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The Reductive Amination of Carbonyl Compounds Using Sodium Hydrogentelluride as a Reducing Reagent

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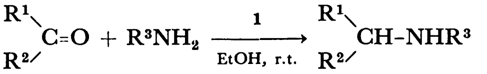
Synopsis. Carbonyl compounds were aminated to secondary amines in moderate yields under mild conditions using sodium hydrogentelluride as a reducing reagent.

Sodium hydrogentelluride (NaTeH, **1**) has been known as a useful reducing reagent and has been used for the reduction of *vic*-dibromo compounds,[1] α,β-unsaturated carbonyl compounds,[2] nitro compounds,[3] α,β-epoxy ketones,[4] *gem*-dibromocyclopropanes,[5] and α-halo carbonyl compounds.[6]

In this paper, we wish to report that **1** is also useful for the reductive amination of carbonyl compounds to secondary amines (Eq. 1).[7]



$$\underset{R^2}{\overset{R^1}{\diagdown}}C{=}O + R^3NH_2 \xrightarrow[\text{EtOH, r.t.}]{\mathbf{1}} \underset{R^2}{\overset{R^1}{\diagdown}}CH\text{-}NHR^3 \qquad (1)$$

For example, benzaldehyde (2 mmol) and butylamine (2 mmol) were added to an ethanolic solution of **1** prepared *in situ* from tellurium and $NaBH_4$, and the mixture wes stirred at room temperature for 20 h. The usual subsequent work-up gave *N*-butylbenzylamine in an 88% yield. The results are summarized in Table 1. As can be seen from Table 1, aliphatic amines afforded the products in good yields, although the yields of the products derived from aniline were rather low. However, when two equivalents of aniline were used, the yield of the corresponding amine was improved (Run 2). In these cases, unreacted aniline and carbonyl compounds were recovered, and no by-product was formed. When glutaraldehyde was treated with amines, *N*-substituted piperidines were obtained as the sole reaction product (Table 2). When 2,5-hexanedione was used, the yield of the pyrrolidine derivative was less than 10%.

Generally, Schiff bases are considered as intermediate of the reductive amination reaction of carbonyl compounds,[7] therefore, in this reaction, the base is also assumed to be formed as an intermediate. In fact, *N*-benzylideneaniline, a representative Schiff base, was reduced by **1** to *N*-benzylaniline in a 70% yield under same reaction conditions.

The good yields of the products, the ease of the reaction procedure, the mildness of the reaction conditions, and the absence of any side reaction make it possible to utilize this reaction for the one-pot synthesis of secondary amines.

Experimental

General. The nuclear magnetic resonance (^{1}H NMR) spectra were recorded on Hitachi R-600 FT-NMR spectrometer (60 MHz), using Me_4Si as the internal standard. The mass spectra were recorded on a Hitachi RM-50 GC-MS spectrometer. The infrared spectra (IR) were recorded on a Hitachi 260-10 infrared spectrometer. Thin-layer chromatography was performed on Merck Silica Gel.

Materials. The tellurium powder and $NaBH_4$ were purchased from Nakarai Chemicals in an extra pure grade and were used without further purification. The ethanol was distilled and stored over 3A molecular sieves. The *N*-benzylideneaniline was synthesized according to the method in the literature.[8] The glutaraldehyde was available as a 25 wt% solution in water and was used without distillation. All the other compounds in this report were commercial products and were used without further purification.

General Procedure for Reductive Amination. Finely divided tellurium powder (0.65 g, 5 mmol) and $NaBH_4$ (0.45 g, 11 mmol) were placed in a two-necked flask containing a

TABLE 1. REDUCTIVE AMINATION OF CARBONYL COMPOUNDS

Run	Carbonyl compound	Amine	Product	Yield/%[a]
1	Benzaldehyde	Aniline	*N*-Benzylaniline	41
2	Benzaldehyde	Aniline[b]	*N*-Benzylaniline	73
3	Benzaldehyde	*p*-Toluidine	*N*-Benzyl-*p*-toluidine	49
4	Benzaldehyde	*p*-Anisidine	*N*-Benzyl-*p*-anisidine	58
5	Benzaldehyde	Cyclohexylamine	*N*-Cyclohexylbenzylamine	80
6	Benzaldehyde	Butylamine	*N*-Butylbenzylamine	88
7	*p*-Tolualdehyde	Aniline	*N*-Phenyl-4-methylbenzylamine	20
8	*p*-Anisaldehyde	Aniline	*N*-Phenyl-4-methoxybenzylamine	44
9	Butyraldehyde	Aniline	*N*-Butylaniline	24
10	Butyraldehyde	Benzylamine	*N*-Butylbenzylamine	96
11	Cyclohexanone	Aniline	*N*-Cyclohexylaniline	6
12	Cyclohexanone	Butylamine	*N*-Butylcyclohexylamine	94
13	Acetone	Benzylamine	*N*-Isopropylbenzylamine	80

a) Isolated yield based on starting carbonyl compounds. b) Two equivalents of aniline were used.

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Table 2. Reductive amination of glutaraldehyde

Run	Amine	Product	Yield/%[a]
1	Aniline	*N*-Phenylpiperidine	34
2	Benzylamine	*N*-Benzylpiperidine	86
3	Butylamine	*N*-Butylpiperidine	54

a) Isolated yield based on starting carbonyl compounds.

Teflon-covered stirring bar. The system was then evacuated and filled with argon. Dry ethanol (25 ml) was injected by means of a syringe, and the suspension was heated at 45 °C until a purple solution was formed. The evolution of hydrogen occurred in this period. This solution was cooled to −20 °C, and then 1 ml of acetic acid in 4 ml of ethanol was injected.[9)]

To a solution of NaTeH, prepared *in situ* as above, a carbonyl compound (2 mmol) and an amine (2 mmol) were added at −20 °C. The resulting mixture was stirred for 20 h at room temperature. The tellurium thus precipitated was filtered, and the filtrate was concentrated *in vacuo*. The residue was dissolved in 20 ml of ethyl acetate and acidified with 3 mol dm^{-3} hydrochloric acid. The combined aqueous layer was made basic with NaOH and extracted with two 30-ml portions of ethyl acetate. The extract was dried over anhydrous Na_2SO_4, concentrated, and purified by TLC (elution with hexane and ethyl acetate). The products were identified by a comparison of their NMR, IR, and mass spectra with those of authentic samples.

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