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A DIASTEREOSELECTIVE SYNTHESIS OF BOTH QUERCUS LACTONE ISOMERS EMPLOYING ALLYL-TYPE ORGANOMETALLICS AS KEY INTERMEDIATES

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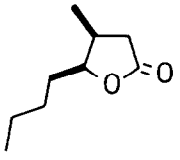
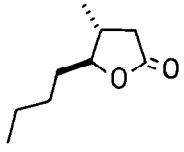
Summary: Consecutive treatment of endo-butenyl potassium or endo-1-(tetrahydropyranyl-oxy)-exo-butenyl lithium with fluorodimethoxyboron and pentanal at -75°C affords an erythro- and, respectively, threo-adduct, the hydrolysis and oxidation of which leads to the cis- and, respectively, trans-isomer of 5-butyl-4-methyl-tetrahydro-2-furanone (4-butyl-3-methyl-4-butanolide), 1, *the so-called quercus or oak lactones.*

The easily accessible 2-alkenyl-dimethoxy-boranes (dimethyl 2-alkeneboronates) combine with aldehydes to give branched homoallyl alcohols in a highly diastereoselective manner [1]. We have already successfully applied this type of reaction as a key step in the synthesis of 4-methyl-3-heptanol, the main constituent of a product mixture that serves the elm bark beetle *Scolytus multistriatus* Marsham as an aggregation pheromone [2]. We now report a stereoselective synthesis of both, *cis*- and *trans*-5-butyl-4-methyl-tetrahydro-2-furanone (*cis*- and *trans*- 1) based on the same method. These two isomers are extracted by wine or other alcoholic beverages like whisky and brandy from oak barrels in which they are kept for maturing [3]. Hence they were nicknamed "quercus lactones" or "oak lactones".

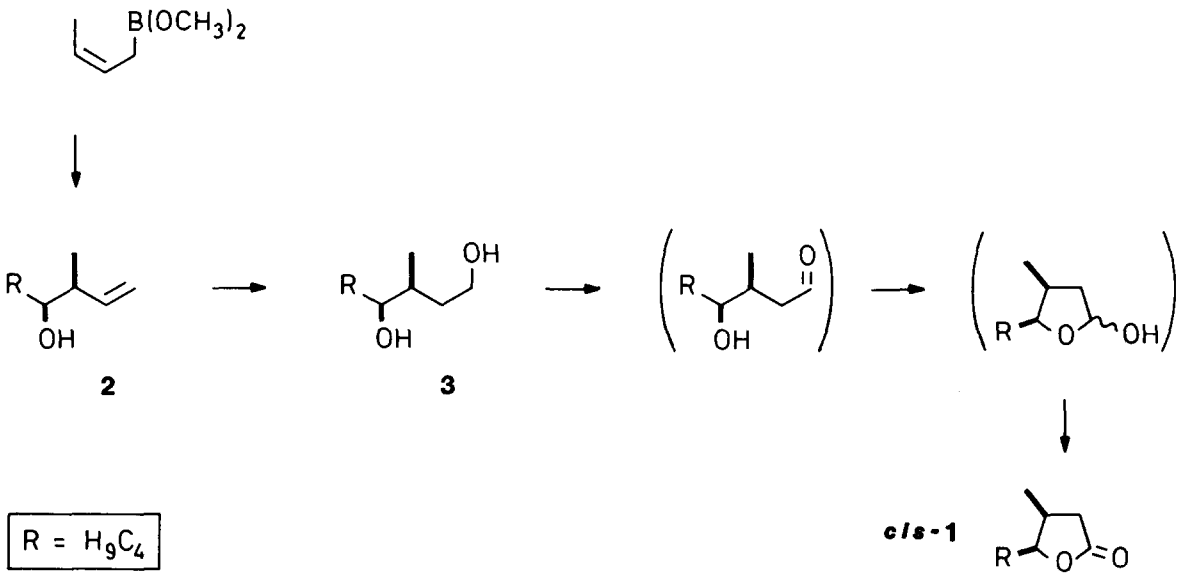


***cis*-1**



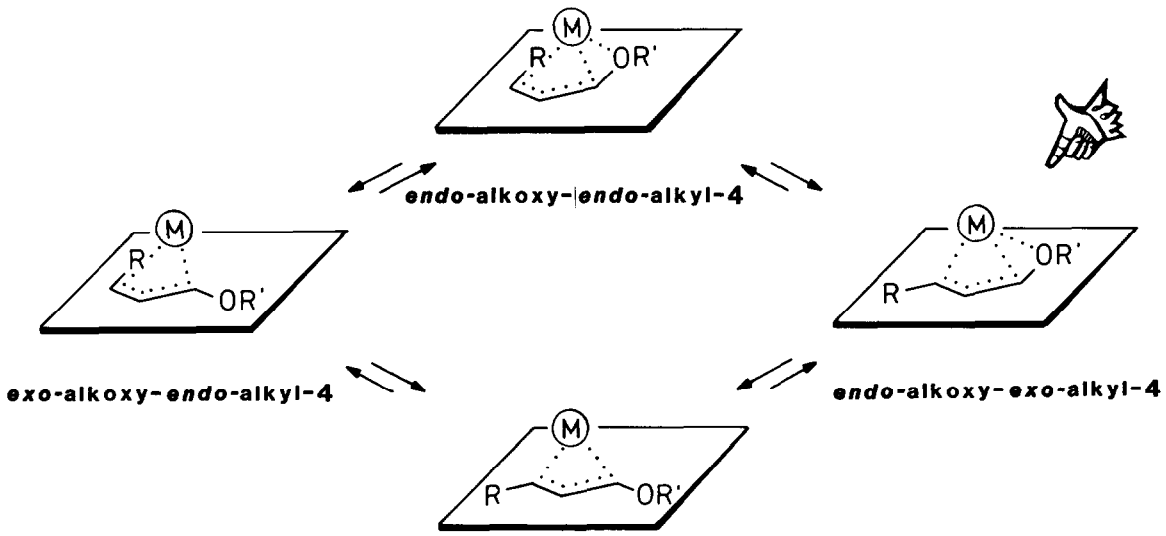
***trans*-1**

The addition of pentanal [4] to *endo*-butenyl-dimethoxy-boron [1] (50 mmol) proceeded rapidly (-120°C to -75°C) and afforded 3-methyl-1-octen-4-ol **2** [5] having an *erythro/threo* [(3*R**,4*R**):(3*S**,4*S**)] ratio of 98 : 2 in 51% yield (bp 74 - 75°C/11 mmHg; n_D^{20} 1.4415). Hydroboration followed by oxidation converted the homoallyl alcohol into the *erythro*-3-methyl-1,4-octandiol **3** [5] (68%; bp 78 - 85°C/0.2 mmHg). Final dehydrogenation with MnO_2 (70 equiv. in CH_3CN, 25 h 25°C) or $RuCl_2[P(C_6H_5)_3]_3$ [6] (1.5 equiv. in benzene, 5 h 25°C) gave the lactone *cis*-**1** [5,7] in 60% yield (*cis/trans* = 98 : 2; bp 114 - 116°C/9 mmHg; n_D^{20} 1.4468).

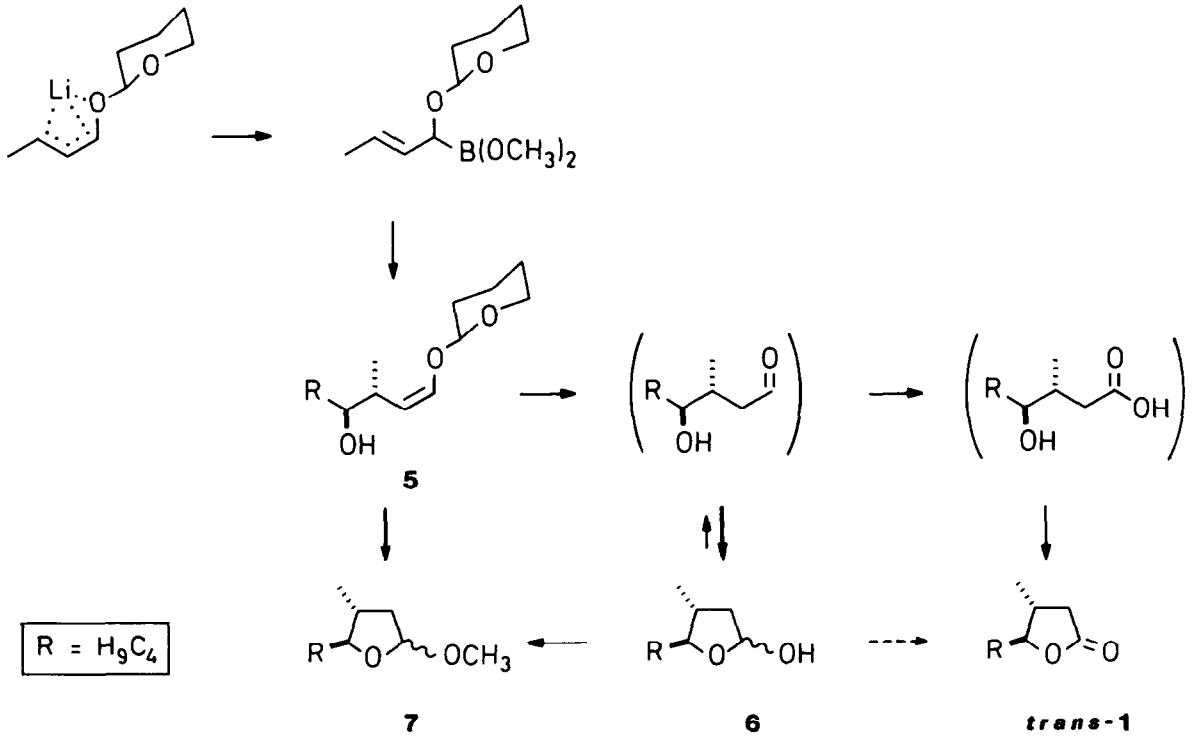


In principle, the *trans*-isomer could be prepared in a strictly analogous fashion starting with *trans*-butenyl-dimethoxy-boron [1]. A related approach, however, which allows the immediate introduction of oxygen-functionality at the unsaturated terminal position appeared more attractive. Allyl-type ethers and, notably, *O*-allyl acetals [8] can be easily deprotonated with *sec*-butyllithium. The resulting organometallic species **4** should be endowed with high torsional mobility. Therefore, the thermodynamically most stable conformer should be produced no matter which isomer of the 2-alkenyl ether is used as the starting material. We expected the *endo*-alkoxy-*exo*-alkyl-substituted allyl conformer to be the most favored one and this assumption proved to be correct indeed.

To a solution of 2-(*E*)-crotyloxy-tetrahydropyrane (30 mmol) in 40 mL of isopentane and 20 mL of tetrahydrofuran (THF) at -75°C, equimolar amounts of *sec*-butyllithium, fluorodimethoxyboron and pentanal were added in 2 h intervals. After 20 min at 25°C and evaporation of the solvents, the acetal-alkenol **5** [9] (not isolated) was submitted to hydrolysis (50 mL 2 N H_2SO_4 + 100 mL acetone,



1 h 25°C) [10] and, without isolation of the lactol intermediate 6 , to oxidation (0.1 mol $KMnO_4$ in a total of 100 mL 2 N H_2SO_4 + 100 mL acetone, 1 h 10 → 25°C) affording virtually pure lactone *trans*- 1 [5,11,12] (50%; *cis/trans* = 1 : 99; bp 112 - 113°C/9 mmHg; n_D^{20} 1.4430).



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2. M. Schlosser & K. Fujita, *Angew. Chem.* 1982, *94*, 320; *Angew. Chem. Int. Ed. Engl.* 1982, *21*, 309; *Angew. Chem. Suppl.* 1982, 646.
3. a) H. Suomalainen & L. Nykänen, *Naeringmittelindustrien* 1970, *23*, 15; b) K. Nishimura & M. Masuda, *J. Food Sci.* 1971, *36*, 819; c) M. Masuda & K. Nishimura, *Phytochem.* 1971, *10*, 1401; d) R.E. Kepner, A.D. Webb & C.J. Muller, *Am. J. Enol. Viticult.* 1972, *23*, 144; f) P. Schreier & F. Drawert, *Chem. Mikrobiol. Techn. Lebensm.* 1974, *3*, 154; g) K. Otsuka, Y. Zenibayashi, M. Itoh & A. Totsuka, *Agr. Biol. Chem.* 1974, *38*, 485; h) M. Masuda & K. Nishimura, *Chem. Lett.* 1981, 1333.
4. The *exo*-isomers react considerably faster than *endo*-boronates with aldehydes. Foregoing addition of 0.05 - 0.1 equiv. of acetaldehyde eliminates eventually present trace amounts of *exo*-boronate and thus may increase the stereoselectivity.
5. Correct elemental analyses (±0.3% C, H) corroborate the identity and purity of these compounds.
6. H. Tomioka, K. Takai, K. Oshima & H. Nozaki, *Tetrahedron Lett.* 1981, 1605.
7. 360 MHz ^{1}H-nmr : 4.44 (1 H, *ddd*, J = 10.0, 5.5, 4.0); 2.70 (1 H, *dd*, J = 7.9, 6.6); 2.6 (1 H, *m*); 2.21 (1 H, *dd*, J = 16.6, 3.9); 1.7 (2 H, *m*); 1.5 (2 H, *m*); 1.4 (2 H, *m*); 1.02 (3 H, *d*, J = 7.0); 0.93 (3 H, *t*, J = 7.0).
8. J. Hartmann, M. Stähle & M. Schlosser, *Synthesis* 1974, 888.
9. Prolonged heating of (*E*)-1-methoxymethoxy-2-butenyl-tributyl-stannane in the presence of aldehydes to 155°C (90 h) or 140°C (11 h) also leads selectively to *threo-O*-(3-alkyl-4-hydroxy-1-alkenyl)-acetals [A.J. Pratt & E.J. Thomas, *Chem. Commun.* 1982, 1115].
10. Alternatively, methanolysis (200 mL CH_3OH + 2 drops of conc. H_2SO_4, 2 h reflux) affords the lactol ether **7** [5] (59%; bp 175 - 176°C/mmHg; n_D^{20} 1.4260).
11. 360 MHz ^{1}H-nmr : 3.99 (1 H, *dt*, J = 7.6, 4.0); 2.67 (1 H, *m*); 2.2 (2 H,*m*); 1.5 (6 H, *m*); 1.14 (3 H, *d*, J = 6.4); 0.92 (3 H, *t*, J = 7.0).
12. For a previous unselective synthesis of **1**, see ref. 3d; for a *trans*-selective synthesis : D. Hoppe & A. Brönnecke, *Tetrahedron Lett.* 1983, 1687.

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