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Tetrahedron
Tetrahedron 63 (2007) 5167–5172

Tellurium/lithium exchange reactions in the synthesis of spiroketals and 1,6-dioxygenated systems

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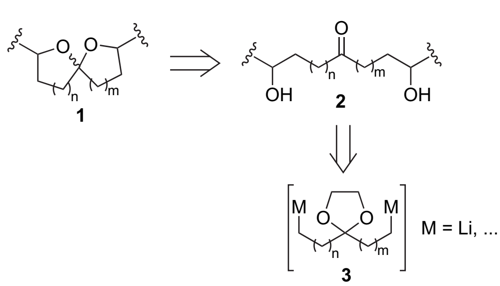
Received 6 March 2007; revised 29 March 2007; accepted 30 March 2007
Available online 6 April 2007

Abstract—1,4-C,O-dianions have been generated through concomitant acid/base and tellurium/lithium exchange reactions. The di-lithium salts were transmetallated with cerium chloride to the corresponding di-cerium salts and subsequently reacted with lactones and carboxylic acid anhydrides to yield the respective spiroketals. The di-lithium entities were also converted into the corresponding cyanocuprates that add in a 1,4-manner to 2-cyclohexen-1-one to form 1,6-dioxygenated compounds.

1. Introduction

The spiroketal ring system (**1**, Scheme 1) is a subunit that is found in naturally occurring compounds derived from a wide variety of different sources including bacteria, fungi, plants and insects.[1] Although the subunit may be encountered both in structurally very simple and in highly complex molecules, the majority of natural products bearing the spiroketal moiety comprises 1,7-dioxaspiro[5.5]undecane, 1,6-dioxaspiro[4.5]decane or 1,6-dioxaspiro[4.4]nonane ring systems.[1,2] Moreover, such systems are also present in most of the pheromones that possess a spiroketal ring,[1] and hence much of the research in this area has focused on these specific structural classes.



Scheme 1.

Recent interest in the biological activities of spiroketal compounds has lead to the development of a number of strategies for the synthesis of this ring system.[1,2] The principal route to **1** involves the acid-catalysed cyclisation of dihydroxy ketones **2** or their equivalents (Scheme 1).[1]

A useful approach to the synthesis of **2** involves organometallic species, particularly organolithium compounds, of the type **3** (Scheme 1). Various methods are available for the preparation of appropriate organolithium analogues, the most common of which involves halogen/lithium or tin/lithium exchange.[3] Organolithium species can be subsequently transformed into other organometallics by transmetallation with salts of metals that are more electronegative than lithium. Formation of organolithium compounds via tellurium/lithium exchange appears to offer a number of advantages over alternative methods in that it is both fast and clean.[4] However, this methodology is not often employed, probably as a consequence of negative comments in the literature concerning the unpleasant odour and the relative instability of organotellurium compounds. As we have pointed out recently, these comments do not always apply.[5]

We have previously demonstrated that the functionalised alkyltellurides **4** and **5** are efficient precursors of homoenolates **6**[6,7] and dianionic species **7**[8] (Scheme 2). In the present study, we have employed the lithium salts **7** and **7a** (derived from hydroxy tellurides **5** and **5a**, respectively) as precursors of 1,6-[4.4]-spiroketals and 1,6-hydroxy-ketones in a reaction sequence involving transformation of the initially obtained lithium compounds into cerium and copper species.

Keywords: Organocerium; Tellurium/lithium exchange; Spiroketals.
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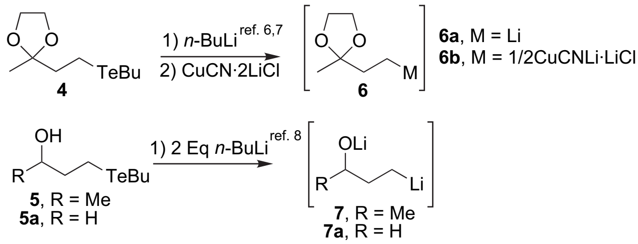
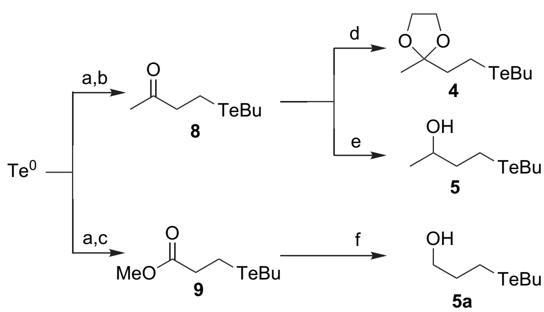
doi:10.1016/j.tet.2007.03.178



Scheme 2.

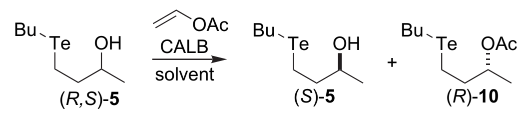
2. Results and discussion

n-Butyltellurol, generated in situ from elemental tellurium and *n*-butyllithium in the presence of a proton source such as water or ethanol, reacts with methyl vinyl ketone to produce the corresponding β-butyltelluro ketone **8**.[9] This telluride can be transformed into the telluro-ketal **1** by reaction with ethylene glycol in the presence of Amberlyst®, and into the hydroxy telluride **5** when treated with an ethanolic or aqueous solution of sodium borohydride (Scheme 3). Alternatively, **5** could be synthesised in 74% isolated yield in a one-pot process by hydrotelluration of methyl vinyl ketone and subsequent in situ reduction of **8** by the addition of sodium borohydride to the reaction mixture. Hydroxy telluride **5a** could be prepared in 78% yield by hydrotelluration of methyl acrylate (**9**), followed by reduction of the ester group with lithium aluminium hydride. These protocols complement our earlier studies on the reduction of butyltelluro carbonyl compounds to the corresponding alcohols.[5]



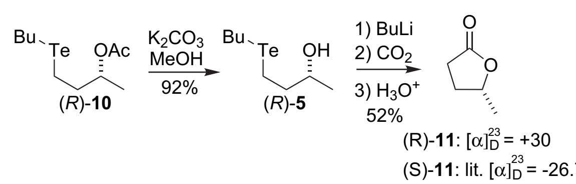
Scheme 3. (a) (1) *n*-BuLi; (2) H_2O; (b) methyl vinyl ketone; (c) methyl acrylate; (d) ethylene glycol, Amberlyst®; (e) $NaBH_4$ (aqueous solution); (f) $LiAlH_4$ (3 equiv).

The enzymatic kinetic resolution of hydroxy telluride **5** was carried out using a typical procedure[10] involving the sequential addition of *Candida antarctica* lipase-B (CALB) and vinyl acetate to a racemic mixture of **5** dissolved in an appropriate solvent (i.e., hexane or THF). In hexane, the chiral acetate (*R*)-**10** was obtained with a 96% enantiomeric excess (ee) but in very low isolated yield (<5%). The observation of a white powder in the reaction medium, coupled with the poor yield obtained, suggested that **5** was probably transformed into a telluroxide. This problem was solved by performing the enzymatic resolution of **5** in THF in which the acetate (*R*)-**10** was produced in 36% yield and with high enantioselectivity (>200). The unreacted alcohol could be recovered in 30% yield and with a high ee (99%) (Scheme 4; Table 1).



Scheme 4.

The absolute configurations of the chiral acetate **10** and of the unreacted alcohol **5** obtained from the enzymatic process were assigned indirectly by conversion of **10** into the natural product γ-valerolactone (**11**) (Scheme 5) followed by comparison of the optical rotation of the synthetic product with literature data.[11] Treatment of the 1,4-C,O-dianion, generated by the reaction of (*R*)-**5** with 2 equiv of *n*-butyllithium in THF, with carbon dioxide followed by an acid workup yielded **11** in 52% isolated yield.



Scheme 5.

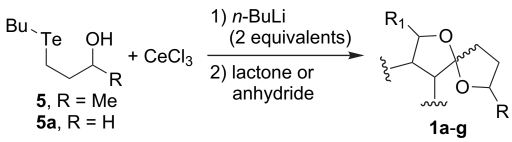
The lithium salts **7** and **7a** (Scheme 2) were transformed into the cerium analogues by transmetallation with cerium trichloride. These intermediates could be reacted with lactones and anhydrides which, following acid workup, afforded the corresponding spiroketals **1a**–**1g**. Initially, these reactions were performed according to the classical procedures for the preparation of organocerium compounds, namely, generation of the organolithium compound followed by addition of a suspension of cerium trichloride in THF.[12] This process is typically carried out at ca. −40 °C, and often requires a long reaction time (>1 h). In the present study, however, mixtures of cerium trichloride and **5** or **5a** in THF were prepared at −70 °C and then reacted with *n*-butyllithium (Scheme 6). TLC analysis revealed that the hydroxy telluride was totally consumed within 5 min following the addition of *n*-butyllithium. The di-cerium salt was then added to the appropriate lactone or anhydride in diethyl ether at

Table 1. Enzymatic resolution of hydroxy telluride (*R*,*S*)-**5**[a]

Entry	Solvent	Reaction time (h)	Conversion (%)	Enantiomeric excess (*S*)-**5** (%)	Enantiomeric excess (*R*)-**10** (%)	Yield (%)	Enantioselectivity
1	Hexane	1	45	80	96	—	
2	Hexane	4	49	90	95	<5	120
3	THF	8	48	93	99		
4	THF	12	50	99	98	36	>200

[a] Substrate (0.5 mmol); CALB 30 mg in hexane (10 mL) or 50 mg in THF (10 mL); temperature 30 °C.

−70 °C (Scheme 6; Table 2). This procedure is operationally far simpler than that of previously published methods.

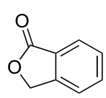
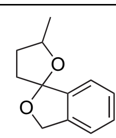
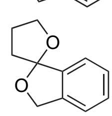
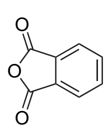
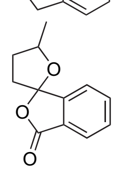
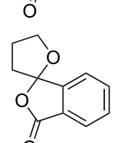
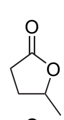
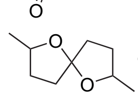
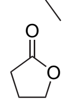
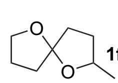
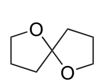


Scheme 6.

Reasonable yields of spiroketals were obtained using the described protocols (Table 2). The mono-spiroketals **1c** and **1d** were the only products formed even when 2 equiv of the di-cerium salt were employed. In the case of spiroketals **1a**, **1c**, **1e** and **1f**, mixtures of *E* and *Z* stereomers were produced and the quoted yields refer to the sum of the isomers.

In the synthesis of the chiral spiroketal **1e**, (*S*)-γ-valerolactone (**11**; produced by the route shown in Scheme 5) was reacted with the chiral di-cerium salt (*R*)-**12** (derived from (*R*)-**5**) with the inverse configuration. Compound **1e** was formed as a 1:1 mixture of *E*,*Z*- and *Z*,*E*-stereomers (Fig. 1B), whilst less than 3% of the other stereomers was detected following chiral GC analysis (Scheme 7, Fig. 1A and B).

Table 2. Reaction of di-cerium salts with lactones and anhydrides

Entry	Substrate	Telluride[a]	Product	Yield (%)
1		**5**	 **1a**	65[b]
2		**5a**	 **1b**	65[b]
3		**5**	 **1c**	52[b]
4		**5a**	 **1d**	56[b]
5		**5**	 **1e**	74[c]
6		**5**	 **1f**	66[c]
7		**5a**	 **1g**	68[d]

[a] *n*-Butyllithium was added to the mixture of hydroxy telluride and cerium trichloride.
[b] Isolated yield.
[c] Yield determined by GC analyses (spiroketal **1g** was employed as internal standard).
[d] Yield determined by GC analyses (spiroketal **1f** was employed as internal standard).

The volatile spiroketals **1e**, **1f** and **1g** were isolated in pure form but only in low yields (<30%), even after most careful distillation of the solvent. This result is in agreement with previous reports concerning this class of volatile compounds.[13]

As a part of our studies concerning the preparation of functionalised organometallics, the dianions **7** and **7a** were also converted into the corresponding cyanocuprates by reacting with the complex CuCN·2LiCl (1/2 equivalent). The preformed cyanocuprate[14] was added to a solution of 2-cyclohexen-1-one and the corresponding hydroxy ketones **13** and **13a** were obtained, respectively, in isolated yields of 62 and 67% (Scheme 8).

Finally, it is noteworthy that, as has been the case for many other tellurides prepared in our laboratory, those described in the present study are light yellow oils and are either odourless or present a smell that is not more unpleasant than other chemicals usually employed in organic synthesis. Moreover, the compounds are stable under ambient conditions and can be manipulated using normal procedures with no appreciable decomposition. However, prolonged contact of telluride solutions, especially those involving hexane, with air should be avoided in order to prevent transformation of substrate into telluroxide. This problem can be minimised through the use of deoxygenated solvents. Tellurides are totally compatible with many common functional group transformations, including carbonyl reduction or protection, enzymatic and chemical acylation and de-acylation. The applicability of hydroxy tellurides as versatile sources of functionalised organometallics has been amply demonstrated in the present study.

3. Experimental section

3.1. General

Tellurium metal (<200 mesh), lithium aluminium hydride, sodium borohydride and cerium trichloride heptahydrate were purchased from Sigma Aldrich. Immobilised lipase-B from *C. antarctica* (CALB; Novozym 435®; 10,000 PLU/g) was kindly donated by Novozymes Inc. All reagents and solvents were previously purified and dried.[15] THF was distilled under nitrogen from sodium/benzophenone just before use. *n*-Butyllithium was titrated using 1,10-phenanthroline as indicator prior to use. Nitrogen gas was deoxygenated and dried. Cerium trichloride heptahydrate was dried according to a reported procedure.[16] All operations were carried out in flame-dried glassware.

Column chromatographic separations were performed over Vetec silica gel 60 (0.063–0.200 mm; 70–230 mesh) or Acros Organics silica gel (0.035–0.075 mm; pore diameter ca. 6 nm). NMR spectra were recorded on Bruker model AC-200 and Varian model FT-300 spectrometers with samples dissolved in deuterochloroform. The internal references were TMS (^{1}H NMR), the central peak of the deuterochloroform signal (^{13}C NMR) and a capillary of diphenyl ditelluride 1 mol L^{-1} (^{125}Te NMR). IR spectra were recorded on a Bomem MB-100 spectrophotometer, whilst optical rotations were determined on a Jasco DIP 370 digital

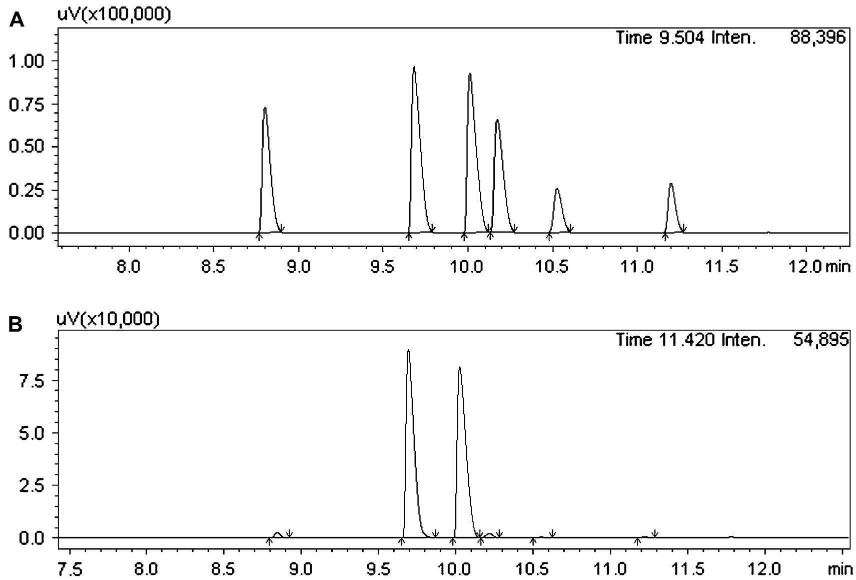
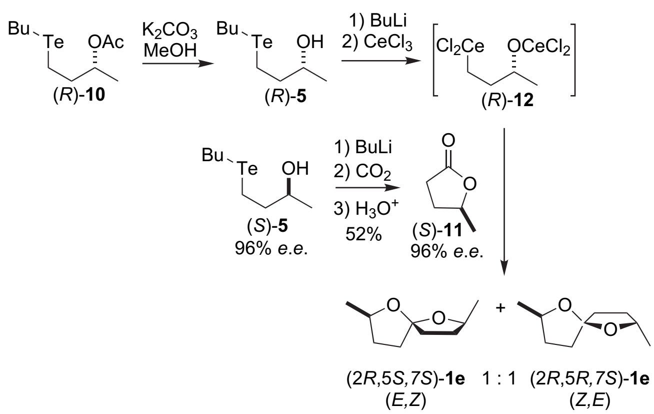
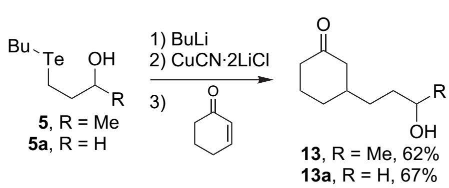


Figure 1.



Scheme 7.



Scheme 8.

polarimeter. Chiral GC analyses were performed on a Shimadzu GC-17A instrument coupled to a flame ionisation detector and equipped with a Varian Chromopack™ Chirasil-Dex CB (β-cyclodextrin packing) capillary column (25 m× 0.25 mm i.d.; 0.25 μm) with hydrogen as the carrier gas. Mass spectra were recorded by coupling the GC to a Shimadzu model QP 5050A mass spectrometer.

3.1.1. One-pot procedure for the preparation of 4-(butyltellanyl)butan-2-ol (5).[8] *n*-Butyllithium (1.69 mol L^{-1} in hexane: 23.7 mL, 40 mmol) was added slowly at room temperature to a suspension of elemental tellurium (5.10 g, 40 mmol) in dry THF (80 mL). Deoxygenated water (1.8 mL, 100 mmol) was added to the light yellow solution of lithium butyl tellurolate so formed, and the resulting red-brown mixture was stirred at room temperature for 10 min and subsequently cooled to 0 °C. Methyl vinyl ketone (3.32 mL, 40 mmol) was added in a single portion, and the resulting mixture was stirred whilst being warmed to room temperature. The progress of the reaction was monitored by TLC. After stirring for 1 h at room temperature, sodium borohydride (1.52 g, 40 mmol) was added to the mixture, which was then gently warmed to 50 °C. After a reaction time of 10 min, all of the telluro ketone had been converted into hydroxy telluride (as determined by TLC analysis), and the resulting brown solution was cooled to room temperature. Deoxygenated water (20 mL) was added slowly over a period of 20 min, the reaction mixture was shaken vigorously, a further 40 mL of deoxygenated water was introduced and the phases were separated. The organic phase was washed with saturated ammonium chloride solution (100 mL), and the aqueous phases were combined and extracted with ethyl acetate (2×200 mL). The organic phases were combined, dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. The crude product was purified by CC over silica gel eluted with cyclohexane/ethyl acetate (4:1) to yield 7.7 g (74%) of oil **5** (CAS No. 861399-10-2).

3.1.2. One-pot procedure for the preparation of 3-(butyltellanyl)propan-1-ol (5a). *n*-Butyllithium (1.69 mol L^{-1} in hexane: 17.7 mL, 30 mmol) was added slowly at room temperature to a suspension of elemental tellurium (3.83 g, 30 mmol) in dry THF (60 mL). Deoxygenated water (1.35 mL, 75 mmol) was added to the light yellow solution of lithium butyl tellurolate so formed, and the resulting red-brown mixture was stirred at room temperature for 10 min and subsequently cooled to 0 °C. Methyl acrylate (2.7 mL, 30 mmol) was added in a single portion, and the resulting mixture was stirred whilst being warmed to room temperature. The progress of the reaction was monitored by TLC. After stirring for 1 h at room temperature, the reaction mixture was cooled to 0 °C and lithium aluminium hydride (3.4 g, 90 mmol) was added slowly in three portions (0.5, 1.0 and 1.9 g, respectively). The mixture was warmed to room temperature and then gently heated at 50 °C. After a reaction time of 20 min, all of the telluro ester had been converted into hydroxy telluride (as determined by TLC analysis), and the resulting mixture was cooled to 0 °C. Deoxygenated water (ca. 30 mL) was added slowly over a period of 30 min, the resulting slurry was filtered and the residue washed with diethyl ether (2×30 mL). The organic phases were combined, washed with saturated ammonium chloride solution (2×30 mL), dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. The crude product was purified by CC over silica gel eluted with cyclohexane/ethyl acetate (3:1) to afford 5.7 g (78%) of oil **5a**—^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.89 (t, ^3J=7.2 Hz, 3H), 1.36 (sext, ^3J=7.2 Hz, 2H), 1.70 (quint, ^3J=7.5 Hz, 2H), 1.91–2.00 (m, 3H), 2.63 (t, ^3J=7.5 Hz), 2.66 (t, ^3J=7.5 Hz), 3.66 (t, ^3J=6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 2.1, 2.8, 13.3, 25.0, 34.2, 34.6, 63.9; ^{125}Te NMR (157.79 MHz, 298 K, $CDCl_3$), δ (ppm): 244.45; MS, *m/z* (%): 246 (26%) [M^{2+}], 244 (24%) [M^+], 242 (15%), 240 (3%), 188 (6%), 186 (7%), 172 (23%), 170 (23%), 168 (13%), 144 (4%), 142 (2%), 130 (6%), 126 (4%), 57 (100%), 41 (86%): Anal. Calcd for $C_7H_{16}OTe$: C, 34.49; H, 6.61. Found: C, 34.79; H, 6.56.

3.1.3. Enzymatic kinetic resolution of 4-(butyltellanyl)-butan-1-ol (5). Hydroxy telluride **5** (0.13 g, 0.5 mmol) was dissolved in 10 mL of deoxygenated hexane or THF, and vinyl acetate (5 equiv) and CALB (0.03 g for hexane or 0.05 g for THF) were added. The reaction mixture was stirred and the course of the reaction was monitored by chiral GC. After ca. 50% conversion had been achieved, the enzyme was removed by filtration and the resulting solution was concentrated under reduced pressure. The organic residue was subjected to CC over silica gel eluted with hexane/ethyl acetate (4:1) to yield 0.019 g (30%) of an oil corresponding to the alcohol (*S*)-**5** ($[\alpha]_D^{22}$ +7 (*c* 1.0, CH_2Cl_2); ee=99%), and 0.027 g (36%) of an oil corresponding to the acetate (*R*)-**10**—^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 0.92 (t, *J*=7.5 Hz, 3H), 1.23 (d, *J*=6.3 Hz, 3H), 1.38 (sext, *J*=7.5 Hz, 2H), 1.72 (quint, *J*=7.5 Hz, 2H), 2.04 (s, 3H), 1.87–2.11 (m, 2H), 2.49–2.67 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 3.6, 2.8, 13.4, 19.5, 21.3, 25.0, 34.2, 38.8, 72.2, 170.6; ^{125}Te NMR (157.79 MHz, 300 K, $CDCl_3$), δ (ppm): 270.15; $[\alpha]_D^{22}$ +18 (*c* 1.0, CH_2Cl_2); ee=98%. Anal. Calcd for $C_{10}H_{20}O_2Te$: C, 40.05; H, 6.72. Found: C, 40.02; H, 6.53.

3.1.4. Hydrolysis of (*R*)-4-(butyltellanyl)butan-2-yl acetate (10). Potassium carbonate (0.03 g, 0.2 mmol) was added to telluride (*R*)-**10** (0.30 g, 1 mmol) dissolved in methanol (5 mL) and water (1 mL), and the mixture stirred for 1 h at room temperature, diluted with water (5 mL) and extracted with ethyl acetate (2×5 mL). The organic phase was washed with brine (2 mL), dried over magnesium sulfate and the solvent removed under reduced pressure. The resulting residue was purified by CC over silica gel eluted with hexane/ethyl acetate (4:1) to yield 0.24 g (92%) of the light yellow oil (*R*)-**5**.

3.1.5. Synthesis of (*R*)-(+)-γ-valerolactone (11). *n*-Butyllithium (1.4 mol L^{-1} in hexane: 7.15 mL, 10 mmol) was added to a solution of hydroxy telluride (*R*)-**5** (96% ee, 1.28 g, 5 mmol) dissolved in dry THF (25 mL) that had been cooled to −70 °C. The resulting light yellow solution was stirred at −70 °C for 5 min and dry carbon dioxide gas was introduced, by means of a needle immersed into the solution, producing a white gel after ca. 15 min. The mixture was warmed to room temperature, hydrochloric acid (50% v/v, 6 mL) was added, the whole stirred for 30 min at room temperature and the phases separated. The aqueous phase was washed with ethyl acetate (2×5 mL), and the combined organic phases dried over magnesium sulfate, filtered and the solvent removed by distillation. The resulting residue was purified by CC over silica gel eluted with hexane/ethyl acetate (1:1) to yield 0.26 g (52%) of the colourless oil (*R*)-**11** (CAS No. 58917-25-2).

3.1.6. General procedure for the preparation of spiroketals. *n*-Butyllithium (1.4 mol L^{-1} in hexane: 2.87 mL, 4 mmol) was added slowly to a mixture of anhydrous cerium chloride (0.98 g, 4 mmol) and hydroxy telluride **5** (0.51 g, 2 mmol) or **5a** (0.48 g, 2 mmol) in dry THF (40 mL) that had been cooled to −70 °C. The whole was stirred at −70 °C for 2 h, warmed to −40 °C, stirred for 1 h at this temperature, re-cooled to −70 °C and finally transferred via a cannula to another flask containing a solution of the appropriate carbonyl compound (lactone or anhydride, 2 mmol) in diethyl ether (5 mL). The resulting mixture was stirred for 1.5 h at −70 °C, warmed to room temperature, and hydrochloric acid (10% v/v, 20 mL) added with constant stirring for 20 min. The phases were separated and the aqueous phase was extracted with diethyl ether (2×5 mL). The combined organic phases were washed, dried and the solvent removed under reduced pressure (compounds **1a–1d**) or by distillation (volatile spiroketals **1e–1g**). In each case the resulting residue was purified by CC over silica gel to produce the respective products.

The oil **1a** was obtained in a yield of 0.74 g (65%) following elution with hexane/diethyl ether (7:1)—^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.32 (d, ^3J=6.3 Hz, 1H), 1.41 (d, ^3J=6.0 Hz, 1H), 1.71–1.87 (m, 1H), 2.30–2.47 (m, 3H), 4.37 (sext, ^3J=6.0 Hz, 1H), 4.45 (sext, ^3J=6.3 Hz, 1H), 4.95 (d, ^1J=12.6 Hz, 1H), 4.98 (d, ^1J=12.6 Hz, 1H), 5.17 (d, ^1J=12.6 Hz, 1H), 5.22 (d, ^1J=12.6 Hz, 1H), 7.23–7.27 (m, 1H), 7.33–7.37 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 21.2, 22.4, 32.6, 32.8, 37.1, 38.5, 70.6, 70.7, 75.4, 77.2, 116.9, 117.0, 121.0, 121.9, 127.6, 127.7, 128.7, 139.4, 139.5, 139.9, 140.0; MS, *m/z* (%): 190 (22%) [M^+], 175 (29%), 146 (35%), 135 (100%), 117 (16%), 105 (25%), 89 (21%), 77 (26%), 63 (10%), 51 (12%), 41 (11%). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.66; H, 7.53.

The oil **1b** (CAS No. 139697-84-0) was obtained in a yield of 0.72 g (65%) following elution with hexane/diethyl ether (7:1).

The oil **1c** (CAS No. 180198-87-2) was obtained in a yield of 0.21 g (52%) following elution with hexane/ethyl acetate (1:2).

The oil **1d** (CAS No. 177780-65-3) was obtained in a yield of 0.21 g (56%) following elution with hexane/ethyl acetate (1:2).

Compound **1e** (CAS No. 106356-13-2) was obtained in a yield of 74% (determined by GC analysis with **1g** as internal standard) following elution with pentane/diethyl ether (5:1).

Compound **1f** (CAS No. 5451-15-0) was obtained in a yield of 66% (determined by GC analysis with **1g** as internal standard) following elution with pentane/diethyl ether (5:1).

Compound **1g** (CAS No. 76041-89-9) was obtained in a yield of 68% (determined by GC analysis with **1f** as internal standard) following elution with pentane/diethyl ether (5:1).

3.1.7. General procedure for the preparation of cyanocuprates from hydroxy tellurides 5 and 5a, and their reaction with 2-cyclohexen-1-one. A solution of the appropriate dianion **7** or **7a** (4 mmol; prepared similarly as described in Section 3.1.5) was added to a solution of the complex $CuCN\cdot 2LiCl$ (1 mol L^{-1} in THF, 2 mL, 2 mmol) that had been further diluted with THF (10 mL) and cooled to −70 °C. The resulting clear, light yellow solution was stirred at −70 °C for 1 h and then transferred via a cannula to another flask containing 2-cyclohexen-1-one (0.2 g, 2 mmol) in THF (4 mL). The resulting mixture was stirred at −70 °C for 30 min, warmed to room temperature and then diluted with ammonium hydroxide/ammonium chloride solution (10% m/v, 5 mL) and diethyl ether (5 mL). The mixture was maintained under vigorous stirring for 30 min and the phases separated. The organic phase was washed with brine (2×3 mL) and the aqueous phase was extracted with ethyl acetate (5 mL). The combined organic phases were dried over magnesium sulfate, filtered and the solvent removed under reduced pressure. In each case the resulting residue was purified by CC over silica gel eluted with ethyl acetate/hexane (3:1).

The oil **13** was obtained in a yield of 0.21 g (62%)—^{1}H NMR (300 MHz, $CDCl_3$), δ (ppm): 1.19 (d, ^3J=6.1 Hz, 3H), 1.33–2.48 (m, 13H), 3.77 (sext, ^3J=6.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ (ppm): 23.4, 25.0, 25.1, 31.0, 31.2, 32.5, 36.1, 36.2, 38.9, 39.0, 41.3, 47.9, 48.0, 67.8, 67.9, 212.0; MS, *m/z* (%): 170 (2%) [M^+], 152 (6%), 110 (69%), 97 (100%), 82 (48%), 67 (62%), 55 (82%), 45 (84%), 41 (88%). Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.35; H, 10.53.

The oil **13a** (CAS No. 69441-81-2) was obtained in a yield of 0.21 g (67%).

Acknowledgements

The authors wish to thank the Brazilian granting authorities FAPESP, CAPES and CNPq for financial support. Generous gifts of lipase and *n*-butyllithium from Novozymes Inc. and Petroflex Inc., respectively, are gratefully acknowledged.

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