CYCLOADDITION REACTIONS OF FURO[2,3-*b*]PYRROLES

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Dedicated to the memory of Dr Miroslav Protiva, an excellent Czech chemist.

Reactions of furo[2,3-*b*]pyrroles with dimethyl butynedioate and ethyl propynoate were investigated. The reaction course is influenced by the substituents on the fused system. Products of [4+2]cycloaddition to the furan ring leading to indole derivatives have been observed. In the case of the reaction of methyl 6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**1a**) with dimethyl butynedioate, products of [4+2]cycloaddition to the furan ring as well as of Michael addition to the pyrrole ring leading to *N*-substituted indole derivative 3 have been observed.
Key words: Furo[2,3-*b*]pyrroles; Indoles; Diels–Alder reactions; [4+2]Cycloadditions; Alkynes.

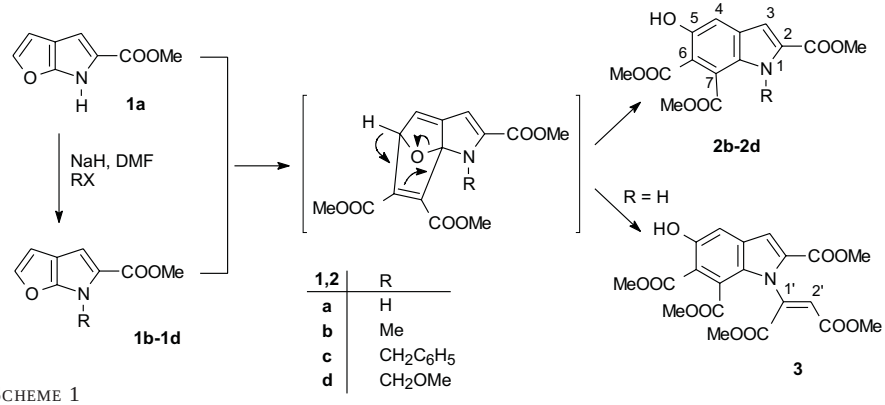
Furo[2,3-*b*]pyrroles belong to A,B-diheteropentalenes which possess different degrees of aromaticity reflected in their chemical behaviour such as the ability to undergo electrophilic substitution reactions. A,B-Diheteropentalenes rank among electron-rich heterocycles, but a quantitative criterion of their aromaticity is not easy to determine[1]. A wide range of potential criteria available for this purpose has been surveyed[1,2]. Most of the available criteria point to an order of decreasing aromaticity of 1,4-diheteropentalene > 1,6-diheteropentalene which is influenced by the heteroatom in the order S > Se ≥ N > O. There is little evidence for an interaction between two rings of the ring system. Substituents attached to the A,B-diheteropentalene structures can strongly influence the aromaticity. Until recently, only 1,6-diheteropentalenes containing S or Se heteroatoms have been studied[1,2] and a few derivatives of the furo[2,3-*b*]pyrrole system were known[3,4]. The parent furo[2,3-*b*]pyrrole has not been reported and synthesis and Diels–Alder reactions of some highly labile furo[2,3-*c*]pyrroles and their benzo[4,5] derivatives have been published just recently[5].

Previously we were interested in syntheses and studies of the reactions of furo[3,2-*b*]pyrroles and their benzo derivatives[6–13]. We also investigated their addition and cycloaddition reactions[7,8]. We described[7] that with furo[3,2-*b*]pyrroles bearing no substituent in position 2, the cycloaddition reaction proceeds on the furan ring giving substituted indoles.

As a continuation of our previous studies, we tried to get a deeper insight into the reactivity of furo[2,3-*b*]pyrroles to compare them with the [3,2-*b*] system. Herein we report the preparation of furo[2,3-*b*]pyrroles and their Diels–Alder reaction.

RESULTS AND DISCUSSION

In our previous paper[4], we described the preparation of **1b** and **1c** from **1a** under phase transfer catalysis conditions. Compounds **1b**–**1d** were obtained more effectively by direct substitution of the *in situ* prepared sodium salt of **1a** in DMF (Scheme 1). Our present study concerns reactions of



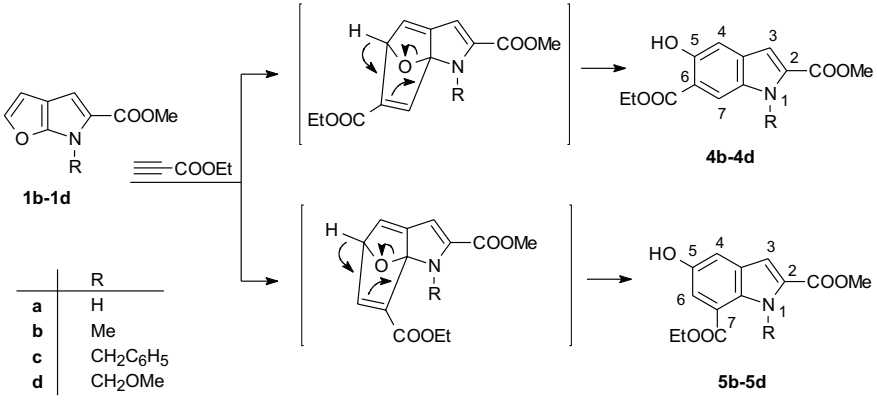
SCHEME 1

methyl 6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**1a**) and its 6-methyl (**1b**), 6-benzyl (**1c**) and 6-(methoxymethyl) (**1d**) derivatives with dimethyl butynedioate (Scheme 1) or ethyl propynoate (Scheme 2).

The reactions of methyl 6-substituted furo[2,3-*b*]pyrrole-5-carboxylates **1b**–**1d** with dimethyl butynedioate in acetonitrile gave only cycloaddition products **2b**–**2d** in good yields. The formed undetected cycloadducts (Scheme 1) are obviously labile, and by opening the furan ring are transformed into the corresponding indole derivatives. The reaction of methyl 6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**1a**) under the same conditions gave **2a**

and a minor addition product **3**. These products were isolated by fractional crystallization from methanol. Since our attempts to get **3** from **2a** under the same conditions were not successful, we can conclude that the Michael addition to **1a** is the first step in formation of **3**.

For the study of the reaction with unsymmetric dienophiles, we used ethyl propynoate (Scheme 2). Theoretically, this reaction can afford two regioisomeric 1 : 1 adducts which, on subsequent rearrangement, can give 6- and 7-ethoxycarbonylindoles **4a**–**4d** and **5a**–**5d**, respectively. Two products were observed by TLC ($CHCl_3$) and separated by column chromatography. The ratio of products **5** : **4** was 93 : 7 for R = H, 85 : 15 for R = methyl, 95 : 5 for R = benzyl, and 95 : 5 for R = methoxymethyl.



SCHEME 2

Earlier we described[7] that the reaction of 4-acetylfuro[3,2-*b*]pyrrole with ethyl propynoate was regiospecific, giving only one product formed analogously as compounds **5a**–**5d**. We demonstrated that formation of the tricyclic intermediate could not be concerted and that furo[3,2-*b*]pyrroles having ethoxycarbonyl group attached at C-5 did not react with ethyl propynoate. Taking these findings into account, it was interesting to study rates of the reaction of compounds **1a**–**1d** with ethyl propynoate in various solvents. We carried this reaction in excess of ethyl propynoate (reaction time 12 h), acetonitrile (reaction time 45 h), and benzene (reaction time 100 h). The fact, that the reaction rate increases with increasing solvent polarity suggests that the formation of the undetected cycloaddition intermediates is not a concerned process and probably proceeds in two separate steps. The first step starts by an attack of more electrophilic center of the dienophile at the more reactive C-2 position of the furo[2,3-*b*]pyrrole sys-

tem. This is in accord with net atomic charges[4] calculated using the AMI method (for C-2 = –0.104 and C-6a = +0.04). In the second step, the formed carbanion attacks the C-6a carbon atom. The formed cycloadduct is then transformed into the indole derivative **5a**–**5d**. The formation of compounds **4a**–**4d** and **5a**–**5d** demonstrated that furo[2,3-*b*]pyrroles **1a**–**1d** behave differently than their furo[3,2-*b*]pyrrole isomers, which do not react with ethyl propynoate at all[7].

The structure of the products was confirmed by ^{1}H and ^{13}C NMR spectroscopy. The ^{1}H and ^{13}C NMR data are given in the Experimental. The structure of addition product **3** was proved by the signal of olefinic proton H-2′. The positions of substituents on the benzene ring in **5a**–**5d** were unequivocally confirmed by the coupling constant $J(4,6)$ = 2.5 Hz, characteristic of coupling of *meta*-proton. The O–H signals in these compounds appear at 4.5–5.5 ppm. The large δ value of the O–H signals (10.5 ppm) in **4a**–**4d** suggests an intramolecular hydrogen bond between the OH and the ethoxycarbonyl group at C-6. Assignment of signals in the ^{13}C NMR spectra was done on the basis of characteristic splitting pattern caused by long-range coupling and was confirmed by selective heteronuclear decoupling. Quaternary carbon atoms were assigned by selective INEPT technique analogously as described in our paper[14].

In summary, we have synthesized new methyl 6-(methoxymethyl)furo-[2,3-*b*]pyrrole (**1d**). Diels–Alder reaction of methyl furo[2,3-*b*]pyrrole-5-carboxylates **1a**–**1d** with dimethyl butynedioate or ethyl propynoate gave substituted indoles which are not accessible by other routes. The reaction with ethyl propynoate afforded two regioisomeric adducts which rearranged into minor methyl 6- and major 7-ethoxycarbonyl-5-hydroxyindole-2-carboxylates **4a**–**4d** and **5a**–**5d**, respectively. The ratio of the products **4** : **5** is not dependent on the substituent attached in position 6 of the furo[2,3-*b*]-pyrroles **1a**–**1d**. Comparing the course of the Diels–Alder reactions of furo-[2,3-*b*]pyrroles with their [3,2-*b*] isomers, we can conclude that the [2,3-*b*] system is more active diene than its [3,2-*b*] isomer.

EXPERIMENTAL

Compound **1a** was prepared according to ref.[4]. Melting points were determined on a Kofler hot plate apparatus and are uncorrected. UV spectra were measured on an M-40 (Zeiss, Jena) spectrophotometer in methanol (λ_{max} (log ε); λ_{max} in nm, ε in m^2 mol^{-1}). IR spectra were taken on a FTIR PU 9802/25 (Philips) spectrometer using KBr technique (0.5 mg in 300 mg KBr, ν in cm^{-1}). ^{1}H NMR (80 MHz) spectra were recorded on a Tesla BS 587 spectrometer and ^{13}C NMR (75.43 MHz) spectra on a Varian VXR-300 in $CDCl_3$. Tetramethylsilane was used as an internal standard; chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz.

Methyl 6-(Methoxymethyl)furo[2,3-*b*]pyrrole-5-carboxylate (**1d**)

A solution of methyl furo[2,3-*b*]pyrrole-5-carboxylate (**1a**) (3.3 g, 20 mmol) in *N*,*N*-dimethylformamide (40 ml) was added slowly to a mixture of sodium hydride (60% in mineral oil, 0.96 g, 24 mmol) in *N*,*N*-dimethylformamide (20 ml). The mixture was stirred at 20 °C till the evolution of hydrogen ceased, then chloromethyl methyl ether (1.8 ml, 1.9 g, 24 mmol) was added and the stirring at room temperature continued for 1 h. The solution was poured into ice water (150 ml), the precipitate was filtered off and crystallized. Yield: 3.0 g (72%), m.p. 65–66 °C (hexane). For $C_{10}H_{11}NO_4$ (209.2) calculated: 57.41% C, 5.30% H, 6.70% N; found: 57.28% C, 5.34% H, 6.76% N. ^{1}H NMR: 3.34 s, 3 H (OCH_3); 3.84 s, 3 H (CO_2CH_3); 5.80 s, 2 H (CH_2); 6.53 d, 1 H, *J*(2,3) = 2.2 (H-3); 6.96 s, 1 H (H-4); 7.30 d, 1 H, *J*(2,3) = 2.2 (H-2). IR: 1 697 (C=O). UV: 291 (4.24).

Reaction of Methyl Furo[2,3-*b*]pyrrole-5-carboxylates (**1a**–**1d**) with Dimethyl Butynedioate. General Procedure

A mixture of methyl furo[2,3-*b*]pyrrole-5-carboxylate **1a**–**1d** (4 mmol) and dimethyl butynedioate (1.15 g, 8 mmol) in acetonitrile (2 ml) was refluxed for 12 h. Evaporation of the solvent and excess dimethyl butynedioate *in vacuo* yielded a crude product as a dark brown oil. Methanol was added to this material and the mixture was boiled and then allowed to stand overnight at 5 °C. The product was collected by filtration, washed with methanol, and dried to provide pure trimethyl 5-hydroxy-1*H*-indole-2,6,7-tricarboxylates **2a**–**2d** as yellow crystals.

Trimethyl 5-hydroxy-1H-indole-2,6,7-tricarboxylate (**2a**). Yield: 0.53 g (43%), m.p. 164–165 °C (methanol). For $C_{14}H_{13}NO_7$ (307.3) calculated: 54.73% C, 4.26% H, 4.56% N; found: 54.62% C, 4.22% H, 4.58% N. ^{1}H NMR: 3.95 s, 6 H (2 × CO_2CH_3); 3.98 s, 3 H (CO_2CH_3); 7.09 d, 1 H, *J*(1,3) = 2.2 (H-3); 7.37 s, 1 H (H-4); 8.82 bs, 1 H (NH); 9.40 bs, 1 H (OH). IR: 3 466 (OH), 3 368 (NH), 1 736 (C=O), 1 720 (C=O), 1 693 (C=O). UV: 214 (4.34), 312 (4.13), 256 (3.20).

Trimethyl 1-[(1,2-bis(methoxycarbonyl)vinyl)]-5-hydroxyindole-2,6,7-tricarboxylate (**3**). This compound was isolated by concentrating the filtrate after the isolation of **2a** to approximately half of its volume and standing overnight in a refrigerator. The product was collected by filtration and recrystallization from methanol gave pure **3** as colorless crystals. Yield: 0.36 g (20%), m.p. 122–124 °C (methanol). For $C_{20}H_{19}NO_{11}$ (449.4) calculated: 53.46% C, 4.26% H, 3.12% N; found: 53.34% C, 4.18% H, 3.22 % N. ^{1}H NMR: 3.66 s, 3 H (CO_2CH_3); 3.93 s, 3 H (CO_2CH_3); 3.97 s, 3 H (CO_2CH_3); 3.98 s, 3 H (CO_2CH_3); 4.02 s, 3 H (CO_2CH_3); 5.15 s, 1 H ($CHCO_2$); 7.23 s, 1 H (H-3); 7.72 s, 1 H (H-4); 10.30 s, 1 H (OH). IR: 3 478 (OH), 1 751 (C=O), 1 724 (C=O), 1 643 (C=O). UV: 216 (4.18), 310 (3.86).

Trimethyl 5-hydroxy-1-methylindole-2,6,7-tricarboxylate (**2b**). Yield: 67%, m.p. 192–194 °C (ethanol). For $C_{15}H_{15}NO_7$ (321.3) calculated: 56.08% C, 4.71% H, 4.36% N; found: 55.98% C, 4.59% H, 4.46% N. ^{1}H NMR: 3.91 s, 3 H (CH_3); 3.97 s, 3 H (CH_3); 3.99 s, 6 H (2 × CH_3); 7.12 s, 1 H (H-3); 7.26 s, 1 H (H-4); 10.37 s, 1 H (OH). ^{13}C NMR: 32.13 (N**C**H_3); 52.10 (CO_2**C**H_3); 52.67 (CO_2**C**H_3); 53.13 (CO_2**C**H_3); 108.50; 108.93 (C-3 or C-4); 109.27 (C-3 or C-4); 120.07; 130.06; 132.85; 133.62; 153.75 (C-5); 161.87 (**C**O_2CH_3); 168.54 (**C**O_2CH_3); 169.65 (**C**O_2CH_3). IR: 3 505 (OH), 1 734 (C=O), 1 709 (C=O), 1 693 (C=O). UV: 238 (saturated solution).

Trimethyl 1-benzyl-5-hydroxyindole-2,6,7-tricarboxylate (**2c**). Yield: 95%, m.p. 178–180 °C (methanol). For $C_{21}H_{19}NO_7$ (397.4) calculated: 63.47% C, 4.82% H, 3.52% N; found: 63.25% C, 4.74% H, 3.58% N. ^{1}H NMR: 3.43 s, 3 H (CO_2CH_3); 3.83 s, 3 H (CO_2CH_3); 3.89 s, 3 H

(CO_2CH_3); 5.85 s, 2 H (CH_2); 6.75–7.37 m, 7 H (H-arom); 10.36 s, 1 H (OH). IR: 3 426 (OH), 1 724 (C=O), 1 674 (C=O). UV: 221 (4.16), 303 (3.95).

Trimethyl 5-hydroxy-1-(methoxymethyl)indole-2,6,7-tricarboxylate (**2d**). Yield: 85%, m.p. 134–136 °C (methanol). For $C_{16}H_{17}NO_8$ (351.3) calculated: 54.70% C, 4.88% H, 3.99% N; found: 54.59% C, 4.82% H, 4.08% N. ^{1}H NMR: 3.16 s, 3 H (OCH_3); 3.93 s, 3 H (CO_2CH_3); 3.94 s, 3 H (CO_2CH_3); 3.96 s, 3 H (CO_2CH_3); 5.90 s, 2 H (CH_2); 7.21 s, 1 H (H-3); 7.30 s, 1 H (H-4); 10.72 s, 1 H (OH). ^{13}C NMR: 52.28 ($CO_2\mathbf{C}H_3$); 52.98 ($CO_2\mathbf{C}H_3$); 53.12 ($CO_2\mathbf{C}H_3$); 55.09 (OCH_3); 75.06 (CH_2); 109.08 (C-4); 109.98; 111.07 (C-3); 120.94; 129.21; 133.54; 133.73; 154.18 (C-5); 161.67 ($\mathbf{C}O_2CH_3$); 167.81 ($\mathbf{C}O_2CH_3$); 169.87 ($\mathbf{C}O_2CH_3$). IR: 3 522 (OH), 2 957, 1 720 (C=O). UV: 232 (4.35), 306 (4.31).

Reaction of Methyl Furo[2,3-*b*]pyrrole-5-carboxylates (**1a**–**1d**) with Ethyl Propynoate. General Procedure

A mixture of methyl furo[2,3-*b*]pyrrole-5-carboxylate **1a**–**1d** (4 mmol) and ethyl propynoate (0.7 ml, 0.8 g, 8 mmol) was stirred at 90 °C for 36 h. Evaporation of the excess ethyl propynoate *in vacuo* yielded crude product, which was chromatographed on silica gel (80 g). Elution with hexane–ethyl acetate (8 : 2) gave two products, compounds **4** and **5**. Minor products **4a**–**4d** had in the used system generally lower elution times than major products **5a**–**5d**.

Methyl 6-ethoxycarbonyl-5-hydroxy-1H-indole-2-carboxylate (**4a**). Yield: 0.04 g (4%), m.p. 133–135 °C (hexane–ethyl acetate, 9 : 1). For $C_{13}H_{13}NO_5$ (263.2) calculated: 59.31% C, 4.98% H, 5.32% N; found: 59.42% C, 5.06% H, 5.28% N. ^{1}H NMR: 1.45 t, 3 H (CH_3); 4.07 s, 3 H (CO_2CH_3); 4.45 q, 2 H (CH_2); 7.24 s, 1 H (H-3); 7.60 s, 1 H (H-4); 7.85 s, 1 H (H-7); 10.06 bs, 10.24 bs, 2 H (OH, NH). IR: 3 460 (OH), 2 982, 1 710 (C=O), 1 693 (C=O). UV: 215 (4.21).

Methyl 7-ethoxycarbonyl-5-hydroxy-1H-indole-2-carboxylate (**5a**). Yield: 0.58 g (55%) m.p. 160–163 °C (hexane–ethyl acetate, 8 : 2). For $C_{13}H_{13}NO_5$ (263.2) calculated: 59.31% C, 4.98% H, 5.32% N; found: 59.25% C, 4.79% H, 5.41% N. ^{1}H NMR: 1.44 t, 3 H (CH_3); 3.94 s, 3 H (CO_2CH_3); 4.44 q, 2 H (CH_2); 4.5 bs, 1 H (OH); 7.08 s, 1 H (H-3); 7.31 d, 1 H, *J*(4,6) = 2.4 (H-6); 7.60 d, 1 H, *J*(4,6) = 2.4 (H-4); 9.95 bs, 1 H (NH). ^{13}C NMR: 14.08 ($CH_2\mathbf{C}H_3$); 51.93 ($CO_2\mathbf{C}H_3$); 61.11 ($\mathbf{C}H_2$); 107.79 (C-3); 112.24 (C-4); 113.70 (C-7); 117.66 (C-6); 128.05; 129.03; 131.26; 150.34 (C-5); 162.05 ($\mathbf{C}O_2CH_3$); 166.44 ($\mathbf{C}O_2C_2H_5$). IR: 3 460 (OH), 1 693 (C=O). UV: 256 (3.20).

Methyl 6-ethoxycarbonyl-5-hydroxy-1-methylindole-2-carboxylate (**4b**). Yield: 11%, m.p. 110–113 °C (hexane–ethyl acetate, 9 : 1). For $C_{14}H_{15}NO_5$ (277.3) calculated: 60.64% C, 5.45% H, 5.05% N; found: 60.52% C, 5.31% H, 4.96% N. ^{1}H NMR: 1.44 t, 3 H (CH_3); 3.88 s, 3 H (CH_3); 4.06 s, 3 H (CH_3); 4.44 q, 2 H (CH_2); 7.53 s, 1 H (H-3); 8.28 s, 1 H (H-4); 8.67 s, 1 H (H-7); 10.4 s, 1 H (OH). IR: 3 385 (OH), 2 973, 1 721 (C=O). UV: 219 (4.32).

Methyl 7-ethoxycarbonyl-5-hydroxy-1-methylindole-2-carboxylate (**5b**). Yield: 60%, m.p. 131–133 °C (hexane–ethyl acetate, 8 : 2). For $C_{14}H_{15}NO_5$ (277.3) calculated: 60.64% C, 5.45% H, 5.05% N; found: 60.85% C, 5.52% H, 5.16% N. ^{1}H NMR: 1.40 t, 3 H (CH_3); 3.90 s, 3 H (CH_3); 3.99 s, 3 H (CH_3); 4.43 q, 2 H (CH_2); 5.8 br, 1 H (OH); 7.17 s, 1 H (H-3); 7.19 d, *J*(4,6) = 2.5 (H-6); 7.36 d, *J*(4,6) = 2.5 (H-4). ^{13}C NMR: 14.22 ($CH_2\mathbf{C}H_3$); 35.45 (NCH_3); 51.88 ($CO_2\mathbf{C}H_3$); 61.75 ($\mathbf{C}H_2CH_3$); 110.53 (C-3); 110.53 (C-4); 118.17 (C-7); 118.37 (C-6); 128.78; 130.78; 132.87; 149.21 (C-5); 162.38 ($\mathbf{C}O_2CH_2CH_3$); 167.52 ($\mathbf{C}O_2CH_2CH_3$). IR: 3 428 (OH), 2 952, 1 698 (C=O). UV: 258 (3.55).

Methyl 1-benzyl-6-ethoxycarbonyl-5-hydroxyindole-2-carboxylate (**4c**). Yield: 2.3%, m.p. 114–116 °C (ethanol). For $C_{20}H_{19}NO_5$ (353.4) calculated: 67.98% C, 5.42% H, 3.96% N; found: 68.12% C, 5.34% H, 3.72% N. ^{1}H NMR: 1.39 t, 3 H (CH_3); 3.87 s, 3 H (CO_2CH_3); 4.41 q, 2 H (CH_2); 5.81 s, 2 H (CH_2Ph); 7.01–7.29 m, 7 H (H-3, H-4, H-arom); 7.95 s, 1 H (H-7); 10.44 s, 1 H (OH). IR: 3 262 (OH), 2 961, 1 704 (C=O). UV: 214 (4.25).

Methyl 1-benzyl-7-ethoxycarbonyl-5-hydroxyindole-2-carboxylate (**5c**). Yield: 62%, m.p. 139–141 °C (hexane–ethyl acetate, 8 : 2). For $C_{20}H_{19}NO_5$ (353.4) calculated: 67.98% C, 5.42% H, 3.96% N; found: 67.63% C, 5.29% H, 3.82% N. ^{1}H NMR: 1.15 t, 3 H (CH_3); 3.86 s, 3 H (CO_2CH_3); 4.15 q, 2 H (CH_2); 5.22 br, 1 H (OH); 6.11 s, 2 H (CH_2); 6.68–7.15 m, 5 H (H-arom); 7.19 d, 1 H, *J*(4,6) = 2.5 (H-6); 7.21 d, 1 H, *J*(4,6) = 2.5 (H-4); 7.32 s, 1 H (H-3). ^{13}C NMR: 13.91 ($CH_2\mathbf{C}H_3$); 49.17 ($\mathbf{C}H_2Ph$); 51.92 ($CO_2\mathbf{C}H_3$); 61.64 ($\mathbf{C}H_2CH_3$); 110.34 (C-3); 111.53 (C-4); 118.19 (C-6); 119.53 (C-7); 125.87 (C-3′); 125.87 (C-5′); 126.76 (C-4′); 128.33 (C-2′); 128.33 (C-6′); 129.3; 130.52; 131.43; 138.66 (C-1′); 149.07 (C-5); 162.21 ($\mathbf{C}O_2CH_2CH_3$); 167.04 ($\mathbf{C}O_2C_2H_5$). IR: 3 443 (OH), 1 711, 1 687 (C=O). UV: 243 (3.84).

Methyl 6-ethoxycarbonyl-5-hydroxy-1-(methoxymethyl)indole-2-carboxylate (**4d**). Yield: 3.5%, m.p. 118–120 °C (hexane–ethyl acetate, 9 : 1). For $C_{15}H_{17}NO_6$ (307.3) calculated: 58.62% C, 5.58% H, 4.56% N; found: 58.31% C, 5.72% H, 4.39% N. ^{1}H NMR: 1.46 t, 3 H (CH_3); 3.29 s, 3 H (OCH_3); 3.93 s, 3 H (CO_2CH_3); 4.46 q, 2 H (CH_2); 5.96 s, 2 H (NCH_2); 7.19 s, 2 H (H-3, H-4); 8.10 s, 1 H (H-7); 10.53 s, 1 H (OH). ^{13}C NMR: 14.34 ($CH_2\mathbf{C}H_3$); 52.10 ($CO_2\mathbf{C}H_3$); 55.99 (OCH_3); 61.68 ($\mathbf{C}H_2CH_3$); 74.68 (NCH_2); 107.54 (C-3); 110.79 (C-4); 112.00 (C-7); 112.98 (C-6); 131.81; 132.07; 133.53; 155.25 (C-5); 161.94 ($\mathbf{C}O_2CH_3$); 170.35 ($\mathbf{C}O_2C_2H_5$). IR: 3 360 (OH), 2 937, 1 709 (C=O). UV: 214 (4.25).

Methyl 7-ethoxycarbonyl-5-hydroxy-1-(methoxymethyl)indole-2-carboxylate (**5d**). Yield: 67%, m.p. 119–122 °C (ethanol–water). For $C_{15}H_{17}NO_6$ (307.3) calculated: 58.63% C, 5.58% H, 4.56% N; found: 58.84% C, 5.41% H, 4.62% N. ^{1}H NMR: 1.41 t, 3 H (CH_3); 2.93 s, 3 H (OCH_3); 3.91 s, 3 H (CO_2CH_3); 4.43 q, 2 H (CH_2); 5.25 bs, 1 H (OH); 6.12 s, 2 H (CH_2); 7.20 d, 1 H, *J*(4,6) = 2.6 (H-4 or H-6); 7.26 s, 1 H (H-3); 7.32 d, 1 H, *J*(4,6) = 2.6 (H-4 or H-6). ^{13}C NMR: 14.23 ($CH_2\mathbf{C}H_3$); 52.04 ($CO_2\mathbf{C}H_3$); 55.34 (OCH_3); 61.79 ($\mathbf{C}H_2CH_3$); 76.63 (NCH_2); 110.33 (C-3); 112.29 (C-4); 118.21 (C-6); 119.99 (C-7); 129.47; 130.54; 149.79 (C-5); 162.28 ($\mathbf{C}O_2CH_3$); 167.37 ($\mathbf{C}O_2C_2H_5$). IR: 3 231 (OH), 2 917, 1 706, 1 682 (C=O). UV: 262 (3.91).

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