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Studies on Heterocyclic Enaminonitriles. IV.[1] Reaction of Ethyl *N*-(3-Cyano-4,5-dihydro-2-thienyl)oxamates with Cyanomethylene Compounds in the Presence of Triethylamine

SHIZUKO HACHIYAMA, KAZUKO KOYANAGI, YUKIHIKO TOMIOKA,
and MOTOYOSHI YAMAZAKI*

*Faculty of Pharmaceutical Sciences, Fukuoka University, 8-19-1
Nanakuma, Jōnan-ku, Fukuoka 814-01, Japan*

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Ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamate (Ia) reacted with ethyl or methyl cyanoacetate, α-cyanoacetamide and 1-cyanoacetylpyrrolidine in the presence of triethylamine to form the corresponding 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetic acid derivatives (IIa-1—IIa-4). Similarly, ethyl *N*-[3-cyano-5-methyl(or 4-phenyl)-4,5-dihydro-2-thienyl]oxamate (Ib or Ic) gave the corresponding 2-[4-amino-5,6-dihydrothieno-[2,3-*d*]pyrimidine]acetic acid derivatives (IIb-1—IIb-4 or IIc-1—IIc-4). On acidic hydrolysis, IIa-1, 2, IIb-1, 2 and IIc-1, 2 were converted to 4-amino-2-methyl-5,6-dihydrothieno[2,3-*d*]pyrimidines (IIIa—c).

Keywords——ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamate; triethylamine; cyanomethylene compounds; hydrolysis; 4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine; acetamidine; 4-amino-2-methyl-5,6-dihydrothieno[2,3-*d*]pyrimidine; cyclization

In an earlier communication,[2] we reported that ethyl *N*-(2-cyanophenyl)oxamate reacts with some cyanomethylene compounds, such as ethyl or methyl cyanoacetate, α-cyanoacetamide and 1-cyanoacetylpyrrolidine, in the presence of potassium cyanide to form the corresponding 4-aminoquinazolines. As a sequel to this study, we examined the reactions of ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamates with cyanomethylene compounds.

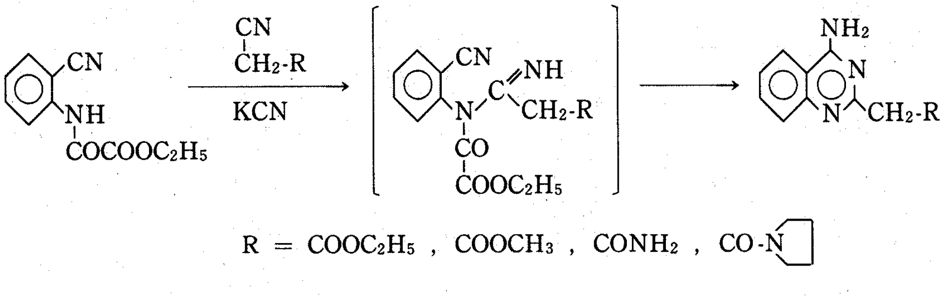


Chart 1

The reactions of 2-amino-3-cyano-4,5-dihydrothiophene[3] and 2-amino-3-cyano-5-methyl-(or 4-phenyl)-4,5-dihydrothiophene[3] with ethoxalyl chloride in pyridine gave the corresponding ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamates (Ia—c).

Ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamate (Ia) was allowed to react with ethyl cyanoacetate (2 eq) and potassium cyanide (3 eq) in dimethylformamide (DMF) at 70°C for 24 h to form the expected ethyl 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetate (IIa-1) in a low yield (6.5%). When the reaction was carried out at 120°C for 12 h, the yield of IIa-1 was not observed, we examined the reaction in the presence of bases other than potassium cyanide, and found that triethylamine was a more effective base for the formation of IIa-1. When a solution of Ia, ethyl cyanoacetate (2 eq) and triethylamine (2 eq) in tetrahydrofuran (THF) was refluxed for 10 h, the yield of IIa-1 increased to 45%. Compound IIa-1 had the molecular composition $C_{10}H_{13}N_3O_2S$, and its infrared (IR) spectrum displayed bands due to an amino group at 3410 cm^{-1}, 3330 cm^{-1} and 3150 cm^{-1}, and a carbonyl group at 1720 cm^{-1}, and no band indicative of a conjugated cyano group was observed. The proton magnetic resonance (PMR) spectrum showed a three-proton triplet at δ 1.17 and a two-proton quartet at δ 4.10 indicative of an ethyl ester, a broad two-proton singlet at δ 6.65 due to an amino group, and a two-proton singlet at δ 3.56 attributable to an isolated methylene group, besides the signals assignable to four protons of C_5–C_6. On the basis of these data, IIa-**1** was assigned as ethyl 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetate.

In a similar manner, the reactions of Ia with methyl cyanoacetate, α-cyanoacetamide and 1-cyanoacetylpyrrolidine resulted in the formation of the corresponding 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetic acid derivatives (IIa-**2**—**4**).

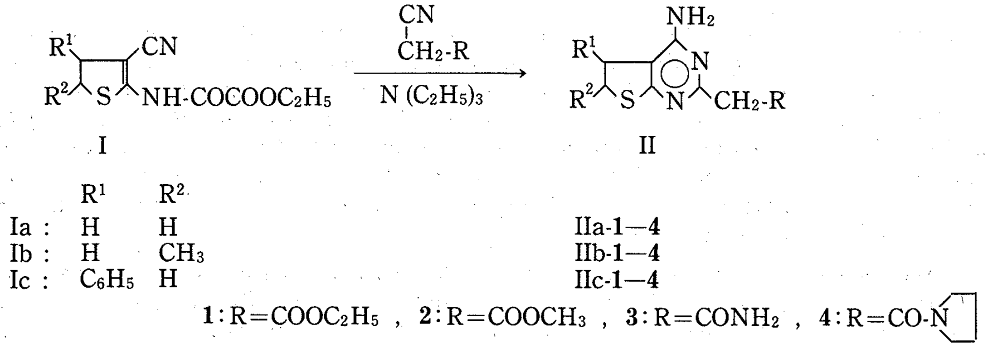


Chart 2

TABLE I. Some Properties of IIa-**1**—**4**, IIb-**1**—**4** and IIc-**1**—**4**

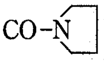
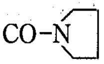
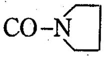
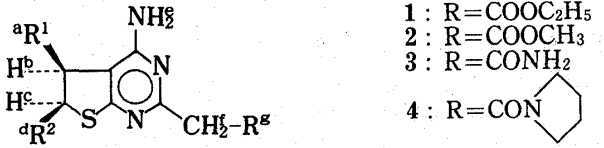
Compd. No.	Reactant CN–CH2-R R	Yield (%)	mp (°C) (Recrystn. solvent)	Appearance	Formula	Analysis (%) Calcd (Found) C	H	N
IIa-**1**	$COOC_2H_5$	45	187—189 ($CHCl_3$-ether)	Pale yellow prisms	$C_{10}H_{13}N_3O_2S$	50.19 (50.19	5.48 5.50	17.56 17.39)
IIa-**2**	$COOCH_3$	36	216 (dec.) (Acetone)	Pale yellow prisms	$C_9H_{11}N_3O_2S$	47.99 (48.09	4.92 5.08	18.65 18.73)
IIa-**3**	$CONH_2$	25	254 (dec.) (MeOH)	Colorless prisms	$C_8H_{10}N_4OS$	45.70 (45.62	4.79 4.71	26.65 26.74)
IIa-**4**	CO-N 	29	226 (dec.) (MeOH)	Colorless needles	$C_{12}H_{16}N_4OS\cdot$ $1/4H_2O$	53.61 (53.68	6.19 6.11	20.84 20.87)
IIb-**1**	$COOC_2H_5$	41	141—142 (Acetone)	Colorless needles	$C_{11}H_{15}N_3O_2S$	52.16 (52.10	5.97 6.06	16.59 16.71)
IIb-**2**	$COOCH_3$	38	176—177 (Acetone)	Colorless needles	$C_{10}H_{13}N_3O_2S$	50.19 (50.14	5.48 5.50	17.56 17.68)
IIb-**3**	$CONH_2$	24	200 (MeOH)	Colorless prisms	$C_9H_{12}N_4OS$	48.20 (47.96	5.39 5.45	24.98 24.73)
IIb-**4**	CO-N 	22	205—207 (Acetone-petr. ether)	Colorless needles	$C_{13}H_{18}N_4OS$	56.09 (55.98	6.52 6.56	20.13 20.30)
IIc-**1**	$COOC_2H_5$	40	133—134 (MeOH)	Pale yellow prisms	$C_{16}H_{17}N_3O_2S$	60.93 (60.92	5.43 5.40	13.32 13.45)
IIc-**2**	$COOCH_3$	40	166—168 (Acetone)	Pale yellow prisms	$C_{15}H_{15}N_3O_2S$	59.78 (59.86	5.02 5.03	13.94 14.05)
IIc-**3**	$CONH_2$	13	206—207 (MeOH)	Colorless needles	$C_{14}H_{14}N_4OS$	58.72 (58.60	4.93 4.81	19.57 19.32)
IIc-**4**	CO-N 	25	244 (dec.) (Acetone)	Colorless needles	$C_{18}H_{20}N_4OS$	63.51 (63.74	5.92 5.90	16.46 16.41)

TABLE II. Some Spectral Data for IIa-**1**—**4**, IIb-**1**—**4** and IIc-**1**—**4**



1 : $R=COOC_2H_5$
2 : $R=COOCH_3$
3 : $R=CONH_2$
4 : $R=CON$

Compd. No.	IR ν^{KBr}_{max} cm^{-1}		^{1}H-NMR spectra (ppm) in DMSO-d_6 solution (J in Hz)							MS m/z (M^+)
	NH$_2$	CO	H^a	H^b	H^c	H^d	H^e	H^f	H^g	
IIa-**1**	3410 3330 3150	1720	2.90—3.26 (m)		3.23—3.48 (m)		6.66 (br s)	3.57 (s)	1.18 $(-OCH_2-C\underline{H}_3)$ 4.09 $(-OC\underline{H}_2-CH_3)$	239
IIa-**2**	3420 3320 3150	1730	2.92—3.18 (m)		3.25—3.50 (m)		6.66 (br s)	3.58 (s)	3.63 $(-OC\underline{H}_3)$	225
IIa-**3**	3380 3140	1665	2.83 ——— 3.50 (m)				6.33 (br s)	3.35 (s)	6.45—7.30 (2H, br s)	210
IIa-**4**	3350 3160	1630	2.92 ——— 3.50 (m)				6.58 (br s)	3.55 (s)	1.70—2.08 (4H, m) 3.20—3.55 (4H, m)	264
IIb-**1**	3400 3310 3150	1710	3.18 (dd) ($J_{a,b}=16$, $J_{a,c}=8$, $J_{b,c}=6$, $J_{c,d}=7$)	2.68 (dd)	3.85—4.20 (m)	1.37 (d)	6.62 (br s)	3.55 (s)	1.17 $(-OCH_2-C\underline{H}_3)$ 4.07 $(-OC\underline{H}_2-CH_3)$	253
IIb-**2**	3310 3140	1735	3.18 (dd) ($J_{a,b}=16$, $J_{a,c}=8$, $J_{b,c}=6$, $J_{c,d}=6.5$)	2.69 (dd)	3.80—4.16 (m)	1.38 (d)	6.14 (br s)	3.57 (s)	3.60 $(-OC\underline{H}_3)$	239
IIb-**3**	3410 3320 3170	1655	3.22 (dd) ($J_{a,b}=16$, $J_{a,c}=8$, $J_{b,c}=6$, $J_{c,d}=6.5$)	2.70 (dd)	3.80—4.17 (m)	1.40 (d)	6.60 (br s)	3.35 (s)	6.90 (1H, br s) 7.40 (1H, br s)	224
IIb-**4**	3340 3160	1625	3.20 (dd) ($J_{a,b}=16$, $J_{a,c}=8$, $J_{b,c}=6$, $J_{c,d}=7$)	2.69 (dd)	3.84—4.10 (m)	1.38 (d)	6.23 (br s)	3.55 (s)	1.65—2.00 (4H, m) 3.25—3.50 (4H, m)	278
IIc-**1**	3480 3300 3110	1730	7.10—7.45 (m) ($J_{b,c}=3$, $J_{b,d}=9$, $J_{c,d}=11.5$)	4.72 (dd)	3.12 (dd)	3.91 (dd)	6.32 (br s)	3.60 (s)	1.18 $(-OCH_2-C\underline{H}_3)$ 4.11 $(-OC\underline{H}_2-CH_3)$	315
IIc-**2**	3420 3310 3160	1720	7.12—7.45 (m) ($J_{b,c}=2.5$, $J_{b,d}=9$, $J_{c,d}=11.5$)	4.80 (dd)	3.12 (dd)	3.92 (dd)	6.42 (br s)	3.30 (s)	3.64 $(-OC\underline{H}_3)$	301
IIc-**3**	3460 3260 3140	1690	7.10—7.48 (m) ($J_{b,c}=3$, $J_{b,d}=9$, $J_{c,d}=11.5$)	4.71 (dd)	3.12 (dd)	3.90 (dd)	6.24 (br s)	3.40 (s)	6.65—7.10 (2H, br s)	286
IIc-**4**	3400 3300 3160	1620	7.10—7.45 (m) ($J_{b,c}=3$, $J_{b,d}=9$, $J_{c,d}=11$)	4.72 (dd)	3.11 (dd)	3.91 (dd)	6.30 (br s)	3.60 (s)	1.67—2.10 (4H, m) 3.22—3.58 (4H, m)	340

Abbreviations: br s, broad singlet; d, doublet; dd, doublet of doublets; m, multipet; s, singlet.

Similarly, ethyl *N*-(3-cyano-5-methyl-4,5-dihydro-2-thienyl)oxamate (Ib) and ethyl *N*-(3-cyano-4-phenyl-4,5-dihydro-2-thienyl)oxamate (Ic) gave the corresponding 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetic acid derivatives (IIb-**1**—**4** and IIc-**1**—**4**). The structural assignments of these products were made on the basis of elemental analysis (Table I) and the spectral data (Table II).

In order to confirm the structures of IIa-**1**—**4** — IIc-**1**—**4**, we carried out the reactions shown in Chart 3.

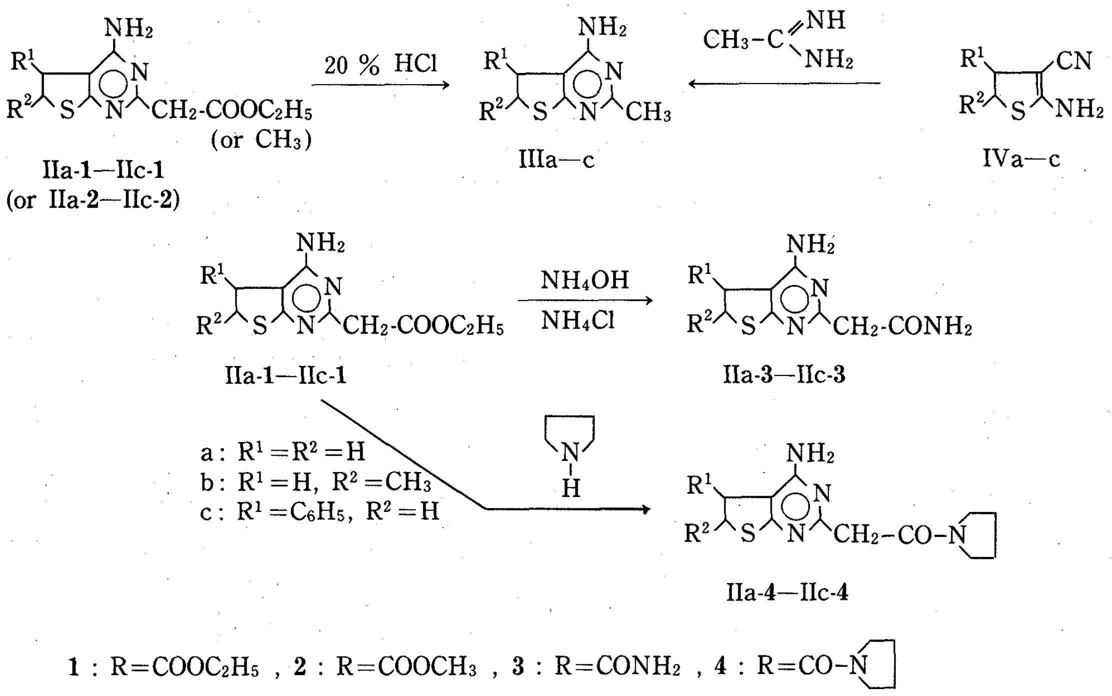


Chart 3

Compounds IIa-**1**,**2**, IIb-**1**,**2** and IIc-**1**,**2** were hydrolyzed by refluxing them with 20% hydrochloric acid to provide 4-amino-2-methyl-5,6-dihydrothieno[2,3-*d*]pyrimidine (IIIa), 4-amino-2,6-dimethyl-5,6-dihydrothieno[2,3-*d*]pyrimidine (IIIb) and 4-amino-2-methyl-5-phenyl-5,6-di-hydrothieno[2,3-*d*]pyrimidine (IIIc) in moderate yields. The structures of IIIa—c were confirmed by direct comparison with the corresponding authentic samples prepared by the reactions of 2-amino-3-cyano-4,5-dihydrothiophene (IVa) and 2-amino-3-cyano-5-methyl(or 4-phenyl)-4,5-dihydrothiophene (IVb or IVc) with acetamidine according to the method of Taylor.[4] On treatment with ammonium hydroxide or pyrrolidine, IIa-**1**, IIb-**1** and IIc-**1** were converted to 2-[4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine]acetamides (IIa-**3**, IIb-**3** and IIc-**3**) or 4-amino-2-(1-pyrrolidinyl)carbonylmethyl-5,6-dihydrothieno[2,3-*d*]pyrimidines (IIa-**4**, IIb-**4** and IIc-**4**).

In order to explore the scope of the reaction, further studies of this reaction using ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydro-2-pyrrolyl)oxamates and cyanomethylene compounds are in progress.

Experimental

THF was prepared by distillation and stored over sodium wire. All melting points are uncorrected. IR spectra were recorded on a JASCO IRA-2 or a JASCO A-302 spectrophotometer. PMR spectra were taken on a Hitachi R-22 spectrometer at 90 MHz or a JNM-MH-100 spectrometer at 100 MHz using tetramethylsilane as an internal standard. Mass spectra (MS) were measured with a JEOL model JMS-01SG spectrometer.

Preparation of Ethyl *N*-(3-Cyano-4,5-dihydro-2-thienyl)oxamates (Ia—c)——Ethoxalyl chloride (24 mmol) was added dropwise to a stirred solution of IVa, IVb or IVc (20 mmol) in pyridine (10 ml) under ice cooling. The reaction mixture was stirred at 50°C for 1 h, then poured into ice water. The precipitate was collected, washed with ice water, dried and recrystallized from ether. The yields of Ia, Ib and Ic were 71, 67 and 66%, respectively.

i) Ethyl *N*-(3-Cyano-4,5-dihydro-2-thienyl)oxamate (Ia): Pale yellow prisms, mp 62°C. *Anal.* Calcd for $C_9H_{10}N_2O_3S$: C, 47.78; H, 4.45; N, 12.38. Found: C, 47.77; H, 4.42; N, 12.37. MS *m/z*: 226 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3200, 3100 (>NH), 2200 (CN), 1750, 1713 (>CO). PMR (in $CDCl_3$) δ: 1.40 (3H, t, J=7 Hz, $-OCH_2-C\underline{H}_3$), 2.85—3.15 (2H, m, C_4-H), 3.25—3.60 (2H, m, C_5-H), 4.95 (2H, q, J=7 Hz, $-OC\underline{H}_2-CH_3$), 9.35 (1H, br s, >NH).

ii) Ethyl *N*-(3-Cyano-5-methyl-4,5-dihydro-2-thienyl)oxamate (Ib): Pale yellow prisms, mp 56—57°C. *Anal.* Calcd for $C_{10}H_{12}N_2O_3S$: C, 49.99; H, 5.03; N, 11.66. Found: C, 49.93; H, 5.06; N, 11.60. MS *m/z*: 240 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3280 (>NH), 2200 (CN), 1735, 1700 (>CO). PMR (in $CDCl_3$) δ: 1.40 (3H, t, $J=$ 7 Hz, $-OCH_2-C\underline{H}_3$), 1.44 (3H, d, $J=7$ Hz, $-C\underline{H}_3$), 2.58 (1H, dd, $J=6$ and 15 Hz, C_4–H), 3.09 (1H, dd, $J=8$ and 15 Hz, C_4–H), 3.70—4.00 (1H, m, C_5–H), 4.44 (2H, q, $J=7$ Hz, $-OC\underline{H}_2-CH_3$), 9.38 (1H, br s, >NH).

iii) Ethyl *N*-(3-Cyano-4-phenyl-4,5-dihydro-2-thienyl)oxamate (Ic): Pale yellow columns, mp 95—96°C. *Anal.* Calcd for $C_{15}H_{14}N_2O_3S$: C, 59.59; H, 4.67; N, 9.27. Found: C, 59.57; H, 4.70; N, 9.18. MS *m/z*: 302 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3360 (>NH), 2200 (CN), 1715 (>CO). PMR (in $CDCl_3$) δ: 1.40 (3H, t, $J=$ 7 Hz, $-OCH_2-C\underline{H}_3$), 3.30 (1H, dd, $J=7$ and 11 Hz, C_5–H), 3.76 (1H, dd, $J=9$ and 11 Hz, C_5–H), 4.40 (2H, q, $J=7$ Hz, $-OC\underline{H}_2-CH_3$), 4.26—4.50 (1H, m, C_4–H), 7.11 (5H, s, aromatic H), 9.44 (1H, br s, >NH).

Reactions of Ia—c with Ethyl Cyanoacetate——A mixture of Ia, Ib or Ic (3 mmol), ethyl cyanoacetate (6 mmol) and triethylamine (6 mmol) in THF (1 ml) was refluxed for 10 h (in the case of Ia and Ib) or 15 h (in the case of Ic).

i) For Ia and Ib: The reaction mixture was cooled, and the deposited crystals [IIa-**1** (285 mg) or IIb-**1** (293 mg)] were collected by filtration. The filtrate was concentrated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$–MeOH (50: 1) as the eluent to give the unchanged ethyl cyanoacetate, and IIa-**1** (38 mg) or IIb-**1** (19 mg).

ii) For Ic: After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel with $CHCl_3$–MeOH (50: 1) as the eluent. The first fraction gave the unchanged ethyl cyanoacetate, and the second fraction gave IIc-**1** (373 mg).

Reactions of Ia—c with Methyl Cyanoacetate——A solution of Ia, Ib or Ic (3 mmol), methyl cyanoacetate (6 mmol) and triethylamine (6 mmol) in THF (1 ml) was refluxed for 10 h.

i) For Ia: The reaction mixture was cooled and the deposited crystals (IIa-**2**, 203 mg) were collected by filtration. The filtrate was concentrated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$–MeOH (50: 1) as the eluent. The first fraction gave the unchanged methyl cyanoacetate, and the second fraction gave IIa-**2** (41 mg).

ii) For Ib and Ic: After removal of the solvent *in vacuo*, the residue was chromatographed on silica gel. Elution with $CHCl_3$–MeOH (50: 1) gave the unchanged methyl cyanoacetate, and further elution gave IIb-**2** (275 mg) or IIc-**2** (363 mg).

Reactions of Ia—c with α-Cyanoacetamide——A mixture of Ia, Ib or Ic (3 mmol), α-cyanoacetamide (6 mmol) and triethylamine (6 mmol) in THF (1 ml) was refluxed for 10 h.

i) For Ia: The mixture was cooled, and the precipitate (IIa-**3**, 130 mg) was collected by filtration. The filtrate was concentrated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$–MeOH (50: 1) as the eluent. The first fraction gave 2-amino-3-cyano-4,5-dihydrothiophene (IVa, 20 mg). The second fraction afforded IIa-**3** (25 mg).

ii) For Ib and Ic: After removal of the THF under reduced pressure, the residue was chromatographed on silica gel with $CHCl_3$–MeOH (50: 1) as the eluent. The first fraction gave IVb (96 mg, 23%) or IVc (356 mg, 59%). The second fraction gave IIb-**3** (160 mg, 24%) or IIc-**3** (110 mg, 13%).

Reactions of Ia—c with 1-Cyanoacetylpyrrolidine——A solution of Ia, Ib or Ic (3 mmol), 1-cyanoacetylpyrrolidine (6 mmol) and triethylamine (6 mmol) in THF (1 ml) was refluxed for 10 h. After removal of the THF *in vacuo*, the residue was purified by column chromatography on alumina with $CHCl_3$–MeOH (50: 1) to give IIa-**4**, IIb-**4** or IIc-**4** in the yields shown in Table I.

Hydrolysis of IIa-1, IIb-1 and IIc-1——A solution of IIa-**1**, IIb-**1** or IIc-**1** (100 mg) in 20% HCl was refluxed for 3 h. The reaction mixture was cooled, and basified with aq. NaOH. The precipitate [IIIa (50 mg, 72%), IIIb (48 mg, 67%) or IIIc (60 mg, 78%)] was collected by filtration. These products were identical with the corresponding authentic samples prepared from IVa—c as described below.

i) 4-Amino-2-methyl-5,6-dihydrothieno[2,3-*d*]pyrimidine (IIIa) was recrystallized from acetone to produce colorless prisms, mp 231—233°C (dec.). *Anal.* Calcd for $C_7H_9N_3S$: C, 50.28; H, 5.42; N, 25.13. Found: C, 50.39; H, 5.39; N, 24.92. MS *m/z*: 167 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3310, 3120 (NH_2). PMR (in DMSO-d_6) δ: 2.25 (3H, s, $-C\underline{H}_3$), 2.90—3.50 (4H, m, C_5 and C_6–H), 6.53 (2H, br s, $-NH_2$).

ii) 4-Amino-2,6-dimethyl-5,6-dihydrothieno[2,3-*d*]pyrimidine (IIIb) was recrystallized from acetone to give colorless columns, mp 197—198°C (dec.). *Anal.* Calcd for $C_8H_{11}N_3S$: C, 53.01; H, 6.12; N, 23.18. Found: C, 53.12; H, 6.31; N, 23.01. MS *m/z*: 181 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3310, 3130 (NH_2). PMR (in DMSO-d_6) δ: 1.37 (3H, d, $J=7$ Hz, $C_6-C\underline{H}_3$), 2.24 (3H, s, $C_2-C\underline{H}_3$), 2.66 (1H, dd, $J=5$ and 16 Hz, C_5–H), 3.18 (1H, dd, $J=8$ and 16 Hz, C_5–H), 3.75—4.15 (1H, m, C_6–H), 6.48 (2H, br s, $-N\underline{H}_2$).

iii) 4-Amino-2-methyl-5-phenyl-5,6-dihydrothieno[2,3-*d*]pyrimidine (IIIc) was recrystallized from acetone to yield colorless needles, mp 221.5—222°C (dec.). *Anal.* Calcd for $C_{13}H_{13}N_3S$: C, 64.17; H, 5.38; N, 17.27. Found: C, 64.04; H, 5.37; N, 16.92. MS *m/z*: 243 (M^+). IR ν_{max}^{KBr} cm^{-1}: 3280, 3120 (NH_2). PMR (in DMSO-d_6) δ: 2.29 (3H, s, $C_2-C\underline{H}_3$), 3.07 (1H, dd, $J=2$ and 11 Hz, C_6–H), 3.86 (1H, dd, $J=9$ and 11 Hz, C_6–H), 4.68 (1H, dd, $J=2$ and 9 Hz, C_5–H), 6.25 (2H, br s, $-N\underline{H}_2$), 7.10—7.40 (5H, m, aromatic H).

Hydrolysis of IIa-2, IIb-2 and IIc-2——A solution of IIa-**2**, IIb-**2** or IIc-**2** (100 mg) in 20% HCl was refluxed for 2 h.

i) For IIa-**2** and IIb-**2**: The reaction mixture was basified with aq. NaOH, and extracted with $CHCl_3$. The $CHCl_3$ layer was evaporated to dryness to give IIIa (59 mg, 79%) or IIIb (55 mg, 73%).

ii) For IIc-**2**: The reaction mixture was basified with aq. NaOH and cooled. The precipitate (IIIc, 68 mg, 84%) was collected by filtration.

Preparation of 4-Amino-2-methyl-5,6-dihydrothieno[2,3-*d*]pyrimidines (IIIa, IIIb and IIIc)——Sodium metal (230 mg) was dissolved in abs. MeOH (10 ml) and the MeOH was removed *in vacuo*. The resulting MeONa was suspended in ethyl cellosolve (10 ml), and acetamidine hydrochloride (7.5 mmol) and IVa, IVb or IVc (5 mmol) was added. The reaction mixture was refluxed for 10 h. After removal of the solvent *in vacuo*, the residue was added to water, and the deposited crystals [IIIa (248 mg), IIIb (280 mg) or IIIc (275 mg)] were collected by filtration. The filtrate was extracted with $CHCl_3$. The $CHCl_3$ extract gave the same substance [IIIa (30 mg), IIIb (60 mg) or IIIc (150 mg)]. The total yields of IIIa, IIIb and IIIc were 33, 38 and 35%, respectively.

Ammonolysis of IIa-1, IIb-1 and IIc-1——A suspension of IIa-**1**, IIb-**1** or IIc-**1** (1 mmol) and NH_4Cl (40 mg) in conc. NH_4OH (20 ml) was heated at 50°C for 5 h (in the case of IIa-**1** and IIb-**1**) or 10 h (in the case of IIc-**1**) with stirring. The reaction mixture was cooled, and the precipitate [IIa-**3** (163 mg, 78%), IIb-**3** (175 mg, 78%) or IIc-**3** (187 mg, 65%)] was collected, washed with water and dried.

Reactions of IIa-1, IIb-1 and IIc-1 with Pyrrolidine——A mixture of IIa-**1**, IIb-**1** or IIc-**1** (1 mmol) and pyrrolidine (5 ml) was refluxed for 30 h. After removal of the pyrrolidine under reduced pressure, the residue was recrystallized from an appropriate solvent (Table I) to give IIa-**4** (166 mg, 63%), IIb-**4** (215 mg, 77%) or IIc-**4** (218 mg, 64%).

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