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Photochemical Conversion of Enaminonitriles to Imidazoles. Scope and Mechanism[1]

J. P. Ferris* and R. W. Trimmer

Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

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The scope of the photolysis of enaminonitriles has been extended to include the conversions of cyclic five-, six-, and seven-membered enaminonitriles to imidazoles and the photochemical synthesis of imidazole-4-carbonitrile. Ketenimine intermediates were detected by ir bands at 2000–2020 cm^{-1} when the photolyses were performed at −77 and −195°. It was determined that pyrazoles are neither reaction intermediates nor products in the photolysis of aliphatic enaminonitriles. Similar rates were observed for the photochemical loss of the enaminonitrile **13b** and for the corresponding formation of imidazole **14b**, a result consistent with a monophotonic process with no buildup of uv-absorbing intermediates. It was not possible to detect excited state species by fluorescence measurements; however, the restricted geometry of these cyclic compounds established that the excited state does not have a trans geometry prior to cyclization to the imidazole.

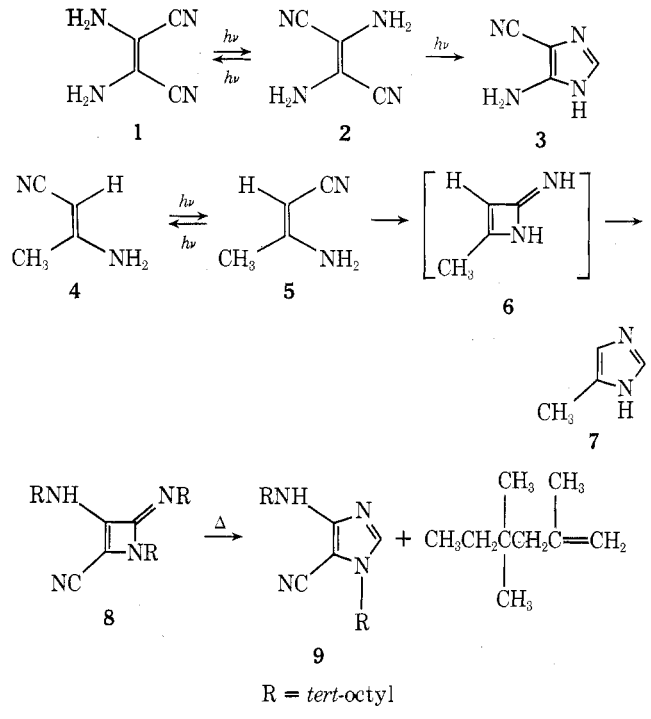
The photochemical conversion of the enaminonitrile diaminomaleonitrile (**1**) to 4-aminoimidazole-5-carbonitrile (**3**) is a key step in the proposed prebiotic formation of purines from HCN (Scheme I).[2] Previous studies established that the simpler enaminonitriles, β-aminoacrylonitrile and β-aminocrotononitrile (**4**), rearrange to imidazole and 4(5)-methylimidazole, respectively.[3,4] Since the trans isomer of β-aminocrotononitrile (**5**) must cyclize to 4(5)-methylimidazole (**7**), it was assumed that diaminofumaronitrile (**2**) is the photochemical precursor to 4-aminoimidazole-5-carbonitrile (**3**). This proposal was questioned by Becker, Kolc, and Rothman;[5] however, Koch and Rodehurst[6] have recently demonstrated that the excited diaminofumaronitrile (**2**) is the precursor to **3**.

We proposed that an iminoazetine intermediate (e.g., **6**, Scheme I) is formed photochemically and this rearranges to the corresponding imidazole in a thermal reaction.[4] The thermal conversion of iminoazetine **8** to imidazole **9** is consistent with this postulate.[7] Becker et al.[5] suggest that a stable intermediate is formed from **1** or **2** which is then photochemically converted to **3** (a two-photon process from **2**). This possibility has been ruled out by the observation that the efficiency of the photoreaction is independent of light intensity.[6]

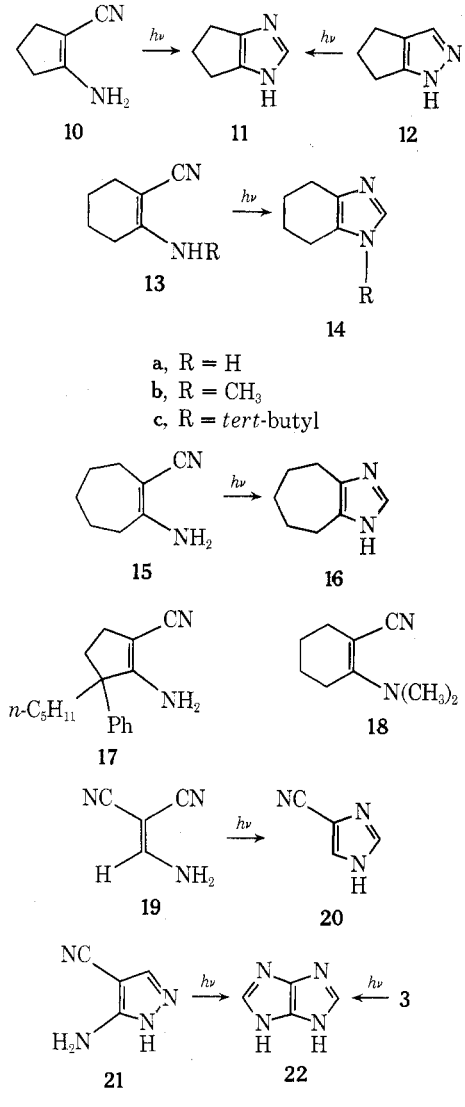
The present study was undertaken with the goal of providing further information concerning the scope and mechanism of this photochemical transformation.[8]

Scope. The photolysis of enaminonitriles provides a convenient and direct one-step synthesis of novel imidazoles (Scheme II). The cyclic enaminonitriles used as starting materials can be readily prepared by the base-catalyzed cyclization of the corresponding dinitriles. The N-substituted

Scheme I



Scheme II



enaminonitriles **13b, 13c,** and **18** were prepared in high yield by the reaction of 2-oxocyclohexanecarbonitrile with the corresponding amine. Lower yields of imidazoles were observed when enaminonitrile concentrations greater than 10^{-2} *M* were used. Presumably this is due to the occurrence of bimolecular reactions in more concentrated solution. No imidazole products were detected on irradiation of the N,N-disubstituted enaminonitrile **18.**

The imidazole photoproducts were characterized by direct comparison with authentic samples prepared by other routes. The *N-tert*-butyl derivative **14c** was an exception since it was characterized by the close similarity of its uv spectrum and color tests with those observed for the *N*-methyl derivative **14b.** Imidazole-4-carbonitrile (**20**) had not been reported previously. A multistep chemical synthesis (Experimental Section) gave a product that was identical with the photoproduct of **19.** We were unable to effect the conversion of **19** to **20** previously[3] because we had not removed oxygen prior to photolysis.[4] It was not possible to prepare useful amounts of 2-aminocyclopentanone, an intermediate in the chemical synthesis of **11,** by the reported procedures.[9] Two alternative syntheses of 2-aminocyclopentanone were devised (Experimental Section) one of which gives a much higher yield than the published syntheses.[9] 1,6-Dihydroimidazo[4,5-*d*]imidazole (**22**) was prepared in the present work by the photochemical rearrangement of 3-aminopyrazole-4-carbonitrile (**21**). No chemical syntheses of **22** have been reported, but it was prepared previously by the photolysis of **3.**[2]

Mechanistic Studies. The enaminonitriles were photolyzed at −77 and −196° as liquid films[10] or in a KBr matrix[11] for 1 hr and their ir spectra were determined to detect reaction intermediates stable at low temperatures.[1,2] Compounds **10, 13, 15,** and **17** exhibited ir absorption at 2000–2020 cm^{-1} after irradiation characteristic of the ketenimine chromophore.[12] This absorption disappeared on warming. No ir absorption was detected in the 2000-cm^{-1} region when **18** was irradiated, demonstrating that at least one NH group is required for ketenimine formation. Two ketenimines (Scheme III, **23, 26**) may be formed from a cyclic enaminonitrile. Ketenimine **26** was eliminated as a possibility because it would be impossible to form, without rearrangement, from the dialkyl-substituted enaminonitrile **17.**

The long-term (5 hr) photolyses of enaminonitriles **10** and **15** at −198° were investigated in an attempt to detect further intermediates. However, only one additional band was observed at 2260 cm^{-1} which did not disappear on warming. This absorption, characteristic of an aliphatic nitrile, was tentatively assigned to **24,** a compound which may be formed by the photolyses of **23.**

An attempt was made to trap the iminoketenimines (e.g., **23**) observed in low-temperature photolyses as amides by performing the photolysis in aqueous solution. In previous studies it was possible to trap the ketoketenimines formed by the photolyses of isoxazoles in this way.[1] However, photolyses of **13a** or **13b** in aqueous solution gave the imidazoles as the major photoproducts. It was not possible to detect any of the corresponding 2-oxocyclohexanecarboxamide either before or after acid hydrolysis of the reaction mixture (detection limit ~1% yield).

The absence of the formation of other definitive ir bands suggested that a pyrazole might be present, a structure which would not exhibit ir absorption above 1700 cm^{-1}. Previous experiments indicated that this intermediate was not likely;[4] however, the photochemical conversion of anthranilonitrile to indazole[2] suggested that this point should be reinvestigated. Photolyses of 3-methylpyrazole with

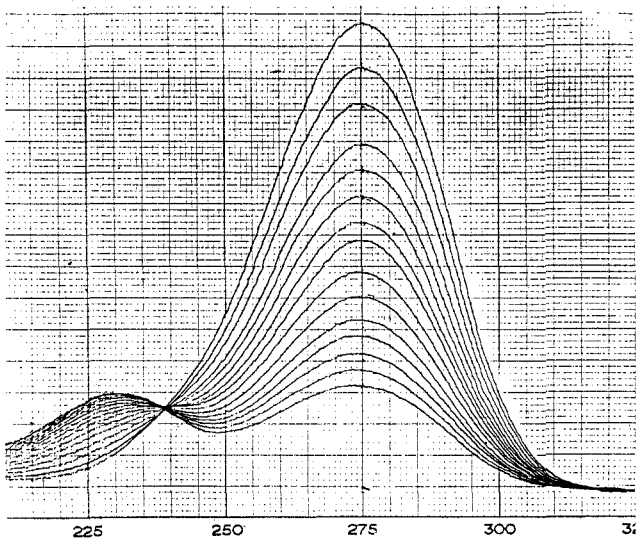


Figure 1. The photochemical conversion of enaminonitrile **13b** (uv max 276 nm) to imidazole **14b** (uv max 226 nm). Samples irradiated in a Rayonet reactor in degassed ethanol solution using lamps with principal emission at 300 nm. UV spectral measurements were made at 60-sec intervals.

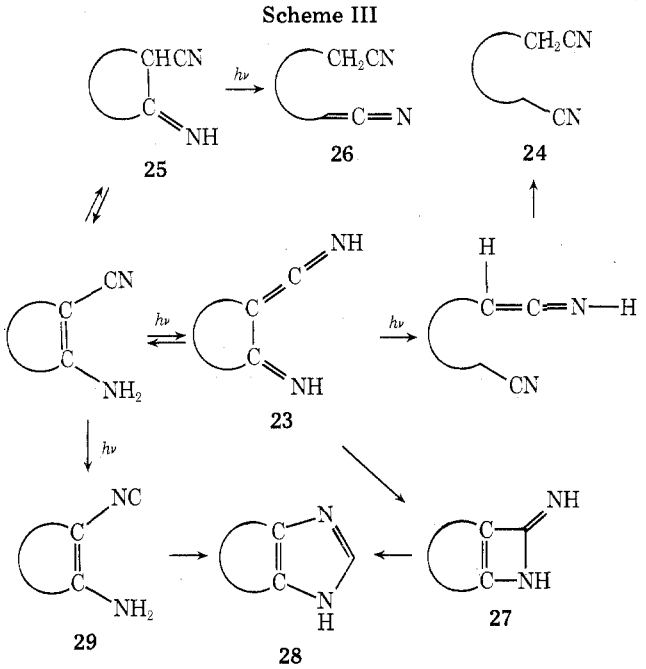
254- or 300-nm light sources resulted in the formation of both the 2-and 4(5)-methylimidazoles.[13] We found that this reaction is not sensitized by benzophenone.[13] Irradiation of β-aminocrotononitrile (**4**) under the same reaction conditions results in the formation of only 4(5)-methylimidazole.[4] In another experiment an attempt was made to detect pyrazole **12** on irradiation of **10;** however, it was not detected in the photolysis mixture. Finally, no new ir absorption bands could be detected in the 4000–1700-cm^{-1} region when pyrazole **12** or 3-methylpyrazole were irradiated at −77 or −195°. The differences observed in the photoproducts obtained from aliphatic enaminonitriles and the corresponding pyrazoles proves that pyrazoles are not formed nor are they intermediates in the photochemical rearrangement of aliphatic enaminonitriles to imidazoles.

The smooth conversion of enaminonitrile **13b** to imidazole **14b** was observed when the uv spectrum of the reaction mixture was monitored at 1-min intervals (Figure 1). The transformation proceeds without formation of a uv-absorbing intermediate as shown by the observation of a clean isosbestic point at 239 nm. In addition the rate of loss of **13b** paralleled the rate of formation of **14b.** The photochemical conversion of **13c** to **14c** proceeds in a similar fashion with an isosbestic point at 238 nm. These data are consistent with a monophotonic process with no buildup of uv-absorbing intermediates. The two or more photon process postulated by Becker et al.[5] would require the buildup of a uv-absorbing intermediate (no isosbestic point), more complex reaction kinetics, and a difference between the rate of the dissappearance of **13b** and the formation of **14b.** Our results require either the concerted formation of the imidazole from the enaminonitrile (no reaction intermediate) or the photochemical formation of a reaction intermediate which is rapidly converted to product and/or starting material by one or more thermal processes.

The photochemical formation of imidazoles from the cyclic enaminonitriles used in this study clearly demonstrates that the cis isomer is the precursor to the imidazole. It is not possible for these cyclic enaminonitriles to isomerize to the corresponding trans isomers. This would require that simple, noncyclic enaminonitriles such as diaminomaleonitrile (**1**) isomerize to the corresponding trans derivative **2** before rearranging to product **3.** This conclusion together with the monophotonic nature of the rearrangement is completely in accord with the conclusions drawn by Koch and Rodehurst[6] from their study of the photolysis of diaminonitrile (**1**).

The precise nature of the reaction intermediates (if any) formed on irradiation of enaminonitriles remains to be determined (Scheme III). The ketenimines (**23**) observed in

Scheme III



the low-temperature studies might thermally cyclize to azetines (**27**) which in turn thermally rearrange to the imidazoles (**28**).[4,7] The ketenimines do not appear to be likely precursors to azirines. Since it was not possible to detect the conversion of the ketenimines to product at low temperature, they may just revert back to the starting enaminonitrile. The observation of isonitrile intermediates on irradiation of isooxazoles[2] and the possible formation of the isonitrile on photolysis of 2-cyanophenol suggests the possibility of a direct conversion of the enaminonitrile to the corresponding isonitrile (**29**). Previous studies eliminated the possibility of tautomerization of the enaminonitrile to the β-iminonitrile (e.g., **25**), prior to the formation of the isonitrile;[4] however, the direct photochemical inversion of the nitrile to isonitrile **29** is a possibility. Finally, azirine intermediates must also be considered. The ir absorption of the 2-unsubstituted azirines in the 1650-cm^{-1} region[14] makes it difficult to detect these intermediates in low-temperature ir experiments.

Sensitization experiments have shown that the rearrangement proceeds from the singlet excited state, while cis–trans isomerization of the enaminonitrile proceeds via the triplet manifold.[4] Previous attempts to detect the excited state species formed from **1** or **4** were unsuccessful.[4] Presumably the absence of luminescence was due to a rapid vibrational relaxation of the excited state. It was anticipated that since the cyclic enaminonitriles possessed fewer degrees of freedom, it might be possible to detect emission from their singlet or triplet states. However, we could not detect luminescence from enaminonitriles **10** or **13a** or from imidazole **14a.**

Experimental Section[15]

Synthesis of 2-Methylamino-1-cyclohexene-1-carbonitrile (13b). To 1.23 g (0.01 mol) of 2-oxocyclohexanecarbonitrile[16] was added 0.25 ml of glacial acetic acid and 75 ml of benzene. Excess of methylamine was then bubbled through the solution and the reac-

tion mixture was then heated to reflux for 30 min and 0.01 mol of H_2O was collected in a Dean-Stark trap. The reaction solution was then concentrated in vacuo to a solid which was twice crystallized from cyclohexane to afford a 70% yield of white crystals: mp 66–67.5°; uv max (ethanol) 276 nm (ε 13200); ir (KBr) 3390 (m), 2190 (s, C≡N), and 1600 cm^{-1} (s, C=C); NMR ($CDCl_3$) δ 4.6 (s, 1, NH), 2.9 (d, 3, CH_3), 2.2 [m, 4, $(CH_2)_2$], and 1.65 [m, 4, $(CH_2)_4$]; the NH signal disappeared and the doublet collapsed to a singlet when D_2O was added.

Anal. Calcd for $C_8H_{12}N_2$: C, 70.54; H, 8.88. Found: C, 70.66; H, 8.90.

Synthesis of *N*-Methyl-4,5,6,7-tetrahydrobenzimidazole (14b). To 1.22 g (0.01 mol) of 4,5,6,7-tetrahydrobenzimidazole (**14a**) in 35 ml of benzene under nitrogen was added 0.0111 mol of NaH. To the vigorously stirred mixture was added 0.011 mol of methyl iodide and after 3 hr of stirring the reaction mixture was poured into 100 ml of ice water and the aqueous mixture was extracted three times with 50-ml portions of benzene. The combined organic layers were then washed once with 25 ml of water and then 25 ml of brine, dried over $MgSO_4$, and concentrated in vacuo to an oil. The oil was distilled to afford a 60% yield of product: bp 135–137° (10 mm) [lit.[17] 110–120° (4 mm)]; uv max (ethanol) 226 nm (ε 6100); NMR ($CDCl_3$) δ 7.3 (s, 1, aromatic H), 3.5 (s, 3, CH_3), 2.55 [m, 4, $(CH_2)_2$], and 1.9 [m, 4, $(CH_2)_2$]. The picrate had mp 219–220° (lit.[17] mp 219–220°).

Synthesis of 2-Dimethylamino-1-cyclohexene-1-carbonitrile (18). To 1.23 g (0.01 mol) of 2-oxocyclohexanecarbonitrile,[16] 0.25 ml of glacial acetic acid, and 20 ml of a 40% aqueous dimethylamine solution was added 50 ml of benzene. The reaction mixture was heated to reflux until no more water was collected in the Dean-Stark trap. The reaction solution was then concentrated in vacuo to an oil, 50 ml of 1 *N* NaOH was added, and the aqueous solution was then extracted three times with 50-ml portions of benzene. The combined organic layers were washed with 50 ml of brine, dried over $MgSO_4$, and concentrated in vacuo to an oil which was distilled to afford a 79% yield of **18**: bp 143–144° (10 mm); uv max (ethanol) 285 nm (ε 13800); ir (neat) 2960 (s), 2190 (s) (C≡N), 1585 (s) (C=C), 1385 (m), and 1115 cm^{-1} (m); NMR ($CDCl_3$) δ 3.05 (s, 6, CH_3), 2.25 [m, 4, $(CH_2)_2$], and 1.65 [m, 4, $(CH_2)_2$].

Anal. Calcd for $C_9H_{14}N_2$: C, 71.95; H, 9.39. Found: C, 71.52; H, 9.24.

Synthesis of 2-*tert*-Butylamino-1-cyclohexene-1-carbonitrile (13c). To 1.23 g (0.01 mol) of 2-oxocyclohexanecarbonitrile[16] and 0.25 ml of glacial acetic acid was added 5 ml of *tert*-butylamine (freshly distilled from NaOH). The reaction mixture was sealed in an ampule and heated at 100° for 48 hr. The cooled reaction mixture was poured into 25 ml of 1*N* NaOH and extracted three times with 30-ml portions of benzene, and the combined organic layers were washed twice with water and once with brine, dried over $MgSO_4$, and then concentrated in vacuo to an oil. The oil was distilled to afford a 73% yield of product: bp 133–134° (9 mm); uv max (ethanol) 278 nm (ε 16200); ir (neat) 3430 (w), 2970 (s), 2195 (s) (C≡N), 1605 (s), 1385 (s), and 1230 cm^{-1} (s); NMR ($CDCl_3$) δ 4.65 (s, 1, NH), 2.4 [m, 4, $(CH_2)_2$], 1.6 [m, 4, $(CH_2)_2$], and 1.3 [s, 9, $(CH_3)_3$].

Anal. Calcd for $C_{11}H_{18}N_2$: C, 74.11; H, 10.18. Found: C, 74.36; H, 10.25.

Irradiation of 2-Amino-1-cyclopentene-1-carbonitrile. A 250-ml solution of the enaminonitrile **10**[18] (10^{-4} *M*, THF) was irradiated at 254 nm for 30 hr. Analysis by TLC (isopropylamine–methanol–benzene, 3:7:90) showed starting material and a substance which gave an R_f and DSA color corresponding to **11**. A 90% yield (based on recovered starting material) was obtained after column chromatography (isopropylamine–methanol–benzene, 1:2:97) on silica gel. The product was recrystallized from water–ethanol (95:5): mp 145.5–147° (lit.[9a] 150–151°); uv max (ethanol) 224 nm; ir (KBr) 2500–3100 (s and br), 1800 (w and br), 1600 (w), 1580 (m), 1420 (s), 1350 (w), 1270 (m), 1220 (s), 1210 sh (m), 1160 (m), 1070 (w), 980 (s), 920–930 (m and br), 785 (s), 715 cm^{-1} (m); NMR ($CDCl_3$) δ 2.6 (m, 6 H, methylene H's), 7.5 (s, 1, aromatic H), and 10.2 (s, 1, NH); mass spectrum *m/e* (rel intensity) 108 (89) (molecular ion), 107 (100), 81 (16), 80 (37), 54 (16), and 53 (24). The picrate was recrystallized from 2-propanol, mp 175–177° (lit.[19] 180–181°).

Irradiation of 2-Amino-1-cyclohexane-1-carbonitrile. A 250-ml solution (10^{-2} *M*, THF) of **13a**[19] was irradiated at 254 nm for 24 hr. Column chromatography (isopropylamine–methanol–benzene, 1:3:96) afforded an 81% yield of 4,5,6,7-tetrahydrobenzimidazole (**14a**). White crystals were obtained after one recrystallization from benzene–ether: mp 146–148° (lit.[17,20] 149–150°); ir (KBr) 3170–2630 (br and s), 1800 (br and w), 1615 (s), 1495 (m), 1490 (s), 1440 (s), 1295 (s), and 955 cm^{-1} (s); NMR ($CDCl_3$) δ 10.0 (s, 1, NH), 7.5 (s, 1, aromatic H), 2.55 [m, 4, $(CH_2)_2$], and 1.9 [m, 4, $(CH_2)_2$]. The picrate was also prepared, mp 191–192° (lit.[21] 189–190°).

Irradiation of 2-Methylamino-1-cyclohexene-1-carbonitrile. A 10^{-3} *M* solution of **13b** in ethanol was degassed and irradiated at 254 nm for 45 min. The product (**14b**) was identified by its uv max at 226 nm and by TLC in three solvent systems (benzene–ethanol–isopropylamine, 92:6:2, and ether–ethanol, 95:5, and ether). The R_f values and color reactions with DSA (orange) and iodoplatinate (yellow) were identical with an authentic sample. A 49% yield of the imidazole **14b** was determined from the extinction coefficient at 226 nm.

Irradiation of 2-Dimethylamino-1-cyclohexene-1-carbonitrile. A 10^{-4} *M* solution of **18** in ethanol was degassed and irradiated at 254 nm for 1 hr. No new peaks were observed in the uv spectrum and the intensity of the uv max of the enaminonitrile **18** diminished by about 50%.

Irradiation of 2-*tert*-Butylamino-1-cyclohexene-1-carbonitrile. 1. A 10^{-2} *M* solution of **13c** in ethanol was degassed and irradiated at 254 nm for 9 hr. The reaction solution was then concentrated in vacuo to an oil. TLC analysis (ether–methanol, 95:5; benzene–methanol–isopropylamine, 92:5:3) of the oil showed that a new product had formed which gave positive DSA (intense orange) and iodoplatinate (yellow) tests indicative of an imidazole formation. 2. A 10^{-4} *M* solution of **13c** in ethanol was degassed and irradiated at 254 nm at six 30-sec intervals. An isosbestic point at 237.5 nm and a new peak at 227 nm were observed. These data, in comparison with the data obtained from the photosynthesis of *N*-methyl-4,5,6,7-tetrahydrobenzimidazole (**14b**) from **13b**, provide a strong support for the *N*-*tert*-butyl-4,5,6,7-tetrahydrobenzimidazole (**14c**) as the photoproduct.

Irradiation of 2-Amino-1-cycloheptene-1-carbonitrile. A 10^{-2} *M* solution of 2-amino-1-cycloheptene-1-carbonitrile (**15**)[22] was prepared in 250 ml of freshly distilled THF. The solution was purged with nitrogen for 25 min and irradiated at 254 nm for 48 hr in a stoppered quartz tube. The solution was concentrated in vacuo to an oil which was chromatographed on 40 g of silica gel and eluted with a solution of isopropylamine–methanol–benzene (1:2:97). A 56% yield of pentamethyleneimidazole (**16**) was achieved based on isolated imidazole. White crystals were obtained on crystallization from benzene after prior treatment with decolorizing charcoal: mp 197–199° (lit.[23] 199°); uv max (methanol) 219 nm (ε 9500); ir (KBr) 2640–3140 (br and s), 1880 (br and s), 1600 (m), 1470 (s), 1440 (s), 1240 (s), 1080 (m), 965 (s), 814 (m), and 796 cm^{-1} (m); mass spectrum *m/e* (rel intensity) 136 (100 (molecular ion), 135 (45), 108 (32), 107 (86), 81 (34), 80 (21), 54 (18), and 53 (23).

Irradiation of Aminomethylenemalononitrile (19). A 10^{-3} *M* acetonitrile (purified) solution of compound **19**[24] [uv max (CH_3CN) 266 nm (ε 17100) and 346 nm (ε 750)] was degassed and irradiated in a quartz cell at 254 nm for 40 hr. Analysis of the product by TLC (ethyl acetate–methanol–isopropylamine, 90:7:3) showed a small amount of starting material (**19**) at the top of the plate (uv visible), the expected 4-cyanoimidazole (**20**) (DSA, dark red) at the center, and some unknown material at the origin. When the irradiation was conducted in water, methanol, dioxane, or unpurified acetonitrile no DSA positive spot was detected.

Synthesis of Imidazole-4-carboxaldehyde Oxime. The procedure of Hubball and Pyman[25] gave a 53% yield of the oxime: mp 181–184° (lit.[25] 183–184°); uv max (ethanol) 247.5 nm (lit.[26] 248 nm); ir (KBr) 2700–3350 (br and s), 1670 (s) (C=N), 1530 (s), 1450 (s), 1220 (s), 1110 (s), 1000 (s), 960 (s), 925 (s), and 825 cm^{-1} (br and s); NMR (acetone-d_6) δ 7.7 (s, 1, aromatic H) and 7.4 (s, 1, aromatic H).

Synthesis of Imidazole-4-carbonitrile (20). To 50 mg of imidazole-4-carboxaldehyde oxime was added 3 ml of acetic anhydride and the mixture was heated at reflux for 2 hr. To the reaction mixture was added 10 ml of cold aqueous 6 *N* HCl and the mixture was washed with ether. The aqueous solution was made basic with excess potassium carbonate, extracted with methylene chloride, and concentrated in vacuo to a small amount of a solid: ir (KBr) 3120 (br and s), 2235 (s) (C≡N), 1665 (m), 1550 (m), and 1400 cm^{-1} (s); NMR (acetone-d_6) 8.0 (s, 1, aromatic H) and 7.9 (s, 1, aromatic H); uv max (ethanol) 237 nm. When this solid was compared to the product obtained by photolysis of **19**, by TLC (ethyl acetate–methanol–isopropylamine, 90:7:3, and chloroform), both were found to have identical R_f values and reaction with DSA

(dark red). The tosylate salt of **20** was recrystallized from 2-propanol: mp 174–175°; ir (KBr) 2245 cm^{-1} (s).

Anal. Calcd for $C_4H_3N_3 \cdot C_7H_8SO_3$: C, 49.80; H, 4.18. Found: C, 49.72; H, 4.15.

Synthesis of 6-Amino-1,4-dioxaspiro[4.4]nonane. To 0.01 mol of 6-phthalimido-1,4-dioxaspiro[4.4]nonane[9a] in 50 ml of ethanol was added 0.01 mol aqueous 64% hydrazine and the stoppered solution was allowed to stand at room temperature overnight. The solution was concentrated at less than 50° (20 mm) to dryness, 50 ml of benzene was added, and the reaction mixture was then dried over magnesium sulfate and concentrated in vacuo to a pale yellow oil: bp 25–26° (0.3 mm) (a water-white oil) (76%); ir (neat) 3430 (m) (NH_2), 2960 (s), 2900 sh (s), 1600 (s and broad), 1470 (m), 1315 (s), 1205 (s), 1125 (s), 1035 (s), and 945 cm^{-1} (s).

Synthesis of 2-Aminocyclopentanone. A. Acid Hydrolysis of 6-Amino-1,4-dioxaspiro[4.4]nonane. To 186 mg of the ketal was added 5 ml of 1 *N* hydrochloric acid and the mixture was heated in a sealed ampule at 50° for 12 hr. The solution was cooled, filtered, and concentrated in vacuo to an oil. The oil was dissolved in a small amount of 2-propanol and triturated with ether to yield 74 mg (40%) of white crystals: mp 139–141° (lit.[9b] 146–147°); ir (KBr) identical with the published spectrum of 2-aminocyclopentanone hydrochloride.[9b] No attempts were made to optimize the yield.

B. Reaction of Cyclopentanone Oxime p-Toluenesulfonate with Sodium Alkoxide. To 60.5 g (0.239 mol) of cyclopentanone oxime *p*-toluenesulfonate[9a] in 100 ml of absolute ethanol at 0° was added a solution of 25.8 g (0.578 mol) of sodium methoxide in 200 ml of absolute ethanol over a period of 1 hr. The reaction mixture was kept under a nitrogen atmosphere at 0° for another 1 hr and then the temperature was allowed to rise to room temperature. Stirring was continued for 2 days. The white solids formed were collected by filtration and washed with absolute alcohol. The filtrate was poured into 300 ml of ice-cold 2 *N* HCl and extracted with 600 ml of ether and the ether extract was then washed with 300 ml of 2 *N* HCl. The combined acidic aqueous ethanolic solutions were treated with Norit and filtered. The filtrate was concentrated in vacuo to a semisolid which was dissolved in 2-propanol (hot), the insolubles were filtered, and white crystals were obtained from the filtrate on cooling: mp 145–146° (lit.[9b] 146–147°); 61%; ir (KBr) identical with the published spectrum.[9b]

Isolation of 1,6-Dihydroimidazo[4,5-*d*]imidazole from the Irradiation of 3-Aminopyrazole-4-carbonitrile. A 250-ml solution of 10^{-2} *M* pyrazole **21** in dioxane was degassed and irradiated at 254 nm for 77 hr. The solution was concentrated in vacuo to a solid and the residue was chromatographed on 50 g of silica gel (benzene–methanol, 95:5). The fractions which gave a blue color with DSA were combined and concentrated in vacuo to a solid. The product exhibited uv and ir spectra identical with those of an authentic sample of **3**.[2]

Irradiation of 2-Methylamino-1-cyclohexene-1-carbonitrile in Aqueous Ethanol. A 10^{-2} *M* solution of the enaminonitrile **13b** in aqueous ethanol (4:1) was degassed and irradiated in quartz at 254 nm for 17 hr. TLC analysis (ether–methanol, 95:5) showed the major product to be *N*-methyl-4,5,6,7-tetrahydrobenzimidazole (**14b**) together with smaller amounts of starting material plus some additional unknown products. The reaction mixture (10 ml) was then hydrolyzed with 5 ml of 6 *N* HCl at room temperature for 24 hr. (These reactions conditions were found in control experiments to hydrolyze the enaminonitrile to 2-oxocyclohexanecarbonitrile but they did not hydrolyze the amide moiety of *N*-methyl-2-oxocyclohexanecarboxamide.) The acidic solution was then extracted four times with methylene chloride, and the methylene chloride extract was washed once with water, dried over $MgSO_4$, and concentrated in vacuo to an oil. TLC analysis (ether–methanol, 95:5) did not reveal even a 1% yield of the desired 2-oxocyclohexanecarboxamide by uv absorption or characteristic purple color with $FeCl_3$.

Irradiation of 2-Amino-1-cyclohexene-1-carbonitrile in Aqueous Ethanol. A 10^{-2} *M* solution of the enaminonitrile **13a** in aqueous ethanol (4:1) was degassed and irradiated in quartz at 254 nm for 9.5 hr. TLC analysis (benzene–methanol–isopropylamine, 92:6:2) showed the major product to be the imidazole **14a** and the minor products to be starting material plus three other unknown compounds. 2-Oxocyclohexanecarboxamide was not detected when an aliquot of the reaction mixture was subjected to acid hydrolysis as described above.

Synthesis of 1,4-Dioxaspiro[4.5]decane-6-carboxamide from Ethyl 1,4-Dioxaspiro[4.5]decane-6-carboxylate.[1] The general procedure of Petit and Poisson was followed.[27] White crystals were obtained which crystallized from *n*-pentane–benzene (1:1): mp 138–140°; ir (KBr) 3380 and 3180 (m) (NH), 2940 (m), 1650 (m) (C=O), 1435 (m), 1155 (m), 1080 (s), and 1030 cm^{-1} (m); NMR ($CDCl_3$) δ 6.7–5.6 (br s, 2, NH_2), 4.0 [s, 4, $(CH_2)_2$], 2.55 (m, 1, methine), and 1.65 [m, 8, $(CH_2)_4$].

Synthesis of 2-Oxocyclohexanecarboxamide. To 170 mg of 1,4-dioxaspiro[4.5]decane-6-carboxamide was added 6 ml of 6 *N* HCl and the mixture was stirred at room temperature for 20 hr. The reaction solution was then extracted four times with 20-ml portions of methylene chloride and the combined organic layers were washed with 25 ml of brine, dried over $MgSO_4$, and concentrated in vacuo to a white residue. The residue was crystallized from 2-propanol: mp 130–132° (lit.[28,29] 131–132°); ir (KBr) 3430 (s), 3330 (w), 3190 (m), 2940 (m), 2840 (m), 1650 (s), 1635 (s), 1585 (m), 1450 (m), 1335 (m), 1225 (m), and 1135 cm^{-1} (m).

Kinetics of the Photoisomerization of 2-Methylamino-1-cyclohexene-1-carbonitrile (13b). Degassed 10^{-4} *M* solutions of **13b** were irradiated at 300 nm in ethanol for 60- or 120- sec time periods and the concentrations of reactant and product (**14b**) were monitored by their uv absorption at 276 and 215 nm, respectively. The absorption of **14b** was not followed at its maximum at 226 nm because of overlapping absorption with **13b**. A 300-nm light source was used in place of the usual 254-nm source to avoid photodecomposition of the imidazole product. The rate of loss of **13b** and formation of **14b** agreed within 15%. An isosbestic point was observed at 239 nm.

Photolysis at Low Temperatures. Photolysis of 2-Amino-1-cyclopentene-1-carbonitrile. Irradiation of the title compound in KBr pellet or Nujol mull using a Rayonet reactor equipped with a 254-nm light source for 1 hr at −195° resulted in the formation of an ir band at 2000 cm^{-1} which disappeared on warming. Irradiation at −77° resulted only in the development of weak bands at 2260, 1080, 820, and 765 cm^{-1}. These bands are not found in the ir spectrum of the imidazole **11** although a small amount of this product was detected by TLC after irradiation at −77°.

Photolysis of 2-Amino-3-*n*-pentyl-3-phenyl-1-cyclopentene-1-carbonitrile (17). Irradiation of **17** as a neat film at 254 nm at −196° for 1 hr resulted in the formation of a new peak at 2020 cm^{-1} which disappeared on warming.

Photolysis of 2-Amino-1-cyclohexene-1-carbonitrile (13a). Irradiation of **13a** in KBr with a 254-nm light source at −195° for 1 hr resulted in the formation of a new band at 2000 cm^{-1}. The absorption disappeared on warming to room temperature.

Photolysis of 2-Methylamino-1-cyclohexene-1-carbonitrile (13b). Irradiation of **13b** in KBr with a 254-nm light source for 1 hr at −195° resulted in the formation of a new band at 2010 cm^{-1}. This absorption disappeared on warming to room temperature.

Photolysis of 2-Dimethylamino-1-cyclohexene-1-carbonitrile (18). No change was observed in the ir spectrum when a neat film of **18** was irradiated with a 254-nm light source for 1 hr.

Photolysis of 2-*tert*-Butylamino-1-cyclohexene-1-carbonitrile (13c). A new band was observed in the ir at 2015 cm^{-1} when a neat film of **13c** was irradiated at −195° for 1 hr with a 254-nm light source. The absorption disappeared when the sample was warmed to room temperature.

Photolysis of 2-Amino-1-cycloheptene-1-carbonitrile (15). A new ir band was observed at 2000 cm^{-1} when a KBr pellet of **15** was irradiated at −195 or −77° for 1 hr. An additional band formed at 2260 cm^{-1} after irradiation for 3 hr. The 2000-cm^{-1} band disappeared on warming while the band at 3260 cm^{-1} was stable to heat. No peaks corresponding to imidazole **16** were observed when the pellet was warmed to room temperature, although a small amount was detected by TLC.

Photolysis of 3-Methylpyrazole. No change in the ir spectrum was observed when a melt of 3-methylpyrazole was irradiated at 254 nm at −196° and −77° for 2 hr.

Photolysis of 1,4,5,6-Tetrahydrocyclopentapyrazole (12). No change in the ir was observed when a KBr pellet of the pyrazole **12** was irradiated at −77° at 254 nm for 5 hr.

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21, 16617-46-2; 2-oxocyclohexanecarbonitrile, 4513-77-3; imidazole-4-carboxaldehyde oxime, 57090-90-1; 6-amino-1,4-dioxaspiro[4.4]nonane, 57090-91-2; 6-phthalimido-1,4-dioxaspiro[4.4]nonane, 10442-96-3; cyclopentanone oxime *p*-toluenesulfonate, 10442-97-4; 1,4-dioxaspiro[4.5]decane-6-carboxamide, 57090-92-3; ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate, 13747-72-3; 2-oxocyclohexanecarboxamide, 22945-27-3; 3-methylpyrazole, 1453-58-3.

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Thallium in Organic Synthesis. XLI. Synthesis of 1-Substituted 2(1*H*)-Pyridones. A New Synthesis of Unsymmetrical Biphenyls via Photochemical N–O Bond Cleavage of 1-Aroyloxy-2(1*H*)-pyridones[1,2]

Edward C. Taylor,* Henry W. Altland, and Frank Kienzle[3]

Department of Chemistry, Princeton University, Princeton, New Jersey 08540

Alexander McKillop

School of Chemical Sciences, University of East Anglia, Norwich, England

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Reaction of the thallium(I) salt of 1-hydroxy-2(1*H*)-pyridone with alkyl iodides, arylsulfonyl chlorides, and aroyl chlorides gave a series of 1-alkoxy-, 1-arylsulfonyloxy-, and 1-aroyloxy-2(1*H*)-pyridones. A similar series was prepared from the thallium(I) salt of 1-hydroxy-3,5-dinitro-2(1*H*)-pyridone. Irradiation of the 1-aroyloxy-3,5-dinitro-2(1*H*)-pyridones in benzene gave unsymmetrical biphenyls in moderate yield. It is suggested that these stable, crystalline pyridone derivatives may be generally useful as sources of aryl radicals.

We have recently described a convenient, high-yield synthesis of 1-acyloxy-2(1*H*)-pyridones by reaction of the thallium(I) salt of 1-hydroxy-2(1*H*)-pyridone (1) with acyl halides in ether suspension.[4] Intrigued by the utility of these active esters for peptide synthesis,[4-6] we have examined the preparation and reactivity of a number of other 1-substituted 2(1*H*)-pyridones which were similarly prepared.

Although 1 was unreactive toward alkyl halides at room temperature in ether suspension, reaction was quantitative when 1 was heated under reflux with an excess of the alkyl halide.[7] Lower boiling halides and secondary halides needed longer reaction times, and not surprisingly, iodobenzene proved unreactive. 1-Phenoxy-2(1*H*)-pyridone was, however, readily prepared in 90% yield by stirring 1 with 1 equiv of diphenyliodonium chloride in *tert*-butyl alcohol for 16 hr at 30°.

1-Aroyloxy-2(1*H*)-pyridones were similarly prepared from 1 and the appropriate aroyl halide at room temperature in ethyl acetate suspension. The various 1-alkoxy- and 1-aroyloxy-2(1*H*)-pyridones prepared in this study, along with pertinent physical data and yields, are summarized in Table I.

An analogous series of 1-alkoxy and 1-aroyloxy derivatives was prepared from the thallium(I) salt of 1-hydroxy-3,5-dinitro-2(1*H*)-pyridone (2). As expected, 2 was weakly nucleophilic and proved to be relatively sluggish in its reac-