

SILICA GEL-PROMOTED SYNTHESIS OF 1,4-OXATHIANE DERIVATIVES FROM β,β' -DICHLORO SULFIDES

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Abstract—Treatment of bis(2-chloro-2-phenylethyl) sulfide, prepared from SCl_2 and styrene, with commercially available silica gel in *n*-hexane and benzene at 30 °C for 6 h gave 2,6-diphenyl-1,4-oxathiane in quantitative yield. The cyclization was successfully applied to other β,β' -dichloro sulfides, affording 1,4-oxathiane derivatives.

Sulfur dichloride (SCl_2) has long been known as a potential enophilic reagent which easily forms bis(2-chloroalkyl) sulfides upon addition to olefins.¹ In the course of our studies on this compound, we discovered that it is a facile sulfur transfer reagent in the preparation of sulfur-containing heterocycles from nitriles² and imines.³ The high reactivity of SCl_2 toward unsaturated bonds has often been utilized in the synthesis of cyclic sulfides from diolefinic compounds.¹ We previously reported the synthesis of sulfur-containing bicyclic β -lactams by the treatment of diolefinic β -lactams with SCl_2 .⁴ Although a considerable amount of knowledge on the addition reaction of SCl_2 to carbon-carbon double bonds has been published,¹ the 2:1 adducts of alkenes and SCl_2 have rarely been utilized in the synthesis of sulfur-containing heterocycles. One example is the synthesis of thiazine derivatives from β,β' -dichloro sulfides by treatment of the sulfide with amines.⁵ In the presence of water, this type of reaction would be expected to lead to the formation of a oxathiane ring. Certain oxathiane derivatives are known to have insecticidal⁶ and fungicidal⁷ activities and, as a result, this prompted us to investigate this reaction as a new procedure for the synthesis of oxathianes. *Herein, we report the silica gel-catalyzed synthesis of 1,4-oxathianes from β,β' -dichloro sulfides, prepared by the reaction of SCl_2 with alkenes.*

β,β' -Dichloro sulfides, the starting materials for the 1,4-oxathianes, were prepared by the addition of SCl_2 to alkenes to give 2:1 adducts. The results are summarized in Table 1. The general procedure is as follows: to a well-stirred solution of styrene (**1a**; 2.08 g, 20 mmol) in dichloromethane (100 mL) at 0 °C under a nitrogen atmosphere, sulfur dichloride (1.03 g, 10 mmol) was added dropwise with stirring over 2 h period to give bis(2-chloro-2-phenylethyl) sulfide (**3a**) in 88% yield. The structures of **3** were determined by spectral analysis. The ^1H -NMR signal of the methine proton at the 2-position did not show a simple dd pattern, indicating that the product was a mixture of diastereomers. The regiochemistry of the

addition reaction was consistent with the known fact that the sulfur atom is attached to the β -position of the aryl group.

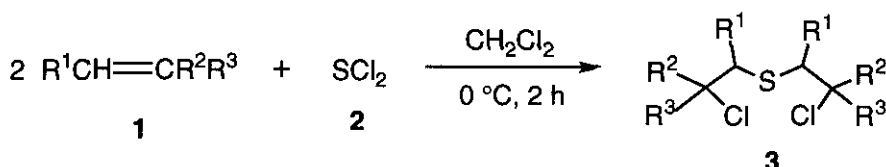
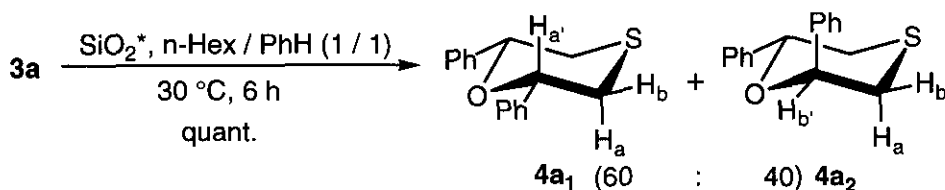


Table 1.

3	R ¹	R ²	R ³	yield (%)
a	H	Ph	H	88
b	H	<i>p</i> -MeOC ₆ H ₄	H	63
c	H	<i>p</i> -ClC ₆ H ₄	H	80
d	H	Me	Ph	71
e	—(CH ₂) ₄ —		H	100
f	PhCH ₂	H	H	81

When β,β' -dichloro sulfide (**3a**) was treated with water and triethylamine in benzene at 30 °C for 18 h, no reaction occurred, and the starting material was recovered. On the other hand, a small amount of an unidentified compound, which was not detected in the crude sulfide (**3a**), was obtained when **3a** was purified by silica gel column chromatography. The mass spectrum suggests that this compound is 3,5-diphenyl-1,4-oxathiane.

Since the above observation suggested that β,β' -dichloro sulfide (**3a**) was able to be converted into oxathiane derivatives by treatment with silica gel, this was investigated further. When β,β' -dichloro sulfide (**3a**) (311 mg, 1 mmol) was treated with silica gel (40 g) in *n*-hexane/benzene (1/1), which was the chromatographic eluent mentioned above, for 6 h at 30 °C, 2,6-diphenyl-1,4-oxathiane (**4a**) was obtained as a mixture of two isomers (**4a₁** and **4a₂**) in nearly quantitative yield. The isomers of thioxane (**4a**) could be separated by silica gel column chromatography and their structures were determined by ¹H-NMR.⁸



* Fuji-Davison BW300 (pH 6.7, H₂O content 4.9 wt%, 325-400 mesh), 40 g / 1 mmol of **3a**

In order to confirm the optimal reaction conditions and to clarify the source of the oxygen in the oxathiane ring, the reaction of **3a** was studied in detail and the results are listed in Table 2.

Decreasing the reaction time from 6 h to 1 h resulted in the quantitative formation of β,β' -dihydroxy sulfide (**5a**) without a trace of oxathiane (**4a**). When the reaction temperature was raised to 50 °C, oxathiane (**4a**) was quantitatively formed within 1 h. The reaction also proceeded even in anhydrous CHCl₃, when used

in place of the commercially available *n*-hexane and benzene. Decreasing the amount of SiO₂ lowered the yield of oxathiane (**4a**). When dried SiO₂ and anhydrous solvent was used, no reaction occurred.

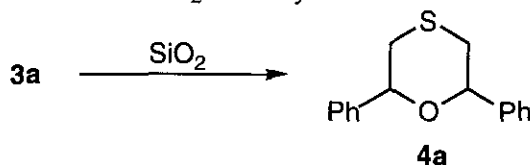


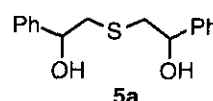
Table 2.

SiO ₂ (g) ^{a)}	solv. ^{b)}	time (h)	temp. (°C)	yield (%)
40	<i>n</i> -Hex-PhH	6	30	100
40	<i>n</i> -Hex-PhH	1	30	— ^{c)}
40	<i>n</i> -Hex-PhH	1	50	100
40	CHCl ₃ ^{d)}	6	30	100
5	<i>n</i> -Hex-PhH	6	30	35 ^{e)}
40 ^{d)}	<i>n</i> -Hex-PhH ^{d)}	6	30	0 ^{f)}

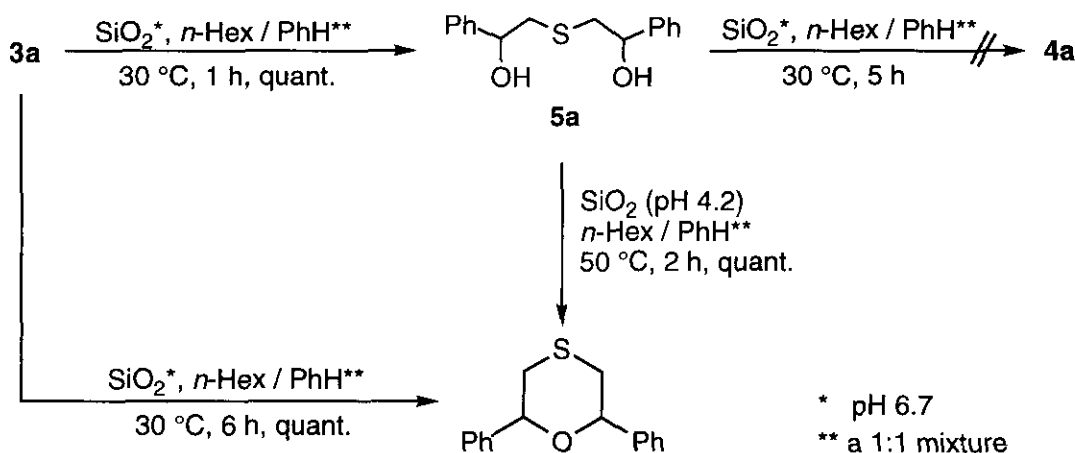
a) Weight per 1 mmol of **3a**. b) *n*-HeX : PhH = 1 : 1

c) β, β'-hydroxy sulfide (**5a**) was obtained. d) Dried.

e) Recovery of **3a**: 65%. f) Recovery of **3a**: 100%.



These results suggest that the source of oxygen is the water contained in the silica gel. Since dihydroxy sulfide (**5a**) was obtained quantitatively after 1 h, **5a** was assumed to be a precursor of **4a**. Contrary to our expectation, treatment of **5a** with SiO₂ under the same conditions did not afford **4a**. The reaction system is acidic, as a result of the liberation of hydrogen chloride during the formation of dihydroxy sulfide (**5a**) from **3a**. When **5a** was treated with acidic silica gel (pH 4.2)⁹ at 30 °C for 5 h, no reaction was observed. This may be attributed to the amount of hydrogen chloride adsorbed in SiO₂ (pH 4.2), whose amount is *ca.* 1/20 of that of HCl generated in the reaction of **3a** with neutral SiO₂. Therefore, dihydroxy sulfide (**5a**) was treated with SiO₂ (pH 4.2) at 50 °C for 2 h to give oxathiane (**4a**) in quantitative yield. Subsequently, it was discovered that the transformation of **3a** to **4a** proceeds *via* **5a**, and, the hydrogen chloride generated *in situ* plays an important role in the cyclodehydration of **5a** to an oxathiane ring.¹⁰



The present cyclization, catalyzed by silica gel, was successfully applied to several other β,β' -dichloro sulfide derivatives. The typical procedure is as follows: to a slurry of silica gel (Fuji Davison BW-300, 40 g) in CHCl_3 (80 mL) was added β,β' -dichloro sulfide (1 mmol) and the mixture was stirred under the conditions shown in Table 3. The reaction mixture was filtered through a Buchner funnel and the filtrate was washed with CHCl_3 (400 mL). The CHCl_3 solution was concentrated under reduced pressure and the residue was separated by silica gel column chromatography.

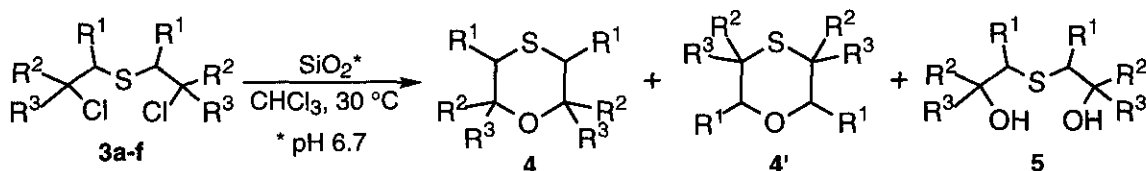


Table 3.

3	R ¹	R ²	R ³	time (h)	4 (%)	4' (%)	5 (%)
a	H	Ph	H	6	100	0	0
b	H	<i>p</i> -MeOC ₆ H ₄	H	6	95	0	0
c	H	<i>p</i> -ClC ₆ H ₄	H	6	48	0	48
d	H	Me	Ph	6	a)		
e	—(CH ₂) ₄ —		H	18	43	0	30
f	PhCH ₂	H	H	6	0	100	0

a) A complicated mixture.

When the adducts of *p*-substituted styrenes with SCl_2 , **3b** and **3c**, were employed in the reaction, the adduct (**3b**) derived from *p*-methoxystyrene was converted to oxathiane (**4b**) in better yield and the *p*-chloro-substituted adduct (**3c**) gave oxathiane (**4c**) in 48% yield, along with considerable amount of β,β' -dihydroxy sulfide (**5c**). This suggests that the reaction proceeds via benzyl cation, which is more stabilized by an electron-donating *para*-substituent. In order to examine whether the reaction occurred at only the benzyl position or at other positions, the adducts of α -methylstyrene, cyclohexene and allylbenzene with SCl_2 were subjected to the cyclization reaction. The reaction of **3d** with SiO_2 gave a complicated mixture containing olefinic products. This result may be explained as follows: while the benzyl cation formed from **3d** is stable because of tertiary cation, the nucleophilic attack of water to **3d** is sterically hindered and, for example, dehydrochlorination proceeds to some extent, giving olefinic products. In spite of increasing the reaction time in the case of adduct (**3e**), derived from cyclohexene and SCl_2 , the cyclization was not complete and gave oxathiane (**4e**) in 43% yield along with dihydroxy sulfide (**5e**) in 30% yield. With adduct (**3f**), which generates a primary carbocation, rearrangement occurred to give oxathiane (**4'f**) in quantitative yield.

Thus, β,β' -dichloro sulfides, which are readily prepared by the reaction of SCl_2 with various alkenes, can be transformed to oxathiane derivatives using commercially available silica gel as the catalyst. The reaction proceeds effectively and cleanly, and pre-treatment or purification either the silica gel or solvent is not

intermediary β,β' -dihydroxy sulfides is catalyzed by the hydrogen chloride generated *in situ*. Further investigations of the cyclization and transformation of β,β' -dichloro sulfides with other nucleophiles are now underway.

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8. ^1H NMR (90 MHz, CDCl_3) and mass spectral data of **4a**: Compound (**4a**₁) δ 6.7-7.7 (m, 10H), 4.90 (dd, J = 10.3, 2.3 Hz, 2H), 2.57 (dd, J = 2.3, 12.4 Hz, 2H), 2.89 (dd, J = 10.3, 12.4 Hz, 2H), MS (m/z) 256 (M^+); Compound (**4a**₂) δ 7.0-7.7 (m, 10H), 5.08 (dd, J = 3.8, 5.8 Hz, 2H), 3.0 (m, 4H), MS (m/z) 256 (M^+).
9. pH of SiO_2 refers to pH of the 5% aqueous slurry of SiO_2 .
10. Formation of oxathianes from β,β' -dihydroxy sulfides by treatment with diethoxytriphenylphosphorane has been reported; see for example, W. T. Murray, J. W. Kelly, and S. A. Evans, Jr., *J. Org. Chem.*, 1987, **52**, 525.

Received, 1st May, 1997