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SIMPLE THREE-COMPONENT SYNTHESIS OF 4-ACYL-5-PHENYL-1-(2-HETERYL)-3-HYDROXY-3-PYRROLIN-2-ONES

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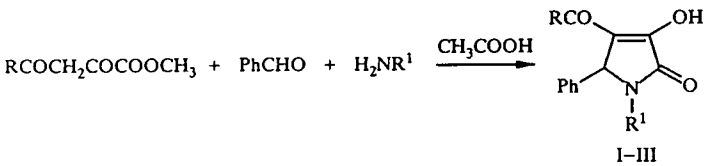
We have discovered that brief heating of a mixture of equimolar amounts of methyl pyruvate, aromatic aldehyde, and a heterylamine (2-aminopyridine or 2-aminothiazole) in glacial acetic acid gives 4-acyl-5-phenyl-1- (2-heteryl)-3-hydroxy-3-pyrrolin-2-ones (I-III) in high yield. Thus, we are the first to report the synthesis of 4,5-disubstituted 3-hydroxy-3-pyrrolin-2-ones containing a heterocyclic substituent at $N_{(1)}$, which are capable of giving condensed heterocyclic systems with possible biological activity.



I–III

I R = Ph; R^1 = 2-pyridyl; II R = Me; R^1 = 2-pyridyl; III R = Ph; R^1 = 2-thiazolyl

Products I-III are colorless, crystalline compounds with limited solubility in acetic acid, dioxane, ethanol, DMSO, and DMF. These compounds give a cherry red color with ethanolic ferric chloride. The PMR spectra of these products have a singlet for the proton at $C_{(5)}$ at 6.36-6.73 ppm and a multiplet for the aromatic protons at 7.46-8.2 ppm. The PMR spectrum of II has a singlet for the acetyl methyl group at 2.43 ppm.

4-Benzoyl-5-phenyl-3-hydroxy-1-(2-pyridyl)-3-pyrrolin-2-one (I). A sample of 5 mmoles methyl benzoylpyruvate was added to a mixture of 5 mmoles benzaldehyde and 5 mmoles 2-aminopyridine in 2 ml glacial acetic acid. The reaction mixture was heated at reflux for 30 min and cooled. The crystalline precipitate was filtered off to give 1.06 g (60%) I, mp 226.5-227.0°C (from acetic acid, dec.). IR Spectrum (Vaseline mull): 3190 (O–H), 1700 (O=C–N), 1690 (C=O), 1640 cm^{-1} (C=C). ^1H NMR Spectrum in DMSO-d_6 (HMDS): 6.36 (1H, s, $C_{(5)}H$), 7.28-7.46 ppm (14H, m, 2Ph, pyridyl). R_f 0.56 (Silufol UV-254, 1:1 benzene–ether). Found: C, 74.05; H, 4.65; N, 7.62%. Calculated for $C_{21}H_{16}N_2O_3$: C, 74.14; H, 4.53; N, 7.86%

4-Acetyl-5-phenyl-3-hydroxy-1-(2-pyridyl)-3-pyrrolin-2-one (II) was obtained in 35% yield, mp 239-239.5°C (from acetic acid, dec.). ^1H NMR Spectrum in DMSO-d_6 (HMDS): 6.41 (1H, s, $C_{(5)}H$), 7.34-7.53 (9H, m, Ph, pyridyl), 2.43 ppm (3H, s, Me). R_f 0.62 (Silufol UV-254, 1:1 benzene–ether). Found: C, 69.18; H, 4.67; N, 9.43%. Calculated: C, 69.38; H, 4.79; N, 9.52%.

4-Benzoyl-5-phenyl-3-hydroxy-1-(2-thiazolyl)-3-pyrrolin-2-one (III) was obtained in 43% yield, mp 226-227°C (from acetic acid, dec.). ^1H NMR Spectrum in DMSO-d_6 (HMDS): 6.23 (1H, s, $C_{(5)}H$), 7.05-7.50 (10H, m, 2Ph), 7.93-8.27 ppm (2H, d, thiazolyl). R_f 0.38 (Silufol UV-254, 1:1 benzene–ether). Found: C, 66.08; H, 3.52; N, 7.93; S, 9.13%. Calculated for $C_{20}H_{14}N_2O_3S$: C, 66.28; H, 3.89; N, 7.73; S, 8.85%.

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