Tetrahedron Vol. 46, No. 2, pp. 587-594, 1990

A Fast Procedure for the Reduction of Azides and Nitro Compounds Based on the Reducing Ability of $Sn(SR)_3^-$ Species

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Abstract. Tin(II) complexes prepared by treatment of $SnCl_2$ or $Sn(SR)_2$ with appropriate amounts of RSH and Et_3N appear to be the best reducing agents for azides (to amines) reported so far. These tin(II) complexes also reduce primary and secondary aliphatic nitro compounds to oximes, usually within minutes at r.t. or hours in cold, and tertiary aliphatic as well as aromatic nitro compounds to afford the corresponding hydroxylamines. In general, azides react more rapidly than nitro substituents, whereas carbonyl groups, sulphoxides, sulphones, nitriles, and esters are practically unreactive under the same conditions. Some mechanistic details of the reaction of $Sn(SPh)_3^-$ with azides and nitro compounds have also been elucidated.

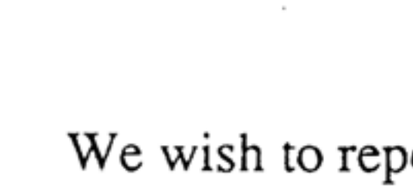
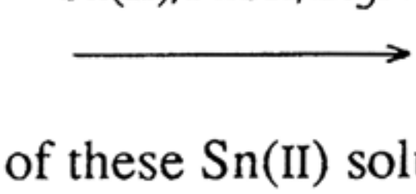
When the insoluble tin(II) benzenethiolate [$Sn(SPh)_2$, easily prepared either from SnO and PhSH in refluxing toluene in a Dean-Stark apparatus,[1] or by precipitation from $SnCl_2$ and sodium benzenethiolate in CH_3CN, EtOH, or H_2O] is treated with one equiv. of PhSH and Et_3N in most organic solvents, it affords yellow solutions which react almost instantaneously with azides to give amines and nitrogen.[2a] A similar reducing power is exhibited by solutions arising from $SnCl_2$ + 3 PhSH + 3 Et_3N (eq 1).[2b] As a matter of fact, most aliphatic and aromatic azides react completely, in less than 5 min at r.t., at 0.1 M reagent concentrations;[2a] treatment of the final mixtures with base and extraction, or filtration through a pad of basic alumina, affords pure amines in practically quantitative yields.

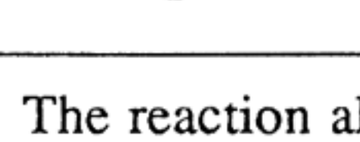
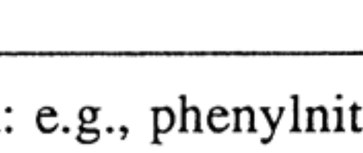
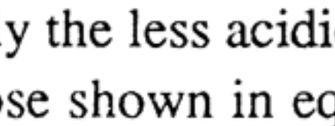
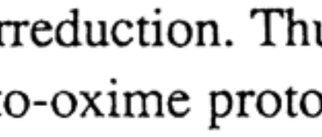
$$R\text{-}N_3 \xrightarrow{Sn(II)/PhSH/Et_3N} R\text{-}NH_2 \qquad (1)$$

We wish to report here on the reactivity of these Sn(II) solutions with nitro compounds, as well as on the nature, reducing ability, and chemoselectivity (vs. azides and nitro compounds) of related complexes. Since azides and nitro compounds are the most common and versatile precursors of other nitrogenated functional groups, we considered it useful to evaluate the scope of these new reducing agents.

Reduction of Primary and Secondary Nitroalkanes to Oximes

Treatment of primary and secondary nitroalkanes with 1.5 equiv. of the $Sn(SPh)_2$/PhSH/Et_3N mixture either in C_6H_6, CH_2Cl_2, THF, CH_3CN, or MeOH, or with 1.5 equiv. of the $SnCl_2$/3PhSH/3Et_3N in THF, CH_3CN, or MeOH, at r. t., readily gives oximes, often in excellent yields:

	nitro compd	solvent	r. time	product	yield	isomer	
1	$PhCH_2NO_2$	C_6H_6[a]	10 min	PhCH=NOH	98%[a]	*E*	[a]The yield is similar in THF, CH_2Cl_2, CH_3CN, and MeOH.
2		C_6H_6	10 min		95%	*E*	
3	$CH_3(CH_2)_3NO_2$	C_6H_6	3 h	$CH_3(CH_2)_2CH$=NOH	75%	*E*/*Z*, 1:1	
		CH_3CN	1 h		82%	*E*/*Z*, 1:1	
4	4-MeOPh$(CH_2)_2NO_2$	C_6H_6	30 min	4-MeOPhCH_2CH=NOH	74%[b]	*E*	[b]88% after 3 h.
		CH_3CN	30 min		93%	*E*/*Z*, 2:1	

5	$MeO_2C(CH_2)_{10}NO_2$	C_6H_6	3 h	$MeO_2C(CH_2)_9CH{=}NOH$	85%	*E* (major)	[c]Plus 23% of the hydroxylamine.
		CH_3CN	1 h		85%	*E*/*Z*, 1:1	
6		C_6H_6	10 min		87%	*E*	
7	$PhCHMeNO_2$	C_6H_6	10 min	PhC(Me)=NOH	60%[c]	*E*	[d]Plus ca. 30% of the hydroxylamine.
		CH_3CN	10 min		85%	*E*	
8		C_6H_6	12 h		35%[d]		
		CH_3CN[e]	6 h		70%[f]		[e]In MeOH, 60% yield after 6 h.
9	4-$MeOPhCH_2CHCH_3$ NO_2	C_6H_6	3 h	4-$MeOPhCH_2CCH_3$ NOH	30%[d]	*E*/*Z*, 3:1	
		CH_3CN	3 h		85%[f]	*E*/*Z*, 2.5:1	
10	CH_3-CH-CO_2Et NO_2	C_6H_6	10 min	CH_3-C-CO_2Et N-OH	100%	*Z*	[f]No hydroxylamine is obtained under these conditions

The reaction also takes places in cold: e.g., phenylnitromethane (entry 1), treated with 2 equiv. of the reducing mixture in CH_2Cl_2 at -20 °C, affords a 40% yield of benzaldehyde oxime after only 30 min and a 80% yield after 3 h; at -78 °C, a 40% reduction is already observed within 4 h.

Further reduction to hydroxylamines is only observed for secondary nitroalkanes in apolar solvents, as if only the less acidic substrates underwent overreduction. Thus, it can be assumed that the reactions involved are those shown in eq 2, where the fast nitroso-to-oxime prototropy may prevent the reduction of NO to NHOH. Indeed, the hydroxylamines obtained as byproducts in entries 7-9 must arise from the nitroso derivatives, since in independent experiments we have confirmed that oximes do not react with our reagent.

$$RR'CH\text{-}NO_2 \xrightarrow{Sn(II)/PhSH/Et_3N} [\,RR'CH\text{-}NO\,] \xrightarrow{Sn(II)/PhSH/Et_3N} RR'CH\text{-}NHOH \qquad (2)$$

$$[\,RR'CH\text{-}NO\,] \rightleftharpoons RR'C{=}NOH$$

Reduction of Tertiary Aliphatic and Aromatic Nitro Compounds to Hydroxylamines

Addition of 2.5 equiv. of $Sn(SPh)_2$/PhSH/Et_3N to tertiary and aromatic nitro compounds, in C_6H_6 at r.t., affords hydroxylamines within 10 min:

	nitro compd	product	yield
11	$PhCMe_2NO_2$	$PhCMe_2NHOH$	91%
12	$PhNO_2$	PhNHOH	81%
13	4-$MePhNO_2$	4-MePhNHOH	82%
14	4-$EtOPhNO_2$	4-EtOPhNHOH	76%
15	4-MeO_2CPhNO_2	4-$MeO_2CPhNHOH$	94%

Yields are generally better in C_6H_6 than in polar solvents like CH_3CN or MeOH, in which coloured byproducts have often been observed. Reduction also occurs in cold: e.g., methyl 4-nitrobenzoate (entry 15 is completely reduced in CH_2Cl_2 at -20 °C in 15 min and at -78 °C in ca. 2 h.

No further reduction to amine has been observed by enhancing the amount of the Sn complex, a fact that seems reasonable since the medium is not acidic. On the other hand, when only 1 equiv. is added, the final mixture only contains $ArNO_2$ and ArNHOH; i.e., in these cases, where the nitroso-to-oxime tautomerisation cannot occur, it is unlikely to stop the cascade reduction ($RNO_2 \rightarrow RNO \rightarrow RNHOH$) at the nitroso step, as the reduction of the NO group seems to be faster than that of the NO_2 group. Moreover, the reduction of the nitroso group is probably so rapid that the dimeric products (azoxy and azo compounds) have no chance.[3]

Thus, we now add to the arsenal of reducing agents an extremely reactive one that stops the reduction at the oxime or hydroxylamine steps.

Nature of the Reducing Agent

The chemical ionization mass spectra (negative ions) of the concentrates arising from Sn(II)/PhSH/Et_3N, Sn(II)/Bu^tSH/Et_3N, Sn(II)/$HSCH_2CH_2SH$/Et_3N, and Sn(II)/PhSeH/Et_3N show as the base peaks those corresponding to the $^{120}Sn(SPh)_3^-$, $^{120}Sn(SBu^t)_3^-$, $[^{120}Sn(SCH_2)_2(SCH_2CH_2SH)]^-$, and $^{120}Sn(SePh)_3^-$ species, in the expected isotopic ratio (bearing in mind the tin isotope distribution, from ^{116}Sn to ^{124}Sn).[4] The ^1H NMR spectra in $CDCl_3$ of the presumed $[Et_3NH][Sn(SPh)_3]$ show the signals expected for Et_3NH^+ cation (identical to those shown, e.g., by $Et_3NH^+CF_3COO^-$). However, attempts to obtain pure crystals of $[Et_3NH][Sn(SPh)_3]$ by adding pentane to CH_2Cl_2 solutions (or water to ethanol solutions) resulted mainly in the precipitation of $Sn(SPh)_2$. Thus, a rapid equilibrium between the reagents and Sn(II) complex (eq 3) may be assumed:

$$:Sn(SR)_2 + RSH + B: \rightleftharpoons BH^+ [:Sn(SR)_3]^- \qquad (3)$$

In fact, $Sn(SPh)_2$ is not solubilized in organic solvents by adding only either PhSH or Et_3N, and neither the $Sn(SPh)_2$/PhSH nor $Sn(SPh)_2$/Et_3N mixtures show any reducing power. Furthermore, the strong reducing ability of Sn(II)/PhSH/Et_3N cannot be attributed to the presence of PhSH/Et_3N, or of $SnCl_2$/Et_3N, in the medium, since these last two reagents require several hours to complete the azide reduction under conditions in which the Sn(II)/PhSH/Et_3N mixture takes only 2-3 min.

The structures of the reduction products also point to the involvement of $Sn(SR)_3^-$ species, since when benzyl azide and $Sn(SPh)_2$/PhSH/Et_3N are mixed at r.t. in equivalent amounts, the resulting product shows a ^1H NMR spectrum in $CDCl_3$ that agrees with structure $PhCH_2NHSn(SPh)_3$ (see eq 4). By using phenylmethanethiol instead of benzenethiol as complexing agent, or dodecyl azide instead of benzyl azide, similar facts are observed. The corresponding residues, when treated with aq. NaOH and extracted, afforded the expected amines in 95-100% yields.

$$PhCH_2N_3 + Sn(SPh)_2 / PhSH \xrightarrow{Et_3N} PhCH_2NHSn(SPh)_3 + N_2 \qquad (4)$$

To investigate the possible involvement of radicals in these reductions, an ESR study of the reaction of benzyl azide with $[Et_3NH][Sn(SPh)_3]$ has been undertaken. Since even in 0.1 M degassed toluene solutions at different temperatures (from -60 °C to r.t.) no ESR signal has been detected, we think that the main pathway does not involve a free-radical, chain mechanism (although certain rapid single-electron transfer steps cannot be excluded, at present).

In view of all these data, the following mechanism for the azide reduction may be proposed:

$$\underset{}{R\text{-}\bar{N}\text{-}\overset{+}{N}\equiv N} + \underset{Et_3NH^+}{:Sn(SPh)_3^-} \rightleftharpoons \underset{Et_3NH^+}{R\text{-}\bar{N}\text{-}N{=}N\text{-}Sn(SPh)_3} \rightleftharpoons \underset{Et_3N}{R\text{-}NH\text{-}N{=}N\text{-}Sn(SPh)_3} \rightarrow \underset{Et_3N}{R\text{-}NHSn(SPh)_3} + N_2 \qquad (5)$$

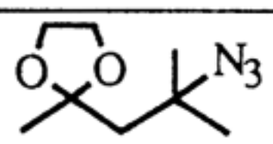
Regarding the reduction of nitro compounds, the fact that oximes and hydroxylamines are not further reduced under the present conditions, as well as the observation that PhNO is reduced even faster than $PhNO_2$,[5] suggest that the mechanism that mainly operates might be summarised as follows:[6]

$$R\text{-}NO_2 \xrightarrow{Sn(SPh)_3^-} [\,R\text{-}N(O^-)(O\text{-}Sn(SPh)_3)\,] \rightarrow R\text{-}N{=}O \xrightarrow{Sn(SPh)_3^-} [\,R\text{-}N^-\text{-}OSn(SPh)_3\,] \xrightarrow[Et_3N]{Et_3NH^+} R\text{-}NHOSn(SPh)_3 \qquad (6)$$

Comparison of $Sn(SR)_3^-$ and Other Reducing Agents (of Azides)

Most reagents reported to reduce aliphatic azides to amines[7] have been checked against a tertiary azide (4-azido-4-methylpentan-2-one ethylene acetal) in a thermostatic bath at 20 °C, by measuring in most cases the nitrogen evolved at identical concentrations of substrates (0.05 M) and reagents (1.5 equiv.) and confirming then

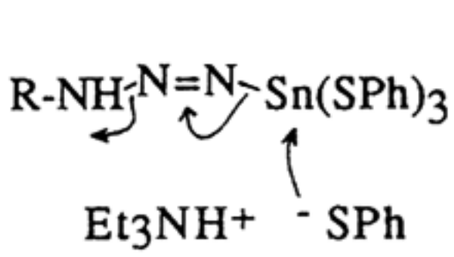
by NMR and chromatography that no azide remained in the crude product; those reagents which do not react with that tertiary azide after several hours have been treated with $PhCH_2N_3$ under similar conditions. In addition, some other reducing species, like $Sn(SR)_3^-$ (R≠Ph), $PhSeH/Et_3N$, $TiCl_2$, NaPhTe, Bu_3SnH/AIBN, and $Pd(PPh_3)_4$, have also been tested. The results are summarised below:

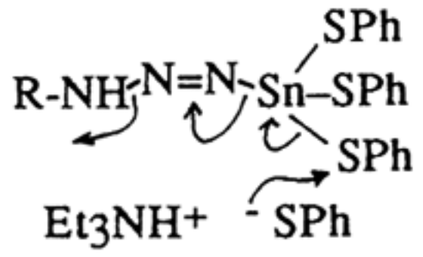
Reactivity vs. 	**% of azide reduced**		
$Sn(II)/HS(CH_2)_nSH/Et_3N/CH_3CN$[a]	100% (2 min)	Et_3P-H_2O/CH_3CN[e]	100% (9 h)
Sn(II)/toluene-3,4-diSH/Et_3N/CH_3CN	100% (3 min)	Sn(II)/py-2-SH/Et_3N/CH_3CN	85% (12 h)
$Sn(II)/PhCH_2SH/Et_3N/CH_3CN$	100% (10 min)		
Sn(II)/PhSH or $PhSeH/Et_3N/CH_3CN$	100% (20 min)	**Reactivity vs. $PhCH_2N_3$**	**% of azide red.**
$TiCl_4/Zn/THF$[b]	100% (25 min)		
$CrCl_2/HCl/MeCOMe$-H_2O	100% (40 min)	Sn(II)/py-2-SH/Et_3N/CH_3CN	100% (2 h)
$NaHTe/EtOH$-Et_2O	100% (45 min)	Na_2SnO_2/H_2O-THF	85% (24 h)
Sn(II)/ButSH/Et_3N/CH_3CN	100% (45 min)	Na_2S/MeOH	70% (24 h)
Sn(II)/$Me_3Si(CH_2)_2SH/Et_3N/CH_3CN$	100% (1 h)	$SnCl_2$/MeOH	60% (24 h)
NaPhTe/EtOH-Et_2O	100% (1 h)	Mg/MeOH	45% (24 h)
H_2/Pd-C/MeOH	100% (2.5 h)[c]	PhSH/Et_3N/CH_3CN	45% (24 h)
$PhSeH/Et_3N/SnCl_2$(cat.)/CH_3CN	100% (3 h)[d]	MeCOSH/MeOH	40% (24 h)[f]
$PhSeH/Et_3N/CH_3CN$	100% (6 h)	Bu_3SnH/C_6H_6	35% (24 h)[g]
$LiAlH_4/Et_2O$	100% (6 h)	$HS(CH_2)_2SH/Et_3N$/MeOH	35% (24 h)
Ph_2SnH_2/C_6H_6	100% (6 h)	$NaBH_4$/MeOH	20% (24 h)
PhSH/$Et_3N/SnCl_2$(cat.)/CH_3CN	100% (7 h)	$TiCl_3$/HCl/MeOH	0% (24 h)
Bu_2SnH_2/C_6H_6	100% (7 h)	$Pd(PPh_3)_4/C_6H_6$	0% (24 h)

[a] n = 2 or 3. [b] Using a $TiCl_4/2Zn$ molar ratio. [c] From ca. 2 equiv. of H_2 (1 atm) and 10 mg of Pd-C (10%); under these conditions, 45% of reduction product was obtained after 30 min and 90% after 2 h. This result corrects an earlier one from us (ref. 2a). In fact, we have observed that this catalytic hydrogenation is very sensitive to the palladium purity and other experimental conditions. Thus, e.g., reduction does not take place in aprotic solvents like EtOAc, C_6H_6, or $MeOCH_2CH_2OMe$, even in the presence of larger amounts of Pd; on the other hand, with a 25-fold excess of hydrogen and only 10 mg of Fluka Pd-C, 100% of reduction may be reached in 20 min. [d] 1.5 equiv. of a $2PhSeH/2Et_3N/0.25SnCl_2$ mixture. [e] Ph_3P had been used earlier (see ref. 8). [f] The corresponding acetamide is obtained. [g] Yields are the same with and without AIBN, or protecting the flask from the light.

The reactivity of most $Sn(SR)_3^-$ complexes is worthwhile, overcoming largely the more usual reducing agents employed so far.[9] This does not mean that $LiAlH_4$ or H_2/Pd, e.g., must be ruled out hereafter but, for extremely hindered azides or when the molecule contains other functional groups amenable to reduction, there are several $Sn(SR)_3^-$ complexes which work faster and, as will commented below, more chemoselectively. Actually, a note should be added concerning reagents in the right list of the above Table: many of them **do reduce** benzyl azide in good yields either at reflux, with excess of reagent, or under more concentrate solutions; what the present Table emphasises is their relative reducing ability under the above-mentioned conditions (temperature controlled by a water bath, dilute solutions, etc.).

Some additional points worthy of mention are: (i) The effect of solvents on the reduction rate of $Sn(SR)_3^-$ complexes is as follows, $CH_3CN \approx C_6H_6 \approx$ MeCOMe › THF › MeCOMe-H_2O › py › DMF › MeOH › THF-H_2O.[10] (ii) Whereas there are no significant differences among the bases Et_2NH, Et_3N, DMAP, TMEDA, $EtPr^i_2N$, the relative rate with pyridine (py) is one third of that of Et_2NH. (iii) We have observed that the 1:2:1 component ratio of $Sn(SPh)_2$/RSH/Et_3N is, depending on the azide, 1.3-2.0 times more active than the 1:1:1 ratio (that is to say, $SnCl_2$/4RSH/$3Et_3N$ is better than $SnCl_2$/3RSH/$3Et_3N$).[11] At first sight, this fact could be related with an easier protonation of the triazene (see eq 5) in the presence of an additional mole of RSH and/or to the probably more rapid cleavage of the triazene to afford the amine and $Sn(SPh)_4$, but there is another possible cleavage of the triazene derivative that would yield PhSSPh, $Sn(SPh)_2$, and RNH_2. We took this possibility into account after observing that the addition of only catalytic amounts (ca. 0.2 equiv.) of $SnCl_2$ to benzyl azide/4PhSH/$3Et_3N$ mixtures increases largely the rate, all the





azide being reduced, and that addition of either $Sn(SPh)_4$ or $SnCl_4$ (!) to a benzyl azide/4PhSH/3Et3N mixture shows the same catalytic effect; thus, redox equilibria involving the Sn(IV)/Sn(II) and PhS^-/PhSSPh pairs, such as $Sn(SPh)_4 \rightleftharpoons Sn(SPh)_2$ + PhSSPh or $YSn(SPh)_3 + PhS^- \rightleftharpoons Y^- + Sn(SPh)_2$ + PhSSPh cannot be ruled out under our reduction conditions.

Comparison of $Sn(SR)_3^-$ and Other Reducing Agents (of Nitro Compounds)

Phenylnitromethane, 1-nitrobutane, 1-(4-methoxyphenyl)-2-nitroethane, 3-methyl-2-nitromethylcyclohexene, and 1-(4-methoxyphenyl)-2-nitropropane (entries 1, 3, 4, 6, and 9, above) have been treated with appropriate reducing agents[12] under identical conditions. By monitoring the disappearance of the nitro derivative by TLC and ^1H NMR, the following scale of reducing power has been established:

$$CrCl_2/HCl \gg Sn(SCH_2Ph)_3^- > Sn(SPh)_3^- > Sn(SBut)_3^- \gg SnCl_2/Et_3N/MeOH > CS_2/Et_3N/CH_3CN > SnCl_2 \cdot 2H_2O/AcOEt$$

For instance, $CrCl_2$, either commercial product or prepared in situ from $CrCl_3/Zn/HCl$,[12a] in $MeCOMe/H_2O$ reduces completely 1-(4-methoxyphenyl)-2-nitroethane (entry 4) within 5 min, but the problem, as reported for other nitroalkanes,[12a] is that a mixture of aldehyde and oxime is actually obtained under these acidic conditions; $Sn(SPh)_3^-$ in CH_3CN gives oxime in 93% isolated yield after 1 h; $SnCl_2/Et_3N/MeOH$, 40% of oxime after 12 h; CS_2/Et_3N in CH_3CN,[12b] 25% of impure oxime after 24 h; and $SnCl_2$ in AcOEt, no reduction at all.[12c]

We have proceeded similarly to evaluate these or related reagents with regard to the potential reduction of 4-nitrotoluene to *N*-(4-tolyl)hydroxylamine.[13] A summary of their relative performance at 20 °C, at identical substrate concentrations (0.2 M), using 2.5 equiv. of each reductant, is shown below:

React. vs. 4-NO_2PhMe	**% reduced**	**main product(s)**
$CrCl_2/HCl/MeCOMe-H_2O$	100% (5 min)	4-$MePhNH_2$ (25%), azoxy (30%)[a]
$Sn(SPh)_2/PhSH/Et_3N/C_6H_6$	100% (10 min)	4-MePhNHOH (82%)
$Zn/NH_4Cl/EtOH-H_2O$ 1:1	100% (1 h)	4-MePhNHOH (55%), azoxy (35%)
$H_2/Pd-C/MeOH$	85% (1 h)	4-$MePhNH_2$ (78%)
$NaHS/CaCl_2/EtOH-H_2O$ 1:1	55% (1 h)	4-$MePhNH_2$ (50%)
$Zn/NH_4Cl/H_2O$	50% (1 h)[b]	4-MePhNHOH (45%)
$SnCl_2/Et_3N/MeOH$	90% (12 h)	azoxy (80%)
$SnCl_2 \cdot 2H_2O$	30% (12 h)	4-$MePhNH_2$ (26%)

[a]Percentage given in weight (w/w).

[b]85% of reduction in 3 h, 65% of hydroxilamine and minor amounts of amine and azoxy being obtained.

Chemoselectivity

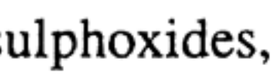
The reactivity of $Sn(SPh)_3^-$ with $PhCH_2N_3$, $PhCH_2NO_2$, 4-MeOPhCHO, $CH_2=CH(CH_2)_8CHO$, $PhCH_2COCH_3$, $PhCH_2SOCH_3$, $PhCH_2SO_2CH_3$, $PhCH_2CN$, and $PhCH_2COOEt$ has been checked at r.t. and 0.1 M reagent concentrations. Whereas benzylamine and benzaldehyde oxime have been produced almost instantaneously, the remaining compounds are not reduced at all after a few hours.[14] Thus, the Sn(II) complex reduces azido and nitro groups with a high selectivity.

In comparing azides and nitro derivatives, it turns out that, with a defect of $Sn(SPh)_3^-$ at 0 °C, an equimolar mixture of $PhCH_2N_3$ and $PhCH_2NO_2$ gives benzylamine and very small amounts of benzaldehyde oxime. Thus, azides are reduced under these conditions even more quickly than nitro compounds. Only the nitroso compounds, among the functional groups we have studied so far, react faster than azides with Sn(II) complexes.

By means of competition experiments, we have also evaluated the approximate reactivity order of some azides with $Sn(SPh)_3^-$ at r.t.:

4-N_3PhCO_2Me	PhN_3	$PhCH_2N_3$	$PhCHMeN_3$	
30	2	1	0.4	0.1

Similarly, the following approximate reactivity order for different nitro compounds has been obtained:

4-NO_2PhCO_2Me	$PhNO_2$	4-$MePhNO_2$	$PhCH_2NO_2$	4-$EtOPhNO_2$	4-$MeOPh(CH_2)_2NO_2$	4-$MeOPhCH_2\underset{\displaystyle Me}{\underset{|}{C}}HNO_2$	
10	1.7	1.5	1	0.6	0.4	0.1	0.05

There is a close parallelism between the two series: aromatic are more readily reduced than primary aliphatic derivatives (although the differences are not relevant except for the aromatic rings with an electron-withdrawing group) whereas secondary aliphatic derivatives outstand out from the remaining compounds for their lower reactivity. In comparing the two series, it appears that, under these conditions, azides are more rapidly reduced than their nitro counterparts by a factor ≥4.

Conclusions

The tin(II) complexes arising from treatment of Sn^{2+} with appropriate amounts of PhSH and base appear to be a extremely reactive and chemoselective reducing agents for azides (which give amines) and nitro compounds (which afford either oximes or hydroxylamines, depending on the substrate). In fact, these reactions can be readily accomplished, even with hindered substrates, and without affecting carbonyl groups, sulphoxides, esters, or nitriles. When similar azides and nitro compounds are compared, it turns out that the azide reacts faster than the nitro group in cold and at room temperature.

From a practical point of view, polar solvents can be recommended for the preparation of ketoximes, while apolar solvents give rise to better yields of *N*-arylhydroxylamines, in general. Future applications to the natural product field (where amine groups are usually introduced through azides), to the chemistry of aromatic and heteroaromatic compounds, and as a suitable method for the conversion at low temperatures of aliphatic nitro derivatives into other organic functions seem promising.

EXPERIMENTAL

Mp's have been determined on a Büchi apparatus and are uncorrected. NMR spectra have been obtained in $CDCl_3$ (unless otherwise indicated) on a 'Gemini-200' Varian spectrometer; ^1H and ^{13}C chemical shifts are reported in ppm with respect to internal TMS, and *J* values are in Hz. IR spectra have been recorded in KBr with a Perkin-Elmer 681 instrument; only the most significant absorptions (in cm^{-1}) are given. Chemical ionisation mass spectra have been recorded on a Hewlett-Packard 5988A spectrometer. A Varian E-109 EPR spectrometer has also been utilised.

Preparation of substrates. Benzyl and cyclohexyl azide have been prepared from the corresponding chlorides and NaN_3 in refluxing aq. EtOH.[15] 4-Azido-4-methylpentan-2-one ethylene acetal has been synthesised from mesityl oxide.[16] Phenyl azide and methyl 4-azidobenzoate have been obtained from their amines, by diazotisation and treatment with NaN_3.[17] 1-Azido-1-phenylethane[18] has been prepared from acetophenone (by reduction with $LiAlH_4$, treatment with Br_2/Ph_3P, and substitution of N_3 for Br under phase-transfer conditions). Phenylnitromethane and 3,4-methylenedioxyphenylnitromethane have been prepared from their bromides and $NaNO_2$ in DMF (in the presence of urea);[19a] the last compound has also been obtained by oxidation of its oxime with MCPBA. 1-Nitrobutane (entry 3), methyl 11-nitroundecanoate (entry 5), and ethyl 2-nitropropanoate (entry 10), from treatment of butyl bromide, methyl 11-bromoundecanoate, and ethyl 2-bromopropanoate, respectively, with $NaNO_2$ in DMSO.[19a] 1-(4-Methoxyphenyl-2-nitroethane (entry 4) and 1-(4-methoxyphenyl)-2-nitropropane (entry 9), from condensation of nitromethane and nitroethane, respectively, with 4-methoxybenzaldehyde,[19b] followed by reduction with $NaBH_4$.[19c] 6-Methyl-1-nitromethylcyclohexene (entry 6), from 2-methylcyclohexanone, nitromethane, and ethylenediamine.[12b] 1-Nitro-1-phenylethane (entry 7) and nitrocyclohexane (entry 8), from acetophenone oxime and cyclohexylamine, respectively, and MCPBA.[19d] 2-Nitro-2-phenylpropane (entry 11), from 2-nitropropane and diphenyliodonium chloride.[19e] 1-Ethoxy-4-nitrobenzene (entry 14) and methyl 4-nitrobenzoate (entry 15) from alkylation of 4-nitrofenol and esterification of 4-nitrobenzoic acid, respectively. Preparation of reagents. 2-Trimethylsilylethanethiol has been prepared from 2-trimethylsilylethanol[20a] (treatment with Br_2/Ph_3P in CH_2Cl_2, reaction with CH_3COSH/Et_3N in THF, and reduction with $LiAlH_4$[20b]). Sodium phenyltelluride has been prepared from diphenyl ditelluride and $NaBH_4$,[20c] phenylselenol from commercially available diphenyl diselenide,[20d] diphenyltin dihydride and dibutyltin dihydride by treatment of the corresponding dichlorides with $LiAlH_4$,[20e] and tetrakis(triphenylphosphine)palladium(0) from $PdCl_2$, N_2H_4, and Ph_3P in DMSO.[20f]

Reduction of azides. Typical example: 185 mg (1 mmol) of 4-azido-4-methylpentan-2-one ethylene acetal are added to a magnetically stirred mixture of 505 mg (1.5 mmol) of $Sn(SPh)_2$, 155 µl (1.5 mmol) of PhSH, and 210 µl (ca. 1.5 mmol) of Et_3N in 10 ml of C_6H_6 (or other organic solvents) at r.t. Twenty min later on, 25 ml of 2 N NaOH and 25 ml of CH_2Cl_2 are added. Separation of the two phases, extraction of the aq. layer twice more with CH_2Cl_2, drying of the organic solutions, and evaporation of the solvent afford 150-156 mg (95-98%) of chromatographically and spectroscopically pure amine.[8a]

Alternative procedure. Typical example: To a solution of anh. $SnCl_2$ (285 mg, 1.5 mmol) in 10 ml of CH_3CN (or THF), stirred magnetically at r.t., 620 µl (6 mmol) of PhSH and 620 µl (4.5 mmol) of Et_3N are added. Then, 185 mg (1 mmol) of 4-azido-2-methylpentan-2-one ethylene acetal are added. Twenty min later, the solvent is evaporated under vacuum. Workup as above gives the amine in almost quantitative yield.

Reduction of nitroalkanes to oximes. Typical example: 181 mg (1 mmol) of 1-(4-methoxyphenyl)-2-nitroethane (entry 4) in 2 ml of C_6H_6 are added to a mixture of 505 mg (1.5 mmol) of $Sn(SPh)_2$, 155 µl (1.5 mmol) of PhSH, and 210 µl (ca. 1.5 mmol) of Et_3N in 3 ml of C_6H_6 maintained at r.t. Thirty min later on, the reaction mixture is directly introduced into a silica gel column and separated by means of CH_2Cl_2 (PhSH and PhSSPh being eluted) and then CH_2Cl_2-MeOH 95:5, to afford 123 mg (74%) of *(E)*-4-methoxylphenylacetaldehyde oxime: mp 111-114 °C, lit.[21a] 111-113 °C; ^{1}H NMR ∂ 9.0 (br s, 1H), 7.15 (pseudo d, 8.8 Hz, 2H), 6.86 (pseudo d, 8.8 Hz, 2H), 6.81 (t, 5.3 Hz, 1H), 3.79 (s, 3H), 3.67 (d, 5.3 Hz, 2H); ^{13}C NMR ∂ 158.8, 151.8 (CH=N), 130.2, 129.0, 114.5, 55.5, 30.8 (CH_2); IR 3400-3100, 1670.

Alternative procedure. Typical example: To a solution of anh. $SnCl_2$ (142 mg, 0.75 mmol) in 1 ml of CH_3CN, magnetically stirred at r.t., 235 µl (2.25 mmol) of PhSH and 345 µl (2.5 mmol) of Et_3N are added. Then, 91 mg (0.5 mmol) of 1-(4-methoxyphenyl)-2-nitroethane in 2 ml of CH_3CN are added. After 30 min, the reaction mixture is concentrated under vacuum and the residue separated by column chromatography as above to give 83 mg (93%) of an *E/Z* mixture (2:1 according to the ^{1}H NMR spectrum). Spectral data of isomer *Z*: ^{1}H NMR ∂ 8.5 (br s, 1H), 7.54 (t, 6.4 Hz, 1H), 7.15 (pseudo d, 8.8 Hz, 2H), 6.86 (pseudo d, 8.8 Hz, 2H), 3.79 (s, 3H), 3.50 (d, 6.4 Hz, 2H); ^{13}C NMR ∂ 151.5 (CH=N), 35.1 (CH_2).

To our knowledge, the oximes here obtained are known compounds[21b] save methyl 11-(hydroxyimino)undecanoate (entry 5), mp 64-67 °C,[21c] ^{1}H NMR ∂ 8.5 (br s, 1H), 6.71 (t, 5.5 Hz, 1H), 3.67 (s, 3H), 2.5-2.1 (m, 4H), 1.7-1.2 (m, 14H); ^{13}C NMR ∂ 174.6, 152.9, 51.3 , 33.9, 29.0-24.7 (eight CH_2); IR 3500-3100, 1745.

Reduction of 2-nitro-2-phenylpropane and nitroarenes to hydroxylamines. Typical example: 122 mg (0.67 mmol) of methyl 4-nitrobenzoate (entry 15) are added to 572 mg (1.7 mmol) of $Sn(SPh)_2$, 180 µl (1.7 mmol) of PhSH, and 240 µl (1.7 mmol) of Et_3N in 3 ml of C_6H_6 at r.t. After 5-10 min, the reaction mixture is separated by column chromatography on silica gel with CH_2Cl_2 and then CH_2Cl_2-MeOH 95:5 to yield 106 mg (94%) of methyl 4-(hydroxylamino)benzoate: mp 120-122 °C (lit.[22] 121-122 °C); ^{1}H NMR in DMSO-d_6 ∂ 8.95 (s, 1H), 8.65 (s, 1H), 7.75 (d, 8.0, 2H), 6.90 (d, 8.0, 2H), 3.75 (s, 3H); IR 3375, 3250, 1690.

To our knowledge, the hydroxylamines here obtained are known compounds[13b] with the exception of 2-hydroxylamino-2-phenylpropane, mp 82-85 °C; ^{1}H NMR ∂ 8.3 (br s, 2H), 7.5-7.1 (m, 5H), 1.55 (s, 6H); IR 3600, 3300-3100; CI-MS m/z 186 ($M+NH_3+NH_4^+$, base peak), 169 ($M+NH_4^+$), 153 ($M+2^+$), 152 ($M+1^+$).

Acknowledgments

Financial support from the CICYT, Ministerio de Educación y Ciencia (grant PB86-0170) is gratefully acknowledged. Thanks are due as well to the Spanish Ministerio de Educación y Ciencia for fellowships (to M. B. and P. R.). We also thank Ms. A. Díaz and Dr. J. Veciana (CSIC, Barcelona) for their assistance with the ESR spectra, Mr. C. Celma for the CI-MS, Ms. C. Caballol for studying the reactivity of the Pd(0) complex with some azides, and Mr. R. Roy for technical help.

References and footnotes

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3. It is known (see Smentowski, F. J. *J. Am. Chem. Soc.* **1963**, *85*, 3036) that nitrosobenzene is readily reduced by thiol(ate)s to azoxybenzene, as we have confirmed by NMR by mixing PhNO, PhSH, and Et_3N in $CDCl_3$. But we have not observed nitroso, azoxy, or azo derivatives as byproducts of the reduction of nitroarenes with Sn(II)/PhSH/Et_3N in apolar solvents.
4. In fact, this only indicates that some $Sn(SR)_3^-$ species are relatively very stable in the gas phase.
5. We have reduced PhNO (prepared independently) to PhNHOH in 93% yield at -78 °C within 1 h, with 1 equiv. of $Sn(SPh)_3^-$.
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9. It may be added that the reduction of azides by Cr(II) and Ti(III) in the presence of thiols and base has also been tried, without success, and that V(II) and V(III) salts (Ho, T. L.; Henninger, M.; Olah, G. A. *Synthesis* **1976**, 815) have not been evaluated since their reported reactivity is similar—a bit lower, indeed—to that of Cr(II).[7]
10. For instance: the reaction of 4-azido-4-methylpentan-2-one ethylene acetal with 1.1 equiv. of the $SnCl_2$/4PhSH/3Et_3N mixture for 30 min gives the following yields in different solvents: CH_3CN, C_6H_6, and MeCOMe, 100% (in fact, only 20 min are required); THF, 90%; MeCOMe-H_2O, 70%; py, 58%; DMF, 55%; MeOH, 50%; and THF-H_2O 8:2, 25%.
11. In practice, only the amount of PhSH is significant, since the Et_3N ratio (from 2 equiv. to an excess) has no effect on the yields.
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13 This is classically effected (a) by hydrogenation, usually under special conditions (cf. Johnstone, R. A. W.; Wilby, A. H.; Entwistle, I. D. *Chem. Rev.* **1985**, *85*, 129) or (b) by treatment with Zn/NH_4Cl or NaHS/$CaCl_2$ [cf. Zeeh, B.; Metzger, H. In 'Houben-Weyl Methoden der Organischen Chemie'; Band 10/1; Müller, E. (Ed.); G. Thieme Verlag, Stuttgart, 1971]. (c) Ytterbium metal also reduces nitrobenzene to phenylhydroxylamine, in 46% yield: Hou, Z.; Fujiwara, Y.; Taniguchi, H. *J. Org. Chem.* **1988**, *53*, 3118. (d) Nitroalkenes may be reduced to *N*-alkylhydroxylamines with BH_3 plus $NaBH_4$ (Mourad, M. S.; Varma, R. S.; Kabalka, G. W. *J. Org. Chem.* **1985**, *50*, 133; and references therein).
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