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Cooperative Catalysis of Samarium Diiodide and Mercaptan in a Stereoselective One-Pot Transformation of 5-Oxopentanals into δ-Lactones

Jue-Liang Hsu, Chao-Tsen Chen, and Jim-Min Fang*

Department of Chemistry, National Taiwan University, Taipei, Taiwan 106, Republic of China

jmfang@mail.ch.ntu.edu.tw

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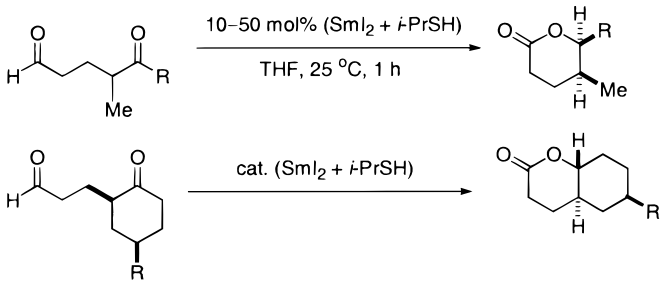
ABSTRACT



We demonstrate a general method for conversion of various 5-oxopentanals to substituted δ-lactones and 1-oxa-2-decalones by the synergistic catalysis of samarium diiodide and 2-propanethiol (or disulfide). The deliberate use of mercaptan is advantageous to facilitate the catalytic cycle. This method shows high stereoselectivities, and an enantioselective procedure is feasible by using the chiral mercaptan (1*R*,2*S*)-1-phenyl-2-(*N*-acetamido)propanethiol as a promoter.

Many natural products, such as insect pheromones and food flavors, incorporate the core structure of δ-lactones, which also attract a number of synthetic approaches.[1] Uenishi and co-workers[2] have demonstrated that 5-oxo-4-silyloxyhexanals can undergo the intramolecular Tishchenko oxidoreductions[3] by reactions with stoichiometric amounts of (*t*-BuO)SmI_2 or an aged SmI_2 solution (presumably containing Sm^{3+} ion) to give the corresponding δ-lactones. The authors also indicated that the silyloxy substituent is essential for such transformations. Otherwise, unsubstituted substrates such as 5-oxohexanal afford only low yields (∼10%) of δ-methyl-δ-lactone on treatment with (*t*-BuO)SmI_2 or simply the pinacolic coupling product on treatment with a freshly prepared SmI_2 solution. We found previously[3e] that transformation of 5-trimethylsilyl-5-oxopentanal into δ-trimethylsilyl-δ-lactone can be carried out by using stoichiometric amounts of SmI_2 and methanol. This reaction is presumably initiated by addition of MeOH to the aldehyde group to form a hemiacetal with the assistance of samarium ion. After an intramolecular hydride transfer to the ketone group (Tishchenko reaction),[3] a cyclization of the δ-hydroxyester intermediate would give the observed δ-lactone product. On the basis of this speculation, one can conceive a catalytic method for transformation of 5-oxopentanals into their

(1) (a) Ohloff, G. *Fortschr. Chem. Org. Naturst.* **1978**, *35*, 431. (b) Mulzer, J. In *Comprehensive Organic Functional Group Transformations*; Katrizky, A. R., Meth-Cohn, O., Rees, C. W., Eds.; Elsevier: Oxford, 1995; Vol. 5, pp 121−179. (c) Ley, S. V.; Cox, L. R.; Meek, G. *Chem. Rev.* **1996**, *96*, 423. (d) Collins, I. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1869.

(2) Uenishi, J.; Masuda, S.; Wakabayashi, S. *Tetrahedron Lett.* **1991**, *32*, 5097.

(3) Examples of samarium ion catalyzed Tishchenko reactions: (a) Collin, J.; Namy, J. L.; Kagan, H. B. *Nouv. J. Chem.* **1986**, *10*, 229. (b) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447. (c) Curran, D. P.; Wolin, R. L. *Synlett* **1991**, 317. (d) Molander, G. A.; McKie, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 5821. (e) Chuang, T.-H.; Fang, J.-M.; Jiaang, W.-T.; Tsai, Y.-M. *J. Org. Chem.* **1996**, *61*, 1794. (f) Lu, L.; Chang, H.-Y.; Fang, J.-M. *J. Org. Chem.* **1999**, *64*, 843.

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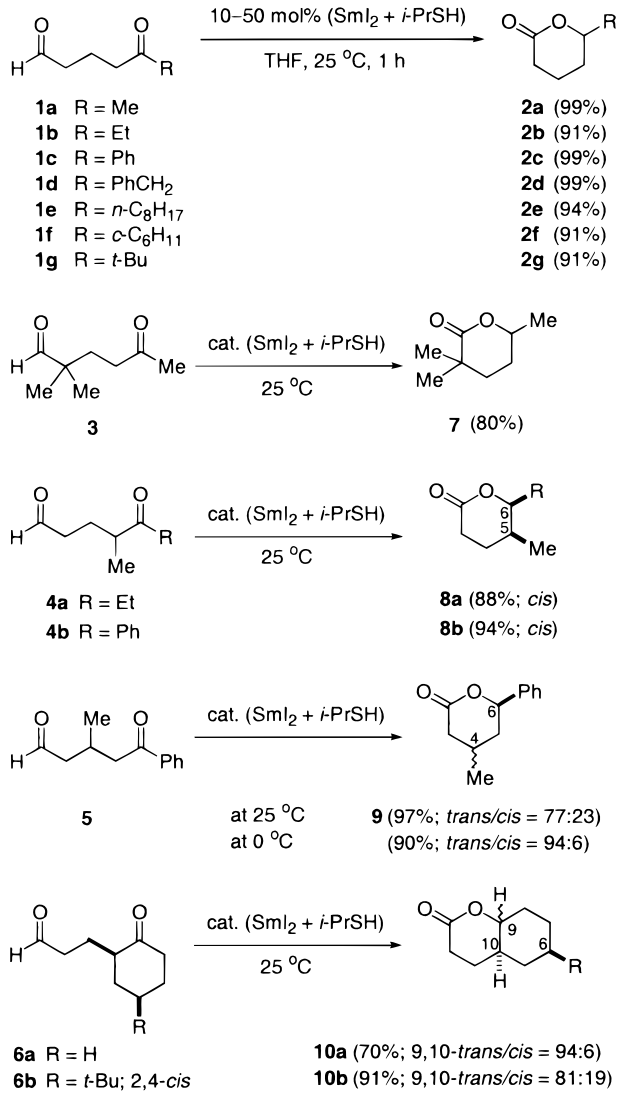
corresponding δ-lactones. Indeed, we report herein a general and efficient one-pot procedure by using SmI_2 and 2-propanethiol (*i*-PrSH) as the combined catalysts.

As shown in Scheme 1, a series of 5-alkyl- and 5-phenyl-5-oxopentanals **1a**−**g** were successfully converted to the corresponding δ-substituted-δ-lactones **2a**−**g**[4] by the catalysis of SmI_2/*i*-PrSH (10−50 mol %). No aldol or pinacol products were observed under these reaction conditions.

Scheme 1



The following procedure is typical. Under an atmosphere of argon, *i*-PrSH (0.01 mL, 0.1 mmol) was added to a deep blue SmI_2 (0.2 mmol) solution freshly prepared from samarium and 1,2-diiodoethane in THF (15 mL). The mixture was stirred for 10 min at room temperature, and a THF solution (5 mL) of 5-oxo-5-phenylpentanal (**1c**, 176 mg, 1.0 mmol) was added dropwise. The mixture was stirred for 1 h and then filtered through a short silica gel column by elution with EtOAc/hexane (1:1). The filtrate was concentrated by rotary evaporation to give the practically pure lactone **2c** (174 mg, 99%). We also conducted reactions using a slightly modified procedure by premixing an aliquot of SmI_2/*i*-PrSH (1−5 mol % in 1 mL of THF) with the substrate (**1a**−**g**) in an oven-dried syringe. The resulting yellow solution, an indication of the presence of trivalent samarium ion, was then added dropwise to the original SmI_2/*i*-PrSH solution. Accordingly, the desired lactones **2a**−**g** were also obtained in excellent yields (>90%).

By replacing SmI_2/*i*-PrSH with SmI_2/$(MeS)_2$,[5] the reaction of **1e** (R = *n*-C_8H_{17}) also proceeded smoothly to give **2e** in a comparable yield. The in situ generated (MeS)SmI_2 was considered as the reactive catalyst.[5] By using SmI_3/*i*-PrSH instead of SmI_2/*i*-PrSH, the reaction gave a 1:1 mixture of isopropyl thioesters of tridec-4-enoic acid and tridec-5-enoic acid according to NMR analysis. It seemed that the intermediary δ-oxyacid thioester (analogue of **B** in Figure 1, R = *n*-C_8H_{17}) was diverted to dehydration under such reaction conditions.[6] The reaction of **1c** (R = Ph) with stoichiometric amounts of SmI_3 and *i*-PrSH also gave an 83% yield of 5-phenylpent-4-enoic acid isopropyl thioester.[6] When **1c** was treated with stoichiometric amounts of SmI_2 and *i*-PrOH, a

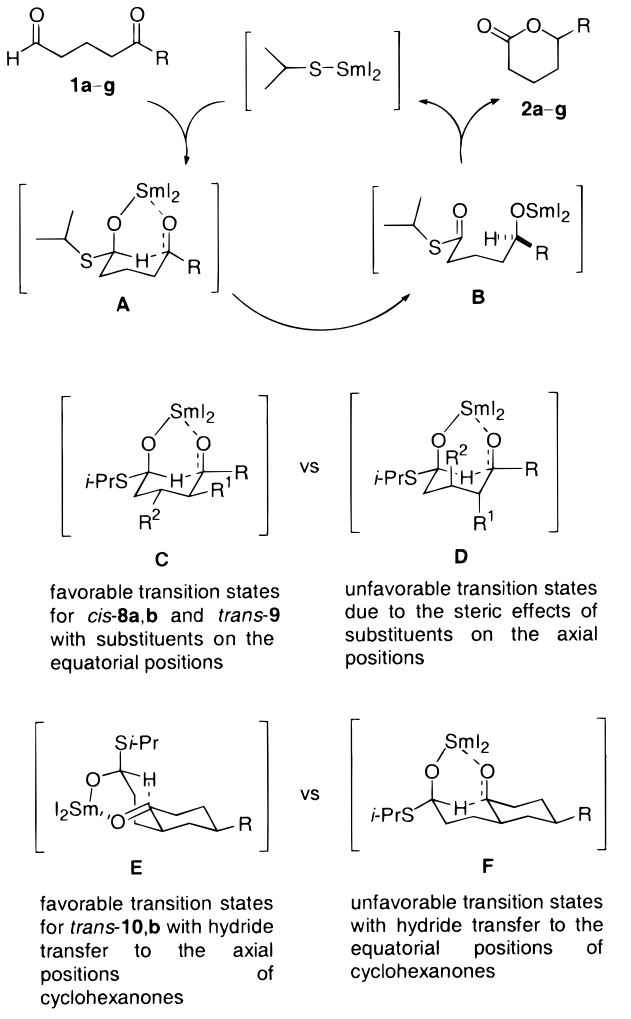


Figure 1. Proposed catalytic cycle and the favorable transition states for the formation of δ-lactones.

1:1 mixture of isopropyl 5-hydroxy-5-phenylpentanoate and 1-phenyl-1,2-cyclopentanediol were obtained as a consequence of the intramolecular Tishchenko oxidoreduction and pinacolic coupling.

On the basis of the above experimental results, one can propose a possible reaction mechanism for the formation of δ-lactones (Figure 1). A Lewis acid such as the presumed (*i*-PrS)SmI_2 or the related samarium species[3a,5,7] can promote the addition of *i*-PrSH to the aldehyde group of a 5-oxopentanal substrate. The samarium-bound hemithiolacetal intermediate (**A**) can undergo an intramolecular hydride shift to give the δ-oxyacid thioester (**B**).[3d] The reaction would proceed further with an irreversible lactonization and release the catalyst (*i*-PrS)SmI_2 (or the related samarium species) for the next cycle. The deliberate use of mercaptan is advantageous, because mercaptan is a better nucleophile than alcohol on addition to the aldehyde group. The resulting thioester is also more reactive than ester in the subsequent lactonization; thus the catalytic cycle is facilitated.

The SmI_2/*i*-PrSH-catalyzed reaction of bulky substrate **3** still proceeded smoothly to give δ-lactone **7** (Scheme 1).[4h] A variety of substituted 5-oxopentanals **4**−**6** also underwent the SmI_2/*i*-PrSH catalyzed reactions in highly stereoselective manners. Lactones **8a**,**b**,[4i,j] derived from 4-methyl-5-oxopentanals **4a**,**b**, had the *cis* configuration as indicated by a small coupling constant (∼3 Hz) between H-5 and H-6. Treatment of 3-methyl-5-oxo-5-phenylpentanal (**5**) in an SmI_2/*i*-PrSH solution at 25 °C gave lactone **9** as a mixture of *trans* and *cis* isomers (77:23).[4k] The *trans*/*cis* isomeric ratio was increased substantially to 94:6 by performing the reaction at a lower temperature (0 °C). The *trans* lactone showed an NOE correlation between Me-4 and H-6, whereas the *cis* isomer was devoid of this effect. The SmI_2/*i*-PrSH-catalyzed reactions of 2-(3-oxopropyl)cyclohexanones **6a**,**b** at 25 °C afforded 1-oxa-2-decalones **10a**,**b** in a preponderance of the 9,10-*trans* isomers.[4l,m,8] The *trans* decalones had H-9 and H-10 at axial positions as characterized by the ddd splitting pattern (J = 10, 10, 4 Hz) of H-9 in the ^{1}H NMR spectra.[4]

The stereochemical outcomes can be interpreted by comparisons of the transition states **C** versus **D** and **E** versus **F** (Figure 1). The transition state **C**, giving *cis*-**8a**,**b** and *trans*-**9**, is energetically favored due to the equatorial dispositions of substituents (R^1 or R^2), whereas the alternative transition state **D** exerts steric repulsions due to the axially oriented substituents. The transition state **E**, giving *trans*-**10a**,**b** by having hydride attack the cyclohexanone moiety from the axial direction, is superior to an equatorial attack in the transition state **F**. Under such circumstances, a product development control also favors the formation of the more stable equatorial alcohol (as shown in **E**). The stereoselectivities are in agreement with the previous findings[3c,f] of the related intermolecular Tishchenko reactions.

Our current study demonstrates an effective stereocontrol in conversion of 5-oxopentanals to δ-lactones by the synergistic catalysis of 2-propanethiol and samarium ion. This study also sheds light on the design of enantioselective catalysis by using chiral mercaptans. Our preliminary result using SmI_2 and (1*R*,2*S*)-1-phenyl-2-(*N*-acetamido)propanethiol as the combined catalysts (50 mol %) indicated that 5-octyl-5-oxopentanal (**1e**) was converted to 6-octyl-3,4,5,6-tetrahydropyran-2-one (**2e**) with predominance of the (*R*)-(+)-enantiomer (52% ee according to the HPLC analysis on a Chiralcel OB column).

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(4) All the δ-lactones **2a**−**g**, **7**, **8a**,**b**, **9**, and **10a**,**b** are fully characterized by spectral methods (IR, MS, HRMS, ^{1}H and ^{13}C NMR). (a) White, J. D.; Somers, T. C.; Reddy, G. N. *J. Org. Chem.* **1992**, *57*, 4991, for compound **2a**. (b) Utaka, M.; Watabu, H.; Takeda, A. *J. Org. Chem.* **1987**, *52*, 4363, for compounds **2b** and **2e**. (c) Downham, R.; Edwards, P. J.; Entwistle, D. A.; Hughes, A. B.; Kim, K. S.; Ley, S. V. *Tetrahedron: Asymmetry* **1995**, *6*, 2403, for compound **2c**. (d) Barluenga, J.; Lopez, P. J.; Campos, J. A. *Tetrahedron* **1983**, *39*, 2863, for compound **2d**. (e) Haase, B.; Schneider, M. P. *Tetrahedron: Asymmetry* **1993**, *4*, 1017, for compound (*R*)-**2e**. (f) Otsubo, K.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987**, 1487, for compound **2f**. (g) Garner, P.; Anderson, J. T. *Tetrahedron Lett.* **1997**, *38*, 6647, for compound **2g**. (h) Souma, Y.; Iyoda, J.; Sano, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3291, for compound **7**. (i) Kobayashi, Y.; Kitano, Y.; Takeda, Y.; Sato, F. *Tetrahedron* **1986**, *42*, 2937, for compound **8a**. (j) Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am. Chem. Soc.* **1989**, *111*, 6280, for compound **8b**. (k) Barbero, A.; Blakemore, D. C.; Fleming, I.; Wesley, R. N. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1329, for compound **9**. (l) Griffiths, D. V.; Wilcox, G. *J. Chem. Soc., Perkin Trans. 2* **1988**, 431, for compound **10a**. (m) Edward, J. T.; Cooke, E.; Paradellis, T. C. *Can. J. Chem.* **1982**, *60*, 2546, for compound **10b**. The data relevant to the stereochemical assignments are shown: **2e**, the (*R*)-enantiomer, $[\alpha]_D = +38.4$ ($CHCl_3$), is more retained than the (*S*)-enantiomer on a Chiralcel OB column by elution with *i*-PrOH/hexane (2:98); **2g**, δ_H 3.85 (1 H, dd, J = 11.7 Hz, J = 2.8 Hz); **8a** (*cis*), δ_H 4.14 (ddd, J = 11.5, 5.5, 2.8 Hz, H-6); **8b** (*cis*), 5.48 (d, J = 3.0 Hz, H-6); *trans*-**9**, δ_H 1.09 (d, J = 6.2 Hz, Me-4), 5.50 (dd, J = 7.3, 4.6 Hz, H-6); *cis*-**9**, δ_H 1.07 (d, J = 6.4 Hz, Me-4), 5.29 (dd, J = 12.0, 3.1 Hz, H-6); *trans*-**10a**, δ_H 3.28 (ddd, J = 10.2, 10.2, 4.2 Hz, H-9); *cis*-**10b**, δ_H 4.44 (br dd, J = 6.7, 3.3 Hz, H-9); *trans*-**10b**, δ_H 3.80 (ddd, J = 10.5, 10.4, 4.5 Hz, H-9); *cis*-**10b**, δ_H 4.42 (br d, J = 2.6 Hz, H-9).

(5) The S−S bond of PhSSPh is reductively cleaved by SmI_2, see: (a) Jia, X.; Zhang, Y.; Zhou, X. *Synth. Commun.* **1994**, *24*, 387. (b) Taniguchi, Y.; Maruo, M.; Takaki, K.; Fujiwara, Y. *Tetrahedron Lett.* **1994**, *35*, 7789.

(6) The reason for the preference of dehydration was unclear, presumably due to SmI_3 exhibiting a property of stronger Lewis acid.

(7) It has been reported (ref 3a) that SmI_2 reacts with alcohol ROH to give (RO)SmI_2 in the presence of a metallic salt as the electron carrier.

(8) Chandrasekhar, S.; Venkatesan, V. *J. Chem. Res, Miniprint* **1995**, 1137. The authors reported that 2-(3-oxopropyl)cyclohexanone (**6a**) underwent an intramolecular Cannizzaro reaction in boiling NaOH solution to give 3-(2-hydroxycyclohexyl)propionic acid, which was subjected to lactonization on treatment with concentrated HCl to give exclusively the *trans* isomer of **10a** (59%), based on an analysis of the ^{1}H NMR spectrum (90 MHz). In our hand, the two-step reaction afforded a *trans/cis* mixture of **10a** in a ratio of 91:9 based on an analysis of the ^{1}H NMR spectrum (300 MHz).