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

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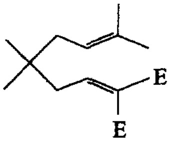
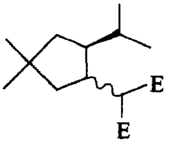
Abstract : SmI_2 presents catalytic activity for ene cyclizations of a series of unsaturated carbonyl compounds, some of which are prone to rearrangement or polymerization under standard conditions. Copyright © 1996 Elsevier Science Ltd

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



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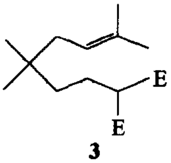

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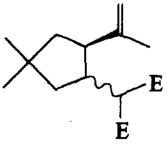


4

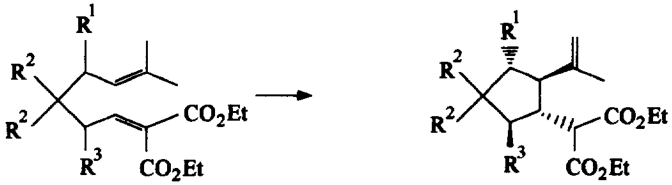
$E = CO_2Et$

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

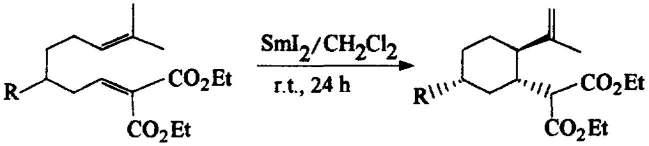


Educts	R^1	R^2	R^3	Ene products[a]	Yield
1	H	Me	H	**9**	100%
5	H	H	H	**10**	95%
6	OTBDPS	Me	H	**11**	100%
7	H	H	Me	**12**	96%
8	H	H	OTBDPS	**13**	95%

[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

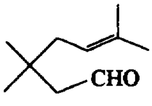
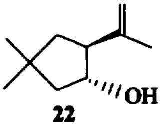
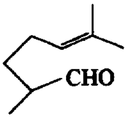
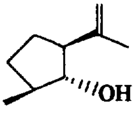
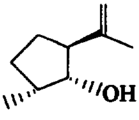
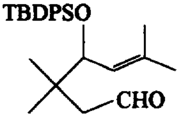
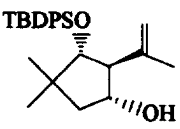
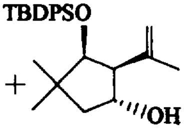
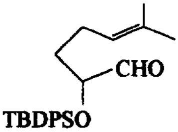
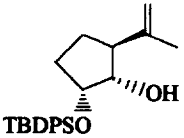
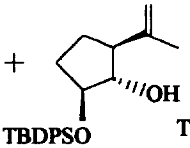
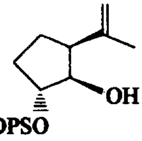


14: R = H
15: R = Me

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] (%)
 **18**	 **22**	60(84)
 **19**	 +  **23** **24** (80 : 20)	53(80)
 **20**	 +  **25** **26** (75 : 25)	57(82)
 **21**	 +  +  **27** **28** **29** (50 : 25 : 25)	62(90)

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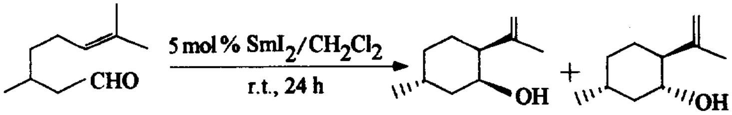
[a] All reactions were carried out in the presence of 5 mol% SmI_2 in CH_2Cl_2 at r.t. for 24 h as described in the general reaction protocol and products were purified by preparative layer chromatography on silica gel.
[b] Yields in parentheses are those based on recovered starting materials.

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 $ZnBr_2$ 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.

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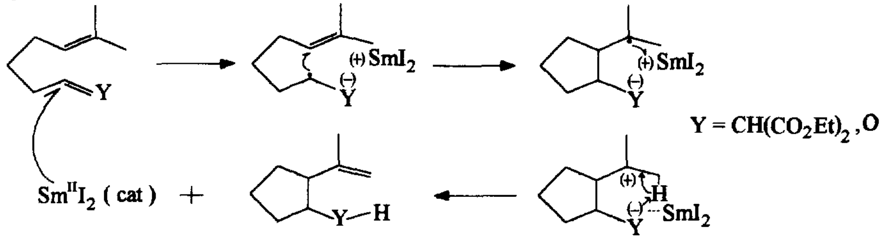
25. A referee has suggested an alternate mechanism based on Molander's work (Scheme 3)[26] involving initial electron transfer from SmI_2 to the substrate followed by radical cyclization of the ketyl (radical anion) to give a tertiary cyclized radical which undergoes electron transfer ($Sm^{III} \longrightarrow Sm^{II}$) to give the cation which 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**.

Scheme 3



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