

STEREOSPECIFIC SYNTHESIS OF γ -BUTYROLACTONES FROM ACYCLIC VINYL SULFOXIDES:
AN ASYMMETRIC SYNTHESIS OF OPTICALLY PURE OAK LACTONES

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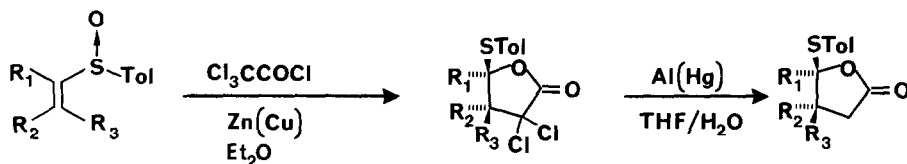
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Summary: The sulfoxide-directed lactonization of several trisubstituted vinyl sulfoxides with dichloroketene proceeds in a completely stereospecific manner. The lactonization of (E)-3(R)-p-tolylsulfinyloctene occurs with complete enantiospecificity to produce a precursor for the synthesis of optically pure oak lactones.

Several years ago we described a new type of stereospecific cyclization of dichloroketene and vinyl sulfoxides to yield γ -arylthio- γ -butyrolactones.¹ More recently we found that optically pure 1-arylsulfinyl cyclohexenes undergo this lactonization process with complete enantiospecificity leading to optically pure bicyclic γ -butyrolactones.² Since this latter study only included cyclic vinyl sulfoxides, it was imperative to test the generality of this chirality transfer from sulfur to carbon in acyclic systems. Furthermore, it was desirable to correlate the configuration of the sulfoxide group with the absolute configurations of the new created carbon centers. In this report we describe the sulfoxide-directed lactonizations of several trisubstituted acyclic vinyl sulfoxides, and the asymmetric synthesis of optically pure (3S,4R) and (3S,4S)-3-methyl-4-octanolides or Quercus (oak) lactones.

When the trisubstituted vinyl sulfoxides,³ 1-3, were treated with an excess of trichloroacetyl chloride and zinc/copper couple in refluxing ether, good yields of the corresponding γ -butyrolactones, 4-6, were obtained⁴ (Scheme I). The dichlorolactones were readily dechlorinated to the γ -thio-aryl- γ -butyrolactones (7,8) with an aluminum amalgam in aqueous THF.⁵ Previous examples¹ reported by us only included 2-substituted vinyl sulfoxides. In the case of sulfoxide 2, the reaction is not affected by the β - β -disubstitution pattern, a fact that is consistent with an intramolecular process.

Scheme I

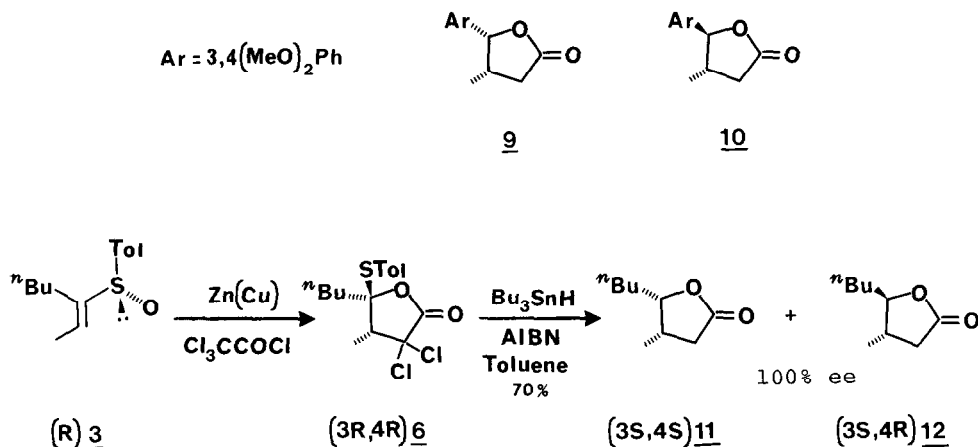


<u>1</u> : R ₁ =3,4(MeO) ₂ Ph, R ₂ =Me; R ₃ =H	<u>4</u> (60%)	<u>7</u> (90%)
<u>2</u> : R ₁ =H, R ₂ = <u>n</u> -Bu, R ₃ =Me	<u>5</u> (70%)	--
<u>3</u> : R ₁ = <u>n</u> -Bu, R ₂ =Me, R ₃ =H	<u>6</u> (75%)	<u>8</u> (90%)

The stereospecific removal of sulfur from lactones 4-8 is an extremely important operation if one is to retain the newly created chiral centers. In general, Raney nickel desulfurizations are not known to be stereospecific.⁶ In the case of cyclohexenylbutyrolactones,² Raney nickel desulfurization was stereospecific because the ring-fused butyrolactone is the thermodynamically more stable cis-lactone. For desulfurizations of lactones 4-8, there is no anticipated thermodynamic control. We found that the Raney nickel desulfurization of lactone 7 proceeded with very high stereoselectivity (~25% chemical yield) to give the cis-lactone 9, contaminated with only a trace of its trans isomer, 10 (ca. 30:1).⁷ On the other hand, Raney nickel desulfurization and dechlorination of lactone 6 produced a 40% yield of a mixture of cis and trans lactones, 11 and 12, respectively, in a ratio of 2:1. In an effort to examine other methods for desulfurizations and dechlorinations, we studied the reactions of tri-n-butyltin hydride⁸ with lactones 4 and 6. In these cases, the yields of lactones (9,10,11,12) were much higher, but again mixtures of cis/trans isomers were produced (9/10, 2.3/1; 11/12, 1/1.8). It is interesting to note that desulfurization of lactones 4 and 7 with tin hydride or Raney nickel results in a higher degree of retention of stereochemistry, suggesting that the aryl group is special.

As a test for the asymmetric induction inherent in the lactonization process, we prepared the optically pure⁹ (R) sulfoxide 3 and converted it into the optically active dichlorolactone 6 ($[\alpha]_D = +13.04$, acetone). Desulfurization and dechlorination of 6 with tri-n-butyltin hydride produced the (3S,4R) and the (3S,4S)-3-methyl-4-octanolides 11 and 12, known as oak lactones (Scheme II). These lactones were separated by flash chromatography, and

Scheme II



their optical rotations were identical to literature values.¹⁰ Since the absolute configurations of the lactones have been determined,¹⁰ our results reveal that the (R) sulfoxide produces the (3R,4R) configurations in the chlorolactone 6 and ultimately the (3S) configuration of the cis and trans oak lactones. This last fact suggests that the chirality transfer proceeds from a sulfoxide conformation in which a double bond bisects the angle created by the sulfur-oxygen bond and the lone pair of electrons.

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References

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3. Sulfoxide 1 was prepared from the lithio reagent of 1-bromo-1-(3,4-dimethoxyphenyl)-1(E)-propene and *p*-toluenesulfinyl chloride. Sulfoxide 2 was prepared from 1-*p*-toluenesulfinyl-1-propyne by addition of *n*-butylcopper. Sulfoxide 3 was derived from the α -alkylation of the vinyl anion of (E)-1-propenyl *p*-tolyl sulfoxide.
4. All new compounds gave satisfactory elemental analyses and possessed spectral properties consistent with the assigned structures (IR, C¹³, 360 MHz H¹ and M.S.).

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7. The stereochemical assignments were based on the 360 MHz H^1 chemical shifts of the methyl group and the benzylic hydrogen, as well as the magnitude of J_{34} ; 9 (Me, 0.70; 5.54, J_{34} 5.7 Hz), 10 (Me, 1.16; 4.86, J_{34} = 8.6 Hz).
8. For some recent examples of tri-*n*-butyltin hydride reductions of unsymmetric sulfides see: (a) C. G. Gutierrez and L. R. Summerhays, J. Org. Chem., 49, 5206 (1984). (b) D. J. Hart and Y.-M. Tsai, J. Am. Chem. Soc., 106, 8209 (1984). (c) D. A. Burnett, J.-K. Choi, D. J. Hart and Y.-M. Tsai, J. Am. Chem. Soc., 106, 8201 (1984).
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