant stereostructural details of these compounds.



Compound (**2a**). The α orientation of H-15 is reflected in the NOE interaction between H-15 and H-3 (*ca.* 6 % in both directions). [In a hypothetical C-15 epimer the long-range H-15 ↔ H-3 NOE

Table 1. ^{1}H Chemical Shifts for Compounds (**2a**, **2b**, **3**, **5**, **6**).

Proton	**2a**	**2b**	**3**	**5**	**6**
H-3	4.02(s)[e]	4.02(s)[e]	4.04(s)[e]	3.91(s)[e]	4.40(s)[d]
H_a-5	3.21(ddd)	3.24(ddd)	3.16(ddd)	3.15-3.36(m)[a]	3.29(ddd)
H_e-5	3.33(ddd)	3.36(ddd)	3.32(ddd)	3.15-3.36(m)[a]	3.38(ddd)
$H\alpha$-6	2.52(dddd)	2.54(dddd)	2.46(dddd)	2.50-2.70(m)[b]	2.54-2.68(m)[a]
$H\beta$-6	3.00(dddd)	3.03(dddd)	2.95(dddd)	2.96(dddd)	3.06(dddd)
H-9	7.48(m)	7.48(m)	7.49(m)	7.48(m)[c]	7.55(m)
H-10	7.10-7.20(m)[c]	7.12-7.19(m)[c]	7.13-7.29(m)[c]	7.11(td)	7.13-7.25(m)[b]
H-11	7.10-7.20(m)[c]	7.12-7.19(m)[c]	7.13-7.29(m)[c]	7.17(td)	7.13-7.25(m)[b]
H-12	7.10-7.20(m)[c]	7.32(m)	7.13-7.29(m)[c]	7.48(m)[c]	7.13-7.25(m)[b]
H-15	4.25(s)	4.31(s)	3.54(s)	4.40(d)	-
H_a-17	1.36-1.45(m)[a]	1.35-1.48(m)[a]	1.01(td)	1.20(td)	1.24-1.38(m)[c]
H_e-17	1.60-1.77(m)[b]	1.35-1.48(m)[a]	1.51(ddd)	1.63(dm)	1.24-1.38(m)[c]
H_a-18	1.60-1.77(m)[b]	1.75(m)	1.66(ddddd)	1.80(ddddd)	1.86(ddddd)
H_e-18	1.36-1.45(m)[a]	1.35-1.48(m)[a]	1.43(ddddd)	1.43(ddddd)	1.46(ddddd)
H_a-19	2.57-2.66(m)[d]	2.55-2.68(m)[d]	2.48(td)	2.50-2.70(m)[b]	2.54-2.68(m)[a]
H_e-19	2.57-2.66(m)[d]	2.55-2.68(m)[d]	2.62(dm)	2.50-2.70(m)[b]	2.54-2.68(m)[a]
H_x-20	2.13(dq)	2.14(dq)	1.75(dq)	1.77(dq)	2.04(dq)
H_y-20	1.78(dq)	1.85(dq)	2.37(dq)	2.17(dq)	2.18(dq)
H_3-21	1.02(t)	1.07(t)	1.08(t)	1.04(t)	1.01(t)
other	3.74(s)(COOMe)	3.73(s)(COOMe)	3.88(s)(COOMe)		
	2.89(br s)(2xOH)	3.22(br s)(OH)		3.15-3.36(m)(2xOH)[a]	
		3.14(s)(14-OMe)		4.05(dd)(-CH_xO-)	4.35(d)($H\alpha$-14)
				4.25(dd)(-CH_yO-)	4.83(d)($H\beta$-14)

[a,b,c] Like superscripts denote overlapping signals. [d] Broadened by long-range couplings to H_2-6 (homoallylic) and H_e-17,19 ('W'). H_x-20 and H_y-20 are defined as before[2], and as depicted in the figures below.

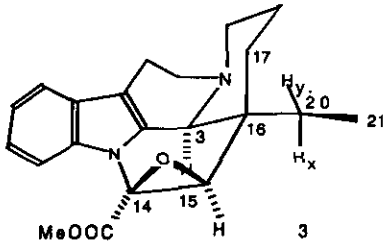
connection may still be measurable due to the relaxationally rather isolated nature of these protons. However, that interaction should be below 1 % (we used an irradiation time of 4 s) by analogy with our previous investigations of compound (**1**).[2] We avoided utilizing the γ-steric effect of the C(15)-OH group on C(17) and C(3) as potential indicators of the C(15) configuration, since the γ_{anti} and γ_{gauche} effect of the OH group can both exert significant upfield shifts on the relevant carbons (cf. 14-epivincamine[2]). Moreover, any C(15) substituent might alter the rotameric equilibrium about the C(16)—C(20) bond, which in turn can influence the chemical shifts of the carbons in the γ position relative to H_3-21.[2] The configuration of C(14) was indicated by the NOE connection between the $COOCH_3$ and H_{eq}-17. [This NOE is small (*ca.* 1 %) but clearly reproducible; a similar NOE connection can be measured in vincamine, while it is absent in 14-epivincamine].

Compound (**2b,c**). For **2b** the stereostructure and the relevant nmr spectroscopic features are entirely analogous to those described for **2a**. In addition, the NOE into the 14-OMe (10%) from $H\alpha$-15 provides further direct evidence for the α orientation of the 14-OMe. For **2c** the structure follows readily from a comparison of the ^{1}H data (see experimental section) with those of **2b**.

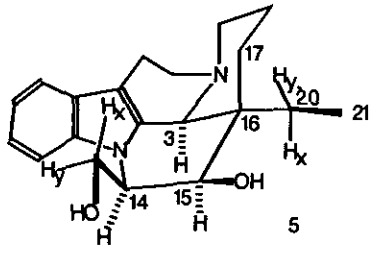
Table 2. ^{13}C Chemical Shifts for Compounds (**2a**, **2b**, **3**, **5**, **6**).

Carbon	**2a**	**2b**	**3**	**5**	**6**
C(2)	131.2	131.9	130.2	130.2	129.5
C(3)	54.2	54.4	56.2	54.7	53.2
C(5)	51.2	51.2	51.4	51.5	51.5
C(6)	16.6	16.7	16.0	16.7	16.8
C(7)	106.4	107.1	107.7	104.8	105.3
C(8)	128.7	128.5	128.6	128.2	127.5
C(9)	118.4	118.0	118.5	118.2	118.5
C(10)	120.4	120.6	120.6	119.6	119.9
C(11)	121.8	122.0	121.9	120.9	121.2
C(12)	110.6	112.0	110.3	110.6	108.8
C(13)	134.5	135.6	135.8	134.7	134.8
C(14)	86.5	90.7	61.6	58.3	50.6
C(15)	81.8	73.7	63.8	72.3	206.9
C(16)	40.6	40.5	37.4	39.6	50.9
C(17)	22.7	23.0	22.9	25.4	27.9
C(18)	20.5	20.5	19.7	20.6	20.6
C(19)	45.0	45.1	44.8	45.1	43.9
C(20)	25.4	25.6	28.2	24.2	23.1
C(21)	8.4	8.3	7.8	8.2	9.3
C=O	171.8	169.0	166.5	-	
COOMe	53.8	53.0	53.4	-	
other		45.5 (14-OMe)		62.2 (CH_2OH)	

Compound (**3**). The β orientation of the epoxy ring is indicated by the NOE found at H_x-20 (3 %) on irradiating H-15, while no NOE was measured into either H-17 proton from H-15. The H-15 ↔ H-3 NOE connection is small (≈1 %) due to the relatively large interproton distance involved, and is in this case an unreliable indicator of the orientation of the epoxy ring.



Compound (**5**). For this compound the indicated geometry, with the C(14)-CH_2-OH being dominantly in the depicted rotameric form, is secured by the following NOE connections: H-15 ↔ H-3: ≈ 5 %; H-15 → H-14: ≈ 10 %; H-14 → H-15: ≈ 5 %; OCH_x → H_{ax}-17: ≈ 5 %; OCH_y → H-12: ≈ 8 %; H-14 → H-12: ≈ 8 %.



Compound (**6**). The structure follows readily from the data collected in the tables. The C-15 position of the C=O group was further corroborated by the strong H_2-14 → H-12 NOEs. Hβ-14 and Hα-14 were assigned (Table 1) on the basis of the measured Hβ-14 → H_{ax}-17 NOE (2 %).

We have previously discussed the conformational characteristics of the C(16)-ethyl for various vincamine analogues.[2] Two main rotamers about the C(16)—C(20) bond must be considered: In

conformer 'a' H_3-21 intersects C(15) and C(17) as depicted in the figures above; in the 'b' rotamer H_3-21 intersects C(3) and C(15). In the present case molecular mechanics (MM+) calculations[6] predict the following $E_{'a'}-E_{'b'} = \Delta E$ (kcal/mol) steric energy differences and corresponding $p_{'a'}$ percentage rotameric populations calculated for 24°C: **2a-c, 5**: $\Delta E \approx +0.17$ ($p_{'a'} \approx 43$ %); **3**: $\Delta E = -0.445$ ($p_{'a'} \approx 68$ %); **6**: $\Delta E = +0.11$ ($p_{'a'} \approx 45$ %). These population distributions are in accord with the fact that for all of these compounds H_3-21 shows NOE connections to H_{eq}-17 as well as to H-3.

EXPERIMENTAL

Mps are uncorrected. Optical rotations were recorded in chloroform or methanol at 25 ± 2 °C. Ir spectra were taken on a Specord IR 75 instrument using KBr pellets. Mass spectra were run on an AEI-MS-902 (70 eV; direct insertion) mass spectrometer. Nmr measurements were carried out on a Varian VXR-300 instrument (300 MHz for ^{1}H and 75 MHz for ^{13}C) at 24 °C in $CDCl_3$. Chemical shifts are given relative to $\delta_{TMS} = 0.00$ ppm. The COSY (COSY-90, magnitude mode), HETCOR and NOE experiments were recorded by using the standard spectrometer software package. The HETCOR experiments were run with ^{1}H decoupling in the F_1 dimension. NOEs were measured in non-degassed samples with 4 s pre-irradiation times. FIDs were exponentially multiplied prior to Fourier transformation (LB = 1 Hz). Molecular mechanics calculations were carried out using the MM+ facility of HyperChem™ with the default parameter-set (in vacuum, Polak-Ribiere algorythm).

Synthesis

14,15 β-Epoxyvincamine (3). A/ To a solution of the hydrochloride salt of **1** (11 g; 25.8 mmol) in benzene (800 ml) at room temperature, sodium methoxide (prepared from 0.7 g /30 mmol/ of sodium and 10 ml of methanol) was added and the mixture refluxed for 1 h. After cooling at room temperature, iced water (200 ml) was added. After extraction, the organic phase was washed with iced water (3 x 100 ml), dried (Na_2SO_4), filtered and the filtrate evaporated to dryness under reduced pressure to give an oil as the product (**3**)[3] (9.2 g; 92 %).

B/ To a solution of **1** (0.77 g; 2 mmol) in benzene (30 ml) at room temperature, sodium hydride (washed with n-hexane, 0.4 g; 8 mmol) was added and the mixture was refluxed for 8 h. After cooling at room temperature, the mixture was treated according to the above procedure to yield **3** (0.66 g; 95.6 %).

C/ To a solution of **1** (0.77 g; 2 mmol) in dry benzene (30 ml) potassium *tert*.-butoxide (0.25 g; 2.22 mmol) was added at room temperature, and the mixture was stirred for 45 min. The mixture was treated according to the above procedure to yield **3** (0.63 g; 91.3 %).

(-)-15 β-Hydroxy-14-epivincamine (**2a**). A/ To a solution of **1** (0.77 g; 2 mmol) in methanol (70 ml) sodium borohydride (0.16 g; 16 mmol) was added at room temperature and the mixture was stirred for 3 h. The solvent was removed by rotary evaporation and the residue was treated with a mixture of water (30 ml) and acetic acid (30 ml). After 5 min the pH of the mixture was adjusted to 8 by adding concentrated aqueous ammonium hydroxide solution (20 ml). The solution was extracted with ethyl acetate (3 x 20 ml) and the extract was washed with water (20 ml), dried (Na_2SO_4). The filtrate was evaporated to dryness under reduced pressure and the residue (0.6 g) was chromatographed on silica (eluent: chloroform 200 ml, chloroform/methanol, 19/1, 300 ml). The solvent was evaporated *in vacuo* and the residue was crystallized from ether (5 ml) to give **2a** (0.16 g; 22 %), mp 89-92 °C, $[\alpha]_D = -8.4°$ (c = 0.2; $CHCl_3$). Ir: 3400, 1720, 1450 cm^{-1}. Ms (m/z, %): 370 (M^+, 93); 369 (80); 355 (6.6, M-15); 341 (8.6, M-29); 325 (12, M-45); 323 (16, M-47); 311 (28, M-59); 300 (5.1; M-70).

B/ **3** (4.4 g; oil; 12.5 mmol) was dissolved in a mixture of water and concentrated sulfuric acid (100 ml/ 4 ml) at room temperature and stirred for 4 h. The mixture was basified by adding concentrated aqueous ammonium hydroxide solution (100 ml), then extracted with chloroform (3 x 50 ml). The combined organic phase was washed with water (2 x 20 ml), dried (Na_2SO_4) and filtered. The filtrate was evaporated to dryness under reduced pressure and the residue (4.5 g) was chromatographed on silica (eluent: chloroform/methanol, 19/1, 500 ml; chloroform/methanol, 19/1, 1000 ml). The solvent was evaporated *in vacuo* and the residue was crystallized from cyclohexane (20 ml) to give **2a** (2.2 g; 47.6 %).

(+)-15β-Hydroxy-14-O-methyl-14-epivincamine (**2b**). A/ To a solution of **1** (0.77 g; 2 mmol) in methanol (70 ml) at room temperature, sodium borohydride (0.6 g; 16 mmol) was added and the mixture refluxed for 4 h. After cooling at room temp., a mixture of acetic acid (20 ml) and water (5 ml) was added. After 24 h the mixture was evaporated to dryness in vacuo and the residue dissolved in a mixture of chloroform/water (40 ml/10 ml). The pH was adjusted to 8 by adding concentrated aqueous ammonium hydroxide solution (5 ml) and the phases were separated. The organic phase was washed with water (3 x 5 ml), dried (Na_2SO_4), filtered. The filtrate was evaporated under reduced pressure and the residue (0.72 g) was chromatographed on silica (eluent: chloroform 200 ml, chloroform/methanol 19/1 300 ml). The solvent was evaporated under reduced pressure and the residue

was crystallized from ether (5 ml) to give **2b** (0.13 g; 17 %), mp 86-90 °C, $[\alpha]_D = +1.6°$ (c =0.2; $CHCl_3$). Ir: 3450, 1720, 1440, 1250, 1090, 1050, 710 cm^{-1}. Ms (m/z, %): 385 (22), 384 (100, M^+), 383 (88, M-1), 369 (22, M-15), 353 (2.6, M-31), 339 (1.5, M-45), 325 (14, M-59), 323 (5, M-61), 309 (3.2, M-75), 263 (4.1, M-121), 253 (15), 252 (71, M-132), 251 (16), 237 (5, M-147), 224 (4.3, M-160), 223 (5.2, M-161), 209 (3.1, M-175).

B/ **3** (4.4 g; 12.5 mmol) was dissolved in a mixture of methanol/concentrated sulfuric acid (50 ml/ 1 ml) at room temperature and stirred. After 4 h the precipitated crystals were filtered off, washed with methanol (5 ml) to give the hydrogensulfate salt of **2b** (2.78 g; 46.1 %), mp 187-192 °C, $[\alpha]_D = +37°$ (c =0.2; $CHCl_3$).

This salt (2.7 g) was dissolved in water (30 ml) and alkalized by adding concentrated aqueous ammonium hydroxide solution (3 ml). The crystals were filtered off, washed with water to give **2b** (2.03 g; 42.3 %), mp 85-90 °C, $[\alpha]_D = +1.6°$ (c =0.18; $CHCl_3$).

(+)-15β-Hydroxy-14-O-ethyl-14-epivincamine (**2c**). Starting from **3** (2.0 g; 5.7 mmol) using ethanol (30 ml) and concentrated sulfuric acid (0.7 ml), the salt of **2c** was obtained (1.5 g; 53.5 %), mp 196-198 °C, $[\alpha]_D = +1.0°$ (c =0.2; MeOH).

This salt was treated with base according to the above procedure to yield **2c** (1.0 g; 44.2 %), mp 85-89 °C, $[\alpha]_D = +1.0°$ (c =0.2; $CHCl_3$). Ir: 3450, 1720, 1440 cm^{-1}. Ms (m/z, %): 404 (35), 403 (29), 402 (100, M^+), 401 (1.7, M-1), 384 (1.7, M-18), 373 (9, M-29), 367 (74, M-Cl), 355 (6, M-47), 349 (17), 337 (7), 332 (9, M-70), 329 (19, M-73), 321 (9), 293 (11), 280 (7), 265 (18), 264 (16), 263 (12), 253 (22), 252 (53), 251 (12), 237 (12), 224 (24), 223 (7), 222(6), 209 (7), 180 (9). ^1H Nmr ($CDCl_3$), δ: 1.08 (3H, t, 7.6 Hz, H_3-21); 1.20 (3H, t, 7.5 Hz, OCH_2CH_3); 1.30-1.53 (3H, m, H_2-17, H_e-18); 1.78 (1H, m, H_a-18); 1.85 (1H, dq, 14.2 and 7.6 Hz, H_x-20); 2.14 (1H, dq, 14.2 and 7.6 Hz, H_y-20); 2.55 (1H, m, H_α-6); 2.57-2.69 (2H, m, H_2-19); 3.02 (1H, m, $H\beta$-6); 3.07 (1H, dq, 14.0 and 7.5 Hz, OCH_xCH_3); 3.26 (2H, ddd, 13.9, 10.6 and 5.7 Hz, H_a-5); 3.36 (1H, dd, 13.9 and 6.6 Hz, H_e-5); 3.59 (1H, dq, 14.0 and 7.5 Hz, OCH_yCH_3); 3.70 (3H, s, OMe); 3.92 (1H, br s, OH); 4.01 (1H, s, H-3); 4.33 (1H, s, H-15); 7.12-7.17 (2H, m, H-10, H-11); 7.38 (1H, m, H-12); 7.48 (1H, m, H-9).

(-)-15β-Hydroxy-14β-hydroxymethyleburnamenine (**5**). To a solution of **1** (2.13 g; 5.5 mmol) in dimethyl sulfoxide (30 ml) at room temperature, sodium borohydride (1.66 g; 43.8 mmol) was added portionwise and the mixture was heated at 80 °C for 2 h. After cooling to room temperature the reaction mixture was poured into water (10 ml) and extracted with ethyl acetate (1 x 30, 3 x 10 ml), dried (Na_2SO_4). The filtrate was evaporated to dryness under reduced pressure and the residue (1.54 g) was

chromatographed on silica (eluent: chloroform / methanol 19/1). The solvent was evaporated under reduced pressure and the residue (1.2 g; 67 %) was crystallized from ether to give **5** (0.68 g; 38 %), mp 108-111 °C, $[\alpha]_D$=- 57.6° (c =0.2; $CHCl_3$). Ir: 3284, 1457 cm^{-1}. Ms (m/z, %): 326 (M^+, 100); 325 (50); 309 (4, M-17); 307 (2.3); 297 (23, M-29); 295 (16); 279 (10); 267 (8, M-59); 256 (25, M-70); 238 (9).

(+)-15-oxo-14,15-dihydroeburnamenine **(6).** A/ To a solution of **1** (5.82 g; 15 mmol) in benzene (300 ml) potassium fluoride on alumina (92 g) was added, and the mixture was refluxed for 2 h during intensive stirring. After cooling, the mixture was filtered off and the precipitate was washed with benzene (2 x 50 ml). The combied filtrate was washed with water (3 x 50 ml) and dried (Na_2SO_4), filtered. The filtrate was evaporated under reduced pressure and the residue (4.1 g; 95 %) was crystallized from methanol to give **6** (3.6 g; 83 %), mp 138-140 °C, $[\alpha]_D$= +63.4° (c =1.0; $CHCl_3$). Ir: 1709 cm^{-1}. Ms (m/z, %): 294 (M+, 12); 265 (100); 224 (70); 180 (9).

B/ Starting from **1** (0.77 g; 2 mM), the epoxide (**3**) was prepared as described above. The crude epoxide (**3**) (0.72 g) was dissolved in benzene (30 ml) and KF on alumina (12 g) was added. The reaction mixture was treated as above. After the usual procedure compound (**6**) (0.49 g; 85.5 %) was obtained.

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