Pergamon

*Tetrahedron Letters*, Vol. 37, No. 29, pp. 5195-5198, 1996

0040-4039/96 \$15.00 + 0.00

PII: S0040-4039(96)01049-0

# Diiodosamarium, a Unique Catalyst Precursor for Ene Reactions of Unsaturated Carbonyl Compounds

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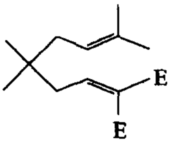
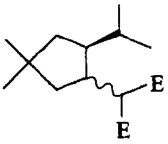
*Abstract :* $SmI_2$ presents catalytic activity for ene cyclizations of a series of unsaturated carbonyl compounds, some of which are prone to rearrangement or polymerization under standard conditions. Copyright © 1996 Elsevier Science Ltd

Recently, diiodosamarium mediated reactions have been used to generate a variety of carbo- and heterocycles.[1] The oxophilic samarium (II) species, a potent reducing agent, induces reaction via two sequential one-electron reductions, and the intermediate radicals thereby formed undergo a range of carbon-carbon bond forming reactions.

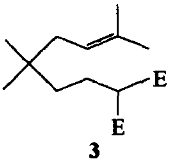
In the course of our investigations aiming at the synthesis of cyclopentanoid natural products,[2] we were interested to study the $SmI_2$ mediated cyclization of the doubly-activated 1,6-diene **1**[3] to the 1,2-disubstituted cyclopentane derivative **2**. Surprisingly, when a THF solution of excess samarium iodide[4] (3-4 equivalents) was added to **1**[3] in THF at room temperature, none of **2** was formed.[5] Instead, the crude reaction product showed the presence of **3** (2%), the cyclized product **4** (66%) as an equal mixture of *cis* and *trans* diastereomers and an unidentified by-product (32%).[5]



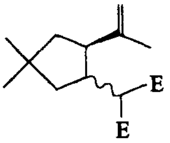
**1**



**2**



**3**



**4**

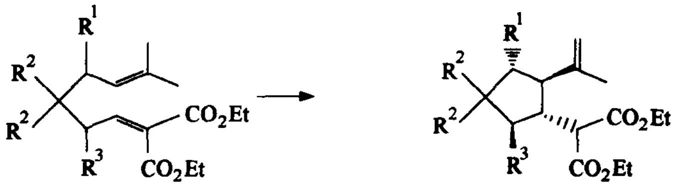
E = $CO_2Et$

Although, the formation of **3** was not unexpected, the formation of **4** appeared most intriguing. It seems likely that during reduction of **1** to **3**, the *in situ* generated Sm(III) species triggered an ene-like cyclization of **1** to **4**.[6] However, the lack of stereoselectivity in this reaction remains difficult to explain.[7]

Prompted by this unusual observation, we began a systematic study of the catalytic activity of diiodosamarium in ene-like cyclizations of a series of unsaturated carbonyl compounds and herein we report our preliminary results.[8]

We have found that ene cyclizations of doubly activated 1,6-dienes proceed in good yields by use of 5% mol eq. $SmI_2$ in $CH_2Cl_2$[6] (Table 1). In a typical experiment, a blue solution of $SmI_2$ in THF (0.025 mmol) is added to 0.5 mmol (150 mg) of **1** in 5 ml $CH_2Cl_2$ at ambient temperature under argon. Reaction mixture turns immediately yellow and after TLC indicated completion of reaction (24 h), the solvent is removed in vacuo, the product dissolved in 3% ethyl acetate-petroleum ether (60 - 80°) and passed through a short plug of silica gel to yield **9** (150 mg, 100%). The $SmI_2$ promoted cyclization in this case and in the cases of **5** and **6** gave yields of cyclization products that were comparable to previously published methods using $ZnBr_2$[3,9] and $LiClO_4$- supported silica gel.[10] The $SmI_2$ induced cyclization of **7** gave a high yield of cyclized product with good selectivity for the all *trans* isomer **12**. It should be noted that attempted cyclization of **7** with $ZnBr_2$ gave a polymeric material that only contained traces of **12**.[11] However, cyclization of **8**[12] gave a high yield of **13**[13] contaminated with traces of a diastereomer.

Table 1 : Ene Cyclizations of Doubly Activated 1,6-Dienes Using $SmI_2$

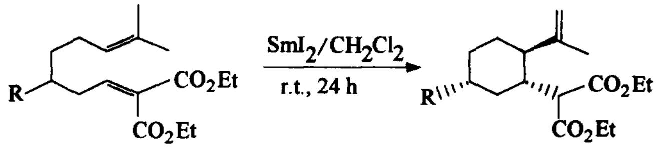


| Educts | $R^1$ | $R^2$ | $R^3$ | Ene products[a] | Yield |
|---|---|---|---|---|---|
| **1** | H | Me | H | **9** | 100% |
| **5** | H | H | H | **10** | 95% |
| **6** | OTBDPS | Me | H | **11** | 100% |
| **7** | H | H | Me | **12** | 96% |
| **8** | H | H | OTBDPS | **13** | 95% |

[a] All reactions were carried out in the presence of 5 mol% $SmI_2$ in $CH_2Cl_2$ at r.t. for 24 h as described in the general reaction protocol.

Like in the previous cases, the unsaturated carbonyl 6-ring precursors **14** and **15** underwent smooth cyclization to **16**[14] and **17**[15] when exposed to 5 mol % eq. $SmI_2$ in $CH_2Cl_2$ (Scheme 1).[16]

**Scheme 1**

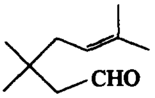
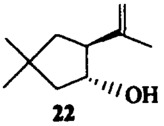
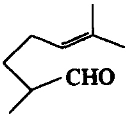
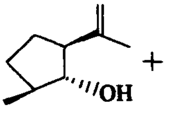
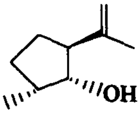
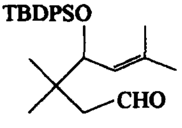
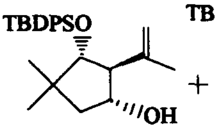
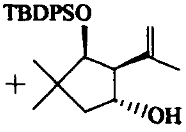
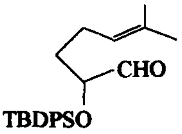
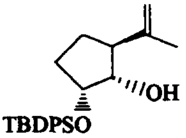
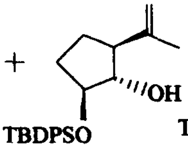
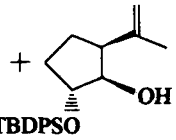


**14**: R=H
**15**: R=Me

**16**: R=H (95%)
**17** : R=Me (90%)

A second series of 5-ring precursors which gave unsaturated alcohols was also investigated (Table II). The cyclization of **18** in the presence of $SnCl_4$ and $Me_2AlCl$ has been reported to give the *cis* isomer of **22** as the major product.[17] However, cyclization of **18** is a demanding reaction and careful control of reaction conditions is required with $SnCl_4$ or $Me_2AlCl$ to avoid by-products that arise from competing ionic pathways.[17] In stark contrast, exposure of **18** to 5 mol % eq. $SmI_2$ in $CH_2Cl_2$ at room temperature gave only the *trans*-alcohol **22**, uncontaminated with any *cis*-product or other rearranged by-products. The cyclization of **19** in the presence of $Me_2AlCl$ is also a complex reaction, giving a variety of rearranged products depending on the reaction condition.[18] The $SmI_2$ promoted cyclization of **19** gave a high yield of ene-like products **23**[18] and **24**[18] in a ratio of 4:1, respectively. Cyclization of other oxygenated aldehydes e.g., **20**[19] and **21**[20] were also studied, although, product stereoselectivity was not high.[22]

Table II : Ene Cyclizations of Unsaturated Aldehydes Using $SmI_2$

| Educts | Ene products[a] | Yield[b] (%) |
|---|---|---|
| <br>**18** | <br>**22** | 60(84) |
| <br>**19** |  + <br>**23** **24**<br>( 80 : 20 ) | 53(80) |
| <br>**20** |  + <br>**25** **26**<br>( 75 : 25 ) | 57(82) |
| <br>**21** |  +  + <br>**27** **28** **29**<br>( 50 : 25 : 25 ) | 62(90) |

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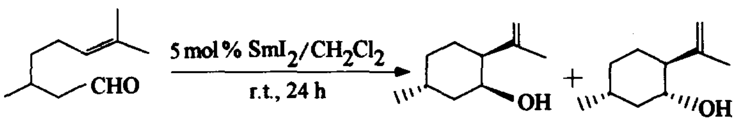
[a] All reactions were carried out in the presence of 5 mol% $SmI_2$ in $CH_2Cl_2$ at r.t. for 24 h as described in the general reaction protocol and products were purified by preparative layer chromatography on silica gel.

[b] Yields in parentheses are those based on recovered starting materials.

The $SmI_2$ induced cyclization is also effective for 6-ring cyclization precursors, e.g., **30** (Scheme 2). However, product stereoselectivity (**31**/**32** = 3:1) in this case is different from that obtained in the ZnBr₂ catalysed cyclization of **30**,[23] but similar to the case of $(Ph_3P)_3RhCl$ catalysed cyclization of **30**.[24] Unfortunately, the methyl ketone analog of **30** was completely stable to $SmI_2$ in $CH_2Cl_2$ at r.t. even after 24h.

**Scheme 2**



**30** **31 (45%)** **32 (15%)**

In summary, the present investigation has demonstrated that $SmI_2$ in $CH_2Cl_2$ is an effective catalytic system for promoting ene-like cyclizations of unsaturated carbonyl compounds. The catalyst is readily available and easy to use, and a small amount of catalyst is needed (5 mol % or less). The change in colour from blue to yellow observed in all cases after the addition of reactants suggests that the actual catalyst is trivalent.[6,25] The effectiveness of $SmI_2$ in promoting cyclization of **7** , **18** and **19** underscores the mildness of the new method.

**Acknowledgements :** The support of CSIR, New Delhi [01(1368)/95-EMR-II] is gratefully acknowledged. The CSIR, New Delhi, is also thanked for the award of SRF to S.K.N. We are thankful to Dr. B.K. Ghorai for some preliminary observations and to Mr. B.Mukherjee for the preparation of **8**.

## References and Notes :

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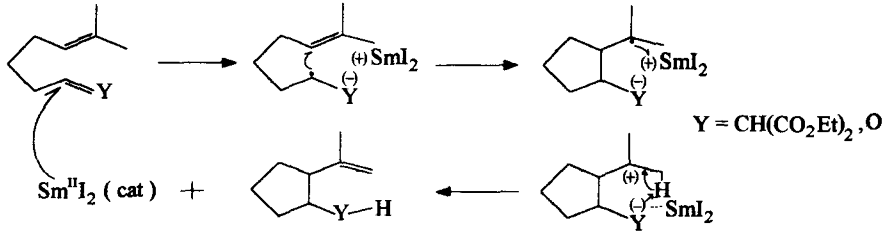
3. Sarkar, T.K.; Subba Rao, P.S.V. *Synth. Commun.* 1989, **19**, 1281.
4. Prepared by reacting samarium metal with diiodomethane in THF solution, see : Girard, P.; Namy, J.L.; Kagan, H.B. *J.Amer.Chem.Soc.* 1980, **102**, 2693.
5. GC/$^1$H-NMR comparison with independently synthesized samples of **2**, **3** and **4** confirmed this.
6. Weghe, P.; Collin, J. *Tetrahedron Lett.* 1994, **35**, 2545.
7. Lewis acid, e.g. $ZnBr_2$ catalysed ene reaction of **1** gives almost exclusively the *trans*-isomer of **4**, see : ref. 3.
8. For the only report of lanthanide catalysis using Eu(III) salts in intramolecular olefinic-aldehyde ene reaction, see : Ziegler, F.E.; Sobolov, S.B. *J. Amer. Chem. Soc.* 1990, **112**, 2749.
9. Tietze, L.F.; Beifuss, U.; Ruther, M.; Ruhlman, A,; Antel, J.; Sheldrick, G.M. *Angew. Chem. Int. Ed. Engl.* 1988, **27**, 1186.
10. Sarkar, T.K.; Nandy, S.K.;Ghorai, B.K.;Mukherjee, B. *Synlett*, 1996, 97.
11. Dauben, W.G.; Hendricks, R.T. *Tetrahedron Lett.* 1992, **33**, 603.
12. Prepared from **21** by Knoevenagel condensation [$CH_2(CO_2Et)_2$ / piperidinium acetate].
13. **13** was characterized by a combination of spectral ($^1$H- & $^{13}$C-NMR) and chemical methods.
14. Tietze, L.F.; Beifuss, U. *Liebigs Ann. Chem.* 1988, 321.
15. Tietze, L.F.; Beifuss, U. *Synthesis* 1988, 359.
16. No other diastereomer was visible by high-field (200 MHz) $^1$H-NMR analysis in these cases.
17. Andersen, N.H.; Hadley, S.W.; Kelly, J.D.; Bacon, E.R. *J. Org. Chem.* 1985, **50**, 4144.
18. Snider, B.B.; Karras, M.; Price, R.T.; Rodini, D.J. *J. Org. Chem.* 1982, **47**, 4538.
19. Sarkar, T.K.; Ghorai, B.K.; Nandy, S.K.; Mukherjee, B. *Tetrahedron Lett.* 1994, **35**, 6903.
20. Prepared from 5-O-(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-glycero pentofuranose (ref. 21) by Wittig olefination (with $Me_2C{=}PPh_3$), silylation (with t-$BuPh_2SiCl$), selective deprotection (with PPTS/MeOH) and Swern oxidation.
21. Dueholm, K.L.; Pederson, E.B. *Synthesis* 1992, 1.
22. **25** and **26** (inseparable mixture) were characterized by spectral (high-field $^1$H- & $^{13}$C-NMR, NOE evidence) analysis of the corresponding acetates (inseparable mixture). **27**, **28** and **29** (separated by preparative TLC) were characterised by a combination of $^1$H- & $^{13}$C-NMR, NOE evidence.
23. Nakatani, Y.; Kawashima, K. *Synthesis* 1978, 147.
24. Sakai, K.; Oda, O. *Tetrahedron Lett.* 1972, 4375.
25. A referee has suggested an alternate mechanism based on Molander's work (Scheme 3)[26] involving initial electron transfer from $SmI_2$ to the substrate followed by radical cyclization of the ketyl (radical anion) to give a tertiary cyclized radical which undergoes electron transfer ($Sm^{III} \longrightarrow Sm^{II}$) to give the cation which

**Scheme 3**



then eliminates to the alkene. *This mechanism does not seem tenable since addition of a catalytic amount of freshly prepared $SmI_3$[27] in THF to* **1** *in $CH_2Cl_2$ at r.t. efficiently converts it to* **9**.

26. Molander, G.A.; McKie, J.A. *J. Org. Chem.* 1992, **57**, 3132.
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(*Received in UK* 3 *April* 1996; *revised* 29 *May* 1996; *accepted* 31 *May* 1996)