

ON THE α -KETOLS OBTAINED FROM α,β -UNSATURATED AROMATIC ALDEHYDES
AND BAKERS' YEAST

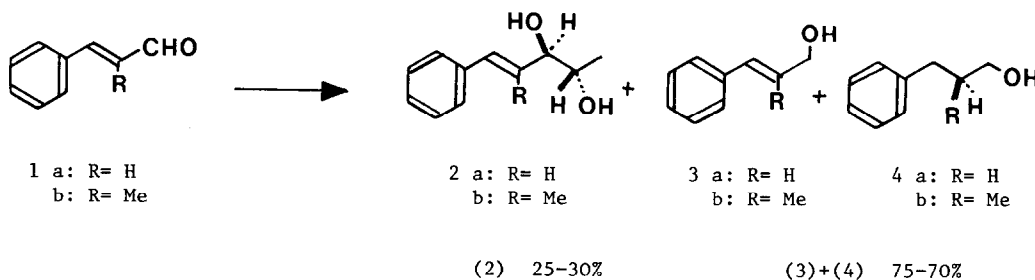
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From α -methylcinnamaldehyde (1b), acetaldehyde and fermenting bakers' yeast, at pH 5, the R α -ketol (6) is obtained in ca. 15% yield, together with unreacted (1b); from cinnamaldehyde (1a), under identical conditions, optically inactive (5) has been isolated as the only transformation product.

For some years now we have been using the (2S,3R) diols (2)¹ obtained from the aldehydes (1) in fermenting bakers' yeast as starting materials for chiral syntheses of natural products.² These include compounds of practical interest such as N-trifluoroacetyl-L-acosamine and -L-adaunosamine,^{2e} and for this reason, and in view of further synthetic applications of (2) we are interested in finding out experimental conditions enabling efficient conversions of (1) into (2). Now we present some results of our studies in this field.

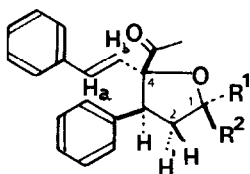
With the procedure described^{1,2d} the transformation of the aldehydes (1) by bakers' yeast fermenting on D-glucose takes place according to the following equation:



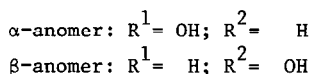
We thought that the rapid reduction of (1) to (2)+(3) might be the major drawback of this method. Indeed, this process subtracts aldehydic species to the slower acyloin-type condensation, leading to the intermediate α -ketols, later reduced to the desired products (2).

Accordingly, in the light of a patent report³ claiming the formation from benzaldehyde, acetaldehyde and bakers' yeast fermenting on sugar beet molasses, at pH 5, of up to 76% of the R α -ketol $C_6H_5CHOHCOCH_3$, we submitted the aldehydes (1) to analogous experimental conditions, in the expectation of obtaining similar yields of the corresponding α -ketols, which might be later reduced enzymatically, by changing the fermentation conditions, or chemically,⁴ to the chiral diols (2).

However, from cinnamaldehyde (1a), under the above-mentioned conditions, together with ca. 70% unreacted aldehyde,⁵ an optically inactive hydroxyketone was isolated in ca. 15% yield. This material, on the basis of analytical and spectroscopic data, was assigned the structure of a tetrahydrofuran with the relative stereochemistry depicted in (5).



(5)



As shown from n.m.r. studies (Table), compound (5) undergoes mutarotational isomerism, reaching the equilibrium value of about 60% of the α -anomer after one day. The relative stereochemistry has been tentatively deduced as follows. Going from the β to the α -anomer, H-3 is shifted downfield by 0.26 ppm, in agreement with the deshielding effect exerted by a substituent on the cis- γ -proton in the 5-membered rings.⁶ Furthermore, the chemical shift difference between H-2 and H-2' becomes smaller, i.e. H-2 is shifted downfield and H-2' upfield, according to the upfield effect indicated by a substituent syn to a vicinal proton in a pentacyclic moiety.^{6,7} These observations strongly support that the phenyl substituent is cis to the hydroxyl group in the β -anomer. The stereochemistry at C-4 seems more difficult to determine. However, an indication comes from the ¹³C chemical shift of the carbonyl carbon, which is shifted downfield by 1.9 ppm in the β -anomer. This so-called δ -effect, i.e. the effect exerted by a substituent on the ¹³C chemical shift through four bonds, is known to be downfield when the two substituents are in a cis configuration.⁸ According to this rule, closely related systems as D-arabinofuranose⁹ and D-ribofuranose¹⁰ show a downfield shift of 1.2 ppm of the CH₂OH carbon in the β respect to the α -anomer. However, since the effects are rather small, and not completely understood, any conclusion must be taken with caution.

Compound (5) is expected to arise upon Michael addition of the anion derived from the α -ketol from cinnamaldehyde (1a) onto a molecule of cinnamaldehyde, followed by ring closure, as shown below.

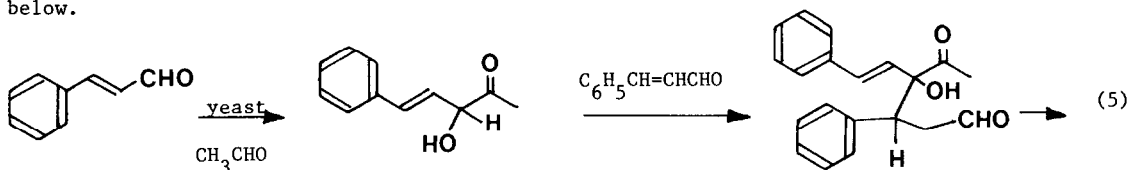


TABLE: ^1H and ^{13}C n.m.r. data of compound (5)^a

	α -anomer ^b		β -anomer		α^c		β^c
H-1	6.11	J(1,2) 3.5	5.86	J(1,2) 4.5	C-1	99.5	99.3
H-2	2.42	J(1,2') 5.0	2.3 ^d	J(1,2') 5.8	C-2	39.5	39.4
H-2'	2.46	J(2,2') 14.0	2.70	J(2,2') 14.0	C-3	54.0	55.5
H-3	3.80	J(2,3) 7.3	3.54	J(2,3) 8.0	C-4	95.2	93.9
H-a	6.66	J(2',3) 7.3	6.57	J(2',3) 9.8	CH ₃	27.9	28.7
H-b	7.09	J(a,b) 16.0	6.97	J(a,b) 16.0	CO	207.6	209.5
CH ₃	1.78	J(1,OH) 4.5	1.72				
OH	3.89						

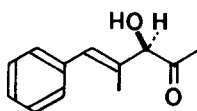
^aSolvent: CDCl_3 ; chemical shift in ppm from int. TMS; J in Hz

^banomeric form present immediately after the solution is made

^cthe aromatic and ethylenic carbons are not reported

^dpartially overlapped signals

At variance with the α -ketol derived from cinnamaldehyde, the corresponding compound from α -methylcinnamaldehyde survives to the above fermentation conditions. Indeed, from (1b) the α -ketol (6), contaminated by some (3b), was isolated in 15–20% yield, alongside ca. 70% unreacted starting aldehyde. The (3R) absolute configuration of (6) is supported by its conversion by yeast fermenting on $\underline{\text{D}}$ -glucose or by LiAlH_4 reduction⁴ to the (2S,3R)-diol (2b).



(6)

The allylic chiral α -ketol (6) might hold some synthetic significance, because, once suitably

protected, could undergo chelation-controlled nucleophilic addition, (by R^-),¹¹ onto the carbonyl carbon, and, subsequently, by ozonolysis, could give rise to a C_5+R methyl ketone, embodying two adjacent chiral centres.

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