Structure and Spectral Properties of β-Carbolines. Part 4.[1] Synthesis of the New Ring System: 9,10,15,15b-Tetrahydroindolo[1′,2′:4,3]pyrazino[2,1-a]-carbolin-7(6*H*)-one

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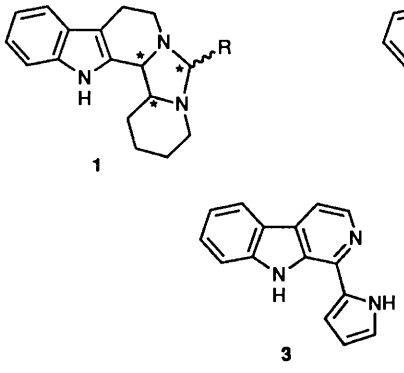
1-Indol-2-yl-1,2,3,4-tetrahydro-β-carboline and its 5-methoxy derivative were synthesized by the Pictet-Spengler reaction between tryptamine or 5-methoxytryptamine and indole-2-carbaldehyde, with a high yield. A step-by-step oxidation of the indolyl carbolines led to formation of the appropriate dihydrocarboline derivatives and two analogues of neoeudistomine, the fully unsaturated carbolines. Condensation of the indolyltetrahydrocarbolines with bromoacetyl chloride yielded the appropriate 2-substituted derivatives, which were cyclized to yield the new ring system compounds 9,10,15,15b-tetrahydroindolo[1′,2′:4,3]pyrazino[2,1-*a*]carbolin-7(6*H*)-ones, the structures of which were determined by using a high-resolution ^{1}H NMR technique.

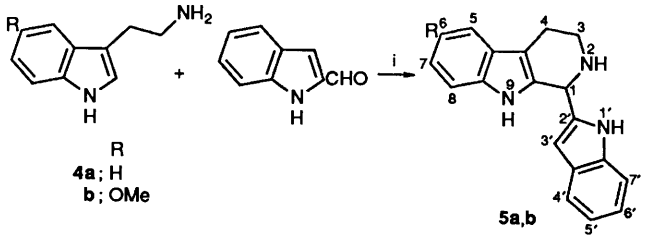
Our previous papers described a highly efficient synthesis of different derivatives of 1-(2-pyridyl)-, 1-(3-pyridyl)-, and 1-(4-pyridyl)-1,2,3,4-tetrahydro-β-carbolines *via* Pictet–Spengler reaction.[2] We also reported a simple method for the synthesis of 1-substituted 3,4-dihydro-β-carbolines, based on a selective oxidation of the readily available 1,2,3,4-tetrahydro-β-carbolines with solid potassium permanganate in tetrahydrofuran (THF) at 0 °C.[3] However, catalytic reduction of 1-(2-pyridyl)-1,2,3,4-tetrahydro-β-carboline yielded (±)-*threo*- and (±)-*erythro*-1-(2-piperidyl)-1,2,3,4-tetrahydro-β-carboline.[4] The two latter compounds were found to be excellent intermediate products for the synthesis of some heterocyclic ring systems, such as species **1**[5] or **2**.[1] We also studied in detail the structure of individual diastereoisomers of compounds **1** and **2**, and then the conformation of the octahydrodipyridoimidazo and decahydrodipyridopyrazino skeletons.[1,5d]



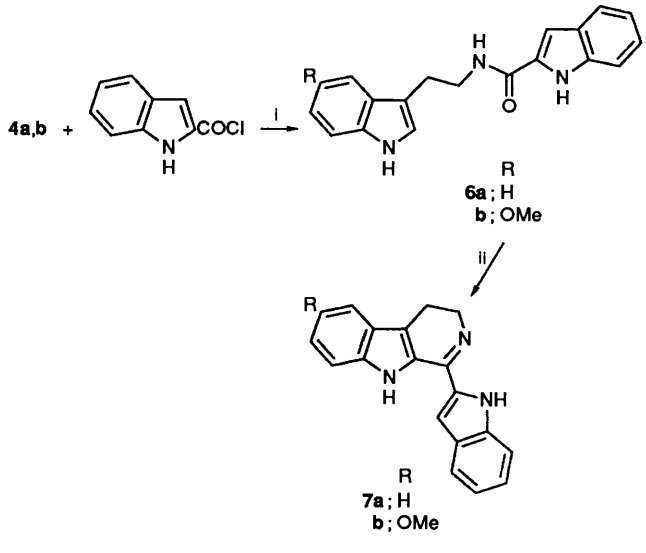
As a continuation of our study, we synthesized the two 1,2,3,4-tetrahydro-β-carboline derivatives **5a** and **5b**, new indole analogues of a neoeudistomine, **3**,[6] **8a** and **8b**, and a new heterocyclic system, the 9,10,15,15b-tetrahydroindolo[1′,2′:4,3]pyrazino[2,1-*a*]carbolin-7(6*H*)-ones **10a** and **10b**.

Results and Discussion

Synthesis.—The Pictet–Spengler reaction between tryptamine **4a** or 5-methoxytryptamine **4b** and indole-2-carbaldehyde afforded the appropriate 1,2,3,4-tetrahydro-β-carboline **5a** or **5b**, respectively, in high yield (81 and 84%, respectively) (Scheme 1). The condensation of compound **4a** or **4b** with indole-2-carbonyl chloride, followed by cyclization of the appropriate

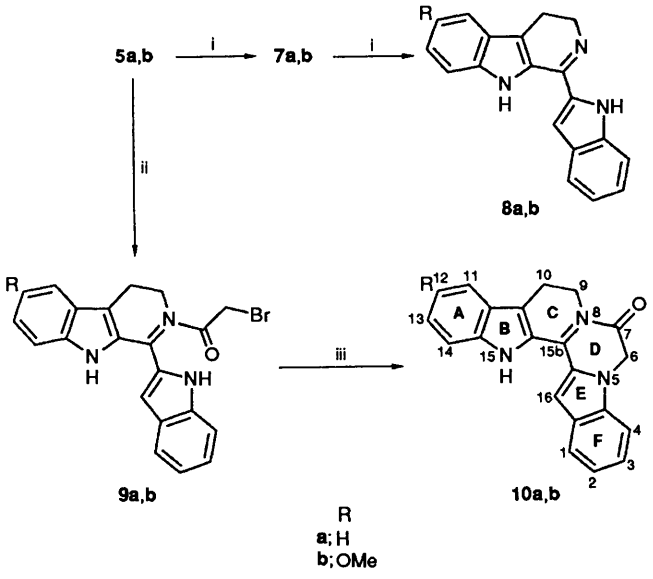


Scheme 1 *Reagents and conditions:* i, BuOH, reflux, 2 h



Scheme 2 *Reagents and conditions:* i, $CHCl_3$, 10% Na_2CO_3, room temp., 2 h; ii, PPE (polyphosphoric esters), 120 °C, 1 h

amide **6a** or **6b** to the 3,4-dihydro-β-carboline derivative **7a** or **7b** (Scheme 2) ensued in low overall yield (≤21%). Oxidation of the tetrahydrocarboline **5a** or **5b** with commercially available manganese dioxide (Merck) in benzene solution under reflux for 45 min afforded a mixture of the 3,4-dihydro-β-carboline **7a** or **7b**, in moderate yield (63 or 53%, respectively), and the appropriate β-carboline **8a** or **8b** in a yield of 14 or 27%, respectively (Scheme 3). The oxidation process was also followed by analytical TLC. After 45 min of reaction only traces of the substrate tetrahydro derivative **5a** or **5b** and a small amount of the corresponding β-carboline **8a** or **8b** were observed on the chromatoplates, while the 3,4-dihydro



Scheme 3 *Reagents and conditions:* i, MnO_2, benzene, reflux; ii, $ClCOCH_2Br$, Na_2CO_3, acetone, room temp., 20 min; iii, NaH, THF, N_2, 0–3 °C, 30 min

derivative **7a** or **7b** was found to be the main product. The spot for substrate **5a** or **5b** disappeared after 1.5 h of reaction. However, lengthening of the reaction time up to 6 h with an additional amount of manganese dioxide resulted in formation of the carboline **8a** or **8b** as the main product, and only a small amount of the dihydro product **7a** or **7b** was detected.

Reaction of compound **5a** or **5b** with bromoacetyl chloride in acetone at room temperature, in the presence of sodium carbonate, gave the corresponding 2-bromoacetyl derivative **9a** or **9b** in 70 or 80% yield, respectively. The 2-bromoacetyl derivative **9a** or **9b** was cyclized in tetrahydrofuran (THF) solution at 0–3 °C, in the presence of sodium hydride, to the appropriate 7-oxo heterocyclic system **10a** or **10b** in high yield (92 or 70%, respectively).

^{1}H *NMR Spectra.*—We reported previously that a strong intramolecular hydrogen bond exists between 2′-N and 9-N atoms of 1-(2-piperidyl)-1,2,3,4-tetrahydro-β-carboline.[4] The NH proton signal position of the indole ring depends strongly on the formation of a hydrogen bond with the solvent. For example, in a carbon tetrachloride solution it appears at δ 7.68, while in a triethylamine solution this signal shifts downfield to δ 11.21.[7] For tetrahydro derivatives the indolic 9-NH signal appears at δ 7.69 and 7.60 in a deuteriochloroform solution for compounds **5a** and **5b**, respectively. However, the appropriate 1′-NH and 2-NH signals are shifted downfield to δ 10.37 and 8.65 for compound **5a**, and to δ 10.45 and 8.71 for compound **5b**. The position and shape of these signals permit a tentative conclusion that there is a strong hydrogen bond between the 1′-H and 2-N atoms for compounds **5a** and **5b**. The position of the hydrogen bond can be unequivocally determined on the basis of the ^{1}H NMR spectra of compounds **10a** or **10b** or those of the 7-oxo derivatives of the structure **2**. As expected, the indole NH signals in compounds **10a** and **10b** (Table 1) and the 7-oxo derivatives of compound **2**[1] appear within the range δ 7.88–8.05; moreover, these signals become sharp. The same position for the hydrogen bond, *i.e.* one between the 1′-H and 2-N atoms, can be attributed to derivatives **8a** and **8b**. Chemical shifts of the 1′-NH indole signals for compounds **8a** and **8b** are δ 10.02 and 10.19, respectively, and are comparable with those of compounds **5a** and **5b**. The appropriate 9-NH signals for the carbolines **8a** and **8b** are shifted downfield by ~1 ppm in relation to those observed for their tetrahydro derivatives **5a** or **5b**. However, the observed downfield shift should be regarded as an effect of aromatization rather than as a result of the intramolecular hydrogen bond between 1′-H and 9-N.

The ^{1}H NMR data for compounds **10a** and **10b** are presented in Table 1. There are several characteristic chemical shifts and coupling constants which are diagnostic for a conformational determination of the investigated structures **10a** and **10b**.

It was found that aromatic and heteroaromatic substituents at position 1 of the 1,2,3,4-tetrahydro-β-carboline system occupy a roughly equatorial position in the twist-chair conformation,[9] and that the 1-H(axial) signal is located within the range δ 5.1–5.5.[2a] The 1-(2-indolyl) substituent in derivatives **5a** and **5b** is arranged in the same conformation since the 1-H signal is observed within the predicted range (δ 5.35). On the other hand, the same H(axial) signal for 1-(2-piperidyl)-1,2,3,4-tetrahydro-β-carboline appears at δ 3.99, and after cyclization to the 7-oxo derivative of compound **2** is shifted downfield by 0.68 ppm.[1,3] The 15b-H atom of compounds **10a** and **10b** resonates at δ 6.72 (Table 1), and the signal is shifted downfield by ~1.4 ppm in relation to the signal for compound **5a** or **5b**. The observed downfield shift can take place when the 15b-H atom occupies a roughly equatorial position on the twist–chair conformation (Fig. 1). In such an arrangement this proton may

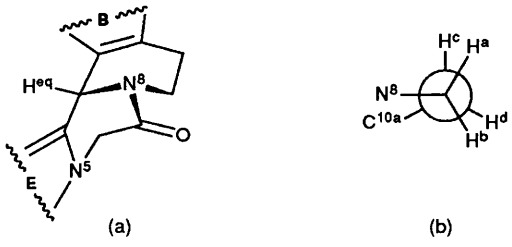


Fig. 1 (a) Observed conformation of the tetrahydropyrazinopyrido skeleton; (b) conformation of the C(9)–C(10) ethylene bridge calculated from the vicinal coupling constants

be additionally deshielded by the aromatic system A/B of the tetrahydro-β-carboline moiety. Other evidence for the existence of the observed conformation is the position of the carboline 1-H signal. In this particular conformation the 1-H atom (15b-H) in structures **10a** and **10b** should be placed under the plane of ring B, as the planes A/B and E/F are almost perpendicular; hence it should be shielded by the aromatic ring system A/B. In fact, this signal appears at δ 6.29 for compound **10a** and at δ 6.23 for compound **10b**, and is shifted upfield by 0.19 and 0.27 ppm, respectively, in relation to the appropriate 3′-H signal observed for compounds **5a** and **5b**. The 9-H(a) resonance signal appears at δ 5.16 for both compounds **10a** and **10b** (Table 1), and is shifted downfield by ~1.7 ppm from the position of the appropriate 3-H(equatorial) signals of derivatives **5a** and **5b**. Such a strong downfield shift is the result of a deshielding effect of the carbonyl group at position 7. Moreover, it may be concluded that the C(9)–H(a) bond and the 7-oxo group should be placed approximately in the same plane. The conformation of the ethylene bridge of ring C of compounds **10a** and **10b** can be determined on the grounds of vicinal coupling constants between particular protons. The dihedral angles (φ) between H(a),H(b)–C(9)–C(10)–H(c),H(d) (see Fig. 1) shown in Table 1 were estimated using the basic Karplus equation (1).[10]

$$J^{vic} = 4.5\cos 2\varphi - 0.5\cos \varphi + 4.22 \qquad (1)$$

The φ-values calculated from the vicinal coupling constants between b–c, b–d, c–a and c–b protons are reasonable and they unequivocally define the conformation shown in Fig. 1. However, the value of φ 68° is too small, and it should be pointed out that for small values of the coupling constants, $J^{vic} < 1.0$ Hz, the condition given by equation (2) is justified.

Table 1 ^{1}H NMR (500 MHz) data of compounds **10a** and **10b** in $CDCl_3$, and calculated dihedral angles (φ) between H(a),H(b)–C(9)–C(10)–H(c),H(d)

	10a			**10b**		
Proton[a]	δ	J(Hz)	Angle (φ/°)[b]	δ	J(Hz)	Angle (φ/°)[b]
1-H	7.70	d, 7.8		7.70	d, 7.8	
2-H	7.22	t, 7.7		7.22	t, 7.9	
3-H	*c*			7.28	t, 8.0	
4-H	*c*			7.31	d, 8.2	
6-H^{eq}	4.83	d, 17.5		4.85	d, 17.4	
6-H^{ax}	4.72	d, 17.5		4.73	d, 17.4	
9-H(a)	5.16	ddd, 12.5, 5.8(a–c), 0.8(a–d)	32(a–c) 68(a–d)	5.16	ddd, 12.5, 5.8(a–c), <0.8(a–d)	32(a–c) >68(a–d)
9-H(b)	3.27	ddd, 12.3, 8.0(b–c), 4.5 (b–d)	159(b–c) 41(b–d)	3.27	ddd, 12.4, 8.1(b–c), 4.8(b–d)	160(b–c) 39(b–d)
10-H(c)	3.18	ddd, 15.2, 5.8(c–a), 7.9(c–b)	32(c–a) 158(c–b)	3.16	ddd, 15.4, 5.8(c–a), 8.1(c–b)	32(c–a) 160(c–b)
10-H(d)	2.86	ddd, 15.4, 0.8(d–a), 4.5(d–b)	68(d–a) 41(d–b)	2.86	ddd, 15.4, <0.8(d–a), 4.8(d–b)	>68(d–a) 39(d–b)
11-H	7.51	d, 7.8		6.99	d, 2.4[d]	
12-H	7.13	t, 7.6				
13-H	7.19	t, 8.0		6.84	dd, 8.8, 2.4[d]	
14-H	*c*			7.20	d, 8.9	
15(N)–H	8.05	s		7.88	s,	
15b-H	6.72	s		6.72	s	
16-H	6.29	br s		6.23	br s	
12-OMe				3.85	s	

[a] Numbering scheme corresponds to that shown in structures **10a** and **b**. [b] Dihedral angles calculated from equation (1). [c] 7.33–7.27 (3 H, m). [d] ^4J(11-H,13-H) (lit.,[8] ^4J 2.9 Hz).

$$66° < \varphi < 90° \quad (2)$$

Conclusions.—Ring C of the investigated compounds **10a** and **10b** adopts a twist–chair conformation, while ring D exists in a flattened boat conformation with the C-6 and C-15b atoms deviating from the plane of atoms N-5, C-7, N-8 and C-15c. Moreover, rings C and D are *cis*-annelated for both derivatives **10a** and **10b**.

Experimental

Uncorrected m.p.s were determined on a Boetius apparatus. Microanalyses were performed on a Perkin-Elmer 240 elemental analyser in the Institute of Organic Chemistry, PAS, Warsaw. EI mass spectra at 70 eV were taken with a LKB 9005 spectrometer, and IR spectra were recorded in KBr pellets on a Specord 71 IR spectrometer. ^{1}H (500 MHz) NMR spectra were recorded on a Bruker 500 spectrometer for solutions in $CDCl_3$ with tetramethylsilane as internal standard. J-Values are given in Hz. Column chromatography was performed using Kieselgel 60 (Art. 7734, Merck). TLC was conducted on precoated Kieselgel 60F_{254} plates [Art. 5554, and Art. 5717 for preparative TLC (PLC), Merck] with $CHCl_3$–MeOH (9:1) as developing solvent. Spots on TLC were detected by their absorption under UV light. Tryptamine **4a** and 5-methoxytryptamine **4b** were commercial products (Aldrich), and syntheses of the other starting materials were described previously: indole-2-carbaldehyde[11] and indole-2-carbonyl chloride.[12]

Condensation of Tryptamines **4a** *and* **4b** *with Indole-2-carbaldehyde.*—A mixture of tryptamine (**4a** or **4b**) hydrochloride (15 mmol), indole-2-carbaldehyde (2.2 g, 15 mmol) and butan-1-ol (100 cm^3) was refluxed for 2 h, cooled and kept in a refrigerator for 12 h. The precipitate was filtered off and dissolved in hot 80% aq. ethanol. The hot solution was made alkaline with 25% aq. ammonia to pH 9–10, and left for crystallization to yield (i) 1-*indol*-2-*yl*-1,2,3,4-*tetrahydro*-β-*carboline* **5a** as crystals from 80% ethanol (3.5 g, 81%), m.p. 191–194 °C (Found: C, 79.2; H, 5.9; N, 14.7. $C_{19}H_{17}N_3$ requires C, 79.4; H, 6.0; N, 14.6%); R_f 0.25; m/z 287 (M^+, 68%), 286 (32), 258 (93), 257 (100), 171 (13) and 144 (11); δ_H 10.37 [1 H, br s, 1′(N)-H], 8.65 [1 H, br s, 2(N)-H], 7.69 [1 H, s, 9(N)–H], 7.57 (1 H, d, J 7.7, 4′-H), 7.52 (1 H, d, J 7.2, 5-H), 7.24–7.07 (6 H, m, 6-, 7-, 8-, 5′-, 6′-and 7′-H), 6.48 (1 H, br s, 3′-H), 5.34 (1 H, br s, 1-H), 3.33 (1 H, ddd, J 12.2, 5.2 and 4.2, 3-H^{eq}), 3.15 (1 H, ddd, J 12.2, 8.8 and 4.7, 3-H^{ax}), 2.90 (1 H, ddd, J 15.3, 4.7 and 1.2, 4-H^{eq}) and 2.78 (1 H, ddd, J 15.3, 8.7 and 4.4, 4-H^{ax}).

(ii) 1-*Indol*-2-*yl*-6-*methoxy*-1,2,3,4-*tetrahydro*-β-*carboline* **5b** as crystals from 80% ethanol (4 g, 84%), m.p. 114–116 °C (Found: C, 75.5; H, 6.0; N, 13.0. $C_{20}H_{19}N_3O$ requires C, 75.7; H, 6.0; N, 13.2%); R_f 0.24; m/z 317 (M^+, 31%), 273 (8), 186 (2), 159 (3) and 31 (100); δ_H 10.45 [1 H, br s, 1′(N)-H], 8.71 [1 H, br s, 2(N)-H], 7.60 [1 H, s, 9(N)-H], 7.57 (1 H, d, J 7.8, 4′-H), 7.24 (1 H, d, J 8.1, 7′-H), 7.15 (1 H, t, J 7.9, 6′-H), 7.09 (1 H, t, J 7.6, 5′-H), 7.07 (1 H, d, J 8.9, 8-H), 6.97 (1 H, d, J 2.4, 5-H), 6.80 (1 H, dd, J 8.8 and 2.5, 7-H), 6.49 (1 H, d, J 1.6, 3′-H), 5.35 (1 H, br s, 1-H), 3.85 (3 H, s, OMe), 3.35 (1 H, ddd, J 12.0, 4.0 and 4.0, 3-H^{eq}), 3.16 (1 H, ddd, J 12.3, 8.9 and 4.5, 3-H^{ax}), 2.87 (1 H, ddd, J 15.3, 4.5 and 1.2, 4-H^{eq}), 2.75 (1 H, ddd, J 15.2, 8.8 and 4.2, 4-H^{ax}).

Condensation of Tryptamines **4a** *and* **4b** *with Indole-2-carbonyl Chloride.*—A mixture of tryptamine (**4a** or **4b**) hydrochloride (4.5 mmol), indole-2-carbonyl chloride (0.9 g, 5 mmol), chloroform (10 cm^3) and 10% aq. sodium carbonate (20 cm^3) was shaken at room temperature for 2 h. The precipitate was filtered off, washed with water (20 cm^3), and crystallized to yield (i) N-[2-(3-*indolyl*)*ethyl*]*indole*-2-*carboxamide* **6a** as crystals from ethanol (0.8 g, 58%), m.p. 204–206 °C (Found: C, 75.0; H, 5.6; N, 13.9. $C_{19}H_{17}N_3O$ requires C, 75.2; H, 5.6; N, 13.8%); R_f 0.68; ν_{max}/cm^{-1} 1650 (CO); m/z 303 (M^+, 8%), 144 (29), 143 (100) and 130 (67).

(ii) N-[2-(5-*Methoxyindol*-3-*yl*)*ethyl*]*indole*-2-*carboxamide* **6b** as crystals from ethanol (0.9 g, 60%), m.p. 206–207 °C (Found: C, 71.9; H, 5.7; N, 12.4. $C_{20}H_{19}N_3O_2$ requires C, 72.0; H, 5.7; N, 12.6%); R_f 0.69; ν_{max}/cm^{-1} 1645 (CO); m/z 333 (M^+, 22%), 173 (100), 160 (71), 159 (34) and 144 (18).

Cyclization of Amides **6a** *and* **6b**.—The appropriate amide **6a**

or **6b** (1 mmol) was heated in polyphosphoric esters (PPE) (2 g) at 120 °C for 1 h. Then the reaction mixture was poured into water (30 cm^3) and made alkaline with 25% aq. ammonia to pH 10–11. The precipitate was filtered off, and the product was isolated by PLC with ethyl acetate–methanol (3:1) as solvent, followed by crystallization to afford (i) 1-*indol*-2-*yl*-3,4-*dihydro*-β-*carboline* **7a** as yellow crystals from benzene (0.1 g, 35%), m.p. 180–182 °C (Found: C, 80.0; H, 5.0; N, 14.9. $C_{19}H_{15}N_3$ requires C, 80.0; H, 5.3; N, 14.7%); R_f 0.38; *m/z* 285 (M^+, 25%), 284 (100), 257 (11), 255 (43) and 89 (20).

(ii) 1-*Indol*-2-*yl*-6-*methoxy*-3,4-*dihydro*-β-*carboline* **7b** as yellow crystals from benzene–heptane (3:1) (0.1 g, 32%), m.p. 196–199 °C (Found: C, 75.9; H, 5.2; N, 13.0. $C_{20}H_{17}N_3O$ requires C, 76.2; H, 5.4; N, 13.3%); R_f 0.38; *m/z* 315 (M^+, 100%), 300 (19), 287 (11) and 271 (11).

Oxidation of Tetrahydro-β-*carbolines* **5a** *and* **5b**.—To a solution of tetrahydrocarboline **5a** or **5b** (5 mmol) in benzene (200 cm^3) was added manganese dioxide (9 g, Merck), and the reaction mixture was refluxed for 45 min. Then the inorganic precipitate was filtered off, and the solvent was evaporated under reduced pressure. The mixture of products was separated by a column chromatography with chloroform–methanol (9:1) as eluent, and crystallized to yield dihydro derivative **7a** from benzene (0.9 g, 63%), m.p. 179–182 °C; R_f 0.38, or dihydro derivative **7b** from benzene–n-heptane (3:1) (0.84 g, 53%), m.p. 197–199 °C; R_f 0.38, and (i) 1-*indol*-2-*yl*-β-*carboline* **8a** as pale yellow crystals from ethyl acetate–n-hexane (3:1) (0.2 g, 14%), m.p. 218–220 °C (Found: C, 80.3; H, 4.3; N, 14.6. $C_{19}H_{13}N_3$ requires C, 80.5; H, 4.6; N, 14.8%); R_f 0.75; *m/z* 283 (M^+, 100%), 282 (54) and 141 (18); δ_H 10.02 [1 H, br s, 1′(N)-H], 8.72 [1 H, br s, 9(N)-H], 8.47 (1 H, d, *J* 5.2, 3-H), 8.14 (1 H, d, *J* 7.8, 5-H), 7.88 (1 H, d, *J* 5.2, 4-H), 7.72 (1 H, d, *J* 7.9, 4′-H), 7.62–7.56 (2 H, m, 7- and 8-H), 7.44 (1 H, d, *J* 8.0, 7′-H), 7.33 (1 H, t, *J* 7.9, 6-H), 7.25 (1 H, t, *J* 8.1, 6′-H), 7.16 (1 H, t, *J* 7.7, 5′-H) and 7.14 (1 H, s, 3′-H).

(ii) 1-*Indol*-2-*yl*-6-*methoxy*-β-*carboline* **8b** as pale yellow crystals from ethyl acetate–hexane (3:1) (0.42 g, 27%), m.p. 217–219 °C (Found: C, 76.6; H, 4.9; N, 13.1. $C_{20}H_{15}N_3O$ requires C, 76.7; H, 4.8; N, 13.4%); R_f 0.75; *m/z* 313 (M^+, 100%), 298 (72) and 270 (18); δ_H 10.19 [1 H, br s, 1′(N)-H], 8.61 [1 H, br s, 9(N)-H], 8.45 (1 H, d, *J* 5.2, 3-H), 7.83 (1 H, d, *J* 5.2, 4-H), 7.72 (1 H, d, *J* 7.9, 4′-H), 7.55 (1 H, d, *J* 2.4, 5-H), 7.50 (1 H, d, *J* 8.8, 8-H), 7.43 (1 H, d, *J* 7.9, 7′-H), 7.25 (1 H, t, *J* 8.0, 6′-H), 7.23 (1 H, dd, *J* 8.8 and 2.5, 7-H), 7.15 (1 H, t, *J* 7.9, 5′-H), 7.14 (1 H, s, 3′-H) and 3.94 (3 H, s, OMe).

Condensation of Tetrahydro-β-*carbolines* **5a** *and* **5b** *with Bromoacetyl Chloride*.—To a solution of tetrahydrocarboline **5a** or **5b** (2 mmol) in acetone (10 cm^3) was added sodium carbonate (0.5 g); then a solution of bromoacetyl chloride (0.95 g, 6 mmol) in acetone (7 cm^3) was added dropwise. The reaction mixture was stirred at room temperature for 10 min, the insoluble material was filtered off, and the solvent was evaporated off to yield (i) 2-*bromoacetyl*-1-*indol*-2-*yl*-1,2,3,4-*tetrahydro*-β-*carboline* **9a** as crystals from ethanol (0.57 g, 70%), m.p. 198–199 °C (Found: C, 61.8; H, 4.4; N, 10.3. $C_{21}H_{18}BrN_3O$ requires C, 61.8; H, 4.5; N, 10.3%); ν_{max}/cm^{-1} 1645 (CO); *m/z* 409 [$M^+(^{81}Br)$, 14%], 407 [$M^+(^{79}Br)$, 14], 328 [$(M - HBr)^+$, 100] and 287 [$(M - COCH_2Br)^+$, 20].

(ii) 2-*Bromoacetyl*-1-*indol*-2-*yl*-6-*methoxy*-1,2,3,4-*tetrahydro*-β-*carboline* **9b** as crystals from ethanol–acetone (4:1) (0.7 g, 80%), m.p. 224–226 °C (Found: C, 60.2; H, 4.5; N, 9.4. $C_{22}H_{20}BrN_3O_2$ requires C, 60.3; H, 4.6; N, 9.6%); ν_{max}/cm^{-1} 1630 (CO); *m/z* 439 [$M^+(^{81}Br)$, 14%], 437 [$M^+(^{79}Br)$, 13], 358 [$(M - HBr)^+$, 100] and 317 [$(M - COCH_2Br)^+$, 26].

Cyclization of Derivatives **9a** *and* **9b**.—To a suspension of sodium hydride (0.1 g; 50% suspension in mineral oil) in THF (10 cm^3) under N_2 at 0–3 °C was added a solution of compound **9a** or **9b** (1 mmol) in THF (10 cm^3) dropwise. The reaction mixture was stirred for 30 min. Then water (10 cm^3) was added, and the mixture was extracted with chloroform (3 × 15 cm^3). The organic layers were combined, dried over anhydrous sodium sulphate, and evaporated under reduced pressure. Purification of the residue by column chromatography with ethyl acetate afforded (i) 9,10,15,15b-*tetrahydroindolo*[1′,2′:4,3]*pyrazino*[2,1-a]*carbolin*-7(6H)-*one* **10a** as crystals from 1,4-dioxane (0.3 g, 92%), m.p. 212–215 °C (Found: C, 76.7; H, 5.1; N, 12.5. $C_{21}H_{17}N_3O$ requires C, 77.0; H, 5.2; N, 12.8%); ν_{max}/cm^{-1} 1655 (CO); *m/z* (M^+, 100%), 326 (59), 299 (11), 298 (27) and 269 (17).

(ii) 12-*Methoxy*-9,10,15,15b-*tetrahydroindolo*[1′,2′:4,3]*pyrazino*[2,1-a]*carbolin*-7(6H)-*one* **10b** as crystals from acetone (0.25 g, 70%), m.p. 231–233 °C (Found: C, 73.7; H, 5.3; N, 11.4. $C_{22}H_{19}N_3O_2$ requires C, 73.9; H, 5.4; N, 11.8%); ν_{max}/cm^{-1} 1655 (CO); *m/z* 357 (M^+, 100%), 356 (51), 342 (10), 329 (6), 328 (14) and 314 (8).

Acknowledgements

We thank Dr. J. Boksa for his helpful discussion of the mass spectra. This work was supported in part by the Research Programme CPBR 3.8.4.

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Paper 1/00050K
Received 3rd *January* 1991
Accepted 28th *March* 1991