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NOVEL SCHEMES FOR THE SYNTHESIS OF PYRROLOCOUMARINS

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Two novel schemes have been developed for the synthesis of pyrrolocoumarin derivatives. A series of previously unknown 4,9-dimethylpyrano[3,2-e]indol-7(3H)-ones have been prepared.

Keywords: benzo[*a*]pyrano[2,3-*g*]carbazol-3(7H)-one, indole, carbazole, coumarin, pyrano[3,2-*e*]indol-7(3H)-one, pyrano[2,3-*c*]carbazol-3(7H)-one, pyrrolocoumarin, Fischer reaction.

Since pyrrolocoumarins are promising compounds in the search for novel antitumor agents [1] it is currently of interest to develop novel synthetic routes for the preparation of differently structured pyrrolocoumarins. In this study we propose two novel schemes for the synthesis of pyrano[3,2-*e*]indol-7(3H)-one derivatives.

Analysis of the literature data shows that there are two possible routes for the construction of pyrrolocoumarin molecules. The first route is based on the formation of the pyrrole fragment condensed with coumarin ring. The second route introduces pyrone fragment into appropriate hydroxyindole or hydroxyindoline molecule.

The first synthetic route is achieved using Bischler and Fischer reactions. The Bischler reaction was used for the preparation of 4,9-dimethyl-1,2-diphenylpyrano[3,2-*e*]indol-7(3H)-one [2]. The Bischler synthesis needs drastic conditions and the halo or hydroxycarbonyl compounds which are not always available and so this narrows its use.

An alternative route is based on the reaction of the corresponding arylhydrazine with carbonyl compounds and subsequent Fischer indolization of hydrazones obtained and this is more versatile. It has been used successfully in the preparation of differently structured pyrrolocoumarins [1, 3]. However, in this case the starting coumarinylhydrazines are prepared directly before the synthesis of pyrrolocoumarins and are used as solution of arylhydrazine hexachlorostannate in hydrochloric acid. The procedure significantly limits the possibility of carrying out the cyclization and in some cases does not permit preparation of pyrrolocoumarins of the desired structure.

In the second route (i.e. from hydroxyindoles) pyrrolocoumarins are also prepared by two routes. One of these includes the formylation of the starting 5-hydroxyindole and subsequent cyclization of aldehyde obtained with acetic anhydride [4].

The second scheme is based on Pechmann cyclization of 5-hydroxyindole with acetoacetic ester [5]. The Pechmann reaction is also used for the preparation of 8-ethyl-4-methylpyrano[3,2-*e*]indol-2(8H)-one from the corresponding hydroxyindoline [6].

The use of this second synthetic route for pyrrolocoumarins is limited by the complexity of preparing the starting hydroxyindoles and hydroxyindolines.

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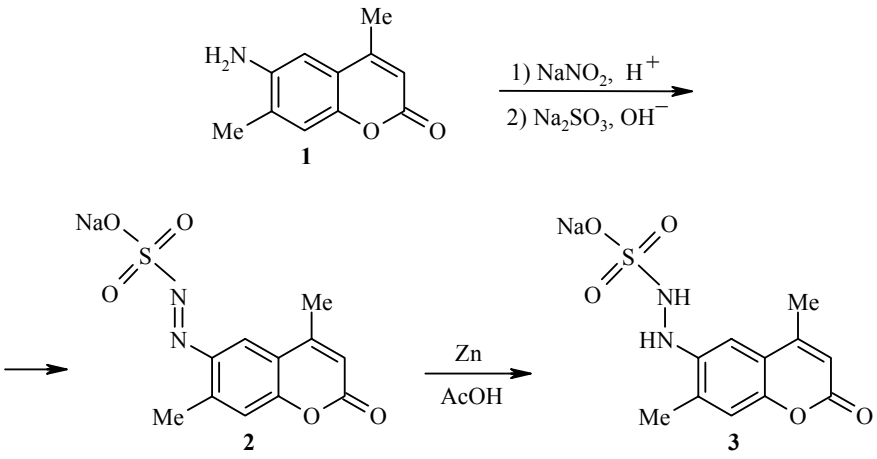
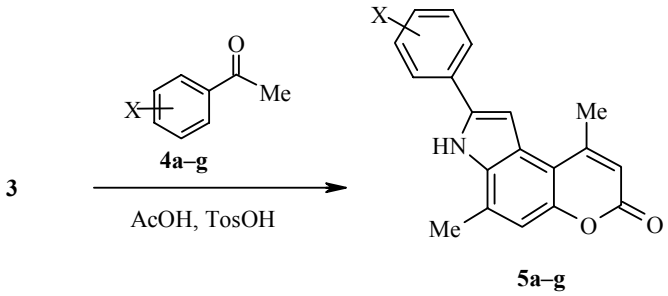
In the current work we report two novel schemes for the synthesis of 4,9-dimethylpyrano[3,2-*e*]indol-7(3H)-ones with different substituents in positions 1 and 2. Both schemes are simple in use and are suitable for obtaining preparative amounts of the target compounds with different structures.

In the first scheme, diazonium chloride obtained from 6-amino-4,7-dimethylcoumarin **1** [2] was treated with sodium sulfite to give 4,7-dimethylcoumarin sodium 6-diazosulfonate (**2**) in 75% yield. It was reduced with zinc in acetic acid to give 4,7-dimethylcoumarin sodium 6-hydrazinosulfonate (**3**) (80% yield).



The reaction of compound **3** with ketones **4** leads to the formation of the corresponding hydrazones, isolation of which was not expedient. From a series of experiments we have found that the use of the system $TsOH \cdot H_2O$-acetic acid at this stage gives good yields of the target pyrrolocoumarins without separation of the intermediate hydrazones. Hence reaction of compound **3** with acetophenones **4a-g** gave 2-arylindoles **5a-g** in a single stage.



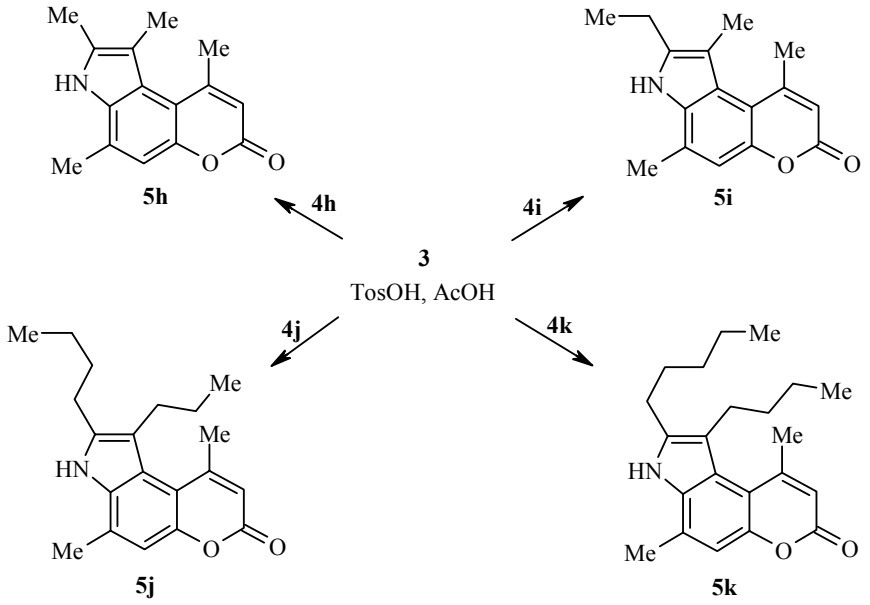
5a–g

4, 5 a X = H, **b** X = 4'-NO_2, **c** X = 3'-NO_2, **d** X = 4'-F, **e** X = 4'-Cl, **f** X = 4'-Br, **g** X = 4'-I

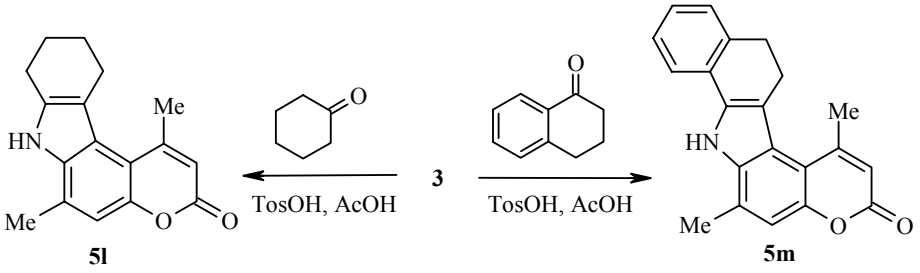
Good results were achieved using these conditions in the synthesis of 1,2-dialkylindoles **5h-k** and also in the preparation of carbazole derivatives **5l,m** (Scheme 1)

The scheme discussed seems quite versatile. It is characterized by good yields and simplicity of separation of the target pyrrolocoumarins.

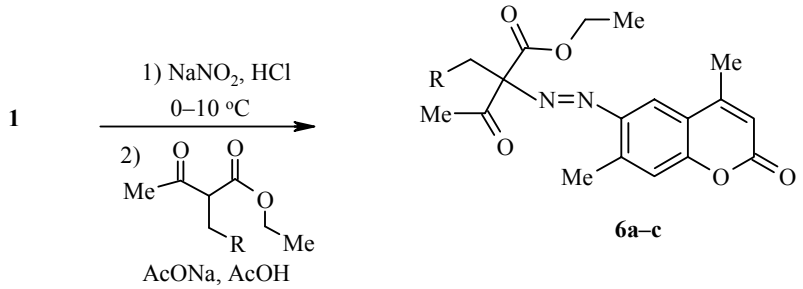
Scheme 1



4 h = MeCOEt, **i** = Et_2CO, **j** = Bu_2CO, **k** = Am_2CO

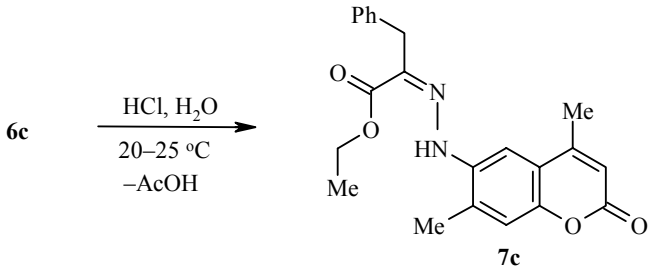


In the second scheme, diazonium chloride obtained from 6-amino-4,7-dimethylcoumarin **1** in the presence of sodium acetate readily undergoes azo coupling with 1,3-dicarbonyl compounds: α-methyl, α-ethyl, and α-benzylacetoacetic ester. As a result of the reaction azo compounds **6a-c** were formed and these were used immediately for the preparation of the indole derivatives.

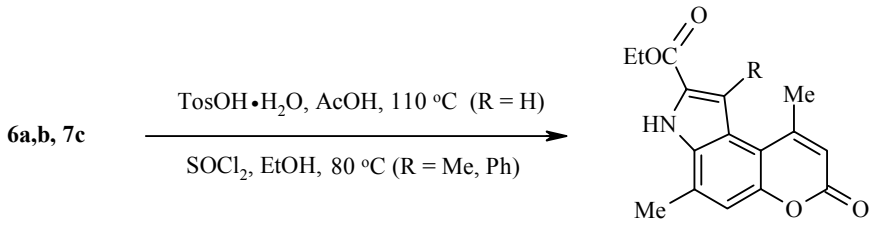


6 a R = H, **b** R = Me, **c** R = Ph

Because the coupling product **6c** is an oil, for convenience of separation and identification it was subjected to fission to hydrazone **7c** using hydrochloric acid at room temperature.



We have used solution of *p*-toluenesulfonic acid in acetic acid for the preparation of compound **8a**. Upon cyclization of coupling products **6b** and **7c** (R = Me, Ph) to **8b** and **8c**, respectively, an alcohol solution, prepared by a careful stirring of ethanol with thionyl chloride, was used as an acid reagent.



8 a R = H, **b** R = Me, **c** R = Ph

The yields and spectroscopic parameters for the synthesized pyrrolocoumarins are given in Tables 1-3.

TABLE 1. Characteristics of 4,9-Dimethylpyrano[3,2-*e*]indol-7(3H)-ones and Intermediate Products

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f	Yield, %
		C	H	N			
1	2	3	4	5	6	7	8
5a	$C_{19}H_{15}NO_2$	79.09 / 78.87	5.40 / 5.23	4.88 / 4.84	278	0.52	72
5b	$C_{19}H_{14}N_2O_4$	68.40 / 68.26	4.26 / 4.22	8.73 / 8.38	>310	0.43	65
5c	$C_{19}H_{14}N_2O_4$	68.31 / 68.26	4.53 / 4.22	8.87 / 8.38	>315	0.41	36
5d	$C_{19}H_{14}FNO_2$	74.34 / 74.26	4.70 / 4.59	6.24 / 6.18	>300	0.52	22
5e	$C_{19}H_{14}ClNO_2$	71.01 / 70.48	4.55 / 4.36	4.30 / 4.33	>310	0.53	65
5f	$C_{19}H_{14}BrNO_2$	62.08 / 61.97	3.95 / 3.83	4.01 / 3.80	>300	0.54	70
5g	$C_{19}H_{14}INO_2$	55.12 / 54.96	3.81 / 3.40	3.45 / 3.37	325 (with dec.)	0.51	67
5h	$C_{15}H_{15}NO_2$	74.95 / 74.67	6.34 / 6.27	5.94 / 5.80	276-278	0.61	85
5i	$C_{16}H_{17}NO_2$	45.48 / 45.27	6.90 / 6.71	5.59 / 5.49	226-227	0.55	85
5j	$C_{20}H_{25}NO_2$	77.81 / 77.14	8.15 / 8.09	4.81 / 4.50	143-145	0.73	72
5k	$C_{22}H_{29}NO_2$	78.01 / 77.84	8.76 / 8.61	4.26 / 4.13	119-121	0.66	72

TABLE 1 (continued)

1	2	3	4	5	6	7	8
5l	$C_{17}H_{17}NO_2$	76.48 76.38	6.60 6.41	5.29 5.24	305-306	0.64	90
5m	$C_{21}H_{17}NO_2$	80.11 79.98	5.66 5.43	4.92 4.44	319-320	0.56	90
6a	$C_{18}H_{20}N_2O_5$	62.78 63.00	5.85 5.81	8.13 8.15	84-85	0.87	87
6b	$C_{19}H_{22}N_2O_5$	63.68 63.83	6.19 6.31	7.82 7.80	88-90	0.83	86
7c	$C_{22}H_{22}N_2O_4$	69.83 69.62	5.86 5.92	7.40 7.34	160-162	0.88	70
8a	$C_{16}H_{15}NO_4$	67.36 67.39	5.30 5.25	4.91 4.89	>300	0.77	36
8b	$C_{17}H_{17}NO_4$	68.22 67.98	5.72 5.68	4.68 4.73	178-180	0.71	85
8c	$C_{22}H_{19}NO_4$	73.12 73.11	5.30 5.28	3.88 3.77	223-225	0.74	50

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker WR-200SV instrument (200 MHz) with TMS as internal standard and mass spectra were taken on a Finnigan MAT SSQ-710 instrument with ionization energy 70 eV. The course of the reactions was monitored using TLC on Silufol UV-254 plates in the system chloroform–acetone (25:1).

Sodium (*E*,*Z*)-2-(4,7-Dimethyl-2-oxo-2H-chromen-6-yl)-1-diazosulfonate (2). Solution of $NaNO_2$ (22 g, 0.32 mol) in water (50 ml) was added at once with vigorous stirring to solution of 6-amino-4,7-dimethylcoumarin (**1**) (51 g, 0.27 mol) in hydrochloric acid (73 ml) at -5°C. The diazo solution was stirred at 0-10°C for 2-3 h and then immediately and with vigorous stirring poured into solution of Na_2SO_3 (52 g,

TABLE 2. Mass Spectral Characteristics of the Novel 4,9-Dimethylpyrano-[3,2-*e*]indol-7(3H)-ones and Intermediate Products

Compound	*m*/*z* (I_{rel}, %)	Compound	*m*/*z* (I_{rel}, %)
5a	289 $[M]^+$ (100), 261 $[M^+ – CO]$ (93)	**5k**	339 $[M]^+$ (72), 296 $[M^+ – CH_3CO]$ (92)
5b	334 $[M]^+$ (93), 306 $[M^+ – CO]$ (93)	**5l**	267 $[M]^+$ (45), 239 $[M^+ – CO]$ (14)
5c	334 $[M]^+$ (68), 306 $[M^+ – CO]$ (67)	**5m**	315 $[M]^+$ (100), 272 $[M^+ – CH_3CO]$ (35)
5d	307 $[M]^+$ (100), 279 $[M^+ – CO]$ (97)	**6a**	302 $[M^+ – CH_2{=}C{=}O]$ (9), 271 $[M^+ – COOEt]$ (25)
5e	323 $[M]^+$ (56), 295 $[M^+ – CO]$ (41)	**6b**	330 $[M^+ – CH_2{=}CH_2]$ (7), 316 $[M^+ – CH_2{=}C{=}O]$ (6)
5f	369 $[M]^+$ (100), 341 $[M^+ – CO]$ (89)	**7c**	378 $[M]^+$ (75)
5g	415 $[M]^+$ (92), 387 $[M^+ – CO]$ (54)	**8a**	285 $[M]^+$ (81), 257 $[M^+ – CH_2{=}CH_2]$ (11)
5h	241 $[M]^+$ (100), 198 $[M^+ – CH_3CO]$ (82)	**8b**	299 $[M]^+$ (80)
5i	255 $[M]^+$ (100), 212 $[M^+ – CH_3CO]$ (80)	**8c**	361 $[M]^+$ (85)
5j	311 $[M]^+$ (66), 282 $[M^+ – CH_3CH_2]$ (97)		

TABLE 3. ^{1}H NMR Spectral Characteristics of the Novel 4,9-Dimethyl-pyrano[3,2-*e*]indol-7(3H)-ones and Intermediate Products

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)*
2	2.4 (3H, d, *J* = 1, 4-CH_3); 2.6 (3H, s, 7-CH_3); 6.4 (1H, d, *J* = 1.0, H-3); 7.4 (1H, s, H-8); 7.6 (1H, s, H-5)
3	2.2 (3H, s, 7-CH_3); 2.4 (3H, s, 4-CH_3); 5.9 (1H, s, 2-NH); 6.2 (1H, s, 1-NH); 6.4 (1H, s, H-3); 7.0 (1H, s, H-5); 7.4 (1H, s, H-8)
5a	2.6 (3H, s, 4-CH_3); 2.8 (3H, d, *J* = 1.0, 9-CH_3); 6.2 (1H, d, *J* = 1.0, H-8); 7.0 (1H, s, H-5); 7.3 (1H, d, *J* = 2.0, H-1); 7.4-8.1 (5H, m, $C_6\underline{H}_5$); 11.5 (1H, s, NH)
5b	2.7 (3H, d, *J* = 0.5, 4-CH_3); 2.8 (3H, d, *J* = 1.0, 9-CH_3); 6.2 (1H, d, *J* = 1.0, H-8); 7.0 (1H, d, *J* = 0.5, H-5); 7.6 (1H, d, *J* = 2.0, H-1); 8.3 (4H, s, $C_6\underline{H}_4$); 11.7 (1H, s, NH)
5c	2.7 (3H, s, 4-CH_3); 2.8 (3H, s, 9-CH_3); 6.2 (1H, s, H-8); 7.0 (1H, s, H-5); 7.5 (1H, d, *J* = 2.0, H-1); 7.7 (1H, t, *J* = 7, H-5); 8.2 (1H, d, *J* = 7, H-6); 8.5 (1H, d, *J* = 7, H-4); 8.9 (1H, s, H-2); 11.8 (1H, s, NH)
5d	2.8 (3H, s, 4-CH_3); 2.9 (3H, d, *J* = 1.0, 9-CH_3); 6.2 (1H, d, *J* = 1.0, H-8); 7.0 (1H, s, H-5); 7.1 (1H, d, *J* = 2.0, H-1); 7.2 (2H, d, *J* = 8.0, H-2, 6); 7.9 (2H, d, *J* = 8, H-3, 5); 1.0 (1H, s, NH)
5e	2.6 (3H, s, 4-CH_3); 2.8 (3H, s, 9-CH_3); 6.2 (1H, s, H-8); 7.0 (1H, s, H-5); 7.4 (1H, d, *J* = 1.5, H-1); 7.8 (4H, dd, *J* = 100, *J* = 8, $C_6\underline{H}_4$); 11.54 (1H, s, NH)
5f	2.6 (3H, s, 4-CH_3); 2.7 (3H, s, 9-CH_3); 6.2 (1H, s, H-8); 7.0 (1H, s, H-5); 7.4 (1H, d, *J* = 1.5, H-1); 7.9 (4H, dd, *J* = 70, *J* = 8, $C_6\underline{H}_4$); 11.5 (1H, s, NH)
5g	2.6 (3H, s, 4-CH_3); 2.7 (3H, d, *J* = 1.0, 9-CH_3); 6.2 (1H, d, *J* = 1.0, H-8); 7.0 (1H, s, H-5); 7.4 (1H, d, *J* = 2.0, H-1); 7.8 (4H, s, $C_6\underline{H}_4$); 11.5 (1H, s, NH)
5h	2.3 (3H, s, 1-CH_3); 2.4 (3H, s, 2-CH_3); 2.5 (3H, d, *J* = 0.4, 4-CH_3); 2.7 (3H, d, *J* = 1.0, 9-CH_3); 6.1 (1H, d, *J* = 1.0, H-8); 6.8 (1H, s, H-5); 11.1 (1H, s, NH)
5i	1.2 (3H, t, *J* = 7.5, 2-$CH_2C\underline{H}_3$); 2.4 (3H, s, 1-CH_3); 2.5 (3H, s, 4-CH_3); 2.6 (3H, s, 9-CH_3); 2.8 (2H, q, *J* = 7.5, 2$C\underline{H}_2CH_3$); 6.1 (1H, s, H-8); 6.8 (1H, s, H-5); 11.0 (1H, s, NH)
5j	0.8-1.0 (6H, m, 1-$(CH_2)_2C\underline{H}_3$, 2-$(CH_2)_3C\underline{H}_3$); 1.4-1.7 (6H, m, 1-$CH_2C\underline{H}_2CH_3$, 2-$CH_2(C\underline{H}_2)_2CH_3$); 2.5 (3H, s, 4-$CH_3$); 2.6 (3H, d, *J* = 1.0, 9-CH_3); 2.8-2.9 (4H, m, 1-$C\underline{H}_2CH_2CH_3$, 2-$C\underline{H}_2(CH_2)_2CH_3$); 6.2 (1H, d, *J* = 1.0, H-8); 6.9 (1H, s, H-5); 8.2 (1H, s, NH)
5k	0.8-1.0 (6H, m, 1-$(CH_2)_3C\underline{H}_3$, 2-$(CH_2)_4C\underline{H}_3$); 1.3-1.7 (10H, m, 1-$CH_2(C\underline{H}_2)_2CH_3$, 2-$CH_2(C\underline{H}_2)_3CH_3$); 2.5 (3H, d, *J* = 0.5, 4-CH_3); 2.6 (3H, d, *J* = 1.0, 9-CH_3); 2.7-2.8 (4H, m, 1-$C\underline{H}_2(CH_2)_2CH_3$, 2-$C\underline{H}_2(CH_2)_3CH_3$); 6.2 (1H, d, *J* = 1.0, H-8); 6.94 (1H, d, *J* = 0.5, H-5); 8.1 (1H, s, NH)
5l*	1.8-1.9 (4H, m, 9-$C\underline{H}_2$, 10-$C\underline{H}_2$); 2.5 (3H, s, 6-CH_3); 2.6 (3H, d, *J* = 1.3, 1-CH_3); 2.8-3.0 (4H, m, 8-$C\underline{H}_2$, 11-$C\underline{H}_2$); 6.2 (1H, d, *J* = 1.3, H-2); 6.7 (1H, s, H-5); 8.0 (1H, s, NH)
5m	2.6 (3H, s, 6-CH_3); 2.7 (3H, s, 1-CH_3); 2.8-3.2 (4H, m, –$C\underline{H}_2C\underline{H}_2$–); 6.2 (1H, s, H-2); 6.9 (1H, s, H-5); 7.2-7.9 (4H, m, $C_6\underline{H}_4$); 11.5 (1H, s, NH)
6a	1.3 (3H, t, *J* = 7.5, $COOCH_2C\underline{H}_3$); 1.7 (3H, s, 2-CH_3); 2.3 (3H, s, 7-CH_3); 2.4 (3H, d, *J* = 1.6, 4-CH_3); 2.6 (3H, s, CH_3CO); 4.3 (2H, q, *J* = 7.5, $COOC\underline{H}_2CH_3$); 6.3 (1H, d, *J* = 1.6, H-3); 7.3 (1H, s, H-8); 7.6 (1H, s, H-5)
6b	1.0 (3H, t, *J* = 7.5, 2-$CH_2C\underline{H}_3$); 1.3 (3H, t, *J* = 7.5, $COOCH_2C\underline{H}_3$); 2.3 (2H, q, *J* = 7.5, 2-$C\underline{H}_2CH_3$); 2.3 (3H, s, 7-CH_3); 2.4 (3H, d, *J* = 1.8, 4-CH_3); 2.6 (3H, s, CH_3CO); 4.3 (2H, q, *J* = 7.5, $COOC\underline{H}_2CH_3$); 6.3 (1H, d, *J* = 1.8, H-3); 7.3 (1H, s, H-8); 7.6 (1H, s, H-5)
7c	1.3 (3H, t, *J* = 7.3, $COOCH_2C\underline{H}_3$); 2.4 (3H, d, *J* = 0.3, 7-CH_3); 2.4 (3H, d, *J* = 1.0, 4-CH_3); 3.9 (2H, s, $C\underline{H}_2C_6H_5$); 4.3 (2H, q, *J* = 7.3, $COOC\underline{H}_2CH_3$); 6.2 (1H, d, *J* = 1.0, H-3); 7.1 (1H, d, *J* = 0.3, H-8); 7.3 (5H, m, $C_6\underline{H}_5$); 7.6 (1H, s, H-5); 12.2 (1H, s, NH)
8a	1.4 (3H, t, *J* = 7.5, $COOCH_2C\underline{H}_3$); 2.6 (3H, d, *J* = 1.0, 4-CH_3); 2.7 (3H, d, *J* = 1.3, 9-CH_3); 4.5 (2H, q, *J* = 7.5, $COOC\underline{H}_2CH_3$); 6.3 (1H, d, *J* = 1.3, H-8); 7.2 (1H, d, *J* = 1.0, H-5); 7.6 (1H, d, *J* = 2.1, H-1); 9.1 (1H, s, NH)
8b	1.4 (3H, t, *J* = 7.5, $COOCH_2C\underline{H}_3$); 2.6 (3H, d, *J* = 0.8, 4-CH_3); 2.7 (3H, d, *J* = 1.1, 9-CH_3); 2.8 (3H, s, 1-CH_3); 4.5 (2H, q, *J* = 7.5, $COOC\underline{H}_2CH_3$); 6.2 (1H, d, *J* = 1.1, H-8); 7.1 (1H, d, *J* = 0.8, H-5); 9.1 (1H, s, NH)
8c	1.1 (3H, t, *J* = 7.5, $COOCH_2C\underline{H}_3$); 1.6 (3H, d, *J* = 1.0, 9-CH_3); 2.6 (3H, d, *J* = 0.8, 4-CH_3); 4.2 (2H, q, *J* = 7.5, $COOC\underline{H}_2CH_3$); 6.0 (1H, d, *J* = 1.0, H-8); 7.2 (1H, d, *J* = 0.8, H-5); 7.4 (5H, m, $C_6\underline{H}_5$); 9.3 (1H, s, NH)

* Spectra of compounds **2**, **3**, **5a-i,m** recorded in DMSO-d_6 and of compounds **5j-l**, **6a,b**, **7c**, **8a-c** in $CDCl_3$.

0.41 mol) and NaOH (11 g, 0.275 mol) in water (250 ml) cooled to 0°C. The yellow solution obtained (pH > 5.5) was stirred for 4 h and the precipitated diazosulfonate was filtered off, washed with isopropanol (10 ml), and dried to give compound **2** as a bright yellow powder (yield 61.5 g, 75%).

Sodium 2-(4,7-Dimethyl-2-oxo-2H-chromen-6-yl)-1-hydrazinosulfonate (3). Zinc dust (2.2 g) was added to suspension of diazosulfonate **2** (10 g, 0.033 mol) in acetic acid (10 ml) and the reaction product was stirred for 3-5 h at 50-60°C until the yellow color had disappeared. It was then treated with water (50 ml), heated to reflux, and the insoluble residue was filtered off and washed with boiling water (30 ml). The filtrate was cooled and the precipitate of hydrazinosulfonate was filtered off. Drying gave compound **3** as white, crystalline needles (yield 8 g, 80%).

4,9-Dimethylpyrano[3,2-*e*]indol-7(3H)-ones (5) (General Method). Suspension of compound **3** (1 g, 0.326 mmol), ketone **4** (0.326 mmol), and *p*-toluenesulfonic acid (1 g, 0.52 mmol) in glacial acetic acid (10-15 ml) was refluxed with stirring under argon atmosphere for 7-12 h and monitored by TLC. The product was cooled and poured into water (150 ml). The precipitated solid was filtered off, washed with water and cold ethanol, and dried to give compounds **5a-m**.

4,9-Dimethyl-2-phenylpyrano[3,2-*e*]indol-7(3H)-one (5a). Yield 0.679 g.

4,9-Dimethyl-2-(4-nitrophenyl)pyrano[3,2-*e*]indol-7(3H)-one (5b). Recrystallized from DMF with activated carbon. Yield 0.708 g.

4,9-Dimethyl-2-(3-nitrophenyl)pyrano[3,2-*e*]indol-7(3H)-one (5c) was purified similarly to compound **5b**. Yield 0.391 g.

2-(4-Fluorophenyl)-4,9-dimethylpyrano[3,2-*e*]indol-7(3H)-one (5d). The compound obtained was suspended in refluxing ethanol, cooled and the precipitate was filtered off and dried to give compound **5d**. Yield 0.217 g.

2-(4-Chlorophenyl)-4,9-dimethylpyrano[3,2-*e*]indol-7(3H)-one (5e) was purified similarly to compound **5d**. Yield 0.691 g.

2-(4-Bromophenyl)-4,9-dimethylpyrano[3,2-*e*]indol-7(3H)-one (5f) was purified similarly to compound **5d**. Yield 0.844 g.

2-(4-Iodophenyl)-4,9-dimethylpyrano[3,2-*e*]indol-7(3H)-one (5g) was purified similarly to compound **5d**. Yield 0.914 g.

1,2,4,9-Tetramethylpyrano[3,2-*e*]indol-7(3H)-one (5h). Yield 0.669 g.

2-Ethyl-1,4,9-trimethylpyrano[3,2-*e*]indol-7(3H)-one (5i). Yield 0.707 g.

2-Butyl-4,9-dimethyl-1-propylpyrano[3,2-*e*]indol-7(3H)-one (5j). Yield 0.731 g.

1-Butyl-4,9-dimethyl-2-pentylpyrano[3,2-*e*]indol-7(3H)-one (5k). Yield 0.787 g.

1,6-Dimethyl-8,9,10,11-tetrahydropyrano[2,3-*c*]carbazol-3(7H)-one (5l). Yield 0.784 g.

1,6-Dimethyl-12,13-dihydrobenzo[*a*]pyrano[2,3-*g*]carbazol-3(7H)-one (5m). Yield 0.925 g.

Azo Coupling Products (6a,b) (General Method). Concentrated HCl (25 ml) and then, at once and with vigorous stirring, solution of sodium nitrite (4 g, 0.055 mol) in water (10 ml) were added to solution of aminocoumarin **1** (9.45 g, 0.05 mol) in acetic acid (50 ml) cooled to -5°C such that the temperature did not exceed 5°C. The reaction product was stirred at this temperature for 2 h and poured into solution of α-alkylacetoacetic ester (0.051 mol) in acetic acid (75 ml) cooled in ice to 0°C and containing crystal hydrate $MeCOONa \cdot 3H_2O$ (50 g, 2.5 mol). The pH should be 5.5. The product was then left for 10 h at room temperature, diluted with equal volume of water, the precipitated solid filtered off, carefully pressed on the filter, and then washed with alcohol and with water, and dried to give **ethyl 2-[(*E*,*Z*-2-(4,7-dimethyl-2-oxo-2H-chromen-6-yl)azo]-2-methyl-3-oxobutanoate (6a)**, yield 15.0 g or **ethyl 2-[(*E*,*Z*-2-(4,7-dimethyl-2-oxo-2H-chromen-6-yl)azo]-3-oxo-2-ethyl-butanoate (6b)**, yield 15.4 g.

Ethyl 2-[(*E*,*Z*)-2-(4,7-Dimethyl-2-oxo-2H-chromen-6-yl)hydrazino]phenylpropionate (7c). Concentrated HCl (25 ml) and then, at once and with vigorous stirring, solution of sodium nitrite (4 g, 0.055 mol) in water (10 ml) was added to solution of aminocoumarin **1** (9.45 g, 0.05 mol) in acetic acid (50 ml)

cooled to -5°C at such a rate that the temperature did not exceed 5°C. The reaction product was stirred at this temperature for 2 h and poured into solution of α-benzylacetoacetic ester (11.22 g, 0.51 mol) in acetic acid (75 ml) cooled in ice to 0°C and containing crystal hydrate $MeCOONa \cdot 3H_2O$ (50 g, 2.5 mol). The pH should be 5.5. The product was then left for 10 h at room temperature, diluted with equal volume of water. The organic phase was separated and treated with hydrochloric acid (20%, 30 ml). After 3 h the solid precipitate was filtered off, carefully pressed on the filter, and washed with alcohol and with water, and dried to give compound **7c**, yield 13 g.

Ethyl 4,9-Dimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indole-2-carboxylate (8a). *p*-Toluenesulfonic acid (1 g) was added to glacial acetic acid (10 ml), the mixture taken to reflux and compound **6a** (1 g, 0.35 mmol) was added, and the product was stirred under reflux for 12 h. The mixture was cooled, poured into ice water (200 ml) and the precipitate was filtered, washed with water, and crystallized from 1,4-dioxane with activated carbon after drying to give compound **8a**. Yield 0.3 g.

Ethyl 1,4,9-Trimethyl-7-oxo-3,7-dihydropyrano[3,2-*e*]indole-2-carboxylate (8b). Thionyl chloride (10-15 ml) was added portionwise to ethanol (30 ml), then compound **6b** (12.4 g, 0.035 mol) was added and the mixture was refluxed under stirring for 12 h. It was then cooled and the precipitate was filtered off, washed with alcohol and with water, and dried to give compound **8b**. Yield 8.8 g.

Ethyl 4,9-Dimethyl-7-oxo-1-phenyl-3,7-dihydropyrano[3,2-*e*]indol-2-carboxylate (8c). Thionyl chloride (10-15 ml) was added portionwise to ethanol (40 ml), then compound **7c** (10.5 g, 0.028 mol) was added and the mixture was refluxed under stirring for 12 h. It was then cooled and the precipitate was filtered off, washed with alcohol and water, and dried to give compound **8c**. Yield 5 g.

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