Lewis acid catalyzed ring-opening reactions of methylenecyclopropanes with diphenylphosphine oxide in the presence of sulfur or selenium†

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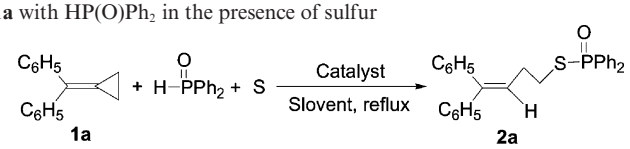
Methylenecyclopropanes undergo an interesting Lewis acid-catalyzed ring-opening reaction with diphenylphosphine oxide in the presence of sulfur or selenium upon heating at 85 °C in 1,2-dichloroethane to give the corresponding homoallylic thiol or selenol derivatives in good to high yields.

Methylenecyclopropanes (MCPs) are highly strained but readily accessible molecules that have served as useful building blocks in organic synthesis.[1] MCPs undergo a variety of ring-opening reactions in the presence of transition metals or Lewis acids because the relief of ring strain provides a potent thermodynamic driving force.[2–8] In this paper, we wish to report that methylenecyclopropanes can undergo an interesting Lewis acid-catalyzed ring-opening reaction with diphenylphosphine oxide in the presence of sulfur or selenium upon heating at 85 °C in 1,2-dichloroethane (DCE) to give the corresponding homoallylic thiol or selenol derivatives in good to high yields.

We first envisioned that MCPs can easily react with diphenylphosphine oxide [$Ph_2P(O)H$], which is in an equilibrium with Ph_2P–OH,[9] to give the corresponding homoallylic alcohol derivatives similar to those of alcohols, aromatic amines or sulfonamides in the presence of Lewis acid.[3–6] However, a disordered reaction was observed. In the following investigation, we found that, with the addition of sulfur, the expected ring-opening reaction of MCP **1a** with diphenylphosphine oxide takes place in the presence of a Lewis acid to give the corresponding homoallylic thiol derivative **2a** in good yield under mild conditions. The results are summarized in Table 1. We found that in the absence of Lewis acid, **2a** was obtained in 67% and 35% yield in DCE under reflux (85 °C) after 12 and 1 h, respectively (Table 1, entries 1 and 2). In the presence of a Lewis acid, **2a** was obtained in good yields within 1 h under otherwise identical conditions (Table 1, entries 3–8). Lewis acid $Sn(OTf)_2$ is the best one for this reaction to give **2a** in 86% yield in DCE under reflux (Table 1, entries 2–8). Further examination of the solvent effects revealed that DCE is the best one for this transformation (Table 1, entries 9–14). In dichloromethane or ether, **2a** was obtained in 67% and 68% at room temperature (20 °C) after 12 h, respectively (Table 1, entries 11 and 13). Only, 25% of **2a** was formed in dichloromethane at room temperature (20 °C) within 1 h (Table 1, entry 12).

Table 1 Optimization of conditions for the ring-opening reaction of MCP **1a** with $HP(O)Ph_2$ in the presence of sulfur



Entry[a]	Catalyst	Solvent	Time/h	Yield/(%)[b] **2b**
1	none	DCE	12	67
2	none	DCE	1	35
3	$Sn(OTf)_2$	DCE	1	86
4	$La(OTf)_3$	DCE	1	74
5	$Zr(OTf)_4$	DCE	1	66
6	$Sc(OTf)_3$	DCE	1	81
7	$Yb(OTf)_3$	DCE	1	77
8	BF_3 Et_2O	DCE	1	66
9	$Sn(OTf)_2$	THF	10	44
10	$Sn(OTf)_2$	CH_3CN	10	64
11	$Sn(OTf)_2$	CH_2Cl_2[c]	12	67
12	$Sn(OTf)_2$	CH_2Cl_2[c]	1	25
13	$Sn(OTf)_2$	ether[c]	12	68
14	$Sn(OTf)_2$	toluene	8	80

[a] Reaction conditions: **1a** (0.2 mmol), $HP(O)Ph_2$ (0.3 mmol), sulfur (0.3 mmol), Lewis acid (10 mol%), solvent (2.0 mL), and the reactions were carried out under reflux. [b] Isolated yields. [c] At room temperature.

Under these optimal reaction conditions, we next carried out $Sn(OTf)_2$-catalyzed ring-opening reactions of a variety of MCPs **1** with diphenylphosphine oxide in the presence of sulfur and selenium. We found that the corresponding ring-opening products **2** were obtained in moderate to good yields within 1–6 h for MCPs **1** with electron-rich, electron-neutral, and electron-poor substituents on the benzene ring (Table 2). For unsymmetrical MCPs **1e**, **1g**, and **1h**, the corresponding products **2e**, **2g**, and **2h** were obtained as mixtures of *E*- and *Z*-isomers (Table 2, entries 4, 6 and 7) (ESI†). But for unsymmetrical MCPs **1i**, **1j**, **1k**, and **1l**, the corresponding products **2i**, **2j**, **2k** and **2l** were obtained as the single *E*-isomer in moderate yields (Table 2, entries 8–11). The possible reason is that the aromatic group is sterically much larger than a hydrogen atom, which results in the high regioselectivity. Moreover, in the presence of selenium, the corresponding products **2m–2p** could be also obtained in good yields under the standard conditions (Table 1, entries 12–15).

The reaction of MCP **1a** with diphenylphosphine oxide has also been examined under identical conditions in the presence of an oxygen atmosphere.[10] However, the corresponding ring-opened product **3a** was formed in 32% yield after 10 h (Scheme 1).

The structures of all the products reported in this paper were determined by ^1H, ^{13}C NMR, and ^{31}P NMR spectroscopic data, HRMS or microanalysis.

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† The spectroscopic data (^1H, ^{13}C, and ^{31}P NMR spectra data), HRMS, analytic data of the compounds shown in Tables 1 and 2 and Scheme 2 and the detailed description of experimental procedures. See DOI: 10.1039/b616378e

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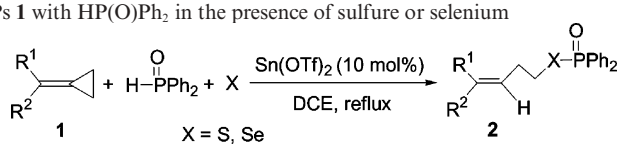
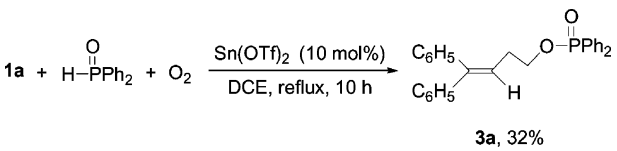
Table 2 Ring-opening reaction of MCPs **1** with $HP(O)Ph_2$ in the presence of sulfure or selenium



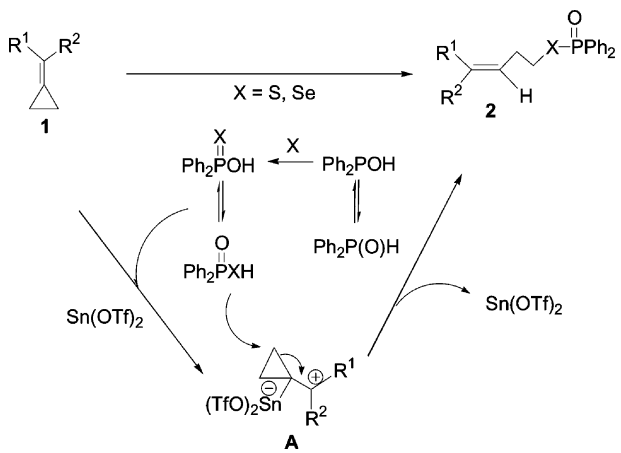
Entry[a]	MCPs (R^1/R^2)	X	Time/h	Yield/(%)[b] **2** (E : Z)
1	**1b** (ρ-MeC_6H_4/ρ-MeC_6H_4)	S	1	**2b**, 71
2	**1c** (ρ-ClC_6H_4/ρ-ClC_6H_4)		1	**2c**, 81
3	**1b** (ρ-$MeOC_6H_4$/ρ-$MeOC_6H_4$)		1	**2d**, 80
4	**1e** (ρ-ClC_6H_4/C_6H_5)		1	**2e**, 66 (1 : 1)[c]
5	**1f** (ρ-FC_6H_4/ρ-FC_6H_4)		1	**2f**, 71
6	**1g** (ρ-$MeOC_6H_4$/ρ-C_6H_5)		1	**2g**, 78 (1 : 1)[c]
7	**1h** (C_6H_5/Me)		1	**2h**, 51 (4 : 1)[c]
8	**1i** (C_6H_5/H)		1	**2i**, 73[d]
9	**1j** (*o*-MeC_6H_4/H)		1	**2j**, 65[d]
10	**1k** (*p*-MeC_6H_4/H)		1	**2k**, 68[d]
11	**1l** (*m*-MeC_6H_4/H)		1	**21**, 61[d]
12	**1a**	Se	1.5	**2m**, 73
13	**1b**		1.5	**2n**, 82
14	**1c**		2.5	**2o**, 66
15	**1i**		6	**2p**, 71[d]

[a] Reactions were carried out in an oil bath at 80 °C. Reaction conditions: **1** (0.3 mmol), $HP(O)Ph_2$ (0.45 mmol), X (0.45 mmol), $Sn(OTf)_2$ (10 mol%), DEC (2.0 mL). [b] Isolated yields. [c] Mixtures of *E*- and *Z*-isomers. [d] Products were obtained as *E*-configuration.



Scheme 1 Reaction of MCP **1a** with $HP(O)\ Ph_2$ under oxygen atmosphere.

The reaction mechanism is outlined in Scheme 2. The reaction of sulfur or selenium with Ph_2POH produces the corresponding $Ph_2P(X)OH$ species (X = S, Se),[11] which is in equilibrium with $Ph_2P(O)XH$.[12] The reaction of $Ph_2P(O)XH$ or $Ph_2P(X)OH$ with $Sn(OTf)_2$ activated MCP **1** (intermediate **A**) produces the corresponding product **2** and regenerates $Sn(OTf)_2$. The stronger nucleophilic properties of sulfur or selenium atoms play a key role in producing the corresponding ring-opened products in higher yields.[13]



Scheme 2 Proposed mechanism of ring-opening reactions of MCPs catalyzed by $Sn(OTf)_2$.

In summary, we have disclosed an interesting Lewis acid-catalyzed ring-opening reaction of MCPs with diphenylphosphine oxide in the presence of sulfur or selenium upon heating at 85 °C in DCE to give the corresponding ring-opening products in moderate to good yields.[14] The corresponding homoallylic thiol or selenol derivatives **2** may be useful intermediates in organic synthesis. Efforts are in progress to elucidate the mechanistic details of this reaction and to determine its scope and limitations.

Acknowledgements

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14 General procedure for the reaction of 1,1-diphenylmethylenecyclopropane **1a** with diphenylphosphine oxide in the presence of $Sn(OTf)_2$ and sulfur. 1,1-Diphenylmethylenecyclopropane **1a** (0.30 mmol), diphenylphosphine oxide (0.45 mmol), sulfur (0.45 mmol) and $Sn(OTf)_2$ (0.03 mmol) were dissolved in 2.0 mL of DCE. The reaction mixture was stirred at 80 °C for 1 h. Then, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2) to give the corresponding product **2a** in 86% yield. **2a**: white solid, mp 102–104 °C; IR (CH_2Cl_2): ν 3075, 3023, 1655, 1596, 1494, 1438, 1200, 1115, 926, 753, 724, 698, 568 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$, TMS): δ 2.43 (2H, dt, $J = 7.2$, 7.2 Hz, CH_2), 2.89 (2H, dt, $J = 7.2$, 7.8 Hz, CH_2), 6.01 (1H, t, $J = 7.8$ Hz, CH), 7.08–7.51 (16H, m, ArH), 7.81–7.88 (4H, m, ArH); ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ 29.1 (d, $J = 2.3$ Hz), 30.4 (d, $J = 5.2$ Hz), 126.1, 127.0, 127.2, 128.0, 128.4, 128.6, 129.6, 131.4, 132.2, 132.4, 133.8, 139.4, 142.0, 143.7; ^{31}P NMR (121.45 MHz, $CDCl_3$, TMS): δ 44.50; MS (EI) m/z (%): 441 (47.12) [M + H^+], 419 (15.10), 409 (12.78), 388 (100.00); HRMS (MALDI) calcd. for $C_{28}H_{26}POS^{+1}$ [M + H^+] requires 441.1442, found: 441.1436.

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