Note

Lipase catalyzed synthesis of epoxy-fatty acids

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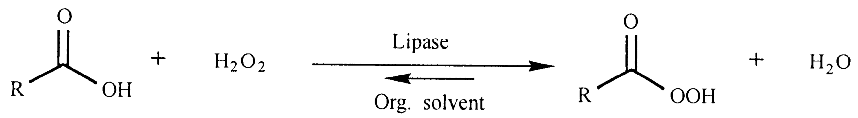
Lipase catalyzed synthesis of epoxy-fatty acids from unsaturated carboxylic acids was investigated. Under mild conditions unsaturated carboxylic acids were converted to peroxycarboxylic acids by lipase with hydrogen peroxide, then the unsaturated peroxycarboxylic acids epoxidised the C = C bond of themselves.

Keywords Lipase, unsaturated acids, epoxidation, peroxy acids

During recent years the use of lipases in organic chemical processing has been studied extensively and the technologies for production and application of lipases have been highly developed. As a consequence, more and more lipases are applied in organic synthesis for various kinds of esterification and ester hydrolysis.[1] In these reactions the lipases often exhibit a high regio- and stereo-selectivity which may be exploited for synthesis of optically active compounds.[2] Furthermore, the conditions of lipase-catalyzed reactions are rather mild and convenient.[1]

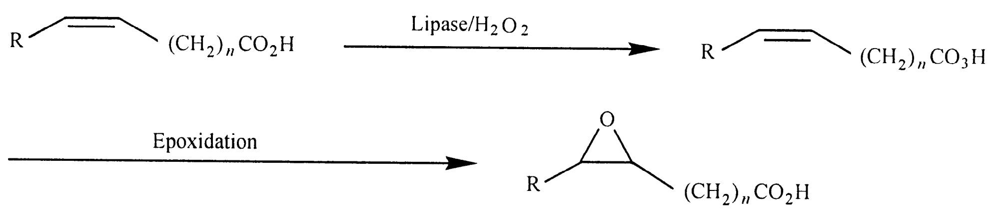
A novel application of lipases was found that lipases catalyze formation of peroxycarboxylic acids from the corresponding carboxylic acids and hydrogen peroxide[3] (Scheme 1). The peroxycarboxylic acids thus formed can be applied *in situ* for oxidation of organic substances such as alkenes and sulphides.

Scheme 1



In this work, we applied lipase-catalyzed formation of peroxycarboxylic acids to unsaturated fatty acids. Unsaturated fatty acids contain both the C = C bond and the carboxyl group suitable for conversion to a peroxy acid. Under the catalysis of lipases, unsaturated fatty acids induced a two-step reaction. In the first step, the unsaturated fatty acid is converted to an unsaturated peroxy acid by lipase/H_2O_2. In the second step, the unsaturated peroxy acid epoxidised the C = C bond of themselves. The reaction principle is shown in Scheme 2.

Scheme 2



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The reaction was simply performed by adding hydrogen peroxide (60% wt/wt) gradually to a suspension of Novozyme 435 in a solution of unsaturated fatty acidsin toluene, and then stirring for a further 16 h at room temperature. Finally 9, 10-epoxystearic acid was achieved from oleic acid in 72% yield[4] and 10, 11-epoxyundecanoic acid was prepared from 10-undecanoic acid in 28% yield.[5]

The difference of conversion between terminal unsaturated acids and internal unsaturated acids can be explained by the peroxycarboxylic acid epoxidation mechanism. To the epoxidation, reaction conversion depends largely upon the number and nature of the group attached to the ethylenic carbon atoms. Substitutes that enhance the nucleophilic character of the double bond (*e.g.* alkyl) promote the reaction, whereas those of opposite effect (*e.g.* carboxyl) inhibit it. Oleic acid, the internal unsaturated acid, has more alkyl group attached to the C = C bond than 10-undecenoic acid. As a consequence, under the same reaction condition, the conversion of oleic acid is better than 10-undecenoic acid. However, the yield of 10, 11-epoxyundecanoic acid can be improved to 61% if the reaction time was prolonged to 72 h and the temperature was increased to 40℃.

In conclusion, compared with traditional organic chemical methods, the procedure of lipase-catalyzed synthesis of epoxy-fatty acids is mild and safe, cost-effective and convenient, and has great potential for large-scale organic chemical manufacture of even sensitive epoxides.

Reference and notes

1. Bjorkling, F.; Godtfredsen, S. E.; Kirk, O., *Trends Biotech.*, **9**, 360(1991).
2. Adelhorst, K.; Bjorkling, F.; Godtfredsen, S.E.; Kirk, O., *Synthesis*, 112(1990).
3. Bjorkling, F.; Godtfredsen, S.E.; Kirk, O., *J. Chem. Soc.*, *Chem. Commum.*, 1301(1990).
4. mp: 57—58℃. ν_{max}: 2918, 2815, 1700, 1262, 919, 847 cm^{-1}. $\delta_H(CDCl_3)$: 2.85—2.95(m, 2H), 2.3(t, J = 7.49 Hz, 2H), 1.20—1.45(m, 26H), 0.85(t, J = 6.7 Hz, 3H). m/z: 299(0.37 M + H), 281(8.09), 155(35.60), 139(9.10).
5. mp: 53—55℃. ν_{max}: 2929, 2815, 1709, 1212, 937, 846 cm^{-1}. $\delta_H(CDCl_3)$: 12.3(1H), 2.88—2.93(m, 1H), 2.73—2.77(m, 1H), 2.46—2.49(m, 1H), 2.3(t, J = 7.46 Hz, 2H), 1.25—1.65(m, 14H). ESI-MS m/z: 223(M + 23), 423(2M + Na), 623(3M + Na). EI-MS m/z: 200(0.50, M^+), 183(0.52), 155(1.11), 71 (100.00).

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