Chlorination of Phenylsulfinylcyclopropanes and Phenylthiocyclopropanes

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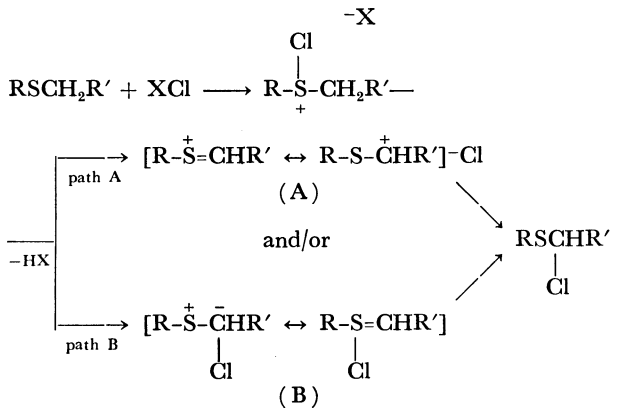
Chlorination of phenylsulfinylcyclopropanes or phenylthiocyclopropanes with various chlorinating agents provides the corresponding 1-chloro-1-(phenylthio)cyclopropanes but not any ring opening product. Kinetic isotope effects, (k_H/k_D), for the chlorination were measured with 1-deuterated cyclopropane derivatives and found to be small, *i.e.*, 1.6—2.8. The chlorination is considered to be a kind of the Pummerer reaction of the chlorosulfonium salt formed as the initial intermediate in the reaction of sulfides or sulfoxides with such chlorinating agents as *N*-chlorosuccinimide (NCS) or thionyl chloride and proceeds *via* the ylide-ylene intermediate.

Earlier, the formation of α-chloro sulfides from the reaction of sulfides with chlorinating agents was suggested to go through an ylide-ylene type intermediate (B) after the initial formation of the chlorosulfonium salt, as shown below,[2] as in the ordinary Pummerer reaction.



Scheme 1.

As to the subsequent S–Cl bond cleavage and the α-C–Cl bond formation, both an E2 like process forming an incipient carbonium ion (A)[3] and an ElcB type mechanism through an ylide-ylene (B)[4] have been proposed. The former involves a free carbonium ion (A) stabilized by the sulfur's lone pair electron while the latter implies a chloro-migration in the ylide-ylene intermediate (B). Thus the whole process is considered to be a kind of the Pummerer reaction. Meanwhile our recent work[5] revealed that the Pummerer reaction of phenylsulfinylcyclopropanes with acetic anhydride afforded the corresponding 1-acetoxy-1-(phenylthio)cyclopropanes nearly quantitatively without any ring opening, whereas the solvolysis of 1-chloro-1-(phenylthio)cyclopropanes gave a concomitant mixture of both the unrearranged solvolysis products and some ring opening allylic products. Accordingly, the Pummerer reaction of this system is considered to proceed *via* an ylide-ion pair but not a free carbonium ion.

As an extension of our studies on the Pummerer reaction, we have carried out the reaction of phenylsulfinylcyclopropanes (**1a—c**) and phenylthiocyclopropanes (**2a—c**) with various chlorinating agents, in order to examine the formation of any ring opening product, since the cyclopropyl cation once formed will definitely give the ring opening products. However, the chlorination afforded nothing but the corresponding 1-chloro-1-(phenylthio)cyclopropanes in good yields.

This paper describes the reaction of phenylsulfinylcyclopropanes (**1a—c**) and phenylthiocyclopropanes (**2a—c**) with various chlorinating agents and the hydrogen–deuterium kinetic isotope effects estimated by the competitive reaction between the 1-deuterated and undeuterated cyclopropane derivatives in the chlorinations.

Results

*Chlorination of Phenylsulfinylcyclopropanes (**1a—c**) and Phenylthiocyclopropanes (**2a—c**).* Chlorination of **1** with thionyl chloride or propionyl chloride under reflux for 1 h in methylene chloride afforded 1-chloro-1-(phenylthio)cyclopropanes (**3**) in good yields without any ring opening (Table 1). The products (**3a—c**) obtained were purified further by distillation *in vacuo* (by bulb to bulb distillation) and identified by their IR and NMR spectra (Table 2) and by conversion to the corresponding sulfoxides (**4a—c**) upon treatment with *m*-chloroperbenzoic acid in dichloromethane (Scheme 2 and Table 2).

Meanwhile, chlorination of **2** with NCS at room temperature for overnight in benzene also afforded **3** in high yields without any ring opening (Scheme 3 and Table 3).

The Hydrogen-Deuterium Kinetic Isotope Effects for the Chlorination. The hydrogen-deuterium kinetic isotope effects were estimated by the competitive reaction of both 1-deuterated phenylsulfinylcyclopropane (**5**) and undeuterated compound (**1a**) with thionyl

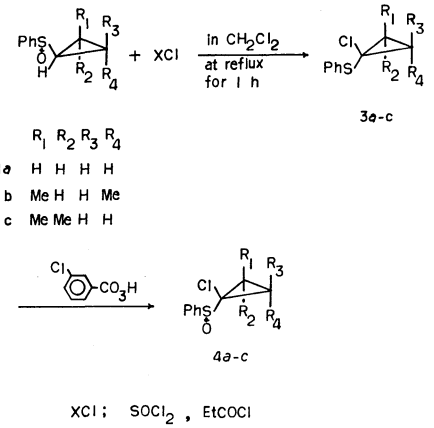
TABLE 1. THE REACTION OF PHENYLSULFINYLCYCLOPROPANES (**1a—c**) WITH CHLORINATING AGENTS IN DICHLOROMETHANE AT REFLUX FOR 1 h

Starting sulfoxide (**1a—c**)	R_1	R_2	R_3	R_4	Chlorinating agent XCl	Products (**3a—c**)	and their yields (%)
1a	H	H	H	H	$SOCl_2$	**3a**	Quant.
1a	H	H	H	H	EtCOCl	**3a**	Quant.
1b	Me	H	H	Me	$SOCl_2$	**3b**	85
1c	Me	Me	H	H	$SOCl_2$	**3c**	71[a]

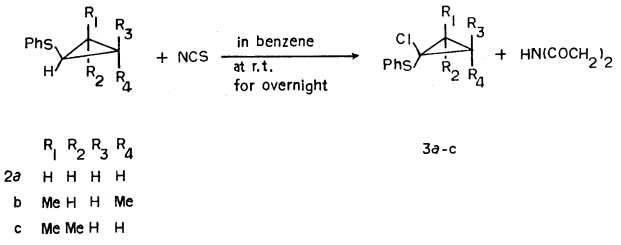
a) 1-(Phenylthio)-2,2-dimethylcyclopropane (**2c**) was obtained in 14% yield.

Table 2. IR and NMR spectrum data of 1-chloro-1-(phenylthio)cyclopropanes (**3a—c**) and 1-chloro-1-(phenylsulfinyl)cyclopropanes (**4a—c**)

3a—c	Bp(bath tempt) (°C/mmHg) (lit)	NMR Spectra ($CDCl_2$) (δ-ppm)	**4a—c**	Mp (°C)	IR Spectra (cm^{-1}) (S=O)	NMR Spectra ($CDCl_3$) (δ-ppm)	Analysis Found (Calcd)
3a	84/3	1.3—1.6(m, 4H, ) 7.0—7.6(m, 5H, PhS-)	**4a**	50—51	1060	1.1—1.8(m, 4H,) 7.2—7.8(m, 5H, PhS(O)-)	C, 54.10 (53.86) H, 4.57 (4.52) S, 15.76 (15.98)
3b	115/1	1.0—1.5(m, 8H, ) 7.0—7.6(m, 5H, PhS-)	**4b**	76—77	1050	1.0—1.8(m, 8H,) 7.3—7.8(m, 5H, PhS(O)-)	C, 58.00 (57.76) H, 5.77 (5.73) S, 14.22 (14.02)
3c	115/1 (85—7/0.2)[13]	1.2(q, 2H,) 1.33 and 1.44 (s, 3H and s, 3H, and) 7.0—7.5(m, 5H, PhS-)	**4c**	76—77	1050	1.13 and 1.52(d, 1H and d, 1H,  and ) 1.40 and 1.63 (s, 3H and s, 3H,  and) 7.3—7.8(m, 5H, PhS(O)-)	C, 58.00 (57.76) H, 5,73 (5.73) S, 13,78 (14.02)



Scheme 2.



Scheme 3.

chloride and acetyl chloride by means of quantitative GLC and GLC-mass spectrometry (Table 4). The kinetic isotope effects of these competitive chlorinations

Table 3. Chlorination of phenylthiocyclopropanes (**2a—c**) with NCS in benzene at room temperature for overnight

Starting sulfide (**2a—c**)	R_1	R_2	R_3	R_4	Products (**3a—c**) and their yields (%)	
2a	H	H	H	H	**3a**	90
2b	Me	H	H	Me	**3b**	81
2c	Me	Me	H	H	**3c**	82

Table 4. The hydrogen-deuterium kinetic isotope effects in competitive reaction of undeuterated phenylsulfinylcyclopropane (**1a**) and 1-deuterated compound (**5**) with thionyl chloride or acetyl chloride

Chlorinating agent XCl	Conversion (%)	[H]/[D] (mmol l^{-1})	k_H/k_D	
$SOCl_2$	0.0	45.31/48.15	—	
	22.8	31.74/40.42	2.0	
	47.1	18.96/30.50	1.9	2.1±0.3
	67.4	7.52/22.97	2.4	
MeCOCl	0.0	45.66/45.78	—	
	16.2	35.58/41.09	2.3	
	32.6	26.17/35.50	2.2	2.1±0.3
	50.8	17.99/27.02	1.8	

were calculated by the following equation:

$$\frac{k_H}{k_D} = \frac{\ln([H]_f/[H]_0)}{\ln([D]_f/[D]_0)}. \quad (1)$$

The extent of conversion of the reaction was estimated by comparing the relative peak areas of phenylsulfinylcyclopropane for each reacting sample with that without thionyl chloride, respectively, in GLC. Ratios of [H]/[D] were determined from the relative intensities of the sulfoxides in the respective molecular peaks in GLC-mass spectrometry.

Meanwhile, the hydrogen-deuterium kinetic isotope effects in the competitive chlorination of 1-deuterated phenylthiocyclopropane (**6**) and undeuterated compound (**2a**) with NCS and sulfuryl chloride were also determined by quantitative GLC and GLC-mass spectrometry (Table 5).

Table 5. The hydrogen-deuterium kinetic isotope effects in competitive chlorination of undeuterated phenylthiocyclopropane (**2a**) and 1-deuterated compound (**6**) with NCS or sulfuryl chloride

Chlorinating agent XCl	Conversion (%)	[H]/[D] (mmol l^{-1})	k_H/k_D	
SO_2Cl_2	0.0	73.94/59.62	—	
	22.8	53.95/49.19	1.6	
	48.7	32.56/35.98	1.6	1.8±0.3
	64.6	15.77/29.61	2.2	
NCS	0.0	73.94/59.62	—	
	18.5	55.94/52.96	2.4	
	38.0	36.48/46.31	2.8	2.3±0.5
	59.3	22.76/31.60	1.9	

Discussion

The Pummerer reaction of sulfoxides with thionyl chloride or acyl chloride has been shown by Bordwell *et al.*[2c,d] to yield α-chlorosulfides. However, the reaction of sulfoxides with such chlorinating agents as acetyl chloride afforded the reduced sulfide though the reaction also involves the initial formation of the chlorosulfonium salt intermediate.[6]

The Pummerer reaction of **1** with thionyl chloride or propionyl chloride in methylene chloride afforded readily the corresponding α-chlorosulfides (**2**) in a good yield without any ring opening, though, in the case of 2,2-dimethyl-1-(phenylsulfinyl)cyclopropane (**1c**), 2,2-dimethyl-1-(phenylthio)cyclopropane (**2c**) was obtained only in 14% yield (Table 1).

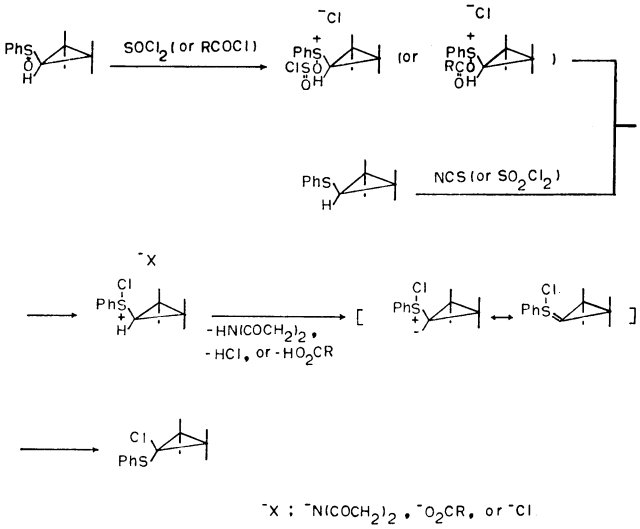
Meanwhile, the reaction of sulfides with such chlorinating agents as NCS is generally considered to proceed *via* the initial formation of the chlorosulfonium salt which then decomposes to afford the α-chlorosulfides. Mechanism of the chlorination of sulfides has previously been proposed by Wilson, Jr. *et al.*[3] to involve a free carbonium ion intermediate. Tuleen *et al.*,[4] however, suggested the reaction to proceed *via* an ylide-ylene intermediate. The chlorination of **2** with NCS was also carried out and was found to afford the corresponding (**3**) in a high yield without any ring opening (Table 3). The lack of any ring opening product both in the Pummerer reaction of **1** with thionyl chloride and acyl chlorides and in the chlorination of **2** with NCS suggests that these chlorinations do not proceed *via* the mechanistic route which involves a free carbonium ion intermediate, since the methanolysis[7] and acetolysis[5a] of 1-chloro-1-(phenylthio)cyclopropanes gave the ring opening products which undoutedly arise from the cyclopropyl carbonium ion as the intermediate.

In the reaction of **1a/5** with thionyl chloride to yield **2a**, the kinetic isotope effect, (k_H/k_D), determined by the competitive chlorinations, was found to be 2.1 (Table 4), while, in chlorination of **2a/6** with sulfuryl chloride the value was 1.8 (Table 5). Thus, the kinetic isotope effects obtained in these chlorinations are quite small in comparison with those of chlorinations of tetrahydrothiophene with chlorine[3b] and of benzyl phenyl sulfide with NCS;[4a] namely 5.1 and 5.7, respectively. These observed values of the kinetic isotope effects are smaller than even those of the general Pummerer reaction (2.9 for the reaction methyl *p*-tolyl sulfoxide with acetic anhydride).[8] The kinetic isotope effects of the chlorination of **1a/5** with thionyl chloride or **2a/6** with sulfuryl chloride are of nearly the same order of magnitude with that of the Pummerer reaction of methylphenylsulfonium methylide with acetic anhydride, *i.e.*, 1.57. Incidentally the Pummerer reaction of methylphenylsulfonium methylide is believed to proceed *via* an ElcB path.[9]

Tuleen[4a] proposed that both the acidity of α-proton of sulfides and the basicity of the counter anion ($^-$X) of the chlorosulfonium salt are two important factors in the chlorination of sulfides.

In Tables 4 and 5 are presented the kinetic isotope effects of chlorination of the sulfoxides (**1a/5**) and the sulfides (**2a/6**) with various chlorinating agents. The basicities of the counter anion ($^-$X) fall in the following order; $^-N(COCH_2)_2 > ^-O_2CMe > ^-Cl$. However, the results obtained cannot be correlated with the order of the basicities; these observed values of kinetic isotope effects are nearly identical. Thus, the results revealed that the basicity of the counter anion ($^-$X) does not significantly affect on the process.

The product distribution, *i.e.*, lack of any ring opening product, the small size of the kinetic isotope effect



Scheme 4.

and the insensitivity of the reaction toward basicity of the counter anion, all seems to suggest that both the Pummerer reaction of **1** and the chlorination of **2** with chlorinating agents such as thionyl chloride or NCS proceed *via* an ylide-ylene intermediate.

Experimental

Material. Spectroscopic grade dichloromethane and benzene and acetic acid-*d*, which were obtained from E. Merck, were used without further purification. All the chlorinating agents, *i.e.*, NCS, thionyl chloride, sulfuryl chloride, acetyl chloride and propionyl chloride were purified by recrystallization or distillation.

*Phenylthiocyclopropanes (**2a—c**).* Phenylthiocyclopropane (**2a**) was prepared by the reaction of 3-chloropropylphenyl sulfide with sodium amide in liquid ammonia.[10] Other phenylthiocyclopropanes (**2b, c**) were prepared by the reaction of chloromethyl phenyl sulfide and potassium *t*-butoxide in 2-methylpropene or *trans*-2-butene.[11]

*Phenylsulfinylcyclopropanes (**1a—c**).* Phenylsulfinylcyclopropanes (**1a—c**) were prepared by the usual oxidation (H_2O_2–AcOH) of the corresponding sulfides (**2a—c**) by the method described in our previous paper.[5c]

*The Reaction of Phenylsulfinylcyclopropanes (**1a—c**) with Chlorinating Agents.* The reaction was carried out as follows. To a solution of 3 mmol of phenylsulfinylcyclopropane (**1**) in 10 ml of dichloromethane was added a 1.2 mol excess of thionyl chloride (or propionyl chloride) in 10 ml of dichloromethane. The mixture was kept refluxing for 1 h and then at room temperature for 2 h. Then, the solution was poured into 50 ml of 5% aqueous sodium carbonate and washed with water. The dichloromethane layer was dried over magnesium sulfate. After removal of dichloromethane, the product (**3**) was purified by distillation *in vacuo* (by bulb to bulb distillation). The products obtained (**3a—c**) were identified by their IR and NMR spectra (see Table 2) and by conversion on treatment with *m*-chloroperbenzoic acid in dichloromethane to the corresponding sulfoxides (**4a—c**) (see Table 2).

*Chlorination of Phenylthiocyclopropanes (**2a—c**) with NCS.* The reaction was carried out as follows. A 1.2 mol excess of NCS was added to a solution of 2 mmol of phenylthiocyclopropane (**2**) in 20 ml of benzene in the presence of a 1.5 mol excess of pyridine at room temperature. After keeping the mixture for overnight at room temperature, the solution was poured into cold water and washed with 5% aqueous sodium thiosulfate, water, 5% aqueous hydrochloric acid, and again water. The product (**3**) was purified further by distillation *in vacuo* (by bulb to bulb distillation).

*Preparation of 1-Chloro-1-(phenylsulfinyl)cyclopropanes (**4a—c**).* A 1.2 mol excess of (dichloroiodo)benzene was added to a solution of 3 mmol of phenylsulfinylcyclopropane (**1**) in 10 ml of dichloromethane in the presence of a 1.5 mol excess of pyridine at 0 °C. After keeping the mixture for 3 h at room temperature, the reaction mixture was poured into cold water and washed with 5% aqueous sodium thiosulfate and water. After removal of dichloromethane, the residue was subjected to the column chromatography packed with silica gel using dichloromethane as eluent. The product (**4**) was purified further by recrystallization from ether–hexane. The structures of these products (**4a—c**) were determined from their IR and NMR spectra (see Table 2). Yields of the products were 92, 87, and 86% for **4a**, **b**, and **c**, respectively.

1-Chloro-1-(phenylsulfinyl) cyclopropanes (**4a—c**) were also prepared in yields of 78, 72, and 73% for **4a**, **b**, and **c**, respectively, by the reaction of **3a—c** with an equimolar amount of *m*-chloroperbenzoic acid in dichloromethane at 0 °C for 5 h. These compounds obtained (**4a—c**) were identified by comparing their IR and NMR spectra with those of the samples obtained by the reaction of **1a—c** with (dichloroiodo)benzene.

*Preparation of 1-Deuterated Phenylsulfinylcyclopropane (**5**).* 1-Deuterated phenylsulfinylcyclopropane (**5**) was prepared by treating the corresponding sulfoxide (**1a**) in NaOD/D_2O-MeOD at reflux for 12 h.[5c]

*Preparation of 1-Deuterated Phenylthiocyclopropane (**6**).* 1-Deuterated phenylthiocyclopropane (**6**) was prepared by treating the corresponding sulfide (**2a**) with butyllithium it tetrahydrofuran at 0 °C for 2 h and then quenching with acetic acid-*d*.[12]

Determination of the Hydrogen-Deuterium Kinetic Isotope Effects in Competitive Chlorination. The kinetic isotope effect in the competitive reaction of phenylsulfinylcyclopropane (**1a**/**5**) was carried out as follows. Three samples, which were dissolved 0.5, 1.0, or 1.5 ml of the dichloromethane solution of thionyl chloride (about 172.8 mmol l^{-1}) in 5 ml of dichloromethane containing known amount of the mixture of **1a** and **5**, respectively, and one sample without thionyl chloride were prepared. These four samples were allowed to react for 24 h at 20±1 °C until the reaction was complete. Then from each sample an aliquot portion (5 μl) of the content was directly injected into the GLC column (1% OV-1; 1 m; 3 mm i.d.; glass column; temperature 100 °C; He flow 40 ml min^{-1}) and the extent of conversion for each sample was calculated from the relative peak areas of phenylsulfinylcyclopropane for each sample and one sample without thionyl chloride, respectively. Meanwhile, ratio of [H]/[D] for each compound was calculated from the intensities of the molecular peaks for undeuterated phenylsulfinylcyclopropane (**5**), respectively, by GLC-mass spectrometry. The hydrogen-deuterium kinetic isotope effects in this competitive reaction were calculated by the Eq. 1. The result was summarized in Table 4.

The kinetic isotope effects in other chlorinations were also estimated similarly in the competitive reactions as described above. These results were summarized in Tables 4 and 5.

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