# RING OPENING OF CYCLOPROPANECARBOXYLATES USING SAMARIUM(II) DIIODIDE ($SmI_2$)-HMPA-THF SYSTEM

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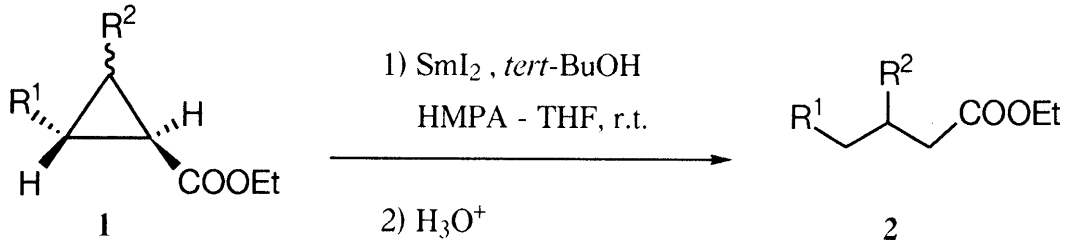
Cyclopropane ring of 2- and 2,3-substituted cyclopropanecarboxylates (**1**) was regioselectively cleaved using $SmI_2$-HMPA-THF system in the presence of *tert*-BuOH to give 4- and 3,4-substituted butyrates (**2**) in moderate to good yields.

**KEY WORDS** samarium diiodide; cyclopropane; ring opening; cyclopropanecarboxylate; 4-arylbutyrate; 4-aryl-3-trimethylsilylbutyrate

Since Kagan and his co-workers reported the first work on the use of samarium diiodide ($SmI_2$) in synthetic organic chemistry,[1] many applications of the reagent have been developed.[2] Due to its reactivity,[3] cyclopropane ring opening has been one of the interesting subjects, and several examples of the cyclopropane ring opening reactions using $SmI_2$ have been reported.[4] We have investigated the reactivity of $SmI_2$[5a] and ring opening of cyclopropanecarboxylates and cyclopropane-1,1-dicarboxylates with $SmI_2$.[5b,c] Recently, Imamoto and his co-workers reported the cyclopropane ring cleavage of cyclopropane-1,1-dicarboxylates with $SmI_2$ in the presence of tris(dibenzoylmethiodo)iron(III), but they stated in the report that cyclopropanemonocarboxylate was not reactive except for a low-yield example of a thioester.[6] In this paper, we describe the cyclopropane ring opening of 2-substituted and 2,3-disubstituted cyclopropanemonocarboxylates (**1**).




1 2

Ethyl 2-phenylcyclopropanecarboxylate (**1a** : $R^1 = C_6H_5$, $R^2$=H) was treated with $SmI_2$ (3.0 eq) in THF-HMPA (10: 1) in the presence of *tert*-BuOH at room temperature (run 1 in Table 1).[7] After 12 h, the cyclopropane was opened regioselectively to give ethyl 4-phenylbutyrate (**2a**) in only 11% yield together with 89% recovery of the starting material (**1a**). In order to optimize this reaction, several reaction conditions were examined, and the results are summarized in Table 1. It has been known that addition of HMPA raises the reducing power of $SmI_2$.[8] In fact, use of a large amount of HMPA markedly promoted the cyclopropane ring opening (Table 1). In run 8, the best

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yield was obtained using $SmI_2$(4 eq) in HMPA-THF (1:1), and the reaction was completed within 1h.

TABLE 1. Cyclopropane Ring Opening of **1a** ($R^1$= $C_6H_5$, $R^2$=H)

| Run | $SmI_2$ (eq) | THF:HMPA (v/v) | Temp. | Reaction time (h) | *tert*-BuOH (eq) | Recovery of **1a** (% ;GLC) | Yield of **2a** (% ;GLC) |
|---|---|---|---|---|---|---|---|
| 1 | 3 | 10:1 | r.t. | 12 | 2 | 89 | 11 |
| 2 | 3 | 5:1 | r.t. | 6 | 2 | 45 | 19 |
| 3 | 3 | 5:2 | r.t. | 6 | 2 | 40 | 44 |
| 4 | 3 | 5:3 | r.t. | 6 | 2 | 35 | 65 |
| 5 | 4 | 5:3 | r.t. | 5 | 2 | - | 59 |
| 6 | 3 | 1:1 | 0°C | 6 | 2 | 81 | 19 |
| 7 | 3 | 1:1 | 0°C | 6 | 4 | 26 | 40 |
| 8 | 4 | 1:1 | 0°C | 1 | 4 | - | 74 |

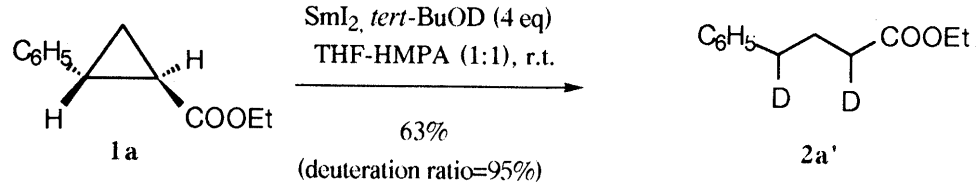
TABLE 2. Cyclopropane Ring Opening of Various Cyclopropane Monoesters (**1**)

| Run | $R^1$ | $R^2$ | Reaction time (h) | Isolated yield (%) | Run | $R^1$ | $R^2$ | Reaction time (h) | Isolated yield (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 4-$MeC_6H_4$- | H | 1 | 47 | 7 | 4-$MeC_6H_4$- | $SiMe_3$ | 1 | 80 |
| 2 | 4-$MeOC_6H_4$- | H | 1 | 44 | 8 | 4-$MeOC_6H_4$- | $SiMe_3$ | 1 | 89 |
| 3 | 3,4-($OCH_2O$)-$C_6H_3$- | H | 1 | 87 | 9 | 2-furyl | $SiMe_3$ | 1 | 16 |
| | | | | | 10 | 2-thienyl | $SiMe_3$ | 1 | 54 |
| 4 | 2-furyl | H | 1 | -a) | 11 | $CH_3(CH_2)_2$- | H | 6 | N.R.b) |
| 5 | 2-thienyl | H | 1 | 30 | 12 | $CH_3(CH_2)_6$- | H | 6 | N.R.b) |
| 6 | $C_6H_5$- | $SiMe_3$ | 1 | 75 | | | | | |

a) A complex mixture was obtained. b) No reaction.

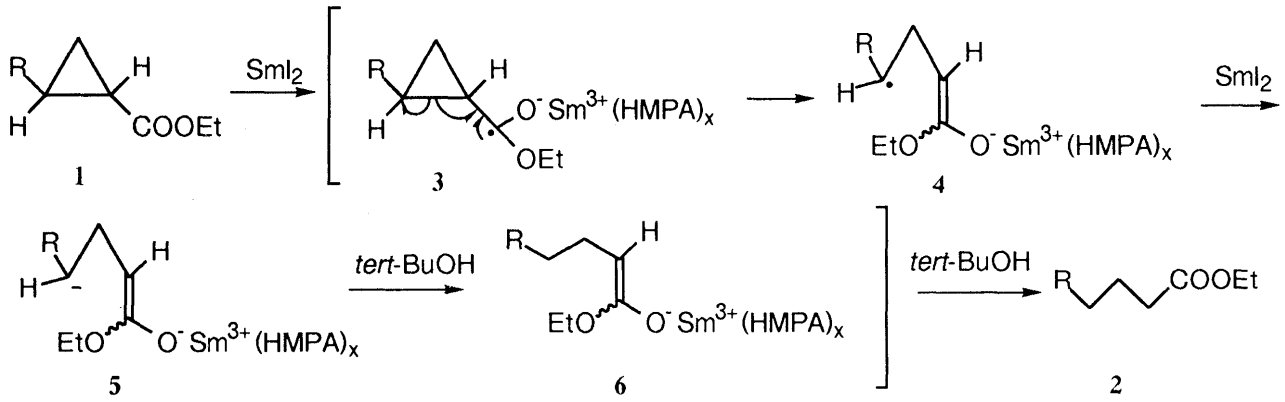
The conditions of run 8 were applied to various cyclopropane compounds (**1**) (Table 2). In the cases of 2-aryl compounds except for run 4,[9] the desired butyrates (**2**) were obtained in moderate to high yields (runs 1,2,3,5). In the cases of 2-aryl-3-trimethylsilyl compounds, the yields were considerably improved (runs 6 - 10). However, substrates having an aliphatic group at 2-position did not react with $SmI_2$ under the same conditions (runs 11, 12). This difference in the reactivity between aliphatic $R^1$ and aromatic $R^1$ may be attributable to the stability of the corresponding intermediate radicals (**4**).

In order to examine the mechanism, the reaction with **1a** was carried out in the presence of *tert*-BuOD instead of *tert*-BuOH to give α,γ-dideuterated product (**2a'**) in 63% chemical yield and 95% deuteration ratio.[10]




**1a** **2a'**

From these results, a possible reaction mechanism for the present cyclopropane opening of **1** can be hypothesized as shown in the following scheme.[11]




## REFERENCES AND NOTES


1) Namy J. L., Girard P., Kagan H. B., *Nouv. J. Chim.*, **1**, 5 (1977); Girard P., Namy J. L., Kagan H. B., *J. Am. Chem. Soc.*, **102**, 2693 (1980).

2) For reviews : Kagan H. B., Namy J. L., *Tetrahedron*, **42**, 6573 (1986); Inanaga J., *Yuki Gosei Kagaku Kyokai Shi*, **47**, 200 (1989); Kagan H. B., *New J. Chem.*, **14**, 453 (1990); Soderquist J. A., *Aldrichimica Acta*, **24**, 15 (1991); Molander G. A., *Chem. Rew.* **92**, 29 (1992).

3) For reviews : Tunemoto D., Kondo K., *Yuki Gosei Kagaku Kyokai Shi*, **35**, 1070 (1977); Murakami M., Nishida S., *ibid.*, **41**, 22 (1983); Saigo K., Shimada S., *ibid.*, **49**, 928 (1991); Nonhebel D. C., *Chem. Soc. Rev.*, **1993**, 347.

4) Molander G. A., McKie J. A., *J. Org. Chem.*, **56**, 4112 (1991); Batey R. A., Motherwell W. B., *Tetrahedron Lett.*, **32**, 6211 (1991); Beerli R., Brunner E. J., Borschberg H-J., *ibid.*, **33**, 6449 (1992).

5) a) Yamashita M., Kitagawa K., Ohhara T., Iida Y., Masumi A., Kawasaki I., Ohta S., *Chem. Lett.*, **1993**, 653; b) Presented at the 113rd Annual Meeting of Pharmaceutical Society of Japan, Osaka, Mar. 1993, Abstracts of papers, No. 2, p. 92; c) Presented at the 43rd Meeting of Kinki Branch, Pharmaceutical Society of Japan, Osaka, Oct. 1993, Abstracts of papers, p. 111.

6) Imamoto T., Hatajima T., Yoshizawa T., *Tetrahedron Lett.*, **35**, 7805 (1994).

7) We applied these reaction conditions to the cyclopropane ring opening of 2-substituted cyclopropane-1,1-dicarboxylates to give (2-substituted ethyl)malonates in good yields.[5c] However, Imamoto reported that dimethyl cyclopropane-1,1-dicarboxylate (1.0 mmol) was opened in low yield (32%) by treatment with $SmI_2$ (4 mmol) in the presence of HMPA (4 eq) and *tert*-BuOH (2 mmol) in THF at room temperature for 24 h.[6]

8) Otsubo K., Inanaga J., Yamaguchi M., *Tetrahedron Lett.*, **27**, 5763 (1986); Otsubo K., Kawamura K., Inanaga J., Yamaguchi M., *Chem. Lett.*, **1987**, 1485; Hasegawa E., Curran D. P., *Tetrahedron Lett.*, **34**, 1717 (1993).

9) The failure may be attributable to the instability of ethyl 2-furylcyclopropanecarboxylate.

10) In $^1$H-NMR spectrum of **2a'**, the signal intensities of γ-position proton at δ 2.31 and α-position proton at δ 2.63 both decreased than those of **2a**.

11) Typical procedure: To a solution of $SmI_2$ [2.0 mmol; prepared from Sm (360 mg, 2.4 mmol) and 1,2-diiodoethane (536 mg, 2.0 mmol)] in THF (5 ml) and HMPA (5 ml) was added dropwise a solution of ethyl cyclopropanecarbonate(**1**) (0.5 mmol) and *tert*-BuOH (0.2 ml, 2.0 mmol) in THF (1 ml) at 0 °C under $N_2$. After 1 h, the reaction mixture was quenched with 3% HCl, and the product was extracted with diethyl ether. The combined organic layer was washed with 3% HCl, saturated $Na_2S_2O_3$, and brine, dried with $Na_2SO_4$, and evaporated. The residue was purified by silica gel chromatography.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