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The Reduction of α,β-Unsaturated Nitriles and α-Halonitriles with Sodium Hydrogen Telluride

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Abstract: Sodium hydrogen telluride reacts chemoselectively with α,β-unsaturated nitriles and α-halonitriles linked to aromatic and aliphatic substituents to give the corresponding saturated nitriles with good yields. Copyright © 1996 Elsevier Science Ltd

Since the first report by Barton[1] in 1975 on a procedure for the preparation of sodium hydrogen telluride a considerable number of papers have been published dealing with the reduction of different functional groups with this reagent,[2] which exhibits great versatility as a selective reducing agent. The reduction of the double bond of α,β-unsaturated carbonyl compounds[3,4] and the dehalogenation of α-halocarbonyl compounds[7] being among its most important applications. Both reactions occur under mild conditions giving high yields of reduced products. Recently we have described the use of this reagent in a highly stereoselective synthesis of sesquiterpenes.[6] Despite the mildness of this method and its synthetic importance no much studies have been made to extent these reactions to other substrates containing electronwithdrawing groups different than carbonyl.[7] Cyano is a very useful synthetic group that shows parallel reactivity to carbonyl group in many aspects. Therefore we have studied the applicability of NaTeH in the reduction of α,β-unsaturated nitriles and α-halonitriles. The results are reported on in this paper.

RESULTS AND DISCUSSION

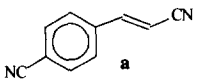
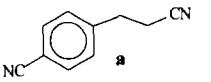
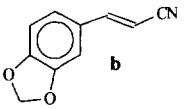
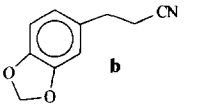
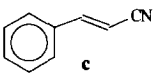
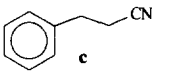
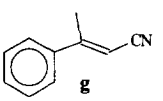
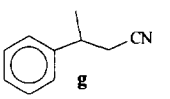
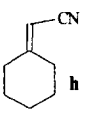
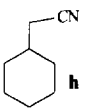
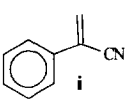
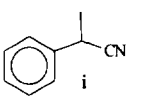
A. Reduction of α,β-unsaturated nitriles

α,β-Unsaturated nitriles can be obtained from aldehydes and ketones by different methods such as dehydration of cyanohydrins[8] or Claisen-like condensations with acetonitrile,[9] which constitute common methods for one or two carbon chain-elongation. Reduction of the double bond affords saturated nitriles (Scheme 1) which can be further transformed in other groups, such as acid, amine, or aldehyde.

$$\underset{\mathbf{1}}{R_\beta R_{\beta'}C{=}CR_\alpha CN} \xrightarrow{NaTeH} \underset{\mathbf{2}}{R_\beta R_{\beta'}HC{-}CHR_\alpha CN}$$

Scheme 1

Table 1. Reduction of α,β-Unsaturated Nitriles with NaTeH

Entry	α,β-unsaturated nitriles **1**	T	time (h)	nitriles **2**	yield[b] (%)
1	 **a**	rt	24	 **a**	85
2	 **b**	rt	24	 **b**	90
3	 **c**	rt	24	 **c**	80
4	$CH_3(CH_2)_7CH{=}CHCN$ **d**	rt	24	$CH_3(CH_2)_9CN$ **d**	90
5	$CH_3OCO(CH_2)_6CH{=}CHCN$ **e**	rt	24	$CH_3OCO(CH_2)_8CN$ **e**	89
6	$CH_2{=}CH(CH_2)_7CH{=}CHCN$ **f**	rt	24	$CH_2{=}CH(CH_2)_9CN$ **f**	90
7	 **g**	reflux	24	 **g**	75[c]
8	 **h**	reflux	24	 **h**	67
9	 **i**	rt	24	 **i**	40

[a] Major E-isomer (entries 1, 2, 3 and 7). Mixtures (entries 4, 5 and 6).

[b] Yields refer to isolated and chromatographically pure compounds.

[c] Starting material **1g** (15 %) was also recovered.

The results of the reduction of several mono and disubstituted acrylonitriles are summarized in Table 1. In general the required reaction times are longer than those in the reduction of unsaturated ketones or esters.[4] The yields are good either with alkyl and aryl acrylonitriles.

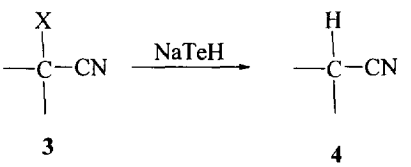
The ease of reduction and yields are sensitive to steric, more than electronic factors. Thus, β-aryl monosubstituted acrylonitriles possessing electron withdrawing groups (entry 1), electron releasing groups (entry 2) or unsubstituted (entry 3), and β-alkyl monosubstituted acrylonitriles (entries 4,5 and 6) react at room temperature with good yields (~ 90%). However β,β-disubstituted acrylonitriles, aromatic (entry 7) or aliphatic (entry 8) were inert under these conditions and were recovered unreacted after 3 days at room temperature. These compounds required reflux temperatures and gave somewhat lower yields. The α-monosubstituted acrylonitrile (entry 9) reacted smoothly at room temperature. However the yield of reduced product was lowered by the formation of an organotellurim byproduct, the structure of which could not be determined.

In order to test the selectivity of NaTeH towards substitution of the double bond, an equimolar mixture of compounds **1c** and **1g** was treated at room temperature for 24 h. The resulting mixture (93 % yield) contained (G.C.) 48% of reduced product **2c**, 42% of starting material **1g** and only 5% of reduced product **2g**.

Other reducible groups such as isolated double bonds (entry 6), and methyl esters (entry 5), were fully compatible with the reaction conditions and remained unaltered after the reduction of the double bond conjugated to the cyano group.

B. Reduction of α-halonitriles

α-Halonitriles can be obtained by reaction of organoboranes with dichloroacetonitrile[10] or by addition of organic halides to acrylonitriles.[11] Alternatively, they can be obtained from the corresponding cyanohydrins by conversion of the hydroxyl group into a halide. The ability of NaTeH to produce hydrogenolysis (Scheme 2) was tested with several α-halonitriles. The results are summarized in Table 2.

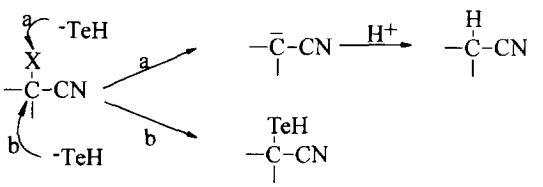


3 **4**

Scheme 2

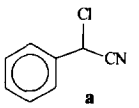
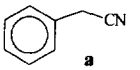
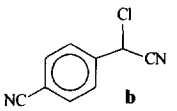
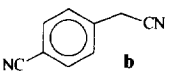
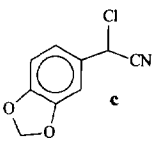
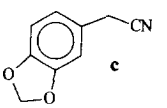
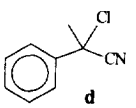
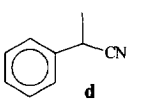
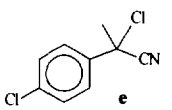
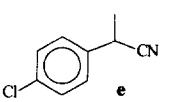
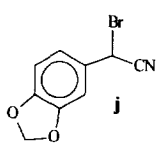
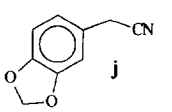
As shown in Table 2, the reduction of α-aryl substituted substrates was complete within 15-20 min at -20 °C whilst α-alkyl substituted substrates required 5 h at room temperature. Some common functional groups as cyano, methyl ester and isolated multiple bond are tolerated by our conditions (entries 2, 7-8) and good yields of dehalogenated products are obtained. Interestingly, this reduction of α-halonitriles is also compatible with the occurrence in the molecule of common good leaving groups (as chloride or mesylate) either on primary or secondary carbons when the reaction is carried out at temperatures between 0 and 5 °C (entries 9-10). Unfortunately, epoxides are not tolerated, and in the reaction conditions (0 - 5 °C) the opening of this group took place faster than the dehalogenation of α-halonitriles. With α-alkyl-α-bromonitriles (entry 12), the reaction of debromination proceeded rapidly (20-30 min) at lower temperatures (- 20 °C), but with somewhat lower yields. However, with the α-aryl substituted bromonitrile **3j** (entry 11) the yields dropped dramatically because of the formation of organotellurium byproducts of undetermined structure.

Conversion of α-halonitriles into nitriles is thought to occur by a similar mechanism as for α-haloketones,[5] via a pathway which involves the attack of hydrogen telluride anion to the halogen atom to give a carbanion (pathway a) which is protonated in the protic solvent to give the final product. When the halogen is chloride either at aliphatic or benzylic positions, this is the most favoured reaction pathway, giving good yields of saturated nitriles. However when the halogen is a bromide ion (a better leaving group), a competitive nucleophilic attack by hydrogen telluride anion can take place (pathway b) to give organotellurium byproducts and, therefore, lowering the yield of the main reaction. This process would be favoured when bromine is at a benzylic position.



It is well known the importance of nitriles in synthetic organic chemistry, since they are versatile intermediates commonly used for many functional group transformations and carbon-carbon bond forming reactions. Nitriles are usually prepared from alkyl halides or sulfonate ester by S_N2 substitutions with cyanide ion.[12] Alternatively, they can be obtained also by one-carbon homologation from a carbonyl group by reaction with tosyl methyl isocyanide (Tosmic)[13] or by cyanophosforylation followed by reduction with samarium diiodide.[14] Therefore our methods constitute interesting complementary methods to others described for the obtention of nitriles with one- or two-carbon homologation, through the corresponding alkenenitriles or α-halonitriles obtained as mentioned above.

Table 2. Reduction of α-Halonitriles with NaTeH

Entry	α-halonitriles **3**	T (°C)	t	Nitriles **4**	yield (%)[a]
1	 **a**	-20	20 min	 **a**	96
2	 **b**	-20	20 min	 **b**	97
3	 **c**	-20	20 min	 **c**	98
4	 **d**	-20	20 min	 **d**	93
5	 **e**	-20	20 min	 **e**	90
6	$CH_3(CH_2)_8CHClCN$ **f**	rt	5 h	$CH_3(CH_2)_9CN$ **f**	97
7	$CH_3OOC(CH_2)_7CHClCN$ **g**	rt	5 h	$CH_3OOC(CH_2)_8CN$ **g**	94
8	$CH_2=CH(CH_2)_8CHClCN$ **h**	rt	5 h	$CH_2=CH(CH_2)_9CN$ **h**	96
9	$ClCH_2(CH_2)_8CHClCN$ **i**	0-5	5 h	$ClCH_2(CH_2)_9CN$ **i**	95
10	$CH_3(CH_2)_8CHClCN$ **f** + $CH_3CHOMs(CH_2)_8CH_3$	0-5	5 h	$CH_3(CH_2)_9CN$ **f** + $CH_3CHOMs(CH_2)_8CH_3$	96 95
11	 **j**	-20	20 min	 **j**	54
12	$CH_3(CH_2)_8CHBrCN$ **k**	-20	30 min	$CH_3(CH_2)_8CHBrCN$ **k**	86

[a] Yields refer to isolated and chromatographically pure compounds

EXPERIMENTAL

NMR spectra were run on a Bruker AC-200 instrument (200.1 MHz for ^{1}H NMR and 50.3 MHz for ^{13}C NMR. Mass spectra were recorded at 70 eV. All the starting materials were obtained from the corresponding carbonyl compounds by standard procedures: α,β-unsaturated nitriles were obtained by condensation of the corresponding carbonyl compounds and acetonitrile with KOH (**1b**, **1h**)[9a] or with buthyllithium followed by dehydration (**1a**, **1g**),[9b] or by dehydration (1. $POCl_3$/py/Bz; 2. Li_2CO_3, LiBr/DMF) of the corresponding cyanohydrins(**1d-1f**, **1i**).[8] α-Chloronitriles were obtained from the corresponding cyanohydrins by treatment with $POCl_3$/py/Bz. Compound **3j** was obtained from the corresponding cyanohydrin and PBr_3 and **3k** was obtained by treatment of the corresponding α-mesyloxynitrile with LiBr in DMF. The preparation of these products were not optimized.

Experimental procedure for the reduction of α,β unsaturated nitriles and α-halonitriles: Te powder (140 mg, 1.09 mmol) and $NaBH_4$ (95 mg, 2.5 mmol) were refluxed in EtOH (4 mL) for 45-60 min. The resulting deep purple solution was cooled at -20 °C and then 0.12 mL of AcOH in 0.5 mL of EtOH were added followed by the substrate (0.5 mmol) in 1 mL of benzene. The reaction mixture was stirred at the indicated temperature for the indicated time. Then, the reaction flask was opened to air and a small amount of silica gel added. After one hour, the mixture was filtered through celite and chromatographed on silica gel.

3-(4'-Cyanophenyl)propanenitrile (**2a**)

^{1}H NMR δ 2.59 (t, J = 7.2 Hz, 2H), 2.93 (t J = 7.2 Hz, 2H), 7.29 (d, J = 8.2 Hz, 1H), 7.54 (d, J = 8.2 Hz) ^{13}C NMR δ 18.4 (t), 31.0 (t), 110.8 (s), 118.3 (s), 129.0 (d), 132.3 (d), 143.2 (s); MS *m/e* 156 (M^+, 100), 128 (30), 117 (82).

3-(3',4'-Methylendioxyphenyl)propanenitrile (**2b**)

^{1}H NMR δ 2.54 (t, J = 7.2 Hz, 2H), 2.83 (t J = 7.2 Hz, 2H), 5.90 (s, 2H), 6.65 (d, J = 7.6 Hz, 1H), 6.68 (s, 1H), 6.74 (d, J = 7.6 Hz, 1H); ^{13}C NMR δ 19.5 (t), 31.5 (t), 101.0 (t), 108.4 (d), 108.6 (d), 119.1 (s), 121.3 (d), 131.7 (s), 146.6 (s), 147.8 (s); MS *m/e* 175 (M^+, 80), 135 (100), 105 (26).

3-Phenylpropanenitrile (**2c**)

^{1}H NMR δ 2.57 (t, J = 7.3 Hz, 2H), 2.92 (t, J = 7.3 Hz, 2H), 7.2-7.4 (m, 5H); ^{13}C NMR δ 19.2 (t), 31.4 (t), 119.1 (s), 127.1 (d), 128.2 (d), 128.8 (d), 138.0 (s); MS *m/e* 131 (M^+, 35), 91 (100).

Undecanenitrile (**2d**), (**4f**) *or* (**4k**)

^{1}H NMR δ 0.84 (t, J = 6.2 Hz, 3H), 1.0-1.4 (m, 14H), 1.59 (m, 2H), 2.29 (t, J = 7.0 Hz, 2H); ^{13}C NMR δ 13.9 (q), 16.9 (t), 22.5 (t), 25.2 (t), 28.5 (t), 28.6 (t), 29.1 (t), 29.2 (t), 29.3 (t), 31.7 (t), 119.7 (s) ; MS *m/e* 152 (M^+-Me, 1), 138 (8), 124 (16), 110 (20), 97 (30).

Methyl 8-cyanooctanoate (**2e**) *or* (**4g**)

^{1}H NMR δ 1.1-1.6 (m, 12 H), 2.20 (m, 4H), 3.58 (s, 3H); ^{13}C NMR δ 16.8 (t), 24.6 (t), 25.1 (t), 28.4 (t), 28.8 (t), 33.8 (t), 51.2 (q), 119.6 (s), 173.9 (s); MS *m/e* 166 (M^+-MeO, 32), 149 (100), 138 (19).

11-Dodecenenitrile (**2f**) *or* (**4h**)

^{1}H NMR δ 0.9-1.4 (m, 12 H), 1.57 (m, 2H), 1.96 (q, J = 6.7 Hz, 2H), 2.25 (t, J = 7.1 Hz, 2H), 4.88 (d, J = 9 Hz, 1H), 4.94 (dd, J = 1.5, 16.9 Hz, 1H), 5.76 (m, 1H); ^{13}C NMR δ 16.9 (t), 25.2(t), 28.5 (t), 28.6 (t), 28.7 (t), 28.9 (t), 29.1 (t), 29.2 (t), 33.6 (t), 114.0 (t), 119.7 (s), 138.9 (s); MS *m/e* 179 (M^+, 2), 164 (8), 150 (44), 136 (93), 122 (100).

3-Phenylbutanenitrile (**2g**).

^{1}H NMR δ 1.44 (d, J = 6.8 Hz, 3H), 2.55 (dd, J = 2.4, 6.5 Hz, 2H), 3.13 (m, 1H), 7.1-7.4 (m, 5H); ^{13}C NMR δ 20.4 (q), 26.0 (t), 36.2 (d), 118.4 (s), 126.4 (d),127.0 (d), 128.6 (d), 142.9 (s); Ms *m/e* 145 (M^+, 27), 105 (100), 77 (56).

Cyclohexylacetonitrile (**2h**)

^{1}H NMR δ 0.8-2.1 (m, 11H), 2.19 (d, J = 6.5 Hz, 2H); ^{13}C NMR δ 24.9 (t), 25.7 (t), 32.4 (t), 34.4 (d), 118.9 (s); MS *m/e* 124 (M^++1, 100), 83 (59), 55 (39).

2-Phenylpropanenitrile (**2i**) *or* (**4d**)

^{1}H NMR δ 1.63 (d, J = 7.3 Hz, 2H), 3.89 (q, J = 7.3 Hz, 1H), 7.3-7.4 (m, 5H); ^{13}C NMR δ 21.4 (q), 31.2 (d), 121.4 (s), 126.6 (d), 127.9 (d), 129.1 (d), 136.9 (s); MS *m/e* 130 (M^+-1, 4), 105 (100).

Phenylacetonitrile (**4a**)

^{1}H NMR δ 3.72 (s, 2H), 7.2-7.4 (m, 5H); ^{13}C NMR δ 23.4 (t), 118.6 (s), 127.8 (d), 127.9 (d), 129.0 (d), 129.9 (s); MS *m/e* 117 (M^+, 100), 90 (42).

4'-Cyanophenylacetonitrile (**4b**)

^{1}H NMR δ 3.82 (s, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.2 Hz, 2H); ^{13}C NMR δ 23.6 (t), 112.0 (s), 116.7 (s), 118.1 (s), 128.7 (d), 132.7 (d), 135.2 (s); MS *m/e* 142 (M^+, 56), 141 (98), 114 (100), 102 (42).

3',4'-Methylendioxyphenylacetonitrile (**4c**) *or* (**4j**)

^{1}H NMR δ 3.61 (s, 2H), 5.93 (s, 2H), 6.74 (s, 3H); ^{13}C NMR δ 23.2 (t), 101.4 (t), 108.4 (d), 108.5 (d), 118.1 (s), 121.2 (d), 123.3 (s), 147.3 (s), 148.2 (s); MS *m/e* 161 (M^+, 98), 160 (100), 131 (73), 103 (98).

2-(4'-Chlorophenyl)propanenitrile (**4e**)

^{1}H NMR δ 1.59 (d, J = 7.2 Hz, 3H), 3.86 (q, J = 7.2 Hz, 1H), 7.1-7.4 (m, 5H); ^{13}C NMR δ 21.1 (q), 30.5 (d), 121.0 (s), 127.9 (d), 129.1 (d), 133.8 (s), 135.4 (s); MS *m/e* 166 (M^+-1, 15), 164 (M^+-1, 43), 129 (62).

11-Chloroundecanenitrile (**4i**)

^{1}H NMR δ 0.9-1.8 (m, 16H), 2.29 (t, J = 6.8 Hz, 2H), 3.49 (t, J = 6.6 Hz, 2H); ^{13}C NMR δ 16.9 (t), 25.2(t), 26.6 (t), 28.4 (t), 28.5 (t), 29.0 (t), 29.1(t), 32.4 (t), 44.9 (t), 119.7 (s); MS *m/e* 202 (M^+-1, 2), 200 (M^++1, 6), 166 (M^+-Cl, 85), 158 (41), 136 (52), 124 (62).

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REFERENCES

1. Barton, D.H.R.; McCombie, S.W. *J.Chem.Soc., Perkin Trans. I* **1975**, 1574.
2. Petragnani, N.; Comasseto, J.V. *Synthesis* **1986**, 1. *Synthesis* **1991**, 793. *Synthesis* **1991**, 897.
3. Yamashita, M.; Kato, Y.; Suemitsu, R. *Chem. Lett.* **1980**, 847.
4. Yamashita, M.; Tanaka, Y.; Arita, A.; Nishida , M. *J. Org. Chem.* **1994**, *59*, 3500.
5. Osuka, A.; Suzuki, H. *Chem. Lett.* **1983**, 119.
6. Blay, G.; Cardona L.; García, B.; Pedro, J.R.; Sánchez, J.J. *J. Org. Chem.* **1996**, in press.
7. Blay, G.; Cardona, L.; García, B.; Pedro, J.R. *Synlett* **1995**, 1189.
8. Oda, M.; Yamamuro, A.; Watabe, T. *Chem. Lett.* **1979**, 1427.
9. a) DiBiase, S.S.; Lipisko, B.A.; Haag, A.; Wolak, R.A.; Gokel, G.W. *J. Org. Chem.* **1979**, *44*, 4640. b) Kaiser, E.W.; Hauser, C.R. *J. Org. Chem.* **1968**, *33*, 3402.
10. Nambu, H.; Brown, H.C. *J. Am. Chem. Soc.* **1970**, *92*, 5790.
11. Mitani, M.; Nakayama, M.; Koyama, K. *Tetrahedron Lett.* **1980**, *21*, 4457.
12. Tennant, G.. *The Synthesis and Reactions of Organic Compounds. Vol 2*. Barton, D.H.R. and Ollis, W.D. Ed. Pergamon Press. Oxford **1979**.
13. Van Leusen, A.M.; Oomkes, P.G. *Synthetic Commun.* **1980**, *10*, 399.
14. Yoneda, R.; Harusawa, S.; Kurihara, T. *Tetrahedron Lett.* **1989**, *30*, 3681.

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