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CONDENSATION OF OXINDOLE WITH ACETOACETIC ESTER AND ACETYLACETONE

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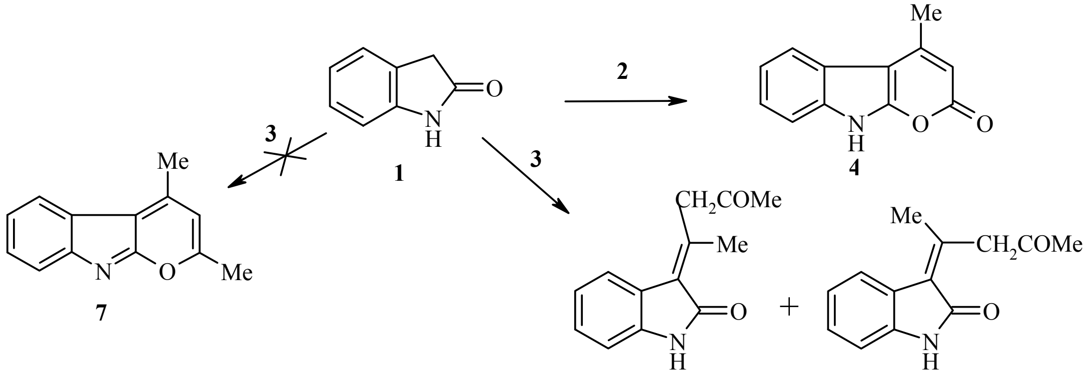
4-Methylpyrano[2,3-b]indol-2-one is formed on thermal condensation of oxindole with acetoacetic ester. The condensation of oxindole with acetylacetone proceeds in position 3 of oxindole without closure in the pyrane ring.

Keywords: acetoacetic ester, acetylacetone, oxindole, pyrano[2,3-*b*]indol-2-one.

Previously we reported the condensation of pyrazolones with β-keto esters leading to pyrano[2,3-*c*]-pyrazol-6-ones.[1]. Results are given in the present report on the condensation of oxindole **1** with acetoacetic ester **2** and acetylacetone **3**.

After heating oxindole **1** with a threefold excess of acetoacetic ester **2** for 12 h (9H)-4-methylpyrano[2,3-*b*]indol-2-one (**4**) was isolated in 18% yield. The composition and structure of compound **4** were confirmed by data of elemental analysis and ^{1}H NMR spectra. The signal of the H-3 proton, like the analogous proton of pyranopyrazolones [1], has a chemical shift of 5.77 ppm, which indicates the formation of a pyrane ring.



1 **4** **7**

5 *E*-isomer, 80%

6 *Z*-isomer, 20%

All attempts to put N-ethyloxindole into this condensation were unsuccessful. Changes in the temperature regimen and also the addition of acidic or basic reagents did not lead to the isolation of an individual compound.

On condensing oxindole with acetylacetone **3** no pyranoindole **7** was obtained. The substance isolated proved to be a mixture of *E*- and *Z*-isomers (**5** and **6**) of 3-(3-oxo-2-pentylylidene)indol-2-one in a ratio of

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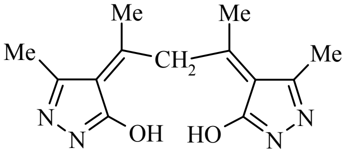
80:20, according to data of ^{1}H NMR spectra, with a total yield of 13%. After repeated recrystallization from methanol pure *E*-isomer was isolated.

Assignment of the *E*- and *Z*-isomers was made on the basis of the fact that the α-methyl (at the carbon atom of the double bond) for the *E*-isomer (2.17 ppm) and the α'-CH_2CO for the *Z*-isomer (3.92 ppm) fall into the region of diamagnetic shift for the anisotropic cone of the C=O group of the indole ring.

It is interesting to note that the condensation of 3-methylpyrazol-5-one with acetylacetone under the same conditions [1] occurs with the participation of one molecule of acetylacetone and two molecules of pyrazolone with the formation of compound **8**.



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EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker MXL 300 (300 MHz) instrument in DMSO-d_6, the UV spectra on a Specord M 40 instrument, and the IR spectra on a Perkin-Elmer instrument (KBr).

(9H)-4-Methylpyrano[2,3-*b*]indol-2-one (4). A mixture of oxindole (2.66 g, 0.02 mol) and acetoacetic ester **2** (3 ml) was heated for 10 h on a metal bath at a bath temperature of 190-200°C, distilling off the water and alcohol. Further ester **2** (about 0.5 ml) was added to the reaction mass after 2, 4, and 6 h from the start of heating. The reaction mixture was then refluxed for 30 min with a mixture of hexane (7 ml) and benzene (5 ml), cooled, and the precipitated crystalline mass was filtered off. This was recrystallized from methanol (5 ml), washed with cold methanol (1 ml), and dried. Pyranoindole **4** (0.73 g, 18%) was obtained; mp 271°C, R_f 0.61 (benzene–acetone, 3:1, Silufol, visualizing with iodine). IR spectrum, ν, cm^{-1}: 1620, 1680 (C=O), 2950-3100. UV spectrum, λ_{max}, nm (log ε): 223 (4.45); 265 (4.03); 274 sh (3.83); 287 sh (3.65); 358 (4.26). ^{1}H NMR spectrum, δ, ppm: 2.61 (3H, s, α-CH_3); 5.77 (1H, s, H-3); 7.24 (1H, m, H-11); 7.24 (1H, m, H-12); 7.43 (1H, t, H-10); 8.78 (1H, t, H-13); 12.5 (1H, s, NH). Found, %: C 72.3; H 4.8; N 7.1. $C_{12}H_9NO_2$. Calculated, %: C 72.4; H 4.5; N 7.0.

1H-3-(3-Oxo-2-pentylidene)indol-2-one (Mixture of *Z*- and *E*-Isomers 5 and 6). A mixture of oxindole (3.99 g, 0.03 mol) and acetylacetone **3** (5 ml) was heated for 14 h in a metal bath at 190°C. Then hexane (7 ml) and benzene (3 ml) were added to the reaction mass and heated to boiling. The crystals precipitated on cooling were filtered off, and recrystallized from methanol (5 ml). Condensation product (0.82 g, 13%) was obtained; mp 170-172°C. IR spectrum, ν, cm^{-1}: 1610, 1690 (C=O), 1715 (C=O), 2900-3100. UV spectrum, λ_{max}, nm (log ε): 224 (3.90); 251 sh (4.27); 261 (4.34); 281 (4.08); 357 (3.08). ^{1}H NMR spectrum *Z*-isomer **6**, δ, ppm: 2.44 (3H, s, α-CH_3); 2.26 (3H, s, $CH_2COC\underline{H}_3$); 3.92 (2H, s, $C\underline{H}_2COCH_3$); 6.83 (1H, d, H-4); 6.98 (1H, m, H-5); 7.21 (1H, m, H-6); 7.56 (1H, d, H-7); 10.38 (1H, s, NH). After repeated recrystallization from methanol pure *E*-isomer **5** was obtained; mp 178-179°C, R_f 0.70 (benzene–acetone, 5:1, Silufol, visualization with iodine). ^{1}H NMR spectrum, δ, ppm: 2.17 (3H, α-CH_3); 2.27 (3H, s, $CH_2COC\underline{H}_3$); 4.25 (2H, s, $C\underline{H}_2COCH_3$); 6.79 (1H, d, H-4); 6.91 (1H, m, H-5); 7.16 (1H, m, H-6); 7.38 (1H, d, H-7); 10.42 (1H, s, NH). Found, %: C 72.4; H 6.4; N 6.5. $C_{13}H_{13}NO_2$. Calculated, %: C 72.6; H 6.0; N 6.5.

REFERENCES

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