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Tetrahedron Letters 44 (2003) 2661–2664

TETRAHEDRON
LETTERS

Selective reduction of carbon–carbon double and triple bonds in conjugated olefins mediated by SmI_2/H_2O/amine in THF

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Received 18 December 2002; revised 28 January 2003; accepted 7 February 2003

Abstract—Conjugated double and triple bonds are reduced into alkenes using non-hazardous SmI_2/H_2O/amine mixtures as reducing agents in THF. Isolated alkenes are not reduced during these reductions. All the reactions studied are quantitative and are completed in less than five minutes. © 2003 Elsevier Science Ltd. All rights reserved.

Recently there has been a rapid development of SmI_2-mediated transformations.[1] SmI_2 has become a versatile and selective reagent that mediates a number of different reduction and coupling reactions.[2] Recently we reported that a mixture of H_2O/amine as co-solvent strongly accelerates the rate of reduction of ketones, α,β-unsaturated esters and imines promoted by SmI_2.[3] Encouraged by the large acceleration of these reactions, we explored the use of SmI_2 in other reduction reactions. SmI_2/H_2O/amine[3] or SmI_2/HMPA[4] mixtures readily reduce α,β-unsaturated esters, but to the best of our knowledge, SmI_2 has so far proved to be too weak a reductant for conjugated olefins.

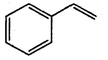
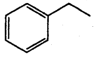
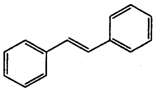
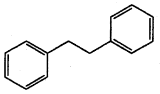
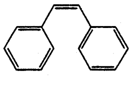
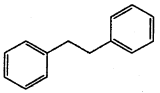
In our exploration of SmI_2/H_2O/amine mixtures in the reduction of various functional groups we have discovered that conjugated olefins can be selectively reduced in the presence of isolated double bonds. Herein we present the use of SmI_2/H_2O/amine mixtures in THF, using either of the amines Et_3N, *N*,*N*,*N′*,*N′*-tetramethylethylene diamine (TMEDA) or *N*,*N*,*N′*,*N″*,*N″*-pentamethylethylene triamine (PMDTA), for the reduction of conjugated olefins.

As we demonstrated in our earlier studies, the facile SmI_2/H_2O/amine mediated reduction of ketones can be understood from the equation described below. We believe that this equation also applies for conjugated olefins.

$$\mathbf{R_2C{=}O + 2\,SmI_2 + 6\,H_2O + 4\,R_3N \rightleftharpoons R_2CHOH + 2\,Sm(OH)_3 + 4\,R_3N{\cdot}HI}$$

Styrene is almost immediately reduced to ethyl benzene in quantitative yield in the presence of SmI_2/H_2O/amine (Table 1), leaving a white precipitate of samarium- and amine-salts. There is no reduction of the phenyl group. The terminal double bonds of styrene are conjugated with the aromatic ring and hence more reactive, therefore it was not surprising that both *cis*- and *trans*-stilbene were reduced to the corresponding saturated compound, dibenzyl.

Table 1. Reduction of styrene derivatives by SmI_2/H_2O/PMDTA

Entry	Alkene	Product	Time / min	Yield / %
1			5	> 99
2			< 1	> 99
3			2	> 99

The transfer of two deuteriums from D_2O to the double bonds of styrene and stilbene was also confirmed by GC/MS. Measurement of the initial rates of the reduction of styrene with SmI_2/H_2O/amine and SmI_2/D_2O/amine, respectively, showed no difference in rates, i.e. there was no primary kinetic isotope effect ($k_H/k_D = 1$). This indicates that the proton transfer is not involved in the rate-determining step; therefore the formation of a conjugated radical or anion is most likely the rate-determining step.

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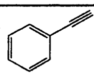
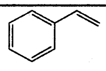
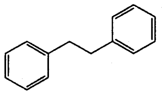
0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)00369-1

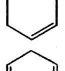
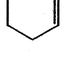
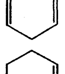
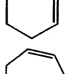
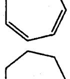
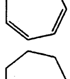
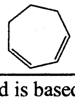
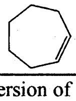
Addition of phenylacetylene to the SmI_2/H_2O/amine mixture resulted in rapid reduction of the triple bond to styrene in ten seconds. Styrene was then further reduced into ethyl benzene within 5 min, provided that an excess of SmI_2/H_2O/amine was used (Table 2). Likewise was diphenylacetylene readily reduced into dibenzyl via stilbene. It should be noted that approximately 2.5 equiv. of SmI_2 is necessary to ensure complete reduction of each conjugated bond.

Table 2. Reduction of phenylacetylene derivatives by SmI_2/H_2O/PMDTA

Entry	Alkyne	Product	Time / min	Yield / %
1			< 0.2	> 99
2			5	> 99

These unsaturated systems are all conjugated with an aromatic ring, but SmI_2/H_2O/amine mixtures are also capable of reducing conjugated dienes and trienes (Table 3). The conjugated diene 1,3-cyclohexadiene was rapidly reduced into cyclohexene with SmI_2/H_2O/amine, but not further reduced into cyclohexane. It appears that the double bonds must be conjugated, otherwise there is no reduction, i.e. 1,4-cyclohexadiene does not undergo reduction with SmI_2/H_2O/amine. Another conjugated cyclic alkene, 1,3,5-cycloheptatriene, with three conjugated double bonds was also reduced to the corresponding cycloalkene. After 10 s in a SmI_2/H_2O/amine mixture at room temperature all the cycloheptatriene was reduced into 1,3-cycloheptadiene and smaller amounts of cycloheptene. The only detected product was cycloheptene after approximately five minutes. Hence it is possible to reduce this triene into the corresponding diene, if desired, or all the way to the corresponding alkene.

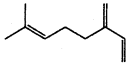
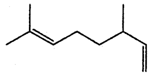
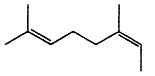
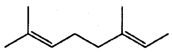
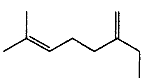
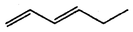
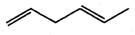
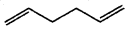
Table 3. Reduction of cyclic alkene derivatives by SmI_2/H_2O/PMDTA

Entry	Alkene	Product	Time / min	Yield / %
1			5	> 99
2		No reaction	3000	-
3		No reaction	3000	-
4			< 0.2	> 99^{a}
5			5	> 99

[a] The yield is based on the conversion of cycloheptatriene.

A different triene is myrcene, which has two of its double bonds conjugated while the third is isolated (Table 4, entry 1). Reduction of myrcene with SmI_2/H_2O/amine gives a mixture of four compounds according to GC/MS analysis. The masses (m/z) of these compounds are identical ($M^+ = 138$) corresponding to the reduction of one conjugated double bond in myrcene. The formation of four products indicates that the reaction is not concerted, and the reaction must proceed via several competing intermediates. A tentative assignment of the four signals in the chromatogram was made based on fragmentation patterns and fitted to a database (NIST)[5] after EI ionization. This assignment was also supported by GC analysis on achiral and chiral columns.[6] The *E* and *Z* isomers have approximately the same retention times. One of the alkenes exists as a racemate, which was resolved using chiral GC (Table 4, entry 1a). Analysis of the product composition indicated that the reduction of the terminal double bond is slightly favored (56%). Interestingly, both the *E* and the *Z* stereoisomers were formed in equal quantities. The product composition shows that the reductions may occur via both 1,2- and 1,4-addition to the diene and, yet again, the isolated double bond was not affected.

Table 4. Reduction of alkene derivatives by $SmI_2/H_2O/Et_3N^a$

Entry	Alkene	Product	Time / min	Yield / %
1		 a	2	20
		 b		12
		 c		12
		 d		56
2		 a	5	~ 20
		 b		~ 40
		 c		~ 40
3		No reaction	3000	-
4		No reaction	3000	-

[a] The product composition varied slightly going from Et_3N to TMEDA or PMDTA.

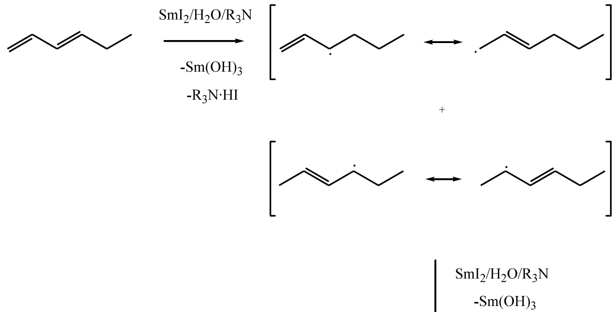
To confirm the importance of conjugation a mixture of *cis*- and *trans*-1,3-hexadiene was also reduced to a mixture of 1-hexene, *cis*- and *trans*-2-hexene and *cis*-

and *trans*-3-hexene (Table 4, entry 2). We could not resolve completely these isomers on GC, however it is clear that the formation of 2- and 3-hexene were favored over 1-hexene. None of these alkenes was further reduced to hexane with SmI_2/H_2O/amine. Furthermore, the unconjugated 1,4- and 1,5-hexadienes were not affected by the SmI_2/H_2O/amine mixtures (Table 4, entries 3 and 4).

Treatment of *cis*-stilbene with SmI_2 only for 24 h did not result in any isomerization to the more stable *trans*-isomer. Hence the reactions do not proceed via a preequilibrium between the alkene and an organosamarium intermediate, since such an intermediate would be expected to isomerize to some extent. The addition of SmI_2 to the conjugated double bond requires both water and an amine.

A mechanism for the reduction of conjugated double and triple bonds is given in Scheme 1. The mixture SmI_2/H_2O/amine is suggested to generate an electron and a proton which, based on these observations, readily add to the conjugated alkene. The radical that is formed is stabilized by delocalization of the unpaired electron into the conjugated π-system. The reduction using SmI_2, being a single electron transfer reagent, must therefore proceed in two steps. The first involves the formation of π- or alkene-stabilized radical intermediates. We suggest that this first step in the reduction reaction proceeds via either a 1,2- or 1,4-addition mechanism. The observation of both the 1,2- and 1,4-reduction products is also explained by equilibrium between two pairs of resonance-stabilized radicals. The driving force in these reduction reactions appears to be the precipitation of $Sm(OH)_3$ and $R_3N{\cdot}HI$.[3] The radical intermediate reacts with a second electron and proton from SmI_2 and water to generate the alkene. In order to operate by this mechanism only conjugated olefins or olefins with aromatic groups can be reduced.

All the reduction reactions reported proceed with any of the tested amines, i.e. triethylamine, TMEDA or PMDTA. However, there is a slightly higher rate of reduction using PMDTA. In the absence of either water or amine none of the reported SmI_2-mediated reductions of any of the alkenes could be observed.



Scheme 1. Suggested mechanism for the reduction of 1,3-hexadiene.

In conclusion, the present development of SmI_2/H_2O/amine mixtures for the selective reduction of conjugated carbon–carbon double bonds is very promising. But a disadvantage is the formation of mixtures of products, which will be obtained from unsymmetrical substrates, such as myrcene. However, this method of reducing double bonds does not require any pyrophoric catalysts,[7] H_2-gas[8] or alkali metal (Li or Na),[9,10] and the reagent mixture SmI_2/H_2O/amine is considered non-hazardous. In addition the reductions are fast and performed under 1 atm at room temperature. Furthermore, the use of H_2O as the hydrogen source allows a simple and inexpensive way for incorporating deuterium from D_2O. High selectivity is a major advantage in SmI_2 reactions, however, the SmI_2/H_2O/amine mixture may prove too powerful for selective reactions involving multifunctional substrates, and this has yet to be determined.

Experimental

The SmI_2 solutions were purchased from Aldrich (0.1 M SmI_2 in THF). All substances, including starting materials and products, were purchased from commercial resources. The products of reduced myrcene were not available; therefore a tentative assignment of these products was carried out based on GC/MS, the NIST Mass Spectral Database, and chiral GC analysis. Verification of the retention times of the products with authentic samples along with GC/MS analysis identified all other products. The non-volatile compounds were also identified using ^{1}H NMR.

General procedure for the reduction of a conjugated double and/or triple bond: SmI_2 in THF (0.1 M, Aldrich, 2.5 equiv.) was added to a dry Schlenk tube, fitted with a septum and containing a magnetic stirrer bar, inside a glove box with a nitrogen atmosphere. The amine, i.e. Et_3N (5 equiv.), TMEDA (2.5 equiv.) or PMDTA (1.7 equiv.), and the alkene (1 equiv.) were added at 20°C. The proton donor, i.e. H_2O (6.25 equiv.), was added dropwise using a gastight syringe. Small portions of the mixture (100 μL) were removed via a syringe and quenched with I_2 in *n*-hexane (0.1 M, 0.1 mL). To the quenched solution diethyl ether (1 mL) and HCl (0.12 M, 0.1 mL) were added to dissolve the inorganic salts and finally $Na_2S_2O_3$ to remove excess iodine. The organic layer was transferred to a vial and the yield of the reaction was analyzed with GC. All products were analyzed by GC/MS and also compared with authentic samples by GC.

The rate measurements of the primary kinetic isotope effect of styrene (1 equiv.) were performed using SmI_2 in THF (0.1 M, 7 equiv.), Et_3N (14 equiv.) and H_2O or D_2O (35 equiv.). Samples from the reaction mixture were quenched every ten seconds, work-up was then carried out as described above, and the yield was determined by GC.

All reported yields are based on GC analysis; however, performing reductions on a larger scale showed that the isolated yields are also nearly quantitative. Reactions on larger scale may be purified by dissolving the inorganic samarium-salts and precipitated amines in HCl (0.1 M), extracting the water layer with diethyl ether and finally washing the ether layer with $Na_2S_2O_3$ and brine. The ether layer is then dried over Na_2SO_4 and, after evaporation, the product was sufficiently pure for further use.

A faster and more convenient work-up procedure for isolation of the crude product is centrifugation of the precipitated salts followed by evaporation of THF.

Acknowledgements

The authors would like to thank Dr. Anna Börje for a sample of myrcene. Financial support from the Carl Trygger foundation and the Swedish Natural Research Council (VR) is also gratefully acknowledged.

References

1. (a) Molander, G. A. In *Organic Reactions*; Paquette, L. A., et al., Eds.; John Wiley & Sons 1994; Vol. 46 (Reductions with Samarium(II) Iodide), pp. 211–367; (b) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745–777; (c) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338; (d) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29–68; (e) Nomura, R.; Endo, T. *Chem. Eur. J.* **1998**, *4*, 1605–1610; (f) Kim, S. M.; Byun, S., II; Kim, Y. H. *Angew Chem.* **2000**, *39*, 728–731; (g) Nakamura, Y.; Takeuchi, S.; Ohira, A.; Ohgo, Y. *Tetrahedron Lett.* **1996**, *37*, 2805–2808; (h) Takeuchi, S.; Nakamura, Y.; Ohgo, Y.; Curran, D. P. *Tetrahedron Lett.* **1998**, *39*, 8691–8694; (i) Pedersen, L. H.; Christensen, T. B.; Enemaerke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Eur. J. Org. Chem.* **1999**, *3*, 565–572; (j) Steel, P. S. *J. Chem. Soc., Perkin Trans. 1* **2001**, *21*, 2727–2751.
2. (a) Molander, G. A.; Etter, J. B. *Synth. Commun.* **1987**, *17*, 901–912; (b) Huang, Z.; Jin, H.; Duan, D. *Synth. Commun.* **2002**, *32*, 565–570; (c) Namy, J. L.; Souppe, J.; Kagan, H. B. *Tetrahedron Lett.* **1983**, *24*, 765–766; (d) Miller, R. S.; Sealy, M. S.; Shabangi, M.; Kuhlman, M. L.; Fuchs, J. R.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2000**, *122*, 7718–7722; (e) Taniguchi, N.; Uemura, M. *J. Am. Chem. Soc.* **2000**, *122*, 8301–8302; (f) Kito, M.; Sakai, T.; Haruta, N.; Shirahama, H.; Matsuda, F. *Synlett* **1996**, *11*, 1057–1060; (g) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059–4071.
3. (a) Dahlén, A.; Hilmersson, G. *Tetrahedron Lett.* **2002**, *43*, 7197–7200; (b) Dahlén, A.; Hilmersson, G. *Chem. Eur. J.* **2003**, in press.
4. (a) Inanaga, J.; Sakai, S.; Handa, Y.; Yamaguchi, M.; Yokoyama, Y. *Chem. Lett.* **1991**, *12*, 2117–2118; (b) Lin, T.-Y.; Fuh, M.-R.; Chan, I. S. *J. Chin. Chem. Soc.* **2001**, *48*, 843–847; (c) Cabrera, A.; Alper, H. *Tetrahedron Lett.* **1992**, *33*, 5007–5008.
5. NIST Mass Spectral Search Program, *Microsoft Corporation*®.
6. GC–MS column: CP-Sil 8 CB Low Bleed column (∅ = 0.25 mm, length = 30 m), Achiral GC column: CPWAX 52CB column (∅ = 0.25 mm, length = 25 m), Chiral GC column: CP Chirasil-Dex CB column (∅ = 0.25 mm, length = 25 m).
7. Pyrophoric catalyst e.g. $LiAlH_4$: Magoon, E. F.; Slaugh, L. H. *Tetrahedron* **1967**, *23*, 4509–4515, or Lindlar's catalyst: Lindlar, H.; Dubuis, R. *Org. Synth.* **1973**, *V*, 880.
8. H_2, Pt: Siegel, S.; Smith, G. V. *J. Am. Chem. Soc.* **1960**, *82*, 6082–6087.
9. Alkali metal (Li or Na), e.g.: Caine, D.; Chao, S. T.; Smith, H. A. *Org. Synth.* **1977**, *56*, 52–58.
10. General references for reduction of various functional groups: *Catalytic Hydrogenation in Organic Synthesis: Procedures and Commentary*; John Wiley & Sons, New York, 1978; Nylander, P. N. *Hydrogenation Methods*, Academic Press: Orlando, FL, 1985.