Novel reduction of isothiocyanates to thioformamides with SmI_2 and *tert*-butyl alcohol in the presence of HMPA

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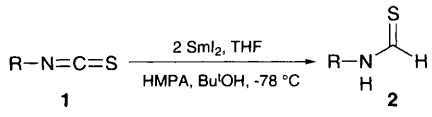
Isocyanates react with SmI_2 and *tert*-butyl alcohol in the presence of HMPA to give thioformamides in excellent yields under mild conditions.

Thioformamides are synthetically useful for a number of chemical transformations such as heterocyclic ring generation,[1] thioacylations,[2] thioamide formations,[3] condensation to iminyl sulfides[4] and enamines.[5] Several methods for the synthesis of thioformamides have been developed. Methods for the preparation of *N,N*-disubstituted formamides include the transformation of amines with dichlorocarbene and hydrogen sulfide,[6] conversion of thioformates to thioformamides,[7] transformation of thiocarbamoyl chloride with alkoxide,[8] amine-exchange between disubstituted amine and dimethyl thioformamide,[9] conversion of tertiary amines with carbon disulfide[10] and other methods using special reagents.[11]

Many of these methods are not directly applicable for the synthesis of *N*-monosubstituted thioformamides and require toxic reagents under strongly basic or acidic conditions at high temperatures. Trials of reduction of isothiocyanates to thioformamides have been performed. Reductions with zinc and hydrochloric acid or lithium aluminium hydride affords the corresponding primary or secondary amines rather than thioformamides.[12] Aryl isothiocyanates reacted with a catalytic amount of sodium borohydride to give the trimers (isocyanurate). Reduction with an excess amount of sodium borohydride resulted in primary amines or thioformamides in low yields.[13]



Scheme 1

Table 1 Reduction of various isothiocyanates with SmI_2

Run	R	SmI_2 (equiv.)	*t*/min	Yield (%)[a]
1	Et	0.5	<3	24
2	Et	1.0	<3	47
3	Et	2.0	<3	92 (32)[b]
4	Me	2.0	<3	91
5	*c*-hex	2.0	5	93
6	Bu^t	2.0	5	87
7	Bn	2.0	<3	91
8	allyl	2.0	<3	89
9	Ph	2.0	5	85

[a] Isolated yield. [b] Yield in the absence of HMPA.

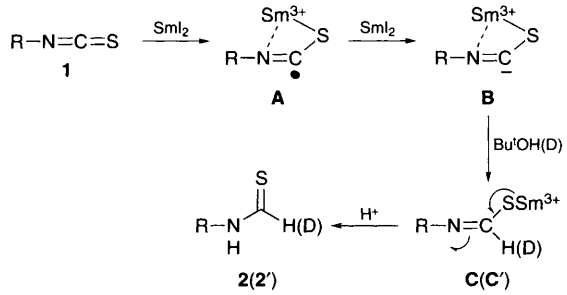


Fig. 1 Possible mechanism of isothiocyanate reduction

Samarium diiodide shows oxophilicity and one electron donor effects,[14] which have been demonstrated by its widespread applications in the reduction of a variety of functional groups in organic synthesis, as well as its mediation of a range of unusual reductive cyclization and intermolecular coupling reactions.[15] Compared with traditional reducing reagents, reductions using samarium diiodide have been carried out with short reaction times at low temperature under mild reaction conditions. These transformations include the reductions of sulfoxides, sulfones, phosphine oxides, halides and carbonyl compounds.[16] However, the reduction of three centred 4π electron systems [*e.g.*–N=C=X (X=O, S)] with samarium diiodide has never been reported.

We have now found that isothiocyanates **1** can be converted into *N*-monosubstituted thioformamides **2** in excellent yields using SmI_2 in the presence of *tert*-butyl alcohol and HMPA in tetrahydrofuran. These reactions were carried out within a few minutes at −78 °C. The results obtained are summarized in Table 1. Various isothiocyanates **1** such as alkyl, aryl and allyl isothiocyanates are readily reduced to thioformamides **2**. Even bulky *tert*-butyl isothiocyanate was converted to *tert*-butyl thioformamide in 87% yield. Most starting materials are commercially available. Benzyl and cyclohexyl isothiocyanates were prepared by the standard method.

This interesting reaction appears to be initiated *via* formation of radical **A** which converts to the anion **B** by one electron transfer from SmI_2. The anion **B** abstracts H^+ (D^+) from *tert*-butyl alcohol (Bu^{t}OD) to form an intermediate **C** (**C′**), which was quenched to give **2** (**2′**) as shown in Fig. 1 The reaction was carefully followed by ^1H NMR without quenching. In order to see the mechanism, Bu^{t}OD was used instead of Bu^{t}OH. The deuteriated **2′** was isolated by column chromatography (silica gel 60, 45–60 μm) and confirmed by ^1H NMR [EtNH–C(=S)H: δ 9.2, EtNH–C(=S)D: no peak at δ 9.2] and mass spectroscopy [EtNH–C(=S)D, M^+: 90.18, at 95 D atom%].

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