SYNTHESIS OF FUSED PYRIMIDINONES BY REACTION OF AMINOARENECARBOXAMIDE 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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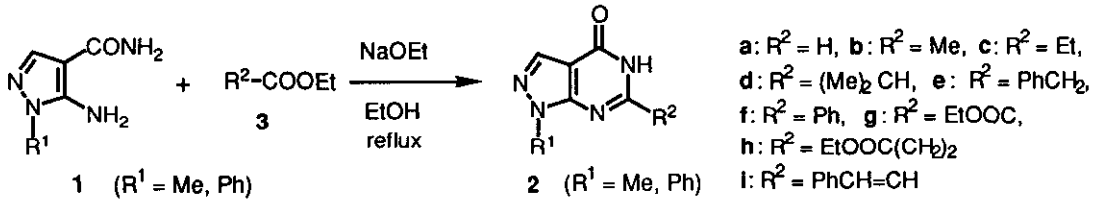
Abstract——Several fused pyrimidinones were synthesized by reaction of aminoarenecarboxamide with esters in moderate to good yields. In the presence of sodium ethoxide, treatments of 2-amino-1-phenyl-3-pyrrolecarboxamide(**4**, **5**, and **6**), 2-amino-3-thiophenecarboxamide (**14**), 3-amino-4-isoxazolecarboxamide (**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.

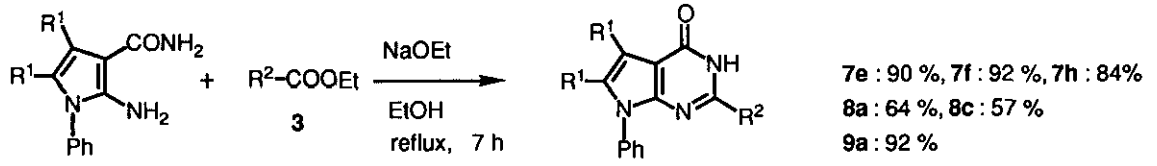
Fused pyrimidines are important compounds in the fields of pharmacy and biology,[1] and a number of these compounds have been found to have biological activities.[2] In our continuous study related to fused pyrimidines, one of our purposes is discovery and establishment of a facilely preparative method 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.



1 (R^1 = Me, Ph) **2** (R^1 = Me, Ph)

Scheme 1

We have already reported that 4,5-dimethyl-2-amino-1-phenyl-3-pyrrolecarboxamide (**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-pyrrolecarboxamides (**4**, **5**, and **6**) with esters (**3**) except reported esters, and obtained the corresponding pyrrolopyrimidinones (**7**, **8** and **9**) in moderate to good yields.

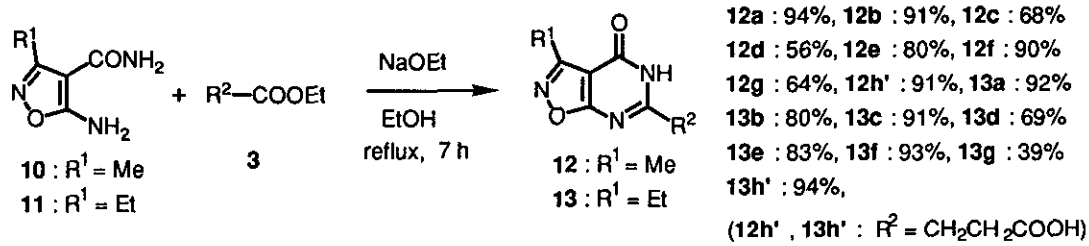


4: R^1 = Me
5: R^1 = -$(CH_2)_4$-
6: R^1 = Ph

7: R^1 = Me
8: R^1 = -$(CH_2)_4$-
9: R^1 = Ph

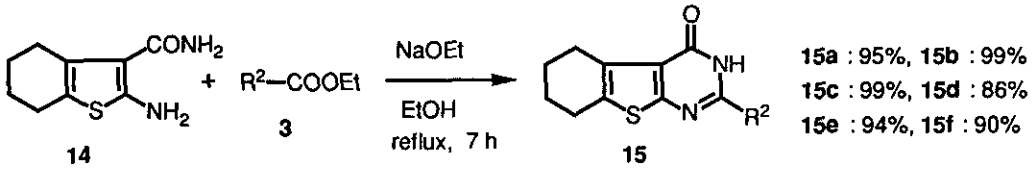
Scheme 2

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 ethoxycarbonylethyl group at the 6-position by reaction of 5-amino-4-isoxazolecarboxamides (**10** and **11**) with ethyl succcinate (**3h**), but the reactions afforded hydrolyzed products (**12h'** and **13h'**) in good yields.



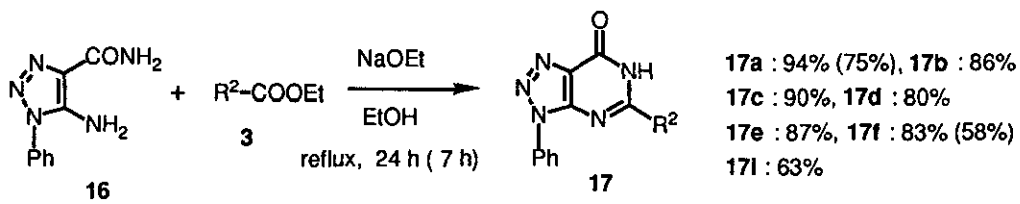
Scheme 3

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.



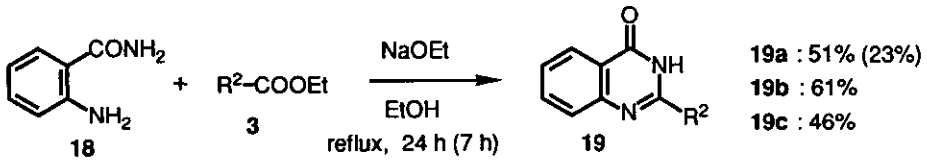
Scheme 4

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 established 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**)



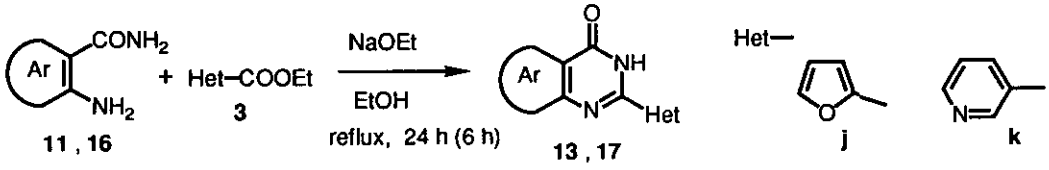
Scheme 5

On the other hand, 4(3*H*)-quinazolone (**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*)-Quinazolone (**19**) was obtained in 51% yield when the reaction was run in refluxing EtOH for 24 h.



Scheme 6

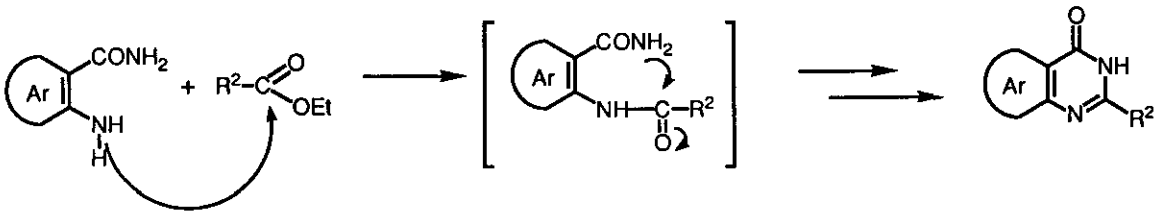
Moreover, compound (**16**)reacted with ethyl heteroarenecarboxylates, such as ethyl 2-furoate (**3j**) and ethyl 3-pyridinecarboxylate (**3k**), to give the corresponding triazolopyrimidinones (**17j** and **17k**), which possess heteroarenyl groups at the 5-position. Similarly 6-furyl-3-ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one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



13j : 43% (10%), **17j** : 67%, **17k** : 81%,

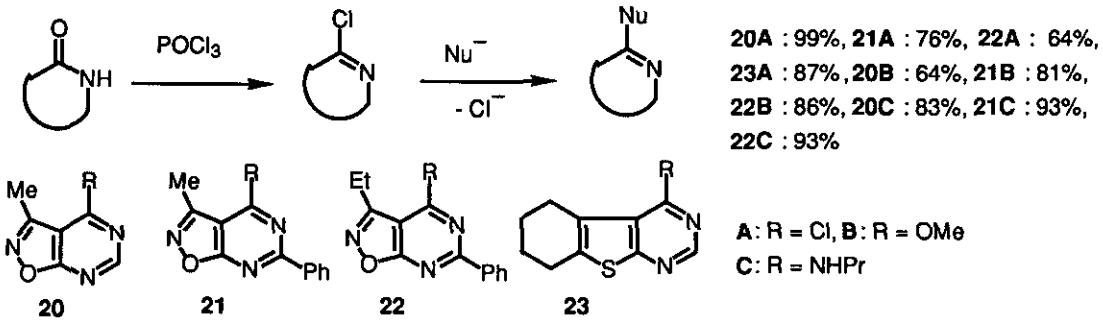
Scheme 7

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 aminoarenecarboxamide (nucleophilicity of the amino group) and the carbonyl group of the esters (electrophilicity of the esters). As the ring-closure requires to produce acylamidoarenecarboxamide by acylation with esters, acylation of five-membered aminoarenecarboxamides, whose amino groups are electron-rich because of the electron-donating-effect of the ring, proceeds easily in comparison with that of six-membered aminoarenecarboxamides. Namely synthesis of 4(3*H*)-quinazolone required prolonged reaction time, but formation of pyrrolo-, isoxazolo-, thieno-, and triazolopyrimidinones easily proceeded. Similarly, ethyl arenecarboxylate 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 $POCl_3$ 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 aminoarenecarboxamide 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 (^{1}H-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 aminoarenecarboxamide (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 H_2O (*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-pyrrolecarboxamide (**4**),[4] 2-amino-4,5-tetramethylene-1-phenyl-3-pyrrolecarboxamide(**5**),[4] 2-amino-1,4,5-triphenyl-3-pyrrolecarboxamide (**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 aminoarenecarboxamide.

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 ^{1}H-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 $POCl_3$ (55 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 resultant solution was poured onto ice-H_2O. The 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-chloroisoxazolo[5,4-*d*]pyrimidine, colorless scales (benzene), mp 58-62 °C. *Anal.* Calcd for $C_6H_4N_3OCl$; C: 42.50, H: 2.38, N: 24.78. Found. C; 42.47, H; 2.19, N; 25.01. ^{1}H-Nmr ($CDCl_3$) 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 $POCl_3$ (40 ml, 0.43 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 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. ^{1}H-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(5*H*)-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. ^{1}H-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, $C\underline{H}_2CH_3$), 1.45 (3H, t, *J* = 7 Hz, $CH_2C\underline{H}_3$).
Preparation of 4-Chloro-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (23A) A mixture of 5,6-tetramethylenethieno[2,3-*d*]pyrimidin-4(3*H*)-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. ^{1}H-Nmr ($CDCl_3$) δ (ppm): 8.65 (1H, s, C^6-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. ^{1}H-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. ^{1}H-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, $C\underline{H}_2CH_3$), 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. ^{1}H-Nmr ($CDCl_3$) δ (ppm): 8.48 (1H, s, C^6-H), 5.50 (1H, br s, NH), 3.64 (2H, q, *J* = 7 Hz, $NHC\underline{H}_2CH_2CH_3$), 2.60 (3H, s, Me), 2.0-1.4 (2H, m, $NHCH_2C\underline{H}_2CH_3$), 1.02 (3H, t, *J* = 7 Hz, $NHCH_2CH_2C\underline{H}_3$).
4-Propylamino-3-methyl-6-phenylisoxazolo[5,4-*d*]pyrimidine (**21C**): Colorless scales from benzene, mp 114-115 °C. *Anal.* Calcd for $C_{15}H_{16}N_4O$; C: 67.15, H: 6.01, N: 20.88. Found. C; 67.13, H; 6.01, N; 20.90. ^{1}H-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, $NHC\underline{H}_2CH_2CH_3$), 2.55 (3H, s, Me), 2.0-1.4 (2H, m, $NHCH_2C\underline{H}_2CH_3$), 1.05 (3H, t, *J* = 6 Hz, $NHCH_2CH_2C\underline{H}_3$).
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. ^{1}H-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, $NHC\underline{H}_2CH_2CH_3$), 2.92 (2H, q, *J* = 6 Hz, $C\underline{H}_2CH_3$), 2.0-1.55 (2H, m, $NHCH_2C\underline{H}_2CH_3$), 1.4 (3H, t, *J* = 6 Hz, $CH_2C\underline{H}_3$), 1.2 (3H, t, *J* = 6 Hz, $NHCH_2CH_2C\underline{H}_3$).

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
7e	Colorless needles (MeOH)	269-272	$C_{21}H_{19}N_3O$	76.57 (76.32)	5.81 (5.89)	12.76 (12.76)
7f	Slightly brown needles (MeOH)	294-297	$C_{20}H_{17}N_3O$	76.17 (75.74)	5.43 (5.45)	13.32 (13.24)
7h	Colorless granules (acetone)	175.5-178	$C_{19}H_{21}N_3O_3$	67.24 (67.18)	6.24 (6.09)	12.38 (12.20)
8a	Slightly brown prisms (MeOH)	>300	$C_{16}H_{15}N_3O$	72.43 (72.23)	5.70 (5.54)	15.84 (15.89)
8c	Slightly brown needles (MeOH)	273-275	$C_{18}H_{19}N_3O$	73.70 (73.83)	6.53 (6.63)	14.32 (14.46)
9a	Yellowish granules (MeOH)	>300	$C_{24}H_{17}N_3O$	79.32 (78.61)	4.72 (4.87)	11.56 (11.33)
12a	Colorless needles (MeOH)	217-219	$C_6H_5N_3O_2$	47.67 (47.82)	3.33 (3.21)	27.80 (27.80)
12b	Colorless needles (benzene-MeOH)	268-269	$C_7H_7N_3O_2$	50.91 (51.06)	4.27 (4.23)	25.44 (25.31)
12c	Colorless needles (MeOH)	247-249	$C_8H_9N_3O_2$	53.63 (53.38)	5.06 (4.90)	23.45 (23.40)
12d	Colorless needles (MeOH)	198-201	$C_9H_{11}N_3O_2$	55.95 (56.09)	5.74 (5.72)	21.75 (21.88)
12e	Colorless needles (MeOH)	241-243	$C_{13}H_{11}N_3O_2$	67.72 (64.87)	4.60 (4.36)	17.42 (17.21)
12f	Colorless needles (MeOH)	284	$C_{12}H_9N_3O_2$	63.43 (63.33)	3.99 (3.98)	18.49 (18.43)
12g	Colorless needles (MeOH)	152-153	$C_9H_9N_3O_4$	48.43 (48.26)	4.06 (4.06)	18.83 (18.95)
12h'	Colorless powder (MeOH)	290	$C_9H_9N_3O_4$	48.43 (48.70)	4.06 (4.07)	18.83 (18.84)
13a	Colorless needles (MeOH)	179-180	$C_7H_7N_3O_2$	50.91 (51.05)	4.27 (3.98)	25.44 (25.60)
13b	Colorless needles (benzene)	216-218	$C_8H_9N_3O_2$	53.63 (53.50)	5.06 (5.09)	23.45 (23.23)
13c	Clorless powder (MeOH)	165-166	$C_9H_{11}N_3O_2$	55.95 (56.03)	5.74 (5.56)	21.75 (21.75)
13d	Colorless needles (MeOH)	158-160	$C_{10}H_{13}N_3O_2$	57.96 (57.97)	6.32 (6.25)	20.28 (20.29)
13e	Colorless needles (MeOH)	197-198	$C_{14}H_{13}N_3O_2$	65.87 (66.07)	5.13 (5.15)	16.46 (16.58)
13f	Slightly yellow scales (MeOH-AcOH)	250-252	$C_{13}H_{11}N_3O_2$	64.72 (64.62)	4.60 (4.48)	17.42 (17.27)
13g	Colorless powder (MeOH)	206-210	$C_{10}H_{11}N_3O_4$	50.63 (50.41)	4.67 (4.61)	17.71 (17.73)
13h'	Colorless powder (MeOH)	223-226	$C_{10}H_{11}N_3O_4$	50.63 (50.54)	4.67 (4.40)	17.71 (17.63)
13j	Colorless needles (MeOH)	255-258	$C_{11}H_9N_3O_3$	57.14 (57.22)	3.92 (3.89)	18.17 (18.14)
15a	Yellow needles (MeOH)	247-250	$C_{10}H_{10}N_2OS$	58.23 (57.98)	4.89 (4.97)	13.58 (13.29)
15b	Yellow needles (MeOH)	286-289 (lit.[11] 270-271)	$C_{11}H_{12}N_2OS$	59.98 (60.06)	5.49 (5.54)	12.72 (12.45)
15c	Yellowish needles (MeOH)	253-254	$C_{12}H_{14}N_2OS$	61.51 (61.71)	6.02 (6.10)	11.96 (11.82)
15d	Yellowish needles (MeOH)	251-252	$C_{13}H_{16}N_2OS$	62.87 (62.74)	6.49 (6.48)	11.28 (11.13)
15e	Yellowish needles (MeOH)	253-255	$C_{17}H_{16}N_2OS$	68.89 (68.69)	5.44 (5.51)	9.45 (9.44)
15f	Yellowish needles (MeOH)	209-211	$C_{16}H_{14}N_2OS$	68.06 (67.92)	5.00 (5.10)	9.92 (10.13)

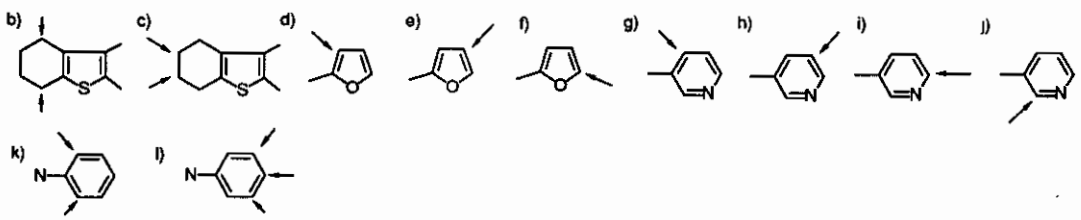
17a	Colorless needles (MeOH)	280 (lit.[12] 279)	$C_{10}H_7N_5O$			
17b	Yellowish needles (MeOH)	267-268 (lit.[12] 268)	$C_{11}H_9N_5O$	58.14 (58.20)	3.99 (4.04)	30.82 (31.08)
17c	Colorless needles (MeOH)	269 (lit.[12] 270)	$C_{12}H_{11}N_5O$	59.74 (59.85)	4.60 (4.65)	29.03 (29.08)
17d	Colorless needles (acetone)	246-249	$C_{13}H_{13}N_5O$	61.17 (61.16)	5.13 (5.12)	27.43 (27.61)
17e	Yellowish needles (MeOH)	258-260 (lit.[12] 281)	$C_{17}H_{13}N_5O$	67.32 (67.05)	4.32 (4.34)	23.09 (22.83)
17f	Yellowish powder (MeOH)	302-303	$C_{18}H_{11}N_5O$	66.42 (66.26)	3.83 (3.94)	24.21 (24.26)
17i	Colorless granules (MeOH)	279-282	$C_{18}H_{13}N_5O$	68.56 (68.76)	4.16 (3.93)	22.21 (22.13)
17j	Yellowish needles (MeOH)	258-259	$C_{14}H_9N_5O_2$	60.21 (60.31)	3.25 (3.12)	25.08 (24.97)
17k	Yellow needles (MeOH)	279-282	$C_{15}H_{10}N_6O$	62.07 (61.76)	3.47 (3.49)	28.95 (29.08)
19a	Colorless needles (MeOH)	215-216 (lit.[10] 215.5-216.5)	$C_8H_6N_2O$			

Table II Ir and ^{1}H-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, J = 7 Hz, $C\underline{H}_2CH_3$), 2.7-3.05 (4H, m, $C\underline{H}_2C\underline{H}_2$), 2.40 (3H, s, Me), 2.09 (3H, s, Me), 1.18 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
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 $C\underline{H}_2CH_3$), 1.29 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
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, J = 7 Hz, $C\underline{H}_2CH_3$), 2.62 (3H, s, Me), 1.45 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
12d	1690 (CO)	A	3.5-2.4 (1H, m, $C\underline{H}(CH_3)_2$), 2.63 (3H, s, Me) 1.45 (6H, d, J = 7 Hz, $CH(C\underline{H}_3)_2$)
12e	1700 (CO)	A	7.26 (5H, s, Ph), 4.20 (2H, s, $C\underline{H}_2Ph$), 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, J = 7 Hz, $COOC\underline{H}_2CH_3$), 2.67 (3H, s, Me), 1.48 (3H, t, J = 7 Hz, $COOCH_2C\underline{H}_3$)
12h'	1690 (CO)	A	2.9-3.5 (4H, m, $C\underline{H}_2C\underline{H}_2COOH$), 2.65 (3H, s, Me)
13a	1700 (CO)	A	8.50 (1H, s, C^6-H), 3.18 (2H, q, J = 6 Hz, $C\underline{H}_2CH_3$), 1.43 (3H, t, J = 6 Hz, $CH_2C\underline{H}_3$)
13b	1700 (CO)	A	2.97 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 2.61 (3H, s, Me) 1.42 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
13c	1720 (CO)	A	2.6-3.3 (4H, m, $C\underline{H}_2CH_3$ x 2), 1.2-1.7 (6H, m, $CH_2C\underline{H}_3$ x 2)
13d	1690 (CO)	A	2.8-3.5 (3H, m, $C\underline{H}_2CH_3$ and $C\underline{H}(CH_3)_2$), 1.2-1.8 (9H, m, $CH_2C\underline{H}_3$ and $CH(C\underline{H}_3)_2$)
13e	1670 (CO)	A	7.25 (5H, s, Ph), 4.15 (2H, s, $C\underline{H}_2Ph$), 3.00 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 1.35 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
13f	1680 (CO)	A	7.3-8.2 (5H, m Ph), 3.07 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 1.45 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)

13g	1690 (CO)	A	4.55 (2H, q, J = 6 Hz, $COOC\underline{H}_2CH_3$), 3.06 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$) 1.7-1.2 (6H, m, $COOCH_2C\underline{H}_3$ and $CH_2C\underline{H}_3$)
13h'	1690 (CO)	A	2.8-3.45 (6H, m, $C\underline{H}_2CH_3$ and $C\underline{H}_2C\underline{H}_2COOH$), 1.42 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
13j	1680 (CO)	B	13.00 (1H, br s, NH), 8.09 (1H, J = 1.9 Hz, furan[f]), 7.78 (1H, d, J = 3.9 Hz, furan[d]), 6.80 (1H, dd, J = 1.9, 3.9 Hz, furan[e]), 2.87 (2H, q, J = 7.8 Hz, $C\underline{H}_2CH_3$), 1.32 (3H, t, J = 7.8 Hz, $CH_2C\underline{H}_3$)
15a	1660 (CO)	A	9.00 (1H, s, C^2-H), 2.6-3.2 (4H, m)[b], 1.65-2.2 (4H, m)[c]
15b	1660 (CO)	A	2.7-3.2 (4H, m)[b][j], 2.83 (3H, s, Me), 1.7-2.15 (4H, m)[c]
15c	1660 (CO)	A	3.15 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 2.7-3.2 (4H, m)[b], 1.7-2.1 (4H, m)[c], 1.53 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)
15d	1650 (CO)	D	2.6-3.2 (5H, m, $C\underline{H}(CH_3)_2$ and methylene[b]), 1.7-2.05 (4H, m)[c] 1.39 (6H, d, J = 7 Hz, $CH(C\underline{H}_3)_2$)
15e	1660 (CO)	A	7.34 (5H, s, $CH_2\underline{Ph}$), 4.35 (2H, s, $C\underline{H}_2Ph$), 2.5-3.1 (4H, m)[b], 1.7-2.15 (4H, m)[c]
15f	1660 (CO)	A	7.55-8.1 (5H, m, Ph), 2.5-3.1 (4H, m)[b], 1.7-2.15 (4H, m)[c]
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[l]), 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[l]), 3.10 (1H, q, J = 7.8 Hz, $C\underline{H}(CH_3)_2$), 1.43 (6H, d, J = 7.8 Hz, $CH(C\underline{H}_3)_2$)
17e	1710 (CO)	A	7.9-8.15 (2H, m, N-Ph[k]), 7.6-7.75 (3H, m, N-Ph[l]), 7.35 (5H, s, $CH_2\underline{Ph}$), 4.20 (2H, s, $C\underline{H}_2Ph$)
17f	1700 (CO)	A	7.9-8.3 (4H, m, N-Ph[k] and Ph), 7.45-7.75 (6H, m, N-Ph[l] and Ph)
17i	1710(CO)	A	8.08 (1H, d, J = 16 Hz, $PhC\underline{H}$=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=$C\underline{H}$)
17j	1700 (CO)	A	8.05-8.1 (2H, m, N-Ph[k]), 7.80 (1H, m, furan[f]), 7.6-7.7 (4H, m, furan[d] and N-Ph[l]), 6.74 (1H, dd, J = 1.9, 3.6 Hz, furan[e])
17k	1720 (CO)	B	13.26 (1H, br s, NH), 9.29-9.3 (1H, m, pyridine[j]), 8.79-8.81 (1H, m, pyridine[i]), 8.48-8.53 (1H, m, pyridine[g]), 8.12-8.15 (2H, m, N-Ph[k]), 7.54-7.72 (4H, m, pyridine[h] and N-Ph[l])
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, $C\underline{H}_2CH_3$), 1.40 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$)

a) A = CF_3COOD+ $CDCl_3$, B = DMSO-d_6, C = CD_3OD, D = $CDCl_3$



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