TUTORIAL REVIEW

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β-Elimination reactions by using samarium diiodide

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The development of methodologies for the formation of carbon–carbon double bonds could be considered one of the most important challenges in organic synthesis. To this end, β-elimination reactions in 1,2-difunctionalised substrates have been one of the most important means of generating C=C bonds.

This review is intended to highlight the use of SmI_2 in β-elimination procedures, such that the organization of this revision highlights conventional β-elimination processes which are promoted by samarium diiodide. The synthetic applications of SmI_2 will be covered, and 1,2-elimination reactions which are involved in sequential reactions promoted by samarium diiodide, will also be illustrated. These methodologies along with the more recent developments in the area are discussed in this *tutorial review*.

1 Introduction

Since the pioneering studies of Kagan,[1] samarium diiodide has rapidly become an important reagent in synthetic organic chemistry because of its versatility in one- and two-electron transfer reactions.

The reduction potential of Sm^{+3}/Sm^{+2} measured in THF is -1.33 V,[2] but it can be widely modulated by using different solvents or additives.[3] This fact makes samarium diiodide an attractive reagent due to the possibility of changing its reactivity and selectivity. In addition, samarium ions are excellent Lewis acids and the species generated during the reaction are very oxophilic, being responsible of the high stereoselectivity exhibited by SmI_2-mediated reactions.

Moreover, samarium diiodide exhibits excellent properties for sequential organic reactions, requiring considerably less time, effort, and material with respect to more traditional multi-step procedures.[4]

For these reasons, few reagents have received as much attention in organic synthesis as samarium diiodide. As a result of this, several reviews, describing its applications, have recently been published.[3–5] In addition, this compound has been applied to a multitude of organic transformations, including β-elimination reactions, which proceed generally with high selectivity.[4]

Samarium diiodide can be prepared without difficulty, in moderate concentrations (0.1 M) in THF by treatment of diiodomethane, 1,2-diiodoethane, or iodine.[1b] Recently a synthesis of samarium diiodide by sonic treatment of these iodo compounds and metallic samarium considerably reducing the reaction time has also been described. In this paper, the first synthesis of SmI_2 using iodoform is also described.[6]

2 Metalation of the sulfonyl group

Transformations of carbonyl compounds into olefins is a useful C–C bond-forming method in organic synthesis, and among

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Humberto Rodríguez Solla was born in Gijón (Asturias) in 1975 and graduated from the University of Oviedo in 1998. He obtained his PhD in the same University in 2002 supervised by Prof. José M. Concellón. In that year he moved to Oxford (United Kingdom) where he is currently a postdoc in the Chemistry Research Laboratory (University of Oxford) under the supervision of Prof. Stephen G. Davies. His research interests are focused on the development of new methodologies by using organometallic compounds. During his PhD, he developed new methodologies to carry out β-elimination, reduction and cyclopropanation reactions using samarium diiodide or samarium carbenoids. Currently, he is working in the area of asymmetric synthesis using organometallic compounds and samarium diiodide with oxazolidinone chiral auxiliaries or DKP templates.

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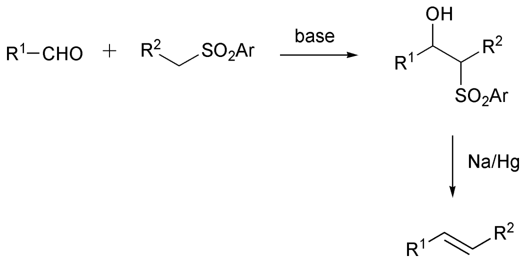
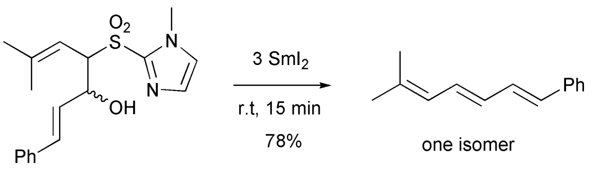
the numerous methodologies reported, Julia–Lythgoe olefination has been extensively utilized as a regio and stereoselective preparation of alkenes.[7]

In Julia–Lythgoe olefin synthesis, the C=C bond forming takes place by a reductive elimination in β-hydroxy sulfones and is commonly effected using sodium amalgam. The β-hydroxy sulfones are principally obtained by an aldolic reaction (Scheme 1).



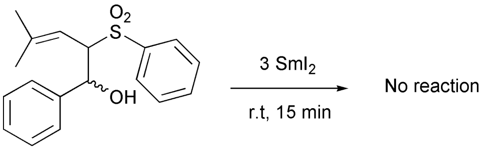
Scheme 1

Kende and Mendoza described an improved variant of the Julia–Lythgoe olefin synthesis by using samarium diiodide instead of a sodium amalgam.[8] In this way, they reported the reaction of β-hydroxy imidazoyl sulfones with a solution of SmI_2 in THF via an electron transfer pathway (Scheme 2).



Scheme 2

However, no reaction was observed when the same reaction conditions, used for the elimination in β-hydroxy imidazoyl sulfones, were applied in the case of the β-hydroxy phenyl sulfones (Scheme 3).

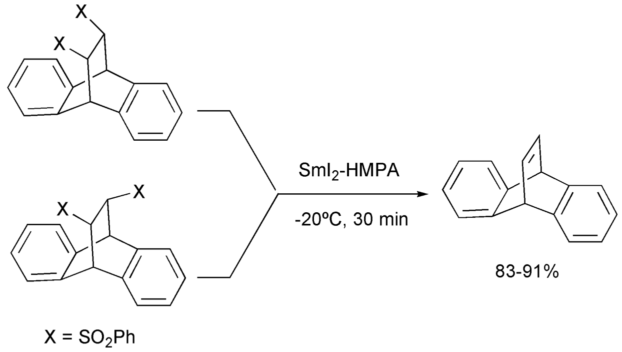


Scheme 3

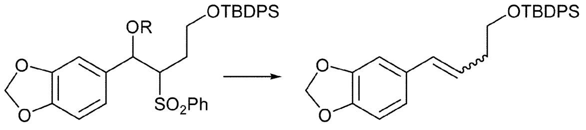
For this reason, an improvement of this methodology was described by Küntzer *et al.*, reporting the use of a mixture of SmI_2–HMPA for the reductive elimination of phenyl sulfones. This mixture was applied to the conversion of vicinal bis(arylsulfonyl) derivatives into the corresponding olefins (Scheme 4).[9]

Following-on from this work, a comparative study of the Julia–Lythgoe reaction by using SmI_2–HMPA or Na(Hg) has been carried out by Fukumoto *et al.*[10] No major differences during the reaction process were observed starting from β-hydroxy sulfones or *O*-acetylated-β-hydroxy sulfones. In general, better yields were obtained by using SmI_2–HMPA than the traditional procedure using sodium amalgam (Scheme 5). Both methodologies afford similar *E*/*Z* ratio of the obtained alkenes, and at the same time, the diastereoselection was fundamentally unaffected by the reaction temperature.

The Julia–Lythgoe olefination of ketones, to prepare trisubstituted alkenes, suffers from a number of drawbacks.

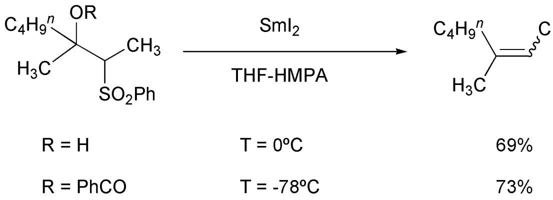


Scheme 4



R	Reagents	*t*(h)	*E*:*Z*	Yield(%)
H	SmI_2-HMPA	2	3:1	73
H	Na(Hg)	2	2.1:1	68
Ac	SmI_2-HMPA	1	3.1:1	95
Ac	Na(Hg)	2	3.7:1	88

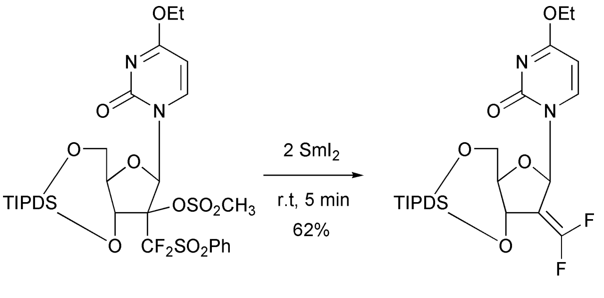
Scheme 5



Scheme 6

The use of Na(Hg) bears poor yields of the alkene and large amounts of the retroaldol products of the starting material. Consequently samarium chemistry has played a crucial role,[11] and β-elimination reactions in β-hydroxysulfones, and β-sulfoxybenzoates afford trisubstituted alkenes in high yields with approximate *E*/*Z* ratios of 2 : 1.

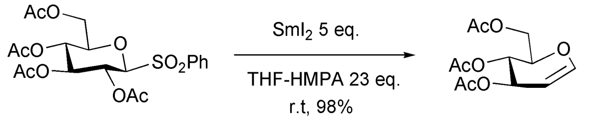
SmI_2–HMPA has also been used in the synthesis of 2′-deoxy-2′-difluoromethylene nucleosides,[12] which can present antitumor activity and inhibition of ribonucleotide diphosphate reductase (Scheme 7). In this case, conventional difluoromethylation strategies such as Wadsworth–Emmons (using difluromethyldiphenylphosphine oxide),[13] and Wittig reaction (by using CF_2Br_2–$(Me_2N)_3P$),[14] were unsuccessful.



Scheme 7

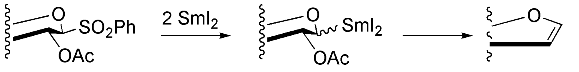
The mesylation of the starting compounds was crucial to afford the C=C bond. Thus, when this reaction was carried out from non-mesylated substrates, desulfonylation products, and starting material were isolated (Scheme 7).[9]

This methodology has been applied to the synthesis of natural products, as demonstrated by Sinaÿ *et al.* These authors, developed the first application of samarium diiodide to bring about the reductive metalation of an anomeric center of carbohydrates promoted by SmI_2–HMPA, obtaining substituted pyranoid glycols.[15] Again, the use of HMPA as a co-solvent was necessary to obtain the corresponding olefination products (Scheme 8).



Scheme 8

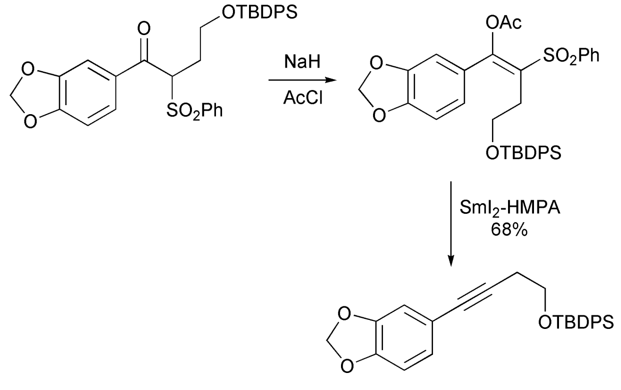
Generally, the 1,2-elimination takes place in the case of glycosyl phenyl sulfones when they are acetylated at the C-2 position. The authors propose a mechanism based on a *β*-elimination of the acetate (Scheme 9) when a transient unstable anomeric organosamarium species is formed.



Scheme 9

Analogously, this monomolecular elimination can also be carried out in glycosyl phenyl sulfones bearing carbonates or carbamates at the C-2 position.[16] It is described that *β*-elimination takes place easily through the anomeric organosamarium species, when an OAc group is present at the C-2 position. In the case of *O*-allyl or *O*-benzyl no elimination or a mixture between the elimination and reduction products is obtained, respectively.[15a]

High yields of acetylenes were obtained from unsaturated *β*-substituted sulfones by using a modification of the SmI_2–HMPA methodology (Scheme 10).[17]



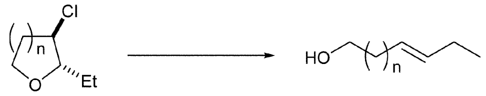
Scheme 10

3 Halogen metalation

One of the most important aspects of samarium diiodide is its utility in halogen metalation. In this instance, there are a large number of examples that belong to this methodology, which are summarised below.

3.1 Metalation of 1-halogeno-2-oxygenated compounds

3.1.1 Synthesis of alkenes. Samarium diiodide has been used for the ring scission of *β*-halogenoethers, such as in a complementary methodology to that where the use of sodium was reported.[18] Different stereochemistry results were observed depending on whether the scission reaction was carried out using sodium or samarium diiodide (Scheme 11).[19]

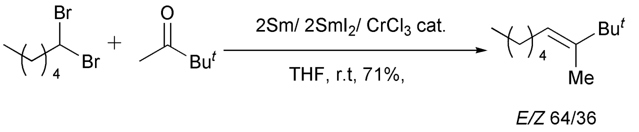


	n = 1	n = 2
SmI_2	89%, *E* >99%	85%, *E/Z* 24/76
Na	75%, *E/Z* 82/18	89%, *E* >95%

Scheme 11

The elimination reaction of 2-aryl or vinyl derivatives promoted by sodium, afforded over-reduction products. Nevertheless, when the same reaction is carried out by using samarium diiodide these products were not observed or were undetectable, and the unsaturated conjugated alcohols were obtained with high yields, and *E*-selectivity.

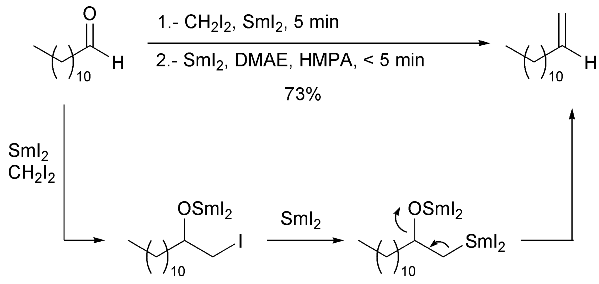
Alkylidenation reaction of ketones with $Sm/SmI_2/CrCl_3$ and *gem*-dibromoalkanes (Scheme 12) had previously been used to obtain olefins.[20]



Scheme 12

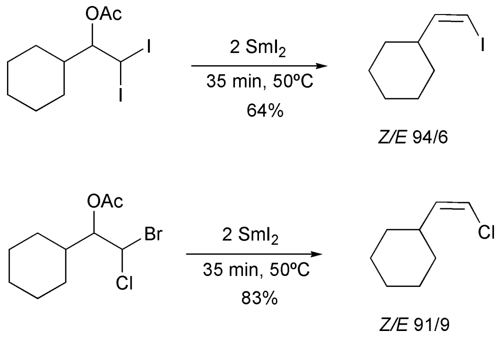
A mechanism based on the generation of *gem*-dimetallic compounds by reduction of *gem*-dihaloalkanes by the Sm/SmI_2 system under $CrCl_3$ catalysis, is proposed.

A methylenation process promoted by samarium diiodide has been described by Inanaga *et al.*[21] The authors depicted a one-pot carbonyl methylenation by an iodomethylation/elimination sequence as depicted in Scheme 13.



Scheme 13

3.1.2 Preparation of vinyl halides. A diastereoselective 1,2-elimination promoted by samarium diiodide was performed in 1,1-dihaloalkan-2-ols in order to obtain the corresponding vinyl halides, demonstrating the first general stereoselective *β*-elimination reaction promoted by SmI_2.[22] A study of the temperature conditions, *O*-protecting groups and addition of different co-solvents is described in this paper. Thus, it was found that the best results were obtained at higher temperatures (surprisingly, the usual diastereoselectivity/temperature trend was not observed), by using acetyl as an *O*-protecting group, and in the absence of co-solvents (Scheme 14).

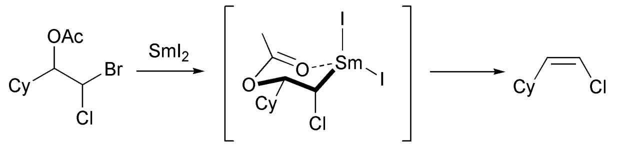


Scheme 14

This elimination was more interesting in dihaloalkanols bearing two different halogen atoms. In this case, complete chemoselectivity was observed and only products resulting from metalation of more reactive halogen (I > Br > Cl) were observed; diastereoselectivity was similar in all cases.

One limitation of this methodology is the lower diastereoselectivity obtained when the resulting double bond is conjugated.

The proposed mechanism (Scheme 15) envisages a chelation control model in which, the metalation takes place in the most reactive halogen generating a six-membered ring, due to the chelation of the oxophilic samarium(III) center with the carbonyl oxygen atom of the acetoxy group.

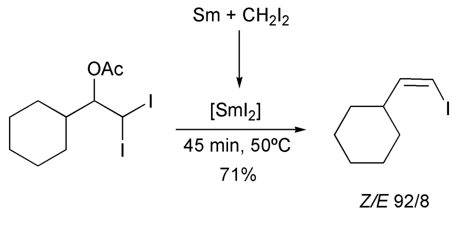


Scheme 15

It is noteworthy that a diastereoisomeric mixture of the starting materials were used and the corresponding vinyl iodides were obtained with high diastereoselectivity. This proposed cyclic model has an equatorial R group (R = Cy in Scheme 15), to avoid 1,3-diaxial interactions, and an axial halogen atom where neither 1,3-diaxial interactions nor dipoles (due to C–halogen and Sm–I are opposed) are present.

This proposal explains the observed stereochemistry of the (*Z*)-vinyl halides obtained.

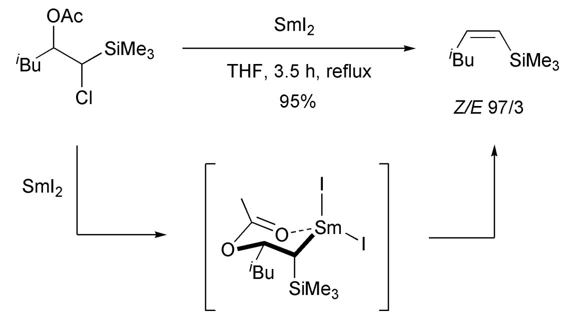
An alternative strategy to the use of SmI_2 is to generate samarium diiodide *in situ* (for example from samarium metal and diiodomethane), in the presence of the starting materials. This method has been reported in a recent publication in which the elimination reaction takes place by using cheaper and more stable metallic samarium instead of preformed SmI_2. The total reaction time using this alternative method is also shorter (Scheme 16).[23]



Scheme 16

3.1.3 Synthesis of vinyl silanes. A highly diastereoselective synthesis of (*Z*)-vinylsilanes was carried out from *O*-acetyl 1-chloro-1-trimethylsilylalkan-2-ols.[24]

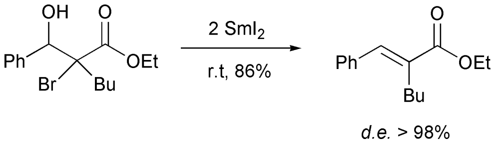
A study of the reaction conditions was accomplished indicating that *O*-acetylation, and refluxing conditions were important factors. When 1-chloro-1-trimethylsilylalkan-2-ols were used (without acetylation) no elimination reaction took place, subsequent reactions performed at room temperature also proved unsuccessful in the formation of *β*-elimination products. The stereoselectivity, through the *β*-elimination process, has also been explained. A chairlike transition state with R group (R = *i*Bu in Scheme 17) in an equatorial position, avoiding 1,3-diaxial interactions is proposed. Similarly, the trimethylsilyl group adopts an axial position to avoid interactions with the samarium coordination sphere taking into account that no 1,3-diaxial interactions are present.



Scheme 17

3.1.4 Synthesis of *α,β*-unsaturated esters or amides. In a recent publication a general synthesis of (*E*)-*α,β*-unsaturated esters with total selectivity,[25] or (*E*)-*α,β*-unsaturated amides with high or total selectivity has been described.[26]

The reaction of 2-halo-3-hydroxyesters (easily prepared by aldolic reaction between the corresponding lithium enolates of *α*-haloesters and aldehydes) with a solution of samarium diiodide in THF gave the corresponding (*E*)-*α,β*-unsaturated esters, with total diastereoselectivity in which the C–C double bond is di- or trisubstituted (Scheme 18). *α,β*-Unsaturated esters in which the double bond is tetrasubstituted can not be prepared by using this method.



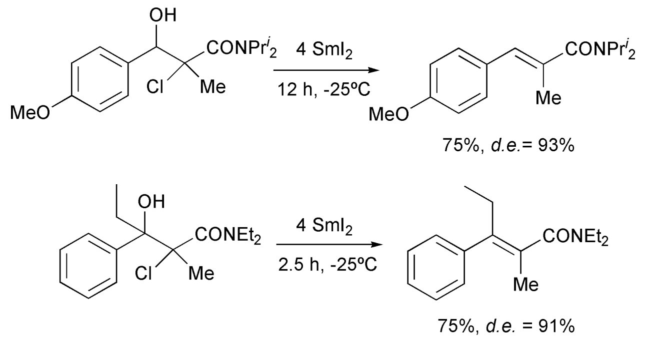
Scheme 18

In a similar way, it is possible to prepare di-, tri-, or tetra-substituted (*E*)-*α,β*-unsaturated amides from 2-chloro-3-hydroxyamides as starting materials with high or total diastereoselectivity.

In the previous case, the stereoselectivity was affected by the structure of the starting compounds as distinguished from the esters. Therefore, a decrease of the selectivity in di-, tri-, and tetra-substituted amides, respectively, was observed and the reaction was performed at lower temperatures to improve the diastereoselection.

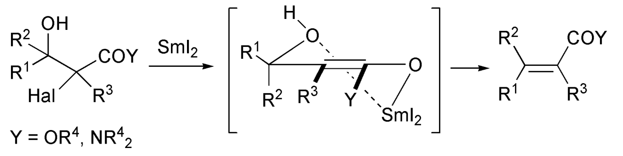
It is noteworthy that (*E*)-*α,β*-unsaturated esters (Scheme 18), or amides (Scheme 19) were obtained with high or total diastereoselectivity from a mixture of diastereoisomers of the corresponding starting compounds.

In the synthesis of *α,β*-unsaturated esters or amides the

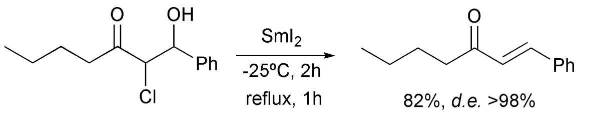


Scheme 19

observed stereochemistry may be explained by assuming the formation of an enolate intermediate, in which the oxophilic Sm(III) center is chelated with the oxygen atom of the alcohol group producing a six-membered ring, with the group R^1 (R^1 bulkier than R^2) in an equatorial position. An elimination from this cyclic transition state afford the α,β-unsaturated ester, or amide (Scheme 20).



Scheme 20



Scheme 21

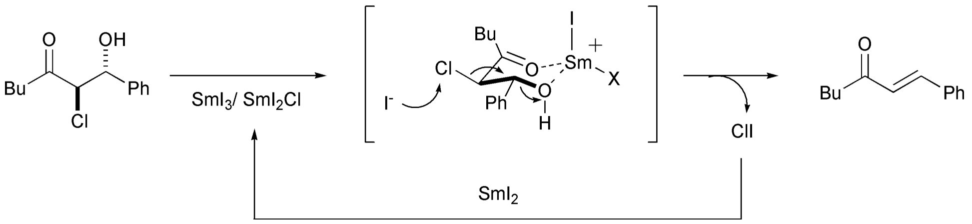
The preparation of α,β-unsaturated esters with total diastereoselectivity can also be carried out by using SmI_2 generated *in situ* from a mixture of samarium powder and diiodomethane, thus reducing the reaction time considerably which achieving higher yields.[23]

3.1.5 Synthesis of α,β-unsaturated ketones.

Analogously, SmI_2 has been used to obtain (*E*)-α,β-unsaturated ketones.[27] So, when the requisite α-chloro-β-hydroxy ketone, as a mixture of diastereoisomers, is added to a solution of SmI_2 or SmI_3 in THF at −25 °C and then heated at reflux, the corresponding (*E*)-α,β-unsaturated ketones are isolated with total or high diastereoselectivity.

In this case only one equivalent of SmI_2 or SmI_3 was necessary to perform the reaction, and two mechanisms are proposed for each starting diastereoisomer. When SmI_2 was used, the reaction is initiated, in both cases, by traces of samarium(III) present in the SmI_2–THF solution (Scheme 22). In the *anti* diastereoisomer a chelation between the oxygen of the alcohol group and the oxygen of the carbonyl group with the samarium(III) center generates a six-membered ring, in which the ability of the hydroxyl group to act as a leaving group is enhanced. An elimination reaction in which the intermediate generates the (*E*)-α,β-unsaturated ketones takes place, and this process is continually repeated by the Sm(III) which is generated *in situ* by reaction of the remaining SmI_2 with the I_2 or ClI.

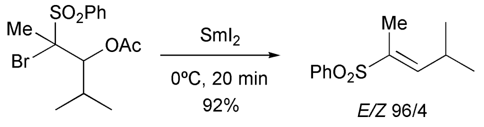
In the *syn* diastereoisomer a substitution of the chlorine atom by iodide (from SmI_3 dissociation) takes place, leading to the *anti* diastereoisomer. Thus the (*E*)-α,β-unsaturated ketones are provided through the same mechanism explained in Scheme 22.



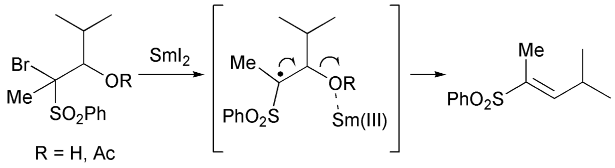
Scheme 22

3.1.6 Synthesis of α,β-unsaturated sulfones.

Similarly, Reutrakul *et al.* developed a method for the synthesis of α,β-unsaturated sulfones by using SmI_2.[28] The reaction of α-halo-β-hydroxy or acetoxy phenylsulfones with SmI_2 at 0 °C afforded unsaturated sulfones in good yields and between moderate and good *E*/*Z* ratios (Scheme 23).



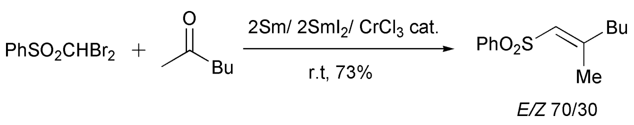
Scheme 23



Scheme 24

When the reaction was carried out using the acetylated starting compounds, and in the absence of co-solvents, better diastereoselectivities and yields were observed. The final products were explained through a radical mechanism in which the proposed radical intermediate undergoes an elimination in order to afford the thermodynamically more stable olefin.

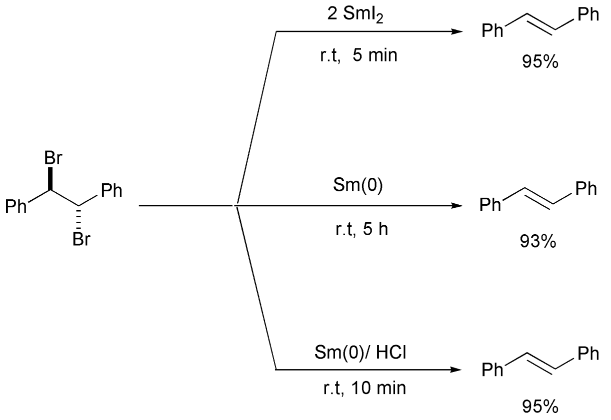
α,β-Unsaturated sulfones have also been synthesised by a sequential reaction from ketones and *gem*-dibromomethyl sulfones by using a $Sm/SmI_2/CrCl_3$ system (Scheme 25).[29] The first stage of the reaction is a synthesis, *in situ*, of the α-halo-β-hydroxy arylsulfones through a sequenced metalation and addition to the carbonyl group. Subsequent elimination from the halogenated sulfone afforded the α,β-unsaturated sulfone.



Scheme 25

3.2 Metalation of 1,2-dihalogenated compounds

SmI_2-promoted elimination reactions occur in other *vicinal* systems such as *vic*-dihalides. Yanada *et al.* published a comparative study of the reductive debromination of *vic*-dibromides to the corresponding alkenes by using, SmI_2, Sm(0), or Sm(0)/HCl (Scheme 26).[30]



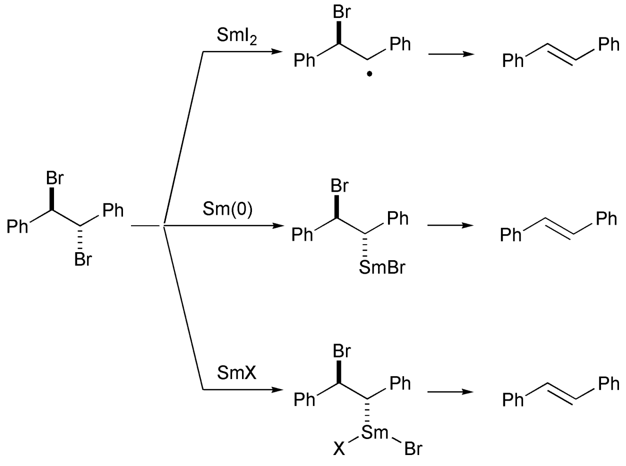
Scheme 26

Similar behaviour was observed when the reaction was carried out by using 2 eq. of SmI_2 or 1 eq. of Sm(0). In most cases, the yields were very similar but the reaction times were much longer when metallic samarium was used. However, the debromination with Sm(0) was accelerated when catalytic amounts of acid were used and, again, 1 eq. of metallic samarium was necessary to perform the reaction.

Different mechanisms have been proposed in each reaction (Scheme 27). Thus, when the reaction is carried out by using SmI_2, a radical or anionic mechanism is taken into account. In the case of Sm(0), an oxidative addition in the C–Br bond is proposed and, when a mixture of Sm(0) and HCl cat. is employed, monovalent samarium species might be produced at the first stage, and after a SmX-insertion in the C–halogen bond the final olefin is obtained.

3.3 Halogen metalation and C–C cleavage

Samarium diiodide has also been used to perform cyclic fragmentations in which a C–C bond is broken. In this sense, SmI_2 complements other methodologies previously described. Thus, in the scheme shown below it is possible to see a different behaviour when the fragmentation reaction is promoted by SmI_2 or NaHTe.[31]

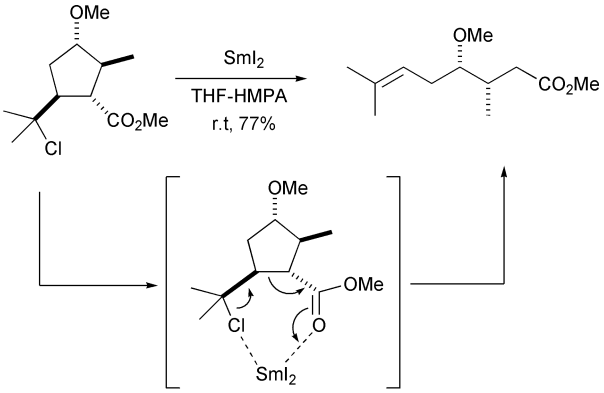


Scheme 27

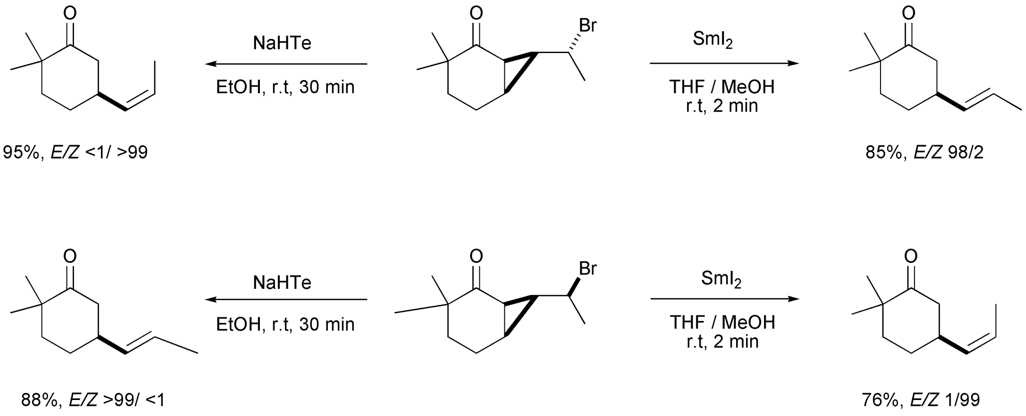
This fragmentation process was also carried out in the same model substrate by using other reducing agents such as Li/NH_3, Zn/AcOH, Cr^{II}, Bu_3SnH/AIBN, and mixtures of the (*E*)- and (*Z*)-olefins were isolated. A clear mechanism that could explain the SmI_2-mediated process has not been addressed by the authors, and different mechanistic proposals have been taken into account.

These elimination–cyclic opening processes have been widely used during the synthesis of some natural products. The reductive fragmentation of γ-halocarbonyl esters has been applied in the course of the enantiospecific synthesis of several natural products such us (−)-oudemansin A, (+)-eldanolide, and (−)-*cis*-whisky lactone.[32]

The authors proposed a mechanism based in an interaction between samarium diiodide with both the halogen atom and the carbonyl functional group (Scheme 29). This interaction



Scheme 29



Scheme 28

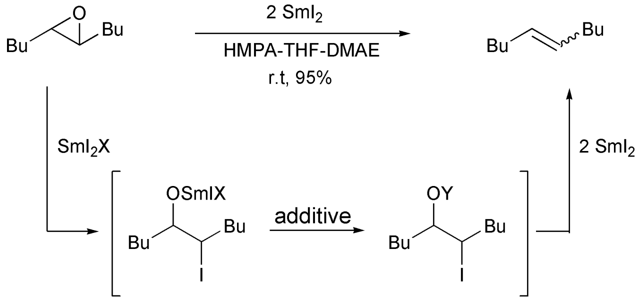
forms a seven-membered transition state, in which a concerted fragmentation leads the corresponding acyclic alkene.

4 Metalation of oxygenated functions

This section covers a wide number of examples in which the metalation takes place in an oxygenated function. This is one of the main advantages of samarium diiodide in comparison with the majority of alternatives, where this possibility does not exist.

4.1 Deoxygenation reactions of epoxides

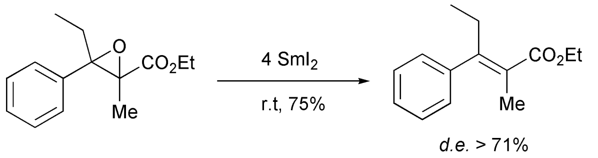
4.1.1 Synthesis of alkenes. Deoxygenation reactions of epoxides have also been carried out by SmI_2–HMPA in the presence of different additives, and the corresponding olefins, were obtained as a mixture of isomers (Scheme 30).[21]



Scheme 30

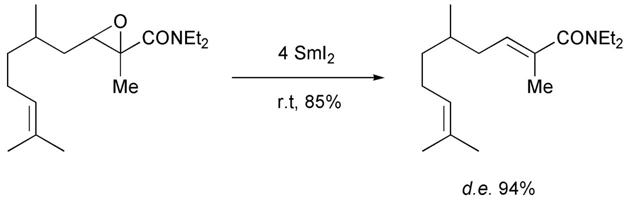
The authors proposed a mechanism based in a oxirane ring opening by a catalytic amount of Sm^{3+}. The alkoxide anion generated is transformed into a better leaving group due to the presence of additives (Y). A two electron process promoted by samarium diiodide affords the olefins through a reductive elimination.

4.1.2 Preparation of *α,β*-unsaturated esters or amides. Deoxygenation reactions were carried out in *α,β*-epoxyesters developing a methodology to synthesise (*E*)-*α,β*-unsaturated esters in which the C–C double bond is di-, tri-, or tetra-substituted, with total or high diastereoselectivity (Scheme 31).[33]

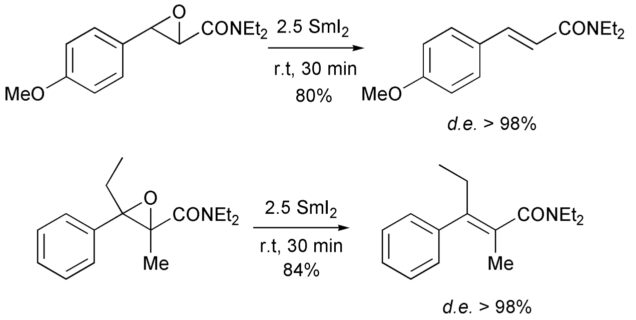


Scheme 31

In this case, the mechanistic proposal is based on the ability of samarium diiodide to reduce α-heterosubstituted carbonyl compounds. Thus, after the C_α–O reduction, a samarium-enolate is formed (Scheme 32). A chelation between the second oxygen atom and the samarium(III), generates a six-membered ring transition state responsible for the high diastereoselectivity observed in the elimination reaction.



Scheme 33



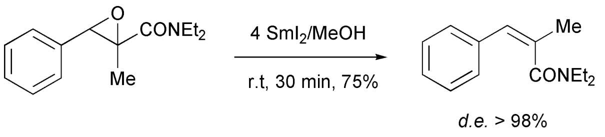
Scheme 34

An extension of this reaction has been use in the synthesis of *α,β*-unsaturated amides. Nevertheless, the reaction conditions and the proposed mechanisms to obtain aliphatic or aromatic *α,β*-unsaturated amides were different.[34]

The elimination reaction of aliphatic *α,β*-epoxyamides was carried out with SmI_2 in the presence of HMPA, and the corresponding (*E*)-*α,β*-unsaturated amides were obtained in good yields, with high diastereoselectivity. The formation of the products obtained is explained using a similar model illustrated in Scheme 32.

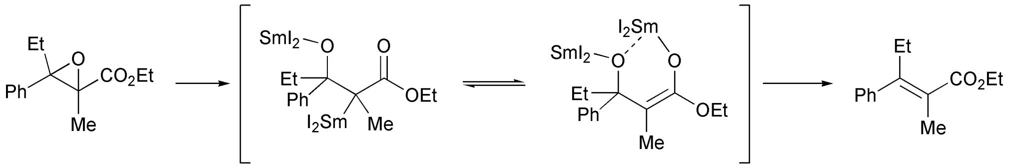
In the case of aromatic epoxyamides, (*E*)- or (*Z*)-*α,β*-unsaturated amides were obtained depending on the substitution in the epoxide. Hence when di- or tetra-substituted epoxyamides were used as starting materials, a (*E*)-diastereoselection was observed in the elimination process.

On the contrary, when trisubstituted starting products were used, the reaction afforded (*Z*)-*α,β*-unsaturated amides in high yields and very high diastereoselectivities (Scheme 35).

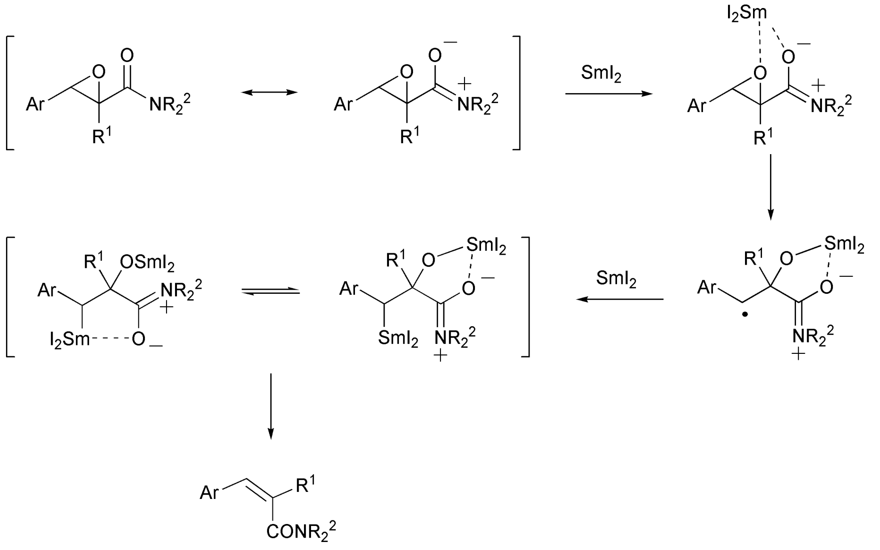


Scheme 35

The different reactivity of di-/tetra- *vs.* tri-substituted epoxides can be rationalised by the following mechanistic proposal. It is assumed that initially samarium forms a double coordination with both oxygen atoms (Scheme 36). This chelation of samarium with the oxirane ring is more favoured in amides rather than esters due to the electron-donating capacity of the nitrogen, producing a similar effect of a Lewis acid. Thus, opening the oxirane ring by reduction of the C_β–O bond (in opposition to the *α,β*-epoxyesters), affords a benzylic radical.



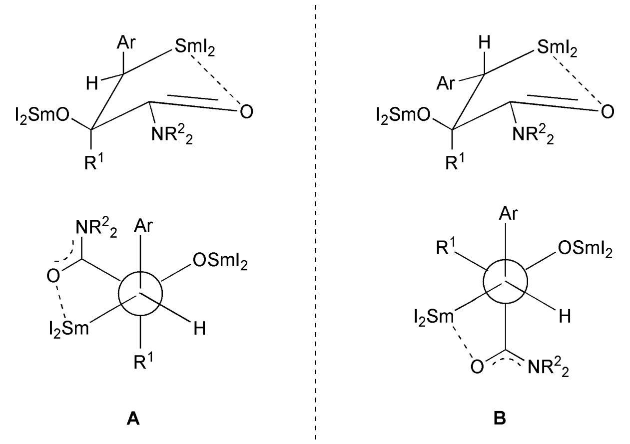
Scheme 32



Scheme 36

A second electron transfer, from another equivalent of samarium diiodide, generates the anion, which suffers a 1,2-elimination affording the unsaturated compounds.

Both diastereoselectivities are explained based on the transition state models (Scheme 37). So, *anti* elimination processes in transition states **A** and **B** are suitable. In the case of (*Z*)-unsaturated compounds, the transition state **A** is preferred due to lower steric clash between the Ar group and R^1. Here, no 1,3-diaxial interactions involving the Ar group are present in either cyclic transition state. When the elimination is carried out in di- or tetra-substituted epoxyamides, the transition state **B** is preferred because the Ar group takes an equatorial orientation. Elimination from **B** would generate di- or tetra-substituted (*E*)-α,β-unsaturated amides.

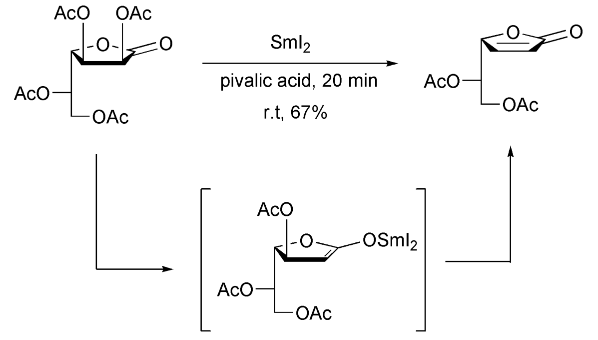


Scheme 37

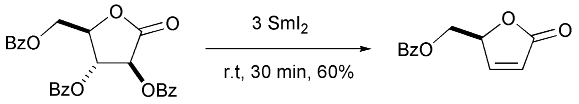
4.2 Reduction of *O*-acylated 2-hydroxylactones

1,2-elimination has been observed in *vicinal* systems, thus, α,β-unsaturated lactones were obtained (Scheme 38) when *O*-acetylsugar lactones were subjected to reduction conditions, achieving the aim of SmI_2-promoted deacetoxylation.[35]

According to the authors, the reaction seems to proceed through the formation of a lactone enolate followed by elimination of the 3-acetoxy group. Analogously, Hanessian *et al.* founded similar elimination reactions in perbenzoylated aldonolactones,[36] in this example, unsaturated lactones were formed in average yields (Scheme 39).



Scheme 38

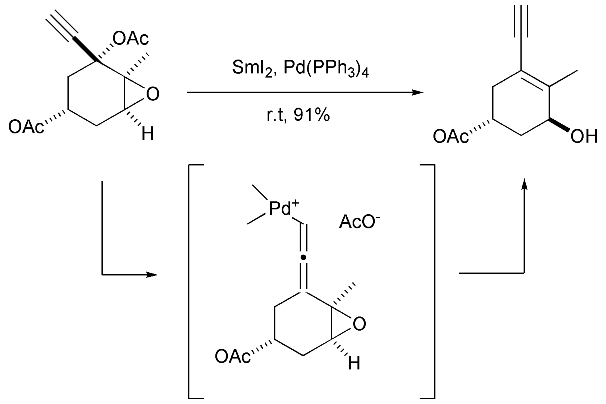


Scheme 39

5 Elimination reactions in the presence of other metals

5.1 Starting from *O*-acetylated propargyl alcohols

Ring opening of oxiranes have been used during the synthesis of vitamin D analogues.[37] Here samarium diiodide serves as stoichiometric reductant in the palladium(0)-catalysed reduction of propargyl acetates (Scheme 40).



Scheme 40

The reductive elimination was effected using a method previously described for the conversion of propargyl acetates into allenes.[38] The authors used modified conditions and without a proton source.[37] With these conditions, a palladium-catalysed samarium diiodide mediated displacement of the propargyl acetate, generates an allenylpalladium intermediate which undergoes the reduction and the ring opening of the epoxide to give the corresponding enynol.[37]

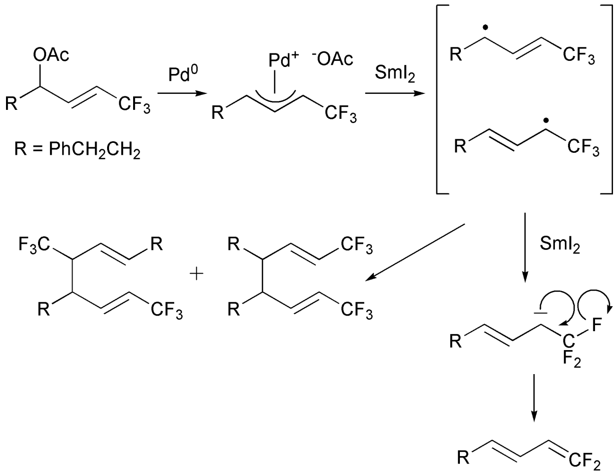
5.2 Starting from *O*-acetylated allylic alcohols

Taguchi *et al.* observed different behaviour in the reaction pathway when using trifluoromethylated allylic alcohol derivatives.[39] In this instance the elimination reaction takes place through an electronic inversion of a π-allylic palladium complex promoted by samarium diiodide (Scheme 41).

Thus, at the first stage of the reaction, a π-allylic palladium complex is generated and is transformed, partially, into the corresponding difluorodiene through the formation of an allylic anion species followed by the β-elimination of a fluoride ion. The formation of dimerization products is observed, presumably by the coupling of the radical intermediates before the second samarium-promoted electron transfer (Scheme 42).

6 Sequential processes

As was indicated in the introduction, samarium diiodide exhibits excellent properties for sequential organic reactions.

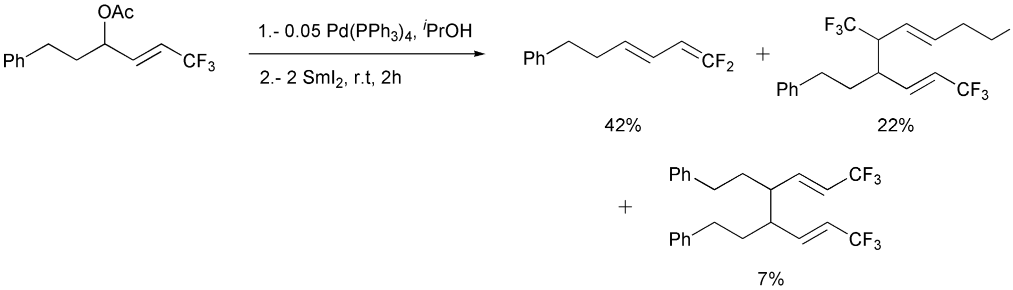


Scheme 42

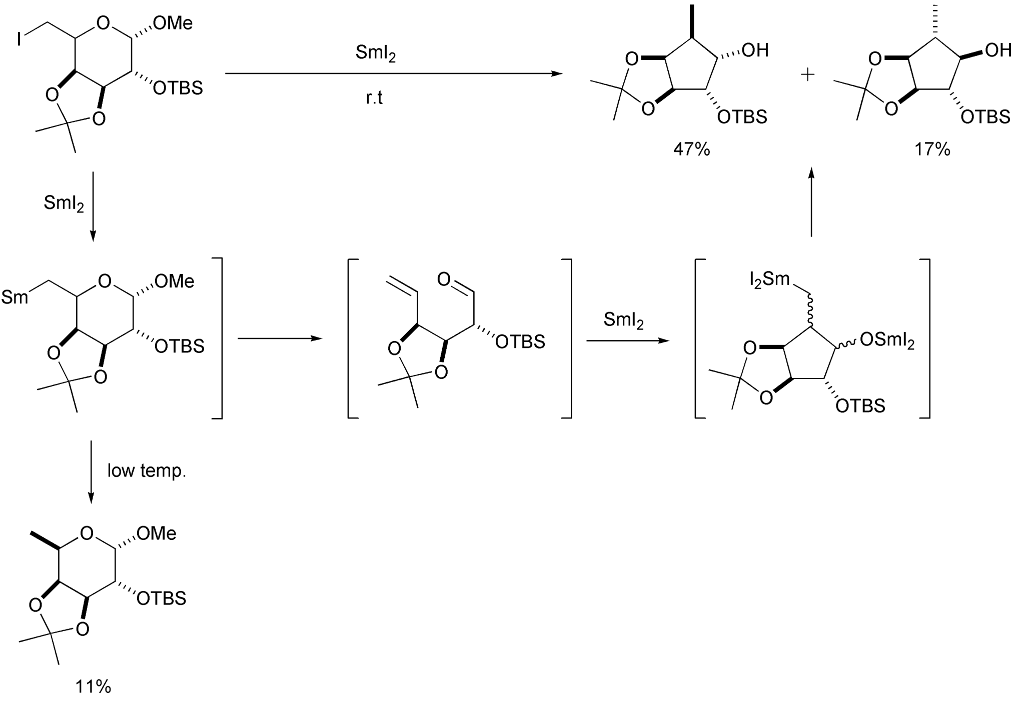
Several examples have been described in which an elimination reaction occurs as a step of a sequential process.

6.1 Elimination–cyclization reactions

Cascade reactions take place in 6-deoxy-6-iodohexopyranosides and lead to a ring contraction of the pyranoside moiety.[40] The sequence described by Chiara *et. al* suggests a four-step process in which the first consists of a reductive



Scheme 41

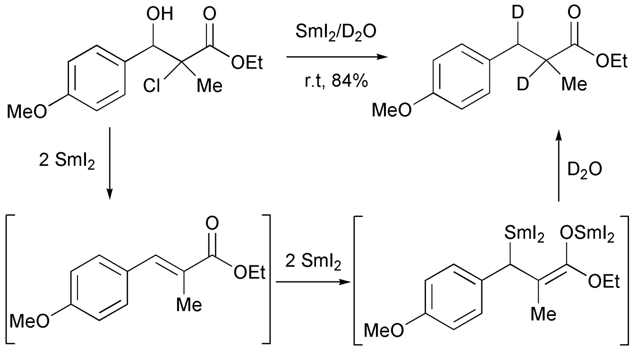


Scheme 43

dealkoxydehalogenation. Further steps generate the corresponding five membered rings with other by-products.

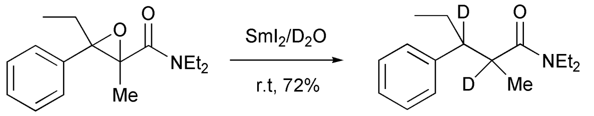
6.2 Elimination–reduction reactions

Sequential elimination–reduction reactions have been employed to synthesise 2,3-deuterioesters or amides employing different methodologies starting from α-halo-β-hydroxyesters or amides, or from α,β-epoxyesters.[41] In the first case the initial step is the same as shown in Scheme 20,[25,26] and α,β-unsaturated esters or amides are generated. Thereafter, SmI_2-promoted 1,4-reduction of the obtained unsaturated compound is initiated by oxidative addition of the reagent to generate the enolate radical, which after a second electron transfer and hydrolysis with D_2O affords the corresponding dideuterio compounds (Scheme 44).



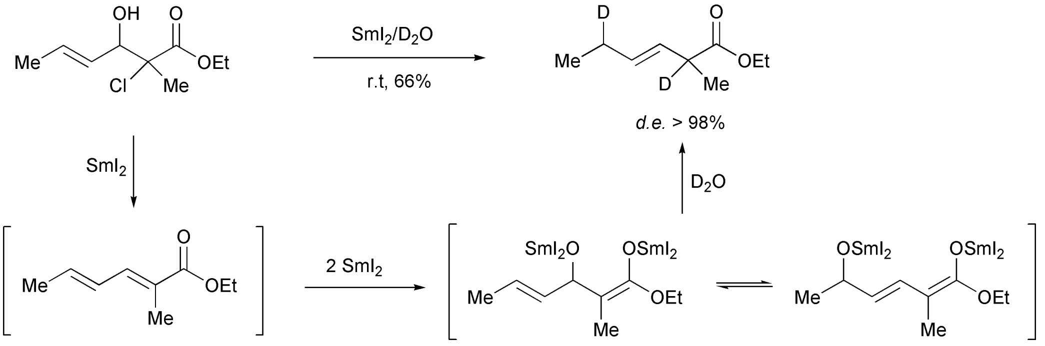
Scheme 44

Similarly, when the reaction is carried out in α,β-epoxyesters or amides the first step is an elimination, as depicted in Scheme 32, generating *in situ* the corresponding α,β-unsaturated esters or amides. These compounds are reduced to the dideuterio compounds such as has been indicated in the previous scheme. When H_2O is used instead of D_2O, saturated compounds are obtained (Scheme 45).

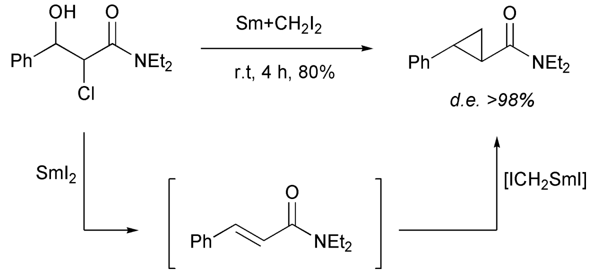


Scheme 45

The same sequential reaction has been used to obtain isotopically labelled (*E*)-β,γ-unsaturated esters.[42] When starting materials were α-halo-β-hydroxy-γ,δ-unsaturated esters, dienes were generated *in situ*, and the subsequent samarium diiodide-promoted 1,4-reduction afforded (*E*)-α,δ-dideuterio-β,γ-unsaturated esters, or (*E*)-β,γ-unsaturated esters when D_2O or H_2O are used respectively (Scheme 46).



Scheme 46



Scheme 47

6.3 Elimination–cyclopropanation reactions

Finally, based on the samarium promoted cyclopropanation reaction of α,β-unsaturated amides sequential elimination–cyclopropanation protocol has recently been developed.[43] Thus, in the first step, starting from α-chloro-β-hydroxyamides, the corresponding α,β-unsaturated amides[26] were generated through a reductive elimination reaction promoted by *in situ* generated SmI_2. In the second step a cyclopropanation reaction is promoted by a samarium carbenoid. Di-, tri-, and tetra-substituted cyclopropylamides are given in high yields and in a diastereospecific manner.

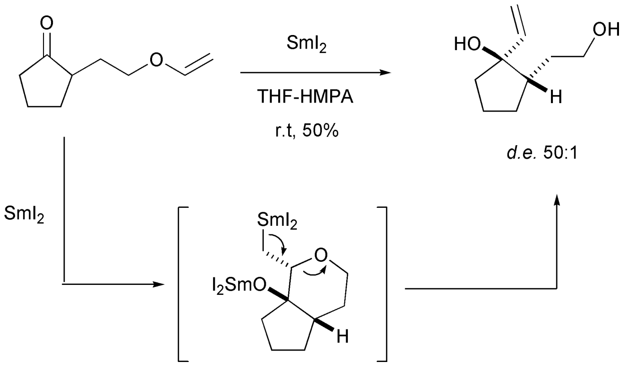
6.4 Sequential ketyl–olefin coupling/β-elimination reaction

A sequential intramolecular ketyl–olefin coupling/β-elimination reaction has been reported with the effective addition of alkenyl species to a ketone carbonyl.[44] This reaction is interesting and potentially very useful when compared to the nucleophilic addition of alkenylmagnesium halides or alkenyllithium to carbonyl compounds which are sometimes problematic for a variety of reasons including: a) preparation of the unsaturated organometallic species; b) organolithium compounds and Grignard derivatives can react as either nucleophiles or bases; and c) diastereoselectivity in the reaction of these organometallic compounds is often low. An alternative to the use of these reagents is this sequential samarium reaction (Scheme 48). It is noteworthy that a high level of diastereoselectivity is observed in this reaction.

This process is explained based on a radical ketyl–olefin coupling reaction, generating an exocyclic organosamarium species that undergoes a rapid β-elimination affording the final products.

7 Conclusions

In summary, samarium diiodide has become an important and useful reagent for the generation of C–C double bonds, in most cases with a high level control of the diastereoselectivity. The interest in samarium diiodide-promoted eliminations has grown in the last two decades due to its higher yielding reactions, which exhibit good stereoselectivities when



Scheme 48

compared with classic methods for C=C generation. Due to its relative infancy in such systems, further work will yield fruitful and rewarding results when dealing with SmI_2.

Acknowledgements

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