ISSN 1070-4280, Russian Journal of Organic Chemistry, 2008, Vol. 44, No. 10, pp. 1562–1563. © Pleiades Publishing, Ltd., 2008.
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SHORT COMMUNICATIONS

Synthesis of Tetrahydropyrimidin-2-one Derivatives from *N-tert*-Butylurea

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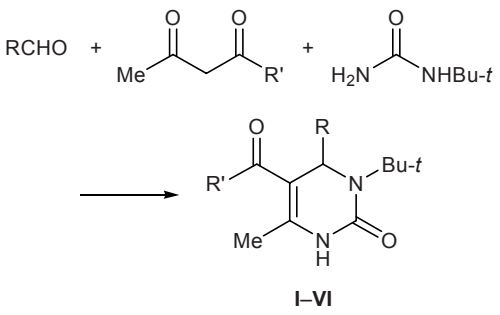
Received October 6, 2007

DOI: 10.1134/S1070428008100321

It is known that some functionalized oxo derivatives of pyrimidines exhibit a broad spectrum of biological and pharmacological activity. Dihydropyrimidine-5-carboxylate moiety is a structural fragment of many natural marine products, in particular *batzelladine* alkaloids which inhibit HIV gp-120-CD_4 [1]. In addition, 4-aryldihydropyrimidinones are potent calcium channel blockers, antihypertensive agents, α_{1a}-adrenergic antagonists, and neuropeptide antagonists [2]. The possibility of using pyrimidinone derivatives as new class of calcium channel blockers has attracted interest of many researchers.

Taking the above stated into account, one-pot synthesis of some pyrimidinone derivatives in the presence of trichloroacetic acid was performed [3]. In continuation of studies in this field, the present communication reports on a new three-component condensation of ethyl acetoacetate with *N-tert*-butylurea and aromatic aldehydes, which leads to the formation of ethyl 3-*tert*-butyl-6-methyl-2-oxo-4-R-1,2,3,4-tetrahydropyrimidine-5-carboxylates **I**–**III** in 70% yield. The condensation with another CH acid, acetylacetone, gave analogous products, 5-acetyl-3-*tert*-butyl-6-methyl-4-R-3,4-dihydropyrimidin-2(1*H*)-ones **IV**–**VI** in ~80% yield. The IR spectra of the condensation products contained strong absorption bands due to stretching vibrations of the C^5=O carbonyl group at 1675–1690 cm^{-1}, ester carbonyl group in compounds **I**–**III** at 1745–1750 cm^{-1}, and NH bond at 3375 cm^{-1}.



I–VI

I, **IV**, R = Ph; **II**, **V**, R = 2-HOC_6H_4; **III**, **VI**, R = 2-HO-5-BrC_6H_3; **I**–**III**, R′ = EtO; **IV**–**VI**, R′ = Me.

General procedure for the synthesis of compounds I–VI. A mixture of 25 mmol of the corresponding aromatic aldehyde, 38 mmol of ethyl acetoacetate or acetylacetone, 5.8 g (0.05 mol) of *N-tert*-butylurea, 25 mg of trichloroacetic acid, and 10 ml of 95% ethanol was stirred for 2–4 h at 78°C. The progress of the reaction was monitored following the disappearance of organic substrate (ethyl acetoacetate or acetylacetone) by TLC using Silufol UV-254 plates (eluent ethyl acetate–hexane, 1:1). When the reaction was complete, the mixture was cooled to room temperature, and the precipitate was filtered off, washed with ethanol, dried, and recrystallized from aqueous ethanol.

Ethyl 3-*tert*-butyl-6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (I). Yield 70%, mp 150–151°C. IR spectrum, ν, cm^{-1}: 1255, 1680, 1745, 3350. ^{1}H NMR spectrum, δ, ppm: 1.31 t (3H, CH_3), 1.40 s (9H, *t*-Bu), 2.50 s (3H, CH_3), 4.35 d (2H, CH_2O), 4.70 s (1H, CH), 7.68–7.89 m (5H, H_{arom}), 8.78 s (1H, NH). Found %: C 68.44; H 7.64; N 8.90. $C_{18}H_{24}N_2O_3$. Calculated, %: C 68.35; H 7.59; N 8.86.

Ethyl 3-*tert*-butyl-4-(2-hydroxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (II). Yield 69%, mp 220–222°C. IR spectrum, ν, cm^{-1}: 1250, 1675, 1740, 3330. ^{1}H NMR spectrum, δ, ppm: 1.30 t (3H, CH_3), 1.47 s (9H, *t*-Bu), 2.55 s (3H, CH_3), 4.30 d (2H, CH_2O), 4.85 s (1H, CH), 7.25–

7.55 m (4H, H_{arom}), 9.40 s (1H, NH), 10.0 s (1H, OH). Found, %: C 65.09; H 7.17; N 8.50. $C_{18}H_{24}N_2O_4$. Calculated, %: C 65.06; H 7.22; N 8.43.

Ethyl 4-(5-bromo-2-hydroxyphenyl)-3-*tert*-butyl-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (III). Yield 67%, mp 240–241°C. IR spectrum, ν, cm^{-1}: 1250, 1675, 1740, 3330. ^1H NMR spectrum, δ, ppm: 1.36 t (3H, CH_3), 1.41 s (9H, *t*-Bu), 2.57 s (3H, CH_3), 4.25 d (2H, CH_2O), 4.70 s (1H, CH), 7.00–7.60 m (3H, H_{arom}), 8.70 s (1H, NH), 10.4 s (1H, OH). Found, %: C 52.60; H 5.65; Br 19.50; N 6.74. $C_{18}H_{23}BrN_2O_4$. Calculated, %: C 52.55; H 5.59; Br 19.46; N 6.81.

5-Acetyl-3-*tert*-butyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1*H*)-one (IV). Yield 80%, mp 130–132°C. IR spectrum, ν, cm^{-1}: 1255, 1675, 3335. ^1H NMR spectrum, δ, ppm: 1.40 s (9H, *t*-Bu), 2.21 s (3H, CH_3), 2.50 s (3H, CH_3), 4.70 s (1H, CH), 7.68–7.89 m (5H, H_{arom}), 8.78 s (1H, NH). Found, %: C 71.36; H 7.52; N 9.68. $C_{17}H_{22}N_2O_2$. Calculated, %: C 71.32; H 7.69; N 9.79.

5-Acetyl-3-*tert*-butyl-4-(2-hydroxyphenyl)-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (V). Yield 77%, mp 196–197°C. IR spectrum, ν, cm^{-1}: 1680, 3335, 1245. ^1H NMR spectrum, δ, ppm: 1.37 s (9H, *t*-Bu), 2.20 s (3H, CH_3), 2.55 s (3H, CH_3), 4.85 s (1H, CH), 7.25–7.55 m (4H, H_{arom}), 9.40 s (1H, NH), 9.8 s (1H, OH). Found, %: C 67.46; H 7.32; N 9.28. $C_{17}H_{22}N_2O_3$. Calculated, %: C 67.54; H 7.28; N 9.27.

5-Acetyl-4-(5-bromo-2-hydroxyphenyl)-3-*tert*-butyl-6-methyl-3,4-dihydropyrimidin-2(1*H*)-one (VI). Yield 78%, mp 215–216°C. IR spectrum, ν, cm^{-1}: 1680, 3335, 1245. ^1H NMR spectrum, δ, ppm: 1.41 s (9H, *t*-Bu), 2.21 s (3H, CH_3), 2.57 s (3H, CH_3), 4.70 s (1H, CH), 7.00–7.58 m (3H, H_{arom}), 8.60 s (1H, NH), 10.4 s (1H, OH). Found, %: C 53.46; H 5.42; Br 20.87; N 7.29. $C_{17}H_{21}BrN_2O_3$. Calculated, %: C 53.54; H 5.51; Br 20.99; N 7.34.

The ^1H NMR spectra were recorded at 25°C on a Bruker spectrometer (300 MHz) from solutions in DMSO-d_6. The IR spectra were measured in mineral oil on a Specord 75IR instrument. The progress of reactions and the purity of products were monitored by thin-layer chromatography.

REFERENCES

1. Snider, B.B, Chen, J., Patil, A.D., and Freyer, A., *Tetrahedron Lett*., 1996, vol. 37, p. 6977.
2. Rovnyak, G.C., Atwal, K.S., Hedberg, A., Kimball, S.D., Moreland, S., Gougoutas, J.Z., Schwartz, J., O'Reilly, B.C., and Malley, M.F., *J. Med. Chem*., 1992, vol. 35, p. 3254.
3. Magerramov, A.M., Kurbanova, M.M., Abdinbekova, R.T., Rzaeva, I.A., Farzaliev, V.M., and Allakhverdiev, M.A., *Zh. Prikl. Khim*., 2006, vol. 79, p. 796.