181. Approaches to the Synthesis of Cytochalasans

Part 11[1])

Further Transformations and Cyclization Attempts Directed towards Proxiphomin

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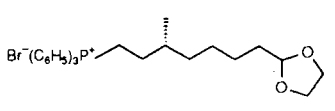
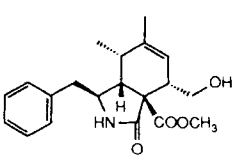
Starting from iodoalcohol **9**, the monoprotected dialdehyde **5** was synthesized (*Scheme 2*) and converted to **17** by reaction with oxo-phosphonate **15** (*Scheme 3*). The latter was prepared from **13**. Cyclisation of **17** to the target compound **18** failed. Also the attachment of thiol **22** to lactone **19** was unsatisfactory (*Scheme 4*). Therefore, the building blocks **28** and **29** were synthesized using diene **33** and diester **30** as starting material for **28** and **9** for **29** (*Schemes 5* and *6*). Hydroxy acid **28** was converted into formyl-ester **46** (*Scheme 7*). However, the condensation of its derivatives **48** and **49** with 'Umpolung' of the carbonyl reactivity was unsuccessful, probably due to steric hindrance.

According to the concept presented earlier [2] [3] for the synthesis of proxiphomin (= (16*R*,13*E*,21*E*)-16-methyl-10-phenyl[13]cytochalasa-6,13,21-triene-1,23-dione; **7**)[2]), the optically active building block **1** should have been linked to the tetrahydroisoindolinone unit **2** leading to the 13,14-didehydro derivative **3**.



1



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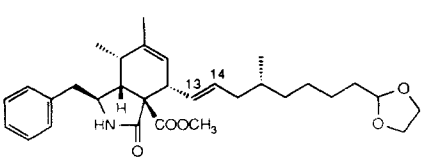


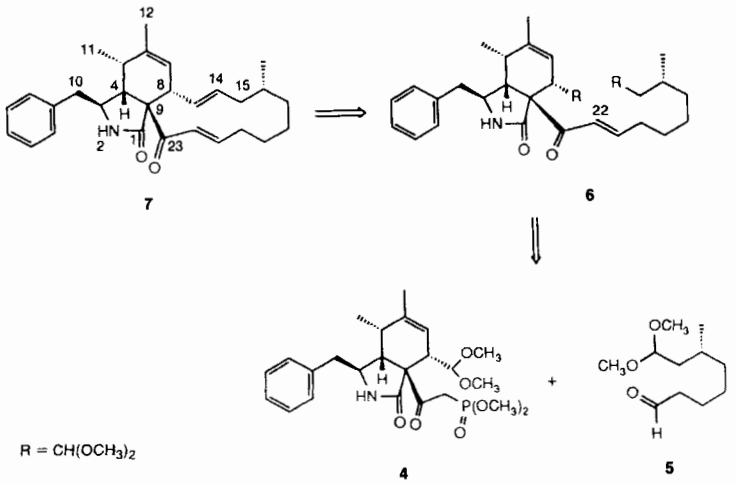
3

This reaction gave the desired product in low yield only once; any attempts to reproduce this condensation failed. Therefore, the strategy was modified in a way that the two synthons should be connected *via* C(22), which could be introduced into compound **2**

[1]) Part 10: [1].

[2]) In the *General Part*, cytochalasan numbering (see **7**) is used; for systematic names, see *Exper. Part.*

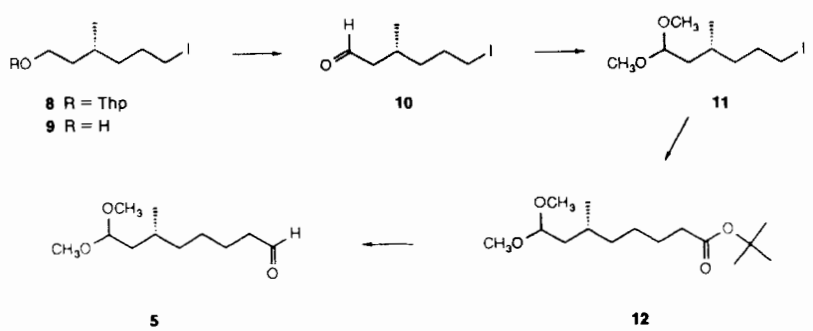
Scheme 1



by alkylation of the ester carbonyl group *e.g.*, by converting it into phosphonate **4** (*Scheme 1*). A *Wadsworth-Emmons* reaction [4] of **4** with aldehyde **5** would lead to the α,β-unsaturated ketone **6**. Cleavage of the two protecting groups would give a dialdehyde which should undergo a *McMurry* reaction [5] yielding the target compound **7**.

Results. – The monoprotected dialdehyde **5** was synthesized starting from iodoalcohol **9** [6] (obtained from its tetrahydropyranyl ether **8** in 95% yield; *Scheme 2*). After

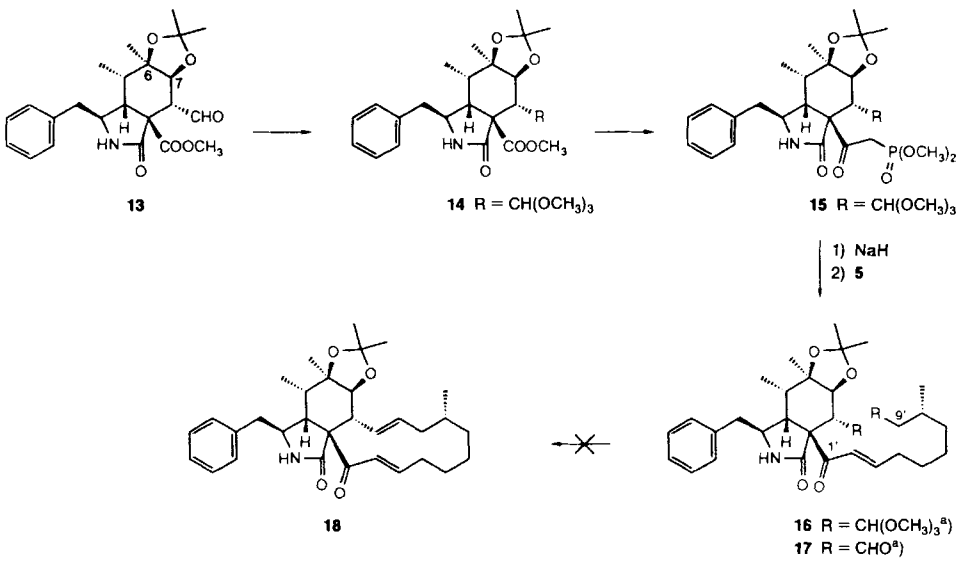
Scheme 2



oxidation to **10** by *Swern*'s method [7] and conversion to dimethyl acetal **11** (75% yield starting from **9**), the elongation of the chain by two additional C-atoms could be achieved by reaction with 1.0 equiv. of *tert*-butyl 2-lithioacetate [8], yielding ester **12** (68%). Subsequent reduction with diisobutylaluminium hydride (DIBAH) in hexane [9] led to aldehyde **5** (96%).

Aldehyde **13** [3] with the protected double bond at C(6) and C(7), to prevent migration, was converted to **14**. Alkylation of the ester carbonyl group with dimethyl

Scheme 3



a) Only one diastereoisomer is shown.

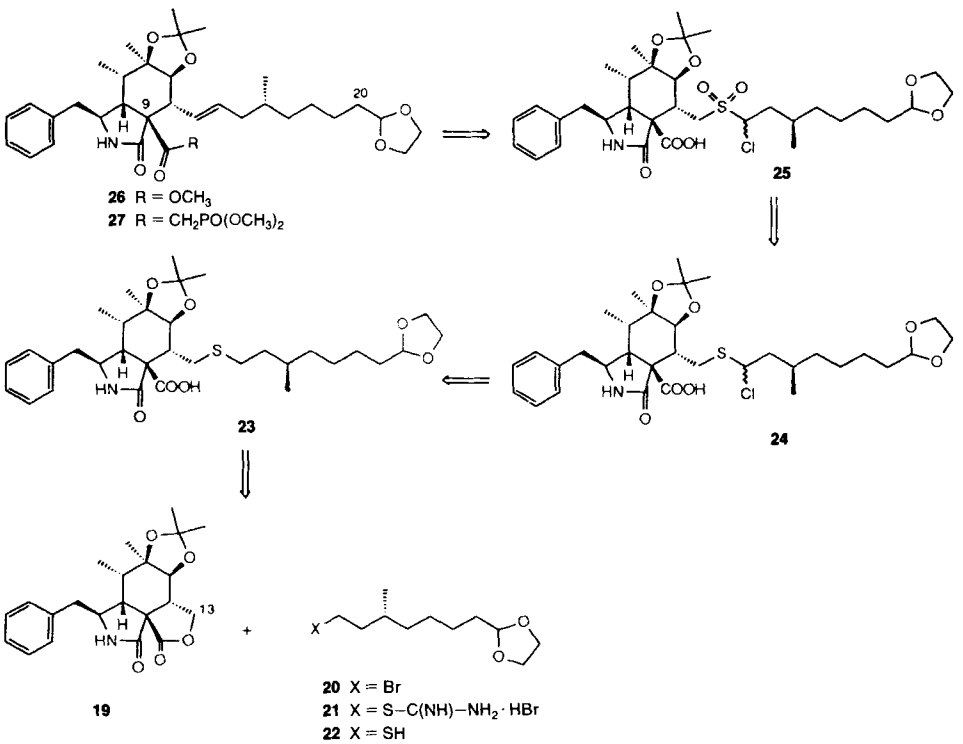
(lithiomethyl)phosphonate led to the (oxoethyl)phosphonate **15** (86%; *Scheme 3*), a derivative of the building block **4**. The condensation of **15** and **5** was carried out according to the method of *Wadsworth* and *Emmons* [4]. Thus, **15** was deprotonated with NaH in diglyme and then reacted with 2 equiv. of **5**, giving the desired olefin **16** in 51% yield, whereby 20% of unreacted **5** were recovered. Cleavage of the dimethyl-acetal protecting groups gave **17** (94%). Finally, a *McMurry* reaction [5] of the two aldehyde groups of **17** should give the macrocyclic compound **18**. But all attempts failed, no product of identified structure could be isolated. The 21,22-dihydro derivative of **17** was also unsuccessful in this reaction.

As it was not possible to obtain target molecule **18** in this way, we changed our strategy and planned to connect lactone **19** and thiol **22** using the *Ramberg-Bäcklund* reaction [10] (*Scheme 4*). The resulting sulfide **23** should be chlorinated with *N*-chlorosuccinimide (→ **24**) and oxidized with 3-chloroperbenzoic acid (→ **25**), and elimination of sulfur dioxide would give the desired olefin **26**. Macrocyclization by conversion of the ester carbonyl group at C(9) into the phosphonate **27**, followed by a *Wadsworth-Emmons* reaction between the phosphonate and the formyl group at C(20), would yield the target molecule **7**.

For the synthesis of thiol **22**, bromide **20** [6] was treated with thiourea yielding derivative **21** which was immediately hydrolyzed with aq. NaOH solution (→ **22**; 71%). Reaction of **22** at C(13) of lactone **19** according to *Fujita* and coworkers [11] led to sulfide **23**, but only in low and not reproducible yields. Modifications of reaction conditions were unsuccessful.

Summarizing all results which we have obtained from our approaches to the synthesis of cytochalasans [2] [3] [6], we decided to modify the concept and to prepare the two new

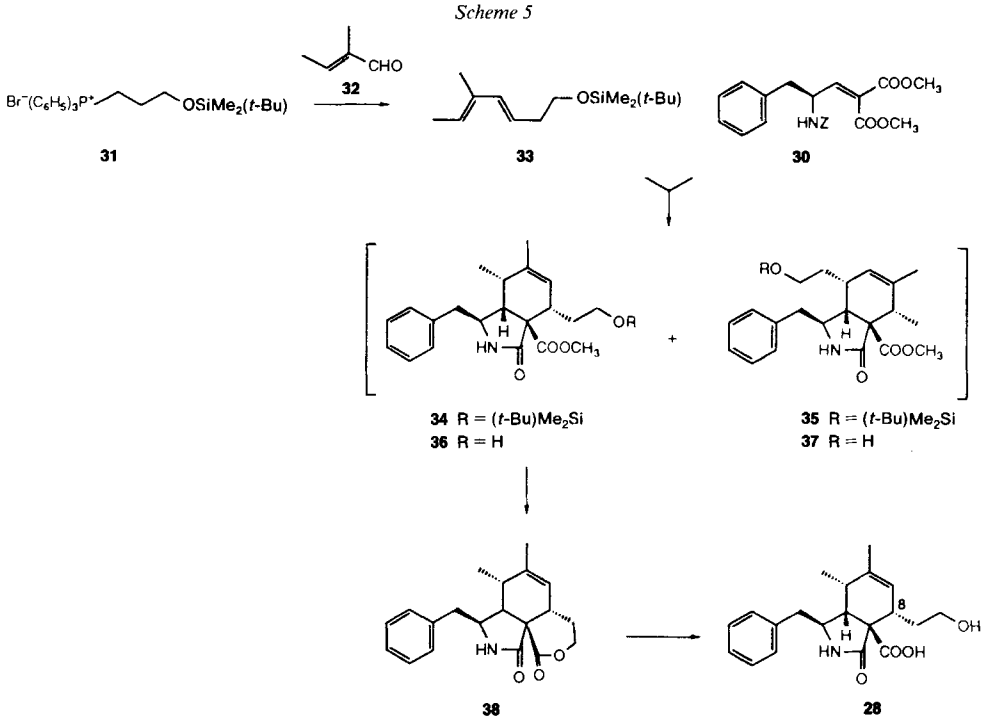
Scheme 4



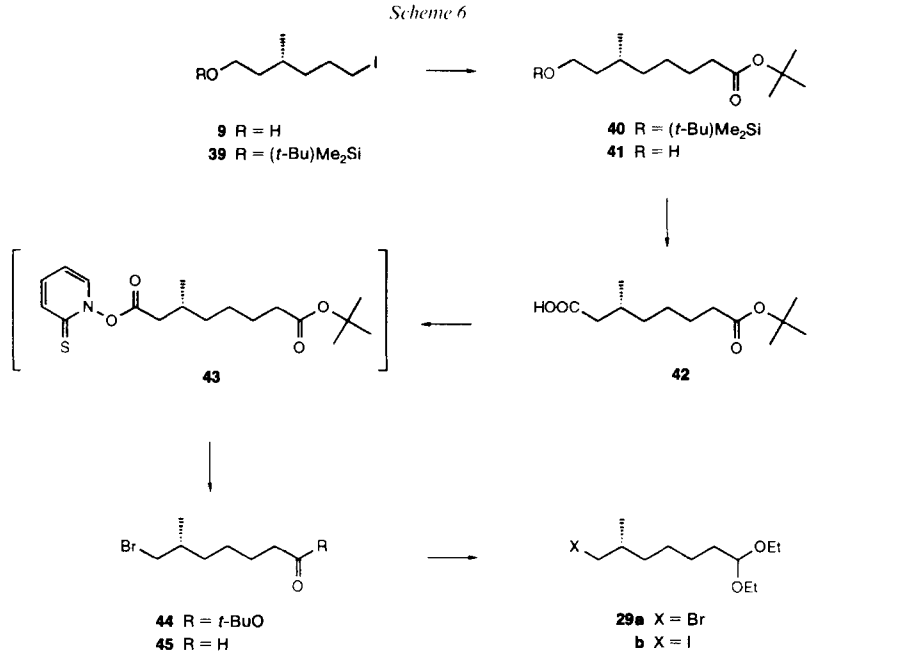
building blocks **28** (*Scheme 5*) and **29a** (*Scheme 6*), which would allow us to connect the synthons between C(14) and C(15) of **7** minimizing the steric hindrance. Building block **28** was synthesized in analogy to the concept for the synthesis of **2** [12]. Thus, unsaturated amino diester **30** [3] [13] and diene **33**, which was obtained from {3-[(*tert*-butyl)-dimethylsilyloxy]propyl}triphenylphosphonium bromide (**31**) and tiglic aldehyde (**32**), reacted in a *Diels-Alder* addition to a 2:1 mixture of the two regioisomers **34** and **35** (40%; *Scheme 5*). Cleavage of the (*t*-Bu)Me_2Si group with AcOH/THF/H_2O 8:1:1 afforded hydroxy esters **36**/**37**, which could be separated on silica gel due to spontaneous lactonization of the desired compound **36** (→ **38**). Subsequent opening of lactone **38** with KOH in THF led to acid **28** (96%).

Bromo derivative **29a**, the second building block, was synthesized from alcohol **9** (*Scheme 6*). Protection with (*t*-Bu)$_2$$Me_2$SiCl (→ **39**) and alkylation with *tert*-butyl 2-lithioacetate gave ester **40** (57%), cleavage of the (*t*-Bu)Me_2Si group (→ **41**; 95%) and oxidation with pyridinium dichromate (PDC) in DMF [14] afforded carboxylic acid **42** (77%). Subsequent esterification with 2-mercaptopyridine 1-oxide gave the light-sensitive compound **43** which was converted into the bromo derivative **44** by irradiation with the light of a mercury lamp in the presence of $CBrCl_3$ [15]. Reduction of **44** with DIBAH (→ **45**) and protection of the aldehyde group with EtOH/pyridinium toluene-4-sulfonate (PPTS) led finally to **29a**.

Scheme 5

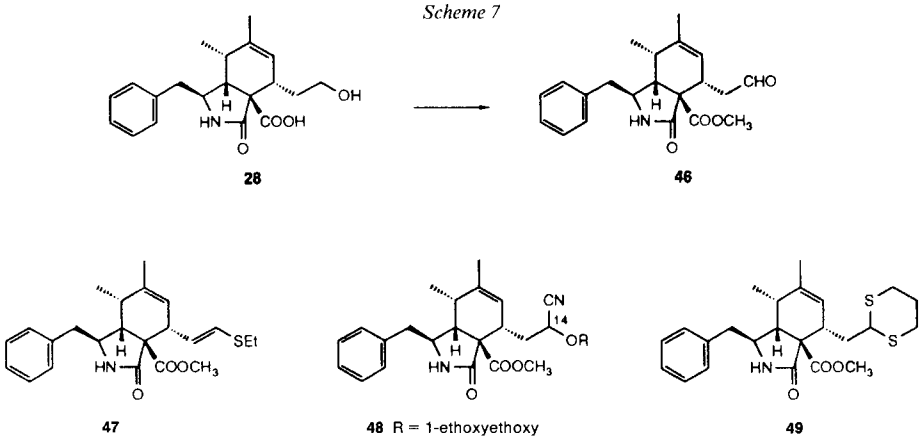


Scheme 6



To connect the synthons **28** and **29a** to an olefin of type **3**, hydroxy acid **28** was converted into formyl ester **46** (60%) by esterification and *Swern* oxidation (*Scheme 7*). Several derivatives of **46** were then synthesized with the intention to find the best conditions for the condensation step. Vinyl sulfide **47** should have been prepared with ethanethiol/$TiCl_4$, providing an intermediate which would react with the magnesium derivative of **29a** to afford the desired olefin [16], but, so far, it was impossible to obtain **47**. Later, we synthesized the derivatives **48** and **49** with 'Umpolung' of the carbonyl reactivity at C(14) [17]. Both compounds were deprotonated with lithium diisopropylamide (LDA) at C(14) and reacted with **29a** (or its iodo derivative **29b**) as electrophile. But all experiments conducted under varying conditions failed to produce the desired condensation product. Whereas, in most experiments, starting material **29a** (or **29b**) could be recovered in high yield, neither **48** or **49** nor related compounds were detected in the reaction mixture.

Scheme 7



28 **46**

47 **48** R = 1-ethoxyethoxy **49**

Conclusions. – The original goal of these investigations, the condensation of (oxoethyl)phosphonate **15** and aldehyde **5** and then of lactone **19** and thiol **22**, with subsequent macrolactonization to a precursor of proxiphomin (**7**), was not achieved. The extension of the heterocyclic building block at C(13) by one C-atom (see **28**) to minimize its steric hindrance did not enhance its reactivity. One reason might be the instability of the carbanions which are generated by the various alkylation reactions. In addition, the side-chain building block **29a** proved to be rather unreactive. Therefore, the concept of changing the point of attachment from C(13) to C(14) to extend the heterocyclic system does not provide any advantage.

Financial support of these investigations by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. H_2O- and air-sensitive reactions were carried out under Ar or N_2. THF was freshly distilled over Na-K alloy. All org. extracts were dried (Na_2SO_4) and evaporated below 40°. TLC: silica gel *60 F254* (*Merck*). Column chromatography (CC): silica gel (60–200 μm or 35–70 μm, *Chemische Fabrik Uetikon*). M.p.: *Kofler* block; corrected. $[\alpha]_D$: *Perkin-Elmer-141* polarimeter. IR Spectra (cm^{-1}): *Perkin-Elmer-781* IR spectrometer. NMR Spectra: *Varian-EM-360* (^1H, 60 MHz); *Varian-EM-390* (^1H, 90 MHz), *Bruker-WH-90* (^1H, 90 MHz; ^{13}C, 22.63 MHz), *Varian-Gemini-300* (^1H, 300 MHz; ^{13}C, 75 MHz), *Varian-VXR-400* (^1H, 400 MHz; ^{13}C, 101 MHz); chemical shifts in ppm rel. to internal Me_4Si (= 0 ppm) or to residual non-deuterated solvent. MS (*m/z* (%)): *VG-70–250* spectrometer (Cl with NH_3).

(3R)-6-Iodo-3-methylhexan-1-ol (**9**). A soln. of **8** (16.0 g, 49 mmol) and pyridinium toluene-4-sulfonate (PPTS; 1.255 g, 5 mmol) in EtOH (100 ml) was stirred for 15 h at 55°. After the addition of Na_2CO_3 (250 mg, 2.36 mmol), the mixture was evaporated, the residue dissolved in Et_2O, the soln. washed with sat. NH_4Cl soln. and brine, dried, and evaporated, and the crude product purified first by vacuum distillation (175°/0.6 Torr) and then by CC (Et_2O): 11.25 g (95%) of pure **9**. IR (film): 3340 (OH); 2960, 2930, 2875 (CH); 1060. ^1H-NMR (60 MHz, $CDCl_3$): 0.94 (*d*, *J* = 6, Me–C(3)); 1.18–2.15 (*m*, 7 H); 2.46 (br. *s*, OH); 3.18 (*t*, *J* = 7, CH_2(6)); 3.65 (*t*, *J* = 6, CH_2(1)). CI-MS: 260 ($[M + NH_4]^+$), 243 ($[M + H]^+$).

(3R)-6-Iodo-3-methylhexanal (**10**). To a soln. of oxalyl chloride (1.90 ml, 22.1 mmol) and MeI (6.2 ml, 100 mmol) CH_2Cl_2 (15 ml) cooled to −78° DMSO (3.1 ml, 43.7 mmol) in CH_2Cl_2 (6 ml) was added. After 15 min, a soln. of **9** (4.1 g, 16.9 mmol) in CH_2Cl_2 (10 ml) was added dropwise during 10 min. Stirring was continued for another 30 min at −78°, followed by the addition of Et_3N (15 ml, 107 mmol). The cooling bath was removed and H_2O (20 ml) added. The aq. layer was extracted with CH_2Cl_2 (70 ml) and the combined org. phase washed with 1M $Na_2S_2O_3$ soln. (20 ml), sat. NH_4Cl soln. (20 ml), and H_2O, dried, and evaporated: 4.0 g (99%) of pure **10** which were used without further purification. IR (film): 2960, 2930, 2880 (CH); 2780 (CO–H); 1725 (C=O). ^1H-NMR (90 MHz, $CDCl_3$): 1.00 (*d*, *J* = 6, Me–C(3)); 1.15–1.75 (*m*, 5 H); 2.35 (*dd*, *J* = 2, 6, CH_2(2)); 3.18 (*t*, *J* = 6, CH_2(6)); 9.75 (*t*, *J* = 2, H–C(1)).

(3R)-6-Iodo-1,1-dimethoxy-3-methylheptane (**11**). A soln. of **10** (4.0 g, 16.7 mmol) and PPTS (250 mg, 1 mmol) in MeOH (25 ml) was stirred under Ar for 3 h at r.t. After diluting with Et_2O (150 ml), the mixture was washed with 2M Na_2CO_3, sat. NH_4Cl soln., and H_2O (20 ml each), the combined aq. phase extracted with Et_2O (2 × 100 ml), the combined org. extract dried and evaporated and the crude product purified by vacuum distillation (120°/0.4 Torr) and CC (CH_2Cl_2): 3.64 g (75%) of **11**. IR (film): 2960, 2940, 2835 (CH); 1125; 1060; 960. ^1H-NMR (90 MHz, $CDCl_3$): 0.97 (*d*, *J* = 6, Me–C(3)); 1.15–2.05 (*m*, 7 H); 3.18 (*t*, *J* = 6, CH_2(6)); 3.32 (*s*, 2 MeO); 4.45 (*t*, *J* = 5, H–C(1)). EI-MS: 285 ($[M - H]^+$), 255, 197, 155, 127, 75.

tert-*Butyl (6R)-8,8-Dimethoxy-6-methyloctanoate* (**12**). To a soln. of $(i\text{-}Pr)_2NH$ (6.2 ml, 43.6 mmol) in dry THF (30 ml), 1.5M BuLi in hexane (29 ml) was added slowly under Ar. After the addition was complete, the yellow soln. was cooled to −78° and AcO(*t*-Bu) (5.8 ml, 43.6 mmol) added dropwise. After 1 h, a soln. of **11** (12.5 g, 43.6 mmol) and hexamethylphosphoric triamide (HMPA; 7.7 ml, 43.6 mmol) in dry THF (40 ml) was added and stirring continued for 2.5 h at −78° and 15 h at r.t. Then sat. NH_4Cl soln. (25 ml) was added, the mixture extracted with Et_2O (3 × 100 ml), and the combined org. phase washed with H_2O, dried, and evaporated. CC ($CH_2Cl_2 \rightarrow CH_2Cl_2$/MeOH) gave 8.13 g (68%) of **12** and 2.25 g (18%) of **11**. **12**: $[\alpha]_D^{20} = +3.6$ (*c* = 0.94, EtOH). IR (film): 2980, 2940, 2835 (CH); 1735 (C=O); 1150; 1130; 1060; 960. ^1H-NMR (90 MHz, $CDCl_3$): 0.90 (*d*, *J* = 6, Me–C(6)); 1.13–1.80 (*m*, 9 H); 1.44 (*s*, *t*-BuO); 2.20 (*t*, *J* = 7, CH_2(2)); 3.27 (*s*, 2 MeO); 4.44 (*t*, *J* = 6, H–C(8)). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 19.8 (Me–C(6)); 25.4, 26.4 (C(3), C(4)); 28.2 (*Me*$_3$C); 29.1 (C(6)); 35.7, 37.0, 39.7 (C(2), C(5), C(7)); 52.4, 52.7 (2 MeO); 79.9 (*Me*$_3$*C*); 103.5 (C(8)); 173.1 (C(1)).

(6R)-8,8-Dimethoxy-6-methyloctanal (**5**). To a soln. of **12** (8.13 g, 29.6 mmol) in hexane (150 ml) at −78°, 36 ml of 1M DIBAH in hexane were added slowly under Ar. After stirring at −78° for 4 h, MeOH (0.5 ml) was added and the soln. warmed to r.t., followed by the addition of H_2O (25 ml). The mixture was neutralized with 2N HCl and extracted with Et_2O (3 × 100 ml), the extract washed with H_2O, dried, and evaporated, and the crude product purified by vacuum distillation (130°/0.7 Torr): 5.74 g (96%) of **5**. Colorless oil. $[\alpha]_D^{20} = +3.4$ (*c* = 1.06, EtOH). IR (film): 2940, 2870; 2730 (CO–H); 1730 (C=O); 1130; 1060; 965. ^1H-NMR (90 MHz, $CDCl_3$): 0.94 (*d*, *J* = 6, Me–C(6)); 1.10–1.85 (*m*, 9 H); 2.45 (*td*, *J* = 2.7, CH_2(2)); 3.31 (*s*, 2 MeO); 4.45 (*t*, *J* = 6, H–C(8)); 9.74 (*t*, *J* = 2, H–C(1)). CI-MS: 220 ($[M + NH_4]^+$), 202 ($[M]^+$).

Methyl (1RS,3aRS,4SR,5RS,6SR,7RS,7aSR)-4-(Dimethoxymethyl)-6,7-dimethyl-5,6-[(1-methylethylidene)dioxy]octahydro-3-oxo-1-(phenylmethyl)-3aH-isoindole-3a-carboxylate (**14**). At r.t., **13** (2.47 g, 5.90 mmol) and PPTS (148 mg, 0.59 mmol) in MeOH (75 ml) were stirred for 21 h. After addition of CH_2Cl_2 (300 ml), the soln. was washed with brine (3 × 50 ml), dried, and evaporated. The resulting material was recrystallized ($(i\text{-}Pr)_2O$/

CH_2Cl_2): 2.428 g (89%) of pure **14**. Colorless prisms. M.p. 206–207°. IR (KBr): 3330 (NH); 3060, 3030, 2990, 2950, 2880, 2840 (CH); 1745 (C=O, ester); 1735 (C=O, lactame); 1710 (N–C=O); 1230, 1080 (C–O); 1055. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.95 (*d*, *J* = 7, Me–C(7)); 1.24 (*s*, Me–C(6)); 1.38, 1.42 (2*s*, Me_2); 2.13 (*qd*, *J* = 7, 7, H–C(7)); 2.53 (*dd*, *J* = 2, 7, H–C(7a)); 2.68 (*d*, *J* = 8, PhCH_2); 2.85 (*dd*, *J* = 8, 8.5, H–C(4)); 3.39, 3.43 (2*s*, $(MeO)_2$C); 3.57 (*td*, *J* = 2, 8, H–C(1)); 3.85 (*s*, COOMe); 3.87 (*d*, *J* = 8.5, H–C(5)); 5.27 (*d*, *J* = 8, $(MeO)_2CH$); 5.69 (br. *s*, NH); 7.02–7.40 (*m*, Ph). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 10.8 (*Me*–C(7)); 22.4 (*Me*–C(6)); 27.4, 29.0 (Me_2C); 37.3 (C(7a)); 44.5 (C(7)); 44.6 (PhCH_2); 49.8 (C(4)); 52.0 (COO*Me*); 52.4 (C(1)); 53.4, 56.0 ((*Me*O)$_2$C); 54.6 (C(3a)); 81.4 (C(6)); 81.7 (C(5)); 105.0 ((MeO)$_2$*C*); 108.3 (Me_2C); 127.1 (C_p); 128.9, 129.4 (C_m, C_o); 137.3 (c_{ipso}); 173.5, 174.4 (C(3), *C*OOMe). EI-MS: 461 (M^+), 446, 386, 372, 370, 312, 280, 248, 220, 91, 75. Anal. calc. for $C_{25}H_{35}NO_7$ (461.56): C 56.05, H 7.64, N 3.04; found: C 64.80, H 7.84, N 2.96.

*Dimethyl {2-[(1*RS,*3a*SR,*4*SR,*5*RS,*6*SR,*7*RS,*7a*SR*)-4-(Dimethoxymethyl)-6,7-dimethyl-5,6-[(1-methylethylidene)dioxy]octahydro-3-oxo-1-(phenylmethyl)-3a*H*-isoindol-3a-yl]-2-oxoethyl}phosphonate* (**15**). To dry THF (35 ml), 1.8M *t*-BuLi in pentane (35 ml) was added at −78° under Ar, followed by dimethyl methylphosphonate (7.55 ml, 70 mmol) in dry THF (10 ml). After stirring for 1 h, **14** (2.028 g, 4.39 mmol) was added with a syringe. The mixture was stirred for an additional 7 h at −78°, then warmed to r.t. within 4 h. After addition of Et_2O/CH_2Cl_2 2:1 (150 ml), the mixture was washed with sat. NH_4Cl soln. (4 × 50 ml) and H_2O (50 ml), dried, and evaporated. Recrystallization ((i-Pr)$_2$O(CH_2Cl_2)) gave 2.078 g (86%) of **15**. Hexagonal prisms. M.p. 182–183°. IR (KBr): 3200; 3100; 3070, 3030 (CH); 2990, 2960, 2940, 2880, 2860 (CH); 1720 (C=O, ketone); 1700 (C=O, lactame); 1610; 1270; 1250; 1110; 1055. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.89 (*d*, *J* = 7, Me–C(7)); 1.22 (*s*, Me–C(6)); 1.36, 1.40 (2*s*, Me_2C); 2.02 (*qd*, *J* = 7, 7, H–C(7)); 2.48–2.80 (*m*, H–C(7a), H–C(4), PhCH_2); 3.34, 3.88 (2*d*, *J*(H,P) = 11, $(MeO)_2$PO); 3.83 (*d*, *J* = 8, H–C(5)); 5.23 (*d*, *J* = 8, $(MeO)_2CH$); 6.41 (br. *s*, NH); 7.18–7.30 (*m*, PH). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 11.0 (*Me*–C(7)); 22.6 (*Me*–C(6)); 27.5, 29.1 (Me_2C); 36.8 (*d*, *J*(C,P) = 141, COCH_2PO); 37.9 (C(3a)); 44.1 (PhCH_2); 45.5, 46.4 (C(7), C(4)); 52.6, 53.3 (*d*, *J*(C,P) = 7, $(MeO)_2$PO); 53.3, 56.0 ((*Me*O)$_2$C); 54.0 (C(1)); 61.8 (*d*, *J*(C,P) = 6, C(3a)); 81.4 (C(6)); 81.8 (C(5)); 105.6 ((MeO)$_2$*C*); 108.5 (Me_2C); 127.0 (C_p); 128.9, 129.4 (C_m, C_o) = 137.7 (C_{ipso}); 173.9 (C(3)); 198.8 (*d*, *J* = (C,P) = 6, *C*OCH$_2$PO). FAB-MS: 592 ([*M* + K]$^+$), 576 ([*M* + Na]$^+$), 554 ([*M* + H]$^+$). Anal. calc. for $C_{27}H_{40}NO_9P$ (553.59): C 58.57, H 7.28, N 2.53; found: C 58.37, H 7.53, N 2.37.

*(1*R,*3a*S,*4*S,*5*R,6S,*7*R,*7a*S,*8′*R,*2′*E*)- and (1*S,*3a*R,*4*R,*5*S,*6*R,*7*S,*7a*R,*8′*R,*2′*E*)-3a-(10,10-Dimethoxy-8-methyldec-2-en-1-oyl)-6,7-dimethyl-5,6-[(1-methylethylidene)dioxy]-3-oxooctahydro-1-(phenylmethyl)-4*H*-isoindole-4-carbaldehyde Dimethyl Acetal* (**16**; 2 diastereoisomers). A soln. of **15** (2.078 g, 3.75 mmol) in diglyme (60 ml) was treated with NaH (45% in mineral oil; 203 mg, 3.8 mmol) and stirred at r.t. After 7 h, a soln. of **5** (1.5 g, 7.5 mmol) in diglyme (10 ml) was added. After stirring for an additional h at r.t., the mixture was heated to 60° for 18 h. The mixture was transferred into CH_2Cl_2/Et_2O 1:4 (300 ml) and washed with H_2O (7 × 25 ml). The aq. layers were extracted with CH_2Cl_2/Et_2O 1:4 (2 × 100 ml) and the combined org. layers dried and evaporated (50°/0.5 Torr): 3.2 g of a light yellow oil. CC (CH_2Cl_2/MeOH 97.5:2.5) afforded 1.21 g (51%) of **16** as a colorless oil oil and 310 mg (20%) of **5**. **16**: IR (film): 3300 (NH); 3090, 3070, 3030, 2990, 2940, 2860, 2840 (CH_2); 1705 (C=O, lactame); 1690 (C=O, ketone); 1630; 1610; 1120; 1055; 975. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.91 (*d*, *J* = 7, Me–C(7)); 0.95 (*d*, *J* = 5, Me–C(8′)); 1.14–1.68 (*m*, CH_2(5′), CH_2(6′), CH_2(7′), CH(8′), CH_2(9′)); 1.26 (*s*, Me–C(6)); 1.40, 1.45 (2*s*, Me_2C); 2.10 (*qd*, *J* = 7, 7, H–C(7)); 2.22–2.42 (*m*, CH_2(4′)); 2.48 (*dd*, *J* = 2, 7, H–C(7a)); 2.62 (*d*, *J* = 8, PhCH_2); 2.88 (*dd*, *J* = 8, 8, H–C(4)); 3.33 (*s*, 2 $(MeO)_2$C); 3.56 (*td*, *J* = 2, 8, H–C(1)); 3.95 (*d*, *J* = 8, H–C(5)); 4.47 (*t*, *J* = 5, H–C(10′)); 5.34 (*d*, *J* = 8, $(MeO_2)CH$–C(4)); 5.87 (br. *s*, NH); 6.52 (br. *d*, *J* = 15, H–C(2′)); 7.02 (*td*, *J* = 6, 15, H–C(3′)); 7.05–7.37 (*m*, PH). ^{13}C-NMR (22.63 MHz, $CDCl_3$): 10.9 (*Me*–C(7)); 19.9 (*Me*–C(8′)); 22.4 (*Me*–C(6)); 26.6 (C(6′)); 27.4, 29.0 (Me_2C); 28.8 (C(5′)); 29.1 (C(8′)); 32.6 (C(4′)); 37.1 (C(7′)); 37.7 (C(7a)); 39.8 (C(9′)); 44.5 (PhCH_2); 45.5 (C(7)); 49.0 (C(4)); 52.0, 52.5, 52.6, 53.5 (2 (*Me*O)$_2$C); 55.3 (C(1)); 59.8 (C(3a)); 81.5 (C(6)); 81.7 (C(5)); 103.5 (C(10′)); 105.0 (*C*H–C(4)); 108.2 (Me_2C); 125.9 (C(2′)); 127.1 (C_p); 128.9, 129.3 (C_m, C_o); 137.3 (C_{ipso}); 143.3 (C(3′)); 175.6 (C(3)); 197.6 (C(1′)). FAB-MS: 629 ([*M*]$^+$).

*(1*R,*3a*S,*4*S,*5*R,*6*S,*7*R,*7a*S,*8′*R,*2′*E*)- and (1*S,*3a*R,4R,*5*S,*6*R,*7*S,*7a*R,*8′*R,*2′*E*)-3a-(9-Formyl-8-methylnon-2-en-1-oyl)-6,7-dimethyl-5,6-[(1-methylethylidene)dioxy]octahydro-3-oxo-1-(phenylmethyl)-4*H*-isoindole-4-carbaldehyde* (**17**; 2 diastereoisomers). To a soln. of **16** (160 mg, 0.254 mmol) in acetone (10 ml), PPTS (10 mg, 0.058 mmol) was added. After stirring for 28 h at r.t., the mixture was diluted with Et_2O (50 ml) and washed with sat. $KHCO_3$ soln. (10 ml) and brine (4 × 10 ml). The aq. layers were extracted with Et_2O (2 × 50 ml), and the combined org. phase was dried and evaporated: 129 mg (94%) of **17**. Colorless foam which was used without further purification. IR (CCl_4): 3440 (NH); 3080, 3030 (arom. and olef. CH); 2990, 2940, 2860 (aliph. CH); 1735 (C=O, ester); 1715 (C=O, aldehyde); 1690 (C=O, ketone); 1225. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.92 (*d*, *J* = 7, Me–C(7)); 0.95 (*d*, *J* = 6, Me–C(8′)); 1.10–1.77 (*m*, CH_2(5′), CH_2(6′), CH_2(7′), CH(8′)); 1.26 (*s*, Me–C(6)); 1.40 (*s*, Me_2C); 1.89–2.76 (*m*, H–C(4), H–C(5), PhCH_2, CH_2(4′), CH_2(9′)); 3.11 (*dd*, *J* = 1, 10, H–C(7a)); 3.56–3.78 (*m*, H–C(3));

4.34 (*d*, *J* = 10, H–C(7)); 5.85 (br. *s*, NH); 6.58 (br. *d*, *J* = 14, H–C(2')); 7.00–7.40 (*m*, H–C(3'), Ph); 9.73 (*t*, *J* = 2, H–C(10')); 9.89 (*t*, *J* = 1, OHC–C(4)). EI-MS: 537 (M^+), 522 ([M – Me]$^+$), 508 ([M – CHO]$^+$), 446 ([M – C_7H_7]).

*(3*R*)-7-(1,3-Dioxolan-2-yl)-3-methyloctane-1-thiol* (**22**). A mixture of **20** (1.23 g, 4.62 mmol) and thiourea (352 mg, 4.62 mmol) in EtOH (1.25 ml) was refluxed for 4 h. After cooling to r.t., 2.5N NaOH (2.8 ml) was added and the mixture refluxed for additonal 2 h. The two layers were separated, the org. layer was dried and evaporated: 720 mg (71%) of a light yellow, pure (TLC, NMR) oil which was used without further purification. IR (film): 2920, 2870 (CH); 1150, 1130 (C–O–C); 1030; 950. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.90 (*d*, *J* = 6, Me–C(3)); 1.10–1.85 (*m*, 12 H); 2.50 (*t*, *J* = 7, CH_2(1)); 3.80–4.05 (*AA'BB'*, CH_2(4'), CH_2(5')); 4.85 (*t*, *J* = 5, H–C(2')). EI-MS: 434 (10, [M_2 – 2 H]$^+$), 123 (128), 95 (7), 81 (15), 73 (100, [$C_3H_5O_2$]$^+$), 69 (12), 55 (20), 45 (20), 41 (14).

*{3-[(*tert*-Butyl)dimethylsilyloxy]propyl}triphenylphosphonium Bromide* (**31**). To 3-bromopropan-1-ol (3.70 ml, 42.6 mmol) in dry CH_2Cl_2 (140 ml), (*t*-Bu)Me_2SiCl (8.10 g, 53.7 mmol), Et_3N (9.0 ml, 64.4 mmol), and 4-(dimethylamino)pyridine (525 mg, 4.3 mmol) were added at r.t. After stirring for 24 h, the mixture was diluted with more CH_2Cl_2 (50 ml) and washed with cold 1N H_2SO_4, sat. Na_2CO_3 soln., sat. NH_4Cl soln., and brine. Drying and evaporation afforded a red oil which was purified by CC (pentane/Et_2O 2:1). The resulting colorless oil (10.62 g, 98%) was dissolved in dry benzene (30 ml) and PPh_3 (12.1 g, 46 mmol) added. After refluxing for 72 h under Ar and evaporation the colorless, hygroscopic foam was dried *in vacuo*. CC (CH_2Cl_2/MeOH 20:1) yielded 14.93 g (69%) of **31**. Colorless foam. IR (CH_2Cl_2): 3035 (CH); 2950, 2930, 2855 (CH); 1585 (C–C); 1440 (C–P); 1110 (Si–O–C); 835 (*Me*Si). ^{1}H-NMR (400 MHz, $CDCl_3$ (= 7.27 ppm)): –0.08 (*s*, Me_2Si); 0.75 (*s*, *t*-BuSi); 1.77–1.83 (*m*, CH_2(2)); 3.64–3.77 (*m*, CH_2(1), CH_2(3)); 7.58–7.75 (*m*, 3 Ph). ^{13}C-NMR (101 MHz, $CDCl_3$ (= 77.0 ppm)): –5.6 (Me_2Si); 17.9 (Me_3*C*Si); 18.8 (*d*, *J*(C,P) = 53, C(1)); 25.7 (*Me*$_3$CSi); 25.8 (*d*, *J*(C,P) = 4, C(2)); 61.5 (*d*, *J*(C,P) = 17, C(3)); 118.0 (*d*, *J*(C,P) = 86, C_{ipso}); 130.3 (*d*, *J*(C,P) = 13, C_m); 133.4 (*d*, *J*(C,P) = 10, C_o); 134.9 (*d*, *J*(C,P) = 3, C_p). FAB-MS: 494 (4), 436 (41), 435 (100, [M – Br]$^+$), 289 (10), 275 (7), 262 (7), 199 (7), 183 (4), 91 (4, [C_7H_7]$^+$), 73 (20).

*(2*E*,4*E*)-7-[(*tert*-Butyl)dimethylsilyloxy]-3-methylhepta-2,4-diene* (**33**). To a suspension of **31** (6.98 g, 13.54 mmol) in abs. THF (22 ml) and dry Et_2O (13.5 ml) under Ar at –78°, 1.5M BuLi in hexane (10.0 ml) was added. After 20 min, (*E*)-2-methylbut-2-enal (= tiglic aldehyde; (**32**); 1.32 ml, 13.54 mmol) in dry Et_2O (9 ml) was added dropwise and the mixture stirred at –78° for 15 min and at –20° for another 30 min. BuLi soln. (9.4 ml) was then added and the mixture stirred at –15° for 10 min. After the addition of 4M HCl in Et_2O (3.8 ml) and 3.8 g (20.3 mmol) of KO(*t*-Bu) (as 1:1 complex with *t*-BuOH), stirring was continued for 2.5 h at r.t. yielding a brownish suspension which was centrifuged. The supernatant was washed with H_2O, dried, and evaporated: 5.6 g of a red oil. CC (CH_2Cl_2) led to a 3:1 mixture of the (2*E*,4*E*)- and (2*E*,4*Z*)-isomer. Separation by spinning-band distillation yielded 1.14 g (35%) of **33**. Colorless oil. B.p. 128–132°/15 Torr. IR (film): 3035, 3020, 3000 (CH); 2960, 2930, 2860 (CH); 1255 (SiC); 1100 (SiO–C); 835 (*Me*Si); 770 (*Me*Si). ^{1}H-NMR (400 MHz, $CDCl_3$ (= 7.24 ppm)): –0.05 (*s*, Me_2Si); 0.81 (*s*, *t*-BuSi); 1.61 (*d*, *J* = 7.0, Me(1)); 1.62 (*s*, Me–C(3)); 2.18–2.25 (*m*, CH_2(6)); 3.56 (*t*, *J* = 7.0, CH_2(7)); 5.37 (*q*, *J* = 6.5, H–C(2)); 5.44 (*td*, *J* = 15.5, 7.0, H–C(5)); 6.01 (*d*, *J* = 15.5, H–C(4)). ^{13}C-NMR (101 MHz, $CDCl_3$ (= 77.0 ppm)): –5.5 (Me_2Si); 11.7 (C(1)); 13.4 (*Me*–C(3)); 18.2 (Me_3*C*Si); 25.8 (*Me*$_3$CSi); 36.4 (C(6)); 63.3 (C(7)); 123.3 (C(2)); 125.1 (C(5)); 134.6 (C(3)); 136.8 (C(4)). CI-MS: 241 (3, [M + H]$^+$), 200 (5), 183 (9), 109 (100).

*Methyl (1*RS*,3a*SR*,4*RS*,7*RS*,7a*SR*)-4-{2-[(*tert*-Butyl)dimethylsilyloxy]ethyl}-1,2,3,4,7,7a-hexahydro-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3a*H*-isoindole-3a-carboxylate* (**34**) *and Methyl (1*RS*,3a*SR*,4*RS*,7*SR*,7a*SR*)-7-{2-[(*tert*-Butyl)dimethylsilyloxy]methyl}-1,2,3,4,7,7a-hexahydro-4,5-dimethyl-3-oxo-1-(phenylmethyl)-3a*H*-isoindole-3a-carboxylate* (**35**). For 72 h, **30** (3.97 g, 10.0 mmol) and **33** (2.88 g, 12.0 mmol) in *o*-xylene (26 ml) were heated to 160° in a sealed vessel. After cooling to r.t. and evaporation, the yellow oil (7.8 g) was submitted to CC (CH_2Cl_2/AcOEt): 1.87 g (40%) of **34**/**35** 65:35. Colorless foam. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.01, 0.03 (2*s*, Me_2Si); 0.86, 0.88 (2*s*, *t*-BuSi); 1.13, 1.34 (2*d*, *J* = 7.0, Me–C(7) resp. Me–C(4)); 1.55–1.75 (*m*, CH_2CH_2O); 1.71, 1.73 (2*s*, Me–C(6) resp. Me–C(5)); 1.80–2.00 (*m*, H–C(7) resp. H–C(4)); 2.50–2.75 (*m*, 1 H of PhCH_2, H–C(4) resp. H–C(7). H–C(7a)); 2.80–2.95 (*m*, 1 H of PhCH_2); 3.20–3.25, 3.30–3.38 (2*m*, H–C(1)); 3.60–3.75 (*m*, CH_2CH_2O); 3.74, 3.77 (2*s*, COOMe); 5.48, 5.51 (br. *s*, H–C(5) resp. H–C(6)); 5.66, 5.75 (br. *s*, NH); 7.13–7.33 (*m*, Ph). EI-MS: 471 (13, [M]$^+$), 414 (100, [M – C_4H_9]$^+$), 380 (16, [M – C_7H_7]$^+$), 288 (61), 280 (48), 216 (11), 193 (17), 109 (33), 91 (63, [C_7H_7]$^+$), 73 (55).

*Methyl (1*RS*,3a*SR*,4*RS*,7*SR*,7a*SR*)-1,2,3,4,7,7a-Hexahydro-7-(2'-hydroxyethyl)-4,5-dimethyl-3-oxo-1-(phenylmethyl)-3a*H*-isoindole-3a-carboxylate* (**37**) *and (1*RS*,3a*SR*,4*RS*,7*RS*,7a*SR*)-4-Ethyl-1,2,3,4,7,7a-hexahydro-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3a*H*-isoindole-3a,2'-carbolactone* (**38**). At 60°, **34**/**35** 65:35 (2.16 g, 4.58 mmol) was stirred in AcOH/H_2O/THF 8:1:1 (40 ml) for 2 h. After neutralization with sat. $NaHCO_3$ soln., the mixture was extracted with Et_2O (1 × 100 ml and 2 × 50 ml). The org. layers were washed with H_2O (40 ml) and

brine (40 ml), dried, and evaporated: 1.90 g of a light yellow oil which were transferred onto a silica-gel column. After 15 h, the products were eluted wtih CH_2Cl_2/MeOH 4:1→1:1: 475 mg (32%) of **38** (recrystallized in CH_2Cl_2/pentane) and 410 mg (25%) of **37**.

Data for **38**: M.p. 187–190.5°. IR (KBr): 3375 (NH); 3050, 3020, 2965, 2925 (CH); 1700 (br., C=O, lactone, lactame); 1450; 1400; 1240; 1190; 1130; 1060. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.07 (*d*, *J* = 7.0, Me–C(7)); 1.76 (br. *s*, Me–C(6)); 1.89–1.98 (*m*, 1 H, CH_2CH$_2$OCO); 2.41–2.51 (*m*, 1 H of CH$_2$CH$_2$OCO, H–C(7)); 2.86–3.01 (*ABX*, J_{AB} = 13.5, PhCH_2); 3.08–3.23 (*m*, H–C(7a), H–C(4)); 3.29–3.34 (*m*, H–C(1)); 4.47 (*ddd*, *J* = 11.0, 11.0, 6.5, 1 H of CH$_2$CH$_2$OCO); 4.80 (*ddd*, *J* = 11.0, 7.5, 2.0, 1 H of CH$_2$CH$_2$OCO); 5.53 (br. *s*, H–C(5)); 7.20–7.35 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$ (= 77.0 ppm)): 13.1 (*Me*–C(7)); 19.6 (*Me*–C(6)); 21.9 (*C*H$_2$CH$_2$OCO); 35.0, 35.7 (C(7a), C(4)); 44.1 (PhCH$_2$); 49.4 (C(7)); 55.2 (C(1)); 58.2 (C(3a)); 70.1 (CH$_2$*C*H$_2$OCO); 125.0 (C(5)); 127.0 (C_p); 129.0, 129.4 (C_m, C_o); 137.9 (C_{ipso}); 141.3 (C(6)); 171.5, 172.8 (*C*O–C(3a), C(3)). EI-MS: 325 (1, M^+), 234 (100, $[M - C_7H_7]^+$), 206 (28), 189 (5), 119 (5), 91 (32, $[C_7H_7]^+$), 77 (7, $[C_6H_5]^+$).

Data for **37**: IR (CH_2Cl_2): 3680, 3610, 3410 (OH, NH); 3040, 2980, 2960 (CH); 1730 (C=O, ester); 1700 (C=O, lactam); 1600; 1430; 1235; 1030. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.36 (*d*, *J* = 10.5, Me–C(4)); 1.61–1.80 (*m*, CH_2CH$_2$OH, OH); 1.73 (br. *s*, Me–C(5)); 2.36–2.45 (*m*, H–C(7)); 2.58–2.66 (*m*, H–C(4), 1 H of PhCH_2); 3.35–3.41 (*m*, H–C(1)); 3.65–3.84 (*m*, CH$_2$CH$_2$OH); 3.80 (*s*, COOMe); 5.50 (br. *s*, H–C(6)); 5.62 (br. *s*, NH); 7.15–7.35 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.3 (*Me*–C(4)); 19.7 (Me–C(5)); 33.9 (C(7a)); 34.4 (*C*H$_2$CH$_2$OH); 37.4 (C(4)); 44.7 (PhCH$_2$); 52.5 (COO*Me*); 53.0 (C(7)); 55.9 (C(1)); 61.4 (C(3)); 61.5 (C(3a)); 126.5 (C(6)); 127.5 (C_p); 129.4, 129.7 (C_m, C_o); 137.9 (C_{ipso}); 141.3 (C(5)); 173.9, 174.3 (C(3), *C*OOMe). EI-MS: 357 (38, M^+), 325 (4, $[M - MeOH]^+$), 298 (40, $[M - COOMe]^+$), 266 (99, $[M - C_7H_7]^+$), 234 (54), 206 (61), 119 (32), 91 (100, $[C_7H_7]^+$), 77 (15, $[C_6H_5]^+$).

*(1*RS,*3a*SR,*4*RS,*7*RS,*7a*SR*)-1,2,3,4,7,7a-Hexahydro-4-(hydroxyethyl)-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3a*H*-isoindole-3a-carboxylic Acid* (**28**). To a soln. of **38** (101 mg, 0.31 mmol) in THF (4 ml) aq. 2M KOH (170 µl) was added, (→colorless precipitate). After 1 h, the mixture was evaporated and the residue transferred onto a *Dowex-50-WX8* column with a little EtOH and eluted with H_2O. Evaporation yielded 102 mg (96%) of **28**. Colorless powder. IR (KBr): 3470 (NH); 3200 (br., OH); 3090, 3060, 3030, 2965, 2920, 2875 (CH); 1715 (C=O, acid); 1685 (C=O, lactame); 1490; 1265; 1120. ^{1}H-NMR (300 MHz, CD_3OD): 0.65 (*d*, *J* = 7.5, Me–C(7)); 1.72 (*s*, Me–C(6)); 1.83–1.91 (*m*, H–C(7a)); 2.24–2.39 (*m*, H–C(7)); 2.60–2.65 (*m*, H–C(4)); 2.91–2.99 (*m*, PhCH_2); 3.10–3.25 (*m*, 1 H, CH_2CH$_2$OH); 3.30–3.43 (*m*, 1 H, CH_2CH$_2$OH); 3.50–3.70 (*m*, H–C(1)); 4.51 (*ddd*, *J* = 11.5, 11.5, 5.0, 1 H, CH$_2$CH_2OH); 4.67 (*ddd*, *J* = 11.0, 7.0, 1.5, 1 H, CH$_2$CH$_2$OH); 5.50 (br. *s*, H–C(5)); 7.18–7.35 (*m*, Ph). FAB-MS: 344 (100, $[M + H]^+$), 218 (33), 200 (30).

*(3*R*)-1-[(*tert*-Butyl)dimethylsilyloxy]-6-iodo-3-methylhexane* (**39**). A soln. of **9** (11.25 g, 46.5 mmol), (*t*-Bu)Me$_2$SiCl (8.7 g, 58.0 mmol), Et$_3$N (10.0 ml, 70.0 mmol), and 4-(dimethylamino)pyridine (611 mg, 5.0 mmol) in CH_2Cl_2 (150 ml) was stirred at r.t. for 20 h. After dilution with CH_2Cl_2 (50 ml), the soln. was washed with 1N H_2SO_4, 2N Na_2CO_3, sat. NH_4Cl soln., and brine, dried, and evaporated and the yellow oil purified by distillation (200°/0.5 Torr): 13.7 g (83%) of pure **39**. IR (film): 2960, 2930, 2860 (CH); 1255; 1100. ^{1}H-NMR (60 MHz, $CDCl_3$): 0.10 (*s*, Me$_2$Si); 0.92–1.10 (br. *s*, *t*-BuSi, Me–C(3)); 1.20–2.20 (*m*, 7 H); 3.19 (*t*, *J* = 7, CH$_2$(6)); 3.68 (*t*, *J* = 6, CH$_2$(1)). CI-MS: 374 ($[M + NH_4]^+$), 357 ($[M + H]^+$).

tert-*Butyl (6*R*)-6-Methyl-8-[(*tert*-butyl)dimethylsilyloxy]octanoate* (**40**). To (i-Pr)$_2$NH (2.11 ml, 15.0 mmol) in dry THF (10 ml) at 0°, 1.5M BuLi in hexane (9.9 ml) was added dropwise. After the addition was complete, the mixture was cooled to −78° and AcO(*t*-Bu) (2.0 ml, 15.0 mmol) added. After 1 h stirring, a soln. of **39** (4.46 g, 10.0 mmol) and HMPT (1.77 ml, 10.0 mmol) in dry THF (5 ml) was added slowly. Stirring was continued for 4 h at −78°, then the mixture was warmed to r.t. and stirred for 11 h. After addition of sat. NH_4Cl soln. (25 ml), the mixture was extracted with Et_2O (3 × 100 ml) and the extract washed with sat. NH_4Cl soln. and brine, dried, and evaporated. After CC (CH_2Cl_2), 1.95 g (57%) of **40** were obtained. Colorless oil. $[\alpha]_D^{25}$ = +2.3 (*c* = 1.45, $CHCl_3$). IR (film): 2960, 2935, 2860 (CH); 1735 (C=O); 1255. ^{1}H-NMR (90 MHz, $CDCl_3$): 0.05 (*s*, Me$_2$Si): 0.85–0.96 (br. *s*, *t*-BuSi, Me–C(6)); 1.11–1.72 (*m*, 9 H); 1.46 (*s*, *t*-BuO); 2.22 (*t*, *J* = 7, CH$_2$(2)); 3.65 (*t*, *J* = 6, CH$_2$(8)). CI-MS: 362 ($[M + NH_4]^+$), 345 ($[M + H]^+$).

tert-*Butyl (6*R*)-8-Hydroxy-6-methyloctanoate* (**41**). A soln. of **40** (4.30 g, 12.5 mmol) in conc. AcOH/H_2O/THF 3:1:1 (36 ml) was stirred for 1 h. Sat. $NaHCO_3$ soln. (20 ml) was added and the mixture extracted with Et_2O (3 × 100 ml). Drying and evaporation afforded 2.7 g (95%) of **41**. Colorless oil. $[\alpha]_D^{24}$ = +2.5 (*c* = 2.35, $CHCl_3$). IR (film): 3400 (br. OH); 2960, 2935, 2860 (CH); 1735 (C=O); 1150. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89 (*d*, *J* = 6.5, Me–C(6)); 1.16–1.62 (*m*, 9 H and OH); 1.43 (*s*, *t*-Bu); 2.20 (*t*, *J* = 7.5, CH$_2$(2)); 3.66 (*td*, *J* = 6.0, 6.0, CH$_2$(8)). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.3 (*Me*–C(6)); 25.1, 26.2 (C(3), C(4)); 27.9 (*Me*$_3$C); 29.1 (C(6)); 35.4 (C(5)); 36.5 (C(2)); 39.7 (C(7)); 61.0 (C(8)); 80.0 (Me$_3$*C*); 173.3 (C(1)). CI-MS: 248 (25, $[M + NH_4]^+$), 231 (6, $[M + H]^+$), 192 (99), 175 (10), 57 (100, $[C_4H_9]^+$).

*8-(*tert*-Butyl) 1-Hydrogen (3*R*)-3-Methyloctanedioate* (**42**). A soln. of **41** (2.40 g, 10.4 mmol) and PDC (19.6 g, 52.1 mmol) in dry DMF (40 ml) was stirred under N_2 for 4 h at r.t. The mixture was poured into H_2O (300 ml) and extracted with Et_2O (3 × 150 ml). The combined org. layers were washed with H_2O (2 × 100 ml), dried, and evaporated. After CC (pentane/Et_2O 7:3), 1.95 (77%) of **42** were obtained. $[\alpha]_D^{24} = +4.7$ ($c = 1.65$, $CHCl_3$). IR (film): 3500–3000 (OH, acid); 2960, 2930, 2860 (CH); 1730 (C=O, ester); 1710 (C=O, acid); 1150. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*d*, $J = 6.5$, Me–C(3)); 1.17–1.62 (*m*, 7 H); 1.45 (*s*, *t*-Bu); 2.22 (*t*, $J = 7.5$, CH_2(7)); 1.95–2.38 (*m*, CH_2(2)). ^{13}C-NMR (75 MHz, $CDCl_3$): 19.4 (*Me*–C(3)); 24.9, 26.1 (C(5), C(6)); 28.0 (*Me*$_3$C); 29.8 (C(3)); 35.3 (C(4)); 36.1 (C(7)); 41.5 (C(2)); 80.1 (Me$_3$*C*); 173.6 (C(8)); 179.3 (C(1)). FAB-MS: 245 (19, $[M + H]^+$), 189 (65), 171 (74, $[M - (t\text{-BuO})]^+$), 157 (4), 137 (16), 83 (7), 57 (100, $[C_4H_9]^+$), 41 (17).

tert*-Butyl (6*R*)-7-Bromo-6-methylheptanoate* (**44**). To **42** (0.66 g, 2.40 mmol) in dry THF (20 ml), ClCOO-(i-Bu) (0.30 ml, 2.40 mmol) was added dropwise at −15°. After 10 min, a soln. of 2-mercaptopyridine 1-oxide (0.46 g, 0.30 mmol) and Et_3N (0.68 ml, 3.60 mmol) in dry THF (10 ml) was added, keeping the temp. at −15°. Stirring was continued for 1 h, then the mixture filtered in the cold, evaporated and dissolved in 40 ml of O_2-free[3]) $CBrCl_3$. The yellow soln. was irradiated for 45 min with a Hg lamp, then evaporated and purified by CC (pentane/Et_2O 95:5): 0.56 g (84%) of **44**. Colorless oil. $[\alpha]_D^{24} = +0.8$ ($c = 2.18$, $CHCl_3$). IR (film): 2960, 2930, 2860 (CH); 1730 (C=O); 1155. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*d*, $J = 7.0$, Me–C(6)); 1.23–1.81 (*m*, 7 H); 1.45 (*s*, *t*-BuO); 2.23 (*t*, $J = 7.5$, CH_2(2)); 3.30–3.42 (*ABX*, $J_{AB} = 10.0$, CH_2(7)). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.8 (*Me*–C(6)); 25.2, 26.4 (C(3), C(4)); 28.2 (*Me*$_3$C); 34.6 (C(5)); 35.1 (C(6)); 35.6 (C(2)); 41.5 (C(7)); 80.3 (Me$_3$*C*); 173.7 (C(1)). FAB-MS: 281 (5), 279 (6, $[M + H]^+$), 235 (21), 223 (23), 207 (7), 205 (8, $[M - (t\text{-BuO})]^+$), 97 (8), 57 (100, $[C_4H_9]^+$), 51 (20), 41 (31).

*(6*R*)-7-Bromo-6-methylheptanal* (**45**). To **44** (137 mg, 0.49 mmol) in dry CH_2Cl_2 (2.5 ml), 1.0M DIBAH in hexane (0.60 ml) was added over 10 min at −78° under Ar. After stirring for 3.5 h at −78°, MeOH (0.1 ml) was added, the cooling bath removed, and the mixture warmed to r.t. After the addition of H_2O (0.5 ml), the mixture was extracted with Et_2O (3 × 10 ml), the extract washed with H_2O (5 ml), dried, and evaporated, and the resulting oil purified by CC (CH_2Cl_2): 90 mg (89%) of **45**. Colorless oil. $[\alpha]_D^{21} = +2.0$ ($c = 4.98$, $CHCl_3$). IR (film): 2960, 2930, 2860 (CH); 1720 (C=O); 1455; 1375; 1230. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*d*, $J = 6.5$, Me–C(6)); 1.22–1.51 (*m*, 4 H); 1.59–1.72 (*m*, 2 H); 1.76–1.84 (*m*, H–C(6)); 2.45 (*td*, $J = 7.0$, 1.5, CH_2(2)); 3.31–3.41 (*ABX*, $J_{AB} = 10.0$, CH_2(7)); 9.77 (*t*, $J = 1.5$, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.7 (*Me*–C(6)); 22.1 (C(3)); 26.4 (C(4)); 34.5 (C(5)); 35.0 (C(6)); 41.2 (C(7)); 43.7 (C(2)); 202.5 (CHO). EI-MS: 180 (1), 178 (1, $[M - CO]^+$), 164 (29), 162 (30, $[M - CHO - Me]^+$), 123 (10), 121 (11), 109 (19), 95 (11), 83 (45), 69 (35), 55 (63), 41 (100).

*(6*R*)-7-Bromo-1,1-diethoxy-6-methylheptane* (**29a**). At 40–50°, **45** (192 mg, 0.927 mmol) and PPTS (25 mg, 0.1 mmol) in abs. EtOH (5 ml) were stirred for 40 min. After dilution with Et_2O (50 ml), the mixture was washed with sat. Na_2CO_3 soln. (2 × 15 ml) and brine, dried, and evaporated. CC (CH_2Cl_2) afforded 214 mg (82%) of **29a**. Colorless oil. $[\alpha]_D^{21} = +0.6$ ($c = 8.37$, $CHCl_3$). IR (film): 2980, 2930, 2870 (CH); 1450; 1370; 1130 (C–O–C); 1065 (C–O). ^{1}H-NMR (300 MHz, $CDCl_3$): 1.01 (*d*, $J = 6.5$, Me–C(6)); 1.21 (*t*, $J = 7.0$, 2 *Me*CH$_2$O); 1.24–1.44 (*m*, 6 H); 1.59–1.63 (*m*, 2 H); 1.70–1.80 (*m*, H–C(6)); 3.29–3.42 (*ABX*, $J_{AB} = 10.0$, 2 H–C(7)); 3.48 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.51 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.63 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.66 (*q*, $J = 7.0$, MeC*H*$_2$O); 4.48 (*t*, $J = 5.5$, H–C(1)). ^{13}C-NMR (75 MHz, $CDCl_3$ (= 77.0 ppm)): 15.3 (2 *Me*CH$_2$O); 18.7 (*Me*–C(6)); 24.8 (C(3)); 26.7 (C(4)); 33.5, 34.7 (C(5), C(2)); 35.1 (C(6)); 41.4 (C(7)); 60.9 (2 *MeCH*$_2$*O*); 102.8 (*C(1)*). EI-MS: 237 (22), 235 (23, $[M - OEt]^+$), 109 (25), 103 (100, $[CH(OEt)_2]^+$), 83 (6), 75 (25), 47 (29).

*(6*R*)-1,1-Diethoxy-7-iodo-6-methylheptane* (**29b**). A soln. of dry NaI (300 mg, 2.0 mmol) in dry acetone (1 ml) was added to **29a** (140 mg, 0.50 mmol) in dry acetone (0.3 ml). After stirring for 24 h at r.t., the mixture was evaporated, suspended in Et_2O (15 ml), filtered, and washed with H_2O (3 × 5 ml; containing 1 crystal of $Na_2S_2O_3$). The combined aq. phase was extracted with Et_2O (5 ml), the combined org. phase dried and evaporated, and the yellow oil purified by CC (CH_2Cl_2): 135 mg (82%) of **29b**. Colorless oil. $[\alpha]_D^{22} = -1.2$ ($c = 10.7$, $CHCl_3$). IR (film): 2970, 2930, 2860 (aliph. CH); 1450; 1375; 1340; 1190; 1125 (C–O–C); 1060 (C–O). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.97 (*d*, $J = 6.5$, Me–C(6)); 1.21 (*t*, $J = 7.0$, 2 *Me*CH$_2$O); 1.26–1.46 (*m*, 7 H); 1.58–1.70 (*m*, 2 H); 3.13–3.25 (*ABX*, $J_{AB} = 9.5$, 2 H–C(7)); 3.47 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.50 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.62 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 3.66 (*q*, $J = 7.0$, 1 H, MeC*H*$_2$O); 4.48 (*t*, $J = 5.5$, H–C(1)). ^{13}C-NMR (75 MHz, $CDCl_3$): 15.3 (2 *Me*CH$_2$O); 17.7 (C(7)); 20.5 (C(*Me*–C(2))); 24.7 (C(3)); 26.7 (C(4)); 33.5 (C(5)); 34.6 (C(6)); 36.3 (C(2)); 60.9 (2 MeCH$_2$O); 102.8 (C(1)). FAB-MS: 327 (1, $[M - H]^+$), 283 (100, $[M - OEt]^+$), 109 (48), 103 (27).

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[3]) N_2, which was passed through 5% benzene-1,2,3-triol in 45% KOH, was bubbled through the solvent for 15 min.

Methyl (1RS,3aSR,4RS,7RS,7aSR)-4-(Formylmethyl)-1,2,3,4,7,7a-hexahydro-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3aH-isoindole-3a-carboxylate (**46**). A soln. of diazomethane in Et_2O was added dropwise to a soln. of **28** (84 mg, 0.246 mmol) in MeOH (4 ml) until a slight yellow color persisted. Then, the mixture was evaporated in the cold and the solid (80 mg) dissolved in dry CH_2Cl_2 (1.4 ml). In a separate flask, dry DMSO (53 µl, 0.740 mmol) was added to a soln. of oxalyl choride (32 µl, 0.368 mmol) in dry CH_2Cl_2 (2 ml) under Ar ar −78°. After 2 min, the previously prepared soln. was added within 5 min at −78°, and stirring was continued for 20 min. Then Et_3N (170 µl) was added, and after 5 min, the mixture was warmed to r.t. and diluted with 50 ml of CH_2Cl_2. The soln. was washed with 1N H_2SO_4 (2 × 15 ml), sat $NaHCO_3$ soln. (15 ml), and brine (15 ml), dried, and evaporated. CC (CH_2Cl_2/MeOH 98:2) gave 52 mg (60%) of **46**. Colorless foam. IR (KBr): 3200 (br., NH); 3030 (arom. CH); 2960, 2920, 2850 (aliph. CH); 1740 (C=O, ester); 1720 (C=O, aldehyde); 1690 (C=O, lactame); 1450; 1430; 1310; 1230; 1120. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.16 (*d*, *J* = 7.5, Me–C(7)); 1.76 (*s*, Me–C(6)); 2.48–2.60 (*m*, H–C(7)); 2.65 (*dd*, *J* = 4.5, 4.5, H–C(7a)); 2.69 (*dd*, *J* = 9.5, 13.5, 1 H, PhC*H*$_2$); 2.89–3.10 (*m*, 1 H of PhC*H*$_2$, CH_2–C(4)); 3.15–3.22 (*m*, H–C(4)); 3.24–3.32 (*m*, H–C(1)); 3.76 (*s*, COOMe); 5.31 (br. *s*, H–C(5)); 6.04 (br. *s*, NH); 7.15–7.35 (*m*, Ph); 9.79 (*s*, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.0 (*Me*–C(7)); 20.2 (*Me*–C(6)); 32.8 (C(7a)); 34.3 (C(7)); 44.6, 45.2 (Ph*C*H$_2$, *C*H$_2$–C(4)); 52.9 (C(4)); 53.0 (COO*Me*); 56.1 (C(1)); 59.6 (C(3a)); 126.0 (C(5)); 127.0 (C_p); 128.9, 129.2 (C_o, C_m); 137.2 (C_{ipso}); 139.8 (C(6)); 172.6, 173.4 (C(3), *C*OOMe); 201.8 (CHO). FAB-MS: 356 (100, $[M + H]^+$), 340 (5), 326 (11), 296 (8), 232 (75), 200 (73), 105 (14), 91 (94, $[C_7H_7]^+$), 77 (18, $[C_6H_5]^+$).

Methyl (1RS,3aSR,4RS,7RS,7aSR)-4-[2-Cyano-2-(1-ethoxyethoxy)ethyl]-1,2,3,4,7,7a-hexahydro-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3aH-isoindole-3a-carboxylate (**48**). To **46** (25 mg, 0.07 mmol) in dry THF (0.5 ml), 38% $NaHSO_3$ soln. (21 µl, 0.07 mmol) was added. After stirring for 15 min at r.t., 2 drops of H_2O were added, followed by NaCN (4.5 mg, 0.09 mmol). Stirring was continued for 2.5 h, then the mixture diluted with 15 ml of CH_2Cl_2, the soln. washed with H_2O (2 × 5 ml), dried, and evaporated, and the resulting foam purified by CC (CH_2Cl_2/AcOEt 97:3): 20 mg (0.052 mmol) of 2 diastereoisomeric cyanohydrins. To a soln. of this mixture (16 mg), in dry THF (0.5 ml), ethyl vinyl ether (10 µl, 0.1 mmol), and TsOH (2 mg, 0.01 mmol) were added, and the soln. was stirred at r.t. After 2 h, CH_2Cl_2 (15 ml) was added, the mixture washed with sat. $NaHSO_3$ soln. (5 ml) and H_2O (5 ml), dried, and evaporated, and the resulting oil purified by CC (CH_2Cl_2→CH_2Cl_2/MeOH 98:2): 14 mg (74%) of **48** (diastereoisomer mixture). IR (CCl_4): 3200 (br., NH); 3020 (arom. CH); 2970, 2920 (aliph. CH); 1735 (C=O, ester); 1700 (C=O, lactame); 1430; 1380; 1230; 1130 (C–O–C); 1080 (C–O); 1050. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.16–1.22 (*m*, Me–C(7), *Me*CH$_2$O); 1.33, 1.38 (2*d*, *J* = 7.0, MeCH$_2$OCH(*Me*)O); 1.78 (*s*, Me–C(6)); 2.22–2.30 (*m*, 1 H, CH_2–C(4)); 2.38–2.50 (*m*, 1 H of CH_2–C(4), H–C(7)); 2.62 (*dd*, *J* = 4.0, 4.0, H–C(7a)); 2.69 (*dd*, *J* = 13.0, 3.0, 1 H, PhC*H*$_2$); 2.72–2.85 (*m*, H–C(4)); 2.90 (*dd*, *J* = 13.0, 4.0, 1 H, PhC*H*$_2$); 3.20–3.30 (*m*, H–C(1)); 3.40–3.70 (*m*, MeC*H*$_2$O); 3.80, 3.81 (2*s*, COOMe); 4.40–4.44, 4.52–4.58 (2*m*, MeCH$_2$OC*H*(Me)O); 4.81–4.85, 4.92–4.96 (2*m*, *CH*(OR)CN); 5.51 (br. *s*, H–C(5)); 5.62 (br. *s*, NH); 7.14–7.36 (*m*, Ph). FAB-MS: 455 (6, $[M + H]^+$), 383 (69), 365 (11), 291 (3), 232 (20), 200 (17), 91 (24, $[C_7H_7]^+$), 73 (100, $[C_4H_9O]^+$), 45 (67, $[C_2H_5O]^+$).

Methyl (1RS,3aSR,4RS,7RS,7aSR)-4-[(1,3-Dithian-2-yl)methyl]-1,2,3,4,7,7a-hexahydro-6,7-dimethyl-3-oxo-1-(phenylmethyl)-3aH-isoindole-3a-carboxylate (**49**). At r.t., propane-1,3-dithiol (14 µl, 0.14 mmol) was added to **46** (46 mg, 0.13 mmol) in $CHCl_3$ (0.5 ml) at r.t. After stirring for 1 h, the mixture was cooled to 0°, TsOH (9.5 mg, 0.05 mmol) added, the mixture allowed to warm to r.t., and stirring continued for 18 h. After dilution with CH_2Cl_2 (10 ml), the soln. was washed with H_2O (2 × 5 ml), cold 7% KOH soln. (3 × 5 ml), and H_2O (2 × 5 ml), dried and evaporated and the colorless foam purified by CC (CH_2Cl_2/MeOH 99:1): 45 mg (78%) of **50**. Colorless foam. IR (KBr): 3300–3200 (NH); 3040 (arom. CH); 2960, 2930, 2870 (aliph. CH); 1735 (C=O, ester); 1690 (C=O, lactame); 1460; 1430; 1305; 1235; 1110. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.13 (*d*, *J* = 7.0, Me–C(7)); 1.77 (*s*, Me–C(6)); 1.82–2.00 (*m*, H_a–C(5′)); 2.05–2.14 (*m*, H_b–C(5′)); 2.20 (*dd*, *J* = 14.0, 4.0, 1 H, CH_2–C(4)); 2.31 (*ddd*, *J* = 2.5, 10.0, 14.0, 1 H, CH_2–C(4)); 2.45–2.58 (*m*, H–C(7)); 2.60 (*dd*, *J* = 4.5, 4.5, H–C(7a)); 2.67 (*dd*, *J* = 9.0, 13.5, 1 H, PhC*H*$_2$); 2.75 (*dd*, *J* = 3.0, 14.0, 1 H, PhC*H*$_2$); 2.81–2.91 (*m*, 2 H–C(4′), 2 H–C(6′)); 2.95–3.02 (*m*, H–C(4)); 3.22–3.27 (*m*, H–C(1)); 3.79 (*s*, COOMe); 4.04 (*dd*, *J* = 4.5, 10.0, H–C(2′)); 5.49 (br. *s*, H–C(5)); 5.80 (br. *s*, NH); 7.14–7.34 (*m*, Ph). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.9 (*Me*–C(7)); 20.3 (*Me*–C(6)); 26.1 (C(5′)); 29.7, 30.3 (C(4′), C(6′)); 34.5 (C(7a)); 36.0 (*C*H$_2$–C(4)); 37.1 (C(7)); 44.9 (Ph*C*H$_2$); 46.7 (C(2′)); 52.8 (C(4)); 53.7 (COO*Me*); 55.8 (C(1)); 60.4 (C(3a)); 126.4, 127.0 (C(5), C_p); 128.9; 129.2 (C_o, C_m); 137.4 (C_{ipso}); 139.8 (C(6)); 172.9, 173.2 (C(3), *C*OOMe). EI-MS: 445 (22, M^+), 386 (4, $[M - COOMe]^+$), 354 (7, $[M - C_7H_7]^+$), 339 (26), 326 (6, $[M - C_4H_7S_2]^+$), 313 (8), 280 (45), 278 (42), 254 (35), 232 (14), 200 (49), 193 (51), 119 (76), 107 (20), 91 (100, $[C_7H_7]^+$).

REFERENCES

[1] M. Matthes, Ch. Tamm, *Helv. Chim. Acta* **1991,** *74,* 1585.

[2] T. Schmidlin, D. Wallach, Ch. Tamm, *Helv. Chim. Acta* **1984,** *67,* 1998.

[3] T. Schmidlin, Dissertation, Basel, 1979.

[4] W.S. Wadsworth, Jr., W.D. Emmons, *J. Am. Chem. Soc.* **1961,** *83,* 1733.

[5] J.E. McMurry, M.P. Fleming, K.L. Kees, L.K. Krepski, *J. Org. Chem.* **1978,** *43,* 3255; J.E. McMurry, *Acc. Chem. Res.* **1983,** *16,* 405; J.E. McMurry, *Chem. Rev.* **1989,** *89,* 1513.

[6] D. Wallach, I.G. Csendes, P.E. Burckhardt, T. Schmidlin, Ch. Tamm, *Helv. Chim. Acta* **1984,** *67,* 1989.

[7] A.J. Mancuso, S.-L. Huang, D. Swern, *J. Org. Chem.* **1978,** *42,* 2480; T.T. Tidwell, *Synthesis* **1990,** 857.

[8] R.J. Cregge, J.L. Herrmann, C.S. Lee, J.E. Richmann, R.H. Schlessinger, *Tetrahedron Lett.* **1973,** 2425.

[9] L.I. Zakharkin, I.M. Khorlina, *Tetrahedron Lett.* **1962,** 619; E. Winterfeldt, *Synthesis* **1975,** 617; J.S. Cha, *Org. Prep. Proc. Int.* **1989,** *21,* 451.

[10] L. Ramberg, B. Bäcklund, *Ark. Kemi Mineral. Geol.* **1940,** *13A,* No. 27, 50 pp.; *Chem. Abstr.* **1940,** *34,* 4725; L.A. Paquette, *Org. React.* **1977,** *25,* 1.

[11] N. Node, K. Nishide, M. Ochiai, K. Fuji, E. Fujita, *J. Org. Chem.* **1981,** *46,* 5163.

[12] T. Schmidlin, P.E. Burckhardt, N. Waespe-Šarčević, Ch. Tamm, *Helv. Chim. Acta* **1983,** *66,* 450.

[13] T. Schmidlin, Ch. Tamm, *Helv. Chim. Acta* **1980,** *63,* 121.

[14] E.J. Corey, G. Schmidt, *Tetrahedron Lett.* **1979,** 399.

[15] D.H.R. Barton, D. Crich, W.B. Motherwell, *Tetrahedron Lett.* **1983,** *24,* 4979; D.H.R. Barton, Y. Herv, P. Poitier, J. Thierry, *J. Am. Chem. Soc., Chem. Commun.* **1984,** 1298.

[16] H. Okamura, M. Miura, H. Takei, *Tetrahedron Lett.* **1979,** 43; H. Okamura, H. Takei, *ibid.* **1979,** 3425; E. Wenkert, T.W. Ferreira, E.L. Michelotti, *J. Chem. Soc., Chem. Commun.* **1979,** 637; T. Mukaiyama, K. Saigo, *Chem. Lett.* **1973,** 479.

[17] D. Seebach, M. Kolb, *Chem. Ind.* **1974,** 687; D. Seebach, *Angew. Chem.* **1979,** *91,* 259; D. Seebach, *Synthesis* **1969,** 17; D. Seebach, E.J. Corey, *J. Org. Chem.* **1975,** *40,* 231; G. Stork, L. Maldonado, *J. Am. Chem. Soc.* **1971,** *93,* 5286; E. Pierson, M. Giella, M. Tishler, *ibid.* **1948,** *70,* 1450; E. Aufderhaar, J.E. Baldwin, D.H.R. Barton, D.J. Faulkner, M. Slaytor, *J. Chem. Soc. C* **1971,** 2175; G. Stork, T. Takahashi, *J. Am. Chem. Soc.* **1977,** *99,* 1275; T. Takahashi, H. Ikeda, J. Tsuji, *Tetrahedron Lett.* **1981,** *22,* 1363; T. Takahashi, I. Minami, J. Tsuji, *ibid.* **1981,** *22,* 2651; T. Takahashi, T. Nagashima, H. Ikeda, J. Tsuji, *ibid.* **1982,** *23,* 4361; S. Hünig, G. Wehner, *Synthesis* **1975,** 180; *ibid.* **1975,** 391; U. Herteinstein, S. Hünig, M. Öller, *ibid.* **1976,** 416; K. Deuchert, U. Hertenstein, S. Hünig, *ibid.* **1973,** 777; A.I. Meyers, D.L. Comins, D.M. Roland, R. Henning, K. Shimizu, *J. Am. Chem. Soc.* **1979,** *101,* 7104.