James W. Pavlik*, Heather St. Martin, Karen A. Lambert, Jennifer A. Lowell, Vikki M. Tsefrikas, Cheryl K. Eddins, and Naod Kebede.[1]

Department of Chemistry and Biochemistry
Worcester Polytechnic Institute, Worcester, MA 01609
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5-Phenylisoxazole (**4**) and 4-phenylisoxazole (**22**) underwent phototransposition to 5-phenyloxazole (**5**) and 4-phenyloxazole (**24**) respectively. Labeling with deuterium or methyl confirmed that these phototranspositions occurred *via* the P_4 pathway which involves only interchange of the N2 and C3 ring position. Thus, 4-deuterio-5-phenylisoxazole (**4-4d**), 4-methyl-5-phenylisoxazole (**10**), and 5-methyl-4-phenylisoxazole (**23**) phototransposed to 4-deuterio-5-phenyloxazole (**5-4d**), 4-methyl-5-phenyloxazole (**11**), and 5-methyl-4-phenyloxazole (**25**) respectively. In addition to phototransposition, isoxazoles **4**, **10**, and **23** also underwent photo-ring cleavage to yield benzoylacetonitrile (**9**), α-benzoylpropionitrile (**15**), and aceto-α-phenylacetonitrile (**26**) respectively. Irradiation of 5-phenyl-3-(trifluoromethyl)isoxazole (**16**) in acetonitrile led to 5-phenyl-2-(trifluoromethyl)oxazole (**17**), the P_4 phototransposition product. Irradiation of **16** in methanol led to a substantial decrease in the yield of **17** and to the formation of a mixture of (*E*) and (*Z*)-2-methoxy-2-(trifluoromethyl)-3-benzoylaziridines **18a** and **18b**.

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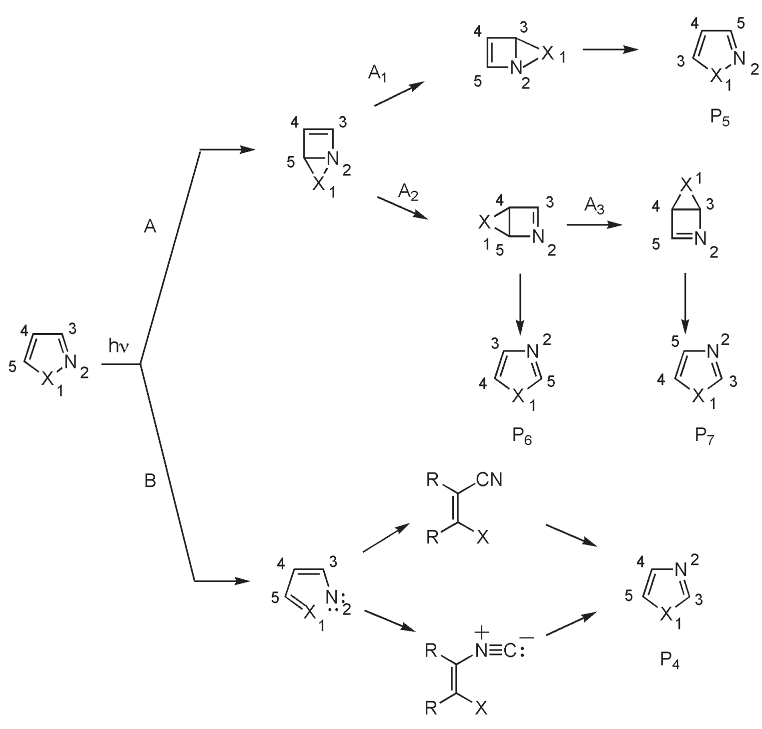
Introduction.

Previous work in this and other laboratories has established that the phototransposition chemistry of 1-methylpyrazoles [2-7] and isothiazoles [8-10] involves competition between electrocyclic ring closure (Path A, Scheme 1) and cleavage of the bond between the two heteroatoms (Path B, Scheme 1). Path A results in the formation of a 1,5-diheterobicyclo[2.1.0]pentene intermediate which undergoes one or two sigmatropic shifts (Paths A1, A2, or A3, Scheme 1) followed by rearomatization to yield heterocyclic products with three different scrambling patterns identified as P_5, P_6 and P_7 [11]. Whereas isothiazoles react by all three pathways resulting in isothiazole to isothiazole (Path A1) and isothiazole to thiazole (Paths A2, A3) transpositions [8], 1-methylpyrazoles react only *via* pathways A2 and A3 resulting only in 1-methylpyrazole to 1-methylimidazole isomerizations [2]. Alternatively, path B leads to a species that can be viewed as a vinyl nitrene that rearranges to a 1-methylimidazole (when

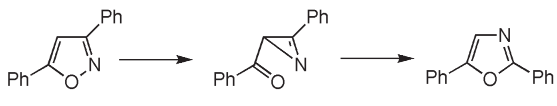
Scheme 1

(X = N-CH$_3$ or S)



X = N-CH_3) or a thiazole (when X = S) with a P_4 scrambling pattern. If the initial heterocycle bears a hydrogen atom at ring position 3, this rearrangement occurs *via* detectable nitrile and/or isocyanide photocleavage products as shown in Scheme 1 [3,9,12,13]. This P_4 scrambling pattern involves only interchange of the N2 and C3 ring atoms.

Isoxazoles have also been the subject of numerous photochemical studies since Ulman and Singh first reported that the photoconversion of 3,5-diphenylisoxazole (**1**) to 2,5-diphenyloxazole (**3**) occurs by way of an initial ring contraction to yield an isolable 3-benzoyl-2-phenylazirine (**2**) which subsequently undergoes photo-ring expansion to the final product **3** [14-16]. Essentially all of the subsequent studies of isoxazole photochemistry in the literature involve isoxazoles substituted at ring position 3 (and other positions) [17-25] because of the thermal stability imparted to the resulting azirine by the substituent at ring position 2.



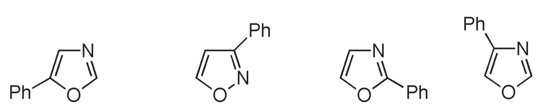
1 **2** **3**

In this paper we report the results of a study of the photochemistry of 4- and 5-phenyl substituted isoxazoles. The effect of additional substitution on the photochemistry of these phenyl substituted isoxazoles is also reported.

Results and Discussion.

Based on the phototransposition pathways outlined in Scheme 1, 5-phenylisoxazole (**4**) would be expected to transpose to 5-phenyloxazole (**5**), 3-phenylisoxazole (**6**), 2-phenyloxazole (**7**), and/or 4-phenyloxazole (**8**) *via* the P_4, P_5, P_6, and/or P_7 pathways respectively (Scheme 2). To investigate these possibilities, a solution of 5-phenylisoxazole (**4**) (3.0 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated at 254 nm. Gas Chromatographic (GC) analysis as a function of irradiation time showed the consumption of the reactant and the formation of two volatile products with retentions relative to the reactant of 0.82 and 1.8.

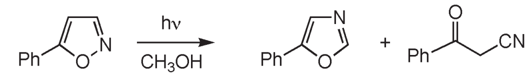
Scheme 2



5 6 **7** **8**

P_4 P_5 P_6 P_7

Mass spectral analysis showed that both products exhibited molecular ions at m/z = 145 and were thus both isomeric with the reactant. These products were identified as 5-phenyloxazole (**5**) and benzoylacetonitrile (**9**) by GC



4 **5** **9**

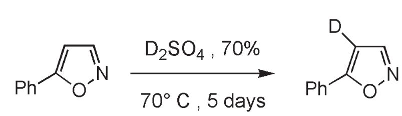
and mass spectral comparison of the products formed with authentic samples of these two compounds. Quantitative GC showed that after 10 minutes of irradiation 48% of **4** had been consumed and that **5** and **9** were formed in yields of 41% and 21% respectively.

On a preparative-scale, a solution of **4** (50 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated at 254 nm for 90 minutes after which GC analysis showed that 96% of **4** had been consumed. Flash column chromatography of the concentrated product mixture provided **5** and **9** in yields of 42% and 27% respectively. These results show that 5-phenylisoxazole (**4**) undergoes photocleavage to yield **9** and regiospecific phototransposition to provide **5**.

These results indicate that 5-phenylisoxazole (**4**) does not phototranspose *via* path A in Scheme 1 to yield 3-phenylisoxazole (**6**), 2-phenyloxazole (**7**), or 4-phenyloxazole (**8**). Indeed, GC co-injection studies using authentic samples of these compounds confirmed that **6**, **7**, and **8** were not formed in this reaction. Formation of **5** and **9**, however, suggests that **4** reacts *via* path B in Scheme 1 since photocleavage and P_4 phototransposition are characteristic of this pathway.

Phototransposition of 5-phenylisoxazole (**4**) to 5-phenyloxazole (**5**) by the P_4 pathway requires that the isomerization involves only interchange of ring atoms N2 and C3. Because C3 and C4 of the reactant **4** both bear H, it is not possible to distinguish where C3 and C4 of the product originated in the reactant. Thus, the isomerization could have occurred by simple N2-C3 interchange, as demanded by the P_4 pathway, or by some "other" more complicated pathway that involves interchange of N2, C3, and C4 of the reactant which would require a different mechanistic explanation.

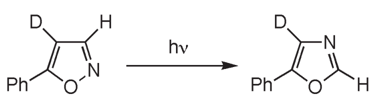
This ambiguity was resolved by studying the photochemistry of 4-deuterio-5-phenylisoxazole (**4-4d**) in which all ring atoms are uniquely labeled. Deuteration was accomplished by treating **4** in 70% D_2SO_4 in D_2O at



4 **4-4d**

70 ºC for 5 days. The mass spectrum of the deuterated product exhibited a molecular ion at m/z = 146, indicating that one proton had been exchanged by one deuterium atom. The ^{1}H-NMR spectrum of the deuterated product showed no signal at δ 6.51 where the H4 proton of 5-phenylisoxazole (**4**) is known to absorb. Furthermore, the signal for the H5 proton, which appeared as a doublet before deuteration, appeared as a singlet in the deuterated product. This confirms that deuterium-hydrogen exchange occurred regiospecifically at the C4 ring position of **4**.

A solution of 4-deuterio-5-phenylisoxazole (**4-4d**) (5.0 mL, 2.0 x 10^{-2} *M*) in acetonitrile was irradiated for 60 minutes [26]. GC analysis of the solution following irradiation showed substantial consumption of the reactant and formation of benzoylacetonitrile (**9**) and 5-phenyloxazole (**5**). The mass spectrum of the latter product exhibited a molecular ion at m/z = 146 (95%) with no peak at m/z = 145 showing that the deuterium label was not lost during the phototransposition. ^{1}H-NMR analysis of the residue following evaporation showed no signal at δ 7.34 where the C4 proton of 5-phenyloxazole (**5**) is known to absorb but did exhibit at sharp singlet at δ 7.89 where the C2 proton of **5** is known to absorb. These results show that the C3 proton of **4-4d** has transposed to ring position **2** and that the



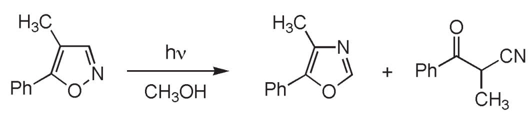
4-4d **5-4d**

product is 4-deuterio-5-phenyloxazole (**5-4d**). This confirms that the isomerization has occurred only with N2-C3 interchange as required by the P_4 permutation pathway.

The photochemistry of 4-methyl-5-phenylisoxazole (**10**) was also investigated. Based on Scheme 1, the anticipated phototransposition and photocleavage products are shown in Scheme 3.

analysis showed that all of these products had molecular ions at m/z = 159 and were thus all isomeric with the reactant. Subsequent studies, which included irradiation of the isolated and purified photoproducts, showed however, that the small peak in the GC trace with a relative retention of 0.82 was a secondary photoproduct formed by photoreaction of the major primary photoproduct with relative retention of 0.6. This product was therefore not further investigated.

GC co-injection studies with authentic samples synthesized in this laboratory allowed identification of the short retention time product as 4-methyl-5-phenyloxazole (**11**). Since each ring position in the reactant **10** and product **11** are uniquely substituted, product identification allowed unambiguous conclusion that the isomerization of **10** to **11** involves only N2-C3 interchange as required by the P_4 pathway. Co-injection studies also allowed identification of the long retention time product as α-benzoylpropionitrile (**15**), the anticipated photocleavage product. Quantitative GC analysis showed that after 5 minutes of irradiation when 34% of the reactant had been consumed, the yields of **11** and **15** were 54% and 26% respectively.

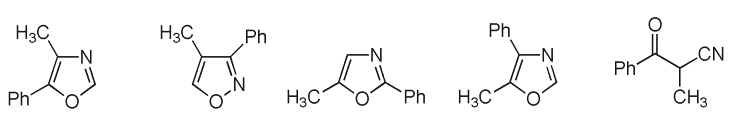


10 **11** **15**

Furthermore, GC coinjection studies and ^{1}H-NMR analysis of the crude reaction mixture confirmed that **12**, **13**, and **14** (Scheme 3), the P_5, P_6, and P_7 compounds, were not formed from the photoreaction of **10**. This confirms that **10** also reacts *via* pathway B (Scheme 1) to yield P_4 phototransposition and photocleavage products.

In order to investigate the effects of a trifluoromethyl substituent on the photochemistry of 5-phenylisoxazole (**4**), the photochemistry of 5-phenyl-3-(trifluoromethyl)-

Scheme 3



P_4 P_5 P_6 P_7 photocleavage

11 12 13 14 15

Irradiation of a solution of **10** (3.0 mL, 2.0 x 10^{-2} *M*) in methanol for 10 minutes led to the consumption of 53% of **10** and to the formation of three GC volatile products with retentions relative to **10** of 0.6, 0.8, and 1.7. Mass spectral

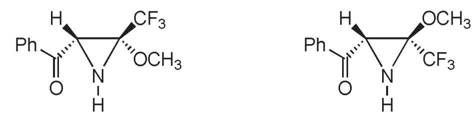
isoxazole (**16**) was also investigated. A solution of **16** (3.0 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated for 10 minutes. GC analysis showed the consumption of **16** and the appearance of two GC-volatile products with relative retentions of 0.75 and 2.25. On a preparative-scale a solution of **16** in methanol (25.0 mL, 1.46 x 10^{-2} *M*) was irradiated for 20 minutes. GC analysis showed the presence of unconsumed starting material as well as the above products. Evaporation of the solvent left a residue (81.2 mg, 104% recovery) which was resolved into three fractions by preparative layer chromatography. The fraction with the highest Rf provided 49.5 mg of a white solid which was shown to be identical to the reactant, 5-phenyl-3-(trifluoromethyl)isoxazole (**16**).

The second fraction provided 3.1 mg of a yellow oil. GC analysis showed that this fraction corresponded to the product with the relative retention of 0.75. Although the yield of this product was very low, it was subsequently discovered that the yield can be significantly increased if the irradiation is carried out in acetonitrile solvent. In acetonitrile this is the only product formed and was isolated as a yellow oil by flash column chromatography. The mass spectrum of this material exhibited a molecular ion at m/z 213 showing that this product is isomeric with the reactant. NMR analysis allowed the compound to be identified as 5-phenyl-2-(trifluoromethyl)oxazole (**17**). As expected for this structure, the ^{1}H-NMR spectrum exhibited one 2H multiplet at δ 7.65-7.72 assigned to the *ortho*-phenyl protons and a 3H multiplet from δ 7.37-7.48, due to the remaining phenyl protons, and a 1H singlet at δ 7.44 assigned to the C4 proton in the oxazole ring.

The ^{13}C-NMR spectrum was also consistent with this assignment. The proton decoupled spectrum exhibits signals at δ 150.0, 122.3, and 153.9 for the C2, C4, and C5 carbons respectively of the oxazole ring. These observed chemical shifts are in good agreement with the chemical shifts for the same ring carbons in 5-phenyloxazole (**5**). In addition, the spectrum exhibits signals at δ 125.0, 126.2, 129.1, and 130.1 for the four different sets of phenyl carbon atoms and a quartet (J = 270.3 Hz) at δ 116.5 for the trifluoromethyl carbon. The position of the trifluoromethyl group was confirmed to be at position 2 of the oxazole ring since the signal for this carbon at δ 150.0 exhibited long range coupling (J = 43.8Hz) with the fluorine nuclei of the trifluoromethyl group. These spectroscopic data confirm that this product is 5-phenyl-2-(trifluoromethyl)oxazole (**17**), the product expected from a P_4 phototransposition.

The third band from the preparative layer plate provided 24.9 mg of a slightly unstable, orange oil. GC analysis of this oil showed a major peak at a retention time identical to the photoproduct with a relative retention of 2.25 and a small peak at a shorter retention due to oxazole **17**. Although GC analysis clearly showed the presence of oxazole **17** in this sample, neither TLC nor ^{1}H-NMR provided any evidence for **17** in this sample. Thus, it appears that **17** is formed during the GC analysis from the compound with the longer retention time. The mass spectrum of the latter material exhibited a molecular ion at m/z 245, consistent with a molecular formula of $C_{11}H_{10}F_3NO_2$. This indicates that this compound has been formed by addition of a molecule of methanol to the reactant, $C_{10}H_6F_3NO$.

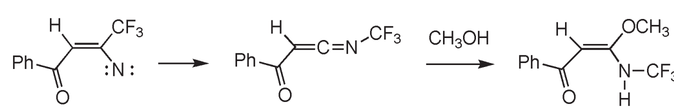
The ^{1}H-NMR spectrum of this material suggests that it is a mixture of (*E*)- and (*Z*)-2-methoxy-2-(trifluoromethyl)-3-benzoylaziridine (**18a**) and (**18b**). Thus, in



18a **18b**

addition to signals at δ 7.99, 7.63 and 7.52, assigned to the protons of the phenyl ring, the spectrum also exhibited a broad singlet at δ 2.80 and a broad doublet (J=9.0 Hz) at δ 2.69, assigned to the N-H proton in **18a** and **18b**, two sharp singlets at δ 3.59 and 3.48, assigned to the protons of the methoxy groups in **18a** and **18b**, and two doublets at δ 3.76 (J = 8.8 Hz) and δ 3.59 (J = 9.0 Hz) for the C3 proton in the aziridine ring in **18a** and **18b** respectively. As demanded by these assignments, addition of D_2O to the sample resulted in the loss of the N-H signals at δ 2.80 and 2.69 with concomitant collapse of the doublets at δ 3.76 and 3.59 to two singlets.

The ^{13}C-NMR spectrum was also consistent with the aziridine **18** structures. The proton decoupled spectrum exhibited signals at δ 43.8 and 46.4 due to the methoxy carbons, at δ 53.9 and 55.2 for the C-H carbon of the aziridine ring, signals for the phenyl carbons from δ 128.9 to 135.1, a quartet (J = 280.9 Hz) at δ 123.1 for the trifluoromethyl carbon, and a signal at δ 190.2 for the carbonyl carbon. These chemical shift values are not consistent with those expected for alternate structures such as **20** which would result from methanol trapping of ketenimine **19** [27].

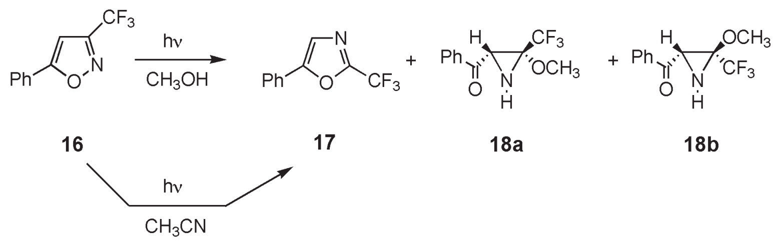


19 **20**

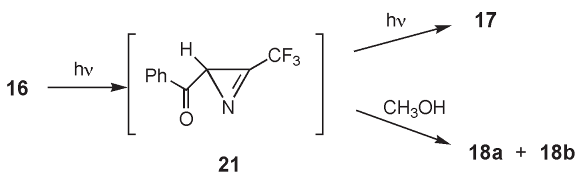
In the NMR spectrum of structure **20** the chemical shifts of the vinyl proton and carbon would be expected to resonate substantially downfield from those observed.

Finally, as expected for the assigned structure, the infrared spectrum showed an intense absorption at 1751.7 cm^{-1} due to the carbonyl functional group.

These results show that upon irradiation in methanol solvent, 5-phenyl-3-(trifluoromethyl)isoxazole (**16**) is converted to 5-phenyl-2-(trifluoromethyl)oxazole (**17**) and to a mixture of (*E*)- and (*Z*)-2-methoxy-2-(trifluoromethyl)-3-benzoylaziridine (**18a**) and (**18b**). Upon irradiation in acetonitrile, however, the only product formed was **17** in a yield of 55%.

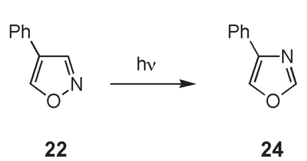


The formation of aziridines **18a** and **18b** is likely to result from the photochemically generated azirine **21** which is either converted to oxazole **17** or is trapped by



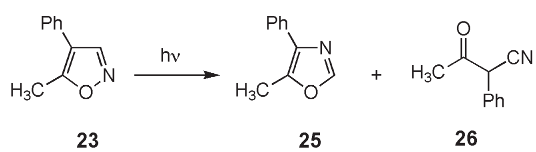
methanol to yield **18a** and **18b**. Interestingly, no analogous trapping was observed when 5-phenylisoxazole **5** was irradiated in methanol solvent. The electron withdrawing trifluoromethyl group apparently renders the azirine more susceptible to nucleophilic reaction with methanol than is the case with the unsubstituted azirine. As expected, in acetonitrile solvent no such trapping occurs and, as a result, the yield of **17** is greatly increased.

The photochemistry of 4-phenylisoxazole (**22**) and 5-methyl-4-phenylisoxazole (**23**) were also studied. A solution of 4-phenylisoxazole (**22**) (3.0 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated for 5 minutes. GC analysis revealed the consumption of 23% of the reactant and the formation of a single GC volatile product with a relative retention of 0.7 which was identified as 4-phenyloxazole (**24**) by direct comparison of its GC retention time and mass spectrum with an authentic sample. Quantitative GC showed that **24** was formed in 94% yield. GC analysis did not reveal the formation of cyanophenylacetaldehyde, the expected photocleavage product. Furthermore, analysis of the crude photoproduct residue by infrared spectroscopy did not show the presence of an absorption around 2300 cm^{-1} as required for a cyano functional group.



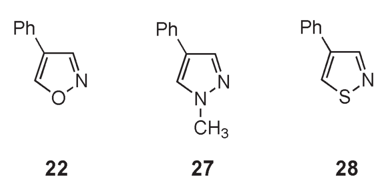
Although the extent of substitution in **22** and **24** does not allow the scrambling pattern to be unambiguously assigned, each ring position in **23** is uniquely substituted which allows the transposition of each ring position to be monitored.

A solution of 5-methyl-4-phenylisoxazole (**23**) (3.0 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated for 10 minutes after which GC analysis showed the consumption of 29% of the reactant and the formation of two GC-volatile products with relative retentions of 0.8 and 1.8 respectively. These products were identified as 5-methyl-4-phenyloxazole (**25**) and α-phenylacetoacetonitrile (**26**) by direct comparison of the



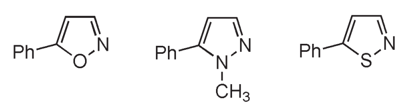
retention times and mass spectra of these products with authentic samples of the compounds. Quantitative GC showed that **25** and **26** were formed in yields of 80% and 18% respectively. These results also show that the phototransposition of **23** has occurred only with interchange of the N2 and C3 atoms and has therefore taken place by the P_4 pathway. By analogy, it is also assumed that the transposition of 4-phenylisoxazole (**22**) to 4-phenyloxazole (**24**) has also followed this pathway.

These studies show that the photochemistry of 4-phenylisoxazole (**22**) is similar to the photochemistry of



1-methyl-4-phenylpyrazole (**27**) [4] and 4-phenylisothiazole (**28**) [9]. All three of these compounds phototranspose solely *via* the P_4 pathway (Path B, Scheme 1) which involves only interchange of the N2-C3 ring atoms. No phototransposition *via* the electrocyclic ring closure-heteroatom migration pathway (Path A, Scheme 1) could be detected for any of these compounds. Although photo-ring cleavage products were observed from both **27** and **28**, an analogous product could not be detected from **22**.

The photochemistry of the three 5-phenyl-substituted heterocycles **4**, **29**, and **30** is, however, quite different.

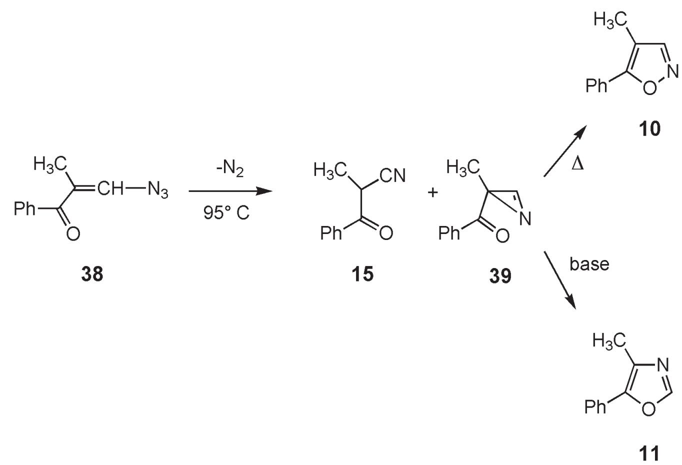


4 **29** **30**

Thus, although the phototransposition chemistry 1-methyl-5-phenylpyrazole (**29**) [4] and 5-phenylisothiazole (**30**) [10] is known to involve competition between heterocyclic ring closure-heteroatom migration (Path A, Scheme 1) and N2-C3 interchange (Path B, Scheme 1), this study reveals that 5-phenylisoxazole (**4**) phototranposes only *via* the P_4 pathway (Path B, Scheme 1).

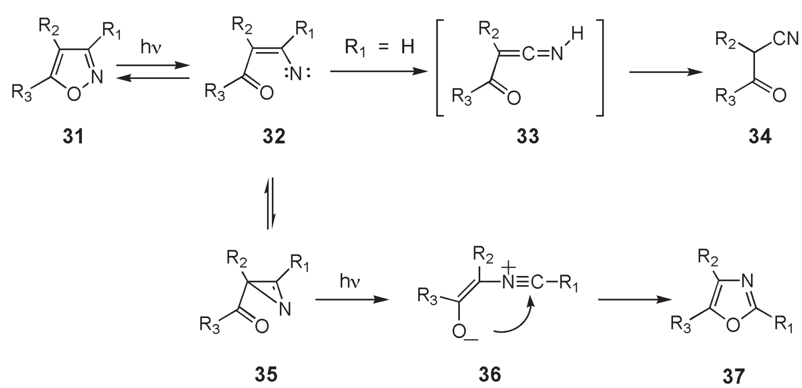
Reaction by the P_4 pathway indicates that photochemical excitation of these isoxazoles results in cleavage of the O-N bond in **31** to yield a species that is generally viewed as a vinylnitrene **32** (Scheme 4). Several reaction pathways can be envisioned for this nitrene. In addition to recyclizing to **31**, when R_1=H, vinyl nitrene **32** would be expected to rearrange to the ketonitrile photocleavage product **34**, possibly by way of keteneimine **33**. Indeed, isomerization to nitriles is a well-documented reaction of terminal vinyl nitrenes [28]. In addition, since vinyl nitrenes are also known to be in thermal equilibrium with their isomeric azirines [29], **32** would be expected to be in equilibrium with ketoazirine **35**. Ketoazirines, such as **35**, have been shown to be photochemically converted to an oxazole **37** by way of nitrile ylide **36** [30,31].

β-Ketovinyl nitrene **32** is a key intermediate in this mechanistic scheme. Interestingly, these same vinyl nitrenes can be generated by elimination of nitrogen from the corresponding vinyl azide. Isomura and colleagues [32] have shown that 3-azido-2-methyl-1-phenylpropen-1-



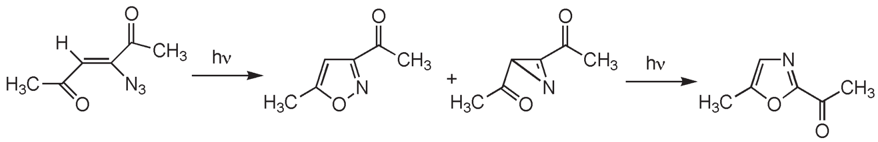
one (**38**) eliminates nitrogen at 95 ºC to give α-benzoylpropionitrile (**15**) and 3-benzoyl-3-methylazirine (**39**) which underwent thermal rearrangement to 4-methyl-5-phenylisoxazole (**10**) and base catalyzed isomerization to 4-methyl-5-phenyloxazole (**11**).

Scheme 4



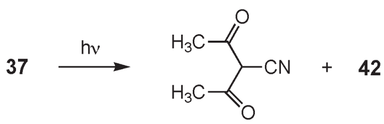
Although no photochemical reactions of azide **38** have appeared in the literature, Sauers and Van Arnum [33] have shown that (*Z*)-3-azido-3-hexene-2,5-dione (**40**) is photochemically converted to 3-acetyl-5-methylisoxazole

(**41**) and 2,3-diacetyl-2*H*-azirine (**42**) which underwent photoisomerization to 2-acetyl-5-methyloxazole (**43**).



40 **41** **42** **43**

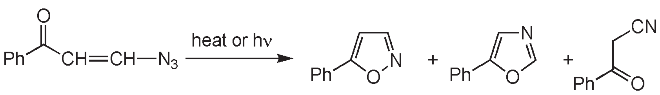
In contrast, irradiation of isoxazole **41** led to the formation of 3-cyano-2,4-pentanedione (**44**) and azirine **42**.



44

As part of this study, 3-azido-1-phenylpropen-1-one (**45**) was synthesized and its thermal and photochemical properties were compared with the photochemistry of 5-phenylisoxazole (**4**).

Azide **45** was decomposed thermally by injection into a gas chromatograph with an injection port temperature of 180 ºC. The resulting GC trace showed the formation of 5-phenylisoxazole (**4**), 5-phenyloxazole (**5**), and benzoylacetonitrile (**9**) in yields of 1.2%, 0.8 % and 16.5% respectively. Thus, thermolysis of azide **41** led to the formation of the nitrile **9** as the major product.



45 **4** **5** **9**

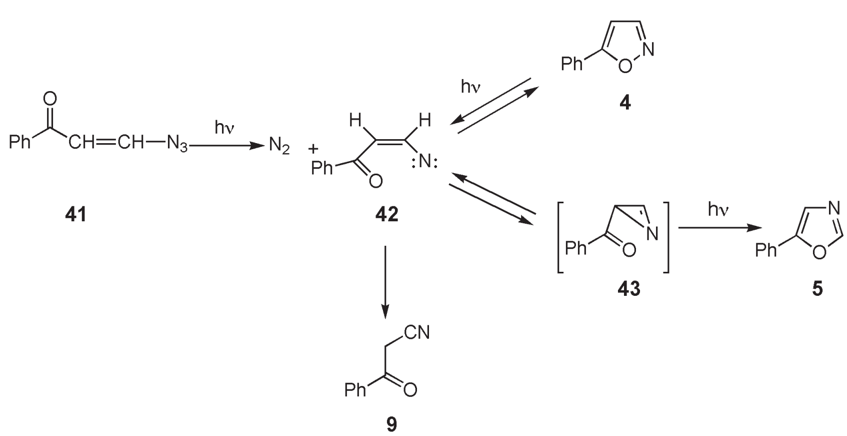
Azide **45** exhibited an absorption band with λ max at 290 nm which extended beyond 300 nm. A solution of **45** (5.0 mL, 2.0 x 10^{-2} *M*) in methanol was irradiated with light of λ > 290 nm until uv absorption spectroscopy confirmed the complete photochemical consumption of the azide **45**. GC analysis of the resulting solution showed the formation of 5-phenylisoxazole (**4**), 5-phenyloxazole (**5**), and benzoylacetonitrile (**9**) in yields of 9.4 %, 10.0 %, and 1.2 % respectively. Thus, in contrast to the thermolysis of azide **45**, photolysis of **45** provides the oxazole **5** as the major product. This was also observed upon irradiation of isoxazole **4**.

These results clearly show that β-benzoylvinyl nitrene **46**, formed photochemically from azide **45**, can cyclize to 5-phenylisoxazole (**4**) and can also rearrange to the observed P_4 phototransposition product, 5-phenyloxazole (**5**), presumably *via* azirine **47**, and to the photo-ring cleavage product, benzoylacetonitrile (**9**). These results are consistent with the suggestion that both 5-phenylisoxazole (**4**) and 3-azido-1-phenylpropen-1-one (**45**) undergo photoreaction by way of the same intermediate, namely, β-benzoylvinyl nitrene **46**, as shown in Scheme 5.

EXPERIMENTAL

^{1}H and ^{13}C-NMR spectra were recorded at 200 and 50.3 MHz respectively in deuteriochloroform on a Bruker FT NMR system.

Scheme 5



^1H and ^{13}C chemical shifts were measured relative to internal tetramethylsilane and chloroform respectively. Mass spectra were recorded with an HP 5970 B mass selective detector interfaced to an HP 5880 capillary column gas chromatograph. Infrared and ultraviolet absorption spectra were recorded using a Perkin Elmer Spectrum One FT-IR spectrometer or a Hitachi U-2000 spectrometer respectively. Gas chromatographic analyses were performed on a Perkin Elmer-9000 FID instrument equipped with a 15-m x 3-μm Carbowax-20M bonded phase capillary column.

Synthesis of Reactants and Possible Products.

5-Phenylisoxazole (**4**) was prepared by reaction of 3-oxo-3-phenylpropionaldehyde oxime with acetyl chloride [33]; 4-methyl-5-phenylisoxazole (**10**) by reaction of 2-benzoylpropanal with hydroxylamine hydrochloride [34]; 4-phenylisoxazole (**22**) by condensation of *N*,*N*-dimethylformamide and phenylacetic acid in the presence of phosphorus oxychloride [36] and treatment of the resulting 3-(*N*,*N*-dimethylamino)-2-phenylpropenal with hydroxylamine hydrochloride [37]; 5-methyl-4-phenylisoxazole (**23**) by reaction of 3-oxo-2-phenylbutanal with hydroxylamine [35]; 5-phenyl-3-(trifluoromethyl)isoxazole (**16)** by condensation of 4-phenyl-1,1,1-trifluorobut-3-yne-2-one with hydroxylamine hydrochloride [38]; 3-azido-1-phenylpropen-1-one (**41**) by reaction of 3-chloro-1-phenyl-2-propen-1-one [39] with sodium azide in methanol [40]; 5-phenyloxazole (**5**) by reaction of benzaldehyde with tosylmethylisocyanide [41]; 3-phenylisoxazole (**6**) by reaction of benzhydroximidoyl chloride [42] with triethylamine in the presence of acetylene [43]; 4-phenyloxazole (**8**) by reaction of α-bromoacetophenone with formamide [44]; 4-methyl-5-phenyloxazole (**11**), by the reaction of benzaldehyde with α-tosylethylisocyanide [41,44]; cyanophenylacetaldehyde by condensation of benzylcyanide and ethyl formate in the presence of sodium ethoxide [45]; α-benzoylpropionitrile (**15**) by condensation of propionitrile and methylbenzoate in the presence of sodium methoxide [46]; 2-phenylacetoacetonitrile (**26**) by condensation of benzylcyanide and ethylacetate in the presence of sodium ethoxide.

4-Deuterio-5-Phenylisoxazole (**4-4d**).

5-Phenylisoxazole (**4**) (0.300 g, 2.1 mmol) was dissolved in a mixture of deuteriosulfuric acid (98%, 2.00 mL) and deuterium oxide (1.44 mL). The solution was protected from the atmosphere and placed in an oil bath at 70 ºC for five days. The resulting solution was cooled, neutralized with aqueous sodium bicarbonate, extracted with dichloromethane (3 x 20 mL), dried (anhydrous sodium sulfate), and evaporated. The residual oil (0.201 g) was distilled (Kugelrohr) to give 4-deuterio-5-phenylisoxazole (**4-4d**) as a colorless oil: bp (Kugelrohr oven temperature) 115-120 ºC (17 Torr); yield 0.131 g (0.90 mmol, 43 %); ^{1}HNMR (deuteriochloroform): δ 7.4-7.5 (m, 3H), 7.7-7.8 (m, 2H), 8.28 (S, IH); MS m/z (%), 146(73), 105(100), 90(16), 77(75).

Irradiation and Analysis Procedures.

A solution of the appropriate reactant (3.0 mL, 2.0 x 10^{-2} *M*) in acetonitrile or methanol was placed in a quartz tube (1.0 cm inside diameter x 12.0 cm long). The tube was sealed with a rubber septum and purged with argon for 10 minutes prior to irradiation. The tubes were then irradiated at 254 nm in a Rayonet photochemical reactor equipped with eight low-pressure Hg lamps.

Reaction progress was monitored by removing aliquots periodically during the irradiation for analysis by GC. GC retentions of all products are given relative to the appropriate reactant. Quantitative GC analysis of reactant consumption and product formation was accomplished using calibration curves constructed for the reactants and products by plotting detector responses versus concentration for five standards of known concentration. Correlation coefficients ranged from 0.994 to 0.998.

5-Phenylisoxazole (**4**).

GC analysis (140º) after 10 minutes of irradiation showed the consumption of **4** (48%) and the formation of 5-phenyloxazole (**5**) (41%) with a relative retention of 0.82; MS, m/z (%); 145(100), 117(52), 105(131), 90(65), 89(31), 77(32), 63(15), 50(15) and benzoylacetonitrile (**9**) (21%) with a relative retention of 1.8: MS, m/z (%); 145 (4), 105(100), 77(71).

4-Phenylisoxazole (**22**).

GC analysis (140º) after 5 minutes of irradiation showed the consumption of **22** (23%) and the formation of 4-phenyloxazole (**24**) (94%) with a relative retention of 0.7: MS m/z (%) 145(100), 89(89), 63(59), 77(16), 146(13).

4-Methyl-5-phenylisoxazole (**10**).

GC analysis (190º) after 5 minutes of irradiation showed the consumption of **10** (34%) and the formation of 4-methyl-5-phenyloxazole (**11**) (54%) with a relative retention of 0.6: MS m/z (%) 159(100) 130(73), 130(19), 90(63), 77(50, 63(131), 51(33) and α-benzoylpropionitrile (**15**) (26%) with a relative retention of 1.7: MS m/z (%) 159(2), 105(100), 77(54), 51(25).

5-Methyl-4-phenylisoxazole (**23**).

GC analysis (190º) after 10 minutes of irradiation showed the consumption of **23** (29%) and the formation of 5-methyl-4-phenyloxazole (**25**) (80%) with a relative retention of 0.8: MS m/z (%) 159(100), 130(23), 104(53), 89(21), 78(40), 63(21) and 2-phenylacetoacetonitrile (**26**) (18%) with a relative retention of 1.8: MS m/z (%) 159(79), 144(14), 117(100), 116(36), 104(28), 103(28), 90(30), 89(47), 78(34), 77(23), 53(34), 52(19), 43(96).

5-Phenyl-3-(trifluoromethyl)isoxazole (**16**).

Irradiation in Methanol.

GC analysis (120-170 ºC) after irradiation showed the consumption of **16** and the formation of 5-phenyl-2-(trifluoromethyl)oxazole (**17**) with a relative retention of 0.75: MS, m/z (%); 213(100), 165(49), 160(16), 105(37), 89(18), 77 (33) and an unresolved mixture of (*E*)- and (*Z*)-2-methoxy-2-(trifluoromethyl)-3-benzoylaziridine (**18a**) and (**18b**) with a relative retention of 2.25: MS, m/z (%); 245(2), 213(101), 105(100), 77(18).

Irradiation in Acetonitrile.

GC analysis (120-170 ºC) after irradiation showed the consumption of **16** and the formation of 5-phenyl-2-(trifluoromethyl)oxazole (**17**) with relative retention and MS as above.

Preparative-scale Irradiation of 5-Phenyl-3-(trifluoromethyl)-isoxazole (**16**) in Methanol.

A solution of **16** (0.080g, 0.37 mmol) in methanol (25.0 mL) was placed in a quartz tube, sealed with a rubber septum, purged with nitrogen for 15 minutes, and irradiated for 25 minutes. After removal of the solvent at reduced pressure the brown residual oil (0.081 g) was subjected to preparative layer chromatography (silica gel, dichloromethane). The band at Rf = 0.77 gave 5-phenyl-

3-(trifluoromethyl)isoxazole (**16**) (0.0495 g, 0.232 mmol, 63% recovery). The band at Rf = 0.57 gave 5-phenyl-2-(trifluoromethyl)oxazole (**17**) (0.0031g, 0.015 mmol, 11% yield) as a yellow oil (lit. [48] mp 2-4 ºC); ^{1}H-NMR (deuteriochloroform): δ 7.44 (S 1H), 7.45 (m, 3H); 7.68 (m, 2H); ^{13}C-NMR (deuteriochloroform): δ (DEPT 135) 153.9(+), 150.0(0), 122.3(+), 129.9(+), 129.1(+), 126.2(0), 124.9(+), 122.3(+), 115.2(q, J=270.3Hz) (0); MS mz(%), 213(100), 165(47), 105(36), 89(15), 77(33), 51(17). The band at Rf = 0.23 gave a mixture of (*E*)- and (*Z*)-2-methoxy-2-(trifluoromethyl)-3-benzoylaziridine (**18a** and **18b**) (0.0249g, 0.10 mmol, 72.5% yield); ^{1}H-NMR (deuteriochloroform) δ 2.7 (br. d, J= 9.0 Hz, 1H), 2.8 (br. s, 1H), 3.5(s, 3H), 3.6 (s, 3H), 3.6 (d, J= 9.0 Hz, IH), 3.8 (d, J=8.8 Hz, IH), 7.5 (m, 4H), 7.6 (m, 2H), 7.9 (m, 4H); ^{13}CNMR (deuteriochloroform) δ 190.5, 190.2, 135.1, 134.9, 129.5, 129.4, 129.1, 128.9, 123.2, 73.3, 55.2, 46.4, 43.8; MS m/z (%) 245(1), 213(12), 110(12), 105 (100), 77(38), 69(10).

Preparative-scale Irradiation of 5-Phenyl-3-(trifuloromethyl)-isoxazole (**16**) in Acetonitrile.

A solution of **16** (0.0156 g, 7.3 x 10^{-2} mmole) in acetonnitrile (5.0 ml) was placed in a quartz tube, sealed with a rubber septum, purged with nitrogen for 15 minutes, and irradiated for 180 minutes. After removal of the solvent at reduced pressure the orange residual oil (0.014 g) was subjected to column chromatography (silcia gel). The column was eluted with hexane:dichloromethane, 2:1 (3.0 ml), and hexane:dichloromethane, 1:1 (25.0 ml). Thirteen fractions (2.0 ml) were collected. Fractions 7-11 were combined and concentrated to yield 5-phenyl-2-(trifluoromethyl)oxazole (**17**) as a yellow oil (0.0094 g, 60% yield).

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