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Reduction of Imines and Enamines with Hydrogen Telluride. An Application to Reductive Alkylation of Amines with Carbonyl Compounds

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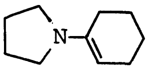
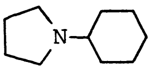
Hydrogen telluride was found to reduce imines and enamines to the corresponding amines under mild conditions. As an application of this reduction,a new method for reductive alkylation of primary and secondary amines with ketones or aldehydes has been developed.

Alkali metal salts[1-9)] of hydrogen telluride (H_2Te) and tellurols (RTeH) have been frequently used in the selective reduction of various functional groups.[10)] On the other hand, little attention has been paid to the reactivity of hydrogen telluride and tellurols themselves. Recently Cava showed that the tellurols act just like as hydrogen telluride in the reduction of some functional groups, but very differently from sodium hydrogen telluride (NaTeH).[11)] We have already reported that hydrogen telluride has a unique reducing ability toward carbonyl groups and some nitrogen containing functional groups.[12,13)] We report here that hydrogen telluride generated in situ from aluminum telluride (Al_2Te_3) and water reduces imines and enamines to the corresponding amines in THF under mild conditions and also that amines react with carbonyl compounds to give alkylated amines in the presence of aluminum telluride under similar conditions.

Reduction of imines and enamines was carried out by the addition of water to a suspension of aluminum telluride and the substrate in THF at -78 °C followed by stirring the mixture for 2 h at 0 °C. Some representative examples are presented in Table 1. The reduction is applicable to aryl and alkyl imines and enamines.

A principal side reaciton is the hydrolysis of the substrates, e.g., aniline (7%) and benzaldehyde (16%) were detected by GLC from a reaction mixture of N-benzylideneaniline. But this has been overcome by the addition of triethylamine. For example, N-butylidenebutylamine gave dibutylamine quantitatively in the presence of triethylamine, although the hydrolysis predominated in the absence of it. Under similar conditions, benzenetellurol is known to reduce N-benzylidene-aniline in a good yield, but the reaction with sodium hydrogen telluride suffered from hydrolysis of N-benzylideneaniline.[11)]

Table 1. Reduction of Imines and Enamine[a)]

Substrate	Product	Yield/%
PhN=CHPh	$PhNHCH_2Ph$	71
EtN=CHPh	$EtNHCH_2Ph$	65
n-BuN=CHPr-n	$n\text{-}Bu_2NH$	45 (100)[b)]
		85

a) Substrate(1 mmol), Al_2Te_3(2 mmol), H_2O(24 mmol), THF(10 ml), 0 °C, 2 h.
b) In the presence of Et_3N(10 mmol).

As an application of the present redution, we attempted reductive N-alkylation of amines with carbonyl compounds by using this reaction system. If condensation of amines and carbonyl compounds proceeds in the presence of aluminum telluride producing one equivalent of water, the imine or enamine formed may be reduced with hydrogen telluride generated from aluminum telluride and the resulting water. Although GLC analysis showed that condensation of butylamine with butanal was complete, desired alkylated amine was not formed when an equimolar amount of butylamine to butanal was used (Table 2, run 1), implying that the stoichiometric amount of water formed was not sufficient for the generation of hydrogen telluride. This was confirmed by the following fact that reductive alkylation proceeded by the use of exess amounts of the amine as a proton source (runs 2-5) or by the addition of water (run 6). The yield was improved when triethylamine was added to the reaction system (run 7).

Table 2. Reductive Alkylation of Butylamine with Butanal[a)]

Run No.	$n\text{-}BuNH_2$ (mmol)	n-PrCHO (mmol)	Additive (mmol)	Time / h	$n\text{-}Bu_2NH$ yield/%[b)]
1	1	1	-	5	0
2	1.5	1	-	5	26
3	2	1	-	5	39
4	5	1	-	5	69
5	10	1	-	5	74
6	1	1	H_2O(24)	0.5	58
7	1	1	H_2O(24), Et_3N(10)	0.5	79

a) Al_2Te_3(2 mmol), THF(10 ml), 66 °C.
b) Based on n-PrCHO used.

In Table 3 are summarized the results obtained from various amines and carbonyl compounds using water and triethylamine.[14] Alkyl substituted amines gave the desired products in satisfactory yields by the reaction with ketones and aldehydes. GLC analysis showed that condensation was complete before addition of water. On the other hand, aniline condensed to a lesser extent (ca. 30%) under similar conditions resulting in poor yields of N-alkylated anilines. When ammonia was used as the substrate, corresponding secondary amine was obtained as the major product together with a tertiary amine. This is probably due to low solubility of ammonia in THF. Use of ammonium acetate and carbonate in place of ammonia did not improve the yields.

Similar reactions are known to proceed using benzeneselenol[15] or sodium hydrogen telluride[16] as the reducing agent. Although a variety of methods are available for reductive N-alkylation of amines,[15-17] the present reaction may be a useful addition to hitherto known methods because of its operational simplicity.

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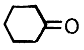
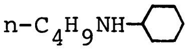
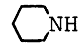
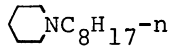
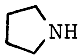
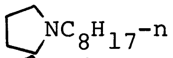
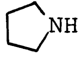
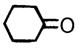
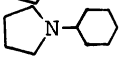
Table 3. Reductive Alkylation of Amines with Carbonyl Compounds[a]

Amine	Carbonyl compound	Product	Yield/%
$n\text{-}C_4H_9NH_2$	$n\text{-}C_7H_{15}CHO$	$n\text{-}C_4H_9NHC_8H_{17}\text{-}n$	96
$n\text{-}C_4H_9NH_2$	PhCHO	$n\text{-}C_4H_9NHCH_2Ph$	89
$n\text{-}C_4H_9NH_2$			82
$t\text{-}C_4H_9NH_2$	$n\text{-}C_7H_{15}CHO$	$t\text{-}C_4H_9NHC_8H_{17}\text{-}n$	86
$PhCH_2NH_2$	$n\text{-}C_7H_{15}CHO$	$PhCH_2NHC_8H_{17}\text{-}n$	80[b]
	$n\text{-}C_7H_{15}CHO$		70[c]
	$n\text{-}C_7H_{15}CHO$		80
			86
$PhNH_2$	$n\text{-}C_7H_{15}CHO$	$PhNHC_8H_{17}\text{-}n$	12[d]
$PhNH_2$	PhCHO	$PhNHCH_2Ph$	22[d]
NH_3[e]	$n\text{-}C_7H_{15}CHO$	$(n\text{-}C_8H_{17})_2NH$	49[f]
NH_3[e]	PhCHO	$(PhCH_2)_2NH$	67[g]

a) Amine(3 mmol), carbonyl compound(3 mmol), Al_2Te_3(2 mmol), H_2O(24 mmol), THF(10 ml), Et_3N(10 mmol).
b) Amine(15 mmol), octanal(15 mmol), Al_2Te_3(14 mmol), H_2O(168 mmol), THF(30 ml), Et_3N(50 mmol).
c) Piperidine(4.5 mmol) was used. d) GLC yield.
e) NH_3 was bubbled. f) Octylamine(0%), trioctylamine(25%).
g) Benzylamine(0%).

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14) A typical experiment is as follows. A THF (30 ml) suspension of benzylamine (15 mmol, 1.67 g), octanal (15 mmol, 1.55 g), triethylamine (50 mmol, 7.0 ml), and aluminum telluride (14 mmol, 6.1 g) was refluxed for 30 min. GLC analysis showed that condensation to give N-octylidenebenzylamine was complete at this stage. Then water (168 mmol, 3.0 g) was added to the suspension at 15 °C. The heterogeneous mixture was refluxed for another 30 min. The black solid was removed by filtration and the filtrate was dried over calcium sulfate. Evaporation of the solvent gave crude product (3.4 g) which was fractionally distilled to give N-octylbenzylamine (2.7 g, 12.3 mmol, 80%, 108-112 °C/1 mmHg).
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