from ethanol; IR 1660 (C=O) cm^{-1}. Anal. Calcd for $C_{29}H_{22}OS$: C, 83.22; H, 5.29. Found: C, 83.02; H, 5.17.

Reaction of 1d with 6. A benzene solution (25 mL) of **6** (1.44 g, 6.87 mmol) was added at room temperature to a benzene solution (25 mL) of **1d** (2.00 g, 6.87 mmol), and the reaction mixture was heated at reflux for 0.5 h. The reaction mixture was evaporated in vacuo, and the resultant residue was triturated with a mixture of ethanol and hexane to give 2.72 g of **7d** as colorless prisms from ethanol–benzene; IR 1670 (C=O) cm^{-1}. Anal. Calcd for $C_{27}H_{16}OCl_2S$: C, 70.59; H, 3.48. Found: C, 70.68; H, 3.50.

Reduction of 7d with $NaBH_4$. A mixture of **7d** (310 mg) and a large excess of $NaBH_4$ in ethanol (20 mL) was stirred at room temperature overnight, and ice-cold water was added to the mixture. The precipitate was collected by filtration to give 195 mg of **8** as pale yellow prisms from hexane–benzene: mp 212–213 °C; IR 3550 (OH) cm^{-1}. Anal. Calcd for $C_{27}H_{18}OCl_2$: C, 75.52; H, 4.19. Found: C, 75.54; H, 4.27.

Pyrolysis of 7d. A xylene solution (10 mL) of **7d** (425 mg) was heated at reflux for 24 h. After being cooled to room temperature, the reaction mixture was evaporated in vacuo and the resultant residue was triturated with a mixture of ether and hexane to give 38 mg (9%) of unreacted **7d**. The filtrate was chilled with dry ice–acetone to give 240 mg of **9** as pale yellow needles from benzene: mp 176–177 °C; IR 1660 (C=O) cm^{-1}. Anal. Calcd for $C_{27}H_{16}OCl_2$: C, 75.88; H, 3.74. Found: C, 75.76; H, 3.82.

Registry No.—**1a**, 3469-17-8; **1b**, 18627-14-0; **1c**, 67069-91-4; **1d**, 67069-90-3; **2**, 1450-31-3; **3**, 64801-82-7; **4a**, 67069-87-8; **4b**, 67069-86-7; **5**, 64801-83-8; **6**, 830-72-8; **7a**, 67069-82-3; **7b**, 67069-83-4; **7c**, 67069-81-2; **7d**, 67069-80-1; **8**, 67069-85-6; **9**, 67069-84-5.

References and Notes

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(7) The transient formation of 1,3-oxathiole might be unlikely because no appreciable decomposition of **3** was observed when **3** was heated at reflux in xylene for 24 h.
(8) "Organic Syntheses", Collect. Vol. 4, Wiley, New York, N.Y., 1963, p 927.
(9) H. Staudinger, *Helv. Chim. Acta*, **3**, 862 (1920).
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Reaction of N-Substituted Thioamides with *gem*-Dicyano Epoxides: A New Synthetic Route to Anhydro-4-hydroxythiazolium Hydroxides

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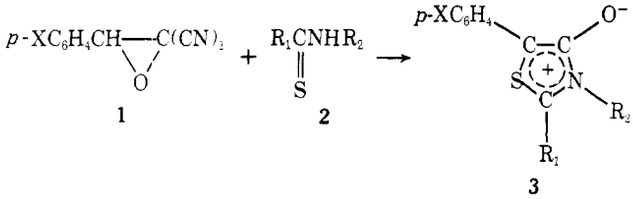
gem-Dicyano epoxides undergo ready reaction under neutral conditions with N-monosubstituted thioamides to provide a new, convenient synthesis of the anhydro-4-hydroxythiazolium hydroxide system. The epoxides act as potential 1,2-bielectrophiles, while the N-monosubstituted thioamides act as 1,3-binucleophiles, and in most cases excellent yields of products are obtained. The mechanism of this reaction is discussed.

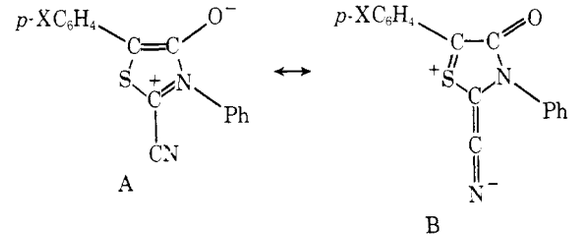
The increasing interest in the field of mesoionic compounds is evident from several recent reviews dealing with this subject.[1-3] Monocyclic anhydro-4-hydroxythiazolium hydroxides have been prepared by S-alkylation of rhodamines,[4-6] or by S-alkylation of N-substituted thioamides with an α-halo acid, followed by cyclodehydration of the resulting acid,[7-9] and recent studies have shown that this last reaction can lead to numerous mesoionic compounds when the α-halo acid is replaced by its acid chloride.[10] In a preliminary communication we described the reaction of N-substituted thioamides with *gem*-dicyano epoxides **1** as a new route to the anhydro-4-hydroxythiazolium hydroxide system[11] and in this paper elaborate further on this very useful and versatile approach to this ring system.

The reaction of the *gem*-dicyano epoxides **1** with the thiocarbonyl compounds **2** was generally carried out under neutral conditions at room temperature in acetone as solvent. The

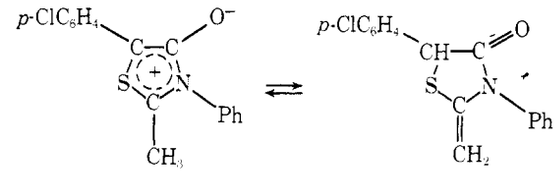


mesoionic thiazoles obtained are described in Table I, which illustrates the general nature of the reaction and the excellent yields obtained.[13]

The mesoionic compounds **3** were generally deep red or violet in color and were characterized by IR carbonyl absorptions at 1650 cm^{-1}. The mesoionic thiazoles **3** (X = NO_2, Cl; R_1 = CN; R_2 = Ph) showed an intense nitrile absorption at 2200 cm^{-1} consistent with that described earlier for the mesoionic thiazole **3** (R_1 = CN; R_2 = Ph; X = H).[10] The presence of the strongly conjugated nitrile group in these representations of **3** is most likely indicative of a significant contribution of the resonance form B.



It is interesting to note that compound **3** (X = Cl; R_1 = CH_3; R_2 = Ph) shows two carbonyl bands in solution in CCl_4 (1628,

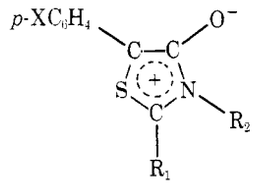


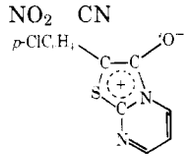
δ 2.48 (s, CH_3) 50%

δ 4.34 (AB system, CH_2)
δ 5.18 (s, CH) 50%

0022-3263/78/1943-3732$01.00/0

Table I. Anhydro-4-hydroxythiazolium Hydroxide Derivatives (3)



registry no.	substituents X	R_1	R_2	mp, °C	% yield
18100-80-6	H	Ph	Ph	270[a]	92
59208-06-9	Cl	Ph	Ph	300	94
66702-52-1	MeO	Ph	Ph	250	90
59208-07-0	NO_2	Ph	Ph	273	95
66702-53-2	Cl	$pNO_2C_6H_4$	Ph	242	60
66702-54-3	NO_2	$pNO_2C_6H_4$	Ph	260	65
13288-65-8	H	Ph	$PhCH_2$	164[b]	60
59208-08-1	Cl	Ph	$PhCH_2$	170	65
59208-09-2	NO_2	Ph	$PhCH_2$	210	71
59208-10-5	Cl	CH_3	Ph	180	30
59208-11-6	NO_2	CH_3	Ph	280	60
66702-55-4	Cl	Ph	Et	174	50
66702-56-5	NO_2	Ph	Et	204	60
66702-57-6	NO_2	NMe_2	Ph	287	96
66702-58-7	NO_2	SPh	Ph	210	60
66702-59-8	Cl	CN	Ph	248	40
66702-60-1	NO_2	CN	Ph	258	80
66702-61-2				278	14

[a] Lit. mp 270 °C.[7] [b] mp 164 °C.[7]

1716 cm^{-1}), whereas the solid (Nujol mull) shows only one band, at 1628 cm^{-1}. Its NMR spectrum ($CDCl_3$) shows the existence of the following tautomeric equilibrium.

The CH_3, CH_2, and CH signals are not observed when a drop of CD_3CO_2D is added in the $CDCl_3$ solution, but these signals are recovered when an excess of CH_3CO_2H is added.

The main mass fragmentations observed for the mesoionic thiazoles **3** are consistent with those described[12] (Scheme I).

The mesoionic thiazoles **3** were accompanied by a small quantity of a secondary product assigned the 2-cyanothiazo-

Scheme I. Mass Fragmentations of Mesoionic Thiazoles

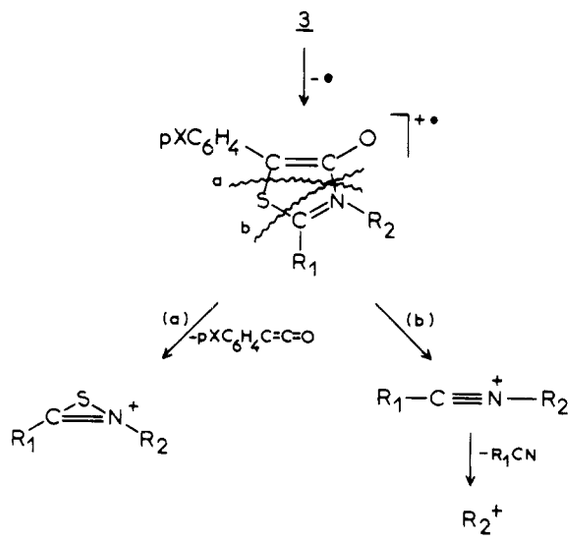
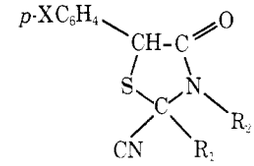


Table II. 2-Cyano-4-Thiazolidinones 4



registry no.	substituents X	R_1	R_2	mp, °C	% yield
66702-62-3	H	Ph	Ph	*a*	1
66702-63-4	Cl	Ph	Ph	191	1
66702-45-2	Cl	Ph	$PhCH_2$	158	13
66702-46-3	Cl	CH_3	Ph	174	15
66702-47-4	NO_2	CH_3	Ph	198	12

[a] Not purified.

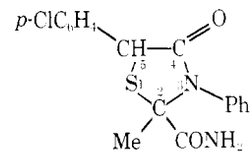
lidinone (**4**) structure on the basis of their spectral characteristics (Table II).[13] The NMR spectra of the crude product (**4**, X = Cl; R_1 = Me; R_2 = Ph) showed signals which may be attributed to the presence of two diastereoisomers, but only one of the diastereoisomers was isolated by successive recrystallizations. The relative configuration of the carbons 2 and 5 has not been determined.

The thiazolidinone **4** (X = Cl; R_1 = Me; R_2 = Ph) reacted with sulfuric acid to give the thiazolidinone **5**, characterized by its IR, NMR, and mass spectrum [IR (Nujol) 3395, 2380, 1702, 1654 cm^{-1}; NMR ($CDCl_3$ + CF_3CO_2H) 7.6–7 (m, 9, Ar), 5.48 (s, 1, CH), 1.82 (s, 3, Me); $M^{+\cdot}$ calcd 346.054272, found 346.0540].

Mechanism of the Reaction of the Thiocarbonyl Compounds 2 with the Epoxides 1. When the reaction of **1** (X = Cl) with **2** (R_1 = R_2 = Ph) was carried out in the presence of **4** (X = Cl; R_1 = Me; R_2 = Ph), a mixture containing exclusively **3** (X = Cl; R_1 = R_2 = Ph) and unchanged **4** (X = Cl; R_1 = Me; R_2 = Ph) was observed by NMR and TLC. This indicates that the thiazolidinone **4** was not a precursor of the mesoionic thiazole **3**. We have also shown that the mesoionic thiazoles **3** were stable under the reaction conditions and that they did not give the thiazolidinones **4**. Thus compounds **3** and **4** must arise from two different pathways.

Scheme II provides a rational mechanism for the formation of **3** and **4**. The first step, a nucleophilic opening of the epoxide **1** by the thiocarbonyl compound **2**, leads to the oxathiolane intermediate **6**. This first step is reminiscent of the well-documented ring opening of epoxides by thiourea or alkaline thiocyanate, leading to episulfide formation via an oxathiolane.[14] The intermediate **6** does not lead to an episulfide. Successive hydrocyanic acid eliminations lead first to the oxathiole **7** and then to the ketene **8** (path a) or alternatively to the α-keto nitrile **9** (path b).

Evidence in favor of the formation of the intermediate **7** comes from the isolation of 2-*N*-acyliminooxathioles **10** when the epoxides **1** were treated with KSCN in acetic anhydride.[15] We were also able to trap the intermediate **7** as its acetylated

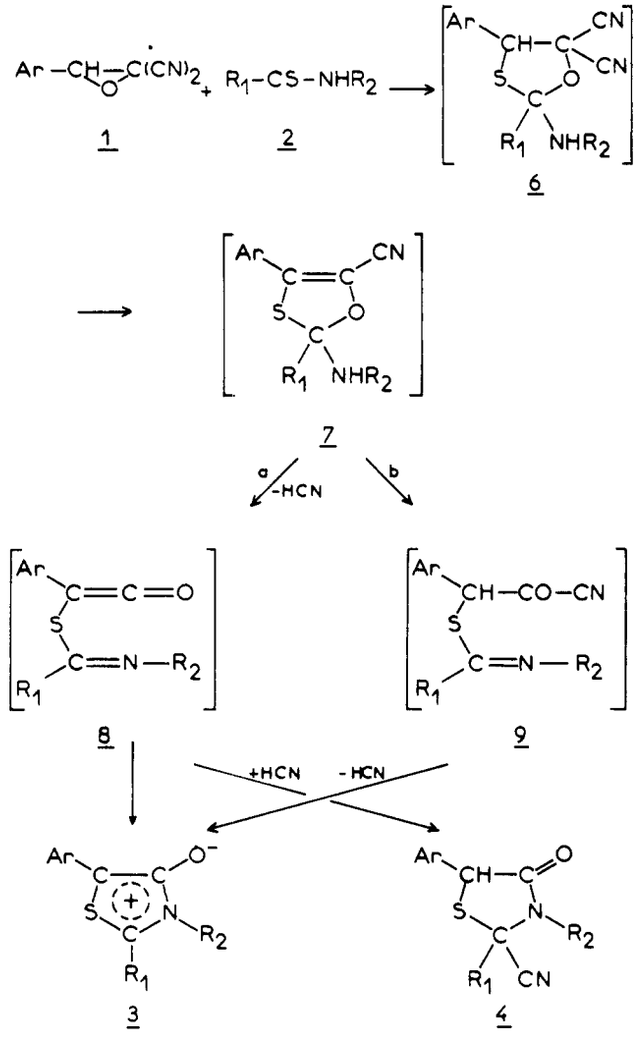


5

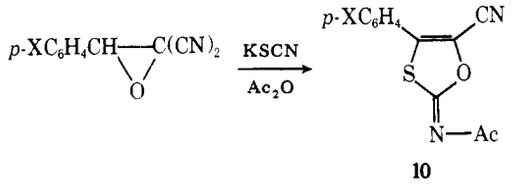
derivative **11** by reacting the epoxide **1** (X = Cl) and thiobenzanilide (**2**, R_1 = R_2 = Ph) in acetic anhydride. The compound **11** decomposed rapidly at 50 °C and gave the mesoionic thiazole **3** (X = Cl; R_1 = R_2 = Ph).

The loss of a hydrocyanic acid molecule from **7** can lead to

Scheme II. Mechanism of the Reaction of the Thiocarbonyl Compounds 2 with the Epoxides 1

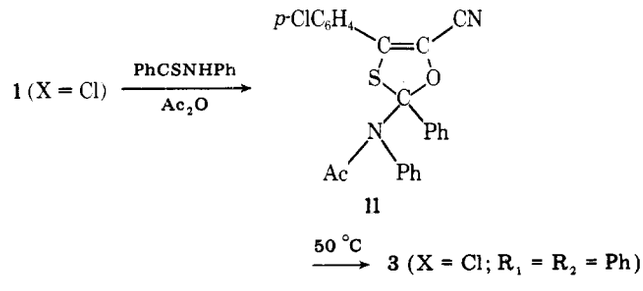


the ketene 8 (path a). However, such a ketene was not trapped by water or alcohol even when the reaction was carried out in methanol as solvent. If formed, the intermediate 8 must cyclize



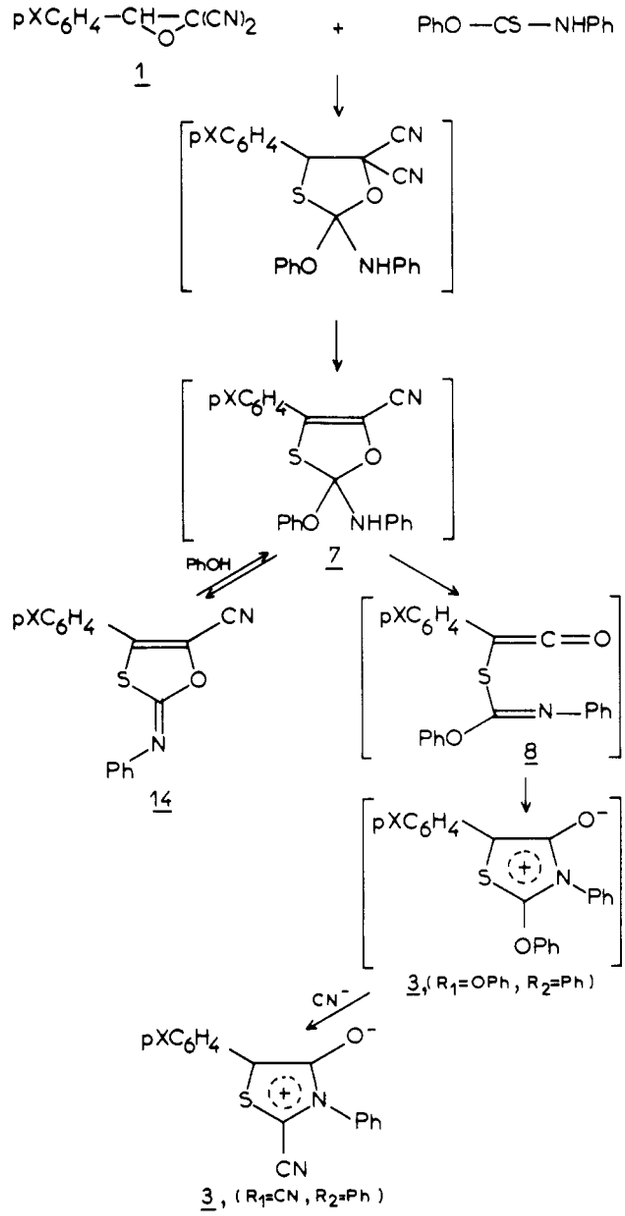
10

rapidly to 3 or react with the cyanide ion present in the medium to give 4. The alternative pathway b, involving the rearrangement of 7 into the α-keto nitrile 9, cannot be definitely excluded and 9 can also be an intermediate leading to the mesoionic thiazole 3 and to the thiazolidinone 4.



It is interesting to note that the mesoionic thiazole 3 (R_1 = CN; R_2 = Ph) was obtained from *O*-phenyl phenylcarbamothioate (2) (R_1 = OPh; R_2 = Ph) and epoxide 1, whereas this same mesoionic thiazole 3 (R_1 = CN; R_2 = Ph) was not isolated from the action of thiocyananilide with epoxide 1. The particular reaction of epoxide 1 and *O*-phenyl phenylcarbamothioate gives a mixture of 2-*N*-phenyliminooxathiole (14) and mesoionic thiazole 3 (R_1 = CN; R_2 = Ph). This unexpected result can be explained by the formation of an oxathiole 7 (R_1 = OPh) as described in Scheme II. The formation of this intermediate 7 (R_1 = OPh) is linked to the presence of the leaving group, R_1 = OPh, as 7 can be an intermediate giving either 2-*N*-phenyliminooxathiole (14) by the loss of phenol, or the ketene 8 by the loss of hydrocyanic acid (Scheme III). It has been shown that 2-alkoxy-substituted mesoionic thiazoles are unstable systems[10] and we postulate that the mesoionic thiazoles 3 (R_1 = CN; R_2 = Ph) obtained arise from the reaction of the cyanide ions present in the medium with the mesoionic thiazoles 3 (R_1 = OPh; R_2 = Ph) (Scheme III).

Scheme III. Formation of 3 (R_1 = CN; R_2 = Ph)



It is of interest to note that when the reaction of 1 and *O*-phenyl phenylcarbamothioate (2, R_1 = OPh; R_2 = Ph) is carried out in the presence of phenol the yield of 14 is lowered, while the yield of mesoionic thiazole 3 (R_1 = CN; R_2 = Ph) is considerably increased. In agreement with Scheme III, this can be explained by a reversible loss of phenol from the in-

termediate 7. Indeed, whereas 14 is thermally stable, it is partially transformed into 3 (R_1 = CN) when it is heated with phenol.

Experimental Section

General. IR spectra were measured in CCl_4 on a Perkin-Elmer 225 spectrophotometer. ^1H NMR spectra were recorded on a Jeolco JNM MH 100 spectrometer using a chloroform-*d* solvent and Me_4Si as internal standard; chemical shifts are reported in δ (ppm) units. Mass spectral data were obtained on Varian Mat 311 spectrometer.

Preparation of *gem*-Dicyano Epoxides 1. The *gem*-dicyano epoxides were prepared according to a known synthetic method[16] and improvements of this procedure are detailed below. The NaClO used was a 2.5 M commercial bleach solution, diluted with water (540 mL of the 2.5 M solution and 460 mL of water).

1 (X = H). The olefin (6 g, 0.032 mol) was dissolved in 50 mL of acetonitrile and 2 mL of 2 N H_2SO_4 was added. The solution was stirred vigorously and 5 mL of the NaClO solution was added and immediately the pH of the reaction mixture was adjusted to about pH 5 with 2 N H_2SO_4. A total of 85 mL of the NaClO solution was added in this way during 10 min and, after this addition, vigorous stirring was continued for 10 min at pH 5. After adding 1000 mL of water and cooling, 4.8 g of the epoxide (X = H) was obtained (more or less rapidly). Generally the product, washed with water, is pure enough to be used without further recrystallization: mp 52–53 °C.

1 (X = Cl). The olefin (20.0 g, 0.11 mol) was dissolved in 200 mL of CH_3CN (the suspension must be warmed) and 4 mL of 2 N H_2SO_4, followed by 200 mL of the diluted bleach solution, was added in about 10 min. During the addition the pH was maintained at 5 by adding 2 N H_2SO_4. The epoxide 1 (X = Cl) readily separated on dilution of the reaction mixture with water: mp 128–129 °C (quantitative).

1 (X = NO_2). The olefin (20.0 g, 0.10 mol) was dissolved in 200 mL of CH_3CN and 7 mL of 2 N H_2SO_4, followed by 120 mL of the NaClO solution, was added rapidly. The pH was maintained at 5 by adding 2 N H_2SO_4. The epoxide 1 (X = NO_2) was obtained by dilution of the reaction mixture with water: mp 183–184 °C.

1 (X = MeO). The olefin (20.0 g, 0.10 mol) was dissolved in 200 mL of CH_3CN and 200 mL of NaClO solution was added in 50-mL portions, the pH of the reaction mixture being maintained at 5 by adding 2 N H_2SO_4. After 5 min of stirring and dilution with water the epoxide precipitated: mp 86–87 °C.

Thiocarbonyl Compounds 2. Thioacetanilide 2 (R_1 = CH_3; R_2 = Ph), thiobenzanilide 2 (R_1 = R_2 = Ph), and 2-imidazolidinethione were commercial products. The other carbonyl compounds 2 were prepared according to procedures described in the following references.

R_1	R_2	ref	R_1	R_2	ref
p-$NO_2C_6H_4$	Ph	17	$N(Me)_2$	Ph	20
Ph	$PhCH_2$	18	SPh	Ph	21
Ph	Et	19	OPh	Ph	22

General Procedure for the Reaction of N-Monosubstituted Thioamides with Epoxides. The epoxide 1 (0.005 mol) and the thioamide (0.005 mol) were dissolved in 20 mL of acetone and after 24 h at room temperature, the precipitate was separated by filtration. The mesoionic compounds 3 were recrystallized from ethanol (Table I).[13]

Modification of the above procedure for the preparation of the following mesoionic thiazoles 3: 3 (X = NO_2; R_1 = R_2 = Ph), 30 mL of acetone was used; 3 (X = NO_2; R_1 = Ph; R_2 = $PhCH_2$), 40 mL of acetone was used and the time of reaction was 160 h; 3 (X = H; R_1 = Ph; R_2 = $PhCH_2$), 3 (X = Cl; R_1 = Ph; R_2 = Et), 3 (X = NO_2; R_1 = Ph; R_2 = Et), the time of reaction was 72, 72, and 96 h, respectively; 3 (X = Cl; R_1 = *p*-$NO_2C_6H_4$; R_2 = Ph), boiling acetone; 3 (X = Cl; R_1 = Ph; R_2 = $PhCH_2$), 3 (X = Cl; R_1 = CH_3; R_2 = Ph), 40 and 20 mL of methanol was used, respectively (instead of acetone), and the time of reaction was 72 and 24 h; 3 (X = NO_2; R_1 = SPh; R_2 = Ph), the epoxide 1 (X = NO_2) and the dithiocarbamate 2 (R_1 = SPh, R_2 = Ph) were heated at 180 °C for 5 min without solvent; 3 (X = Cl; R_1, R_2 = –N=CHCH=CH–) was prepared by reacting the epoxide 1 (X = Cl) (0.005 mol) and 2(1*H*)-pyrimidinethione (0.005 mol) in solution in 20 mL of DMF for 15 min at room temperature.

2-Cyano-4-thiazolidinones 4 were obtained by refluxing the epoxides 1 (0.005 mol) and the thioamides 2 (0.005 mol) in acetone (20 mL) for 24 h. The mesoionic compounds 3 were filtered and removal of the solvent under reduced pressure and trituration of the resultant residue with ether afforded the colorless crystals of 4 (Table II).[13]

Hydrolysis of 2-(Cyanomethyl)-5-*p*-chlorophenyl-3-phenyl-4-thiazoldinone (4). The thiazolidinone (4, R_1 = CH_3; R_2 = Ph) (0.5 g, 0.0015 mol) was added to 8 mL of H_2SO_4. After 3 h of stirring the compound 5 precipitated on dilution with water: 0.4 g (80%); mp 282 °C after crystallization from EtOH.

Table III. Oxathioles 14

registry no.	X	mp, °C	% yield
62501-56-8	H	112	50
66702-48-5	Cl	120	60
66702-49-6	MeO	112	50
62501-57-9	NO_2	82	56

Stability of Mesoionic Thiazoles 3. Epoxide 1 (X = Cl) (0.005 mol), thiobenzanilide (0.005 mol), and 3 (X = Cl; R_1 = Ph; R_2 = $PhCH_2$) (0.001 mol) were dissolved in acetone (40 mL). After 27 h the solvent was removed. IR, NMR, and TLC data show that the mixture consisted of 3 (X = Cl; R_1 = R_2 = Ph), 3 (X = Cl; R_1 = Ph; R_2 = $PhCH_2$), and 4 (X = Cl; R_1 = R_2 = Ph). The formation of 4 (X = Cl; R_1 = Ph; R_2 = $PhCH_2$) was not observed.

Stability of 2-Cyano-4-thiazolidinones 4. Epoxide 1 (X = Cl) (0.005 mol), thiobenzanilide (0.005 mol), and 4 (X = Cl; R_1 = CH_3; R_2 = Ph) (0.001 mol) were dissolved in acetone (20 mL). After 24 h the solvent was removed. IR, NMR, and TLC data show that the mixture consisted of 3 (X = Cl; R_1 = R_2 = Ph), 4 (X = Cl; R_1 = R_2 = Ph), and 4 (X = Cl; R_1 = CH_3; R_2 = Ph). The formation of 3 (X = Cl; R_1 = CH_3; R_2 = Ph) was not observed.

Preparation of 2-*N*-Acyliminooxathiole 10 (X = H). Epoxide 1 (X = H) (0.005 mol) and KSCN (0.005 mol) were dissolved in acetic anhydride (6 mL). After 3 h at room temperature the mixture was cooled and the 2-*N*-acyliminooxathiole was filtered and washed with water (to eliminate CH_3CO_2K). The compound was crystallized from EtOH: mp 100 °C; yield 42%; ^1H NMR ($CDCl_3$) δ 2.42 (s, 3, CH_3); IR (CCl_4) 2229 (ν_{CN}), 1668 cm^{-1} (ν_{CO}). Anal. Calcd for $C_{12}H_8N_2O_2S$: C, 59.00; H, 3.30; N, 11.47.Found: C, 58.58; H, 3.34; N, 11.49.

Preparation of the Oxathiole 11. Epoxide 1 (X = Cl) (0.005 mol) and thiobenzanilide (0.005 mol) were dissolved in acetic anhydride (10 mL). After 24 h, successive fractions of 3 (R_1 = R_2 = Ph) were filtered and characterized by IR. After 48 h, a colorless precipitate was isolated. The compound crystallized rapidly from EtOH: mp 150 °C; IR (CCl_4) 2224 (C≡N), 1722 cm^{-1} (C=O); NMR ($CDCl_3$) δ 2.54 (s, 3, CH_3).

Compound 11 decomposed on electron impact. The observed spectrum was the same as that of the corresponding mesoionic thiazole 3 (R_1 = R_2 = Ph).

Preparation of the Mesoionic Thiazoles 3 (R_1 = CN; R_2 = Ph) and of the Oxathioles 14. When epoxides 1 (0.005 mol) and *O*-phenyl phenylcarbamothioate were heated together a mixture of the compounds 3 (R_1 = CN; R_2 = Ph) and 14 was obtained. The relative yield of these two compounds was very dependent of the reaction conditions.

Preparation of 3 (X = NO_2, Cl; R_1 = CN; R_2 = Ph). Epoxides 1 (X = NO_2, Cl) (0.005 mol), *O*-phenyl phenylcarbamothioate (0.005 mol), and phenol (0.02 mol) were heated at 180 °C for 5 min (oil bath). The mixture was then dissolved in the minimum volume of acetone and the mesoionic compound 3 (R_1 = CN; R_2 = Ph) precipitated on addition of ether (Table I).[13]

Preparation of 14 (X = H, Cl, MeO). Oxathioles 14 were obtained by fusion of epoxides 1 and *O*-phenyl phenylcarbamothioate. The mixture was purified by column chromatography (alumina, ether as eluent) (Table III).[13]

Preparation of 14 (X = NO_2). When X = NO_2, the best yield of oxathiole 14 was obtained when epoxide 1 (0.005 mol) and *O*-phenyl phenylcarbamothioate (0.005 mol) in dioxane (20 mL) were heated for 24 h. Removal of the solvent and column chromatography (alumina, ether as eluant) of the residue give the oxathiole 14 (X = NO_2) (Table III).[13]

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Registry No.—1 (X = H), 33512-02-6; 1 (X = Cl), 33512-03-7; 1 (X = NO_2), 34559-52-9; 1 (X = MeO), 33441-62-2; 2 (R_1 = CH_3; R_2 = Ph), 637-53-6; 2 (R_1 = R_2 = Ph), 636-04-4; 2 (R_1 = *p*-$NO_2C_6H_4$; R_2 = Ph), 6244-77-5; 2 (R_1 = Ph; R_2 = $PhCH_2$), 14309-89-8; 2 (R_1 = Ph; R_2 = Et), 39203-76-4; 2 (R_1 = $N(Me)_2$; R_2 = Ph), 705-62-4; 2 (R_1 = SPh; R_2 = Ph), 27063-57-6; 2 (R_1 = OPh; R_2 = Ph), 2423-29-2; 5, 66702-50-9; 10 (X = H), 66702-51-0; 11, 66758-66-5; 2-imidazolidinethione, 96-45-7; 2(1*H*)-pyrimidinethione, 1450-85-7.

Supplementary Material Available: Full color, NMR, IR, UV, and mass spectral data for compounds **3** (Table I); NMR, IR, and mass spectral data for compounds **4** (Table II); IR, UV, and mass spectral data for compounds **14** (Table III) (3 pages). Ordering information is given on any current masthead page.

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Cycloaddition Reactions of Nitrile Sulfides with Acetylenic Esters. Synthesis of Isothiazolecarboxylates

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Evidence is reported for production of nitrile sulfides as reactive intermediates in the thermolysis of 1,3,4-oxathiazol-2-ones. The nitrile sulfides were trapped with dimethyl acetylenedicarboxylate to give good yields of dimethyl 3-substituted-4,5-isothiazoledicarboxylates **6a–t.** The diacids **7a–r** were readily converted to 3-substituted-4-isothiazolecarboxylic acids **8a–r** by thermal decarboxylation. 3-Aryl-4-isothiazolecarboxylates **9a,j,u–w** and 3-aryl-5-isothiazolecarboxylates **10a,j, u–w** were obtained in nearly equivalent amounts from nitrile sulfides and ethyl propiolate. Thermolysis of 5-methyl- and 5-phenyl-1,3,4-oxathiazol-2-ones in excess ethyl 2-butynoate and of 5-methyl-1,3,4-oxathiazol-2-one in excess ethyl phenylpropiolate resulted in excessive byproduct formation and low yields of isothiazoles. Thermolysis of 5-(α,α,α-trifluoro-*m*-tolyl)-1,3,4-oxathiazol-2-one (**5u**) in the presence of excess ethyl phenylpropiolate gave a product mixture which contained ethyl 3-(α,α,α-trifluoro-*m*-tolyl)-5-phenyl-4-isothiazolecarboxylate (**18**) (47% yield by GC) and ethyl 3-(α,α,α-trifluoro-*m*-tolyl)-4-phenyl-5-isothiazolecarboxylate (**19**) (9.5% yield by GC).

Nitrile ylides (**1**), nitrile imines (**2**), and nitrile oxides (**3**) all have been utilized in 1,3-dipolar cycloaddition reactions to form heterocycles.[1] Until very recently,[2–6] nitrile sulfides (**4**) were conspicuously missing from this series of 1,3-dipoles.

$RC{\equiv}N^+{-}C^-R'R''$ (**1**) $\quad RC{\equiv}N^+{-}N^-R'$ (**2**)

$RC{\equiv}N{\rightarrow}O$ (**3**) $\quad RC{\equiv}N{\rightarrow}S$ (**4**)

We report here evidence for the production of nitrile sulfides as reactive intermediates in the thermolysis of 1,3,4-oxathiazol-2-ones and reaction of the nitrile sulfides with acetylenic esters to form isothiazolecarboxylates in preparatively significant reactions.[7]

A report[8] that thermolysis of 5-phenyl-1,3,4-oxathiazol-2-one (**5a**) produced benzonitrile and sulfur suggested to us that benzonitrile sulfide **4a** was a possible intermediate in this reaction. Thermolysis of **5a** in the presence of dimethyl acetylenedicarboxylate (DMAD), in an experiment designed to trap the nitrile sulfide, resulted in isothiazoledicarboxylate **6a** (>90% yield); similarly, thermolysis of **5a** in the presence of ethyl propiolate gave isothiazolecarboxylates **9a** and **10a.**[2] These reactions now have been extended to a large variety of 5-substituted-1,3,4-oxathiazol-2-ones to produce the products outlined in Scheme I.

Formation of nearly equivalent amounts of **9** and **10** from ethyl propiolate and the various oxathiazolones is consistent only with a 1,3-dipolar cycloaddition reaction[9] (e.g., path A or path B, Scheme II). An alternative mechanism, path C, involving heterolysis of a bond of **5** to produce an ionic species **12,** followed by Michael addition of **12** to ethyl propiolate to give **13** and eventually **9,** is contrary to the observed formation of both **9** and **10.** Path C, as well as a similar homolytic mechanism, should produce **9** exclusively.[10]

A choice between path A and path B, which involves adduct (**11**) formation prior to loss of carbon dioxide, was made possible by the kinetic studies summarized in Table I. These studies, performed with varied concentrations of DMAD as the trapping agent, show that the rate of disappearance of **5a** is independent of the concentration of DMAD and is first order. Furthermore, the rate constants for formation of isothiazole and benzonitrile are both first order and equal to the rate constant for disappearance of **5a.** In the absence of DMAD, **5a** gave benzonitrile in 100% yield. These results rule out path B as a possible reaction mechanism and thus provide support for path A and benzonitrile sulfide as the reactive intermediate.

The order of rates of thermolysis of several 5-substituted-1,3,4-oxathiazol-2-ones is 5-CH_3 ≫ 5-$ClCH_2$ > 5-EtO_2C and 5-*o*-$CH_3C_6H_4$, 5-*m*-$CH_3C_6H_4$, 5-*p*-$CH_3C_6H_4$ > 5-C_6H_5 > 5-*m*-ClC_6H_4 > 5-*m*-$CF_3C_6H_4$ > 5-[3,5-$(CF_3)_2C_6H_3$], 5-*p*-NCC_6H_4, 5-*p*-$O_2NC_6H_4$, indicative of development of a partial positive charge at the 5 position in the transition state for

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