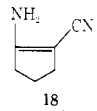
(2) (a) S. Danishefsky and G. Rovnyak, *J. Chem. Soc., Chem. Commun.*, 821 (1972); (b) *J. Org. Chem.*, **40**, 114 (1975).
(3) S. Danishefsky, G. Rovnyak, and R. Cavanaugh, *Chem. Commun.*, 636 (1969).
(4) J. E. Dolfini, K. Menich, P. Corliss, R. Cavanaugh, S. Danishefsky, and S. Chakrabartty, *Tetrahedron Lett.*, 4421 (1966).
(5) P. Boldt, L. Schulz, and J. Etzmuller, *Chem. Ber.*, **100**, 1281 (1967).
(6) Enamines characteristically exhibit strong absorption in the region of 220–235 nm (ϵ 5000–10000): S. K. Malhotra, "Enamines", A. G. Cook, Ed., Marcel Dekker, New York, N.Y., 1969.
(7) S. Baldwin, *J. Org. Chem.*, **26**, 3288 (1961): ir ($CHCl_3$) 3512, 3420,



18

2189, 1645, 1605 cm^{-1}; uv λ 263 (ϵ 13000). **13**: ir ($CHCl_3$) 3472, 3367, 2188, 1645, 1597 cm^{-1}; uv λ 264 (ϵ 11900).
(8) A 10 ft × 0.38 in. column packed with Chromosorb coated with 20% by weight of SE-30 silicone gum was used.
(9) A satisfactory elemental analysis was obtained for this material.
(10) We are indebted to W. C. Jankowski of Varian for this spectrum.
(11) W. Herz, *J. Org. Chem.*, **22**, 630 (1957): 2-oxocyclopentanepentanoic acid ir 1730, 1710 cm^{-1}.
(12) (a) R. N. Chakravarti, *J. Chem. Soc.*, 1028 (1947); (b) S. Kagawa et al., *Tetrahedron Lett.*, 3913 (1969); neither reference reports physical data for **16**.
(13) M. Pines, F. J. Pavlik, and V. N. Ipatieff, *J. Am. Chem. Soc.*, **73**, 5738 (1951).
(14) A 6 ft × 0.25 in. column packed with Chromosorb P coated with 30% by weight of SE-30 silicone gum was used.
(15) N. J. Leonard, H. S. Gutowsky, W. J. Middleton, and E. M. Petersen, *J. Am. Chem. Soc.*, **74**, 4070 (1952): 2-carbethoxycyclopentanone ir 1756, 1725, 1660, 1618 cm^{-1}.
(16) H. O. House and H. Babad, *J. Org. Chem.*, **28**, 90 (1963).
(17) W. Herz, *J. Am. Chem. Soc.*, **78**, 1485 (1956): ethyl 1-carbethoxy-2-oxocyclopentanepentanoate ir 1735, 1755 cm^{-1} (sh).
(18) A modification of the procedure of W. Kreiser, W. Haumesser, and A. Thomas, *Helv. Chim. Acta*, **57**, 164 (1974).
(19) A 4 ft × 0.25 in. column packed with Chromosorb W coated with 20% by weight of DC 200 silicone oil was used.

Mechanistic Studies on the Photochemical Reactions of Isoxazoles[1]

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

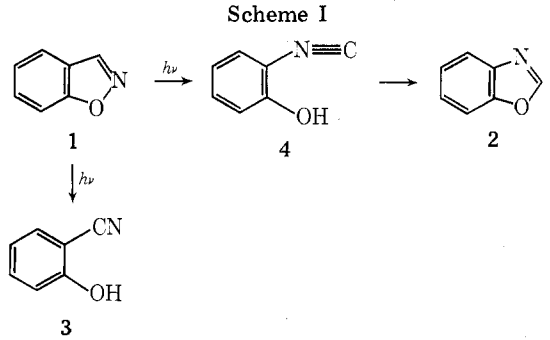
Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181

Received September 22, 1975

The mechanisms of the photochemical conversion of isoxazoles to oxazoles and ketoketenimines have been investigated. Isonitrile **14** was detected by an ir band at 2160 cm^{-1} in the photoconversion of **5** to **15** at −77°. Compound **14** was further identified by independent synthesis and by hydrolysis to formamide **17** in acid. Ir bands at 1690 and 1655 cm^{-1} are consistent with the hypothesis that azirine **13** is the precursor to isonitrile **14.** It is postulated that a vinyl nitrene is the immediate precursor to **13.** Photolysis of **10** at −77 or −196° resulted in the formation of an ir band at 2050 cm^{-1}. This band was assigned to ketoketenimine **23.** The structure of **23** was proved by independent synthesis and trapping with water. No intermediates in the photochemical conversion of **10** to **21** were detected by trapping or low-temperature ir studies. New syntheses of isoxazoles **5** and **10** were developed.

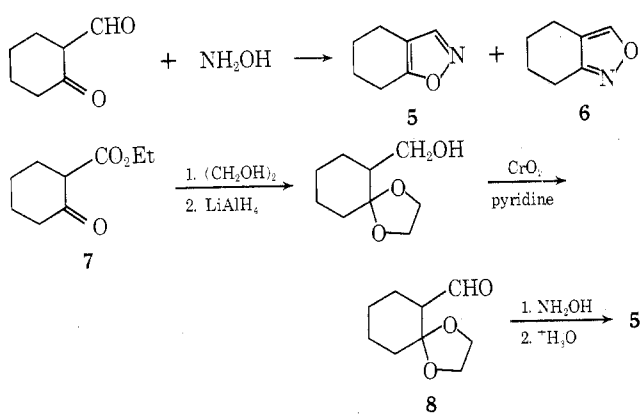
A study of the mechanisms of the photochemical rearrangement of indoxazene (**1**) to benzoxazole (**2**) and 2-cyanophenol (**3**) has been reported (Scheme I).[2] The isonitrile (**4**) was detected spectrally by trapping experiments and by independent synthesis. The present study was undertaken with the objective of learning more about the mechanism of the photochemical isomerization of isoxazoles to oxazoles.[3–5]

Scheme I

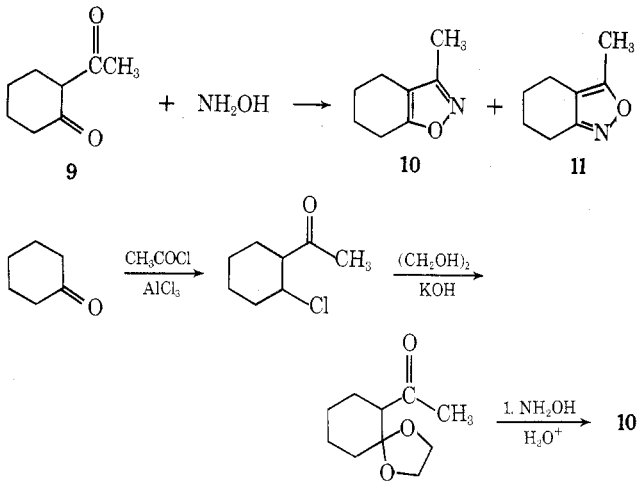


Results and Discussion

Synthesis of Isoxazoles. The reported synthesis of 4,5,6,7-tetrahydro-1,2-benzisoxazole (**5**) from 2-oxocyclohexanecarboxaldehyde was complicated by the formation of isomer **6,** which we were unable to separate from **5.**[6,7] A successful synthesis of pure **5** was devised starting from ethyl 2-oxocyclohexanecarboxylate (**7**) via aldehyde **8.**[8]



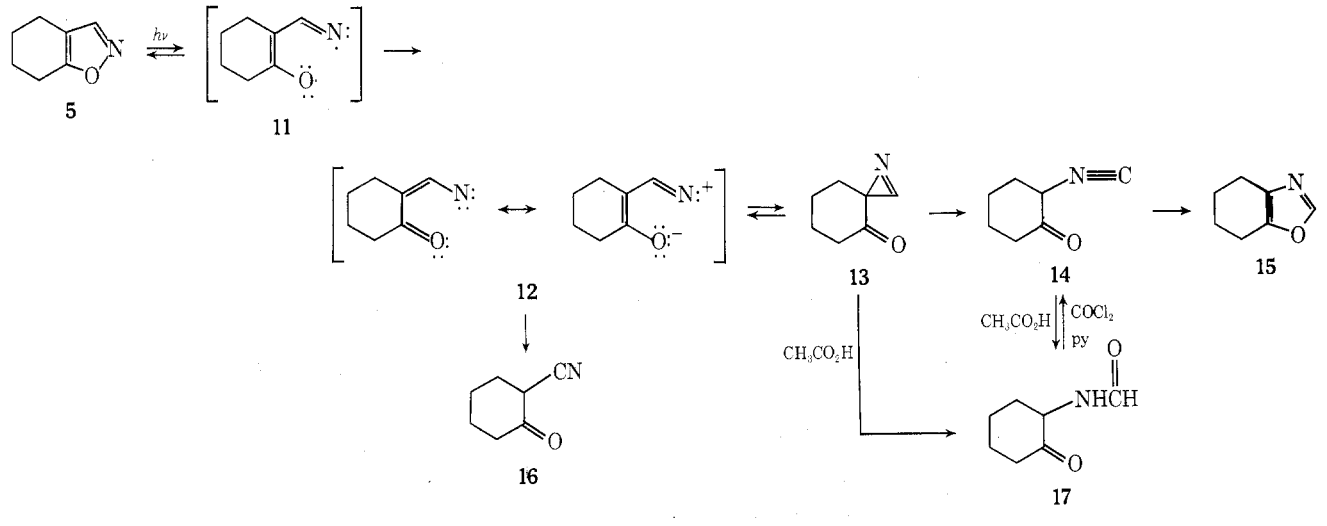
Attempted direct synthesis of 3-methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole (**10**) from 2-acetylcyclohexanone (**9**) led to a 1:4 mixture of the desired isomer **10** and isomer **11,** respectively. A higher proportion (5:1) of **10** was obtained by preferential ketalization of the cyclohexanone carbonyl of **9** followed by its reaction with hydroxylamine and acid hydrolysis of the ketal. We succeeded in obtaining pure **10** starting from cyclohexanone and proceeding via 1-acetyl-2-chloro-1-cyclohexene.



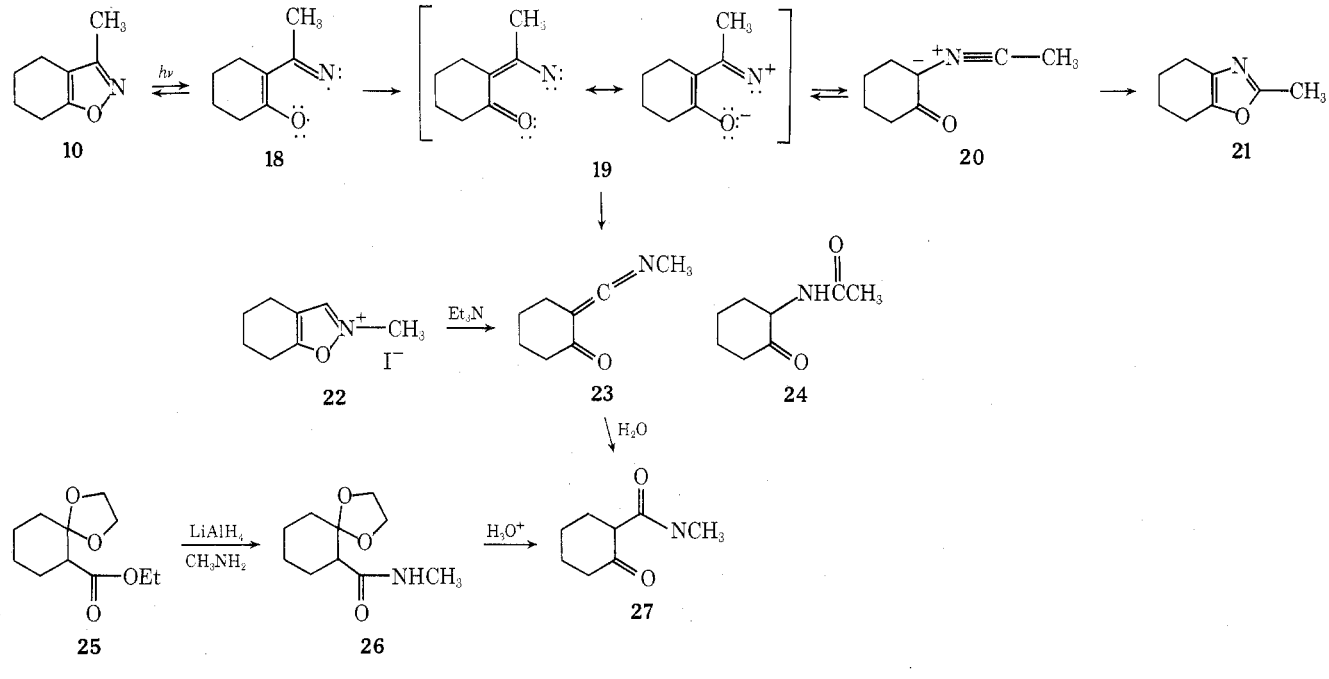
Photochemical Studies. The photochemical rearrangement of **5** to 4,5,6,7-tetrahydrobenzoxazole (**15**) proceeds in 99% yield in degassed ethanol (Scheme II). A 63% yield of **21** was obtained on irradiation of **10** in degassed ethanol (Scheme III). Other unidentified photoproducts were detected by TLC when the photolysis of **10** was performed in degassed methylcyclohexane. The photolysis of 2-oxocyclohexanecarbonitrile (**16**) gives a 2% yield of **15** in degassed aqueous solution; however, no **15** could be detected when the photolysis of **16** was performed in tetrahydrofuran or ethanol. None of the corresponding oxazole was detected when 2-oxocyclopentanecarbonitrile was photolyzed in a variety of solvents.

The mechanism of the photochemical rearrangements of **5** and **10** was first investigated by low-temperature ir techniques. Photolysis of a neat film of **5** at −77° resulted in the development of new ir bands at 2210, 1720, 1690, and 1655 cm^{-1}. The bands at 2210 and 1720 cm^{-1} were assigned to the ketonitrile **16** since they were also observed in the ir spectrum of an authentic sample of **16.** These ir bands did not change when the film was warmed to room temperature. The absorption bands at 1690 and 1655 cm^{-1} decrease when the film is warmed to room temperature and a new band develops at 2160 cm^{-1} together with intensified absorption in the 1720-cm^{-1} region. On continued standing at room temperature the infrared bands at 2160 and 1720 cm^{-1} decrease in intensity and absorption bands character-

Scheme II



Scheme III



istic of **15** appear. The presence of **15** in the liquid film was verified by TLC analysis.

The transitory ir absorptions at 1720 and 2160 cm^{-1} were assigned to the ketoisonitrile **14** (Scheme II) since identical bands were observed in the ir spectrum of an authentic sample prepared by the dehydration of the formamide **17**. The formation of oxazoles from β-ketoisonitriles has been reported.[9] The initially observed ir bands at 1690 and 1655 cm^{-1} are tentatively assigned to azirine **13**. The band at 1655 cm^{-1} is consistent with those reported for an azirine with no substituent in the 2 position.[10,11] The 1690-cm^{-1} absorption is consistent with a cyclohexanone carbonyl the frequency of which is shifted to longer wavelengths by conjugation with the spiroazirine group.[12,13] The azirine is probably formed from **5** via the vinyl nitrene **12**, since it has been suggested that vinyl nitrenes are in thermal equilibrium with azirines.[14] Vinyl nitrene **12** is also a likely precursor to ketonitrile **16**.[15,16]

Photolysis of 3-methyl-4,5,6,7-tetrahydro-1,2-benzoisoxazole (**10**) as a neat film at −77 or −196° resulted in the formation of a new ir band at 2050 cm^{-1}. This band disappeared on warming to room temperature. Absorption at 2050 cm^{-1} is characteristic of the ketenimine group in compound **23**. Ketenimines have been noted as photoproducts of isoxazoles[13b] and similar *N*-alkylketenimines are known to be stable at −77°.[8,17] No infrared bands characteristic of 2-methyl-4,5,6,7-tetrahydrobenzoxazole (**21**) were observed on warming the film to room temperature and only a trace of **21** could be detected by TLC analysis. The virtual absence of **21** when **10** was irradiated as a liquid film or in methylcyclohexane solution is due to the low polarity of the medium, since it has been observed that ketenimine and nitrile formation is favored when isoxazoles are irradiated in nonhydroxylic solvents.[2,5] However, the possibility of a greater temperature coefficient for the rate constant for the rearrangement of **10** to **21** as compared to **23** cannot be ruled out.

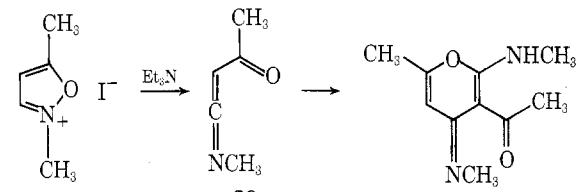
Trapping studies provided further evidence for the intermediates postulated as a result of the low-temperature experiments. Photolysis of **5** in glacial acetic acid resulted in a 50% yield of the corresponding formamide **17**. This product is probably formed by the acid hydrolysis of isonitrile **14**.[2] There is one report[15] of the acid hydrolysis of a 2-unsubstituted azirine to a formamide so the possibility exists that we are intercepting **13** as well as **14**. Only a 5% yield of **17** was obtained when **15** was photolyzed in acetic acid. This eliminates the possibility that **17** was formed after **5** had been converted to oxazole **15**.

A low yield (5%) of the acetamide **24** (corresponding to formamide **17**) along with **21** was obtained on photolysis of **10** in acetic acid. The low yield of **24** that was observed probably is not due to the trapping of a reaction intermediate, because a similar yield of **24** was obtained when **21** was irradiated for the same time period under the same reaction conditions. The absence of trapping by acetic acid suggests that neither azirine nor isonitrile type intermediates (e.g., **20**) are formed in the photochemical conversion of **10** to **21**. There does exist the possibility that intermediates of this type are formed but that they rearrange faster to **21** than they react with acetic acid.

The photochemically produced ketenimine **23** reacted with water in aqueous solution to give a 5% yield of amide **27** together with oxazole **21**. The low yield of **27** is probably due to the use of a polar solvent. It has been demonstrated that higher yields of amides are obtained when nonhydroxylic solvents containing 5% water or methanol are used.[5] There is one report of the predominant formation of a methanol adduct of the ketenimine formed by the photolysis of 3,5-disubstituted isoxazoles in methanol solution.[18]

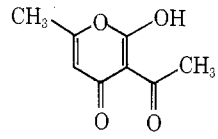
Direct comparison of the spectral and chemical properties of ketenimine **23** prepared synthetically with that prepared photochemically provides further evidence for its formation on irradiation of **10**. The ir spectrum of the reaction mixture formed by the treatment of methiodide **22** with Et_3N exhibited a band for the ketenimine chromophore at the same frequency (2050 cm^{-1}) as was observed in the ir spectrum of photolyzed **10**. Furthermore, addition of water to a solution of the ketenimine prepared from **22** resulted in the formation of the same amide (**27**) as was obtained by photolysis of **10**. Our sample of **27** prepared photochemically was identical in all respects with that prepared chemically but both samples exhibited a melting point that was considerable lower (64–70°) than that in the literature (82–84°).[8] An unambiguous synthesis of **27** from **25**, the ketal of 2-oxocyclohexanecarboxylate, resulted in the formation of a product that was identical with those samples prepared previously in our laboratory. The spectral properties of all our samples were identical with those of an authentic sample provided by Olofson.[8] The melting point of the sample provided by Professor Olofson decreased with time from 84° to the melting point we observed. Presumably this variation is due to different proportions of the two possible tautomeric forms of **27**.

In our initial studies on the chemical synthesis of ketenimines for comparison with those produced photochemically we synthesized ketenimine **29** from 2,5-dimethylisoxazolium iodide (**28**). Ketenimine **29** formed readily as shown



28 **29** **30**

by a band at 2075 cm^{-1} in the ir spectrum of the reaction mixture. However, treatment with water did not result in the expected amide but instead a dimer (**30**) was produced. Structure **30** is consistent with spectral studies and with the structure of dehydroacetic acid (**31**), a compound which



31

forms spontaneously from acetylketene.[19] Presumably the steric requirements of **23** mediate against its forming a similar dimer.

No tetrahydrosalicylamide was formed on irradiation of **5** in aqueous solution. This finding is consistent with the absence of the development of ketenimine absorption in the 2050–2090 cm^{-1} region when **5** was irradiated at −77 and −198°.

Attempts were made to trap the radical (e.g., **18**), or nitrenes (e.g., **19**) or nitrile ylides (e.g., **20**) derived from radicals using olefins.[20-22] Many of the olefins used previously to trap nitrile ylides absorb light at the same wavelengths as isoxazole **9**, so we were limited to the use of the weakly uv absorbing cyclohexene and norbornene as trapping agents. Considerable rearrangement of **10** to **21** was observed during the course of the photolysis of **10** in the presence of these olefins but there was no evidence of adduct formation. The failure to detect olefin adducts is not in conflict with the formation of **18**, **19**, or **20** as intermediates but instead suggests that the rate of the intramolecular re-

arrangement is much faster than the rate of the intermolecular reaction with the olefin.

Experimental Section

General Procedures. The same experimental procedures and instruments were used as described previously.[2] In addition some spectral measurements were performed on a Perkin-Elmer Model 337 ir spectrophotometer and a Varian HA-100 NMR spectrometer. Gas chromatography was performed on a F & M Model 810 equipped with a flame ionization detector and Aerograph Model A-700 equipped with a thermal conductivity detector. The liquid phase noted was supported on Chromosorb W. Samples for irradiation were degassed by at least three freeze–pump–thaw cycles. Thin layer chromatography (TLC) was conducted on Merck's precoated plates of silica gel (F-254) unless otherwise noted. Quantitative analysis was done visually with known amounts of standards chromatographed on the same plate. The accuracy is within ±10%.

The following compounds, prepared essentially by literature procedures, are listed together with the yields and physical constants we observed: 2-oxocyclohexanecarboxaldehyde,[23] 60%, bp 70–75° (7 mm); ethyl 2-oxocyclohexanecarboxylate,[24] bp 115–120° (22–25 mm); 2-aminocyclohexanone hydrochloride,[25] 60%, mp 159–160°, ir in agreement with the reported spectrum; *N*-methyl-5-methylisoxazolium iodide (**28**),[26] mp 125.5–126.5°; 4,5,6,7-tetrahydrobenzoxazole (**15**),[27] bp 67–69° (8 mm); NMR ($CDCl_3$) δ 7.7 (s, 1, aromatic H), 2.55 [m, 4, $(CH_2)_2$], and 1.75 [m, 4, $(CH_2)_2$].

Synthesis of 4,5,6,7-Tetrahydro-1,2-benzisoxazole (5) from 2-Oxocyclohexanecarboxaldehyde. The procedure of von Auwers et al.[6] was followed. The oil was distilled through a Vigreux column: 83%, bp 82–86° (7–8 mm) [lit. 90–95° (14 mm)]; NMR (neat) δ 8.15 (s, 1, aromatic H), 8.05 (s, 1, aromatic H), 2.55 [m, 4, $(CH_2)_2$], and 1.7 [m, 4, $(CH_2)_2$]. The signal at δ 8.05 was assigned to the aromatic proton of **5** while the one at δ 8.15 was assigned to the aromatic proton in **6**. A 6:1 ratio of **5** to **6** was obtained as determined from the NMR spectrum. Compound **6** was prepared previously.[28]

Synthesis of Ethyl 1,4-Dioxaspiro[4.5]decane-6-carboxylate (25). To 0.03 mol of ethyl 2-oxocyclohexanecarboxylate dissolved in 75 ml of benzene was added 0.03 mol of ethyl glycol, and a catalytic amount of *p*-toluenesulfonic acid. This solution was heated to reflux and after 10 hr 1 equiv of water was collected in a Dean-Stark trap. The solution was cooled and then poured into dilute aqueous sodium hydroxide and extracted three times with ether, and the combined ether phases were washed with water and then brine. The ether extract was dried over magnesium sulfate and concentrated in vacuo to an oil. The oil was distilled: bp 140–142° (19 mm); NMR (neat) δ 4.05 (q, 2, ester), 3.85 (s, 4, ketal), 2.75 (m, 1, $-CHCO_2Et$), 2.65 [m, 8, $(CH_2)_4$], and 1.2 (t, 3, ester); ir (neat) spectrum gives no evidence for starting material.

Synthesis of 6-Hydroxymethyl-1,4-dioxaspiro[4.5]decane. To a solution of 0.01 mol of lithium aluminum hydride in 150 ml of dry tetrahydrofuran (THF) was added dropwise 0.0317 mol of the ester **25** over a 10-min period at room temperature. The mixture was then heated to reflux for 9 hr and then allowed to stir overnight at room temperature. Water was added (4 ml) and then 12 ml of a saturated solution of sodium potassium tartrate was added to the mixture and it was stirred for an additional 1 hr. The solids were filtered and washed with THF and the filtrate was concentrated in vacuo to a yellow oil which was distilled: 70%; bp 136–145° (19–20 mm); ir (neat) 3460 cm^{-1} (s) (OH) and the carbonyl region (1760–1620 cm^{-1}) was blank.

Synthesis of 1,4-Dioxaspiro[4.5]decane-6-carboxaldehyde (8). The general oxidation procedure of Ratcliffe and Rodehorst was followed.[29] To a solution of 0.157 mol of dry chromium trioxide and 0.316 mol of dry pyridine in 450 ml of methylene chloride was added 0.26 mol of the above alcohol in a small volume of methylene chloride with vigorous stirring. The solution was stirred for 45 min and then decanted from the black solids. The filtrate was concentrated in vacuo to dryness. Ether was added to the residue and the ether was then washed with dilute aqueous potassium hydroxide. The basic aqueous phase was extracted three times with ether and the combined ether layers were washed once with water and two times with brine. The ether extract was dried over magnesium sulfate and concentrated in vacuo to a pale yellow oil which was distilled: 79%; bp 123–133° (20 mm); ir (neat) 2780 (w) (OCH) and 1720 cm^{-1} (s) (O=CH).

Synthesis of 4,5,6,7-Tetrahydro-1,2-benzisoxazole (5) from 1,4-Dioxaspiro[4.5]decane-6-carboxaldehyde (8). To 20 ml of 1:1 aqueous ethanol was added 0.01 mol each of hydroxylamine hydrochloride and potassium carbonate, then 0.01 mol of the above aldehyde (**8**) and the solution was stirred for 6 hr. The solution was acidified with 1 *N* HCl and then heated on a steam bath for 1.5 hr. The solution was then cooled and extracted four times with ether, and the combined ether layers were washed once with a small amount of water and then brine. The ether extract was dried over magnesium sulfate and concentrated in vacuo (20 mm) at 50° to an oil. The oil was distilled and the fraction of bp 102–105° (20 mm) was retained, affording a 72% yield of **5**: NMR (neat) δ 8.05 (s, 1, aromatic H), 2.5 [m, 4, $(CH_2)_2$], and 1.7 [m, 4, $(CH_2)_2$]. The peaks obtained in this NMR spectrum have the same chemical shifts as those peaks assigned to the major component present in the previous synthesis where a mixture of isoxazoles (**5** and **6**) was obtained.

Synthesis of 3-Methyl-4,5,6,7-tetrahydro-1,2- and -2,1-benzisoxazoles from 2-Acetylcyclohexanone. To a solution of 10 ml of ethanol, 20 ml of water, and 0.0359 mol of hydroxylamine hydrochloride was added 0.0350 mol of 2-acetylcyclohexanone (Eastman). The reaction mixture was heated to reflux for 1.5 hr, cooled, and made basic with potassium carbonate. The basic mixture was extracted three times with ether and the combined ether layers were washed twice with brine, dried with magnesium sulfate, and concentrated in vacuo to an oil which was distilled: bp 90–96° (8 mm); NMR ($CDCl_3$) δ 2.7 [m, 4, $(CH_2)_2$], 2.3 (s, 3, CH_3) (**11**, major), 2.2 (s, 3, CH_3) (**10**, minor), and 1.75 [m, 4, $(CH_2)_2$]; TLC analysis (ether–cyclohexane, 1:1) showed only one spot which was bright yellow when sprayed with iodoplatinate;[30a] VPC (5% Carbowax, 6 ft at 135°) showed two peaks with appreciable overlap in the ratio of 1:4, the one with the shortest retention time being 25% of the mixture.

Synthesis of 6-Acetyl-1,4-dioxaspiro[4.5]decane. To 0.03 mol of 2-acetylcyclohexanone in 50 ml of benzene was added 0.03 mol of ethylene glycol and 0.1 g of *p*-toluenesulfonic acid monohydrate and the mixture was heated to reflux for 20 hr. At the end of this time about 75% of 1 equiv of water was collected in a Dean-Stark trap. The solution was cooled, made basic by addition of a cold aqueous potassium carbonate solution, and extracted with ether, and the combined ether layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo to a yellow oil which was then distilled. The fraction boiling at 112–118° (9 mm) was collected: ir (neat) 1720 cm^{-1} (C=O); NMR ($CDCl_3$) δ 3.9 [s, 4, $(CH_2)_2$], 2.75 (t, 1, methine), 2.2 (s, 3, CH_3), and 1.7 [m, 8, $(CH_2)_4$]. Minor peaks were observed at δ 2.1, 1.35, and 1.4 which indicate that about 85–95% of the ketalization took place on the ring carbonyl. The major peaks in the NMR are in agreement with the published spectrum.[31] The oil was redistilled before use at 130–132° (15 mm) [lit.[31] 119–120° (7 mm)].

Synthesis of 3-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole (10) from the Crude 6-Acetyl-1,4-dioxaspiro[4.5]decane. To 40 ml of a 3:1 aqueous ethanolic solution of 0.004 mol of hydroxylamine hydrochloride were added 0.01 mol of sodium acetate and 0.004 mol of the above crude 2-acetylcyclohexanone ethylene ketal and the solution was stirred overnight. This solution was acidified with dilute aqueous HCl and heated to reflux on the steam bath for 2.5 hr. The solution was cooled, poured into water, and extracted three times with ether. The combined ether layers were washed successively with brine, dilute potassium hydroxide, and brine, dried over $MgSO_4$, and concentrated in vacuo to an oil which was distilled: bp 101–102° (11 mm); ir (neat) exhibited no bands in the 1700-cm^{-1} region; NMR ($CDCl_3$) δ 2.65 [m, 4, $(CH_2)_2$], 2.2 (s, 3, CH_3), and 1.8 [m, 4, $(CH_2)_2$]. A peak was observed at δ 2.3 (s, CH_3) which was assigned to isomer **11**. Based on the peak height at δ 2.2 (vs. δ 2.3) isoxazole isomer **10** represents about 85% of the isomer mixture.

Synthesis of 1-Acetyl-2-chloro-1-cyclohexane. The desired product was not obtained when the procedure of Kochetkov was followed exactly.[32] The procedure was modified by increasing the amount of aluminum chloride (11 g) by a factor of 13, i.e., 3 mol each of aluminum chloride and acetyl chloride per mole of cyclohexanone, which resulted in a satisfactory yield of the product, bp 92–108° (9 mm). Redistillation gave a water-white oil, bp 91–96° (7 mm) [lit.[32] 125–129° (30 mm)].

Synthesis of 6-Acetyl-1,4-dioxaspiro[4.5]decane from the Vinyl Chloride (1-Acetyl-2-chloro-1-cyclohexene). The procedure of Kochetkov et al.[32] was followed. Distillation of the oil, bp 115–119° (9 mm) [lit.[32] 121–122° (10 mm)], afforded a satisfactory yield of the above ketal: ir (neat) 1720 cm^{-1} (s); NMR ($CDCl_3$) δ 3.9 [s, 4, $(CH_2)_2$], 2.8 (t, 1, methine), 2.2 (s, 3, CH_3), and 1.65 [m, 8, $(CH_2)_4$]. This product was used directly in the following experiment.

Synthesis of the Oxime of 6-Acetyl-1,4-dioxaspiro[4.5]dec-

ane. To 0.01 mol of 6-acetyl-1,4-dioxaspiro[4.5]decane was added a solution of 0.01 mol of hydroxylamine hydrochloride, 0.02 mol of sodium acetate, 30 ml of water, and 15 ml of ethanol. The reaction mixture was stirred at room temperature for 18 hr. The crystals were collected by filtration and washed with water and air dried. White crystals were obtained after one recrystallization from cyclohexane: mp 115–117°; ir (KBr) 3320 (s) (OH), 2980 (s), 1680 (w), 1440 (m), 1160 (s), 1080 (s), 955 (s) (NO), and 930 cm^{-1} (s); NMR ($CDCl_3$) δ 8.65 (s, 1, OH), 3.85 [s, 4, $(CH_2)_2$], 2.5 (m, 1, methine), 1.95 (s, 3, CH_3), and 1.65 [m, 8, $(CH_2)_4$].

Synthesis of 3-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole (10) from the Oxime of 6-Acetyl-1,4-dioxaspiro[4.5]decane. To 1 g of the above oxime were added 10 ml of ethanol and 25 ml of 1 *N* HCl. The reaction mixture was heated on a steam bath for 5 hr, cooled, poured into 40 ml of 1 *N* NaOH, and extracted three times with ether. The combined ether layers were washed with water and brine, dried over $MgSO_4$, and concentrated in vacuo to an oil which was then distilled: bp 98–100° (10 mm); ir (neat) spectrum was superimposable on the spectrum of the product obtained by the monoketalization of 2-acetycyclohexanone; NMR ($CDCl_3$) was consistent with pure **10** since the δ 2.2 singlet peak assigned to **11** was absent. Analysis by VPC (5% Carbowax, 6 ft column) showed only one peak which corresponded to the major component (**10**) in the previous synthesis. Uv max (ethanol–methanol, 4:1 v/v) 226 nm.

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08. Found: C, 70.13; H, 8.31.

Synthesis of 2-Methyl-4,5,6,7-tetrahydrobenzoxazole (21). To 9.5 g (0.0834 mol) of adipoin were added 8.1 g (0.0825 mol) of concentrated H_2SO_4 and recrystallized acetamide (from methanol–ether) and the reaction mixture was then stirred on a steam bath for 3 hr. The mixture was then heated at 150° for 0.5 hr. The solution was then cooled, poured into ice water, made basic with KOH, and extracted three times with ether, the combined ether layers were washed once with water and then with brine and dried over $MgSO_4$, and the solvent was distilled. Distillation of the oily residue afforded a water-white oil: bp 74–76° (10 mm); NMR ($CDCl_3$) δ 2.45 [m, 4, $(CH_2)_2$], 2.4 (s, 3, CH_3), and 1.8 [m, 4, $(CH_2)_2$]; ir (neat) 2850 (s), 1670 (m) (C=N), 1585 (s), 1270 (s), and 1215 cm^{-1} (s); uv max (4:1 ethanol–methanol, v/v) 225 nm.

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08. Found: C, 70.03; H, 8.26.

Irradiation of 4,5,6,7-Tetrahydro-1,2-benzisoxazole in Ethanol. A 10^{-2} *M* ethanol solution of **5** was degassed and irradiated in a quartz cell at 254 nm for 2 hr. Analysis by VPC (10% SE-30, 6-ft column), using a 10^{-2} *M* ethanolic solution of the oxazole isomer **15** as a reference standard, indicated a 99% yield of the 4,5,6,7-tetrahydrobenzoxazole.

Photochemical Synthesis of 3-Methyl-4,5,6,7-tetrahydrobenzoxazole (21) from Isoxazole 5. A 10^{-2} *M* ethanolic solution of 3-methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole (**10**) was degassed and irradiated at 254 nm for 0.5 hr. Analysis by VPC (5% Carbowax, 6-ft column) at 145°, using a 10^{-2} *M* ethanolic solution of the oxazole isomer **21** as a standard, indicated a 63% yield of the desired oxazole **21**; TLC (ether) further confirmed that only two materials were present, namely, unreacted starting material (**10**) and the oxazole **21**.

Photochemical Synthesis of 3-Methyl-4,5,6,7-tetrahydrobenzoxazole from 10 in Methylcyclohexane. A 10^{-2} *M* solution of **10** in methylcyclohexane was degassed and irradiated at 254 nm for 30 min. TLC analysis (ether) showed the major product to be the oxazole **21**, some starting material, and large amounts of polar substances at the origin of the TLC plate.

Irradiation of 2-Oxocyclohexanecarbonitrile (16). A 10^{-3} *M* aqueous solution of the 2-cyanocyclohexanone **16** was degassed and irradiated in a quartz cell using 254-nm lamps for 1 hr. A 10-ml sample was then concentrated in vacuo to an oil and analyzed by TLC using both ethyl acetate and ether. In both cases a spot corresponding to the 4,5,6,7-tetrahydrobenzoxazole (**15**) was observed which gave the same color test with iodoplatinate[30a] and the same R_f value as an authentic sample. From the TLC analysis (benzene–methanol, 95:5) using a known amount of the authentic oxazole **15**, it was estimated that the oxazole **15** was produced photochemically in a 2% yield. Analysis by VPC (6-ft column of 10% SE-30 at 130° and 6-ft column of 5% Carbowax at 160°) also indicated about a 2% yield of the oxazole isomer.

Photolysis of 4,5,6,7-Tetrahydro-1,2-benzisoxazole at −77°. The isoxazole **5** was irradiated at 254 nm as a neat film at −77° for several hours. New peaks formed at 2210 (w), 1720 (w), and 1690 (m) and shoulder at 1655 cm^{-1}. On slowly warming to room temperature, the 1690- and 1655-cm^{-1} peaks diminished and a 2160-cm^{-1} peak formed, and the 1720-cm^{-1} peak intensified. After 3 hr of such warming the 2160-cm^{-1} peak was sharply diminished and the 1720-cm^{-1} peak moderately diminished. Ir peaks corresponding to the oxazole isomer **15** were observed at 1705 (w), 1665 (w), 1110 (w), 1070 (w), and 905 cm^{-1} (w). The peak at 2210 cm^{-1} did not change in intensity. Its position corresponds with that of the nitrile moiety in 2-oxocyclohexanecarbonitrile. Analysis of this irradiated sample by TLC (cyclohexane–ether, 2:1) showed starting material (**5**), the oxazole isomer (**15**), and 2-oxocyclohexanecarbonitrile (**16**).

Synthesis of 2-Formamidocyclohexanone (17). The formylation procedure of Sheehan and Yang[33] was followed. To 9.2 g (0.057 mol) of the 2-aminocyclohexanone hydrochloride in 30 ml of 97–100% formic acid under a nitrogen cover at 0–5° was added 5 ml of dry pyridine with stirring followed by the slow addition of 20 ml of acetic anhydride. At the end of the addition of the acetic anhydride the ice bath was allowed to melt and the stirring was continued overnight. Ethanol was added to the reaction mixture and the solution was concentrated in vacuo to an oil. Ice was added to the oil and the mixture was extracted three times with chloroform, dried, filtered, and concentrated in vacuo. Distillation afforded a water-white oil: bp 108–109° (0.4 mm); ir (neat) 3330 (s), 3070 (w), 2960 (s), 1740–1650 (s and br), and 1530 cm^{-1} (s).

Anal. Calcd for $C_7H_{11}NO_2$: C, 59.56; H, 7.85. Found: C, 59.58; H, 7.90.

Synthesis of 2-Acetamidocyclohexanone (24). To 500 mg (0.00309 mol) of 2-aminocyclohexanone hydrochloride were added 15 ml of acetic anhydride and 260 mg (0.00317 mol) of anhydrous sodium acetate and the mixture was stirred at room temperature overnight. Methanol was added to the solution and it was stirred for an additional 4 hr and then concentrated to a small volume in vacuo (20 mm) while keeping the temperature at 30–40°. Dilute aqueous potassium carbonate was added to the solution and it was extracted with ether three times. The combined ether phases were washed with brine once, dried over $MgSO_4$, filtered, and concentrated to dryness. The residue obtained was recrystallized from cyclohexane to afford white crystals: mp 91–92° (lit.[34] 92°); ir (KBr) 3320 (s) (NH), 1715 (s) (ketone), 1650 (s) (amide), and 1550 cm^{-1} (m).

Synthesis of 4,5,6,7-Tetrahydrobenzoxazole (15) from 2-Isocyanocyclohexanone (14). The general procedure of isonitrile synthesis by Ugi[35] was followed. To 1.4 g (0.01 mol) of 2-formamidocyclohexanone (**17**) in 50 ml of methylene chloride and 10 ml of triethylamine was bubbled in phosgene for about 5 min while allowing the temperature to rise to about 35°. The mixture was cooled and then nitrogen was bubbled through the solution to remove the excess phosgene; then ammonia was bubbled through the solution for about 20 min. After chilling the solution the salts were collected by filtration and the filter cake was washed with methylene chloride. The filtrate was concentrated at less than 30° (20 mm) to a light brown oil. Analysis by uv (ethanol) showed a strong max at 268 nm, and ir (neat) showed isonitrile peaks at 2160 (s) (keto) and 2130 cm^{-1} (w) (enol) (the enol is probably due to the base present). Distillation of the crude isonitrile at 7 mm afforded only one fraction: bp 55–62°; ir (neat) spectrum was identical with that of a sample of oxazole **15** made by a known procedure;[36] TLC analysis in two different systems also afforded the same R_f values and color (yellow) as **15** when sprayed with iodoplatinate reagent; the sample had the same retention time as an authentic sample of **15** by VPC (6-ft column of 10% SE-30).

Photolysis of 3-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole at −77°. The trisubstituted isoxazole **10** was irradiated at 254 nm as a neat film at −77°. After 1 hr new peaks formed at 2050 (m), 1695 (w), and 1590 cm^{-1} (w). On slowly warming to room temperature for 0.5 hr the 2050-cm^{-1} band had completely disappeared and two new bands emerged at 3400–3500 (broad) and 1620 cm^{-1} which were thermally stable but do not correspond to the ir spectrum of the oxazole **21**. Analysis by TLC (ether) showed largely starting material (**10**), a smaller amount of the oxazole isomer (**21**) (same R_f value and yellow color when treated with the iodoplatinate reagent), and some unknown material at the origin.

Irradiation of 4,5,6,7-Tetrahydro-1,2-benzisoxazole in Glacial Acetic Acid. A 10^{-2} *M* solution of isoxazole **5** in acetic acid and was degassed and irradiated in a quartz cell at 254 nm for 1 hr. Quantitative analysis of the reaction mixture by TLC (ethyl acetate) using a 10^{-2} *M* acetic acid solution of 2-formamidocyclohexanone (**17**) as a reference standard, indicated a 50% yield of the formyl compound (**17**). A 50% yield of 2-oxocyclohexanecarbonitrile (**16**) was also estimated by TLC.

Irradiation of 4,5,6,7-Tetrahydrobenzoxazole in Glacial Acetic Acid. In a control experiment to determine if **17** was a hydrolysis product of the oxazole **15** a 10^{-2} *M* solution of the oxazole **15** was degassed and irradiated in a quartz cell at 254 nm for 1 hr. A 5% yield of the formyl derivative (**17**) was detected by TLC analysis (ethyl acetate) of the reaction mixture using a 10^{-2} *M* acetic acid solution of 2-formamidocyclohexanone as reference standard.

Irradiation of 3-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole in Glacial Acetic Acid. A 10^{-2} *M* solution of the isoxazole **10** in glacial acetic acid was degassed and irradiated in a quartz cell at 254 nm for 0.5 hr. The solution was concentrated in vacuo at less than 40° to an oil. Analysis by TLC (ethyl acetate) using chloroform–iodine and DNP spray reagents[30b] indicated a small yield of *N*-acetyl-2-aminocyclohexanone (**24**); TLC on alumina (chloroform–pyridine, 2:1) also afforded a spot corresponding in color and R_f value to amide **24**. Analysis by VPC (10% SE-30, 6-ft column) at 210 and 230° showed some starting material, the oxazole isomer **21**, and about a 5% yield of amide **24**; VPC (5% Carbowax, 6-ft column) at 210° gave identical results, but there were seven other unidentifiable peaks. In a control experiment where oxazole **21** was irradiated more than 5% of **24** was formed.

Irradiation of 3-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazole in Water. A 10^{-2} *M* solution of the isoxazole **10** in water was degassed and irradiated in quartz at 254 nm for 30 min. TLC analysis (ether–methanol, 95:5; ether) of the reaction solution showed the presence of starting material, 2-methyl-4,5,6,7-tetrahydrobenzoxazole, and *N*-methyl-2-oxocyclohexanecarboxamide. Ether was added to the reaction solution which was then extracted with 10% NaOH. The combined aqueous layers were washed once with ether and then acidified with 6 *N* HCl. The acidic aqueous solution was then extracted four times with methylene chloride and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. TLC analysis (ether) showed only the presence of *N*-methyl-2-oxocyclohexanecarboxamide (**27**); a yield of 5% was ascertained based on the uv absorption of **27** after elution from the TLC plate.

Synthesis of *N*-Methyl-4,5,6,7-tetrahydro-2,1-benzisoxazolium Iodide. To 500 mg of 4,5,6,7-tetrahydro-2,1-benzisoxazole (**6**) was added 5 ml of methyl iodide. This mixture was heated in a sealed tube at about 95° for 27 hr. Pale yellow crystals were collected from the cooled reaction mixture which were recrystallized from ethanol–ether (1:1) and again from 2-propanol: mp 120–121°; NMR ($CDCl_3$) δ 9.1 (s, 1, aromatic H), 4.5 (s, 3, CH_3), 3.3 (t, 2, CH_2), 2.8 (t, 2, CH_2), and 2.0 [m, 4, $(CH_2)_2$].

Synthesis of *N*-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazolium Iodide (22). To 1 g of isoxazole **5** was added 5 ml of methyl iodide. This mixture was heated in a sealed tube at about 95° for 22 hr and was then concentrated in vacuo to an oil. The oil crystallized from ethanol–ether (1:1) affording pale yellow crystals: mp 135–136°; NMR ($CDCl_3$) δ 10.4 (s, 1, aromatic H), 4.65 (s, 3, CH_3), 2.8 [m, 4, $(CH_2)_2$], and 2.0 [m, 4, $(CH_2)_2$].

Synthesis of the Ketoketenimine 23 and Its Hydrolysis Product (27) from *N*-Methyl-4,5,6,7-tetrahydro-1,2-benzisoxazolium Iodide (22). A solution of 1 g of **22** in 3 ml of methylene chloride at −77° was poured into 10 ml of a triethylamine–methylene chloride (1:2) solution at −77°. The chilled reaction solution was next poured into 15 ml of cold (−77°) *n*-hexane and the crystals of triethylamine hydriodide were collected by filtration. The ir spectrum of the filtrate exhibited a strong absorption at 2050 cm^{-1} (COC=C=N) (lit.[8] 2062 cm^{-1}). To the cold filtrate was added 50 ml of 1 *N* HCl and the acidic solution was then extracted four times with methylene chloride. The combined organic layers were washed once with brine, dried ($MgSO_4$), and concentrated to an oil which crystallized upon chilling in an ice bath: mp 59–64° and after one recrystallization from benzene–*n*-hexane (1:1) mp 68–70° (lit.[8] 82–84°) mixture melting point; ir (KBr) was superimposable with the spectrum of the *N*-methyl-2-oxocyclohexanecarboxamide prepared by the hydrolysis of *N*-methyl-1,4-dioxaspiro[4.5]decane-6-carboxamide (**26**).

Synthesis of *N*-Methyl-1,4-dioxaspiro[4.5]decane-6-carboxamide (26). The general procedure of Petit and Poisson was followed.[37] Methylamine was bubbled through a suspension of 0.0003 mol of $LiAlH_4$ in 50 ml of ether at −10°. To the solution was added 0.0002 mol of ethyl 1,4-dioxaspiro[4.5]decane-6-carboxylate (**25**) in 10 ml of absolute ether. The solution was stirred for 17 hr at room temperature. To the reaction solution was then added 0.5 ml of water with 1 ml of ethanol and then 1.5 ml of a saturated solution of sodium potassium tartrate. The reaction mixture was stirred for 30 min and filtered, and the filtrate was concentrated in vacuo to a clear oil which crystallized upon cooling to room temperature. The solid residue was crystallized from ether and the crystals were then washed with ether–*n*-pentane (1:1) to afford a 56% yield of amide **26**: mp 105.5–106.5°; ir (KBr) 3330 (s), 3130 (w), 2960 (s), 1640 (s) (amide C=O), 1565 (s), 1400 (m), 1250 (m), 1160 (s), and 1090 cm^{-1} (s); NMR ($CDCl_3$) δ 6.4 (br s, 1, NH), 4.0 [s, 4, $(CH_2)_2$], 2.8 (d, 3, methyl), 2.5 (t, 1, methine), and 1.65 [m, 8, $(CH_2)_4$]. After treatment with D_2O for 24 hr the doublet at δ 2.8 collapsed into a singlet and the broad singlet at δ 6.4 completely disappeared.

Synthesis of *N*-Methyl-2-oxocyclohexanecarboxamide (27). To 600 mg of *N*-methyl-1,4-dioxaspiro[4.5]decane-6-carboxamide (**26**) was added 7 ml of 6 *N* HCl and the resulting solution was allowed to stand for 48 hr at room temperature. The reaction solution was extracted four times with methylene chloride and the combined layers were then washed once with brine. The organic phase was then extracted three times with 10% NaOH and the combined aqueous layers were washed once with methylene chloride. The basic solution was acidified with 6 *N* HCl and then extracted four times with methylene chloride. The combined organic layers were then washed once with brine and dried ($MgSO_4$). Evaporation of the solvent afforded an oil which crystallized. White crystals (63%) were collected after one crystallization from benzene–*n*-pentane (1:1), mp 63–65.5°. The melting point of these crystals changed after a few hours to 58–70° (lit.[8] 82–84°); further recrystallizations of **27** did not appreciably change the melting point; ir (KBr) 3450 (s), 2990 (s), 1655 (s), 1620 (s), 1550 (s), 1370 (s), 1310 (s), 1225 (m), and 1160 cm^{-1} (s). This ir spectrum was superimposable with an ir spectrum taken from a sample obtained from Professor Olofson[8] whose sample was synthesized by a different procedure; NMR ($CDCl_3$) δ 14.2 (s, 0.5, OH), 7.1 (br s, 0.5, NH), 5.5 (br s, 0.5, NH), 3.1 (t, 0.5, methine), 2.8 (dd, 3, methyl), and 1.9 [m, 8, $(CH_2)_4$]; uv max (water) 256 nm (ε 100) and in 0.1 *N* NaOH 284 nm (ε 10400).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.92; H, 8.44. Found: C, 62.10; H, 8.43.

Synthesis of the Ketoketenimine 29 and Its Dimer 30 from *N*-Methyl-5-methylisoxazolium Iodide. A mixture of 0.5 g of quaternary salt **28** in 3 ml of methylene chloride at −77° was poured into 10 ml of triethylamine–methylene chloride (1:2) at −77°. The reaction mixture was then poured into 15 ml of cold (−77°) *n*-hexane and the triethylamine hydriodide crystals were collected by filtration. The filtrate exhibited a strong absorption at 2075 cm^{-1} (COC=C=N) in the ir. The filtrate was then poured into 50 ml of vigorously stirred water. After several hours white crystals precipitated from the reaction mixture, which were filtered to afford a 40% yield of the dimer **30**. The dimer was recrystallized from ethyl acetate and was not soluble in 1 *N* HCl nor 1 *N* NaOH: mp 176–178°; uv max (EtOH) 233 nm (ε 31600) and 315.5 (16200); ir (KBr) 3230 (m), 2950 (w), 1640 (s), 1610 (s), 1580 (sh), 1525 (s), and 1310 cm^{-1} (m); NMR ($CDCl_3$) δ 10.7 (s, 1, NH), 5.6 (s, 1, vinyl H), 3.4 (s, 3, $C{=}NCH_3$), 2.85 (d, 3, $NHCH_3$), 2.6 (s, 3, $COCH_3$), and 2.3 (s, 3, vinyl CH_3); mass spectrum *m/e* (rel intensity) 194 (43), 193 (7), 180 (12), 179 (100), 177 (12), 123 (6), and 56 (20).

Anal. Calcd for $C_{10}H_{14}N_2O_2$: C, 61.83; H, 7.26. Found: C, 61.66; H, 7.16.

Acknowledgment. This investigation was supported by Public Health Service Research Grant CA-14511 from the National Cancer Institute and Career Development Award G. M. 6380 (to J.P.F.) from the National Institutes of Health.

Registry No.—**5**, 5626-82-4; **6**, 2305-78-4; **7**, 1655-07-8; **8**, 57091-28-8; **9**, 874-23-7; **10**, 24010-93-3; **11**, 29146-79-0; **15**, 40814-50-4; **16**, 4513-77-3; **17**, 40814-51-5; **21**, 33793-98-5; **22**, 57091-29-9; **23**, 27439-90-3; **24**, 17578-82-4; **25**, 13747-72-3; **26**, 57091-30-2; **27**, 27439-91-4; **28**, 57091-31-3; **30**, 57091-32-4; 2-oxocyclohexanecarboxaldehyde, 1193-63-1; 6-hydroxymethyl-1,4-dioxaspiro[4.5]decane, 23153-80-2; 6-acetyl-1,4-dioxaspiro[4.5]decane, 16111-99-2; 1-acetyl-2-chloro-1-cyclohexene, 16111-92-5; 6-acetyl-1,4-dioxaspiro[4.5]decane oxime, 57091-33-5; adipoin, 533-60-8; 2-aminocyclohexane HCl, 6946-05-0.

References and Notes

(1) Chemical Evolution. XXVII. For the previous paper in the series see J. P. Ferris and C. T. Chen, *J. Am. Chem. Soc.*, **97**, 2962 (1975).
(2) J. P. Ferris and F. R. Antonucci, *J. Am. Chem. Soc.*, **96**, 2014 (1974).

(3) A portion of this work has been reported in preliminary form: J. P. Ferris, F. R. Antonucci, and R. W. Trimmer, *J. Am. Chem. Soc.*, **95**, 919 (1973).
(4) This research is described in detail in the Ph.D. Dissertation of R. W. Trimmer, Rensselaer Polytechnic Institute, 1973.
(5) A preliminary communication of some related results was recently reported: W. Heinzelmann and M. Märky, *Helv. Chim. Acta*, **57**, 376 (1974).
(6) K. von Auwers, T. Bahr, and E. Frese, *Justus Liebigs Ann. Chem.*, **441**, 54 (1925).
(7) L. Aspart-Pascot and J. Lematre, *Bull. Soc. Chim. Fr.*, 483 (1971).
(8) A synthesis of **5** was reported independently by another route by R. A. Olofson and Y. L. Marino, *Tetrahedron*, **26**, 1779 (1970).
(9) I. Hagedorn, U. Eholzer, and H. Etling, *Chem. Ber.*, **98**, 193 (1965).
(10) K. Isomura, S. Kobayashi, and H. Taniguchi, *Tetrahedron Lett.*, 3499 (1968); K. Isomura, M. Okada, and H. Taniguchi, *ibid.*, 4073 (1969).
(11) We did not realize that 2-unsubstituted azirines could adsorb in the 1650–1665-cm^{-1} region when we submitted our preliminary communication.[3]
(12) Examples of conjugation between cyclopropyl and carbonyl groups are given by W. G. Dauben and G. H. Berezen, *J. Am. Chem. Soc.*, **89**, 3449 (1967).
(13) There have been several observations of the formation of azirine intermediates in the photochemical conversion of isoxazoles to oxazoles: (a) E. F. Ullman and B. Singh, *J. Am. Chem. Soc.*, **88**, 1844 (1966); B. Singh and E. F. Ullmann, *ibid.*, **89**, 6911 (1967); B, Singh, A. Zweig, and J. B. Gallivan, *J. Am. Chem. Soc.*, **94**, 1199 (1972); (b) D. W. Kurtz and H. Schechter, *Chem. Commun.*, 689 (1966).
(14) F. W. Fowler, *Adv. Heterocycl. Chem.*, **13**, 45–76 (1971); T. Nishiwaki, *J. Chem. Soc., Chem. Commun.*, 565 (1972).
(15) W. Bauer and K. Hafner, *Angew. Chem., Int. Ed. Engl.*, **8**, 772 (1969).
(16) G. Smolinsky and C. A. Pryde, "The Chemistry of the Azide Group", S. Patai, Ed., Interscience, New York, N.Y., 1971, pp 555–585.
(17) R. B. Woodward and R. A. Olofson, *J. Am. Chem. Soc.*, **83**, 1007 (1961).
(18) T. Sato, K. Yamamoto, and K. Fukui, *Chem. Lett.*, 111 (1973).
(19) H. Ullrich, "Cycloaddition Reactions of Heterocumulenes", Academic Press, New York, N.Y., 1967, p 40.
(20) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 565 (1963); *Helv. Chim. Acta*, **50**, 2421 (1967).
(21) A. Padwa and S. I. Wetmore, Jr., *J. Org. Chem.*, **39**, 1396 (1974), and previous papers in this series.
(22) P. Claus et al., *Pure Appl. Chem.*, **33**, 339 (1973); P. Gilgen, H. Heimgartner, and H. Schmid, *Helv. Chim. Acta*, **57**, 1382 (1974), and previous papers in this series; K. Burger, J. Albanbauer, and F. Manz, *Chem. Ber.*, **107**, 1823 (1974).
(23) C. F. Hammer and R. A. Hines, *J. Am. Chem. Soc.*, **77**, 3649 (1955).
(24) H. R. Snyder, L. A. Brooks, and S. H. Shapiro in "Organic Syntheses", Collect. Vol. II, A. H. Blatt, Wiley, New York, N.Y., 1943, p 531.
(25) H. E. Baumgarten and F. A. Bower, *J. Am. Chem. Soc.*, **82**, 460 (1960).
(26) L. Claisen, *Chem. Ber.*, **42**, 59 (1909).
(27) H. Bredereck and R. Gomper, *Chem. Ber.*, **87**, 726 (1954).
(28) H. Bredereck, F. Effenberger, H. Botsch, and H. Rehn, *Chem. Ber.*, **98**, 1081 (1965).
(29) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).
(30) (a) E. Stahl, "Thin Layer Chromatography", Springer-Verlag New York, New York, N.Y., 1969, p 899; (b) *ibid.*, p 888.
(31) R. Jacquier and G. Maury, *Bull. Soc. Chim. Fr.*, 306 (1967).
(32) N. K. Kochetkov, E. E. Nifantev, and V. N. Shibaev, *J. Gen. Chem. USSR (Engl. Transl.)*, **30**, 2257 (1960).
(33) J. C. Sheehan and D.-D. H. Yang, *J. Am. Chem. Soc.*, **80**, 1156 (1958).
(34) H. K. Müller and H. Reschke, *Z. Chem.*, **4**, 30 (1964).
(35) I. Ugi, U. Fetzer, U. Eholzer, H. Krupfer, and K. Offermann, *Angew. Chem., Int. Ed. Engl.*, **4**, 472 (1965).
(36) A. Lablanche-Combier and A. Pottet, *Tetrahedron*, **28**, 3141 (1972).
(37) J. Petit and R. Poisson, *C. R. Acad. Sci.*, **247**, 1628 (1958).

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

Received September 22, 1975

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