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Direct Conversion of 1,2-Diol into Allyl Sulfide. Regioselective Transformation of (-)-Quinic Acid to (-)-Shikimic Acid.

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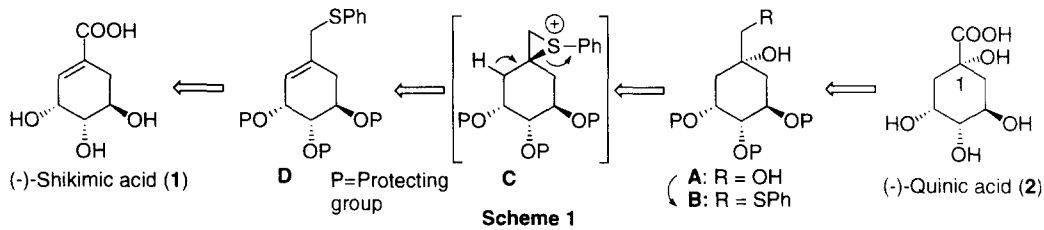
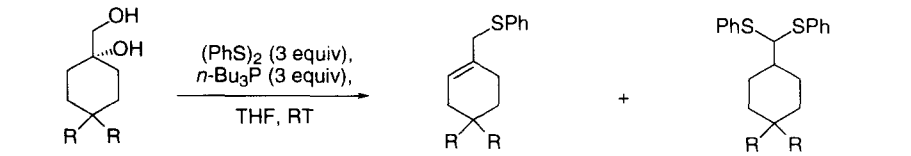
Abstract: *Exo*-1,2-diols **3** and **4** were efficiently converted into the corresponding allyl sulfides by means of tri-*n*-butylphosphine (Bu_3P) and diphenyl disulfide $(PhS)_2$. This method was applied to the introduction of a carbon-carbon double bond from diol **11** to give allyl sulfide **12** in a highly regioselective manner. The allyl sulfide **12** was transformed into (-)-shikimic acid (**1**) in four steps. © 1998 Elsevier Science Ltd. All rights reserved.

Shikimic acid (**1**) is a common precursor for the biosynthesis of aromatic compounds. The biological significance of this compound as well as the fact that the stereocontrolled construction of the three contiguous asymmetric carbon centers and the regiocontrolled introduction of the olefin moiety make it a challenging synthetic target have led to numerous synthetic studies.[1] Dehydration of the hydroxy group at C-1 of readily available (-)-quinic acid (**2**) would be a concise route to **1**, while moderate regioselectivity of the dehydration step was observed in an earlier paper.[2] We herein report an alternative synthetic route to **1** which involves a direct transformation of diol **A** to allyl sulfide **D** using Bu_3P and $(PhS)_2$.



Scheme 1

The key to our route relied on the dehydration *via* a thiiranium ion **C**, which could be generated from sulfinyl alcohol **B** prepared by a simple replacement of the primary alcohol of **A** (Scheme 1).[3] In this context, the substitution of the hydroxy group of diols **3** and **4** was examined using the $(PhS)_2$ and Ph_3P reaction system. However, these reactions resulted in complete recovery of the starting materials. We considered that the use of the more nucleophilic Bu_3P could effect the desired substitution reaction.[4] Treatment of **3** with 3 equiv of Bu_3P and $(PhS)_2$ in THF at room temperature for 18 h did not give any substituted product such as **B**, but afforded,



3: R=R=H
4: R=R=-OCH_2CH_2O-

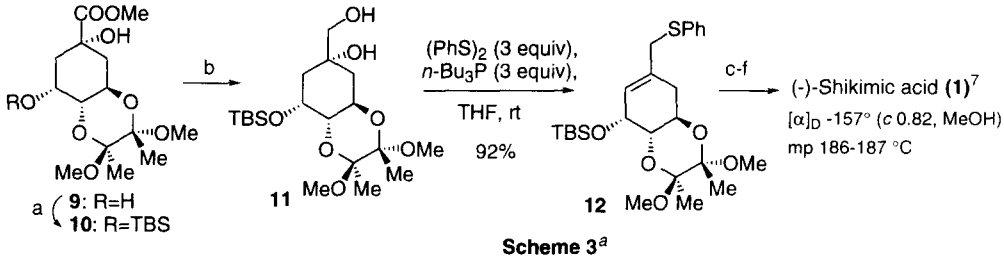
5: R=R=H (70%)
6: R=R=-OCH_2CH_2O- (34%)

7: R=R=H (20%)
8: R=R=-OCH_2CH_2O- (34%)

Scheme 2

PII: S0040-4039(98)01239-8

unexpectedly, allyl sulfide **5** in 70% yield along with dithioacetal **7** (20%). The reaction of diol **4** also gave a mixture of allyl sulfide **6** and dithioacetal **8** (**6**:**8** = 1:1) in good yield. Thus, we found that the allyl sulfide of type **D** can be synthesized directly from the *exo*-1,2-diol.[5]



Scheme 3[a]

[a](a) TBSCl, CH_2Cl_2, imidazole (94%); (b) DIBAL, THF, 0 °C (79%); (c) MCPBA, CH_2Cl_2, 0 °C (90%); (d) TFAA, 2,6-lutidine, CH_2Cl_2 (43%); (e) $NaClO_2$, Na_2PO_4, 2-methyl-2-butene, *t*-BuOH, H_2O (59%); (f) TFA, H_2O (53%).

Based on the above experiments, the conversion of the diol **A** to the allyl sulfide **D,** which is a key step for the synthesis of **1** from **2,** was examined next (Scheme 3). Surprisingly, the treatment of **11** afforded in 92% yield the desired allyl sulfide **12** as an exclusive regioisomer which corresponded to **1**.[6] None of the dithioacetal was detected. The resulting allyl sulfide **12** was treated with the following sequence of reactions to give **1**; (i) oxidation with *m*-chloroperoxybenzoic acid, (ii) Pummerer reaction, (iii) oxidation of the resulting aldehyde to the carboxylic acid, and (iv) removal of the protecting groups with trifluoroacetic acid. Spectroscopic data and physical constants of the synthetic **1** were identical in all respects with those of commercially available **1**.[7]

Acknowledgments. We gratefully acknowledge financial support from Yamada Science Foundation, SUNBOR Grant, and the Ministry of Education, Science, Sports, and Culture, Japan. This paper is dedicated to the memory of the late Professor D. H. R. Barton.

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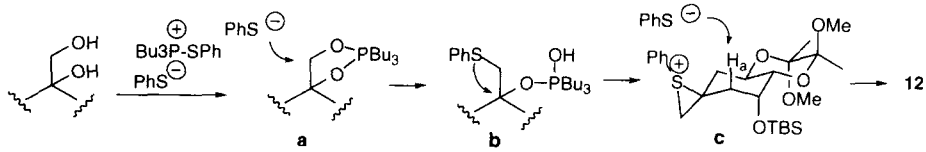
2. Snyder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1973**, *95*, 7821.
3. Acid-catalyzed conversion of hydroxysulfide *via* thiiranium ion to allyl sulfide has been reported, see: Hannaby, M.;Warren, S. *J. Chem. Soc. Perkin Trans. 1* **1989**, 303.
4. (a) Nakagawa, I.; Hata, T. *Tetrahedron Lett.* **1975**, 1409. (b) Nakagawa, I.; Aki, K.; Hata, T. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1315.
5. To our knowledge, the one-step conversion of 1,2-diol into allyl sulfide has not been reported.
6. The following reaction mechanism is proposed for this reaction; (i) formation of a cyclic phosphorane **a**, (ii) substitution at the methylene position with PhS^-, (iii) formation of a thiiranium cation **c** from **b**, and (iv) deprotonation of H_a. This remarkable regioselectivity would be due to the stereoelectronic effect of the neighboring silyoxy group.



7. Purchased from NACALAI TESQUE, Inc. $[\alpha]_D$ -157° (*c* 0.82, MeOH); mp 186-187 °C (MeOH-AcOEt).