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# Samarium(II) Iodide Mediated Transformations of Carbohydrate Derived Alkenyl Iodides

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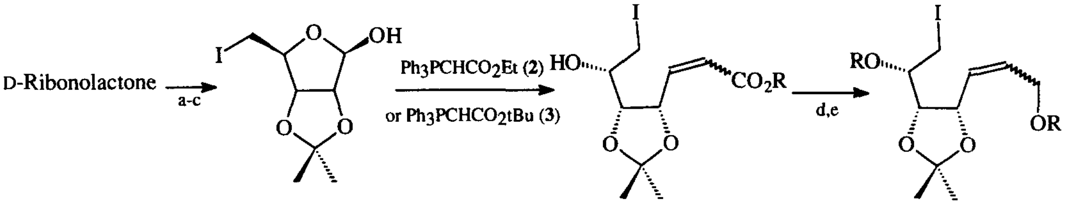
**Abstract:** D-ribonolactone derived acyclic alkenyl iodides were treated with samarium(II) iodide in THF/MeOH/HMPA at low temperature. Highly functionalized carbocycles are formed if the iodide is tethered to an allylic alcohol, an allylic acetate or an α, β - unsaturated *t*-butyl ester. The chemoselectivity and diastereoselectively of these transformations vary with the solvent system and with the reaction temperature.

Samarium(II) iodide is a useful reagent for the formation of carbon-carbon bonds by radical or carbanionic processes.[1] We have used $SmI_2$ to form carbocyclic compounds from simple alkynyl halides[2] and, in this letter, we describe the reactions of some D-ribonolactone derived acyclic alkenyl iodides with $SmI_2$ and $Bu_3SnH$.[3-7]

The synthesis of our acyclic alkenyl iodides (**Scheme 1**) was based on a strategy used by Wilcox and Thomasco.[5] Compound **1** was prepared from D-ribonolactone via a protection[8], iodination[9] and reduction[5] sequence and then reacted with the stabilized Wittig reagents **2** and **3**.[10] Reaction of **1** with ylide **3**, to give **5a** (86%) and **5b** (11%), was the cleaner of the two transformations.[11] The *cis* ester **5a** was used to prepare **6a** and **7a** and the *trans* ester **5b** was used to prepare **6b** and **7b**.



**1**

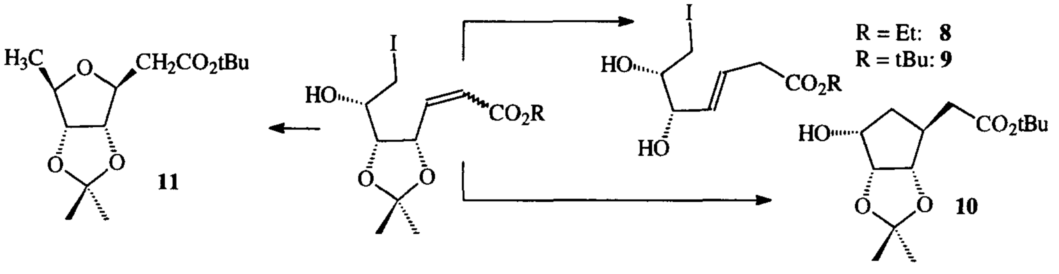
R = Et: **4a** (*Z*), **4b** (*E*)
R = tBu: **5a** (*Z*), **5b** (*E*)

R = H: **6a** (*Z*), **6b** (*E*)
R = Ac: **7a** (*Z*), **7b** (*E*)

**Scheme 1:** (a) See Reference 8; (b) $Ph_3P$, imidazole, $I_2$, $CH_2Cl_2$; 74%; (c) DIBAL-H, $CH_2Cl_2$, -78°C; 86%; (d) DIBAL-H, THF, -78°C[12]: **6a** [73% from **5a**], **6b** ( 76% from **5b**); (e) $Ac_2O$, $NEt_3$, DMAP, $CH_2Cl_2$, -78°C to rt[13]: **7a** [ 95% from **6a**],**7b** [93 % from 7b].[14]

Upon exposure to 3 equiv of $SmI_2$ in THF at rt (1 h), **4a** undergoes a reductive cleavage of the *carbon - oxygen* bond at the γ-position to give the β, γ -unsaturated ester **8** (42%).[15] The formation of this product is consistent with an organosamarium reaction intermediate.[15] We found no evidence for carbon-iodine bond reduction under these conditions. Substrate **5a** also reacts with $SmI_2$ in THF/MeOH at rt to give **9** (44%). We observed a dramatic change in chemoselectivity when HMPA and MeOH are used as cosolvents and when the reaction temperature is lowered. Interestingly, reaction of **5a** with 4 equiv of $SmI_2$ in *THF/MeOH/HMPA at low temperature* (-78°C, 4h; 0°C, 50 min)[16] gives the cyclized product **10** in 70% yield. We saw none of the γ-deoxygenation under these conditions. The $SmI_2$ mediated cyclization compares well with the corresponding $Bu_3SnH$ mediated radical cyclization.[5] Slow simultaneous addition of 1.2 equiv of $Bu_3SnH$ and 0.12 equiv of AIBN over 3.5 h to a refluxing solution of **5a** in benzene (final concentration: *ca.* 0.015 M, reaction time: 4 h total) gave compound **11** (18%) in addition to compound **10** (36%).[17,18]

**Scheme 2**



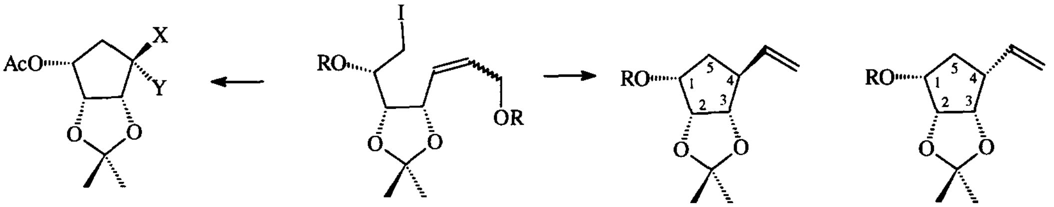
**11**

R = Et: **8**
R = tBu: **9**

**10**

The diacetates **7a** and **7b** react with 5 equiv of $SmI_2$ in THF/HMPA/MeOH at low temperature (-78°C 2h; 0°C 1.3h) in a stereodivergent manner to give vinylcyclopentane compounds **12** and **13**. The *Z* isomer **7a** gave **12** (76 %) as the major reaction product together with a little of the diastereoisomer **13** (6%). The reaction with the *E* isomer **7b** gave **12** and **13** in 25% and 65% yield respectively.[18] The corresponding $Bu_3SnH$ reactions are less diastereoselective and lead to the formation of different products. When **7a** is treated with $Bu_3SnH$/AIBN under reflux conditions overnight we isolated the β-diacetate **14** (59%) and the α-diacetate **15** (16%). The reaction of **7b** with $Bu_3SnH$ and AIBN gave **14** and **15** in a 1:1.7 ratio.

**Scheme 3**



**14** : X = $CH_2CH_2OAc$; Y = H
**15** : X = H; Y = $CH_2CH_2OAc$

R = Ac: **7a** (*Z*), **7b** (*E*)
R = H: **6a** (*Z*)

**12**: R = Ac
**16**: R = H

**13**:R = Ac
**17**: R = H

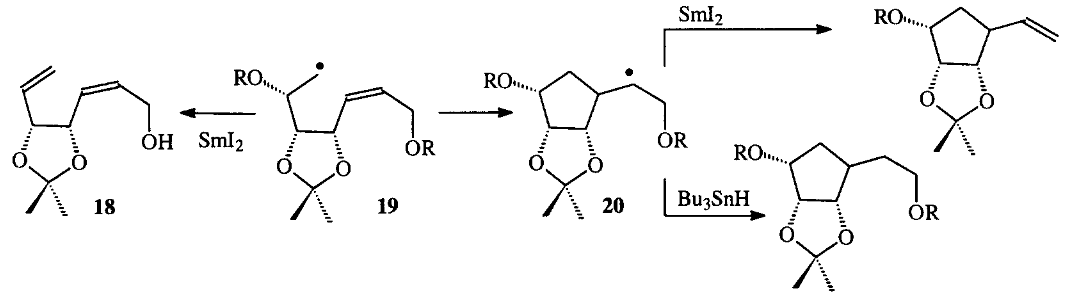
The ω-iodo (*Z*) allylic alcohol **6a** also cleanly reacts with $SmI_2$ in THF/HMPA/MeOH under low temperature conditions to exclusively give the diastereoisomer **16** (51%)[19] together with some unreacted starting material (30%). The reaction was incomplete under these conditions but attempts to push the reaction to completion, by running it at rt in THF/MeOH, resulted in a poorer mass balance and in the isolation of compounds **16**, **17**, **18** and **6a** from the reaction mixture.

Our interpretation of these results is summarized in scheme 4. The reaction of **7a** and **7b** with $Bu_3SnH$ or $SmI_2$ involves formation of the primary alkyl radical **19** and a 5-*exo* cyclization then gives the cyclized secondary radical **20**. In the $SmI_2$ reactions, reduction of the cyclized radical by a second equivalent of $SmI_2$ gives an organosamarium species which then undergoes β-elimination to give vinylcyclopentanes.[20] In the tin hydride reactions, the cyclized radical abstracts a hydrogen atom from $Bu_3SnH$ to give compounds **14** and **15**.

The acyclic β-elimination compound **18** is formed when the acyclic primary radical **19** is reduced to the corresponding organosamarium species before it can cyclize.[21] Compound **18** *is not formed* when the reactions are run under the low temperature conditions in THF/HMPA/MeOH.

We are continuing our work with other carbohydrate derived substrates in order to determine the generality of these reactions.

**Scheme 4**



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11. The purification of the **4a** and **4b** was complicated by the presence of tetrahydrofuran side products (formed by an intramolecular 1,4 - addition of the hydroxyl group onto the α, β-unsaturated ester).
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14. Our spectral data ($^1H$ and $^{13}C$ NMR, FTIR, MS) are in agreement with the proposed structures. Yields refer to isolated yields of pure products.
15. For some examples of reductive cleavage of γ-oxygenated α, β-unsaturated esters by $SmI_2$ see : (a) Molander, G.A.; La Belle, B.E.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 5259-5264. (b) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, *28*, 4437-4440. (c) Kang, S.K.; Kim, S.G.; Park, D.C.; Lee, J.S.; Yoo, W.J., Pak, C.S. *J.C.S., Perkin Trans I* **1993**, 9-10.
16. **General procedure for reactions with $SmI_2$:** A soln of the starting material (0.15 mmol) in THF (2.5 - 5.5 mL) was prepared under an argon atmosphere. HMPA (5% v/v) and MeOH (1.5 mmol) were then added. $SmI_2$ [0.1 M THF soln (Aldrich), 4.5 - 7.5 mL, 0.45 - 0.75 mmol] was transferred via cannula to the reaction mixture. The final concn of starting material was *ca.* 0.015 M. The reactions were quenched by addition of a saturated aq soln of $NH_4Cl$ (5 mL) and worked up as follows: the mixture was diluted with $H_2O$ (5 mL) and extracted with EtOAc (3 x 10 mL). The combined extracts were washed with $H_2O$ (3 x 20 mL), saturated aq $Na_2S_2O_3$ (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$ and concd. The crude products were purified by flash column chromatography or by radial chromatography [Harrison Research Chromatotron, silica gel or adsorbosil plates] using a mixture of EtOAc and hexanes.
17. The poor mass balance is due in part to the difficulties we encountered in separating our reaction products from the organotin species. We have not optimized conditions for the $Bu_3SnH$ reactions.
18. The stereochemistry of the cyclization products was determined with the help of nOe experiments.
19. As determined by TLC and $^1H$ NMR analysis of both the crude and purified products.
20. A $SmI_2$ radical addition/reductive elimination sequence involving a simple *aromatic* bromide tethered to an allylic acetate has been reported. See: Inanaga, J.; Ujikawa, O.; Yamaguchi, M. *Tetrahedron Lett.* **1991**, *32*, 1737-1740.
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