

ENANTIOSELECTIVITY IN ENEDIOL-HYDROXYKETONE TAUTOMERIZATION

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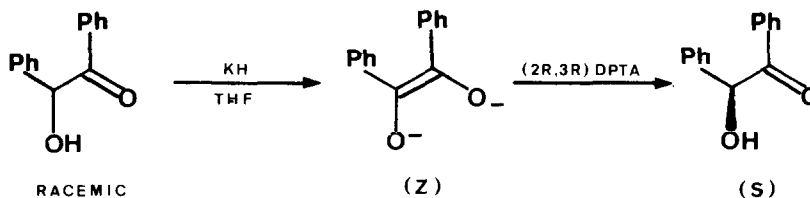
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ABSTRACT : The conversion of racemic α -hydroxyketone into optically active α -hydroxyketone with e.e. as high as 80 % and in good yield is reported. This is accomplished by a low temperature enantioselective protonation of the enediol using (2R,3R) O,O-dipivaloyltartaric acid.

The production of optically active compounds from racemic mixtures via enantioselective protonation has been of increasing interest in recent years (1).

We now wish to disclose our finding that the protonation of an enediolate with (2R,2R) O,O-dipivaloyltartaric acid (2) ((2R,3R)DPTA) can lead to an optically active α -hydroxyketone with an enantiomeric ratio as high as 90:10 (80 % e.e.) (scheme I). This is the highest percent enantiomeric excess yet reported for a deracemization (1) by enantioselective protonation. This is also the first reported experimental evidence of the enantioselective tautomerization of an enolic into a ketonic form.

SCHEME I



The Z configuration enediolate used in these experiments (table I) was prepared by the reaction of potassium hydride with benzoin (3).

Among numerous assays of enantioselective protonation of the previous enediolate by (2R,3R) DPTA, most significant are the two extrema results recorded in the first two entries of table I.

TABLE I : Product distribution after protonation of benzoin potassium enediolate

(2R,3R) DPTA	Protonation Conditions		Benzoin isolated Yield %	Benzoin e.e.% ^a	Benzil isolated Yield %
3.3 eq	+ 20°C,	1 h	78	1 (S)	18
3.3 eq	- 70°C,	1 h	20	41 (S)	75
1.06 eq	- 70°C,	15 h	82	80 (S)	13

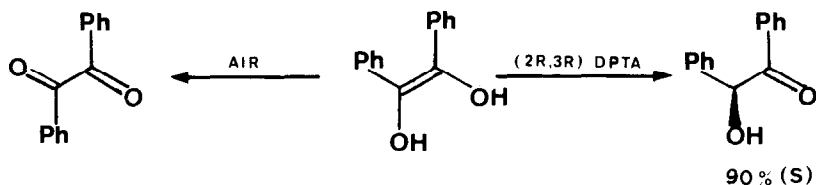
^a Reference 8.

Thus, if protonation of the enediolate is carried out, in a short reaction time, at room temperature, by an excess of (2R,3R)DPTA, benzoin is obtained with a good chemical yield, but without any enantiomeric excess. In contrast, other things being equal, carrying out the protonation, at - 70°C, led to a moderate enantiomeric excess, but resulted in a disappointingly low chemical yield of benzoin, with benzil as the major product. These results can be rationalized by assuming that in such reaction conditions the enediolate reacts under kinetic control, via a fast protonation on the oxygen atoms (4). At room temperature, the resulting enediol quickly tautomerizes to benzoin without stereoselectivity. At - 70°C, tautomerization occurs with good enantioselectivity, but very slowly, and the untautomerized enediol is immediately oxidized to benzil by the oxygen of the air during work-up (5) (scheme II).

These observations led us to the conclusion that carrying out the protonation at - 70°C, for a period long enough to give complete tautomerization of the enediol, would result in both higher chemical yield and higher enantiomeric excess. Thus, the reaction mixture after standing under argon for 15 h, at - 70°C, afforded benzoin 90 % S (e.e. 80 %) with 82 % chemical yield (6) (table I - entry n° 3).

Moreover, this high e.e. causes the major enantiomer to crystallize spontaneously in methanol : filtration gave optically pure crystalline benzoin of (S) configuration according to (7).

SCHEME II



In a typical procedure, 0.32 g (1.5 mmol) of benzoin in 5 ml of THF was added at 0°C, under argon with stirring to 0.46 g (3.8 mmol) of KH (33 % in oil) washed three times with petroleum ether, in 10 ml of THF. Stirring was continued for one hour at 0°C. Cooling (-70°C) was followed by dropwise addition of 0.51 g (1.6 mmol) of (2R,3R)DPTA in 3 ml of THF and the solution was kept at -70°C for 15 h after the addition. A solution of 0.35 g (1.1 mmol) of (2R,3R) DPTA in 2 ml of THF was added (9); the mixture was rapidly warmed to -40°C and 10 ml of H₂O was added. After the usual work-up, flash chromatography afforded benzoin in 80 % e.e. (82 % yield). (2R,3R) DPTA was recovered with 94 % yield without racemization.

Finally, we suggest that the enantioselective enediol tautomerization could also be involved in the enantioselective hydrogenation of benzil in the presence of achiral cobalt complexes and chiral amines, instead of the reported 1-2 enantioselective addition of hydrogen (10).

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REFERENCES and NOTES

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- (2) L. Duhamel and J.C. Plaquevent, Org.Prep.Proc.Int. 1982, 14, 347.
- (3) Configuration of enediolate ($Z \geq 95\%$) was established by quenching with acetic anhydride; according to L.F. Fieser, J.Chem.Educ. 1954, 31, 291; G. Rio and J. Berthelot, Bull.Soc.Chim.Fr. 1972, 822 and Y. Ogata and I. Urasaki, J.Org.Chem. 1973, 38, 100.
- (4) Adding (2R,3R)DPTA at -70°C to the red solution of the enediolate led to a

discoloured solution. By the quenching with acetylchloride-Et₃N, this discoloured solution led to Z-diacetoxystilbene. In the same experimental conditions, the benzoin was transformed into O-acetylbenzoin.

- (5) The oxidation of potassium benzoin enediolate by dissolved oxygen must be ruled out : protonation by (2R,3R)DPTA, at 20°C (table I, entry n° 1) or by water, at - 70°C, led to a good yield in benzoin; moreover, according to H. Staudinger and H. Binkert, *Helv.Chim.Acta* 1922, 5, 703 and W.E. Bachmann, *J.Amer.Chem.Soc.* 1934, 56, 93, the oxidation of this enediolate by air leads chiefly to benzoic acid which was never detected in our experiments.
- (6) We have verified that the optical enrichment was not due to an asymmetric transformation of benzoin : when reagents were added in the following order : KH, DPTA, benzoin, the benzoin recovered was inactive. Thus, the enantioselectivity is determined by the difference in energy of activation for approach of the proton carrier from the two enantiotopic faces of trigonal carbon atoms.
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 (S) benzoin : $[\alpha]_D^{12} = + 118,5^\circ$, acetone, c = 1.
- (9) Tautomerization of enediol was hindered by an excess of acid. Addition of acid allows the air oxidation of the residual enediol during the work-up, thus avoiding its transformation in racemic benzoin.
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