Synthesis of 1*H*-[1,2]Diazepino[4,5-*b*]indole Derivatives

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A synthesis of four 1*H*-[1,2]diazepino[4,5-*b*]indole derivatives and some preliminary information about their biological activity are presented. The starting materials were 2-ethoxycarbonylindoles and 2-ethoxycarbonyl-3-formylindoles, **1a, b** and **2a, b**, respectively. 2-Ethoxycarbonyls **1a, b** reacted with 1-dimethylamino-2-nitroethylene and -2-ethoxycarbonyl-3-formylindoles **2a, b** in the presence of nitroalkanes (nitromethane or nitroethane) giving 3-(2-nitrovinyl)indoles **3a, b**. Reduction of **3a, b** yielded β-(2-oxoalkyl)indoles **4**. On reaction with an excess of hydrazine hydrate, compounds **4** gave satisfactory yields of 5-oxo-1*H*-[1,2]diazepino[4,5-*b*]indoles **5**.

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Since the discovery in 1957 of the activity of chlordiazepoxide on the central nervous system, a considerable number of benzodiazepines (1) have been prepared. In the last few years attention has been drawn to the synthesis of diazepines which are fused to different heterocyclic systems such as pyrrole (2), thiophene (3), imidazole (4), pyrazole (5), isoxazole (6) and also different types of indoles (7) and isoindoles (8). However, to our knowledge, [1,2]diazepinoindoles have not yet been described (9). The chemistry of 1,2-diazepines has been recently reviewed (10). This paper reports on the syntheses of four 1*H*-[1,2]-diazepino[4,5-*b*]indole derivatives and also some preliminary information on their activity on the central nervous system. The scheme illustrates the sequence of reactions utilized in the synthesis. The starting materials were the 2-ethoxycarbonylindoles **1a,b** and the 2-ethoxycarbonyl-3-formylindoles **2a,b**, which were all prepared by well known methods (21-24). The introduction of the 3-(2-nitrovinyl) group was carried out by two procedures: a) condensation of the 2-ethoxycarbonyl-3-formylindoles **2a,b** with the appropriate nitroalkane (nitromethane or nitroethane), using ammonium acetate as a catalyst (11-13); and b) condensation of the 2-ethoxycarbonylindoles **1a,b** with 1-dimethylamino-2-nitroethylene (14,15) using trifluoroacetic acid as a solvent to give compounds **3a,b**, respectively. Both methods gave similar and satisfactory results (yields 73-80%). The structural properties of the 3-(2-nitrovinyl)indoles have been previously discussed in detail (12,16,17) and it has been suggested that their formation occurs by means of an ammonium salt intermediate. From the J_{AB} values of about 11-14 Hz which we have obtained, we would surmise a *trans*-configuration for compounds **3a,b**.

The 3-(2-nitrovinyl)indoles **3** were reduced to the corresponding 3-(2-oxoalkyl)indoles **4** using a toluene (or acetone)/iron/acid system (18). This reaction has been previously reported for the preparation of 3-indolylacetone from 3-(2-nitrovinyl)indole (16). However, to our knowledge, it has never been used in the preparation of 3-indolylacetaldehydes, which are generally obtained through other procedures (19). Compounds **4a,b** were obtained as crude brown oils (yields 40-45%) and were characterized by their ir and ^{1}H-nmr spectra. Compounds **4c,d** were obtained in crystalline form by both methods (yields 50% and 26-30%, respectively) and they were characterized by elemental analysis and spectral properties (ir and ^{1}H-nmr).

The reactions of compounds **4** with an excess of hydrazine hydrate in dioxane or ethanol gave satisfactory yields of compounds **5** (69-70% for the compounds **5a,b** and 90% for the compounds **5c,d**). The four compounds were obtained as white or yellow cream crystals and they were characterized by analysis and spectral properties (ir and ^{1}H-nmr). They are derivatives of the new heterocyclic system of 1*H*-[1,2]diazepino[4,5-*b*]indole. However, the compound **5b** seems to be an exception as its ^{1}H-nmr spectrum does not show the expected signal at about δ 3.65-3.75 ppm (a doublet for compounds **5a** and a singlet for compounds **5c,d**), which has been assigned to the C-1-methylene group, but does show a complex multiplet at about δ 6.70-7.65 ppm, which integrated for 6H. This multiplet was assigned to the protons H-7, H-8, H-9, a -CH=CH group and a CONH group. On this basis, we believe that compound **5b** is better represented by the formula **5'b**, as a derivative of 3*H*-[1,2]diazepino[4,5-*b*]indole, and we have alternatively named it 4,5-dihydro-5-oxo-6-methyl-3*H*-[1,2]diazepino[4,5-*b*]indole (**5'b**). The tautomerism of benzo[1,2]diazepines and related systems has been widely studied (26).

Boiling of compound **5a** with hydrazine hydrate in toluene or with hydrochloric acid gave compound **6**. This was not an unexpected reaction, as the ring contraction of 1,2-diazepines to pyridines is a well known transformation (20) which takes place under thermal treatment, or acid or basic catalysis. The structure of compound **6** was confirmed by elemental analysis and a study of its ir and ^{1}H-nmr

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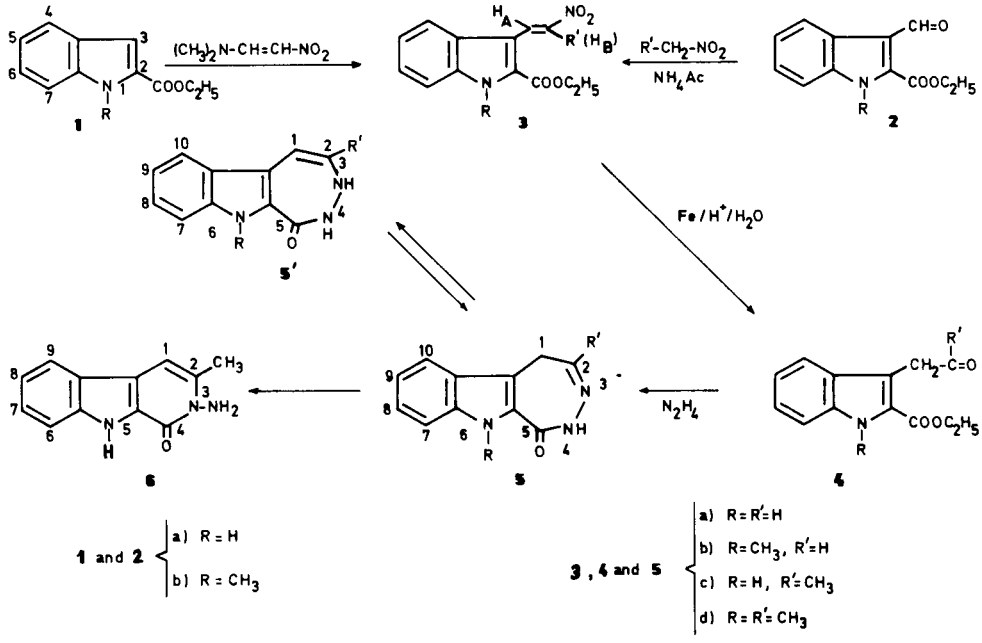
Scheme



spectra. On the other hand, when compound **5a** was boiled with phosphorus oxychloride in order to introduce an atom of chlorine on C-5, or when the compound **5a** was treated with chloranil in boiling toluene in order to dehydrogenate the 1,2-diazepine ring, only compound **6** was obtained in both cases.

Compound **5b** was assayed (i.p. in 1.5% Tween suspension) for toxicity using male wistar mice, and the general behaviour of the animals was observed. At a dose of 75 mg/kg (the smallest dose assayed) we observed, starting 5 minutes after injection and lasting 2 hours, significant sedation with a remarkable decline in spontaneous motor activity, but no loss of response to external stimulation. The LD_{50} was 335 mg/kg (353-316 for seven lots of 5 animals in each lot). These and other results, which will soon be published, suggest that the 1,2-diazepino[4,5-*b*]-indoles could be of interest as potential tranquilizing drugs.

EXPERIMENTAL

Melting points were determined in a Kofler and they are uncorrected. Elemental analyses were obtained from vacuum-dried samples (over phosphorus pentoxide at 3-5 mm Hg, 2-3 hours, at about 60-70°). Ir spectra were recorded on a Perkin-Elmer 257 apparatus using potassium bromide tablets for solid products and placing the products between crystals of sodium chloride for liquid products and the frequencies expressed in cm^{-1}. ^1H-nmr spectra were obtained on a Perkin-Elmer R-32 (90 MHz) instrument, with TMS as the internal reference, at a concentration of about 0.1 g/ml and with solvents as indicated; the chemical shifts are reported in ppm from TMS as an internal standard and are given in δ units.

The thin-layer chromatographies (tlc) were carried out on silicagel (DSF-5 Cammag, 0.3 mm thickness) with benzene:dioxane:acetic acid, 90:25:4 (v/v) as solvent and the plates were scanned under ultraviolet light λ = 254 and 366 nm.

The following starting products were prepared by previously reported methods: 2-ethoxycarbonylindole **1a**, mp 123-124°, yield 65% (21); 1-methyl-2-ethoxycarbonylindole **1b**, mp 61°, yield 90% (22); 2-ethoxycarbonyl-3-formylindole **2a**, mp 189-190°, yield 90% (23); 1-methyl-2-ethoxycarbonyl-3-formylindole **2b**, mp 112-113°, yield 93% (24); 1-dimethylamino-2-nitroethylene, mp 103-105°, yield 60% (15).

1-Methyl-2-ethoxycarbonylindole (**1b**).

A mixture of 15.0 g (80 mmoles) of 2-ethoxycarbonylindole (22), 300 g of anhydrous potassium carbonate, 25 ml (33.4 g, 0.26 mole) of dimethyl sulfate and 500 ml of acetone was boiled for 18 hours under a reflux-condenser with mechanical stirring while protecting the mixtures with a tube of anhydrous calcium chloride. The addition of an excess of 10% ammonium hydroxide solution to the cold reaction mixture neutralized any remaining reagent. Then, most of the acetone was removed *in vacuo* in a rotavapor and water was added to the residual material in order to dissolve the potassium carbonate. The aqueous mixture was extracted with benzene, the organic solution dried on anhydrous sodium sulfate, and the solvent once again removed *in vacuo*. The residual solid was recrystallized from ethanol, mp 60-61°, yield 14.6 g (90%). With this procedure we were able to obtain a higher yield than that previously described (22), mp 60-61°.

2-Ethoxycarbonyl-3-(2-nitrovinyl)indoles (**3**).

2-Ethoxycarbonyl-3-(2-nitrovinyl)indole (**3a**).

Method A.

A mixture of compound **2a** (15.5 g, 60 mmoles), ammonium acetate (1.5 g) and nitromethane (15 ml) was boiled under reflux until the tlc showed total disappearance of compound **2a** (about 3 hours are required). On cooling, compound **3a** crystallized, mp 236° (ethanol), yield about 80%.

Method B.

With constant stirring, 2-ethoxycarbonylindole **1a** (5.67 g, 30 mmoles) was added to a solution of 1-dimethylamino-2-nitroethylene (3.48 g, 30 mmoles) in an ice-bath and the mixture then stirred in a nitrogen atmosphere for 15 minutes. The color of the solution changed from yellow

to dark. The mixture was then allowed to warm to room temperature and was poured onto crushed ice (300 g). A yellow semisolid precipitated.

The aqueous suspension was extracted three times with ethyl acetate, first using 350 ml and then using 100 ml. The combined organic extracts were washed with saturated sodium bicarbonate solution (150 ml) and then with diluted hydrochloric acid (100 ml, 1:5 v/v) and dried over anhydrous sodium sulfate. Removal of the solvent *in vacuo* afforded a yellow solid (6.0 g, 78%), mp 236° (ethanol); ir (potassium bromide): 3280 (s, NH), 1680 (s, C=O), 1625 (s), 1320 (s, NO_2), 1275 (s), 1160 (s, C-O), 970 &s, CH=CH, *trans*), 745 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.41 (t, CH_3, 3H), 4.45 (q, CH_2, 2H), 7.15-7.70 (m, H-5, H-6 and H-7, 3H), 8.00 (d, H-4, 1H, $J_{4\text{-}5}$ = 7 Hz, $J_{4\text{-}6}$ = 1 Hz), 8.10 (d, H_A, 1H), 8.89 (d, H_B, 1H, J_{AB} = 11 Hz, *trans*), 11.75 (bs, H-1, 1H).

Anal. Calcd. for $C_{13}H_{12}N_2O_4$: C, 60.00; H, 4.65; N, 10.76. Found: C, 59.90; H, 4.63; N, 10.50.

1-Methyl-2-ethoxycarbonyl-3-(2-nitrovinyl)indole (**3b**).

This compound was prepared in a similar way to that of compound **3a**. Through method A, from compound **2a**, (16.5 g, 60 mmoles), yellow crystals were obtained (13.2 g, 80%), mp 143° (ethanol). Through method B, from compound **1b** (6.02 g, 30 mmoles), 6.74 g were obtained (80%), mp 143° (ethanol); ir (potassium bromide): 1700 (s, C=O), 1630 (s, CH=CH, *trans*), 1520 (s), 1320 (s, NO_2), 1275 (s), 1100 (s, C-O), 965 (s, CH=CH, *trans*), 745 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.37 (t, C-CH_3, 3H), 4.00 (s, N-CH_3, 3H), 4.45 (q, CH_2, 2H), 7.10-7.70 (m, H-5, H-6 and H-7, 3H), 7.80-8.20 (m, H-4, 1H), 8.13 (d, H_A, 1H), 9.00 (d, H_B, 1H, J_{AB} 5 14 Hz, *trans*).

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.59; H, 5.18; N, 9.98.

2-Ethoxycarbonyl-3-(2-nitropropenyl)indole (**3c**).

This compound was prepared similarly according to the above described method A for compound **3a**. From compound **2a** (16.5 g, 60 mmoles), nitroethane (78 ml) and ammonium acetate (1.5 g), yellow crystals were obtained (12.0 g, 73%), mp 175-176° (ethanol); ir (potassium bromide): 3320 (s, NH), 1700 (s, C=O), 1650 (s, CH=CH, *trans*), 1525 (s), 1300 (s, NO_2), 1240 (s), 1110 (s, C=O), 985 (s, CH=CH, *trans*), 745 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.48 (t, CH_3, 3H), 2.33 (s, =C-CH_3, 3H), 4.53 (q, CH_2, 2H), 7.20-7.80 (m, H-4, H-5, H-6 and H-7, 4H), 8.20 (s, C=CH_A, 1H), 12.6 (bs, H-1, 1H).

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 61.31; H, 5.14; N, 10.21. Found: C, 61.45; H, 5.18; N, 10.11.

1-Methyl-2-ethoxycarbonyl-3-(2-nitropropen-1-yl)indole (**3d**).

This compound was prepared as described in method A for compound **3a**. From compound **2b** (17.3 g, 60 mmoles), nitroethane (78 ml) and ammonium acetate (1.5 g), yellow needles were obtained (13.0 g, 75%), mp 122-123° (ethanol); ir (potassium bromide): 1710 (s, C=O), 1660 (s, C=C, *trans*), 1520 (s), 1320 (s, NO_2), 1255 (s), 1140 (s, C-O), 972 (s, CH=C, *trans*); 745 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.21 (t, CH_2-CH_3, 3H), 2.05 (s, =C-CH_3, 3H), 3.95 (s, N-CH_3, 3H), 4.25 (q, CH_2, 2H), 6.90-7.60 (m, H-4, H-5, H-6 and H-7, 4H), 8.35 (s, C=CH, 1H).

Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.43; H, 5.47; N, 9.69.

2-Ethoxycarbonyl-3-(2-oxoalkyl)indoles (**4**).

2-Ethoxycarbonin-3-(2-oxoethyl)indole (**4a**).

Using a three neck flask with a dropping-funnel, reflux condenser and vigorous mechanical stirring, a mixture of 14.0 g (54 mmoles) of compound **3a**, 250 ml of water, 100 ml of toluene, 11.0 g (0.2 atom. gr.) of iron powder and 1.0 g of ferric chloride was heated to about 60°.

While at this temperature, 25 ml of concentrated hydrochloric acid was dropped into the reaction mixture. Then, the mixture was maintained under these conditions until tlc showed that all of the starting product **3a** had reacted (about 24 hours). The mixture was finally cooled to room temperature, filtered on a bed of celite and the organic phase separated. The aqueous solution was extracted twice with toluene (100 ml). The combined organic extracts were dried on anhydrous sodium sulfate and the toluene was removed *in vacuo*. A brown oil was obtained, which was used without further purification, yield 10.4 g (45%); ir (within crystals of sodium chloride): 3320 (s, NH), 1720 (s, CH=O), 1680 (s, C=O, ester), 1260 (s), 1100 (s, C-O), 745 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.34 (t, CH_3, 3H), 4.18 (d, CH_2-CHO, 2H), 4.35 (d, O-CH_2, 2H), 7.00-7.80 (m, H-4, H-5, H-6 and H-7, 4H), 9.68 (t, CHO, 1H, J 5 1.5 Hz), 11.85 (bs, H-1, 1H).

The following compounds **4** were obtained in a similar way.

1-Methyl-3-(2-oxoethyl)indole **4b**.

From 15.0 g (54 mmoles) of compound **3b**, 9.80 g (40%) were obtained, as a crude brown oil which was used without further purification; ir (within crystals of sodium chloride): 1700 (s, C=O, ketone and ester), 1265 (s), 1140 (s, C-O), 740 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.38 (t, C-CH_3, 3H), 4.00 (s, N-CH_3, 3H), 4.08 (d, CH_2-CHO, 2H), 4.38 (d, O-CH_2, 2H), 6.70 (t, CHO, 1H, J = 3 Hz), 7.00-7.85 (m, H-4, H-5, H-6 and H-7, 4H).

2-Ethoxycarbonyl-3-(2-oxopropyl)indole (**4c**).

Method A.

Compound **4c** was prepared from compound **3c** (15.0 g, 54 mmoles) in a way similar to that described above for compound **4a**, but maintaining the reaction temperature at about 80°. When tlc showed that all the starting compound **3c** had reacted (about 15 hours), the reaction mixture was cooled and filtered on a celite bed. The organic phase was separated and the aqueous phase extracted twice with toluene (100 ml).

The combined organic extracts were washed with a solution of 26 g of sodium bisulfite in 500 ml of water in order to remove any aldehydic material, and then washed with water and dried on anydrous sodium sulfate. The solvent was removed *in vacuo* and the residual solid recrystallized, yield 6.60 g (50%) of white crystals, mp 115° (2-propanol).

Method B.

In a 250 ml flask with reflux-condenser, dropping funnel and mechanical stirring, a mixture of compound **3c** (5.20 g, 90 mmoles), acetone (70 ml), iron powder (6.5 g) and ferric chloride (1.5 g) was heated to about 50°. While this temperature and vigorous stirring were maintained, a solution of acetic acid (17 ml) in water (50 ml) was dropped into the reaction mixture.

The mixture was then boiled for 4 hours, cooled to room temperature and filtered on a celite bed. Most of the acetone was removed *in vacuo* and the residual material extracted with methylene chloride, which had been previously washed with diluted sulfuric acid (1/10, v/v). The organic extract was washed first with a saturated aqueous solution of sodium bicarbonate, then several times with water, and finally dried on anhydrous sodium sulfate. Removal of solvent *in vacuo* gave an oil, which crystallized on cooling, yield 26%, mp 115° (2-propanol); ir (potassium bromide): 3320 (s, NH), 1720 (s, -CH=O), 1680 (s, C=O ester), 1260 (s), 1105 (s, C-O), 750 (s, 1,2-arom. disubst.); ^{1}H-nmr (deuteriochloroform): 1.28 (t, CH_2-CH_3, 3H), 2.05 (s, CO-CH_3, 3H), 4.13 (s, CH_2-CO, 2H), 4.30 (q, O-CH2, 2H), 6.80-7.80 (m, H-4, H-5, H-6 and H-7, 4H), 9.25 (bs, H-1, 1H).

Anal. Calcd. for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.52; H, 6.25; N, 5.59.

1-Methyl-2-ethoxycarbonyl-3-(2-oxopropyl)indole (**4d**).

Method A.

This compound was prepared from compound **3d** (14.0 g, 54 mmoles) as described above for compound **4c**, method A, yield 7.0 g (50%) of white crystals with mp 79° (2-propanol).

Method B.

This compound was obtained from compound **3d** (5.50 g, 10 mmoles) in a similar way as described above for compound **4c**, method B, yield 30%, mp 79° (2-propanol); ir (potassium bromide): 1722 (s, CO, ketone), 1690 (s, CO ester), 1245 (s), 1110 (s, C-O), 750 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 1.22 (t, CH_2-CH_3, 3H), 2.08 (s, CO-CH_3, 3H), 3.90 (s,

N-CH_3, 3H), 4.09 (s, CH_2-CO, 2H), 4.25 (q, O-CH_2, 2H), 6.80-7.80 (m, H-4, H-5, H-6 and H-7, 4H).

Anal. Calcd. for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.56; N, 5.40. Found: C, 69.21; H, 6.90; N, 5.33.

5-Oxo-1*H*-[1,2]diazepino[4,5-*b*]indoles (**5**).

4,5-Dihydro-5-oxo-1*H*-[1,2]diazepino[4,5-*b*]indole (**5a**).

A mixture of compound **4a** (2.30 g, 10 mmoles), 80% hydrazine hydrate (5 ml) and ethanol (or dioxane, 25-50 ml) was boiled until tlc showed that all compound **4a** had reacted (about 3 hours). The ethanol was removed *in vacuo* and the residual material diluted with water. The product **5a** precipitated and was collected by filtration and washed with water, yield 1.40 g (70%) as a yellow powder, with mp 170° (ethanol); ir (potassium bromide): 3200 (bs, NH), 1650 (bs, C=O and C=N), 1330 (s), 1265 (s, C-N), 740 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 3.75 (d, CH_2, 2H), 6.80-7.75 (m, H-2, H-7, H-8 and H-9, 4H), 7.65-7.95 (m, H-10, 1H), 10.70 (bs, H-4, 1H), 11.70 (bs, H-6, 1H).

Anal. Calcd. for $C_{11}H_9N_3O$: C, 66.32; H, 4.52; N, 21.09. Found: C, 66.15; H, 4.24; N, 21.11.

In a similar way the following compounds **5** were prepared.

4,5-Dihydro-5-oxo-6-methyl-3*H*-[1,2]diazepino[4,5-*b*]indole (**5'b**).

This compound was obtained from compound **4b** (1.10 g, 4 mmoles), yield 0.5 g (69%) as a yellow-green powder, mp 154.5° (ethanol); ir (potassium bromide): 3300 (bs, NH), 3180 (s, NH), 1645 (s, C=O), 1270 (s, C-N), 740 (s, 1,2-arom. disub.); ^{1}H-nmr (DMSO-d_6): 4.14 (s, N-CH_3, 3H), 6.70-7.65 (m, H-1, H-2, H-4, H-7, H-8 and H-9, 6H), 7.75-8.10 (m, H-10, 1H).

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.62; H, 5.38; N, 20.00.

4,5-Dihydro-2-methyl-5-oxo-1*H*-[1,2]diazepino[4,5-*b*]indole (**5c**).

This compound was obtained from compound **4c** (2.50 g, 10 mmoles, reaction time 5 hours), yield 1.90 g (90%) as white needles, mp 227° (ethanol); ir (potassium bromide): 3280 (s, NH), 1675 (s, C=O), 1630 (s, C=N), 1330 (s), 1265 (s, C-N), 725 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 2.13 (s, CH_3, 3H), 3.67 (s, CH_2, 2H), 7.00-7.60 (m, H-7, H-8 and H-9, 3H), 7.70-7.90 (d, H-10, 1H), 10.55 (s, CONH, 1H), 11.85 (s, H-6 1H).

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.41; H, 5.30; N, 19.63.

4,5-Dihydro-2,6-dimethyl-5-oxo-1*H*-[1,2]diazepino[4,5-*b*]indole (**5d**).

This compound was obtained from compound **4d** (2.60 g, 10 mmoles, reaction time 7 hours), yield 2.10 g (90%) as yellow-cream plates, mp 146.5° (ethanol); ir (potassium bromide): 3360 (s), 3260 (s), 3140 (s, NH), 1625 (bs, C=O, C=N), 1370 (s), 1300 (s, C-N), 740 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 2.11 (s, C-CH_3, 3H), 3.65 (s, CH_2, 2H), 4.05 (s, N-CH_3, 3H), 6.90-7.80 (m, H-4, H-7, H-8 and H-9, 4H), 7.80-8.10 (m, H-10, 1H).

Anal. Calcd. for $C_{13}H_{13}N_3O$: C, 68.71; H, 5.77; N, 18.49. Found: C, 68.90; H, 5.88; N, 18.64.

3,4-Dihydro-2-methyl-3-amino-4-oxo-5*H*-pyrido[3,4-*b*]indole (**6**).

A mixture of compound **5c** (0.30 g, 1.4 mmoles), toluene (15 ml) and 80% hydrazine hydrate (1 ml) was boiled until tlc showed the total transformation of compound **5c**. Upon cooling of the reaction mixture white crystals were obtained (0.20 g, 66%), mp 274° (hot ethanol with a few drops of DMF).

The same product was obtained boiling compound **5c** with: a) toluene; b) hydrochloric acid; c) chloranil in toluene; d) phosphorous oxychloride; ir (potassium bromide): 3170 (bs, NH), 1660 (s, C=O), 1620 (m), 1590 (s), 1540 (m, C=C), 750 (s, 1,2-arom. disubst.); ^{1}H-nmr (DMSO-d_6): 2.53 (s, CH_3, 3H), 6.02 (s, NH_2, 2H), 6.95 (s, H-1, 1H), 7.07-7.70 (m, H-6, H-7, H-8 and H-9, 4H), 11.75 (s, H-5, 1H).

Anal. Calcd. for $C_{12}H_{11}N_3O$: C, 67.59; H, 5.20; N, 19.71. Found: C, 67.61; H, 5.33; N, 19.66.

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