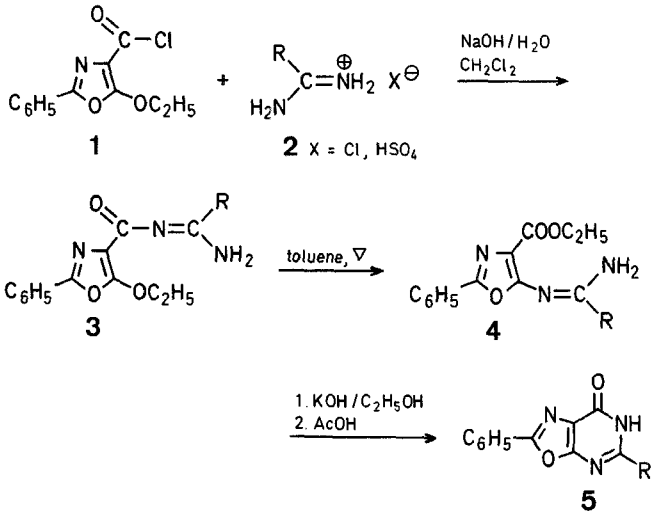
azolo[5,4-*d*]pyrimid-7-ones **5a–f** via base-induced cyclization of intermediates **4**. Thus, when 4-chlorocarbonyl-5-ethoxy-2-phenyloxazole **(1)** is treated with amidines **2a–d**, guanidine **2e** or isourea **2f**, the *N*-(4-oxazolyl)amidines **3a–d**, -guanidine **3e** or -isourea **3f** result, respectively. Thermolysis of **3a–f** in refluxing toluene affords **4a–f**, which yield the oxazolopyrimidones **5a–f** upon treatment with ethanolic potassium hydroxide followed by acidification with acetic acid (Table). The oxazolylamidines **4a–d** obtained from thermolysis of **3a–d** are contaminated with trace amounts of the cyclized materials **5a–d** (T.L.C., chloroform/methanol, 95/5). This does not affect the yields or purity of the products **5a–d** produced in the subsequent step. Prolonged heating of **4a–d** (refluxing toluene) converts these species to the pyrimidones **5a–d**. Under these conditions the cyclization of **4a** and **4f** is slow. However, the base-induced cyclization of intermediates **4** constitutes a superior procedure for the formation of **5** since the latter is faster and affords **5** in higher yields without competing side reactions.



2-5	a	b	c	d	e	f
R	H	H_3C				H_3CO

The reaction of acid chloride **1** with *S*-methylisothiourea (**2**, R = SCH_3) gives **3** (R = SCH_3) in low yield. The major and as yet unidentified product appears to arise via elimination of methanethiol. We are at present attempting to elucidate the structure of this material.

A New Synthesis of Oxazolo[5,4-*d*]pyrimid-7-ones

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The Cornforth rearrangement of 5-alkoxyoxazole-4-carboxamides is a general method for the preparation of alkyl 5-aminooxazole-4-carboxylates[3,4]. The mechanism of this transformation is thought to involve electrocyclic ring opening of the oxazoles to provide carbonylnitrile ylides as transient intermediates. 1,5-Dipolar electrocyclization[5] of these species leads to the observed 5-aminooxazole-4-carboxylates[6].

We have applied this process to a synthesis of *N*-(5-oxazolyl)-amidines **4a–d**, the *N*-(5-oxazolyl)-guanidine **4e**, and the *N*-(5-oxazolyl)-isourea **4f**, and ultimately to a synthesis of oxazolo[5,4-*d*]pyrimid-7-ones **5**. Oxazolo[5,4-*d*]pyrimid-7-ones **5** have been prepared in moderate yields by reaction of 4,6-dihydroxy-5-aminopyrimidines with acid anhydrides[7–10], and in low to moderate yields from 5-acylaminooxazole-4-carboxamides[11,12,13]. The method presented here represents a convenient synthesis of 5-oxazolylamidines **4a–d** and oxazolo[5,4-*d*]pyrimid-7-ones **5** and, in particular, for the preparation of the less readily available 2-heteroatom-substituted systems such as **5e** and **5f**. In addition, oxazolo[5,4-*d*]pyrimidines are useful in the preparation of the biologically important purine and hypoxanthine systems[14,15].

4-Chlorocarbonyl-5-ethoxy-2-phenyloxazole (1):
To a well-stirred suspension of 4-carboxy-5-ethoxy-2-phenyloxazole[16] (2.33 g, 10 mmol) in dichloromethane (150 ml) and dimethylformamide (0.05 ml) at 5°C is added dropwise a solution of oxalyl chloride (1.90 g, 15 mmol) in ether (100 ml). After the addition, the mixture is allowed to reach room temperature and stirring is continued for 2 h.

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The solvent and excess oxalyl chloride are removed under reduced pressure and the solid residue is recrystallized from cyclohexane; yield: 2.15 g (86%); m.p. 105–106°C (Ref.[16], m.p. 105–106°C).

N-(4-Oxazolyl)-amidines 3a–d, -guanidine 3e, and -isourea 3f; General Procedure:

To a well-stirred suspension of the amidine hydrochloride, *N,N*-dimethylguanidine hydrochloride, or *O*-methylisourea hydrogen sulfate **2** (10 mmol) in dichloromethane (40 ml) at 5°C is added a solution of sodium hydroxide (0.8 g, 20 mmol) in water (10 ml). To this mixture is added dropwise **1** (2.52 g, 10 mmol) in dichloromethane (30 ml). After 3 h at room temperature, the organic phase is separated, washed with water (50 ml), dried with magnesium sulfate and the solvent removed under reduced pressure. The solid residue is recrystallized from ethanol (**3b–f**) or from dichloromethane/hexane (**3a**).

Oxazolyl-amidines 4a–d, -guanidine 4e, and -isourea 4f; General Procedure:

Compounds **3** (10 mmol) are heated under reflux in toluene (50 ml) for 1.5 h for **3a–d** and **3f**, 4 h for **3e**. The solvent is removed under reduced pressure and the residue recrystallized from ethanol.

Table. Compounds **3**, **4**, and **5** prepared

Product No.	Yield [%]	m.p. [°C]	Molecular formula[a] or Lit. m.p. [°C]	I.R. (KBr) ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6) δ [ppm]	M.S. (70 eV) m/e (M^+)
3a	78	146–148°[b]	$C_{13}H_{13}N_3O_3$ (259.3)	3410, 3390, 3225, 1680, 1645	1.45 (distorted t, 3H, J=7 Hz); 4.65 (distorted q, 2H, J=7 Hz); 7.0–7.7 (m, 4H); 7.7–8.0 (m, 3H); 8.45 (d, 1H)	259
3b[c]	—	—	$C_{14}H_{15}N_3O_3$ (273.3)	—	—	273
3c	72	—[d]	$C_{19}H_{17}N_3O_3$ (335.4)	3330, 3200, 1595, 1560, 1475	1.55 (t, 3H, J=7 Hz); 4.6 (q, 2H, J=7 Hz); 7.4 (m, 8H); 8.0 (m, 4H)	335
3d	88	118–119°[b]	$C_{18}H_{16}N_4O_3$[b] (336.4)	3430, 3290, 1685, 1610, 1490	1.54 (t, 3H, J=6 Hz); 4.65 (q, 2H, J=6 Hz); 7.48 (m, 4H); 7.93 (m, 4H); 8.42 (m, 2H); 8.67 (d, 1H, J=5 Hz)	336
3e	91	177–179°[b]	$C_{15}H_{18}N_4O_3$ (302.3)	3330, 3170, 2980, 1580, 1445	1.5 (distorted t, 3H, J=7 Hz); 3.15 (s, 6H); 4.58 (distorted q, 2H, J=7 Hz); 7.43 (m, 5H); 8.02 (m, 2H)	302
3f	89	158–159°	$C_{14}H_{15}N_3O_4$ (289.3)	3360, 3250, 1600, 1495, 1435	1.38, 1.50 (overlapping t, 3H, J=7 Hz); 4.13, 4.34 (overlapping q, 2H, J=7 Hz); 3.78, 3.88, 3.94 (s, 3H); 7.94 (m, 5H); 2.52, 5.47, 8.38, 8.66 (br. m, 2H)	289
4a	84	184–185°[b]	$C_{13}H_{13}N_3O_3$ (259.3)	3510, 3225, 1710, 1645, 1460	1.3 (t, 3H, J=7 Hz); 4.3 (q, 2H, J=7 Hz); 7.45 (m, 5H); 7.8 (m, 2H)	259
4b[c]	—	—	$C_{14}H_{15}N_3O_3$ (273.3)	—	—	273
4c	75	173–174°	$C_{19}H_{17}N_3O_3$ (335.4)	3350, 1700, 1625, 1585, 1565	1.26 (t, 3H, J=7 Hz); 4.21 (q, 2H, J=7 Hz); 7.43 (m, 6H); 7.64 (m, 2H); 7.97 (m, 4H)	335
4d	92	156–157°[b]	$C_{18}H_{16}N_4O_3$ (336.4)	3430, 2980, 1700, 1620, 1570	1.31 (t, 3H, J=7 Hz); 4.24 (q, 2H, J=7 Hz); 7.45 (m, 4H); 7.74 (m, 2H); 8.0 (m, 3H); 8.43 (dd, 1H); 8.64 (dd, 1H)	336
4e	90	201–202°[b]	$C_{15}H_{18}N_4O_3$ (302.3)	3480, 2980, 1690, 1565, 1415	1.25 (t, 3H, J=7 Hz); 3.0 (s, 6H); 4.14 (q, 2H, J=7 Hz); 6.36 (br s, 2H); 7.37 (m, 3H); 7.84 (m, 2H)	302
4f	93	197–199°[b]	$C_{14}H_{15}N_3O_4$ (289.3)	3490, 3280, 1705, 1595, 1450	1.28 (t, 3H, J=6 Hz); 3.81 (s, 3H); 4.19 (q, 2H, J=6 Hz); 7.01 (br. s, 2H); 7.44 (m, 3H); 7.88 (m, 2H)	289
5a	85	315–317°	320–321°[8]	—	—[e]	—
5b	79	306–308°	314–316°[11]	—	—[e]	—
5c	86	374–376°	376–379°[13]	3060, 1690, 1580, 1560, 1530	—[e]	289
5d	94	260–262°	$C_{16}H_{10}N_4O_2$ (290.3)	3300, 1705, 1540, 1485, 1450	—[e]	290
5e	96	319–321°[b]	$C_{13}H_{12}N_4O_2$ (256.3)	3120, 3050, 1685, 1590, 1510	2.9 (br. s, 1H); 3.16 (s, 6H); 7.63 (m, 3H); 8.08 (m, 2H)	256
5f	96	248–249°[b]	$C_{12}H_9N_3O_3$ (243.2)	3050, 2950, 1675, 1565, 1310	3.4 (br. s, 1H); 4.02 (s, 3H); 7.65 (m, 2H); 8.05 (m, 3H)	243

[a] Satisfactory microanalyses obtained: C ±0.3, H ±0.3, N ±0.27.
[b] Analyses as the hemihydrate. Karl Fischer analysis gives 2.25% water; the calculated value is 2.68%.
[c] This intermediate was not fully characterized since it was contaminated with the final product **5b**.
[d] Compound softens at 165°C, but does not melt until ~370°C, the melting point of **5c**.
[e] The compound is too insoluble to obtain the ^{1}H-N.M.R. spectrum.

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Oxazolo[5,4-*d*]pyrimid-7-ones 5; General Procedure:
To a solution of potassium hydroxide (1.32 g, 20 mmol) in ethanol (20 ml), the appropriate compound **4a–f** (10 mmol) is added. The mixture is allowed to stir at room temperature for 8 h and the resulting potassium salt of **5a–f** is isolated by filtration, dissolved in water (30 ml) and acidified with glacial acetic acid (5 ml). The product is filtered and recrystallized from ethanol or methanol with the exception of **5c** which is recrystallized from aqueous dimethylformamide.

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