

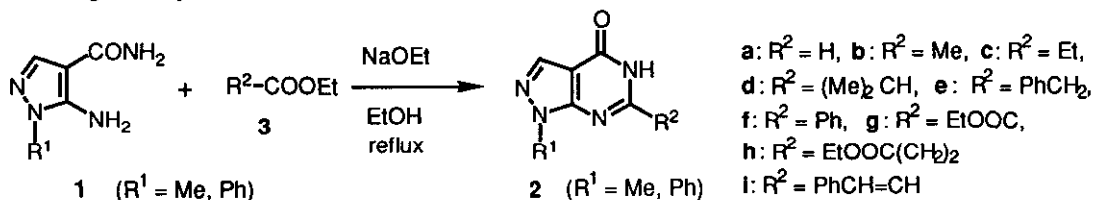
SYNTHESIS OF FUSED PYRIMIDINONES BY REACTION OF AMINOARENE-CARBOXAMIDE WITH ESTERS; PREPARATION OF PYRROLO[2,3-*d*]-, THIENO[2,3-*d*]-, ISOXAZOLO[5,4-*d*]-, AND 1,2,3-TRIAZOLO[4,5-*d*]PYRIMIDINONES, AND QUINAZOLONES

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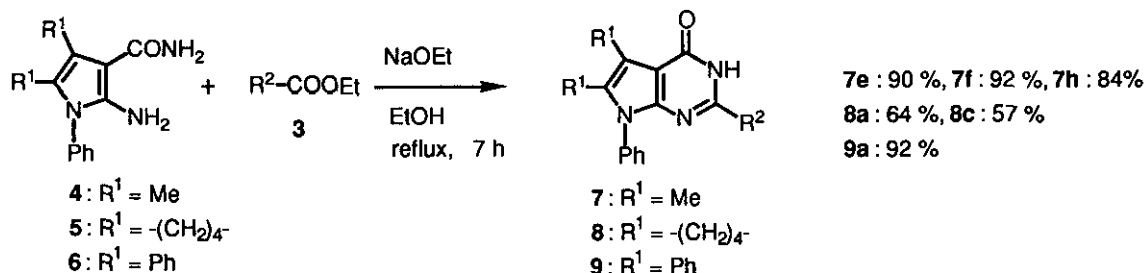
Abstract—Several fused pyrimidinones were synthesized by reaction of aminoarenecarboxamide with esters in moderate to good yields. In the presence of sodium ethoxide, treatments of 2-amino-1-phenyl-3-pyrrolicarboxamide (4, 5, and 6), 2-amino-3-thiophenecarboxamide (14), 3-amino-4-isoxazolecarboxamide (10 and 11), 4-amino-1,2,3-triazole-5-carboxamide (16), and *o*-aminobenzamide (18) with esters (3) such as ethyl formate (3a) and ethyl acetate (3b) led to the corresponding pyrrolo[2,3-*d*]- (7, 8, and 9), and thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (15), isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones (12 and 13), 1,2,3-triazolo[4,5-*d*]pyrimidin-7(6*H*)-ones (17), and 4(3*H*)-quinazolones (19), respectively.

Fused pyrimidines are important compounds in the fields of pharmacy and biology,¹ and a number of these compounds have been found to have biological activities.² In our continuous study related to fused pyrimidines, one of our purposes is discovery and establishment of a facilely preparative method of fused pyrimidines. In the previous paper, we have reported that pyrazolo[3,4-*d*]pyrimidin-4(5*H*)-ones (2)³ are easily prepared by reaction of 3-amino-4-pyrazolecarboxamide (1) with esters. We tried to extend this synthetic method to preparation of several fused pyrimidinones. To establish the generality, we used various aminoarenecarboxamides.



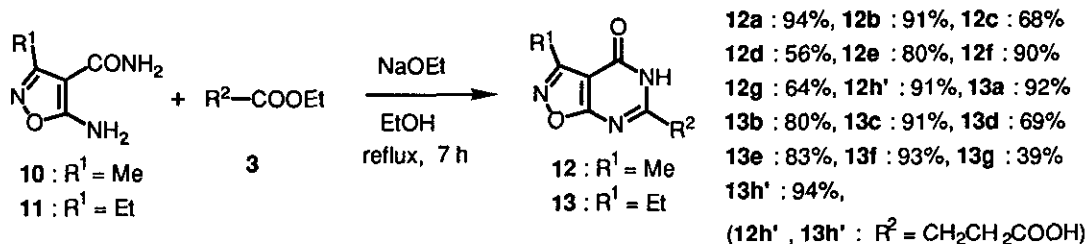
Scheme 1

We have already reported that 4,5-dimethyl-2-amino-1-phenyl-3-pyrrolicarboxamide (4)⁴ reacted with ethyl formate (3a), ethyl acetate (3b), and ethyl propionate (3c) in the presence of sodium ethoxide to give 7*H*-pyrrolo[2,3-*d*]pyrimidin-4(3*H*)-ones (7)⁵ in similar manner as described above. We further examined the formation of pyrrolopyrimidinones by reaction of 2-amino-3-pyrrolicarboxamides (4, 5, and 6) with esters (3) except reported esters, and obtained the corresponding pyrrolopyrimidinones (7, 8 and 9) in moderate to good yields.



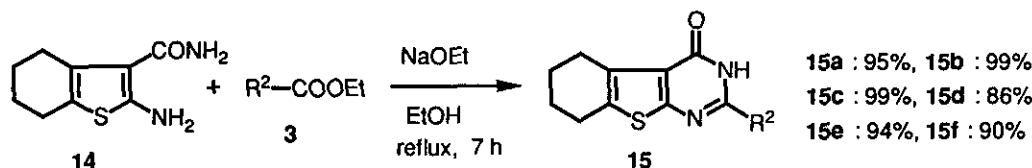
Scheme 2

A few synthetic methods of isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones have been reported, but these methods are complex.⁶ Treatment of 5-amino-3-methyl-4-isoxazolecarboxamide (**10**) with ethyl acetate (**3b**) in EtOH in the presence of EtONa underwent ring-closure, giving 3,6-dimethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one (**12b**). Similarly, the treatment of **10** with several esters (**3**) resulted in the formation of the corresponding 6-substituted 3-methylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones (**12**) in good yields. A similar result was obtained in the reaction of 5-amino-3-ethyl-4-isoxazolecarboxamide (**11**). Namely, synthesis of 3-ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones (**13**) was achieved by treatment of **11** with various esters (**3**). It failed to produce isoxazolopyrimidinones (**12h** and **13h**) having ethoxycarbonyl group at the 6-position by reaction of 5-amino-4-isoxazolecarboxamides (**10** and **11**) with ethyl succinate (**3h**), but the reactions afforded hydrolyzed products (**12h'** and **13h'**) in good yields.



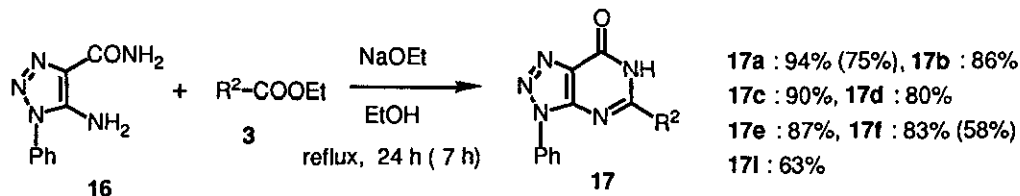
Scheme 3

We tried this synthetic procedure to prepare thieno[2,3-*d*]pyrimidin-4(3*H*)-ones (**15**). As shown in Scheme 4, 2-amino-4,5-tetramethylene-3-thiophenecarboxamide (**14**)⁷ reacted with esters (**3**) to give 5,6-tetramethylenethieno[2,3-*d*]pyrimidin-4(3*H*)-ones (**15**) in good yields.



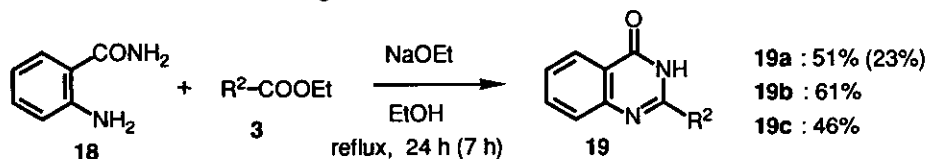
Scheme 4

This synthetic method could be extended to prepare triazolopyrimidinones (**17**) and quinazolones (**19**). Barili and co-workers reported that one-pot reaction involved formation of 1-benzyl-5-amino-1,2,3-triazole-4-carboxamide from benzyl azide and cyanoacetamide followed by reaction with esters resulted in the formation of 3-benzyl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidinones.⁸ Then we examined to prepare triazolopyrimidinones (**17**) by this procedure using 5-amino-1-phenyl-1,2,3-triazole-4-carboxamide (**16**). As shown in Scheme 5, we could establish a preparative method of triazolopyrimidinones (**17**) by reaction of **16** with esters (**3**). 3-Phenyl-5-styryl-3*H*-1,2,3-triazolo[4,5-*d*]pyrimidin-7(6*H*)-one (**17i**) which possesses a functional group at the 5-position was given by this synthetic method using ethyl cinnamate (**3i**)



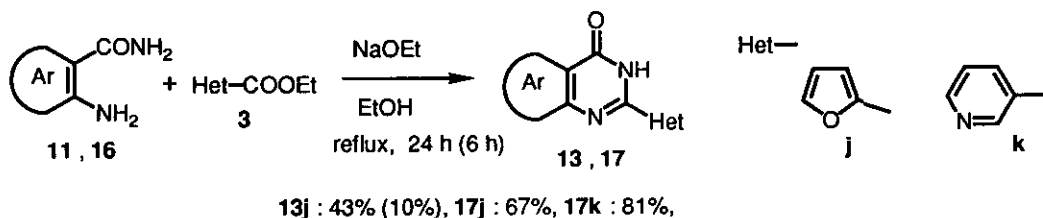
Scheme 5

On the other hand, 4(3*H*)-quinazolinone (**19a**) was given by reaction of *o*-aminobenzamide (**18**) with ethyl formate (**3a**) under similar conditions as described in the preparation of pyrrolo[2,3-*d*]-, isoxazolo[5,4-*d*]-, and thieno[2,3-*d*]pyrimidinones (refluxed for 7 h), but the yield was low (23%). 4(3*H*)-Quinazolinone (**19**) was obtained in 51% yield when the reaction was run in refluxing EtOH for 24 h.



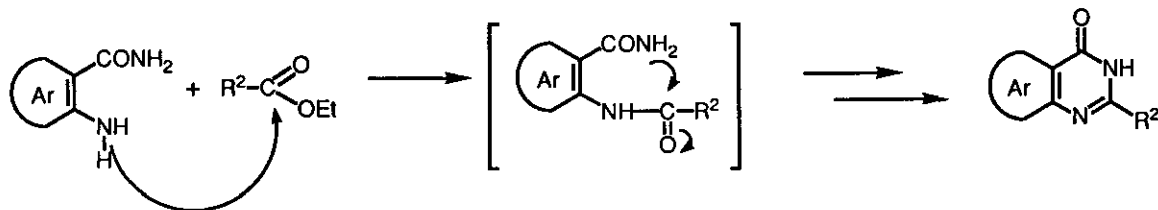
Scheme 6

Moreover, compound (**16**) reacted with ethyl heteroarene-carboxylates, such as ethyl 2-furoate (**3j**) and ethyl 3-pyridine-carboxylate (**3k**), to give the corresponding triazolopyrimidinones (**17j** and **17k**), which possess heteroarenyl groups at the 5-position. Similarly 6-furyl-3-ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one (**13j**) was synthesized by treatment of **11** with ester (**3j**).



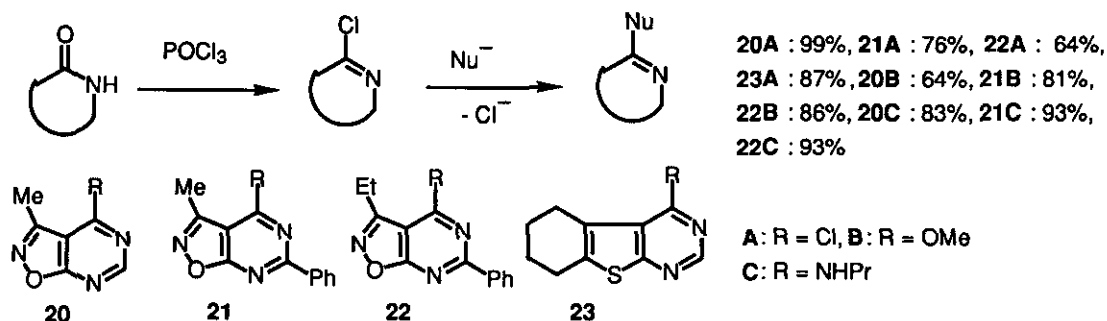
Scheme 7

The reaction pathway can be illustrated as Scheme 8. The facility of the reaction is correlated to the electron density of the amino group of the aminoarene-carboxamide (nucleophilicity of the amino group) and the carbonyl group of the esters (electrophilicity of the esters). As the ring-closure requires to produce acylamidoarene-carboxamide by acylation with esters, acylation of five-membered aminoarene-carboxamides, whose amino groups are electron-rich because of the electron-donating-effect of the ring, proceeds easily in comparison with that of six-membered aminoarene-carboxamides. Namely synthesis of 4(3*H*)-quinazolinone required prolonged reaction time, but formation of pyrrolo-, isoxazolo-, thieno-, and triazolopyrimidinones easily proceeded. Similarly, ethyl arene-carboxylate requires stronger reaction conditions in comparison with ethyl alkanecarboxylate because of low electrophilicity of the carbonyl group.



Scheme 8

In addition, treatment of the fused pyrimidinones with POCl₃ gave the corresponding fused chloropyrimidines. As shown in Scheme 9, the fused chloropyrimidines reacted with nucleophiles to give the substituted pyrimidines.



Scheme 9

We established a preparative method of fused pyrimidinones by reaction of aminoarene carboxamide with esters. Pyrrolo[2,3-*d*]-, isoxazolo[5,4-*d*]-, thieno[2,3-*d*]-, and 1,2,3-triazolo[4,5-*d*]pyrimidinones, and 4(3*H*)-quinazolones were synthesized by this method. Among synthetic methods of fused pyrimidinones, this is easy and simple procedure.

EXPERIMENTAL

All melting points were uncorrected. Ir spectra were recorded on a JASCO A-102 diffraction grating infrared spectrophotometer. Proton magnetic resonance (¹H-nmr) spectra were measured at 60 MHz on a HITACHI NMR R-1100 spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane (TMS) as an internal standard, and coupling constants (*J*) are given in hertz (Hz).

Preparation of Fused Pyrimidinones (7, 8, 9, 12, 13, 15, 17, and 19); General Procedure A mixture of aminoarene carboxamide (20 mmol) and an ester (80 mmol) in 200 ml of EtOH-NaOEt solution [prepared by 2.3 g (100 mmol) of Na and 200 ml of EtOH] was refluxed with stirring. The reaction mixture was concentrated under reduced pressure and the residue was dissolved in H₂O (ca. 200 ml). The resulting solution was acidified by AcOH and the separated solid was collected. The solid was dried and recrystallized from MeOH.

In this paper, 2-amino-4,5-dimethyl-1-phenyl-3-pyrrolocarboxamide (4),⁴ 2-amino-4,5-tetramethylene-1-phenyl-3-pyrrolocarboxamide (5),⁴ 2-amino-1,4,5-triphenyl-3-pyrrolocarboxamide (6),⁴ 5-amino-3-methyl-4-isoxazolecarboxamide (10),^{6c} 5-amino-3-ethyl-4-isoxazolecarboxamide (11),^{6c} 2-amino-4,5-tetramethylene-3-thiophenecarboxamide (14),⁷ 5-amino-1-phenyl-1,2,3-triazole-4-carboxamide (16),¹⁰ and *o*-aminobenzamide (18) were used as the starting aminoarene carboxamide.

Reaction conditions are shown in Schemes 1-7. Appearance, melting point, and elemental analysis for the fused pyrimidinones obtained are shown in Table I, and Table II shows the ¹H-nmr and ir spectra.

Preparation of 4-Chloro-3-methylisoxazolo[5,4-*d*]pyrimidine (20A) A mixture of 3-methylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one (12a, 10 g, 66 mmol) and POCl₃ (55 ml, 0.54 mol) was refluxed for 2 h, and excess POCl₃ was removed under reduced pressure. The residue was dissolved in CHCl₃ and the resultant solution was poured onto ice-H₂O. The mixture was made to alkali with 20% NH₄OH. The CHCl₃ layer was separated, washed with H₂O, and dried over Na₂SO₄. The solvent was removed under reduced pressure and the residue was purified by column chromatography on Al₂O₃ with CHCl₃. The first fraction gave the 4-chloroisoxazolo[5,4-*d*]pyrimidine, colorless scales (benzene), mp 58-62 °C. *Anal.* Calcd for C₆H₄N₂OCl: C, 42.50; H, 2.38; N, 24.78. Found: C, 42.47; H, 2.19; N, 25.01. ¹H-Nmr (CDCl₃) δ (ppm): 8.90 (1H, s, C-H), 2.75 (3H, s, Me).

Preparation of 4-Chloro-6-phenyl-3-methylisoxazolo[5,4-*d*]pyrimidine (21A) A mixture of 3-methyl-6-phenyl-isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one (12f, 4.55 g, 20 mmol) and POCl₃ (40 ml, 0.43 mol) was refluxed for 2 h, and excess POCl₃ was removed under reduced pressure. The residue was dissolved in CHCl₃ and the solution was poured onto ice-H₂O. The resulting mixture was made to alkali with 20% NH₄OH. The CHCl₃ layer was separated,

washed with H_2O , and dried over Na_2SO_4 . The solvent was concentrated under reduced pressure and the residue was purified by column chromatography on Al_2O_3 with $CHCl_3$. The first fraction gave the 4-chloroisoxazolo[5,4-*d*]pyrimidine (21A), yellowish needles (benzene), mp 157-158 °C. *Anal.* Calcd for $C_{12}H_8N_3OCl$; C: 58.67, H: 3.28, N: 17.10. Found: C: 58.83, H: 3.11, N: 17.24. 1H -Nmr ($CDCl_3$) δ (ppm): 8.54-8.26 (5H, m, Ph), 2.68 (3H, s, Me). Similar treatment of 3-ethyl-6-phenylisoxazolo[5,4-*d*]pyrimidin-4(5H)-one (13f, 4.6 g, 20 mmol) and $POCl_3$ (40 ml, 0.43 mol) yielded 4-chloroisoxazolo[5,4-*d*]pyrimidine (22A), yellowish needles (benzene), mp 88-90 °C. *Anal.* Calcd for $C_{13}H_{10}N_3OCl$; C: 60.13, H: 3.88, N: 16.20. Found: C: 60.77, H: 4.05, N: 15.95. 1H -Nmr ($CDCl_3$) δ (ppm): 8.6-8.3 (2H, m, Ph), 7.6-7.3 (3H, m, Ph), 3.10 (2H, q, $J = 7$ Hz, CH_2CH_3), 1.45 (3H, t, $J = 7$ Hz, CH_2CH_3).

Preparation of 4-Chloro-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (23A) A mixture of 5,6-tetramethylenethieno[2,3-*d*]pyrimidin-4(3H)-one (15a, 9.8 g, 48 mmol) and $POCl_3$ (50 ml, 0.54 mol) was refluxed for 2 h, and excess $POCl_3$ was removed under reduced pressure. The residue was dissolved in $CHCl_3$ and the solution was poured onto ice- H_2O . The resulting mixture was made to alkali with 20% NH_4OH . The $CHCl_3$ layer was separated, washed with H_2O , and dried over Na_2SO_4 . The solvent was removed under reduced pressure and the residue was purified by column chromatography on Al_2O_3 with $CHCl_3$. The first fraction gave the 4-chlorothieno[2,3-*d*]pyrimidine (23A), colorless needles (hexane), mp 110-111 °C.

Reaction of Fused Chloropyrimidine with Sodium Methoxide; General Procedure Fused chloropyrimidine (3 mmol) was added to MeOH-NaOMe solution [prepared by 0.2 g (8.7 mmol) of Na and 10 ml of MeOH] and the mixture was refluxed for 1 h with stirring. The reaction mixture was concentrated under reduced pressure and H_2O was added to the residue. The resulting mixture was extracted with $CHCl_3$, and the extract was dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on SiO_2 with $CHCl_3$ to give methoxyheteroarene.

4-Methoxy-3-methylisoxazolo[5,4-*d*]pyrimidine (20B): Colorless powder from hexane, mp 76-77 °C. *Anal.* Calcd for $C_7H_7N_3O_2$; C: 50.91, H: 4.27, N: 25.44. Found: C: 50.95, H: 4.01, N: 25.68. 1H -Nmr ($CDCl_3$) δ (ppm): 8.65 (1H, s, C⁶-H), 4.20 (3H, s, OMe), 2.62 (3H, s, Me).

4-Methoxy-3-methyl-6-phenylisoxazolo[5,4-*d*]pyrimidine (21B): Colorless needles from hexane, mp 134-136. *Anal.* Calcd for $C_{13}H_{11}N_3O_2$; C: 64.72, H: 4.60, N: 17.42. Found: C: 64.91, H: 4.48, N: 17.67. 1H -Nmr ($CDCl_3$) δ (ppm): 8.6-8.2 (2H, m, Ph), 7.6-7.2 (3H, m, Ph), 4.18 (3H, s, OMe), 2.54 (3H, s, Me).

4-Methoxy-3-ethyl-6-phenylisoxazolo[5,4-*d*]pyrimidine (22B): Colorless needles from hexane, mp 100-101. *Anal.* Calcd for $C_{14}H_{13}N_3O_2$; C: 65.82, H: 5.13, N: 16.46. Found: C: 65.91, H: 4.95, N: 16.58. 1H -Nmr ($CDCl_3$) δ (ppm): 8.55-8.25 (2H, m, Ph), 7.6-7.2 (3H, m, Ph), 4.19 (3H, s, OMe), 2.95 (2H, q, $J = 7$ Hz, CH_2CH_3), 1.38 (3H, t, $J = 7$ Hz, CH_2CH_3).

Reaction of Fused Chloropyrimidine with *n*-Propylamine; General Procedure A mixture of fused chloropyrimidine (2 mmol) and 10 ml (0.17 mol) of *n*-propylamine was refluxed for 1 h with stirring. Excess of *n*-propylamine was removed under reduced pressure. The obtained residue was dissolved in $CHCl_3$, and the solution was washed with H_2O , dried over Na_2SO_4 , and concentrated. The residue was purified by column chromatography on SiO_2 with $CHCl_3$ to give propylaminoheteroarene.

4-Propylamino-3-methylisoxazolo[5,4-*d*]pyrimidine (20C): Colorless scales from hexane, mp 128-130 °C. *Anal.* Calcd for $C_9H_{12}N_4O$; C: 56.24, H: 6.29, N: 29.15. Found: C: 56.44, H: 6.43, N: 29.18. 1H -Nmr ($CDCl_3$) δ (ppm): 8.48 (1H, s, C⁶-H), 5.50 (1H, br s, NH), 3.64 (2H, q, $J = 7$ Hz, $NHCH_2CH_2CH_3$), 2.60 (3H, s, Me), 2.0-1.4 (2H, m, $NHCH_2CH_2CH_3$), 1.02 (3H, t, $J = 7$ Hz, $NHCH_2CH_2CH_3$).

4-Propylamino-3-methyl-6-phenylisoxazolo[5,4-*d*]pyrimidine (21C): Colorless scales from benzene, mp 114-115 °C. *Anal.* Calcd for $C_{13}H_{16}N_4O$; C: 67.15, H: 6.01, N: 20.88. Found: C: 67.13, H: 6.01, N: 20.90. 1H -Nmr ($CDCl_3$) δ (ppm): 8.5-8.2 (2H, m, Ph), 7.5-7.2 (3H, m, Ph), 5.4-4.9 (1H, br s, NH), 3.70 (2H, q, $J = 6$ Hz, $NHCH_2CH_2CH_3$), 2.55 (3H, s, Me), 2.0-1.4 (2H, m, $NHCH_2CH_2CH_3$), 1.05 (3H, t, $J = 6$ Hz, $NHCH_2CH_2CH_3$).

4-Propylamino-3-ethyl-6-phenylisoxazolo[5,4-*d*]pyrimidine (22C): Colorless powder from benzene, mp 126-128 °C. *Anal.* Calcd for $C_{16}H_{18}N_4O$; C: 68.06, H: 6.43, N: 19.84. Found: C: 67.97, H: 6.43, N: 19.77. 1H -Nmr ($CDCl_3$) δ (ppm): 8.53-8.26 (2H, m, Ph), 7.5-7.25 (3H, m, Ph), 5.3-5.0 (1H, br s, NH), 3.72 (2H, q, $J = 6$ Hz, $NHCH_2CH_2CH_3$), 2.92 (2H, q, $J = 6$ Hz, CH_2CH_3), 2.0-1.55 (2H, m, $NHCH_2CH_2CH_3$), 1.4 (3H, t, $J = 6$ Hz, CH_2CH_3), 1.2 (3H, t, $J = 6$ Hz, $NHCH_2CH_2CH_3$).

Table I. Appearance, Melting Point (mp), and Elemental Analysis for the Fused Pyrimidinones (7-9, 12-13, 15, and 17)

Compd	Appearance	mp (°C)	Formula	Analysis, Calcd (Found)		
				C	H	N
7a	Colorless needles (MeOH)	269-272	C ₂₁ H ₁₉ N ₃ O	76.57 (76.32)	5.81 (5.89)	12.76 (12.76)
7f	Slightly brown needles (MeOH)	294-297	C ₂₀ H ₁₇ N ₃ O	76.17 (75.74)	5.43 (5.45)	13.32 (13.24)
7h	Colorless granules (acetone)	175.5-178	C ₁₉ H ₂₁ N ₃ O ₃	67.24 (67.18)	6.24 (6.09)	12.38 (12.20)
8a	Slightly brown prisms (MeOH)	>300	C ₁₈ H ₁₅ N ₃ O	72.43 (72.23)	5.70 (5.54)	15.84 (15.89)
8c	Slightly brown needles (MeOH)	273-275	C ₁₈ H ₁₉ N ₃ O	73.70 (73.83)	6.53 (6.63)	14.32 (14.46)
9a	Yellowish granules (MeOH)	>300	C ₂₄ H ₁₇ N ₃ O	79.32 (78.61)	4.72 (4.87)	11.56 (11.33)
12a	Colorless needles (MeOH)	217-219	C ₈ H ₅ N ₃ O ₂	47.67 (47.82)	3.33 (3.21)	27.80 (27.80)
12b	Colorless needles (benzene-MeOH)	268-269	C ₇ H ₇ N ₃ O ₂	50.91 (51.06)	4.27 (4.23)	25.44 (25.31)
12c	Colorless needles (MeOH)	247-249	C ₈ H ₉ N ₃ O ₂	53.63 (53.38)	5.06 (4.90)	23.45 (23.40)
12d	Colorless needles (MeOH)	198-201	C ₉ H ₁₁ N ₃ O ₂	55.95 (56.09)	5.74 (5.72)	21.75 (21.88)
12e	Colorless needles (MeOH)	241-243	C ₁₃ H ₁₁ N ₃ O ₂	67.72 (64.87)	4.60 (4.36)	17.42 (17.21)
12f	Colorless needles (MeOH)	284	C ₁₂ H ₉ N ₃ O ₂	63.43 (63.33)	3.99 (3.98)	18.49 (18.43)
12g	Colorless needles (MeOH)	152-153	C ₉ H ₉ N ₃ O ₄	48.43 (48.26)	4.06 (4.06)	18.83 (18.95)
12h'	Colorless powder (MeOH)	290	C ₉ H ₉ N ₃ O ₄	48.43 (48.70)	4.06 (4.07)	18.83 (18.84)
13a	Colorless needles (MeOH)	179-180	C ₇ H ₇ N ₃ O ₂	50.91 (51.05)	4.27 (3.98)	25.44 (25.60)
13b	Colorless needles (benzene)	216-218	C ₈ H ₉ N ₃ O ₂	53.63 (53.50)	5.06 (5.09)	23.45 (23.23)
13c	Colorless powder (MeOH)	165-166	C ₉ H ₁₁ N ₃ O ₂	55.95 (56.03)	5.74 (5.56)	21.75 (21.75)
13d	Colorless needles (MeOH)	158-160	C ₁₀ H ₁₃ N ₃ O ₂	57.96 (57.97)	6.32 (6.25)	20.28 (20.29)
13e	Colorless needles (MeOH)	197-198	C ₁₄ H ₁₃ N ₃ O ₂	65.87 (66.07)	5.13 (5.15)	16.46 (16.58)
13f	Slightly yellow scales (MeOH-AcOH)	250-252	C ₁₃ H ₁₁ N ₃ O ₂	64.72 (64.62)	4.60 (4.48)	17.42 (17.27)
13g	Colorless powder (MeOH)	206-210	C ₁₀ H ₁₁ N ₃ O ₄	50.63 (50.41)	4.67 (4.61)	17.71 (17.73)
13h'	Colorless powder (MeOH)	223-226	C ₁₀ H ₁₁ N ₃ O ₄	50.63 (50.54)	4.67 (4.40)	17.71 (17.63)
13j	Colorless needles (MeOH)	255-258	C ₁₁ H ₉ N ₃ O ₃	57.14 (57.22)	3.92 (3.89)	18.17 (18.14)
15a	Yellow needles (MeOH)	247-250	C ₁₀ H ₁₀ N ₂ OS	58.23 (57.98)	4.89 (4.97)	13.58 (13.29)
15b	Yellow needles (MeOH)	286-289 (lit. ¹¹ 270-271)	C ₁₁ H ₁₂ N ₂ OS	59.98 (60.06)	5.49 (5.54)	12.72 (12.45)
15c	Yellowish needles (MeOH)	253-254	C ₁₂ H ₁₄ N ₂ OS	61.51 (61.71)	6.02 (6.10)	11.96 (11.82)
15d	Yellowish needles (MeOH)	251-252	C ₁₃ H ₁₆ N ₂ OS	62.87 (62.74)	6.49 (6.48)	11.28 (11.13)
15e	Yellowish needles (MeOH)	253-255	C ₁₇ H ₁₈ N ₂ OS	68.89 (68.69)	5.44 (5.51)	9.45 (9.44)
15f	Yellowish needles (MeOH)	209-211	C ₁₆ H ₁₄ N ₂ OS	68.06 (67.92)	5.00 (5.10)	9.92 (10.13)

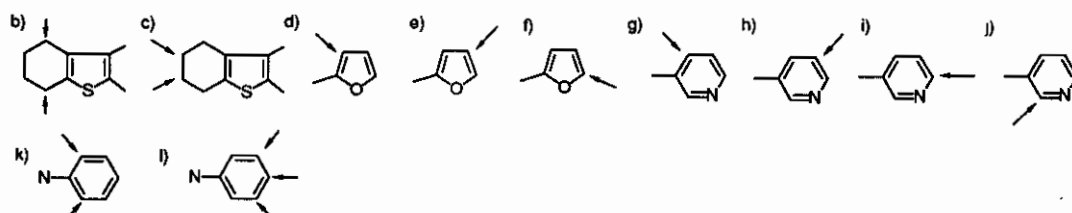
17a	Colorless needles (MeOH)	280 (lit. ¹² 279)	C ₁₀ H ₇ N ₅ O			
17b	Yellowish needles (MeOH)	267-268 (lit. ¹² 268)	C ₁₁ H ₉ N ₅ O	58.14 (58.20)	3.99 (4.04)	30.82 (31.08)
17c	Colorless needles (MeOH)	269 (lit. ¹² 270)	C ₁₂ H ₁₁ N ₅ O	59.74 (59.85)	4.60 (4.65)	29.03 (29.08)
17d	Colorless needles (acetone)	246-249	C ₁₃ H ₁₃ N ₅ O	61.17 (61.16)	5.13 (5.12)	27.43 (27.61)
17e	Yellowish needles (MeOH)	258-260 (lit. ¹² 281)	C ₁₇ H ₁₃ N ₅ O	67.32 (67.05)	4.32 (4.34)	23.09 (22.83)
17f	Yellowish powder (MeOH)	302-303	C ₁₆ H ₁₁ N ₅ O	66.42 (66.26)	3.83 (3.94)	24.21 (24.26)
17i	Colorless granules (MeOH)	279-282	C ₁₆ H ₁₃ N ₅ O	68.56 (68.76)	4.16 (3.93)	22.21 (22.13)
17j	Yellowish needles (MeOH)	258-259	C ₁₄ H ₉ N ₅ O ₂	60.21 (60.31)	3.25 (3.12)	25.08 (24.97)
17k	Yellow needles (MeOH)	279-282	C ₁₅ H ₁₀ N ₆ O	62.07 (61.76)	3.47 (3.49)	28.95 (29.08)
19a	Colorless needles (MeOH)	215-216 (lit. ¹⁰ 215.5-216.5)	C ₈ H ₆ N ₂ O			

Table II Ir and ¹H-Nmr Spectral Data for the Fused Pyrimidinones (7-9, 12-13, 15, and 17)

Compd	Ir (KBr)	Solvent ^{a)}	¹ H-Nmr δ (ppm)
7e	1660(CO)	A	7.15-7.7 (10H, m, aromatic H), 4.15 (2H, s, CH ₂), 2.35 (3H, s, Me) 2.17 (3H, s, Me)
7f	1665(CO)	A	7.4-7.8 (10H, m, aromatic H), 2.48 (3H, s, Me), 2.15 (3H, s, Me)
7h	1670(CO)	D	7.3-7.45 (5H, m, aromatic H), 4.05 (2H, q, <i>J</i> = 7 Hz, CH ₂ CH ₃), 2.7-3.05 (4H, m, CH ₂ CH ₃), 2.40 (3H, s, Me), 2.09 (3H, s, Me), 1.18 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)
8a	1660(CO)	A	8.41 (1H, s, C ² -H), 7.15-7.7 (5H, m, aromatic H), 1.7-3.1 (8H, m, aliphatic H)
8c	1660(CO)	A	7.2-7.6 (5H, m, aromatic H), 1.7-2.15 (10H, m, aliphatic H and CH ₂ CH ₃), 1.29 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)
9a	1660(CO)	A	8.21 (1H, s, C ² -H), 7.0-7.5 (15H, m, aromatic H)
12a	1700 (CO)	A	8.40 (1H, s, C ⁶ -H), 2.68 (3H, s, Me)
12b	1700 (CO)	A	2.69 (3H, s, Me), 2.61 (3H, s, Me)
12c	1690 (CO)	A	2.97 (2H, q, <i>J</i> = 7 Hz, CH ₂ CH ₃), 2.62 (3H, s, Me), 1.45 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)
12d	1690 (CO)	A	3.5-2.4 (1H, m, CH(CH ₃) ₂), 2.63 (3H, s, Me) 1.45 (6H, d, <i>J</i> = 7 Hz, CH(CH ₃) ₂)
12e	1700 (CO)	A	7.26 (5H, s, Ph), 4.20 (2H, s, CH ₂ Ph), 2.61 (3H, s, Me)
12f	1680 (CO)	A	7.3-8.2 (5H, m, Ph), 2.68 (3H, s, Me)
12g	1710(CO)	A	4.05 (2H, q, <i>J</i> = 7 Hz, COOCH ₂ CH ₃), 2.67 (3H, s, Me), 1.48 (3H, t, <i>J</i> = 7 Hz, COOCH ₂ CH ₃)
12h'	1690 (CO)	A	2.9-3.5 (4H, m, CH ₂ CH ₂ COOH), 2.65 (3H, s, Me)
13a	1700 (CO)	A	8.50 (1H, s, C ⁶ -H), 3.18 (2H, q, <i>J</i> = 6 Hz, CH ₂ CH ₃), 1.43 (3H, t, <i>J</i> = 6 Hz, CH ₂ CH ₃)
13b	1700 (CO)	A	2.97 (2H, q, <i>J</i> = 7 Hz, CH ₂ CH ₃), 2.61 (3H, s, Me) 1.42 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)
13c	1720 (CO)	A	2.6-3.3 (4H, m, CH ₂ CH ₃ x 2), 1.2-1.7 (6H, m, CH ₂ CH ₃ x 2)
13d	1690 (CO)	A	2.8-3.5 (3H, m, CH ₂ CH ₃ and CH(CH ₃) ₂), 1.2-1.8 (9H, m, CH ₂ CH ₃ and CH(CH ₃) ₂)
13e	1670 (CO)	A	7.25 (5H, s, Ph), 4.15 (2H, s, CH ₂ Ph), 3.00 (2H, q, <i>J</i> = 7 Hz, CH ₂ CH ₃), 1.35 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)
13f	1680 (CO)	A	7.3-8.2 (5H, m Ph), 3.07 (2H, q, <i>J</i> = 7 Hz, CH ₂ CH ₃), 1.45 (3H, t, <i>J</i> = 7 Hz, CH ₂ CH ₃)

13g	1690 (CO)	A	4.55 (2H, q, $J = 6$ Hz, $\text{COOCH}_2\text{CH}_3$), 3.06 (2H, q, $J = 7$ Hz, CH_2CH_3) 1.7-1.2 (6H, m, $\text{COOCH}_2\text{CH}_3$ and CH_2CH_3)
13h'	1690 (CO)	A	2.8-3.45 (6H, m, CH_2CH_3 and $\text{CH}_2\text{CH}_2\text{COOH}$), 1.42 (3H, t, $J = 7$ Hz, CH_2CH_3)
13j	1680 (CO)	B	13.00 (1H, br s, NH), 8.09 (1H, $J = 1.9$ Hz, furan ^b), 7.78 (1H, d, $J = 3.9$ Hz, furan ^b), 6.80 (1H, dd, $J = 1.9, 3.9$ Hz, furan ^b), 2.87 (2H, q, $J = 7.8$ Hz, CH_2CH_3), 1.32 (3H, t, $J = 7.8$ Hz, CH_2CH_3)
15a	1660 (CO)	A	9.00 (1H, s, $\text{C}^2\text{-H}$), 2.6-3.2 (4H, m) ^b , 1.65-2.2 (4H, m) ^a
15b	1660 (CO)	A	2.7-3.2 (4H, m) ^b , 2.83 (3H, s, Me), 1.7-2.15 (4H, m) ^a
15c	1660 (CO)	A	3.15 (2H, q, $J = 7$ Hz, CH_2CH_3), 2.7-3.2 (4H, m) ^b , 1.7-2.1 (4H, m) ^a , 1.53 (3H, t, $J = 7$ Hz, CH_2CH_3)
15d	1650 (CO)	D	2.6-3.2 (5H, m, $\text{CH}(\text{CH}_3)_2$ and methylene ^b), 1.7-2.05 (4H, m) ^a 1.39 (6H, d, $J = 7$ Hz, $\text{CH}(\text{CH}_3)_2$)
15e	1660 (CO)	A	7.34 (5H, s, CH_2Ph), 4.35 (2H, s, CH_2Ph), 2.5-3.1 (4H, m) ^b , 1.7-2.15 (4H, m) ^a
15f	1660 (CO)	A	7.55-8.1 (5H, m, Ph), 2.5-3.1 (4H, m) ^b , 1.7-2.15 (4H, m) ^a
17b	1695 (CO)	A	7.5-7.9 (5H, m, aromatic H), 2.70 (3H, s, Me)
17c	1695 (CO)	B	7.9-8.2 (2H, m, N-Ph ^k), 7.45-7.8 (3H, m, N-Ph ^h), 2.65 (2H, q, $J = 7.8$ Hz, CH_2CH_3), 1.26 (3H, t, $J = 7.8$ Hz, CH_2CH_3)
17d	1710 (CO)	A	7.9-8.25 (2H, m, N-Ph ^k), 7.5-7.7 (3H, m, N-Ph ^h), 3.10 (1H, q, $J = 7.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.43 (6H, d, $J = 7.8$ Hz, $\text{CH}(\text{CH}_3)_2$)
17e	1710 (CO)	A	7.9-8.15 (2H, m, N-Ph ^k), 7.6-7.75 (3H, m, N-Ph ^h), 7.35 (5H, s, CH_2Ph), 4.20 (2H, s, CH_2Ph)
17f	1700 (CO)	A	7.9-8.3 (4H, m, N-Ph ^k and Ph), 7.45-7.75 (6H, m, N-Ph ^h and Ph)
17i	1710 (CO)	A	8.08 (1H, d, $J = 16$ Hz, PhCH=CH), 8.0-8.1 (2H, m, aromatic H), 7.6-7.7 (5H, m, aromatic H), 7.45-7.5 (3H, m, aromatic H), 6.99 (1H, d, $J = 16$ Hz, PhCH=CH)
17j	1700 (CO)	A	8.05-8.1 (2H, m, N-Ph ^k), 7.80 (1H, m, furan ^b), 7.6-7.7 (4H, m, furan ^a and N-Ph ^h), 6.74 (1H, dd, $J = 1.9, 3.6$ Hz, furan ^b)
17k	1720 (CO)	B	13.26 (1H, br s, NH), 9.29-9.3 (1H, m, pyridine ^b), 8.79-8.81 (1H, m, pyridine ^b), 8.48-8.53 (1H, m, pyridine ^a), 8.12-8.15 (2H, m, N-Ph ^k), 7.54-7.72 (4H, m, pyridine ^b and N-Ph ^h)
19b	1680 (CO)	D	8.2-8.4 (1H, m, aromatic H), 7.3-7.7 (3H, m, aromatic H), 2.60 (3H, s, Me)
19c	1680 (CO)	C	8.1-8.35 (1H, m, aromatic H), 7.3-7.75 (3H, m, aromatic H), 2.72 (2H, q, $J = 7$ Hz, CH_2CH_3), 1.40 (3H, t, $J = 7$ Hz, CH_2CH_3)

a) $\text{A} = \text{CF}_3\text{COOD} + \text{CDCl}_3$, $\text{B} = \text{DMSO}-d_6$, $\text{C} = \text{CD}_3\text{OD}$, $\text{D} = \text{CDCl}_3$



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