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# SYNTHESIS OF 1,6-POLYMETHYLENE PYRIMIDINES BASED ON 4-(1-AZA-CYCLOALKYLIDENE)-1,3-OXAZOL-5-ONES

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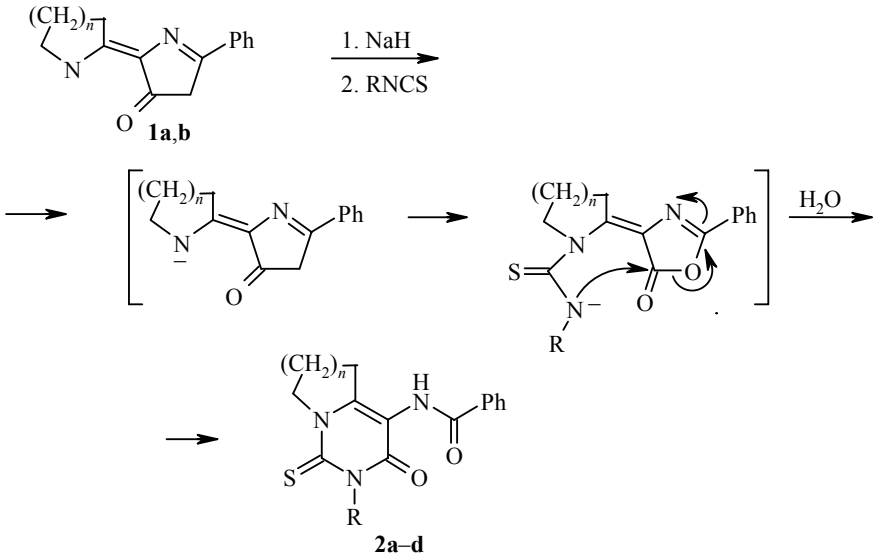
We propose a novel method for obtaining derivatives of 1,6-polymethylene pyrimidines, which are intermediates in synthesis of some alkaloids [1]. The method is based on reaction of 4-(2-azacycloalkylidene)-1,3-oxazol-5-ones **1a,b** with isothiocyanates in DMF in the presence of sodium hydride. We hypothesize that during the reaction, the anion formed from compound **1** is added to the isothiocyanate molecule, which is followed by recyclization, leading to the 4-oxo-2-thioxo-5-benzoylamino-1,6-polymethylene pyrimidine derivatives **2a-d**.

The structure of compounds **2a-d** has been proven based on the $^{1}H$ and $^{13}C$ NMR spectra and elemental analysis data.

Enamines that are structurally similar to **1**, containing an ester and a nitrile group in the β-position, react with heterocumulenes, yielding 1,6-polymethylene pyrimidine derivatives.




**1 a** *n* = 1, **b** *n* = 3; **2 a** *n* = 1, R = Ph, **b** *n* = 1, R = 2-methylpropen-2-yl, **c** *n* = 3, R = Ph, **d** *n* = 3, R = Me

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**General Procedure for Obtaining Compounds 2a-d.** Sodium hydride (12 mmol, 60% suspension in mineral oil) was added to a solution of the appropriate oxazolone [2, 3] (10 mmol) in dry DMF. The mixture was stirred at room temperature for 30 min, the appropriate isothiocyanate was added (10 mmol), and the mixture was stirred for another 8 h. Water was added, the mixture was stirred for 1 h, and the precipitate formed was filtered out.

**N-(3-Oxo-2-phenyl-1-thioxo-1,2,3,5,6,7-hexahydropyrrolo[1,2-*c*]pyrimidin-4-yl)benzamide (2a).** Yield 36%; mp 243-245°C (*i*-PrOH–EtOH). $^1$H NMR spectrum (DMSO-$d_6$, 300 MHz), δ, ppm (*J*, Hz): 2.15-2.25 (2H, m, 6-$CH_2$); 3.14 (2H, t, *J* = 7.8, 5-$CH_2$); 4.33 (2H, t, *J* = 7.8, 7-$CH_2$); 7.14-7.17 (2H, m, arom.); 7.38-7.59 (6H, m, arom.); 7.96-7.99 (2H, m, arom.); 9.74 (1H, s, NH). $^{13}$C NMR spectrum (DMSO-$d_6$, 75 MHz), δ, ppm: 20.21 (6-C), 31.14 (5-C), 56.61 (7-C), 111.86 (4-C), 128.32, 128.39, 129.20, 129.03, 129.85, 132.45, 133.96, 140.28, 154.48, 159.59 (CO), 165.77 (NHCOPh), 174.38 (CS). Found, %: C 66.43; N 11.23. $C_{20}H_{17}N_3O_2S$. Calculated, %: C 66.10; N 11.56.

**N-[2-(2-Methylpropen-2-yl)-3-oxo-1-thioxo-1,2,3,5,6,7-hexahydropyrrolo[1,2-*c*]-pyrimidin-4-yl]-benzamide (2b).** Yield 42%; mp 202-204°C (*i*-PrOH–EtOH). $^1$H NMR spectrum (DMSO-$d_6$, 300 MHz), δ, ppm (*J*, Hz): 1.76 (3H, s, $CH_3$); 2.10-2.21 (2H, m, 6-$CH_2$); 3.07 (2H, t, *J* = 7.3, 5-$CH_2$); 4.33 (2H, t, *J* = 7.3, 7-$CH_2$); 4.51 (1H, s, C$H_2$=C); 4.75 (1H, s, C$H_2$=C); 4.89 (2H, s, N–$CH_2$); 7.46-7.59 (3H, m, arom.); 7.95 (2H, d, *J* = 7.1, arom.); 9.68 (1H, s, NH). Found, %: C 63.65; N 12.17. $C_{18}H_{19}N_3O_2S$. Calculated, %: C 63.32; N 12.31.

**N-(3-Oxo-2-phenyl-1-thioxo-1,2,3,5,6,7,8,9-octahydropyrimido[1,6-*a*]azepin-4-yl)benzamide (2c).** Yield 63%; mp 236-238°C (EtOH). $^1$H NMR spectrum (DMSO-$d_6$, 300 MHz), δ, ppm (*J*, Hz): 1.79 (6H, m, 6-, 7-, 8-$CH_2$); 2.98 (2H, m, 5-$CH_2$); 4.87 (2H, m, 9-$CH_2$); 7.11 (2H, d, *J* = 7.7, arom.); 7.34-7.57 (6H, m, arom.); 7.94 (2H, d, *J* = 7.7, arom.); 9.65 (1H, s, NH). Found, %: C 67.34; N 10.43. $C_{22}H_{21}N_3O_2S$. Calculated, %: C 67.50; N 10.73.

**N-(2-Methyl-3-oxo-1-thioxo-1,2,3,5,6,7,8,9-octahydropyrimido[1,6-*a*]azepin-4-yl)benzamide (2d).** Yield 62%; mp 179-181°C (EtOAc–heptane). $^1$H NMR spectrum (DMSO-$d_6$, 300 MHz), δ, ppm (*J*, Hz): 1.74 (6H, m, 6-, 7-, 8-$CH_2$); 2.91 (2H, m, 5-$CH_2$); 3.68 (3H, s, $NCH_3$); 4.88 (2H, m, 9-$CH_2$); 7.46-7.59 (3H, m, arom.); 7.95 (2H, d, *J* = 6.9, arom.); 9.60 (1H, s, NH). $^{13}$C NMR spectrum (DMSO-$d_6$, 75 MHz), δ, ppm: 24.85 (6-C), 25.76 (7-C), 26.73 (8-C), 27.62 (5-C), 35.36 ($NCH_3$), 52.27 (9-C), 112.25, 127.15, 127.81, 131.24, 132.93, 155.11, 157.13 (CO), 165.78 (NHCOPh), 176.10 (CS). Found, %: C 61.64; N 12.95. $C_{17}H_{19}N_3O_2S$. Calculated, %: C 61.98; N 12.76.

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