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

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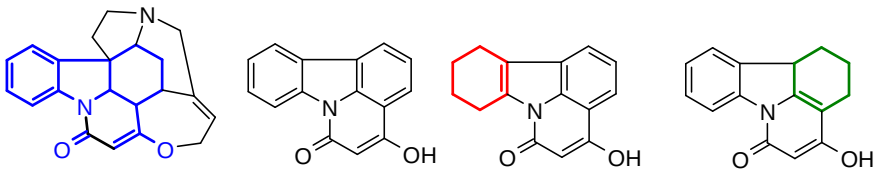
Abstract

Arylhydrazines **1** react with 2-methylcyclohexanone **2** via *Fischer indole synthesis* to 4a-methyl-2,3,3,4a-tetrahydro-1*H*-carbazoles **3**, which cyclize with 2-substituted malonates **5** to give 5-aryl- and 5-alkylsubstituted 4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-ones **6**. Pyridocarbazoles **6** can be shown to give a series of reactions, such as electrophilic halogenation to 5-chloro-pyridocarbazole-4,6-dione **9**, and nucleophilic halogenation to 4-chloro-pyridocarbazol-6-one **11**. 4-Azido-5-phenylpyridocarbazol-6-one **13** cyclizes under thermolysis to the indolo derivative **14**. This reaction was studied by differential scanning calorimetry (DSC).

Introduction

Tetrahydropyrido[3,2,1-*jk*]carbazol-6-one (**blue** 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], e.g. Brucine (dimethoxystrychnin) [3b] and Vomicin (12-hydroxy-N-methylpseudostrychnine) [3c]. It possesses the biological interesting combination of the well-known indole structure [4] and the 4-hydroxy-2-pyridone structure.



A **B** **C** **D**

Especially the pyridone system is noteworthy for several reasons: The basic structure 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 [5]), and the yellow fungal pigment Tenellin [6]. A whole class of 4-hydroxy-5,6-dihydro-2-pyridones with antibiotic activity (e.g. Mocimycin [3e]) is produced by *Streptomyces* species. 4-Hydroxy-2-pyridone itself has been used as

"3-Deaza-uracil" for the preparation of nucleoside analogs [7] and some halogenated derivatives have shown herbicidal activity [8].

Recently we published the syntheses and reactions of a series of pyrido[3,2,1-*jk*]carbazol-6-ones **B** with two aromatic benzo rings in the carbazole moiety [9], and of tetrahydropyrido[3,2,1-*jk*]carbazol-6-ones with one hydrogenated benzo ring of type **C** [10] (**red** partial structure), having the pyridone part fused to the aromatic part of the carbazole. Building up the 4-hydroxy-2-pyridone part starting with enamines or azomethines on one side, and reactive malonic acid derivatives on the other side, has attracted our attention for many years [11]. To direct the ring closure reaction to the desired position, in the present work 2,3,4,9-tetrahydrocarbazoles **3** ("indolenines") are tested as substrates for diethyl and trichlorophenyl malonates. The resulting tetrahydro-pyrido[3,2,1-*jk*]carbazoles of type **D** (**green** saturated ring) comprise already four rings as found in Strychnos alkaloids [2] with the two oxygen functions at the correct positions and having the pyridone part fused to the hydrogenated ring.

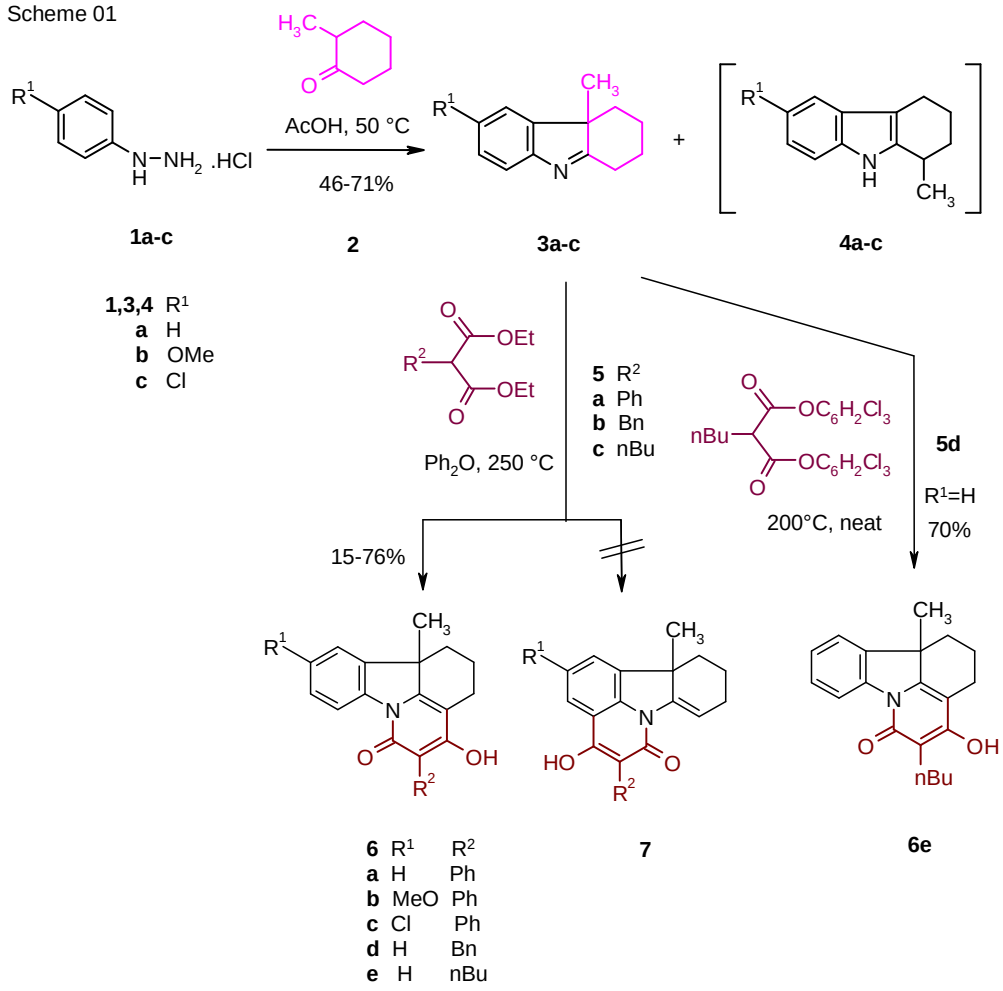
Results and Discussion

1. Synthesis of tetrahydrocarbazoles 3 and cyclocondensation with malonates to tetrahydro-pyrido-carbazolones 6

Our approach to the tetrahydro-pyridocarbazole system started with the synthesis of 2,3,4,4a-tetrahydro-1*H*-carbazoles **3** with suitable substituents at the desired positions. 2-Methylcyclohexanone (**2**, pink colored) gives, depending on the reaction conditions, via a *Fischer indole synthesis* 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]. The isomers were called as the neutral (**4**) and the basic product (**3**) [13], a property which makes it easy to separate them [14]. Mechanistic investigations support an intermolecular rearrangement by radical cleavage of the intermediate hydrazones which allow a free rotation of the radical molecules [15]; the structures were assigned in ref. [16]. The ratio of both isomers, **3** and **4**, is influenced by the structure of the substituent in position 2 of the cyclohexanone and the kind of the acid catalyst: with soft acids such as acetic acid, product **3** is preferably formed, with hard acids such as sulfuric acid, preferable **4** is formed [17]; however, the yields are low. Our synthetic approach started from commercially available phenylhydrazine hydrochlorides **1a-c** and 2-methylcyclohexanone (**2**), which were brought to reaction directly in glacial acetic acid as solvent without releasing the free phenylhydrazine bases. The work-up includes the extraction of **3** with diethyl ether from the alkaline solution to isolate the crude so-called "basic products" as oils, which crystallized in the case of **3a** and **3c** on addition of hexane; **3b** was obtained as an yellowish oil. Comparison of the ^{1}H nmr spectra of **3** with spectra of the isomer 1-methyl-2,3,4,9-tetrahydro-1*H*-carbazoles **4** [10] show, that the methyl groups in the hydrogenated carbazole rings are located between 1.07-1.08 ppm, whereas the 4a-methyl group in **3** has a signal at 1.30 ppm. In addition, the NH-signal in 9-position, which is visible in all spectra of type **4** at 10.40-10.50 ppm, is missing in structures **3** (Scheme 01).

The thermal cyclocondensation of 4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazoles **3a-c** with diethyl phenylmalonate and diethyl benzylmalonate (red colored) in diphenylether as the solvent gave via reactive ketene intermediates [11] pyrido-carbazolones, which could be formed in two isomeric structures. The spectral analysis showed that a ring closure directed to the aromatic ring producing **7** can be ruled out, because of the lack of an olefinic proton at position 8 and an fourth aromatic proton from the carbazole part. In this way, tetrahydro-pyridocarbazolones **6a-d** were obtained in good yields.

Scheme 01



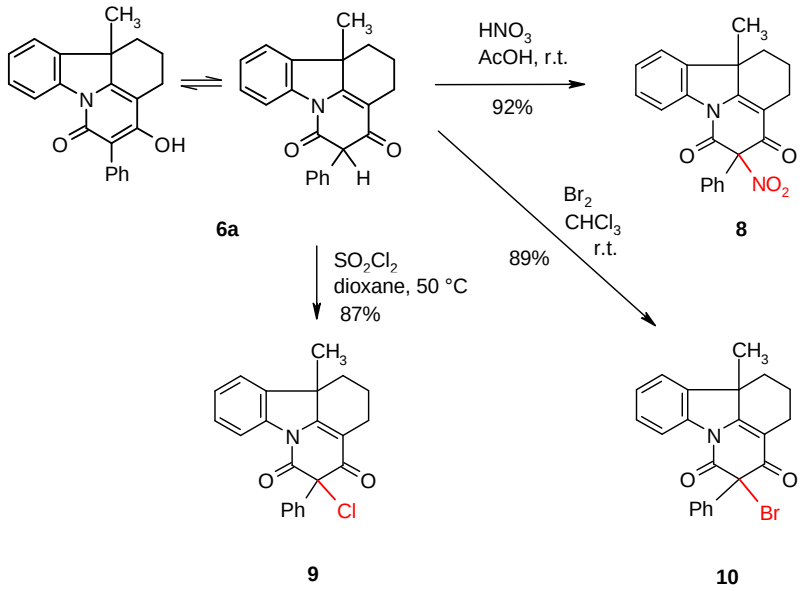
Thermal cyclocondensation of **3a** with diethyl butylmalonate **5c** gave only very low yields of **6e**. However, when the cyclization reaction was performed without solvent at 200 °C with the highly reactive bis-(2,4,6-trichlorophenyl) n-butylmalonate (**5d**), the so-called "active malonate" [11, 18], the ring closure proceeded in good yields of 70% to **6e**.

2. Electrophilic attack directed to 4-hydroxy-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (6a)

The attack with electrophilic reagents on 4-hydroxy-5-phenyl-tetrahydropyridocarbazolone **6a** has three possible targets: the positions 1-4 of the benzo ring in carbazole, the phenyl ring in position 5 and position 5 itself in the heterocyclic ring, which can be considered as tautomeric CH-acidic position. Under mild conditions, only position 5 (red marked substituents) is attacked, similar as found in rela-

ted quinoline systems [19] . With concentrated nitric acid in glacial acetic acid already at room temperature 5-nitro-5-phenyl-tetrahydropyrido[3,2,1-jk]carbazoledione **8** was formed in excellent yields (Scheme 02). Chlorination of **6a** with sulfuryl chloride in dioxane as the solvent gave at 50 °C in excellent yields 5-chloro-5-phenyl-tetrahydropyrido[3,2,1-jk]carbazoledione **9**. Bromination with bromine in chloroform formed already at room temperature in similar excellent yields 5-bromo-5-phenyl-tetrahydropyrido[3,2,1-jk]carbazoledione **10**.

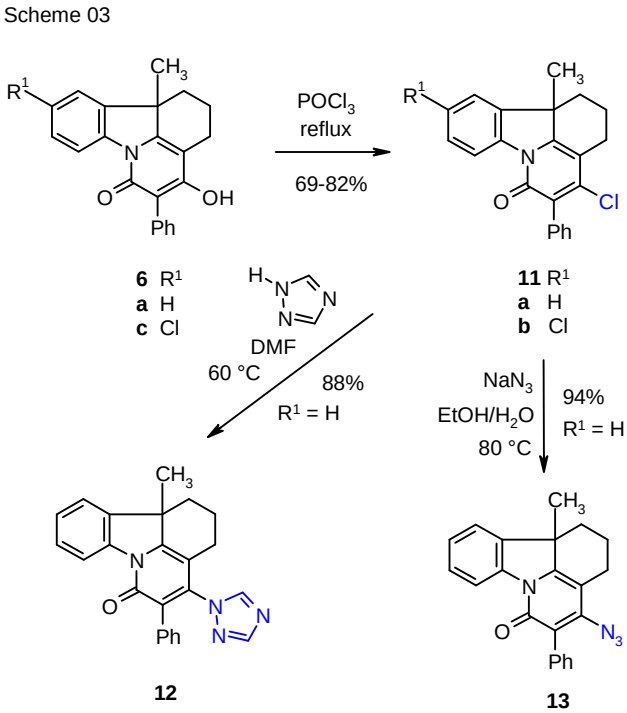
Scheme 02



The electrophilic attack formed in all three examples a 5,5-disubstituted pyridinedione structure deriving from the CH-acidic group of the α,γ-dioxo tautomer of **6a** in position 5.

3. Nucleophilic displacement of the 4-hydroxy-group in tetrahydro-pyridocarbazolone 6a

Scheme 03



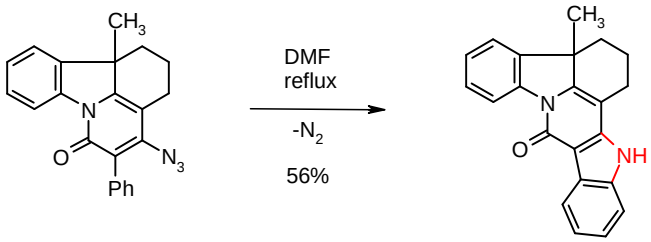
Reaction of boiling phosphoryl chloride with 4-hydroxy-5-phenyl-tetrahydropyridocarbazolones **6a,c** gave similar as in quinoline series [20] in very good yields 4-chloro-5-phenyl-tetrahydropyridocarbazolone **11a,b** by replacing the 4-hydroxy group in a nucleophilic substitution reaction against the 4-chloro group (Scheme 03, blue marked substituents). The formed 4-chloro derivatives are reactive intermediates and can easily converted to other derivatives, e.g. nitrogen bases or azido groups.

1,2,4-Triazole sodium reacted in dimethylformamide solution with 4-chloro derivative **11a** at 60 °C in excellent yields to 5-phenyl-4-triazolyl-tetrahydropyridocarbazolone **12**, a structure related to anti-fungal agents [21] . 4-Chloro derivative **11a** and sodium azide gave in boiling ethanol in excellent yields 4-azido-5-phenyl-tetrahydropyridocarbazolone **13**. The structure of **13** is supported by the IR signal of the azido group at 2109 cm^{-1}. Both reactions demonstrated the high reactivity of the 4-chloro group against nucleophiles.

4. Thermal cyclization of 4-azido-5-phenyl-tetrahydropyridocarbazolone 13

In the last years we investigated a series of cyclization reactions of azides with reactive ortho-substituents [22, 23]. The thermal cyclization of ortho-phenyl azides in pyridocarbazoles proceeds via nitrene intermediates [24] and is known to produce indolo products [25]. The conditions of the ring closure reaction of the 4-azido derivative **13** was investigated by differential scanning calorimetry (DSC) to obtain the information on the cyclization temperature to indole **14** (red marked) and possible further decomposition. The DSC diagram shows a cyclization range with 139.1 °C onset and 171.8 °C maximum, which allows to use dimethylformamide at reflux temperature as the cyclization solvent (Scheme 04).

Scheme04



13 **14**

The reaction enthalpy with a value of ΔH = -547 J/g is rather large, which must be taken into consideration when larger batches are thermolyzed. At 236.4 °C a melting point is observed, which is identical with the data obtained from the cyclized indolo-pyridocarbazole **14**. The structure of 3a-methyl-2,3,3a,14-tetrahydroindolo[2',3':4,5]pyrido[3,2,1-*jk*]carbazol-9(1*H*)-one (**14**) is supported by NMR data, which contain a NH signal at δ 11.97 ppm, and by mass spectral data, which show the molecule peak.

Conclusion

It could be shown, that 4a-methyl-2,3,4,4a-tetrahydro-1*H*-carbazoles **3** are obtained without by-products of the isomeric 1-methyl-2,3,4,9-tetrahydro-1H-carbazoles **4** in yields of 50-70%. Cyclocondensation of tetrahydrocarbazoles **3** with substituted malonates results in the formation of 4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-ones **6** without formation of the isomeric pyridocarbazoles **7**. Both electrophilic as well as nucleophilic attacks at **6** gave regioselective substitutions in the heterocyclic pyridone ring either in position 5 or position 4, respectively. Thermal

cyclization of 4-azido-5-phenyl-tetrahydropyridocarbazolone **13** was investigated by differential scanning calorimetry (DSC) and produced indolo-pyridocarbazole **14** 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 reflection 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 [26] 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): A suspension of phenylhydrazinium chloride (**1a)** (30.8 g, 0.21 mol) in glacial acetic acid (170 mL) was warmed to 50 °C. To this suspension, a solution of 2-methylcyclohexanone **2** (22.7 g, 0.20 mol) in glacial acetic acid (35 mL) was added dropwise rapidly under stirring. After addition, the mixture was heated under reflux for further 2 hours and then cooled to room temperature. The solvent was removed under reduced pressure, the residual brown oil diluted with water (10 mL) and then 2 *M* aq. sodium hydroxide solution (130 mL) was added to the residue until an alkaline pH was reached. The product was extracted with diethyl ether (100 mL), the organic phase dried with sodium sulfate, filtered and the solvent removed at the rotary evaporator. The residue was distilled under reduced pressure to get a light yellow oil at 144–155 °C / 13 mm Hg.; lit. bp 158 °C/20 mm Hg [27]. On addition of a few drops of hexane, transparent crystals were formed within a few minutes. The yield was 27.7 g (71%); colorless prisms, mp 68 °C (hexane) lit. mp 69 °C [27]. 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). Anal. calcd for $C_{13}H_{15}N$ (185.27): C, 84.28; H, 8.16; N, 7.56. Found: C, 83.81; H, 8.36; N, 7.66.

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 described for **3a**. The yield was 9.89 g (46%), yellowish oil, bp 190 °C/14 mm Hg; lit. bp 122 °C/2 mm Hg [28].

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 for **3a** to obtain after distillation a yellowish oil, bp 170 °C/14 mm Hg. The oily liquid crystallized on addition of hexane. The solid was filtered by suction, washed with cold hexane and dried at room temperature under reduced pressure The yield was 3.05 g (47%), colorless crystals, mp 66 °C (hexane); its yellow picrate showed a mp of 181 °C. IR: 3050 w, 2920 m, b, 1610 w, 1580 s cm^{-1}. Anal. calcd for $C_{13}H_{14}ClN$ (219.72): C, 71.07; H, 6.42; N, 6.37. Found: C, 70.85; H, 6.56; N, 6.41.

4-Hydroxy-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**6a**): A mixture of tetrahydrocarbazole **3a** (1.85 g, 10 mmol) and diethyl phenylmalonate (**5a**) (2.37g, 10 mmol) in diphenyl ether (10 mL) was heated in a 2-necked flask equipped with a distillation bridge and a 20 cm Vigreux column to 230-240 °C internal temperature and kept for 3 hours at this temperature. Then the temperature was raised to 250 °C and the distillation was continued until no more ethanol was liberated (about 1 hour). The reaction mixture was cooled to room temperature, treated with hexane (50 mL) and stirred for 24 hours. The resulting solid product was filtered by suction, dissolved in hot toluene (200 mL), heated with char-coal, filtered and the solvent reduced to 50 mL i. vac.. The residue was filtered, washed with cold methanol (20 mL) and dried under reduced pressure at 40 °C. The yield was 1.61 g (49%), gray-white powder, mp 213 °C (toluene). IR: 3044 w, 2981 w, 2962 m, 2881 w, 1682 s, 1608 m, 1556 s cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.44 (s, 3 H, Me), 1.63-1.69 and 2.01-2.35 (2 m, 4 H, 1-CH_2, 2-CH_2), 2.72 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.24-7.26 (t, J = 7.0 Hz, 1 H, 9-H), 7.33-7.38 and 7.41-7.56 (2 m, 7 H, 10-H, 11-H, 5 PhH), 8.56 (dd, J = 7.0+2.0 Hz, 1 H, 8-H). Anal. calcd for $C_{22}H_{19}NO_2$ (329.40): C, 80.22; H, 5.81; N, 4.25. Found: C, 80.40; H, 5.85; N, 4.21.

4-Hydroxy-10-methoxy-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**6b**): This compound was obtained from 6-methoxy-tetrahydrocarbazole **3b** (2.15 g, 10 mmol) and diethyl phenylmalonate (**5a**) (2.37g, 10 mmol) using the procedure and work-up described for **6a**.. The yield was 1.97 g (55%), colorless prisms, mp 251 °C (toluene). IR: 3050 m, 2930 m, 2720 m, 1610 m, 1600 m cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.25 (s, 3 H, Me), 1.55-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.60 (t, J = 7.0 Hz, 2 H, 3-CH_2), 3.60 (s, OMe), 6.80-7.00 (5 H, Ph), 7.20-7.40 (s, (m, 3 H, 8-H, 9-H, 11-H), 11.20 (s, OH). Anal. calcd for $C_{23}H_{21}NO_3$ (359.43): C, 76.86 H, 5.89 N, 3.90. Found: C, 76.93 H, 5.91 N, 3.76.

10-Chloro-4-hydroxy-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (6c): This compound was obtained from 6-chloro-tetrahydrocarbazole **3c** (2.19 g, 10 mmol) and diethyl phenylmalonate (**5a**) (2.37g, 10 mmol) using the procedure and work-up described for **6a**. The yield was 2.76 g (76%), colorless prisms, mp 237 °C (toluene). IR: 2920 m, b, 1750 w, 1730 w, 1710 m, 1680 s, 1630 s, 1560 m cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.20 (s, 3 H, Me), 1.55-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.65 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.20 (s, 5 H, Ph), 7.30-7.40 (m, 1 H, 9-H), 7.40-7.60 (m, 1 H, 11-H), 8.30 (dd, J = 7.0+1.0 Hz, 8-H), 11.20 (s, OH). Anal. calcd for $C_{22}H_{18}ClNO_2$ (363.85): C, 72.63; H, 4.99; N, 3.85. Found: C, 72.24; H, 5.18; N, 3.51.

5-Benzyl-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**6d**)**:** This compound was obtained from tetrahydrocarbazole **3a** (2.81 g, 15 mmol) and diethyl benzylmalonate (**5b**) (3.75 g, 15 mmol) using the procedure and work-up described for **6a**. The yield was 2.92 g (52%), gray prisms, mp 216 °C (1-butanol). IR**:** 3200-3300 b, m, 2920 m, 1680 s, 1610 s, 1560 b,s cm^{-1}. ^{1}H NMR (DMSO-d_6): δ 1.30 (s, 3 H, Me), 1.35-2.30 (m, 4 H, 1-CH_2, 2-CH_2), 2.65 (t, J = 7.0 Hz, 2 H, 3-CH_2), 3.87 (s, 2 H, benzyl-CH_2), 7.10-7.50 (m, 8 H, ArH, Ph), 8.42 (dd, J = 7.0+1.0 Hz, 1 H, 8-H). Anal. calcd for $C_{23}H_{21}NO_2$ (343.44): C, 80.44; H, 6.16; N, 4.08. Found: C, 80.64; H, 6.22; N, 4.04.

5-Butyl-4-hydroxy-11b-methyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazole-6-one (**6e**)**:**

Method A: This compound was obtained from tetrahydrocarbazole **3a** (2.81 g, 15 mmol) and diethyl n-butylmalonate (**5c**) (3.24 g, 15 mmol) using the procedure and work-up described for **6a**. The yield was 0.69 g (15%).

Method B: An intimate mixture of tetrahydrocarbazole **3a** (1.85 g, 10 mmol) and bis-(2,4,6-trichlorophenyl) n-butylmalonate (**5d**) (5.19 g, 10 mmol) was heated to 200 °C for 20 minutes without solvent. The product was cooled to room temperature and digested with hexane several times to remove 2,4,6-trichlorophenol. The remaining solid was filtered by suction, washed with hexane and dried under reduced pressure at 40 °C. The yield was 2.16 g (70%), colorless powder, mp 198 °C (methanol). IR**:** 3350 m, 2960 m, 1675 s, 1610 m, 1555 s cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.91 (t, J = 7.0 Hz, butyl-CH_3), 1.23 (s, 3 H, Me) 1.35-2.30 (m, 6 H, 1-CH_2, 2-CH_2, 2 butyl-CH_2), 2.60-2.80 (m, 4 H, 3-CH_2, butyl-CH_2), 7.10-7.50 (m, 3 H, 9-H, 10-H, 11-H), 8.33 (dd, J = 7.0+1.5 Hz, 8-H), 10.80 (s, br, 1 H, OH). Anal. calcd for $C_{20}H_{23}NO_2$ (309.41): C, 77.64; H, 7.49; N, 4.53. Found: C, 77.38; H, 7.12; N, 4.62.

11b-Methyl-5-nitro-5-phenyl-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazole-4,6(5*H*)-dione (8): To a solution of 2-phenyl-tetrahydropyridocarbazolone **6a** (1.98 g, 6 mmol) in glacial acetic acid (20 mL), concentrated nitric acid (8.0 mL) was added slowly with stirring at room temperature. The reaction mixture was kept at room temperature for 12 hours to afford a solid product, which was filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 2.10 g (92%), yellow prisms, mp 145 °C (ethanol). IR: 2950 w, 1710 m, 1685 s, 1640 s, 1590 m cm^{-1}. Anal. calcd for $C_{22}H_{18}N_2O_4$ (374.40): C, 70.58; H, 4.85; N, 7.48. Found: C, 70.96; H, 5.04; N, 7.30.

5-Chloro-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazole-4,6(5*H*)-dione (**9**)**:** To a suspension of 2-phenyl-tetrahydropyridcarbazolone **6a** (1.98 g, 6 mmol) in dioxane (20 mL), sulfuryl chloride (1.0 g = 0.6 mL, 7.4 mmol) was added dropwise, keeping the temperature at 50 °C. After further 10 minutes at this temperature, the reaction mixture was poured onto ice-water (300 mL) and the precipitate filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 1.87 g (87%), yellow prisms, mp 158 °C (cyclohexane). IR: 1705 m, 1680 s, 1650 s cm^{-1}. Anal. calcd for $C_{22}H_{18}ClNO_2$ (363.85): C, 72.63; H, 4.99; N, 3.85; Found: C, 72.72; H, 5.06; N, 3.81.

5-Bromo-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-pyrido[3,2,1-*jk*]carbazole-4,6(5*H*)-dione (**10**): To a solution of 2-phenyl-tetrahydropyridocarbazolone **6a** (1.98 g, 6 mmol) in chloroform (20 mL), a solution of bromine (0.96 g, 6 mmol) in chloroform (5 mL) of was slowly added. The reaction mixture was stirred at room temperature for 20 minutes and then extracted with water. The organic layer was dried with sodium sulfate and taken to dryness under reduced pressure. The solid was digested with cyclohexane, filtered by suction and dried at reduced pressure at room temperature. The yield was 2.20 g (89%), pale yellow crystals, mp 150 °C (cyclohexane). IR: 2970 w, 1710 m, 1685 m, 1655 s, 1605 w cm^{-1}. Anal. calcd for $C_{22}H_{18}BrNO_2$ (408.30): C, 64.72; H, 4.44; N, 3.43. Found: C, 64.53; H, 4.76; N, 3.37.

4-Chloro-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**11a**): A mixture of 2-phenyl-tetrahydropyridocarbazolone **6a** (1.00 g, 3 mmol) and phosphoryl chloride (10 mL) was heated under reflux for 4 hours. The resulting solution was poured onto ice/water (100 mL) and brought to pH = 4–6 with 2 *M* aqueous sodium hydroxide solution. The solid was filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 0.72 g (69%), grayish prisms, mp 191 °C (ethanol). IR: 3051 w, 2964 m, 2861 w, 1647 s, 1624 s, 1587 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.45 (s, 3 H, Me), 2.13-2.38 (m, 4 H, 1-CH_2, 2-CH_2) 2.80 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.37-7.39, 7.41-7.47, 7.50-7.69 (3 m, 8 H, Ph, 9-H, 10-H, 11-H), 8.58 (dd, J = 7.0+1.5 Hz, 8-H). Anal. calcd for $C_{22}H_{18}ClNO$ (347.85): C, 75.97; H, 5.22; N, 4.03. Found: C, 76.36; H, 5.64; N, 3.82.

4,10-Dichloro-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido-[3,2,1-*jk*]carbazol-6-one (11b): A mixture of 8-chloro-2-phenyltetrahydropyridocarbazolone **6c** (1.10 g, 3 mmol) and phosphoryl chloride (10 mL) was heated under reflux for 4 hours. The excess phosphoryl chloride was removed under reduced pressure, the

residue was poured on ice/water (200 mL) and then brought to pH = 4–6 with 2 *M* aqueous sodium hydroxide solution. The resulting solid was filtered by suction, washed with water (50 mL) and dried under reduced pressure at room temperature. The yield was 0.94 g (82%), colorless prisms, mp 175 °C (ethanol). IR: 2950 w, 2920 w, 1665 s, 1630 s, 1600 w, 1585 w cm^{-1}. Anal. calcd for $C_{22}H_{17}Cl_2NO$ (382.29): C, 69.12; H, 4.48; N, 3.66. Found: C, 69.17; H, 4.57; N, 3.61.

11b-Methyl-5-phenyl-4-(1,2,4-triazol-1-yl)-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (**12**): To a solution of 4-chloro-5-phenyl-tetrahydropyridocarbazolone **11a** (1.16 g, 3 mmol) in dimethylformamide (10 mL), 1,2,4-triazole sodium (0.36 g, 3 mmol) was added and the resulting mixture stirred at 50–60 °C for 30 minutes. After cooling to room temperature the mixture was poured into cold water (200 mL), the solid filtered by suction, washed with cold water (50 mL) and dried under reduced pressure at room temperature. The yield was 1.00 g (88%), colorless prisms, mp 202 °C (ethanol). IR: 2940 w, 1670 s, 1630 m, 1600 w, 1580 m cm^{-1}. Anal. calcd for $C_{24}H_{20}N_4O$ (380.45): C, 75.77; H, 5.30; N, 14.73. Found: C, 75.86; H, 5.01: N, 14.64.

4-Azido-11b-methyl-5-phenyl-1,2,3,11b-tetrahydro-6*H*-pyrido[3,2,1-*jk*]carbazol-6-one (13): To a solution of 4-chloro-5-phenyl-tetrahydropyridocarbazolone **11a** (1.16 g, 3 mmol) in ethanol (15 mL) and water (5 mL), sodium azide (0.26 g, 4 mmol) was added and the resulting mixture was heated to 80 °C for 12 hours. Insoluble inorganic material was removed by 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 1.00 g (94%), colorless prisms**,** mp/dec. 138 °C (ethanol). Calorimetric data for the thermolysis: decomposition at 139.1 °C onset, 171.8 °C maximum, ΔH = -547 J/g; mp at 236.1 °C onset, 236.4 °C maximum, ΔH = 2.2 J/g. IR: 3052 w, 2924 m, 2860 w, 2109 s, 1663 s, 1625 s, 1591 m cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 3 H, Me), 1.62-1.68 and 2.00-2.33 (2 m, 4 H, 1-CH_2, 2-CH_2), 2.69 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.32-7.35 (m, 3 H, 9-H, 10-H, 11-H), 7.38-7.46 (m, 5 H, Ph), 8.59 (dd, J = 7.0 + 2.0 Hz, 8-H). Anal. calcd for $C_{22}H_{18}N_4O$ (354.41): C, 74.56; H, 5.12; N, 15.81. Found: C, 74.50; H, 5.21; N, 15.67.

3a-Methyl-2,3,3a,14-tetrahydroindolo[2',3':4,5]pyrido[3,2,1-*jk*]carbazol-9(1*H*)-one (**14**): A solution of 4-azido-5-phenyl-tetrahydropyridocarbazolone (**13**) (100 mg, 0.3 mmol) in dimethylformamide (6 mL) was heated under reflux for 12 hours, then cooled to room temperature and poured onto ice/water (100 mL). The resulting precipitate was filtered by suction, washed with a small amount of water and dried under reduced pressure at 40 °C. The yield was 53mg (56%), light yellow prisms, mp 236 °C (dimethylformamide/methanol). IR: 3215 w, 3198 w, 3055 w, 2948 w, 2928 w, 2661 w, 1664 s, 1622 s, 1579 s, 1558 m cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 3 H, Me), 1.66-1.72, 2.16-2.21 and 2.32-2.39 (3 m, 4 H, 1-CH_2, 2-CH_2), 2.81 (t, J = 7.0 Hz, 2 H, 3-CH_2), 7.24-7.32 (m, 1 H, 5-H), 7.35-7.47 (m, 5 H, 4-H, 6-H, 11-H, 12-H, 13-H), 8.48-8.51 and 8.58-8.78 (2 m, 2 H, 7-H, 10-H), 11.97 (s, 1 H, NH). MS (API-ESI neg): m/z (%) = 326 (M+1, 35), 325 (M, 100); MS (API-ESI pos): m/z (%) = 328 (M+1, 25), 327 (M, 100). Anal. calcd for $C_{22}H_{18}N_2O$ (326.40): C, 80.96; H, 5.56; N, 8.58. Found: C, 81.30; H, 5.62; N, 8.72.

References and Notes

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