Synthesis and Some Reactions of 2-Amino-1-azaazulene-3-carbaldehyde

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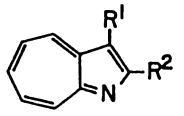
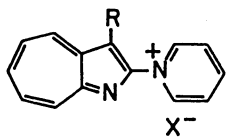
2-Chloro-1-azaazulene-3-carbaldehyde (**1a**) reacted with pyridine, followed by a reacion with piperidine to give 2-amino-1-azaazulene-3-carbaldehyde (**1b**) in excellent yield. Compound **1b** was also obtained by a Vilsmeier–Haack reaction of 2-amino-1-azaazulene. Acetylation of **1b** yielded a 2-acetylamino derivative, whereas methylation gave a 1-methylated compound. Reactions of **1b** with hydrazines and alkylamines gave the corresponding hydrazones and Schiff bases, respectively, in excellent yields. The reactions of **1b** with active methylene compounds gave 1,10-diazabenz[*a*]azulen-2(1*H*)-one derivatives. The reaction of **1b** with guanidine gave pyrimidine-fuzed 1-azaazulene.

It is known that ortho-substituted amino aldehyde on heterocycles, such as 2-amino-3-pyridinecarbaldehyde (2-aminonicotinaldehyde), are useful for the syntheses of fuzed heterocycles.[1] We have studied the reaction of 1-azaazulenes and syntheses of fuzed 1-azaazulenes.[2] In spite of its synthetical interest and usefulness, 2-amino-1-azaazulene-3-carbaldehyde (**1b**) has not yet been synthesized. We focused our attention on the preparation and reactions of this new compound **1b**. It is known that the cleavage of Zincke salt gives 2,4-dinitroaniline and 2-pentenedial.[3] We tried to apply this method to 2-chloro-1-azaazulenes, and succeeded in the preparation of 2-amino-1-azaazulene derivatives. The obtained 2-amino-1-azaazulene-3-carbaldehyde (**1b**) was synthetically useful and afforded novel fuzed heterocycles in excellent yields.

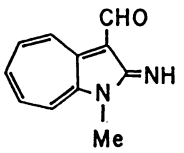
The treatment of 2-chloro-1-azaazulene-3-carbaldehyde[4] (**1a**) with pyridine for 30 min gave a pyridinium salt **2a** in nearly quantitative yield; the structure was confirmed to be the perchlorate **2b**. The treatment of **2a** with piperidine gave 2-amino-1-azaazulene-3-



1a: R^1=CHO, R^2=Cl
1b: R^1= CHO, R^2=NH_2
1c: R^1=H, R^2=NH_2
1d: R^1=H, R^2=Cl
1e: R^1=CO_2Et, R^2=Cl
1f: R^1=CO_2Et, R^2=NH_2
1g: R^1=CHO, R^2=NHAc



2a: R=CHO, X=Cl
2b: R=CHO, X=ClO_4
2c: R=H, X=Cl
2d: R=H, X=ClO_4
2e: R=CO_2Et, X=Cl
2f: R=CO_2Et, X=ClO_4



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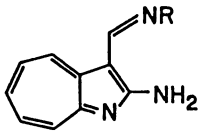
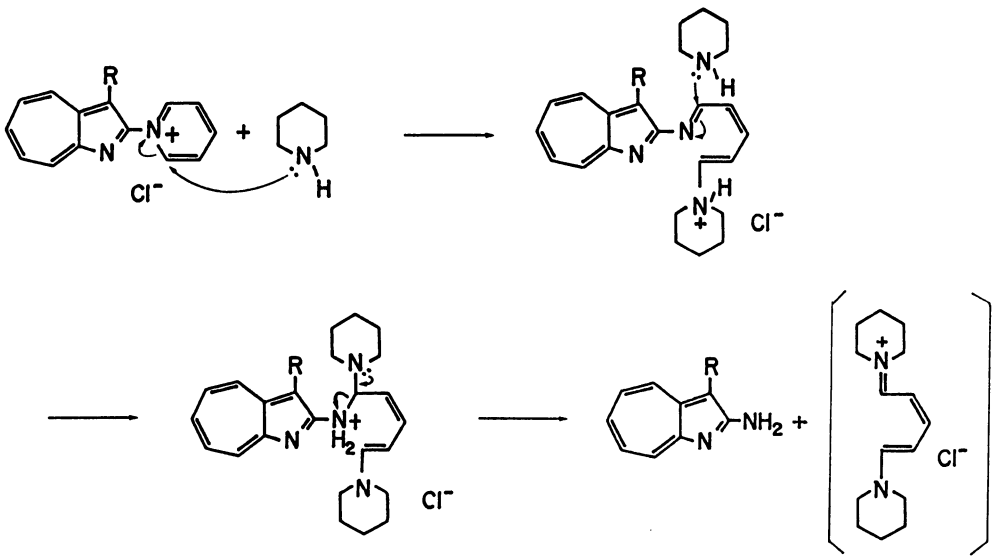


4a: R=NH_2
4b: R=NHPh
4c: R=Et
4d: R=$CH_2CH{=}CH_2$
4e: R=*t*-butyl
4f: R=$CH_2CH(OMe)_2$



Scheme 1.

carbaldehyde (**1b**) in 93% yield. The reaction proceeded as shown in Scheme 1. Compound **1b** was also synthesized by the Vilsmeier–Haack reaction of 2-amino-1-azaazulene[5] (**1c**) in 94% yield.

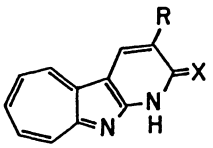
In order to expand the reaction, we treated 2-chloro-1-azaazulene (**1d**) and ethyl 2-chloro-1-azaazulene-3-carboxylate (**1e**) with pyridine, followed by piperidine, and obtained **1c** and **1f**,[6] respectively, in excellent yields.

In comparison with the known amino substitution of 2-chloro-1-azaazulenes, in which such conditions as the heating of **1d** or **1e** with ammonia–methanol in a sealed tube under high temperature were employed,[5,6] the reaction conditions were mild, the procedure was convenient, and the yields were excellent. This procedure is therefore synthetically useful for 2-amino-1-aza-azulenes.

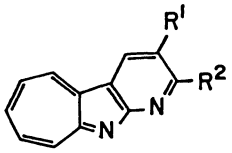
Compound **1b** was acetylated with acetic anhydride and gave the 2-acetylamino derivative (**1g**) in 72% yield. The treatment of **1b** with methyl iodide in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in refluxing acetonitrile for 48 h gave 1-methylated compound **3** quantitatively.

The formyl group of **1b** was reacted with hydrazine hydrate and phenylhydrazine to give the corresponding hydrazones, **4a** and **4b**, respectively. Compound **1b** condensed with alkylamines RNH_2 (R=ethyl, allyl, *t*-butyl, 2,2-dimethoxyethyl) in the presence of molecular sieves or under azeotropical refluxing conditions to give Schiff bases **4c**—**4f** in good to excellent yields.

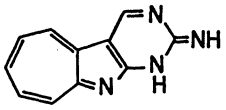
In order to synthesize heterocycles-fuzed 1-aza-azulenes, **1b** was treated with some active methylene compounds. The reactions of **1b** with active methylene compounds (diethyl malonate, ethyl cyanoacetate, ethyl acetoacetate, ethyl benzoylacetate, cycnoactamide, and malononitrile) under reflux in the presence of pyrrolidine gave 1,10-diazabenz[*a*]azulene-2(1*H*)-ones (**5a**—**5f**)



5a: X=O, R=CO_2Et
5b: X=O, R=CN
5c: X=O, R=Ac
5d: X=O, R=COPh
5e: X=NH, R=$CONH_2$
5f: X=NH, R=CN
5g: X=O, R=CO_2H
5h: X=O, R=H



6a: R^1=CO_2Et, R^2=Ph
6b: R^1=H, R^2=Cl
6c: R^1=CO_2Et, R^2=Cl
6a: R^1=CN, R^2=Cl



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in excellent yields. These heterocyclic systems would be produced by the initial Knoevenagel condensation and successive cyclizations by an attack of the amino group on the ester group.

When **1b** was treated with ethyl benzoylacetate under refluxing ethanol in the presence of pyrrolidine, the result was somewhat different; **5d** (17%) and ethyl 2-phenyl-1,10-diazabenz[*a*]azulene-3-carboxylate (**6a**, 41%) were obtained. When an intramolecular attack of the amino group on the ester group on the intermediate Knoevenagel condensation product occured, the former was produced, while an attack of the amino group on the benzoyl group produced the latter.

The reaction of **1b** with malononitrile proceeded to reflux 1-butanol in the presence of pyrrolidine, giving **5f** in 99.5% yield.

The reactions of **1b** with active methylene compounds in the presence of sodium hydroxide or sodium ethoxide gave complex mixtures. Pyrrolidine (or piperidine) is prominent as a catalyst for condensation; sodium hydroxide and sodium ethoxide were not suited.

The reaction of **1b** with guanidine hydrochloride in the presence of sodium ethoxide in refluxing ethanol for 3 h gave 1,3,10-triazabenz[*a*]azulen-2-(1*H*)-imine **7** in 70% yield.

The treatment of **5a** and **5b** with refluxing 48% hydrobromic acid for 2 h gave carboxylic acid **5g** in nearly quantitative yields. The acid (**5g**) was decarboxylated by a further treatment with refluxing hydrobromic acid for 24 h to give **5h** in 80% yield. Prolonged heating of **5a** in refluxing hydrobromic acid also gave **5h** in 86% yield.

The treatment of **5h**, **5a**, and **5b** with phosphoryl chloride gave 2-chloro-1,10-diazabenz[*a*]azulenes **6b** (20%), **6c** (95%), and **6d** (47%), respectively.

In ^{1}H NMR spectra of **5h**, H-5 and H-9 protons were found at δ=8.21 ($J_{5,6}$=9.8 Hz) and 9.09 ($J_{8,9}$=9.8 Hz), respectively. On the other hand, in the ^{1}H NMR spectrum of **6b**, the H-5 and H-9 protons were found at δ=8.86 ($J_{5,6}$=9.2 Hz) and 8.85 ($J_{8,9}$=11.6 Hz), respectively. In the former, vicinal spin–spin coupling ($J_{8,9}$ and $J_{5,6}$) was equal, showing that the azaazulene ring has no bond alternation and maintains aromaticity. In the latter, however, the large divergence of the vicinal spin–spin coupling constant, $\Delta J=J_{8,9}-J_{5,6}$=2.4 Hz, was observed, indicating a bond alternation in the azaazulene ring, and reflecting the large aromaticity of the pyridine ring. This phenomenon resembles the case of 1-azabenz[*a*]azulene.[7] A larger divergence of the coupling constant in the azaazulene ring (2.4 Hz) than in the azulene ring (1.8 Hz)[7] suggests that the aromaticity of the azaazulene is smaller than that in azulene.[8]

Experimental

All of the melting points are uncorrected. ^{1}H (250 MHz) and ^{13}C (62.87 MHz) NMR spectra were taken on a Hitachi R-250H spectrometer using $CDCl_3$ as a solvent (TMS as an

internal standard). The IR spectra were recorded for Nujol mulls with a Hitachi 270-50 infrared spectrophotometer. The mass spectra, including high-resolution, were determined with a JEOL-01SG-2 spectrometer. Column chromatography was performed on a Kieselgel 60.

Synthesis of 1b. a) A mixture of **1a**[4] (1.380 g) and pyridine (7 ml) was warmed at 90 °C on a water bath for 30 min and then cooled. The precipitate was collected and washed with benzene to give **2a** (1.920 g, 98.5%) as yellow prisms, mp 202—204 °C. A small portion of **2a** was dissolved in water; the addition of 60% perchloric acid to the solution gave the perchlorate **2b** as yellow needles, mp 214 °C (decomp). Found: C, 53.51; H, 3.40; N, 8.41%. Calcd for $C_{15}H_{11}ClN_2O_5$: C, 53.87; H, 3.31; N, 8.37%.

A mixture of **2a** (1.920 g), piperidine (6 ml), and abs ethanol (60 ml) was set aside for 1 d at room temperature. The precipitate was collected and washed with ethanol to give **1b** (0.760 g, 62%), which was recrystallized from ethyl acetate to give yellow needles, mp 220—222 °C. The filtrate was evaporated and the residue was chromatographed with chloroform to give **1b** (0.380 g, 31%). ^{1}H NMR δ=6.2—7.6 (2H, br), 7.60 (1H, dd, J=10.4 and 9.8 Hz), 7.70 (1H, d, J=9.8 Hz), 7.77 (1H, d, J=9.8 Hz), 8.12 (1H, d, J=10.4 Hz), 8.42 (1H, d, J=9.8 Hz), and 10.40 (1H, s); IR 3392, 3272 (NH), and 1644 cm^{-1} (C=O). Found: C, 69.96; H, 4.81; N, 16.14%. Calcd for $C_{10}H_8N_2O$: C, 69.75; H, 4.68; N, 16.27%.

In a similar manner, we synthesized **2c** (79.5%), **2d**, **1c**[5] (96%), **2e** (94%), **2f**, and **1f**[6] (85%).

2d: Brown needles, mp 223—224 °C. Found: C, 55.04; H, 3.67; N, 9.01%. Calcd for $C_{14}H_{11}ClN_2O_4$: C, 54.82; H, 3.61; N, 9.18%.

2f: Yellow powder, mp 212—213 °C (decomp). Found: C, 53.35; H, 4.19; N, 7.23%. Calcd for $C_{17}H_{15}ClN_2O_6$: C, 53.89; H, 3.99; N, 7.39%.

b) To a solution of **1c** (0.500 g) in *N,N*-dimethylformamide (DMF) (10 ml) cooling in an ice bath, a mixture of DMF (5 ml) and phosphoryl chloride (2.00 g) was added dropwise. The mixture was heated at 80 °C for 8 h with stirring and then allowed to stand for 1 d at room temperature. The mixture was then warmed at 50 °C with stirring after the addition of sodium acetate (1.00 g), and poured into cold water (200 ml). The solution was neutralized with sodium hydrogencarbonate and extracted with dichloromethane. The extract was dried (Na_2SO_4) and evaporated. The residue was chromatographed with chloroform to give **1b** (0.568 g, 94%).

Acetylation of 1b. A mixture of **1b** (0.100 g), acetic anhydride (5 ml), and concd H_2SO_4 (2 drops) was warmed at 90 °C on a water bath for 30 min, and then allowed to stand for 3 d at room temperature. The mixture was poured into cold water (100 ml). The solution was neutralized with sodium hydrogencarbonate and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated. The residue was crystallized from hexane–dichloromethane to give **1g** (0.090 g, 72%) as red prisms, mp 156—157 °C; 1H NMR δ=2.58 (3H, s), 7.85—8.05 (3H, m), 8.67 (1H, d, J=9.8 Hz), 8.73—8.82 (1H, m), 10.46 (1H, s), and 10.60 (1H, brs); IR 3300—2700 (NH), 1702, and 1645 cm^{-1} (C=O). Found: C, 59.64; H, 4.45; N, 10.68%. Calcd for $C_{12}H_{10}N_2O_2 \cdot 0.5CH_2Cl_2$: C, 60.05; H, 4.32; N, 10.91%. HRMS; Found: m/z 214.0742. Calcd for $C_{12}H_{10}N_2O_2$: M, 214.0741.

Methylation of 1b. A mixture of **1b** (0.100 g), methyl iodide (1.0 g), and DBU (0.30 g) in acetonitrile (30 ml) was refluxed for 48 h, and the precipitate was collected. The precipitate was dissolved in water and neutralized with sodium hydrogencarbonate. The mixture was extracted with chloroform. The extracts were dried (Na_2SO_4), and evaporation of the solvent gave **3** (0.108 g, 100%), which was recrystallized from hexane–dichloromethane to give yellow needles, mp 110—111 °C; ^{1}H NMR δ=3.53 (3H, s), 6.90—7.01 (2H, m), 7.26—7.40 (2H, m), 8.06 (1H, d, J=11.3 Hz), and 10.27 (1H, s);[9] IR 3296 (NH) and 1652 cm^{-1} (C=O). Found: C, 62.24; H, 5.93; N, 12.93%. Calcd for $C_{11}H_{10}N_2O \cdot 1.5CH_2Cl_2$: C, 61.96; H, 6.14; N, 13.14%. MS M$^+$, m/z 186. Calcd for $C_{11}H_{10}N_2O$: M, 186.

Reaction of 1b with Hydrazines. A mixture of **1b** (0.100 g) and hydrazine hydrate (0.5 ml) in ethanol (30 ml) was warmed on a water bath for 5 min. Evaporation of the solvent gave **4a** (0.104 g, 96%), which was recrystallized from ethanol to give red leaflets, mp >300 °C; ^{1}H NMR δ=1.6—2.4 (1H, br), 3.3—4.0 (1H, br), 6.5—6.9 (2H, br), 7.3—7.6 (3H, m), 7.90 (2H, d, J=9.2 Hz), and 8.33 (1H, s); IR 3360, 3264 (NH), and 1626 cm^{-1} (C=N). Found: C, 64.55; H, 5.49; N, 30.18%. Calcd for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41; N, 30.09%.

Similarly, reaction of **1b** with pheylhydrazine gave **4b** (89%).

4b: Red needles (from ethanol), mp 270—271 °C; ^{1}H NMR δ=3.3—3.9 (1H, br), 6.4—7.2 (2H, br), 6.77 (1H, t, J=7.3 Hz), 7.03 (2H, d, J=8.5 Hz), 7.20—7.60 (5H, m), 7.88—7.97 (2H, m), and 8.03 (1H, s); IR 3368, 3288 (NH), 1628 (C=N), 764, and 684 cm^{-1} (phenyl). Found: C, 73.12; H, 5.49; N, 21.30%. Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36%.

Reaction of 1b with Amines. A mixture of **1b** (0.100 g), 70% ethylamine (4 ml), and molecular sieves 4A (5.0 g) in toluene (50 ml) was refluxed for 3 d. The mixture was filtered and washed with chloroform. The filtrate was evaporated, giving orange crystals (0.088 g), which were purified by fractional crystallization from hexane–dichloromethane to give **4c** (0.045 g, 39%) and **1b** (0.005 g, 5%).

4c: Red needles, mp 169—170 °C; ^{1}H NMR δ=1.32 (3H, t, J=7.3 Hz), 3.65 (2H, q, J=7.3 Hz), 6.7—7.15 (2H, br), 7.36 (1H, t, J=9.8 Hz), 7.45 (1H, t, J=9.8 Hz), 7.54 (1H, t, J=9.8 Hz), 7.96 (1H, d, J=9.8 Hz), 8.08 (1H, d, J=9.8 Hz), and 8.84 (1H, s); IR 3360, 3280 (NH), and 1640 cm^{-1} (C=N). Found: C, 72.21; H, 6.54; N, 21.31%. Calcd for $C_{12}H_{13}N_3$: C, 72.34; H, 6.57; N, 21.09%.

In a similar manner, we synthesized **4d** (99%) and **4e** (85%).

4d: Orange scales (from hexane–dichloromethane), mp 133—134 °C; ^{1}H NMR δ=4.28 (2H, d, J=5.5 Hz), 5.15 (1H, dd, J=9.8 and 1.8 Hz), 5.25 (1H, dd, J=17.1 and 1.8 Hz), 6.10 (1H, ddd, J=17.1, 9.8, and 5.5 Hz), 6.4—8.0 (2H, br), 7.40 (1H, dd, J=10.4 and 9.8 Hz), 7.47 (1H, t, J=9.8 Hz), 7.56 (1H, t, J=9.8 Hz), 7.97 (1H, d, J=9.8 Hz), 8.10 (1H, d, J=10.4 Hz), and 8.84 (1H, s); IR 3344, 3284 (NH), and 1640 cm^{-1} (C=N). Found: C, 73.83; H, 6.24; N, 19.93%. Calcd for $C_{13}H_{13}N_3$: C, 73.91; H, 6.20; N, 19.89%.

4e: Orange needles (from hexane–dichloromethane), mp 182—184 °C; ^{1}H NMR δ=1.34 (9H, s), 6.2—8.0 (2H, br), 7.35 (1H, dd, J=10.4 and 9.8 Hz), 7.45 (1H, t, J=9.8 Hz), 7.53 (1H, t, J=9.8 Hz), 7.95 (1H, d, J=9.8 Hz), 8.11 (1H, d, J=9.8 Hz) and 8.86 (1H, s); IR 3336, 3255 (NH), and 1640 cm^{-1} (C=N). Found: C, 73.77; H, 7.47; N, 18.63%. Calcd for $C_{14}H_{17}N_3$: C, 73.97; H, 7.54; N, 18.49%.

Reaction of 1b with 2,2-Dimethoxyethylamine. A mixture of **1b** (1.380 g), 2,2-dimethoxyethylamine (2.520 g), diethylamine (1.760 g) in dry xylene (150 ml) was azeotropically

refluxed for 50 h by use of a Dean-Stark trap; the solvent was then evaporated. The residue was recrystallized from ethanol to give **4f** (1.680 g, 81%) as red scales, mp 169—170 °C; ^{1}H NMR δ=3.48 (3H, s), 3.80 (2H, d, J=5.5 Hz), 4.66 (1H, t, J=3.5 Hz), 7.37 (1H, t, J=9.8 Hz) 7.48 (1H, t, 9.8 Hz), 7.56 (1H, t, J=9.8 Hz), 7.97 (1H, d, J=9.8 Hz), 8.09 (1H, d, J=9.8 Hz), and 8.83 (1H, s); IR 3320, 3150 (NH), and 1646 cm^{-1} (C=N). Found: C, 65.11; H, 6.59; N, 15.95%. Calcd for $C_{14}H_{17}N_3O_2$: C, 64.85; H, 6.61; N, 16.20%.

Reaction of 1b with Active Methylene Compounds. a) A mixture of **1b** (0.207 g), diethyl malonate (5 ml), and pyrrolidine (4 drops) was refluxed for 2 h and cooled. The precipitates were collected by filtration and washed with ethanol to give **5a** (0.267 g, 83%) as orange needles, mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=1.61 (3H, t, J=7.0 Hz), 4.73 (2H, q, J=7.0 Hz), 8.80—9.00 (3H, m), 9.40—9.46 (1H, m), 9.77 (1H, s), and 9.73—9.81 (1H, m); IR 3100—2600 (NH), 1724, and 1646 cm^{-1} (C=O). Found: C, 67.03; H, 4.61; N, 10.49%. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44%. The filtrate was concentrated and gave **5a** (0.028 g, 9%).

Similarly, reactions of **1b** with ethyl cyanoacetate, ethyl acetoacetate, ethyl benzoylacetate, cyanoacetamide, and malononitrile gave **5b** (94%), **5c** (85%), **5d** (73%), **5e** (81%), and **5f** (97.5%), respectively.

5b: Orange needles (from ethanol), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=8.75—8.95 (3H, m), 9.31 (1H, d, J=11.0 Hz), 9.33 (1H, s), and 9.57 (1H, d, J=9.8 Hz). Found: C, 70.48; H, 3.25; N, 19.03%. Calcd for $C_{13}H_7N_3O$: C, 70.58; H, 3.19; N, 18.99%.

5c: Orange needles (from ethanol), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=3.02 (3H, s), 8.80—9.00 (3H, m), 9.30—9.40 (1H, m), 9.77 (1H, s), and 9.73—9.83 (1H, m); IR 3100—2700 (NH), 1668, and 1646 cm^{-1} (C=O). Found: C, 70.73; H, 4.43; N, 11.52%. Calcd for $C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76%.

5d: Red needles (from ethanol-chloroform), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=7.67 (2H, t, J=7.3 Hz), 7.85 (1H, t, J=7.3 Hz), 7.93 (2H, d, J=7.3 Hz), 8.50—8.90 (3H, m), 9.27 (1H, s), 9.32 (1H, dm, J=11.0 Hz), and 9.56 (1H, d, J=9.2 Hz); IR 3100—2700 (NH), 1660, 1644 (C=O), 746, and 674 cm^{-1} (phenyl). Found: C, 76.22; H, 4.20; N, 9.33%. Calcd for $C_{19}H_{12}N_2O_2$: C, 75.99; H, 4.03; N, 9.33%.

5e: Red prisms, mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)= 8.85—9.05 (3H, m), 9.44 (1H, d, J=9.8 Hz), 9.70 (1H, d, J=11.0 Hz), and 9.72 (1H, s); IR 3430, 3390, 3345, 3275 (NH), 1660 (C=O), and 1620 cm^{-1} (C=N). Found: C, 65.43; H, 4.32; N, 23.13%. Calcd for $C_{13}H_{10}N_4O$: C, 65.54; H, 4.23; N, 23.52%.

5f: Red prisms (from ethanol), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=7.60—7.90 (3H, m), 8.00 (1H, d, J=12.2 Hz), 8.89—8.90 (1H, m), and 8.97 (1H, s); IR 3320 (NH), 2204 (CN), and 1622 cm^{-1} (C=N). Found: N, 25.58%; MS M$^+$, m/z 220. Calcd for $C_{13}H_8N_4$: N, 25.44%; M, 220.

b) A mixture of **1b** (0.340 g), ethyl benzoylacetate (1 ml), and pyrrolidine (0.5 ml) in ethanol (50 ml) was refluxed for 15 h; the solvent was then evaporated. The residue was chromatographed. Elution with chloroform gave **6a** (0.267 g, 41%). Elution with acetone gave **5d** (0.101 g, 17%).

6a: Red prisms (from hexane-dichloromethane), mp 163—164 °C; ^{1}H NMR δ=1.08 (3H, t, J=7.0 Hz), 4.21 (2H, q, J=7.0 Hz), 7.42—7.53 (3H, m), 7.74—7.81 (2H, m), 7.85—8.05 (3H, m), 8.82—8.95 (2H, m), and 9.13 (1H, s); IR 1702 (C=O), 776, and 700 cm^{-1} (phenyl). Found: C, 76.36; H, 5.02; N, 8.21%. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53%.

Reaction of 1b with Guanidine Hydrochloride. Guanidine hydrochloride (0.200 g) was added to a sodium ethoxide solution prepared from sodium (0.045 g) and abs ethanol (20 ml). To the mixture **1b** (0.340 g) was added; this mixture was refluxed for 3 h, and then allowed to stand for 24 h at room temperature. A precipitate **7** (0.270 g, 70%) was obtained.

7: Yellow needles (from aq ethanol), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=8.90—9.15 (3H, m), 9.29 (1H, d, J=9.2 Hz), 9.73—9.83 (1H, m), and 10.00 (1H, s); IR 3268, 3096 (NH), and 1668 cm^{-1} (C=N). Found: C, 67.37; H, 3.86; N, 28.52%. Calcd for $C_{11}H_8N_4$: C, 67.33; H, 4.11; N, 28.56%.

Conversion of 5a to 5h. a) A mixture of **5a** (0.250 g) and 48% hydrobromic acid (10 ml) was refluxed for 1 h, and then poured into water (200 ml). The precipitate was filtered, washed with water, and dried. The carboxylic acid **5g** was obtained as an orange powder (0.220 g, 98%), mp >300 °C; ^{1}H NMR δ (CF_3CO_2D)=8.60—8.95 (3H, m), 9.36 (1H, d, J=8.6 Hz), 9.76 (1H, d, J=9.2 Hz), and 9.96 (1H, s); IR 2900—2400 (ON and NH), 1718, 1632 cm^{-1} (C=O). A mixture of (0.170 g) and 48% hydrobromic acid (20 ml) was refluxted for 24 h, and then poured into water (200 ml). The mixture was neutralized with sodium hydrogencarbonate and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporation of the solvent gave **5h** (0.110 g, 80%).

5h: Red needles (from ethyl acetate-dichloromethane), mp >300 °C; ^{1}H NMR δ=3.2—3.8 (1H, br), 6.62 (1H, d, J=9.2 Hz), 7.80—8.07 (3H, m), 8.21 (1H, d, J=9.8 Hz), 8.63 (1H, d, J=9.2 Hz), and 9.09 (1H, d, J=9.8 Hz); IR 2800—2500 (NH), 1652 cm^{-1} (C=O); Found: C, 73.46; H, 4.23; N, 14.12%. Calcd for $C_{12}H_8N_2O$: C, 73.46; H, 4.11; N, 14.28%.

b) A mixture of **5a** (0.250 g) and 48% hydrobromic acid (30 ml) was refluxed for 24 h and worked up as mentioned above to give **5h** (0.157 g, 86%).

Hydrolysis of 5b. A mixture of **5b** (0.200 g) and 48% hydrobromic acid (10 ml) was refluxed for 1 h, and then poured into water (100 ml). The precipitate was collected by filtration, washed with water and dried. Carboxylic acid **5g** (0.216 g, 99.5%) was obtained.

Chlorination of 5a. A mixture of **5a** (0.100 g) and phosphoryl chloride (10 ml) was refluxed for 3 h, and then poured into ice-water (200 ml). The mixture was neutralized with sodium hydrogencarbonate and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated. The residue was chromatographed with chloroform to give **6c** (0.102 g, 95%).

6c: Orange needles (from hexane-dichloromethane), mp 206—209 °C; ^{1}H NMR δ=1.48 (3H, t, J=7.0 Hz), 4.49 (2H, q, J=7.0 Hz), 7.90—8.20 (3H, m), 8.83—8.89 (1H, m), 8.91 (1H, d, J=8.5 Hz), and 9.14 (1H, s); IR 1714 cm^{-1} (C=O). Found: C, 62.87; H, 3.86; N, 9.43%. Calcd for $C_{15}H_{11}N_2O_2Cl$: C, 62.84; H, 3.87; N, 9.77%.

In a similar manner, chlorination of **5b** and **5h** gave **6d** (47%) and **6b** (20%), respectively.

6d: Orange needles, mp >300 °C; ^{1}H NMR δ (CF_3CO_2D) =8.95—9.18 (3H, m), 9.50—9.60 (1H, m), 9.66 (1H, s), and 10.02 (1H, d, J=9.2 Hz); IR 2208 cm^{-1} (CN). Found: C, 65.23; H, 2.89; N, 17.85%. Calcd for $C_{13}H_6N_3Cl$: C, 65.16; H, 2.52; N, 17.95%.

6b: Red needles (from hexane-dichloromethane), mp 197—199 °C; ^{1}H NMR δ=7.45 (1H, d, J=7.9 Hz), 7.70—8.10 (3H, m), 8.58 (1H, d, J=7.9 Hz), 8.85 (1H, d, J=11.6 Hz), and

8.86 (1H, d, J=9.2 Hz). Found: C, 66.87; H, 3.53; N, 12.68%. Calcd for $C_{12}H_7N_2Cl$: C, 67.15; H, 3.29; N, 13.05%.

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References

1) J. E. Harper and D. G. Wibberley, *J. Chem. Soc. C,* **1971**, 2991; E. Eichler, C. S. Rooney, and H. W. R. Williams, *J. Heterocycl. Chem.,* **13**, 43 (1976); W. W. Paudler and R. M. Sheets, *Adv. Heterocycl. Chem.,* **33**, 150 (1983).

2) N. Abe and K. Yatabe, *Bull. Chem. Soc. Jpn.,* **64**, 1704 (1991); N. Abe and T. Ueno, *ibid.,* **63**, 2121 (1990); N. Abe, N. Ishikawa, T. Hayashi, and Y. Miura, *ibid.,* **63**, 1617 (1990); N. Abe and T. Takehiro, *ibid.,* **61**, 1225 (1988); N. Abe, *ibid.,* **60**, 1053 (1987); N. Abe, *Heterocycles,* **26**, 51, (1987); **26**, 59 (1987); T. Nishiwaki and N. Abe, *ibid.,* **15**, 547 (1981).

3) T. Zincke, *Ann.,* **330**, 367 (1904); T. Zincke, G. Hauser, and W. Moller, *ibid.,* **333**, 296 (1904).

4) T. Toda, *Bull. Chem. Soc. Jpn.,* **40**, 590 (1967).

5) T. Nozoe, S. Seto, S. Matsumura, and T. Terasawa, *Chem. Ind.,* **1954**, 1357; K. Fujimori, N. Nirako, and K. Yamane, *Bull. Chem. Soc. Jpn.,* **56**, 1247 (1983).

6) T. Nozoe, S. Seto, and T. Toda, *Bull. Chem. Soc. Jpn.,* **41**, 208 (1968); N. Abe, T. Nishiwaki, H. Yamamoto, and N. Kunishige, *ibid.,* **56**, 3703 (1983).

7) N. Abe, *Bull. Chem. Soc. Jpn.,* **64**, 2393 (1991).

8) M. Kimura, *Yuki Gosei Kagaku Kyokai Shi,* **39**, 690 (1981), and references cited therein.

9) No signal of the NH protons was observed.