

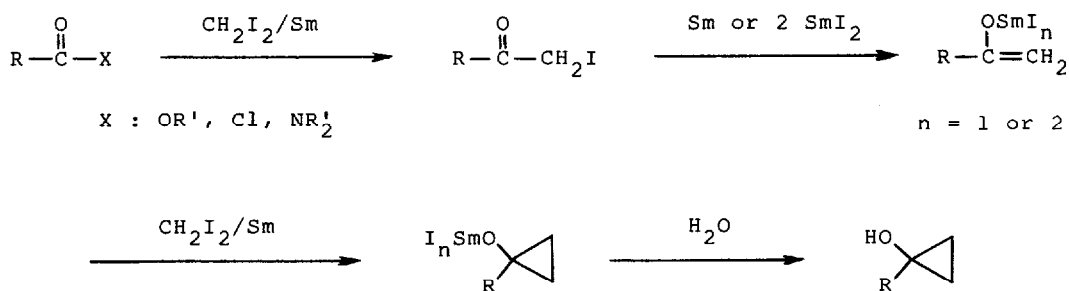
TANDEM ONE-CARBON HOMOLOGATION OF ESTERS TO CYCLOPROPANOLS

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Summary: Esters react with diiodomethane in the presence of samarium to afford 1-substituted cyclopropanols in good yields.

Previously, we reported that  $\alpha$ -haloketones reacted with diiodomethane in the presence of samarium to give cyclopropanols.<sup>1</sup> This cyclopropanation reaction is considered to proceed through the following pathway.  $\alpha$ -Haloketones are reduced with samarium or divalent samarium to generate samarium enolates, which are subsequently subjected to the Simmons-Smith type cyclopropanation with samarium carbene species.<sup>2,3</sup>

These mechanistic considerations have led us to develop a new one-pot synthesis of 1-substituted cyclopropanols from carboxylic acid derivatives via tandem one-carbon homologation. Thus, we have envisioned that cyclopropanols might be produced through the following reaction pathway.



Our preliminary experiments to demonstrate this presumption were carried out using benzoic acid derivatives. The results are summarized in Table 1. The expected product, 1-phenylcyclopropanol, was produced in all cases except for benzamide; the highest yield was obtained in the case of ethyl benzoate. Benzoyl chloride was converted to the cyclopropanol in 16% yield; significant amounts of benzoin and benzil were produced in this reaction.<sup>4</sup> It is noted that benzoic acid itself provided the cyclopropanol under these conditions although the yield was poor.

Table 1. One-pot Cyclopropanation of Benzoic Acid Derivatives

$$\text{PhCOX} \xrightarrow[\text{THF}]{\text{excess CH}_2\text{I}_2/\text{Sm}} \text{HO}-\text{C}(\text{R})-\text{Cyclopropane}$$

PhCOX	Molar ratio of PhCOX/CH <sub>2</sub> I <sub>2</sub> /Sm	Conditions	Yield (%)
PhCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	1:2:3	reflux, 0.7 h	42
"	1:3:4	reflux, 0.7 h	66
"	1:3:4	50 °C, 1.5 h	71
"	1:3:4	20 °C, 1.5 h	58
"	1:4:4	20 °C, 0.7 h	66
"	1:4:6	reflux, 0.7 h	56
"	1:5:6	reflux, 0.7 h	65
"	1:5:6	50 °C, 1.2 h	76
"	1:5:6	0 °C, 1 h	45
"	1:5:6	-78-0 °C, 2 h	33
"	1:8:6	reflux, 0.7 h	44
PhCO <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	1:3:4	50 °C, 1.5 h	34
PhCOCl	1:3:4	50 °C, 1.5 h	16
PhCOSC <sub>4</sub> H <sub>9</sub>	1:3:4	50 °C, 1.5 h	23
PhCON(CH <sub>3</sub> ) <sub>2</sub>	1:3:4	50 °C, 1.5 h	34
PhCONH <sub>2</sub>	1:3:4	50 °C, 1.5 h	0
PhCO <sub>2</sub> H	1:3:4	50 °C, 1.5 h	19

Other lanthanoid metals (La, Ce, Yb) were also tested for the reaction of ethyl benzoate under similar conditions.<sup>5</sup> Lanthanum, cerium, and ytterbium provided 1-phenylcyclopropanol in 19%, 32%, and 10% yields, respectively. However, no or only a trace of the expected cyclopropanol was produced by the use of other metals or reducing agents such as magnesium, zinc-copper couple, lithium naphthalenide, or diethyl zinc.

On the basis of these results, we next examined the reaction of various esters with CH<sub>2</sub>I<sub>2</sub>/Sm in order to clarify the general scope of the reaction. Some representative results are shown in Table 2.<sup>6</sup>

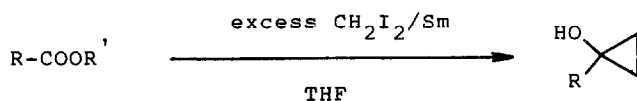

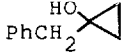
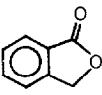
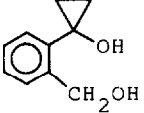


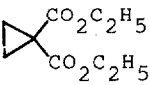
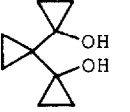
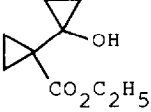
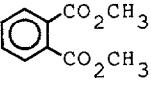
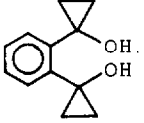
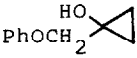
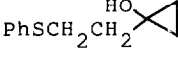


Table 2. One-pot Synthesis of 1-Substituted Cyclopropanols from Esters<sup>a</sup>

Ester	Molar ratio of Ester/CH <sub>2</sub> I <sub>2</sub> /Sm	Product	Yield (%) <sup>b</sup>
PhCO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	1:3:4		71
PhCO <sub>2</sub> C(CH <sub>3</sub> ) <sub>3</sub>	1:3:4	"	34
PhCH <sub>2</sub> CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	1:3:4		51
	1:3:4		59
	1:3:4		70
	1:6:8	 22 + 	14
	1:6:8		21
PhOCH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	1:3:4		55
PhSCH <sub>2</sub> CO <sub>2</sub> CH <sub>3</sub>	1:3:4		9 <sup>c</sup>

<sup>a</sup>All reactions were carried out in THF at 50 °C. The conditions were not optimized. <sup>b</sup>Isolated yield. <sup>c</sup>Thioanisole and (phenylthio)acetone were obtained in 29% and 12% yields, respectively.

A characteristic feature of this method is that cyclopropanols are synthesized directly from esters via tandem one-carbon homologation. It should be also noted that other carbon-carbon double bond remained unchanged during the reaction.

Another interesting fact is that three methylene components were incorporated in the reaction of phenylthioacetic acid methyl ester.<sup>7</sup>

The reaction described herein provides a new method for the synthesis of cyclopropanols<sup>8-10</sup> and may be useful in organic synthesis.<sup>11</sup>

References and Notes

1. T. Imamoto, T. Takeyama, and H. Koto, *Tetrahedron Lett.*, 27, 3243 (1986).
2. T. Imamoto and N. Takiyama, *Tetrahedron Lett.*, 28, 1307 (1987).
3. Samarium-promoted cyclopropanation of allyl alcohols was reported by Molander et al. G. A. Molander and J. B. Etter, *J. Org. Chem.*, 52, 3942 (1987).
4. Low-valent samarium-promoted coupling reaction of acid chlorides to  $\alpha$ -diketones and acyloins was reported by Kagan et al. P. Girard, R. Couffignal, and H. B. Kagan, *Tetrahedron Lett.*, 22, 3959 (1981).
5. The reactions were carried out in THF at 50 °C with a molar ratio of 1:3:4 (ethyl benzoate/diiodomethane/lanthanoid metal).
6. General procedure: Samarium powder (ca. 40 mesh) (600 mg, 4 matom) was placed in a 30 ml two-necked flask and covered with 2 ml of dry THF. The mixture was warmed to 50 °C, and to this mixture was added a solution of ester (1 mmol) and diiodomethane (804 mg, 3 mmol) in THF (8 ml) under argon. The reaction was usually initiated within a few minutes after addition of several drops of the solution. The remainder of the solution was slowly added over a period of 1.5 h with vigorous stirring. After addition, the mixture was cooled, treated with 1N HCl, and extracted with ether. The product was isolated by chromatography on silica gel.
7. The formation of this compound is reasonably explained by assuming the occurrence of the Stevens rearrangement of a sulfonium ylide produced by the reaction of the sulfide with the samarium carbenoid.
8. Recently, Kagan et al. reported that cyclopropanols were easily obtained by an unusual double cyclization of 2-allyloxybenzoic acid chlorides mediated by samarium diiodide. M. Sasaki, J. Collin, and H. B. Kagan, *Tetrahedron Lett.*, 29, 6105 (1988).
9. Barluenga et al. reported a new one-pot synthesis of 1-substituted cyclopropanols from acid chlorides by the reaction with two equivalents of chloromethyl lithium, followed by treatment with lithium powder. J. Barluenga, J. L. Fernandez-Simon, J. M. Concellon, and M. Yus, *Synthesis*, 1987, 584.
10. For other methods for the preparation of cyclopropanols, see the following: (a) D. H. Gibson and C. H. DePuy, *Chem. Rev.*, 74, 605 (1974) and references cited therein. (b) J. Barluenga, J. Florez, and M. Yus, *Synthesis*, 1983, 647. (c) T. Sato, M. Watanabe, T. Watanabe, Y. Onoda, and E. Murayama, *J. Org. Chem.*, 53, 1894 (1988).
11. This work was supported by a grant from the Ministry of Education, Science and Culture of the Japanese Government.

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