



Thermolytic decomposition of benzylic dialkoxy disulfides

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ABSTRACT

Dialkoxy disulfides have been used as an alkoxy radical source under photolytic conditions. In addition, this class of disulfide thermally decomposes to deliver S_2 to dienes. We examined benzylic dialkoxy disulfides ($X-Ph-CH_2-O-S-S-O-CH_2-Ph-X$) under thermolytic conditions and observed that the rates of decomposition are related to Swain and Lupton's field constant, \mathcal{F} . In addition, the observed non 1:1 ratio of alcohol to aldehyde reaffirms Harpp's-postulated cage mechanism. We have shown that the ratio is dependant upon the substituent present which can enhance the pi-stacking ability with the solvent, and thus favor diffusion out of the solvation cage yielding the non 1:1 ratio observed.

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In 1895, Lengfield reported the first synthesis of dialkoxy disulfides by the reaction of an alcohol with sulfur monochloride (S_2Cl_2).¹ However, the structure was not unambiguously confirmed for over 100 years.² Prior to this there was debate as to whether this structure existed as a linear molecule, **1**, or as the branched thionosulfite, **2** (Fig. 1).³ However in 1997, an X-ray crystal structure study was carried out and it confirmed the linear dialkoxy disulfide structure, **1**.² Subsequently, branched thionosulfites have been synthesized, however only when cyclic.⁴ The dialkoxy disulfide has unique characteristics; including a short S–S bond length of 1.95 Å and a high barrier of rotation of 18 kcal/mol,⁶ compared to ~2.05 Å and ~8 kcal/mol for simple disulfides,⁷ respectively. These traits have been attributed to electronic modulation of the S–S σ -bond where it is believed that a lone pair of electrons from one of the sulfurs donates its electrons to the σ^* orbital of the adjacent S–O bond, hence providing double bond characteristic.⁸

The synthetic use of dialkoxy disulfides have been examined in two major areas. Lunazzi and Placucci have successfully used this moiety as an alkoxy radical donor when irradiated.⁹ In addition, Harpp has shown that dialkoxy disulfides can donate S_2 , which can be trapped in a pseudo Diels–Alder reaction with dienes to form cyclic di- and tetrasulfides, under thermolytic conditions.¹⁰ Thompson had postulated that this latter thermolytic fragmentation went through a concerted mechanism (Scheme 1).³ However, recently Zysman-Colman and Harpp have provided an alternate theory on this, whereby there is an initial homolytic cleavage of the S–O bond, followed by liberation of S_2 (Scheme 2).⁸

We have recently examined the photolytic behavior of a series of *para*-substituted benzylic dialkoxy disulfides (**1**).¹¹ A correlation of rate of decomposition, to their corresponding alcohols, with Swain

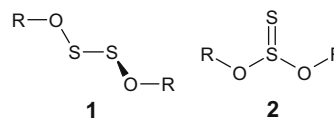
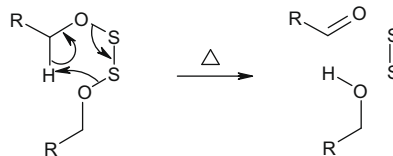


Figure 1. Structure of dialkoxy disulfide, **1**, and thionosulfite, **2**.

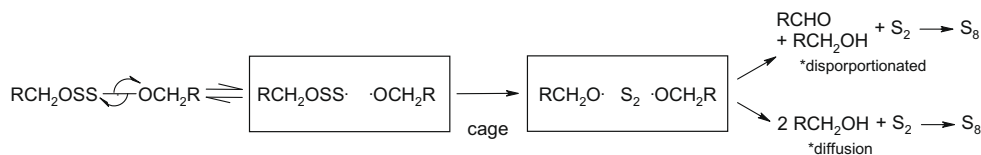
and Lupton's field constant, \mathcal{F} ,¹² was deduced. We now wish to report the thermolytic behavior of this series of dialkoxy disulfides.

The synthesis of the library of dialkoxy disulfides was performed as previously described.¹¹ {**1**(H): bis(benzyloxy) disulfide; **1**(Me): bis(*p*-methylbenzyloxy) disulfide; **1**(OMe): bis(*p*-methoxybenzyloxy) disulfide; **1**(NO₂): bis(*p*-nitrobenzyloxy) disulfide; **1**(Cl): bis(*p*-chlorobenzyloxy) disulfide; **1**(tBu): bis(*p*-*t*-butylbenzyloxy) disulfide; **1**(Ph): bis(*p*-phenylbenzyloxy) disulfide} (Scheme 3). The rate of thermolytic decomposition of **1**(NO₂) has been previously reported.⁸ In that study three solvents, spanning a large range of polarities were explored. It was determined that in all cases the rate of decomposition was first order.⁸ What we wished to examine was how the substitution on the aromatic ring would affect the rate of decomposition. For our system we examined toluene as the solvent. The dialkoxy disulfides were refluxed in toluene (110 °C), while being protected from ambient light with aluminum foil. As

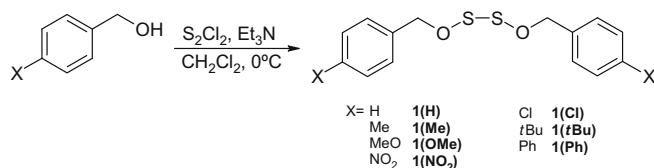


Scheme 1. Thompson's proposed mechanism of intramolecular thermolytic fragmentation of dialkoxy disulfides.³

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Scheme 2. Harpp's-proposed cage mechanism of thermolytic decomposition of dialkoxy disulfides.⁸



Scheme 3. Library of dialkoxy disulfides synthesized.

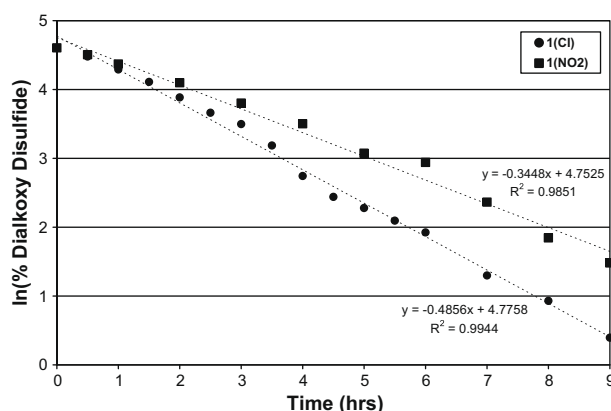


Figure 2. Plot of ln(%dialkoxy disulfide) versus time, illustrates a first order reaction.

Table 1
Rates of reaction compared to Swain and Lupton's \mathcal{F} values

Compound	\mathcal{F} -value	Rate constant (k_d) hrs ⁻¹
1(NO₂)	1.109	−0.3448
1(Cl)	0.69	−0.4856
1(OMe)	0.413	−0.4809
1(Ph)	0.139	−0.4237
1(H)	0	−0.3303
1(Me)	−0.052	−0.3193
1(tBu)	−0.104	−0.2921

with **1(NO₂)**, all decompositions were first order (i.e., rate = $k_d[1]$) (Fig. 2).

The rates of decomposition showed no correlation with Hammett's constants, similar to our photolytic work.¹¹ We therefore explored other variables and indeed discovered a relationship with Swain and Lupton's field constant, \mathcal{F} ¹² (Table 1). By comparing the rate constant (k_d) versus \mathcal{F} -values we obtained a parabolic correlation (Fig. 3). This type of relationship to the rate of decomposition with \mathcal{F} -values was also observed for a photolytic study on the same system.¹¹

As shown above, there are two competing theories for the mechanism of decomposition (Schemes 1 and 2). With Thompson's mechanism the products formed should be in a 1:1 ratio of alcohol to aldehyde.³ However, experimentally this is not the case. Zysman-Colman and Harpp's proposal suggests two successive

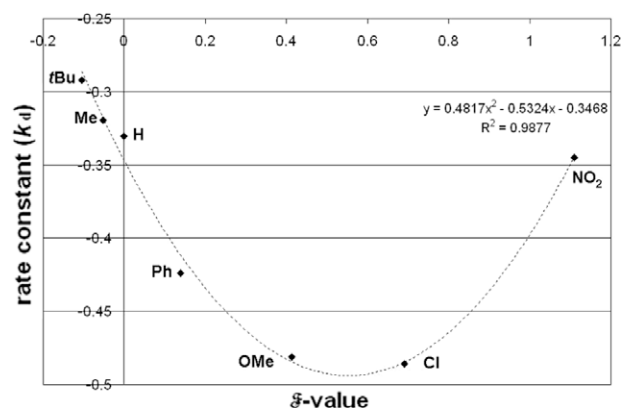


Figure 3. Rate constant (k_d) of a library of *para*-substituted bis(benzyloxy) disulfides versus Swain and Lupton's field constant, \mathcal{F} .

homolytic S–O bond cleavages, at which point the alkoxy radical can either diffuse out of the cage to yield alcohol, or stay within and disproportionate to a 1:1 ratio of alcohol to aldehyde.⁸ With **1(NO₂)**, it was reported that alcohol to aldehyde ratios ranged from just under 2:1 up to ~8:1 depending on solvent and temperature.⁸ We also observed a range of ratios (1.09–2.03:1; alcohol to aldehyde) for our system. This however was not as drastic as in previous studies.⁸ Harpp noted that the greatest deviation from the 1:1 ratio was when the most polar solvent (i.e., DMSO) was used. By employing a less polar solvent, the ability for the alkoxy radical to diffuse out of the cage should be hampered, thus a near 1:1 ratio of alcohol to aldehyde for **1(tBu)** is observed.

In an effort to understand the experimental ratios of alcohol to aldehyde we computationally examined the abilities of these compounds to pi-stack using toluene as our model solvent. Starting with crystallographic structural analysis to determine starting packing,¹³ the benzylic alcohol analogs were modeled with the solvent, toluene, with the pi-systems stacking at 3.0 Å apart from each other simultaneously minimizing steric interactions. The total energy of the modeled system was calculated using SYBYL with a Tripos force field and MMFF94 charges.¹⁴ The termination gradient was set to 0.05 kcal/(mol Å) with a non-bonded cutoff of 8 Å. The total energy of the modeled stacked system was calculated (Table 2).

Table 2
Experimental ratio of alcohol to aldehyde during thermolytic decomposition of dialkoxy disulfide (**1**) and total energy calculated for pi-stacked model systems of benzylic alcohols with toluene

Compound	Ratio of alcohol to aldehyde	Total energy (kcal/mol)	1/Total energy (mol/kcal)
1(NO₂)	1.44	22.526	0.04439
1(Cl)	2.03	7.772	0.1287
1(OMe)	1.39	31.847	0.03140
1(Ph)	1.25	52.616	0.01901
1(H)	1.69	11.004	0.09088
1(Me)	1.85	10.854	0.09213
1(tBu)	1.09	318.100	0.003144

The energy of stacking for **1**(*t*Bu) with toluene was by far the highest with 318.00 kcal/mol. This can most likely be attributed to the steric bulk of the *tert*-butyl group. Similarly, **1**(Ph) possesses a relatively high stacking energy (52.616 kcal/mol) due to the twist of the biphenyl, increasing the steric interactions of the system. The lowest stacking energy was observed with **1**(Cl) (7.772 kcal/mol), which possesses not only pi-stacking but also a LP_{Cl}– π interaction.¹⁵ Graphing the experimental ratio versus the inverse of the total energy demonstrates a linear relationship (Fig. 4). This shows that there is a correlation between pi-stacking and product ratios, thus supporting Harpp's cage mechanism model.⁸

We have examined the thermolytic decay of a range of *para*-substituted bis(benzyloxy) disulfides (**1**). Their rates of decomposition were all first order, and their rate constants (k_d) were correlated to Swain and Lupton's field constant, \mathcal{F} . The ratio of alcohol to aldehyde obtained for this series of compounds provides further evidence for the cage mechanism of thermolytic decompo-

sition of dialkoxy disulfides. Current studies are underway on the *ortho* and *meta*-substituted bis(benzyloxy) disulfides to see how their rates and product ratios may be altered.

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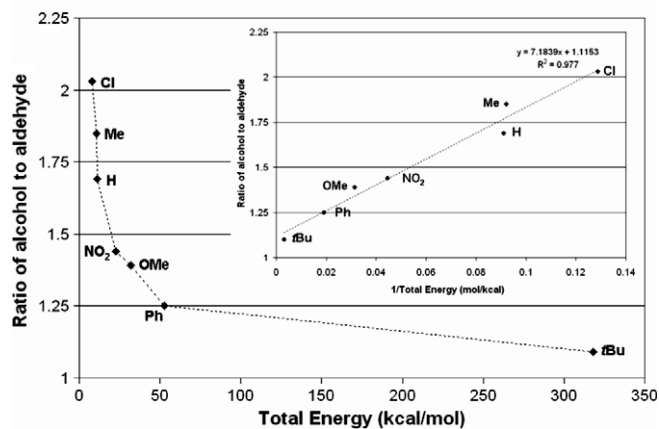


Figure 4. Relationship of ratio of alcohol to aldehyde with the total energies of the modeled system.