Synthesis of Eburnamine, Isoeburnamine, and Eburnamonine *via* a Spirocyclic Intermediate

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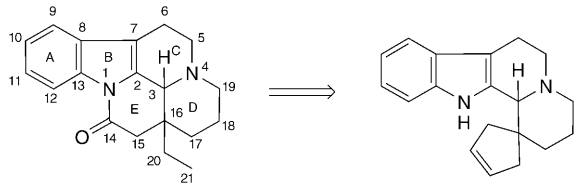
Racemic eburnamonine (**1**) was synthesized *via* **6**, an intermediate possessing local symmetry. Cleavage of the cyclopentene subunit led to pentacyclic aldehydes **8a**/**8b** which on subsequent borohydride and *Wolff–Kishner* reductions gave **12**. The final steps included a $RuCl_3$-catalyzed periodate oxidation and pyridinium chlorochromate (PCC) oxidation. The penultimate intermediates were racemic eburnamine (**2**) and racemic isoeburnamine (**3**).

The pentacyclic indole alkaloids represented by eburnamonine (**1**), eburnamine (**2**), and isoeburnamine (**3**) have been isolated from numerous species of the plant family Apocyanaceae [1] (an extensive tabulation of isolation of these alkaloids from numerous plants is found in [2d]). Interestingly, dextrorotatory, levorotatory, and racemic forms of eburnamonine exist in nature. The (−)-form, also known as vincamone (isolated from *Vinca minor*), is a drug that possesses a stimulating activity for muscle and is used as cerebrotonic, whereas both enantiomers have hypotensive effects. The interesting pharmacological activities triggered much effort for the synthesis of this type of compounds [2–4] (for an extensive compilation of eburnamonine syntheses from 1960–1991, see [3a]; for pharmacological aspects, see [2d] and ref. cit. therein). It is the synthetic work of *Wenkert* and *Wickberg* [5] that established the *cis* D/E-ring junction of the *Eburna* alkaloids.

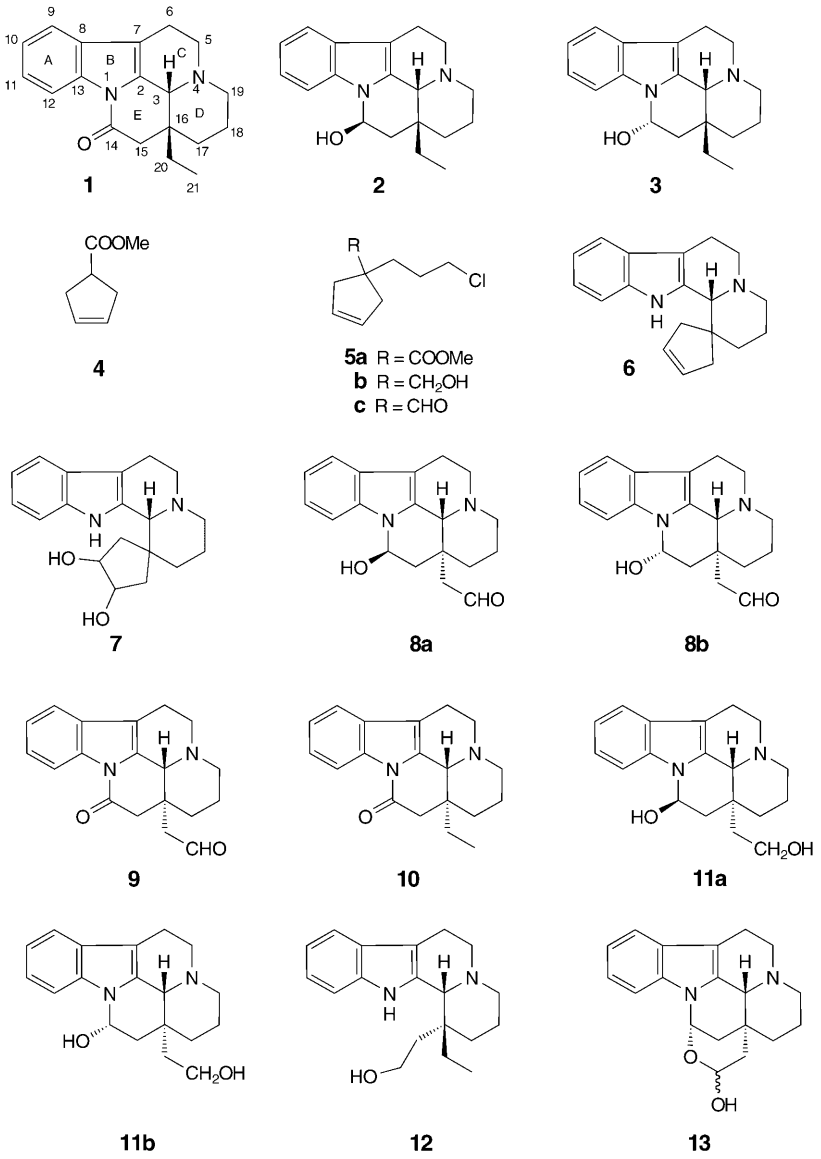
With molecular symmetry or hidden symmetry as a guide for synthetic design [6] for natural products [7], our attention was turned to the possibility of elaborating some of the *Eburna* alkaloids from a precursor with local symmetry. Our analysis focused on the racemic spirocyclic intermediate **6** (*Scheme*[1])) which on oxidative cleavage (at the iso-

Scheme[1])



1 **6**

[1]) Throughout this report, racemates are described; for convenience, only the formula of one enantiomer is depicted. The absolute configuration of the corresponding stereoparent 'eburnamenine' is (3*β*,16*β*), *cf.* names in the *Exper. Part.*



lated double bond) would release two functionalized C-chains necessary for completing the ring system as well as the erection of the angular ethyl group. As the stereochemical issue is concerned, we believed that adjustment is possible even if the E-ring formation led to the epimeric series.

Aldehyde **5c** was identified as a component for combining with tryptamine by a *Pictet–Spengler* reaction [8]. Access to **5c** from methyl cyclopent-3-enecarboxylate **4** [9] in 3 steps *via* **5a**,**b** was straightforward: alkylation with 1-bromo-3-chloropropane, reduction with *Dibal-H* (diisopropylaluminium hydride), and PCC (pyridinium chlorochro-

mate) oxidation. Initially, we attempted to convert the ester group into a formyl group with *Dibal-H* but only the alcohol was obtained. Probably due to the steric hindrance of **5c**, we observed its optimal transformation into **6** by a CF_3COOH-promoted *Pictet–Spengler* reaction to the extent of only 50% completion. Concomitant formation of the D-ring was observed. Next, we carried out a vicinal-dihydroxylation with a catalytic amount of OsO_4 and 4-methylmorpholine 4-oxide as the reoxidant. Only one product, diol **7**, was isolated (66% yield). On treatment of the diol with $NaIO_4$, a mixture of pentacyclic hydroxyaldehydes (later identified as **8a** and **8b** which are epimeric at the alcohol center) was isolated. To establish the identity of these hydroxyaldehydes, particularly the nature of the ring junction, the mixture was oxidized with PDC (pyridinium dichromate). Production of a single product confirmed the presence of epimers in the cyclization product and showed that the cyclization was selective. Dithioacetalization of the hydroxyaldehyde mixture followed by desulfurization with *Raney*-Ni led to 3-epieburnamonine (**10**) [3g][5]. Therefore, our objective was yet to be reached.

Further identification of the pentacyclic hydroxyaldehydes proved rather trivial since **8b** readily underwent cyclization to lactol **13** upon column chromatography. Exposure of **8a** and **13** to $NaBH_4$ delivered **11a** and **11b** [3b], respectively. Deoxygenation of **11a**/**11b** to **12** by a *Wolff–Kishner* reduction under *Huang–Minlon* conditions proceeded smoothly. Alcohol **12** is a known compound, and its conversion to eburnamonine has been described [3b][10]. However, we were not able to repeat the transformation, using either $BF_3 \cdot OEt_2$/PCC [3b][10] or the perrhenate protocols [3d][3g]. We had to carry out a $RuCl_3$-catalyzed periodate oxidation [11] to obtain a 1:1 mixture of eburnamine (**2**) and isoeburnamine (**3**) [12], before treatment with PCC to afford eburnamonine (**1**) [12b][1]).

In summary, we have completed a synthesis of eburnamine, isoeburnamine, and eburnamonine utilizing racemic **6** that possesses local symmetry as a pivotal intermediate.

We thank the *National Science Council* of ROC for financial support.

Experimental Part

General. All reactions were conducted under N_2. For drying org. solns. during workup, Na_2SO_4 was used. Column chromatography (CC): *Merck* silica gel (63–200 mesh). TLC: *Merck* silica gel *60 F 254* plates. M.p.: *Laboratory Devices*; uncorrected. IR Spectra: *Bio-Rad FTS 165*; $\tilde{\nu}$ in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: *Varian Unity-300*; $CDCl_3$ unless otherwise indicated; δ in ppm, J in Hz. EI-MS: *Trio-2000* and *Jeol SX-102A*; ionization potential 70 eV unless otherwise indicated.

Methyl Cyclopent-3-enecarboxylate (**4**). According to [9], from dimethyl malonate and (2*Z*)-1,4-dichlorobut-2-ene: **4** (*ca.* 50%). ^{1}H-NMR: 2.63 (*d*, J = 8.4, 4 H); 3.05–3.15 (*m*, 1 H); 3.68 (*s*, 3 H); 5.64 (*s*, 2 H).

Methyl 1-(3-Chloropropyl)cyclopent-3-enecarboxylate (**5a**). To a stirred soln. of lithium diisopropylamide (LDA; 28 mmol; prepared from BuLi and ^{i}Pr$_2$NH in anh. THF (20 ml)) was added a soln. of **4** (3.0 g, 23.7 mmol) in THF (5 ml) during 5 min, while the temp. was maintained at −78°. After 30 min, a soln. of 1-bromo-3-chloropropane (3.78 g, 24 mmol) in THF (5 ml) was added dropwise. After an additional hour, the mixture was allowed to gradually warm up to r.t. and then kept overnight. After quenching with sat. aq. NH_4Cl soln. (20 ml), the product was extracted into Et_2O, the combined org. phase washed with brine, dried, and evaporated, and the residue subjected to CC (AcOEt/hexane 1:9): **5a** (4.22 g, 88%). Colorless liquid. R_f 0.4 (AcOEt/hexane 1:9). IR: 1723 (C=O). ^{1}H-NMR: 1.67–1.72 (*m*, 2 H); 1.76–1.80 (*m*, 2 H); 2.28 (*d*, J = 15, 2 H); 2.88 (*d*, J = 15, 2 H), 3.48 (*t*, J = 6, 2 H); 3.67 (*s*, 3 H); 5.58 (*s*, 2 H). ^{13}C-NMR: 28.58 (*t*); 36.55 (*t*); 42.34 (*t*); 45.04 (*t*); 51.83 (*s*);

51.95 (*q*); 128.33 (*d*); 177.59 (*s*). EI-MS (30 eV): 204 (0.40), 202 (1.05, M^+), 187 (2.13), 145 (35.95), 143 (100), 125 (16.83). Anal. calc. for $C_{10}H_{15}ClO_2$: C 59.26, H 7.46; found: C 59.12, H 7.86.

1-(3-Chloropropyl)cyclopent-3-ene-1-methanol (**5b**). A soln. of **5a** (3.55 g, 17.5 mmol) in anh. THF (25 ml) was cooled to $-78°$ and treated with *Dibal-H* (38.5 mmol, 32 ml; 20% (*w*/*w*) in PhMe) during 10 min. The resulting soln. was stirred for 30 min at $-78°$ and for 2 h at 0°, and then cautiously quenched by MeOH (5 ml). After dilution with H_2O (15 ml) while warming up to r.t. during an additional 2 h, the mixture was poured into 5% HCl soln. (50 ml) and extracted with Et_2O. The extract was washed with aq. $NaHCO_3$ soln. and brine, dried, and evaporated and the residue subjected to CC (AcOEt/hexane 15:85): **5b** (2.99 g, 98%). Colorless liquid. R_f 0.15 (AcOEt/hexane 1:9). IR: 3385 (OH). ^{1}H-NMR: 1.52–1.58 (*m*, 2 H); 1.67–1.76 (*m*, 2 H); 1.83 (br., 1 H); 2.21 (*d*, *J* = 15, 2 H); 2.09 (*d*, *J* = 15, 2 H); 3.42 (*s*, 2 H); 3.50 (*t*, *J* = 6.6, 2 H); 5.56 (*s*, 2 H). ^{13}C-NMR: 28.07 (*t*); 34.62 (*t*); 41.07 (*t*); 45.69 (*s*); 45.74 (*t*); 69.02 (*t*); 129.12 (*d*). Anal. calc. for $C_9H_{15}ClO$: C 61.89, H 8.66; found: C 61.79, H 8.90.

1-(3-Chloropropyl)cyclopent-3-ene-1-carboxaldehyde (**5c**). PCC (6.47 g, 30 mmol) was added in portions within 10 min to a mixture of **5b** (2.62 g, 15 mmol), Na_2CO_3 (5.24 g, 49.5 mmol), and powdered 4-Å molecular sieves (7.67 g) in anh. CH_2Cl_2 (60 ml) at r.t. After 1 h, the mixture was diluted with Et_2O (25 ml) and passed through a pad of *Florisil*. The *Florisil* bed was thoroughly rinsed with Et_2O the combined soln. evaporated, and the residue subjected to CC (AcOEt/hexane 5:95): **5c** (2.04 g, 79%). Colorless liquid. R_f 0.4 (AcOEt/hexane 1:9). IR: 1724 (C=O). ^{1}H-NMR: 1.64–1.70 (*m*, 2 H); 1.77–1.83 (*m*, 2 H); 2.23 (*d*, *J* = 15, 2 H); 2.71 (*d*, *J* = 15, 2 H); 3.51 (*t*, *J* = 6.3, 2 H); 5.61 (*s*, 2 H); 9.49 (*s*, 1 H). ^{13}C-NMR: 28.24 (*t*); 32.66 (*t*); 38.82 (*t*); 45.11 (*t*); 56.05 (*t*); 128.68 (*d*); 203.42 (*d*). EI-MS (30 eV): 174 (0.91), 172 (2.29, M^+), 145 (2.48), 143 (9.28). Anal. calc. for $C_9H_{13}ClO$: C 62.61, H 7.59; found: C 62.75, H 7.88.

*(12′b*RS*)-3′,4′,6′,7′,12′,12′b-Hexahydro-spiro[cyclopent-3-ene-1,1′(2′*H*)-indolo[2,3-*a*]quinolizine]* (**6**). A soln. of **5c** (1.85 g, 10.7 mmol) in anh. CH_2Cl_2 (30 ml) was mixed with a soln. of tryptamine (= 1*H*-indole-3-ethanamine; 1.88 g, 11.8 mmol) in CH_2Cl_2 (30 ml) at r.t. and stirred for 2 h. The mixture was cooled to 0° and treated with CF_3COOH (45.0 mmol, 3.45 ml) in CH_2Cl_2 (5 ml) during 10 min. After 1 h, the ice bath was removed and the mixture kept at r.t. overnight and then poured into an ice-cold 5% aq. $NaHCO_3$ soln. (50 ml). The mixture was extracted with CH_2Cl_2, washed with aq. $NaHCO_3$ soln. and brine, dried, and evaporated, and the residue subjected to CC (AcOEt/hexane 10:90 → 50:50): recovered **5c** (0.68 g) and **6** (0.68 g, 36% based on reacted **5c**). Pale yellow solid. R_f 0.25 (AcOEt/hexane 1:1). M.p. 101–103°. IR: 2803, 2849, 2919 (CH), 3439 (NH). ^{1}H-NMR: 1.47–1.69 (*m*, 2 H); 1.79–1.63 (*m*, 2 H); 2.16–2.45 (*m*, 4 H); 2.62–2.73 (*m*, 2 H); 2.98–3.13 (*m*, 4 H); 3.34 (*s*, 1 H); 5.71–5.74 (*m*, 1 H); 5.80–5.84 (*m*, 1 H); 7.04–7.15 (*m*, 2 H); 7.24 (*d*, *J* = 7.2, 1 H); 7.46 (*d*, *J* = 7.2, 1 H); 7.90 (*s*, 1 H). ^{13}C-NMR: 21.38 (*t*); 22.60 (*t*); 40.05 (*t*); 40.83 (*t*); 43.14 (*s*); 47.94 (*t*); 54.56 (*t*); 56.10 (*t*); 69.15 (*d*); 110.63 (*s*); 110.78 (*d*); 117.74 (*d*); 119.08 (*d*); 121.31 (*d*); 126.69 (*d*); 126.86 (*s*); 134.07(*d*); 134.58(*s*); 136.02 (*s*). EI-MS: 279 (5.88), 278 (31.66, M^+), 211 (2.79), 198 (5.37), 197 (4.11), 184 (3.19), 171 (6.25), 170 (14.95), 168 (10.60). HR-MS: 278.1777 ($C_{19}H_{22}N_2^+$; calc. 278.1785).

*(12′b*RS*)-3′,4′,6′,7′,12′,12′b-Hexahydrospiro[cyclopentane-1,1′-(2′*H*)-indolo[2,3-*a*]quinolizine]-3,4-diol* (**7**). A soln. of **6** (0.38 g, 1.37 mmol), 2.5% OsO_4 in *t*-BuOH (2 drops), and 4-methylmorpholine 4-oxide monohydrate (NMO; 0.54 g, 4.0 mmol) in THF (9.0 ml), H_2O (0.45 ml), and *t*-BuOH 0.90 ml) was stirred at r.t. overnight. Addition of CH_2Cl_2 (25 ml) was followed by washing with H_2O and brine. The org. soln. was dried and evaporated and the residue subjected to CC (AcOEt): **7** (0.28 g, 66%). Very light yellow solid. R_f 0.15 (AcOEt). M.p. 122–124°. IR: 2807, 2850, 2931 (CH), 3342 (NH, OH). ^{1}H-NMR: 1.53–1.79 (*m*, 4 H); 1.93–2.03 (*m*, 1 H); 2.34–2.64 (*m*, 6 H); 2.85–2.92 (*m*, 3 H); 3.32 (br., 1 H); 3.78 (br., 1 H); 4.12 (br., 1 H); 7.02–7.12 (*m*, 2 H); 7.31 (*d*, *J* = 7.8, 1 H); 7.42 (*d*, *J* = 7.8, 1 H); 8.29 (*s*, 1 H). ^{13}C-NMR: 21.07 (*t*); 22.20 (*t*); 36.00 (*t*); 40.78 (*t*); 42.81 (*t*); 43.30 (*s*); 52.23 (*t*); 55.43 (*t*); 68.16 (*d*); 72.59 (*d*); 72.76 (*d*); 110.32 (*d*); 110.93 (*s*); 116.50 (*d*); 117.90 (*d*); 120.11 (*d*); 125.94 (*s*); 132.79 (*s*); 135.89 (*s*). EI-MS: 312 (39, M^+), 311 (100), 310 (79), 295 (3), 185 (4), 170 (15). HR-MS: 312.1833 ($C_{19}H_{24}N_2O_2^+$; calc. 312.1839).

rac-*(14β,16α)-14,15-Dihydro-14-hydroxyeburnamenin-21-al*[1]) (**8a**). To a soln. of **7** (0.30 g, 0.97 mmol) in 50% THF/H_2O (16.0 ml) was added $NaIO_4$ (1.28 g, 5.98 mmol). The mixture was stirred for 30 min at r.t. when CH_2Cl_2 (50 ml) was added. The org. layer was washed with H_2O and brine, dried, and evaporated: crude **8a**/**8b** *ca.* 2.5:1.0 (by ^{1}H-NMR). CC (10% → 100% AcOEt/hexane): gave **8a** (0.18 g, 0.58 mmol) and **13** (80 mg, 0.26 mmol), the latter being formed from **8b** on CC. Combined yield 87%. Attempts to purify **13** failed; its identity was confirmed by $NaBH_4$ reduction to **11b** (*vide infra*).

Data of **8a**: Pale yellow amorphous solid. R_f 0.50 (AcOEt). IR: 1711 (C=O), 2806, 2852, 2940 (CH), 3363 (NH, OH). ^{1}H-NMR: 1.08–1.20 (*m*, 1 H); 1.43 (*ddd*, *J* = 13.8, 9.0, 1.2, 1 H); 1.49–1.59 (*m*, 2 H); 1.80–1.92 (*m*, 2 H); 2.14 (*dt*, *J* = 11.1, 3.3, 1 H); 2.38 (*dt*, *J* = 11.1, 4.2, 1 H); 2.53 (*dd*, *J* = 13.8, 5.7, 1 H); 2.57–2.64 (*m*, 2 H); 2.74–2.88 (*m*, 2 H); 2.92–2.98 (*m*, 2 H); 3.60 (br., 1 H); 5.53 (*dd*, *J* = 9.0, 6.0, 1 H); 7.09–7.18 (*m*, 2 H); 7.40–7.46 (*m*,

1 H); 7.57–7.60 (*m*, 1 H); 9.56 (*t*, *J* = 2.4, 1 H). ^{13}C-NMR: 21.22 (*t*); 32.79 (*s*); 37.75 (*s*); 42.10 (*t*); 43.00 (*t*); 52.14 (*t*); 55.17 (*t*); 66.40 (*d*); 76.44 (*d*); 106.79 (*s*); 111.76 (*d*); 118.28 (*d*); 120.30 (*d*); 121.51 (*d*); 128.29 (*s*); 133.07 (*s*); 137.61 (*s*); 202.61 (*d*). EI-MS: 310 (20, M^+), 309 (30), 308 (16), 282 (72), 281 (100), 280 (52), 266 (20), 248 (14), 238 (63). HR-MS: 310.1676 ($C_{19}H_{22}N_2O_2^+$; calc. 310.1683).

rac-*(16α)-14,15-Dihydro-14-oxoeburnamenin-21-al* (**9**). PDC (0.11 g, 0.29 mmol) was added to crude **8a**/**8b** (70 mg, 0.23 mmol) in anh. CH_2Cl_2 (5 ml), and the mixture was stirred at r.t. overnight. The oxidation product was diluted with AcOEt (20 ml) and passed through *Celite*. The *Celite* pad was further rinsed, the combined filtrate evaporated, and the residue subjected to CC (AcOEt/hexane 1:1): **9** (30 mg, 43%). Thick oil. R_f 0.50 (AcOEt/hexane 3:1). IR: 1656, 1707 (C=O), 2943 (CH). ^{1}H-NMR: 1.31 (*ddt*, *J* = 13.4, 4.3, 1.5, 1 H); 1.59–1.70 (*m*, 1 H); 1.79–1.93 (*m*, 3 H); 2.11 (*td*, *J* = 13.5, 3.3, 1 H); 2.28 (*dt*, *J* = 11.7, 3.6, 1 H); 2.44–2.53 (*m*, 2 H); 2.56–2.64 (*m*, 1 H); 2.74–2.86 (*m*, 1 H); 2.92 (*td*, *J* = 14.1, 2.4, 1 H); 2.98–3.08 (*m*, 3 H); 7.20–7.28 (*m*, 2 H); 7.35–7.38 (*m*, 1 H); 8.26–8.29 (*m*, 1 H); 9.66 (*t*, *J* = 2.1, 1 H). ^{13}C-NMR: 21.08 (*t*); 21.43 (*t*); 32.92 (*t*); 39.12 (*s*); 43.16 (*t*); 44.62 (*s*); 51.86 (*t*); 55.00 (*t*); 65.07 (*d*); 113.72 (*s*); 116.27 (*d*); 118.27 (*d*); 124.04 (*d*); 124.45 (*d*); 129.62 (*s*); 131.92 (*s*); 134.96 (*s*); 166.52 (*s*); 200.99 (*d*). EI-MS: 308 (3.53, M^+), 307 (14.73), 282 (10.45), 281 (56.79), 279 (100), 263 (15.54), 237 (22.77). HR-MS: 308.1529 ($C_{19}H_{20}N_2O_2^+$; calc. 308.1526).

3-Epieburnamonine[1]) (= rac-*(16α)-Eburnamenin-14(15*H*)-one*[1]); **10**). A mixture of **9** (30 mg, 0.098 mmol), ethane-1,2-dithiol (0.03 ml, 0.35 mmol) and BF_3·Et_2O (0.02 ml, 0.16 mmol) in CH_2Cl_2 (5 ml) was stirred at 0° for 1 h, then at r.t. for 8 h. It was diluted with CH_2Cl_2 (15 ml), washed with 5% aq. $NaHCO_3$ soln. and, brine, dried, and evaporated. The residue was dissolved in EtOH (8 ml), treated with *Raney*-Ni (50% aq. slurry, *ca*. 0.5 ml) and refluxed for 8 h. The cooled mixture was filtered through *Celite*, the latter washed with CH_2Cl_2 (15 ml), the filtrate evaporated, and the residue subjected to CC (AcOEt/hexane 1:1): **10** (20 mg, 69%). White solid. R_f 0.40 (AcOEt/hexane 1:1). M.p. 135–137° ([5]: 138–139°). IR: 1654, 1708 (C=O), 2854, 2926 (CH). ^{1}H-NMR: 0.73–0.87 (*m*, 4 H); 1.12–1.23 (*m*, 2 H); 1.57–1.63 (*m*, 2 H); 1.79–1.86 (*m*, 2 H); 2.29 (*dt*, *J* = 14.4, 3.3, 1 H); 2.33 (*dd*, *J* = 16.8, 1.8, 1 H); 2.54 (*dt*, *J* = 11.2, 4.2, 1 H); 2.58–2.68 (*m*, 1 H); 2.78 (*d*, *J* = 17.1, 1 H); 2.78–2.92 (*m*, 1 H); 3.01–3.11 (*m*, 2 H); 7.22–7.30 (*m*, 2 H); 7.37–7.40 (*m*, 1 H); 8.29–8.32 (*m*, 1 H). ^{13}C-NMR: 7.36 (*q*); 20.66 (*t*); 20.95 (*t*); 21.25 (*t*); 31.51 (*t*); 39.42 (*s*), 44.09 (*t*), 52.30 (*t*), 55.22 (*t*), 65.71 (*d*), 112.95 (*s*), 116.12 (*d*), 118.20 (*d*), 123.86 (*d*), 124.22 (*d*), 129.69 (*s*), 133.60 (*s*), 135.00 (*s*), 167.34 (*s*). EI-MS: 294 (64.6, M^+), 293 (100), 265 (12.94), 237 (32.96). HR-MS: 294.1729 ($C_{19}H_{22}N_2O^+$; calc. 294.17336).

rac-*(14β,16α)-14,15-Dihydroeburnamenine-14,21-diol*[1]) (**11a**). To a soln. of **8a** (0.12 g, 0.39 mmol) in EtOH (5 ml) was added at r.t. $NaBH_4$ (0.10 g, 2.64 mmol) in portions during 5 min. The resulting mixture was stirred for 1 h. Then H_2O/CH_2Cl_2 1:5 (30 ml) was added, the org. layer washed with H_2O and brine, dried, and evaporated, and the residue subjected to CC (MeOH/CH_2Cl_2 5:95): **11a** (0.10 g, 82%). White solid. R_f 0.15 (MeOH/CH_2Cl_2 5:95). M.p. 100–102° ([3b]: 102–103°). IR: 2809, 2852, 2928 (CH), 3303 (OH). ^{1}H-NMR: 0.96–1.04 (*m*, 1 H); 1.12–1.24 (*m*, 1 H); 1.41–1.60 (*m*, 3 H); 1.74 (*d*, *J* = 13.5, 1 H); 1.85–2.04 (*m*, 1 H); 2.15–2.27 (*m*, 2 H); 2.44 (*dt*, *J* = 11.1, 4.2, 1 H); 2.63 (*dd*, *J* = 14.4, 2.4, 1 H); 2.81 (*s*, 1 H); 2.81–3.00 (*m*, 3 H); 3.22–3.30 (*m*, 1 H); 3.52–3.60 (*m*, 1 H); 5.58 (*dd*, *J* = 9.0, 5.7, 1 H); 7.08–7.15 (*m*, 2 H); 7.40–7.43 (*m*, 1 H); 7.55–7.58 (*m*, 1 H). ^{13}C-NMR: 21.06 (*t*); 21.97 (*t*); 33.29 (*t*); 33.55 (*t*); 38.26 (*s*); 47.03 (*t*); 52.29 (*t*); 55.22 (*t*); 58.41 (*t*); 66.08 (*d*); 76.84(*d*); 106.31 (*s*); 111.54 (*d*); 118.30 (*d*); 120.23 (*d*); 121.40 (*d*); 128.32 (*s*); 133.05 (*s*); 137.59 (*s*). EI-MS: 312 (80, M^+), 311 (100), 310 (30), 294 (44), 293 (67), 267 (34), 249 (21), 237 (14). HR-MS: 312.1840 ($C_{19}H_{24}N_2O_2^+$; calc. 312.1839).

rac-*(14α,16α)-14,15-Dihydroeburnamenin-14,21-diol*[1]) (**11b**). As described for **11a**, with **13** (70 mg, 0.23 mmol), EtOH (5 ml), and $NaBH_4$ (70 mg, 2.59 mmol): **11b** (60 mg, 83%). White solid. R_f 0.33 (5% MeOH/CH_2Cl_2). M.p. 168–170° ([3b]: 172–174°). IR: 2803, 2852, 2935 (CH), 3292 (OH). ^{1}H-NMR: 1.08–1.16 (*m*, 1 H); 1.44–1.58 (*m*, 2 H); 1.78–1.89 (*m*, 3 H); 2.07 (*d*, *J* = 16.5, 1 H); 2.20 (*dt*, *J* = 16.5, 3.3, 1 H); 2.35 (*d*, *J* = 15, 1 H); 2.43 (*dt*, *J* = 11.1, 4.5, 1 H); 2.67 (*dd*, *J* = 15, 4.2, 1 H); 2.77 (*s*, 1 H); 2.86–2.92 (*m*, 1 H); 2.99–3.08 (*m*, 2 H); 3.60–3.70 (*m*, 2 H); 5.84 (*d*, *J* = 5.1, 1 H); 7.05–7.15 (*m*, 2 H); 7.45 (*dd*, *J* = 10.5, 7.5, 2 H). ^{13}C-NMR: 21.10 (*t*); 29.84 (*t*); 32.25 (*t*); 33.96 (*s*); 41.59 (*t*); 53.30 (*t*); 55.76 (*t*); 58.43 (*t*); 67.74 (*d*); 74.61 (*d*); 105.10 (*s*); 111.10 (*d*); 118.04 (*d*); 119.56 (*d*); 120.80 (*d*); 128.16 (*s*); 131.25 (*s*); 135.73 (*s*). EI-MS: 312 (18, M^+), 311 (33), 310 (22), 294 (29), 293 (100), 265 (8), 249 (7). HR-MS: 312.1836 ($C_{19}H_{24}N_2O_2^+$; calc. 312.1839).

*[(1*RS*,12b*RS*)-1-Ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine-1-ethanol* (**12**). According to a modified literature procedure [3b], a mixture **11a**/**11b** (60 mg, 0.19 mmol), KOH (30 mg, 0.52 mmol), and hydrazine hydrate (0.32 ml, 6.6 mmol) in ethylene glycol (1.0 ml) was heated at 130° for 2 h and then refluxed for 8 h. After cooling to r.t., the mixture was diluted with H_2O, and extracted with CH_2Cl_2, the org. soln. washed with H_2O and, brine, dried, and evaporated, and the residue subjected to CC (MeOH/CH_2Cl_2 5:95) **12** (30 mg, 53%). M.p. 168–170° ([3b]: 173–174°). IR: 2758, 2808, 2852, 2929 (CH), 3317, 3480 (NH, OH). ^{1}H-NMR: 1.08 (*t*, *J* = 7.5, 3 H); 1.29 (*td*, *J* = 14.7, 3.3, 1 H); 1.55–1.82 (*m*, 6 H); 2.00–2.12 (*m*, 1 H); 2.41; (*dt*, *J* = 12.0, 3.0, 1 H);

2.60–2.70 (*m*, 1 H); 2.66 (*d*, *J* = 12.6, 1 H); 2.94–3.08 (*m*, 3 H); 3.32 (*s*, 1 H); 3.41 (*td*, *J* = 11.7, 4.5, 1 H); 3.73 (*dt*, *J* = 11.7, 3.0, 1 H); 7.04–7.15 (*m*, 2 H); 7.29 (*d*, *J* = 7.5, 1 H); 7.45 (*d*, *J* = 7.5, 1 H); 7.89 (*s*, 1 H). ^{13}C-NMR: 8.43 (*q*); 21.27 (*t*); 22.91 (*t*); 32.22 (*t*); 35.46 (*t*); 38.58 (*t*); 40.73 (*s*); 53.94 (*t*); 58.56 (*t*); 67.10 (*d*); 110.61 (*d*); 111.71 (*d*); 118.06 (*d*); 119.33 (*d*); 121.62 (*d*); 126.61 (*s*); 132.19 (*s*); 136.04 (*s*). EI-MS: 299 (8.09), 298 (100, M^+), 297 (48.42), 283 (6.25), 267 (19.47), 253 (10.13), 237 (8.62). HR-MS: 298.2048 ($C_{19}H_{26}N_2O^+$; calc. 298.20468).

Eburnamine[1]) (= rac-*(14β)-14,15-Dihydroeburnamenin-14-el*[1]); **2**) *and Isoeburnamine* (= rac-*(14α)-14,15-Dihydroeburnamenin-14-ol*[1]); **3**). A mixture of **12** (40 mg, 0.13 mmol), $RuCl_3 \cdot xH_2O$ (5 mg, 0.02 mmol), and $NaIO_4$ (80 mg, 0.37 mmol) in CH_2Cl_2 (1.0 ml), MeCN (1.0 ml), and H_2O (1.5 ml) was stirred at 0° for 6 h. The mixture was diluted with CH_2Cl_2 (15 ml), the org. phase washed with H_2O and brine, dried, and evaporated, and the residue subjected to CC (1 → 5% MeOH/CH_2Cl_2 containing 0.25% Et_3N): **2** [12] (10 mg, 26%) and **3** [12] (10 mg, 26%).

Data of **2**: IR: 2933 (CH), 3346 (OH). ^{1}H-NMR: 0.80–0.94 (*m*, 4 H); 1.23 – 1.70 (*m*, 5 H); 1.95–2.06 (*m*, 1 H); 2.26–2.39 (*m*, 2 H); 2.45–2.67 (*m*, 2 H); 2.88–3.10 (*m*, 2 H); 3.15–3.25 (*m*, 2 H); 3.76 (*s*, 1 H); 5.53 (*m*, 1 H); 7.06–7.19 (*m*, 2 H); 7.43 (*d*, *J* = 6.9, 1 H); 7.72 (*d*, *J* = 6.9, 1 H). ^{13}C-NMR: 7.5 (*q*); 16.7 (*t*); 20.4 (*t*); 25.0 (*t*); 28.5 (*t*); 36.8 (*s*); 43.4 (*t*); 44.3 (*t*); 50.8 (*t*); 58.7 (*d*); 76.7 (*d*); 105.5 (*s*); 112.2 (*d*); 118.0 (*d*); 120.0 (*d*); 121.2 (*d*); 128.6 (*s*); 132.6 (*s*); 136.6 (*s*). EI-MS: 296 (40, M^+), 295 (31), 278 (25), 249 (90), 208 (100). HR-MS: 296.1886 ($C_{19}H_{24}N_2O^+$; calc. 296.1890).

Data of **3**: IR: 2929 (CH), 3310 (OH). ^{1}H-NMR: 0.91 (*t*, *J* = 7.5, 3 H); 1.40–1.83 (*m*, 5 H); 1.99 (*d*, *J* = 7.8, 1 H); 2.17–2.25 (*m*, 2 H); 2.57–2.75 (*m*, 3 H); 2.98–3.03 (*m*, 1 H); 3.25–3.38 (*m*, 2 H); 3.91 (*s*, 1 H); 6.06 (*s*, 1 H); 7.13–7.23 (*m*, 2 H); 7.43 (*d*, *J* = 7.8, 1 H); 7.48 (*d*, *J* = 7.8, 1 H). ^{13}C-NMR: 7.5 (*q*); 16.5 (*t*); 20.2 (*t*); 25.8 (*t*); 29.0 (*t*); 34.8 (*s*); 39.7 (*t*); 44.8 (*t*); 51.4 (*t*); 59.5 (*d*); 74.3 (*d*); 105.2 (*s*); 110.1 (*d*); 118.5 (*d*); 120.4 (*d*); 121.7 (*d*); 128.4 (*s*); 129.3 (*s*); 135.0 (*s*). EI-MS: 296 (81, M^+), 295 (100), 278 (20), 267 (38), 249 (50), 208 (36). HR-MS: 296.1888 ($C_{19}H_{24}N_2O^+$; calc. 296.1890).

Eburnamonine[1]) (rac-*Eburnamenin-14(15*H*)-one*; **1**). A mixture of **2**/**3** (35 mg, 0.12 mmol) in anh. CH_2Cl_2 (4 ml) and PDC (60 mg, 0.16 mmol) was stirred at r.t. for 3 h. Then the mixture was diluted with AcOEt (20 ml) and passed through a short column of *Celite*. The filtrate was evaporated, and the residue subjected to CC (AcOEt/hexane 1:1): **1** (15 mg, 42%). White solid. R_f 0.40 (AcOEt/hexane 1:1). M.p. 195–197° ([5]: 199.5–200.5°). IR: 1703 (C=O), 2855, 2931 (CH). ^{1}H-NMR: 0.91 (*t*, *J* = 7.5, 3 H); 1.01 (*dt*, *J* = 13.8, 3.9, 1 H); 1.39–1.49 (*m*, 1 H); 1.58–1.80 (*m*, 3 H); 2.02 (*m*, 1 H); 2.35–2.71 (*m*, 5 H); 2.80–3.00 (*m*, 1 H); 3.18–3.35 (*m*, 2 H); 3.96 (*s*, 1 H); 7.24–7.32 (*m*, 2 H); 7.40–7.43 (*m*, 1 H); 8.33–8.36 (*m*, 1 H). ^{13}C-NMR: 7.63 (*q*); 16.52 (*t*); 20.59 (*t*); 26.91 (*t*); 28.32 (*t*); 38.43 (*s*); 44.29 (*t*); 44.33 (*t*); 50.62 (*t*); 57.67 (*d*); 112.59 (*s*); 116.23 (*d*); 118.07 (*d*); 123.82 (*d*); 124.31 (*d*); 130.07 (*s*); 131.95 (*s*); 134.18 (*s*); 167.64 (*s*). EI-MS: 294 (100, M^+), 293 (63.87), 278 (2.78), 265 (57.42), 237 (67.10), 224 (20.81). HR-MS: 294.1722 ($C_{19}H_{22}N_2O^+$; calc. 294.17336).

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Received May 16, 2005