Chemistry of Aliphatic Disulfides. IX. Alkoxide Cleavage of Unsymmetrical Disulfides[1,2]

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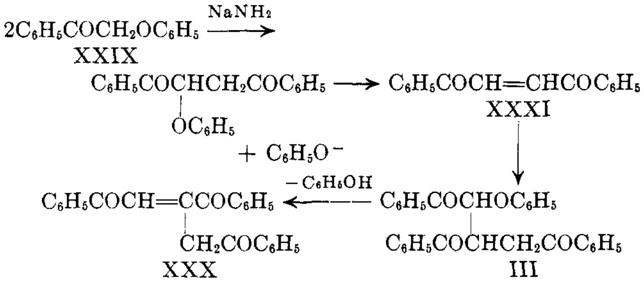
Treatment of several unsymmetrical disulfides with alkoxide ion has been shown to initially provide the corresponding symmetrical disulfides. When the symmetrical disulfides produced by disulfide interchange contain an α-carbonyl group, the disulfides are further degraded to a variety of products. A mechanism for the formation of 3,5-dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione from 6,7-dibenzoyl-3-carboxy-4,5-dithiaheptanoic acid is proposed.

In the preceding paper, the report of Groth[5,6] concerning the transformation of 1,6-diphenyl-3,4-dithia-1,6-hexanedione (diphenacyl disulfide, I) to 1,4-diphenyl-1,4-butanedione (V) and other products, with 1 equiv. of potassium ethoxide was re-examined and verified. A seemingly analogous reaction, investigated in some detail by Yates, *et al.*,[7] involved the conversion of 1-phenoxyacetophenone (XXIX) to 1,2,3-tribenzoylpropene (XXX) *via* the intermediate 1,2-dibenzoylethylene (XXXI). The intermediacy of XXXI in the formation of XXX was suggested from the fact that addition of XXXI to the reaction mixture provided a greater than theoretical yield of XXX.

$$\underset{\text{I}}{[C_6H_5COCH_2S]_2} \xrightarrow{^-OC_2H_5} \underset{\text{V, }39\%}{C_6H_5COCH_2CH_2COC_6H_5} + \underset{14\%}{C_6H_5COCH_3}$$



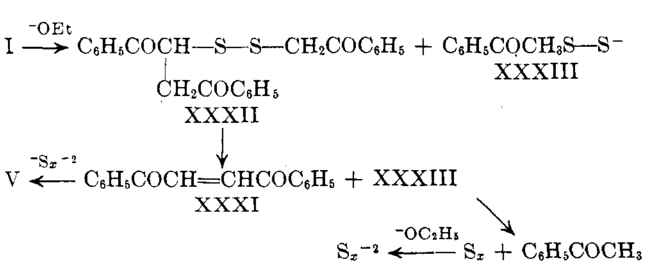
$$\underset{\text{XXIX}}{2C_6H_5COCH_2OC_6H_5} \xrightarrow{NaNH_2}$$

$$\underset{OC_6H_5}{C_6H_5COCHCH_2COC_6H_5} \longrightarrow \underset{\text{XXXI}}{C_6H_5COCH{=}CHCOC_6H_5}$$

$$+\ C_6H_5O^-$$

$$\underset{\text{XXX}}{\underset{CH_2COC_6H_5}{C_6H_5COCH{=}CCOC_6H_5}} \xleftarrow{-C_6H_5OH} \underset{\text{III}}{\begin{array}{c}C_6H_5COCHOC_6H_5\\ C_6H_5COCHCH_2COC_6H_5\end{array}}$$

Bimolecular condensation of a similar type could also be envisaged for I. Loss of thiolsulfenate ion (XXXIII) from the unsymmetrical disulfide (XXXII) would yield XXXI which could be reduced by polysulfide ion to the observed product V. The present paper concerns (a) a test of the bimolecular condensation mechanism (involving XXXI as an intermediate) and (b) a study of the possible role of intermediate unsymmetrical disulfides, such as XXXII, in the conversion of I to V.

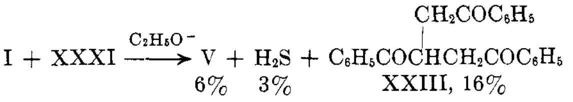


$$\text{I} \xrightarrow{^-OEt} \underset{\text{XXXII}}{\underset{CH_2COC_6H_5}{C_6H_5COCH{-}S{-}S{-}CH_2COC_6H_5}} + \underset{\text{XXXIII}}{C_6H_5COCH_2S{-}S^-}$$

$$\text{V} \xleftarrow{^-S_x{}^{-2}} \underset{\text{XXXI}}{C_6H_5COCH{=}CHCOC_6H_5} + \text{XXXIII}$$

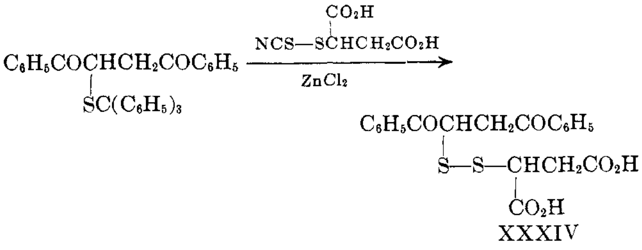
$$S_x{}^{-2} \xleftarrow{^-OC_2H_5} S_x + C_6H_5COCH_3$$

1,2-Dibenzoylethylene (XXXI) as a Possible Intermediate.—Since the bimolecular mechanism implied that V was produced from XXXI by reduction with polysulfide ion, this aspect was initially tested. Indeed, incubation of an ethanolic solution containing elemental sulfur, potassium ethoxide, and XXXI at room temperature provided V in 42% yield.[8] However, when I was allowed to react with ethoxide in the presence of XXXI, the yield of V was reduced to only 6%; other products of this reaction were identified as hydrogen sulfide and 1,2,3-tribenzoylpropane (XXIII). Thus the function of XXXI in the reaction appeared to be that of a scavenger of acetophenone anion rather than an intermediate in the formation of V. The fact that an enhanced yield of V was not obtained in this experiment provides the strongest available evidence against the intermediacy of XXXI in the conversion of I to V. The cleavage of I was also followed by thin layer chromatography but in no instance could spots due to XXXI or its base-catalyzed decomposition products be detected. In view of these results, mechanisms involving XXXI in the production of V were tentatively discarded.



$$\text{I} + \text{XXXI} \xrightarrow{C_2H_5O^-} \underset{6\%}{\text{V}} + \underset{3\%}{H_2S} + \underset{\text{XXIII, }16\%}{\overset{CH_2COC_6H_5}{C_6H_5COCHCH_2COC_6H_5}}$$

Methoxide Cleavage of XXXIV.—Since the formation of V could have occurred from an intermediate unsymmetrical disulfide, such as XXXII, without the formation of XXXI, the action of alkoxide ion on molecules of this type was investigated. A convenient model disulfide for these experiments was 6,7-dibenzoyl-3-carboxy-4,5-dithiaheptanoic acid (XXXIV). The substance was readily prepared as shown below.



$$\underset{SC(C_6H_5)_3}{C_6H_5COCHCH_2COC_6H_5} \xrightarrow[ZnCl_2]{NCS{-}S\overset{CO_2H}{CH}CH_2CO_2H} \underset{\text{XXXIV}}{\underset{S{-}S{-}\underset{CO_2H}{CH}CH_2CO_2H}{C_6H_5COCHCH_2COC_6H_5}}$$

Treatment of XXXIV with 1 or 2 equiv. of methoxide ion failed to provide any appreciable reaction. How-

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[1] Supported in part by Research Grant RG-7966 from the National Institute of General Medical Sciences of the National Institutes of Health, U. S. Public Health Service.

[2] For part VIII of this series, see R. G. Hiskey, B. D. Thomas, and J. A. Kepler, *J. Org. Chem.*, **29**, 3671 (1964).

[3] Abstracted in part from a dissertation submitted by J. A. Kepler to the University of North Carolina in partial fulfillment of the requirements for the Ph.D., August, 1963.

[4] Shell Chemical Corp. Fellow, 1962–1963.

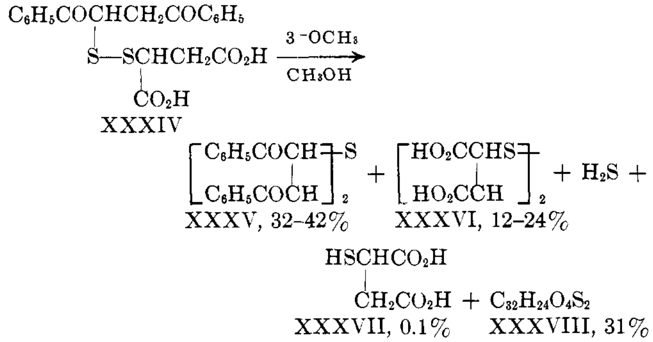
[5] B. Groth. *Arkiv Kemi Mineral Geol.*, **9**, 1 (1924).

[6] B. Groth, Dissertation, Uppsala, 1926.

[7] P. Yates, D. G. Farnum, and H. G. Stout, *J. Am. Chem. Soc.*, **80**, 196 (1958).

[8] B. D. Thomas, Dissertation, University of North Carolina, 1962.

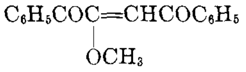
ever, when XXXIV was allowed to react with 3 equiv. of methoxide ion in methanol, a 32–42% yield of 3,5-dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione (XXXV) was isolated. The other identifiable products included α,α-dithiadisuccinic acid (XXXVI), α-mercaptosuccinic acid (XXXVII), and hydrogen sulfide. A yellow crystalline solid (XXXVIII, $C_{32}H_{24}O_4S_2$) was also obtained by acidification of a bicarbonate extract of the reaction mixture.



$$\underset{\text{XXXIV}}{C_6H_5COCH(S\text{—}SCH(CO_2H)CH_2CO_2H)CH_2COC_6H_5} \xrightarrow[CH_3OH]{3\,^-OCH_3} \underset{\text{XXXV, 32–42\%}}{\left[\begin{matrix}C_6H_5COCH\\ C_6H_5COCH\end{matrix}\right]_2S} + \underset{\text{XXXVI, 12–24\%}}{\left[\begin{matrix}HO_2CCHS\\ HO_2CCH\end{matrix}\right]_2} + H_2S + \underset{\text{XXXVII, 0.1\%}}{HSCH(CO_2H)CH_2CO_2H} + \underset{\text{XXXVIII, 31\%}}{C_{32}H_{24}O_4S_2}$$

Structure of XXXVIII.—Considerable difficulty was experienced in the purification of XXXVIII; the best elemental analysis was obtained on a sample melting at 174–180°. The empirical formula, $C_{32}H_{24}O_4S_2$, is based on elemental analysis, the integrated n.m.r. spectrum, and several molecular weight determinations.

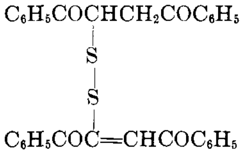
Additional evidence concerning the nature of XXXVIII was obtained from the infrared spectrum of the substance. The absorption of XXXVIII in the carbonyl region is virtually identical with the absorption exhibited by 1-methoxy-1,2-dibenzoylethylene (XXXIX). Treatment of XXXVIII with sodium nitroprusside failed to provide the characteristic color; however, a positive test was obtained with the sodium



$$C_6H_5COC(OCH_3)\!=\!CHCOC_6H_5$$

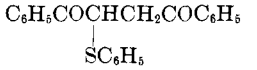
XXXIX

azide–iodine reagent indicating the presence of a mercaptan, thio ketone, or a labile disulfide. All attempts to prepare a thio ether derivative of XXXVIII failed. The n.m.r. spectrum of XXXVIII exhibited the following proton groups (the integrated ratios are given in parentheses): an aromatic multiplet at approximately τ 2.29 (19.2), an apparent quartet centered at 4.79 (1), and a pair of doublets exhibiting AB splitting at 5.98 and 6.26 (1.92). The n.m.r. spectrum of XXXVIII is very similar to that of a model compound, 1,4-diphenyl-2-thiophenyl-1,4-butanedione (XL). The thio ether XL exhibits an aromatic multiplet at τ 2.22, an apparent quartet at 4.76 (1), and an octet centered at 6.25 (1.94). The octet consists of a group of four central peaks, similar in intensities to the group observed for XXXVIII, at τ 5.98 and 6.26, and four less intense, satellite peaks. The low solubility of XXXVIII would not permit the observation of the satellite peaks in the spectrum of XXXVIII, if they were present. From the foregoing data XXXVIII is tentatively assigned as the unsymmetrical disulfide. The fact that the vinyl proton in the proposed structure is not observed may be explained by assuming that it resonates in the aromatic hydrogen region and is obscured by the aromatic multiplet. The absence of the vinyl proton in the spectrum of XXXIX supports this assumption.



$$C_6H_5COCH(CH_2COC_6H_5)\text{—}S\text{—}S\text{—}C(COC_6H_5)\!=\!CHCOC_6H_5$$

XXXVIII



$$C_6H_5COCH(SC_6H_5)CH_2COC_6H_5$$

XL

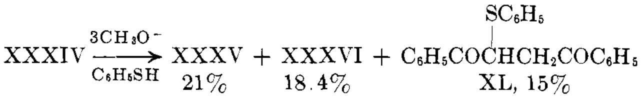
Cleavage of XXXIV with 3 equiv. of methoxide in purified dioxane, rather than methanol, provided essentially the same products. When the cleavage

$$\text{XXXIV} \xrightarrow[\text{dioxane}]{3CH_3O^-} \underset{37\%}{\text{XXXV}} + \underset{43.4\%}{\text{XXXVI}} + \underset{0.3\%}{\text{XXXVII}} + \underset{11\%}{\text{XXXVIII}} + H_2S$$

was conducted with 2.5 equiv. of sodium methoxide in dioxane, similar results were obtained.

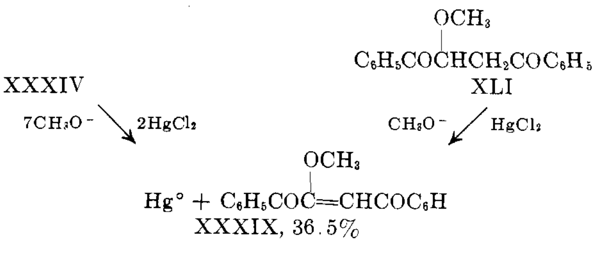
A number of experiments were performed in attempts to isolate V and/or XXXI from the methoxide decomposition of XXXIV. However, no trace of either material could be detected. When the reaction was followed with thin layer chromatography, no spots due to XXXI or its decomposition products appeared.

Methoxide Cleavage of XXXIV in the Presence of Thiophenol.—Treatment of XXXIV with 3 equiv. of methoxide in the presence of 1 equiv. of thiophenol afforded 21% of XXXV, 18.4% of XXXVI, and 15% of 3-benzoyl-1,2-diphenyl-4-thiabutanone (XL). The formation of XL at the expense of XXXV indicates that XXXV probably results from an intermolecular reaction between an intermediate thio ketone and a mercaptide.



$$\text{XXXIV} \xrightarrow[C_6H_5SH]{3CH_3O^-} \underset{21\%}{\text{XXXV}} + \underset{18.4\%}{\text{XXXVI}} + \underset{\text{XL, 15\%}}{C_6H_5COCH(SC_6H_5)CH_2COC_6H_5}$$

Methoxide Cleavage of XXXIV in the Presence of Mercury(II) Chloride.—The alkaline cleavage of XXXIV was carried out in the presence of mercury(II) chloride in order to remove any mercaptide ion from the reaction as it was formed. Unexpectedly, the reaction provided 1-methoxy-1,2-dibenzoylethylene (XXXIX) and elemental mercury. Subsequently, it was determined that XXXIX could also be produced from 1-methoxy-1,2-dibenzoylethane (XLI) under the reaction conditions. When 1,2-dibenzoylethylene (XXXI) was treated with mercury(II) chloride in the presence of sodium methoxide, neither XXXIX nor mercury was produced. Thus, XXXIX and XLI do not arise from XXXI. However, the fact that XXXIV was decomposed when treated with mercury(II) chloride in the absence of base makes the significance of the base-catalyzed formation of XXXIX from XXXIV and mercury(II) chloride uncertain.



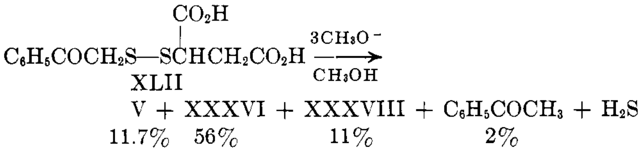
$$\text{XXXIV} \xrightarrow[2HgCl_2]{7CH_3O^-} Hg^\circ + \underset{\text{XXXIX, 36.5\%}}{C_6H_5COC(OCH_3)\!=\!CHCOC_6H}$$

$$\underset{\text{XLI}}{C_6H_5COCH(OCH_3)CH_2COC_6H_5} \xrightarrow[HgCl_2]{CH_3O^-} \text{XXXIX}$$

The fact that alkoxide treatment of XXXIV did not yield V or XXXI provides additional evidence against a mechanism involving XXXI or an unsymmetrical disulfide such as XXXII as intermediates. Also the absence of XXXI from the cleavage of XXXIV indicates that a β-elimination mechanism is not operative under the conditions employed.

Methoxide Cleavage of XLII.—Since an intermediate unsymmetrical disulfide containing a 1,2-dibenzoylethane fragment, XXXIV, was apparently not a precursor to V, as suggested by the bimolecular condensation mechanism, an unsymmetrical disulfide containing a phenacyl fragment XLII was synthesized and cleaved.

When XLII was treated with 3 equiv. of methoxide, rapid decomposition occurred. Analysis of the reaction products indicated the presence of 11.7% of V in addition to XXXVI and XXXVIII. Similar results were observed when the cleavage was performed in dioxane.



$$\underset{\text{XLII}}{C_6H_5COCH_2S{-}S\overset{CO_2H}{\overset{|}{C}}HCH_2CO_2H} \xrightarrow[CH_3OH]{3CH_3O^-} \underset{11.7\%}{V} + \underset{56\%}{XXXVI} + \underset{11\%}{XXXVIII} + \underset{2\%}{C_6H_5COCH_3} + H_2S$$

The methoxide cleavage of XLII in methanol was followed by thin layer chromatography. During the initial phase of the reaction, the chromatogram exhibited only a single mobile spot, in addition to the spot due to XLII which remained at the origin. The mobile substance was shown to be diphenacyl disulfide (I) by a comparison of R_f values on the same chromatogram. After 45 min. other spots appeared which were identical with those resulting from the cleavage of I. Positive evidence for the formation I, from the methoxide treatment of XLII, was obtained by quenching the reaction after 25 min. A 2.7% yield of I resulted together with 66% of starting disulfide.

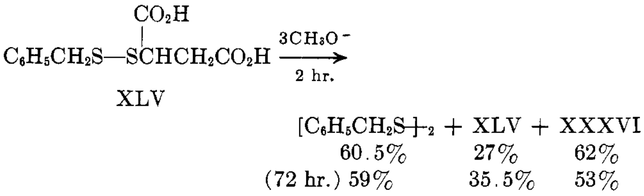
$$\text{XLII} \xrightarrow[CH_3OH]{3CH_3O^-} \underset{2.7\%}{\text{I}} + \underset{66\%}{\text{XLII}}$$

Disulfide Interchange.—These data suggest that XLII undergoes base-catalyzed "disulfide interchange" and is converted to I and XXXVI prior to the formation of V and the other products. To confirm this possibility, several other unsymmetrical disulfides were studied. Treatment of methyl 5-phenyl-3,4-dithiapentanoate (XLIII) with 0.25 equiv. of *t*-butoxide provided 83–92% yields of benzyl disulfide. Cleavage of XLIII with 1 equiv. of methoxide in the presence of 1 equiv. of N,N-diphenylcarbamyl chloride (DPCC) provided the N,N-diphenylthiocarbamate derivative of methyl thioglycolate (XLIV) and benzyl disulfide. The isolation of XLIV parallels the results obtained from treatment of XLIII with cyanide ion and DPCC.[9]

$$\underset{\text{XLIII}}{C_6H_5CH_2S{-}SCH_2CO_2CH_3} \xrightarrow{t\text{-}C_4H_9O^-} [C_6H_5CH_2S]_2$$

$$\text{XLIII} \xrightarrow[DPCC]{CH_3O^-} \underset{35\%}{[C_6H_5CH_2S]_2} + \underset{\text{XLIV, }25\%}{(C_6H_5)_2NCOSCH_2CO_2CH_3} + \underset{36\%}{(C_6H_5)_2NCO_2CH_3}$$

Incubation of 3-carboxy-6-phenyl-4,5-dithiahexanoic acid (XLV) with 3 equiv. of methoxide for 2 or 72 hr. produced the same mixture of symmetrical disulfides in nearly identical yield. Thus, an equilibrium-type mechanism is apparently involved. From these data the most plausible scheme for disulfide interchange would involve "direct displacement of a mercaptide"[2] by attack of methoxide on the disulfide bond. Reaction of the mercaptide and intermediate sulfenate ester (presumably unstable) would ultimately provide an equilibrium mixture of the three disulfides. Similar results involving recombination of the primary cleavage products were previously observed in the cyanide cleavage of the unsymmetrical disulfide XLIII[9] and of methyl 5-methyl-3,4-dithiahexanoate (XLVI).[10] In both cases, cleavage in the absence of a mercaptide scavenger led to the formation of symmetrical disulfides. Although the driving force for disulfide interchange is not known with certainty, it is probably associated with the greater stability of symmetrical disulfides, as compared to unsymmetrical disulfides, toward nucleophiles. This increased stability in turn may be related to the lack of polarization of the sulfur–sulfur bond in symmetrical disulfides.



$$\underset{\text{XLV}}{C_6H_5CH_2S{-}S\overset{CO_2H}{\overset{|}{C}}HCH_2CO_2H} \xrightarrow[2\text{ hr.}]{3CH_3O^-} [C_6H_5CH_2S]_2 + \text{XLV} + \text{XXXVI}$$

$$\begin{array}{rccc} & 60.5\% & 27\% & 62\% \\ (72\text{ hr.}) & 59\% & 35.5\% & 53\% \end{array}$$

$$RS^- + [R'SOR''] \rightleftharpoons RS{-}SR' \rightleftharpoons R'S^- + [RSOR''] + {}^-OR''$$

$$RS^- + [RSOR''] \rightleftharpoons RS{-}SR + {}^-OR''$$

$$R'S^- + [R'SOR''] \rightleftharpoons R'S{-}SR' + {}^-OR''$$

$$\underset{\text{XLIII}}{C_6H_5CH_2S{-}SCH_2CO_2CH_3} \xrightarrow{^-CN} [C_6H_5CH_2S]_2$$

$$\underset{\text{XLVI}}{(CH_3)_2CHS{-}SCH_2CO_2CH_3} \xrightarrow{^-CN} (CH_3)_2CHSCN + [CH_3O_2CCH_2S]_2 + \text{XLVI}$$

The Formation of XXXV and XXXVIII.—It is apparent from the product analysis of the cleavage reactions of the unsymmetrical disulfides XXXIV and XLII that although initial "disulfide interchange" provides the symmetrical β-keto disulfides (XLVII and I) both further decompose under the reaction conditions. Thus, XLII provides I and ultimately V, whereas by analogy XXXIV presumably gave XLVII and eventually XXXV. The presence of the other symmetrical disulfide XXXVI in both reactions is consistent with this view. Since XXXVI is present in the reaction mixture as the tetrasodium salt, further decomposition of this substance would not be expected.

The formation of XXXV can be rationalized by several mechanisms. Although XXXV could arise by "β-elimination,"[2,11] the fact that 1,2-dibenzoylethylene could not be detected in any of the alkoxide cleav-

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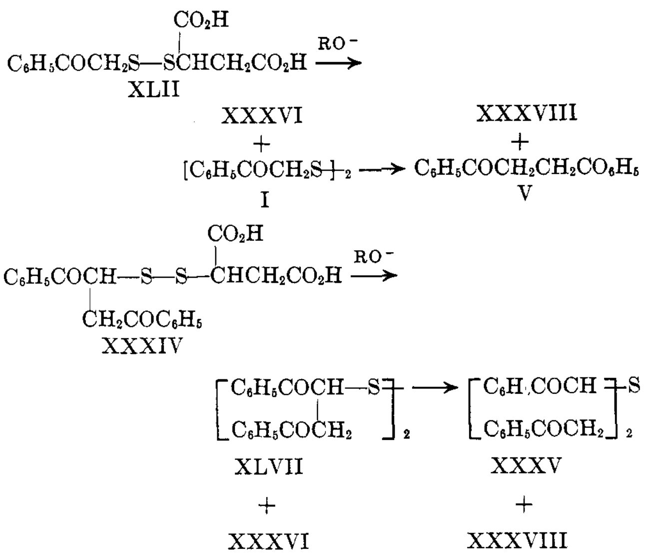
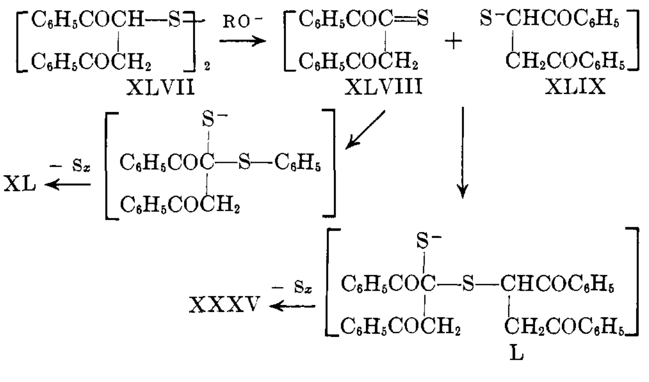
(9) R. G. Hiskey and F. I. Carroll, *J. Am. Chem. Soc.*, **83**, 4644 (1961).

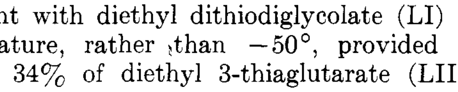
(10) R. G. Hiskey, W. H. Bowers, and D. N. Harpp, *ibid.*, **86**, 2010 (1964).

(11) J. M. Swan, *Angew. Chem.*, **68**, 215 (1956).



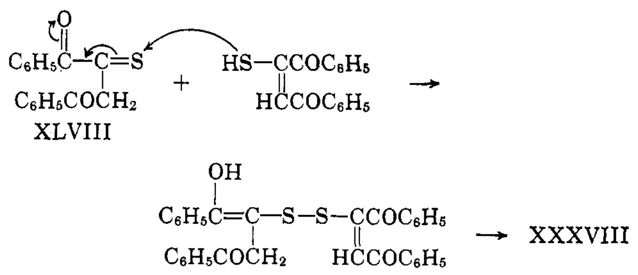
age reactions casts some doubt on the importance of β-elimination in these circumstances. On the other hand, the production of both XXXV and XXXVIII, from XLVII, can be rationalized assuming an initial "α-elimination"[2] reaction. In the case of XXXV, α-elimination would provide the thio ketone XLVIII and the mercaptide XLIX. Nucleophilic addition of the latter to the former would afford a hemidithioketal (L) of the type isolated by Howard.[2,12] Loss of elemental sulfur from L would yield XXXV. The formation of the unsymmetrical sulfide XL from methoxide cleavage of XXXIV in the presence of thiophenol can be rationalized by a similar process. Although the loss of elemental sulfur from hemidithioacetals of the type isolated by Howard[12] has not been experimentally demonstrated, repetition of Howard's experiment with diethyl dithiodiglycolate (LI) at room temperature, rather than −50°, provided approximately 34% of diethyl 3-thiaglutarate (LII). This result would suggest that the intermediate hemidithioacetal isolated by Howard lost elemental sulfur in the manner proposed and provided LII.





$$\underset{\text{LI}}{[C_2H_5O_2CCH_2S\text{+}_2} \xrightarrow{C_2H_5O^-} \underset{\text{LII}}{[C_2H_5O_2CCH_2\text{+}_2S}$$

The formation of XXXVIII from XLVII is also readily explained in terms of the thio ketone XLVIII. Dimerization of XLVIII *via* nucleophilic addition of the enol form to the keto form would account for this product. Dimerizations of this type have previously been reported for thio ketones containing electron-withdrawing groups.[13] The fact that the methoxide cleavage of XLII also provided XXXVIII now becomes of considerable significance; that is, any mechanistic scheme written for the formation of V from I must also account for the formation of XXXVIII *via* the thio ketone XLVIII. A proposal which incorporates this data is presented in the accompanying report.



Experimental[14]

Preparation of Triphenylmethyl Mercaptan.—A suspension of 75 g. (0.29 mole) of triphenylmethanol in 600 ml. of purified dioxane containing 0.29 mole of boron trifluoride etherate complex was stirred magnetically until the solid dissolved. The solution was then treated with hydrogen sulfide until the color disappeared (about 5 hr.). The reaction mixture was poured on ice and the solid was recrystallized from isopropyl alcohol (using 5 ml. of solvent/g. of triphenylmethyl mercaptan) to yield 74.3 g. (93%) of yellow needles, m.p. 106–107°, lit.[15] m.p. 107°.

Preparation of 3,4-Dibenzoyl-1,1,1-triphenyl-2-thiabutane.—To a solution of 11.8 g. (0.05 mole) of *trans*-1,2-dibenzoylethylene in 400 ml. of benzene was added 13.8 g. (0.05 mole) of triphenylmethyl mercaptan. When the mercaptan dissolved, 1 ml. of piperidine was added, and the solution was allowed to stand at room temperature for 6 hr. The solvent was removed and the resulting oil solidified when triturated with methanol. Recrystallization from a mixture of 75 ml. of acetone and 300 ml. of methanol provided 19.35 g. (79%) of colorless needles, m.p. 146–147°.

Anal. Calcd. for $C_{35}H_{28}O_2S$: C, 82.05; H, 5.51; S. 6.25. Found: C, 81.90; H, 5.63; S, 6.12.

Preparation of 6,7-Dibenzoyl-3-carboxy-4,5-dithiaheptanoic Acid (XXXIV).—A solution of 6.0 g. (0.04 mole) of α-mercaptosuccinic acid in a mixture of 50 ml. of dry dioxane and 50 ml. of ether was added in 30 min. to 0.044 mole of thiocyanogen in 500 ml. of ether. The reaction mixture was stirred an additional 30 min. at ice bath temperature. Zinc chloride (14.0 g.) was then added to the solution with vigorous stirring. A solution of 0.04 mole of the S-trityl derivative in a mixture of 100 ml. of dioxane and 100 ml. of ether was then added to the suspension in one portion. The ice bath was removed and the solution was refluxed for 2 hr. The suspension was then stirred 8 hr. at room temperature. The mixture was filtered and evaporated and the residue was dissolved in 200 ml. of hot benzene. Filtration and drying of the crystalline solid gave 4.94 g. (29.4%) of XXXIV, m.p. 187–188°.

Anal. Calcd. for $C_{20}H_{18}O_6S_2$: C, 57.39; H, 4.34; S, 15.33. Found: C, 57.43, 57.77; H, 4.61, 4.57; S, 14.80; 14.95.

Dilution of the hot mother liquor to the cloud point with petroleum ether (60–90°) and cooling gave 4.24 g. (25.3%) of additional solid, m.p. 152–154°. The infrared spectrum of this substance was identical with that of the 187–188° solid.

Preparation of 1,4,4,4-Tetraphenyl-2-thiabutanone.—To 19.9 g. (0.1 mole) of ω-bromoacetophenone in 600 ml. of methanol was added 27.6 g. (0.1 mole) of triphenylmethyl mercaptan. The solution was heated to dissolve the solid, cooled, and carefully treated with 9.3 g. (0.11 mole) of piperidine. On cooling, the solution deposited 33.5 g. (85%) of the product, m.p. 114–116°.

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

[13] W. J. Middleton, E. G. Howard, and W. H. Sharkey, *J. Am. Chem. Soc.*, **83**, 2589 (1961).

[14] Melting points and boiling points are uncorrected. Elemental analyses were performed by Micro-Tech Laboratories, Skokie, Ill.; molecular weight determinations were by Alfred Bernhardt, Mülheim (Ruhr), Germany, and Huffman Micro-Analytical Laboratories, Wheatridge, Colo.

[15] F. Asinger, M. Theil, and E. Pallus, *Ann.*, **602**, 37 (1957).

The analytical sample was prepared by recrystallization from an acetone–methanol mixture, m.p. 116–117°.

Anal. Calcd. for $C_{27}H_{22}OS$: C, 82.29; H, 5.62; S, 8.13. Found: C, 82.03; H, 5.56; S, 8.01.

Preparation of 5,6-Dicarboxy-1-phenyl-3,4-dithiahexanone (XLII).—A solution of 0.044 mole of thiocyanogen in 500 ml. of ether was treated with 6.0 g. (0.04 mole) of α-mercaptosuccinic acid as previously described. The solution of sulfenylthiocyanate was then treated with 14.0 g. of zinc chloride and 15.8 g. (0.04 mole) of 1,4,4,4-tetraphenyl-2-thiabutanone. Isolation in the manner previously described provided 7.56 g. (62%) of XLII, m.p. 140–141°. The analytical sample was prepared by recrystallization from an ethyl acetate–petroleum ether (60–90°) mixture, m.p. 140–141°.

Anal. Calcd. for $C_{12}H_{12}O_5S$: C, 47.97; H, 4.03; S, 21.32. Found: C, 47.75; H, 4.15; S, 21.28.

The anhydride of XLII was prepared by refluxing a benzene solution of the acid overnight using a Dean–Stark trap to collect the water. Filtration of the benzene solution and dilution with two volumes of petroleum ether provided the anhydride, m.p. 121–123°.

Anal. Calcd. for $C_{12}H_{10}O_4S_2$: C, 51.06; H, 3.59; S, 22.71. Found: C, 50.78; H, 3.78; S, 22.33.

Preparation of 3,5-Dibenzoyl-1,7-diphenyl-4-thia-1,7-heptanedione (XXXV).—A 0.78-g. (3.23 mmoles) sample of disodium sulfide nonahydrate was dissolved in 100 ml. of ethanol and treated with a suspension containing 2.0 g. (6.56 mmoles) of 2-chloro-1,4-diphenyl-1,4-butanedione in a 1:1 mixture of ethanol-benzene. The resulting solid was filtered and washed with water, ethanol, and ether to provide 1.38 g. (86%) of XXXV, m.p. 194–196°, lit.[16] m.p. 188–192°.

Oxidation of 1,2-Dibenzoyl-1-methoxyethane (XLI) with Mercury(II) Chloride.—To a solution of 0.21 g. (0.78 mmole) of mercury(II) chloride and 0.2 g. (0.75 mmole) of XLI[17] in 25 ml. of methanol was added 3 equiv. of sodium methoxide in 20 ml. of methanol. An immediate precipitate of mercury was observed and the mixture was kept at room temperature for 24 hr. The solution was acidified to pH 2, filtered, and evaporated. The residual oil was dissolved in 15 ml. of ether and diluted with 15 ml. of *n*-pentane. The resulting solid, 0.07 g. (36.5%), XLI, melted at 103–105°, lit.[17] m.p. 105–106°. A mixture melting point with an authentic sample was not depressed.

Preparation of 3-Benzoyl-1,2-diphenyl-4-thiabutanone (XL).—To a solution of 2.4 g. (0.01 mole) of *trans*-1,2-dibenzoylethylene in 40 ml. of hot methanol was added 1.1 g. (0.01 mole) of thiophenol. The yellow solution immediately became colorless upon the addition of 1 drop of piperidine. The solution was cooled and 3.4 g. (97%) of XL was obtained, m.p. 82–84°.

Anal. Calcd. for $C_{22}N_{18}SO_2$: C, 76.32; H, 5.23; S, 9.25. Found: C, 76.30; H, 5.14; S, 9.26.

3-Carboxy-6-phenyl-4,5-dithiahexanoic acid (XLV) and methyl 5-phenyl-3,4-dithiapentanoate (XLIII) were prepared as previously described.[18]

Cleavage of XXXIV with Sodium Methoxide in Methanol.—A 1.01-g. (2.39 mmoles) sample of XXXIV in 75 ml. of methanol was treated with a solution of 0.16 g. (7.2 mg.-atoms) of sodium in 15 ml. of methanol. The solution was stirred at room temperature for 20 hr. The precipitated salt, 0.29 g., was filtered and washed with water to give 0.08 g. of XXXV, m.p. 185–190°. The methanol was removed from the original filtrate; the residue was dissolved in water and filtered to give an additional 0.1 g. (total yield, 31.5%) of XXXV, m.p. 187–190°. The yield of XXXV could be increased by chromatography of the residue on Florisil using benzene as the eluent.

The aqueous solutions were combined and acidified with dilute hydrochloric acid. The acidified solution was extracted with ether; the ether extracts were dried and evaporated to provide a red gum. The material was crystallized from acetone to afford 0.20 g. (31.2%) of XXXVIII, m.p. 181–189°. The infrared spectrum of XXXVIII was identical with the sample of XXXVIII, m.p. 174–180°, obtained from XLII.

The aqueous solution was evaporated to dryness and the residual solid was treated with excess ethereal diazomethane. Removal of the ether provided 0.1 g. of an oil which was analyzed for dimethyl α-mercaptosuccinate and tetramethyl α,α-dithiasuccinate in the vapor fractometer. A silicon rubber column was employed using a helium flow rate of 75 cc./min. The analysis for mercaptan was conducted at 100°, programmed for a temperature rise of 4.6°/min. For the disulfide the starting temperature was 150°, programmed for a rise of 13°/min. Nitrobenzene was used as the internal standard and the peak areas were determined with a Disc Integrator used in conjunction with the recorder. The oil was found to contain 11.9% of disulfide and 0.12% mercaptan.

Cleavage of XXXIV with Sodium Methoxide in Dioxane.—A 1.0-g. (2.39 mmoles) sample of XXXIV dissolved in 75 ml. of dry dioxane was treated with a solution of 0.16 g. (7.2 mg.-atoms) of sodium in 5 ml. of methanol. After 70 hr. the dioxane was removed and the residue was partitioned between water and ether. The unsoluble material was filtered. The solid appeared as 0.22 g. (37%) of XXXV, m.p. 192–193°. A mixture melting point with an authentic sample was not depressed.

The aqueous solution was acidified and extracted with ether, and the ether extracts were combined and evaporated. The residue was crystallized from acetone to provide 0.05 g. (10.9%) of XXXVIII, m.p. 178–182°.

The aqueous layer was analyzed for disulfide and mercaptan using the previous procedure. The analysis indicated the presence of 43.4% of XXXVI and 0.35% of XXXVIII.

Cleavage of XXXIV with Sodium Methoxide in the Presence of Thiophenol.—To a solution of 2.0 g. (4.8 mmoles) of XXXIV and 0.53 g. (4.8 mmoles) of thiophenol in 200 ml. of dry dioxane was added 3 equiv. of sodium methoxide in 5 ml. of methanol. After 20 hr. the precipitated salt was filtered and provided 0.21 g. (18.4%) of XXXVI, m.p. 162–167°, lit.[19] m.p. 172–173°. The infrared spectrum of the material was identical with that of an authentic sample.

The filtrate was acidified with 6 *N* hydrochloric acid, and the solvent was removed. The resulting oil was dried and triturated with cold methanol to provide 0.15 g. of XXXV, m.p. 189–192°. Concentration and cooling of the filtrate gave an additional 0.1 g. (total yield, 21%) of XXXV. A thin layer chromatogram of the filtrate indicated the presence of XXXV as well as XL and six other products. The methanol was removed and the resulting oil was filtered through a 3-in. alumina column. The eluent was concentrated and analyzed by thin layer chromatography. The chromatogram indicated the presence of XXXV and XL. Removal of the solvent provided 0.98 g. of oil which yielded 0.25 g. (15%) of XL, m.p. 80–84°, when crystallized from a methanol–petroleum ether mixture. A mixture melting point with an authentic sample of XL melted at 81–84°.

Cleavage of XXXIV in the Presence of Mercury(II) Chloride.—To a solution of 1.30 g. (4.8 mmoles) of mercury(II) chloride in 300 ml. of dry methanol was added 1.0 g. (2.39 mmoles) of XXXIV. The solution was treated with a solution containing 0.48 g. (0.31 mg.-atom) of sodium in 50 ml. of methanol. A yellow solid immediately precipitated. The mixture was stirred 28 hr. at room temperature during which time elemental mercury precipitated. The mixture was acidified to approximately pH 6 and filtered, and the filtrate was evaporated to dryness. The resulting oil was dissolved in ether, washed with 1 *N* hydrochloric acid, 10% bicarbonate solution, and water. Removal of the solvent provided an oil which crystallized from an ether–*n*-pentane mixture to give 0.36 g. (56.6%) of yellow needles, m.p. 105–106°. A mixture melting point with authentic XXXIX was not depressed.

Anal. Calcd. for $C_{17}H_{14}O_3$: C, 76.69; H, 5.30. Found: C, 76.65; H, 5.43.

Evaporation of the mother liquor provided a yellow oil whose n.m.r. spectrum exhibited a single peak at τ 6.66 similar to the methoxy signal given by XLI; however, the spectrum did not exhibit the triplet centered at τ 4.57 present in XLI.

Cleavage of XXXIV with Sodium Methoxide in Dioxane.—To a solution of 2.0 g. (4.8 mmoles) of XXXIV in 150 ml. of dioxane was added 0.274 g. (0.011 g.-atom) of sodium in 10 ml. of methanol (2.5 equiv. of sodium methoxide). After 1 hr., a 1-ml. aliquot of the reaction mixture was acidified and chromatographed on a thin layer of silica gel. The developing solvent was chloroform–benzene (3:4). The chromatogram exhibited two spots, one of which remained at the origin. After 20 hr. an aliquot exhibited four spots, two of which had R_f values similar to those of XXXV and XLI. No spots due to XXXI or its alkaline decomposition products could be detected in any experiment using

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[16] E. Campaigne and W. O. Foye, *J. Org. Chem.*, **17**, 1405 (1952).

[17] R. E. Lutz, *J. Am. Chem. Soc.*, **51**, 3008 (1929).

[18] R. G. Hiskey, F. I. Carroll, R. M. Babb, J. O. Bledsoe, R. T. Puckett, and B. W. Roberts, *J. Org. Chem.*, **26**, 1152 (1961).

[19] A. Rosenheim and W. Stadler, *Ber.*, **38**, 2687 (1905).

either 2.5 or 3 equiv. of methoxide in either methanol, dioxane, or benzene.

Work-up in the manner previously described gave 0.15 g. (21%) of XXXVI, m.p. 165–170°, and 0.41 g. (37%) of XXXV, m.p. 190–191°. The combined oils gave a positive Tollens test as did XXXIX and XLI; attempts to isolate XXXIX from the oxidation failed.

Cleavage of XLII with Sodium Methoxide in Dioxane.—To 50 ml. of methanol was added 0.69 g. (0.03 g.-atom) of sodium. Removal of the solvent provided sodium methoxide which was ground to a powder and suspended in a solution containing 3.0 g. (0.01 mole) of XLII in 150 ml. of dioxane. The reaction mixture was stirred at room temperature for 48 hr. and filtered, and the resulting solid was dried over phosphorus pentoxide. The solid 2.96 g. exhibited an infrared spectrum identical with the tetrasodium salt of XXXVI. Purification of the salt as previously described gave 1.11 g. (41%) of XXXVI.

The dioxane solution was evaporated to a red oil which was dissolved in 100 ml. of water and washed with chloroform, carbon disulfide, and ether. The organic extracts were combined, dried, and evaporated to give 0.40 g. of an oil which provided 0.13 g. (11%) of V when chromatographed on Florisil.

The aqueous solution was acidified with 6 *N* hydrochloric acid, and the hydrogen sulfide evolved was trapped as lead sulfide, 0.2 g. (10%). Extraction of the aqueous solution with ether and then extraction of the ether layer with 10% sodium bicarbonate solution provided a yellow bicarbonate extract. Evaporation of the ether layer gave 0.15 g. of an unidentified red oil.

The bicarbonate extract was acidified with 6 *N* hydrochloric acid and extracted with ether. The red oil resulting from removal of the ether was dissolved in carbon tetrachloride and crystallized on standing to give 0.16 g. (11%) of yellow solid XXXVIII, m.p. 180–187°. Recrystallization from acetone lowered the melting point to 174–180°. The infrared spectrum of this substance was identical with the sample of XXXVIII obtained from XXXIV.

Anal. Calcd. for $C_{32}H_{24}O_4S_2$: C, 71.61; H, 4.51; S, 12.24; mol. wt., 536. Found: C, 71.55, 71.31; H, 4.51, 4.91; S, 12.24, 11.88; mol. wt., 403, 436 (Rast), 448 (ebulscopic).

The material XXXVIII gave a negative nitroprusside test for disulfide and mercaptan, but a positive sodium azide–iodine test and a positive phosphomolybdic acid test for mercaptan. Attempts to prepare 2,4-dinitrochlorobenzene derivatives of XXXVIII failed as did the reaction of XXXVIII with alcoholic potassium hydroxide and methyl iodide. In these cases the starting material was usually recovered unchanged.

The infrared spectrum of XXXVIII exhibited major peaks at 1664, 1642, and 1543 cm.$^{-1}$. The n.m.r. spectrum of XXXVIII showed the following proton groups: a doublet centered at τ 6.26 (J = 6 c.p.s.) and another doublet at 5.98 (J = 7 c.p.s.). The integration of these two groups corresponded to 1.92 protons. A group at lower field integrated for one proton. The group consisted of a doublet centered at τ 4.78 (J = 6 c.p.s.) and another doublet centered at 4.67 (J = 7 c.p.s.). The aromatic proton multiplet integrated for 19.2 protons. The spectrum was obtained in a trifluoroacetic acid–carbon tetrachloride mixture using tetramethylsilane as an internal reference. The material was recovered unchanged from this solvent system.

Cleavage of XLII with Sodium Methoxide in Methanol. Isolation of I.—A 3.0-g. (0.01-mole) sample of XLII was dissolved in 400 ml. of methanol and treated with a solution containing 0.03 mole of sodium methoxide in 100 ml. of methanol. The reaction mixture was stirred for 20 min. and acidified with 6 *N* hydrochloric acid. The solvent was removed and the residue was partitioned between methylene chloride and water. The insoluble material dissolved when a little sodium bicarbonate was added. The methylene chloride extract was evaporated and provided 2.0 g. (66%) of XLII.

A similar reaction conducted on 0.3 g. (0.001 mole) of XLII was followed by thin layer chromatography on silica gel G. Benzene–chloroform (4:3) was used as the developing solvent. Aliquots were spotted before the addition of base, at zero time and at 15-min. intervals for 1.75 hr. Aliquots were taken at 3, 4, 6, 9, 19, and 25 hr.

Aliquots from the cleavage of I with 1 mole of base were taken at the same times and spotted on the same chromatogram. The chromatogram of XLII showed only one spot during the initial 45 min. The spot had the same R_f value as I. The later aliquots showed several spots, most of which had the same R_f values as the spots from the cleavage of I.

Cleavage of Methyl 5-Phenyl-3,4-dithiapentanoate (XLIII) with Potassium *t*-Butoxide.—A solution of 5.61 g. (0.024 mole) of XLIII in 25 ml. of *t*-butyl alcohol and 3.0 mmoles of potassium *t*-butoxide was refluxed for 6 hr. under nitrogen. Removal of the solvent and extraction of the resulting oil with petroleum ether (30–60°) gave 4.55 g. of oil which provided 1.05 g. of dibenzyl disulfide, m.p. 70–72°, when crystallized from methanol. Chromatography of the mother liquor (3.40 g.) on alumina gave an additional 0.51 g. of dibenzyl disulfide (total yield, 83%). When the cleavage was conducted at room temperature for 24 hr., 49% of dibenzyl disulfide was isolated.

Cleavage of XLIII with Sodium Methoxide in the Presence of DPCC.—A solution of 4.00 g. (0.018 mole) of XLIII and 4.25 g. (0.018 mole) of DPCC in 100 ml. of methanol was treated with a solution of 0.018 mole of sodium methoxide in 150 ml. of methanol. The dropwise addition was carried out in 1 hr. The solution was stirred under nitrogen for 4 hr. and evaporated, and the resulting oil was extracted with ether. Removal of the ether provided 1.33 g. (24.5%) of N,N-diphenylthiocarbamate derivative of methyl thioglycolate (XLIV), m.p. 82–83°. A mixture melting point with an authentic sample melted at 82–85°.

Cleavage of 3-Carboxy-6-phenyl-4,5-dithiahexanoic Acid (XLV) with Sodium Methoxide.—To a solution of 0.01 mole of XLV in 200 ml. of methanol was added 0.03 mole of sodium methoxide in 10 ml. of methanol. After 2 hr. at room temperature, the solvent was removed, and the residue was extracted with ether. Evaporation of the ether gave dibenzyl disulfide in 60% yield, m.p. 71–72%.

The residue was dissolved in water, acidified, and extracted with ether. The ether extract provided 30% of XLV, m.p. 144–147°. A mixture melting point with an authentic sample was not depressed.

The aqueous layer was evaporated and the resulting solid partially dissolved in 150 ml. of ethyl acetate. The solution was filtered, concentrated to 50 ml., and diluted with petroleum ether (60–90°). The disulfide XXXVI (62%) was obtained as a white solid, m.p. 169–172°.

When the cleavage of XLV was conducted at room temperature for 72 hr., similar yields of the same products were obtained.

Cleavage of Diethyl Dithiodiglycolate (LI) with Potassium Ethoxide.—To a solution of 1.76 g. (0.021 mole) of potassium ethoxide in 15 ml. of dry ethanol was added 5.0 g. (0.021 mole) of LI. The reaction mixture was stirred magnetically for 9 days at 30°. After removal of a water-soluble salt, the filtrate was evaporated to dryness, and the residue was partitioned between water and ether. The ether extracts were dried and evaporated to a residual oil (3.1 g.). Analysis of the oil in the vapor fractometer indicated 1.06 g. (34.5%) of diethyl 3-thiaglutarate (LII) and 65% of LI were present. A 40-in. glass column packed with 30–60-mesh Celite containing 1% Carbowax 400 was employed (ethyl benzoate; 117°; helium flow, 218 cc./min; elution time, 28 and 192 sec.).