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Samarium(II) Iodide Promoted Reductive Ring Opening Reaction of Cyclopropane-1,1-dicarboxylic Esters. Synthesis of Substituted 5-Pentanolides from Carbonyl Compounds and Dimethyl Cyclopropane-1,1-dicarboxylate

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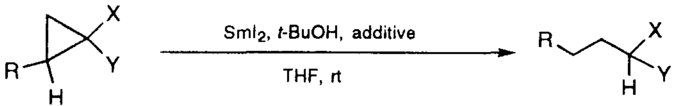
Abstract: Dimethyl cyclopropane-1,1-dicarboxylate is readily subjected to reductive ring opening reaction with samarium(II) iodide in the presence of tris(dibenzoylmethiodo)iron(III). The generated organosamarium intermediate is trapped by aliphatic ketones to afford 5,5-disubstituted 2-methoxycarbonyl-5-pentanolides.

It has been well documented that cyclopropyl ketones, on treatment with reducing agents, undergo reductive cyclopropane ring opening reaction, and that the generated radicals or organometallic species are utilized for further organic transformations.[1] The same type of the ring opening reaction of cyclopropanecarboxylic esters has been scarcely reported,[2] despite its anticipated utility for the generation of γ-metalloesters which are useful for the synthesis of δ-hydroxy esters and related substrates.[3] Here we report a reductive ring opening reaction of cyclopropane-1,1-dicarboxylic esters. In addition, we wish to describe a direct synthesis of 5,5-disubstituted 2-methoxycarbonyl-5-pentanolides from dimethyl cyclopropane-1,1-dicarboxylate and aliphatic ketones.

Previously, it was reported that cyclopropyl ketones were reduced with ring opening by samarium(II) iodide or metallic samarium.[1d–g] Based on the facts, we examined samarium(II) iodide promoted reductive ring opening reaction of several cyclopropane carboxylic esters in the presence of *t*-butyl alcohol as a proton source. A cursory experiment using dimethyl cyclopropane-1,1-dicarboxylate (**1a**) indicated that the expected reduction did not proceed smoothly without additives (Entry 1 in Table 1). Hexamethylphosphoric triamide (HMPA), which is known to enhance the reducing ability of SmI_2,[4] was not effective in this case (entry 2). In sharp contrast, the use of a catalytic amount of iron compounds such as tris(dibenzoylmethiodo)iron(III) ($Fe(DBM)_3$) greatly accelerated the reductive ring opening reaction (entry 3–5).[5] Similarly, other cyclopropane-1,1-dicarboxylic esters including thiol esters underwent facile ring opening reaction (entries 6, 7, 8, 11, and 12). On the other hand, monocarboxylic esters (**1e**, **1f**, and **1i**) were difficultly subjected to reduction under these conditions.



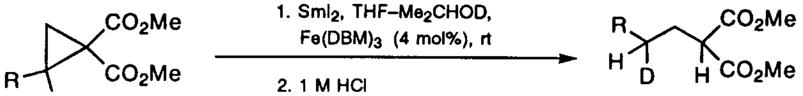
1a–l
R = H, Me
X, Y = CO_2Me, CO_2Et, CO_2Bu-*t*, CO_2Ph, COSPh, CN, H

Table 1. Reductive Ring Opening Reaction of Compounds **1a-j** with SmI_2

Entry [a]	Compound	Additive	Time	Yield (%)[b]
1	**1a** (R = H, X = CO_2Me, Y = CO_2Me)	none	24 h	15
2	"	HMPA (4 eq.)	24 h	32
3	"	$FeCl_2$ (4 mol%)	20 min	82
4	"	$FeCl_3$ (4 mol%)	20 min	74
5	"	$Fe(DBM)_3$ (4 mol%)	10 min	92
6	**1b** (R = H, X = CO_2Et, Y = CO_2Et)	$Fe(DBM)_3$ (4 mol%)	30 min	89
7	**1c** (R = H, X = CO_2Bu-*t*, Y = CO_2Bu-*t*)	$Fe(DBM)_3$ (4 mol%)	1 h	72
8	**1d** (R = H, X = CO_2Ph, Y = CO_2Ph)	$Fe(DBM)_3$ (4 mol%)	5 min	96
9	**1e** (R = H, X = CO_2Et, Y = H)	$Fe(DBM)_3$ (4 mol%)	24 h	0
10	**1f** (R = H, X = CO_2Me, Y = CN)	$Fe(DBM)_3$ (4 mol%)	24 h	0
11	**1g** (R = H, X = COSPh, Y = COSPh)	$Fe(DBM)_3$ (2 mol%)	1 min	82
12	**1h** (R = H, X = CO_2Et, Y = COSPh)	$Fe(DBM)_3$ (2 mol%)	1 min	97
13	**1i** (R = H, COSPh, Y = H)	$Fe(DBM)_3$ (2 mol%)	24 h	21
14	**1j** (R = Me, X = CO_2Me, Y = CO_2Me)	$Fe(DBM)_3$ (4 mol%)	10 min	95[c]

[a] All reactions were carried out by using compond **1a-j** (1 mmol), *t*-butyl alcohol (2 mmol), and SmI_2 (4 mmol) in THF at room temperature. [b] Isolated yield of ring-opened product. [c] The product was identified as dimethyl propylmalonate. Dimethyl isopropylmalonate was not detected.

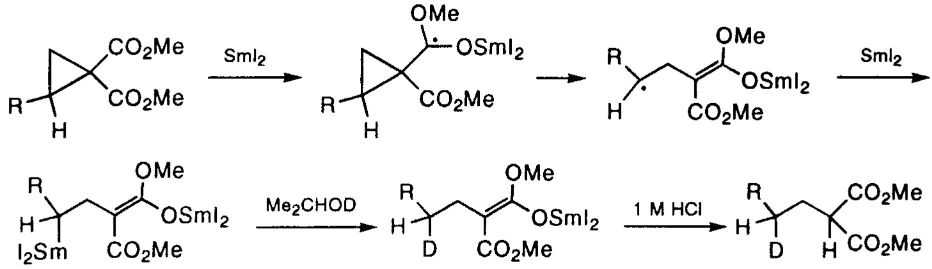
In order to obtain the mechanistic aspects of these reactions, compound **1a** was treated with SmI_2 in the presence of $(CH_3)_2CHOD$, and the isolated product was assigned as compound **2** by ^1H NMR and mass spectroscopy. Similarly, dimethyl 2-methylcyclopropane-1,1-dicarboxylate (**1j**) was treated with SmI_2 under the same conditions. In this case, compound **3** was isolated in 92% yield.



1a : R = H
1J : R = Me

2 : R = H
3 : R = Me

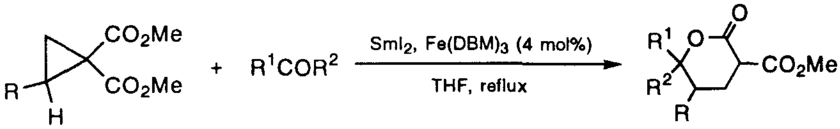
These results are reasonably interpreted by assuming that the reaction proceeds through a pathway shown in Scheme 1. It is noted that not only radicals but also organosamarium species **4** are proposed as conceivable intermediates.[6]



4

Scheme 1

Based on these results, we tried to synthesize 5-pentanolide derivatives from compounds **1a** or **1j** and carbonyl compounds using SmI_2–$Fe(DBM)_3$ reagent system. As shown in Table 2, the reactions in the presence of aliphatic ketones were best carried out at refluxing temperature to give 2-methoxycarbonyl-5,5-disubstituted 5-pentanolides in good yields.[7] On the other hand, the reactions with aldehydes or aromatic ketones resulted in relatively low yields of the expected 5-pentanolides; significant amounts of pinacol coupling products were formed in these reactions.



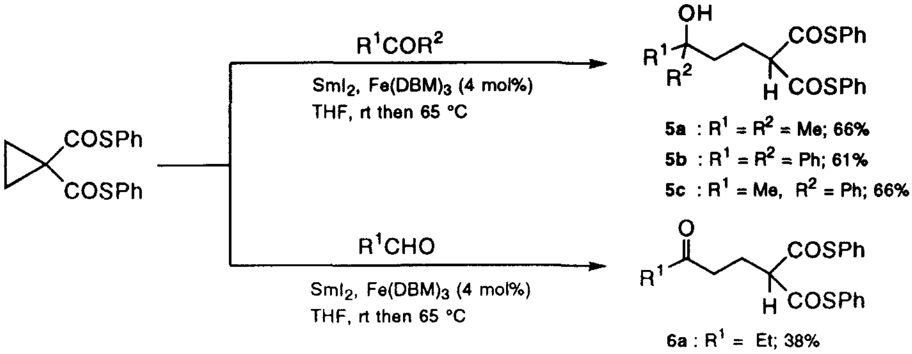
1a : R = H
1J : R = Me

Table 2. Synthesis of 5-Pentanolides from Carbonyl Compounds and **1a** or **1j**[a]

Entry	Cyclopropane derivative	Carbonyl compound	Yield (%)[b]
1	**1a**	Acetone	74
2	**1a**	3-Pentanone	76
3	**1a**	Cyclohexanone	72
4	**1a**	2-Adamantanone	65
5	**1a**	Cyclododecanone	71
6	**1a**	4-Phenyl-2-butanone	76 (54 : 46)[c]
7	**1a**	1,3-Diphenyl-2-propanone	51
8	**1a**	Acetophenone	15 (52 : 48)[c]
9	**1a**	Cyclohexanecarboxaldehyde	30 (63 : 37)[c]
10	**1j**	Cyclohexanone	67 (55 : 45)[c]

[a] All reactions were carried out in THF at reflux with a molar ratio of **1a** or **1j** : carbonyl compound : SmI_2 : $Fe(DBM)_3$ = 1 : 1 : 4 : 0.04. [b] Isolated yield. [c] The diastereomer ratio was determined by ^1H NMR.

S,S'-Diphenyl cyclopropane-1,1-dicarbothioate (**1g**) was allowed to react with carbonyl compounds under similar conditions. In contrast to the reactions of **1a**, 5-pentanolide derivatives were not produced and instead δ-hydroxy thiol esters **5a–c**[8] or δ-keto thiol esters **6a,b** were formed from ketones or aldehydes, respectively (Scheme 2). The formation of δ-keto thiol esters can be interpreted by considering Meerwein-Ponndorf-Verley reaction of the initially formed samarium alkoxide with remaining aldehydes.[9]



5a : $R^1 = R^2 = Me$; 66%
5b : $R^1 = R^2 = Ph$; 61%
5c : $R^1 = Me$, $R^2 = Ph$; 66%

6a : R^1 = Et; 38%
6b : R^1 = c-C_6H_{11}; 36%

Scheme 2

In conclusion, SmI_2–$Fe(DBM)_3$ reagent system promotes the reductive ring opening reaction of cyclopropane-1,1-dicarboxylic esters. The generated organosamarium species were trapped by carbonyl compounds to give 5-pentanolides and related substrates.

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6. It has been demonstrated that organosamarium(III) compounds are produced by the reduction of alkyl radicals by SmI_2. Curran, D. P.; Fevig, T. L.; Jasperse, C. P.; Totleben, M. J. *Synlett* **1992**, 943 and references cited therein.
7. A typical procedure for the preparation of 5,5-dibenzyl-2-methoxycarbonyl-5-pentanolide is as follows. Tris(dibenzoylmethiodo)iron(III) (28 mg, 0.04 mmol) was added to a suspension of SmI_2 prepared by the reaction of CH_2I_2 (1.07 g, 4 mmol) with samarium powder (600 mg, 4 mmol) in THF (10 mL) under argon. The mixture was refluxed, and a solution of dimethyl cyclopropane-1,1-dicarboxylate (**1a**) (158 mg, 1 mmol) and 1,3-diphenyl-2-propanone (210 mg, 1 mmol) in THF (5 mL) was added over a period of 1 h with vigorous stirring. After addition, the reaction mixture was cooled, treated with 1 M HCl, and extracted with ether. The combined extracts were washed with $Na_2S_2O_3$ solution and brine, and dried over Na_2SO_4. Purification by preparative thin layer chromatography on silica gel with ethyl acetate/hexane (1/5) afforded the product (173 mg) in 51% yield. Mp 90–91 °C (hexane); IR (KBr) 3010, 2920, 1720, 1435, 1160, 760, 740, 710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.66–1.99 (m, 4H), 2.82 (d, $J = 13.8$ Hz, 1H), 2.99 (dd, $J = 6.1$ Hz, 8.7 Hz, 1H), 3.01 (d, $J = 13.8$ Hz, 1H), 3.12 (d, $J = 13.8$ Hz, 1H), 3.13 (d, $J = 13.8$ Hz, 1H), 3.60 (s, 3H), 7.17–7.34 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 20.65, 26.06, 46.26, 46.71, 46.81, 52.63, 86.80, 127.06, 127.09, 128.39, 128.45, 130.78, 130.82, 135.43, 135.46, 166.80, 169.31; MS *m/z* (rel intensity) 338 (M^+, 4%), 247 (100), 215 (55), 171 (25), 147 (14), 113 (10), 91 (65), 55 (11). Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.53; H, 6.55. Found: C, 74.27; H, 6.37.
8. These compounds were readily cyclized to the corresponding 5-pentanolides by refluxing in THF in the presence of a catalytic amount of *p*-toluenesulfonic acid.
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