The Alkaline Decomposition of Organic Disulfides. V. Experimental Variants of α Elimination

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Several compounds, which might have been expected to undergo α elimination in aqueous alkaline solution, failed to give the anticipated mixtures of thiol, carbonyl compound, and hydrogen sulfide. Rather, fairly stable hemidithioketals were formed, apparently by the rapid conversion of the initially formed carbanions into stable thiolate anions. *meso*-1,2-Dithiane-3,6-dicarboxylic acid (1) in 0.1 *N* NaOH was transformed into *trans*-2-mercaptothiolane-2,5-dicarboxylic acid about 100 times as rapidly as the corresponding racemic disulfide was transformed into the cis isomer. The bicyclic anhydride of 1 decomposed at pH 8.6 in the same fashion, but even faster than did 1 in 0.1 *N* NaOH. The diethyl ester of 1 is about as sensitive to alkali as is the anhydride. Dithiodisuccinic acid decomposed predominantly by the alternative method and to a small extent by α elimination.

Organic disulfides appear to undergo alkaline decomposition by one of three alternative pathways, as determined by their molecular structures.[2] In the cases of disulfides in which a proton on a carbon atom α to a sulfur is sufficiently acidic, abstraction of this proton is the initiating step in alkaline decomposition, followed by the completion of an α elimination.[3] These reactions are characterized by the formation of carbonyl compounds and of thiol and hydrogen sulfide in a simple, integral ratio. Authenticated cases of β elimination are much less common,[4] although some version of this mechanism is invoked to explain transformation of cystinyl residues into lanthionyl residues, a process which is still not understood. Finally, direct nucleophilic displacement of sulfur from sulfur by hydroxide ion appears to cover the majority of all cases reported.[2,4]

Quantitative data in support of α elimination have been obtained for dithiodiacetate, which gives mercaptoacetic acid and hydrogen sulfide in the ratio of 3:1, and for 2,2′-dithiodipropionate, which gives 2-mercaptopropionic acid, hydrogen sulfide, and pyruvate in a ratio of 1:1:1.[3] It was expected that *meso*-1,2-dithiane-3,6-dicarboxylic acid (**1**), because of its structural analogy to 2,2′-dithiodipropionic acid, would decompose in a similar fashion to afford 2-keto-5-mercaptohexanedioic acid and an equivalent amount of hydrogen sulfide. Actually, they decompose at about the same speed (see Table I), but the cyclic compound gives not a trace of hydrogen sulfide, and the disappearance of each disulfide group corresponds quantitatively to the appearance of one thiol group. To account for these facts we suggest that the carbanion formed by the abstraction of the proton from the α carbon is rapidly converted into a stable thiolate anion, a five-membered cyclic hemidithioketal, *trans*-2-mercaptothiolane-2,5-dicarboxylic acid (**2**) (Scheme I). Actually, **2** was recovered as a crystalline product whose thiol content and neutralization equivalent corresponded to the assigned structure. **2** was readily alkylated in good yield by ethyl iodide to furnish **3**, a crystalline product whose elemental analysis, neutralization equivalent, and nmr spectrum corresponded to the structure assigned.

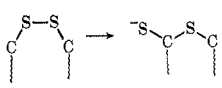
Fredga,[5] who first prepared the meso compound **1**, showed that it could easily be converted into the more stable racemic one (**4**) by heating above its melting point for a few minutes. The racemic compound **4** decomposes (see Table II) in exactly the same fashion as does the meso one (**1**), but the decomposition of **1** is approximately 100 times as rapid as that of **4** under comparably alkaline conditions. In order to account for this substantial difference it should be noted that in **1** one of the α protons must be axial and the other equatorial, while in **4**, since both carboxyl groups can scarcely be axial, both α protons probably are axial and therefore equally difficult to abstract.

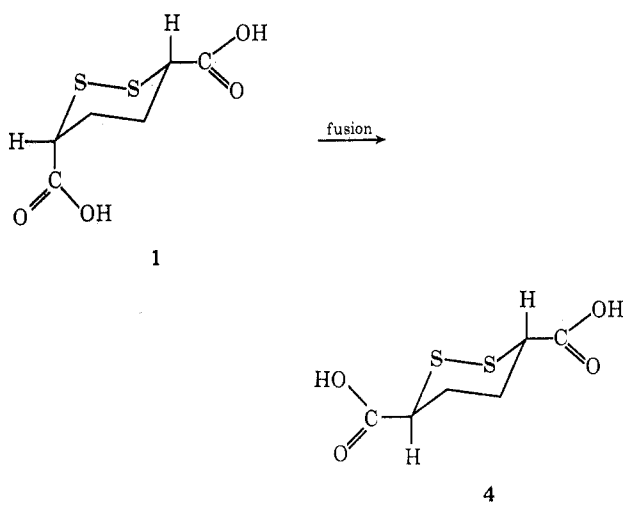
TABLE I

DECOMPOSITION OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID (1) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

Time, hr	RSSR	RSH	% dec	% S accounted for[c]
0	15.9[a]	0[a]	0	100
1	13.0	3.50	18.2	103
2	10.2	5.91	35.3	102
4	6.10	9.10	61.0	96
6	4.67	11.40	71.0	101
0	14.1[b]	0[b]	0	100
0.5	11.7	3.15	17.3	105
1	9.21	5.45	34.7	104
2	6.16	8.40	56.4	103
3	4.36	10.13	69.1	103

[a] $M \times 10^4$ in 0.0580 *N* NaOH. [b] $M \times 10^4$ in 0.1188 *N* NaOH. [c] On assumption that





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(1) Postodoctoral Research Associate, 1969–1970.
(2) J. P. Danehy and K. N. Parameswaran, *J. Org. Chem.*, **33**, 568 (1968).
(3) J. P. Danehy and J. A. Kreuz, *J. Amer. Chem. Soc.*, **83**, 1109 (1961).
(4) J. P. Danehy and W. E. Hunter, *J. Org. Chem.*, **32**, 2047 (1967).
(5) A. Fredga, *Ber.*, **71B**, 289 (1938).

SCHEME I

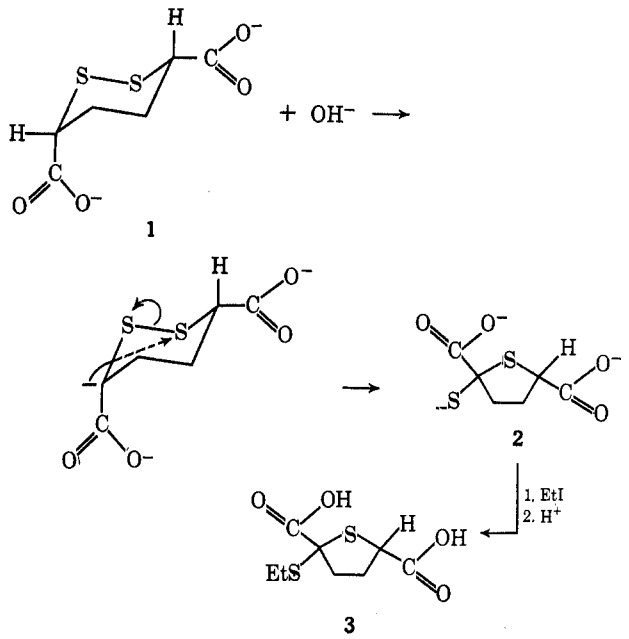


TABLE II

DECOMPOSITION OF RACEMIC 1,2-DITHIANE-3,6-DICARBOXYLIC ACID (4) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

Time, hr	RSSR	RSH	% dec	% S accounted for
0	17.1[a]	0[a]	0	100
7	16.7	0.35	2.0	100
24	16.5	0.48	3.0	99.7
0	16.3[b]	0[b]	0	100
3	15.8	0.52	3.1	100.1
8	15.0	1.07	8.2	98.4
24	13.7	2.72	16.2	100.3
0	15.9[c]	0[c]	0	100
1	15.5	0.64	2.3	99.6
4	14.2	2.18	10.7	96.3
6	12.6	2.95	20.9	97.8
9	11.7	3.92	26.6	98.4

[a] $M \times 10^4$ in 0.0578 N NaOH. [b] $M \times 10^4$ in 0.1984 N NaOH. [c] $M \times 10^4$ in 0.500 N NaOH.

Consideration of a difference between the reaction products from the alkaline decompositions of **1** and **4** supports the mechanism proposed. Decomposition of **1**, in which the carboxyl groups are cis, should give **2** (and **3**) in which the carboxyl groups are trans. Decomposition of **4**, in which the carboxyl groups are trans, should give the hemidithioketal **5** and its *S*-ethyl derivative **6** in which the carboxyl groups are cis. As a matter of fact, **3** and **6** are diastereomers;[6] the former melts at 115°, and the latter at 156–158°. That **3** and **6** have almost identical nmr spectra is not inconsistent with their structures. The known structures of **1** and **4**, and the considerations just given, are the bases for assigning trans configurations to **2** and **3** and cis configurations to **5** and **6**.

(6) As shown in detail in the Experimental Section, **1** gives both **2** and **5** in the ratio of 65:35, and **4** gives both **2** and **5** in the ratio of 30:70, respectively. While the reactions are not stereochemically clean, perhaps because of some scrambling at the carbanion stage, the observed predominances support our conclusion.

The bicyclic anhydride **7**[7] of **1** is exceedingly sensitive to alkaline decomposition, more sensitive than any other disulfide that has ever been reported (see Table III). At pH 8.6, **7** decomposed much more rapidly

TABLE III

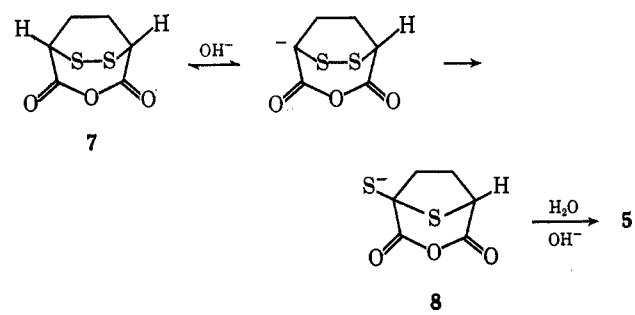
DECOMPOSITION OF THE ANHYDRIDE OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID (**7**) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2° AT pH 8.68

Time, min	RSSR	RSH	% dec	% S accounted for
0	16.60[a]			
20	11.39	5.21[a]	31.3	100
40	9.18	6.75	44.7	96
60	8.42	7.58	49.3	96
90	7.50	8.62	54.9	97
120	6.86	9.14	58.7	96
180	5.53	10.42	66.7	96

[a] $M \times 10^4$ in 0.2 M phosphate buffer at pH 8.68.

than did **1** in 0.1 N NaOH. The analytical results certainly are in accord with the idea that decomposition proceeds in the same manner (see Scheme II), and

SCHEME II



the observed speed precludes the possibility that hydrolysis of **7** to **1** is followed by alkaline decomposition of **1**. However, the isolation and characterization of the 2-mercaptothiolane-2,5-dicarboxylic acid anhydride (**8**) is not claimed. Indeed, by reason of the rotation required for the attack of the carbanion on the remote sulfur, it may be that **8** is never formed; the breaking of the sulfur–sulfur bond may induce the simultaneous hydrolysis of the anhydride bond to give **5**. Two supplementary factors probably account for the large difference in sensitivity. In **7** the inductive effect of the oxygens, which increases the lability of the α protons, is not mitigated by the negative charge which is necessarily present in **1**. Construction of a model shows that both α protons are unequivocally equatorial. That the first of these factors is more important than the second is indicated by the fact that the alkaline decomposition of the diethyl ester of **1** is almost as facile as that of **7** (see Table IV). Nor should it be overlooked that ring strain makes some contribution to the ease with which the hypothetical carbanion attacks the remote sulfur. While the dihedral angle about the sulfur–sulfur bond is ~90° in a wide variety of acyclic disulfides,[8] it has been shown to be only 60° in **4**[9] and presumably is about the same in **1**.

(7) L. DeMytt, U. S. Patent 2,930,799 (March 29, 1960).

(8) O. Foss in "Organic Sulphur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, Oxford, 1961.

(9) O. Foss and T. Reistad, *Acta Chem. Scand.*, **11**, 1427 (1957).

TABLE IV

DECOMPOSITION OF *meso*-1,2-DITHIANE-3,6-DICARBOXYLIC ACID DIETHYL ESTER IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

Time, min	RSSR	RSH	% dec	% S accounted for
0	11.35[a]		0	100
20	9.42	1.79[a]	16.7	99
40	7.91	2.91	30.3	96
60	7.43	3.50	34.6	97
90	6.51	3.91	42.6	92
120	6.22	4.43	45.3	94
180	5.67	5.18	49.0	96
0	9.30[b]		0	100
4 hr	8.12	1.10[b]	12.7	99
22 hr	7.97	1.19	14.3	99

[a] $M \times 10^4$ in 0.2 M phosphate buffer at pH 8.68. [b] $M \times 10^4$ in 0.2 M phosphate buffer at pH 7.00; no hydrogen sulfide detectable at any time.

In view of the extreme sensitivity of the anhydride **7** to decomposition in mildly alkaline solution, it is particularly interesting that in order to hydrolyze it to the corresponding dicarboxylic acid (**1**) it is necessary to reflux it in aqueous 2 N HCl for several hours. The disulfide linkage survives this treatment quantitatively.

However, a cyclic disulfide is not a necessary condition for the kind of reaction described here. Howard[10] found that diethyl dithiodiacetate was cleaved at a low temperature by sodium methoxide in anhydrous methanol to give the rather unstable ester of 2-mercapto-3-thiaglutaric acid and proposed a mechanism essentially the same as the one invoked here. It was expected that dithiodisuccinic acid (**9**) would decompose readily by α elimination to give equivalent amounts of oxaloacetate (ketosuccinate), mercaptosuccinate, and hydrosulfide. The determination of relatively small amounts of hydrogen sulfide (a maximum of 5% of the total sulfur rather than the expected 50%) gave evidence that this may be a minor pathway. An approximate sulfur balance is obtained (see Table V) when the

TABLE V

DECOMPOSITION OF DITHIODISUCCINIC ACID (**9**) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

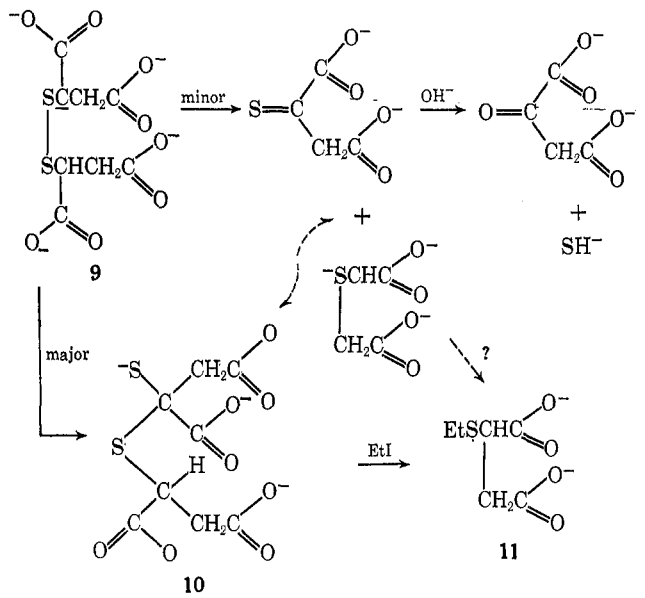
Time, hr	RSSR	RSH	% dec	% S accounted for
0	8.30[a]	0	0	100
24	6.10	2.47[a]	26.5	103
48	4.80	4.50	42.2	112
0	8.95[b]	0[b]	0	100
1	8.14	1.28	9.1	105
3	6.68	2.75	25.4	105
6	5.64	3.90	37.0	106

[a] $M \times 10^4$ in 0.1492 N NaOH. [b] $M \times 10^4$ in 0.5112 N NaOH.

data are treated on the assumption that a hemidithioketal **10** is the principal product (Scheme III). However, attempts to prepare the *S*-ethyl derivative of **10** resulted only in the formation of 2 mol of the *S*-ethyl derivative of mercaptosuccinic acid (**11**) for each mole of the original disulfide **9**. It would not be difficult to account for the formation of 1 mol of **11**; **10** might be

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

SCHEME III



in equilibrium with a very small amount of the same products which would result directly from an α elimination (dotted arrow in Scheme III), and under alkylating conditions the mercaptosuccinate might compete for the ethyl iodide to the exclusion of its precursor. The formation of a small but significant amount of hydrogen sulfide is in agreement with this view. However, we are at a loss to account for the repeated recovery of almost 2 mol of **11** for each mol of **10**.

At least two other experimental facts support the view that the hemidithioketal **10** is formed and persists in alkaline solution. During the alkaline decomposition of **9**, absorption with a well-defined maximum at 296 nm gradually increases to a maximal value which persists indefinitely. Treatment with ethyl iodide dissipates the absorption. Also, acidification of an alkaline solution to pH 1–2 destroys the absorption, and it does not reappear upon making the solution alkaline again. However, when an alkaline solution is neutralized only to pH 10, evaporated to dryness, and redissolved in water, the absorption at 296 nm is still present. Aliphatic thiolate ions absorb maximally in the range of 235–250 nm and aromatic ones in the range of 265–305 nm.[11] Fleury and Tohier[12] have observed the development of absorption at 315 nm, which gradually passes over to 335 nm, during the alkaline decomposition of dithiodiacetic acid. Earlier, Rosenthal and Oster[13] observed the absorption at 335 nm and attributed it to thioglyoxylic acid, S=CHCO$_2$H. It seems reasonable, then, that the persistent absorption at 296 nm is attributable to the alkali-stable **10** and that the absorption at 315 nm is attributable to the transient 2-mercapto-3-thiaglutarate ion which Fleury and Tohier have isolated.

All of these facts furnish a basis for resolving the apparent contradiction between our earlier results on the alkaline decomposition of dithiodiacetate and the report of Fleury and Tohier who, following the decomposition spectrophotometrically and polarographically, could find no evidence for hydrogen sulfide. In our

(11) J. P. Danehy and K. N. Parameswaran, *J. Chem. Eng. Data*, **13**, 386 (1968).

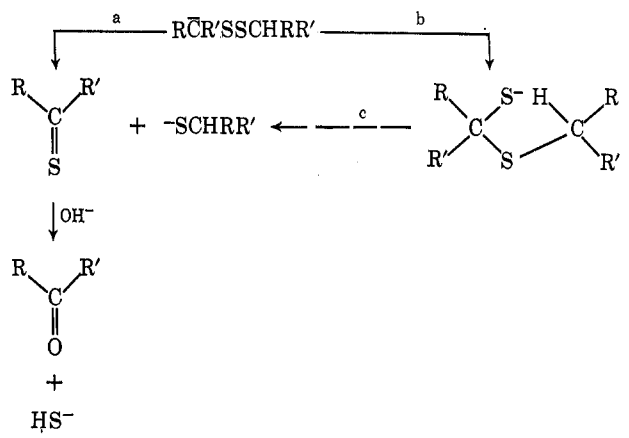
(12) M. Fleury and J. Tohier, *C. R. Acad. Sci., Ser. C*, **264**, 693 (1967).

(13) N. A. Rosenthal and G. Oster, *J. Amer. Chem. Soc.*, **83**, 4445 (1961).

work, aliquots of the reaction mixture were quenched in acid before analysis, and it might be that the hemidithiomercaptal undergoes hydrolysis and that hydrogen sulfide appears only at that stage. We have recently followed the decomposition of dithiodiacetate in aqueous alkali spectrophotometrically and have found that under the same conditions that led to ~50% decomposition[3] according to our analyses the absorption at 315 nm was still maximal. The conditions under which Fleury and Tohier oberved the transition from 315 to 335 nm were much more alkaline.

It appears likely then that in the cases of those disulfides in which a proton on a carbon α to sulfur is sufficiently acidic so that proton abstraction is the operative initial step in alkaline decomposition, three alternatives are possible (Scheme IV), and the one most difficult to

SCHEME IV



authenticate, direct α elimination (a), is the one we have until recently considered to be the most likely. It is now clear that pathway b can lead to stable cyclic products. After the fact, this is not too surprising since Owen[14] has shown that cyclic hemimonothioacetals are more stable than their oxygen analogs, and Field[15] has reported several quite stable hemimercaptals. With acyclic disulfides, pathway b can lead to relatively unstable intermediates and final products *via* pathway c, as in the case of dithiodiacetate, or to relatively stable products whose final disposition is not completely understood, as in the case of dithiodisuccinate.

Recently, Reeve and Nees[16] reported that 2,2'-diphenyldithiodiacetic acid (**12**) was resistant to attack by aqueous ammonia at 80° and by 15% KOH in methanol at 50°. These results are surprising for two quite different reasons. First, Schöberl[17] found that this disulfide decomposes readily in aqueous alkali. Second, it is to be expected that the phenyl groups would labilize the protons on the α carbons so that carbanion formation in this disulfide would be more facile than in the already sensitive dithiodiacetic acid.[3] We have investigated the behavior of **12** in aqueous alkali and find that it is indeed more sensitive than dithiodiacetic acid (see Table VI) and that the results correspond formally to an α elimination (Scheme IV, pathway a), irrespective of whether the reaction proceeds *via* a or b plus c. As expected, the order of decreasing sensitivity is $(-SCHPhCO_2H)_2 > (-SCH_2CO_2H)_2 > (-SCHMeCO_2H)_2$.

TABLE VI

DECOMPOSITION OF 2,2'-DIPHENYLDITHIODIACETIC ACID (12) IN AQUEOUS ALKALINE SOLUTIONS AT 35.2°

Time, hr	RSSR	RSH	H_2S	% dec	% S accounted for
0	9.65[a]			0	100
1	5.08	4.86[a]	3.88[a]	47.3	98
2	4.44	6.03	5.06	54.0	102
0	9.70[b]			0	100
1	8.22	1.66[b]	0.82[b]	15.2	98
2	7.18	2.90	1.44	26.0	97
3	6.96	3.24	1.82	28.2	98
5	6.68	3.68	2.56	31.1	101
10.5	5.49	4.64	3.73	43.4	100
24	4.00	6.04	5.13	68.8	99

[a] In 0.100 *N* NaOH. [b] In 0.0180 *N* NaOH.

Experimental Section

Materials.—*meso*-2,5-Dimercaptoadipic acid, melting at 175–177° (lit.[5] mp 188°), 94.5% thiol by titration with aqueous potassium triiodide, *meso*-2,5-dimercaptoadipic acid diethyl ester, melting at 54–56°, 97.4% thiol by titration with aqueous potassium triiodide, *meso*-1,2-dithiane-3,6-dicarboxylic acid anhydride (**7**), melting at 74–76° (lit.[6] mp 77°), and 2,2'-diphenyldithiodiacetic acid (**12**), melting at 201–205° (lit.[16] mp 210–212°), were gifts from the Toni Division of the Gillette Co., Chicago, Ill. Mercaptosuccinic acid, melting at 154° (lit.[18] mp 149–150°), 99.3% pure by determination of neutralization equivalent, was a gift from Evans Chemetics, New York, N. Y. *meso*-1,2-Dithiane-3,6-dicarboxylic acid (**1**) was prepared by oxidation of the corresponding thiol in aqueous solution with either aqueous potassium iodide or aqueous hydrogen peroxide. After recrystallization from water, **1** melted at 197–199° (lit.[5] mp 199°). Racemic 1,2-dithiane-3,6-dicarboxylic acid (**4**) was prepared by heating ~5 g of **1** in a porcelain dish at ~230° for 7–8 min until the melt resolidified. After recrystallization from glacial acetic acid, **4** melted at 267–279° (lit.[5] mp 275° dec). *meso*-1,2-Dithiane-3,6-dicarboxylic acid diethyl ester was prepared by oxidation of the corresponding thiol in ethanol solution with a solution of iodine in ethanol; evaporation, extraction of the residue with ethyl ether, and evaporation of the ethereal extract gave an oil which distilled at 117° (0.5 mm). Dithiodisuccinic acid (**9**) was prepared by oxidation of the corresponding thiol in aqueous solution with aqueous hydrogen peroxide. After recrystallization from acetic acid–benzene, it melted at 171–173° (lit.[19] mp 168.5°).

Transformation of *meso*-1,2-Dithiane-3,6-dicarboxylic Acid (1) into 2-Mercaptothiolane-2,5-dicarboxylic Acid and of the Latter into 2-Ethylmercaptothiolane-2,5-dicarboxylic Acid.—**1** (4.9 g) was dissolved in 200 ml of aqueous sodium hydroxide (10 g of NaOH) under nitrogen at 35.2°. After 4 hr analysis[3] showed that the decomposition was substantially complete. The solution was acidified to pH 1 with hydrochloric acid and extracted with ethyl ether, and the ethereal extract was dried with magnesium sulfate and evaporated to dryness to give 3.5 g of a solid thiol. Extraction of this solid with chloroform left 2.3 g (65%) of a thiol insoluble in chloroform which, after recrystallization from ethyl ether–Skellysolve B, melted at 139–142°: ir (KBr) 3000 (CH), 2600 (SH), and 1690 cm^{-1} (COOH); nmr (D_2O) δ 2.58 (J = 155 Hz, multiplet, 4 H, methylene), 4.38 (J = 263 Hz, t, 1 H, methine). This compound is considered to be **2**, the trans isomer. Evaporation of the chloroform solution gave 1.2 g (35%) of a thiol which, after recrystallization from chloroform–Skellysolve B, melted at 117–120°: ir (KBr) 3000 (CH), 2600 (S H), and 1690 cm^{-1} (COOH); nmr (CF_3COOH) δ 2.71 (J = 163 Hz, multiplet, 4

(14) J. M. Cox and L. N. Owen, *J. Chem. Soc.*, 1130 (1967).
(15) L. Field, B. J. Sweetman, and M. Bellas, *J. Med. Chem.*, **12**, 624 (1969).
(16) W. Reeve and M. Nees, *J. Amer. Chem. Soc.*, **89**, 647 (1967).
(17) A. Schöberl, *Ber.*, **67B**, 1545 (1934).
(18) B. Holmberg, *Ark. Kemi. Mineral Geol.*, **6** (1), 1 (1915).
(19) A. Schöberl and H. Eck, *Justus Liebigs Ann. Chem.*, **522**, 97 (1936).

H, methylene), 4.38 (J = 264 Hz, t, 1 H, methine). This compound is considered to be **5**, the cis isomer. To 0.300 g of **2** dissolved in 50% aqueous ethanol was added sufficient aqueous sodium hydroxide to give a pH value of 10. Ethyl iodide (0.30 g) was added, the solution stirred until a negative value for sulfhydryl group was obtained (Folin's reagent), the solution acidified to pH 1, the ethanol removed by flash evaporation under reduced pressure, the residual aqueous solution extracted with ethyl ether, and the ethereal extract evaporated to leave 0.180 g of **3** which, after recrystallization from ethyl ether–Skellysolve B, melted at 115–117°: neutralization equivalent, 120.5 (calcd 118.2); nmr (CF_3COOH) δ 1.31 (J = 79 Hz, t, 3 H, methyl), 2.75 (J = 165 Hz, multiplet, 6 H, methylene), 4.47 (J = 257 Hz, t, 1 H, methine). *Anal.* Calcd: C, 40.66; H, 5.12; S, 27.14. Found: C, 41.11; H, 5.38; S, 26.64.

Treatment of 0.300 g of **5** with 0.30 g of ethyl iodide as above gave 0.245 g of **6** which, after recrystallization from chloroform–ethyl ether, melted at 156–158°: nmr (CF_3COOH) δ 1.31 (J = 79 Hz, t, 3 H, methyl), 2.75 (J = 165 Hz, multiplet, 6 H, methylene), 4.47 (J = 258 Hz t, 1 H, methine.) *Anal.* Calcd: C, 40.66; H, 5.12; S, 27.14. Found: C, 40.78; H, 5.14; S, 26.91.

Transformation of Racemic 1,2-Dithiane-3,6-dicarboxylic Acid (4) into 2-Mercaptothiolane-2,5-dicarboxylic Acid and of the Latter into Its *S*-Ethyl Derivative.—In a procedure that differed from the immediately preceding one only in that the concentration of sodium hydroxide was ~3 N, 3.30 g of **4** was transformed into 2.70 g of solid thiol which was fractionated into 0.80 g of **2** (30%) and 1.90 g of **5** (70%). From both **2** and **5** the *S*-ethyl derivatives, **3** and **6**, were prepared as before.

Transformation of Dithiodisuccinic Acid (9) into 2-Mercapto-3-thiapentane-1,2,4,5-tetracarboxylic Acid (10) and of 10 into *S*-Ethylmercaptosuccinic Acid (11).—**9** (1.12 g) was dissolved in a solution of 12.5 g of sodium hydroxide in 100 ml of water at room temperature under nitrogen. After ~2 hr the absorbance at 296 nm had reached a maximum. Ethyl iodide and sufficient ethanol to give a homogeneous solution were then added. When the test for the sulfhydryl group was negative, the solution was acidified to pH 2 and partially evaporated under reduced pressure, the residual aqueous solution extracted with ethyl ether, and the ethereal extract dried with magnesium sulfate and evaporated to dryness to give 1.17 g of a product which, after recrystallization from chloroform–Skellysolve B, melted at 95–97°. This product was identical in melting point and nmr spectrum with an authentic specimen of **11** prepared by alkylating mercaptosuccinate with ethyl iodide. Again, 3.14 g of **9** was dissolved in a solution of 6.0 g of sodium hydroxide in 100 ml of water under nitrogen. When the absorbance maximum at 296 nm was attained, the solution was neutralized to pH 10.0 and evaporated to dryness. After holding the residue over phosphorus pentoxide for some time, it was redissolved in water and the absorbance at 296 nm was found to be comparable to the previous value.

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Registry No.—**1**, 28463-60-7; **2**, 28463-61-8; **3**, 28463-62-9; **4**, 2611-41-8; **5**, 28463-64-1; **6**, 28463-65-2; **7**, 28463-66-3; **9**, 3384-95-0; **12**, 4695-07-2; *meso*-1,2-dithiane-3,6-dicarboxylic acid diethyl ester, 28463-67-4.

The Synthesis of 6,6′-Diethynyldiphenic Anhydride[1]

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The synthesis of 6,6′-diethynyldiphenic anhydride (**10**) is described (Scheme I). Methyl 2,3-diiodobenzoate (**2**) was heated with copper bronze to yield dimethyl 6,6′-diiododiphenate (**3**). Heating **3** with carbethoxyethynylcopper in pyridine yielded dimethyl 6,6′-bis(carbethoxyethynyl)diphenate (**6**) which, by preferential alkaline hydrolysis, was converted into dimethyl 6,6′-bis(carboxyethynyl)diphenate (**8**). After decarboxylation of **8**, the resulting ester was hydrolyzed to 6,6′-diethynyldiphenic acid (**9**). Treatment of **9** with ethoxyacetylene afforded **10** which is stable thermally up to about 200° when decomposition to yield dark polymeric material occurs. A few attempts at photolysis of **10** yielded unchanged **10** in almost quantitative yield. Heating of **2** with copper in dimethylformamide at 55° yielded 1,5-dicarbomethoxybiphenylene (**4**). In pyridine **3** yielded a small amount of 1,8-dicarbomethoxybiphenylene (**5**) on heating with copper. Intramolecular Ullmann coupling of 2-iodo-3-ethylbenzoic anhydride (**15**) proceeded in 90% yield on refluxing in DMF for 15 min, whereas conventional Ullmann coupling of methyl 2-iodo-3-ethylbenzoate (**14**) was much slower.

In this paper, the synthesis of 6,6′-diethynyldiphenic anhydride (**10**) is reported. This compound was synthesized because we wished to know whether or not the substituted tetrahedrane (**11**) would be formed on pyrolysis or photolysis. The most highly strained and condensed ring system containing carbon–carbon single bonds is that of tricyclo[1.1.0.0.^{2,4}]butane (tetrahedrane). The strain energy for tetrahedrane has been calculated to be 90 and 151 kcal/mol, respectively.[3,4]

Since attempted syntheses of tetrahedranetricarboxylic acid were reported,[5,6] a number of papers[7-11] dealing with unsuccessful attempts to prepare tetrahedranes have appeared. The synthesis of 6,6′-diethynyldiphenic anhydride (**10**) was undertaken because **10** seemed to offer the greatest chance to yield a tetrahedrane compound. Molecular models indicated that the two ethyl groups cross each other at about an 80° angle and the anhydride function supposedly would force the two ethynyl groups as close to each other as nonbonded interaction would allow. Furthermore, nmr analysis would readily show the loss of the acetylenic hydrogens in any product.

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