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Lewis Acid-mediated Highly Regioselective Ring-expansion of Methyl 2-Phenyl-1-(arylhydroxymethyl)cyclopropanecarboxylates

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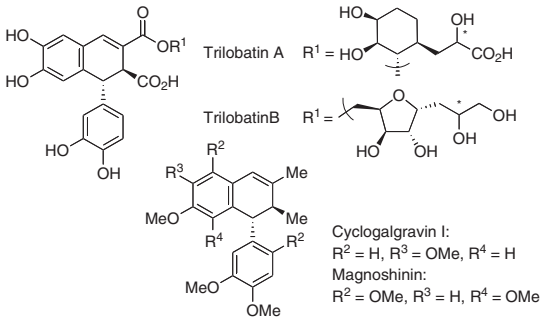
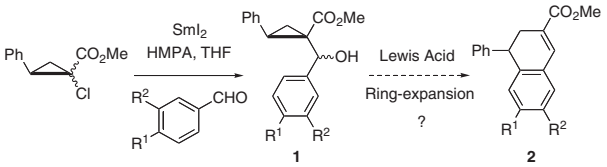
A novel ring-expansion of methyl (arylhydroxymethyl)-cyclopropanecarboxylates **1** using $Sc(OTf)_3$ or $BF_3 \cdot OEt_2$ afforded 1,2-dihydronaphthalene-3-carboxylic acid ester **2** in high to excellent yields. In the reaction, highly regioselective ring opening of cyclopropane and sequential cyclization occurred.

1-Aryl-1,2-dihydronaphthalene analogs are attracting considerable attention due to their distribution in nature (for examples, trilobatin A, B, cyclogalgravin, and magnoshinin, Scheme 1), multiple biological activities, and usefulness as important synthetic intermediates.[1] As a part of our ongoing program of synthetic studies on the transformation of *gem*-dihalocyclopropanes,[2] we have recently reported highly stereoselective SmI_2-promoted Reformatsky-type reactions of 1-chlorocyclopropanecarboxylate to afford (arylhydroxymethyl)-cyclopropanecarboxylates **1** (Scheme 2).[3] Here we report a Lewis acid-mediated highly regioselective ring expansion of methyl (arylhydroxymethyl)cyclopropanecarboxylates **1**[4] to give 1-aryl-1,2-dihydronaphthalene-3-carboxylic acid esters **2**.[5]

Initially, we investigated the reaction of cyclopropanecarboxylate **1a** with various Lewis acids. Table 1 lists the results of the ring-expansion. $TiCl_4$, $SnCl_4$, or TBDMSOTf promoted ring-expansion to afford dihydronaphthalene **2a** in low to moderate yields (Entries 1–4). These results are inconsistent with those for benzannulation of *gem*-dichlorocyclopropylmethanol.[2b] Under Seebach's condition,[5] no amount of ester **2a** was obtained (Entry 5). In this case, hydrolysis of ester occurred along with the ring-expansion to give corresponding 1,2-dihydronaphthalene-3-carboxylic acid in 71% yield. The use of CF_3CO_2H decreased the yield of ring-expansion (Entry 6). A similar reaction with $BF_3 \cdot Et_2O$ proceeded in good yields (Entries 7 and 8). The use of lanthanide triflates, $Yb(OTf)_3$ and $Sc(OTf)_3$, at 83 °C promoted ring-expansion in high yields (Entries 10 and 12). Similar reactions at room temperature resulted in a decrease in the yield (Entries 9 and 11). Thus, the use of $Sc(OTf)_3$ at 83 °C in EDC (1,2-dichloroethane) is the most efficient condition for this ring-expansion.[6] The structures of **2a** were determined by analogy with a known compound, based on spectral data.[7]



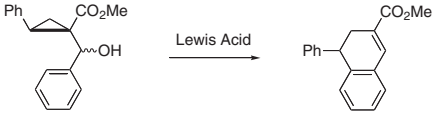
Scheme 1.



Scheme 2.

Next we investigated the ring-expansion of (arylhydroxymethyl)cyclopropanecarboxylates **1b–1e** with $Sc(OTf)_3$ at 83 °C. As expected, the ring-expansion of ester **1b–1e** proceeded smoothly to afford dihydronaphthalene **2b–2e** in good to high yields (Table 2, Entries 1–4). In the case of **1d**, hydrolysis of ester **2d** occurred as a side reaction (Entry 3). In addition, we also investigated similar reaction of diaryl analogs **1f–1i** (Table 3). Every case of ester **1f–1i** underwent the desired ring-expansion to give dihydronaphthalene **2f–2i** in good to excellent yields. Treatment of **1f** with $Sc(OTf)_3$ at 83 °C afforded dihydronaphthalene **2f** in high yield (Entry 1). The use of $Yb(OTf)_3$ or $TiCl_4$ decrease the yield of ring-expansion (Entries 2 and 3). In the case of diaryl analog **1f**, $BF_3 \cdot Et_2O$ also promoted the ring-expansion in excellent yield (Entry 4).

Table 1. Highly regioselective ring-expansion of methyl (phenylhydroxymethyl)cyclopropanecarboxylates **1a**[a–d]



1a **2a**

Entry	Acid	Temp/°C	Solvent	Yield[e]/%
1	$TiCl_4$	rt	CH_2Cl_2	43
2	$TiCl_4$	83	EDC	36
3	$SnCl_4$	rt	CH_2Cl_2	25
4	TBDMSOTf	rt	CH_2Cl_2	54
5	H_2SO_4[f]	35	Et_2O	0
6	CF_3CO_2H	rt	none	10
7	$BF_3 \cdot Et_2O$	rt	CH_2Cl_2	70
8	$BF_3 \cdot Et_2O$	83	EDC	62
9	$Yb(OTf)_3$	rt	CH_2Cl_2	10
10	$Yb(OTf)_3$	83	EDC	90
11	$Sc(OTf)_3$	rt	CH_2Cl_2	66
12	$Sc(OTf)_3$	83	EDC	95

[a]Reactions were carried out under an Ar atmosphere. [b]Reaction time is 1 h. [c]1.1 equiv of Lewis acid was used. [d]A mixture of diastereo isomers (ratio = 1/1) was used for the reactions of **1a**. [e]Isolated. [f]Based on Ref. 5, 1000 equiv of H_2SO_4 was used.

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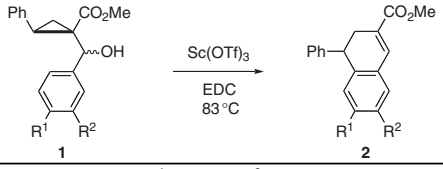
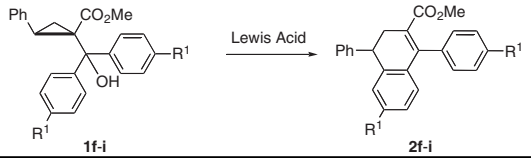
Table 2. Highly regioselective $Sc(OTf)_3$-mediated ring-expansion of methyl (arylhydroxymethyl)cyclopropanecarboxylates **1b–1e**[a–d]



Entry	Substrate	R^1	R^2	Product	Yield[e]/%
1	**1b**	Cl	H	**2b**	88
2	**1c**	Me	H	**2c**	82
3	**1d**	OMe	H	**2d**	60
4	**1e**	OMe	OMe	**2e**	80

[a]Reactions were carried out under an Ar atmosphere. [b]Reaction time is 1 h. [c]1.1 equiv of Lewis acid was used. [d]A mixture of diastereo isomers (ratio = 1/1) was used for the reactions of **1a**. [e]Isolated.

Table 3. Highly regioselective ring-expansion of methyl (diarylhydroxymethyl)cyclopropanecarboxylates **1f–1i**[a–c]



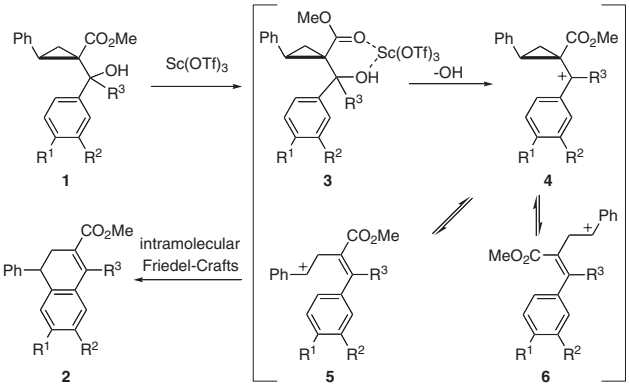
Entry	Substrate	R^1	Acid	Temp /°C	Solvent	Product	Yield[d] /%
1	**1f**	H	$Sc(OTf)_3$	83	EDC	**2f**	92
2	**1f**	H	$Yb(OTf)_3$	83	EDC	**2f**	85
3	**1f**	H	$TiCl_4$	rt	CH_2Cl_2	**2f**	60
4	**1f**	H	$BF_3{\cdot}Et_2O$	rt	CH_2Cl_2	**2f**	99
5	**1g**	Cl	$BF_3{\cdot}Et_2O$	rt	CH_2Cl_2	**2g**	68
6	**1h**	Me	$BF_3{\cdot}Et_2O$	rt	CH_2Cl_2	**2h**	82
7	**1i**	OMe	$BF_3{\cdot}Et_2O$	rt	CH_2Cl_2	**2i**	71

[a]Reactions were carried out under an Ar atmosphere. [b]Reaction time is 1 h. [c]1.1 equiv of Lewis acid was used. [d]Isolated.

Similar reaction of diaryl analogs **1g–1i** proceeded in good to high yields (Entries 5–7).

The proposed mechanism of the ring-expansion mediated by $Sc(OTf)_3$ is as follows (Scheme 3). First, $Sc(OTf)_3$ chelates with the OH and carbonyl of β-hyrdoxyester **1** to give an intermediate **3**. Successive $Sc(OTf)_3$-promoted elimination of the OH group gives the cationic intermediate **4**. Then, highly regioselective ring-opening and Friedel–Crafts-type cyclization sequentially occur to give dihydronaphthalene **2**. Cyclization proceeds smoothly in the Z-intermediate **5** of the cation. In the reaction using $TiCl_4$ or $SnCl_4$, the presence of Cl^- adversely affects the cyclization, causing the chlorination of benzyl cation to occur. $BF_3{\cdot}OEt_2$ also promotes the ring-expansion of symmetrically substituted diaryl analog **1f** in excellent yield. In this case ($R^3 = p$-R^1-Ph, R^2 = H, intermediate **5** = **6**), the ring-expansion proceeds smoothly without the problem of the E-intermediate.

In conclusion, we developed a novel synthesis of 1-aryl-1,2-dihydronaphthalene-3-carboxylic acid esters utilizing a Lewis acid-mediated regioselective ring-expansion of methyl (arylhydroxymethyl)cyclopropanecarboxylate. Application of the present method to a total synthesis of natural product is now being performed.



Scheme 3.

This paper is dedicated to the first principal, Chotaro Harizuka, on the occasion of 100th anniversary of Faculty of Textile Science and Technology, Shinshu University. This research was partially supported by Grant-in-Aids for Scientific Research on Basic Area (C) "No. 20550036" and for Global COE Program from MEXT.

References and Notes

1 a) J. M. Scher, J. Zapp, H. Becker, *Phytochemistry* **2003**, *62*, 769. b) C. Cow, C. Leung, J. L. Charlton, *Can. J. Chem.* **2000**, *78*, 553. c) B. L. Yvon, P. K. Datta, T. N. Le, J. L. Charlton, *Synthesis* **2001**, 1556. d) H. Yoda, Y. Nakaseko, K. Takabe, *Tetrahedron Lett.* **2004**, *45*, 4217. e) L. F. Silva, Jr., F. A. Siqueira, E. C. Pedrozo, F. Y. M. Vieira, A. C. Doriguetto, *Org. Lett.* **2007**, *9*, 1433. f) M. Sriram, J. J. Hall, N. C. Grohmann, T. E. Strecker, T. Wootton, A. Franken, M. L. Trawick, K. G. Pinney, *Bioorg. Med. Chem.* **2008**, *16*, 8161.

2 a) Y. Nishii, K. Wakasugi, K. Koga, Y. Tanabe, *J. Am. Chem. Soc.* **2004**, *126*, 5358. b) Y. Nishii, T. Yoshida, H. Asano, K. Wakasugi, J. Morita, Y. Aso, E. Yoshida, J. Motoyoshiya, H. Aoyama, Y. Tanabe, *J. Org. Chem.* **2005**, *70*, 2667. c) Y. Nishii, T. Nagano, H. Gotoh, R. Nagase, J. Motoyoshiya, H. Aoyama, Y. Tanabe, *Org. Lett.* **2007**, *9*, 563, other references cited therein.

3 a) T. Nagano, J. Motoyoshiya, A. Kakehi, Y. Nishii, *Org. Lett.* **2008**, *10*, 5453. b) E. Yoshida, T. Nagano, J. Motoyoshiya, Y. Nishii, *Chem. Lett.* **2009**, *38*, 1078.

4 (Arylhydroxymethyl)cyclopropanecarboxylates **1a–1i** were prepared by the similar method of our previous report: see Ref. 3a.

5 As a similar reaction, an example has been reported to synthesize 3-bromo-1,1-dimethyl-4-phenyl-2-hydronaphthalene: R. Dammann, D. Seebach, *Chem. Ber.* **1979**, *112*, 2167.

6 Procedures were described in Supporting Information, which is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

7 a) J. Vebrel, R. Carrié, *Tetrahedron* **1983**, *39*, 4163. b) J. Vebrel, D. Grée, R. Carrié, *Can. J. Chem.* **1984**, *62*, 939. c) J. Vebrel, R. Carrie, *Bull. Chem. Soc. Fr* **1982**, *3–4*, Part II, 116.

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