

Communications

Efficient Synthesis of Iodohydrins by Selective Cleavage of Epoxides with Samarium Iodide Complex[†]

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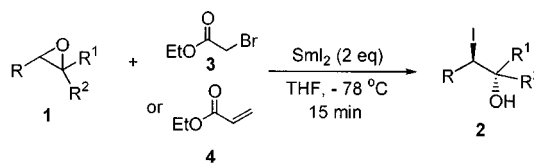
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Iodohydrins are useful intermediates in organic synthesis since they contain two functional groups of alcohol and iodide. The synthesis and application of iodohydrins and hydroxy iodohydrins have been intensively developed for a long time.¹ In the 2,3-epoxy alcohols, two problems have existed to be solved: the one is the regioselectivity at C-2 or C-3 in 2,3-epoxy alcohols to avoid or minimize the side reactions and the other is the stereoselectivity with *syn* or *anti* form of the product. Reactions with a mixture of hydrohalic acids and metals are limited by giving the mixture of epoxide and olefin by side reactions.² Metal halides, such as Li,^{1c,3} Al,⁴ Mg,^{1e,1c,5} Ti⁶ halides gave the better results in selectivity for the preparation of iodohydrins from epoxides.

The iodide donation from samarium iodide complex has been reported in a few papers. In the rearrangement of epoxides to carbonyl compounds, samarium oxide and *t*-butyldiiodosamarium complex gave iodohydrins as the side products.⁷ In the deoxygenation of epoxides with SmI₂, formation of an iodide addition intermediates has been postulated.⁸ The nucleophilic addition reactions using samarium complex with azide to epoxides were reported.⁹ The chiral iodohydrins have been prepared from the chiral epoxides and applied to organic synthesis.^{1c,3h,6h,10} However, these reactions have demonstrated limitation of regio and stereoselectivity for some substrates. Recently, chiral iodohydrins have been synthesized with high stereoselectivity by the reaction of diiodomethane or diiodo alkane and secondary



Scheme 1

chiral aldehydes with SmI₂.¹¹ The ring opening cyclic ethers with samarium(II) diiodide-BF₃·Et₂O-benzene-HMPA was reported.¹² SmI₂ shows strong oxophilicity and one electron donor ability which have been demonstrated by its wide spread application in organic synthesis. During the course of investigation on the reactivity of samarium oxophilicity, on the supposition that interaction between SmI₂, oxygens of epoxy alcohol may exist, a variety of functionalized epoxides 1 have been prepared and examined to react with samarium complexes. We have found that functionalized epoxides reacted with SmI₂ in the presence of ethyl bromoacetate 3 or ethyl acrylate 4 to afford 2 in high chemical yields with high regio and stereoselectivity as shown in Scheme 1.

Several additives to make samarium complex with SmI₂ have been examined and 3 and 4 resulted in the best results. The 3 may accept two electrons from 2 eq. of samarium(II) diiodide to generate the vinyl samarium complex¹³ which should increase the electron density of samarium metal to interact with the epoxide.

The additive 3 or 4 is essential in the reaction. Cyclohexene oxide 1a did not undergo the reaction with SmI₂ in the absence of 3 or 4. In the case of styrene oxide 1b which

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Table 1. Iodinations of **1a** Using Samarium Complexes at $-78\text{ }^{\circ}\text{C}$













| SmI ₂ | Additive | Time (min) | Product | Yields (%) ^a |
|-------------------|-----------------|------------|--------------------------------|-------------------------|
| SmI ₂ | — | 180 | — | — ^b |
| SmI ₂ | Br ₂ | 30 | 2a (trans) ^c | 48 |
| SmI ₂ | I ₂ | 30 | 2a (trans) ^c | 65 |
| SmCl ₃ | I ₂ | 300 | — | — ^d |
| SmI ₂ | 3 | <3 | — | >99 |
| SmI ₂ | 4 | <3 | — | 98 |

^aIsolated yields. ^bWithout additive starting material **1a** was recovered. ^cThe ratio of *trans* : *cis* = >99 : 1 was determined by ¹H NMR spectroscopy. ^dNo reaction occurred.

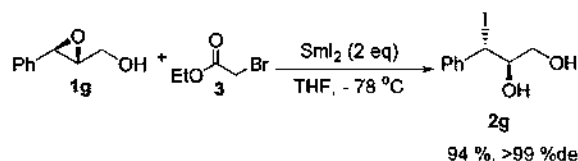
contains the more active benzyl carbon oxygen bond, the coupled diol was obtained as major product in the absence of **3** or **4**. Iodine or bromine with SmI₂, or iodine with trichloro samarium also gave low yields. The best results are obtained with the additive of **3** or **4**. The effects of additives and the samarium complex are summarized in Table 1.

Optically active epoxy alcohol was prepared by Sharpless epoxidation method.¹⁴ All the reactions were carried out with **3** within a few min with extremely high regio and stereoselectivity. The aliphatic terminal epoxide **1c** gave the primary iodide **2c** where iodination occurred at the less hindered terminal carbon, but aryl terminal epoxide **1b** resulted in **2b** by cleavage between benzylic C and O with the complete regioselectivity, which may be explained by a possible formation of a stable positive charge in the benzylic position. The α -epoxy alcohols **1e** and **1f** gave the corresponding 3-iodo-1, 2 diols **2e** and **2f** respectively with the complete regio and stereoselectivities without formation of any other side products. The opening of both *trans* **1e** and *cis* **1f** epoxy alcohols were transformed to *threo* **2e** and *erythro* **2f** iodohydrins respectively (entry 5 and 6). The results obtained are summarized in Table 2.

Table 2. Synthesis of Iodohydrins using SmI₂ (2 eq.) with **3** at $-78\text{ }^{\circ}\text{C}$

| Entry | Substrates | Time (min) | Products | Yields (%) ^a |
|-------|---|------------|---|-------------------------|
| 1 | 1a  | <3 | 2a  | >99 |
| 2 | 1b  | <3 | 2b  | 93 |
| 3 | 1c  | 5 | 2c  | 94 |
| 4 | 1d  | 5 | 2d  | 97 |
| 5 | 1e  | 15 | 2e  | 94 ^b |
| 6 | 1f  | 15 | 2f  | 94 ^c |

^aIsolated yields. ^bRegioselectivity: >99:1. Stereoselectivity: *threo* : *erythro* = >99 : 1. *Erythro* form of **2e** can not be observed by ¹H NMR spectroscopy. ^c*Erythro* form of **2f** was determined by comparison with the known ¹H NMR spectral data. Regioselectivity: 99 : 1. Stereoselectivity: *threo* : *erythro* = 1 : >99. *Threo* form of **2f** can not be observed by ¹H NMR spectroscopy.

**Scheme 2**

In order to see the stereochemistry of cleavages and iodinations of the functionalized epoxides, (2*R*, 3*R*)-(+)-3-phenylglycidol **1g** was reacted with SmI₂ and **3** under the same conditions.

The complete regioselectivity (C-3 attack of iodine) was determined by ¹H NMR spectra. The diastereoselectivity (>99%de; **1g** : (2*R*, 3*R*) : (2*S*, 3*S*) = 95 : 5; **2g** : (2*S*, 3*R*) : (2*R*, 3*S*) = 95 : 5) was determined by HPLC on chiral column (Daicel OD column).

It can be concluded that the additive **3** or **4** plays an important role to form vinyl alkoxy samarium complex. Since the iodo vinyl alkoxy samarium complex increases electron density of samarium as well as a soft nucleophilic character of I⁻, the donation of iodide is more feasible than that of the simple trivalent trihalosamarium complexes.⁷

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