Cyclization and Ring-expansion Reactions Involving Reductive Formation and Oxidative Ring-opening of Cyclopropanol Derivatives

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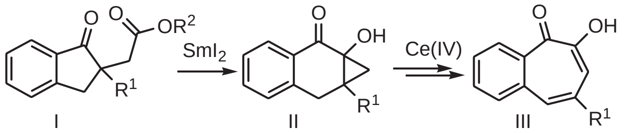
$FeCl_3$-promoted regioselective ring-opening reactions of cyclopropyl trimethylsilyl ethers, obtained by SmI_2 reduction followed by silylation with Me_3SiCl of bromoalkyl ketones and acyl chloride, were performed. Eventually, the sequential reduction and oxidation reactions starting from bromoalkyl ketones to give ring-expanded enones were achieved in one-pot.

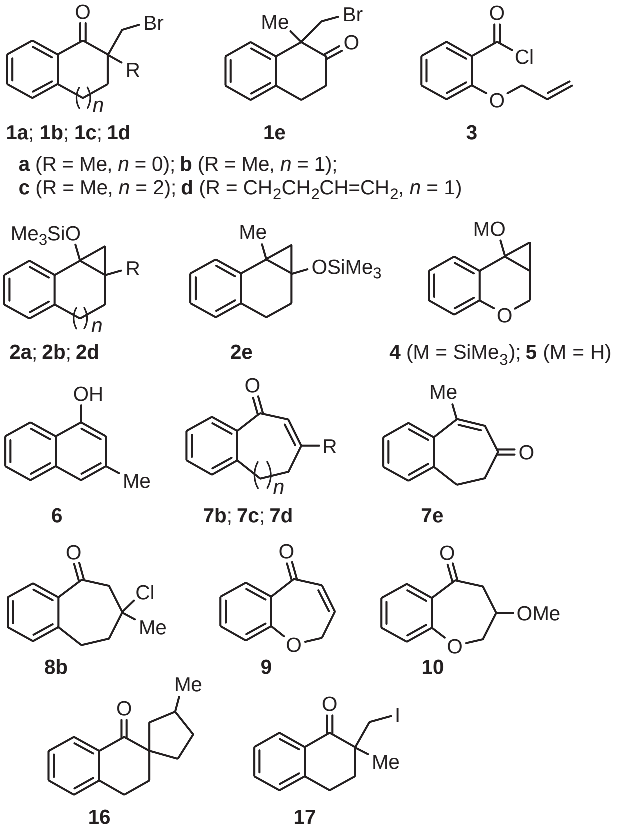
Cyclization and ring-expansion reactions provide an effective protocol to construct various cyclic compounds, particularly medium-sized rings.[1] We recently discovered novel sets of reduction by samarium diiodide (SmI_2)[2] and following oxidation to promote cyclization and ring-expansion reactions.[3] For example, keto esters I were reduced by SmI_2, and Ce(IV)-promoted ring-opening of the resulting cyclopropanols II led to seven-membered-ring ketones III (Scheme 1).[3b]



Scheme 1.

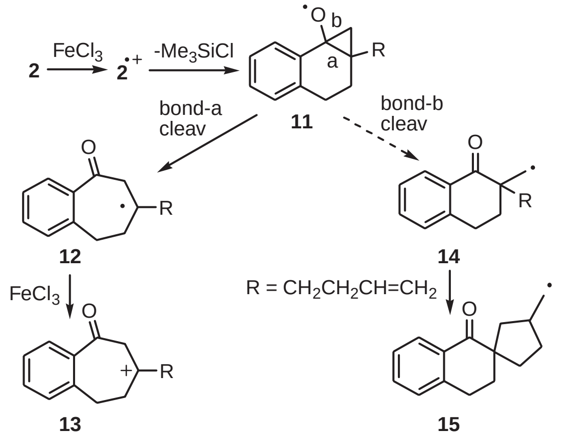
In principle, SmI_2-promoted formation and oxidative ring-opening of cyclopropanol derivatives[4] using other types of substrates should be also possible. For example, the intramolecular samarium Barbier reactions[5] giving cyclopropanols must be compatible with this idea. In this paper, we will describe the sequential reductive formation and oxidation reactions of cyclopropanol derivatives obtained from α-bromomethyl ketones **1**[6] and acyl chloride **3** (Figure 1).[7]

Cyclopropanols prepared by the SmI_2 reductions of **1** and **3** were silylated to give **2** and **4**, respectively, because the unprotected cyclopropanols were less stable than the corresponding silyl ethers.[8] Then, we examined the reaction of **2a** with various single electron oxidants to find a suitable reagent to promote the oxidative ring-opening of **2**. While the reactions of **2a** with $Ce(NH_4)_2(NO_3)_6$, $Mn(OAc)_3 \cdot 2H_2O$, or $PhI(OAc)_2$ which was effective for the transformation of II to III gave the complex mixtures, $FeCl_3$ was found to work well.[4b,4d,9] The reaction of **2a** with $FeCl_3$ in DMF allowed us to isolate 1-naphthol **6** in moderate yield (67%).[10] Interestingly, an addition of pyridine (1 equiv. vs **2a**) significantly increased the yield of **6** (95%). Therefore, the combination of $FeCl_3$ and pyridine was used for the reactions of other **2** and **4**.[10] When **2b** was treated with $FeCl_3$ and pyridine, a crude product that was tentatively assigned as **8b** was obtained. Subsequently **8b** was treated with NaOAc in MeOH to give cycloheptenone **7b** in 72%.[10] Similarly, **7e** was obtained in 47% yield from **2e**. In the case of **4**, the same treatment afforded not only enone **9** (18%) but also MeO-adduct **10** (30%). When the corresponding cyclopropanol **5** was used, similar product distributions (**9**, 24%; **10**, 32%) were observed.



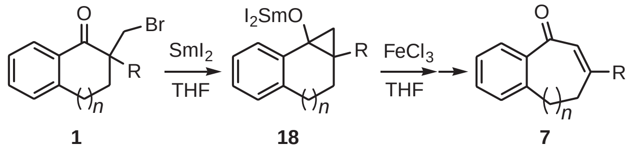
a (R = Me, *n* = 0); **b** (R = Me, *n* = 1); **c** (R = Me, *n* = 2); **d** (R = $CH_2CH_2CH=CH_2$, *n* = 1)

Figure 1.



Scheme 2.

In Scheme 2, a plausible mechanism is proposed. Oxidation of **2** by $FeCl_3$ and the subsequent release of Me_3SiCl affords the



Scheme 3.

Table 1. One-pot reduction and oxidation reactions starting from bromo ketones **1**

Entry	**1**	Pyridine	Product	Yields/%^{a}
1	**1a**	add	**6**	65 [47]
2	**1b**	add	**7b**	71 [65]
3	**1b**	not add	**7b**	25
4	**1c**	add	**7c**	60 [—]
5	**1d**	add	**7d**	72 [28]
6	**1e**	add	**7e**	66 [57]

^{a}Isolated yields and the numbers in brackets represent the yields of the enones from **1** by the stepwise procedures.

oxy radical **11**.[4b,4d] Selective cleavage of bond-a of **11** gives the alkyl radical **12** that is oxidized by another equivalent of FeCl$_3$ to give carbocation **13**. **13** is finally converted to the observed products. It should be interesting to discuss the regioselectivity of the bond cleavage of the cyclopropane ring in **11**. If an equilibrium between **11** and **14** exists,[11] and if a fast reaction of **14** proceeds, cleavage of bond-b of **11** would be also possible. To ascertain this hypothesis, we conducted the reaction of **2d** expecting that the fast 5-exo cyclization[12] of **14d** giving **15d** would proceed. However, cycloheptenone **7d** was obtained as a major product (71%) along with only a small amount of the spiro-cyclization product **16**[13] (5%).

Our next interest was to determine if these sequential reduction–oxidation reactions would proceed in one-pot as shown in Scheme 3 (represented by the conversion of **1b**–**1d** to **7b**–**7d**). In this one-pot reaction, the formation of samarium alkoxide **18** and its oxidation by FeCl$_3$ was anticipated. To this end, all experiments would have to be conducted in a single solvent. We then found that THF was tolerable for the reaction of FeCl$_3$. The results are presented in Table 1.[14]

In the case of **1a**, **6** was isolated and its yield was better than that in the corresponding stepwise reactions (Entry 1). Similarly, one-pot reactions of **1b**–**1e** were performed to obtain **7b**–**7e** in good yields (Entries 2, 4, 5, and 6). Notably, the yield of **7b** significantly varied depending on the presence or absence of pyridine (compare Entry 2 to Entry 3). In these cases, iodide **17** was also obtained. While the yield of **17** was low (3%) in the presence of pyridine (Entry 2), **17** became a major product (38%) in the absence of pyridine (Entry 3).[15] We also conducted one-pot reaction of **3**; however, the reaction was complicated and **9** could not be obtained.

In the results described above, the one-pot procedure is particularly noteworthy. Although the condition was not completely optimized yet and some limitation exists at the moment, further exploration of this procedure involving in-situ generation and oxidation of cyclopropoxy intermediates must be interesting. And, application of this concept to other cyclopropanol derivatives generated under various conditions[16] is also promising.

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[8] Crude cyclopropanol obtained from the reaction of **1b** (0.50 mmol) with SmI$_2$ (1.10 mmol) in a similar manner to the previously reported procedure,[3b] were treated under N$_2$ with Me$_3$SiCl (1.10 mmol) and NEt$_3$ (1.50 mmol) in CH$_2$Cl$_2$ (3 mL) at room temp for 30 min. The reaction was quenched by H$_2$O and worked-up (extracted with ether; treated with sat aqueous Na$_2$S$_2$O$_3$, NaHCO$_3$, NaCl, anhydrous MgSO$_4$; concentrated). This quenching and work-up procedure was also applied to other reactions unless otherwise stated (see Refs. 10 and 14). Silica-gel column chromatography (EtOAc/nC$_6$H$_{14}$ = 1/5) gave **2b** (0.44 mmol, 88%). **2a**, **2d**, **2e**, and **4** were similarly prepared (**2a** 42%, **2d** 80%, **2e** 88%, **4** 16%).

[9] To find a suitable reagent for each substrate was rather confusing. For example, while FeCl$_3$ was ineffective for the transformation of II to III,[3b] it turned out that Ce(NH$_4$)$_2$(NO$_3$)$_6$ could promote the conversion of **2e** to **7e** in MeCN without further base treatment.

[10] A DMF solution (4 mL) of **2b** (0.50 mmol) and FeCl$_3$ (1.10 mmol) with pyridine (0.50 mmol) was stirred under N$_2$ at room temp for 1 h. Then, a MeOH solution (5 mL) of **8b** and NaOAc (2.50 mmol) was heated at 85 °C under N$_2$ for 2 h. Silica-gel TLC (CH$_2$Cl$_2$) gave **7b** (0.36 mmol). Reactions of **2d**, **2e**, and **4** were similarly performed. In the case of **2a**, NaOAc was not necessary to obtain **6**.

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[14] A THF solution (4 mL) of FeCl$_3$ (1.10 mmol) and pyridine (0.50 mmol) was added under N$_2$ to the THF solution (12 mL) of **1b** (0.50 mmol) with SmI$_2$ (1.10 mmol), and the mixture was stirred for 1 h at room temp and heated at 85 °C for 2 h. Silica-gel TLC (CH$_2$Cl$_2$) of the crude products gave **7b** (0.35 mmol, 71%). Further TLC (CH$_2$Cl$_2$/nC$_6$H$_{14}$ = 1/1, twice) of the remained part gave **16** (0.016 mmol, 3%). Reactions of **1c**, **1d**, and **4** were similarly performed. In the case of **1a**, the heating was not performed.

[15] The origin of this pyridine effect is unclear. A possible explanation would be that FeCl$_3$ acts as a Lewis acid in the absence of pyridine since Lewis acids are known to prefer similar regioselective bond cleavage of cyclopropanols incorporated in bicyclic systems (S. Murai, T. Aya, T. Renge, I. Ryu, and N. Sonoda, *J. Org. Chem.*, **39**, 858 (1974); I. Ryu, M. Ando, A. Ogawa, S. Murai, and N. Sonoda, *J. Am. Chem. Soc.*, **105**, 7192 (1983); I. Ryu, S. Murai, and N. Sonoda, *J. Org. Chem.*, **51**, 2389 (1986)).

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