SYNTHESIS OF 4-HYDROXYTHIENO[2,3-d]PYRIMIDINE DERIVATIVES

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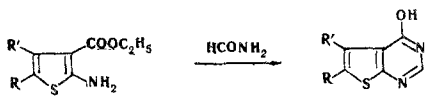
Condensation of 2-amino-3-ethoxycarbonylthiophenes with formide at 200° C gives a number of 4-hydroxythieno [2, 3-d]-pyrimidine derivatives.

4-Hydroxythieno[2,3-d]pyrimidine has been synthesized in 4% yield by prolonged action of ammonia on 2-formylamino-3-methoxycarbonylthiophene[1].

We have offered a method of synthesizing 4-hydroxythieno[2,3-d]pyrimidine derivatives by condensing 2-amino-3-ethoxycarbonylthiophenes with formamide [2]. The reaction is carried out by heating the derivatives of 2-aminothiophene [3–6] with excess formamide at 200° C, when 69–93% yields of 4-hydroxythieno[2,3-d]pyrimidines are obtained.



The IR spectra of these latter compounds exhibit absorption at 1670 cm^{-1}, evidence in favor of a ketone structure for them [7]. There is a complex absorption band at 3320–3030 cm^{-1}, evidently due to superposition of bands characteristic of the NH groups of amido compounds. The synthesized derivatives show absorption at 990 cm^{-1}, corresponding to pyrimidine ring vibrations [7]. Conjugation of the thiophene ring with the pyrimidine one leads to one of the thiophene frequencies of vibration being lowered by 35–50 cm^{-1}, i.e. to 1360 to 1375 cm^{-1}, while a second band at 785 cm^{-1}, characteristic of the thiophene ring [3,5], is not displaced.

EXPERIMENTAL

4-Hydroxy-5-methyl-6-(ω-acetoxyethyl)thieno[2,3-d]pyrimidine. 5 g (0.02 mole) 2-amino-3-ethoxycarbonyl-4-methyl-5-(ω-acetoxyethyl)thiophene in 20 ml (0.04 mole) formamide was refluxed for 1 hr 30 min. The products were cooled, the crystals which came out separated off, washed on the funnel with MeOH, and dried at 120° C, yield 4 g (86%), mp 196°-197° (ex MeOH). Found: C 51.87; 51.93; H 4.74; 4.61; N 11.21; 11.32; S 12.50; 12.48%. Calculated for $C_{11}H_{12}N_2O_3S$: C 52.36; H 4.79; N 11.10; S 12.71%.

The table gives data for 4-hydroxythieno[2,3-d] pyrimidines.

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4-Hydroxythieno[2,3-d]pyrimidine Derivatives

R	R′	Amounts of starting compounds		Mp, °C (solvent for crystallizing)	Formula	Found, %				Calculated, %				Yield, %
		2-Amino-3-ethoxycarbonylthiophene derivative, g (mole)	Formamide, ml (mole)			C	H	N	S	C	H	N	S	
$CH_2CH_2OCOCH_3$	CH_3	5 (0.02)	20 (0.4)	196—197 (MeOH)	$C_{11}H_{12}N_2O_3S$	51.87 51.93	4.74 4.61	11.21 11.32	12.50 12.48	52.36	4.79	11.10	12.71	86
$COOC_2H_5$	CH_3	10 (0.04)	20 (0.4)	233—234 (MeOH)	$C_{10}H_{10}N_2O_3S$	50.38 50.20	4.62 4.40	11.81	13.12 13.51	50.41	4.23	11.76	13.46	78.8
$(CH_2)_3$		2 (0.01)	8 (0.16)	247—248 (MeOH)	$C_9H_8N_2OS$	56.02 56.30	4.41 4.20	14.74 14.72	16.76 16.50	56.23	4.19	14.57	16.68	71.4
$(CH_2)_4$		4.5 (0.02)	10 (0.2)	255—256 (dimethylformamide)	$C_{10}H_{10}N_2OS$	58.20 58.38	4.92 5.20	13.73 14.04	15.28 15.34	58.22	4.88	13.58	15.54	92.3
H	C_6H_5	6.2 (0.025)	20 (0.4)	210—211 (MeOH)	$C_{12}H_8N_2OS$	62.92 62.92	3.42 3.62	12.28 11.79	14.11 13.76	63.14	3.53	12.27	14.05	91
H	p-$CH_3C_6H_4$	3.5 (0.01)	6 (0.1)	201.5—202.5 (MeOH)	$C_{13}H_{10}N_2OS$	64.85	4.49	11.88 11.36	13.40 13.22	64.44	4.16	11.56	13.23	93
H	p-$C_2H_5C_6H_4$	1.2 (0.004)	2.5 (0.05)	181—182 (MeOH)	$C_{14}H_{12}N_2OS$	65.23 65.15	4.53 4.76	11.07 11.13	12.46 12.71	65.59	4.72	10.93	12.51	69
H	2,4-$(CH_2)_2C_6H_4$	3 (0.01)	6 (0.12)	258—259 (ethylcellosolve)	$C_{14}H_{12}N_2OS$	66.00 65.50	5.01 4.70	10.66 10.71	12.30 12.13	65.59	4.72	10.93	12.51	89.4
H	2,5-$(CH_3)_2C_6H_3$	1.1 (0.004)	2.5 (0.05)	254—254.5 (ethylcellosolve)	$C_{14}H_{12}N_2OS$	65.93 65.71	4.81 4.79	10.90 10.95	12.12 12.16	65.59	4.72	10.93	12.51	83.4
H	p-$CH_3OC_6H_4$	4.4 (0.016)	13 (0.25)	274—275 (dimethylformamide)	$C_{13}H_{10}N_2O_2S$	60.70 60.39	4.00 4.04	10.76 10.74	12.39 12.68	60.45	3.90	10.85	12.41	70.2
H	3,4-$(CH_3O)_2C_6H_3$	3 (0.01)	12 (0.2)	232—233 (MeOH)	$C_{14}H_{12}N_2O_3S$	58.23 58.02	4.41 4.51	9.36 9.68	11.32 11.00	58.31	4.20	9.71	11.12	92.5
H	2,4-$(CH_3O)_2C_6H_3$	3 (0.01)	12 (0.2)	200—201 (MeOH)	$C_{14}H_{12}N_2O_3S$	58.14 58.18	4.46 4.38	9.36 9.53	10.84 10.88	58.31	4.20	9.71	11.12	92.6
H	2,5-$(CH_3O)_2C_6H_3$	3 (0.01)	12 (0.2)	191.5—192.5 (MeOH)	$C_{14}H_{12}N_2O_3S$	57.75 57.80	4.18 3.90	9.52 9.65	11.18 10.84	58.31	4.20	9.71	11.12	74.7