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A Novel Oxidative Cleavage Reaction with $Pb(OAc)_4$ *via* Dithioacetal Derivatives[1]

Kunio Hiroi, Shuko Sato, and Kazuhide Matsuo

Tohoku College of Pharmacy[2]

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The oxidative cleavage of 2-alkyl-2-(1-hydroxyalkyl)-1,3-dithianes (**1**—**5**) and 2-(1-hydroxyethyl)-2-methyl-1,3-dithiolane (**11**) with $Pb(OAc)_4$ gave 3-alkyl-1,4-dithiepan-2-ones (**7a**—**e**) and 1,4-dithian-2-one (**12**), respectively, in fairly good yields.

Analogously, the treatment of 2-alkylidene-1,3-dithianes (**13a**—**e**) with $Pb(OAc)_4$ resulted in a ring expansion to give **7a**—**e**, whereas the reaction of 2-benzylidene-1,3-dithiane (**13f**) with $Pb(OAc)_4$ did not produce the expected ring expansion product, instead giving 2-(α-acetoxybenzylidene)-1,3-dithiane (**8**).

Keywords——bond cleavage; ring expansion; dithioacetal; 1,3-dithiane; 1,3-dithiolane; 1,4-dithiane; 1,4-dithiepan-2-one; $Pb(OAc)_4$

In recent years many new synthetic strategies have been devised for the completion of total syntheses of natural products and pharmaceuticals, and carbon-carbon bond cleavage[3,4] is one of the most useful synthetic tools for the stereoselective construction[5] of such complex molecules.

Recently, one of us (K.H.)[6] has reported a valuable method for the ring cleavage of cyclic carbon compounds, involving oxidative cleavage of cyclic β-sulfenyl alcohols with $Pb(OAc)_4$[7,8] under extremely mild conditions. However this method is restricted to cyclic systems possessing some strain energy, such as four or five membered rings, and is not

1) Preliminary results were presented at the 11th Congress of Heterocyclic Chemistry, Kanazawa, Japan, October 1978. For a preliminary report of a portion of this work see Kunio Hiroi and Shuko Sato, *Chem. Lett.*, **1979**, 923.

2) Location: *4-4-1, Komatsushima, Sendai, Miyagi 983, Japan.*

3) For leading reviews see *a*) H.O. House, "Modern Synthetic Reactions," W.A. Benjamin, 2nd ed. 1972, Chapters 5—7; *b*) C.H. Hassall, "Organic, Reactions," Vol. 9, John wiley and Sons, Inc., New York, 1957, pp. 73—106; *c*) E.L. Jackson, *ibid.*, Vol. 2, 1944, pp. 341—375.

4) For cleavage *via* organo-sulfur compounds see *a*) R.L. Autrey and P.W. Scullard, *J. Am. Chem. Soc.*, **90**, 4917, 4924 (1968); *b*) J.A. Marshall and J.L. Belletire, *Tetrahedron Lett.*, **1971**, 871; *c*) J.A. Marshall and H. Roebke, *ibid.*, **1970**, 1555; *d*) J.A. Marshall, C.T. Buse, and D.E. Seitz, *Synth. Commun.*, **3**, 85 (1973); *e*) J.A. Marshall and D.E. Seitz, *J. Org. Chem.*, **39**, 1814 (1974); *f*) *Idem*, *Synth. Commun.*, **4**, 395 (1974); *g*) *Idem*, *J. Org. Chem.*, **40**, 534 (1975); *h*) E. Cossement, *Tetrahedron Lett.*, **1974**, 997; *i*) B.M. Trost, M. Preckel, and L.M. Leichter, *J. Am. Chem. Soc.*, **97**, 2224 (1975); *j*) R.J. Bryant, *Tetrahedron Lett.*, **1975**, 3841.

5) For examples of related works see *a*) P.A. Grieco and K. Hiroi, *Tetrahedron Lett.*, **1973**, 1831; *b*) P.A. Grieco, K. Hiroi, J.J. Reap, and J.A. Noguez, *J. Org. Chem.*, **40**, 1450 (1975); *c*) P.A. Grieco, M. Nishizawa, S.D. Burke, and N. Marinovic, *J. Am. Chem. Soc.*, **98**, 1612 (1976); *d*) S. Danishefsky, T. Kitahara, P.F. Shuda, and S.J. Etheredge, *ibid.*, **98**, 3030 (1976); *e*) B.M. Trost, K. Hiroi, and N. Holy, *ibid.*, **97**, 5873 (1975).

6) B.M. Trost and K. Hiroi, *J. Am. Chem. Soc.*, **97**, 6911 (1975).

7) For leading reviews regarding lead tetraacetate see *a*) R.N. Butler, "Synthetic Reagents," Vol. 3, ed. by J.S. Pizey, Ellis Horwood Limited Publisher, England, 1977, pp. 277—419; *b*) L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. 1, John Wiley and Sons, Inc., New York, 1967, p. 537; *c*) R.N. Butler, *Chem. Ind.* (London), **1976**, 499; *d*) D.J. Rawlinson and G. Sosnovsky, *Synthesis*, **1973**, 567; *e*) M.L. Mihailović and Z. Čeković, *ibid.*, **1970**, 209.

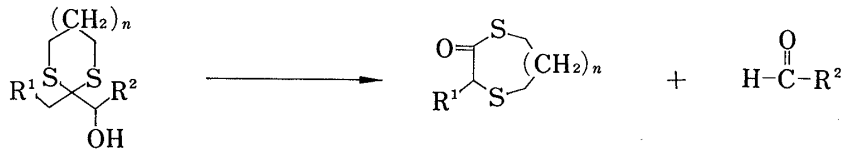
8) For examples of cleavage with lead tetraacetate see *a*) G.M. Rubottom, R. Marrero, D.S. Krueger, and J.L. Schreiner, *Tetrahedron Lett.*, **1977**, 4013; *b*) E. Zbiral, *Synthesis*, **1972**, 285; *c*) E. Zbiral, G. Nestler, and K. Kischa, *Tetrahedron*, **26**, 1427 (1970); *d*) H.E. Baumgarten, D.F. McLaen, and H.W. Taylor, Jr., *J. Org. Chem.*, **36**, 3668 (1971).

applicable to ring systems with more than six members, or to open-chain carbon compounds.

More recently, one of us (K.H.)[9] has communicated an alternative method for ring cleavage, which involves the reaction of 2,2-(1,3-propanedithio)cycloalkanols with $Pb(OAc)_4$ and has the advantage of applicability to larger ring systems.

We report here an extension of this method to open-chain systems, and its availability not only for 1,3-dithiane, but also for 1,3-dithiolane derivatives. A recent study on the same cleavage reaction by another group[10] has recently appeared, in which an example of an open-chain system was discussed.

Treatment of 2-alkyl-2-(1-hydroxyalkyl)-1,3-dithiolanes (Ia) or -1,3-dithianes (Ib)[11] with $Pb(OAc)_4$ leads to a carbon-carbon bond cleavage reaction, accompanied by migration of the sulfur group, to give 3-alkyl-1,4-dithian-2-ones (IIa) or -1,4-dithiepan-2-ones (IIb), respectively, as a counterpart of the bond cleaved products.

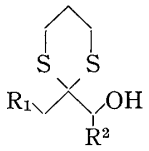


Ia : $n=0$
Ib : $n=1$

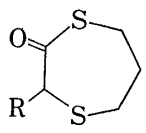
IIa : $n=0$
IIb : $n=1$

Chart 1

Several workers in recent years have reported this kind of ring enlargement reaction of cyclic thioacetal derivatives, involving migration of the thio group, with BF_3 etherate,[12] PPA,[13] pyridine hydrochloride,[14] P_2O_5,[15] Cl_2,[16] heating,[17] and others.[18] These kinds of ring



1a: $R^1=H$, $R^2=CH_3$
1b: $R^1=H$, $R^2=CH_3CH_2CH_2$
1c: $R^1=H$, $R^2=C_6H_5$
2 : $R^1=CH_3$, $R^2=CH_3CH_2CH_2$
3 : $R^1=CH_3CH_2$, $R^2=CH_3CH_2CH_2$
4 : $R^1=CH_3CH_2CH_2$ $R^2=CH_3CH_2CH_2$
5 : $R^1=C_6H_5CH_2$, $R^2=CH_3CH_2CH_2$
6a: $R^1=C_6H_5$, $R^2=CH_3CH_2CH_2$
6b: $R^1=C_6H_5$, $R^2=C_6H_5$



7a: R=H
7b: $R=CH_3$
7c: $R=CH_3CH_2$
7d: $R=CH_3CH_2CH_2$
7e: $R=C_6H_5CH_2$
7f: $R=C_6H_5$

Fig. 1

9) B.M. Trost and K. Hiroi, *J. Am. Chem. Soc.*, **98**, 4313 (1976).
10) W. Lottenbach and W. Graf, *Helv. Chim. Acta*, **61**, 3087 (1978).
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12) L.F. Fieser, C. Yuan, and T. Goto, *J. Am. Chem. Soc.*, **82**, 1996 (1960).
13) M. Tomoeda, M. Ishizaki, H. Kobayashi, S. Kanamoto, T. Koga, M. Inuzuka, and T. Furuta, *Chem. Pharm. Bull.*, **12**, 383 (1964); *idem*, *Tetrahedron*, **21**, 733 (1965).
14) G. Karmas, *J. Org. Chem.*, **32**, 3147 (1967).
15) J.L. Massingill, Jr., M.G. Reinecke, and J.E. Hodgkins, *J. Org. Chem.*, **35**, 823 (1970).
16) G.E. Wilson, Jr., and M-G. Huang, *J. Org. Chem.*, **41**, 966 (1976).
17) C.H. Chen, *Tetrahedron Lett.*, **1976**, 25; C.H. Chen and B.A. Donatelli, *J. Org. Chem.*, **41**, 3053 (1976); K. Hiratani, T. Nakai, and M. Okawara, *Bull. Chem. Soc. Jpn.*, **49**, 2339 (1976).
18) H. Rubinstein and M. Wuerthele, *J. Org. Chem.*, **34**, 2762 (1969); J.A. Marshall and H. Roebke, *ibid.*, **34**, 4188 (1969); H. Yoshino, Y. Kawazoi, and T. Taguchi, *Synthesis*, **1974**, 713.

transformations of cyclic thioacetal derivatives appear to offer an attractive route to other heterocycles containing sulfur in the main skeleton.

The initial attempts to produce bond cleavage in an open-chain system were made under various reaction conditions, employing 2-(1-hydroxybutyl)-2-phenethyl-1,3-dithiane (**5**) as a model compound. The bond cleavage reaction of **5** with 2.4 equivalents of $Pb(OAc)_4$ was carried out under the reaction conditions given in Table I to afford 3-benzyl-1,4-dithiepan-2-one (**7e**) as colorless needles of mp 109—110° in moderate yields.

Characterization of this compound was accomplished by spectral analyses as follows. A carbonyl absorption of the thio ester (**7e**) appears at 1662 cm^{-1} in the infrared (IR) spectrum and a proton α to the carbonyl group appears at δ 3.95 as a triplet in the nuclear magnetic resonance (NMR) spectrum. Furthermore, to confirm the structure of **7e**, it was converted into methyl cinnamate by the ester exchange reaction of **7e** under reflux in methanol in the presence of iodine, and subsequent oxidation with $NaIO_4$ to the sulfoxide, followed by thermolysis in refluxing toluene.[9,19]

Table I. Oxidative Cleavage of 2-(1-Hydroxybutyl)-2-phenethyl-1,3-dithiane (**5**) with $Pb(OAc)_4$

Solvent	Reaction temp.	Yield of **7e** %
C_6H_6	Room temp.	67
C_6H_6	55°	50
$CHCl_3$	Room temp.	60
CCl_4	Room temp.	54

Compound **5** was reacted with 2.4 equiv. of $Pb(OAc)_4$ for 16 hr.

The application of this method to other 1,3-dithiane derivatives (**1**—**4**) was achieved in the same way by heating in benzene at 55° to give the corresponding 3-alkyl-1,4-dithiepan-2-ones (**7a**—**d**) in the yields listed in Table II.

Table II. Oxidative Cleavage of 2-Alkyl-2-(1-hydroxyalkyl)-1,3-dithianes (**1**—**4**) with $Pb(OAc)_4$

Starting material	Reaction time hr	Product	Yield %
1a	16.0	**7a**	40
1b	16.0	**7a**	49
1c	18.5	**7a**	34
2	16.0	**7b**	51
3	13.5	**7c**	42
4	12.0	**7d**	58

Compounds **1**—**4** were reacted with 2.4 equiv. of $Pb(OAc)_4$ in benzene at 55°.

The structures of these products were fully consistent with the observed spectral data. All of the products have carbonyl absorptions of the thio esters at around 1660 cm^{-1} in the IR spectra and the protons α to the carbonyl groups appear at α 3.60 as a two-proton singlet (**7a**), at δ 3.82 as a one-proton quartet (**7b**), at δ 3.60 as a one-proton triplet (**7c**), or at 3.68 as a one-proton triplet (**7d**) in the NMR spectra. The structures of **7a** and **7b** were confirmed by direct comparison with authentic samples, prepared from chloroacetyl chloride and 1,3-propanedithiol, and α-chloropropionic acid and 1,3-propanedithiol, respectively.

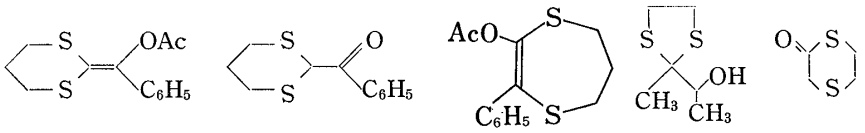
19) B.M. Trost, T.N. Salzmann, and K. Hiroi, *J. Am. Chem. Soc.*, **98**, 4887 (1976).

In the case of 2-(α-hydroxybenzyl)-2-methyl-1,3-dithiane (**1c**), benzaldehyde was obtained together with **7a** as another counterpart of the bond cleaved products.

It is somewhat surprising, however, that the oxidative cleavage reaction of 2-benzyl-2-(1-hydroxyalkyl)-1,3-dithiane (**6**) with 2.4 equivalents of $Pb(OAc)_4$ did not produce the corresponding 1,4-dithiepane derivative (**7f**), instead giving 2-(α-acetoxybenzylidene)-1,3-dithiane (**8**) in good yield.

The structure of **8** was determined unequivocally by hydrolytic conversion into 2-benzoyl-1,3-dithiane (**9**), mp 92—92.5°; this was identical with an authentic sample prepared from 1,3-dithiane and benzoyl chloride (spectral properties and mixed melting point determination). Furthermore, the product (**8**) was completely different from an authentic specimen of 3-phenyl-1,4-dithiepan-2-one (**7f**), mp 131.5—132.5°, prepared from α-bromophenylacetic acid and 1,3-propanedithiol.

Very recently, Lottenbach and Graf proposed the structure 2-acetoxy-3-phenyl-6,7-dihydro-5H-dithiepin (**10**) for the product of an analogous reaction.[10] However, the structure reported by them appears to be incorrect.



8 **9** **10** **11** **12**

Fig. 2

The versatility of this oxidative bond cleavage reaction was further evaluated by applying to a 1,3-dithiolane derivative. 2-(1-Hydroxyethyl)-2-methyl-1,3-dithiolane (**11**) underwent, upon treatment with 2.4 equivalents of $Pb(OAc)_4$, the same cleavage reaction accompanied by migration of the sulfur group to give 1,4-dithian-2-one (**12**).

This reaction was studied in detail to improve the yield, and the results are summarized in Table III. The reaction in benzene at 55° for 16 hr resulted in the best yield (80%) of **12**. A carbonyl absorption of the thio ester appears at 1660 cm^{-1} in the IR spectrum of **12** and the methylene protons α to the carbonyl appear at δ 3.35 as a two-proton singlet in the NMR spectrum. These spectral data are superimposable with those of an authentic sample prepared from chloroacetyl chloride and 1,2-ethanedithiol.

Table III. Oxidative Cleavage of 2-(1-Hydroxyethyl)-2-methyl-1,3-dithiolane (**11**) with $Pb(OAc)_4$

Solvent	Reaction temp.	Reaction time hr	Yield of **12** %
C_6H_6	Room temp.	13.0	66
C_6H_6	55°	4.5	54
C_6H_6	55°	16.0	80
C_6H_6	80°	3.5	57
$CHCl_3$	55°	2.5	49
CCl_4	55°	3.5	40

A reasonable mechanistic hypothesis which explains this anomalous cleavage reaction involves the formation of 2-alkylidene-1,3-dithianes as key intermediates. Accordingly, 2-alkylidene-1,3-dithianes (**13a—e**)[20] were treated with 1.2 equivalents of $Pb(OAc)_4$ under

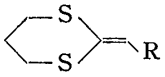
20) *a*) P.F. Jones and M.F. Lappert, *J. Chem. Soc., Chem. Commun.*, **1972**, 526; *b*) D. Seebach, M. Kolb, and B-T. Gröbel, *Chem. Ber.*, **106**, 2277 (1973); *c*) *Idem, Tetrahedron Lett.*, **1974**, 3171.

the reaction conditions employed above to give, as expected, the corresponding 3-alkyl-1, 4-dithiepan-2-ones (**7a**—**e**) in the yields listed in Table IV.

A detailed examination was carried out of the reaction of 2-ethylidene-1,3-dithiane (**13b**) with $Pb(OAc)_4$ to find suitable reaction conditions; the reaction in benzene at 55° led to the best yield (74%) of 3-methyl-1,4-dithiepan-2-one (**7b**).

Exceptionally, the reaction of 2-benzylidene-1,3-dithiane (**13f**) with 1.2 equivalents of $Pb(OAc)_4$ in benzene at 55° produced **8** in 69% yield. These compounds prepared from **13a**—**f** were identical with the products obtained previously.

Table IV. Oxidative Ring Expansion of 2-Alkylidene-1,3-dithianes (13) with $Pb(OAc)_4$



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	Starting material (**13**) R	Solvent	Reaction temp.	Reaction time (hr)	Product	Yield (%)
13a	H	C_6H_6	55°	12.5	**7a**	67
13b	CH_3	C_6H_6	Room temp.	12.0	**7b**	55
13b	CH_3	C_6H_6	55°	16.5	**7b**	74
13b	CH_3	C_6H_6	80°	12.0	**7b**	47
13b	CH_3	$CHCl_3$	55°	8.0	**7b**	65
13b	CH_3	CCl_4	55°	8.0	**7b**	64
13c	CH_3CH_2	C_6H_6	55°	16.0	**7c**	58
13d	$CH_3CH_2CH_2$	C_6H_6	55°	14.5	**7d**	59
13e	$C_6H_5CH_2$	C_6H_6	55°	9.5	**7e**	34
13f	C_6H_5	C_6H_6	55°	12.0	**8**	69

In view of the above results, the mechanism of this reaction is probably as shown in Chart 2, involving C–C bond cleavage *via* **14** and ring enlargement of the key intermediate (**15**) by migration of the sulfur group *via* **17** and subsequent hydrolysis of **18**.[9,10] The results observed in the cases of **6** and **13f** can be reasonably explained by preferable oxidation

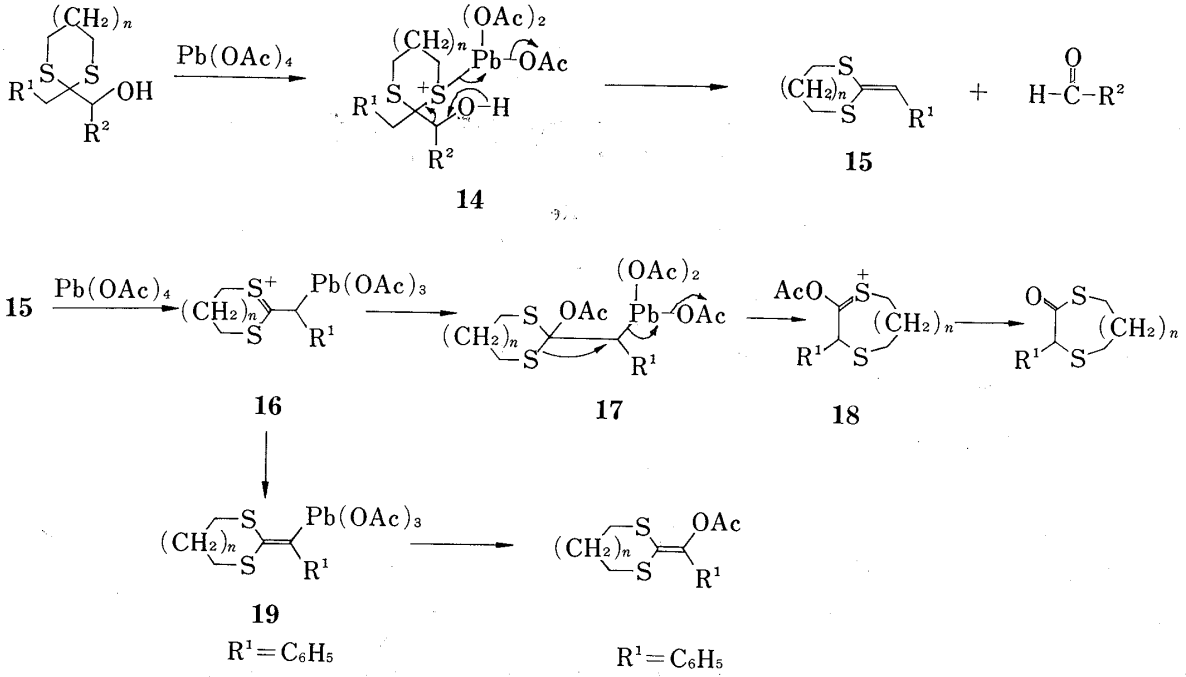
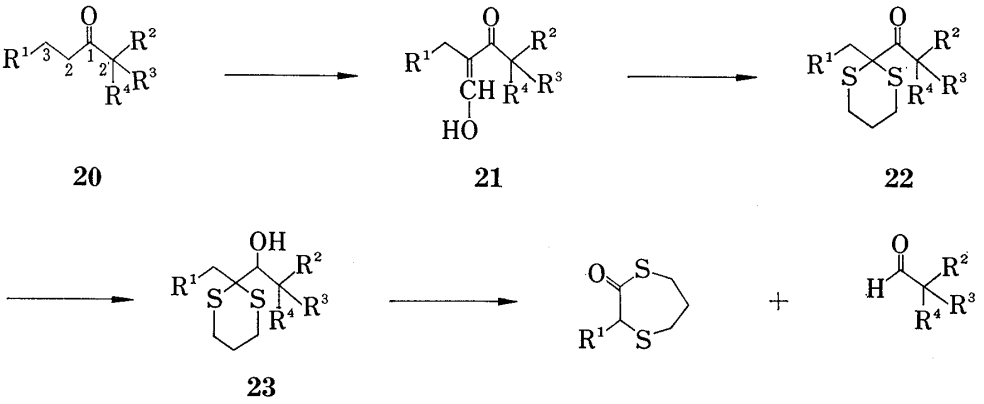


Chart 2

(**16**) of the benzylic moiety and stabilization by transformation into **19**, due to conjugation with the phenyl ring.

This new procedure for the bond cleavage or for the preparation of the 3-alkyl-1,4-dithiepan-2-one derivatives (**7**) clearly has advantages in terms of yield and mildness of the reaction conditions. In addition, this method is applicable to the selective 1,2′-bond cleavage of *prim*-alkyl *sec*- or *tert*-alkyl ketones (**20**) *via* the thioacetal derivatives (**22**) and (**23**), as shown in Chart 3.



20 **21** **22**

23

Chart 3

Experimental

General

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Thin-layer or preparative thick layer plates were made of E. Merck Silica gel 60PF-254 activated by drying at 140° for 3.5 hr.

Infrared spectra were obtained in the indicated state with a Hitachi 215 spectrometer. Nuclear magnetic resonance spectra were determined in the indicated solvent with a Hitachi R-24B high resolution NMR spectrometer; chemical shifts are given in ppm from tetramethylsilane. Splitting patterns are designated as s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Mass spectra were taken on a Hitachi RMU-6MG spectrometer.

The materials, 2-alkyl-2-(1-hydroxyalkyl)-1,3-dithianes (**1**—**6**) and 2-alkylidene-1,3-dithianes (**13a**—**f**), were prepared according to the Seebach–Corey[11] and Jones–Seebach[20] methods, respectively.

Reaction of 2-Alkyl-2-(1-hydroxyalkyl)-1,3-dithianes (1—6) with $Pb(OAc)_4$

1,4-Dithiepan-2-one (7a)——A suspension of 610 mg (2.96 mmol) of 2-(1-hydroxybutyl)-2-methyl-1,3-dithiane (**1b**) and 3.706 g (7.11 mmol) of 85% pure $Pb(OAc)_4$ in 18 ml of benzene was stirred at 55° for 13 hr under nitrogen. After cooling, the reaction mixture was quenched with ethylene glycol (800 mg) and extracted with ether. The organic extracts were washed successively with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residual oil was subjected to preparative TLC (benzene–ether 10: 1) to give 214 mg (49% yield) of **7a** as colorless needles of mp 87—88° (recryst. from CCl_4). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (thio ester). NMR ($CDCl_3$) δ: 2.15—2.70 (2H, m), 2.75—3.25 (4H, m, 2 SCH_2), 3.60 (2H, s, $\overset{O}{\overset{\|}{C}}-CH_2-S$). MS *m/e*: 148 ($M^+$). *Anal.* Calcd for $C_5H_8OS_2$: C, 40.54; H, 5.44; S, 43.21. Found: C, 40.58; H, 5.40; S, 43.32.

The reactions of the other analogs **1a** and **1c** with $Pb(OAc)_4$ were carried out as described above under the reaction conditions given in Table II, to give **7a** in the yields listed in Table II.

In the reaction of 248 mg (1.00 mmol) of **1c** with 1.25 g (2.40 mmol) of 85% pure $Pb(OAc)_4$, benzaldehyde (40 mg, 38% yield) was obtained together with **7a** (51 mg, 34% yield).

3-Methyl-1,4-dithiepan-2-one (7b)——A suspension of 300 mg (1.40 mmol) of 2-ethyl-2-(1-hydroxybutyl)-1,3-dithiane (**2**) and 1.770 g (3.40 mmol) of 85% pure $Pb(OAc)_4$ in 10 ml of benzene was stirred at 55° for 16 hr. After cooling, the reaction mixture was quenched with ethylene glycol (400 mg) and diluted with ether.

Work-up as described above, followed by preparative TLC (benzene), gave 116 mg (51% yield) of **7b** as colorless prisms of mp 54—55° (recryst. from hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1662 (thio ester). NMR (CCl_4) δ: 1.35 (3H, d, J=7 Hz, CH_3), 1.80—2.65 (2H, m), 2.70—3.30 (4H, m, 2 SCH_2), 3.82 (1H, q, J=7 Hz, $\overset{O}{\overset{\|}{C}}-CH-S$).

MS *m/e*: 162 (M^+). *Anal.* Calcd for $C_6H_{10}OS_2$: C, 44.40; H, 6.21; S, 39.52. Found: C, 44.14; H, 6.38; S, 39.99.

3-Ethyl-1,4-dithiepan-2-one (7c)——A suspension of 97 mg (0.39 mmol) of 2-(1-hydroxybutyl)-2-propyl-1,3-dithiane (**3**) and 555 mg (1.00 mmol) of 80% pure $Pb(OAc)_4$ in 5 ml of benzene was stirred at 55° for 13.5 hr. The reaction mixture was worked up as described above, and the crude product obtained was subjected to preparative TLC (benzene) to give 29 mg (42% yield) of **7c** as colorless plates of mp 65—65.5° (recryst. from hexane–CCl_4). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1660 (thio ester). NMR (CCl_4) δ: 1.00 (3H, t, J=7 Hz, CH_3), 1.30—2.50 (4H, m), 2.50—3.30 (4H, m, 2 SCH_2), 3.60 (1H, t, J=7 Hz, $\overset{O}{\overset{\|}{C}}$–CH–S). MS *m/e*: 176 ($M^+$). *Anal.* Calcd for $C_7H_{12}OS_2$: C, 47.72; H, 6.87; S, 36.33. Found: C, 47.83; H, 6.83; S, 36.29.

3-Propyl-1,4-dithiepan-2-one (7d)——A suspension of 200 mg (0.81 mmol) of 2-butyl-2-(1-hydroxybutyl)-1,3-dithiane (**4**) and 1.070 g (1.93 mmol) of 80% pure $Pb(OAc)_4$ in 10 ml of benzene was stirred at 55° for 12 hr. Work-up as described above, followed by preparative TLC (benzene), gave 89 mg (58% yield) of **7d** as colorless needles of mp 60—61° (recryst. from hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1662 (thio ester). NMR (CCl_4) δ: 0.93 (3H, t, CH_3), 1.20—2.65 (6H, m), 2.70—3.35 (4H, m, 2 SCH_2), 3.68 (1H, t, J=7 Hz, $\overset{O}{\overset{\|}{C}}$–CH–S). MS *m/e*: 190 ($M^+$). *Anal.* Calcd for $C_8H_{14}OS_2$: C, 50.52; H, 7.42; S, 33.70. Found: C, 50.46; H, 7.43; S, 34.18.

3-Benzyl-1,4-dithiepan-2-one (7e)——A suspension of 300 mg (1.00 mmol) of 2-(1-hydroxybutyl)-2-phenethyl-1,3-dithiane (**5**) and 1.250 g (2.40 mmol) of 85% pure $Pb(OAc)_4$ in 10 ml of benzene was stirred at 55° for 16 hr. After cooling, the reaction mixture was quenched with ethylene glycol (400 mg) and extracted with ether. Work up as described above, followed by preparative TLC (benzene), gave 118 mg (50% yield) of **7e** as colorless needles of mp 109—110° (recryst. from hexane–ether). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1662 (thio ester), 1597 (phenyl). NMR ($CDCl_3$) δ: 2.00—2.60 (2H, m), 2.66—3.50 (6H, m, 2 SCH_2 and CH_2–Ph), 3.95 (1H, t, J=7 Hz, $\overset{O}{\overset{\|}{C}}$–CH–S), 7.10—7.40 (5H, C_6H_5). MS *m/e*: 238 (M^+). *Anal.* Calcd for $C_{12}H_{14}OS_2$: C, 60.50; H, 5.92; S, 26.86. Found: C, 60.33; H, 5.92; S, 26.55.

The reaction of **5** with $Pb(OAc)_4$ was carried out under various reaction conditions, as described above, to give **7e** in the yields listed in Table I.

Reaction of 2-Benzyl-2-(1-hydroxyalkyl)-1,3-dithiane (6) with $Pb(OAc)_4$——A suspension of 746 mg (2.60 mmol) of 2-benzyl-2-(1-hydroxybutyl)-1,3-dithiane (**6a**) and 3.26 g (6.20 mmol) of 85% pure $Pb(OAc)_4$ in 28 ml of benzene was stirred at 55° for 16 hr. After cooling, the reaction mixture was worked up as described above and the crude product obtained was subjected to preparative TLC (benzene) to give 464 mg (67% yield) of 2-(α-acetoxybenzylidene)-1,3-dithiane (**8**) as a colorless oil of bp 160° (1 mmHg) (oil bath). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1770 (enol ester), 1600 (phenyl). NMR (CCl_4) δ: 2.10 (3H, s, O–$\overset{O}{\overset{\|}{C}}$–$CH_3$), 1.80—2.26 (2H, m), 2.78 (2H, t, J=6 Hz, SCH_2), 2.90 (2H, t, J=6 Hz, SCH_2), 7.10—7.50 (5H, m, C_6H_5). MS *m/e*: 266 (M^+). *Anal.* Calcd for $C_{13}H_{14}O_2S_2$: C, 58.64; H, 5.30; S, 24.04. Found: C, 58.58; H, 5.25; S, 24.33.

The reaction of 2-benzyl-2-(α-hydroxybenzyl)-1,3-dithiane (**6b**) with $Pb(OAc)_4$ was carried out as described above to give **8** in 34% yield.

Preparation of 7a from Chloroacetyl Chloride and 1,3-Propanedithiol——A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirrer, and containing 265 mg (5.50 mmol) of sodium hydride (50% oil dispersion, washed with hexane to remove mineral oil), was flushed with nitrogen and maintained under a positive pressure of nitrogen. Freshly distilled anhydrous THF (5 ml) was added followed by the dropwise addition of 0.23 ml (2.30 mmol) of 1,3-propanedithiol. The mixture was stirred at 0° for 35 min, then at room temperature for 1.5 hr, and a solution of 0.20 ml (2.50 mmol) of chloroacetyl chloride in 1 ml of THF was added dropwise. The reaction mixture was stirred at 0° for 2 hr, then warmed to room temperature, and stirred for a further 41 hr. The reaction mixture was diluted with ether. The solution was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was subjected to preparative TLC (ether–hexane 2: 1) to give **7a** (15 mg, 4% yield) as colorless needles of mp 87—88° (recryst. from CCl_4); this material was identical with the product obtained by the reaction of **1a—c** with $Pb(OAc)_4$ (spectral properties and mixed melting point determination).

Preparation of 7b from 2-Chloropropionic Acid and 1,3-Propanedithiol——A solution of 0.31 ml (3.60 mmol) of 2-chloropropionic acid in 3 ml of THF was added at 0° to a suspension of disodium 1,3-propanedithiolate in 10 ml of THF, prepared from 0.40 ml (4.00 mmol) of 1,3-propanedithiol and 570 mg (11.9 mmol) of sodium hydride (50% oil dispersion, washed with hexane to remove mineral oil before use). The reaction mixture was stirred at room temperature for 18 hr, then diluted with methylene chloride, and washed with 10% aqueous HCl. The organic layer was washed with saturated aqueous $NaHCO_3$. The aqueous washings were acidified with 10% aqueous HCl and the separated oil was extracted with methylene chloride. The organic extracts were washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give 2-(3-mercaptopropylthio)propionic acid (650 mg) as a yellow oil. IR ν_{max}^{film}

cm^{-1}: 1710 (CO_2H). NMR ($CDCl_3$) δ: 1.46 (3H, d, $J=8$ Hz, CH_3), 1.70—2.25 (2H, m), 2.40—3.20 (6H, m, 2 SCH_2, SH, and CO_2H), 3.45 (1H, q, $J=8$ Hz, C<u>H</u>–CH_3).

Ethyl chlorocarbonate (0.42 ml, 4.30 mmol) was added to an ice-cooled solution of the crude product obtained above and 0.61 ml (4.30 mmol) of triethylamine in 7 ml of THF. The reaction mixture was stirred at 0° for 2 hr and the precipitates were filtered off. The filtrate was concentrated *in vacuo* to give the mixed anhydride (869 mg): IR ν_{max}^{film} cm^{-1}: 1820, 1760 (anhydride).

A solution of this crude mixed anhydride in 20 ml of benzene was refluxed for 7 hr in the presence of a catalytic amount of *p*-toluenesulfonic acid with a Dean–Stark apparatus. After cooling, the reaction mixture was diluted with ether. The solution was washed successively with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residual oil was twice subjected to preparative TLC, eluting with benzene the first time and with hexane–ether (3: 2) the second time, to give **7b** (14 mg) as colorless prisms of mp 54—55°; the spectral and physical properties of this material were identical with those of the product obtained by the reaction of **2** with $Pb(OAc)_4$.

Preparation of 3-Phenyl-1,4-dithiepan-2-one (7f) from α-Bromophenylacetic Acid and 1,3-Propanedithiol——A solution of 774 mg (3.60 mmol) of α-bromophenylacetic acid in 7 ml of THF was added to an ice-cooled suspension of disodium 1,3-propanedithiolate in 8 ml of THF, prepared from 0.40 ml (3.60 mmol) of 1,3-propanedithiol and 570 mg (11.88 mmol) of sodium hydride (50% oil dispersion, washed with hexane to remove mineral oil). The reaction mixture was stirred at room temperature for 11 hr, then quenched with 10% aqueous HCl and extracted with ether. The organic extracts were washed with saturated aqueous $NaHCO_3$. The aqueous washings were acidified with 10% aqueous HCl and the separated oil was extracted with ether. The combined extracts were washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated to dryness under reduced pressure to give α-(3-mercaptopropylthio)phenylacetic acid (814 mg). IR ν_{max}^{film} cm^{-1}: 1715 (CO_2H). NMR (CCl_4) δ: 1.50—2.20 (2H, m), 2.30—2.80 (4H, m, 2 SCH_2), 3.66 (1H, s, $\overset{O}{\overset{\|}{C}}$–CH–S), 4.42 (2H, bs, CO_2H and SH), 7.00—7.50 (5H, C_6H_5).

Ethyl chlorocarbonate (0.31 ml, 3.30 mmol) was added at −5° to a mixture of the crude carboxylic acid obtained and 0.55 ml (3.96 mmol) of triethylamine in 11 ml of THF. The reaction mixture was stirred at 0° for 2 hr. The precipitates were filtered off and the filtrate was concentrated *in vacuo* to give the mixed anhydride (816 mg). IR ν_{max}^{film} cm^{-1}: 1820, 1740 (anhydride).

This crude mixed anhydride was heated in refluxing benzene (20 ml) for 20.6 hr in the presence of a catalytic amount of *p*-toluenesulfonic acid using a Dean–Stark apparatus. The usual work-up, followed by preparative TLC (hexane–ether 5: 4), gave **7f** (11 mg, 21% yield from α-bromophenylacetic acid) as colorless prisms of mp 131.5—132.5° (recryst. from CCl_4). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1675 (thio ester), 1600, 1590 (phenyl). NMR ($CDCl_3$) δ: 2.10—2.50 (2H, m), 2.90—3.30 (4H, m, 2 SCH_2), 4.92 (1H, s, $\overset{O}{\overset{\|}{C}}$–CH–S), 7.23—7.50 (5H, C_6H_5). MS *m/e*: 224 (M^+). *Anal.* Calcd for $C_{11}H_{12}OS_2$: C, 58.92; H, 5.40; S, 28.54. Found: C, 58.69; H, 5.48; S, 28.77.

Conversion of 7e into Methyl Cinnamate——A solution of 100 mg (0.42 mmol) of **7e** in 3 ml of methanol was refluxed in the presence of 213 mg (0.84 mmol) of iodine for 4 hr. The solvent was evaporated off under reduced pressure and the residue was dissolved in ether. The solution was washed successively with 10% aqueous $Na_2S_2O_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The oxidation to the sulfoxide was carried out by treatment of the residual oil (105 mg) with 216 mg (1.01 mmol) of $NaIO_4$ in 3 ml of methanol at room temperature for 20 hr. The solvent was removed *in vacuo* and the residue was triturated with chloroform. The precipitates were filtered off and the filtrate was concentrated to dryness under reduced pressure. The residue (125 mg) was heated in refluxing carbon tetrachloride (3 ml) for 3 hr. Removal of the solvent, followed by preparative TLC (benzene), gave methyl cinnamate (34 mg, 50% yield from **7e**), which was identical with a commercial sample (spectral and physical properties).

Hydrolysis of 8——A solution of 100 mg (0.38 mmol) of **8** in 2.5 ml of THF was added to an ice-cooled solution of 25 mg (0.38 mmol) of 85% pure KOH in 2.5 ml of H_2O. The reaction mixture was stirred at 0° for 10 hr and then extracted with ether. The combined organic extracts were washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to preparative TLC (hexane–ether 3: 1) to give 34 mg (40% yield) of 2-benzoyl-1,3-dithiane (**9**) as colorless needles of mp 92—92.5° (recryst. from hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (–$\overset{O}{\overset{\|}{C}}$–$C_6H_5$), 1595, 1580 (phenyl). NMR ($CDCl_3$) δ: 1.90—2.30 (2H, m), 2.40—2.80 (2H, m, SCH_2), 3.14—3.60 (2H, m, SCH_2), 5.12 (1H, s, S–CH–S), 7.26—7.66 and 7.78—8.00 (5H, m, C_6H_5). MS *m/e*: 224 (M^+). *Anal.* Calcd for $C_{11}H_{12}OS_2$: C, 58.92; H, 5.40; S, 28.54. Found: C, 59.20; H, 5.56; S, 28.93.

Preparation of 9 from 1,3-Dithiane and Benzoyl Chloride——A 1.5 M hexane solution of butyllithium (2.5 ml, 3.70 mmol) was added at −20° to a solution of 300 mg (2.50 mmol) of 1,3-dithiane in 5 ml of THF. After stirring at −20° for 2.5 hr, a solution of benzoyl chloride (0.29 ml, 2.50 mmol) in 3 ml of THF was added at −78°. The reaction mixture was stirred at −78° for 2.5 hr, warmed to room temperature, then

quenched with 10% aqueous HCl, and extracted with ether. The usual work-up, followed by preparative TLC (hexane–ether 3: 1), gave 213 mg (38% yield) of **9** as colorless needles of mp 92—92.5°; this material was identical with the compound obtained by hydrolysis of **8** (spectral properties and mixed melting point determination).

Reaction of 2-Alkylidene-1,3-dithianes (13a—f) with $Pb(OAc)_4$ General Procedure——A suspension of **13a—e** (1.10 mmol) and $Pb(OAc)_4$ (85% pure, 2.64 mmol) in benzene (12 ml) was stirred under the conditions given in Table IV. Work-up as described above, followed by preparative TLC (benzene), gave the corresponding 1,4-dithiepan-2-ones (**7a—e**) in the yields listed in Table IV. The spectral and physical properties of these products were completely superimposable on those of the compounds obtained by the reaction of **1—5** with $Pb(OAc)_4$.

Reaction of 2-Benzylidene-1,3-dithiane (13f) with $Pb(OAc)_4$——A suspension of **13f** (150 mg, 0.72 mmol) and $Pb(OAc)_4$ (80% pure, 480 mg, 0.87 mmol) in benzene (8 ml) was stirred at 55° for 12 hr.

Work-up as described above, followed by preparative TLC (hexane–ether 3: 2), gave **8** (133 mg, 69% yield), which was identical with the product obtained by the reaction of **6a, b** with $Pb(OAc)_4$.

Oxidative Cleavage of 2-(1-Hydroxyethyl)-2-methyl-1,3-dithiolane (11)

Preparation of 11——A solution of 300 mg (3.40 mmol) of acetoin and 320 mg (3.40 mmol) of 1,2-ethanedithiol in 3 ml of toluene was stirred in the presence of BF_3 etherate (0.05 ml) at 0° for 20 hr. The reaction mixture was diluted with ether. The solution was washed successively with 10% aqueous NaOH and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was subjected to preparative TLC (benzene–ether 10: 1) to give 357 mg (64% yield) of **11**. bp 90° (bath temp.) (5 mmHg). IR ν_{max}^{film} cm^{-1}: 3470 (OH). NMR (CCl_4) δ: 1.20 (3H, d, J=6 Hz, $C\underline{H}_3$–CH–O), 1.66 (3H, s, CH_3), 2.35 (1H, bs, OH), 3.23 (4H, s, 2 SCH_2), 3.70 (1H, q, J=6 Hz, CH–O). *Anal.* Calcd for $C_6H_{12}OS_2$: C, 43.90; H, 7.37; S, 38.98. Found: C, 44.02; H, 7.49; S, 39.45.

Reaction of 11 with $Pb(OAc)_4$ General Procedure——A suspension of **11** (572 mg, 3.50 mmol) and $Pb(OAc)_4$ (85% pure, 4.38 g, 8.40 mmol) in 24 ml of a solvent (benzene, $CHCl_3$, or CCl_4) was stirred under the conditions given in Table III. The usual work-up as described above, followed by preparative TLC (benzene), gave 1,4-dithian-2-one (**12**) in the yields listed in Table III. bp 105° (3 mmHg). IR ν_{max}^{film} cm^{-1}: 1660 (thio ester). NMR (CCl_4) δ: 2.90—3.50 (4H, m, 2 SCH_2), 3.35 (2H, s, $\overset{O}{\overset{\|}{C}}$–$CH_2$–S). MS *m/e*: 134 ($M^+$). *Anal.* Calcd for $C_4H_6OS_2$: C, 35.83; H, 4.51; S, 47.73. Found: C, 36.06; H, 4.45; S, 47.55.

Preparation of 12 from Chloroacetyl Chloride and 1,2-Ethanedithiol——A solution of 250 mg (2.66 mmol) of 1,2-ethanedithiol in 1 ml of THF was added to a suspension of sodium hydride (50% oil dispersion, 306 mg, 6.38 mmol, washed with hexane to remove mineral oil) in 4 ml of THF. After stirring the mixture at 0° for 2 hr, then at room temperature for 2.5 hr, a solution of 2.30 ml (2.93 mmol) of chloroacetyl chloride in 1 ml of THF was added at 0°. The reaction mixture was stirred at 0° for 17.5 hr, warmed to room temperature, and then stirred for a further 28.5 hr. The usual work-up, followed by preparative TLC (benzene), gave 189 mg (53% yield) of **12**, which was identical with the product obtained by the reaction of **11** with $Pb(OAc)_4$.