Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 48 (2007) 1485–1487

Tellurium in organic synthesis: synthesis of bioactive butenolides

Bruno K. Bassora,[a] Carlos E. Da Costa,[a] Rogério A. Gariani,[a] João V. Comasseto[a] and Alcindo A. Dos Santos[b,*]

[a]*Instituto de Química, Universidade de São Paulo, CP 26077, 05599-070, São Paulo SP, Brazil*
[b]*Departamento de Química, Universidade Federal de São Carlos, 13565-905, São Carlos SP, Brazil*

Received 27 October 2006; revised 1 December 2006; accepted 12 December 2006
Available online 16 January 2007

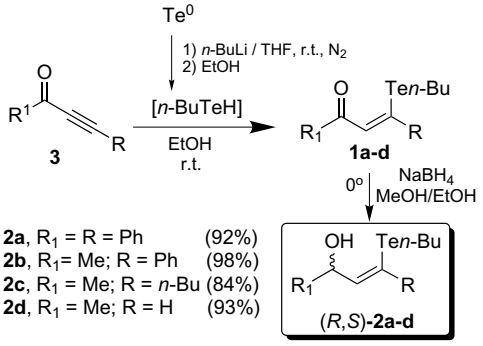
Abstract—Reduction of (*Z*)-β-butyltelluro-enones gives the corresponding γ-hydroxy vinylic tellurides with retention of the double bond configuration. Reaction of γ-hydroxy vinylic tellurides with 2 equiv of *n*-butyllithium produces 1,4-C,O-dianions, which on reaction with carbon dioxide give the corresponding butenolides.

Several methods are available to introduce tellurium into organic molecules with high regio- and stereoselectivity.[1] The tellurium atom can be removed from the resulting organotellurides under mild conditions. The most employed methods for this purpose are the tellurium/metal exchange reaction[1,2] and the coupling reaction promoted by Pd^0 [3] and Ni^0.[4] These facts make organotellurium compounds versatile reagents for organic synthesis.[1b,d] It is worth mentioning that most of the functionalized tellurides, contrary to comments found in the literature, are not bad smelling compounds and can be manipulated safely in the presence of light and air, provided a long contact with these agents is avoided.[5] In recent years, the unique features of the organic chemistry of tellurium were explored in the synthesis of some bioactive natural products.[5b,6]

In this work we describe a route to butenolides starting from γ-hydroxy vinyl tellurides **2**, which can be prepared by the reduction of **1** with common reducing systems.[7]

The β-butyltelluro enones **1** were prepared by hydrotelluration of the corresponding alkynones **3**.[8] The γ-hydroxy vinylic tellurides **2a**–**d** were prepared by reacting the appropriate β-butyltelluro enones **1** with sodium borohydride in methanol/ethanol at 0 °C (Scheme 1).[7]

With the (*Z*)-γ-hydroxy vinylic tellurides **2** in hand, the butenolides were obtained in an one-pot procedure, by



Scheme 1. Preparation of γ-hydroxy vinylic tellurides.

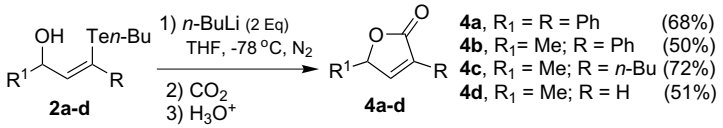
treating **2** with *n*-BuLi and then with carbon dioxide, followed by an acid workup (Scheme 2).[9]

It is worth mentioning that butenolides **4b** present a moderate activity against filamentous fungi,[10] while **4c** is a metabolite from *Streptomyces griseus*[11] and **4d** is angelicalactone, a flavoring agent.[12]

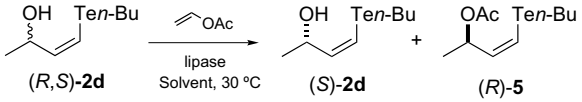
In order to demonstrate that the methodology can be stereoselective, telluride **2d** was submitted to an enzymatic screening aiming to its kinetic resolution. Three lipases were investigated, **PPL** (free porcine pancreatic lipase—42 units/mg prot), **PSL** (Amano PS—free *Pseudomonas* sp. Lipase—30,000 u/g), and **CALB** (NOVOZYM 435®—immobilized *Candida antartica* lipase type B—10,000 PLU/g). Scheme 3 and Table 1 summarize the enzymatic performance of those lipases with **2d** in hexane, THF, and a 1:1 mixture of hexane/THF.

* Corresponding author. Tel./fax: +55 (016) 3351 8299; e-mail: alcindo@dq.ufscar.br

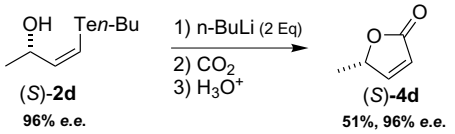
0040-4039/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.12.063



Scheme 2. Tellurium/lithium exchange mediated synthesis of butenolides.



Scheme 3. Enzymatic resolution of telluride (*R*,*S*)-**2d**.



Scheme 4. Synthesis of (*S*)-β-angelicalactone from (*S*)-**2d**.

The enantioenriched acetate (*R*)-**5** was obtained in a high enantiomeric excess using **CALB** and **PPL** in different solvent systems (entries 1–11). Modest and poor ee values were obtained for acetate (*R*)-**5** and alcohol (*S*)-**2**, respectively, when **PSL** was employed as a biocatalyst (entries 12 and 13). On the other hand, the enantiomeric excess of the unreacted alcohol (*S*)-**2d** was good in presence of **CALB** using hexane as a solvent (entry 3) and moderate in a 1:1 mixture of THF/hexane (entry 9). In all other cases the optical purity of the (*S*)-**2d** was only modest.

The absolute configuration of alcohol **2d** and acetate **5** were indirectly assigned as (*S*) and (*R*), respectively, by conversion of the optically enriched alcohol into β-angelicalactone (**4d**—Scheme 4). Comparison of the rotation signal (+) of the synthetic sample of **4d** with the literature data[13] revealed that the stereochemistry of the synthetic lactone is (*S*).

We point out that all tellurides prepared in this work are not bad smelling compounds.

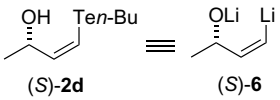


Figure 1. (*S*)-**2d** as a synthetic equivalent of a chiral building block.

In conclusion, a simple and straightforward route to butenolides was developed. In addition, telluride **2d** constitutes a precursor of the (*Z*) chiral lithium dianion **6** (Fig. 1), an important chiral building block, which could be used in the synthesis of bioactive compounds containing this structural unity.

The enzymatic kinetic resolution of **2d** complements the tin methodology reported some time ago, which describes the preparation of *R* and *S* (*E*)-4-(tributylstannanyl)but-3-en-2-ol (**7**) proposed as a precursor of the (*E*)-chiral lithium dianion **8** (Fig. 2).[14]

Table 1. Enzymatic kinetic resolution[a] of (*R*,*S*)-**2d**

Entry	Lipase	Solvent	Time (h)	Conversion (%)	ee (*S*)-**2d**[b] (%)	ee (*R*)-**5**[c] (%)	Yield (%) (alcohol/acetate)[d]	*E*[e]
1	**CALB**	Hexane	2	39	62	>99		
2			3	45	79	98		
3			4	49	96	98	36/32	>200
4		THF	6	27	37	99		
5			24	28	38	99	36/26	
6			48	36	54	96		84
7		Hexane/THF	4	29	40	99		
8			6	32	46	97		
9			24	48	89	98	36/49	>200
10	**PPL**	Hexane	2	9	10	98		
11			5	26	35	98		139
12	**PSL**	Hexane	2	4	3	65		
13			6.5	12	9	64		5

[a] The reactions were performed with 1 mmol of (*R*,*S*)-**2d** and 50 mg of CALB or 0.5 mmol of (*R*,*S*)-**2d** and 1 g of PPL, 100 mg of PSL in hexane (20 mL for CALB or 10 mL for PPL and PSL), THF (20 mL) or 1:1 mixture hexane/THF (10 mL).

[b] Enantiomeric excess (ee) of the recovered alcohol (*S*)-**2d**; Conditions for chiral-GC analysis: CHIRASIL-DEX CB (packed β-cyclodextrin, 25 m × 0.25 mm × 0.25 μm, CRHOMOPACK-Varian®), $p = 120$ kPa; 80 °C, 120 min hold, 80–160 °C\2 °C/min. $t_R1 = 144.1$ min, $t_R2 = 145.2$ min.

[c] Enantiomeric excess (ee) of the acetate (*R*)-**5**; Conditions for chiral-GC analysis: CHIRASIL-DEX CB, $p = 120$ kPa; 80 °C, 120 min hold, 80–160 °C\2 °C/min. $t_R1 = 142.5$ min, $t_R2 = 143.3$ min.

[d] Isolated yields.

[e] Enantiomeric ratio: this parameter describes the enantioselectivity of the enzyme.

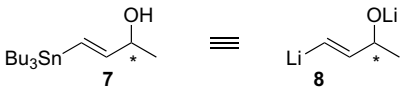


Figure 2. Compound **7** as a possible precursor of a (*E*)-chiral building block.

Acknowledgments

We thank FAPESP, CAPES, and CNPq for support. Amano Pharmaceutical CO and Novozymes Inc are acknowledged for donation of the lipases.

References and notes

1. (a) Petragnani, N. *Tellurium in Organic Synthesis*; Academic Press: London, UK, 1994; (b) Comasseto, J. V.; Barrientos-Astigarraga, R. E. *Aldrichim. Acta* **2000**, *33*, 66; (c) Petragnani, N.; Stefani, H. A. *Tetrahedron* **2005**, *61*, 1613; (d) Comasseto, J. V.; Cunha, R. L. O. R.; Clososki, G. C. In *Comprehensive Organometallic Chemistry*, Knochel, P., Ed.; Elsevier: London, in press.
2. (a) Seebach, D.; Beck, A. K. *Chem. Ber.* **1975**, *108*, 314; (b) Kauffman, T. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 4110; (c) Hiiro, T.; Kambe, N.; Ogowa, A.; Miyoshi, N.; Murei, T.; Sonoda, N. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1187; (d) Barros, S. M.; Comasseto, J. V.; Berriel, J. *Tetrahedron Lett.* **1989**, *30*, 7353; (e) Comasseto, J. V.; Berriel, J. *Synth. Commun.* **1990**, *20*, 1681; (f) Tucci, F. C.; Chieffi, A.; Comasseto, J. V. *Tetrahedron Lett.* **1992**, *33*, 5721; (g) Tucci, F.; Chieffi, A.; Comasseto, J. V. *J. Org. Chem.* **1996**, *61*, 4975; For recent review, see: (h) Zeni, G.; Lüdtke, D. S.; Panatieri, R. S.; Braga, A. L. *Chem. Rev.* **2006**, *106*, 1032.
3. (a) Zeni, G.; Comasseto, J. V. *Tetrahedron Lett.* **1999**, *40*, 4619; (b) Stefani, H. A.; Cella, R.; Dörr, F. A.; Pereira, C. M. P.; Zeni, G.; Gomes, M. *Tetrahedron Lett.* **2005**, *46*, 563; (c) Silveira, C. C.; Braga, A. L.; Vieira, A. S.; Zeni, G. *J. Org. Chem.* **2003**, *68*, 662; For review, see: (d) Zeni, G.; Braga, A. L.; Stefani, H. A. *Acc. Chem. Res.* **2003**, *36*, 731.
4. Raminelli, C.; Gargalaka, C. C.; Silveira, C. C.; Comasseto, J. V. *Tetrahedron Lett.* **2004**, *45*, 4927.
5. (a) Dos Santos, A. A.; Da Costa, C. E.; Princival, J. L.; Comasseto, J. V. *Tetrahedron: Asymmetry* **2006**, *17*, 2252; (b) Dos Santos, A. A.; Ferrarini, R. S.; Princival, J. L.; Comasseto, J. V. *Tetrahedron Lett.* **2006**, *47*, 8933; (c) Princival, J. L.; Barros, S. M. G.; Comasseto, J. V.; Dos Santos, A. A. *Tetrahedron Lett.* **2005**, *46*, 4423.
6. (a) Oliveira, J. M.; Zeni, G.; Malvestiti, I.; Menezes, P. H. *Tetrahedron Lett.* **2006**, *47*, 8183; (b) Diego, D. G.; Cunha, R. L. O. R.; Comasseto, J. V. *Tetrahedron Lett.* **2006**, *47*, 7147; (c) Alves, D.; Nogueira, C. W.; Zeni, G. *Tetrahedron Lett.* **2005**, *46*, 8761; (d) Marino, J. P.; McClure, M. S.; Holub, D. P.; Comasseto, J. V.; Tucci, F. C. *J. Am. Chem. Soc.* **2002**, *124*, 1664; (e) Zeni, G.; Panatieri, R. B.; Lissner, E.; Menezes, P. H.; Braga, A. L.; Stefani, H. A. *Org. Lett.* **2001**, *3*, 819; (f) Yang, J.; Cohn, S. T.; Romo, D. *Org. Lett.* **2000**, *2*, 763; (g) Stefani, H. A.; Costa, I. M.; Zeni, G. *Tetrahedron Lett.* **1999**, *40*, 9215.
7. Dos Santos, A. A.; Castelani, P.; Bassora, B. K.; Fogo Junior, J. C.; Costa, C. E.; Comasseto, J. V. *Tetrahedron* **2005**, *61*, 9173.
8. Zeni, G.; Formiga, H. B.; Comasseto, J. V. *Tetrahedron Lett.* **2000**, *41*, 1311.
9. *Typical procedure*: Preparation of (*S*)-(+)-β-angelicalactone [(*S*)-**4d**]—In a two necked round-bottomed flask equipped with rubber septum, magnetic stirring, and under nitrogen atmosphere was placed the γ-hydroxy vinylic teluride (*S*)-**2d** (0.256 g, 1 mmol, 96% ee) in dry THF (5 mL). The solution was cooled to −78 °C and then *n*-butyllithium (1.69 mL, 1.3 mol L^{-1} in hexane, 2.2 mmol) was slowly added. After 20 min under stirring at −78 °C, dry CO_2 was bubbled through the solution for 30 min. In the following the mixture was allowed to reach the room temperature and then treated with diluted 14% HCl solution (3 mL) and extracted with diethylether (4 × 3 mL). The organic phase was dried with $MgSO_4$, filtered, and the solvent was distilled. The residue was purified by silica gel flash column chromatography eluting with pentane:diethylether (1:1) to give 0.050 g (51%) of (*S*)-(+)-β-angelicalactone as an oil. CAS NR: 92694-51-4; 96% ee; Conditions for chiral-GC analysis: CHIRASIL-DEX CB (packed β-cyclodextrin, 25 m × 0.25 mm × 0.25 μm, CRHOMOPACK-Varian®), $p = 120$ kPa; 60 °C, 10 min hold, 60–90 °C\2 °C/min. $t_R1 = 15.6$ min, $t_R2 = 16.0$ min; $[\alpha]_D^{23}$ +100 (*c* 0.25; $CHCl_3$) {lit.[13] (*S*)-enantiomer: $[\alpha]_D$ +110.6 (*c* 1.23 $CHCl_3$) 99% ee}; ^1H NMR (200 MHz): δ 1.46 (d, $J = 6.6$ Hz, 3H); 5.09–5.21 (m, 1H); 6.11 (dd, $J = 5.7$ Hz, 2.2 Hz, 1H); 7.47 (dd; $J = 5.7$ Hz, 1.7 Hz, 1H); ^{13}C NMR (50 MHz): δ 18.7; 79.6; 121.2; 157.3; MS *m*/*z* (rel int): 98 (M^+ 34); 83 (40); 69 (12); 55 (100), 43 (58).
10. (a) Matheus, C. J.; Taylor, J.; Tyte, M. J.; Worthington, P. A. *Synlett* **2005**, 538; (b) Pour, M.; Špulák, M.; Balšánek, V.; Kuneš, J.; Buchta, V.; Waisser, K. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1893.
11. Amonkar, C. P.; Tilve, S. G.; Parameswaran, P. S. *Synthesis* **2005**, 2314.
12. Aldrich, Catalogue of Flavors and Fragrances, 1998–1999.
13. Tsuboi, S.; Sakamoto, J.; Yamashita, H.; Sakai, T.; Utaka, M. *J. Org. Chem.* **1998**, *63*, 1102.
14. Lee, T.; Kim, S. *Tetrahedron: Asymmetry* **2003**, *14*, 1951.