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pH DEPENDENT OXIDATION-REDUCTION OF 1-BENZENESULFENYL-2-PROPANONE AND ITS OXIDES BY A MICROORGANISM[1)]

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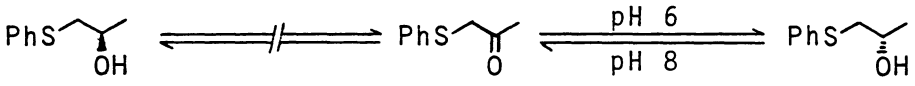
Incubation of 1-benzenesulfenyl-2-propanone with Corynebacterium equi IFO 3730 in a weakly acidic medium afforded (S)-1-benzenesulfenyl-2-propanol. On the contrary, when the cultivation was carried out at pH 8 with the same bacterium, only the (S)-alcohol was transformed into the starting ketone, the (R)-alcohol being recovered intact. The similar enantioselectivities were also observed in the reaction of 1-benzenesulfinyl-2-propanone.

Utilization of enzymatic reactions on synthetic substrates is one of convenient methods for introduction of asymmetric centers to achiral molecules.[2)] The crucial limitation of this method is that, in general, only one enantiomer of optically active catalysts (=enzymes) is available,[3)] and accordingly the product is limited to one of two optical isomers. We are pleased to report in this letter that we have succeeded in obtaining both enantiomers of sulfur-containing alcohols, taking advantage of the reversibility of enzymatic reactions or switching the direction of reaction by simply regulating the pH of the reaction medium.

We have already reported that Corynebacterium equi IFO 3730 has an ability to transform sulfur-containing compounds.[4)] As sulfur compounds having a carbonyl or a hydroxy group are useful in organic synthesis,[5)] we applied this system to acetone and propanol derivatives (Scheme 1). Incubation of 1-benzenesulfenyl-2-propanone (1) with C. equi at 30 °C for 7 days in a medium of pH 6-6.5 containing 2% of hexadecane as a sole source of carbon[6)] (concentration of substrate, 0.1%), resulted in the formation of (S)-1-benzenesulfenyl-2-propanol (S-2) in a yield of 65%, after purification with preparative TLC. The structure was confirmed by

comparison of spectroscopic data[7] with those of the authentic racemic sample of 2. The reduction product exhibited $[\alpha]_D^{20}$ +6.75° (c 0.86, MeOH) indicating that its absolute configuration is S.[8] The optical purity was determined by derivation to the Mosher's ester,[9] in which no signal originated from R-2 was observed.[10] These results show that the optical purity of S-2 is at least over 95%.

Changing the pH of the medium to weakly basic brought about a dramatic inversion of the reaction course. The pH of the medium was adjusted to 8 by adding 2N NaOH after the growth of the bacterium, followed by addition of racemic 1-benzenesulfenyl-2-propanol (2, 0.1% to the medium). A half of the alcohol 2 was oxidized to the corresponding ketone 1 (yield, 50%) as identified spectroscopically, the other half being remained unaffected (yield, 50%). Interestingly, the recovered 2 showed $[\alpha]_D^{22}$ -6.42° (c 0.87, MeOH), opposite to the value of the one obtained by reduction of ketone 1 with the same microbe. The optical purity of this sample was determined to be over 95% by the method mentioned above. Thus, the recovery of 2 is attributed to the stereospecificity of alcohol dehydrogenase of C. equi. This result can be explained by assuming that a single enzyme acts on 1 and 2, the methyl and benzenesulfenylmethyl group of the substrates being sterically and/or electronically distinguished by the enzyme, and that accordingly, addition and removal of hydrogen occurred from the same side of the substrate.[11] In this case R-2 is considered not to be incorporated in the active site of the enzyme. Thus, a slight change in cultivation condition enables to afford both enantiomers of 1-benzenesulfenyl-2-propanol (R- and S-2, Scheme 1), although the driving force for the inversion of direction of the reaction is not clear at present.



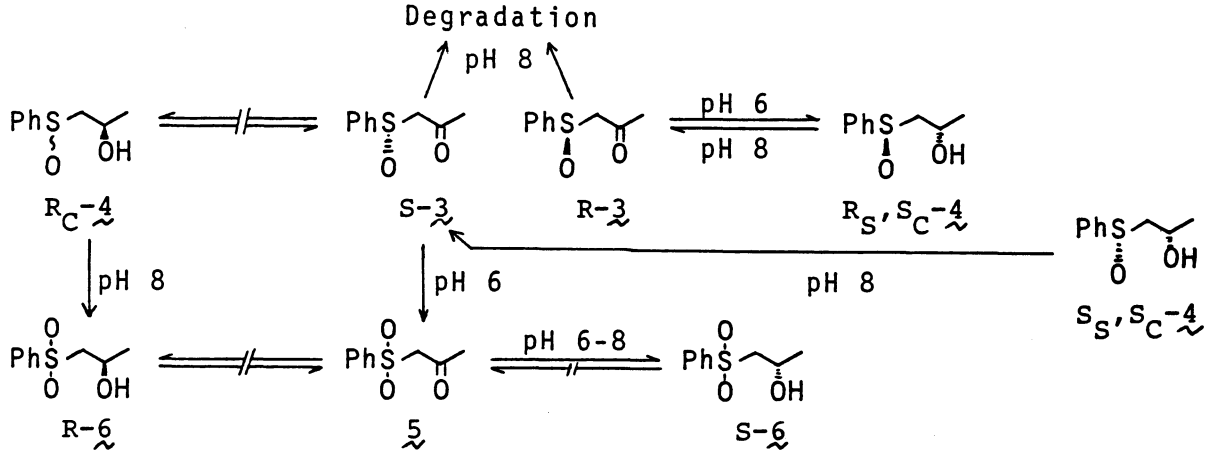
R-2 1 S-2

Scheme 1.

This enzyme system was also applied to the redox reactions of benzenesulfinyl derivatives (3) (Scheme 2). Alcohol dehydrogenase catalyzed the reduction of (R)-benzenesulfinyl-2-propanone (R-3) to give smoothly (R_S, S_C)-1-benzenesulfinyl-2-propanol (R_S, S_C-4) in a yield of 38%. The diastereomeric ratio of this compound was confirmed to be erythro:threo = 5:95[12] by HPLC analysis. Sulfinyl alcohol R_S,

S_c-4 gave R-3, $[\alpha]_D^{22}$ +269° (c 0.80, MeOH), on oxidation with active MnO_2, indicating that the absolute configuration of the alcohol is as depicted in Scheme 2. On the other hand, S-3 gave (S)-1-benzenesulfonyl-2-propanol (S-6) in a yield of 62%, $[\alpha]_D^{22}$ +7.4° (c 4.68, MeOH), the optical purity being determined to be 84% by ^{1}H-NMR spectra taken in the presence of Eu(TFC)$_3$. While S_s,S_c-4[13] was inactive under the fermentation conditions, sulfone 5 was smoothly reduced to afford S-6 (76% e.e.) in a yield of 97%. Thus, it can be concluded that S-3 is converted to S-6 via sulfonyl ketone 5. In contrust to sulfenyl alcohol 2, both enantiomers of sulfonyl alcohol 6 was recovered unchanged by cultivation even at pH 8.

Finally, a mixture of four diastereoisomers of 1-benzenesulfinyl-2-propanol (4) was submitted to the reaction in the medium of pH 8. R-Alcohol 6 was obtained in a yield of 23%. The specific rotation $[\alpha]_D^{25}$ -13.9° (c 0.36, MeOH) indicates that its absolute configuration is R. It is not confirmed whether both the epimers different in configuration at the sulfur atom were transformed to R-6. No other products were obtained from the broth. It is considered that the other isomers were further metabolized after oxidation to carbonyl compounds.



Scheme 2.

In conclusion, both enantiomers of 1-benzenesulfenyl- and benzenesulfonyl-2-propanols (S- and R-2, S- and R-6) were obtained by the catalytic action of a single microorganism with a little variation of the cultivation conditions.

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References

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7) All products gave agreeable IR, ^{1}H-NMR, and mass spectra.
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