Pergamon

Tetrahedron Letters 39 (1998) 7075–7078

TETRAHEDRON LETTERS

Studies on the Diastereoselectivity of Samarium(II) Iodide Mediated Reductive Carbocyclizations of ω-Iodo-α,β-Unsaturated Esters Prepared from 2-Deoxy-D-ribose

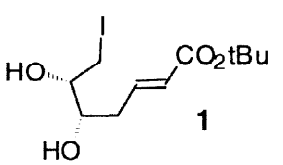
Sharon M. Bennett,* Raphinos Kouya Biboutou and Bita Samim Firouz Salari

Département de chimie et de biochimie, Université du Québec à Montréal, Case postale 8888, succursale Centre-Ville, Montréal, Québec, Canada, H3C 3P8. *e-mail: bennett.sharon_m@uqam.ca

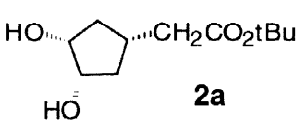
Received 30 June 1998; accepted 16 July 1998

Abstract: The title compounds were reduced with SmI_2 or Bu_3SnH to give carbocyclic compounds in good yield. The stereoselectivity of the SmI_2 reductive carbocyclizations varies with the reaction conditions, the double bond geometry and with the identity of the hydroxyl protecting groups. **Keywords**: Alkenyl halides, carbohydrates, cyclisation, samarium and compounds.

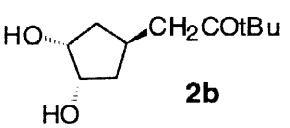
The chemoselective reduction of the carbon-halogen bond of *multifunctional* alkenyl halides by Sm(II) reagents can be challenging.[1-3] We found that reactions of D-ribonolactone derived ω-halo-α,β-unsaturated esters with SmI_2 gave products resulting from reduction of the carbon-halogen bond and/or reduction of the conjugated ester.[4a] Reductive carbocyclization to give highly functionalized cyclopentanes is favored when HMPA is used as a cosolvent,[5] the halogen is an iodine atom and when *t*-butyl esters are used.[4a] Molander and Harris have also used SmI_2 , in the presence of a proton source and a catalytic amount of NiI_2, to promote conjugate addition reactions of alkyl halides onto α,β-unsaturated esters, amides, lactones, lactams and nitriles.[6] Similar transformations have been accomplished with Bu_3SnH.[7] While the Bu_3SnH mediated reactions of γ-substituted *Z* ω-halo-α,β-unsaturated esters can be quite selective this is often not the case for the corresponding *E* substrates.[7,8,9]



1



2a



2b

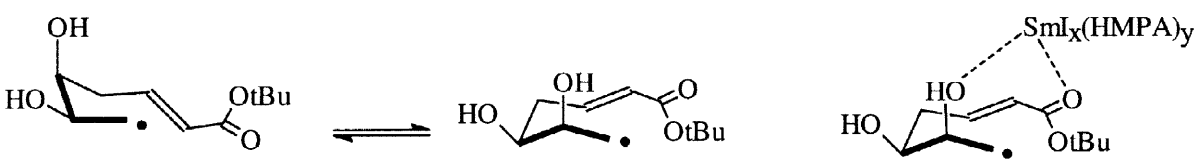
We reported that **1** reacts with both Bu_3SnH and SmI_2/THF/HMPA/MeOH to give the *cis* and *trans* carbocyclic compounds **2a** and **2b** (Table 1, entries a,c). Bu_3SnH gives a *cis:trans* ratio of 2.3:1 whereas the addition of SmI_2 in THF/HMPA to a solution of **1** in THF/MeOH at -78°C gives a **2a**:**2b** ratio of 7.2:1.[4a] These results prompted us to initiate a study on the *diastereoselectivity* of SmI_2 mediated transformations of carbohydrate derived ω-iodo-α,β-unsaturated esters to carbocycles.[10] This letter describes reactions, carried out with SmI_2

0040-4039/98/$ - see front matter
PII: S0040-4039(98)01552-4

and Bu_3SnH, for some new substrates prepared from 2-deoxy-D-ribose (**3**,**4**, **5**, **7** and **9**) and it also includes new results for compound **1** (Table 1, entry b).

Substrates **1** and **3** were prepared by a Wittig and iodination sequence as previously described;[4a] protection of the hydroxyl groups under standard conditions (Ac_2O/pyridine/CH_2Cl_2 or dimethoxypropane/pTSA) then gave substrates **4**, **5** and **7** in good yield. The preparation of **9** involved: monoiodination of 2-deoxy-D-ribonolactone[11] (CI_4, Ph_3P, imidazole, CH_2Cl_2), protection of the 2° hydroxyl group as a silyl ether (TBDMSCl, imidazole, CH_2Cl_2), reduction of the lactone with DIBAL-H and reaction of the resulting iodolactol with a stabilized Wittig reagent (Ph_3PCHCO_2tBu, CH_2Cl_2). The substrates were reduced with SmI_2 in THF/MeOH/HMPA at -78 °C and comparative studies were done with Bu_3SnH for most of the substrates.[12]

The *Z* esters **3** and **5** give the *trans* compounds as the major isomers but the diastereoselectivity is low. The most interesting levels of diastereoselectivity were observed for the *E* substrates **1**, **7** and **9** (Table 1, entries b, k, l, o).[12] *The major products from these reactions are the more sterically hindered cis isomers.* The stereochemistry of the cyclized products was determined from nOe experiments and from the known configuration of carbons 1 and 2. SmI_2 offers a distinct stereochemical advantage over Bu_3SnH (entries c, m) for these *E* substrates. The stereoselectivity, of the samarium(II) reductions of **1** and **9**, is better when the reactions are run *without* precomplexation of SmI_2 and HMPA (see entries a,b and n,o).[12] Complexation of a samarium ion with the carbonyl oxygen and one or more of the hydroxyl groups, or acetyl groups, is a likely explanation for the difference in the levels of diastereoselectivity observed in the Bu_3SnH and the SmI_2 reactions (figure 1).[13]

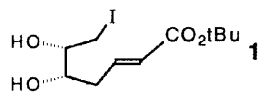
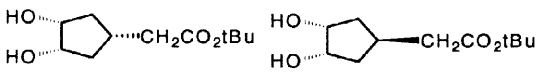
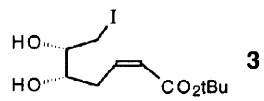
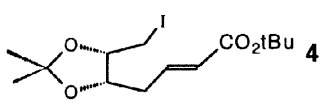
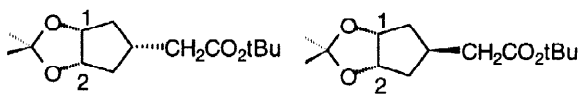
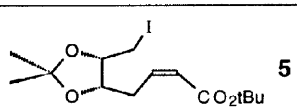
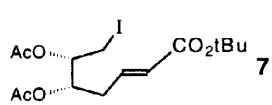
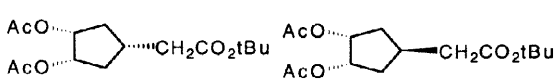
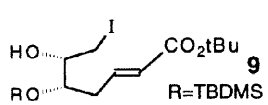
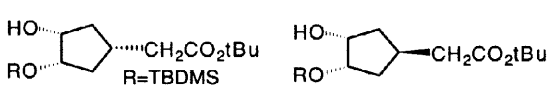


(gives *trans*) (gives *cis*) (gives *cis*)

Figure 1: Rationalization of the diastereoselectivity observed with SmI_2 for compound **1**.

Introduction of an *iso*propylidene group (**4**) blocks such a complexation; the *trans* isomer **6b** is the major compound and there is no advantage in using SmI_2 over Bu_3SnH.[14] We are continuing our studies with other carbohydrate derived substrates and a full account will be published in due course.

Table 1: Results of the Reductive Carbocyclization Reactions

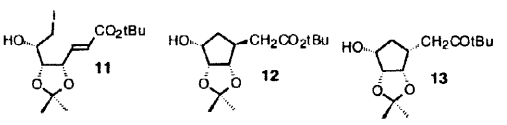
Entry	Substrate, Reagents and Reaction Conditions	Products % yield (*cis/trans*)[d,e]
	 **1**	 **2a** **2b**
a	SmI_2 (4 eq)[a], MeOH/ THF/HMPA, -78°C 4.5 h.	91 (7.2/1.0)[f]
b	SmI_2 (4 eq)[b], MeOH/THF/HMPA, -78°C 4.3 h.	83 (20.7/1.0)[g]
c	Bu_3SnH (1.4 eq), AIBN, Benzene, 80°C, 3 h.	79 (2.3/1.0)[f]
	 **3**	**2a** (*cis*) and **2b** (*trans*)
d	SmI_2 (4 eq)[a], MeOH/THF/HMPA, -78°C 4.2 h.	49 (1.0/2.0)[g]
e	SmI_2 (4 eq)[b], MeOH/THF/HMPA, -78°C 3 h, 0°C 0.4h.	71 (1.0/2.1)[f]
	 **4**	 **6a** **6b**
f	SmI_2 (4 eq)[a], MeOH/THF/HMPA, -78°C 3.5 h, 0°C 0.8 h.	89 (1.0/1.2)[g]
g	SmI_2 (4 eq)[b], MeOH/THF/HMPA, -78°C 3.5 h, 0°C 0.7h.	83 (1.0/1.3)[f]
h	Bu_3SnH (1.4 eq), AIBN, Benzene, 80°C, 3 h.	71 (1.0/1.6)[f]
	 **5**	**6a** (*cis*) and **6b** (*trans*)
i	SmI_2 (4 eq)[a], MeOH/THF/HMPA, -78°C 4 h, 0°C 0.5 h.	51 (1.0/1.9)[f]
j	Bu_3SnH (1.4 eq), AIBN, Benzene, 80°C, 3 h.	68 (1.0/3.0)[f]
	 **7**	 **8a** **8b**
k	SmI_2 (5 eq)[a], MeOH/THF/HMPA, -78°C, 1 h.	92 (16.1/1.0)[g]
l	SmI_2 (4 eq)[b], MeOH/THF/HMPA, -78°C, 1 h.	85 (14.9/1.0)[g]
m	Bu_3SnH (1.5 eq), AIBN, Benzene, 80°C, 3.5 h.	88 (1.7/1.0)[g]
	 **9** R=TBDMS	 **10a** **10b**
n	SmI_2 (4 eq)[a], MeOH/THF/HMPA[c], -78°C 4.5 h.	75 (3.4/1.0)[f]
o	SmI_2 (4 eq)[b], MeOH/THF/HMPA, -78°C h, 0°C h.	92 (13.1/1.0)[f]

a) SmI_2 *Precomplexation conditions*[12,4a] b) SmI_2 *Without precomplexation*[12, 4b] c) For this reaction only we used 2% v/v of HMPA
d) Isolated yield of purified compounds e) Isomers were not separable by radial chromatography. f) GC-MS ratio. g) ^1H NMR ratio.

Acknowledgements: We are grateful to the Natural Sciences and Engineering Research Council of Canada (NSERC), Bio-Méga/Boehringer Ingelheim Canada Ltd. and to the Université du Québec à Montréal (UQAM) for research funding. We thank Mr. N. Saade (McGill University) for mass spectra results, Dr. H. Le Thanh (UQAM) for help with the nOe and HMQC NMR experiments and Dr. G. Sauvé (Institut Armand Frappier) for providing access a polarimeter.

REFERENCES AND NOTES

1. For some recent reviews on SmI_2 see: (a) Molander, G.A.; Harris, C.R. *Chem. Rev.* **1996**, *96*, 307-338. (b) Molander, G.A. *Chem Rev.* **1992**, *92*, 29-68. (c) Curran, D. P. ; Fevig, T.L.; Jasperse, C.P.; Totleben, M.J. *Synlett* **1992**, 943-961. (d) Soderquist, J.A. *Aldrichchimica Acta* **1991**, 24, 15-23. (d) Kagan, H.B. *New J. Chem.* **1990**, *14*, 453-460.
2. The SmI_2 reduction of alkyl halides to the corresponding alkanes was first demonstrated by Kagan. See: (a) Girard, P.; Namy, J.L.; Kagan, H.B. *J. Am. Chem. Soc.* **1980**, *102*, 2693 - 2698. (b) Kagan, H.B.; Namy, J.L.; Girard, P. *Tetrahedron* **1981**, *37*, Suppl. 1, 175-180.
3. For a discussion of SmI_2 reactions of unsaturated halides see references 1a and 1c and references therein. Also see Curran, D.P.; Gu, X.; Zhang, W.; Dowd, P. *Tetrahedron* **1997**, *53*, 9023-9042.
4. (a) Bennett, S. M., Kouya Biboutou, R., Zhou, Z. and Pion, R. *Tetrahedron* **1998**, *54*, 4761 - 4786. (b) Zhou, Z. and Bennett, S. M. *Tetrahedron Lett.* **1997**, *38*, 1153 - 1156.
5. (a) The addition of HMPA as a cosolvent to facilitate the SmI_2 reduction of alkyl halides was first reported in: Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485-14866. (b) For an X-ray structure of $SmI_2(HMPA)_4$ see: Hou, Z.; Wakatsuki, Y. *J.C.S., Chem. Commun.* **1994**, 1205-1206. (c) For a report on electrochemical studies of SmI_2/THF/HMPA solutions see: Shabangi, M.; Flowers, Robert A. *Tetrahedron Lett.* **1997**, *38*, 1137-1140. (d) For some kinetic studies on SmI_2-HMPA see: Hasegawa, E.; Curran, D.P. *Tetrahedron Lett.* **1993**, *34*, 1717-1720.
6. Molander, G.A. and Harris, C.R. *J. Org. Chem.* **1997**, *62*, 7418 - 7429.
7. Bu_3SnH mediated radical cyclizations of ω-bromo-α,β-unsaturated ethyl esters, derived from D-ribonolactone, have been reported in the literature. See: Wilcox, C.S.; Thomasco, L.M. *J. Org. Chem.* **1985**, *50*, 546-547.
8. For a discussion on the stereochemistry of radical cyclizations see: Curran, D.P.; Porter, N.A.; Giese, B. *Stereochemistry of Radical Reactions - Concepts, Guidelines and Synthetic Applications*, VCH, Weinheim, **1996**.
9. Compound **11** reacts with Bu_3SnH to give **12** and **13** in a 1:2.6 ratio whereas SmI_2 gives a **12**:**13** ratio of 78:1. We suggested that the SmI_2 stereoselectivity is due to unfavorable steric interactions, between a bulky samarium-complexed carbonyl oxygen and the *iso*propylidene methyl groups, that leads to the formation of mainly the *trans* isomer.[4a]



10. For some examples of SmI_2 mediated transformations of carbohydrates to carbocycles via an intramolecular coupling of an aldehyde carbonyl with an α,β-unsaturated ester see: (a) Enholm, E. J. ; Trivellas, A. *Tetrahedron Lett.* **1994**, *35*, 1627-1628. (b) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463-6465. (c) Grové, J.J.C.; Holzapfel, C.W.; Williams, D.B.G.; *Tetrahedron Lett.* **1996**, *37*, 5817-5820. (d) Chiara, J.L.; Martínez, S.; Bernabé, M. *J. Org. Chem.*, **1996**, *61*, 6488.
11. Han, S.-Y.; Jouillié, M.M.; Petasis, N.A.; Bigorra, J.; Corbera, J.; Font, J.; Ortuño, R.M. *Tetrahedron*, **1993**, *49*, 349 - 362.
12. The SmI_2 reactions were run at -78°C in THF in the presence of HMPA (5 % v/v) and 10-14 equivalents of MeOH ([substrate] = 0.015 M; ratio of HMPA: SmI_2 : substrate = 19:4:1). In some cases HMPA was first precomplexed with a commercial solution of SmI_2 in THF at rt and the resulting deep purple solution was then added dropwise to cold solutions of the substrate in THF/MeOH (method A).[4a] In other cases, the commercial solutions of SmI_2 in THF were added dropwise directly to cold solutions of the substrates in THF, MeOH and HMPA (method B).[4b] The Bu_3SnH reactions were run as follows: a 0.015 M benzene soln of the substrate, Bu_3SnH (1.4 eq) and AIBN (0.1 eq) was prepared at rt under anhyd conditions under an argon atmosphere and then heated to 80 °C. The workup was as described in reference 4a.
13. Complexation is believed to be the controlling factor in the stereoselective SmI_2 mediated intermolecular coupling of α-(alkoxycarbonyl)amino ketones with α,β-unsaturated esters. See: Kawatsura, M.; Dekura, F.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, 373-376.
14. The level of stereoselectivity for **4** is much lower than we observed for **11**. This is likely the result of an increase in the distance between the *iso*propylidene methyl groups and the ester carbonyl.[9]