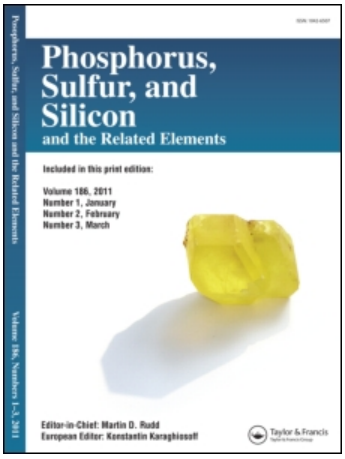

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A Thio-Staudinger Reaction: Thermolysis of a Vinyl Azide in the Presence of t -Butyl Mercaptan

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A THIO-STAUDINGER REACTION: THERMOLYSIS OF A VINYL AZIDE IN THE PRESENCE OF *t*-BUTYL MERCAPTAN

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*The thermal decomposition of E-3-azido-3-hexene-2,5-dione (**1**) in protic media gave rise to several novel reactions of the azide **1** including adducts derived from keteneimine **11**. Reaction with t-butyl mercaptan yielded two products, keteneimine-derived mercaptan addition product **20** and a sulfenimine **6**. Trapping of a vinyl nitrene intermediate or a thio-Staudinger reaction was considered as a possible mechanism for the formation of sulfenimine **6**. The absence of the vinyl nitrene addition products **3** and **5** when the thermal decomposition was conducted in either methanol or t-butylamine suggests a thio-Staudinger reaction is operative.*

Keywords: Staudinger reaction; sulfenimines; vinyl azides

Sulfenimines[1] have been prepared from a variety of starting materials such as aromatic disulfides,[2] sulfenamides,[3] thioketenes,[4] thioamides,[5] and other substrates.[6] They also are an important functional constituent of substituted cephalosporins and penicillins.[7] Furthermore, trityl sulfenimine recently has been used as a reagent in a highly diastereoselective coupling reaction to prepare an intermediate in the synthesis of an influenza neuraminidase inhibitor.[8] Despite the availability of different approaches to sulfenimines, the formation of these compounds by reaction of a mercaptan with an azide has not yet been

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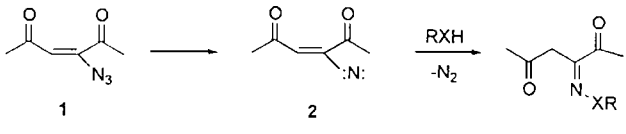
reported. We report on an unexpected reaction when the thermolysis of *E*-3-azido-3-hexene-2,5-dione (**1**) was conducted in *t*-butyl mercaptan and to provide evidence that a thio-Staudinger reaction is operative.[9]

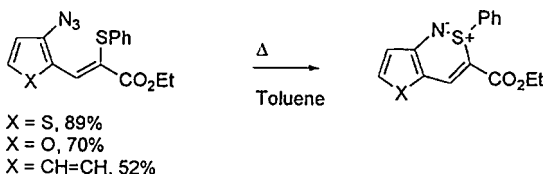
RESULTS

Earlier studies on vinyl azides led us to examine the properties of *E*-3-azido-3-hexene-2,5-dione (**1**) for comparison with the corresponding *Z*-isomer.[10] Of particular interest was the possibility that thermolysis of the former would produce a vinyl nitrene **2** that could be trapped with nucleophiles (Eq. 1). A recent review has highlighted the synthetic



(1)

utility of this concept in the synthesis of heterocycles by intramolecular trapping of nitrenes by heteroatoms.[11] For example, thermolysis of either the azido benzene, thiophene or furan with a vinylthiol substituent yielded the corresponding ylide in good yields (Eq. 2).[12]



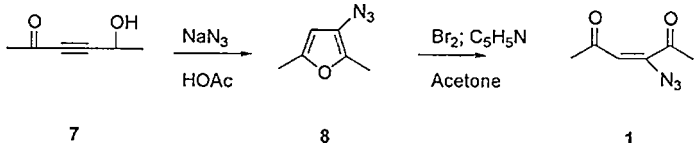
X = S, 89%
X = O, 70%
X = CH=CH. 52%

(2)

However, in the case of vinyl azides, calculations have suggested that the formation of azirines from vinyl azides involves either rate determining formation of vinyl nitrenes with no activation energy for the conversion of the nitrene to the azirine or that azirines are formed from vinyl azides via a concerted losss of nitrogen.[13] Kinetic studies by Hassner have reinforced the latter hypothesis for those vinyl azides which yield azirines and, in particular, a concerted mechanism is favored when the α-position is functionalized by substituents that are capable of stabilizing a positive charge such as aryl, alkyl, heteroatoms, or alkoylcarboxyl.[14] In addition, Hassner's work also suggests that these conclusions may not be general, and the mechanism for the decomposition of an azide will depend on the nature of the substituents. L'Abbé and Matthys also have determined kinetic parameters for

the thermolysis of vinyl azides that support either a mechanism involving a concerted loss of nitrogen or a pathway that involves an intermediate 4*H*-triazole.[15] We report herein the synthesis of vinyl azide **1** and its thermolysis under a variety of conditions in the presence of water, methyl alcohol, *t*-butyl alcohol, *t*-butylamine, and *t*-butyl mercaptan.

The *E*-vinyl azide **1** was prepared stereospecifically from 3-azido-2,5-dimethyl furan (**8**) using a modified Clauson-Kaas method.[16,17] The required furyl azide **8** was synthesized in a 53% yield by a Michael addition of sodium azide to 5-hydroxy-hex-3-yne-2-one (**7**) (Eq. 3).[18,19] The unstable furyl azide **8** was characterized by preparation of the



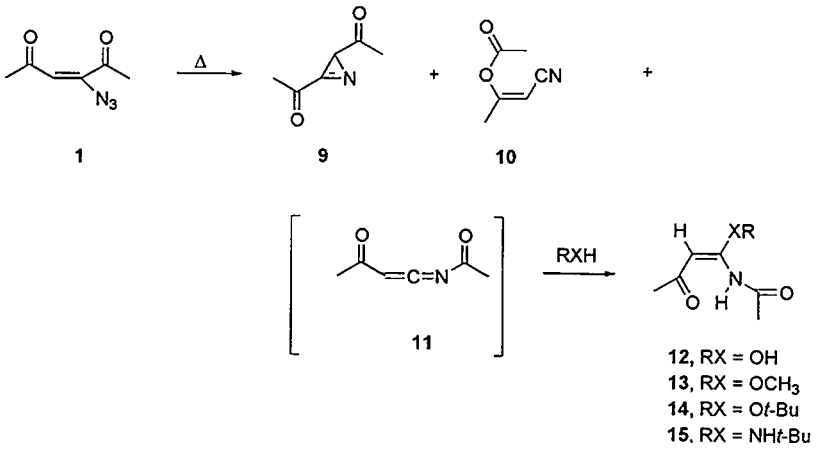
7 8 1 (3)

corresponding iminophosphorane by reaction with triphenylphosphine. After purification by chromatography, the azide **1** was immediately dissolved in either an appropriate solvent or in the presence of a reactive additive in an inert solvent and allowed to thermalize in the dark at room temperature.

Studies on the thermolysis of the *E*-3-azido-3-hexene-2,5-dione (**1**) in acetonitrile, which contained water or in the presence of alcohols or *t*-butylamine gave rise to three different products: azirine **9**,[10] *Z*-acetoxybut-2-enenitrile (**10**),[20] and compounds derived from keteneimine **11** (Scheme 1).[10] The ratios of these products were solvent dependent. The formation of compound **10** probably involves cyclization of the azide **1** to form a dihydroxydihydrofuran derivative that undergoes loss of water and nitrogen. In Hassner's review of experimental work on vinyl azides which give rise to products derived from a keteneimine intermediate, a concerted mechanism was favored.[14,21,22] By analogy, the keteneimine **11** is believed to arise by a concerted loss of nitrogen from the vinyl azide **1** via a 1,2-shift of the acetyl group. Isolation of its derived addition products **12**,[23] **13**, **14**,* and **15** served to characterize this molecule.

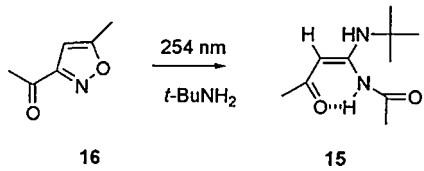
The *t*-butylamine adduct **15** was isolated from both the decomposition of the *E*-vinyl azide **1** in *t*-butylamine and from the photolysis

*The adduct **14** had ^{1}H NMR data ($CDCl_3$) δ 1.57 (s, 9H), 2.13 (s, 3H), 2.17 (s, 3H), 5.00 (s, 1H), 13.3 (b, 1H).



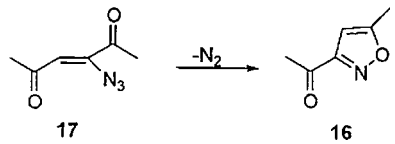
SCHEME 1

of 3-acetyl-5-methylisoxazole **16** in *t*-butylamine (Eq. 4). The decomposition of the *E*-vinyl azide **1** in *t*-butylamine also



(4)

gave rise to isoxazole ketone **16**.[24] Under these conditions and the relative ease by which ene-diones can isomerize,[25] the isoxazole ketone **16** probably arises from isomerization of the *E*-vinyl azide **1** to *Z*-3-azido-3-hexene-2,5-dione **17** followed by expulsion of nitrogen (Eq. 5). Indeed, the significant difference in the semi-quantitative rates for the



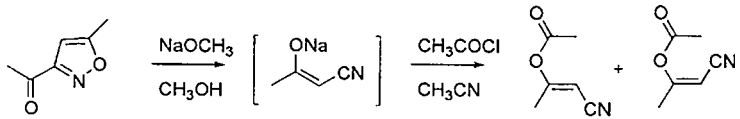
(5)

decomposition of the vinyl azides **1** and **17** further suggests that a concerted mechanism is operative.* In the case of the *Z*-vinyl azide **17**, a pathway in which the oxygen atom on the γ-carbonyl group functions

*At room temperature, the thermolysis of the *E*-vinyl azide **1** required approximately 15 h whereas the decomposition of the *Z*-vinyl azide **17** was complete in approximately 4 h.

as an internal nucleophile, via SN2 attack on the C-terminus nitrogen of the azide group, is a likely mechanism.[26]

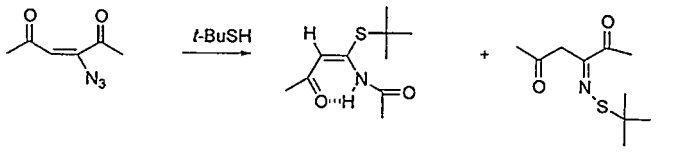
An authentic sample of *Z*-3-acetoxybut-2-enenitrile (**10**) was prepared by the acetylation of the anion of 3-oxo-butanenitrile (**18**) to afford a mixture of *E*- and *Z*-isomers **19** and **10**. The anion of cyanoacetone (**18**) was prepared *in situ* by the base-catalyzed cleavage of the isoxazole ketone **16** (Eq. 6).



(6)

16 18 19 10

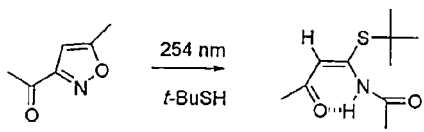
In contrast, decomposition of the *E*-vinyl azide **1** in *t*-butyl mercaptan at room temperature yielded two products, the expected keteneimine addition product **20** and a new product, which is assigned as sulfenimine **6**. No azirine **9** or acrylonitrile **10** were detected. Compounds **20** and **6** were isolated respectively in yields of 17% and 19% based on the furyl azide **8** (Eq. 7). The spectral properties of the mercaptan adduct



(7)

1 20 6

20 were in agreement with the product obtained from the photolysis of the isoxazole ketone **16** in the presence of *t*-butyl mercaptan (Eq. 8).



(8)

16 20

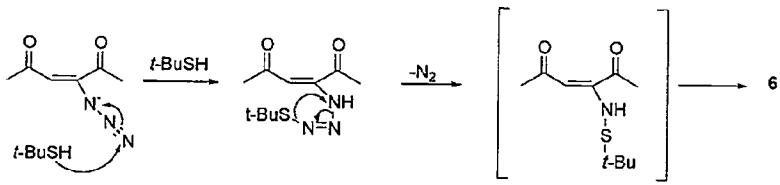
The structural assignment of the sulfenimine **6**, isolated as a single stereoisomer, was based on the correct exact mass for $C_{10}H_{17}NO_2S$. The IR spectrum had two intense carbonyl absorbances at 1720 and 1690 cm^{-1} and another absorbance at 1360 cm^{-1}, which was assigned to the imine stretch.[27,*] The ^1H NMR spectrum had resonances at 1.43 ppm (s, 9H, *t*-Bu), 2.20 ppm (s, 3H, CH_3), 2.43 ppm (s, 3H, CH_3), and

*The IR imine stretch of nonconjugated thiooximes occurs between 1618 and 1622 cm^{-1}.

3.70 ppm (s, 2H, CH_2).[28] The mercaptan adduct **20** also had a correct exact mass for $C_{10}H_{17}NO_2S$. The IR spectrum displayed a broad absorbance at 2900–2850 cm^{-1}, two strong carbonyl absorbances at 1700 and 1620 cm^{-1}, and two other intense absorbances at 1550 and 1220 cm^{-1}. The ^1H NMR spectrum for the adduct **20** had resonances at 1.67 ppm (s, 9H, *t*-Bu), 2.20 ppm (s, 6H, 2 × CH_3), 5.60 ppm (s, 1H, CH), and 13.3 ppm (b, 1H, NH).

DISCUSSION

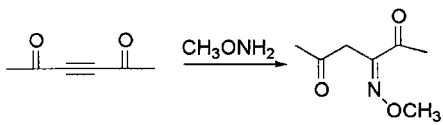
In the case of the thermolysis of vinyl azide **1**, the formation of the sulfenimine **6** is most likely explained by attack of *t*-butyl mercaptan on the N-terminus of the azide in a similar manner as in the Staudinger reaction.[9,14] Migration of the mercapto group to the C-terminus nitrogen, followed by expulsion of nitrogen, affords an ene-sulfenamine that gives rise to sulfenimine **6** on tautomerization (Eq. 9).[29]



(9)

1

As an alternative mechanism, we considered the possibility that sulfenimine **6** might be formed by trapping of a vinyl nitrene intermediate. However, when the thermolysis of the vinyl azide **1** was conducted in either methanol or *t*-butylamine, there was no evidence for the analogous insertion products, **3** and **5**. For comparison purposes in this study, an authentic sample of the 3-O-methyl oxime of 2,3,5-hexanetrione (**3**) was prepared by the addition of methoxyamine to 3-hex-yne-2,5-dione (**21**) (Eq. 10).[30]



(10)

21 **3**

These findings are consistent with the proposal by Hassner et al. that vinyl nitrenes are not intermediates in the thermolysis of vinyl azides.[14] In contrast, the photolytic production of **20** from the isoxazole ketone **16** is believed to involve the singlet state of the incipient *Z*-nitrene, which may be stabilized by the lone pairs on sulfur. As a

consequence, the importance of the triplet state, the source of rearrangement products for compounds such as azirine **9** is reduced with concomitant formation of **20**.[10,31]

CONCLUSION

In summary, the decomposition of the *E*-vinyl azide **1** in *t*-butyl mercaptan affords the *t*-butyl mercaptan addition product **20** and an unexpected product, sulfenimine **6**. The absence of the vinyl nitrene-like addition products **3** and **5** when the thermal decomposition was conducted in either methanol or *t*-butylamine suggests that a thio-Staudinger reaction is operative as opposed to trapping of a vinyl nitrene intermediate. Aside from the potential utility of this chemistry to prepare sulfenimines, this thio-Staudinger reaction may have applicability as a method to probe active sites in enzymes. In a similar way that aromatic azides are used in photoaffinity labeling studies, the selectivity in this reaction for mercaptans may allow for specific identification of cysteine residues in enzymes.[32]

EXPERIMENTAL

Melting points were taken on a Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Varian Model T-60 spectrophotometer in deuterochloroform using tetramethylsilane as an internal standard. ^{13}C NMR spectra were recorded on a Varian XL-400 spectrophotometer in deuterochloroform using tetramethylsilane as an internal standard. IR spectra were obtained on a Perkin-Elmer Model 727 IR spectrophotometer. Low resolution mass spectra were obtained on a VG Analytical model and high resolution spectra were obtained on a 7070 EQ high resolution mass spectrophotometer. UV spectra were taken on either a Perkin-Elmer UV-VIS or a Cary 17D spectrophotometer. The ^{31}P NMR spectrum was taken on a Varian Model FT 80 NMR using a broad band probe operating at 32.203 MHz. An external standard of 85% H_3PO_4 was used. Elemental analyses were done by Robertson Laboratories, Florham Park, NJ.

Preparation of 3-Azido-2,5-dimethylfuran (7)

To 4.23 g (0.038 mmol) of 5-hydroxy-hex-3-yne-2-one (**7**)[30,33] in 90 mL of acetic acid was added a solution of 2.64 g (0.041 mmol) of sodium azide in 20 mL of water. The solution was placed in a freezer at

−10 to 5°C for 17 h during which time the mixture eventually froze. Chloroform (250 mL) and water (100 mL) were added. The organic layer was washed with aqueous sodium bicarbonate solution (3 × 150 mL) and saturated sodium chloride solution (150 mL). Drying over magnesium sulfate was followed by evaporation of the solvent at room temperature. There was obtained 5.84 g of crude product. Flash chromatography on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent yielded 2.71 g (53% yield) of the furyl azide **8** as a bright yellow oil. ^{1}H NMR ($CDCl_3$) δ 2.06 (s, 3H), 2.17 (s, 3H), 5.83 (s, 1H); IR (film) 4.65 (vs), 6.06 (m), 7.69 (s), 13.33 (m) μm. The furyl azide **8** is not a stable compound and decomposes on standing. The azide **8** was further characterized by the preparation of the corresponding phosphinimine by reaction with triphenylphosphine. Under a nitrogen atmosphere and in glassware, which had been washed with concentrated ammonium hydroxide and dried in an oven overnight at 120°C, a solution of 0.1500 g (1.09 mmol) of freshly chromatographed furyl azide **8** in 2 mL of anhydrous diethyl ether was prepared. A solution of 0.286 g (1.09 mmol) of triphenylphosphine in 2 mL of anhydrous ether was added. Additional ether was added and, under a nitrogen atmosphere, the product was filtered and the solid was washed with anhydrous ether. This phosphinimine had m.p. 134–136°C (dec); ^{1}H NMR ($CDCl_3$) δ 2.06–2.17 (d, 6H), 5.30 (s, 1H), 6.83–7.90 (m, 15H); ^{31}P NMR (CH_2Cl_2) δ 4.45; IR (KBr) 6.17 (s), 6.97 (m), 7.07 (m), 7.69 (m), 9.01 (s), 14.3 (s) μm. Anal. Calcd. for $C_{24}H_{22}NOP$: C, 77.62; H, 5.97; N, 3.77; P, 8.34. Found: C, 77.49; H, 6.17; N, 4.03; P, 8.23.

Preparation of *E*-Azido-hex-3-ene-2,5-dione (1)

To 2.07 g (0.015 mmol) of 3-azido-2,5-dimethylfuran (**8**) in 130 mL of acetone and 20 mmL of water was added 4.78 g (0.060 mmol) of pyridine.[17] The solution was cooled to −20°C in a dry-ice/carbon tetrachloride bath. A solution of bromine (2.43 g, 0.015 mmol) in 13 mL of acetone and 3 mL of water was added over a 10-min period. After 20 min, the reaction was complete as shown by TLC. Ether (140 mL) and saturated sodium chloride solution (70 mL) were added, and the layers were separated. The ether layer was washed with saturated aqueous cupric sulfate (2 × 70 mL) and dried over magnesium sulfate. The solvent was removed at room temperature under reduced pressure. The *E*-azide **1** was immediately purified by flash chromatography on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent. The *E*-azide **1** decomposed explosively when neat upon standing. Solutions containing the *E*-vinyl azide **1** were not evaporated to dryness. ^{1}H NMR

($CDCl_3$) δ 2.23 (s, 3H), 2.36 (s, 3H), 5.87 (s, 1H); IR (CCl_4) 4.76 (s), 6.10 (m), 7.19 (m), 9.17 (m) μm. UV (CH_3CN) $\lambda = 400$ nm (ε = ca. 14); λ = 280 (ε = ca. 2700).

Thermolysis of *E*-Azido-hex-3-ene-2,5-dione (1) in *t*-Butyl Mercaptan

To approximately 4.4 mmol of the *E*-vinyl azide **1**, based on 0.60 g (4.4 mmol) of the furyl azide **8** was added 30 mL of *t*-butyl mercaptan and the solution was stirred overnight at room temperature. The solvent was removed, and the products were purified to yield 0.16 g (17%) of the *t*-butyl mercaptan adduct **20** and 0.18 g (19%) of the sulfenimine **6**. The adduct **20**, isolated as a pale yellow solid, had the following properties: m.p. 50–52°C. Exact mass calcd for $C_{10}H_{17}NO_2S$: 215.0980007. Found: 215.0978200. MS, m/z 159 (55%), 116 (100%), 102 (25%), 84 (29%). ^{1}H NMR ($CDCl_3$) δ 1.67 (s, 9H), 2.20 (s, 6H), 5.60 (s, 1H), 13.3 (b, 1H). IR (KBr) 3.45–3.51 (b), 5.88 (s), 6.17 (s), 6.45 (s), 8.20 (s) μm. The sulfenimine **6** had the following properties: Exact mass calcd for $C_{10}H_{17}NO_2S$: 215.0980007. Found: 215.0974100. MS, m/z 215 (8%), 159 (100%), 116 (65%), 89 (35%), 74 (28%). ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 9H), 2.20 (s, 3H), 2.43 (s, 3H), 3.70 (s, 2H); IR (film) 5.81 (s), 5.91 (s), 7.35 (s), 8.62 (m), 13.5 (m) μm.

Photolysis of 3-Acetyl-5-methylisoxazole (16) in *t*-Butyl Mercaptan

A nitrogen degassed solution of 3-acetyl-5-methylisoxazole (**16**) (0.50 g, 0.4 mmol)[24] in 10 mL of *t*-butyl mercaptan was irradiated in quartz NMR tubes at 254 nm in a Rayonet photochemical reactor (Southern New England Ultraviolet Co.) for 16 h. The solvent was removed under vacuum, and the residue was filtered through silica gel using methylene chloride as the eluent. The fractions containing the *t*-butyl mercaptan adduct **20** were combined and purified again via flash chromatography on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent to yield 0.07 g (8.1%) of the adduct **20**. The spectral properties of this compound were in agreement with those obtained from the thermolysis of the *E*-vinyl azide **1**.

Thermolysis of *E*-Azido-hex-3-ene-2,5-dione (1) in Acetonitrile

To the *E*-vinyl azide **1** prepared from 2.07 g (15.1 mmol) of furyl azide **8** was added to 100 mL of acetonitrile which contained approximately

0.1% water. The solution was wrapped in aluminum foil and held at room temperature for 17 h. Solvent was removed under vacuum to yield a yellow oil. ^{1}H NMR integration revealed the products to be a mixture of imide **12** (61%),[23] azirine **9** (6%),[10] and enol ester **10** (33%).[10] This oil darkened very rapidly when neat upon standing. Anhydrous ether was added, and imide **12** (0.25 g, 12%) was filtered and air dried. The imide **12** had m.p. 89–91°C (lit.[23] m.p. 86–86.5°C); ^{1}H NMR ($CDCl_3$) δ 2.00 (s, 3H enol), 2.23 (s, 3H), 2.33 (s, 3H, keto), 3.82 (s, 2H, enol), 5.82 (s, 1H enol), 9.60 (b, 1H), 13.6 (b, 1H enol), keto:enol ratio 5:1; IR (KBr) 3.05 (s), 5.75 (s), 5.88 (sh), 6.62 (s), 7.94 (s), 8.62 (m) μm. The filtrate was concentrated and the residue was chromatographed on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent to yield 0.07g (3.7%) of the *Z*-enol ester **10**.[20] ^{1}H NMR ($CDCl_3$) δ 2.13 (d, 3H), 2.23 (s, 3H), 4.95 (q, 1H); IR (film) 4.50 (s), 5.65 (s), 6.02 (s), 8.33 (s), 8.47 (s), 12.5 (m) μm; Anal. Calcd. for $C_6H_7NO_2$: C, 57.59; H, 5.64; N, 11.19. Found: C, 57.37; H, 5.55; N, 11.01.

Thermolysis of *E*-Azido-hex-3-ene-2,5-dione (1) in Methanol

E-vinyl azide **1** was prepared from 2.07 g (15.1 mmol) of the furyl azide **8** and was dissolved in 100 mL of methanol. The solution was held in the dark at room temperature for 17 h. Solvent was removed under vacuum to yield 0.80 g of product. ^{1}H NMR integration revealed the mixture to contain 70% of enol ether **13** and 30% of enol ester **10**. An analytical sample of the enol ether **13** was prepared via a distillation at 50–55°C (0.1 mm), followed by flash chromatography on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent. The enol ether **13** had ^{1}H NMR ($CDCl_3$) δ 2.12 (s, 3H), 2.13 (s, 3H), 4.90 (s, 1H), 12.40 (b, 1H); IR (film) 2.82–3.51 (b), 5.78–6.33 (b), 6.67 (s), 6.90 (s), 7.25 (s), 7.58 (s), 8.26 (s) μm; Anal. Calcd. for $C_7H_{11}NO_3$: C, 53.49; H, 7.06; N, 8.90. Found: C, 52.98; H, 7.40; N, 9.05. To a sample of the enol ether **13** in $CDCl_3$, was added an aqueous overlay of trifluoroacetic acid and the two-phase system was held at room temperature for 2 days. The course of the hydrolysis was monitored by ^{1}H NMR analysis and indicated that the enol ether **13** had yielded the imide **12** under these conditions.

Thermolysis of *E*-Azido-hex-3-ene-2,5-dione (1) in *t*-Butylamine

Azide **1** was prepared from 1.00 g (7.3 mmol) of furyl azide **8** and was dissolved in 50 mL of freshly distilled *t*-butylamine. After 15 h in the

dark at room temperature, solvent was removed under vacuum to afford a black tar. By ^{1}H NMR analysis, the mixture contained nearly equal amounts of isoxazole ketone **16**[26] and the *t*-butylamine adduct **15**. The tar was triturated in ether, and the supernatant was decanted. An analytical sample of the *t*-butylamine adduct **15** was prepared by flash chromatography on silica gel using a mixture of 65% hexane and 35% ethyl acetate as the eluent. The adduct **15**, isolated as a yellow oil, had exact mass calcd. for $C_{10}H_{18}N_2O_2$: 198.1368280. Found: 198.1355100. MS, m/z 198 (80%), 127 (87%), 101 (80%), 85 (100%), 57 (55%). ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 9H), 2.03 (s, 3H), 2.13 (s, 3H), 4.80 (s, 1H), 9.15 (b, 1H), 14.17 (b, 1H). IR (film) 3.13 (b), 5.95 (m), 6.17 (s), 6.33 (s), 7.25 (m), 8.20 (m). ^{13}C NMR ($CDCl_3$)δ 25.22, 28.94, 30.83, 51.29, 83.14, 155.66, 173.15, 180.28, 192.95.

Preparation of the 3-O-Methyloxime of 2,3,5-Hexanetrione (3)

To a magnetically stirred solution of 0.33 g (5.00 mmol) of potassium hydroxide in 2 mL of water was added 10 mL of chloroform. Methoxyamine hydrochloride (0.42 g, 5 mmol) was added, and the mixture was stirred for 5 min. 3-Hex-yne-2,5-dione (**21**) (0.55 g, 5.0 mmol) was added.[30] After the addition, the reaction was complete as shown by ^{1}H NMR analysis. Drying over magnesium sulfate was followed by evaporation of the solvent. There was obtained 0.70 g (90%) of the 3-O-methyloxime (**3**) of 2,3,5-hexanetrione. An analytical sample was prepared by flash chromatography using a mixture of 65% hexane and 35% ethyl acetate as the eluent; ^{1}H NMR δ 2.17 (s, 3H), 2.40 (s, 3H), 3.62 (s, 2H), 4.05 (s, 3H); IR (film) 5.81(s), 5.92 (s), 6.25 (w), 7.35 (m) μm. Anal. Calcd. For $C_7H_{11}NO_3$: C, 53.49; H, 7.06; N, 8.90. Found: C, 53.30; H, 7.44; N, 8.89.

Preparation of *E*-3-Acetoxybut-2-enenitrile (19) and *Z*-3-Acetoxybut-2-enenitrile (10)

Under a nitrogen atmosphere, 0.23 g (0.01 mmol) of sodium was added to 25 mL of methanol. A solution of 1.25 g (0.01 mmol) of 3-acetyl-5-methylisoxazole (**16**)[24] in 5 mL of methanol was added. The reaction was stirred at room temperature overnight, and the solvent was removed under reduced pressure to yield a reddish-brown solid. The salt was suspended in 50 mL of acetonitrile, and 1.0 mL (0.014 mmol) of acetyl chloride was added. The reaction was exothermic, and the precipitation of sodium chloride occurred immediately. Solvent was removed under vacuum, and water (50 mL) and ether (100 mL) were added. The

layers were separated and the organic layer was washed with saturated aqueous sodium bicarbonate solution (3 × 50 mL) and saturated sodium chloride solution (50 mL). Drying over magnesium sulfate was followed by evaporation of the solvent to yield 1.20 g of crude product. Distillation at 20–25°C (0.1 mm) [lit[20a] b.p. 85°C (13 mm)] yielded 0.22 g (22%) of a mixture of *E*- and *Z*-3-acetoxybut-2-enenitriles (**19** and **10**). By ^{1}H NMR analysis, the mixture contained 75% of the *E*-isomer **19** and 25% of the Z-isomer **10**. The *E*-isomer **19** had ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 6H), 5.40 (s, 1H). The *Z*-isomer **10** had ^{1}H NMR ($CDCl_3$) δ 2.13 (d, 3H), 2.23 (s, 3H), 4.95 (q, 1H). IR (film) (mixture) 4.50 (s), 5.65 (s), 6.02 (s), 8.33 (s), 8.47 (s), 11.1 (m), 12.5 (m) μm.

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