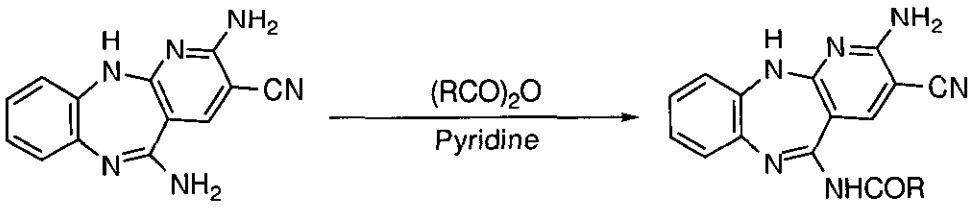
REGIOSELECTIVE ACYLATION OF 2,5-DIAMINO-3-CYANO-11*H*-PYRIDO[2,3-*b*][1,5]BENZODIAZEPINE AND STRUCTURAL DETERMINATION BY X RAY ANALYSIS

Yoshihisa Okamoto*, Yoshimi Zama, and Kaname Takagi
Division of Chemistry, College of Liberal Arts and Sciences, Kitasato University, 1-15-1, Kitasato, Sagamihara-shi, Kanagawa-ken 228, Japan
Yoshihisa Kurasawa, Kazuho Harada, and Atsushi Takada
School of Pharmaceutical Sciences, Kitasato University, Shirokane, Minato-ku, Tokyo 108, Japan

Abstract---The acylation of 2,5-diamino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]-benzodiazepine (**1**) with acid anhydrides selectively gave the 5-acylamino derivatives (**2a-d** and **3**). The structure of **3** was determined by X ray analysis. A similar reaction of **1** with chloroacetic anhydride afforded a bridgehead double bonded compound (**4**) *via* acylation at the 5-amino group of **1**. Cyclic anhydrides also reacted with **1** at the 5-amino group to provide the 5-imido derivatives (**5a,b** and **6**). The reaction of **1** with maleic anhydride unexpectedly afforded the 2,3-dimethylmaleimido derivative (**12**).

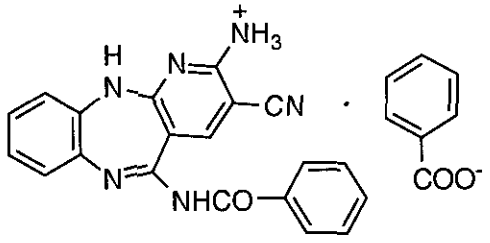
In a previous paper,[1] we described the novel and versatile synthesis of pyrido[2,3-*b*][1,5]-benzodiazepine derivatives by cyclization of 3-substituted 2-amino-6-(2-aminoanilino)-5-cyanopyridines, which were readily formed by ring transformation of 4-amino-1*H*-1,5-benzodiazepine-3-carbonitrile with some active methylene compounds under basic conditions.[2] Among the compounds obtained by the above synthetic method, 2,5-diamino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**1**) was found to have a remarkable antiulcer activity.[3] These results prompted us to synthesize a series of derivatives of **1** in order to obtain compounds with biological interest. The present paper deals with regioselective acylation of **1**.

Treatment of **1** with excess acid anhydride such as acetic, propionic or benzoic anhydride in dry pyridine readily gave the 5-acylamino-2-amino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepines (**2a-c**) in moderate yields (Scheme 1). A similar reaction of **1** with diethyl pyrocarbonate in tetrahydrofuran afforded 2-amino-3-cyano-5-ethoxycarbonylamino-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**2d**) in 69% yield. Each ^{1}H-nmr spectra of **2a-d** showed a broad singlet signal due to one amido proton (**2a**:9.84, **2b**:9.82, **2c**:13.29, **2d**:11,60 ppm), while a signal due to the amino proton at the 5-position (6.38 ppm, broad singlet, 2H) observed in the spectrum of **1** disappeared. These results indicate that the acylation selectively took place at the 5-amino group of **1**. Both the exo nitrogen at the 2-position and the endo nitrogen at the 11- position of **1** seem to be less reactive to the acylating reagents.



1

2a , R=CH_3
2b , R=C_2H_5
2c , R=C_6H_5
2d , R=OC_2H_5

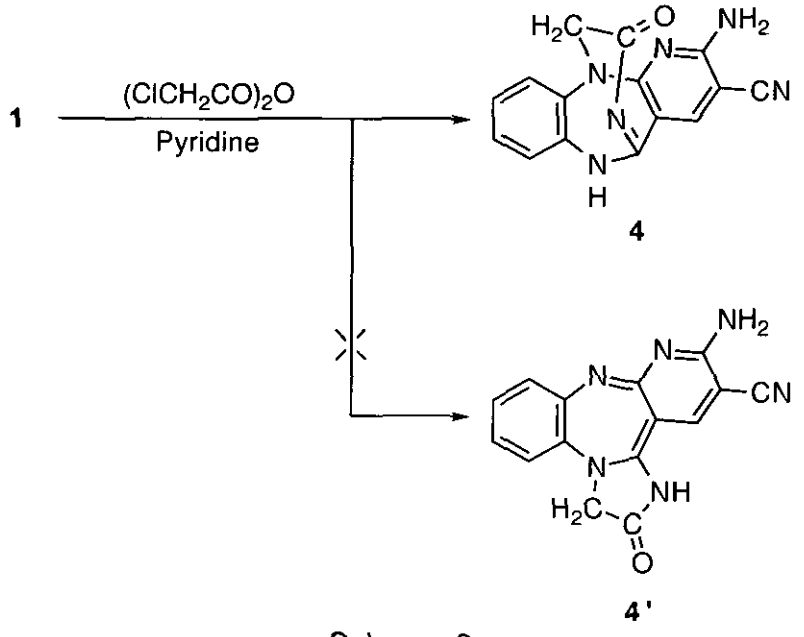


3

Scheme 1

From the reaction of **1** with benzoic anhydride, we isolated red crystals (**3**) which consisted of **2c** and benzoic acid (1:1molar ratio) besides the main product (**2c**) (Scheme 1). The red crystalline compound (**3**) was transformed into yellow crystals (**2c**) by heating above at 160°C, or by treatment with an alkaline solusion. An equimolecular solution of **2c** and benzoic acid in chloroform

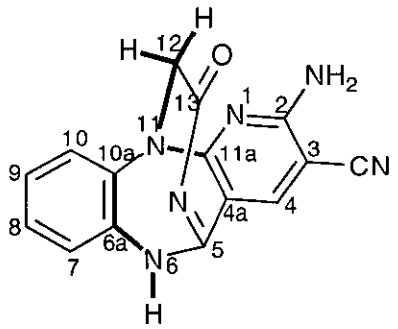
gradually produced the red crystals (**3**), however, a similar attempt to crystallize **3** from a similar solution in ethanol failed. To clarify the problem whether the red compound (**3**) is an acid-base salt or a molecular complex between **2c** and benzoic acid, an X ray analysis was performed on the red crystals, and the structure was determined to be the benzoic acid salt of **2c**, but not the molecular complex (Figure 1). Other X ray analysis data are summarized in Tables I ~Ⅳ. For the structure of the red crystals, it is worth noting that the protonation occurs at the exo nitrogen at the 2-position, but not at the endo nitrogen at the 1 position of **2c**, and a hydrogen bond is formed between the oxygen of the benzoate anion and the 11-amino proton of **2c** (1.89 Å). Since the red color disappeared when compound (**3**) was dissolved in solvents such as alcohols and dimethyl sulfoxide, the hydrogen bond plays an important role on the red coloration. On the other hand, no such salt formation was observed between **2a** and acetic acid, **2b** and propionic acid, or **2c** and ethoxyformic acid in the above reactions. The reason for these results is thought to be that the pKa values of these acids are larger than that of benzoic acid.



Scheme 2

The reaction of **1** with chloroacetic anhydride in dry pyridine at room temperature afforded 2-amino-3-cyano-11,5-(methylcarbonylnitrilo)pyrido[2,3-*b*][1,5]benzodiazepine (**4**), but not the condensed tetracyclic compound (**4'**) (Scheme 2). The structure of **4** was determined on the basis of elemental analytical and spectral data. Especially, the ^{3}J-couplings between the 11a-carbon

and CH_2-protons and between the 10a-carbon and NH-proton observed in the LSPD analysis established the bridgehead double bonded structure of **4** (Chart 1).



4

^3J { 10a-carbon / NH-proton } ^3J { 11a-carbon / CH_2-proton }

Chart 1

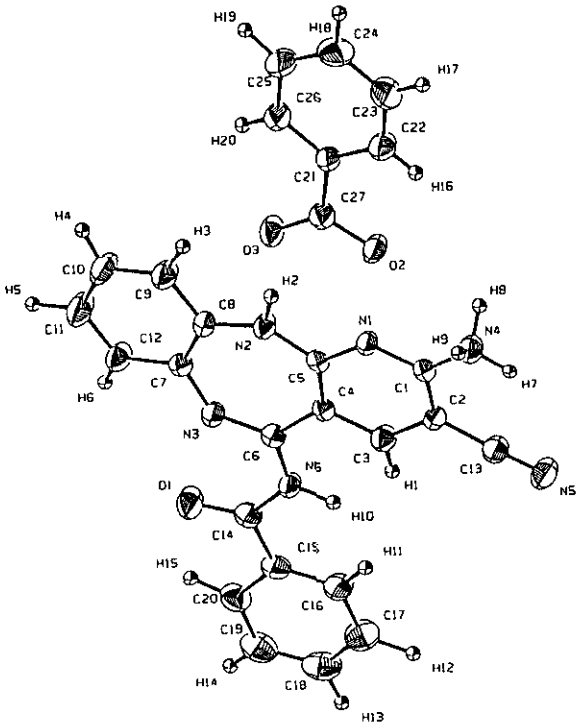


Figure 1. X Ray structure of **3** showing crystallographic numbering scheme

Cyclic anhydrides also reacted with **1** to give the corresponding imido derivatives (Scheme 3). When **1** was heated with an excess of phthalic anhydrides in dry pyridine, the corresponding phthalimido derivatives, 2-amino-3-cyano-5-phthalimido-11*H*-pyrido[2,3-*b*][1,5]benzodiazepines (**5a**) and 2-amino-3-cyano-5-(4-methylphthalimido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**5b**), were obtained in 10-17% yields. The structures of **5a,b** were elucidated on the basis of their elemental analytical and spectral data. Similarly, *cis*-1,2-cyclohexanedicarboxylic anhydride and succinic anhydride reacted with **1** to give 2-amino-3-cyano-5-(1,2-cyclohexanedicarboxylimido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**6**) in 22% yield and 2-amino-3-cyano-5-(succinimido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**7**) in 44% yield, respectively.

Table I Positional Parameters and Their Estimated Standard Deviations for Compound (3)

Atom	*x*	*y*	*z*	*Beq*
O(1)	0.4803(5)	- 0.2396(3)	0.5925(1)	5.2(1)
O(2)	- 0.0646(4)	0.1302(2)	0.3385(1)	4.0(1)
O(3)	- 0.0140(4)	- 0.0672(2)	0.3282(1)	4.4(2)
N(1)	0.0867(4)	0.1105(3)	0.4274(1)	2.9(1)
N(2)	0.1587(5)	- 0.0857(3)	0.4204(1)	3.2(2)
N(3)	0.3470(4)	- 0.1915(3)	0.5101(1)	3.3(2)
N(4)	- 0.0017(5)	0.3102(3)	0.4261(1)	3.9(2)
N(5)	0.1301(5)	0.4423(3)	0.5406(1)	4.9(2)
N(6)	0.3784(4)	- 0.0473(3)	0.5704(1)	3.2(2)
C(1)	0.0785(5)	0.2183(3)	0.4502(1)	3.0(2)
C(2)	0.1500(5)	0.2344(3)	0.4974(1)	3.0(2)
C(3)	0.2290(6)	0.1349(4)	0.5196(1)	3.1(2)
C(4)	0.2398(5)	0.0214(3)	0.4971(1)	2.6(2)
C(5)	0.1660(5)	0.0138(3)	0.4496(1)	2.6(2)
C(6)	0.3239(5)	- 0.0765(3)	0.5260(1)	2.8(2)
C(7)	0.3181(5)	- 0.2500(3)	0.4648(1)	3.1(2)
C(8)	0.2325(5)	- 0.2027(3)	0.4241(1)	3.0(2)
C(9)	0.2142(7)	- 0.2760(4)	0.3826(2)	4.2(2)
C(10)	0.2792(8)	- 0.3936(4)	0.3820(2)	5.3(3)
C(11)	0.3641(8)	- 0.4405(4)	0.4221(2)	5.3(3)
C(12)	0.3832(7)	- 0.3687(4)	0.4630(2)	4.2(2)
C(13)	0.1389(6)	0.3497(4)	0.5218(1)	3.6(2)
C(14)	0.4576(6)	- 0.1284(4)	0.6010(1)	3.6(2)
C(15)	0.5208(6)	- 0.0789(4)	0.6491(1)	3.4(2)
C(16)	0.4937(6)	0.0413(4)	0.6624(2)	4.0(2)
C(17)	0.5509(7)	0.0837(5)	0.7074(2)	4.8(3)
C(18)	0.6350(7)	0.0051(6)	0.7392(2)	5.3(3)
C(19)	0.6633(7)	- 0.1149(6)	0.7264(2)	5.1(3)
C(20)	0.6089(6)	- 0.1568(5)	0.6813(2)	4.2(2)
C(21)	- 0.1275(5)	0.0436(4)	0.2605(1)	3.1(2)
C(22)	- 0.2074(7)	0.1492(4)	0.2443(2)	4.1(2)
C(23)	- 0.2684(7)	0.1575(5)	0.1969(2)	5.0(3)
C(24)	- 0.2489(7)	0.0610(5)	0.1652(2)	5.4(3)
C(25)	- 0.1667(7)	- 0.0450(5)	0.1809(2)	4.8(3)
C(26)	- 0.1071(7)	- 0.0536(4)	0.2286(2)	3.9(2)
C(27)	- 0.0643(6)	0.0298(4)	0.3114(1)	3.4(2)

Table II Selected Bond Lengths of 3

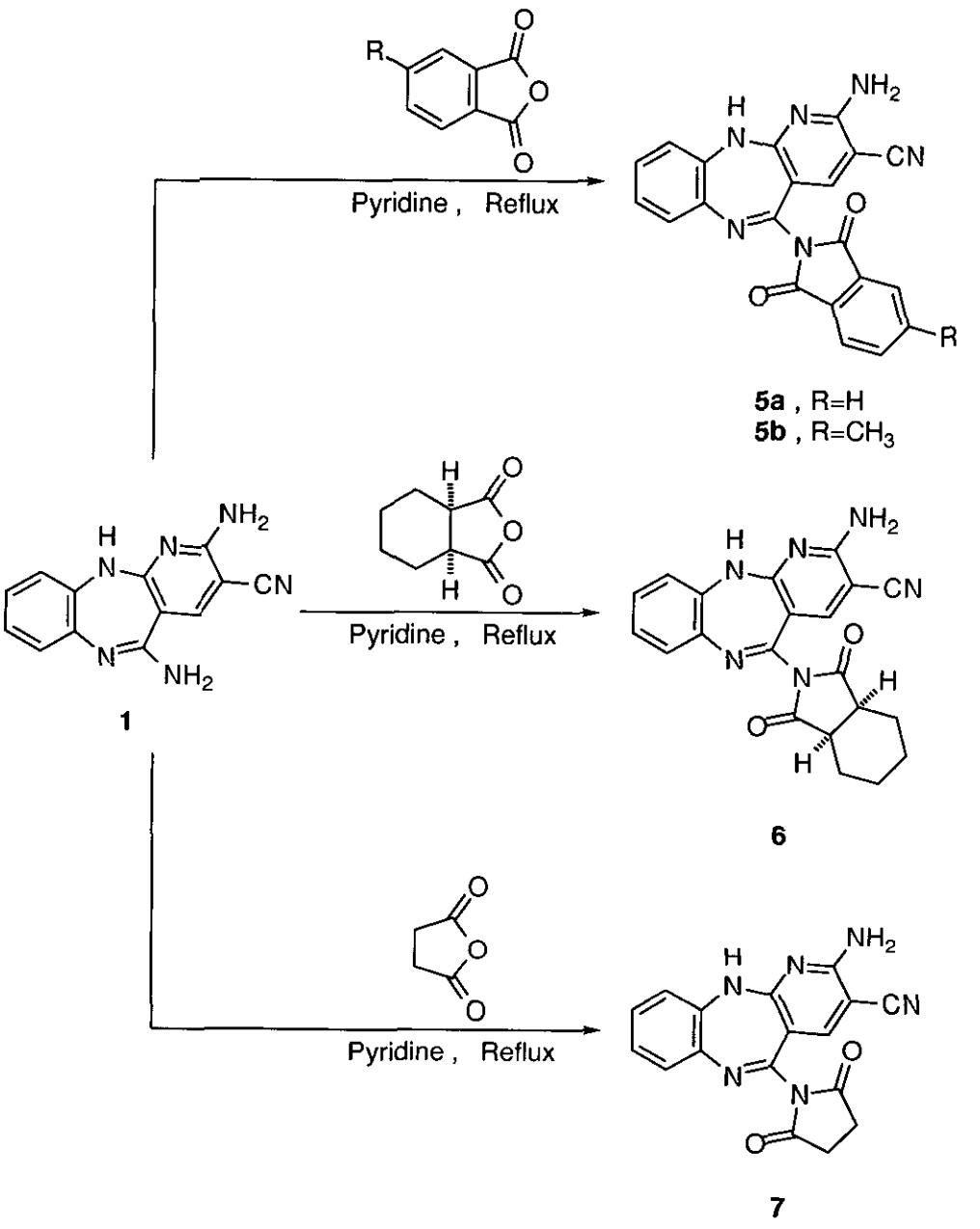
Bond Length (Å)		Bond Length (Å)	
O(1)-C(14)	1.254 (5)	N(5)-C(13)	1.142 (5)
O(2)-C(27)	1.327 (4)	N(6)-C(6)	1.319 (4)
O(3)-C(27)	1.218 (5)	N(6)-C(14)	1.357 (5)
N(1)-C(1)	1.338 (4)	C(1)-C(2)	1.406 (5)
N(2)-C(5)	1.354 (4)	C(2)-C(3)	1.383 (5)
N(2)-C(8)	1.403 (5)	C(2)-C(13)	1.432 (5)
N(3)-C(6)	1.346 (5)	C(3)-C(4)	1.391 (5)
N(3)-C(7)	1.413 (5)	C(4)-C(5)	1.412 (5)
N(4)-C(1)	1.346 (5)	C(4)-C(6)	1.475 (5)

Table III Selected Bond Angles of 3

Bond Angle (°)		Bond Angle (°)	
O(1)-C(14)-N(6)	125.6 (4)	N(3)-C(6)-N(6)	119.0 (3)
O(1)-C(14)-C(15)	118.3 (4)	N(3)-C(6)-C(4)	116.6 (3)
O(2)-C(27)-C(21)	116.1 (4)	C(1)-N(1)-C(5)	120.2 (3)
O(3)-C(27)-C(21)	122.8 (4)	C(1)-C(2)-C(3)	117.7 (4)
N(1)-C(1)-N(4)	117.1 (3)	C(2)-C(3)-C(4)	122.6 (4)
N(1)-C(1)-C(2)	121.3 (3)	C(3)-C(4)-C(5)	115.9 (3)
N(1)-C(5)-C(4)	122.3 (3)	C(5)-C(4)-C(6)	128.0 (3)
N(2)-C(5)-C(4)	127.2 (3)	C(5)-N(2)-C(8)	132.9 (3)
N(2)-C(8)-C(7)	125.8 (3)	C(6)-N(3)-C(7)	133.7 (3)

Table IV Selected Torsion Angles of 3

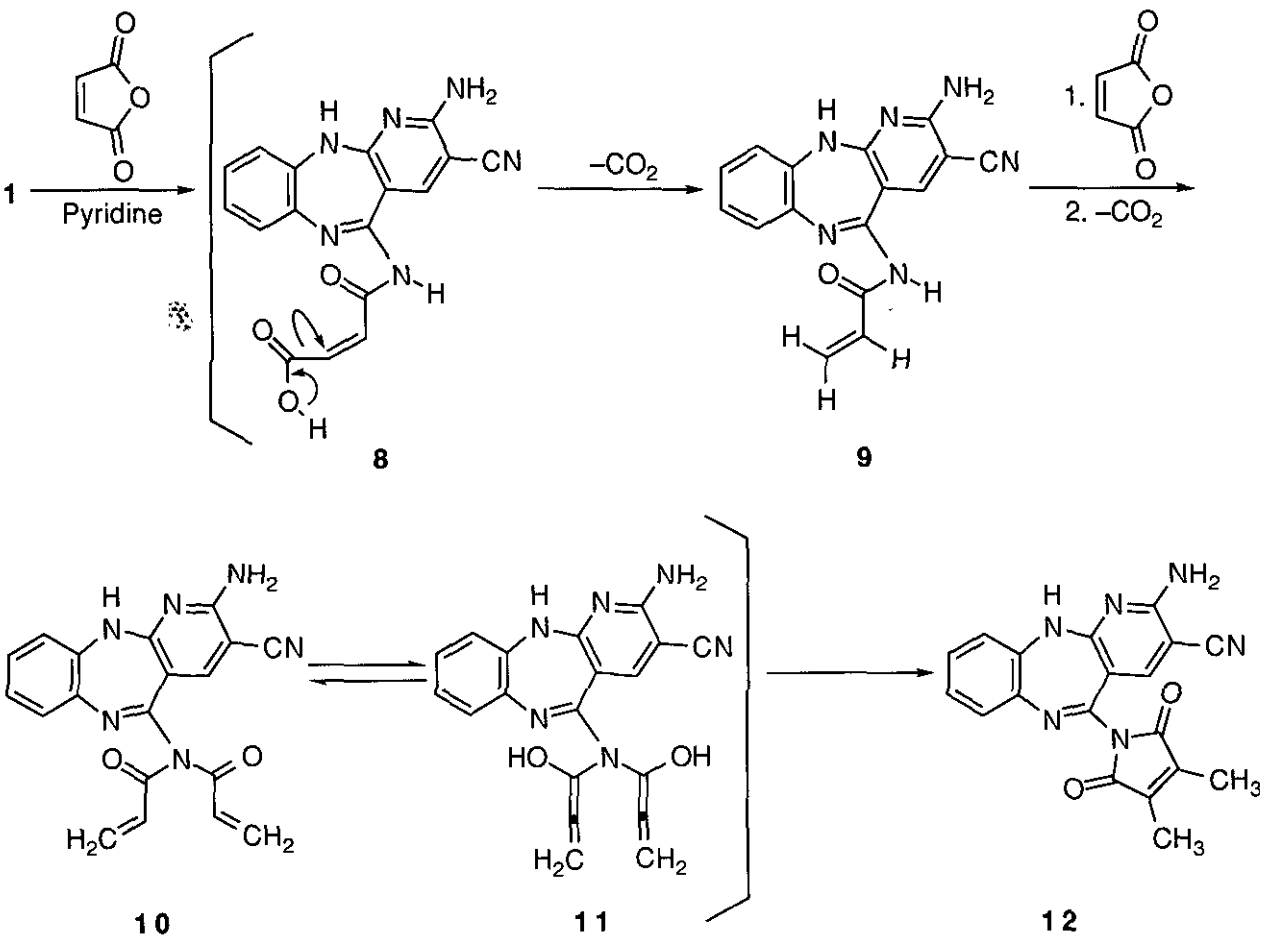
Torsion Angle (°)		Torsion Angle (°)	
O(2)-C(27)-C(21)-C(22)	- 9.7 (6)	C(1)-N(1)-C(5)-N(2)	179.7 (4)
N(1)-C(1)-C(2)-C(3)	- 0.1 (6)	C(1)-N(1)-C(5)-C(4)	1.0 (6)
N(1)-C(5)-N(2)-C(8)	173.6 (4)	C(1)-C(2)-C(3)-C(4)	0.0 (7)
N(1)-C(5)-C(4)-C(3)	- 1.0 (6)	C(2)-C(3)-C(4)-C(5)	0.5 (6)
N(2)-C(5)-C(4)-C(6)	- 0.7 (7)	C(2)-C(3)-C(4)-C(6)	- 178.5 (4)
N(2)-C(8)-C(7)-N(3)	0.4 (7)	C(4)-C(5)-N(2)-C(8)	- 7.8 (8)
N(3)-C(6)-C(4)-C(5)	1.7 (7)	C(4)-C(6)-N(3)-C(7)	6.0 (7)
N(6)-C(6)-N(3)-C(7)	- 174.3 (4)	C(5)-N(2)-C(8)-C(7)	9.2 (7)
N(6)-C(6)-C(4)-C(3)	0.8 (6)	C(6)-N(3)-C(7)-C(8)	- 9.0 (8)
N(6)-C(14)-C(15)-C(16)	2.5 (6)	C(6)-N(6)-C(14)-C(15)	176.6 (4)



Scheme 3

However, similar treatment of **1** with maleic anhydride provided the unexpected product, 2-amino-3-cyano-5-(2,3-dimethylmaleimido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (**12**), in 20% yield (Scheme 4). The structure of **12** was determined on the basis of its elemental analytical and spectral data. The ^{1}H-nmr spectrum of **12** showed a characteristic singlet signal corresponding to the methyl protons (1.95 ppm, 6H) which suggested the presence of two methyl groups in the

molecule. Other signals were in good agreement with the proposed structure (**12**).



Scheme 4

A possible mechanism for the formation of **12** is shown in Scheme 4. The amino group at the 5-position of compound (**1**) was at first acylated with maleic anhydride to give **8** followed by decarboxylation to the acryloylamino derivative (**9**), which reacted with maleic anhydride followed by decarboxylated to **10**. The intermediate (**10**) was isomerized to the allene derivative (**11**) which cyclized to **12**.

In conclusion, the acylation of **1** *with acid anhydrides selectively took place at the 5-amino group* to give **2a-d** and **4**. Cyclic anhydrides also reacted with **1** to produce the cyclic imides (**5a,b**, **6**, and **7**). However, the reaction of **1** with maleic anhydride produced the 2,3-dimethylmaleimido derivative (**12**) where the 5-amino group of compound (**1**) was entirely acylated with two molecule

of maleic anhydride.

EXPERIMENTAL

All melting points were determined on a Yazawa micro melting point BY-2 apparatus and are uncorrected. The ir spectra (potassium bromide) were recorded on a JASCO IRA-1 spectrophotometer, and all acylated compounds showed the characteristic absorption bands at 1600-1630 cm^{-1} due to amido carbonyl group. The nmr spectra were determined with a Varian VXR-300 spectrometer using deuteriodimethyl sulfoxide as the solvent and tetramethylsilane as the standard. The ms spectra were recorded using a JMS D-100. Elemental analyses were performed using a Perkin-Elmer 240B instrument.

5-Acylamino-2-amino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepines (2a,b)

General Procedure

To a suspension of **1** (0.5 g, 2 mmol) in dry pyridine (5 ml, 62 mmol) was gradually added acetic anhydride or propionic anhydride (25 mmol) at 0-5°C with stirring. The mixture was stirred at room temperature for 30 min, and then heated at 80-85°C for 5 min. After cooling, the reaction mixture was poured into ice water, and crystalline precipitates were collected by filtration, washed with water and recrystallized from ethanol to yield **2a** or **2b**.

5-Acetamido-2-amino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (2a): Yield 65%; mp 258-259°C; ms(m/z):292(M^+); ^{1}H-nmr: 2.09(s, 3H, CH_3), 6.80-7.01(m, 4H, arom), 7.17(br s, 2H, 2-NH_2), 7.62(s, 1H, H-4), 8.00(br s, 1H, H-11), 9.84(br s, 1H, CONH). *Anal.* Calcd for $C_{15}H_{12}N_6O$: C, 61.64; H, 4.14; N, 28.75. Found: C, 61.53; H, 4.15; N, 28.64.

5-Propionamido-2-amino-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (2b): Yield 80%; mp 219-221°C; ms(m/z):306(M^+); ^{1}H-nmr: 1.02(t, J=6.9Hz, 3H, CH_3), 2.42(q, J=6.9Hz, 2H, CH_2), 6.83-7.20(m, 4H, arom), 7.17(br s, 2H, 2-NH_2), 7.58(s, 1H, H-4), 8.00(br s, 1H, H-11), 9.82(br s, 1H, CONH). *Anal.* Calcd for $C_{16}H_{14}N_6O$: C, 62.74; H, 4.61; N, 27.43. Found: C, 62.71; H, 4.67; N, 27.39.

2-Amino-5-benzamido-3-cyano-11*H* -pyrido[2,3-*b*][1,5]benzodiazepine (2c)

To a suspension of **1** (0.5 g, 2 mmol) in dry pyridine (5 ml, 62 mmol) was gradually added benzoic anhydride (0.3 g, 1.32 mmol) at 0-5°C with stirring. The mixture was stirred at room temperature

for 30 min, and then heated at 80-85°C for 15 min. After cooling, the reaction mixture was poured into ice water, and the crystalline precipitates were collected by filtration, washed with water, dried and purified by column chromatography using chloroform as the eluant to provide **2c** (0.47 g, 66% yield), mp 267-269°C; ms(m/z): 354(M^+); ^{1}H-nmr: 6.88-7.17(m, 4H, arom), 7.45(br s, 2H, 2-NH_2), 7.47-8.22(m, 5H, arom), 8.65(br s, 1H, H-4), 8.95(br s, 1H, H-11), 13.29(br s, 1H, CONH). *Anal.* Calcd for $C_{20}H_{14}N_6O$: C, 67.79; H, 3.98; N, 23.72. Found: C, 66.89; H, 3.97; N, 23.51.

2-Amino-5-benzamido-3-cyano-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine Benzoic Acid Salt (3)

Method A: To a suspension of **1** (0.5 g, 2 mmol) in chloroform (20 ml) were added sodium benzoate (0.3 g, 2mmol) and benzoic anhydride (0.9 g, 4 mmol) at 0-5°C with stirring. The mixture was refluxed for 1 h to provide red crystals and **2c**. Chloroform was added to the reaction mixture to dissolve the red crystals, and the reaction mixture was filtered off. The filtrate was evaporated, and the precipitates were recrystallized from chloroform-ethanol to give **3** (95 mg, 10% yield); ms(m/z): 354(M^+ as the free base), 122(M^+ as the acid); ^{1}H-nmr: 6.90-7.14(m, 4H, H-7, H-8, H-9, and H-10), 7.46-8.20(m, 5H, benzoyl arom), 7.42(br s, 2H, 2-NH_2), 8.53(s, 1H, H-4), 8.80(br s, 1H, H-11), 13.15(br s, 1H, CONH). *Anal.* Calcd for $C_{27}H_{20}N_6O_3$: C, 68.06; H, 4.23; N, 17.64. Found: C, 67.86; H, 4.31; N, 17.52.

Method B: A solution of **2c** (50 mg, 0.14 mmol) and benzoic acid (18 mg, 0.14 mmol) in 80 ml of chloroform was evaporated to provide **3** quantitatively.

2-Amino-3-cyano-5-ethoxycarbonylamino-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (2d)

To a suspension of **1** (0.5 g, 2 mmol) in tetrahydrofuran (5 ml) was added ethyl carbonate (0.39 g, 2.4 mmol) at 0-5°C with stirring. The mixture was treated in the same manner as described for the synthesis of **2a,b**. Recrystallization from ethanol gave **2d** (0.44 g, 69% yield) as pale yellow needles, mp>300°C; ms(m/z): 322(M^+); 1H-nmr: 1.23(t, J=6.9 Hz, 3H, CH_3), 4.10(q, J=6.9 Hz, 2H, CH_2), 6.85-7.15(m, 4H, arom), 7.37(br s, 2H, 2-NH_2), 8.28(s, 1H, H-4), 8.92(br s, 1H, H-11), 11.60(br s, 1H, CONH). *Anal.* Calcd for $C_{16}H_{14}N_6O_2$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59.52; H, 4.39; N, 25.98.

2-Amino-3-cyano-11,5-(methanocarbonylnitrilo)-5*H*,6*H*,11*H*-pyrido[2,3-*b*][1,5]-benzodiazepine (4)

To a suspension of **1** (1.0 g, 4 mmol) in dry pyridine (10 ml, 124 mmol) was added chloroacetic

anhydride (2.5 g, 14.6 mmol) at 0-5°C with stirring. The mixture was stirred at room temperature for 3 h, and then poured into ice water. The precipitates were collected by filtratrion, washed with water and dried. The crude product was treated in boiling chloroform for 30 min and the insoluble solid was recrystallized from chloroform-methanol to give **4** (0.35 g, 30% yield), mp> 300°C; ms(m/z): 290(M^+); ^{1}H-nmr: 4.65(s, 2H, CH_2), 6.92-7.20(m, 4H, arom), 7.55(br s, 2H, NH_2), 8.22(s, 1H, H-4), 9.06(br s, 1H, NH); ^{13}C-nmr: 55.27(12), 83.43(3), 99.22(4a), 116.46(CN), 120.90(7), 121.72(10), 124.28(9), 126.03(8), 128.41(10a), 133.88(6a), 149.15(4), 160.82(5), 161.03(2), 174.10(11a), 185.14(13). *Anal.* Calcd for $C_{15}H_{10}N_6O \cdot 1/2H_2O$: C, 60.20; H, 3.70; N, 28.08. Found: C, 60.51; H, 4.09; N, 27.78.

2-Amino-3-cyano-5-imido-11*H*-pyrido[2,3-*b*][1,5]benzodiazepines (5a,b, 6, 7, and 12) General Prodedure

A mixture of **1** (0.2 g, 0.8 mmol) and phthalic anhydrides (2.4 mmol) in dry pyridine (5 ml, 62mmol) was heated at 120°C for 3 h (for **5a**,**b**) or 30 min (for **6**, **7**, and **12**) with stirring. After cooling, the reaction mixture was poured into ice water. The crystalline precipitates were collected by filtration, washed with water, and dried. The crude product was then dissolved in chloroform and the resulting solution was chromatographed on a silica gel column with chloroform to yield **5a**,**b**, **6**, and **7**.

2-Amino-3-cyano-5-phthalimido-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (5a): Yield, 17%; mp 173-175°C; ms(m/z): 380(M^+); ^{1}H-nmr: 6.80-7.14(m, 4H, arom), 7.34(br s, 2H, 2-NH_2), 7.88-7.98(m, 4H, phthalic arom), 8.01(s, 1H, H-4), 8.30(br s, 1H, H-11). *Anal.* Calcd for $C_{21}H_{12}N_6O_2 \cdot 1/3H_2O$: C, 66.31; H, 3.18; N, 22.09. Found. C, 65.28; H, 3.28; N, 21.76.

2-Amino-3-cyano-5-(4-methylphthalimido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (5b): Yield, 10%; mp 284-286°C; ms(m/z): 394(M^+); ^{1}H-nmr: 2.52(s, 3H, CH_3), 6.83-7.11(m, 4H, arom), 7.33(br s, 2H, 2-NH_2), 7.67-7.85(m, 3H, phthalic arom), 7.93(s, 1H, H-4), 8.29(br s, 1H, H-11). *Anal.* Calcd for $C_{22}H_{14}N_6O_2 \cdot 5/12H_2O$: C, 65.75; H, 3.28; N, 21.76. Found. C, 65.75; H, 3.67; N, 20.78.

2-Amino-3-cyano-5-(1,2-cyclohexanedicarboximido)-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (6): Yield, 22%; mp 200-201°C; ms(m/z): 386(M^+); ^{1}H-nmr: 1.28-1.84(m, 8H, cyclohexyl CH_2), 3.15(dt, *J*=9 Hz and 7.5 Hz, 2H, cyclohexyl CH), 6.78-7.06(m, 4H, arom), 7.34(br s, 2H, 2-NH_2), 7.63(br s, 1H, H-4), 8.29(br s, 1H, H-11). *Anal.* Calcd for $C_{21}H_{18}N_6O_2$: C, 65.28; H, 4.66; N, 21.76. Found. C, 65.40; H, 4.80; N, 21.62.

2-Amino-3-cyano-5-succinimido-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (7): Yield, 44%; mp 270°C; ms(m/z): 332(M^+); ^{1}H-nmr: 2.76(s, 4H, CH_2), 6.76-7.07(m, 4H, arom), 7.30(br s, 2H, 2-NH_2), 7.68(s, 1H, H-4), 8.25(br s, 1H, H-11). *Anal.* Calcd for $C_{17}H_{12}N_6O_2$: C, 61.44; H, 3.64; N, 25.29. Found. C, 61.21; H, 3.78; N, 25.13.

2-Amino-3-cyano-5-dimethylmaleimido-11*H*-pyrido[2,3-*b*][1,5]benzodiazepine (12) Yield, 20%; mp 220°C; ms(m/z): 358(M^+); ^{1}H-nmr: 1.95(s, 6H, CH_3), 6.78-7.10(m, 4H, arom), 7.32(br s, 2H, 2-NH_2), 7.76(s, 1H, H-4), 8.24(br s, 1H, H-11). *Anal.* Calcd for $C_{19}H_{14}N_6O_2$: C, 63.69; H, 3.91; N, 23.46. Found. C, 63.28; H, 4.25; N, 23.41.

X Ray Analysis of 3

A crystal was mounted on a Rigaku AFC-5R diffractometer, and the cell parameters and the intensity data were measured using graphite-monochromated Cu $K\alpha$ (λ =1.54179 Å) radiation at 23°C. Approximate atomic coordinates were obtained by the direct method using MITHRIL.[4] The parameters of non-hydrogen atoms were refined using the full-matrix least-squares method with anisotropic temperature factors. The hydrogen atoms were located from a difference Fourie synthesis, and refined with isotropic temperature factors. The crystal data are as follows: Chemical formula $C_{27}H_{20}N_6O_3$; M W 476.49; monoclinic; space group $P2_1/n$; Z=4; unit cell dimensions a=7.557 (6) Å, b=10.965 (4) Å, β=90.52 (5)° , V=2267 (3) Å^3; D_{cal}=1.396 gcm^{-1}; μ (Cu$K\alpha$)=7.34 cm^{-1}; crystal size 0.2×0.3×0.8 mm. Of the total of 4782 reflections up to the 2θ range of 140.2° (unique reflections: 4423), 2801 were measured as being above the 3σ (I) level and were used. The final R value was 0.062. The positional parameters for **3** are listed in Table Ⅰ. The selected bond lengths, bond angles, and torsion angles for **3** are listed in Tables Ⅱ, Ⅲ, and Ⅳ, respectively.

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