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SYNTHESIS OF DERIVATIVES OF 3-METHYL-4-PHENYL-3*a*,4,5,6,7*a*-HEXAHYDRO-1H-PYRAZOLO-[4,5-*d*]PYRIMIDIN-6-ONE

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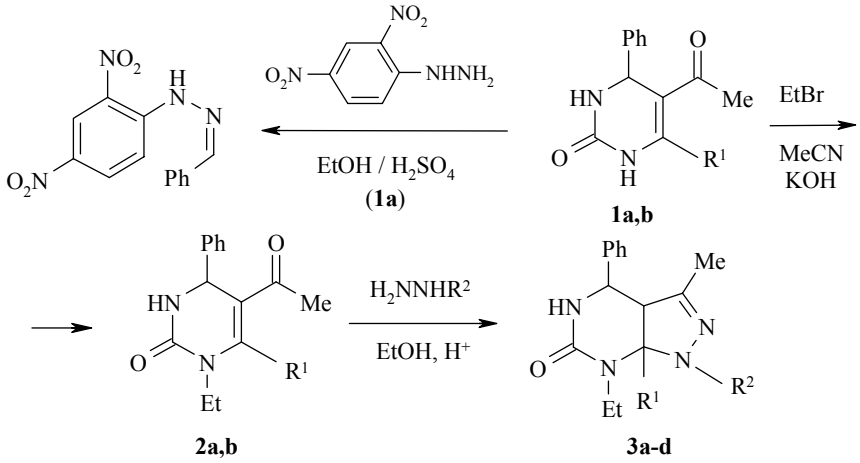
Derivatives of 4-phenyl-3,4-dihydro-2(1H)-pyrimidinones have a broad spectrum of pharmacological properties [1, 2].

We have studied the reaction of compounds **1** and **2** with hydrazines in ethanolic medium in the presence of catalytic amounts of acid. There have been reports concerning the reaction of compound **1a** with 2,4-dinitrophenylhydrazine and NH_2OH [3] but we were unable to reproduce these results. Furthermore, heating **1a** with 2,4-dinitrophenylhydrazine in the presence of conc. H_2SO_4 (the conditions for carrying out the qualitative test for a CO group [4]) led to the complete destruction of the ring, leading to the isolation only of the 2,4-dinitrophenylhydrazone of benzaldehyde.

Even though derivatives of 5-acetyltriazolo[4,5-*b*]pyrimidine with a structure similar to **1a** react readily with 1,2-binucleophiles [5], pyrimidinone **1a**, which is not substituted at $N_{(1)}$ in the 3,4-dihydropyrimidine ring, does not react with NH_2OH, hydrazine, or hydrazine derivatives.



1,2 a R^1 = H, **b** R^1 = Me; **3 a** $R^1 = R^2$ = H, **b** R^1 = Me, R^2 = H, **c** R^1 = H, R^2 = Ph, **d** R^1 = Me, R^2 = Ph

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On the other hand, the reaction of 1-ethyl derivatives **2a**,**b** with excess hydrazine or phenylhydrazine in the presence of conc. HCl proceeds rather readily to give bicyclic pyrimidinones **3a,d**.

The lack of reactivity of **1a** is likely related to the acidic proton $N_{(1)}H$ and the tendency of this compound to undergo amide-imidol tautomerization.

The ^1H NMR spectra were taken on a Varian Mercury VX-200 spectrometer at 200 MHz in DMSO-d_6 using TMS as the internal standard. The IR spectra were taken on a Specord-75 IR spectrometer for KBr pellets. The mass spectra were taken on an Agillent mass spectrometer.

Pyrimidinones 1a,b, 2a,b were obtained according to our previous procedure [6].

Pyrimidinones 3a-d (General Method). A solution of 1(N)-alkyl derivative **2** (1.16 mmol), corresponding hydrazine (11.6 mmol), and four drops of concentrated hydrochloric acid in ethanol (3 ml) was heated at reflux for 3 h and left for 15-20 h. The crystalline precipitate was filtered off and washed thrice with 3-ml portions of 10:20:1 ethanol–water–piperidine.

7-Ethyl-3-methyl-4-phenyl-3*a*,4,5,6,7,7*a*-hexahydro-1H-pyrazolo[4,5-*d*]pyrimidin-6-one (3a). Yield 32%; mp 183-185°C (ethanol). IR spectrum, ν, cm^{-1}: 1682, 2930, 3080, 3216, 3370. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.22 (1H, m, H-7a); 7.10-7.35 (5H, m, C_6H_5); 6.70 (1H, s, H-4); 6.0 (1H, br. s, $N_{(1)}H$); 5.92 (1H, br. s, $N_{(5)}H$); 5.32 (1H, d, *J* = 3.2, H-3a); 3.28-3.62 (2H, m, CH_2); 1.75 (3H, s, 3-CH_3); 1.07 (3H, t, *J* = 7, $CH_2C\underline{H}_3$). Found, %: N 21.90. $C_{14}H_{18}N_4O$. Calculated, %: N, 21.69.

7-Ethyl-3,7*a*-dimethyl-4-phenyl-3*a*,4,5,6,7,7*a*-hexahydro-1H-pyrazolo[4,5-*d*]pyrimidin-6-one (3b). Yield 44%; mp 216-218°C (ethanol). IR spectrum, ν, cm^{-1}: 1582, 1622, 2970. ^1H NMR spectrum, δ, ppm (*J*, Hz): 12.0 (1H, br. s, $N_{(1)}H$); 7.09-7.5 (5H, m, C_6H_5); 6.34 (1H, d, *J* = 8.2, H-4); 5.86 (1H, d, *J* = 8.2, $N_{(5)}H$); 5.77-5.95 (1H, m, H-3a); 2.90-3.15 (2H, m, CH_2); 1.93 (3H, s, 3-CH_3); 1.93 (3H, s, 7a-CH_3); 0.98 (3H, t, *J* = 7, $CH_2C\underline{H}_3$). Mass spectrum (electron impact, 70 eV), *m/z* (I_{rel}, %): 273 [M+1] (100), 203 (10). Found, %: N 20.92. $C_{15}H_{20}N_4O$. Calculated, %: N 20.57.

7-Ethyl-3-methyl-1,4-diphenyl-3*a*,4,5,6,7,7*a*-hexahydro-1H-pyrazolo[4,5-*d*]pyrimidin-6-one (3c). Yield 22%; mp 185-187°C (ethanol). IR spectrum, ν, cm^{-1}: 1602, 1682, 3080, 3223. ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.89 (1H, s, $N_{(5)}H$); 7.40-7.45 (1H, m, ArH); 7.25-7.35 (4H, m, ArH); 7.18 (1H, t, *J* = 6.4, ArH); 7.13 (2H, t, *J* = 7.6, ArH); 6.98 (2H, d, *J* = 7.6, ArH); 6.89 (1H, s, H-7a); 6.66 (1H, t, *J* = 7.2, H-4); 5.51 (1H, d, *J* = 2.8, H-3a); 3.40-3.65 (2H, m, CH_2); 1.98 (3H, s, 3-CH_3); 1.14 (3H, t, *J* = 6.8, $CH_2C\underline{H}_3$). Found, %: N 17.01. $C_{20}H_{22}N_4O$. Calculated. %: N, 16.75.

7-Ethyl-3,7*a*-dimethyl-1,4-diphenyl-3*a*,4,5,6,7,7*a*-hexahydro-1H-pyrazolo[4,5-*d*]pyrimidin-6-one (3d). Yield 33%; mp 168-170°C (ethanol). IR spectrum, ν, cm^{-1}: 1600, 1669, 2923, 3196. ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.83 (1H, s, $N_{(5)}H$); 6.93-7.38 (10H, m, ArH); 6.66 (1H, t, *J* = 7.0, H-4); 5.13 (1H, d, *J* = 2.4, H-3a); 3.3-3.9 (2H, m, CH_2); 2.05 (3H, s, 3-CH_3); 1.88 (3H, s, 7a-CH_3); 1.05 (3H, t, *J* = 7.0, $CH_2C\underline{H}_3$). Found, %: N 16.33. $C_{21}H_{24}N_4O$. Calculated, %: N 16.08.

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