AROYLATION OF FUSED PYRIMIDINES; SYNTHESIS OF 4-AROYLFURO[2,3-*d*]-, 4-AROYLTHIENO[2,3-*d*]-, AND 4-AROYL-ISOXAZOLO[5,4-*d*]PYRIMIDINES

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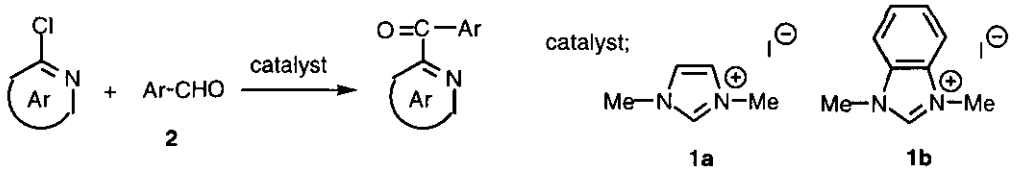
Abstract ——— 4-Aroylfuro[2,3-*d*]- (**4**), 4-aroylthieno[2,3-*d*]- (**7** and **8**), and 4-aroylisoxazolo[5,4-*d*]pyrimidines (**13**) were synthesized by aroylation of the fused chloro- (**3a** and **12**) or bromopyrimidines (**3b**, **5**, and **6**) with arenecarbaldehydes (**2**) catalyzed by an imidazolium salt (**1a**). The fused aroylpyrimidines (**4** and **7**) were also synthesized by oxidative decyanation of α-phenylheteroareneacetonitriles (**10** and **11**).

As a continuation of our studies on the syntheses and reactivities of fused pyrimidines,[1] we tried to establish a synthetic method for ketones having a fused pyrimidine ring system. Fused pyrimidine derivatives occur widely in nature,[2] and many of them have biological activities.[3]

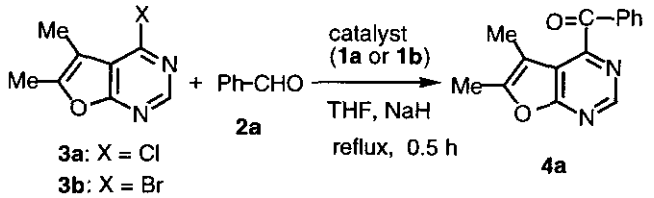
We have already developed a catalytic aroylation method using arenecarbaldehydes (**2**) as the aroyl sources; the aroyl groups are nucleophilically introduced by the catalytic action of azolium salts (**1a** and **1b**).[4] This is a facile method of synthesizing aroylheteroarenes such as fused aroylpyrimidines. In this paper, we wish to describe the synthesis of 4-aroylfuropyrimidines (**4**), 4-aroylthienopyrimidines (**7** and **8**), and 4-aroylisoxazolopyrimidines (**13**) using 1,3-dimethylimidazolium iodide (**1a**) and 1,3-dimethylbenzimidazolium



Scheme 1

iodide (**1b**) as catalysts.

4-Chloro-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3a**) reacted with benzaldehyde (**2a**) in the presence of 1,3-dimethylimidazolium iodide (**1a**) to give 4-benzoyl-5,6-dimethylfuro[2,3-*d*]pyrimidine (**4a**). However the yield was low (43%). We considered that this might have been due to low activity of the chlorine atom as the leaving group. In an attempt to improve the yield, 4-bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3b**) was synthesized and its aroylation was examined. 4-Benzoyl-5,6-dimethylfuro[2,3-*d*]pyrimidine (**4a**) was obtained in good yield (79%), when **3b** was treated with benzaldehyde (**2a**) in the presence of the imidazolium salt (**1a**). When 1,3-dimethylbenzimidazolium iodide (**1b**) was used in this aroylation as the catalyst, however, the expected benzoylfuropyrimidine (**4a**) was not formed and the starting compound (**3b**) was recovered (60%). In further experiments, the 4-bromofuropyrimidine (**3b**) and the imidazolium salt (**1a**) were used.



3a: X = Cl
3b: X = Br

4a

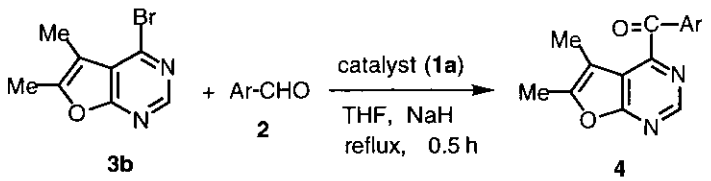
Substrate	Catalyst	Ketone (**4a**) Yield (%)
3a	**1a**	43
3b	**1a**	79
3b	**1b**	– [a] (60)[b]

[a] The ketone (**4a**) was not isolated.

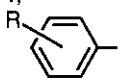
[b] Recovery of the starting **3b**.

Scheme 2

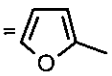
As shown in Scheme 3, synthesis of several 4-aroyl-5,6-dimethylfuro[2,3-*d*]pyrimidines (**4**) was achieved by treatment of the bromofuropyrimidine (**3b**) with arenecarbaldehydes (**2**) catalyzed by the imidazolium salt (**1a**) in refluxing THF. Namely, on treatment with *p*-fluoro- (**2b**), *p*-chloro- (**2c**), *p*-bromo- (**2d**), *p*-methyl- (**2g**), and *p*-methoxybenzaldehyde (**2h**), bromofuropyrimidine (**3b**) was converted to aroylfuropyrimidines (**4**) in moderate to good yields. On similar treatment with *p*-nitro- (**2k**) and *p*-dimethylaminobenzaldehyde (**2l**), the aroylated compounds (**4k** and **4l**) could not be obtained because of the extremely powerful electron–donating and –withdrawing effects of the substituents.[4a] In the case of *o*-methoxybenzaldehyde (**2i**), the aroylation failed to proceed because of the steric hindrance and the electron–donating effect of the methoxy group. Reaction with heteroarenecarbaldehydes, 2-furaldehyde (**2m**) and 2-thiophenecarbaldehyde (**2n**) furnished the corresponding aroylfuropyrimidines (**4m** and **4n**).



2 and **4**;

Ar = 

a: R = H (Ph), **b**: R = *p*–F, **c**: R = *p*–Cl, **d**: R = *p*–Br, **e**: *o*–Br, **f**: *m*–Br, **g**: R = *p*–Me, **h**: R = *p*–OMe, **i**: *o*–OMe, **j**: *m*–OMe, **k**: R = *p*–NO_2, **l**: R = *p*–NMe_2

m: Ar =  **n**: Ar = 

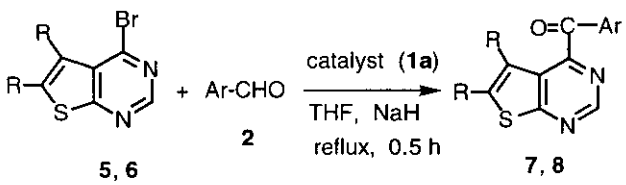
Aldehyde	Ketone (4)	Yield (%)
2b	**4b**	74
2c	**4c**	95
2d	**4d**	99
2e	**4e**	67
2f	**4f**	50 (38)[a]
2g	**4g**	42 (8)[a]
2h	**4h**	53 (20)[a]
2i	**4i**	–[b] (39)[a]
2j	**4j**	82
2k	**4k**	–[b] (90)[a]
2l	**4l**	–[b] (93)[a]
2m	**4m**	38 (43)[a]
2n	**4n**	27 (29)[a]

[a] Recovery of the starting **3b**.

[b] The ketone (**4**) was not isolated.

Scheme 3

This aroylation method (Method a) was next applied to the synthesis of 4-aroylthieno[2,3-*d*]pyrimidines (**7** and **8**). 4-Bromo-5,6-dimethylthieno[2,3-*d*]pyrimidine (**5**) reacted with arenecarbaldehydes (**2**) under the same conditions as described for the furopyrimidine (**3**) to give 4-aroyl-5,6-dimethylthieno[2,3-*d*]pyrimidines (**7**) in moderate yields. However, in the case of the arenecarbaldehydes (**2g** and **2h**) having an electron-donating



5, **7**: R = Me

6, **8**: R, R = –$(CH_2)_4$–

Substrate		Ketone	
Compd	Aldehyde		Yield (%)
5	**2a**	**7a**	52
5	**2b**	**7b**	70
5	**2c**	**7c**	53
5	**2d**	**7d**	68
5	**2g**	**7g**	5 (44)[a]
5	**2h**	**7h**	–[b] (43)[a]
6	**2c**	**8c**	81

[a] Recovery of the starting **5**.

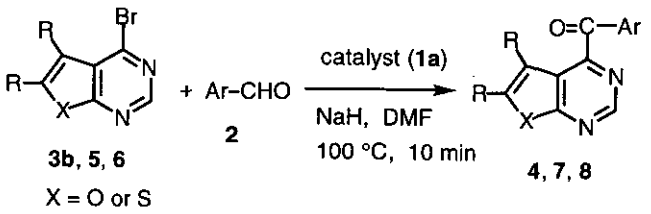
[b] The ketone (**7h**) was not isolated.

Scheme 4

substituent, the aroylation did not proceed under these conditions or proceeded with difficulty. Similar results were obtained in the aroylation of 4-bromo-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**6**) (Scheme 4).

We have already shown that DMF is an effective solvent in this aroylation, but further reactions proceeded if

the aroyl compounds formed were reactive.[4a] In the aroylation of the furopyrimidine (**3b**) and thienopyrimidines (**5** and **6**), DMF was used as the solvent. As shown in Scheme 5, the aroylation proceeded successfully, and the corresponding ketones (**4**, **7**, and **8**) were formed in moderate to good yields. The aroylthienopyrimidines (**7g**



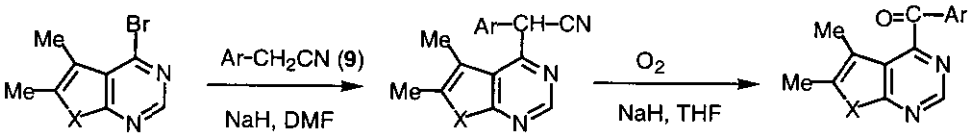
3b, **5**, **6**
X = O or S

4, **7**, **8**

Substrate		Ketone	
Compd	Aldehyde		Yield (%)
3b	**2a**	**4a**	87
3b	**2g**	**4g**	76
3b	**2h**	**4h**	89
5	**2a**	**7a**	94
5	**2g**	**7g**	96
5	**2h**	**7h**	65
6	**2a**	**8a**	55
6	**2g**	**8g**	45
6	**2h**	**8h**	34

Scheme 5

and **7h**), which could not be obtained or were obtained in low yields in THF, were formed in moderate to good yields in DMF.



3b, **5**
X = O or S

10: X = O
11: X = S

Ar = **a**, **c**, **g**, and **h**

4, **7**

Starting substrates		Products			
		α-Phenylheteroareneacetonitrile		Ketone (**4** or **7**)	
Bromo compd	Benzyl cyanide (**9**)	**10** or **11**;	Yield (%)		Yield (%)
3b	**9a**	**10a**	94	**4a**	94
3b	**9c**	**10c**	85	**4c**	85
3b	**9g**	**10g**	74	**4g**	74
3b	**9h**	**10h**	99	**4h**	99
5	**9a**	**11a**	54	**7a**	74
5	**9c**	**11c**	33	**7c**	94
5	**9g**	**11g**	46	**7g**	90
5	**9h**	**11h**	73	**7h**	96

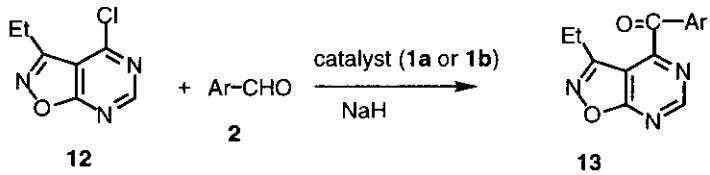
Scheme 6

Yamanaka and Ohba reported a method of aroylheteroarene preparation,[5] which involves introduction of benzyl cyanide (**9**) into heteroarenes followed by oxidative decyanation (Method b). We applied this procedure to the synthesis of the aroylfuro- (**4**) and the aroylthienopyrimidines (**7**) (Scheme 6).

The yields of the ketones (**4** and **7**) obtained from the bromo compounds (**3b** and **5**) by Method a in DMF were similar to those obtained by Method b as overall yields including the two steps. However, Method a is simple and easy to carry out.

The catalytic aroylation was applied to the synthesis of 4-aroylisoxazolo[5,4-*d*]pyrimidines (**13**). Various isoxazolo[5,4-*d*]pyrimidine derivatives and their analogues are known to have biological activities.[6]

The treatment of 3-ethyl-4-chloroisoxazolo[5,4-*d*]pyrimidine (**12**) with arenecarbaldehydes (**2**) in the presence of the imidazolium iodide (**1a**) in dioxane or DMF furnished the corresponding 4-aroyl-3-ethylisoxazolo[5,4-*d*]pyrimidines (**13**). However the yields were moderate. The imidazolium salt (**1a**) was a more effective catalyst than the benzimidazolium salt (**1b**), as found in the aroylation of furopyrimidine. These results are shown in Scheme 7.



12 **13**

Substrate	Reaction conditions				Ketone (**13**)	
Aldehyde	Catalyst	Solvent	Temp	Time (min)		Yield (%)
2a	**1a**	DMF	80 °C	10	**13a**	22 (12)[a]
2a	**1b**	THF	reflux	30	**13a**	–[b] (56)[a]
2a	**1b**	DMF	120 °C	30	**13a**	–[b] (33)[a]
2c	**1a**	dioxane	reflux	20	**13c**	67
2d	**1a**	dioxane	reflux	30	**13d**	83
2h	**1a**	DMF	80 °C	10	**13h**	22
2h	**1b**	dioxane	reflux	40	**13h**	–[b] (42)[a]
2m	**1a**	dioxane	reflux	15	**13m**	49
2n	**1a**	dioxane	reflux	20	**13n**	67

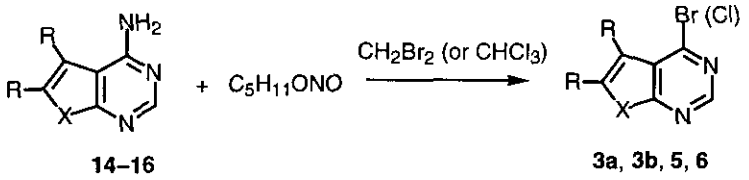
[a] Recovery of the starting **12**.

[b] The ketone (**13**) was not isolated.

Scheme 7

The structures of the newly obtained ketones (**4**, **7**, **8**, and **13**) in this paper were supported by the spectral data and the elemental analyses.

The starting halofuropyrimidines (**3a** and **3b**) and bromothienopyrimidines (**5** and **6**) were synthesized by chlorination or bromination of the amino compounds (**14–16**) (Scheme 8).[7]



14–16 3a, 3b, 5, 6

	X	R
14	O	Me
15	S	Me
16	S	-$(CH_2)_4$-

Scheme 8

In conclusion, we have synthesized various 4-aroylfuro[2,3-*d*]pyrimidines (**4**), 4-aroylthieno[2,3-*d*]pyrimidines (**7** and **8**), and 4-aroylisoxazolo[5,4-*d*]pyrimidines (**13**) *via* two methods, catalytic aroylation (Method a) and oxidative decyanation of α-phenylheteroareneacetonitrile (Method b). Catalytic aroylation (Method a) is an easy and simple procedure.

EXPERIMENTAL

All melting points were measured without correction. IR spectra were recorded on a JASCO A-102 diffraction grating IR spectrophotometer. ^{1}H-NMR spectra were measured at 60 MHz on a JEOL PMX60SI NMR spectrometer, and at 270 MHz on a JEOL JNM-GSX270 FT-NMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (*J*) are given in Hz.

Catalytic Aroylation (Method a):

Reaction of 4-Chloro-5,6-dimethylfuro[2,3-*d*]pyrimidine (3a) with Benzaldehyde (2a) in the Presence of 1,3-Dimethylimidazolium Iodide (1a). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of 4-chloro-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3a**, 681 mg, 3.7 mmol), benzaldehyde (**2a**, 471 mg, 4.4 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with *n*-hexane–benzene (1:1) afforded the starting **3a** in 16% yield (110 mg). The fraction eluted with benzene gave 4-benzoyl-5,6-dimethylfuro[2,3-*d*]pyrimidine (**4a**) in 43% yield (400 mg).

Reaction of 4-Bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (3b) with Benzaldehyde (2a) in the Presence of 1,3-Dimethylimidazolium Iodide (1a). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to

a mixture of 4-bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3b**, 681 mg, 3.7 mmol), benzaldehyde (**2a**, 382mg, 3.6 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with benzene gave 4-benzoyl-5,6-dimethylfuro[2,3-*d*]pyrimidine (**4a**) in 79% yield (598 mg).

Reaction of 4-Bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (3b) with Benzaldehyde (2a) in the Presence of 1,3-Dimethylbenzimidazolium Iodide (1b). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of 4-bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3b**, 681 mg, 3.0 mmol), benzaldehyde (**2a**, 382 mg, 3.6 mmol), and 1,3-dimethylbenzimidazolium iodide (**1b**, 274 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with benzene. The fraction eluted with benzene afforded the starting **3b** in 60% yield (381 mg).

Synthesis of 4-Aroyl-5,6-dimethylfuro[2,3-*d*]pyrimidines (4); General Procedure (in THF). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of 4-bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3b**, 681 mg, 3.0 mmol), an arenecarbaldehyde (**2**, 3.6 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and/or benzene. The fraction eluted with benzene gave 4-aroyl-5,6-dimethylfuro[2,3-*d*]pyrimidine (**4**). These results are shown in Scheme 3. Appearance, recrystallization solvent, and the spectral data are shown in Tables 1 and 2.

Synthesis of 4-Aroyl-5,6-dimethylthieno[2,3-*d*]pyrimidines (7); General Procedure (in THF). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of 4-bromo-5,6-dimethylthieno[2,3-*d*]pyrimidine (**5**, 729 mg, 3.0 mmol), an arenecarbaldehyde (**2**, 3.6 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with benzene and/or $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (1:1) gave 4-aroyl-5,6-dimethylthieno[2,3-*d*]pyrimidine (**7**). These results are shown Scheme 4. Appearance, recrystallization solvent, and the spectral

data are shown in Tables 1 and 2.

Synthesis of 4-Aroyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidines (8); General Procedure (in THF). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of 4-bromo-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**6**, 808 mg, 3.0 mmol), an arenecarbaldehyde (**2**, 3.6 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in THF (20 mL), and the resulting mixture was refluxed for 30 min with stirring. Work-up as described for the synthesis of **7** gave 4-aroyl-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**8**). These results are shown Scheme 4. Appearance, recrystallization solvent, and the spectral data are shown in Tables 1 and 2.

Synthesis of 4-Aroylfuro[2,3-*d*]pyrimidines (4) and 4-Aroylthieno[2,3-*d*]pyrimidines (7 and 8); General Procedure (in DMF). Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was added to a mixture of a bromoheteroarene (**3b**, **5**, or **6**, 3.0 mmol), an arenecarbaldehyde (**2**, 3.6 mmol), and 1,3-dimethylimidazolium iodide (**1a**, 224 mg, 1.0 mmol) in DMF (20 mL), and the resulting mixture was stirred at 100 °C for 10 min. The reaction mixture was poured into ice–H_2O and extracted with AcOEt. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with benzene and/or $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (1:1) gave an aroylheteroarene (**4**, **7**, or **8**). These results are shown in Scheme 5.

Oxidative Decyanation (Method b):

Synthesis of α-Phenyl-5,6-dimethylfuro[2,3-*d*]pyrimidine-4-acetonitrile (10) and α-Phenyl-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (10); Reaction of Bromoheteroarene (3b and 5) with Benzyl Cyanide (9). General Procedure. Sodium hydride (60% in oil, 180 mg, 4.5 mmol) was slowly added to a mixture of a bromoheteroarene (**3b** or **5**, 3.0 mmol), and phenylacetonitrile (**9**, 3.6 mmol) in DMF (20 mL), and the resulting mixture was stirred at 130 °C for 30 min. The reaction mixture was poured into ice–H_2O, neutralized with AcOH, and extracted with AcOEt. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with benzene and/or $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (1:1) gave α-phenyl-5,6-dimethylfuro[2,3-*d*]- (**10**) or α-phenyl-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11**).

α-Phenyl-5,6-dimethylfuro[2,3-*d*]pyrimidine-4-acetonitrile (**10a**): Yield 94% (744 mg). Colorless needles (MeOH), mp 139–140 °C. *Anal.* Calcd for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96. Found: C, 73.15; H, 5.00; N, 16.00. IR (KBr) cm^{-1}: 2240 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.16 (3H, s, Me), 2.40 (3H, s, Me), 5.67 (1H, s, CH), 7.21–7.51 (5H, m, aromatic H), 8.86 (1H, s, C^2–H).

α-(4-Chlorophenyl)-5,6-dimethylfuro[2,3-*d*]pyrimidine-4-acetonitrile (**10c**): Yield 85% (834 mg). Colorless

needles (MeOH), mp 133–134 °C. *Anal.* Calcd for $C_{16}H_{12}N_3OCl$: C, 64.54; H, 4.06; N, 14.11. Found: C, 64.42; H, 4.09; N, 14.12. IR (KBr) cm^{-1}: 2238 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.23 (3H, s, Me), 2.41 (3H, s, Me), 5.67 (1H, s, CH), 7.32 (4H, s, aromatic H), 8.89 (1H, s, C^2–H).

α-(4-Methylphenyl)-5,6-dimethylfuro[2,3-*d*]pyrimidine-4-acetonitrile (**10g**): Yield 74% (613 mg). Colorless needles (MeOH), mp 125–126 °C. *Anal.* Calcd for $C_{17}H_{15}N_3O$: C, 73.63; H, 5.45; N, 15.15. Found: C, 73.45; H, 5.47; N, 15.14. IR (KBr) cm^{-1}: 2238 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.25 (3H, s, Me), 2.33 (3H, s, Me), 2.44 (3H, s, Me), 5.70 (1H, s, CH), 7.04–7.37 (4H, m, aromatic H), 8.88 (1H, s, C^2–H).

α-(4-Methoxyphenyl)-5,6-dimethylfuro[2,3-*d*]pyrimidine-4-acetonitrile (**10h**): Yield 99% (872 mg). Colorless needles (MeOH), mp 194–195 °C. *Anal.* Calcd for $C_{17}H_{15}N_3O_2$: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.46; H, 5.08; N, 14.41. IR (KBr) cm^{-1}: 2236 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.18 (3H, s, Me), 2.36 (3H, s, Me), 3.67 (3H, s, OMe), 5.57 (1H, s, CH), 6.64–7.21 (4H, m, aromatic H), 8.68 (1H, s, C^2–H).

α-Phenyl-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11a**): Yield 54% (449 mg). Colorless needles (MeOH), mp 131–132 °C. *Anal.* Calcd for $C_{16}H_{13}N_3S$: C, 68.79; H, 4.69; N, 15.04. Found: C, 68.69; H, 4.46; N, 15.13. IR (KBr) cm^{-1}: 2236 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s, Me), 2.50 (3H, s, Me), 6.00 (1H, s, CH), 7.23–7.34 (5H, m, aromatic H), 9.00 (1H, s, C^2–H).

α-(4-Chlorophenyl)-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11c**): Yield 33% (309 mg). Colorless needles (MeOH), mp 167–168 °C. *Anal.* Calcd for $C_{16}H_{12}N_3ClS$: C, 61.24; H, 3.85; N, 13.39. Found: C, 61.01; H, 3.71; N, 13.42. IR (KBr) cm^{-1}: 2238 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s, Me), 2.47 (3H, s, Me), 5.91 (1H, s, CH), 7.21 (4H, s, aromatic H), 8.91 (1H, s, C^2–H).

α-(4-Methylphenyl)-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11g**): Yield 46% (407 mg). Colorless needles (MeOH), mp 175–176 °C. *Anal.* Calcd for $C_{17}H_{15}N_3S$: C, 69.60; H, 5.15; N, 14.32. Found: C, 69.46; H, 5.08; N, 14.41. IR (KBr) cm^{-1}: 2238 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.32 (3H, s, Me), 2.44 (3H, s, Me), 2.52 (3H, s, Me), 6.00 (1H, s, CH), 7.21–7.35 (4H, m, aromatic H), 9.01 (1H, s, C^2–H).

α-(4-Methoxyphenyl)-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11h**): Yield 74% (684 mg). Colorless needles (MeOH), mp 142–143 °C. *Anal.* Calcd for $C_{17}H_{15}N_3OS$: C, 66.00; H, 4.89; N, 13.58. Found: C, 65.90; H, 4.71; N, 13.62. IR (KBr) cm^{-1}: 2234 (CN). ^{1}H-NMR ($CDCl_3$) δ: 2.44 (3H, s, Me), 2.50 (3H, s, Me), 3.76 (3H, s, OMe), 5.98 (1H, s, CH), 6.74–7.30 (4H, m, aromatic H), 8.98 (1H, s, C^2–H).

Synthesis of Fused Aroylpyrimidines (4 and 7) by Oxidative Decyanation; General Procedure. Sodium hydride (60% in oil, 120 mg, 3.0 mmol) was added to a solution of α-phenyl-5,6-dimethylfuro[2,3-*d*]- (**10**) or α-phenyl-5,6-dimethylthieno[2,3-*d*]pyrimidine-4-acetonitrile (**11**, 3.0 mmol) in THF (20 mL), and the mixture was stirred at rt for 5 min. Oxygen gas was bubbled through the resulting mixture at rt with stirring for 3 h. The reaction mixture was concentrated, and the residue was poured into H_2O and then extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by

column chromatography on SiO_2 with benzene and/or $CHCl_3$. The fraction eluted with benzene–$CHCl_3$ (1:1) gave an aroylheteroarene (**4** or **7**).

Synthesis of 4-Aroyl-3-ethylisoxazolo[5,4-*d*]pyrimidines (Method a); General Procedure. Sodium hydride (60% in oil, 300 mg, 7.5 mmol) was added to a mixture of 4-chloro-3-ethylisoxazolo[5,4-*d*]pyrimidine (**12**, 920 mg, 5.0 mmol), an arenecarbaldehyde (**2**, 6.0 mmol), and 1,3-dimethylbenzimidazolium iodide (**1b**, 274 mg, 1.0 mmol) in THF, dioxane, or DMF (20 mL), and the resulting mixture was stirred under appropriate conditions (reaction conditions are shown in Scheme 7). The reaction mixture was poured into ice–H_2O and extracted with $CHCl_3$ (in THF or dioxane) or AcOEt (in DMF). The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on SiO_2 with benzene. The first fraction afforded the starting **12**. The second fraction gave 4-aroyl-3-ethylisoxazolo[5,4-*d*]pyrimidine (**13**). These results are shown in Scheme 7. Appearance, recrystallization solvent, and the IR and ^{1}H-NMR spectral data are shown in Tables 1 and 2. ^{13}C-NMR spectral data are shown in Table 3.

Table 1. Appearance, Recrystallization Solvent, Melting Point, and Elemental Analyses for 4-Aroylfuro[2,3-*d*]pyrimidines (**4**), 4-Aroylthieno[2,3-*d*]pyrimidines (**7** and **8**), and 4-Aroylisoxazolo[5,4-*d*]pyrimidines (**13**).

	Appearance			Analysis (%); Calcd (Found)			
Compd	mp (°C)	(Recrystallization solvent)	Formula	C	H	N	MS (m/z)
4a	143–144	Yellow needles (petroleum benzin)	$C_{15}H_{12}N_2O_2$	71.42 (71.30)	4.79 (4.98)	11.10 (11.07)	
4b	154–155	Yellow needles (petroleum benzin)	$C_{15}H_{11}N_2O_2F$	66.66 (66.62)	4.10 (3.88)	11.37 (10.09)	270 (M^+)
4c	190–192	Yellow needles (petroleum benzin)	$C_{15}H_{11}N_2O_2Cl$	62.84 (62.71)	3.87 (3.79)	9.77 (9.68)	286 (M^+)
4d	190–192	Yellow needles (petroleum benzin)	$C_{15}H_{11}N_2O_2Br$	54.40 (54.30)	3.35 (3.29)	8.46 (8.29)	330, 332 (M^+)
4e	138–139	Yellow needles (petroleum benzin)	$C_{15}H_{11}N_2O_2Br$	54.40 (54.62)	3.35 (3.09)	8.46 (8.29)	
4f	135–136	Yellow needles (petroleum benzin)	$C_{15}H_{11}N_2O_2Br$	54.40 (54.36)	3.35 (3.24)	8.46 (8.32)	
4g	149–150	Yellow needles (petroleum benzin)	$C_{16}H_{14}N_2O_2$	72.13 (71.76)	5.30 (5.26)	10.52 (10.54)	
4h	185–186	Yellow needles (petroleum benzin)	$C_{16}H_{14}N_2O_3$	68.08 (68.11)	5.00 (5.13)	9.92 (9.83)	
4j	125–126	Yellow needles (petroleum benzin)	$C_{16}H_{14}N_2O_3$	68.08 (67.89)	5.00 (4.85)	9.92 (9.76)	
4m	165–167	Yellow needles (petroleum benzin)	$C_{13}H_{10}N_2O_3$	64.46 (64.18)	4.16 (4.11)	11.56 (11.42)	
4n	144–145	Yellow needles (petroleum benzin)	$C_{13}H_{10}N_2O_2S$	60.45 (60.24)	3.90 (3.72)	10.85 (10.84)	

7a	68–69	Yellow needles (MeOH)	$C_{15}H_{12}N_2OS$	67.14 (67.25)	4.51 (4.48)	10.44 (10.38)	268 (M^+)
7b	119–120	Yellow needles (MeOH)	$C_{15}H_{11}N_2OFS$	62.92 (62.92)	3.87 (3.85)	9.74 (9.74)	
7c	131–132	Yellow needles (MeOH)	$C_{15}H_{11}N_2OClS$	59.50 (59.31)	3.66 (3.61)	9.25 (9.23)	
7d	113–114	Yellow needles (MeOH)	$C_{15}H_{11}N_2OBrS$	51.89 (52.05)	3.19 (3.09)	8.07 (8.05)	
7g	141–142	Yellow needles (MeOH)	$C_{16}H_{14}N_2OS$	68.06 (68.34)	5.00 (5.14)	9.92 (9.62)	
7h	126–127	Yellow needles (MeOH)	$C_{16}H_{14}N_2O_2S$	64.41 (64.41)	4.73 (4.70)	9.39 (9.21)	
8a	93–94	Yellow needles (MeOH)	$C_{17}H_{14}N_2OS$	69.36 (69.53)	4.79 (4.87)	9.52 (9.27)	294 (M^+)
8c	119–120	Yellow needles (MeOH)	$C_{17}H_{13}N_2OClS$	62.10 (61.87)	3.99 (3.91)	8.52 (8.39)	
8g	133–134	Yellow needles (MeOH)	$C_{18}H_{16}N_2OS$	70.10 (69.79)	5.23 (5.07)	9.08 (8.99)	308 (M^+)
8h	114–116	Yellow needles (MeOH)	$C_{18}H_{16}N_2O_2S$	66.65 (66.51)	4.97 (4.98)	8.64 (8.64)	
13a	85–86	Slightly yellow needles (petroleum benzin)	$C_{14}H_{11}N_3O_2$	66.40 (66.54)	4.38 (4.11)	16.59 (16.60)	253 (M^+)
13c	103–104	Colorless needles (petroleum benzin)	$C_{14}H_{10}N_3O_2Cl$	58.45 (58.59)	3.50 (3.54)	14.61 (14.50)	
13d	108–109	Pale orange needles (petroleum benzin)	$C_{14}H_{10}N_3O_2Br$	50.62 (50.86)	3.03 (3.04)	12.65 (12.69)	
13h	82–84	Slightly yellow needles (petroleum benzin)	$C_{15}H_{13}N_3O_3$	63.60 (63.92)	4.63 (4.63)	14.83 (14.83)	
13m	85–87	Yellow needles (petroleum benzin)	$C_{12}H_9N_3O_3$	59.26 (59.15)	3.73 (3.50)	17.28 (17.20)	
13n	93	Yellow needles (petroleum benzin)	$C_{12}H_9N_3O_2S$	55.59 (55.73)	3.50 (3.35)	16.21 (16.10)	259 (M^+)

Table 2. IR and ^{1}H-NMR Spectral Data for 4-Aroylfuro[2,3-*d*]pyrimidines (**4**), 4-Aroylthieno[2,3-*d*]pyrimidines (**7** and **8**), and 4-Aroylisoxazolo[5,4-*d*]pyrimidines (**13**).

Compd	IR (KBr) cm^{-1}	^{1}H-NMR ($CDCl_3$) δ
4a	1663 (CO)	2.10 (3H, s, Me), 2.49 (3H, s, Me), 7.40–7.61 (3H, m, aromatic H), 7.86–8.02 (2H, m, aromatic H), 8.87 (1H, s, C^2-H)
4b	1665 (CO)	2.16 (3H, s, Me), 2.55 (3H, s, Me), 7.09–7.38 (2H, m, aromatic H), 8.01–8.22 (2H, m, aromatic H), 8.99 (1H, s, C^2-H)
4c	1661 (CO)	2.13 (3H, s, Me), 2.51 (3H, s, Me), 7.53 (2H, d, J = 8 Hz, aromatic H), 8.05 (2H, d, J = 8 Hz, aromatic H), 9.01 (1H, s, C^2-H)
4d	1661 (CO)	2.15 (3H, s, Me), 2.53 (3H, s, Me), 7.71 (2H, d, J = 8 Hz, aromatic H), 8.00 (2H, d, J = 8 Hz, aromatic H), 9.01 (1H, s, C^2-H)
4e	1676 (CO)	2.35 (3H, s, Me), 2.52 (3H, s, Me), 7.41–7.78 (4H, m, aromatic H), 8.94 (1H, s, C^2-H)
4f	1667 (CO)	2.11 (3H, s, Me), 2.50 (3H, s, Me), 7.21–8.21 (4H, m, aromatic H), 8.93 (1H, s, C^2-H)
4g	1658 (CO)	2.18 (3H, s, Me), 2.58 (6H, s, 2 x Me), 7.47 (2H, d, J = 8 Hz, aromatic H), 8.01 (2H, d, J = 8 Hz, aromatic H), 9.08 (1H, s, C^2-H)

4h	1652 (CO)	2.08 (3H, s, Me), 2.49 (3H, s, Me), 3.94 (3H, s, OMe), 7.01 (2H, d, J = 8 Hz, aromatic H), 8.05 (2H, d, J = 8 Hz, aromatic H), 9.01 (1H, s, C^2-H)
4j	1654 (CO)	2.11 (3H, s, Me), 2.52 (3H, s, Me), 3.88 (3H, s, OMe), 7.20–7.63 (4H, m, aromatic H), 8.99 (1H, s, C^2-H)
4m	1649 (CO)	2.28 (3H, s, Me), 2.52 (3H, s, Me), 6.64–6.74 (1H, m, furan), 7.69–7.85 (2H, m, furan), 9.01 (1H, s, C^2-H)
4n	1628 (CO)	2.26 (3H, s, Me), 2.53 (3H, s, Me), 7.17–7.25 (1H, m, thiophene), 7.81–7.92 (1H, m, thiophene), 8.10–8.18 (1H, m, thiophene), 9.02 (1H, s, C2-H)
7a	1674 (CO)	2.08 (3H, s, Me), 2.51 (3H, s, Me), 7.24–7.62 (3H, m, aromatic H), 7.78–7.92 (2H, m, aromatic H), 8.10–8.18 (1H, m, thiophene), 8.99 (1H, s, C^2-H)
7b	1674 (CO)	2.05 (3H, s, Me), 2.50 (6H, s, 2 x Me), 7.00–7.30 (2H, m, aromatic H), 7.81–8.05 (2H, m, aromatic H), 9.00 (1H, s, C^2-H)
7c	1679 (CO)	2.07 (3H, s, Me), 2.50 (6H, s, 2 x Me), 7.40 (2H, d, J = 9 Hz, aromatic H), 7.81 (2H, d, J = 9 Hz, aromatic H), 8.96 (1H, s, C^2-H)
7d	1671 (CO)	2.03 (3H, s, Me), 2.46 (3H, s, Me), 7.21–7.80 (4H, m, aromatic H), 8.90 (1H, s, C^2-H)
7g	1670 (CO)	2.10 (3H, s, Me), 2.50 (3H, s, Me), 2.55 (3H, s, Me), 7.26 (2H, d, J = 7 Hz, aromatic H), 7.76 (2H, d, J = 7 Hz, aromatic H), 9.02 (1H, s, C^2-H)
7h	1652 (CO)	2.10 (3H, s, Me), 2.55 (3H, s, Me), 3.93 (3H, s, OMe), 6.99 (2H, d, J = 10 Hz, aromatic H), 7.90 (2H, d, J = 10 Hz, aromatic H), 9.08 (1H, s, C^2-H)
8a	1672 (CO)	1.68–1.92 (4H, m, methylene), 2.35–2.55 (2H, m, methylene), 2.78–2.92 (2H, m, methylene), 7.42–7.63 (3H, m, aromatic H), 7.80–7.94 (2H, m, aromatic H), 9.00 (1H, s, C^2-H)
8c	1674 (CO)	1.70–1.95 (4H, m, methylene), 2.38–2.60 (2H, m, methylene), 2.79–3.09 (2H, m, methylene), 7.60 (2H, d, J = 9 Hz, aromatic H), 7.85 (2H, d, J = 9 Hz, aromatic H), 9.00 (1H, s, C^2-H)
8g	1668 (CO)	1.72–1.94 (4H, m, methylene), 2.42 (3H, s, Me), 2.75–2.99 (4H, m, methylene), 7.27 (2H, d, J = 9 Hz, aromatic H), 7.77 (2H, d, J = 9 Hz, aromatic H), 9.00 (1H, s, C^2-H)
8h	1664 (CO)	1.78–1.97 (4H, m, methylene), 2.40–2.60 (2H, m, methylene), 2.79–3.09 (2H, m, methylene), 3.90 (3H, s, OMe), 7.02 (2H, d, J = 10 Hz, aromatic H), 7.92 (2H, d, J = 10 Hz, aromatic H), 9.10 (1H, s, C^2-H)
13a	1670 (CO)	1.17 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 2.86 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 7.34–7.56 (3H, m, aromatic H), 7.77–7.93 (2H, m, aromatic H), 9.05 (1H, s, C^6-H)
13c	1660 (CO)	1.29 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 3.01 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 7.39 (2H, d, J = 9 Hz, aromatic H), 7.91 (2H, d, J = 9 Hz, aromatic H), 9.10 (1H, s, C^6-H)
13d	1665 (CO)	1.29 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 2.98 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 7.57 (2H, d, J = 9 Hz, aromatic H), 7.86 (2H, d, J = 9 Hz, aromatic H), 9.12 (1H, s, C^6-H)
13h	1653 (CO)	1.26 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 2.86 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 3.87 (3H, s, OMe), 6.91 (2H, d, J = 9 Hz, aromatic H), 7.93 (2H, d, J = 9 Hz, aromatic H), 9.11 (1H, s, C^6-H)
13m	1648 (CO)	1.35 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 3.15 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 6.52–6.61 (1H, m, furan), 7.68–7.74 (2H, m, furan), 9.01 (1H, s, C^6-H)
13n	1650 (CO)	1.35 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 3.26 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 7.13 (1H, dd, J = 5, 4 Hz, thiophene), 7.67 (1H,dd, J = 5, 1 Hz, thiophene), 8.09 (1H, dd, J = 4, 1 Hz, thiophene), 9.01 (1H, s, C^6-H)

Table 3. ^{13}C-NMR Spectral Data for 4-Aroylisoxazolo[5,4-*d*]pyrimidines (**13**).

Compd	^{13}C-NMR ($CDCl_3$) δ
13a	11.5 (q, $CH_2\underline{C}H_3$), 20.9 (t, $\underline{C}H_2CH_3$), 110.2 (s), 128.9 (d), 130.9 (d), 134.1 (s), 134.9 (d), 157.0 (d),159.0 (s), 159.8 (s), 175.0 (s), 190.8 (s, CO).

13c	11.5 (q, $CH_2\underline{C}H_3$), 21.0 (t, $\underline{C}H_2CH_3$), 110.3 (s), 129.3 (d), 132.3 (d), 132.4 (s), 141.6 (s), 157.0 (d), 159.1 (s), 159.6 (s), 175.1 (s), 189.5 (s, CO)
13d	11.5 (q, $CH_2\underline{C}H_3$), 21.0 (t, $\underline{C}H_2CH_3$), 110.3 (s), 130.5 (s), 132.2 (d), 132.3 (d), 132.8 (d), 157.0 (d), 159.0 (s), 159.6 (s), 175.1 (s), 189.7 (s, CO)
13h	11.4 (q, $CH_2\underline{C}H_3$), 20.8 (t, $\underline{C}H_2CH_3$), 55.7 (q, OMe), 110.2 (s), 114.3 (d), 127.0 (s), 133.4 (d), 157.0 (d), 159.0 (s), 160.6 (s), 165.1 (s), 175.0 (s), 189.0 (s, CO)
13m	11.8 (q, $CH_2\underline{C}H_3$), 21.7 (t, $\underline{C}H_2CH_3$), 110.3 (s), 113.2 (d), 125.5 (d), 149.6 (d), 150.4 (s), 157.0 (d), 157.9 (s), 160.1 (s), 175.2 (s), 177.0 (CO)
13n	11.7 (q, $CH_2\underline{C}H_3$), 21.7 (t, $\underline{C}H_2CH_3$), 110.1 (s), 128.6 (d), 137.87 (d), 137.89 (d), 139.8 (s), 156.9 (d), 158.3 (s), 160.1 (s), 175.3 (s), 182.1 (s, CO)

4-Chloro-5,6-dimethylfuro[2,3-*d*]pyrimidine (3a). Isoamyl nitrite (11 mL, *ca.* 100 mmol) was added dropwise to a stirred suspension of 4-amino-5,6-dimethylfuro[2,3-*d*]pyrimidine[8] (**14**, 7.5 g, 46 mmol) in $CHCl_3$ (45 mL). The resulting mixture was refluxed for 1 h and then concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with benzene gave 4-chloro-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3a**) in 19% yield (1.6 g). Colorless needles (*n*-hexane), mp 100–101 °C. *Anal.* Calcd for $C_8H_7N_2OCl$: C, 52.62; H, 3.86; N, 15.34. Found: C, 52.52; H, 3.73; N, 15.22. ^{1}H-NMR ($CDCl_3$) δ: 2.37 (3H, s, Me), 2.47 (3H, s, Me), 8.65 (1H, s, C^2–H).

4-Bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (3b). Isoamyl nitrite (11 mL, *ca.* 100 mmol) was added dropwise to a stirred suspension of 4-amino-5,6-dimethylfuro[2,3-*d*]pyrimidine (**14**, 7.5 g, 46 mmol) in CH_2Br_2 (45 mL) with temperature control at 80–85 °C. The resulting mixture was refluxed for 1 h and then concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with benzene gave 4-bromo-5,6-dimethylfuro[2,3-*d*]pyrimidine (**3b**) in 47% yield (4.9 g). Slightly yellow needles (*n*-hexane), mp 115–117 °C (lit.,[9] 115–117 °C). MS (m/z): 226, 228 (M^+). ^{13}C-NMR ($CDCl_3$) δ: 9.1 (q), 11.8 (q), 109.2 (s), 121.6 (s), 142.4 (s), 151.7 (d), 152.7 (s), 165.0 (s).

4-Bromo-5,6-dimethylthieno[2,3-*d*]pyrimidine (5). Isoamyl nitrite (11 mL, *ca.* 100 mmol) was added dropwise to a stirred suspension of 4-amino-5,6-dimethylthieno[2,3-*d*]pyrimidine[10] (**15**, 8.0 g, 45 mmol) in CH_2Br_2 (45 mL) with temperature control at 80–85 °C. The resulting mixture was refluxed for 1 h and then concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with *n*-hexane–benzene (1:1) gave 4-bromo-5,6-dimethylthieno[2,3-*d*]pyrimidine (**5**) in 33% yield (3.6 g). Slightly yellow needles (*n*-hexane), mp 137–139 °C. *Anal.* Calcd for $C_8H_7N_2BrS$: C, 39.52; H, 2.90; N, 11.52. Found: C, 39.61; H, 2.69; N, 11.60. ^{1}H-NMR ($CDCl_3$) δ: 2.50 (3H, s, Me), 2.56 (3H, s, Me), 8.63 (1H, s, C^2–H). ^{13}C-NMR ($CDCl_3$) δ:14.1 (q), 14.2 (q), 125.3 (s), 131.4 (s), 136.4 (s), 144.9 (d), 151.1 (s), 167.5 (s).

4-Bromo-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (6). Isoamyl nitrite (11 mL, *ca.* 100 mmol) was added dropwise to a stirred suspension of 4-amino-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**16**, 7.5 g, 40 mmol) in CH_2Br_2 (45 mL) with temperature control at 80–85 °C. The resulting mixture was refluxed for 1 h and then concentrated. The residue was purified by column chromatography on SiO_2 with *n*-hexane and benzene. The fraction eluted with *n*-hexane–benzene (1:1) gave 4-bromo-5,6-tetramethylenethieno[2,3-*d*]pyrimidine (**6**) in 26% yield (2.5 g). Slightly yellow needles (*n*-hexane), mp 113–114 °C. *Anal.* Calcd for $C_{10}H_9N_2BrS$: C, 44.62; H, 3.37; N, 10.41. Found: C, 44.68; H, 3.32; N, 10.44. MS (m/z): 268, 270 (M^+). ^{1}H-NMR ($CDCl_3$) δ: 1.82–2.04 (4H, m, methylene), 2.24–3.22 (4H, m, methylene), 8.60 (1H, s, C^2–H). ^{13}C-NMR ($CDCl_3$) δ: 22.1 (t), 22.3 (t), 26.2 (t), 26.5 (t),127.3 (s), 131.0 (s), 139.8 (s), 144.4 (d), 150.8 (s), 168.2 (s).

4-Chloro-3-ethylisoxazolo[5,4-*d*]pyrimidine (12). A mixture of 3-ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one[11] (10 g, 0.06 mol) and $POCl_3$ (50 mL, *ca.* 0.54 mol) was refluxed for 2 h. The excess $POCl_3$ was evaporated, and the residue was poured into ice–H_2O and then extracted with $CHCl_3$. The organic layer was washed with H_2O, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on Al_2O_3 with $CHCl_3$ to give 4-chloro-3-ethylisoxazolo[5,4-*d*]pyrimidine (**6**) in quantitative yield. Slightly yellow oil. *Anal.* Calcd for $C_7H_6N_3OCl$: C, 45.79; H, 3.29; N, 22.89. Found: C, 45.48; H, 3.25; N, 22.40. ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, t, J = 7 Hz, $CH_2C\underline{H}_3$), 3.15 (2H, q, J = 7 Hz, $C\underline{H}_2CH_3$), 8.71 (1H, s, C^6–H).

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