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4-Amino-3-cyanopyrazole (6) had once been considered to be a possible intermediate in the photochemical conversion at 350 nm of diaminomaleonitrile (1) into 4-amino-5-cyanoimidazole (3), a precursor of adenine. The pyrazole was synthesized and irradiated at 350 nm. No isomerization into the imidazole was observed, even when the photolysis was carried out in the presence of an excess of 1, where sensitization by this or one of its photolysis products might have operated. At 254 nm, complete decomposition of 6 was observed, with formation of polymeric products. At 300 nm, 6 underwent isomerization to 3, as well as extensive decomposition. Hydrogen cyanide was probably produced, which reacted with the remaining starting material to yield 7-aminopyrazolo[4,3-d]pyrimidine (10), which did not isomerize into adenine under the photolysis conditions. A polymer was also obtained, from which glycine was identified after hydrolysis.

Introduction

One remarkable reaction was reported by Ferris and Orgel (1), in which diaminomaleonitrile (1), a hydrogen cyanide tetramer, was converted photochemically into 4-amino-5-cyanoimidazole (3) through a singlet excited state of diaminofumaronitrile (2) (2,3,4). The imidazole in turn, may be converted into adenine (4) by reaction with either formamidine acetate (5) or hydrogen cyanide (6). These reactions are presumed to be important in the field of chemical evolution (7).
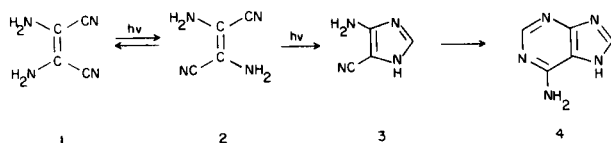
Neglecting the amino and cyano substituents common to 2 and 3, the clockwise sequence of atoms N-C-C-C-N in 2 was replaced by N-C-C-N-C in 3, and the mechanism of this reorganization has still not been satisfactorily explained. The possibility that the conversion of 1 into 3 had taken place at 350 nm *via* a pyrazole had been considered by Ferris and Orgel (1) who irradiated 3-amino-4-cyanopyrazole (5), and found it to isomerize into 3 only at 253 nm and not at 350 nm. However, 5 was not structurally related to 1 in a direct manner, and Ferris and Kuder later acknowledged that the experiment had been designed incorrectly (2), and that it was 4-amino-3-cyanopyrazole (6) which should have been investigated instead. Later work by Ferris and Trimmer (3) showed that although selected pyrazoles rearranged into imidazoles, they were not likely intermediates in the direct conversion of the corresponding enaminonitriles into these imidazoles. Low temperature experiments were also interpreted in terms of the absence of a pyrazole intermediate in these conversions. These results suggested that the conversion of 1 to 3

likewise did not involve a pyrazole intermediate, although one conclusion reached by Koch and Rodehurst was that the photochemistry of 1 was not inconsistent with a photochemical rearrangement of an (unspecified) intermediate (4). To the best of our knowledge, 6 was still unknown and the final determination of whether or not it was an intermediate in the conversion of 1 into 3 still remained to be made.

Since 3-carboxamide-4-nitropyrazole (7) was known (8), it was an attractive precursor for 6, through conversion of the amide into a nitrile, and reduction of the nitro into an amino group. The same product was obtained whether 7 was initially converted into 8 or 9. 4-Amino-3-cyanopyrazole (6) melted at 143.5-145°, gave a tolylate salt, m.p. 206.5-208°, and had its structure supported by the results of elemental analysis, nmr, uv, ir and mass spectral analyses. Furthermore, the R_f value on silica gel using benzene-ethanol (3:1) was different from those of 1, 2, and 3, and the monitoring of the course of the photolysis of 1 by tlc therefore appeared possible.
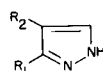
5   $R_1 = NH_2, R_2 = CN$
6   $R_1 = CN, R_2 = NH_2$
7   $R_1 = CONH_2, R_2 = NO_2$
8   $R_1 = CN, R_2 = NO_2$
9   $R_1 = CONH_2, R_2 = NH_2$

The photolysis of 6 was performed in acetonitrile at 350 nm in the dilute solution reported by Ferris and Orgel (1). Even after extended irradiation (48 hours), the compound had not undergone any transformation. Under these conditions 1 was found to show approximately 50% conversion into 3, and no spot corresponding to 6 was found in the tlc of the crude protolysis mixture of 1. These results suggested that 6 was not an intermediate in the conversion of 1 into 3. The possibility remained, however, that the conversion of 6 into 3 required sensitization by either the

starting material or one of its photoproducts. We found that 6 survived the irradiation at 350 nm in the presence of a tenfold molar excess of 1, conditions in which the latter absorbed essentially all the light. These experiments provided conclusive proof that the formation of 3 from 1 at 350 nm does not involve a pyrazole intermediate.

The photochemistry of 6 was investigated below 350 nm, since the λ max is at 272 nm. At 254 nm, extensive decomposition took place and led to a brown polymer which coated the walls. No discrete products could be isolated from the solution, and the structure of the polymer was not investigated.

At 300 nm, the photolysis of 6 also led to a brown polymer, which was hydrolyzed in 6N hydrochloric acid, and analyzed by glc after esterification with 1-butanol, followed by trifluoroacetylation (9). Glycine and two other unidentified compounds were observed, suggesting that the material had been an HCN polymer. The acetonitrile solution was found by tlc to contain at least ten products, in addition to some starting material. All these products were present in minute quantities, and only two could be isolated and characterized. One was shown to be 3 by direct comparison, and even though 6 had now been proved to undergo photochemical conversion to 3 at 300 nm, it was not detected in the photolysis mixture of 1 at this wavelength under conditions where 50% conversion to 3 had taken place. Thus 6 was not an intermediate in the conversion of 1 into 3 at 300 nm.

The second product in the photolysis of 6 at 300 nm had a molecular weight of 135, higher than that of 6 by 27 units, corresponding to the addition of HCN to the starting material. Since the addition of HCN to an enaminonitrile was expected to yield an aminopyrimidine, and the product was not adenine (4), the pyrazolopyrimidine 10 was synthesized for comparison. Although a previous synthesis had been described (8), we preferred to condense the tolylate salt of 6 with formamidine acetate (10). This new synthesis of 10 yielded a product which was identical in all respects with the above photolysis product.

6   3   10
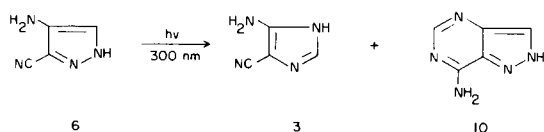
Although neither 1 nor 2 were detected, the photolysis of 6 must have generated HCN in order to account for the formation of 10. This decomposition parallels that in the mass spectrometer, where the fragments corresponding to the loss of one and two molecules of HCN were very intense.

In order to counter the argument that it was the oligomerization of the HCN produced from 6 which led to 3 at 300 nm, rather than the direct isomerization of 6, we note that had 3 been formed from HCN, 1 and 2 would

have been its immediate precursors. Monitoring for these during the photolysis of 6 failed to detect their formation. Since independent photolysis of 1 at 300 nm showed that 50% remained unreacted after 8 hours, it is reasonable to conclude that 1 would have been observed in the photolysis of 6, had it been formed prior to 3. The absence of 1 in the photolysis of 6 therefore supports the suggestion that the formation of 3 in the photolysis of 6 at 300 nm was the result of a direct isomerization. It is also worth noting that the photolysis of 1 at 300 nm did not produce any 10, as would have been expected if 6 had been an intermediate.

Finally, although the irradiation of 10 could have been expected to produce adenine (4), this compound was definitely absent in the crude photolysis mixture of 6, and was not produced in an independent photolysis of 10 at 300 nm for 48 hours.

In conclusion, the mechanism of the rearrangement of 1 into 3 is still an open problem, and no definitive information is yet available concerning the possible involvement of an isonitrile, an iminoazetine, an azirine, or some other intermediate, although one option must no longer be considered (11).

EXPERIMENTAL

All irradiations were conducted under nitrogen after three freeze-pump-thaw cycles, and a Rayonet reactor was used, with lamps having their principal emission at either 254, 300, or 350 nm.

3-Cyano-4-nitropyrazole (8).

A mixture of finely ground 7 (9) (2.0 g.) and phosphorus pentoxide ((1.5 g.) was treated at 250° until foaming subsided. The product was sublimed under vacuum and recrystallized from water to yield 690 mg. (39%) of the nitrile as white plates, m.p. 162-163°; ir (potassium bromide): 3275 (s), 3150 (s), and 2280 cm^{-1} (s); nmr (DMSO-d₆): 9.1 ppm (s); uv λ max (ethanol): 263 (ε, 6,100) and 209 nm (ε, 8,500); ms: m/e (% intensity) 138 (100), 122 (24), 108 (22), 94 (40) and 66 amu (45).

Anal. Calcd. for C₄H₂N₄O₂: C, 34.79; H, 1.45; N, 40.57. Found: C, 34.71; H, 1.53; N, 40.13.

4-Amino-3-cyanopyrazole Toluenesulfonate Salt.

Compound 8 (2 g.) was hydrogenated in methanol over 10% palladium/carbon at 15 psi. After treatment with 1 equivalent of p-toluenes sulfonic acid and recrystallization from acetonitrile, there was obtained 2.38 g. (59%) of salt. A second recrystallization gave long white needles, m.p. 206.5-208°; ir (potassium bromide): 3400 (m), 2900 (s), 2275 (m), 1605 (m), 1540 (m), 1210-1150 (s, br), 1040 (s), 1020 (s), 820 (s), and 690 cm^{-1} (s); nmr (DMSO-d₆): 8.0 (s, 1H), 7.6 (d, 2H, J = 8 Hz), 7.15 (d, 2H, J = 8 Hz) and 2.33 ppm (s, 3H); uv λ max (methanol): 272 (ε, 3,290) and 219 nm (ε 13,000); ms: m/e (% intensity), 172 (64), 108 (100), 91 (100) and 77 amu (19).

Anal. Calcd. for C₁₁H₂₂N₄O₃S: C, 47.13; H, 4.31; N, 19.98. Found: C, 47.19; H, 4.29; N, 19.90.

4-Amino-3-cyanopyrazole (6).

A solution of 175 mg. of tosylate in 0.7 ml. of water was adjusted to pH 8 with ammonium hydroxide and treated with 15 mg. of charcoal, which was then filtered and washed with 0.7 ml. of water. The combined solutions were concentrated to 0.7 ml. and the pH readjusted to 8. Refrigeration overnight and filtration afforded 45 mg. (67%) of 6 as near-white, rectangular prisms. The yield was 89% when scaled up to 1 g. of salt.

Although decomposition of the amine was observed in solution, the pure solid could be stored in the refrigerator indefinitely. Sublimation yielded white grains, m.p. 143.5-145°; ir (potassium bromide): 3250 (s), 3050 (m), 2975 (m), and 2260 cm⁻¹ (s); nmr (deuterioacetonitrile): 7.2 ppm (s); uv λ max (acetonitrile): 276 (ϵ, 3,900) and 198 nm (ϵ, 11,400); λ max (methanol): 276 (ϵ, 3,390) and 205 nm (ϵ, 6,990); ms: (20 eV) m/e (% intensity), 108 (100), 81 (26), 80 (4), 66 (3) and 54 amu (20).

Anal. Calcd. for $C_4H_4N_4$: C, 44.44; H, 3.73; N, 51.82. Found: C, 44.68; H, 3.61; N, 51.51.

Preparation of 6 from 4-Amino-3-pyrazolecarboxamide (9).

A mixture of 85 mg. of 9 and 180 mg. of phosphorus pentoxide was heated until the foaming stopped, and was sublimed under vacuum. The mixture contained (tlc) 6, 9, and four unidentified compounds. After preparative tlc there was obtained 3.5 mg. of 6 (5% based on reacted starting material), m.p. 141-143°, and 3.2 mg. of 9.

7-Aminopyrazolo[4,3-*d*]pyrimidine (10).

A mixture of 0.35 g. of the tosylate of 6 and 0.26 g. of formamidine acetate (10) in 7 ml. of methyl cellosolve was refluxed for 1 hour, cooled, and made basic to litmus with ammonia. Preparative tlc purification yielded a mixture of 10 with its acetate and sulfonate salts. Treatment with ammonia gave 60 mg. (50%) of 10 as pale pink grains, m.p. 350° and uv λ max (water) of 294 (ϵ, 9,100) at pH 1 and 293 nm (ϵ, 7,900) at pH 11, in accord with literature values (8).

Irradiation of 6 at 300 nm.

A solution of 120 mg. of 6 in 10 ml. of acetonitrile was irradiated at 300 nm. Periodically the solution was separated from the insoluble polymer and irradiated further. Five runs were combined, and preparative tlc of the solution yielded 210 mg. of crystalline starting material, 1 mg. of 3, and 3 mg. of 10, which were identified by direct comparison.

Irradiation of 3 at 300 nm.

A solution of 5 mg. of 3 in 20 ml. of acetonitrile was irradiated at 300 nm. After 72 hours the solution was filtered, concentrated, and shown by tlc to contain roughly equal amounts of starting material and four other compounds, none of which being 4. The brown precipitate weighed 1 mg.

Irradiation of 10 at 300 mn.

A solution of 6 mg. of 10 in 20 ml. of acetonitrile was irradiated at 300 nm. It was concentrated after 72 hours to yield 4 mg. of solid starting

material and a solution which was shown by tlc to be almost entirely 10, with a small amount of a highly mobile component which was not identified. A band corresponding to 4 was not detected.

Irradiation of 1 at 300 nm.

A solution of 20 mg. of 1 in 10 ml. of acetonitrile was irradiated at 300 nm for 8 hours. After concentration, the tlc was similar to that obtained from the 350 nm irradiation of 1. Neither 10 nor 6 could be detected, although roughly 50% conversion of 1 into 3 had occurred.

Irradiation of 6 at 350 nm.

A solution of 20 mg. of 6 in 10 ml. of acetonitrile was irradiated at 350 nm. After 48 hours the solution was concentrated and analyzed by tlc. No conversion of starting material had occurred.

Irradiation of 6 at 254 nm.

A solution of 7.5 mg. of 6 in 20 ml. of acetonitrile was irradiated at 254 nm. After 1 hour a heavy brown precipitate was filtered off and the solution concentrated. Tlc analysis showed a trailing component superimposed upon a complex mixture of barely detectable components. The mixture was not analyzed further.

Irradiation of 6 in the Presence of 1 at 350 nm.

A solution (10 ml.) which was 0.0001 M in 6 and 0.001 M in 1 was irradiated at 350 nm. After 15 hours, the solution was filtered, concentrated, and analyzed by tlc. Formation of 3 had occurred to a large extent, but little if any conversion of 6 had taken place.

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