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SOME NOVEL ISOXAZOLE PHOTOCHEMISTRY:
A COMPARISON WITH VINYL AZIDE CHEMISTRY

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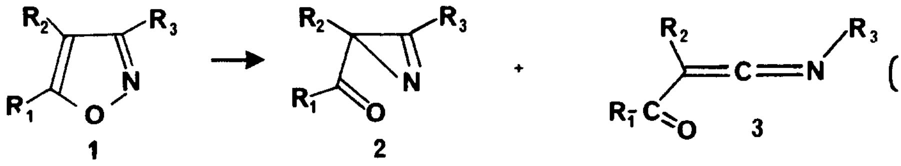
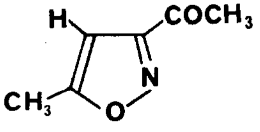
Summary: Product profiles from the irradiations of 3-acetyl-5-methylisoxazole (4) and Z-3-azido-3-hexene-2,5-dione (5) were compared. Whereas both compounds gave rise to azirine 7, diacetylacetonitrile (6) was produced only from (4).

Isoxazole (1) photochemistry has been routinely characterized by formation of a 2H-azirines (2) and, less frequently, ketenimines (3) by way of alkyl migrations from C_3 to nitrogen (eq 1).[1] These products have generally been assumed to arise



via rearrangements of a common intermediate described either as a vinyl nitrene or a diradical of unspecified multiplicity.[2] Theoretical studies,[3] on the other hand, have led to the suggestion that azirine formation may proceed in a "nearly concerted" manner from an excited state of 1.

Because vinyl azides are also believed to produce vinyl nitrenes on irradiation,[4,5] it appeared that a fruitful approach to furthering our understanding of the importance of these intermediates would be to generate them from different sources and compare product profiles. To this end we synthesized and monitored the photochemistry of 3-acetyl-5-methylisoxazole[6] (4) and Z-3-azido-3-hexene-2,5-dione (5).



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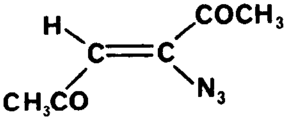
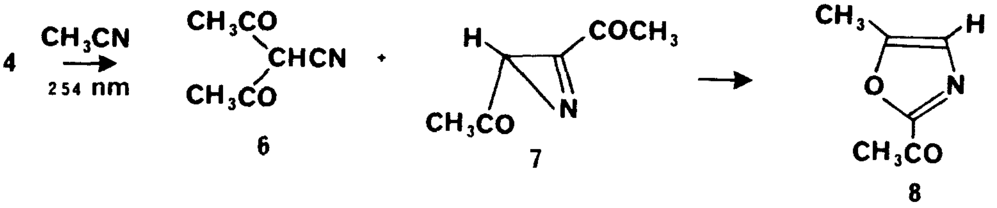
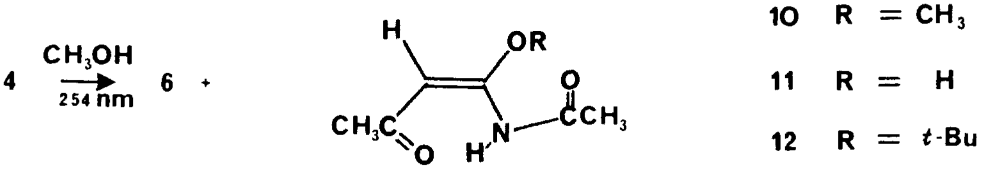


5

Isoxazole 4 was inert toward irradiation at long wavelengths ($\lambda > 300$ nm), but reacted readily ($\phi_{-K} = 0.20 \pm 0.02$) at 254 nm to form two products. The minor product (ca. 35%) was isolated and identified as diacetylacetonitrile (6) by comparison with an independently synthesized sample.[7,8] Attempts to isolate and purify the major product were unsuccessful but spectral data were consistent with azirine 7 (^{1}H NMR δ 2.13 (s, 3H), 2.67 (s, 3H), 3.10 (s, 1H). Further support for this assignment was provided by the finding that this substance was converted on long term irradiation into an oxazole (8) that was independently synthesized.[9]

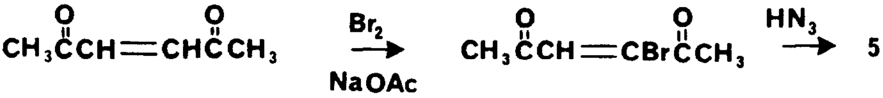


When the irradiation was carried out in methanol, nitrile 6 was again produced (ca. 70%), but no azirine was detected by ^{1}H NMR. Instead, a new product to which structure 10 is assigned was found. The identity of 10 is based on ^{1}H NMR data[10] and the fact that it was readily hydrolyzed[11] to a known imide 11.[12] In a control experiment, it was demonstrated that azirine 7 was not converted to 10 on irradiation in methanol. It is presumed that the latter arises via thermal addition of methanol to an intermediate ketenimine (3, $R_1 = CH_3$, $R_2 = H$, $R_3 = C(O)CH_3$) and is a primary product. In contrast, use of t-butanol as solvent led to all three products: 6 (32%), 7 (43%) and 12[13] (25%). These remarkable solvent effects most likely represent a combination of the effects of solvation on both excited states and intermediates.



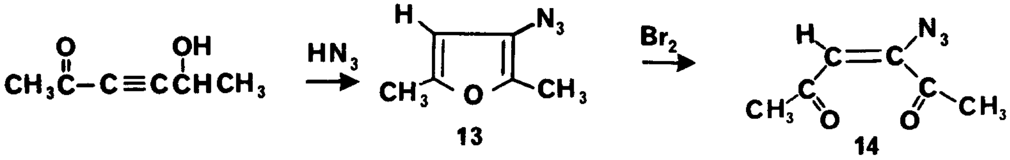
(2)

We next synthesized azide 5 to compare its photochemistry with that of 4. Application of the method of Hassner[14] (eq 3) to diacetylethylene gave rise to an unstable yellow oil[15] that decomposed thermally (4h, 27°) to produce isoxazole



$$CH_3\overset{O}{\overset{\|}{C}}CH{=}CH\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[NaOAc]{Br_2} CH_3\overset{O}{\overset{\|}{C}}CH{=}CBr\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{HN_3} 5 \qquad (3)$$

4 in high yield. Although this result is best construed as evidence for the Z-configuration of 5, this point was verified by an independent synthesis of the E-isomer 14.[16] The latter, in turn, was prepared by a modified Clauson-Kaas reaction (eq 4).[17] Thermolysis of 14 in methanol gave mainly 10, an acrylonitrile derivative,[18] and no isoxazole.



Irradiations of 5 at 300 nm (acetonitrile, methanol) gave rise to isoxazole 4 (51%, 32%), azirine 7 (27%, 26%), and E-azide 14 (22%, 34%) as the major products. The absence of 6 in these reactions is striking, and indicates that different product-forming intermediates are involved. Because it is likely that vinyl nitenes are involved from both precursors, the most obvious differences would involve the multiplicity of these species. Thus, 6 (and 10) could arise from singlet vinyl nitrenes[19] and 7 could arise from the triplet form. In support of these ideas, we have shown that acetone-sensitized irradiation of 4 did not produce 6; instead oxazole 8 was produced, presumably via azirine 7; this conversion was independently verified. In addition, it was shown that the presence of 1 M isoprene quenched the rate of disappearance of 5 ($\phi_0/\phi \approx 1.5$). This finding is consistent with triplet state precursors for the photo products of 5. Attempts to perturb the photochemistry of 4 by heavy atom additives (e.g., t-C_4H_9Br, CH_2Br_2, $(CH_3)_4Sn$) were not conclusive, but additives with lone pairs reduced the yields of 7. These results and the solvent effects may reflect stabilization of singlet nitrenes.[20]

Acknowledgement. We are grateful to the Garden State Fellowship Commission and the J.L.R. Morgan Fellowship Fund for financial support.

References and Notes

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(6) Ketone **4** was conveniently prepared by nitrosation of 2,5-hexanedione followed by cyclization; bp 73-77°C (13 torr). Lit. bp 76-77°C (19 torr): Meister, H.; Peitscher, G. Justus Liebigs Ann. Chem. **1974**, 1908.

(7) Nitrile **6** was prepared by the method of Fackler[8] from 2,4-pentanedione and cyanogen and had mp 53-56°C. Lit. mp 53-54°C; Lock, G.A.; Thompson, D.W. J. Chem. Soc. Dalton Trans. **1980**, 1265.

(8) Fackler, J.P. J. Chem. Soc. **1962**, 1957.

(9) Prepared by cyclization of N-acetonylpyruvyl amide with phosphorous oxychloride; bp 70-73°C (4.3 torr); ^{1}H NMR δ 2.46 (s, 3H), 2.60 (s, 3H), 6.90 (s, 1H). Anal. Found for $C_6H_7NO_2$: C, 57.21; H, 5.76; N, 11.37.

(10) Amide **10** was isolated in 15% yield and had bp 50-60° (0.05 torr); ^{1}H NMR δ 2.07 (s, 3H), 2.13 (s, 3H), 3.80 (s, 3H), 4.80 (s 1H), 12.40 (b, 1H). Anal. Found for $C_7H_{11}NO_3$: C, 52.98; H, 7.40; N, 9.05.

(11) Hydrolysis was effected using a two-phase system ($CDCl_3$- aq. trifluoroacetic acid) for 2 days at 27°.

(12) Yamamoto, Y.; Ohnishi, S.; Azuma, Y. Synthesis, **1981**, 122.

(13) This compound was unstable and rapidly hydrolyzed to **11**.

(14) Hassner, A.; L'abbe, G.; Miller, M.J. J. Am. Chem. Soc. **1971**, 93, 981.

(15) Compound **5** was characterized by IR (CCl_4) 4.65 (vs) and 5.88(s)μm; ^{1}H NMR δ 2.47 (s, 6H), 5.93 (s, 1H). Caution: overheating can cause detonation.

(16) Furan **13** was characterized by IR (film) 4.65 (vs) μm; ^{1}H NMR δ 2.06 (s, 3H), 2.17 (s, 3H), 5.83 (s, 1H) and elemental analyses of the phosphinimine derivative prepared by reaction with triphenyl phosphine. Anal. Found for $C_{24}H_{22}NOP$: C, 77.47; H, 6.17; N, 4.03; P, 8.23. E-azide **14** had the following properties: IR 4.76 (s) μm; ^{1}H NMR δ 2.23 (s, 3H), 2.36 (s, 3H), 5.87 (s, 1H).

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