Tetrahedron Letters,Vol.27,No.40,pp 4817-4820,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

CHEMISTRY OF BAKER'S YEAST REDUCTION PRODUCTS: USE OF OPTICALLY ACTIVE (S)-(+)-1-(p-TOLUENESULFONYL)PROPAN-2-OL AND (S)-(+)-1-(PHENYLSULFONYL)PROPAN-2-OL IN SYNTHESIS.

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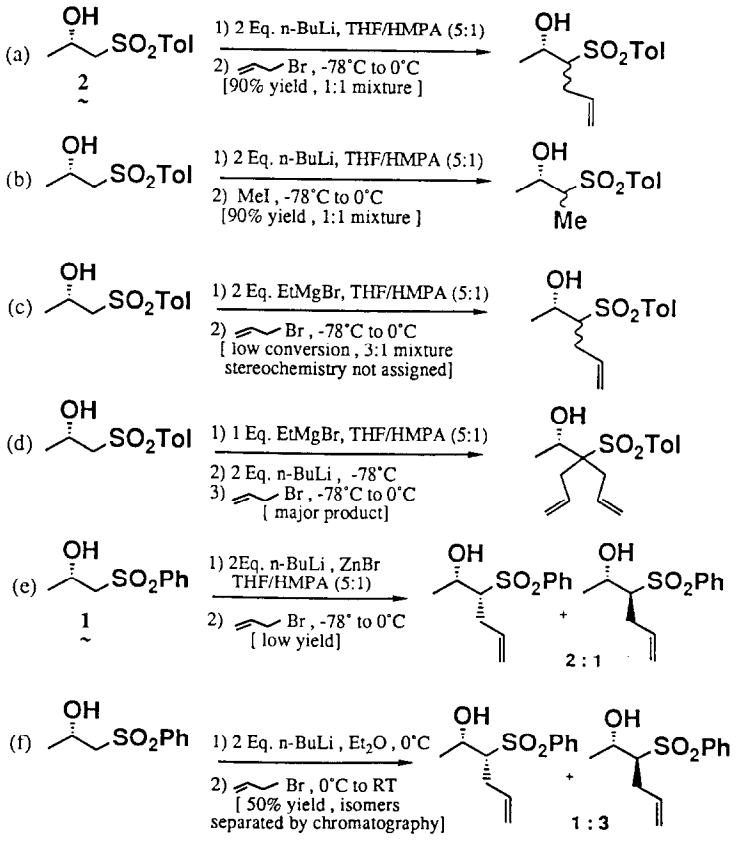
Summary: The utility of the title compounds in the preparation of optically active lactones and alcohols is detailed.

In order to further expand the organic chemist's ability to access useful homo-chiral alcohols for organic synthesis through NADH reductions[1], we have examined in further detail the nature of the baker's yeast reduction products formed from ß-keto sulfones. Additionally, we have examined the metallation/alkylation chemistry of the ß-hydroxy sulfones so generated.

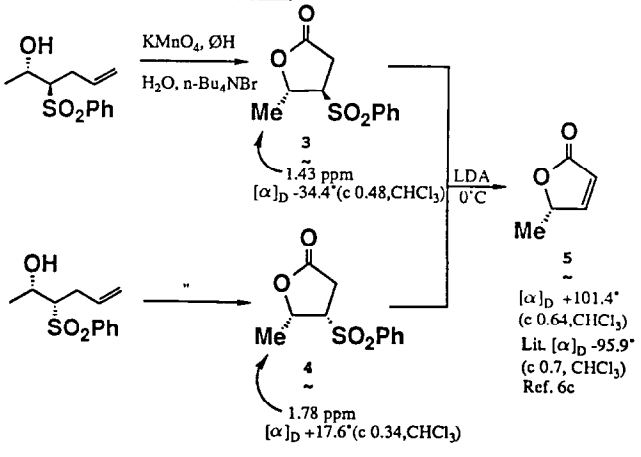


The reduction of both 1-(phenylsulfonyl)propan-2-one (**6**) and 1-(*p*-toluenesulfonyl)propan-2-one by baker's yeast (*Saccharomyces cerevisiae*) was carried out in the same fashion as first described by Ridley[2] for phenylsulfone **6**. The optical purity of the reduction product had been determined by Ridley to be >95% through a chiral shift study. The absolute configuration of the 1-(phenylsulfonyl)propan-2-ol (**1**) was assigned as *S* as determined by the method of Horeau. By converting each of the title compounds to its MTPA ester[3], we were able to assign an optical purity of >97% to each alcohol as determined by NMR integrations. Additionally, we have confirmed the *S*-stereochemistry of **1** through a chemical correlation described below. Compound **2** is thus also reasonably assigned the *S*-configuration.

On transforming **1** and **2** to their corresponding dianions[4] under a variety of conditions, little stereoselectivity was observed in the subsequent alkylation step. The tolylsulfone did, however, generally afford the alkylation product in higher yield. These results are shown in the accompanying equations (a-f).

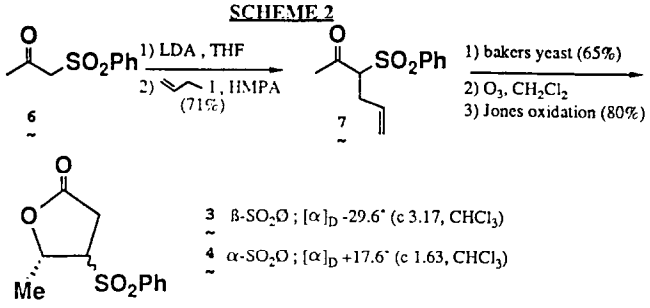
The assignment of stereochemistry to products of the allylation reaction (eqn. f) follows from their conversion to the corresponding lactones **3** and **4**. Since the phenylsulfonyl group exhibits a deshielding effect[5] on the neighboring cis-methyl group (cf. chemical shifts for **3** and **4**), it follows that the major isomer from reaction (e) has a syn relationship between sulfonyl and hydroxyl groups. These sulfonyl substituted lactones were then converted to the optically pure butenolide **5**, a compound previously prepared by Font[6a] in eleven steps from tartaric acid. Hydrogenation[6b] of butenolide **5** also provides a lactone which Mori has used in the synthesis of the aggregation pheromone of *Gnathotrichus sulcatus*, an ambrosia beetle found in the Pacific coast area of North America[6c].

SCHEME 1



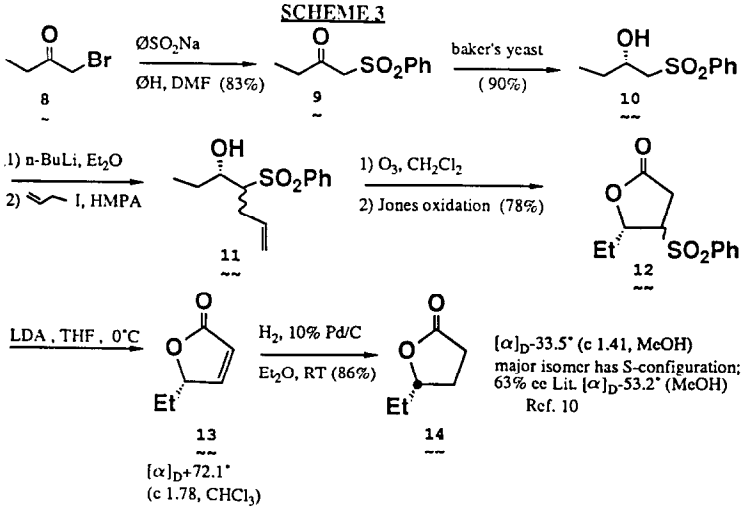
Since in some cases both the yields and the stereoselectivity of the alkylation chemistry of the ß-hydroxy sulfone dianions were marginal, we examined the baker's yeast reduction of the allylated ß-keto sulfone **7**, a compound easily prepared from phenylsulfonylacetone (scheme 2). Both enantiomers of **7** were, in fact, reduced, for a 2.5:1 cis/trans mixture of diastereomeric ß-hydroxy sulfones was generated. These diastereomers were separated and individually converted to lactones **3** and **4**. Since these lactones were found to have nearly the same rotations as found for those reported above, we conclude that the yeast reduction remains (in this case) *S*-selective regardless of the stereochemistry of the sulfone bearing center.

SCHEME 2



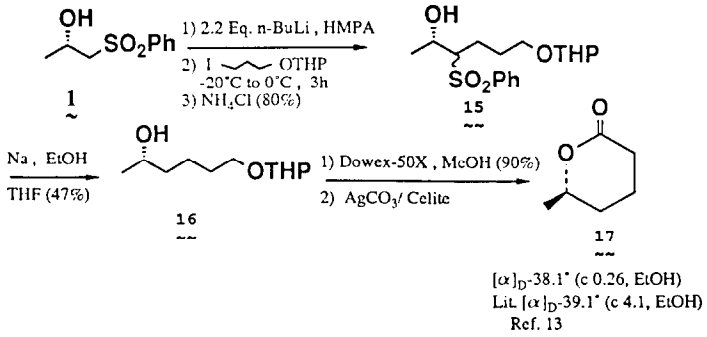
To extend this chemistry to other γ-lactone systems, we prepared the sulfonyl substituted 2-butanone **9** and subjected it to actively fermenting baker's yeast. The alcohol **10** was obtained in 90% yield[7]. In order to ascertain the level of asymmetric induction in this reduction, the alcohol was converted to 4-hexanolide **14**, a component of the pheromone secreted by the female dermisted beetle *Trogoderma glabrum* [8]. Several syntheses of both enantiomers of this lactone have been reported[9], and thus the appropriate rotations are available for comparison. As described below, the sulfonyl substituted lactone **12** was prepared from **11** by ozonolysis followed by Jones oxidation. The sulfonyl group was eliminated by base treatment and the resulting butenolide[10] was hydrogenated. The γ-lactone obtained exhibited a rotation of -33.5° (c 1.41, MeOH) and was judged to be at least 60% optically pure on the basis of literature comparisons[11]. Apparently in this case the larger ethyl group has caused some erosion in the enantioface discrimination by the baker's yeast.

SCHEME 3



Lastly, we have also examined the possibility of removing the sulfonyl group of these alkylated ß-hydroxy sulfones through chemical reduction methods. As illustrated below (scheme 4) for the product formed from the reaction of the dianion of **1** with the tetrahydropyranyl ether of 3-iodopropanol, the use of sodium in ethanol[12] does lead to a reasonable yield of the mono-protected diol **16**. A small amount of the olefin resulting from loss of both the sulfonyl and hydroxyl groups was also detected. The mono-protected diol was then converted to the known optically active δ-lactone **17**[13] by THP group removal followed by Fetizon oxidation[14] with silver carbonate on Celite. The optical rotation of lactone **17** further attests to the optical purity of the starting ß-hydroxy sulfone **1**.

SCHEME 4



In summary, the chemistry discussed herein reveals several ways in which ß-hydroxy sulfones prepared from actively fermenting baker's yeast may serve as chiral educts for organic synthesis[15].

Acknowledgment: We are indebted to the Petroleum Research Fund (Grant No. 14068-ACI) for support of these studies.

References and Notes

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(Received in USA 23 June 1986)