The Reaction of 2-Indolecarbohydrazones With Ethoxycarbonyl Chloride. New Synthesis of 2,3-Dihydro-2-oxo-1,3,4-oxadiazoles and 1,2,3,4-Tetrahydro-4-oxo-5*H*-pyridazino[4,5-*b*]indoles

A. Monge*, J. A. Palop and P. Tabar

Facultad de Farmacia, Departamento de Química Orgánica y Farmaceutica, Universidad de Navarra, Pamplona, Spain

E. Fernández-Alvarez

Instituto de Química Orgánica del C.S.I.C., Juan de la Cierva, No. 3 Madrid 6, Spain

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The synthesis of 2,3-dihydro-2-oxo-1,3,4-oxadiazole (**4**) and 5*H*-pyridazino[4,5-*b*]indole (**7**), are described. Compounds **4** were obtained by reduction of *O*-ethoxycarbonylcarbohydrazones **3** with sodium borohydride. Compounds **7** were obtained by cyclization of compounds with ethanol/hydrochloric acid and removing the ethoxycarbonyl group with hydrazine. Compounds **3** were obtained by reaction of 2-indolecarbohydrazones **1** with ethoxycarbonyl chloride.

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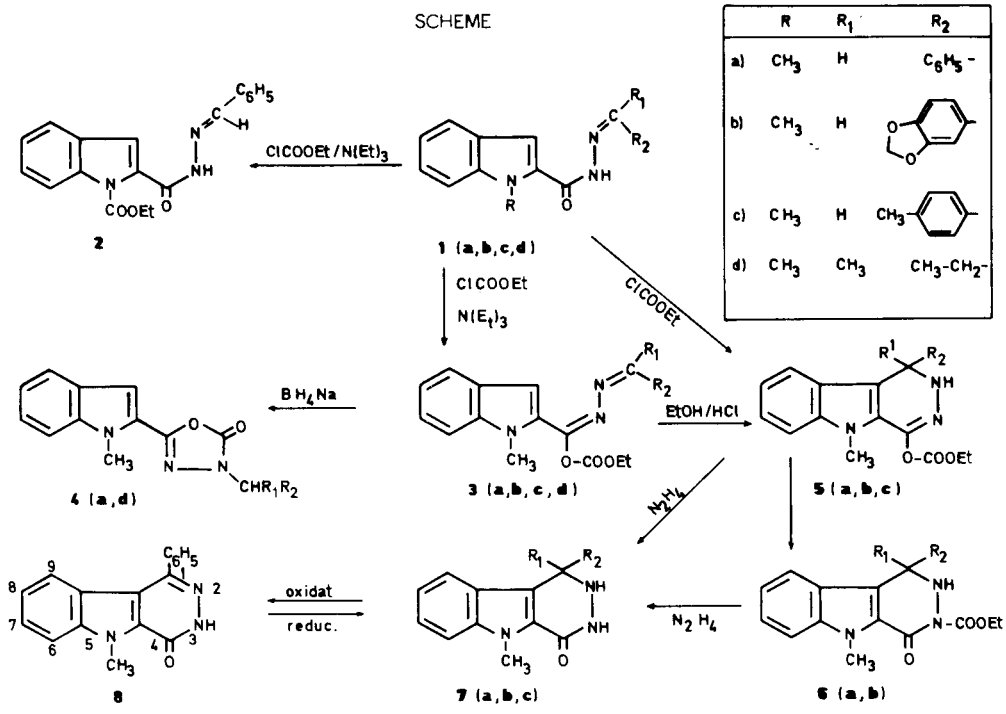
As a part of our work on the preparation and study of the biological properties of 5*H*-pyridazino[4,5-*b*]indole derivatives, particularly as antihypertensive agents [1-3], we have reported in previous papers [3,4] the reactions of 2-indolecarbohydrazones and 3-indolecarbohydrazones with acyl halides as new methods for the synthesis of 4-oxo- and 1-oxo derivatives of 5*H*-pyridazino[4,5-*b*]indole. In fact, treating 2-indolecarbohydrazones with acyl (acetyl, benzoyl) halides in the presence of triethylamine, cyclization and acylation reactions take place to give 2-acyl-1,2,3,4-tetrahydro-4-oxo-5*H*-pyridazino[4,5-*b*]indoles; in a similar way, 3-indolecarbohydrazones yield 3-acyl-1,2,3,4-tetrahydro-1-oxo-5*H*-pyridazino[4,5-*b*]indoles [3,4].

In this paper we have studied the reactions of 2-indolecarbohydrazones with ethoxycarbonyl chloride in the presence or absence of triethylamine, which has provided new methods for the preparation of 2,3-dihydro-2-oxo-1,3,4-oxadiazole and 5*H*-pyridazino[4,5-*b*]indole derivatives (see Scheme).

The reactions of 2-indolecarbohydrazones **1** with ethoxycarbonyl chloride and with other acyl (acetyl, benzoyl) chlorides, take place in different ways, probably as a con-

SCHEME



sequence of the poor reactivity of the ethoxycarbonyl chloride. So, compound **1e** reacts to give the *N*-ethoxycarbonyl derivative **2**, while the reaction with acetyl (or benzoyl) chloride yields 2,5-diacetyl-(or benzoyl)-1,2,3,4-tetrahydro-4-oxo-5*H*-pyridazino[4,5-*b*]indole [4]. Probably, the introduction of the *N*-ethoxycarbonyl group lowers the electronic density on the carbon atom in position 3 of the indole and further cyclization is forbidden.

When the indole is *N*-substituted with a methyl group (**1a-1d**), the reaction takes a different course, and we obtain (85-90%) the *O*-ethoxycarbonyl-carbohydrazones **3a-3d**, which were characterized by their analytical and spectroanalytical (ir, ^{1}H-nmr) data. The structure of these compounds was supported by the reduction of **3a** and **3d** with sodium borohydride in ethanol to give (75-80%) the oxadiazoles **4a** and **4d**, respectively, which were also characterized by their analytical and spectroanalytical (ir, ^{1}H-nmr) data. This reaction involves the reduction of the double-bond C=NR^{1}R^2 and further cyclization with elimination of ethanol, which confirms the position of the ethoxycarbonyl group in compound **3**.

Compound **3a** recovery was unchanged after boiling (6 hours) in dioxane with catalytic amounts of sodium hydroxide. However, when **3a-3d** were boiled with ethanol/-hydrochloric acid, a progressive change in the composition of the reaction mixture was observed by tlc. After 1-2 hours of reactions, depending on the starting compound, these compounds disappeared with the formation of new ones, which after isolation were characterized by analytical and spectroanalytical (ir, ^{1}H-nmr) data as the 5*H*-pyridazino[4,5-*b*]indole derivatives **5**. The ir spectra of these compounds show bands at 3200 cm^{-1} (s-m), 1705-1725 cm^{-1} (s) and 1660-1675 cm^{-1} (s), which were assigned, respectively, to the groups -NH-, -O-C(=O)- and -C=N-. On the other hand, a signal at δ 6.68-6.83 (s, 1H) in the ^{1}H-nmr spectra was assigned to the H_1. Although these δ values may seem too high for this proton, we [4-7] and other authors [8] have registered values of δ 6.00-7.00 for this proton in several 1,2,3,4-tetrahydro-4-oxopyridazino[4,5-*b*]indole derivatives.

When the boiling of compounds **3a-3c** with ethanol/-hydrochloric acid was prolonged approximately 6 hours, tlc of the reaction mixture demonstrated presence of two principal components: one was identified as the corresponding compound **5**, and the other one was a new compound formed from the respective **5**. In the case of **3a** and **3b** as starting materials, both of the above mentioned compounds were easily separated by hplc and characterized. In each case, the new compound was identified by analytical and spectroanalytical (ir, ^{1}H-nmr) data as the corresponding **6**, generated by an O → N shift of the ethoxycarbonyl group. The ir spectra of **6a** and **6b** show bands at 3200-3215 (s), 1740-1750 (s) and 1690-1700 (s), assigned to the groups -NH-, C=O ester and C=O cyclic amide, respectively. The ^{1}H-nmr spectra show signals at δ 6.83 (s, 1H) for **6a** and δ 5.70 (s, 1H) for **6b**, assigned to the H_1. However, we can not give an explanation for this unusual difference. Further, the two protons of the methylenedioxy group in **6b** were not equivalent, forming an AB system with two signals very close to each other showing two singlets at δ 6.00 (1H) and δ 6.04 (1H).

Treating compounds **5a-5c**, or **6a-6c**, or mixtures of the respective compounds **5** and **6** with hydrazine, the ethoxycarbonyl group was removed and compounds **7** were obtained, and their structures were confirmed by analytical and spectroanalytical (ir, ^{1}H-nmr) data. The ir spectra of **7a-7c** show bands at 3200-3300 cm^{-1} (s-m, NH), and 1650-1660 cm^{-1} (s, C=O); the ^{1}H-nmr spectra show signals at δ 8.80-8.90 (s, 1H, CONH), δ 6.10-6.15 (d, 1H, NH) and δ 5.40-5.45 (d, 1H, H_1), J (NH, CH) 4-5 Hz. According to these assignments treating the samples for ^{1}H-nmr with deuterium oxide, the signals for the CONH and NH groups disappear, and the doublet for H_1 is collapsed to a singlet at about δ 5.40-5.45 (s, 1H, H_1). These and other data support unequivocally the structure of **7**. Compound **7a**, mp 234-236°, has been previously reported by us [5,7] erroneously (mp 279-280°) and correctly by other authors [8]. This mistake, as we have now probed, was due to an easy partial spontaneous oxidation of **7a** to **8** (mp 250°) [5], even in the solid state. Oxidation of **7a** with potassium permanganate gives **8** quantitatively and reduction of **8** with sodium borohydride, as previously reported by us [5], gives **7a**.

EXPERIMENTAL

Melting points were determined in an automatic Mettler FP5 apparatus and they are uncorrected. Elemental analyses were obtained from vacuum-dried samples (over phosphorus pentoxide at 1-3 mm Hg, for 2-3 hours, at about 60-70°). The ir spectra were recorded on a Perkin-Elmer 681 apparatus in potassium bromide tablets, and the frequencies are expressed in cm^{-1}. The ^{1}H-nmr spectra were obtained on a Perkin-Elmer R-24A (60 MHz) or R-32 (90 MHz) instrument in the indicated solvent, at a concentration of about 0.1 g/ml. Chemical shifts are reported in ppm from TMS as an internal standard and they are given in δ units (s, d, t... for singlet, doublet, triplet...; dd, double doublet; bs, broad signal). Thin-layer chromatography (tlc) was performed in the usual way on glass-plaques coated with silica-gel DSF-5 (Cammaga), using benzene:dioxane:acetic acid (90:25:40 v/v) as solvent; spots were revealed by spraying the plaques with a solution of ammonium molibdate (40 mmoles), sulfuric acid (1.33 moles) and phosphoric acid (1.0 mole). High pressure liquid chromatography (hplc) was performed on a Waters Associates apparatus, model 450, provided with UV-detector (λ 254 nm), pump model 6000 A, manual injector M-U6K, and module for data; solvent was acetonitrile:-water (60:40 v/v, in analytical experiments and 50:50 v/v in semipreparative experiments) at pressure values of 1200-2000 psi. A μ-Bondapak C_{18} column was used with a flow of 1 ml/minute (analytical) and 2 ml/minute (preparative).

2-(*N*-Methylindole)carbohydrazones (**1**).

They were obtained as previously reported: **1a**, **1c** and **1d** [9], **1b** [4] and **1e** [10].

2-(*N*-Ethoxycarbonyl)benzylidenecarbohydrazone (**2**).

Compound **1e** is treated with ethoxycarbonyl chloride and triethylam-

ine as is posteriorly described to obtain **3** from **1**; orange-coloured crystals, mp 168-169° (from 2-propanol), yield 90%; ir: 3300 (s, broad, NH), 1660 (s, broad and multiple, C=O), 1640 (s, C=N), 690 (s), 740 (s), aromatic monosubstitution; ^{1}H-nmr (deuteriochloroform): 1.28 (s, 3H, CH_3), 4.30 (q, 2H, CH_2O), 6.98 (s, 1H, CH=N), 7.05-7.85 (m, 10H, $H_{3,4,5,6,7}$ and C_6H_5), 9.10 (s, 1H, CONH). This last signal disappears on treating the sample with deuterium oxide.

Compounds **3**.

On a boiling suspension of the respective hydrazone **1** (10 mmoles) in dry chloroform (60 ml) and triethylamine (30 ml), a solution of ethoxycarbonyl chloride (12.0 ml, 13.6 g, 125 mmoles) in dry chloroform (30 ml) was slowly added. The reaction mixture was protected with an anhydrous calcium chloride tube. In about 2-2.5 hours all the starting product **1** disappears (tlc). The cold reaction mixture is repeatedly washed with water, then with 1% hydrochloric acid, (until all the triethylamine was removed) and after with water, and dried on anhydrous sodium sulfate. The solvent was removed in vacuum and the residual material recrystallized from 2-propanol, yield about 85-90%. The following compounds were obtained:

Compound **3a**.

This compound was obtained as a white crystalline powder, mp 144-145°; ir: 1710 (s, C=O), 1635 (s, C=N), 1350 (s), 1430 (s), CH_3, 1060 (s), 1125 (s), 1235 (s), 1260 (s), C-O; 700 (s), 750 (s), aromatic monosubstitution; ^{1}H-nmr (deuteriochloroform): 1.30 (t, 3H, CH_3), 4.18 (s, 3H, N-CH_3), 4.33 (q, 2H, CH_2O), 6.92 (s, 1H, CH=N), 7.15 (s, 1H, H_3), 7.20-7.90 (m, 9H, $H_{4,5,6,7}$ and C_6H_5).

Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.69; H, 5.60; N, 11.85.

Compound **3b**.

This compound was obtained as a white crystalline powder, mp 155-156°; ir: 1700 (s, C=O), 1630 (s, C=N), 1345 (s), 1430 (s) CH_3, 1030 (s), 1050 (s), 1105 (s), 1125 (s), 1225 (s), 1250 (s), C-O; 870 (s), 855 (s), 1,2,4-aromatic trisubstitution; ^{1}H-nmr (DMSO-d_6): 1.22 (t, 3H, CH_3), 4.10 (s, 3H, N-CH_3), 4.18 (q, 2H, CH_2O), 6.10 (s, 2H, CH_2O_2), 6.98 (s, 1H, CH=N), 7.05 (s, 1H, H_3), 6.90-7.80 (m, 7H, 3H-piperonyl and $H_{4,5,6,7}$).

Anal. Calcd. for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68. Found: C, 64.36; H, 5.23; H, 10.84.

Compound **3c**.

This compound was obtained as pale orange coloured needles, mp 145-146°; ir: 1730 (s, C=O), 1632 (s, C=N), 1340 (s) CH_3, 1055 (m), 1120 (s), 1230 (m), 1250 (m), C-O; 803 (m), 1,4-aromatic disubstitution; ^{1}H-nmr (DMSO-d_6): 1.20 (t, 3H, CH_3), 2.38 (s, 3H, CH_3-aryl), 4.11 (s, 3H, N-CH_3), 4.15 (q, 2H, CH_2O), 7.03 (s, 1H, CH=N), 7.08 (s, 1H, H_3), 7.10-7.80 (m, 8H, 4H-tolyl and $H_{4,5,6,7}$).

Anal. Calcd. for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.40; H, 6.01; N, 11.43.

Compound **3d**.

This compound was obtained as pale orange coloured needles, mp 73-74°; ir: 1695 (s, C=O), 1630 (s, C=N), 1350 (s), 1460 (s), CH_3, 1060 (m), 1095 (s), 1235 (s), 1265 (m), C-O; ^{1}H-nmr (DMSO-d_6): 0.90 (t, 3H, CH_3), 1.31 (t, 3H, CH_3), 1.80 (s, 3H, =C-CH_3), 1.95-2.45 (m, 2H, =C-CH_2), 4.05 (s, 3H, N-CH_3), 4.26 (q, 2H, CH_2O), 7.09 (s, 1H, H_3), 7.10-7.80 (m, 4H, $H_{4,5,6,7}$).

Anal. Calcd. for $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.32. Found: C, 64.56; H, 6.88; N, 13.49.

3-Alkyl-2,3-dihydro-5-[2-(*N*-methylindolyl)]-2-oxo-1,3,4-oxadiazoles (**4**).

To a solution of the corresponding **3** (2 mmoles) in dioxane (50 ml) sodium borohydride (0.25 g, 6.6 mmoles) were added. The mixture was boiled until the reaction was completed (tlc, about 8 hours). To the cold mixture diluted acetic acid was added to destroy the excess borohydride; solvent was removed in vacuum and the residual material recrystallized from 2-propanol.

Compound **4a**.

This compound was obtained as a white crystalline powder, mp 124-125°, yield 80%; ir: 1790 (s, C=O), 1620 (m, C=N), 1040 (s), 1150 (m), 1240 (s), C-O; 740 (s), aromatic monosubstitution; ^{1}H-nmr (DMSO-d_6): 4.02 (s, 3H, N-CH_3), 5.05 (s, 2H, N-CH_2), 7.18 (s, 1H, H_3 indole), 7.45 (s, 5H, C_6H_5), 7.20-7.90 (m, 4H, $H_{4,5,6,7}$ indole).

Anal. Calcd. for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.86; H, 4.98; N, 13.56.

Compound **4d**.

This compound was obtained as a cream coloured crystalline powder mp 96-97°; ir: 1775 (s, C=O), 1622 (s, C=N), 1380 (m), 1465 (m) CH_3, 1040 (m), 1195 (m), 1240 (m), 1285 (m), C-O; ^{1}H-nmr (deuteriochloroform): 0.98 (t, 3H, CH_3), 1.45 (d, 3H, CH_3), 1.60-2.10 (m, 2H, CH_2), 4.0-4.40 (m, 1H, CH), 4.05 (s, 3H, N-CH_3), 7.04 (s, 1H, H_3 indole), 7.10-7.80 (m, 4H, $H_{4,5,6,7}$ indole).

Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.13; H, 6.58; N, 15.38.

1-Aryl-4-ethoxycarbonyl-1,2-dihydro-5-methyl-5*H*-pyridazino[4,5-*b*]indoles **5** and 1-Aryl-3-ethoxycarbonyl-1,2,3,4-tetrahydro-4-oxo-5-methyl-5*H*-pyridazino[4,5-*b*]indoles **6**.

A mixture of the corresponding compound **3** (3 mmoles) ethanol (40 ml) and concentrated hydrochloric acid (1 ml) was boiled for the indicated time and the composition of the mixture followed by tlc.

From Compound **3a**.

After about 1 hour all of compound **3a** had disappeared and tlc showed the presence of a new compound. Solvent was removed in vacuum and the syrupy residual material treated with a few drops of ethanol. A solid material crystallized, which was recovered by filtration, washed with water and recrystallized from ethanol, yield 85%, mp 175-177°, as a white powder; ir: 3200 (s, NH), 1725 (m, C=O), 1675 (s, C=N), 1375 (m), 1440 (m), CH_3, 1100 (m), 1260 (s), C-O; 700 (m), 750 (s), aromatic monosubstitution; ^{1}H-nmr (DMSO-d_6): 1.28 (t, 3H, CH_3), 4.12 (s, 3H, N-CH_3), 4.25 (q, 2H, CH_2O), 6.83 (s, 1H, H_1), 7.32 (s, 5H, C_6H_5), 7.00-7.80 (m, 4H, $H_{6,7,8,9}$), 11.3 (bs, 1H, NH). This last signal disappears by the addition of deuterium oxide.

Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.42; H, 5.57; N, 11.86.

If the reaction time was continued for about 6 hours, the mixture gave (tlc) two principal components identified as **5a** (~60%) and **6a** (~40%). Both products were separated by hplc. Compound **5a** had a retention time of 34.2 minutes and **6a**, 28.4 minutes in semipreparative experiments.

Compound **6a**.

This compound had mp 213-215° (from ethanol); ir: 3215 (s, NH), 1740 (s, C=O), 1690 (s, C=O), 1510 (m), 1370 (m), CH_3, 1250 (s), 1205 (s), 1140 (m), 1060 (m), C-O; 740 (s), 715 (m), aromatic monosubstitution; ^{1}H-nmr (DMSO-d_6): 1.20 (t, 3H, CH_3), 4.02 (s, 3H, N-CH_3), 4.10 (q, 2H, CH_2O), 5.82 (s, 1H, H_1), 7.00-7.80 (m, 4H, $H_{6,7,8,9}$), 7.40 (s, 5H, C_6H_5), 9.80 (bs, 1H, NH). This last signal disappeared by addition of deuterium oxide.

Anal. Calcd. for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.49; H, 5.42; N, 11.82.

If the reaction time was prolonged further, new products appeared; at least four after 12 hours which were not studied.

From Compound **3b**.

After about 2 hours of reaction, all the starting material had disappeared, and tlc showed the presence of a new principal compound, which was isolated and identified as **5b** (75%), mp 186-188° (from ethanol); ir: 3200 (s, NH), 1710 (s, C=O), 1670 (s, C=N), 1360 (m), 1440 (m), CH_3, 1040 (s), 1120 (m), 1100 (m), 1230-1290 (s, several bands), C-O; 805 (m), 870 (m), for 1,2,4-aromatic trisubstitution; ^{1}H-nmr (DMSO-d_6): 1.28 (t, 3H, CH_3), 4.10 (s, 3H, N-CH_3), 4.23 (q, 2H, CH_2O), 6.04 (s, 2H, CH_2O), 6.83 (s, 1H, H_1), 6.60-7.80 (m, 7H, 3H-piperonyl and $H_{6,7,8,9}$), 10.30 (s, 1H, NH). This last signal disappeared by addition of deuterium oxide.

Anal. Calcd. for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68. Found: C,

64.37; H, 5.07; N, 10.40.

After about 6.5 hours, the mixture contained two principal components (tlc), which were isolated and characterized as **5b** and **6b**. Both components were separated by hplc (at *p*H 5.0 adjusted with acetic acid); retention times in semipreparative experiments: 24.5 minutes (**5b**) and 20.7 minutes (**6b**).

Compound **6b**.

This compound had mp 190-192° (from ethanol); ir: 3200 (s, NH), 1750 (s, double, C=O), 1700, (s, C=O), 1380 (w), 1450 (m), CH_3, 1035 (m), 1100 (m), 1205 (s), 1260 (s), C-O; 800 (w), 860 (m), 1,2,4-aromatic trisubstitution; ^{1}H-nmr (DMSO-d_6): 1.20 (t, 3H, CH_3), 4.00 (s, 3H, N-CH_3), 4.15 (q, 2H, CH_2O), 5.70 (s, 1H, H_1), 6.00 (s, 1H), 6.04 (s, 1H) for CH_2O_2, 6.80-7.75 (m, 7H, 3H-piperonyl and $H_{6,7,8,9}$), 9.70 (bs, 1H, NH). This last signal disappeared by the addition of deuterium oxide.

Anal. Calcd. for $C_{21}H_{19}N_3O_5$: C, 64.12; H, 4.87; N, 10.68. Found: C, 64.56; H, 4.39; N, 10.87.

When the reaction time was prolonged for more than about 6.5 hours, new products appeared (four, at least, after 12 hours), which were not studied.

From Compound **3c**.

After about 1 hour, the reaction mixture contained only one new product (tlc), identified as **5c**, mp 209° (from ethanol); ir: 3200 (s, NH), 1705 (s, C=O), 1660 (s, C=N), 1370 (m), 1420 (m), CH_3, 1110 (s), 1260 (s), 1280 (s), C-O; 830 (m), 1,4-aromatic disubstitution; ^{1}H-nmr (DMSO-d_6): 1.28 (t, 3H, CH_3), 2.30 (s, 3H, CH_3-aryl), 4.13 (s, 3H, N-CH_3), 4.25 (q, 2H, CH_2O), 6.68 (s, 1H, H_1), 7.10-7.80 (m, 8H, 4H-*p*-tolyl and $H_{6,7,8,9}$), 10.2 (s, 1H, NH). This last signal disappeared by addition of deuterium oxide.

Anal. Calcd. for $C_{21}H_{21}N_3O_3$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.53; H, 5.95; N, 11.63.

After about 6 hours of reaction, the mixture contained two principal products: one identified (tlc) as **5c** and the other, probably **6c**, was not characterized.

4-Ethoxycarbonyl-1,2-dihydro-5-methyl-5*H*-pyridazino[4,5-*b*]indole (**5a**).

On a boiling suspension of **1a** (10 mmoles) in dry chloroform (60 ml) a solution of ethoxycarbonyl chloride (12.0 ml, 13.6 g, 125 mmoles) was slowly added dropwise. The reaction was completed in about 25 hours. Solvent was removed in vacuum and the residual material crystallized from ethanol to give **5a** (85%), mp 175-177° (see above ir and ^{1}H-nmr spectra).

1-Aryl-1,2,3,4-tetrahydro-5-methyl-4-oxo-5*H*-pyridazino[4,5-*b*]indole (**7**).

A suspension of the corresponding **5**, or **6**, or a mixture of **5** and **6** (see the preparation of these mixtures from the corresponding **3** above) (10 mmoles) in 80% hydrazine hydrate (25 ml) was boiled. After total dissolution of the starting compound(s), a new white product began to crystallize in about 30 minutes. After about 6 hours, the reaction mixture was cooled and filtered, and the solid washed with 50% ethanol-water and recrystallized. The following compounds were obtained:

Compound **7a**.

From **5a**, or **6a**, or a mixture of **5a** and **6a**, white crystals were obtained, mp 234-236° (from ethanol), yield 70%; ir: 3210 (s, NH), 1660 (s, C=O), 1375 (w), 1440 (m), CH_3, 745 (s), 695 (m), for aromatic monosubstitution; ^{1}H-nmr (DMSO-d_6): 4.10 (s, 3H, N-CH_3), 5.40 (d, 1H, H_1), J (CH, NH) 4 Hz, 6.10 (d, 1H, NH), 6.95-7.65 (m, 4H, $H_{6,7,8,9}$), 7.30 (s, 5H, C_6H_5), 8.80 (s, 1H, CONH). By the addition of deuterium oxide to the sample (or yet registering the spectra at about 100°), the signals assigned to the groups NH and CONH disappeared and the signal for H_1 collapsed to a singlet (δ 5.40).

Anal. Calcd. for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.23; H, 5.41; N, 15.21.

Compound **7b**.

From **5b**, or **6b**, or a mixture of **5b** and **6b**, white crystals were obtained, mp 246-248° (from ethanol), yield 70%; ir: 3220 (m, NH), 1655 (s, C=O), 1370 (w), 1450 (m), CH_3, 1050 (s), 1250 (s), C-O; 875 (m), 870 (m), for 1,2,4-aromatic trisubstitution; ^{1}H-nmr (DMSO-d_6): 4.20 (s, 3H, N-CH_3), 5.45 (d, 1H, H_1), J (CH, NH) 5 Hz, 6.10 (s, 2H, CH_2O_2), 6.15 (s, 1H, NH), 6.80-7.80 (m, 7H, piperonyl and $H_{6,7,8,9}$), 8.93 (s, 1H, CONH). By the addition of deuterium oxide to the sample, signals assigned to the groups NH and CONH disappeared and the signal for H_1 collapsed to a singlet.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.32; H, 4.67; N, 13.22.

Compound **7c**.

From **5c**, or **6c**, or a mixture of **5c** and **6c**, white crystals were obtained, mp >300° (from ethanol), yield 75%; ir: 3200 (s, NH), 1650 (s, C=O), 1370 (w), 1440 (m), CH_3, 820 (s) for 1,4-aromatic disubstitution; ^{1}H-nmr (DMSO-d_6): 2.38 (s, 3H, CH_3-aryl), 4.18 (s, 3H, N-CH_3), 5.45 (d, 1H, H_1), J (CH, NH) 5 Hz, 6.10 (d, 1H, NH), 7.00-7.70 (m, 8H, 4H-*p*-tolyl and $H_{6,7,8,9}$), 8.90 (s, 1H, CONH). By the addition of deuterium oxide the signals for NH and CONH disappeared and the signal for H_1 collapsed to a singlet.

Anal. Calcd. for $C_{18}H_{17}N_3O$: C, 74.21; H, 5.88; N, 14.42. Found: C, 73.85; H, 6.24; N, 14.73.

3,4-Dihydro-5-methyl-4-oxo-1-phenyl-5*H*-pyridazino[4,5-*b*]indole (**8**).

A mixture of **7a** (10 mmoles) in chloroform (50 ml) and 0.1 *M* potassium permanganate (100 ml) was vigorously stirred at room temperature for 6 hours. The organic phase was separated, washed with water and dried over anhydrous sodium sulfate. The solvent was removed in vacuum and the solid residue crystallized to give **8** (98%), mp 250° (2-propanol); reported [5] mp 250°, with identical ir and ^{1}H-nmr spectra.

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