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MICROBIAL OXIDATION OF α-ALLENIC ALCOHOLS

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SUMMARY : By microbial oxidation of α-allenic alcohols, α-allenic acids are formed.

While the synthesis of α-allenic alcohols is now easy (1), methods to obtain the corresponding acids are few and much delicate (2).

The partial oxidation of prenol (unsaturated at the α-position with respect to alcohol group) by a bacterium, *Pseudomonas aeruginosa* (ATCC'17504), incited us to substitute chemical oxidation of primary alcohols to acids by enzymatic catalysis.

Our results show that this microbial pathway enables the formation of α-allenic acids from variously substituted α-allenic alcohols without any alteration of the allenic bond (Scheme I).

SCHEME I

Pseudomonas aeruginosa was chosen for the broadness of its metabolitic potentialities (3), in particular n-alkanes can be used as the only source of carbone and energy ; the oxidation of substrate is then complete, a reaction which does not attract a chimist interested in organic synthesis.

Partial oxidation of prenol has been obtained, while the corresponding saturated compound is completely metabolized.

In order to subject the substrate only to a "cooxidation" the energy required for this reaction and for good microbial development is supplied in the form of organic compound which can be easily metabolized (peptone, beef extract). The culture is developped within a 400 ml liquide medium put in 1 liter erlenmeyer which is swirled on a rotatory shaker (250 rpm) at 30°C. The substrate to be oxidized is added after 24 hours of culture.

Measurement of the oxygen uptake of the bacterial suspension by the Warburg manometric method (4) enables one to determine if a given substrate is oxidized.

After the elimination of bacterial cells from the medium by centrifugation, the unoxidized alcohols are recovered by ether extraction of the slightly basic supernatant. The α-allenic acids are obtained by identical treatment of the acidified supernatant, and are sufficiently pure to be used as such. The reaction yield for the various traited α-allenic alcohols are given in Table I.

TABLE I

	R_1	R_2	R_3	Yield in alcohol recovered	Yield in acid
a	H	H	H	20 %	65 %
b	H	H	CH_3	15 %	72 %
c	CH_3	H	H	10 %	75 %
d	CH_3	CH_3	H	< 1 %	82 %
e	CH_3	C_2H_5	H	1 %	87 %
f	$-(CH_2)_5-$		H	30 %	60 %

Biological reaction often being stereospecific (5), it would be interesting to examine the possibility of partial resolution of racemic mixtures by preferential oxidation of one enantiomer.

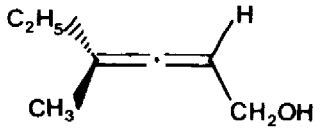
Table I shows that at least 75 and 84 % of alcohols c and e are transformed respectively, which indicates that both enantiomers of the racemic mixture at the start were enzymatically oxidized. On the other hand, in the case of the alcohol e, the recovered acid has a rotatory power corresponding to an enrichment of up to 3 % in the enantiomer (+) S (6).

This result suggests to us that the oxidation rates of the two stereoisomers are different.

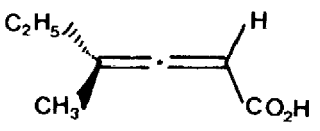
It has also helped us to plan experimental procedures to avoid a complete oxidation of the alcohol.

We have thus carried out a kinetic study on four identical flasks of culture which were analysed 19, 43, 67 and 91 hours respectively after the addition of the substrate. In this experiment we used 4-Methylhexa-2,3 diene ol as substrate since the absolute configurations and the rotatory

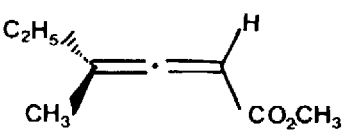
powers of the pure enantiomers of the allenic alcohol (7), of the acid and its methyl ester (5) are known (Scheme II).



1e, (-), R
$[\alpha]_D^{20} = -33°,1$



2e, (-), R
$[\alpha]_D^{20} = -36°,01$



(-), R
$[\alpha]_D^{20} = -29°,40$

SCHEME II

The results obtained are summarized in Table II.

TABLE II

Time of contact bacteria-substrat	Yield in crude product		$[\alpha]_D^{20}$ neat		Optical Yield	
	Alcohol	Acid	Alcohol	Methyl ester *	Alcohol	Methyl ester *
19 H	69 %	-	+ 3°,7	-	11 % (+)	-
43 H	13 %	90 %	+ 21°,5	- 1°,9	65 % (+)	6 % (-)
67 H	<2 %	91 %	-	+ 4°,4	-	15 % (+)
91 H	<1 %	92 %	-	+ 4°,9	-	16 % (+)

* The polarimetric analyses are carried out on the methyl ester, the purity of which is easy to verify.

The difference between the oxidation rates of the two enantiomers is supported by the results of this study which, besides, show an inversion of the sign of the acid obtained between 43 and 67 hours transformation time. An oxidation of the alcohol (-) S to acid (-) S followed by a degradation of the latter offers a possible explanation of this surprising observation.

This method gives access to all substituted α-allenic acids by alkyl group and in this it presents an advantage over chemical synthesis.

From β-allenic alcohols the corresponding acids certainly can be produced, 3-Methyl 3-butene 1-ol is oxidized with neither degradation nor migration of the double-bond.

The preferential oxidation by a microbial pathway of one of the two optical antipodes should be able to be optimized in respect of the optical yield after a more complete study of the bacteria-substrate contact.

This is certainly the most interesting result because microorganisms, by their enzymes, distinguish the two optical antipods of a molecule with an axial chirality and yield is higher than that obtained, in most cases, by pure chemical methods (8).

In this case the reaction is rendered especially attractive as the separation of the optically enriched acids and alcohols is carried out by simple extraction.

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