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Photoinduced Metalation of Nonactivated C–Cl Bonds with Samarium Diiodide: Synthesis of Alkenes with High (*Z*)-Selectivity through *β*-Elimination Reactions[†]

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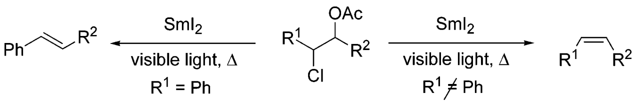
ABSTRACT



The photoinduced metalation of nonactivated C–Cl bonds of *O*-acetyl chlorohydrins is promoted by samarium diiodide. As a result of this, *β*-elimination of *O*-acetyl chlorohydrins is achieved, affording the corresponding (*Z*)-alkenes with total or high stereoselectivity.

(*Z*)-Alkenes are important intermediates for the synthesis of relevant substances such as pheromones[1] amid other natural products.[2] These alkenes are more difficult to prepare than those with (*E*)-stereochemistry, and as consequence, there are few publications dealing with their preparation.[3] Usually, (*Z*)-alkenes are obtained through Wittig-type reactions,[4] elimination reactions of vicinal alkoxyiodoalkanes,[5] manganese-induced migration−elimination processes,[6] Peterson reactions,[7] or condensation of aldehydes with dimesitylboryl stabilized carbanions.[8] However, in most of these articles, (*Z*)- or (*E*)-alkenes are obtained depending on the diastereoisomer of the starting material utilized.[4b−d,5,7] Some methods are limited by their poor generality[4a−c,6−8] or because the control of the stereoselectivity of the C−C double bond formation remains unsolved.[6,8]

Samarium diiodide is an important reducing agent used to create C−C bonds through radical or anionic mechanisms, as documented in several reviews.[9] Despite its wide applicability, and to the best of our knowledge, synthetic applications of SmI_2 regarding the metalation of nonactivated C−Cl bonds have not been described.[10] In this field, only

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[†] This paper is dedicated with best wishes to Professor Dr. Víctor Riera on the ocassion of his 70th birthday.

(1) Henrick, C. A. *Tetrahedron* **1977**, *33*, 1845−1889.

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(3) Synthesis of (*Z*)-alkenes can be achieved starting from acetylenic compounds through partial hydrogenation of alkynes: (a) Gruttadauria, M.; Liotta, L. F.; Noto, R.; Deganello, G. *Tetrahedron Lett.* **2001**, *42*, 2015−2017. (b) Lee, S. E.; Vyle, J. S.; Williams, D. M.; Grasby, J. A. *Tetrahedron Lett.* **2000**, *41*, 267−270. Or synthesizing the corresponding vinylic organoboranes: (c) Periasamy, M.; Prasad, A. S. B.; Suseela, Y. *Tetrahedron* **1995**, *51*, 2743−2748. (d) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U.; Bhat, N. G.; Vara Prasad, J. V. N. *J. Org. Chem.* **1988**, *53*, 239−246. (e) Brown, H. C.; Molander, G. A. *J. Org. Chem.* **1986**, *51*, 4512−4514. (f) Wang, K. K.; Chu, K.-H. *J. Org. Chem.* **1984**, *49*, 5175−5178. Also olefinic starting materials can be used: (g) Cahiez, G.; Avedissian, H. *Synthesis* **1998**, 1199−1205.

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(6) Kayika, H.; Shinokubo, H.; Oshima, K. *Tetrahedron* **2001**, *57*, 10063−10069.

(7) Barbero, A.; Blanco, Y.; García, C.; Pulido, F. J. *Synthesis* **2000**, 1223−1228.

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the photoinduced metalation processes of nonactivated C−Cl bonds by SmI_2 have been recently reported.[11]

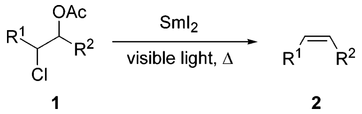
In particular, SmI_2 has been used to promote elimination reactions to afford C−C double bonds with high stereoselectivity.[12] For instance, our group has previously described the preparation of vinyl halides,[13] vinyl silanes,[14] α,β-unsaturated esters,[15] amides,[16] or ketones[17] by using this reagent. In all these preceding examples, the β-elimination reaction was triggered by the metalation of the activated C-halogen bond with SmI_2.

In this paper, we describe an efficient and highly stereoselective preparation of alkenes from O-acetylated chlorohydrins, in which the β-elimination reaction is initiated by metalating the nonactivated C−Cl bond with SmI_2 in the presence of visible light. To the best of our knowledge, this is the first method to promote 1,2-elimination reactions by treating chlorinated compounds in which the C−Cl bond is nonactivated with SmI_2. Although this elimination process seems appropriate to be also performed on *O*-acetyl bromohydrins, the use of *O*-acetyl chlorohydrins **1** presents some advantages: *O*-acetyl chlorohydrins are easier to prepare and, in general, more accessible than the equivalent bromo derivatives.[18]

The starting chlorohydrins **1** were prepared by subsequent treatment of several α-chloroaldehydes[19] with different Grignard reagents and acetyl chloride.[20]

Thus, when a mixture of *O*-acetyl chlorohydrins **1** and SmI_2 (0.1 M THF solution) was refluxed in THF in the presence of visible light (five household tungsten lamps × 100 W), alkenes **2** were obtained with total or very high stereoselectivity after 8 h of reaction (Scheme 1). When this process was carried out in the absence of light no reaction took place.

Scheme 1. Synthesis of Alkenes **2**



This transformation is general, and aliphatic (linear, branched, or cyclic) alkenes **2a−f** were obtained with total or very high (*Z*)-selectivity (Table 1, entries 1−6). R^1 and R^2 can be varied using diverse α-chloroaldehydes and Grignard derivatives, respectively.

Table 1. Synthesis of Alkenes **2** by Using SmI_2

entry	2	R¹	R²	*Z/E*[a]	yield[b]
1	**2a**	n-C_6H_{13}	Et	>98/2	53
2	**2b**	n-C_6H_{13}	n-Bu	>98/2	72
3	**2c**	n-C_6H_{13}	s-Bu[c]	91/9	51
4	**2d**	n-Pr	n-$C_{10}H_{21}$	>98/2	65
5	**2e**	n-Pr	Cy	94/6	56
6	**2f**	i-Pr	n-C_8H_{17}	90/10	87
7	**2g**	$-(CH_2)_5-$	n-Bu[c]	−	79
8	**2h**	Ph	Et	8/92	60
9	**2i**	Ph	Cy	20/80	67
10	**2j**	Ph	H	−	65

[a] *Z/E* ratio was determined by GC−MS and/or 300 MHz ^1H NMR analysis of the crude products **2**. [b] Isolated yield after column chromatography based on compound **1**. [c] *s*-BuLi and *n*-BuLi were used, instead of Grignard reagents, for the synthesis of starting materials **1c** and **1g**, respectively.

When aromatic *O*-acetyl chlorohydrins **1h**,**i** were used, (*E*)-alkenes were obtained with high stereoselectivity (Table 1, entries 8 and 9). In addition, this method can be also employed to obtain terminal alkenes such as **2j** (Table 1, entry 10).

The *Z*/*E* ratio was determined on the crude reaction products by ^1H NMR (300 MHz) spectroscopy and/or GC−MS. The (*Z*)- or (*E*)-stereochemistry of the C−C double bond in alkenes **2** was assigned on the basis of the value of the ^1H NMR coupling constants between the olefinic protons of compounds **2a−f** and **2h**,**i** and/or by comparison with NMR data previously reported in the literature for **2b** and **2g−i** (see Supporting Information). Two aspects of this process are worthy of mention: (a) although the *O*-acetyl chlorohydrins **1** were synthesized and used as mixtures of diastereoisomers (roughly 1:1), the corresponding alkenes **2** were obtained with total or high stereoselectivity and (b) in terms of cost, safety, and cleanliness, no cosolvents are necessary for these reactions.[11c]

The acetyl group in compound **1** is believed to play a key role on the observed reaction outcome. Accordingly, when

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(9) (a) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351−10372. (b) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727−2751. (c) Krief, A.; Laval, A. M. *Chem. Rev.* **1999**, *99*, 745−777. (d) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321−3354. (e) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307−338. (f) Molander G. A. In *Organic Reactions*; Paquette, L. A., Ed.; Wiley: New York, 1994; Vol. 46, pp 211−367. (g) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29−68. (h) Soderquist, J. A. *Aldrichimica Acta* **1991**, *24*, 15−23.

(10) Reaction of samarium diiodide with nonactivated C−Cl bonds is generally difficult to achieve, and normally no reaction is observed. See ref 9b.

(11) (a) Prasad, E.; Knettle, B. W.; Flowers, R. A., II. *Chem.−Eur. J.* **2005**, *11*, 3105−3112. (b) Sumino, Y.; Harato, N.; Tomisaka, Y.; Ogawa, A. *Tetrahedron* **2003**, *59*, 10499−10508. (c) Molander, G. A.; Alonso-Alija, C. *J. Org. Chem.* **1998**, *63*, 4366−4373. (d) Molander, G. A.; Wolfe, C. N. *J. Org. Chem.* **1998**, *63*, 9031−9036. (e) Ogawa, A.; Sumino, Y.; Nanke, T.; Ohya, S.; Sonoda, N.; Hirao, T. *J. Am. Chem. Soc.* **1997**, *119*, 2745−2746. (f) Skene, W. G.; Scaiano, J. C.; Cozens, F. L. *J. Org. Chem.* **1996**, *61*, 7918−7921.

(12) For a review of β-elimination reactions promoted by SmI_2, see: Concellón, J. M.; Rodríguez-Solla, H. *Chem. Soc. Rev.* **2004**, *33*, 599−609.

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(14) Concellón, J. M.; Bernad, P. L.; Bardales, E. *Org. Lett.* **2001**, *3*, 937−939.

(15) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Angew. Chem.* **2000**, *112*, 2866−2868; *Angew. Chem., Int. Ed.* **2000**, *39*, 2773−2775.

(16) Concellón, J. M.; Pérez-Andrés, J. A.; Rodríguez-Solla, H. *Chem.−Eur. J.* **2001**, *7*, 3062−3068.

(17) Concellón, J. M.; Huerta, M. *Tetrahedron Lett.* **2003**, *44*, 1931−1934.

(18) Addition of Grignard derivatives to α-bromoaldehydes afforded the corresponding epoxide (Darzens'-type reaction).

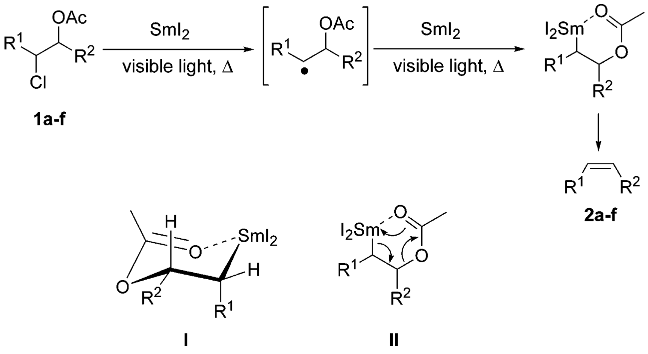
(19) α-Chloroaldehydes can be easily obtained by chlorination of aldehydes with sulfuryl chloride: Stevens, C. L.; Farkas, E.; Gillis, B. *J. Am. Chem. Soc.* **1954**, *76*, 2695−2698.

(20) Barluenga, J.; Yus, M.; Concellón, J. M.; Bernad, P. *J. Chem. Res., Synop.* **1980**, 41; *J. Chem. Res., Miniprint* **1980**, 677−692.

the reaction was carried out on nonacetylated chlorohydrins, a complex mixture of products was obtained.

The observed stereochemistry of alkenes **2a**−**f** might be explained assuming a chelation-control model. In this sense, after metalation of the C−Cl bond in compounds **1**, mediated by the presence of visible light, a six-membered ring intermediate (depicted as **I** or **II** in Scheme 2) is generated through chelation of the Sm^{III} center with the carbonyl oxygen atom of the acetoxy group.[13] In the proposed transition state model **I**, R^2 adopts an equatorial disposition (to avoid 1,3-diaxial interactions), and R^1 adopts an axial disposition (to avoid interactions with the samarium coordination sphere and taking into account that no 1,3-diaxial interactions are present).

Scheme 2. Mechanistic Proposal for the Conversion of **1a**−**f** to **2a**−**f**[a]



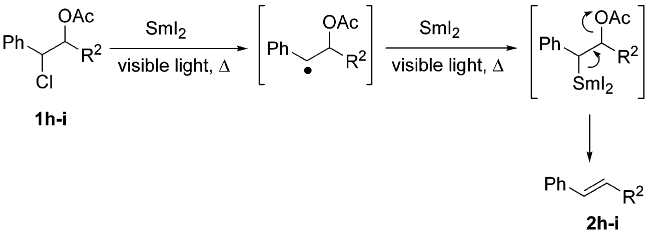
[a] **I**, alternatively **II**, is the proposed transition state model.

An elimination process from **I** as that shown in **II**, affords (*Z*)-alkenes.

The isolation of **2** with high levels of (*Z*)-stereoselectivity from the mixture of diastereoisomers **1** can be explained assuming that the diastereoisomer with a more suitable conformation for coordination of the Sm(III) center with the carbonyl oxygen from the acetoxy group reacts more readily, while the other diastereoisomer epimerizes before the elimination takes place.

On the other hand, reaction of SmI_2 with aromatic *O*-acetyl chlorohydrins **1h**,**i** resulted in the synthesis of (*E*)-alkenes **2h**,**i**. One possible mechanism accounting for this elimination selectivity involves the successive generation of a benzylic radical and a benzylic anion intermediate, which is sufficiently stabilized by the phenyl group and would suffer a *β*-elimination process without the formation of the cyclic chelate **I** discussed above and shown in Scheme 2. In this case, the *β*-elimination reaction is more favored due to the generated C−C double bond conjugated to the phenyl ring. Thus, a 1,2-elimination process takes place to afford the thermodynamically more stable (*E*)-alkene rather than the chelation-controlled product with (*Z*)-configuration (Scheme 3).[13,21]

Scheme 3. Mechanistic Proposal for the Conversion of **1h**,**i** to **2h**,**i**



When compound **1** in which $R^1 = n\text{-}C_6H_{13}$ and $R^2 = Ph$ was treated with SmI_2 in the presence of visible light, the corresponding acetate was obtained instead of the alkene **2**. This result could be explained as a consequence of a metalation of the C−Cl bond by SmI_2 and subsequent hydrolysis of the *β*-functionalized organosamarium intermediate.

In conclusion, the first photoinduced *β*-elimination reaction promoted by samarium diiodide has been achieved. Stereoselective synthesis of alkenes has been carried out through metalation of nonactivated C−Cl bonds on *O*-acetyl chlorohydrins.

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Supporting Information Available: General procedure and spectroscopic data for compounds **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(21) A similar behavior has been observed in other samarium diiodide-promoted processes when benzylic radicals are generated: Davies, S. G.; Rodríguez-Solla, H.; Tamayo, J. A.; Cowley, A. R.; Concellón, C.; Garner, A. C.; Parkes, A. L.; Smith, A. D. *Org. Biomol. Chem.* **2005**, *3*, 1435−1447.