

Thermal and Photochemical 1,3-Dipolar Cycloaddition of a Sulfine (Fluorenethione *S*-Oxide) to the Strained Triple Bond of Cyclooctyne

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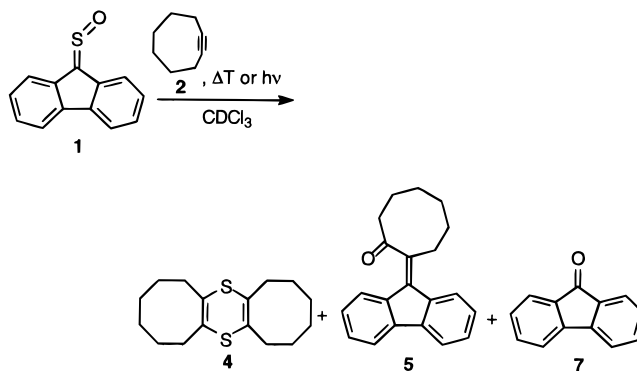
Thiocarbonyl *S*-oxides (sulfines) are known to react as 1,3 dipoles in [3 + 2] cycloadditions with thioketones. The latter have been designated as “super dipolarophiles” by Huisgen,¹ and they are the only effective ones for the sluggish sulfine 1,3-dipoles. However, recent work from our group showed that fluorenethione *S*-oxide (**1**) cycloadds as 1,3-dipole to *trans*-cyclooctene,² the first example of a thermal 1,3-dipolar cycloaddition between a sulfine and a CC double bond. The resulting sultene was isolated and displayed a remarkable propensity for sulfur transfer toward *cis/trans*-cyclooctene and norbornene under acid catalysis. In view of this exalted 1,3-dipolarophilic reactivity of such strained molecules, we have investigated the thermal and photochemical reaction of sulfine **1** with cyclooctyne (**2**) to assess whether the reactive triple bond may serve this purpose. Indeed, we report herein that the initial step in both the thermal and photochemical reaction is a 1,3-dipolar cycloaddition of sulfine **1** to cyclooctyne, followed by efficient sulfur transfer to cyclooctyne to afford dithiin **4**³ (Scheme 1).

The thermolysis (40 °C, 20–88 h) of a CDCl₃ solution of sulfine **1** in the presence of excess cyclooctyne (**2**) led to dithiin **4** and enone **5** as the desulfurized product (Table 1).

The extent of conversion of sulfine **1** depends on the concentration of **2** (Table 1, entries 1,2), which indicates that cyclooctyne (**2**) is involved in the rate-determining step. Unlike *trans*-cyclooctene,² the analogous unsaturated sultene expected as 1,3 cycloadduct between sulfine **1** and cyclooctyne could not be detected even in the presence of bases (entries 3 and 4). Nevertheless, the formation of the enone **5** unequivocally speaks for 1,3-dipolar cycloaddition of the sulfine to cyclooctyne.

The results of the photolysis (5 °C, 350 nm, 3 h) of fluorenethione *S*-oxide in the presence of cyclooctyne were rather surprising. While sulfine **1** was converted solely to fluorenone (**7**) when irradiated in the presence of *trans*-cyclooctene,⁴ for cyclooctyne we observed both enone **5** and fluorenone in almost equal amounts (Table 1, entries 5 and 6). The yield of the photochemical sulfur-transfer product, the dithiin **4**, was the same as for the thermal reaction. These results imply that two different pathways operate in the photochemical sulfur transfer by sulfine **1**: On one hand, we propose photochemical cyclization to the oxathiirane **6**,^{2,5} followed by sulfur transfer and formation of fluorenone; on

Table 1. Product Studies of the Thermal and Photochemical Sulfur Transfer from Sulfine **1** to Cyclooctyne in Chloroform

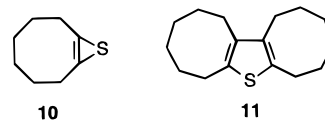


entry	mode ^c	2 ^a (mmol)	t (h)	convn ^{a,b} (mmol)		products ^{a,b} (mmol)		
				1	2	4	5	7
1	ΔT	2.10	24	0.545	0.990	0.271	0.512	traces
			88	0.783	1.42	0.341	0.767	traces
2	ΔT	4.71	41	0.927	1.71	0.355 (0.249) ^d	0.749 (0.556) ^d	traces
3	ΔT ^b	3.65	20	0.771	1.22	0.289	0.652	traces
4	ΔT ^b	3.51	20	0.674	1.43	0.279	0.645	traces
5	hν	2.01	3	1.00	1.52	0.319	0.363	0.543
6	hν	3.55	3	1.00	2.08	0.392	0.452	0.528

^a Relative to 1.00 mmol of sulfine **1**. ^b Determined from the ¹H NMR spectra of the crude reaction mixture by comparison of characteristic signals with the sum of aromatic signals as internal standard (error ± 5% of the stated values). ^c ΔT: 40 °C, exclusion of light. hν: 350 nm (Rayonet), 5 °C. ^d Yield of isolated product after silica gel chromatography. ^e K₂CO₃ (0.04 mmol). ^f NEt₃ (0.02 mmol).

the other hand, 1,3-dipolar cycloaddition between the sulfine **1** with cyclooctyne generates the 1,2-oxathiole **3**, which after sulfur transfer leads to the enone **5** (Scheme 1). The sulfur that is not transferred to afford the dithiin **4** is extruded as elemental sulfur, an undesired side reaction that is well-known for photochemical sulfur-transfer reactions.⁴ Since there are only traces of enone **5** formed within 3 h in the thermal process, the photochemical 1,3 cycloaddition must operate.

The 1,2-oxathiole **3** proposed for both the thermal and photochemical reactions of sulfine **1** with cyclooctyne (**2**), analogous to the sultene derived from the cycloaddition of sulfine **1** with *trans*-cyclooctene, transfers its sulfur atom directly to cyclooctyne to form thiirene **10**, which then dimerizes to dithiin **4**. The formation of a thiirene has been



proposed in the literature when elemental sulfur is allowed to react with triple bonds.⁶ Therefore, an alternative reaction pathway could be the extrusion of elemental sulfur from the 1,2-oxathiole **3** and subsequent formation of thiirene **10** and dimerization of the latter to the dithiin **4**. Indeed, a small amount of elemental sulfur is observed in these reactions; however, a control experiment showed that cyclooctyne and elemental sulfur afford, besides the dithiin **4**, also equal

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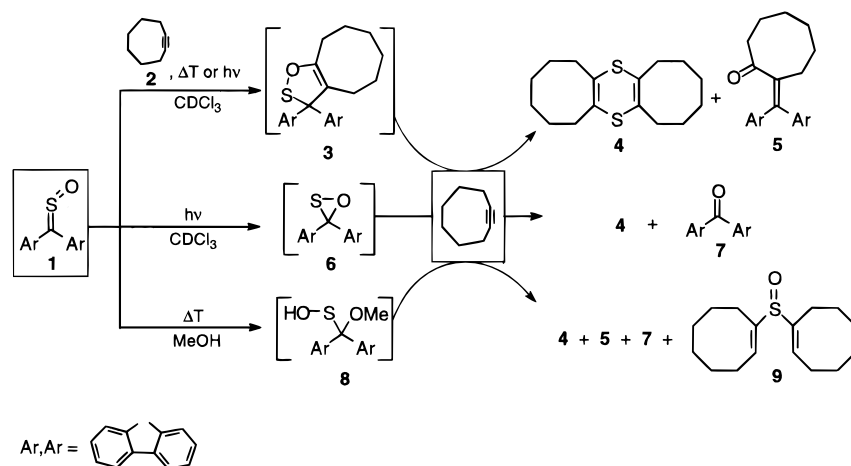
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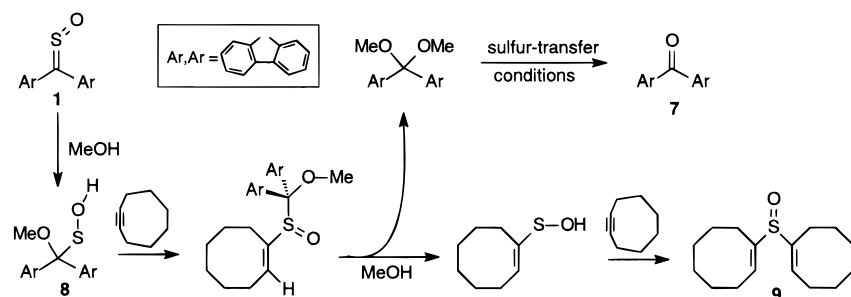
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Scheme 1



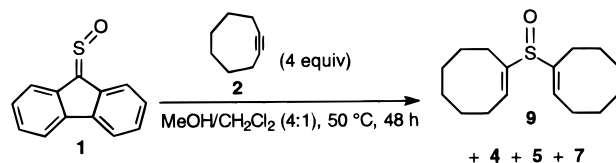
Scheme 2



quantities of the thiophene **11**. Since the latter is not observed in the reaction of sulfine **1** with cyclooctyne and neither dithiin **4** nor thiophene **11** can be transformed into each other under sulfur-transfer conditions, sulfurization by extruded elemental sulfur is unlikely to be a significant reaction pathway.

The thermal reaction of sulfine **1** with cyclooctyne was also performed in methanol to trap possible cationic intermediates.² Surprisingly, the fluorene moiety was not only transformed into enone **5**, but besides the dithiin **4** (sulfur transfer product), up to 48% fluorenone and considerable amounts (ca. 26%) of the unexpected sulfoxide **9** were observed (Table 2). The sulfoxide yield did not depend on the presence of molecular oxygen, so that the oxidation of intermediary sulfides may be excluded to reconcile the formation of the sulfoxide **9**. To explain these unusual results, we suggest nucleophilic attack of methanol on the carbon atom of the sulfine functionality of **1** (Scheme 2). This rather rare carbophilic reactivity of sulfine **1** leads to the sulfenic acid **8**. The analogous addition reaction of sulfines is known for amines.⁷ The sulfenic acid **8** may then add to the triple bond of cyclooctyne under formation of the sulfoxy group, which is a documented reaction for sulfenic acids.⁸ Solvolysis of the adduct sets free the unsaturated sulfenic acid, and subsequent addition to cyclooctyne affords sulfoxide **9**. The released dimethoxyfluorene is hydrolyzed to fluorenone, as confirmed by submission of the authentic fluorenone acetal to the sulfur-transfer conditions.

In conclusion, 1,3-dipolar cycloaddition of fluorene S-oxide (**1**) with cyclooctyne (**2**) is the first example of a

Table 2. Thermal Reaction of Sulfine **1** with Cyclooctyne in Methanol/Methylene Chloride Mixture

entry	conditions	products ^{a,b} (mmol)		
		5 ^c	7 ^d	9 ^c
1	air	0.252	0.451	0.356 (0.268) ^e
2	N ₂	0.368	0.475	0.248
3	degassed ^f	0.458	0.361	0.275

^a Relative to 1.00 mmol sulfine **1**, conversion of **1** >95%. ^b Yield of dithiin **4** not determinable because of severe signal overlap in the ¹H NMR spectra and HPLC chromatograms. ^c Determined from the ¹H NMR spectra of the crude reaction mixture by comparison of characteristic signals with the sum of aromatic signals as internal standard (error ± 5% of the stated values). ^d Determined by HPLC analysis (Eurospheer 100 silica gel column, 98:2 hexane/MTBE). ^e Yield of isolated product after silica gel chromatography and recrystallization. ^f Three freeze-pump-thaw cycles.

reaction between a sulfine and a triple bond under thermal as well as photochemical conditions. The unexpected formation of the sulfoxide **9** in methanol uncovers novel reaction pathways for this versatile sulfine.

Supporting Information Available: Experimental section (4 pages).

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