# Unprecedented Reactions Mediated by Samarium: An Approach to Nonstabilized Carbonyl Ylides[1]

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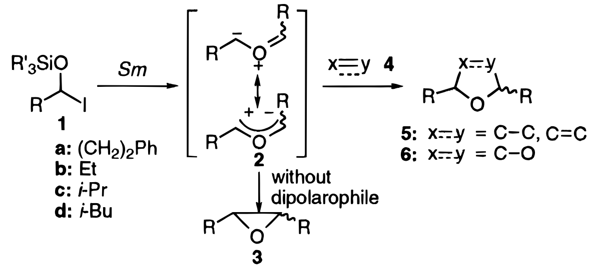
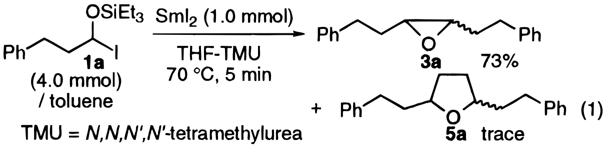
Samarium is widely applied to organic synthesis in the formation of carbon−carbon bonds and the transformation of a variety of functionalities with high selectivities.[2] In these reactions, carbanions[3] and radicals[4] are thought to be involved as transient active species.[5] We report herein the generation of novel active species,[6] nonstabilized carbonyl ylides from iodomethyl silyl ethers mediated by samarium, otherwise inaccessible, and their [3 + 2] cycloadditions to a variety of unsaturated compounds such as aldehydes, alkenes, allenes, and alkynes (Scheme 1).

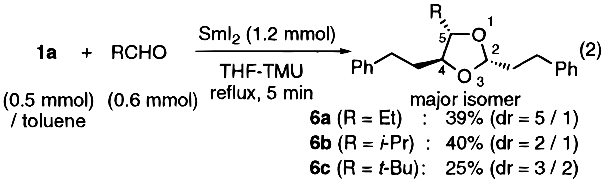
**Scheme 1**



At first we found 1-iodo-3-phenylpropyl triethylsilyl ether (**1a**)[7] prepared quantitatively from 3-phenylpropanal and iodotriethylsilane[8] in toluene was transformed to symmetrical oxirane **3a** by $SmI_2$ (eq 1). Without reflux, a tetrahydrofuran derivative **5a** was produced in 33% yield together with **3a** (17%). Considering the formation of both products **3a** and **5a**, it is strongly and reasonably suggested that the oxirane **3a** is produced from carbonyl ylide **2a** (Scheme 1, R = $Ph(CH_2)_2$) and that **5a** is the cycloadduct of **2a** to ethylene (**4a**) which is produced in the preparation of $SmI_2$ from samarium metal and 1,2-diiodoethane.[3a] An equimolar amount of $SmI_2$ to iodohydrin silyl ether **1a** was sufficient for this reaction. As the result, the oxirane **3a** was obtained in 73% isolated yield on the basis of $SmI_2$ accompanied by a trace amount of **5a**, when the solution of $SmI_2$ (1.0 mmol)/THF (10 mL)−TMU (*N,N,N′,N′*-tetramethylurea, 0.5 mL) was refluxed in advance and successively added to the toluene solution of **1a** (4 mmol/4 mL), and then the mixture was stirred at reflux for 5 min.[9] The same transformation can also be attained using the Sm (0)−$HgCl_2$ (cat.) system;[5a] **1a** (2 mmol)/THF−toluene (10:2 mL), 63% yield. In contrast, tetrahydrofuran **5a** was obtained (64% yield) when ethylene was passed through a reaction mixture (*vide infra*).



In addition to these results, we further found that the [3 + 2] cycloaddition of the carbonyl ylide **2a** to a carbon−oxygen double bond occurred.[12] Thus, when the reaction of iodohydrin silyl ether **1a** was carried out in the presence of an aldehyde, the corresponding cycloadducts, 1,3-dioxolanes **6**, were obtained (eq 2). Marginal yields were obtained from the competing reduction and pinacol coupling of aldehydes.[13] Interestingly, in these reactions, dioxolanes **6** are stereoselectively produced as a mixture of only two isomers, and the major isomer has the 2,4-*trans* and 2,5-*cis* configurations shown in eq 2.[14] These reactions are synthetically equivalent to the intermolecular stereoselective cross-pinacol coupling reaction (RCHO and $PhCH_2CH_2CHO$).[15]



The carbonyl ylides known so far are those bearing some functionalities, and these groups may affect their reactivities electronically.[16] The reactivities of *nonstabilized carbonyl ylides* still remain unknown. In such a context and also from a synthetic point of view, we tried to generate other carbonyl

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[1] Studies on Organosilicon Chemistry. No. 133.

[2] (a) Imamoto, T. *Lanthanides in Organic Synthesis*; Katritzky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Academic Press: London, 1994. (b) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29−68. (c) Sonderquist, J. A. *Aldrichimica Acta* **1991**, *24*, 15−23. (d) Kagan, H. B.; Namy, J. L. *Tetrahedron* **1986**, *42*, 6573−6614.

[3] (a) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698. (b) Ananthanarayan, T. P.; Gallagher, T.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1982**, 709−710. (c) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1986**, *51*, 1778−1786. (d) Imamoto, T.; Takeyama, Y.; Koto, H. *Tetrahedron Lett.* **1986**, *27*, 3243−3246. (e) Tabuchi, T.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 3891−3894. (f) Evans, D. A.; Kaldor, S. W.; Jones, T. K.; Clardy, J.; Stout, T. J. *J. Am. Chem. Soc.* **1990**, *112*, 7001−7031. (g) Hojo, M.; Yoshizawa, J.; Harada, H.; Hosomi, A. *J. Org. Chem.* **1993**, *58*, 6541−6542.

[4] (a) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485−1486. (b) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1990**, *55*, 6171−6176. (c) Curran, D. P.; Totleben, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 6050−6058.

[5] (a) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1987**, *52*, 3942−3944. (b) Molander, G. A.; Harring, L. S. *J. Org. Chem.* **1989**, *54*, 3525−3532. (c) Imamoto, Y.; Takiyama, N. *Tetrahedron Lett.* **1987**, *28*, 1307−1308.

[6] Our recent works; see: (a) Hosomi, A. *Acc. Chem. Res.* **1988**, *21*, 200−206 and references cited therein. (b) Hojo, M.; Ohkuma, M.; Ishibashi, N.; Hosomi, A. *Tetrahedron Lett.* **1993**, *34*, 5943−5946 and ref 3g.

[7] In dichloromethane; see: Jung, M. E.; Mossman, A. B.; Lyster, M. A. *J. Org. Chem.* **1978**, *43*, 3698−3701. A solution of **1** in toluene was also prepared quantitatively.

[8] Ishikawa, M.; Kunai, A.; Sakurai, T.; Toyoda, E.; Yamamoto, Y. *Organometallics* **1994**, *13*, 3233−3236.

[9] Essentially similar results were obtained using $SmI_2$ prepared from samarium metal−diiodomethane[10] and samarium metal−iodine.[11]

[10] Namy, J. L.; Girard, P.; Kagan, H. B. *Nouv. J. Chim.* **1981**, *5*, 479.

[11] Imamoto, T.; Ono, M. *Chem. Lett.* **1987**, 501−502.

[12] For the cycloaddition of a stabilized carbonyl ylide to aldehydes, see e.g.: March, P.-d.; Huisgen, R. *J. Am. Chem. Soc.* **1982**, *104*, 4952.

[13] (a) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765−766. (b) Souppe, J.; Danon, L.; Namy, J. L.; Kagan, H. B. *J. Organomet. Chem.* **1983**, *250*, 227.

[14] The structure of the major isomer was determined by NOE experiments.

[15] Intermolecular cross coupling: (a) Hou, Z.; Takamine, K.; Aoki, O.; Shiraishi, H.; Fujiwara, Y.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1988**, 668−670. (b) Idem *J. Org. Chem.* **1988**, *53*, 6077−6084. (c) Kraynack, E. A.; Pedersen, S. F. *J. Org. Chem.* **1993**, *58*, 6114−6117. (d) Konradi, A. W.; Kemp, S. J.; Pedersen, S. F. *J. Am. Chem. Soc.* **1994**, *116*, 1316−1323. Intramolecular cross coupling: (e) Molander, G. A.; Kenny, C. *J. Org. Chem.* **1988**, *53*, 2132−2134. (f) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236−8246.

[16] For a review, see: Huisgen, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley-Interscience: New York, 1984; pp 1−176.

[17] A suspension of samarium metal (316 mg, 2.1 mmol) and $HgCl_2$ (109 mg, 0.4 mmol) in toluene (5 mL) was well stirred for 20 min. **4** (1.0 mmol) was added to the white suspension, and the mixture was cooled to −78 °C. A solution of **1** in toluene (4.0 mmol/2.4 mL) was introduced, the temperature was allowed to raise to room temperature, and the mixture then was stirred for an additional 1 h. The resultant deep blue solution was poured into saturated aqueous $NaHCO_3$. After the conventional workup and purification, a pure cycloadduct **5** was obtained.

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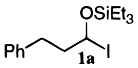
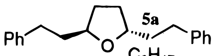
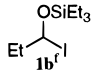
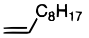
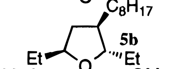
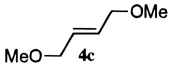
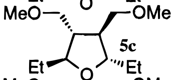
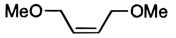
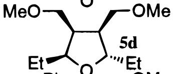
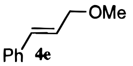
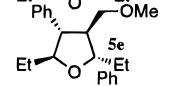
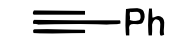
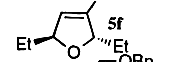
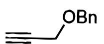
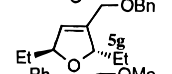
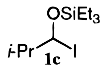
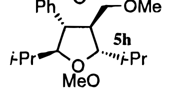
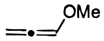
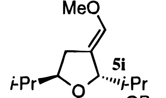
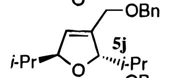
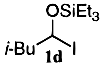
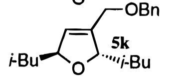
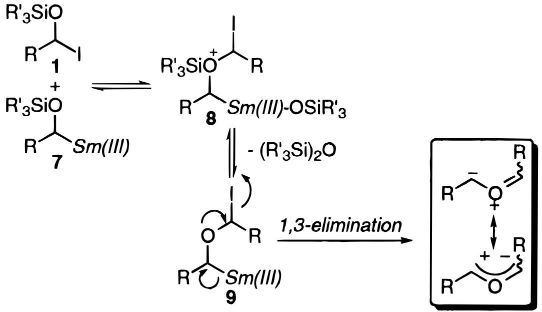
**Table 1.** [3 + 2] Cycloaddition of Carbonyl Ylide **2** to Dipolarophiles **4**[a]

| iodomethyl silyl ether **1** | dipolarophile **4** | cycloadduct **5**[b] | % yield[c,d] |
|---|---|---|---|
|  **1a** | $CH_2=CH_2$ **4a** |  **5a** | 64[e] (84/16) |
|  **1b**[f] |  **4b** |  **5b** | 89[g] (87/13) |
| **1b** |  **4c** |  **5c** | 65 (>95/<5) |
| **1b** |  **4d** |  **5d** | 99 (>95/<5) |
| **1b** |  **4e** |  **5e** | 74 (71/29) |
| **1b**[f] |  **4f** |  **5f** | 99 (>95/<5) |
| **1b** |  **4g** |  **5g** | 88 (85/15) |
|  **1c** | **4e** |  **5h** | 67 (82/18) |
| **1c** |  **4h** |  **5i** | 78 (82/18) |
| **1c** | **4g** |  **5j** | 94 (>95/<5) |
|  **1d** | **4g** |  **5k** | 68 (>95/<5) |

[a] For the procedure, see ref 17, otherwise noted. [b] The major stereoisomer. The stereochemistry for **5e** and **5h** were tentatively assigned. [c] Isolated yield of **5** as a mixture of stereoisomers based on **4**. [d] The ratio of stereoisomers was shown in parentheses. [e] A reaction was carried out using excess ethylene, and the yield was based on **1a**. [f] See ref 18. [g] Under conditions in ref 17, **5b** was obtained in 50% yield.

ylides substituted by only alkyl groups and to examine their reactivities toward a variety of dipolarophiles in intermolecular [3 + 2] cycloadditions. All of the carbon dipolarophiles, alkenes, allenes, and alkynes reacted with nonstabilized carbonyl ylides **2a**−**d** to afford the corresponding [3 + 2] cycloadducts, tetrahydrofurans and dihydrofurans **5**.[17] Selected results are summarized in Table 1. Irrespective of the structures of carbonyl ylides and dipolarophiles, the corresponding cycloadducts were obtained in good to excellent yields. Dipolarophiles bearing an ether moiety tend to react relatively efficiently with carbonyl ylides, while for efficiency, even simple alkenes and alkynes react conveniently under $SmI_2$−Sm(0) conditions.[18] Although these cycloadducts may possibly be 2−8 isomers, up to two isomers were observed in these reaction mixtures, and the structures of the major isomer are shown in the table. It should be noted that these reactions proceed in a stereospecific manner and the configurations of olefins are retained in the cycloadducts, suggesting a concerted process; *(E)*-1,4-dimethoxy-2-butene (**4c**) and its *(Z)*-isomer (**4d**) gave the corresponding cycloadducts bearing *trans*- and *cis*-methoxymethyl substituents at the 3,4-position, respectively. Interestingly, all major isomers possess 2,5-*trans* stereochemistry, and this is consistent with our understanding of the calculation which shows that the most stable conformation of the 1,3-disubstituted carbonyl ylide is a sickle form.[20]

**Scheme 2.** Plausible Pathway for the Generation of Nonstabilized Carbonyl Ylides **2**



The pathway for the generation of carbonyl ylides from iodomethyl silyl ethers is not clear at present, and a plausible route to carbonyl ylides **2** is shown in Scheme 2. It was reported that alkoxymethyl chlorides[21] and siloxymethyl chlorides[22] react with carbonyl compounds in the presence of $SmI_2$ under Barbier-type conditions to afford the corresponding adducts where α-alkoxy- and siloxymethyl carbanions or their equivalents seem to be involved as intermediates. Iodomethyl silyl ethers **1** may be also metalated to siloxymethyl carbanion species such as **7**. After successive reactions of **7** with **1** induced by the oxophilicity of samarium *via* **8** to form 1-samaroalkyl 1′-iodoalkyl ether **9**, spontaneous 1,3-elimination of samarium and iodide ions of **9** may occur to generate carbonyl ylide **2** just as in the generation of carbonyl ylides from (trimethylsilyl)(aryl)methyl chloromethyl ether.[6b,23]

The protocol presented here provides a truly unprecedented method for the generation of alkyl-substituted carbonyl ylides, novel reactive species which are not only a new class of chemical species mediated by samarium but also those otherwise inaccessible.

**Acknowledgment.** The present work was partly supported by the Ministry of Education, Science, Sports and Culture, Japan.

**Supporting Information Available:** Experimental procedures and $^1H$ and $^{13}C$ NMR, IR, and mass spectral data for the products (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(18) $SmI_2$−Sm(0) conditions: A mixture of samarium metal (0.601 g, 4.0 mmol) and $I_2$ (1.016 g, 4.0 mmol) in THF (6.0 mL) was refluxed for 5 h. To this flask, **4** (1.0 mmol) and a solution of **1** in toluene (4.0 mmol/2.4 mL) were added at −78 °C, and the mixture was stirred at room temperature for 3 h. The reaction mixture was poured into saturated aqueous $NaHCO_3$. After the conventional workup and purification, a pure cycloadduct **5** was obtained. Although the reason for high yields is not clear, this system was found to be preferable for the [3 + 2] cycloaddition, and this efficiency is not attributed to the special reducing ability of $SmI_2$−Sm(0) conditions reported.[19] In our case, carbonyl ylides generate even under ordinary $SmI_2$ conditions.

(19) Ogawa, A.; Nanke, T.; Takami, N.; Sumino, Y.; Ryu, I.; Sonoda, N. *Chem. Lett.* **1994**, 379−380 and references cited therein.

(20) From *ab initio* calculation (STO-3G) for 1,3-dimethylcarbonyl ylide, a *sickle* coplanar conformation is most stable.

(21) (a) Imamoto, T.; Takeyama, T.; Yokoyama, M. *Tetrahedron Lett.* **1984**, *25*, 3225−3226. (b) White, J. D.; Somers, T. C. *J. Am. Chem. Soc.* **1987**, *109*, 4424−4426. (c) Sasaki, M.; Collin, J.; Kagan, H. B. *Tetrahedron Lett.* **1988**, *29*, 4847−4850.

(22) Antonsen, ϕ.; Benneche, Y.; Undheim, K. *Acta Chem. Scand.* **1992**, *46*, 757−760.

(23) For the 1,3-elimination access to azomethine and thiocarbonyl ylides, see, e.g.: (a) Hosomi, A.; Sakata, Y.; Sakurai, H. *Chem. Lett.* **1984** 1117−1120. (b) Hosomi, A.; Matsuyama, Y.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1073−1074.