Oxidative Hydrolysis of 1,3-Dithiane Derivatives to Carbonyl Compounds Using *N*-Halosuccinimide Reagents

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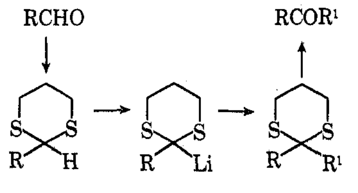
Specific and effective procedures are described for the conversion of a variety of substituted 1,3-dithianes to carbonyl compounds by means of mercury(II)-promoted hydrolysis or oxidative cleavage by *N*-bromo- or *N*-chlorosuccinimide. The conditions required for the mercury(II)-promoted hydrolysis of 1,3-dithianes may be correlated with the ease of C–S heterolysis and the electron-supplying ability of the substituents at C(2). The hydrolysis by the mercury method of 2,2-dialkyl derivatives is generally very facile and more rapid than that of 2-monoalkyl-1,3-dithianes, while the hydrolysis of 2-acyl-1,3-dithianes is very slow. For the latter cases especially the use of the *N*-halosuccinimides is advantageous, and three reagents of this type have been devised for use in aqueous acetonitrile or acetone: (1) *N*-bromosuccinimide alone, (2) *N*-bromosuccinimide with silver ion, and (3) *N*-chlorosuccinimide with silver ion. The use of the *N*-chlorosuccinimide–silver ion reagent is advantageous for unsaturated dithianes, since olefinic linkages are unaffected by it. 2,6-Lutidine and 2,4,6-collidine may be employed to buffer the three reagents in applications to acid-sensitive substrates. A number of aldehydes and ketones have been obtained in 70–100% yields using the halosuccinimide reagents.

1,3-Dithiane derivatives are versatile intermediates in the synthesis and interconversion of monocarbonyl and 1,2-dicarbonyl compounds. For example, numerous synthetic operations have been performed that involve the 2-acyl-1,3-dithiane moiety, including the extension of carbon chains, the masking and unmasking of carbonyl groups, the blocking and unblocking of activated methylene groups, the nucleophilic acylation of carboxylic acid derivatives,[1,2] the reduction of carbonyl groups to methylene groups, and the interchange[3] of a carbonyl group with an adjacent methylene group. Temporary inversion of the electrophilic reactivity of the aldehydic carbonyl group permits the synthesis of carbonyl compounds by the coupling of a nucleophilic aldehyde derivative with electrophiles. A useful procedure[1,2] for accomplishing this synthetic operation involves (1) conversion of the aldehyde to the 1,3-dithiane derivative, (2) metalation of this derivative with *n*-butyllithium in tetrahydrofuran, (3) reaction of the 2-lithio-1,3-dithiane derivative with an electrophile, and (4) hydrolysis of the resulting 1,3-dithiane derivative to the carbonyl compound using mercuric chloride. Among the many carbonyl compounds synthesized by this lithiodithiane procedure are 1-deuterioaldehydes,[4] acylsilanes and -germanes,[5,6] cyclic monoketones anddi ketones,[7,8] optically active aldehydes and ketones,[9] metacyclophanes,[10] acyclic monoterpenes,[11] and 21-keto steroids.[12] The present paper reports the oxidative hydrolysis of 1,3-dithiane derivatives to carbonyl compounds using *N*-halosuccinimide reagents. These oxidative reagents, unlike the mercury(II) reagents, permit the efficient hydrolysis of 2-acyl-1,3-dithiane derivatives to 1,2-dicarbonyl compounds and thus significantly extend the synthetic utility of the lithiodithiane method.



Hydrolysis Using Mercuric Chloride.—Mercuric chloride usually forms a sparingly soluble complex[13] with 1,3-dithiane derivatives that can be hydrolyzed in good yield (60–90%) when heated at 60–90° for 1–8 hr in an aqueous polar organic solvent (methanol,[2,4,5,7–10] ethanol,[11] ethylene glycol,[7] tetrahydrofuran,[10] acetone[6,11]). Insoluble bases (mercuric oxide, cadmium carbonate,[14] calcium carbonate[15]) are often added to neutralize the HCl formed during hydrolysis. Other reagents that also function as Lewis acids to promote the hydrolysis of 1,3-dithiane derivatives include acidic mercuric acetate,[16] mercuric oxide–boron trifluoride etherate,[17] and silver nitrate.[11] Although 2-aryl- and 2,2-dialkyl-1,3-dithianes undergo hydrolysis with mercuric chloride more readily than do the 2-alkyl derivatives,[2] even the latter are slowly hydrolyzed at 25°. 2-Benzyl-1,3-dithiane, for example, is hydrolyzed about 100 times slower at 25° than at 60° (Table I).

A variety of ketones bearing interrelated functional groups can be economically prepared by the lithiodithiane method using mercury(II)-promoted hydrolysis to generate the carbonyl group. The synthesis of 3-acetyl-2-cyclohexenone (6) by the indirect coupling of acetaldehyde and 2-cyclohexenone is exemplary. 2-Methyl-1,3-dithiane, prepared from acetaldehyde and

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[1] E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4**, 1075, 1077 (1965).

[2] For a recent review, see D. Seebach, *Syn.*, **1**, 17 (1969).

[3] J. A. Marshall and H. Roebke, *J. Org. Chem.*, **34**, 4188 (1969).

[4] D. Seebach, B. W. Erickson, and G. Singh, *ibid.*, **31**, 4303 (1966).

[5] E. J. Corey, D. Seebach, and R. Freedman, *J. Amer. Chem. Soc.*, **89**, 434 (1967).

[6] A. G. Brook, J. M. Duff, P. F. Jones, and N. R. Davis, *ibid.*, **89**, 431 (1967); A. G. Brook, D. G. Anderson, J. M. Duff, P. F. Jones, and D. M. MacRae, *ibid.*, **90**, 1076 (1968); A. G. Brook, P. F. Jones, and G. J. D. Peddle, *Can. J. Chem.*, **46**, 2119 (1968); P. R. Jones and R. West, *J. Amer. Chem. Soc.*, **90**, 6978 (1968).

[7] D. Seebach, N. R. Jones, and E. J. Corey, *J. Org. Chem.*, **33**, 300 (1968).

[8] E. J. Corey and D. Crouse, *ibid.*, **33**, 298 (1968).

[9] D. Seebach and D. Steinmüller, *Angew. Chem., Int. Ed. Engl.*, **7**, 619 (1968); D. Seebach, D. Steinmüller, and F. Demuth, *ibid.*, **7**, 620 (1968).

[10] T. Hylton and V. Boekelheide, *J. Amer. Chem. Soc.*, **90**, 6887 (1968).

[11] C. A. Reece, J. O. Rodin, R. G. Brownlee, W. G. Duncan, and R. M. Silverstein, *Tetrahedron*, **24**, 4249 (1968).

[12] J. B. Jones and R. Grayshan, *Chem. Commun.*, 741 (1970).

[13] Infrared data suggest that the Hg–S σ bonds in mercuric halide complexes of 1,3-dithiane and related sulfides are formed by donation of an equatorial sulfur electron pair, whereas both axial and equatorial electron pairs are involved in the Ag–S bonds of the silver nitrate adducts: see J. A. W. Dalziel, M. J. Hitch, and S. D. Ross, *Spectrochim. Acta, Part A*, **25**, 1055, 1061 (1969).

[14] M. L. Wolfrom, *J. Amer. Chem. Soc.*, **51**, 2188 (1929).

[15] The use of inexpensive $CaCO_3$ powder avoids the fresh precipitation of hydrated $CdCO_3$ and the difficulty of keeping heavy HgO powder in suspension.

[16] J. Z. Gougoutas, Ph.D. Thesis, Harvard University, 1964; R. B. Woodward, *Harvey Lect.*, **59**, 31 (1965).

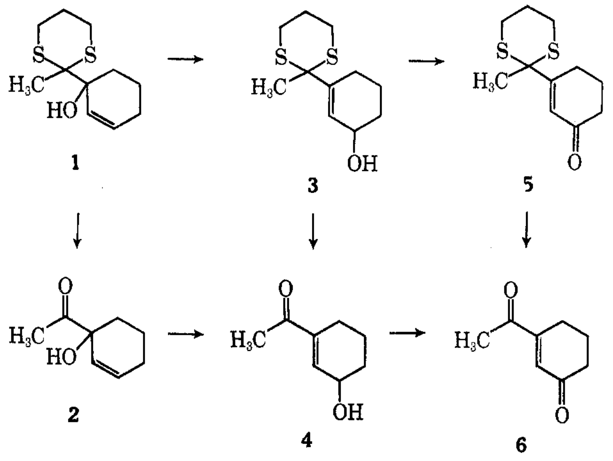
[17] E. Vedejs and P. L. Fuchs, *J. Org. Chem.*, **36**, 366 (1971).

Table I
Mercury(II)-Promoted Hydrolysis of 2-Benzyl-1,3-dithiane to Phenylacetaldehyde[a]

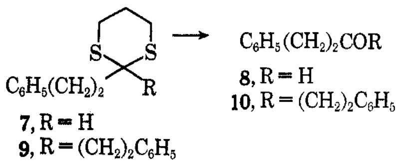
Temp, °C	Time, hr	Yield,[b] %
25	48	19
25	192	62
60	2	66
60	4	77

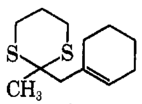
[a] Dithiane (1.0 mol), HgCl$_2$ (2.2 mol), and HgO (2.2 mol) in 90% aqueous CH$_3$OH. [b] Isolated as the 2,4-dinitrophenylhydrazone.

1,3-propanedithiol (91%), was treated sequentially with *n*-butyllithium and 2-cyclohexenone to afford the α-hydroxy dithiane **1** (70%). The γ-hydroxy dithiane **3**, prepared by the isomerization of **1** with acid, has been hydrolyzed with mercuric chloride–cadmium carbonate to the γ-hydroxyenone **4** (80%).[8] In extending this work, the mercuric chloride hydrolysis of the α-hydroxy dithiane **1** to the α-hydroxy enone **2** required the presence of a buffer (CaCO$_3$) to prevent the HCl liberated during hydrolysis from catalyzing the partial isomerization[18] of **2** to **4**. Further, hydrolysis of the γ-keto dithiane **5** with the usual 2 mol of mercuric chloride was very slow; the use of 4 mol, however, provided the enedione **6** in 84% yield. As oxidation of the allylic alcohols **3** and **4** with active MnO$_2$ has afforded the corresponding enones in high yield,[8,19] conversion of the adduct **1** into the enedione **6** has been accomplished by three routes, each in about 70% yield overall.



The hydrolysis of several other 1,3-dithiane derivatives with mercuric chloride was examined to test the generality of the method. Several examples that proceeded in good yield are summarized in Table II. Initially run in aqueous alcohol, the hydrolyses were later conducted in aqueous 80% acetonitrile due to the greater solubility of both mercuric chloride and the dithiane substrates in this medium. Treatment of the dithiane **7** with mercuric chloride–mercuric oxide in aqueous methanol produced mainly the dimethyl ketal,[20] which gave the desired aldehyde on acid hydrolysis. The reaction of cyclohexenyl acetone, a 9:1 mixture of the enone **12** and the conjugated isomer **13**, with acidic 1,3-propanedithiol furnished only the dithiane **11** bearing an endocyclic double bond (85%). Mercury(II)-promoted hydrolysis of this dithiane afforded solely the unconjugated enone **12** by nmr, ir, and tlc criteria; use of these reactions allowed complete removal of the conjugated isomer from the initial enone mixture.

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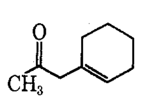
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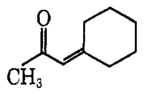
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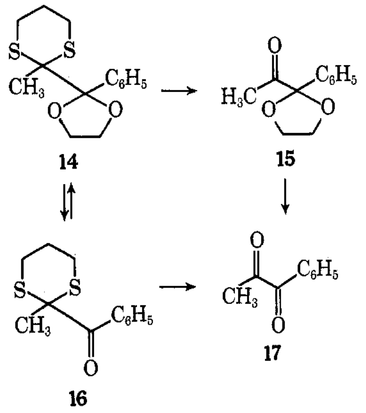
The slow ketalization of the α-keto dithiane **16** with ethylene glycol and nmr evidence that the dithiane ring of the product **14** is frozen in one chair conformation both attest to the steric congestion at the adjacent tetrasubstituted carbon atoms of **14**. Yet the dithiane ring was readily cleaved with twice the usual proportion of mercuric chloride and calcium carbonate.



Two of the dithianes examined, the 2-acyl-1,3-dithianes **16** and **18**, were relatively resistant to hydrolysis with mercuric chloride (Table III). Even prolonged hydrolysis of the α-keto dithiane **16** did not increase significantly the low yield of the α-dione **17** observed under the usual hydrolysis conditions.[22] Previous attempts[23] to hydrolyze α-keto dithioacetals with buffered mercuric chloride were unsuccessful; further, the reaction[17] of 2-benzoyl-1,3-dithiane with HgO–BF$_3$ etherate afforded not phenylglyoxal but benzoic acid (73%). Although mercuric acetate in aqueous acetic acid has been used

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[18] This facile isomerization was accomplished preparatively by treatment of the α-hydroxyenone **2** with trifluoroacetic acid (25°, 20 hr) to give the trifluoroacetate of rearranged alcohol **4** (85%) and solvolysis of the latter in methanolic sodium bicarbonate (25°, 25 hr) to liberate **4** (95%); see Experimental Section.

[19] Dithioketals are also stable to oxidation with chromium trioxide in pyridine; see N. Pappas and H. R. Nace, *J. Amer. Chem. Soc.*, **81**, 4556 (1959).

[20] 1,3-Dithiane derivatives have been converted into ketals using HgCl$_2$–anhydrous alcohol[10,21] and into *gem*-diacetates using Hg(OAc)$_2$–BF$_3$ etherate–acetic acid.[17]

[21] E. J. Corey, N. H. Andersen, R. M. Carlson, J. Paust, E. Vedejs, I. Vlattas, and R. E. K. Winter, *J. Amer. Chem. Soc.*, **90**, 3245 (1968); A. G. Brook and P. J. Dillon, *Can. J. Chem.*, **47**, 4347 (1969).

[22] An indirect conversion of the acyldithiane **16** into the dione **17** was accomplished in 55% yield overall by (1) vigorous ketalization of **16** with acidic ethylene glycol (90%), (2) hydrolysis of the dithiane ring of the bis ketal **14** with mercuric chloride (76%), and (3) prolonged hydrolysis of the acyldioxolane **15** with 9 *M* sulfuric acid in aqueous THF (87%); see Experimental Section.

[23] F. Weygand and H. J. Bestmann, *Z. Naturforsch., B*, **10**, 296 (1955).

TABLE II

HYDROLYSIS OF SIX 1,3-DITHIANES USING MERCURIC CHLORIDE[a]

Dithiane substrate	Buffer, mol	Aqueous solvent (%)	Time, hr	Carbonyl product	Yield, %
1	$CaCO_3$, 2.5	CH_3CN (80)	5.0	α-Hydroxyenone **2**	93
5	None	CH_3CN (80)	6.0	Enedione **6**	84
7	HgO, 1.1	CH_3OH (95)	4.5	3-Phenylpropional (**8**)	68
9	None	CH_3OH (90)	4.2	Ketone **10**	86
11	$CaCO_3$, 2.2	CH_3CN (80)	5.0	Nonconjugated enone **12**	90
14	$CaCO_3$, 4.4	CH_3CN (80)	4.0	α-Keto ketal **15**	76

[a] Dithiane (1.0 mol), mercuric chloride (2.2 mol, except 4.0 mol for **5** and **14**), buffer, and solvent were heated at reflux under nitrogen.

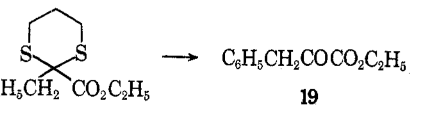
TABLE III

HYDROLYSIS OF TWO 2-ACYL-1,3-DITHIANES USING MERCURIC CHLORIDE, MERCURIC ACETATE, OR BROMINE

Dithiane substrate	Reactant, ratio[a]	Aqueous solvent (%)	Temp, °C (time, hr)	Yield,[b] %
16	$HgCl_2$, 2.2	CH_3CN (80)	80 (4)	13 (78)
16	$HgCl_2$, 2.2	CH_3CN (80)	80 (24)	20 (55)
18	$HgCl_2$, 2.2	C_2H_5OH (95)	80 (4)	0 (89)
16	$Hg(OAc)_2$, 2.0	HCO_2H (95)	75 (2.5)	37 (0)
16	$Hg(OAc)_2$, 2.2	HOAc (80)	90 (4)	40 (0)
16	Br_2, 2.0	0.33 *M* HCl, HOAc (65)	50 (1.5), 25 (36)	48 (40)
16	Br_2, 4.0	0.17 *M* HCl, HOAc (65)	25 (21)	47 (7)
16	Br_2, 4.0	0.33 *M* HCl, HOAc (65)	50 (1), 25 (21)	34 (5)
18	Br_2, 2.0	0.33 *M* HCl, HOAc (65)	50 (0.7)	33 (55)

[a] Moles per mole of dithiane. [b] Recovered dithiane (%) in parentheses.

to prepare a 1,2-cycloheptanedione derivative from a 2-acyl-1,3-dithiane,[16] hydrolysis of the α-keto dithiane **16** with mercuric acetate proceeded in only 40% yield (Table III).



18 **19**

A great variety of 2-acyl-1,3-dithianes are available by the acylation of 2-lithio-1,3-dithiane derivatives[1,2] or by the reaction of ketones bearing an enolizable methylene group with 1,3-propylene bis(*p*-toluenethiolsulfonate).[24,25] First applied in the Woodward–Barton synthesis of lanosterol,[26] the thiolsulfonate route has been used for the preparation of 2-acyl-1,3-dithianes from 3-keto steroids,[27] 11-keto steroids,[28] 2-decalones,[3,29] 17-yohimbone,[30] cyclohexanones,[31] and cycloheptanones.[16,32] Direct hydrolysis of these readily available 2-acyl-1,3-dithiane derivatives to 1,2-dicarbonyl compounds is a useful synthetic operation; the inefficiency of mercury(II) reagents in promoting this transformation emphasized the need for a more general method of 1,3-dithiane hydrolysis.

Oxidative Hydrolysis Using *N*-Halosuccinimides.—Dithioacetals and acyclic dithioketals undergo oxidative hydrolysis on treatment with bromine,[24,33–38] chlorine,[35] or iodine.[39] The oxidative hydrolysis of acyclic α-acyldithioacetals to α-ketoaldehydes using 2 mol of bromine in hydrochloric acid–acetic acid[34] proceeds in 75–90% yield; this method is useful for the hydrolysis of sugar dithioacetals.[37] Yet only moderate yields of 1,2-dicarbonyl compounds were obtained on hydrolysis of the model 2-acyl-1,3-dithianes using either 2 or 4 mol of bromine (Table III).

One mole of *N*-bromosuccinimide (NBS) or *N*-chlorosuccinimide (NCS) in anhydrous methanol rapidly oxidizes organic sulfides to sulfoxides (60–90%),[40] but carbon–sulfur bond cleavage predominates in the reaction of alkyl sulfides with 2 mol of NBS or NCS in dry methanol[40] or with aqueous NBS.[41] The latter observation suggested the use of the *N*-halosuccinimides for 1,3-dithiane hydrolysis, for this reaction requires a reagent that cleaves C–S bonds more readily than it oxidizes divalent sulfur.

2-Benzoyl-2-methyl-1,3-dithiane (**16**) was hydrolyzed to the α-dione **17** in high yield using NBS or NCS, especially in the presence of a silver(I) salt (Table IV).

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(24) J. C. A. Chivers and S. Smiles, *J. Chem. Soc.*, 697 (1928).

(25) The enamine derivatives of certain ketones also couple with this thiolsulfonate reagent to form 2-acyl-1,3-dithiane derivatives (M. L. Scheinbaum, Ph.D. Thesis, Harvard University, 1963).

(26) R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1131 (1957).

(27) J. L. Beton, T. G. Halsall, E. R. H. Jones, and P. C. Phillips, *ibid.*, 753 (1957); J. S. G. Cox, F. E. King, and T. J. King, *ibid.*, 514 (1959); S. Binns, J. S. G. Cox, E. R. H. Jones, and B. G. Ketcheson, *ibid.*, 1161 (1964); Y. M. Y. Haddad, W. T. Pike, G. H. R. Summers, and W. Klyne, *ibid.*, 6117 (1965); J. M. Midgley, W. B. Whalley, G. F. Katekar, and B. A. Lodge, *Chem. Commun.*, 169 (1965); J. M. Midgley, B. J. Millard, W. B. Whalley, and J. C. Smith, *ibid.*, 84 (1969).

(28) C. Djerassi, O. Halpern, G. R. Pettit, and G. H. Thomas, *J. Org. Chem.*, **24**, 1 (1959).

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(31) C. Djerassi, J. Osiecki, and E. J. Eisenbraun, *J. Amer. Chem. Soc.*, **83**, 4433 (1961).

(32) T. A. Crabb and K. Schofield, *J. Chem. Soc.*, 643 (1960).

(33) E. Fischer, *Chem. Ber.*, **27**, 673 (1894).

(34) F. Weygand and H. J. Bestmann, *ibid.*, **90**, 1230 (1957).

(35) The acylthio moiety is successively oxidized by chlorine to the disulfide, the thiosulfonate, and the sulfonyl chloride; see S. W. Lee and G. Dougherty, *J. Org. Chem.*, **5**, 81 (1940).

(36) C. B. Gauthier and C. Vaniscotte, *Bull. Soc. Chim. Fr.*, [5] **23**, 30 (1956), and previous papers.

(37) F. Weygand, H. J. Bestmann, and H. Ziemann, *Chem. Ber.*, **91**, 1040 (1958); F. Weygand, H. J. Bestmann, H. Ziemann, and E. Klieger, *ibid.*, **91**, 1043 (1958); H. Baganz and H. J. May, *ibid.*, **99**, 3771 (1966); R. Kuhn, W. Baschang-Bister, and W. Dafeldecker, *Justus Liebigs Ann. Chem.*, **641**, 160 (1961).

(38) W. E. Truce and F. E. Roberts, *J. Org. Chem.*, **28**, 961 (1963).

(39) G. A. Russell and L. A. Ochrymowycz, *ibid.*, **34**, 3618 (1969).

(40) R. Harville and S. F. Reed, Jr., *ibid.*, **33**, 3976 (1968).

(41) W. Tagaki, K. Kikukawa, K. Ando, and S. Oae, *Chem. Ind.* (*London*), 1624 (1964).

TABLE IV

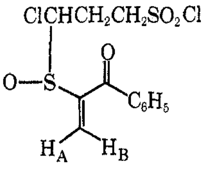
OXIDATIVE HYDROLYSIS OF 2-BENZOYL-2-METHYL-1,3-DITHIANE TO 1-PHENYL-1,2-PROPANEDIONE USING *N*-BROMOSUCCINIMIDE AND *N*-CHLOROSUCCINIMIDE

Reactant, ratio[a]					
Haloimide	Additives	Aqueous solvent (%)	Temp, °C	Time, min	Yield,[b] %
NBS, 4.0		$(CH_3)_2CO$ (97)	-5	2	48 (40)
NBS, 4.0		THF (90)	35	10	63 (27)
NBS, 6.0		$(CH_3)_2CO$ (97)	-5	2	85 (0)
NBS, 8.0		$(CH_3)_2CO$ (97)	0	2	91 (0)
NCS, 4.0		$(CH_3)_2CO$ (90)	30	10	38 (0)
NCS, 6.0		$(CH_3)_2CO$ (90)	30	10	60 (0)
NCS, 4.0	$Cd(NO_3)_2 \cdot 4H_2O$, 4.0	CH_3CN (90)	40	5	50 (0)
NCS, 8.0	$Cd(NO_3)_2 \cdot 4H_2O$, 8.0	CH_3CN (90)	10	5	50 (0)
NCS, 4.0	$CuCl_2 \cdot 2H_2O$, 4.0	CH_3CN (80)	30	10	60 (0)
NCS, 1.0	$AgClO_4$, 1.2	$(CH_3)_2CO$ (90)	30	10	34 (56)
NCS, 2.0	$AgClO_4$, 2.3	$(CH_3)_2CO$ (90)	30	10	75 (15)
NCS, 3.0	$AgNO_3$, 3.5	CH_3CN (90)	2	7	80 (0)
NCS, 4.0	$AgClO_4$, 4.5	$(CH_3)_2CO$ (90)	30	10	92 (0)
NCS, 8.0	$AgNO_3$, 8.1	CH_3CN (80)	32	5	62 (0)
NBS, 2.2	$AgClO_4$, 2.2	$(CH_3)_2CO$ (97)	20	15	55 (43)
NBS, 4.1	$AgClO_4$, 5.0	$(CH_3)_2CO$ (97)	20	15	85 (0)
NBS, 7.0	$AgNO_3$, 7.5; DMP, 16	CH_3CN (80)	-5	17	85 (0)
NBS, 6.0	$AgNO_3$, 6.3; TMP, 12	CH_3CN (85)	30	10	100 (0)

[a] Moles per mole of dithiane (DMP, 2,6-dimethylpyridine; TMP, 2,4,6-trimethylpyridine). [b] Recovered dithiane (%) in parentheses.

Aqueous 90–97% acetone and aqueous 80% acetonitrile were suitable solvent systems when NBS or NCS was used alone or with silver perchlorate. Reactions using silver nitrate were conducted in aqueous 80% acetonitrile, for this salt is only sparingly soluble in aqueous acetone. In each case, a solution of the dithiane was added *to* a homogeneous solution containing the *N*-halosuccinimide and additives; when the reagents were added to the dithiane, the yield of ketone was consistently lower and occasionally vanishing.

In contrast to the 2 mol of bromine[34] needed to hydrolyze acyl dithioacetals to α-ketoaldehydes and to the single mole of chlorine[35] or bromine[36] required to convert other dithioacetals to aldehydes, about 6 mol of NBS was necessary for complete hydrolysis of **16** in the absence of silver ion. Hydrolysis using NBS (6 mol) in aqueous acetone, which occurred even at −20°, was complete within 2 min at 0°; a similar reaction in aqueous 70% dioxane was 83% complete in 4 min at 30° and complete in 9 min (nmr). Four moles of NBS or NCS was sufficient when the molar amount of silver ion present exceeded that of the haloimide; this decrease in stoichiometry may be due to a change in the electrophilic halogen species caused by the presence of silver ion.[42] The use of NCS alone or with cadmium nitrate or cupric chloride furnished only moderate yields of the α-dione; the major by-product (30% yield) with or without cupric chloride was the highly functionalized α-chlorosulfoxide **20**.[35,43]



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A buffer system compatible with silver ion and the *N*-halosuccinimides was desired to prevent the rapid rise in acidity that occurs during hydrolysis. High recovery of the 2-acyl-1,3-dithiane **16** was observed on attempted hydrolysis with NBS in the presence of triethylamine (pK_a = 10.8) or sodium succinimide (pK_a = 9.3), for these bases are evidently incompatible with protonated NBS. In the presence of potassium acetate or an equimolar mixture of sodium acetate and acetic acid, the dithiane was completely consumed but the α-dione was formed in low yield (12 and 24%, respectively). Though the use of pyridine[44] (pK_a = 5.17[45]) as buffer afforded only moderate yields of the dione, 2.6-dimethylpyridine (pK_a = 6.75[45]) or 2,4,6-trimethylpyridine (pK_a = 7.3[46]) furnished the dione **17** in excellent yield (Table IV). These sterically hindered pyridines had little effect on the rate of hydrolysis or the role of silver ion; even though both pyridines form crystalline complexes with silver ion, a moderate concentration[47] of uncomplexed silver ion is still available during hydrolysis.

Oxidative hydrolysis of the seven other model dithianes with NBS or NCS–silver nitrate was also successful (Table V), the isolated yield of the carbonyl product generally being greater for the oxidative procedure than

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[42] (a) The presence of Ag(I) salts during the oxidation of anisole by HOCl reduces the chloride ion concentration sufficiently to suppress completely any reaction through Cl_2 [P. B. D. de la Mare, A. D. Ketley, and C. A. Vernon, *J. Chem. Soc.*, 1290 (1954)]. (b) The NBS oxidation of secondary alcohols to ketones, which initially proceeds with NBS as oxidant, *mainly occurs by oxidation with bromine generated rapidly in situ; the* oxidation by Br_2 is completely suppressed in the presence of Hg(II) salts [N. Venkatasubramanian and V. Thiajarajan, *Can. J. Chem.*, **47**, 694 (1969)]. (c) The rate-limiting step in the oxidation of secondary alcohols with NCS in aqueous HCl is the generation of Cl_2, the major oxidant, by reaction of chloride ion with protonated NCS [N. S. Srinivasan and N. Venkatasubramanian, *Tetrahedron Lett.*, 2099 (1970)].

[43] The ratio of α-halogenation to C–S bond cleavage observed on reaction of the following electrophilic halogen reagents with dibenzyl sulfide ($CDCl_3$, 35°) was 3.6 for NCS, 0.78 for Br_2, and 0.29 for NBS: see G. E. Wilson, Jr., and M. G. Huang, *J. Org. Chem.*, **35**, 3002 (1970).

[44] C. Walling and M. J. Mintz, *ibid.*, **32**, 1286 (1967).

[45] W. J. Peard and R. T. Pflaum, *J. Amer. Chem. Soc.*, **80**, 1593 (1958).

[46] H. Lunden, *Chem. Zentralbl.*, 788 (1908).

[47] The concentration of uncomplexed silver ion in a saturated (0.2 *M*) solution of $Ag(2,6\text{-dimethylpyridine})_2NO_3$ in 4:1 acetonitrile–water is near 5×10^{-3} *M*, *for the dissociation constant of the complex ion* $Ag(2,6\text{-dimethylpyridine})^+$ is 3.4×10^{-6} *M* in acetonitrile.[45]

TABLE V

OXIDATIVE HYDROLYSIS OF SEVEN 1,3-DITHIANES WITH *N*-BROMOSUCCINIMIDE OR *N*-CHLOROSUCCINIMIDE–SILVER NITRATE

Dithiane substrate	Reactant, ratio[a]	Aqueous solvent (%)	Temp, °C	Time, min	Carbonyl product	Yield, %
1	NCS, 4.0 $AgNO_3$, 4.5	CH_3CN (80)	55	5	α-Hydroxyenone **2**	71
5	NCS, 4.0 $AgNO_3$, 4.5	CH_3CN (71)	0	25	Enedione **6**	100[b]
7	NBS, 6.0	CH_3CN (80)	5	5	3-Phenylpropional (**8**)	90
9	NBS, 8.0	$(CH_3)_2CO$ (96)	−5	5	Ketone **10**	97
11	NCS, 4.0 $AgNO_3$, 4.5	CH_3CN (80)	25	10	Nonconjugated enone **12**	94
14	NBS, 6.0	CH_3CN (80)	15	10	α-Keto ketal **15**	100
18	NBS, 9.0	$(CH_3)_2CO$ (97)	−5	3	α-Keto ester **19**	78

[a] Moles per mole of dithiane. [b] Reference 8.

for the mercuric chloride method.[48] Even 2-benzoyl-2-ethoxycarbonyl-1,3-dithiane (**18**), which gave no ethyl phenylpyruvate on treatment with mercuric chloride, afforded this α-keto ester in 78% yield on reaction with NBS for 3 min at −5°.

Hydrolysis of the olefinic dithiane **11** using NBS and silver nitrate proceeded with concomitant reaction of the double bond.[49] Even though silver bromide precipitated immediately and the usual transient red color of molecular bromine was absent, the resulting methyl ketone showed no olefinic protons by nmr assay. In contrast, each of the olefinic dithianes tested was converted to the unsaturated ketone in high yield using *N*-chlorosuccinimide–silver nitrate. Evidently the presence of silver ion during the NCS hydrolysis reduced the chloride ion concentration sufficiently to suppress completely the reaction of the olefinic bond with molecular chlorine.[42] In addition, neither NCS nor its O-protonated conjugate acid was effective in attacking the olefinic bond under these conditions.

N-Bromosuccinimide or *N*-chlorosuccinimide–silver nitrate has thus proven suitable for the oxidative hydrolysis of 1,3-dithiane derivatives bearing a variety of unsaturated and oxygenated substituents. The corresponding carbonyl compound is rapidly formed in high yield at low temperatures; the reaction is readily buffered near neutrality with a 2,6-dimethylpyridine. In contrast to the mercury(II) salts and bromine, these *N*-halosuccinimide reagents efficiently hydrolyze 2-acyl-1,3-dithianes to 1,2-dicarbonyl compounds. Unlike the oxidative hydrolysis with bromine or NBS, the NCS–silver nitrate procedure is compatible with olefinic substrates.

Experimental Section

Melting points and boiling points are uncorrected. Thin layer chromatography (tlc) was performed with Merck fluorescent silica gel plates (0.25 mm for analytical and 2.0 mm for preparative work) using one solvent development unless otherwise stated; compounds were visualized with 254-nm light, with iodine vapor, or by spraying with 2% 2,4-dinitrophenylhydrazine in acidic ethanol followed by heating. Ultraviolet (uv spectra were recorded with a Cary Model 14 spectrophotometer and infrared (ir) data were obtained using a Perkin-Elmer Model 137 (Infracord) spectrophotometer. Nuclear magnetic resonance (nmr) spectra were measured with a Varian Associates A-60 or T-60 spectrometer; chemical shifts are expressed in parts per million (ppm) downfield from internal tetramethylsilane (b = broad). The ir and nmr spectra were observed in CCl_4 solution. Mass spectra (ms) were determined in these laboratories with an AEI-MS 9 spectrometer at 70 eV. *n*-Butyllithium solutions (Foote Mineral Co.) were periodically assayed for active alkyl by titration with 2-butanol in xylene using 1,10-phenanthroline as indicator.[50] NBS was recrystallized from benzene or nitromethane and NCS was recrystallized from CCl_4; both reagents assayed for >98% available halogen by titration with sodium thiosulfate.

General Procedures for the Hydrolysis of 1,3-Dithiane Derivatives. A. Mercuric Chloride Method.—A solution of the dithiane (1.0 mmol) in aqueous 80% acetonitrile (10 ml), unless otherwise state, was added at 25° to an efficiently stirring solution of mercuric chloride (2.2 mmol) in the same solvent mixture (15 ml). Mercuric oxide (1.1 mmol) or powdered calcium carbonate (2.2 mmol) often was added to buffer the reaction mixture near pH 7. The dithiane–mercuric chloride complex usually separated as a flocculent white precipitate. The mixture was stirred and heated at reflux under nitrogen for 4–6 hr, cooled, and filtered through Super Cel; the filter cake was washed thoroughly with 1:1 hexane–dichloromethane. The organic phase of the filtrate was washed with 5 *M* aqueous ammonium acetate, water, and brine, dried ($MgSO_4$), and freed of solvent. Specific reaction conditions are listed in Tables II and III.

B. *N*-Bromosuccinimide Method.—A solution of the dithiane (1.0 mmol) in acetonitrile or acetone (1–5 ml) at 25° was added dropwise *to* a solution of NBS (6–8 mmol) in aqueous 80% acetonitrile or 90–97% acetone (10–25 ml) stirring at −5 to 30°. The solution quickly turned red (bromine) but soon faded to yellow-orange; it was stirred for 5–10 min and shaken with a mixture of saturated aqueous sodium sulfite and 1:1 hexane-dichloromethane. The organic phase was washed with 1.0 *M* aqueous sodium bicarbonate, water, and brine, dried ($MgSO_4$), and freed of solvent. When a 2,6-dimethylpyridine (12–16 mmol) was initially present to buffer the reaction mixture near neutrality, the organic phase was also washed well with 5 *M* aqueous cupric nitrate. Specific reaction conditions are shown in Tables IV and V.

C. *N*-Chlorosuccinimide–Silver Nitrate Method.—A solution of the dithiane (1.0 mmol) in acetonitrile (0.5–2 ml) was added quickly *to* a well-stirred solution of NCS (4.0 mmol) and silver nitrate (4.5 mmol) in aqueous 80% acetonitrile (10–25 ml) at 25°. Silver chloride separated immediately as a voluminous white precipitate and the liquid phase became yellow. The mixture was stirred for 5–10 min and treated successively at 1-min intervals with saturated aqueous sodium sulfite, saturated aqueous sodium carbonate, and brine (1 ml each); 1:1 hexane-dichloromethane (20 ml) was added; and the mixture was filtered through Super Cel. After the filter cake was washed thoroughly with 1:1 hexane–dichloromethane, the organic phase of the filtrate was dried ($MgSO_4$) and freed of solvent. Specific reaction conditions are given in Tables IV and V.

2-Benzyl-1,3-dithiane.—2-Lithio-1,3-dithiane (120 mmol) in dry THF (200 ml) under nitrogen at 0° was treated with benzyl bromide (108 mmol) in dry THF (100 ml) and kept at 0° for 3

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[48] Either or both ketal groups of the doubly masked derivative **14** can be hydrolyzed in excellent yield. Reaction of **14** with 2.5 *M* sulfuric acid in aqueous THF (25°, 104 hr) gave the acyldithiane **16** (99%), which was oxidatively hydrolyzed to the α-dione **17** in quantitative yield. Alternatively, NBS hydrolysis of **14** quantitatively yielded the acyldioxolane **15**, which on acid hydrolysis also furnished **17** (87%); see Experimental Section.

[49] Olefins are readily converted to bromohydrins with aqueous NBS; see C. O. Guss and R. Rosenthal, *J. Amer. Chem. Soc.*, **77**, 2549 (1955); E. E. van Tamelen and T. J. Curphy, *Tetrahedron Lett.*, 121 (1962).

[50] S. C. Watson and J. F. Eastham, *J. Organometal. Chem.*, **9**, 165 (1967).

hr. The oil obtained on extractive work-up was sublimed at 120° (0.6 Torr) to remove 1,3-dithiane and the residue was distilled at 112–115° (0.25 Torr) to afford 2-benzyl-1,3-dithiane (65%), pure by nmr assay, as a pale yellow oil. Crystallization from pentane at 0° furnished white needles: mp 34.5–34.9°; ir 6.69 (m), 6.88 (m), 14.42 (vs) (all C_6H_5), 6.97 (m), 7.04 (s), 7.84 (s), 8.06 (m), 8.43 (m), and 8.52 (m), 10.97 (m), and 11.52 μ (w) (all dithiane[51]); nmr 1.83 (m, 2 H, CCH_2C), 2.63 (m, 4, CH_2S), 2.88 (d, 2 H, $J = 7.0$ Hz, $CH_2C_6H_5$), 4.07 (t, 1 H, $J = 7.0$ Hz, SCHS), and 7.15 ppm (s, 5 H, C_6H_5).

Anal. Calcd for $C_{11}H_{14}S_2$: C, 62.80; H, 6.71; S, 30.49. Found: C, 62.99; H, 6.73; S, 30.61.

Phenylacetaldehyde 2,4-Dinitrophenylhydrazone.—2-Benzyl-1,3-dithiane was hydrolyzed with mercuric chloride and mercuric oxide in aqueous 95% methanol (see Table I). The crude product in ethanol was treated with 2,4-dinitrophenylhydrazine (1.2 equiv) in 7 *M* aqueous sulfuric acid; crystallization of the resulting precipitate from ethanol furnished the title compound as yellow plates, mp 117–118° (lit.[52] mp 121°).

2-Methyl-1,3-dithiane.—A stirring solution of acetaldehyde (23.6 g, 0.54 mol) and 1,3-propanedithiol (49 ml, 0.48 mol) in trichloromethane (300 ml) was treated with a moderate stream of HCl gas for 40 min, during which time the temperature rose to 60° and an aqueous phase separated. The organic phase was washed with water, 2.5 *M* aqueous sodium hydroxide, water, and brine, dried (K_2CO_3), and freed of solvent. Distillation afforded 2-methyl-1,3-dithiane (58.3 g, 91%) as a colorless liquid: bp 53–54° (1.1 Torr) [lit.[53] bp 79–80° (8–10 Torr); lit.[54] bp 66° (5 Torr)]; ir 6.87, 7.30, and 9.43 (all m, CH_3) and 6.99 (m), 7.03 (s), 7.08 (m), 7.84 (m), 8.09 (m), 8.40 (m), 8.54 (w), 10.99 (m), and 11.55 μ (w) (all dithiane[51]); nmr, identical with the published spectrum.[2]

Anal. Calcd for $C_5H_{10}S_2$: C, 44.77; H, 7.52; S, 47.71. Found: C, 44.76; H, 7.31; S, 48.04.

1-Acetyl-2-cyclohexenol (**2**) was prepared from the α-hydroxy dithiane **1**[8] (a) in 93% yield with mercuric chloride and calcium carbonate and (b) in 71% yield with NCS–silver nitrate at 55° for 5 min. The filtered reaction solution from (a) was freed of acetonitrile before extraction, as the title alcohol was moderately water soluble. Short-path distillation afforded the analytical sample: bp 83° (10 Torr), 32° (0.08 Torr); tlc R_f 0.30 ($CHCl_3$); ir 2.87 (m, OH), 5.84 (vs, C=O), 7.40 (s), 8.59 (s), 9.10 (s), 9.75 (m), and 10.42 μ (m); nmr 1.3–2.3 (m, 6 H, $(CH_2)_3$), 2.17 (s, 3 H, CH_3), 3.95 (s, 1 H, OH), 5.46 (d, 1 H, $J_1 = 10$ Hz, C=CH), and 6.02 ppm (dt, 1 H, $J_1 = 10$, $J_2 = 3.5$ Hz, CH_2CH=C).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.39; H, 8.59.

Alcohol **2** was recovered unchanged after being heated at reflux for 45 min with 0.4 *M* methanolic sodium methoxide (1.1 mol).

3-Acetyl-2-cyclohexenyl Trifluoroacetate.—A solution of 1-acetyl-2-cyclohexenol (**2**, 0.280 g, 2.00 mol) in trifluoroacetic acid (0.75 ml, 10 mmol) was kept at 25° for 20 hr, diluted with dichloromethane, washed with 1 *M* aqueous sodium bicarbonate–brine (1:1), dried ($NaHCO_3$–$MgSO_4$), and freed of solvent to furnish the title ester (0.399 g; 85%), pure by ir and nmr assay. Distillation afforded the analytical sample: bp 52° (0.09 Torr); uv max (95% EtOH) 225 nm (ε 11,600); ir 5.62 (s, CF_3C=O), 5.96 (s, CH_3C=O), 8.17, 8.51, and 8.69 μ (all vs, CF_3CO); nmr 1.5–2.4 (m, 6 H, $(CH_2)_3$), 2.26 (s, 3 H, CH_3), 5.4–5.7 (m, 1 H, OCH), and 6.5–6.7 ppm (m, 1 H, C=CH); mass spectrum *m/e* (rel intensity, assignment) 236 (100, molecular ion M), 221 (41, M − CH_3), 193 (70, M − $COCH_3$), and 139 (47, M − $COCF_3$).

Anal. Calcd for $C_{10}H_{11}F_3O_3$: C, 50.85; H, 4.69. Found: C, 50.89; H, 4.84.

3-Acetyl-2-cyclohexenol (**4**).—A solution of the trifluoroacetate of **4** (64 mg, 0.27 mmol) and sodium bicarbonate (32 mg, 0.38 mmol) in methanol (1.0 ml) was stirred at 25° for 25 hr and freed of solvent. Trituration of the residue with dichloromethane and evaporation of the resulting solution provided the title alcohol (36 mg, 95%) as a liquid: ir 2.91 (m, OH), 5.96 (s, C=O), 6.07 (sh, C=C), 7.30, 7.45, 8.03, 8.15, 9.37, 9.55, and 10.55 μ (all m–s); nmr 1.2–2.4 (m, 6 H, $(CH_2)_3$), 2.25 (s, 3 H, CH_3), 4.0–4.5 (b s, 2 H, CHOH), and 6.72 ppm (b s, 1 H, C=CH). This product was identical with an authentic sample[8] by ir and nmr assay.

Treatment of the α-hydroxyenone **2** with CCl_4 saturated with HCl (25°, 23 hr) gave a mixture of **2** and the title alcohol **4** in the ratio of **2**/**4** = 6:4 (nmr).

3-Acetyl-2-cyclohexenone (**6**).—3-(2-Methyl-1,3-dithianyl-2)-2-cyclohexenone[8] (**5**), R_f 0.61 ($CHCl_3$, 3 developments), was hydrolyzed for 6 hr with mercuric chloride (4 mol); the product was crystallized from 1:1 hexane–benzene to afford the enedione **6** in 84% yield as light yellow plates: mp 48.8–49.8° (lit.[8] mp 49.9–50.4°); tlc R_f 0.52 ($CHCl_3$, 3 developments); ir 5.92 (s, C=O), 8.0 (m), 8.23 (s), 8.46 (m), and 10.35 μ (m). This product was identical with an authentic sample[8] by ir and tlc assay. Treatment of **5** with 2 mol of mercuric chloride for 4 hr gave a mixture containing **5**/**6** = 1:3. The quantitative hydrolysis of **5** to the title enedione **6** using NCS and silver nitrate (0°, 25 min) has been described.[8]

2-(2-Phenylethyl)-1,3-dithiane (**7**).—1,3-Dithiane[7] (5.75 g, 47.4 mmol) in dry THF (90 ml) under nitrogen was cooled to −75° and treated with 1.60 *M* *n*-butyllithium in hexane (30 ml, 48 mmol). The solution was kept at −10° for 2.5 hr, cooled to −90° with an ether–ethanol slush, and treated dropwise over 3 min with (2-bromoethyl)benzene. The solution was stored at −10° for 10 hr, diluted with 1:1 pentane–dichloromethane (200 ml), and washed with 0.5 *M* aqueous ammonium chloride, water, and brine; the organic phase was dried (K_2CO_3) and freed of solvent. Short-path distillation afforded the dithiane **7** (7.4 g, 69%) as a colorless liquid: bp 130° (0.06 Torr); ir 7.03 (s), 7.06 (m), 7.84 (s), 8.04 (m), 8.34 (m), 8.47 (m), 11.01 (s), and 11.50 μ (m) (all dithiane[51]); nmr 1.8–2.2 (m, 4 H, CCH_2C), 2.6–2.9 (m, 6 H, CH_2S and $CH_2C_6H_5$), 3.88 (t, 1 H, SCHS), and 7.15 ppm (s, 5 H, C_6H_5).

Anal. Calcd for $C_{12}H_{16}S_2$: C, 64.23; H, 7.19. Found: C, 64.33; H, 7.30.

3-Phenylpropanal (**8**).—Treatment of the dithiane **7** with mercuric chloride–mercuric oxide in aqueous 95% methanol afforded an oil that was primarily 1,1-dimethoxy-3-phenylpropane: nmr 1.7–2.1 (m, 2 H, $CH_2CH_2C_6H_5$), 2.5–2.8 (m, 2 H, $CH_2C_6H_5$), 3.28 (s, 6 H, CH_3), 4.30 (t, 1 H, OCHO), and 7.18 ppm (m, 5 H, C_6H_5). It was hydrolyzed with 2:1 dioxane–1.0 *M* aqueous hydrochloride acid (50°, 1.0 hr) to furnish 3-phenylpropanal (68% yield overall) as a colorless liquid: ir 3.49, 3.61 (both m, O=CH), and 5.86 μ (vs, C=O); nmr 2.3–3.0 (A_2B_2 m, 4 H, CH_2CH_2), 7.12 (s, 5 H, C_6H_5), and 9.57 ppm (s, 1 H, CHO); 2,4-dinitrophenylhydrazone, mp 152–153° (lit.[55] mp 149°; lit.[56] mp 155–157°).

Reaction of the dithiane **7** with NBS (6 mol) in aqueous 80% acetonitrile at 5° provided the title aldehyde in 90% yield.

2,2-Bis(2-phenylethyl)-1,3-dithiane (**9**).—1,3-Dithiane[7] (9.00 g, 75 mmol) in dry THF (140 ml) was cooled to −50° under nitrogen, treated with 1.60 *M* *n*-butyllithium in hexane (56 ml, 82 mmol), and stored at 0°. Anion formation was judged complete after 2 hr by adding part of the solution to D_2O and measuring the deuterium incorporation at C-2 by nmr. The solution was cooled to −50°, treated with (2-bromoethyl)benzene (15.2 g, 82 mmol) in dry THF (25 ml), and stored at 0°. After 15 hr (80% alkylation by the above assay) the solution was cooled to −60°, treated with 1.60 *M* *n*-butyllithium in hexane (60 ml, 96 mmol), and stored at 0°. After 2 hr (complete anion formation) the solution was cooled to −60°, treated with (2-bromoethyl)benzene (17.7 g, 96 mmol) in dry THF (20 ml), stored at 0° for 40 hr, diluted with water, and extracted with 1:1 pentane–dichloromethane. The extracts were washed with 1.0 *M* aqueous hydrochloric acid, water, and brine, dried (K_2CO_3), and freed of solvent.

Vacuum distillation of the remaining oil provided, after a forerun containing the monoalkyl dithiane **7**, the title dithiane (8.6 g, 35% yield), pure by tlc, as a viscous oil: bp 220° (0.20 Torr); tlc R_f 0.5 (1:1 pentane–benzene). Filtration through silica gel and crystallization four times from pentane at −20° afforded small white crystals: mp 46.4–46.6°; ir 7.03 (m), 7.07 (m), 7.84 (m), 8.07 (w), 10.98 (m), and 11.47 μ (w) (all di-

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(51) Examination of the ir spectra of over 100 1,3-dithiane derivatives bearing C-2 substituents has permitted assignment of the following bands to this ring system: ir max (rel intensity) 6.99 (m), 7.02 (m–s), 7.06 (m), 7.84 (m–s), 8.06 (w–m), 10.98 (m–s), and 11.5 μ (w–m). In addition, bands are seen at 8.44 and 8.53 μ (w–m) when C-2 bears one proton (N. H. Andersen and B. W. Erickson, unpublished results).

(52) "Tables for Identification of Organic Compounds," 2nd ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1964, p 86.

(53) L. Autenrieth and K. Wolff, *Chem. Ber.*, **32**, 1375 (1899).

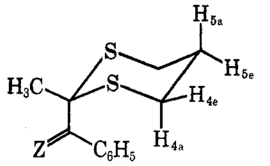
(54) E. E. Campaigne and G. F. Schaefer, *Bol. Col. Quim. P. R.*, **9**, 25 (1952); *Chem. Abstr.*, **46**, 10884 (1952).

(55) C. F. H. Allen and J. H. Richmond, *J. Org. Chem.*, **2**, 222 (1937).

(56) M. Stiles and A. J. Sisti, *ibid.*, **25**, 1691 (1960).

Table VI

220-MHz Nmr Data for Two Compounds with Conformationally Rigid 1,3-Dithiane Rings[a]



	Chemical shift, ppm				Coupling constant, Hz					
Compd	δ_{4a} (ddd)	δ_{4e} (ddd)	δ_{5a} (dtt)	δ_{5e} (dtt)	$J_{4a,4e}$	$J_{4a,5a}$	$J_{4a,5e}$	$J_{4e,5a}$	$J_{4e,5e}$	$J_{5a,5e}$
Ketal **14**[b]	3.23	2.65	1.88	2.08	13.8	10.4	3.0	3.4	6.1	13.8
Ketone **16**[c]	3.32	2.71	1.89	2.15	14.2	12.4	2.7	3.2	4.4	14.0

[a] Varian HR-220 spectrometer, $CDCl_3$ solvent. [b] Also 1.50 (s, 3 H, CH_3), 3.5–4.3 (A_2B_2 m, 4 H, OCH_2CH_2O), and 7.1–7.6 ppm (m, 5 H, C_6H_5). [c] Plus 1.75 (s, 3 H, CH_3) and 7.2–8.1 ppm (m, 5 H, C_6H_5).

thiane[51]); nmr 1.6–2.4 (m, 6 H, CCH_2C). 2.5–2.9 (m, 8 H, CH_2S and $CH_2C_6H_5$), and 7.13 ppm (s, 5 H, C_6H_5).

Anal. Calcd for $C_{20}H_{24}S_2$: C, 73.11; H, 7.36; S, 19.52. Found: C, 73.07; H, 7.24; S, 19.65.

1,5-Diphenyl-3-pentanone (10) was prepared from the dithiane **9** (a) in 86% yield with mercuric chloride in aqueous 90% methanol and (b) in 97% yield with NBS (8 mol) in aqueous 96% acetone at −5°. Short-path distillation afforded the ketone **10** as a colorless oil: bp 160° (0.1 Torr); ir 5.80 (s, C═O), 6.70, 6.90 (both m, CH_2 bend), and 14.30 μ (s, C_6H_5); nmr 2.68 (A_2B_2 sextet, 4 H, CH_2CH_2) and 7.12 ppm (s, 5 H, C_6H_5).

Anal. Calcd for $C_{17}H_{18}O$: C, 85.68; H, 7.61. Found: C, 85.51; H, 7.60.

2-Methyl-2-(1-cyclohexenyl)methyl-1,3-dithiane (11).—Cyclohexenyl acetone and 1,3-propanedithiol were condensed by the procedure described above for the preparation of 2-methyl-1,3-dithiane to provide the title dithiane in 85% yield as a colorless liquid: bp 125–127° (0.12 Torr); tlc R_f 0.17 (CCl_4), R_f 0.74 (CH_2Cl_2); ir 7.00, 7.06, 7.86, 8.09, 10.98, and 11.53 μ (all m, dithiane[51]); nmr 1.57 (s, 3 H, CH_3), 1.4–2.3 (m, 10 H), 2.50 (s, 2 H, CH_2C═O), 2.7–2.9 (m, 4 H, CH_2S), and 5.48 ppm (b s, 1 H, C═CH).

Anal. Calcd for $C_{12}H_{20}S_2$: C, 63.10; H, 8.83. Found: C, 62.92; H, 8.87.

1-Cyclohexenyl-2-propanone (12) was prepared by hydrolysis of the dithiane **11** (a) in 90% yield with mercuric chloride and calcium carbonate and (b) in 94% yield with NCS and silver nitrate (25°, 10 min). These methods furnished identical samples of the nonconjugated ketone **12**: tlc R_f 0.36 (CH_2Cl_2); ir 5.81 μ (s, C═O); nmr 1.4–2.2 (m, 8 H, $(CH_2)_4$), 2.02 (s, 3 H, CH_3), 2.93 (s, 2 H, CH_2C═O), and 5.49 ppm (b s, 1 H, C═CH). Neither sample contained any trace of the conjugated ketone **13** by tlc, nmr, or ir assay; **13** is readily detected in 1-cyclohexenylacetone, a mixture of **12**/**13** = 90:10 (nmr), by a tlc spot at R_f 0.12 (CH_2Cl_2), by an nmr peak at 5.94 ppm (b s, C═CH), and by ir bands at 6.00 (C═O), 6.17 (C═C), and 10.40 μ.

2-(2-Methyl-1,3-dithianyl-2)-2-phenyl-1,3-dioxolane (14).—A mixture of 2-benzoyl-2-methyl-1,3-dithiane (**16**; 3.58 g, 15.0 mmol), ethylene glycol (4.2 g, 75 mmol), *p*-toluenesulfonic acid (0.2 g), and benzene (60 ml) was heated at reflux in a flask equipped with a Dean-Stark water separator. After 24 and 48 hr, additional 0.2-g portions of the acid catalyst were added; after 72 hr the mixture showed no ir carbonyl adsorption. It was cooled, diluted with 1:1 pentane–dichloromethane, washed with 0.5 *M* aqueous sodium bicarbonate, water, and brine, dried, and freed of solvent. The residue was recrystallized from cyclohexane to afford the dioxolane **14** (3.96 g, 90%) as white needles: mp 118.4–119.0°; tlc, R_f 0.43 (CH_2Cl_2); ir 7.00, 7.02, 7.08, 7.82, 10.99, 11.46 (all m, dithiane[51]), 9.09, and 9.24 μ (both s, dioxolane); nmr, see Table VI; mass spectrum *m/e* (rel intensity, assignment) 282 (0.25, molecular ion M), 149 (100, M − $C_5H_9S_2$), and 133 (8, M − $C_9H_9O_2$).

Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.54; H, 6.42; S, 22.71. Found: C, 59.84; H, 6.48; S, 22.73.

2-Acetyl-2-phenyl-1,3-dioxolane (15) was obtained from the dioxolane **14** (a) in 76% yield using mercuric chloride (4.0 mol) and calcium carbonate (4.4 mol) and (b) in quantitative yield with NBS (6 mol) at 15°. Short-path distillation provided the analytical sample, bp 79–80° (0.06 Torr). On standing at 0° it crystallized as colorless plates: mp 27–29°; tlc R_f 0.16 (CH_2Cl_2); ir 5.75 (s, C═O), 9.05, 9.68 (both s, dioxolane), and 14.33 μ (s, C_6H_5); nmr 2.02 (s, 3 H, CH_3), 3.8–4.0 (m, 4 H, CH_2CH_2), and 7.1–7.6 ppm (m, 5 H, C_6H_5).

Hydrolysis of the ketal–dithioketal **14** to the acyldioxolane **15** was slow and incomplete using 2.2 or 3.0 mol of mercuric chloride (Table VII).

Table VII

Mercuric Chloride Hydrolysis of Ketal–Dithioketal **14** to Acyl Ketal **15**

Reactant ratios[a]			
$HgCl_2$	$CaCO_3$	Time,[b] hr	Yield,[c] %
2.2	2.3	5	51 (29)
2.2	2.3	24	52 (17)
3.0	3.1	10	69 (7)
4.0	4.4	1	74 (14)
4.0	4.4	4	81 (5)

[a] Moles per mole of **14**. [b] Aqueous 80% CH_3CN at reflux under N_2. [c] Recovery of **14** (%) in parentheses.

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.70; H, 6.23.

2-Benzoyl-2-methyl-1,3-dithiane (16). A. Addition of 2-Lithio2-methyl-1,3-dithiane to Benzonitrile.—The published procedure[1] was modified. 2-Methyl-1,3-dithiane (28.0 g, 0.208 mol) in dry THF (400 ml) was cooled under nitrogen to −75°, treated with 1.60 *M* *n*-butyllithium in hexane (135 ml, 0.216 mol), stored at −20° for 16 hr, cooled to −75°, and treated dropwise with benzonitrile (22.7 g, 0.220 mol). The bright orange solution was maintained at −75° for 1.0 hr, warmed to 0° over 1.0 hr, treated with 3 *M* aqueous HCl (80 ml), and heated at reflux (65°) for 1.0 hr. The mixture was freed of organic solvents and extracted with 1:1 dichloromethane–ether; the extract was washed with 2 *M* aqueous sodium hydroxide, 1 *M* aqueous HCl, water, and brine, dried, and freed of solvent. The crystalline residue was treated with charcoal and recrystallized from methanol to furnish the acyldithiane **16** (46.9 g, 94.5%) as white crystals: mp 98.6–98.9° (lit.[1] mp 98.4–98.8°); tlc R_f 0.52 (CH_2Cl_2), R_f 0.80 (acetone); ir 5.95 (s, C═O), 6.99, 7.02, 7.08, 7.84, 11.01, and 11.54 μ (all m, dithiane[51]); nmr, see Table VI.

Anal. Calcd for $C_{12}H_{14}OS_2$: C, 60.50; H, 5.92; S, 26.86. Found: C, 60.33; H, 5.99; S. 27.10.

B. Selective Hydrolysis of the Dioxolane 14.—Compound **14** (0.283 g, 1.00 mmol), THF (6 ml), and aqueous 48% sulfuric acid (2 ml) were stirred at 25° for 4.3 days, treated with 1.2 *M* aqueous sodium hydroxide (16 ml), and extracted with ether. The extract was washed with 1 *M* aqueous sodium bicarbonate and brine, dried, and freed of solvent to furnish the acyldithiane **16** (0.236 g, 99%), pure by nmr assay, as white crystals, mp 96.8–98.0°.

1-Phenyl-1,2-propanedione (17). A. Hydrolysis of 2-Benzoyl-2-methyl-1,3-dithiane (16).—The reaction conditions and results are listed in Tables III and IV.

B. Hydrolysis of 2-Acetyl-2-phenyl-1,3-dioxolane (15).—The acyldioxolane **15** (0.335 g, 1.74 mmol), THF (10 ml), and aqueous 48% sulfuric acid (10 ml) were stirred at 25° for 48 hr and extracted with 1:1 pentane–dichloromethane; the extract was washed with 2 *M* aqueous ammonium acetate, water, and brine, dried, and freed of solvent. Short-path distillation of the residual liquid afforded the diketone **17** (0.224 g, 87%), pure by nmr, as a clear yellow liquid: bp 100° (15 Torr) [lit.[57] bp 123° (23 Torr)]; ir 5.83 (s, $CH_3C{=}O$), 5.95 (s, $C_6H_5C{=}O$), 8.63 (s), 11.41 (s), and 14.33 μ (s, C_6H_5); nmr 2.45 (s, 3 H, CH_3) and 7.3–8.1 ppm (m, 5 H, C_6H_5). Lower acidity or a shorter reaction period resulted in incomplete conversion (see Table VIII).

TABLE VIII

ACID HYDROLYSIS OF α-KETO KETAL **15** TO α-DIONE **17**[a]

Sulfuric acid, *M*	Time, hr	Yield,[b] %
6	75	44 (46)
9	12	78 (12)
9	18	81 (9)
9	48	87 (1)

[a] THF–water (2:1, 10 ml/mmol of **15**) at 25°. [b] Recovery of **15** (%) in parentheses.

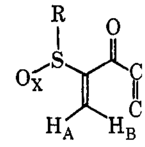
2-Benzyl-2-ethoxycarbonyl-1,3-dithiane (18).—2-Benzyl-1,3-dithiane (4.37 g, 20.8 mmol) in dry THF (100 ml) was cooled under nitrogen to −50°, treated with 1.60 *M* *n*-butyllithium in hexane (14 ml, 23 mmol), and warmed to −20° over 2 hr. The resulting anion solution was cooled to −75° and added over 1 hr through a narrow stainless steel tube to a solution of ethyl chloroformate (31 ml, 0.33 mol) in dry THF (31 ml) stirring under nitrogen at −75°. The reaction mixture was stored at 0° for 12 hr and freed of most solvent; ether extracts of the residual oil were washed with 1 *M* aqueous sodium bicarbonate, water, and brine, dried, and freed of solvent. Short-path distillation furnished the ester **18** (4.40 g, 75%), pure by nmr assay, as a colorless oil: bp 144° (0.01 Torr); ir 5.79 (s, C=O), 7.02, 7.07, 7.85, and 11.00 (all m, dithiane[51]), 8.32, and 8.47 μ (both s, CO); nmr 1.25 (t, 3 H, J = 7 Hz, CH_3), 1.5–2.1 (m, 2 H, H_{5a} and H_{5e}), 2.50 (dt, 1 H, H_{4e}), 3.29 (ddd, 1 H, H_{4a}), 3.29 (s, 2 H, $CH_2C_6H_5$), 4.15 (q, 2 H, J = 7 Hz, CH_2O), and 7.19 ppm (s, 5 H, C_6H_5) with $J_{4a,4e} = 14$, $J_{4a,5a} = 12$, and $J_{4a,5e} = J_{4e,5a} = J_{4e,5e} =$ 4 Hz.

Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.54; H, 6.42; S, 22.71. Found: C, 59.82; H, 6.58; S, 22.50.

Ethyl 3-Phenylpyruvate (19).—Reaction of the acyldithiane **18** with NBS (8 mol) in aqueous 95% acetone at −5° provided the α-keto ester **19** in 78% yield as a colorless liquid: ir 5.76 μ (s, C=O); nmr 1.20 (t, 3 H, J = 7.0 Hz, CH_3), 3.95 (s, 2 H, $CH_2C_6H_5$), 4.11 (q, 2 H, J = 7.0 Hz, CH_2O), and 7.11 ppm (s, 5 H, C_6H_5). On treatment with 1:1 pyridine–CCl_4 the keto ester was mainly converted to an enol tautomer[58] [partial nmr 1.25 (t, 3 H, J = 7.0 Hz, CH_3), 4.23 (q, 2 H, J = 7.0 Hz, CH_2O), and 6.47 ppm (s, 1 H, $C{=}CHC_6H_5$)]; the equilibrium ratio was keto/enol = 3:17 by nmr assay.

3-Chloro-3-(1-oxo-1-phenyl-2-propenyl-2-sulfinyl)propanesulfonyl Chloride (20).—Treatment of the acyldithiane **16** with NCS (4.0 mol) and cupric chloride dihydrate (4.0 mol) in aqueous 80% acetonitrile (30°, 10 min) afforded an oil that was subjected to preparative tlc. The polar material (R_f 0.09, $CHCl_3$) was predominately the title compound: ir 6.08 (m, C=O), 6.28 (w, C=C), 7.29 (s, asym SO_2Cl), 8.58 (s, sym SO_2Cl), 9.55 (m, S=O), and 14.5 μ (m, C_6H_5); nmr 2.2–4.1 (m, 5 H, CH_2CH_2CH), 6.65 (s, 1 H, H_A), 6.82 (s, 1 H, H_B), and 7.3–7.9 ppm (m, 5 H, C_6H_5); mass spectrum *m/e* (rel intensity) 338 (45), 339 (8), 340 (32), 341 (6), and 342 (9) [calcd for $C_{12}H_{12}Cl_2O_4S_2$: 338 (44), 339 (8), 340 (34), 341 (6), and 342 (8)] plus *m/e* 302 (molecular ion − HCl), 105 ($C_7H_5O^+$), and 77 ($C_6H_5^+$).

Use of the tables of Pascual, Meier, and Simon,[59] which correlate chemical shifts of olefinic protons with their chemical environment, predicts that the vinylic protons A and B in the partial structure **21** will appear at 5.99 and 6.25 ppm, respectively, when X = 0 and at 7.38 and 7.24 ppm, respectively, when X = 2. By interpolation, protons A and B should appear at 6.68 and 6.74 ppm, respectively, when X = 1. The observed values for the vinylic protons of the sulfoxide **20** (6.65 and 6.82 ppm) are in good accord with this prediction.



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Registry No.—**2,** 31593-36-9; **4,** 15040-95-6; **6,** 15040-96-7; **7,** 31593-39-2; **8,** 104-53-0; **9,** 31593-41-6; **10,** 5396-91-8; **11,** 31593-43-8; **12,** 768-50-3; **14,** 31593-45-0; **15,** 31593-46-1; **16,** 4883-01-6; **17,** 579-07-7; **18,** 4882-96-6; **19,** 6613-41-8; **20,** 31593-50-7; mercuric chloride, 7487-94-7; *N*-bromosuccinimide, 128-08-5; *N*-chlorosuccinimide, 128-09-6; silver nitrate 7761-88-8; 2-benzyl-1,3-dithiane, 31593-52-9; 2-methyl-1,3-dithiane, 6007-26-7; 3-acetyl-2-cyclohexenyl trifluoroacetate, 31593-54-1; 1,1-dimethoxy-3-phenylpropane, 30076-98-3.

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[57] I. Smedley, *J. Chem. Soc.*, **95**, 218 (1909).

[58] Ester **19** is reported to exist in two enol forms [α, mp 52°; β, bp 152° (15 Torr)] and a keto form (γ, mp 79°): see H. Gault and R. Weick, *Bull. Soc. Chim. Fr.*, [4] **31**, 867 (1922).

[59] C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta*, **49**, 164 (1966).