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# A Novel Stereoselective Synthesis of *cis*-Configured Erythrinane and Erythrinane Type Analogues

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**Summary.** *N*-Alkylation of certain angularly substituted heterocycles by $C_2$- and $C_3$-units provided appropriate precursors to construct stereoselectively the erythrinanone and several erythrinanone type analogues by intramolecular *Friedel-Crafts* acylation. The resulting aromatic ketones were catalytically reduced affording the corresponding parent frameworks including the hitherto unknown tetracyclus A-norschelhammerane. On the other hand, the stereoselective reduction of the carbonyl moiety offered a convenient approach to 11-hydroxylated erythrinanes with the natural occurring $\beta$-configuration. The structures and the stereochemistry of the target compounds were proved by NMR spectroscopy.

**Keywords.** Alkaloids; Spiro compounds; Diastereoselective cyclizations; Erythrinane type frameworks; 11$\beta$-Hydroxy-15-methoxyerythrinane.

## Introduction

Over recent years much work has been devoted to the total synthesis of *Erythrina* alkaloids and their homologues called C-homoerythrinanes or schelhammeranes [1], a group of natural products possessing the unique tetracyclic spiroamine framework and exhibiting a variety of interesting pharmacological activities, *e.g.*, curare-like, sedative, hypotensive, or CNS depressant properties. Furthermore the alkaloidal extracts have been used in indigenous medicine (overviews and further Refs. cited therein see Refs. [2–6], Fig. 1).

The numerous synthetic approaches to the aromatic *Erythrina* alkaloids hitherto reported are based on three strategies according to the number of the alicyclic rings (A–C, Fig. 1), namely in the sense which of them is formed in

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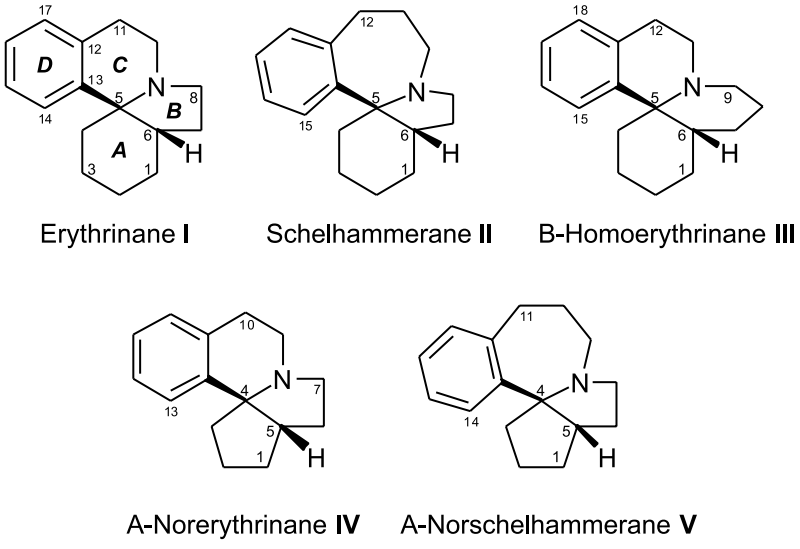
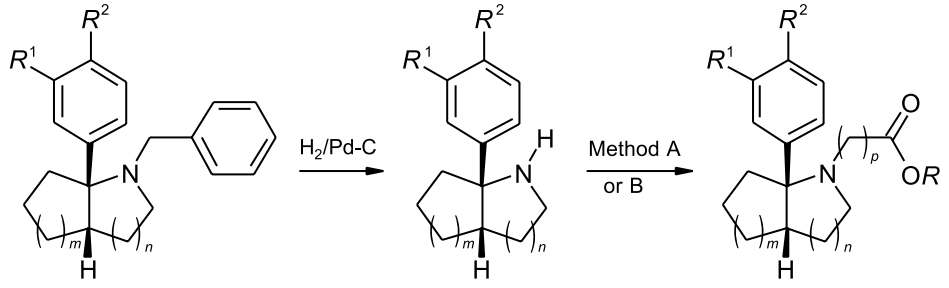



**Fig. 1.** *cis*-Erythrinane and structural related analogues

the last step [4, 5]. Thus in early syntheses the erythrina core mostly has been completed by C ring formation connecting the carbon atoms C-5 and C-13. In contrast, the final generation of the C-ring by connecting the atoms C-11 and C-12 has been achieved only in one case using a *Pummerer*-type cyclization [4]. Following this strategy, the angularly aryl substituted heterocycles **1** previously prepared [7] appeared to be attractive building blocks to construct the erythrinane type framework **I** and related tetracyclic ring systems **II**–**V** by an alternative intramolecular cyclization. Herein we would like to present the results concerning these investigations.

## Results and Discussion

We envisioned a synthetic route as outlined in Schemes 1 and 2. First the educts **1** were catalytically debenzylated affording the secondary amines **2** in 91 to 99% yields. The deprotection caused a marked downfield shift ($\Delta^{13C}\delta \sim 13$ ppm) of the signal originating from the $CH_2$-group which is attached to the quaternary bridgehead carbon atom (Experimental). The compounds **2** in turn were realkylated with a $C_2$- or $C_3$-unit, *e.g.* with bromoacetic ester or methyl acrylat (method A or B, Experimental), providing the desired unknown precursors **3** in excellent yields. These esters were found to be sensitive to air and light and therefore should be stored under nitrogen in the refrigerator. With compounds **3** in hand, the intramolecular acylation of the aromatic unit was investigated which was expected to provide the aromatic ketones of type **4**. Naturally occurring compounds of this structural type are reported [8]. Specific total syntheses of 11-oxoerythrinanes or corresponding homologues are lacking to our knowledge. Merely one synthetic compound isolated as an by-product in very low yield had been described until now [9].



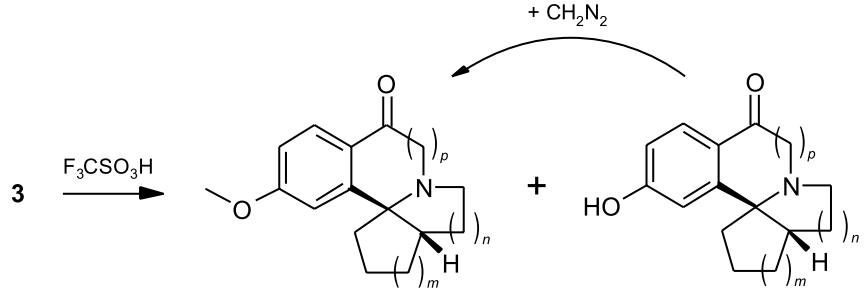

**1** **2** **3**

| 1,2 | *m* | *n* | $R^1$ | $R^2$ | **2**: yield/% |
|---|---|---|---|---|---|
| **a** | 2 | 1 | H | H | 99 |
| **b** | 2 | 1 | O*Me* | H | 98 |
| **c** | 2 | 1 | O*Me* | O*Me* | 91 |
| **d** | 2 | 1 | O-$CH_2$-O | | 92 |
| **e** | 2 | 2 | O*Me* | H | 95* |
| **f** | 1 | 1 | O*Me* | H | 94 |

* see Ref. [7]

| **3** | *m* | *n* | *p* | $R^1$ | $R^2$ | *R* | yield/% |
|---|---|---|---|---|---|---|---|
| **a** | 2 | 1 | 1 | H | H | *Et* | 95 |
| **b** | 2 | 1 | 1 | H | H | *Me* | 90 |
| **c** | 2 | 1 | 1 | O*Me* | H | *Et* | 90 |
| **d** | 2 | 1 | 1 | O*Me* | O*Me* | *Et* | 90 |
| **e** | 2 | 1 | 1 | O-$CH_2$-O | | *Et* | 91 |
| **f** | 2 | 1 | 2 | O*Me* | H | *Me* | 92 |
| **g** | 2 | 2 | 1 | O*Me* | H | *Et* | 93 |
| **h** | 2 | 2 | 2 | O*Me* | H | *Me* | 88 |
| **i** | 1 | 1 | 1 | O*Me* | H | *Et* | 95 |
| **k** | 1 | 1 | 2 | O*Me* | H | *Me* | 82 |

**Scheme 1**




**4** **5**

| **4, 5** | *m* | *n* | *p* | | yield/% | |
|---|---|---|---|---|---|---|
| | | | | Σ **4** | **4** | **5** |
| **a** | 2 | 1 | 1 | 43 | 23 | 17 |
| **b** | 2 | 1 | 2 | 49 | 25 | 20 |
| **c** | 2 | 2 | 1 | 20 | - | - |
| **d** | 1 | 1 | 1 | 66 | 31 | 20 |
| **e** | 1 | 1 | 2 | 35 | 25 | 14 |

**Scheme 2**

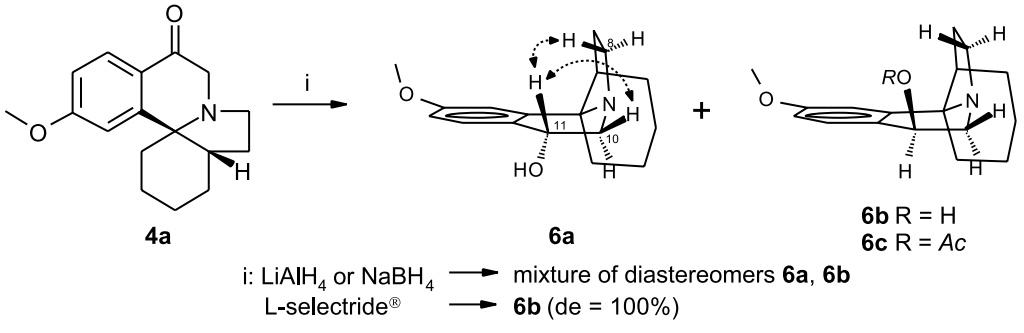
Thus treatment of **3c**, **3f**, **3g**, **3i**, and **3k** with trifluoromethane sulfonic acid effected the intended cyclizations as well as a partial cleavage of the phenol ether group yielding a mixture of the tetracyclic compounds **4a**–**4e** and **5a**–**5e**, which could be easily separated by flash chromatography. For a more convenient working up the reaction mixture was treated with diazomethane thus affording the aromatic

methoxyketones **4** in low to moderate total yields (Scheme 2 and Experimental). On the other hand, attempted cyclization of **3a** and **3b** lacking an activating para substituent in the aromatic unit failed. The same was true for the educts **3d** and **3e** although possessing a dihydroxylated aromatic moiety, as well as for **3h** which defied all our attemps to cyclize to the corresponding schelhammerane. The structures of the products **4** and **5** were confirmed by NMR spectroscopy and their *cis* configurations were deduced from the parent compounds **7** (see below).

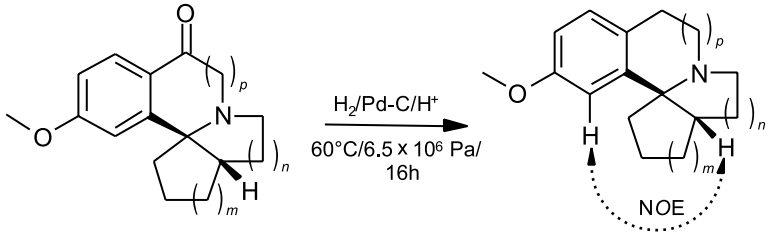
In this connection we were interested in 11-hydroxylated erythrinanes occurring in *Erythrina* species mostly as hydroxy-, methoxy-, and acetoxy-derivatives [10–12]. Surprisingly only three investigations have been devoted as yet to the total synthesis of this type of alkaloids using the *Pummerer* like reaction mentioned above to complete the C-ring or the *CAN* oxidation of the C-11 methylene group [4, 9, 13]. The yields were moderate and the products obtained were mixtures of hydroxy-, carbonyl-, and D-ring degraded compounds. Therefore it appeared worthwhile to prepare 11-hydroxylated erythrinanes, *e.g.* **6** by reduction of the corresponding ketone **4a**. Treatment with lithium aluminum hydride or sodium borohydride afforded a 1:1-mixture of the expected diastereomeric alcohols **6a** and **6b**, which could be separated be flash chromatography. In contrast to the acetyl derivative **6c** the preparation of the corresponding 11-methoxy derivative failed.

The stereochemistry in position 11 as well as that of the A/B-ring fusion was determined by N*O*E measurements. Thus, in the alcohol **6a** the 11-H proton gave a N*O*E to $\beta$-10-H and $\beta$-8-H. Although the latter was obscured by the $\alpha$-10-H exhibiting a multiplett at $\delta = 2.9$ ppm, irradiation of 11-H gave a double triplett of only one proton at the $\delta$-value concerned, which exclusively had to be assigned to the $\beta$-8-H. On the other hand the 11-H of the product **6b** gave no N*O*E to the 8-H-protons. Consequently, compound **6a** represented the $\alpha$-11-hydroxy- and **6b** the $\beta$-11-hydroxy diastereomer. The latter also could be obtained in quantitative yield by reduction of **4a** with L-selectride®. The NMR spectra showed only one set of signals indicating the diastereoselective formation of **6b**. This route to 11-hydroxyerythrinanes may be an interesting alternative to those mentioned above, since many of the natural alkaloids of this structural type possess 11-$\beta$-OH configuration [9–12, 14].

The configuration of the A/B-ring of the compounds **6** was easily deduced by a positve N*O*E between the angularly 6-H and the aromatic 14-H proton indicating the *cis* fusion of the rings concerned. This also implied, that the cyclization of the




**Scheme 3**




**4** **7**

| **4, 7** | *m* | *n* | *p* | **7**: yield/% |
|---|---|---|---|---|
| **a** | 2 | 1 | 1 | 77 |
| **b** | 2 | 1 | 2 | 75 |
| **c** | 2 | 2 | 1 | 68 |
| **d** | 1 | 1 | 1 | 73 |
| **e** | 1 | 1 | 2 | 77 |

**Scheme 4**

*cis* configured educt **3a** to the tetracyclic ketone **4a** (see above) had occurred with retention of the configuration and therefore the A/B-rings in **4a** were *cis* fused, too. Even the same should be true for the 11-deoxygenated target compound **7a**, since an inversion of the A/B configuration was not to be expected under the reaction conditions used (see below).

In the last step the carbonyl group of **4** was catalytically removed to obtain the methoxylated parent ring systems of erythrinane **7a**, C-homoerythrinane **7b** (= schelhammerane), B-homoerythrinane **7c**, A-norerythrinane **7d**, and the hitherto unknown cyclopenta[b]pyrrolo[2]benzazepine **7e**, which we have called A-norschelhammerane in direct analogy to the erythrina serie (Scheme 4 and Fig. 1, **I–V**). It should be mentioned, that naturally occurring examples of **7c** and **7d** or corresponding derivatives of them have not been found hitherto.

The *cis*-configuration of the compounds **7** was proved by NMR spectroscopy and also deduced by comparison with those of the precursors **2**. Thus the $^{1H}\delta$ values of the 15-methoxyerythrinane (**7a**), especially that of 14-H being an appropriate distinctive mark for the A/B-ring fusion [15], were completely in line with those reported [16]. This was confirmed by the positive N*O*E between 6-H and 14-H. Applying the same reasoning the *cis* configurations of the schelhammerane **7b**, of the A-norerythrinane **7d**, and of the A-norschelhammerane **7e** were assigned. An unseparable multiplett caused by the 2-H protons blocked the definite evaluation of the N*O*E between 6-H and 15-H in the B-homoerythrinane **7c**; thus the assignment was achieved starting from the defined *cis* configuration of the educt **1e** [7] and assuming that the consecutive sequence **1e** → **2g** → **4c** → **7c** occurred with retention of the configuration as proved above. Moreover MMX force field calculations [17] generally revealed the *cis*-configured stereoisomers **7** to be markedly more stable than the *trans* stereoisomers.

In conclusion, we have developed a general strategy for the construction of the aromatic erythrinane skeleton and structural related ring systems *via* intramolecular acylation. Additionally, in comparison with the methods mentioned above [4, 9, 13] the route offers a more convenient, stereoselective approach to

derivatives like **6** hydroxylated at the benzyl position. Further investigations in the synthesis of the title compounds are currently in progress in our laboratories.

## Experimental

Melting points are measured with a Reichert hot-stage microscope and are uncorrected. IR: Perkin Elmer FT-IR Paragon 1000 and Jasco FT-IR 410. NMR: Jeol GSX 400 and Jeol GSX 500 ($^1$H: 400 and 500 MHz, $^{13}$C: 100 and 125 MHz, $CDCl_3$, *TMS* as internal reference); MS (70 eV): Hewlett Packard MS-Engine. Elemental analyses: Heraeus CHN-Rapid and Elementar Vario EL; the results are in good agreement with the calculated values. Thin layer chromatography (TLC): aluminum sheets Kieselgel 60 $F_{254}$ (Merck) and aluminum sheets Aluminiumoxid $F_{254}$ (Fluka), each thickness of layer 0.2 mm. Flash chromatography (FC): ICN-Sili Tech 32–63, 60 A and Aluminiumoxid Typ 507 C neutral 0.05–0.15 mm. *cis*-8a-(3-Methoxyphenyl)decahydroquinoline (**2e**) was already reported [7].

*Catalytic Debenzylation of Compounds **1**, General Procedure According to Ref. [7]*

*cis-7a-Phenyloctahydroindole* (**2a**, $C_{14}H_{19}N$)

**1a** 770 mg (2.65 mmol), 2 *N* HCl 1.3 cm$^3$ (2.6 mmol), Pd-C 105 mg, MeOH 10 cm$^3$; yield 528 mg (99%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:5:0.5): $R_f$ = 0.27; MS (EI): $m/z$ (%) = 201 ($M^{+\bullet}$, 20), 158 (100), 120 (42); $^1$H NMR ($CDCl_3$): $\delta$ = 7.47 (dt, $J$ = 8.3, 1.4 Hz, 2arom H), 7.28–7.22 (m, 2arom H), 7.13 (tt, $J$ = 7.3, 1.4 Hz, 1arom H), 3.04 and 2.84 (2ddd, $J$ = 11.3, 8.9, 7.3 and 11.3, 10.0, 3.9 Hz, each 1H), 2.29–2.23 (m, 1H), 2.21 (br s, NH), 1.81–1.69, 1.69–1.58, 1.57–1.47, and 1.47–1.19 (4m, 2, 2, 1, and 5H) ppm; $^{13}$C NMR ($CDCl_3$): $\delta$ = 148.67, 128.15 (2C), 126.16, 125.99 (2C), 66.67, 42.95, 42.76, 36.25, 31.99, 28.50, 24.26, 22.36 ppm.

*cis-7a-(3-Methoxyphenyl)octahydroindole* (**2b**, $C_{15}H_{21}NO$)

**1b** 780 mg (2.43 mmol), 2 *N* HCl 1.2 cm$^3$ (2.4 mmol), Pd-C 100 mg, MeOH 10 cm$^3$; yield 552 mg (98%); TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:5:0.5): $R_f$ = 0.23; MS (EI): $m/z$ (%) = 231 ($M^{+\bullet}$, 26), 202 (100); $^1$H NMR ($CDCl_3$): $\delta$ = 7.23 (br t, $J$ = 7.9 Hz, 1arom H), 7.15 (dd, $J$ = 2.5, 1.7 Hz, 1arom H), 7.10 and 6.74 (2ddd, $J$ = 7.9, 1.7, 0.9 and 7.9, 2.5, 0.9 Hz, each 1arom H), 3.82 (s, $OCH_3$), 3.10 and 2.91 (2ddd, $J$ = 11.2, 8.9, 7.4 and 11.2, 10.1, 3.9, each 1H), 2.33–2.27 (m, 1H), 2.0 (s, NH), 1.86–1.74, 1.74–1.63, 1.63–1.54, and 1.54–1.20 (4m, 2, 2, 1, and 5H) ppm; $^{13}$C NMR ($CDCl_3$): $\delta$ = 159.53, 150.66, 128.91, 118.29, 112.13, 111.12, 66.70, 55.20, 42.94, 42.80, 36.21, 31.04, 28.55, 24.30, 22.34 ppm.

*cis-7a-(3,4-Dimethoxyphenyl)octahydroindole* (**2c**, $C_{16}H_{23}NO_2$)

**1c** 696 mg (1.98 mmol), 2 *N* HCl 1.0 cm$^3$ (2 mmol), Pd-C 91 mg, MeOH 10 cm$^3$; yield 471 mg (91%); TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:8:0.5): $R_f$ = 0.33; MS (EI): $m/z$ (%) = 261 ($M^{+\bullet}$, 18), 218 (100); $^1$H NMR: $\delta$ = 7.15 (d, $J$ = 2.1 Hz, 1arom H), 7.03 (dd, $J$ = 8.3, 2.1 Hz, 1arom H), 6.82 (d, $J$ = 8.3 Hz, 1arom H), 3.91 and 3.87 (2s, 2$OCH_3$), 3.10 and 2.91 (2ddd, $J$ = 11.3, 10.2, 7.1 and 11.3, 10.2, 4.3, each 1H), 2.34–2.27 (m, 1H), 2.21 (br s, NH), 1.86–1.75, 1.75–1.58, and 1.56–1.29 (3m, 2, 3, and 5H) ppm; $^{13}$C NMR: $\delta$ = 148.52, 147.23, 141.01, 117.74, 110.66, 109.79, 66.33, 55.84, 55.78, 42.92, 42.73, 36.08, 30.94, 28.31, 23.96, 22.36 ppm.

*cis-7a-(3,4-Methylenedioxyphenyl)octahydroindole* (**2d**, $C_{15}H_{19}NO_2$)

**1d** 724 mg (2.16 mmol), 2 *N* HCl 1.1 cm$^3$ (2.2 mmol), Pd-C 94 mg, MeOH 10 cm$^3$; yield 487 mg (92%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:7:0.5): $R_f$ = 0.34; MS (EI): $m/z$

(%) = 245 ($M^{+\bullet}$, 20), 202 (100); $^1$H NMR: $\delta = 7.07$ (d, $J = 1.7$ Hz, 1H), 7.00 and 6.75 (2dd, $J = 8.2$, 1.7 and 8.2, 0.4 Hz, each 1H), 5.93 and 5.92 (2d, each $J = 1.6$ Hz, O–$CH_2$–O), 3.08 and 2.88 (2ddd, $J = 11.2$, 8.9, 7.4 and 11.2, 10.1, 3.8 Hz, each 1H), 2.27–2.21 (m, 1H), 2.00 (br s, NH), 1.80 (dt, $J = 14.3$, 3.8 Hz, 1H), 1.75–1.55, 1.54–1.42, and 1.42–1.21 (3m, 4, 2, and 3H) ppm; $^{13}$C NMR: $\delta = 147.43$, 145.62, 142.81, 118.79, 107.66, 106.90, 100.79, 66.60, 42.95, 42.86, 36.32, 30.97, 28.46, 24.21, 22.39 ppm.

*cis-6a-(3-Methoxyphenyl)octahydrocyclopenta[b]pyrrole* (**2f**, $C_{14}H_{19}NO$)

**1f** 890 mg (2.90 mmol), 2 *N* HCl 1.45 $cm^3$ (2.90 mmol), Pd-C 100 mg, MeOH 13 $cm^3$; yield 592 mg (94%); TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:4:0.5): $R_f = 0.26$; MS (EI): $m/z$ (%) = 217 ($M^{+\bullet}$, 22), 188 (100), 174 (32); $^1$H NMR: $\delta = 7.23$ and 7.09 (2m, each 1H), 7.04 and 6.73 (2ddd, $J = 7.7$, 1.7, 0.9 and 8.0, 2.6, 0.9 Hz, each 1H), 3.81 (s, $OCH_3$), 3.03 and 2.75 (2br ddd, $J = 11.1$, 6.8, 4.7 and 11.1, 7.9, 6.5 Hz, each 1H), 2.69 (dt, $J = 8.6$, 5.5, 3.2 Hz, 1H), 2.11–2.02 (dddd, $J = 12.4$, 8.6, 6.5, 4.7 Hz, 1H), 2.03–1.96, 1.95–1.89, and 1.88–1.68 (3m, 1, 2, and 3H), 1.58 (ddt, $J = 12.5$, 6.3, 3.2 Hz, 1H), 1.50–1.43 (dddd, $J = 12.4$, 7.9, 6.8, 5.5 Hz, 1H) ppm; $^{13}$C NMR: $\delta = 159.57$, 151.55, 129.10, 118.01, 111.74, 110.85, 76.61, 55.19, 51.13, 46.88, 44.05, 36.32, 34.64, 25.47 ppm.

*Realkylated Amines* **3**, *General Procedure*

*Method A*: A mixture of the amine **2** (1 mol equiv), $Na_2CO_3$ (2 equiv), and bromoacetic acid ester (1.3 equiv) in $CHCl_3$ was stirred for 16 h at 50°C. After evaporating the solvent *in vacuo*, the residue was dissolved in 15 $cm^3$ of 1 *N* HCl and washed with *Et*$_2$O (3×10 $cm^3$). The aqueous layer was rendered alkaline with 32% NaOH and extracted with *Et*$_2$O (3×15 $cm^3$). The combined organic phases were dried ($Na_2SO_4$) and evaporated *in vacuo*. The residue was purified by FC (eluents were the same as used for TLC).

*Method B*: A mixture of the amine **2** and acrylic acid methyl ester in $CHCl_3$ was stirred for 16 h at 50°C, diluted with 10 $cm^3$ of *Et*$_2$O, and extracted with 0.5 *N* HCl (3×10 $cm^3$). The combined aqueous layers were rendered alkaline with 32% NaOH and extracted with *Et*$_2$O (3×10 $cm^3$). Further workup was the same as given under method A.

*cis-(7a-Phenyloctahydroindol-1-yl)acetic acid ethyl ester* (**3a**, $C_{18}H_{25}NO_2$)

Method A: **2a** 420 mg (2.09 mmol), $Na_2CO_3$ 442 mg (4.18 mmol), $CHCl_3$ 5 $cm^3$, bromoacetic acid ethyl ester 454 mg (2.71 mmol); yield 571 mg (95%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:1): $R_f = 0.48$; IR (film): $\bar{\nu} = 1750$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 287 ($M^{+\bullet}$, 34), 258 (11), 244 (100), 214 (66); $^1$H NMR: $\delta = 7.50$–7.47 (m, 2arom H), 7.23 (m, 2arom H), 7.13 (tt, $J = 7.1$, 1.5 Hz, 1H), 3.98 (q, $J = 7.1$ Hz, 2H), 3.36 (dt, $J = 9.3$, 4.4 Hz, 3.05 and 2.93 (2d, each $J = 16.4$ Hz, each 1H), 2.63 (ddd, $J = 10.3$, 9.3, 5.8 Hz, 1H), 2.41 (m, 1H), 1.94–1.83, 1.81–1.71, 1.71–1.64, 1.52–1.31, and 1.29–1.17 (5m, 2, 1, 1, 5, and 1H), 1.12 (t, $J = 7.1$ Hz, $CH_3$) ppm; $^{13}$C NMR: $\delta = 171.83$, 145.06, 127.99 (2C), 127.86 (2C), 126.51, 66.96, 60.18, 50.51, 49.57, 46.18, 26.27, 25.57, 24.62, 23.47, 20.59, 14.16 ppm.

*cis-(7a-Phenyloctahydroindol-1-yl)acetic acid methyl ester* (**3b**, $C_{17}H_{23}NO_2$)

Method A: **2a** 330 mg (1.64 mmol), $Na_2CO_3$ 348 mg (3.28 mmol), $CHCl_3$ 4 $cm^3$, bromoacetic acid methyl ester 411 mg (2.13 mmol); yield 542 mg (90%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:1): $R_f = 0.39$; IR (film): $\bar{\nu} = 1754$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 273 ($M^{+\bullet}$, 29), 230 (100), 214 (30), 158 (13), 86 (45), 84 (69); $^1$H NMR: $\delta = 7.57$ (m, 2arom H), 7.31 and 7.21 (2tt, $J = 7.5$, 1.7 and 7.5, 1.4 Hz, 2 and 1arom H), 3.58 (s, $OCH_3$), 3.44 (dt, $J = 9.4$, 4.6 Hz, 1H), 3.14 and 3.02 (2d, each $J = 16.4$ Hz, $CH_2CO_2$), 2.74–2.66 and 2.56–2.49 (2m, each 1H), 2.02–1.92 (m, 2H), 1.91–1.80,

1.78–1.71, 1.59–1.28, and 1.35–1.25 (4m, 1, 1, 5, and 1H) ppm; $^{13}$C NMR: $\delta = 172.17$, 144.66, 128.01 (2C), 127.92 (2C), 126.62, 67.07, 51.40, 50.34, 49.66, 46.02, 26.20, 25.49, 24.44, 23.44, 20.51 ppm.

*cis-[7a-(3-Methoxyphenyl)octahydroindol-1-yl]acetic acid ethyl ester* (**3c**, $C_{19}H_{27}NO_3$)

Method A: **2b** 440 mg (1.90 mmol), $Na_2CO_3$ 403 mg (3.80 mmol), $CHCl_3$ 5 cm$^3$, bromoacetic acid ethyl ester 412 mg (2.47 mmol); yield 542 mg (90%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:1): $R_f = 0.44$; IR (film): $\bar{\nu} = 1748$ (CO) cm$^{-1}$; MS (EI): $m/z$ (%) = 317 ($M^{+\bullet}$, 55), 275 (38), 260 (13), 244 (100); $^1$H NMR: $\delta = 7.22$ (br t, $J = 7.9$ Hz, 1arom H), 7.17 (m, 1arom H), 7.14 and 6.76 (2ddd, $J = 7.9$, 1.7, 1.0 and 7.9, 2.5, 1.0, each 1H), 4.06 (q, $J = 7.1$ Hz, $OCH_2$), 3.81 (s, $OCH_3$), 3.42 (dt, $J = 9.5$, 4.3 Hz, 1H), 3.16 and 3.02 (2d, each $J = 16.5$ Hz, $CH_2CO_2$), 2.71 (dt, $J = 9.5$, 6.1 Hz, 1H), 2.49–2.42, 2.00–1.90, and 1.87–1.77 (3m, 1, 2, and 1H), 1.77–1.69, 1.59–1.39, and 1.39–1.28 (3m, 1, 5, and 1H), 1.20 (t, $J = 7.1$ Hz, C–$CH_3$) ppm; $^{13}$C NMR: $\delta = 171.89$, 159.45, 147.30, 128.65, 120.43, 113.96, 111.81, 67.07, 60.20, 55.21, 50.53, 49.50, 46.15, 26.31, 25.65, 25.05, 23.48, 20.65, 14.18 ppm.

*cis-[7a-(3,4-Dimethoxyphenyl)octahydroindol-1-yl]acetic acid ethyl ester* (**3d**, $C_{20}H_{29}NO_4$)

Method A: **2c** 420 mg (1.61 mmol), $Na_2CO_3$ 341 mg (3.22 mmol), $CHCl_3$ 5 cm$^3$, bromoacetic acid ethyl ester 350 mg (2.1 mmol); yield 508 mg (90%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:3): $R_f = 0.43$; IR (film): $\bar{\nu} = 1747$ (CO) cm$^{-1}$; MS (EI): $m/z$ (%) = 347 ($M^{+\bullet}$, 30), 274 (37), 304 (100), 210 (11); $^1$H NMR: $\delta = 7.25$ (d, $J = 2.1$ Hz, 1arom H), 7.05 (dd, $J = 8.4$, 2.1 Hz, 1arom H), 6.78 (d, $J = 8.4$ Hz, 1arom H), 4.06 (dq, $J = 7.1$, 0.4 Hz, $OCH_2$), 3.89 and 3.87 (2s, 2$OCH_3$), 3.43 (dt, $J = 9.2$, 4.4 Hz, 1H), 3.11 and 2.94 (each d, $J = 16.5$ Hz, $CH_2CO_2$), 2.67–2.58, 2.49–2.39, and 2.03–1.80 (3m, 1, 1, and 3H), 1.81–1.63, 1.58–1.41, and 1.37–1.23 (3m, 1, 5, and 1H), 1.19 (t, $J = 7.1$ Hz, C–$CH_3$) ppm; $^{13}$C NMR: $\delta = 148.75$, 147.71, 120.28, 111.47, 109.90, 66.66, 60.19, 55.91, 55.77, 50.40, 49.27, 46.12, 25.99, 25.37, 24.29, 23.73, 20.27, 14.16 (CO and $C_{aryl}$-1 were not found) ppm.

*cis-[7a-(3,4-Methylenedioxyphenyl)octahydroindol-1-yl]acetic acid ethyl ester* (**3e**, $C_{19}H_{25}NO_4$)

Method A: **2d** 252 mg (1.03 mmol), $Na_2CO_3$ 218 mg (2.06 mmol), $CHCl_3$ 3 cm$^3$, bromoacetic acid ethyl ester 412 mg (2.46 mmol); yield 310 mg (91%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:1): $R_f = 0.41$; IR (film): $\bar{\nu} = 1749$ (CO) cm$^{-1}$; MS (EI): $m/z$ (%) = 331 ($M^{+\bullet}$, 35), 288 (100), 258 (49); $^1$H NMR: $\delta = 7.13$ (d, $J = 1.9$ Hz, 1H), 6.99 (dd, $J = 8.1$, 1.9 Hz, 1H), 6.73 (d, $J = 8.1$ Hz, 1H), 5.94 and 5.92 (2d, each $J = 1.5$ Hz, $OCH_2O$), 4.07 (q, $J = 7.1$ Hz, $OCH_2$), 3.42 (dt, $J = 9.4$, 4.6 Hz, 1H), 3.13 and 2.95 (2d, each $J = 16.5$ Hz, $CH_2CO_2$), 2.63 (dt, $J = 9.9$, 5.7 Hz, 1H), 2.45–2.37, 2.00–1.77, and 1.77–1.68 (3m, 1, 3, and 1H), 1.55–1.40 and 1.36–1.20 (2m, 5 and 1H), 1.21 (t, $J = 7.1$ Hz, $CH_3$) ppm; $^{13}$C NMR: $\delta = 171.91$, 147.61, 146.06, 139.20, 121.20, 108.68, 107.15, 100.80, 66.76, 60.20, 50.44, 49.36, 46.25, 26.05, 25.43, 24.54, 23.54, 20.42, 14.18 ppm.

*cis-[7a-(3-Methoxyphenyl)octahydroindol-1-yl]propionic acid methyl ester* (**3f**, $C_{19}H_{27}NO_3$)

Method B: **2b** 376 mg (1.17 mmol), acrylic acid methyl ester 2 cm$^3$ (~22 mmol), $CHCl_3$ 3 cm$^3$; yield 341 mg (92%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:4): $R_f = 0.44$; IR (film): $\bar{\nu} = 1739$ (CO) cm$^{-1}$; MS (EI): $m/z$ (%) = 317 ($M^{+\bullet}$, 23), 274 (100), 244 (13), 210 (18); $^1$H NMR: $\delta = 7.21$ (br t, $J = 8.2$ Hz, 1arom H), 7.16–7.11 and 6.77–6.73 (2m, 2 and 1arom H), 3.81 (s, aryl–$OCH_3$), 3.55 (s, $OCH_3$), 3.29 (dt, $J = 8.9$, 4.5 Hz, 1H), 2.63–2.52, 2.49–2.37, and 2.36–2.21 (3m, each 2H), 2.02–1.79, 1.79–1.69, and 1.56–1.37 (3m, 3, 1, and 5H), 1.33–1.23 (m, 1H) ppm; $^{13}$C NMR: $\delta = 173.15$, 159.21, 147.26, 128.34, 120.55, 114.42, 111.13, 66.52, 55.11, 51.27, 48.81, 46.47, 44.33, 34.56, 25.81, 25.32, 23.52, 23.19, 20.24 ppm.

*cis-[8a-(3-Methoxyphenyl)octahydroquinolin-1-yl]acetic acid ethyl ester* (**3g**, $C_{20}H_{29}NO_3$)

Method A: **2e** 314 mg (1.28 mmol), $Na_2CO_3$ 271 mg (2.56 mmol), $CHCl_3$ 4 $cm^3$, bromoacetic acid methyl ester 277 mg (1.66 mmol); yield 394 mg (93%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:3): $R_f = 0.52$; IR (film): $\bar{\nu} = 1750$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 331 ($M^{+\bullet}$, 29), 288 (100), 258 (45), 224 (20), 202 (12); $^1$H NMR: $\delta = 7.25$–7.18 (m, 3arom H), 6.76 (br ddd, $J = 6.8$, 2.5, 2.5 Hz, 1arom H), 4.07–3.95 (m, $OCH_2$), 3.82 (s, $OCH_3$), 3.05 and 2.90 (2d, each $J = 16.2$ Hz, $CH_2CO_2$), 2.82–2.76, 2.65–2.58, 2.34–2.18, and 2.12–2.03 (4m, each 1H), 1.84–1.71 (m, 6H), 1.59–1.44 and 1.48–1.21 (2m, each 2H), 1.22–1.13 (m, 1H), 1.16 (t, $J = 7.1$ Hz, $CCH_3$) ppm; $^{13}$C NMR: $\delta = 172.32$, 159.47, 148.21, 128.54, 121.12, 114.93, 111.64, 62.86, 60.02, 55.19, 52.71, 47.65, 41.73, 28.61, 26.27, 25.36, 23.58, 22.69 (br), 20.39, 14.15 ppm.

*cis-[8a-(3-Methoxyphenyl)octahydroquinolin-1-yl]propionic acid methyl ester* (**3h**, $C_{20}H_{29}NO_3$)

Method B: **2e** 85 mg (0.35 mmol), acrylic acid methyl ester 0.5 $cm^3$ (~5.5 mmol), $CHCl_3$ 3 $cm^3$; yield 102 mg (88%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:3): $R_f = 0.45$; IR (film): $\bar{\nu} = 1738$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 331 ($M^{+\bullet}$, 23), 288 (100), 258 (10); $^1$H NMR: $\delta = 7.21$ (t, $J = 7.9$ Hz, 1arom H), 7.17–7.12 and 6.76–6.73 (2m, 2 and 1arom H), 3.81 (s, aryl–$CH_3$), 3.50 (s, $OCH_3$), 2.81–2.75 (m, 1H), 2.60 and 2.46 (2dt, $J = 8.2$, 2.6 and 11.5, 3.0, each 1H), 2.33–2.21, 2.21–1.98, and 1.93–1.64 (3m, 1, 3, and 7H), 1.56–1.40 and 1.35–1.21 (2m, each 2H), 1.11 (tt, $J = 13.1$, 3.9 Hz, 1H) ppm; $^{13}$C NMR: $\delta = 173.10$, 159.25, 148.43, 128.23, 121.28, 115.25, 110.00, 63.00, 55.15, 51.16, 46.19, 46.07, 41.95, 34.52, 28.62, 26.39, 25.96, 23.62, 20.67 (br), 20.24 ppm.

*cis-[6a-(3-Methoxyphenyl)hexahydrocyclopenta[b]pyrrol-1-yl]acetic acid ethyl ester* (**3i**, $C_{18}H_{25}NO_3$)

Method A: **2f** 460 mg (2.12 mmol), $Na_2CO_3$ 448 mg (4.24 mmol), $CHCl_3$ 5 $cm^3$, bromoacetic acid ethyl ester 462 mg (2.76 mmol); yield 610 mg (95%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:0.5): $R_f = 0.44$; IR (film): $\bar{\nu} = 1748$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 303 ($M^{+\bullet}$, 47), 274 (100), 260 (17), 246 (16), 230 (85), 202 (10), 186 (13), 121 (15); $^1$H NMR: $\delta = 7.21$ (t, $J = 8.0$ Hz, 1arom H), 7.16 (t, $J = 2.1$ Hz, 1arom H), 7.03 and 6.74 (2m, each 1arom H), 4.13 (d, $J = 7.1$ Hz, $OCH_2$), 3.81 (s, $OCH_3$), 3.13 and 3.05 (2d, each $J = 16.5$ Hz, $CH_2CO_2$), 3.12–3.07 (m, 1H), 2.84–2.77, 2.54–2.46, and 2.19–2.08 (3m, each 1H), 2.00–1.80 and 1.79–1.69 (2m, 4 and 1H), 1.50 (ddt, $J = 12.4$, 6.2, 3.1 Hz, 1H), 1.44–1.37 (m, 1H), 1.23 (dt, $J = 7.1$, 0.7 Hz, $CCH_3$) ppm; $^{13}$C NMR: $\delta = 171.92$, 159.51, 149.39, 128.87, 119.10, 112.75, 111.36, 77.84, 60.28, 55.15, 52.42, 51.57, 51.09, 34.50, 34.16, 31.44, 26.61, 14.21 ppm.

*cis-[6a-(3-Methoxyphenyl)hexahydrocyclopenta[b]pyrrol-1-yl]propionic acid methyl ester* (**3k**, $C_{19}H_{27}NO_3$)

Method B: **2f** 177 mg (0.81 mmol), acrylic acid methyl ester 2 $cm^3$ (~22 mmol), $CHCl_3$ 3 $cm^3$; yield 202 mg (82%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:1): $R_f = 0.33$; IR (film): $\bar{\nu} = 1739$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 303 ($M^{+\bullet}$, 24), 274 (100), 260 (13), 230 (12); $^1$H NMR: $\delta = 7.20$ (t, $J = 8.1$ Hz, 1arom H), 6.99 and 6.98–6.95 (2m, each 1arom H), 6.73 (ddd, $J = 8.1$, 2.6, 0.8 Hz, 1arom H), 3.80 (s, aryl–$OCH_3$), 3.61 (s, $OCH_3$), 2.88 (ddd, $J = 8.9$, 7.1, 4.4 Hz, 1H), 2.75–2.65 (m, 2H), 2.49 (ddt, $J = 8.9$, 5.4, 3.6 Hz, 1H), 2.41–2.31 (m, 3H), 2.11 (ddt, $J = 12.5$, 8.9, 7.5 Hz, 1H), 1.99–1.84 (m, 3H), 1.78, 1.65, 1.50–1.42, and 1.37–1.29 (4m, each 1H) ppm; $^{13}$C NMR: $\delta = 173.21$, 159.28, 149.30, 128.59, 119.29, 113.27, 110.71, 77.56, 55.14, 51.96, 51.35, 49.92, 45.24, 34.78, 34.40, 33.23, 31.69, 26.06 ppm.

*Tetracyclic Ketones **4** and **5**, General Procedure*

The mixture of ester **3** and 0.6 $cm^3$ of trifluoromethanesulfonic acid was stirred for 12 min at 110°C. After cooling in an ice bath the solution was diluted with 1 $cm^3$ of $H_2O$, and then adjusted to $pH = 7$

with aqueous $NaHCO_3$. After addition of $Et_2O$ and brine (each 10 $cm^3$) the ether phase was separated and the aqueous layer was extracted with $Et_2O$ ($3\times15$ $cm^3$). The combined ether extracts were dried ($Na_2SO_4$) and the solvent was removed *in vacuo*. The residual mixture of the products **4** and **5** was separated by FC (*route A*).

Alternatively the residue was redissolved in 2 $cm^3$ of $Et_2O$ and 2 drops of *Me*OH. The solution was reacted with an excess of diazomethane for 16 h at ambient temperature. After evaporating the solvent *in vacuo* the residue was purified by FC affording only the phenol ether **4** (*route B*).

Eluents were the same as used for TLC.

*cis-15-Methoxyerythrinan-11-one* (**4a**, $C_{17}H_{21}NO_2$) *and cis-15-Hydroxyerythrinan-11-one* (**5a**, $C_{16}H_{19}NO_2$)

A. From 111 mg (0.35 mmol) of **3c** and 0.6 $cm^3$ of $F_3CSO_3H$; **4a:** yield 22 mg (23%) light yellowish amorphous solid, mp 82–83°C; TLC ($CH_2Cl_2$:*Me*OH = 100:5): $R_f = 0.60$; IR (KBr): $\bar{\nu} = 1674$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 271 ($M^{+\bullet}$, 25), 242 (6), 228 (100), 214 (18), 186 (5); $^1$H NMR: $\delta = 7.99$ (d, $J = 8.7$ Hz, 1arom H), 6.83 (d, $J = 2.5$ Hz, 1arom H), 6.79 (dd, $J = 8.7$, 2.5 Hz, 1arom H), 3.88 (s, $OCH_3$), 3.75 and 3.48 (2d, each $J = 18.1$ Hz, $COCH_2$–N), 3.26 (dt, $J = 9.3$, 7.0 Hz, 1H), 2.70 (ddd, $J = 11.3$, 9.3, 3.4 Hz, 1H), 2.42 (br dt, $J = 10.8$, 6.3 Hz, 1H), 2.11–2.05, 1.80–1.65, 1.64–1.47, and 1.45–1.25 (4m, 1, 2, 5, and 2H) ppm; $^{13}$C NMR: $\delta = 196.95$, 164.52, 151.77, 128.75, 124.34, 112.10, 110.14, 64.65, 55.43, 53.26, 49.40, 43.38, 33.63, 29.21, 28.06, 25.30, 21.44 ppm.

**5**: yield 15 mg (17%) yellowish solid, mp 68–71°C; TLC ($CH_2Cl_2$:*Me*OH = 100:5): $R_f = 0.35$; IR (KBr): $\bar{\nu} = 1660$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 257 ($M^{+\bullet}$, 26), 214 (96), 200 (22), 149 (100); $^1$H NMR: $\delta = 7.93$ (d, $J = 8.5$ Hz, 1arom H), 6.80–6.76 (dd, $J = 8.5$ Hz, 2arom H), 3.76 and 3.51 (2d, each $J = 18.1$ Hz, $COCH_2$–N), 3.26 (dt, $J = 9.4$, 7.1 Hz, 1H), 2.71 (ddd, $J = 11.1$, 9.4, 3.4 Hz, 1H), 2.43–2.35 and 2.09–2.02 (2m, each 1H), 1.78–1.64, 1.64–1.47, and 1.41–1.21 (3m, 2, 5, and 2H) ppm; $^{13}$C NMR: $\delta = 197.58$, 162.01, 151.87, 129.16, 123.93, 114.51, 111.38, 64.67, 53.32, 49.47, 43.33, 33.42, 29.13, 28.04, 25.17, 21.40 ppm.

B. **4a**: From 115 mg (0.36 mmol) of **3c** and 0.6 $cm^3$ of $F_3CSO_3H$; yield 42 mg (43%); identical data with those given under A (see above).

*cis-16-Methoxyschelhammeran-12-one* (**4b**, $C_{18}H_{23}NO_2$)
*and cis-16-Hydroxyschelhammeran-12-one* (**5b**, $C_{17}H_{21}NO_2$)

A. From 75 mg (0.24 mmol) of **3f** and 0.6 $cm^3$ of $F_3CSO_3H$; **4b:** yield 17 mg (25%) beige solid, mp 81°C; TLC ($CH_2Cl_2$:*Me*OH = 100:5): $R_f = 0.60$; IR (KBr): $\bar{\nu} = 1671$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 285 ($M^{+\bullet}$, 26), 242 (100), 227 (10), 214 (12); $^1$H NMR: $\delta = 7.48$ (d, $J = 8.6$ Hz, 1arom H), 6.99 (d, $J = 2.5$ Hz, 1arom H), 6.77 (dd, $J = 8.6$, 2.5 Hz, 1arom H), 3.85 (s, $OCH_3$), 3.30 and 3.15 (2ddd, $J = 13.7$, 6.2, 4.7 and 13.7, 9.8, 5.7 Hz, each 1H), 3.07 (dt, $J = 8.8$, 6.6 Hz, 1H), 2.97 (ddd, $J = 13.4$, 9.8, 6.2 Hz, 1H), 2.89 (dt, $J = 8.8$, 4.4 Hz, 1H), 2.73 (br dt, $J = 13.4$, 4.7 Hz, 1H), 2.45–2.39 (m, 1H), 2.06 (ddd, $J = 14.0$, 5.8, 3.0 Hz, 1H), 1.77–1.49 and 1.49–1.27 (2m, 5 and 4H) ppm; $^{13}$C NMR: $\delta = 205.42$, 161.37, 150.03, 133.76, 130.44, 113.98, 110.39, 68.01, 55.35, 50.50, 44.82, 44.10, 43.37, 34.60, 28.96, 27.71, 23.94, 21.74 ppm.

**5b**: yield 13 mg (20%) yellowish solid, mp 68–72°C; TLC ($CH_2Cl_2$:*Me*OH = 100:5): $R_f = 0.39$; MS (EI): $m/z$ (%) = 271 ($M^{+\bullet}$, 23), 228 (100), 200 (14); $^1$H NMR: $\delta = 7.30$ (d, $J = 8.4$ Hz, 1arom H), 6.86 (d, $J = 2.3$ Hz, 1arom H), 6.56 (br d, $J = 8.4$ Hz, 1arom H), 4.87 (br s, OH), 3.23 (dt, $J = 13.8$, 5.9 Hz, 1H), 3.08 (ddd, $J = 13.8$, 8.7, 5.9 Hz, 1H), 2.98 (dt, $J = 8.7$, 6.5 Hz, 1H), 2.93–2.74 (m, 3H), 2.41–2.33 and 1.96–1.87 (2m, each 1H), 1.68–1.27 (m, 9H) ppm; $^{13}$C NMR: $\delta = 205.87$, 158.53, 133.20, 130.65, 114.92, 113.64, 68.15, 50.72, 44.52, 43.97, 43.78, 33.97, 28.51, 27.41, 23.41, 21.63 (1quart. C is lacking) ppm.

B. **4b**: From 73 mg (0.23 mmol) of **3f** and 0.6 $cm^3$ of $F_3CSO_3H$; yield 32 mg (49%) beige solid; identical data with those given under A.

*cis-16-Methoxy-B-homoerythrinan-12-one* (**4c**, $C_{18}H_{23}NO_2$)

B. From 120 mg (0.36 mmol) of **3g** and 0.6 $cm^3$ of $F_3CSO_3H$; yield 21 mg (20%) yellowish solid, mp 107–108°C; TLC ($CH_2Cl_2$:*Me*OH = 100:4): $R_f = 0.56$; IR (KBr): $\bar{\nu} = 1677$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 285 ($M^{+\bullet} + H$, 26), 256 (14), 242 (100), 228 (24), 200 (7), 57 (38); $^1H$ NMR: $\delta = 8.02$ (d, $J = 8.6$ Hz, 1arom H), 6.83 (dd, $J = 8.6$, 2.5 Hz, 1arom H), 6.80 (d, $J = 2.5$ Hz, 1arom H), 4.02 and 3.17 (2d, each $J = 18.7$ Hz, each 1H), 3.88 (s, $OCH_3$), 2.70 (br dd, $J = 9.2$, 2.7 Hz, 2H), 2.31–2.25 and 2.24–2.17 (2m, 2 and 1H), 2.01–1.84 and 1.76–1.60 (2m, each 2H), 1.50–1.24 (m, 6H) ppm; $^{13}C$ NMR: $\delta = 196.07$, 164.79, 150.47, 129.44, 124.49, 111.45, 110.91, 59.74, 58.48, 55.46, 51.13, 40.74, 36.57, 26.75 (2C), 26.31, 22.23, 20.98 ppm.

*cis-13-Methoxy-A-norerythrinan-10-one* (**4d**, $C_{16}H_{19}NO_2$)
*and cis-13-Hydroxy-A-norerythrinan-10-one* (**5d**, $C_{17}H_{21}NO_2$)

A. From 75 mg (0.25 mmol) of **3i** and 0.6 $cm^3$ of $F_3CSO_3H$; **4d:** yield 31 mg (48%) yellowish solid, mp 74–75°C; TLC ($CH_2Cl_2$:*Me*OH = 100:4): $R_f = 0.49$; IR (KBr): $\bar{\nu} = 1671$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 258 ($M^{+\bullet} + H$, 29), 257 ($M^{+\bullet}$, 41), 228 (100), 214 (79), 200 (18); $^1H$ NMR: $\delta = 7.92$ (d, $J = 8.8$ Hz, 1arom H), 6.81 (dd, $J = 8.8$, 2.5 Hz, 1arom H), 6.65 (d, $J = 2.5$ Hz, 1arom H), 3.87 and 3.61 (2d, each $J = 17.3$ Hz, each 1H), 3.86 (s, $OCH_3$), 3.01–2.94, 2.84–2.74, and 2.37–2.29 (3m, 1, 2, and 1H), 2.10–1.82, 1.75–1.69, and 1.62–1.46 (3m, 4, 1, and 2H) ppm; $^{13}C$ NMR: $\delta = 195.60$, 164.64, 151.90, 127.87, 123.49, 112.27, 111.42, 73.71, 55.42, 54.56, 54.21, 52.81, 40.06, 35.29, 32.41, 25.93 ppm.

**5d**: yield 15 mg (20%) yellowish solid; mp 65–68°C; TLC ($CH_2Cl_2$:*Me*OH = 100: 4): $R_f = 0.32$; IR (KBr): $\bar{\nu} = 1659$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 244 ($M^{+\bullet} + H$, 25), 243 ($M^{+\bullet}$, 41), 214 (100), 200 (83), 186 (18); $^1H$ NMR: $\delta = 7.87$ (d, $J = 8.6$ Hz, 1arom H), 6.76 (dd, $J = 8.6$, 2.4 Hz, 1arom H), 6.66 (d, $J = 2.4$ Hz, 1arom H), 3.88 and 3.63 (2d, each $J = 17.4$ Hz, each 1H), 3.05–2.94, 2.85–2.74, and 2.39–2.28 (3m, 1, 2, and 1H), 2.12–1.80, 1.77–1.66, and 1.63–1.46 (3m, 4, 1, and 2H) ppm; $^{13}C$ NMR: $\delta = 168.05$, 162.05, 128.31, 122.93, 114.62, 112.66, 54.50, 54.21, 52.94, 39.89, 35.17, 32.25, 25.97 (C-4 did not appear) ppm.

B. **4d**: From 90 mg (0.3 mmol) of **3i** and 0.6 $cm^3$ of $F_3CSO_3H$; yield 50 mg (66%) yellowish solid; identical data with those given under A.

*cis-15-Methoxy-A-norschelhammeran-11-one* (**4e**, $C_{17}H_{21}NO_2$)
*and cis-15-Hydroxy-A-norschelhammeran-11-one* (**5e**, $C_{16}H_{19}NO_2$)

A. From 95 mg (0.31 mmol) of **3k** and 0.6 $cm^3$ of $F_3CSO_3H$; **4e:** yield 21 mg (25%) yellowish solid, mp 98°C; TLC ($CH_2Cl_2$:*Me*OH = 100:4): $R_f = 0.51$; IR (film): $\bar{\nu} = 1682$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 271 ($M^{+\bullet}$, 28), 242 (100), 228 (46), 214 (17); $^1H$ NMR: $\delta = 7.54$ (d, $J = 8.6$ Hz, 1arom H), 6.83 (dd, $J = 8.6$, 2.4 Hz, 1arom H), 6.74 (d, $J = 2.4$ Hz, 1arom H), 3.83 (s, $OCH_3$), 3.20–3.10 (m, 1H), 3.06–2.95 (m, 3H), 2.85 (ddd, $J = 9.0$, 7.2, 2.3 Hz, 1H), 2.81–2.72 and 2.61–2.54 (2 m, each 1H), 2.31 (dt, $J = 12.5$, 6.3 Hz, 1H), 2.13 (br ddd, $J = 14.8$, 12.7, 6.2 Hz, 1H), 1.98–1.67 and 1.53–1.41 (2m, 4 and 2H) ppm; $^{13}C$ NMR: $\delta = 203.93$, 161.12, 153.65, 132.60, 129.60, 113.50, 109.77, 63.62, 55.36, 54.88, 54.72, 45.57, 41.80, 36.21, 34.51, 30.70, 27.60 ppm.

**5e**: yield 11 mg (14%) yellowish solid, mp 66–70°C; TLC ($CH_2Cl_2$:*Me*OH = 100:4): $R_f = 0.36$; IR (film): $\bar{\nu} = 1676$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 257 ($M^{+\bullet}$, 31), 228 (100), 200 (20), 186 (9); $^1H$ NMR: $\delta = 7.45$ (d, $J = 8.2$ Hz, 1arom H), 6.83 (dd, $J = 8.2$, 2.3 Hz, 1arom H), 6.66 (d, $J = 2.3$ Hz, 1arom H), 3.20–3.11 (m, 1H), 3.11–2.96 and 2.87–2.72 (2m, 3 and 2H), 2.62–2.57, 2.37–2.26, and 2.15–2.04 (3m, each 1H), 1.98–1.75, 1.75–1.66, and 1.53–1.41 (3m, 3, 1, and 2H) ppm; $^{13}C$ NMR: $\delta = 204.79$, 158.50, 131.59, 129.95, 114.02, 113.16, 54.80, 54.61 (br), 45.75, 41.58, 36.50 (br), 34.27, 30.50, 27.39 (2quart. C were lacking) ppm.

B. **4e**: From 96 mg (0.32 mmol) of **3k** and 0.6 $cm^3$ of $F_3CSO_3H$; yield 30 mg (35%) yellowish solid; identical data with those given under A.

*cis-(11α- and 11β*-Hydroxy-15-methoxy)erythrinane (**6a** and **6b**, $C_{17}H_{23}NO_2$)

To a solution of 50 mg (0.19 mmol) of **4a** in 3 $cm^3$ of anhydrous *THF* was added 30 mg (0.89 mmol) of $LiAlH_4$. After stirring for 20 min at ambient temperature the suspension was poured into a mixture of 10 $cm^3$ of $Et_2O$ and 10 $cm^3$ of 2 *N* NaOH under ice cooling. The organic layer was separated and the aqueous phase was extracted with $Et_2O$ (2×10 $cm^3$). After drying the combined ether layers with $Na_2SO_4$ the solvent was evaporated *in vacuo* and the residual products first were separated by FC (silica gel; *EtOAc*:*Me*OH:25% $NH_3$ = 100:5:0.5) and finally crystallized from *n*-hexane.

Fraction I: **6a**: yield 21 mg (42%) colourless crystals, mp 121°C; TLC (eluent see FC): $R_f = 0.54$; IR (KBr): $\bar{\nu} = 1047$ (C–OH) $cm^{-1}$; MS (EI): $m/z$ (%) = 255 ($M^{+\bullet}$–$H_2O$, 19), 212 (62), 198 (20), 57 (100); $^1$H NMR: $\delta = 7.45$ and 6.78 (2dd, $J = 8.5$, 0.5 and 8.5, 2.7 Hz, each 1arom H), 6.75 (d, $J = 2.7$ Hz, 1arom H), 4.97 (dd, $J = 9.7$, 6.5 Hz, 1H), 3.81 (s, $OCH_3$), 3.36 (dd, $J = 13.9$, 6.5 Hz, 1H), 3.23 (dt, $J = 9.7$, 8.5 Hz, 1H), 2.90–2.84 (m, 2H), 2.33–2.26 and 2.00–1.93 (2m, each 1H), 1.76–1.63, 1.60–1.35, and 1.31–1.24 (3m, 2, 6, and 1H) ppm; $^{13}$C NMR: $\delta = 158.68$, 146.08, 131.02, 127.89, 111.71, 111.00, 64.91, 61.55, 55.24, 49.37, 48.04, 43.82, 35.34, 28.81, 28.42, 24.62, 21.50 ppm.

Fraction II: **6b**: yield 26 mg (51%) colourless crystals, mp 124°C; TLC (eluent see FC): $R_f = 0.48$; IR (KBr): $\bar{\nu} = 1035$ (C–OH) $cm^{-1}$; MS (EI): $m/z$ (%) = 255 ($M^{+\bullet}$–$H_2O$, 30), 212 (100), 198 (30); $^1$H NMR: $\delta = 7.32$ and 6.78 (2d, $J = 8.4$ and 2.6 Hz, each 1arom H), 6.75 (dd, $J = 8.4$, 2.6 Hz, 1arom H), 4.51 (d, $J = 3.7$ Hz, 1H), 3.82 (s, $OCH_3$), 3.36–3.30 (m, 2H), 3.23 (d, $J = 14.5$ Hz, 1H), 3.13 (q, $J = 8.5$ Hz, 1H), 2.43–2.37 (m, 1H), 2.15 (br s, 1H), 1.83–1.77, 1.76–1.69, and 1.69–1.36 (3m, 1, 2, and 7H) ppm; $^{13}$C NMR: $\delta = 158.98$, 145.47, 130.85, 129.08, 111.75, 110.82, 65.71, 63.47, 55.25, 49.12, 48.57, 43.03, 32.35, 28.56, 28.03, 24.70, 21.01 ppm.

**6b** *by Stereoselective Reduction*

To a solution of 37 mg (0.14 mmol) of **4a** in 2 $cm^3$ of anhydrous *THF* was added 0.28 $cm^3$ of 1 *M* L-selectride® (*THF*) at −78°C under $N_2$. After stirring for 2 h and rapid warm up to ambient temperature the mixture was quenched with 2 $cm^3$ of saturated $NH_4Cl$ solution, diluted with 10 $cm^3$ of $H_2O$, and then acidified with 2 *N* HCl. The aqueous phase was washed with $Et_2O$ (2×10 $cm^3$), rendered alkaline with 2 *N* NaOH, and then extracted with $Et_2O$ (3×10 $cm^3$). After drying the combined ether extracts with $Na_2SO_4$ the solvent was removed and the residue crystallized from *n*-hexane. Yield 36 mg (97%) colourless crystals; identical data with those given under fraction II (see above).

*cis-(11β-Acetoxy-15-methoxy)erythrinane* (**6c**, $C_{19}H_{25}NO_3$)

The mixture of 10 mg (0.04 mmol) of **6b**, 50 mg of acetic anhydride, and 2 $cm^3$ of anhydrous pyridine was stirred for 24 h at ambient temperature, then diluted with 10 $cm^3$ of $H_2O$ and 1 $cm^3$ of saturated $Na_2CO_3$ solution and extracted with $Et_2O$ (3×10 $cm^3$). After drying the combined organic extracts with $Na_2SO_4$, the solvent was removed *in vacuo* and the residue was purified by FC ($CH_2Cl_2$:*Me*OH = 100:3). Yield 8 mg (70%) colourless oil; TLC (eluent see FC): $R_f = 0.39$; IR (film): $\bar{\nu} = 1732$ (CO) $cm^{-1}$; MS (EI): $m/z$ (%) = 315 ($M^{+\bullet}$, 30), 272 (48), 255 (10), 212 (100), 198 (30); $^1$H NMR: $\delta = 7.18$ and 6.83 (2d, $J = 8.4$ and 2.5 Hz, each 1arom H), 6.78 (dd, $J = 8.4$, 2.5 Hz, 1arom H), 5.72 (d, $J = 3.9$ Hz, 1H), 3.82 (s, $OCH_3$), 3.44 (dd, $J = 16.9$, 3.9 Hz, 1H), 3.31–3.11 (m, 3H), 2.46–2.38 (m, 1H), 2.10 (s, $CCH_3$), 1.73–1.50, 1.50–1.26, and 1.26–1.17 (3m, 5, 4 and 1H) ppm; $^{13}$C NMR: $\delta = 170.01$, 159.30, 145.34, 120.42, 122.60, 110.90, 109.43, 65.81, 63.13, 54.25, 47.11, 45.35, 42.58, 33.28, 27.83, 27.14, 23.76, 20.62, 20.00 ppm.

*Tetracycles* **7**, *General Procedure*

A mixture of ketone **4**, glacial acetic acid, acetanhydride, 71% $HClO_4$, and 10% Pd-C was hydrogenated 16 h at 60°C and 6.5×$10^6$ Pa initial pressure of $H_2$. The catalyst was filtered off (glass frit P4)

and washed with 15 $cm^3$ of $H_2O$. The filtrate was rendered alkaline with 32% NaOH solution and extracted with $Et_2O$ ($3\times10$ $cm^3$). After drying the combined organic extracts with $Na_2SO_4$ the solvent was evaporated *in vacuo* and the residue purified by FC (eluents are the same as used for TLC).

*cis-15-Methoxyerythrinane* (**7a** [16])

**4a** 40 mg (0.15 mmol), *Ac*OH 5 $cm^3$/$Ac_2O$ 0.2 $cm^3$, $HClO_4$ 0.1 $cm^3$, Pd-C 9 mg; yield 29 mg (77%) colourless oil; TLC (*Et*OAc:*Me*OH:25% $NH_3$ = 100:5:0.5): $R_f$ = 0.45; MS (EI): $m/z$ (%) = 257 ($M^{+\bullet}$, 22), 214 (100), 200 (25), 149 (30); $^1$H NMR: $\delta$ = 6.95 (d, $J$ = 8.3 Hz, H-17), 6.78 (d, $J$ = 2.6 Hz, H-14), 6.68 (dd, $J$ = 8.3, 2.6 Hz, H-16), 3.79 (s, $OCH_3$), 3.21–3.02 (m, 4H), 2.85 (ddd, $J$ = 10.4, 9.8, 2.9 Hz, 1H), 2.36–2.25, 1.97–1.90, and 1.78–1.64 (3m, 2, 1, and 2H), 1.60–1.32 and 1.31–1.24 (2m, 6 and 1H) ppm; $^{13}$C NMR: $\delta$ = 157.67, 145.68, 129.67, 127.15, 111.36, 111.21, 65.78, 55.25, 46.34, 43.66, 40.51, 35.75, 29.01, 28.66, 24.96, 21.36, 21.09 ppm.

*cis-16-Methoxyschelhammerane* (**7b**, $C_{18}H_{25}NO$)

**4b** 45 mg (0.16 mmol), *Ac*OH 5 $cm^3$/$Ac_2O$ 0.2 $cm^3$, $HClO_4$ 0.1 $cm^3$, Pd-C 11 mg; yield 32 mg (75%) colourless oil; TLC (*Et*OAc:*Me*OH = 100:5): $R_f$ = 0.25; MS (EI): $m/z$ (%) = 271 ($M^{+\bullet}$, 18), 228 (100), 214 (5), 149 (20); $^1$H NMR: $\delta$ = 7.03 and 6.99 (2d, $J$ = 2.8 and 8.3 Hz, each 1arom H), 6.61 (dd, $J$ = 8.3, 2.8 Hz, 1arom H), 3.78 (s, $OCH_3$), 5.15–2.94, 2.80–2.69, and 1.93–1.78 (3m, 4, 3, and 4H), 1.78–1.57, 1.57–1.37, and 1.16–1.06 (3m, 4, 3, and 1H) ppm; $^{13}$C NMR: $\delta$ = 157.58, 147.02, 134.20, 132.01, 115.26, 109.87, 67.37, 55.20, 50.45, 49.85, 42.24, 36.38, 29.14, 28.13, 27.37, 26.82, 23.14, 22.08 ppm.

*cis-16-Methoxy-B-homoerythrinane* (**7c**, $C_{18}H_{25}NO$)

**4c** 60 mg (0.21 mmol), *Ac*OH 5 $cm^3$/$Ac_2O$ 0.2 $cm^3$, $HClO_4$ 0.1 $cm^3$, Pd-C 10 mg; yield 39 mg (68%) colourless oil; TLC (*Et*OAc:*Me*OH:25% $NH_3$ = 100:5:1): $R_f$ = 0.52; MS (EI): $m/z$ (%) = 271 ($M^{+\bullet}$, 22), 242 (16), 228 (100), 214 (27); $^1$H NMR: $\delta$ = 6.99 (br d, $J$ = 8.3 Hz, 1arom H), 6.89 (d, $J$ = 2.6 Hz, 1arom H), 6.65 (dd, $J$ = 8.3, 2.6 Hz, 1arom H), 3.79 (s, $OCH_3$), 3.53 and 3.00 (2ddd, $J$ = 14.3, 10.8, 7.4 and 17.3, 10.8, 8.6 Hz, each 1H), 2.81 (dd, $J$ = 14.3, 8.6 Hz, 1H), 2.67–2.63 (m, 2H), 2.46 (dd, $J$ = 17.3, 7.4 Hz, 1H), 2.29–2.21 (m, 2H), 2.18–2.12, 2.00–1.88, and 1.88–1.80 (3m, each 1H), 1.69–1.55, 1.44–1.33, 1.31–1.22, and 1.26–1.21 (4m, 2, 3, 2, and 1H) ppm; $^{13}$C NMR: $\delta$ = 157.92, 144.11, 130.19, 125.98, 110.73 (2C), 59.26, 55.24, 48.90, 43.94, 41.21, 36.63, 27.04, 26.86, 26.61, 21.46, 21.17, 21.00 ppm.

*cis-14-Methoxy-A-norerythrinane* (**7d**, $C_{16}H_{21}NO$)

**4d** 95 mg (0.37 mmol), *Ac*OH 5 $cm^3$/$Ac_2O$ 0.2 $cm^3$, $HClO_4$ 0.1 $cm^3$, Pd-C 20 mg; yield 66 mg (73%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH = 100:5): $R_f$ = 0.28; MS (EI): $m/z$ (%) = 243 ($M^{+\bullet}$, 35), 230 (10), 228 (14), 214 (100), 200 (90), 186 (13); $^1$H NMR: $\delta$ = 6.93 (d, $J$ = 8.2 Hz, 1arom H), 6.68 (dd, $J$ = 8.2, 2.5 Hz, 1arom H), 6.65 (d, $J$ = 2.5 Hz, 1arom H), 3.77 (s, $OCH_3$), 3.24 (m, 1H), 3.19 and 2.98 (each ddd, $J$ = 13.9, 12.3, 4.0 and 16.4, 12.3, 6.0 Hz, each 1H), 2.82–2.76 (m, 1H), 2.74 (ddd, $J$ = 11.4, 8.6, 5.5 Hz, 1H), 2.61–2.54 (m, 1H), 2.35 (br dd, $J$ = 16.4, 4 Hz, 1H), 2.08–2.03, 2.03–1.67, and 1.65–1.56 (3 m, 1, 5, and 1H), 1.47 (ddt, $J$ = 11.5, 8.6, 7.2 Hz, 1H) ppm; $^{13}$C NMR: $\delta$ = 158.09, 145.62, 129.21, 125.82, 112.51, 111.81, 74.02, 55.25, 53.70, 49.63, 44.35, 43.10, 35.14, 32.04, 25.54, 21.26 ppm.

*cis-15-Methoxy-A-norschelhammerane* (**7e**, $C_{17}H_{23}NO$)

**4e** 40 mg (0.15 mmol), *Ac*OH 5 $cm^3$/$Ac_2O$ 0.2 $cm^3$, $HClO_4$ 0.1 $cm^3$, Pd-C 9 mg; yield 29 mg (77%) colourless oil; TLC ($CH_2Cl_2$:*Me*OH:25% $NH_3$ = 100:5:0.5): $R_f$ = 0.45; MS (EI): $m/z$ (%) = 257 ($M^{+\bullet}$,

64), 242 (23), 228 (100), 214 (94); $^1$H NMR (45°C): $\delta = 6.99$ (d, $J = 8.3$ Hz, 1arom H), 6.81 (dd, $J = 8.3$, 2.3 Hz, 1arom H), 6.61 (d, $J = 2.3$ Hz, 1arom H), 3.77 (s, $OCH_3$), 3.16–3.07, 3.05–2.71, and 2.31–1.96 (3m, 1, 4, and 3H), 1.93–1.73, 1.73–1.54, and 1.54–1.36 (3m, 9H) ppm; $^{13}$C NMR: $\delta = 157.33$, 149.30 (br), 133.50 (br), 131.73, 114.09, 109.53, 55.34 (2C), 52.01 (br), 50.67, 35.01 (br), 34.41 (br, 2C), 30.72, 27.61 (br), 26.82 (br), (1quart. C was lacking) ppm.

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