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REVIEW

Dialkoxy disulfides and their branch-bonded thionosulfite isomers

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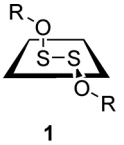
A historical review on the synthesis, physical properties and chemistry of the highly chalcogenated dialkoxy disulfides (ROSSOR) and their isomeric thionosulfites (ROS(S)OR) is provided.

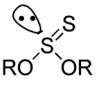
Keywords: Dialkoxy disulfides; Thionosulfite isomers; Synthesis and characterization; Thermochemistry

1. Introduction to compounds containing the OSSO moiety

Although molecules of the form ROSSOR **1**, ester derivatives of hydrothiosulfurous acid HOSSOH, have been known for over a century [1], it was not until 1964 that Thompson and coworkers [2–4] confirmed that this functionality could potentially exist in two separate isomeric forms, namely dialkoxy disulfides **1** and a branch-bonded arrangement, the thionosulfites **2**. Other isomers such as the thiosulfite **3** or the thiosulfonate ester (RSO_2SR) **4** earlier proposed by Zinner [5] were readily ruled out by ^{1}H NMR spectroscopy, while other early work [6–9] (Raman, [10, 11] dipole moment measurements [10]) failed to fully distinguish **1** from **2** though it did suggest the connectivity in **1**.



1



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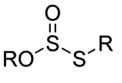

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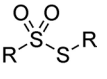

4

For R = Et, Thompson observed a characteristic magnetic non-equivalence of the methylene protons in the ^{1}H NMR at room temperature. The origin of this diastereotopicity was not determined: one of two possible conclusions could be drawn. The compound could have connectivity of form **2**, which would have an associated high thermal barrier to pyramidal

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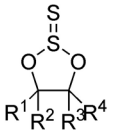
inversion [12–14] about the branched sulfur, as exists with analogous sulfite [15–17] and sulfoxide [18–27] systems. As examples, Thompson has reported that the non-equivalence of the methylene protons in diethyl sulfite is maintained at 145 °C [28] and the barrier to inversion for DMSO is reported [27] to be 39.7 kcal mol^{-1}. Conversely, an inherently high barrier about the sulfur–sulfur bond could be responsible. Here, the compound would adopt a *gauche* conformation in the ground state and would have form **1** [29]. A coalescence of the ABX_3 pattern to that of a simple A_2X_3 pattern for **1** has been observed at 100 °C, suggesting the connectivity of **1** over that of the branched **2** (barriers [22] for sulfoxide inversion can be as high as 85 kcal mol^{-1}).

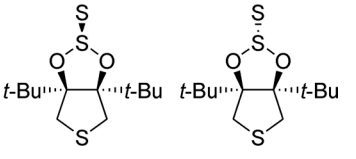
Since Thompson's original work, few investigations into the physical properties of dialkoxy disulfides have been published [30–34]. As well as two other papers from our laboratory [35, 36], these results are profiled in detail throughout this review. Besides their unusual physical properties, substituted benzyloxy disulfides inhibit the growth of certain microorganisms (*E. coli* and *S. aureus*) [37].

Although compounds with a branched sulfur are known [38], there are relatively few examples. Foss [39] had originally suggested that valence expansion of the branched sulfur could be stabilized by adjoining electronegative atoms (F, O). Those of form **2** are rare, having been characterized [2, 40–42] only four times, with each of the thionosulfites containing a five-membered ring core (**5a**–**5n**). Only in cyclic compounds has the thionosulfite connectivity been structurally verified (**5g**, **5i**, **5m** and **5n** by X-ray) [40–42].



5

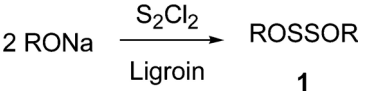
5a $R^1 = R^4 = Me$ (*cis*); $R^2 = R^3 = H$
5b $R^1 = R^3 = Me$ (*trans*); $R^2 = R^4 = H$
5c $R^1 = R^2 = R^3 = R^4 = H$
5d $R^1 = H$; $R^2 = R^3 = H$; $R^4 = Me$
5e $R^1 = R^4 = Ph$ (*cis*); $R^2 = R^3 = H$
5f $R^1 = R^3 = Ph$ (*trans*); $R^2 = R^4 = H$
5g $R^1,R^2 = R^3,R^4 = -(CH_2)_5-$
5h $R^1,R^2 = R^3,R^4 = -(CH_2)_4-$
5i $R^1,R^2 = R^3,R^4 = -(CH_2)_6-$
5j $R^1,R^2 = R^3,R^4 = -(CH_2)_7-$
5k $R^1,R^2 = -(CH_2)_5-$; $R^3 = R^4 = Me$
5l $R^1,R^2 = -(CH_2)_6-$; $R^3 = R^4 = Me$



5m **5n**

2. Synthesis of dialkoxy disulfides

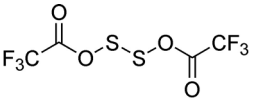
Dialkoxy disulfides **1** (where R = Me **6**, Et **7**) were originally synthesized from the reaction of S_2Cl_2 with a suspension of the sodium alkoxide in ligroin [43] (scheme 1) [1].



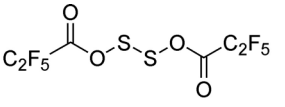
SCHEME 1

Larger homologues (R = *n*-Pr **8**, *n*-Bu **9**) were subsequently synthesized by Stamm [44] using the same procedure. Hackling [45] reported the synthesis of fluorinated derivatives (R = $(CF_3)_2CH$- **10**, CF_3CH_2- **11**) using lithium alkoxides at 50 °C. As will become evident, the use of S_2Cl_2 at elevated temperatures is quite uncommon. Although not strictly dialkoxy

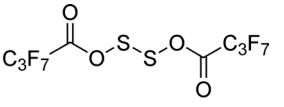
disulfides, as they are derived from silver acid salts and not alcohols, **12a**–**12c** synthesized by Wang [46] in excellent yield (>90%) are included for completeness. These compounds are thermally unstable and decompose readily to form the anhydride, SO_2 and sulfur [47].



12a

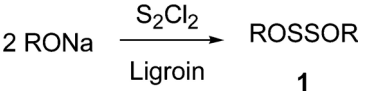


12b



12c

In 1965, Thompson modified the procedure as it became increasingly difficult to prepare dry alcohol-free sodium alcoholates of higher molecular weight homologs. He synthesized several dialkoxy disulfides in good yield by coupling S_2Cl_2 to the alcohol **13** in the presence of an amine base (in his case NEt_3) which would serve as an HCl scavenger (scheme 2). His work is highlighted within tables 1, 2, 4 and 5.

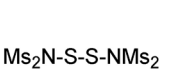


SCHEME 2

Thompson used long addition (or reaction) times under relatively dilute conditions ($[S_2Cl_2] = 3.3$ M), employing a slight excess of alcohol at 10–15 °C (though the reaction could be performed at room temperature). This work has been patented [48] and the general procedure has been used by others [33, 35, 49–51]. Some groups have claimed better yields with ethereal solvents [52, 53] and low temperature work-up and still others have synthesized **1** in THF [54] (no yield reported) or have used pyridine [55] as the HCl acceptor. Most recently, we [56] have modified the reaction conditions to optimize yields for a wide range of substrates. Here, addition (or reaction) times of S_2Cl_2 have been reduced by 90%, though addition (or reaction) times have increased and the purity of the reagents and the use of dilute conditions during the S_2Cl_2 addition were both deemed important factors in obtaining high yields.

Dialkoxy disulfides appear to be formed *via* two simple nucleophilic displacements of chloride by the alcohol, but Steudel [57] as well as Möckel [58, 59] have reported the presence of many other homologs ROS_nOR (with R = Me, n = 1, 2, 4–15; with R = Bu, n = 1–15) by reversed-phase HPLC; peaks were identified based on the relationship that the natural logarithm of the retention time is linearly related to the number of sulfur atoms. The addition of Na_2S_x (from Na_2S and S_8) in the reaction promoted the formation of sulfur allotropes S_7 and S_8.

The formation of **1** is not limited to the use of S_2Cl_2 as the sulfur transfer reagent, though it is the one most frequently employed and the one whereby the highest yields have been reported. Blanschette [60] reported the synthesis of dibutoxy disulfide **9** in moderate yield (46%) using **14** in CH_2Cl_2 at room temperature, whereas the use of other sulfur transfer reagents such as **15a** and **15b** [51], developed in our laboratory [61], has had limited success [56].



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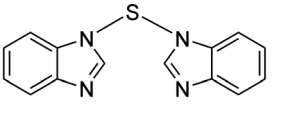
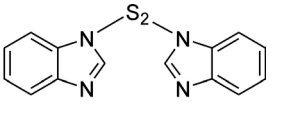


15a



15b

Wenschuh and Rotzel [62] reported the formation of dipropoxy disulfide **8** and di-isopropoxy disulfide **16** through the metathesis of n-Bu_3SnOR (where R = n-Pr, i-Pr) with S_2Cl_2 in excellent yields. This method has not been exploited, most likely due to the need to use toxic stannyl alkoxides as the alcohol derivatives.

Tables 1–5 list the acyclic dialkoxy disulfides synthesized to date in the literature.

As is evident from the tables, the synthesis of dialkoxy disulfides using the method developed by Thompson [3] or derivatives thereof is extremely tolerant to substitution. In general, as the amount of substitution and steric bulk increases on the α-carbon the yield decreases.

We have carried out the first synthesis of cyclic dialkoxy disulfides in moderate-to-excellent yield (table 6).

Compound **61** was the desired synthetic target but we could isolate novel bis(dialkoxy disulfide) **62** in poor yield, which is a dimerized by-product of **61**. Crystal structures for both of these compounds have been obtained. Independent synthesis of **62** with 2 equivalents of S_2Cl_2 to diol proved unsuccessful. Using similar methodology, we isolated **63** in moderate yield. From our theoretical investigation, coupled with our experimental results, it appears that form **1** is the more stable isomer only when the core ring size is greater than seven atoms.

3. Synthesis and characterization of thionosulfites

In 1964, Thompson treated dl-2,3-butanediol with S_2Cl_2 and NEt_3 at 10 °C under high dilution conditions in CH_2Cl_2; the unstable product did not exhibit coalescence of the AB pattern and was proposed to exist as a thionosulfite (form **2**). Evidence for this conclusion was derived from the close spectroscopic similarities between the ^{1}H NMR of this class of compounds compared with the sulfite analog as well as similar UV and IR data; in general, **2** are not shelf-stable [36]. Thompson also prepared and isolated pure thionosulfites **5e** and **5f** from *meso*-hydrobenzoin **64a** in low yield (5–44%) through fractional recrystallization [2, 64]. In this particular case, he synthesized the products from the magnesium alcoholates (scheme 3). The corresponding

Table 1. Conditions and yields for the synthesis of simple dialkyloxy disulfides.

Entry	R	Compd	Method[a]	Solvent [43]	Temp (°C)[b]	Yield (%)[c]	Bp (°C, mmHg)	Ref.[d]
1	Me	**6**	A	ligroin		37 [1]		1, 11
2	Et	**7**	A	ligroin		41 [1]		1, 10
3	n-Pr	**8**	A	ligroin				44
4	n-Pr	**8**	C	CH_2Cl_2	10–15	74 [3]		3
5	n-Pr	**8**	G			94	36–38 (3.9)	62
6	i-Pr	**16**	C	CH_2Cl_2	10–15	71 [3]	48 (100.0)	3, 49
7	i-Pr	**16**	G			87	55–56 (2.0)	62
8	n-Bu	**9**	A	ligroin				44
9	n-Bu	**9**	C	CH_2Cl_2	10–15	70 [3]	71 (0.7)	3
10	n-Bu	**9**	E		Room temp	46	71 (0.7)	60
11	s-Bu	**17**	C	CH_2Cl_2	10–15		58 (1.0)	49
12	t-Bu	**18**	C	CH_2Cl_2	10–15		49 (1.0)	49
13	t-Bu, Me[e]	**19**	C	CH_2Cl_2	10–15			33
14	t-Bu-CH_2–	**20**	C	CH_2Cl_2	10–15	72 (0.8)	49	

[a]Method A: 2RONa + S_2Cl_2; method C: 2ROH + S_2Cl_2 + 2NEt_3, 1 h addition time, 1.25 h total reaction time; method E: 2ROH + $(Ms_2N)_2S_2$, 4 h; method G: 2 Bu_3SnOR + S_2Cl_2. [b]Temperature during the addition of S_2Cl_2 or, if none, the reaction temperature. [c]Yields after distillation and correcting for impurities by GLC. [d]References reported for all those who synthesized the compound. [e]Only known asymmetric dialkoxy disulfide.

Table 2. Conditions and yields for the synthesis of simple dialkyloxy disulfides.

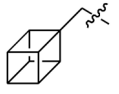
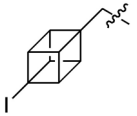
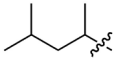
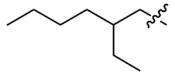
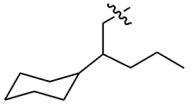
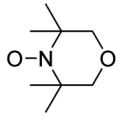
Entry	R	Compd	Method[a]	Solvent	Temp (°C)[b]	Yield (%)	Bp (°C, mmHg)	Mp(°C)	Ref.[c]
1		**21**	C	CH_2Cl_2	0	85			50
2		**22**	C	CH_2Cl_2	0	89			50
3[e]		**23**	C	CH_2Cl_2	10–15	83	67 (0.8)	3	
4		**24**	C	CH_2Cl_2	10–15	80[3]			3
5		**24**	G	CH_2Cl_2	0	69			56
6	$n-C_8H_{17}$	**25**	C	CH_2Cl_2	10–15	90		−22	3
7[e]		**26**	C	CH_2Cl_2	10–15	85	147 (0.8)[d]		3

Table 2. Continued.

Entry	R	Compd	Method[a]	Solvent	Temp (°C)[b]	Yield (%)	Bp (°C, mmHg)	Mp(°C)	Ref.[c]
8	n-$C_{12}H_{25}$	**27**	C	CH_2Cl_2	10–15	85		15–16	3
9	n-$C_{18}H_{37}$	**28**	C	CH_2Cl_2	10–15	85		50–51	3
10[e]		**29**	C	CH_2Cl_2	10–15	90			3
11	cholesteryl	**30**	C	CH_2Cl_2	10–15	48		179–180[d]	3
12	$EtSCH_2CH_2$–	**31**	C	CH_2Cl_2	10–15	70	135 (0.5)[d]		3
13	$EtOCH_2CH_2$–	**32**	C	CH_2Cl_2	10–15	85	117 (1.1)[d]		3
14		**33**	C	−30	68			100–104	55

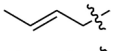
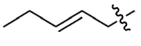
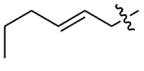
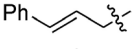
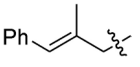
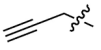
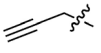
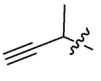
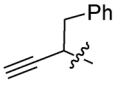
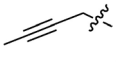
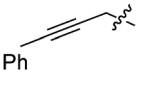
[a]Method C: $2ROH + S_2Cl_2 + 2NEt_3$, 1 h addition time, 1.25 h total reaction time; method G: $2ROH + S_2Cl_2 + 2NEt_3$, 5 min addition time, 5 h total reaction time. [b]Temperature during the addition of S_2Cl_2 or if none, the reaction temperature. [c]References reported for all those who synthesized the compound. [d]Decomposed upon heating. [e]No stereochemistry reported.

Table 3. Conditions and yields for the synthesis of fluorinated dialkoxy disulfides and related compounds.

Entry	R	Compd	Method[a]	Temp (°C)[b]	Yield (%)	Bp (°C, mmHg)	Mp(°C)	Ref.[c]
1	$(CF_3)_2CH$-	**10**	B	50	80	61 (30.0)		45
2	CF_3CH_2–	**11**	B	50	80	78 (76.0)		45
3	CF_3CO_2	**12a**	F		>90		TU[d]	46
4	$C_2F_5CO_2$	**12b**	F		>90		TU[d]	46
5	$C_3F_7CO_2$	**12c**	F		>90		TU[d]	46

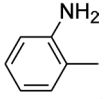
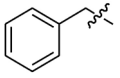
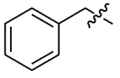
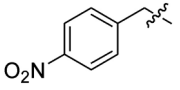
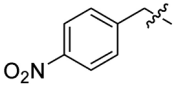
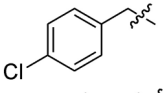
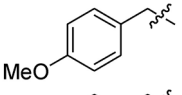
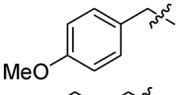
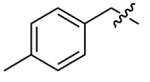
[a]Method B: $2ROLi + S_2Cl_2$; method F: $ROAg + S_2Cl_2$, under vacuum. [b]Temperature during the addition of S_2Cl_2 or, if none, the reaction temperature. [c]References reported for all those who synthesized the compound. [d]TU – thermally unstable.

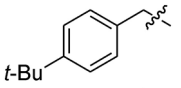
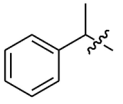
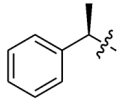
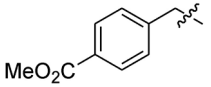
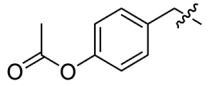
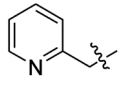
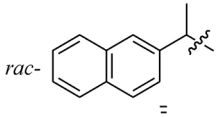
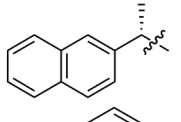
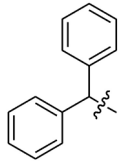
Table 4. Conditions and yields for the synthesis of allylic and propargylic dialkoxy disulfides.

Entry	R	Compd	Method[a]	Solvent	Temp (°C)[b]	Yield (%)	Ref.[c]
1		**34**	C	Et_2O[d]	0	87 [52]	3, 52
2		**34**	G	CH_2Cl_2	0	82	56
3[e]		**35**	C	Et_2O[d]	0	62	52
4		**36**	C	Et_2O[d]	0	95	52
5		**37**	C	Et_2O[d]	0	98	52
6		**38**	C	Et_2O[d]	0	87	52
7		**39**	C	Et_2O[d]	0	90	52
8		**40**	C	Et_2O[d]	0	95	52
9		**41**	C	Et_2O[d]	0	93	52
10		**42**	C	Et_2O[d]	0	98	53
11		**42**	G	CH_2Cl_2	0	57	56
12[e]		**43**	C	Et_2O[d]	0	>91, <98	53
13[e]		**44**	C	Et_2O[d]	0	>91, <98	53
14		**45**	C	Et_2O[d]	0	>91, <98	53
15		**46**	C	Et_2O[d]	0	>91, <98	53

[a]Method C: $2ROH + S_2Cl_2 + 2NEt_3$, 1 h addition time, 1.25 h total reaction time; method G: $2ROH + S_2Cl_2 + 2NEt_3$, 5 min addition time; 5 h total reaction time. [b]Temperature during the addition of S_2Cl_2 or, if none, the reaction temperature. [c]References reported for all those who synthesized the compound. [d]Low temperature work-up. [e]No stereochemistry reported.

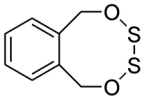
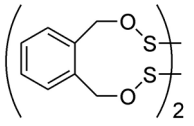
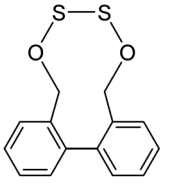
Table 5. Conditions and yields for the synthesis of aryl and benzyl dialkoxy disulfides.

Entry	R	Compd	Method[a]	Solvent	Temp (°C)[b]	Yield (%)	Bp (°C, mmHg)	Mp(°C)	Ref.[c]
1		**47**	C	THF	0–4			84.2	54
2		**48**	C	CH_2Cl_2	0	88 [35]		50–51 [35]; 58–59[49]	3, 35, 49
3		**48**	G	CH_2Cl_2	0	83		47–52	56
4		**49**	C	CH_2Cl_2	0	90 [35]		92–93 [35]; 100–101[33]	33, 35
5		**49**	G	CH_2Cl_2	0	97		95–96	56
6		**50**	C	CH_2Cl_2	0	86		45–47	35
7[d]		**51**	C	CH_2Cl_2	0	62		34–36	35
8[d]		**51**	G	CH_2Cl_2	0	93		37–38	56
9		**52**	C	CH_2Cl_2	0	82		Liquid	35

10		**52a**	G	CH_2Cl_2	0	90		ca. -10	56
11	*rac*- 	**53**	C	CH_2Cl_2	0	80			51
12		**54**	C	CH_2Cl_2	0				51
13		**55**	C	CH_2Cl_2	0	63	44–46		51
14		**56**	C	CH_2Cl_2	0	25			51
15		**57**	C	CH_2Cl_2	0	75[d]			51
16	*rac*- 	**58**	C	CH_2Cl_2	0	12			51
17		**59**	C	CH_2Cl_2	0	69			51
18		**60**	G	CH_2Cl_2	0	86		42–46	56

[a]Method C: $2ROH + S_2Cl_2 + 2NEt_3$, 1 h addition time, 1.25 h total reaction time; method G: $2ROH + S_2Cl_2 + 2NEt_3$, 5 min addition time, 5 h total reaction time. [b]Temperature during the addition of S_2Cl_2 or if none, the reaction temperature. [c]References reported for all those who synthesized the compound. [d]Decomposed entirely upon chromatography.

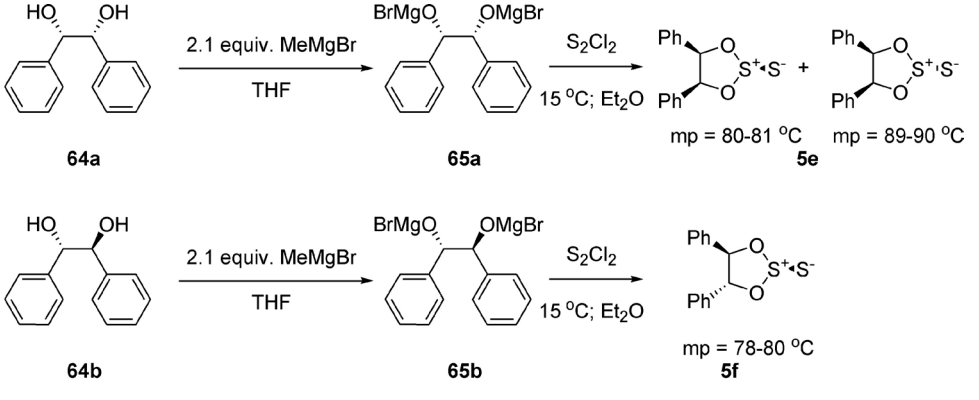
Table 6. Conditions and yields for the synthesis of cyclic dialkoxy disulfides.

Entry	Compd	Method[a]	Solvent	Temp (°C)[b]	Yield (%)	Addition time min	Mp(°C)	Ref.[c]
1	 **61**	H	CH_2Cl_2	0	96	10	59–60	63
2	 **62**	H	THF	0	9	10	153–155	63
3	 **63**	H	CH_2Cl_2	0	25	10	ca. -10	63

[a]Method H: 1ROH + S_2Cl_2 + 2NEt_3, 5.5 h addition time. [b]Temperature during the addition of S_2Cl_2 or if none, the reaction temperature. [c]References reported for all those who synthesized the compound.

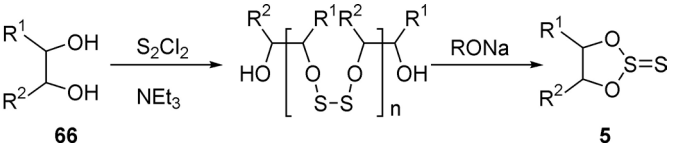
sulfites [65] for the two isomeric forms of **5e** and of **5f** were thermally more stable (130–131, 129–131, and 85–86 °C respectively – scheme 3) than the thionosulfites.

A diagnostic feature of thionosulfites is the presence of non-equivalent protons on the α-carbons in the proton NMR spectrum that are similar to the spectra of the corresponding sulfites, suggesting a similar orientation of the S=S bond with respect to the S=O moiety. For instance **5c**, a lachrymatory liquid, displays an A_2B_2 pattern.



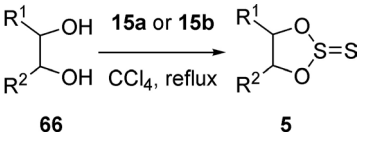
SCHEME 3

Thompson [64] proposed that the reaction pathway involved the formation of a polymer under high dilution conditions of S_2Cl_2. He suggested (scheme 4) that an alkoxide-catalyzed unzipping of the proposed polymeric intermediate would yield a thionosulfite as a cyclic monomeric product (this reaction was performed under reduced pressure at 80–120 °C).



SCHEME 4 Proposed mechanism for the formation of thionosulfites.

Our method [41] of preparation, using sulfur transfer reagents **15a** and **15b**, resulted in similar yields but with no polymeric side-products (scheme 5). While both **15a** and **15b** were effective sulfur transfer reagents in the synthesis of thionosulfites, they proved quite ineffective during the synthesis of isomeric dialkoxy disulfides (*vide supra*). In this manner, thionosulfites **5g–5l** were synthesized (table 7). The *mono*sulfur transfer reagent **15a**, produced thionosulfites in moderate yield (21–50%) while the *di*sulfur transfer reagent **15b** was generally more effective (14–80%) and was used for all the precursor 1,2-diols (**66**) examined. For all thionosulfites, column chromatography was sufficient to obtain analytically pure samples. While isolable, some of the thionosulfites were nevertheless unstable at room temperature or upon extended exposure to light.



SCHEME 5 Synthesis of thionosulfites using either method A or B (cf. table 7).

The mechanism of the formation of thionosulfites remains unclear, particularly with respect to the involvement of *mono*sulfur reagent **15a**. The lack of polymeric side-products suggests that the mechanism for the process in scheme 5 is different to that originally advanced by Thompson (scheme 4). No evidence for the formation of a sulfoxylate ester (ROSOR) intermediate has been found, though Nakayama [42] postulated its existence in the formation of his thionosulfites **5m** and **5n**. Moreover, the only by-product observed was that of benzimidazole; Nakayama [42] has postulated the formation of bibenzimidazole, which was never directly detected.

The proton decoupled ^{13}C NMR spectra of thionosulfites **5g–5l** reveal the expected magnetic anisotropy resulting from the presence of a stereogenic branched-sulfur center. The extent of the influence of the branch-bonded sulfur atom has been hypothesized to be due to its pseudo-axial

Table 7. Yields of some thionosulfites.

Entry	R^1	R^2	R^3	R^4	Diol	Product	Yield (%)
1	$-(CH_2)_5-$		$-(CH_2)_5-$		**66a**	**5g**	50[a]; 41[b]
2	$-(CH_2)_4-$		$-(CH_2)_4-$		**66b**	**5h**[c]	21[a]; 80[b]
3	$-(CH_2)_6-$		$-(CH_2)_6-$		**66c**	**5i**	47[b]
4	$-(CH_2)_7-$		$-(CH_2)_7-$		**66d**	**5j**	14[b]
5	$-(CH_2)_5-$		Me	Me	**66e**	**5k**[c]	72[b]
6	$-(CH_2)_6-$		Me	Me	**66f**	**5l**	77[b]

[a]Method A: 1:1 diol:**15a** in refluxing CCl_4. [b]Method B: 1:1 diol: **15b** in refluxing CCl_4. [c] ^1H NMR data is missing for these two entries; the characterization is therefore incomplete although existing data is consistent with the assigned structures.

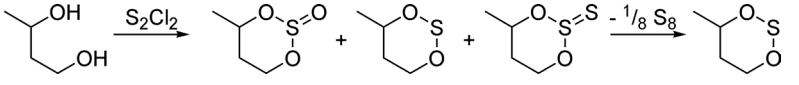
orientation with respect to the five-membered ring core as well as the polarization that exists within the S-S bond. Indeed, Steudel and co-workers showed *via* calculations that the branched sulfur–sulfur bond is polarized, with the terminal sulfur being negatively charged [30]. The observed downfield shift of the signal of the γ-carbon with respect to the S=S bond as compared with the parent diol **66** is a manifestation of this polarization. In fact, the deshielding and shielding zones of the thionosulfite functionality are analogous to that of the sulfite [42].

Although quite similar, the NMR spectra of the thionosulfites are distinct from the analogous sulfites. In addition, the absence of a strong band between 1180 and 1240 cm^{-1} indicates the absence of the sulfite (S=O) moiety. A consistent feature in the infrared of the thionosulfites synthesized is a strong band at 655 cm^{-1}, indicating an S−S (S=S) stretch; this is in clear agreement with the theoretical [36] and experimental literature [42, 63].

One characteristic feature of the MS common to all the thionosulfites is the base peak representing the loss of the HS_2O_2 (m/z 97) moiety from the parent ion. The feature common to the MS of dialkoxy disulfides is the initial loss of SO (m/z 48) from the parent ion.

Most recently, using our procedure (solvent: MeCN at room temperature), Nakayama [42] have reported the synthesis of a fused 5,5-bicycle containing a thionosulfite moiety in two diastereomeric forms. These were isolated by column chromatography then by HPLC to afford **5m** (45%) and **5n** (10%). No thermal isomerization between **5m** and **5n** was possible, even at 120 °C.

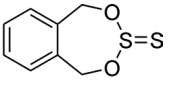
The formation of larger ring homologues has to date generally proven unsuccessful [64]. The reaction of 1,3-butanediols **67** with S_2Cl_2 primarily gave low molecular weight polymeric product which, when subjected to an aklomide-catalyzed degradation, afforded sulfite **68**, sulfoxylate **69** as well as transient formation of what was believed to be thionosulfite **70**. This latter compound decomposed to the sulfoxylate **69** due to facile loss of elemental sulfur (scheme 6). Attempts to form thionosulfites from 1,4-butanediols proved completely unsuccessful, affording only polymeric mixtures of products. No other attempts with larger diols have been reported.



67 **68** **69** **70** **69**

SCHEME 6

As part of our investigation [63] into the factors that govern dialkoxy disulfide and thionosulfite stability we were able to isolate and crystallize **71** in 22% yield. Compound **71** is the first isolated non-five-membered ring thionosulfite.



71

4. Comparison of thionosulfites with other compounds containing branched sulfur atoms directly bonded to sulfur

There are few examples of stable molecules containing a branch-bonded sulfur atom directly bonded to another sulfur atom [38]. The concept of the existence of branch-bonded S−S species has generated considerable debate and investigation [66]. Foss first popularized the notion that branch-bonded sulfur molecules of the form $X_2S{=}S$, bonded *via* $S_{3d}-S_p$ orbital interactions, and that these were only stabilized when the branched sulfur was attached to an electronegative

Table 8. Experimentally determined r(S−S) for hypervalent sulfur–sulfur bond-containing compounds.

Compd	r(S−S) Å	Method	Ref
			67,
$F_2S{=}S$ (**72**)	1.860 ± 0.015	ED, MW	68
O=S=S	1.884 ± 0.010	MW	69
S=S	1.892	MW	70
RN=S=S	1.898	X-ray	71
$(RO)_2S{=}S$ (**5g**)	1.901	X-ray	40
$(RO)_2S{=}S$ (**5i**)	1.910	X-ray	41
$(RO)_2S{=}S$ (**5m**)	1.9154 ± 0.0006	X-ray	42
$(RO)_2S{=}S$ (**5n**)	1.8964 ± 0.0013	X-ray	42
$(RO)_2S{=}S$ (**71**)	1.9361 ± 0.0006	X-ray	63
$Ph_3P{=}NSN{=}S{=}S$	1.908 ± 0.002	X-ray	72
O=S=S=O	2.024	ED	73

group [39, 66]. The S−S bond in these compounds is classically written as if it were a true double bond. Their r(S−S)s are shown in table 8.

The structure of **72** was confirmed by MW and ED studies and contains the shortest known S-S bond [67, 68, 74]. The long S−S bond for planar S_2O_2 has been ascribed to a partial delocalization of the oxygen lone pairs into the σ^*_{S-S} bond, leading to a strengthening of the S−O bond at the expense of the S−S bond. Nevertheless, most compounds in table 8 possess an extremely short S−S bond, indicative of their double bond character. The thionosulfites **5g**, **5i**, **5m** and **5n** have a r_{av}(S−S) = 1.906 ± 0.009 Å. Thionosulfite **71** has a longer r(S−S) than any other reported S=S bond (except gaseous S_2O_2). This is due to the two $n_O \rightarrow \sigma^*_{S=S}$ stereoelectronic donations present in **71**, which contribute to a lengthening of the S=S bond. The greater orbital overlap in **71** *vs*. the other thionosulfites is due to the axial orientation of the S=S bond with respect to the chair conformation of the seven-membered ring core.

5. RO−S−S−OR *vs*. $(RO)_2S{=}S$, (R = H, R') connectivity

Steudel and co-workers have carefully investigated *via* calculations the isomerization between alkoxydisulfides and thionosulfites. The transient preparation of dihydroxy disulfide HOSSOH (**73a**), the unbranched form of thiosulfurous acid, has been reported [75, 76]; however, there is no information on its physical properties, but it has been observed in the EI mass spectrometry of parent ROSSOR compounds (R = alkyl), which are known to exist [77].

There are at least 11 isomeric structures of HOSSOH (**73**) and their geometries and energies have been calculated. The four lowest energy isomers are shown in table 9 [30].

The relative energy differences of the first three structures (**73a–73c**) are small as compared with the fourth, **73d**. When the energies of these three structures are further refined using larger basis sets (MP2/6-311G**//HF/6-311G^{**} + ZPE), their relative energy differences decrease

Table 9. Calculated [30] relative energies (kcal mol^{-1}) of the four most stable isomers of HOSSOH (73).

	HO−S−S−OH **73a**	HO−S(=O)−SH **73b**	HO−S(=S)−OH **73c**	H−S(=O)(=O)−SH **73d**
MP4/6-31g*//HF/6-31G*	0	3.2	3.9	23.5

(**73a** = 0, **73b** = −0.3, **73c** = 3.2 kcal mol^{-1}); **73b** has not been experimentally detected. The related tetrasulfide HSSSSH (**74a**) is 33.0 kcal mol^{-1} more stable than its branch-bonded analog $(HS)_2S{=}S$ (**74b**) [74] whereas the branch-bonded S_2F_2 (**72**) is the more stable isomer in that system [78]. The inclusion of electronegative atoms such as oxygen then stabilizes the branch bonded form **73b** over the unbranched **73a**.

Esters of dihydroxy disulfide can be easily prepared (*vide supra*). To date, the unbranched geometry ROSSOR has been structurally resolved in both acyclic and, more recently, in cyclic forms (acyclic − R = Me **6**, [31, 32, 79] *p*-NO_2-Bn **49**, [35, 36] *p*-Cl-Bn **50** [51]; cyclic - **61**, **62** [63]).

As highlighted earlier, thionosulfites containing a five-membered ring core can be prepared. To our knowledge **71** is the only thionosulfite synthesized that does not contain this defining structural feature; no acyclic thionosulfite is known. Recently, we investigated the source of isomeric stability and concluded, from a combined theoretical and experimental study, that dialkoxy disulfides are the more stable isomeric forms when the core ring size is sufficiently large (eight atoms or larger) or acyclic (which may be thought of as an infinitely large ring). Below this threshold, thionosulfites are more stable. This appears to be due to the decreased conformational stability in small-ringed dialkoxy disulfides which must significantly distort their O−S−S−O dihedral angles from ca. 90° to accommodate the ring [63].

6. Physical properties of acyclic dialkoxy disulfides

Dialkoxy disulfides possess novel structural features. Of note is the very short S−S bond for MeOS–SOMe (**6**) r(S−S) = 1.972 Å [32]; for **22** r(S−S) = 1.970 Å [50]; for *p*-NO_2-BnOS−SOBn-*p*-NO_2 (**49**) r(S−S) = 1.968 Å [36]; for *p*-Cl-BnOS−SOBn-*p*-Cl **50** r(S−S) = 1.933 Å [51]; for **61** r(S−S) = 1.959 Å [63]; for **62** r(S−S) of 1.964 Å [63]. τ(OS−SO) for all of these examples is ca. 90°, which is unremarkable for XSSX systems but the θ(O−S−S) of ca. 108° is larger than θ(C−S−S) in standard disulfides. Stabilization of the 90° conformation is due to two observed 'generalized anomeric effects' resulting from the two n(S) → σ^*(S−O) MO interactions [33, 80].

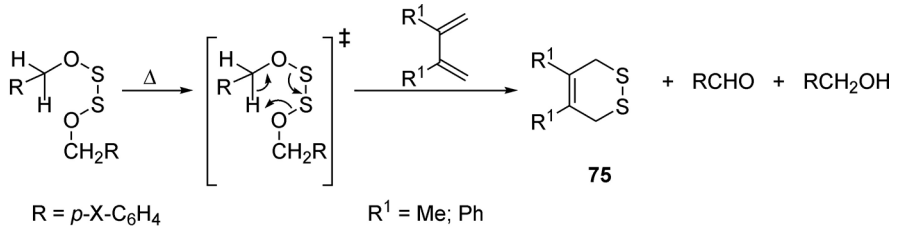
A manifestation of this bond shortening is the high rotational barrier about the S−S bond. Although Thompson first concluded that this barrier to rotation similar to that of disulfides (E_a = 8.6 ± 1.7 kcal mol^{-1}) [3], such a low value would require an unexpectedly [81] large negative $\Delta S^{\ddagger}$. Subsequent work has shown that the reported value is erroneous [82].

Seel [82] demonstrated that such a barrier for **6** (MeOSSOMe) was much higher ($\Delta G^{\ddagger}$ = 17.8 ± 0.1 kcal mol^{-1}). Lunazzi and co-workers [33] determined the thermodynamic properties for **49** in perchloroethene (C_2Cl_4) at 105 °C ($\Delta G^{\ddagger}$ = 19.0 ± 0.2 kcal mol^{-1}, $\Delta H^{\ddagger}$ = 20 ± 1 kcal mol^{-1}, $\Delta S^{\ddagger}$ = 2 ± 5 eu). Additionally, they determined similar activation parameters for other dialkoxy disulfides. We have measured the rotational barrier for a set of 4-substituted bis(benzyloxy) disulfides over a wide range of solvents and confirmed a barrier height of ca. 19 kcal mol^{-1} [56]. These experimental results corroborate with theoretical work performed by us [80].

7. Chemistry of dialkoxy disulfides

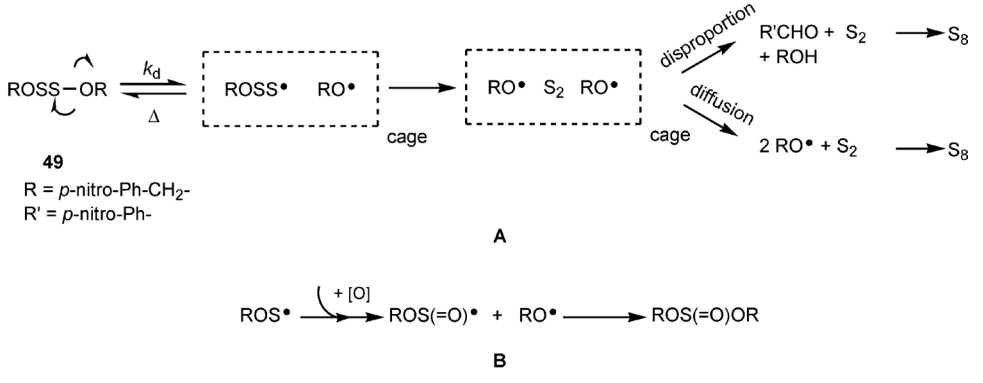
7.1 *Thermochemistry of dialkoxy disulfides*

Of particular interest in the context of this review is the report that dialkoxy disulfides at higher temperatures efficiently (>75% trapped **75**) deliver a 2-sulfur unit [35]. It was originally suggested that such S_2 generation results from the concerted disproportionation of the parent dialkoxy disulfide (scheme 7) [3, 35] though the actual source of sulfur in these thermolysis reactions has been questioned [83]. In particular, Thompson [3] observed that the origin of the R group of the dialkoxy disulfide affected their thermal stability (secondary > primary > allyl > propargyl). He proposed the intriguing cycloreversion mechanism shown in scheme 7.



SCHEME 7 Proposed mechanism in the thermolysis of dialkoxy disulfides.

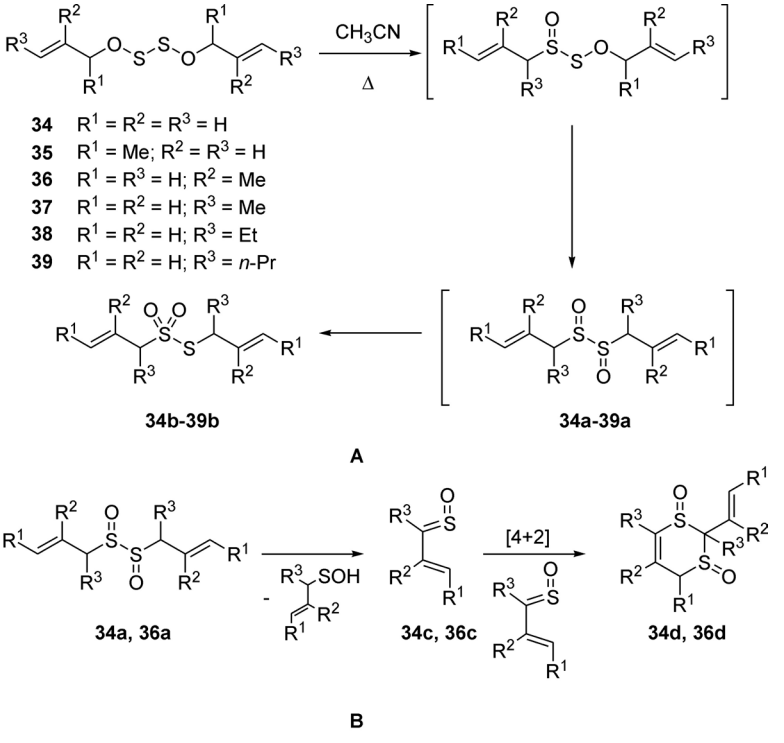
Recently, we revisited the mechanism behind S_2 delivery during the thermolysis of dialkoxy disulfides [56]. We have proposed that dialkoxy disulfides undergo initial asymmetric S−O homolytic bond cleavage to ultimately yield a transient source of diatomic sulfur. Dialkoxy disulfides decompose under first order kinetics with $\Delta G^{\ddagger}_{298} = 24$ kcal mol^{-1} (scheme 8).



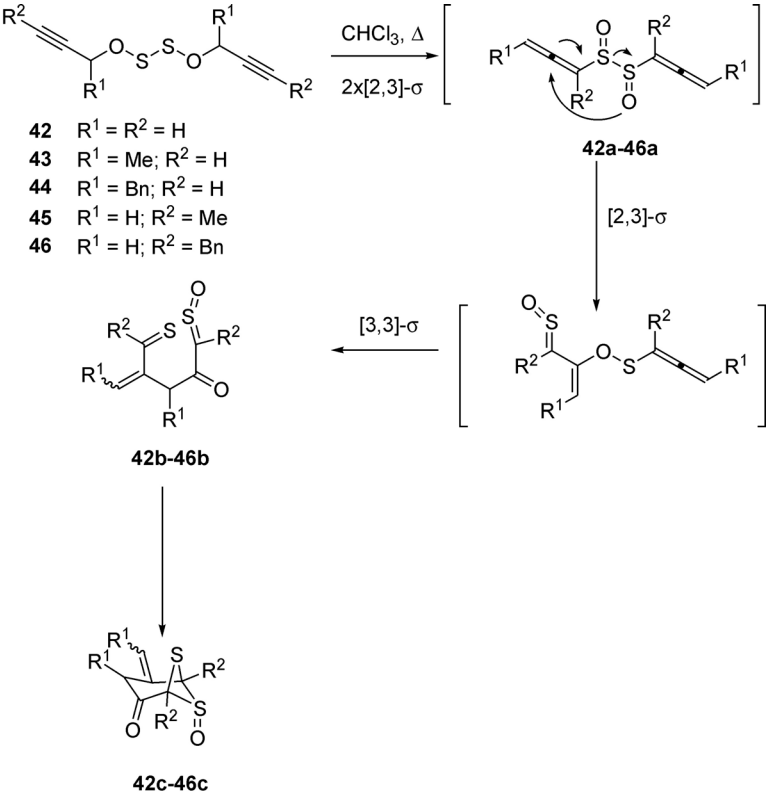
SCHEME 8 Thermally-induced radical decomposition mechanism of ROSSOR (R = p-NO_2-Ph-CH_2) **49**.

Lunazzi [49, 84] has shown that photolysis of *t*-dialkoxy disulfides with subsequent trapping with fullerene-C_{60} or fullerene-C_{70} provides an alternative source of alkoxyl radicals. The mechanism shown in scheme 8 is consistent with the ESR studies by Lunazzi.

Braverman [52, 53], in two related papers, outlined the thermal rearrangements of diallyloxy disulfides **34–41** and dipropargyloxy disulfides **42–46**. Addition (or reaction) times were influenced by substitution patterns of the starting alcohols. Diallyloxy disulfides [52] in refluxing acetonitrile were shown to undergo double [2, 3]-sigmatropic rearrangements to the corresponding *vic*-disulfoxides **34a–39a**, which then rearranged further to the more stable thiosulfonate isomers **34b–39b** (scheme 9A). Cinnamyl dialkoxydisulfides **40–41** (R^1 = H, R^3 = Ph, R^2 = H or Me) do not undergo this tandem rearrangement but instead disproportionate to the corresponding alcohol, aldehyde and elemental sulfur. This is not surprising as cinnamyl sulfenates [85] also do not thermally rearrange due to the loss of conjugation that would result during the allylic shift. Detected **34d** and **36d** could be formed *via* the intermolecular self-[4 + 2]-cycloadditions of the corresponding conjugated vinyl sulfines **34c** and **36c**. These intermediates in turn would have been generated by either H-abstraction from a sulfinyl radical by another *in situ* radical species or by a cycloelimination reaction of precursors **34a** or **36a** (scheme 9B).



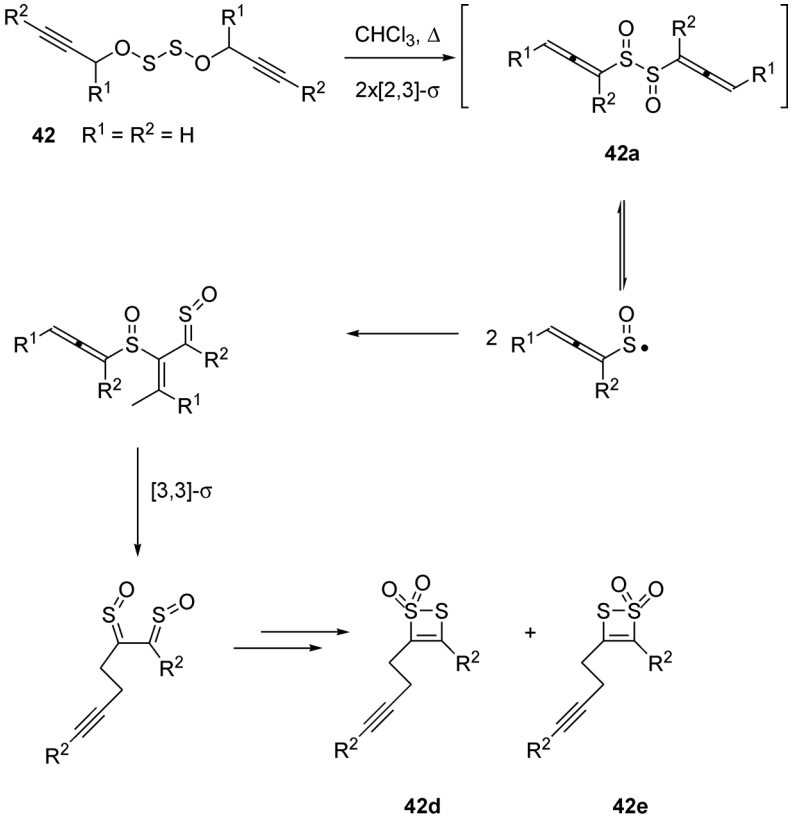
SCHEME 9



SCHEME 10

Analogously, propargyloxy disulfides [53] **42–46** undergo a double [2, 3]-sigmatropic shift to afford the corresponding diallenic *vic*-disulfoxide (scheme 10). These intermediates then undergo tandem [2, 3]-, [3, 3]-sigmatropic rearrangements to form **42b–46b**. This is then followed by a head-to-tail intramolecular [2 + 2] cycloaddition to afford the dithiabicyclo product **42c–46c**. To date this represents the only method to access such substituted dithiabicycles that have similar functionality to the natural product class of bioactive zwiebelanes found in onions [86].

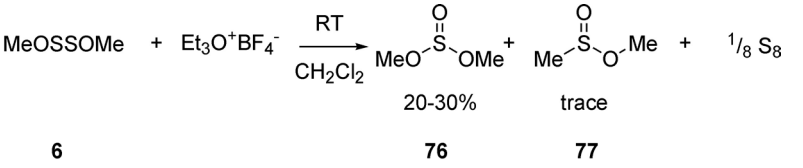
Braverman and co-workers [87] recently isolated as minor products isomeric thiosulfonates **42d** and **42e**. The yield of these unsaturated and previously unreported cyclic products could be relatively increased by substitution at the propargylic carbon of the original dialkoxy disulfide. A rationale for their formation is shown in scheme 11.



SCHEME 11

7.2 *Chemistry involving the dialkoxy disulfides as the nucleophile*

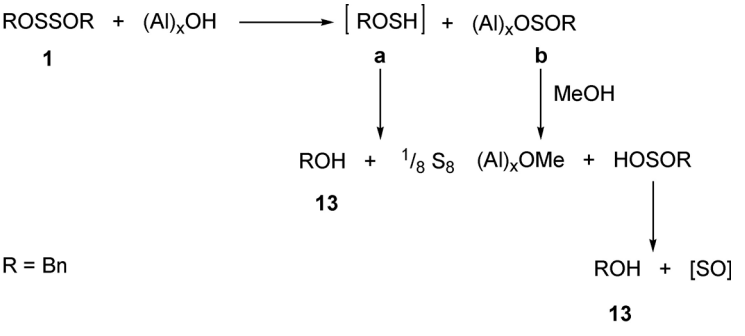
Dialkoxy disulfides are acid labile. In the presence of a stoichiometric amount of Lewis Acid, MeOSSOMe (**6**) was found to readily decompose *via* alkylation to the corresponding sulfite **76** with trace amounts of the sulfinate **77**; sulfur was observed as a precipitate in the reaction (scheme 12) [88].



SCHEME 12

The yield of sulfinate **77** increased when only a catalytic amount of triethyloxonium tetrafluoroborate was used. Other Lewis acids such as $SbCl_5$ and BF_3OEt_2 also effected the same decomposition. When the decomposition was followed by ^1H NMR, other low-boiling products were observed, including dimethyl sulfate and dimethyl ether. The decomposition products most likely result from the concomitant desulfurization/disproportionation/isomerization of **6** [88].

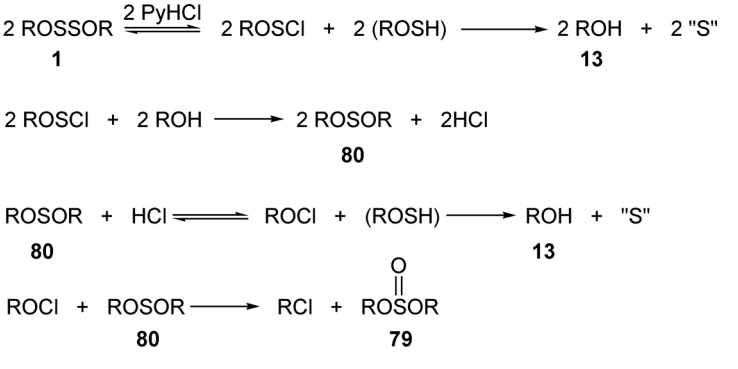
Decomposition of ROSSOR (**1**) has also been observed on acidic and basic alumina during chromatography. In the latter case, it has been proposed [3] that there is S−S bond cleavage, resulting in hydrolysis to the parent alcohol **13** (scheme 13, fragment **a**); the use of MeOH as eluant was required to saponify the aluminium ester, which then afforded another equivalent of alcohol and ca. half of the remaining sulfur, fragment **b**.



SCHEME 13 Decomposition of **1** on basic alumina [$(Al)_xOH$].

Disproportionation to the alcohol **13**, aldehyde **78** and sulfur was observed when using acidic alumina.

When alkoxydisulfides are allowed to stand in solution in the presence of pyridine hydrochloride, decomposition ensues with formation of the alcohol **13**, sulfite (ca. 30%) **79**, sulfoxylate **80** (trace) and sulfur. A rationale was provided to account for the product distribution, as outlined in scheme 14. The observed percentage of sulfite is similar to that observed by Kobayashi [88].

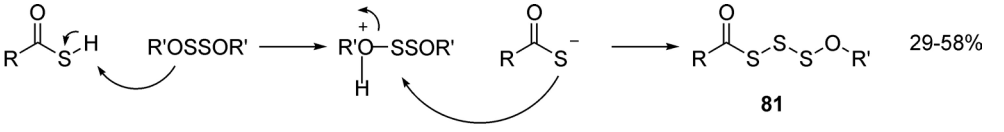


SCHEME 14 Decomposition of ROSSOR with pyridine hydrochloride.

In this scheme 75% of the sulfur is converted into elemental sulfur while the rest can be found as the sulfite **79** [89].

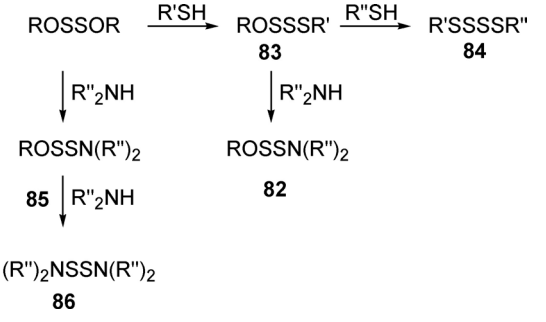
7.3 *Chemistry involving nucleophilic attack on dialkoxy disulfides*

Kagami [90] showed that dialkoxy disulfides could serve as an SSOR source to form **81** when he reacted alkanecarbothioic acids with R′OSSOR′ (R′ = Me **6**, Et **7**, *n*-Pr **8**, *i*-Pr **16**) in CCl_4 in moderate yield (29–58%). A plausible mechanism for this reaction is outlined in scheme 15.



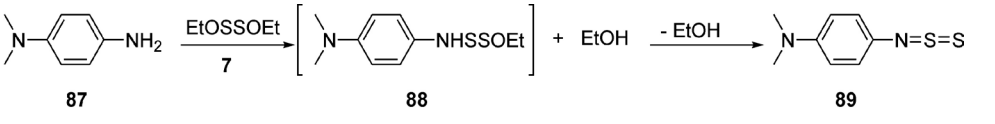
SCHEME 15

In related work, Kagami demonstrated that the SSOR moiety could also be transferred when amines or thiols were used as nucleophiles [91]. These substitution reactions also proceed in moderate yield. Steudel [92] has also used thiols as nucleophiles in related substitution reactions. The work is summarized in scheme 16.



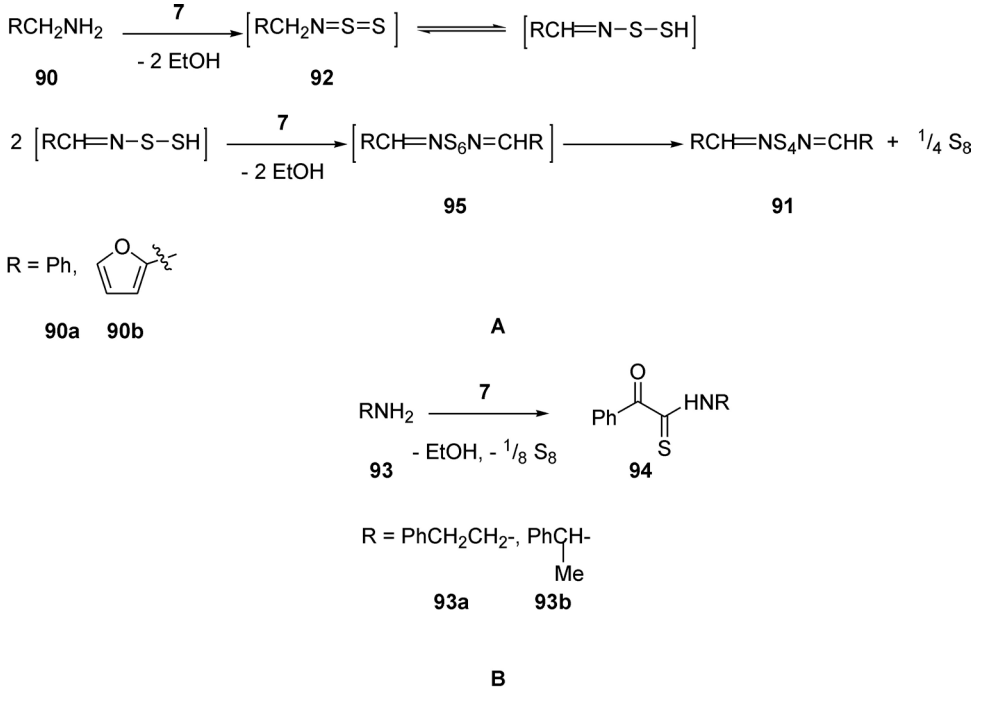
SCHEME 16

Their sequential addition of nucleophiles illustrates well the increasing leaving group capacity of N < S < O. The reaction of EtOSSOEt (**7**) with primary amines was less straightforward than that of the thiols. For instance, reacting **7** with **87** in refluxing benzene resulted in the initial formation of **88**, which then eliminated EtOH to form *N*-thiosulfinylaniline **89** (scheme 17). This reaction was characterized by the solution turning deep violet.



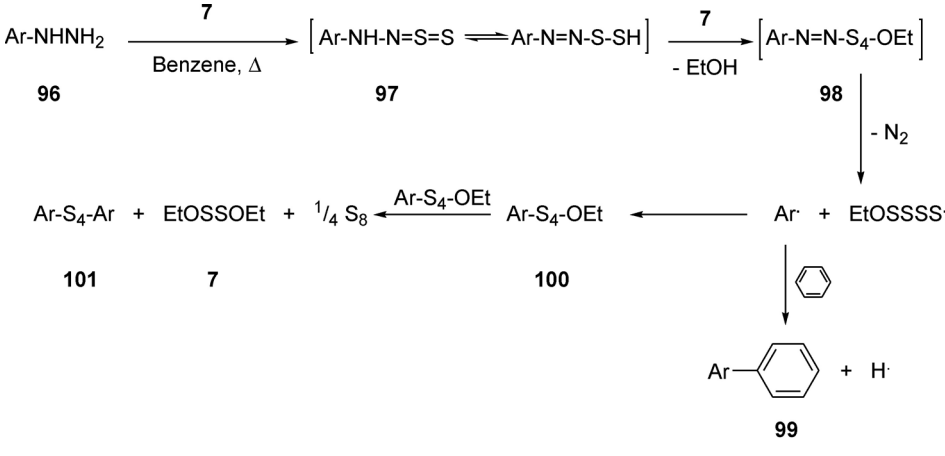
SCHEME 17

When the amine was changed to one that contained protons α but not β to the amine functionality as in benzylamine **90a** or furfurylamine **90b**, under similar reaction conditions, tetrasulfides **91a–91b** were formed *via* intermediate **92** (scheme 18A). When β protons are present (**93a–93b**), α-oxothioamides **94a–94b** are isolated after column chromatography (scheme 18B); notably, no ν_{NH} or $\nu_{C=O}$ stretches were detected in the IR of the crude mixture, suggesting that **94** is formed as a result of decomposition on the column from some unknown intermediate. No attempts were made to trap the extruded sulfur from **95**.



SCHEME 18

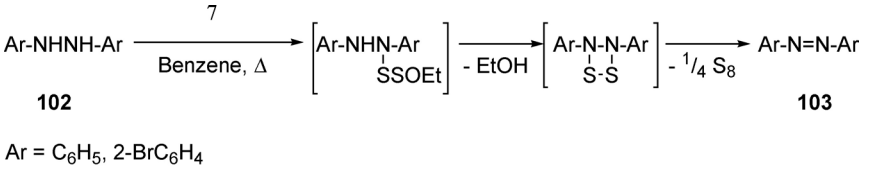
Kagami [93] also investigated the corresponding reaction with hydrazines **96** ($RNHNH_2$) and found that not only is the alkoxy group displaced, as with their other work highlighted in this section, but in addition there is the elimination of sulfur and nitrogen. Analogously to attack by amines (*vide supra*), it is reasonable to assume that here a thiosulfinyl intermediate is formed (**97**). After tautomerization of **97**, a second equivalent of EtOSSOEt (**7**) is attacked to give a highly unstable arylazo ethoxytetrasulfide (**98**). In a radical decomposition mechanism, nitrogen would then evolve with the formation of aryl and highly chalcogenized radicals. Indeed, the formation of an aryl radical from thermal decomposition of diazonium salts is well known [94]. These radicals then concatenate or react with the solvent to give biphenyl (**99**)



SCHEME 19

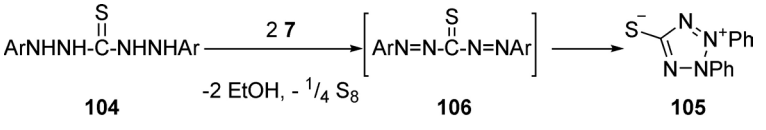
(0–27%) or aryl ethoxy tetrasulfide (**100**, 0–29%). This latter compound can then self-react to form aryl tetrasulfides **101** (13–38%). Reported yields were low due to difficulty in separating the products by chromatography. The results are summarized in scheme 19.

Derivatives of hydrazobenzene **102** reacted much more simply with **7** to afford azobenzenes **103** in near quantitative yields. Their synthesis was originally rationalized as in scheme 20, where **7** acts as an oxidizing agent. based on related work with **102** [95] the mechanism by which S_2 is released may also proceed *via* a six-membered transition state.



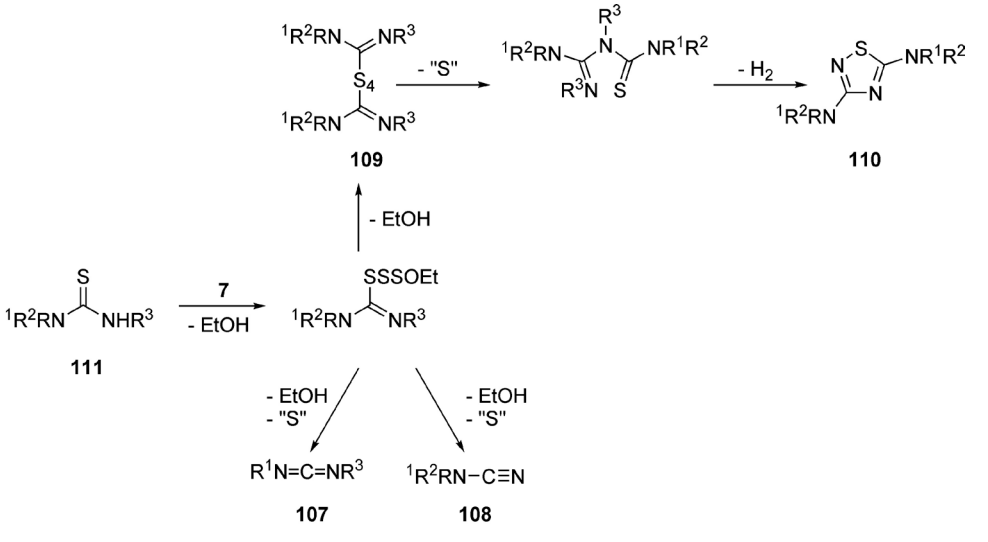
SCHEME 20

Reaction of **7** with $(PhNHNH)_2C(=S)$ **104** gave tetrazoliumthiolate (**105**) *via* **106** (scheme 21).



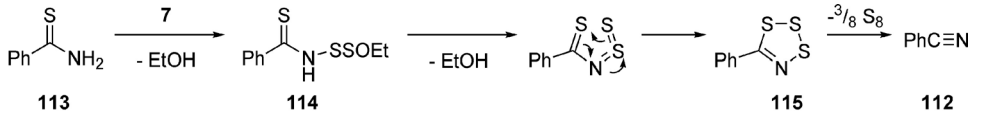
SCHEME 21

Not all nucleophilic attack is so straightforward. Kagami reported [96] the formation of carbodiimidides **107**, cyanamides **108**, tetrasulfides **109** or thiadiazoles **110** from the sequential attack of 1 or 2 equivalents of thiourea **111** on **7**; unsubstituted thioureas were needed to obtain the thiadiazoles. The product formation is rationalized in scheme 22.



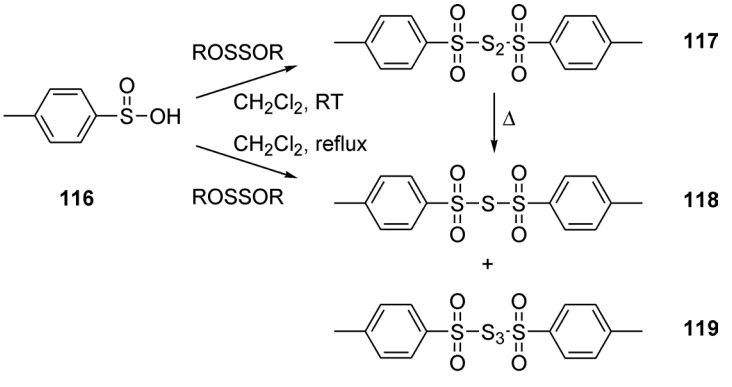
SCHEME 22

Cyanamides **108** are most probably formed by a similar mechanism to that proposed [91] for the formation of benzonitrile (**112**) from thiobenzamide **113** (scheme 23). Notably, a common intermediate in schemes 17–19 is a substituted-*N*-thiosulfinylamine (**89**, **92**, **97**). Interestingly, no reaction was observed when benzamide was used as the nucleophile. The proposed mechanism includes the desulfurization of **115**, which would involve the loss of an 'S_3' unit. Transfer of S_3 is rare though not unprecedented [97] and it would have been interesting if some kind of trapping experiments had been carried out.



SCHEME 23

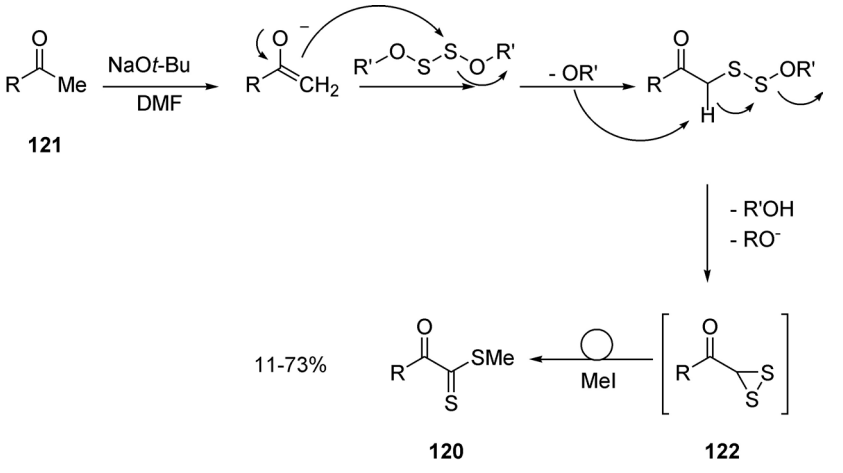
Reaction of *p*-toluenesulfinic acid (**116**) with dialkoxy disulfides does not undergo the same chemistry as that of the thioamides. Instead, simple nucleophilic displacement of alkoxide followed by O−S migration occurs at room temperature to afford di-*p*-toluenesulfonyl disulfide (**117**) in good yield (68–75%), depending on the dialkoxy disulfide used. At elevated temperatures, disproportionation occurs to afford a mixture of di-*p*-toluenesulfonyl sulfide (**118**) and di-*p*-toluenesulfonyl trisulfide (**119**) in yields of ca. 30% each (scheme 24). Indeed, when **117** was heated, **118** and **119** were obtained in yields of 36 and 33% respectively.



SCHEME 24

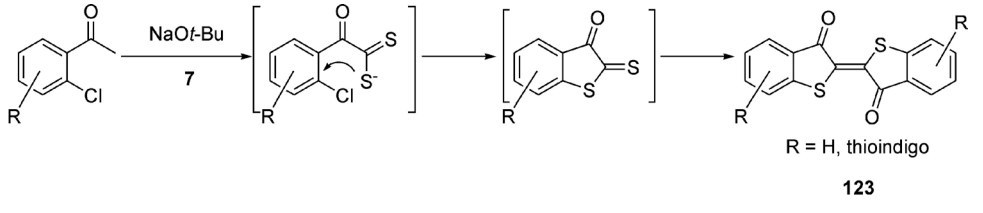
Braverman and Pechenick [98] recently reported a new efficient and general method for the synthesis of mixed sulfoxylates (ROSOR′) from the treatment of dialkoxy disulfides with alcohols at room temperature over 20 h. The use of allylic and propargylic alcohols allows for access to a rapid [2, 3]-sigmatropic rearrangement of the mixed sulfoxylate to ultimately form the mixed alkyl allyl and alkyl allenesulfinates in good yield.

Hoepping [99] has reported the synthesis of α-oxodithioic acid esters **120** in moderate-to-good yields from aryl or *t*-alkyl methyl ketones **121**. A mechanism is proposed, though not confirmed, involving a highly strained dithiirane intermediate **122** (outlined in scheme 25).



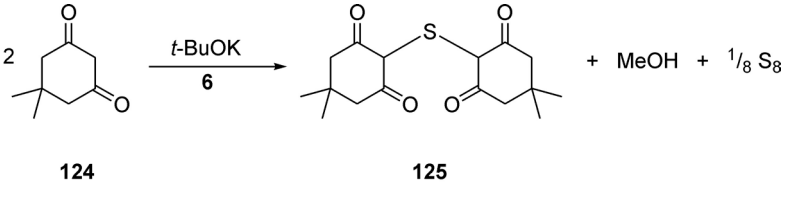
SCHEME 25

This chemistry has been used [100] in the facile synthesis of the dye thioindigo (**123**) (56%) and chlorinated derivatives thereof. Its synthesis is outlined in scheme 26.



SCHEME 26

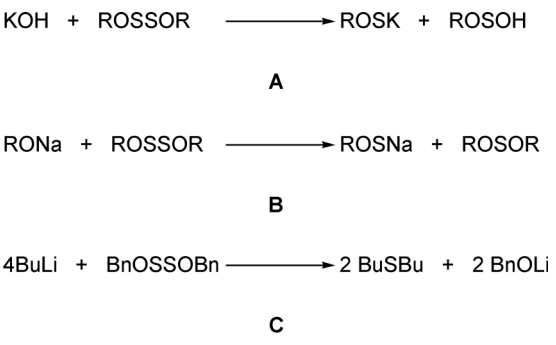
Interestingly, when the enolate of β-diketone **124** is reacted with MeOSSOMe (**6**), the only isolated product was the sulfide **125** (scheme 27).



SCHEME 27

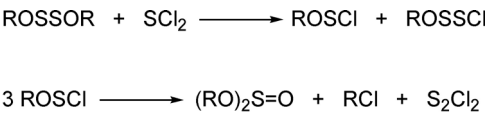
A gas phase nucleophilic substitution with hard nucleophiles on dialkoxy disulfides (R = Me **6**, Et **7**) was detected on carbon, sulfur and oxygen (attack on oxygen occurs less frequently than on carbon or sulfur) has been reported [101]. Meuwsen hypothesized that nucleophilic attack in the solution phase by hard nucleophiles such as potassium hydroxide [8] (scheme 28A) or sodium alkoxides [102, 103] (scheme 28B) or alkyl lithium reagents [3, 102]

(scheme 28C) occurs at sulfur, which is consistent with that observed in the gas phase by Smith and O'Hair [101]. This is intriguing as sulfur would normally be considered the soft site.



SCHEME 28

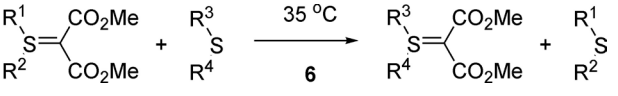
Under careful conditions, ROSSCl can be formed from ROSSOR **1** and SCl_2. Steudel [77] used this key intermediate in his synthesis of a nonasulfide. The formation of ROSSCl is quantitative because the by-product ROSCl decomposes to form a highly stable sulfite (scheme 29).



SCHEME 29

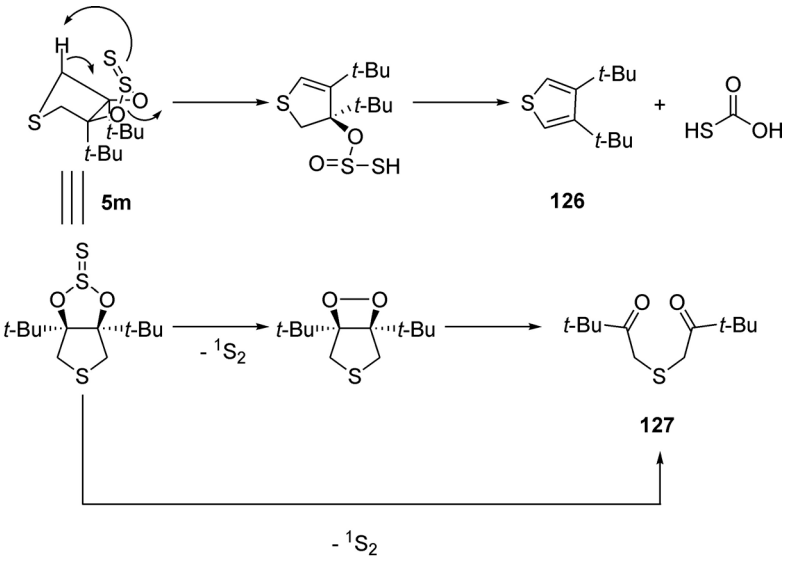
7.4 *Dialkoxy disulfides as catalysts*

Catalytic use of MeOSSOMe (**6**) promotes the transylidation of sulfur ylids containing two electron-withdrawing groups ($R^1R^2S^+C^-$-$(CO_2Me)_2$) on carbon (scheme 30) [104] Examples of transylidation are rare owing to the very strong stability of the sulfur ylid due to the two electron-withdrawing groups attached to carbon. The reaction proceeds quite easily and affords good to excellent yields of the transylidated product. Increasing steric bulk of R^3 and R^4 (scheme 30) decreases the efficiency of the reaction. Other catalysts successfully employed for this reaction include thiocyanogen (NC−SS−CN) and benzoyl disulfide (Bz-SS-Bz). Electron-withdrawing groups adjacent to the disulfide moiety of the catalyst seem to be the key to proper reactivity; during the reaction the catalyst does not decompose but in the absence of the sulfide the ylid does (leading to an olefinic by-product) [105]. Although no mechanism was given, a zwitterionic sulfonium ylid complex most probably forms [106] in an analogous fashion to that when Cu(II) sulfate reacts with ylids to quantitatively decompose them [107].



SCHEME 30

8. Chemistry of thionosulfites

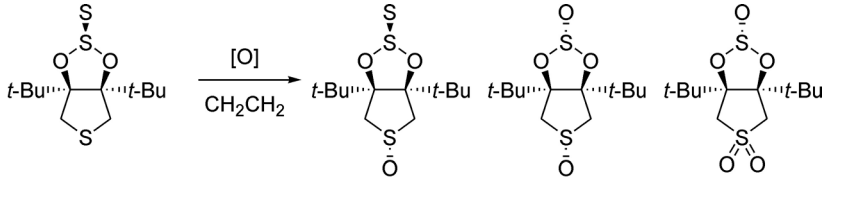


SCHEME 31

The chemistry of thionosulfites remains a relatively unexplored topic. Recently, Nakayama synthesized two diastereomeric thionosulfites **5m** and **5n** and explored some of their chemistry [42]. Thermalization of these thionosulfites gave decomposition products thiophene **126** and sulfide **127** in different relative yields (scheme 31). While **5m** decomposed in 96 h at 120 °C to afford ratio of 39:13:48 of **126:127:5m**, **5n** decomposed completely in 24 h to solely produce a 6:94 ratio of **126:127**. The increased yield of **127** in the thermolysis of **5n** was thought to be due to the retardation of the formation of **126** for steric reasons. Though compound **5m** proved to be the thermodynamically most stable thionosulfite, the relative yield between the two isomers (in a ratio of 82:18) and the lack of isomerization between the two indicates that the synthesis is kinetically controlled. DFT calculations correctly predicted that **5m** would be the more stable isomer by 1.69 kcal mol^{-1}.

These two thionosulfites were also readily hydrolyzed under alkaline conditions. For instance, **5m** was hydrolyzed (1:1 H_2O-THF) in the presence of $NaHCO_3$ to give diol **66m** in 93%.

Oxidation of **5m** with 1.1 equivalents of MCPBA afforded a 94:6 ratio of **128** to **129** (**128** was isolated in 77% yield). Oxidation of **5m** in excess (3.3 equivalent) MCPBA gave a 90:10



5m		128		129		130
MCPBA (1.1 equiv)		94	:	6		
MCPBA (3.3 equiv)				90	:	10

SCHEME 32

ratio of **129** to **130**. These results indicate that the S=S bond is more resistant to oxidation than a simple sulfide sulfur atom. An interesting feature is the inversion of stereochemistry in **129**. A mechanism for this inversion is posited in the supporting information of the paper. The product ratios are summarized in scheme 32.

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