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HLAD-CATALYZED OXIDATIONS OF ALCOHOLS WITH ACETALDEHYDE AS A COENZYME RECYCLING SUBSTRATE.

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As far as we know, the title reaction is mentioned only once in the literature (1). Nevertheless the possible applications are very attractive. To explore the possibilities of this reaction we examined in identical reaction conditions the oxidation of nine structurally different alcohols. The results are shown in figure 1.

Cyclohexanol is oxidized nearly quantitatively within 1 hour, 2-cyclohexenol within 6 hours. The smooth curve indicates that the oxidation rates of (R) and (S)-cyclohexenol are not very different.

For racemic 3-methyl-2-cyclohexenol clearly both enantiomers are highly differentiated, since after 1 hour the reaction sharply stops at a 50% conversion.

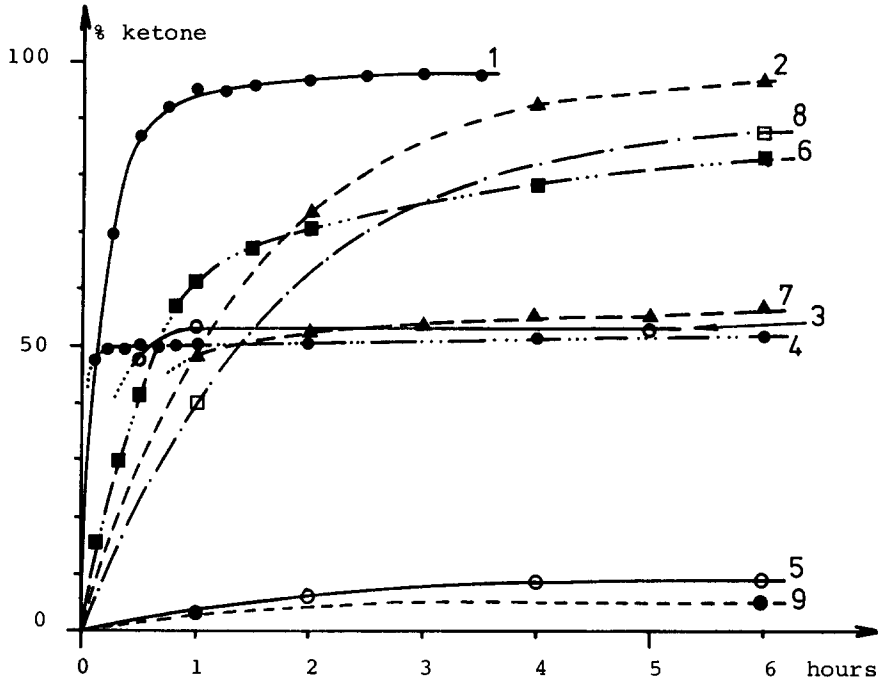
An analogous result is found for *trans*-3-methylcyclohexanol, whereas the *cis* isomer is oxidized very slowly. This is in full accordance with the reverse selective reaction, *i.e.* the formation of *trans*-(1S,3S)-3-methylcyclohexanol from 3-methylcyclohexanone (2).

The overall oxidation rate of 3-methylcyclopentanol (*cis* + *trans*) is of the same magnitude as the oxidation rate of *trans*-3-methylcyclohexanol. This is not the case for the reduction of cyclopentanones, which are poor substrates in comparison with cyclohexanones (3).

Trans-2-methylcyclopentanol is oxidized very slowly but 50% of the *cis* isomer is oxidized within 1 hour, after which a sharp decrease of the oxidation rate is observed. This smooth oxidation is very unexpected since 2-methylcyclopentanone is not reduced at all.

Both enantiomers of 2-octanol were oxidized separately. (2S)-2-Octanol is oxidized ten times faster than its (2R)-enantiomer, which confirms earlier observations (4).

Figure 1 : HLAD-catalyzed oxidation of alcohols.



Reaction circumstances : alcohol : 0.010 M, acetaldehyde : 0.10 M, NAD^+ : 2.0×10^{-4} M, HLAD : 1 mg/10 ml, in MOPS buffer pH 7.

1 = cyclohexanol ; 2 = 2-cyclohexenol ; 3 = 3-methyl-2-cyclohexenol ; 4 = *trans*-3-methylcyclohexanol ; 5 = *cis*-3-methylcyclohexanol ; 6 = 3-methylcyclopentanol (*cis* + *trans*) ; 7 = *cis*-2-methylcyclopentanol; 8 = (2S)-2-octanol ; 9 = (2R)-2-octanol.

Further analytical and preparative scale experiments are in progress. In preparative scale oxidations, higher substrate concentrations are used. Higher acetaldehyde concentrations are deleterious to the enzyme. Coenzyme recycling numbers of up to 50 in analytical tests and up to 1000 in preparative scale reactions are obtained.

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