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Oxidation of Dithia Compounds: Comparative Experimental and Theoretical Studies on 1,3-Bis(methylthio)propane, Bis(methylthio)methane, and *meso*-4,6-Dimethyl-1,3-dithiane

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Dedicated to Günter Szeimies on the occasion of his 85th birthday

1,3-Bis(methylthio)propane, bis(methylthio)methane, and *meso*-4,6-dimethyl-1,3-dithiane were oxidized with 1–4 equivalents of hydrogen peroxide, *meta*-chloroperbenzoic acid, sodium periodate, or potassium permanganate, respectively, and the amounts of oxidized substrates (sulfoxides and/or sulfones) were determined by NMR spectroscopy. Sulfanyl groups in the former starting material turned out to behave like independent functions, while a mutual influence of the sulfur functions was verified in the latter compounds. A meaningful investigation was possible in the conformationally constrained dithiane derivative. Oxidation of the dithiane with stoichiometric amounts of periodate led to exclusive formation of bissulfoxides, while hydrogen peroxide and *meta*-chloroperbenzoic acid yielded the possible products less specifically and permanganate preferentially furnished sulfones. The experimental investigations were supported by calculations on energies and stereoelectronic effects of starting materials, products, and transition states. The unique property of permanganate to exclusively yield sulfones might be due to its special oxidation mechanism, where the sulfur is not only acting as nucleophile, but concomitantly as electrophilic moiety.

Introduction

Oxidations of sulfides to sulfoxides or sulfones, and of sulfoxides to sulfones are widely applied methods for the synthesis of the latter compounds which are given even in basic textbooks and have been summarized repeatedly.[1] A plethora of reagents have been presented for these transformations, where the oxidation of sulfides either to sulfoxides or to sulfones is usually ruled by the amount of oxidant used. During our efforts on the synthesis and evaluation of oxidized derivatives of 1,3-dithianes[2] we noticed a distinct interference between the sulfur atoms and a mutual influence on their oxidations. Oxidations of monosulfides and monosulfoxides with different types of oxidants are mechanistically well understood, while the oxidation of 1,3-dithia compounds (i.e., of dithioacetals) and of other disulfides has never been investigated systematically and comparatively. We thus decided to undertake a thorough and systematic investigation on the oxidation of dithia compounds to provide a deeper understanding of the interactions in these compounds, which are the basis for their structure, their stability, and their reactivity, including their stereochemical reactivity. For this purpose, we used 1,3-bis(methylthio)propane (2,6-dithiaheptane, **1**), in which both sulfanyl groups should be virtually independent, bis(methylthio)methane (2,4-dithiapentane, **2**), in which a strong interaction could be expected, and *meso*-4,6-dimethyl-1,3-dithiane (**3**), in which the two sulfur atoms (and all involved bonds and lone pairs) are in defined orientations with respect to each other. The methyl substituents in dithiane **3** fix an unambiguous chair conformation of the six-membered ring with the methyl groups adopting equatorial positions.[3] The utilized test compounds **1**–**3** and all possible oxidized derivatives **4**–**23** are given in Figure 1.

We chose a selection of four oxidizing agents for this investigation: hydrogen peroxide (35% H_2O_2, acetic acid), *meta*-chloroperbenzoic acid (mcpba), sodium periodate ($NaIO_4$),[4] and potassium permanganate ($KMnO_4$). Hydrogen peroxide was reported to oxidize sulfides to sulfoxides and, albeit significantly slower, sulfoxides to sulfones.[5] Since its reactions are quite sluggish, it is occasionally used together with activating agents, e.g. with acids (especially carboxylic acids) or with transition metal catalysts.[6] Oxidations of sulfides or sulfoxides involve the nucleophilic attack of the sulfurs' lone pairs at one of the hydrogen peroxide's oxygens with concomitant leaving of hydroxide (Scheme 1, 1st reaction). Transprotonation eventually delivers the sulfoxide or the sulfone, respectively, and one equivalent of water.[7] It has been proposed that a further equivalent of water is participating in the transition state.[8] A different mechanism seems to be relevant for the attack of hydrogen peroxide at sulfoxides in basic media (Scheme 1, 2nd reaction).[9] Nucleophilic attack of the hydroperoxide anion at

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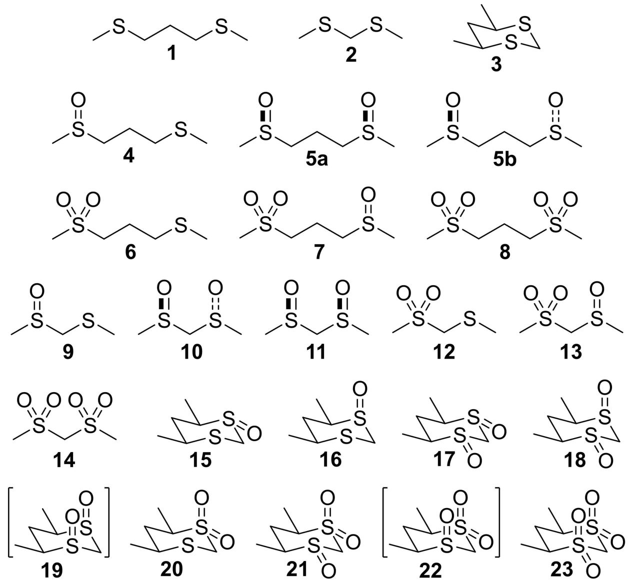
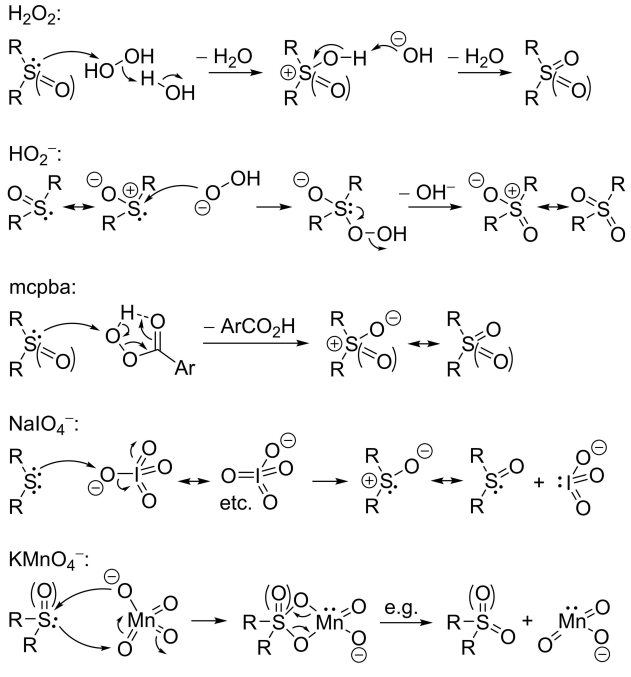


Figure 1. Investigated dithia compounds and their possible oxidized derivatives. Compounds in squared brackets could not be synthesized up to now.



Scheme 1. Mechanistic rationales for the attack of H_2O_2, HO_2^-, mcpba, $NaIO_4^-$, and MnO_4^-, respectively.

the electrophilic sulfur could here be facilitated by the partial positive charge at this position. Nevertheless, hydrogen peroxide is usually used in acetic acid or acetone, where the reactive moieties should be peracetic acid[10] and acetone peroxides, respectively. The former agent could be expected to react like *meta*-chloroperbenzoic acid (mcpba, *vide infra*), while the latter oxidants possibly show similar behavior as dimethyldioxirane (DMDO)[11] or comparable epoxides.

Oxidations of sulfides and sulfoxides with peracids like mcpba yield the respective sulfoxides and sulfones; these reactions can be expected to proceed in one step as depicted in Scheme 1 (3rd reaction).[12] It has been reported that oxidations of sulfides proceed much faster (even at −78 °C) than reactions of sulfoxides, what can be utilized for the clean formation of sulfoxides without over-oxidation.[13]

Sodium periodate is known to selectively oxidize sulfides to sulfoxides; the reaction of sulfoxides to the respective sulfones is scarcely observed. Theoretical investigations suggest a one-step mechanism in which the sulfur's lone pair attacks at one of the four equivalent periodate oxygens with concomitant cleavage of the O–I bond and liberation of the respective sulfoxide and of iodate (Scheme 1, 4th reaction).[14]

Potassium permanganate turned out to be the ideal reagent for the formation of sulfones from sulfides since oxidations of both sulfides and of sulfoxides proceed fast.[15] The even faster reaction of sulfoxides was suggested to be an entropic rather than enthalpic effect,[16] although this could not be confirmed in theoretical investigations.[17] A multi-stage mechanism has been proposed for this oxidation: Simultaneous attack of the sulfur's lone pair at one of the permanganate's oxygens and concomitant attack of another oxygen's lone pair at the sulfur (as given in Scheme 1, last reaction) leads to a four-membered ring. Several possibilities for the final liberation of the sulfoxides or sulfones, respectively, have been proposed, but only a metathesis dissociation has been investigated by quantum chemical methods; it turned out to be a possible reaction path.[17] A previous proposal that sulfides are oxidized by initial attack of the sulfur's lone pair at the permanganate's central atom seems to be not very likely in view of the more recent findings and is here not taken into further consideration.[16]

At this stage it could be mentioned that the usually given double bonds in sulfoxides and sulfones should be understood as simplified depictions. The character of these bonds has been investigated previously by us[18] and by others.[19] They are much better described as single bonds with charge separation and an unambiguous depiction would give a resonance hybrid of contributing formulae **A** and **B** (Figure 2). A simplified representation **C** is occasionally used to face this problem. This argumentation is similarly valid for sulfones, where the sulfurs carry a charge of close to +2 and the S–O bonds should possibly better be depicted as single rather than double bonds (**D**).[19a,c,20]

Results and Discussion

We started our investigations with the synthesis of dithia compounds **1** and **3** (**2** could be purchased) and of their

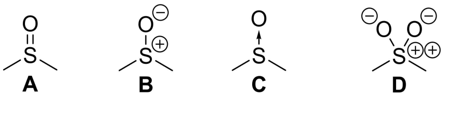


Figure 2. Possible representations of sulfoxides and sulfones.

oxidized derivatives **4**–**18**, **20**, and **22**, which should be used as reference compounds. For most of these compounds we could come back to published procedures or we could use protocols, which had been developed for similar compounds. Details on the utilized procedures are given in the Experimental Section. All dithiaheptane and dithiapentane derivatives were thus accessible, where the bissulfoxides **5 a** (*meso*) and **5 b** (*rac*) could not be separated by the applied chromatographic methods. Since their ^{1}H NMR spectra turned out to be virtually identical, we used these compounds as a mixture of isomers. The similarity of their physical characteristics supported our assumption, that sulfur functions separated by three carbons should behave as virtually independent functionalities. Synthesis of dithiane-derived sulfoxides with two axial S═O bonds (**19** and **21**) could not be synthesized to date. Consequently, they should not result as possible products in oxidations of dithiane **3** and were thus not needed as reference compounds in our investigations.

Oxidations of 2,6-dithiaheptane

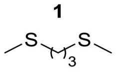
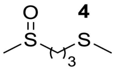
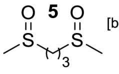
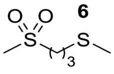
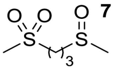
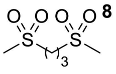
Table 1 summarizes the results of the oxidations of 2,6-dithiaheptane (**1**) as determined by ^{1}H NMR spectroscopy. Normalized ratios of the oxidation products **4**–**8** together with yields (measured in relation to the internal standard *o*-xylene) in brackets are given for the oxidants H_2O_2, mcpba, $NaIO_4$, and $KMnO_4$, where 1, 2 3, and 4 equivalents, respectively, of the respective oxidant were used. Recovery rates and yields of the oxidation equivalents are furthermore given for comparison in the last column. Amounts of the products were determined after a minimum of work-up (see Experimental Section) to avoid losses of material. Nevertheless, it seems as if especially the starting material could not fully be recovered in some of the experiments, possibly due to its volatility and/or water solubility. This has to be considered in the respective evaluations.

The oxidations with H_2O_2 were performed in acetic acid as solvent. Utilization of 1 eq. H_2O_2 led to a roughly statistic formation of monosulfoxide **4** and bissulfoxides **5 a** and **5 b**. A clearly statistic oxidation would give rise to a 25 : 50 : 25 ratio of non-oxidized starting material **1**, mono-oxidized product **4**, and of the bis-oxidized product(s) **5**.[21] This allows the conclusion that both sulfanyl groups in **1** seem to behave as independent functionalities. Only bissulfoxides **5** were obtained with 2 eq. of the oxidant and even with 3 and 4 eq. hardly any overoxidation to the sulfones **6**–**8** was observed.

Oxidation of 2,6-dithiaheptane (**1**) with 1 eq. of mcpba again led to a roughly statistical ratio of the non-oxidized, the singly, and the doubly oxidized products **1**, **4**, and **5**. With 2 eq. of mcpba a predominant formation of bissulfoxides **5** together with somewhat smaller amounts of sulfoxide/sulfone **7** was observed. Oxidation to sulfones **7** and **8** became dominant with 3 or 4 eq. of the oxidant. No intermediate monosulfone **6** was observed in neither of these experiments, giving clear evidence for the much slower oxidation of sulfoxides to sulfones as compared with the oxidation of sulfides to sulfoxides.

The product ratios in reactions of **1** with $NaIO_4$ suggest that formation of the sulfoxides again is much faster than their further oxidation to the respective sulfones. Monosulfoxide **4** was the major product with 1 eq. of the oxidant, while bissulfoxides **5** were the only products observed with 2 eq. of $NaIO_4$. Reaction with 3 eq. of the oxidant led to a statistical oxidation of the intermediate bissulfoxides **5** with a roughly 25 : 50 : 25 formation of **5**, **7**, and **8** (actually a 27 : 56 : 17 ratio).

Table 1. Oxidation of 1,3-bis(methylthio)propane (**1**; 2,6-dithiaheptane).[a]

Oxidant	Eq.	**1** 	**4** 	**5** [b] 	**6** 	**7** 	**8** 	Recovered material (yield of oxidation equivalents[d]) [%]
H_2O_2	1	3 (1)	55 (27)	42 (21)				49 (69)
	2		3 (2)	97 (65)				67 (132/2 = 66)
	3			99 (75)		1 (1)		76 (153/3 = 51)
	4			97 (69)		3 (2)		71 (144/4 = 36)
mcpba	1	28 (16)	41 (23)	31 (17)				56 (57)
	2	6 (2)	4 (1)	67 (26)		23 (9)	1 (1)	39 (84/2 = 42)
	3			15 (8)		58 (30)	26 (14)	52 (162/3 = 54)
	4					14 (7)	86 (45)	52 (201/4 = 50)
$NaIO_4$	1		70 (54)	30 (23)				77 (100)
	2			100 (87)				87 (174/2 = 87)
	3			27 (25)		56 (53)	17 (16)	94 (273/3 = 91)
	4					51 (37)	49 (36)	73 (255/4 = 64)
$KMnO_4$	1		3 (1)		83 (29)	4 (1)	10 (3)	34 (74)
	2		1 (1)		72 (56)	3 (2)	24 (19)	78 (195/2 = 98)
	3		0.6 (1)[c]		58 (54)	4 (2)	38 (35)	92 (255/3 = 85)
	4				50 (49)	3 (3)	47 (46)	98 (291/4 = 73)

[a] Normalized percentage of the respective product. The detected share of the respective compound based on an internal standard (*o*-xylene) is given in brackets (%). [b] As mixtures of diastereoisomers **5 a** and **5 b**. [c] All values are given as determined. Obviously, the precision especially of the small values is much lower than suggested by the precise numbers. [d] Percentage of the oxidant found in the products (as oxygen).

The sulfones **7** and **8** were the only products with 4 eq. of $NaIO_4$ employed.

$KMnO_4$ is known to preferentially yield sulfones instead of the respective sulfoxides. Even application of only 1 eq. of this oxidant led to almost exclusive formation of monosulfone **6**; only vanishingly small amounts of monosulfoxide **4** could be detected. Obviously, **4** is rapidly oxidized to sulfone **6**. Analogous observations were made with larger amounts of the oxidant: Sulfoxide/sulfone **7** was only observed in trace amounts, since its oxidation to bissulfone **8** seems to be similarly fast. The smaller total yields with 1 eq. and to some extend with 2 eq. $KMnO_4$ account for the necessarily significant shares of non-oxidized bissulfide **1**, which again seem to have partly been lost during the work-up procedures.

From these results one can deduce that oxidation of sulfides to sulfoxides is probably best achieved with H_2O_2 in acetic acid since this oxidant leads to hardly any overoxidation. On the other hand, $KMnO_4$ turned out to be the best oxidant for the oxidation of sulfides to sulfones. High yields and effective transfer of oxidation equivalents are observed with this reagent. The data given in Table 1 furthermore suggest that the two sulfanyl groups in 2,6-dithiaheptane (**1**) essentially behave as independent functionalities. Small deviations from an unambiguous statistical oxidation behavior could be attributed to inconsistencies arising from the work-up procedures or to putative intramolecular interactions between the sulfanyl and the intermediately formed sulfinyl group.[22] A discussion on this kind of interaction is given in the Supporting Information; they turned out to be of minor significance in the herein investigated compounds.

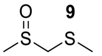
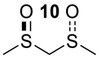
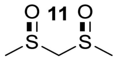
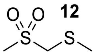
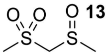
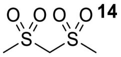
Oxidations of 2,4-dithiapentane

The results summarized in Table 2 suggest that both sulfanyl groups in 2,4-dithiapentane (**2**) no longer behave like independent functionalities. While the oxidation of 2,6-dithiaheptane (**1**) with 1 eq. H_2O_2 led to a roughly statistical oxidation of both sulfanyl groups, the oxidation of **2** with these conditions exclusively yielded the mono-oxidized product **9**. Only vanishingly small amounts of bissulfoxides **10** and **11**, and of sulfone **12** could here be detected. Utilization of further equivalents of this oxidant furnished increasing amounts of the bissulfoxides, but no over-oxidation to any of the sulfones **12**–**14** was observed. It could be mentioned that in either of the oxidant stoichiometries a larger fraction of the *meso*-bissulfoxide **11** was detected as compared with the chiral (but of course racemic) bissulfoxide **10**. This is in conflict with the fact that *meso* compound **11** is about 0.77 kJ/mol less stable than its isomer **10**, but is in line with calculated transition states for the formation of these compounds (*vide infra*): The formation of **11** is kinetically favored.

Utilization of 1 or 2 eq. mcpba in the oxidation of **2** led to largely identical results as obtained with H_2O_2. However, large fractions of sulfoxide/sulfone **13** and of bissulfone **14** were observed, when 3 and 4 eq. of mcpba were applied. This could possibly be attributed to a higher oxidation power of mcpba as compared with H_2O_2 or peracetic acid (which might be formed when H_2O_2 is used in acetic acid as solvent).[24]

Oxidation of **2** with $NaIO_4$ preferentially led to the mono-oxygenated product **9**. Hardly any bissulfoxide was obtained with 1 eq. of the oxidant, again giving clear evidence that both sulfanyl groups are no longer independent. Still a significant fraction of **9** was observed together with somewhat smaller amounts of bissulfoxides **10** and **11** when 2 eq. periodate were used. A predominant oxidation to sulfoxide/sulfone **13** and to

Table 2. Oxidation of bis(methylthio)methane (**2**; 2,4-dithiapentane).[a]

Oxidant	Eq.	 **9**	 **10**	 **11**	 **12**	 **13**	 **14**	Recovered material (yield of oxidation equivalents[c]) [%]
H_2O_2	1	98 (59)	0.8 (0.5)[b]	1 (0.7)	0.09 (0.06)[b]			60 (62)
	2	47 (32)	21 (14)	32 (21)	0.1 (0.08)[b]			67 (102/2 = 51)
	3	19 (16)	32 (27)	49 (41)	0.2 (0.1)[b]			74 (152/3 = 51)
	4	8 (6)	37 (30)	56 (45)				81 (156/4 = 39)
mcpba	1	93 (61)	3 (2)	4 (3)	0.07 (0.07)	0.1 (0.07)[b]		66 (71)
	2	33 (15)	25 (11)	41 (19)	1 (0.3)	1 (0.5)		46 (77/2 = 39)
	3		8 (4)	10 (5)		71 (38)	12 (6)	53 (156/3 = 52)
	4		0.3 (0.2)[b]	0.3 (0.2)[b]		40 (28)	60 (43)	71 (256/4 = 64)
$NaIO_4$	1	94 (87)	2 (2)	4 (3)	0.1 (0.1)[b]			92 (97)
	2	63 (43)	13 (9)	23 (15)	1 (0.5)	0.1 (0.1)[b]		68 (92/2 = 46)
	3		8 (7)	10 (9)		70 (63)	13 (11)	80 (265/3 = 88)
	4		1 (0.4)	1 (0.7)		58 (32)	41 (23)	56 (190/4 = 48)
$KMnO_4$	1	1 (0.2)			99 (13)			13 (26)
	2	0.6 (0.4)[b]			99 (66)			66 (132/2 = 66)
	3				100 (60)			60 (120/3 = 40)
	4				100 (65)			65 (130/4 = 33)

[a] Normalized percentage of the respective product. The detected share of the respective compound based on an internal standard (*o*-xylene) is given in brackets (%). [b] All values are given as determined. Obviously, the precision especially of the small values is much lower than suggested by the precise numbers. [c] Percentage of the oxidant found in the products (as oxygen).

bissulfone **14** turned out to occur with 3 and 4 eq. of the oxidant, respectively.

The outcome with $KMnO_4$ is quite clear: Regardless of what stoichiometry of the oxidant was used, only monosulfone **12** was observed as the single product. Obviously, oxidation of monosulfoxide **9** is significantly faster than that of 2,4-dithiapentane (**2**). Oxidations of **9** to bissulfoxides **10** or **11** or of sulfone **12** to sulfoxide/sulfone **13** are not even observed in traces. A discussion about the special oxidation behavior of $KMnO_4$ is given below in the context of dithiane oxidations.

Theoretical investigations on the oxidation of 2,4-dithiapentane

Wolfe et al.[25] and Alabugin et al.[26] calculated and investigated the structure of methanedithiol (**24**). Its preferred conformation (as given in Figure 3) is stabilized by $\sigma_{\text{H-S}}\rightarrow\sigma^*_{\text{C-Heq}}$, $\sigma_{\text{Heq-C}}\rightarrow\sigma^*_{\text{S-H}}$, and $n_{\text{S}}\rightarrow\sigma^*_{\text{C-Hax}}$ interactions. Apparently, an analogous conformation of bis(methylthio)methane **2** and of other oxidized derivatives is not favorable due to steric hindrance of the methyl groups. The most stable conformation of **2** is given in the Supporting Information where other conformations are at least 6.1 kJ/mol higher in energy and might thus be less relevant. A more ambiguous picture is already observed for monosulfoxide **9**, where four conformers **9 a**–**d** have to be considered, differing by at most 3.5 kJ/mol. (See Supporting Information; all other conformations of **9** are at least 5.3 kJ/mol higher in energy than conformation **9 a**.) An NBO analysis[23] to identify relevant stereoelectronic interactions was thus not considered to be helpful; any stereoelectronic effect stabilizing one specific conformer might not be present (or might be significantly smaller) in other relevant conformers. Any discrete significant effect might thus be countervailed by other effects in other conformers and thus be obsolete.

Instead we calculated the kinetics for an attack of hydrogen peroxide to sulfide and sulfoxide derivatives of dithiapentane. Transition states with different oxidants, especially with peracids or with periodate, and the therein active effects and stabilizations should be comparable and essentially be identical.

It should be noted that the (simplified) attack of H_2O_2 initially leads to protonated species and to hydroxide as a side product. The actual products are formed after transprotonation, which is not considered in these calculations. Again, a comprehensive examination of the obtained kinetic data for compounds **2** and **9**–**13** turned out to be hardly meaningful (thiapentane derivatives **25**–**27** were additionally investigated for comparison). Several conformations of quite similar energy would have to be considered for most of these compounds, low transition state barriers occasionally go along with high transition state dipole momenta (and *vice versa*), and some of the transition states are obscured either by a steric hindrance of virtually non-involved molecule parts or by hydrogen bonding between the attacking hydrogen peroxide and distal S=O bonds. However, some notable points can be extracted from the data (Table 3): 1) Activation barriers for the oxidations are dependent on the conformation. Activation energies for, e.g., reactions of monosulfoxide **9** to sulfone **12** differ by 12.9 kJ/mol for two of the calculated conformations (**9 b** and **9 c**). 2) Activation barriers in reactions towards bissulfoxide **11** are somewhat smaller than those for the formation of **10** and dipole momenta of the transition states in the formation of the former are smaller than those for the formation of the latter. This should explain the preferential formation of **11** over **10** as given in Table 2. 3) Activation energies are smallest for the oxidation of the parent compound **2** ($\geq$65 kJ/mol), are higher for oxidations of monosulfoxide **9** to bissulfoxides ($\geq$78 kJ/mol), are even higher for oxidations of monosulfoxides to sulfone **12** ($\geq$86 kJ/mol), of **12** to sulfoxide/sulfone **13** ($\geq$93 kJ/mol), and of bissulfoxides to **13** ($\geq$94 kJ/mol), and are highest for the oxidation of **13** to bissulfone **14** ($\geq$105 kJ/mol). 4) The activation barrier for the oxidation of dithiapentane **2** is somewhat higher than that for reference compound **25** ($\geq$65 *vs.* $\geq$62 kJ/mol). A similar tendency in the activation barriers is observed for the oxidations of sulfoxide **26** ($\geq$85 kJ/mol) and of bissulfoxides **10** or **11** ($\geq$94 kJ/mol). A clear and helpful

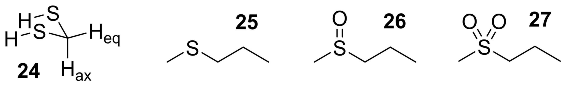


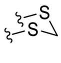
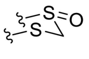
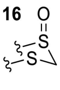
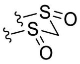
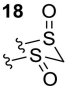
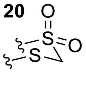
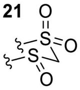
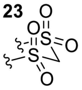
Figure 3. Comparative compounds of dithiapentane derivatives.

Table 3. Activation energies for oxidations of dithiapentane and thiapentane derivatives with H_2O_2.[a]

Educt (E_{rel} [kJ/mol][b])	Transition state	μ [D][c]	Product[d]	E_a [kJ/mol][e]
2	**TS-2/1**	8.6	**9**·H^+	65.1
9 a (:=0)	**TS-9 a/1**	10.3	**10**·H^+	88.5
9 b (1.9)	**TS-9 b/1**	17.9	**10**·H^+	81.2
9 a (:=0)	**TS-9 a/2**	8.7	**11**·H^+	81.5
9 d (3.5)	**TS-9 d/2**	12.8	**11**·H^+	78.0
9 a (:=0)	**TS-9 a/3**	7.3	**12**·H^+	93.8
9 b (1.9)	**TS-9 b/3**	11.5	**12**·H^+	98.9
9 c (2.3)	**TS-9 c/3**	9.4	**12**·H^+	86.0
10 a	**TS-10 a/1**	16.7	**13**·H^+	94.4
11 a	**TS-11 a/1**	7.1	**13**·H^+	97.6
11 a	**TS-11 a/2**	15.5	**13**·H^+	105.8
12 a (:=0)	**TS-12 a**	7.3	**13**·H^+	94.2
12 b (2.9)	**TS-12 b/1**	15.4	**13**·H^+	92.5
13 a	**TS-13 a**	14.0	**14**·H^+	104.8
25 a (:=0)	**TS-25 a/1**	9.6	**26**·H^+	62.3
25 a	**TS-25 a/2**	11.0	**26**·H^+	67.3
25 d (3.3)	**TS-25 d/1**	10.5	**26**·H^+	67.2
26 a (:=0)	**TS-26 a**	10.1	**27**·H^+	87.2
26 d (3.2)	**TS-26 d**	9.5	**27**·H^+	84.8

[a] All optimizations and calculations at the B3LYP/6-311++G(d,p) level with a modeled solvent field (CPCM, H_2O). Only data for reactions of the minimum conformation and for reactions with the lowest activation energies are given. A more comprehensive table is given in the Supporting Information. [b] Relative conformational energies. Only conformations with a relative energy <4.2 kJ/mol were considered. Further information is given in the table in the Supporting Information. [c] Electric dipole momentum of the transition state. [d] The actual products of the calculated elementary reactions are the respective protonated species. [e] Including zero-point correction. The presence of only one imaginary frequency was confirmed for transition states by frequency analyses.

Table 4. Oxidation of *meso*-4,6-dimethyl-1,3-dithiane (**3**).[a]

Oxidant	Eq.	**3** 	**15** 	**16** 	**17** 	**18** 	**20** 	**21** 	**23** 	Recovered material (yield of oxidation equivalents[c]) [%]
H_2O_2	1		90 (76)	10 (8)						84 (84)
	2		79 (69)	2 (2)	9 (8)	9 (8)				87 (103/2 = 52)
	3		56 (54)		20 (19)	24 (24)				97 (140/3 = 47)
	4		46 (40)		27 (23)	27 (23)				86 (132/4 = 33)
mcpba	1	11 (9)	75 (66)	10 (8)	2 (2)	2 (2)				78 (82)
	2		23 (15)		46 (30)	29 (19)	0.4 (0.3)[b]	1 (1)		65 (117/2 = 59)
	3				16 (12)	16 (12)		66 (51)	3 (2)	77 (209/3 = 70)
	4					1 (1)		91 (77)	8 (7)	85 (261/4 = 65)
$NaIO_4$	1		88 (87)	8 (8)	1 (1)	3 (3)				99 (103)
	2		5 (5)		21 (21)	72 (70)	0.5 (0.5)[b]	2 (2)		99 (194/2 = 97)
	3				8 (5)	61 (54)		32 (28)		87 (202/3 = 67)
	4				4 (4)	50 (47)		46 (44)	1 (1)	96 (238/4 = 60)
$KMnO_4$	1	21 (6)	23 (7)				55 (17)			30 (41)
	2	41 (39)	5 (5)				54 (52)			96 (109/2 = 55)
	3	27 (25)	3 (3)				70 (63)			91 (129/3 = 43)
	4	8 (6)	2 (2)				90 (70)			78 (142/4 = 36)

[a] Normalized percentage of the respective product. The detected share of the respective compound based on an internal standard (*o*-xylene) is given in brackets (%). [b] All values are given as determined. Obviously, the precision especially of the small values is much lower than suggested by the precise numbers. [c] Percentage of the oxidant found in the products (as oxygen).

explanation for these observations can hardly be given due to the variety of conformations participating in these reactions.

Oxidations of *meso*-4,6-dimethyl-1,3-dithiane

Although the sulfur functionalities in **2** and its oxidized derivatives turned out to be not independent, these compounds are still present in different conformations. Any mutual effect working in any of the conformations could possibly be attenuated or even countervailed by further effects in other conformations. Even high-energy conformations might be involved and could have an influence on the reaction outcome (Curtin-Hammett principle[27]). For this we additionally investigated oxidations of *meso*-4,6-dimethyl-1,3-dithiane (**3**), in which the functionalities are not independent *and* are in defined orientations towards each other. Only one conformation is relevant for **3** and any of its oxidized derivatives.

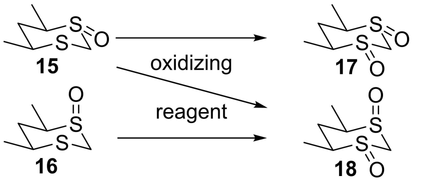
Whatever stoichiometry was used in the oxidation of **3** with H_2O_2, main product was the equatorially oxidized monosulfoxide **15** (Table 4). Since high recovery rates (84–97 %) were observed in these experiments, one could dare a quantitative examination: It looks as if most of the axial sulfoxide **16**, which was obtained in minor amounts with 1 eq. of the oxidant, was reacting to the axial/equatorial bissulfoxide **18**, while equatorial sulfoxide **15** was predominantly oxidized at the second equatorial position (→**17**). The outcome of these reactions suggests a strong preference for oxidations at equatorial positions. Over-oxidations to any of the sulfones were not observed with this oxidant.

Oxidation of dithiane **3** with mcpba was once again faster than with H_2O_2. Larger amounts of the bissulfoxides **17** and **18** were obtained with 2 eq. of the oxidant and over-oxidation to sulfoxide/sulfone **21** was significant with 3 eq.; it became close to quantitative with 4 eq. mcpba. However, bissulfone **23** was only observed in trace amounts.

Oxidation of dithiane **3** with 1 eq. $NaIO_4$ similarly led to equatorial monosulfoxide **15** with minor amounts of axial sulfoxide **16** and trace amounts of bissulfoxides **17** and **18**. Utilization of 2 eq. of this oxidant predominantly furnished axial/equatorial bissulfoxide **18**; obviously, the second oxidation occurred at the axial position. Significant amounts of sulfone/sulfoxide **21** were obtained with 3 or 4 eq. of the reagent; bissulfone **23** was only observed in vanishingly small quantities.

Only equatorial sulfoxide **15**, monosulfone **20**, and significant shares of the starting material were observed with different stoichiometries of $KMnO_4$. Obviously, oxidation of dithiane **3** to sulfoxide **15** is comparatively slow; its further oxidation to sulfone **20** is much faster. An astonishingly small recovery rate is conspicuous with 1 eq. $KMnO_4$, however, very similar product rates were obtained in two further runs with this stoichiometry. This finding might be possibly due to a particularly high solubility of dithiane **3** in the herein applied aqueous reaction mixture, which impeded its extraction during the work-up procedure.

We additionally performed competitive experiments, in which 1 : 1 mixtures of monosulfoxides **15** and **16** were reacted with 0.5 equivalents H_2O_2, mcpba, or $NaIO_4$, respectively (Scheme 2 and Table 5). A significantly larger fraction of the equatorial sulfoxide **15** was recovered in the oxidation with H_2O_2, allowing the assumption that axial sulfoxide **16** is reacting much faster. This is supported by the predominant formation of **18**; bis-equatorial bissulfoxide **17**, which obviously can only result from **15**, is detected only in trace amounts.



Scheme 2. Competitive oxidation of dithiane-derived monosulfoxides.

Table 5. Competitive oxidation of monosulfoxides **15** and **16**.[a,b]

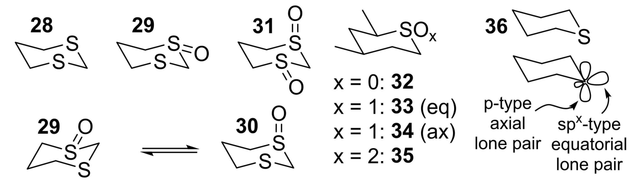
Oxidant[c]	**15**	**16**	**17**	**18**	Recovered material (yield of oxidation equivalents[d]) [%]
H_2O_2	45 (25)	19 (10)	5 (3)	31 (17)	55 (20/0.5 = 40)
mcpba	43 (22)	16 (8)	8 (4)	32 (16)	50 (20/0.5 = 40)
$NaIO_4$	27 (15)	15 (8)	8 (4)	50 (27)	54 (31/0.5 = 62)

[a] Normalized percentage of the respective product. The detected share of the respective compound based on an internal standard (*o*-xylene) is given in brackets (%). [b] 1:1 mixtures of monosulfoxides **15** and **16** were used. [c] 0.5 equivalents. [d] Percentage of the oxidant found in the products (as *additionally* introduced oxygen).

Utilization of mcpba in an analogous experiment led to a comparable outcome, except for a somewhat increased conversion, which is even higher with $NaIO_4$. None of the dithiane-derived sulfones **20**, **21**, and **23** was observed in these reactions, which is essentially consistent with the summarized data in Table 2: No sulfones were observed in the oxidation of **3** with H_2O_2 or with 1 or 2 eq. of mcpba or $NaIO_4$.

Theoretical investigations on the oxidation of dimethyl-1,3-dithiane

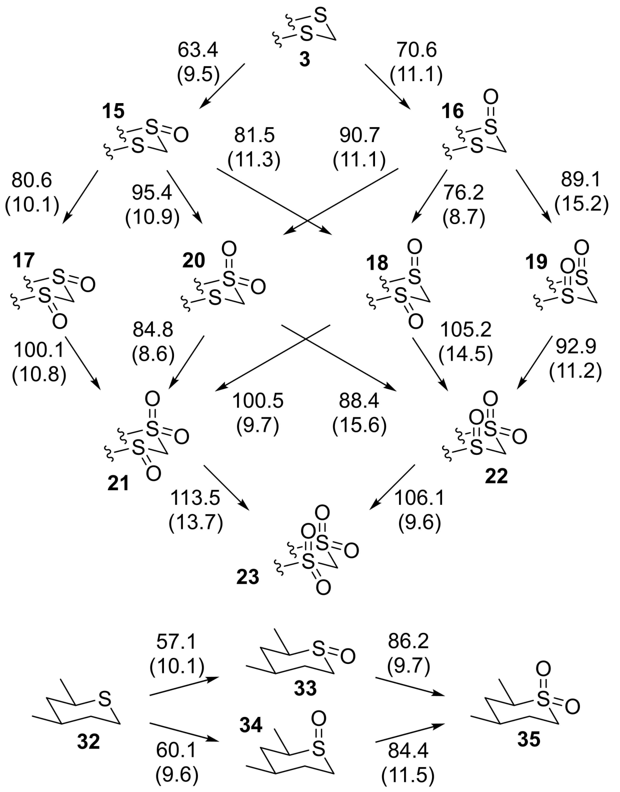
Oxidations of the parent 1,3-dithiane **28** have already been investigated previously,[2f,28] where the preferential formation of equatorial monosulfoxide **29** and in the further course of *trans* bissulfoxide **31** with $NaIO_4$ has been explained by favorable dipole effects (Scheme 3).[28a] Furthermore, it has already been mentioned that equatorial sulfoxide **29** is somewhat more stable than its axial isomer **30**.[2f] In fact we calculated dimethylated monosulfoxide **15** to be not more than 1.8 kJ/mol more stable than its axial isomer **16**. This difference is rather insignificant, where it is especially small in this calculation since the now applied polar solvent field attenuates possible dipole effects. The small difference might furthermore be due to the fact that stereoelectronic effects with participation of the sulfur lone pairs and of the C–S, S=O, and C–H bonds (see Supporting Information) sum up to quite similar stabilizations in both isomers.



Scheme 3. Derivatives of the parent 1,3-dithiane and of thiane. The possibility of a ring flip.

Unfortunately the preferred formation of **29** or **31** does not give any dependable hint on the mechanism of the respective oxidations, since a subsequent ring flip (Scheme 3) could obscure any initially formed conformer. However, further insight into these reactions came from theoretical investigations on the interactions and the intramolecular stabilizations of the lone pairs in 1,3-dithiane (**28**) and in thiane (**36**).[26,29] Alabugin stated that "the sulfur atom in thiacyclohexane [*i.e.* in thiane (**36**)] uses more p-character ($sp^{5.55}$) in its bond with carbon than one would expect from the idealized model. As a result, only a little p-character is left for the equatorial lone pair ($sp^{0.4}$). This makes this lone pair a relatively poor donor […]."[29] The axial lone pair on the other hand can be considered in this view as a virtually perfect p-orbital, which is significantly higher in energy and thus should be a better donor. This can similarly be deduced from calculations of dithiane **28** and its methylated derivative **3**. But when the equatorial lone pair of **3** is less nucleophilic, why is the equatorial sulfoxide **15** formed preferentially in an oxidation? We considered the possibility that any effect accounting for the thermodynamic stability of **15** could to some extend be already valid in the transition state of its oxidative formation. To gain further insight in these oxidations, we calculated transition states for oxidations of dithiane derivatives **3** and **15**–**22**, including the not (yet) synthesized diaxial compounds **19** and **22**. Again we took hydrogen peroxide as oxidant in these calculations. Transition states were determined and calculated for all possible equatorial and axial attacks (Scheme 4).

Several trends can be identified in the calculated data: 1) Dipole momenta of the transition states cannot be taken to explain most of the observed selectivities whereas they possibly might contribute to the non-formation of diaxial compounds **19** and **22**. 2) The higher the oxidation state (primarily of the sulfur to be oxidized, but then of the compound on the whole), the higher the oxidation's activation barrier: Activation energies for the oxidation of the parent dithiane **3** are smallest (63.4, 70.6 kJ/mol), those for the oxidation of monosulfoxides to bissulfoxides (76.2–89.1 kJ/mol), of monosulfones to sulfoxides/sulfones (84.8, 88.4 kJ/mol), of monosulfoxides to sulfones (90.7, 95.4 kJ/mol), and of bissulfoxides to sulfoxides/sulfones (92.9–105.2 kJ/mol) are increasingly higher, and are highest for oxidations of sulfoxides/sulfones to bissulfone **23** (106.1, 113.5 kJ/mol). 3) Whenever an equatorial and an axial attack is possible, the former is favored. This can be seen in the oxidation of the parent compound **3** (63.4 *vs.* 70.6 kJ/mol), of sulfoxides **15** (80.6 *vs.* 81.5 kJ/mol) and **16** (76.2 *vs.* 89.1 kJ/mol), of bissulfoxide **18** (100.5 *vs.* 105.2 kJ/mol), and of sulfone **20** (84.8 *vs.* 88.4 kJ/mol). 4) Axial sulfoxides (*e.g.* **16**) are formed less likely. Bissulfoxide **19** and sulfoxide/sulfone **22** are not even formed at all; they could not be synthesized so far. Nevertheless, according to the calculations, their further oxidation proceeds with significantly lower activation barriers than those of the equatorial analogs. Axial sulfoxide **16** is equatorially



Scheme 4. Oxidations of 1,3-dithiane and thiane derivatives with H_2O_2: calculated activation energies (in kJ/mol) and electric dipole momenta of the respective transition states in parentheses (in Debye). Further annotations are given in footnotes a and e of Table 3.

oxidized to bissulfoxide **18** with an activation energy of 76.2 kJ/mol, while equatorial sulfoxide **15** is oxidized to **17** with a barrier of 80.6 kJ/mol. This is even more pronounced in the oxidation of diaxial bissulfoxide **19** ($E_a = 92.9$ kJ/mol) as compared with the oxidations of **17** and **18** (100.1–105.2 kJ/mol) or in the oxidation of axial sulfoxide/sulfone **22** (106.1 kJ/mol) *vs.* the analogous oxidation of **21** (113.5 kJ/mol). With these observations one could go as far to conclude that the not yet synthesized compounds **19** and **22** might in fact be formed to some extent with specific conditions, but react fast to further products and are thus not detected. The sequence **16**→**19**→**22** has two quite similar consecutive activation energies of 89.1 and 92.9 kJ/mol. This is even more distinct for the sequence **18**→**22**→**23** with activation energies of 105.2 and 106.1 kJ/mol. A similar mechanism might explain the fact that hardly any sulfone **20** is formed with mcpba or NaIO$_4$, although the higher oxidized sulfoxide/sulfone **21** is formed with significant shares. Activation barriers for the formation of **20** are 90.7 and 95.4 kJ/mol, while the calculated activation energy for its further reaction to **21** is only 84.8 kJ/mol.

These theoretical results are quite in line with the experimental findings summarized in Table 4. Oxidations with H_2O_2 in acetic acid (the attacking reagent might in fact be peracetic acid) are with the applied reaction conditions actually observed for transformations with calculated activation barriers up to 81.5 kJ/mol and those with the more reactive oxidants mcpba or NaIO$_4$ are possible up to calculated activation energies of 90.7 kJ/mol and to a very small extent up to 106.1 or 113.5 (depending on the route taken to bissulfone **23**).

In an attempt to shed light on the observed selectivities, especially on the preferential equatorial oxidations, we performed NBO analyses on some of the hydrogen peroxide oxidations' transition states, i.e., on those of the equatorial and axial oxidations of dithiane **3** and of monosulfoxides **15** and **16**, and on the ipso oxidations of **15** and **16** (Figure 4 and Table 6). We calculated all relevant stereoelectronic interactions with participation of the sulfur lone pair, of the emerging $S–O_2H_2$ bond, and of the attacking oxygen's lone pairs. The summarized stereoelectronic effects are given in Table 6, where a detailed and differentiated compilation of these data is given in the Supporting Information.

It turned out that these stereoelectronic interactions are neither able to explain the preferred equatorial oxidation (stereoelectronic stabilization in, e.g., **TS-3-ax** is more pronounced than in **TS-3-eq**), nor do they account for the preferred formation of bissulfoxides rather than sulfones (**TS-16-i** and **TS-15-i** are better stabilized by stereoelectronic interactions than any of the other investigated transition states). As claimed previously,[28a] dipole effects might thus actually be responsible for the preferred equatorial oxidations. The differences in the dipole momenta were calculated to be quite small in the simulated H_2O solvent field, but might be more pronounced, if more expanded transition states with explicit inclusion of further water molecules were considered in the calculations. It

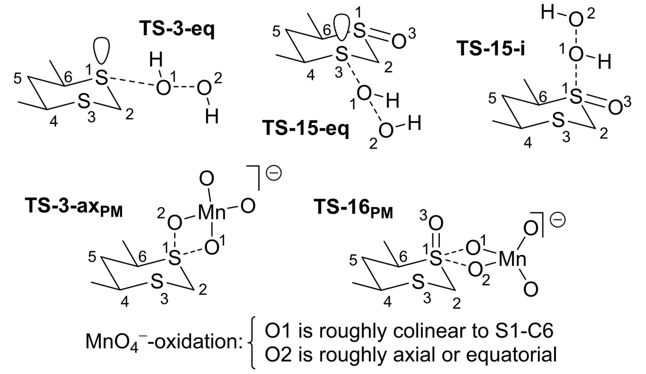


Figure 4. Exemplary transition states for oxidations of dithiane derivatives with H_2O and MnO_4^-, respectively.

Table 6. Summarized and aggregated stereoelectronic effects in transition states (oxidation with H_2O_2).[a]

Transition state[b]	E_{del} [kJ/mol][c]	Transition state[b]	E_{del} [kJ/mol][c]
TS-3-eq	121	**TS-3-ax**	153
TS-15-eq	132	**TS-15-ax**	143
TS-16-eq	130		
TS-16-i	174	**TS-15-i**	187

[a] All optimizations and calculations at the B3LYP/6-311++G(d,p) level with a modeled solvent field (CPCM, H_2O). A differentiated compilation with indication of the summarized stereoelectronic effects is given in the Supporting Information. [b] Transition states are defined in Figure 4. [c] Summarized NBO deletion energies.

Table 7. Activation energies and reaction enthalpies for oxidations of dithiane derivatives with MnO_4^-.[a]

Educt	Transition state	μ [D][b]	Product[c]	E_a [kJ/mol][d]	ΔH [kJ/mol][d]
3	**TS-3-eq**$_{\mathrm{PM}}$	20.4	**15**$\cdot$**MnO**$_3^-$	71.0	57.0
3	**TS-3-ax**$_{\mathrm{PM}}$	18.9	**16**$\cdot$**MnO**$_3^-$	76.6	61.2
15	**TS-15**$_{\mathrm{PM}}$	17.9	**20**$\cdot$**eq-MnO**$_3^-$	63.4	46.2
16	**TS-16**$_{\mathrm{PM}}$	17.1	**20**$\cdot$**ax-MnO**$_3^-$	57.8	48.6

[a] All optimizations and calculations at the B3LYP/6-311++G(d,p) level with a modeled solvent field (CPCM, H_2O). [b] Electric dipole momentum of the transition state. [c] cf. Scheme 1; these products require a metathesis dissociation to liberate the respective sulfoxides or the sulfone, which is not considered in these calculations. [d] Including zero-point correction. The presence of only one imaginary frequency was confirmed for the transition states by frequency analyses.

has been stated previously that at least one further water molecule is participating in the transition state of the hydrogen peroxide oxidation.[8] We furthermore suspect the different hybridization of the axial and the equatorial lone pairs in thianes and dithianes to be hardly relevant for the reaction outcome in oxidations. If it was, the selectivities should be significantly better than observed and should be vice versa (axial oxidations should be preferred, *vide supra*). The strong differentiation of the lone pairs with respect to their hybridization should possibly not be overrated, since a rehybridization of the orbitals might occur together with the oxidation process, making the energetic differences of the lone pairs hardly relevant. This is supported by the following observations: 1) The calculated p character of the *axial* lone pair in dithiane **3** changes during equatorial attack at H_2O_2 discontinuously from 96% to 37% when the S–O distance is only slightly decreased from 212.0 to 211.9 pm (the distance is 209.9 pm in the transition state; further details are given in the Supporting Information). 2) Below the very same bond distance (212 pm), the NBO software does no longer consider the sulfur's equatorial lone pair to be a lone pair, but a part of the evolving S–O bond. This discontinuity is quite likely an artifact of the attempt to consider all bonds and lone pairs as discrete units within the calculated molecules.

The orbital energies in the parent thiane **36** (which is not conformationally constrained!) have been measured by photoelectron spectroscopy and only one value (8.45 eV[30] as a vertical ionization energy) or two very close values (8.39, 8.49 eV[31]) were given for the sulfur's lone pairs. Two values (8.54 and 8.95 eV) were determined for the lone pairs in 1,3-dithiane (**28**), which was then not attributed to different hybridizations of the lone pairs, but to a putative through-space interaction of the axial lone pairs.[30]

On assuming that the strict correlation of the p-type character with the axial lone pairs might be ambiguous and can change in the reaction course, we understand the preferred oxidation of monosulfoxides **15** or **16** towards bissulfoxides **17** or **18** rather than sulfone **20**. This is obviously not due to stereoelectronic effects, but might be due to the different orbital energies of the respective sulfur lone pairs. Orbital energies of the S-1 lone pairs in sulfoxides **15** and **16** were calculated to be −15.4 and −16.0 eV (as converted from values in atomic units), respectively, while the energies of the S-3 lone pairs are −17.8 and −6.9 eV (sp^x-type, p-type, respectively, in **15**), and −17.4 and −6.7 eV (in **16**), respectively. The average orbital energies of the S-3 lone pairs in **15** (−12.4 eV) and in **16** (−12.1 eV) are thus higher than those of the respective sulfur lone pairs at S-1 (S=O) and are consequently oxidized preferentially, whenever the nucleophilic attack of the lone pair is mechanistically relevant in an oxidation.

A special property of $KMnO_4$ has already been noted previously: Oxidations of sulfoxides with this reagent are faster than that of the respective sulfides.[16–17] This could now be confirmed again by calculation of transition states (Figure 4) for permanganate oxidations of dithiane **3** and of monosulfoxides **15** and **16** (Table 7). Equatorial oxidation of **3** with MnO_4^- en route to sulfoxide **15** (cf. Scheme 1 for the mechanism of this oxidation) is preferred over the respective axial oxidation (activation energies: 71.0 *vs.* 76.6 kJ/mol) and the further oxidations of both sulfoxides en route to sulfone **20** are significantly faster. The respective activation barriers were calculated to be 63.4 kJ/mol (**15**→**20**$\cdot$**MnO**$_3^-$) and 57.8 kJ/mol (**16**→**20**$\cdot$**MnO**$_3^-$). This goes in line with the observation that hardly any of the sulfoxides is formed (their further oxidation obviously is faster than their formation) and that axial sulfoxide **16** is not detected at all: In comparison with **15** it has a higher barrier for its formation but its further oxidation is much faster.

It has previously been suggested that the preferred oxidation of sulfoxides (as compared with the respective sulfides) with $KMnO_4$ is due to entropic effects,[16] albeit this could not be affirmed in theoretical investigations.[17] We performed NBO analyses and had to realize that the stereochemical outcome of dithiane oxidations with MnO_4^- is (as in H_2O_2 oxidations) presumably not ruled by stereoelectronic effects. A detailed discussion is thus only given in the Supporting information.

Nevertheless, a clue for the different rates for oxidations of dithiane **3** and of sulfoxides **15** and **16** came from the transition states' geometries. In **TS-3-eq**$_{\mathrm{PM}}$ the bonds between the oxidized sulfur and the former permanganate's oxygens show different bond length of 197 and 234 pm, respectively. The equivalent bonds in **TS-16**$_{\mathrm{PM}}$ are overall significantly shorter (203 and 204 pm) suggesting a stronger bond and a later transition state (within the reasoning of the Hammond postulate).[32] Reaction of dithiane **16** with permanganate to the initially formed product **20**$\cdot$**eq-MnO**$_3^-$ is less endothermic (46.2 kJ/mol) than reaction of **3** to **15**$\cdot$**MnO**$_3^-$ (57.0 kJ/mol). For an understanding we recall the mechanism of the permanganate oxidation (Scheme 1) in which a sulfur lone pair attacks at one of the permanganate's oxygens and a lone pair of another oxygen concomitantly attacks at the sulfur. The combined stereoelectronic interactions of both oxygens' lone pairs with all Rydberg orbitals at the sulfur were calculated to be only 14.4+14.8 kJ/mol for **TS-3-eq**$_{\mathrm{PM}}$, but contribute 23.8+60.0 kJ/mol in **TS-16**$_{\mathrm{PM}}$ (see table in the Supporting Information) This can be attributed to the electron withdrawing effect of the S=O bond's oxygen. A similar interaction is not possible with the other oxidants considered in our investigation. A corresponding rationale can be followed in the comparison of transition states **TS-3-ax$_{\mathbf{PM}}$** and **TS-15$_{\mathbf{PM}}$**.

Conclusion

It could clearly be shown that two distal sulfanyl groups behave in oxidations as virtually independent functions, while both the sulfur groups in 2,4-dithiapentane (**2**) and dithiane **3**, respectively are mutually influencing each other. Investigation of the conformationally constrained dithiane **3** and its oxidized derivatives revealed preferential oxidation in equatorial positions and (except for potassium permanganate) oxidation to bissulfoxides rather than sulfones, which could not be traced back to stereoelectronic interactions in starting materials or transition states. Nevertheless, calculated activation barriers are in excellent agreement with the experimental results. The preferential formation of sulfones with $KMnO_4$ might possibly be due to the quite special mechanism of its action in which not only the sulfur lone pair acts as nucleophile, but the sulfur additionally as electrophilic moiety.

Experimental Section

General. Compound **2** was purchased and dithianes **3**,[33] **16**, **18**, **20**, **21**, and **23**[2f] were synthesized according to published procedures. Technical solvents (acetone, CH_2Cl_2, and *n*-pentane) were distilled prior to use. EtOH, MeOH, and MeCN were purchased as HPLC-grade solvents and used without further purification. Flash column chromatography[34] was carried out using Merck SiO_2 60 (230–400 mesh) and thin layer chromatography (TLC) was carried out using commercially available Merck F_{254} pre-coated sheets. ^{1}H and ^{13}C NMR spectra were recorded with Bruker Avance 300, 500, or 600 instruments. Chemical shifts are given in ppm and are referenced by using the residual signals of the solvent as internal standard. IR spectra were recorded with a Bruker Alpha spectrometer and mass spectra were recorded with a Q Exactive Orbitrap or a Finnigan MAT-95 mass spectrometer.

1,3-Bis(methylthio)propane (1). 1,3-Propanedithiol (3.00 g, 2.79 mL, 27.7 mmol) and MeI (9.83 g, 4.31 mL, 69.3 mmol) were successively added to a suspension of K_2CO_3 (11.5 g, 83.2 mmol) in MeCN (150 mL) and the mixture was stirred for 67 h at rt. H_2O (300 mL) was added and the mixture was extracted with pentane (3×150 mL). The combined organic layers were washed with 10% NaOH (1×200 mL) and H_2O (3×150 mL), dried (Na_2SO_4), concentrated at reduced pressure (~400 mbar), and distilled with a short path vacuum distillation apparatus to yield **1** as a yellow viscous liquid (1.48 g, 10.9 mmol, 39%). bp. 77–78 °C (15–16 mbar); ^{1}H NMR (600 MHz, DMSO-d$_6$): $\delta = 1.78$ (quint, $^3J = 7.1$ Hz, 2 H, 2-H$_2$), 2.04 (s, 6 H, 2×CH$_3$), 2.53 (t, $^3J = 7.2$ Hz, 4 H, 1-H$_2$, 3-H$_2$). The ^{1}H NMR data are in agreement with published data.[35]

***rac*-Methyl[3-(methylsulfinyl)propyl]sulfane (4)**. In analogy to a published procedure[36] a solution of bissulfane **1** (610 mg, 4.48 mmol) in CH_2Cl_2 (20 mL) was added dropwise to a cooled (−78 °C) solution of Tf_2O (750 mg, 2.66 mmol) in CH_2Cl_2 (50 mL) and the mixture was stirred for 4 h at this temperature. A saturated solution of $NaHCO_3$ (20 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3×40 mL), dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 30:1) to yield **4** as a yellow liquid (289 mg, 1.90 mmol, 42%). $R_f = 0.4$ (CH_2Cl_2/MeOH, 20:1); ^{1}H NMR (600 MHz, DMSO-d$_6$): $\delta = 1.87$–1.93 (m, 2 H, 2-H$_2$), 2.06 (s, 3 H, SCH$_3$), 2.53 (s, 3 H, SOCH$_3$), 2.59 (td, $^3J = 7.2$ Hz, $^2J = 1.1$ Hz, 2 H, 3-H$_2$), 2.71 (dt, $^2J = 12.5$ Hz, $^3J = 7.4$ Hz, 1 H, 1-H$_a$), 2.83 (dt„ $^2J = 13.0$ Hz, $^3J = 7.9$ Hz, 1 H, 1-H$_b$). The ^{1}H NMR data are in agreement with published data.[22]

1,3-Bis(methylsulfinyl)propane (5). In analogy to a published procedure[36b] H_2O_2 (35%, 100 mg, 88.3 μL, 1.03 mmol) was added to a cooled (0 °C) solution of bissulfane **1** (610 mg, 4.41 mmol) in AcOH (5 mL) and the mixture was stirred for 1 h at rt. CH_2Cl_2 (30 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 30:1→10:1) to yield **5** as a colorless solid (234 mg, 1.39 mmol, 32%) together with a smaller amount of monosulfoxide **4** (34.4 mg, 0.226 mmol, 5%). $R_f = 0.22$ (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (600 MHz, DMSO-d$_6$): $\delta = 1.97$–2.09 (m, 2 H, 2-H$_2$), 2.55 (s, 6 H, 2×CH$_3$), 2.74–2.81 (m, 2 H, 1-H$_a$, 3-H$_a$), 2.86–2.93 (m, 2 H, 1-H$_b$, 3-H$_b$). The ^{1}H NMR data are in agreement with published data.[22]

Methyl[3-(methylsulfonyl)propyl]sulfane (6). In variation of a published procedure[37] $KMnO_4$ (176 mg, 1.11 mmol) was added in small portions to a solution of monosulfoxide **4** (100 mg, 0.657 mmol) in a cooled (0 °C) mixture of acetone (15 mL) and H_2O (5 mL) and the mixture was stirred for 17.5 h at rt. The precipitate was filtered and washed repeatedly with acetone. CH_2Cl_2 (10 mL) was added to the filtrate and the aqueous phase was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 100:1→50:1) to yield **6** as a yellow liquid (81.2 mg, 0.483 mmol, 74%). $R_f = 0.5$ (CH_2Cl_2/MeOH, 50:1); ^{1}H NMR (600 MHz, DMSO-d$_6$): $\delta = 1.93$–1.99 (m, 2 H, 2-H$_2$), 2.06 (s, 3 H, SCH$_3$), 2.59 (t, $^3J = 7.2$ Hz, 2 H, 3-H$_2$), 2.98 (s, 3 H, SO$_2$CH$_3$), 3.16–3.20 (m, 2 H, 1-H$_2$); ^{13}C NMR (150 MHz, DMSO-d$_6$): $\delta =$ 14.3 (CH$_2$), 21.5 (CH$_3$), 31.5 (CH$_2$), 40.2 (CH$_3$), 52.3 (CH$_2$); IR (ATR): $\tilde{\upsilon}$ (cm^{-1}) = 2919 (w), 1700 (vw), 1426 (w), 1352 (vw), 1287 (s), 1135 (m), 1116 (m); MS (APCI, 280 °C): *m/z* (%) = 171 (9), 169 (100) [(M+1)$^+$], 168 (2) [M$^+$], 143 (1); HRMS (APCI): calcd. for $C_5H_{13}O_2{}^{32}S_2{}^+$: 169.0351; found: 169.0350.

1-(Methylsulfinyl)-3-(methylsulfonyl)propane (7). In analogy to a published procedure[36b] H_2O_2 (35%, 77.4 mg, 68.4 μL, 0.797 mmol) was added to a cooled (0 °C) solution of monosulfone **6** (133 mg, 0.790 mmol) in AcOH (5.00 mL) and the mixture was stirred for 1 h at rt. CH_2Cl_2 (30 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 20:1→10:1) to yield **7** as a colorless solid (115 mg, 0.624 mmol, 79%). $R_f = 0.43$ (CH_2Cl_2/MeOH, 10:1); ^{1}H NMR (500 MHz, DMSO-d$_6$): $\delta = 2.05$–2.12 (m, 2 H, 2-H$_2$), 2.56 (s, 3 H, SOCH$_3$)„ 2.77 (dt, $^2J = 13.0$ Hz, $^3J = 7.6$ Hz, 1 H, 1-H$_a$); 2.90 (dt, $^2J = 13.0$ Hz, $^3J = 7.9$ Hz, 1 H, 1-H$_b$), 3.00 (s, 3 H, SO$_2$CH$_3$), 3.24–3.29 (m, 2 H, 1-H$_2$); ^{13}C NMR (125 MHz, DMSO-d$_6$): $\delta = 15.7$ (CH$_2$), 22.2 (CH$_3$), 37.9 (CH$_2$), 50.9 (CH$_3$), 52.3 (CH$_2$); IR (ATR): $\tilde{\upsilon}$ (cm^{-1}) = 2996 (s), 2912 (vs), 1429 (vs), 1352 (vs), 1288 (s), 1258 (vs), 1191 (s), 1113 (m), 1041 (s), 791 (s).; MS (EI, 280 °C): *m/z* (%) = 185 (2) [(M+1)$^+$], 184 (14) [M$^+$], 121 (100), 89 (10), 79 (52), 63 (57), 57 (18); HRMS (EI): calcd. for $C_5H_{12}O_3{}^{32}S_2$: 184.0222; found: 184.0221.

1,3-Bis(methylsulfonyl)propane (8). In analogy to a published procedure[37] mcpba (77%, 111 mg, 0.0.495 mmol) was added in portions to a cooled (0 °C) solution of bissulfoxide **5** (51.2 g, 0.304 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred for 2 h at 0 °C. H_2O (~2 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4), concentrated at reduced pressure, and purified by crystallization (EtOH) to yield **8** as a colorless solid (23.1 mg, 0.115 mmol, 38 %). ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.10–2.16 (m, 2 H, 2-H_2), 3.01 (s, 6 H, 2×CH_3), 3.24–3.29 (m, 4 H, 1-H_2, 3-H_2); ^{13}C NMR (150 MHz, DMSO-d_6): $\delta = 15.9$ (CH_2), 40.1 (2×CH_3), 51.7 (2×CH_2); IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2933 (vw), 1440 (w), 1318 (w), 1272 (m), 1242 (m), 1124 (m); MS (APCI, 280 °C): *m/z* (%) = 203 (8), 201 (100) [$(M+1)^+$], 199 (16), 193 (9), 185 (10), 165 (20); HRMS (APCI): calcd. for $C_5H_{13}O_4{}^{32}S_2{}^+$: 201.0250; found: 201.0248.

***rac*-Methyl[(methylsulfinyl)methyl]sulfane (9)**. In analogy to a published procedure[36b] H_2O_2 (35 %, 2.51 g, 2.22 mL, 25.8 mmol) was added to a cooled (0 °C) solution of bissulfane **2** (2.54 g, 2.40 mL, 23.5 mmol) in AcOH (5 mL) and the mixture was stirred for 0.5 h at rt. CH_2Cl_2 (30 mL) was added and the mixture was neutralized by addition of K_2CO_3, dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 50 : 1→10 : 1→5 : 1) to yield **9** as a yellowish liquid (2.20 g, 17.7 mmol, 75 %). $R_f = 0.5$ (CH_2Cl_2/MeOH, 10 : 1); ^{1}H NMR (600 MHz, DMSO-d_6): $\delta = 2.25$ (s, 3 H, SCH_3), 2.58 (s, 3 H, $SOCH_3$), 3.77 (d, $^{2}J = 13.6$ Hz, 1 H, CH_aH_b), 3.96 (d, $^{2}J = 13.6$ Hz, 1 H, CH_aH_b). The ^{1}H NMR data are in agreement with published data.[38]

***rac*-Bis(methylsulfinyl)methane (10) and *meso*-Bis(methylsulfinyl) methane (11)**. In variation of a published procedure[37] mcpba (77 %, 1.00 g, 4.46 mmol) was added in portions to a cooled (0 °C) solution of monosulfoxide **9** (437 mg, 3.52 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred for 3 h at 0 °C. H_2O (~2 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 10 : 1) to yield a mixture of bissulfoxides **10** and **11** as a yellowish oil (136 mg, 0.970 mmol, 28 %). The product ratio was determined by NMR spectroscopy (**10**/**11** = 33 : 67; lit.:[37] **10**/**11** = 39 : 61). $R_f = 0.37$ (CH_2Cl_2/MeOH, 10 : 1); **10**: ^{1}H NMR (600 MHz, DMSO-d_6): $\delta = 2.75$ (s, 6 H, 2×$SOCH_3$), 4.34 (s, 2 H, CH_2); **11**: ^{1}H NMR (600 MHz, DMSO-d_6): $\delta = 2.81$ (s, 6 H, 2×$SOCH_3$), 4.15 (d, $^{2}J = 13.0$ Hz, 1 H, CH_aH_b), 4.44 (d, $^{2}J = 13.0$ Hz, 1 H, CH_aH_b). The ^{1}H NMR data are in agreement with published data.[37]

Methyl[(methylsulfonyl)methyl]sulfane (12). In variation of a published procedure[37] $KMnO_4$ (0.840 g, 5.32 mmol) was added in small portions to a solution of monosulfoxide **9** (660 mg, 5.31 mmol) in a mixture of acetone (25 mL) and H_2O (1 mL) and the mixture was stirred for 24 h at rt. The precipitate was filtered, repeatedly washed with acetone, and concentrated at reduced pressure. The residue was dissolved in CH_2Cl_2, dried (Na_2SO_4), and concentrated at reduced pressure to yield **12** as a colorless oil (334 mg, 2.38 mmol, 45 %). $R_f = 0.5$ (CH_2Cl_2/MeOH, 50 : 1); ^{1}H NMR (600 MHz, DMSO-d_6): $\delta = 2.31$ (s, 3 H, SCH_3), 3.01 (s, 3 H, SO_2CH_3), 4.20 (s, 2 H, CH_2). The ^{1}H NMR data are in agreement with published data.[37]

***rac*-(Methylsulfinyl)(methylsulfonyl)methane (13)**. In analogy to a published procedure[37] mcpba (77 %, 223 mg, 0.995 mmol) was added in portions to a cooled (0 °C) solution of monosulfone **12** (120 mg, 0.856 mmol) in CH_2Cl_2 (10 mL) and the mixture was stirred for 2 h at 0 °C. H_2O (~2 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4) and concentrated at reduced pressure to yield **13** as a colorless oil (93.6 mg, 0.600 mmol, 70 %). ^{1}H NMR (600 MHz, DMSO-d_6): $\delta = 2.78$ (s, 3 H, $SOCH_3$), 3.12 (s, 3 H, SO_2CH_3), 4.75–4.82 (m, 2 H, CH_2). The ^{1}H NMR data are in full agreement with published data.[39]

Bis(methylsulfonyl)methane (14). In analogy to a published procedure[37] $KMnO_4$ (464 mg, 2.94 mmol) was slowly added to a solution of bissulfane **2** (159 mg, 0.150 mL, 1.47 mmol) in a mixture of AcOH (15 mL) and H_2O (1.5 mL) and the mixture was stirred for 1 h at rt. A saturated solution of $Na_2S_2O_5$ was added until the solution became colorless and ice (~30 g) was added. The aqueous phase was extracted with CH_2Cl_2 (3×25 mL), dried (Na_2SO_4), concentrated at reduced pressure, and purified by crystallization (EtOH) to yield **14** as a colorless solid (55.4 mg, 0.322 mmol, 22 %). ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 3.20$ (s, 6 H, 2×SO_2CH_3), 5.44 (s, 2 H, CH_2). The ^{1}H NMR data are in agreement with published data.[40]

***rac*-(1*R*,4*R*,6*S*)-4,6-Dimethyl-1,3-dithiane-1-oxide (15) and *meso*-(1*R*,3*S*,4*R*,6*S*)-4,6-Dimethyl-1,3-dithiane-1,3-dioxide (17)**. In analogy to a published procedure[36b] H_2O_2 (35 %, 198 mg, 2.04 mmol) was added to a cooled (0 °C) solution of dithiane **3** (300 mg, 2.02 mmol) in AcOH (5 m) and the mixture was stirred for 2.5 h at rt. CH_2Cl_2 (30 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The solid was extracted with CH_2Cl_2 and the filtrate was dried (Na_2SO_4), concentrated at reduced pressure, and purified by column chromatography (CH_2Cl_2/MeOH, 50 : 1→30 : 1→10 : 1) to yield monosulfoxide **15** (303 mg, 1.84 mmol, 91 %) and bissulfoxide **17** (25 mg, 0.14 mmol, 7 %) as colorless solids. **15**: $R_f = 0.6$ (CH_2Cl_2/MeOH, 20 : 1); ^{1}H NMR (500 MHz, DMSO-d_6): $\delta = 1.10$ (d, $^{3}J = 6.9$ Hz, 3 H, CH_3), 1.27 (d, $^{3}J = 6.9$ Hz, 3 H, CH_3), 1.72 (ddd, $^{2}J = 14.8$ Hz, $^{3}J = 12$ Hz, $^{3}J = 11.8$ Hz, 1 H, 5-H_{ax}), 2.26 (dt, $^{2}J = 14.8$ Hz, $^{3}J = 2.5$ Hz, 1 H, 5-H_{eq}), 2.81 (ddd, $^{3}J = 12.2$ Hz, $^{3}J = 6.9$ Hz, $^{3}J = 2.3$ Hz, 1 H, 4-H), 3.16 (ddd, $^{3}J = 11.4$ Hz, $^{3}J = 6.9$ Hz, $^{3}J = 2.4$ Hz, 1 H, 6-H), 3.97 (d, $^{2}J = 12.3$ Hz, 1 H, 2-H_{ax}), 4.15 (d, $^{2}J = 12.3$ Hz, 1 H, 2-H_{eq}). The ^{1}H NMR data are in full agreement with published data.[2f] **17**: $R_f = 0.38$ (CH_2Cl_2/MeOH, 20 : 1); ^{1}H NMR (300 MHz, DMSO-d_6): $\delta = 1.28$ (d, $^{3}J = 6.9$ Hz, 6 H, 2×CH_3), 1.30–1.38 (m, 1 H, 5-H_{ax}), 2.23 (dq, $^{2}J = 16.8$ Hz, $^{3}J = 2.9$ H, 1 H, 5-H_{eq}), 3.11 (ddd, $^{3}J = 12.3$ Hz, $^{3}J = 6.9$ Hz, $^{3}J = 2.6$ Hz, 2 H, 4-H, 6-H), 4.32 (dd, $^{2}J = 9.8$ Hz, $^{4}J = 0.9$ Hz, 1 H, 2-H_{ax}), 4.97 (d, $^{2}J = 9.8$ Hz, 1 H, 2-H_{eq}). The ^{1}H NMR data are in full agreement with published data.[2f]

Oxidations with H_2O_2. H_2O_2 (35 %, 1–4 eq.) was added to a cooled (0 °C) solution of bissulfide **1**, **2**, or **3**, respectively (0.674–1.50 mmol) in AcOH (5 mL) and the mixture was stirred for 2 h at rt. CH_2Cl_2 (30 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The residue was thoroughly extracted with CH_2Cl_2, the filtrate was dried (Na_2SO_4, repeatedly extracted with CH_2Cl_2) and the washings were concentrated at reduced pressure.

Oxidations with *meta*-Chloroperbenzoic Acid (mcpba). mcpba (77 %, 1–4 eq.) was slowly added to a cooled (0 °C) solution of bissulfide **1**, **2**, or **3**, respectively (0.674–1.53 mmol) in CH_2Cl_2 (15 mL) and the mixture was stirred for 2 h at 0 °C. H_2O (1–2 mL) was added and the mixture was neutralized by addition of K_2CO_3 and filtered. The residue was thoroughly extracted with CH_2Cl_2 and the filtrate concentrated at reduced pressure.

Oxidations with Sodium Periodate ($NaIO_4$). $NaIO_4$ (1–4 eq.) was slowly added to a cooled (0 °C) solution of bissulfide **1**, **2**, or **3**, respectively (0.674–1.04 mmol) in MeOH/H_2O (3 : 1, 20 mL) and the mixture was stirred for 23 h at rt and filtered. The residue was thoroughly extracted with MeOH and the filtrate concentrated at reduced pressure.

Oxidations with Potassium Permanganate ($KMnO_4$). $KMnO_4$ (1–4 eq.) was added to a cooled (0 °C) solution of bissulfide **1**, **2**, or **3**, respectively (0.674–1.16 mmol) in acetone/H_2O (3 : 1, 20 mL) and stirred for 20 h at rt and filtered. The residue was thoroughly extracted with acetone and the filtrate concentrated at reduced pressure.

Evaluation of the Data. The quantitative determination of the composition in multi-component systems was achieved by referencing to an internal standard. The mandatory prerequisites (no signal overlap, sufficient signal-to-noise ratio) were sufficiently met by performing modern NMR experiments (pulsed mode) on highresolution spectrometers (500 or 600 MHz) with consistent measurement parameters (number of scans: 32; relaxation delay D1: 30 s). ^{1}H NMR spectra were measured with DMSO-d_6 as solvent and with *ortho*-xylene as internal standard. Analyte and standard were weighted to ensure comparable concentrations in all experiments. The concentration of the internal standard was kept at 20 mg/mL. The evaluation of the data was performed by comparison with reference compounds. The amounts of substances are given as shares of the total amount of substances for all identified products while the yields are given relative to the internal standard. The obtained averaged integrals were compared with those of the signals obtained for the methyl groups in *ortho*-xylene (singlet at 2.21 ppm).

Calculations. All structures were optimized at the B3LYP[41]/6-311++G(d,p)[42] level by using the Gaussian 09 software package.[43] The solvent H_2O was modeled with the CPCM-SCRF method.[44] Transition states were calculated at the same level of theory using the QST2 optimization routine[45] where the existence of only one imaginary frequency was confirmed by vibrational analyses.[46] Activation energies are given including zero-point correction without thermal correction. The NBO 3.1 software for natural bond orbital (NBO) analyses[23] was used as implemented in Gaussian 09.

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Conflict of Interest

The authors declare no conflict of interest.

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[1] a) M. Madesclaire, *Tetrahedron* **1986**, *42*, 5459–5495; b) N. S. Simpkins, *Sulphones in Organic Synthesis*, Pergamon Press, Oxford, **1993**; c) P. Metzner, A. Thuillier, *Sulfur Reagents in Organic Synthesis.*, Academic Press, London, **1994**; d) E. G. Mata, *Phosphorus Sulfur Silicon Relat. Elem.* **1996**, *117*, 231–286; e) C. Bolm, K. Muñiz, J. P. Hildebrand, in *Comprehensive Asymmetric Catalysis I–III, Vol. 2* (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer-Verlag, Berlin, **1999**, pp. 697–710; f) D. J. Procter, *J. Chem. Soc. Perkin Trans. 1* **2001**, 335–354; g) A. Lattanzi, in *Stereoselective Synthesis 3: Stereoselective Pericyclic Reactions, Cross Coupling, and C-H and C–X Activation, Vol. 3* (Ed.: P. A. Evans), Georg Thieme Verlag, Stuttgart, New York, **2011**, pp. 973–1015.

[2] a) T. Wedel, J. Podlech, *Org. Lett.* **2005**, *7*, 4013–4015; b) T. Wedel, M. Müller, J. Podlech, H. Goesmann, C. Feldmann, *Chem. Eur. J.* **2007**, *13*, 4273–4281; c) T. Wedel, T. Gehring, J. Podlech, E. Kordel, A. Bihlmeier, W. Klopper, *Chem. Eur. J.* **2008**, *14*, 4631–4639; d) T. Gehring, J. Podlech, A. Rothenberger, *Synthesis* **2008**, 2476–2487; e) R. Ulshöfer, J. Podlech, *J. Am. Chem. Soc.* **2009**, *131*, 16618–16619; f) R. Ulshöfer, T. Wedel, B. Süveges, J. Podlech, *Eur. J. Org. Chem.* **2012**, 6867–6877; g) B. D. Süveges, J. Podlech, *Eur. J. Org. Chem.* **2015**, 987–994.

[3] a) E. L. Eliel, R. O. Hutchins, *J. Am. Chem. Soc.* **1969**, *91*, 2703–2715; b) E. L. Eliel, *Acc. Chem. Res.* **1970**, *3*, 1–8.

[4] P. Kowalski, K. Mitka, K. Ossowska, Z. Kolarska, *Tetrahedron* **2005**, *61*, 1933–1953.

[5] a) A. Schöberl, A. Wagner, in *Houben-Weyl – Methoden der Organischen Chemie. Band IX Schwefel-, Selen-, Tellur-Verbindungen, Vol. IX* (Eds.: E. Müller, O. Bayer, H. Meerwein, K. Ziegler), Georg Thieme Verlag, Stuttgart, **1955**, pp. 207–221; b) K. Kaczorowska, Z. Kolarska, K. Mitka, P. Kowalski, *Tetrahedron* **2005**, *61*, 8315–8327.

[6] a) Y. G. Adewuyi, G. R. Carmichael, *Environ. Sci. Technol.* **1986**, *20*, 1017–1022; b) K. A. Vassell, J. H. Espenson, *Inorg. Chem.* **1994**, *33*, 5491–5498; c) P. Moreau, V. Hulea, S. Gomez, D. Brunel, F. Di Renzo, *Appl. Catal. A* **1997**, *155*, 253–263; d) V. R. Tumula, S. Bondwal, P. Bisht, C. Pendem, J. Kumar, *React. Kinet. Mech. Catal.* **2012**, *107*, 449–466.

[7] a) R. D. Bach, M.-D. Su, H. B. Schlegel, *J. Am. Chem. Soc.* **1994**, *116*, 5379–5391; b) S. L. Litvinenko, V. L. Lobachev, L. M. Dyatlenko, N. A. Turovskii, *Theor. Exp. Chem.* **2011**, *47*, 2–8.

[8] J.-W. Chu, B. L. Trout, *J. Am. Chem. Soc.* **2004**, *126*, 900–908.

[9] R. Curci, F. DiFuria, G. Modena, *J. Chem. Soc. Perkin Trans. 2* **1978**, 603–607.

[10] J. Kim, C.-H. Huang, *ACS ES&T Water* **2021**, *1*, 15–33.

[11] P. Hanson, R. A. A. J. Hendrickx, J. R. Lindsay Smith, *New J. Chem.* **2010**, *34*, 65–84.

[12] a) G. Modena, P. E. Todesco, *J. Chem. Soc.* **1962**, 4920–4926; b) R. Curci, R. A. DiPrete, J. O. Edwards, G. Modena, *J. Org. Chem.* **1970**, *35*, 740–745; c) S. Oae, T. Takata, *Tetrahedron Lett.* **1980**, *21*, 3213–3216; d) R. D. Bach, J. E. Winter, J. J. W. McDouall, *J. Am. Chem. Soc.* **1995**, *117*, 8586–8593; e) R. Benassi, L. G. Fiandri, F. Taddei, *J. Org. Chem.* **1997**, *62*, 8018–8023.

[13] B. M. Trost, T. N. Salzmann, K. Hiroi, *J. Am. Chem. Soc.* **1976**, *98*, 4887–4902.

[14] a) F. Ruff, Á. Kucsman, *J. Chem. Soc. Perkin Trans. 2* **1985**, 683–687; b) F. Ruff, A. Fábián, Ö. Farkas, Á. Kucsman, *Eur. J. Org. Chem.* **2009**, 2102–2111.

[15] L. I. Simándi, M. Jáky, A. M. Khenkin, *Inorg. Chim. Acta* **1987**, *134*, 187–189.

[16] D. G. Lee, T. Chen, *J. Org. Chem.* **1991**, *56*, 5346–5348.

[17] A. Jayaraman, A. L. L. East, *J. Org. Chem.* **2012**, *77*, 351–356.

[18] S. Jung, J. Podlech, *J. Phys. Chem. A* **2018**, *122*, 5764–5772.

[19] a) D. B. Chesnut, L. D. Quin, *J. Comput. Chem.* **2004**, *25*, 734–738; b) V. M. Bzhezovskii, N. N. Il'chenko, M. B. Chura, L. G. Gorb, L. M. Yagupol'skii, *Russ. J. Gen. Chem.* **2005**, *75*, 86–93; c) T. Clark, J. S. Murray, P. Lane, P. Politzer, *J. Mol. Model.* **2008**, *14*, 689–697.

[20] J. Podlech, *J. Phys. Chem. A* **2010**, *114*, 8480–8487.

[21] V. Rautenstrauch, *Bull. Soc. Chim. Fr.* **1994**, *131*, 515–524.

[22] P. B. Roush, W. K. Musker, *J. Org. Chem.* **1978**, *43*, 4295–4298.

[23] a) NBO, Version 3.1, E. D. Glendening, A. E. Reed, J. E. Carpenter, F. Weinhold,Theoretical Chemistry Institute, University of Wisconsin: Madison, WI, 2001; b) A. E. Reed, F. Weinhold, *J. Chem. Phys.* **1985**, *83*, 1736–1740; c) A. E. Reed, L. A. Curtiss, F. Weinhold, *Chem. Rev.* **1988**, *88*, 899–926; d) F. Weinhold, in *Encyclopedia of Computational Chemistry* (Ed.: P. von R. Schleyer), John Wiley & Sons, New York, **1998**, pp. 1792–1811.

[24] H. H. Szmant, H. F. Harnsberger, F. Krahe, *J. Am. Chem. Soc.* **1954**, *76*, 2185–2187.

[25] S. Wolfe, C.-K. Kim, *Can. J. Chem.* **1991**, *69*, 1408–1412.

[26] I. V. Alabugin, *J. Org. Chem.* **2000**, *65*, 3910–3919.

[27] J. I. Seeman, *Chem. Rev.* **1983**, *83*, 83–134.

[28] a) V. K. Aggarwal, I. W. Davies, R. J. Franklin, J. Maddock, M. F. Mahon, K. C. Molloy, *J. Chem. Soc. Perkin Trans. 1* **1991**, 662–664; b) V. K. Aggarwal, R. J. Franklin, M. J. Rice, *Tetrahedron Lett.* **1991**, *32*, 7743–7746; c) V. K. Aggarwal, I. W. Davies, R. Franklin, J. Maddock, M. F. Mahon, K. C. Molloy, *J. Chem. Soc. Perkin Trans. 1* **1994**, 2363–2368.

[29] I. V. Alabugin, M. Manoharan, T. A. Zeidan, *J. Am. Chem. Soc.* **2003**, *125*, 14014–14031.

[30] D. A. Sweigart, D. W. Turner, *J. Am. Chem. Soc.* **1972**, *94*, 5599–5603.

[31] A. A. Planckaert, J. Doucet, C. Sandorfy, *J. Chem. Phys.* **1974**, *60*, 4846–4853.

[32] a) G. S. Hammond, *J. Am. Chem. Soc.* **1955**, *77*, 334–338; b) D. Fărcasiu, *J. Chem. Educ.* **1975**, *52*, 76–79.

[33] a) E. J. Corey, D. Seebach, *Org. Synth.* **1970**, *50*, 72–74; *Org. Synth.* **1988**, *Coll. Vol. VI*, 556–559; b) E. L. Eliel, A. A. Hartmann, A. G. Abatjoglou, *J. Am. Chem. Soc.* **1974**, *96*, 1807–1816.

[34] W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* **1978**, *43*, 2923–2925.

[35] E. Anklam, *Synthesis* **1987**, 841–843.

[36] a) N. E. Shevchenko, V. G. Nenaidenko, E. S. Balenkova, *Russ. Chem. Bull.* **2000**, *49*, 1415–1420; b) K. Ogura, G.-i. Tsuchihashi, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 2203–2204.

[37] K. Ogura, M. Suzuki, G.-i. Tsuchihashi, *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1414–1416.

[38] Y. Arroyo-Gómez, J. A. López-Sastre, J. F. Rodríguez-Amo, M. Santos-García, M. A. Sanz-Tejedor, *J. Chem. Soc. Perkin Trans. 1* **1994**, 2177–2180.

[39] H. Böhme, U. Sitorius, *Chem.-Ztg.* **1972**, *96*, 37–38.

[40] C. McLaughlin, A. M. Z. Slawin, A. D. Smith, *Angew. Chem.* **2019**, *131*, 15255–15263; *Angew. Chem. Int. Ed.* **2019**, *58*, 15111–15119.

[41] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648–5652; c) W. Koch, M. C. Holthausen, *A Chemist's Guide to Density Functional Theory*, 2. ed., Wiley-VCH, Weinheim, **2002**.

[42] a) A. J. H. Wachters, *J. Chem. Phys.* **1970**, *52*, 1033–1036; b) P. J. Hay, *J. Chem. Phys.* **1977**, *66*, 4377–4384; c) A. D. McLean, G. S. Chandler, *J. Chem. Phys.* **1980**, *72*, 5639–5648; d) R. Krishnan, J. S. Binkley, R. Seeger, J. A. Pople, *J. Chem. Phys.* **1980**, *72*, 650–654; e) T. Clark, J. Chandrasekhar, G. W. Spitznagel, P. von R. Schleyer, *J. Comput. Chem.* **1983**, *4*, 294–301; f) K. Raghavachari, G. W. Trucks, *J. Chem. Phys.* **1989**, *91*, 1062–1065.

[43] Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. L. Caricato, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J., S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc.: Wallingford CT, 2009.

[44] a) A. Klamt, G. Schüürmann, *J. Chem. Soc. Perkin Trans. 2* **1993**, 799–805; b) V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995–2001; c) M. Cossi, N. Rega, G. Scalmani, V. Barone, *J. Comput. Chem.* **2003**, *24*, 669–681.

[45] a) C. Peng, H. Bernhard Schlegel, *Isr. J. Chem.* **1993**, *33*, 449–454; b) C. Peng, P. Y. Ayala, H. B. Schlegel, M. J. Frisch, *J. Comput. Chem.* **1996**, *17*, 49–56.

[46] a) B. G. Johnson, M. J. Frisch, *Chem. Phys. Lett.* **1993**, *216*, 133–140; b) B. G. Johnson, M. J. Fisch, *J. Chem. Phys.* **1994**, *100*, 7429–7442; c) R. E. Stratmann, J. C. Burant, G. E. Scuseria, M. J. Frisch, *J. Chem. Phys.* **1997**, *106*, 10175–10183.

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