JOC Article

Reactions of Methylenecyclopropanes with Phenylsulfenyl Chloride and Phenylselenyl Chloride

Le-Ping Liu[‡] and Min Shi*[,†]

Department of Chemistry, East China Normal University, 3663 Zhong Shan Bei Lu, Shanghai 20062, China and State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

mshi@pub.sioc.ac.cn

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The reaction of methylenecyclopropanes **1** with phenylsulfenyl chloride or phenylselenyl chloride gives (cyclobut-1-enylsulfanyl)benzene or (cyclobut-1-enylselanyl)benzene along with ring-opened product in good total yields at 0 °C in various solvents. A plausible mechanism has been proposed.

Introduction

Methylenecyclopropanes (MCPs) **1** are highly strained but readily accessible molecules that have served as useful building blocks in organic synthesis.[1,2] Previously, Dunkelblum reported that the addition of 2,4-dinitrobenzenesulfenyl chloride (ArSCl) to a number of phenylmethylenecyclopropanes **1** in dichloromethane (DCM) or AcOH produced the normal addition product **2** or **2** along with ring-opened product **3** (Scheme 1).[3]

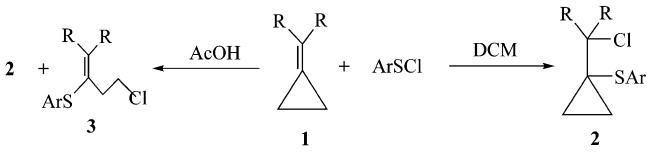
Recently, we have been investigating the Lewis acid-mediated ring-opening reactions of MCPs **1** with a number of nucleophiles such as alcohols, aromatic amines, and other reactants under mild conditions.[4] In this paper, we wish to report that the reaction of MCPs **1** with phenylsulfenyl chloride or phenylselenyl chloride produces the corresponding *gem*-disubstituted (cyclobut-1-enylsulfanyl)benzene **4** or *gem*-disubstituted (cyclobut-1-enylselanyl)benzene **5** along with ring-opened product **3** or **6** under mild conditions.

Results and Discussion

Using diphenylmethylenecyclopropane **1a** as the substrate, we examined the reaction with phenylsulfenyl chloride and phenylselenyl chloride in various solvents at 0 °C. The results are summarized in Tables 1 and 2, respectively. As can be seen from Tables 1 and 2, the reactions proceeded smoothly in various solvents at 0 °C to give (cyclobut-1-enylsulfanyl)benzene **4a** and (cyclobut-1-enylselanyl)benzene **5a** along with ring-opened products **3a** and **6a**, respectively, in about 63−89% total yields (Table 1, entries 1−5; Table 2, entries 1−6). Their structures are determined by ^{1}H and ^{13}C NMR spectroscopic data and HRMS analyses (Supporting Information) and X-ray diffraction. The X-ray crystal structure of **5a** is shown in Figure 1 in the Supporting Information.[5] In DCM, these reactions can complete within 2 min to give **4a** and **5a** in relatively higher yields (Table 1, entry 1; Table 2, entry 1).

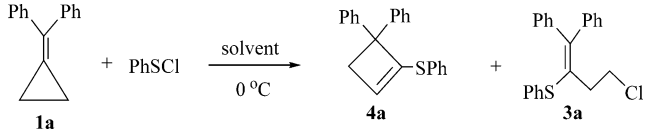
Next, we carried out the reactions of various *gem*-aryldisubstituted MCPs **1** with phenylsulfenyl chloride or phenylselenyl chloride in DCM at 0 °C. The results are summarized in Tables 3 and 4, respectively. We found that the substituents on the benzene ring of MCPs **1**

SCHEME 1. The Reaction of MCPs 1 with 2,4-Dinitrobenzenesulfenyl Chloride



R= aromatic group, Ar= 2,4-$(NO_2)_2C_6H_3$

TABLE 1. The Reaction of MCP 1a (0.3 mmol) with Phenylsulfenyl Chloride (0.3 mmol) in Various Solvents



			yield, %[a]	
entry	solvent	time, min	**4a**	**3a**
1	CH_2Cl_2 (DCM)	2	48	41
2	THF	20	35	41
3	MeCN	2	45	21
4	Et_2O	20	42	22
5	$PhCH_3$	20	44	27

[a] Isolated yields.

† Chinese Academy of Sciences.

‡ East China Normal University.

(1) For synthesis of MCPs, see: Brandi, A.; Goti, A. *Chem. Rev.* **1998**, *98*, 598.

(2) For recent reviews, see: (a) Nakamura, I.; Yamamoto, Y. *Adv. Synth. Catal.* **2002**, *344*, 111. (b) Brandi, A.; Cicchi, S.; Cordero, F. M.; Goti, A. *Chem. Rev.* **2003**, *103*, 1213.

(3) Dunkelblum, E. *Tetrahedron* **1974**, *30*, 3991.

(4) (a) Shi, M.; Xu, B. *Org. Lett.* **2002**, *4*, 2145. (b) Shi, M.; Chen, Y.; Xu, B.; Tang, J. *Tetrahedron Lett.* **2002**, *43*, 8019. (c) Shi, M.; Xu, B. *Tetrahedron Lett.* **2003**, *44*, 3839. (d) Shi, M.; Chen, Y.; Xu, B. *Org. Lett.* **2003**, *5*, 1225.

(5) The crystal data for **5a** have been deposited in the CCDC, number 227147. Empirical formula, $C_{22}H_{18}Se$; formula weight, 361.32; crystal color, colorless; habit, prismatic; crystal system, monoclinic; lattice type, primitive; lattice parameters, a = 11.9201(12) Å, b = 9.1090(10) Å, c = 16.1219(16) Å, α = 90°, β = 105.248(2)°, γ = 90°, V = 1688.9(3) Å^3; space group, $P2(1)/n$; Z = 4; D_{calc} = 1.421 g/cm^3; F_{000} = 736; diffractometer, Rigaku AFC7R; residuals, R = 0.0459, R_w = 0.1012.

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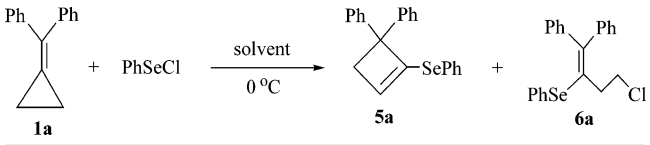
TABLE 2. The Reaction of MCP 1a (0.3 mmol) with Phenylselenyl Chloride (0.3 mmol) in Various Solvents

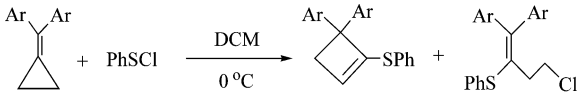


1a 5a 6a

			yield, %[a]	
entry	solvent	time, min	**5a**	**6a**
1	CH_2Cl_2 (DCM)	2	49	37
2	THF	20	44	32
3	MeCN	2	47	23
4	Et_2O	20	39	28
5	$PhCH_3$	20	41	22
6	CH_2ClCH_2Cl	10	45	32

[a] Isolated yields.

TABLE 3. The Reaction of MCPs 1 (0.3 mmol) with Phenylsulfenyl (0.3 mmol) Chloride in DCM at 0 °C

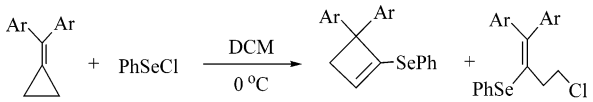


1 4 3

		yield, %[a]	
entry	Ar	**4**	**3**
1	*p*-MeC_6H_4 **1b**	**4b**, 15	**3b**, 69
2	*p*-$MeOC_6H_4$ **1c**	**4c**, trace	**3c**, 80
3	*p*-ClC_6H_4 **1d**	**4d**, 62	**3d**, 23
4	*p*-FC_6H_4 **1e**	**4e**, 55	**3e**, 31

[a] Isolated yields.

TABLE 4. The Reaction of MCPs 1 (0.3 mmol) with Phenylselenyl Chloride (0.3 mmol) in DCM at 0 °C



1 5 6

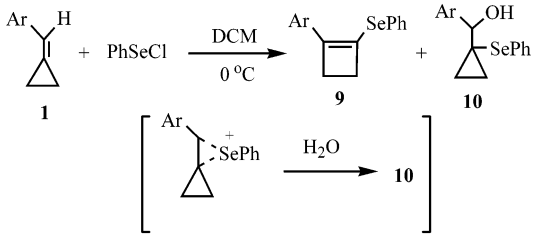
		yield, %[a]	
entry	Ar	**5**	**6**
1	*p*-MeC_6H_4 **1b**	**5b**, trace	**6b**, 75
2	*p*-$MeOC_6H_4$ **1c**	**5c**, trace	**6c**, 76
3	*p*-ClC_6H_4 **1d**	**5d**, 47	**6d**, 41
4	*p*-FC_6H_4 **1e**	**5e**, 45	**6e**, 36

[a] Isolated yields.

significantly affected the distribution of products. For MCPs **1b** and **1c** having an electron-donating group on the benzene ring, the reactions produced (cyclobut-1-enylsulfanyl)benzene **4b**, **4c** or (cyclobut-1-enylselanyl)-benzene **5b**, **5c** in either trace or low yields. The major reaction products are the ring-opened products **3b**, **3c** and **6b**, **6c**, respectively (Table 3, entries 1 and 2; Table 4, entries 1 and 2). For MCPs **1d** and **1e** having an electron-withdrawing group on the benzene ring, the reactions produced (cyclobut-1-enylsulfanyl)benzene **4** or (cyclobut-1-enylselanyl)benzene **5** in higher yields (Table 3, entries 3 and 4; Table 4, entries 3 and 4).

For unsymmetric MCPs **1f** or **1g** having a methyl group or **1h** having a cyclic aliphatic group, the reactions yielded the products of the proton elimination with

TABLE 5. The Reaction of MCPs 1i–*l* (0.3 mmol) with Phenylselenyl Chloride (0.3 mmol) in DCM



1 9 10

		yield, %[a]	
entry	Ar	**9**	**10**
1	*m*,*m*,*p*-$(MeO)_3C_6H_2$ **1i**	**9a**, 37	**10a**, 46
2	*p*-$MeOC_6H_4$ **1j**	**9b**, 38	**10b**, 45
3	C_6H_5 **1k**	**9c**, 29	**10c**, 41
4	*p*-BrC_6H_4 **1l**	**9d**, 36	**10d**, 31
5[b]	*m*,*m*,*p*-$(MeO)_3C_6H_2$ **1i**	**9a**, 7	**10a**, 82

[a] Isolated yields. [b] 3 equiv of H_2O was added.

retention of cyclopropane ring **7a**, **7b**, **8a**, and **8b** in moderate to good yields under the same conditions, respectively (Scheme 2).

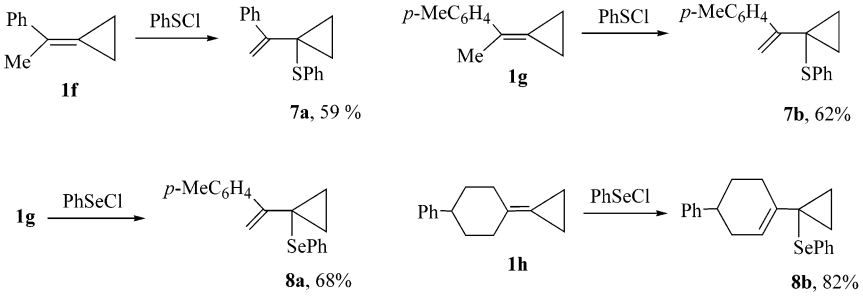
Interestingly for unsymmetric MCPs **1i**–***l*** having a hydrogen atom, the reactions with phenylselenyl chloride produced novel (cyclobut-1-enylselanyl)benzenes **9a**–**d** along with hydrolyzed products **10a**–**d** derived from the nucleophilic attack of the episelenium intermediates[3,6] by ambient moisture (H_2O) in moderate to good total yields (Table 5, entries 1–4). To confirm the formation route of product **10**, we carried out the same reaction in the presence of 3 equiv of water under the same conditions. The corresponding hydrolyzed product **10a** was obtained in 82% yield (Table 5, entry 5).[6] This result suggests that this type of MCPs **1** is very moisture sensitive during the reaction with phenylselenyl chloride and workup. Their structures are determined by ^1H and ^{13}C NMR spectroscopic data and HRMS analyses and X-ray diffraction. The ORTEP draw of **9a** is shown in Figure 2 in the Supporting Information.[7] For aliphatic MCP **1m**, this reaction produced many unidentified products (Scheme 3). Therefore, one aromatic group in MCPs **1** is required for this type of transformation based on the above results.

On the basis of the above results, a plausible mechanism for the reaction of MCPs **1** with phenylsulfenyl chloride or phenylselenyl chloride is outlined in Scheme 4. The addition of phenylsulfenyl chloride or phenylselenyl chloride to MCPs **1** gives intermediate **A** as the episulfonium or episelenium ion, which leads to the intermediate carbonium ion **B**. The nucleophilic attack by Cl^- furnishes the ring-opened product **3** or **6**. The rearrangement of carbonium ion **B** gives ring-expanded

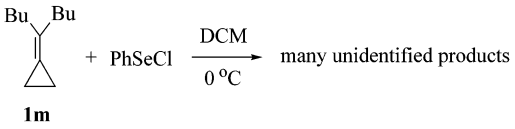
(6) It is conceivable that this less hindered episelenium ion is more easily subject to the influence of ambient water. (a) Slobodkin, R.; Kharash, N. *J. Org. Chem.* **1960**, *25*, 866. (b) Cristol, S. J.; Jarvis, B. B. *J. Am. Chem. Soc.* **1966**, *88*, 3091.

(7) The crystal data for **9a** have been deposited in the CCDC, number 227246. Empirical formula, $C_{19}H_{20}SeO_3$; formula weight, 375.31; crystal color, colorless; habit, prismatic; crystal system, triclinic; lattice type, primitive; lattice parameters, $a = 8.1918(11)$ Å, $b = 9.9371(13)$ Å, $c = 11.6367(16)$ Å, $\alpha = 112.611(2)°$, $\beta = 91.577(2)°$, $\gamma = 100.579(3)°$, $V = 854.5(2)$Å^3; space group, $P\bar{1}$; $Z = 2$; $D_{calc} = 1.459$ g/cm^3; $F_{000} = 384$; diffractometer, Rigaku AFC7R.; residuals, $R = 0.0495$, $R_w = 0.1104$.

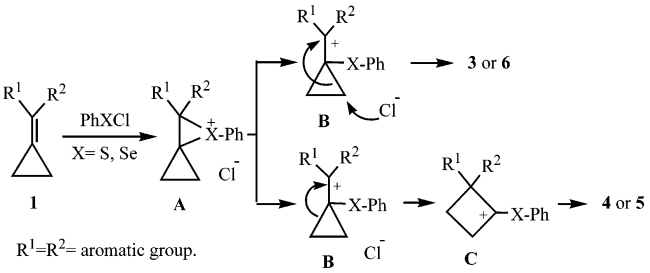
SCHEME 2. The Reaction of MCPs 1f, 1g, and 1h (0.3 mmol) with Phenylsulfenyl Chloride (0.3 mmol) or Phenylselenyl Chloride (0.3 mmol) in DCM

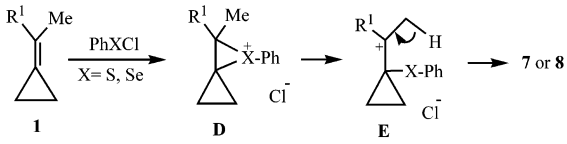


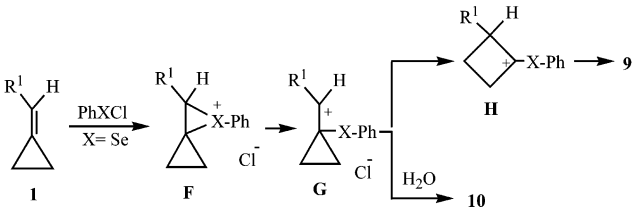
SCHEME 3. The Reaction of Aliphatic MCP 1m (0.3 mmol) with Phenylselenyl Chloride (0.3 mmol) in DCM



SCHEME 4. The Plausible Reaction Mechanism of MCPs 1 with Phenylsulfenyl Chloride and Phenylselenyl Chloride in DCM







cyclobutyl cation **C**,[8] which affords product **4** or **5** via a β-proton elimination (Scheme 4). For MCPs **1b** and **1c** which have an electron-donating group on the benzene ring, the carbonium ion **B** is more stabilized by aromatic groups. Therefore, it is more likely to react with Cl^- to furnish the ring-opened product **3** or **6**. If R^2 = Me, the intermediate carbonium ion **E** derived from the corresponding episulfonium or episelenium ion **D** gives **7** or **8** via a β-proton elimination. For MCP **1h** (R^2 = H), the intermediate carbonium ion **G** derived from the corresponding episulfonium or episelenium ion **F** affords the ring-expanded cyclobutyl cation **G**, which produces the product **9** via a β-proton elimination as well. In the presence of ambient water, this less hindered cation will be attacked by H_2O to produce the product **10** (Scheme 4). One aromatic group is at least required to stabilize the formed cyclopropyl cationic intermediates **B**, **E**, and **G**. This is why aliphatic MCP **1m** gives a disordered reaction.

On the basis of the above mechanism, we can explain why the addition of 2,4-dinitrobenzenesulfenyl chloride (ArSCl) to a number of phenylmethylenecyclopropanes in dichloromethane (DCM) produced the normal addition product **2**. The two strongly electron-withdrawing groups (NO_2−) on the benzene ring of ArSCl cause the corresponding episulfonium ion **A** to be a relatively electron deficient species that can more easily accept the nucleophilic attack by Cl^-. Thus, the normal addition product **2** was formed as the major product in this reaction.

Conclusion

We have found that the reaction of MCPs **1** with phenylsulfenyl chloride or phenylselenyl chloride gives the ring-opened homoallylic chloride and (cyclobut-1-enylsulfanyl)benzene and (cyclobut-1-enylselanyl)benzene depending on the structure of MCPs **1**. A plausible mechanism has been proposed based on the above experiments and previous reports. The novelty in this paper is the formation of an unsaturated four-membered ring under mild conditions. Efforts are underway to elucidate the mechanistic details of this reaction and to disclose the scope and limitation of this transformation. Work along this line is currently in progress.

Experimental Section

All of the MCPs **1**, phenylsulfenyl chloride, and phenylselenyl chloride were prepared according to literature methods.[9,10]

Typical Reaction Procedure for the Reaction of MCPs 1 with Phenylselenyl Chloride. To a solution of MCP **1a** (62 mg, 0.3 mmol) in dichloromethane (1.0 mL) was added phenylselenyl chloride (57 mg, 0.3 mmol) in dichloromethane (1.0 mL) at 0 °C, and the reaction mixture was stirred for 2 min (monitored by TLC). After the starting materials (MCPs **1**) were consumed, the solvent was removed under reduced pressure and the residue was subjected to a flash column chromatography to give the desired products **5a** (53 mg, 49%) and **6a** (44 mg, 37%) as colorless solids.

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(10) (a) Barrett, A. G. M.; Dhanak, D.; Graboski, G. G.; Taylor, S. J. *Organic Syntheses*; Wiley: New York, 1993; Collect. Vol. VIII, p 550. (b) Reich, H. J.; Cohen, M. L.; Clark, P. S. *Org. Synth.* **1979**, *59*, 141.

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Supporting Information Available: The X-ray diffraction data for **5a** and **9a**, spectroscopic data (^{1}H and ^{13}C NMR spectra data) and analytic data for the compounds shown in Tables 1−5 and Schemes 1−3, and a detailed description of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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