Synthesis of Nitrogen-Containing Heterocycles 10 [1]. Reaction of 2-Amino-1*H*-imidazole Derivatives with Ethoxymethylene Compounds

Yoshiko Miyamoto

Department of Chemistry, School of Science, Kitasato University,
Kitasato, Sagamihara, Kanagawa 228-8555 Japan

Received July 23, 2001

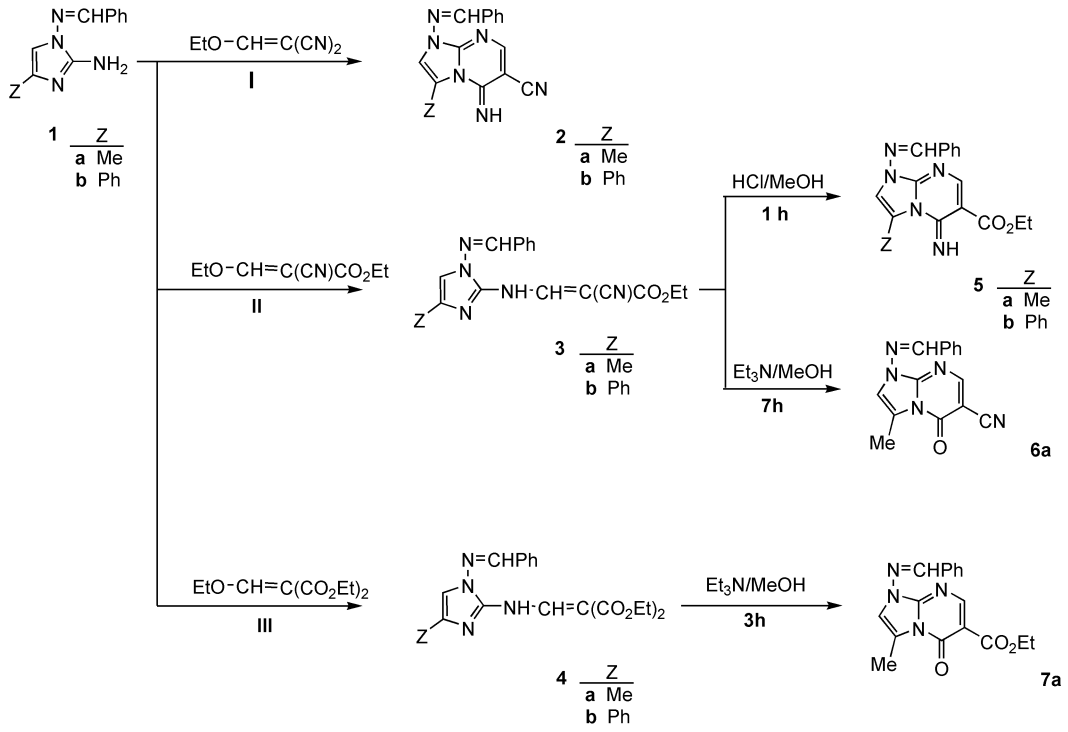
The direct annelation reaction of 4-substituted 2-amino-1-benzylideneamino-1*H*-imidazoles (**1**) or 2-amino-1-isopropylideneamino-1*H*-imidazole (**8**) with ethoxymethylenemalononitrile (**I**) gave successfully bicyclic imidazo[1,2-*a*]pyrimidine compounds **2** and **9** in high yields. The reactions of other ethoxymethylene compounds of lower reactivity, *i.e.*, ethyl ethoxymethylenecyanoacetate (**II**) and diethyl ethoxymethylenemalonate (**III**), with 2-amino-1*H*-imidazoles under similar conditions afforded the corresponding enamines **3**, **4** and **10**, which, upon heating in the presence of an acid or a base, could readily be cyclized to form imidazopyrimidines except for 1-isopropylideneamino compound **10**. In general, the 3-phenyl compounds (**3b** and **4b**) did not cyclize to the type **2** compound resulting in a full recovery of the starting enamines.

J. Heterocyclic Chem., **39**, 157 (2002).

In a previous paper [2], the author has reported the direct cyclization of diaminomethylenehydrazones with ethoxymethylenemalononitrile (**I**) to bicyclic triazolopyrimidines. The author has also reported that treatment of diaminomethylenehydrazones with ethyl ethoxymethylenecyanoacetate (**II**) gave the corresponding 2,3-dihydro- or 2,3-dehydro[1,2,4]triazolo[1,5-*c*]pyrimidines [3]. In the present work, an attempt was made to extend this cyclization to the reaction of ethoxymethylene compounds (**I**-**III**) with 2-amino-1*H*-imidazoles (**1, 8**) and 1,2-diamino-1*H*-imidazole (**14**), which have rarely been used as a starting material for the synthesis of new heterocycles. The 1-isopropylidene- or 1-benzylideneamino-2-amino-1*H*-imidazoles is considered as an already-cyclized diaminomethylenehydrazone, including an imidazole ring.

The reaction of 4-substituted-1-benzylideneamino-2-amino-1*H*-imidazoles (**1**) with ethoxymethylenemalononitrile (**I**) was performed by heating an equimolar mixture of the starting materials in acetonitrile at 80° for 1 hour. The desired 1*H*-imidazo[1,2-*a*]pyrimidines (**2**) crys-

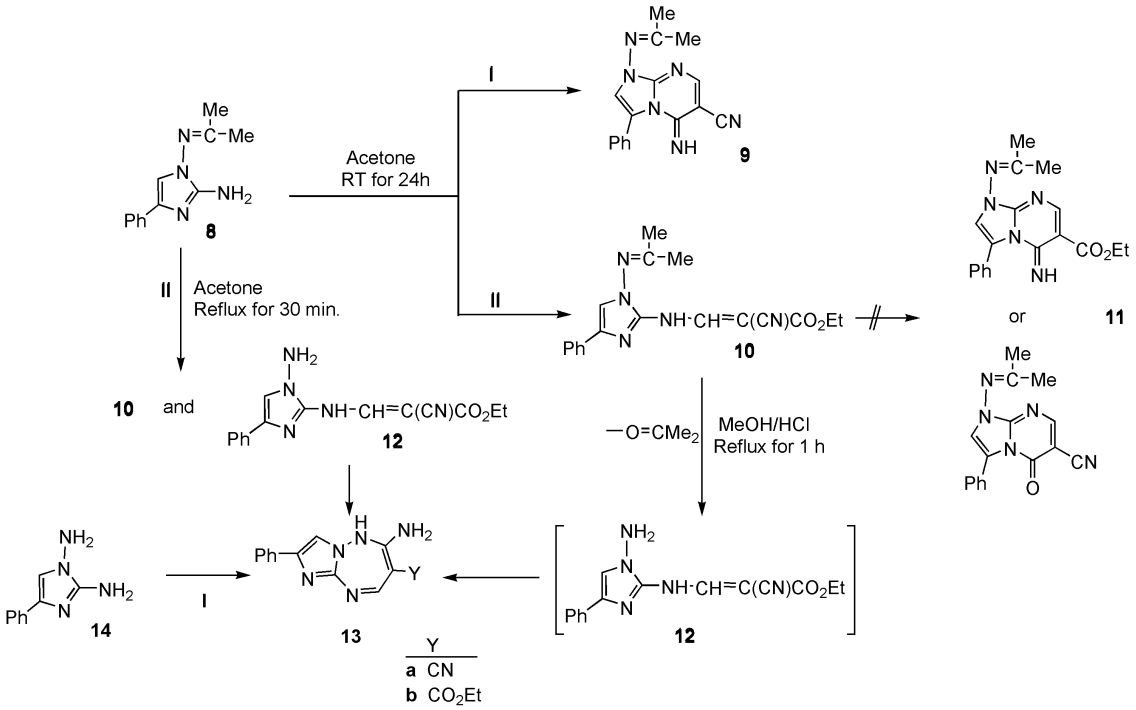
Scheme 1



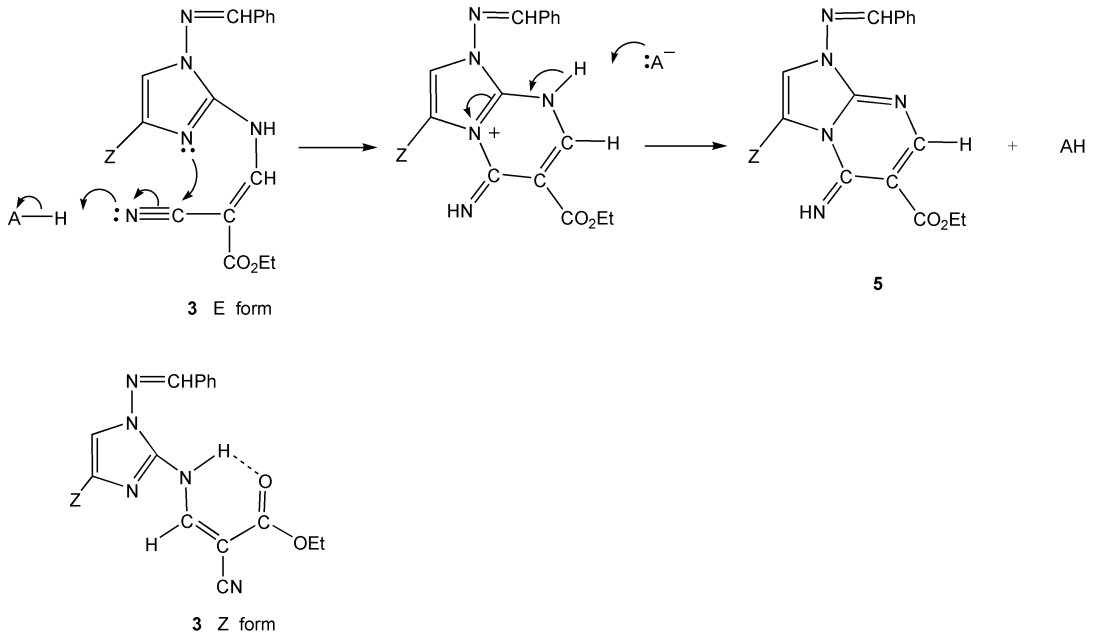
tallized out of the solution and were easily isolated as crystalline compounds in good yields. 1-Isopropylideneaminoimidazole (**8**) gave similar bicyclic imidazopyrimidine compounds (**9**) upon reacting with **I** at room temperature in the presence of acetone to prevent hydrolytic cleavage of the isopropylideneamino group.

When the reaction of ethyl ethoxymethylenecyanoacetate (**II**) with 2-aminoimidazoles (**1**,**8**) was carried out under the conditions of the general procedure, the reaction stopped at the initial condensation stage as was expected from the early study [2] and the open-chain compounds **3** were obtained in 85-98 % yield. Compounds **3** thus produced were homoge-

Scheme 2



Scheme 3



neous upon isolation and found to have a *Z* form on the basis of spectral data [4]. In order to promote the reaction toward the bicyclic products **5** or **6**, it was required to add an acid or a base as a catalyst into the reaction medium. It was unexpectedly found that when the cyclization of **3** was performed under the influence of acid, the cyanocarbon on the vinylidene carbon of the side chain did act as the electrophilic center that attacked the N-3 nitrogen of the imidazole ring to give **5**, whereas, in the presence of a base, nucleophilic attack by the N-3 nitrogen occurred on the ethoxycarbonyl carbon of **3a** (Z=Me) to give **6a** and thus the alternative cyclization could be realized.

In the acid-catalized cyclization (Scheme 3), the protonated cyano-nitrogen may generate a strong electrophilic center at the cyano carbon, which may easily be subjected to nucleophilic attack by the lone-pair of N-3 nitrogen of the imidazole ring, without the unfavorable electron-withdrawing effects of the adjacent phenyl group. The *Z* conformer of **3** is evidently unfavorable to afford **5** unless the geometry is inverted to the *E* form before cyclization. Under the conditions of acid catalysis, the positive charge on the cyano nitrogen should lower the bond order of the vinylic double bond to which it is attached and thus make it possible to approach the cyano group to the N-3 of the imidazole ring in the transition state. While the cyclization of **3a**, for example, in hot acetic acid gave **5a** only in 9 % yield, further improvement in the yield of **5** could be achieved (38 %) by conducting the reaction in a mixture of concentrated HCl and methanol at the reflux temperature. On the other hand, in the base-catalyzed cyclization of **3** (Scheme 4), the adjacent phenyl group (Z=Ph) will sterically block the approach of the ethoxycarbonyl group. Furthermore, the phenyl group will lower the nucleophilicity of the N-3 nitrogen in contrast to the electron-donating effects of the methyl group (Z=Me), thus the formation of 3-phenyl compound corresponding to **6a** being completely inhibited. Thus the base-catalyzed cyclization of **3a** (Z=Me) was performed in methanol containing triethylamine at the reflux temperature and the product **6a** was obtained in 36 % yield. Similarly, the bis(ethoxycarbonyl)vinylamino compound **4a** underwent the base-catalyzed cyclization to form **7a**, whereas **4b** did not cyclize to **7b**.

1-Isopropylideneamino-2-amino-4-phenyl-1*H*-imidazole (**8**) reacted with **I** at room temperature to give 1-isoprpopylideneaminoimidazopyrimidine (**9**) in moderate yield. The imidazole **8** gave 2-cyanovinylaminoimidazole (**10**) in the reaction with **II**, but the resulting cyanovinyl compound (**10**) failed to give **11** under the con-

Scheme 4

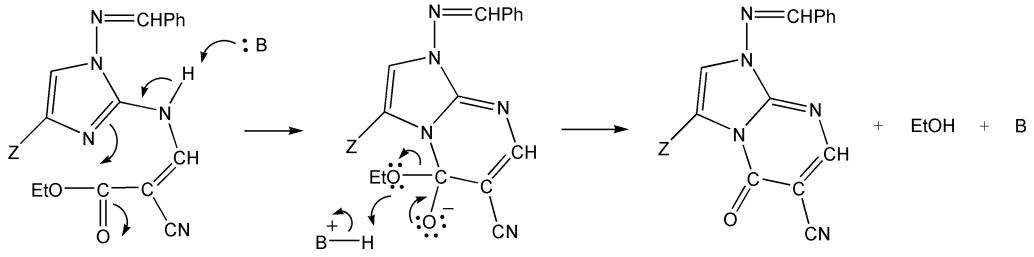


Table 1

Analytical and Physical Data for 1,4-Disubstituted 2-Imidazolamimomethylene Compounds

Compd. No.	Yield (%)	MP (ºC)	Formula	Calcd/Found C	H	N	MS,m/z(Rel.Int.)	^{1}H NMR Spectral Data
3b	85	201-202	$C_{22}H_{19}N_5O_2$	68.56 68.33	4.97 4.98	18.17 18.12	385(M^+,79),209(100)	1.39 (t, J=7.3, 3H, CH_3),4.35 (q,J=7.3, 2H, CH_2), 7.26 (s, 1H, C_5-H),7.30 (t, J=7.3, 1H,Ph), 7.40 (t, J=7.3, 2H, Ph),7.52 (m, 3H, Ph), 7.77 (t, J=8.3, 2H, Ph), 7.85 (m, 2H, Ph), 8.23 (s,1H,=CH), 8.39 (d, J=13, 1H, CH),11.70 (d, J=13, 1H, NH)
4a	78	132-136	$C_{19}H_{22}N_4O_4$	61.61 61.40	5.99 5.92	15.13 15.14	370(M^+,100),175(77)	1.33 (t, J=6.8, 3H, CH_3),1.40 (t, J=6.8, 3H, CH_3), 4.25 (q, J=6.8, 2H, CH_2), 4.38 (q, J=6.8, 2H, CH_2), 7.03 (s, 1H, C_5-H), 7.48 (m, 3H, Ph), 7.84 (m, 3H, Ph), 8.16 (s, 1H,=CH), 8.81 (d, J=13, 1H, CH),11.70 (d, J=13, 1H, NH)
4b	86	160-161	$C_{24}H_{24}N_4O_4$	66.65 66.78	5.59 5.61	12.96 12.89	432(M^+,36),283(100)	1.37 (t, J=7.3, 3H, CH_3), 1.41 (t, J=7.3, 3H, CH_3), 4.29 (q, J=6.8, 2H, CH_2), 4.40 (q, J=6.8, 2H, CH_2), 7.26 (s, 1H, C_5-H), 7.30 (t, J=7.3, 1H, Ph), 7.42 (t, J=7.3, 2H, Ph), 7.55 (m, 3H, Ph), 7.84 (d, J=8.3 ,2H, Ph), 7.90 (m, 2H, Ph), 8.31 (s, 1H,=CH), 8.97 (d, J=13, 1H, CH), 11.75 (d, J=13, 1H, NH)

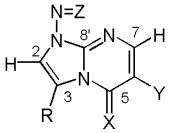
Table 2

Analytical and Physical Data for 1*H*-Imidazo[1,2-*a*]pyrimidines

Compd. No.	Yield (%)	Mpºc	Formula	Calcd/Found C	H	N	MS,m/z(Rel.Int.)
2b	96	196-197	$C_{20}H_{14}N_6$	68.56	4.97	18.17	338(M^+,10),234(100)
				68.50	4.97	18.17	
5b	43	221-222	$C_{22}H_{19}N_5O_2$	68.38	4.70,	14.50	385(M^+,32),281(100)
				68.32	4.72	14.37	
7a	25	205-206	$C_{17}H_{16}N_4O_3$	62.95	4.98	17.27	324(M^+,100),175(80)
				62.94	5.00	17.28	

Table 3

^{1}H and ^{13}C NMR Chemical Shift Values of Imidazopyrimidine Ring Protons and Carbons



	R	Z	X	Y	^{1}H NMR H-2	H-7	^{13}C NMR(J in Hz) C-2	C-3	C-5	C-6	C-7	C-8'
2b	Ph	CHPh	NH	CN	7.11	9.01	111.4(d,202)	122.6	154.2	86.8	155.7(d,184)	144.3
5b	Ph	CHPh	NH	CO_2Et	7.58	8.88	117.2(d,199)	123.2	157.0	105.5	159.0(d,182)	142.5
7a	Me	CHPh	O	CO_2Et	7.14	9.42	113.9(d,199)	122.4	157.0	105.1	159.4(d,184)	145.4
9	Ph	CMe_2	NH	CN	7.76	8.36	111.7(d,202)	125.9	119.3	52.5	164.8(d,162)	144.8

ditions for cyclization of the 1-benzylideneaminoimidazole (**3**). When the reaction of **8** with **II** was carried out in acetonitrile at the reflux temperature, the reaction mixture was found to contain both **10** and 1-aminoimidazole compound (**12**) in an approximately equimolar proportion. The isoprpopylideneamino group of **10** was highly susceptible to hydrolysis in the reaction medium and the hydrolyzate, 1-aminoimidazole compound (**12**), may spontaneously cyclize to a triazepine (**13b**). The formation of **13** was confirmed through an alternative route starting from 1,2-diaminoimidazole (**14**).

The structures of 1*H*-imidazo[1,2-*a*]pyrimidine **2**, **5**-**7**, **9** and 2-vinylamino-1*H*-imidazoles **3** and **4** were confirmed on the basis of the spectral data and the elemental analyses which appear in Tables 1-3.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. ^{1}H and ^{13}C nmr spectra were obtained with a JNM EX-400 (400 MHz) or JNM FX-90Q (90 MHz) spectrometer. The chemical shift values were recorded in parts per million (ppm) on the δ scale with tetramethylsilane as the internal reference. The mass spectra (75 eV) were obtained on a JMS-D100 mass spectrometer. Preparative high-performance liquid chromatography (hplc) was carried out in a Kusano Kagaku KHLC-201 instrument with a 300 X 22 mm glass column packed with silica gel. Microanalyses were performed with a Perkin-Elmer 240D elemental analyzer at the Microanalytical Laboratory of Kitasato University.

2-Amino-1-benzylideneamino-4-methyl-1*H*-imidazole (**1a**).

A mixture of benzaldehyde diaminomethylenehydrazone (1.62 g, 0.01 mol), α-chloroacetone (0.9 g) and triethylamine (2.02 g, 0.02 mol) was heated under reflux for 3 hours and the solvent was removed under reduced pressure. The residue was taken up in chloroform and the solution was thoroughly washed with water, dried over anhydrous sodium sulfate and evaporated under reduced pressure to give substantially pure compound as yellow crystals (1.35g, 68 %), mp 195-199º. Recrystallization from acetonitrile gave yellow needles (0.61 g, 40 %), mp 196-199º; ^{1}H nmr (deuteriochloroform): δ 2.15 (s, 3H, CH_3), 4.70 (s, 2H, NH_2), 7.26 (s, 1H, C_5-H), 7.44 (m, 2H, Ph), 7.74 (m, 2H, Ph), 8.02 (s, 1H, =CH), ^{13}C nmr (deuteriochloroform): δ 14.4(q), 100.6(d), 127.5(d), 128.9(d), 130.8(d), 133.4(s), 135.4(s), 145.6(d), 148.0(s); ms: m/z (relative intensity): 200(M^+, 55), 96(100).

Anal. Calcd. for $C_{11}H_{12}N_4$: C, 65.98; H, 6.04; N, 27.98. Found: C, 65.87, H, 6.18, N, 27.89.

2-Amino-1-benzylideneamino-4-phenyl-1*H*-imidazole (**1b**).

In a similar manner as described for **1a**, treatment of benzaldehyde diaminomethylenehydrazone (1.62 g, 0.01 mol) with α-chloroacetophenone (1.6 g, 0.01 mol) in triethylamine (2.20 g, 0.02 mol) and ethanol (30 ml) afforded **1b** as yellow crystals (1.60 g, 61.1 %), mp 198-203º. Recrystallization from acetonitrile gave yellow needles (1.38 g, 55 %), mp 200-203º; ^{1}H nmr (deuteriochloroform): δ 6.21 (s, 2H, NH_2), 7.21 (t, J=7.3, 1H, Ph), 7.36 (t, J=7.3, 2H, Ph), 7.50 (m, 3H, Ph), 7.73 (d, J=7.3, Ph), 7.94 (m, 2H, Ph), 8.02 (s, 1H, C_5-H), 8.58 (s, 1H, =CH); ^{13}C nmr

(deuteriochloroform): δ 101.2(d), 124.0(d), 126.2(d), 127.6(d), 128.3(d), 128.7(d), 130.4(d), 133.7(s), 134.3(s), 136.6(s), 146.5(d), 149.5(s); ms: m/z (relative intensity): 262 (M^+, 66), 158 (100).

Anal. Calcd. for $C_{16}H_{14}N_4$; C, 73.26, H, 5.38; N, 21.36. Found: C, 73.27; H 5.60; N, 21.63.

2-Amino-1-isopropylideneamino-4-phenyl-1*H*-imidazol (**8**).

A mixture of 1,2-diamino-4-phenyl-1*H*-imidazole (**14**) (0.87 g, 5 mmol), acetone (10 ml), acetic acid (0.2 ml) and ethanol (5 ml) was heated under reflux for 2 hours and then evaporated under reduced pressure. The residue was partitioned between 10 % aqueous sodium carbonate and chloroform. The organic phase was washed with water, dried over sodium sulfate, and then evaporation under reduced pressure to give pale yellow crystals (0.76 g, 71 %), mp 164-165°. Recrystallization from 2-propanol gave pale yellow prisms (0.66 g, 62 %), mp 167°; ^{1}H nmr (deuteriochloroform): δ 2.21 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 4.65 (s, 2H, NH_2), 6.91 (s, 1H, C_5-H), 7.18 (t, J=7.8, 1H, Ph), 7.33 (t, J=7.8, 2H, Ph), 7.67 (t, J=7.8, 2H, Ph); ^{13}C nmr (deuteriochloroform): δ 20.1(q), 25.9(q), 107.4(d), 124.3(d), 126.4(d), 128.5(d), 134.3(s), 135.5(s), 147.3(s), 170.4(s); ms m/z (relative intensity): 214(M^+, 35), 158(100).

Anal. Calcd. for $C_{12}H_{14}N_4$: C, 67.27; H, 6.58; N, 26.15. Found: C, 67.27; H, 6.60; N, 26.36.

1-Benzylideneamino-6-cyano-5-imino-3-methyl-1*H*-imidazo[1,2-*a*]-pyrimidine (**2a**).

A solution of **1a** (0.2 g, 0.01 mol), ethoxymethylenemalononitrile (**I**) (0.122 g, 0.01 mol) in acetonitrile (10 ml) was heated under reflux for 1 hour and then cooled to ambient temperature. The precipitated crystals were collected, washed with acetonitrile, and then dried to give yellow crystals (0.23 g, 83 %), mp 218-220°. Recrystallization from methanol gave yellow needles (0.21 g, 76 %), mp 218-220°; ^{1}H nmr (DMSO-d_6): δ 2.72 (s, 3H, CH_3), 7.12 (s, 1H, C_7-H), 7.57 (m, 3H, Ph), 7.85 (m,2H, Ph), 7.96 (s,1H, =CH), 8.01 (s, 1H, NH), 9.01 (s, 1H, C_7-H); ^{13}C nmr (DMSO-d_6): δ 14.0(q), 85.8(s), 111.0(d), 117.1(s), 122.4(s), 128.1(d), 129.0(d), 131.9(d), 132.4(s), 144.9(s), 153.2(s), 155.4(d), 155.7(d); ms: m/z(relative intensity): 276(M^+, 12), 172(100).

Anal. Calcd. For $C_{15}H_{12}N_6$: C,65.22; H,4.35; N, 30.43. Found: C, 65.19; H, 4.46; N, 30.27.

(1,4-Disubstituted Ethyl Imidazol-2-yl)aminomethylenecyanoacetate.

General Procedure.

A mixture of **1** (0.001 mol) and active ethoxymethylene compounds (0.001 mol) in acetonitrile (2 ml) was heated under reflux for 1 hour. The solid product was recrystallize for acetonitrile to give product.

Ethyl (1-Benzylideneamino-4-methylimidazol-2-yl)aminomethylenecyanoacetate (**3a**).

This compound was obtained in 98 % yield as yellow needles, mp 186-187°; ^{1}H nmr(deuteriochloroform): δ 1.39 (t, J=7.3, 3H, CH_2CH_3), 4.36 (q, J=7.3, CH_2CH_3), 7.05 (s, 1H, C_5-H), 7.50 (m, 3H, Ph), 7.84 (m, 2H, Ph), 8.18 (s, 1H, =CH), 8.33 (d, J=13, CH-NH), 11.49 (d, J=13, CH-NH). ^{13}C nmr (deuteriochloroform): δ 14.2(q), 14.3(q), 61.5(t), 78.6(s), 103.6(d), 116.9(s), 128.1(d), 129.2(d), 131.8(d), 132.3(s), 136.6(s), 139.9(s), 148.7(d), 149.5(d), 166.8(s). ms: m/z (relative intensity): 323(M^+, 72), 147(100).

Anal. Calcd. For $C_{17}H_{17}N_5O_2$: C, 63.14; H, 5.30; N, 21.66. Found: C, 62.94; H, 5.27; N, 21.54.

Ethyl 1-Benzylideneamino-5-imino-3-methyl-1*H*-imidazo-[1,2-*a*]pyrimidine-6-carboxylate (**5a**).

To a solution of **3a** (0.1 g) in methanol (5 ml) was added 1 ml of concentrated HCl solution. The mixture was heated under reflux for 1 hour and then allowed to cool to ambient temperature. The separated crystals were collected by filtration and converted to the free base in usual manner to give **5a** as a crystalline powder (0.09 g, 90 %). Recrystallization from methanol gave the analytically pure sample of **5a** as yellow needles (0.031 g, 31 %), mp 168-170°; ^{1}H nmr (deuteriochloroform): δ 1.35 (t, 3H, J=7.3, CH_2CH_3), 2.84 (s, 3H, CH_3), 4.28 (q, 2H,J=7.3, CH_2CH_3), 6.98 (s, 1H, C_2-H), 7.48 (m, 3H, Ph), 7.85 (m, 2H, Ph), 8.37 (s, 1H, N=CH), 8.95 (s,1H, NH), 9.26 (s, 1H, C_7-H); ^{13}C nmr (deuteriochloroform): δ 14.4 (q), 14.7(q), 60.1(t), 101.4(s), 112.3(d), 123.5(s), 128.4(d), 128.9(d),131.9(d), 132.7(s), 145.6(s), 154.6(s), 155.2(d), 155.8(d), 166.6(s); ms: m/z (relative intensity): 323(M^+, 32), 219(100).

Anal. Calcd. For $C_{17}H_{17}N_5O_2$: C, 63.14; H, 5.30; N, 21.66. Found: C, 62.89; H, 5.31; N, 21.81.

1-Benzylideneamino-6-cyano-3-methyl-5-oxo-1*H*-imdazo[1,2-*a*]-pyrimidine (**6a**).

To a solution of **3a** (0.1 g) in 5 ml of methanol was added 1 ml of triethylamine. The mixture was heated under reflux for 7 hours and then allowed to cool to ambient temperature. The separated crystals were collected, washed with methanol, and then dried to give **6a** as a crystalline powder (0.035 g, 41 %). Recrystallization from methanol gave the analytically pure sample of as yellow needles (0.031 g, 36 %), mp 238-240°; ^{1}H nmr (DMSO-d_6): δ 2.67 (s, 3H, CH_3), 7.57 (m, 3H, Ph), 7.88 (m, 2H, Ph), 8.18 (s, 1H, C_5-H, 8.45 (s, 1H, N=CH), 9.07 (s, 1H, C_7-H); ^{13}C nmr (DMSO-d_6): δ 12.2(q), 87.3(s), 111.8(d), 116.4(s), 121.5(s), 128.2(d), 129.1(d), 132.1(s), 132.1(d), 144.9(s), 157.4(s), 156.9(d), 159.1(d); ms: m/z (relative intensity): 277(M^+, 30), 174(100).

Anal. Calcd. for $C_{15}H_{11}N_5O$: C, 64.97 H, 4.00; N, 25.26. Found: C, 64.87; H, 4.05; N, 25.00.

6-Cyano-5-imino-1-isopropylideneamino-3-phenyl-1*H*-imidazo[1,2-*a*]pyrimidine (**9**).

A mixture of **8** (0.15 g, 0.7 mmol) and **I** (0.10 g, 0.84 mmol) was dissolved in a mixed solvent of acetonitrile (2 ml) and acetone (2 ml) and the reaction mixture was allowed to stand at room temperature with occasional agitation for 1 day. The crystals gradually deposited from the solution, and were collected by filtration to give 0.1 g (50 %) of analytically pure **9** as pale yellow needles, mp 148-151°; ^{1}H nmr (deuteriochloroform): δ 1.99 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 7.49 (t, J=7.3, 2H, Ph), 7.73 (d, J=7.3, 2H, Ph), 7.76 (s, 1H, C_2-H), 7.88 (t, J=7.3, 1H, Ph), 8.36 (s, 1H, C_7-H), 12.8 (s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 20.4(q), 24.7(q), 52.5(d), 111.7(d), 116.5(s), 119.3(s), 124.3(d), 125.9(s), 127.4(s), 128.3(d), 128.9(d), 144.7(d), 164.8(d), 180.6(s): ms: m/z (relative intensity): 290(M^+, 24), 158(100).

Anal. Calcd. For $C_{16}H_{14}N_6$: C, 66.19; H, 4.86; N, 28.95. Found: C, 66.36; H, 4.98; N, 29.02.

Ethyl (4-Phenyl-1-isopropylideneaminoimidazol-2-yl)aminomethyenecyanoacetate (**10**).

A solution of **8** (0.17, 0.001 mol) and ethyl ethoxymethylenecyanoacetate (**II**) (0.203 g, 0.0012 mol) in acetone (2 ml) was

allowed to stand at room temperature. During 24 hours, crystals gradually deposited from the solution, and were collected by filtration to give 0.13 g (89 %) of analytically pure **10** as pale yellow needles, mp 168°; ^{1}H nmr (deuteriochloroform): δ 1.37 (t, J=7.3, 3H, CH_3), 2.20 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 4.31 (q, J=7.3, 2H, CH_2), 7.12 (s, 1H, C_5-H), 7.26 (t, J=7.3, 1H, Ph), 7.39 (t, J=7.8, 2H, Ph), 7.73 (d, J=7.8, 1H, Ph), 8.43 (d, J=13, 1H, CH), 10.99 (d, J=13, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 14.2(q), 20.5(q), 26.3(q), 61.5(t), 78.1(s), 109.5(q), 117.0(s), 124.6(d), 127.3(d), 128.7(d), 133.1(s), 137.4(s), 139.2(s), 150.2(d), 166.9(s), 172.0(s); ms: m/z (relatuve intensity): 337(M^+, 57), 209(100).

Anal. Calcd. for $C_{18}H_{12}N_5O_2$: C, 64.08; H, 5.68; N, 20.76. Found: C, 64.18; H, 5.69; N, 20.76.

Ethyl (1-Amino-4-phenylimidazol-2-yl)aminomethyenecyanoacetate (**12**).

A solution of **8**(0.17 g, 0.001 mol) and **II** (0.203 1.2 mol) in acetone (2 ml) was heated under reflux for 30 minutes and then allowed to cool to ambient temperature. The separated crystals were isolated by filtration and washed acetone to give **10** (0.12 g, 37 %), mp 178°. The filtrate was evaporated to give yellow oil. The oil was crystallized from chloroform and the crystals found were collected by filtration to give 0.06 g, (20 %) of **12** as pale yellow crystals with mp 197-198°; ^{1}H nmr(DMSO-d_6): δ 1.29 (t, J=7.3, 3H, CH_3), 4.25 (q, J=7.3, 2H,CH_2), 6.17 (bs,2H, NH_2), 7.20 (t, J=7.3, 1H, Ph), 7.35 (t, J=7.3 and 7.8, 2H, Ph), 7.55 (s, 1H, C_5-H), 7.76 (d, J=7.8, 2H, Ph), 8.38 (d, J=13, 1H, CH), 11.13 (d, J=13, 1H, NH); ^{13}C nmr(DMSO-d_6): 14.0(q), 61.0(t), 75.5(s), 116.3(d), 117.1(s), 124.0(d), 126.4(d), 128.4(d), 133.7(s), 134.6(s), 140.2(s), 150.5(d), 166.1(s); ms m/z (relative intensity): 297(M^+, 100), 250(96).

Anal. Calcd. for $C_{15}H_{15}N_5O_2$: C, 60.60; H, 5.09; N, 23.59. Found: C, 60.49; H, 5.11; N, 23.50.

6-Amino-7-ethoxycarbonyl-2-phenyl-1*H*-imidazo[1,2-*b*]-[1,2,4]triazepine (**13b**).

To a solution of **10** (0.1 g) in methanol (2 ml) was added 0.2 ml of concentrated HCl. The mixture was heated under reflux for 1 hour and then allowed to cool to ambient temperature. The separated crystals were collected by filtration and converted to the free base in the usual manner to give **13b** as a crystalline powder (0.09 g, 86%), mp 188°(d); ^{1}H nmr (DMSO-d_6): δ 1.23 (t, 3H, J=7.1, CH_2CH_3), 4.29 (q, 2H,J=7.1, CH_2CH_3), 7.33 (t, J=7.3, 1H,Ph), 7.44 (t, J=7.3 and 7.8, 2H, Ph), 7.82 (s, 1H, C_8-H), 7.89 (d, 2H, Ph), 8.91 (s, 1H, C_2-H), 12.01 (s, 2H, C_6-H); ^{13}C nmr (DMSO-d_6): δ 13.9(q), 61.4(t), 78.4(s), 116.1(s), 116.4(d), 124.3(s), 124.4(d), 127.6(s), 127.7(d), 128.6(d), 139.6(s), 150.8(d), 165.3(s); ms: m/z (relative intensity): 297(M^+, 23), 296(100).

Anal. Calcd. For $C_{15}H_{15}N_5O_2$: C, 60.60; H, 5.08; N, 23.56. Found: C, 60.31; H, 4.82; N, 23.68.

6-Amino-7-cyano-2-phenyl-1*H*-imidazo[1,2-*b*][1,2,4]triazepine (**13a**).

A solution of 1,2-diamono-4-phenyl-1*H*-imidazole (**14**) (0.174 g, 0.001 mol), **I** (0.07g, 0.001 mol) in acetonitrile (5 ml) was heated under reflux for 1 hour and then allowed to cool to ambient temperature. The separated crystals were collected, washed with acetonitrile, and then dried to give **13a** as yellow crystals (0.24 g, 96 %), mp 181-182°. Recrystallization from acetonitrile gave yellow needles (0.20 g, 80 %), mp 184-185°; ^{1}H nmr (DMSO-d_6): δ 6.07 (s, 1H, NH), 7.34 (t, J=7.3, 1H, Ph), 7.45 (t, J=7.3 and J=7.8, 2H, Ph), 7.67 (s, 1H, C_8-H), 7.71 (d, J=7.8, 2H, Ph), 8.46 (s, 1H, C_2-H), 12.68 (s, 2H, C_6-NH); ^{13}C nmr (DMSO-d_6): δ 51.6(s), 115.9(d), 117.8(s), 119.6(s), 124.1(s), 124.1(d), 127.6(s), 128.1(d), 128.9(d), 148.5(d), 164.8(d); ms m/z(relative intensity): 250(M^+, 47), 249(100).

Anal. Calcd. for $C_{13}H_{10}N_6$: C, 62.39; H, 4.03; N, 33.58. Found: C, 62.14; H, 4.01; N, 33.48.

REFERENCES AND NOTES

[1] Part 9: Y. Miyamoto, *J. Heterocyclic Chem*., **37**, 1587 (2000).

[2] Y. Miyamoto, R. Kobana and C. Yamazaki, *Chem. Pharm. Bull*. **36**(6), 1963 (1988).

[3] Y. Miyamoto and C. Yamazaki, *J. Heterocyclic Chem*., **26**, 763 (1989).

[4] The carbonyl frequencies in the internal (ir) spectra of **3** appears in the range of 1690-1675 cm^{-1}, which corresponds to the internally bonded bands of the bis(ethoxycarbonyl)vinylamino compounds **4**. Thus the geometry about the CH=C bond of **3** should be *Z* form.