

emphasis should be placed on studying the involvement of cysteine residues in the mechanisms of interaction between B₁₂ apoenzymes and their coenzymes.

Acknowledgment. This research was supported by a grant from the United States Public Health Service (USPH AM-12599).

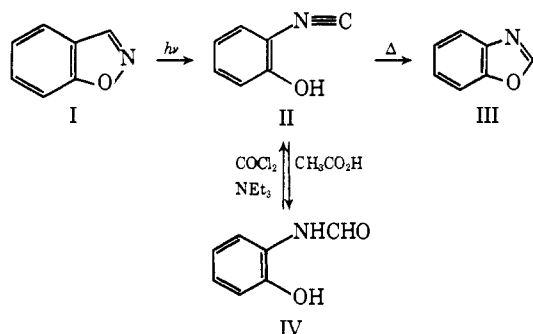
Communications to the Editor

Mechanism of the Photoisomerization of Isoxazoles and 2-Cyanophenol to Oxazoles

Sir:

The photochemical rearrangement of isoxazoles to oxazoles is usually assumed to proceed *via* an azirine intermediate.¹⁻⁴ In this communication, we present evidence for the formation of isonitrile intermediates in this photoisomerization. In addition, some evidence has been obtained for the direct photochemical conversion of a nitrile to an isonitrile.

Benzoxazole (III) and 2-cyanophenol are the photo-products of indoxazene (I) at room temperature.⁵ When indoxazene is photolyzed at -77 and -196° with a 254-nm light source in a KBr matrix or neat film, ir bands are observed at 3350 (-OH), 2220 (-C≡N), and 2130 (-N≡C) cm⁻¹.⁷ The bands at 3350 and 2130 cm⁻¹, assigned to II, disappear on warming in the dark, and a band at 1065 cm⁻¹, an intense band in the ir spectrum of benzoxazole, appears. The 2220-cm⁻¹ band, assigned to the cyano grouping in 2-cyanophenol, does not change in intensity in the dark reaction. The presence of benzoxazole and 2-cyanophenol was confirmed by tlc and uv. Azirine infrared absorption was not observed.^{3,8}



(1) H. Wamhoff, *Chem. Ber.*, **105**, 748 (1972); M. Kojima and M. Maeda, *Tetrahedron Lett.*, 2379 (1969); P. Beak and W. Messer, "Organic Photochemistry," Vol. II, O. Chapman Ed., Marcel Dekker, New York, N. Y., 1969, pp 136-139.

(2) H. Goth, A. R. Gagneux, C. H. Eugster, and H. Schmid, *Helv. Chim. Acta*, **50**, 137 (1967).

(3) B. Singh and E. F. Ullman, *J. Amer. Chem. Soc.*, **89**, 6911 (1967); B. Singh, A. Zweig, and J. B. Gallivan, *ibid.*, **94**, 1199 (1972).

(4) D. W. Kurz and H. Schechter, *Chem. Commun.*, 689 (1966).

(5) J. P. Ferris and F. R. Antonucci, *J. Chem. Soc., Chem. Commun.*, 126 (1972); H. Goth and H. Schmid, *Chimia*, **20**, 148 (1966).

(6) O. L. Chapman and C. L. McIntosh, *J. Amer. Chem. Soc.*, **92**, 7001 (1970).

(7) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 37.

(8) Azirines exhibit moderate to strong ir bands in the 1740-1800 cm⁻¹ region.^{3,9} (The complete spectrum of an azirine is reproduced in ref 9a.) A band of this intensity would have been detected in our studies.

(9) (a) D. J. Cram and M. J. Hatch, *J. Amer. Chem. Soc.*, **75**, 33 (1953); (b) G. Smolinsky, *J. Org. Chem.*, **27**, 3557 (1962).

Irradiation of I in glacial acetic acid yields IV (14%) along with benzoxazole (10%) and 2-cyanophenol (10%).¹⁰ The acid-catalyzed hydration of isonitriles is a well-documented reaction.¹¹ Reaction of IV with phosgene at -78° followed by rapid work-up gave a product with absorption at 2130 cm⁻¹. This absorption decreased in intensity on warming, and benzoxazole (III) was isolated from the crude reaction mixture.¹²

The uv spectrum of II was observed (λ_{\max} 288 nm) when a 10⁻⁴ M solution of I was irradiated for 10 min at -77° in 95% ethanol. The characteristic sharp uv maxima of benzoxazole at 269 and 276 nm were observed when the solution was allowed to warm to room temperature. Irradiation of a 10⁻⁴ M solution of 2-cyanophenol for 1 hr at -77° in methanol-water (3:2 by volume) resulted in a shift of the uv maximum from 295 to 293 nm. The intensity of the absorption at 293 nm decreased markedly and the characteristic uv absorption of benzoxazole at 269 and 276 nm was observed when the solution was allowed to warm to room temperature. These data suggest that II is an intermediate in the photochemical conversion of cyanophenol to benzoxazole.¹³

Indoxazene (I) is converted to 2-cyanophenol *via* the triplet manifold. This was demonstrated by quenching studies using piperylene, cyclohexene,¹⁴ and biacetyl as quenchers (Table I). Quenching by exciplex formation was ruled out because similar quenching efficiency was observed with three structurally different quenchers and because quenching was still observed at low (0.01 M) piperylene concentrations.¹⁵

The conversion of indoxazene ($E_s = 94$, $E_t = 82$ kcal/mol)¹⁶ to benzoxazole appears to proceed from the singlet excited state. The reaction is sensitized by benzene ($E_s = 109$, $E_t = 82$ kcal/mol) but not acetone ($E_s \approx 92$, $E_t = 79$ kcal/mol).¹⁷ The formation of 2-methylbenzoxazole from 3-methylindoxazene ($E_s = 92$ kcal/mol, E_t could not be determined) is sensitized by

(10) A different reaction pathway is followed in 98% H₂SO₄: M. Georganakis, Th. Doppler, M. Märky, H.-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, **54**, 2916 (1971).

(11) T. Saegusa and Y. Ito, "Isonitrile Chemistry," I. Ugi Ed., Academic Press, New York, N. Y., 1971, p 73.

(12) P. Hoffmann, G. Gokel, D. Marquarding, and I. Ugi, *ibid.*, pp 11-14; E. Bamberger, *Chem. Ber.*, **36**, 2042 (1903).

(13) The photolysis of cyanophenol in aqueous acid yields IV. However, this is not evidence for II as a reaction intermediate because III is hydrolyzed to IV at about the same rate.

(14) R. B. Cundall and P. A. Griffiths, *Chem. Commun.*, 194 (1966); G. A. Haninger, Jr., and E. K. C. Lee, *J. Phys. Chem.*, **73**, 1815 (1969); R. B. Cundall, G. B. Evans, and E. L. Land, *ibid.*, **73**, 3982 (1969); I. H. Kochevar and P. J. Wagner, *J. Amer. Chem. Soc.*, **92**, 5742 (1970).

(15) L. Stephenson, D. G. Whitten, G. F. Vesley, and G. S. Hammond, *J. Amer. Chem. Soc.*, **88**, 3665, 3893 (1966).

(16) S. D. Carson and H. M. Rosenberg, *J. Mol. Spectrosc.*, **32**, 242 (1969); report from absorption spectra $E_s = 97.7$ kcal/mol and from phosphorescence $E_t = 81.7$ kcal/mol.

(17) M. A. Golub, *J. Amer. Chem. Soc.*, **91**, 4925 (1969).

Table I. Effect of Solvent and Quenchers on Indoxazene Photoproducts^a

Solvent	Indoxazene, <i>M</i>	Quencher (<i>M</i>)	Benzoxazole, %	Cyanophenol, %
H ₂ O	6.2 × 10 ⁻⁴		70 ^b	13 ^b
Diglyme ^c			18	17
Cyclohexane	10 ⁻⁴		nd	42 ^d
Cyclohexane	10 ⁻⁴	Cyclohexene (0.1)	nd	11 ^d
Cyclohexane	10 ⁻⁴	Cyclohexene (1)	nd	5 ^d
Cyclohexane	10 ⁻⁴	Biacetyl (0.1)	nd	10 ^d
Cyclohexane	10 ⁻³		36 ^e	29 ^d
Cyclohexane	10 ⁻³	Cyclohexene (0.1)	43 ^e	21 ^d
Cyclohexane	10 ⁻⁴	Piperylene (0.1)	nd	5 ^d
Cyclohexane	10 ⁻⁴	Piperylene (0.01)	nd	22 ^d

^a Irradiated with 300-nm light source for 15 min; nd, not determined. ^b Yield determined from uv spectrum. ^c Yield determined by vpc. ^d Yield determined by uv spectra after separation by tlc on silica gel. ^e Details given in ref 7.

both benzene and acetone. These studies, together with our failure to observe the inhibition of benzoxazole formation in the presence of triplet quenchers, suggest singlet sensitization by benzene^{3,18} and acetone.¹⁷

The variation in luminescence and photoproducts with solvent polarity is also consistent with the conclusion derived from the sensitization and quenching experiments. Fluorescence but no phosphorescence is observed in a polar glass (4:1 ethanol-methanol) while phosphorescence is observed along with the fluorescence in a nonpolar glass (5:1 methylcyclohexane-isopentane). Benzoxazole is the predominant product in hydroxylic solvents while cyanophenol is the predominant photoproduct in hydrocarbon solvents. These solvent effects are consistent with benzoxazole formation from a π, π^* state and cyanophenol formation from a n, π^* state.¹⁹

An isonitrile was also detected in the photochemical conversion of V²⁰ to VII. A precursor to the isonitrile was detected by an ir band at 1695 cm⁻¹ when V was irradiated for 1-3 hr at -77° with a 254-nm light source.²² The 1695-cm⁻¹ absorption gradually disappeared and bands at 2160 and 1725 cm⁻¹ gradually appeared when the cryostat was allowed to warm to room temperature. The 2160- and 1725-cm⁻¹ bands are consistent with the ketoisonitrile VI. After 4 hr at room temperature, these maxima disappeared and several of the ir bands characteristic of oxazole VII had formed. The presence of VII together with a lesser amount of 2-cyanocyclohexanone was detected by tlc analysis of the reaction mixture.

A 99% yield of VII was obtained when the photolysis of V was performed at room temperature in ethanol solution. A 50% yield of the formamide VIII²³ was obtained when the photolysis was performed in acetic acid, a result consistent with VI as a reaction intermediate.¹¹ Furthermore, the ir spectrum of the crude reaction product obtained by the reaction of VIII with phosgene¹² also exhibited an ir band at 2160 cm⁻¹ which decreased in intensity at room temperature; oxazole VII was isolated from this reaction mixture.

(18) W. A. Henderson, Jr., R. Lopresti, and A. Zweig, *J. Amer. Chem. Soc.*, **91**, 6049 (1969); J. T. Dubois and F. Wilkinson, *J. Chem. Phys.*, **38**, 2541 (1963).

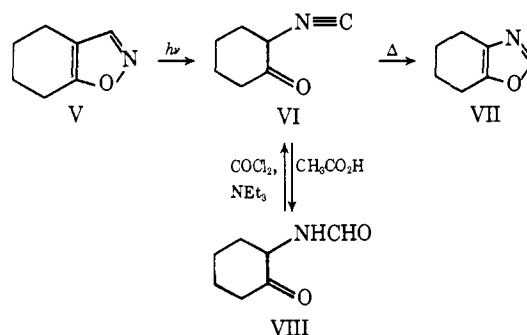
(19) E. Lim and J. Yu, *ibid.*, **45**, 4742 (1966).

(20) Previous syntheses yielded a mixture of V and another isomer.²¹ A new synthesis was devised which yields only V. The details of this synthesis will be reported later.

(21) K. v. Auwers, Th. Bahr, and E. Frese, *Justus Liebigs Ann. Chem.*, **441**, 54 (1925).

(22) The structure of this intermediate is currently under investigation.

(23) Satisfactory analytical and spectral data have been obtained on this new compound.



Acknowledgment. This research was sponsored by the National Institutes of Health in the form of a research grant (GM 15915) and a Research Career Development Award (to J. P. F., GM 6380).

J. P. Ferris,* F. R. Antonucci, R. W. Trimmer
 Department of Chemistry, Rensselaer Polytechnic Institute
 Troy, New York 12181
 Received August 24, 1972

Sulfur Monoxide Chemistry. Stereochemistry of the Thiirane Oxide-Diene Reaction

Sir:

Dodson and his coworkers¹ discovered that SO generated by thermolysis of thiirane oxide² could be trapped by dienes and trienes in the form of 2,5-dihydrothiophene (3-thiolenes) and 2,7-dihydrothiepin S-oxides. Following up an earlier study of the SO₂-diene reaction in this laboratory,³ we have now examined the stereochemistry of the theoretically interesting⁴ SO-diene cycloaddition.

The three 2,4-hexadienes **1** were chosen for this purpose, and all three of the related 3-thiolenes **2** were obtained (eq 1, Table I).⁵ Mixtures of the isomers were separated by column chromatography on silica gel. All three compounds displayed strong sulfoxide S-O stretching absorption; all suffered SO and (SO + methyl) loss as major fragmentation path-

(1) R. M. Dodson and R. F. Sauer, *Chem. Commun.*, 1189 (1967); R. M. Dodson and J. P. Nelson, *ibid.*, 1159 (1969). The reaction with dienes has also been used to trap SO from another source: Y. L. Chow, J. N. S. Taru, J. E. Blier, and H. H. Szmant, *ibid.*, 1604 (1970).

(2) G. E. Hartzell and J. N. Paige, *J. Amer. Chem. Soc.*, **88**, 2616 (1966).

(3) S. D. McGregor and D. M. Lemal, *ibid.*, **88**, 2858 (1966); see also W. L. Mock, *ibid.*, **88**, 2857 (1966).

(4) D. M. Lemal and P. Chao, *ibid.*, **95**, 922 (1973).

(5) Dodson and Sikstrom have studied the same reactions: R. A. Sikstrom, Ph.D. Dissertation, University of Minnesota, 1971.