Reaction of Azibenzil with Thiobenzophenone and Thiofluorenone: Isolation of 1,3-Oxathiole and α-Keto Episulfide[1]

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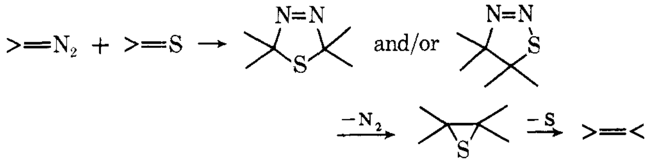
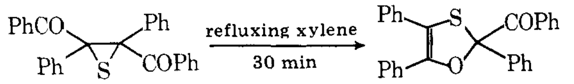
The reactions of azibenzil (1) with thiobenzophenone (2) and thiofluorenone (6) were investigated. In the reaction of 1 with 2, the 1,3-oxathiole 3 and/or the 1:1 adduct 4 of diarylketene and 2 were isolated, while α-keto episulfide 7 was obtained in the reaction of 1 with 6.

The reaction of diazo alkanes with thioketones has been extensively studied and is useful for olefin synthesis. The intermediate episulfides were often isolated, and recently even the unstable initial adducts, Δ^3-1,3,4- and/or Δ^2-1,2,3-thiadiazolines, have been isolated.[2,3]

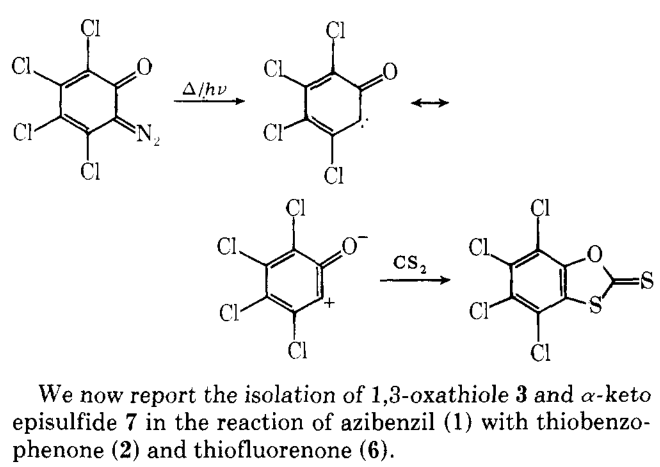


The reaction of α-diazo ketones and α-diazo esters with thiocarbonyls is considered to proceed similarly, and the α,β-unsaturated carbonyl compounds were obtained;[4] however, the intermediate α-keto episulfide has not been isolated.

Recently, the thermal conversion of *trans*-1,2-dibenzoyl-1,2-diphenyl episulfide into the corresponding 1,3-oxathiole was reported to take place smoothly and quantitatively.[5]



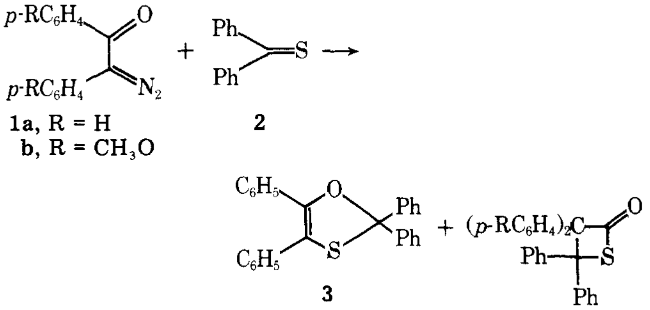
It seems curious that no paper deals with 1,3-oxathiole formation by the reaction of α-diazo compounds with thiocarbonyls except that of Huisgen et al.; the 1,3-dipolar addition of ketocarbene generated thermally and photochemically from α-diazo compounds to phenyl isothiocyanate, carbon disulfide, and *o*-ethyl thiobenzoate gave the corresponding 1,3-oxathioles.[6]



We now report the isolation of 1,3-oxathiole 3 and α-keto episulfide 7 in the reaction of azibenzil (1) with thiobenzophenone (2) and thiofluorenone (6).

Results and Discussion

An equimolecular mixture of azibenzil (**1a**) and **2** in benzene was heated at reflux for 30 min. After removal of the solvent in vacuo, the residue was column chromatographed on alumina using benzene as an eluent to give 2,2,4,5-tetraphenyl-1,3-oxathiole (**3**) and the 1:1 adduct **4a** of diphenylketene and **2** in 31 and 8% yields, respectively. The reaction of 4,4′-dimethoxyazibenzil (**1b**) with **2** under the same reaction conditions gave only **4b**, and no 1,3-oxathiole was isolated.



1a, R = H
b, R = CH_3O

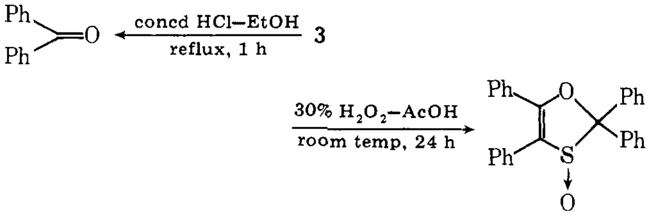
2

3

4a, R = H
b, R = CH_3O

When anhydrous cuprous sulfate was added to the mixture of **1a** and **2** in order to surpress the Wolff rearrangement of **1a**, vigorous gas evolution was observed even at room temperature. The oxathiole **3** was not observed, and only a large amount of intractable resinous materials was obtained. This suggests that not ketocarbene but **1a** itself might participate in the formation of **3**.

The structure of **3** was deduced on the basis of analysis and spectral data, as well as from its chemical conversions. Comparison of the ^{13}C NMR spectrum of **3** with those of 1,3-oxathioles[5] known heretofore was especially helpful. Hydrolysis gave benzophenone, and hydrogen peroxide oxidation in acetic acid afforded the corresponding *S*-oxide **5** at room temperature in 43% yield.



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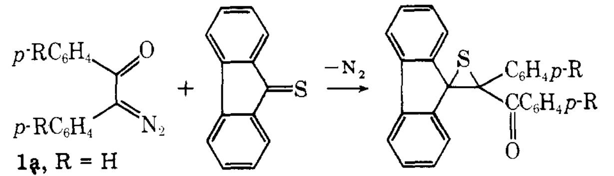
When benzene solutions of **1a–d** were added at room temperature in one portion to a benzene solution of thiofluorenone (**6**), the initial deep color of **1** and **6** disappeared immediately with evolution of nitrogen. This observation is a further indication that the reaction of **1** with **6** also does not proceed via



1a, R = H
b, R = CH_3O
c, R = CH_3
d, R = Cl

6

7a, R = H
b, R = CH_3O
c, R = CH_3
d, R = Cl

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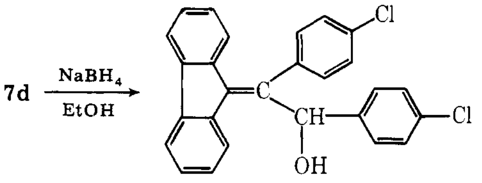
Table I. 1-Aryl-1-aroyl-2,2-fluorenylidene Episulfide (7)

			^{13}C NMR, δ			
Compd	Yield, %	Mp, °C	C_1	C_2	C=O	CH_3
7a	35	131–133	63.9	55.9	193.0	
7b	82	159–160	63.5	56.1	191.6	55.2 55.4
7c	20	182–184	63.9	55.9	192.7	21.1 21.6
7d	86	211–213	62.9	56.1	191.7	

the carbene. Then the reaction mixture was heated at reflux for 30 min for the completion of the reaction. The residue obtained by removal of the solvent in vacuo was subjected to trituration with solvent and/or to silica gel column chromatography to give colorless prisms (**7a–d**) in the yields shown in Table I. The yields of **7a** and **7c** are very low compared with those of **7b** and **7d**; however, the reason for this is not clear.

The empirical formula of 7 agreed with those of 1,3-oxathioles; however, the presence of a carbonyl group was disclosed by the IR and ^{13}C NMR spectra. Reduction of **7d** with $NaBH_4$ gave the alcohol **8**. The structure of 7 was determined to be 1-aryl-1-aroyl-2,2-fluorenylidene episulfide.



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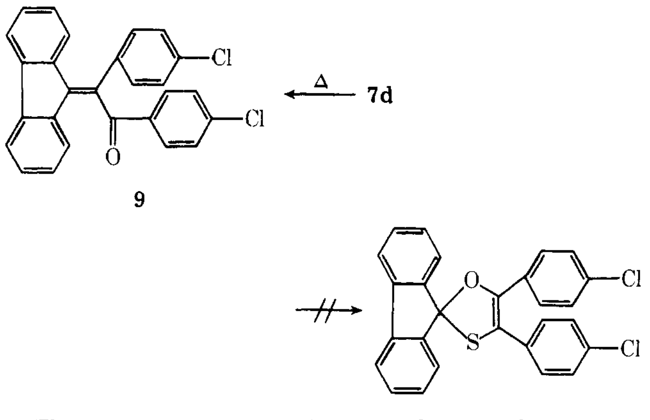
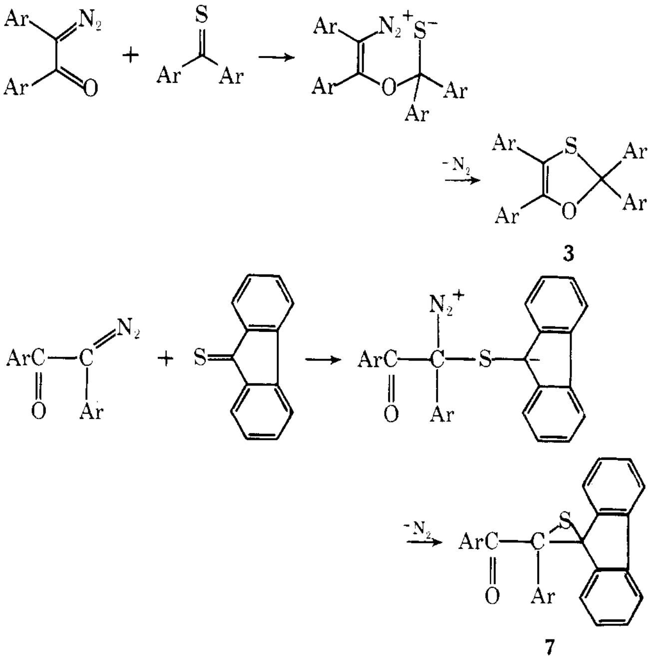
As mentioned earlier, *trans*-1,2-dibenzoyl-1,2-diphenyl episulfide was easily converted into the corresponding 1,3-oxathiole quantitatively.[5] Thus, the pyrolysis of **7d** was studied. The compound **7d** was found to be thermally rather stable, and after being refluxed in xylene for 24 h still 9% of **7d** was recovered with the corresponding α,β-unsaturated ketone **9**; however, the corresponding 1,3-oxathiole was not isolated.[7]



The formation of 1,3-oxathiole 3 and episulfide 7 is interpreted by the terms of the ambident electrophilic character of the thiocarbonyl group and also the ambident nucleophilic character of the diazocarbonyl function. The cyclopentadienide might be responsible for the "anomalous" behavior of thiofluorenone.

Experimental Section

All melting points are uncorrected. IR spectra were measured on a Nippon Bunko IR-A spectrometer as KBr pellets. ^{13}C NMR spectra were determined with a Nihon Denshi Jeol FT-100 spectrometer with Me_4Si as an internal standard in $CDCl_3$. Mass spectra were obtained on a Hitachi R-4 mass spectrometer at 70 eV using a direct inlet. UV spectra were measured on a Hitachi 124 spectrophotometer in ethanol.



Reaction of Azibenzil (1a) with Thiobenzophenone[8] (2). An equimolecular mixture of **1a** (1.00 g) and **2** (0.90 g) in benzene (20 mL) was heated at reflux for 0.5 h. The reaction mixture was condensed to half of its volume and subjected to column chromatography on silica gel (Wako gel C-300) using benzene as an eluent to afford **3** (0.59 g, 31%) and **4a**[9] (0.15 g, 8%). Recrystallization of **3** from ethanol gave pale yellow prisms of mp 146–146.5 °C: IR 1610 (C=C), 1220 (C=C—O-) cm^{-1}; UV λ_{max} 343 nm (ϵ 7550); MS *m/e* (relative intensity) 392 (M^+, 51), 360 ($M^+ - S$, 100); ^{13}C NMR δ 99.7 (C_2), 111.4 (C_4), 143.8 (C_5). Anal. Calcd for $C_{27}H_{20}OS$: C, 82.63; H, 5.14. Found: C, 82.47; H, 5.12.

Reaction of 4,4′-Dimethoxyazibenzil (1b) with Thiobenzophenone (2). An equimolecular mixture (3.55 mmol) of **1b** and **2** in benzene (15 mL) was heated at reflux for 30 min. Evaporation of the solvent in vacuo and trituration of the residue with ethanol afforded **4b** in 44% yield as colorless needles from ethanol: mp 177–179 °C dec; IR 1738 (C=O) cm^{-1}. Anal. Calcd for $C_{29}H_{24}O_3S$: C, 76.97; H, 5.35. Found: C, 76.81; H, 5.32.

Oxidation of 2,2,4,5-Tetraphenyl-1,3-oxathiole (3) with Hydrogen Peroxide. A mixture of 130 mg of **3** and 0.5 mL of a 30% aqueous H_2O_2 solution in 4 mL of acetic acid was stirred at room temperature for 24 h. The reaction mixture was poured into water, and white precipitate was collected by filtration and then washed with ethanol. The ethanol washings were evaporated in vacuo, and the residue was triturated with a small amount of ethanol to give 58 mg (43%) of **5** as colorless prisms from hexane–ethanol: mp 192–193 °C; IR 1070 (S-O) cm^{-1}. Anal. Calcd for $C_{27}H_{20}O_2S$: C, 79.39; H, 4.94. Found: C, 79.42; H, 4.96.

Reaction of 1a with Thiofluorenone (6).[10] A benzene solution (25 mL) of **6** (1.65 g, 8.45 mmol) was added at room temperature to a benzene solution (25 mL) of **1a** (1.86 g, 8.45 mmol). Immediately the deep color of the starting materials faded away with evolution of nitrogen. The reaction mixture was heated at reflux for 0.5 h for the completion of the reaction. After being cooled to room temperature, the residue was treated with ether to give 545 mg of **7a**. The ether filtrate was column chromatographed on silica gel (Wako gel C-300) using benzene as an eluent to give 601 mg of **7a** as colorless prisms from ethanol; IR 1660 (C=O) cm^{-1}. Anal. Calcd for $C_{27}H_{10}OS$: C, 83.06; H, 4.64. Found: C, 83.01; H, 4.58.

Reaction of 1b with 6. A benzene solution (10 mL) of **6** (0.32 g, 1.6 mmol) was added at room temperature to a benzene solution (10 mL) of **1b** (0.46 g, 1.6 mmol), and the mixture was heated at reflux for 0.5 h. The reaction mixture was condensed to half of its volume in vacuo and column chromatographed on silica gel (Wako gel C-300) using benzene as an eluent to give 602 mg of **7b** as colorless prisms from ethanol; IR 1660 (C=O) cm^{-1}. Anal. Calcd for $C_{29}H_{22}O_3S$: C, 77.32; H, 4.92. Found: C, 76.96; H, 4.85.

Reaction of 1c with 6. A benzene solution (15 mL) of **6** (814 mg, 3.26 mmol) was added at room temperature to a benzene solution (15 mL) of **1c** (637 mg, 3.26 mmol), and the reaction mixture was heated at reflux for 0.5 h. The reaction mixture was evaporated, and the residue was column chromatographed on silica gel (Wako gel C-300) using benzene as an eluent to give 277 mg of **7c** as colorless prisms 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

(1) A part of this paper was reported in a preliminary communication: S. Mataka, S. Ishi-i, and M. Tashiro, *Chem. Lett.*, 955 (1977).
(2) C. E. Dieber, *J. Org. Chem.*, **35**, 1501 (1970).
(3) A. P. Krapcho, D. R. Rao, M. P. Silvon, and B. Abegaz, *J. Org. Chem.*, **36**, 3885 (1971).
(4) A. Schönberg and E. Frese, *Chem. Ber.*, **96**, 2420 (1963).
(5) U. Jacobsson, T. Kempe, and T. Norin, *J. Org. Chem.*, **39**, 2722 (1974).
(6) R. Huisgen, H. König, G. Brinsch, and H. J. S. Sturm, *Angew. Chem.*, **73**, 368 (1961).
(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).
(10) E. Campaigne and W. B. Reid, *J. Am. Chem. Soc.*, **68**, 769 (1946).

Reaction of N-Substituted Thioamides with *gem*-Dicyano Epoxides: A New Synthetic Route to Anhydro-4-hydroxythiazolium Hydroxides

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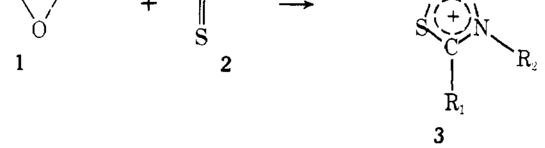
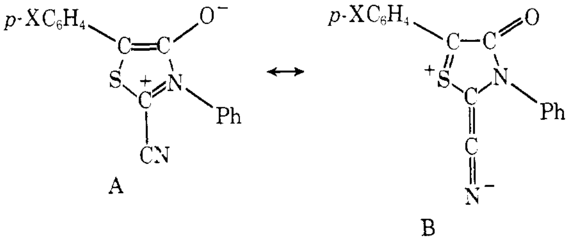
gem-Dicyano epoxides undergo ready reaction under neutral conditions with N-monosubstituted thioamides to provide a new, convenient synthesis of the anhydro-4-hydroxythiazolium hydroxide system. The epoxides act as potential 1,2-bielectrophiles, while the N-monosubstituted thioamides act as 1,3-binucleophiles, 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.

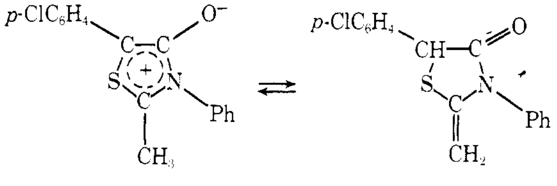
The reaction of the *gem*-dicyano epoxides **1** with the thiocarbonyl compounds **2** was generally carried out under neutral conditions at room temperature in acetone as solvent. The mesoionic thiazoles obtained are described in Table I, which illustrates the general nature of the reaction and the 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%

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