Regioselective Reduction and Ring Cleavage of Polycyclic Barbituric Acid Analogues Derived from Intramolecular Hetero-Diels–Alder Reactions

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Dedicated to Professor Richard Neidlein on the occasion of his 70th birthday

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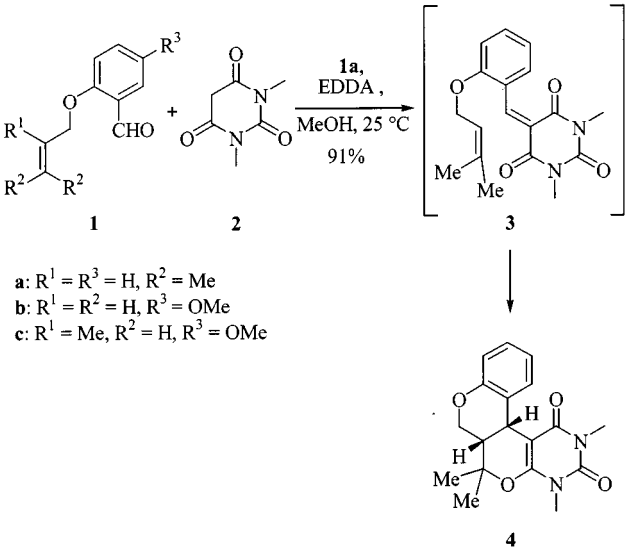
The annulated and bridged dihydropyrans **6**–**8** obtained by a domino-Knoevenagel-hetero-Diels–Alder reaction with *N*,*N*′-dimethylbarbituric acid were reduced with excess DIBAL-H at –78 °C to give the corresponding 3-desoxy derivatives, which were then hydrolyzed to the lactones **14**–**16** with HCl. Compounds **15** and **16** were further reduced to the corresponding lactols. Elimination finally yielded the new functionalized heterocycles **18** and **20**.

Introduction

The hetero-Diels–Alder reaction of 1-oxa-1,3-butadienes is a valuable method for the construction of dihydropyrans, a structural element which is found in many natural products.[1,2] We have shown that electronically activated 1-oxa-1,3-butadienes can easily be formed in situ by condensation of an aldehyde with a 1,3-dicarbonyl compound to allow a cycloaddition even at room temperature. The use of aromatic aldehydes or α,β-unsaturated aldehydes containing a dienophile moiety give *cis*-annulated and, with aliphatic aldehydes, *trans*-annulated dihydropyrans highly stereoselectively.[3–8] Moreover, bridged dihydropyrans can also be obtained by changing the substitution pattern at the dienophile moiety and thus altering the coefficients.[9]

The scope of this domino-Knoevenagel-hetero-Diels–Alder reaction is very broad;[10–13] it is also suitable in combinatorial chemistry for the preparation of substance libraries with high diversity either in the solid phase or in solution, thus allowing the efficient preparation of complex molecules starting from simple substrates. For these transformations any aromatic or aliphatic aldehyde, as well as any 1,3-dicarbonyl compound or hetero analogue such as pyrazolones and isoxazolones, may be employed; thus, in the reaction of the aromatic aldehyde **1a** with *N*,*N*′-dimethylbarbituric acid (**2**) at room temperature a 1-oxa-1,3-butadiene **3** is formed in situ which undergoes a hetero-Diels–Alder-reaction with inverse electron demand to give the annulated tetracycle **4** exclusively in 91% yield (Scheme 1).

N,*N*′-dimethylbarbituric acid (**2**) is a very suitable 1,3-dicarbonyl compound in these domino reactions due to its high reactivity and the stability of the formed products; moreover, the barbituric acid moiety is a pharmacophoric group. However, further transformations of the cycloadducts were limited. We have therefore been looking for quite a long time for a feasible procedure to convert these stable compounds into reactive functionalized derivatives. In this paper we describe our protocol for the facile reduction and ring cleavage of annulated and bridged polycyclic barbituric acid derivatives.



Scheme 1. Domino-Knoevenagel-hetero-Diels–Alder reaction leading to annulated heterocycles

Results and Discussion

For our investigations towards the cleavage of the barbituric acid moiety *N*,*N*′-dimethylpyrimidinetrione (**5**) and the dimethylpyrimidinediones **6**–**8** were prepared (Scheme 2). The benzylidene dimethylbarbituric acid derivative **5** was obtained at 20 °C by a Knoevenagel condensation of 2-allyloxy-5-methoxy-benzaldehyde (**1b**) and *N*,*N*′-dimethylbarbituric acid (**2**) in 93% yield. The compound is stable at

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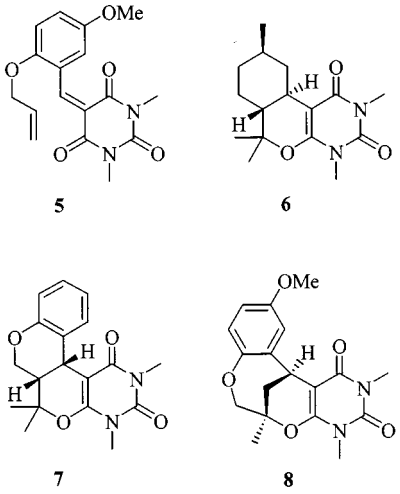
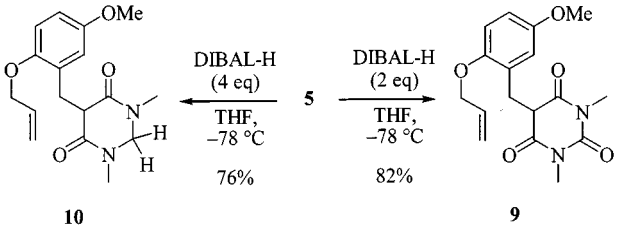
this temperature due to the high HOMO of its dienophile moiety relative to **3**. The aromatic and aliphatic annulated tetracycles **6** and **7** were prepared according to published procedures.[7] The bridged heterocycle **8** was obtained by a domino-Knoevenagel-hetero-Diels–Alder reaction of 2-(2-methylallyloxy)-5-methoxybenzaldehyde (**1c**) and *N*,*N*′-dimethylbarbituric acid (**2**) in 91% yield.



Scheme 2. Barbituric acid derivatives **5**–**8**

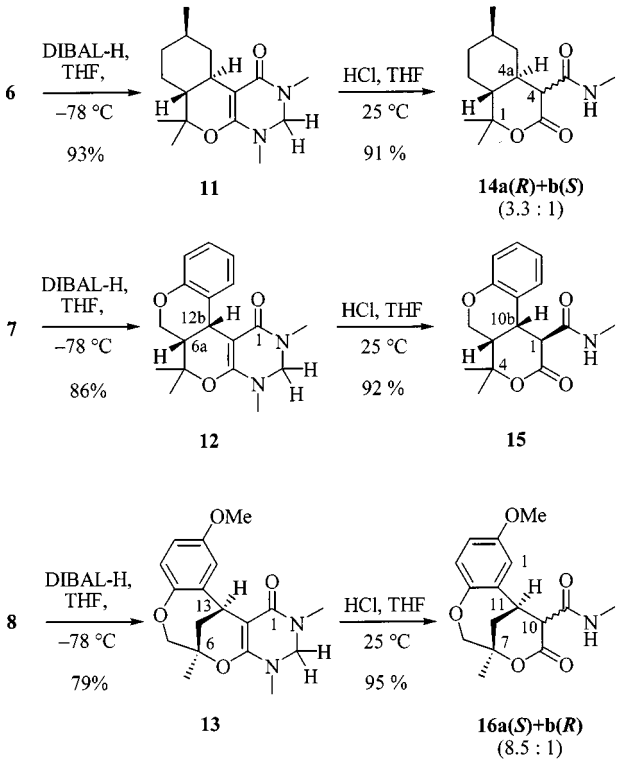
In our first attempts to cleave the barbituric acid moiety in **5**–**8** we employed lithium borohydride, lithium triethylborohydride and PtO_2/H_2 in analogy to published procedures.[14,15] However, either no reaction or decomposition was observed. Furthermore, oxidation with potassium permanganate or ozone again did not lead to the desired products. Treatment of **5** with two equivalents of DIBAL-H exclusively furnished a Michael-type hydrogen transfer to form **9** in 82% yield. In contrast, the use of four equivalents of DIBAL-H led not only to a reduction of the benzylidene 1,3-dicarbonyl scaffold but also to a regioselective reduction of one of the three carbonyl groups of the barbituric acid moiety to give **10** in 76% yield (Scheme 3).



Scheme 3. Reduction of **5**

Similarly, treatment of the annulated and bridged barbituric acid derivatives **6**–**8** with four equivalents of DIBAL-H in dry THF at −78 °C gave the desired 3-desoxy compounds **11**–**13** in a clean reaction in 93%, 86% and 79% yield, respectively (Scheme 4).

The reduction occurred completely regioselectively at the carbonyl group of the urea moiety without the formation of any by-products.



Scheme 4. Regioselective reduction and hydrolysis of barbituric acid derivatives **6**–**8**

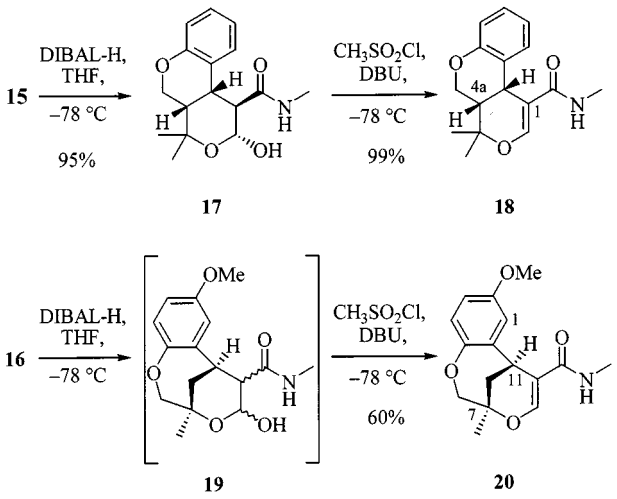
The obtained products which correspond to aminals of formaldehyde can easily be hydrolysed with an excess of 1 N HCl (≈ 10 equiv.) in tetrahydrofuran in excellent yield to give the lactones **14**–**16** containing a carboxamide moiety (Scheme 4). The hydrolysis of **11**–**13** with catalytic amounts of acid (HCl in methanol and tetrahydrofuran, camphorsulfonic acid in methanol, acetic acid in methanol) was generally less suitable since large amounts of decomposed material was formed.

In the hydrolysis step a new stereogenic centre is introduced and thus a mixture of two diastereomers may be formed; however, **15** was obtained as a single diastereomer. In contrast, **14** and **16** were indeed formed as mixtures of two diastereomers (**14a:14b** = 3.3:1; **16a:16b** = 8.5:1). The diastereomers **16a** and **16b** could not be separated, whereas **14a** was obtained diastereomerically pure by slow crystallization from dichloromethane/pentane.

The whole cleavage procedure can also be performed as a one-pot transformation. Thus, treatment of the cycloadducts **6**–**8** with four equivalents of DIBAL-H followed by the successive addition of 2 N HCl gave the desired lactones **14a**, **15** and **16a+b** in 57% (after fractional crystallization), 97% and 95% yield, respectively.

The obtained products can be further functionalized to give novel heterocyclic systems by a fresh reduction with DIBAL-H followed by an elimination step. Thus, reaction of lactone **15** with two equivalents of DIBAL-H provided **17** in 95% yield diastereoselectively. The *trans* arrangement of the substituents at C-1 and C-2 is confirmed by the comparatively large vicinal coupling (J = 8.5 Hz) of 1-H and 2-H. Treatment of **17** with methanesulfonyl chloride in the

presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) then led to the dihydropyran **18** in nearly quantitative yield; the mixture **16a/b** was transformed to give the diastereomerically pure **20** via **19** in 60% yield in a similar manner (Scheme 5).



Scheme 5. Synthesis of the dihydropyrans **18** and **20**

The structures of the newly formed compounds were mainly determined by NMR spectroscopy. As examples, the spectra of the heterocycles **12**, **14a**, **15**, **16a**, and **20** are discussed below. In the ^{1}H NMR spectrum of **12** the signals for the diastereotopic protons at C-3 are found at δ = 3.08 and δ = 3.70 with a geminal coupling of J = 10.0 Hz. The proton 6a-H resonates as a ddd at δ = 1.50 with J = 8.1, 6.5 and 3.8 Hz. The coupling constant of J = 6.5 Hz for the signal for 12b-H at δ = 4.39 is in agreement with the *cis*-annulation of the two oxacycles. From the doublet for 1-H at δ = 3.39 with J = 8.0 Hz in the ^{1}H NMR spectrum of **15** a *trans* orientation of 1-H and 10b-H can be deduced. In the ^{1}H NMR spectrum of **14a**, 4-H resonates at δ = 2.88 with J = 9.5 Hz indicating a *trans* orientation of 4-H and 4a-H. The structure assignment of **16a** with a *trans* orientation of 10-H and 11-H is based on the doublet for 10-H at δ = 3.40 with a coupling of J = 1.0 Hz. In the ^{1}H NMR spectrum of **20** the diastereotopic protons of the methano bridge (C-12) resonate at δ = 2.01 and δ = 2.13 with a large geminal coupling constant of J = 14.1 Hz. For the aminomethyl group a doublet at δ = 2.72 with J = 5.0 Hz is observed. In the ^{13}C NMR spectrum of **20** the quaternary C-7 resonates at δ = 78.5 and thus verifies the bridged structure.

Conclusion

The domino-Knoevenagel-hetero-Diels−Alder reaction of any type of aldehyde containing a dienophile moiety with barbituric acid is a powerful procedure for the synthesis of annulated and bridged dihydropyrans. However, the obtained products are rather stable and were not very suitable for further transformations. With the new protocol for a regioselective reduction of one of the carbonyl moieties in barbituric acid derivatives using an excess of DIBAL-H and successive hydrolysis with HCl an excellent access to lactones was developed which can be further functionalized.

Experimental Section

General: All reactions were performed under nitrogen or argon atmosphere in flame-dried flasks, and the reactants were introduced by syringe. All solvents were dried by standard methods. All reagents obtained from commercial sources were used without further purification. − Thin-layer chromatography was performed on precoated silica gel SIL G/UV$_{254}$ plates (Macherey−Nagel GmbH & Co. KG), and silica gel 32−63 (0.032−0.064 mm; Macherey−Nagel GmbH & Co. KG) was used for column chromatography. − UV/Vis spectra were measured in CH_3CN with a Perkin−Elmer Lambda 2 spectrometer. − IR spectra were recorded as KBr pellets or as films with a Bruker IFS 25 spectrometer. − ^{1}H and ^{13}C NMR spectra were recorded with a Varian XL 200, VXR 200 and VXR 500 or a Bruker AMX-300 with tetramethylsilane (TMS) as internal standard in [D]chloroform, [D$_6$]benzene or [D$_6$]DMSO. Multiplicities of ^{13}C NMR peaks were determined with the APT pulse sequence. − Mass spectra were measured at 70 eV with a Varian MAT 311A and high-resolution mass spectra with a Varian MAT 731 instrument. − Melting points are uncorrected and were measured with a Mettler FP 61. The following abbreviations are used in the text: EA = ethyl acetate, PE = petroleum ether, EDDA = ethylenediammonium diacetate.

5-[2-Allyloxy-5-methoxybenzylidene]-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione (5): A solution of 2-allyloxy-5-methoxybenzaldehyde (**1b**; 3.27 g, 17.0 mmol) and EDDA (0.03 g) in CH_2Cl_2 (120 mL) was treated for 4 h with *N*,*N*′-dimethylbarbituric acid (**2**; 2.34 g, 15.0 mmol) at room temperature. After removal of the solvent in vacuo the yellow oily residue was crystallized from methanol to afford **5** (4.51 g, 13.6 mmol, 93% yield). − m.p. 134 °C − IR (KBr): $\tilde{\nu}$ = 3100, 3014, 2954, 2920 (C−H), 1670 (C=O), 1574 (C=C), 1470, 1418 (CH_2, CH_3) cm^{-1}. − UV (CH_3CN): λ_{max} (lg ε) = 226 nm (4.12), 257 (3.99), 317 (3.91), 409 (3.80). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, N−CH_3), 3.43 (s, 3 H, N−CH_3), 3.82 (s, 3 H, 5′-OCH_3), 4.60 (dt, J = 5.1, 1.5 Hz, 2 H, 1′′-H_2), 5.30 (dq, J = 10.6, 1.5 Hz, 1 H, 3′′-H), 5.42 (dq, J = 17.4, 1.5 Hz, 1 H, 3′′-H), 6.04 (m, 1 H, 2′′-H), 6.88 (d, J = 9.2 Hz, 1 H, 3′-H), 7.06 (dd, J = 9.2, 3.0 Hz, 1 H, 4′-H), 7.77 (d, J = 3.0 Hz, 1 H, 6′-H), 8.92 (s, 1-H, α-H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.4 (N−CH_3), 28.9 (N−CH_3), 55.8 (5′-OCH_3), 69.8 (C-1′′), 112.8 (C-3′), 116.8 (C-4′), 117.4 (C-5), 117.7 (C-3′′), 121.0 (C-6′), 122.7 (C-1′), 132.7 (C-2′′), 151.4 (C=O), 152.5 (C-5′), 153.4 (C-2′), 154.2 (α-C), 160.4 (C=O), 162.5 (C=O). − MS (70 eV, EI): *m*/*z* (%) = 330 (26) [M$^+$], 175 (100) [M$^+$ − $C_6H_7N_2O_3$]. − $C_{17}H_{18}N_2O_5$ (330.3): calcd. C 61.81, H 5.49; found C 61.88, H 5.57.

(6*S*,13*R*)-(±)-6,7-Dihydro-6,13-methano-11-methoxy-2,4,6-trimethyl-13*H*-[1,4]benzodioxonino[5,6-*d*]pyrimidine-1,3(2*H*,4*H*)-dione (8): A solution of 5-methoxy-2-(2-methylallyloxy)benzaldehyde (**1c**; 1.78 g, 8.62 mmol), 30 mg of ethylenediammonium diacetate (EDDA) and *N*,*N*′-dimethylbarbituric acid (**2**; 1.30 g, 8.30 mmol) in 60 mL CH_2Cl_2 was stirred for 4 h at room temperature. After removal of the solvent in vacuo the yellow oily residue was crystallized from methanol to afford 5-[5-methoxy-2-(2-methylallyloxy)benzylidene]-1,3-dimethylpyrimidine-2,4,6(1*H*,3*H*,5*H*)trione (2.77 g, 8.04 mmol, 97% yield) as yellow-orange crystals. The pyrimidinetrione was dissolved in 500 mL toluene and refluxed for 47 h. Removal of the solvent and purification by column chromato-

graphy (EA:PE = 2:1) yielded **8** (2.60 g, 7.55 mmol, 91%) as a colorless solid. – R_f = 0.35 (EA:PE = 2:1). – m.p. 195 °C – IR (KBr): $\tilde{\nu}$ = 3044, 2942, 2914 (C–H), 1700 (C=O), 1642 (C=C), 1494, 1456 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 200 nm (4.68), 223 (4.14), 264 (4.00). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.42 (s, 3 H, 6-CH_3), 2.11 (dd, *J* = 14.3, 2.1 Hz, 1 H, 14-H), 2.20 (ddd, *J* = 14.3, 5.5, 2.4 Hz, 1 H, 14-H), 3.25 (s, 3 H, N–CH_3), 3.42 (s, 3 H, N–CH_3), 3.58 (d, *J* = 13.1 Hz, 1 H, 7-H_{ax}), 3.79 (s, 3 H, OCH_3), 3.94 (dd, *J* = 5.5, 2.0 Hz, 1 H, 13-H), 4.26 (dd, *J* = 13.1, 2.4 Hz, 1 H, 7-H_{eq}), 6.65 (dd, *J* = 9.0, 3.3 Hz, 1 H, 10-H), 6.84 (d, *J* = 9.0 Hz, 1 H, 9-H), 6.98 (d, *J* = 3.3 Hz, 1 H, 12-H). – ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 24.4 (6-CH_3), 27.8 (N–CH_3), 28.7 (N–CH_3), 33.9 (C-13), 35.7 (C-14), 55.5 (O–CH_3), 78.0 (C-7), 81.7 (C-6), 88.1 (C-13a), 113.2 (C-10), 115.6 (C-9), 122.1 (C-12), 136.1 (C-12a), 151.1 (C-11), 151.8 (C-3), 156.0 (C-4a), 156.4 (C-8a), 162.2 (C-1). – MS (70 eV, EI): *m/z* (%) = 344 (100) [M^+]. – $C_{18}H_{20}N_2O_5$ (344.4): calcd. C 62.78, H 5.85; found C 62.62, H 5.99.

5-[2-Allyloxy-5-methoxybenzyl]-1,3-dimethylpyrimidine-2,4,6-(1*H*,3*H*,5*H*)-trione (9): A solution of benzylidene (**5**; 0.53 g, 1.60 mmol) in dry THF (80 mL) was treated with DIBAL-H (4.27 mL, 6.40 mmol, 1.5 M in toluene) at −78 °C. The crude product was purified by column chromatography (EA:PE = 1:2) to give **9** (0.43 g, 1.30 mmol, 82% yield). – R_f = 0.34 (EA:PE = 1:2). – IR (KBr): $\tilde{\nu}$ = 3006, 2956, 2934 (C–H), 1698 (C=O), 1674, 1502 (C=C), 1456 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 225 nm (4.11), 295 (3.53). – ^1H NMR (200 MHz, $CDCl_3$): δ = 3.13 (s, 6 H, 2 × N–CH_3), 3.43 (d, *J* = 5.5 Hz, 2 H, Ar–CH_2), 3.72 (s, 3 H, 5′-OCH_3), 3.81 (t, *J* = 5.5 Hz, 1 H, 5-H), 4.42 (dt, *J* = 4.9, 1.5 Hz, 2 H, 1′′-H_2), 5.27 (dq, *J* = 10.5, 1.6 Hz, 1 H, 3′′-H), 5.38 (dq, *J* = 17.0, 1.6 Hz, 1 H, 3′′-H), 6.01 (ddt, *J* = 17.0, 10.5, 4.9 Hz, 1 H, 2′′-H), 6.61 (m_c, 1 H, 4′-H), 6.74 (m_c, 2 H, 3′-, 6′-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.3 (N–CH_3), 33.4 (Ar–CH_2), 50.3 (C-5), 55.6 (5′-OCH_3), 69.7 (C-1′′), 112.8 (C-4′), 113.5 (C-3′), 116.9 (C-6′), 117.2 (C-3′′), 124.9 (C-1′), 133.2 (C-2′′), 150.6 (C-5′), 151.6 (C-2), 153.4 (C-2′), 168.3 (C-4/C-6). – MS (70 eV, EI): *m/z* (%) = 332 (51) [M^+], 291 (100) [$M^+ - C_3H_5$], 203 (83) [$M^+ - C_3H_7 - CO(NCH_3)_2$]. – $C_{17}H_{20}N_2O_4$ (332.4): calcd. C 61.44, H 6.07; found C 61.39, H 6.05.

General Procedure I for the Preparation of the *N,N′*-Dimethylpyrimidinedione 10 and the *N,N′*-Dimethylpyrimidinones 11–13: To a solution of 3.50 mmol of the *N,N′*-dimethylpyrimidinedione **10** and the *N,N′*-dimethylpyrimidinones **11–13** in dry THF (40–80 mL) was added DIBAL-H (4 equiv., 1.5 M in toluene) at −78 °C. The reaction mixture was then allowed to warm to room temperature overnight and the reaction was quenched by careful hydrolysis with a saturated aqueous solution of potassium sodium tartrate. The organic layer was separated, the aqueous phase extracted with ethyl acetate and the combined organic phases were washed with brine, dried over Na_2SO_4 and concentrated in vacuo.

5-[2-Allyloxy-5-methoxybenzyl]-2,3-dihydro-1,3-dimethylpyrimidine-4,6(1*H*,5*H*)-dione (10): A solution of **5** (0.50 g, 1.51 mmol) in dry THF (80 mL) was treated with DIBAL-H (4.03 mL, 6.04 mmol, 1.5 M in toluene) at −78 °C according to the general procedure I. The crude product was purified by column chromatography (EA) to give **10** (0.37 g, 1.14 mmol, 76% yield). – R_f = 0.17 (EA). – IR (KBr): $\tilde{\nu}$ = 2936 (C–H), 1690 (C=O), 1664, 1500 (C=C), 1462 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 197 nm (4.68), 291 (3.54). – ^1H NMR (200 MHz, $CDCl_3$): δ = 2.90 (s, 6 H, 2 × N–CH_3), 3.33 (d, *J* = 5.5 Hz, 2 H, Ar–CH_2), 3.46 (t, *J* = 5.5 Hz, 1 H, 5-H), 3.74 (s, 3 H, 5′-OCH_3), 3.80 (d, *J* = 10.9 Hz, 1 H, 2-H_{ax}), 4.24 (d, *J* = 10.9 Hz, 1 H, 2-H_{eq}), 4.45 (dt, *J* = 5.0, 1.5 Hz, 2 H, 1′′-H_2), 5.26 (dq, *J* = 10.4, 1.5 Hz, 1 H, 3′′-H), 5.42 (dq, *J* = 17.2, 1.5 Hz, 1 H, 3′′-H), 6.05 (ddt, *J* = 17.2, 10.4, 5.0 Hz, 1 H, 2′′-H), 6.70–6.75 (m, 2 H, 3′-, 4′-H), 6.81–6.86 (m, 1 H, 6′-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 28.7 (Ar–CH_2), 32.1 (N–CH_3), 50.4 (C-5), 55.5 (5′-OCH_3), 63.1 (C-2), 69.5 (C-1′′), 133.3 (C-2′′), 150.6 (C-5′), 153.2 (C-2′), 167.9 (C-4/C-6). – MS (70 eV, EI): *m/z* (%) = 318 (16) [M^+], 203 (20) [$M^+ - C_3H_7 - CH_2(NCH_3)_2$], 43 (100) [$C_3H_7^+$]. – $C_{17}H_{22}N_2O_4$ (318.4): calcd. 318.1579; found 318.1579.

(6a*R*,9*R*,10a*R*,)-(±)-3,4,6,6a,7,8,9,10,10a-Nonahydro-2,4,6,6,9-pentamethyl-[2]benzopyrano[3,4-*d*]pyrimidine-1(2*H*)-one (11): A solution of **6** (2.14 g, 7.34 mmol) in dry THF (40 mL) was treated with DIBAL-H (12.3 mL, 18.4 mmol, 1.5 M in toluene) at −78 °C according to the general procedure I. The crude product was purified by column chromatography (EA: PE = 1:3) to give 1.90 g of **11** (6.83 mmol, 93% yield). – R_f = 0.16 (EA:PE = 1:3). – m.p. 151 °C – IR (KBr): $\tilde{\nu}$ = 2980, 2936, 2860 (C–H), 1628 (C=O) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 279 nm (3.81). – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.50 (q, *J* = 11.0 Hz, 1 H, 10-H), 0.83 (d, *J* = 6.5 Hz, 3 H, 9-CH_3), 0.97 (m, 1 H, 8-H_{ax}), 1.02 (m, 1 H, 7-H_{ax}), 1.07 (s, 3 H, 6-CH_3), 1.23 (td, *J* = 11.0, 2.2 Hz, 1 H, 6a-H), 1.29 (s, 3 H, 6-CH_3), 1.48–1.52 (m, 1 H, 9-H), 1.67 (m, 1 H, 7-H_{eq}), 1.75 (m, 1 H, 8-H_{eq}), 2.13 (td, *J* = 11.0, 3.2 Hz, 1 H, 10a-H), 2.62 (dtd, *J* = 11.0, 3.2, 2.2 Hz, 1 H, 10-H), 2.73, 2.87 (2s, 6 H, 2-CH_3, 4-CH_3), 3.93 (d, *J* = 10.1 Hz, 1 H, 3-H), 4.36 (d, *J* = 10.1 Hz, 1 H, 3-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 19.4 (6-CH_3), 22.4 (9-CH_3), 27.2 (6-CH_3), 27.5 (C-7), 31.7, 32.1 (C-9, C-10a), 33.9, 34.1 (N–CH_3), 35.6 (C-8), 40.5 (C-10), 48.7 (C-6a), 65.8 (C-3), 81.7 (C-6), 87.8 (C-10b), 159.5 (C-4a), 167.3 (C-1). – MS (70 eV, EI): *m/z* (%) = 278 (64) [M^+]. – $C_{16}H_{26}N_2O_2$ (278.4): calcd. C 69.03, H 9.41; found C 69.26, H 9.50.

(6a*R*,12b*S*)-(±)-3,4,6a,7-Tetrahydro-2,4,6,6-tetramethyl-6*H*,12b*H*-[1]benzopyrano[3′,4′:5,4]pyrano[2,3-*d*]pyrimidine-1(2*H*)-one (12): A solution of **7** (0.20 g, 0.61 mmol) in dry THF (80 mL) was treated with DIBAL-H (1.63 mL, 2.44 mmol, 1.5 M in toluene) at −78 °C according to the general procedure I. The crude product was purified by column chromatography (EA) to give **12** (0.16 g, 0.52 mmol, 86% yield) as colorless crystals. – R_f = 0.32 (EA). – m.p. 178 °C – IR (film): $\tilde{\nu}$ = 3068, 2978, 2932 (C–H), 1628 (C=O), 1594 (C=C), 1460, 1436 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 198 nm (4.69), 277 (3.97), 283 (3.96). – ^1H NMR (300 MHz, C_6D_6): δ = 0.98 (s, 3 H, 6-CH_3), 1.00 (s, 3 H, 6-CH_3), 1.50 (ddd, *J* = 8.1, 6.5, 3.8 Hz, 1 H, 6a-H), 2.25 (s, 3 H, N–CH_3), 2.70 (s, 3 H, N–CH_3), 3.08 (d, *J* = 10.0 Hz, 1 H, 3-H_{ax}), 3.70 (d, *J* = 10.0 Hz, 1 H, 3-H_{eq}), 3.92 (dd, *J* = 11.5, 8.1 Hz, 1 H, 7-H_{ax}), 4.07 (ddd, *J* = 11.5, 3.8, 1.0 Hz, 1 H, 7-H_{eq}), 4.39 (d_{br}, *J* = 6.5 Hz, 1 H, 12b-H), 6.95–7.10 (m, 3 H, 9-H, 10-H, 11-H), 8.70 (m_c, 1 H, 12-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.9 (4-CH_3), 25.7 (4-CH_3), 29.1 (C-6a), 32.1 (N–CH_3), 33.7 (N–CH_3), 38.9 (C-12b), 63.6 (C-7), 64.9 (C-3), 79.1 (C-6), 86.1 (C-12c), 115.3 (C-9), 120.0 (C-11), 124.4 (C-12a), 127.1 (C-10), 132.3 (C-12), 153.3 (C-8a), 158.5 (C-4a), 167.0 (C-1). – MS (70 eV, EI): *m/z* (%) = 314 (100) [M^+], 244 (30) [$M^+ - C(NCH_3)_2$], 173 (37) [$C_{12}H_6O^+$]. – $C_{18}H_{22}N_2O_3$ (314.4): calcd. C 68.77, H 7.05; found C 68.59, H 7.12.

(6*S*,13*R*)-(±)-3,4,6,7-Tetrahydro-6,13-methano-11-methoxy-2,4,6-trimethyl-13*H*-[1,4]benzodioxonino[5,6-*d*]pyrimidine-1(2*H*)-one (13): To a solution of **8** (0.30 g, 0.87 mmol) in dry THF (80 mL) was added DIBAL-H (2.32 mL, 3.48 mmol, 1.5 M in toluene) at −78 °C according to the general procedure I. Purification of the crude product by column chromatography (EA) yielded **13** (0.23 g, 0.68 mmol, 79% yield). – R_f = 0.21 (EA). – m.p. 196 °C – IR

(KBr): $\tilde{\nu}$ = 3092, 2918, 2852 (C−H), 1700 (C=O), 1608 (C=C), 1442, 1408 (CH_2, CH_3) cm^{-1}. − UV (CH_3CN): λ_{max} (lg ε) = 197 nm (4.68), 288 (3.97). − ^1H NMR (300 MHz, C_6D_6): δ = 0.80 (s, 3 H, 6-CH_3), 1.52 (dd, *J* = 13.9, 2.0 Hz, 1 H, 14-H), 1.65 (ddd, *J* = 13.9, 5.5, 2.5 Hz, 1 H, 14-H), 2.40 (s, 3 H, N−CH_3), 2.53 (s, 3 H, N−CH_3), 3.09 (d, *J* = 12.5 Hz, 1 H, 7-H_{ax}), 3.32 (d, *J* = 8.0 Hz, 1 H, 3-H_{ax}), 3.40 (s, 3 H, OCH_3), 3.55 (d, *J* = 8.0 Hz, 1 H, 3-H_{eq}), 3.94 (dd, *J* = 12.5, 2.5 Hz, 1 H, 7-H_{eq}), 4.28 (dd, *J* = 5.5, 2.0 Hz, 1 H, 13-H), 6.59 (dd, *J* = 9.0, 3.2 Hz, 1 H, 10-H), 6.92 (d, *J* = 9.0 Hz, 1 H, 9-H), 7.36 (d, *J* = 3.2 Hz, 1 H, 12-H). − ^{13}C NMR (50.3 MHz, C_6D_6): δ = 24.4 (6-CH_3), 31.3 (N−CH_3), 34.6 (C-13), 35.9 (C-14), 55.2 (OCH_3), 66.5 (C-3), 78.2 (C-7), 78.9 (C-6), 83.9 (C-13a), 112.9 (C-10), 116.1 (C-9), 122.2 (C-12), 139.0 (C-12a), 152.7 (C-11), 156.4 (C-4a), 161.1 (C-8a), 166.8 (C-1). − MS (70 eV, EI): *m*/*z* (%) = 330 (37) [M^+], 57 (72) [$C_4H_9^+$], 43 (100) [$C_3H_7^+$]. − $C_{18}H_{22}N_2O_4$ (330.4): calcd. C 65.44, H 6.71; found C 65.32, H 6.76.

General Procedure II for the Preparation of Compounds 14−16: To a solution of 3.50 mmol of the *N,N′*-dimethylpyrimidinedione in dry THF (80 mL) was added DIBAL-H (4 equiv., 1.5 M in toluene) at −78 °C. The reaction mixture was allowed to warm to room temperature overnight and the reaction was quenched by addition of 2 N HCl (40 mL). After additional stirring for 24 h at room temperature and addition of NEt_3 (80 mL) with vigorous stirring the layers were separated and the aqueous layer extracted with ethyl acetate. The combined organic phases were washed with brine and NH_4Cl solution, dried over Na_2SO_4 and the solvent was evaporated in vacuo.

(4*R*,4a*R*,6*R*,8a*R*)-(±)-*N*,1,1,6-Tetramethyl-3-oxo-octahydro-[2]benzopyran-4-carboxamide (14a): Reaction of **6** (1.00 g, 3.42 mmol) in dry THF (80 mL) with DIBAL-H (9.12 mL, 13.68 mmol, 1.5 M in toluene) at −78 °C according to the general procedure II and crystallization from dichloromethane/pentane gave **14a** (0.49 g, 1.93 mmol, 57% yield). − R_f = 0.22 (EA). − m.p. 194 °C − IR (film): $\tilde{\nu}$ = 2984, 2938, 2914 (C−H), 1716 (C=O, lactone), 1648, 1580 (C=O, amide), 1454, 1410 (CH_2, CH_3) cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.65 (q, *J* = 12.0 Hz, 1 H, 5-H_{ax}), 0.89 (d, *J* = 6.5 Hz, 3 H, 6-CH_3), 0.92−1.24 (m, 2 H, 7-H_{ax}, 8-H_{ax}), 1.34 (s, 3 H, 1-CH_3), 1.34 (s, 3 H, 1-CH_3), 1.35−1.62 (m, 2 H, 6-, 8a-H), 1.71−1.94 (m, 3 H, 5-H_{eq}, 7-H_{eq}, 8-H_{eq}), 2.44 (m, 1 H, 4a-H), 2.85 (d, *J* = 5.0 Hz, 3 H, N−CH_3), 2.88 (d, *J* = 9.5 Hz, 1 H, 4-H), 6.66 (s_{br}, 1 H, N−H). − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 22.1 (6-CH_3), 23.1 (1-CH_3), 26.7 (N−CH_3), 27.4 (C-8), 28.2 (1-CH_3), 31.7 (C-6), 34.5 (C-7), 34.7 (C-4a), 41.2 (C-5), 46.0 (C-8a), 54.7 (C-4), 86.3 (C-1), 168.0 (N−C=O), 169.5 (O−C=O). − MS (70 eV, EI): *m*/*z* (%) = 253 (43) [M^+], 136 (90) [$C_{10}H_{16}^+$], 117 (100) [$M^+ - C_{10}H_{16}$], 41 (57) [$C_3H_5^+$] − $C_{14}H_{23}NO_3$ (253.3): calcd. C 66.37, H 9.15; found C 66.54, H 8.93.

(1*R*,4a*R*,10b*R*)-(±)-1,4a,5,10b-Tetrahydro-*N*,4,4-trimethyl-2-oxo-2*H*,4*H*-pyrano[3,4-*c*][1]benzopyran-1-carboxamide (15): A solution of cycloadduct **7** (0.30 g, 0.91 mmol) in dry THF (80 mL) was treated with DIBAL-H (2.43 mL, 3.64 mmol, 1.5 M in toluene) at −78 °C according to general procedure II. The crude product was dissolved in dichloromethane/pentane and crystallized to give **15** (0.26 g, 0.88 mmol, 97% yield). − R_f = 0.48 (EA:PE = 1:1). − m.p. 241 °C − IR (KBr): $\tilde{\nu}$ = 3322 (N−H), 2982, 2940 (C−H), 1726 (C=O, lactone), 1654 (C=O, amide), 1456 (CH_2, CH_3) cm^{-1}. − UV (CH_3CN): λ_{max} (lg ε) = 197 nm (4.68), 275 (3.42), 282 (3.39). − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.50 (s, 3 H, 4-CH_3), 1.61 (s, 3 H, 4-CH_3), 2.33 (ddd, *J* = 12.2, 5.6, 4.0 Hz, 1 H, 4a-H), 2.91 (d, *J* = 5.0 Hz, 3 H, N−CH_3), 3.39 (d, *J* = 8.0 Hz, 1 H, 1-H), 3.79 (t, *J* = 12.2 Hz, 1 H, 5-H_{ax}), 4.39 (ddd, *J* = 8.0, 5.6, 2.0 Hz, 1 H, 10b-H), 4.53 (ddd, *J* = 12.2, 4.0, 2.0 Hz, 1 H, 5-H_{eq}), 6.52 (s_{br}, 1 H, N−H), 6.79−6.92 (m, 2 H, 7-H, 9-H), 7.10−7.21 (m, 2 H, 8-H, 10-H) − ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 26.2 (4-CH_3), 27.2 (4-CH_3), 28.5 (N−CH_3), 29.9 (C-4a), 37.8 (C-10b), 52.6 (C-1), 62.7 (C-5), 82.1 (C-4), 116.8 (C-7), 121.1 (C-9), 124.2 (C-10b), 128.6 (C-8), 129.3 (C-10), 152.5 (C-6a), 166.4 (N−C=O), 168.2 (C-2). − MS (70 eV, EI): *m*/*z* (%) = 289 (7) [M^+], 244 (58) [$M^+ - CH_3NO$], 71 (100) [$C_5H_{11}^+$]. − $C_{16}H_{19}NO_4$ (289.3): calcd. C 66.42, H 6.62; found C 66.60, H 6.62.

(7*S*,10*S*,11*S*)-(±)-6,7,10,11-Tetrahydro-7,11-methano-*N*-methyl-9-oxo-9*H*-[1,4]benzodioxonine-10-carboxamide (16a/b): A solution of cycloadduct **8** (0.20 g, 0.58 mmol) in dry THF (80 mL) was treated with DIBAL-H (1.55 mL, 2.32 mmol, 1.5 M in toluene) at −78° C according to general procedure II. The crude product was purified by column chromatography (EA:PE = 2:1) to give **16a/b** (0.17 g, 0.55 mmol, 95% yield; **a:b =** 8.5:1). − R_f = 0.37 (EA:PE = 2:1). − IR (KBr): $\tilde{\nu}$ = 3398 (N−H), 3076, 2938 (C−H), 1724 (C=O, lactone), 1674 (C=O, amide), 1500 (C=C), 1452 (CH_2, CH_3) cm^{-1}. − UV (CH_3CN): λ_{max} (lg ε) = 196 nm (4.72), 226 (3.87), 281 (3.40). − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.37 (s, 3 H, 7-CH_3), 1.90 (ddd, *J* = 14.8, 2.1, 1.0 Hz, 1 H, 12-H), 2.33 (ddd, *J* = 14.8, 5.5, 2.6 Hz, 1 H, 12-H), [2.50 (d, *J* = 5.0 Hz, 3 H, N−CH_3, diastereomer **16b**)], 2.81 (d, *J* = 5.0 Hz, 3 H, N−CH_3), 3.40 (d, *J* = 1.0 Hz, 1 H, 10-H), 3.50 (d, *J* = 12.5 Hz, 1 H, 6-H_{ax}), 3.76 (s, 3 H, OCH_3), 4.00 (dd, *J* = 5.5, 2.1 Hz, 1 H, 11-H), 4.18 (dd, *J* = 12.5, 2.6 Hz, 1 H, 6-H_{eq}), 6.66−6.77 (m, 2 H, 1-H, 3-H), 6.85 (s_{br}, 1 H, N−H), 6.96 (d, *J* = 8.0 Hz, 1 H, 4-H). − ^{13}C NMR (75.3 MHz, $CDCl_3$): δ = 24.2 (7-CH_3), 26.9 (N−CH_3), 33.9 (C-12), 36.9 (C-11), 50.3 (C-10), 55.5 (OCH_3), 77.8 (C-6), 83.4 (C-7), 113.5 (C-3), 114.7 (C-4), 122.4 (C-1), 137.8 (C-11a), 152.5 (C-2), 156.1 (C-4a), 166.4 (C=O), 170.4 (C-9). − MS (70 eV, EI): *m*/*z* (%) = 305 (100) [M^+], 188 (90) [$M^+ - CH_3 - C_3H_4NO_3$], 43 (97) [$C_3H_7^+$]. − $C_{16}H_{19}NO_5$ (305.3): calcd. C 62.94, H 6.27; found C 62.89, H 6.25.

(1*R*,2*S*,4a*R*,10b*R*)-(±)-1,4a,5,10b-Tetrahydro-2-hydroxy-*N*,4,4-trimethyl-2*H*,4*H*-pyrano[3,4-*c*][1]benzopyran-1-carboxamide (17): DIBAL-H (0.47 mL, 0.70 mmol, 1.5 M in toluene) was slowly added to a solution of lactone **15** (0.10 g, 0.35 mmol) in dry THF (8 mL) at −78 °C. After complete addition the mixture was stirred for 2 h at −78 °C and the reaction was quenched by addition of water (6 mL) at −78 °C and consequent warming to room temperature. The product was extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. Removal of the solvent in vacuo without any further purification step furnished **17** (96.3 mg, 0.33 mmol, 95% yield). − R_f = 0.22 (EA). − m.p. >250 °C − IR (KBr): $\tilde{\nu}$ = 3322 (N−H, O−H), 2978, 2938 (C−H), 1648, 1564 (C=O, amide), 1456, 1412, 1372 (CH_2, CH_3) cm^{-1}. − UV (CH_3CN): λ_{max} (lg ε) = 198 nm (4.66), 218 (3.86), 276 (3.42), 283 (3.41). − ^1H NMR (200 MHz, [D_6]DMSO): δ = 1.20 (s, 3 H, 4-CH_3), 1.40 (s, 3 H, 4-CH_3), 1.85 (dd, *J* = 11.0, 4.5 Hz, 1 H, 4a-H), 2.27 (dd, *J* = 12.2, 8.5 Hz, 1 H, 1-H), 2.50 (d, *J* = 5.0 Hz, 3 H, N−CH_3), 3.45 (dd, *J* = 12.2, 4.7 Hz, 1 H, 10b-H), 4.09 (t, *J* = 11.0 Hz, 1 H, 5-H_{ax}), 4.35 (ddd, *J* = 11.0, 4.7, 1.5 Hz, 1 H, 5-H_{eq}), 5.02 (dd, *J* = 8.5, 6.0 Hz, 1 H, 2-H), 6.36 (d, *J* = 6.0 Hz, 1 H, O−H), 6.68−6.75 (m, 2 H, 7-H, 9-H), 6.85−6.90 (m, 1 H, 10-H), 7.02−7.09 (m, 1 H, 8-H), 7.58 (q, *J* = 5.0 Hz, 1 H, N−H). − ^{13}C NMR (50.3 MHz, [D_6]DMSO): δ = 24.8 (4-CH_3), 25.2 (4-CH_3), 27.0 (N−CH_3), 33.3 (C-4a), 36.4 (C-10b), 53.4 (C-1), 62.7 (C-5), 72.7 (C-4), 91.2 (C-2), 115.9 (C-7), 119.1 (C-9), 123.4 (C-10b), 127.7 (C-8), 129.5 (C-10), 153.1 (C-6a), 171.5 (C=O). − MS (70 eV, EI): *m*/*z* (%) = 291 (6) [M^+], 244 (59) [$M^+ - OH - NHCH_3$], 215 (100)

$[M^+ - OH - CONH_2CH_3]$. – $C_{16}H_{21}NO_4$ (291.3): calcd. C 65.97, H 7.27; found C 65.97, H 7.17.

(4a*R*,10b*S*)-(±)-4a,10b-Dihydro-*N*,4,4-trimethyl-4*H*,5*H*-pyrano-[3,4-*c*][1]benzopyran-1-carboxamide (18): A solution of lactol **17** (60.2 mg, 0.21 mmol) in dry CH_2Cl_2 (40 mL) was treated with NEt_3 (0.35 mL, 0.25 mmol) and a catalytic amount of DMAP at 0° C. The reaction mixture was stirred for 15 min. and then treated dropwise with CH_3SO_2Cl (114 mg, 1.00 mmol) and DBU (32 mg, 0.21 mmol). The reaction was quenched after 2 h at 0 °C by addition of water and the product extracted with CH_2Cl_2. The combined organic layers were washed with saturated NH_4Cl and $NaHCO_3$ solutions and brine, and dried over Na_2SO_4. Removal of the solvent in vacuo and purification by column chromatography (EA:PE = 2:1) provided **18** (56.9 mg, 0.21 mmol, 99% yield) as a colorless solid. – R_f = 0.34 (EA:PE = 2:1). – m.p. 178 °C – IR (KBr): $\tilde{\nu}$ = 3274 (N–H), 3062, 3038, 2982, 2940 (C–H), 1638, 1538 (C=O, amide), 1614 (C=C), 1490, 1452 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 198 nm (4.45), 276 (3.20), 283 (3.17). – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 3 H, 4-CH_3), 1.42 (s, 3 H, 4-CH_3), 2.09 (ddd, *J* = 8.7, 6.0, 4.3 Hz, 1 H, 4a-H) 2.79 (d, *J* = 5.1 Hz, 3 H, N–CH_3), 4.03 (dd, *J* = 11.5, 8.7 Hz, 1 H, 5-H_{ax}), 4.09 (d_{br}, *J* = 6.0 Hz, 1 H, 10b-H), 4.39 (ddd, *J* = 11.5, 4.3, 1.0 Hz, 1 H, 5-H_{eq}), 5.51 (d_{br}, *J* = 5.1 Hz, 1 H, N–H), 6.74–6.88 (m, 2 H, 7-H, 9-H), 6.84 (s, 1 H, 2-H), 7.10 (m, 1 H, 8-H), 7.42 (m, 1 H, 10-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.5 (4-CH_3), 26.4 (N–CH_3), 30.0 (C-4a), 38.1 (C-10b), 63.9 (C-5), 76.8 (C-4), 113.3 (C-1), 116.1 (C-7), 120.5 (C-9), 121.9 (C-10a), 127.9 (C-8), 130.9 (C-10), 144.6 (C-2), 153.9 (C-6a), 169.2 (C=O). – MS (70 eV, EI): *m/z* (%) = 273 (100) $[M^+]$, 242 (36) $[M^+ - NH_2CH_3]$, 214 (50) $[M^+ - CONHCH_3]$, 199 (37) $[M^+ - CONHCH_3]$, 69 (19) $[C_5H_9^+]$. – $C_{16}H_{19}NO_3$ (273.3): calcd. 273.1365; found 273.1364.

(7*S*,11*R*)-(±)-6,7-Dihydro-2-methoxy-*N*,7-dimethyl-11*H*-5,8-dioxa-benzocyclononene-10-carboxamide (20): DIBAL-H (1.10 mL, 1.58 mmol, 1.5 M in toluene) was slowly added to a solution of lactone **16a/b** (0.24 g, 0.79 mmol) in dry THF (8 mL) at −78° C. After complete addition the mixture was stirred for 2 h at −78 °C and the reaction quenched by addition of water (10 mL) at −78 °C and subsequent warming to room temperature. The product was extracted with ethyl acetate and the organic layer washed with NaCl solution and dried over Na_2SO_4. Removal of the solvent in vacuo furnished crude **19** (0.23 g, 0.73 mmol, 93% yield).

A solution of the crude lactol **19** (0.17 g, 0.57 mmol) in dry CH_2Cl_2 (40 mL) was treated with NEt_3 (0.95 mL, 0.68 mmol, 1.5 M in toluene) and a catalytic amount of DMAP at 0 °C. The reaction mixture was stirred for 15 min. and then treated dropwise with CH_3SO_2Cl (344 mg, 3.00 mmol) and DBU (91 mg, 0.60 mmol). The reaction was quenched after 2 h at 0 °C by addition of water and the product extracted with CH_2Cl_2. The combined organic layers were washed with saturated NH_4Cl and $NaHCO_3$ solutions and brine, and dried over Na_2SO_4. Removal of the solvent in vacuo and purification by column chromatography (EA:PE = 2:1) provided **20** (105 mg, 0.36 mmol, 64% yield) as a colorless solid. – R_f = 0.35 (EA). – m.p. 147 °C – IR (KBr): $\tilde{\nu}$ = 3436 (N–H), 3030, 3008, 2974, 2964, 2936 (C–H), 1652, 1590 (C=O, amide), 1550, 1590 (C=C), 1458 (CH_2, CH_3) cm^{-1}. – UV (CH_3CN): λ_{max} (lg ε) = 196 nm (4.61), 224 (4.19), 242 (3.84), 284 (3.47). – ^1H NMR (200 MHz, $CDCl_3$): δ = 1.24 (s, 3 H, 7-CH_3), 2.01 (dd, *J* = 14.1, 1.9 Hz, 1 H, 12-H), 2.13 (ddd, *J* = 14.1, 5.5, 1.9 Hz, 1 H, 12-H), 2.72 (d, *J* = 5.0 Hz, 3 H, N–CH_3), 3.48 (d, *J* = 12.5 Hz, 1 H, 6-H_{ax}), 3.70 (dd, *J* = 5.5, 1.9 Hz, 1 H, 11-H), 3.77 (s, 3 H, OCH_3), 4.18 (dd, *J* = 12.5, 2.0 Hz, 1 H, 6-H_{eq}), 5.38 (d_{br}, *J* = 5.0 Hz, 1 H, N–H), 6.66 (dd, *J* = 8.5, 3.3 Hz, 1 H, 3-H), 6.80 (d, *J* = 3.3 Hz, 1 H, 1-H), 6.90 (d, *J* = 8.5 Hz, 1 H, 4-H), 7.45 (s, 1 H, 9-H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 24.4 (7-CH_3), 26.3 (N–CH_3), 35.4 (C-11), 35.5 (C-12), 55.5 (OCH_3), 76.0 (C-6), 78.5 (C-7), 109.4 (C-10), 112.7 (C-3), 114.9 (C-4), 122.8 (C-1), 135.8 (C-11a), 150.6 (C-9), 152.5 (C-2), 155.9 (C-4a), 168.1 (C=O). – MS (70 eV, EI): *m/z* (%) = 289 (100) $[M^+]$. – $C_{16}H_{19}NO_4$ (289.3): calcd. C 66.42, H 6.62; found C 66.24, H 6.56.

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