[Chem. Pharm. Bull.]
34(2) 886-892 (1986)

Studies on Heterocyclic Enaminonitriles. X.¹⁾ Synthesis of 4-Amino-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo- [2,3-*d*]pyrimidine-2-acetic Acid Derivatives

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(Received July 11, 1985)

The reactions of ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamate (IIa) with methyl or ethyl cyanoacetate, α -cyanoacetamide and 1-cyanoacetylpyrrolidine gave the corresponding 4-amino-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine-2-acetic acid derivatives (IIIa-1—IIIa-4). Similarly, ethyl *N*-(3-cyano-1-ethoxycarbonyl-5-methyl(or 4-phenyl)-4,5-dihydro-1*H*-2-pyrrolyl)oxamate (IIb or IIc) gave the acetic acid derivatives (IIIb-1—IIIb-4 or IIIc-1—IIIc-4) corresponding to IIIa-1—IIIa-4. On acidic hydrolysis, IIIa-c-1 and IIIa-c-2 provided 4-amino-7-ethoxycarbonyl-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (IVa-c), which were converted to 4-amino-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (Va-c) on alkaline hydrolysis.

Keywords—ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamate; 4-amino-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine; cyanomethylene compound; hydrolysis; cyclization

In the previous papers, we showed that ethyl *N*-(2-cyanophenyl)oxamate²⁾ and ethyl *N*-(3-cyano-4,5-dihydro-2-thienyl)oxamates³⁾ react with some cyanomethylene compounds in the presence of a base to form the corresponding 4-amino-2-quinazolineacetic acid and 4-amino-5,6-dihydrothieno[2,3-*d*]pyrimidine-2-acetic acid derivatives. With the aim of widening the scope of this type of reaction, we studied the reactions of ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamates with some cyanomethylene compounds.

a: R¹=R²=H, b: R¹=H, R²=CH₃, c: R¹=C₆H₅, R²=H

1: R=COOCH₃, 2: R=COOC₂H₅, 3: R=CONH₂, 4: R=CO-N $\begin{array}{c} \diagup \\ \diagdown \end{array}$

Chart 1

On treatment with ethoxalyl chloride in pyridine, 2-amino-3-cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-pyrrole (Ia) and 2-amino-1-ethoxycarbonyl-5-methyl(or 4-phenyl)-4,5-dihydro-1*H*-pyrrole (Ib or Ic)⁴⁾ gave the corresponding ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydropyrrolyl)oxamates (IIa—c).

When a mixture of IIa—c, methyl cyanoacetate (2 eq) and triethylamine (2 eq) in tetrahydrofuran (THF) was heated for 8 h at 65—70 °C, the corresponding methyl 4-amino-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine-2-acetates (IIIa—c-1) were obtained in moderate yields together with Ia—c. The infrared (IR) spectra of IIIa—c-1 exhibited bands due to a primary amino group at near 3400, 3320 and 3130 cm⁻¹, and carbonyl groups at near 1740 and 1710 cm⁻¹, and no band indicative of a cyano group was observed. The proton magnetic resonance (¹H-NMR) spectra showed a three-proton singlet at δ 3.60—3.71 attributable to a methyl ester, a two-proton singlet at δ 3.57—3.84 due to an isolated methylene group, and a broad two-proton singlet at δ 4.58—6.59 assignable to an amino group in addition to the signals due to the protons of the dihydropyrrole moiety. These data are consistent with the proposed structures. On the other hand, when 2-benzamido-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrrole⁴⁾ was used in place of IIa—c, no reaction occurred and the starting material was recovered.

Similarly, ethyl cyanoacetate, α -cyanoacetamide and 1-cyanoacetylpyrrolidine react with IIa—c to provide the corresponding ethyl 4-amino-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine-2-acetates (IIIa—c-2), 4-amino-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine-2-acetamides (IIIa—c-3), and 4-amino-2-(1-pyrrolidinyl)car-

TABLE I. Yields, Melting Points and Elemental Analyses of IIIa-1—4, IIIb-1—4 and IIIc-1—4

Compd. No.	Yield (%)		mp (°C) (Recrystallization solvent)	Appearance (Colorless)	Formula	Analysis (%) Calcd (Found)		
		(%) ^{a)}				C	H	N
IIIa-1	41	(17)	191—192 (Acetone)	Needles	C ₁₂ H ₁₆ N ₄ O ₄	51.42 (51.63)	5.75 (5.95)	19.99 (19.58)
IIIa-2	52	(21)	163—164 (Acetone)	Needles	C ₁₃ H ₁₈ N ₄ O ₄	53.05 (53.25)	6.16 (6.18)	19.04 (18.60)
IIIa-3	16	(36)	257—258 (MeOH—CHCl ₃)	Scales	C ₁₁ H ₁₅ N ₅ O ₃	49.80 (49.67)	5.70 (5.74)	26.40 (26.45)
IIIa-4	24	(25)	231—233 (Acetone)	Needles	C ₁₅ H ₂₁ N ₅ O ₃	56.41 (56.53)	6.63 (6.69)	21.93 (21.56)
IIIb-1	53	(19)	154—156 (Acetone)	Needles	C ₁₃ H ₁₈ N ₄ O ₄	53.05 (53.15)	6.16 (6.21)	19.04 (19.05)
IIIb-2	52	(13)	164—165 (Acetone)	Needles	C ₁₄ H ₂₀ N ₄ O ₄	54.53 (54.39)	6.54 (6.78)	18.17 (18.10)
IIIb-3	20	(28)	208—210 (Acetone)	Needles	C ₁₂ H ₁₇ N ₅ O ₃ · 1/2 H ₂ O	49.99 (49.94)	6.29 (5.79)	24.29 (23.83)
IIIb-4	27	(44)	207—208 (Acetone)	Needles	C ₁₆ H ₂₃ N ₅ O ₃	57.64 (57.20)	6.95 (6.98)	21.01 (20.86)
IIIc-1	40	(40)	153—154 (Acetone)	Needles	C ₁₈ H ₂₀ N ₄ O ₄	60.66 (60.47)	5.66 (5.69)	15.72 (15.40)
IIIc-2	43	(35)	157—158 (Acetone)	Needles	C ₁₉ H ₂₂ N ₄ O ₄	61.61 (61.72)	5.99 (6.03)	15.13 (14.83)
IIIc-3	20	(56)	232—234 (MeOH)	Prisms	C ₁₇ H ₁₉ N ₅ O ₃	59.81 (59.54)	5.61 (5.43)	20.52 (20.71)
IIIc-4	27	(33)	247—248 (Acetone)	Needles	C ₂₁ H ₂₅ N ₅ O ₃	63.78 (63.64)	6.37 (6.48)	17.71 (17.41)

a) Yields of Ia—c.

TABLE II. Spectral Data for IIIa-1—4, IIIb-1—4 and IIIc-1—4

Compd. No.	IR $\nu_{\max}^{\text{KBr cm}^{-1}}$		$^1\text{H-NMR}$ spectra (ppm) (J in Hz)										MS m/z (M^+)
	NH_2	CO	H^a	H^b	H^c	H^d	$\text{H}^{e,c}$	H^f	H^g	H^h	H^i		
IIIa-1	3390	1740	$\text{---}2.75\text{---}$ (t)	$\text{---}2.75\text{---}$	$\text{---}3.95\text{---}$ (t)	---	6.59 (br s)	3.60 (s)	3.62	4.18	1.24	280	
	3340	1710							(s)	(q)	(t)		
	3130												
	IIIa-2	3400	1740	$\text{---}2.79\text{---}$ (t)	$\text{---}2.79\text{---}$	$\text{---}4.03\text{---}$ (t)	---	5.00 (br s)	3.79 (s)	$\text{---}1.25\text{ (3H, t) 4.18 (2H, q) 1.32 (3H, t) 4.29 (2H, q) \text{---}}$			294
3340		1710	(s)										
3160													
IIIa-3		3360	1710	$\text{---}2.75\text{---}$ (t)	$\text{---}2.75\text{---}$	$\text{---}3.94\text{---}$ (t)	---	6.61 (br s)	3.41 (s)	7.01 ^c	4.20	1.28	265
	3120	1680	(1H, br s)							(q)	(t)		
			7.98 ^c										
	IIIa-4	3320	1730	$\text{---}2.72\text{---}$ (t)	$\text{---}2.72\text{---}$	$\text{---}3.91\text{---}$ (t)	---	6.50 (br s)	3.55 (s)	$\text{---}1.56\text{---}2.08\text{---}$ (1H, br s)			319
3240		1660	(4H, m)							(q)	(t)		
			3.19—3.68 (4H, m)										
IIIb-1		3400	1725	$\text{---}2.98\text{---}$ (dd)	2.30 (dd)	4.27—4.54 (m)	1.21 (d)	6.55 (br s)	3.57 (s)	3.60	4.14	1.22	294
	3320	1692	(s)							(q)	(t)		
	3120												
	$(J_{a,b}=16, J_{a,c}=9, J_{b,c}=3, J_{c,d}=7)$												

IIIb-2	3400	1735	b)	3.06	2.30	4.44—4.69	1.33	4.94	3.79	1.24 (3H, t) 4.20 (2H, q) 1.34 (3H, t) 4.31 (2H, q)	308
	3340	1710		(dd)	(dd)	(m)	(d)	(brs)	(s)		
	3160										
IIIb-3	3370	1730	a)	3.01	$J_{a,b}=15, J_{a,c}=10, J_{b,c}=3, J_{c,d}=7$	4.32—4.61	1.22	6.64	3.42	7.03 ^{c)} (1H, brs)	279
	3120	1700		(dd)	(dd)	(m)	(d)	(brs)	(s)	8.01 ^{c)} (1H, brs)	
IIIb-4	3370	1730	a)	2.99	2.31	4.31—4.59	1.23	6.51	3.55	1.65—2.00 (4H, m)	333
	3150	1660		(dd)	(dd)	(m)	(d)	(brs)	(s)	3.28—3.79 (4H, m)	
IIIc-1	3410	1740	b)	7.11—7.40	—	3.91—4.51	—	4.58	3.84	3.71 (s)	356
	3300	1720		(m)	(m)	(m)		(brs)	(s)	4.30 (q)	
	3160										
IIIc-2	3430	1740	b)	7.13—7.37	—	3.78—4.78	—	4.53	3.80	1.24 (3H, t) 4.16 (2H, q) 1.31 (3H, t) 4.29 (2H, q)	370
	3320	1715		(m)	(m)	(m)		(brs)	(s)		
	3180										
IIIc-3	3440	1730	a)	6.96—7.42	—	3.56—4.51	—	6.33	3.46	4.19 (q)	341
	3340	1660		(m)	(m)	(m)		(brs)	(s)	8.01 ^{c)} (1H, brs)	
IIIc-4	3400	1735	a)	7.01—7.40	—	3.11—4.50	—	6.20	3.60	1.56—2.04 (4H, m)	395
	3320	1630		(m)	(m)	(m)		(brs)	(s)	3.11—3.78 (4H, m)	

Abbreviations: br s, broad singlet; d, doublet; dd, doublet of doublets; m, multiplet; q, quartet; s, singlet; t, triplet. a) In CDCl_3 . b) In $\text{DMSO}-d_6$. c) Disappeared on treatment with D_2O ; amine ($-\text{NH}_2$) proton. d) Overlapping with the H^a signal.

bonylmethyl-7-ethoxycarbonyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (IIIa—c-4), respectively. The structure assignments of these products were based on the satisfactory elemental analyses (Table I), the spectral data (Table II), and the following chemical reactions (Chart 2).

Chart 2

The reactions of IIIa—c-2 with ammonia resulted in the formation of IIIa—c-3. The treatment of IIIa—c-2 with pyrrolidine gave IIIa—c-4. On hydrolysis with 10% hydrochloric acid, IIIa-1,2, IIIb-1,2 and IIIc-1,2 were converted to the corresponding 4-amino-7-ethoxycarbonyl-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (IVa—c). The structures of IVa—c were confirmed by the analytical and spectral data. In the IR spectra, no absorption band at near 1740 cm^{-1} indicative of the ester carbonyl group was observed. The $^1\text{H-NMR}$ spectra revealed a three-proton singlet at near δ 2.3 assignable to the methyl group at C_2 in IVa—c, but no signal due to an isolated methylene group was observed. Compounds IVa—c were further hydrolyzed by refluxing them with 5% sodium hydroxide to yield the corresponding 4-amino-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (Va—c). The structures of Va—c were confirmed by direct comparison with corresponding authentic specimens prepared by the reactions of Ia—c with acetamidine according to the method of Taylor *et al.*⁵⁾

Experimental

All melting points are uncorrected. IR spectra were recorded on an IRA-2 spectrophotometer. $^1\text{H-NMR}$ spectra were taken on a Hitachi R-22 spectrometer (90 MHz) with tetramethylsilane as an internal standard. Mass spectra (MS) were measured with a JEOL model JMS-D 300 mass spectrometer.

Preparation of Ethyl *N*-(3-Cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamates (IIa—c)—Ethoxalyl chloride (12 mmol) was added dropwise to a stirred solution of Ia, Ib or Ic (10 mmol) in pyridine (10 ml) under ice-cooling. The reaction mixture was stirred for 1 h at 50–55 °C, and then poured into ice water. The precipitate was collected, washed with water, and dried.

i) Ethyl *N*-(3-cyano-1-ethoxycarbonyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamate (IIa) was recrystallized from acetone–petr. benzin to give colorless needles (2.3 g, 82%), mp 145 °C. *Anal.* Calcd for $C_{12}H_{15}N_3O_5$: C, 51.24; H, 5.38; N, 14.94. Found: C, 51.10; H, 5.57; N, 14.63. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3240, 3160 ($>\text{NH}$), 2200 (CN), 1720, 1690 (CO). $^1\text{H-NMR}$ (in CDCl_3) δ : 1.32 (3H, t, $J=7$ Hz, $-\text{COOCH}_2-\text{CH}_3$), 1.40 (3H, t, $J=7$ Hz, $-\text{COOCH}_2-\text{CH}_3$), 2.91 (2H, dd, $J=10, 8$ Hz, $C_4-\text{H}$), 3.93 (2H, dd, $J=10, 8$ Hz, $C_5-\text{H}$), 4.29 (2H, q, $J=7$ Hz, $-\text{OCH}_2-\text{CH}_3$), 4.55 (2H, q, $J=7$ Hz, $-\text{OCH}_2-\text{CH}_3$), 11.68 (1H, brs, $>\text{NH}$).

ii) Ethyl *N*-(3-cyano-1-ethoxycarbonyl-5-methyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamate (IIb) was recrystallized from ether to provide colorless prisms (2.0 g, 68%), mp 83–85 °C. *Anal.* Calcd for $C_{13}H_{17}N_3O_5$: C, 52.87; H, 5.80; N, 14.23. Found: C, 52.98; H, 6.03; N, 14.29. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3240, 3160 ($>\text{NH}$), 2200 (CN), 1720, 1690 (CO). $^1\text{H-NMR}$ (in CDCl_3) δ : 1.32 (3H, d, $J=6$ Hz, $C_5-\text{CH}_3$), 1.33 (3H, t, $J=7$ Hz, $-\text{OCH}_2-\text{CH}_3$), 1.40 (3H, t, $J=7$ Hz, $-\text{OCH}_2-\text{CH}_3$),

2.40 (1H, dd, $J = 15, 3$ Hz, C_4 -H), 3.15 (1H, dd, $J = 15, 10$ Hz, C_4 -H), 4.11–4.51 (1H, m, C_5 -H), 4.31 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 4.40 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 11.58 (1H, br s, $>NH$).

iii) Ethyl *N*-(3-cyano-1-ethoxycarbonyl-4-phenyl-4,5-dihydro-1*H*-2-pyrrolyl)oxamate (IIc) was recrystallized from acetone–petr. benzine to give colorless prisms (2.96 g, 83%). mp 119–120 °C. *Anal.* Calcd for $C_{18}H_{19}N_3O_5$: C, 60.49; H, 5.36; N, 11.76. Found: C, 60.38; H, 5.35; N, 11.61. IR ν_{max}^{KBr} cm^{-1} : 3280, 3220 (NH), 2200 (CN), 1725, 1695 (CO). ^1H -NMR (in $CDCl_3$) δ : 1.29 (3H, t, $J = 7$ Hz, $-OCH_2-CH_3$), 1.40 (3H, t, $J = 7$ Hz, $-OCH_2-CH_3$), 3.72–4.55 (3H, m, $C_{4,5}$ -H), 4.28 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 4.41 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 7.17–7.44 (5H, m, aromatic H), 11.64 (1H, br s, $>NH$).

Reactions of IIa–c with Methyl or Ethyl Cyanoacetate—A mixture of IIa, IIb or IIc (5 mmol), methyl or ethyl cyanoacetate (15 mmol) and triethylamine (10 mmol) in THF (1 ml) was stirred for 8 h at 65–70 °C. After removal of the THF *in vacuo*, the residue was chromatographed on silica gel. The first fraction eluted with $CHCl_3$ gave the unchanged methyl or ethyl cyanoacetate and the second fraction gave Ia–c. The third fraction eluted with $CHCl_3$ –acetone (4:1) gave IIIa–c-1 or IIIa–c-2.

Reactions of IIa–c with α -Cyanoacetamide and 1-Cyanoacetylpyrrolidine—A mixture of IIa, IIb or IIc (5 mmol), α -cyanoacetamide or 1-cyanoacetylpyrrolidine (15 mmol) and triethylamine (10 mmol) in THF (2 ml in the case of α -cyanoacetamide or 1 ml in the case of 1-cyanoacetylpyrrolidine) was heated for 8 h at 65–70 °C with stirring. The solvent was removed *in vacuo*, and then the residue was poured into ice water and salted out with NaCl. The precipitate was collected, washed with water to remove the unchanged cyanomethylene compounds, dried, and chromatographed on Al_2O_3 . The first fraction eluted with $CHCl_3$ gave Ia–c and the second fraction eluted with $CHCl_3$ –MeOH (5:1) gave IIIa–c-3 or IIIa–c-4.

Ammonolysis of IIIa–c-2—A solution of IIIa-2, IIIb-2 or IIIc-2 (2 mmol) in MeOH (15 ml) was saturated with NH_3 under ice-cooling. The reaction mixture was kept at room temperature overnight, and heated for 1 h at 40 °C (in the case of IIIa-2 and IIIc-2) or at 70 °C (in the case of IIIb-2). After removal of the MeOH *in vacuo*, the residue was recrystallized from acetone to give IIIa-3 (87%), IIIb-3 (72%) or IIIc-3 (69%).

Conversion of IIIa–c-2 to IIIa–c-4—A mixture of IIIa-2, IIIb-2 or IIIc-2 (2 mmol) and pyrrolidine (2 ml) was refluxed for 3 h. After removal of the pyrrolidine *in vacuo*, the residue was recrystallized from acetone to yield IIIa-4 (77%), IIIb-4 (81%) or IIIc-4 (68%).

Hydrolysis of IIIa–c-1—A solution of IIIa-1, IIIb-1 or IIIc-1 (1 mmol) in 10% HCl (5 ml) was refluxed for 1 h. The reaction mixture was cooled, and basified with aqueous $NaHCO_3$. The precipitate was collected, dried and recrystallized from acetone to give IVa (83%), IVb (81%) or IVc (88%).

Hydrolysis of IIIa–c-2—A solution of IIIa-2, IIIb-2 or IIIc-2 (1 mmol) in 10% HCl (5 ml) was refluxed for 1 h. Work-up of the reaction mixture as described above gave IVa (96%), IVb (80%) or IVc (89%).

i) 4-Amino-7-ethoxycarbonyl-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (IVa): Colorless prisms, mp 202–204 °C. *Anal.* Calcd for $C_{10}H_{14}N_4O_2$: C, 54.04; H, 6.35; N, 25.21. Found: C, 53.80; H, 6.52; N, 25.30. MS m/z : 222 (M^+). IR ν_{max}^{KBr} cm^{-1} : 3480, 3420, 3320 (NH_2), 1720 (CO). ^1H -NMR (in $DMSO-d_6$) δ : 1.23 (3H, t, $J = 7$ Hz, $-OCH_2-CH_3$), 2.27 (3H, s, C_2-CH_3), 2.71 (2H, t, $J = 9$ Hz, C_5 -H), 3.90 (2H, t, $J = 9$ Hz, C_6 -H), 4.15 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 6.42 (2H, br s, NH_2).

ii) 4-Amino-7-ethoxycarbonyl-2,6-dimethyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (IVb): Colorless needles, mp 179–181 °C. *Anal.* Calcd for $C_{11}H_{16}N_4O_2$: C, 55.91; H, 6.83; N, 23.72. Found: C, 55.79; H, 6.82; N, 23.60. MS m/z : 236 (M^+). IR ν_{max}^{KBr} cm^{-1} : 3380, 3320 (NH_2), 1720 (CO). ^1H -NMR (in $DMSO-d_6$) δ : 1.21 (3H, d, $J = 7$ Hz, C_6-CH_3), 1.24 (3H, t, $J = 7$ Hz, $-OCH_2-CH_3$), 2.27 (3H, s, C_2-CH_3), 2.29 (1H, dd, $J = 15, 3$ Hz, C_5 -H), 2.95 (1H, dd, $J = 15, 10$ Hz, C_5 -H), 4.18 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 4.29–4.54 (1H, m, C_6 -H), 6.44 (2H, br s, NH_2).

iii) 4-Amino-7-ethoxycarbonyl-2-methyl-5-phenyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (IVc): Colorless prisms, mp 227 °C. *Anal.* Calcd for $C_{16}H_{18}N_4O_2$: C, 64.41; H, 6.08; N, 18.78. Found: C, 64.22; H, 6.20; N, 18.94. IR ν_{max}^{KBr} cm^{-1} : 3360, 3320 (NH_2), 1725 (CO). ^1H -NMR (in $DMSO-d_6$) δ : 1.21 (3H, t, $J = 7$ Hz, $-OCH_2-CH_3$), 2.31 (3H, s, C_2-CH_3), 3.12–3.52 (1H, m, C_6 -H), 3.90–4.45 (2H, m, C_5 -H and C_6 -H), 4.15 (2H, q, $J = 7$ Hz, $-OCH_2-CH_3$), 6.15 (2H, br s, NH_2), 7.11–7.33 (5H, m, aromatic H).

Hydrolysis of IVa–c—A suspension of IVa, IVb or IVc (1 mmol) in 5% NaOH (2 ml) was heated at 120–130 °C for 1 h (in the case of IVa and IVb) or 2 h (in the case of IVc) with stirring. The reaction mixture was cooled and the deposited crystals were collected, washed with water, dried, and recrystallized from CH_2Cl_2 to furnish Va (75%), Vb (82%) or Vc (95%).

Preparation of 4-Amino-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidines (Va, Vb and Vc)—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 (10 mmol) and Ia, Ib or Ic (5 mmol) were added. The mixture was refluxed for 3 h (in the case of Ia), 5 h (in the case of Ib) or 9 h (in the case of Ic). After removal of the solvent *in vacuo*, the residue was poured into ice water, and extracted with $CHCl_3$. The $CHCl_3$ layer was dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was recrystallized from CH_2Cl_2 to afford Va (46%), Vb (70%) or Vc (44%).

i) 4-Amino-2-methyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (Va): Colorless needles, mp 258 °C. *Anal.* Calcd for $C_7H_{10}N_4$: C, 55.98; H, 6.71; N, 37.31. Found: C, 56.12; H, 6.71; N, 37.00. MS m/z : 150 (M^+). IR ν_{max}^{KBr} cm^{-1} : 3480,

3260 (NH₂). ¹H-NMR (in DMSO-*d*₆) δ: 2.12 (3H, s, C₂-CH₃), 2.70 (2H, t, *J* = 9 Hz, C₅-H), 3.42 (2H, t, *J* = 9 Hz, C₆-H), 5.84 (2H, br s, NH₂), 6.24 (1H, br s, >NH).

ii) 4-Amino-2,6-dimethyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (Vb): Colorless needles, mp 225–227 °C. *Anal.* Calcd for C₈H₁₂N₄: C, 58.51; H, 7.37; N, 34.12. Found: C, 58.30; H, 7.39; N, 34.01. MS *m/z*: 164 (M⁺). IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3460, 3280 (NH₂). ¹H-NMR (in DMSO-*d*₆) δ: 1.13 (3H, d, *J* = 6 Hz, C₆-CH₃), 2.11 (3H, s, C₂-CH₃), 2.20 (1H, dd, *J* = 15, 6 Hz, C₅-H), 2.88 (1H, dd, *J* = 15, 9 Hz, C₅-H), 3.70–4.00 (1H, m, C₆-H), 5.80 (2H, br s, NH₂), 6.40 (1H, br s, >NH).

iii) 4-Amino-2-methyl-5-phenyl-5,6-dihydro-7*H*-pyrrolo[2,3-*d*]pyrimidine (Vc): Colorless prisms, mp 242 °C. *Anal.* Calcd for C₁₃H₁₄N₄: C, 69.00; H, 6.24; N, 24.76. Found: C, 68.82; H, 6.14; N, 24.75. MS *m/z*: 226 (M⁺). IR $\nu_{\max}^{\text{KBr}}$ cm⁻¹: 3460, 3280 (NH₂). ¹H-NMR (in DMSO-*d*₆) δ: 2.16 (3H, s, C₂-CH₃), 3.26 (1H, dd, *J* = 10, 4 Hz, C₆-H), 3.87 (1H, dd, *J* = 10, 9 Hz, C₆-H), 4.32 (1H, dd, *J* = 9, 4 Hz, C₅-H), 5.49 (2H, br s, NH₂), 6.45 (1H, br s, >NH), 7.20 (5H, s, aromatic H).

Acknowledgement The authors are grateful to Messrs. M. Nishi, Y. Furukawa, and S. Hara of Fukuoka University for ¹H-NMR spectra, mass spectra and elemental analyses.

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