SYNTHESIS OF DERIVATIVES OF 5-(4,5-DIHYDRO-1H-3-PYRAZOLYL)-3,4-DIHYDRO-2(1H)-PYRIMIDONE

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In previous work [1], we showed that hydrazines react with 5-acetyl-1-ethyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidones at the acetyl group and C-6 in the heterocyclic ring to give derivatives of hexahydro-[4,5-*d*]pyrimidin-6-one. The presence of a cinnamoyl group in compound **1a-f** complicates the reaction of these compounds with hydrazines since both cross-conjugated enone fragments can enter the reaction. *A priori*, such a reaction could take place either at the 5-cinnamoyl group (a) or at the endocyclic enone group (b).

We have found that compound **1a-f** in ethanol react with hydrazines in the presence of HCl upon heating at reflux as heterocyclic chalcone analogs. The reaction of compound **1d** with phenylhydrazine was also carried out in ethanol in the presence of KOH but the yield of compound **2f** in this case is only 25% in contrast to 43% in acid medium.

Products **2a-h** are solid colorless or yellow compounds possessing luminescence in the solid state as well as in neutral and alkaline ethanolic solutions.

The ^{1}H NMR spectra were taken on a Varian Mercury VX-200 spectrometer at 200 MHz in DMSO-d_6 with TMS as the internal standard. The IR spectra were taken on a Specord IR-75 spectrometer for KBr pellets. The mass spectra were taken on an Agillent 1100 LC-MS.

Ketones 1a-f were obtained according to our previous work [2].

Pyrimidones 2a-h (General Method). A solution of corresponding ketone **1** (0.8 mmol), hydrazine (8 mmol), and five drops of concentrated hydrochloric acid in 4 ml ethanol was heated at reflux for 3 h. The product was filtered off and washed thrice with 5 ml portions of 10:20:1 ethanol–water–piperidine.

1-Ethyl-5-[5-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2a) was obtained in 22% yield; mp 188-190°C (EtOH). IR spectrum, ν, cm^{-1}: 1502, 1608, 1682, 2923, 3063. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.58 (1H, br. d, *J* = 2.8, NH); 6.72 (1H, s, H-6); 6.40-7.40 (14H, m, ArH); 5.43 (1H, d, *J* = 2.8, H-4); 5.07-5.32 (1H, m, CH); 3.68 (3H, s, OCH_3); 3.0-3.4 (3H, m, $CH_3C\underline{H}_2$ + CH); 2.60-2.90 (1H, m, CH); 1.09 (3H, t, *J* = 7.0, CH_3). Found, %: N 12.57. $C_{28}H_{28}N_4O_2$. Calculated, %: N 12.38.

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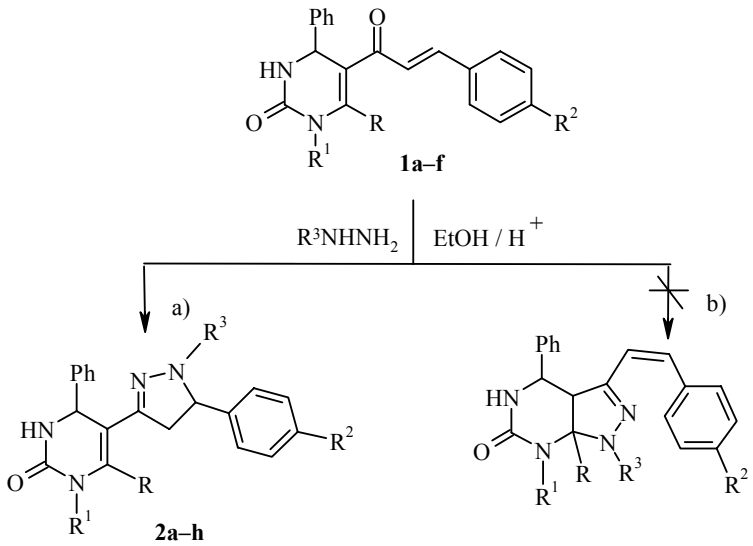

1 a R = H, **b–f** R = Me; **a**, **c–f** R^1 = Et, **b** R^1 = Me; **a**, **b**, **d** R^2 = OMe, **c** R^2 = H, **e** R^2= NMe_2, **f** R = Br; **2 a** R = H, **b–h** R = Me; **a**, **c–h** R^1 = Et, **b** R^1 = Me, **a**, **b**, **d–f** R^2 = OMe, **c** R^2 = H, **g** R^2 = NMe_2, **h** R^2 = Br; **a–c**, **f–h** R^3 = Ph, **d** R^3 = H, **e** R^3 = Et

5-[5-(4-Methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-1,6-dimethyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2b) was obtained in 32% yield; mp 243-245°C (EtOH). IR spectrum, ν, cm^{-1}: 1502, 1596, 1675, 2916, 3076. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.69 (1H, br. d, *J* = 3.2, NH); 7.15-7.40 (5H, m, ArH); 7.05 (2H, t, *J* = 7.6, ArH); 6.36-7.00 (7H, m, ArH); 5.37 (1H, d, *J* = 3.2, H-4); 5.21 (1H, dd, J_1 = 11.2, J_2 = 4.4, CH); 3.72 (1H, dd, J_1 = 16.8, J_2 = 11.2, CH); 3.64 (3H, s, OCH_3); 3.05 (3H, s, NCH_3); 2.75 (1H, dd, J_1 = 16.8, J_2 = 4.4, CH); 2.22 (3H, s, 6-CH_3). Found, %: N 12.53. $C_{28}H_{28}N_4O_2$. Calculated, %: N 12.38.

1-Ethyl-5-(1,5-diphenyl-4,5-dihydro-1H-pyrazol-3-yl)-6-methyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2c) was obtained in 37% yield; mp 204-206°C (EtOH). IR spectrum, ν, cm^{-1}: 1595, 1662, 3056, 3210, 3403. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.60 (1H, br. d, *J* = 2.8, NH); 6.86-7.40 (12H, m, ArH); 6.79 (2H, t, *J* = 7.8, ArH); 6.60 (1H, t, *J* = 7.4, ArH); 5.36 (1H, d, *J* = 2.8, H-4); 5.17-5.32 (1H, m, CH); 3.30-3.90 (3H, m, $CH_3C\underline{H}_2$ + CH); 2.80 (1H, dd, J_1 = 16.6, J_2 = 4.8, CH); 2.24 (3H, s, 6-CH_3); 1.04 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Found, %: N 13.02. $C_{28}H_{28}N_4O$. Calculated, %: N 12.83.

1-Ethyl-5-[5-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-6-methyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2d) was obtained in 29% yield; mp 157-159°C (EtOH). IR spectrum, ν, cm^{-1}: 1682, 2923, 3230, 3290. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.47 (1H, br. d, *J* = 2.8, N(3)H); 6.70-7.50 (6H, m, C_6H_5 + NH); 7.05 (2H, d, *J* = 8.6, ArH); 6.74 (2H, d, *J* = 8.6, ArH); 5.15 (1H, d, *J* = 2.8, H-4); 4.55 (1H, t, *J* = 9.4, CH); 3.68 (3H, s, OCH_3); 3.60-3.90 (1H, m, CH); 3.00-3.60 (2H, m, CH_2); 2.55 (1H, dd, J_1 = 15.0, J_2 = 9.4, CH); 2.16 (3H, s, 6-CH_3); 0.99 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Found, %: N 14.57. $C_{23}H_{26}N_4O_2$. Calculated, %: N 14.35.

1-Ethyl-5-[5-(1-ethyl-4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-3-yl]-6-methyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2e) was obtained in 21% yield; mp 183-185°C (EtOH). IR spectrum, ν, cm^{-1}: 1662, 2956, 3210. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.54 (1H. br. d, *J* = 3.2, N(3)H); 7.10-7.40 (7H, m, ArH); 6.85 (2H, d, *J* = 8.6, ArH); 5.14 (1H, d, *J* = 4.0, H-4); 3.71 (3H, s, OCH_3); 3.60-4.20 (2H, m, CH_2); 3.00-3.60 (3H, m, H Alk); 2.40-2.90 (2H, m, H Alk); 2.17 (3H, s, 6-CH_3); 1.00 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$); 0.97 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Found, %: N 13.20. $C_{25}H_{30}N_4O_2$. Calculated, %: N 13.39.

1-Ethyl-5-[5-(4-methoxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-6-methyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2f) was obtained in 43% yield; mp 194-195°C (EtOH); IR spectrum, ν, cm^{-1}: 1596,

1669, 3050, 3183. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.57 (1H, br. d, *J* = 2.6, NH); 6.40-7.40 (14H, m, ArH); 5.36 (1H, d, *J* = 2.6, H-4); 5.21 (1H, dd, J_1 = 11.8, J_2 = 5.0, CH); 3.66 (3H, s, OCH_3); 3.40-4.00 (3H, m, $CH_3C\underline{H}_2$ + CH); 2.79 (1H, dd, J_1 = 17.0, J_2 = 5.0, CH); 2.25 (3H, s, 6-CH_3); 1.05 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Mass spectrum, *m/z* (I_{rel}, %): 467 $[M+1]^+$ (100). Found, %: N 11.95. $C_{29}H_{30}N_4O_2$. Calculated, %: N 12.01.

5-[5-(4-Dimethylaminophenyl)-6-methyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-1-ethyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2g) was obtained in 13% yield; mp 225-227°C (EtOH). IR spectrum, ν, cm^{-1}: 1495, 1596, 1675, 2910, 3430. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.59 (1H, br. d, *J* = 2.8, NH); 7.15-7.40 (5H, m, ArH); 7.04 (2H, t, *J* = 8.0, ArH); 6.82 (2H, d, *J* = 8.0, ArH); 6.76 (2H, d, *J* = 8.0, ArH); 6.59 (1H, t, *J* = 8.0, ArH); 6.47 (2H, d, *J* = 8.0, ArH); 5.34 (1H, d, *J* = 2.8, H-4); 5.12 (1H, dd, J_1 = 11.2, J_2 = 4.8, CH); 3.40-4.00 (3H, m, $CH_3C\underline{H}_2$ + CH); 2.67-2.85 (1H, m, CH); 2.78 (6H, s, $N(CH_3)_2$); 2.23 (3H, s, 6-CH_3); 1.03 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Found, %: N 14.91. $C_{30}H_{33}N_5O$. Calculated, %: N 14.60.

5-[5-(4-Bromophenyl)-6-methyl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl]-1-ethyl-4-phenyl-3,4-dihydro-2(1H)-pyrimidone (2h) was obtained in 25% yield; mp 233-235°C (EtOH). IR spectrum, ν, cm^{-1}: 1595, 1669, 2916, 3063, 3210. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.60 (1H, br. d, *J* = 2.8, NH); 7.20-7.40 (7H, m, ArH); 7.08 (2H, t, *J* = 8.0, ArH); 6.87 (2H, d, *J* = 8.0, ArH); 6.81 (2H, d, *J* = 8.0, ArH); 6.63 (1H, t, *J* = 7.4, ArH); 5.35 (1H, d, *J* = 2.8, H-4); 5.29 (1H, dd, J_1 = 11.6, J_2 = 4.6, CH); 3.20-4.00 (3H, m, $CH_3C\underline{H}_2$ + CH); 2.82 (1H, dd, J_1 = 16.0, J_2 = 4.8, CH); 2.25 (3H, s, 6-CH_3); 1.05 (3H, t, *J* = 7.0, $C\underline{H}_3CH_2$). Found, %: N 10.81. $C_{28}H_{27}BrN_4O$. Calculated, %: N 10.87.

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