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DERIVATIVES OF CONDENSED THIENO[2,3-*d*]-PYRIMIDINES. 20*. SYNTHESIS OF 2-SUBSTITUTED 5,6-DIHYDRO-8H-PYRANO[4',3':4,5]THIENO[2,3-*d*]PYRIMIDIN-4(3H)-ONES AND 5,6,7,8-TETRAHYDROBENZO-[*b*]THIENO[2,3-*d*]PYRIMIDIN-4-ONES

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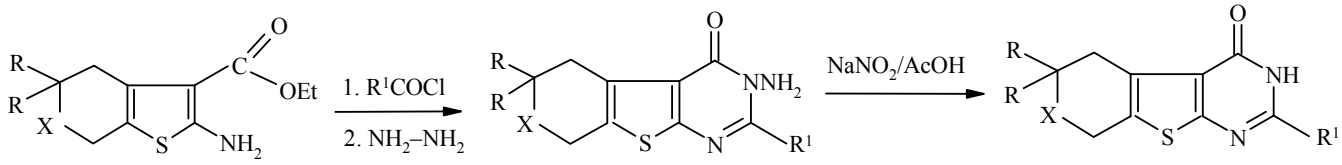
We have developed a method for obtaining 2-substituted 3-amino-6,6-dimethyl-5,6-dihydro-8H-pyrano[4',3':4,5]- and 5,6,7,8-tetrahydrobenzo[b]thieno[2,3-d]pyrimidin-4(3H)-ones, converted by deamination to the corresponding dihydropyranothieno-3H-pyrimidinones.

Keywords: substituted 5,6-dihydro-8H-pyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3H)-ones, 5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3H)-ones, acylation, deamination.

Continuing our research on synthesis of condensed thieno[2,3-*d*]pyrimidin-4-ones [2], we have developed a convenient method for obtaining 2-substituted 3-amino-6,6-dimethyl-5,6-dihydro-8H-pyrano[4',3':4,5]- and 5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3H)-ones **3a-g** and **4a-e** respectively, without separating the intermediate N-acylated 2-amino-3-ethoxycarbonylthiophenes, by treatment of the reaction mixture after acylation of compounds **1, 2** with hydrazine hydrate. The method is convenient, and ensures a good yield of the end products **3a-g, 4a-e**.



1, **2** — **3a–g**, **4a–e** — **5a**,**b, 6a**,**b**

1, **3a-g**, **5a**,**b** X = O, R = Me, **2**, **4a-e**, **6a**,**b** X = CH_2, R = H; **3a**, **4a**, **6a** R^1 = $–(CH_2)_6Me$, **3b**, **4b**, **5a**, **6b** R^1 = $–(CH_2)_7Me$, **3c**, **4c** R^1 = $–CH_2CHMe_2$, **3d**, **4d** R^1 = $–CH_2C_6H_4OMe$-4, **3e**, **4e**, **5b** R^1 = $–(CH_2)_2Ph$, **3f** R^1 = $–CH_2C_6H_3Cl_2$-2,6, **3g** R^1= $–CH_2C_6H_3(OMe)_2$-3,4

* For Communication 19, see [1].

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Earlier [3] we developed a method for deamination of 2-substituted 3-aminothieno[2,3-*d*]pyrimidin-4(3H)-ones to form 2-substituted 3H-thieno[2,3-*d*]pyrimidin-4(3H)-ones by treatment with a mixture of nitrous and acetic acids. We used this method to obtain the corresponding 2-R^1-3H-pyrimidin-4-ones **5a,b, 6a,b** in high yields from compounds **3b,e, 4a,b**.

TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %		mp, °C	Yield %
		N	S		
3a	$C_{18}H_{27}N_3O_2S$	12.11 / 12.02	9.25 / 9.20	143-145	64.7
3b	$C_{19}H_{29}N_3O_2S$	11.60 / 11.56	8.90 / 8.82	186-188	88.8
3c	$C_{15}H_{21}N_3O_2S$	13.70 / 13.66	10.52 / 10.43	162-163	83.3
3d	$C_{19}H_{21}N_3O_3S$	11.45 / 11.31	8.70 / 8.63	199-200	78.5
3e	$C_{19}H_{21}N_3O_2S$	11.93 / 11.82	9.22 / 9.02	178-179	62.5
3f	$C_{18}H_{17}Cl_2N_3O_2S$	10.36 / 10.25	7.94 / 7.81	227-228	61.0
3g	$C_{20}H_{23}N_3O_4S$	10.55 / 10.47	8.19 / 7.99	194-195	75.6
4a	$C_{17}H_{25}N_3OS$	13.46 / 13.15	10.26 / 10.03	120-121	70.0
4b	$C_{18}H_{27}N_3OS$	12.64 / 12.59	9.87 / 9.61	126-128	67.2
4c	$C_{14}H_{19}N_3OS$	15.37 / 15.14	11.77 / 11.56	149-152	85.08
4d	$C_{18}H_{19}N_3O_2S$	12.53 / 12.30	9.62 / 9.40	156-158	68.40
4e	$C_{18}H_{19}N_3OS$	13.02 / 12.91	9.98 / 9.85	200-202	73.15
5a	$C_{19}H_{28}N_2O_2S$	8.15 / 8.03	9.34 / 9.20	186-188	88.80
5b	$C_{19}H_{20}N_2O_2S$	8.39 / 8.22	9.42 / 9.41	226-227	80.00
6a	$C_{17}H_{24}N_2OS$	9.36 / 9.20	10.60 / 10.53	170-172	89.70
6b	$C_{18}H_{26}N_2OS$	8.93 / 8.80	10.18 / 10.06	157-158	98.50

TABLE 2. IR Spectra and ^{1}H NMR Spectra of Synthesized Compounds

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
1	2	3
3a	1665-1670 (CO), 3170-3345 (NH_2)	4.84 (2H, s, NH_2); 4.80 (2H, t, *J* = 1.8, H_2-8,8); 3.01 (2H, t, *J* = 1.8, H_2-5,5); 2.99 (2H, t, *J* = 8.0, 2-$C\underline{H_2}$–); 1.80 (2H, m, 2-$CH_2\underline{CH_2}$–); 1.50-1.25 (8H, m, 2-$CH_2CH_2(\underline{CH_2})_4$–); 1.35 (6H, s, 6,6-$(CH_3)_2$); 0.90 (3H, t, *J* = 6.8, 2-$(CH_2)_6\underline{CH_3}$)
3b	1665-1672 (CO), 3173-3325 (NH_2)	4.83 (2H, br. s, NH_2); 4.80 (2H, t, *J* = 1.8, H_2-8,8); 3.00 (2H, t, *J* = 1.8, H_2-5,5); 2.99 (2H, t, *J* = 8.0, 2-$\underline{CH_2}$–); 1.80 (2H, m, 2-$CH_2\underline{CH_2}$–); 1.25-1.50 (10H, m, 2-$CH_2CH_2(\underline{CH_2})_5$–); 1.35 (6H, s, 6,6-$(CH_3)_2$); 0.90 (3H, t, *J* = 6.8, 2-$(CH_2)_7\underline{CH_3}$)
3c	1660-1675 (CO), 3140-3340 (NH_2)	4.83 (2H, s, NH_2); 4.79 (2H, t, *J* = 1.7, H_2-8,8); 3.00 (2H, t, *J* = 1.7, H_2-5,5); 2.90 (2H, d, *J* = 7.2, 2-$\underline{CH_2}$); 2.29 (1H, d, *J* = 6.6, 2-$CH_2\underline{CH}$); 1.34 (6H, s, 6,6-$(CH_3)_2$); 1.03 (6H, d, *J* = 6.6, 2-$CH_2CH(\underline{CH_3})_2$)

TABLE 2 (continued)

1	2	3
3d	1680-1700 (CO), 3125-3335 (NH_2)	7.28 (2H, d, J = 8.7, H_{Ar}); 6.86 (2H, d, J = 8.7, H_{Ar}); 4.82 (2H, s, NH_2); 4.81 (2H, t, J = 1.9, H_2-8,8); 4.29 (2H, s, 2-CH_2); 3.79 (3H, s, OCH_3); 2.99 (2H, t, J = 1.9, H_2-5,5)
3e	1675-1680 (CO), 3155-3320 (NH_2)	7.20-7.35 (5H, m, H_{Ar}); 4.67 (2H, br. s, NH_2); 4.81 (2H, br. s, H_2-8,8); 3.32-3.15 (4H, m, 2-CH_2CH_2Ph); 3.01 (2H, br. s, H_2-5,5); 1.35 (6H, s, 6,6-$(CH_3)_2$)
3f	1685-1660 (CO), 3200-3395 (NH_2)	7.38 (2H, m, H_{Ar}); 7.27 (1H, m, H_{Ar}); 5.79 (2H, br. s, NH_2); 4.67 (2H, t, J = 1.9, H_2-8,8); 4.64 (2H, s, 2-CH_2); 3.90 (2H, t, J = 1.9, H_2-5,5); 1.30 (6H, s, 6,6-$(CH_3)_2$)
3g	1660-1680 (CO), 3170-3380 (NH_2)	6.92 (1H, d, J = 1.8, H_{Ar}); 6.89 (1H, dd, J_1 = 8.1, J_2 = 1.8, H_{Ar}); 6.81 (1H, d, J = 8.1, H_{Ar}); 4.87 (2H, br. s, NH_2); 4.81 (2H, t, J = 1.8, H_2-8,8); 4.29 (2H, s, 2-CH_2); 3.00 (2H, t, J = 1.8, H_2-5,5); 3.86 (6H, s, $(OCH_3)_2$); 1.35 (6H, s, 6,6-$(CH_3)_2$)
4a	1660-1680 (CO), 3160-3380 (NH_2)	4.83 (2H, br. s, NH_2); 2.99 (2H, m, H_2-5,5); 2.76 (2H, m, H_2-8,8); 2.97 (2H, t, J = 8.0, 2-CH_2–); 1.78 (2H, m, 2-CH_2CH_2–); 1.86 (4H, m, H_2-6,6, H_2-7,7); 1.25-1.50 (8H, m, 2-CH_2–$CH_2(CH_2)_4$); 0.89 (3H, t, J = 6.6, 2-$(CH_2)_6CH_3$)
4b	1670-1680 (CO), 3165-3390 (NH_2)	4.82 (2H, br. s, NH_2); 2.77 (2H, t, J = 7.0, 2-CH_2–); 2.75 (2H, m, H_2-5,5); 2.96 (2H, m, H_2-8,8); 1.87 (4H, m, H_2-6,6, H_2-7,7); 1.80 (2H, m, 2-CH_2CH_2–); 1.20-1.50 (10H, m, 2-$CH_2CH_2(CH_2)_5$); 0.97 (3H, t, J = 6.7, 2-$(CH_2)_7CH_3$)
4c	1660-1690 (CO), 3170-3355 (NH_2)	4.82 (2H, br. s, NH_2); 2.77 (2H, m, H_2-5,5); 3.00 (2H, m, H_2-8,8); 1.87 (4H, m, H_2-6,6, H_2-7,7); 2.89 (2H, d, J = 7.2, 2-CH_2CH); 2.29 (1H, sept, J = 6.6, 2-CH_2CH); 1.02 (6H, d, J = 6.6, 2-$CH_2CH(CH_3)_2$)
4d	1680-1690 (CO), 3175-3385 (NH_2)	7.26 (2H, d, J = 8.7, H_{Ar}); 6.85 (2H, d, J = 8.7, H_{Ar}); 4.81 (2H, br. s, NH_2); 4.26 (2H, s, 2-CH_2); 3.79 (3H, s, OCH_3); 2.79 (2H, m, H_2-8,8); 2.99 (2H, m, H_2-5,5); 1.87 (4H, m, H_2-6,6, H_2-7,7)
4e	1665-1685 (CO), 3175-3390 (NH_2)	7.20–7.35 (5H, m, H_{Ph}); 3.12 (2H, t, J = 8.0, 2-CH_2); 3.35 (2H, t, J = 8.0, $CH_2C_6H_5$); 4.70 (2H, br. s, NH_2); 2.78 (2H, m, H_2-5,5); 3.00 (2H, m, H_2-8,8)
5a	1665-1670 (CO), 3170 (NH)	11.72 (1H, br. s, NH); 4.83 (2H, br. s, H_2-8,8); 3.02 (2H, br. s, H_2-5,5); 2.73 (2H, t, J = 7.1, 2-CH_2); 1.85 (2H, q, J = 7, 2-CH_2CH_2); 1.20-1.50 (10H, m, 2-$CH_2CH_2(CH_2)_5$); 0.89 (3H, t, J = 6.7, 2-$(CH_2)_7CH_3$); 1.38 (6H, s, 6,6-$(CH_3)_2$)
5b	1670-1675 (CO), 3170 (NH)	12.54 (1H, br. s, NH); 7.18-7.30 (5H, m, H_{Ph}); 4.84 (2H, t, J = 1.7, H_2-8,8); 3.03 (2H, t, J = 1.7, H_2-5,5); 3.05-3.20 (4H, m, 2-$CH_2CH_2C_6H_5$); 1.35 (6H, s, 6,6-$(CH_3)_2$)
6a	1670-1673 (CO), 3185 (NH)	11.91 (1H, s, NH); 3.02 (2H, m, H_2-8,8); 2.79 (2H, m, H_2-5,5); 1.88 (4H, m, H_2-6,6, H_2-7,7); 2.73 (2H, t, J = 7.8, 2-CH_2); 1.83 (2H, m, 2-CH_2CH_2); 1.24-1.46 (8H, m, 2-$CH_2CH_2(CH_2)_4$); 0.88 (3H, t, J = 6.6, 2-$(CH_2)_6CH_3$)
6b	1661-1675 (CO), 3180 (NH)	11.90 (1H, br. s, NH); 3.00 (2H, br. s, H_2-5,5); 2.80 (2H, br. s, H_2-8,8); 1.84 (4H, m, H_2-6,6, H_2-7,7); 2.73 (2H, t, J = 6.2, 2-CH_2); 1.80 (2H, m, 2-CH_2CH_2); 1.20-1.50 (10H, m, 2-$CH_2CH_2(CH_2)_5$); 0.90 (3H, t, J = 7.0, 2-$(CH_2)_7CH_3$)

EXPERIMENTAL

The ^{1}H NMR spectra were obtained on a Varian Mercury-300 spectrometer (300 MHz), provided under a grant within the US CRDF RESC 17-S program. The solvent was $CDCl_3$ or DMSO-d_6 (in the case of compound **2f**). The IR spectra were taken on a UR-20 in nujol. The purity of the compounds obtained was monitored by TLC on Silufol UV-254 plates in the system 1:1:1 chloroform–ethyl acetate–acetone or 2:1 ethyl alcohol–chloroform.

The characteristics of the synthesized compounds are given in Tables 1 and 2.

2-R[1]-3-Amino-6,6-dimethyl-5,6-dihydro-8H-pyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3H)-ones 3a-e and -5,6,7,8-tetrahydrobenzo[*b*]thieno[2,3-*d*]pyrimidin-4(3H)-ones 4a-e. Dry triethylamine (0.01 mol) was added to a solution of compounds **1** and **2** (0.01 mol) in dry benzene (30 ml), and then the corresponding acid chloride (0.01 mol) in benzene (5 ml) was added dropwise. The mixture obtained was boiled for 4 h, then water (30 ml) was added and the benzene was evaporated off. The precipitate formed was filtered out, washed with water, and boiled for 8 h with hydrazine hydrate (5 ml) and *n*-butanol (15 ml). The crystals of products **3** and **4** precipitating out upon cooling were filtered out, washed with alcohol and then water, and then dried at 50°C and recrystallized from alcohol.

2-R[1]-3H-6,6-Dimethyl-5,6-dihydro-8H-pyrano[4',3':4,5]thieno[2,3-*d*]pyrimidin-4(3H)-ones 5a,b and -5,6,7,8-tetrahydrobenzo[*b*]thieno]2,3-*d*]pyrimidin-4(3H)-ones 6a,b. A solution of sodium nitrite (1.0 g, 0.015 mol) in water (3 ml) was added dropwise to a solution of compounds **3b,e** and **4a,b** (0.01 mol) in acetic acid (15 ml) at room temperature. After 5 h, the mixture was diluted with water and recrystallized from a 10:1 *n*-butanol–DMF mixture. The crystals of product **5** and **6** were filtered out and dried.

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