Anal. Calcd for $C_{45}H_{61}N_5O_9S_5$: C, 55.36; H, 6.30; N, 7.17; S, 16.42. Found: C, 55.89; H, 6.44; N, 7.15; S, 16.62.

N-[N-Carboxy-3-({2-[3-(phenyldithio)propionamido]ethyl} dithio)-N-benzyl-L-alanyl]-DL-methionine ethyl ester (XV) was prepared at −10° by adding 0.40 g (2.1 mmoles) of WSC to a solution of 1.05 g (2 mmoles) of III and 0.35 g (2 mmoles) of DCC in 40 ml of ethyl acetate. The mixture was stirred at ice temperature for 1 hr, then for 4 hr while warming to room temperature. The solution was transferred to a separatory funnel and washed with 200-ml portions of water, 2 *N* sulfuric acid, water, 5% sodium bicarbonate solution, water, and saturated sodium chloride solution. After drying, the solvent was removed *in vacuo* and the residual oil solidified upon drying *in vacuo*. The crude product was recrystallized from ethyl acetate–*n*-hexane to obtain 0.95 g (70%) of white buttons: mp 85–87°; homogeneous on tlc (system A); ν_{max}^{KBr} 3280, 3050, 2960, 2910, 1735, 1690, 1660, 1270, 1225, 1040, 740, 695 cm^{-1}. Two recrystallizations raised the melting point to 94–95°; $[\alpha]^{24}D$ 4.5° (*c* 1.0, chloroform).

Anal. Calcd for $C_{29}H_{39}N_3O_6S_5$: C, 50.78; H, 5.73; N, 6.13; S, 23.37. Found: C, 51.05; H, 5.91; N, 6.02; S, 23.23.

Ethyl DL-methionate (XVII) was prepared by the thionyl chloride esterification method of Brenner and Huber.[16] Fractional distillation gave product with bp 110–113° (1.7–2.0 mm); $n^{31}D$ 1.4763 (17% of theory based on DL-methionine) (lit.[17] bp 112° (2.5 mm); $n^{20}D$ 1.4819).

Registry No.—V, 15297-41-3; VI, 15297-42-4; 2-tritylthioethylamine hydrochloride, 15297-43-5; VII, 15296-99-8; VIII, 15297-01-5; IX, 15297-32-2; Xa, 15297-02-6; XI, 15297-03-7; XII, 15297-04-8; diethyl N,N-dibenzhydryloxycarbonyl-L-cystinyldiglycinate, 15297-05-9; XIV, 15297-00-4; XV, 15297-06-0.

Acknowledgment.—We are indebted to Dr. Kurt L. Loening of the Chemical Abstracts Service for assistance in the nomenclature of the bisdisulfide derivatives.

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[16] M. Brenner and W. Huber, *Helv. Chim. Acta*, **36**, 1109 (1953).

[17] E. Booth, V. Burnop, and W. Jones, *J. Chem. Soc.*, 666 (1944).

Chemistry of Aliphatic Disulfides. XVI. Studies on the Alkoxide Cleavage of 1,6-Diphenyl-3,4-dithia-1,6-hexanedione[1,2]

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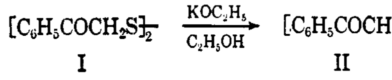
Received August 22, 1967

Treatment of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (I) with 2 equiv of potassium ethoxide provides dipotassio-1,4-diphenyl-1,4-butanedione 2,3-dimercaptide (VI) and potassio-1,4-diphenyl-2-butene-1,4-dione 2-mercaptide (VII) as the major products. A mechanism for the formation of VII is proposed to involve VI as the precursor

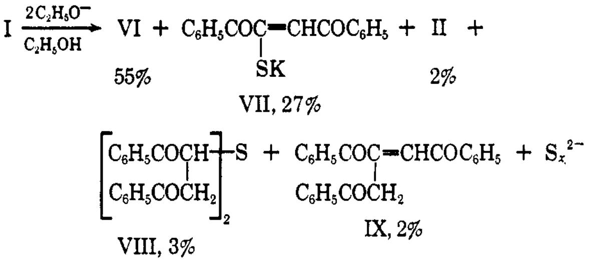
Groth[4] reported the unique conversion of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (diphenacyl disulfide, I) into 1,4-diphenyl-1,4-butanedione (II) with 1



$$\underset{\text{I}}{[C_6H_5COCH_2S]_2} \xrightarrow[C_2H_5OH]{KOC_2H_5} \underset{\text{II}}{[C_6H_5COCH_2]_2}$$

equiv of potassium ethoxide. Subsequent studies[5,6] confirmed these observations and clarified the structures of other products formed by the action of alkoxides on I. The results of these experiments are summarized in Chart I. It is pertinent to note that the nature of the products resulting from the action of ethoxide ion on I vary with the concentration of base used; at low base concentration 1,5-diphenyl-3-thiapentane-1,5-dione (III) resulted while at higher base concentrations the dipotassio mercaptide, VI, was formed. Since VI was previously proposed as a possible precursor of II, the formation and reactions of this substance were studied in more detail.

Cleavage of I with 2 Equiv of Potassium Ethoxide.—Treatment of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (I) with 2 equiv of potassium ethoxide in ethanol gave dipotassio-1,4-diphenyl-1,4-butanedione-2,3



$$\text{I} \xrightarrow[C_2H_5OH]{2C_2H_5O^-} \underset{55\%}{\text{VI}} + \underset{\text{VII, 27\%}}{C_6H_5C\underset{|}{O}C(SK){=}CHCOC_6H_5} + \underset{2\%}{\text{II}} + \underset{\text{VIII, 3\%}}{\left[\begin{matrix} C_6H_5COCH \\ C_6H_5COCH_2 \end{matrix}\right]_2 S} + \underset{\text{IX, 2\%}}{C_6H_5COC(CH_2COC_6H_5){=}CHCOC_6H_5} + S_x^{2-} \qquad (1)$$

dimercaptide (VI) in 55.2% yield (eq 1). In addition small amounts of 1,4-diphenyl-1,4-butanedione (II), 3,5-dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione (VIII), and 3-benzoyl-1,5-diphenyl-2-pentene 1,5-dione (IX) were isolated. When the aqueous extract of the reaction mixture was adjusted to pH 9 with carbon dioxide, a red-brown, nitroprusside-positive solid was obtained in 26.8% yield. The water-soluble salt was identified as potassio-1,4-diphenyl-2-butene-1,4-dione 2-mercaptide (VII) on the basis of the following evidence. The nmr spectrum of VII in D_2O showed an aromatic multiplet centered at τ 1.27 (3.85 H), a singlet at 2.00 (1.00 H), and an aromatic multiplet centered at 2.30 (6.30 H). The infrared spectrum of the salt showed a broad peak at 1635–1625, a medium peak at 1560, and a broad peak at 1500–1425 cm^{-1}. The infrared spectrum of VII along with its alkylation and acylation products contain a band in the 1560–1550-cm^{-1} region which is assigned as C=C absorption. Although this band falls considerably lower than the usual C=C stretching frequency, there is evidence that sulfur-linked C=C ab-

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[1] This investigation was supported by Public Health Service Fellowship 1-F3-GM-31,871-01 and by Research Grant RG 7966 from the National Institutes of General Medical Sciences.

[2] For part XV of the series, see R. G. Hiskey and M. A. Harpold, *J. Org. Chem.*, **33**, 559 (1968).

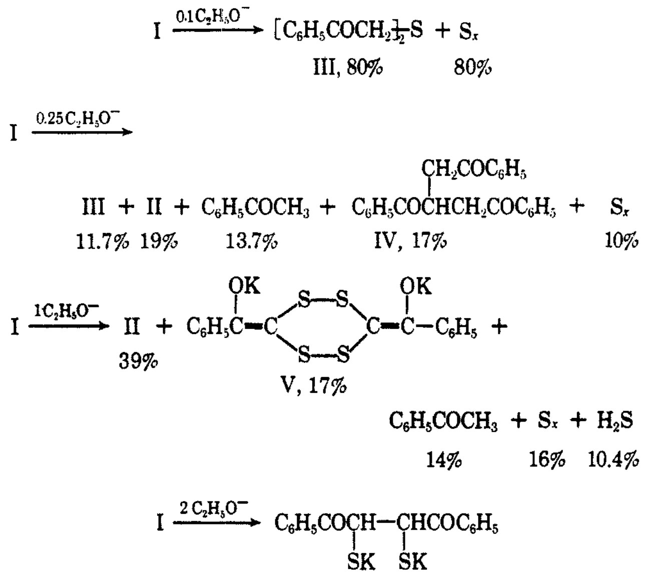
[3] Special Fellow, National Institute of General Medical Sciences, 1966–1967.

[4] B. Groth, *Arkiv Kemi Mineral. Geol.*, **9**, 1 (1924).

[5] R. G. Hiskey, B. D. Thomas, and J. A. Kepler, *J. Org. Chem.*, **29**, 3671 (1964).

[6] R. G. Hiskey, B. D. Thomas, and J. A. Kepler, *ibid.*, **29**, 3684 (1964).

Chart I



$$I \xrightarrow{0.1C_2H_5O^-} [C_6H_5COCH_2]_2S + S_x \quad \text{III, 80\%} \quad 80\%$$

$$I \xrightarrow{0.25C_2H_5O^-} \text{III} + \text{II} + C_6H_5COCH_3 + C_6H_5CO\underset{}{\overset{CH_2COC_6H_5}{CH}}CH_2COC_6H_5 + S_x$$

11.7% 19% 13.7% IV, 17% 10%

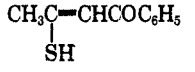
$$I \xrightarrow{1C_2H_5O^-} \text{II} + \text{V} + C_6H_5COCH_3 + S_x + H_2S$$

39% V, 17% 14% 16% 10.4%

$$I \xrightarrow{2C_2H_5O^-} C_6H_5CO\underset{SK}{CH}-\underset{SK}{CH}COC_6H_5$$

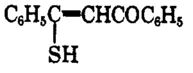
VI

sorption appears in this region.[7,8] In the spectra of two similar compounds, 3-mercapto-1-phenyl-2-buten-1-one (X) and 3-mercapto-1,3-diphenyl-2-propen-1-one (XI), C=C bands are found at 1530 and 1555 cm^{-1}, respectively.



$$CH_3\underset{SH}{C}=CHCOC_6H_5$$

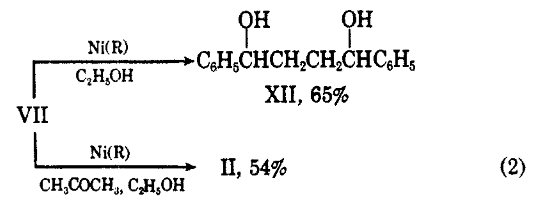
X



$$C_6H_5\underset{SH}{C}=CHCOC_6H_5$$

XI

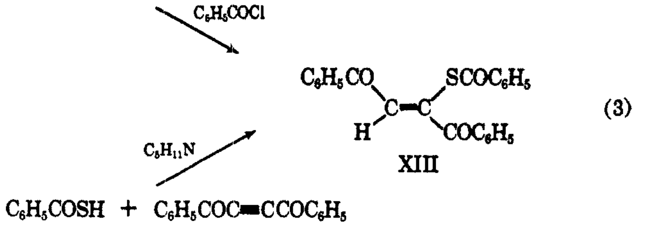
Desulfurization of VII with Raney nickel gave 1,4-diphenyl-1,4-butanediol (XII) in 65% yield; desulfurization with deactivated Raney nickel gave 1,4-diphenyl-1,4-butanedione (II) in 54% yield (eq 2).



$$\text{VII} \xrightarrow[C_2H_5OH]{Ni(R)} C_6H_5\overset{OH}{CH}CH_2CH_2\overset{OH}{CH}C_6H_5 \quad \text{XII, 65\%}$$

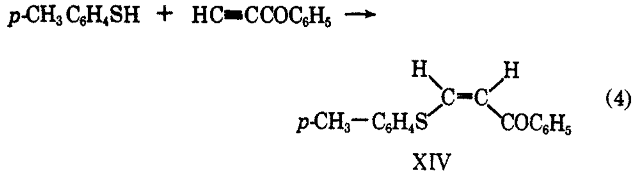
$$\text{VII} \xrightarrow[CH_3COCH_3,\ C_2H_5OH]{Ni(R)} \text{II, 54\%} \qquad (2)$$

Treatment of VII with benzoyl chloride in ether provided the unsaturated thiobenzoate XIII (eq 3). The infrared spectrum of XIII exhibited major peaks at 1680, 1670, 1650, and 1560 cm^{-1}. The nmr spectrum of XIII showed the following proton groups: an aromatic multiplet centered at τ 2.04 (6.3 H), a singlet at 2.16 (1.0 H), and an aromatic multiplet centered at 2.62 (9.3 H). Confirmation of the structure of XIII was obtained through an independent synthesis utilizing the addition of 1 mole of thiolbenzoic acid to 1,4-diphenyl-2-butyne-1,4-dione. The stereochemistry of XIII is inferred from previous studies by Truce, *et al.*[9a,c] These investigations have firmly established that nucleophilic addition of thiols to acetylenes occurs by *trans* addition; for example, the addition of *p*-toluenethiol to phenyl ethynyl ketone (eq 4) provided *cis*-1-benzoyl-2-(*p*-tolylthio)-1-butene (XIV).[9b]



$$\text{VII} \xrightarrow{C_6H_5COCl} (C_6H_5CO)HC=C(SCOC_6H_5)(COC_6H_5) \xleftarrow{C_5H_{11}N} C_6H_5COSH + C_6H_5COC\equiv CCOC_6H_5 \qquad (3)$$

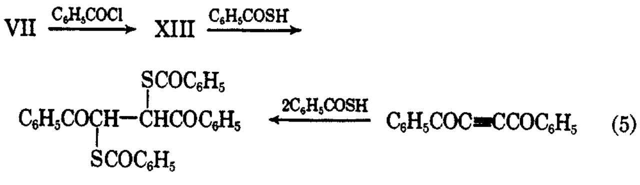
XIII



$$p\text{-}CH_3C_6H_4SH + HC\equiv CCOC_6H_5 \longrightarrow (p\text{-}CH_3-C_6H_4S)HC=CH(COC_6H_5) \qquad (4)$$

XIV

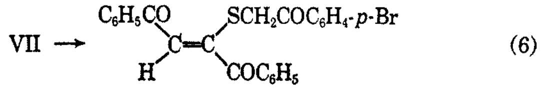
Additional support for the structure of XIII and, subsequently VII, was obtained by allowing the addition of thiolbenzoic acid to 1,4-diphenyl-2-butyne-1,4-dione to go to completion. The dithiolbenzoate XV could be obtained either from the addition of 2 moles of thiolbenzoic acid to 1,4-diphenyl-2-butyne-1,4-dione or from the addition of 1 mole of thiolbenzoic acid to XIII obtained through benzoylation of VII (eq 5).



$$\text{VII} \xrightarrow{C_6H_5COCl} \text{XIII} \xrightarrow{C_6H_5COSH} C_6H_5CO\underset{SCOC_6H_5}{CH}-\overset{SCOC_6H_5}{CH}COC_6H_5 \xleftarrow{2C_6H_5COSH} C_6H_5COC\equiv CCOC_6H_5 \qquad (5)$$

XV

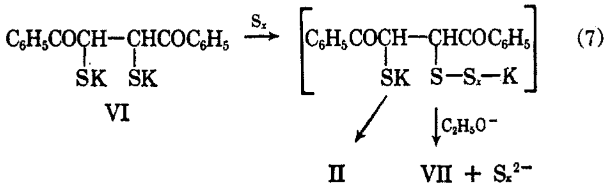
Alkylation of VII with *p*-bromophenacyl bromide provided the sulfide XVI (eq 6). This substance exhibited major peaks in the infrared at 1690, 1670, 1640, and 1550 cm^{-1}.



$$\text{VII} \longrightarrow (C_6H_5CO)HC=C(SCH_2COC_6H_4\text{-}p\text{-}Br)(COC_6H_5) \qquad (6)$$

XVI

Dipotassio-1,4-diphenyl-1,4-butanedione 2,3-Dimercaptide (VI) as the Precursor of VII.—Of the products isolated from the potassium ethoxide cleavage of I, the dimercaptide VI was considered to be the most likely source of VII. The dimercaptide VI was previously shown to provide 1,4-diphenyl-1,4-butanedione (II) when treated with elemental sulfur[6] (eq 7), and the base-catalyzed loss of hydrosulfide ion giving VII appeared likely. However, when a suspension of VI in ethanol was treated with either 1 or 2 equiv of potassium ethoxide, only starting material was recovered. Thus, a second possibility involving the loss of polysulfide rather than sulfide from VI was tested. Indeed,



$$C_6H_5CO\underset{SK}{CH}-\underset{SK}{CH}COC_6H_5 \xrightarrow{S_x} \left[C_6H_5CO\underset{SK}{CH}-\underset{S-S_x-K}{CH}COC_6H_5\right] \longrightarrow \text{II};\ \xrightarrow{C_2H_5O^-} \text{VII} + S_x^{2-} \qquad (7)$$

VI

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[7] S. H. H. Chaston, S. E. Livingstone, T. N. Locyer, V. A. Pickles, and J. S. Shannon, *Australian J. Chem.*, **18**, 673 (1965).

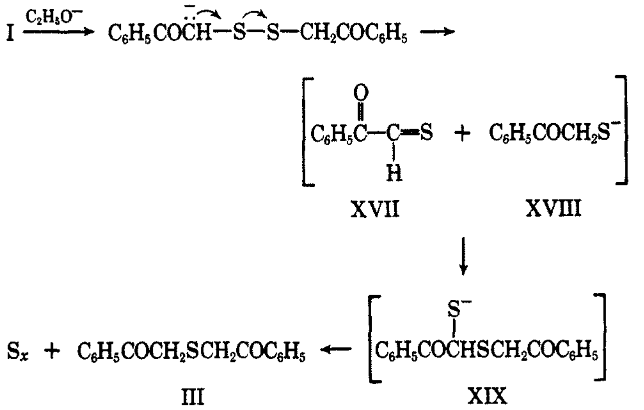
[8] L. J. Bellamy in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961, p 54.

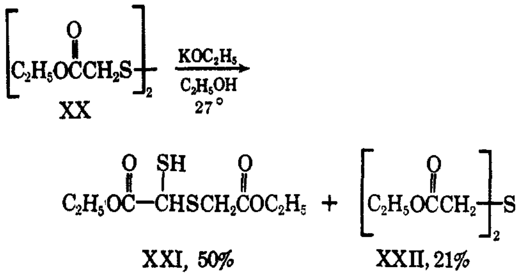
[9] (a) W. F. Truce and J. A. Simms, *J. Am. Chem. Soc.*, **78**, 2756 (1956); (b) S. I. Miller, *ibid.*, **78**, 6091 (1956); (c) W. F. Truce and R. F. Heine, *ibid.*, **79**, 5311 (1957).

when a suspension of VI in ethanol was treated with elemental sulfur followed by addition of potassium ethoxide, VII was produced. When 1 equiv of ethoxide was employed, a 50% yield of VII was obtained; the yield of VII increased to 63.4% when the ratio of ethoxide to VI was increased to 2:1.

Mechanism of the Alkoxide Cleavage of 1,6-Diphenyl-3,4-dithia-1,6-hexanedione (I).—Of the mechanistic pathways which have been proposed for alkaline disulfide cleavage, the one most compatible with our data involves "α elimination" of a mercaptide from I. The active methylene group between the carbonyl group and sulfur atom would readily lose a proton upon treatment with ethoxide giving rise to an intermediate carbanion which could decompose by "α elimination" producing phenylglyoxthial (XVII) and phenacyl mercaptide (XVIII). Recombination of XVII and XVIII would yield the hemidithioacetal XIX (see Scheme I). Although XIX could not be isolated, the formation of the sulfide III in 80% yield from the treatment of I with 0.1 equiv of potassium ethoxide suggests an intermediate of this type may be formed. Although relatively little is known of the preparations or reactions of hemidithioacetals, Howard[10] has reported that treatment of diethyl 3,4-dithiadipate (XX) with sodium methoxide in ether at −20° gives diethyl 2-mercapto-3-thiaglutarate (XXI) *via* an intramolecular pathway. These results could also be rationalized by "α elimination" of the mercaptide, followed by addition of the mercaptide to the thiocarbonyl as in the conversion of I to III. In order to determine whether a hemidithioacetal could yield a sulfide by a pathway of this type, the generation of XXI was reinvestigated. When Howard's procedure using sodium methoxide in ether was repeated, a mixture of two products was obtained. The mass spectral fragmentation pattern of the mixture revealed the presence of XXI and the corresponding methyl ester indicating that ester interchange had occurred. When Howard's experiment was repeated at −20° using potassium ethoxide rather than sodium methoxide, a 62% yield of XXI was obtained; however, when the procedure was repeated at 27°, a 50% yield of XXI was obtained along with a 21% yield of diethyl 3-thiaglutarate (XXII) (eq 8). Although the isolation of XXII from the reaction mixture supports the proposed conversion of I into III, a more detailed knowledge of the decomposition of XXI was desired. In that XXII is similar to the production of III and suggests the loss of elemental sulfur from the hemidithioacetal XXI, the potassium salt of XXI was treated with elemental sulfur. In accord with the proposed pathway for the formation of III, the sulfide XXII was obtained in 10% yield. The low yield of XXII can probably be attributed to its instability in the presence of base; for example, treatment of the sulfide XXII with 1 equiv of potassium ethoxide gave a mixture of products when followed by thin layer chromatography. Additional support for the instability of XXII to base was obtained from treatment of the disulfide XX with 2 equiv of potassium ethoxide. Only a 0.1% yield of XXII was obtained along with a 68% yield of XXI.

SCHEME I

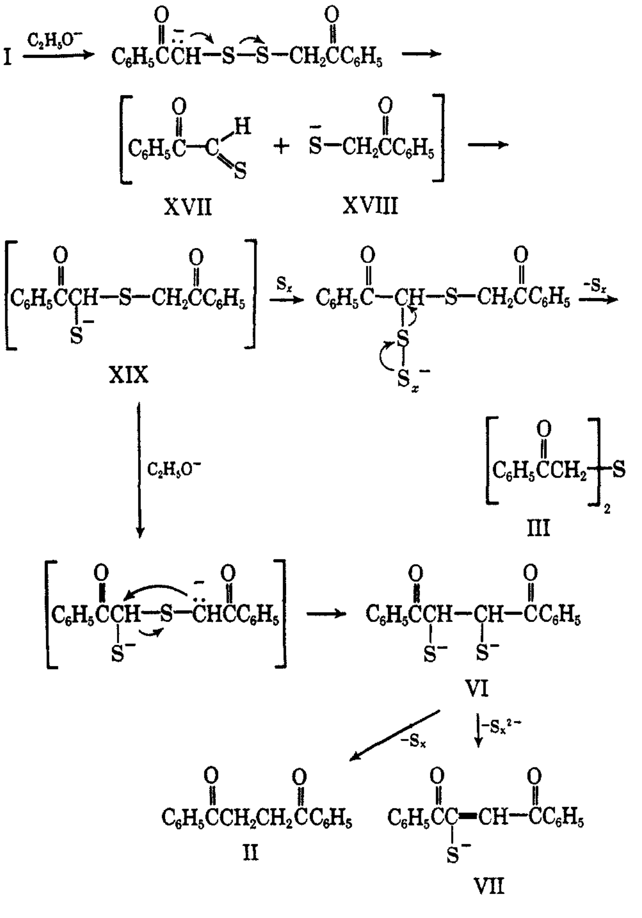




(8)

These data provide additional evidence for the route[6] by which I is converted to products. The concentration of base would be expected to be a significant factor in determining the favored pathway. Low base concentration would lead to III, whereas higher base concentrations would afford VI and subsequently II or VII. The mechanistic pathway that best incorporates the available data is summarized in Chart II.

CHART II



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[10] E. G. Howard, *J. Org. Chem.*, **27**, 2212 (1962).

Experimental Section[11]

Preparation of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (I) was according to the procedure of Hiskey, *et al.*,[5] mp 78–79° (lit.[4] mp 81°).

Preparation of 1,4-diphenyl-1,4-butanedione (II) was according to the procedure of Conant and Lutz[12] mp 144–145° (lit.[12] mp 144–145°).

Preparation of 3,5-dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione (VIII) was according to the procedure of Hiskey and Kepler,[13] mp 196–197° (lit.[13] mp 194–196°).

Preparationof 1,4-diphenyl-2-butyne-1,4-dione was according to the procedure of Lutz and Smithey[14] in 78% yield, mp 109–111° (lit.[14] mp 110–111°).

Preparation of 1,4-Diphenyl-1,4-butanediol (XII).—To 1.0 g (4.2 mmoles) of 1,4-diphenyl-1,4-butanedione (II) in 20 ml of 95% ethanol was added a solution containing 0.38 g (10 mmoles) of sodium borohydride in 5 ml of ethanolic 0.2 *N* sodium hydroxide. The reaction mixture was stirred at reflux temperature for 1 hr. The mixture was concentrated to 5 ml and the residue partitioned between 10 ml of chloroform and 10 ml of water. The chloroform layer was heated to 50° and petroleum ether (30–60°) added until cloudiness persisted. Cooling gave 0.63 g (62.5%) of colorless needles, mp 89–90°. Recrystallization from chloroform–hexane raised the melting point to 91–92° (lit.[15] mp 89–90°).

Preparation of 3-benzoyl-1,5-diphenyl-2-pentene-1,5-dione (IX) was according to the procedure of Yates, *et al.*,[16] in 18.8% yield, mp 124–125° (lit. mp[16] 122–123°).

Preparation of Diethyl 3,4-Dithiadipate (XX).—A solution of 78.0 g (0.65 mole) of ethyl mercaptoacetate in 325 ml of dimethyl sulfoxide was stirred at 85° for 15 hr. After cooling to room temperature, the reaction mixture was poured into 2.5 l. of cold water bringing about separation of a colorless oil. The oil was extracted with 500 ml of ether. The ether layer was washed with water, dried over anhydrous magnesium sulfate, and evaporated *in vacuo* giving 77.0 g of colorless liquid. The liquid was distilled giving 66.2 g (85.5%) of diethyl 3,4-dithiadipate: bp 122° (0.5 mm) (lit.[17] bp 164° (14 mm)); n^{25}_{D} 1.4975 (lit.[18] n^{25}_{D} 1.4979).

Anal. Calcd for $C_8H_{14}O_4S_2$: C, 40.31; H, 5.92; S, 26.91; mol wt, 238. Found: C, 40.58; H, 5.97; S, 26.98; mol wt, 238 (mass spectrometry).

Preparation of Diethyl 3-Thiaglutarate (XXII).—To 60 g (0.25 mole) of sodium sulfide nonahydrate dissolved in a mixture of 250 ml of ethanol and 150 ml of water was added 83.5 g (0.50 mole) of ethyl bromoacetate. The reaction mixture was stirred at 80° for 16 hr. The ethanol was removed *in vacuo* leaving a turbid aqueous solution. The mixture was extracted with two 150-ml portions of ether. The ether layers were combined, dried over anhydrous magnesium sulfate, and evaporated *in vacuo* leaving 31.0 g of colorless liquid. Distillation gave 23.7 g (51.5%) of diethyl 3-thiaglutarate (LII): bp 97° (0.5 mm) (lit.[19] bp 267–268°); n^{25}_{D} 1.4632.

Anal. Calcd for $C_8H_{14}O_4S$: C, 46.58; H, 6.84; S, 15.55; mol wt, 206. Found: C, 46.34; H, 6.81; S, 15.60; mol wt, 206 (mass spectrometry).

Preparation of Diethyl 2-Mercapto-3-thiaglutarate (XXI).—Following the procedure of Howard,[10] a sodium ethoxide solution prepared by the addition of 1.73 g (0.074 g-atom) of sodium to 45 ml of ethanol was diluted with 150 ml of anhydrous ether and cooled to −20°. To the stirred mixture was added 17.85 g (0.074 mole) of diethyl 3,4-dithiadipate (XX). To the yellow reaction mixture at −20° was added a cold solution of 15 ml of concentrated hydrochloric acid in 150 ml of water. The yellow ether layer was removed, dried over anhydrous magnesium sulfate, and evaporated *in vacuo* giving 16.2 g of a yellow liquid. Analysis of the liquid by gas chromatography indicated 10.0 g (62%) of XXI and 6.2 g (38%) of recovered XX were present. The sample was distilled giving 7.7 g of diethyl 2-mercapto-3-thiaglutarate (XXI), bp 135–138° (0.5 mm) (lit.[10] bp 103–104° (0.10 mm)). The infrared spectrum showed peaks at 2550 and 1740 cm^{-1}. The nmr spectrum showed a doublet centered at τ 5.4 (J = 9.5 cps, 1.0 H), two superimposed quartets centered at 5.9 (J = 8.0 cps, 4.0 H), a doublet centered at 6.5 (J = 6.0 cps, 2.3 H), a doublet centered at 7.2 (J = 9.5 cps, 1.0 H), and two superimposed triplets centered at 8.8 (J = 8.0 cps, 6.0 H).

Cleavage of 1,6-Diphenyl-3,4-dithia-1,6-hexanedione (I) with 2 Equiv of Potassium Ethoxide.—To a solution of 11.12 g (0.133 moles) of potassium ethoxide in 60 ml of ethanol was added 20 g (0.066 mole) of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (I). The disulfide reacted immediately giving a clear red solution. After 5 min the solution became cloudy and after 10 min solid formation was observed. The mixture was allowed to stand at 28° for 24 hr, 150 ml of anhydrous ether was added, and the mixture cooled for 2 hr. The solid was filtered and washed with ethanol to give 15.1 g of yellow solid and a red filtrate.

The solid was triturated in 100 ml of water giving a yellow solution and white solid. The solid was removed by filtration and washed with water to give 0.55 g (3.3%) of 3,5-dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione (VIII), mp 185–190°. Recrystallization from ethanol–chloroform raised the melting point to 194–196° (lit.[13] mp 194–196°).

Anal. Calcd for $C_{32}H_{26}O_4S$: C, 75.86; H, 5.17; S, 6.33; mol wt, 506. Found: C, 75.96; H, 5.10; S, 6.78; mol wt, 506 (mass spectrometry).

The product was found to be identical with authentic VIII by mixture melting point determination and infrared spectral comparison. The aqueous filtrate from separation of VIII was evaporated *in vacuo* to give 14.0 g (55.2%) of dipotassio 1,4-diphenyl-1,4-butanedione 2,3-dimercaptide (VI), mp 160–165° (lit.[5] mp 167–170°). When VI was treated with acetyl chloride in ether, 2,3-diacetylthio-1,4-diphenyl-1,4-butanedione was obtained in 76% yield, mp 200–202° (lit.[5] mp 200–204°).

The red filtrate from the separation of the mixture of VIII and VI was evaporated *in vacuo* leaving a red residue which was partitioned between 75 ml of water and 75 ml of ether.

The ether layer was evaporated *in vacuo* giving a pale orange gum which gave two spots on tlc. The gum was dissolved in hot chloroform–methanol. Cooling gave 0.26 g (1.1%) of 3-benzoyl-1,5-diphenyl-2-pentene-1,5-dione (IX), mp 119–122°. Recrystallization from methanol gave orange needles, mp 124–125° (lit.[20] mp 122–123°).

Anal. Calcd for $C_{24}H_{18}O_3$: C, 81.37; H, 5.12; mol wt, 354. Found: C, 81.17, 81.05, 81.20, 81.38; H, 5.00, 5.47, 5.28, 5.12; mol wt, 354 (mass spectrometry).

The sample was found to be identical with authentic IX by mixture melting point determination and infrared spectral comparison. The filtrate from separation of IX was reduced in volume and cooled to give 0.26 g (1.7%) of 1,4-diphenyl-1,4-butanedione (II), mp 139–142°. Recrystallization from ethanol raised the melting point to 144–145° (lit.[12] mp 144–145°). The sample was found to be identical with authentic II by mixture melting point determination and infrared spectral comparison.

The aqueous layer of pH 12.5 was treated with carbon dioxide until pH 9 was reached. The solution was filtered giving an additional 0.12 g (0.5%) of IX, mp 118–122°; total yield of IX was 0.38 g (1.6%). The filtrate was evaporated *in vacuo* leaving a red residue which was treated with 50 ml of absolute ethanol. The solution was filtered removing potassium carbonate and the filtrate evaporated *in vacuo* to give 5.4 g (26.8%) of potassio-1,4-diphenyl-2-butene-1,4-dione 2-mercaptide (VII), mp 118–121°. The hygroscopic red-brown solid gave a positive mercaptide test with sodium nitroprusside. The ultraviolet and visible spectra showed $\lambda_{\max}^{\mathrm{EtOH}}$ 245 mμ (ϵ 15,200) and $\lambda_{\max}^{\mathrm{EtOH}}$ 405 mμ (ϵ 14,150).

Formation of 2,3-Dimercapto-1,4-diphenyl-1,4-butanedione.—To a solution containing 0.80 g (0.0035 mole) of VI in 20 ml of water was added with stirring 60 ml of 0.1 *M* hydrochloric acid. The resulting solid was removed by filtration and washed with water and ether to 0.61 g (95.5%) of pale yellow solid, mp 157–162°. Recrystallization from acetone raised the melting point to 165–166°.

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(11) Melting points were taken on a Fisher-Johns block and are uncorrected. Spectra were determined on a Perkin-Elmer Model 237B (infrared), Perkin-Elmer Model 202 (ultraviolet and visible), Varian Associates A-60 (nmr), and Hitachi Perkin-Elmer RMU-6E (mass spectrometry). Vapor phase chromatography was carried out with a F & M Model 500 gas chromatograph. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.

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Anal. Calcd for $C_{16}H_{14}O_2S_2$: C, 63.54; H, 4.67; S, 21.21; mol wt, 302. Found: C, 63.48; H, 4.60; S, 20.94; mol wt, 302 (mass spectrometry).

The infrared spectrum (KBr) showed a sharp peak at 2525 and a strong peak at 1655 cm^{-1}.

Formation of *trans*-2-(*p*-Bromophenacylthio)-1,4-diphenyl-2-butene-1,4-dione (XVI).—To a solution of 1.00 g (0.0033 mole) of VII in 10 ml of ethanol was added a solution containing 0.92 g (0.0033 mole) of *p*-bromophenacyl bromide in 10 ml of hot ethanol. The mixture was stirred at reflux temperature for 1 hr. The mixture was cooled to room temperature; the resulting white solid was removed by filtration and washed with water and cold ethanol to give 1.26 g (82.5%) of XVI, mp 147–150°. Recrystallization from ethanol–chloroform raised the melting point to 155°.

Anal. Calcd for $C_{24}H_{17}O_3SBr$: C, 61.94; H, 3.68; S, 6.89; Br, 17.17; mol wt, 465. Found: C, 61.68; H, 4.00; S, 6.80; Br, 17.03; mol wt, 465 (mass spectrometry).

The nmr spectrum ($DCCl_3$) showed a multiplet centered at τ 2.08 and a singlet at 5.53 integrating 7.4 to 1.0. The ultraviolet spectrum showed λ_{max}^{EtOH} 263 mμ (ϵ 24,700) and λ_{infl}^{EtOH} 310 mμ (ϵ 9370).

Formation of *trans*-2-Benzoylthio-1,4-diphenyl-2-butene-1,4-dione (XIII).—To a suspension of 0.75 g (0.0021 mole) of VII in 10 ml of ether was added a solution of 1 ml of benzoyl chloride in 10 ml of ether. The mixture was stirred at room temperature for 2 hr. The resulting yellow solid was filtered, washed with 5% sodium bicarbonate, water, and ether to give 0.75 g (60%) of 2-benzoylthio *trans*-1,4-diphenyl-2-butene-1,4-dione (XIII), mp 117–120°. Recrystallization from ethanol–chloroform raised the melting point to 121°.

Anal. Calcd for $C_{23}H_{16}O_3S$: C, 74.17; H, 4.33; S, 8.61; mol wt, 372. Found: C, 73.84, 73.53; H, 4.53, 4.31; S, 9.15, 8.63; mol wt, 372 (mass spectrometry), 369 (osmometry, benzene).

The ultraviolet and visible spectra showed λ_{max}^{EtOH} 265 mμ (ϵ 25,700), 310 (14,050), and 402 (3470).

Preparation of *trans*-2-Benzoylthio-1,4-diphenyl-2-butene-1,4-dione (XIII).—To a solution of 1.0 g (0.0043 mole) of 1,4-diphenyl-2-butyne-1,4-dione in 50 ml of ether was added 0.60 g (0.0043 mole) of thiolbenzoic acid. The reaction mixture was stirred at reflux temperature for 1.5 hr. The solution was concentrated to 20 ml and cooled producing 1.03 g (64.5%) of yellow crystals, mp 119–120°. Recrystallization from ethanol–chloroform raised the melting point to 121°. The product was shown to be identical with XIII obtained from VII by mixture melting point determination and infrared spectral comparison. When the preparation was repeated using two drops of piperidine as catalyst, 1.14 g (71.8%) of XIII (mp 116–119°) was obtained.

Preparation of 2,3-Dibenzoylithio-1,4-diphenyl-1,4-butanedione (XV). A. From Addition of 2 Moles of Thiolbenzoic Acid to 1,4-Diphenyl-2-butyne-1,4-dione.—To a solution of 1.0 g (0.0043 mole) of 1,4-diphenyl-2-butyne-1,4-dione in 20 ml of benzene was added 1.2 g (0.0086 mole) of thiolbenzoic acid. The mixture was stirred at reflux temperature for 1.5 hr; 50 ml of hexane was added and the solution cooled to room temperature giving 1.76 g (81%) of colorless solid, mp 195–197°. Recrystallization from benzene raised the melting point to 198–199°.

Anal. Calcd for $C_{30}H_{22}O_4S_2$: C, 70.56; H, 4.34; S, 12.56; mol wt, 510. Found: C, 70.86; H, 4.53; S, 12.26; mol wt, 516 (osmometry, benzene).

The infrared spectrum (KBr) showed a doublet at 1675 cm^{-1}. The nmr spectrum showed a multiplet centered at τ 2.05 and a singlet at 3.50 integrating 10.0 to 1.0. The ultraviolet spectrum showed λ_{max}^{EtOH} 252 mμ (ϵ 45,700).

B. From Addition of 1 Mole of Thiolbenzoic Acid to XIII.—Compound XIII (500 mg, 1.34 mmoles) prepared from VII was dissolved in 50 ml of hot ether. Thiolbenzoic acid (192 mg, 1.34 mmoles) was added and the mixture heated at reflux temperature for 30 min. The solution was allowed to stand at room temperature for 10 hr giving 301 mg (44.5%) of colorless solid, mp 194–196°. The product was shown to be identical with product from procedure A by mixture melting point determination and infrared spectral comparison.

Desulfurization of VII with Raney Nickel.—To a solution of 1.0 g (0.0033 mole) of VII in 30 ml of ethanol was added 2 tsp of W-2 Raney nickel. The mixture was stirred at reflux temperature for 24 hr, then filtered. The filtrate was evaporated *in vacuo* giving a gummy solid which crystallized when treated with cold ether giving 0.514 g (65%) of 1,4-diphenyl-1,4-butanediol, mp 90–92° (lit.[15] mp 89–90°). The product was found to be identical with an authentic sample by mixture point determination and infrared spectral comparison.

Desulfurization of VII with Deactivated Raney Nickel.—W-2 Raney nickel (2 tsp) in 100 ml of acetone was deactivated by stirring under reflux for 2 hr.[21] To the solution of deactivated Raney nickel was added a solution of 1.0 g (0.0033 mole) of VII in 20 ml of acetone. The mixture was stirred at reflux temperature for 1 hr, then filtered. The filtrate was evaporated *in vacuo* giving 0.424 g (54%) of 1,4-diphenyl-1,4-butanedione (II), mp 140–144°. Recrystallization from ethanol raised the melting point to 144–145° (lit.[12] mp 144–145°). The product was found to be identical with authentic II by mixture melting point determination and infrared spectral comparison.

Cleavage of Diethyl 3,4-Dithiadipate (XX) with 1 Equiv of Potassium Ethoxide at 27°.—To a solution of 4.2 g (0.05 mole) of potassium ethoxide in 35 ml of ethanol was added with stirring 11.9 g (0.05 mole) of diethyl 3,4-dithiadipate (XX). The reaction mixture immediately took on a deep red color. The mixture was allowed to stand at 27° for 72 hr. After removal of a small amount of water-soluble salt, the filtrate was evaporated to dryness *in vacuo* and the residue partitioned between 75 ml of water and 75 ml of ether.

The red aqueous layer was neutralized by addition of 25 ml of cold 3 *M* sulfuric acid bringing about evolution of H_2S and the separation of a yellow oil. The oil was extracted with 50 ml of ether. The ether layer was dried over anhydrous magnesium sulfate and evaporated *in vacuo* giving 6.03 g (50.5%) of diethyl 2-mercapto-2-thiaglutarate (XXI).

The ether extract was dried over anhydrous magnesium sulfate and evaporated *in vacuo* giving 4.0 g of a colorless liquid. Gas chromatographic analysis indicated that the sample was 56% diethyl 3-thiaglutarate (XXII) and 44% diethyl 3,4-dithiadipate (XX) representing 2.2 g (21.2%) of XXII and 1.8 g (15.1%) of recovered XX. A 24-in. silicon rubber column was employed (flow rate, 30 cc/min; column temperature, programmed from 100–200° at 12°/min; elution times, 480 and 660 sec). Samples collected from the fractometer were identical with authentic samples by infrared spectral comparison.

Cleavage of diethyl 3,4-dithiadipate (XX) with 2 equiv of potassium ethoxide at 27° was carried out as described in the cleavage of XX with 1 equiv of potassium ethoxide. The yields were 68% XXI, 0.1% XXII, and 0.07% recovered XX.

Treatment of Diethyl 2-Mercapto-3-thiaglutarate (XXI) with Potassium Ethoxide and Sulfur.—To a solution of 1.51 g (0.018 mole) of potassium ethoxide in 15 ml of ethanol was added 4.30 g (0.018 mole) of diethyl 2-mercapto-3-thiaglutarate (XXI) and 0.58 g (0.018 g-atom) of sulfur. The red mixture was stirred at 27° for 72 hr. After removal of a small amount of solid, 6 ml of 6 *N* hydrochloric acid was added, bringing about a color transition from red to yellow. The mixture was partitioned between 150 ml of ether and 150 ml of water. Evaporation of the aqueous layer *in vacuo* gave negligible residue. The ether layer was dried over anhydrous magnesium sulfate and evaporated *in vacuo* giving 3.75 g of yellow liquid. Gas chromatographic analysis indicated that the sample was 9.9% diethyl 3-thiaglutarate (XXII) and 90.1% diethyl 2-mercapto-3-thiaglutarate (XXI) representing 0.37 g (9.8%) of XXII and 3.38 g (79.5%) of recovered XXI.

Treatment of VI with Potassium Ethoxide in the Presence of Sulfur. A. With 1 Equiv of Potassium Ethoxide.—To a stirred suspension of 3.8 g (0.01 mole) of the dipotassio salt of 2,3-dimercapto-1,4-diphenyl-1,4-butanedione (VI) and 0.64 g (0.02 g-atom) of sulfur in 40 ml of ethanol was added 0.84 g (0.01 mole) of potassium ethoxide in 10 ml of ethanol. The resulting mixture was stirred at 27° for 72 hr. Ether (50 ml) was added and the solution filtered to give 3.1 g of a mixture of VI, sulfur, and potassium polysulfides. The filtrate was evaporated to dryness *in vacuo* giving a red solid which was partitioned between 50 ml of ether and 50 ml of water. Evaporation of the ether solution gave no residue. The aqueous layer was treated with carbon dioxide until pH 9 was reached. The aqueous solution was evaporated *in vacuo* leaving a red solid which was treated with 20 ml of ethanol. The mixture was filtered removing potassium carbonate and the filtrate was evaporated *in vacuo* to give 1.53 g (50%) of VII, mp 119–123°.

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B. With 2 Equiv of Potassium Ethoxide.—Following procedure A, 1.0 g (0.00267 mole) of VI and 0.17 g (0.00534 g-atom) of sulfur in 10 ml of ethanol was treated with 0.44 g (0.00534 mole) of potassium ethoxide in 5 ml of ethanol to give 0.52 g (63.4%) of VII, mp 118–122°.

Registry No.—I, 2461-75-8; VI, 2786-92-7; VII, 15441-13-1; VIII, 15441-14-2; IX, 15441-15-3; XIII, 15441-16-4; XV, 2461-79-2; 2,3-mercapto-1,4-diphenyl-1,4-butanedione, 15441-18-6; XVI, 15441-19-7; XX, 1665-65-2; XXI, 15441-21-1; XXII, 925-47-3.

The Alkaline Decomposition of Organic Disulfides. III. Substituent Effects among Aromatic Disulfides[1]

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Received October 2, 1967

Eleven variously substituted aromatic disulfides have been found to undergo extensive cleavage at 35.2° in 0.1 *N* sodium hydroxide in water, aqueous ethanol, or aqueous 1,4-dioxane, according to the stoichiometry $2ArSSAr + 4OH^- \rightarrow 3ArS^- + ArSO_2^- + 2H_2O$. The relative speeds of decomposition correlate rather well with the pK_a values of the thiols which are conjugate to the thiolate anions displaced from the disulfides by the nucleophilic attack of the hydroxide ion: the more sensitive the disulfide, the more stable the thiolate anion. This generalization extends to those aliphatic disulfides which have previously been shown to decompose by nucleophilic attack, or not at all, in aqueous alkali. Benzyl disulfide decomposes more rapidly than would have been anticipated from the pK value of benzyl mercaptan, but the products of decomposition (benzyl mercaptan, hydrogen sulfide, and benzaldehyde) indicate the probability that it has decomposed by an α elimination. The behavior of 4,4′-dithiodiphenol is anomalous: stable for at least 10 days in 0.1 *N* NaOH, it decomposes readily in 1 *N* NaOH at 35.2°. The slow addition of aqueous hydrogen peroxide to an alkaline solution of an aromatic disulfide which is sufficiently sensitive to alkali, by oxidizing the thiolate anion back to disulfide, provides a convenient way for preparing aromatic sulfinic acids.

Recently, from a consideration of the relative speeds of decomposition, and of the products of decomposition, of variously substituted symmetrical alkyl disulfides, Danehy and Hunter[3] concluded that direct nucleophilic attack of hydroxide ion on one sulfur atom, with displacement of the other as thiolate anion, will take place unless attack is inhibited by a negative charge not too far removed from the sulfur atoms or, in rarer cases, by steric hindrance. It was suggested that the sulfenate anion immediately attacked disulfide to form more thiolate anion and thiolsulfinate, which underwent further alkaline decomposition to furnish sulfinate anion and more thiolate anion. Actually, under strictly anaerobic conditions, more of the oxidized sulfur was accounted for as sulfonate rather than as sulfinate, for which we as yet have no explanation (see Scheme I). Alternatively, if a sufficiently labile proton is bonded to a carbon atom which is α or β to a sulfur atom, decomposition may be initiated by proton abstraction followed by an α or β elimination reaction.

While in principle the displacement and elimination reactions could be competitive, the 17 cases examined were quite clean: evidence for elimination was observed only in those cases in which neighboring carboxylate anions inhibited direct nucleophilic attack by hydroxide ion.

In investigating further the extent and significance of inhibition of direct attack by negative charge, the three isomeric dithiodibenzoic acids seemed particularly suitable. Forty years ago, Smiles[4] reported that 3,3′-dithiodibenzoate anion was extremely susceptible to attack by aqueous alkali, while 2,2′-dithiodibenzoate anion was far less so. While he made some reference to 4,4′-dithiodibenzoic acid, he never completed a quantitative comparison of the three isomers in relation to alkali. He did report that the corresponding mercaptobenzoate anion is the major product in each case. By reinvestigation we have established that at 35.2° the 4,4′ and 3,3′ isomers are 80 and 46% cleaved, respectively, in 12–15 min in a 12:1 molar excess of 0.125 *N* NaOH, while the 2,2′ isomer under the same experimental conditions is only 6.6% cleaved in 6 hr and only 15.5% cleaved in 24 hr.

While these results placed the three isomers in the expected order of reactivity, they are surprising for another reason. There is a long-standing opinion that aromatic disulfides are considerably more resistant to alkaline attack than the suitably substituted, water-soluble alkyl disulfides. Smiles[4a] stated that "in this behavior with cold aqueous alkali, *m*-dithiobenzoic acid [*sic*] is exceptional: other aromatic disulfides which do not contain the acid group appear to be unattacked by the reagent." Earlier investigators[5] had established that some aromatic disulfides decompose under strongly alkaline conditions at elevated temperatures to give thiophenols and aromatic sulfinic acids, though they examined neither the differences in sensitivity to base of different disulfides nor the level of basicity required. The more recently published data of Pappalardo[6] imply support for the notion that relatively concentrated alkali and high temperature are required. Our data for the decomposition of the three dithiodibenzoic acids prompted us to investigate this previously neglected problem. We found that a dozen aromatic disulfides, with a single remarkable exception, decompose more or less readily in 0.1 *N* NaOH in an effective solvent at 35.2°.

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[1] Presented at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 11, 1967.

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