Phototransposition Chemistry of 4-Substituted Isothiazoles. The P_4 Permutation Pathway

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Upon irradiation in the presence of a small quantity of base, 4-substituted isothiazoles undergo photocleavage to yield substituted cyanosulfides, which can be trapped as their benzyl thioether derivatives, and substituted isocyanosulfides. Both products are suggested to arise via initial photocleavage of the sulfur−nitrogen bond, resulting in the formation of a substituted *β*-thioformylvinyl nitrene, which can rearrange to the observed cyanosulfide, or cyclize to an undetected thioformylazirine. Deprotonation of the azirine leads directly to the isocyanosulfide. The plight of the isocyanosulfide depends on the C-4 substituent. If the substituent is aromatic, the isocyanosulfide is reprotonated at the isocyanide carbon and spontaneously cyclizes to a 4-substituted thiazole, the observed transposition product. If the substituent is not aromatic, the isocyanosulfide is reprotonated at sulfur and the resulting species has a higher energy barrier to cyclization. In these cases, the isocyanosulfides can be observed spectroscopically and can be trapped as their *N*-formylaminobenzyl thioether derivatives.

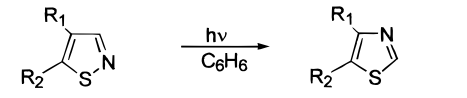
Introduction

Phenylisothiazoles and phenylthiazoles undergo phototransposition in benzene solution via the P_5-P_7 permutation pathways.[1,2] These permutations are consistent with mechanistic pathways involving initial electrocyclic ring closure and one or two subsequent sigmatropic shifts of sulfur around the azetine ring.[4] A perplexing feature of these reactions is the almost complete absence of reaction by the P_4 phototransposition process, a reaction involving interchange of N-2 and C-3 of the heterocyclic ring. Thus, although it was observed that 5-phenylthiazole is formed in less than 1% yield from 5-phenylisothiazole, presumably via a P_4 pathway,[5] neither 3-phenylisothiazole nor 4-phenylisothiazole was observed to yield P_4 products in greater than trace quantities.[4] These results are unusual since the P_4 permutation process is known to be a major pathway for pyrazoles[3,6−8] and isoxazoles[9] which also have two heteroatoms in adjacent ring positions.

In this paper, we present the results of our study of the photochemistry of 4-substituted isothiazoles in various solvents and the effects of added bases or acid on the reaction pathways. In particular, these results show that the addition of acid or base to the reaction media can dramatically affect the yield of phototransposition via the P_4 pathway and can substantially alter the ratio of phototransposition to photocleavage.

Results and Discussion

By analogy with the known photochemistry of pyrazoles and isoxazoles, 4-substituted isothiazoles are expected to be the most reactive isothiazoles via the P_4 pathway. Despite this expectation, Vernin and colleagues irradiated 4-phenylisothiazole (**1a**) in benzene solution but were unable to detect the formation of any phototransposition product.[10] In our laboratory, when a



1 a - e **2 a - e**

a: R_1 = Ph : R_2 = H **b**: R_1 = Ph : R_2 = D

c: R_1 = $PhCH_2$: R_2 = H **d**: R_1 = $PhCH_2$: R_2 = D

e: R_1 = CH_3 : R_2 = H

solution of **1a** in benzene was irradiated for 30 min, gas liquid chromatography (GLC) analysis showed that 82%

(1) For a discussion of permutation pattern analysis in aromatic phototransposition chemistry, see: (a) Barltrop, J. A.; Day, A. C. *J. Chem. Soc., Chem. Commun.* **1975**, 177−179. (b) Barltrop, J. A.; Day, A. C.; Moxon, P. D.; Ward, R. W. *J. Chem. Soc., Chem. Commun.* **1975**, 786−787. (c) Barltrop, J. A.; Day, A. C.; Ward, R. W. *J. Chem. Soc., Chem. Commun.* **1978**, 131−133.

(2) For five-membered heterocycles containing two heteroatoms, there are 12 different ways of transposing the five ring atoms resulting in 12 permutation patterns identified P_1-P_{12}. For a table showing these permutation patterns, see ref 3.

(3) Pavlik, J. W.; Kurzweil, E. M. *J. Org. Chem.* **1991**, *56*, 6313−6320.

(4) Pavlik, J. W.; Tongcharoensirikul, P.; Bird, N. P.; Day, A. C.; Barltrop, J. A. *J. Am. Chem. Soc.* **1994**, *116*, 2292−2300.

(5) The yield of 5-phenylthiazole was too low to be able to confirm the permutation pathway. Since C-2 and C-4 in 5-phenylthiazole are both bonded to hydrogen, it is not possible to determine their origins in 5-phenylisothiazole. Accordingly, the transposition could have occurred by either a P_4 or P_9 permutation pathway.

(6) Pavlik, J. W.; Connors, R. E.; Burns, D. S.; Kurzweil, E. M. *J. Am. Chem. Soc.* **1993**, *115*, 7645−7652.

(7) Pavlik, J. W.; Kebede, N.; Bird, N. P.; Day, A. C.; Barltrop, J. A. *J. Org. Chem.* **1995**, *60*, 8138−8139.

(8) Pavlik, J. W.; Kebede, N. *J. Org. Chem.* **1997**, *62*, 8325−8334.

(9) (a) Kurtz, D. W.; Schechter, H. J. *J. Chem. Soc., Chem. Commun.* **1966**, 689−690. (b) Ullman, E. G.; Singh, B. *J. Am. Chem. Soc.* **1966**, *88*, 1844−1845. (c) Ullman, E. G.; Singh, B. *J. Am. Chem. Soc.* **1967**, *89*, 6911−6916. (d) Singh, B.; Zweig, A.; Gallivan, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 1199−1206. (e) Nishiwaki, T.; Nakano, A.; Matsuoka, J. *J. Chem. Soc. C* **1970**, 1825−1829. (f) Nishiwaki, T.; Fujiyama, F. *J. Chem. Soc., Perkin Trans.* **1972**, 1456−1459. (g) Wamhoff, H. *Chem. Ber.* **1972**, *105*, 748−752. (h) Good, R. H.; Jones, G. *J. Chem. Soc. C* **1971**, 1196−1198. (i) Goeth, H.; Gagneux, A. R.; Eugster, C. H.; Schmid, H. *Helv. Chim. Acta* **1967**, *50*, 137−142. (j) Padwa, A.; Chen, E.; Ku, A. *J. Am. Chem. Soc.* **1975**, *97*, 6484−6491. (k) Dietliker, K.; Gilgen, P.; Heimgartner, H.; Schmid, H. *Helv. Chim. Acta* **1976**, *59*, 2074−2099.

(10) Vernin, G.; Riou, C.; Dou, H. J. M.; Bouscasse, J.; Metzger, J.; Loridan, G. *Bull Soc. Chim. Fr.* **1973**, 1743−1751.

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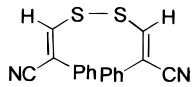
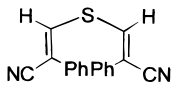
of the reactant had been consumed and that 3% of the P_4 product, 4-phenylthiazole (**2a**), had been formed. No other volatile product could be detected by GLC analysis.

The photoreaction of **1a** in benzene was also monitored by UV absorption spectroscopy. As expected, the absorption maximum of **1a** at 269 nm was obscured by the intense absorption of the benzene solvent. When a solution of **1a** (3.0 mL, 6.2×10^{-5} M) was irradiated, UV analysis revealed the formation of a new absorption at 290 nm which appeared as a shoulder on the benzene absorption.

To avoid competition with the solvent for the incident light, the photoreaction of **1a** was also carried out in diethyl ether solvent. Maeda and Ohashi have previously reported that in this solvent **1a** is converted to β-cyanostyryl disulfide **3**.[11] However, no spectral or analytical



3



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data were presented to support this structural assignment.

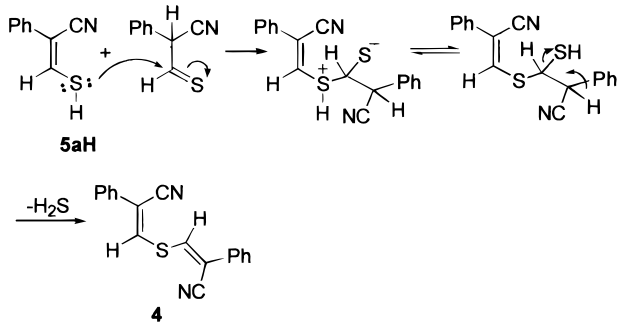
Irradiation of **1a** in diethyl ether was monitored by GLC and, after dilution, by UV absorption spectroscopy. After irradiation for 30 min, GLC analysis showed the consumption of 89% of **1a** without the formation of any volatile product. During this irradiation, UV analysis showed the consumption of **1a** and an increase in the optical density at 290 nm from 0.242 to 0.779 due to the formation of a photoproduct. This absorption maximum is at the same wavelength as was observed after irradiation in benzene, indicating that the same nonvolatile product that formed in diethyl ether is also formed upon irradiation of **1a** in benzene.

On a preparative scale, a solution of **1a** in diethyl ether was irradiated for 30 min. Evaporation of the diethyl ether provided a viscous yellow oil which exhibited an infrared absorption at 2212 cm^{-1} indicating the presence of a nitrile functional group. This oil solidified after standing briefly at room temperature to yield a solid which was purified by repeated recrystallization. The ^1H and ^{13}C NMR and IR spectral data are consistent with the β-cyanostyryl moiety of the disulfide structure **3** suggested by Maeda and Ohashi. Thus, the ^1H NMR spectrum shows only a one-proton singlet at δ 7.66 due to the vinyl proton and a five-proton multiplet at δ 7.41−7.58 due to the five phenyl protons. The ^{13}C NMR spectrum exhibits signals at δ 115.32, 137.77, and 114.37 due to the cyano and vinyl carbons and signals at δ 125.69, 129.63, 129.97, and 132.62 for the carbon atoms of the phenyl ring. Furthermore, the infrared spectrum exhibited an intense absorption at 2208 cm^{-1} characteristic of a nitrile functional group.

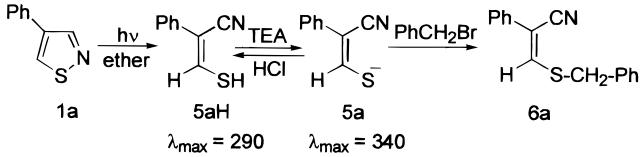
Although these spectral data are consistent with the β-cyanostyryl structure, the mass spectrum exhibited a molecular ion at *m/z* 288, consistent with thioether structure **4**, rather than at *m/z* 320 as required by the disulfide structure **3**. Elemental analyses, however, repeatedly gave results that were slightly low for carbon and slightly high for sulfur, suggesting that the thioether **4** was contaminated with a small amount of the disulfide **3**.

(11) Ohashi, M.; Iio, A.; Ezaki, A.; Yonezawa, T. *Heterocycles* **1975**, *3*, 69.

Scheme 1



Scheme 2



Either structure **3** or **4** suggests that it was formed from 2-cyano-2-phenylethene-1-thiol (**5aH**), the anticipated photocleavage product from 4-phenylisothiazole (**1a**).[12] The formation of either disulfide **3** or thioether **4** from thiol **5aH** can occur either by air oxidation[13] or via an aldol condensation[14] of the enethiol and its thioaldehyde tautomer[15] with elimination of H_2S as shown in Scheme 1.

In an attempt to trap the suggested photocleavage product, a solution of **1a** in diethyl ether was irradiated until after 30 min the optical density at 290 nm was maximized. Triethylamine (TEA) was added to the solution. This caused the absorption maximum to shift from 290 to 340 nm which is consistent with deprotonation of cyanothiol **5aH**, resulting in the formation of its conjugate base, cyanosulfide **5a** (Scheme 2). As expected, this change was reversible. Thus, if the TEA was neutralized with HCl, the absorption maximum shifted back to 290 nm. This confirms that the species absorbing at 290 and 340 nm are the acidic and basic forms of the same compound, respectively. To trap cyanosulfide **5a** as its benzyl thioether derivative, benzyl bromide was added to the solution absorbing at 340 nm. This resulted in the disappearance of the absorption band at 340 nm and the formation of a new absorption band with a maximum at 318 nm confirming that a reaction had taken place.

The ^1H NMR spectrum of the residue obtained from the above reaction mixture revealed the presence of unreacted 4-phenylisothiazole (**1a**) and unreacted benzyl bromide. The spectrum also exhibited two singlets at δ 4.14 and 4.00 in a ratio of 3.5:1 for two sets of benzyl protons. The infrared spectrum exhibited a strong absorption at 2207 cm^{-1} indicating the presence of a nitrile functional group and a weaker signal at 2103 cm^{-1} where isocyanides are known to absorb. Preparative

(12) Although isothiazoles have not been reported to undergo photocleavage to α,β-unsaturated cyanothiols, the analogous photocleavage of pyrazoles to enaminonitriles is well-known. See ref 3 and literature cited therein.

(13) Tarbell, D. S. In *The Chemistry of Organic Sulfur Compounds*; Kharasch, N., Ed.; Pergamon Press: Oxford, 1961; Vol. 1, pp 97−102.

(14) Campaigne, E.; Moss, R. D. *J. Am. Chem. Soc.* **1954**, *76*, 1269−1271.

(15) Reyes, A.; Silverstein, R. M. *J. Am. Chem. Soc.* **1958**, *80*, 6367−6372, 6373−6379.

layer chromatography led to the isolation of a white crystalline nitrile, as evidenced by the strong absorption band in the infrared spectrum at 2207 cm^{-1}, but did not allow isolation of an isocyanide. The mass spectrum of the nitrile exhibited a molecular ion at *m*/*z* 251, consistent with benzyl thioether **6a**, expected by reaction of cyanosulfide **5a** with benzyl bromide as shown in Scheme 2. Furthermore, the mass spectrum also exhibited an intense signal at *m*/*z* 91 as expected for a benzyl derivative.

The ^{1}H NMR spectrum exhibits a singlet at δ 4.14 assigned to the benzyl protons and a multiplet at δ 7.24−7.54 due to the aromatic protons with an integral ratio of 1:5. The ^{13}C NMR spectrum also exhibits signals at δ 38.33 and 116.16 consistent with benzyl and nitrile carbon atoms, respectively. These spectral data are consistent with the 2-cyano-2-phenylethenylbenzyl thioether structure **6a**. Since the ^{1}H and ^{13}C NMR spectra each exhibit one signal in the benzyl region at δ 4.14 and 38.33, respectively, the isolated thioether **6a** apparently consists of a single isomer. Although no ^{1}H NMR signal appears at δ 7.04 where the vinyl proton of the *E* isomer is estimated to absorb,[16] the region at δ 7.27 where the vinyl proton of the *Z* isomer is estimated to absorb is obscured by the signals due to the phenyl protons. Despite this, the product is tentatively assigned the *Z* configuration of **6a** due to the absence of a signal for the *E* isomer and because the *Z* isomer is expected to be formed in the ring cleavage reaction.

Isolation of benzyl thioether **6a** is excellent evidence that irradiation of 4-phenylisothiazole (**1a**) in diethyl ether results in the formation of 2-cyano-2-phenylethene-1-thiol (**5aH**). The infrared spectrum of the crude product mixture, however, also suggested that an isocyanide was also being formed in the photoreaction of 4-phenylisothiazole (**1a**). This possibility is of particular interest since Ferris and colleagues have detected isocyanides at low temperatures in the analogous P_4 phototransposition reactions of 4-substituted isoxazoles[17,18] while work in this laboratory has recently shown that isocyanides are general intermediates in the P_4 phototransposition of *N*-methylpyrazoles to *N*-methylimidazoles.[7,8]

In an attempt to detect the isocyanide intermediate in this reaction, the photochemistry of 4-phenylisothiazole (**1a**) was briefly investigated in an argon matrix at 12 K.[19] After irradiation, infrared analysis at 12 K showed the formation of a new absorption band at 2225 cm^{-1}, consistent with the formation of a nitrile, as well as new absorption bands at 1480, 814, 770, and 722 cm^{-1} where 4-phenylthiazole (**2a**) is known to absorb. Thus, even before the matrix was allowed to warm, there is evidence that some 4-phenylthiazole (**2a**) has been formed. On warming to 50 K, the nitrile band was observed to shift from 2225 to 2213 cm^{-1}. This is most likely due to evaporation of the matrix rather than reaction since all other bands in the spectrum were also observed to shift similarly. More importantly, however, warming to 50 K was also accompanied by the formation of a new low-intensity absorption band at 2075 cm^{-1}. Although this new band may be due to the formation of an isocyanide, the absorption position at 2075 cm^{-1} is outside of the 2100−2150 cm^{-1} range where unsaturated isocyanides generally absorb.[20] Vinyl isocyanide, for example, absorbs in the infrared at 2125 cm^{-1}.[21] Although both of these absorption bands were still observed after warming to 100 K, only the nitrile absorption band, which shifted to 2211 cm^{-1}, was still present at 200 K. During this warming, the species responsible for the absorption band at 2075 cm^{-1} could have either reacted or evaporated. Finally, at 250 K, the absorption band at 2211 cm^{-1} was still present but greatly diminished in intensity.

The photoreaction took a different path when it was carried out in methanol solvent. Thus, after a solution of **1a** (10.0 mL, 2.0×10^{-2} M) in methanol was irradiated for 30 min, GLC analysis showed that 74% of the reactant was consumed and that 4-phenylthiazole (**2a**) was formed in 38% yield. In addition to the consumption of **1a** and the formation of **2a**, analysis by UV absorption spectroscopy showed an increase in the optical density at 340 nm from 0 to 0.287. This absorption maximum is identical to that of the basic form of the photocleavage product **5aH**. Thus, in methanol solvent, 4-phenylisothiazole (**1a**) undergoes both phototransposition to **2a** and photocleavage to yield cyanosulfide **5a**.

Since C-2 and C-5 of 4-phenylthiazole (**2a**) are both bonded to hydrogen, either of these two ring atoms could have originated at either ring position 3 or 5 in the reactant. As a result, this phototransposition can be rationalized by either a P_4 or a P_{11} permutation pathway. This ambiguity was removed by studying the phototransposition chemistry of 5-deuterio-4-phenylisothiazole (**1b**), prepared by the base-catalyzed deuteration of 4-phenylisothiazole (**1a**). The mass spectrum of the deuterated product exhibited a molecular ion at *m*/*z* 162, consistent with monodeuteration, and an intense peak at *m*/*z* 135 due to the loss of HC-3≡N,[22,23] indicating that the deuterium is located at ring position 5. The ^{1}H NMR spectrum confirmed this by showing a 1-H singlet at δ 8.75 where the C-3 proton is known to absorb but no signal at δ 8.65 where the C-5 proton is expected to appear.[24]

5-Deuterio-4-phenylisothiazole (**1b**) is a reactant in which each ring position is uniquely substituted. Product identification thus allows unambiguous assignment of the permutation pattern. A solution of 5-deuterio-4-phenylisothiazole (**1b**) in methanol was irradiated for 30 min. GLC−MS analysis of the 4-phenylthiazole photoproduct showed a molecular ion at *m*/*z* 162 confirming that the loss of deuterium had not occurred during the photolysis. The mass spectrum also exhibited an intense signal at *m*/*z* 135 due to loss of HC-2≡N, indicating that the deuterium is at C-5 of the 4-phenylthiazole ring.[22,23] The ^{1}H NMR spectrum confirmed this by exhibiting a sharp singlet at δ 8.86 where H-2 of 4-phenylthiazole is known

(16) Frieboln, H. *Basic One- and Two-Dimensional NMR Spectroscopy*, 2nd ed.; VCH Publishers: New York, 1993; pp 139−143.
(17) Ferris, J. P.; Antonucci, F. R. *J. Am. Chem. Soc.* **1974**, *96*, 2010−2014, 2014−2019.
(18) Ferris, J. P.; Trimmer, J. *J. Org. Chem.* **1976**, *41*, 13−19.
(19) The matrix isolation experiment was carried out by Max P. Bernstein and Scott A. Sandford, NASA-Ames Research Center, Moffett Field, CA.
(20) Juchnovski, I. N.; Binev, I. G. in *Supplement C: The Chemistry of the Triple-Bonded Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1983; pp 107−135.
(21) Bolton, K.; Owen, N. L.; Sheridan, *J. Spectrochim. Acta* **1970**, *26*, 909−917.
(22) Salmona, G.; Vincent, E.-J. *Org. Mass Spectrom.* **1978**, *13*, 119−120.
(23) Clarke, G. M.; Grigg, R.; Williams, D. H. *J. Chem. Soc. B* **1966**, 339−343.
(24) Staab, H. A.; Mannschreck, A. *Chem. Ber.* **1965**, *98*, 1111−1121.

to absorb but there is no signal for H-5 at δ 7.52.[25] This shows that 5-deuterio-4-phenylisothiazole (**1b**) had been transposed to 5-deuterio-4-phenylthiazole (**2b**) via a P_4 permutation pathway which involves only the interchange of N-2 and C-3 of the isothiazole ring.

The photoreaction in methanol was found to be very dependent on the purity of the methanol used. The above results were obtained only when the methanol was freshly distilled from magnesium methoxide. When the photoreaction was carried out in unpurified methanol, 4-phenylthiazole (**2a**) could not be detected either by UV absorption spectroscopy or by GLC analysis. Under these conditions, UV analysis showed that the optical density at 269 nm decreased from 0.862 to 0.622 due to consumption of **1a**, while the optical densities at 290 and 340 nm increased from 0.322 to 0.756 and from 0 to 0.427, respectively. This shows that if acidic impurities are not removed from the methanol solvent, 4-phenylisothiazole (**1a**) undergoes only photocleavage to yield a mixture of cyanothiol **5aH** and cyanosulfide **5a**.

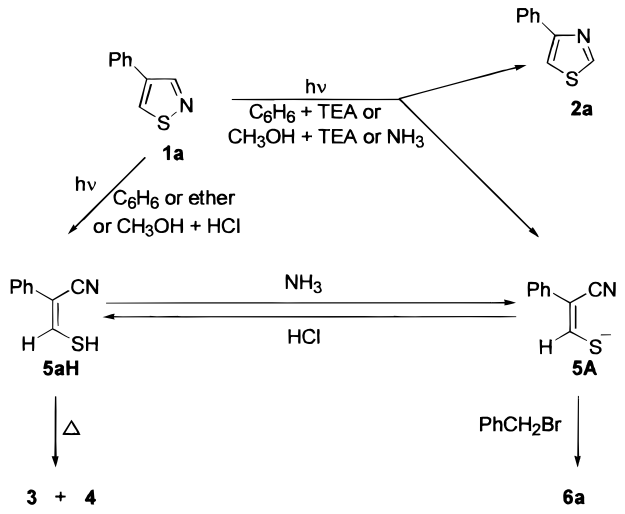
Additional experiments have also shown that the yield of the phototransposition product is substantially enhanced if the irradiation is carried out in methanol containing a small quantity of an added base. Thus, when three solutions of 4-phenylisothiazole (**1a**) (3.0 mL, 2.0×10^{-2} M) in methanol containing 0, 1.0×10^{-2}, or 2.4×10^{-1} M TEA were simultaneously irradiated on a merry-go-round apparatus, GLC analysis showed that consumption of 4-phenylisothiazole (**1a**) decreased slightly from 82% in the absence of TEA to 75 or 76% in the presence of 1.0×10^{-2} or 2.4×10^{-2} M TEA, respectively. At the same time, however, the yield of 4-phenylthiazole (**2a**) increased dramatically from 37% in the absence of TEA to 86 or 82% in the presence of TEA. GLC analysis also showed that TEA is not consumed during these irradiations. This increase in the yield of the phototransposition product is not dependent on the particular base used. Thus, essentially identical results were observed when the photolysis was carried out in methanol containing small quantities of aqueous sodium bicarbonate, aqueous ammonia, or propylamine.

Interestingly, the effect of added base is not observed only in methanol solvent. Thus, when three solutions of 4-phenylisothiazole (**1a**) (3.0 mL, 2.0×10^{-2} M) in benzene containing 0, 1.0×10^{-2}, or 2.4×10^{-1} M TEA were simultaneously irradiated on the merry-go-round, GLC analysis showed that the consumption of 4-phenylisothiazole (**1a**) increased from 63% in the absence of TEA to 77 or 65% in the presence of 1.0×10^{-2} or 2.4×10^{-1} M TEA, respectively. The yield of 4-phenylthiazole (**2a**) increased from 3% in the absence of TEA to 72 or 68% in the presence of 1.0×10^{-2} or 2.4×10^{-1} M TEA, respectively. Again, TEA was not consumed during these irradiations.

Finally, in either methanol or benzene containing TEA, 5-deuterio-4-phenylisothiazole (**1b**) was also converted to 5-deuterio-4-phenylthiazole (**2b**), showing that the added base has not changed the permutation pathway for the phototransposition.

Whereas the presence of base enhances the yield of the phototransposition product, the addition of acid has the opposite effect. Thus, the UV absorption spectrum before and after irradiation of a solution of **1a** in methanol (3.0 mL, 1.15×10^{-4} M) containing 1.0 μL of concentrated HCl showed that consumption of **1a** was not accompanied by an increase in the optical density at 250 nm, indicating that in acid solution the phototransposition is completely suppressed.[26] Instead, irradiation was accompanied by an increase in the optical denisty at 290 nm to a value of 1.18, indicating the formation of cyanothiol **5aH**. If after irradiation the HCl was neutralized by the addition of aqueous ammonia, the absorption band at 290 nm disappeared while the optical density at 340 nm due to the formation of cyanosulfide **5a** increased to 1.35. On the basis of the optical densities, the yield of cyanosulfide **5a** is approximately 5 times greater when it is formed indirectly via cyanothiol **5aH** than when it is formed directly by irradiation of **1a** in methanol containing aqueous ammonia. Finally, experiments show that neither cyanothiol **5aH** nor cyanosulfide **5a** is photochemically converted to either **1a** or **2a**. These results are summarized in Scheme 3.

Scheme 3



Convincing evidence for the involvement of an isocyanide intermediate in the P_4 isothiazole-to-thiazole phototransposition was obtained by studying the photochemistry of 4-benzylisothiazole (**1c**).

Irradiation of a solution of **1c** in methanol containing ammonia (7.5×10^{-2} M) was monitored by GLC and, after dilution, by UV absorption spectroscopy. After irradiation for 30 min, GLC analysis showed the presence of unreacted 4-benzylisothiazole (**1c**) (22%) and the formation of a single product that was identified by its spectroscopic properties as 4-benzylthiazole (**2c**) formed in 51% yield.

The mass spectrum of the photoproduct, which shows a molecular ion at *m*/*z* 175, and the elemental analysis are consistent with $C_{10}H_9NS$, confirming that the photoproduct is an isomer of 4-benzylisothiazole (**1c**). The ^{1}H NMR spectrum of the photoproduct exhibits signals at δ 8.75 and 6.86 where the C-2 and C-5 protons of the thiazole ring are known to absorb, respectively, but no signal at δ 7.98 where the C-4 proton is expected.[25] Furthermore, as anticipated for protons in ring positions

(25) Aune, J. D.; Dou, H. J. M.; Crousier, J. In *Thiazoles and Its Derivatives, Part One*; Metzger, J. V., Ed.; Wiley: New York, 1979; Vol. 34, Part 1, pp 342−347.

(26) Addition of 1.0 μL of concentrated HCl does not change the UV absorption spectrum, indicating that **1a** is not protonated under these conditions. This is consistent with the low basicity of isothiazoles. See: Clementi, S.; Forsythe, P. P.; Johnson, C. D.; Katritzky, A. A.; Terem, B. *J. Chem. Soc., Perkin Trans. 2* **1974**, 399−402.

2 and 5, the spectrum shows that these protons are spin coupled with a J_d of 2.05 Hz. Finally, the signal at δ 6.86 due to the C-5 proton is further split into a triplet of doublets (J_t = 1.99 Hz) due to its coupling with the methylene protons of the benzyl group at position 4 of the thiazole ring. The ^{13}C NMR spectrum is also consistent with the proposed product. The spectrum thus exhibits signals at δ 152.77 and 114.07 where C-2 and C-5 of the thiazole ring are known to resonate, respectively.[25] The signal of C-4 is shifted from δ 143.7 in unsubstituted thiazole to δ 157.20 due to the benzyl group bonded to that carbon. As expected for a quaternary carbon, the intensity of this signal is low. Finally, the spectrum also exhibits a signal at δ 37.69 due to the methylene group of the benzyl group.

The resulting solution was evaporated to dryness and examined by ^{1}H NMR. The spectrum showed the singlet at δ 4.02 due to the benzyl protons of unreacted 4-benzylisothiazole (**1c**) and a singlet at δ 4.17 due to the benzyl protons of the photoproduct, 4-benzylthiazole (**2c**). The spectrum was quite clean and showed only the presence of the unreacted 4-benzylisothiazole (**1c**) and the photoproduct **2c**.

The P_4 permutation pattern for the transposition was confirmed by showing that 5-deuterio-4-benzylisothiazole (**1d**) undergoes photoisomerization in methanol/ammonia to yield 5-deuterio-4-benzylthiazole (**2d**). The location of the deuterium at ring position 5 in the photoproduct was confirmed by the ^{1}H NMR spectrum which exhibited a one-proton singlet for the C-2 proton at δ 8.75 but no signal at δ 6.86 where the C-5 proton is known to absorb.

Although both GLC and ^{1}H NMR show the clean photoconversion of 4-benzylisothiazole (**1c**) to 4-benzylthiazole (**2c**), analysis by UV absorption spectroscopy shows that **2c** is not a primary product in this reaction. Thus, a solution of **1c** (10.0 mL, 2.0 $\times$ 10^{-2} M) in methanol containing aqueous ammonia (50 μL) was irradiated for 30 min. Analysis by UV absorption spectroscopy of an aliquot of the resulting solution after dilution showed a decrease in the optical density at 251 nm due to the consumption of 4-benzylisothiazole (**1c**) and to an increase in the optical density at 294 nm from 0 to 0.861. Neither the reactant nor the expected photoproduct, 4-benzylthiazole (**2c**), absorbs at 294 nm. Interestingly, after a portion (2.0 mL) of the irradiated solution was refluxed for 2 h, UV absorption spectroscopy showed that the optical denisty at 294 nm decreased from 0.861 to 0.369 while the optical density at 248 nm, where 4-benzylthiazole (**2c**) absorbs, increased from 0.632 to 0.887. This indicates that a portion of the species absorbing at 294 nm was converted to 4-benzylthiazole (**2c**) during the reflux. The remaining portion of the refluxed solution (1.5 mL) and the portion of the irradiated solution that had not been refluxed were each concentrated and analyzed by ^{1}H NMR. In both cases, the ^{1}H NMR spectra showed singlets at δ 4.02 and 4.17 due to the benzyl protons of 4-benzylisothiazole (**1c**) and 4-benzylthiazole (**2c**), respectively, in a ratio of 1:2.54 (after refluxing) or 1:2.49 (without refluxing). Both spectra were very clean and showed only the reactant 4-benzylisothiazole (**1c**) and the photoproduct 4-benzylthiazole (**2c**). These results show that upon irradiation in methanol containing ammonia 4-benzylisothiazole (**1c**) is photochemically converted to a primary product or products absorbing at 294 nm which are thermally converted to 4-benzylthiazole (**2c**) during refluxing or under the conditions of our GLC and ^{1}H NMR analyses.

To gain further information about the intermediate or intermediates absorbing at 294 nm, an identical photoreaction (10.0 mL, 2.0 $\times$ 10^{-2} M, 50 μL of aqueous ammonia) was carried out. Aliquots (2.0 mL) of the resulting solution were analyzed by infrared spectroscopy immediately after irradiation and after the solution remained in the dark at room temperature for 12 and 48 h. Immediately after irradiation, the infrared spectrum exhibited absorption signals at 2207 and 2104 cm^{-1} in a ratio of 1:1.2 indicating the presence of a nitrile and suggesting that an isocyanide was also present. After 12 and 48 h, the relative intensities of these bands changed from 1:1.2 immediately after photolysis to 1:0.96 after 12 h and 1:0.5 after 48 h. At the same time, the spectrum revealed an increase in an absorption band at 1407 cm^{-1} where 4-benzylthiazole (**2c**) absorbs. These results indicate that 4-benzylisothiazole (**1c**) is photochemically converted to a mixture of a nitrile and an isocyanide and that the isocyanide is thermally converted to the phototransposition product, 4-benzylthiazole (**2c**).

To further investigate the structures of the photochemically generated primary products, a solution of 4-benzylisothiazole (**1c**) in methanol containing ammonia was irradiated until after 30 min the absorption at 294 nm was maximized. Benzyl bromide was added to the solution, resulting in a change in the UV absorption maximum from 294 to 278 nm. The infrared spectrum of the residue resulting from this solution showed strong absorption bands at 2200 and 2100 cm^{-1} due to nitrile and isocyanide functional groups. This residue was treated with glacial acetic acid. After neutralization, infrared analysis showed no change in the absorption band at 2200 cm^{-1}, as expected for a nitrile functional group. In contrast, the absorption band present before acid treatment at 2100 cm^{-1} was replaced by a new strong band at 1683 cm^{-1}. This is consistent with the acid-catalyzed hydrolysis of the isocyanide to a formamide functional group.[27,28] Preparative layer chromatography allowed the isolation of unreacted benzyl bromide, unreacted 4-benzylisothiazole (**1c**), 4-benzylthiazole (**2c**), and two new compounds identified as 2-cyano-3-phenylpropen-1-ylbenzyl thioether (**7c**) and 2-(*N*-formylamino)-3-phenylpropen-1-ylbenzyl thioether (**8c**).

7 c,e **8 c,e**

c : R_1 = $PhCH_2$ e: R_1 = CH_3

2-Cyano-3-phenylpropen-1-ylbenzyl thioether (**7c**) was isolated as a pale yellow liquid. As required by the assigned structure, the mass spectrum exhibited a molecular ion at *m/z* 265 while the infrared spectrum showed an absorption band for the nitrile functional group at 2200 cm^{-1}. Although the isolated product **7c** appeared to be homogeneous by GLC and TLC, the ^{1}H NMR spectrum revealed the presence of two sets of signals suggesting the presence of two geometrical isomers. Thus, in addition to a 10-H multiplet absorbing

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(28) Lim, Y. Y.; Stein, A. R. *Can. J. Chem.* **1971**, *49*, 2455−2459.

at δ 7.07−7.36, the spectrum also showed two 1-H triplets for the vinyl protons at δ 7.05 (J = 0.90 Hz) and 6.66 (J = 1.34 Hz), two 2-H broad singlets for the benzyl protons at δ 3.46 and 3.51, and two 2-H sharp singlets for the thiobenzyl protons at δ 3.96 and 4.02.

The signals at δ 7.05 and 6.66 were assigned to the vinyl protons of the *E* and *Z* isomers, respectively, since in the *E* configuration the vinyl proton is situated in the deshielding zone of the cyano group and is expected to resonate downfield from the vinyl proton in the *Z* isomer. Similarly, the vinyl proton of (*E*)-3-methoxyacrylonitrile is reported to appear at δ 7.25, while in the *Z* isomer, the vinyl proton is upfield at δ 6.75.[29]

The absorptions at δ 3.51 and 3.46 and at δ 4.02 and 3.96 were assigned to the benzyl and thiobenzyl protons of the *E* and *Z* isomers, respectively, on the basis of the results of NOE experiments.[30] Thus, when the decoupler was set on the vinyl proton absorption at δ 6.66, the signal at δ 3.46 due to the benzyl protons was enhanced due to the NOE effect while the signal at δ 3.96 due to the thiobenzyl protons was slightly enhanced due to the decoupling. This confirms that the vinyl and benzyl protons absorbing at δ 6.66 and 3.46 are situated in close spatial proximity as required by the *Z* configuration and that the signal at δ 3.96 is due to the thiobenzyl protons of the same isomer. Conversely, when the decoupler was set on the vinyl proton absorption at δ 7.05, the thiobenzyl proton signal at δ 4.02 was slightly enhanced, but no NOE enhancement of the signal at δ 3.51 due to the benzyl protons was observed. This shows that these sets of benzyl and vinyl protons are not situated in close spatial proximity and were accordingly assigned to the *E* isomer.

The ^{13}C NMR spectrum is also consistent with the assigned structure. The spectrum exhibits signals at δ 118.87 and 117.02 for the nitrile carbons and at δ 108.37 and 145.56 and at δ 108.73 and 144.45 for the α- and β-vinyl carbon atoms of the *E* and *Z* isomers. These chemical shifts are consistent with the expected polarization due to the resonance interaction of the nitrile and thiobenzyl moieties. Similarly, the *E* and *Z* isomers of 3-methoxyacrylonitrile in the ^{13}C NMR spectrum are reported to resonate at δ 74.84 and 165.23 and at δ 74.27 and 164.32.[29]

As demanded by the proposed structure, the ^{13}C spectrum should also exhibit four signals due to the benzyl and thiobenzyl carbon atoms. These were observed for the benzyl carbons of the *E* and *Z* isomers at δ 36.49 and 40.16 and for the thiobenzyl carbons of the *E* and *Z* isomers at δ 38.07 and 36.95, respectively. These signals were confidently assigned on the basis of ^{13}C−^{1}H NMR correlation analysis.[31]

2-(*N*-Formylamino)-3-phenylpropen-1-ylbenzyl thioether (**8c**) was also isolated as a yellow oil. The mass spectrum, which exhibited a molecular ion at *m*/*z* 283 and a base peak at 91 due to the benzyl cation radical, and the infrared spectrum, which confirmed the presence of the formamide functional group by showing an intense absorption band at 1683 cm^{-1}, were consistent with the assigned structure.

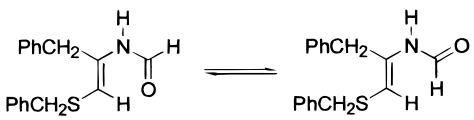
The ^{1}H and ^{13}C NMR spectra of this product again show two sets of signals suggesting the presence of two isomers. Thus, in DMSO-d_6, the ^{1}H NMR spectrum exhibits signals for the amino proton as a doublet at δ 9.57 (J = 10.72 Hz) and a broad singlet at δ 9.38 while the aldehyde proton is observed as two doublets at δ 8.18 (J = 10.72 Hz) and 8.01 (J = 1.72 Hz). As required by these assignments, upon addition of D_2O, the signals assigned to the amino proton disappeared while the doublets assigned to the aldehyde proton collapsed to two broad singlets.

In $CDCl_3$, the aldehyde proton appears in the ^{1}H NMR spectrum as two doublets at δ 8.19 (J = 11.12 Hz) and 8.08 (J = 4.0 Hz) and correlate with signals in the ^{13}C NMR spectrum at δ 161.34 and 158.94, respectively, which were therefore assigned to the carbonyl carbons of the formamide group. These chemical shifts are similar to those of the analogous carbons in *N*-vinylformamide which resonate at δ 163.50 and 159.16.

In DMSO-d_6, the benzyl protons, thiobenzyl protons, and vinyl protons each appear as pairs of singlets at δ 3.59 and 3.52, at δ 3.90 and 3.88, and at δ 6.89 and 5.89, respectively. In $CDCl_3$, the vinyl protons appear at δ 7.14 and 5.77 and correlate with signals in the ^{13}C NMR spectrum at δ 112.78 and 109.38 which were therefore assigned to the C-2 vinyl carbon. The ^{13}C NMR spectrum also exhibits signals at δ 133.03 and 136.38 which do not correlate with any signals in the ^{1}H NMR spectrum and were therefore assigned to the quaternary vinyl carbon atoms.

Substantial changes were observed when the ^{1}H NMR spectrum was recorded in DMSO-d_6 at 80 °C. First, the two pairs of singlets due to the benzyl and thiobenzyl protons each coalesced into two broad singlets at δ 3.58 and 3.89, while the singlets due to the vinyl protons broaden and shift to δ 6.85 and 5.92. More significantly, the two doublets due to the aldehyde proton collapsed to two broad singlets at δ 8.15 and 8.02, while the doublet and broad singlet due to the amino group changed to two broad singlets at δ 9.38 and 9.23, respectively. These changes were reversed upon cooling the solution to 20 °C.

The temperature-dependent changes show that the pairs of signals observed for the various sets of protons are not due to the existence of geometrical isomers but that the isolated photoproduct **8c** consists of a single stereoisomer with two rotamers due to restricted rotation around the C−N bond in the formamide group.[32] Since decoupling of the vinyl proton was not accompanied by an NOE enhancement of the signal due to the benzyl protons, the structure of the isolated product was assigned the *E* configuration with the two rotamers as shown below.



8c

On the basis of the Karplus equation,[33] the rotamer in which the amino and aldehyde protons absorb at δ 9.38

(29) Pouchet, C. J.; Behnke, J. *The Aldrich Library of ^{13}C and ^{1}H NMR Spectra*, 1st ed.; Aldrich Chemical Co.,1993; Vol. 1, spectrum no. 1374A.

(30) Neuhaus, D.; Williamson, M. P. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*; VCH Publishers: New York, 1989; pp 380−386.

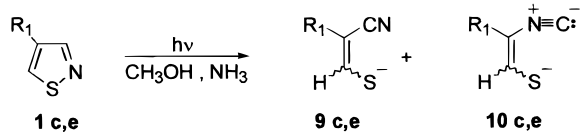
(31) See ref 16, pp 203−250.

(32) Kemp, W. *Organic Spectroscopy*, 3rd ed.; W. H. Freeman: New York, 1991; p 130.

(33) Pavia, D. L.; Lampman, G. M.; Friz, G. S. *Introduction to Spectroscopy*, 2nd ed.; Saunders: New York, 1996; pp 193−194.

and 8.01 (J = 1.72 Hz) was assigned to the structure in which these protons are syn with respect to each other while the rotamer in which the amino and aldehyde protons absorb at δ 9.57 and 8.18 (J = 10.72 Hz) was assigned to the structure in which these protons are anti with respect to each other. NOE experiments confirmed these assignments.

Isolation of nitrile **7c** and formamide **8c** provides excellent evidence that the initial photoproducts absorbing at 294 nm are a mixture of cyanosulfide **9c** and isocyanosulfide **10c**.

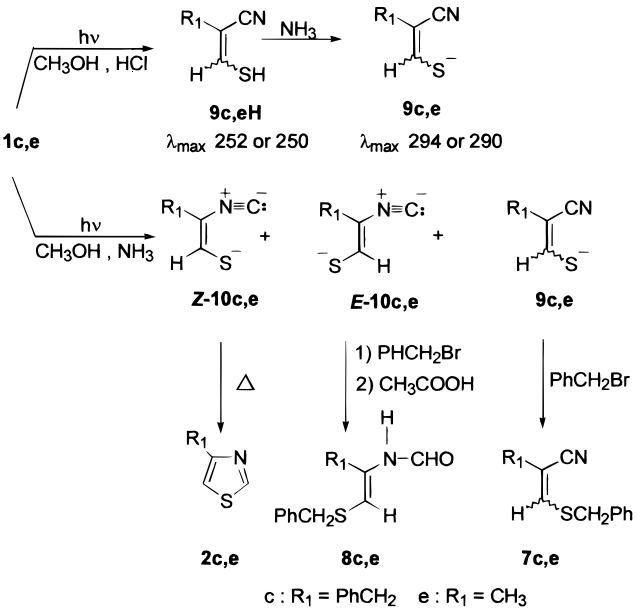


As in the case of 4-phenylisothiazole (**1a**), the presence of acid has a substantial effect on the photochemistry of 4-benzylisothiazole (**1c**). When a solution of **1c** (3.0 mL, 1.6 × 10^{-4} M) in methanol containing ammonia was irradiated for 10 s, the optical density at 251 nm due to the absorption of 4-benzylisothiazole (**1c**) decreased from 0.962 to 0.550 while the optical density at 294 nm increased from 0 to 0.930 due to the formation of **9c** and **10c**. After acidification with concentrated HCl, the absorption maximum shifted from 294 to 251 nm. When this solution was again made basic with ammonia, the absorption maximum shifted back to 294 nm but with a decrease in the optical density from 0.930 to 0.626. Further acidification followed by basification was also accompanied by changes in the absorption maximum from 294 to 251 nm and back to 294 nm but without any additional significant changes in the optical density. This suggests that a portion of the mixture absorbing at 294 nm is unstable in acidic solution. Isocyanides are known to be quite sensitive to acid.[27,28] Thus, it seems likely that although cyanosulfide **9c** and isocyanosulfide **10c** are both formed photochemically in methanol/ammonia, the isocyanide **10c** is decomposed upon acidification and only the cyanothiol **9cH**, which is relatively insensitive to acid, remains in the solution. Further experiments support this suggestion.

A solution of 4-benzylisothiazole (**1c**) (3.0 mL, 1.6 × 10^{-4} M) in methanol containing concentrated HCl (1.0 μL) was irradiated for 10 s, during which the optical density at 251 nm increased slightly from 0.948 to 0.960 but no increase in the optical density at 294 nm was observed. After this solution was made basic with ammonia, however, the absorption maximum shifted from 251 to 294 nm with an optical density of 0.867. After this solution was reacidified, the absorption maximum shifted back to 251 nm with only a very slight decrease in the optical density due to dilution of the sample. This suggests that only the cyanothiol **9cH** is formed photochemically in methanol/HCl and is stable with respect to subsequent changes in acidity.

To confirm this, three solutions of 4-benzylisothiazole (**1c**) in methanol, methanol containing ammonia, or methanol containing HCl were irradiated simultaneously on a merry-go-round apparatus. GLC analysis of the resulting neutral methanol solution showed 70% consumption of the reactant and formation of 4-benzylthiazole (**2c**) in 18% yield. In addition, the infrared spectrum of the residue remaining after evaporation of this solution showed sharp absorption bands at 2207 and 2104 cm^{-1} in a ratio of 1.77:1 showing the presence of cyanosulfide **9c** and isocyanosulfide **10c**. GLC analysis of the irradiated alkaline solution, however, showed 88% consumption of the reactant and formation of **2c** in 43% yield, while infrared analysis of the resulting residue showed the sharp bands due to the **9c** and **10c** in a ratio of 1.23:1. In contrast, after neutralization of the irradiated methanol/HCl solution, GLC analysis showed 57% consumption of **1c** but did not reveal the formation of any volatile photoproduct while infrared analysis of the residue from this solution showed an absorption band at 2207 cm^{-1}, indicating the presence of **9c**, but did not show absorption at 2104 cm^{-1}, showing that **10c** is not present in this mixture.

Scheme 4



These results demonstrate (Scheme 4) that 4-benzylisothiazole (**1c**) undergoes photocleavage in methanol containing HCl to 2-cyano-3-phenylpropene-1-thiol (**9cH**) absorbing at 251 nm which can be deprotonated by addition of ammonia to yield the conjugate base **9c** absorbing at 294 nm. UV and infrared spectroscopy indicate that 2-isocyano-3-phenylpropene-1-thiol (**10cH**) is not formed in this reaction. Furthermore, no 4-benzylthiazole (**2c**) was observed when **1c** was irradiated in methanol containing HCl or after the solution was made alkaline by the addition of aqueous ammonia. These results show that 2-cyano-3-phenylpropene-1-thiol (**9cH**) is not an intermediate in the conversion of **1c** to **2c**.

Alternatively, photolysis of 4-benzylisothiazole (**1c**) in methanol containing ammonia leads to the formation of cyanosulfide **9c** and isocyanosulfide **10c** as primary products. Reaction of cyanosulfide **9c** with benzyl bromide led to the formation of (*E*)- and (*Z*)-2-cyano-3-phenylpropen-1-ylbenzyl thioether **7c**, whereas reaction of isocyanosulfide **10c** with benzyl bromide followed by hydrolysis led to the formation of (*E*)-2-(*N*-formylamino)-3-phenylpropen-1-ylbenzyl thioether (**8c**). Isolation of only the *E* isomer suggests that (*Z*)-2-isocyano-3-phenylpropene-1-sulfide (**10c**) undergoes thermal cyclization to 4-benzylthiazole (**2c**).

The photochemistry of 4-methylisothiazole (**1e**) was also investigated and found to be similar to the photo-

chemistry of 4-benzylisothiazole (**1c**). Thus, GLC analysis showed that the yield of 4-methylthiazole (**2e**) is increased from 10% in the absence of ammonia to 32% when the irradiation is carried out in methanol containing ammonia. Also, UV absorption analysis again revealed that thiazole **2e** is not the primary product in this reaction but that in methanol containing ammonia **1e** undergoes photocleavage to yield a mixture of cyanosulfide **9e** and isocyanosulfide **10e**, absorbing in the UV at 290 nm, or in methanol containing HCl to yield only cyanothiol **9eH** which absorbs at 250 nm (Scheme 4).

In an attempt to trap **9e** and **10e**, a solution of 4-methylisothiazole (**1e**) in methanol containing TEA was irradiated for 30 min. Benzyl bromide was added, and after 6 h in the dark, the absorption maximum had shifted from 290 to 272 nm, confirming that the reaction of **9e** and **10e** with benzyl bromide was complete. The infrared spectrum of the resulting residue showed intense absorption bands at 2209 and 2106 cm^{-1} confirming the presence of the benzyl derivatives of **9e** and **10e**. After treatment of this residue with acetic acid, infrared analysis showed that the absorption due to the isocyanide at 2106 cm^{-1} was replaced by a new absorption band at 1684 cm^{-1}, consistent with the hydrolysis of the benzyl derivative of **10e** to the formylbenzyl thioether **8e**. The absorption at 2209 cm^{-1} remained unchanged during treatment with acetic acid, indicating that 2-cyanopropen-1-ylbenzyl thioether **7e** was unchanged by the reaction conditions.

2-Cyanopropen-1-ylbenzyl thioether **7e** was isolated by preparative layer chromatography as a colorless oil which exhibited an intense absorption in the infrared spectrum at 2209 cm^{-1} as required by the nitrile functional group. The mass spectrum, which exhibited a molecular ion at *m/z* 189, and the elemental analysis are consistent with the molecular formula of $C_{11}H_{11}NS$ required by **7e**. The ^1H NMR spectrum indicated that the isolated product was a mixture of two geometrical isomers. Thus, in addition to the two 2-H singlets in the ^1H NMR spectrum at δ 3.97 and 3.98 due to the thiobenzyl protons of the two isomers, the spectrum also exhibits two quartets at δ 6.64 (J = 1.42 Hz) and 6.94 (J = 1.34 Hz) in an integrated ratio of 2:1 assigned to the vinyl protons of (*Z*)- and (*E*)-**7e** which are spin coupled to the allylic methyl protons which appear as two doublets (ratio of 2:1) in the ^1H NMR spectrum at δ 1.88 and 1.83 and which absorb at δ 20.35 and 16.45 in the ^{13}C NMR spectrum. Similarly, the carbons of the methylene and cyano groups in the *Z* and *E* isomers were observed at δ 37.81 and 117.63 and at δ 37.98 and 119.75, respectively. All of these spectroscopic data confirm that the isolated product is a 2:1 mixture of (*Z*)- and (*E*)-2-cyanopropen-1-ylbenzyl thioether (**7e**) formed by the reaction of (*Z*)- and (*E*)-**9e** with benzyl bromide.

Although our results show that isocyanosulfide **10e** was also formed and reacted with benzyl bromide and then with acetic acid to form **8e**, the quantity of **8e** was insufficient to allow isolation by preparative layer chromatography.

Quantum Yields. The quantum yields for the consumption of isothiazoles **1a** and **1c** and for the formation of the P_4 phototransposition products **2a** and **2c** were determined in triplicate in cyclohexane or methanol solutions in the absence and presence of TEA and are shown in Table 1. 1,3-Cycloheptadiene was used as the actinometer.[34]

Table 1. Quantum Yield Results

reactant (solvent)	ϕ(consumption)	P_4 product	ϕ(formation)
1a (C_6H_{12})	0.41 ± 0.06	**2a**	0
1a (C_6H_{12}/TEA)	0.40 ± 0.06	**2a**	0.25 ± 0.04
1c (CH_3OH)	0.21 ± 0.03	**2c**	0.08 ± 0.01
1c (CH_3OH/TEA)	0.25 ± 0.04	**2c**	0.13 ± 0.02

Table 2. Spectroscopic and Photophysical Properties

	λ_{max} (nm)	log ϵ	ϕ_f ($\times 10^4$)	τ_f^0 (ns)	τ_f (ps)	τ_p (s)
1a	241, 270 (288 sh)	4.20, 4.16 (3.84)	1.32	1.9	0.25	3.8×10^{-1}
1c	251	4.00	~0.4	7.2	0.29	5.2×10^{-3}

Spectroscopic Properties. 4-Phenylisothiazole (**1a**) and 4-benzylisothiazole (**1c**) exhibit structureless absorption spectra in methanol solvent (Table 2) with extinction coefficients consistent with $\pi \rightarrow \pi^*$ transitions. Both compounds exhibit very weak fluorescence and phosphorescence in methanol/ethanol (1:1) solvent. Discernible 0,0 bands in the fluorescence and phosphorescence spectra of **1a** and **1c** indicate that E_{S_1} values are 90.8 and 91.1 kcal mol^{-1} while E_{T_1} values are 65.7 and 71.5 kcal mol^{-1}, respectively. The quantum yields of fluorescence at room temperature were measured relative to hexaphenylbenzene[35] and are shown in Table 2. Intrinsic fluorescence lifetimes (τ_f^0) were determined from Strickler−Berg calculations in which areas under the absorption and emission curves are evaluated.[36,37] The fluorescence lifetimes (τ_f) were then estimated from $\tau_f = \tau_f^0 \phi_f$. The phosphorescence lifetimes (τ_p) were determined from plots of the natural logarithm of the phosphorescense decay versus time. These lifetimes and energy gaps are consistent with π and π^* states.

Sensitized Irradiations. The photoreaction of 4-phenylisothiazole (**1a**) (E_T = 65.7 kcal mol^{-1}) could not be sensitized in acetonitrile by butyrophenone (E_T = 74.7 kcal mol^{-1}) despite the observation that **1a** efficiently quenched the Norrish type II reaction of the sensitizer with a rate constant of 3.2×10^9 M^{-1} s^{-1}. 4-Benzylisothiazole (**1c**) (E_T = 71.5 kcal mol^{-1}) was also unreactive when irradiated in the presence of butyrophenone. In this case, however, the type II reaction of butyrophenone was not quenched, indicating that energy transfer had not occurred.

Mechanistic Discussion. The experimental results reported here show that the phototransposition reaction is greatly enhanced by the presence of small quantities of bases such as triethylamine in the reaction medium. Amines are known to be good electron donors in electron transfer reactions to excited states of electron acceptors.[38] Considering the reduction potential of TEA (1.15 eV vs SCE in acetonitrile), and the $\Delta E_{0,0}$ for 4-phenylisothiazole (97.9 kcal mol^{-1}), the reduction potential of 4-phenylisothiazole (**1a**) can be no more negative than 3.08 eV for the electron transfer to be thermodynamically feasible. Although 4-phenylisothiazole (**1a**) was not observed to undergo reduction in the range of 0 to −2.2 eV versus SCE, the reduction could not be evaluated at more

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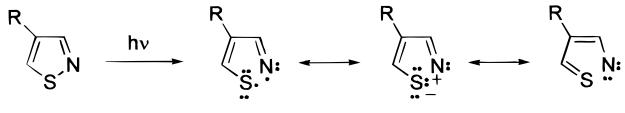
(35) Berlman, I. B. *Handbook of Fluorescence Spectra of Aromatic Molecules*, 2nd ed.; Academic Press: New York, 1971; p 237.
(36) Strickler, S. J.; Berg, R. A. *J. Chem. Phys.* **1962**, *37*, 814−822.
(37) We are thankful to Dr. R. E. Connors of this department for carrying out these calculations.
(38) Pienta, N. J. In *Photoinduced Electron Transfer. Part C. Photoinduced Electron-Transfer Reactions: Organic Substrates*; Fox, M. A., Chanon, M., Eds.; Elsevier: New York, 1988; pp 421−486.

negative potentials since the acetonitrile solvent is reduced at this potential. Therefore, we cannot exclude the possibility that it is thermodynamically feasible for an electron to transfer from TEA to the excited singlet state of 4-phenylisothiazole (**1a**). Kinetically, however, this transfer does not seem likely. Thus, the calculated lifetime for the excited singlet of 4-phenylisothiazole (**1a**) is 2.5×10^{-13} s and the rate of unimolecular decay is 4.0×10^{12} s^{-1}. If we assume that the diffusion-controlled rate constant is 1.0×10^{10} L mol^{-1} s^{-1}, the rate of unimolecular decay in the presence of 1.0×10^{-2} M TEA is calculated to be 4 orders of magnitude faster than the rate of bimolecular diffusion-controlled electron transfer. Clearly, under these conditions, electron transfer would not be expected to compete with unimolecular decay of the singlet state.

In contrast, however, the lifetime of the triplet state of 4-phenylisothiazole (**1a**), measured from the phosphorescence decay, is 0.4 s. Thus, even at a TEA concentration of 1.0×10^{-2} M, electron transfer to the triplet state of 4-phenylisothiazole (**1a**) should be kinetically quite possible. In this case, however, since the triplet energy is 67.8 kcal mol^{-1}, the reduction potential of 4-phenylisothiazole (**1a**) can be no more negative than 1.79 eV versus SCE for the electron transfer to be thermodynamically feasible. Cyclic voltammetry, however, indicates that the reduction potential is considerably more negative than this value.

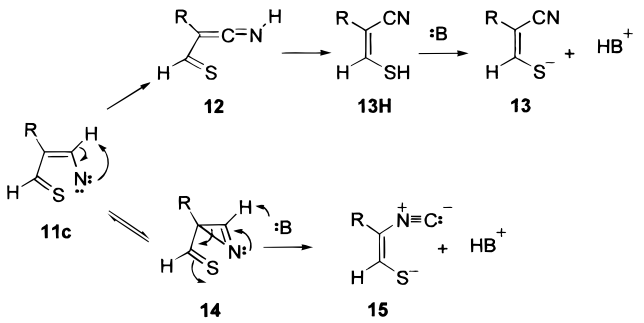
In addition to the above arguments, several other experimental observations are also inconsistent with an electron transfer mechanism. First, the effect of TEA on the photoreaction was not sensitive to changing the solvent polarity from benzene to methanol. Second, although TEA, propylamine, ammonia, and bicarbonate have substantially different ionization potentials, they all affect the reaction to essentially the same extent. Accordingly, a mechanism involving electron transfer to either the excited singlet or triplet of the 4-substituted isothiazole can be excluded.

By analogy with the photochemistry of isoxazoles and pyrazoles, photoexcitation of 4-substituted isothiazoles **11** is suggested to result in cleavage of the S−N bond, resulting in the formation of a species that can be viewed as diradical **11a** or zwitterion **11b**, which are resonance forms of β-thioformylvinyl nitrene **11c**.

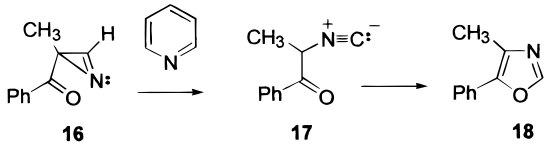


In addition to recyclizing to the isothiazole reactant, β-thioformylvinyl nitrene **11c** would be expected to rearrange as shown in Scheme 5 to the cyanothiol photocleavage product **13H**, plausibly by way of thioformylketeneimine **12**. Indeed, isomerization to nitriles is a well-documented reaction of terminal vinyl nitrenes.[39] In addition, since vinyl nitrenes are also known to be in thermal equilibrium with their isomeric azirines,[40] β-thioformylvinyl nitrene **11c** would also be expected to be in equilibrium with thioformylazirine **14**. In the absence of other reaction pathways, β-thioformylvinyl nitrene **11c** is thus converted totally to cyanothiol **13H**. As a result, upon irradiation in benzene, ether, or methanol containing HCl, 4-substituted isothiazoles such as **11c** undergo only photocleavage to cyanothiols such as **13H**.

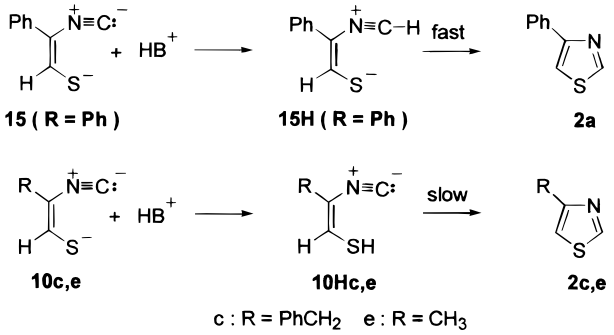
Scheme 5



If the photolysis is carried out in the presence of ammonia or TEA, the base will convert cyanothiol **13H** to cyanosulfide **13**. More importantly, however, it is envisioned that the base will also deprotonate azirine **14**, resulting in its conversion to isocyanide **15**. This suggestion is not without precedent. Thus, although benzoylazirine **16** is stable in solution at room temperature, Isomura and colleagues have shown that upon addition of pyridine the azirine is converted to oxazole **18** via isocyanide **17** which was detected by ^{1}H NMR and infrared spectroscopy.[41]



It is suggested that the fate of isocyanide **15** depends on the nature of the substituent originally at C-4 of the isothiazole ring. If R is aryl, as in **15(R=Ph)**, the extended conjugation of the sulfide and the aryl group is expected to lower the basicity of the sulfide, leaving the isocyanide carbon as the more basic site. Protonation thus converts **15** to **15H**. The net effect of this protonation is to render the carbon more susceptible to nucleophilic attack by the negative sulfur. As a result, these substituted isocyanides cannot be detected or chemically trapped because they spontaneously cyclize to the 4-arylthiazole **2a**.



(39) See Hassner, A. In *Azides and Nitrenes. Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic Press: Orlando, 1984; pp 35−94, and references therein.

(40) Hassner, A.; Wiegand, N. H.; Gottlieb, H. E. *J. Org. Chem.* **1986**, *51*, 3176−3180.

(41) Isomura, K.; Hirose, Y.; Shuyama, H.; Abe, S.; Ayabe, G.; Taniguchi, H. *Heterocycles* **1978**, *9*, 1207−1216.

If the C-4 substituent is alkyl or a substituted alkyl as in **10c,e**, the reduced conjugation raises the energy of the sulfide so that sulfur is more basic than the isocyanide carbon. Protonation of **10c,e** at sulfur reduces the nucleophilic character of the sulfide and also leaves the negatively charged carbon less susceptible to nucleophilic attack. As a result, cyclization requires a higher energy of activation, and hence, the alkyl-substituted isocyanides can be detected spectroscopically and trapped by benzyl bromide.

The effects of acid and base added to the photochemistry of 3- and 5-substituted isothiazoles are currently being investigated and will be reported at a later time.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded at 200 and 50.3 MHz, respectively. GLC was performed using a 30 m × 0.25 μm Supelcowax 10 bonded phase column. Preparative layer chromatography was carried out on 20 cm × 20 cm glass plates coated with 2 mm Kieselgel 60 F_{254} (Merck). Elemental analyses were determined by Desert Analytics (Tucson, AZ).

Materials. EM hydrochloric acid GH (36.5−38.0%) and EM ammonium hydroxide GH (28−30%) were used. Benzene was purified by refluxing over calcium hydride followed by fractional distillation. Diethyl either was purified by refluxing over a 40% dispersion of sodium in paraffin containing benzophenone until the benzophenone ketyl radical was bright blue followed by fractional distillation. Methanol was purified by refluxing over magnesium methoxide followed by fractional distillation.

Synthesis of Reactants and Products. 4-Phenylisothiazole (**1a**) and 4-phenylthiazole (**2a**) were prepared by procedures previously published.[4] 4-Methylisothiazole[42] (**1e**) was prepared from 3-chloro-2-methylpropenal[42] and ammonium thiocyanate and purified by fractional distillation. 4-Benzylisothiazole (**1c**) and 4-methylthiazole (**1e**) were obtained from Aldrich Chemical Co. and purified by distillation.

5-Deuterio-4-phenylisothiazole (1b). Sodium metal (0.20 g, 8.8 mmol) was added to CH_3OD (30 mL). After the reaction was complete, 4-phenylisothiazole (**1a**) (0.98 g, 6.1 mmol) was added and the flask was tightly closed and allowed to stand at room temperature in the dark for 3 days. The resulting solution was added to aqueous HCl (5 M, 60 mL), and the mixture was extracted with chloroform (3 × 100 mL). The extract was dried (Na_2SO_4) and concentrated to yield a white solid that was sublimed (40 °C, 1 Torr) to give 5-deuterio-4-phenylisothiazole (**1b**) as white crystals: mp 35−36 °C; yield 0.90 g (5.57 mmol, 91%); ^{1}H NMR ($CDCl_3$) δ 8.75 (s, 1H), 7.61−7.55 (m, 2H), 7.47−7.24 (m, 3H); MS *m*/*z* (relative intensity) 164 (5), 163 (11), 162 (100), 161 (27), 135 (44).

5-Deuterio-4-benzylisothiazole (1d). 4-Benzylisothiazole (**1c**) (0.54 g, 3.1 mmol) was allowed to react with a solution prepared by dissolving sodium metal (0.1 g, 4.4 mmol) in CH_3OD (25 mL) as described above to yield a yellow oil that was distilled (Kugelrohr) to give 5-deuterio-4-benzylisothiazole (**1d**) as a colorless oil: bp (Kugelrohr oven temperature) 120 °C (0.5 Torr); yield 0.50 g (2.8 mmol, 92%); ^{1}H NMR ($CDCl_3$) δ 8.31 (s, 1H), 7.32−7.13 (m, 5H), 4.02 (s, 2H); MS *m*/*z* (relative intensity) 177 (15), 176 (100), 175 (75), 149 (14), 148 (39), 117 (12), 116 (36).

Irradiation and Analysis Procedures. Photoreactions of 4-substituted isothiazoles **1a**, **1c**, and **1e** on an analytical scale were monitored by GLC and by UV absorption spectroscopy.

UV Absorption Analysis. A solution of **1a**, **1c**, or **1e** (3.0 mL) in methanol in the presence or absence of either 1.0 μL of aqueous ammonia (density of 0.88 g/mL) or concentrated HCl was placed in a quartz UV cell (1.0 cm path length) and the cell purged with argon for 15 min and closed with a Teflon cap. The cell was irradiated with one low-pressure Hg lamp for six consecutive 5 s irradiations and analyzed by UV absorption spectroscopy after every 5 s.

GLC Analysis. A solution of **1a**, **1c**, or **1e** (3.0 mL, 2.0 × 10^{-2} M) in benzene, methanol, or diethyl ether solvent in the absence or presence of the appropriate quantity of aqueous ammonia, triethylamine, or concentrated HCl was placed in a quartz tube (0.70 cm inside diameter × 15 cm long) and the tube sealed with a rubber septum and purged with argon for 30 min. The tubes were then irradiated at 254 nm in a Rayonet photochemical reactor equipped with eight low-pressure Hg lamps.

Solutions without added aqueous ammonia or HCl were analyzed directly by GLC. Solutions containing aqueous ammonia were dried (Na_2SO_4) prior to analysis, while solutions containing concentrated HCl were first neutralized ($NaHCO_3$) and then dried (Na_2SO_4) prior to GLC analysis.

Quantitative GLC analysis of reactant consumption and product formation was accomplished using calibration curves constructed for 4-substituted isothiazoles **1a**, **1c**, and **1e** and for 4-substituted thiazoles **2a**, **2c**, and **2e** by plotting detector responses versus 10 standards with known concentrations. Correlation coefficients ranged from 0.993 to 0.999.

Irradiation of 4-Phenylisothiazole (1a) in Benzene. A solution of **1a** (3.0 mL, 2.0 × 10^{-2} M) in benzene was irradiated for 30 min. GLC analysis showed the consumption of **1a** (82%) and the formation of 4-phenylthiazole (**2a**) (3%) with a relative retention of 1.07.[43]

Irradiation of 4-Phenylisothiazole (1a) in Diethyl Ether. A solution of **1a** (3.0 mL, 6.7 × 10^{-3} M) in diethyl ether was irradiated for 30 min. GLC analysis showed the consumption of **1a** (89%) but did not show the formation of any volatile product. Analysis by UV absorption spectroscopy after dilution (1:200) showed a decrease in the optical density at 269 nm from 0.891 to 0.726 and an increase in the optical density at 290 nm from 0.242 to 0.779.

Irradiation of 4-Phenylisothiazole (1a) in Methanol. A solution of **1a** (3.0 mL, 2.0 × 10^{-2} M) in methanol was irradiated for 30 min. GLC analysis showed the consumption of **1a** (74%) and the formation of 4-phenylthiazole (**2a**) (38%) with a relative retention of 1.07. Analysis by UV absorption spectroscopy after dilution (1:1000) showed an increase in the optical density at 340 nm from 0 to 0.287.

Irradiation of 4-Phenylisothiazole (1a) in Methanol. Effect of Added TEA. Three solutions of **1a** (3.0 mL, 2.0 × 10^{-2} M) in methanol containing 0, 1.0 × 10^{-2}, or 2.4 × 10^{-1} M TEA were simultaneously irradiated on a merry-go-round apparatus for 30 min. GLC analysis showed the consumption of **1a** (82, 75, or 76%, respectively) and the formation of 4-phenylthiazole (**2a**) (37, 86, or 82%, respectively) with a relative retention of 1.07. GLC analysis at 50 °C showed no consumption of TEA.

Irradiation of 4-Phenylisothiazole (1a) in Benzene. Effect of Added TEA. Three solutions of **1a** (3.0 mL, 2.0 × 10^{-2} M) in benzene containing 0, 1.0 × 10^{-2}, or 2.4 × 10^{-1} M TEA were simultaneously irradiated on a merry-go-round apparatus for 30 min. GLC analysis showed the consumption of **1a** (63, 77, or 65%, respectively) and the formation of 4-phenylthiazole (**2a**) (3, 72, or 68%, respectively) with a relative retention of 1.07. GLC analysis at 50 °C showed no consumption of TEA.

Irradiation of 4-Benzylisothiazole (1c) in Methanol. Effects of Added Ammonia or HCl. Three solutions of **1c** (3.0 mL, 2.0 × 10^{-2} M) in methanol, in methanol containing aqueous ammonia (10 μL, density of 0.88 g/mL), or in concentrated HCl (10 μL) were simultaneously irradiated on a merry-go-round apparatus for 30 min. GLC analysis showed the consumption of **1c** (70, 88, or 57%, respectively) and the formation of 4-benzylthiazole (**2c**) (18, 43, or 0%, respectively) with a relative retention of 0.86. Each of these solutions was

(42) Arnold, Z.; Zemlicka J. *Collect. Czech. Chem. Commun.* **1959**, *24*, 2385−2392.

(43) The retentions of products are given relative to the appropriate reactant.

evaporated to dryness, and the infrared spectrum (KBr) of each residue was recorded. The spectra showed bands at 2207 and 2104 cm^{-1} (1.77:1), 2207 and 2104 cm^{-1} (1.23:1), and 2207 cm^{-1}, respectively.

Irradiation of 4-Methylisothiazole (1e). Effect of Added TEA. Two solutions of **1e** (3.0 mL, 2.0×10^{-2} M) in methanol or in methanol containing TEA (10 μL, 0.072 mmol) were simultaneously irradiated on a merry-go-round apparatus for 30 min. GLC analysis showed the consumption of **1e** (68 or 82%, respectively) and the formation of 4-methylthiazole (**2e**) (10 or 32%, respectively) with a relative retention of 0.80.

Preparative Scale Irradiations. A solution of the reactant was dissolved in the appropriate solvent (10.0, 50.0, or 90.0 mL) and the mixture placed in a quartz tube [1.45 cm inside diameter × 13 cm long (for 10.0 mL) or 2.5 cm inner diameter × 30 cm long (for 50.0 or 90.0 mL)] which was closed with a rubber septum, purged with argon for 30 min, and irradiated in a Rayonet reactor equipped with eight low-pressure lamps for 30 min while the solution was continuously purged with a fine stream of argon.

Irradiation of 4-Phenylisothiazole (1a) in Diethyl Ether. 4-Phenylisothiazole (**1a**) (0.097 g, 0.60 mmol) was dissolved in purified diethyl ether (90.0 mL) and irradiated. The solutions from two such reactions were combined and evaporated to dryness to yield a yellow viscous liquid (0.19 g) which solidified after standing at room temperature. The residue was repeatedly recrystallized from diethyl ether and methylene chloride to give 2-cyano-2-phenylethenyl thioether (**4**) as colorless crystals: mp 192−193 °C; yield 0.012 g (0.042 mmol, 3.5%); ^{1}H NMR (CD_2Cl_2) δ 7.66 (s, 2H), 7.41−7.58 (m, 10H); ^{13}C NMR (CD_2Cl_2) δ 137.77, 132.62, 129.97, 129.63, 125.69, 115.32, 114.37; IR (KBr) 2208 (C≡N), 680.9 (C−S) cm^{-1}; HRMS calcd for $C_{18}H_{12}N_2S$ 288.07226, found 288.07234. Anal. Calcd for $C_{18}H_{12}N_2S$: C, 74.97; H, 4.19; N, 9.71. Found: C, 74.35; H, 4.13; N, 9.60.

Irradiation of 4-Phenylisothiazole (1a) in Diethyl Ether. Trapping of Cyanosulfide 5a. 4-Phenylisothiazole (**1a**) (0.050 g, 0.21 mmol) was dissolved in purified diethyl ether (50.0 mL) and irradiated. To the resulting solution was added TEA (5.0 mL) followed by benzyl bromide (0.100 mL, 0.84 mmol). The mixture was allowed to stand overnight at room temperature. The solutions from two such reactions were combined and evaporated to dryness, and the residue (0.096 g) was subjected to preparative layer chromatography (silica gel, CH_2Cl_2). The band at $R_f = 0.76$ (0.050 g) was rechromatographed (silica gel, 1:1 CH_2Cl_2/hexane), and the band at $R_f = 0.50$ gave 2-cyano-2-phenylethenylbenzyl thioether (**6a**) as a white solid, with a melting point of 58−60 °C and a yield of 0.036 g (0.14 mmol, 22.6%) which was further purified by sublimation (60 °C, 0.2 Torr) to give white crystals: mp 58−60 °C; ^{1}H NMR ($CDCl_3$) δ 4.14 (s, 2H), 7.24−7.54 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 143.75, 136.05, 133.11, 129.03, 128.96, 128.91, 128.37, 128.02, 124.79, 116.16, 109.75, 38.33; IR (KBr) 2207 (C≡N) cm^{-1}; MS *m*/*z* (relative intensity) 251 (16.7), 91 (100). Anal. Calcd for $C_{16}H_{13}NS$: C, 76.46; H, 5.21; N, 5.57. Found: C, 76.52; H, 5.07; N, 5.52.

Irradiation of 5-Deuterio-4-phenylisothiazole (1b) in Methanol Containing Ammonia. 5-Deuterio-4-phenylisothiazole (**1b**) (0.44 g, 0.27 mmol) was dissolved in methanol (10.0 mL) containing aqueous ammonia (0.10 mL, density of 0.88 g/mL) and irradiated. The resulting solution was evaporated to dryness, and the residue (0.040 g) was subjected to preparative layer chromatography (silica gel, CH_2Cl_2) which gave two bands. Band 1 ($R_f = 0.2$) contained 5-deuterio-4-phenylthiazole (**2b**) (0.012 g, 0.076 mmol, 48% yield): ^{1}H NMR ($CDCl_3$) δ 8.86 (s, 1H), 7.60−7.55 (m, 2H), 7.47−7.24 (m, 3H); MS *m*/*z* (relative intensity) 164 (5), 163 (12), 162 (100), 161 (26), 135 (37).

Irradiation of 5-Deuterio-4-phenylisothiazole (1b) in Methanol. A solution of **1b** (0.044 g, 0.27 mmol) in methanol (10.0 mL) was irradiated for 30 min. GLC−MS analysis of **2b** showed ions at *m*/*z* (relative intensity) 164 (5), 163 (12), 162 (100), 161 (26), and 135 (37). The solution was evaporated to dryness. ^{1}H NMR ($CDCl_3$) analysis of the residue showed a singlet at δ 8.75 due to the C-3 proton of residual **1b** and a singlet at δ 8.86 due to the C-2 proton of **2b** formed in the reaction.

Irradiation of 4-Benzylisothiazole (1c) in Methanol Containing Ammonia. 4-Benzylisothiazole (**1c**) (0.18 g, 1.03 mmol) was dissolved in methanol (50 mL) containing aqueous ammonia (0.25 mL, density of 0.88 g/mL) and irradiated. The resulting solution was evaporated to dryness, and the residue (0.18 g) was subjected to preparative layer chromatography (silica gel, CH_2Cl_2) which gave two major bands. Band 1 ($R_f = 0.50$) contained recovered 4-benzylisothiazole (**1c**) (0.036 g, 0.21 mmol, 20.4% recovery). Band 2 ($R_f = 0.34$) contained 4-benzylthiazole (**2c**) (0.073 g, 0.42 mmol, 51% yield): ^{1}H NMR ($CDCl_3$) δ 8.75 (d, $J = 2.02$ Hz, 1H), 7.35−7.18 (m, 5H), 6.86 (triplet of doublet, $J_t = 1.99$ Hz, $J_d = 2.02$ Hz), 4.17 (br s, 2H); ^{13}C NMR ($CDCl_3$) δ 157.20, 152.77, 139.01, 128.96, 128.57, 126.47, 114.07, 37.69; MS *m*/*z* (relative intensity) 176 (14.6), 175 (100), 174 (75.9), 148 (32.3), 147 (34.6), 115 (69.1); IR (KBr) 3107, 3063, 3028, 2909, 2839, 1604 cm^{-1}. Anal. Calcd for $C_{10}H_9NS$: C, 68.53; H, 5.18; N, 7.96. Found: C, 68.31; H, 5.08; N, 7.99.

Irradiation of 5-Deuterio-4-benzylisothiazole (1d) in Methanol Containing Ammonia. 5-Deuterio-4-benzylisothiazole (**1d**) (0.12 g 0.68 mmol) was dissolved in methanol (50 mL) containing aqueous ammonia (0.25 mL, density of 0.88 g/mL) and irradiated. The resulting solution was evaporated to dryness, and the residue (0.10 g) was subjected to preparative layer chromatography (silica gel, CH_2Cl_2) which gave two major bands. Band 1 ($R_f = 0.50$) contained recovered 5-deuterio-4-benzylisothiazole (**1d**) (0.024 g, 0.14 mmol, 19.5% recovery). Band 2 ($R_f = 0.34$) contained 5-deuterio-4-benzylthiazole (**2d**) (0.044 g, 0.25 mmol, 46% yield): ^{1}H NMR ($CDCl_3$) δ 8.75 (s, 1H), 7.35−7.13 (m, 5H), 4.17 (s, 1H); MS *m*/*z* (relative intensity) 177 (14.7), 176 (100), 175 (76.3), 149 (30.4), 148 (33.7).

Irradiation of 4-Benzylisothiazole (1c) in Methanol Containing Ammonia. Trapping of Cyanosulfide 9c and Isocyanosulfide 10c. 4-Benzylisothiazole (**1c**) (0.12 g, 0.69 mmol) was dissolved in methanol (50 mL) containing aqueous ammonia (0.25 mL, density of 0.88 g/mL) and irradiated. Benzyl bromide (84 μL, 0.2 g, 0.70 mmol) was added to the resulting solution, and the mixture was allowed to stand for 30 min and then evaporated to dryness. Glacial acetic acid (1.0 mL) was added to the residue, and the mixture was allowed to stand at room temperature overnight. It was subsequently neutralized with saturated aqueous sodium bicarbonate and extracted with CH_2Cl_2 (3 × 20 mL), dried (Na_2SO_4), and concentrated. The yellow residual oil (0.19 g) was subjected to preparative layer chromatography (silica gel, CH_2Cl_2). The band at $R_f = 0.79$ gave (*E*)- or (*Z*)-2-cyano-3-phenylpropen-1-ylbenzyl thioether (**7c**) as a yellow oil (0.04 g, 0.15 mmol, 21.4% yield): ^{1}H NMR ($CDCl_3$) δ 7.36−7.07 (m, 10H), 7.05 (t, $J = 0.90$ Hz, vinyl proton of *E* isomer), 6.66 (t, $J = 1.34$ Hz, vinyl proton of *Z* isomer), 4.02 (s, *E* isomer), 3.96 (s, *Z* isomer), 3.51 (br s, *E* isomer), 3.46 (br s, *Z* isomer); ^{13}C NMR ($CDCl_3$) δ 145.56, 144.45, 136.21, 136.05, 135.95, 135.90, 128.83, 128.69, 128.58, 128.40, 123.38, 128.37, 127.82, 127.58, 127.02, 126.96, 118.87 (C≡N, *E* isomer), 117.02 (C≡N, *Z* isomer), 108.73, 108.37, 40.16 (*Z* isomer), 38.07 (*E* isomer), 36.95 (*Z* isomer), 36.49 (*E* isomer); MS *m*/*z* (relative intensity) 265 (4.8), 91 (100); IR (KBr) 2200 (C≡N) cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{16}NS$ (M^+) 266.1003, found 266.10181.

The band at $R_f = 0.16$ gave (*E*)-2-(*N*-formylamino)-3-phenylpropen-1-ylbenzyl thioether (**8c**) as a yellow oil (0.02 g, 0.07 mmol, 10.0% yield): ^{1}H NMR (DMSO-d_6) δ 9.57 (d, $J = 10.72$ Hz, exchangeable), 9.38 (br s, exchangeable), 8.18 (d, $J = 10.72$ Hz), 8.01 (d, $J = 1.72$ Hz), 7.32−6.97 (m, 10H), 6.89 (s), 5.89 (s), 3.90 (s, 0.75H), 3.88 (s, 1.25H), 3.59 (s, 0.75H), 3.52 (s, 1.25 H); ^{13}C NMR ($CDCl_3$) δ 161.34, 158.94, 138.13, 137.57, 136.38, 135.69, 133.03, 128.90, 128.68, 128.54, 127.37, 127.09, 112.78, 109.38, 39.00, 38.34, 37.29, 36.66; IR (KBr) 1683 cm^{-1}; MS *m*/*z* (relative intensity) 284 (3), 283 (15.8), 91 (100); HRMS (FAB) calcd for $C_{17}H_{18}NSO$ (M^+) 284.1104, found 284.1092.

Irradiation of 4-Methylisothiazole (1e) in Methanol Containing TEA. Trapping of Cyanosulfide 9e. A solution of **1e** (0.26 g, 2.67 mmol) in methanol (90.0 mL) containing TEA (1.0 mL) was irradiated for 30 min. Benzyl bromide (0.3 mL, 2.67 mmol) was added, and the mixture was allowed to stand at room temperature for 2 h and then evaporated to dryness. Glacial acetic acid (1.0 mL) was added, and the mixture was allowed to stand overnight at room temperature. It was then neutralized with saturated aqueous sodium bicarbonate and extracted with CH_2Cl_2 (3 × 20 mL). The CH_2Cl_2 extract was washed with saturated aqueous sodium bicarbonate (3 × 5 mL), dried (Na_2SO_4), and concentrated. The residues from two such reactions (yellow oil, 0.56 g) were subjected to preparative layer chromatography (silica gel, CH_2Cl_2). The band at R_f = 0.80 gave 2-cyanopropen-1-ylbenzyl thioether (**7e**) as a yellow oil (0.14 g, 0.74 mmol, 16% yield).

The total amount of **7e** from six photoreactions (0.50 g) was subjected to preparative layer chromatography (silica gel, 3:4 CH_2Cl_2/hexane). The band at R_f = 0.25 gave **7e** as a yellow oil (0.25 g) which was again subjected to preparative layer chromatography (silica gel, 1:1 CH_2Cl_2/hexane). The band at R_f = 0.40 gave **7e** as a slightly yellow oil (0.24 g) which was further purified by distillation (Kugelrohr) to give **7e** as a colorless oil: bp (Kugelrohr oven temperature) 40 °C (0.2 Torr); yield 0.18 g; ^{1}H NMR ($CDCl_3$) δ 7.37−7.24 (m, 5H), 6.94 (q, J = 1.34 Hz, vinyl proton of *E* isomer), 6.64 (q, J = 1.42 Hz, vinyl proton of *Z* isomer), 3.98 (s, *E* isomer), 3.97 (s, *Z* isomer), 1.88 (d, J = 1.42 Hz, *Z* isomer), 1.83 (d, J = 1.34 Hz, *E* isomer); ^{13}C NMR ($CDCl_3$) δ 145.28 (*E* isomer), 143.56 (*Z* isomer), 136.43, 136.20, 129.09, 128.97, 128.85, 128.22, 127.94, 119.75 (C≡N, *E* isomer), 117.63 (C≡N, *Z* isomer), 104.57 (*Z* isomer), 103.62 (*E* isomer), 37.98 (*E* isomer), 37.81 (*Z* isomer), 20.35 (*Z* isomer), 16.45 (*E* isomer); MS *m*/*z* (relative intensity) 189 (2), 91 (100); IR (KBr) 2209 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NS$: C, 69.80; H, 5.86; N, 7.40. Found: C, 69.99; H, 5.61; N, 7.37.

Quantum Yields of Reactions. Quantum yields of reactions were determined in triplicate by simultaneously irradiating solutions of 4-phenylisothiazole (**1a**) or 4-benzylisothiazole (**1c**) (2.0 × 10^{-2} M, 3.0 mL) in cyclohexane or methanol solvent in the absence or presence of TEA (7.2 × 10^{-3} M) and the actinometer (1,3-cycloheptadiene) in a Rayonet reactor equipped with a merry-go-round. The consumption of the reactants or actinometer and the formation of the P_4 phototransposition products (**2a** or **2c**) were measured using GLC.

Sensitizations. Six solutions of butyrophenone (3.0 mL, 3.0 × 10^{-2} M) in cyclohexane containing 4-phenylisothiazole (**1a**) (0, 1.52 × 10^{-3}, 3.03 × 10^{-3}, 4.55 × 10^{-3}, 6.06 × 10^{-6}, or 7.58 × 10^{-3} M) were irradiated simultaneously in Pyrex tubes in a Rayonet reactor equipped with a merry-go-round and one 350 nm lamp. The concentrations of **1a**, butyrophenone, and acetophenone were measured using GLC. A plot of $\phi°/\phi$ versus [**1a**] was linear with a slope of 771 M^{-1}.

A similar irradiation was conducted in CH_3CN using an initial butyrophenone concentration of 0.20 M and concentrations of **1a** of 11.92 × 10^{-3}, 23.85 × 10^{-3}, 35.78 × 10^{-3}, 47.70 × 10^{-3}, and 59.63 × 10^{-3} M. A plot of $\phi°/\phi$ versus [**1**] was linear with a slope of 488 M^{-1}. In neither case could any reaction of **1a** be detected.

Luminescence Spectra, Energies, and Lifetimes of Excited States. The fluorescence spectrum of **1a** or **1c** was recorded at room temperature in cyclohexane (A_{265nm} = 0.345) or in a 1:1 methanol/ethanol solvent (A_{250nm} = 0.250) after excitation at 265 or 250 nm, respectively. Quantum yields of fluorescence were determined relative to hexaphenylbenzene (ϕ_f = 0.01).[35]

The phosphorescence spectrum of **1a** or **1c** was recorded at 77 K in methylcyclohexane or a 1:1 methanol/ethanol solvent after excitation at 265 or 250 nm. Decay constants and triplet lifetimes were obtained from plots of the natural logarithm of the phosphorescence decay versus time.

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