

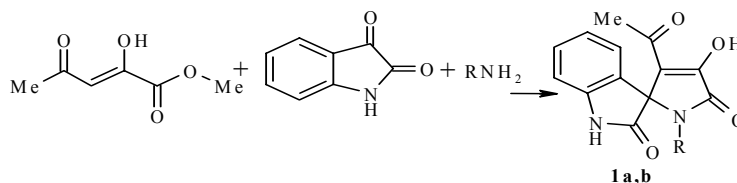
### THREE-COMPONENT SYNTHESIS OF 1-SUBSTITUTED 4-ACETYL- 3-HYDROXYSPIRO[2,5-DIHYDRO- PYRROL-5,3'-INDOLE]-2,2'-DIONES

V. L. Gein<sup>1</sup>, L. F. Gein<sup>2</sup>, E. D. Kuznetsova<sup>1</sup>, M. A. Sheptukha<sup>1</sup>,  
E. P. Tsypliakova<sup>1</sup>, and K. D. Potiemkin<sup>1</sup>

**Keywords:** isatin, methylamine, methyl acetylpyruvate, tryptamine.

It is known that the reaction of esters of acylpyruvic acids with a mixture of an aromatic aldehyde and alkylamine leads to 4-acyl-1-alkyl-5-aryl-3-hydroxy-3-pyrrolin-2-ones [1]. The replacement of the aromatic aldehyde by ninhydrin leads to the formation of alkylammonium 4-acetyl-2,1',3'-trioxospiro[2,5-dihydrofuran-5,2'-indan]olates [2].

We have observed that the brief heating of equivalent amounts of methyl acetylpyruvate, isatin, and methylamine or tryptamine in dioxane leads to the formation of 1-substituted 4-acetyl-3-hydroxyspiro[2,5-dihydropyrrol-5,3'-indole]-2,2'-diones (**1a,b**), which are colorless compounds soluble in ordinary organic solvents.



**1 a** R = Me, **b** R = 2-(indol-3-yl)ethyl

The <sup>1</sup>H NMR spectra were obtained on a Bruker DRX 500 spectrometer at 500 MHz in DMSO-d<sub>6</sub> with TMS as the internal standard. The IR spectra were taken on a UR-20 spectrometer for vaseline mulls. The mass spectra were taken on an MKh-1320 mass spectrometer. The ionizing electron energy was 70 eV.

**4-Acetyl-3-hydroxy-1-methylspiro[2,5-dihydropyrrol-5,3'-indole]-2,2'-dione (1a).** A mixture of methyl acetylpyruvate (1.44 g, 0.01 mol) and isatin (1.47 g, 0.01 mol) in dioxane (10 ml) was heated until the components dissolved. The solution obtained was cooled to room temperature and 1.3 ml aqueous methylamine was added. The reaction mixture was maintained for 5-6 h at room temperature. The precipitate formed was filtered off and recrystallized from ethanol to give compound **1a** (1.12 g, 47%); mp 302-304°C (ethanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 1664 (CH<sub>3</sub>CO), 1726 (C(2)=O), 1832 (C(2')=O), 3144 (NH), 3456 (OH). <sup>1</sup>H NMR spectrum,

<sup>1</sup>Perm State Pharmaceutical Academy, Perm 614990, Russia; e-mail: geinv148@mail.ru. <sup>2</sup>Perm State Medical Academy, Perm 614000, Russia. Translated from *Khimiya Geterotsiklicheskikh Soedinenii*, No. 5, pp. 786-787, May, 2008. Original article submitted March 19, 2008.

$\delta$ , ppm: 2.26 (3H, s, CH<sub>3</sub>); 2.45 (3H, s, CH<sub>3</sub>N); 6.93 (2H, m, H-6' and H-4'); 7.00 (1H, d, H-7'); 7.28 (1H, d, H-5'); 10.86 (1H, s, NH); 13.05 (1H, br. s, OH). Mass spectrum,  $m/z$  ( $I_{\text{rel}}$ , %): [M]<sup>+</sup> 272 (20). Found, %: C 61.62, 61.69; H 4.39, 4.47; N 10.22, 10.31. C<sub>14</sub>H<sub>12</sub>N<sub>2</sub>O<sub>4</sub>. Calculated, %: C 61.76; H 4.44; N 10.29.

**4-Acetyl-3-hydroxy-1-[2-(indol-3-yl)ethyl]spiro[2,5-dihydropyrrol-5,3'-indole]-2,2'-dione (1b)** was obtained analogously in 67% yield (2.68 g); mp 276-278°C (ethanol). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 1664 (CH<sub>3</sub>CO), 1712 (C(2)=O), 1840 (C(2)=O), 3296 (NH), 3456 (OH). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.27 (3H, s, CH<sub>3</sub>); 2.58 (1H, m, CH<sub>A</sub>CH<sub>B</sub>); 2.81 (1H, m, CH<sub>A</sub>CH<sub>B</sub>); 3.14 (2H, m, CH<sub>2</sub>); 6.88-7.46 (9H, m, ArH); 10.80 (1H, s, NH); 10.99 (1H, s, NH); 13.04 (1H, br. s, OH). Found, %: C 61.86, 61.76; H 4.80, 4.69; N 10.55, 10.38. C<sub>23</sub>H<sub>19</sub>N<sub>3</sub>O<sub>4</sub>. Calculated, %: C 68.82; H 4.77; N 10.47.

## REFERENCES

1. V. L. Gein, E. V. Shumilovskikh, E. V. Voronina, R. F. Saraeva, L. F. Gein, B. I. Ugrak, and Yu. S. Andreichikov, *Zh. Org. Khim.*, **64**, 1203 (1994).
2. V. L. Gein, L. F. Gein, E. D. Kuznetsova, and Z. G. Aliev, *Khim. Geterotsykl. Soedin.*, 288 (2005)]. [*Chem. Heterocycl. Comp.*, **41**, 255 (2005)].