

β -Butyltellanyl Carbonyl Compounds: A Useful Source of Masked Metal Homo-enolates

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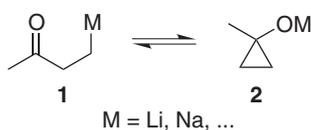
Cianocupratos de ordem superior e homo-enolatos de lítio secundários, foram eficientemente gerados a partir de β -butil teluro cetais e submetidos a reação com benzaldeído e 2-ciclohexen-1-ona.

Secondary higher order cyanocuprates and lithium homo-enolates, were efficiently generated from β -butyltellanylketals and reacted with benzaldehyde and 2-cyclohexen-1-one.

Keywords: tellurides, tellurium / lithium exchange, secondary lithium homo-enolates and higher order cyanocuprates

Introduction

Homo-enolate anions are important synthons in the Umpolung concept.¹ Unlike the enolate anions, the homo-enolate anions cannot be stoichiometrically generated by deprotonation of a carbonyl compound, since the pK_a value of the β -hydrogen is only very slightly lowered.² In addition, the reactive homo-enolates **1**, especially lithium and sodium derivatives, spontaneously cyclize to the corresponding cyclopropanolate tautomer **2** (Scheme 1),² which does not react as a carbon-nucleophile with standard electrophiles.

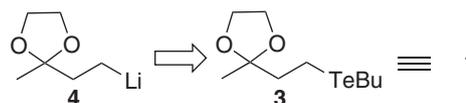


Scheme 1.

Although the α -enolization of carbonyl compounds is readily carried out under mild conditions to yield high equilibrium concentrations of α -enolates, vigorous conditions are required to give low concentrations of short-lived intermediate homo-enolates by β -deprotonation of nonenolizable ketones.² This fact makes the direct β -deprotonation of carbonyl compounds an impracticable method for preparative purposes. The use of a masked carbonyl unit is an alternative to circumvent this problem.³

However, this strategy is also limited to the presence of strongly electron-attracting substituents at the β -position to the masked carbonyl groups that promotes the stabilization of the carbanion formed. Classically, for this purpose nitro,⁴ phosphorus⁵ and sulphur⁶ based compounds are used. Moreover, this method requires previous preparation of the nitro, phosphorus or sulphur organic substrates and another further step, to remove reductively the activating group.

A simple strategy to circumvent this problem should be the preparation of β -butyltellanyl masked carbonyl compounds such as **3**,⁷ and their transformation into the corresponding lithium homo-enolates through a tellurium/lithium exchange reaction (Scheme 2).⁸

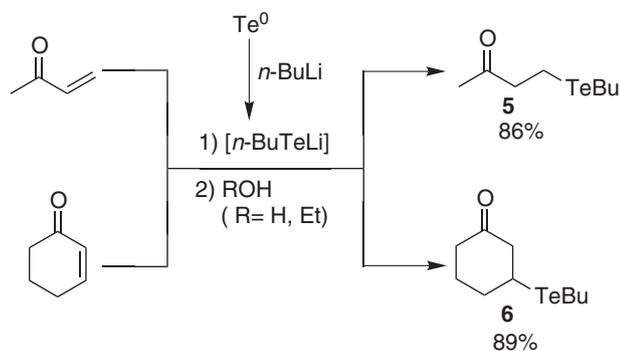


Scheme 2.

A general way to obtain compounds of type **3** should be the Michael addition of *n*-butyltellurol to α,β -unsaturated ketones, as recently described by us,⁹ followed by a ketalization reaction.

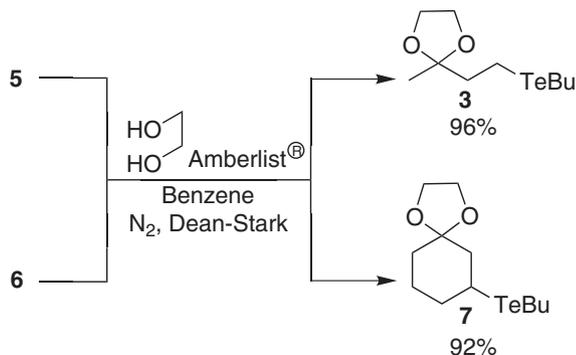
The *n*-butyltellurol, generated in situ by reaction of elemental tellurium with *n*-BuLi in THF, followed by addition of a proton source such as ethanol or water, reacts rapidly with Michael acceptors.⁹ Under these conditions the β -butyltellanylketones **5** and **6** were successfully prepared in 86% and 89% yield respectively (Scheme 3).

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Scheme 3.

The β -butyrtellanylketones **5** and **6** were converted into the corresponding β -butyrtellanylketals **3** and **7** in high yields by reaction with ethylene glycol in benzene in a Dean-Stark apparatus (Scheme 4).^{9,10}



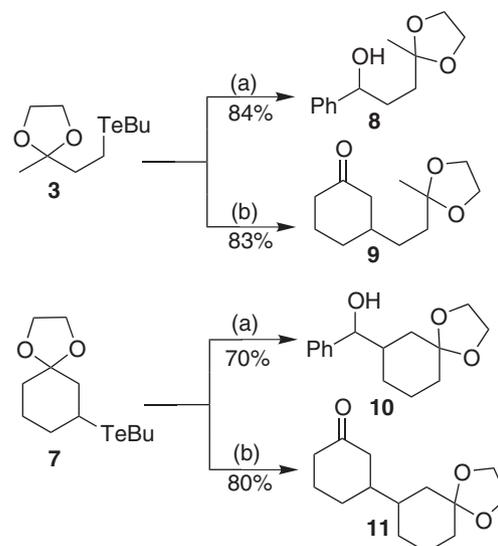
Scheme 4.

The light yellow tellurides **3** and **7** were transformed into the corresponding lithium masked homoenolates by reaction with *t*-butyllithium in THF at -70 °C. The tellurium/lithium exchange showed to be very fast even to generate a secondary anion.

Trapping the lithium anions with benzaldehyde afforded the corresponding alcohols **8** and **10** (Scheme 5).¹¹ The lithium intermediates were also submitted to reaction with the copper soluble species $\text{CuCN}\cdot 2\text{LiCl}$ ¹² producing the corresponding higher order cyanocuprates.¹³ Michael addition of these intermediates to 2-cyclohexen-1-one produced the corresponding saturated ketones (Scheme 5).¹³

All tellurides described in this paper are stable to the ambient light and can be manipulated in the air. Most of them are almost odourless or present a smell not more unpleasant than most of the laboratory chemicals normally used in an organic synthesis laboratory.

It is worthy of note that the dibutyrtelluride originated in the tellurium/lithium exchange step, is totally compatible



Scheme 5. (a): 1) *t*-BuLi (1 Equiv); 2) benzaldehyde. (b): 1) *t*-BuLi (1 Equiv.); 2) $\text{CuCN}\cdot 2\text{LiCl}$ (0.5 Equiv.); 3) 2-cyclohexen-1-one (1 Equiv.).

with all the subsequent operations. It can be easily eliminated in an odourless operation by washing the organic phase with a diluted sodium hypochlorite solution.

In conclusion, β -butyrtellanyl carbonyl compounds are a very practical source of homoenolate equivalents.

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10. General procedure for the preparation of the β -butyltellanylketals **3** and **7**: To a two bottomed flask equipped with a Dean-Stark reflux apparatus were added the appropriate β -butyltellanylketone **5** or **6** (5 mmol), benzene (10 mL), ethylene glycol (8 mmol, 0.44 mL) and Amberlist® (30 mg). The reaction mixture was refluxed under nitrogen atmosphere for 5 hours. The mixture was filtered and the residue washed with ethyl acetate. The solvents were removed under reduced pressure. The residue was purified by silica gel chromatography eluting with a mixture of hexane:ethyl acetate (15:1), to give 2-(2-(butyltellanyl)ethyl)-2-methyl-1,3-dioxolane (**3**). Yield: 1.43 g (96%); ¹H NMR: (300 MHz, CDCl₃, ppm) δ 3.95 (m, 4 H); 2.60-2.66 (m, 4 H); 2.10-2.16 (m, 2 H); 1.72 (quint, *J* 7.3 Hz, 2 H); 1.38 (sext, *J* 7.3 Hz, 2 H); 1.32 (s, 3H); 0.92 (t, *J* 7.3 Hz, 3H); ¹³C NMR: (75 MHz, CDCl₃, ppm) δ 110.2; 64.7; 42.1; 34.2; 25.0; 23.5; 13.3; 2.7; -5.6; LRMS *m/z* (rel. int.) 302 (M⁺, 3); 99 (4); 87 (100); 55 (15); 43 (58); IR (film) ν_{\max} /cm⁻¹: 2979; 2958; 2927; 2874; 1457; 1378; 1246; 1212; 1040; 944; ¹²⁵Te NMR (CDCl₃, 157.79 MHz / 298 K / Ph₂Te₂) δ (ppm) 263.3; Anal. Calc. for C₁₀H₂₀O₂Te: C, 40.13; H, 6.68; Found: C, 40.35; H, 6.46. 7-butyltellanyl-1,4-dioxaspiro [4.5]hexane (**7**). Yield: 1.49 g (92%); ¹H NMR: (300 MHz, CDCl₃, ppm) δ 3.94 (t, *J* 0.8 Hz, 4 H); 3.30 (m, 1 H); 2.66 (t, *J* 7.2 Hz, 2 H); 2.00-2.23 (m, 2 H); 1.50-1.90 (m, 8 H); 1.37 (sext, *J* 7.2 Hz, 2H); 0.91 (t, *J* 7.2 Hz, 3H); ¹³C NMR: (75 MHz, CDCl₃, ppm) δ 108.7; 64.2; 44.8; 35.5; 34.5; 34.4; 25.2; 25.0; 16.1; 13.4; 2.3; LRMS *m/z* (rel. int.) 328 (M⁺, 10); 141 (87); 99 (100); 79 (12); 69 (18); 57 (13); 55 (44); 41 (70). IR(film) ν_{\max} /cm⁻¹: 2953; 2933; 1448; 1356; 1299; 1164; 1063; 1025; ¹²⁵Te NMR (CDCl₃, 157.79 MHz / 298 K / Ph₂Te₂) δ (ppm) 423.31; Anal. Calc. for C₁₂H₂₂O₂Te: C, 44.30; H, 6.76; Found: C, 44.49; H, 6.72.
11. Typical procedure for the tellurium / lithium exchange reaction and capture of the resulting organolithium with benzaldehyde: to a solution of telluride **3** (1 mmol, 0.29 g) in THF (5 mL), at -70 °C was added *t*-butyllithium (1.0 mmol, 0.89 mL, 1.12 mol L⁻¹ in pentane). After 5 min was added benzaldehyde (1 mmol, 0.1 mL). The reaction mixture was allowed to warm to 0 °C. The mixture was stirred for 1 h and then diluted with ethyl acetate (5 mL). The organic phase was sequentially washed with a diluted solution of sodium hypochlorite (2 x 5 mL) and brine (2 x 5 mL), dried over magnesium sulphate, filtrated and evaporated. The residue was purified by column chromatography on silica gel using a 2:1 hexane:ethyl acetate mixture as eluent, to give 3-(2-methyl-1,3-dioxolan-2-yl)-1-phenylpropan-1-ol (**8**). Yield: 0.18 g (84%); CAS N^o: 167644-51-1.
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13. Typical procedure to prepare the higher order cyanocuprate and its reaction with 2-cyclohexen-1-one: To a solution of the lithium anion of telluride **7** (1 mmol, 0.32 g, generated by the same procedure described in ref. 11) at -70 °C, was added a solution of CuCN.2LiCl (0.5 mmol, 1 mol⁻¹ / THF, 0.5 Equiv.). The resulting orange solution was stirred for 20 min at the same temperature and then 2-cyclohexen-1-one (1 Equiv.) was added in one portion. The resulting solution was stirred for 1 h at -70 °C and then allowed to warm to 0 °C. A solution of saturated aqueous ammonium chloride and ammonium hydroxide was added (3 mL) and the mixture was stirred for 40 min. The organic phase was sequentially washed with a diluted solution of sodium hypochlorite (2 x 5 mL) and then with brine (2 x 10 mL), dried over magnesium sulphate, filtered and the solvents were removed. The residue was purified by silica gel chromatography using a 3:1 hexane:ethyl acetate mixture, to give a diastereomeric mixture of 3-(1,4-Dioxaspiro[4.5]dec-7-yl)-cyclohexanone (**II**). Yield: 0.19 g (80%); ¹H NMR: (300 MHz, CDCl₃, ppm) δ 3.92-3.94 (m, 4H); 2.22-2.50 (m, 3 H); 2.04-2.13 (m, 2 H); 1.04-1.7 (m, 12 H); 0.86-0.98 (m, 1 H); ¹³C NMR: (75 MHz, CDCl₃, ppm) δ 212.1; 109.4; 64.3; 64.2; 45.4; 44.0; 43.9; 41.5; 40.3; 38.7; 38.5; 34.9; 34.8; 28.5; 28.4; 28.3; 25.5; 25.4; 23.2; 23.1; LRMS *m/z* (rel. int.) 238 (M⁺, 2); 195 (3); 141 (100); 113 (11); 112 (12); 99 (90); 86 (28); 55 (33); 42 (16); 41 (41); IR(film) ν_{\max} /cm⁻¹: 2938; 2866; 1711; 1448; 1355; 1159; 1085; 919; 516; Anal. Calc. for C₁₄H₂₂O₃: C, 70.49; H, 9.23; Found: C, 70.29; H, 9.11.

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