SYNTHESES AND REACTIONS OF 5-UNSUBSTITUTED 11B-METHYL-1,2,3,11B-TETRAHYDRO-PYRIDO[3,2,1-*JK*]CARBAZOLES HAVING A STRYCHNOS ALKALOIDS PARTIAL STRUCTURE [1]

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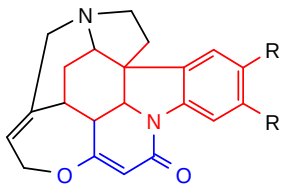
Abstract

4a-Methyl-2,3,3,4a-tetrahydro-1*H*-carbazoles **3**, obtained from arylhydrazines **1** and 2-methylcyclohexanone **2**, react with diethyl malonate **5a** by cyclocondensation to 7-hydroxy-13b-methyl-tetrahydro-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazolediones **6**. With methanetricarboxylates **5b,c**, cyclocondensation forms a mixture of pyrano-pyrido-carbazole-carboxylates **7** and pyrido-carbazole-carboxylates **8**. Degradation of pyrano-pyrido-carbazolediones **6** by alkaline ring-opening and decarboxylation leads to 5-acetyl derivatives **10**. Deacetylation with sulfuric acid reveals the 5-unsubstituted 4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-jk]carbazol-6-one (**9**). Pyrido-carbazolone **9** was also obtained in a single step reaction from tetrahydrocarbazole **3a** and malonic acid **5d** with phosphoryl chloride as catalyst in low yields.

Electrophilic halogenation of **9** takes place at position 5 and gives 5-bromo compound **15** or 5,5-dihalogenated products **14**, **16** or **17**, depending on the reaction conditions. Nitration takes also place in an electrophilic reaction to give 4-hydroxy-5-nitro-pyrido-carbazolone **20**. Nucleophilic exchange of the 4-hydroxy group in pyridocarbazolones **9** and **20** by reaction with phosphoryl chloride gives reactive 4-chloro intermediates **18** and **21**, which react with sodium azide to 4-azido derivatives **19** and **22**. 4-Azido-5-nitro-pyrido-carbazolone **22** with the reactive ortho-nitro group in the neighborship of the azido group cyclizes thermolytically to furoxane **23**. This reaction was studied by differential scanning calorimetry (DSC).

Introduction



A

Tetrahydropyrido[3,2,1-*jk*]carbazol-6-one (colored partial structure in **A**) is part of the heterocyclic skeleton of many natural products, e. g. Strychnos alkaloids **A** such as strychninolones and derivatives [2, 3a], Brucine (dimethoxystrychnin) [3b] and Vomicin (12-hydroxy-N-methylpseudostrychnine) [3c]. It possesses the biological interesting combination of the well-known indole structure [4, 5] and the 4-hydroxy-2-pyridone structure.

The basic structure of the the pyridone system can be found in many natural products, such as the highly toxic Ricinine (a 4-methoxy-2-oxo-3-pyridinecarbonitrile [3d]), in compounds with antibiotic activity (e.g. Flavipucin [6]), and the yellow fungal pigment Tenellin [7]. A whole class of 4-hydroxy-5,6-dihydro-2-pyridones with antibiotic activity (e.g. Mocimycin [3e]) is produced by *Streptomyces* species.

In the last years we published the syntheses and reactions of a series of pyrido[3,2,1-*jk*]carbazol-6-ones, tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones [1, 8, 9]. Recently we described the reaction of 2,3,4,9-tetrahydrocarbazoles **3** ("indolenines") with 2-substituted malonates which forms 5-substituted tetrahydro-pyrido[3,2,1-*jk*]carbazoles [1] in a 1:1 cyclocondensation reaction. However, this reaction sequence is not applicable to produce 5-unsubstituted tetrahydro-pyrido[3,2,1-*jk*]carbazoles.

A one-step reaction was adapted from similar systems [8g,h, 9]: it starts from tetrahydrocarbazole **3a** using malonic acid (**5d**)/phosphoryl chloride. However, this reaction path has some disadvantages. As second possibility, the formation of tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones **9** was investigated by building up the 4-hydroxy-2-pyridone part from tetrahydrocarbazoles **3** as enamine part, and malonate **5a** as C-3 source, via a 3-step reaction sequence which has attracted our attention in similar ring systems for many years [10, 11]. In this reaction way, the formation of a pyrono-pyridocarbazole ring system takes place, followed by the stepwise degradation to the pyrido-carbazole ring system.

Results and Discussion

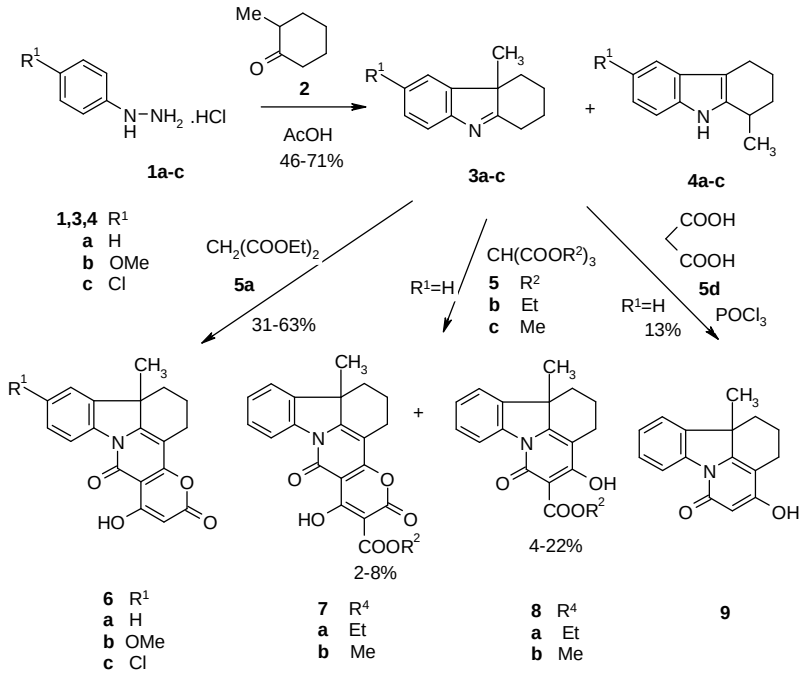
1. Cyclocondensation of tetrahydrocarbazoles 3 with malonates 5 to pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazolediones 6 and 7 and to tetrahydro-pyrido[3,2,1-*jk*]carbazolones 8 and 9.

The synthesis of the tetrahydro-pyridocarbazole system started from 2,3,4,4a-tetrahydro-1*H*-carbazoles **3**, obtained from phenylhydrazines **1** and 2-methylcyclohexanone (**2**) via a *Fischer indole synthesis*, **1a** and **2** give a mixture of two isomers, 4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazole (**3a**) and 1-methyl-2,3,4,9-tetrahydro-1H-carbazole (**4a**) [12] which are easy to separate according to their chemical properties [13]. The synthesis of **3a-c** was performed as described recently in ref [1].

Attempts to perform a cyclocondensation of 2-unsubstituted diethyl malonate **5a** with carbazoles **3** gives in a 1:1 reaction a mixture of compounds, which cannot not be simply separated. In a 2:1 cyclocondensation, however, a single compound **6** is obtained in good yields, which has been shown to consist of one molecule of tetrahydrocarbazole **3** and two molecules deriving from malonate **5a**. The structure was assigned to 7-hydroxy-13b-methyl-1,2,3,13b-tetrahydro-5*H*,8*H*-pyrano[2',3':4,5]pyrido-[3,2,1-*jk*]carbazole-5,8-diones **6** similar as obtained from related systems [10, 11]. We could further show that the use of boiling diphenyl ether (bp. 258 °C) as solvent gives the best results, when the formed four molecules of ethanol were removed by distillation during the reaction. Such pyrones can serve as precursors for the synthesis of 5-unsubstituted 4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-ones **9**.

To develop a shorter reaction sequence to 4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-ones, cyclocondensation of methanetricarboxylates **5b,c** with carbazoles **3** was investigated. It was intended that the additional ester group of **5b,c** at 2-position gives a 1:1 cyclization product **8** which should then react by hydrolysis and decarboxylation to 5-unsubstituted derivatives **9**. However, the reaction produces a mixture of the pyrano-pyridocarbazole-carboxylates **7** and the desired pyridocarbazole-carboxylates **8** in low yields only.

Scheme 01



As an alternative way to pyridocarbazoles with two aromatic rings we have recently investigated a one-step reaction to pyridocarbazoles starting from malonic acid (**5d**), carbazole and phosphoryl chloride [8g,h] following a reaction described in ref. [9], which gives pyridocarbazoles in moderate yields. Transformation of this reaction sequence to tetrahydrocarbazole **3a** gave in low yields tetrahydropyridocarbazole **9**. Further disadvantages were, that the reaction gives no reliable results, because in several batches a very impure product was obtained, which needed cumbersome purification lowering again the yield. So the short reaction path was not really advantageous.

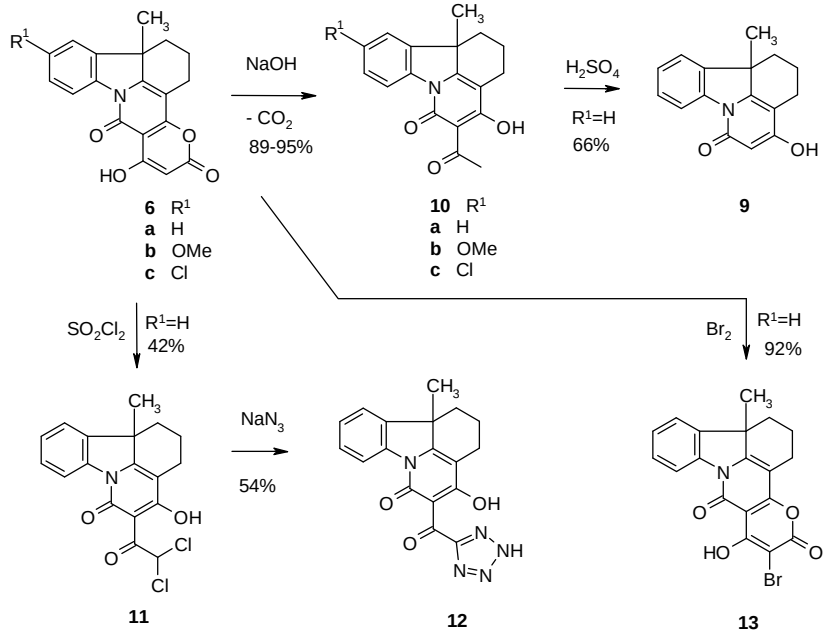
2. Degradation of pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-5,8-diones 6 to tetrahydro-6*H*-pyrido[3,2,1-jk]carbazol-6-ones 9

Pyrano-pyridocarbazoles **6** have a sensitive lactone structure in its pyrano ring, which reacts as cyclic ester with sodium or potassium hydroxide by hydrolytic ring opening as the first degradation step. Best results were obtained when glycol was used as the solvent in order to obtain a higher reaction temperature and shorter reaction time. Acidification of the basic reaction mixture with hydrochloric acid results in the formation of an acetoacetic acid fragment as substituent, which decarboxylates spontaneously at elevated temperatures already in weak acidic media to give 5-acetyl-pyridocarbazoles **10** in excellent yields. Because strong foaming by evolution of carbon dioxide accompanies this reaction, there must be taken care to perform this reaction with caution.

The 5-acetyl group in pyridocarbazole **10** can be removed in a smooth reaction with 90% sulfuric acid at 140 °C by ipso-substitution and results in a good overall yield of highly pure 5-unsubstituted pyridocarbazole **9** after 3 steps.

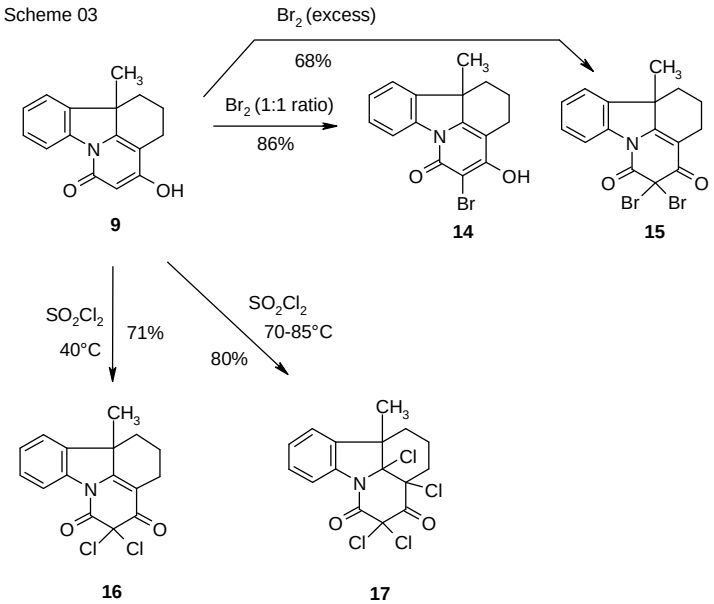
A similar degradation of the pyrone **6** takes place, when it was brought to reaction with sulfuryl chloride. This reaction is known to give in an electrocyclic reaction bis-chlorination at the 2-position of the 1,3-dioxo structure or its tautomeric form, as shown in Scheme 03 for compound **16**. Bis-chlorination of pyrone **6a**, however, resulted in a subsequent ring opening and decarboxylation step to give as the product 5-dichloroacetyl-pyridocarbazole **11**. Exchange of the chloro atoms of **11** against azido groups with sodium azide and further elimination of nitrogen resulted in the formation of 5-tetrazolylcarbonyl-pyridocarbazole **12**, a compound class which is known to possess interesting biological properties, e.g. antiinflammatory activities [14]. Bromination of **6a** under mild conditions gave a single bromination in position 6 without degradation of the pyrone ring and formed compound **13**. Higher temperatures or excess of bromine gave a mixture of compounds.

Scheme 02



3. Halogenation of tetrahydro-6*H*-pyrido[3,2,1-jk]carbazol-6-one 9

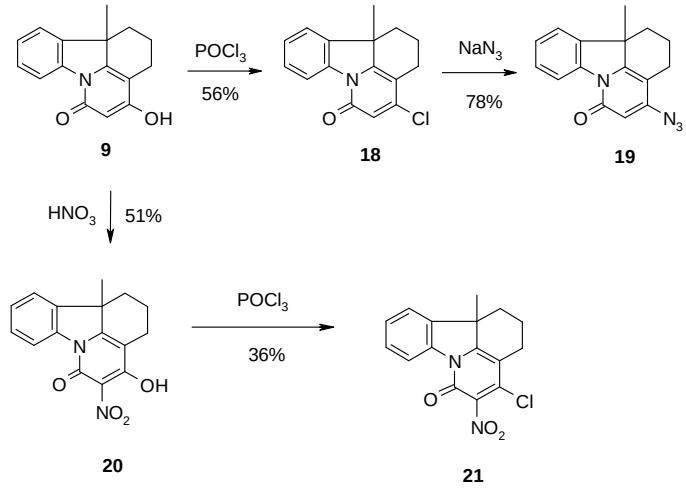
Scheme 03



Electrophilic halogenation of pyridocarbazole **9** with bromine at room temperature results either in a mono-halogenation to 5-bromo-4-hydroxy-pyridocarbazolone **14**, when bromine was added in a 1:1 ratio, or in a bis-halogenation to 5,5-dibromo-pyridocarbazoledione **15** with a four-fold excess of bromine.

Electrophilic chlorination of **9** with sulfuryl chloride gave at temperatures below 40 °C 5,5-dichloro-pyridocarbazoledione **16** by attack at the CH-acidic position of the 1,3-diketone moiety. Slightly higher temperatures showed an additional halogenation at the isolated double bond at the 3a,11c-position and produced 3a,5,5,11c-tetrachloro-pyridocarbazoledione **17**.

Scheme 04

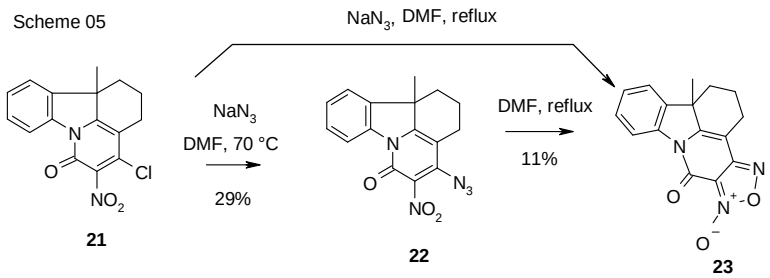


Chlorination of pyridocarbazole **9** with phosphoryl chloride leads to 4-chloro-pyridocarbazole **18** by a nucleophilic exchange of the 4-hydroxy group. A further nucleophilic exchange with sodium azide produces 4-azido-pyridocarbazole **19**. A similar reaction sequence was started from 5-nitro-pyridocarbazole **20**, which was obtained from 4-hydroxy-pyridocarbazole **9** by nitration with nitric acid in glacial acetic acid at room temperature using sodium nitrite as catalyst. The chlorination to 4-chloro compound **21** was not so easy to perform because the hydrogen bonding between the hydroxy- and the nitro group hindered an attack of phosphoryl chloride. Destroying of this bondings could be accomplished by the addition of triethylamine and the 4-chloro-5-nitro compound was obtained in moderate yields. The introduction of the azido group took place in ethanol at 70 °C. The temperature had to be controlled rather exactly because otherwise partial decomposition of **22** took place.

4. Thermal cyclization of 4-azido-5-nitro-tetrahydropyrido[3,2,1-jk]carbazol-6-one 22

In the last years we investigated a series of cyclization reactions of azides with reactive ortho-substituents [15, 16]. The thermal cyclization of ortho-phenyl azides in pyridocarbazoles proceeds via nitrene intermediates [17] and is known to produce indolo products [18]. The conditions of the ring closure reaction of the 4-azido derivative **22** was investigated by differential scanning calorimetry (DSC) to obtain the information on the cyclization temperature to furoxane **23** and possible further decomposition. The DSC diagram shows a cyclization range with 142.8 °C onset and 174.7 °C maximum, which allows to use dimethylformamide at reflux temperature as the suitable cyclization solvent.

Scheme 05



The reaction enthalpy with a value of ΔH = -110 J/g is rather high, which must be taken into consideration when larger batches are thermolyzed. The structure of **23** is supported by IR data, which show that the azide signal of **22** at 2113 cm^{-1} is missing. For synthetic purposes it is important that the introduction of the azido group from chloro derivative **21** to azido derivative **22** must be carried out below 70 °C, otherwise a partial decomposition takes place, which can be observed by the detection of furoxane **23** in the TLC analysis.

Conclusion

4a-Methyl-2,3,4,4a-tetrahydro-1*H*-carbazoles **3** was shown to cyclize with diethylmalonate **5a** to pyranopyridocarbazole-5,8-diones **6**, which can be degraded in a two-step reaction via an acetyl intermediate **10** to 5-unsubstituted tetrahydropyridocarbazolones **9**. Attempts to use shorter reaction pathways gave too low yields of tetrahydropyridocarbazolones **9**. Electrophilic substitution of tetrahydropyridocarbazolones **9** was shown to take place mainly at position 5 and produces 5-bromo, 5,5-dibromo- and 5,5-dichloro derivatives **14**, **15** and **16**. Nitration affords 5-nitro derivative **20**. Nucleophilic substitution results in the exchange of the 4-hydroxy-group against a chloro- or an azido group to afford derivatives **18**, **19**, **21** and **22**.

Thermal cyclization of 4-azido-5-nitro-tetrahydropyridocarbazolone **22** was investigated by differential scanning calorimetry (DSC) and produced furoxano-pyridocarbazole **23** under suitable conditions obtained from DSC data.

Methods and Experimental

General

Melting points were determined using a Stuart SMP3 Melting Point Apparatus (Bibby Scientific Limited, Stone, Staffordshire, UK) in open capillary tubes. Calorimetric data (DSC data) were obtained on a Perkin Elmer Pyris 1 DSC instrument (Perkin Elmer Corp., Waltham, MA, USA) with the Pyris Software for Windows (Pyris Thermal Analysis System) V3.72. The differential scanning calorimetry plots were recorded between 25-600 °C, with a heating rate of 2-10 °C/min, and 1.5-3.0 mg of compound in sealed aluminum crucibles (11 bar). IR spectra were recorded with a Bruker Alpha-P instrument (Bruker GmbH, Karlsruhe, Germany) with Attenuated Total Reflectance (ATR) measurement, using a reflexion method. NMR spectra were recorded on a Bruker Avance III instrument (Bruker GmbH) (300 MHz ^{1}H). Chemical shifts are given in ppm (δ) from the internal TMS standard. Elemental analyses were performed at the Microanalytical Laboratory of the University of Vienna, Austria. Mass spectra were obtained from a HP 1100 LC/MSD mass spectral instrument (Agilent Technologies, Santa Clara, CA, USA) with either positive or negative atmospheric pressure chemical ionization (APCI) ion source, 50–200 V, nitrogen, or atmospheric pressure electrospray (AP-ES) method. Analytical HPLC was performed on a Shimadzu LC 20 system equipped with a diode array detector (215 and 254 nm) on a Pathfinder AS reversed phase (4.6150 mm, 5 µm) column, running in acetonitrile/water gradient (30–100% acetonitrile). Dry column flash chromatography [19] was carried out on silica gel 60 H (5–40 µm) (Merck, Darmstadt, Germany). All reactions were monitored by thin layer chromatography on 0.2 mm silica gel F 254 plates (Merck, Darmstadt, Germany) using UV light (254 and 366 nm) for detection. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

4a-Methyl-2,3,3,4a-tetrahydro-1*H*-carbazole (3a): This compound was obtained from phenylhydrazinium chloride (**1a)** (30.8 g, 0.21 mol) and 2-methylcyclohexanone **2** (22.7 g, 0.20 mol) using the procedure and work-up as described in ref [1]. The yield was 27.7 g (71%); colorless prisms, mp 68 °C (hexane) lit. mp 68 °C [1]. IR: 3043 w, 2968 w, 2942 m, 2852 w, 1609 w, 1574 s cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.19 (dt, 1 H, J = 7.0 + 2.0 Hz, 3-$CH_{2(ax)}$), 1.33 (s, 3 H, Me), 1.44 (dt, J = 7.0+ 2.0 Hz, 1 H, 3-$CH_{2(eq)}$), 1.72-1.84 (m, 2 H, 2-H), 2.19-2.30 (m, 2 H, 4-CH_2), 2.55-2.66 (dt, J = 7.0 + 2.0 Hz, 1 H, 1-$CH_{2(ax)}$), 2.85-2.91 (m, 1 H, 1-$CH_{2(eq)}$), 7.21 (dt, J = 7.0+1.5 Hz, 1 H, ArH), 7.30-7.36 (m, 2 H, ArH), 7.61 (d, J = 7.0 Hz, 1 H, 5-H).

6-Methoxy-4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazole (**3b**)*:* This compound was obtained from 4-methoxyphenylhydrazinium chloride (**1b**) (17.7 g, 0.10 mol) and 2-methylcyclohexanone (**2**) (11.2 g, 0.10 mol) using the procedure and work-up as described in ref [1]. The yield was 9.89 g (46%), yellowish oil, bp 190 °C/14 mm Hg; lit. bp 190 °C/14 mm Hg [1].

6-Chloro-4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazole (**3c**)*:* This compound was obtained from 4-chlorophenylhydrazinium chloride (**1c**) (7.16 g, 40 mmol) and 2-methylcyclohexanone (**2**) (4.49 g, 40 mmol) using the procedure and work-up described in ref [1]. The yield was 3.05 g (47%), colorless crystals, mp 66 °C (hexane); lit. mp 66°C [1]. IR: 3050 w, 2920 m, b, 1610 w, 1580 s cm^{-1}.

7-Hydroxy-13b-methyl-1,2,3,13b-tetrahydro-5*H*,8*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-5,8-dione (**6a**): A mixture of tetrahydrocarbazole **3a** (1.85 g, 10 mmol), diethyl malonate (**5a**) (3.20 g, 20 mmol) and diphenyl ether (10 g) was heated in a 2-necked flask equipped with a distillation bridge and a 20 cm Vigreux column. Liberation of ethanol starts at about 180 °C. The temperature was raised to 205-210 °C internal temperature and kept there for 3 hours. Then the temperature was raised to 230 °C and kept there until no more ethanol was formed (about 2-3 hours). The reaction mixture was then cooled to approx. 40 °C and triturated with diethyl ether (50 mL). The resulting solid was filtered by suction, washed with methanol and dried under reduced pressure at 40 °C. The yield was 2.02 g (63%), yellowish prisms, mp 254 °C (1-butanol). IR: 3066 w, 3038 w, 2924 m, 2865 w, 1735 s, 1676 s, 1640 m, 1562 s cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 3 H, Me), 2.14-2.26 and 2.38-2.44 (2 m, 4 H, 1-CH_2, 2-CH_2) 2.76-2.91 (m, 2 H, 3-CH_2), 5.57 (s, 1 H, 6-H), 7.02 (dd, J = 7.0+1.0 Hz, 1 H, 13-H), 7.32-7.49 (m, 2 H, 11-H, 12-H), 8.48 (dd, J = 7.0+1.0 Hz, 1 H, 10-H), 13.01 (s, 1 H, OH). Anal. calcd for $C_{19}H_{15}NO_4$ (321.34): C, 71.02; H, 4.71; N, 4.36. Found: C, 70.92; H, 4.57; N, 4.18.

7-Hydroxy-12-methoxy-13b-methyl-1,2,3,13b-tetrahydro-5*H*,8*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-5,8-dione (**6b**): This compound was obtained from 6-methoxy-tetrahydrocarbazole **3b** (2.15 g, 10 mmol) and diethyl malonate (**5a**) (3.20 g, 20 mmol) using the procedure and work-up described for **6a**. The yield was 1.09 g (31%), colorless prisms, mp 271°C (acetic acid). IR: 2950 w, 1730 s, 1670 s, 1610 w, 1560 m cm^{-1}. ^{1}H NMR (CF_3COOH): δ 1.50 (s, 3 H, Me), 2.20-2.60 (m, 4 H, 1-CH_2, 2-CH_2), 2.90 (t, J = 7.0 Hz, 2 H, 3-CH_2), 4.00 (s, 3 H, OMe), 5.90 (s, 1 H, 6-H), 7.00-7.20 (m, 2 H, 11-H, 13-H), 8.35 (dd, J=7.0+1.5 Hz, 1 H, 10-H). Anal. calcd for $C_{20}H_{17}NO_5$ (351.36): C, 68.37; H, 4.88; N, 3.99. Found: C, 67.98; H, 4.97; N, 3.96.

12-Chloro-7-hydroxy-13b-methyl-1,2,3,13b-tetrahydro-5*H*,8*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-5,8-dione (6c): This compound was obtained from 6-chloro-tetrahydrocarbazole **3c** (2.19 g, 10 mmol) and diethyl malonate (**2a**) (3.20 g, 20 mmol) using the procedure and work-up described for **6a**. The yield was 1.53 g (43%), colorless prisms, mp 309 °C (acetic acid). IR: 2910 w, 1725 m, 1675 s, 1610 w, 1580 m cm^{-1}. Anal. calcd for $C_{19}H_{14}ClNO_4$ (355.78): C, 64.14; H, 3.97; N, 3.94. Found: C, 64.23; H, 4.13; N, 3.86.

Ethyl 7-hydroxy-13b-methyl-5,8-dioxo-2,3,8,13b-tetrahydro-1*H*,5*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-6-carboxylate (**7a**): This compound was obtained as by-product during the preparation of pyridocarbazole-5-carboxylate **8a** as first crop of the fractionated recrystallization. The yield was 0.70 g (8%), light yellow prisms, mp 230-233 °C (1-butanol). IR: 1750 s, 1670 s, 1640 m, 1610 w, 1570 m cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.30 (t, J = 7.0 Hz, ester-CH_3), 1.45 (s, 3 H, Me), 1.90-2.40 (m, 4 H, 1-CH_2, 2-CH_2), 2.75 (t, J = 7.0 Hz, 2 H, 3-CH_2), 4.25 (q, ester-CH_2), 7.50-7.60 (m, 2 H, 11-H, 12-H), 7.70 (dd, J = 7.0+1.0 Hz, 1 H, 13-H), 8.35 (dd, J = 7.0+1.0 Hz, 10-H). ^{13}C NMR (DMSO-d_6): δ 13.5 (13b-Me), 15.7 (1-C), 16.2 (2-C), 24.6 (ethyl-CH_3), 28.6 (3-C), 44.6 (13a-C), 60.1 (ethyl-CH_2), 94.6 (7a-C), 98.9 (6-C), 105.3 (3a-C), 116.5 (10-C), 122.9 (12-C), 126.9 (11-C), 128.0 (13-C), 138.3 (9a-C), 140.0 (13b-C), 156.9 (7-C), 157.9 (13c-C), 160.4 (8-C), 161.2 (3b-C), 162.1 (ester-CO), 168.9 (5-C). Anal. calcd for $C_{22}H_{19}NO_6$ (393.40): C, 67.17; H, 4.87; N, 3.56. Found: C, 67.56; H, 4.72; N, 3.53.

Methyl 7-hydroxy-13b-methyl-5,8-dioxo-2,3,8,13b-tetrahydro-1*H*,5*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-6-carboxylate (**7b**): This compound was obtained as by-product during the preparation of pyridocarbazole-5-carboxylate **8b** by fractionated recrystallization. The yield was 0.60 g (2%), beige prisms, mp 242-247 °C (ethanol). IR: 2950 w, 1750 s, 1675 s, 1645 m, 1610 w, 1565 m cm^{-1}. ^{1}H NMR (DMSO-d_6): 1.40 (s, 3 H, Me), 1.70-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.70 (t, J = 7.0 Hz, 2 H, 3-CH_2), 3.90 (s, 2 H, ester-CH_2),

7.40-7.55 (m, 2 H, 11-H, 12-H), 7.70 (dd, J = 7.0+1.0 Hz, 1 H, 13-H), 8.40 (dd, J = 7.0+1.0 Hz, 10-H). Anal. calcd for $C_{21}H_{17}NO_6$ (379.37): C, 66.49; H, 4.52; N, 3.69. C, 66.66; H, 4.75; N, 3.51.

Ethyl 4-hydroxy-11b-methyl-6-oxo-2,3,6,11b-tetrahydro-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylate (8a): A neat mixture of tetrahydrocarbazole **3a** (4.10 g, 22 mmol) and triethyl methanetricarboxylate (**5b**) (6.10 g, 26 mmol) was heated in a 2-necked flask equipped with a distillation bridge and a 20 cm Vigreux column at 230-240 °C internal temperature until no more ethanol was liberated (about 10-15 minutes). After cooling, the reaction mixture was triturated with diethyl ether (30 mL) and kept overnight at room temperature. The resulting solid product was filtered by suction, washed with cold diethyl ether (50 mL) and dried under reduced pressure at 40 °C. The crude yield was 5.30 g (74%)**,** which was fractionated recrystallized from ethanol (200 mL) to afford as first crop the by-product **7a** (0.70 g, 8%), the second crop gave the product **8a** (1.6 g, 22%) yield, light brown prisms, mp 177 °C (ethanol). IR: 2980-2900 w, 1680 s, 1645 m, 1620 sh, 1600 w, 1550 m cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.25 (s, 3 H, 11b-Me), 1.30 (t, J = 7.0 Hz, ethyl-CH_3), 1.40-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.65 (t, J = 7.0 Hz, 2 H, 3-CH_2), 4.20 (q, J = 7.0 Hz, 2 H, ethyl-CH_2), 7.00-7.40 (m, 2 H, 9-H, 10-H) 7.50 (dd, J = 7.0+1.0 Hz, 1 H, 11-H), 8.20 (dd, J = 7.0+1.0 Hz, 8-H), 13.10 (s, OH). Anal. calcd for $C_{19}H_{19}NO_4$ (325.37): C, 70.14 H, 5.89 N, 4.30. Found: C, 70.39; H, 5.69; N, 4.30.

Methyl 4-hydroxy-11b-methyl-6-oxo-2,3,6,11b-tetrahydro-1*H*-pyrido[3,2,1-*jk*]carbazole-5-carboxylate (8b): A neat mixture of tetrahydrocarbazole **3a** (12.70 g, 69 mmol) and trimethyl methanetricarboxylate (**5c**) (15.70 g, 83 mmol) was heated in a 2-necked flask equipped with a distillation bridge and a 20 cm Vigreux column at 220 °C internal temperature until no more ethanol was liberated (about 20 minutes). After cooling, the reaction mixture was triturated with hexane (3x100 mL) and diethyl ether (30 mL) and kept overnight at room temperature. The resulting solid product was filtered by suction, washed with cold diethyl ether (100 mL) and dried under reduced pressure at 40 °C. A crude orange solid of 3.00 g was isolated, which was treated with boiling ethanol (150 mL) and gave 0.60 g (2%) of the by-product **7b** on fractionated crystallization. Product **8b** was isolated from the ether phase, which was taken to dryness and gave 8.00 g of an impure product. Purification by dry column flash chromatography (toluene and ethyl acetate as eluents) yielded **8b** (0.90 g, 4%), beige powder, mp 155 °C (ethanol). IR: 2960 m, 1750 s, 1715 m, 1670 s, 1640 m, 1610 w, 1570 s cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.42 (s, 3 H, 11b-Me), 1.50-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.78 (t, J = 7.0 Hz, 2 H, 3-CH_2), 3.81 (s, 3 H, ester-CH_3), 7.40-7.60 (m, 2 H, 9-H, 10-H), 7.72 (dd, J = 7.0+1.0 Hz, 1 H, 11-H), 8.39 (dd, J = 7.0+1.0 Hz, 8-H). Anal. calcd for $C_{18}H_{17}NO_4$ (311.34): C, 69.44; H, 5.50; N, 4.50. Found: C, 69.31; H, 5.65; N, 4.25.

4-Hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**9**): *Method A:* To a stirred mixture of tetrahydrocarbazole **3a** (1.85 g, 10 mmol), malonic acid (**5d**) (3.02 g, 29 mmol), naphthalene (3.00 g) and phosphoryl chloride (16.8 g, 10 mL, 110 mmol) was slowly added. The reaction mixture was heated to 70-80 °C and stirred until the mixture dissolved. The solution was kept for 45 minutes at this temperature, then the mixture was heated for further 10 minutes to 120 °C (attention: strong foaming occurs). The bright brown color of the reaction mixture changed to dark brown. After cooling to 20 °C, excess phosphoryl chloride was removed by distillation in vacuo, the residue poured onto crushed ice/water (100 mL) and stirred for 3 hours at 20 °C until the solid precipitated. The solid was filtered by suction, dissolved in 0.5 *M* aq. sodium hydroxide solution (250 mL) and the remaining insoluble by-products filtered off. The mother liquor was acidified with 2 *M* hydrochloric acid to pH = 2, the formed solid filtered by suction, washed with water (100 mL) and dried at 40 °C. The yield was 0.33 g (13 %), brown powder, mp 250 °C (ethanol/water).

Method B: A solution of 5-acetyl-pyridocarbazolone **10a** (2.95 g, 10 mmol) in 90% sulfuric acid (10 mL) was heated for 15 minutes to 135-140 °C. Then the solution was poured onto ice/water (300 mL) and allowed to stand overnight at room temperature. The precipitate was filtered by suction, washed with water (3x 50 mL) and dried under reduced pressure at 40 °C. The yield was 1.66 g (66%), colorless prisms, mp 255 °C (dimethylformamide). IR: 3069 m, 2925 m, 2858 w, 1665 s, 1612 m, 1585 w, 1549 m cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.31 (s, 3 H, Me), 1.42-1.46, 1.88-2.04, 2.07-2.12 and 2.27-2.32 (4 m, 4 H, 1-CH_2, 2-CH_2), 2.49-2.55 (m, 2 H, 3-CH_2), 5.67 (s, 1 H, 5-H), 6.93 (dd, J = 7.0+1.5 Hz, 1 H, 11-H), 7.23-7.38 and 7.45-7.63 (2 m, 2 H, 9-H, 10-H), 8.29 (dd, J = 7.0+1.5 Hz, 8-H), 11.20 (s, br, 1 H, OH). Anal. calcd for $C_{16}H_{15}NO_2$ (253.30): C, 75.87; H, 5.97; N, 5.53. Found C, 75.75; H, 5.83; N, 5.58.

5-Acetyl-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**10a**): To a suspension of pyrano-pyridocarbazoledione **6a** (3.21 g, 10 mmol) in 1,2-ethanediol (50 mL), sodium hydroxide (5.0 g in 5 mL of water) was added. The reaction mixture was heated under reflux for 1 hour, then poured onto ice/water (300 mL), and slowly acidified with concentrated hydrochloric acid**.** The obtained precipitate was filtered by suction, washed with water and dried under reduced pressure at 40 °C. The yield was 2.80 g (95%), colorless prisms, mp 113 °C (methanol). IR: 3309 s, 2924 m, 2866 m, 1676 s, 1638 m, 1592s, 1550 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.41 (s, 3 H, Me), 1.55-1.66 and 2.02-2.36 (2 m, 4 H, 1-CH_2, 2-CH_2), 2.59-2.69 (m, 2 H, 3-CH_2), 2.83 (s, 3 H, COMe), 7.24-7.42 (m, 3 H, 9-H, 10-H, 11-H), 8.52 (dd, J = 7.0+1.5 Hz, 8-H), 11.30 (s, 1 H, OH). Anal. calcd for $C_{18}H_{17}NO_3$ (295.34): C, 73.20; H, 5.80; N, 4.74. Found C, 73.02; H, 5.79; N, 4.70.

5-Acetyl-4-hydroxy-10-methoxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**10b**): This compound was obtained from pyrano-pyridocarbazoledione **6b** (3.51 g, 10 mmol) using the procedure and work-up described for **10a**. The yield was 3.06 g (94%), colorless prisms, mp 139-140 °C (methanol). IR: 2930 m, 1670 s, 1630 m, 1610 sh, 1595 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.35 (s, 3 H, Me), 1.40-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.65 (t, J = 7.0 Hz, 2 H, 3-CH_2), 2.80 (s, 3 H, COMe), 3.85 (s, 3 H, OMe), 6.75-7.00 (m, 2 H, 9-H, 11-H), 8.45 (dd, J = 7.0+1.0 Hz, 8-H). Anal. calcd for $C_{19}H_{19}NO_4$ (325.37): C, 70.14; H, 5.89; N, 4.30. Found: C, 70.12; H, 6.25; N, 4.25.

5-Acetyl-10-chloro-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (10c): This compound was obtained from pyrano-pyridocarbazoledione **6c** (3.55 g, 10 mmol) using the procedure and work-up described for **10a**. The yield was 2.93 g (89%), colorless prisms, mp 186 °C (methanol). IR: 2940 w, 1675 s, 1640 m, 1600 m, 1550 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.30 (s, 3 H, Me), 1.40-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.65 (t, J = 7.0 Hz, 2 H, 3-CH_2), 2.80 (s, 3 H, COMe), 7.20-7.50 (m, 2 H, 9-H, 11-H), 7.55 (dd, J = 7.0+1.0 Hz, 8-H). Anal. calcd for $C_{18}H_{16}ClNO_3$ (329.79): C, 65.56; H, 4.89; N, 4.25. Found: C, 65.50; H, 4.86; N, 4.16.

5-(2,2-Dichloroacetyl)-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3, 2,1-*jk*]carbazol-6-one (**11**): To a suspension of pyrano-pyridocarbazoledione **6a** (4.82 g, 15 mmol) in dioxane (30 mL), sulfuryl chloride (4.72 g = 2.8 mL, 35 mmol) was added portionwise, while the temperature was kept below 50 °C. After the addition was ready (about 10 minutes) the mixture was heated to boil for 5 minutes, then poured onto crushed ice/water (400 mL). The obtained solid was stirred for 12 hours, then filtered by suction, washed with water neutral and dried under reduced pressure at 40 °C. The yield was 2.30 g (42%), colorless prisms, mp 192 °C (acetic acid). IR: 3119 w, 3060 m, 2920 b, m, 1730 w, 1665 s, 1645 s, 1600 m, 1550 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.55 (s, 3 H, Me), 1.70-2.40 (m, 4 H, 1-CH_2, 2-CH_2), 2.80-2.90 (m, 2 H, 3-CH_2), 7.25-7.50 (m, 3 H, 9-H, 10-H, 11-H), 7.90 (s, 1 H, $CHCl_2$), 8.50 (dd, J = 7+1.5 Hz, 1 H, 8-H). Anal. calcd for $C_{18}H_{15}Cl_2NO_3$ (364.23): C, 59.36; H, 4.15; N, 3.85. Found: C, 59.72; H, 4.32; N, 3.78.

4-Hydroxy-11b-methyl-5-(2*H*-tetrazol-5-ylcarbonyl)-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**12**): To a solution of dichloroacetyl-pyridocarbazolone **11** (1.10 g, 3 mmol) in dimethylformamide (20 mL), sodium azide (0.65 g, 10 mmol) was added. The mixture was stirred at room temperature for 24 hours, and then diluted with water (200 mL), and brought to pH~3 with 2 *M* hydrochloric acid. The formed precipitate was filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 0.57 g (54%), colorless prisms, mp 151 °C (ethanol). IR: 3220 w, 2950 w, 1665 s, 1640 m, 1590 s cm^{-1}. Anal. calcd for $C_{18}H_{15}N_5O_3$ (349.35): C, 61.89; H, 4.33; N, 20.05. Found: C, 62.17; H, 4.52; N, 19.70.

6-Bromo-7-hydroxy-13b-methyl-1,2,3,13b-tetrahydro-5*H*,8*H*-pyrano[2',3':4,5]pyrido[3,2,1-*jk*]carbazole-5,8-dione (13): To a stirred solution of pyrano-pyridocarbazoledione **6a** (1.28 g, 4 mmol) in chloroform (20 mL), bromine (0.64 g, 4 mmol) in chloroform (5 mL) was added slowly at room temperature. The mixture was kept 12 hours at room temperature, the precipitated solid filtered by suction, washed with chloroform (20 mL) and dried under reduced pressure at 40 °C. The yield was 1.44 g (92%), yellow prisms, mp 271 °C (dimethylformamide). IR: 2929 w, 1780 s, 1670 s, 1640 w, 1560 m cm^{-1}. Anal. calcd for $C_{19}H_{14}BrNO_4$ (400.23): C, 57.02; H, 3.53; N, 3.50. Found: C, 57.20; H, 3.72; N, 3.55.

5-Bromo-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (14): To a suspension of 4-hydroxy-tetrahydropyridocarbazolone **9** (1.01 g, 4 mmol) in chloroform (15 mL), bromine (0.64 g, 4 mmol) in chloroform (5 mL) was added dropwise at room temperature. The reaction mixture was stirred for

15 minutes at this temperature and then extracted with water (50 mL). The organic layer was taken to dryness under reduced pressure. The oily residue was triturated with diethyl ether (3x50 mL), the obtained solid filtered by suction, washed with diethyl ether (50 mL) and dried under reduced pressure at 40 °C. The yield was 1.13 g (86%) yellow crystals, mp 298 °C (ethanol). IR: 2910 m, 1660 s, 1605 w, 1590 m cm^{-1}. Anal. calcd for $C_{16}H_{14}BrNO_2$ (332.20): C, 57.85; H, 4.25; N, 4.22. Found: C, 57.82; H, 4.33; N, 4.18.

5,5-Dibromo-11b-methyl-3,11b-dihydro-1*H*-pyrido[3,2,1-*jk*]carbazole-4,6(2*H*,5*H*)-dione (**15**): To a suspension of 4-hydroxy-pyridocarbazolone **9** (1.01 g, 4 mmol) in chloroform (15 mL) was added dropwise a solution of bromine (2.60 g, 16 mmol) in chloroform (5 mL). The reaction mixture was stirred for 15 minutes at room temperature and then extracted with water (50 mL). The organic layer was taken to dryness under reduced pressure and the oily residue triturated with diethyl ether until a solid product was formed. The solid was filtered by suction, washed with diethyl ether (50 mL) and dried under reduced pressure at 40 °C. The yield was 1.10 g (68%), yellow prisms, mp 147 °C (ethanol). IR: 2950 m, 1710 m, 1680 w, 1655 s, 1600 w cm^{-1}. Anal. calcd for $C_{16}H_{13}Br_2NO_2$ (411.10): C, 46.75 H, 3.19 N, 3.41.Found: C, 46.37; H, 3.16; N, 3.35.

5,5-Dichloro-11b-methyl-3,11b-dihydro-1*H*-pyrido[3,2,1-*jk*]carbazole-4,6(2*H*,5*H*)-dione (**16**): To a suspension of 4-hydroxy-pyridocarbazolone **9** (1.01 g, 4 mmol) in dioxane (20 mL), sulfuryl chloride (1.08 g = 0.65 mL, 8 mmol) was added dropwise keeping the temperature below 40 °C. The solution was poured onto ice/ water (50 mL), the formed solid filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 0.90 g (71%), yellow crystals, mp 149 °C (ethanol). IR: 2980-2860 m, b, 1720 s, 1690 m, 1655 s, 1605 m cm^{-1}. Anal. calcd for $C_{16}H_{13}Cl_2NO_2$ (322.19): C, 59.65; H, 4.07; N, 4.35. Found: C, 59.34, H, 4.25, N, 4.29.

3a,5,5,11c-Tetrachloro-11b-methyl-3,3a,11b,11c-tetrahydro-1*H*-pyrido[3,2,1-*jk*]carbazole-4,6(2*H*,5*H*)-dione (**17**): To a suspension of 4-hydroxy-pyridocarbazolone **9** (1.01 g, 4 mmol) in dioxane (20 ml), sulfuryl chloride (1.62 g = 0.97 mL, 12 mmol) was added dropwise while the temperature was kept between 50-70 °C. Then the solution was heated to 85 °C for 10 minutes and the cooled reaction mixture poured onto ice/water (300 mL). The formed solid was filtered by suction, washed with water (100 mL) and dried under reduced pressure at 40 °C. The yield was 1.00 g (80%), colorless prisms, mp 178 °C. IR: 2950 m, 1760 m, 1700 s, 1600 w cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.40 (m, 1 H, 2-H_{ax}), 1.70 (m, 1 H, 2-H_{eq}), 1.82 (s, 3 H, Me), 2.05 (m, 1 H, 1-H_{ax}), 2.15 (m, 1 H, 1-H_{eq}), 2.35 (m, 1 H, 3-H_{ax}), 2.45 (m, 1 H, 3-H_{eq}), 7.27 (m, 2 H, 10-H), 7.39 (m, 1 H, 9-H, 11-H), 8.23 (d, J = 7.0 Hz, 1 H, 8-H). ^{13}C NMR ($CDCl_3$): δ 17.1 (2-C), 19.3 (Me), 36.6 (1-C) 40.6 (3-C), 52.3 (11b-C), 75.0 (3a-C), 78.6 (5-C), 96.1 (11c-C), 118.9 (8-C), 121.7 (10-C) 127.5 (9-C), 129.2 (11-C), 137.3 (11a-C), 139.9 (7a-C), 160.0 (6-C), 188.3 (4-C). Anal. calcd for $C_{16}H_{13}Cl_4NO_2$ (393.10): C, 48.89; H, 3.33; N, 3.56. Found: C, 48.91; H, 3.48; N, 3.51.

4-Chloro-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**18**): A solution of 4-hydroxy-pyridocarbazolone **9** (1.00 g, 40 mmol) in phosphoryl chloride (15 mL) was heated under reflux for 15 minutes. After cooling, the reaction mixture was poured onto ice/water (100 mL) and brought to pH = 4-6 with 2 M aq. sodium hydroxide solution. The alkaline mixture was extracted with chloroform (3x100 mL), the combined organic phases taken to dryness under reduced pressure, the obtained solid filtered by suction, washed with hexane and dried under reduced pressure at 40 °C. The yield was 0.61 g (56%), mp 125 °C (ethanol). IR: 3450 m, b, 2931 s, 1661 m, 1616 s, 1594 m, 1556 m cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.40 (s, 3 H, Me), 1.70-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.50-2.55 (m, 2 H, 3-CH_2), 5.70 (s, 1 H, 5-H), 7.10-7.50 (m, 3 H, 9-H, 10-H, 11-H), 8.30-8.35 (m, 1 H, 8-H), Anal. calcd for $C_{16}H_{14}ClNO$ (271.75): C, 70.72; H, 5.19; N, 5.15. Found: C, 70.36, H, 5.16; N, 5.03.

4-Azido-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (19): To a solution of 4-chloro-tetrahydropyridocarbazolone **18** (1.00 g, 3.3 mmol) in ethanol (20 mL) and water (2 mL), sodium azide (0.65 g, 10 mmol) was added and the resulting mixture was heated to 80 °C for 3 hours. The end of the reaction was detected by tlc control. Insoluble inorganic material was removed by hot filtration and the solvent of the filtrate was removed under reduced pressure. The solid residue was digested with water (50 mL), filtered by suction, washed with water (50 mL) and dried under reduced pressure at room temperature. The yield was 0.80 g (78%), colorless prisms**,** mp 159 °C (ethanol). IR: 2930 m, 2865 w, 2124 m, 1671 s, 1626 s, 1594 s, 1560 s cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.35 (s, 3 H, Me), 1.20-2.10 (m, 4 H, 1-CH_2, 2-CH_2), 2.50-2.60 (m, 2 H, 3-CH_2),

5.65 (s, 1 H, 5-H), 7.20-7.70 (m, 3 H, 9-H, 10-H, 11-H), 8.30-8.35 (m, 1 H, 8-H). Anal. calcd for $C_{16}H_{14}N_4O$ (278.32): C, 69.05; H, 5.07; N, 20.13, Found: C, 69.42; H, 5.12; N, 19.78.

4-Hydroxy-11b-methyl-5-nitro-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazol-6-one (20): To a solution of 4-hydroxy-pyridocarbazolone **10** (1.50 g, 6 mmol) in glacial acetic acid (20 mL), concentrated nitric acid (8.0 mL, 120 mmol) was slowly added at room temperature. Then sodium nitrite (0.25 g, 3.6 mmol) was added as a catalyst. The mixture was stirred for 1.5 hours until a precipitate was formed. Then it was poured onto ice/water (150 mL), stirred, and the precipitated solid filtered by suction. The product was washed with water until acid-free (pH=6) and dried under reduced pressure at 40 °C. The yield was 0.90 g (51%), mp 224 °C, yellow needles (ethanol). IR: 2930 m, 1660 s, 1610 w, 1595 m cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.33 (s, 3 H, Me), 1.40-1.49, 1.90-1.97, 2.08-2.12 and 2.31-2.36 (4 m, 4 H, 1-CH_2, 2-CH_2), 2.61 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.29-7.33 and 7.38-7.43 (2 t, J = 7.0 Hz, 2 H, 9-H, 10-H), 7.56-7.58 (dd, J = 7.0+1.5 Hz, 1 H, 11-H), 8.29-8.31 (dd, J = 7.0+1.5 Hz, 1 H, 8-H). Anal. calcd for $C_{16}H_{14}N_2O_4$ (298.30): C, 64.42; H, 4.73; N, 9.39. Found: C, 64.51; H, 4.67; N, 9.04.

4-Chloro-11b-methyl-5-nitro-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazol-6-one (21): A solution of 4-hydroxy-pyridocarbazolone **20** (0.50 g, 1.7 mmol) and triethylamine (0.5 mL) in phosphoryl chloride (8 mL) was heated under reflux for 2 hours. After cooling to room temperature, the reaction mixture was poured onto ice/water (150 mL), brought to pH = 4-6 with 2 M aq. sodium hydroxide solution and kept for 12 hours at 20 °C. The obtained solid was filtered by suction, washed with water and dried under reduced pressure at 40 °C. The yield was 0.19 g (36 %), brown crystals, mp 205 °C (dec) (ethanol). IR: 2931 w, 1668 m, 1627 m, 1597 w, 1535 s cm^{-1}. ^1H NMR (DMSO-d_6): δ 1.38 (s, 3 H, Me), 1.40-1.45, 1.90-2.00, 2.10-2.15 and 2.30-2.40 (4 m, 4 H, 1-CH_2, 2-CH_2), 2.52 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.43-7.50 (m, 2 H, 9-H, 10-H), 7.65-7.68 (dd, J = 7.0+1.5 Hz, 1 H, 11-H), 8.36-8.39 (dd, J = 7.0+1.5 Hz, 1 H, 8-H). MS (APCI pos): m/z (%) = 319 (M+2, 30%), 317 (M, 100%), 244 (10%), 186 (8%). Anal. calcd for $C_{16}H_{13}ClN_2O_3$ (316.75): C, 60.67; H, 4.14; N; 8.84. Found: C, 60.48; H, 4.34; N, 8.52.

4-Azido-11b-methyl-5-nitro-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazol-6-one (22): To a solution of 4-chloro-pyridocarbazolone **21** (1.00 g, 3.1 mmol) in dimethylformamide (30 mL), sodium azide (6.5 g, 100 mmol) was added and the resulting mixture was heated to 70 °C for about 4 hours. The end of the reaction was detected by tlc check. The mixture was cooled to room temperature, poured onto ice/water (50 mL) and kept for 12 hours at 20 °C. The solid was filtered by suction, washed with water (50 mL) and dried under reduced pressure at 30 °C. The yield was 0.30 g (29%), brown prisms**,** mp 175 °C (ethanol). DSC: reaction onset 142.8 °C, peak maximum 174.7 °C (-110 mcal/mg). IR: 3308 w, b, 2951 m, 2926 m, 2864 w, 2113 m, 1666 s, 1600 w cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.33 (s, 3 H, Me), 1.40-1.90 (m, 4 H, 1-CH_2, 2-CH_2), 2.30-2.55 (m, 2 H, 3-CH_2), 7.25-7.45 (m, 3 H, 9-H, 10-H, 11-H), 8.45-8.55 (m, 1 H, 8-H). Anal. calcd for $C_{16}H_{13}N_5O_3$ (323.31): C, 59.44; H, 4.05; N, 21.66, Found: C, 59.42; H, 4.12; N, 21.28.

12b-methyl-1,2,3,12b-tetrahydro-7*H*-[1,2,5]oxadiazolo[3',4':4,5]pyrido[3,2,1-*jk*]carbazol-7-one 6-oxide (23): A solution of 4-azidopyridocarbazolone **22** (10 mg, 0.034 mmol) in dimethylformamide (2 mL) was heated under reflux for 2 h. After cooling to room temperature, the mixture was poured onto crushed ice/water (20 mL). The formed solid was filtered by suction, washed with water and dried. The yield was 1 mg (11%), brown powder, mp 271 °C (methanol). DSC: mp onset 265.1 °C, peak maximum 272.5 °C (30 mcal/mg). IR: 3360, 3310 w, b, 2950 m, 2925 m, 1695 s, 1650 m, 1610 s, 1595 s cm^{-1}.

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