

Titanocene Dichloride as a Convenient Catalyst for the Diastereoselective Oxidation of 2-Substituted 1,3-Dithianes and 1,3-Dithiolanes

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Dedicated to the memory of Professor Guido Sodano, deceased on June 7th, 2001

Abstract: Cp₂TiCl₂ is an efficient catalyst for the diastereoselective mono-oxidation of 2-substituted 1,3-dithianes and 1,3-dithiolanes by *tert*-butyl hydroperoxide; comparable stereoselectivities and better yields than Ti(*i*-PrO)₄ were obtained. Activities are similar, provided activated 4Å molecular sieves are present in the titanocene-promoted process. Furthermore, Cp₂TiCl₂ is a more moisture stable compound than Ti(*i*-PrO)₄ and therefore can be used in catalytic amounts of 1 mol%.

Key words: diastereoselectivity, oxidations, metallocenes, sulfoxides, titanium

The d⁰ transition metal/alkyl hydroperoxide system has been extensively used for the oxidation of a number of organic compounds, in particular alkenes and thioethers.¹ In several instances, fairly good diastereoselectivities can be obtained in the oxidation of allylic alcohols² and thioethers³ containing a stereogenic center. The level of the stereoselectivity, however, is dependent on the metal catalyst and the substrate structure.

Ti(IV) alkoxides are commonly employed as catalysts in the diastereo-^{2b,4} and enantioselective⁵ epoxidation of allylic alcohols as well as in the enantioselective oxidation of thioethers.⁶

Surprisingly, cyclopentadienyl Ti(IV) compounds, despite their great availability and wide employment as catalysts in many homogeneous processes,⁷ have been scarcely used in these oxidation reactions.⁸

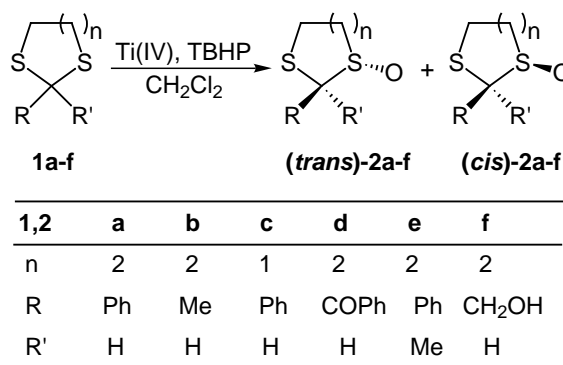
We have recently shown the applicability of titanocenes such as Cp₂TiCl₂, CpTiCl₃ and bis(cyclopentadienyl)titanium (IV) bis(trifluoromethanesulfonate) [Cp₂Ti(OTf)₂] in the diastereoselective epoxidation of allylic⁹ and bishomoallylic¹⁰ alcohols and in the enantioselective sulfoxidation¹¹ using *tert*-butyl hydroperoxide (TBHP) as oxidant; the catalytic activity is markedly enhanced in the presence of activated 4Å molecular sieves.

As an extension of our work, we became interested in the diastereoselective oxidation of dithianes. A great deal of data is available in the literature on the oxidation of racemic 2-substituted 1,3-dithianes and 1,3-dithiolanes as models of cyclic thioethers. Except for enzymatic reactions,¹² d⁰ transition metal/alkyl hydroperoxides proved to

be the most stereoselective oxidizing systems for this type of substrates.¹³ However, the chiral Kagan and Modena catalyst, a Ti(*i*-PrO)₄/(+)-diethyl tartrate [(+)-DET] modified system,^{13a,b,14,15} has been mostly used in stoichiometric amount to achieve a diastereo- and enantioselective process. The diastereoselectivity is merely associated with facial discrimination, whereas the enantioselectivity is a result of both facial selectivity and selection between the two enantiotopic sulfur atoms. In order to perform a diastereoselective transformation, a simple achiral transition-metal catalyst can be employed.

Very few systematic reports¹⁶ have appeared concerning the use of an achiral reagent for the diastereoselective oxidation of thioethers. Indeed, a catalytic (using minimal amount of catalyst) process would be highly desirable and the use of cheap, safe and stable catalysts should be highly preferable.

In the present work, we compare some simple achiral titanocenes with the traditional Ti(IV) catalyst, namely Ti(*i*-PrO)₄, as promoters in the TBHP oxidation of 2-substituted 1,3-dithianes and 1,3-dithiolanes **1a–f** (Scheme 1). Diastereoselectivity, yield, catalyst loading as well as its cost and ease of handling, were taken into account for each titanium compound.



Scheme 1

Initially, we performed a set of preliminary experiments on 2-phenyl-1,3-dithiane (**1a**) as model compound (Table 1) using our previously reported procedure for the titanocene-promoted sulfoxidation.¹¹ For the titanocene-catalyzed oxidation an aqueous workup (Method A: see

Table 1 Ti(IV)-Catalyzed Oxidation of **1a** by TBHP

Run	Catalyst (% mol)	Temp. (°C)	Time (h)	Yield 2a ^a (%)	<i>trans/cis</i> Ratio ^b (%)
1	Ti(<i>i</i> -PrO) ₄ (5)	0	3	72	98:2
2	Cp ₂ TiCl ₂ (5)	0	22	81	99:1
3	Cp ₂ TiCl ₂ (1)	r.t.	22	79	97:3
4	Cp ₂ TiCl ₂ /MS (5) ^c	0	5	86	98:2
5	Cp ₂ TiCl ₂ /MS (1) ^c	0	21	84	98:2
6	Cp ₂ Ti(OTf) ₂ (1)	0	5	42	96:4
7	Cp ₂ Ti(OTf) ₂ /MS (1) ^c	0	5	76	99:1

^a Isolated yield.

^b Determined by ¹H NMR analysis (400 MHz) on the crude reaction mixture.

^c MS = 4 Å molecular sieves. Ratio of titanocene to MS = 1 mmol/3.5 g

experimental section) or a simple filtration through a silica gel pad (Method B), could be indifferently used.

At 0 °C and in 5 mol% catalytic amount, Ti(*i*-PrO)₄ reacted faster than Cp₂TiCl₂ (runs 1 and 2), the former required a short reaction time to reach a good conversion, while a better yield was obtained using the more chemoselective titanocene. Comparable stereoselectivities were observed.

At room temperature (run 3), a 1 mol% catalytic amount of Cp₂TiCl₂ furnished a good conversion after 22 hours while the diastereoselectivity was slightly decreased.

As expected,^{10,11} titanocene activity was improved by adding activated 4 Å molecular sieves. In fact, under the same conditions, at 0 °C and 5 mol% catalyst loading, the reaction time and the stereoselectivity were comparable in those obtained with Ti(*i*-PrO)₄, yield being still higher (runs 4 and 1). In the presence of molecular sieves, simply by prolonging the reaction time (runs 4 and 5), the amount of titanocene can be lowered to 1 mol% without affecting the yield and the facial selectivity.

According to what we reported in our previous paper,¹¹ Cp₂Ti(OTf)₂ worked better than Cp₂TiCl₂ (runs 5–7). However, because of its higher cost and lower moisture stability, the bis-triflate complex is less convenient than the dichloride.

Once we had recognized the best conditions for the titanocene-promoted oxidation, we investigated variously 2-substituted substrates **1b–f** (Table 2).

The stereochemical outcome for all the Ti(IV)-catalyzed reactions was similar, while Cp₂TiCl₂ furnished systematically higher yields than Ti(*i*-PrO)₄. The *trans/cis* ratios slightly decreased changing the R group from Ph to Me (**1b**), a result that can be ascribed to the less sterically demanding Me group. Again (runs 2 and 3), as a general rule, Cp₂TiCl₂ worked better in the presence of molecular

Table 2 Ti(IV)-Catalyzed Oxidation of 2-Substituted Dithianes and Dithiolanes **1b–f** by TBHP^a

Run	Substrate	Catalyst (% mol)	Time (h)	Yield of 2 ^b (%)	<i>trans/cis</i> Ratio ^c (%)
1	1b	Ti(<i>i</i> -PrO) ₄ (5)	3	70	95:5
2	1b	Cp ₂ TiCl ₂ (5)	20	71	96:4
3	1b	Cp ₂ TiCl ₂ /MS (5)	5	91	96:4
4	1b	Cp ₂ TiCl ₂ /MS (1)	22	78	96:4
5	1c	Ti(<i>i</i> -PrO) ₄ (5)	5	78	94:6
6	1c	Cp ₂ TiCl ₂ /MS (1)	16	85	98:2
7	1d	Ti(<i>i</i> -PrO) ₄ (5)	21	47	80:20
8	1d	Cp ₂ TiCl ₂ /MS (1)	21	40	81:19
9	1d	Cp ₂ TiCl ₂ /MS (5)	25	63	80:20
10	1d	Cp ₂ TiCl ₂ /MS (5) ^d	25	65	82:18
11	1d	<i>rac</i> -(EBTHI)TiCl ₂ /MS (5)	48	42	77:23
12	1e	Ti(<i>i</i> -PrO) ₄ (5)	8 ^e	56	75:25
13	1e	Cp ₂ TiCl ₂ /MS (1)	30	69	72:28
14	1e	<i>rac</i> -(EBTHI)TiCl ₂ /MS (5) ^f	24	75	67:33
15	1f	Cp ₂ TiCl ₂ /MS (1)	22	69 ^g	93:7

^a All the reactions were conducted at 0 °C. MS = Molecular sieves. Ratio of 4; **MS**/titanocene = 3.5 g/1 mmol.

^b Isolated yield.

^c Determined by ¹H NMR analysis (400 MHz) of the crude reaction mixture.

^d 2,6-Di-*tert*-butyl-4-methylpyridine was used (molar ratio = 2:1 with respect to Cp₂TiCl₂).

^e The same yield and diastereoselectivity were obtained after 24 h.

^f [(±)-Ethylene(4,5,6,7-tetrahydro-1-indenyl)dichlorotitanium(IV)].

^g 4% Yield of bis-sulfoxide was obtained.

sieves. Furthermore, we confirmed that with prolonged reaction time, a reduced 1 mol% catalyst loading can be used without altering the efficiency and the diastereoselectivity (run 4).

Comparable results to the titanocene-catalyzed oxidation of dithiane **1a** were achieved for dithiolane **1c** and a better stereoselectivity was observed with respect to the Ti(*i*-PrO)₄ promoted process (runs 5 and 6). From this point of view it is interesting to note that in the oxidation of **1c** Cp₂TiCl₂/MS is superior to Mo(VI) catalyst and behaves similarly to VO(acac)₂.^{13a}

According to the literature,^{14,15} the oxidation of 2-carbonyl dithianes proceeds with low *trans* stereoselectivities: for example, in the oxidation of **1d**, a diastereomeric ratio of 75:25 was reported using the Modena^{13a} catalyst, whereas an almost completely stereospecific *trans* oxidation resulted on **1a** and **1b**.¹⁵ The reason of the lower ste-

reochemical ratio was attributed to the enolizability of H-2 in the 2-carbonyl dithiane oxides. The diastereomeric mixture may be obtained with high stereoselectivity but, then the Lewis acidic titanium might equilibrate the isomeric mixture. $\text{Cp}_2\text{TiCl}_2/\text{MS}$ and $\text{Ti}(i\text{-PrO})_4$ produced lower diastereomeric ratios (runs 7–9), when compared with the oxidation of dithianes **1a** and **1b**. Interestingly, $\text{Ti}(i\text{-PrO})_4$ showed to be, in this instance, more diastereoselective in the absence of (+)-DET ligand (run 7 and literature data¹⁵). In order to prevent the acid catalyzed equilibration of diastereomers a non-nucleophilic base, namely the 2,6-di-*tert*-butyl-4-methylpyridine, was added, but no significant improvement in the *trans/cis* ratio was observed (run 10).

Similarly, the more sterically hindered titanocene (\pm)-ethylene-bis-(4,5,6,7-tetrahydro-1-indenyl)dichlorotitanium(IV) [**3**, *rac*-(EBTHI) TiCl_2], (Figure 1) turned out to be less stereoselective and active catalyst (run 11). In the 2,2-disubstituted dithiane **1e**, the ability of the catalyst to discriminate between the two faces of the ring is expectedly reduced. In fact, using Modena catalyst, a 85:15 *trans/cis* diastereomeric ratio was obtained in the oxidation of **1e**,^{13a,b} while surprisingly, using the Kagan modification the stereospecific *trans* oxidation was reported.¹⁴ Since both faces of the ring are shielded, a lower reactivity is predictable. Our results confirmed these expectations (runs 12 and 13). Titanocene **3** did not lead to any improvement of the facial selectivity (run 14).

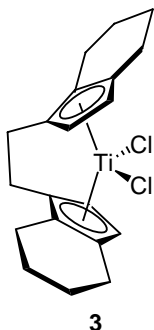
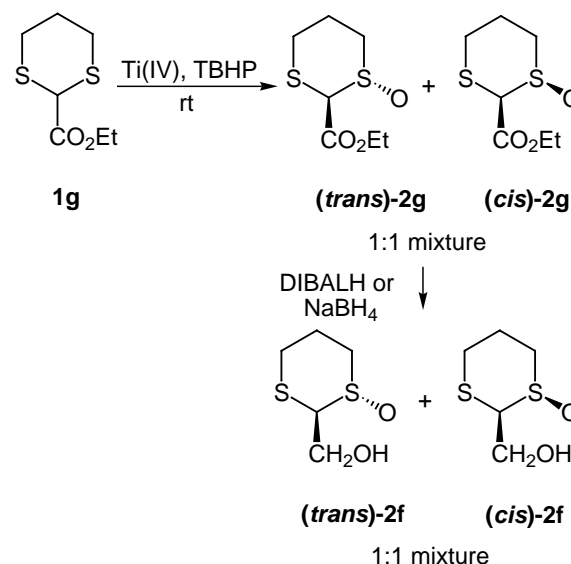


Figure 1 The structure of titanocene **3**.

The hydroxymethyl dithiane **1f** deserves some attention. So far the sulfoxidation of this substrate has never been reported. We envisioned a mechanism involving the initial coordination of the hydroxy group to the metal center, followed by an intramolecular oxygen transfer by the coordinated alkyl hydroperoxide. Such behaviour is, indeed, well documented for β -hydroxy sulfides.¹⁷ This transition state could have afforded a different stereochemical outcome compared to unfunctionalized 2-substituted dithianes. The oxidation of **1f** catalyzed by $\text{Cp}_2\text{TiCl}_2/\text{MS}$ under the usual conditions, furnished two main products as inseparable mixture by silica gel chromatography in 93:7 ratio (run 15). They were identified as the two geometric isomers of the monosulfoxide **2f**.

A confirmation of their structure was gained by performing the synthetic sequence depicted in Scheme 2. The known 1:1 *trans/cis* mixture of monosulfoxide **2g**^{14,18} was obtained by $\text{Ti}(i\text{-PrO})_4$ -catalyzed oxidation of commercially available 1,3-dithiane **1g**. The reduction of **2g** by DIBAL-H or NaBH_4 , afforded a 1:1 mixture of the same compounds isolated after the titanocene oxidation of **1f**, as confirmed by ^1H NMR analysis.



Scheme 2

Crystals suitable for X-ray analysis of the more abundant **2f** diastereomer were obtained by slow evaporation from a benzene- CHCl_3 solution. X-ray structure analysis showed a *trans* relative configuration (Figure 2).

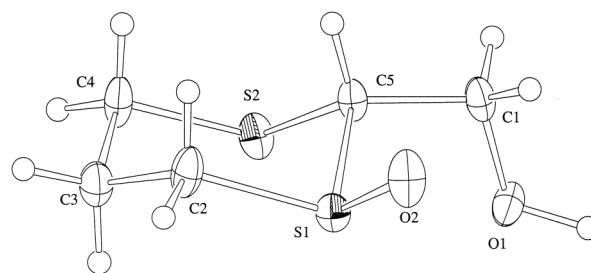


Figure 2 Crystal structure of the more abundant **2f** diastereoisomer (ORTEP plot). Thermal ellipsoids are drawn at 30% probability level.

From our findings, in the present paper we have shown that titanocene Cp_2TiCl_2 is an efficient catalyst for the diastereoselective mono-oxidation of 2-substituted 1,3-dithianes and 1,3-dithiolanes. It is a valuable alternative to $\text{Ti}(i\text{-PrO})_4$, the most frequently employed Ti(IV) promoter for this type of reaction. Titanocene-catalyzed oxidations are more chemoselective and as a consequence higher yields of monosulfoxides **2** can be obtained.

Cp_2TiCl_2 catalyst is as active as $\text{Ti}(i\text{-PrO})_4$, provided activated 4Å molecular sieves are present. The stereoselectiv-

ities achieved with both the Ti(IV) catalysts are similar in most of the examples.

The employment of a compound in minimal amounts is one of the main goals of green chemistry. In this respect Cp_2TiCl_2 is preferable to $\text{Ti}(i\text{-PrO})_4$. The former is very cheap and moisture stable compound,¹⁹ so it can be used in catalytic amount of 1 mol%, whereas for the more sensitive $\text{Ti}(i\text{-PrO})_4$, less than 5 mol% has never been reported. Moreover, with $\text{Cp}_2\text{TiCl}_2/\text{MS}$ only a simple filtration is needed to remove the catalyst (Method B: see experimental section).

All reactions were carried out under dry N_2 . Glassware was flame-dried (0.05 Torr) before use. The solvents employed were freshly distilled and dried. Temperatures were measured externally; reactions were monitored by TLC on Merck silica gel plates (0.25 mm) and visualized by UV light and by exposition to I_2 vapours. Cp_2TiCl_2 , $\text{Ti}(i\text{-PrO})_4$ and $\text{rac}(\text{-EBTHI})_2\text{TiCl}_2$ (**3**), as well as TBHP 5–6 M in decane, were all purchased from Aldrich and used without further purifications. Dithianes **1a**, **1b** and **1g** were purchased by Aldrich. Dithiolane **1c**^{13a} and dithianes **1d**¹⁵ and **1e**^{13a} were prepared as described in literature; **1f**²⁰ was prepared by LiAlH_4 reduction of **1g**.

Diastereomeric ratios of products **2** were determined by integration of characteristic ^1H NMR peaks directly on the crude reaction mixtures. Yields refer to isolated pure compounds. *trans*- and *cis*-isomers of products **2a**,^{13c,15} **2b**,^{13c,15} **2c**,^{13a} **2d**¹⁵ and **2e**^{13a,14} were identified by comparison of their ^1H NMR, ^{13}C NMR and mp data with those reported in the literature.

Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). NMR spectra were recorded on a Bruker DRX 400 spectrometer (400 MHz) at r.t. EIMS spectra (EI, 30 eV) were performed on a Finnigan Polaris spectrometer. IR spectra were recorded on a Bruker Vector 22 instrument. Mps were measured on a digital Electrothermal 9100 apparatus.

Titanium-Catalyzed Oxidation of **1a–f**; General Procedure

To a stirred mixture of the appropriate Ti(IV) catalyst (see Tables 1 and 2 for the amount) and, if present, activated 4Å molecular sieves (see Tables 1 and 2 for the amount) in anhyd CH_2Cl_2 (4 mL) was added a 5–6 M solution of TBHP in decane (0.22 mL, 1.2 mmol) at r.t. After 30 min the mixture was cooled at 0 °C and the substrate **1** (1 mmol) was introduced. After completion of the reaction, the mixture was treated according to workup procedure using Method A, B or, as is the case of **2f**, Method C.

Method A (Products **2a–e**)

The mixture was poured into a beaker containing sat. aq Na_2SO_4 . After stirring for 10 min it was diluted with EtOAc and the aqueous layer and the molecular sieves were separated by centrifugation and again extracted twice with EtOAc. The combined organic extracts were dried (MgSO_4), filtered, and then the solvent was removed in vacuo.

Method B (Products **2a–e**)

The reaction mixture was filtered through a short silica gel column to remove catalyst and molecular sieves. Then the solvent was removed in vacuo.

Method C (Product **2f**)

The reaction mixture containing **2f** was filtered through a pad of Celite eluting with EtOH. Then, the solvent was removed in vacuo. The residue was purified by flash chromatography on silica gel (eluent: CHCl_3 to $\text{CHCl}_3\text{-MeOH}$, 98:2). The monosulfoxides were ob-

tained as *trans/cis*-mixture (**2b–d,f**) or as separated isomers (**2a,e**). The *E*-isomer of **2f** was obtained pure (white needles) by crystallization from MeOH.

trans-2-Phenyl-1λ⁴,3-dithian-1-one (*trans*-**2a**)

^1H NMR (400 MHz, CDCl_3): δ = 7.45–7.36 (m, 5 H, ArH), 4.56 (s, 1 H, H-2), 3.58 (m, 1 H, H-6), 2.90 (ddd, 1 H, J = 14.1, 12.4, 2.6 Hz, H-4), 2.77 (ddd, 1 H, J = 13.1, 13.1, 2.9 Hz, H'-6), 2.70 (ddd, 1 H, J = 14.1, 3.4, 1.4 Hz, H'-4), 2.59–2.49 (m, 1 H, H-5), 2.45–2.31 (m, 1 H, H'-5).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 133.3, 129.4, 129.2, 128.8, 69.7, 54.8, 31.5, 29.6.

cis-2-Phenyl-1λ⁴,3-dithian-1-one (*cis*-**2a**)

^1H NMR (400 MHz, CDCl_3): δ = 7.46–7.34 (m, 5 H, Ar-H), 4.77 (s, 1 H, H-2), 3.22 (m, 1 H), 3.05 (m, 1 H), 2.81–2.61 (m, 3 H), 1.87 (m, 1 H).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 135.5, 129.1, 128.9, 128.4, 64.7, 47.4, 30.0, 13.9.

trans-2-Methyl-1λ⁴,3-dithian-1-one (*trans*-**2b**)

^1H NMR (400 MHz, CDCl_3): δ = 3.62 (q, 1 H, J = 7.0 Hz, H-2), 3.41 (m, 1 H, H-6), 2.74 (ddd, 1 H, J = 14.0, 12.3, 2.5 Hz, H-4), 2.62 (ddd, 1 H, J = 13.3, 12.8, 2.8 Hz, H'-6), 2.54 (m, 1 H, H'-4) 2.51–2.43 (m, 1 H, H-5), 2.35–2.22 (m, 1 H, H'-5), 1.64 (d, 3 H, J = 7.0 Hz, CH_3).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 60.0, 53.4, 30.0, 29.5, 15.1.

trans-2-Phenyl-1λ⁴,3-dithiolan-1-one (*trans*-**2c**)

^1H NMR (400 MHz, CDCl_3): δ = 7.49 (m, 2 H, *ortho* ArH), 7.42–7.31 (m, 3 H, *meta* and *para* ArH), 5.41 (s, 1 H, H-2), 3.85 (ddd, 1 H, J = 11.5, 11.3, 5.5 Hz, H-5), 3.62 (ddd, 1 H, J = 11.5, 7.0, 2.2 Hz, H'-5), 3.36 (ddd, 1 H, J = 13.5, 5.4, 2.2 Hz, H-4), 2.91 (ddd, 1 H, J = 13.5, 11.3, 7.0 Hz, H'-4).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 132.9, 128.8, 128.8, 128.3, 77.5, 52.9, 32.3.

2-Benzoyl-1λ⁴,3-dithian-1-one (**2d**) (*trans/cis*-Mixture)

^1H NMR (400 MHz, CDCl_3): δ (*trans*-isomer, distinct signals) = 8.02 (m, 2 H, *ortho* ArH), 7.64 (m, 1 H, *para* ArH), 7.51 (m, 2 H, *meta* ArH), 5.25 (s, 1 H, H-2), 3.60 (ddd, 1 H, J = 13.6, 8.7, 3.1 Hz, H-6), 2.96 (ddd, 1 H, J = 13.6, 9.4, 2.9 Hz, H'-6), 2.84 (ddd, 1 H, J = 14.3, 7.7, 2.9 Hz, H-4), 2.19–2.08 (m, 1 H, H-5). δ (*cis*-isomer, distinct signals) = 7.96 (m, 2 H, *ortho* ArH), 7.61 (m, 1 H, *para* ArH), 7.49 (m, 2 H, *meta* ArH), 5.56 (s, 1 H, H-2), 3.88 (ddd, 1 H, J = 12.8, 12.8, 2.9 Hz, H-6), 3.27 (m, 1 H, H-4), 3.10 (m, 1 H, H'-6), 2.45–2.27 (m, 2 H, H-5, H'-5). Overlapped signals: δ = 2.72–2.53 [m, 2 H (*trans*), H'-4, H'-5, 1 H (*cis*), H'-4].

trans-2-Methyl-2-phenyl-1λ⁴,3-dithian-1-one (*trans*-**2e**)

^1H NMR (400 MHz, CDCl_3): δ = 7.66 (m, 2 H, *ortho* ArH), 7.41 (m, 2 H, *meta* ArH), 7.33 (m, 1 H, *para* ArH), 2.88–2.60 (m, 4 H, H-4, H'-4, H-6, H'-6), 2.53–2.43 (m, 1 H, H-5), 2.09–1.96 (m, 1 H, H'-5), 1.92 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 138.5, 129.0, 128.6, 127.3, 64.7, 45.2, 26.5, 22.5, 19.3.

cis-2-Methyl-2-phenyl-1λ⁴,3-dithian-1-one (*cis*-**2e**)

^1H NMR (400 MHz, CDCl_3): δ = 8.00 (m, 2 H, *ortho* ArH), 7.43 (m, 2 H, *meta* ArH), 7.36 (m, 1 H, *para* ArH), 2.91 (m, 1 H), 2.79–2.65 (m, 2 H), 2.47–2.28 (m, 3 H), 1.93 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, CDCl_3): δ = 137.8, 128.7, 128.2, 128.1, 65.7, 47.1, 28.7, 28.0, 27.5.

trans-2-(Hydroxymethyl)-1 λ^4 ,3-dithian-1-one (trans-2f)

White needles from MeOH; mp 179–181 °C.

IR (KBr/nujol): 3233, 1424, 1083, 982, 720, 668 cm⁻¹.

¹H NMR (400 MHz, CDCl₃): δ = 4.27 (dd, 1 H, J = 12.3, 4.1 Hz, CHHOH), 4.02 (dd, 1 H, J = 12.3, 2.8 Hz, CHHOH), 3.94 (dd, 1 H, J = 4.1, 2.8 Hz, H-2), 3.52 (m, 1 H, H-6), 2.88 (ddd, 1 H, J = 14.0, 12.3, J_3 = 2.6 Hz, H-4), 2.80 (ddd, 1 H, J = 13.3, 12.4, 2.9 Hz, H'-6), 2.67 (m, 1 H, H'-4), 2.55–2.46 (m, 1 H, H-5), 2.31–2.18 (m, 1 H, H'-5).

¹³C NMR (100.6 MHz, CDCl₃): δ = 67.8, 57.9, 52.7, 29.3, 28.8.

MS: m/z (%) = 166 (M⁺, 12), 164 (45), 150 (39), 131 (99), 119 (50), 107 (44), 91 (100).

Anal. Calcd. for C₅H₁₀S₂O₂: C, 36.12; S, 38.07; H, 6.06. Found: C, 36.24; S, 38.01; H, 6.14.

X-ray Crystal Structure Analysis of 2f

Formula: C₅H₉O₂S₂, FW = 165.24, system: orthorhombic, space group *Pna*2₁, Z = 4, a = 18.663(2) Å, b = 4.656(2) Å, c = 8.344(2) Å, V = 725.1(4) Å³, D_c = 1.514 g cm⁻³, μ (CuK α) = 60.68 cm⁻¹.

A suitable crystal of **2f** (0.2 × 0.2 × 0.4 mm) was selected and mounted on a glass fiber. Diffraction measurements were performed at room temperature on a Rigaku AFC7S diffractometer using graphite monochromated *CuK α* radiation (λ = 1.54178 Å). Intensity data were corrected for Lorentz, polarization, and absorption effects (ψ -scan). No decay correction was applied.

The structure was solved by direct methods using SIR92²¹ and refined by means of full matrix least-squares procedure based on F² with SHELXL97.²² Eightyone variable parameters against 584 reflections were considered in the final refinement cycle. Anisotropic displacement factors were used for all non-hydrogen atoms. Hydrogen atoms were included (considering a riding model) but not refined. Maximum and minimum residual density were respectively 0.34 eÅ⁻³ and -0.45 eÅ⁻³. Final disagreement indices are R_1 = 0.033 ($I > 2\sigma_I$) and R_w = 0.082 (all 584 data).²³

Mixture of cis- and trans-2-(Hydroxymethyl)-1 λ^4 ,3-dithian-1-one (cis- and trans-2f)

¹H NMR (400 MHz, CDCl₃): δ (distinct signals) = 4.15 (dd, AB system, 1 H, J = 7.7, 6.1 Hz, H-6), 3.88 (dd, 1 H, J = 11.9, 7.7 Hz, CHHOH), 3.83 (dd, AB system, 1 H, J = 11.9, 6.1 Hz, CHHOH), 3.21 (ddd, 1 H, J = 14.3, 6.5 Hz, 2.6 Hz), 2.04–1.92 (m, 1 H).

Ethyl 1-Oxo-1 λ^4 ,3-dithiane-2-carboxylate (2g), trans/cis-Mixture

To a stirred mixture of Ti(*i*-PrO)₄ (74 mg, 0.26 mmol) in anhyd CH₂Cl₂ (2 mL), at r.t. were added sequentially a 5–6 M solution of TBHP in decane (1.13 mL, 6.2 mmol) and dithiane **1g** (1.0 g, 5.2 mmol). After 6 h, the reaction was quenched by pouring the mixture into a beaker containing sat. aq Na₂SO₄. After stirring for 10 min, the mixture was extracted with EtOAc; the combined extracts were dried (MgSO₄) and filtered, and then the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (eluent: CHCl₃ to CHCl₃-MeOH, 98:2) to give a nearly 1:1 *trans/cis*-mixture of sulfoxide **2g** (0.78 g, 72%) identified by the literature NMR data.¹⁴

DIBAL-H Reduction of 2g, trans/cis-Mixture

A stirred mixture of nearly 1:1 *trans/cis*-**2g** (89 mg, 0.44 mmol) in anhyd CH₂Cl₂ (1.5 mL) was cooled to 0 °C and DIBAL-H (1 M in CH₂Cl₂) was added (1.3 mL, 1.31 mmol). After 24 h, the reaction was stopped by adding a 1:1 mixture MeOH-H₂O (2 mL) and stirring for 20 min. The mixture was filtered through a Celite pad and washed with MeOH. After evaporation of the solvent a crude mixture was obtained, whose ¹H NMR spectrum revealed, as main

products, a nearly 1:1 mixture of the stereoisomers obtained by the oxidation of **1f** and identified as *trans/cis*-**2f**.

NaBH₄ Reduction of 2g, trans/cis-Mixture

To a stirred solution of nearly 1:1 *trans/cis*-**2g** (72 mg, 0.35 mmol) in EtOH (1.5 mL) was added NaBH₄ (26 mg, 0.70 mmol). After 4 h, the reaction mixture was filtered through a Celite pad and washed with EtOH. After evaporation of the solvent a crude mixture was obtained whose ¹H NMR spectrum revealed, as main products, a nearly 1:1 mixture of the stereoisomers obtained by oxidation of **1f** and by DIBAL-H reduction of **2g**, identified as *trans/cis*-**2f**.

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