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Hydrogen Cyanide Chemistry. 6. [1]Cyanogen Condensation with Cyanide, $C_7N_7^-$

D. W. Wiley,* O. W. Webster, and E. P. Blanchard

Contribution No. 1962 from the Central Research and Development Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

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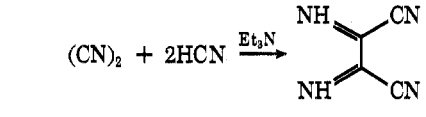
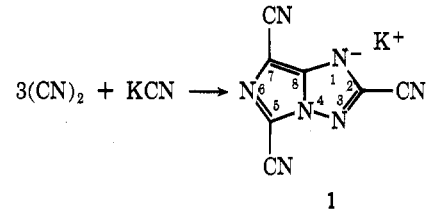
Three moles of cyanogen react with cyanide ion to give the salt of 1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile ($C_7N_7^-$, 1). This structure is confirmed by its chemistry.

In the base-catalyzed condensation of hydrogen cyanide with cyanogen, diiminosuccinonitrile is formed via the additions of cyanide ion across the nitrile groups.[2] In the absence



of a proton source, we have found that cyanide ion reacts with 3 mol of cyanogen to give a C_7N_7 anion. For example, cyanogen reacts with an acetonitrile slurry of potassium cyanide to give KC_7N_7. This material, isolated as the dioxane solvate in 65% yield, is the potassium salt of 1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile[3] (1).



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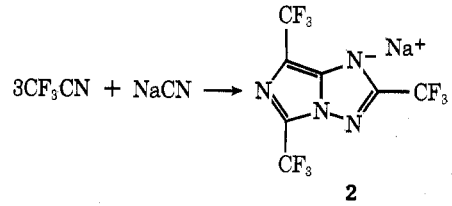
Trifluoroacetonitrile, another activated nitrile, undergoes the same type of cyclization reaction to give the corresponding tris(trifluoromethyl) compound **2**.[4] The structure of **2** was in



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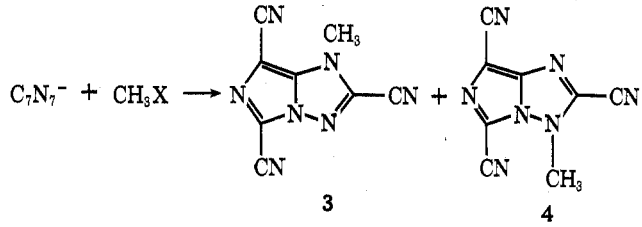
part based on the structure of **1**. This paper will describe work on which the structure of **1** is based.

The free acid from **1**, obtained either by treating the potassium salt with 9 N sulfuric acid or preferably by ion exchange, has a pK_a of −3 (extrapolated to water from spectrophotometric measurements in acetonitrile). Polarographic studies on $C_7N_7^-$ have shown an oxidation which is chemically but not electrochemically reversible. However, oxidation with chlorine yields only a chloro-C_7N_7 which reverts to C_7N_7H on contact with water.

The natural abundance ^{13}C NMR spectrum of KC_7N_7 in water shows seven peaks (87.8, 102.0, 110.7, 112.6, 114.9, 141.2, and 151.3 ppm downfield from Me_4Si) ruling out any symmetrical structure for **1**. The three peaks between 110 and 115 ppm (downfield from Me_4Si) occur in a range which has been reported for nitrile groups.[5]

KC_7N_7 can be alkylated to give a mixture of two isomers. Methylation gives the two isomers in a ratio of 1:3 with NMR peaks at δ 4.51 and 4.27, respectively, indicating *N*-methyl groups. Methylation can be carried out using a variety of methylating agents and solvents with not much change in the ratio of the isomers. The major isomer was shown to be the 1-methyl compound **3** by its ultimate conversion to 3-methylguanine **13** (see below) with the minor isomer being the

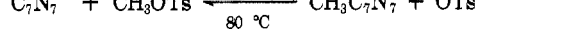


3 4

3-methyl compound **4**, supported by the presence of a $N_2CH_3^+$ ion in its mass spectrum.

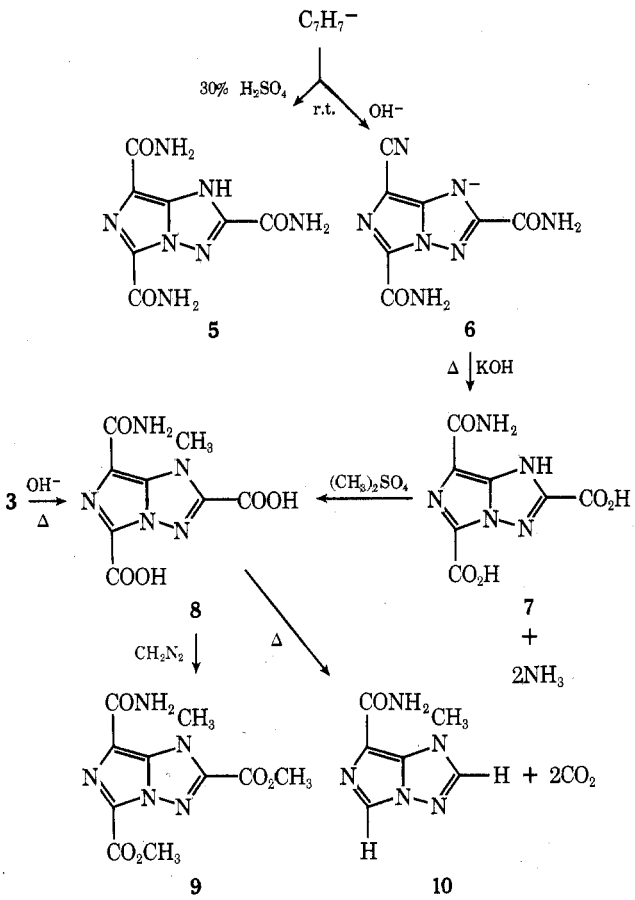
Methylation of the tris(trifluoromethyl) compound **2** gives a 1-methylated to 3-methylated product ratio of 93:7.[4]

Interestingly, methylation of $C_7N_7^-$ with methyl *p*-toluenesulfonate is an equilibrium reaction. The reverse reaction can be observed in the reaction of potassium *p*-toluenesulfonate with a pure single isomer of $CH_3C_7N_7$ to give $C_7N_7^-$ and the 1:3 mixture of methyl isomers.

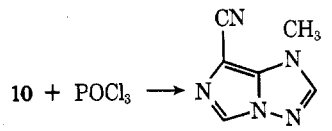


Hydrolysis of $C_7N_7^-$ in both acidic and basic media indicated three nitrile groups. With 30% sulfuric acid at room temperature, a base-soluble triamide (**5**) was formed in high yield. Other acidic conditions afforded mixtures. When $C_7N_7^-$ was allowed to stand for a few minutes at room temperature in 0.6 N hydroxide, the salt of a diamide nitrile **6**, $pK_a \simeq 4.5$, was quantitatively precipitated. Further basic hydrolysis at reflux (1.5 h) afforded 2 mol of ammonia and the tribasic amido dicarboxylic acid (**7**), pK_a = 0.93, 3.66, and 7.34.

Compound **7** was methylated at pH 10 to the methyl amido dicarboxylic acid (**8**), pK_a = 0.99 and 3.78, which was also obtained by base hydrolysis of the major $CH_3C_7N_7$ isomer **3**. Further methylation of **8** with diazomethane gave the trimethyl derivative **9** whose NMR spectrum showed 1 NCH_3 (δ 4.12) and 2 OCH_3 (δ 3.76). The presence of the two carboxylic acid groups was also substantiated by the ready decarboxylation of **8** to the *N*-methyl monoamide compound (**10**) whose NMR spectrum in D_2O showed two heterocyclic CH peaks at δ 8.17 and 7.79 and a NCH_3 at δ 4.00 along with a DOH peak indicating two exchanged hydrogens.



Conversion of the amide function in compound **10** with phosphorus oxychloride to a nitrile group, along with the two lost carboxylic groups, accounts for all three of the original nitrile groups. The NMR spectrum of the *N*-methyl nitrile compound **11** in deuterioacetone showed two heterocyclic CH's at δ 7.76 and 7.25 and the NCH_3 at δ 3.33. An attempt to dehydrate the amide group in **10** with acetic anhydride gave a monoacetyl compound which was hydrolyzed back to **10** in hot 2 N sodium carbonate. The solubility of the acetyl compound in cold base favors a structure with an acetylimide



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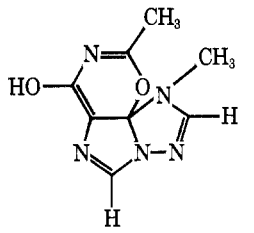

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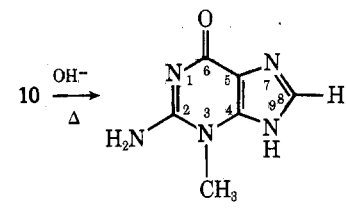
group but the shift in uv from 276 nm in **10** to 299 nm indicates the possibility of an *O*-acetyl derivative or the cyclized structure **12**.

The *N*-methyl monoamide **10** quantitatively isomerizes (30 min) in hot 0.5 N sodium hydroxide to 3-methylguanine **13**.[6] Assuming that there have been no rearrangements in the skeleton of $C_7N_7^-$, compound **10** has two of the original *C*-nitrile groups as CH with the other nitrile as an amide group. This leaves a nucleus of C_4N_4 with a methyl attached to one of the nitrogens. If the carbonyl of the amide group in **10** is the same as the carbonyl at carbon atom 6 in the 3-methylguanine, then a partial structure of **10** is **14**. Assuming minimum rearrangement in the isomerization, structure **15** is also possible for **10** where nitrogen atom c is connected to either carbon a. Structure **15** is eliminated, however, because $C_7N_7^-$ would be the symmetrical **16** which should have a ^{13}C NMR spectrum of five peaks at the most, with two peaks of relative intensity 2.



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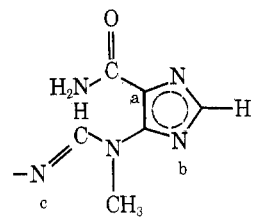

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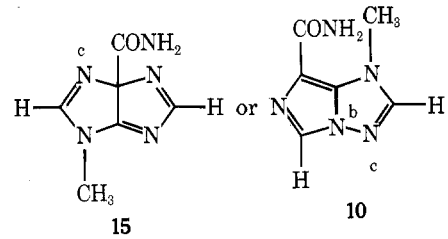

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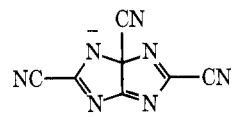

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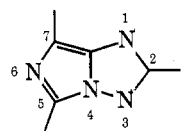
Therefore, barring any gross rearrangements in the degradations, $C_7N_7^-$ contains the heterocyclic nucleus 1*H*- or 3*H*-imidazo[1,5-*b*]-*s*-triazole (**17**) and KC_7N_7 is its 2,5,7-tricyano derivative.



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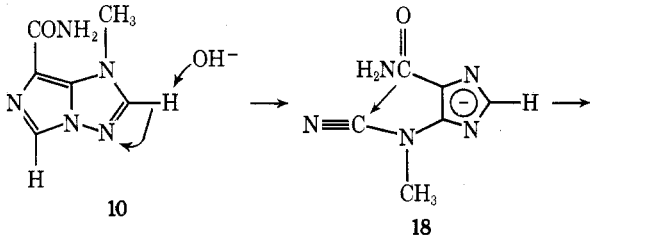
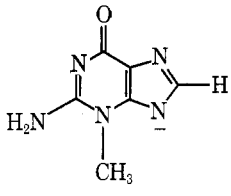
The rearrangement of **10** to 3-methylguanine is postulated to occur as follows:



10 **18**



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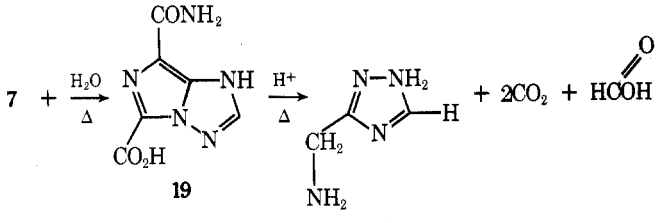
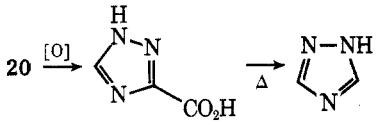
The attack of base on the triazole ring hydrogen gives the *N*-cyano intermediate, **18**, with the formation of the imidazole anion (further stabilized by resonance on the amide carbonyl) as the driving force.[7] This is followed by ring closure and tautomerization to 3-methylguanine.

The presence of the triazole ring is also shown by the acid hydrolysis and degradation of the tribasic amido dicarboxylic acid **7**. Refluxing its monopotassium salt in water (pH 5.60) gave 1 mol of carbon dioxide and the monodecarboxylation



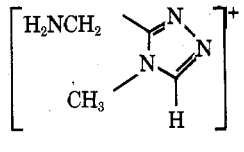
19 **20**



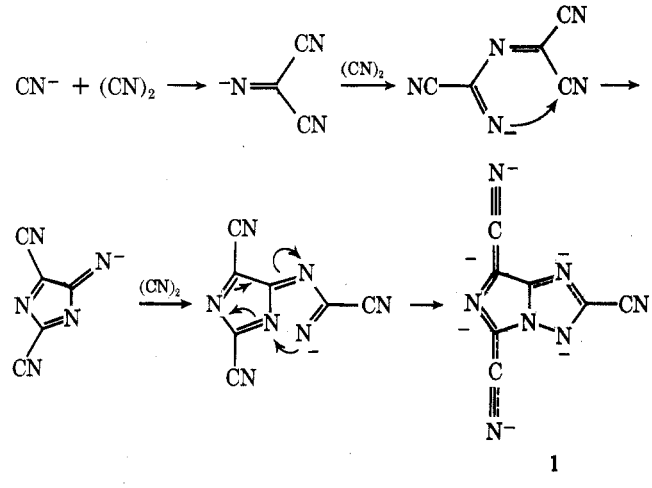
21 **22**

product **19**, which incidentally could be converted to the methyl amide **10** by methylation and decarboxylation. Prolonged treatment with more concentrated acid gave 3 mol of CO_2, 1 mol of formic acid, and 3-aminomethyl-1,2,4-triazole (**20**). Although 3-aminomethyl-1,2,4-triazole is described in the literature[8,9] (as the 2HCl and 2HBr salts), its structure was confirmed by oxidation to 1,2,4-triazole-3-carboxylic acid (**21**),[10] which was decarboxylated to 1,2,4-triazole (**22**).

The triazole ring was further noted in the very slow HCl hydrolysis of the methyl amide **10** to give a crude product characterized only by its lack of uv absorption and its mass spectrum which had a peak at *m/e* 112 as its highest mass peak of reasonable intensity. This corresponds to the fragment



The formation of KC_7N_7 with its structure defined by the chemical transformations described above must occur through the following reactions:



1

The anion is stabilized by having the negative charge delocalized over the ring system as well as two of the cyano groups.

Experimental Section

The mass spectral data were in general obtained using direct injection techniques and the intensities of the *m/e* peaks are grossly variable and only strong or pertinent peaks are listed. Detailed interpretations of the mass spectral data were hampered by the lack of related compounds, but empirical formulas assigned to *m/e* peaks are based on related deuterated isomers.

Potassium 1*H*-Imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile (1, KC_7N_7). A three-necked 1-l. flask equipped with a magnetic stirrer, thermometer, gas inlet tube, and dry ice condenser was flamed out under N_2. Anhydrous potassium cyanide (50 g, 0.8 mol, excess) and 500 ml of anhydrous acetonitrile were placed in the flask. The slurry was cooled under N_2 to 15 °C with a cold-water bath. Cyanogen gas (104 g, 2 mol) was then added over 50–90 min while maintaining the mildly exothermic reaction mixture between 20 and 25 °C. The resulting dark brown-red mixture was allowed to stir at 25 °C for an additional 1 h or until removal of the water bath caused no rise in temperature. The excess potassium cyanide was removed by filtration (washing with 50 ml of acetonitrile). The combined filtrates were carefully diluted with ca. 4 l. of ether to effect precipitation of a brown, water-sensitive, flocculent solid which was removed by filtration. The clear orange solution was concentrated under vacuum to give 135 g of **1** as an orange solid. Three recrystallizations from acetonitrile–dioxane (1:4 by volume) using Darco gave 110 g of colorless **1** 2 dioxane. An additional 55 g of colorless product was obtained from the mother liquors for a total yield of 165 g (63%). The dioxane (44.3% by weight) was removed by drying at 140 °C (refluxing xylene) for 2 h under vacuum: uv (H_2O) max 313 nm (ϵ 16 600), 279 (11 300), and 220 (33 500), ir 2250 (m), 2220 (s), 2170 (w), 1560 (s), 1420 (m), 1380 (s), 1305 (s), 1290 (w), 1210 (s), 1185 (s), 997 (m), 740 (m), 715 (w), and 695 cm^{-1} (w). (Raman was not taken because of the fluorescence of $C_7N_7^-$ in the 430-nm range.)

The ^{13}C NMR spectrum of **1** in water was determined using a saturated solution (ca. 60%) of the dioxane-solvated salt in water. Using the dioxane as an internal standard, seven peaks were observed at 87.8, 102.0, 110.7, 112.6, 114.9, 141.2, and 151.3 ppm downfield from Me_4Si.

Anal. Calcd for C_7N_7K: C, 38.0; N, 44.3; K, 17.7; mol wt, 221. Found: C, 37.8, 37.9; N, 31.2, 37.0; K, 17.3; mol wt (by acetonitrile boiling point), 115–116 (indicating dissociation).

We could not obtain satisfactory nitrogen analyses on the anhydrous potassium salt presumably because of nitride formation. However, other salts described below obviated this problem.

This preparation has been run on two to three times this scale with yields varying from 45 to 65%. The 1 2 dioxane salt so obtained could be converted to the dihydrate by exposure to a stream of moist air. It was most convenient to store **1** as the dioxane salt since the dioxane (44% by weight) could easily be removed at 130 °C (refluxing xylene) under vacuum for 2 h, whereas the dihydrate was only difficultly dried (160 °C, 8 h or longer).

Other salts of $C_7N_7^-$ were prepared as described below. Aside from the sodium salt, they were prepared either by metathesis or by neutralizing the free acid HC_7N_7 (preparation below) with a carbonate or hydroxide of the desired metallic ion. An example of each procedure is illustrated. The others listed were prepared similarly and had satisfactory analyses.

Sodium C_7N_7. This was prepared from sodium cyanide and cyanogen in essentially the same manner as above at 25–29 °C. The crude reaction solution was passed through an alumina column (ethyl acetate eluent) to remove the bulk of the colored impurities. Recrystallization from dioxane–acetonitrile (2:1 by volume) gave the colorless salt, no mp <390 °C. A sample was analyzed as the hydrate (by alternate drying at 130 °C and exposing to moist air).

Anal. Calcd for $C_7N_7Na \cdot 2H_2O$: C, 34.9; H, 1.7; N, 40.7. Found: C, 34.8, 34.9; H, 1.9, 1.9; N, 40.7, 40.7.

Tetramethylammonium C_7N_7. A solution of 6.61 g (25.5 mmol) of 1 $2H_2O$ in 35 ml of water was treated with 5 g (excess) of tetramethylammonium chloride in 30 ml of water. The resulting precipitate was redissolved by heating the mixture to boiling. Cooling gave white, feathery needles, mp >300 °C, weighing 6.30 g (96%) after collecting, washing (25 ml of ice water), and air drying. It was recrystallized from water.

Anal. Calcd for $C_{11}H_{12}N_8$: C, 51.5; H, 4.7; N, 43.7. Found: C, 51.6; H, 4.7; N, 43.6.

Zinc $(C_7N_7)_2$. In an aqueous solution (60 ml) of 4.57 g (25 mmol) of HC_7N_7 (see below), zinc carbonate (1.57 g) was dissolved in small portions until the pH became 4. The slightly cloudy solution was filtered, treated with Darco (if necessary), and concentrated in vacuo at 80 °C to a dry foam which upon crushing and drying gave 4.3 g of free-flowing white powder.

Anal. Calcd for $C_{14}N_{14}Zn \cdot 1.5H_2O$: C, 36.8; H, 0.7; N, 43.0; Zn, 14.3. Found: C, 36.6; H, 0.4; N, 42.9; Zn, 14.2.

Lithium $C_7N_7 \cdot 2H_2O$: white powder, mp 320 °C dec.

Manganous $(C_7N_7)_2 \cdot 2C_2H_5OH$: yellow powder, darkening above 200 °C.

Cupric $(C_7N_7)_2 \cdot H_2O$: chocolate brown powder, darkening above 300 °C (water insoluble).

Silver C_7N_7: white needles from acetonitrile–water (water insoluble), no mp <300 °C.

Tetraethylammonium C_7N_7: white needles, mp 221–222 °C (7:1 H_2O–acetonitrile).

Trimethyloctadecylammonium C_7N_7: mp 118–119 °C (H_2O).

***N*-Methylphenazinium C_7N_7:** mixture of orange-yellow and deep red needles (3:1 H_2O–acetonitrile). Upon standing the orange needles turned red. Both forms behaved similarly upon heating, turned orange-red at 70–80 °C, and melted with decomposition at 159 °C.

Trimethylsulfonium C_7N_7: needles (2-propanol), mp 194–197 °C with bubbling to give mixture of methyl C_7N_7 isomers (see below).

Methyltriphenylphosphonium C_7N_7: white platelets, mp 152–153 °C (3:1 H_2O–ethanol).

1*H*-Imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile (HC_7N_7). A strong acid ion-exchange column was prepared by taking 100 ml of resin [Rexyn RG 50 (H), exchange capacity 1.9 mequiv/ml] and washing with water, 100 ml of 2 N HCl, and then water until pH 6. A solution of 1 $2H_2O$ [made from 39.7 g (0.1 mol) of KC_7N_7 2 dioxane by air drying overnight, weight loss 14 g] in 100 ml of water was passed through the column, collecting a total of 400 ml of solution washings. Concentration of the strongly acidic aqueous solution on a Rinco evaporator at 60 °C gave 19.0 g of crude HC_7N_7 as a red solid (theory 18.3 g). The uv spectrum of this material in water indicated it to be 96% pure.

An analytical sample was obtained by careful recrystallizations from anhydrous acetonitrile (1:5 w/v with 40% weight loss each time) to give almost white prisms, no melting point, turned dark brown by 200 °C and black at 250 °C. Recrystallization could also be effected from ethyl acetate–chloroform (35% weight loss) to give salmon-pink platelets: ir (KBr) 3225 (broad, m), 2260 (s), *1622 (s)*, 1505 (m), 1480 (m), 1450 (s), 1410 (m), 1332 (s), 1323 (sh, s), 1244 (w), 1227 (m), 1208 (s), 1185 (m), 1002 (m), 971 (w), 797 (m), 722 (w), 710 (m), 700 (m), and 657 cm^{-1} (s); uv (H_2O) same as I; (EtOH) max 325 nm (ϵ 13 000), 313 (17 300), 279 (11 700), and 229 (30 500); (CH_3CN) max 305 nm (ϵ 6900), 282 (5100), 262 (12 600), and 219 (27 000); NMR (Me_4Si internal) one sharp peak which shifted with solvent and traces of water, in CD_3COCD_3, δ 13.36; in CD_3SOCD_3, δ 10.28; and in CH_3CN, δ 8.98; MS *m/e* 183 (parent), with other strong peaks at *m/e* 131, 103, 79, 77, 53, and 38.

Anal. Calcd for C_7HN_7: C, 45.9; H, 0.6; N, 53.6; mol wt, 183. Found: C, 45.3; H, 0.9; N, 53.2, 53.6; neut equiv, 185.

Molecular weight, measured by vapor pressure osmometry in acetonitrile, was found to be 142, whereas by freezing point lowering in dimethyl sulfoxide, strong dissociation was noted in the values of 91 and 108, varying with concentration.

The pK_a was determined spectrophotometrically in acetonitrile, using tetraalkylammonium C_7N_7 salts.[11] Picric acid was used as hydrogen ion indicator as well as source of hydrogen ion. The pK_a values of HC_7N_7 in acetonitrile were 5.55 and 5.32. When converted to aqueous scale, using picric acid as conversion reference standard, the pK_a of HC_7N_7 is -3.1 ± 0.2. The validity of this conversion is based on the assumption that $C_7N_7^-$ behaves similarly to picrate ion in both acetonitrile and water.

Chlorination of 1. To a solution of 4.42 g (20 mmol) of KC_7N_7 in 35 ml of acetonitrile at 10 °C, 22 mmol of chlorine gas was added in a slow flow of N_2. The resulting colorless mixture was filtered to remove the bulk of the KCl. Concentration gave a very viscous oil which was then evaporatively distilled at 140 °C (0.1 mm). The colorless distillate of **1-chloro-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile** was resinous at room temperature and quite soluble in most organic solvents.

Anal. Calcd for C_7ClN_7: Cl, 16.3. Found: Cl, 16.2. 16.1.

The uv spectrum in dioxane showed a max of 285 nm (*k* varied markedly with concentration indicating strong π complexing). The addition of water caused the immediate appearance of those peaks characteristic of the $C_7N_7^-$ ion. The mass spectrum showed strong peaks (reported as ^{35}Cl peaks only) at *m/e* 217 ($C_7N_7Cl^+$), 189 ($C_7N_5Cl^+$), 182 ($C_7N_7^+$), *137* ($C_5N_3Cl^+$), 128 ($C_6N_4^+$), *102* ($C_5N_3^+$), 85 (C_3NCl^+), etc. It is the presence of the *m/e* 137 peak ($P - C_2N_4^+$) on which the 1-isomer structure is assigned.

Methylation of 1. A solution of 158.8 g (0.40 mol) of 1 2 dioxane in 1 l. of CH_3CN and 59.5 g (0.47 mol) of dimethyl sulfate was heated at reflux for 2 h with stirring. The solid, which deposited in the hot solution, was collected after cooling to 5 °C, thoroughly washed with 350 ml of CH_3CN, and dried under N_2 to give 54.1 g (90%) of methyl potassium sulfate. Concentration of the filtrate gave a gummy solid, which was washed with 250 ml of H_2O to give 77.0 g (97%) of a mixture of 1- and 3-methyl isomers, mp 180–198 °C. Four successive 100-ml extractions with tetrahydrofuran afforded 40.2 g of almost pure **1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile (3)**, mp 231–234 °C. An analytical sample, mp 234–235 °C, was obtained after three crystallizations from methyl ethyl ketone (MEK). Concentration of the tetrahydrofuran extracts, followed by fractional crystallization of the total mixture from MEK, afforded a total of 49.7 g of pure 1-methyl $C_7N_7^-$, mp 234.5–235 °C, in the head fractions: uv (EtOH) max 298 nm (ϵ 6600), 264 (12 500), and 221 (22 400); ir (KBr) 1630 cm^{-1}; NMR (CD_3COCD_3, Me_4Si internal) δ 4.27; MS *m/e* 197 (parent), other strong peaks at *m/e* 15 (CH_3^+), 38 (C_2N^+), 40 ($C_2H_2N^+$), 41 (CH_3CN^+), 52 ($C_2N_2^+$ and $C_3H_2N^+$), 64 ($C_3N_2^+$), 66 ($CH_2C_2N_2^+$), 67 ($CH_3C_2N_2^+$), 93 ($CH_3C_3N_3^+$), 102 ($C_5N_3^+$), 116 ($CH_2C_5N_3^+$), and 117 ($CH_3C_5N_3^+$). Empirical formulas were assigned from MS of $CD_3C_7N_7$ (1 isomer).

Anal. Calcd for $C_8H_3N_7$: C, 48.7; H, 1.5; N, 49.7. Found: C, 48.6, 48.7; H, 1.8, 1.7; N, 49.6, 49.8, 49.9.

Pure **3-methyl-3*H*-imdiazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile (4)**, mp 179.5–181 °C, was obtained from the tail fractions. An analytical sample, mp 182–183 °C (crystalline transition at 176 °C), was obtained by two recrystallizations from 1:1 chloroform–ethyl acetate (25 ml/g): uv (EtOH) max 336 nm (ϵ 20 900), 325 (16 600), 271 (3100), 248 (16 700), 240 (15 000), and 217 (22 100); ir (KBr) 1610 cm^{-1}; NMR (CD_3COCD_3, Me_4Si internal) δ 4.51; MS *m/e* 197 (parent), other strong peaks at *m/e* 15 (CH_3^+), 38 (C_2N^+), 43 ($CH_3N_2^+$), 52 ($C_2N_2^+$), 64 ($C_3N_2^+$), 66 ($C_3H_2N_2^+$), 93 ($C_4H_3N_3^+$), 102 ($C_5N_3^+$), and 145 ($CH_3C_5N_5^+$).

Anal. Found: C, 48.9, 48.7; H, 1.6, 1.7; N, 49.6, 49.7.

Analysis by NMR of the crude reaction product showed an isomer ratio of 3:1 for 1-:3-methyl isomers. Both isomers could be sublimed at 120–130 °C (0.1 mm), with no evidence (by NMR) for thermal interconversion at temperatures up to 230 °C. (The 3-methyl isomer slowly darkened in the melt at this temperature.) The same 3:1 ratio was noted when methylation was carried out with methyl iodide, methyl tosylate, trimethyloxonium fluoroborate, trimethylsulfonium iodide, and by reaction of diazomethane with HC_7N_7.

1-Methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarboxamide. To 10 ml of concentrated HCl was added 0.65 g of powdered **3** and the mixture was stirred for 36 h. After dilution with 10 ml of water, the solid was collected and washed with 95% ethanol and ether. The crude hydrolysate (0.90 g) was heated in dimethylformamide on a steam bath and filtered. After thorough drying, 0.63 g (79%) of the triamide was obtained as a microcrystalline solid, no mp <350 °C, ir no C≡N.

Anal. Calcd for $C_8H_9N_7O_3$: C, 38.2; H, 3.6; N, 30.1. Found: C, 38.6; H, 3.8, 3.5; N, 37.8, 38.1.

1-Benzyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile. A solution of 3.38 g of 1 and 10 ml of benzyl chloride in 25 ml of 1,2-dimethoxyethane was heated at reflux for 5 days. After cooling, 1.09 g of KCl was removed by filtration. Concentration of the filtrate gave a mixture of oil and solid which was slurried with ether. The resulting solid was collected and recrystallized to give 3.0 g of white needles, mp 149–152 °C.

Anal. Calcd for $C_{14}H_7N_7$: C, 61.5; H, 2.6; N, 35.9. Found: C, 61.2, 61.2; H, 2.6, 2.5; N, 35.2, 35.6.

1*H*-Imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarboxamide (5). To 25 ml of warm 30% (by weight, 20% by volume) H_2SO_4 was added 1.00 g of HC_7N_7. After standing overnight, the clear solution was diluted with 1 l. of H_2O to give **5** as a gelatinous precipitate. The solid was collected (very slow filtration) and washed extensively with H_2O. After air drying the white powder (electrostatic) weighed 1.23 g (95%). An analytical sample was dried at 80 °C for 12 h. The identical product was obtained using KC_7N_7 2 dioxane: uv (pH 13) max 335 nm (ε 20 600), 295 (8400), and 238 (24 400).

Anal. Calcd for $C_7H_7N_7O_3$: C, 35.4; H, 3.0; N, 41.3. Found: C, 35.5, 35.7; H, 2.9, 2.8; N, 41.6.

7-Cyano-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5-dicarboxamide (6). To 3.66 g (20 mmol) of HC_7N_7 in 7 ml of H_2O was added 60 ml of 1.000 N NaOH. The clear solution was stirred for 20 min and to the resulting slurry was added 40 ml of 1.000 N HCl. The pH was adjusted to 7 by adding 0.5 ml of saturated sodium bicarbonate. The entire mixture was heated to boiling and additional water was added to give a clear solution (total volume 350 ml). Cooling slowly to room temperature gave 3.51 g of the **sodium salt of 7-cyano-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5-dicarboxamide (6)** as fine needles, no mp <400 °C. An analytical sample was obtained by two recrystallizations from water. The free acid could be prepared by digestion in hot 30% acetic acid: uv (pH 12) max 323 nm (ε 17 700), 290 (8700), and 234 (29 600) with fluorescence at 491 nm (356-nm excitation); ir (KBr) 2230 (C≡N), and characteristic $CONH_2$ at 3160–3550 and 1695 cm^{-1}.

Anal. Calcd for $C_7H_4N_7O_2Na$: C, 34.9; H, 1.7; N, 40.7; Na, 9.5. Found: C, 34.4, 34.6; H, 2.1, 2.0; N, 40.4, 40.6; Na, 9.2.

7-Carboxamido-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5-dicarboxylic Acid. (7). A solution of 39.7 g (0.10 mol) of **1** 2 dioxane in 200 ml of H_2O and 200 ml of 20% KOH (0.60 mol) was heated with stirring in an apparatus designed to collect distillate in 2 N H_2SO_4. A precipitate formed in a few minutes which slowly dissolved upon distilling over the evolved ammonia. Additional water was added as needed to keep the volume at 450 ml. After 1.5 h, a total of 0.20 ml of ammonia had been collected, and a considerable amount of solid was present in the hot reaction solution. The reaction mixture was cooled to 35 °C and 425 ml of 2 N HCl was slowly added with stirring. The initial solid dissolved and another precipitate formed during the acidification. The precipitate was collected, washed with water, ethanol, and ether, and air dried to give 28.8 g (theory 27.7 g) of white, powdery **monopotassium salt of 7-carboxamido-1*H*-imidazo-[1,5-*b*]-*s*-triazole-2,5-dicarboxylic acid,** no melting point darkening at 210 °C, evolved gas at 255–260 °C. Thin layer chromatography (TLC) on cellulose using 0.2 N NH_4OH showed one major fluorescent spot with three minor slower spots. Titration required 1 equiv of base to give solution and another 1 equiv for titrating acidity of pK_a 7.40 with neut equiv 271 (theory 277).

Anal. Calcd for $C_7H_4N_5O_5K$: C, 30.3, H, 1.5; N, 25.3; K, 14.1. Found: C, 30.8; H, 1.9; N, 26.2; K, 12.8.

A small sample (5 g) was purified as the dipotassium salt by taking up in 60 ml of 3% KOH and 10 ml of saturated KCl. The dark solution was saturated with CO_2 to precipitate 4.3 g of light-blue crystals. Four recrystallizations from 1:1 isopropyl alcohol–H_2O removed the blue color and gave 1.3 g of the dipotassium salt of **7** as white needles (TLC pure), no melting point, darkened by 340 °C. The pK_a (spectrophotometric) = 0.93, 3.66, 7.34 with H_3A having max at 311 nm (ε 12 400), 276 (9700), 221 (21 200); H_2A^- at 307 nm (ε 16 000), 270 (7500), 220 (19 900); HA^{2-} at 302 nm (ε 11 900), 268 (9300), 238 (13 400), 204 (20 000); and A^{3-} at 328 nm (ε 22 300), 283 (6200), 237 (21 400).

Anal. Calcd for $C_7H_3N_5O_5K_2$: C, 26.7; H, 1.0; N, 22.2; K, 24.8. Found: C, 26.7, 26.6; H, 1.1, 1.3; N, 22.4, 22.3; K, 25.1.

1-Methyl-7-carboxamido-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5-dicarboxylic Acid (8). From 7. The monopotassium salt (2.72 g, 10 mmol) of **7** suspended in 35 ml of H_2O was dissolved by adding 6 N NaOH. Dimethyl sulfate (15 g, excess) and 6 N NaOH were added over 3 h with stirring at 36 °C while maintaining the pH between 9 and 10. After stirring overnight, the solution (pH 9.5) was heated to boiling, filtered, and acidified with 20 ml of 2 N HCl. The resulting precipitate was collected and washed with water to give 1.75 g (69%) of white, powdery **8**, evolved gas at 180 °C changing from powder to a crystalline form and then melted at 280–283 °C (darkening 260–280 °C). This material was identical (ir, TLC, and uv) with material obtained below.

From 3. In a 300-ml flask, equipped with a magnetic stirrer, addition funnel, and Claisen distillation head, was placed 11.82 g (60 mmol) of pure 1-methyl-1*H*-imidazo-[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile (**3**). A NaOH solution (7.30 g, 180 mmol, in 100 ml of H_2O) was added in one portion. Heating the mixture caused rapid solution followed by formation of precipitate. After 1.5 h, 20 ml of distillate was collected in 2 N H_2SO_4 and shown to contain 1l9.3 mmol of evolved ammonia. The reaction mixture was diluted with 100 ml of EtOH and cooled to 5 °C. The product was collected and washed with 100 ml of 50% ethanol, 100 ml of absolute EtOH, and ether. Air drying gave 18.04 g of the disodium salt of **8** as a white, fluffy solid, no mp below 400 °C. An analytical sample was obtained by two recrystallizations from 1:1 EtOH–H_2O (1 g in 70 ml) followed by vacuum drying at 80 °C overnight. Two different solvated modifications were sometimes obtained with different ir spectra, but reverted to the same material upon drying: NMR (D_2O,Me_4Si external) δ 4.73 (DOH exchange peak, wt 2.3) and 4.16 (wt 3).

Anal. Calcd for $C_8H_5N_5O_5Na_2$: C, 32.3; H, 1.7; N, 23.6; Na, 15.5. Found: C, 31.7, 31.7; H, 1.9, 1.7; N, 23.8, 23.7; Na, 15.1.

The disodium salt was converted to the free acid by dissolving 1.0 g in 50 ml of warm (60 °C) H_2O and acidifying with 2 N HCl until pH 1. The light cream precipitate (monohydrate by analysis) was collected and dried at 64 °C to give 0.69 g of **8**, evolved gas at 175–180 °C and melted with some decomposition at 275–280 °C. Drying at higher temperatures caused slow loss of CO_2. Uv (pH 7 and 10) max 302 nm (ε 14 200), 273 (sh, 8900), and 250 (13 900); (pH 3) max 307 nm (ε 16 400), 272 (6600), and 247 (12 700); (2 N HCl) max 313 nm (ε 12 300), 278 (9900), 245 (sh, 12 900), and 224 (17 900); pK_a (spectrophotometric) = 0.99 and 3.78.

Anal. Calcd for $C_8H_7N_5O_5$: C, 35.4; H, 3.4; N, 25.8; neut equiv, 135.5. Found: C, 35.3; H, 3.6; N, 25.6; neut equiv, 137, 138.

Reaction of 8 with Diazomethane. To a slurry of 253 mg (1 mmol) of **8** in 20 ml of ethanol was added 3 mmol of ethereal diazomethane. After stirring for 2 days, the solid phase was collected and washed with benzene to give 191 mg of **dimethyl 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5-dicarboxylate (9),** mp 198–200 °C dec. An analytical sample, mp 218–219 °C dec, was obtained by recrystallization from DMF–H_2O and drying overnight at 64 °C: uv (H_2O and 2 N HCl) max 315 nm (ε 11 600), 280 (11 300), and 228 (19 600); NMR (CF_3COOH, Me_4Si external) δ 4.12 (wt 3) and 3.76 (wt 6).

Anal. Calcd for $C_{10}H_{11}N_5O_5$: C, 42.7; H, 4.0; N, 24.9. Found: C, 42.2; H, 4.4; N, 25.0, 24.7.

7-Carboxamido-1*H*-imidazo[1,5-*b*]-*s*-triazole-2- (or 5-) carboxylic Acid (19). A 150-ml solution of the monopotassium salt of **7** was prepared by dissolving 10 g (33 mmol by titration) of the crude salt in water to which enough dilute KOH was added to give a clear solution and carefully adjusting the pH to exactly 5.60. The clear, light-blue solution was then heated to reflux for 3 h under N_2. (In air, there was considerable darkening.) The pH had changed to 9.4. The still-hot solution was acidified with 2N HCl to pH 6 and cooled. The solid was collected, washed with water and ethanol, and dried to give 7.65 g of crude **potassium 7-carboxamido-1*H*-imidazo[1,5-*b*]-*s*-triazole-2- (or 5-) carboxylate.** An analytical sample was obtained as glistening platelets, mp darkening above 340 °C, by recrystallizations under N_2 from CO_2-free water. (Recrystallization in air gave blue crystals.) The product was dried at 80 °C for 15 h, uv max (H_2O) 280 nm (ε 6120) and 255 (12 700).

Anal. Calcd for $C_6H_4N_5O_3K\cdot H_2O$: C, 28.7; H, 2.4; N, 27.9; K, 15.6. Found: C, 29.0, 28.9; H, 2.3; N, 27.4, 27.6; K, 15.3.

The free acid **19** was prepared by acidification of a dilute solution of the monopotassium salt. The precipitate was collected, washed, and dried at 80 °C for 6 h to give a white, amorphous powder, no mp <350 °C (darkened at 260 °C); uv (pH 1) max 279 nm (ε 7200) and 240 (shoulder, 8000); (pH 10) max 310 nm (ε 13 900) and 263 (7400). Potentiometric titration indicated two buffer zones with pK_a = <4 and 7.25 with neut equiv 189 and 194, respectively (theory, 195).

Anal. Calcd for $C_6H_5N_5O_3$: C, 36.9; H, 2.6; N, 35.9. Found: C, 36.8; 36.4; H, 2.8, 3.1; N, 34.9, 35.6, 35.8.

7-Carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2- (or 5-) carboxylic Acid. 19 (3.1 g) was dissolved in 25 ml of water and 6 N NAOH. Dimethyl sulfate (15 ml excess) and 6 N NaOH were added in alternate small portions while maintaining the pH between 9 and 10 and the temperature at 35 °C. The solution was acidified to pH 4 with 2 N HCl and the product collected. The crude product was taken up in 50 ml of hot 0.1 N NaOH, acidified to pH 7, and cooled. The **sodium 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2- (or 5-) carboxylate** was collected, washed, and dried to give 1.85 g of white needles, no mp <400 °C. An analytical sample was recrystallized from water: NMR (CF_3COOH, Me_4Si external) δ 8.67 (wt 1) and 4.13 (wt 3).

Anal. Calcd for $C_7H_6N_5O_3Na$: C, 36.4; H, 2.6; N, 30.3. Found: C, 36.0, 36.0; H, 3.0, 3.1; N, 30.3, 30.7, 30.5.

The free acid was prepared by acidifying a warm solution of the salt with 2 N HCl and cooling. The solid was collected, washed, and dried

at 64 °C for 8 h to give the acid as small cubes: evolves CO_2 at 195 °C and melts with decomposition at 270 °C; uv (pH 7) max 261 nm (ϵ 12 400) and 285 (sh, 7900); (2 N HCl) 285 nm (ϵ 6200) and 244 (8300). Attempts to determine the pK_a spectrophotometrically were unsuccessful giving a wide range of values (1.20–1.60) with shifts of the maxima indicating further protonation in the strong acids.

Anal. Calcd for $C_7H_7N_5O_3$: C, 40.2; H, 3.4; N, 33.5; neut equiv, 209. Found: C, 40.0, 39.7; H, 3.5, 3.5; N, 33.5; neut equiv, 208.

Hydrolysis of 7 with Acid. A mixture of 14.0 g (50 mmol) of the monopotassium salt of **7**, 100 ml of water, and 42.0 ml of 6 N H_2SO_4 was placed in a 500-ml flask fitted with a reflux condenser leading to three gas scrubbing towers in series with 100 ml of 1.0 N NaOH solution in each. A slow N_2 sweep was maintained through a tube leading down the condenser. The reaction mixture (thick slurry) was then heated to reflux for 12 h. After 3 h, the initially rapid gas evolution appeared to subside and a clear solution (5 h) gradually formed. Analyses of the trapping solutions indicated the evolution of 147 mmol of carbon dioxide (3 equiv).

The hot, clear reaction solution was then diluted with ethanol until turbid (300 ml) and cooled. The crystalline solid mixture of needles and amorphous powder was collected and dried to give 3.86 g of potassium sulfate with some ammonium ion present (ir and titration). The mother liquors were warmed and diluted with additional ethanol (total volume 1 l.) until turbid. Cooling afforded 7.43 g of crude **3-aminomethyl-1,2,4-triazole H_2SO_4 (20).** An additional 3.22 g was obtained from workup of the mother liquors. An analytical sample was prepared by three recrystallizations from 85% ethanol (100 ml/g) and dried at 80 °C for 5 h: NMR (D_2O, Me_4Si external) δ 8.88 (wt 1), 4.86 (DOH, wt 5.4), and 4.47 (wt 2). Potentiometric titration indicated three buffer zones corresponding to <4, 7.8 and 9.9 with neut equiv values of 204, 204, and 190, respectively (theory, 196).

Anal. Calcd for $C_3H_8N_4O_4S$: C, 18.4; H, 4.1; N, 28.6; S, 16.3. Found: C, 18.1, 18.3; H, 4.1, 4.1; N, 28.1, 28.4; S, 16.6, 16.4.

In another experiment the original hydrolysis solution was distilled to a low volume, fresh water was added, and the solution was redistilled successively until no more acid was collected in the distillate. There was obtained 99% of 1 equiv of volatile acid per mole of starting material. Concentration to dryness of the resulting titrated solution gave sodium formate (identified by ir).

The free base **20** was isolated by dissolving the crude H_2SO_4 salt (10.0 g) in 150 ml of H_2O and 35 ml of 6 N NaOH. The solution was boiled until no more ammonia was evolved. The pH was then adjusted to 9.00 with 2 N H_2SO_4. Concentration of the clear solution to dryness followed by sublimation (130 °C, 0.1 mm) afforded 4.25 g of **3-aminomethyl-1,2,4-triazole (20)** as a very water-soluble white solid: mp 104–143 °C; NMR (D_2O, Me_4Si external) δ 8.13 (wt 1), 4.74 (DOH, wt 3), and 3.92 (wt 2); MS parent at *m/e* 98 and base peak at *m/e* 30 ($NH_2CH_2^+$) with other strong peaks at *m/e* 28, 42, 70 ($P - N_2^+$), and 97 ($P - H^+$).

Anal. Calcd for $C_3H_6N_4$: C, 36.7; H, 6.2; N, 57.1. Found: C, 37.0, 36.8; H, 6.0, 6.0; N, 57.4, 57.4, 57.5.

Oxidation of 20. The crude 3-aminomethyl-1,2,4-triazole H_2SO_4 (4.66 g) in 50 ml of 3 N NaOH was oxidized by adding 7.95 g of potassium permanganate in small portions while stirring and heating on a hot plate for 1 hr. The clear basic filtrate was acidified first to pH 4, and then an additional 6.0 ml of 6 N H_2SO_4 was added to give a precipitate. The 1,2,4-triazole-3-carboxylic acid (**21**) was collected, washed, and dried to give 2.31 g (86%) of fine white needles, mp 140 °C with evolution of gas (reported[10] 137 °C); NMR (D_2O with 1 drop NaOH) δ 8.33 and 4.86 (DOH).

This structure was confirmed by decarboxylation at 140 °C and sublimation of the residue to give 1,2,4-triazole (**22**), mp 120 °C (reported[10] 121 °C), identified by its ir spectrum.[12]

1-Methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-7-carboxamide (10). **8** monohydrate (705 mg, 2.60 mmol) was placed in a micro sublimer and covered with a loose cotton plug. Sublimation under vacuum at 180–240 °C was accompanied by initial CO_2 evolution to give 306 mg (71%) of **10**, mp 281–285 °C dec. Two recrystallizations from water (7.5 ml) followed by sublimation at 210–220 °C gave an analytical sample (217 mg): mp 289–292 °C dec; uv (pH 7 and 12) max 276 nm (ϵ 17 000) and (pH 1) max 273 nm (ϵ 15 200) and 232 (6900); NMR (CF_3COOH, Me_4Si external) δ 8.68 (wt 1), 8.17 (wt 1), and 3.89 (wt 3); (D_2O at 80 °C, Me_4Si external) δ 8.17 (wt 1), 7.79 (wt 1), 4.33 (DOH, wt 2.5), and 4.00 (wt 3); MS parent at *m/e* 165 and base at *m/e* 109. (From the MS of **10** containing CD_3 group, this peak contains the CD_3 group and is $P - CCONH_2^+$.)

Anal. Calcd for $C_6H_7N_5O$: C, 43.6; H, 4.3; N, 42.4. Found: C, 43.8; H, 4.4; N, 42.3, 42.1.

When the above reaction was carried out on a larger scale (12–15 g), the sublimation required 5–6 days to give **10** in 65% yield. Attempts to isolate **10** from the crude decarboxylated mixture by recrystallizations resulted in severe loss.

10 appears to form a crystalline hydrochloride when recrystallized from HCl which reverts to free amide on treatment with $NaHCO_3$. Potentiometric titration gave a pK_a of 1.82 ± 0.04 but this may be a mirage[13] (5×10^{-3} N at halfway titration).

Under the same conditions, decarboxylation of 1-methyl-7-carboxamido-1*H*-imidazo[1,5-*b*]-*s*-triazole-2- (or 5-) carboxylic acid (**19**) gave **10.**

1-Methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-7-carbonitrile (11). A mixture of 1.65 g (10 mmol) of **10** and 12 ml of phosphorus oxychloride was refluxed for 2 h. The original thin slurry became very thick with solid which slowly dissolved to give a black solution. The excess phosphorus oxychloride was removed under vacuum and the tarry residue was treated with 12 ml of ice and water. The black solution was neutralized to pH 7.0 with dilute NaOH. The greenish solid was collected, washed, and dried to give 0.78 g (53%) of crude **11.** Sublimation (160 °C, 0.05 mm) removed the color. An analytical sample, mp 219–220 °C, was obtained by recrystallizations from dichloroethane (90 ml/g) followed by sublimation: uv (pH 1 and 11) max 260 nm (ϵ 12 200) and 235 (10 400); (2 N HCl) max 265 nm (ϵ 21 000) and 227 (7000); ir (KBr C≡N at 2205 (s), C=C and C=N at 1620 (s), 1570 (w), and 1520 (m), with other strong bands at 1185, 1080, 1060, and 860 cm^{-1}; NMR (CD_3COCD_3, Me_4Si external) δ 7.76 (wt 1), 7.25 (wt 1), and 3.33 (wt 3); MS *m/e* 147 (parent, base), 15, 28, 41 (CHN_2^+), 53, 68, 77 ($P - C_2H_4N_3^+$), 91 ($P - C_2H_4N_2^+$), 107, and 120 ($P - HCN^+$).

Anal. Calcd for $C_6H_5N_5$: C, 49.0; H, 3.4; N, 47.6. Found: C, 48.7, 48.8; H, 3.2, 3.3; N, 47.8, 47.9, 48.4.

Using CF_3OOH as a solvent, peaks were at δ 8.70, 8.16, and 3.64 in a ratio of 1:1:4. The latter peak was resolved to two peaks with a 2.2-Hz separation. Dilution with D_2O caused the δ 3.64 peak to coalesce to one peak but the relative area remained 4. Apparently, trifluoroacetic acid reacted with the compound to give a new CH bond (nonexchangeable).

Acetylation of 10. A mixture of 200 mg of **10** and 5 ml of acetic anhydride was refluxed until solution occurred. The solvent was evaporated and the residue sublimed to give 236 mg of **acetyl 1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-7-carboxamide,** mp 207–212 °C. An analytical sample, mp 220–221 °C, was obtained by recrystallization from water: uv (pH 1) max 297 nm (ϵ 20 600) and 239 (3600); (pH 7) max 299 nm (ϵ 23 600) and 250 (2900); (pH 11) max 298 nm (ϵ 17 500) and 286 (sh, 16 000, concentration dependent); NMR (CF_3COOH, Me_4Si external) δ 8.20, 7.70, 3.43, and 1.65 (wt 1:1:3:3, respectively); MS parent at *m/e* 207* with base peak 149* ($P - CH_3CONH^+$), other strong peaks at 15*, 28, 42*, 43, 53, 109*, 122*, 136*, 165*, and 192*. (Peaks marked contain the NCH_3 group as shown by the MS of the NCD_3 compound.)

Anal. Calcd for $C_8H_9N_5O_2$: C, 46.4; H, 4.4; N, 33.8. Found: C, 46.4, 46.2; H, 4.4, 4.4; N, 33.9.

Acidifying the pH 11 uv solution showed that no change had occurred. However, dissolving the acetyl compound in hot 1 N sodium carbonate caused a rapid precipitation of the unacetylated material **10.**

Rearrangement of 10 to 3-Methylguanine (13). A mixture of 990 mg (6 mmol) of **10** and 30 ml of 0.5 N NaOH was heated at reflux for 1 h (reaction complete after 30 min). The solution was cooled and acidified to pH 7.0 with 1 N HCl. The precipitate was redissolved by heating and adding more water (total volume 90 ml). After cooling 883 mg of 3-methylguanine (**13**) was obtained as small needles, mp 366–371 °C dec. Two recrystallizations from water raised the melting point to 375–377 °C dec. An analytical sample was dried at 80 °C for 7 h: uv (pH 1) max 265 nm (ϵ 10 600), 245 (sh, 7250), and (pH 11) 247 nm (ϵ 14 100) [reported[6] (pH 1) 265 nm (ϵ 10 900), 245 (sh, 8060), and 274 (13 000)]; pK_a (potentiometric, concentration 4.44 M, halfway) 4.41 ± 0.02 and 9.60 ± 0.04; (spectrophotometric) 4.43 and 9.62; NMR (0.1 N NaOD, Me_4Si external) δ 7.47 (wt 1), 4.86 (DOH), and 3.27 (wt 3).

The material was identical with 3-methylguanine obtained from Cyclo Chemical Corp. Los Angeles, Calif., by uv, ir, MS, and paper chromatography (Whatman No. 1, *n*-BuOH saturated with H_2O, ammonia atmosphere, $R_{adenine}$ 0.53, 0.52).

Anal. Calcd for $C_6H_7N_5O$: C, 43.6; H, 4.3; N, 42.4. Found: C, 44.0, 43.8; H, 4.5, 4.3; N, 42.4.

Registry No.—**1**, 58520-76-8; **3**, 58502-13-9; **4**, 58502-14-0; **5**, 58502-15-1; **6** Na salt, 58502-16-2; **7** mono-K salt, 58502-17-3; **7** di-K salt, 58502-18-4; **8**, 58502-19-5; **8** di-Na salt, 58502-20-8; **9**, 58502-21-9; **10**, 58502-22-0; **10** acetyl derivative, 58502-23-1; **11**, 58502-24-2; **13**, 2958-98-7; **19** 2 isomer, 58502-25-3; **19** 2 isomer K salt, 58502-26-4; **19**

5 isomer, 58502-27-5; **19** 5 isomer K salt, 58502-28-6; **20**, 15285-16-2; **20** H_2SO_4, 58502-30-0; **21**, 4928-87-4; sodium C_7N_7, 58502-31-1; tetramethylammonium C_7N_7, 58502-33-3; zinc $(C_7N_7)_2$, 58502-34-4; lithium C_7N_7, 58502-35-5; manganous $(C_7N_7)_2$, 58502-36-6; cupric $(C_7N_7)_2$, 58502-37-7; silver C_7N_7, 58502-38-8; tetraethylammonium C_7N_7, 58502, 39-9; trimethylactadecylammonium C_7N_7, 58502-40-2; *N*-methylphenazinium C_7N_7, 58526-69-5; trimethylsulfonium C_7N_7, 58502-42-4; methyltriphenylphosphonium C_7N_7, 58502-43-5; HC_7N_7, 58502-44-6; potassium cyanide, 151-50-8; cyanogen, 2074-87-5; sodium cyanide, 143-33-9; tetramethylammonium chloride, 75-57-0; zinc carbonate, 3486-35-9; 1-chloro-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile, 58502-45-7; 1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarboxamide, 58502-46-8; dimethylformamide, 68-12-2; 1-benzyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2,5,7-tricarbonitrile, 58502-47-9; benzyl chloride, 98-88-4; diazomethane, 334-88-3; 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2-carboxylic acid, 58502-48-0; 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-5-carboxylic acid, 58502-49-1; sodium 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-2-carboxylate, 58502-50-4; sodium 7-carboxamido-1-methyl-1*H*-imidazo[1,5-*b*]-*s*-triazole-5-carboxylate, 58502-51-5.

References and Notes

(1) Part 5: W. A. Sheppard and O. W. Webster, *J. Am. Chem. Soc.*, **95**, 2695 (1973).
(2) R. W. Begland, A. Cairncross, D. S. Donald, D. R. Hartter, W. A. Sheppard, and O. W. Webster, *J. Am. Chem. Soc.*, **93**, 4953 (1971).
(3) O. W. Webster, U.S. Patent 3 093 653 (1963).
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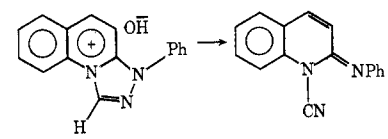
(5) For example, see T. Pehk and E. Lippaa, *Org. Magn. Reson.*, **3**, 679 (1971); P. C. Lauterbur, *J. Chem. Phys.*, **26**, 217 (1957).
(6) G. B. Elion, *J. Org. Chem.*, **27**, 2478 (1962).
(7) There are numerous examples in the literature of the formation of nitrile compounds from five-membered heterocyclics; the most pertinent is the rearrangement



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(13) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases", Wiley, New York, N.Y., 1962, p 41.

Rearrangement of *N*-Acylaziridines in Strong Acid Media[1]

Samuel P. McManus* and Richard A. Hearn

Department of Chemistry, The University of Alabama in Huntsville, Huntsville, Alabama 35807

Charles U. Pittman, Jr.

Department of Chemistry, University of Alabama, University, Alabama 35486

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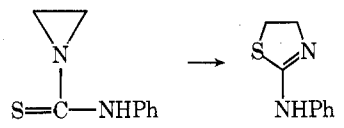
The rearrangement of *trans*-1-*p*-nitrobenzoyl-2,3-dimethylaziridine (**8**) in either sulfuric or fluorosulfuric acid occurs stereoselectively to give the *trans*-2-phenyl-4,5-dimethyloxazolinium cation and after neutralization the trans oxazoline **10**. In contrast, the isomeric cis aziridine derivative **7** gives a mixture of the cis and trans oxazolines, **9** and **10**, respectively, in a 28:72 ratio. These results implicate acyclic carbocationic intermediates in the rearrangement. The mechanism of the acid-catalyzed isomerization of acylaziridines is discussed in light of these results and other available data.

Gabriel and Stelzer[2] reported the acid-catalyzed isomerization of thioacylaziridines in 1895. Their report described the conversion of the thiourea derivative **1** to the thiazoline **2** upon heating the former in concentrated hydrochloric acid.

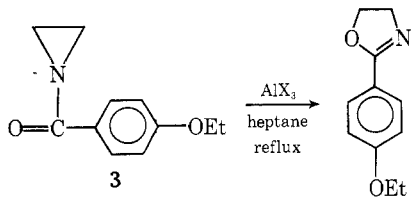


(1)

1 **2**

The reaction lay dormant until the late 1950s when a number of workers confirmed[3] and extended[4,5] the reaction.[6] One of these reports included isomerizations of several aziridines utilizing other aqueous mineral acid catalysts.[5]

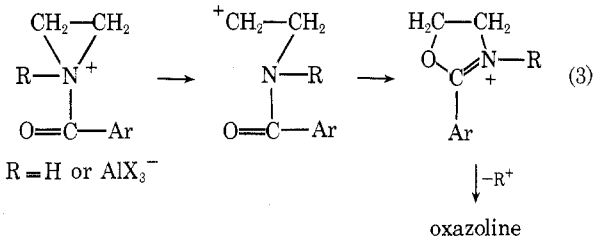
Heine and Proctor[7] carried out a similar isomerization on acylaziridines using aluminum halides in refluxing heptane, eq 2. Two mechanisms for the isomerization were considered;



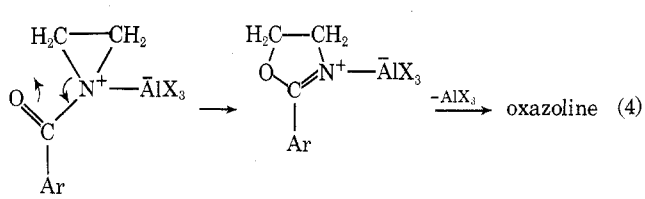
(2)

3

one involved sequentially acid attack at nitrogen, ring opening, and cyclization, eq 3; the second involved a four-centered transition state, eq 4. Owing to the low dielectric constant of



(3)



(4)

the solvent (heptane) and the high energy of the primary carbocationic intermediate formed from *N*-(*p*-ethoxybenzyl)aziridine (**3**), Heine and Proctor[7] preferred the mechanism shown in eq 4 for the isomerization of **3**.

In subsequent work, Heine et al.[8] used concentrated sulfuric