SHORT PAPER

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Nickel mediated reduction of azides by Bu_3SnH

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The use of two equivalents of Bu_3SnH (TBTH), in the presence of a catalytic amount of $NidppeCl_2$, provides a new procedure for the reduction of organic azides under mild conditions. While non-sterically hindered aliphatic azides readily undergo reduction to produce primary amines in good yields, benzyl azide gives N_3 displacement by the hydrido group.

The reduction of azides to primary amines constitutes a synthetically useful process[1]. A wide variety of reagents including lithium aluminium hydride[2], catalytic hydrogenation[3], triphenylphosphine[4], boron hydride[5], stannous chloride[6], propane-1,3-dithiol[7] and magnesium or calcium in methanol[8], among others have been reported for this conversion. However, most of them have some drawbacks in terms of their general applicability, selectivity and availability. For instance, $LiAlH_4$ does not tolerate too many functionalities such as –COOR, $–NO_2$, *etc.* On the other hand, catalytic hydrogenation and diborane reduction cannot be applicable to unsaturated compounds containing a double or triple bond. Surprisingly, to our knowledge, there are only a few references about the reduction of azides to amines by Bu_3SnH[9]. The traditional protocol for this conversion entails drastic conditions, such as the use of AIBN as a radical initiator (or long reaction times in its absence), and high boiling solvents.

In exploring the chemistry of Ni-hydrido species as catalytic reducing agents[10], we have tested the possibility of reducing the readily available azides[1,11] by employing TBTH as a hydride source in the presence of a catalytic amount of $NidppeCl_2$ (dppe=Diphenylphosphinoethane).

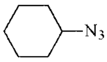
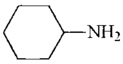
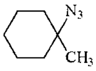
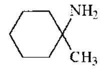
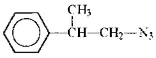
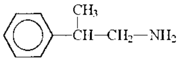
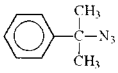
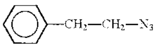
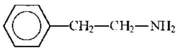
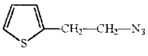
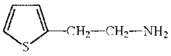
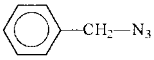
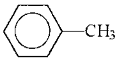
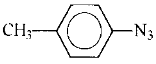
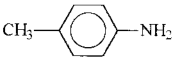
In a typical experiment, to 0.01 mol of *n*-octyl azide, in THF, in the presence of $NidppeCl_2$, at 0 °C, was slowly added 0.01 mol of TBTH, under N_2 atmosphere (Table 1, run 1). The reaction produced amine with a conversion of 50%, although the conversion is 95% when two equivalents of TBTH were used.

Table 1 summarises our results for the reduction of a variety of azides employing two equivalents of TBTH.

The Table highlights that the success of the reaction is strictly dependent on the nature of the substrate employed. Primary and secondary azides are reduced in good yields while sterically hindered substrates do not seem to be affected (Run 6, 8, Table 1). As shown in Table 1, even *p*-tolyl azide is almost transformed to the corresponding amine (Run 12), whereas under analogous conditions, benzylic acid undergoes the displacement of the N_3 group with the formation of the corresponding aromatic hydrocarbon (Run 11). In this last case only one equivalent of TBTH per mole of precursor is sufficient to promote the reaction. Attempts to carry out the reaction on allylic azides produce (in low conversions) a mixture of allylic amines and corresponding alkanes, deriving from the reduction ($RN_3 \rightarrow RNH_2$) or the substitution of ($RN_3 \rightarrow RH$) of the N_3 group, respectively. Unexpectedly, some reductions on precursors of a similar structure [Run 7, 9, 10, (Table 1)] give the corresponding amines with quite different conversions (16%–95%). These reactions seem to depend on the nature of the aromatic or heteroaromatic ring in α position to the azido group.

Thus, at temperatures under –20 °C all the catalytic processes are inhibited, included the TBTH dimerization that in these reaction conditions normally takes place.[12]

Table 1 Reduction of azides by using two equivalents TBTH and $NidppeCl_2$[a]

Run	RN_3 (0.05 mol)	Product	Yield[b]
1	n-$C_8H_{17}N_3$	n-$C_8H_{17}NH_2$	50 %[c]
2	n-$C_8H_{17}N_3$	n-$C_8H_{17}NH_2$	95 %
3	n-$C_{10}H_{21}N_3$	n-$C_{10}H_{21}NH_2$	83 %[d]
4	5-azidononane	50-aminononane	95 %
5			60 %
6			Traces
7			16%
8		-----------	0 %[e]
9			27 %
10			95 %
11			75 %[e]
12			95 %[f]

[a] 1.90×10^{-4} mol of $NidppeCl_2$ were employed; [b] GC yields; [c] only one equivalent of TBTH per mole of precursor was used; [d] decane is identified as the by-product; [e] only the formation of $n.Bu_6Sn_2$ is observed; [f] only traces of toluene are present as the by-product.

The reaction must be performed at 0°C by adding the TBTH to the reaction mixture. The mechanism for the reaction proposed is shown in Scheme 1.

The reaction presumably proceeds in three steps, the first of which (Step **A**) involves the initial reduction of $NidppeCl_2$ due to action of the TBTH, to give a Ni(0) species, followed (Step **B**) by the probable formation of an azido nickel complex[13], which reacts with TBTH to give an intermediate **I**, evolving into the more stable alkyl tri *n*-butyl stannyl triazene (**II**).[14]

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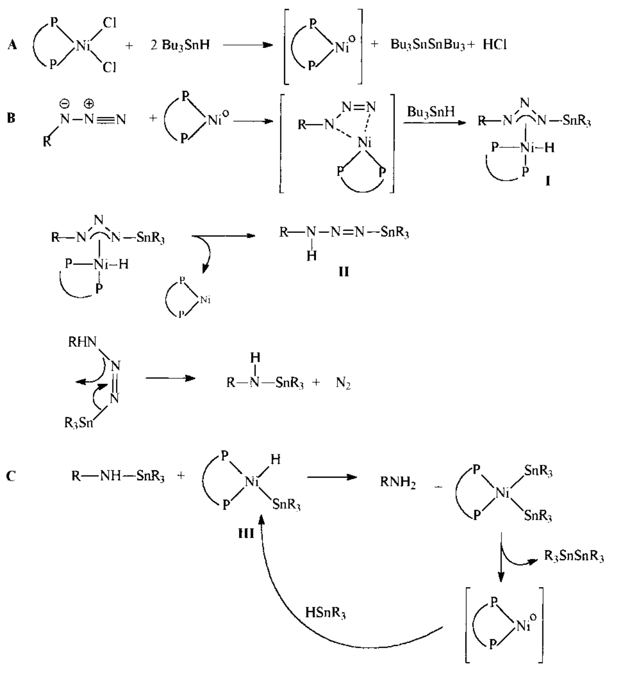

Scheme 1

The triazene (**II**) eliminates N_2 thus giving the corresponding alkyl stannyl amine in accordance to what was obtained in similar intermediates (Staudinger reaction).[15] The stannyl amine rapidly reacts with Nidppe tri-*n*-butyl stannyl hydride (**III**), to give alkyl amines (Step **C**).

The formation of the stannyl amine seems to be in accordance with the formation of traces of corresponding hydroxylamine (GC-MS) observed when the hydrolysis of the final reaction mixture is carried out with oxygen saturated water. It must be underlined that the stannyl amine rapidly reacts with **III** (Step **C**, Scheme 1), so it is impossible to employ only one equivalent of TBTH to obtain the corresponding amine in high yield (Run 1, Table 1). On the other hand, the formation of amine starting from stannyl amine and TBTH or similar hydrides in absence of Ni(0) catalysts is reported[16] and occurs in more drastic reaction conditions. Note that species **III**, characterised by Ni–Sn, Ni–H bonds, seems to be similar to compounds reported in the literature[16a,17] such as acid hydrides (metal hydrides with reverse polarity) in which the hydrogen bonded to the nickel metal atom should have real acidic properties.[18,19] The *p*-tolyl azide (Run 12, Table 1) showed a pseudohalide behaviour and undergoes the replacement of N_3 group through a S_H2 process.

The reaction of TBTH with NidppeCl_2 represents a new and useful approach to the synthesis of catalytically active nickel-hydride species, able to perform many functional groups interconversion[10] and, in particular, the azido group reduction to primary amines.

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