Synthesis of Substituted Pyrrolo[3,4-a]carbazoles

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The cycloaddition between *N*-protected 3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indoles and substituted maleimides (=1*H*-pyrrole-2,5-diones) yielded substituted pyrrolo[3,4-*a*]carbazole derivatives bearing an additional succinimide (=pyrrolidine-2,5-dione) moiety either at C(5a) or C(10b) depending on the type of the protection group at the indole N-atom. Derivatives substituted at C(10b) were isolated when the protection group, Me$_3$Si or Boc (^{t}BuOCO), was eliminated during the reaction (*Schemes 2* and *3*), whereas a substitution at C(5a) was observed when an electron-withdrawing group, Tos (4-MeC$_6$H$_4$SO$_2$) or pivaloyl (Me$_3$CCO), was not eliminated (*Scheme 1*). Complex results were found in reactions between 1-(trimethylsilyl)-3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indole, in contrast to formerly reported results (*Scheme 3*). Some derivatives of 1*H*,5*H*-[1,2,4]triazolo[1′,2:1,2]pyridazino[3,4-*b*]indole-1,3(2*H*)-dione were obtained from reactions with 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (*Scheme 2*). All structures were established by spectroscopic data, by calculations, and one representative structure was confirmed by an X-ray crystallographic analysis (*Fig.*). Finally, the formation of the different structure types was discussed, and compared with similar reactions reported in the literature.

Introduction. – Fused indole derivatives like carbazoles were found in a large number of highly potent natural products like ellipticine, a drug used in tumor therapy, vincamine, used against *Alzheimer* disease, or the large group of secale alkaloids [1]. During the last decade, camptothecine and some synthetic derivatives like topotecane and irinotecane gained great importance as inhibitors of topoisomerase I and are today used against different types of cancer. The cycloaddition of appropriate dienophiles to 2- or 3-ethenyl-1*H*-indoles is used as a standard procedure for the synthesis of those fused indoles [2]. As we have studied reactions between cyclopentadiene and 1-[(1-silyloxy)ethenyl]naphthalene derivatives and maleimides (=1*H*-pyrrole-2,5-diones) [3], we continue here with the report on the cycloaddition between *N*-substituted 3-[(1-silyloxy)ethenyl]-1*H*-indoles and maleimides and on some reactions of the cycloadducts.

Results. – Although a protecting group at the indole N-atom was described as not being necessary for some reactions [4], we noticed that in most cycloadditions, a protecting group at the N-atom supported the reactions and increased the yields. Therefore, we used the *N*-protected compounds **1a**–**c**, **9**, and **14** as starting materials. Compound **14** was prepared according to a known procedure [5], the other compounds were synthesized from the parent acetyl derivatives following a standard procedure [6] in nearly quantitative yields. All compounds were obtained as sensitive liquids

Scheme 1

1a R' = Tos   **2a** R = Ph   **3a** R = Ph, R' = Tos   **3e** R = Me, R' = Piv
b R' = Piv   **b** R = Me   **b** R = Me, R' = Tos   **f** R = Et, R' = Piv
c R' = Boc   **c** R = Et   **c** R = Et, R' = Tos   **g** R = Ph, R' = Boc
                                d R = Ph, R' = Piv   **h** R = Me, R' = Boc

3d $\xrightarrow{\text{MeONa}}$
$\xrightarrow{\text{MeOH}}$

3g $\xrightarrow{\text{M.p.}}$

3f, 3h $\longrightarrow$

TMS = Me$_3$Si
Tos = 4-MeC$_6$H$_4$SO$_2$
Piv = Me$_3$CCO
Boc = ^{t}BuOCO

5 R = Et, R' = Piv
7 R = Me, R' = Boc

which tend to polymerize and were, therefore, used as crude products without further purification.

When the reactions between the 1-[(4-methylphenyl)sulfonyl]-3-{1-[(trimethyl-silyl)oxy]ethenyl}-1*H*-indole (**1a**) and the *N*-substituted maleimides **2a**, **2b**, or **2c** were carried out in a reactant ratio of 1:1, a mixture of starting materials, degradation products, and small amounts of 1:2 adducts but no 1:1 adduct were obtained after workup. But when 1:2 mixtures of the reactants were stirred in toluene at room temperature for some hours, the crystalline compounds **3a–c** were isolated after evaporation of the solvent and purification by crystallization or CC (*Scheme 1*).

Inspection of the elemental analyses and of the spectroscopic data immediately revealed that **3a–c** are not, as first expected, 1:1 adducts, but were formed by a 1:2 addition. The IR spectra showed strong bands of the imide CO groups at *ca.* 1780 and 1720 cm^{-1}, another carbonyl band at 1702–1712 cm^{-1} (saturated cyclic ketone), and the bands of the protecting sulfonamide group at *ca.* 1350 and 1170 cm^{-1}. Furthermore, the ^{1}H-NMR spectra of **3b** showed two signals for the MeN group, and that of **3c**

gave two sets of signals for the EtN group. NMR Spectroscopy and X-ray crystallographic analysis (see below) finally established the proposed structures.

The analogous reaction between the *N*-pivaloyl derivative **1b** (Piv = Me₃CCO) and the maleimides **2a–c** yielded the analogous structures **3d–f**. The carbonyl group in position 5 of the products **3** can react with MeOH/MeONa yielding the hemiketal, as was demonstrated in the case of **3d** by the formation of **4** (*Scheme 1*). During chromatographic workup of **3f**, the substituent at C(5a) was eliminated, and we isolated **5**. As demonstrated by other experiments, this elimination can occur either during chromatography on silica gel or during prolonged heating for recrystallization.

The elimination of the substituent at C(5a) is in agreement with the observations we made in reactions with the Boc-protected **1c** (Boc = (*tert*-butoxy)carbonyl = ʹBuOCO). The reaction with **2a** at room temperature yielded the expected product **3g**. But from the reaction between **1c** and **2b** at room temperature, we obtained the addition product **3h** and the elimination product **7**. When **3g** was heated to the melting point, we observed cleavage of the Boc group but no elimination of the substituent at C(5a), and we isolated **6**.

As the spectroscopic data of compounds **3a–h** showed analogous patterns, the structure elucidation is discussed by means of the data of compound **3c**. The identification of the signals was possible from ^{1}H,^{13}C-HETCOR (300 MHz), ^{1}H,^{1}H-COSY (300 MHz), and NOE experiments. The ^{13}C-NMR data (75.43 MHz) were compared with those obtained by SPECINFO [7] and showed satisfactory agreement (*Table*).

Table. *Experimental and Calculated* (SPECINFO) ^{13}C-NMR Shift Data of **3c**

	C(1)	C(3)	C(3a)	C(4)	C(5)	C(5a)	C(5b)	C(9a)	C(10a)	C(10b)
Exper.	172.72	175.9	38.21	38.7	204.71	58.20	128.72	141.41	65.39	39.93
Calc.	175.16	177.40	40.04	46.73	208.17	54.98	129.6	143.6	71.87	50.14

The ^{1}H-NMR signal of H−C(3a) of **3c** at δ 3.32 showed a coupling constant *J* = 9.8 (9.5) Hz with the signal of H−C(10b) at δ 3.66, and a coupling constant *J* = 5.9 Hz with both H−C(4) at δ 2.83, whereas the signal of H−C(10b) coupled with the signal of H−C(10a) (*J* = 8.5 (8.3) Hz) at δ 5.89. This signal did not exhibit any other coupling, and thereby demonstrated that the additional substituent should be located at C(5a). The signals of the protons of the succinimide (= pyrrolidine-2,5-dione) moiety at C(5a) were found as an *ABX* system.

Finally, the structure deduced from spectroscopic data was confirmed by an X-ray crystallographic analysis of **3c** (*Fig. 1,a*) clearly showing that the succinimide moiety is attached at C(5a), that the succinimide moiety and H−C(10a) are *cis* oriented with a torsion angle H−C(10a)−C(10a)−C(5a)−C(13) = 33.1(1.2)°, that H−C(10a) and H−C(10b) are also *cis* oriented, and finally that even H−C(10b) and H−C(3a) are *cis* oriented. A PM3 calculation (HYPERCHEM) [8] gave a similar structure (*Fig. 1,b*).

A surprising result was obtained from the reaction between the Boc-protected derivative **1c** and **2c** in refluxing toluene. After evaporation of the solvent and crystallization, a compound was obtained whose elemental analysis and MS showed a 1:2 ratio of the reaction partners, but the ^{1}H-NMR data exhibited significant differences when compared with the data of compounds like **3a** or **3c**. The Boc group was lost probably by a thermal decomposition, and in the ^{1}H-NMR spectrum, a broad *s* at δ 11.7 caused by H−N(10) was detected. Further spectroscopic data established the proposed
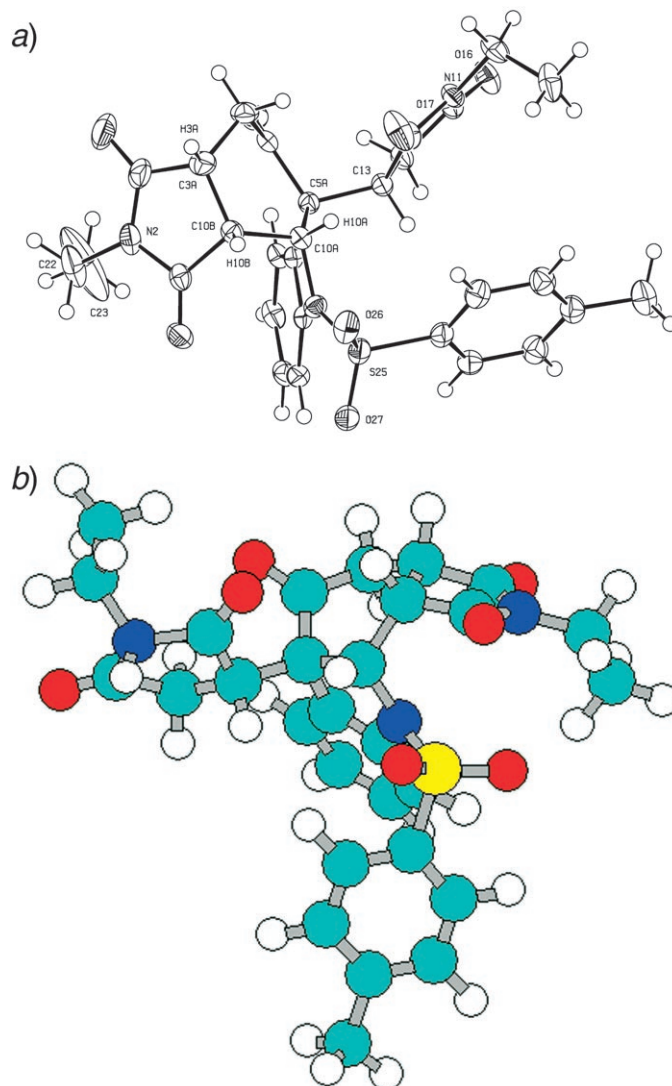
Figure. a) *Structure of* **3c** *in the crystal* [9] (ellipsoids drawn at 50% probability, radii of H-atoms arbitrary; arbitrary atom numbering). b) *Structure of* **3c** *obtained by a PM3 calculation.*

structure **8** (*Scheme 2*) in which the additional succinimide moiety is not fixed at C(5a) but at C(10b). Calculations of the distances for the favored conformation of **8** (MM2, SYBYL [9]) resulted in the following values: $H-C(3a)/H_{trans}-C(4')$ 2.497 Å, $H-C(3')/H_{cis}-C(4')$ 2.364 Å, and $H-C(3')/H-N(10)$ 2.596 Å, in agreement with the observed NOEs.

Analyzing the data of the COSY and NOE experiments performed with **8** revealed two groups of 3 protons each from which one was caused by the H-atoms of the succinimide moiety and the other one belonged to the

Scheme 2
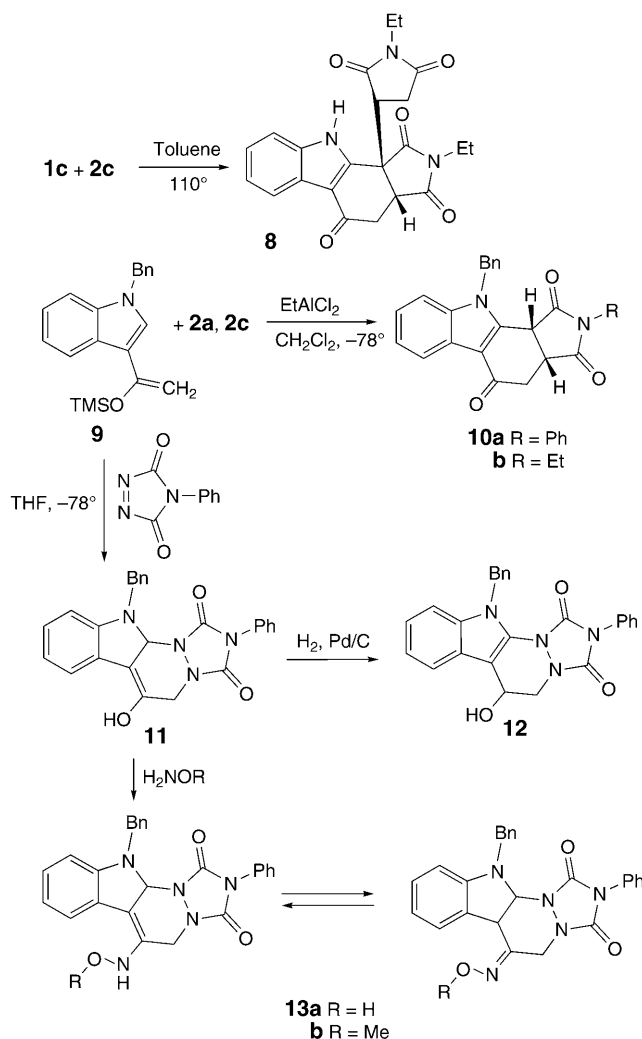
pyrrolocarbazole system indicating that neither at C(5a) nor at C(10a) a proton was located. Irradiation at δ 4.06 (H−C(3′)) simplified both signals at δ 2.05 and 2.28 to *d* with $J = 18$ Hz, which therefore could be caused solely by the two H−C(4′) of the succinimide moiety. The second 3-H system, an *ABC* system, showed signals at δ 2.50, 2.80, and 2.86 with $J_{gem} = 18.0$, $J_{cis} = 8.6$, and $J_{trans} = 1.4$ Hz and was caused by the pyrrolocarbazole part. NOEs were found between H−C(3a) and H_{trans}−C(4′), H−C(3′) and H−C(4′), and H−C(3′) and H−N(10).

Compounds **1a**–**c** reacted as 1,3-dienes substituted in position 2 by a Me₃SiO group, in position 3 by an aryl group, and in position 4 by an N-atom which is substituted by an electron-withdrawing group. In contrast, the benzyl substituent at the N-atom of diene **9** is not an electron-withdrawing substituent. This 1,3-diene did not react with male-imides in toluene at room temperature, and when the mixtures were refluxed for sev-

eral hours or days, only decomposition occurred. A successful reaction, but with lower yields, was observed when we performed the reaction in CH_2Cl_2 at $-78°$ in the presence of $EtAlCl_2$. The products **10a** and **10b** were isolated after hydrolytic (HCl) workup (*Scheme 2*). Interestingly, this reaction did not result in the addition of a second maleimide molecule. Probably, the re-aromatization after hydrolysis of the Me_3SiO group is favored compared to a further addition. All analytical data were in agreement with the structures **10a** and **10b**.

The IR spectra of **10a,b** were characterized by the strong C=O absorptions at 1783 and 1720 cm^{-1} of the imide part, and at 1650 cm^{-1} of the α,β-unsaturated ketone moiety. The ^{1}H-NMR spectra contained a 4-H system caused by H−C(10b), H−C(3a), and the two H−C(4) at δ 2.99, 3.15, 3.82, and 4.46, and $J_{gem} = 17.1$ Hz, $J(3a,4) = 6.6$, and 8.2 Hz, and $J(3a,10b) = 8.1$ Hz (values from **10a**) establishing the *cis* configuration.

In contrast to the less reactive maleimides, the highly reactive 4-phenyl-3H-1,2,4-triazole-3,5(4H)-dione reacted at $-78°$ in THF nearly quantitative with **9** yielding **11** after hydrolytic workup with MeOH, without addition of a second molecule of the dienophile (*Scheme 2*). The IR spectrum (KBr) of **11** showed a strong absorption at 3445 cm^{-1}; in the ^{1}H-NMR spectrum in CDCl$_3$, (D$_6$)DMSO, or (D$_6$)acetone, a broad *s* at δ ca. 10, and the signal at δ 154 in the ^{13}C-NMR spectrum indicated that **11** preferred the enol structure in the solid state and in solution. The attempt to cleave the N−benzyl bond by catalytic hydrogenation (Pd/C) was not successful, but the spectra of the isolated product were consistent with the proposed structure of isomer **12**. Reactions of **11** with $H_2NOH \cdot HCl$ and $H_2NOMe \cdot HCl$ following standard procedures yielded **13a** and **13b**, respectively, which exist, according to spectroscopic data, in solution as an equilibrium between the imine and the enamine structure.

A very complex behavior was observed in the reactions of the bis-silylated 1H-indole derivative **14**. Its synthesis and reaction with *N*-phenylmaleimide is described in [5]. According to this report, the normal addition product **I** should be obtained which by dehydrogenation should be transformed into the more stable structure **II** (*Scheme 3*). Repeating the reaction, we could not verify these reported results. Following exactly the reported procedure, we isolated from the reaction between **14** and **2a** always two products. According to the NMR data, the first one, **15a**, was a mixture of two diastereoisomers, which differ only in the configuration at C(3′) of the succinimide moiety attached at C(10b), and which were deprotected at N(10). The second product, **16**, was not deprotected at N(10) and bore the additional succinimide moiety at C(5a). The analogous reaction between **14** and **2b** yielded **15b** and **19**, whereas the reaction with **2c** only yielded **8** (*Scheme 3*).

The reaction of **14** with *N*-phenylcitraconimide (**17**) was very slow, the yield was poor, and in the isolated product **18**, the additional Me group was found at C(3a) [3].

The ^{1}H-NMR spectrum of **18** showed 1 *s* at δ 1.50 (Me), an *AB* system at δ 2.55 and 3.00 with $J_{gem} = 16.8$ Hz for the two H−C(4), and a *s* at δ 4.10 caused by H−C(10b), indicating the *cis* orientation between H−C(10b) and Me−C(3a).

Discussion. – The reaction between *N*-substituted maleimides and *N*-protected 3-[(1-trimethylsilyl)oxy]ethenyl]-1H-indoles did not end up with the expected 1:1 adduct, the silylated enol. This structure was not detected in any reaction. Instead,

Scheme 3
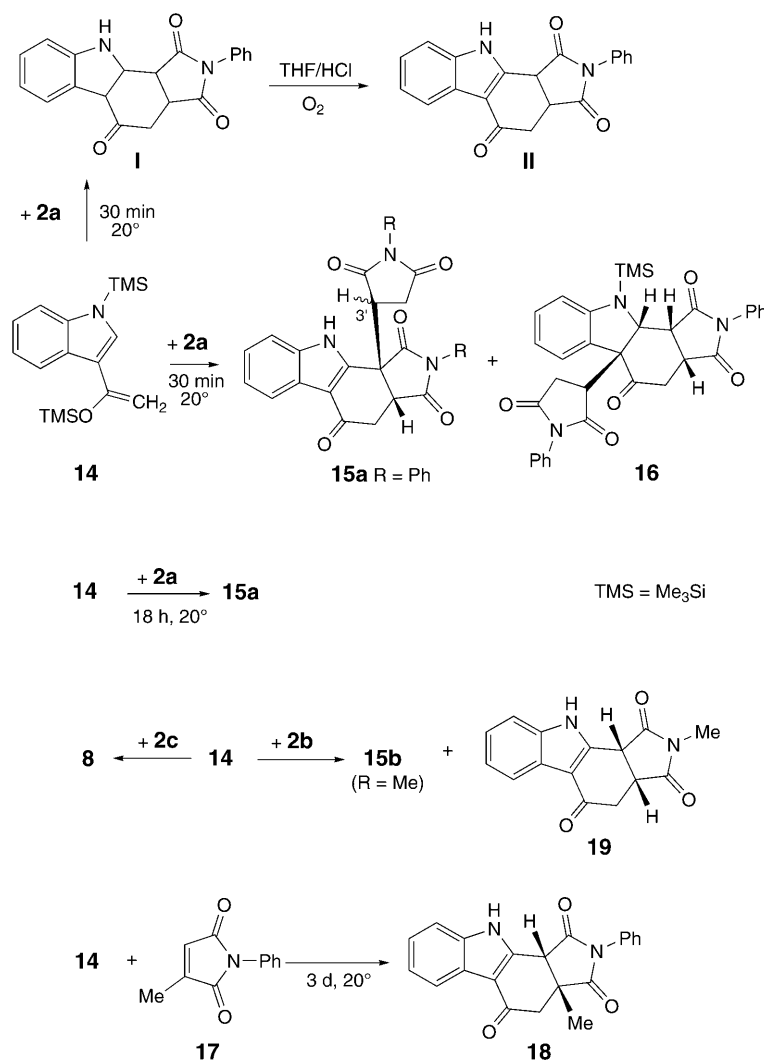
the cycloaddition was followed by the addition of a second maleimide molecule. This addition occurred either at C(5a) or at C(10b) of the pyrrolocarbazole, and depended on the protecting group at the indole N-atom. *Pindur* and *Rogge* [10] described reactions between **2a** and unprotected 3-{1-[(trimethylsilyl)oxy]ethenyl}-1-*H*-indole, and isolated, as a by-product, a 1:2 adduct, but the second addition – the authors discussed a hetero-ene or a conjugate addition reaction for its formation – occurred at C(4). In our experiments, the protecting group was a relatively bulky electron-withdrawing group, Tos, pivaloyl, or Boc (see **1a–c**), which could not be deleted during the reaction at room temperature. The addition of a second maleimide molecule to C(5a) and the formation of **3a–h**, therefore, might be explained as a sequence of a 1:1 cycloaddition

between the 1,3-diene **1** and the maleimide (**2**), followed by an ene addition of a second maleimide molecule to the (silyloxy)ene moiety at C(5a) of the first adduct, and followed finally by the hydrolysis of the silyloxy group to the C(5) ketone. Structures like **5** and **7** could be formed either by a thermal elimination from the 1:2 adduct or, if they were found together with the addition product, by a partial re-aromatization of the indole moiety before the second addition ocurred. If the N-atom in the starting material was protected by a benzyl group (see **9**), a cycloadduct was found only from reactions in the presence of a *Lewis* acid (EtAlCl₂), and stabilization of the adduct was faster than the addition of a second molecule. If the protecting group was easily deleted like the Me₃Si or the Boc group, the formation of a reactive center at C(10b) and the addition of the second maleimide molecule at this position was favored (→ **8**, **15a**, **15b**). This addition possibly might be understood either as a *Michael*-type addition of an anion intermediate at C(10b) to the second maleimide molecule, or as an ene reaction between an intermediately formed enamine structure (indol N-atom, C(10a), C(10b)) and the second maleimide molecule. All additions occurred as 'syn' additions, and thereby led to products with all-*cis* configurations.

Experimental Part

General. Abbreviations: HMPA, hexamethylphosphoric triamide; LDA, lithium diisopropylamide. The following compounds were prepared according to known procedures: 3-Acetyl-1-[(4-methylphenyl)sulfonyl]-1*H*-indole [11], 3-acetyl-1-(2,2-dimethylpropanoyl)-1*H*-indole [12], 3-acetyl-1-benzyl-1*H*-indole [13], 3-acetyl-1-[(*tert*-butoxy)carbonyl]-1*H*-indole [14], and 1-(trimethylsilyl)-3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indole (**14**) [5]. THF was stored under CaCl₂ protection, and distilled from Na and benzophenone prior to use. Other solvents were dried/purified according to literature procedures. LDA was prepared by mixing equivalent amounts of ⁱPr₂NH and BuLi (15% in hexane). All reactions at −78° were done under N₂. Column chromatography (CC): silica gel *60*, *Merck 7734*. TLC precoated silica-gel *60* F₂₅₄ plates *Merck 5549*. M.p.: *Mel-Temp-II* apparatus; not corrected. IR Spectra (KBr, cm⁻¹): *Perkin-Elmer IR 841*. NMR Spectra: *Varian T 60*, *Bruker WP 80*, *Varian Unity 300* for ¹H; *Varian Unity 300* (75.43 MHz) for ¹³C; δ in ppm rel. to SiMe₄ as internal standard, *J* in Hz; δ(H) from spectra in CDCl₃, if not otherwise noted. MS: *Finnigan MAT 312*, *MAT 44 S*; EI spectra at 200° and 70 eV; CI spectra with CH₄ or NH₃ at *ca.* 300 μbar. Elemental analyses: Institute of Pharmacy, University of Greifswald, or Chemisches Laboratorium, University of Freiburg.

*1-[(4-Methylphenyl)sulfonyl]-3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indole* (**1a**). A soln. of 3-acetyl-1-[(4-methylphenyl)sulfonyl]-1*H*-indole (3.12 g, 10 mmol) in THF (20 ml) was added dropwise at −78° to a LDA soln. in THF (20 ml), and after stirring for 10 min, Me₃SiCl (2.5 ml, 20 mmol) was added in one portion. When the mixture was warmed to r.t. (*ca.* 2 h), pentane (50 ml) was added. The org. layer was washed with an aq. sat. NaHCO₃ soln. (100 ml), dried (MgSO₄), and evaporated: 3.8 g (99%; not purified) of **1a** which was immediately used for further reactions. IR (film): 2959 (CH), 1670 (C=C), 1596 (arom. C−C), 1377, 1174 (SO₂), 1252 (Me-Si), 1090 (Si–O), 961 (=CH), 848, 750 (SiMe₃). ¹H-NMR (60 MHz): 0.26 (*s*, Me₃Si); 2.30 (*s*, Me); 4.54, 4.88 (*d*, *J* = 1.7, C=CH₂); 7.00–8.00 (*m*, 9 arom. H). MS: 385 (45, *M*⁺˙, C₂₀H₂₃NO₃SSi⁺), 313 (6, [acetyltosylindole]⁺˙).

*1-(2,2-Dimethylpropanoyl)-3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indole* (**1b**). From 3-acetyl-1-(2,2-dimethylpropanoyl)-1*H*-indole (2.43 g, 10 mmol), as described for **1a**: 3 g (95%; not purified) of **1b** which was immediately used for further reactions. IR (film): 2959 (CH), 1696 (C=C), 1622, 1549 (CO), 1253 (Si–Me), 958 (=CH), 1074 (Si–O), 845, 753 (SiMe₃).

*1-[(tert-Butoxy)carbonyl]-3-{1-[(trimethylsilyl)oxy]ethenyl}-1*H*-indole* (**1c**). From 3-acetyl-1-[(*tert*-butoxy)carbonyl]-1*H*-indole (2.59 g, 10 mmol), as described for **1a**: 3.2 g (95%; not purified) of **1c** which was

immediately used for further reactions. IR (film): 3053 (=CH$_2$), 2978 (CH), 1630 (C=C, CO), 1451 (Me), 1065, 1013 (Si–O), 845, 748 (SiMe$_3$).

5a-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-3a,4,5a,10,10a,10b-hexahydro-10-[(4-methylphenyl)sulfonyl]-2-phenylpyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3a**). Under N$_2$ and at r.t., a soln. of **1a** (3.86 g, 10 mmol) and **2a** (3.46 g, 20 mmol) in toluene (100 ml) was stirred until the precipitation was complete. Then, the solvent was evaporated and the residue in MeOH (100 ml) refluxed for 1 h. After cooling to r.t., the precipitate was collected: 2.04 g (31%) of **3a**. R_f (cyclohexane/AcOEt 1:1) 0.53. Colorless crystals. M.p. 280° (AcOEt). IR: 2926 (CH), 1781, 1712 (CO), 1597 (C–C), 1382, 1170 (SO$_2$), 755, 696 (arom.). ^{1}H-NMR (300 MHz): 1.94 (*dd*, *J*(3′,4′; *trans*) = 6.1, *J*(3′,4′; *cis*) = 9.3, H–C(3′)); 2.05 (*dd*, *J*(4′,3′; *cis*) = 9.3, *J*(4′,4′) = 17.5, H$_{cis}$–C(4′)); 2.38 (*s*, Me); 2.85 (*dd*, *J*(4A, 3a) = 9.0, *J*(4A,4B) = 15.3, H$_A$–C(4)); 2.97 (*dd*, *J*(4B,3a) = 3.7, *J*(4B,4A) = 15.4, H$_B$–C(4)); 3.02 (*dd*, *J*(4′,3′; *trans*) = 6.1, *J*(4′,4′) = 17.5, H$_{trans}$–C(4′)); 3.50 (*ddd*, *J*(3a,4B) = 3.7, *J*(3a,4A) = 9.0, *J*(3a,10b) = 9.3, H–C(3a)); 3.82 (*dd*, *J*(10b,10a) = 8.5, *J*(10b,3a) = 9.3, H–C(10b)); 5.95 (*d*, *J*(10a,10b) = 8.3, H–C(10a)); 6.84 (*dd*, *J* = 2.0, *J* = 7.8, 2 arom. H); 7.11–7.53 (*m*, 13 arom. H); 7.7 (*d*, *J* = 8.1, H–C(9)); 7.81 (*d*, *J* = 8.3, 2 arom. H). Anal. calc. for C$_{37}$H$_{29}$N$_3$O$_7$S (659.72): C 67.36, H 4.43, N 6.37; found: C 66.87, H 4.44, N 6.07.

3a,4,5a,10,10a,10b-Hexahydro-2-methyl-5a-(1-methyl-2,5-dioxopyrrolidin-3-yl)-10-[(4-methylphenyl)sulfonyl]-pyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3b**). From **1a** (3.86 g, 10 mmol) and **2b** (2.2 g, 20 mmol), as described for **3a** (72 h) at r.t., 1.9 g (36%) of **3b**. Colorless crystals. M.p. 226° (cyclohexane/AcOEt 1:1). IR: 2949 (CH), 1781, 1702 (CO), 1598 (C–C), 1461, 1435 (CH), 1364, 1168 (SO$_2$). ^{1}H-NMR (300 MHz): 1.80–1.90 (*m*, H–C(3′), H$_{cis}$–C(4′)); 2.34, 2.58 (2*s*, 2 Me); 2.80 (*m*, H$_A$–C(4), H$_B$–C(4), H$_{trans}$–C(4′)); 2.90 (*s*, Me); 3.32 (*dt*, *J*(3a,4) = 5.9, *J*(3a,10b) = 9.3, H–C(3a)); 3.67 (*dd*, *J*(10b,3a) = 9.1, *J*(10b,10a) = 8.6, H–C(10b)); 5.86 (*d*, *J*(10a,10b) = 8.6, H–C(10a)); 7.00 (*ddd*, *J*(7,9) = 1, *J*(7,6) = 7.6, *J*(7,8) = 7.6, H–C(7)); 7.18 (*dd*, *J*(6,8) = 0.7, *J*(6,7) = 7.6, H–C(6)); 7.23 (*d*, *J* = 7.8, 2 arom. H); 7.32 (*ddd*, *J*(8,6) = 1.2, *J*(8,7) = 7.6, *J*(8,9) = 8.1, H–C(8)); 7.64 (*d*, *J*(9,8) = 8.1, H–C(9)); 7.80 (*d*, *J* = 8.3, 2 arom. H). ^{13}C-NMR (75.43 MHz): 21.46 (Me); 24.70 (MeN); 24.81 (MeN); 31.27 (CH$_2$); 38.27 (C(3a)); 38.42 (CH$_2$); 40.31 (C(10b)); 45.17 (C(3′)); 58.27 (C(5a)); 65.76 (C(10a)); 117.05 (C(9)); 124.58 (C(7)); 124.66 (C(6)); 127.00 (arom. C); 128.63 (C(5b)); 129.81 (arom. C); 130.64 (C(8)); 136.02 (arom. C); 141.34 (C(9a)); 144.80 (arom. C); 173.10, 174.28, 176.06, 176.67, 204.86 (CO). MS: 535 (100, M^+). Anal. calc. for C$_{27}$H$_{25}$N$_3$O$_7$S (535.58): C 60.55, H 4.71, N 7.85; found: C 60.94, H 4.79, N 7.23.

2-Ethyl-5a-(1-ethyl-2,5-dioxopyrrolidin-3-yl)-3a,4,5a,10,10a,10b-hexahydro-10-[(4-methylphenyl)sulfonyl]-pyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3c**). From **1a** (3.86 g, 10 mmol) and **2c** (2.5 g, 20 mmol), as described for **3a**. CC (cyclohexane/AcOEt 1:1; R_f 0.38) gave 1.45 g (26%) of **3c**. Colorless crystals. M.p. 208° (MeOH). IR: 2980 (CH), 1777, 1704 (CO), 1597 (arom. C–C), 1461, 1402 (CH), 1350, 1169 (SO$_2$), 1225 (C–C), 815, 797 (arom.). ^{1}H-NMR (300 MHz): 0.60 (*t*, *J* = 7.3, Me); 1.07 (*t*, *J* = 7.3, Me); 1.68 (*dd*, *J*(3′,4′; *trans*) = 5.6, *J*(3′,4′; *cis*) = 9.0, H–C(3′)); 1.81 (*dd*, *J*(4′,3′; *cis*) = 9.0, *J*(4′,4′) = 17.8, H$_{cis}$–C(4′)); 2.32 (*s*, Me); 2.80 (*dd*, *J*(4′,3′; *trans*) = 5.6, *J*(4′,4′) = 17.6, H$_{trans}$–C(4′)); 2.83 (*d*, *J*(4,3a) = 5.9, H$_A$–C(4), H$_B$–C(4)); 3.19 (*q*, *J* = 7.3, CH$_2$); 3.32 (*dt*, *J*(3a,4) = 5.9, *J*(3a,10b) = 9.8, H–C(3a)); 3.43 (*q*, *J* = 7.3, CH$_2$); 3.66 (*dd*, *J*(10b,10a) = 8.5, *J*(10b,3a) = 9.5, H–C(10b)); 5.89 (*d*, *J*(10a,10b) = 8.3, H–C(10a)); 6.98 (*ddd*, *J*(7,9) = 1, *J*(7,6) = 7.6, *J*(7,8) = 7.6, H–C(7)); 7.21 (*d*, *J* = 8.1, 2 arom. H); 7.23 (*d*, *J*(6,7) = 7.3, H–C(6)); 7.32 (*ddd*, *J*(8,6) = 1.2, *J*(8,7) = 7.8, *J*(8,9) = 8.1, H–C(8)); 7.67 (*d*, *J*(9,8) = 8.1, H–C(9)); 7.80 (*d*, *J* = 8.3, 2 arom. H). ^{13}C-NMR (75.43 MHz): 12.33 (Me); 12.77(Me); 21.50 (Me); 31.16 (C(4′)); 33.74 (CH$_2$); 33.87 (CH$_2$); 38.21 (C(3a)); 38.70 (C(4)); 39.93 (C(10b)); 45.20 (C(3′)); 58.20 (C(5a)); 65.39 (C(10a)); 117.09 (C(9)); 124.52 (C(7)); 124.92 (C(6)); 126.99 (arom. C); 128.72 (C(5b)); 129.86 (arom. C); 130.72 (C(8)); 136.22 (arom. C); 141.41 (C(9a)); 144.73 (arom. C); 172.72 (C(1)); 173.99 (C(2′)); 175.90 (C(3)); 176.35 (C(5′)); 204.71 (C(5)). FAB-MS (FAB gun, Xe, 6 kV, 2 mA): 564 (M^+), 437 ([M – ethylsuccinimide]$^+$), 409 ([M + 1 – Tos]$^+$), 283 ([M + 1 – Tos-ethylsuccinimide]$^+$). Anal. calc. for C$_{29}$H$_{29}$N$_3$O$_7$S (563.63): C 61.80, H 5.19, N 7.46; found: C 61.59, H 4.98, N 7.23.

Crystal-Structure Analysis of **3c**. Crystals suitable for diffraction experiments were grown from EtOH. C$_{29}$H$_{29}$N$_3$O$_7$S, M_r 563.61, monoclinic, space group $P2_1/c$ with a = 8.738(2), b = 16.516(3), c = 18.913(3) Å, β = 101.613(9)°, V = 2673.6(9) Å^3, Z = 4, D_c = 1.400 g·cm^{-3}, 34253 reflections measured, 4877 independent (R_{int} = 0.0455), 3.59° < θ < 69.23°, 379 parameters, no restraints, R_1 = 0.0369, wR_2 = 0.0911 for 4057 reflections with I > 2σ(*I*), R_1 = 0.0482, wR_2 = 0.0996 for all 4877 data, goodness-of-fit = 1.039, res. electron density = +0.37/–0.34 e·Å^3. Diffraction data were collected at 100 K with a *Bruker AXS-SMART-6000-CCD* detector on a three-circle platform goniometer with Cu*Kα* radiation from a fine-focus sealed tube generator equipped with a graphite monochromator. A semi-empirical absorption correction was applied, based on the intensities of symmetry-related reflections measured at different angular settings [15]. The structure was solved and refined on F^2 with the SHELXTL suite of programs [16]. Non-H-atoms were refined with anisotropic displacement parameters, H-atoms at tertiary C-atoms were located in difference *Fourier* maps and refined isotropically,

all other H-atoms were calculated in idealized positions and refined using a riding model. Displacement parameters and bond lengths of the ethyl side chain at N(2) indicate disorder. The disorder was not modeled. CCDC-261131 contains the supplementary crystallographic data (excluding structure factors) for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

10-(2,2-Dimethylpropanoyl)-5a-(2,5-dioxo-1-phenylpyrrolidin-3-yl)-3a,4,5a,10,10a,10b-hexahydro-2-phenylpyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3d**). From **1b** (3.15 g, 10 mmol) and **2a** (1.73 g, 10 mmol), as described for **3a** (96 h) at r.t.: 1.04 g (35%) of **3d**. Colorless crystals. TLC (cyclohexane/AcOEt 1:1): R_f 0.53. M.p. 288–292° (AcOEt). IR: 1778, 1719 (CO), 1660, 1595 (CO, amide). ^{1}H-NMR (300 MHz): 1.53 (*s*, Me$_3$C); 2.42 (*dd*, $J(4',3';\ cis) = 11.8$, $J(4',4') = 20.5$, H$_{cis}$−C(4')); 2.90 (*dd*, $J(4A,3a) = 7.8$, $J(4A,4B) = 16.4$, H$_A$−C(4)); 3.23 (*dd*, $J(4B,3a) = 2.9$, $J(4B,4A) = 16.4$, H$_B$−C(4)); 3.23 (*dd*, $J(3',4';\ trans) = 5.6$, $J(3',4';\ cis) = 11.9$, H−C(3')); 3.26 (*dd*, $J(4',3';\ trans) = 5.6$, $J(4',4') = 20.1$, H$_{trans}$−C(4')); 3.47 (*ddd*, $J(3a,4B) = 2.9$, $J(3a,4A) = 7.8$, $J(3a, 10b) = 10.3$, H−C(3a)); 3.99 (*dd*, $J(10b,10a) = 9.8$, $J(10b,3a) = 9.9$, H−C(10b)); 6.25 (*d*, $J(10a,10b) = 9.8$, H−C(10a)); 6,54–8,00 (*m*, 14 arom. H). MS: 589 (6, $M^{+\cdot}$), 505 (8, $[M − C_5H_9O]^+$), 331 (45), 174, 85, 57 (100, $C_4H_9^+$). EI-HR-MS: 589.221287 (calc. 589.221171). Anal. calc. for $C_{35}H_{31}N_3O_6$ (589.64): C 71.29, H 5.30, N 7.13; found: C 68.88, H 5.31, N 6.84.

10-(2,2-Dimethylpropanoyl)-3a,4,5a,10,10a,10b-hexahydro-2-methyl-5a-(1-methyl-2,5-dioxopyrrolidin-3-yl)pyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3e**). From **1b** (3.15 g, 10 mmol) and **2b** (1.1 g, 10 mmol), as described for **3a** (3 weeks at r.t.). Then the solvent was evaporated, the residue stirred with MeOH (a few ml) for 2–5 h, and the solvent evaporated: 710 mg (30%) of **3e**. Colorless crystals. M.p. 226° (AcOEt). IR: 2971 (CH), 1769, 1702 (CO), 1649 (CO amide), 1466, 1439 (Me), 1381, 1354, 1209 (Me$_3$C). ^{1}H-NMR (300 MHz): 1.53 (*s*, Me$_3$C); 2.24 (*dd*, $J(4',3';\ cis) = 10.7$, $J(4',4') = 19.5$, H$_{cis}$−C(4')); 2.80 (*dd*, $J(4A,4B) = 16.6$, $J(4A,3a) = 7.6$, H$_A$−C(4)); 3.06 (*dd*, $J(3',4';\ trans) = 5.6$, $J(3',4';\ cis) = 11$, H−C(3')); 3.08 (*dd*, $J(4',4') = 19.4$, $J(4',3';\ trans) = 5.6$, H$_{trans}$−C(4')); 3.13 (*dd*, $J(4B,4A) = 16.5$, $J(4B,3a) = 2.7$, H$_B$−C(4)); 3.26 (*ddd*, $J(3a,4B) = 2.7$, $J(3a,4A) = 7.5$, $J(3a,10b) = 9.7$, H−C(3a)); 3.82 (*dd*, $J(10b,10a) = 9.5$, $J(10b,3a) = 9.5$, H−C(10b)); 6.09 (*d*, $J(10a,10b) = 9.5$, H−C(10a)); 7.01 (*ddd*, $J(7,9) = 1.2$, $J(7,6) = 7.6$, $J(7,8) = 7.6$, H−C(7)); 7.11 (*dd*, $J(6,8) = 1.5$, $J(6,7) = 7.6$, H−C(6)); 7.28 (*ddd*, $J(8,6) = 1.2$, $J(8,7) = 7.3$, $J(8,9) = 8.1$, H−C(8)); 7.99 (*d*, $J(9,8) = 8.1$, H−C(9)). Anal. calc. for $C_{25}H_{27}N_3O_6$ (465.50): C 64.50, H 5.85, N 9.03; found: C 64.25, H 5.74, N 8.97.

10-[(tert-Butoxy)carbonyl]-5a-(2,5-dioxo-1-phenylpyrrolidin-3-yl)-3a,4,5a,10,10a,10b-hexahydro-2-phenylpyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3g**). A soln. of **1c** (3.31 g, 10 mmol) and **2a** (1.73 g, 10 mmol) in toluene (30–50 ml) was stirred at r.t. for 4 d. Then the solvent was evaporated: 1.5 g (50%) of **3g**. Colorless crystals. M.p. 240–243° (AcOEt). IR: 2980 (CH), 1783, 1720 (CO), 1598 (arom. C−C), 1390, 1256 (Me$_3$C). ^{1}H-NMR (300 MHz, (D$_6$)DMSO): 1.60 (*s*, Me$_3$C); 2.60 (*dd*, $J(4',3';\ cis) = 9.3$, $J(4',4') = 18.1$, H$_{cis}$−C(4')); 2.82 (*m*, H$_A$−C(4)); 2.82 (*dd*, $J(4',4') = 18.2$, H$_{trans}$−C(4')); 3.1 (*m*, H$_B$−C(4)), 3.60 (*dd*, $J(3',4';\ trans) = 4.6$, $J(3', 4';\ cis) = 9.4$, H−C(3')); 3.80 (*ddd*, $J(3a,10b) = 9.0$, $J(3a,4B) = 2.4$, $J(3a,4A) = 9.0$, H−C(3a)); 4.02 (*dd*, $J(10b, 10a) = 9.3$, $J(10b,3a) = 9.3$, H−C(10b)); 5.75 (*d*, $J(10a,10b) = 8.8$, H−C(10a)); 6.50–7.70 (*m*, 14 arom. H). FAB-MS (FAB gun, Xe, 8 kV, 1 mV): 605 (1.14, $M^{+\cdot}$). MS: 605 (0.29, $M^{+\cdot}$), 505 (10.11, $[M + 1 − \text{Boc}]^+$), 331 (75.55, $[M + 1 − \text{Boc-phenylmaleimide}]^+$). Anal. calc. for $C_{35}H_{31}N_3O_7$ (605.64): C 69.41, H 5.16, N 6.94; found: C 68.92, H 5.16, N 6.79.

10-[(tert-Butoxy)carbonyl]-3a,4,5a,10,10a,10b-hexahydro-2-methyl-5a-(1-methyl-2,5-dioxopyrrolidin-3-yl)-pyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**3h**). As described for **3g**, from **1c** (3.31 g, 10 mmol) and **2b** (1.1 g, 10 mmol). MeOH (a few ml) was added to the residue, the mixture was filtered, and from the filtrate, **3h/7** (520 mg, 14%) was isolated. The insoluble residue was separated by filtration: 500 mg (20%) of **3h**. Colorless crystals. M.p. 245–248° (AcOEt). IR: 2977 (CH), 1777, 1703 (CO), 1480, 1385, 1244 (Me). ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 1.48 (*s*, Me$_3$C); 2.3 (*m*, H$_{cis}$−C(4'), H$_{trans}$−C(4')); 2.40, 2.44 (2*s*, 2 MeN); 2.75 (*dd*, $J(4B, 3a) = 3.7$, $J(4B,4A) = 14.5$, H$_B$−C(4)); 3.07 (*dd*, $J(4A,3a) = 8.3$, $J(4A,4B) = 14.5$, H$_A$−C(4)); 3.26 (*ddd*, $J(3a, 4B) = 3.7$, $J(3a,4A) = 8.3$, $J(3a,10b) = 8.7$, H−C(3a)); 3.50 (*dd*, $J(3',4';\ trans) = 5.6$, $J(3',4';\ cis) = 8.8$, H−C(3')); 3.64 (*dd*, $J(10b,3a) = 8.8$, $J(10b,10a) = 8.6$, H−C(10b)); 4.99 (*d*, $J(10a,10b) = 8.3$, H−C(10a)); 6.78 (*ddd*, $J(7, 9) = 1$, $J(7,8) = 7.6$, $J(7,6) = 7.6$, H−C(7)); 7.10 (*ddd*, $J(8,6) = 1.5$, $J(8,7) = 7.6$, $J(8,9) = 7.8$, H−C(8)); 7.18 (*dd*, $J(9,7) = 1$, $J(9,8) = 7.7$, H−C(9)); 7.44 (*d*, $J(6,7) = 8.1$, H−C(6)). Anal. calc. for $C_{25}H_{26}N_3O_7$ (480.49): C 62.49, H 5.45, N 8.75; found: C 61.49, H 5.52, N 8.53.

10-(2,2-Dimethylpropanoyl)-5a-(2,5-dioxo-1-phenylpyrrolidin-3-yl)-4,5,5a,10,10a,10b-hexahydro-5-hydroxy-5-methoxy-2-phenylpyrrolo[3,4-a]carbazole-1,3(2H,3a,H)-dione (**4**). A soln. of **3d** (400 mg, 0.68 mmol) in MeOH (20 ml) and 0.1ɴ MeONa/MeOH (1 ml) was stirred for 30 min. Then H$_2$O (50 ml) and AcOEt (50 ml) were added. The aq. layer was twice extracted with AcOEt, the combined org. layer washed with an aq. sat. NaCl soln., dried (MgSO$_4$), and evaporated: 240 mg (38%) of **4**. Colorless crystals. M.p. 270° (MeOH). IR:

3431 (OH), 2956 (CH), 1712, 1632 (CO), 1597 (arom. C−C), 1475, 1437, 1387 (Me). ^{1}H-NMR (300 MHz): 1.46 (*s*, Me$_3$C); 1.82 (*dd*, *J*(4′,4′) = 17.7, *J*(4′,3′; *cis*) = 8.1, H$_{cis}$−C(4′)); 2.35 (*ddd*, *J*(4*A*,4*B*) = 14.3, *J*(4*A*,3a) = 8.3, *J*(4*A*, OH) = 2.4, H$_A$−C(4)); 2.77(*dd*, *J*(4*B*,4*A*) = 14.5, *J*(4*B*,3a) = 0.9, H$_B$−C(4)); 2.80 (*dd*, *J*(4′,4′) = 17.7, *J*(4′,3′; *trans*) = 4.6, H$_{trans}$−C(4′)); 2.95 (*d*, *J*(OH,4*A*) = 2.4, OH); 3.34 (*m*, H−C(3a)); 3.58 (*dd*, *J*(3′,4′; *trans*) = 4.6, *J*(3′,4′; *cis*) = 8.0, H−C(3′)); 3.62 (*s*, MeO); 4.26 (*dd*, *J*(10b,10a) = 7.8, *J*(10b,3a) = 10.1, H−C(10b)); 5.42 (*d*, *J*(10a,10b) = 7.9, H−C(10a)); 6.90–7.65 (*m*, 14 arom. H). MS: 621 (12, $M^{+\cdot}$), 590 (1.4, [M − MeO]$^+$), 505 (1.1, [M − OMe − C$_4$H$_9$O]$^+$), 174 (1.3, [*N*-phenylsuccinimide]$^+$), 130 (4), 57 (100, C$_4$H$_9^+$). EI-HR-MS: 621.247502 (C$_{36}$-H$_{35}$N$_3$O$_7^+$); calc. 621.247508, 0.0 ppm).

10-(2,2-Dimethylpropanoyl)-2-ethyl-3a,4,10,10b-tetrahydropyrrolo[3,4-a]carbazole-1,3,5(2H)-trione   (**5**). From **1b** (3.15 g, 10 mmol) and **2c**, as described for **3e**. CC (cyclohexane/AcOEt 1 : 1) gave 340 mg (9.3%) of **5**. Colorless crystals. M.p. 197–200°. IR: 2973, 2917 (CH), 1778, 1708 (CO), 1671, 1569 (CO, amide), 1449 (Me), 1397, 1378, 1222 (Me$_3$C). ^{1}H-NMR (300 MHz): 1.15 (*t*, *J* = 7.3, Me); 3.00 (*d*, *J*(4,3a) = 7.1, H$_A$−C(4), H$_B$−C(4)); 3.55 (*q*, *J* = 7.3, CH$_2$); 3.71 (*dt*, *J*(3a,4) = 7.1, *J*(3a,10b) = 8.6, H−C(3a)); 5.0 (*d*, *J*(10b,3a) = 8.6, H−C(10b)); 7.37 (*m*, 2 arom. H); 7.67 (*d*, 1 arom. H); 8.32 (*dd*, 1 arom. H). MS: 366 (16, $M^{+\cdot}$), 282 (61, [M + 1 − pivaloyl]$^+$), 57(100). Anal. calc. for C$_{21}$H$_{22}$N$_2$O$_4$ (366.41): C 68.84, H 6.05, N 7.65; found: C 68.67, H 5.99, N 7.59.

3a,4,5a,10,10a,10b-Hexahydro-2-phenyl-5a-(1-phenyl-2,5-dioxopyrrolidin-3-yl)pyrrolo[3,4-a]carbazole-1,3,5-(2H)-trione (**6**). Dry **3g** was heated until melting occurred. M.p. *ca.* 300°. IR: 3354 (NH), 1778, 1708 (CO), 1597, 1500 (arom. C−C), 1261, 1187 (CH). ^{1}H-NMR (300 MHz): 2.71 (*dd*, *J*(4*B*,3a) = 7.9, *J*(4*B*,4*A*) = 12.5, H$_B$−C(4)); 2.84 (*dd*, *J*(4*A*,3a) = 12.4, *J*(4*A*,4*B*) = 12.4, H$_A$−C(4)); 3.08 (*dd*, *J*(4′,3′; *cis*) = 9.0, *J*(4′,4′) = 17.1, H$_{cis}$−C(4′)); 3.43 (*dd*, *J*(3′,4′; *trans*) = 7.3, *J*(3′,4′; *cis*) = 9.0, H−C(3′)); 3.50 (*ddd*, *J*(3a,4*B*) = 7.9, *J*(3a,4*A*) = 12.2, *J*(3a,10b) = 10.0, H−C(3a)); 3.66 (*dd*, *J*(4′,3′; *trans*) = 7.3, *J*(4′,4′) = 17.3, H$_{trans}$−C(4′)); 4.24 (*dd*, *J*(10b,3a) = 10.0, *J*(10b,10a) = 5.3, H−C(10b)); 4.51 (*d*, *J*(NH,10a) = 5.5, NH); 5.1 (*dd*, *J*(10a,10b) = 5.3, *J*(10a,NH) = 5.3, H−C(10a)); 6.70–7.50 (*m*, 14 arom. H). EI-HR-MS: 505.163772 (C$_{30}$H$_{23}$N$_3$O$_5^+$; calc. 505.163603; − 0.3 ppm).

10-[(tert-*Butoxy)carbonyl]-3a,4,10,10b-tetrahydro-2-methylpyrrolo[3,4-a]carbazole-1,3,5(2H)-trione*   (**7**). As a by-product from the synthesis of **3h**. Colorless crystals. M.p. 176°. IR: 2982 (CH), 1745, 1697, 1666 (CO), 1454, 1375 (Me). ^{1}H-NMR (300 MHz): 1.8 (*s*, Me$_3$C); 2.98 (*s*, MeN); 2.99 (*d*, *J*(4*A*,3a) = 8.1, H$_A$−C(4)); 3.01 (*d*, *J*(4*B*,3a) = 5.6, H$_B$−C(4)); 3.70 (*ddd*, *J*(3a,4*B*) = 6.1, *J*(3a,4*A*) = 8.3, *J*(3a,10b) = 8.3, H−C(3a)); 5.32 (*d*, *J*(10b,3a) = 8.3, H−C(10b)); 7.7–8.25 (*m*, 4 arom. H). Anal. calc. for C$_{20}$H$_{20}$N$_2$O$_5$ (368.39): C 65.21, H 5.47, N 7.60; found: C 64.87, H 5.39, N 7.58.

2-Ethyl-10b-(1-ethyl-2,5-dioxopyrrolidin-3-yl)-3a,4,10,10b-tetrahydropyrrolo[3,4-a]carbazole-1,3,5(2H)-tri-one (**8**). *a*) From **1c** (3.31 g, 10 mmol) and **2c** (1.25 g, 10 mmol), as described for **3g** (3 d under reflux, then evaporation): 960 mg (47%) of **8**. *b*) From **14** (3.0 g, 10 mmol) and **2c** (1.3 g, 10 mmol) as described for **15b**: 980 mg (48%) of **8**. Colorless crystals. M.p. 241–243° (AcOEt). IR: 3181 (NH), 2982 (CH), 1778, 1701, 1619 (CO), 1584 (arom. C−C), 1460, 1380 (Me). ^{1}H-NMR (300 MHz, CDCl$_3$/(D$_6$)DMSO): 0.7 (2*t*, *J* = 7.3, 2 Me); 2.05 (*dd*, *J*(4′,3′; *trans*) = 6.7, *J*(4′,4′) = 18.1, H$_{trans}$−C(4′)); 2.28 (*dd*, *J*(4′,3′; *cis*) = 9.5, *J*(4′,4′) = 18.2, H$_{cis}$−C(4′)); 2.50 (*dd*, *J*(4*B*, 3a) = 8.7, *J*(4*B*,4*A*) = 18.0, H$_B$−C(4)); 2.80 (*dd*, *J*(4*A*,3a) = 1.4, *J*(4*A*,4*B*) = 18.1, H$_A$−C(4)); 2.86 (*dd*, *J*(3a, 4*A*) = 1.4, *J*(3a,4*B*) = 8.6, H−C(3a)); 3.10 (*m*, 2 CH$_2$); 4.06 (*dd*, *J*(3′,4′; *trans*) = 6.7, *J*(3′,4′; *cis*) = 9.4, H−C(3′)); 6.80 (*ddd*, *J*(7,9) = 1.4, *J*(7,6) = 7.3, *J*(7,8) = 7.5, H−C(7)); 6.86 (*ddd*, *J*(8,6) = 1.5, *J*(8,7) = 7.5, *J*(8, 9) = 7.5, H−C(8)); 7.08 (*dd*, *J*(9,6) = 0.9, *J*(9,7) = 1.4, *J*(9,8) = 7.5, H−C(9)); 7.71(*ddd*, *J*(6,9) = 0.6, *J*(6,8) = 1.5, *J*(6,7) = 7, H−C(6)). Anal. calc. for C$_{22}$H$_{21}$N$_3$O$_5$ (407.42): C 64.86, H 5.20, N 10.31; found: C 64.08, H 5.23, N 9.91.

1-Benzyl-3-{1-[(trimethylsilyl)oxy]ethenyl}-1H-indole (**9**). From 3-acetyl-1-benzyl-1*H*-indole (2.5 g, 10 mmol), LDA (20 mmol), and Me$_3$SiCl (2.5 ml, 20 mmol), as described for **1a**. After stirring for 90 min at − 78°, the mixture was poured into Et$_2$O (100 ml), the org. layer washed with aq. sat. NH$_4$Cl soln. (3 × 100 ml), dried (MgSO$_4$), and evaporated: 3.0 g (93%; not purified) of **9** which was immediately used for further reactions. IR (film): 2958 (CH), 1636 (C=C), 1528 (arom. C−C), 1252 (Si−Me), 1090 (Si−O), 845 (Me$_3$Si). ^{1}H-NMR (60 MHz): 0.2 (*s*, Me$_3$Si); 4.48, 4.90 (2*d*, *J* = 1.2, =CH$_2$); 5.04, 5.31 (2*s*, CH$_2$); 7.00–7.92 (*m*, 9 arom. H).

10-Benzyl-3a,4,10,10b-tetrahydro-2-phenylpyrrolo[3,4-a]carbazole-1,3,5(2H)-trione (**10a**). At − 78°, 1M EtAlCl$_2$ in hexane (10 ml) was injected *via* a septum into a vigorously stirred soln. of **2a** (1.73 g, 10 mmol) in CH$_2$Cl$_2$ (40 ml), and after 30 min a soln. of **9** (3.2 g, 10 mmol) in CH$_2$Cl$_2$ (20 ml) was added. Stirring was continued for 2 h at − 78°, then the mixture allowed to warm to r.t., and stirring continued for 2 d. After hydrolysis with dil. HCl soln. (*caution!*), the mixture was extracted with CH$_2$Cl$_2$ and the org. layer dried (MgSO$_4$) and evaporated. A few ml MeOH and dil. HCl soln. were added to the residue, and the mixture was refluxed for 2 h. After evaporation, the residue was purified by CC (AcOEt/cyclohexane 1 : 1): 80 mg (2%) of **10a**. Colorless crystals. M.p. 244° (MeOH). IR: 1783, 1720, 1649 (CO), 1528, 1495 (arom. C−C). ^{1}H-NMR (300 MHz): 2.99 (*dd*, *J*(4*B*, 3a) = 8.1, *J*(4*B*,4*A*) = 17.1, H$_B$−C(4)); 3.15 (*dd*, *J*(4*A*,3a) = 6.6, *J*(4*A*,4*B*) = 17.1, H$_A$−C(4)); 3.82 (*ddd*, *J*(3a,

$4A) = 6.6, J(3a,4B) = 8.2, J(3a,10b) = 8.2, H−C(3a)$); 4.46 ($d, J(10b,3a) = 8.1, H−C(10b)$); 5.66, 6.13 ($2d, J = 17.1$, CH$_2$); 6.98–8.36 ($m$, 14 arom. H). Anal. calc. for C$_{27}$H$_{20}$N$_2$O$_3$ (420.47): C 77.13, H 4.79, N 6.66; found: C 76.07, H 4.86, N 6.47.

*10-Benzyl-2-ethyl-3a,4,10,10b-tetrahydropyrrolo[3,4-a]carbazole-1,3,5(2*H*)-trione* (**10b**). From **2c** (1.25 g, 10 mmol) and **9** (3.21 g, 10 mmol), as described for **10a**, but after warming to r.t., the mixture was refluxed for 72 h and then cooled to r.t.: 84 mg (2.3%) of **10b**. Colorless crystals. M.p. 190° (MeOH). IR: 1779, 1708, 1642 (CO), 1529, 1497 (arom. C−C). ^{1}H-NMR (300 MHz): 1.16 ($t, J = 7.3$, Me); 2.91 ($dd, J(4B,4A) = 17.2$, $J(4B,3a) = 8.2, H_B−C(4)$); 3.04 ($dd, J(4A,4B) = 17.1, J(4A,3a) = 6.1, H_A−C(4)$); 3.58 ($q, J = 7.3$, CH$_2$); 3.64 ($ddd, J(3a,4A) = 6.1, J(3a,4B) = 8.2, J(3a,10b) = 8.2, H−C(3a)$); 4.29 ($d, J(10b,3a) = 8.1, H−C(10b)$); 5.66, 6.14 ($2d, J = 16.9$, CH$_2$); 6.99–8.31 ($m$, 9 arom. H). Anal. calc. for C$_{23}$H$_{20}$N$_2$O$_3$ (372.42): C 74.18, H 5.41, N 7.52; found: C 73.98, H 5.43, N 7.44.

*11-Benzyl-11,11a-dihydro-6-hydroxy-2-phenyl-1*H,5*H-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-b]indole-1,3-(2*H*)-dione* (**11**). At −78°, a soln. of 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (1.16 g, 6 mmol) in THF (10 ml) was dropwise added with stirring to a soln. of **9** (3.2 g, 10 mmol) in THF (50 ml). After 2 h at −78°, the mixture was allowed to warm to r.t., the solvent evaporated, and the residue stirred with MeOH (a few ml) for 5–6 h. The solvent was evaporated, and after addition of toluene (a few ml), the insoluble part was separated: 2.4 g (92%) of **11**. Colorless crystals. M.p. 212°. IR: 3445 (OH), 1706 (CO), 1187 (arom. C−OH). ^{1}H-NMR (CDCl$_3$/(D$_6$)DMSO 5:1): 4.72 (s, H$_A$−C(5), H$_B$−C(5)); 5.2 (s, CH$_2$); 6.99–8.15 (m, 15 arom. H); 9.9 (br. s, OH). Anal. calc. for C$_{25}$H$_{20}$N$_4$O$_3$ (424.46): C 70.74, H 4.75, N 13.20; found: C 70.53, H 4.82, N 13.12.

*11-Benzyl-6,11-dihydro-6-hydroxy-2-phenyl-1*H,5*H-[1,2,4]triazolo[1′,2′:1,2]pyridazino[3,4-b]indole-1,3-(2*H*)-dione* (**12**). From **11** (400 mg, 0.9 mmol) by hydrogenation with H$_2$ (Pd/C) in MeOH/CH$_2$Cl$_2$ 1:1 at r. t. for 72 h: 280 mg (70%) of **12**. Colorless crystals. ^{1}H-NMR (300 MHz): 3.90 ($dd, J(5,6) = 9.4, J(5,5) = 14.5$, H$_A$−C(5)); 4.20 ($dd, J(5,6) = 3.5, J(5,5) = 14.5$, H$_B$−C(5)); 4.84 ($dd, J(6,5) = 3.4, J(6,5) = 9.5$, H−C(6)); 5.30 ($s$, CH$_2$); 7.0–7.8 ($m$, 15 arom. H); 8.05 (br. s, OH).

*11-Benzyl-6,6a,11,11a-tetrahydro-6-(hydroxyimino)-2-phenyl-1*H,5*H-[1,2,4]triazolo[1′,2′:1,2]pyridazino-[3,4-b]indole-1,3(2*H*)-dione* (**13a**). A mixture of AcONa (5.0 g, 60 mmol), and H$_2$NOH·HCl (4.2 g, 60 mmol) in EtOH (50 ml) was refluxed for some min and then filtered. To the filtrate, **11** (1.0 g, 2.35 mmol) was added and the mixture was then refluxed for 3 h. After evaporation, EtOH (20 ml) was added to the residue, followed by H$_2$O until the mixture was cloudy: 840 mg (81%) of **13a**. Colorless needles. M.p. 166° (EtOH). IR: 3385 (OH), 1691 (CO). ^{1}H-NMR ((D$_6$)DMSO): 4.82 (s, H$_A$−C(5), H$_B$−C(5)); 5.40 (s, CH$_2$); 7.07–8.16 (m, 15 arom. H, OH); 11.9 (br. s, NH). Anal. calc. for C$_{25}$H$_{21}$N$_5$O$_3$ (439.47): C 68.33, H 4.82, N 15.94; found: C 68.67, H 5.01, N 15.44.

*11-Benzyl-6,6a,11,11a-tetrahydro-6-(methoxyimino)-2-phenyl-1*H,5*H[1,2,4]triazolo[1′,2′:1,2]pyridazino-[3,4-b]indole-1,3(2*H*)-dione* (**13b**). As described for **13a**, from AcONa (2.0 g, 24 mmol), H$_2$NOMe·HCl (2.0 g, 24 mmol), and **11** (0.43 g, 1 mmol): 385 mg (85%) of **13b**. Colorless needles. M.p. 221–223° (EtOH). IR: 3434 (NH), 1703 (CO), 1600 (arom. C−C). ^{1}H-NMR ((D$_6$)DMSO): 3.95 (s, MeO); 4.8 (s, H$_A$−C(5), H$_B$−C(5)); 5.4 (s, CH$_2$); 7–8.2 (m, 15 arom. H); 10.6 (br. s, NH). MS: 453 (16.8, M^+), 91 (100, PhC$_2^+$), 77 (6.5, Ph). EI-HR-MS: 453.1801 (C$_{26}$H$_{23}$N$_5$O$_3^+$; calc. 453.1810, 2.0 ppm).

*10b-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-3a,4,10,10b-tetrahydro-2-phenylpyrrolo[3,4-a]carbazole-1,3,5(2*H*)-trione* (**15a**). A soln. of **2a** (1.73 g, 10 mmol) and **14** (3 g, 10 mmol) in toluene was stirred for 24 h. After evaporation, the residue was stirred with MeOH (a few ml) at r.t., the solvent evaporated, and the residue purified by CC (cyclohexane/AcOEt 1:1): 1.2 g (48%) of isomers **15aa/15ab** 4:1. Colorless crystals. M.p. 272°. IR: 3411 (NH), 1782, 1712, 1650 (CO), 1597 (arom. C−C). **15aa**: ^{1}H-NMR (300 MHz): 2.43 ($dd, J(4′,3′; trans) = 7.5$, $J(4′,4′) = 17.9$, H$_{trans}$−C(4′)); 2.57 ($dd, J(4′,3′; cis) = 9.4, J(4′,4′) = 17.9$, H$_{cis}$−C(4′)); 2.80 ($dd, J(4B,3a) = 8.8$, $J(4B,4A) = 18.1$, H$_B$−C(4)); 3.04 ($dd, J(4A,3a) = 1.5, J(4A,4B) = 18.2$, H$_A$−C(4)); 3.45 ($dd, J(3a,4A) = 1.5$, $J(3a,4B) = 8.8$, H−C(3a)); 4.47 ($dd, J(3′,4′; trans) = 7.5, J(3′,4′; cis) = 8.9$, H−C(3′)); 6.80–7.90 ($m$, 14 arom. H); 11.80 ($s$, NH). MS: 503 (79, $M^{+\cdot}$), 330 (71, $[M+1−$ phenylmaleimide$]^+$), 329 (40, $[M−$ phenylmaleimide$]^+$), 174 (14, [phenylmaleimide]$^+$), 130 (4), 77(4). EI-HR-MS: 503.1481 (C$_{30}$H$_{21}$N$_3$O$_5^+$; calc. 503.1483, 0.4 ppm).

*3a,4,10,10b-Tetrahydro-2-methyl-10b-(1-methyl-2,5-dioxopyrrolidin-3-yl)-pyrrolo[3,4-a]carbazole-1,3,5-(2*H*)-trione* (**15b**). As described for **15a**, with **14** (3.0 g, 10 mmol), **2b** (1.1 g, 10 mmol), and toluene (30 ml) (3 d at r.t.; stirring of MeOH soln. for 1 h): 135 mg (7%) of **15b/19**. **15b**: Colorless crystals. M.p. 275° (AcOEt). IR: 3333 (NH), 1778, 1704, 1636 (CO), 1583 (arom. C−C). ^{1}H-NMR (300 MHz): 2.46 ($dd, J(4′,3′; trans) = 6.7, J(4′, 4′) = 18.4$, H$_{trans}$−C(4′)); 2.75 ($dd, J(4′,3′; cis) = 9.5, J(4′,4′) = 18.4$, H$_{cis}$−C(4′)); 2.88 ($dd, J(4B,3a) = 8.7, J(4B, 4A) = 18.4$, H$_B$−C(4)); 3.14 ($dd, J(3a,4A) = 1.2, J(3a,4B) = 8.7$, H−C(3)); 3.43 ($dd, J(4A,3a) = 1.2, J(4A, 4B) = 18.4$, H$_A$−C(4)); 4.18 ($dd, J(3′,4′; trans) = 6.7, J(3′,4′; cis) = 9.4$, H−C(3′)); 7.26–8.26 ($m$, 4 arom. H); 9.7 (br. s, NH). MS: 379 (96, $M^{+\cdot}$), 268 (90.11, $[M−$maleimide$]^+$). EI-HR-MS: 379.1168 (C$_{20}$H$_{17}$N$_3$O$_5^+$ calc.; 379.1169, 0.2 ppm).

*5a-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-3a,4,5a,10,10a,10b-hexahydro-2-phenyl-10-(trimethylsilyl)pyrrolo-[3,4-*a*]carbazole-1,3,5(2*H*)-trione* (**16**). As described **15a**, from **14** (3 g, 10 mmol) and **2a** (1.73 g, 10 mmol) (30 min at r.t., stirring of MeOH soln. for only 1 h): 850 mg (30%) of **16**. Colorless crystals. M.p. 300°. IR: 1777, 1714 (CO), 1596 (arom. C−C), 1187, 1110, 1068, 1026, 983 (Si−N), 842, 757 (SiMe$_3$). ^{1}H-NMR (300 MHz): 0.40 (*s*, Me$_3$Si); 2.47 (*dd*, *J*(4′,3′; *cis*) = 9, *J*(4′,4′) = 18.1, H$_{cis}$−C(4′)); 2.83 (*dd*, *J*(4*A*,3a) = 8.54, *J*(4*A*,4*B*) = 15.9, H$_A$−C(4)); 3.06 (*dd*, *J*(3′,4′; *trans*) = 5.6, *J*(3′,4′; *cis*) = 9, H−C(3′)); 3.16 (*dd*, *J*(4′,3; *trans*) = 5.6, *J*(4′,4′) = 18.1, H$_{trans}$−C(4′)); 3.21 (*dd*, *J*(4*B*,3a) = 2.7, *J*(4*B*,4*A*) = 15.8, H$_B$−C(4)); 3.42 (*dd*, *J*(10b,10a) = 8.6, *J*(10b,3a) = 9.5, H−C(10b)); 3.48 (*ddd*, *J*(3a,4*B*) = 2.7, *J*(3a,4*A*) = 9.2, *J*(3a,10b) = 9.2, H−C(3a)); 5.52 (*d*, *J*(10a,10b) = 8.5, H−C(10a)); 6.70−7.55 (*m*, 14 arom. H). Anal. calc. for C$_{33}$H$_{31}$N$_3$O$_5$Si (577.71): C 68.61, H 5.41, N 7.27; found: C 68.75, H 5.49, N 7.16.

*3a,4,10,10b-Tetrahydro-3a-methyl-2-phenylpyrrolo[3,4-*a*]carbazole-1,3,5(2*H*)-trione* (**18**). As described for **15b**, from **14** (3.0 g, 10 mmol) and *N*-phenylcitraconimide (= 3-methyl-1-phenyl-1*H*-pyrrole-2,5-dione; **17**; 1.87 g, 10 mmol): 70 mg (2%) of **18**. Colorless crystals. M.p. 272−275° (MeOH). IR: 3185 (NH), 1719 1633 (CO). ^{1}H-NMR (300 MHz): 1.5 (*s*, Me); 2.55 (*d*, *J* = 16.1, H$_B$−C(4)); 3.0 (*d*, *J* = 16.8, H$_A$−C(4)); 4.1 (*s*, H−C(10b)); 7.0−8.0 (*m*, 9 arom. H); 11.6 (br. *s*, NH). MS: 344 (100, *M*$^+$). EI-HR-MS: 344.1161 (C$_{21}$H$_{16}$N$_2$O$_3^+$; calc. 344.1162).

*3a,4,10,10b-Tetrahydro-2-methylpyrrolo[3,4-*a*]carbazole-1,3,5(2*H*)-trione* (**19**). From the mixture **15b/19** by crystallization from AcOEt, or by heating of **7** (368 mg, 1 mmol) until the product was melting (*ca.* 300°), and crystallization of the residue from MeOH: 242 mg (90%) of **19**. Colorless crystals. M.p. 282°. IR: 3227 (NH), 1779, 1703 (C=O), 1626 (α,β-unsatd. C=O). ^{1}H-NMR (300 MHz): 2.59 (*dd*, *J*(4*A*,3a) = 8.8, *J*(4*A*,4*B*) = 17.6, H$_A$−C(4)); 2.68 (*s*, Me); 2.88 (*dd*, *J*(4*B*,3a) = 2.7, *J*(4*B*,4*A*) = 17.3, H$_B$−C(4)); 3.45 (*ddd*, *J*(3a,4*B*) = 2.7, *J*(3a, 4*A*) = 8.6, *J*(3a,10b) = 8.6, H−C(3a)); 4.19 (*d*, *J*(10b,3a) = 8.3, H−C(10b)); 6.93 (*m*, 2 arom. H); 7.22 (*m*, 1 arom. H); 7.84 (*m*, 1 arom. H); 11.4 (br. *s*, NH). MS: 268 (24, *M*$^+$). EI-HR-MS: 268.0848 (C$_{15}$H$_{12}$N$_2$O$_3^+$; calc. 268.0849). Anal. calc. for C$_{15}$H$_{12}$N$_2$O$_3$ (268.27): C 67.16, H 4.51, N 10.44; found: C 66.52, H 4.47, N 10.29.

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