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Studies on Heterocyclic Enaminonitriles. I. Synthesis and Aromatization of 2-Amino-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrroles

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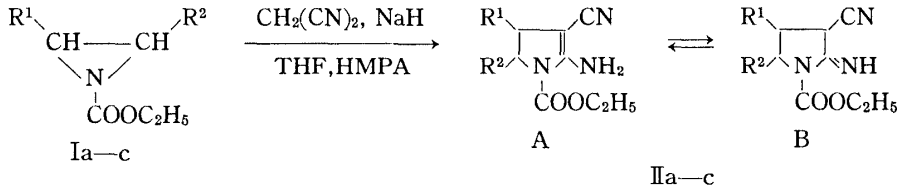
The reaction of 1-ethoxycarbonylaziridine with malononitrile in the presence of sodium hydride gave 2-amino-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrrole (IIa) in 47% yield. Similarly, 1-ethoxycarbonyl-2-methyl(or phenyl)aziridine reacted with malononitrile to give 2-amino-3-cyano-5-methyl(or 4-phenyl)-4,5-dihydropyrrole (IIb or c). Compounds IIa—c were dehydrogenated to the corresponding pyrroles (IVa—c) when heated with chloranil in benzene. 2-Amino-3-cyano-1-ethoxycarbonyl-4-phenylpyrrole (IVc) was also synthesized from ethyl *N*-phenacylcarbamate and malononitrile. The 2-benzamido derivatives of IIa—c reacted with *N*-bromosuccinimide in the presence of 2,2′-azobisisobutyronitrile to produce the corresponding 2-benzamido-3-cyano-1-ethoxycarbonylpyrroles (Va—c) as major products.

Keywords——malononitrile; 1-ethoxycarbonylaziridines; 2-amino-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrroles; NBS; chloranil; 2-amino-3-cyano-1-ethoxycarbonylpyrroles; benzoylation; aromatization

Enaminonitriles are versatile synthons and their chemistry has been reviewed by Taylor *et al.*[1] However, few papers have been published on the heterocyclic enaminonitriles.[1,2] We report here a synthesis of 2-amino-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrroles and we also describe their aromatization.

Stamm *et al.*[3] reported that 1-ethoxycarbonylaziridine (Ia) reacts with diethyl malonate to form 1,3-diethoxycarbonyl-2-pyrrolidone. We examined this reaction with malononitrile in place of diethyl malonate.

When a solution of Ia, malononitrile, and sodium hydride in tetrahydrofuran (THF) was refluxed with hexamethylphosphoric triamide (HMPA) for 4 h, 2-amino-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrrole (IIa) was obtained in 47% yield. Similarly, the reactions of malononitrile with 1-ethoxycarbonyl-2-methylaziridine (Ib) and 1-ethoxycarbonyl-2-phenylaziridine (Ic) gave 2-amino-3-cyano-1-ethoxycarbonyl-5-methyl-4,5-dihydropyrrole (IIb) and 2-amino-3-cyano-1-ethoxycarbonyl-4-phenyl-4,5-dihydropyrrole (IIc) in 50 and 49% yields, respectively. When II a—c were treated with benzoyl chloride in pyridine, the corresponding 2-benzamido-3-cyano-4,5-dihydropyrroles (IIIa—c) were obtained. Some properties of II and III are shown in Table I, and the spectral data are listed in Table II.



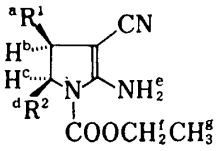
a: $R^1=R^2=H$ b: $R^1=H$, $R^2=CH_3$ c: $R^1=C_6H_5$, $R^2=H$

As regards the structures of II a—c, the imine forms (B) are possible besides the enamine forms (A). However, the infrared (IR) spectra of II a—c displayed bands due to an amino group at near 3400 cm^{-1}, 3300 cm^{-1} and 3250 cm^{-1}, and a characteristic conjugated nitrile group at 2190 cm^{-1}. The proton magnetic resonance (PMR) spectra showed a broad singlet

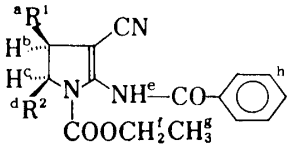
Table I. Some Properties of II and III

Compd. No.	mp (°C) (Recrystn. solvent)	Appearance (Colorless)	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	N
IIa	188—190 (CH_2Cl_2–Petr. benzin)	Prisms	47	$C_8H_{11}N_3O_2$	53.03 (53.04	6.12 6.06	23.19 22.92)
IIb	135—137 (Acetone)	Prisms	50	$C_9H_{13}N_3O_2$	55.37 (55.19	6.17 6.60	21.53 21.63)
IIc	213—214 ($CHCl_3$–EtOH)	Needles	49	$C_{14}H_{15}N_3O_2$	65.35 (65.31	5.88 5.73	16.33 16.45)
IIIa	173—174 (Acetone)	Scales	83	$C_{15}H_{15}N_3O_3$	63.15 (63.14	5.30 5.14	14.73 14.62)
IIIb	147 (Acetone–Petr. benzin)	Scales	83	$C_{16}H_{17}N_3O_3$	64.20 (63.95	5.72 5.63	14.04 14.23)
IIIc	178—179 (Acetone–Petr. benzin)	Columns	73	$C_{21}H_{19}N_3O_3$	69.79 (69.74	5.30 5.24	11.63 11.61)

Table II. Some Spectral Data for II and III



II a—c



III a—c

a: $R^1=R^2=H$
b: $R^1=H$, $R^2=CH_3$
c: $R^1=C_6H_5$, $R^2=H$

Compd. No.	IR ν_{max}^{KBr} cm^{-1} NH	CN	CO	Proton NMR spectra (ppm) in $CDCl_3$ solution (J in Hz) H^a	H^b	H^c	H^d	H^e	H^f	H^g	H^h
IIa	3400 3300 3250	2190	1700	2.55—4.03 (m)		3.74 — 4.03 (m)		6.13 (br s)	4.26 (q)	1.35 (t)	—
IIb	3400 3300 3250	2190	1705	2.90 (dd)	2.14 (dd)	4.10— 4.37 (m)	1.29 (d)	6.04 (br s)	4.24 (q)	1.32 (t)	—
				($J_{a,b}=12$, $J_{a,c}=8$, $J_{b,c}=3$)							
IIc	3410 3320 3250	2190	1715	7.37 (s)	4.20— 4.32 (m)	3.74 or 4.01 (d) ($J_{c,d}=7.5$)	(d)	6.10 (br s)	4.31 (q)	1.32 (t)	—
IIIa	3240 3120	2200	1700 1690	2.79—2.99 (m)		3.79 — 3.96 (m)		11.38 (br s)	4.26 (q)	1.31 (t)	7.46—7.53(3H, m) 7.88—7.99(2H, m)
IIIb	3250 3170	2200	1705 1690	3.16 (dd)	2.39 (dd)	4.2—4.4 (m)	1.32 (d)	11.49 (br s)	4.27 (q)	1.32 (t)	7.42—7.56(3H, m) 7.85—7.96(2H, m)
				($J_{a,b}=14$, $J_{a,c}=10$, $J_{b,c}=3.2$, $J_{c,d}=7.6$)							
IIIc	3260 3180	2200	1705 1695	7.30 (s)		3.75—4.25 (m)		11.38 (br s)	4.25 (q)	1.30 (t)	7.44—7.52(3H, m) 7.89—8.00(2H, m)

Abbreviations: br s, broad singlet; d, doublet; dd, doublet of doublets; m, multiplet; q, quartet; s, singlet; t, triplet.

at near δ 6.1 (2H) attributable to the primary amino protons. These observations are consistent with the enamine structures (A) rather than the imine structures (B).

In order to confirm the structures of II a—c, we aromatized the compounds. When II a—c were refluxed with chloranil in benzene, the corresponding pyrroles IV a—c were obtained in yields of 45, 39 and 90%, respectively. The treatment of IV(a—c) with benzoyl chloride in refluxing acetonitrile was carried out for 3 h to give the corresponding 2-benzamido-3-cyanopyrroles V a—c. Table III shows some properties of IV and V, and Table IV shows the spectral data.

2-Amino-3-cyano-1-ethoxycarbonyl-4-phenylpyrrole (IVc) was proved to be identical with an authentic sample prepared by the reaction of ethyl *N*-phenacyclarbamate and malononitrile. In a similar fashion, the reaction of ethyl *N*-acetonylearbamate with malononitrile gave 2-amino-3-cyano-1-ethoxycarbonyl-4-methylpyrrole (IVd) in 45% yield. These reactions are formulated in Chart 1.

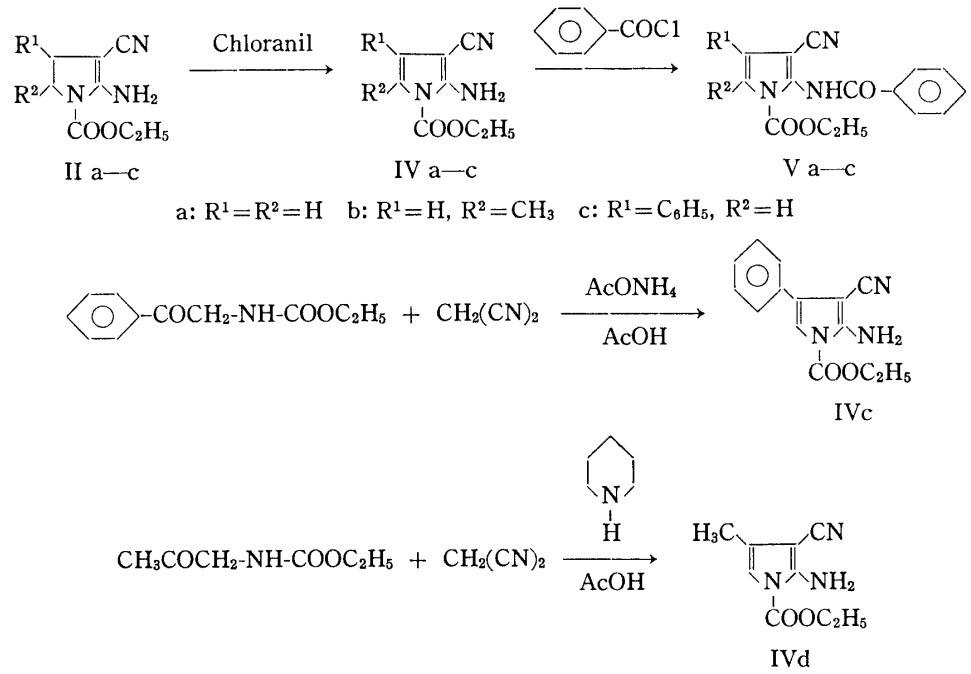


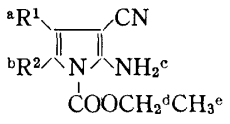
Chart 1

Although IVb (mp 180—182°C) had the molecular composition $C_9H_{11}N_3O_2$, which is the same as that of IVd (mp 170—171°C), IVb was obviously not identical with the latter compound. In the PMR spectra of IV(b and d), the aromatic proton signal (1H) of IVb appeared at higher magnetic field than that of IVd (δ 5.90 and δ 6.39 for IVb and IVd, respectively). On the other hand, the methyl protons at C-5 in IVb absorbed at lower field than the methyl protons at C-4 in IVd (δ 2.22 and δ 1.92 for IVb and IVd, respectively). On the basis of these spectral data, IVb was assigned as 2-amino-3-cyano-1-ethoxycarbonyl-5-methylpyrrole.

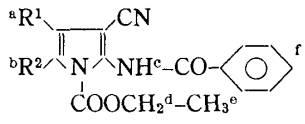
TABLE III. Some Properties of IV and V

Compd. No.	mp (°C) (Recrystn. solvent)	Appearance (Colorless)	Yield (%)	Formula	Analysis (%) Calcd (Found) C	H	N
IVa	141—142 (CH_2Cl_2-Petr. benzin)	Prisms	45	$C_8H_9N_3O_2$	53.62 (53.78	5.06 4.99	23.45 23.62)
IVb	180—182 (Acetone)	Prisms	39	$C_9H_{11}N_3O_2$	55.95 (56.14	5.74 5.77	21.75 21.58)
IVc	177—178 (EtOH-$CHCl_3$)	Prisms	90	$C_{14}H_{13}N_3O_2$	65.87 (65.52	5.13 4.90	16.46 16.32)
IVd	170—171 (CH_2Cl_2-Petr. benzin)	Prisms	45	$C_9H_{11}N_3O_2$	55.95 (55.85	5.74 5.81	21.75 21.48)
Va	136—137 (CH_2Cl_2-Petr. benzin)	Prisms	78	$C_{15}H_{13}N_3O_3$	63.59 (63.81	4.63 4.41	14.83 14.33)
Vb	112 (CH_2Cl_2-Petr. benzin)	Needles	61	$C_{16}H_{15}N_3O_3$	64.63 (64.69	5.09 4.94	14.14 13.88)
Vc	196—197 (CH_2Cl_2-Petr. benzin)	Needles	52	$C_{21}H_{17}N_3O_3$	70.18 (70.18	4.77 4.50	11.69 11.37)

TABLE IV. Some Spectral Data for IV and V



IV(a—d)



V(a—c)

a: $R^1=R^2=H$
b: $R^1=H$, $R^2=CH_3$
c: $R^1=C_6H_5$, $R^2=H$
d: $R^1=CH_3$, $R^2=H$

Compd. No.	IR ν_{max}^{KBr} cm^{-1} NH	CN	CO	Proton NMR spectra ppm (J in Hz) H^a	H^b	H^c	H^d	H^e	H^f	MS m/e (M^+)
IVa	3420 3320 3220	2190	1740	a) 6.08 (d) ($J_{a,b}=4$)	6.56 (d)	5.78 (br s)	4.43 (q)	1.40 (t)	—	179
IVb	3430 3320 3230	2200	1730	b) 5.90 (q) ($J_{a,b}=1.8$)	2.22 (d)	6.75 (br s)	4.37 (q)	1.32 (t)	—	193
IVc	3420 3320 3230	2190	1740	b) 7.29— 7.65 (m)	6.94 (s)	7.06 (br s)	4.41 (q)	1.33 (t)	—	255
IVd	3420 3320 3230	2190	1735	b) 1.92 (d) ($J_{a,b}=2$)	6.39 (q)	6.90 (br s)	4.34 (q)	1.30 (t)	—	193
Va	3290 3250	2200	1730 1690	a) 6.38 (d) ($J_{a,b}=4$)	7.01 (d)	10.41 (br s)	4.48 (q)	1.41 (t)	7.38—7.60(3H, m) 7.88—8.00(2H, m)	—
Vb	3280 3230	2210	1730 1690	a) 6.11 (s)	2.38 (s)	9.89 (br s)	4.47 (q)	1.38 (t)	7.38—7.58(3H, m) 7.88—8.00(2H, m)	—
Vc	3280 3220	2200	1730 1690	a) 7.36— 7.72 (5H, m)	7.20 (s)	10.21 (br s)	4.52 (q)	1.43 (t)	7.36—7.72(3H, m) 7.94—8.05(2H, m)	—

Abbreviations: br s, broad singlet; d, doublet; m, multiplet; q, quartet; s, singlet; t, triplet.
a) In $CDCl_3$. *b*) In $(CD_3)_2SO$.

The reaction of Ib with malononitrile led to the formation of IIb, while a similar reaction with Ic gave IIc. Therefore, it appeared that the malononitrile anion attacked at C-3 of Ib, whereas the anion attacked at C-2 of Ic. In contrast with this reaction, in the case of the reaction of 2-phenyloxirane with malononitrile, the malononitrile anion attacks at C-3 of the

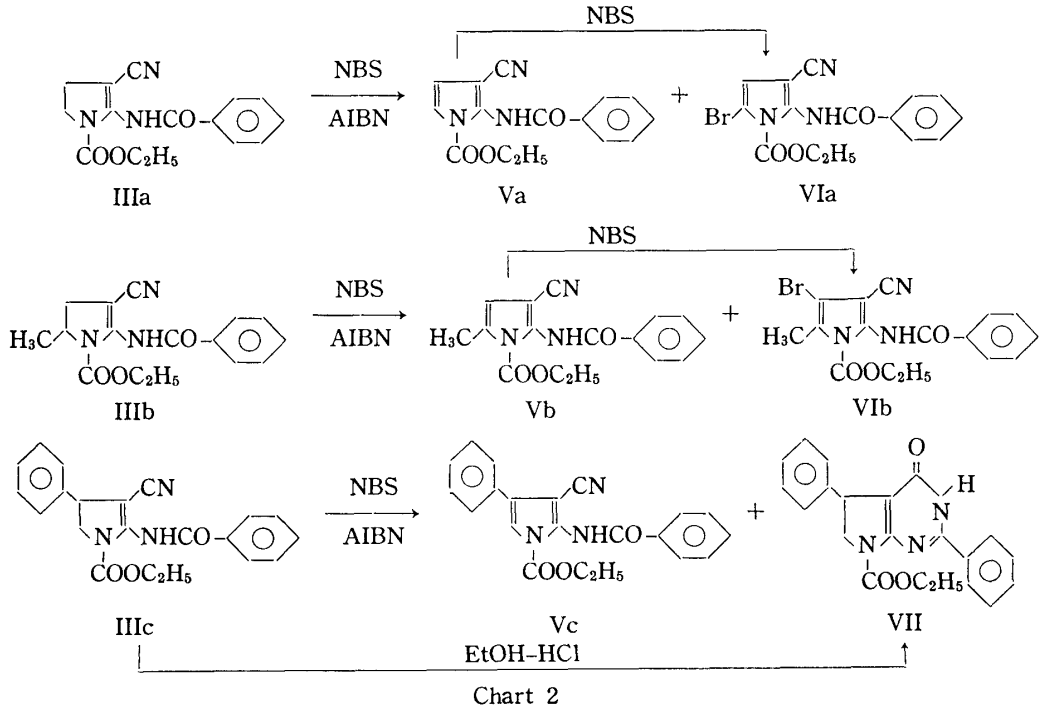


Chart 2

oxirane to give 2-amino-3-cyano-5-phenyl-4,5-dihydrofuran.[2)]

Subsequently, the reactions of 2-benzamido-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrroles (III a—c) with *N*-bromosuccinimide (NBS) were examined (Chart 2). It is known that hydroaromatic compounds are converted to aromatic compounds on reaction with NBS.[4)] For example, isoxazoles are prepared by the treatment of 2-isoxazolines with NBS.[5)] When a solution of 2-benzamido-3-cyano-1-ethoxycarbonyl-4,5-dihydropyrrole (IIIa), NBS, and 2,2′-azobisisobutyronitrile (AIBN) in carbon tetrachloride was refluxed for 1 h, 2-benzamido-3-cyano-1-ethoxycarbonylpyrrole (Va) and 2-benzamido-5-bromo-3-cyano-1-ethoxycarbonylpyrrole (VIa) were obtained in 42 and 15% yields, respectively.

Compound Va was converted to VIa when heated with NBS in carbon tetrachloride. The structure of VIa was supported by the analytical and spectral data. In particular, its PMR spectrum showed a one-proton singlet at δ 6.50 assigned to the proton at C-4. This absorption position is at lower field than that of the C_4-proton (δ 6.38) of Va, and at higher field than that of the C_5-proton (δ 7.01) of Va. These observations are consistent with the assigned structure.

Similarly, the reaction of IIIb with NBS gave 2-benzamido-3-cyano-1-ethoxycarbonyl-5-methylpyrrole (Vb) and 2-benzamido-4-bromo-3-cyano-1-ethoxycarbonyl-5-methylpyrrole (VIb) in 58 and 11% yields, respectively, and no formation of the 5-bromomethyl derivative was noted. On treatment with NBS, Vb was converted to VIb in 53% yield. The structure assignment of VIb was made on the basis of elemental analysis and its spectral data (see "Experimental").

Finally, the reaction of IIIc with NBS resulted in the formation of the corresponding pyrrole (Vc) and 7-ethoxycarbonyl-4-oxo-2,5-diphenyl-3,4,5,6-tetrahydropyrrolo[2,3-*d*]pyrimidine (VII) in yields of 44 and 15%, respectively, no bromo derivative being isolated. Bretschneider *et al.*[6)] reported that 2-acetamidonaphthalene-1-carbonitrile is cyclized to 3-methylbenzo[*f*]quinazolin-1(2*H*)-one by treatment with hydrogen chloride. Under the same conditions, compound IIIc was readily cyclized to VII in 76% yield. Therefore, the formation of VII can be accounted for by cyclization of IIIc with hydrogen bromide which was produced in the course of the reaction. The structures of Va—c were confirmed by direct comparison with the corresponding authentic specimens prepared from IIIa—c and benzoyl chloride, respectively.

Experimental

THF was purified by refluxing it over sodium metal and by distilling it, and the product was stored over sodium wire. HMPA was distilled under reduced pressure and stored over molecular sieve 4A. All melting points were taken in capillary tubes and are uncorrected. IR spectra were recorded on an IRA-2 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 were measured with a JEOL model JMS-01SG spectrometer.

Reaction of Malononitrile with Ia—c. General Procedure for the Preparation of IIa—c——Malononitrile (0.2 mol) was added dropwise to a stirred suspension of 50% NaH (0.12 mol) in HMPA (10 ml) and THF (50 ml). The stirring was continued until evolution of gas ceased. A solution of Ia—c (0.1 mol) in THF (50 ml) was then added, and the mixture was refluxed for 4 h. After removal of the THF *in vacuo*, the residue was poured into ice water. The precipitate was collected, washed with ice water and petr. ether, dried, and recrystallized from the solvent indicated in Table I.

Benzoylation of IIa—c——A solution of IIa, b or c (10 mmol) and benzoyl chloride (12 mmol) in pyridine (20 ml) was heated at 80—90°C for 3 h. The reaction mixture was kept at room temperature overnight. The reactants were poured into ice water, and the deposited crystals were collected, washed with water, dried and recrystallized from the solvent listed in Table I.

Reaction of IIa—c with Chloranil——A solution of IIa, b or c (10 mmol) and chloranil (12 mmol) in benzene (80 ml) was refluxed for 3 h. After removal of the benzene *in vacuo*, the residue was dissolved in $CHCl_3$ and the $CHCl_3$ layer was washed with 4% NaOH solution containing 1% $NaHSO_3$ and then water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with $CHCl_3$ as the eluent to give IVa, b or c (Table III).

Benzoylation of 2-Amino-3-cyano-1-ethoxycarbonylpyrroles——A solution of IVa, b or c (3 mmol)

and benzoyl chloride (3.6 mmol) in CH_3CN (10 ml) was refluxed for 3 h. After removal of the solvent *in vacuo*, the residue was recrystallized from CH_2Cl_2–petr. benzin to give Va, b or c.

Preparation of 2-Amino-3-cyano-1-ethoxycarbonyl-4-phenylpyrrole (IVc)——Ethyl *N*-phenacylcarbamate (5 mmol) and malononitrile (7.5 mmol) were refluxed (with removal of water) in benzene (30 ml) together with $AcONH_4$ (100 mg) and AcOH (1 ml). After 5 h of refluxing, the benzene was evaporated off *in vacuo*, and the residue was basified with $NaHCO_3$, and extracted with $CHCl_3$. The $CHCl_3$ extract was purified by column chromatography on Al_2O_3 with $CHCl_3$ as the eluent to give IVc (800 mg, 63%), which was identical with 2-amino-3-cyano-1-ethoxycarbonyl-4-phenylpyrrole prepared by the above reaction of IIc with chloranil.

Preparation of 2-Amino-3-cyano-1-ethoxycarbonyl-4-methylpyrrole (IVd). i) Ethyl *N*-Acetonylcarbamate——A solution of acetamidoacetone[7] (0.1 mol) and conc. HCl (20 ml) in MeOH (50 ml) was refluxed for 4 h. After removal of the MeOH *in vacuo*, the residue was diluted with water (20 ml), and ethyl chloroformate (0.13 mol) was added with stirring and ice cooling. The mixture was made alkaline with K_2CO_3. The stirring was continued at room temperature until the odor of ethyl chloroformate was absent. The reactants were extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried over Na_2SO_4, and concentrated. The residue was distilled to give ethyl *N*-acetonylcarbamate (5.74 g) as a colorless oil, bp 100—102°C/4 mmHg. PMR (in $CDCl_3$) δ: 1.25 (3H, t, J=7 Hz, $-CH_2-C\underline{H}_3$), 2.19 (3H, s, $-COC\underline{H}_3$), 4.08 (2H, d, J=4.5 Hz, $-NH-C\underline{H}_2-$), 4.14 (2H, q, J=7 Hz, $-C\underline{H}_2-CH_3$), 5.42 (1H, br s, $-N\underline{H}-$). This product was used for the preparation of IVd without further purification.

ii) Preparation of IVd——A mixture of ethyl *N*-acetonylcarbamate (2.9 g), malononitrile (1.58 g), AcOH (0.5 ml), and piperidine (200 mg) was refluxed for 3 h with removal of water in benzene (30 ml). The benzene was evaporated off *in vacuo*, and the residue was basified with $NaHCO_3$, and extracted with $CHCl_3$. The $CHCl_3$ extract was purified by column chromatography on Al_2O_3 with $CHCl_3$ as the eluent to give IVd (1.75 g, 45%).

Reaction of IIIa—c with NBS——2,2′-Azobisisobutyronitrile (AIBN) (100 mg) was added to a refluxed solution of NBS [5.5 mmol in the case of IIIa and c or 3.5 mmol in the case of IIIb in CCl_4 (150 ml)], and the dropwise addition of a solution of IIIa, b or c (5 mmol) and AIBN (100 mg) in $CHCl_3$ (20 ml) was immediately started. When the addition was complete (10 min later), the mixture was refluxed for another 1 h. The solvent was removed under reduced pressure, and the residue was dissolved in $CHCl_3$. The $CHCl_3$ layer was washed successively with aq. $NaHCO_3$ and water, dried over Na_2SO_4, and then concentrated *in vacuo*. The residue was chromatographed on silica gel.

(i) for IIIa: The first fraction eluted with $CHCl_3$ gave 2-benzamido-5-bromo-3-cyano-1-ethoxycarbonylpyrrole (VIa: 270 mg, 15%) which was recrystallized from ether to give colorless needles, mp 136—137°C. *Anal.* Calcd for $C_{15}H_{12}BrN_3O_3$: C, 49.74; H, 3.34; N, 11.60. Found: C, 49.58; H, 3.14; N, 11.56. IR ν_{max}^{KBr} cm^{-1}: 3220 (>NH), 2200 (CN), 1770, 1660 (>CO). PMR (in $CDCl_3$) δ: 1.42 (3H, t, J=7 Hz, $-CH_2-C\underline{H}_3$), 4.51 (2H, q, J=7 Hz, $-C\underline{H}_2-CH_3$), 6.50 (1H, s, C_4–H), 7.38—7.61 (3H, m, aromatic H), 7.81—7.97 (2H, m, aromatic H), 9.77 (1H, br s, >N$\underline{H}$). The second product to appear was Va (590 mg, 42%).

(ii) for IIIb: The first fraction eluted with $CHCl_3$ gave 2-benzamido-4-bromo-3-cyano-1-ethoxycarbonyl-5-methylpyrrole (VIb: 210 mg, 11%) which was recrystallized from $CHCl_3$–ether to give colorless needles, mp 154—155°C. *Anal.* Calcd for $C_{16}H_{14}BrN_3O_3$: C, 51.08; H, 3.75; N, 11.16. Found: C, 51.09; H, 3.53; N, 11.14. IR ν_{max}^{KBr} cm^{-1}: 3280 (>NH), 2200 (CN), 1720, 1690 (>CO). PMR (in $CDCl_3$) δ: 1.40 (3H, t, J= 7 Hz, $-CH_2-C\underline{H}_3$), 2.40 (3H, s, $C_5-C\underline{H}_3$), 4.49 (2H, q, J=7 Hz, $-C\underline{H}_2-CH_3$), 7.25—7.60 (3H, m, aromatic H), 7.82—8.00 (2H, m, aromatic H), 10.09 (1H, br s, >N$\underline{H}$). Further elution with $CHCl_3$ gave Vb (860 mg, 58%).

(iii) for IIIc: The first fraction eluted with $CHCl_3$ gave Vc (800 mg, 44%). The second product to appear was 7-ethoxycarbonyl-4-oxo-2,5-diphenyl-3,4,5,6-tetrahydropyrrolo[2,3-*d*]pyrimidine (VII; 270 mg, 15%), which was identical with an authentic sample prepared from IIIc by the method described later in this paper.

Reaction of Va with NBS——A solution of Va (1 mmol) and NBS (1.1 mmol) in CCl_4 (10 ml) was refluxed for 1 h. After removal of the CCl_4, the residue was dissolved in $CHCl_3$. The $CHCl_3$ layer was washed with $NaHCO_3$ and water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with $CHCl_3$ as the eluent to give VIa (180 mg, 50%), mp 136°C (from ether), colorless needles.

Reaction of Vb with NBS——A solution of Vb (5 mmol) and NBS (5.5 mmol) in CCl_4 (50 ml) was refluxed for 4 h. After removal of the CCl_4, the residue was dissolved in $CHCl_3$. The $CHCl_3$ layer was washed with $NaHCO_3$ and water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with $CHCl_3$ as the eluent to give VIb (990 mg, 53%), which was recrystallized from $CHCl_3$–ether to yield colorless needles, mp 154—155°C.

Preparation of 7-Ethoxycarbonyl-4-oxo-2,5-diphenyl-3,4,5,6-tetrahydropyrrolo[2,3-*d*]pyrimidine (VII)——A suspension of IIIc (3 mmol) in abs. EtOH (20 ml) was saturated with dry HCl under ice cooling. The reaction mixture was then refluxed for 30 min. After removal of the EtOH, the residue was basified with $NaHCO_3$, and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4, and concentrated *in vacuo*. The residue was recrystallized from CH_2Cl_2 to afford VII (820 mg, 76%) as colorless feathery crystals, mp 266°C. *Anal.* Calcd for $C_{21}H_{19}N_3O_3$: C, 69.79; H, 5.30; N, 11.63. Found: C, 69.81; H, 5.13; N, 11.74. IR

ν_{max}^{KBr} cm^{-1}: 3200 (>NH), 1740, 1640 (>CO). PMR (in DMSO-d_6) δ: 1.38 (3H, t, J=7 Hz, $-CH_2-CH_3$), 4.22 (2H, q, J=7 Hz, $-CH_2-CH_3$), 3.55—3.80 (1H, m, C_5-H), 4.34—4.44 (2H, m, C_6-H), 7.10—7.43 (5H, m, aromatic H), 7.43—7.60 (3H, m, aromatic H), 8.12—8.30 (2H, m, aromatic H), 12.11 (1H, br s, >NH).

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