

Novel Reaction of Dibutyl(cyanomethyl)telluronium Chloride with Carbonyl Compounds Mediated by Organolithium Reagents: Highly Efficient Synthesis of β -Hydroxy Nitriles†

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Dibutyl(cyanomethyl)telluronium chloride, a precursor of stabilized telluronium ylides, after being treated with organolithium reagents reacted with carbonyl compounds to afford β -hydroxy nitriles instead of α,β -unsaturated nitriles in excellent yields.

Recently there has been a remarkable interest in the synthetic application of organotellurium reagents.¹⁻³ However, little attention has been paid to telluronium ylides compared with sulphonium and selenium ylides.⁴⁻⁶ Osuka *et al.* reported that the stabilized and moderately stabilized tellurium ylides are reactive towards carbonyl compounds, giving rise to alkenes and epoxides, respectively.⁷⁻⁹ We found that diphenyl-telluronium methylide, the first non-stabilized telluronium ylide, generated from methyldiphenyltelluronium tetraphenylborate with lithium, 2,2,6,6-tetramethylpiperidide (LiTMP), reacted with aldehydes or ketones to form substituted oxiranes.¹⁰ In our previous paper we reported that the reactions of trimethyl- and methyldiphenyl-telluronium salts (precursors of non-stabilized telluronium ylides) with aldehydes gave secondary alcohols by the use of organolithium reagents.¹¹ We also reported that reactions of carbonyl compounds with benzylidibutyltelluronium bromide (precursor of a semi-stabilized telluronium ylide) afforded homobenzylic alcohols in a reaction mediated by organolithium reagents.¹²

In 1988, X. Huang *et al.* reported that dibutyl(cyanomethyl)-telluronium chloride **1**, on treatment with potassium *t*-butoxide, gave the stabilized telluronium ylide dibutyltelluronium cyanomethylide, which condensed with carbonyl compounds to yield α,β -unsaturated nitriles in moderate yields.¹³ In this paper we report a quite different result, in that dibutyl(cyanomethyl)-telluronium chloride **1**, a precursor of a stabilized telluronium ylide, after being treated with a nucleophilic organolithium reagent, reacts with a variety of carbonyl compounds to afford β -hydroxy nitriles instead of α,β -unsaturated nitriles in excellent yields.

β -Hydroxy nitriles are an important class of compounds because the cyano group can undergo several transformations.¹⁴ Among many methods for generating nitrile anions,¹⁵ the Reformatsky-type reaction between bromoacetonitrile and carbonyl compounds induced by zinc represents one of the most useful methods for the preparation of β -hydroxy nitriles.¹⁶ However, under standard conditions the expected β -hydroxy nitriles are produced only in moderate yield.¹⁷ Although somewhat better yields could be obtained from the preformed organozinc intermediate¹⁸ or by the use of other metals,¹⁹ the reaction is still limited in scope. We report herein a novel synthesis of β -hydroxy nitriles with the advantages of easy availability of the reagent **1**, simplicity of procedure, and excellent yields.

Dibutyl(cyanomethyl)telluronium chloride **1** was easily prepared from the reaction of dibutyl telluride and chloroacetonitrile at room temperature. The telluronium salt **1**, after

Table 1 Synthesis of β -hydroxy nitriles 3^a

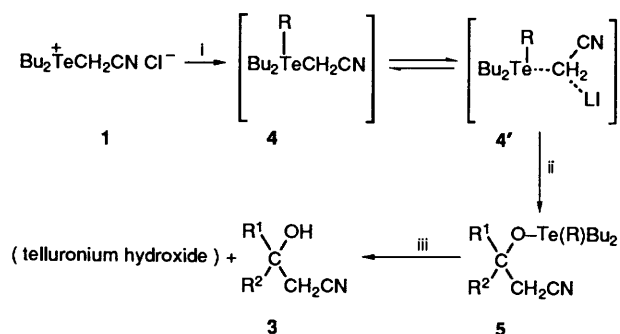
Product 3	RLi	R ¹	R ²	Yield (%) ^b
a	Bu	Ph	H	95
b	Me	4-ClC ₆ H ₄	H	92
b	Ph	4-ClC ₆ H ₄	H	91
b	4-MeC ₆ H ₄	4-ClC ₆ H ₄	H	93
b	Bu	4-ClC ₆ H ₄	H	98
c	Bu	2-ClC ₆ H ₄	H	95
d	Bu	4-FC ₆ H ₄	H	96
e	Bu	4-BrC ₆ H ₄	H	97
f	Bu	2-Naphthyl	H	98
g	Bu	4-MeOC ₆ H ₄	H	97
h	Bu	4-Me ₂ NC ₆ H ₄	H	95
i	Bu	2,4-(MeO) ₂ C ₆ H ₃	H	95
j	Bu	3,4-(OCH ₂) ₂ C ₆ H ₃	H	92
k	Bu	Cyclohexyl	H	88
l	Bu	Pr	H	90
m	Bu	Pentyl	H	92
n	Bu	Ph	Ph	85
o	Bu	Ph	Me	94

^a All reactions were performed as described in the text. ^b For the isolated product.

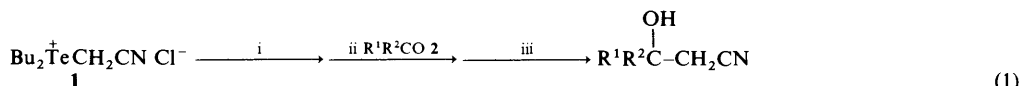
being treated with an alkyl- or phenyl-lithium, reacted with carbonyl compounds **2** to give alcohols, *viz.* β -hydroxy nitriles **3** in excellent yields [eqn. (1)], instead of the corresponding alkenes²⁰ or epoxides,²¹ the Wittig-type reaction products expected by analogy with the reactions of other heteroatom ylides. The preparation of compounds **3** has been performed on a variety of structurally different carbonyl compounds to determine the scope of the reaction. Some experimental results are summarized in Table 1 and illustrate the efficiency, the applicability, and the scope of the present method. Conversion of carbonyl compounds into β -hydroxy nitriles usually proceeds completely when the mixture was allowed to warm to room temperature, and the reaction works well with both enolizable and non-enolizable carbonyl compounds. As for the potentially unreactive substrates, such as 2,4-dimethoxybenzaldehyde, 4-(dimethylamino)benzaldehyde, and piperonal, the yields of the expected β -hydroxy nitriles are still excellent. It is particularly noteworthy that, in the absence of RLi, the reaction did not take place under the same conditions unless the mixture was refluxed in tetrahydrofuran (THF) to give α,β -unsaturated nitrile.¹³

This RLi-promoted condensation of dibutyl(cyanomethyl)-telluronium chloride with carbonyl compounds giving rise to β -hydroxy nitriles is novel. Various lithium reagents such as BuLi, MeLi, *p*-MeC₆H₄Li and PhLi could promote the reaction effectively. Instead of formation of a telluronium ylide, as in the case of phosphonium²⁰ or arsonium²¹ analogues, an unstable tetraorganyltellurium intermediate **4** may be formed, as in the

† This paper is the 92nd report on the synthetic application of elemento-organic compounds of the 15th and 16th groups.



Scheme 1 Reagents: i, RLi; ii, 2; iii, water



2a; R ¹ = Ph	R ² = H	2i; R ¹ = 2,4-(MeO) ₂ C ₆ H ₃	R ² = H
2b; R ¹ = 4-ClC ₆ H ₄	R ² = H	2j; R ¹ = 3,4-OCH ₂ OC ₆ H ₃	R ² = H
2c; R ¹ = 2-ClC ₆ H ₄	R ² = H	2k; R ¹ = Cyclohexyl,	R ² = H
2d; R ¹ = 4-FC ₆ H ₄	R ² = H	2l; R ¹ = Pr,	R ² = H
2e; R ¹ = 4-BrC ₆ H ₄	R ² = H	2m; R ¹ = Pentyl,	R ² = H
2f; R ¹ = 2-Naphthyl,	R ² = H	2n; R ¹ = Ph,	R ² = Ph
2g; R ¹ = 4-MeOC ₆ H ₄ ,	R ² = H	2o; R ¹ = Ph,	R ² = Me
2h; R ¹ = 4-Me ₂ NC ₆ H ₄ ,	R ² = H		

Reagents and conditions: i, RLi, THF, -70 °C; ii, -70 °C to room temp.; iii, water

case of Bu_3TeI .²² Owing to the weakness of the Te-C bond which is polarized in the presence of Li^+ , species **4** underwent nucleophilic addition to carbonyl compounds through cleavage of one of the substituents as shown in Scheme 1. The cyanomethyl group is transferred preferentially, so we obtained only the β -hydroxy nitriles and no other alkylated alcohols.

In addition to the synthetic utility for the preparation of β -hydroxy nitriles, this reaction is of mechanistic interest in view of the first demonstration that dibutyl(cyanomethyl)telluronium chloride, a precursor of a stabilized telluronium ylide, reacts with carbonyl compounds to give exclusively β -hydroxy nitriles when treated with strong nucleophilic bases, a result quite different from that obtained with phosphonium and arsonium analogues.

Experimental

M.p.s and b.p.s are uncorrected. M.p.s were measured on a Thiele apparatus. ¹H NMR spectra were determined in CDCl_3 on a Varian EM-360L (60 MHz) spectrometer with SiMe_4 as the internal standard; *J*-values are given in Hz. IR spectra were recorded on a Shimadzu IR-400 instrument. Mass spectral data were obtained by electron ionization (EI) on a Finnigan 4021 spectrometer.

All the reactions were carried out under nitrogen. All solvents and materials were dried and redistilled before use. Dibutyl telluride was prepared according to the procedure reported by Balfe *et al.*²³

Synthesis of Dibutyl(cyanomethyl)telluronium Chloride 1.—Dibutyl telluride (12 mmol) was syringed into chloroacetonitrile (12 mmol) under nitrogen. The mixture was stirred for 4 h to afford a crystalline product (95%), m.p. 93–94 °C (lit.,¹³ 92–93 °C); δ_{H} 1.05 (6 H, t, *J* 4), 1.50 (4 H, m), 2.10 (4 H, m), 3.10 (2 H, s) and 3.15 (4 H, t, *J* 4); $\nu_{\text{max}}(\text{KCl})/\text{cm}^{-1}$ 2230.

Synthesis of β -Hydroxy Nitriles 3. General Procedure.—A solution of RLi (1.5 mmol) in hexane was syringed into a

solution of dibutyl(cyanomethyl)telluronium chloride (1.5 mmol) in dry THF at -70 °C under nitrogen. After 1 h, a solution of a carbonyl compound (1.0 mmol) in THF (2 cm³) was added. After the reaction was complete (monitored by TLC), ethyl acetate was added. The resulting mixture was filtered through a short column of silica gel. The solvent was evaporated off under reduced pressure, and flash chromatography gave the pure product.

3-Hydroxy-3-phenylpropanenitrile 3a (95%), b.p. 165–166 °C/2 mmHg (lit.,²⁴ 154–155 °C/1 mmHg); δ_{H} 2.53 (2 H, d, *J* 6), 3.65 (1 H, br), 4.75 (1 H, t, *J* 6) and 7.20 (5 H, s); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3450vs and 2230m; *m/z* (%) 147 (M^+ , 3), 130 (5), 107 (94) and 77 (100).

3-(4-Chlorophenyl)-3-hydroxypropanenitrile 3b (98%), oil;²⁵ δ_{H} 2.63 (2 H, d, *J* 6), 3.62 (1 H, br), 4.90 (1 H, t, *J* 6) and 7.22 (4 H, s); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3450s and 2240m; *m/z* (%) 182 (M^+ + 1, 22), 181 (M^+ , 8), 165 (37) and 142 (100).

3-(2-Chlorophenyl)-3-hydroxypropanenitrile 3c (95%), oil;²⁵ δ_{H} 2.65 (2 H, d, *J* 6), 3.60 (1 H, br), 4.92 (1 H, t, *J* 6) and 7.45 (4 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3455s and 2235m.

3-(4-Fluorophenyl)-3-hydroxypropanenitrile 3d (96%), b.p. 150–152 °C/1 mmHg; δ_{H} 2.53 (2 H, d, *J* 6), 3.59 (1 H, br), 4.77 (1 H, t, *J* 6) and 6.97 (4 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3450s and 2240m; *m/z* (%) 165 (M^+ , 20), 148 (5), 125 (48), 123 (55), 95 (55) and 71 (100) (Found: C, 65.1; H, 5.15; N, 8.45; F, 11.5. $\text{C}_9\text{H}_8\text{FNO}$ requires C, 65.45; H, 4.88; N, 8.48; F, 11.50%).

3-(4-Bromophenyl)-3-hydroxypropanenitrile 3e (97%), b.p. 159–160 °C/1 mmHg (lit.,¹⁹ 147–148 °C/0.49 mmHg); δ_{H} 2.60 (2 H, d, *J* 6), 3.67 (1 H, br), 4.82 (1 H, t, *J* 6) and 7.27 (4 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3440s and 2245m; *m/z* (%) 227, 225 (M^+ , 5), 210, 208 (2), 187, 185 (100) and 157 (23).

3-Hydroxy-3-(2-naphthyl)propanenitrile 3f (98%), m.p. 68–70 °C; δ_{H} 2.40 (2 H, d, *J* 6), 3.73 (1 H, br), 4.73 (1 H, t, *J* 6) and 7.38 (7 H, m); $\nu_{\text{max}}(\text{KCl})/\text{cm}^{-1}$ 3430s and 2240m; *m/z* (%) 197 (M^+ , 43), 180 (5), 157 (83), 129 (100) and 127 (60) (Found: C, 79.2; H, 5.6; N, 6.9. $\text{C}_{13}\text{H}_{11}\text{NO}$ requires C, 79.17; H, 5.62; N, 7.10%).

3-Hydroxy-3-(4-methoxyphenyl)propanenitrile 3g (97%), b.p. 175 °C/4 mmHg (lit.,²⁶ 173 °C/4 mmHg); δ_{H} 2.70 (2 H, d, *J* 6), 3.28 (1 H, br), 3.75 (3 H, s), 4.95 (1 H, t, *J* 6), 6.85 (2 H, d, *J* 8) and 7.25 (2 H, d, *J* 8); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3450vs and 2240s; *m/z* (%) 177 (M^+ , 5), 169 (5) and 137 (100).

3-(4-Dimethylaminophenyl)-3-hydroxypropanenitrile 3h (95%), oil;²⁵ δ_{H} 2.51 (2 H, d, *J* 6), 2.78 (6 H, s), 3.42 (1 H, br), 4.68 (1 H, t, *J* 6), 6.58 (2 H, d, *J* 8) and 7.11 (2 H, d, *J* 8); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3430vs and 2235m; *m/z* (%) 190 (M^+ , 26), 173 (8) and 150 (100).

3-(2,4-Dimethoxyphenyl)-3-hydroxypropanenitrile 3i (95%), m.p. 90–91 °C (lit.,²⁶ 89.5–90.5 °C); δ_{H} 2.75 (2 H, d, *J* 6), 3.20 (1 H, s), 3.82 (3 H, s), 3.86 (3 H, s), 5.10 (1 H, t, *J* 6), 6.49 (1 H, s), 6.59 (1 H, d, *J* 7) and 7.38 (1 H, d, *J* 7); $\nu_{\text{max}}(\text{KCl})/\text{cm}^{-1}$ 3450s and 2250m.

3-Hydroxy-3-(3,4-methylenedioxyphenyl)propanenitrile **3j** (92%), m.p. 79–80 °C (lit.,²⁶ 80.5–81.0 °C); δ_{H} 2.70 (2 H, d, *J* 6), 3.64 (1 H, br), 4.89 (1 H, t, *J* 6), 5.94 (2 H, s) and 6.85–6.95 (3 H, m); $\nu_{\text{max}}(\text{KCl})/\text{cm}^{-1}$ 3450vs and 2250m; *m/z* (%) 191 (M^+ , 32), 174 (5), 151 (100), 93 (75) and 65 (52).

3-Cyclohexyl-3-hydroxypropanenitrile **3k** (88%), b.p. 100–102 °C/1 mmHg; δ_{H} 1.26–1.73 (11 H, m), 2.60 (2 H, d, *J* 6), 3.16 (1 H, br) and 3.70 (1 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3450s and 2245m; *m/z* (%) 154 ($\text{M} + 1$, 89), 136 (50), 113 (9), 95 (100), 83 (76) and 55 (80) (Found: C, 70.5; H, 9.85; N, 9.15. $\text{C}_9\text{H}_{15}\text{NO}$ requires C, 70.55; H, 9.87; N, 9.14%).

3-Hydroxyhexanenitrile **3l** (90%), b.p. 96 °C/5 mmHg (lit.,¹⁹ 114 °C/11 mmHg); δ_{H} 0.90 (3 H, t, *J* 4), 1.35 (4 H, m), 2.55 (2 H, d, *J* 6), 3.25 (1 H, br) and 3.92 (1 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3455s and 2240m.

3-Hydroxyoctanenitrile **3m** (92%), b.p. 115 °C/2 mmHg (lit.,¹⁹ 83 °C/0.34 mmHg); δ_{H} 0.88 (3 H, t, *J* 4), 1.33 (8 H, m), 2.53 (2 H, d, *J* 6), 3.23 (1 H, br) and 3.93 (1 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3455vs and 2240m.

3-Hydroxy-3,3-diphenylpropanenitrile **3n** (85%), m.p. 142–143 °C (lit.,²⁴ 141.5–143 °C); δ_{H} 2.82 (1 H, br), 3.25 (2 H, s) and 7.38 (10 H, s); $\nu_{\text{max}}(\text{KCl})/\text{cm}^{-1}$ 3450s and 2290m; *m/z* (%) 223 (M^+ , 5), 206 (3), 183 (100), 105 (95) and 77 (62).

3-Hydroxy-3-phenylbutanenitrile **3o** (94%), b.p. 150–151 °C/4 mmHg (lit.,²⁴ 149–150 °C/4 mmHg); δ_{H} 1.63 (3 H, s), 2.78 (2 H, s), 3.44 (1 H, br) and 7.33 (5 H, m); $\nu_{\text{max}}(\text{neat})/\text{cm}^{-1}$ 3420s and 2240m; *m/z* (%) 161 (M^+ , 40), 144 (10), 121 (80), 105 (100) and 77 (68).

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References

- 1 T. G. Back, *The Chemistry of Organic Selenium and Tellurium Compounds*, ed. S. Patai, Wiley, New York, 1987, p. 2.
- 2 L. Engman, *Acc. Chem. Res.*, 1985, **18**, 274.

- 3 N. Petragnani and J. V. Comasset, *Synthesis*, 1986, 1.
- 4 B. M. Trost and L. S. Melvin, Jr., *Sulfur Ylides*, Academic, New York, 1975.
- 5 W. Dumont, P. Bayet and A. Krief, *Angew. Chem., Int. Ed. Engl.*, 1974, **13**, 2574.
- 6 K. Jakaki, M. Yasumura and K. Negoro, *Angew. Chem., Int. Ed. Engl.*, 1981, **20**, 671.
- 7 A. Osuka, Y. Mori, H. Shimizu and H. Suzuki, *Tetrahedron Lett.*, 1983, **24**, 2599.
- 8 A. Osuka and H. Suzuki, *Tetrahedron Lett.*, 1983, **24**, 5109.
- 9 A. Osuka, Y. Hanasaki and H. Suzuki, *Nippon Kagaku Kaishi*, 1987, 1505 (*Chem. Abstr.*, 1988, **108**, 131 223w).
- 10 L. L. Shi, Z. L. Zhou and Y. Z. Huang, *Tetrahedron Lett.*, 1990, **31**, 4173.
- 11 L. L. Shi, Z. L. Zhou and Y. Z. Huang, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2847.
- 12 S. W. Li, Z. L. Zhou, Y. Z. Huang and L. L. Shi, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1099.
- 13 X. Huang, L. H. Xie and H. Wu, *J. Org. Chem.*, 1988, **53**, 4862.
- 14 H. Henecka and O. Erwin, in *Houben-Weyl, Methoden der Organischen Chemie*, 4th ed., ed. E. Muller, Georg Thieme Verlag, Stuttgart, 1952, vol. 8, pp. 427, 661.
- 15 For a review on nitrile-stabilized carbanions, see S. Areniyadis, K. S. Kyler and D. S. Watt, *Org. React.*, 1984, **31**, 1.
- 16 For a recent reviews, see M. Gaudemar, *Organomet. Chem. Rev.*, 1972, **8**, 183; L. Miginiac, in *The Chemistry of the Metal-Carbon Bond*, ed. F. R. Hartley and S. Patai, Wiley, New York, 1985, vol. 3, p. 99.
- 17 N. S. Vul'fson and L. K. Vinograd, *Zh. Obshch. Khim.*, 1959, **29**, 2690; J. Canceill and J. Jacques, *Bull. Soc. Chim. Fr.*, 1970, 2180.
- 18 N. Goasdoue and M. Gaudemar, *J. Organomet. Chem.*, 1972, **39**, 17; *Organometallic Synthesis*, ed. R. B. King and J. J. Eisch, Elsevier: Amsterdam, 1988, vol. 4, p. 414.
- 19 S. I. Inaba and R. D. Rieke, *Tetrahedron Lett.*, 1985, **26**, 155.
- 20 A. Maercker, *Org. React.*, 1965, **14**, 270.
- 21 A. W. Johnson and J. O. Martin, *Chem. Ind. (London)*, 1965, 1726.
- 22 D. Hellwinkle and G. Farbach, *Chem. Ber.*, 1968, **101**, 574.
- 23 M. P. Balfe, C. A. Chaplin and H. Phillips, *J. Chem. Soc.*, 1938, 341.
- 24 E. M. Kaiser and C. R. Hauser, *J. Org. Chem.*, 1968, **33**, 3402.
- 25 H. Hamana and T. Sugawara, *Chem. Lett.*, 1982, 1401.
- 26 K. Takahashi, K. Sasaki, H. Tanabe, K. Yamada and H. Iida, *Nippon Kagaku Kaishi*, 1973, 2347 (*Chem. Abstr.*, 1974, **80**, 70 499v).

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