

LETTERS
TO THE EDITOR

Simple Three-Component Synthesis of 4-Acyl-1-(2-aminoethyl)-5-aryl-3-hydroxy-2,5-dihydropyrrol-2(1*H*)-ones

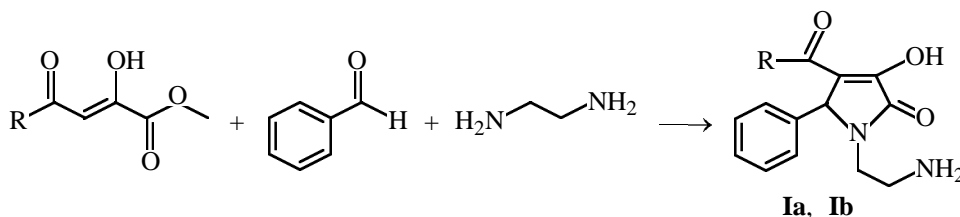
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Ethylenediamine is known [1] to react with acylpyruvic acid esters, yielding 3-acylmethylenehexahydropiperazin-2-ones. We have found that short heating of ethylenediamine with methyl acylpyruvates in dioxane in the presence of an aromatic aldehyde

yields 4-acyl-1-(2-aminoethyl)-5-aryl-3-hydroxy-2,5-dihydropyrrol-2(1*H*)-ones **Ia** and **Ib**. Presumably, in the initial stage ethylenediamine reacts with aromatic aldehyde to give a Schiff base which undergoes intermolecular cyclization with acylpyruvic acid ester.



R = CH₃ (**a**), C₆H₅ (**b**).

Compounds **Ia** and **Ib** are colorless crystalline substances which are poorly soluble in dimethyl sulfoxide and dimethylformamide. Product **Ia** is soluble in hot water. The ¹H NMR spectra of **Ia** and **Ib** contain multiplets from methylene protons of the aliphatic residue at the nitrogen atom: δ 2.70–2.86 (C¹H_A), 2.80–2.90 (C²H₂), 3.59–3.64 ppm (C¹H_B); the 5-H proton gives a singlet at δ 5.04–5.27 ppm; aromatic protons appear as a multiplet at δ 7.15–7.75 ppm; and a broadened two-proton signal at δ 7.85–7.95 ppm belongs to the aliphatic amino group. In the IR spectra of **Ia** and **Ib** we observed absorption bands from the lactam carbonyl group (1680–1697 cm⁻¹), side-chain ketone carbonyl (1635–1650 cm⁻¹), enol hydroxy group (3020–3030 cm⁻¹), and amino group (3230–3240 cm⁻¹). The mass spectra of **Ia** and **Ib** contain the molecular and fragment ion peaks which are consistent with the proposed structures. Compounds **Ia** and **Ib** give an intense cherry color with an alcoholic solution of iron(III) chloride; this test, together with the above spectral data, confirms the enol structure of the products.

4-Acetyl-1-(2-aminoethyl)-3-hydroxy-5-phenyl-2,5-dihydropyrrol-2(1*H*)-one (Ia). To a solution of 0.01 mol of methyl acetylpyruvate and 0.01 mol of benzaldehyde in 10 ml of 1,4-dioxane, we added at room temperature 0.01 mol of ethylenediamine, and the mixture was kept for 3 h at that temperature. The precipitate was filtered off; 1.63 g (63%) of **Ia** was obtained, mp >300°C (from ethanol). IR spectrum, ν, cm⁻¹: 1682 (CON), 1646 (CO), 3023 (OH), 3230 (NH₂). ¹H NMR spectrum (DMSO-*d*₆), δ, ppm: 2.11 s (3H, CH₃), 2.70 m (1H, 1-CH_A), 2.80 m and 2.90 m (2H, CH₂NH₂), 3.59 m (1H, 1-CH_B), 5.04 s (1H, 5-H), 7.20 m (5H, H_{arom}), 7.95 m (2H, NH₂). Mass spectrum, *m/z*: 260 [*M*]⁺, 218 [*M*-CH₃CO]⁺, 184 [*M*-C₆H₅]⁺, 77 [C₆H₅]⁺, 43 [CH₃CO]⁺. Found, %: C 65.10, 64.62; H 6.38, 6.42; N 10.70, 9.98. C₁₄H₁₆N₂O₃. Calculated, %: C 64.60; H 6.20; N 10.76.

1-(2-Aminoethyl)-4-benzoyl-3-hydroxy-5-phenyl-2,5-dihydropyrrol-2(1*H*)-one (Ib). To a solution of 0.01 mol of methyl benzoylpyruvate and 0.01 mol of benzaldehyde in 10 ml of 1,4-dioxane, we added at room temperature 0.01 mol of ethylenediamine, and

the mixture was kept for 3 h at that temperature. The precipitate was filtered off; 1.94 g (60%) of **1b** was obtained, mp 241–243°C (from ethanol). IR spectrum, ν , cm^{-1} : 1697 (CON), 1635 (CO), 3029 (OH), 3236 (NH_2). ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm: 2.83 m (2H, NH_2CH_2), 2.86 m (1H, 1- CH_A), 3.64 m (1H, 1- CH_B), 5.27 s (1H, 5-H), 7.25 m (8H, H_{arom}), 7.74 d (2H, H_{arom}), 7.85 m (2H, NH_2). Mass spectrum, m/z : 322 $[\text{M}]^+$, 208 $[\text{C}_6\text{H}_5\text{CH}=\text{CHCOC}_6\text{H}_5]^+$, 105 $[\text{C}_6\text{H}_5\text{CO}]^+$, 77 $[\text{C}_6\text{H}_5]^+$. Found, %: C 70.65, 70.71; H 5.60, 5.64; N 8.68, 8.71. $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}_3$. Calculated, %: C 70.79; H 5.63; N 8.69.

The IR spectra were recorded on a UR-20 spectrometer in mineral oil, the ^1H NMR spectra were measured on a Bruker DRX-500 instrument at 500.13 MHz, and the mass spectra (electron impact, 70 eV) were run on an MKh-1320 mass spectrometer.

REFERENCES

1. Milyutin, A.V., Safonova, N.V., Goleneva, A.F., Andreichikov, Yu.S., Tul'bovich, G.A., and Makhmudov, R.R., *Khim.-Farm. Zh.*, 1994, vol. 28, no. 12, p. 37.