Anion Reactions of 1,3-Dithiane 1,3-Dioxide with Carbonyl Compounds: High Diastereoselectivity with Aromatic Aldehydes under Conditions of Equilibrium Control

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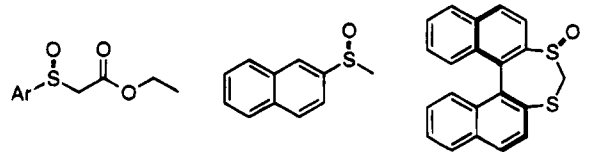
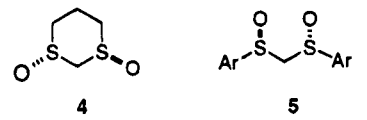
We have investigated the anion chemistry of *trans*-1,3-dithiane 1,3-dioxide (**4**) with aldehydes and ketones, and we have found that this reagent undergoes highly selective addition reactions with aromatic aldehydes but only when reactions are under equilibrium control (achieved using Na anion of **4**). Other metals invetsigated (Li, Mg, Al, Ce, Ti) gave either poorer selectivity or caused decomposition of **4**. Zn-**4** did give improved selectivity at low temperature but only with aromatic aldehydes. Reactions with ketones were limited to those without α-branching. A model that accounts for the high diastereoselectivity observed with aromatic aldehydes is presented.

Sulfoxide-stabilized carbanions have found a permanent position in asymmetric synthesis primarily due to the work of Kunieda and Solladie.[1-3] Over a decade ago they showed that the magnesium enolates of **1** reacted with aldehydes with very high diastereocontrol,[4-6] and since then variations in the structure of **1** have been explored and found to give similarly high diastereoselectivity.[2,7-10] This has led to the perception that



1 **2** **3**



4 **5**

sulfoxide-stabilized carbanions usually give very high diastereoselectivity in addition reactions with aldehydes. However, while sulfoxide-stabilized carbanions do usually show high stereoselectivity α to the sulfoxide, β-stereoselectivity is often very poor.[11-16] Apart from α-sulfinyl esters described above, there are only a few exceptions to this situation. Lithiated naphthyl methyl sulfoxide **2**[17] and the binaphthyl-based dithiepine **3**[18,19] show high diastereoselectivity with benzaldehyde. In our own studies, we have found that *trans*-1,3-dithiane 1,3-dioxide (**4**) reacts with very high diastereoselectivity with aromatic aldehydes,[20-22] and in this paper we describe our results in full. The 1,3-dithiane 1,3-dioxide moiety can be readily converted to a thioester which in turn can be transformed into an acid, ester, amide, ketone, or aldehyde.[23] During the course of this work, Solladie reported anion reactions of bis(*p*-tolylsulfinyl)methane (**5**) which also gave high diastereoselectivity with aromatic aldehydes.[24]

Anion Reactions with Aldehydes. Racemic *trans*-1,3-dithiane 1,3-dioxide (**4**) was prepared as previously described.[22,25] Problems were initially encountered with the poor solubility of **4** in ethereal solvents. It was, however, soluble in polar solvents, e.g., DMF and pyridine. While it was found that anion reactions could be carried out in these polar solvents better yields were

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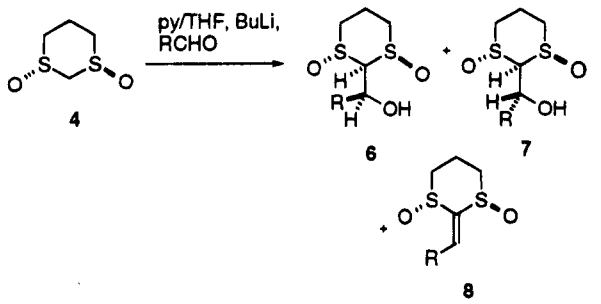
Scheme 1



a R = Ph
b R = *n*-Bu
c R = *i*-Pr
d R = *t*-Bu
e R = *m*-$MeOC_6H_4$
f R = *p*-$MeOC_6H_4$
g R = *o*-$MeOC_6H_4$
h R = 3,4-$(TBDMSO)_2C_6H_3$
i R = *p*-$NO_2C_6H_4$
j R = 3-pyridyl
k R = 9-anthracenyl
l R = 2,6-$(MeO)_2C_6H_3$
m R = 2,4,6-$Me_3C_6H_2$
n R = 2,6-$F_2C_6H_3$
o R = 2,4-$F_2C_6H_3$
p R = C_6F_5
q R = furfuryl

Table 1. Reaction of Li-4 with Aldehydes

entry	aldehyde	temp (°C)	time	ratio of products[a] **6:7:8**
1	PhCHO	−78	30 min[b]	66:34:0[c]
2	*n*-BuCHO	−78	30 min[b]	63:37:0[c]
3	*i*-PrCHO	−78	30 min[b]	50:50:0[c]
4	*t*-BuCHO	−78	30 min[b]	64:36:0[c]
5	PhCHO	0	1 min[d]	62:38:0
6			30 min[d]	45:55:0
7			60 min[d]	36:64:0
8			3.5 h[d]	13:77:10
9	*n*-BuCHO	0	5 min[d]	50:50:0
10			60 min[d]	50:50:0
11			6 h[d]	15:56:29
12	*i*-PrCHO	0	5 min[d]	50:50:0
13			60 min[d]	50:34:16
14			6 h[d]	38:26:36
15	*t*-BuCHO	0	5 min[d]	33:67:0
16			60 min[d]	10:90:0
17			6 h[d]	31:38:31

[a] Ratios determined by HPLC analysis. [b] Reactions were completed after 1 min and ratios did not vary with time. [c] Isolated yields of **6a−d** were 58%, 49%, 34%, and 42%, respectively. [d] Aliquots were removed from a single reaction at the times indicated and ratios determined by HPLC analysis.

obtained in dual solvent systems, particularly pyridine/THF. Most reactions have been conducted in this solvent system. Metalation with *n*-BuLi at 0 °C, followed by addition of an aldehyde at −78 °C and quenching with HCl (aq)/EtOH, gave adducts **6** and **7** in high yield but with poor diastereoselectivity (Scheme 1, Table 1, entries 1−4).

Several points are worthy of note. During addition of *n*-BuLi a transient yellow color appeared which remained when a slight excess of *n*-BuLi had been added. These observations are interpreted as follows. *n*-BuLi adds to pyridine[26] to give the lithiated dihydropyridine **9** (yellow), and this deprotonates **4** to give lithiated dithiane dioxide (colorless) and the dihydropyridine (colorless) (Scheme 2). When all the dithiane dioxide has been deprotonated a small amount of lithiated dihydropyridine **9** remains giving rise to the yellow solution at the end. Using the *n*-BuLi/pyridine system we were able to simply titrate the base into solution, and this obviated the need to

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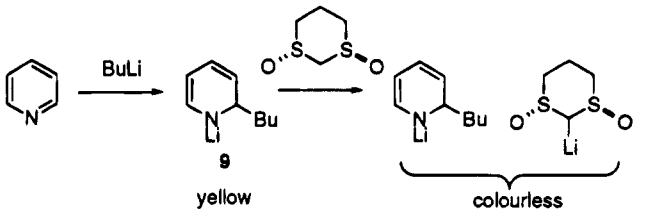
Scheme 2



determine the molarity of the *n*-BuLi used. To our knowledge this combination of BuLi/pyridine as a titratable base has not previously been used.

The nature of the quench was critical. Use of H_2O or NH_4Cl (aq) resulted in only starting material being isolated, and use of AcOH gave variable amounts of adducts (depending on the aldehyde used) whereas use of HCl (aq)/EtOH afforded good yields of products. Higher yields were obtained when the reaction mixture was added to a rapidly stirring solution of HCl (aq) in EtOH. The requirement for a fast quench to isolate the adducts in good yield and the observation of reduced yields with slower quenches indicated that the addition reaction was reversible.

Other workers have found that the stereoselectivity in kinetically controlled reactions of sulfoxide-stabilized carbanions can be dramatically influenced by the temperature of formation of the anion since at higher temperatures reorganization of the lithium species can occur, giving a chelated anion.[27] This effect was investigated with dithiane dioxide. In two separate experiments, the *n*-butyllithium-derived anion of **4** was formed at both 0 °C and −45 °C and then reacted with pivalaldehyde at −78 °C. However, the product distribution (65:35, **6**:**7**) was very similar in both experiments. In all further experiments, *n*-BuLi addition was carried out at 0 °C.

The reactions were repeated at 0 °C, and it was found that improved diastereoselectivity was obtained with benzaldehyde and pivalaldehyde after 1 h (Table 1, entries 5−8, 15, 16). It was found that under these reaction conditions equilibration was occurring as the ratios of **6:7** changed with time. The ratios obtained were not true equilibrium ratios as elimination began to occur over long periods of time with benzaldehyde and pivalaldehyde to give **8**, Scheme 1 (Table 1, entries 8, 17). Less hindered aliphatic aldehydes did not equilibrate and gave poor ratios at short reaction times and elimination over longer reaction times (Table 1, entries 9−11, 12−14). In order to obtain true equilibrium ratios we required faster equilibration rates to try to avoid the elimination reaction that occurred over extended times and so changed the counterion from Li to Na. We therefore replaced *n*-BuLi with NaHMDS,[28] and the results of reactions with a variety of aldehydes are summarized in Table 2. For comparison, reactions were also conducted with KHMDS and LiHMDS as base, and again the results are presented in Table 2. While aliphatic aldehydes showed only poor selectivity (Table 2, entries 2−4) with all bases, benzaldehyde gave very high selectivity (Table 2, entry 1) with the sodium base. Reactions with LiHMDS were

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(28) The greater acidity of *trans*-1,3-dithiane 1,3-dioxide (pK_a 25, see ref 25) relative to dithiane (pK_a 39) itself allows metalation with relatively weak bases. NaHMDS did not give the same color changes that were observed with *n*-BuLi, and it is presumed that this base does not add to pyridine.

Table 2. Reaction of M-HMDS-4 with Aldehydes at 0 °C

entry	aldehyde	ratio of products 6:7 LiHMDS	NaHMDS	KHMDS
1	PhCHO	12:88	4:96	10:90
2	*n*-BuCHO	50:50	23:77	20:80
3	*i*-PrCHO	40:60	40:60	30:70
4	*t*-BuCHO	18:82	60:40	70:30

Table 3. Reaction of Na-4 with Aldehydes at 0 °C

entry	aldehyde	equilibration time[a]	ratio[b]	isolated yield of 7 (%)
1	PhCHO	30 min	4:96	87
2	*m*-$MeOC_6H_4CHO$	3 h	5:95	64
3	*p*-$MeOC_6H_4CHO$	3 h	5:95	72
4	*o*-$MeOC_6H_4CHO$	18 h	5:95	76
5	3,4-$(TBDMSO)_2C_6H_3CHO$	30 min	4:96	56
6	*p*-$NO_2C_6H_4CHO$	5 h	5:95	42
7	3-pyridylcarboxaldehyde	30 min	3:97[c]	71[c]
8	9-anthracenecarboxaldehyde	30 min	<2:98	91
9	$2,6\text{-}(MeO)_2C_6H_3CHO$	1 h	30:70	66[d]
10	$2,4,6\text{-}Me_3C_6H_2CHO$	10 min[e]	40:60	26 (47[f])
11	$2,6\text{-}F_2C_6H_3CHO$	30 min[e]	40:60	25[g]
12	$2,4\text{-}F_2C_6H_3CHO$	30 min[e]	3:97	34[h]
13	C_6F_5CHO	1 min	i	65[i]
14	furfuraldehyde	5 min	i	70[i]

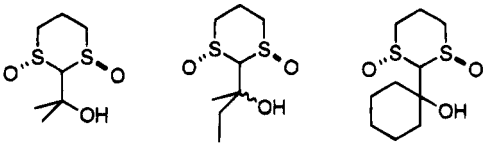
[a] Reactions were monitored over time by HPLC and indicate time before elimination began to occur. [b] Ratios determined by integration of crude NMR. [c] Ratio and yield determined after formation of TMS silyl ether. [d] Combined yield of **6m** and **7m** (inseparable by chromatography). [e] A significant amount of elimination occurred even at very short reaction times. [f] Yield based on recovered starting material. [g] 35% of **7n** and 22% of **8n** was isolated. [h] 22% of **8o** was isolated. [i] Only **8p,q** was isolated.

similar in selectivity to reactions conducted with BuLi/pyridine and similar in that only benzaldehyde and pivaldehde were under equilibrium control. All of the sodium and potassium reactions were now under equilibrium control but the sodium anion showed the highest selectivity.[29] To determine the scope of the diastereoselectivity observed with the sodium base we investigated a large number of aromatic aldehydes, and the results are presented in Table 3. As can be seen, high selectivity is maintained for electron rich aromatics (Table 3, entries 2–5), electron deficient aromatics (Table 3, entries 6,-12), and heteroaromatics (Table 3, entry 7). The only class of aromatic aldehydes that gave poor selectivity were 2,6-disubstituted aromatics (Table 3, entries 9–11) with the exception of 9-anthracenecarboxaldehyde (Table 3, entry 8), and this prompted us to examine a number of aldehydes in this class (Table 3, entries 8–11). Whether electron rich (entry 9, 10) or electron deficient (entry 11), 2,6-disubstituted aldehydes gave adducts with low diastereoselectivity. Furfuraldehyde and pentafluorobenzaldehyde did not give hydroxy adducts but only gave the eliminated product **8** (entries 13, 14). While the result with furfuraldehyde is anomalous for electron rich aldehydes, as a general rule, electron deficient aldehydes (entries 11–13) showed a greater propensity for elimination than electron rich aromatic aldehydes.

While the yields in the anion reactions are generally high (Table 3, entries 1-8), slightly lower yields were obtained with 3,4-dialkoxybenzaldehyde, and by TLC it was observed that some 1,3-dithiane 1,3-dioxide remained. In anion reactions with such electron rich aromatic aldehydes, the equilibrium mixture now included an observable amount of starting material. Solladie found that in the reaction between the analogous C_2 symmetric bis-sulfoxide **5** and a similar aromatic aldehyde, the equilibrium was entirely on the side of starting material and no product was obtained.[24] 1,3-Dithiane 1,3-dioxide is less hindered and has a higher pK_a than **5**[28,30] making it more reactive and thereby favoring formation of adducts with less electrophilic aldehydes.

The rates of equilibration for the different aromatic aldehydes varied considerably without any correlation emerging between time taken to reach equilibrium and electronic properties of the aromatic ring. The particularly slow rate of equilibration for *o*-methoxybenzaldehyde probably results from the product metal alkoxide chelating to the *ortho* substituent and slowing down the rate of the reverse reaction. The time taken to achieve maximum selectivity was determined experimentally for each aldehyde by HPLC analysis of aliquots at various time intervals.

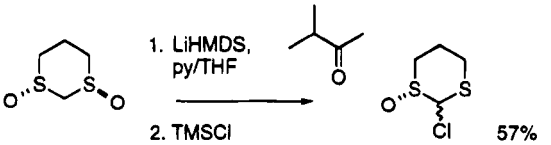
Reactions with Ketones. Anion reactions of Li-**4** were carried out by the method depicted in Scheme 1 with acetone, 2-butanone, cyclohexanone, 3-methyl-2-butanone, acetophenone, and trifluoracetophenone. Adducts were only obtained with acetone, 2-butanone, and cyclohexanone, indicating that the equilibrium for the reaction with ketones is now dominated by steric interactions. If there are groups larger than ethyl flanking a carbonyl group then no adduct is obtained. Even the presence of electron-withdrawing groups α-to the carbonyl group (trifluoracetophenone) was not sufficient to promote the reaction.[31,32]



77% 67% (3:1) 83%

10 **11** **12**

Attempts to push the equilibrium in favor of products using $MgBr_2.Et_2O$[33] or TMSCl failed. The former simply gave starting material while the latter gave the chlorosulfoxide **13**, as a mixture of diastereoisomers, presumably by a silyl Pummerer reaction.[34]



4 **13**

Solvent Effects. Initial attempts at carrying out anion reactions of **4** in THF were unsuccessful due to its

(29) Treatment of isomer **6b** with NaHMDS for 1 h at 0 °C gave a 35:65 ratio of **6b:7b**. As aliphatic aldehydes equilibrated under these conditions one would expect aromatic aldehydes to equilibrate more readily.

(30) The pK_a of **5** is 18.1. See: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

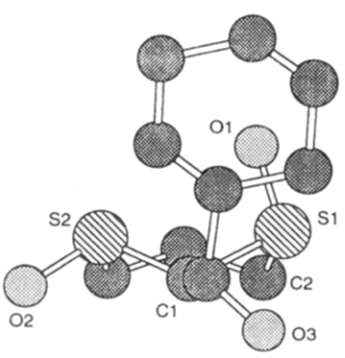
(31) Das, G.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 5360–5362.

(32) Das, G.; Thornton, E. R. *J. Am. Chem. Soc.* **1993**, *115*, 1302–1312.

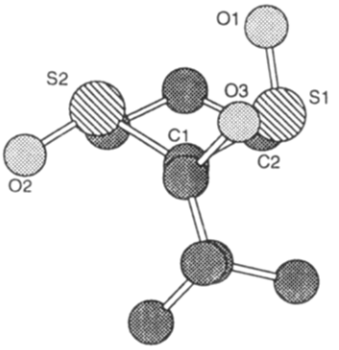
(33) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310–3324.

(34) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77–84.

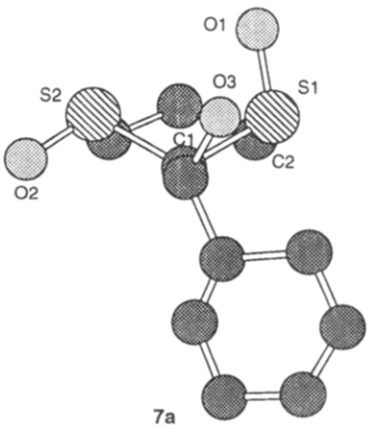
Chart 1



6a



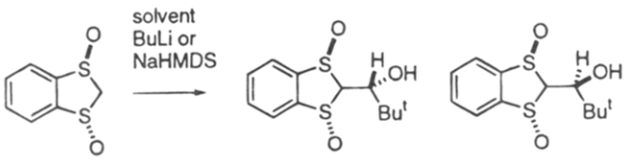
6d



7a

poor solubility. It was found that anion reactions could be conducted in dual solvent systems like pyridine/THF, and we wanted to investigated how changes to the pyridine/THF ratio effected stereoselectivity of the reaction under conditions of both kinetic and thermodynamic control.

Due to the poor solubility of **4** in nonpolar solvents, the more lipophilic analogue **14** was prepared[35] (so that a complete range of ratios of pyridine/THF could be investigated) and anion reactions with pivaldehyde were conducted at both −42 °C (the freezing point of pyridine) and 0 °C in pyridine, pyridine−THF (1.6:1), and neat THF. At −42 °C all three solvents gave similar ratios of products (1:2, **15**:**16**), and the reactions were under kinetic control. At 0 °C again all three solvents gave similar ratios of products (85:15, **15**:**16**), and the reactions were under thermodynamic control.



14 **15** **16**

It was concluded from these experiments that pyridine/THF ratios had little or no effect upon the selectivity of the reaction under conditions of either thermodynamic or kinetic control. Since the absence of THF had no effect upon selectivity, some reactions at 0 °C were carried out in neat pyridine. However, when using NaHMDS as base, reaction yields were diminished. Pyridine/THF (1.6:1), therefore, remains the solvent system of choice for anion reactions with aldehydes. Reactions were also tried in DMF under a variety of conditions. In all cases, the selectivity was the same as reactions performed in pyridine/THF, but due to the difficulties in removing DMF on workup, this was not considered a good alternative.

It has since been discovered that anion reactions can been conducted in neat THF if **4** was finely ground prior to suspension in THF. The only disadvantage in using neat THF is the large volume of solvent required for anion chemistry (typically 1 mmol in 20 mL of THF). Reactions can also be conducted in neat MeCN, and **4** is much more soluble in this solvent.

(35) Aggarwal, V. K.; Lightowler, M.; Lindell, S. D. *Synlett* **1992**, 730−732.

Alternative Metals. There have been several reports in the literature where the diastereoselectivity of reactions of α-sulfinyl carbanions has been improved by using counterions other than lithium. Reactions of metalated-**4** involving magnesium, aluminium, cerium, and zinc as counterions with benzaldehyde at −78 °C were investigated.

Mg-**4** (derived from transmetalation of Li-**4** with $MgBr_2{\cdot}Et_2O$[33] or treatment of **4** with Me-/Ph-/*t*-BuMgBr[5]), Ce-**4** (derived from transmetalation of Li-**4** with $CeCl_3$[36,37]), or Ti-**4** (derived from transmetalation of Li-**4** with $Ti(OiPr)_3Cl$[38]) did not improve selectivity. Transmetalation of Li-**4** with Et_2AlCl or $TiCl_4$ caused decomposition of **4**. Transmetalation of Li-**4** with $ZnCl_2$ led to improved selectivity (93:7, **6a**:**7a**) but only with benzaldehyde; isobutyraldehyde showed low selectivity (68:32, **6c**:**7c**). The reactivity of Zn-**4** at −78 °C was rather low, as has been noted with other zinc α-sulfinyl carbanions,[13] and a large amount of starting material (*ca.* 50%) was apparent from the HPLC traces of these reactions.

It is notable that of the reactions described above only benzaldehyde showed good selectivity, but now in favor of isomer **6a** rather than isomer **7a**. Isomer **7a** is strongly favored in the reaction of aromatic aldehydes and Na-**4** under equilibrating conditions.

Determination of Stereochemistry. X-ray crystal structures of the benzaldehyde adducts **6a** and **7a** were obtained and are shown in Chart 1 as is the X-ray crystal structure of **7d**.[20,42] From analysis of the crystal packing, intermolecular hydrogen bonding to the sulfoxides was observed for all the adducts. Sulfoxide−hydroxyl hydrogen bonds are relatively strong and are believed to be worth ~2.6 kcal mol^{-1} and therefore contribute significantly to the lattice energy.[39]

From a comparison of the C-13 data in d_6-DMSO for all the adducts obtained a correlation between stereochemistry and chemical shift difference was observed. For all the adducts diastereoisomer **7** showed a larger chemical shift difference between carbons C4 and C6 than diastereoisomer **6**. In general, adduct **7** had a chemical shift difference of 4.7−8 ppm for the C4 and C6 carbons of the dithiane ring with most of the values falling within a relatively narrow range of 5−6 ppm while adduct **6** had

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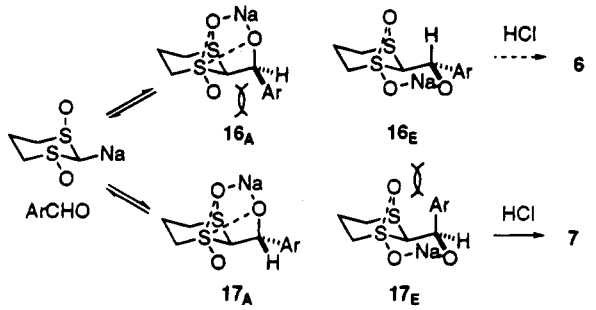
(39) Eliel, E. L.; Olefirowicz, E. M.; Alvarez, M. T.; Hodgson, D. J.; Towle, D. K. *Heterocycles* **1989**, *28*, 937−950.

Scheme 3



Scheme 4

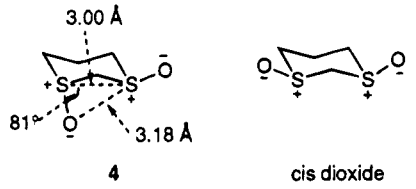


Table 4. C-13 Chemical Shift Differences for Isomers 6 and 7 in d_6-DMSO

aldehyde	**6** $\Delta\delta_C$(C4−C6)	**7** $\Delta\delta_C$(C4−C6)
a	3.1	5.6
b	4.9	6.1
c	3.1	6.0
d	1.6	7.7
e		5.2
f		5.1
g		5.1
i		5.4
k		5.5
l	3.5	4.7
m	4.4	6.0
n	2.8	6.4
o		5.6

a chemical shift difference of 2−5 ppm for the same carbons (Table 4) with most of the values falling within a relatively narrow range of 2−3.5 ppm. Those adducts at the extremities of these ranges were aromatic aldehydes with two electron-donating groups (**6/7l**) and α-unsubstituted aldehydes (**6/7b**).

Discussion

Anion reactions of **4** with aldehydes at low temperature gave adducts but with poor diastereoselectivity under kinetic control. In contrast, anion reactions at higher temperature (0 °C) gave adducts with high diastereoselectivity but only with aromatic aldehydes. Under these conditions the reactions were under thermodynamic control. Thus, in attempting to rationalize the stereochemical outcome of these reactions only the diastereomeric alkoxides **16** and **17** need to be considered. These metal alkoxides can each chelate to either the axial or equatorial sulfoxide, and the two sets of conformations are shown in Scheme 3.

In the parent X-ray crystal structure of dithiane dioxide[22] and in the X-rays shown above, it was noted that the axial sulfoxide was bent quite considerably toward the equatorial sulfoxide; the O1−S1−S2 angle was 81° and the O1−S2 distance was only marginally greater than S1−S2 (Scheme 4). Presumably, conformational changes of the six-membered ring occur to allow more favorable interactions between the sulfoxide groups.[40] It was also thought that such electrostatic interactions were responsible for the *trans* dioxide being thermodynamically more stable than the *cis* diastereoisomer where such electrostatic interactions are not possible (Scheme 4).

Each of the four conformations of the metal alkoxides (Scheme 3) retain this electrostatic interaction, but alkoxide conformations $\mathbf{16_A}$ and $\mathbf{17_A}$ possess an additional electrostatic interaction from the alkoxide to the equatorial sulfoxide. Of these two alkoxides, $\mathbf{16_A}$ suffers from electronic repulsions between the lone pairs of the sulfinyl oxygen and the π-system of the aromatic ring, so diastereoisomer $\mathbf{17_A}$ is favored. As aliphatic aldehydes reacted with poor diastereoselectivity under the same equilibrating conditions, it is assumed that electronic rather than steric repulsions between the sulfinyl oxygen and the aldehyde substituent are responsible for controlling the outcome of the reaction. The X-ray crystal structure of the major diastereoisomer **7a** does indeed mirror the more stable conformation $\mathbf{17_A}$.

The low selectivity observed with 2,6-disubstituted aromatic aldehydes could simply be due to the increased rate of elimination relative to equilibration as a result of the extra steric hindrance of such substrates. Thus, the ratios observed are preequilibrium ratios; the true equilibrium ratios are never obtained.

Conclusion

We have demonstrated that *trans*-1,3-dithiane 1,3-dioxide undergoes highly selective addition reactions with aromatic aldehydes but only when reactions are under equilibrium control. Such conditions are achieved using the sodium anion of *trans*-1,3-dithiane 1,3-dioxide and conducting reactions at 0 °C. Other metals either gave poorer selectivity or caused decomposition of *trans*-1,3-dithiane 1,3-dioxide. Reactions with ketones are limited to those without α-branching indicating that the equilibrium for the reactions was sensitive to steric factors. A model that accounts for the high diastereoselectivity observed with aromatic aldehydes is presented. The key components of this model include preferential complexation of the metal alkoxide with the axial sulfoxide, and in this conformation, electronic repulsion of the aromatic ring with the equatorial sulfoxide disfavors one of the two possible diastereoisomers.

Experimental Section

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. Proton and ^{13}C NMR spectra were recorded on a JEOL 270 MHz or a Bruker 250 MHz instrument. *J* values are given in Hz. Infrared spectra were measured on a Perkin-Elmer 1310 spectrophotometer. THF was distilled from sodium immediately prior to use. Pyridine was distilled from potassium hydroxide and then stored over molecular sieves and under nitrogen until required. DMF was distilled from molecular sieves and then stored over more molecular sieves and under nitrogen until required. Dichloromethane was distilled from CaH_2 and stored over molecular sieves and under nitrogen until required. All anion reactions were performed in flame-dried apparatus under a nitrogen atmosphere. All aldehydes were recrystallized or distilled from $CaCl_2$ and stored under nitrogen until required. 3,4-Bis[(*tert*-butyldimethylsilyl)oxy]benzaldehyde was prepared as previously described.[41]

(40) It is well known that π-rich systems (e.g., benzene) coordinate to the sulfur atom of sulfoxides: Ledaal, T. *Tetrahedron Lett.* **1968**, 1683−1688. We believe that a neighboring sulfinyl oxygen (also a π-rich system) coordinates similarly to the sulfur atom of the sulfoxide.

(41) Cardona, L.; Fernandez, I.; Garcia, B.; Pedro, J. R. *Tetrahedron* **1986**, *42*, 2725−2730.

General Method for Monitoring *n*-BuLi Reactions. Dithiane dioxide (**4**) (0.05 g, 0.328 mmol) was dissolved in pyridine (2.5 mL) with warming and then diluted with THF (1.5 mL) before cooling to 0 °C, under nitrogen. A solution of *n*-BuLi (1.6 M in hexanes) was then added dropwise until permanent appearance of a yellow-orange color. An excess of aldehyde (typically 0.5 mmol) was then added at the required reaction temperature and stirring continued. Aliquots (0.5 mL) were removed by syringe and quenched by addition to a 9:1 mixture (1 mL) of ethanol/ aqueous HCl (2 M, 0.1 mL, 0.2 mmol) at the reaction temperature. The solvents were then evaporated, the residue taken up in aqueous ammonia solution (2 M, 1.5 mL), and the mixture concentrated under reduced pressure. The residue was dissolved in 50% ethanol/water (1 mL) and the solution either analyzed by HPLC or filtered through a short pad of silica gel, eluting with acetone, and analyzed by NMR after evaporation of the acetone.

For monitoring NaHMDS reactions *n*-BuLi was replaced with a solution of NaHMDS in THF (0.394 mmol).

General Procedure for Carrying out *n*-BuLi Reactions. Dithiane dioxide (**4**) (0.328 mmol) was dissolved in pyridine (2.5 mL) with warming and then diluted with THF (1.5 mL) before cooling to 0 °C under nitrogen. A solution of *n*-BuLi (1.6 M in hexanes) was then added dropwise at that temperature until permanent appearance of a yellow-orange color. An excess of aldehyde (typically 0.5 mmol) was then added at the required reaction temperature (0 or −78 °C) and stirring continued. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (10 mL) and aqueous HCl (2 M, 0.82 mL, 1.64 mmol) at the same temperature as the reaction. The solvents were then evaporated and the residue purified by chromatography on silica gel.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-Butyl-1,3-dioxo-1,3-dithiane-2-methanol (7b). With valeraldehyde (0.05 mL, 0.48 mmol) stirring was continued for 10 min at 0 °C. Chromatography on silica gel with 80% acetone/petrol as the eluant afforded **7b** (0.025 g, 32%). An analytical sample was recrystallized from toluene: mp 150-152 °C; R_f (acetone) 0.25; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1020 (SO); δ_H (DMSO) 5.40 (1H, d, *J* 6.6), 4.26 (1H, m), 3.83 (1H, d, *J* 4.4), 3.51 (1H, m), 3.00 (3H, m), 2.60−2.15 (2H, m), 1.68 (2H, q, *J* 1.7), 1.50−1.20 (4H, m), 0.88 (3H, t, *J* 7.1); δ_C (DMSO) 78.1, 66.5, 51.9, 45.8, 35.6, 27.9, 22.4, 15.6, 14.4; m/z (EI) 238 (M$^+$, 100), 122 (80), 103 (40), 85 (30), 73 (35). Found: C, 44.7; H, 7.70. Requires for $C_9H_{18}O_3S_2$: C, 45.1; H, 7.60.

1-(*RS*)-3-(*RS*)-α-(*SR*)-α-Butyl-1,3-dioxo-1,3-dithiane-2-methanol (6b). With valeraldehyde (0.05 mL, 0.48 mmol) stirring was continued for 10 min at −78 °C. Chromatography on silica gel with 80% acetone/petrol as the eluant afforded **6b** (0.031 g, 40%). An analytical sample was recrystallized from chlorobenzene: mp 111−112 °C; R_f (acetone) 0.35; υ_{max} (Nujol)/cm^{-1} 3300 (OH), 990 (SO); δ_H (DMSO) 5.50 (1H, d, *J* 5.5), 4.29 (1H, m), 4.04 (1H, d, *J* 3.9), 3.47 (1H, ddd, *J* 12.3, 6.2 and 4.0), 3.06 (3H, m), 2.50−2.20 (2H, m), 1.77 (2H, q, *J* 7.0), 1.52 (1H, m), 1.30 (3H, m), 0.88 (3H, t, *J* 7.1); δ_C (DMSO) 77.2, 67.0, 50.7, 45.8, 34.0, 28.5, 22.4, 15.3, 14.4; m/z (EI) 238 (M$^+$, 100), 172 (50), 122 (90), 73 (50). Found: C, 45.5; H, 7.70. Requires for $C_9H_{18}O_3S_2$: C, 45.4; H, 7.60.

1-(*RS*)-3-(*RS*)-α-(*SR*)-α-(1-Methylethyl)-1,3-dioxo-1,3-dithiane-2-methanol (7c) and 1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(1-Methylethyl)-1,3-dioxo-1,3-dithiane-2-methanol (6c). With isobutyraldehyde (0.05 mL, 0.55 mmol) stirring was continued for 2 min at −78 °C. Chromatography on silica gel with 80% acetone/petrol as the eluant afforded **7c** (0.026 g, 35%). An analytical sample was recrystallized from toluene: mp 135 °C; R_f (acetone) 0.35; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1000 (SO); δ_H (DMSO) 5.39 (1H, d, *J* 5.3), 4.20 (1H, d, *J* 3.7), 4.07 (1H, ddd, *J* 6.7, 5.2 and 3.7), 3.49 (1H, ddd, *J* 12.7, 6.7 and 4.5), 3.20−3.00 (3H, m), 2.37 (2H, m), 2.03 (1H, octet, *J* 6.7), 0.96 (3H, d, *J* 6.8), 0.93 (3H, d, *J* 6.8); δ_C (DMSO) 76.1, 71.3, 51.6, 45.6, 32.5, 19.9, 18.2, 15.6; m/z (EI) 224 (M$^+$, 7), 123 (20), 119 (25). Found: C, 42.9; H, 7.40. Requires for $C_8H_{16}O_3S_2$: C, 42.8; H, 7.20.

Continued elution of the column gave **6c** (0.026 g, 35%). An analytical sample was recrystallized from chlorobenzene: mp 177−178 °C; R_f (acetone) 0.25; υ_{max} (Nujol)/cm^{-1} 3230 (OH), 1010 (SO); δ_H (DMSO) 5.44 (1H, d, *J* 6.8), 3.97 (2H, m), 3.50 (1H, ddd, *J* 12.0, 5.2 and 2.2), 3.15−3.00 (3H, m), 2.53 (1H, m), 2.22 (1H, m), 2.04 (1H, octet, *J* 6.6), 0.95 (3H, d, *J* 6.6), 0.88 (3H, d, *J* 6.6); δ_C (DMSO) 73.7, 72.0, 48.6, 45.5, 33.0, 19.7, 18.3, 15.1; m/z (EI) 224 (M$^+$, 3), 181 (10), 123 (25). Found: C, 42.9; H, 7.40. Requires for $C_8H_{16}O_3S_2$: C, 42.8; H, 7.20.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(1,1-Dimethylethyl)-1,3-dioxo-1,3-dithiane-2-methanol (7d). With pivalaldehyde (0.05 mL, 0.46 mmol) stirring was continued for 60 min at 0 °C. Chromatography on silica gel with 80% acetone/petrol as the eluant afforded **7d** (0.053 g, 68%). An analytical sample was recrystallized from CCl_4/EtOAc: mp 188−190 °C; R_f (acetone) 0.30; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1020 (SO); δ_H (DMSO) 5.76 (1H, d, *J* 6.2), 4.02 (1H, d, *J* 6.2), 3.95 (1H, s), 3.57 (1H, dm, *J* 13.0), 3.18 (1H, ddd, *J* 13.0, 13.0 and 3.0), 3.05 (1H, ddd, *J* 14.0, 14.0 and 2.5), 2.91 (1H, dm, *J* 14.0), 2.60 (1H, m), 2.22 (1H, dm), 0.89 (9H, s); δ_C (DMSO) 75.8, 71.2, 52.6, 44.9, 35.7, 26.0, 15.5; m/z (CI) 239 ((M + 1)$^+$, 50), 153 (60), 92 (100), 87 (60). Found: C, 45.4; H, 7.90. Requires for $C_9H_{18}O_3S_2$: C, 45.4; H, 7.50.

1-(*RS*)-3-(*RS*)-α-(*SR*)-α-(1,1-Dimethylethyl)-1,3-dioxo-1,3-dithiane-2-methanol, (6d). With pivalaldehyde (0.05 mL, 0.46 mmol) stirring was continued for 40 min at −78 °C. Chromatography on silica gel with 80% acetone/petrol as the eluant afforded **6d** (0.022 g, 28%). An analytical sample was recrystallized from toluene: mp 157−160 °C; R_f (acetone) 0.35; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1020 (SO); δ_H ($CDCl_3$) 4.28 (1H, d, *J* 2.0), 3.96 (1H, br.s), 3.52 (1H, ddd, *J* 14.1, 11.4 and 4.9), 3.37 (1H, ddd, *J* 13.4, 7.9 and 4.6), 3.25 (1H, ddd, *J* 13.2, 8.3 and 4.4), 3.08 (1H, ddd, *J* 14.1, 4.0 and 4.0), 2.67 (1H, m), 2.42 (1H, m), 1.07 (9H, s); δ_C (DMSO) 75.2, 73.7, 50.3, 48.7, 40.3, 30.0, 19.1; m/z (EI) 238 (M$^+$, 100), 181 (40), 122 (40). Found: C, 45.4; H, 7.90. Requires for $C_9H_{18}O_3S_2$: C, 45.4; H, 7.60.

General Method for Carrying out NaHMDS Reactions with Aromatic Aldehydes. Dithiane dioxide **4** (0.657 mmol) was dissolved in pyridine (5 mL) with warming and then diluted with THF (3 mL) before cooling to 0 °C, under nitrogen. To this was added a 1.0 M solution of NaHMDS in THF (0.99 mmol). Stirring was continued at 0 °C for 0.5 h. An excess of aldehyde (0.98 mmol) was then added in one portion at the required reaction temperature and stirring continued for the required time. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (15 mL) and aqueous HCl (2 M, 1.6 mL, 3.2 mmol) at 0 °C. The solvents were then evaporated and the residue purified.

1-(*RS*)-3-(*RS*)-α-(*RS*)-1,3-Dioxo-α-phenyl-1,3-dithiane-2-methanol (7a). Reaction with benzaldehyde (0.1 mL, 0.98 mmol) at 0 °C for 0.5 h. After workup the solvents were evaporated under vacuum and the resulting white solid recrystallized from ethanol to give **7a** (0.13 g, 77%). The mother liquor was evaporated to dryness. Chromatography on silica gel with acetone as the eluant afforded more **7a** (0.017 g, 10%). Total yield of **7a** 0.147 g (87%): mp 187−188 °C; R_f (acetone) 0.25; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1045 and 1010 (SO); δ_H (DMSO) 7.5−7.25, 6.07 (1H, d, *J* 4.3), 5.49 (1H, br. t, *J* 4.4), 4.16 (1H, d, *J* 4.3), 3.53 (1H, ddd, *J* 12.0, 4.8 and 1.5), 3.09 (1H, ddd, *J* 12.0, 12.0 and 2.3), 3.0−2.6 (2H, m), 2.55 (1H, m), 2.22 (1H, m); δ_C (DMSO) 141.5, 128.4, 127.7, 126.7, 79.0, 67.8, 51.5, 45.9, 15.3; m/z (CI) 259 (M + 1, 10), 153 (50), 107 (100). Found: C, 51.0; H, 5.50. Requires for $C_{11}H_{14}O_3S_2$: C, 51.1; H, 5.46.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(3-Methoxyphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7e). Reaction with *m*-anisaldehyde (0.075 mL, 0.61 mmol) at 0 °C for 2.5 h. Following workup the residue was chromatographed on silica gel with acetone as the eluant to afford **7e**. The chromatographed material was recrystallized from ethanol (two crops) to give colorless needles (0.091 g, 64%): mp 202−203 °C; R_f (acetone) 0.24; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1010 (S-O); δ_H (DMSO) 7.56 (1H, m, Ar), 7.28 (2H, m, Ar), 7.11 (1H, m, Ar), 6.32 (1H, d, *J*

(42) The author has deposited atomic coordinates for **6a**, **6d**, and **7a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

5.0, OH), 5.71 (1H, dd, *J* 5.0 and 3.3), 4.42 (1H, d, *J* 3.3), 4.02 (3H, s), 3.78 (1H, dm, *J* 12.1), 3.36 (1H, dt, *J* 11.2 and 2.3), 3.19–3.03 (2H, m), 2.55 (1H, m), 2.22 (1H, m); δ_C (DMSO) 159.1, 143.0, 118.5, 112.7, 112.0, 78.7, 67.5, 54.9, 50.9, 15.0; m/z (EI) 288 (M^+, 15), 222 (15), 152 (30), 136 (100), 103 (40). Found: C, 49.7; H, 5.62. Requires for $C_{12}H_{16}O_4S_2$: C, 50.0; H, 5.59.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(4-Methoxyphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7f). Reaction with *p*-anisaldehyde (0.075 mL, 0.61 mmol) at 0 °C for 2.5 h. Following work up the residue was chromatographed on silica gel with acetone as the eluant afforded **7f**. The chromatographed material was recrystallized from ethanol (two crops) to give colorless needles (0.072 g, 72%): mp 158 °C; R_f (acetone) 0.21; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1005 (SO); δ_H (DMSO) 7.62 (2H, d, *J* 8.7), 7.20 (2H, d, *J* 8.7), 6.22 (1H, d, *J* 4.8), 5.69 (1H, dd, *J* 4.8 and 3.5), 4.35 (1H, d, *J* 3.5), 4.01 (3H, s), 3.77 (1H, dm, *J* 11.7), 3.33 (1H, dt, *J* 12.4 and 2.3), 3.22–3.01 (2H, m), 2.82 (1H, dm, *J* 15.0), 2.46 (1H, dm, *J* 15.0); δ_C (DMSO) 158.7, 133.2, 127.7, 113.6, 78.9, 67.4, 55.1, 50.8, 45.7, 15.0; m/z (CI) 271 (M − H_2O, 100), 255 (80), 238 (70). Found: C, 50.1; H, 5.67. Requires for $C_{12}H_{16}O_4S_2$: C, 50.0; H, 5.59.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(2-Methoxyphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7g). Dithiane dioxide (**4**) (0.15 g, 0.49 mmol), pyridine (7.5 mL), THF (4.5 mL), NaHMDS in THF (1.2 mL, 1.20 mmol), and *o*-anisaldehyde (0.16 g, 1.20 mmol) were used and stirred for 7.5 h at 0 °C. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (20 mL) and aqueous HCl (2 M, 2.5 mL, 4.93 mmol) at 0 °C. The solvents were then evaporated under vacuum, and the residue was taken up in aqueous ammonia solution (2 M, 20 mL). The solution was evaporated to dryness. Chromatography on silica gel with 70–100% acetone/petrol as the eluant afforded **7g** (0.216 g, 76%). An analytical sample was recrystallized from ethanol: mp 167 °C; R_f (acetone) 0.16; υ_{max} (Nujol)/cm^{-1} 3230 (OH), 1010 (SO); δ_H (DMSO) 7.67 (1H, dd, *J* 7.5 and 1.8), 7.30 (1H, ddd, *J* 7.5, 7.5 and 1.8), 7.02 (2H, m), 5.80 (1H, d, *J* 5.8), 5.76 (1H, dd, *J* 5.8 and 3.5), 3.86 (1H, d, *J* 3.5), 3.78 (3H, s), 3.51 (1H, ddd, *J* 12.4, 5.1 and 2.2), 3.09 (1H, ddd, *J* 12.4, 12.4 and 2.3), 2.89 (2H, m), 2.51 (1H, m), 2.18 (1H, dm, *J* 15.0); δ_C (DMSO) 155.2, 128.9, 128.7, 128.1, 120.2, 110.7, 77.1, 63.0, 55.6, 50.9, 45.8, 15.1; m/z (EI) 288 (M^+, 100), 222 (35), 206 (45), 136 (60), 119 (70). Found: C, 49.9; H, 5.82. Requires for $C_{12}H_{16}O_4S_2$: C, 50.0; H, 5.59.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-[3,4-Bis[(*tert*-butyldimethylsilyl)oxy]phenyl]-1,3-dioxo-1,3-dithiane-2-methanol (7h). The dithiane dioxide (**4**) (0.311 g, 2.05 mmol), pyridine (15 mL), THF (9 mL), NaHMDS in THF (2.45 mL, 2.45 mmol), and 3,4-bis[(*tert*-butyldimethylsilyl)oxy]benzaldehyde (0.075 mL, 0.61 mmol) (0.9 g, 2.45 mmol) were used and stirred for 10 min at 0 °C. Following workup the residue was chromatographed on silica gel with 25–50% acetone/EtOAc as the eluant and afforded **7h** (0.59 g, 56%). An analytical sample was recrystallized from EtOAc: mp 141 °C; R_f (acetone) 0.58; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1010 (S-O); δ_H (DMSO) 6.98 (1H, s), 6.80 (2H, s), 5.91 (1H, d, *J* 4.4), 5.31 (1H, dd, *J* 4.4 and 4.4), 4.02 (1H, d, *J* 4.4), 3.45 (1H, dm, *J* 11.6), 3.15 (1H, dm, *J* 11.6), 2.90–2.70 (2H, m), 2.45 (1H, m), 2.13 (1H, dm, *J* 16), 0.90 (18H, s), 0.12 (12H, s); δ_C ($CDCl_3$) 147.8, 131.6, 121.3 119.0, 118.9, 78.3, 70.3, 48.6, 45.5, 25.9, 18.4, 14.0, −4.1. Found: C, 52.7; H, 8.48. Requires for $C_{23}H_{42}O_5S_2Si_2$: C, 53.2; H, 8.16.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(4-Nitrophenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7i). Dithiane dioxide (**4**) (0.15 g, 0.99 mmol), pyridine (7.5 mL), THF (4.5 mL), NaHMDS in THF (1.18 mL, 1.18 mmol), and *p*-nitrobenzaldehyde were used and stirred for 5 h at 0 °C. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (20 mL) and aqueous HCl (2 M, 2.5 mL, 4.93 mmol) at 0 °C. The solvents were then evaporated under vacuum and the residue taken up in aqueous ammonia solution (2 M, 20 mL). The solution was evaporated to dryness. Chromatography on silica gel with acetone as the eluant afforded **7i** (0.127 g, 42%). An analytical sample was recrystallized from ethanol: mp 227-230 °C; R_f (50% acetone/ethanol) 0.55; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1020 (S-O); δ_H (DMSO) 8.26 (2H, d, *J* 8.7), 7.75 (2H, d, *J* 8.7), 6.49 (1H, d, *J* 5.1), 5.60 (1H, dd, *J* 5.1 and 3.6), 4.32 (1H, d, *J* 3.7), 3.57 (1H, ddm, *J* 11.7 and 3.0), 3.10 (1H, dt, *J* 12.2 and 2.3), 3.00–2.78 (2H, m), 2.60 (1H, dm, *J* 15.0), 2.24 (1H, dm, *J* 15.0); δ_C (DMSO) 147.0, 128.1, 123.5, 78.5, 67.6, 51.4, 46.0, 15.3; m/z (CI) (M+1, 2%), 153 (100), 122 (40). Found: C, 43.4; H, 4.35; N, 4.55. Requires for $C_{11}H_{13}NO_5S_2$: C, 43.6; H, 4.32; N, 4.62.

1-(*RS*)-3-(*RS*)-α-(*RS*)-1,3-Dioxo-α-(3-pyridyl)-1,3-dithiane-2-[(trimethylsilyl)oxy]methane (7jT). Dithiane dioxide (**4**) (0.10 g, 0.657 mmol), pyridine (5 mL), THF (3 mL), NaHMDS in THF (0.8 mL, 0.8 mmol), and 3-pyridinecarboxaldehyde were used and stirred for 0.5 h at 0 °C. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (15 mL) and aqueous HCl (2 M, 1.6 mL, 3.2 mmol) at 0 °C. The solvents were then evaporated under vacuum. The mixture was suspended in pyridine (5 mL) at room temperature in a dried flask, under nitrogen. To this was added chlorotrimethylsilane (0.29 mL, 2.30 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (0.41 mL, 3.61 mmol). Stirring was continued at room temperature for 1.5 h. The reaction mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (50 mL × 2). Combined organics were washed with brine, dried ($MgSO_4$), and evaporated. Chromatography on silica gel with acetone as the eluant afforded **7jT** (0.121 g, 56%) and a mixture of **7jT** and **6jT** (0.37 g, 17%). An analytical sample of **7jT** was recrystallized from EtOAc: mp 170–171 °C; R_f (acetone) 0.18; υ_{max} (Nujol)/cm^{-1} 1025 (S-O); δ_H ($CDCl_3$) 8.64 (1H, br. s), 8.56 (1H, d, *J* 4.8), 7.87 (1H, *J* 7.9), 7.33 (1H, dd, *J* 7.9 and 4.8), 5.70 (1H, d, *J* 4.4), 3.67 (1H, dd, *J* 10 and 6.0), 3.32 (1H, d, *J* 4.4), 3.11 (1H, dt, *J* 14.0 and 3.5), 2.88 (2H, m), 2.58 (1H, m), 2.35 (1H, m), 0,13 (9H, s, 3 × CH_3); δ_C ($CDCl_3$) 149.8, 148.1, 135.9, 134.6, 123.5, 82.0, 67.9, 51.6, 46.2, 14.5, −0.16; m/z (CI) 332 (M + 1, 40), 331 (60), 314 (60), 283 (100), 193 (70), 177 (60), 73 (80). Found: C, 47.3; H, 6.47; N, 4.23. Requires for $C_{13}H_{21}NO_3S_2Si$: C, 47.1; H, 6.38; N, 4.25.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(9-Anthracenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7k). Reaction with 9-anthracenecarboxaldehyde (0.2 g, 0.971 mmol, 1.48 equiv) at 0 °C for 0.5 h. Following workup the residue was chromatographed on silica gel with acetone as the eluant to afford **7k** as a yellow solid (219 mg, 93%). An analytical sample was recrystallized from ethanol: mp 126 °C dec; υ_{max} (KBr)/cm^{-1} 3370 (OH), 1025 (SO); δ_H (DMSO) 8.80 (2H, br s), 8.54 (1H, s), 8.08 (2H, br d, *J* 7.0), 7.46–7.56 (4H, m), 7.04 (1H, d, *J* 5.0), 4.38 (1H, d, *J* 5.0), 3.40–3.46 (1H, m), 2.96–3.05 (3H, m), 2.57–2.65 (1H, m), 2.17–2.23 (1H, m); δ_C (DMSO, 343 K) 134.0, 131.3, 130.8, 129.3, 128.5, 127.8, 126.2, 125.0, 124.2, 78.9, 65.1, 50.1, 44.6, 13.8; m/z (EI) 358 (M^+, 14), 320 (68), 182 (92), 139 (100), 111 (80), 98 (93), 55 (83). Found: 340.05989. Requires for $C_{19}H_{18}O_3S_2-H_2O$: 340.05980.

1-(*RS*)-3-(*RS*)-α-(*RS/SR*)-α-(2,6-Dimethoxyphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (6/7l). Reaction with 2,6-dimethoxybenzaldehyde (0.13 g, 0.8 mmol) at 0 °C for 1 h. Following workup the residue was chromatographed on silica gel with acetone as the eluant afforded **6/7l** (0.139 g, 66%) as a 1:1.3 ratio of diastereomers. An analytical sample was recrystallized from acetone/petrol mp 142–145 °C; R_f (acetone) 0.33; υ_{max} (Nujol)/cm^{-1} 3530 (OH), 1040 (SO); δ_H (DMSO) 7.29[b] (1H, t, *J* 8.5), 7.26[a] (1H, t, *J* 8.5), 6.68[b] (2H, d, *J* 8.5), 6.67[a] (2H, d, *J* 8.5), 5.99[b] (1H, dd, *J* 8.1 and 5.7), 5.85[a] (1H, dd, *J* 9.4 and 7.0), 5.12[a] (1H, d, *J* 9.4), 4.81[b] (1H, d, *J* 5.7), 4.44[b] (1H, d, *J* 8.1). 4.08[a] (1H, d, *J* 7.0), 3.79[a] (3H, s), 3.78[b] (3H, s), 3.52 (1H, m), 3.40–2.95 (3H, m), 2.52–2.12 (2H, m); δ_C (DMSO) 158.9[b], 158.7[a], 130.8[a], 130.3[b], 116.1[a], 115.6[b], 105.22[a], 105.17[b], 77.4[b], 75.9[a], 64.2[b], 62.4[a], 56.5, 49.4[a], 49.2[b], 45.7[a], 44.7[b], 15.1[a], 14.7[b]; m/z (EI) 318 (M^+, 10), 180 (30), 167 (100), 151 (50), 107 (40), 41 (35). [a]Major diastereoisomer. [b]Minor diastereoisomer Found: C, 48.8; H, 5.76. Requires for $C_{13}H_{18}O_5S_2$: C, 49.0; H, 5.70.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(2,4,6-Trimethylphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7m). Dithiane dioxide (**4**) (0.25 g, 1.64 mmol), pyridine (12.5 mL), THF (7.5 mL), NaHMDS in THF (1.97 mL, 1.97 mmol), and mesitaldehyde (0.36 mL, 2.46 mmol) were used and stirred for 0.5 h at 0 °C. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (40 mL) and aqueous HCl (2 M, 4.1 mL, 8.2 mmol) at 0 °C. The solvents were then

evaporated under vacuum. The residue was partitioned between water and CH_2Cl_2, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (50 mL × 2). Combined organic extracts were washed with brine, dried ($MgSO_4$), and evaporated. Chromatography on silica gel with 25–50% acetone/EtOAc as the eluant afforded **7m** (0.108 g, 22%). An analytical sample was recrystallized from CH_2Cl_2/$^iPr_2O$: mp 172 °C; R_f (acetone) 0.37; υ_{max} (Nujol)/cm^{-1} 3220 (OH), 1000 (SO); δ_H (DMSO) 6.76 (2H, s), 6.00 (1H, d, *J* 5.1), 5.72 (1H, dd, *J* 7.3 and 5.1), 4.02 (1H, d, *J* 7.3), 3.37 (1H, m), 3.06–2.92 (3H, m), 2.55–2.25 (8H, m), 2.13 (3H, s); δ_C (DMSO) 136.5, 136.0, 134.3, 129.6, 77.1, 65.5, 50.3, 44.3, 20.8, 20.4, 14.4; m/z (CI) 283 ((M − H_2O) + 1, 1), 153 (70), 149 (100).

1-(*RS*)-3-(*RS*)-α-(*SR*)-α-(2,4,6-Trimethylphenyl)-1,3-dioxo-1,3-dithiane-2-methanol (6m). Dithiane dioxide (**4**) (0.4 g, 2.63 mmol) was dissolved in pyridine (20 mL) with warming and then diluted with THF (12 mL) before being cooled to 0 °C, under nitrogen. To this was added a 1.0 M solution of LiHMDS in THF (3.15 mL, 3.15 mmol). Stirring was continued at 0 °C for 0.5 h. The mixture was cooled to −78 °C. Mesitaldehyde (0.46 mL, 3.15 mmol) was then added in one portion. Stirring was continued for 0.5 h at −78 °C. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (66 mL) and aqueous HCl (2 M, 6.6 mL, 13.1 mmol) at −78 °C. The solvents were then evaporated under vacuum. Chromatography on silica gel with 25–50% acetone/EtOAc as the eluant afforded **6m** (0.068 g, 9%). An analytical sample was recrystallized from EtOAc: mp 167 °C; R_f (acetone) 0.54; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1030 (SO); δ_H (DMSO) 6.75 (2H, s), 5.80 (1H, dd, *J* 8.0 and 3.6), 5.37 (1H, d, *J* 3.6), 4.35 (1H, d, *J* 8.0), 3.47 (1H, m), 3.18 (1H, m), 3.01 (2H, m), 2.42–2.10 (11H, m); δ_C (DMSO) 136.9, 136.8, 132.9, 129.6, 75.4, 68.6, 49.3, 44.9, 20.6, 20.4, 14.5; m/z (EI) 300 (M$^+$, 1), 147 (100), 119 (50), 41 (40). Found: C, 55.7; H, 6.69. Requires for $C_{14}H_{20}O_3S_2$: C, 56.0; H, 6.71.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(2,6-Difluorophenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7n), 1-(*RS*)-3-(*RS*)-α-(*SR*)-α-(2,6-Difluorophenyl)-1,3-dioxo-1,3-dithiane-2-methanol (6n), and 1-(*RS*)-3-(*RS*)-α-(2,6-Difluorophenyl)-2-methylene-1,3-dithiane 1,3-Dioxide (8n). Dithiane dioxide (**4**) (0.25 g, 1.64 mmol), pyridine (12.5 mL), THF (7.5 mL), NaHMDS in THF (1.97 mL, 1.97 mmol), and 2,6-difluorobenzaldehyde (0.21 mL, 1.97 mmol) were used and stirred for 1.0 min at 0 °C. Following workup, chromatography on silica gel with 25–60% acetone/petrol as the eluant afforded

(**7n**) (0.123 g, 25%). An analytical sample was recrystallized from ethanol: mp 182-6 °C; R_f (acetone) 0.33; υ_{max} (Nujol)/cm^{-1} 3400 (OH), 1010 (SO); δ_H (DMSO) 7.36 (1H, m), 7.04 (2H, t, *J* 8.3), 6.60 (1H, d, *J* 6.8), 5.70 (1H, dd, *J* 9.4 and 6.8), 4.28 (1H, d, *J* 9.4), 3.40 (1H, m), 3.30–3.00 (3H, m), 2.60–2.15 (2H, m); δ_C (DMSO) 161.2, 130.7, 118.2, 112.1, 76.8, 61.0, 51.1, 44.7, 15.1; m/z (CI) 294 (M$^+$, 30), 152 (100), 140 (95), 74 (30), 41 (30). Found: C, 44.7; H, 4.04. Requires for $C_{11}H_{12}F_2O_3S_2$: C, 44.9; H, 4.11.

6n (0.17 g, 35%). An analytical sample was recrystallized from ethanol: mp 181–3 °C; R_f (acetone) 0.41; υ_{max} (Nujol)/cm^{-1} 3240 (OH), 995 (SO); δ_H (DMSO) 7.45 (1H, m), 7.12 (2H, t, *J* 8.3), 6.20 (1H, d, *J* 6.0), 5.87 (1H, dd, *J* 7.5 and 6.0), 4.50 (1H, d, *J* 7.5) 3.50 (1H, m), 3.25 (1H, m), 2.40 (2H, m); δ_C (DMSO) 161.0, 131.4, 116.8, 112.4, 74.8, 62.0, 48.2, 45.4, 14.6; m/z (CI) 294 (M$^+$, 40), 276 (30), 153 (100), 141 (90), 74 (40), 63 (35), 41 (45). Found: C, 44.8; H, 4.09. Requires for $C_{11}H_{12}F_2O_3S_2$: C, 44.9; H, 4.11.

8n (0.101 g, 22%). An analytical sample was recrystallized from EtOAc/petrol: mp 139 °C; R_f (50% acetone/petrol) 0.32; υ_{max} (Nujol)/cm^{-1} 1040 (SO); δ_H ($CDCl_3$) 7.50–7.30 (2H, m), 7.00 (2H, t, *J* 7.5), 3.75 (1H, m), 3.38–2.88 (4H, m), 2.45 (1H, m); δ_C ($CDCl_3$) 159.6, 151.2, 132.1, 122.5, 111.8, 110.1, 56.2, 48.3, 15.1; m/z (CI) 276 (M$^+$, 100), 228 (90), 170 (35), 41 (20). Found: C, 47.8; H, 3.52. Requires for $C_{11}H_{10}F_2O_2S_2$: C, 47.8; H, 3.65.

1-(*RS*)-3-(*RS*)-α-(*RS*)-α-(2,4-Difluorophenyl)-1,3-dioxo-1,3-dithiane-2-methanol (7o) and 1-(*RS*)-3-(*RS*)-α-(2,4-Difluorophenyl)-2-methylene-1,3-dithiane 1,3-Dioxide (8o). Dithiane dioxide (**4**) (0.15 g, 0.985 mmol), pyridine (7.5 mL), THF (4.5 mL), NaHMDS in THF (1.18 mL, 1.18 mmol), and 2,4-difluorobenzaldehyde (0.13 mL, 1.18 mmol) were used and stirred for 18 min at 0 °C. Following workup, chromatography on silica gel with 25–100% acetone/petrol as the eluant afforded

7o (0.099 g, 34%). An analytical sample was recrystallized from ethanol: mp 198-208 °C; R_f (acetone) 0.33; υ_{max} (Nujol)/cm^{-1} 3260 (OH), 1000 (S-O); δ_H (DMSO) 7.73 (1H, m), 7.15 (1H, m), 6.25 (1H, d, *J* 5.6), 5.68 (1H, dd, *J* 5.6 and 4.5), 4.03 (1H, d, *J* 4.5), 3.50 (1H, m), 3.20–2.85 (3H, m), 2.55 (1H, m), 2.23 (1H, m); δ_C (DMSO) 162.6, 158.7, 130.8, 125.4 , 111.8 , 104.1, 78.0, 62.5, 51.6, 46.0, 15.5; m/z (CI) 294 (M$^+$, 15), 276 (15), 261 (10), 152 (100), 140 (70). Found: C, 44.8; H, 4.07. Requires for $C_{11}H_{12}F_2O_3S_2$: C, 44.9; H, 4.11.

8o (0.112 g, 41%). An analytical sample was recrystallized from EtOAc/petrol: mp 190–192 °C; R_f (acetone) 0.64; υ_{max} (Nujol)/cm^{-1} 1040 (SO); δ_H ($CDCl_3$) 7.50–7.30 (2H, m), 7.07–6.86 (2H, m), 3.78 (1H, m), 3.35–2.80 (4H, m), 2.45 (1H, m); δ_C ($CDCl_3$) 164.0, 160.0, 148.5, 132.1, 127.8, 116.4, 112.2, 104.7, 56.0, 48.6, 15.0; m/z (CI) 277 (M + 1, 30), 228 (80), 170 (100), 125 (80). Found: C, 47.7; H, 3.56. Requires for $C_{11}H_{10}F_2O_2S_2$: C, 47.8; H, 3.65.

Zinc Anion Reaction: 1-(*RS*)-3-(*RS*)-α-(*SR*)-1,3-Dioxo-α-phenyl-1,3-dithiane-2-methanol (6a). Dithiane dioxide (**4**) (0.2 g, 1.31 mmol) was dissolved in pyridine (10 mL) with warming and then diluted with THF (6 mL) before cooling to 0 °C, under nitrogen. To this was added a 1.0 M solution of LiHMDS in THF (1.6 mL, 1.6 mmol). Stirring was continued at 0 °C for 0.5 h. A 1.0 M solution of $ZnCl_2$ in THF (2.0 mL, 2.0 mmol), was then added and stirring continued at 0 °C for a further 0.5 h. The mixture was then cooled to −78 °C and benzaldehyde (0.20 mL, 2.0 mmol) added. Stirring was continued at −78 °C for 45 min. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol (35 mL) and aqueous HCl (2 M, 3.3 mL, 6.55 mmol) at −78 °C. The solvents were then evaporated under vacuum. Chromatography on silica gel with 50–100% acetone/petrol as the eluant afforded **6a** (0.114 g, 34%). An analytical sample was recrystallized from ethanol: mp 177-178 °C; R_f (acetone) 0.45; υ_{max} (Nujol)/cm^{-1} 3180 (OH), 975 (S-O); δ_H (DMSO) 7.50–7.25 (5H, m), 6.19 (1H, d, *J* 4.0), 5.47 (1H, dd, *J* 4.7 and 4.4), 4.43 (1H, *J* 4.7), 3.46 (1H, m), 3.25 (1H, m), 3.10 (2H, m), 2.35 (2H, m); δ_C (DMSO) 141.4, 128.2, 127.8, 126.9, 76.0, 67.8, 48.4, 14.7; m/z (CI) 259 (M + 1, 2), 153 (85), 107 (100), 105 (60). Found: C, 50.9; H, 5.45. Requires for $C_{11}H_{14}O_3S_2$: C, 51.1; H, 5.46.

Monitoring Reactions of 14 and Synthesis of the Pivaldehyde Adduct 15. Dithiolane dioxide (**14**) (0.25 g, 1.34 mmol) was dissolved in the appropriate solvent (8 mL). To this was added a solution of base (1.5 mmol), and stirring was continued at 0 °C for 0.5 h. An excess of aldehyde (typically 1.6 mmol) was then added at the required reaction temperature and stirring continued. Samples (0.2 mL) were removed by syringe and quenched by addition to ethanol (1 mL) and aqueous HCl (2 M, 0.1 mL, 0.2 mmol) at the reaction temperature and then neutralized with $NaHCO_3$. The solvents were then evaporated, and the residue was taken up in CH_2Cl_2 and filtered through a plug of silica gel and analyzed by NMR after evaporation. On a synthetic scale, the same procedure as that used for the preparation of **6d** was followed and **15** was isolated as a single isomer: mp 140 °C (petrol:EtOAc); R_f [DCM:*i*-PrOH (95:5)] 0.63; υ_{max} (Nujol)/cm^{-1} 3290 (OH), δ_H ($CDCl_3$) 8.03 (1H, d, *J* 7), 7.94 (1H, d, *J* 7), 7.87 (1H, dt, *J* 7 and 1.3), 7.75 (1H, dt, *J* 7 and *J* 1.3), 4.48 (1H, d, *J* 4.4), 4.04 (1H, d, *J* 4.4) 3.5 (1H, bs), 1.23 (9H, s); m/z (70e V, E. I.) 215 (M$^+$-57, 100), 156 (65), 57 (95, Me_3C^+), (*i*-Bu, CI) 273 ([M + 1]$^+$, 50) 215 (30), 187 (100), 87 (100). Found: C, 52.6; H, 5.85. Requires for $C_{12}H_{16}O_3S_2$; C, 52.9; H, 5.92.

General Method for Carrying out LiHMDS Reactions with Ketones. Dithiane dioxide (**4**) (1 mmol) was dissolved in pyridine (7.5 mL) with warming and then diluted with THF (5 mL) before cooling to 0 °C, under nitrogen. To this was added a 1.0 M solution of LiHMDS in THF (1.2 mmol). Stirring was continued at 0 °C for 30 min. An excess of ketone (1.5 mmol) was then added in one portion and stirring continued for the 30 min. The reaction mixture was then transferred by syringe into a rapidly stirred mixture of ethanol

(22 mL) and aqueous HCl (2 M, 2.4 mL, 4.8 mmol) at 0 °C. The solvents were then evaporated, and the residue was purified by column chromatography.

1-(*RS*)-3-(*RS*)-α,α-Dimethyl-1,3-dioxo-1,3-dithiane-2-methanol (10). Using acetone (87 mg, 100 μL, 1.5 mmol) and following workup, the residue was preadsorbed onto silica and columned on silica, eluting with acetone to afford the desired alcohol as a white solid: 158.8 mg (77%); mp 162 °C dec (acetone/ethyl acetate); R_f (acetone) 0.27; υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1045 and 1010 (S-O); δ_H (DMSO) 1.44 (3H, s); 1.49 (3H, s); 2.20–2.30 (1H, m); 2.40–2.60 (1H, m); 2.92 (1H, dt, *J* 3.5, 14.0), 3.08 (1H, dt, *J* 15, 3.0); 3.15 (1H, td, *J* 2.5, 12.4); 3.45–3.55 (1H, m); 3.82 (1H, s); 5.35 (1H, s); δ_C (DMSO) 15.44, 27.11, 31.33, 45.41, 51.11, 71.84, 80.08; m/z (CI) 211 (M + 1, 20); HRMS (found 210.03935, $C_7H_{14}O_3S_2$ requires 210.03844).

1-(*RS*)-3-(*RS*)-α-(*RS*/*SR*)-α-Methyl-α-ethyl-1,3-dioxo-1,3-dithiane-2-methanol (11). Using butanone (108 mg, 130 μL, 1.5 mmol) and following workup, the residue was preadsorbed onto silica and columned on silica, eluting with ethyl acetate/acetone 1/1 → acetone to afford the desired *alcohols* as white solids. First diastereomer from column 107.8 mg (49%) had R_f (ethyl acetate/acetone 1/1) 0.24: υ_{max} (Nujol)/cm^{-1} 3220 (OH), 1045 and 1010 (SO); δ_H (DMSO) 0.86 (3H, t *J* 7.4), 1.37 (3H, s), 1.67 (1H, dq, *J* 7 and 14), 1.90 (1H, dq, *J* 7 and 14), 2.14–2.27 (1H, m), 2.35–2.53 (1H, m), 2.93 (1H, dt, *J* 3.5, 14), 3.04 (1H, dt, *J* 3.6, 14), 3.16 (1H, dt, *J* 3, 12), 3.41–3.50 (1H, m), 3.87 (1H, s), 5.03 (1H, s); δ_C (DMSO) 7.46, 15.21, 26.76, 31.95, 45.34 50.76, 74.27, 79.33; m/z (CI) 225 (M + 1, 16). Found: C, 42.4; H, 7.02. Requires for $C_8H_{16}O_3S_2$: C, 42.5; H, 7.07.

Second diastereomer from column, 39.4 mg (18%), had R_f (ethyl acetate/acetone 1/1) 0.16: υ_{max} (Nujol)/cm^{-1} 3200 (OH), 1045 and 1010 (SO); δ_H (DMSO) 0.88 (3H, t *J* 7.3), 1.46 (3H, s), 1.72 (1H, dq, *J* 7 and14), 1.97 (1H, dq, *J* 7 and 14), 2.19–2.30 (1H, m), 2.43–2.60 (1H, m), 2.95 (1H, dt, *J* 3.4, 14.3), 3.2 (1H, m), 3.44–3.54 (1H, m), 3.94 (1H, s), 5.1 (1H, s); m/z (CI) 225 (M + 1, 12).

1-(*RS*)-3-(*RS*)-α-Cyclohexyl-1,3-dioxo-1,3-dithiane-2-methanol (12). Using cyclohexanone (147 mg, 160 μL, 1.5 mmol) and following workup, the residue was preadsorbed onto silica and columned on silica, eluting with ethyl acetate/acetone 1/1 → acetone to afford the desired *alcohol* as a white solid, 205.8 mg, (83%): R_f (acetone) 0.35; υ_{max} (Nujol)/cm^{-1} 3250 (OH), 1040 and 1010 (SO); δ_H ($CDCl_3$) 1.3–1.4 (1H, m), 1.6–2.3 (9H, m), 2.4–2.55 (1H, m), 2.67–2.85 (1H, m), 2.92–3.04 (1H, m), 3.18–3.35 (2H, m), 3.35 (1H, s), 3.62–3.73 (1H, m), 3.99 (1H, s); δ_C ($CDCl_3$) 12.45, 21.01, 21.47, 25.23, 36.03, 36.33, 43.49, 47.52, 75.38, 80.37; m/z (CI) 251 (M + 1, 10). Found: C, 48.2; H, 7.57. Requires for $C_{10}H_{18}O_3S_2$: C, 48.0; H, 7.25.

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